ORGANOGERMANE CHEMISTRY.

PREPARATION OF REAGENTS USEFUL IN SYNTHESIS

by

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ABSTRACT

This thesis is divided into three parts. The first part describes the preparation of regio-isomerically pure functionalized 2-trimethylgermylalk-1-enes of general structure **26**, which are useful in synthesis. The vinylgermane iodide **18**, for example, has been shown in our laboratories to be a good synthetic equivalent to the but-1-ene d^2,d^4- and a^2,d^4-synthons **11** and **22**, respectively. The preparation of the 2-trimethylgermylalk-1-enes of general structure **26** was accomplished via i) $H_2PtCl_6 \bullet 6H_2O$ catalyzed addition of Me_3GeH (**53**) to the carbon–carbon triple bond of 1-trimethylsilylalk-1-ynes **52**, and ii) treatment of the resultant product mixtures with *p*-TsOH•H_2O in dichloromethane.

The second part delineates the new and experimentally simple preparation of Me_3GeLi (**149**) in THF solution. The novel reagent $Me_3GeCu \bullet Me_2S$ (**168**) was obtained by treatment of **149** with $CuBr \bullet Me_2S$. $Me_3GeCu \bullet Me_2S$ (**168**), in the presence of chlorotrimethylsilane, serves as a good reagent for the conversion of functionalized acyl chlorides of general structure **35** (X = Cl) into the acyltrimethylgermanes **37**. Functionalized *S*-(pyridin-2-yl) thioesters of general structure **35** (X = *S*-(pyridin-2-yl)) also serve as good substrates for the preparation of acyltrimethylgermanes **37** with reagent **168**. The acyltrimethylgermanes **37** are efficiently transformed into the 2-trimethylgermylalk-1-enes **26** via olefination with methylene-triphenylphosphorane.

The third part of this thesis outlines the preparation of the novel (trimethylgermyl)-copper(I) reagents **222–225**. The conjugate addition of reagents **222–225**, as well as $Me_3GeCu \bullet Me_2S$ (**168**), to selected unsaturated carbonyl systems was investigated. The substances **229** and **234–238** were synthesized from the corresponding enones via 1,4-addition

of the (trimethylgermyl)copper(I) reagents. The (*E*)-3-trimethylgermylalk-2-enoate **242** was prepared stereoselectively via 1,4-addition of reagents **168** or **223** onto the corresponding alk-2-ynoate, whereas the (*Z*) isomer **243** was obtained predominantly when reagent **225** was employed.

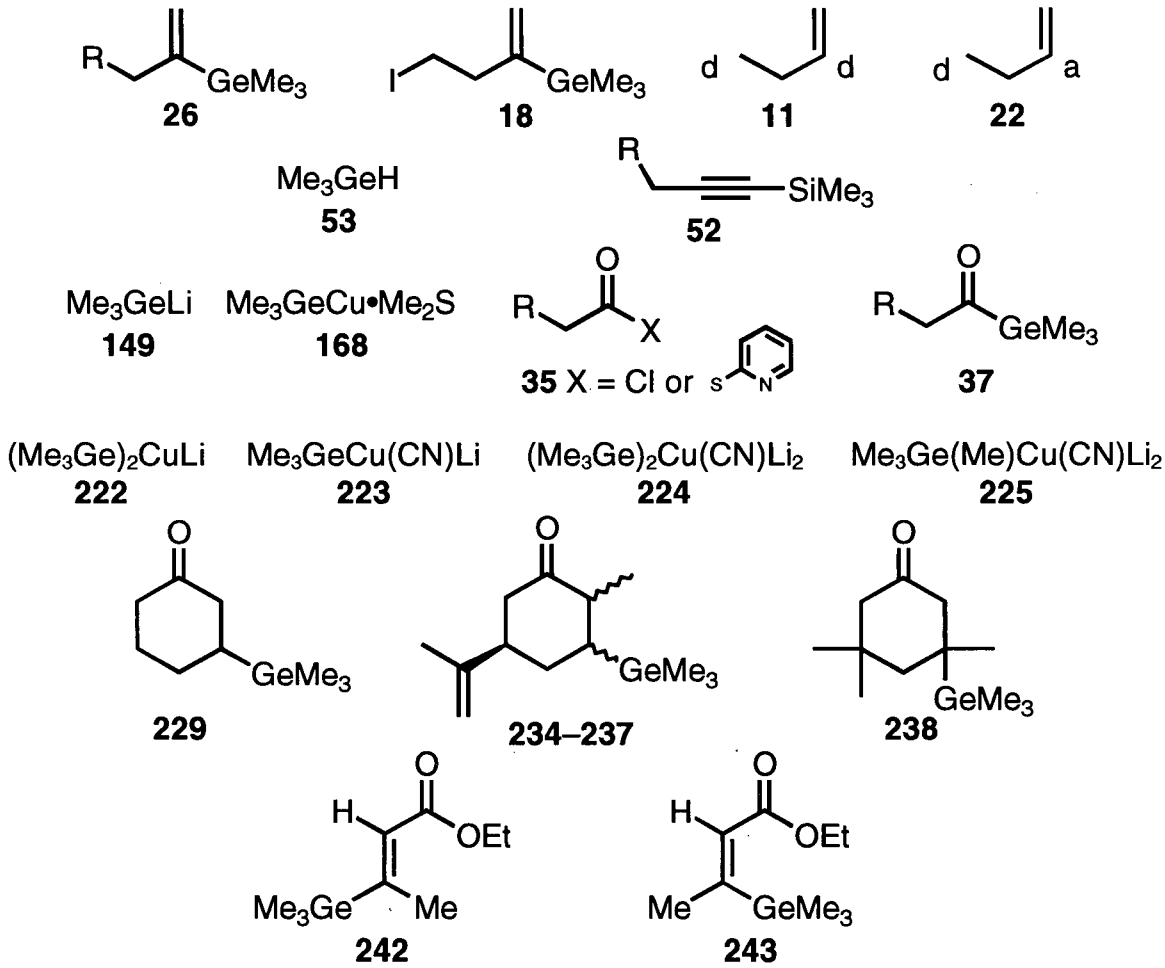

TABLE OF CONTENTS

ABSTRACT ii

TABLE OF CONTENTS iv

LIST OF TABLES xvi

LIST OF GENERAL PROCEDURES xviii

LIST OF ABBREVIATIONS xix

ACKNOWLEDGMENTS xx

DEDICATION xxi

1 INTRODUCTION 1

1.1 GENERAL 1

1.2 BACKGROUND 3

1.3 PROPOSALS 13

2 DISCUSSION 16

2.1 SYNTHESIS OF 2-TRIMETHYLGERMYLALK-1-ENES VIA PLATINUM CATALYZED HYDROGERMYLATION OF 1-TRIMETHYLSILYLALK-1-YNES 16

2.1.1 INTRODUCTORY REMARKS 16

2.1.2 SYNTHESIS OF 1-TRIMETHYLSILYLALK-1-YNES 22

2.1.3 SYNTHESIS OF TRIMETHYLGERMANE (53) 25

2.1.4 ISOLATION OF THE PRODUCTS OF HYDROGERMYLATION OF 6-TRIMETHYLSILYLHEX-5-YN-1-OL (62) AND THEIR TREATMENT WITH P-TOLUENESULFONIC ACID MONOHYDRATE IN DICHLOROMETHANE 26

2.1.4.1 HYDROGERMYLATION OF 6-TRIMETHYLSILYLHEX-5-YN-1-OL (**62**) 26

2.1.4.2 ISOLATION OF THE PRODUCTS OF HYDROGERMYLATION OF 6-TRIMETHYLSILYLHEX-5-YN-1-OL (**62**) 37

2.1.4.2.1 Isolation and Characterization of (*E*)-5-Trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**73**) 38

2.1.4.2.2 Isolation and Characterization of (*Z*)-5-Trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**75**) 40

2.1.4.2.3 Isolation and Characterization of (*E*)-6-Trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**74**) 42

2.1.4.2.4 Isolation and Characterization of (*Z*)-6-Trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**76**) 46

2.1.4.2.5 Summary 48

2.1.4.3 TREATMENT OF THE PRODUCTS OF HYDROGERMYLATION OF 6-TRIMETHYLSILYLHEX-5-YN-1-OL (**62**) WITH *P*-TOLUENESULFONIC ACID MONOHYDRATE IN DICHLOROMETHANE 50

2.1.4.3.1 Protiodesilylation of (*E*)-5-Trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**73**) to 5-Trimethylgermylhex-5-en-1-ol (**92**) 50

2.1.4.3.2 Protiodesilylation of (*Z*)-5-Trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**75**) to 5-Trimethylgermylhex-5-en-1-ol (**92**) 51

2.1.4.3.3 Protiodesilylation of (*Z*)-6-Trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**76**) to 5-Trimethylgermylhex-5-en-1-ol (**92**) 52

2.1.4.3.4 Protiodegermylation of (*E*)-6-Trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**74**) to (*E*)-6-Trimethylsilylhex-5-en-1-ol (**94a**) and (*Z*)-6-Trimethylsilylhex-5-en-1-ol (**94b**) 57

2.1.4.3.5 Summary 63

2.1.5 SYNTHESIS OF 2-TRIMETHYLGERMYLALK-1-ENES 65

2.1.5.1 CHARACTERISTIC SPECTRAL DATA OF 2-TRIMETHYLGERMYLALK-1-ENES 74

2.1.6 CONCLUSIONS 79

2.2 SYNTHESIS OF ACYLTRIMETHYLGERMANES VIA ADDITION OF (TRIMETHYLGERMYL)COPPER(I)–DIMETHYL SULFIDE TO ACYL ELECTROPHILES AND THEIR OLEFINATION TO 2-TRIMETHYLGERMYLALK-1-ENES 81

2.2.1 INTRODUCTORY REMARKS 81

2.2.2 SYNTHESIS OF ACYLTRIMETHYLGERMANES FROM ACYL CHLORIDES 89

2.2.2.1 SYNTHESIS OF ACYL CHLORIDES 89

2.2.2.2 PREPARATION OF TRIMETHYLGERMYLLITHIUM (**149**) AND (TRIMETHYLGERMYL)COPPER(I)–DIMETHYL SULFIDE (**168**) 92

2.2.2.3 SYNTHESIS OF ACYLTRIMETHYLGERMANES 97

2.2.2.4 CHARACTERISTIC SPECTRAL DATA OF ACYLTRIMETHYLGERMANES 121

2.2.3 SYNTHESIS OF ACYLTRIMETHYLGERMANES FROM S-(PYRIDIN-2-YL) THIOESTERS 123

2.2.3.1 SYNTHESIS OF *S*-(PYRIDIN-2-YL) THIOESTERS 123

2.2.3.2 SYNTHESIS OF ACYLTRIMETHYLGERMANES 125

2.2.4 OLEFINATION OF ACYLTRIMETHYLGERMANES TO 2-TRIMETHYLGERMYLALK-1-ENES 128

2.2.5 CONCLUSIONS 132

2.3 CONJUGATE ADDITION OF (TRIMETHYLGERMYL)COPPER(I)–DIMETHYL SULFIDE (168) AND LITHIUM (TRIMETHYLGERMYL)-CUPRATES TO SELECTED UNSATURATED CARBONYL SYSTEMS 134

2.3.1 INTRODUCTORY REMARKS 134

2.3.2 PREPARATION OF THE (TRIMETHYLGERMYL)CUPRATES 222–225 136

2.3.3 ADDITION OF (TRIMETHYLGERMYL)COPPER(I)–DIMETHYL SULFIDE (168) AND (TRIMETHYLGERMYL)CUPRATES 222–225 TO CYCLIC ENONES 138

2.3.3.1 CONJUGATE ADDITION TO CYCLOHEX-2-EN-1-ONE (**226**) 138

2.3.3.1.1 Mechanistic Considerations 142

2.3.3.2 CONJUGATE ADDITION TO *L*-CARVONE (**227**) 143

2.3.3.2.1 Isolation and Characterization of the Four Diastereomers **234–237** 145

2.3.3.2.2 Conjugate Addition of Reagents **168** and **223–225** to *l*-Carvone (**227**) 151

2.3.3.3 CONJUGATE ADDITION TO ISOPHORONE (**228**) 153

2.3.4 ADDITION OF (TRIMETHYLGERMYL)COPPER(I)–DIMETHYL SULFIDE (168) AND (TRIMETHYLGERMYL)CUPRATES TO ALK-2-YNOATES 156

2.3.4.1 ADDITION TO ETHYL BUT-2-YNOATE (**241**) 156

2.3.4.1.1 Mechanistic Considerations 160

2.3.4.2 SYNTHESIS OF METHYL (*E*)-6-CHLORO-3-TRIMETHYLGERMYLHEX-2-ENOATE (**248**) 162

2.3.5 CONCLUSIONS 164

3 EXPERIMENTAL 165

3.1 GENERAL 165

3.1.1 DATA ACQUISITION AND METHODS 165

3.1.2 SOLVENTS AND REAGENTS 169

3.2 SYNTHESIS OF 2-TRIMETHYLGERMYLALK-1-ENES VIA PLATINUM CATALYZED HYDROGERMYLATION OF 1-TRIMETHYLSILYLALK-1-YNES 171

3.2.1 SYNTHESIS OF 1-TRIMETHYLSILYLALK-1-YNES 171

3.2.1.1 GENERAL PROCEDURE 1: PREPARATION OF THE 1-TRIMETHYLSILYLALK-1-YNES **61** AND **63** 171

3.2.1.1.1 Synthesis of 1-Trimethylsilyl-6-(trimethylsilyloxy)hex-1-yne (**61**) . 171

3.2.1.1.2 Synthesis of 1-Trimethylsilyl-4-(trimethylsilyloxy)but-1-yne (**63**) . 172

3.2.1.2 SYNTHESIS OF 6-TRIMETHYLSILYLHEX-5-YN-1-OL (**62**) 173

3.2.1.3 GENERAL PROCEDURE 2: PREPARATION OF THE 1-TRIMETHYLSILYLALK-1-YNES **64–66** 174

3.2.1.3.1 Synthesis of 1-Trimethylsilyldodec-1-yne (**64**) 175

3.2.1.3.2 Synthesis of 5-Chloro-1-trimethylsilylpent-1-yne (**65**) 176

3.2.1.3.3 Synthesis of 1-Phenyl-2-trimethylsilylacetylene (**66**) 177

3.2.1.4 SYNTHESIS OF 1,6-BIS(TRIMETHYLSILYL)HEXA-1,5-DIYNE (**67**) 178

3.2.1.5 SYNTHESIS OF 2-(CYCLOPENT-2-EN-1-YL)ETHANOL (**69**), 1-(CYCLOPENT-2-EN-1-YL)-2-IODOETHANE (**70**) AND 4-(CYCLOPENT-2-EN-1-YL)-1-TRIMETHYLSILYLBUT-1-YNE (**72**) 179

*a) 2-(Cyclopent-2-en-1-yl)ethanol (**69**)* *179*

*b) 2-(Cyclopent-2-en-1-yl)ethanol (**70**)* *180*

*c) 2-(Cyclopent-2-en-1-yl)ethanol (**72**)* *181*

3.2.2 SYNTHESIS OF TRIMETHYLGERMANE (53) 183

3.2.3 ISOLATION OF THE PRODUCTS OF HYDROGERMYLATION OF 6-TRIMETHYLSILYLHEX-5-YN-1-OL (62) AND THEIR TREATMENT WITH P-TOLUENESULFONIC ACID MONOHYDRATE IN DICHLOROMETHANE 185

3.2.3.1 SYNTHESIS, ISOLATION AND CHARACTERIZATION OF (*E*)- AND (*Z*)-5-TRIMETHYLGERMYL-6-TRIMETHYLSILYLHEX-5-EN-1-OLS (**73**) AND (**75**), AND (*E*)- AND (*Z*)-6-TRIMETHYLGERMYL-6-TRIMETHYLSILYLHEX-5-EN-1-OLS (**74**) AND (**76**) 185

*a) Isolation and Characterization of (E)-5-Trimethylgermyl-6-trimethylsilylhex-5-en-1ol (**73**)* *186*

*b) Isolation and Characterization of (Z)-5-Trimethylgermyl-6-trimethylsilylhex-5-en-1ol (**75**)* *188*

*c) Isolation and Characterization of (E)-6-Trimethylgermyl-6-trimethylsilylhex-5-en-1ol (**74**)* *190*

*d) Isolation and Characterization of (Z)-6-Trimethylgermyl-6-trimethylsilylhex-5-en-1ol (**76**)* *191*

3.2.3.2 TREATMENT OF (*E*)- AND (*Z*)-5-TRIMETHYLGERMYL-6-TRIMETHYLSILYLHEX-5-EN-1-OLS (**73**) AND (**75**), AND (*E*)- AND (*Z*)-6-TRIMETHYLGERMYL-6-TRIMETHYLSILYLHEX-5-EN-1-OLS (**74**) AND (**76**) WITH *P*-TOLUENESULFONIC ACID MONOHYDRATE IN DICHLOROMETHANE 194

3.2.3.2.1 Protiodesilylation of (*E*)-5-Trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**73**) to 5-Trimethylgermylhex-5-en-1-ol (**92**) 194

3.2.3.2.2 Protiodesilylation of (*Z*)-5-Trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**75**) to 5-Trimethylgermylhex-5-en-1-ol (**92**) 195

3.2.3.2.3 Protiodesilylation of (*Z*)-6-Trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**76**) to 5-Trimethylgermylhex-5-en-1-ol (**92**) 195

3.2.3.2.4 Protiodegermylation of (*E*)-6-Trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**74**) to (*E*)- and (*Z*)-6-Trimethylsilylhex-5-en-1-ol (**94a**) and (**94b**) 196

3.2.4 SYNTHESIS OF 2-TRIMETHYLGERMYLALK-1-ENES 199

3.2.4.1 GENERAL PROCEDURE 3: PREPARATION OF THE 2-TRIMETHYLGERMYLALK-1-ENES 199

3.2.4.1.1 Synthesis of 5-Trimethylgermylhex-5-en-1-ol (**92**) and 5-Trimethylgermyl-6-trimethylsilylhexan-1-ol (**122**) 200

3.2.4.1.2 Synthesis of 3-Trimethylgermylbut-3-en-1-ol (**115**) 204

3.2.4.1.3 Synthesis of 2-Trimethylgermyldodec-1-ene (**116**) 205

3.2.4.1.4 Synthesis of 5-Chloro-2-trimethylgermylpent-1-ene (**117**) 206

3.2.4.1.5 Synthesis of 1-Phenyl-1-trimethylgermylethene (**118**) 207

3.2.4.1.6 Synthesis of 2,5-bis(Trimethylgermyl)hexa-1,5-diene (**119**) 209

3.2.4.1.7 Synthesis of 4-(Cyclopent-1-en-1-yl)-2-trimethylgermylbut-1-ene (**120**) 210

3.2.4.1.8 Synthesis of 4-Trimethylgermylpent-4-enoyltrimethylgermane (**121**) 211

3.3 SYNTHESIS OF ACYLTRIMETHYLGERMANES VIA ADDITION OF (TRIMETHYLGERMYL)COPPER(I)–DIMETHYL SULFIDE TO ACYL ELECTROPHILES, AND THEIR OLEFINATION TO 2-TRIMETHYL-GERMYLALK-1-ENES 213

3.3.1 SYNTHESIS OF ACYL CHLORIDES 213

3.3.1.1 GENERAL PROCEDURE 4: PREPARATION OF THE ACYL CHLORIDES **157–160** AND **164** 213

3.3.1.1.1 Synthesis of Decanoyl Chloride (**157**) 213

3.3.1.1.2 Synthesis of (Cyclopent-2-en-1-yl)acetyl Chloride (**158**) 214

3.3.1.1.3 Synthesis of Adipoyl Chloride (**159**) 214

3.3.1.1.4 Synthesis of Pent-4-ynoyl Chloride (**160**) 215

3.3.1.1.5 Synthesis of 5-Trimethylsilylpent-4-yn-1-ol (**162**), 5-Trimethylsilylpent-4-ynoic Acid (**163**) and 5-Trimethylsilylpent-4-ynoyl Chloride (**164**) 215

*a) 5-Trimethylsilylpent-4-yn-1-ol (**162**)* *215*

*b) 5-Trimethylsilylpent-4-ynoic Acid (**163**)* *216*

*c) 5-Trimethylsilylpent-4-ynoyl Chloride (**164**)* *217*

3.3.1.2 SYNTHESIS OF ((4-METHOXYBENZYL)OXY)ACETIC ACID (**166**) AND ((4-METHOXYBENZYL)OXY)ACETYL CHLORIDE (**167**) 218

*a) ((4-Methoxybenzyl)oxy)acetic Acid (**166**)* *218*

*b) ((4-Methoxybenzyl)oxy)acetyl Chloride (**167**)* *219*

3.3.2 SYNTHESIS OF ACYLTRIMETHYLGERMANES FROM ACYL CHLORIDES 221

3.3.2.1 SYNTHESIS OF TRIMETHYLGERMYLLITHIUM (**149**) 221

3.3.2.1.1 Preparation of the Trimethylgermyllithium Reagent (**149**) 221

3.3.2.1.2 Treatment of Trimethylgermyllithium with 1-Bromodecane: Synthesis of 1-Trimethylgermyldecane (**172**) 221

3.3.2.1.3 Determination of the Yield of Trimethylgermyllithium (**149**) Formation from Trimethylgermane (**53**) via the Internal Standard Method 222

3.3.2.2 PREPARATION OF (TRIMETHYLGERMYL)COPPER(I)–DIMETHYL SULFIDE (**168**) 223

*a) Via Addition of the Solution of Me_3GeLi (**149**) to a Suspension of $CuBr{\bullet}Me_2S$ in THF ("Normal" Addition Method)* *223*

*b) Via Addition of Solid $CuBr{\bullet}Me_2S$ to the Solution of Me_3GeLi (**149**) in THF ("Inverse" Addition Method)* *223*

3.3.2.3 GENERAL PROCEDURE 5: PREPARATION OF THE ACYLTRIMETHYLGERMANES FROM ACYL CHLORIDES 224

3.3.2.3.1 Synthesis of Decanoyltrimethylgermane (**170**) 225

a) With Chlorotrimethylsilane as Additive *225*

b) Without Additive *226*

3.3.2.3.2 Synthesis of (Cyclopent-2-en-1-yl)acetyltrimethylgermane (**178**).. 226

3.3.2.3.3 Synthesis of (Cyclohexanecarbonyl)trimethylgermane (**179**)..... 227

3.3.2.3.4 Synthesis of ((4-Methoxybenzyl)oxy)acetyltrimethylgermane (**180**) 228

3.3.2.3.5 Synthesis of (Benzyloxy)acetyltrimethylgermane (**181**)..... 229

a) With Chlorotrimethylsilane as Additive *229*

b) Without Additive *230*

c) With Bromotrimethylsilane as Additive..... *232*

3.3.2.3.6 Synthesis of 5-Chloropentanoyltrimethylgermane (**182**) 234

3.3.2.3.7 Synthesis of 3-Chloropropanoyltrimethylgermane (**183**)..... 235

a) With Bromotrimethylsilane as Additive *235*

b) Without Additive *236*

3.3.2.3.8 Synthesis of Hexanedioylbis(trimethylgermane) (**184**) 238

a) With Chlorotrimethylsilane as Additive..... *238*

b) Without Additive *239*

3.3.2.3.9 Attempts at Synthesizing Pent-4-ynoyltrimethylgermane (**185**)..... 241

a) With Chlorotrimethylsilane as Additive..... *241*

b) Without Additive *242*

3.3.2.3.10 Synthesis of 5-Trimethylsilylpent-4-ynoyltrimethylgermane (**114**)246

3.3.2.4 LARGE SCALE PREPARATION OF ((4-METHOXYBENZYL)OXY)ACETYL-TRIMETHYLGERMANE (**180**)..... 247

3.3.3 SYNTHESIS OF S-(PYRIDIN-2-YL) THIOESTERS 249

3.3.3.1 GENERAL PROCEDURE 6: PREPARATION OF THE *S*-(PYRIDIN-2-YL) THIOESTERS..... 249

3.3.3.1.1 Synthesis of *S*-(Pyridin-2-yl) Decanethioate (**210**)..... 249

3.3.3.1.2 Synthesis of *S*-(Pyridin-2-yl) Pent-4-ynethioate (**211**)..... 250

3.3.3.1.3 Synthesis of *S*-(Pyridin-2-yl) ((4-Methoxybenzyl)oxy)ethanethioate (**212**) 251

3.3.3.1.4 Synthesis of *S*-(Pyridin-2-yl) 3-Chloropropanethioate (**213**) 252

3.3.4 SYNTHESIS OF ACYLTRIMETHYLGERMANES FROM S-(PYRIDIN-2-YL) THIOESTERS 253

3.3.4.1 GENERAL PROCEDURE 7: PREPARATION OF THE ACYLTRIMETHYLGERMANES FROM *S*-(PYRIDIN-2-YL) THIOESTERS 253

3.3.4.1.1 Synthesis of Decanoyltrimethylgermane (**170**) 254

3.3.4.1.2 Synthesis of ((4-Methoxybenzyl)oxy)acetyltrimethylgermane (**180**) 254

3.3.4.1.3 Synthesis of 3-Chloropropanoyltrimethylgermane (**183**) 255

3.3.4.1.4 Attempt at Synthesizing Pent-4-ynoyltrimethylgermane (**185**) 255

3.3.5 SYNTHESIS OF 2-TRIMETHYLGERMYLALK-1-ENES VIA WITTIG OLEFINATION OF ACYLTRIMETHYLGERMANES 257

3.3.5.1 GENERAL PROCEDURE 8: PREPARATION OF THE 2-TRIMETHYLGERMYLALK-1-ENES 257

3.3.5.1.1 Synthesis of 2-Trimethylgermylundec-1-ene (**214**) 257

3.3.5.1.2 Synthesis of 2-Trimethylgermyl-6-trimethylsilylhex-5-yn-1-ene (**215**) 258

3.3.5.1.3 Synthesis of 1-((4-Methoxybenzyl)oxy)-2-trimethylgermylprop-2-ene (**216**) and 2-Trimethylgermylprop-2-en-1-ol (**219**) 260

*a) 1-((4-Methoxybenzyl)oxy)-2-trimethylgermylprop-2-ene (**216**) 260*

*b) 2-Trimethylgermylprop-2-en-1-ol (**219**) 261*

3.3.5.1.4 Synthesis of 6-Chloro-2-trimethylgermylhex-1-ene (**217**) 262

3.3.5.1.5 Synthesis of 2,7-bis(Trimethylgermyl)octa-1,7-diene (**218**) 263

3.4 CONJUGATE ADDITION OF (TRIMETHYLGERMYL)COPPER(I)–DIMETHYL SULFIDE (168) AND LITHIUM (TRIMETHYLGERMYL)-CUPRATES 222–225 TO SELECTED UNSATURATED CARBONYL SYSTEMS 265

3.4.1 PREPARATION OF THE (TRIMETHYLGERMYL)CUPRATES 222–225 265

3.4.1.1 PREPARATION OF THE LITHIUM BIS(TRIMETHYLGERMYL)CUPRATE (**222**) 265

3.4.1.2 PREPARATION OF THE LITHIUM (TRIMETHYLGERMYL)CYANOCUPRATE (**223**) 265

3.4.1.3 PREPARATION OF THE DILITHIUM BIS(TRIMETHYLGERMYL)CYANOCUPRATE (**224**) 266

3.4.1.4 PREPARATION OF THE DILITHIUM METHYL(TRIMETHYLGERMYL)CYANOCUPRATE (**225**) 266

3.4.2 ADDITION OF (TRIMETHYLGERMYL)COPPER(I)–DIMETHYL SULFIDE (168) AND (TRIMETHYLGERMYL)CUPRATES 222–225 TO CYCLIC ENONES 268

3.4.2.1 GENERAL PROCEDURE 9: SYNTHESIS OF 3-TRIMETHYLGERMYLCYCLOHEXANONE (**229**) FROM CYCLOHEX-2-EN-1-ONE (**226**) 268

3.4.2.1.1 Preparation of 3-Trimethylgermylcyclohexanone (**229**) Using (Trimethylgermyl)copper(I)–Dimethyl Sulfide (**168**) 269

3.4.2.1.2 Preparation of 3-Trimethylgermylcyclohexanone (**229**) Using Lithium Bis(trimethylgermyl)cuprate (**222**) 270

3.4.2.1.3 Preparation of 3-Trimethylgermylcyclohexanone (**229**) Using Lithium (Trimethylgermyl)cyanocuprate (**223**) 270

3.4.2.1.4 Preparation of 3-Trimethylgermylcyclohexanone (**229**) Using Dilithium Bis(trimethylgermyl)cyanocuprate (**224**) 271

3.4.2.1.5 Preparation of 3-Trimethylgermylcyclohexanone (**229**) Using Dilithium Methyl(trimethylgermyl)cyanocuprate (**225**) 272

3.4.2.2 ADDITION OF TRIMETHYLGERMYLLITHIUM (**149**) TO CYCLOHEX-2-EN-1-ONE (**226**) 272

3.4.2.2.1 Synthesis of 1-Trimethylgermylcyclohex-2-en-1-ol (**230**) 272

3.4.2.3 GENERAL PROCEDURE 10: SYNTHESIS OF (2*R*,3*S*,5*S*)-, (2*S*,3*S*,5*S*)-(2*R*,3*R*,5*S*)- AND (2*S*,3*R*,5*S*)-5-ISOPROPENYL-2-METHYL-3-TRIMETHYLGERMYLCYCLOHEXANONE (**234**)–(**237**) FROM *L*-CARVONE (**227**) 274

3.4.2.3.1 Isolation and Characterization of the Four Diastereomeric 5(*S*)-Isopropenyl-2-methyl-3-trimethylgermylcyclohexanones (**234**)–(**237**) 275

*a) Isolation and Characterization of (2R,3S,5S)-Isopropenyl-2-methyl-3-trimethylgermylcyclohexanone (**234**)* *275*

*b) Isolation and Characterization of (2S,3R,5S)- and (2S,3S,5S)-5-Isopropenyl-2-methyl-3-trimethylgermylcyclohexanone (**237**) and (**235**)*.... *278*

*c) Isolation and Characterization of (2R,3R,5S)-Isopropenyl-2-methyl-3-trimethylgermylcyclohexanone (**236**)* *282*

3.4.2.3.2 Preparation of the Diastereomeric Mixture of Four 5(*S*)-Isopropenyl-2-methyl-3-trimethylgermylcyclohexanones (**234**)–(**237**) Using (Trimethylgermyl)copper(I)–Dimethyl Sulfide (**168**) 285

3.4.2.3.3 Preparation of the Diastereomeric Mixture of Four 5(*S*)-Isopropenyl-2-methyl-3-trimethylgermylcyclohexanones (**234**)–(**237**) Using Lithium (Trimethylgermyl)cyanocuprate (**223**) 286

3.4.2.3.4 Preparation of the Diastereomeric Mixture of Four 5(*S*)-Isopropenyl-2-methyl-3-trimethylgermylcyclohexanones (**234**)–(**237**) Using Dilithium Bis(trimethylgermyl)cyanocuprate (**224**) 287

3.4.2.3.5 Preparation of the Diastereomeric Mixture of Four 5(*S*)-Isopropenyl-2-methyl-3-trimethylgermylcyclohexanones (**234**)–(**237**) Using Dilithium Methyl(trimethylgermyl)cyanocuprate (**225**) 288

3.4.2.4 GENERAL PROCEDURE 11: SYNTHESIS OF 3,5,5-TRIMETHYL-3-TRIMETHYLGERMYLCYCLOHEXANONE (**238**) FROM ISOPHORONE (**228**) 289

3.4.2.4.1 Preparation of 3,5,5-Trimethyl-3-trimethylgermylcyclohexanone (**238**) Using Dilithium Bis(trimethylgermyl)cyanocuprate (**224**) ... 290

3.4.2.4.2 Preparation of 3,5,5-Trimethyl-3-trimethylgermylcyclohexanone (**238**) Using Dilithium Methyl(trimethylgermyl)cyanocuprate (**225**) 291

3.4.2.4.3 Preparation of 3,5,5-Trimethyl-3-trimethylgermylcyclohexanone (**238**) Using Dilithium Methyl(trimethylgermyl)cyanocuprate (**225**) and Chlorotrimethylsilane as Additive 292

3.4.2.4.4 Preparation of 3,5,5-Trimethyl-3-trimethylgermylcyclohexanone (**238**) Using Dilithium Methyl(trimethylgermyl)cyanocuprate (**225**) and Bromotrimethylsilane as Additive 293

3.4.3 ADDITION OF (TRIMETHYLGERMYL)COPPER(I)–DIMETHYL SULFIDE (168) AND (TRIMETHYLGERMYL)CUPRATES TO ACETYLENIC ESTERS 294

3.4.3.1 GENERAL PROCEDURE 12: SYNTHESIS OF ETHYL (*E*)-3-TRIMETHYLGERMYLBUT-2-ENOATE (**242**) FROM ETHYL BUT-2-YNOATE (**241**) 294

3.4.3.1.1 Preparation of Ethyl (*E*)-3-Trimethylgermylbut-2-enoate (**242**) Using Trimethylgermylcopper(I)–Dimethyl Sulfide (**168**)..... 296

3.4.3.1.2 Preparation of Ethyl (*E*)-3-Trimethylgermylbut-2-enoate (**242**) Using Lithium (Trimethylgermyl)cyanocuprate (**223**)..... 296

3.4.3.2 SYNTHESIS OF ETHYL (*Z*)-3-TRIMETHYLGERMYLBUT-2-ENOATE (**243**) FROM ETHYL BUT-2-YNOATE (**241**) USING DILITHIUM METHYL(TRIMETHYLGERMYL)CYANOCUPRATE (**225**) 297

3.4.3.3 SYNTHESIS OF ETHYL (*E*)- AND (*Z*)-3-TRIMETHYLGERMYLBUT-2-ENOATE (**242**) AND (**243**) FROM ETHYL BUT-2-YNOATE (**241**) USING LITHIUM BIS(TRIMETHYLGERMYL)CUPRATE (**222**) 300

3.4.3.4 SYNTHESIS OF METHYL (*E*)-6-CHLORO-3-TRIMETHYLGERMYLHEX-2-ENOATE (**248**) 301

4 FOOTNOTES AND REFERENCES 303

LIST OF TABLES

Table 1: Preparation of the 1-Trimethylsilylalk-1-ynes **61–67** 23

Table 2: Preparation of the 2-Trimethylgermylalk-1-enes **92, 115–121** 66

Table 3: Characteristic Spectral Data of 2-Trimethylgermylalk-1-enes **92, 115–121** 76

Table 4: Preparation of the Acyl Chlorides **157–160** 89

Table 5: Optimization of the Experimental Conditions for the Formation of Decanoyl-trimethylgermane (**170**) 97

Table 6: Preparation of the Acyltrimethylgermanes **170, 178–184** and **114** 101

Table 7: Characteristic Spectral Data of the Acyltrimethylgermanes **114, 170, 178–184** 121

Table 8: Preparation of the *S*-(Pyridin-2-yl) Thioesters **210–213** 124

Table 9: Preparation of the Acyltrimethylgermanes **170, 180** and **183** 126

Table 10: Preparation of the 2-Trimethylgermylalk-1-enes **214–218** 129

Table 11: Conjugate Addition of Reagents **168** and **222–225** to Cyclohex-2-en-1-one (**226**) 139

Table 12: Conjugate Addition of Reagents **168** and **223–225** to *l*-Carvone (**227**) 152

Table 13: Conjugate Addition of Reagents **224** and **225** to Isophorone (**228**) 154

Table 14: Addition of (Trimethylgermyl)copper(I) Reagents to Ethyl But-2-ynoate (**241**) . 158

Table 15: ^{1}H NMR Data from Nuclear Overhauser Enhancement Difference Experiments for (*E*)-5-Trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**73**) 187

Table 16: ^{1}H NMR Data from Nuclear Overhauser Enhancement Difference Experiments for (*Z*)-5-Trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**75**) 189

Table 17: ^{1}H NMR Data from Nuclear Overhauser Enhancement Difference Experiments for (*E*)-6-Trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**74**) 191

Table 18: ^{1}H NMR Data from Nuclear Overhauser Enhancement Difference Experiments for (*Z*)-6-Trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**76**) 193

Table 19: ^{1}H NMR Data from Homonuclear Decoupling Experiments for 5-Trimethylgermyl-6-trimethylsilylhexan-1-ol (**122**) 201

Table 20: ^{1}H NMR Data from Nuclear Overhauser Enhancement Difference Experiments for 5-Trimethylgermylhex-5-en-1-ol (**92**) 203

Table 21: ^{1}H NMR Data from Nuclear Overhauser Enhancement Difference Experiments for (*E*)-2-Benzyloxy-1-(benzyloxy)acetoxy-1-trimethylgermylethene (**186**) 232

Table 22: ^{1}H NMR Data from Homonuclear Decoupling Experiments for 5-(But-3-yn-1-yl)-4-(bis(trimethylgermyl)methyl)pent-4-eno-5-lactone (**205**) 245

Table 23: ^{1}H NMR Data from ^{1}H–^{1}H Homonuclear Correlation Spectroscopy and Nuclear Overhauser Enhancement Difference Experiments for (2*R*,3*S*,5*S*)-5-Isopropenyl-2-methyl-3-trimethylgermylcyclohexan-1-one (**234**) 277

Table 24: ^{1}H NMR Data from ^{1}H–^{1}H Homonuclear Correlation Spectroscopy and Nuclear Overhauser Enhancement Difference Experiments for (2*S*,3*R*,5*S*)-5-Isopropenyl-2-methyl-3-trimethylgermylcyclohexanone (**237**) 279

Table 25: ^{1}H NMR Data from ^{1}H–^{1}H Homonuclear Correlation Spectroscopy and Nuclear Overhauser Enhancement Difference Experiments for (2*S*,3*S*,5*S*)-5-Isopropenyl-2-methyl-3-trimethylgermylcyclohexanone (**235**) 281

Table 26: ^{1}H NMR Data from ^{1}H–^{1}H Homonuclear Correlation Spectroscopy and Nuclear Overhauser Enhancement Difference Experiments for (2*R*,3*R*,5*S*)-5-Isopropenyl-2-methyl-3-trimethylgermylcyclohexanone (**236**) 284

Table 27: ^{1}H NMR Data from Nuclear Overhauser Enhancement Difference Experiments for Ethyl (*E*)-3-Trimethylgermylbut-2-enoate (**242**) 295

Table 28: ^{1}H NMR Data from Nuclear Overhauser Enhancement Difference Experiments for Ethyl (*Z*)-3-Trimethylgermylbut-2-enoate (**243**) 299

LIST OF GENERAL PROCEDURES

General Procedure 1: Preparation of the 1-Trimethylsilylalk-1-ynes **61** and **63** 171

General Procedure 2: Preparation of the 1-Trimethylsilylalk-1-ynes **64–66** 174

General Procedure 3: Preparation of the 2-Trimethylgermylalk-1-enes 199

General Procedure 4: Preparation of the Acyl Chlorides **157–160** and **164** 213

General Procedure 5: Preparation of the Acyltrimethylgermanes from Acyl Chlorides 224

General Procedure 6: Preparation of the *S*-(Pyridin-2-yl) Thioesters 249

General Procedure 7: Preparation of the Acyltrimethylgermanes from *S*-(Pyridin-2-yl) Thioesters 253

General Procedure 8: Preparation of the 2-Trimethylgermylalk-1-enes 257

General Procedure 9: Synthesis of 3-Trimethylgermylcyclohexanone (**229**) from Cyclohex-2-en-1-one (**226**) 268

General Procedure 10: Synthesis of (2*R*,3*S*,5*S*)-, (2*S*,3*S*,5*S*)- (2*R*,3*R*,5*S*)- and (2*S*,3*R*,5*S*)-5-Isopropenyl-2-methyl-3-trimethylgermylcyclohexanone (**234**)–(**237**) from *l*-Carvone (**227**) 274

General Procedure 11: Synthesis of 3,5,5-Trimethyl-3-trimethylgermylcyclohexanone (**238**) from Isophorone (**228**) 289

General Procedure 12: Synthesis of Ethyl (*E*)-3-Trimethylgermylbut-2-enoate (**242**) from Ethyl But-2-ynoate (**241**) 294

LIST OF ABBREVIATIONS

δ	–	chemical shift in part per million from Me_4Si
Δ	–	reflux
^{13}C NMR	–	carbon nuclear magnetic resonance
^{1}H NMR	–	proton nuclear magnetic resonance
br	–	broad
C-x	–	carbon number x
COSY	–	^{1}H-^{1}H homonuclear correlation spectroscopy
DCI	–	desorption chemical ionization
GLC	–	gas–liquid chromatography
H-x	–	hydrogen number x
HMPA	–	hexamethylphosphoramide
HRMS	–	high resolution mass spectrometry
J	–	coupling constant in hertz
LRMS	–	low resolution mass spectrometry
M	–	$mol \cdot L^{-1}$
MHz	–	mega hertz
mmol	–	millimole
NOE	–	nuclear Overhauser enhancement
ppm	–	part per million
RI	–	refractive index
THF	–	tetrahydrofuran
TLC	–	thin layer chromatography

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to my best friend, my sister

1 INTRODUCTION

1.1 GENERAL

Over the past decades, organic chemists have striven to increase their understanding of chemical reactions and, hence, to expand the repertoire of bond forming processes that allow the construction of increasingly more complex molecules. Some of these target molecules are naturally occurring and have important biological activities. Such compounds, though, are often in scarce supply by virtue of a lack of natural sources. Therefore, to prevent depletion of a living species for the sole purpose of isolating biologically valuable compounds, supplying the latter via synthesis would be ecologically warranted. Alternatively, analogs of such compounds may also have important biological activity. Generally, the preparation of such analogs is most conveniently accomplished via synthesis, which requires the preparation of a very large number of diversely functionalized compounds. Since different target organic compounds may differ widely in their structure and functionalization, it would be advantageous to have access to a wide variety of methods to synthesize such target substances.

Due to the fact that the carbon skeletons of target organic compounds often possess structural features such as stereogenic centers, stereodefined unsaturations, and carbocyclic rings, many different types of reactions are required to construct such compounds. To assemble the components required to obtain the synthetic goal, it is generally advantageous to use "building blocks" that contain carbon atoms bearing key required structural features and functional groups. When properly functionalized, such "building blocks" or synthons[1,2]

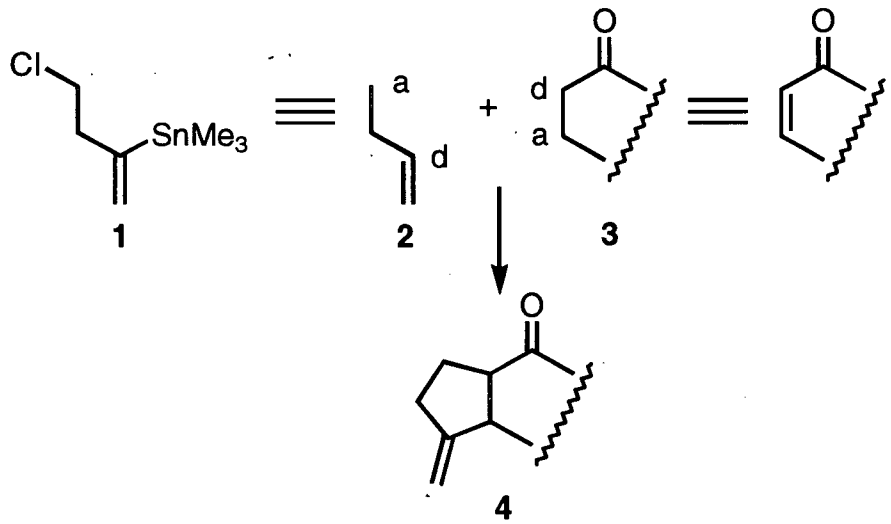
become a great asset to the synthetic chemist.

The incorporation of group XIV elements into reagents used for the synthesis of natural products has seen tremendous growth over the last few years, although the scene has been mainly dominated by silicon[3] and tin.[4] The amount of literature that has been published on these subjects is too great to discuss here, but the reader is referred to some excellent reviews.[5-14] The organic derivatives of these two elements have found widespread applicability in coupling reactions and cyclizations, often forming key steps in natural product syntheses. For some recent examples see references (15)–(22). The popularity of these elements in organic chemistry stems from their compatibility with a wide variety of standard reactions such as reductions, oxidations, alkylations, etc., and to the fact that their (latent) reactivity can be employed when required.

Remarkably, germanium is almost completely absent from the literature on the use of group XIV elements in natural product synthesis. Although some recent reports[23,24] have appeared, the research in this area is still minimal. In response to the under utilization of organogermane compounds in organic synthesis, it was decided to explore methods that could lead to the preparation of certain classes of functionalized organogermanes that should prove useful in organic synthesis. The details of these investigations and the developments of these new methods are described in this thesis.

1.2 BACKGROUND

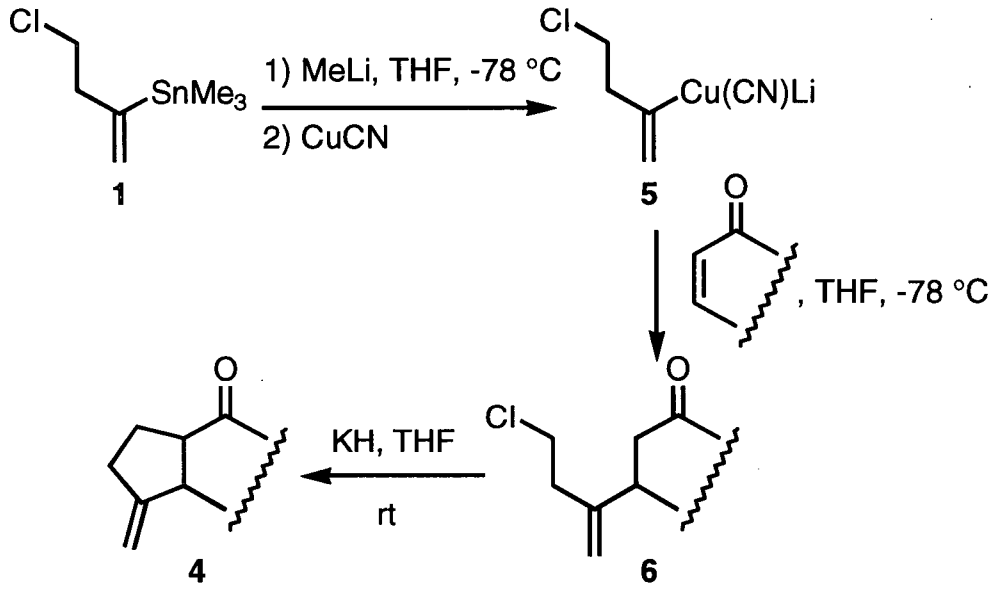
A recent report from our laboratories has described the preparation[25] of 4-chloro-2-trimethylstannylbut-1-ene (**1**). This reagent has been shown to serve well as a synthetic equivalent of the donor–acceptor[26] but-1-ene d^2,a^4-synthon **2**.[27] The usefulness of the bifunctional reagent **1** becomes apparent in the annulation sequence depicted below (**Scheme 1**). A cyclic enone serves as the synthetic equivalent of the donor–acceptor synthon **3** to produce, after annulation with **2**, a bicyclic system such as **4**.



Scheme 1

Conjunctive reagents have been defined by Trost[28] as "...those reagents which are simple building blocks that are incorporated in whole or in part into a more complex system...". Substance **1** may be referred to as a *bifunctional* conjunctive reagent. To illustrate this concept, when a solution of **1** in THF at –78 °C is treated with one equivalent of a solution of methyllithium and then with one equivalent of copper cyanide, the corresponding cuprate **5**[27] is formed (**Scheme 2**). To this mixture the appropriate enone is added and after

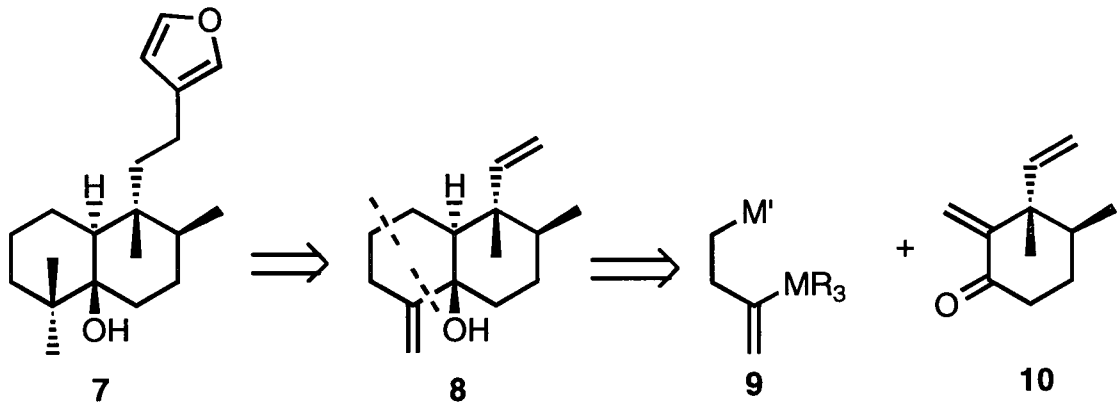
work-up the ketone **6** is isolated. This product is then treated with potassium hydride in THF at room temperature to generate the bicyclic ketone **4**.[27]



Scheme 2

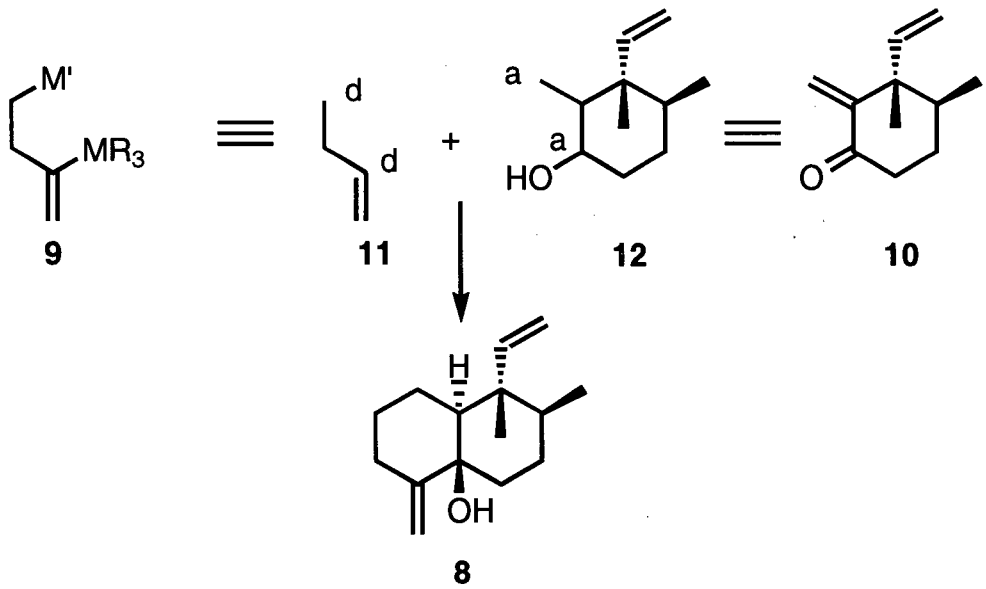
Therefore, in this example, the donor site of **1** was deployed first during the conjugate addition to the enone, and the acceptor site was used in a second step during the intra-molecular alkylation.

Recently, in our laboratories, the total synthesis of the diterpenoid (±)-ambliol B (**7**) was completed.[23] The retrosynthetic analysis of (±)-ambliol B that formed the basis of this synthesis is outlined in **Scheme 3**. It was thought that **7** could be derived from the bicyclic alcohol **8**. Thus, the exocyclic methylidene group in **8** would serve to introduce the gem-dimethyl group, and the vinyl moiety would be used to attach the furan ring. This bicyclic alcohol **8** could, in turn, be obtained via a key annulation sequence which would connect the bifunctional reagent **9** and the enone **10**.



Scheme 3

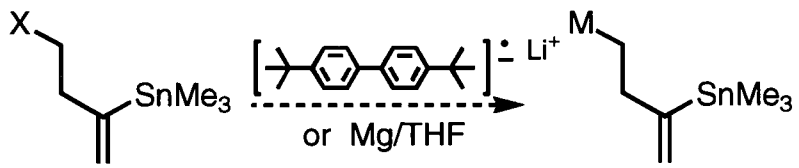
Such a sequence can be seen as the theoretical assembly of the donor–donor and acceptor–acceptor synthons **11** and **12** (**Scheme 4**) that are the synthetic equivalents of the organometallic bifunctional reagent **9** (M' = metal) and the enone **10**, respectively. In this sequence of events, the but-1-ene synthon must now be used as the d^2,d^4-synthon **11**.



Scheme 4

To accomplish such a transformation using the 4-halo-2-trimethylstannylbut-1-enes (**1**,

X = Cl or **13**, X = I), it would be necessary to transform one of these substances into the corresponding lithio (**14**, M = Li) or Grignard (**15**, M = MgI) derivatives (**Scheme 5**). However, treatment[29] of **1** with lithium 4,4'-di-*tert*-butylbiphenyl[30] failed to produce significant quantities of **14**. Moreover, treatment of **13** with magnesium turnings in THF heated to reflux failed to produce the expected Grignard reagent **15**.[29] It was rationalized that the labile alkenyl carbon–tin bond interfered with the preparation of the organometallic derivatives **14** and **15**.



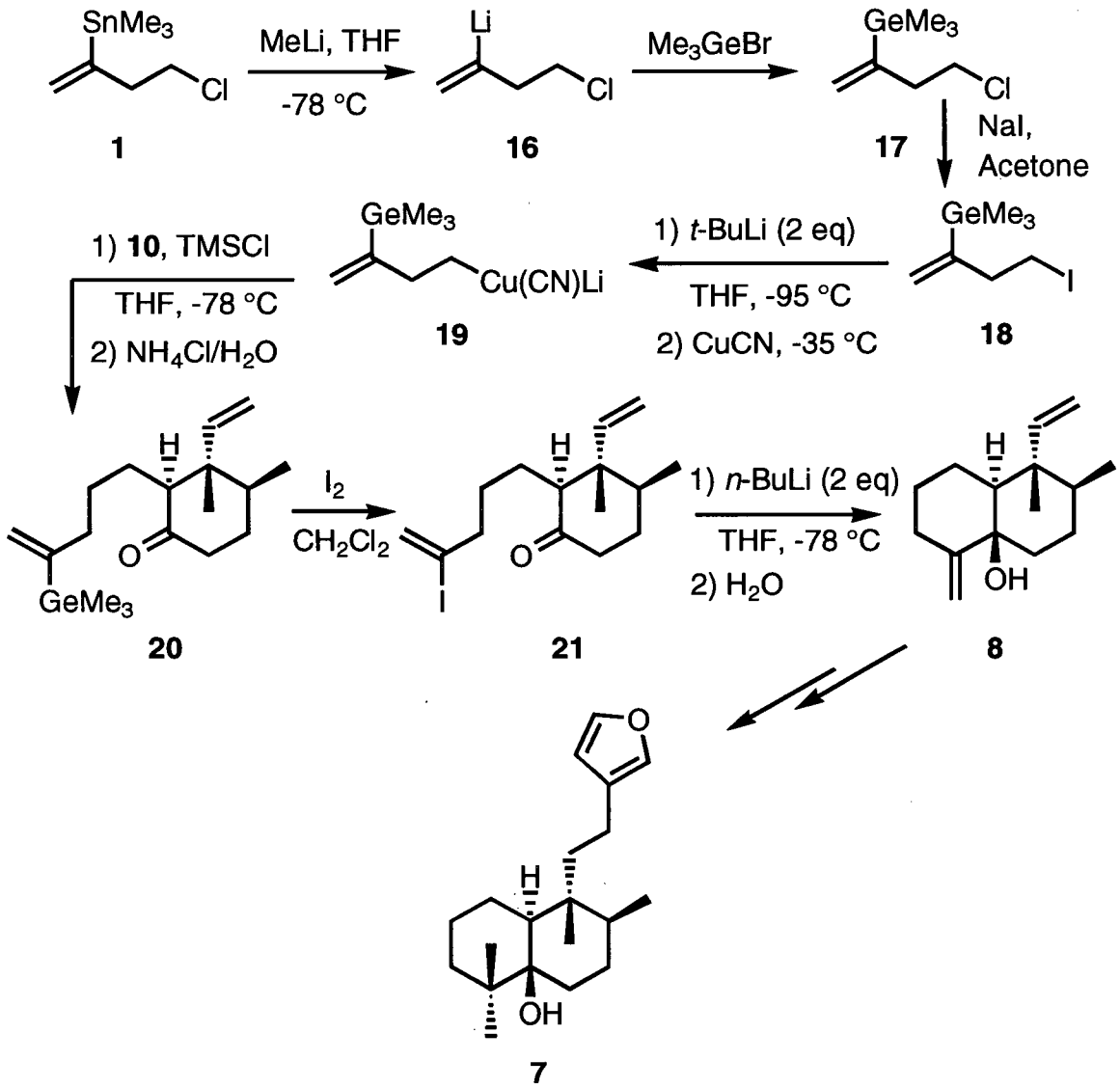
1 X = Cl **14** M = Li

13 X = I **15** M = MgI

Scheme 5

To overcome this problem it was decided to replace the trimethylstannyl moiety with another group that would be stable under the conditions used to generate the organometallic reagent required for the first carbon–carbon bond formation and yet would allow the formation of a vinyl anion at a later stage. To do this is was necessary to find a replacement with a greater alkenyl carbon–metal bond strength. The chemical bond strength, often expressed as the bond dissociation energy, for the carbon–tin bond in Me_4Sn has been determined[31] to be 65 kcal·mol^{-1}. Comparatively, the carbon–germanium bond dissociation energy for Me_4Ge was found[31] to be 76 kcal·mol^{-1}. It was thought that the greater alkyl carbon–germanium bond strength compared to the alkyl carbon–tin bond strength would be

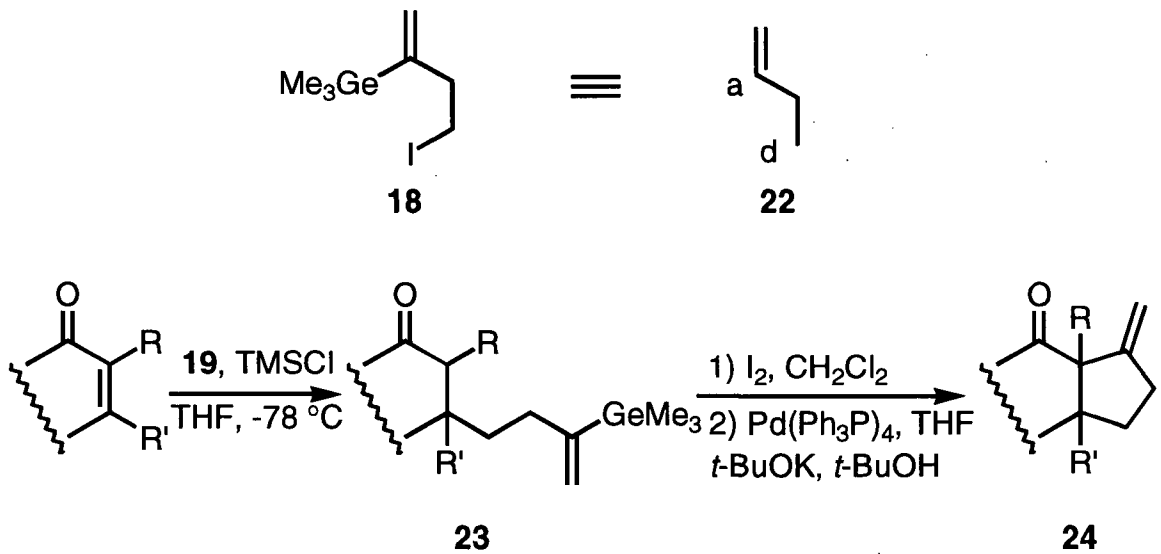
paralleled in the corresponding alkenyl carbon–metal systems. Therefore, it was envisaged that the trimethylgermyl group would be a good substitute for the trimethylstannyl moiety in the required transformation.



Scheme 6

Transmetallation of **1** at low temperature with a solution of methyllithium (**Scheme 6**) generated the corresponding vinyllithium[27] species **16**, which was then treated with bromo-

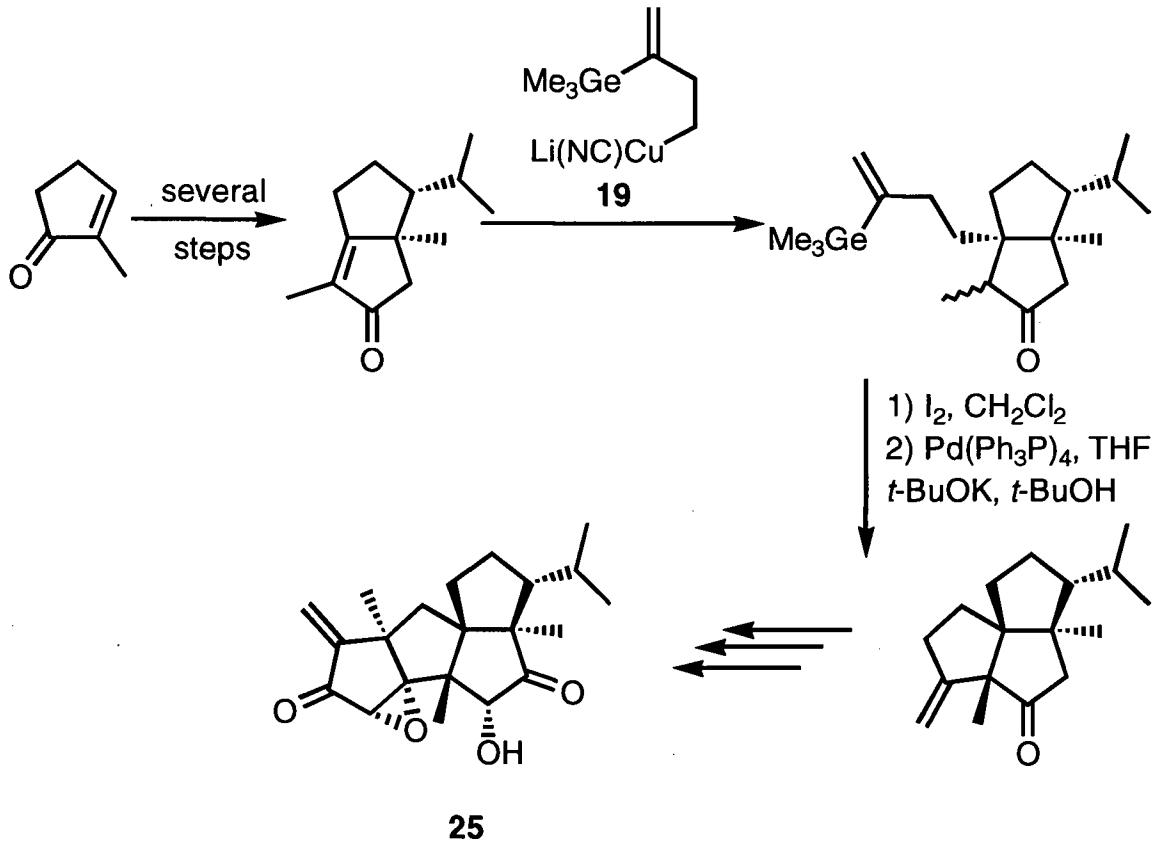
trimethylgermane to produce 4-chloro-2-trimethylgermylbut-1-ene (**17**). Following this, the chloride **17** was allowed to react with sodium iodide in acetone to yield the iodide **18**. Metal–halogen exchange performed on the iodide **18** using a solution of *tert*-butyllithium (2 equiv) at –95 °C, followed by treatment of the resultant lithio reagent with one equivalent of copper(I) cyanide, resulted in the formation of the cuprate reagent **19**. The successful preparation of **19** allowed the formation of adduct **20** from conjugate addition of **19** to the enone **10**. Straightforward iododegermylation[32] of **20** under standard conditions led to **21**. This keto iodide was treated with a solution of *n*-butyllithium (2 equiv) at low temperature to chemoselectively effect a facile lithium–halogen exchange reaction. The resultant vinyllithium intermediate underwent a ring-closure reaction to provide the alcohol **8**. Having this key intermediate in hand, the synthesis of (±)-ambliol B (**7**)[23] could be completed.



Scheme 7

Following the successful preparation of reagent **19** a related, complementary use of this reagent was developed in our laboratories. In the synthetic sequence depicted in **Scheme**

7, the reagent **18** serves as the synthetic equivalent to the but-1-ene a^2,d^4-synthon **22** and possesses umpolung[26] reactivity when compared to that of synthon **11**. Conjugate addition of **19** (prepared from **18**, *vide supra*) to a substituted cyclic enone resulted in the formation of adduct **23**. Iododegermylation of **23** under standard conditions, followed by treatment of the resulting vinyl iodide with a catalytic amount of $Pd(Ph_3P)_4$ in the presence of *t*-BuOK and *t*-BuOH generated the bicyclic ring system **24**. Thus, this annulation method exhibits a regio-selectivity that is opposite to that of the method outlined in **Scheme 1**.

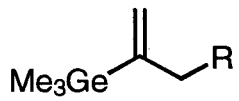


Scheme 8

The general applicability of this method was shown by the preparation of a number of bicyclic[33,34] and tricyclic[34] ring systems. Moreover, the usefulness of this method in organic

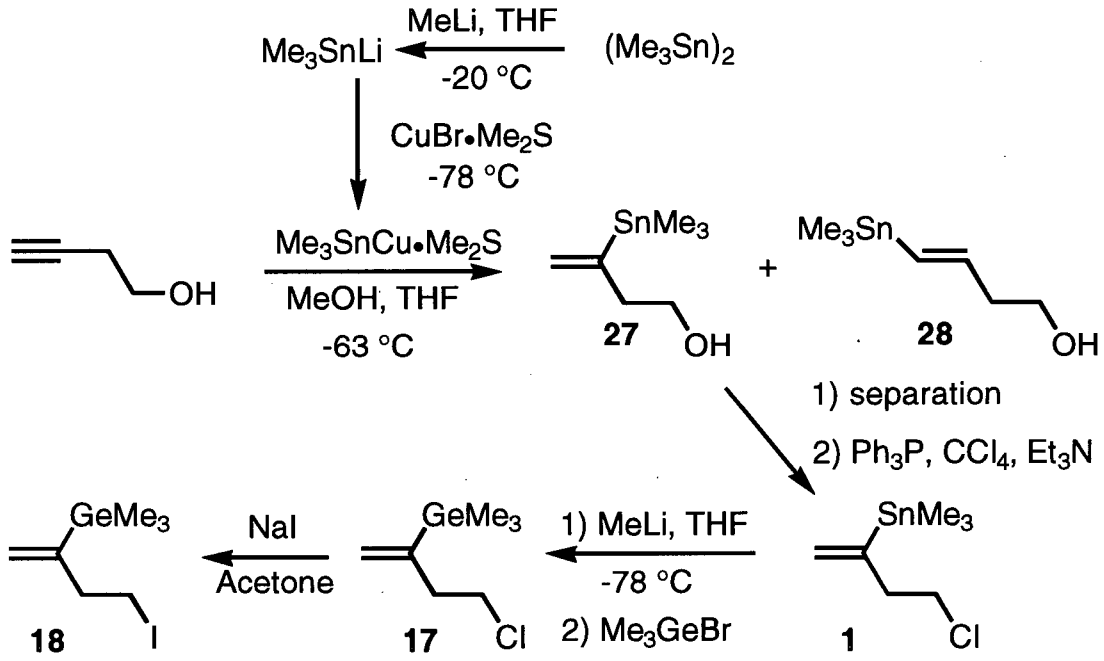
synthesis was demonstrated when this 5-membered ring annulation, using the reagent **19**, played a key role in the total synthesis of (±)-crinipellin B (**25**) (**Scheme 8**).[24]

Following the discovery by Marais[23,29,33] that 4-iodo-2-trimethylgermylbut-1-ene (**18**) i) *can* undergo controlled metal–halogen exchange to produce 4-lithio-2-trimethylgermylbut-1-ene and ii) serves as an excellent synthetic equivalent to the but-1-ene d^2,d^4- and a^2,d^4-synthons **11** and **22** respectively, it became of interest to consider the possibility of preparing a wide variety of diversely functionalized 2-trimethylgermylalk-1-ene bifunctional reagents of general structure **26**. Such substances should prove very useful in organic synthesis.



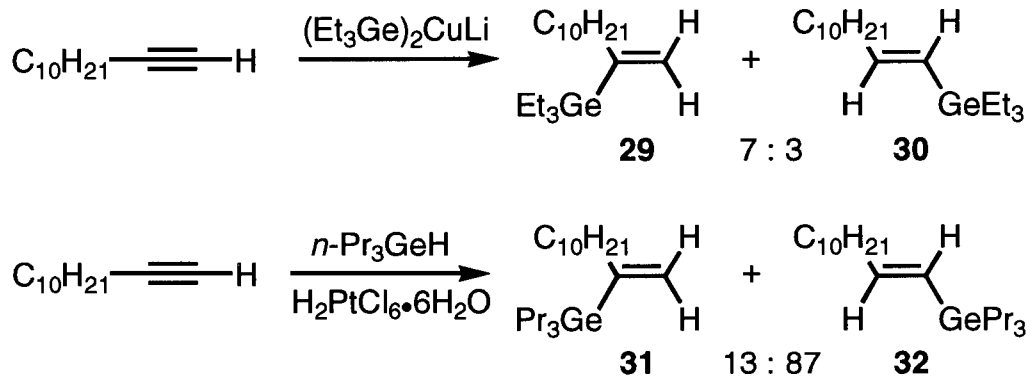
26

The synthetic sequence initially used to prepare the bifunctional reagent **18** from but-3-yn-1-ol proceeds in satisfactory yield (**Scheme 9**). However, this synthesis suffers from i) a tedious separation of the regioisomers **27** and **28** formed during the trimethylstannyl-cupration[25] of but-3-yn-1-ol and ii) requires the use of two expensive reagents, namely hexamethylditin and bromotrimethylgermane. To overcome these problems, it would be advantageous to prepare compounds of general structure **26** from an alternative precursor such that the intermediacy of the vinylstannane would be avoided.



Scheme 9

Examination of the literature revealed that a number of reports have appeared over the last three decades on the preparation of vinylgermanes. Although a certain number of these described the preparation of 2-trialkylgermylalk-1-enes, the latter are usually isolated as an inseparable mixture with the corresponding 1-trialkylgermylalk-1-enes. The following results reported by Oshima and co-workers[32,35] illustrate well the difficulty (**Scheme 10**). Germyl-cupration[35] of dodec-1-yne afforded, after workup, a 7:3 mixture of the regioisomeric adducts **29** and **30** in 81% yield. Alternatively, when dodec-1-yne was treated with *n*-Pr_3GeH in the presence of a catalytic amount of $H_2PtCl_6 \cdot 6H_2O$, a 13:87 mixture of the regioisomers **31** and **32** was formed in 93% yield.[32]

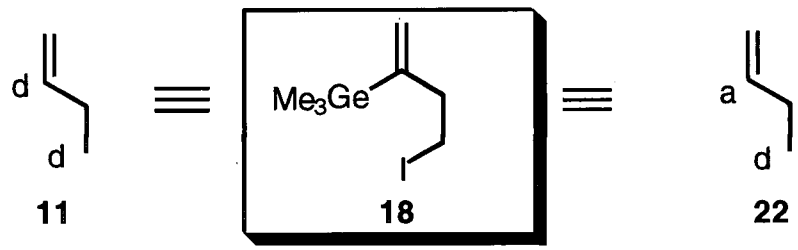


Scheme 10

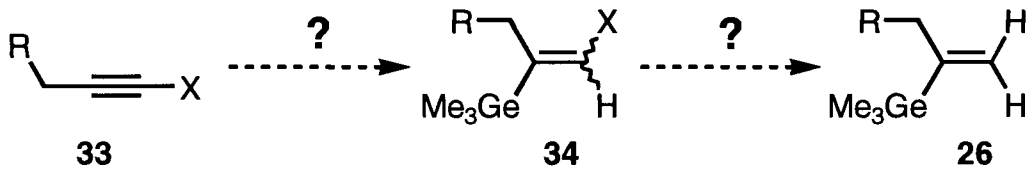
Obviously, it would be advantageous, in the context of using 2-trialkylgermylalk-1-enes in synthesis, to have access to a method that would produce these substances in regio-isomerically pure form. Based on the above precedents, it was felt that the preparation of such compounds from terminal alkynes would be troublesome. In the next pages, proposals to prepare regioisomerically pure 2-trimethylgermylalk-1-enes from 1-trimethylsilylalk-1-ynes will be outlined.

1.3 PROPOSALS

The successful preparation *and* use of the vinylgermane iodide **18** as a synthetic equivalent to the but-1-ene d^2,d^4- and a^2,d^4-synthons **11** and **22**, respectively, prompted us to investigate the development of general synthetic methods for the synthesis of functionalized 2-



trimethylgermylalk-1-enes. Because of the lack of regioselectivity displayed by reactions in which terminal alkynes were converted directly into 2-trialkylgermylalk-1-enes (see previous section), the possibility of using substituted alkynes of general structure **33** to prepare the desired trimethylgermyl compounds **26** became appealing (**Equation 1**). What reaction would be employed to add the elements of Me_3GeH across the carbon–carbon triple bond? Would the use of a substituent **X** be sufficient to effect complete regiocontrol in the addition process? If so, what would the nature of **X** need to be? What functional groups in **R** would be compatible with this transformation?

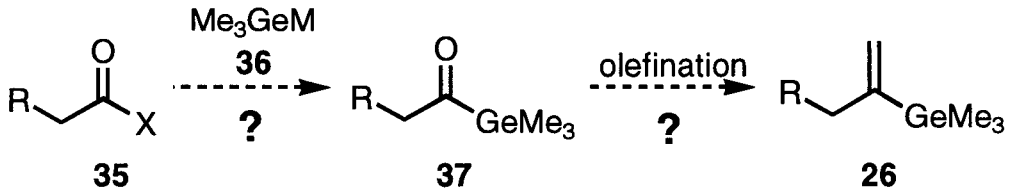


(1)

If the first step of this sequence proved to be successful, the second aspect of the overall transformation remained to be examined. Could the **X** group in **34** be replaced by a hydrogen atom (**Equation 1**) in the presence of the newly introduced trimethylgermyl group?

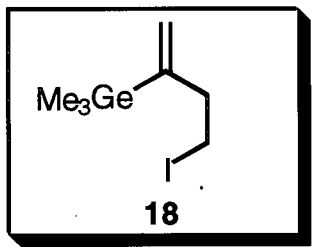
Since functionalization of the **R** group was imperative, what other functional groups would be compatible with this substitution?

An alternative approach to the synthesis of 2-trimethylgermylalk-1-enes was also envisaged. This method, due to the intrinsic nature of the transformations involved, would preclude the formation of regioisomers. Thus, it was postulated that nucleophilic acyl substitution involving reaction of substrates of general structure **35** with a suitable metallo-(trimethylgermane) reagent **36** would generate the corresponding trimethylgermyl ketones **37**. The latter compounds could then be olefinated to generate substances **26** (**Equation 2**). In order for this sequence to be viable, the rate of reaction of reagent **36** with **35** would have to be considerably faster than that of reaction of **36** with **37**. What, then, would the requirements be on the nature of **X**? Could a (trimethylgermyl)copper(I) derivative (**36**, M = Cu) be used to affect such a transformation? Once again, what functional groups in **R** would be compatible with such a transformation? Is the olefination of **37** possible?



(2)

As seen in the previous section (**Scheme 10**), (triethylgermyl)cuprates are known reagents. In contrast, (trimethylgermyl)copper(I) reagents had not been reported prior to the work described in this thesis. If (trimethylgermyl)copper(I) reagents could be prepared, what other synthetic applications would these reagents have?



18

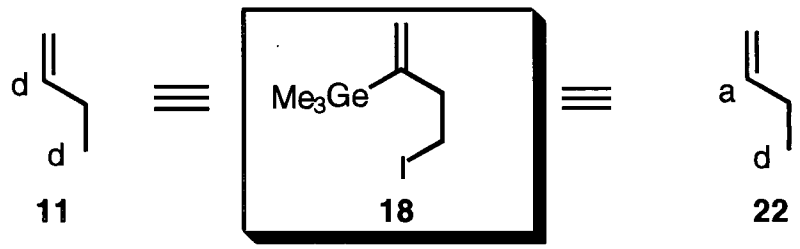
The utilization of the vinylgermane iodide **18** in the syntheses of (±)-ambliol B (**7**)[23] and (±)-crinipellin B (**25**),[24] and the possibility of employing **18** and structurally related substances in synthesis were important motivations for the development of methods for the preparation of other functionalized, regioisomerically pure 2-trimethylgermylalk-1-enes. This thesis is divided into three parts and describes the results of research related to the proposed investigations outlined above. The first part describes the preparation of 2-trimethylgermyl-alk-1-enes from 1-trimethylsilylalk-1-ynes in two experimentally simple steps: platinum catalyzed hydrogermylation of the 1-trimethylsilylalk-1-ynes followed by *p*-toluenesulfonic acid mediated protiodesilylation to afford the 2-trimethylgermylalk-1-enes. The second part details the preparation of acyltrimethylgermanes from the corresponding acyl chlorides using the novel (trimethylgermyl)copper(I)–dimethyl sulfide reagent. The olefination of selected acyltrimethylgermanes into the corresponding 2-trimethylgermylalk-1-enes will also be described. Finally, the third part delineates the preparation of new (trimethylgermyl)cuprate reagents and describes their reaction with selected unsaturated carbonyl systems.

2 DISCUSSION

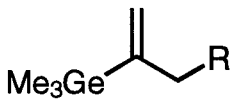
2.1 SYNTHESIS OF 2-TRIMETHYLGERMYLALK-1-ENES VIA PLATINUM CATALYZED HYDROGERMYLATION OF 1-TRIMETHYLSILYLALK-1-YNES

2.1.1 INTRODUCTORY REMARKS

Recent reports[23,24,29,33,34] from our laboratories have shown the vinylgermane iodide **18** to be a good synthetic equivalent to the but-1-ene d^2,d^4- and a^2,d^4-synthons **11** and **22**, respectively. The usefulness of reagent **18** was demonstrated through the development of two new annulation methods (see Introduction section, **Scheme 6**, p 7 and **Scheme 7**, p 9).



The utilization of the vinylgermane iodide **18** in the syntheses of (±)-ambliol B (**7**)[23] (see **Scheme 6**, p 7) and (±)-crinipellin B (**25**)[24] (see **Scheme 8**, p 9) as well as the possibility of using structurally related substances in synthesis, prompted an investigation into the development of a method that would allow the preparation of regioisomerically pure 2-trimethylgermylalk-1-enes of general structure **26**.

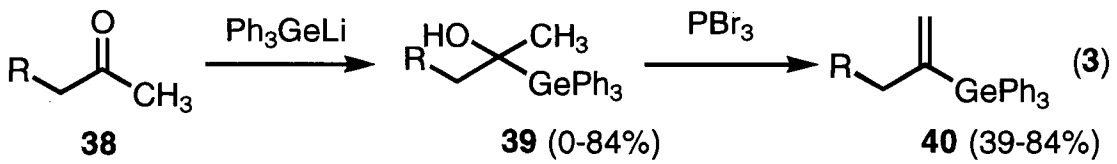


26

A survey of the literature revealed that a number of methods for the preparation of 2-

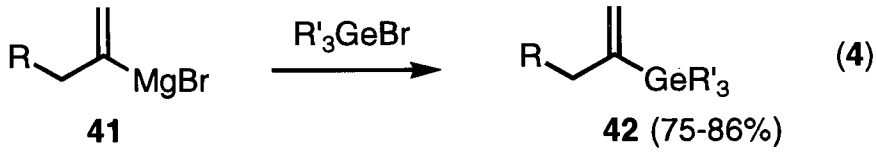
trialkylgermylalk-1-enes and 2-triphenylgermylalk-1-enes have been reported. These methods employ, collectively, four different classes of substrates to achieve the preparation of the 2-trialkylgermylalk-1-enes and 2-triphenylgermylalk-1-enes. A brief description of these methods is presented in the following pages.

Nicholson and Allred[36] reported the preparation of 2-triphenylgermylalk-1-enes in a two step sequence from alkan-2-ones (**Equation 3**). In this protocol, triphenylgermyllithium was allowed to react with an alkan-2-one **38** to give the corresponding alcohol **39**. This alcohol was then treated with phosphorous tribromide to afford the 2-triphenylgermylalk-1-ene **40**. The overall yield for these two transformations varies from poor to moderate. The applicability of this method for the preparation of functionalized 2-triphenylgermylalk-1-enes is greatly limited by the fact that a powerful nucleophile, triphenylgermyllithium, is required in the first step. Moreover, the conditions used for the dehydration (PBr_3, benzene, reflux 16 h) also limits the number of functional groups that are compatible with the overall method.



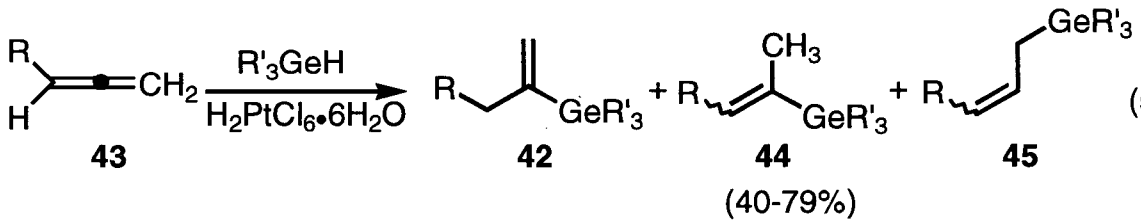
(3)

A different approach to the preparation of 2-trialkylgermylalk-1-enes was used by Manulkin and co-workers.[37,38] In this synthetic transformation (**Equation 4**), a vinyl Grignard reagent **41** is treated with a suitable trialkylgermanium bromide reagent to give the 2-trialkyl-germylalk-1-ene **42**. Although the yield for this transformation is good and the formation of regioisomers is precluded, the general applicability of this method is limited by the availability of the regioisomerically pure 2-bromoalk-1-enes, precursors to the Grignard reagents **41**.



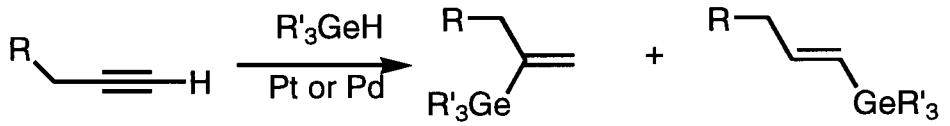
(4)

2-Trialkylgermylalk-1-enes were also prepared from allenes (**Equation 5**).[39,40] In this chemical transformation, $H_2PtCl_6 \bullet 6H_2O$ catalyzed addition of a trialkylgermane to an allene **43** resulted in the formation of the desired 2-trialkylgermylalk-1-ene **42**. However, the vinylgermane **44** and the allylgermane **45** were also produced. In fact, the three adducts were obtained as a mixture in an almost equimolar amounts (40–79% combined yield). Therefore, the low selectivity displayed by this reaction would not allow the preparation of regioisomerically pure 2-trialkylgermylalk-1-enes.



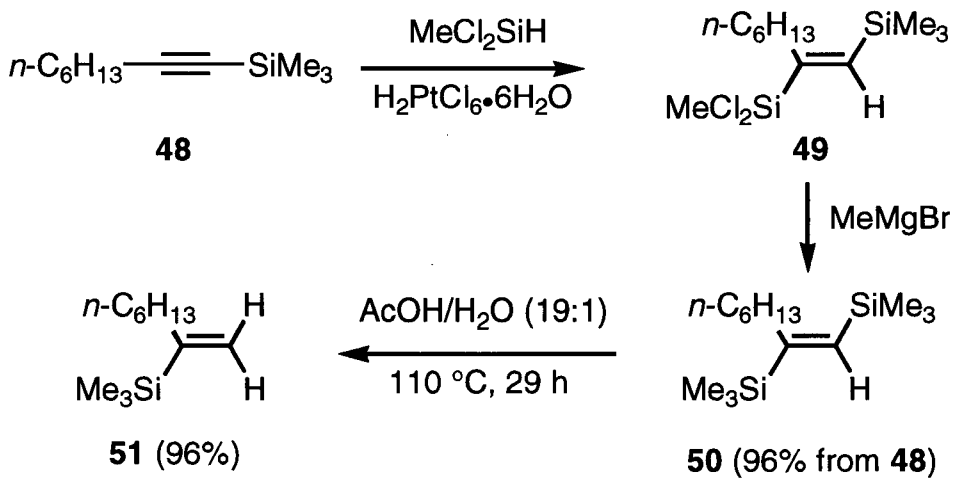
(5)

Terminal alkynes are a fourth class of substrates that have been used to prepare 2-trialkylgermylalk-1-enes. As presented in the Introduction section (**Scheme 10**, p 12), germylcupration of a terminal alkyne has been reported by Oshima and co-workers[35] to result in the formation of regioisomeric adducts. Similarly, platinum[32,41] or palladium[42] catalyzed addition of a trialkylgermane to a terminal alkyne **46** (**Equation 6**) resulted in the formation of a mixture of the regioisomers **42** and **47** (35–97% combined yield), in which isomer **47** had been predominantly formed.



46 **42** (35-97%) **47** (6)

In light of the literature surveyed, it appears that the methods reported i) have a limited scope and lack generality in the preparation of functionalized 2-trialkylgermylalk-1-enes *or* ii) yield regioisomeric mixtures of 1- and 2-trialkylgermylalk-1-enes. As outlined in the Proposals (section 1.3, p 13 ff.), the possibility of effecting regiocontrolled addition of the elements of Me_3GeH to 1-substituted alk-1-ynes became an appealing alternative. Support for the possibility of this type of transformation was found in a related reaction reported by Hudrlik and co-workers[43] (**Scheme 11**).

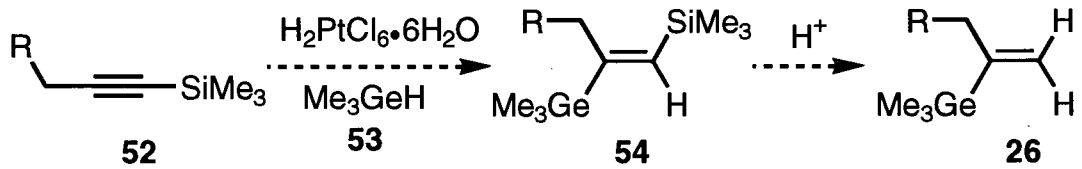


48 **49** **51** (96%) **50** (96% from **48**)

Scheme 11

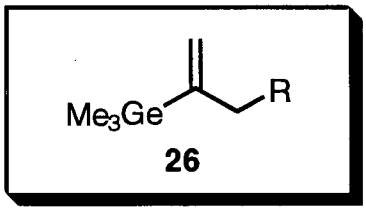
Thus, treatment of 1-trimethylsilyloct-1-yne (**48**) with methyldichlorosilane (**Scheme 11**) in the presence of a catalytic amount of $H_2PtCl_6{\bullet}6H_2O$, in the absence of solvent (neat), resulted in the formation of adduct **49**. Treatment of **49** with methylmagnesium bromide afforded (*E*)-1,2-bis(trimethylsilyl)oct-1-ene (**50**) in 96% yield. The regioisomeric purity of

50 was shown to be ≥96% by GLC.[43] 2-Trimethylsilyloct-1-ene (**51**) was obtained in 96% yield by heating at reflux a solution of **50** in glacial acetic acid–water (19:1) for 29 h.



(7)

The synthetic sequence depicted above (**Scheme 11**) effects an overall transformation similar to that required for the preparation of the 2-trimethylgermylalk-1-enes. Since the 1-trimethylsilylalk-1-ynes are easily accessible from the corresponding alk-1-ynes in high yields,[3] it was of interest to determine whether or not the 1-trimethylsilylalk-1-ynes **52** (**Equation 7**) could be used as substrates for a regioselective hydrogermylation process. In other words, could trimethylgermane (**53**) be used instead of the methyldichlorosilane in this transformation? If so, this would render the method more versatile, since the utilization of the Grignard reagent would no longer be required. Would the high regioselectivity exhibited in the hydrosilylation be retained in the hydrogermylation leading to the formation of **54** (**Equation 7**)? If the (*E*)-2-trimethylgermyl-1-trimethylsilylalk-1-ene **54** could be prepared in a regioisomerically pure form, the removal of the trimethylsilyl group from **54** would have to be addressed. Would it be possible to remove the trimethylsilyl group in the presence of the trimethylgermyl group?



The answer to these questions, as well as the details of the investigations leading to the

successful preparation of the regioisomerically pure 2-trimethylgermylalk-1-enes **26** from the 1-trimethylsilylalk-1-ynes **52** will be disclosed in sections 2.1.4 (p 26 ff.) and 2.1.5 (p 65 ff.) of this thesis.

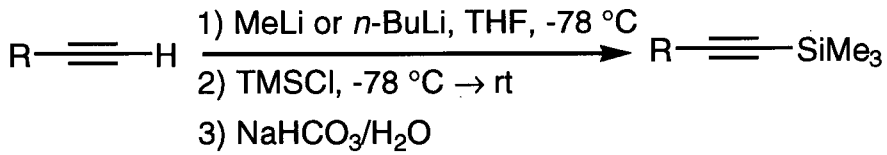
2.1.2 SYNTHESIS OF 1-TRIMETHYLSILYLALK-1-YNES

In order to prepare the 1-trimethylsilylalk-1-ynes required for this study, the commercially available alk-1-ynes **55–60** shown in **Table 1** were chosen as substrates. **Table 1** also contains a summary of the conversions of **55–60** into the 1-trimethylsilylalk-1-ynes **61–67**.

The 1-trimethylsilylalk-1-ynes were prepared in high yield in a straightforward way. The synthesis of 1-trimethylsilyl-6-(trimethylsilyloxy)hex-1-yne (**61**) (**Table 1**, entry 1) for example, was accomplished in the following manner. A solution of hex-5-yn-1-ol (**55**) in etheral solvent at low temperature (–78 °C) was treated with a solution of methyllithium followed by addition of chlorotrimethylsilane, and the reaction mixture was warmed to room temperature. After isolation and purification of the crude product, the compound **61** was obtained in 96% yield as a clear colorless oil. Confirmation of the assigned structure was obtained from the ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **61**, which exhibited two nine-proton singlets at δ 0.12 and 0.09, characteristic of Me_3Si- functions. Additional evidence was provided by the IR spectrum which exhibited an intense band at 2176 cm^{-1}, diagnostic of Me_3Si- substituted alkynes, as well as a lack of a broad absorption in the 3200–3600 cm^{-1} (-OH) region.

The 1-trimethylsilylalk-1-ynes **63–67** were synthesized from the corresponding alk-1-ynes **56–60** in a manner identical with that outlined above. The 1-trimethylsilylalk-1-yne **62** was obtained by treatment of **61** with aqueous hydrochloric acid during the workup of the reaction sequence described above.

Table 1: Preparation of the 1-Trimethylsilylalk-1-ynes **61–67**

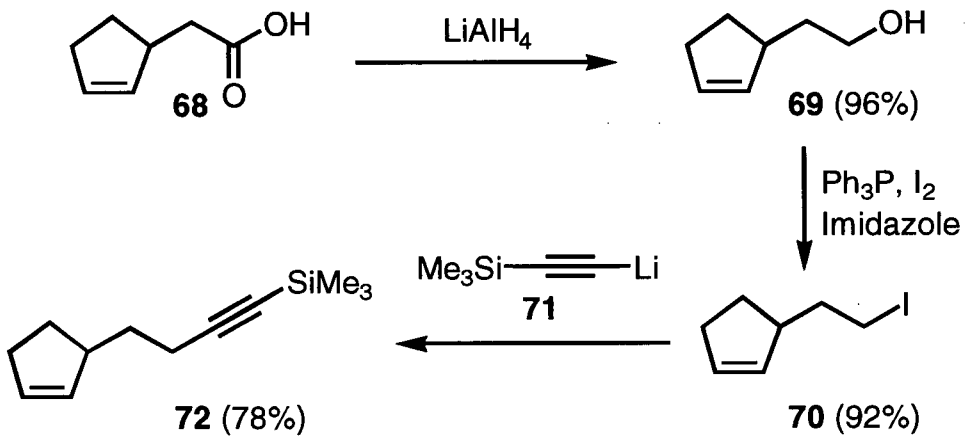


Entry	Alk-1-yne	1-Trimethylsilylalk-1-yne	Yield (%)[a]
1	HO **55**	Me_3SiO **61** $SiMe_3$	96
2[b]	HO **55**	HO **62** $SiMe_3$	82
3	HO **56**	Me_3SiO **63** $SiMe_3$	96
4	n-$C_{10}H_{21}$—≡ **57**	n-$C_{10}H_{21}$—≡—$SiMe_3$ **64**	98
5	Cl **58**	Cl **65** $SiMe_3$	91
6	**59**	**66** $SiMe_3$	96
7	**60**	Me_3Si **67** $SiMe_3$	71

[a] Yield of isolated and purified product. [b] For the workup, 1 N aqueous HCl was used instead of saturated aqueous $NaHCO_3$.

The synthesis of 4-(cyclopent-2-en-1-yl)-1-trimethylsilylbut-1-yne (**72**) was effected via a three step sequence from (cyclopent-2-en-1-yl)acetic acid (**68**) (**Scheme 12**). Thus, lithium aluminum hydride reduction of **68** afforded the corresponding alcohol **69** in 96% yield. This alcohol was treated with triphenylphosphine–iodine complex[44] in the presence of

imidazole to yield the primary iodide **70** in 92% yield. Finally, the iodide **70** was allowed to react with lithium trimethylsilylacetylide (**71**) (prepared by treatment of trimethylsilylacetylene



Scheme 12

with *n*-butyllithium) in the presence of HMPA. Isolation and purification of the resultant product afforded 4-(cyclopent-2-en-1-yl)-1-trimethylsilylbut-1-yne (**72**) in 78% yield (69% overall from **68**) as a clear colorless oil.

2.1.3 SYNTHESIS OF TRIMETHYLGERMANE (53)

$$Me_3GeBr \xrightarrow[Bu_2O]{LiAlH_4} \underset{\mathbf{53}}{Me_3GeH} \qquad (8)$$

Trimethylgermane (**53**) was prepared using a procedure reported by Coates and Tedder,[45] with a minor modification. In the original procedure,[45] a solution of trimethylgermanium bromide in dry dibutyl ether was added to a slurry of lithium aluminum hydride in the same solvent (**Equation 8**). The heterogeneous mixture was then heated to 75 °C and the volatile liquid (bp 26 °C) was distilled directly from the reaction mixture into a cold (–78 °C) receiving flask. This procedure afforded trimethylgermane (**53**) in 75% yield.

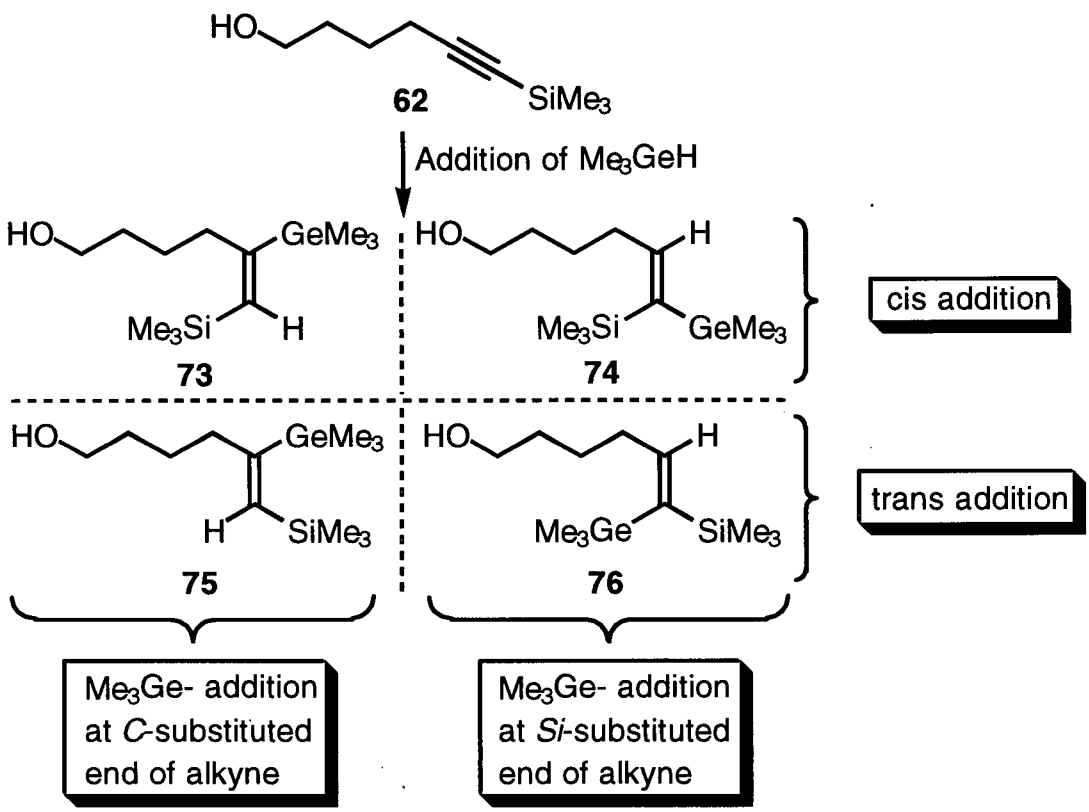
Since trimethylgermanium bromide required for this reaction is a fairly expensive reagent (≈$5 per gram), it appeared worthwhile to try to improve the yield of this conversion. After some investigation, it was found that raising the distillation temperature to 110 °C resulted in a significantly improved yield. Moreover, the time required to complete the distillation at 110 °C was 3 h as compared to 6–8 h at 75 °C. Examination of the ^{1}H NMR spectrum of the acquired liquid revealed the presence of a small amount (5–10%) of dibutyl ether. Distillation of this material (bulb-to-bulb) from –78 °C to 40 °C (directly from the initial receiving flask) afforded essentially pure trimethylgermane (**53**) in 95% yield. This reaction can be easily carried out on a 20–30 g scale of trimethylgermanium bromide with reproducible yields.

2.1.4 ISOLATION OF THE PRODUCTS OF HYDROGERMYLATION OF 6-TRIMETHYLSILYLHEX-5-YN-1-OL (62) AND THEIR TREATMENT WITH *p*-TOLUENESULFONIC ACID MONOHYDRATE IN DICHLOROMETHANE

2.1.4.1 HYDROGERMYLATION OF 6-TRIMETHYLSILYLHEX-5-YN-1-OL (**62**)

6-Trimethylsilylhex-5-yn-1-ol (**62**) was chosen as the initial substrate for the investigation of the hydrogermylation reaction, since it could be readily prepared from the commercially available hex-5-yn-1-ol (**55**). This compound also has a moderately high boiling point which would facilitate, in the event, the recovery of any unreacted starting material.

From the chemical transformation involved in the hydrogermylation of **62**, it is possible to form four isomers as a result of adding the elements of Me_3GeH (**53**) across the alkyne function of **62** (**Scheme 13**). The isomers **73** and **74** arise due to cis addition of Me_3GeH (**53**) to the carbon–carbon triple bond of **62**. Alternatively, the isomers **75** and **76** are the consequence of trans addition of the elements of Me_3GeH (**53**) across the alkyne function of **62**. The regiochemistry of the addition of Me_3GeH (**53**) can proceed in two different orientations. The trimethylgermyl group can add to the *C*-substituted end of the alkyne, yielding the isomers **73** and **75**. On the other hand, the trimethylgermyl group can add to the *Si*-substituted end of the triple bond, thus generating isomers the **74** and **76**.

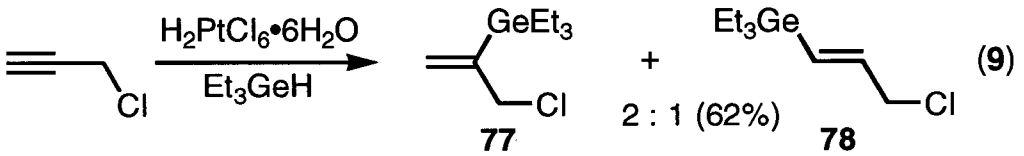


Scheme 13

Since the objective of this investigation was to develop a method that would ultimately provide 2-trimethylgermylalk-1-enes after removal of the trimethylsilyl group, generation of the isomers **73** and/or **75** from the hydrogermylation of **62** was desired. The regiochemistry of the addition of Me_3GeH (**53**) to the alkyne function of **62** should be relatively straight-forward to establish via ^1H NMR spectroscopic analysis. The ^1H NMR spectra of **73** and **75** should contain a singlet (or a triplet with J = 1–2 Hz) for the vinylic proton. On the other hand, the spectra of **74** and **76** should exhibit a triplet, with a vicinal coupling constant of 5–10 Hz, for the corresponding signal.

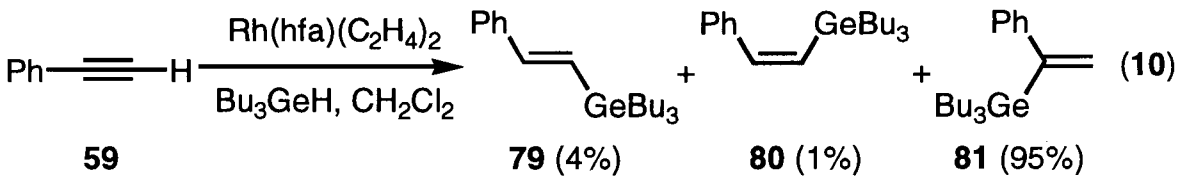
Experimentally, hydrogermylations of various types of substrates, with trialkyl-

germanes, have been carried out with $H_2PtCl_6 \cdot 6H_2O$ in the absence of solvent.[32,39-41] These procedures usually result in a vigorous exothermic reaction, accompanied by a significant increase in the temperature of the reaction mixture.



(9)

For example, when a mixture of propargyl chloride and triethylgermane (neat) was treated with a catalytic amount of $H_2PtCl_6 \cdot 6H_2O$, a vigorous exothermic reaction occurred to generate the adducts **77** and **78** (**Equation 9**).[41] Alternatively, hydrogermylations of alkynes with tributylgermane and a catalytic amount of $H_2PtCl_6 \cdot 6H_2O$ have also been carried out in 1,2-dichloroethane.[46] In a similar transformation, but using a $Rh(hfa)(C_2H_4)_2$ as catalyst, the hydrogermylation of phenylacetylene (**59**) with tributylgermane has been performed in dichloromethane to afford a mixture of adducts **79–81** (**Equation 10**).[47]



(10)

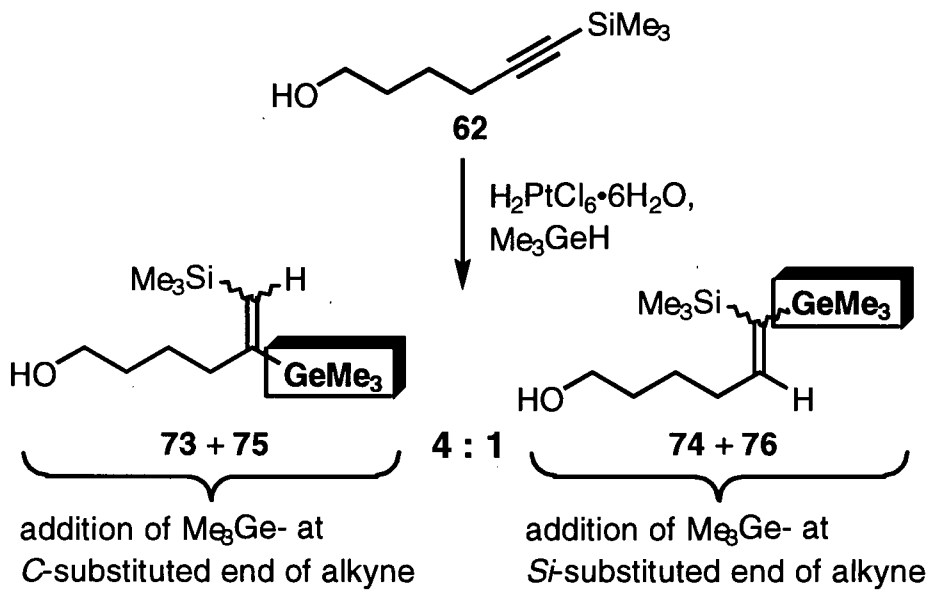
Since trimethylgermane (**53**) is a very volatile liquid (bp 26 °C), performing the hydrogermylation in the absence of solvent would not be suitable, since it is likely that due to the (expected) exothermic reaction, the volatile trimethylgermane (**53**) would be lost. $H_2PtCl_6 \cdot 6H_2O$ was selected to effect the proposed transformation since it is commercially available and is known to be an effective catalyst for these reactions. It was also decided to perform the reaction in dichloromethane solution to prevent significant temperature increase.

Speier[48] has investigated in detail the nature of the catalyst involved in the

homogeneous catalysis of hydrosilylation by $H_2PtCl_6 \cdot 6H_2O$. Although no direct proof of the structure of the soluble complex was obtained, many observations suggest that it is likely to be a Pt(0) species. For example, the reduction of $H_2PtCl_6 \cdot 6H_2O$ with Me_3GeH (**53**) to a Pt(0) species probably occurs as depicted in **Equation 11**.

$$H_2PtCl_6 \cdot 6H_2O + 18Me_3GeH \rightarrow Pt(0) + 6Me_3GeCl + 6(Me_3Ge)_2O + 16H_2 \qquad \textbf{(11)}$$

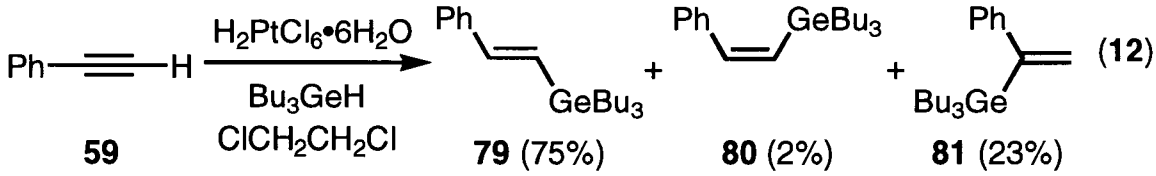
Initial investigations were performed using substrate **62** in dichloromethane and focused on finding experimental conditions that would allow the conversion of the starting material to product within a reasonable length of time. Thus, hydrogermylations of **62** were performed in the presence of approximately two equivalents of Me_3GeH (**53**) with 1–2% of $H_2PtCl_6 \cdot 6H_2O$ at 0 and –10 °C initially, in order to minimize the loss of Me_3GeH (**53**) through evaporation. GLC and TLC analyses of the reaction mixtures revealed that the conversion of the starting material to product was proceeding very slowly.



Scheme 14

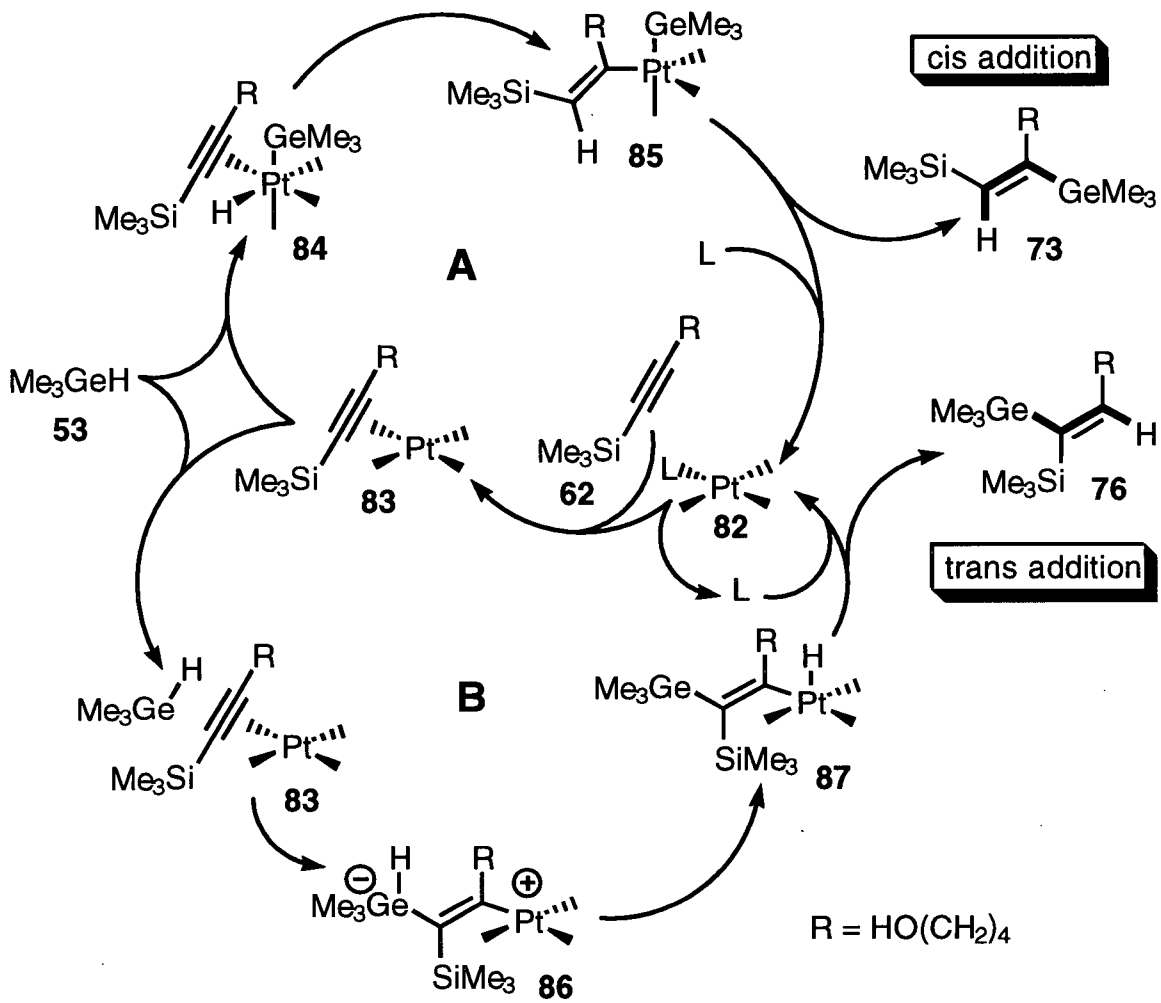
In a separate experiment, two equivalents of Me_3GeH (**53**) were added to a cold (0 °C) solution of **62** (1 equiv) and ≈1 mol% of $H_2PtCl_6 \bullet 6H_2O$ and the resultant mixture was allowed to stir at room temperature for 15 h (**Scheme 14**). GLC analysis of the crude reaction mixture indicated that the starting material had been completely consumed; this analysis also revealed the presence of several products. The two major products constituted approximately 75% and 19% of the mixture, whereas the minor components accounted for the balance of the material at 1–2% each. Preliminary ^{1}H NMR spectroscopic analysis of this crude mixture revealed that the region of δ 6.5–5.5 contained four distinct signals. These signals were as follows: a triplet at δ 5.7, a singlet at δ 5.8, a singlet at δ 6.2 and finally a triplet at δ ≈6.4. The singlet at δ 5.8 and triplet at δ 5.7 were present in a ratio of approximately 4:1, whereas the other two signals at δ 6.2 and 6.4 were present in approximately equal, very small amounts.

Thus, the hydrogermylation of **62** appeared to have generated an approximately 4:1 mixture of regioisomers. The addition of the Me_3Ge- group occurred primarily at the *C*-substituted end of the alkyne function of **62** (**Scheme 14**). The poor regioselectivity exhibited by this reaction was disappointing. The platinum catalyzed addition of Me_3GeH (**53**) to the carbon–carbon triple bond of **62** did not display the high regioselectivity obtained in an analogous reaction, as reported by Hudrlik and co-workers (see **Scheme 11**, p 19).[43]



A mechanism for the hydrogermylation of phenylacetylene (**59**) catalyzed by

$H_2PtCl_6 \cdot 6H_2O$ has been proposed by Corriu and Moreau.[46] This mechanism is based on the observations made by Chalk and Harrod[49-51] on the homogeneous catalysis with group VIII metal complexes. Corriu and Moreau[46] have shown that *n*-Bu_3GeH adds to phenylacetylene (**59**) in 1,2-dichloroethane solution at room temperature in the presence of a catalytic amount of $H_2PtCl_6 \cdot 6H_2O$ to generate three products (**Equation 12**). The major product (75%) obtained from this reaction, **79**, resulted from cis addition of the *n*-Bu_3GeH, with the Bu_3Ge-group located on the terminal carbon of the alkene product. The second most abundant adduct was **81** (23%), whereas **80** was formed in 2% yield.[46] The formation of **80** is the result of a trans addition of the elements of *n*-Bu_3GeH across the alkyne function of **59**, while **81** can be produced from one or both of cis and trans modes of addition of *n*-Bu_3GeH. Although it could be argued that the formation of **80** might arise from a trans to cis isomerization subsequent to the generation of **79**, Corriu and Moreau[46] have shown that this process is slow compared to the rate of addition of *n*-Bu_3GeH to **59** under comparable experimental conditions.



Scheme 15

Scheme 15 depicts a reaction pathway that rationalizes the formation of the adducts **73–76** from the catalyzed hydrogermylation of the 1-trimethylsilylalk-1-yne **62**. This reaction scheme is based entirely on the proposals of Corriu and Moreau.[46] Cycle **A** depicts the cis addition of trimethylgermane (**53**) to the 1-trimethylsilylalk-1-yne **62**, whereas path **B** accounts for the formation of the adducts resulting from a trans addition of Me_3GeH (**53**) to the substrate.

The catalytic cycle **A** proceeds as follows: the active form of the Pt catalyst, **82**,

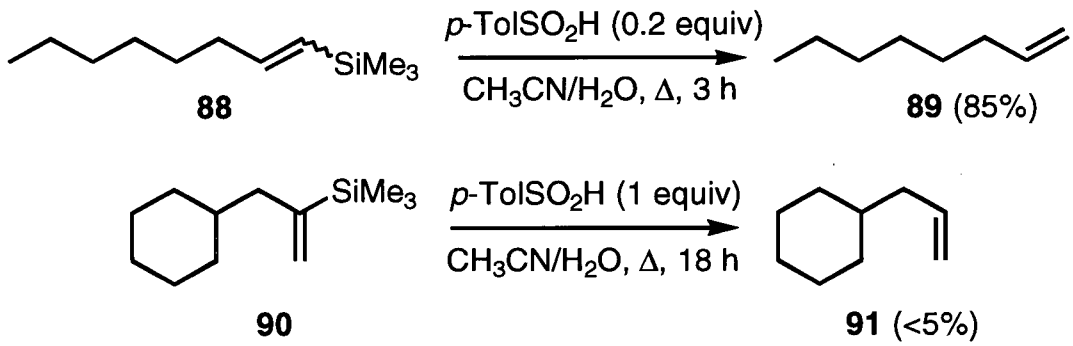
coordinates to the 1-trimethylsilylalk-1-yne **62** to generate the complex **83**. Oxidative addition of trimethylgermane (**53**) to this complex results in the formation of the hexa-coordinated complex **84**. Intramolecular hydrogen transfer to the carbon–carbon triple bond generates the vinyl platinate **85**, which then undergoes reductive elimination to the (*E*)-2-trimethylgermyl-1-trimethylsilylalk-1-ene **73**, simultaneously regenerating the catalytic species **82**. Alternatively, migration of the trimethylgermyl group from **84** onto the *C*-substituted end of the alkyne function, followed by reductive elimination, leads to the same adduct.

The first step of the catalytic cycle **B** also involves coordination of **62** to the active form of the catalyst **82**, generating the complex **83**. However, in this case, the trimethylgermane (**53**) reacts intermolecularly with complex **83** to form the vinyl platinate **86**. Hydride transfer from germanium to platinum generates **87**, which subsequently undergoes reductive elimination to form the (*Z*)-1-trimethylgermyl-1-trimethylsilylalk-1-ene **76** and regenerates the catalytic species **82**.

TLC analyses of the crude mixture of the newly formed adducts **73–76** (see **Scheme 14**, p 29) indicated that the products could not be separated by conventional flash chromatography on silica gel. Therefore, protiodesilylation of the crude mixture was attempted.

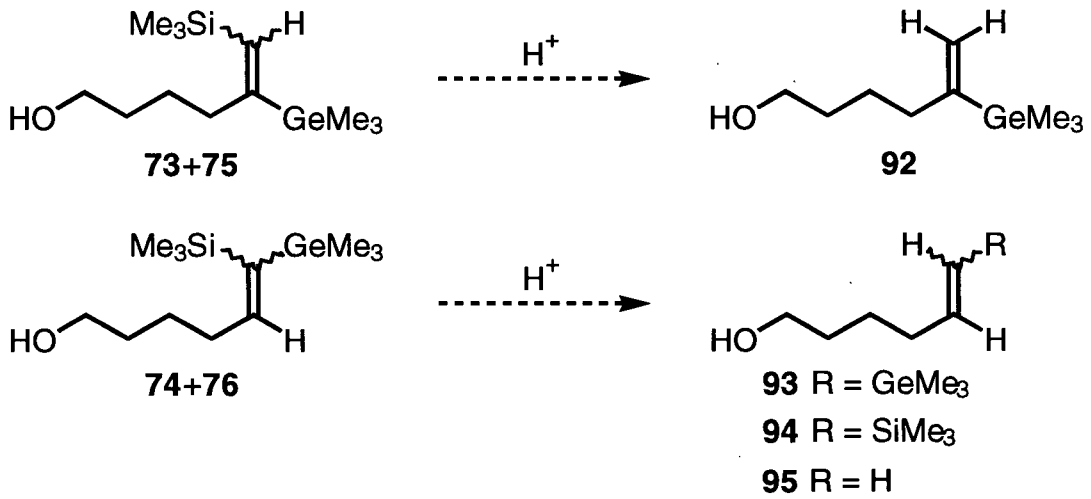
Büchi and Wüest[52] have shown the dramatic difference in the rate of protiodesilylation between the (*E*/*Z*)-1-trimethylsilylalk-1-ene **88** and the 2-trimethylsilylalk-1-ene **90** (**Scheme 16**). When (*E*/*Z*)-1-trimethylsilyloct-1-ene (**88**) was allowed to react with 0.2 equivalent of *p*-toluenesulfinic acid in wet acetonitrile heated at reflux for 3 h, the oct-1-ene (**89**) was formed in 85% yield.[52] Alternatively, treatment of vinylsilane **90** with one equivalent of *p*-toluene-

sulfinic acid in wet acetonitrile heated at reflux generated less than 5% of the alkene **91** after 18 h.[52] The remainder of the vinylsilane **90** was recovered unchanged. Consistent with these findings, Hudrlik and co-workers[43] found that (*E*)-1,2-bis(trimethylsilyl)oct-1-ene (**50**) underwent protiodesilylation to yield 2-trimethylsilyloct-1-ene (**51**) (see **Scheme 11**, p 19).



Scheme 16

Although the carbon–silicon bond strength is greater than the corresponding carbon–germanium bond strength (90 kcal·mol^{-1} for Me_4Si vs 76 kcal·mol^{-1} for Me_4Ge,[31] it was expected that the difference in ease of protiodemetallation between 1-trialkylmetal- and 2-trialkylmetalalk-1-enes would be the dominant factor controlling the outcome of the acidic treatment of **73** and **75** (**Scheme 17**).



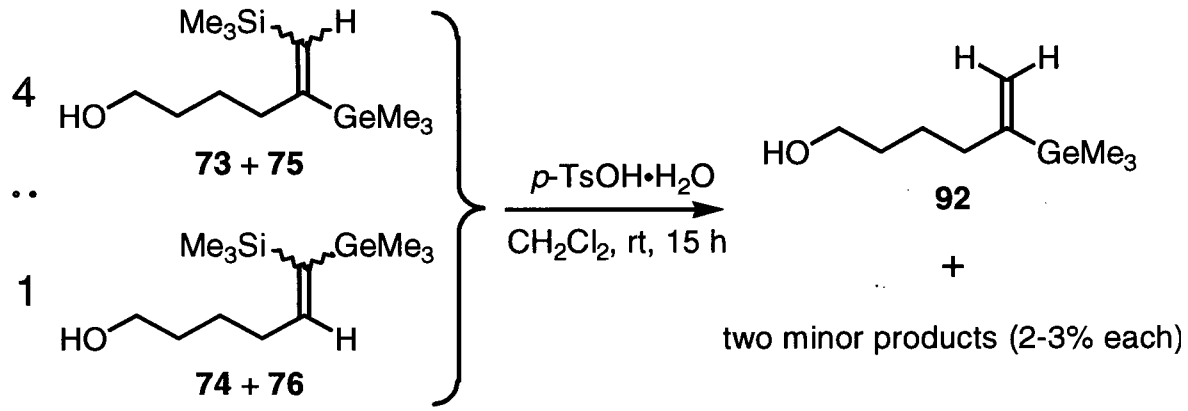
Scheme 17

Therefore, treatment of both **73** and **75** under acidic conditions was expected to generate 5-trimethylgermylhex-5-en-1-ol (**92**) (**Scheme 17**). On the other hand, the isomers **74** and **76** could potentially give three different types of products. Protiodesilylation of **74** and **76** would afford the vinylgermanes **93**. Alternatively, protiodegermylation of the same substrates would lead to the formation of the corresponding vinylsilanes **94**. Finally, both **93** and **94** could undergo further protiodemetallation to afford hex-5-en-1-ol (**95**).

Protiodesilylation of vinylsilanes has been carried out under a variety of acidic conditions.[6] Traditionally strong acids such as hydrochloric acid,[53,54] hydrobromic acid[53] or hydriodic acid[55] have been used, but other acid systems including *p*-toluenesulfinic acid in wet acetonitrile[52] heated at reflux and aqueous acetic acid[43] heated at reflux have also been employed to effect this type of process. Since the objective of this study was the preparation of functionalized 2-trimethylgermylalk-1-enes, the use of strong acids in the protiodesilylation step was avoided in order to allow for a large number of functional groups to be compatible with this transformation. Moreover, wet acetonitrile was reported to have a poor solubility[52]

for the substrates, whereas Hudrlik and co-workers noted that the protiodesilylation in aqueous acetic acid required extensive heating at reflux.[43] More convenient reaction conditions were therefore sought and the first system investigated was the *p*-toluenesulfonic acid monohydrate in dichloromethane.

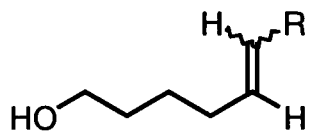
Treatment of the mixture of the isomers **73–76** with 1.1 equivalents of *p*-toluenesulfonic acid monohydrate in dichloromethane at room temperature for 15 h effected smoothly the conversion of the starting materials into a single new product (TLC analysis) (**Scheme 18**). Isolation and flash column chromatography of the crude product, followed by distillation of the acquired oil afforded the newly formed substance as a clear colorless oil in 80% overall yield (from the 1-trimethylsilylalk-1-yne **62**). The ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of this substance exhibited two characteristic doublets (J = 2.6 Hz) at δ 5.49 and 5.16 integrating for one proton each (terminal alkenyl protons), a two-proton triplet (J = 6.4 Hz) at δ 3.63, a two-proton triplet (J = 7.4 Hz) at δ 2.19, a two-proton multiplet at δ 1.60–1.50, a two-proton multiplet δ 1.50–1.40, a broad one-proton signal at δ 1.31 (exchanges with D_2O), as well as a nine-proton singlet at δ 0.18 for the Me_3Ge- group. These data are consistent with the structure 5-trimethylgermylhex-5-en-1-ol (**92**) (**Scheme 18**). However, GLC analysis of the acquired oil indicated that the vinylgermane **92** was contaminated with two minor components, each present in 2–3%.



Scheme 18

The failure to detect significant amounts (≈20% combined yield expected) of the products **93–95** resulting from the protiodemetallation of the isomers **74** and **76**, cast doubt on the structural assignments of the isomers **73–76**.

93 R = $GeMe_3$
94 R = $SiMe_3$
95 R = H



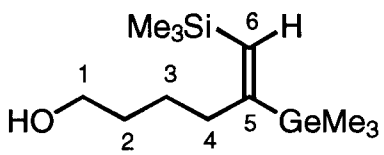
Moreover, the high overall yield of the two-step sequence for the generation of 5-trimethylgermylhex-5-en-1-ol (**92**) from the isomers **73** and **75** was unexpected. Therefore, isolation of the (initially presumed) isomers **73–76** was attempted so that they could be completely characterized and then subjected individually to the protiodesilylation conditions.

2.1.4.2 Isolation of the Products of Hydrogermylation of 6-Trimethylsilylhex-5-yn-1-ol (62)

For the purpose of isolating the different isomeric products from the hydrogermylation of 6-trimethylsilylhex-5-yn-1-ol (**62**), it was decided to perform the reaction on a larger scale

under experimental conditions similar with that outlined above. Thus, to a cold (0 °C) stirred solution of **62** (932 mg, 5.47 mmol, 1 equiv) and $H_2PtCl_6 \cdot 6H_2O$ (57 mg, 0.11 mmol, 0.020 equiv) in dry dichloromethane (27 mL) was added Me_3GeH (**53**) (974 mg, 8.21 mmol, 1.50 equiv). The cooling bath was removed and the reaction mixture was allowed to stir at room temperature overnight. Isolation and flash column chromatography of the acquired oil on silica gel, afforded 1.32 g (83%) of a mixture of the four isomers **73–76**. This liquid was subjected to semi-preparative HPLC (silica Partisil, 10 μm; 22 mm × 250 mm column, 22:3 hexane–ethyl acetate) in four approximately equal portions. These chromatographies resulted in a rough separation to afford three fractions. The corresponding fractions of the separate injections were combined and concentrated under reduced pressure. The first fraction to be eluted, fraction ***A*** (retention time 28–40 min), afforded 985 mg of a mixture of two components. The second fraction to be eluted, fraction ***B*** (retention time 40–46 min) afforded 105 mg of an oil which was constituted of a mixture of three components (HPLC analysis). The third fraction to be eluted, fraction ***C*** (retention time 46–52 min) afforded 75 mg of an oil which was constituted of a mixture of five components (HPLC analysis).

2.1.4.2.1 Isolation and Characterization of (*E*)-5-Trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**73**)

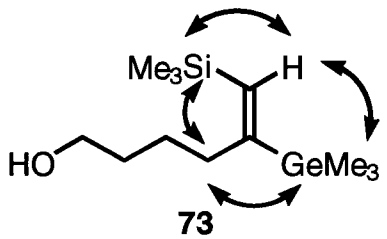


73

Part of fraction ***A*** (≈200 mg) was subjected to reversed phase HPLC (C_{18} μBondapak, 10 μm; 25 mm × 100 mm column, 3:1 methanol–water) in approximately eight equal portions.

The corresponding fractions of the separate injections were combined and concentrated under reduced pressure. The first component to be eluted (retention time 30 min) was distilled to afford 43 mg of a clear colorless oil. This compound, (*E*)-5-trimethylgermyl-6-trimethylsilyl-hex-5-en-1-ol (**73**), is the major component formed during the hydrogermylation of 6-trimethylsilylhex-5-yn-1-ol (**62**).

The ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of this liquid exhibited two nine-proton singlets at δ 0.17 and 0.09, assigned to the Me_3Ge- and Me_3Si- groups. The spectrum also showed a one-proton singlet at δ 5.81 and a multiplet at δ 2.34–2.30 (allylic methylene protons). The singlet at δ 5.81 can be assigned confidently to a vinylic proton that has no *vicinal* protons. Therefore, the vinylic proton must be on C-6 and the Me_3Ge- group must be on C-5. HRMS (DCI, CH_4) analysis was consistent with the presence of a Si and a Ge atom in the formula $C_{12}H_{29}{}^{74}GeO^{28}Si$ $(M + 1)^+$ for the proposed structure with a calculated mass of 291.1199 and an experimentally found value of 291.1185.



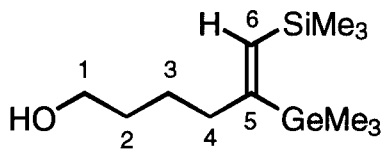
73

After determining the position of the Me_3Ge- group, the configuration of the double bond needed to be established. This was accomplished through ^{1}H NMR NOE difference experiments (see **73**). Thus, irradiation of the signal at δ 0.09 (Me_3Si-) generated an enhancement of the resonances at δ 5.81 (vinylic proton) and 2.34–2.30 (allylic methylene protons). Likewise, irradiation at δ 0.17 (Me_3Ge-) caused the same two signals to be enhanced. These experiments suggest that the Me_3Si- and the Me_3Ge- groups are trans to

each other so that both of these functions have the vinylic proton *and* the allylic methylene protons as immediate neighbors. Additional support for this assignment came from observing signal enhancements of the singlets at δ 0.09 and 0.17 (Me_3Si- and Me_3Ge-) from irradiation of the signal at δ 5.81 (vinylic proton) or from irradiation of the allylic methylene resonance at δ 2.34–2.30. Since the Me_3Si- group in the starting material, 6-trimethylsilylhex-5-yn-1-ol (**62**), was initially located on C-6, the Me_3Ge- group in the product **73** must be on C-5 and trans to the Me_3Si- moiety.

The second compound to be eluted from the reversed phase HPLC (retention time 33 min) was concentrated under reduced pressure to provide 40 mg of an oil which was still a mixture, but had been enriched with the 33 min component. This sample was resubjected to identical HPLC conditions to afford 13 mg of an oil, fraction ***D*** (vide infra), which was 93% pure by GLC analysis. This fraction, which contains the second most abundant product from the hydrogermylation of 6-trimethylsilylhex-5-yn-1-ol (**62**), was processed further as described in section 2.1.4.2.4 (p 46 ff.).

2.1.4.2.2 Isolation and Characterization of (*Z*)-5-Trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**75**)

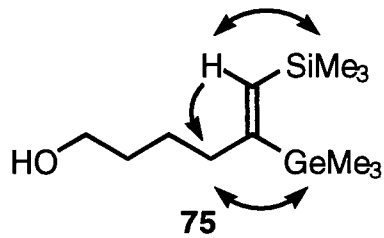


75

The fraction ***B*** (105 mg) from the initial HPLC separation (section 2.1.4.2, p 37) was subjected to HPLC (silica Partisil, 10 μm; 22 mm × 250 mm, 9:1 hexane–ethyl acetate). The last component to be eluted (retention time 51 min) was concentrated under reduced pressure

to afford 10.8 mg of an oil which was still a mixture but had been enriched with the 51 min component. This sample was resubjected to HPLC under identical conditions to afford 5.6 mg of an oil which was 92% pure (GLC analysis).

The ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of this liquid exhibited two nine-proton singlets at δ 0.27 and 0.10, which are assigned to the Me_3Ge- and Me_3Si- groups. A two-proton triplet of doublets (J = 7.8 and 1.2 Hz) at δ 2.24 as well as a one-proton triplet (J = 1.2 Hz) at δ 6.18 (vinylic proton) suggest an allylic coupling between the vinylic proton and the allylic methylene protons. It may therefore be proposed with confidence that this compound has the vinylic proton on C-6 and, therefore, the Me_3Ge- group on C-5 (see **75**). It may be further concluded that the Me_3Ge- and the Me_3Si- groups are cis to each other since compound **73** (vide supra) has the two moieties in a trans relationship. HRMS (DCI, NH_3 + CH_4) analysis of compound **75** indicated a signal at *m/z* 291.1193, which is in good agreement with the calculated value of 291.1199 for $C_{12}H_{29}{}^{74}GeO^{28}Si$ $(M + 1)^+$.

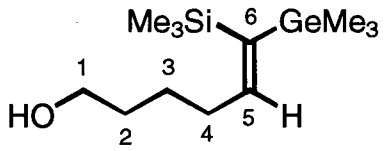


75

^{1}H NMR NOE difference experiments were performed to establish the relationship between the Me_3Si- and Me_3Ge- groups (see **75**). Irradiation at δ 6.18 (vinylic proton) caused signal enhancements of the resonances at δ 0.10 (Me_3Si-) and 2.24 (allylic methylene protons). Alternatively, irradiation of the allylic methylene protons at δ 2.24 caused the signal at δ 0.27 (Me_3Ge-) to be enhanced. Moreover, irradiation at δ 0.27 (Me_3Ge-) caused the allylic

methylene signal to be enhanced, whereas irradiation of the Me_3Si- group at δ 0.10 generated an enhancement of the triplet at δ 6.18 (vinylic proton). These experiments establish the cis relationship between the Me_3Si- and the Me_3Ge- groups.

2.1.4.2.3 Isolation and Characterization of (*E*)-6-Trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**74**)

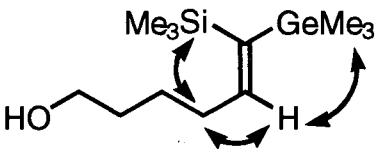


74

The fraction ***C*** (75 mg) from the initial HPLC separation (section 2.1.4.2, p 37) was subjected to HPLC (silica Partisil, 10 μm; 22 mm × 250 mm, 9:1 hexane–ethyl acetate). The fourth component to be eluted (retention time 54 min) was concentrated under reduced pressure to give an oil which was still a mixture, but had been enriched with the 54 min component. This sample was resubjected twice to HPLC under identical conditions, and the acquired liquid was distilled to afford 13 mg of a clear colorless oil (95% pure by GLC analysis). This sample contained a small (5%) amount of (*Z*)-5-trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**75**), as determined by GLC and ^{1}H NMR analyses.

The ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of this oil exhibited two nine-proton singlets at δ 0.17 and 0.12 (Me_3Ge- and Me_3Si-), a doublet of triplets (J = 7.0 and 7.0 Hz) at δ 2.21 (allylic methylene protons) and a one-proton triplet (J = 7.0 Hz) at δ 6.43 (vinylic proton). The multiplicity and coupling constant of the vinylic proton suggest a vicinal coupling to the allylic methylene protons. Therefore, both the Me_3Ge- and the Me_3Si- moieties must be located on C-6 of the alkene function. HRMS (DCI, NH_3 + CH_4) analysis of

this compound gave a signal at *m/z* 291.1190, which is in agreement with the calculated value for $C_{12}H_{29}{}^{74}GeO^{28}Si$ $(M + 1)^+$ of 291.1199.



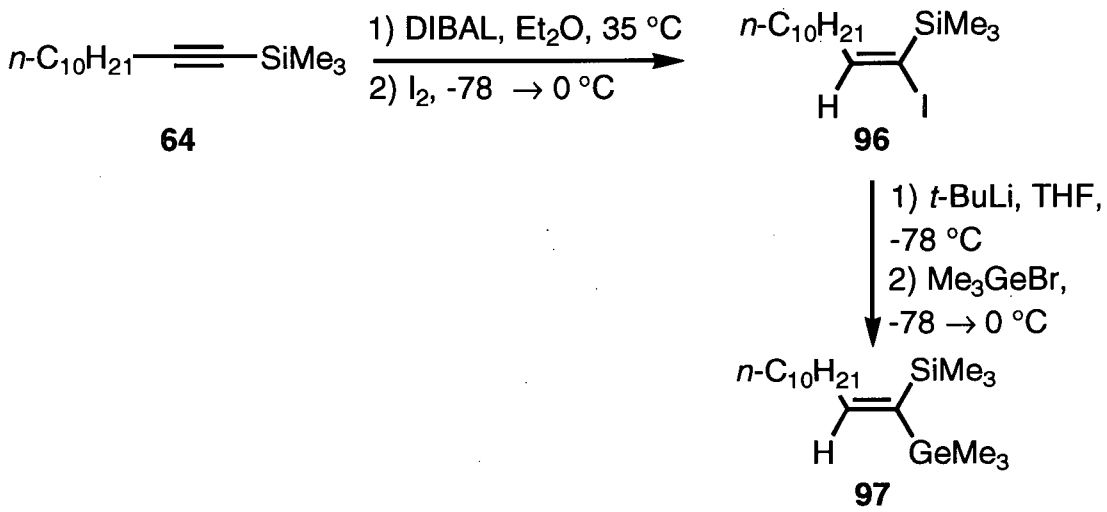
74

^{1}H NMR NOE difference experiments were performed to establish the orientation of the Me_3Si- and Me_3Ge- groups (see **74**). Irradiation of the signal at δ 6.43 (vinylic proton) caused enhancements of the resonances at δ 2.21 (allylic methylene protons) and 0.17 (Me_3Ge-). Alternatively, irradiation of the allylic methylene protons (δ 2.21) caused the signals at δ 6.43 (vinylic proton) and 0.12 (Me_3Si-) to be enhanced. Irradiation of the Me_3Ge- singlet at δ 0.17 generated an enhancement of the triplet at δ 6.43 (vinylic proton), whereas irradiation of the singlet at δ 0.12 (Me_3Si-) caused the signal at δ 2.21 (allylic methylene protons) to be enhanced. These experiments establish the cis relationship between the Me_3Ge- group and the vinylic proton and at the same time, demonstrate that the Me_3Si- group and the side chain are on the same side of the alkene.

Although the above analysis appears reasonable, it could be argued that the determination of the geometry of the alkene from the NOE experiments hinges ultimately on the assignments of the Me_3Ge- group at δ 0.17 and the Me_3Si- at δ 0.12. Since these signals are in very close proximity, it was decided to prepare an alkene bearing the same functional groups via a method that would generate a double bond of known geometry and thus ascertain the identity of the two signals.

Following the procedure described by Zweifel and Lewis,[56] 1-trimethylsilyldodec-1-

yne (**64**) (144 mg, 0.60 mmol) was transformed into (*E*)-1-iodo-1-trimethylsilyldodec-1-ene (**96**) via hydroalumination and iodination of the resulting vinylalane (**Scheme 19**). GLC and ^{1}H NMR spectroscopic analyses of the crude mixture indicated the presence of the starting alkyne **64** (19 %), the expected vinyl iodide **96** (69%) and a small amount (12%) of another product assigned to be (*Z*)-1-trimethylsilyldodec-1-ene. Flash column chromatography of this mixture using C_{18} silica gel and acetonitrile as eluant afforded 116 mg of an inseparable mixture of (*Z*)-1-trimethylsilyldodec-1-ene and (*E*)-1-iodo-1-trimethylsilyldodec-1-ene (**96**) in a ratio of 1:6. The ^{1}H NMR spectrum (200 MHz, $CDCl_3$) of this mixture showed that the major product **96** exhibits a one-proton triplet (J = 8 Hz) at δ 7.14, a two-proton doublet of triplets (J = 8 and 8 Hz) at δ 2.04, a sixteen-proton multiplet at δ 1.42–1.16, a three-proton triplet at δ 0.86 and a nine-proton singlet at δ 0.26. The characteristic signals of this material are in good agreement with the spectroscopic data reported by Zweifel and Lewis[56] for (*E*)-1-iodo-1-trimethylsilylhex-1-ene. Zweifel and Lewis also reported that metal–halogen exchange of 1-halo-1-trimethylsilylalk-1-enes by treatment with *n*-butyllithium generates the corresponding vinyllithium species, which can subsequently be alkylated without loss of the stereochemical integrity of the alkene function.[56]

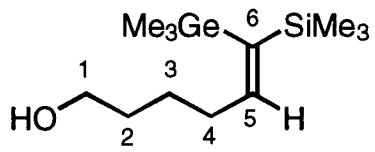


Scheme 19

Thus, (*E*)-1-iodo-1-trimethylsilyldodec-1-ene (**96**) was transformed into (*E*)-1-trimethylgermyl-1-trimethylsilyldodec-1-ene (**97**) via a lithium–halogen exchange, followed by germylation of the corresponding vinyllithium species (**Scheme 19**). A cold (–78 °C) stirred solution of a mixture of **96** and (*Z*)-1-trimethylsilyldodec-1-ene (ratio of ≈6:1) (56 mg, 0.15 mmol, 1 equiv) in anhydrous THF (2 mL) was treated with a solution of *tert*-butyllithium (1.62 M in pentane, 0.21 mL, 0.33 mmol, 2.2 equiv) via a syringe. The yellow heterogeneous reaction mixture was stirred at –78 °C for 15 min and then Me_3GeBr (89 mg, 0.45 mmol, 3.0 equiv) was added. The resulting colorless heterogeneous mixture was stirred at –78 °C for 15 min, then was warmed to room temperature and was allowed to stir for an additional 10 min. Water (1 mL) and diethyl ether (15 mL) were added. The layers were separated and the organic extract was washed with water (5 mL) and brine (5 mL), was dried over anhydrous magnesium sulfate and then was filtered and concentrated under reduced pressure. The crude oil acquired was flash chromatographed (C_{18} silica gel, methanol) to afford 30 mg (56%) of

the (*E*)-1-trimethylgermyl-1-trimethylsilyldodec-1-ene (**97**). The ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of this oil exhibited the following signals: δ 6.44 (t, 1H, J = 7.0 Hz), 2.17 (dt, 2H, J = 7.0 and 7.0 Hz), 1.48–1.15 (m, 16H), 0.86 (t, 3H, J = 6.8 Hz), 0.17 (s, 9H) and 0.12 (s, 9H). The ^{1}H NMR chemical shifts for the vinylic proton (δ 6.44), the Me_3Ge- group (δ 0.17) and the Me_3Si- group (δ 0.12) of (**97**) are in excellent agreement with those of (*E*)-6-trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**74**) (vide supra), therefore establishing the geometry of the alkene function of **74**.

2.1.4.2.4 Isolation and Characterization of (*Z*)-6-Trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**76**)

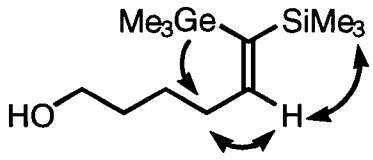


76

The fraction ***D*** (13 mg), isolated from the reversed phase HPLC separation of fraction ***A*** (see section 2.1.4.2.1, p 38 ff.), was subjected to HPLC (silica μPorasil, 10 μm; 25 mm × 100 mm, 9:1 hexane–ethyl acetate). The major component (retention time 17 min) was separated from a small amount of a more polar impurity (retention time 19 min) and was concentrated under reduced pressure to afford 5.8 mg of a clear colorless oil (98 % pure by GLC analysis).

The ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of this liquid possessed a one-proton triplet (J = 7.4 Hz) at δ 5.70 (vinylic proton), a two-proton doublet of triplets (J = 7.4 and 7.4 Hz) at δ 2.12 (allylic methylene protons) and two nine-proton singlets at δ 0.24 (Me_3Ge-) and –0.04 (Me_3Si-). The multiplicity and coupling constant of the vinylic proton indicated a

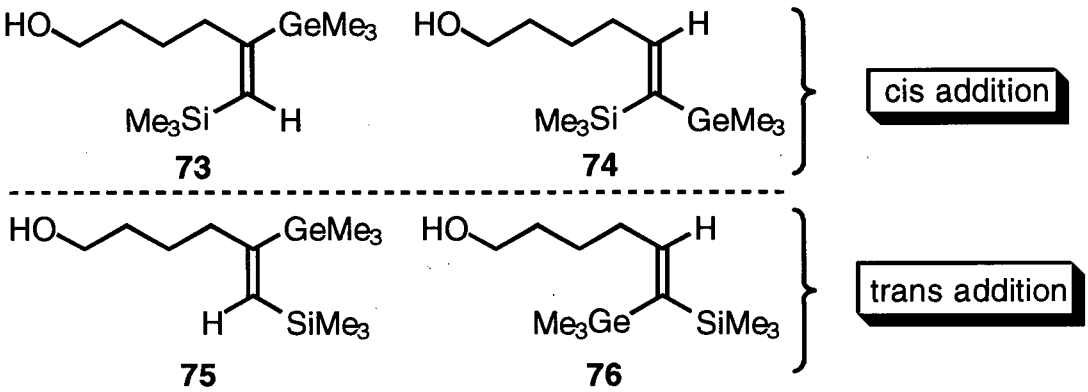
vicinal coupling to the allylic methylene protons, therefore locating the Me_3Ge- group on C-6. HRMS (DCI, NH_3 + CH_4) analysis of this compound revealed a signal at *m/z* 291.1180, in agreement with the calculated value of 291.1173 for $C_{12}H_{29}{}^{72}GeO^{30}Si$ $(M + 1)^+$. Since all three other possible isomers **73**, **74** and **75** from the hydrogermylation of 6-trimethylsilylhex-5-yn-1-ol (**62**) had been characterized (vide supra), this compound was assigned structure **76** (see **Scheme 13**, p 27). To confirm further the configuration of this compound, the following ^1H NMR NOE difference experiments were performed.



76

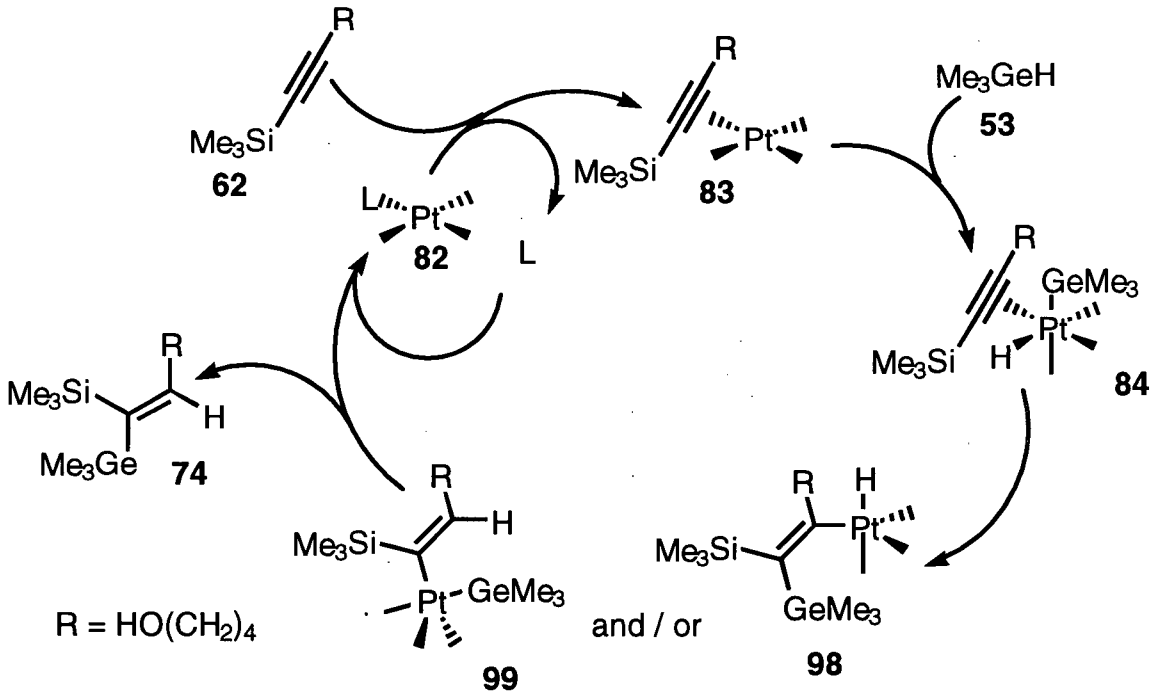
Irradiation of the signal at δ 5.70 (vinylic proton) generated an enhancement of the resonances at δ 2.12 (allylic methylene protons) and –0.04 (Me_3Si-). Alternatively, irradiation of the allylic methylene protons at δ 2.12 caused the signal at δ 5.70 to be enhanced (vinylic proton). Irradiation of the singlet at δ 0.24 (Me_3Ge-) generated an enhancement of the signal at δ 2.12 (allylic methylene protons), whereas irradiation of the Me_3Si- group at δ –0.04 caused the triplet due to the vinylic proton (δ 5.70) to be enhanced. These experiments establish the cis relationship between the Me_3Si- group and the vinylic proton and demonstrate that the Me_3Ge- group is on the same side of the alkene as the side chain.

2.1.4.2.5 Summary



The experimentation summarized above established that the hydrogermylation of 6-trimethylsilylhex-5-yn-1-ol (**62**) with trimethylgermane (**53**) in the presence of a catalytic amount of $H_2PtCl_6 \cdot 6H_2O$ generates four products. The major product obtained (75%), (*E*)-5-trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**73**), arises from the cis addition of Me_3GeH (**53**) across the alkyne function of **62** (see the formation of **73** from loop **A** in the catalytic cycle depicted in **Scheme 15**, p 32). This primary mode of addition was that expected, based on previously described hydrogermylations of alkynes.[32,46] The second major product (19%) was (*Z*)-6-trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**76**). This product emanates from a trans addition of the elements of Me_3GeH (**53**) across the alkyne function of **62** (see the formation of **76** from loop **B** in the catalytic cycle depicted in **Scheme 15**, p 32). This result is somewhat unexpected since the hydrogermylation of alk-1-ynes in the presence of $H_2PtCl_6 \cdot 6H_2O$ generally provides predominantly, if not exclusively, products of cis addition. Although no reports of hydrogermylation of 1-trimethylsilylalk-1-ynes have been reported to this date, it appears that this class of substrates behaves somewhat differently from the alk-1-ynes.

Scheme 20 depicts the reaction pathway that would lead to the formation of the other cis addition product, (*E*)-6-trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**74**), from the 1-trimethylsilylalk-1-yne **62**. Thus, coordination of the active form of the catalyst **82** to the substrate **62** leads to the formation of the complex **83**. Oxidative addition of Me_3GeH (**53**) generates complex **84**, which upon transfer of the Me_3Ge- or H fragment yields the vinyl platinates **98** or **99**. Reductive elimination from either **98** or **99** generates the alkene **74**. Finally, the formation of the other minor product (≈2%), (*Z*)-5-trimethylgermyl-6-trimethyl-silylhex-5-en-1-ol (**75**), arises from a pathway analogous to that of the production of compound **76**, that is from a trans addition of the elements of Me_3GeH (**53**) across the carbon–carbon triple bond of **62** (see **Scheme 15**, p 32).



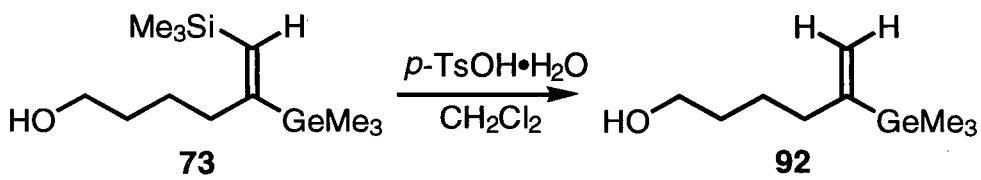
Scheme 20

The spectroscopic data presented above support the original assignments for the

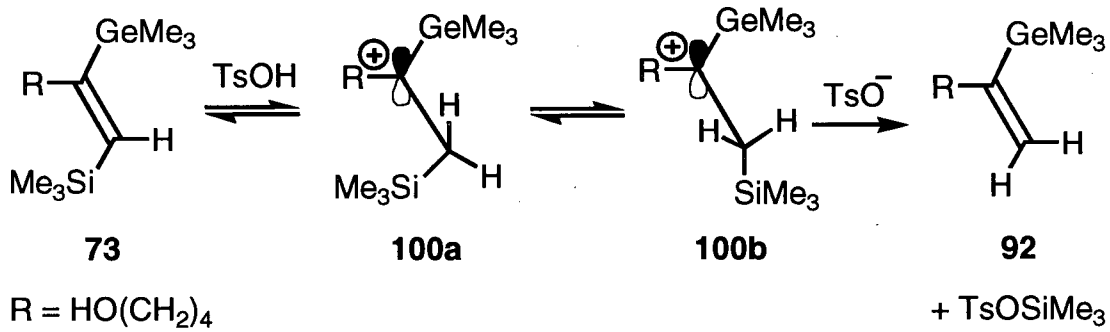
structure of compounds **73–76**. Therefore, the next step in the attempt to elucidate the transformation was to submit individually the products **73–76** derived from the hydrogermylation of 6-trimethylsilylhex-5-yn-1-ol (**62**) to the *p*-TsOH•H_2O mediated protiodesilylation reaction conditions.

2.1.4.3 Treatment of the Products of Hydrogermylation of 6-Trimethylsilylhex-5-yn-1-ol (62) with *p*-Toluenesulfonic Acid Monohydrate in Dichloromethane

2.1.4.3.1 Protiodesilylation of (*E*)-5-Trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (73) to 5-Trimethylgermylhex-5-en-1-ol (92)



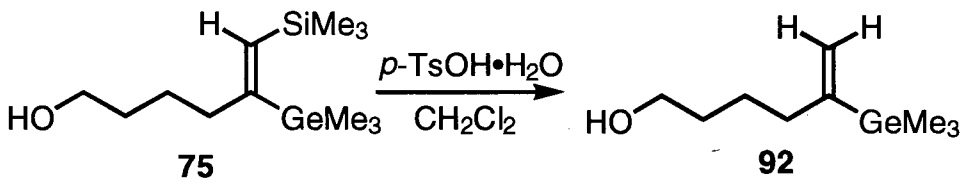
A dichloromethane solution of 8.8 mg of (*E*)-5-trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**73**) (the major product obtained from the hydrogermylation of **62**) was treated with 1.2 equivalents of *p*-TsOH•H_2O at room temperature for 1 h. GLC analysis of an aliquot of the reaction mixture revealed that a single product had been formed. After isolation and purification, 6.6 mg of 5-trimethylgermylhex-5-en-1-ol (**92**) was obtained (quantitative). The ^{1}H NMR spectrum of the acquired liquid was identical with that obtained from the hydrogermylation–protiodesilylation sequence of 6-trimethylsilylhex-5-yn-1-ol (**62**) as described in section 2.1.4.1, p 26 ff. As anticipated, the removal of the trimethylsilyl group was effected selectively.



Scheme 21

The protiodesilylation of (*E*)-5-trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**73**) can be rationalized using a mechanism similar to that proposed by Koenig and Weber.[53] Thus, when **73** is treated with *p*-TsOH•H_2O, protonation of the carbon–carbon double bond leads to **100a** (**Scheme 21**). Bond rotation about the carbon–carbon single bond with the least nuclear motion (**100a** → **100b**) permits increasing stabilization of the carbocation from the trimethylsilyl group via hyperconjugation (also referred to as "vertical stabilization").[57] This property of R_3Si- groups (as well as R_3Ge-, R_3Sn- and R_3Pb-) to stabilize β carbocations[58] is now well recognized.[6] Finally, attack of the nucleophile (TsO^-) on the trimethylsilyl group, with reformation of the carbon–carbon double bond effects the production of the vinylgermane **92**.

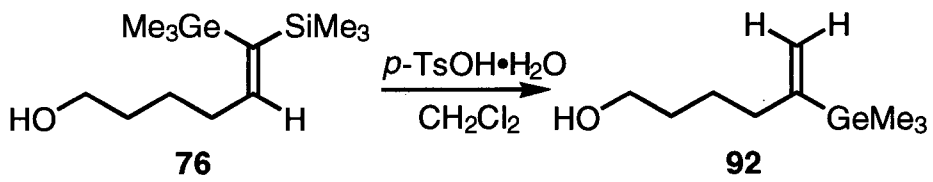
2.1.4.3.2 Protiodesilylation of (*Z*)-5-Trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**75**) to 5-Trimethylgermylhex-5-en-1-ol (**92**)



Similarly, a solution of 2.7 mg of (*Z*)-5-trimethylgermyl-6-trimethylsilylhex-5-en-1-ol

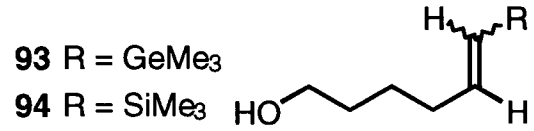
(**75**) (obtained in trace amounts from the hydrogermylation of **62**) in dichloromethane was treated with 1.2 equivalents of *p*-TsOH•H_2O at room temperature for 1.5 h. GLC analysis of an aliquot of the reaction mixture revealed that the vinylgermane **92** was the sole product formed. After isolation and purification of the crude product, 1.1 mg of 5-trimethylgermyl-hex-5-en-1-ol (**92**) was obtained (54%). A mechanism similar to that depicted in **Scheme 21** (vide supra) can be used to rationalize the protiodesilylation of **75** to yield the vinylgermane **92**.

2.1.4.3.3 Protiodesilylation of (*Z*)-6-Trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**76**) to 5-Trimethylgermylhex-5-en-1-ol (**92**)

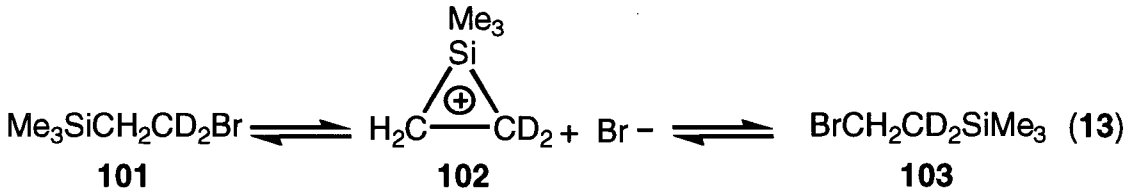


The treatment of (*Z*)-6-trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**76**) (the second most abundant product from the hydrogermylation of 6-trimethylsilylhex-5-yn-1-ol (**62**)) with *p*-TsOH•H_2O will now be discussed. A solution of **76** (9.6 mg) in dichloromethane was treated with 1.2 equivalents of *p*-TsOH•H_2O at room temperature for 1.5 h. After isolation and purification of the crude product, 5-trimethylgermylhex-5-en-1-ol (**92**) was obtained in 85% yield. The spectral data derived from this product were identical with those reported in section 2.1.4.1 (p 26). GLC analysis of the crude product, as well as GLC and GLC-MS analyses of the chromatographed product, revealed that a small amount (≈2.5%) of (*E*)-6-trimethylsilylhex-5-en-1-ol (**94a**) had also been formed during the reaction (vide infra). The structural assignment of this compound was made by comparison of the GLC retention time

and GLC-MS data presented in the next section.



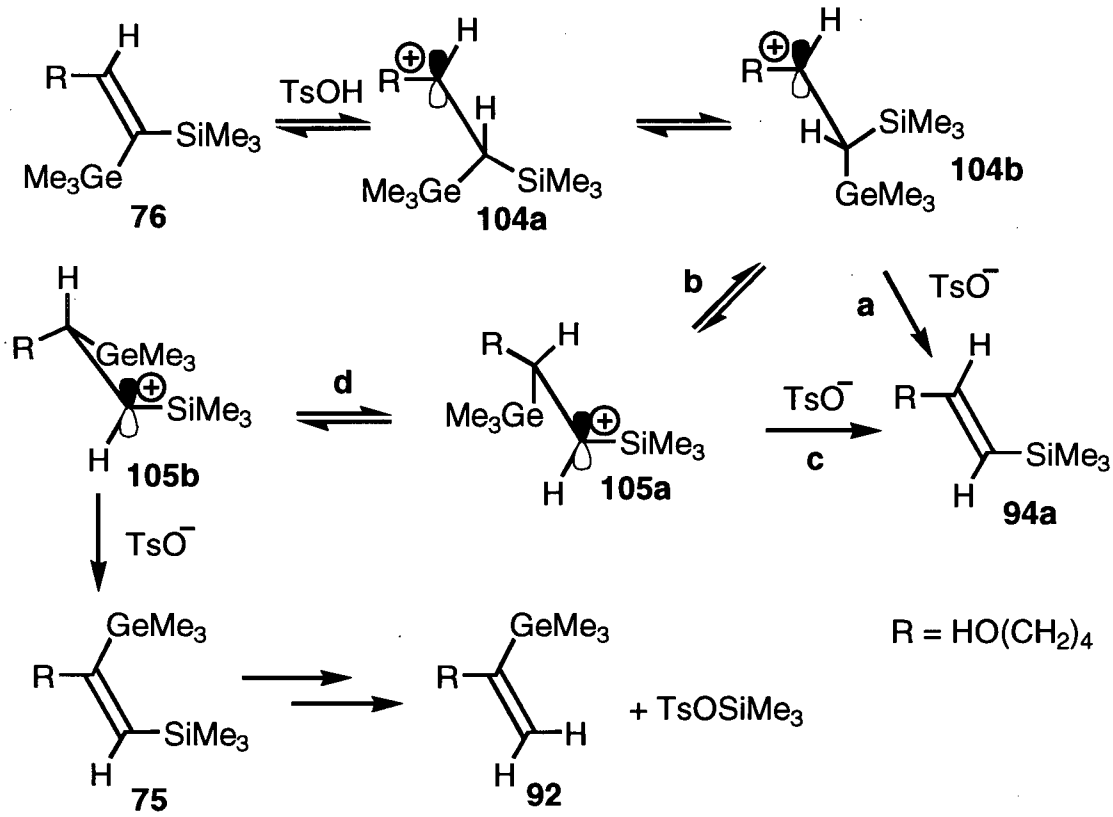
The results described above were rather surprising and certainly not predicted. Based on the analysis outlined in **Scheme 17** (p 35), it was expected that **76** would undergo simple protiodesilylation to the vinylgermanes **93** or protiodegermylation to the vinylsilanes **94**. The fact that (*Z*)-6-trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**76**) is transformed almost entirely (>97%) into 5-trimethylgermylhex-5-en-1-ol (**92**) seems to be the key to the high overall yield of the hydrogermylation–protiodesilylation sequence. It therefore appears that upon treatment of **76** with *p*-TsOH•H_2O in dichloromethane at room temperature, the trimethylgermyl group underwent a 1,2 shift. Although this migration was not expected, there is precedent for a related process in the literature involving trialkylsilyl chemistry.



Eaborn and co-workers[59] carried out the solvolysis of **101** in aqueous methanol to 50% completion and recovered the bromide. ^{1}H NMR spectroscopic analysis revealed that the recovered bromide was comprised of a mixture of **101** and **103** (**Equation 13**). The formation of **103** was rationalized by postulating the reversible ionization of the bromide **101** to a non-classical silacyclopropenium ion **102**, as depicted in **Equation 13**. It was also concluded that, under the reaction conditions used, the rate of rearrangement was somewhat faster than that of the solvolysis. Similar results obtained from related experiments have been

rationalized via silacyclopropenium ions.[60,61]

A possible reaction pathway accounting for the formation of the vinylgermane **92** and the vinylsilane **94a** from (Z)-6-trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**76**), rationalized in terms of classical carbocations, is depicted in **Scheme 22**. Thus, protonation of the alkene function of **76** with *p*-TsOH•H_2O generates the carbocation **104a**. Bond rotation about the carbon–carbon single bond of **104a** with the least nuclear motion allows increasing stabilization of the carbocation from hyperconjugation by the trimethylgermyl group leading to the formation of **104b**. Since the hyperconjugative[58,62] electron release from the carbon–germanium bond is greater than that from the carbon–silicon bond (the electron release through hyperconjugation for the C–M bond is in the order M = Si < Ge << Sn < Pb),[62] it is reasonable to assume that rotation around the carbon–carbon single bond will be such as to favor a stabilization of the carbocation from the trimethylgermyl group. At this point, nucleophilic attack from the tosylate (path **a**) onto the trimethylgermyl group of **104b** with reformation of the carbon–carbon double bond results in the production of the vinylsilane **94a**.



Scheme 22

Alternatively, the Me_3Ge- group from **104b** may undergo a 1,2 shift (path **b**) to generate the carbocation **105a**. This migration would relieve some steric encumbrance from the crowded terminal carbon of **104b**, which bears both a Me_3Ge- and a Me_3Si- group. From the carbocation **105a**, nucleophilic attack from the tosylate onto the trimethylgermyl group (path **c**) would produce the vinylsilane **94a**, whereas carbon–carbon single bond rotation with the least nuclear motion (path **d**) would lead to **105b**, which can undergo loss of a proton to form **75**. Compound **75** can subsequently undergo protiodesilylation to **92**, as discussed in the previous section. Although no attempts were made to demonstrate the presence of compound **75** in the reaction mixture, the pathway leading to **92** seems nonetheless reasonable. This

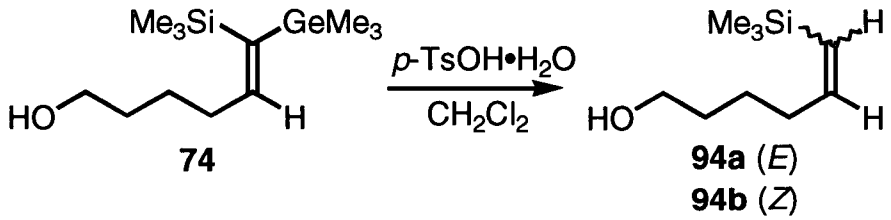
does not preclude a possible alternative pathway that would lead to the formation of **92** without going through the intermediacy of **75**.

Assuming that i) from **104b** the 1,2 shift of the Me_3Ge- group (path **b**) is fast compared to the attack by the nucleophile (path **a**), and ii) that from the carbocation **105a** rotation (path **d**) and proton elimination leading to the production of **75** is fast compared to the nucleophilic attack by the tosylate (path **c**) one would expect the major product to arise via the rearrangement process. This is, in fact, what is experimentally observed: the ratio of the observed products **92** and **94a** is ≈49:1. This shows that the proposed pathways **b** and **d** are favored over pathways **a** and **c** respectively.

It may be possible to rationalize the preferential formation of 5-trimethylgermylhex-5-en-1-ol (**92**) over (*E*)-6-trimethylsilylhex-5-en-1-ol (**94a**) in terms of counter-ion control.[63] The tosylate anion should be initially located on the same face as the newly introduced proton in **104a**. After bond rotation to carbocation **104b**, the elimination of the Me_3Ge- group (path **a**) requires participation of the tosylate anion, which necessitates that the latter moves to the other side of the molecule. On the other hand, the 1,2 shift of the Me_3Ge- group (path **b**) does not require such a participation of the tosylate and accordingly should be the favored process.

A similar argument may be formulated from carbocation **105a** for the preferential proton elimination (path **d**: **105a** ↔ **105b** → **75**) to form **75**, which then undergoes protio-desilylation to **92**, as opposed to the Me_3Ge- group elimination (path **c**) to produce **94a**.

2.1.4.3.4 Protiodegermylation of (*E*)-6-Trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**74**) to (*E*)-6-Trimethylsilylhex-5-en-1-ol (**94a**) and (*Z*)-6-Trimethylsilylhex-5-en-1-ol (**94b**)



A solution of 6.6 mg of (*E*)-6-trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**74**) (obtained in trace amounts from the hydrogermylation of (**62**); this sample contained a small (5%) amount of (*Z*)-5-trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**75**)) in dichloromethane was treated with 1.2 equivalents of *p*-TsOH•H_2O at room temperature for 1.25 h. After isolation and purification of the crude product, ^{1}H NMR (400 MHz, $CDCl_3$) spectroscopic, GLC and GLC-MS analyses of the acquired oil revealed the presence of three products, as well as a small amount (5%) of unreacted starting material. The ^{1}H NMR spectrum of the mixture showed six signals in the region δ 6.5–5.1, integrating for a total of two protons, a two-proton triplet at δ 3.62, a two-proton multiplet at δ 2.26–2.08, a four-proton multiplet at δ 1.63–1.40 and five singlets in the δ 0.20–0.02 region integrating for a total of nine protons.

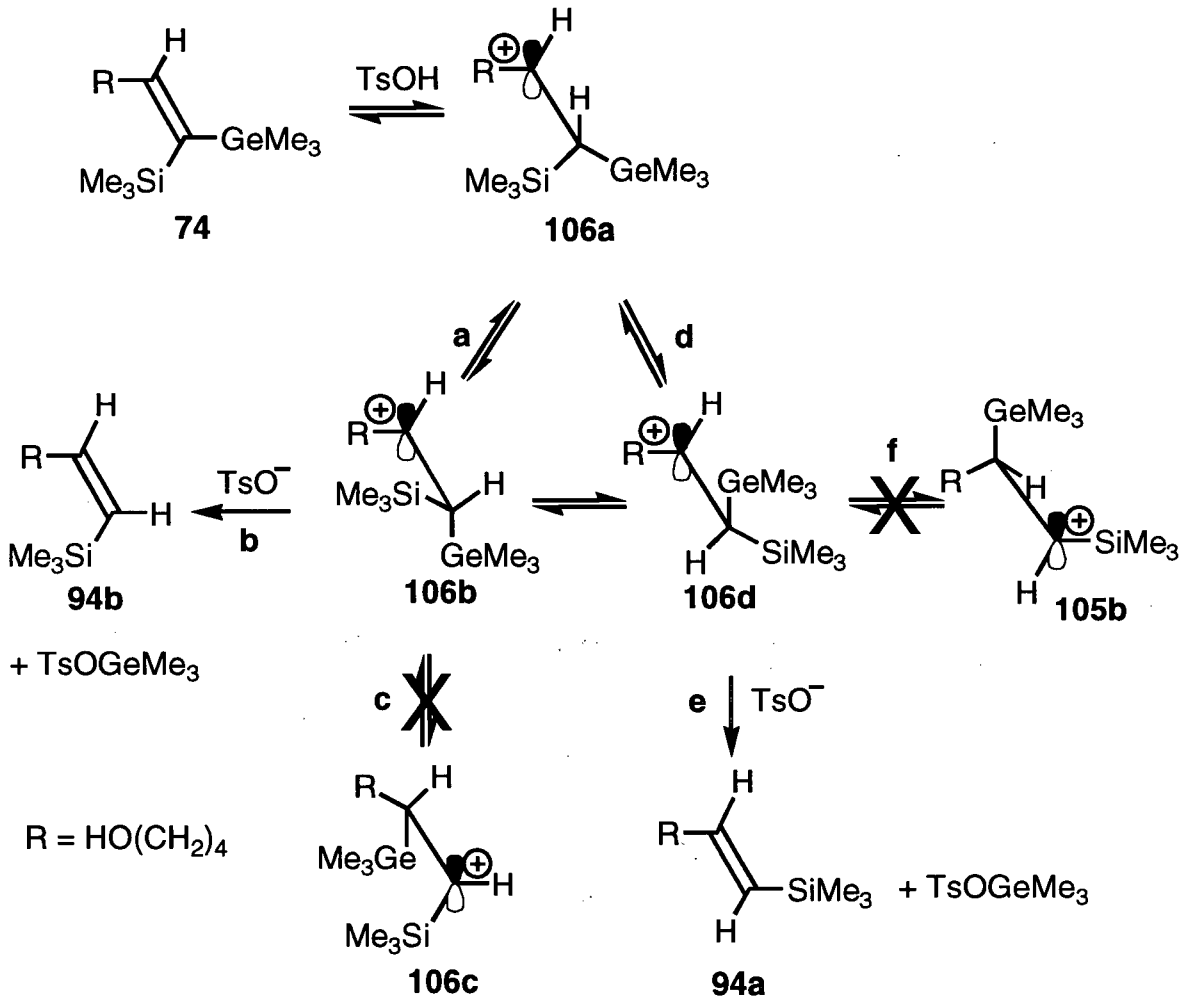
The major product (72% by GLC analysis) in the mixture was assigned structure **94b**, (*Z*)-6-trimethylsilylhex-5-en-1-ol, formed by protiodegermylation of the starting material **74**. The assignment was based on the following data: the ^{1}H NMR spectrum exhibited a doublet of triplets (J = 14.0 and 7.0 Hz) at δ 6.27, as well as another doublet of triplets (J = 14.0 and 1.2 Hz), of equal intensity, at δ 5.48. Homonuclear decoupling of the δ 6.27 signal resulted in the collapse of the δ 5.48 doublet of triplets to a triplet, simultaneously revealing the presence of a small doublet at δ 5.49, previously hidden, due to a small amount of 5-trimethylgermyl-

hex-5-en-1-ol (**92**) present in the mixture (vide infra). The two signals at δ 6.27 and δ 5.48, together with the data given below, suggest a cis arrangement between two vinylic protons of a 1,2-disubstituted alkene. GLC-MS (CI, NH_3) analysis indicated an ion at 173 $(M + 1)^+$, which is consistent with the expected mass for $C_9H_{20}O^{28}Si$ (172), as well as diagnostic fragments at 157 $(M - CH_3)^+$ and 73 $(-Si(CH_3)_3)^+$.

Similarly, the next major component (18%) was assigned structure **94a**, (*E*)-6-trimethylsilylhex-5-en-1-ol, also formed by protiodegermylation of the starting material **74**, on the basis of the following data: the ^1H NMR spectrum exhibited a doublet of triplets (J = 18.6 and 6.2 Hz) at δ 6.00 as well as another doublet of triplets (J = 18.6 and 1.5 Hz), of equal intensity, at δ 5.62. These signals are consistent with a trans arrangement between two vinylic protons of a 1,2-disubstituted alkene. GLC-MS (CI, NH_3) analysis indicated an ion at 173 $(M + 1)^+$, in agreement with the expected mass for $C_9H_{20}O^{28}Si$ (172), as well as diagnostic fragments at 157 $(M - CH_3)^+$ and 73 $(-Si(CH_3)_3)^+$.

The minor product (5%) (vide supra) formed during the reaction was 5-trimethylgermylhex-5-en-1-ol (**92**). The assignment was established as follows: the ^1H NMR spectrum displayed characteristic doublets at δ 5.49 (revealed during the homonuclear decoupling experiment at δ 6.27, vide supra) and 5.16. GLC-MS (CI, NH_3) indicated an ion at 219 $(M + 1)^+$ with an isotopic cluster consistent with the expected distribution for $C_9H_{20}O^{74}Ge$ (218) and finally, coinjection with an authentic sample on GLC ascertained that this product has a retention time identical with that of 5-trimethylgermylhex-5-en-1-ol (**92**). The presence of this compound can be linked to the small (5%) amount of (*Z*)-5-trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**75**) in the starting material, incompletely separated from **74** during the

isolation, which underwent protiodesilylation (vide supra).



Scheme 23

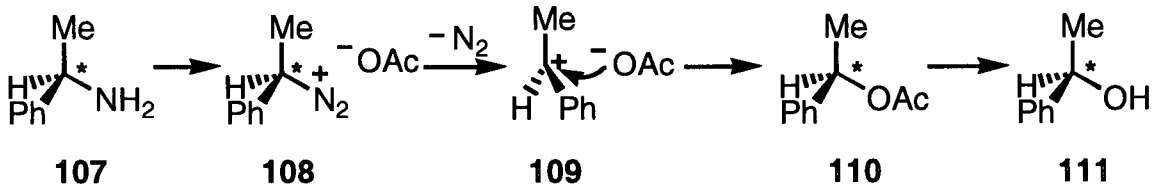
The formation of the vinylsilanes **94a** and **94b** from **74** can be rationalized in a fashion similar to that used for the formation of the vinylgermane **92** from **73** (**Scheme 21**, p 51), following the mechanism proposed by Koenig and Weber.[53] **Scheme 23** depicts the proposed transformations. Thus, when **74** is treated with *p*-TsOH•H_2O, protonation of the alkene function leads to the formation of carbocation **106a**. Rotation about the carbon–carbon single bond with the least nuclear motion (path **a**), simultaneously causing the side chain **R**

and the Me_3Si- group to eclipse each other, allows increased stabilization of the carbocation **106b** from the trimethylgermyl group through hyperconjugation. Elimination of the Me_3Ge-group, through nucleophilic attack from the tosylate on **106b**, results in the formation of the vinylsilane **94b** (path **b**). The product obtained as a result of pathway **b**, (*Z*)-6-trimethylsilyl-hex-5-en-1-ol (**94b**), is the major component produced from the treatment of **74** under acidic conditions.

As outlined above, no rearranged product was observed from the treatment of **74** with *p*-TsOH•H_2O. It appears that the carbocation **106b** does not undergo a 1,2 Me_3Ge- shift. It is possible that pathway **c** is not favored since migration of the trimethylgermyl group would require that the side chain **R** becomes eclipsed the Me_3Si- group going from **106b** to **106c**. This interaction may be responsible for inhibiting the migration of the Me_3Ge- group.

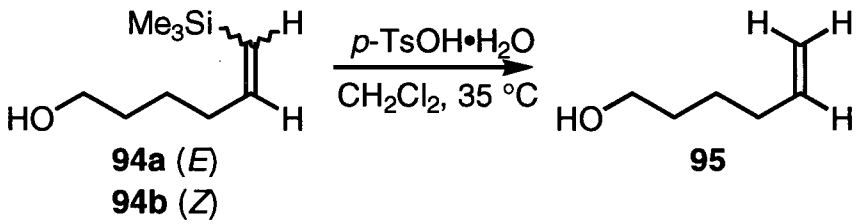
Alternatively, rotation about the carbon–carbon single bond of **106a** (path **d**) would form **106d**. At this time, elimination of the trimethylgermyl group through nucleophilic attack from the tosylate yields vinylsilane **94a** (path **e**). Additional comments are required on the formation of **94a** from **106a**. Firstly, the formation of **106d**, which is stabilized through hyperconjugation from the Me_3Ge- group, alleviates the steric encumbrance between the Me_3Si- group and the side chain **R** present in both **106a** and **106b**. Secondly, the carbocation **106d** possesses a conformation analogous to that of carbocation **104b** which underwent a 1,2 Me_3Ge- shift (**Scheme 22**, p 55). The "anomalous" behavior of carbocation **106d** may be rationalized in terms of counter-ion control.[63] The tosylate anion should be initially located on the same face as the newly introduced proton in **106a**, and hence on the same face as the Me_3Ge- group of **106d**. Therefore, the tosylate anion may compete effectively for the

elimination of the Me_3Ge- group (path **e**), instead of undergoing a 1,2 shift (path **f**). This was not the case for carbocation **104b** (see **Scheme 22**, p 55 and accompanying text).



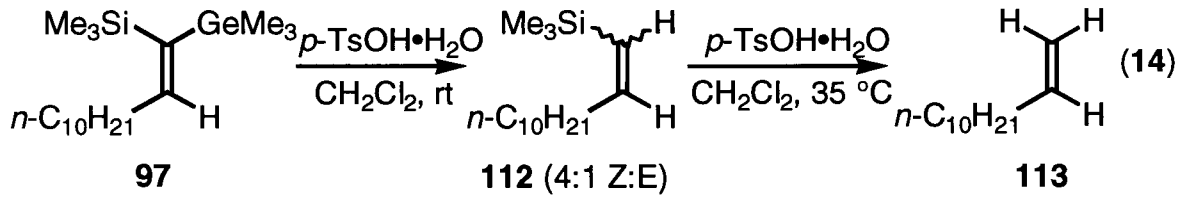
Scheme 24

Counter-ion control[63] has been used successfully to rationalize the outcome of examples in which identical carbocation intermediates lead to different products. This rationale uses ion-pairing to explain the selectivity of certain transformations. The example in **Scheme 24** illustrates this concept. Deamination of optically active amine **107** in acetic acid solution in the presence of sodium nitrite generated the optically active acetate **110**, which upon hydrolysis, formed the optically active alcohol **111**. The optical activity of the alcohol **111** was largely retained. To explain this retention of configuration,[63] it has been postulated that the intermediate diazonium acetate **108** decomposes to the ion pair **109**, which then recombines to form the acetate **110**. The hydrolysis of **110** leads to the optically active alcohol **111**.



When the mixture of vinylsilanes **94a** and **94b**, obtained from the protiodegermylation of (*E*)-6-trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**74**) (vide supra), was treated with *p*-

TsOH•H_2O (1.2 equiv) in dichloromethane at 35 °C for 1h, protiodesilylation occurred. GLC analysis of the crude mixture indicated that the substrates had been completely consumed. However, due to the small scale of the reaction (≈1 mg) the (expected) product, hex-5-en-1-ol (**95**), could not be isolated.

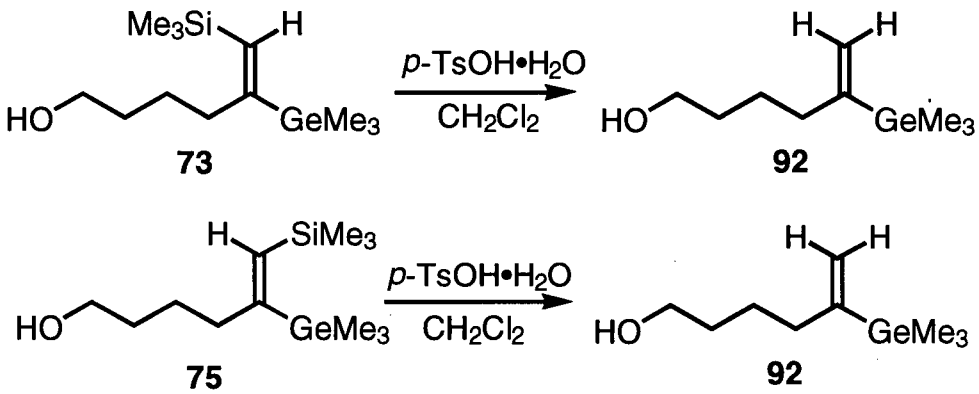


In order to gain further information on the outcome of treating (*E*)-6-trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**74**) with *p*-TsOH•H_2O, a similar experiment was carried out employing (*E*)-1-trimethylgermyl-1-trimethylsilyldodec-1-ene (**97**) as substrate (**Equation 14**). Thus, treatment of **97** with 1.2 equivalents of *p*-TsOH•H_2O in dichloromethane at room temperature for 2.5 h resulted in the formation of the vinylsilanes **112**. GLC and ^{1}H NMR spectroscopic analyses indicated that the vinylsilanes **112** had been formed in a ratio of approximately 4:1, with the *Z* isomer being the major compound. The signals in the vinylic region of the ^{1}H NMR spectrum of the crude mixture were similar to those reported for the product mixture derived from protiodegermylation of **74** (vide supra). Periodic GLC analyses of aliquots of the reaction mixture indicated that neither the substrate nor the vinylsilanes **112** underwent E to Z isomerization under the reaction conditions during the time required to effect protiodegermylation. Therefore, both vinylsilanes **112** arose from the same substrate. Moreover, the ^{1}H NMR spectrum clearly showed that *no* product originating from the migration of the Me_3Ge- group had been formed during the reaction. When the reaction mixture containing the vinylsilanes **112** was heated to 35 °C for 1 h, protiodesilylation

occurred to generate dodec-1-ene (**113**) (**Equation 14**). This assignment was based on the ^{1}H NMR (400 MHz, $CDCl_3$) spectroscopic analysis of the crude oil isolated from the reaction mixture. The spectrum exhibited the following signals: δ 5.80 (ddt, 1H, J = 17.1, 10.3 and 6.7 Hz), 4.98 (ddt, 1H, J = 17.1, 2.0 and 2.0 Hz), 4.91 (ddt, 1H, J = 10.3, 2.0 and 2.0 Hz), 2.10–1.98 (m, 2H), 1.45–1.15 (m, 16H), 0.88 (t, 3H, J = 7.0 Hz). This experiment, along with those derived from the study involving treatment of **74** with acid (vide supra), demonstrates that the minor isomer (*E*)-6-trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**74**) obtained from the hydrogermylation of 6-trimethylsilylhex-5-yn-1-ol (**62**) can be chemically "destroyed" to form hex-5-en-1-ol (**95**) and (possibly) removed via chromatography from the desired 5-trimethylgermylhex-5-en-1-ol (**92**).

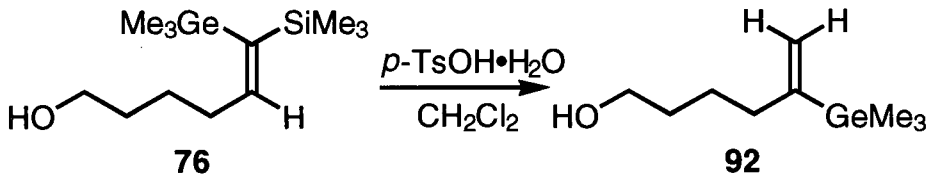
2.1.4.3.5 Summary

The isomers **73**–**76**, products from the hydrogermylation of 6-trimethylsilylhex-5-yn-1-ol (**62**), were treated individually with *p*-TsOH•H_2O in dichloromethane.

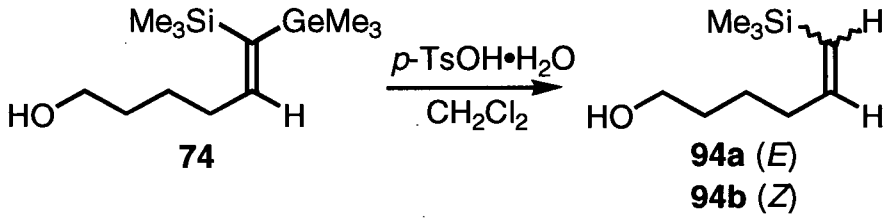


As outlined above, (*E*)-5-trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**73**) and (*Z*)-5-trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**75**) react chemospecifically, as anticipated, with *p*-TsOH•H_2O in dichloromethane to undergo C–Si bond cleavage to generate 5-

trimethylgermylhex-5-en-1-ol (**92**).



Unexpectedly, (*Z*)-6-trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**76**) also produced 5-trimethylgermylhex-5-en-1-ol (**92**) when treated with *p*-TsOH•H_2O in dichloromethane. It is postulated that this transformation occurs via an acid mediated 1,2 Me_3Ge- shift (**Scheme 22**, p 55), to generate eventually (*Z*)-5-trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**75**). The latter undergoes protiodesilylation to give (**92**).



Finally, (*E*)-6-trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**74**) underwent protio-degermylation to a mixture (*E*)- and (*Z*)-6-trimethylsilylhex-5-en-1-ols (**94a**) and (**94b**). Furthermore, when the reaction mixture containing *p*-TsOH•H_2O along with the vinylsilanes **94a** and **94b** was heated to 35 °C, protiodesilylation occurred to generate hex-5-en-1-ol (**95**).

These transformations proved to be general for a series of diversely functionalized 1-trimethylsilylalk-1-ynes. The results are presented in the following section.

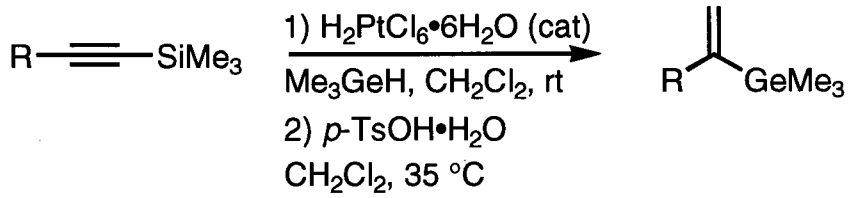
2.1.5 SYNTHESIS OF 2-TRIMETHYLGERMYLALK-1-ENES

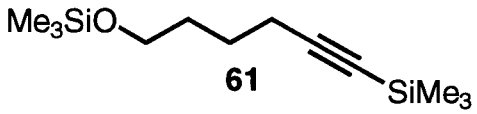
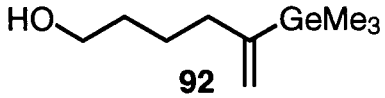
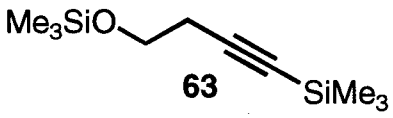
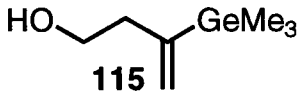
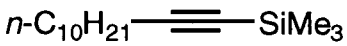
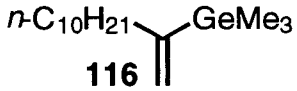
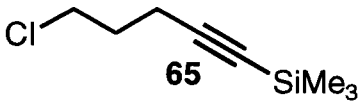
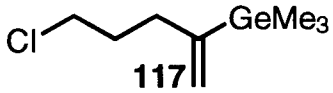
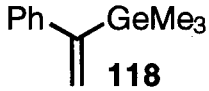
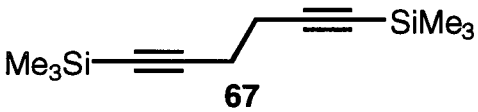
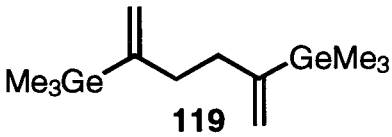
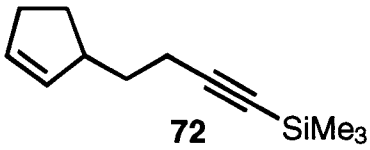
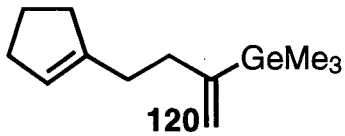
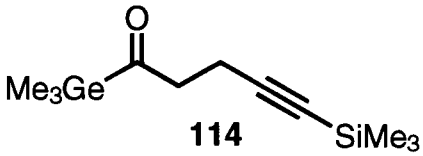
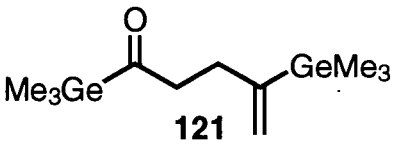
The optimized experimental conditions devised as described in the previous section were successfully applied to a number of 1-trimethylsilylalk-1-ynes to generate the corresponding 2-trimethylgermylalk-1-enes.

Table 2 summarizes the conversion of the 1-trimethylsilylalk-1-ynes **61**, **63–67**, **72** and **114** into the 2-trimethylgermylalk-1-enes **92** and **115–121**. The synthesis of 5-chloro-2-trimethylgermylpent-1-ene (**117**) (**Table 2**, entry 4), for example, was accomplished in the following manner. A mixture of 5-chloro-1-trimethylsilylpent-1-yne (**65**) (1 equiv) and $H_2PtCl_6 \cdot 6H_2O$ (≈0.02 equiv) in dichloromethane at 0 °C was treated with trimethylgermane (**53**) (1.5 equiv). The reaction mixture was then stirred at room temperature until complete consumption of the starting material. After isolation, the crude oil was dissolved in dichloromethane and treated with *p*-TsOH•H_2O (1.2 equiv) at 30–35 °C for 1 h. Isolation and purification of the crude product afforded 5-chloro-2-trimethylgermylpent-1-ene (**117**) in 74% overall yield as a clear colorless oil.

The remainder of the 2-trimethylgermylalk-1-enes listed in **Table 2** were synthesized from the corresponding 1-trimethylsilylalk-1-ynes in a manner identical with that outlined above. As seen in **Table 2**, the experimental conditions used for the preparation of the 2-trimethylgermylalk-1-enes are compatible with a wide variety of functional groups. Entries 1 and 2 (**Table 2**) show that this method accommodates trimethylsilyl ethers. Investigations showed that under similar experimental conditions, substrates bearing a trimethylsilyl ether function underwent hydrogermylation faster than the corresponding substrate with a free hydroxy group.

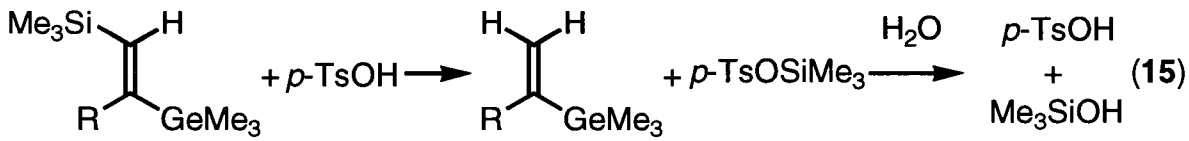
Table 2: Preparation of the 2-Trimethylgermylalk-1-enes **92, 115–121**



Entry	1-Trimethylsilylalk-1-yne	2-Trimethylgermylalk-1-ene[a]	Yield (%)[b]
1	 **61**	 **92**	74
2	 **63**	 **115**	63
3	 **64**	 **116**	72
4	 **65**	 **117**	74
5	**66**	 **118**	68
6[c]	 **67**	 **119**	71
7	 **72**	 **120**	72
8	 **114**	 **121**	68

[a] Conditions: 1) Me_3GeH (1.5 equiv), $H_2PtCl_6{\bullet}6H_2O$ (≈0.02 equiv), CH_2Cl_2 (1 M), rt 1–21 h. 2) *p*-TsOH•H_2O (1.2 equiv), CH_2Cl_2 (0.1 M), 30–35 °C 1–7 h. [b] Overall yield of isolated and purified product. [c] The amounts of reagents were doubled for this substrate.

Thus, hydrogermylation followed by protiodesilylation of the trimethylsilyl ethers **61** and **63** afforded the alcohols **92** and **115** in 74 and 63% overall yield, respectively. TLC analyses of the product mixtures after hydrogermylation indicated that the trimethylsilyl ether protecting groups had been largely retained. However, the trimethylsilyl ether functions were cleaved during the step involving treatment of the crude product with *p*-TsOH•H_2O in dichloromethane. Two Me_3Si- groups were removed from each of the substrates **61** and **63** during the protiodesilylation step. Since only 1.2 equivalents of *p*-TsOH•H_2O were used, the acid must therefore have been regenerated within the reaction mixture. It is plausible to envisage that, after protiodesilylation of a substrate of general structure depicted in **Equation 15**, for example, the resulting trimethylsilyl-*para*-toluenesulfonate was hydrolyzed with water (from the monohydrate of *p*-TsOH•H_2O or from the CH_2Cl_2 which is not anhydrous) to *p*-TsOH and trimethylsilanol.[64]



(15)

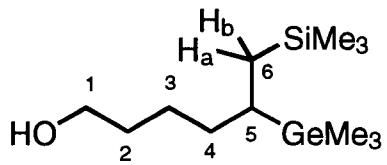
1-Trimethylsilyldodec-1-yne (**64**) (entry 3) was transformed into 2-trimethylgermyl-dodec-1-ene (**116**) in 72% yield. The two-step sequence leading to the formation of the 2-trimethylgermylalk-1-enes also allows for the presence of a primary chloride (entry 4) as well as a phenyl group (entry 5). 1,6-bis(Trimethylsilyl)hexa-1,5-diyne (**67**) (entry 6) was smoothly converted into the structurally novel 2,5-bis(trimethylgermyl)hexa-1,5-diene (**119**) in 71% via the same set of transformations. Substrate **67** underwent a double hydrogermylation followed by protiodesilylation and thus required that the amounts of reagents used be doubled.

The presence of an alkene function is also tolerated, as seen in entry 7, in which **72** is

transformed into **120**. However, the endocyclic alkene function of **72** isomerized during the platinum catalyzed step leading to the formation of **120**. A possible rationale for this isomerization will be presented later (vide infra). Finally, as summarized in entry 8, 5-trimethylsilylpent-4-ynoyltrimethylgermane (**114**) (the preparation of **114** is described later in section 2.2.2.3, p 97 ff.) was efficiently transformed into the structurally unique 4-trimethylgermylpent-4-enoyltrimethylgermane (**121**), which possesses two Me_3Ge- groups in different chemical environments.

Although the regioselectivity of addition of the Me_3Ge- group varied from one substrate to another (from 5:1 for **64** to 17:1 for **66**), the ratio was generally about 12:1 in favor of the Me_3Ge- group having undergone addition at the *C*-substituted end of the alkyne for the 1-trimethylsilylalk-1-ynes depicted in **Table 2**.

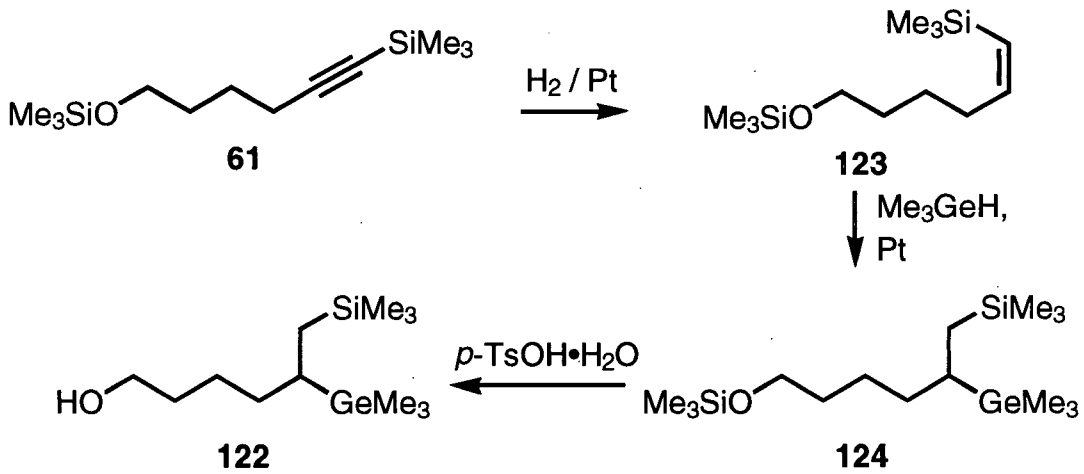
The formation of **92** from **61** (entry 1), **116** from **64** (entry 3) and **120** from **72** (entry 7) require additional comments.



122

Firstly, during the purification of 5-trimethylgermylhex-5-en-1-ol (**92**) (entry 1), two by-products were also isolated in trace amounts. The first component, which was assigned structure **122**, 5-trimethylgermyl-6-trimethylsilylhexan-1-ol, was isolated in ≈1.5% yield. The structural assignment was based on the following data. The ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **122** exhibited several distinctive signals, including a one-proton multiplet at δ 1.05–0.98 (H-5), a one-proton doublet of doublets (J = 15.0 and 3.6 Hz) at δ 0.60 (H-6a), a

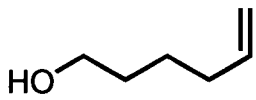
one-proton doublet of doublets (J = 15.0 and 10.4 Hz) at δ 0.48 (H-6b) and two nine-proton singlets at δ 0.06 and –0.02 (Me_3Ge- and Me_3Si-). Additional evidence for the proposed structure was obtained from homonuclear decoupling experiments. Thus, irradiation of the multiplet at δ 1.05–0.98 (H-5) resulted in the simplification of the signals at δ 0.60 (H-6a) and 0.48 (H-6b) to doublets (J = 15 Hz). Alternatively, when H-6a (δ 0.60) was irradiated, H-5 (δ 1.05–0.98) was simplified and at the same time H-6b (δ 0.48) collapsed to a doublet (J = 10.4 Hz). Similarly, when H-6b (δ 0.48) was irradiated, H-5 (δ 1.05–0.98) was again simplified and H-6a (δ 0.60) became a doublet (J = 3.6 Hz). In addition, HRMS analysis of **122** showed a signal at *m/z* 292.1270, in good agreement with the calculated value of 292.1278 for $C_{12}H_{30}{}^{74}GeO^{28}Si$.



Scheme 25

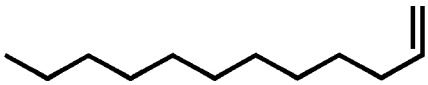
A possible rationale accounting for the formation of **122** is depicted in **Scheme 25**. It is conceivable that, during the early stages of the reaction, the hydrogen produced by the reduction of $H_2PtCl_6{\bullet}6H_2O$ to the active Pt(0) form of the catalyst (see **Equation 11** and accompanying text in section 2.1.4.1) hydrogenated a small amount of **61**, resulting in the

formation of the vinylsilane **123**. Hydrogermylation of the latter substance could then generate **124**. Hydrogermylation of alkenes[65] are usually slow compared to the hydrogermylation of the corresponding alkynes[46] under similar experimental conditions. However, it is possible that vinylsilanes such as **123** are better substrates towards Pt catalyzed addition of trimethylgermane (**53**) than the parent carbon analogues. Subsequent treatment of **124** with *p*-TsOH•H_2O in dichloromethane would afford 5-trimethylgermyl-6-trimethylsilylhexan-1-ol (**122**). In spite of the fact that no other by-products related in structure to **122** were isolated from the materials derived from hydrogermylation of the remainder of the substrates depicted in **Table 2**, it is reasonable to assume that by-products analogous to **122** were formed in trace amounts and were separated during the purification step.



95

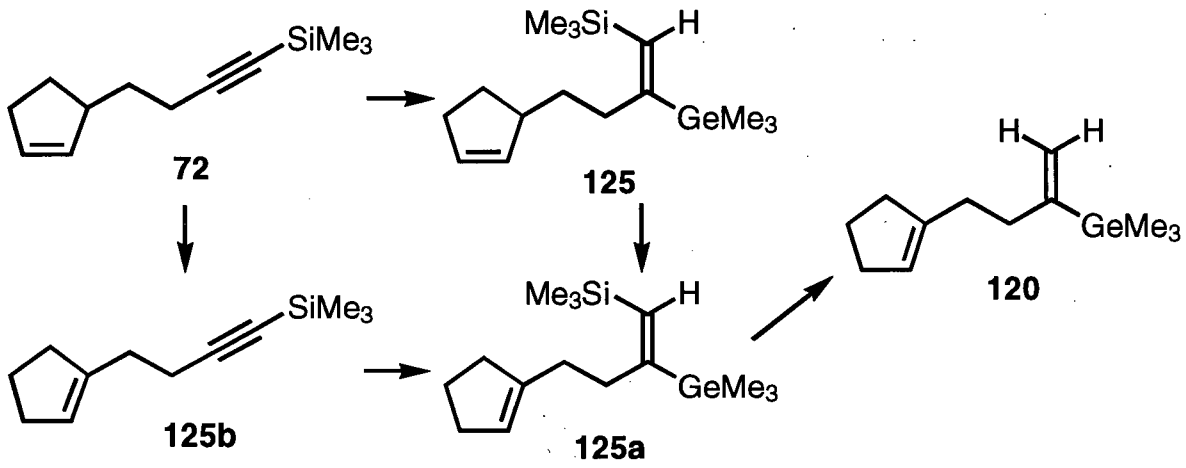
The second by-product that arose from the synthesis of **92** was hex-5-en-1-ol (**95**), isolated as a mixture with an equal amount of **92** (≈3% combined). The structural assignment related to **95** was based on the examination of the vinylic region of the ^{1}H NMR spectrum of this mixture. Thus, the spectrum exhibited the following distinctive signals: a one-proton doublet of doublets of triplets (J = 17.0, 10.2 and 6.8 Hz) at δ 5.79, a one-proton doublet of doublets (J = 17.0 and 2.0 Hz) at δ 4.99 and a one-proton doublet of doublets (J = 10.2 and 2.0 Hz) at δ 4.94. Presumably, hex-5-en-1-ol (**95**) is produced by protiodemetallation of one of the isomers generated in trace amounts during the hydrogermylation of **61** (for a complete discussion of an identical transformation see section 2.1.4.3.4, p 57 ff.).



113

Secondly, the preparation of 2-trimethylgermyldodec-1-ene (**116**) from 1-trimethylsilyldodec-1-yne (**64**) (**Table 2**, entry 3) also yielded a small amount (≈1.5%) of the corresponding monosubstituted alkene, dodec-1-ene (**113**). The ^{1}H NMR data for this compound are consistent with that reported earlier (see **Equation 14** and the accompanying discussion in section 2.1.4.3.4, p 57 ff.). Although the corresponding alk-1-enes were not isolated from the hydrogermylations of the other 1-trimethylsilylalk-1-ynes depicted in **Table 2**, it can be assumed that the alk-1-enes were generated in trace amounts in all cases and were separated during the purification procedures.

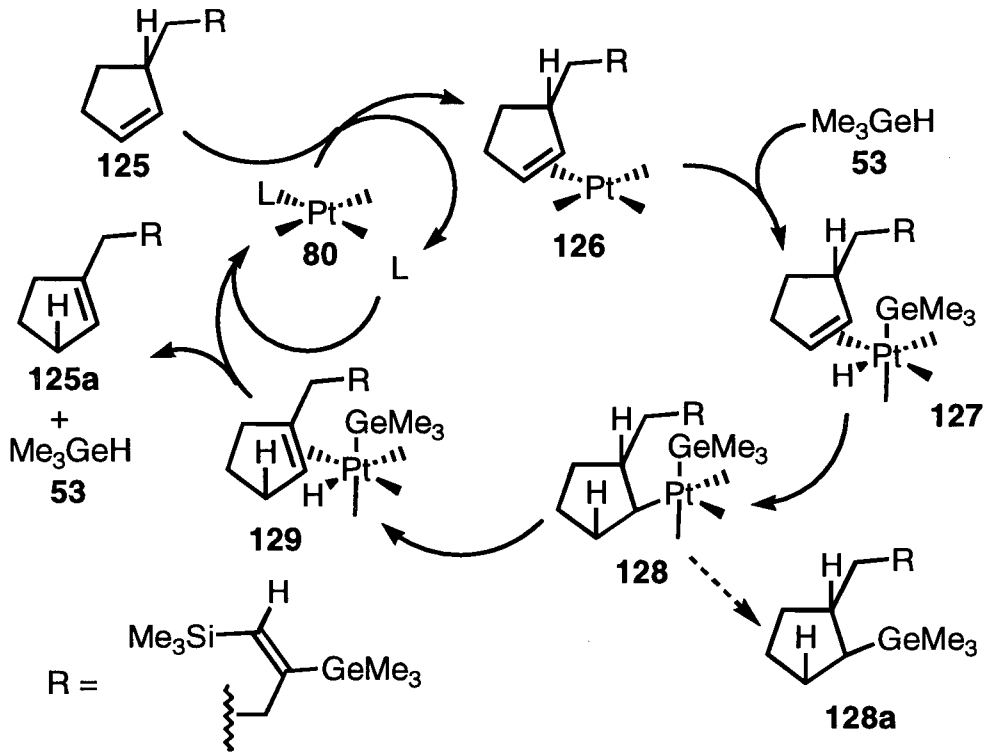
Thirdly, during the transformation of **72** into the product **120** (**Table 2**, entry 7) the cyclopentene alkene function underwent isomerization. The fact that compound **72** had undergone isomerization was established as follows. GLC analysis of the crude hydrogermylation mixture indicated the presence of one major component. ^{1}H NMR spectroscopic analysis of this crude mixture showed that the cyclopentene alkene function of this component had isomerized during the course of the hydrogermylation. This conclusion was based on the examination of the vinylic region of the spectrum which exhibited a one-proton singlet at δ 5.82 and a one-proton triplet (J ≈2 Hz) at δ 5.33. The singlet (δ 5.82) was assigned to the vinylic proton geminal to the Me_3Si- group in **125a** (**Scheme 26**), whereas the triplet (δ 5.33) was assigned to the cyclopentene vinylic proton.



Scheme 26

During a duplicate experiment, periodic GLC analyses of aliquots of the hydrogermylation mixture of **72** suggested that the starting material also underwent isomerization, to **125b** (**Scheme 26**). After 2 h at room temperature, an aliquot of the reaction mixture was withdrawn. After isolation and purification, GLC and ^{1}H NMR spectroscopic analyses of the unreacted 1-trimethylsilylalk-1-yne indicated the presence of two compounds. The vinylic region of the ^{1}H NMR spectrum indicated three one-proton signals: δ 5.73–5.70 (m), δ 5.67–5.64 (m), 5.33 (t, J = ≈2 Hz). The triplet at δ 5.33 was attributed to **125b** whereas the two multiplet were from **72**. After 8 h at room temperature, the hydrogermylation of **72** and **125b** was essentially complete. GLC analysis of an aliquot of the mixture at this time indicated that **125** and **125a** were present in a 1:12 ratio. TLC analysis of this mixture revealed that it would not be possible to separate **125** from **125a** by conventional chromatography. The reaction mixture was therefore allowed to stir at room temperature for an additional 13 h (total of 21 h), at which time the isomerization of **125** into **125a** was essentially complete (**125**:**125a** 1:>30). Protiodesilylation of the latter mixture under standard conditions yielded

essentially pure **120**.

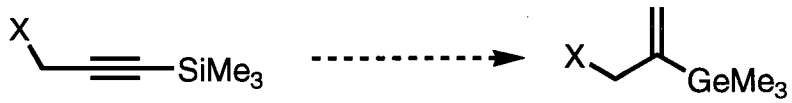


Scheme 27

Scheme 27 depicts a pathway, analogous to that proposed by Harrod and Chalk[49,51] for the isomerization of alkenes by group VIII metal hydrides complexes, that can account for the isomerization of **125** into **125a**. Thus, coordination of the active form of the catalyst **80** to the cyclopentene alkene function of **125** would generate the π-complex **126**. Oxidative addition of trimethylgermane (**53**) would give **127**, which can subsequently undergo hydrogen transfer to form the alkyl platinate **128**. The latter can loose the newly incorporated elements, hydrogen and platinum, but via a different pathway to produce the isomerized π-complex **129**. Decomplexation and reductive elimination of trimethylgermane (**53**) regenerates the catalyst **80** and yields **125a**. Although the isomerization of **125** to **125a** is a rather facile process, at

no point in this study was the isomerization of the vinylgermane function of the products **92**, **115–121** in **Table 2** (p 66) ever observed. The isomerization of alkenes using group VIII metals hydrides is a well known process.[49,51,66,67]

The hydrogermylation of substituted alkenes through reductive elimination of alkyl platinates such as **128** to produce **128a** (**Scheme 27**) under these experimental conditions, although possible, is a slow process[65] compared to the hydrogermylation of alkyne functions.



(16)

(X = Cl, Br, OAc, $OSiMe_3$) (X = Cl, Br, OAc, OH)

A perusal of the structures of the 2-trimethylgermylalk-1-enes depicted in **Table 2** (p 66) reveals that none of the products are functionalized at the allylic position. This is not coincidental. Although several attempts were made to hydrogermylate propargylic substrates (**Equation 16**), reaction under standard conditions always gave rise to complex mixtures. Examination of the ^{1}H NMR spectrum of the crude reaction mixtures revealed that while the corresponding allylic products (X = Cl, Br, OAc, OH) were present, they were always accompanied by significant amounts of several by-products. Attempts to isolate and characterize these by-products proved unsuccessful. Investigations into the use of this method for the synthesis of 2-trimethylgermylalk-1-enes bearing an allylic functional group were therefore abandoned.

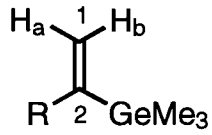
2.1.5.1 Characteristic Spectral Data of 2-Trimethylgermylalk-1-enes

The 2-trimethylgermylalk-1-enes prepared in this study possess a number of representative features which are correlated in their spectral data. **Table 3** summarizes the charac-

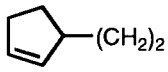
teristic IR, ^{1}H and ^{13}C NMR data of compounds **92** and **115–121**.

The carbon–carbon double bond stretching frequency of the 2-trimethylgermylalk-1-enes appears around 1606 cm^{-1} for most compounds in **Table 3**, whereas it appears at 1599 cm^{-1} for **118** (entry 5). The carbon–carbon double bond stretching frequencies of the 2-trimethylgermylalk-1-enes ($\approx$1606 cm^{-1}) is somewhat lower than those of the corresponding carbon analogs, for which the expected frequencies would be around 1660–1630 cm^{-1}.[68]

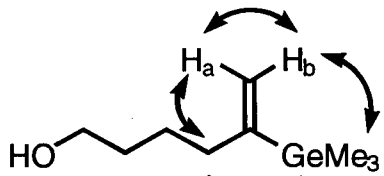
Table 3: Characteristic Spectral Data of 2-Trimethylgermylalk-1-enes **92, 115–121**



		IR	^{1}H NMR (δ ppm)[a]			^{13}C NMR (δ ppm)[b]		
Entry	R	ν C=C[c]	H-a[d]	H-b[d]	Me_3Ge-	C-1	C-2	Me_3Ge-
1	$HO(CH_2)_4$ **92**	1606	5.49	5.16	0.18	121.5	153.8	–1.9
2	$HO(CH_2)_2$ **115**	1606	5.61	5.32	0.21	124.6	150.3	–1.9
3	*n*-$C_{10}H_{21}$ **116**	n/a	5.48	5.14	0.18	121.3	154.4	–1.8
4	$Cl(CH_2)_3$ **117**	1607	5.53	5.22	0.20	122.5	152.2	–1.9
5	Ph **118**	1599	5.84	5.47	0.29	124.2	154.1	–1.1
6	$Me_3GeC(=CH_2)(CH_2)_2$ **119**	1607	5.52	5.18	0.20	121.4	153.8	–1.8
7	*c*-$C_5H_7(CH_2)_2$[e] **120**	1606	5.51	5.33	0.20	121.1	153.9	–1.9
8	$Me_3GeCO(CH_2)_2$ **121**	n/a	5.44	5.17	0.19	121.2	152.5	–2.1

[a] 400 MHz, $CDCl_3$. [b] 75 MHz, $CDCl_3$. [c] in cm^{-1}. [d] These assignments were made by correlation with the ^{1}H NMR NOE difference experiments performed on **92** (see text). [e] *c*-$C_5H_7(CH_2)_2$ = 

The ^{1}H NMR spectra of the 2-trimethylgermylalk-1-enes display three distinctive signals: the two alkenyl proton resonances due to H-a and H-b as well as the singlets due to the methyl protons from the Me_3Ge- group. The protons H-a and H-b give rise to doublets with a small mutual coupling constant (≈2.5 Hz). Since the H-a and H-b signals could not be assigned on the sole basis of their chemical shifts and coupling constants, ^{1}H NMR NOE difference experiments were performed on 5-trimethylgermylhex-5-en-1-ol (**92**).



92

Irradiation of the signal at δ 5.49 (H-a) generated an enhancement at δ 5.16 (H-b) as well as at δ 2.19 (allylic methylene protons). Alternatively, when the allylic methylene protons were irradiated (δ 2.19) an enhancement was observed at δ 5.49 (H-a) and at δ 0.18 (Me_3Ge-). These experiments demonstrate that H-a is the alkenyl proton trans to the Me_3Ge-group. When the signal at δ 5.16 (H-b) was irradiated, a signal enhancement was observed at δ 5.49 (H-a) and at δ 0.18 (Me_3Ge-). Furthermore, irradiation of the signal at δ 0.18 (Me_3Ge-) caused the signals at δ 5.16 (H-b) and at δ 2.19 (allylic methylene protons) to be enhanced. The latter experiments establish that the alkenyl proton H-b and the Me_3Ge- are cis to each other.

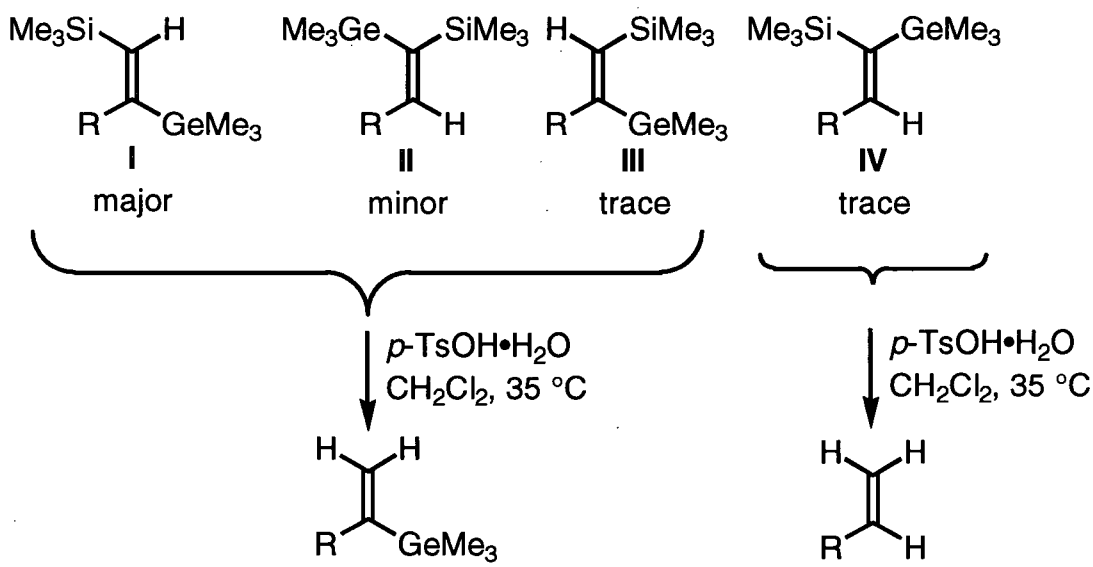
The assignments of H-a and H-b for the compounds **115–121** depicted in **Table 3** were made by correlation with the data obtained from the ^{1}H NMR NOE difference experiments for 5-trimethylgermylhex-5-en-1-ol (**92**). The signals for H-a, the protons trans to the Me_3Ge- group, appear between δ 5.61–5.44, whereas the resonances derived from the protons H-b, (cis to the Me_3Ge- group) appear between δ 5.33–5.14. The signals of H-a and H-b are somewhat deshielded in 1-phenyl-1-trimethylgermylethene (**118**) (entry 5). Thus, for **118**, H-a appears at δ 5.84, whereas H-b resonates at δ 5.47. The protons of the Me_3Ge- group for the compounds depicted in **Table 3** appear as a singlet between δ 0.18–0.20, except for **118** in which the Me_3Ge- protons resonate at δ 0.29.

Each of the ^{13}C NMR spectra of the 2-trimethylgermylalk-1-enes depicted in **Table 3** also exhibit three distinctive signals: the resonances due to the two alkenyl carbons C-1 and C-2 and the signal derived from the methyl carbons of the Me_3Ge- group. The signals from the terminal alkenyl carbons (C-1) appear within the region δ 125–121, whereas the C-2 alkenyl carbons give rise to resonances between δ 155 and 150. In each case, the alkenyl carbons C-1 and C-2 were assigned by examination of the intensity of their signals in the ^{13}C NMR spectra. The alkenyl carbon C-1 bearing two protons exhibits a more intense signal, due to a faster relaxation,[69] than the adjacent alkenyl carbon C-2, which has no attached protons. The signals of the methyl carbons of the Me_3Ge- group in the ^{13}C spectra appears near δ –1.8, except for compound **118** which exhibits the corresponding signal at δ –1.1.

2.1.6 CONCLUSIONS

The aim of this study was to develop a method that would allow the efficient preparation of diversely functionalized 2-trimethylgermylalk-1-enes from the corresponding 1-trimethylsilylalk-1-ynes.

The 1-trimethylsilylalk-1-ynes are easily prepared from the corresponding alk-1-ynes in high yield. 1-Trimethylsilylalk-1-ynes serve as good substrates for the $H_2PtCl_6 \cdot 6H_2O$ catalyzed addition of Me_3GeH (**53**) to the carbon–carbon triple bond. Although the regioselectivity of this type of addition was generally only moderate (≈12:1), this lack of selectivity turned out to be of no consequence.



The isomers of general structure **I–IV** were formed as a result of the hydrogermylation of the 1-trimethylsilylalk-1-ynes. The major component produced from this transformation was isomer **I**, whereas isomer **II** was the second most abundant. Isomers **III** and **IV** were generated in trace amounts.

Isomers **I** and **III** upon treatment with p-TsOH•H_2O in dichloromethane undergo

protiodesilylation to afford the 2-trimethylgermylalk-1-ene. Isomer **II**, when treated under identical experimental conditions, undergoes a 1,2 Me_3Ge- shift followed by protiodesilylation to also produce the 2-trimethylgermylalk-1-ene. Isomer **IV** undergoes sequential protio-degermylation *and* protiodesilylation to the corresponding alk-1-ene when treated with *p*-TsOH•H_2O in dichloromethane.

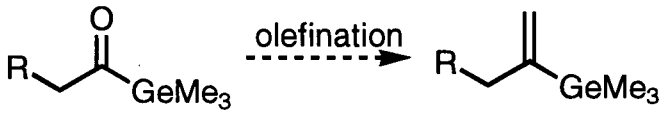
This two-step procedure for the conversion of 1-trimethylsilylalk-1-ynes into 2-trimethylgermylalk-1-enes is experimentally simple, accommodates a variety of functional groups and provides the products regioisomerically pure.

2.2 SYNTHESIS OF ACYLTRIMETHYLGERMANES VIA ADDITION OF (TRIMETHYLGERMYL)COPPER(I)–DIMETHYL SULFIDE TO ACYL ELECTROPHILES AND THEIR OLEFINATION TO 2-TRIMETHYLGERMYLALK-1-ENES

2.2.1 INTRODUCTORY REMARKS

As outlined in the Proposals (section 1.3, p 13 ff.), an approach to the synthesis of 2-trimethylgermylalk-1-enes, alternative to that involving catalyzed hydrogermylation of 1-trimethylsilylalk-1-ynes, was envisaged. This method, due to the inherent nature of the transformations involved, would preclude the formation of regioisomers.

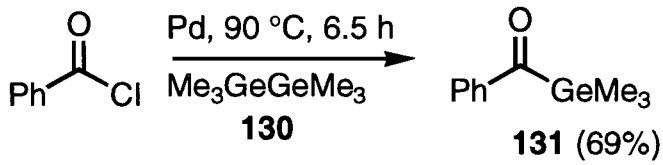
It was postulated that olefination of acyltrimethylgermanes of general structure **37** (**Equation 17**) would generate the corresponding 2-trimethylgermylalk-1-enes **26**. The first objective of this study was, therefore, to prepare the key acyltrimethylgermanes. A survey of the literature revealed that a number of methods have been reported for the preparation of acyltrialkylgermanes. A brief summary of these methods, which can be separated into four categories, is presented in the following pages.



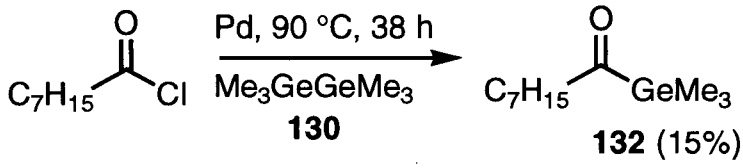
37 **26** **(17)**

In the first category, Yamamoto and co-workers[70] reported the preparation of the acyltrimethylgermanes **131** (**Equation 18**) and **132** (**Equation 19**) via a Pd-catalyzed acyl substitution with hexamethyldigermane (**130**). In this protocol, treatment of benzoyl chloride (**Equation 18**) with $Me_3GeGeMe_3$ (**130**) and a catalytic amount of Pd(0) at 90 °C for 6.5 h provided the acyltrimethylgermane **131** in 69% yield. Alternatively, when octanoyl chloride

(**Equation 19**) was allowed to react under similar conditions, the acyltrimethylgermane **132** was generated in 15% after 38 h at 90 °C. These results suggest that an aryloyl chloride is a much better substrate in this reaction than an alkanoyl chloride. Therefore, this method appears to be unsuitable for the preparation of diversely functionalized acyltrimethylgermanes.

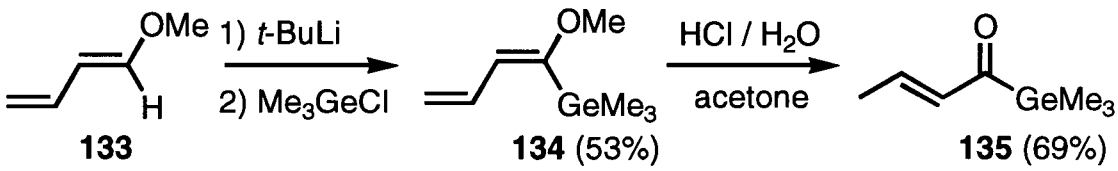


(**18**)



(**19**)

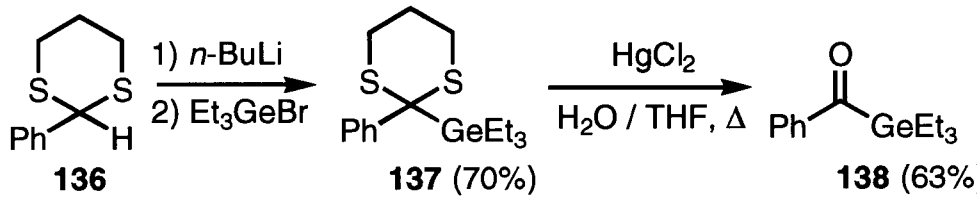
In the second category, a sequence of transformations generates a precursor to the acyltrimethylgermane in which the carbonyl group is masked. Hydrolysis of the latter function affords the final product. An example utilizing this strategy is depicted in **Equation 20**. Soderquist and Hassner[71] reported that lithiation of the dienol ether **133** with *tert*-butyllithium, followed by treatment of the corresponding lithio species with Me_3GeCl, afforded **134** in 53% yield. Subsequent hydrolysis of the latter in a dilute hydrochloric acid–acetone mixture, gave the unsaturated acyltrimethylgermane **135** in 69% yield.



(**20**)

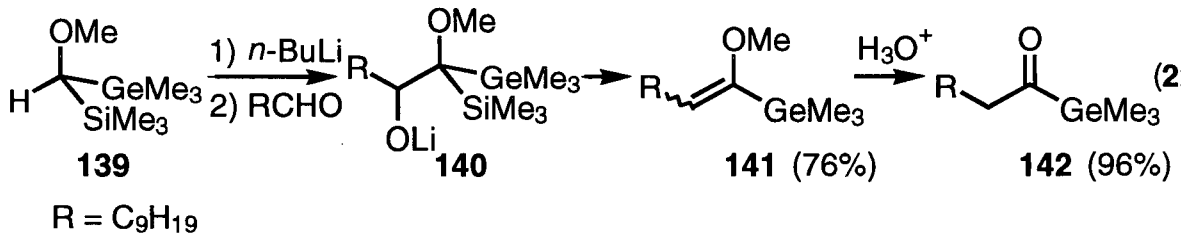
A similar approach was used by Brook and co-workers.[72] Thus, when the dithiane **136** (**Equation 21**) was deprotonated with *n*-butyllithium and the resulting lithio species treated with Et_3GeBr, the substituted dithiane **137** was obtained in 70% yield. Subsequent

hydrolysis of **137** with $HgCl_2$ in aqueous THF heated at reflux afforded the acyltriethylgermane **138** in 63% yield.



(21)

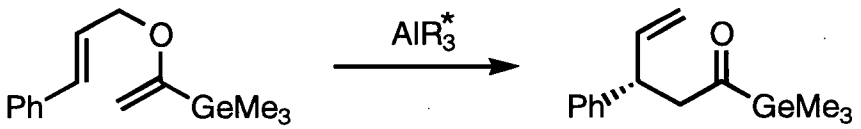
Equation 22 depicts a somewhat different, but related, method devised by Yoshida and co-workers[73] for the synthesis of acyltrimethylgermanes. In this protocol, the methyl ether **139** was treated with *n*-butyllithium and the resultant carbanion was allowed to react with decanal to form the alkoxide **140**. The latter underwent in situ carbon–silicon bond cleavage (Peterson reaction)[74] to form the enol ethers **141** (*E*/*Z* = 1:1) in 76% yield. This compound was subsequently hydrolyzed in aqueous acid to generate the acyltrimethylgermane **142** in 96% yield.



(22)

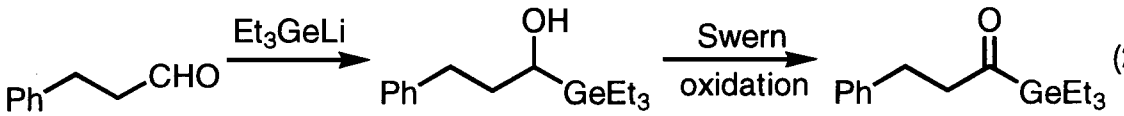
Although the above three methods (**Equations 20–22**) have, collectively, the potential to accomplish the preparation of a certain number of acyltrialkylgermanes, in poor to good overall yield, they all suffer from one limitation: a carbanion intermediate is formed at one stage during the sequence of transformations. The strongly nucleophilic and basic nature of such anions seriously limits the type of functional groups that could be introduced into the acyltrialkylgermanes.

In the third category, a Claisen rearrangement is used to introduce the carbonyl function of the acyltrimethylgermane. Yamamoto and co-workers[75] have shown that when the enol ether **143** (**Equation 23**) was treated with a chiral organoaluminum reagent, rearrangement occurred to generate the optically active acyltrimethylgermane **144** in 73% yield (91% ee). Although this method provides good yields of the acyltrimethylgermane, it is limited to the preparation of γ,δ-enones.



143 **144** (73%) **(23)**

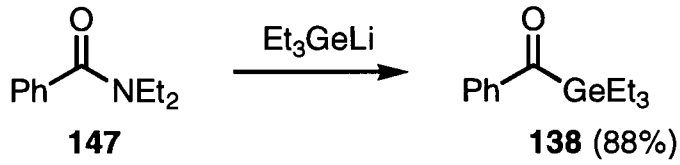
Finally, the fourth category of transformations employs the addition of a trialkylgermyllithium reagent to a carbonyl electrophile (**Equation 24**). In this protocol, described by Sato and co-workers,[76] treatment of 3-phenylpropanal with triethylgermyllithium afforded the alcohol **145** in 76% yield. Oxidation of the latter compound using the conditions of Swern[77] generated the acyltriethylgermane **146** in 72% yield.



145 (76%) **146** (72%) **(24)**

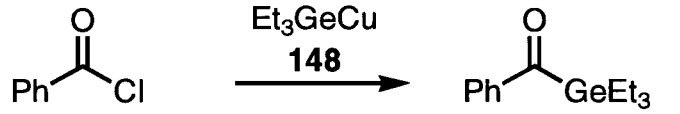
A similar method was developed by Vyazankin and co-workers,[78] in which triethylgermyllithium was allowed to react with *N,N*-dialkylamides (**Equation 25**). For example, when the amide **147** was treated with triethylgermyllithium, the acyltriethylgermane **138** was obtained in 88% yield. While the methods depicted in **Equations 24** and **25** provide the acyltriethylgermanes in good yields, they require the use of the triethylgermyllithium reagent, which is a powerful nucleophile. The use of such a nucleophile again limits the possible

functional groups that can be present in the acyltrialkylgermanes.



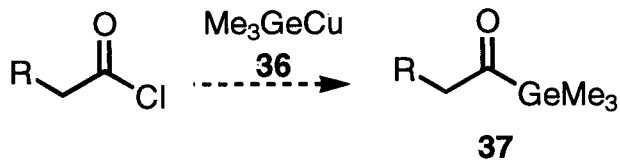
147 **138** (88%) **(25)**

Vyazankin and co-workers[78] noted that adding one equivalent of copper(I) iodide to triethylgermyllithium formed the corresponding copper reagent. When the (triethylgermyl)copper(I) reagent (**148**) (**Equation 26**) was allowed to react with benzoyl chloride at –30 °C, the acyltriethylgermane **138** was formed in 60% yield. No additional examples were reported.



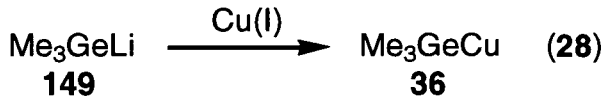
138 (60%) **(26)**

In light of this report, the utilization of a trimethylgermylcopper(I) reagent to effect the synthesis of acyltrimethylgermanes from acyl chlorides became appealing (**Equation 27**). Three questions then arose: i) can the nucleophilic substitution of an acyl chloride be effected by a reagent such as trimethylgermylcopper(I) (**36**) to generate the corresponding acyltrimethylgermane **37**, ii) is the transformation general, or to put it in other words, what functional groups, other than phenyl, are compatible with this transformation (since functionalization of the side chain was imperative) and iii) can the method be developed to provide the required products in high yields? The trimethylgermylcopper(I) reagent would certainly be a milder nucleophile than the corresponding lithio species and the experimental conditions would then possibly allow for a large number of functional groups to be present in the acyl chloride.



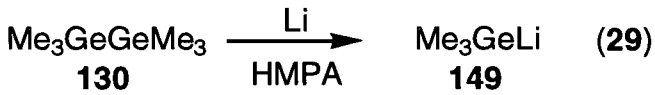
(27)

In order to prepare the trimethylgermylcopper(I) reagent (**36**), the corresponding lithio species **149** was required (**Equation 28**). Examination of the literature revealed that only two methods had been reported for the preparation of the trimethylgermyllithium (**149**).



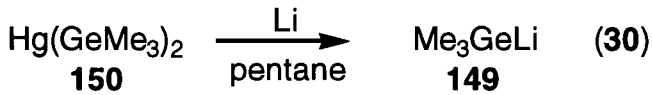
(28)

Bulten and Noltes[79] have developed a general method for the preparation of solutions of R_3GeM (R = alkyl, M = alkali metal) in HMPA. For example, in this protocol, when a solution of hexamethyldigermane (**130**) in HMPA was stirred with lithium metal, trimethylgermyllithium (**149**) was generated quantitatively (**Equation 29**).



(29)

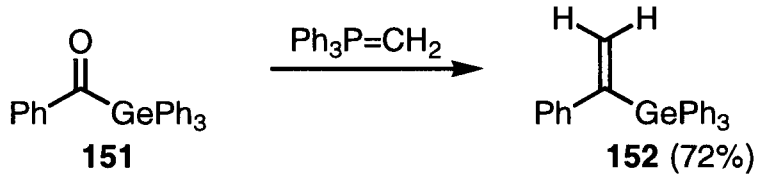
Alternatively, a solution of Me_3GeLi (**149**) has been prepared in pentane by Schumann and co-workers.[80] Thus, when bis(trimethylgermyl)mercury (**150**) was treated with lithium metal in pentane, Me_3GeLi (**149**) was obtained in 12% yield (**Equation 30**).



(30)

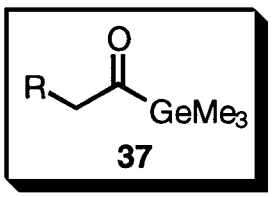
Although both methods (**Equations 29** and **30**) depicted above provide access to Me_3GeLi (**149**), the latter protocol, using bis(trimethylgermyl)mercury (**150**) (**Equation 30**), is clearly unsatisfactory due to the low yield of this reaction. On the other hand, the former method (**Equation 29**) generates Me_3GeLi (**149**), quantitatively, in HMPA solution. The

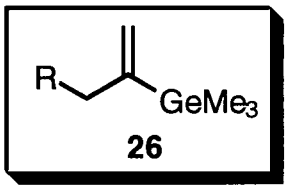
Me_3GeLi (**149**) needs to be converted in situ into the corresponding copper reagent **36** (see **Equation 28**) for reaction with the acyl chloride. Since most reactions involving organo-copper reagents are performed in etheral solvents, it was unclear what effects a co-solvent such as HMPA would have on the outcome of the reaction. The details of the investigations describing the development of a new method for the in situ preparation of the Me_3GeLi (**149**) in etheral solvent will be disclosed in the following section.



(**31**)

Finally, if the preparation of the acyltrimethylgermanes proved successful, their conversion into the corresponding 2-trialkylgermylalk-1-enes remained to be accomplished. Examination of the literature revealed that one example of olefination of an acyltriphenyl-germane into the corresponding 2-triphenylgermylalk-1-ene had been reported. Brook and Fieldhouse[81] reported that when the acyltriphenylgermane **151** was treated with $Ph_3P{=}CH_2$, the 2-triphenylgermylalk-1-ene **152** was formed in 72% yield (**Equation 31**). Would the olefination depicted in **Equation 31** be applicable to the synthesis of the functionalized acyl-trimethylgermanes?





The answer to the questions raised in the previous pages, as well as the details of the investigations leading to the successful preparation of the acyltrimethylgermanes of general

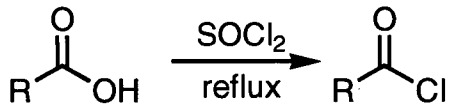
structure **37** and their olefination into the 2-trimethylgermylalk-1-enes **26** will be disclosed in the following sections.

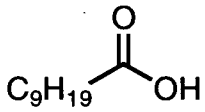
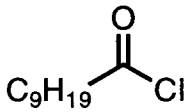
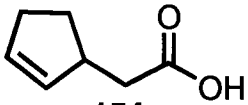
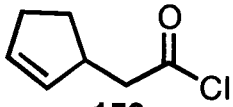
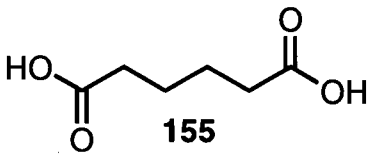
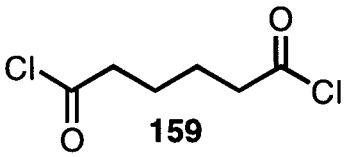
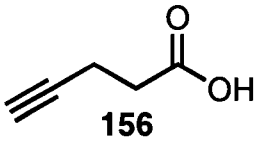
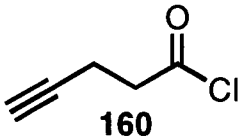
2.2.2 SYNTHESIS OF ACYLTRIMETHYLGERMANES FROM ACYL CHLORIDES

2.2.2.1 SYNTHESIS OF ACYL CHLORIDES

In order to prepare the acyl chlorides required for this study, the commercially available carboxylic acids **153–156** shown in **Table 4** were chosen as substrates. **Table 4** also contains a summary of the conversions of **153–156** into the acyl chlorides **157–160**.

Table 4: Preparation of the Acyl Chlorides **157–160**



Entry	Alkanoic Acid	Acyl Chloride	Yield (%)[a]
1	 **153**	 **157**	98
2	 **154**	 **158**	94
3	 **155**	 **159**	92
4	 **156**	 **160**	62[b]

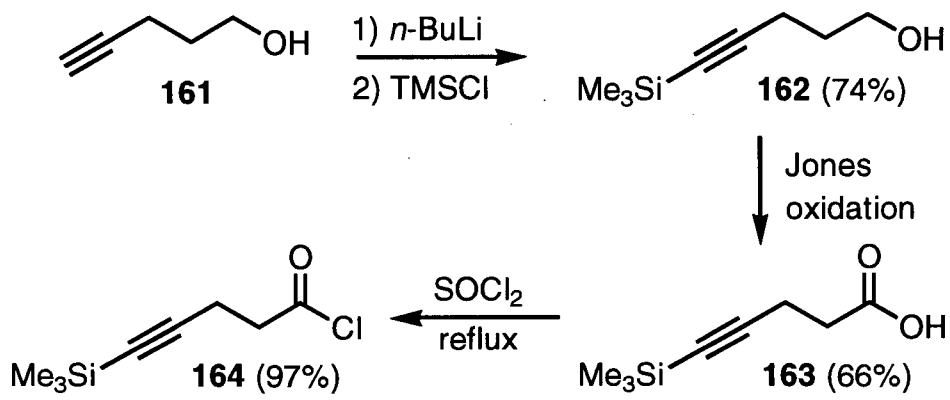
[a] Yield of isolated and purified product. [b] Volatile liquid.

The acyl chlorides depicted in **Table 4** were prepared in a straightforward manner.

The synthesis of decanoyl chloride (**157**), for example, was accomplished as follows. Decanoic acid (**153**) was treated with an excess of thionyl chloride and the reaction mixture was heated at reflux for 0.5 h. After the mixture had been cooled to room temperature, removal of the excess thionyl chloride under reduced pressure, followed by distillation (bulb-to-bulb 70–80 °C/0.06 Torr, lit. bp 94–96 °C/5 Torr[82]) of the residue, afforded decanoyl chloride (**157**) in 98% yield as a clear colorless oil.

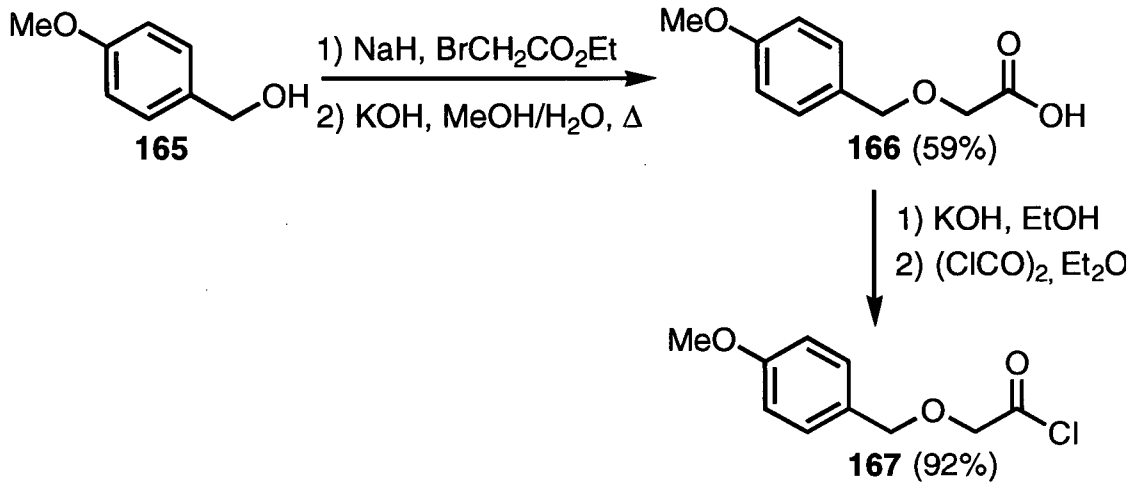
The acyl chlorides **158–160** were obtained in a manner identical with that outlined above. Although the acyl chlorides **157** and **159** are commercially available, they were prepared by this simple method since the corresponding alkanoic acids were readily available.

Two additional substrates were prepared for this study. The first, 5-trimethylsilylpent-4-ynoyl chloride (**164**), was synthesized from pent-4-yn-1-ol (**161**) via a three step sequence, reported by Utimoto and co-workers,[83] as outlined in **Scheme 28**. A solution of **161** in etheral solvent was treated sequentially with a solution of *n*-butyllithium and chlorotrimethylsilane. Subsequent treatment of the mixture with aqueous acid afforded 5-trimethylsilylpent-4-yn-1-ol (**162**) in 74% yield. Jones oxidation of the latter compound gave 5-trimethylsilylpent-4-ynoic acid (**163**) in 66% yield.[84] This alkanoic acid was treated with thionyl chloride, as described above, to generate 5-trimethylsilylpent-4-ynoyl chloride (**164**) in 97% yield.



Scheme 28

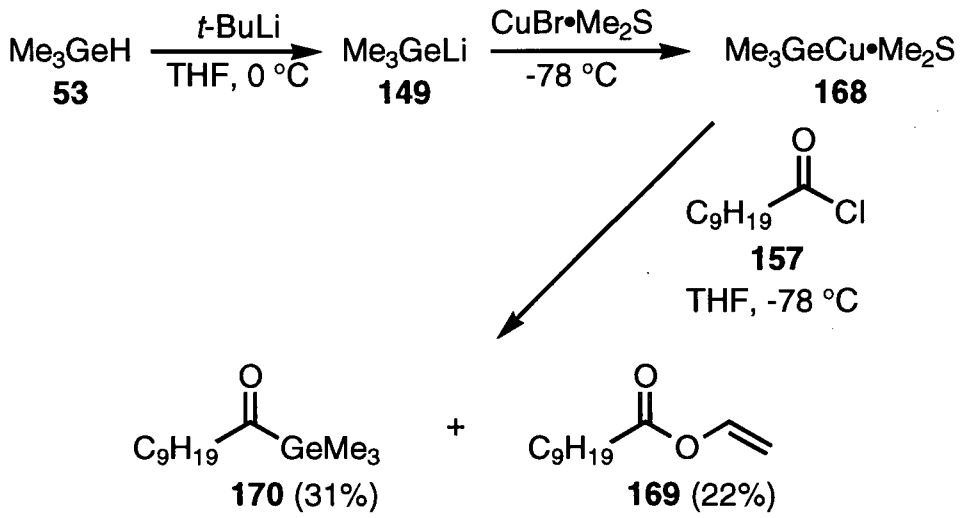
The second substrate, ((4-methoxybenzyl)oxy)acetyl chloride (**167**), was prepared via a three step sequence from (4-methoxyphenyl)methanol (**165**), via a procedure reported by Kukla and Fortunato[85] for a related substrate, as outlined in **Scheme 29**. Treatment of an excess of (4-methoxyphenyl)methanol (**165**) with sodium hydride, followed by addition of ethyl bromoacetate and subsequent saponification of the mixture, resulted in the formation of ((4-methoxybenzyl)oxy)acetic acid (**166**) in 59% yield. Attempted formation of the acyl chloride **167** from **166** under standard conditions (thionyl chloride, reflux) failed to generate the expected product. However, a procedure to form acyl chlorides under neutral conditions reported by Beeby[86] proved to be successful. Thus, treatment of the alkanoic acid **166** with a solution of potassium hydroxide in ethanol formed a precipitate, the potassium salt of **166**, which was collected by suction filtration. This salt was subsequently treated with oxalyl chloride in dry diethyl ether to afford ((4-methoxybenzyl)oxy)acetyl chloride (**167**) in 92% yield from **166**.



Scheme 29

2.2.2.2 PREPARATION OF TRIMETHYLGERMYLLITHIUM (**149**) AND (TRIMETHYLGERMYL)-COPPER(I)–DIMETHYL SULFIDE (**168**)

As outlined in the Introductory Remarks (section 2.2.1, p 81 ff.), the reported procedures[79,80] for the preparation of Me_3GeLi (**149**) were unsuitable for the present study. Following initial investigations performed by Dr. Guy Plourde from our laboratories, attention was focused on the development of a satisfactory preparation of Me_3GeLi (**149**) for which the following protocol was devised. Treatment of 1.4 equivalents of Me_3GeH (**53**) in THF (≈0.18 M solution of Me_3GeH in THF) with 1.2 equivalents of a solution of *tert*-butyllithium at 0 °C for 20 min afforded a clear and colorless solution (**Scheme 30**). Indications that metallation had occurred were the rapid disappearance of the initial yellow color, caused by the presence of *tert*-butyllithium in THF.



Scheme 30

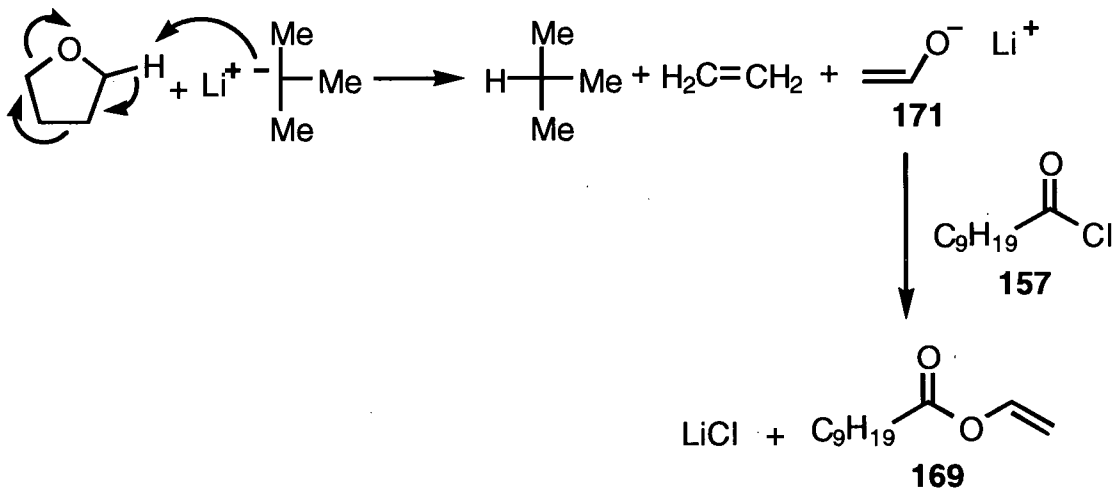
In order to assess the extent of the formation of the lithium reagent **149**, it was decided to form the corresponding copper reagent **168** in situ, and to treat the latter with an acyl electrophile (**Scheme 30**). Thus, addition of 1.2 equivalents of $CuBr{\bullet}Me_2S$ to the resultant solution of Me_3GeLi (**149**) ("inverse" addition method) at –78 °C, followed by stirring of this mixture at –78 °C for 45 min, resulted in the formation of a dark red–black solution of the reagent $Me_3GeCu{\bullet}Me_2S$ (**168**). This solution was treated with one equivalent of decanoyl chloride (**157**), the resultant reaction mixture was stirred for an hour at –78 °C, and then was treated with an aqueous solution of NH_4Cl–NH_4OH. Isolation and flash chromatography of the crude product afforded two compounds.

The first component to be eluted, obtained in 22% yield, was assigned structure **169** (**Scheme 30**). This assignment was established as follows. The ^1H NMR (400 MHz, $CDCl_3$) spectrum of **169** exhibited a one-proton doublet of doublets (J = 14.0 and 6.3 Hz) at δ 7.27, a one-proton doublet of doublets (J = 14.0 and 1.5 Hz) at δ 4.86, a one-proton doublet of

doublets (J = 6.3 and 1.5 Hz) at δ 4.54, a two-proton triplet (J = 7.5 Hz) at δ 2.36, a two-proton multiplet at δ 1.69–1.57, a twelve-proton multiplet at δ 1.37–1.16 and a three-proton broad triplet (J = 6.8 Hz) at δ 0.86. Additional evidence supporting the structural assignment of **169** was provided by the IR spectrum, which showed an intense band at 1758 cm^{-1} (ν C=O) as well as a band of medium intensity at 1648 cm^{-1} (ν C=C) for the vinyl ester function. These frequencies are in good agreement with the literature values for this type of functionality.[87]

The second compound to be eluted, obtained in 31% yield, was decanoyltrimethylgermane (**170**) (**Scheme 30**). The ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **170** exhibited a two-proton triplet (J = 7.4 Hz) at δ 2.58, a two-proton multiplet at δ 1.57–1.45, a twelve-proton multiplet at δ 1.39–1.18, a three-proton broad triplet (J = 6.8 Hz) at δ 0.85 and a nine-proton singlet at δ 0.31. Additional evidence to support the structural assignment of **170** was provided by the IR spectrum, which contained a band at 1658 cm^{-1} for the acyl germane carbonyl, as well as from HRMS analysis, which exhibited a signal at *m/z* 274.1354, in good agreement with the calculated value of 274.1352 for $C_{13}H_{28}{}^{74}GeO$.

Two conclusions were drawn from the experiment depicted in **Scheme 30**. First, the formation of an acyltrimethylgermane via addition of (trimethylgermyl)copper(I)–dimethyl sulfide reagent (**168**) to an acyl chloride is possible and, second, the lithiation of Me_3GeH (**53**) is incomplete, as indicated by the generation of the by-product **169** (vide infra).



Scheme 31

Scheme 31 depicts a rationale for the formation of **169**. Under the reaction conditions used for the lithiation of Me_3GeH (**53**), competitive fragmentation of THF by *tert*-butyl-lithium[88] generates isobutane, ethylene and the lithium enolate of acetaldehyde **171**. Upon addition of decanoyl chloride (**157**) to the reaction mixture, **171** reacts with **157** to form **169** and lithium chloride.

Further investigations pertaining to the lithiation of Me_3GeH (**53**) showed that deprotonation of **53** with *tert*-butyllithium did not occur when diethyl ether was used as solvent or in the absence of solvent (neat), even at room temperature. Moreover, the formation of Me_3GeLi (**149**) in THF with *tert*-butyllithium did not occur below –15 °C. In order to minimize the fragmentation of THF by *tert*-butyllithium, the lithiation of Me_3GeH (**53**) was performed in the presence of a *minimum* amount of THF.

$$\underset{\mathbf{53}}{Me_3GeH} \xrightarrow[\text{THF, -10 °C}]{t\text{-BuLi}} \underset{\mathbf{149}}{Me_3GeLi} \xrightarrow[\text{THF, -78 °C}]{C_{10}H_{21}Br} \underset{\mathbf{172}}{C_{10}H_{21}GeMe_3} \quad (\mathbf{32})$$

Thus, treatment of a cold (–10 °C) solution of 1.2 equivalents of trimethylgermane

(**53**) in anhydrous THF (≈2.5 M solution of Me_3GeH in THF) with 1 equivalent of a solution of *tert*-butyllithium for 5 min generated Me_3GeLi (**149**) (**Equation 32**). In order to quantify the yield of **149**, the following experiment was carried out. The solution of Me_3GeLi (**149**) was diluted with additional anhydrous THF (final concentration of ≈0.6 M with respect to Me_3GeH), was then cooled to –78 °C and 1.2 equivalents of 1-bromodecane were added. After the mixture had been warmed to room temperature, an internal standard was added and the mixture was treated with water and diethyl ether (for complete experimental details, see section 3.3.2.1.3, p 222). GLC analysis of an aliquot of this mixture revealed that 1-trimethylgermyldecane (**172**) (**Equation 32**), and, therefore, Me_3GeLi (**149**), had been formed in >97% yield. The remaining 2–3% can be accounted for by the formation of the lithium enolate of acetaldehyde **171** (vide infra), from the reaction of *tert*-butyllithium with THF (see **Scheme 31**).

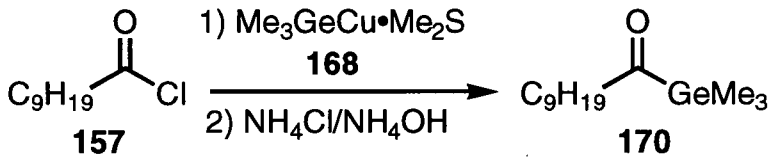
$$Et_3GeH \xrightarrow[\text{THF, 0 °C, 30 min}]{t\text{-BuLi, TMEDA}} Et_3GeLi \quad \textbf{(33)}$$

During the course of these investigations, a preparation of Et_3GeLi via a related method was reported by Takeda and co-workers.[89] In this protocol, a solution of one equivalent of Et_3GeH in THF (≈1 M solution of Et_3GeH in THF) was treated with 1.1 equivalents of a solution of *tert*-butyllithium and 1.1 equivalents of *N,N,N′,N′*-tetramethylethylenediamine (TMEDA) at 0 °C for 30 min to generate Et_3GeLi quantitatively (**Equation 33**). However, since 1.1 equivalents of *tert*-butyllithium were employed, it is likely that under the experimental conditions used the excess reagent (≈0.1 equivalent) reacted with THF to form the lithium enolate of acetaldehyde **171** (see **Scheme 31**).

2.2.2.3 Synthesis of Acyltrimethylgermanes

As described in the previous section, the formation of decanoyltrimethylgermane (**170**) via reaction of $Me_3GeCu{\bullet}Me_2S$ (**168**) with decanoyl chloride (**157**) is possible. Further investigations were therefore conducted with the same substrate, in an effort to improve the yield of decanoyltrimethylgermane (**170**) using this method.

Table 5: Optimization of the Experimental Conditions for the Formation of Decanoyltrimethylgermane (**170**)

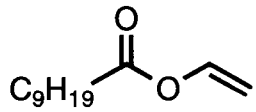


Entry	$Me_3GeCu{\bullet}Me_2S$ (equiv)	T (°C), time	Yield[a]
1	1.2[b,c]	–78, 1 h	31
2	1.2[c]	–78, 0.3 h	43
3	1.2[c]	–78, 1 h; –30, 2 h	70
4	2.2[c]	–78, 1 h; –30, 2 h	71
5	1.5[d]	–78, 1 h; –30, 2 h	81
6	1.5[d] / 1 equiv TMSCl	–78, 1 h; –30, 2 h	92

[a] Yield of isolated and purified product. [b] Preparation of Me_3GeLi under non-optimum conditions; see text. [c] Preparation of $Me_3GeCu{\bullet}Me_2S$ via the "inverse" addition method; see text. [d] Preparation of $Me_3GeCu{\bullet}Me_2S$ via the "normal" addition method; see text.

Table 5 summarizes the key experimental modifications that rendered the transformation synthetically useful. Entry 1 displays the initial conditions under which **170** was synthesized in 31% yield. This experiment was used to assess the formation of the Me_3GeLi

(**149**), via lithiation of Me_3GeH (**53**), in a solution of THF (see previous section, 2.2.2.2, p 92 ff.). In entry 2, the product was obtained in 43% yield, using the optimized preparation of Me_3GeLi (**149**) (see previous section, 2.2.2.2, p 92 ff.) and, consequently, the formation of the by-product **169** was significantly reduced.

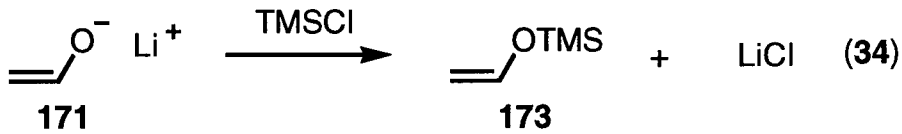


169

The yield of decanoyltrimethylgermane (**170**) increased dramatically when the reaction mixture was stirred for 1 h at –78 °C, was warmed to –30 °C and then was allowed to stir for an additional 2 h (entry 3). This result suggests that the conversion of the starting material is incomplete at –78 °C. When the same experiment was repeated using 2.2 equivalents of $Me_3GeCu{\bullet}Me_2S$ (**168**) (entry 4), the yield of **170** was unchanged.

In entry 5, the reagent $Me_3GeCu{\bullet}Me_2S$ (**168**) was prepared via a protocol very similar to that previously described, but with a minor modification. In entries 1–4, the reagent **168** was obtained by addition of solid $CuBr{\bullet}Me_2S$ *to* a solution of the Me_3GeLi (**149**) in THF at –78 °C ("inverse" addition), as described in the previous section (2.2.2.2, p 92 ff.). In entry 5, the $Me_3GeCu{\bullet}Me_2S$ (**168**) was prepared by addition, via a cannula, of a solution of reagent **149** *to* a suspension of $CuBr{\bullet}Me_2S$ in THF at –78 °C ("normal" addition). While both of these preparations should generate the same reagent, $Me_3GeCu{\bullet}Me_2S$ (**168**), it appears that the "normal" addition method affords decanoyltrimethylgermane (**170**) in better yield than the "inverse" addition method. The fact that 1.5 equivalents of **168** were used in entry 5, as opposed to 1.2 equivalents, is not likely to be responsible for the increase in yield (compare, for example, entries 3 and 4). The reasons for the different yields of **170** obtained from the

preparation of $Me_3GeCu{\bullet}Me_2S$ (**168**) via the "normal" and "inverse" addition methods remain unclear.



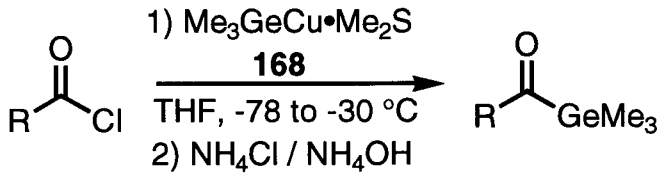
The optimized preparation of Me_3GeLi (**149**) virtually eliminated the formation of **169** in the reactions summarized in entries 2–5. However, GLC analyses of aliquots of the crude reaction mixtures indicated the presence of trace amounts (≈2–3%) of **169**. In an attempt to completely inhibit the production of **169**, the solution of $Me_3GeCu{\bullet}Me_2S$ (**168**) was treated with chlorotrimethylsilane *prior* to the addition of decanoyl chloride (**157**). It was anticipated that the lithium enolate of acetaldehyde **171** would react with chlorotrimethylsilane to form the corresponding vinyl silyl ether **173** (**Equation 34**) and, consequently, suppress the formation of **169**. Thus, when a solution of 1.5 equivalents of $Me_3GeCu{\bullet}Me_2S$ (**168**) and one equivalent of chlorotrimethylsilane in THF were treated with one equivalent of the acyl chloride **157** (**Table 5**, entry 6), decanoyltrimethylgermane (**170**) was obtained in 92% yield. GLC analysis of an aliquot of the crude reaction mixture showed that the formation of **169** had been completely inhibited. Additional benefits of chlorotrimethylsilane as an additive in the formation of acyltrimethylgermanes in high yield will be discussed on the following pages. The experimental conditions outlined above to prepare decanoyltrimethylgermane (**170**) proved to be general for a number of diversely functionalized acyl chlorides, as described below.

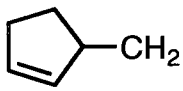
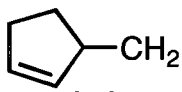
The acyl chlorides **157**, **158**, **174**, **167**, **175–177**, **159**, **160** and **164** depicted in **Table 6** were chosen as substrates. **Table 6** also contains a summary of the conversions of these

acyl chlorides into the acyltrimethylgermanes **170**, **178–185** and **114**.

The substrates **157–160**, **164** and **167** were synthesized as described previously (section 2.2.2, p 89 ff.), whereas the acyl chlorides **174–177** are commercially available.

Table 6: Preparation of the Acyltrimethylgermanes **170, 178–184** and **114**



	Acyl Chloride	Acyltrimethylgermane	Yield (%)[a]		
Entry[b]	R	R	without additive	with TMSCl[c]	with TMSBr[d]
1	C_9H_{19} **157**	C_9H_{19} **170**	81	92	n/a
2	 **158**	 **178**	n/a	88	n/a
3	c-C_6H_{11} **174**	c-C_6H_{11} **179**	n/a	88	n/a
4	4-MeO(C_6H_4)CH_2OCH_2 **167**	4-MeO(C_6H_4)CH_2OCH_2 **180**	n/a	82	n/a
5	(C_6H_5)CH_2OCH_2 **175**	(C_6H_5)CH_2OCH_2 **181**	63[e,f]	89	0[e,f]
6	Cl(CH_2)$_4$ **176**	Cl(CH_2)$_4$ **182**	n/a	90	n/a
7	Cl(CH_2)$_2$ **177**	Cl(CH_2)$_2$ **183**	23	35[g]	58[f]
8[h]	ClCO(CH_2)$_4$ **159**	$Me_3GeCO(CH_2)_4$ **184**	33[e]	92	n/a
9[e,i]	HC≡C(CH_2)$_2$ **160**	HC≡C(CH_2)$_2$ **185**	0[j]	0	n/a
10	$Me_3SiC{\equiv}C(CH_2)_2$ **164**	$Me_3SiC{\equiv}C(CH_2)_2$ **114**	n/a	82	n/a

[a] Yield of isolated and purified product. [b] 1.5 equiv of $Me_3GeCu{\bullet}Me_2S$, prepared via the "normal" addition method, were used unless otherwise stated. [c] One equiv of TMSCl was used unless otherwise stated. [d] 2.5–4 equiv of TMSBr were used. [e] $Me_3GeCu{\bullet}Me_2S$ was prepared via the "inverse" addition method. [f] 2.2 equiv of $Me_3GeCu{\bullet}Me_2S$ were used. [g] 4.5 equiv of TMSCl were used. [h] The amounts of reagents were doubled for this experiment. [i] 1–1.06 equiv of $Me_3GeCu{\bullet}Me_2S$ were used, and the reaction was carried out at –78 °C for 2.5–3 h. [j] 2.5 equiv of pyridine and 2 equiv of dry methanol were added prior to work-up.

The results summarized in entry 1 of **Table 6** for the synthesis of decanoyltrimethylgermane (**170**) have already been discussed in detail (see **Table 5**, p 97 and accompanying text). The synthesis of (cyclopent-2-en-1-yl)acetyltrimethylgermane (**178**) (entry 2) was accomplished in the following manner. A cold (–78 °C) solution of $Me_3GeCu{\bullet}Me_2S$ (**168**) (1.5 equiv) prepared via the "normal" addition method (vide supra) in dry THF (≈0.18 M) was treated sequentially with chlorotrimethylsilane (1 equiv) and (cyclopent-2-en-1-yl)acetyl chloride (**158**). The reaction mixture was stirred at –78 °C for 1 h, then was warmed to –30 °C and was allowed to stir for an additional 2 h. After isolation and purification of the crude product, (cyclopent-2-en-1-yl)acetyltrimethylgermane (**178**) was obtained in 88% yield as a light yellow oil.

The remainder of the acyltrimethylgermanes listed in **Table 6**, except for **185**, were synthesized from the corresponding acyl chlorides in a manner similar to or identical with that outlined above. In an effort to further understand the (additional) benefits of using chlorotrimethylsilane as additive, a number of selected substrates were also allowed to react with $Me_3GeCu{\bullet}Me_2S$ (**168**) *in the absence of* chlorotrimethylsilane, whereas two of these substrates were also allowed to undergo reaction with **168** in the presence of bromotrimethylsilane as additive.

The acyl chloride **174**, which bears a "bulky" cyclohexyl group α to the carbonyl, was smoothly converted into the corresponding acyltrimethylgermane under standard experimental conditions (entry 3).

This transformation is also compatible with benzylic ethers. ((4-Methoxybenzyl)oxy)-acetyl chloride (**167**) (entry 4) was converted into ((4-methoxybenzyl)oxy)acetyltrimethyl-

germane (**180**) in 82% yield. On the other hand, treatment of (benzyloxy)acetyl chloride (**175**) (entry 5) with $Me_3GeCu{\bullet}Me_2S$ (**168**) prepared via the "inverse" addition method (vide supra) without additive afforded (benzyloxy)acetyltrimethylgermane (**181**) in 63% yield. Alternatively, when **175** was allowed to react with $Me_3GeCu{\bullet}Me_2S$ (**168**) (prepared via the "normal" addition method) in the presence of chlorotrimethylsilane, the yield of **181** was increased to 89%. Attempted conversion of **175** into **181** with 2.2 equivalents of $Me_3GeCu{\bullet}Me_2S$ (**168**) (prepared via the "inverse" addition method) using bromotrimethylsilane as additive failed to produce any of the "expected" product.

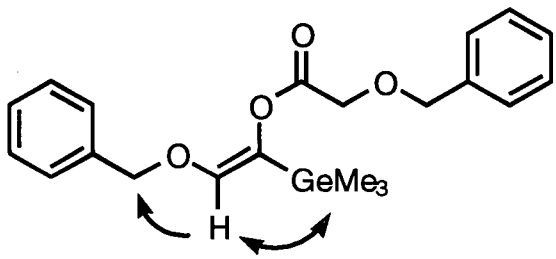
5-Chloropentanoyl chloride (**176**) (entry 6) was efficiently (90% yield) converted into 5-chloropentanoyltrimethylgermane (**182**) under standard experimental conditions. Reaction of 3-chloropropanoyltrimethylgermane (**177**) with reagent **168** (entry 7) in the absence of additive afforded 3-chloropropanoyltrimethylgermane (**183**) in only 23% yield. On the other hand, treatment of **177** with **168** in the presence of 4.5 equivalents of chlorotrimethylsilane gave the acyltrimethylgermane **183** in 35% yield. When the same reaction was performed using 2.2 equivalents of $Me_3GeCu{\bullet}Me_2S$ (**168**) and bromotrimethylsilane (4.5 equiv) as additive, **183** was generated in 58% yield.

When adipoyl chloride (**159**) (entry 8) was treated with three equivalents of $Me_3GeCu{\bullet}Me_2S$ (**168**) (prepared via the "inverse" addition method) without chlorotrimethylsilane, the structurally novel hexanedioylbis(trimethylgermane) (**184**) was obtained in 33% yield. On the other hand, when **159** was allowed to react with **168** (3 equiv) in the presence of two equivalents of chlorotrimethylsilane, the product **184** was generated in 92% yield. Since **159** possesses two acyl chloride functions which can undergo reaction with **168**, the

amounts of reagents for this substrate were doubled.

Treatment of pent-4-ynoyl chloride (**160**) (entry 9) with approximately one equivalent of $Me_3GeCu{\bullet}Me_2S$ (**168**) at –78 °C for 2.5–3 h, with or without chlorotrimethylsilane, failed to produce the expected pent-4-ynoyltrimethylgermane (**185**). Remarkably, reaction of **168** with 5-trimethylsilylpent-4-ynoyl chloride (**164**), the Me_3Si- substituted analog of **160**, under standard conditions generated 5-trimethylsilylpent-4-ynoyltrimethylgermane (**114**) in 82% yield (entry 10).

The reactions summarized in entries 5, 7, 8 and 9 of **Table 6** require additional comments. During the purification of (benzyloxy)acetyltrimethylgermane (**181**) (entry 5), formed by reaction of **175** with $Me_3GeCu{\bullet}Me_2S$ (**168**) *in the absence* of chlorotrimethylsilane, a by-product was isolated in ≈2.5% yield. This material was assigned structure **186**, (*E*)-2-benzyloxy-1-(benzyloxy)acetoxy-1-trimethylgermylethene.

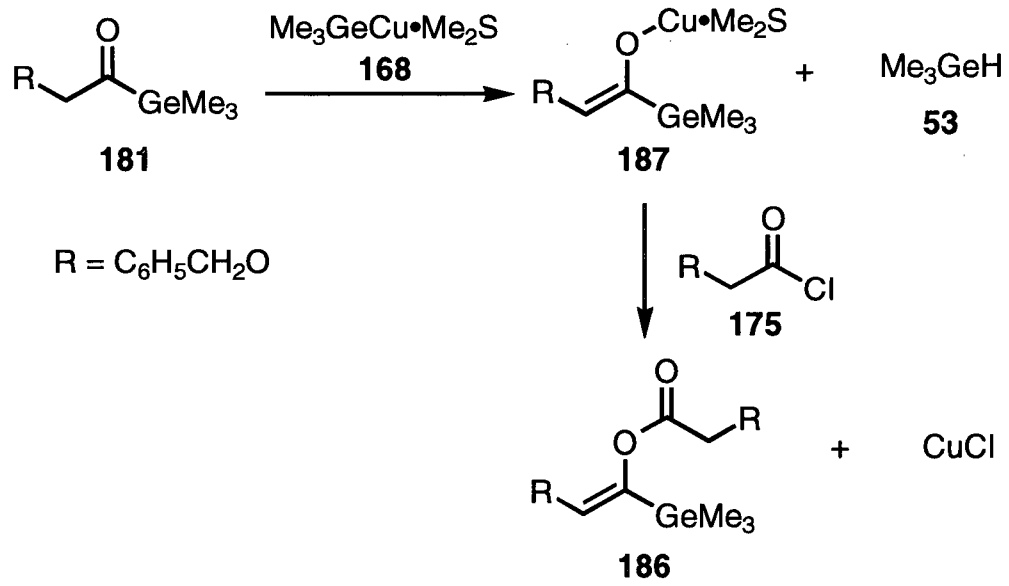


186

The assignment was based on the following data. The ^1H NMR (400 MHz, $CDCl_3$) spectrum exhibited a ten-proton multiplet at δ 7.52–7.23 (aromatic protons), a one-proton singlet at δ 5.87 (vinylic proton), three two-proton singlets at δ 4.84, 4.62 and 4.19 as well as a nine-proton singlet at δ 0.27 (Me_3Ge-). Additional evidence was provided by the IR spectrum of **186** which showed a strong band at 1760 cm^{-1} (ν C=O), together with HRMS

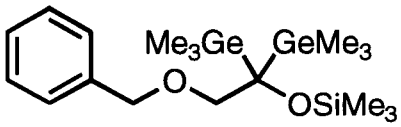
analysis which showed a signal at *m/z* 416.1043, a value identical with that calculated for $C_{21}H_{26}{}^{74}GeO_4$. To establish the geometry of the alkene function, ^{1}H NMR NOE difference experiments were performed. Thus, irradiation of the singlet at δ 5.87 (vinylic proton) caused the resonances at δ 4.84 (benzylic protons) and 0.27 (Me_3Ge-) to be enhanced. Alternatively, when the Me_3Ge- signal (δ 0.27) was irradiated, the vinylic proton (δ 5.87) was enhanced. These experiments establish the cis relationship between the vinylic proton and the Me_3Ge-group.

A possible rationale accounting for the formation of **186** is depicted in **Scheme 32**. Thus, during the course of the reaction of $Me_3GeCu{\bullet}Me_2S$ (**168**) with **181**, the reagent **168** may have served as a base to form a small amount of the copper enolate **187**, together with Me_3GeH (**53**), from the acyltrimethylgermane **181**. This enolate could then undergo *O*-acylation with **175**, still present in the reaction mixture, to afford the enol acetate **186**.



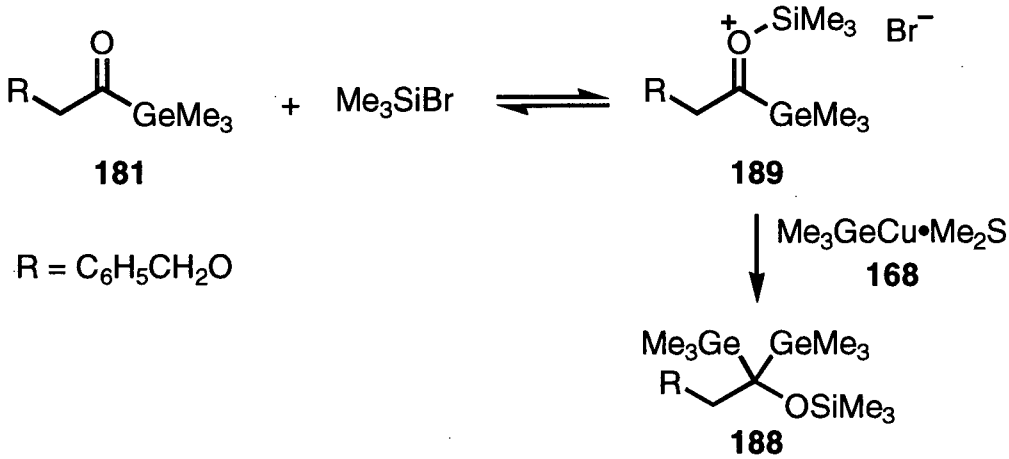
Scheme 32

When (benzyloxy)acetyl chloride (**175**) was allowed to react with **168** (**Table 6**, entry 5) in the presence of bromotrimethylsilane, none of the expected acyltrimethylgermane **181** was formed. The only product that was isolated from the complex mixture was assigned structure **188**, 2-benzyloxy-1-trimethylsilyloxy-1,1-bis(trimethylgermyl)ethane, which was obtained in 52% yield.



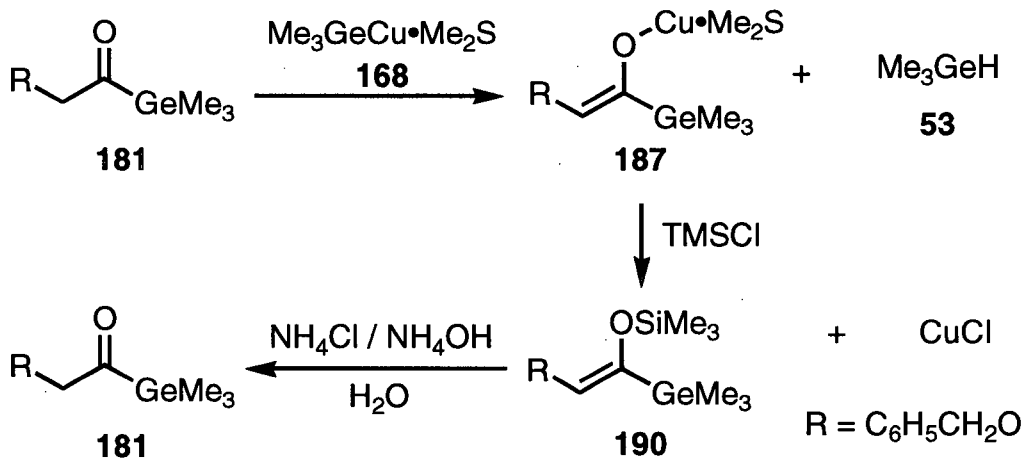
188

This assignment was based on the following data. The ^{1}H NMR (400 MHz, $CDCl_3$) spectrum exhibited a 5-proton multiplet at δ 7.45–7.35, a two-proton singlet at δ 4.43, a two-proton singlet at δ 3.77, an eighteen-proton singlet at δ 0.15 as well as a nine-proton singlet at δ 0.07. Additional evidence to support the structural assignment of **188** was provided from HRMS analysis which indicated a signal at *m/z* 443.0686 $(M - CH_3)^+$. This data is consistent with the calculated value of 443.0682 for $C_{17}H_{33}{}^{72}Ge^{74}GeO_2{}^{28}Si$.



Scheme 33

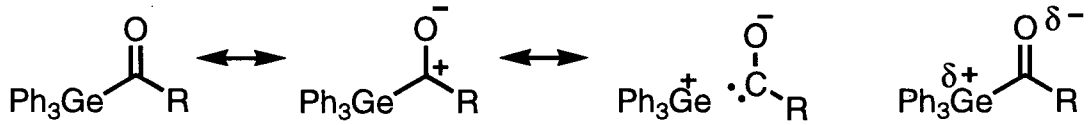
Scheme 33 depicts a possible reaction pathway that rationalizes the formation of **188**. During the course of the reaction of **181** with **168**, bromotrimethylsilane could have acted as a Lewis acid to form (reversibly) the oxonium ion **189** from the initially formed acyltrimethylgermane **181**, thus enhancing the electrophilic character of the carbonyl carbon. Subsequent nucleophilic addition of the $Me_3GeCu{\bullet}Me_2S$ (**168**) to **189** would generate the trimethylsilyl ether **188**.



Scheme 34

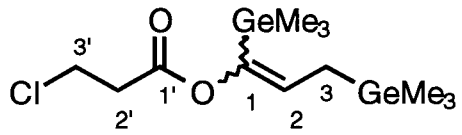
The data derived from the reaction of **168** with **175** (**Table 6**, entry 5) also shed some light on the possible role of chlorotrimethylsilane as additive. A mechanistic pathway rationalizing the role of chlorotrimethylsilane in the formation of the acyltrimethylgermane **181** is depicted in **Scheme 34**. The small amount of the (postulated) copper enolate **187** produced from the acyltrimethylgermane **181** could be trapped efficiently by chlorotrimethylsilane, as opposed to reacting with the acyl chloride substrate (compare **Scheme 34** with **Scheme 32**), to produce the enol trimethylsilyl ether **190**. After complete conversion of the acyl chloride into product, treatment of the reaction mixture with aqueous NH_4Cl/NH_4OH would hydrolyze

190 to regenerate the product **181**. Several attempts to isolate and characterize the (postulated) enol trimethylsilyl ether **190** proved unsuccessful.



I **II** **III** **IV**

The notable tendency of acyltrimethylgermanes to undergo enolization (or enolate anion formation) may be understood by examining the properties associated with the acyl-germane function. Yates and Agolini[90] have shown that benzoyltriphenylgermane (**I**) (R = phenyl) and related substances have an increased amount of electron density at the carbonyl oxygen, compared to the carbon analog. This increase was attributed to a larger contribution of the canonical form (**II**), due to a strong inductive effect of germanium[91] on the carbonyl carbon–germanium bond. Trotter and Harrison[92] suggested that a third resonance form (**III**), in which there is no formal bond between the germanium and the carbonyl carbon, may contribute to the structural representation of the acylgermanes. The contribution from this resonance form was suggested by a single crystal X-ray crystallographic analysis of a related substance (R = Me), in which the carbonyl carbon–germanium bond is abnormally long at 2.01 Å, compared to the phenyl carbon–germanium bond length of 1.95 Å. Thus, it was suggested that compounds such as acetyltriphenylgermane (R = Me) would be best illustrated by (**IV**), which represents both the increased electron availability at the carbonyl carbon and the lengthened germanium–carbonyl carbon bond.[92]



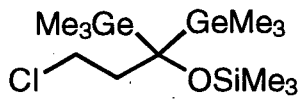
191-192

During the chromatographic purification of 3-chloropropanoyltrimethylgermane (**183**), synthesized by reaction of reagent **168** with 3-chloropropanoyl chloride (**177**) in the absence of any additive (**Table 6**, entry 7, p 101), an additional fraction, which was constituted of two compounds, was obtained in 10% yield. An analytically pure sample of each component was obtained by subjecting this mixture to reversed phase HPLC (C_{18} μBondapak 10 μm, 25 mm × 100 mm column, 3:2 acetonitrile–water). The first component to be eluted (retention time 53 min) was assigned structure **191**, (*E*)- or (*Z*)-1-((3-chloropropanoyl)oxy)-1,3-bis(trimethylgermyl)prop-1-ene. The structural assignment of **191** was based on the following data. The ^{1}H NMR (400 MHz, $CDCl_3$) spectrum exhibited a one-proton triplet (J = 9.2 Hz) at δ 5.80 (H-2), a two-proton triplet (J = 6.8 Hz) at δ 3.75 (H-3'), a two-proton triplet (J = 6.8 Hz) at δ 2.82 (H-2'), a two-proton doublet (J = 9.2 Hz) at δ 1.58 (H-3), as well as two nine-proton singlets at δ 0.30 and 0.16 for the Me_3Ge- groups. Additional evidence to support the structural assignment of **191** was provided by the IR spectrum, which showed a band at 1741 cm^{-1} (ν C=O). In addition, HRMS analysis indicated a signal at *m/z* of 383.9985 which is in good agreement with the calculated value of 383.9967 for $C_{12}H_{25}{}^{35}Cl^{74}Ge_2O_2$.

The second component to be eluted (retention time 57 min) was assigned structure **192**, (*Z*)- or (*E*)-1-((3-chloropropanoyl)oxy)-1,3-bis(trimethylgermyl)prop-1-ene. This assignment was based on the following data. The ^{1}H NMR (400 MHz, $CDCl_3$) spectrum exhibited a one-proton triplet (J = 8.8 Hz) at δ 5.34 (H-2), a two-proton triplet (J = 6.6 Hz)

at δ 3.77 (H-3'), a two-proton triplet (J = 6.6 Hz) at δ 2.86 (H-2'), a two-proton doublet (J = 8.8 Hz) at δ 1.64 (H-3), as well as two nine-proton singlets at δ 0.25 and 0.13 for the Me_3Ge-groups. Additional evidence was provided by the IR spectrum which showed a band at 1742 cm^{-1} (ν C=O). In addition, HRMS analysis indicated a signal at m/z 383.9975, which is in good agreement with the calculated value of 383.9967 for $C_{12}H_{25}{}^{35}Cl^{74}Ge_2O_2$.

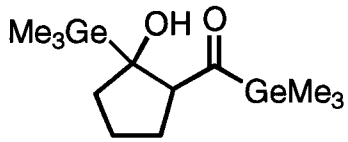
Although the geometry of the alkene functions of compounds **191** and **192** was not established, it is obvious from the data presented above that **191** and **192** are constitutionally identical and must, therefore, be geometric isomers. Compounds **191** and **192** are, in part, structurally related to **186** and thus, are likely to be formed via a pathway similar to that depicted in **Scheme 32** (p 105) for the production of **186**. In addition, **191** and **192** possess an allylic Me_3Ge- group which results from the substitution of the chloride by a Me_3Ge-function.



193

When 3-chloropropanoyl chloride (**177**) was allowed to react with $Me_3GeCu{\bullet}Me_2S$ (**168**) in the presence of bromotrimethylsilane (**Table 6**, entry 7, p 101), an additional fraction was isolated during the purification of 3-chloropropanoyltrimethylgermane (**183**). GLC and ^1H NMR analyses showed that this fraction was constituted of a mixture of compounds, but contained a major (≈75%) component. The major component was assigned structure **193**, 3-chloro-1,1-bis(trimethylgermyl)-1-(trimethylsilyloxy)propane. The structural assignment of **193** was based on the following data. The ^1H NMR (400 MHz, $CDCl_3$) spectrum exhibited a two-proton multiplet at δ 3.55–3.48, a two-proton multiplet at δ 2.40–2.32, an eighteen-

proton singlet at δ 0.20 as well as a nine-proton singlet at δ 0.12. The compound **193** is structurally related to **188** and thus, it is postulated to be formed via a pathway identical with that depicted in **Scheme 33** (p 106) for the production of **188**.

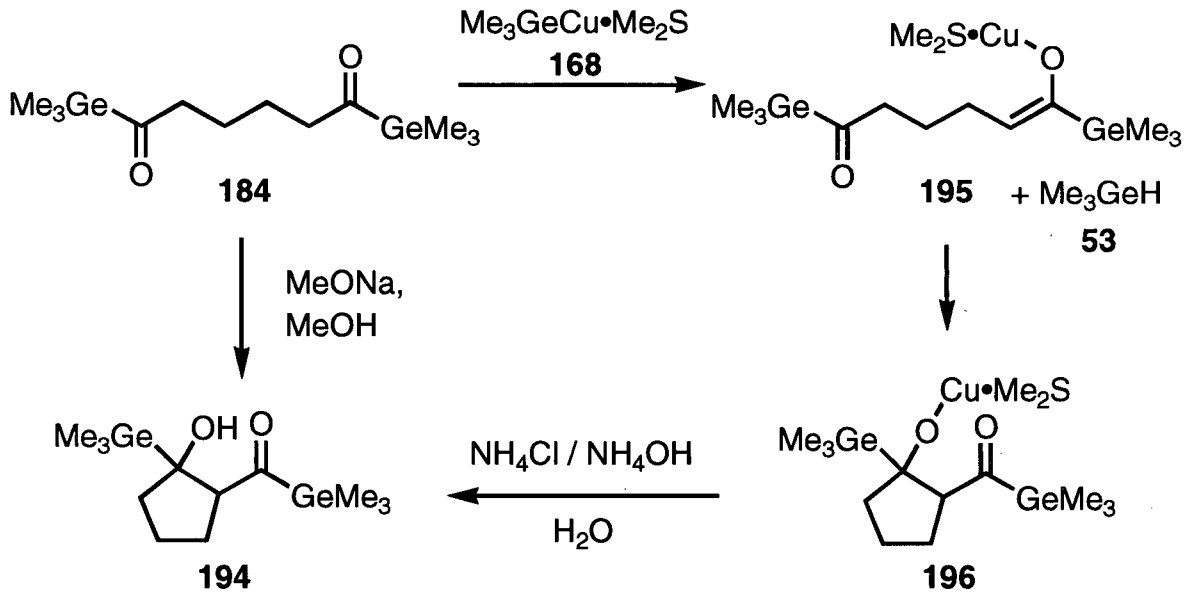


194

During the purification of hexanedioylbis(trimethylgermane) (**184**), synthesized by treatment of adipoyl chloride (**159**) with $Me_3GeCu{\bullet}Me_2S$ (**168**) in the absence of any additive (**Table 6**, entry 8, p 101), a by-product was isolated. This component, which was assigned structure **194**, 2-hydroxy-2-trimethylgermyl(cyclopentanecarbonyl)trimethylgermane, was obtained in 6% yield. This assignment was based on the following data. The ^{1}H NMR (400 MHz, $CDCl_3$) spectrum exhibited a one-proton broad signal (exchanges with D_2O) at δ 3.92 (-OH), a one-proton doublet of doublets (J = 11.0 and 8.6 Hz) at δ 3.11, a two-proton multiplet at δ 2.10–1.95, a two-proton multiplet at δ 1.85–1.75, a one-proton multiplet at δ 1.72–1.61, a one-proton multiplet at δ 1.59–1.52, a nine-proton singlet at δ 0.34 as well as a nine-proton singlet at δ 0.10. Additional evidence was provided by the IR spectrum which showed bands at 3464 (-OH) and 1634 cm^{-1} (ν C=O), together with HRMS analysis which indicated a signal at *m/z* 348.0359, in good agreement with the calculated value of 348.0365 for $C_{12}H_{26}{}^{72}Ge^{74}GeO_2$.

A mechanistic pathway accounting for the formation of **194** is depicted in **Scheme 35**. During the course of the formation of **184**, the $Me_3GeCu{\bullet}Me_2S$ (**168**) may have served as a base to generate a small amount of the copper enolate **195** and Me_3GeH (**53**) from the

compound **184**. This enolate can undergo ring closure to the copper alkoxide **196**, which upon work-up produces the alcohol **194**. In order to gain further information on the production of **194**, the following experiment was performed. A solution of **184** (1 equiv) in dry methanol was treated with sodium methoxide (1 equiv) at room temperature, and then was allowed to stir for 15 h. TLC analysis of an aliquot of the mixture indicated that the conversion of **184** into **194** was essentially complete (>95%). However, due to the small scale on the reaction (≈10 mg), isolation and purification of the crude oil obtained afforded the alcohol **194** in 30% yield. The spectral data derived from **194** were identical with that reported above.

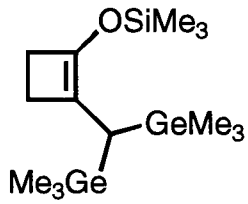


Scheme 35

The experiments described above, along with the data derived from the reaction of substrates **175** and **177** with reagent **168** (**Table 6**, entries 5 and 7, p 101), indicate that the acyltrimethylgermanes partially undergo enolate formation under the experimental conditions

used. This enolization results in the formation of by-products through *O*-acylation or aldol condensation in the case of the reaction in which adipoyl chloride (**159**) is the substrate.

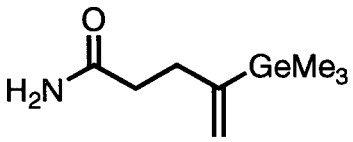
Treatment of pent-4-ynoyl chloride (**160**) (**Table 6**, entry 9, p 101) with approximately one equivalent of $Me_3GeCu{\bullet}Me_2S$ (**168**), with or without chlorotrimethylsilane, failed to produce pent-4-ynoyltrimethylgermane (**185**). Pent-4-ynoyl chloride (**160**) was chosen as a substrate to investigate the possibility of effecting a chemoselective reaction of the $Me_3GeCu{\bullet}Me_2S$ (**168**) with an acyl chloride function in the presence of another potentially reactive function (alk-1-yne) within the same substrate. Although neither of the two attempts afforded the expected acyltrimethylgermane **185**, isolation and characterization of the by-products formed under these experimental conditions gave some insights into the chemoselectivity of the overall reaction.



197

Treatment of pent-4-ynoyl chloride (**160**) with $Me_3GeCu{\bullet}Me_2S$ (**168**) in the presence of chlorotrimethylsilane gave a complex mixture of products. The crude oil obtained was subjected to flash column chromatography on silica gel to afford two components. The first compound, which was assigned structure **197**, 2-(bis(trimethylgermyl)methyl)-1-((trimethylsilyl)oxy)cyclobutene, was obtained in 10% yield. The structural assignment was based on the following data. The ^{1}H NMR (400 MHz, $CDCl_3$) spectrum exhibited a two-proton triplet (J = 3.2 Hz) at δ 2.47, a two-proton triplet (J = 3.2 Hz) at δ 1.89, a one-proton singlet at δ 1.29, a

nine-proton singlet at δ 0.16 as well as an eighteen-proton singlet at δ 0.15. Additional evidence was provided by the IR spectrum which showed a band at 1681 cm^{-1} (ν C=O). HRMS analysis of **197** indicated a signal at *m/z* 390.0660, which is consistent with the calculated value of 390.0655 for $C_{14}H_{32}{}^{72}Ge^{74}GeO^{28}Si$.

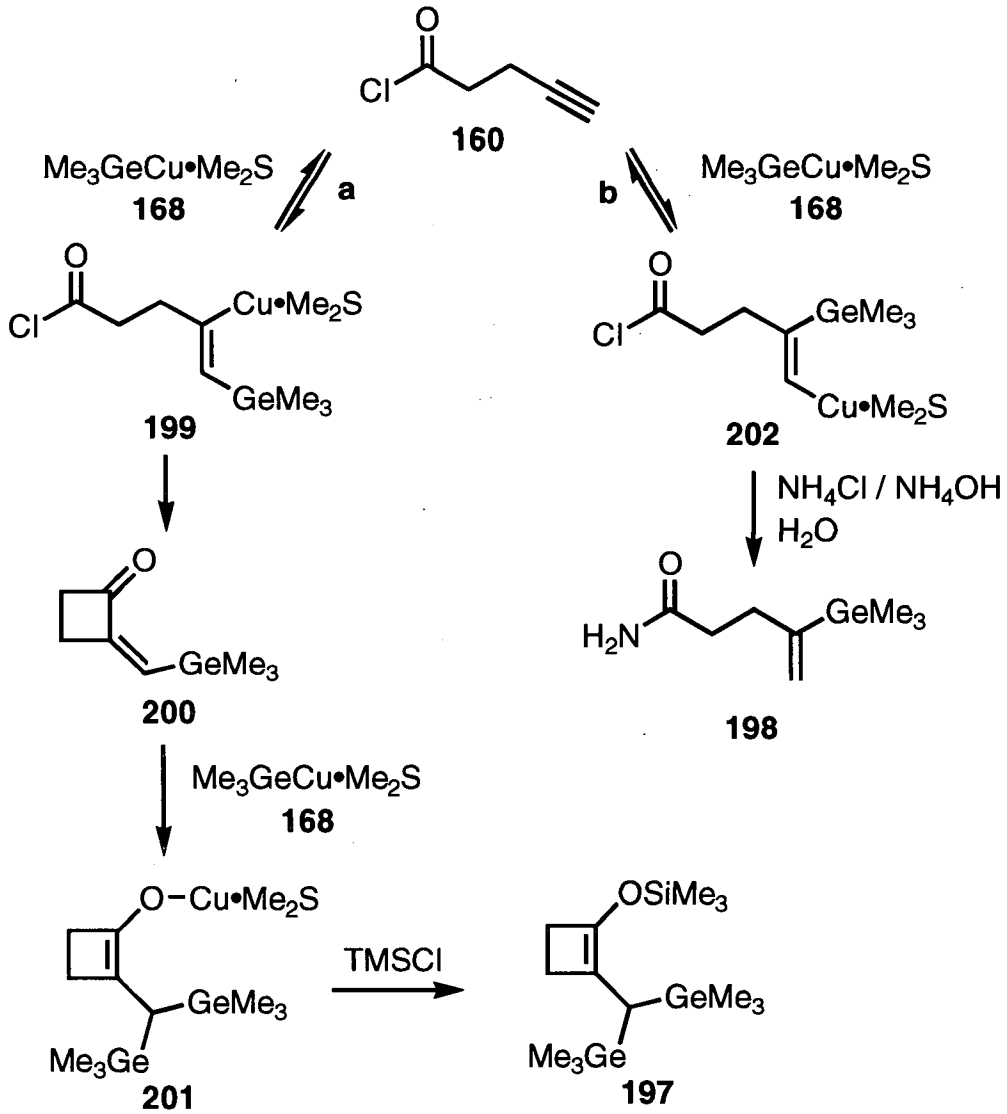


198

The second component, which was assigned structure **198**, 4-trimethylgermylpent-4-enamide, was isolated in 42% yield. This assignment was based on the following data. The ^1H NMR (400 MHz, $CDCl_3$) spectrum exhibited a two-proton broad signal at δ 5.62–5.40, a one-proton doublet (J = 2.0 Hz) at δ 5.53, a one-proton doublet (J = 2.0 Hz) at δ 5.22, a two-proton multiplet at δ 2.53–2.47, a two-proton multiplet at δ 2.37–2.30 as well as a nine-proton singlet at δ 0.21. Additional evidence was provided by the IR spectrum of **198** which showed two broad bands at 3365 and 3193 cm^{-1} ($-NH_2$) along with another band at 1667 cm^{-1} (ν C=O). HRMS analysis of this component indicated a signal at *m/z* 217.0513, in good agreement with the calculated value of 217.0522 for $C_8H_{17}{}^{74}GeNO$.

A rationale accounting for the formation of 2-(bis(trimethylgermyl)methyl)-1-((trimethylsilyl)oxy)cyclobutene (**197**) and 4-trimethylgermylpent-4-enamide (**198**) is depicted in **Scheme 36**. Thus, in one possible pathway, cis addition[93-95] of $Me_3GeCu{\bullet}Me_2S$ (**168**) to the alkyne function of **160** results in the formation of the vinylcopper species **199**, which bears the Me_3Ge- group on the terminal carbon of the alkene function (path **a**). The adduct **199** can undergo ring closure to generate the cyclobutenone **200**. Conjugate addition of

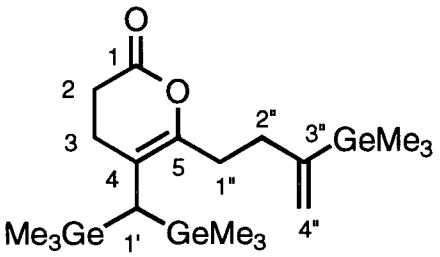
$Me_3GeCu{\bullet}Me_2S$ (**168**) to the enone function of **200** generates the copper enolate **201** which can subsequently react with chlorotrimethylsilane to form the enol trimethylsilyl ether **197**.



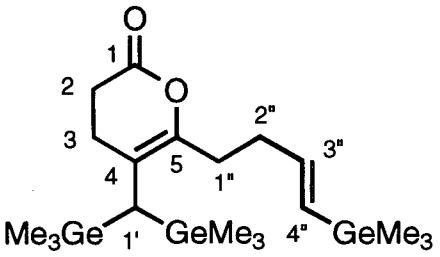
Scheme 36

Alternatively, cis addition of $Me_3GeCu{\bullet}Me_2S$ (**168**) to the alkyne function of **160**, in a manner regio-opposite to that producing **199**, results in the formation of the vinylcopper species **202** (path **b**) in which the Me_3Ge- group is located on the internal carbon of the alkene

function. Upon work-up (aqueous NH_4Cl/NH_4OH), nucleophilic substitution of the acyl chloride function by NH_3 and protonation of the vinylcopper species affords **198**.



203

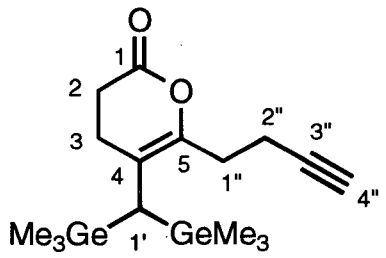


204

The reaction mixture derived from treatment of pent-4-ynoyl chloride (**160**) with $Me_3GeCu{\bullet}Me_2S$ (**168**) in the absence of chlorotrimethylsilane was treated with pyridine and dry methanol immediately prior to work-up. This treatment would transform any unreacted acyl chloride into the corresponding methyl ester, as opposed to a primary amide (vide supra), and consequently, would facilitate the isolation and purification procedures. The crude oil (a complex mixture) obtained was subjected to flash column chromatography to afford three fractions.

^{1}H NMR spectroscopic, GLC and GLC-MS analyses of the first fraction (obtained in 9% yield) suggested that it was constituted of two components, which were assigned structures **203**, 5-(3-trimethylgermylbut-3-en-1-yl)-4-(bis(trimethylgermyl)methyl)pent-4-eno-5-lactone (≈80% by GLC analysis) and **204**, (*E*)-5-(4-trimethylgermylbut-3-en-1-yl)-4-(bis(trimethylgermyl)methyl)pent-4-eno-5-lactone (≈20%). These assignments were based on the following data and by correlation with the ^{1}H NMR spectroscopic data derived from **205** (vide infra). The ^{1}H NMR (400 MHz, $CDCl_3$) spectrum showed four signals in the δ 5.95–5.15 region integrating for a total of two protons: δ 5.92 (m, 0.2H, H-3"–**204**), δ 5.83 (d,

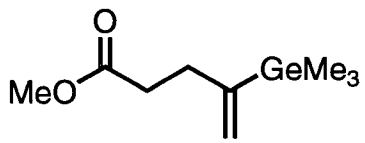
0.2H, J = 18.2 Hz, H-4"–**204**), δ 5.52 (d, 0.8H, J = 1.8 Hz, H-4"–**203**) and δ 5.22 (d, 0.8H, J = 1.8 Hz, H-4"–**203**); then a two-proton triplet (J = 3.2 Hz, H-3–**203** + **204**) at δ 2.79, a four-proton multiplet at δ 2.60–2.38 (H-1" and H-2"–**203** + **204**), a two-proton triplet (J = 3.2 Hz, H-3–**203** + **204**) at δ 2.08, a one-proton singlet at δ 1.34 (H-1'–**203** + **204**) and three singlets in the δ 0.26–0.15 region integrating for a total of 27 protons. The doublet (J = 18.2 Hz) at δ 5.83 indicates a trans coupling of a 1,2-disubsituted alkene with the signal at δ 5.92 consistent with the proposed structure for **204**. On the other hand, the doublets (J = 1.8 Hz) at δ 5.52 and 5.22 are characteristic of terminal alkenyl protons in the 2-trimethylgermylalk-1-ene moiety of **203**. GLC-MS analysis showed that both components have a mass of 516, and the isotopic clusters are consistent with the calculated isotopic distribution for $C_{19}H_{38}Ge_3O_2$.



205

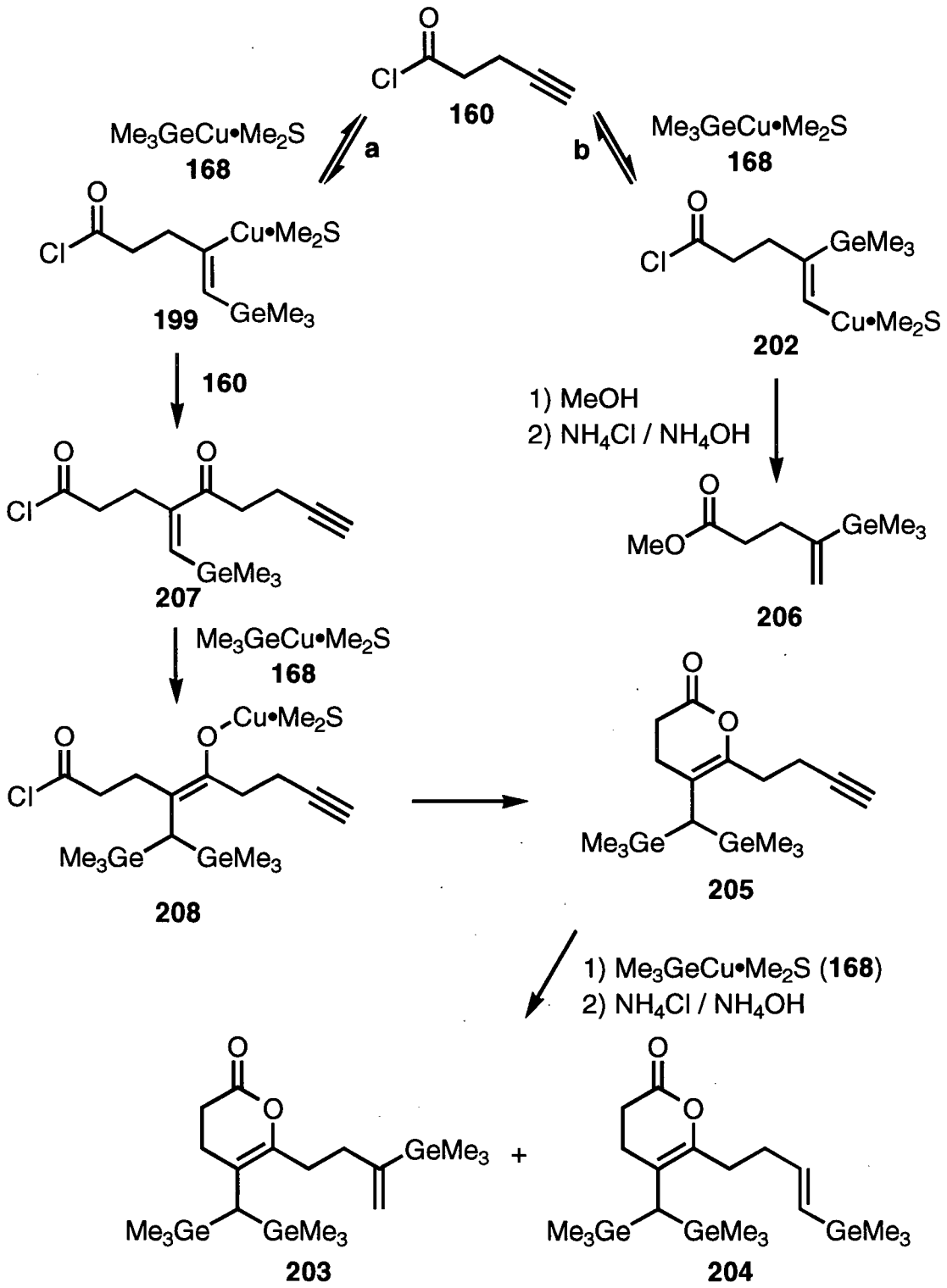
The second fraction (obtained in 16% yield) was constituted of a single component which was assigned structure **205**, 5-(but-3-yn-1-yl)-4-(bis(trimethylgermyl)methyl)pent-4-eno-5-lactone. This assignment was based on the following data. The ^{1}H NMR (400 MHz, $CDCl_3$) spectrum exhibited a two-proton triplet (J = 3.0 Hz) at δ 2.79 (H-2), a two-proton multiplet at δ 2.62–2.55 (H-1"), a two-proton multiplet at δ 2.53–2.46 (H-2"), a two-proton triplet (J = 3.0 Hz) at δ 2.06 (H-3), a one-proton triplet (J = 2.6 Hz) at δ 1.96 (H-4"), a one-proton singlet at δ 1.34 (H-1') as well as an eighteen-proton singlet at δ 0.17 (Me_3Ge-).

These assignments were supported by the following decoupling experiments. Thus, irradiation of the triplet at δ 2.79 (H-2) resulted in the collapse of the signal at δ 2.06 (H-3) to a singlet. Similarly, irradiation of H-3 (δ 2.06) caused H-2 (δ 2.79) to collapse to a singlet. When the multiplet at δ 2.62–2.55 (H-1") was irradiated, the resonance at δ 2.53–2.46 (H-2") was simplified to a doublet (J = 2.6 Hz). Irradiation of the multiplet at δ 2.53–2.46 (H-2") caused the signals at δ 2.62–2.55 (H-1") and 1.96 (H-4") to collapse to singlets. Finally, when the triplet at δ 1.96 (H-4") was irradiated the multiplet at δ 2.53–2.46 (H-2") was simplified. Additional evidence was provided by the IR spectrum which showed bands at 3313 (ν alkynyl C-H), 2140 (ν C≡C) and 1757 cm^{-1} (ν C=O), together with HRMS analysis which indicated a signal at m/z 398.0521, in good agreement with the calculated value of 398.0522 for $C_{16}H_{28}{}^{72}Ge^{74}GeO_2$.



206

The third fraction, which consisted of a single component, was obtained in 4% yield and was assigned structure **206**, methyl 4-trimethylgermylpent-4-enoate. This assignment was based on the data derived from the ^{1}H NMR (400 MHz, $CDCl_3$) spectrum, which exhibits a one-proton doublet (J = 2.0 Hz) at δ 5.50, a one-proton doublet (J = 2.0 Hz) at δ 5.20, a three-proton singlet at δ 3.67, a four-proton multiplet at δ 2.52–2.39 as well as a nine-proton singlet at δ 0.22.


160
Me3GeCu•Me2S
168
a
b
Cu•Me2S
GeMe3
199
202
160
1) MeOH
2) NH4Cl / NH4OH
207
206
Me3GeCu•Me2S
168
208
205
1) Me3GeCu•Me2S (168)
2) NH4Cl / NH4OH
203
204

Scheme 37

Possible mechanistic pathways rationalizing the formation of compounds **203–206** are depicted in **Scheme 37**. Thus, in one possible pathway, cis addition[93-95] of the reagent $Me_3GeCu{\bullet}Me_2S$ (**168**) to the alkyne function of pent-4-ynoyl chloride (**160**) results in the formation of the vinylcopper species **199** (path **a**). Intermolecular acylation of the latter with **160** generates the enone **207**, which can subsequently undergo further conjugate addition with $Me_3GeCu{\bullet}Me_2S$ (**168**) to produce the copper enolate **208**. This enolate can undergo intramolecular acyl substitution to form the six-membered ring lactone **205**. Germylcupration of the carbon–carbon triple bond of **205** affords the regioisomeric vinylgermanes **203** and **204** upon work-up.

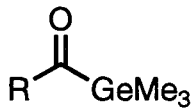
The formation of methyl 4-trimethylgermylpent-4-enoate (**206**) can be rationalized via pathway **b**, depicted in **Scheme 37**. Addition of $Me_3GeCu{\bullet}Me_2S$ (**168**) to the alkyne function of pent-4-ynoyl chloride (**160**) affords the vinylcopper species **202**. Treatment of the latter intermediate with dry methanol prior to work-up affords methyl 4-trimethylgermylpent-4-enoate (**206**).

The data presented above, along with that derived from the reaction of pent-4-ynoyl chloride (**160**) with $Me_3GeCu{\bullet}Me_2S$ (**168**) in the presence of chlorotrimethylsilane as additive (see **Scheme 36**, p 115), demonstrate somewhat surprisingly that reagent **168** adds preferentially, if not exclusively, to the alkyne moiety of a substrate bearing both a terminal alkyne and an acyl chloride function. Interestingly, when the alkynyl H was replaced by a Me_3Si- group, the chemoselectivity of addition of $Me_3GeCu{\bullet}Me_2S$ (**168**) was completely reversed from that observed for **160**, affording the "normal" addition product (compare entries 9 and 10 in **Table 6**, p 101).

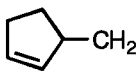
2.2.2.4 Characteristic Spectral Data of Acyltrimethylgermanes

The acyltrimethylgermanes prepared in this study exhibit a number of characteristic spectral features. **Table 7** summarizes some of the IR, ^{1}H and ^{13}C NMR data derived from compounds **114, 170, 178–184**.

Table 7: Characteristic Spectral Data of the Acyltrimethylgermanes **114, 170, 178–184**

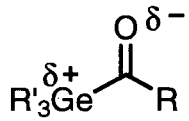


			NMR (δ ppm)		
		IR	$^{1}H^{a}$	$^{13}C^{b}$	
Entry	R	ν C=O	Me_3Ge-	C=O	Me_3Ge-
1	$Me_3SiC{\equiv}C(CH_2)$ **114**	1660	0.33	242.9	–3.1
2	*n*-C_9H_{19} **170**	1658	0.31	245.9	–2.9
3	*c*-$C_5H_7CH_2$[c] **178**	1657	0.31	245.4	–3.0
4	*c*-C_6H_{11} **179**	1654	0.31	247.2	–2.2
5	4-$MeO(C_6H_4)CH_2OCH_2$ **180**	1667	0.32	244.8	–2.7
6	$(C_6H_5)CH_2OCH_2$ **181**	1668	0.34	244.8	–2.6
7	$Cl(CH_2)_4$ **182**	1657	0.32	244.9	–3.0
8	$Cl(CH_2)_2$ **183**	1661	0.34	242.5	–3.3
9	$Me_3GeCO(CH_2)_4$ **184**	1657	0.31	245.1	–3.0

[a] 400 MHz, $CDCl_3$. [b] 75 MHz, $CDCl_3$. [c] *c*-$C_5H_7CH_2$ = 

The carbonyl stretching frequencies of the acyltrimethylgermanes depicted in **Table 7**

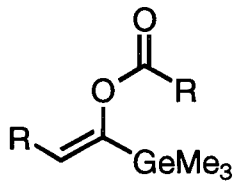
appear in the 1668–1654 cm^{-1} region. These absorptions are found at frequencies lower than those of the corresponding carbon analogs, for which the expected frequencies would be approximately 1730–1700 cm^{-1}.[96] The lowering in the carbonyl stretching frequencies of acylgermanes has been attributed to a strong inductive effect of the germanium atom, resulting in an increase in the electron density at the carbonyl oxygen.[90,92]



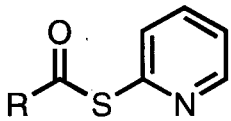
The ^{1}H NMR spectra of the acyltrimethylgermanes exhibit singlets for the Me_3Ge-group at approximately δ 0.32 for the compounds depicted in **Table 7**. The ^{13}C spectra of the acyltrimethylgermanes display two distinctive signals. The resonances due to the carbonyl carbons appear within the region δ 248–242, and the signals derived from the methyl carbons of the Me_3Ge- groups appear near δ –3.0, except for compound **179**, which exhibits the corresponding signal at δ –2.2. Finally, the acyltrimethylgermanes are pale yellow oils. This color is consistent with that of other reported acylgermanes and is due to the n–π* transition of the carbonyl group occurring in the visible region.[97] The shifted absorption, compared to the corresponding carbon analogs, has been rationalized in terms of inductive effects.[97]

2.2.3 SYNTHESIS OF ACYLTRIMETHYLGERMANES FROM *S*-(PYRIDIN-2-YL) THIOESTERS

As described in section 2.2.2.3 (p 97 ff.), the reaction of acyl chlorides with $Me_3GeCu{\bullet}Me_2S$ (**168**) in the absence of an additive generally produced small amounts of enol ester by-products. These substances are thought to be produced by formation of enolate anions from the initial products (acyltrimethylgermanes), followed by *O*-acylation of these intermediates with the acyl chloride substrates.



In an effort to circumvent the formation of such by-products, investigations were directed towards the conversion of *S*-(pyridin-2-yl) thioesters into acyltrimethylgermanes. It was hoped that the less reactive electrophilic substrates, *S*-(pyridin-2-yl) thioesters, would not form by-products resulting from *O*-acylation as readily as their acyl chlorides counterparts.

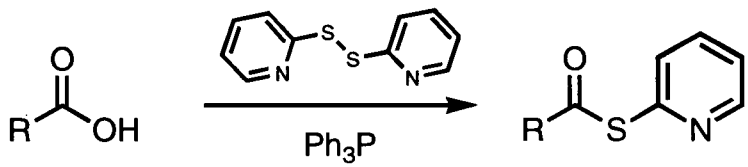


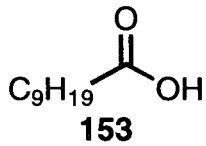
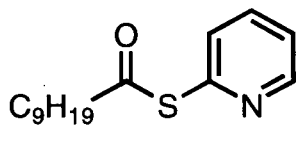
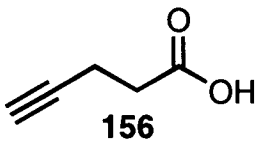
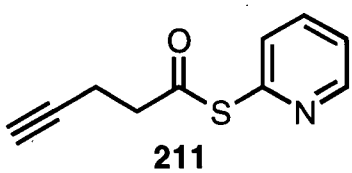
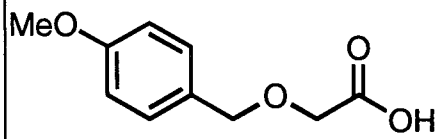
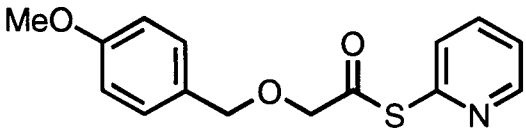
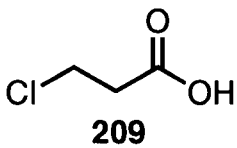
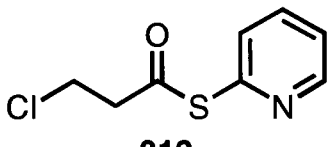
2.2.3.1 SYNTHESIS OF *S*-(PYRIDIN-2-YL) THIOESTERS

In order to prepare the *S*-(pyridin-2-yl) thioesters chosen for this study, the carboxylic acids **153**, **156**, **166** and **209** shown in **Table 8** were employed as substrates. **Table 8** also contains a summary of the conversion of the carboxylic acids **153**, **156**, **166** and **209** into the *S*-(pyridin-2-yl) thioesters **210–213**. In particular, compound **211** was synthesized to deter-

mine whether the chemoselectivity of the reaction of $Me_3GeCu{\bullet}Me_2S$ (**168**) would be altered from that of the parent pent-4-ynoyl chloride (**160**) (exclusive addition on the alkyne function of **160**; see **Table 6**, entry 9, p 101 and accompanying text). On the other hand, **213** was selected in an attempt to improve the efficiency of the synthesis of 3-chloropropanoyl-trimethylgermane (**183**) (see **Table 6**, entry 7, p 101).

Table 8: Preparation of the *S*-(Pyridin-2-yl) Thioesters **210–213**



Entry	Alkanoic Acid	*S*-(Pyridin-2-yl) Thioester	Yield (%)[a]
1	 **153**	 **210**	78
2	 **156**	 **211**	56
3	 **166**	 **212**	83
4	 **209**	 **213**	56[b]

[a] Yield of isolated and purified product. [b] This compound decomposed readily when stored at room temperature.

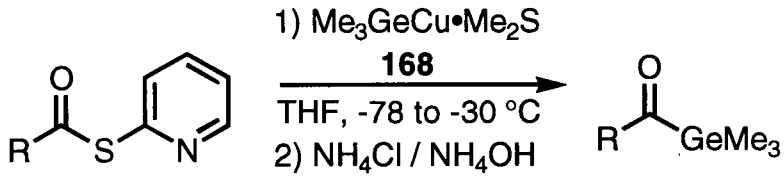
The synthesis of *S*-(pyridin-2-yl) decanethioate (**210**) (**Table 8**, entry 1), for example, was accomplished in the following manner. A solution of decanoic acid (**153**) (1 equiv) in acetonitrile was treated sequentially with triphenylphosphine (≈1.1 equiv) and 2,2'-disulfanediyldipyridine[98] (≈1.1 equiv) and the resultant mixture was stirred for 1 h at room temperature. After isolation and purification of the crude product, *S*-(pyridin-2-yl) decanethioate (**210**) was obtained in 78% yield as a light yellow oil. The remainder of the *S*-(pyridin-2-yl) thioesters listed in **Table 8** were prepared from the corresponding alkanoic acids in a manner identical with that outlined above.

2.2.3.2 SYNTHESIS OF ACYLTRIMETHYLGERMANES

Table 9 contains a summary of the conversion of the *S*-(pyridin-2-yl) thioesters **210**, **212** and **213** into the acyltrimethylgermanes **170**, **180** and **183**. For example, the synthesis of decanoyltrimethylgermane (**170**) (entry 1) was accomplished in the following manner. A cold (–78 °C) stirred solution of $Me_3GeCu{\bullet}Me_2S$ (**168**) (≈1.5 equiv), prepared via the "inverse" addition method (see section 2.2.2.2, p 92 ff.), in dry THF was treated with one equivalent of *S*-(pyridin-2-yl) decanethioate (**210**). The reaction mixture was stirred at –78 °C for 1 h, then was warmed to –30 °C and was allowed to stir for an additional 2 h. After isolation and purification of the crude product, decanoyltrimethylgermane (**170**) was obtained in 64% yield, along with 10% of **210** which was recovered unchanged.

The acyltrimethylgermanes **180** and **183** listed in **Table 9** were prepared in a manner identical with that outlined above from the corresponding *S*-(pyridin-2-yl) thioesters. **Table 9** also summarizes the yields of acyltrimethylgermanes obtained from the related conversions using the corresponding acyl chlorides as substrates (taken from **Table 6**, p 101).

Table 9: Preparation of the Acyltrimethylgermanes **170**, **180** and **183**

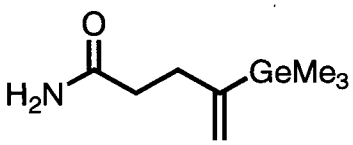


	S-(pyridin-2-yl) Thioester	Acyltrimethylgermane	Yield (%)[a]	
Entry[b]	R	R	from thioester	from acyl chloride[c]
1	*n*-C_9H_{19} **210**	*n*-C_9H_{19} **170**	64	81
2	4-MeO(C_6H_4)CH_2OCH_2 **212**	4-MeO(C_6H_4)CH_2OCH_2 **180**	62	n/a
3	Cl(CH_2)$_2$ **213**	Cl(CH_2)$_2$ **183**	23	23
4	HC≡C(CH_2)$_2$ **211**	HC≡C(CH_2)$_2$ **185**	0	0

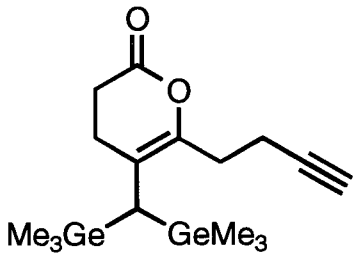
[a] Yield of isolated and purified product. [b] The $Me_3GeCu{\bullet}Me_2S$ (**168**) reagent was prepared via the "inverse" addition method (see section 2.2.2.2, p 92 ff.). [c] Yields taken from **Table 6**, p 101.

Decanoyltrimethylgermane (**170**) (entry 1) was synthesized in 64% yield from *S*-(pyridin-2-yl) decanethioate **210**, whereas **170** was obtained in 81% yield from the corresponding acyl chloride **157** under similar experimental conditions. Treatment of **212** with $Me_3GeCu{\bullet}Me_2S$ (**168**) resulted in the formation of **180** in 62% yield (entry 2). *S*-(Pyridin-2-yl) 3-chloropropanethioate **213** (entry 3) was converted into 3-chloropropanoyltrimethylgermane (**183**) in 23% yield, a yield identical with that obtained from a similar reaction involving 3-chloropropanoyl chloride (**177**) as the substrate. Finally, treatment of *S*-(pyridin-2-yl) pent-4-ynethioate (**211**) (entry 4) gave none of the expected pent-4-ynoyltrimethylgermane (**185**), an outcome analogous with that observed from pent-4-ynoyl chloride (**160**). Purification of the crude oil (complex mixture) obtained from the reaction of **211** with **168**

(entry 4), provided the products **198** and **205** in small amounts. The spectral data of these materials were identical with those reported in section 2.2.2.3, p 97 ff.



198



205

The data presented above suggest that, for the synthesis of acyltrimethylgermanes by reaction with $Me_3GeCu{\bullet}Me_2S$ (**168**), acyl chlorides are better substrates than *S*-(pyridin-2-yl) thioesters, at least under the experimental conditions investigated. Moreover, many acyl chlorides are commercially available or are more readily prepared than the *S*-(pyridin-2-yl) thioesters from the parent carboxylic acids.

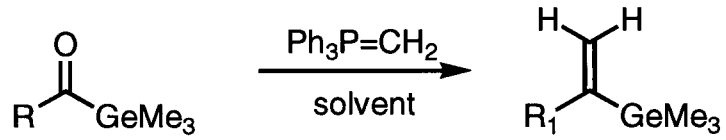
2.2.4 OLEFINATION OF ACYLTRIMETHYLGERMANES TO 2-TRIMETHYL-GERMYLALK-1-ENES

As outlined in the Introductory Remarks (section 2.2.1, p 81 ff.), following the successful development of a method for the preparation of acyltrimethylgermanes, the olefination of the latter compounds into the corresponding 2-trimethylgermylalk-1-enes remained to be accomplished.

Brook and Fieldhouse[81] reported the conversion of an acyltriphenylgermane to the corresponding 2-triphenylgermylalk-1-ene using a Wittig reagent (see **Equation 31** in the Introductory Remarks, section 2.2.1, p 81 ff.). It was therefore decided to investigate the applicability of this transformation to the conversion of functionalized acyltrimethylgermanes into the corresponding 2-trimethylgermylalk-1-enes.

Table 10 contains a summary of the conversion of selected acyltrimethylgermanes (**170, 114, 180, 182, 184**) into the 2-trimethylgermylalk-1-enes **214–218**.

Table 10: Preparation of the 2-Trimethylgermylalk-1-enes **214–218**



Entry	R	R_1	Solvent	Yield (%)[a]
1	C_9H_{19} **170**	C_9H_{19} **214**	THF	90
2	$Me_3SiC{\equiv}C(CH_2)_2$ **114**	$Me_3SiC{\equiv}C(CH_2)_2$ **215**	benzene	86[b]
3	$4\text{-}MeO(C_6H_4)CH_2OCH_2$ **180**	$4\text{-}MeO(C_6H_4)CH_2OCH_2$ **216**	THF	91
4	$Cl(CH_2)_4$ **182**	$Cl(CH_2)_4$ **217**	diethyl ether	84
5	$Me_3Ge(C{=}O)(CH_2)_4$ **184**	$Me_3Ge(C{=}CH_2)(CH_2)_4$ **218**	benzene	85[c]

[a] Yield of isolated and purified product using 1.2 equiv of $Ph_3P{=}CH_2$ (unless otherwise noted). [b] 1.6 equiv of $Ph_3P{=}CH_2$ were used. [c] Using 2.5 equiv of $Ph_3P{=}CH_2$ were used.

For example, the synthesis of 2-trimethylgermylundec-1-ene (**214**) (entry 1) was accomplished in the following manner. A mixture of methylenetriphenylphosphorane (1.2 equiv) in dry THF, prepared by treating methyltriphenylphosphonium bromide (1.25 equiv) with a solution of *n*-BuLi (1.2 equiv), was allowed to react with decanoyltrimethylgermane (**170**) (1 equiv) at room temperature for 20 min. After isolation and purification of the crude product, 2-trimethylgermylundec-1-ene (**214**) was obtained in 90% yield. The ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **214** exhibited a one-proton doublet (J = 2.8 Hz) at δ 5.48, a one-proton doublet (J = 2.8 Hz) at δ 5.14, a two-proton triplet (J = 7.6 Hz) at δ 2.16, a fourteen-proton multiplet at δ 1.44–1.16, a three-proton triplet (J = 7.0 Hz) at δ 0.86 as well as a nine-proton singlet at δ 0.19. Additional structural evidence was provided by the IR spectrum

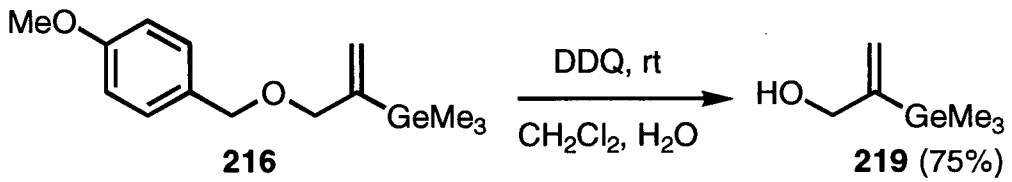
which showed a band at 1604 cm^{-1} (ν C=C), together with HRMS analysis which indicated a signal at *m/z* 257.1329 $(M - CH_3)^+$, in good agreement with the calculated value of 257.1325 for $C_{13}H_{27}{}^{74}Ge$.

The 2-trimethylgermylalk-1-enes **215–218** listed in **Table 10** were prepared from the corresponding acyltrimethylgermanes in a manner analogous with that outlined above. Thus, treatment of 5-trimethylsilylpent-4-ynoyltrimethylgermane (**114**) (entry 2) with 1.6 equivalents of methylenetriphenylphosphorane in dry benzene afforded 2-trimethylgermyl-6-trimethylsilyl-hex-5-yn-1-ene (**215**) in 86% yield. When the same reaction was performed in THF or with 1.2 equivalents of methylenetriphenylphosphorane, the yield of **215** decreased by ≈10%. It is noteworthy that 2-trimethylgermyl-6-trimethylsilylhex-5-yn-1-ene (**215**) possesses a 2-trimethylgermylalk-1-ene *as well as* a 1-trimethylsilylalk-1-yne function. Using the method developed as described in section 2.1 of this thesis (p 16 ff.), the 1-trimethylsilylalk-1-yne function of **215** could be submitted (theoretically) to the platinum catalyzed hydrogermylation conditions to produce, sequentially, a second vinylgermane function.

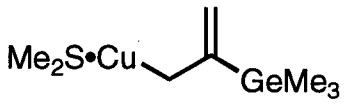
Treatment of the acyltrimethylgermane **180** (entry 3) with 1.2 equivalents of methylenetriphenylphosphorane in dry THF afforded the 2-trimethylgermylalk-1-ene **216** in 91% yield. Interestingly, product **216** bears an ether function in the allylic position, a type of compound that could not be synthesized via the method involving platinum catalyzed hydro-germylation of 1-trimethylsilylalk-1-ynes (see section 2.1.5, p 65 ff.). 5-Chloropentanoyl-trimethylgermane (**182**) (entry 4) was converted into 6-chloro-2-trimethylgermylhex-1-ene (**217**) in 84% yield using dry diethyl ether as solvent. When the olefination of **182** was effected in THF, **217** was obtained in 80% yield, whereas with benzene as solvent the yield of

217 was essentially the same as with diethyl ether (83%).

Finally, treatment of hexanedioylbis(trimethylgermane) (**184**) with 2.5 equivalents of methylenetriphenylphosphorane in benzene afforded 2,7-bis(trimethylgermyl)octa-1,7-diene (**218**) in 85% yield. Since substrate **184** underwent a double olefination reaction, the amount of reagent employed was increased. When the olefination of **184** was effected in diethyl ether, the yield of **218** was lowered slightly (82%).



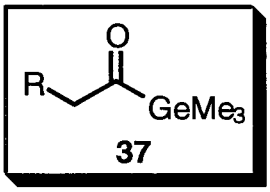
The vinylgermane **216** can serve as an ether-protected form of an allylic bifunctional reagent. Thus, 1-((4-methoxybenzyl)oxy)-2-trimethylgermylprop-2-ene (**216**) was treated with DDQ[99] in a dichloromethane–water mixture at room temperature. After isolation and purification of the crude product, 2-trimethylgermylprop-2-en-1-ol (**219**) was obtained in 75% yield. Substance **219** has been employed as a precursor for the preparation of the synthetically useful bifunctional reagent 2-(trimethylgermyl)allylcopper(I)–dimethyl sulfide.[100]



2.2.5 CONCLUSIONS

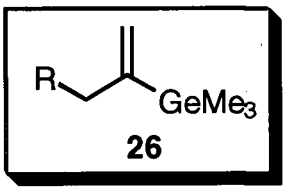
The aim of this study was to develop a method for the preparation of functionalized acyltrimethylgermanes and, subsequently, to convert the latter compounds into the corresponding 2-trimethylgermylalk-1-enes.

The acyl chlorides required as substrates for this study are easily synthesized from the alkanoic acids precursors. A new and, more importantly, experimentally simple method was devised for the preparation of Me_3GeLi (**149**) in high yield in THF solution. The novel reagent $Me_3GeCu{\bullet}Me_2S$ (**168**) was obtained by treatment of a solution of Me_3GeLi (**149**) with $CuBr{\bullet}Me_2S$.



37

$Me_3GeCu{\bullet}Me_2S$ (**168**) serves as a good reagent for the conversion of functionalized acyl chlorides into the corresponding acyltrimethylgermanes of general structure **37**. The formation of the acyltrimethylgermanes is accompanied by the production of small amounts of by-products, apparently originating from the enolization of the acyltrimethylgermanes. The formation of these by-products can be completely inhibited by addition of chlorotrimethylsilane to the reaction mixture prior to addition of the substrate. The reaction of *S*-(pyridin-2-yl) thioesters with $Me_3GeCu{\bullet}Me_2S$ (**168**) provides the corresponding acyltrimethylgermanes. The yields are comparable or lower than that obtained with the parent acyl chlorides.



26

Finally, the acyltrimethylgermanes **37** are efficiently converted into the corresponding 2-trimethylgermylalk-1-enes of general structure **26** via olefination with methylenetriphenyl-phosphorane.

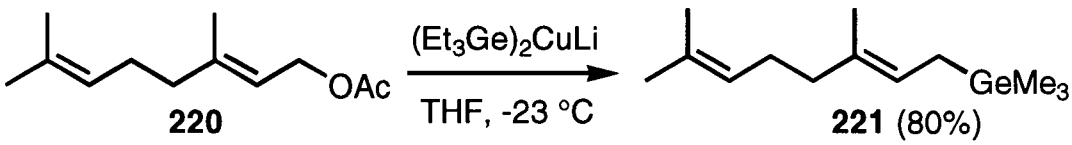
2.3 CONJUGATE ADDITION OF (TRIMETHYLGERMYL)COPPER(I)–DIMETHYL SULFIDE (168) AND LITHIUM (TRIMETHYLGERMYL)CUPRATES TO SELECTED UNSATURATED CARBONYL SYSTEMS

2.3.1 INTRODUCTORY REMARKS

Following the successful preparation of $Me_3GeCu{\bullet}Me_2S$ (**168**) (section 2.2.2.2, p 92 ff.), and the demonstration that **168** serves as useful reagent for the synthesis of functionalized acyltrimethylgermanes (section 2.2.2.3, p 97 ff.), it became of interest to undertake the preparation of additional (trimethylgermyl)copper(I) reagents. In addition, as outlined in the Proposals (section 1.3, p 13 ff.), given that (trimethylgermyl)copper(I) reagents could be prepared, what synthetic applications would these reagents have?

A survey of the literature showed that three reports have appeared describing the preparation and use of triphenyl- and (triethylgermyl)copper(I) reagents. In contrast, (trimethylgermyl)copper(I) reagents had not been reported prior this work.[101] A brief summary of these reports will be presented below.

In the first report, as outlined in the Introductory Remarks from the previous section (2.2.1, p 81 ff.), Vyazankin and co-workers[78] described the use of Et_3GeCu to convert an acyl chloride into the corresponding acyltriethylgermane (see **Equation 26**).

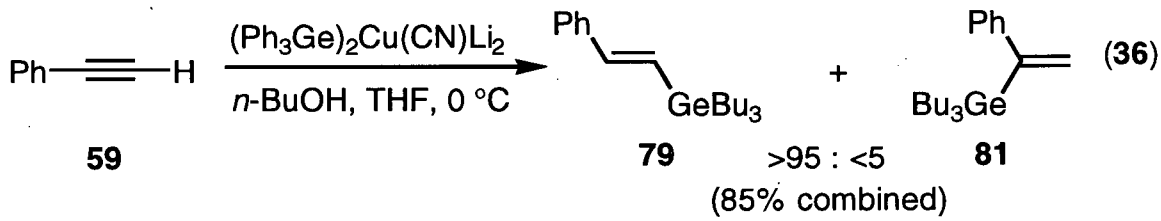


220 **221** (80%) **(35)**

Takeda and co-workers,[89] in the second report, utilized $(Et_3Ge)_2CuLi$ for the preparation of allylgermanes. In this protocol, for example, a cold (–23 °C) solution of

$(Et_3Ge)_2CuLi$ (1 equiv) in THF was treated with the allylic acetate **220** (1 equiv) to afford the allylgermane **221** in 80% yield (**Equation 35**).

In the third report, Oshima and co-workers,[35] outlined the use of $(Et_3Ge)_2CuLi$ in the synthesis of vinylgermanes, as depicted in **Scheme 10** (p 12) of the Introduction.



Oshima and co-workers,[35] also employed $(Ph_3Ge)_2Cu(CN)Li_2$ in the formation of vinylgermanes from alk-1-ynes. For example, in this protocol, a solution of $(Ph_3Ge)_2Cu(CN)Li_2$ (1.5 equiv) in THF at 0 °C was treated sequentially with phenylacetylene (**59**) (1 equiv) and *n*-butanol (4.6 equiv) as a proton source,[35] to afford the regioisomeric vinylgermanes **79** and **81**, as a mixture, in 85% yield (**Equation 36**).

As outlined above, the triphenyl- and (triethylgermyl)copper(I) reagents have been used sparingly with a limited number of substrates. In an effort to develop the use of organo-germanes reagents in synthesis, a number of new (trimethylgermyl)copper(I) reagents have been prepared. The following pages describes the preparation of these reagents as well as their conjugate addition to selected α,β-unsaturated carbonyl systems.

2.3.2 PREPARATION OF THE (TRIMETHYLGERMYL)CUPRATES 222–225

Following the development of the new and experimentally simple formation of Me_3GeLi (**149**) (section 2.2.2.2, p 92 ff.), the preparation of the (trimethylgermyl)cuprates reagents **222–225** was easily accomplished.

$(Me_3Ge)_2CuLi$	$Me_3GeCu(CN)Li$	$(Me_3Ge)_2Cu(CN)Li_2$	$Me_3Ge(Me)Cu(CN)Li_2$
222	**223**	**224**	**225**

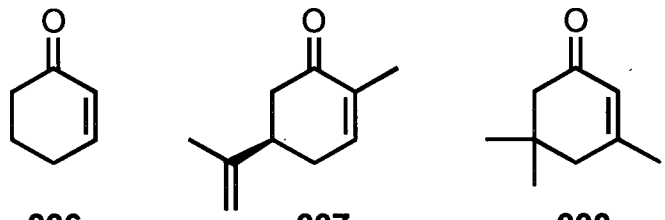
For example, the formation of lithium bis(trimethylgermyl)cuprate (**222**) was accomplished as follows. A cold (–10 °C) solution of Me_3GeLi (**149**) (2 equiv) in dry THF was transferred to a cold (–78 °C) stirred suspension of $CuBr{\bullet}Me_2S$ (1 equiv) in dry THF via a cannula. The resultant mixture was stirred at –78 °C for 1 h to afford a clear golden solution of the reagent **222**, which was then ready to use.

The (trimethylgermyl)cuprate reagents **223–225** were prepare in a manner analogous to that described above, using CuCN as the copper(I) source. A yellow opaque solution of reagent **223** in THF was obtained by mixing together a 1:1 molar ratio of Me_3GeLi (**149**) and CuCN, whereas treatment of one equivalent of CuCN with 2 equivalents of Me_3GeLi (**149**) in THF generated a clear colorless solution of reagent **224**. When a suspension of CuCN (1 equiv) in THF was treated with one equivalent each of solutions of Me_3GeLi (**149**) and MeLi, the dilithium methyl(trimethylgermyl)cyanocuprate (**225**) was obtained as a clear colorless solution.

The formulae depicting the (trimethylgermyl)cuprates **222–225** are intended to indicate the stoichiometry of the reagents used for their preparation and not an actual structural representation or state of aggregation. While reagents **222–225** will be treated as

monomeric species, in order to facilitate the discussion of the results, the reader should keep in mind that they possibly possess some degree of aggregation like their carbocuprate analogs.[102-104]

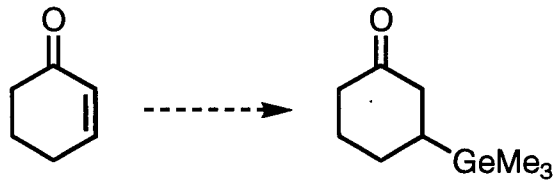
2.3.3 ADDITION OF (TRIMETHYLGERMYL)COPPER(I)–DIMETHYL SULFIDE (168) AND (TRIMETHYLGERMYL)CUPRATES 222–225 TO CYCLIC ENONES



226 **227** **228**

In order to evaluate the effectiveness of $Me_3GeCu{\bullet}Me_2S$ (**168**) and the (trimethylgermyl)cuprates reagents **222–225** to undergo conjugate addition, cyclohex-2-en-1-one (**226**), *l*-carvone (**227**) and isophorone (**228**) were chosen as substrates.

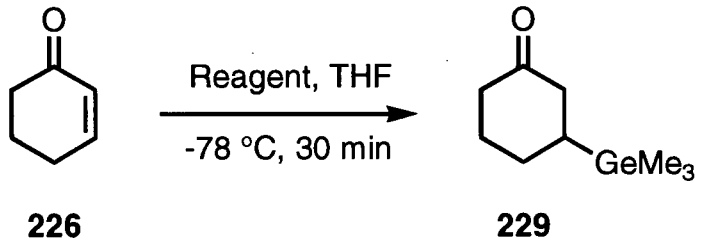
2.3.3.1 CONJUGATE ADDITION TO CYCLOHEX-2-EN-1-ONE (226)



226 **229**

Initial investigations were performed using cyclohex-2-en-1-one (**226**) as substrate. **Table 11** contains a summary of the conversion of **226** into 3-trimethylgermylcyclohexanone (**229**) with reagents **168** and **222–225**.

Table 11: Conjugate Addition of Reagents **168** and **222–225** to Cyclohex-2-en-1-one (**226**)



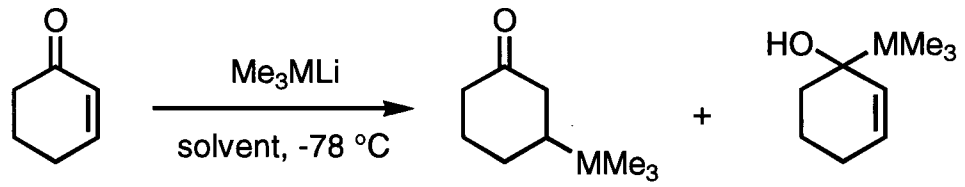
Entry	Reagent[a]	Yield (%)[b]
1	$Me_3GeCu{\bullet}Me_2S$ **168**	77
2[c]	$(Me_3Ge)_2CuLi$ **222**	86
3	$Me_3GeCu(CN)Li$ **223**	90
4[c]	$(Me_3Ge)_2Cu(CN)Li_2$ **224**	85
5	$Me_3Ge(Me)Cu(CN)Li_2$ **225**	87

[a] 1.3 equiv of reagent were used unless otherwise stated. [b] Yield of isolated and purified product. [c] 0.65 equiv of reagent was used.

For example, the conjugate addition of $Me_3GeCu{\bullet}Me_2S$ (**168**) to **226** (entry 1) was accomplished as follows. A cold (–78 °C) solution of reagent **168** (1.3 equiv) in dry THF was treated with cyclohex-2-en-1-one (**226**) (1 equiv). The resultant black mixture was stirred at –78 °C for 0.5 h, and then was treated with aqueous NH_4Cl–NH_4OH (pH 8–9). Isolation and purification of the crude product obtained afforded 3-trimethylgermylcyclohexanone (**229**) in 77% yield. The ^1H NMR (400 MHz, $CDCl_3$) spectrum derived from **229** exhibits a three-proton multiplet at δ 2.41–2.24, a two-proton multiplet at δ 2.20–2.10, a one-proton multiplet at δ 1.86–1.78, a one-proton ddddd (J = 12.8, 12.8, 12.8, 5.0 and 3.8 Hz) at δ 1.71, a one-proton dddd (J = 12.8, 12.8, 12.8 and 3.6 Hz) at δ 1.46, a one-proton dddd (J = 13.6, 12.8, 3.4 and 3.4 Hz) at δ 1.30, as well as a nine-proton singlet at δ 0.10. The IR spectrum derived

from **229** showed a band at 1713 cm^{-1} (ν C=O), whereas HRMS analysis indicated a signal at *m/z* 216.0565, which is consistent with the calculated value of 216.0569 for $C_9H_{18}{}^{74}GeO$.

The conjugate addition of the other (trimethylgermyl)cuprate reagents **222–225** listed in **Table 11** to cyclohex-2-en-1-one (**226**) was effected in a manner similar to that described above. It is noteworthy that reagents **222** (entry 2) and **224** (entry 4), which possess two Me_3Ge- ligands, were employed in sub-stoichiometric amounts (0.65 equivalent) with **226** to afford the adduct **229** in 86 and 85% yield respectively. These results demonstrate that *both* ligands are transferable in a conjugate addition reaction to an enone and, thus, "throwing away" a valuable (Me_3Ge-) ligand is precluded. Similarly, this concept of "ligand economy" instigated the preparation of reagent **225**, which possesses an expendable non-transferable ligand (Me-).[105] Thus, when 1.3 equivalents of reagent **225** were treated with one equivalent of the enone **226**, the adduct **229** was obtained in 87% yield (entry 5).



226 | **229** M = Ge, **229a** M = Si, **229b** M = Sn | **230** M = Ge, **230a** M = Si, **230b** M = Sn

M	Solvent			
Si	THF-HMPA	>99	:	<1
Sn	THF	>99	:	<1
Sn	Et_2O	1	:	9
Ge	THF	1	:	3.8

Scheme 38

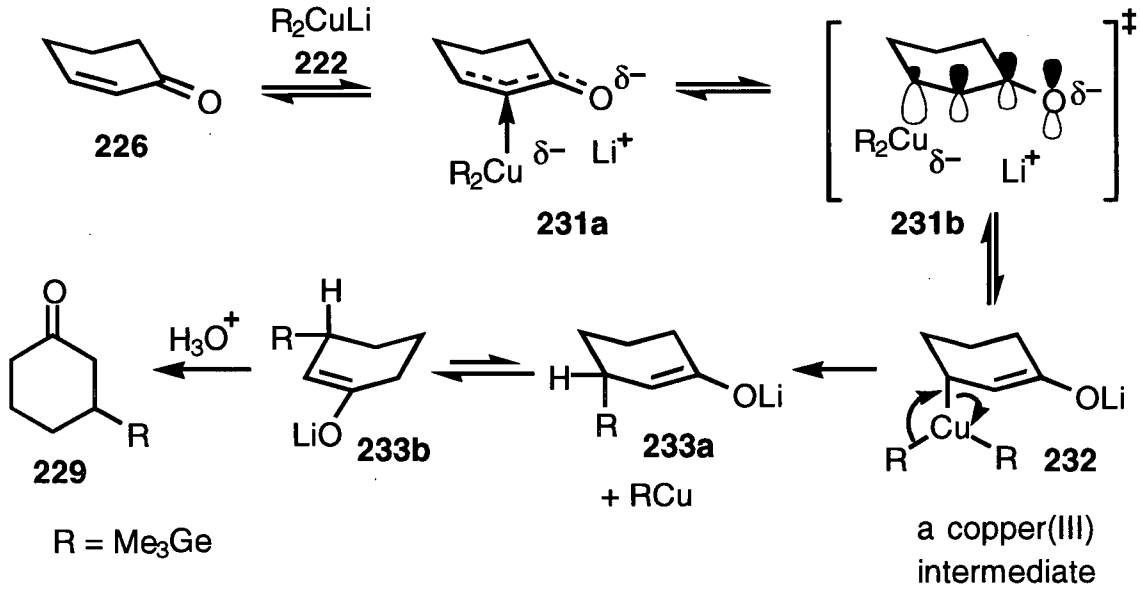
Still[106,107] has shown that Me_3MLi (M = Si, Sn) reagents undergo smooth 1,4-addition to cyclohex-2-en-1-one (**226**) in a THF–HMPA solvent mixture or in THF respectively, to produce exclusively the adduct **229a** and **229b**, respectively (**Scheme 38**). Alternatively, when a solution of Me_3SnLi in diethyl ether was treated with **226**, the allylic alcohol **230b** was formed predominantly.[107]

Therefore, it could be argued that Me_3GeLi (**149**) might also add in a 1,4-fashion to the enone **226** in THF solution. When cyclohex-2-en-1-one (**226**) was allowed to react with Me_3GeLi (**149**) in THF at –78 °C for 5 min, a mixture of two compounds was obtained in a ratio of 1:3.8 (GLC analysis). Isolation and purification of the crude oil obtained afforded compound **229** in 20% yield as well as product **230** in 59% yield. The ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **230** exhibited the following signals: a one-proton ddd (J = 9.8, 3.8 and 3.0 Hz) at δ 5.75 (vinylic proton), a one-proton ddd (J = 9.8, 1.4 and 1.4 Hz) at δ 5.69, a one-proton multiplet at δ 2.08–1.98, a three-proton multiplet at δ 1.94–1.72, a two-proton multiplet at δ 1.68–1.50, a one-proton broad signal at δ 1.27 (-OH) as well as a nine-proton singlet at δ 0.17 (Me_3Ge-). The IR spectrum derived from **230** showed a broad signal at 3425 cm^{-1} (-OH) and HRMS analysis indicated a signal at m/z 216.0567, in good agreement with the calculated value of 216.0569 for $C_9H_{18}{}^{74}GeO$.

Thus, under the experimental conditions used, the chemoselectivity of addition of Me_3SiLi and Me_3SnLi is higher than that derived from addition of Me_3GeLi (**149**). The selectivity of addition of reagents **168** and **222–225** (**Table 11**) to **226** is also superior to that of Me_3GeLi (**149**), evident from the exclusive formation of **229**.

2.3.3.1.1 Mechanistic Considerations

Attempts to gain insight into the mechanistic picture of cuprate addition to α,β-unsaturated ketones has generated a lot of research over the past years. Several different proposals, such as single electron transfer[108] between the organocopper an the enone substrate, as well as formation of a charge transfer complex between the reactants,[109] have been put forth. Another proposal delineates the reversible formation of an intermediate d,π* cuprate–enone complex[110] in the conjugate addition of organocopper(I) reagents to enones. The latter proposal is summarized in **Scheme 39** and depicts, for example, the conjugate addition of $(Me_3Ge)_2CuLi$ (**222**) to cyclohex-2-en-1-one (**226**).

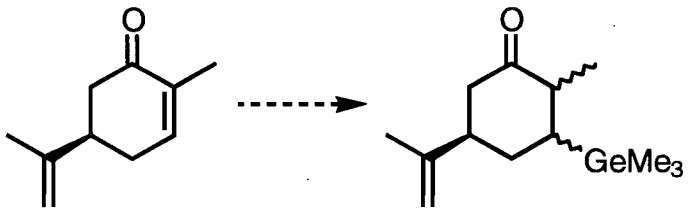


Scheme 39

Initially, complexation of the cuprate reagent **222** to the enone moiety of **226** generates the d,π* intermediate **231a**. Subsequently, C–Cu bond formation perpendicular to the plane of the p orbital system (**231b**) leads to the copper(III) intermediate **232**. Reductive

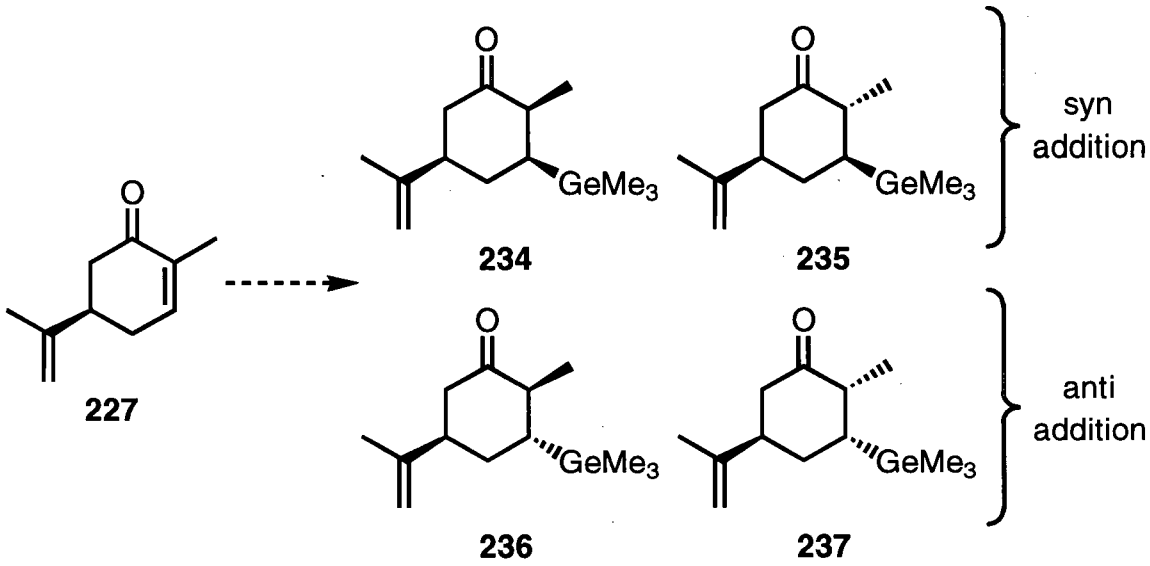
elimination generates the copper(I) species RCu as well as the enolate **233a**. The latter enolate can undergo conformational change to **233b**, thus changing the R group from an axial to a more stable equatorial orientation. Protonation of the enolate during work-up affords 3-trimethylgermylcyclohexanone (**229**).

2.3.3.2 CONJUGATE ADDITION TO *l*-CARVONE (**227**)



227 **234–237**

l-Carvone (**227**) was the next substrate selected for the conjugate addition of the (trimethylgermyl)copper(I) reagents **168** and **223–225**. In this transformation, the four diastereomeric adducts **234–237** can be formed. The diastereomeric pair **234** and **235** is the result of a syn addition of the Me_3Ge- group with respect to the isopropenyl moiety in **227**, whereas the **236** and **237** pair arises from an anti addition of the Me_3Ge- group. Each member of a pair shares an epimeric relationship at the carbon bearing the methyl group.



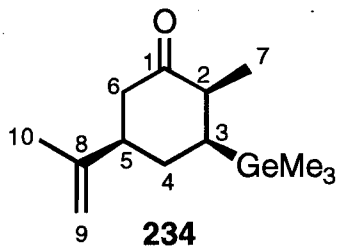
The reagent $(Me_3Ge)_2Cu(CN)Li_2$ (**224**) was employed to effect the initial conjugate addition to *l*-carvone (**227**). Thus, treatment of a solution of reagent **224** (0.6 equiv) in THF with the enone **227** (1 equiv) at –78 °C for 1 h resulted in the formation of a complex mixture. Periodic TLC analyses of aliquots of the reaction mixture indicated that the conversion of the starting material was incomplete after 1 h and was no longer progressing.

In a separate experiment, a solution of reagent **224** (0.65 equiv) in THF was treated sequentially with chlorotrimethylsilane (1.3 equiv) and the enone **227** (1 equiv) at –78 °C. TLC analysis of an aliquot of the reaction mixture after 0.5 h at –78 °C indicated that the conversion of starting material to product (enol trimethylsilyl ether) was incomplete. Therefore, the mixture was warmed gradually to 0 °C over a 0.5 h period, at which time the conversion of the starting material appeared to be complete (TLC analysis). After isolation, GLC analysis of an aliquot of the crude oil indicated that two products had been formed in a ratio of 1.4:1. This oil was dissolved in THF and the solution was treated with 1 M hydrochloric acid (few drops) at room temperature for 1 h in order to hydrolyze the enol

trimethylsilyl ether function. Isolation and purification of the crude product gave a clear and colorless oil in 86% yield. ^{1}H NMR (400 MHz, C_6D_6) spectroscopic analysis of this oil indicated the presence of four products, evident from the four singlets in the region δ 0.10 and δ –0.02 in a ratio of 1.1:2.5:1:3.9, attributed to the Me_3Ge- group of the four diastereomeric products **234–237**, respectively. In order to ascertain the identity and stereochemistry of each products, it was decided to isolate the four compounds **234–237**.

2.3.3.2.1 Isolation and Characterization of the Four Diastereomers **234–237**

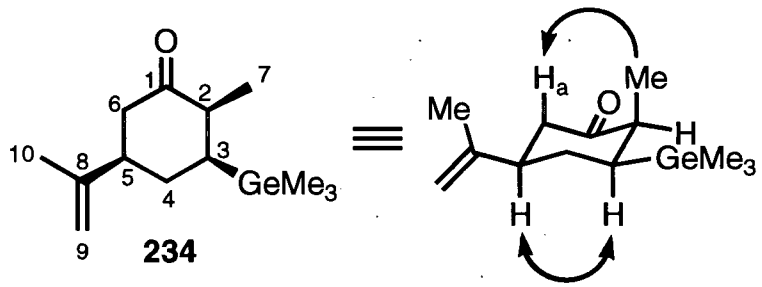
Two samples (≈100 mg each) of the mixture obtained as described above were subjected to HPLC (silica Partisil, 10 μm; 22 mm × 250 mm column, 99:1 hexane–ethyl acetate) individually. These chromatographies resulted in a rough separation to afford three fractions. The corresponding fractions of the separate injections were combined and concentrated under reduced pressure. The first fraction to be eluted, fraction ***A*** (retention time 42–45 min), afforded 45 mg of an oil which consisted of a mixture of two components (compounds **237** and **235**). The second fraction to be eluted, fraction ***B*** (retention time 53–62 min), afforded 28 mg of an oil which was mostly one component (compound **236**). Fractions ***A*** and ***B*** were processed further as described below. The third fraction to be eluted (retention time 65–78 min) afforded 28 mg of compound **234** as a clear colorless oil.



234

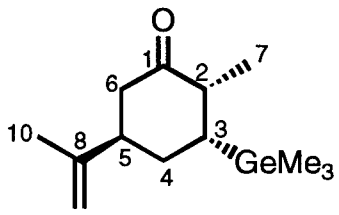
The ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of this oil exhibited the following charac-

teristic signals: two one-proton singlets at δ 4.75 and 4.73 (H-9a, H-9b), a three-proton singlet at δ 1.73 (Me-10), a three-proton doublet (J = 7.2 Hz) at δ 1.12 (Me-7) as well as a nine-proton singlet at δ 0.15 (Me_3Ge-). The proton H-2 was evident as a quadruplet of doublets (J = 7.2 and 4.0 Hz) at δ 2.55 with a 7.2 Hz coupling to the Me-7. The COSY spectrum allowed the assignment of proton H-3 (δ 1.39 ddd, J = 13.4, 4.0 and 3.8 Hz) through the correlation of its signal to that of proton H-2 (the majority of the signals could be assigned from the data derived from the COSY spectrum; see Experimental section **Table 23**, p 277). Proton H-6a was evident as a doublet of doublets (J = 13.0 and 13.0 Hz) at δ 2.50 and, consequently, a trans-diaxial relationship between H-5 and H-6a with a 13.0 Hz coupling constant, was established. The COSY spectrum allowed the assignment of proton H-5 (δ 2.42–2.32 m) through the correlation of its signal to that of proton H-6a.



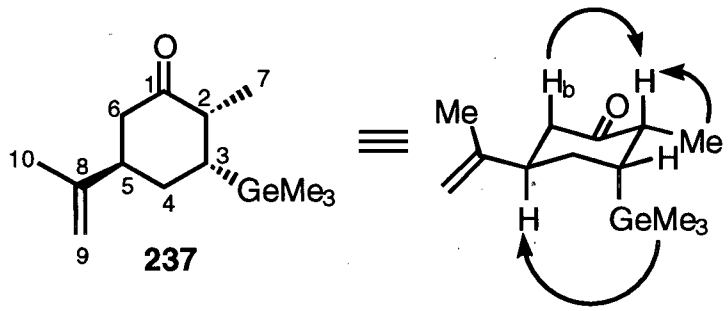
^{1}H NMR NOE difference experiments were performed to establish the stereochemistry of this compound. Thus, irradiation of the doublet at δ 1.12 (Me-7) caused the signal at δ 2.50 (H-6a) to be enhanced. When the resonance for H-5 (δ 2.42–2.32) was irradiated an enhancement was observed for H-3 (δ 1.39). Similarly, irradiation of the signal at δ 1.39 (H-3) caused the signal at δ 2.42–2.32 (H-5) to be enhanced. These experiments, along with the data derived from the ^{1}H NMR and COSY spectra presented above, are consistent with the structural assignment for compound **234**.

Fraction *A* (45 mg) from the first HPLC separation (vide supra) was subjected to reversed phase HPLC (C_{18} μBondapak, 10 μm; 8 mm × 100 mm column, acetonitrile–water step gradient) in four approximately equal portions. The combined first fractions to be eluted (retention time 56 min) afforded 23 mg of compound **237** as a clear colorless oil.

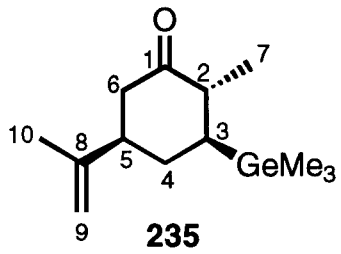


237

The ^{1}H NMR (400 MHz, C_6D_6) spectrum derived from this oil exhibits the following characteristic signals: a two-proton singlet at δ 4.73 (H-9a, H-9b), a three-proton singlet (Me-10) at δ 1.52 (part of the δ 1.56–1.47 multiplet), a three-proton doublet (J = 6.2 Hz) at δ 1.07 (Me-7) as well as a nine-proton singlet at δ 0.10 (Me_3Ge-). The proton H-6b was evident as a doublet of doublets (J = 13.6 and 11.2 Hz) at δ 2.07 and, consequently, a trans-diaxial arrangement between H-6a and H-5 was established. The COSY spectrum allowed the assignment of proton H-5 (part of δ 2.35–2.25 m) through the correlation of its signal to that of proton H-6b (the majority of the signals could be assigned from the data derived from the COSY spectrum; see Experimental section **Table 24**, p 279). The proton H-3 was evident as the highest field one-proton signal (ddd, J = 6.2, 4.6 and 4.6 Hz) at δ 1.38. These coupling constants indicate that H-3 is not part of a trans-diaxial arrangement and, therefore, must be in an equatorial orientation. The COSY spectrum allowed the assignment of the proton H-2 through the correlations of its signal (part of δ 2.35–2.25 m) to that of proton H-3 and Me-7.

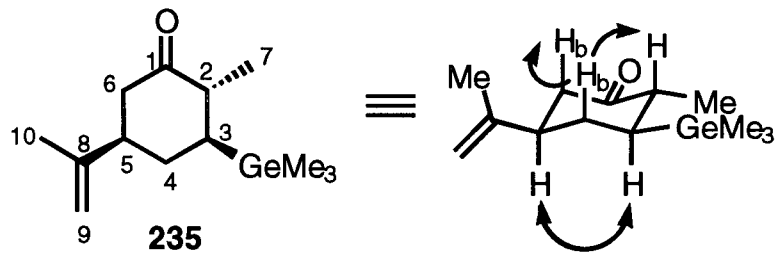


^{1}H NMR NOE difference experiments were performed to establish the stereochemistry of compound **237**. Thus, irradiation of the doublet at δ 1.07 (Me-7) caused a quadruplet of doublets (J = 6.2 and 6.2 Hz) at δ 2.31 (H-2) to be enhanced. This experiment was performed to differentiate the resonance derived from H-2 from the multiplet expected from H-5 (vide infra), both of which are part of the δ 2.35–2.25 multiplet. When the signal for H-6b (δ 2.07) was irradiated, an enhancement was observed at δ 2.31 (qd, J = 6.2 and 6.2 Hz) for H-2. On the other hand, irradiation of the singlet derived from the Me_3Ge- group (δ 0.10) caused the multiplet at δ 2.32–2.25 to be enhanced (H-5). This signal was *different* from the multiplet observed in the non-irradiated spectrum for H-2 and H-5 together. These experiments, along with the data derived from the ^{1}H NMR and COSY spectra, are consistent with the structural assignment for compound **237**.



The combined second fractions to be eluted (retention time 59 min) from the reversed phase HPLC of fraction ***A*** (vide supra) afforded 9.8 mg of compound **235** as a clear colorless oil. The ^{1}H NMR (400 MHz, C_6D_6) spectrum of this oil exhibited the following characteristic

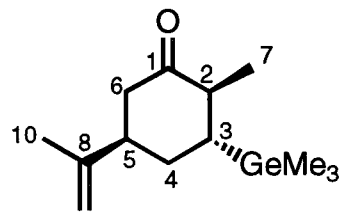
signals: two one-proton doublets (J = 1.4 Hz) at δ 4.69 and 4.64 (H-9a, H-9b), a three-proton singlet at δ 1.50 (Me-10), a three-proton doublet (J = 6.6 Hz) at δ 1.08 (Me-7) as well as a nine-proton singlet at δ 0.04 (Me_3Ge-). The proton H-2 was evident as a doublet of quadruplets (J = 13.2 and 6.6 Hz) at δ 1.92. The COSY spectrum allowed the assignment of H-3 through the correlation of its signal (δ 0.77 ddd, J = 13.2, 13.2 and 3.2) to that of proton H-2 (the majority of the signals could be assigned from the data derived from the COSY spectrum; see Experimental section **Table 25**, p 281). The 13.2 Hz coupling constant between protons H-2 and H-3 indicates a trans-diaxial arrangement. The proton H-4b was assigned through the correlation of its signal (δ 1.22 ddd, J = 13.2, 13.2 and 11.8 Hz) to that of proton H-3. These coupling constants indicate that H-4b possesses two neighboring protons in trans-diaxial arrangements. The proton H-6b was evident as a doublet of doublets (J = 13.2 and 12.4 Hz) at δ 1.97 and, thus, a trans-diaxial arrangement between protons H-5 and H-6b was established. The COSY spectrum allowed the assignment of proton H-5 through the correlation of its signal (δ 2.21–2.11 m) to that of proton H-6b.



^{1}H NMR NOE difference experiments were performed in order to establish the stereochemistry of compound **235**. Thus, irradiation of the resonance for H-4b (δ 1.22) caused the signals for H-2 (δ 1.92) and H-6b (δ 1.97) to be enhanced. When the multiplet at δ 2.21–2.11 (H-5) was irradiated the signal at δ 0.77 (H-3) was enhanced. Similarly, irradiation

of H-3 (δ 0.77) resulted in an enhancement of the resonance for H-5 (δ 2.21–2.11). The results of these experiments, along with the data derived from the ^{1}H NMR and COSY spectra, are consistent with the structural assignment for compound **235**.

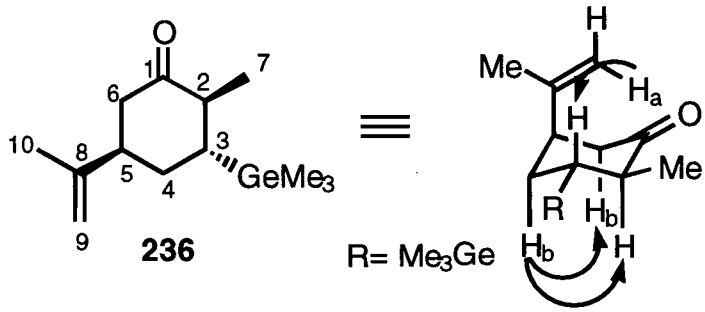
Fraction ***B*** (28 mg) from the initial chromatography was resubjected to HPLC under identical conditions (silica Partisil, 10 μm; 22 mm × 250 mm column, 99:1 hexane–ethyl acetate) to afford 8.2 mg of compound **236** as a clear colorless oil.



236

The ^{1}H NMR (400 MHz, C_6D_6) spectrum derived from this oil exhibits the following characteristic signals: two one-proton singlets at δ 4.94 and 4.86 (H-9a, H-9b), a three-proton singlet at δ 1.50 (Me-10), a three-proton doublet (J = 6.8 Hz) at δ 1.07 (Me-7) as well as a nine-proton singlet at δ 0.05 (Me_3Ge-). The proton H-2 was evident as a doublet of quadruplets (J = 11.0 and 6.8 Hz) at δ 2.01. The COSY spectrum allowed the assignment of proton H-3 through the correlation of its signal (δ 1.12 ddd, J = 11.0, 11.0 and 3.6 Hz) to that of proton H-2 (the majority of the signals could be assigned from the data derived from the COSY spectrum; see Experimental section **Table 26**, p 284). The large coupling constants (J = 11.0 and 11.0 Hz) associated with the signal due to H-3 indicate that this proton is in a trans-diaxial arrangement with two neighboring protons. The COSY spectrum also allowed the assignment of the following protons through sequential correlations of their signals: H-4b (δ 1.38 ddd, J = 13.8, 11.0 and 4.6 Hz, correlation with H-3), H-5 (δ 2.41–2.34 m,

correlation with H-4b) and H-6b (δ 2.11 dd, J = 14.2 and 6.0 Hz, correlation with H-5).



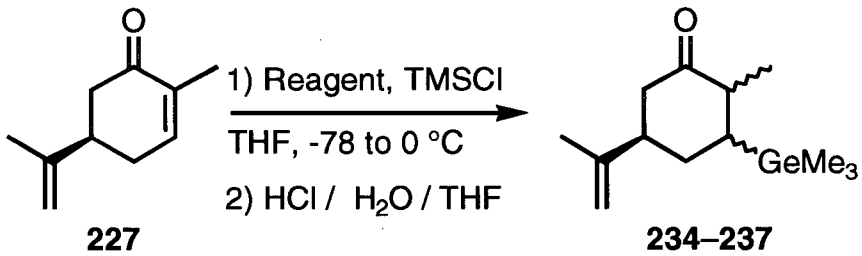
^{1}H NMR NOE difference experiments were performed to establish the stereochemistry of compound **236**. Thus, irradiation of H-9a (δ 4.94) caused the resonance for H-3 (δ 1.12) to be enhanced. When the signal for H-4b (δ 1.38) was irradiated, the resonances at H-2 (δ 2.01) and H-6b (δ 2.11) were enhanced. The results of these experiments, along with the data derived from the ^{1}H NMR and COSY spectra, are consistent with the structural assignment for compound **236**.

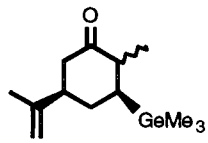
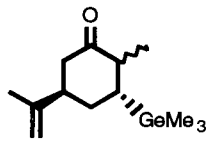
2.3.3.2.2 Conjugate Addition of Reagents **168** and **223–225** to *l*-Carvone (**227**)

Table 12 contains a summary of the conjugate addition of reagents **168** and **223–225** to *l*-carvone (**227**). The reaction of $Me_3GeCu{\bullet}Me_2S$ (**168**) with **227** (entry 1), for example, was accomplished in the following manner. A cold (–78 °C) solution of reagent **168** (1.3 equiv) in dry THF was sequentially treated with chlorotrimethylsilane (1.3 equiv) and **227** (1 equiv). The reaction mixture was stirred at –78 °C for 0.5 h, then was allowed to warm to 0 °C over a 0.5 h period. After isolation, the crude oil was dissolved in THF and the solution was treated with 1 M hydrochloric acid (few drops) at room temperature for 1 h. ^{1}H NMR (400 MHz, C_6D_6) spectroscopic analysis of the crude mixture indicated that the addition of the Me_3Ge- group occurred predominantly (1.4:1) in a fashion syn to the isopropenyl moiety

(**234** + **235**). After isolation and purification, the products **234–237** were obtained as a mixture in 82% yield.

Table 12: Conjugate Addition of Reagents **168** and **223–225** to *l*-Carvone (**227**)



Entry	Reagent[a]	 **234 + 235**		 **236 + 237**	Yield (%)[b]
1	$Me_3GeCu{\bullet}Me_2S$ **168**	1.4	:	1[c]	82
2	$Me_3GeCu(CN)Li$ **223**	1.4	:	1[c]	80
3	$(Me_3Ge)_2Cu(CN)Li_2$ **224**	1	:	1.4[c]	86
4	$Me_3Ge(Me)Cu(CN)Li_2$ **225**	1	:	3.9[c]	90

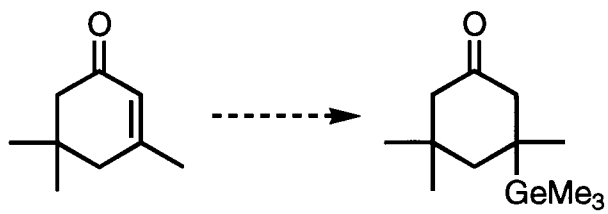
[a] 1.3 equiv of reagent were employed, except for reagent **224** for which 0.65 equiv was utilized. [b] Yield of isolated and purified product mixture (**234–237**). [c] Ratio determined from ^1H NMR (400 MHz, C_6D_6) spectroscopic analysis of the crude mixture (integration of the Me_3Ge- singlets).

The remainder of the reagents listed in **Table 12** were employed in a manner similar with that outlined above. For the conversion summarized in entry 2, the stereoselectivity of addition of the Me_3Ge- group, using $Me_3GeCu(CN)Li$ (**223**), was comparable with that of reagent **168** affording predominantly (1.4:1) products of syn addition in 80% yield. When reagent **224** (entry 3) was employed (see previous discussion), the selectivity was reversed: the addition of the Me_3Ge- group occurred to give mainly (1.4:1) the anti adducts (**236** +

237). The yield of the mixture obtained was 86%. In the reaction summarized in entry 4, conjugate addition of reagent **225** to *l*-carvone (**227**) afforded predominantly (3.9:1) the products of anti addition (**236** + **237**) (overall yield, 90%). The epimeric ratio at the α-carbon varied for the different experiments, but was generally ≈2.5:1 for the syn adducts, with the epimer **235** predominating, whereas for the anti adducts the ratio was ≈3:1, with the epimer **237** being dominant.

The results summarized in **Table 12** require additional comments. It is well documented that cuprate additions to enones bearing a substituent at C-5, such as *l*-carvone (**227**), result largely in the formation of adducts with the newly introduced group anti to the C-5 substituent.[105,111,112] As shown in **Table 12**, the ratios obtained for the different trimethylgermylcuprates indicate that the reactions of these reagents with *l*-carvone (**227**) proceed with poor stereoselectivity. The reasons for this lack of selectivity remain unclear.

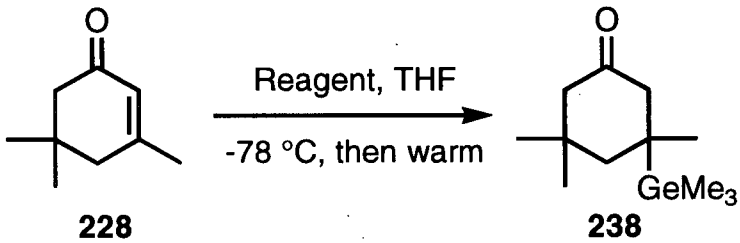
2.3.3.3 CONJUGATE ADDITION TO ISOPHORONE (**228**)



228 **238**

Isophorone (**228**) was selected as substrate for the conjugate addition of the (trimethylgermyl)cuprates to evaluate their ability to undergo addition to a sterically hindered substrate. **Table 13** contains a summary of the conjugate addition of reagents **224** and **225** to isophorone (**228**). The effect of certain additives on the production of **238** was also evaluated.

Table 13: Conjugate Addition of Reagents **224** and **225** to Isophorone (**228**)



Entry	Reagent[a]	Additive	Yield (%)[b]
1[c]	$(Me_3Ge)_2Cu(CN)Li_2$ **224**	HMPA (2.6 equiv)	42
2[d]	$Me_3Ge(Me)Cu(CN)Li_2$ **225**	none	33
3[e]	$Me_3Ge(Me)Cu(CN)Li_2$ **225**	TMSCl (1.2 equiv)	33
4[f]	$Me_3Ge(Me)Cu(CN)Li_2$ **225**	TMSBr (4 equiv)	66

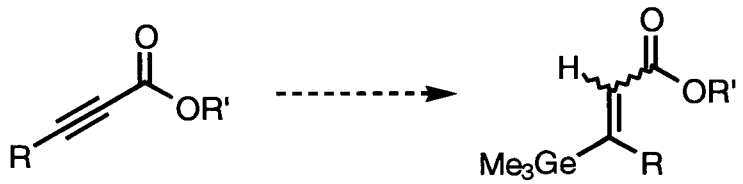
[a] 0.64 equiv of reagent **224** was used whereas 1.2–1.3 equiv of reagent **225** were employed.
[b] Yield of isolated and purified product. [c] Conditions: –78 °C 1 h, then HMPA, –78 → 0 °C.
[d] Conditions: –78 → 0 °C. [e] Conditions: –78 → –30 °C. [f] Conditions: –78 → –15 °C.

A solution of **224** (0.64 equiv) in dry THF (entry 1) was treated with isophorone (**228**) (1 equiv) at –78 °C. After the reaction mixture had been stirred at –78 °C for 1 h, HMPA (2.6 equiv) was added. The mixture was allowed to stir for an additional 0.5 h, then was warmed to 0 °C over 0.5 h to afford the product **238** in 42% yield. When 1.2 equivalents of a solution of reagent **225** was treated with 1 equivalent of **228** at –78 °C for 1h, then was warmed to 0 °C over 0.75 h, the adduct **238** was formed in 33% yield (entry 2). Entry 3 summarizes a similar experiment in which 1.2 equivalents of chlorotrimethylsilane were used as additive, prior to the addition of isophorone (**238**), to afford **238** in 33% yield after hydrolysis of the intermediate enol trimethylsilyl ether. A solution of reagent **225** (1.3 equiv) was treated sequentially with bromotrimethylsilane (4 equiv) and **228** (1 equiv) at –78 °C (entry 4). The reaction mixture was stirred at –78 °C for 1 h, then was allowed to warm

slowly to –30 °C over 2 h. After hydrolysis of the intermediate enol trimethylsilyl ether, the product **238** was obtained in 66% yield.

The results summarized in **Table 13** suggest that neither HMPA nor chlorotrimethylsilane are very effective additives in this transformation. On the other hand, bromotrimethylsilane served as an effective additive for the production of **238**, increasing the yield from 33% to 66% under similar experimental conditions (compare entries 2 and 4).

2.3.4 ADDITION OF (TRIMETHYLGERMYL)COPPER(I)–DIMETHYL SULFIDE (168) AND (TRIMETHYLGERMYL)CUPRATES TO ALK-2-YNOATES



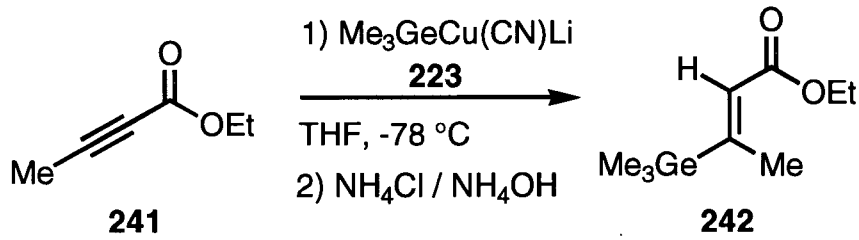
239 **240**

As outlined in the previous section, (trimethylgermyl)copper(I)–dimethyl sulfide (**168**) and the (trimethylgermyl)cuprates **222**–**225** serve as efficient reagents for the conjugate addition to cyclohex-2-en-1-ones. The possibility of employing these reagents for the preparation of (*E*)- and/or (*Z*)-3-trimethylgermylalk-2-enoates of general structure **240**, via addition to alk-2-ynoates of general structure **239**, was envisaged.

2.3.4.1 ADDITION TO ETHYL BUT-2-YNOATE (241)

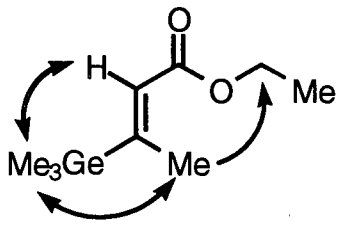
241 **242** **243**

The 1,4-addition of the Me_3Ge- group onto the conjugated carbonyl system of **241** can result in the formation of one or both of two adducts, ethyl (*E*)- and/or (*Z*)-3-trimethylgermyl-but-2-enoate (**242**) and (**243**), respectively. The (*E*) isomer **242** was expected to be the major product resulting from the germylcupration of **241** by analogy with the literature precedents for the stannylcupration of alk-2-ynoates.[113,114]



(37)

The initial investigation was carried out using $Me_3GeCu(CN)Li$ (**223**) and the commercially available ethyl but-2-ynoate (**241**) was selected as substrate (**Equation 37**). Thus, a cold (–78 °C) solution of 1.3 equivalents of reagent **223** in THF, prepared as described above (section 2.3.2, p 136 ff.), was treated with one equivalent of ethyl but-2-ynoate (**241**). The reaction mixture was stirred at –78 °C for 20 min, then was treated sequentially with glacial acetic acid (≈4 equiv) and NH_4Cl/NH_4OH (pH 8–9). GLC analysis of the crude product indicated that a single substance (>99% by GLC) had been formed. Isolation and purification of the crude product obtained afforded a clear colorless oil in 90% yield. The ^1H NMR (400 MHz, $CDCl_3$) spectrum derived from this oil exhibits the following signals: a one-proton quadruplet (J = 1.8 Hz) at δ 5.95, a two-proton quadruplet (J = 7.2 Hz) at δ 4.14, a three-proton doublet (J = 1.8 Hz) at δ 2.26, a three-proton triplet (J = 7.2 Hz) at δ 1.27 as well as a nine-proton singlet at δ 0.23. The IR spectrum of this oil showed bands at 1718 (ν C=O) and 1614 cm^{-1} (ν C=C), whereas HRMS (DCI, NH_3 + CH_4) analysis indicated a signal at *m/z* 233.0597, a value identical with that calculated for $C_9H_{19}{}^{74}GeO_2$ $(M + 1)^+$.

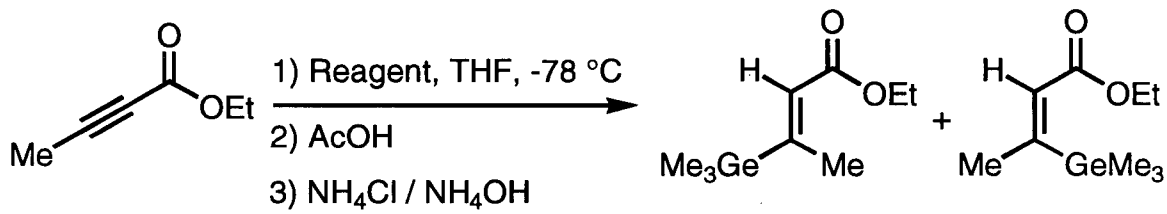


242

^1H NMR NOE difference experiments were performed to establish the geometry of the

alkene function of the isolated compound. Thus, irradiation of the resonance for the vinylic proton (δ 5.95) caused the signal for the Me_3Ge- group (δ 0.23) to be enhanced. When the singlet for the Me_3Ge- group (δ 0.23) was irradiated, enhancements were observed for the vinylic proton (δ 5.95) and the alkenyl methyl (δ 2.26). Irradiation of the doublet at δ 2.26 (alkenyl methyl) caused the resonances for the Me_3Ge- group (δ 0.23) and the methylene protons (δ 4.14) to be enhanced. These experiments, along with the spectral data presented above are consistent with the structural assignment for ethyl (*E*)-3-trimethylgermylbut-2-enoate (**242**).

Table 14: Addition of (Trimethylgermyl)copper(I) Reagents to Ethyl But-2-ynoate (**241**)



241 **242** **243**

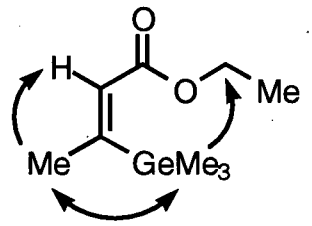
Entry	Reagent[a]	Ratio[b] **242** : **243**	Yield[c]
1	$Me_3GeCu{\bullet}Me_2S$ **168**	>99 : <1	81
2	$Me_3GeCu(CN)Li$ **223**	>99 : <1	90
3	$(Me_3Ge)_2CuLi$ **222**	1.7 : 1	90[d]
4	$Me_3Ge(Me)Cu(CN)Li_2$ **225**	1 : 3.9	(*E*) 17, (*Z*) 69

[a] ≈1.3 equiv of reagent were employed except for reagent **222**, for which 0.66 equiv was used. [b] Ratio determined by GLC analysis of an aliquot of the crude product. [c] Yield of isolated and purified product unless otherwise stated. [d] Isolated as a mixture of (*E*/*Z*) isomers.

Table 14 summarizes the reaction of reagents **168**, **223**, **222** and **225** with ethyl but-2-

ynoate (**241**). The reaction of **241** with reagents **168**, **222** and **225** was effected in manner similar to that outlined above for $Me_3GeCu(CN)Li$ (**223**) (entry 2). Treatment of a solution of ≈1.3 equivalents of $Me_3GeCu{\bullet}Me_2S$ (**168**) (entry 1) in THF with one equivalent of **241** afforded the (*E*) isomer **242** in 81% yield. In the reaction summarized in entry 3, when a solution of reagent **222** (0.66 equiv) was treated with **241** (1 equiv), a mixture of isomers **242** and **243** (vide infra) was obtained in 90% yield (1.7:1, *E*:*Z*).

Treatment of a solution of reagent **225** (1.3 equiv) (entry 4) with **241** (1 equiv) gave a mixture of products **242** and **243**, in a ratio of 1:3.9 respectively (GLC analysis). The crude oil obtained was subjected to flash chromatography to afford two fractions. The first fraction to be eluted, compound **243** (vide infra), was obtained in 69% yield as a clear colorless oil. The second fraction to be eluted afforded ethyl (*E*)-3-trimethylgermylbut-2-enoate (**242**) in 17% yield. The structural assignment for **243** was based on the following data. The ^1H NMR (400 MHz, $CDCl_3$) spectrum exhibited a one-proton quadruplet (J = 1.6 Hz) at δ 6.28, a two-proton quadruplet (J = 7.2 Hz) at δ 4.13, a three-proton doublet (J = 1.6 Hz) at δ 2.01, a three-proton triplet (J = 7.2 Hz) at δ 1.26 as well as a nine-proton singlet at δ 0.29. The IR spectrum of this oil showed bands at 1718 (ν C=O) and 1610 cm^{-1} (ν C=C). In addition, HRMS analysis indicated a signal at *m/z* 217.0291, in good agreement with the calculated value of 217.0284 for $C_8H_{15}{}^{74}GeO_2$ $(M - CH_3)^+$.



243

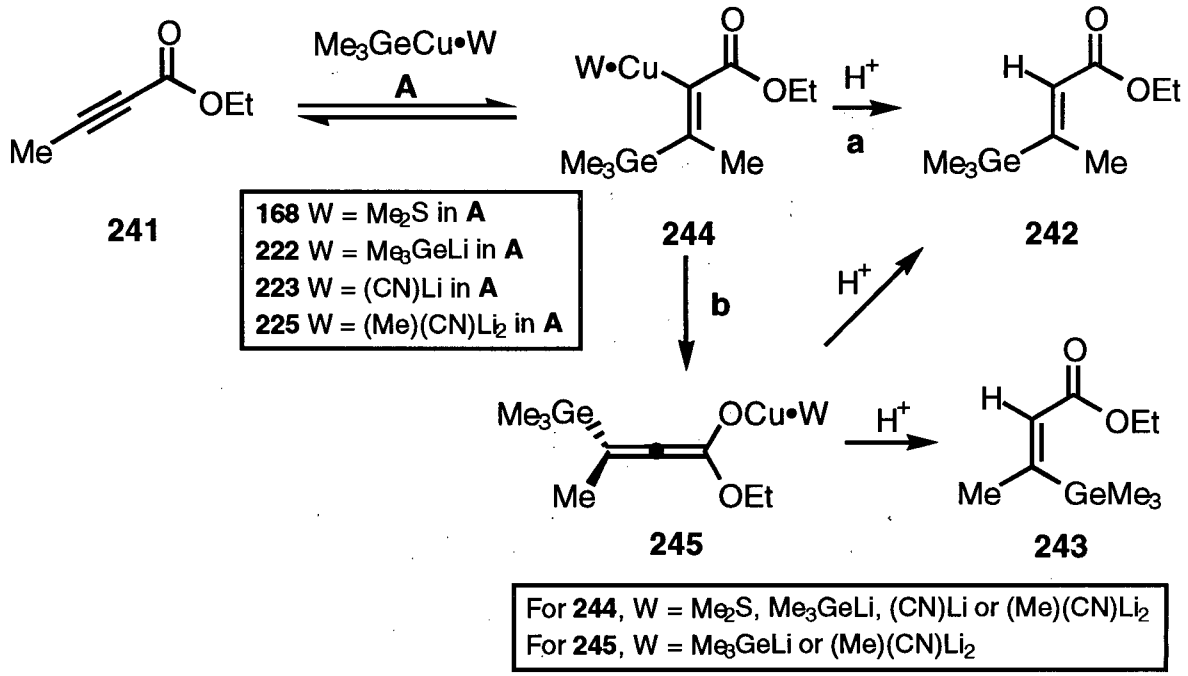
^{1}H NMR NOE difference experiments were performed to establish the geometry of the alkene function of **243**. Thus, irradiation of the alkenyl methyl doublet (δ 2.01) caused an enhancement of the signals for the vinylic proton (δ 6.28) and the Me_3Ge- group (δ 0.29). When the singlet at δ 0.29 (Me_3Ge-) was irradiated, the resonances at δ 4.13 (methylene protons) and 2.01 (alkenyl methyl) were enhanced. The results of these experiments, along with the spectral data presented above, are consistent with the structural assignment for ethyl (*Z*)-3-trimethylgermylbut-2-enoate (**243**).

The experimental conditions outlined above did not allow a completely stereoselective preparation of ethyl (*Z*)-3-trimethylgermylbut-2-ynoate (**243**). However, compound **243** can be obtained as a single stereoisomer, in a synthetically useful yield (≈70%), via facile chromatographic separation from the corresponding (*E*) isomer (see entry 4, **Table 14**).

2.3.4.1.1 Mechanistic Considerations

A possible reaction pathway rationalizing the formation of stereoisomers **242** and **243** is depicted in **Scheme 40**. Thus, cis addition[93-95] of a (trimethylgermyl)copper(I) reagent to the alkyne function of **241** generates the alkenylcopper intermediate **244**. Protonation of the latter intermediate (path **a**) produces the (*E*) isomer **242**. The formation of **242** via path **a** is predominant for the reagents $Me_3GeCu{\bullet}Me_2S$ (**168**) and $Me_3GeCu(CN)Li$ (**223**) (see entries 1 and 2 in **Table 14**, p 158). Alternatively, **244** can isomerize (path **b**) to the (postulated)

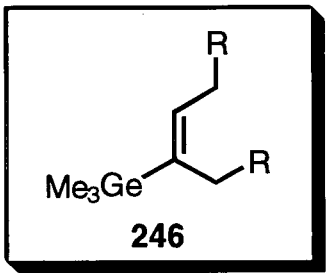
allenoate species **245** (a similar intermediate has been proposed to rationalize the formation of alkyl (Z)-2-trimethylstannylalk-2-enoates[113] from reaction of $Me_3SnCu(SPh)Li$ with alkyl alk-2-ynoates). Protonation of the allenoate **245** from the same side as the Me_3Ge- group leads to the formation of **242**. On the other hand, protonation of the allenoate from the opposite side of the Me_3Ge- group generates **243**.



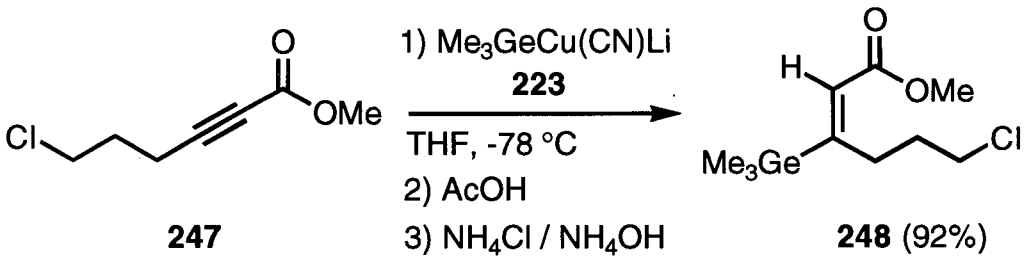
Scheme 40

Pathways **a** and **b** are probably both in effect with reagents $(Me_3Ge)_2CuLi$ (**222**) and $Me_3Ge(Me)Cu(CN)Li_2$ (**225**) (see **Table 14**, entries 3 and 4). Interestingly, the nature of **W** seem to have a profound influence on the ease of formation of the allenoate **245**. Under identical experimental conditions, while reagents **168** and **223** appear to generate a stable intermediate **244**, reagents **222** and **225** seem to undergo (at least in part) isomerization to the (postulated) allenoate intermediate **245**.

2.3.4.2 Synthesis of Methyl (*E*)-6-Chloro-3-trimethylgermylhex-2-enoate (**248**)

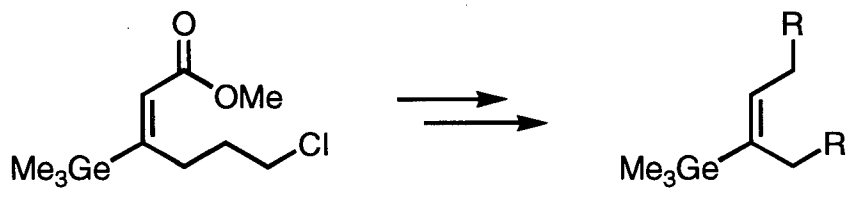


The preparation of trifunctional reagents of general structure **246**, which should prove useful in synthesis, can possibly be achieved through the germylcupration of functionalized alk-2-ynoates. The stereocontrolled conversion of methyl 6-chlorohex-2-ynoate[115] (**247**) into methyl (*E*)-6-chloro-3-trimethylgermylhex-2-enoate (**248**) illustrates this concept (**Equation 38**).



(**38**)

A cold (–78 °C) solution of 1.3 equivalents of $Me_3GeCu(CN)Li$ (**223**) in THF was treated with one equivalent of **247**. The reaction mixture was stirred at –78 °C for 30 min, then was treated sequentially with glacial acetic acid (1.6 equiv) and aqueous NH_4Cl/NH_4OH (pH 8–9). Isolation and purification of the crude product obtained gave methyl (*E*)-6-chloro-3-trimethylgermylhex-2-enoate (**248**) in 92% yield.



248 **246**

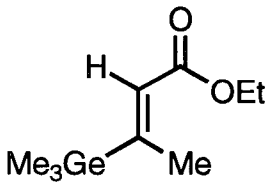
Conversion of **248**, and other structurally related substances, into trifunctional reagents (of general structure **246**) should be accomplished in a straightforward manner via functional group interconversions.

2.3.5 CONCLUSIONS

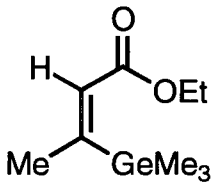
The novel (trimethylgermyl)cuprates **222–225** have been prepared by treatment of solutions of Me_3GeLi (**149**) in THF with copper(I) salts. These (trimethylgermyl)cuprates serve as excellent reagents in the conjugate addition of the Me_3Ge- group to cyclohex-2-en-1-ones.

$(Me_3Ge)_2CuLi$	$Me_3GeCu(CN)Li$	$(Me_3Ge)_2Cu(CN)Li_2$	$Me_3Ge(Me)Cu(CN)Li_2$
222	**223**	**224**	**225**

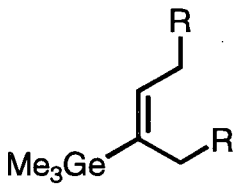
Reagents $Me_3GeCu{\bullet}Me_2S$ (**168**) and $Me_3GeCu(CN)Li$ (**223**) undergo stereocontrolled cis addition to the alkyne function of ethyl but-2-ynoate (**241**) at low temperature to produce ethyl (*E*)-2-trimethylgermylbut-2-enoate (**242**) in high yield. The completely stereoselective synthesis of ethyl (*Z*)-2-trimethylgermylbut-2-enoate (**243**) could not be achieved under the experimental conditions used. However, facile chromatographic separation of the mixture of (*E*/*Z*) isomers produced affords the (*Z*) isomer **243** in a synthetically useful yield (≈70%).



242



243



246

Finally, stereocontrolled germylcupration of functionalized alkynoates, followed by functional group interconversions, should provide convenient access to trifunctional reagents of general structure **246**.

3 EXPERIMENTAL

3.1 GENERAL

3.1.1 DATA ACQUISITION AND METHODS

Unless otherwise stated all glassware was dried at ≈140 °C in an oven or flame dried prior to use, and all reactions were performed under an atmosphere of dry argon. The Teflon cannulae (purchased from Canlab, 0.38 mm × 0.23 mm, catalogue # R5360-111 and 0.97 mm × 0.30 mm, catalogue # R5360-117) and stainless steel needles used to handle various anhydrous solvents and reagents were oven dried. The plastic syringes were flushed with dry argon prior to use. The glass microliter syringes were dried under reduced pressure (vacuum pump), stored in a desiccator and flushed with dry argon prior to use.

The following cooling baths were used to maintain sub-zero temperatures: –10 °C and –30 °C: aqueous $CaCl_2$–solid CO_2 (16.5 and 34.8 g $CaCl_2$/100 g water, respectively);[116] –78 °C: acetone–solid CO_2.

Solvent removal or concentration refers to solvent removal under reduced pressure (water aspirator) via a Büchi rotary evaporator at ≈15 Torr.

Thin layer chromatography (TLC) was performed using commercial aluminum-backed silica gel 60 F_{254} plates from E. Merck, type 5554, 0.2 mm. Reversed phase TLC was carried out on commercially available glass backed plates from Whatman, type $KC_{18}/KC_{18}F$. Visualization was accomplished using ultraviolet light (254 nm) and/or iodine, followed by heating the plates after staining with an appropriate reagent. The following stains were used:

1) phosphomolybdic acid in ethanol from Aldrich Chemical Co. Inc., 2) cerium sulfate–ammonium molybdate in aqueous H_2SO_4 (0.40 g $Ce(SO_4)_2$, 20 g $(NH_4)_6Mo_7O_{24}\bullet 4H_2O$, 400 mL 10% aqueous H_2SO_4), 3) anisaldehyde in H_2SO_4–ethanol (20 mL anisaldehyde, 20 mL concentrated H_2SO_4, 400 mL ethanol), 4) basic aqueous $KMnO_4$ (3 g $KMnO_4$, 20 g K_2CO_3, 5 mL 5% aqueous NaOH, 300 mL water). Flash chromatography[117] was performed using 230–400 mesh silica gel 60 from E. Merck. Reversed phase chromatography was performed using C_{18} functionalized[118] silica gel 60 with an appropriate solvent system applied to the technique described by Still.[117] TLC grade flash chromatography was performed using Sigma type H silica gel 10–40 μm, no binder, following the technique described by Taber.[119]

Gas–liquid chromatography (GLC) was performed on Hewlett-Packard model 5830A, 5880A or 5890 gas chromatographs, all three equipped with flame ionization detectors and fused capillary columns, either 25 m × 0.20 mm coated with 5% phenylmethyl silicone or Stabilwax 30 m × 0.25 mm × 0.25 μm.

High performance liquid chromatography (HPLC) was performed using a Waters 600E Multisolvent Delivery System connected in series, to 1) a Waters 486 Tunable Absorbance Detector and 2) a Waters 410 Differential Refractometer. The following columns were used: 1) Waters μPorasil silica 10 μm, 8 mm × 100 mm; 2) Waters μBondapak 10 μm, 8 mm × 100 mm and 25 mm × 100 mm; 3) Whatman Magnum 20 Partisil silica 10 μm, 20 mm × 250 mm.

Unless otherwise noted, distillations refer to bulb-to-bulb distillations; the temperature is indicated in parentheses and is uncorrected. Melting points were recorded on a Fisher-Johns melting point apparatus and are uncorrected.

Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded on Bruker models AC-200 (200.1 MHz) or WH-400 (400.1 MHz) spectrometers using deuteriochloroform ($CDCl_3$) or deuteriobenzene (C_6D_6) as solvents. Signal positions (δ) are given in parts per million from tetramethylsilane and were measured relative to the residual signal of chloroform (δ 7.24) or benzene (δ 7.15). The following abbreviations are used to describe the multiplicity: br = broad, d = doublet, m = multiplet, q = quartet, s = singlet, t = triplet. Coupling constants (*J* values) are given in Hertz (Hz). Data are reported in the following format: chemical shift (ppm), multiplicity, number of protons, coupling constants (Hz) and assignment (when known). In some instances the assignments are supported by COSY (^{1}H-^{1}H homonuclear correlation spectroscopy) and ^{1}H NMR NOE (nuclear Overhauser enhancement) difference experiments. These experiments were carried out using the Bruker WH-400 spectrometer.

Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on Varian XL-300 (75.4 MHz) or Bruker AMX-500 (125.7 MHz) spectrometers, using deuteriochloroform or deuteriobenzene as solvents. Signal positions are given in parts per million from tetramethylsilane and were measured relative to the signal of deuteriochloroform (δ 77.0) or deuteriobenzene (δ 128.0). Attached proton test (APT) experiments were used to differentiate methyl and methine from methylene and quaternary carbons.

Infrared (IR) spectra were recorded on a Perkin Elmer 1710 Fourier transform spectrophotometer with internal calibration using sodium chloride plates for liquids and potassium bromide pellets for solid samples.

Low and high resolution electron impact (EI) mass spectra were recorded on Kratos

MS 50 or MS 80 mass spectrometers at 70 eV. The molecular ion (M^+) masses are given unless otherwise stated. Low and high resolution desorption chemical ionization (DCI) spectra were recorded on a Delsi Nermag R10-10 C mass spectrometer using CH_4, isobutane or a NH_3 + CH_4 mixture and masses are given as $(M + 1)^+$ unless otherwise stated. Gas–liquid chromatography–low resolution mass spectrometry was performed on a Carlo Erba model 4160 capillary gas chromatograph (15 m × 0.25 mm fused silica column coated with DB-5) and a Kratos MS 80 mass spectrometer, interfaced with a hollow capillary tube. The following masses were used to calculate the mass of the ions in the high resolution mass spectra (HRMS): ^{1}H 1.007825, ^{12}C 12.000000, ^{14}N 14.003074, ^{16}O 15.994915, ^{28}Si 27.976927, ^{30}Si 29.973770, ^{32}S 31.972070, ^{35}Cl 34.968852, ^{37}Cl 36.965903, ^{72}Ge 71.922079, ^{74}Ge 73.921177. All compounds subjected to HRMS were homogeneous by TLC and/or GLC analyses.

Elemental analyses were performed on a Carlo Erba CHN model 1106 or on a Fisons EA model 1108 elemental analyzer, by the UBC Microanalytical Laboratory.

3.1.2 SOLVENTS AND REAGENTS

All solvents and reagents were purified using established procedures.[120] Diethyl ether, dibutyl ether and tetrahydrofuran (THF) were heated at reflux over and distilled from sodium–benzophenone ketyl radical. Dichloromethane and benzene were heated at reflux over and distilled from calcium hydride. The five aforementioned solvents were distilled under an atmosphere of argon and used immediately. Acetonitrile, HMPA and *N,N*–dimethylformamide were heated at reflux over and distilled from calcium hydride under an atmosphere of argon and stored under argon in bottles sealed with a Sure/Seal (Aldrich Chemical Co. Inc.). Magnesium turnings were added to methanol and the mixture was heated at reflux under an atmosphere of argon. The methanol was distilled from the formed magnesium methoxide and stored under argon over 4Å molecular sieves in bottles sealed with a Sure/Seal (Aldrich Chemical Co. Inc.). Chlorotrimethylsilane was heated at reflux over and distilled from calcium hydride and was used immediately. Bromotrimethylsilane was distilled (bulb-to-bulb) from calcium hydride and was used immediately. Petroleum ether refers to a mixture of hydrocarbon with a boiling range of 35–60 °C. All others solvents were used without further purification.

Solutions of methyllithium in diethyl ether, *n*-butyllithium in hexanes and *tert*-butyllithium in pentane were obtained from Aldrich Chemical Co. Inc., and were standardized using the procedure of Kofron and Baclawski.[121]

Copper(I) bromide–dimethyl sulfide complex was prepared by the method described by Wuts[122] and was stored in a desiccator under an atmosphere of dry argon.

Methyltriphenylphosphonium bromide was heated at 110–120 °C (using an oil bath)

under reduced pressure (0.05 Torr) for 3 h and then was stored under an atmosphere of argon.

Aqueous ammonium chloride–ammonium hydroxide (NH_4Cl–NH_4OH, pH 8–9) was prepared by the addition of 50 mL of concentrated aqueous ammonium hydroxide to 950 mL of saturated aqueous ammonium chloride solution.

All other reagents are commercially available and were used without further purification.

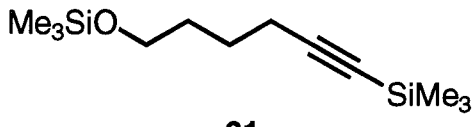
3.2 SYNTHESIS OF 2-TRIMETHYLGERMYLALK-1-ENES VIA PLATINUM CATALYZED HYDROGERMYLATION OF 1-TRIMETHYLSILYLALK-1-YNES

3.2.1 SYNTHESIS OF 1-TRIMETHYLSILYLALK-1-YNES

3.2.1.1 GENERAL PROCEDURE 1: PREPARATION OF THE 1-TRIMETHYLSILYLALK-1-YNES **61** AND **63**

To a cold (–78 °C) stirred solution of the alk-1-yne (1 equiv) in dry THF (0.2–0.3 M) was added a solution of MeLi in diethyl ether (2.2–2.3 equiv). The resultant mixture was stirred at –78 °C for 1.25–2 h. Chlorotrimethylsilane (2.5–2.6 equiv) was added, the cooling bath was removed and the mixture was allowed to stir at rt for at least 1.5 h. Ice-cold saturated aqueous $NaHCO_3$ (≈10 mL per mmol of alkyne) was added. The mixture was diluted with diethyl ether (≈10 mL per mmol of alkyne) and the layers were separated. Ice was added to the aqueous layer and the latter was extracted with diethyl ether (2 × ≈3 mL per mmol of alkyne). The pooled organic extracts were washed with an ice–water mixture (≈3 mL per mmol of alkyne) and with ice-cold brine (2 × ≈3 mL per mmol of alkyne), were dried over anhydrous magnesium sulfate, and then were filtered and concentrated under reduced pressure. The oil thus obtained was distilled to provide the desired 1-trimethylsilylalk-1-yne.

3.2.1.1.1 Synthesis of 1-Trimethylsilyl-6-(trimethylsilyloxy)hex-1-yne (**61**)



61

Following general procedure 1, to a solution of hex-5-yn-1-ol (**55**) (1.10 g, 11.2

mmol, 1 equiv) in dry THF (57 mL) was added a solution of MeLi (1.40 M in diethyl ether, 17.6 mL, 24.6 mmol, 2.20 equiv). The thick mixture was stirred at –78 °C for 2 h, then chlorotrimethylsilane (3.04 g, 28.0 mmol, 2.50 equiv) was added. The resulting solution was warmed to rt and was allowed to stir for an additional 1.5 h. The crude oil acquired was distilled (60–69 °C/0.04 Torr) to yield 2.61 g (96%) of the title compound as a clear colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.58 (t, 2H, J = 6.2 Hz, -CH_2O-), 2.22 (t, 2H, J = 6.8 Hz, -$CH_2C{\equiv}C$-), 1.68–1.50 (m, 4H), 0.12 (s, 9H, -$C{\equiv}CSi(CH_3)_3$), 0.09 (s, 9H, -$OSi(CH_3)_3$).

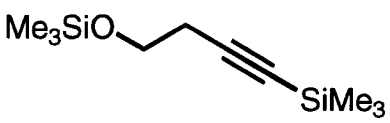
^{13}C NMR (75.4 MHz, $CDCl_3$): δ 107.1 (-$C{\equiv}\underline{C}Si(CH_3)_3$), 84.4 (-$\underline{C}{\equiv}CSi(CH_3)_3$), 62.0 (-$CH_2O$-), 31.7 (-$\underline{C}H_2CH_2O$-), 24.9 (-$\underline{C}H_2CH_2C{\equiv}C$-), 19.5 (-$\underline{C}H_2C{\equiv}C$-), 0.1 (-$C{\equiv}CSi(\underline{C}H_3)_3$), –0.6 (-$OSi(CH_3)_3$).

IR (film): 2176, 1251, 1106, 841, 760 cm^{-1}.

HRMS for $C_{12}H_{26}O^{28}Si_2$: calcd 242.1522, found 242.1513.

Anal. calcd for $C_{12}H_{26}OSi_2$: C 59.43, H 10.81; found: C 59.10, H 10.71.

3.2.1.1.2 Synthesis of 1-Trimethylsilyl-4-(trimethylsilyloxy)but-1-yne (**63**)



63

Following general procedure 1, to a solution of but-3-yn-1-ol (**56**) (2.51 g, 35.8 mmol, 1 equiv) in dry THF (120 mL) was added a solution of MeLi (1.40 M in diethyl ether, 59 mL, 82 mmol, 2.3 equiv). The resulting solution was stirred at –78 °C for 1.25 h, then chloro-

trimethylsilane (10.1 g, 93.0 mmol, 2.60 equiv) was added. The mixture was warmed to rt and was allowed to stir overnight. The crude oil acquired was distilled (bp 85 °C/12 Torr) to yield 7.36 g (96%) of the title compound as a clear colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.67 (t, 2H, J = 7.2 Hz, -OCH_2-), 2.43 (t, 2H, J = 7.2 Hz, -$CH_2C{\equiv}C$-), 0.13 (s, 9H, -$C{\equiv}CSi(CH_3)_3$), 0.11 (s, 9H, -$OSi(CH_3)_3$).

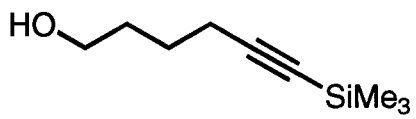
^{13}C NMR (75.4 MHz, $CDCl_3$): δ 103.9 (-$C{\equiv}\underline{C}Si(CH_3)_3$), 85.5 (-$\underline{C}{\equiv}CSi(CH_3)_3$), 61.2 (-$CH_2O$-), 24.1 (-$\underline{C}H_2C{\equiv}C$-), 0.0 (-$C{\equiv}CSi(\underline{C}H_3)_3$), –0.5 (-$OSi(CH_3)_3$).

IR (film): 2179, 1252, 1104, 843, 760 cm^{-1}.

HRMS for $C_{10}H_{22}O^{28}Si_2$: calcd 214.1209, found 214.1202.

Anal. calcd for $C_{10}H_{22}OSi_2$: C 56.01, H 10.34; found: C 55.75, H 10.45.

3.2.1.2 SYNTHESIS OF 6-TRIMETHYLSILYLHEX-5-YN-1-OL (**62**)



62

To a cold (–78 °C) stirred solution of hex-5-yn-1-ol (**55**) (1.47 g, 15.0 mmol, 1 equiv) in dry THF (134 mL) was added a solution of MeLi (1.46 M in diethyl ether, 22.6 mL, 33.0 mmol, 2.20 equiv). The reaction mixture was warmed to 0 °C and was allowed to stir for 2 h at 0 °C, after which time it became a white opaque mixture. Chlorotrimethylsilane (4.07 g, 37.5 mmol, 2.50 equiv) was added, then the cooling bath was removed and the solution was allowed to stir at rt for 2.5 h. The reaction mixture was treated with 1 M hydrochloric acid (50 mL) and ethyl acetate (300 mL) was added. The layers were separated and the aqueous portion was extracted with ethyl acetate (2 × 100 mL). The combined organic extracts were

washed with brine (2 × 100 mL), were dried over anhydrous magnesium sulfate, and then were filtered and concentrated under reduced pressure. The crude oil thus acquired was subjected to flash chromatography (100 g TLC grade silica gel, 7:3 petroleum ether–ethyl acetate) and distilled (68–82 °C/0.05 Torr) to afford 2.11 g (82%) of the title compound as a clear colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.66 (t, 2H, J = 6.2 Hz, -C$\underline{H}_2$OH), 2.25 (t, 2H, J = 6.8 Hz, -C$\underline{H}_2$C≡C-), 1.71–1.55 (m, 4H, -(C$\underline{H}_2$)$_2$CH$_2$OH), 1.42 (br s, 1H, exchanges with D_2O, -OH), 0.12 (s, 9H, Si(CH$_3$)$_3$).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 107.1 (-C≡$\underline{C}$Si(CH$_3$)$_3$), 84.6 (-$\underline{C}$≡CSi(CH$_3$)$_3$), 61.9 (-CH$_2$OH), 31.6 (-$\underline{C}$H$_2$CH$_2$OH), 24.8 (-$\underline{C}$H$_2$CH$_2$C≡C-), 19.5 (-$\underline{C}$H$_2$C≡C-), 0.0 (-Si(CH$_3$)$_3$).

IR (film): 3348, 2957, 2175, 1250, 1047, 844, 760 cm^{-1}.

HRMS for $C_8H_{15}O^{28}Si$ (M – CH$_3$)$^+$: calcd 155.0892, found 155.0892.

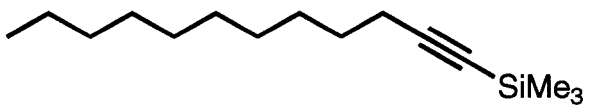
Anal. calcd for $C_9H_{18}OSi$: C 63.47, H 10.65; found: C 63.33, H 10.52.

3.2.1.3 General Procedure 2: Preparation of the 1-Trimethylsilylalk-1-ynes **64–66**

To a cold (–78 °C) stirred solution of the alk-1-yne (1 equiv) in dry etheral solvent (diethyl ether or THF, 0.1–0.25 M) was added a solution of MeLi in diethyl ether or *n*-BuLi in hexanes (1.1–1.25 equiv) via a syringe. The resulting solution was stirred at –78 °C for 1.5–2 h, then chlorotrimethylsilane (1.3–1.5 equiv) was added. The reaction mixture was stirred at –78 °C for a short period of time, then the cooling bath was removed and the mixture was

allowed to stir at rt for at least 1 h. Saturated aqueous $NaHCO_3$ (≈2 mL per mmol of alkyne) was added. The mixture was diluted with diethyl ether (≈10 mL per mmol of alkyne) and the layers were separated. The organic layer was washed with saturated aqueous $NaHCO_3$ (1 × ≈2 mL per mmol of alkyne) and the pooled aqueous layers were extracted with diethyl ether (2 × ≈3 mL per mmol of alkyne). The combined organic extracts were washed with water (2 × ≈3 mL per mmol of alkyne) and brine (1 × ≈3 mL per mmol of alkyne), were dried over anhydrous magnesium sulfate, and then were filtered and concentrated under reduced pressure. The oil thus acquired was distilled to provide the desired 1-trimethylsilylalk-1-yne.

3.2.1.3.1 Synthesis of 1-Trimethylsilyldodec-1-yne (**64**)



64

Following general procedure 2, to a solution of dodec-1-yne (**57**) (1.04 g, 6.27 mmol, 1 equiv) in dry THF (63 mL) was added a solution of *n*-BuLi (1.58 M in hexanes, 4.76 mL, 7.53 mmol, 1.20 equiv). The reaction mixture was stirred at –78 °C for 2 h, then chlorotrimethylsilane (1.02 g, 9.41 mmol, 1.50 equiv) was added. The resultant solution was warmed to rt and was allowed to stir overnight. The crude oil obtained was distilled (72–77 °C/0.04 Torr) to afford 1.46 g (98%) of the title compound as a clear colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.19 (t, 2H, J = 7.2 Hz, -C$\underline{H}_2$C≡C-), 1.49 (quintuplet, 2H, J = 7.2 Hz, -C$\underline{H}_2$CH$_2$C≡C-), 1.40–1.33 (br m, 3H), 1.33–1.20 (br s, 11H), 0.86 (br t, 3H, J = 6.8 Hz, -CH$_2$C$\underline{H}_3$), 0.12 (s, 9H, -Si(CH$_3$)$_3$).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 107.5 (-C≡$\underline{C}$Si(CH$_3$)$_3$), 84.1 (-$\underline{C}$≡CSi(CH$_3$)$_3$), 32.0, 29.62,

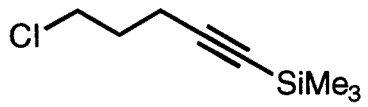
29.57, 29.4, 29.1, 28.8, 28.7, 22.7, 19.9 (-$\underline{C}H_2C{\equiv}C$-), 14.1 (-$CH_2\underline{C}H_3$), 0.1 (-$Si(CH_3)_3$).

IR (film): 2176, 1250, 843, 760 cm^{-1}.

HRMS for $C_{15}H_{30}{}^{28}Si$: calcd 238.2117, found 238.2123.

Anal. calcd for $C_{15}H_{30}Si$: C 75.54, H 12.68; found: C 75.29, H 12.77.

3.2.1.3.2 Synthesis of 5-Chloro-1-trimethylsilylpent-1-yne (**65**)



65

Following general procedure 2, to a solution of 5-chloropent-1-yne (**58**) (5.05 g, 49.2 mmol, 1 equiv) in dry diethyl ether (200 mL) was added a solution of MeLi (1.40 M in diethyl ether, 43.9 mL, 61.5 mmol, 1.25 equiv). The resultant mixture was stirred at –78 °C for 1.5 h. Chlorotrimethylsilane (8.02 g, 73.8 mmol, 1.50 equiv) was added and the mixture was stirred for an additional 45 min at –78 °C. The cooling bath was removed and the solution was stirred at rt overnight. The crude oil obtained was distilled (bp 108–112 °C/70 Torr) to provide 7.82 g (91%) of the title compound as a clear colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.62 (t, 2H, J = 6.6 Hz, -CH_2Cl), 2.39 (t, 2H, J = 6.6 Hz, -$C\underline{H}_2C{\equiv}C$-), 1.94 (quintuplet, 2H, J = 6.6 Hz, -$CH_2C\underline{H}_2CH_2$-), 0.13 (s, 9H, -$Si(CH_3)_3$).

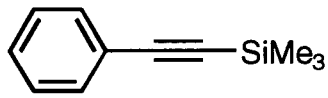
^{13}C NMR (75.4 MHz, $CDCl_3$): δ 105.1 (-$C{\equiv}\underline{C}Si(CH_3)_3$), 85.5 (-$\underline{C}{\equiv}CSi(CH_3)_3$), 43.4, 31.3, 17.2, 0.0 (-$Si(CH_3)_3$).

IR (film): 2177, 1250, 844, 761 cm^{-1}.

HRMS for $C_8H_{15}{}^{35}Cl^{28}Si$: calcd 174.0632, found 174.0624.

Anal. calcd for $C_8H_{15}ClSi$: C 54.99, H 8.65; found: C 55.18, H 8.80.

3.2.1.3.3 Synthesis of 1-Phenyl-2-trimethylsilylacetylene (**66**)



66

Following general procedure 2, to a solution of phenylacetylene (**59**) (2.64 g, 25.9 mmol, 1 equiv) in dry THF (130 mL) was added a solution of *n*-BuLi (1.59 M in hexanes, 17.9 mL, 28.5 mmol, 1.10 equiv). The solution was stirred at –78 °C for 1 h, after which time a white suspension formed. The mixture was stirred for an additional hour, then chlorotrimethylsilane (3.65 g, 33.6 mmol, 1.30 equiv) was added. The resulting solution was warmed to rt and was allowed to stir for 1 h. The crude oil obtained was distilled (110–120 °C/11 Torr) to provide 4.31 g (96%) of the title compound as a clear colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50–7.42 (m, 2H), 7.32–7.26 (m, 3H), 0.24 (s, 9H, $-Si(CH_3)_3$).

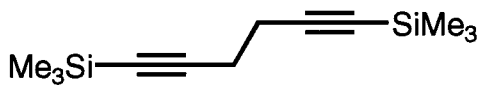
^{13}C NMR (75.4 MHz, $CDCl_3$): δ 131.9, 128.4, 128.2, 123.1 (aromatic *ipso* carbon), 105.1 ($-C\equiv\underline{C}Si(CH_3)_3$), 94.0 ($-\underline{C}\equiv CSi(CH_3)_3$), 0.0 ($-Si(CH_3)_3$).

IR (film): 3081, 2961, 2900, 2160, 1599, 1489, 1445, 864, 758, 691, 645 cm^{-1}.

HRMS for $C_{11}H_{14}{}^{28}Si$: calcd 174.0865, found 174.0866.

Anal. calcd for $C_{11}H_{14}Si$: C 75.79, H 8.10; found: C 75.51, H 8.03.

3.2.1.4 SYNTHESIS OF 1,6-BIS(TRIMETHYLSILYL)HEXA-1,5-DIYNE (**67**)



67

To a cold (–78 °C) stirred solution of hexa-1,5-diyne (**60**) (558 mg, 7.15 mmol, 1 equiv) in dry THF (36 mL) was added a solution of MeLi (1.40 M in diethyl ether, 12.3 mL, 17.2 mmol, 2.40 equiv). The resulting solution was stirred at –78 °C for 0.5 h, then chlorotrimethylsilane (2.02 g, 18.6 mmol, 2.60 equiv) was added. The reaction mixture was warmed to rt and was allowed to stir for an additional hour. Saturated aqueous $NaHCO_3$ (25 mL) was added. The mixture was diluted with diethyl ether (175 mL), the layers were separated and the organic layer was washed with another portion of saturated aqueous $NaHCO_3$ (25 mL). The pooled aqueous layers were extracted with diethyl ether (2 × 20 mL). The combined organic extracts were washed with water (20 mL) and brine (20 mL), were dried over anhydrous magnesium sulfate, and then were filtered and concentrated under reduced pressure. The crude solid thus acquired was recrystallized from a pentane–methanol mixture to afford 1.14 g (71%) of the title compound as colorless crystals (mp 46–46.5 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.41 (s, 4H, $-CH_2CH_2-$), 0.13 (s, 18H, 2 × $-Si(CH_3)_3$).

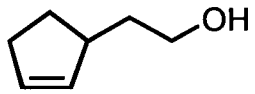
^{13}C NMR (75.4 MHz, $CDCl_3$): δ 105.1 ($-C{\equiv}\underline{C}Si(CH_3)_3$), 85.5 ($-\underline{C}{\equiv}CSi(CH_3)_3$), 20.0 ($-CH_2-$), 0.1 ($-Si(CH_3)_3$).

IR (KBr pellet): 2180, 1249, 1023, 844, 759, 637 cm^{-1}.

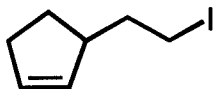
HRMS for $C_{12}H_{22}{}^{28}Si_2$: calcd 222.1260, found 222.1258.

Anal. calcd for $C_{12}H_{22}Si_2$: C 64.78, H 9.97; found: C 64.50, H 10.11.

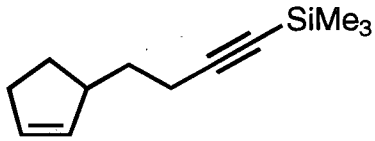
3.2.1.5 SYNTHESIS OF 2-(CYCLOPENT-2-EN-1-YL)ETHANOL (**69**), 1-(CYCLOPENT-2-EN-1-YL)-2-IODOETHANE (**70**) AND 4-(CYCLOPENT-2-EN-1-YL)-1-TRIMETHYLSILYLBUT-1-YNE (**72**)



69



70



72

*a) 2-(Cyclopent-2-en-1-yl)ethanol (**69**)*

To a cold (0 °C) stirred slurry of $LiAlH_4$ (1.15 g, 30.3 mmol, 1.20 equiv) in dry diethyl ether (225 mL) was added dropwise, via a cannula, a solution of (cyclopent-2-en-1-yl)acetic acid (**68**) (3.18 g, 25.2 mmol, 1 equiv) in diethyl ether (25 mL). The heterogeneous mixture was allowed to stir at rt for 1.5 h, then 1 M hydrochloric acid (≈55 mL total) was cautiously added until the pH of the aqueous layer reached ≈3. Diethyl ether (200 mL) was added and the layers were separated. The aqueous layer was extracted with diethyl ether (3 × 50 mL). The combined organic extracts were washed with water (25 mL), saturated aqueous $NaHCO_3$ (25 mL), and brine (2 × 25 mL), were dried over anhydrous magnesium sulfate, and then were filtered and concentrated under reduced pressure. The crude oil thus obtained was distilled (118–128 °C/11 Torr) to afford 2.72 g (96%) of 2-(cyclopent-2-en-1-yl)ethanol (**69**) as a clear colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.73–5.70 (m, 1H, vinylic proton), 5.68–5.65 (m, 1H, vinylic proton), 3.73–3.63 (m, 2H, -C<u>H</u>$_2$OH), 2.80–2.70 (m, 1H, allylic methine proton), 2.39–2.21 (m, 2H), 2.05 (dtd, 1H, J = 13.2, 8.4 and 4.8 Hz), 1.72–1.63 (m, 1H), 1.60–1.51 (m, 1H), 1.46–1.37 (m, 1H), 1.32 (br s, 1H, exchanges with D_2O, -OH).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 134.6 (vinylic carbon), 130.5 (vinylic carbon), 61.6 (-CH_2OH), 42.0 (allylic methine carbon), 38.8, 31.8, 29.7.

IR (film): 3338, 3051, 2931, 1614, 1433, 1359, 1059, 720 cm^{-1}.

HRMS for $C_7H_{12}O$: calcd 112.0888, found 112.0890.

*b) 1-(Cyclopent-2-en-1-yl)-2-iodoethane (**70**)*

To a stirred mixture of dry diethyl ether–acetonitrile (3:1, 236 mL total) at rt was added sequentially triphenylphosphine (19.2 g, 73.1 mmol, 3.10 equiv) and imidazole (4.98 g, 73.1 mmol, 3.10 equiv). The clear colorless solution was cooled to 0 °C and iodine (18.6 g, 73.1 mmol, 3.10 equiv) was added in three approximately equal portions. After the mixture had been stirred for 20 min at 0 °C, the mustard-yellow suspension was treated, via a cannula, with a solution of 2-(cyclopent-2-en-1-yl)ethanol (**69**) (2.64 g, 23.6 mmol, 1 equiv) in dry diethyl ether (10 mL). The reaction mixture was stirred for an additional 20 min, then was treated with saturated aqueous $Na_2S_2O_3$ (150 mL). Diethyl ether (200 mL) was added and the layers were separated. The organic layer was washed with saturated aqueous $Na_2S_2O_3$ (6 × 25 mL). The pooled aqueous layers were extracted with diethyl ether (3 × 25 mL). The combined organic extracts were washed with 10% aqueous $CuSO_4$ (2 × 25 mL), water (2 × 25 mL), and brine (2 × 25 mL), were dried over anhydrous magnesium sulfate, and then were filtered and concentrated under reduced pressure. The residue was passed through a column of Florisil (85 g, elution with petroleum ether, 200 mL) and the eluate was concentrated under reduced pressure. The crude oil thus acquired was distilled (118–128 °C/11 Torr) to yield 4.82 g (92%) of 1-(cyclopent-2-en-1-yl)-2-iodoethane (**70**) as a clear colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.77–5.73 (m, 1H, vinylic proton), 5.65–5.61 (m, 1H, vinylic proton), 3.25–3.12 (m, 2H, -CH_2I), 2.80–2.70 (m, 1H, allylic methine proton), 2.40–2.22 (m, 2H), 2.05 (dtd, 1H, J = 12.8, 8.4 and 5.2 Hz), 1.99–1.90 (m, 1H), 1.85–1.76 (m, 1H), 1.42–1.33 (m, 1H).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 133.2 (vinylic carbon), 131.2 (vinylic carbon), 46.4 (allylic methine carbon), 39.9, 31.9, 29.0, 4.9 (-CH_2I).

IR (film): 3050, 2931, 1614, 1427, 1231, 1181, 720 cm^{-1}.

HRMS for $C_7H_{11}I$: calcd 221.9906, found 221.9904.

*c) 4-(Cyclopent-2-en-1-yl)-1-trimethylsilylbut-1-yne (**72**)*

To a cold (–78 °C) stirred solution of trimethylsilylacetylene (1.73 g, 17.6 mmol, 1.50 equiv) in dry THF (14 mL) was added a solution of *n*-BuLi (1.55 M in hexanes, 9.10 mL, 14.1 mmol, 1.20 equiv). The reaction mixture was stirred at –78 °C for 5 min, then was warmed to 0 °C and was allowed to stir at 0 °C for an additional 10 min. A solution of 1-(cyclopent-2-en-1-yl)-2-iodoethane (**70**) (2.60 g, 11.7 mmol, 1 equiv) in dry HMPA (12 mL) was added dropwise over 30 min via a cannula. The resulting mixture was stirred at 0 °C for 30 min, then was treated with water (10 mL). Diethyl ether (120 mL) was added and the layers were separated. The aqueous layer was extracted with diethyl ether (3 × 50 mL). The pooled organic extracts were washed with 10% aqueous $CuSO_4$ (3 × 25 mL), saturated aqueous $Na_2S_2O_3$ (25 mL), water (2 × 20 mL), and brine (2 × 20 mL), were dried over anhydrous magnesium sulfate, and then were filtered and concentrated under reduced pressure. The crude oil thus obtained was distilled. A forerun (distillation temperature 80–120 °C/39 Torr) was collected in a first bulb (155 mg, volatile material as indicated by GLC

analysis). The remainder of the material was collected in a second bulb (distillation temperature 120–140 °C/39 Torr) to afford 1.76 g (78%) of 4-(cyclopent-2-en-1-yl)-1-trimethylsilylbut-1-yne (**72**) as a clear colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.73–5.70 (m, 1H, vinylic proton), 5.67–5.64 (m, 1H, vinylic proton), 2.80–2.68 (m, 1H, allylic methine proton), 2.38–2.19 (m, 4H), 2.03 (dtd, 1H, J = 13.2, 8.4 and 5.0 Hz), 1.67–1.58 (m, 1H), 1.53–1.44 (m, 1H), 1.43–1.34 (m, 1H), 0.12 (s, 9H, $-Si(CH_3)_3$).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 134.3 (vinylic carbon), 130.7 (vinylic carbon), 107.5 ($-C\equiv\underline{C}Si(CH_3)_3$), 84.1 ($-\underline{C}\equiv CSi(CH_3)_3$), 44.8 (allylic methine carbon), 34.8, 31.9, 29.4, 18.3 ($-\underline{C}H_2C\equiv C-$), 0.1 ($-Si(CH_3)_3$).

IR (film): 3053, 2957, 2176, 1614, 1250, 843, 760 cm^{-1}.

HRMS for $C_{12}H_{20}{}^{28}Si$: calcd 192.1334, found 192.1334.

Anal. calcd for $C_{12}H_{20}Si$: C 74.92, H 10.48; found: C 75.10, H 10.38.

3.2.2 SYNTHESIS OF TRIMETHYLGERMANE (53)

Me_3GeH
53

The apparatus for this reaction was as follows: a 250 mL three-necked flask was equipped with a stir bar, two septa and a water-cooled condenser (15 cm). The condenser was surmounted with a short-path distillation apparatus fitted with a 100 mL receiving flask. This distillation apparatus *must* have a drip end that can reach deep inside the 100 mL flask. An argon flow through the system was created using an inlet (needle) on one neck of the reaction flask, and a bleed was created on the short path distillation apparatus by inserting a needle through a septum covering the outlet side arm. All joints were sealed with Teflon tape. The 100 mL receiving flask was immersed deep inside a dry ice–acetone bath.

To a cold (0 °C) stirred slurry of $LiAlH_4$ (2.5 g, 65 mmol, 0.5 equiv) in dry dibutyl ether (100 mL) in the three-necked flask, was added a solution of bromotrimethylgermane (25.7 g, 130 mmol, 1 equiv, freshly distilled from CaH_2) in dry dibutyl ether (17 mL) via a cannula. The mixture was stirred for 5 min at 0 °C, then was heated to 110 °C, with an oil bath, and stirred at this temperature for 3 h while distilling the volatile liquid into the receiving flask cooled to –78 °C. The distilled liquid generally contained 5–10% of dibutyl ether. This liquid was then redistilled (bulb-to-bulb distillation) from –78 °C to 40 °C, under an atmosphere of argon, to afford 14.70 (95%) of essentially pure trimethylgermane (**53**). The volatile liquid was transferred to a 25 mL round bottom flask fitted with a Teflon Mininert Valve (purchased from the Aldrich Chemical Co. Inc.) and stored at –25 °C in a freezer.

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.83 (deciplet, 1H, J = 3.6 Hz, $\underline{H}Ge(CH_3)_3$), 0.22 (d, 9H,

J = 3.6 Hz, HGe(C$\underline{H}_3$)$_3$).

^{13}C NMR (50.3 MHz, $CDCl_3$): δ –3.5 (HGe(CH_3)$_3$).

3.2.3 ISOLATION OF THE PRODUCTS OF HYDROGERMYLATION OF 6-TRIMETHYLSILYLHEX-5-YN-1-OL (62) AND THEIR TREATMENT WITH *p*-TOLUENESULFONIC ACID MONOHYDRATE IN DICHLOROMETHANE

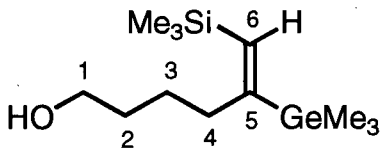
3.2.3.1 SYNTHESIS, ISOLATION AND CHARACTERIZATION OF (*E*)- AND (*Z*)-5-TRIMETHYLGERMYL-6-TRIMETHYLSILYLHEX-5-EN-1-OLS (**73**) AND (**75**), AND (*E*)- AND (*Z*)-6-TRIMETHYLGERMYL-6-TRIMETHYLSILYLHEX-5-EN-1-OLS (**74**) AND (**76**)

To a stirred solution of 6-trimethylsilylhex-5-yn-1-ol (**62**) (932 mg, 5.47 mmol, 1 equiv) in CH_2Cl_2 (27 mL) at rt was added $H_2PtCl_6 \cdot 6H_2O$ (57 mg, 0.11 mmol, 0.020 equiv). The orange solution was cooled to 0° C, stirred for 5 min and Me_3GeH (**53**) (974 mg, 8.21 mmol, 1.50 equiv) was added via a precooled gas-tight syringe (cooled by running cold water on the barrel). The cooling bath was removed and the reaction mixture was allowed to stir at rt overnight. The black solution was treated with saturated aqueous $NaHCO_3$ (5 mL) and diethyl ether (150 mL) and the layers were separated. The organic layer was washed with saturated aqueous $NaHCO_3$ (25 mL) and water (25 mL). The combined aqueous portions were extracted with diethyl ether (2 × 25 mL). The pooled organic extracts were washed with brine (2 × 25 mL), were dried over anhydrous magnesium sulfate, and then were filtered and concentrated under reduced pressure. The crude oil thus obtained was subjected to flash chromatography (80 g TLC grade silica gel, 17:3 petroleum ether–ethyl acetate) to afford 1.32 g (83%) of the four title compounds as a mixture.

The acquired liquid was subjected to HPLC (silica Partisil, 10 μm; 22 mm × 250 mm column, 22:3 hexane–ethyl acetate, 9 mL/min, RI detector, UV-vis detector λ = 254 nm) in

four approximately equal portions. This chromatography resulted in a rough separation to afford three fractions, which were concentrated under reduced pressure. The first fraction to be eluted, fraction ***A*** (retention time 28–40 min), afforded 985 mg of a mixture of two components. The second fraction to be eluted, fraction ***B*** (retention time 40–46 min), afforded 105 mg of an oil which was constituted of a mixture of three components (HPLC analysis). The third fraction to be eluted, fraction ***C*** (retention time 46–52 min), afforded 75 mg of an oil which was constituted of a mixture of five components (HPLC analysis).

a) Isolation and Characterization of (E)-5-Trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (73)



73

Part of fraction ***A*** (≈200 mg) was submitted to reversed phase HPLC (C_{18} μBondapak, 10 μm; 25 mm × 100 mm column, 3:1 methanol–water, 9 mL/min, UV-vis detector $\lambda = 230$ nm) in eight approximately equal portions. The first component to be eluted (retention time 30 min) was concentrated under reduced pressure and then was distilled (72–80 °C/0.04 Torr) to provide 43 mg of pure (*E*)-5-trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**73**) as a clear colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.81 (s, 1H, vinylic proton), 3.63 (t, 2H, J = 6.6 Hz, -C<u>H</u>$_2$OH), 2.34–2.30 (m, 2H, allylic protons), 1.60–1.53 (m, 2H, -C<u>H</u>$_2$CH$_2$OH), 1.43–1.35 (m, 2H, homoallylic protons), 1.21 (br s, 1H, exchanges with D_2O,

-OH), 0.17 (s, 9H, -Ge(CH_3)$_3$), 0.09 (s, 9H, -Si(CH_3)$_3$).

Additional ^{1}H NMR data, derived from NOE difference experiments, are given in **Table 15**.

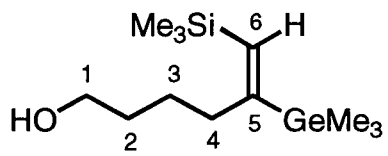
^{13}C NMR (125.7 MHz, $CDCl_3$): δ 166.7 (C-5), 138.8 (C-6), 62.9 (C-1), 37.4, 33.0, 26.6, 0.6, –1.2.

IR (film): 3318, 2937, 1566, 1411, 1247, 1066, 823, 756, 597 cm^{-1}.

HRMS (DCI, CH_4) for $C_{12}H_{29}{}^{74}GeO^{28}Si$ $(M + 1)^+$: calcd 291.1199, found 291.1185.

Anal. calcd for $C_{12}H_{28}GeOSi$: C 49.87, H 9.76; found: C 49.83, H 9.79.

Table 15: ^{1}H NMR Data from Nuclear Overhauser Enhancement Difference Experiments for (*E*)-5-Trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**73**)



73

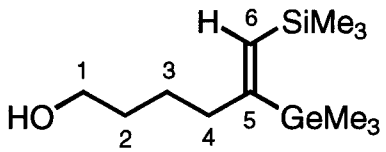
Assignments H-x	^{1}H NMR[a] δ ppm (mult, *J* (Hz))	Observed NOEs
H-6[b]	5.81 (s)	-Ge(CH_3)$_3$, -Si(CH_3)$_3$
H-1	3.63 (t, *J* = 6.6)	
H-4[b]	2.34–2.30 (m)	H-2, H-3, -Ge(CH_3)$_3$, -Si(CH_3)$_3$
H-2	1.60–1.53 (m)	
H-3	1.43–1.35 (m)	
-OH	1.21 (br s)	
-Ge(CH_3)$_3$[b]	0.17 (s)	H-1, H-2, H-3, H-4, H-6
-Si(CH_3)$_3$[b]	0.09 (s)	H-4, H-6

[a] 400 MHz, $CDCl_3$. [b] Irradiation of this signal generated the corresponding NOEs in the right hand column.

The second component to be eluted from the reversed phase HPLC (retention time 33

min), was concentrated under reduced pressure to provide 40 mg of an oil which was still a mixture, but had been enriched with the 33 min component. This sample was resubjected to identical HPLC conditions to afford 13 mg of an oil, fraction ***D***, which was 93% pure by GLC analysis.

b) Isolation and Characterization of (Z)-5-Trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (75)



75

The fraction ***B*** (105 mg) from the initial HPLC separation was subjected to HPLC (silica Partisil, 10 μm; 22 mm × 250 mm column, 9:1 hexane–ethyl acetate, 9 mL/min, RI detector, UV-vis detector λ = 254 nm). The last component to be eluted (retention time 51 min) was concentrated under reduced pressure to afford 10.8 mg of an oil which was still a mixture, but had been enriched with the 51 min component. This sample was resubjected to HPLC under identical conditions to afford 5.6 mg of (Z)-5-trimethylgermyl-6-trimethyl-silylhex-5-en-1-ol (**75**) (92% pure by GLC analysis).

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.18 (t, 1H, J = 1.2 Hz, vinylic proton), 3.63 (t, 2H, J = 6.6 Hz, -C<u>H</u>$_2$OH), 2.24 (td, 2H, J = 7.8 and 1.2 Hz, allylic protons), 1.57–1.50 (m, 2H, -C<u>H</u>$_2$CH$_2$OH), 1.43–1.36 (m, 2H, homoallylic protons), 1.23 (br s, 1H, exchanges with D_2O, -OH), 0.27 (s, 9H, -Ge(CH$_3$)$_3$), 0.10 (s, 9H, -Si(CH$_3$)$_3$).

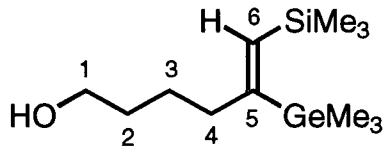
Additional ^{1}H NMR data, derived from NOE difference experiments, are given in **Table 16**.

^{13}C NMR (125.7 MHz, $CDCl_3$): δ 163.9 (C-5), 140.9 (C-6), 62.9 (C-1), 44.4, 32.4, 25.8, 0.83, 0.81.

IR (film): 3325, 2928, 1564, 1461, 1249, 1067, 826, 595 cm^{-1}.

HRMS (DCI, NH_3 + CH_4) for $C_{12}H_{29}{}^{74}GeO^{28}Si$ $(M + 1)^+$: calcd 291.1199, found 291.1193.

Table 16: ^{1}H NMR Data from Nuclear Overhauser Enhancement Difference Experiments for (*Z*)-5-Trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**75**)

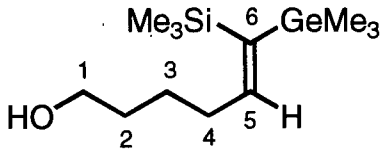


75

Assignments H-x	^{1}H NMR[a] δ ppm (mult, *J* (Hz))	Observed NOEs
H-6[b]	6.18 (t, *J* = 1.2)	H-3, H-4, -Si(CH_3)$_3$
H-1	3.63 (t, *J* = 6.6)	
H-4[b]	2.24 (td, *J* = 7.8, 1.2)	H-1, H-2, H-3, H-4, -Ge(CH_3)$_3$
H-2	1.57–1.50 (m)	
H-3	1.43–1.36 (m)	
-OH	1.23 (br s)	
-Ge(CH_3)$_3$[b]	0.27 (s)	H-4
-Si(CH_3)$_3$[b]	0.10 (s)	H-6

[a] 400 MHz, $CDCl_3$. [b] Irradiation of this signal generated the corresponding NOEs in the right hand column.

c) Isolation and Characterization of (E)-6-Trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (74)



74

The fraction ***C*** (75 mg) from the initial HPLC separation was subjected to HPLC (silica Partisil, 10 μm; 22 mm × 250 mm column, 9:1 hexane–ethyl acetate, 9 mL/min, RI detector, UV-vis detector λ = 254 nm). The fourth component to be eluted (retention time 54 min) was concentrated under reduced pressure to give an oil which was still a mixture, but had been enriched with the 54 min component. This sample was resubjected twice to HPLC under identical conditions and then was distilled (80–89 °C/0.04 Torr) to afford 13 mg of (*E*)-6-trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**74**) (95% pure by GLC analysis). This sample contained a small amount (5%) of (*Z*)-5-trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**75**).

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.43 (t, 1H, J = 7.0 Hz, vinylic proton), 3.64 (t, 2H, J = 6.4 Hz, -C<u>H</u>$_2$OH), 2.21 (dt, 2H, J = 7.0 and 7.0 Hz, allylic protons), 1.61–1.54 (m, 2H, -C<u>H</u>$_2$CH$_2$OH), 1.49–1.43 (m, 2H, homoallylic protons), 1.24 (br s, 1H, exchanges with D_2O, -OH), 0.17 (s, 9H, -Ge(CH$_3$)$_3$), 0.12 (s, 9H, -Si(CH$_3$)$_3$).

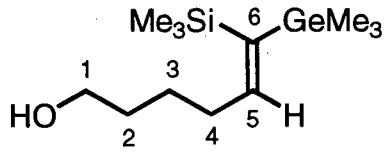
Additional ^{1}H NMR data, derived from NOE difference experiments, are given in **Table 17**.

^{13}C NMR (125.7 MHz, $CDCl_3$): δ 154.7 (C-5), 141.6 (C-6), 62.9 (C-1), 35.1, 32.5, 25.8, 1.6, 0.0.

IR (film): 3317, 2954, 1574, 1407, 1249, 837, 594 cm^{-1}.

HRMS (DCI, NH_3 + CH_4) for $C_{12}H_{29}{}^{74}GeO^{28}Si$ (M + 1)$^+$: calcd 291.1199, found 291.1190.

Table 17: ^{1}H NMR Data from Nuclear Overhauser Enhancement Difference Experiments for (*E*)-6-Trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**74**)

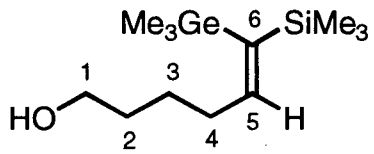


74

Assignments H-x	^{1}H NMR[a] δ ppm (mult, *J* (Hz))	Observed NOEs
H-5[b]	6.43 (t, *J* = 7.0)	H-4, -Ge(CH$_3$)$_3$
H-1	3.64 (t, *J* = 6.4)	
H-4[b]	2.21 (dt, *J* = 7.0, 7.0)	H-1, H-2, H-3, H-5, -Si(CH$_3$)$_3$
H-2	1.61–1.54 (m)	
H-3	1.49–1.43 (m)	
-OH	1.24 (br s)	
-Ge(CH$_3$)$_3$[b]	0.17 (s)	H-5
-Si(CH$_3$)$_3$[b]	0.12 (s)	H-4

[a] 400 MHz, CDCl$_3$. [b] Irradiation of this signal generated the corresponding NOEs in the right hand column.

d) Isolation and Characterization of (Z)-6-Trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (76)



76

The fraction ***D*** (13 mg) from the reversed phase HPLC separation of fraction ***A***, was subjected to HPLC (silica μPorasil, 10 μm; 25 mm × 100 mm column, 9:1 hexane–ethyl

acetate, 10 mL/min, RI detector, UV-vis detector λ = 254 nm). The major component (retention time 17 min) was separated from a small amount of a more polar impurity (retention time 19 min) and was concentrated under reduced pressure to afford 5.8 mg of (*Z*)-6-trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**76**), which was now 98% pure by GLC analysis.

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.70 (t, 1H, J = 7.4 Hz, vinylic proton), 3.64 (t, 2H, J = 6.6 Hz, -C$\underline{H}_2$OH), 2.12 (dt, 2H, J = 7.4 and 7.4 Hz, allylic protons), 1.65–1.61 (m, 4H, -(C$\underline{H}_2$)$_2$CH$_2$OH), 1.34–1.20 (br s, 1H, exchanges with D_2O, -OH), 0.24 (s, 9H, -Ge(CH$_3$)$_3$), –0.04 (s, 9H, -Si(CH$_3$)$_3$).

Additional ^{1}H NMR data, derived from NOE difference experiments, are given in **Table 18**.

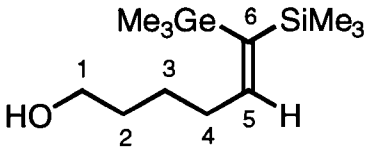
^{13}C NMR (125.7 MHz, $CDCl_3$): δ 138.9 (C-6), 136.5 (C-5), 62.8 (C-1), 33.6, 28.8, 26.7, 0.1, –1.3.

IR (film): 3316, 2953, 1612, 1413, 1247, 1055, 852, 595 cm^{-1}.

HRMS (DCI, NH_3 + CH_4) for $C_{12}H_{29}{}^{72}GeO^{30}Si$ $(M + 1)^+$: calcd 291.1173, found 291.1180.

Anal. calcd for $C_{12}H_{28}GeOSi$: C 49.87, H 9.76; found C 49.74, H 9.80.

Table 18: ^{1}H NMR Data from Nuclear Overhauser Enhancement Difference Experiments for (*Z*)-6-Trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**76**)



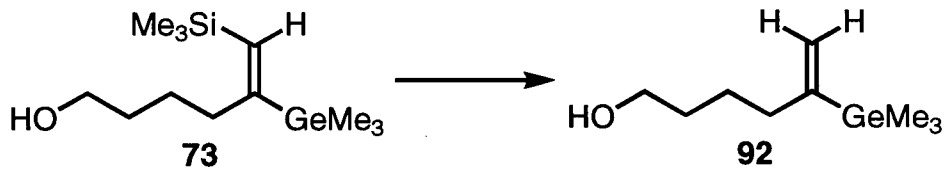
76

Assignments H-x	^{1}H NMR[a] δ ppm (mult, *J* (Hz))	Observed NOEs
H-5[b]	5.70 (t, *J* = 7.4)	H-3, H-4, -Si(CH$_3$)$_3$
H-1	3.64 (t, *J* = 6.6)	
H-4[b]	2.12 (dt, *J* = 7.4, 7.4)	H-1, H-5
H-2, H-3	1.65–1.61 (m)	
-OH	1.34–1.20 (br s)	
-Ge(CH$_3$)$_3$[b]	0.24 (s)	H-4
-Si(CH$_3$)$_3$[b]	–0.04 (s)	H-5

[a] 400 MHz, CDCl$_3$. [b] Irradiation of this signal generated the corresponding NOEs in the right hand column.

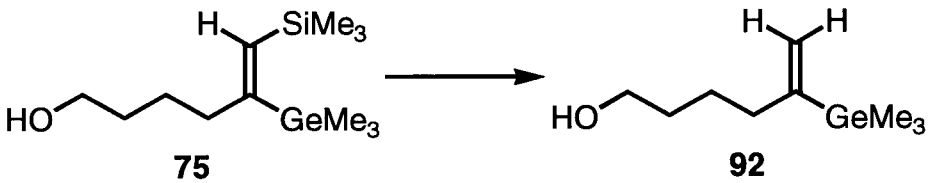
3.2.3.2 TREATMENT OF (*E*)- AND (*Z*)-5-TRIMETHYLGERMYL-6-TRIMETHYLSILYLHEX-5-EN-1-OLS (**73**) AND (**75**), AND (*E*)- AND (*Z*)-6-TRIMETHYLGERMYL-6-TRIMETHYLSILYLHEX-5-EN-1-OLS (**74**) AND (**76**) WITH *p*-TOLUENESULFONIC ACID MONOHYDRATE IN DICHLOROMETHANE

3.2.3.2.1 Protiodesilylation of (*E*)-5-Trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**73**) to 5-Trimethylgermylhex-5-en-1-ol (**92**)



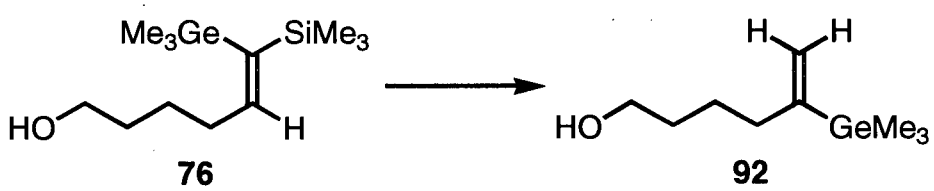
To a stirred solution of (*E*)-5-trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**73**) (8.8 mg, 0.030 mmol, 1 equiv) in CH_2Cl_2 (0.5 mL) at rt was added *p*-TsOH•H_2O (6.9 mg, 0.036 mmol, 1.2 equiv). The heterogeneous mixture was stirred at rt for 1 h, then was treated with saturated aqueous $NaHCO_3$ (1 mL) and diethyl ether (20 mL). The layers were separated and the organic extract was washed with water (2 mL) and brine (3 mL), was dried over anhydrous magnesium sulfate, and then was filtered and concentrated under reduced pressure. The crude oil thus acquired was subjected to flash chromatography (4 g silica gel, 7:3 petroleum ether–diethyl ether) and distilled (84–90 °C/8 Torr) to afford 6.6 mg (100%) of 5-trimethylgermylhex-5-en-1-ol (**92**) as a clear colorless oil. Spectral data were identical with those reported in section 3.2.4.1.1 (p 200 ff.).

3.2.3.2.2 Protiodesilylation of (*Z*)-5-Trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**75**) to 5-Trimethylgermylhex-5-en-1-ol (**92**)



To a stirred solution of (*Z*)-5-trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**75**) (92% pure by GLC analysis, 2.7 mg, 0.0093 mmol, 1 equiv) in CH_2Cl_2 (0.5 mL) at rt was added *p*-TsOH•H_2O (2.1 mg, 0.011 mmol, 1.2 equiv). The heterogeneous mixture was stirred at rt for 1.5 h, then was treated with saturated aqueous $NaHCO_3$ (1 mL) and diethyl ether (15 mL). The layers were separated and the organic extract was washed with water (1 mL) and brine (2 mL), was dried over anhydrous magnesium sulfate and then was filtered and concentrated under reduced pressure. The oil thus acquired was subjected to flash chromatography (4 g silica gel, 17:3 petroleum ether–ethyl acetate) to afford 1.1 mg (54%, as a single product) of 5-trimethylgermylhex-5-en-1-ol (**92**) as a clear colorless oil. The spectral data were identical with those reported in section 3.2.4.1.1 (p 200 ff.).

3.2.3.2.3 Protiodesilylation of (*Z*)-6-Trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**76**) to 5-Trimethylgermylhex-5-en-1-ol (**92**)



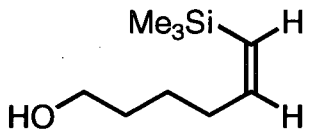
To a stirred solution of (*Z*)-6-trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**76**) (9.6 mg, 0.033 mmol, 1 equiv) in CH_2Cl_2 (0.5 mL) at rt was added *p*-TsOH•H_2O (7.6 mg, 0.040

mmol, 1.2 equiv). The heterogeneous mixture was stirred at rt for 1.5 h, then was treated with saturated aqueous $NaHCO_3$ (1 mL) and diethyl ether (15 mL). The layers were separated and the organic extract was washed with water (1 mL) and brine (1 mL), was dried over anhydrous magnesium sulfate and then was filtered and concentrated under reduced pressure. The oil thus acquired was subjected to flash chromatography (4 g silica gel, 17:3 petroleum ether–ethyl acetate) to afford 6.1 mg (85%) of 5-trimethylgermylhex-5-en-1-ol (**92**) as a clear colorless oil. The spectral data were identical with those reported in section 3.2.4.1.1 (p 200 ff.). GLC analysis of the crude mixture as well as GLC–MS analyses of the chromatographed product revealed the presence of a small amount (≈2.5%) of (*E*)-6-trimethylsilylhex-5-en-1-ol (**94a**) (vide infra) also formed during the reaction.

3.2.3.2.4 Protiodegermylation of (*E*)-6-Trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**74**) to (*E*)- and (*Z*)-6-Trimethylsilylhex-5-en-1-ol (**94a**) and (**94b**)

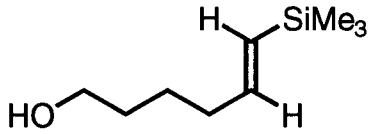
To a stirred solution of (*E*)-6-trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**74**) (6.6 mg, 0.023 mmol, 1 equiv) in CH_2Cl_2 (0.5 mL) at rt was added *p*-TsOH•H_2O (5.2 mg, 0.027 mmol, 1.2 equiv). The heterogeneous mixture was stirred at rt for 1.25 h, then was treated with saturated aqueous $NaHCO_3$ (1 mL) and diethyl ether (15 mL). The layers were separated and the organic extract was washed with water (1 mL) and brine (1 mL), was dried over anhydrous magnesium sulfate, and then was filtered and concentrated under reduced

pressure. The oil thus acquired was subjected to flash chromatography (4 g silica gel, 17:3 petroleum ether–ethyl acetate) to afford 4.4 mg of a clear colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) spectroscopic, GLC and GLC–MS (CI, NH_3) analyses of the mixture revealed the presence of three products, as well as a small amount (≈5%) of unreacted starting material. The ^{1}H NMR spectrum showed 6 signals in the 6.50–5.10 ppm region integrating for a total of 2 protons, a triplet at 3.62 ppm (2H), a multiplet at 2.26–2.08 ppm (2H), a multiplet at 1.63–1.40 ppm (4H) and 5 singlets in the 0.20–0.02 ppm region integrating for a total of 9 protons.



94b

The major product (≈72%) was assigned structure **94b**, (*Z*)-6-trimethylsilylhex-5-en-1-ol, formed by protiodegermylation of the starting material, based on the following data. ^{1}H NMR: δ 6.27 (dt, 1H, J = 14.0 and 7.0 Hz), 5.48 (dt, 1H, J = 14.0 and 1.2 Hz). Homonuclear decoupling of the 6.27 signal resulted in the collapse of the 5.48 ppm doublet of triplets to a triplet, also revealing a small doublet previously hidden (vide infra). GLC-MS indicated an ion at 173 $(M + 1)^+$, as well as diagnostic fragments at 157 $(M - CH_3)^+$ and 73 $(\text{-}Si(CH_3)_3)^+$.



94a

Similarly, the next major component (18%) was assigned structure **94a**, (*E*)-6-trimethylsilylhex-5-en-1-ol, based on the following data. ^{1}H NMR: δ 6.00 (dt, 1H, J = 18.6

and 6.2 Hz), 5.62 (dt, 1H, J = 18.6 and 1.5 Hz). GLC-MS indicated an ion at 173 $(M + 1)^+$, as well as diagnostic fragments at 157 $(M - CH_3)^+$ and 73 $(-Si(CH_3)_3)^+$. The minor product (≈5%) formed during the reaction was 5-trimethylgermylhex-5-en-1-ol (**92**). The assignment was established based on the following: characteristic doublets at 5.49 (revealed during the decoupling experiment at 6.27 ppm) and 5.16 ppm in the ^1H NMR spectrum, GLC-MS indicated an ion 219 $(M + 1)^+$ with an isotopic cluster consistent with the expected isotopic distribution and finally, coinjection with an authentic sample on GLC ascertained that this product has a retention time identical with that of 5-trimethylgermylhex-5-en-1-ol (**92**). The presence of this compound can be linked to the small (5%) amount of (*Z*)-5-trimethylgermyl-6-trimethylsilylhex-5-en-1-ol (**75**) in the starting material, incompletely separated from **74** during the isolation, which underwent protiodesilylation (vide supra).

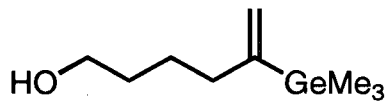
3.2.4 SYNTHESIS OF 2-TRIMETHYLGERMYLALK-1-ENES

3.2.4.1 GENERAL PROCEDURE 3: PREPARATION OF THE 2-TRIMETHYLGERMYLALK-1-ENES

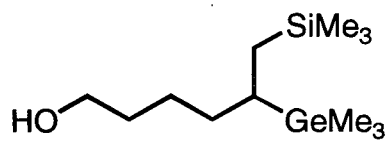
To a stirred solution of the appropriate 1-trimethylsilylalk-1-yne (1 equiv) in dry CH_2Cl_2 (1 M solution) at rt was added $H_2PtCl_6 \cdot 6H_2O$ (≈0.02 equiv unless otherwise noted). The mixture was cooled to 0 °C, stirred for 5 min and Me_3GeH (**53**) (1.50 equiv unless otherwise noted) was added via a precooled gas-tight syringe (cooled by running cold water on the barrel). The reaction mixture was warmed to rt and stirred until the conversion of the starting material appeared to be complete (1–21 h) by TLC or GLC analysis of an aliquot of the reaction mixture. The mixture was filtered through a short column of Florisil or silica gel (≈3 g per mmol of 1-trimethylsilylalk-1-yne) and the column was eluted with CH_2Cl_2 or diethyl ether (≈30 mL per mmol of 1-trimethylsilylalk-1-yne). The eluate was concentrated under reduced pressure. The dark oil thus obtained was dissolved in CH_2Cl_2 (0.1 M, nonanhydrous; reaction not performed under inert atmosphere) and *p*-TsOH•H_2O (1.20 equiv unless otherwise noted) was added. The stirred heterogeneous mixture was heated, using an oil bath, at 30–34 °C until the protiodesilylation appeared to be complete (1–7 h) by GLC analysis of an aliquot of the reaction mixture. After the mixture had been cooled, it was diluted with diethyl ether (≈20 mL per mmol of 1-trimethylsilylalk-1-yne) and saturated aqueous $NaHCO_3$ (≈3 mL per mmol of 1-trimethylsilylalk-1-yne) was added. The layers were separated and the aqueous portion was extracted with diethyl ether (2 × ≈3 mL per mmol of 1-trimethylsilylalk-1-yne). The pooled organic extracts were washed with water (≈3 mL per mmol of 1-trimethylsilylalk-1-yne), and brine (≈3 mL per mmol of 1-trimethylsilylalk-1-yne),

were dried over anhydrous magnesium sulfate, and then were filtered and concentrated under reduced pressure. The crude oil was flash chromatographed and the acquired oil was distilled to afford the desired 2-trimethylgermylalk-1-ene.

3.2.4.1.1 Synthesis of 5-Trimethylgermylhex-5-en-1-ol (**92**) and 5-Trimethylgermyl-6-trimethylsilylhexan-1-ol (**122**)



92



122

Following general procedure 3, to a stirred solution of 1-trimethylsilyl-6-(trimethylsilyloxy)hex-1-yne (**61**) (305 mg, 1.26 mmol, 1 equiv) in dry CH_2Cl_2 (1.2 mL), was added sequentially $H_2PtCl_6{\bullet}6H_2O$ (13 mg, 0.025 mmol, 0.019 equiv) and Me_3GeH (**53**) (224 mg, 1.89 mmol, 1.50 equiv). The orange solution was stirred at rt for 1 h. The mixture was filtered through a short column of silica gel (elution with diethyl ether) and the eluate was concentrated under reduced pressure. The dark oil thus acquired was dissolved in CH_2Cl_2 (12 mL) and *p*-TsOH•H_2O (287 mg, 1.51 mmol, 1.20 equiv) was added. The heterogeneous mixture was heated at 30 °C and stirred for 1.5 h. The crude oil obtained was subjected to flash chromatography (30 g TLC grade silica gel, 17:3 then 4:1 petroleum ether–ethyl acetate) to afford three fractions which were concentrated under reduced pressure. The first fraction to be eluted afforded 5.8 mg of 5-trimethylgermyl-6-trimethylsilylhexan-1-ol (**122**) as a clear colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.61 (t, 2H, J = 6.6 Hz, -C<u>H</u>$_2$OH), 1.56–1.18 (m, 7H), 1.05–

0.98 (m, 1H, -C<u>H</u>Ge(CH_3)$_3$-), 0.60 (dd, 1H, J = 15.0 and 3.6 Hz, -C<u>H</u>$_a$H$_b$Si(CH_3)$_3$), 0.48 (dd, 1H, J = 15.0 and 10.4 Hz, -CH$_a$<u>H</u>$_b$Si(CH_3)$_3$), 0.06 (s, 9H), –0.02 (s, 9H).

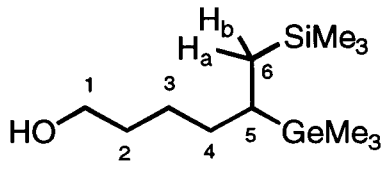
Additional ^{1}H NMR data, derived from homonuclear decoupling experiments, are given in **Table 19**.

^{13}C NMR (125.7 MHz, $CDCl_3$): δ 63.0 (-CH_2OH), 34.1, 33.3, 25.0, 22.9 (-<u>C</u>HGe(CH_3)$_3$-), 17.5 (-<u>C</u>H$_2$Si(CH_3)$_3$), 0.8, –3.0.

IR (film): 3328, 2952, 1413, 1248, 1060, 839, 751, 692 cm^{-1}.

HRMS for $C_{12}H_{30}{}^{74}GeO^{28}Si$: calcd 292.1278, found 292.1270.

Table 19: ^{1}H NMR Data from Homonuclear Decoupling Experiments for 5-Trimethylgermyl-6-trimethylsilylhexan-1-ol (**122**)



122

Assignments H-x	^{1}H NMR[a] δ ppm (mult, J (Hz))	Simplified Signals (mult, J (Hz))
H-1	3.61 (t, J = 6.6)	
H-2,3,4, -OH	1.56–1.18 (m)	
H-5[b]	1.05–0.98 (m)	1.49–1.41 (H-4) portion of 1.56–1.18 m, H-6a (d, 15.0) H-6b (d, 15.0)
H-6a[b]	0.60 (dd, J = 15.0, 3.6)	H-5 (dt; 10.4, 6.0), H-6b (d, 10.4)
H-6b[b]	0.48 (dd, J = 15.0, 10.4)	H-5 (td; 6.0, 3.6), H-6a (d, 3.6)
	0.06 (s)	
	–0.02 (s)	

[a] 400 MHz, $CDCl_3$. [b] Irradiation of this signal simplified the corresponding signals in the right hand column.

The second fraction to be eluted was distilled (118–124 °C/24 Torr) to afford 202 mg (74%) of 5-trimethylgermylhex-5-en-1-ol (**92**) as a clear colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.49 (d, 1H, J = 2.6 Hz, vinylic proton trans to -Ge(CH_3)$_3$), 5.16 (d, 1H, J = 2.6 Hz, vinylic proton cis to -Ge(CH_3)$_3$), 3.63 (t, 2H, J = 6.4 Hz, -C$\underline{H}_2$OH), 2.19 (t, 2H, J = 7.4 Hz, -C$\underline{H}_2$C(=CH_2)-), 1.60–1.50 (m, 2H, -C$\underline{H}_2$$CH_2$OH), 1.50–1.40 (m, 2H, -C$\underline{H}_2$$CH_2$C(=$CH_2$)-), 1.31 (br s, 1H, exchanges with D_2O, -OH), 0.18 (s, 9H, -Ge(CH_3)$_3$).

Additional ^{1}H NMR data, derived from NOE difference experiments, are given in **Table 20**.

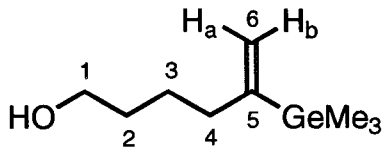
^{13}C NMR (75.4 MHz, $CDCl_3$): δ 153.8 (-$\underline{C}$(=CH_2)-), 121.5 (-C(=$\underline{C}$$H_2$)-), 62.6 (-$CH_2$OH), 37.0, 32.4, 24.9, –1.9 (-Ge(CH_3)$_3$).

IR (film): 3328, 3046, 2937, 1833, 1606, 1413, 1236, 1062, 916, 825, 760, 599 cm^{-1}.

HRMS for $C_8H_{17}{}^{74}GeO$ (M – CH_3)$^+$: calcd 203.0491, found 203.0482.

Anal. calcd for $C_9H_{20}GeO$: C 49.85, H 9.30; found: C 49.83, H 9.28.

Table 20: ^{1}H NMR Data from Nuclear Overhauser Enhancement Difference Experiments for 5-Trimethylgermylhex-5-en-1-ol (**92**)



92

Assignments H-x	^{1}H NMR[a] δ ppm (mult, *J* (Hz))	Observed NOEs
H-6a[b]	5.49 (d)	H-3, H-4, H-6b
H-6b[b]	5.16 (d)	H-6a, -Ge(CH$_3$)$_3$
H-1	3.63 (t, *J* = 6.4)	
H-4[b]	2.19 (t, *J* = 7.4)	H-2, H-3, H-6a, -Ge(CH$_3$)$_3$
H-2	1.60–1.50 (m)	
H-3	1.50–1.40 (m)	
-OH	1.31 (br s)	
-Ge(CH$_3$)$_3$[b]	0.18 (s)	H-2, H-3, H-4, H-6b

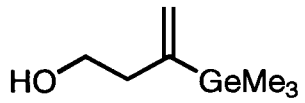
[a] 400 MHz, CDCl$_3$. [b] Irradiation of this signal generated the corresponding NOEs in the right hand column.

The third fraction to be eluted afforded 8.5 mg and was shown, by GLC analysis, to be a mixture of four compounds. ^{1}H NMR analysis of the mixture suggested that it was comprised mainly of two components, hex-5-en-1-ol (**95**) and 5-trimethylgermylhex-5-en-1-ol (**92**), in about equal amounts. Spectral data for hex-5-en-1-ol (**95**) are as follows:

^{1}H NMR (400 MHz, CDCl$_3$): δ 5.79 (ddt, 1H, *J* = 17.0, 10.2 and 6.8 Hz, -C<u>H</u>=CH$_2$), 4.99 (dd, 1H, *J* = 17.0 and 2.0 Hz, -CH=C<u>H</u>$_a$H$_b$), 4.94 (dd, 1H, *J* = 10.2 and 2.0 Hz, -CH=CH$_a$<u>H</u>$_b$), 3.63 (t, 2H, *J* = 6.4 Hz, -C<u>H</u>$_2$OH), 2.07 (dt, 2H, *J* = 6.8 and 6.8 Hz,

-C$\underline{H}_2$CH=CH_2), 1.58–1.40 (m, 4H, -C$\underline{H}_2$C$\underline{H}_2$$CH_2$OH), 1.28 (br s, 1H, exchanges with D_2O -OH).

3.2.4.1.2 Synthesis of 3-Trimethylgermylbut-3-en-1-ol (**115**)



115

Following general procedure 3, to a stirred solution of 1-trimethylsilyl-4-(trimethylsilyloxy)but-1-yne (**63**) (279 mg, 1.30 mmol, 1 equiv) in dry CH_2Cl_2 (1.3 mL) was added sequentially H_2PtCl_6•$6H_2O$ (8.8 mg, 0.017 mmol, 0.013 equiv) and Me_3GeH (**53**) (232 mg, 1.95 mmol, 1.50 equiv). The orange solution was stirred at rt for 1 h and was then filtered through a short column of silica gel (elution with diethyl ether). The eluate was concentrated under reduced pressure. The dark oil thus obtained was dissolved in CH_2Cl_2 (13 mL) and *p*-TsOH•H_2O (297 mg, 1.56 mmol, 1.20 equiv) was added. The heterogeneous mixture was heated at 30–32 °C and stirred for 1.5 h. The crude oil acquired was flash chromatographed (20 g TLC grade silica gel, 17:3 petroleum ether–diethyl ether) and distilled (95–102 °C/9 Torr) to afford 155 mg (63%) of the title compound as a clear colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.61 (d, 1H, J = 2.4 Hz, vinylic proton trans to -Ge(CH_3)$_3$), 5.32 (d, 1H, J = 2.4 Hz, vinylic proton cis to -Ge(CH_3)$_3$), 3.65 (td, 2H, J = 6.4 and 6.4 Hz, -C$\underline{H}_2$OH), 2.46 (t, 2H, J = 6.4 Hz, -C$\underline{H}_2$C(=CH_2)-), 1.41 (br t, 1H, J = 6.4 Hz, exchanges with D_2O, -OH), 0.21 (s, 9H, -Ge(CH_3)$_3$).

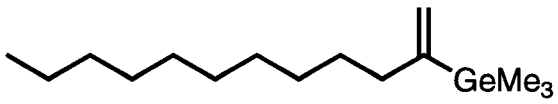
^{13}C NMR (75.4 MHz, $CDCl_3$): δ 150.3 (-$\underline{C}$(=CH_2)-), 124.6 (-C(=$\underline{C}$$H_2$)-), 61.1 (-$CH_2$OH), 40.4 (-$\underline{C}$$H_2$C(=$CH_2$)-), –1.9 (-Ge($CH_3$)$_3$).

IR (film): 3365, 3048, 2971, 1606, 1417, 1237, 1047, 920, 825, 760 cm^{-1}.

HRMS for $C_6H_{13}{}^{74}GeO$ $(M - CH_3)^+$: calcd 175.0178, found 175.0179.

Anal. calcd for $C_7H_{16}GeO$: C 44.53, H 8.54; found: C 44.64, H 8.70.

3.2.4.1.3 Synthesis of 2-Trimethylgermyldodec-1-ene (**116**)



116

Following general procedure 3, to a stirred solution of 1-trimethylsilyldodec-1-yne (**64**) (314 mg, 1.32 mmol, 1 equiv) in dry CH_2Cl_2 (1.3 mL) was added sequentially $H_2PtCl_6{\bullet}6H_2O$ (12 mg, 0.024 mmol, 0.018 equiv) and Me_3GeH (**53**) (235 mg, 1.98 mmol, 1.50 equiv). The heterogeneous mixture was stirred at rt for 3.5 h. The green solution which contained a fine black suspension was filtered through Florisil (elution with CH_2Cl_2) and the eluate was concentrated under reduced pressure. The dark oil thus acquired was dissolved in CH_2Cl_2 (13 mL) and *p*-TsOH•H_2O (301 mg, 1.58 mmol, 1.20 equiv) was added. The heterogeneous mixture was heated at 34 °C and stirred for 1.5 h. The crude liquid was flash chromatographed (40 g of C_{18} silica gel, 3:2 acetonitrile–methanol) to afford two fractions which were concentrated under reduced pressure. The first fraction to be eluted afforded 3.9 mg and was shown, by GLC analysis, to be a mixture of several compounds. ^{1}H NMR spectroscopic analysis of the mixture suggested that the major component of this mixture was dodec-1-ene (**113**).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.80 (ddt, 1H, J = 17.1, 10.3 and 6.7 Hz), 4.98 (ddt, 1H, J = 17.1, 2.0 and 2.0 Hz), 4.91 (ddt, 1H, J = 10.3, 2.0 and 2.0 Hz), 2.10–1.98 (m, 2H),

1.45–1.15 (m, 16H), 0.88 (t, 3H, J = 7.0 Hz).

The second fraction to be eluted was distilled (102–110 °C/0.2 Torr) to afford 269 mg (72%) of the title compound as a clear colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.48 (d, 1H, J = 2.7 Hz, vinylic proton trans to -Ge(CH_3)$_3$), 5.14 (d, 1H, J = 2.7 Hz, vinylic proton cis to -Ge(CH_3)$_3$), 2.16 (br t, 2H, J = 7.6 Hz, -C$\underline{H}_2$C(=CH_2)-), 1.42–1.33 (br m, 3H), 1.33–1.20 (br s, 13H), 0.86 (br t, 3H, J = 6.8 Hz, -CH_2C$\underline{H}_3$), 0.18 (s, 9H, -Ge(CH_3)$_3$).

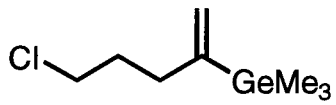
^{13}C NMR (75.4 MHz, $CDCl_3$): δ 154.4 (-$\underline{C}$(=CH_2)-), 121.3 (-C(=$\underline{C}H_2$)-), 37.6, 32.1, 29.8 (2 overlapping signals), 29.7, 29.52, 29.49, 29.1, 22.8, 14.2 (-$CH_2\underline{C}H_3$), –1.8 (-Ge(CH_3)$_3$).

IR (film): 3050, 2926, 1467, 1236, 824, 759 cm^{-1}.

HRMS for $C_{15}H_{32}{}^{74}Ge$: calcd 286.1716, found 286.1724.

Anal. calcd for $C_{15}H_{32}Ge$: C 63.21, H 11.32; found: C 62.89, H 11.60.

3.2.4.1.4 Synthesis of 5-Chloro-2-trimethylgermylpent-1-ene (**117**)



117

Following general procedure 3, to a stirred solution of 5-chloro-1-trimethylsilylpent-1-yne (**65**) (256 mg, 1.47 mmol, 1 equiv) in dry CH_2Cl_2 (1.5 mL) was added sequentially H_2PtCl_6•$6H_2O$ (10 mg, 0.020 mmol, 0.014 equiv) and Me_3GeH (**53**) (261 mg, 2.20 mmol, 1.50 equiv). The heterogeneous mixture was stirred at rt for 3.5 h. The green solution which contained a fine black suspension was filtered through Florisil (elution with CH_2Cl_2) and the

eluate was concentrated under reduced pressure. The dark oil thus obtained was dissolved in CH_2Cl_2 (15 mL) and *p*-TsOH•H_2O (335 mg, 1.76 mmol, 1.20 equiv) was added. The heterogeneous mixture was heated at 30 °C and stirred for 2.5 h. The crude oil acquired was flash chromatographed (20 g TLC grade silica gel, petroleum ether) and distilled (103–112 °C/16 Torr) to afford 243 mg (74%) of the title compound as a clear colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.53 (d, 1H, J = 2.4 Hz, vinylic proton trans to -Ge(CH_3)$_3$), 5.22 (d, 1H, J = 2.4 Hz, vinylic proton cis to -Ge(CH_3)$_3$), 3.51 (t, 2H, J = 6.6 Hz, -CH_2Cl), 2.32 (br t, 2H, J = 7.4 Hz, -C$\underline{H}_2$C(=CH_2)-), 1.86 (tt, 2H, J = 7.4 and 6.6 Hz, -CH_2C$\underline{H}_2$$CH_2$-), 0.20 (s, 9H, -Ge($CH_3$)$_3$).

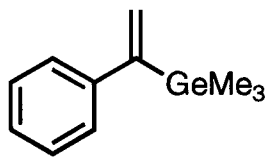
^{13}C NMR (75.4 MHz, $CDCl_3$): δ 152.2 (-$\underline{C}$(=CH_2)-), 122.5 (-C(=$\underline{C}$$H_2$)-), 44.3, 34.2, 31.6, –1.9 (-Ge(CH_3)$_3$).

IR (film): 3048, 2970, 1839, 1607, 1237, 920, 826, 601 cm^{-1}.

HRMS for $C_7H_{14}{}^{35}Cl^{74}Ge$ (M – CH_3)$^+$: calcd 206.9996, found 206.9999.

Anal. calcd for $C_8H_{17}ClGe$: C 43.43, H 7.74; found: C 43.60, H 7.90.

3.2.4.1.5 Synthesis of 1-Phenyl-1-trimethylgermylethene (**118**)



118

Following general procedure 3, to a stirred solution of 1-phenyl-2-trimethylsilyl-acetylene (**66**) (201 mg, 1.15 mmol, 1 equiv) in dry CH_2Cl_2 (1.2 mL) was added H_2PtCl_6•6H_2O (16 mg, 0.030 mmol, 0.026 equiv). The mixture soon became green and

contained a fine black suspension. After cooling to 0 °C, Me_3GeH (**53**) (205 mg, 1.73 mmol, 1.50 equiv) was added and the mixture became bright yellow. The heterogeneous mixture was stirred at rt for 4 h, during which time it became green again. The mixture was filtered through Florisil (elution with CH_2Cl_2) and the eluate was concentrated under reduced pressure. The dark oil thus obtained was dissolved in CH_2Cl_2 (12 mL) and *p*-TsOH•H_2O (263 mg, 1.38 mmol, 1.20 equiv) was added. The suspension was heated at 30 °C and stirred for 7 h. The crude liquid acquired was subjected to flash chromatography (25 g TLC grade silica gel, petroleum ether) and distilled (105–108 °C/8 Torr) to afford 174 mg (68%) of the title compound as a clear colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31–7.27 (m, 2H), 7.23–7.19 (m, 3H), 5.84 (d, 1H, J = 2.4 Hz, vinylic proton trans to -$Ge(CH_3)_3$), 5.47 (d, 1H, J = 2.4 Hz, vinylic proton cis to -$Ge(CH_3)_3$), 0.29 (s, 9H, -$Ge(CH_3)_3$).

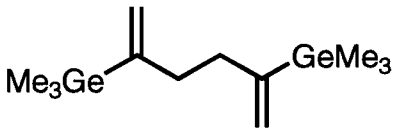
^{13}C NMR (75.4 MHz, $CDCl_3$): δ 154.1 (-$\underline{C}$(=CH_2)-), 144.4 (aromatic *ipso* carbon), 128.2, 126.4 (2 overlapping signals), 124.2 (-C(=$\underline{C}H_2$)-), –1.1 (-$Ge(CH_3)_3$).

IR (film): 3055, 2974, 1599, 1573, 1490, 1412, 1237, 924, 827, 778, 705, 601 cm^{-1}.

HRMS for $C_{11}H_{16}{}^{74}Ge$: calcd 222.0464, found 222.0470.

Anal. calcd for $C_{11}H_{16}Ge$: C 59.83, H 7.30; found: C 59.60, H 7.25.

3.2.4.1.6 Synthesis of 2,5-bis(Trimethylgermyl)hexa-1,5-diene (**119**)



119

Following general procedure 3, to a stirred solution of 1,6-bis(trimethylsilyl)hexa-1,5-diyne (**67**) (250 mg, 1.12 mmol, 1 equiv) in dry CH_2Cl_2 (1.1 mL) was added sequentially $H_2PtCl_6 \cdot 6H_2O$ (22 mg, 0.043 mmol, 0.038 equiv) and Me_3GeH (**53**) (400 mg, 3.37 mmol, 3.00 equiv). The heterogeneous mixture was stirred at rt for 4.5 h. The green solution which contained a fine black suspension was filtered through Florisil (elution with CH_2Cl_2) and the eluate was concentrated under reduced pressure. The dark oil thus acquired was dissolved in CH_2Cl_2 (11 mL) and *p*-TsOH•H_2O (513 mg, 2.70 mmol, 2.40 equiv) was added. The suspension was heated at 30 °C and stirred for 5 h. The crude oil obtained was flash chromatographed (20 g TLC grade silica gel, petroleum ether) and distilled. A forerun (distillation temperature 50–70 °C/9 Torr) was collected in a first bulb (26 mg, volatile material as indicated by GLC analysis). The remainder of the liquid was collected in a second bulb (distillation temperature 88–98 °C/9 Torr) to afford 251 mg (71%) of the title compound as a clear colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.52 (d, 2H, J = 2.4 Hz, 2 × vinylic proton trans to -Ge$(CH_3)_3$), 5.18 (d, 2H, J = 2.4 Hz, 2 × vinylic proton cis to -Ge$(CH_3)_3$), 2.26 (s, 4H, -CH_2CH_2-), 0.20 (s, 18H, 2 × -Ge$(CH_3)_3$).

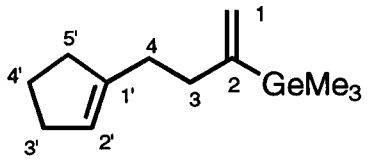
^{13}C NMR (75.4 MHz, $CDCl_3$): δ 153.8 (-<u>C</u>(=CH_2)-), 121.4 (-C(=<u>C</u>H_2)-), 36.9 (-CH_2-), –1.8 (-Ge$(CH_3)_3$).

IR (film): 3048, 2972, 1838, 1607, 1412, 1236, 916, 825, 759, 598 cm^{-1}.

HRMS (DCI, NH_3 + CH_4) for $C_{12}H_{27}{}^{72}Ge^{74}Ge$ $(M + 1)^+$: calcd 317.0545, found 317.0541.

Anal. calcd for $C_{12}H_{26}Ge_2$: C 45.68, H 8.31; found: C 45.47, H 8.27.

3.2.4.1.7 Synthesis of 4-(Cyclopent-1-en-1-yl)-2-trimethylgermylbut-1-ene (**120**)



120

Following general procedure 3, to a stirred solution of 4-(cyclopent-2-en-1-yl)-1-trimethylsilylbut-1-yne (**72**) (228 mg, 1.19 mmol, 1 equiv) in dry CH_2Cl_2 (1.2 mL) was added sequentially $H_2PtCl_6{\bullet}6H_2O$ (9.0 mg, 0.017 mmol, 0.015 equiv) and Me_3GeH (**53**) (211 mg, 1.78 mmol, 1.50 equiv). The heterogeneous mixture was stirred at rt for 21 h. The green solution which contained a fine black suspension was filtered through Florisil (elution with CH_2Cl_2) and the eluate was concentrated under reduced pressure. The dark oil thus acquired was dissolved in CH_2Cl_2 (12 mL) and *p*-TsOH•H_2O (270 mg, 1.42 mmol, 1.20 equiv) was added. The heterogeneous mixture was heated at 30 °C and stirred for 2 h. The crude oil obtained was filtered through a short column of silica gel (2.5 g, elution with petroleum ether, 50 mL), and the eluate was concentrated under reduced pressure. The crude oil thus acquired was distilled. A forerun was collected in a first bulb (31 mg, distillation temperature 70–100 °C/17 Torr). The remainder of the material was collected in a second bulb (distillation temperature 130–150 °C/17 Torr) to afford 205 mg (72%) of the title compound as a clear colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.51 (d, 1H, J = 2.6 Hz, vinylic proton trans to -Ge(CH_3)$_3$), 5.33 (t, 1H, J = 1.8 Hz, cyclopentene vinylic proton), 5.16 (d, 1H, J = 2.6 Hz, vinylic proton cis to -Ge(CH_3)$_3$), 2.39–2.12 (m, 8H), 1.87–1.80 (m, 2H), 0.20 (s, 9H, -Ge(CH_3)$_3$).

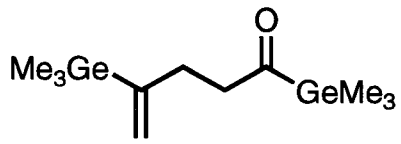
^{13}C NMR (75.4 MHz, $CDCl_3$): δ 153.9 (-C(=CH_2)-), 144.5 (C-1'), 123.3 (C-2'), 121.1 (-C(=CH_2)-), 35.5, 35.2, 32.4, 30.6, 23.4, –1.9 (-Ge(CH_3)$_3$).

IR (film): 3046, 2907, 1835, 1651, 1606, 1439, 1236, 916, 824, 759, 599 cm^{-1}.

HRMS for $C_{12}H_{22}{}^{74}Ge$: calcd 240.0933, found 240.0935.

Anal. calcd for $C_{12}H_{22}Ge$: C 60.33, H 9.28; found: C 60.13, H 9.20.

3.2.4.1.8 Synthesis of 4-Trimethylgermylpent-4-enoyltrimethylgermane (**121**)



121

Following general procedure 3, to a stirred solution of 5-trimethylsilylpent-4-ynoyl-trimethylgermane (**114**) (see section 3.3.2.3.10, p 246 for the preparation of **114**; 296 mg, 1.09 mmol, 1 equiv) in dry CH_2Cl_2 (1.1 mL) was added sequentially H_2PtCl_6•$6H_2O$ (9.0 mg, 0.017 mmol, 0.016 equiv) and Me_3GeH (**53**) (194 mg, 1.63 mmol, 1.50 equiv). The orange solution was stirred at rt for 6 h. The mixture was filtered through a short column of silica gel (elution with diethyl ether) and the eluate was concentrated under reduced pressure. The dark oil thus obtained was dissolved in CH_2Cl_2 (11 mL) and p-TsOH•H_2O (249 mg, 1.31 mmol, 1.20 equiv) was added. The heterogeneous mixture was heated at 32–34 °C for 1 h. The crude oil acquired was subjected to flash chromatography (35 g TLC grade silica gel, 97:3

petroleum ether–diethyl ether) and distilled (75–85 °C/0.1 Torr) to afford 235 mg (68%) of the title compound as a light yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.44 (d, 1H, J = 2.0 Hz, vinylic proton trans to -Ge(CH_3)$_3$), 5.17 (d, 1H, J = 2.0 Hz, vinylic proton cis to -Ge(CH_3)$_3$), 2.75–2.71 (m, 2H), 2.40–2.36 (m, 2H), 0.32 (s, 9H, -COGe(CH_3)$_3$), 0.19 (s, 9H, -C(=CH_2)Ge($C\underline{H}_3$)$_3$).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 244.4 (-$\underline{C}$OGe(CH_3)$_3$), 152.5 (-$\underline{C}$(=CH_2)-), 121.2 (-C(=$\underline{C}H_2$)-), 48.3 (-$\underline{C}H_2$CO-), 28.8 (-$\underline{C}H_2$C(=CH_2)-), –2.1 (-C(=CH_2)Ge($\underline{C}H_3$)$_3$), –2.9 (-COGe($\underline{C}H_3$)$_3$).

IR (film): 3049, 2974, 1840, 1658, 1412, 1237, 1053, 828, 602 cm^{-1}.

HRMS for $C_{10}H_{21}{}^{72}Ge^{74}GeO$ (M – CH_3)$^+$: calcd 303.0025, found 303.0027.

Anal. calcd for $C_{11}H_{24}Ge_2O$: C 41.61, H 7.62; C 41.40, H 7.83.

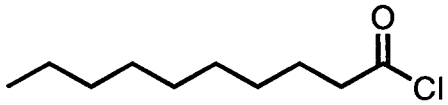
3.3 SYNTHESIS OF ACYLTRIMETHYLGERMANES VIA ADDITION OF (TRIMETHYLGERMYL)COPPER(I)–DIMETHYL SULFIDE TO ACYL ELECTROPHILES, AND THEIR OLEFINATION TO 2-TRIMETHYLGERMYLALK-1-ENES

3.3.1 SYNTHESIS OF ACYL CHLORIDES

3.3.1.1 GENERAL PROCEDURE 4: PREPARATION OF THE ACYL CHLORIDES **157–160** AND **164**

To the appropriate carboxylic acid (1 equiv) was added $SOCl_2$ (2–8 equiv). The mixture was heated at reflux for 0.5–3 h, then the excess $SOCl_2$ was removed via distillation under reduced pressure. The crude oil thus obtained was distilled to afford the desired acyl chloride.

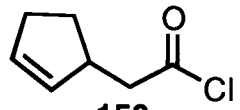
3.3.1.1.1 Synthesis of Decanoyl Chloride (**157**)



157

Following general procedure 4, to decanoic acid (**153**) (2.00 g, 11.6 mmol, 1 equiv) was added $SOCl_2$ (2.76 g, 23.2 mmol, 2.00 equiv). The mixture was heated at reflux for 0.5 h. The crude oil obtained was distilled (70–80 °C/0.06 Torr, lit. bp 94–96 °C/5 Torr[82]) to afford 2.16 g (98%) of the title compound as a clear colorless oil. Decanoyl chloride (**157**) is commercially available, but it was prepared by this simple method since decanoic acid (**153**) was readily available.

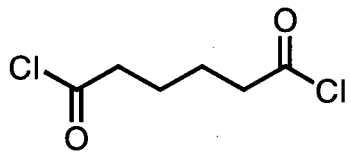
3.3.1.1.2 Synthesis of (Cyclopent-2-en-1-yl)acetyl Chloride (**158**)



158

Following general procedure 4, to (cyclopent-2-en-1-yl)acetic acid (**154**) (1.84 g, 14.6 mmol, 1 equiv) was added $SOCl_2$ (3.46 g, 29.1 mmol, 2.00 equiv). The mixture was heated at reflux for 0.75 h. The crude oil obtained was distilled (90–110 °C/9 Torr, lit. bp 65 °C/18 Torr[123]) to afford 1.99 g (94%) of the title compound as a clear colorless oil.

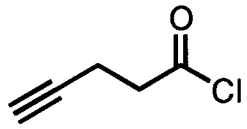
3.3.1.1.3 Synthesis of Adipoyl Chloride (**159**)



159

Following general procedure 4, to adipic acid (**155**) (2.00 g, 13.7 mmol, 1 equiv) was added $SOCl_2$ (6.51 g, 54.7 mmol, 4 equiv). The mixture was heated at reflux for 3 h. The crude oil obtained was distilled (76–86 °C/0.05 Torr, lit. bp 105–107 °C/2 Torr[82]) to afford 2.30 g (92%) of the title compound as a clear colorless oil. Adipoyl chloride (**159**) is commercially available, but it was prepared by this simple method since adipic acid (**155**) was readily available.

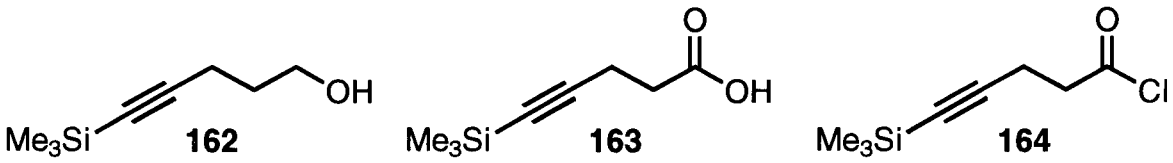
3.3.1.1.4 Synthesis of Pent-4-ynoyl Chloride (**160**)



160

Following general procedure 4, to pent-4-ynoic acid (**156**) (990 mg, 10.1 mmol, 1 equiv) was added $SOCl_2$ (2.40 g, 20.2 mmol, 2 equiv). The mixture was heated at reflux for 0.75 h. The crude oil obtained was distilled (62–72 °C/23 Torr, lit. bp 46–48 °C/19 Torr[124]) to afford 733 mg (62%) of the title compound as a volatile clear colorless oil.

3.3.1.1.5 Synthesis of 5-Trimethylsilylpent-4-yn-1-ol (**162**), 5-Trimethylsilylpent-4-ynoic Acid (**163**) and 5-Trimethylsilylpent-4-ynoyl Chloride (**164**)[83]



*a) 5-Trimethylsilylpent-4-yn-1-ol (**162**)*

To a cold (–78 °C) stirred solution of pent-4-yn-1-ol (**161**) (2.29 g, 27.2 mmol, 1 equiv) in dry THF (270 mL) was added a solution of *n*-BuLi (1.60 M in hexanes, 37.4 mL, 59.9 mmol, 2.20 equiv) via a syringe over 10 min. The resulting thick slurry was stirred at –78 °C for 2 h, then chlorotrimethylsilane (7.39 g, 68.0 mmol, 2.50 equiv) was added via a syringe. The solution was stirred at –78 °C for 5 min, then was warmed to rt and was allowed to stir for an additional 0.5 h. Water (100 mL) was added and the mixture was stirred overnight. Diethyl ether (100 mL) was added and the layers were separated. The aqueous portion was extracted with diethyl ether (2 × 100 mL). The pooled organic extracts were

washed with brine (2 × 50 mL), were dried over anhydrous magnesium sulfate, and then were filtered and concentrated under reduced pressure. The crude oil thus acquired was subjected to flash chromatography (200 g silica gel, 3:2 diethyl ether–petroleum ether) and distilled (130–140 °C/11 Torr) to afford 3.53 g (74%) of 5-trimethylsilylpent-4-yn-1-ol (**162**) as a clear colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.74 (t, 2H, J = 6.2 Hz, -C$\underline{H}_2$OH), 2.33 (t, 2H, J = 6.8 Hz, -CH_2C≡C-), 1.75 (tt, 2H, J = 6.8 and 6.2 Hz, -CH_2C$\underline{H}_2$$CH_2$-), 1.56 (br s, 1H, exchanges with D_2O, -OH), 0.12 (s, 9H, -Si(CH_3)$_3$).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 106.6 (-C≡$\underline{C}$Si(CH_3)$_3$), 85.3 (-$\underline{C}$≡CSi(CH_3)$_3$), 61.9 (-CH_2OH), 31.1 (-$CH_2$$\underline{C}$$H_2$$CH_2$-), 16.5 (-$\underline{C}$$H_2$C≡C-), 0.1 (-Si($CH_3$)$_3$).

IR (film): 3327, 2958, 2176, 1250, 843, 761 cm^{-1}.

HRMS for $C_7H_{13}O^{28}Si$ (M – CH_3)$^+$: calcd 141.0736, found 141.0730.

Anal. calcd for $C_8H_{16}OSi$: C 61.48, H 10.32; found: C 61.25, H 10.23.

*b) 5-Trimethylsilylpent-4-ynoic Acid (**163**)*

To a stirred solution of CrO_3 (7.20 g, 72.0 mmol, 3.75 equiv) in 1.5 M aqueous H_2SO_4 (115 mL) at 0 °C, was added a solution of 5-trimethylsilylpent-4-yn-1-ol (**162**) (3.00 g, 19.2 mmol, 1 equiv) in acetone (230 mL) over 3 h. The reaction mixture was allowed to slowly warm up to rt and was stirred overnight. Diethyl ether (100 mL) was added and the aqueous layer was saturated with NaCl. The layers were separated and the aqueous portion was extracted with diethyl ether (3 × 100 mL). The combined organic extracts were washed with water (8 × 50 mL) and brine (2 × 100 mL), were dried over anhydrous magnesium sulfate,

and then were filtered and concentrated under reduced pressure. The crude oil thus acquired was subjected to flash chromatography (325 g silica gel, 85:15:1 petroleum ether–ethyl acetate–acetic acid) to afford a beige solid. This solid was sublimed (42–44 °C/0.007 Torr) to afford 2.16 g (66%) of 5-trimethylsilylpent-4-ynoic acid (**163**) as a colorless solid (mp 47.5–48.0 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ 11.00–10.40 (br s, 1H, exchanges with D_2O, $-CO_2H$), 2.62–2.49 (m, 4H, $-CH_2CH_2-$), 0.12 (s, 9H, $-Si(CH_3)_3$).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 178.4 ($-CO_2H$), 104.5 ($-C\equiv\underline{C}Si(CH_3)_3$), 85.7 ($-\underline{C}\equiv CSi(CH_3)_3$), 33.4 ($-\underline{C}H_2CO_2H$), 15.4 ($-\underline{C}H_2C\equiv C-$), 0.0 ($-Si(CH_3)_3$).

IR (KBr pellet): 3600–2300, 2178, 1718, 1430, 1296, 1255, 1212, 1014, 844, 761 cm^{-1}.

HRMS for $C_8H_{14}O_2{}^{28}Si$: calcd 170.0763, found 170.0758.

Anal. calcd for $C_8H_{14}O_2Si$: C 56.43, H 8.29; found: C 56.37, H 8.20.

*c) 5-Trimethylsilylpent-4-ynoyl Chloride (**164**)*

Following general procedure 4, to 5-trimethylsilylpent-4-ynoic acid (**163**) (150 mg, 0.88 mmol, 1 equiv) was added $SOCl_2$ (0.84 g, 7.1 mmol, 8.0 equiv). The mixture was heated at reflux for 0.75 h. The crude oil obtained was distilled (80–85 °C/11 Torr) to afford 161 mg (97%) of 5-trimethylsilylpent-4-ynoyl chloride (**164**) as a clear colorless oil.

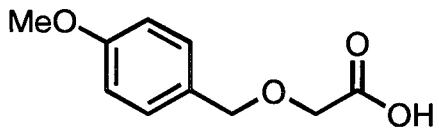
^{1}H NMR (400 MHz, $CDCl_3$): δ 3.09 (t, 2H, J = 7.2 Hz), 2.58 (t, 2H, J = 7.2 Hz), 0.13 (s, 9H, $-Si(CH_3)_3$).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 172.1 (-COCl), 102.6 ($-C\equiv\underline{C}Si(CH_3)_3$), 86.8 ($-\underline{C}\equiv CSi(CH_3)_3$), 45.8 ($-\underline{C}H_2COCl$), 16.0 ($-\underline{C}H_2C\equiv C-$), –0.1 ($-Si(CH_3)_3$).

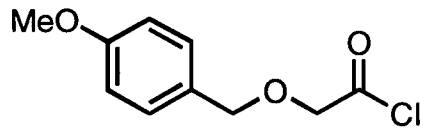
IR (film): 2182, 1801, 1252, 844, 761 cm^{-1}.

LRMS for $C_7H_{10}{}^{35}ClO^{28}Si$ $(M - CH_3)^+$: calcd 173, found 173.

3.3.1.2 SYNTHESIS OF ((4-METHOXYBENZYL)OXY)ACETIC ACID (**166**) AND ((4-METHOXY-BENZYL)OXY)ACETYL CHLORIDE (**167**)



166



167

*a) ((4-Methoxybenzyl)oxy)acetic Acid (**166**)*[85]

To stirred neat (4-methoxyphenyl)methanol (**165**) (78.7 g, 570 mmol, 6.30 equiv) at rt was added, portionwise, NaH (dry powder 98%, 4.56 g, 190 mmol, 2.10 equiv) over 1 h. The resulting thick slurry was heated at 60 °C and stirred for 3 h. Ethyl bromoacetate (15.1 g, 90.4 mmol, 1 equiv) was added dropwise over 10 min. The mixture was stirred at 60 °C for an additional 2 h. After the solution had been cooled, methanol (30 mL), water (20 mL) and KOH (5.58 g, 99.5 mmol, 1.10 equiv) were added. The reaction mixture was heated at 60 °C and stirred overnight (this reaction was not performed under an atmosphere of argon). After the solution had been cooled, water (200 mL) and diethyl ether (100 mL) were added. The layers were separated and the aqueous portion was extracted with diethyl ether (8 × 100 mL). The aqueous layer was acidified with concentrated hydrochloric acid (25 mL) and was extracted with diethyl ether (100 mL). The aqueous layer was saturated with NaCl, and then was extracted with diethyl ether (2 × 200 mL). The combined organic extracts were washed with brine (50 mL), were dried over anhydrous magnesium sulfate, and then were filtered and concentrated under reduced pressure. The crude solid (16.1 g) thus obtained was dissolved in

2:1 benzene–petroleum ether (160 mL total) at rt and was stored in the refrigerator for 48 h to allow crystallization. The crystals were collected by suction filtration and washed with ice-cold pentane (3 × 30 mL) to afford 10.5 g (59%) of ((4-methoxybenzyl)oxy)acetic acid (**166**) as a colorless solid (mp 52.5–53.5 °C, lit. mp 49–52 °C[125]).

^{1}H NMR (400 MHz, $CDCl_3$): δ 10.00–8.50 (br s, 1H, -CO_2H), 7.26 (d, 2H, J = 8.6 Hz), 6.88 (d, 2H, J = 8.6 Hz), 4.56 (s, 2H), 4.09 (s, 2H), 3.79 (s, 3H, -OCH_3).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 175.5 (-CO_2H), 159.5, 129.8, 128.5, 113.9, 73.0 (-$\underline{C}H_2OCH_2CO$-), 66.1 (-$CH_2O\underline{C}H_2CO$-), 55.2 (-OCH_3).

IR (KBr pellet): 3600–2500, 1727, 1614, 1584, 1253, 1178, 1097, 1028, 819 cm^{-1}.

HRMS for $C_{10}H_{12}O_4$: calcd 196.0736, found 196.0739.

Anal. calcd for $C_{10}H_{12}O_4$: C 61.22, H 6.16; found: C 61.16, H 6.10.

*b) ((4-Methoxybenzyl)oxy)acetyl Chloride (**167**)*

To a stirred solution of ((4-methoxybenzyl)oxy)acetic acid (**166**) (1.84 g, 9.38 mmol, 1 equiv) in absolute ethanol (38 mL) at rt was added a solution of KOH[86] (2.69 M in ethanol, 3.49 mL, 9.38 mmol, 1 equiv; this reaction was not performed under an atmosphere of argon). The thick slurry was stirred at rt for 20 min, then the solvent was removed under reduced pressure. The solid obtained was triturated in acetone (40 mL), and the solvent was removed under reduced pressure. The residual solid was suspended in dry diethyl ether (27 mL; under an atmosphere of argon) and was cooled to 0 °C. Dry *N,N*-dimethylformamide (2 drops) and oxalyl chloride (3.57 g, 28.1 mmol, 3.00 equiv) were sequentially added. The heterogeneous mixture was stirred at 0 °C for 2 h, then was filtered through a dry sintered glass funnel under

an atmosphere of argon. The solvent was removed from the filtrate via distillation under reduced pressure at rt, and the crude oil thus obtained was distilled (92–96 °C/0.02 Torr) to afford 1.85 g (92%) of ((4-methoxybenzyl)oxy)acetyl chloride (**167**)[126] as a clear colorless oil. This compound was either used immediately or kept overnight in a freezer (–25 °C) under an argon atmosphere and used the following day. Storage of this compound at rt, even for a few hours resulted in decomposition of the material.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26 (d, 2H, J = 8.8 Hz), 6.88 (d, 2H, J = 8.8 Hz), 4.58 (s, 2H), 4.37 (s, 2H), 3.80 (s, 3H, -OCH_3).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 171.9 (-CO-), 159.6, 129.8, 128.0, 113.9, 74.4 (-$CH_2O\underline{C}H_2CO$-), 73.0 (-$\underline{C}H_2OCH_2CO$-), 55.1 (-OCH_3).

IR (film): 1801, 1614, 1515, 1251, 1127, 1034, 937, 746 cm^{-1}.

LRMS for $C_{10}H_{11}{}^{35}ClO_3$: calcd 214, found 214.

3.3.2 SYNTHESIS OF ACYLTRIMETHYLGERMANES FROM ACYL CHLORIDES

3.3.2.1 SYNTHESIS OF TRIMETHYLGERMYLLITHIUM (**149**)

3.3.2.1.1 Preparation of the Trimethylgermyllithium Reagent (**149**)

Me_3GeLi
149

To cold (–10 °C) dry THF (0.6 mL) was added Me_3GeH (**53**) (202 mg, 1.70 mmol, 1.20 equiv to give an ≈2.5 M solution of Me_3GeH in THF) via a precooled syringe (cooled by running cold water on the barrel). A solution of *t*-BuLi (1.69 M in pentane, 837 μL, 1.41 mmol, 1 equiv) was added via a syringe, and the resulting yellow solution was stirred at –10 °C for 5 min to afford a clear colorless solution. The solution of Me_3GeLi (**149**) thus obtained was used immediately. For a large scale preparation of Me_3GeLi (**149**) see section 3.3.2.4, p 247.

3.3.2.1.2 Treatment of Trimethylgermyllithium with 1-Bromodecane: Synthesis of 1-Trimethylgermyldecane (**172**)

172

A cold (–10 °C) stirred solution of Me_3GeLi (**149**) (1.25 mmol, 1.25 equiv) in dry THF (0.5 mL), prepared as described above (section 3.3.2.1.1, p 221), was diluted with dry THF (2 mL) and the solution was cooled to –78 °C. 1-Bromodecane (221 mg, 1.00 mmol, 1 equiv, freshly distilled from CaH_2) was added via a syringe. The reaction mixture was stirred

at –78 °C for 5 min, then was warmed to rt and was allowed to stir for an additional 15 min. The mixture was diluted with diethyl ether (15 mL), then water (0.5 mL) was added and the layers were separated. The organic extract was washed with brine (2 mL), was dried over anhydrous magnesium sulfate, and then was filtered and concentrated under reduced pressure. The crude oil thus obtained was distilled (48–54 °C/0.06 Torr) to afford 241 mg (93%) of the title compound as a clear colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.40–1.18 (br s, 16H), 0.86 (br t, 3H, J = 6.8 Hz, -$CH_2C\underline{H}_3$), 0.67 (br dd, 2H, J = 8.2 and 7.8 Hz, -$C\underline{H}_2Ge(CH_3)_3$), 0.07 (s, 9H, -$Ge(CH_3)_3$).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 33.3, 32.0, 29.72, 29.68, 29.43, 29.40, 25.1, 22.7, 16.9, 14.2 (-$CH_2\underline{C}H_3$), –2.3 (-$Ge(CH_3)_3$).

IR (film): 2925, 823, 598 cm^{-1}.

HRMS (DCI, NH_3 + CH_4) for $C_{12}H_{27}{}^{74}Ge$ $(M - CH_3)^+$: calcd 245.1325, found 245.1328.

Anal. calcd for $C_{13}H_{30}Ge$: C 60.29, H 11.68; found: C 60.47, H 11.65.

3.3.2.1.3 Determination of the Yield of Trimethylgermyllithium (**149**) Formation from Trimethylgermane (**53**) via the Internal Standard Method

A cold (–10 °C) stirred solution of Me_3GeLi (**149**) (1.25 mmol, 1 equiv) in dry THF (0.5 mL), prepared as described above (section 3.3.2.1.1, p 221), was diluted with THF (2 mL) and the solution was cooled to –78 °C. 1-Bromodecane (323 mg, 1.50 mmol, 1.20 equiv, freshly distilled from CaH_2) was added via a syringe. The reaction mixture was stirred at –78 °C for 15 min, then was warmed to rt and was allowed to stir for an additional 45 min. The internal standard *n*-tridecane (191.5 ± 1.2 mg) was added via a syringe calibrated by

delivering 250 μL of tridecane multiple times. The mixture was treated with water (1 mL) and diethyl ether (1 mL) was added. The GLC was calibrated using a mixture prepared as follows: 64 mg of *n*-tridecane and 107 mg of 1-trimethylgermyldecane (**172**). An aliquot of the reaction mixture was injected and it was determined that 1-trimethylgermyldecane (**172**) had been formed in >97% yield.

3.3.2.2 PREPARATION OF (TRIMETHYLGERMYL)COPPER(I)–DIMETHYL SULFIDE (**168**)

$Me_3GeCu{\bullet}Me_2S$
168

*a) Via Addition of the Solution of Me_3GeLi (**149**) to a Suspension of $CuBr{\bullet}Me_2S$ in THF ("Normal" Addition Method)*

A cold (–10 °C) stirred solution of Me_3GeLi (**149**) (1.41 mmol, 1 equiv) in dry THF (0.6 mL), prepared as described above (section 3.3.2.1.1, p 221), was transferred via a cannula to a cold (–78 °C) stirred suspension of $CuBr{\bullet}Me_2S$ (290 mg, 1.41 mmol, 1 equiv) in dry THF (6 mL). The flask that initially contained the Me_3GeLi (**149**) was rinsed with dry THF (2 × 0.5 mL) and the rinses were transferred via a cannula to the suspension of $CuBr{\bullet}Me_2S$. The suspension was stirred at –78 °C for 1 h to afford a dark red–black solution of the title reagent (≈0.18 M). The reagent **168** was then ready to use. For a large scale preparation of $Me_3GeCu{\bullet}Me_2S$ (**168**) using this procedure see section 3.3.2.4, p 247.

*b) Via Addition of Solid $CuBr{\bullet}Me_2S$ to the Solution of Me_3GeLi (**149**) in THF ("Inverse" Addition Method)*

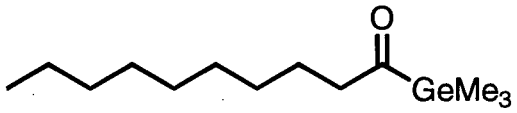
A cold (–10 °C) stirred solution of Me_3GeLi (**149**) (4.40 mmol, 1 equiv) in dry THF (1.8 mL), prepared as described above (section 3.3.2.1.1, p 221), was diluted with dry THF

(23 mL) and the solution was cooled to –78 °C. After the solution had been stirred for 10 min, solid $CuBr{\bullet}Me_2S$ (905 mg, 4.40 mmol, 1 equiv) was added in one portion. The suspension was stirred at –78 °C for 1 h to afford a dark red–black solution of the title reagent (≈0.18 M). The reagent **168** was then ready to use.

3.3.2.3 General Procedure 5: Preparation of the Acyltrimethylgermanes from Acyl Chlorides

To a cold (–78 °C) stirred solution of $Me_3GeCu{\bullet}Me_2S$ (**168**) (1.0–3.0 equiv) in dry THF (≈0.18 M), prepared as described above (section 3.3.2.2, p 223), was added a solution of the appropriate acyl chloride (1 equiv) in dry THF, via a cannula, to generate a final concentration of ≈0.1 M of the acyl chloride. The reaction mixture was stirred at –78 °C for 1 h, was then warmed to –30 °C and was allowed to stir for an additional 2 h. The black mixture was poured into a stirred aqueous NH_4Cl–NH_4OH solution (pH 8–9, ≈15 mL per mmol of acyl chloride) and diethyl ether (≈30 mL per mmol of acyl chloride) was added. The two-phase system was stirred vigorously open to the atmosphere until the aqueous layer was deep blue. The layers were separated and the aqueous portion was extracted with diethyl ether (2 × ≈10 mL per mmol of acyl chloride). The combined organic extracts were washed with water (2 × ≈10 mL per mmol of acyl chloride) and brine (≈10 mL per mmol of acyl chloride), were dried over anhydrous magnesium sulfate, and then were filtered and concentrated under reduced pressure. The crude oil thus acquired was subjected to flash chromatography and the acquired oil was distilled to provide the desired acyltrimethylgermane.

3.3.2.3.1 Synthesis of Decanoyltrimethylgermane (**170**)



170

a) With Chlorotrimethylsilane as Additive

Following general procedure 5, to a cold (–78 °C) stirred solution of $Me_3GeCu{\bullet}Me_2S$ (**168**) (1.47 mmol, 1.50 equiv) in dry THF (8.5 mL total), prepared via the "normal" addition method (section 3.3.2.2(a), p 223), was added chlorotrimethylsilane (107 mg, 0.98 mmol, 1 equiv) via a syringe. After the mixture had been stirred for 5 min at –78 °C, a solution of decanoyl chloride (**157**) (187 mg, 0.98 mmol, 1 equiv) in dry THF (2 mL) was added via a cannula. The oil acquired was subjected to flash chromatography (30 g TLC grade silica gel, 24:1 petroleum ether–diethyl ether) and the derived oil was distilled (86–94 °C/0.04 Torr) to afford 247 mg (92%) of the title compound as a light yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.58 (t, 2H, J = 7.4 Hz, -CH_2CO-), 1.57–1.45 (m, 2H), 1.39–1.18 (m, 12H), 0.85 (br t, 3H, J = 6.8 Hz, -$CH_2C\underline{H}_3$), 0.31 (s, 9H, -$Ge(CH_3)_3$).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 245.9 (-CO-), 49.7 (-$\underline{C}H_2$CO-), 31.9, 29.5, 29.4, 29.30, 29.27, 22.7, 22.3, 14.1 (-$CH_2\underline{C}H_3$), –2.9 (-$Ge(CH_3)_3$).

IR (film): 1658, 1466, 1237, 829, 603 cm^{-1}.

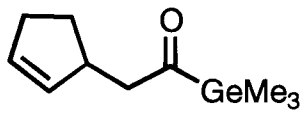
HRMS for $C_{13}H_{28}{}^{74}GeO$: calcd 274.1352, found 274.1354.

Anal. calcd for $C_{13}H_{28}GeO$: C 57.20, H 10.34; found: C 56.90, H 10.45.

b) Without Additive

Following general procedure 5, to a cold (–78 °C) stirred solution of $Me_3GeCu{\bullet}Me_2S$ (**168**) (1.59 mmol, 1.50 equiv) in dry THF (8.7 mL total), prepared via the "normal" addition method (section 3.3.2.2(a), p 223), was added a solution of decanoyl chloride (**157**) (202 mg, 1.06 mmol, 1 equiv) in dry THF (2 mL) via a cannula. The oil acquired was subjected to flash chromatography (25 g TLC grade silica gel, 24:1 petroleum ether–diethyl ether) and the acquired oil was distilled to afford 234 mg (81%) of the title compound as a light yellow oil. The spectral data were identical with those reported above.

3.3.2.3.2 Synthesis of (Cyclopent-2-en-1-yl)acetyltrimethylgermane (**178**)



178

Following general procedure 5, to a cold (–78 °C) stirred solution of $Me_3GeCu{\bullet}Me_2S$ (**168**) (1.69 mmol, 1.50 equiv) in dry THF (9.2 mL total), prepared via the "normal" addition method (section 3.3.2.2(a), p 223), was added chlorotrimethylsilane (122 mg, 1.13 mmol, 1 equiv) via a syringe. After the mixture had been stirred for 5 min, a solution of (cyclopent-2-en-1-yl)acetyl chloride (**158**) (163 mg, 1.13 mmol, 1 equiv) in dry THF (2 mL) was added via a cannula. The oil acquired was subjected to flash chromatography (35 g TLC grade silica gel, 24:1 petroleum ether–diethyl ether) and the derived oil was distilled (120–130 °C/12 Torr) to afford 225 mg (88%) of the title compound as a light yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.73–5.68 (m, 1H, vinylic proton), 5.60–5.56 (m, 1H, vinylic proton), 3.16–3.06 (m, 1H, allylic methine proton), 2.71 (dd, 1H, J = 16.7 and 6.4

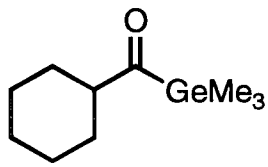
Hz, -C$\underline{H}_a$H$_b$CO-), 2.62 (dd, 1H, J = 16.7 and 7.9 Hz, -CH$_a$$\underline{H}_b$CO-), 2.36–2.20 (m, 2H), 2.07 (dtd, 1H, J = 12.9, 8.4 and 5.4 Hz), 1.34–1.24 (m, 1H), 0.31 (s, 9H, -Ge(CH$_3$)$_3$).

^{13}C NMR (75.4 MHz, CDCl$_3$): δ 245.4 (-CO-), 134.1 (vinylic carbon), 130.9 (vinylic carbon), 55.7 (-$\underline{C}$H$_2$CO-), 39.5 (allylic methine carbon), 31.7, 29.9, –3.0 (-Ge(CH$_3$)$_3$).

IR (film): 3053, 2910, 1657, 1238, 830, 605 cm^{-1}.

HRMS for C$_{10}$H$_{18}$^{74}GeO: calcd 228.0569, found 228.0570.

3.3.2.3.3 Synthesis of (Cyclohexanecarbonyl)trimethylgermane (**179**)



179

Following general procedure 5, to a cold (–78 °C) stirred solution of Me$_3$GeCu•Me$_2$S (**168**) (2.10 mmol, 1.50 equiv) in dry THF (11.9 mL total), prepared via the "normal" addition method (section 3.3.2.2(a), p 223), was added chlorotrimethylsilane (153 mg, 1.40 mmol, 1 equiv). After the solution had been stirred for 5 min at –78 °C, a solution of cyclohexane-carbonyl chloride (**174**) (206 mg, 1.40 mmol, 1 equiv) in dry THF (2 mL) was added via a cannula. The oil acquired was subjected to flash chromatography (40 g TLC grade silica gel, 24:1 petroleum ether–diethyl ether) and the derived oil was distilled (120–130 °C/10 Torr) to afford 282 mg (88%) of the title compound as a light yellow oil.

^{1}H NMR (400 MHz, CDCl$_3$): δ 2.63–2.54 (m, 1H, -C$\underline{H}$(COGe(CH$_3$)$_3$)-), 1.85–1.58 (m, 5H), 1.34–1.10 (m, 5H), 0.31 (s, 9H, -Ge(CH$_3$)$_3$).

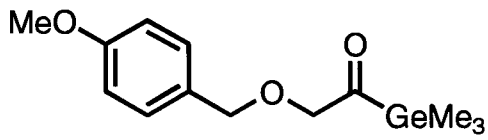
^{13}C NMR (75.4 MHz, $CDCl_3$): δ 247.2 (-CO-), 56.5 (-<u>C</u>HCO-), 26.5, 26.0, 25.5, –2.2 (-Ge(CH_3)$_3$).

IR (film): 1654, 1450, 1236, 1137, 830, 604 cm^{-1}.

HRMS for $C_{10}H_{20}{}^{74}GeO$: calcd 230.0726, found 230.0732.

Anal. calcd for $C_{10}H_{20}GeO$: C 52.48, H 8.81; found: C 52.64, H 8.98.

3.3.2.3.4 Synthesis of ((4-Methoxybenzyl)oxy)acetyltrimethylgermane (**180**)



180

Following general procedure 5, to a cold (–78 °C) stirred solution of $Me_3GeCu{\bullet}Me_2S$ (**168**) (1.60 mmol, 1.50 equiv) in dry THF (9.2 mL total), prepared via the "normal" addition method (section 3.3.2.2(a), p 223), was added chlorotrimethylsilane (116 mg, 1.07 mmol, 1 equiv) via a syringe. After the mixture had been stirred for 5 min, a solution of ((4-methoxybenzyl)oxy)acetyl chloride (**167**) (229 mg, 1.07 mmol, 1 equiv) in dry THF (1.5 mL) was added via a cannula. The oil acquired was subjected to flash chromatography (30 g TLC grade silica gel, 17:3 petroleum ether–diethyl ether) and the derived oil was distilled (120–130 °C/0.06 Torr) to afford 259 mg (82%) of the title compound as a light yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25 (d, 2H, J = 8.6 Hz, aromatic protons), 6.87 (d, 2H, J = 8.6 Hz, aromatic protons), 4.50 (s, 2H), 4.00 (s, 2H), 3.79 (s, 3H, -OCH_3), 0.32 (s, 9H, -Ge(CH_3)$_3$).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 244.8 (-CO-), 159.3, 129.4, 129.3, 113.7, 80.7

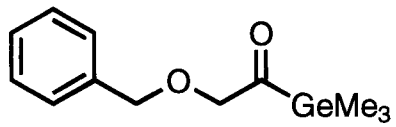
(-$CH_2O\underline{C}H_2CO$-), 73.0 (-$\underline{C}H_2OCH_2CO$-), 55.1 (-OCH_3), –2.7 (-$Ge(CH_3)_3$).

IR (film): 1667, 1614, 1515, 1303, 1250, 1175, 1117, 1036, 830, 607 cm^{-1}.

HRMS for $C_{13}H_{20}{}^{74}GeO_3$: calcd 298.0624, found 298.0628.

Anal. calcd for $C_{13}H_{20}GeO_3$: C 52.59, H 6.79; found: C 52.47, H 6.56.

3.3.2.3.5 Synthesis of (Benzyloxy)acetyltrimethylgermane (**181**)



181

a) With Chlorotrimethylsilane as Additive

Following general procedure 5, to a cold (–78 °C) stirred solution of $Me_3GeCu{\bullet}Me_2S$ (**168**) (1.42 mmol, 1.50 equiv) in dry THF (8.1 mL total), prepared via the "normal" addition method (section 3.3.2.2(a), p 223), was added chlorotrimethylsilane (103 mg, 0.94 mmol, 1 equiv) via a syringe. After the mixture had been stirred at –78 °C for 5 min, a solution of benzyloxyacetyl chloride (**175**) (174 mg, 0.94 mmol, 1 equiv) in dry THF (1.5 mL) was added via a cannula. The oil acquired was subjected to flash chromatography (26 g TLC grade silica gel, 9:1 petroleum ether–diethyl ether) and the oil derived was distilled (130–140 °C/0.05 Torr) to afford 224 mg (89%) of the title compound as a light yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33 (br s, 5H, aromatic protons), 4.56 (s, 2H), 4.03 (s, 2H), 0.34 (s, 9H, -$Ge(CH_3)_3$).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 244.8 (-CO-), 137.2 (aromatic *ipso* carbon), 128.4, 127.81, 127.75, 81.1 (-$CH_2O\underline{C}H_2CO$-), 73.4 (-$\underline{C}H_2OCH_2CO$-), –2.6 (-$Ge(CH_3)_3$).

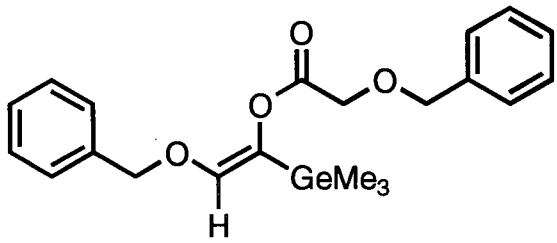
IR (film): 3033, 2911, 1668, 1455, 1236, 1123, 833, 739, 699, 606 cm^{-1}.

HRMS for $C_{11}H_{15}{}^{74}GeO_2$ $(M - CH_3)^+$: calcd 253.0284, found 253.0283.

Anal. calcd for $C_{12}H_{18}GeO_2$: C 54.01, H 6.80; found: C 54.13, H 6.82.

b) Without Additive

Following general procedure 5, to a cold (–78 °C) stirred solution of $Me_3GeCu{\bullet}Me_2S$ (**168**) (4.40 mmol, 2.20 equiv) in dry THF (26.8 mL total), prepared via the "inverse" addition method (section 3.3.2.2(b), p 223), was added benzyloxyacetyl chloride (**175**) (369 mg, 2.00 mmol, 1 equiv) via a syringe. The reaction mixture was stirred at –78 °C for 1.5 h, then was treated with aqueous NH_4Cl–NH_4OH (pH 8–9, 6 mL) and diethyl ether (10 mL) was added to the mixture. The cooling bath was removed and the mixture was stirred vigorously at rt, open to the atmosphere, until the aqueous layer was deep blue. The crude oil obtained was subjected to flash chromatography (50 g TLC grade silica gel, 9:1 then 3:1 petroleum ether–diethyl ether) to afford four fractions which were concentrated under reduced pressure. The first fraction to be eluted afforded 337 mg (63%) of (benzyloxy)acetyltrimethylgermane (**181**). The spectral data were identical with those reported above. The second fraction to be eluted afforded 8.9 mg of an unidentified compound. The third fraction to be eluted afforded 22 mg (2.6%) of (*E*)-2-benzyloxy-1-(benzyloxy)acetoxy-1-trimethylgermylethene (**186**). An analytically pure sample of this compound was obtained by resubjecting this material to flash chromatography (5 g TLC grade silica gel, 17:3 petroleum ether–diethyl ether).



186

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52–7.23 (m, 10H, aromatic protons), 5.87 (s, 1H, -C<u>H</u>=C(Ge(CH_3)$_3$)-), 4.84 (s, 2H, -C<u>H</u>$_2$OCH=C(Ge(CH_3)$_3$)-), 4.62 (s, 2H, -C<u>H</u>$_2$OCH$_2$CO-), 4.19 (s, 2H, -CH$_2$CO-), 0.27 (s, 9H, -Ge(CH_3)$_3$).

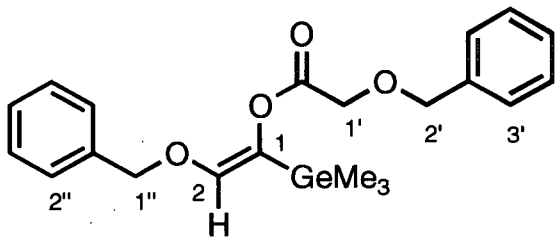
Additional ^{1}H NMR data, derived from NOE difference experiments, are given in **Table 21**.

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 168.4 (-CO-) 142.0 (-<u>C</u>H=C(Ge(CH_3)$_3$)-), 137.1, 136.7, 134.2, 128.5, 128.4, 128.14, 128.08, 127.9, 127.4, 74.4, 73.1, 66.8, –1.4 (-Ge(CH_3)$_3$).

IR (film): 3032, 2909, 1760, 1647, 1238, 1202, 1117, 830, 738, 698, 606 cm^{-1}.

HRMS for $C_{21}H_{26}{}^{74}GeO_4$: calcd 416.1043, found 416.1043.

Table 21: ^{1}H NMR Data from Nuclear Overhauser Enhancement Difference Experiments for (*E*)-2-Benzyloxy-1-(benzyloxy)acetoxy-1-trimethylgermylethene (**186**)



186

Assignments H-x	^{1}H NMR[a] δ ppm (mult, *J* (Hz))	Observed NOEs
Aromatic	7.52–7.23 (m)	
H-2[b]	5.87 (s)	H-1", -Ge(CH$_3$)$_3$
H-1"[b]	4.84 (s)	H-2, H-2"
H-2'[b]	4.62 (s)	H-1', H-3'
H-1'[b]	4.19 (s)	H-2'
-Ge(CH$_3$)$_3$[b]	0.27 (s)	H-2

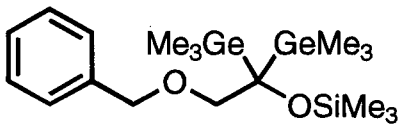
[a] 400 MHz, $CDCl_3$. [b] Irradiation of this signal generated the corresponding NOEs in the right hand column.

The fourth fraction to be eluted afforded 4.2 mg of an unidentified compound.

c) With Bromotrimethylsilane as Additive

Following general procedure 5, to a cold (–78 °C) stirred solution of $Me_3GeCu{\bullet}Me_2S$ (**168**) (2.40 mmol, 2.20 equiv) in dry THF (14 mL total), prepared via the "inverse" addition method (section 3.3.2.2(b), p 223), was added a solution of bromotrimethylsilane (659 mg, 4.30 mmol, 3.93 equiv, freshly distilled from CaH_2) in THF (1 mL) via a cannula. After the mixture had been stirred for 5 min, a solution of (benzyloxy)acetyl chloride (**175**) (202 mg,

1.09 mmol, 1 equiv) in dry THF (1 mL) was added via a cannula. The reaction mixture was stirred at –78 °C for 2.5 h, then was treated with aqueous NH_4Cl–NH_4OH (pH 8–9, 7 mL) and diethyl ether (10 mL) was added to the mixture. The cooling bath was removed and the heterogeneous mixture was vigorously stirred, open to the atmosphere, until the aqueous layer was deep blue. The crude oil obtained was subjected to flash chromatography (16 g TLC grade silica gel, 19:1 petroleum ether–diethyl ether) to afford four fractions which were concentrated under reduced pressure. The first fraction to be eluted afforded 262 mg (52%) of 2-benzyloxy-1-trimethylsilyloxy-1,1-bis(trimethylgermyl)ethane (**188**).



188

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45–7.35 (m, 5H, aromatic protons), 4.43 (s, 2H), 3.77 (s, 2H), 0.15 (s, 18H, 2 × -$Ge(CH_3)_3$), 0.07 (s, 9H, -$Si(CH_3)_3$).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 138.3 (aromatic *ipso* carbon), 128.2, 127.9, 127.4, 76.9 ($C_6H_5CH_2O\underline{C}H_2$-), 74.3 (-$\underline{C}(Ge(CH_3)_3)_2OSi(CH_3)_3$-), 73.0 ($C_6H_5\underline{C}H_2$-), 2.6 (-$Si(CH_3)_3$), –1.6 (-$Ge(CH_3)_3$).

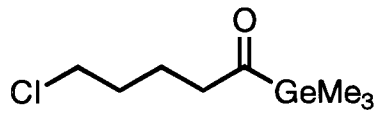
IR (film): 1498, 1455, 1402, 1351, 1248, 1111, 1065, 976, 838, 599 cm^{-1}.

HRMS for $C_{17}H_{33}{}^{72}Ge^{74}GeO_2{}^{28}Si$ $(M - CH_3)^+$: calcd 443.0682, found 443.0686.

Anal. calcd for $C_{18}H_{36}Ge_2O_2Si$: C 47.23, H 7.93; found: C 47.19, H 7.71.

The following three fractions to be eluted afforded only trace amounts of unidentified compounds.

3.3.2.3.6 Synthesis of 5-Chloropentanoyltrimethylgermane (**182**)



182

Following general procedure 5, to a cold (–78 °C) stirred solution of $Me_3GeCu{\bullet}Me_2S$ (**168**) (1.81 mmol, 1.50 equiv) in dry THF (9.8 mL total), prepared via the "normal" addition method (section 3.3.2.2(a), p 223), was added chlorotrimethylsilane (131 mg, 1.21 mmol, 1 equiv) via a syringe. After the mixture had been stirred for 5 min, a solution of 5-chloropentanoyl chloride (**176**) (186 mg, 1.21 mmol, 1 equiv) in dry THF (2 mL) was added via a cannula. The crude oil acquired was subjected to flash chromatography (20 g TLC grade silica gel, 19:1 petroleum ether–diethyl ether) and the resultant oil was distilled (145–155 °C/15 Torr) to afford 256 mg (90%) of the title compound as a light yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.49 (t, 2H, J = 6.4 Hz, -CH_2Cl), 2.64 (t, 2H, J = 7.0 Hz, -CH_2CO-), 1.78–1.62 (m, 4H), 0.32 (s, 9H, -$Ge(CH_3)_3$).

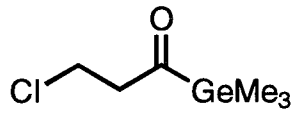
^{13}C NMR (75.4 MHz, $CDCl_3$): δ 244.9 (-CO-), 48.4, 44.6, 31.9, 19.5, –3.0 (-$Ge(CH_3)_3$).

IR (film): 1657, 1238, 830, 605 cm^{-1}.

HRMS for $C_8H_{17}{}^{35}Cl^{74}GeO$: calcd 238.0180, found 238.0179.

Anal. calcd for $C_8H_{17}ClGeO$: C 40.50, H 7.22; found: C 40.80, H 7.40.

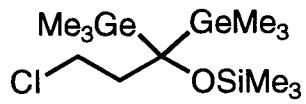
3.3.2.3.7 Synthesis of 3-Chloropropanoyltrimethylgermane (**183**)



183

a) With Bromotrimethylsilane as Additive

Following general procedure 5, to a cold (–78 °C) stirred solution of $Me_3GeCu{\bullet}Me_2S$ (**168**) (4.70 mmol, 2.20 equiv) in dry THF (26.5 mL total), prepared via the "inverse" addition method (section 3.3.2.2(b), p 223), was added a solution of bromotrimethylsilane (815 mg, 5.32 mmol, 2.50 equiv) in dry THF (3 mL) via a cannula. After the mixture had been stirred for 5 min, a solution of 3-chloropropanoyl chloride (**177**) (271 mg, 2.13 mmol, 1 equiv) in dry THF (2 mL) was added via a cannula. The reaction mixture was stirred at –78 °C for 2.25 h, then was treated with aqueous NH_4Cl–NH_4OH (pH 8–9, 8 mL) and diethyl ether (10 mL) was added to the mixture. The cooling bath was removed and the heterogeneous mixture was stirred vigorously, open to the atmosphere, until the aqueous layer was deep blue. The combined dried organic extracts were concentrated via distillation of the solvent at atmospheric pressure. The crude oil obtained was subjected to flash chromatography (50 g TLC grade silica gel, 24:1 petroleum ether–diethyl ether) to afford two fractions which were concentrated via distillation of the solvent at atmospheric pressure. The first fraction to be eluted afforded 65 mg of an oil as a mixture of compounds. ^{1}H NMR spectroscopic and GLC analysis suggested that this material was mainly composed (≈75%) of 3-chloro-1,1-bis-(trimethylgermyl)-1-(trimethylsilyloxy)propane (**193**).



193

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.55–3.48 (m, 2H, -CH_2Cl), 2.40–2.32 (m, 2H, -C<u>H</u>$_2$CH$_2$Cl), 0.20 (s, 18H, 2 × -Ge(CH_3)$_3$), 0.12 (s, 9H, -Si(CH_3)$_3$).

The second compound to be eluted was distilled. A forerun was collected in a first bulb (distillation temperature 20–40 °C/9 Torr) to afford 31 mg of volatile material (by GLC analysis). The remainder of the oil was collected in a second bulb (distillation temperature 105–115 °C/9 Torr) to afford 261 mg (58%) of 3-chloropropanoyltrimethylgermane (**183**) as a light yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.69 (t, 2H, J = 6.8 Hz, -CH_2Cl), 3.09 (t, 2H, J = 6.8 Hz, -CH_2CO-), 0.34 (s, 9H, -Ge(CH_3)$_3$).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 242.5 (-CO-), 51.1 (-CH_2Cl), 37.4 (-<u>C</u>H$_2$CO-), –3.3 (-Ge(CH_3)$_3$).

IR (film): 1661, 1326, 1239, 832, 668, 606 cm^{-1}.

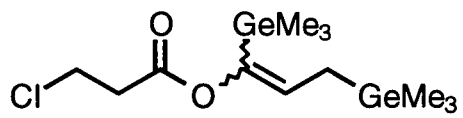
HRMS for $C_6H_{13}{}^{35}Cl^{74}GeO$: calcd 209.9867, found 209.9872.

Anal. calcd for $C_6H_{13}ClGeO$: C 34.45, H 6.26; found: C 34.46, H 6.36.

b) Without Additive

Following general procedure 5, to a cold (–78 °C) stirred solution of $Me_3GeCu{\bullet}Me_2S$ (**168**) (2.59 mmol, 1.50 equiv) in dry THF (14.1 mL total), prepared via the "inverse" addition method (section 3.3.2.2(b), p 223), was added a solution of 3-chloropropanoyl chloride (**177**) (220 mg, 1.73 mmol, 1 equiv) in dry THF (3 mL) via a cannula. The reaction mixture was

stirred at –78 °C for 3 h, then was treated with aqueous NH_4Cl–NH_4OH (pH 8–9, 8 mL) and diethyl ether (10 mL) was added to the mixture. The cooling bath was removed and the heterogeneous mixture was stirred vigorously, open to the atmosphere, until the aqueous layer was deep blue. The crude oil obtained was subjected to flash chromatography (29 g TLC grade silica gel, 32:1 petroleum ether–diethyl ether) to afford two fractions which were concentrated under reduced pressure. The first fraction to be eluted afforded 34 mg of a mixture of two compounds. An analytically pure sample of each compound was obtained by HPLC separation (vide infra). The second fraction to be eluted afforded 82 mg (23%) of 3-chloropropanoyltrimethylgermane (**183**). The spectral data were identical with those reported above. The mixture of two compounds (fraction one) was subjected to reversed phase HPLC (C_{18} μBondapak 10 μm, 25 mm × 100 mm column; 3:2 acetonitrile–water, 10 mL/min, UV-vis detector λ = 254 nm) to give two fractions which were concentrated under reduced pressure. The first fraction to be eluted, retention time 53 min, afforded 3.5 mg of (*E*)- or (*Z*)-1-((3-chloropropanoyl)oxy)-1,3-bis(trimethylgermyl)prop-1-ene (**191**).



191

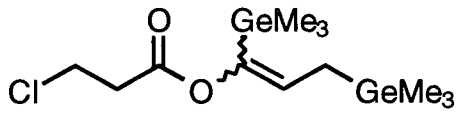
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.80 (t, 1H, J = 9.2 Hz, -C<u>H</u>=C(Ge(CH_3)$_3$)-), 3.75 (t, 2H, J = 6.8 Hz, -CH_2Cl), 2.82 (t, 2H, J = 6.8 Hz, -CH_2CO-), 1.58 (d, 2H, J = 9.2 Hz, -C<u>H</u>$_2$Ge(CH_3)$_3$), 0.30 (s, 9H, -CH=C(Ge(C<u>H</u>$_3$)$_3$)-), 0.16 (s, 9H, -CH_2Ge(C<u>H</u>$_3$)$_3$).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 169.8 (-CO-), 152.7 (-CH=<u>C</u>(Ge(CH_3)$_3$)-), 129.5 (-<u>C</u>H=C(Ge(CH_3)$_3$)-), 39.0, 37.4, 17.2 (-<u>C</u>H_2Ge(CH_3)$_3$), –0.7, –2.3.

IR (film): 1741, 1238, 1146, 827, 603 cm^{-1}.

HRMS for $C_{12}H_{25}{}^{35}Cl^{74}Ge_2O_2$: calcd 383.9967, found 383.9985.

The second fraction to be eluted, retention time 57 min, afforded 7.4 mg of (*Z*)- or (*E*)-1-((3-chloropropanoyl)oxy)-1,3-bis(trimethylgermyl)prop-1-ene (**192**).



192

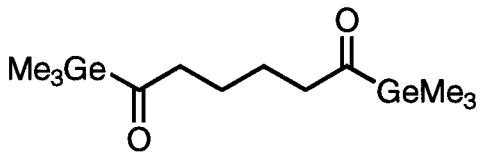
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.34 (t, 1H, J = 8.8 Hz, -C<u>H</u>=C(Ge(CH_3)$_3$)-), 3.77 (t, 2H, J = 6.6 Hz, -CH_2Cl), 2.86 (t, 2H, J = 6.6 Hz, -CH_2CO-), 1.64 (d, 2H, J = 8.8 Hz, -C<u>H</u>$_2$Ge(CH_3)$_3$), 0.25 (s, 9H, -CH=C(Ge(C<u>H</u>$_3$)$_3$)-), 0.13 (s, 9H, -CH_2Ge(C<u>H</u>$_3$)$_3$).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 168.5 (-CO-), 153.1 (-CH=<u>C</u>(Ge(CH_3)$_3$)-), 126.5 (-<u>C</u>H=C(Ge(CH_3)$_3$)-), 39.1, 37.5, 16.4 (-<u>C</u>H$_2$Ge(CH_3)$_3$), –1.0, –2.2.

IR (film): 1742, 1629, 1237, 1148, 825, 602 cm^{-1}.

HRMS for $C_{12}H_{25}{}^{35}Cl^{74}Ge_2O_2$: calcd 383.9967, found 383.9975.

3.3.2.3.8 Synthesis of Hexanedioylbis(trimethylgermane) (**184**)



184

a) With Chlorotrimethylsilane as Additive

Following general procedure 5 (amounts of reagents and solvents were doubled for this substrate), to a cold (–78 °C) stirred solution of $Me_3GeCu{\bullet}Me_2S$ (**168**) (3.53 mmol, 3.00

equiv) in dry THF (21.4 mL total), prepared via the "normal" addition method (section 3.3.2.2(a), p 223), was added chlorotrimethylsilane (256 mg, 2.35 mmol, 2.00 equiv) via a syringe. After the solution had been stirred for 5 min, a solution of adipoyl chloride (**159**) (215 mg, 1.18 mmol, 1 equiv) in dry THF (2 mL) was added via a cannula. The crude oil acquired was subjected to flash chromatography (50 g TLC grade silica gel, 17:3 petroleum ether–diethyl ether) and the derived liquid was distilled (110–120 °C/0.05 Torr) to afford 375 mg (92%) of the title compound as a light yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.69–2.56 (m, 4H, 2 × -CH_2CO-), 1.53–1.44 (m, 4H, 2 × -C$\underline{H}_2$$CH_2$CO-), 0.31 (s, 18H, 2 × -Ge(CH_3)$_3$).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 245.1 (-CO-), 49.2 (-$\underline{C}H_2$CO-), 21.8 (-$\underline{C}H_2CH_2$CO-), –3.0 (-Ge(CH_3)$_3$).

IR (film): 1657, 1237, 830, 604 cm^{-1}.

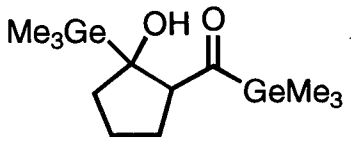
HRMS for $C_{12}H_{26}{}^{74}Ge_2O_2$: calcd 350.0356, found 350.0355.

Anal. calcd for $C_{12}H_{26}Ge_2O_2$: C 41.47, H 7.54; found: C 41.58, H 7.58.

b) Without Additive

Following general procedure 5 (amounts of reagents and solvents were doubled for this substrate), to a cold (–78 °C) stirred solution of $Me_3GeCu{\bullet}Me_2S$ (**168**) (3.45 mmol, 3.00 equiv) in dry THF (18.4 mL total), prepared via the "inverse" addition method (section 3.3.2.2(b), p 223), was added a solution of adipoyl chloride (**159**) (210 mg, 1.15 mmol, 1 equiv) in dry THF (2 mL) via a cannula. The crude oil obtained was subjected to flash chromatography (60 g TLC grade silica gel, 29:20:1 petroleum ether–CH_2Cl_2–diethyl ether)

to afford 229 mg of a mixture of 2 components. The mixture was resubjected to flash chromatography (25 g TLC grade silica gel, 9:1 petroleum ether–diethyl ether) to afford two fractions, which were concentrated under reduced pressure. The first fraction to be eluted was distilled (105–115 °C/0.07 Torr) to afford 25 mg (6%) of 2-hydroxy-2-trimethylgermyl-(cyclopentanecarbonyl)trimethylgermane (**194**) as a light yellow oil.



194

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.92 (br s, 1H, exchanges with D_2O, -OH), 3.11 (dd, 1H, J = 11.0 and 8.6 Hz, -C<u>H</u>(COGe(CH_3)$_3$)-), 2.10–1.95 (m, 2H), 1.85–1.75 (m, 2H), 1.72–1.61 (m, 1H), 1.59–1.52 (m, 1H), 0.34 (s, 9H, -COGe(CH_3)$_3$), 0.10 (s, 9H, -C(OH)Ge(C<u>H</u>$_3$)$_3$-).

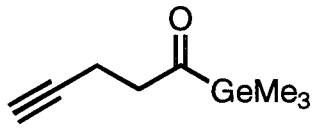
^{13}C NMR (75.4 MHz, $CDCl_3$): δ 254.4 (-CO-), 79.1 (-<u>C</u>(OH)Ge(CH_3)$_3$-), 62.8 (-<u>C</u>H(COGe(CH_3)$_3$)-), 37.7, 26.9, 22.5, –2.8, –3.7.

IR (film): 3464, 2969, 1634, 1358, 1291, 1236, 1031, 826, 602 cm^{-1}.

HRMS for $C_{12}H_{26}{}^{72}Ge^{74}GeO_2$: calcd 348.0365, found 348.0359.

The second fraction to be eluted was distilled to afford 131 mg (33%) of hexanedioyl-bis(trimethylgermane) (**184**). Spectral data were identical with those reported above.

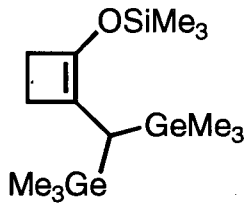
3.3.2.3.9 Attempts at Synthesizing Pent-4-ynoyltrimethylgermane (**185**)



185

a) With Chlorotrimethylsilane as Additive

Following general procedure 5, to a cold (–78 °C) stirred solution of $Me_3GeCu{\bullet}Me_2S$ (**168**) (0.92 mmol, 1.06 equiv) in dry THF (5 mL total), prepared via the "inverse" addition method (section 3.3.2.2(b), p 223), was added chlorotrimethylsilane (99 mg, 0.91 mmol, 1.05 equiv) via a syringe. After the mixture had been stirred for 5 min, a solution of pent-4-ynoyl chloride (**160**) (101 mg, 0.87 mmol, 1 equiv) in dry THF (1 mL) was added via a cannula. The reaction mixture was stirred for 3 h at –78 °C. The crude oil obtained was subjected to flash chromatography (5 g TLC grade silica gel, petroleum ether then ethyl acetate) to afford two fractions which were concentrated under reduced pressure. The first fraction to be eluted was distilled (70–80 °C/0.08 Torr) to afford 34 mg (10%) of 2-(bis(trimethylgermyl)methyl)-1-((trimethylsilyl)oxy)cyclobutene (**197**) as a clear colorless oil.



197

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.47 (t, 2H, J = 3.2 Hz), 1.89 (t, 2H, J = 3.2 Hz), 1.29 (s, 1H, -C<u>H</u>(Ge(CH$_3$)$_3$)$_2$), 0.16 (s, 9H, -Si(CH$_3$)$_3$), 0.15 (s, 18H, 2 × -Ge(CH$_3$)$_3$).

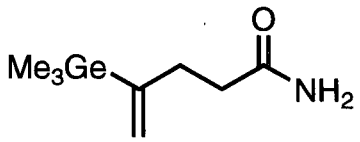
^{13}C NMR (75.4 MHz, $CDCl_3$): δ 137.3 (vinylic carbon), 117.2 (vinylic carbon), 31.7, 24.9,

19.0 (-$\underline{C}$H(Ge(CH$_3$)$_3$)$_2$), 0.7 (-Si(CH$_3$)$_3$), 0.1 (-Ge(CH$_3$)$_3$).

IR (film): 1681, 1296, 1185, 1151, 1026, 924, 884, 845, 598 cm^{-1}.

HRMS for $C_{14}H_{32}{}^{72}Ge^{74}GeO^{28}Si$: calcd 390.0655, found 390.0660.

The second fraction to be eluted afforded 78 mg (42%) of 4-trimethylgermylpent-4-enamide (**198**) as a colorless solid. An analytically pure sample of this compound was obtained by sublimation (35–36 °C/0.007 Torr; mp 52.5–54.5 °C).



198

^{1}H NMR (400 MHz, CDCl$_3$): δ 5.62–5.40 (br s, 2H, -NH$_2$), 5.53 (d, 1H, J = 2.0 Hz, vinylic proton trans to -Ge(CH$_3$)$_3$), 5.22 (d, 1H, J = 2.0 Hz, vinylic proton cis to -Ge(CH$_3$)$_3$), 2.53–2.47 (m, 2H), 2.37–2.30 (m, 2H), 0.21 (s, 9H, -Ge(CH$_3$)$_3$).

^{13}C NMR (75.4 MHz, CDCl$_3$): δ 175.3 (-CO-), 152.4 (-$\underline{C}$(=CH$_2$)-), 121.7 (-C(=$\underline{C}$H$_2$)-), 34.8, 32.1, –2.1 (-Ge(CH$_3$)$_3$).

IR (KBr pellet): 3365, 3193, 3050, 2972, 1667, 1631, 1413, 1236, 921, 826, 599 cm^{-1}.

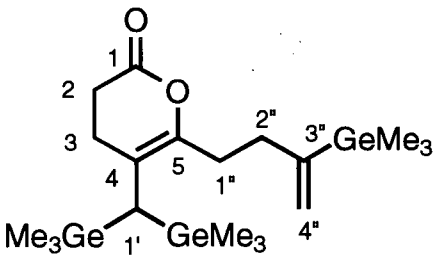
HRMS for $C_8H_{17}{}^{74}GeNO$: calcd 217.0522, found 217.0513.

Anal. calcd for $C_8H_{17}GeNO$: C 44.52, H 7.94, N 6.49; found: C 44.78, H 7.95, N 6.44.

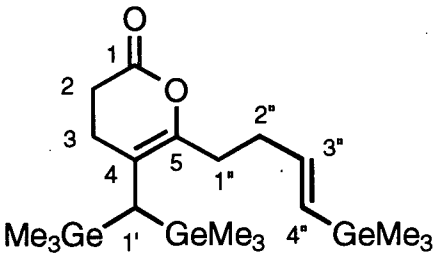
b) Without Additive

Following general procedure 5, to a cold (–78 °C) stirred solution of Me$_3$GeCu•Me$_2$S (**168**) (0.94 mmol, 1 equiv) in dry THF (5 mL total), prepared via the "inverse" addition method (section 3.3.2.2(b), p 223), was added a solution of pent-4-ynoyl chloride (**160**) (110

mg, 0.94 mmol, 1 equiv) in dry THF (1 mL) via a cannula. The reaction mixture was stirred at –78 °C for 2.5 h, then pyridine (187 mg, 2.36 mmol, 2.50 equiv) and dry methanol (61 mg, 1.90 mmol, 2.00 equiv) were added sequentially. The cooling bath was removed, and the mixture was allowed to stir for an additional 15 min. The mixture was poured into aqueous NH_4Cl–NH_4OH (pH 8–9, 5 mL) and diethyl ether (10 mL) was added to the mixture. The heterogeneous mixture was stirred vigorously, open to the atmosphere, until the aqueous layer was deep blue. The crude oil of the complex mixture obtained was subjected to flash chromatography (35 g TLC grade silica gel, 49:1, then 24:1, petroleum ether–diethyl ether) to afford three major fractions, which were concentrated under reduced pressure. The first substantial fraction to be eluted afforded 23 mg (9%) of a mixture of two compounds. ^{1}H NMR, GLC and GLC–MS analyses of this mixture suggested that it was composed of 5-(3-trimethylgermylbut-3-en-1-yl)-4-(bis(trimethylgermyl)methyl)pent-4-eno-5-lactone (**203**) (≈80% by GLC analysis) as well as of (*E*)-5-(4-trimethylgermylbut-3-en-1-yl)-4-(bis(trimethylgermyl)-methyl)pent-4-eno-5-lactone (**204**) (≈20%) based on the following: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum showed four signals in the 5.95–5.15 ppm region integrating for a total of two protons: 5.92 (m, 0.2H, H-3"–**204**), 5.83 (d, 0.2H, J = 18.2 Hz, H-4"–**204**), 5.52 (d, 0.8H, J = 1.8 Hz, H-4"–**203**) and 5.22 (d, 0.8H, J = 1.8 Hz, H-4"–**203**); then 2.79 (t, 2H, J = 3.2 Hz, H-3–**203** + **204**), 2.60–2.38 (m, 4H, H-1" and H-2"–**203** + **204**), 2.08 (t, 2H,J = 3.2 Hz, H-3–**203** + **204**), 1.34 (s, 1H, H-1'–**203** + **204**) and three singlets in the 0.26–0.15 ppm region integrating for a total of 27 protons. GLC-MS showed both components to have molecular ions of 516 whose isotopic clusters are consistent with the calculated isotopic distribution for $C_{19}H_{38}Ge_3O_2$.

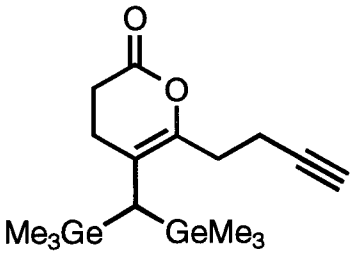


203



204

The second sizable fraction to be eluted was distilled (98–107 °C/0.07 Torr) to afford 30 mg (16%) of 5-(but-3-yn-1-yl)-4-(bis(trimethylgermyl)methyl)pent-4-eno-5-lactone (**205**) as a clear colorless oil.



205

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.79 (t, 2H, J = 3.0 Hz, -CH_2CO-), 2.62–2.55 (m, 2H, -C$\underline{H}_2$$CH_2$C≡CH), 2.53–2.46 (m, 2H, -C$\underline{H}_2$C≡CH), 2.06 (t, 2H, J = 3.0 Hz, -C$\underline{H}_2$$CH_2$CO-), 1.96 (t, 1H, J = 2.6 Hz, -C≡CH), 1.34 (s, 1H, -C$\underline{H}$(Ge(CH_3)$_3$)$_2$), 0.17 (s, 18H, 2 × -Ge(CH_3)$_3$).

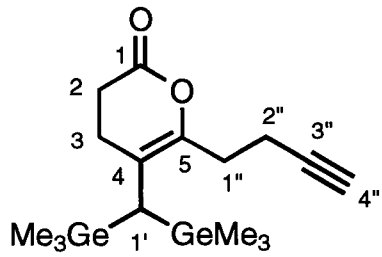
Additional ^{1}H NMR data, derived from homonuclear decoupling experiments, are given in **Table 22**.

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 168.9 (-CO-), 133.3 (vinylic carbon), 126.9 (vinylic carbon), 82.3 (-$\underline{C}$≡CH), 69.2 (-C≡$\underline{C}$H), 33.2, 31.2, 26.8, 19.9 (-$\underline{C}$H(Ge(CH_3)$_3$)$_2$), 14.3 (-$\underline{C}$$H_2$C≡CH), –0.1 (-Ge($CH_3$)$_3$).

IR (film): 3313, 2970, 2140, 1757, 1682, 1269, 1236, 1144, 823, 600 cm^{-1}.

HRMS for $C_{16}H_{28}{}^{72}Ge^{74}GeO_2$: calcd 398.0522, found 398.0521.

Table 22: ^{1}H NMR Data from Homonuclear Decoupling Experiments for 5-(But-3-yn-1-yl)-4-(bis(trimethylgermyl)methyl)pent-4-eno-5-lactone (**205**)

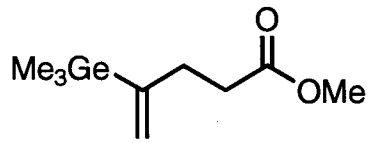


205

Assignments H-x	^{1}H NMR[a] δ ppm (mult, *J* (Hz))	Simplified Signals (mult, *J* (Hz))
H-2[b]	2.79 (t, 3.0)	H-3 (s)
H-1"[b]	2.62–2.55 (m)	H-2" (d, 2.6)
H-2"[b]	2.53–2.46 (m)	H-1" (s), H-4" (s)
H-3[b]	2.06 (t, 3.0)	H-2 (s)
H-4"[b]	1.96 (t, 2.6)	H-2" (m)
H-1'	1.34 (s)	
-Ge(CH$_3$)$_3$	0.17	

[a] 400 MHz, $CDCl_3$. [b] Irradiation of this signal simplified the corresponding signals in the right hand column.

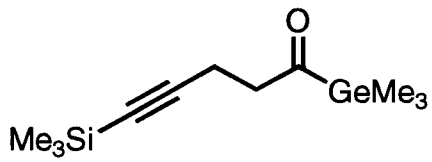
The third substantial fraction to be eluted afforded 9 mg (4%) of methyl 4-trimethylgermylpent-4-enoate (**206**) as a clear colorless oil.



206

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.50 (d, 1H, J = 2.0 Hz, vinylic proton trans to -Ge(CH_3)$_3$), 5.20 (d, 1H, J = 2.0 Hz, vinylic proton cis to -Ge(CH_3)$_3$), 3.67 (s, 3H, -OCH_3), 2.52–2.39 (m, 4H, -CH_2CH_2-), 0.22 (s, 9H, -Ge(CH_3)$_3$).

3.3.2.3.10 Synthesis of 5-Trimethylsilylpent-4-ynoyltrimethylgermane (**114**)



114

Following general procedure 5, to a cold (–78 °C) stirred solution of $Me_3GeCu{\bullet}Me_2S$ (**168**) (1.79 mmol, 1.50 equiv) in dry THF (9.8 mL total), prepared via the "normal" addition method (section 3.3.2.2(a), p 223), was added chlorotrimethylsilane (130 mg, 1.19 mmol, 1 equiv) via a syringe. After the mixture had been stirred for 5 min, a solution of 5-trimethylsilylpent-4-ynoyl chloride (**164**) (225 mg, 1.19 mmol, 1 equiv) in dry THF (2 mL) was added via a cannula. The oil acquired was subjected to flash chromatography (40 g TLC grade silica gel, 26:1 petroleum ether–diethyl ether) and the derived oil was distilled (68–76 °C/0.05 Torr) to afford 265 mg (82%) of the title compound as a light yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.89–2.83 (m, 2H), 2.45–2.38 (m, 2H), 0.33 (s, 9H, -Ge(CH_3)$_3$), 0.11 (s, 9H, -Si(CH_3)$_3$).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 242.9 (-CO-), 106.1 (-C≡$\underline{C}$Si(CH_3)$_3$), 84.8 (-$\underline{C}$≡CSi(CH_3)$_3$),

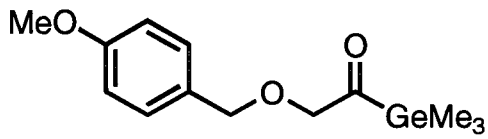
47.9 (-$\underline{C}H_2CO$-), 12.9 (-$\underline{C}H_2C{\equiv}C$-), 0.0 (-$Si(CH_3)_3$), –3.1 (-$Ge(CH_3)_3$).

IR (film): 2177, 1660, 1251, 843, 760, 606 cm^{-1}.

HRMS for $C_{11}H_{22}{}^{74}GeO^{28}Si$: calcd 272.0652, found 272.0644.

Anal. calcd for $C_{11}H_{22}GeOSi$: C 48.76, H 8.18; found: C 48.79, H 8.16.

3.3.2.4 LARGE SCALE PREPARATION OF ((4-METHOXYBENZYL)OXY)ACETYLTRIMETHYL-GERMANE (**180**)



180

To cold (–10 °C) stirred dry THF (25 mL) was added cold (0 °C) Me_3GeH (**53**) (8.55 g, 72.0 mmol, 1.80 equiv) via a cannula. A solution of *t*-BuLi (1.77 M in pentane, 33.9 mL, 60.0 mmol, 1.50 equiv) was added via a syringe over 3 min (***Warning! Gas evolution!***). The resulting yellow solution was stirred at –10 °C for 5 min to afford a clear colorless solution. This solution was transferred via a cannula to a cold (–78 °C) stirred suspension of CuBr•Me_2S (12.34 g, 60.0 mmol, 1.50 equiv) in dry THF (325 mL). The flask that initially contained the Me_3GeLi (**149**) was rinsed with dry THF (2 × 10 mL) and the rinses were transferred via a cannula to the suspension of CuBr•Me_2S. The mixture was stirred at –78 °C for 1 h to afford a dark red–black solution. Chlorotrimethylsilane (4.35 g, 40.0 mmol, 1 equiv) was added via a syringe. After the mixture had been stirred for 5 min, a solution of ((4-methoxybenzyl)oxy)acetyl chloride (**167**) (8.59 g, 40.0 mmol, 1 equiv) in dry THF (30 mL) was added via a cannula. The black reaction mixture was stirred at –78 °C for 1 h, then was warmed to –30 °C and was allowed to stir for an additional 2 h. The mixture was poured

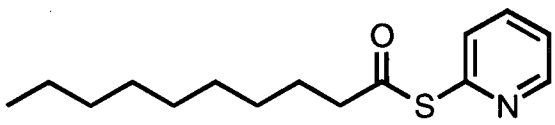
into a stirred solution of aqueous NH_4Cl–NH_4OH (pH 8–9, 400 mL) and diethyl ether (400 mL) was added to the mixture. The heterogeneous mixture was stirred vigorously, open to the atmosphere, until the aqueous layer was deep blue. The layers were separated and the aqueous portion was extracted with diethyl ether (3 × 200 mL). The combined organic extracts were washed with water (2 × 100 mL) and brine (100 mL), were dried over anhydrous magnesium sulfate and then were filtered and concentrated under reduced pressure. The crude oil obtained was subjected to chromatography (Prep LC 500, two silica gel cartridges (57 mm × 300 mm) in tandem, 23:2 petroleum ether–diethyl ether, 250 mL/min) and the acquired oil was distilled to afford 9.76 g (82%) of the title compound as a clear colorless oil. The spectral data were identical with those reported above (section 3.3.2.3.4, p 228).

3.3.3 SYNTHESIS OF *S*-(PYRIDIN-2-YL) THIOESTERS

3.3.3.1 GENERAL PROCEDURE 6: PREPARATION OF THE *S*-(PYRIDIN-2-YL) THIOESTERS

To a stirred solution of the appropriate carboxylic acid (1 equiv) in dry acetonitrile (0.3 M solution) at rt was added sequentially triphenylphosphine (1.0–1.1 equiv) and 2,2'-disulfanediyldipyridine[98] (1.0–1.1 equiv). The yellow solution was stirred at rt 0.5–1 h, then the solvent was removed under reduced pressure. The residue was flash chromatographed to afford the desired *S*-(pyridin-2-yl) thioester.

3.3.3.1.1 Synthesis of *S*-(Pyridin-2-yl) Decanethioate (**210**)



210

Following general procedure 6, to a solution of decanoic acid (**153**) (1.02 g, 5.92 mmol, 1 equiv) in dry acetonitrile (20 mL) was sequentially added triphenylphosphine (1.55 g, 5.92 mmol, 1.00 equiv) and 2,2'-disulfanediyldipyridine (1.31 g, 5.92 mmol, 1.00 equiv). The reaction mixture was stirred at rt for 0.5 h. The residue was subjected to flash chromatography (140 g silica gel, 2:1 petroleum ether–diethyl ether) to afford 1.23 g (78%) of the title compound as a light yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.59 (ddd, 1H, J = 4.8, 1.8 and 1.0 Hz), 7.71 (td, 1H, J = 7.8 and 1.8 Hz), 7.59 (dt, 1H, J = 7.8 and 1.0 Hz), 7.25 (ddd, 1H, J = 7.8, 4.8 and 1.0 Hz), 2.67 (t, 2H, J = 7.4 Hz, -CH_2CO-), 1.70 (quintuplet, 2H, J = 7.4 Hz, -C$\underline{H}_2$$CH_2$CO-), 1.48–1.19 (m, 12H), 0.85 (t, 3H, J = 7.8 Hz, -CH_2C$\underline{H}_3$).

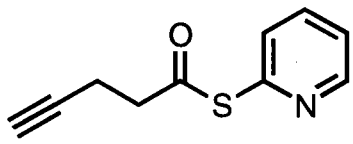
^{13}C NMR (75.4 MHz, $CDCl_3$): δ 196.1 (-CO-), 151.4, 150.0, 136.7, 129.8, 123.1, 43.9, 31.6, 29.1, 29.0 (2 overlapping signals), 28.6, 25.1, 22.4, 13.8 (-$CH_2\underline{C}H_3$).

IR (film): 1708, 1573, 1563, 1451, 1421, 1120, 990, 766 cm^{-1}.

HRMS for $C_{15}H_{23}NOS$: calcd 265.1500, found 265.1496.

Anal. calcd for $C_{15}H_{23}NOS$: C 67.88, H 8.73, N 5.28; found: C 67.84, H 8.91, N 5.16.

3.3.3.1.2 Synthesis of *S*-(Pyridin-2-yl) Pent-4-ynethioate (**211**)



211

Following general procedure 6, to a solution of pent-4-ynoic acid (**156**) (343 mg, 3.50 mmol, 1 equiv) in dry acetonitrile (12 mL) was added sequentially triphenylphosphine (1.01 g, 3.85 mmol, 1.10 equiv) and 2,2'-disulfanediyldipyridine (848 mg, 3.85 mmol, 1.10 equiv). The reaction mixture was stirred at rt for 0.5 h. The residue was subjected to flash chromatography (140 g silica gel, 7:3 petroleum ether–ethyl acetate) to afford 624 mg (56%) of the title compound as a light yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.60 (ddd, 1H, J = 4.8, 1.8 and 1.0 Hz), 7.72 (ddd, 1H, J = 7.6, 7.6 and 1.8 Hz), 7.60 (ddd, 1H, 7.6, 1.0 and 1.0 Hz), 7.27 (ddd, 1H, J = 7.6, 4.8 and 1.0 Hz), 2.92 (t, 2H, J = 7.4 Hz, -$C\underline{H}_2CH_2C{\equiv}CH$), 2.56 (td, 2H, J = 7.4 and 2.6 Hz, -$C\underline{H}_2C{\equiv}CH$), 1.99 (t, 1H, J = 2.6 Hz, -C≡CH).

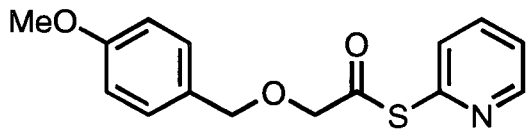
^{13}C NMR (75.4 MHz, $CDCl_3$): δ 194.3 (-CO-), 150.7, 150.2. 137.0, 129.9, 123.5, 81.4 (-$\underline{C}{\equiv}CH$), 69.5 (-$C{\equiv}\underline{C}H$), 42.3 (-$\underline{C}H_2CH_2C{\equiv}CH$), 14.2 (-$\underline{C}H_2C{\equiv}CH$).

IR (film): 3293, 2121, 1703, 1573, 1563, 1451, 1422, 1051, 974, 769 cm^{-1}.

HRMS (DCI, isobutane) for $C_{10}H_{10}NOS$ $(M + 1)^+$: calcd 192.0483, found 192.0484.

Anal. calcd for $C_{10}H_9NOS$: C 62.80, H 4.74, N 7.32; found: C 62.58, H 4.61, N 7.51.

3.3.3.1.3 Synthesis of *S*-(Pyridin-2-yl) ((4-Methoxybenzyl)oxy)ethanethioate (**212**)



212

Following general procedure 6, to a solution of ((4-methoxybenzyl)oxy)acetic acid (**166**) (694 mg, 3.53 mmol, 1 equiv) in dry acetonitrile (12 mL) was added sequentially triphenylphosphine (1.02 g, 3.89 mmol, 1.10 equiv) and 2,2'-disulfanediyldipyridine (857 mg, 3.89 mmol, 1.10 equiv). The reaction mixture was stirred at rt for 1 h. The residue was subjected to flash chromatography (140 g silica gel, 3:2 petroleum ether–ethyl acetate) to afford 851 mg (83%) of the title compound as a light yellow oil.

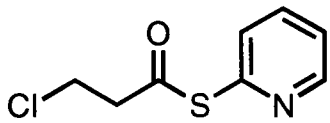
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.64 (ddd, 1H, J = 4.8, 2.0 and 1.0 Hz), 7.73 (ddd, 1H, J = 7.8, 7.8 and 2.0), 7.58 (ddd, 1H, J = 7.8, 1.0 and 1.0 Hz), 7.33 (d, 2H, J = 8.6 Hz), 7.28 (ddd, 1H, J = 7.8, 4.8 and 1.0 Hz), 6.89 (d, 2H, J = 8.6 Hz), 4.65 (s, 2H), 4.23 (s, 2H), 3.80 (s, 3H, $-OCH_3$).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 197.6 (-CO-), 159.4, 150.7, 150.3, 137.0, 130.4, 129.5, 128.5, 123.4, 113.7, 74.3, 73.7, 55.0 ($-OCH_3$).

IR (film): 1708, 1613, 1574, 1563, 1515, 1451, 1422, 1250, 1121, 1076, 1034, 769 cm^{-1}.

HRMS (DCI, isobutane) for $C_{15}H_{16}NO_3S$ $(M + 1)^+$: calcd 290.0851, found 290.0850.

3.3.3.1.4 Synthesis of *S*-(Pyridin-2-yl) 3-Chloropropanethioate (**213**)



213

Following general procedure 6, to a solution of 3-chloropropanoic acid (**209**) (380 mg, 3.50 mmol, 1 equiv) in dry acetonitrile (12 mL) was added sequentially triphenylphosphine (1.01 g, 3.85 mmol, 1.10 equiv) and 2,2'-disulfanediyldipyridine (848 mg, 3.85 mmol, 1.10 equiv). The reaction mixture was stirred at rt for 0.5 h. The residue was subjected to flash chromatography (50 g TLC grade silica gel, 3:2 petroleum ether–ethyl acetate) to afford 395 mg (56%) of the title compound as a light yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.61 (ddd, 1H, J = 4.8, 2.0 and 1.0 Hz), 7.74 (ddd, 1H, J = 7.6, 7.6 and 2.0 Hz), 7.61 (ddd, 1H, J = 7.6, 1.0 and 1.0 Hz), 7.29 (ddd, 1H, J = 7.6, 4.8 and 1.0 Hz), 3.78 (t, 2H, J = 6.8 Hz), 3.14 (t, 2H, J = 6.8 Hz).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 193.2 (-CO-), 150.21, 150.17, 137.4, 130.1, 123.8, 46.1, 38.3.

IR (film): 1708, 1573, 1563, 1451, 1421, 1050, 969, 768 cm^{-1}.

LRMS for $C_8H_8{}^{35}ClNOS$: calcd 201, found 201.

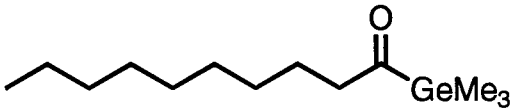
Due to the fact that this compound was unstable, satisfactory HRMS and elemental analysis could not be obtained.

3.3.4 SYNTHESIS OF ACYLTRIMETHYLGERMANES FROM *S*-(PYRIDIN-2-YL) THIOESTERS

3.3.4.1 GENERAL PROCEDURE 7: PREPARATION OF THE ACYLTRIMETHYLGERMANES FROM *S*-(PYRIDIN-2-YL) THIOESTERS

To a cold (–78 °C) stirred solution of $Me_3GeCu{\bullet}Me_2S$ (**168**) (1.0–1.5 equiv) in dry THF, prepared via the "inverse" addition method (section 3.3.2.2(b), p 223), was added a solution of the appropriate *S*-(pyridin-2-yl) thioester (1 equiv) in dry THF, via a cannula, to generate a final concentration of ≈0.1 M solution of the *S*-(pyridin-2-yl) thioester. The reaction mixture was stirred at –78 °C for 1 h, then was warmed to –30 °C and was allowed to stir for an additional 2 h. The black mixture was poured into a stirred aqueous NH_4Cl–NH_4OH solution (pH 8–9, ≈15 mL per mmol of *S*-(pyridin-2-yl) thioester) and diethyl ether (≈30 mL per mmol of *S*-(pyridin-2-yl) thioester) was added to the mixture. The two-phase system was stirred vigorously, open to the atmosphere, until the aqueous layer was deep blue and an orange precipitate was present. The solid was removed by filtration of the mixture through a plug of glass wool in a funnel. The layers of the filtrate were separated and the aqueous portion was extracted with diethyl ether (2 × ≈10 mL per mmol of *S*-(pyridin-2-yl) thioester). The combined organic extracts were washed with water (2 × ≈10 mL per mmol of *S*-(pyridin-2-yl) thioester) and brine (≈10 mL per mmol of *S*-(pyridin-2-yl) thioester), were dried over anhydrous magnesium sulfate, and then were filtered and concentrated under reduced pressure. The crude oil thus acquired was subjected to flash chromatography to provide the desired acyltrimethylgermane.

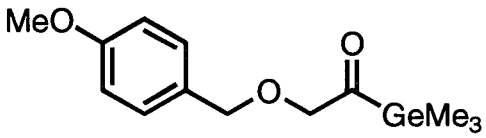
3.3.4.1.1 Synthesis of Decanoyltrimethylgermane (**170**)



170

Following general procedure 7, to a cold (–78 °C) stirred solution of $Me_3GeCu{\bullet}Me_2S$ (**168**) (1.28 mmol, 1.47 equiv) in dry THF (7.5 mL total) was added a solution of *S*-(pyridin-2-yl) decanethioate (**210**) (232 mg, 0.87 mmol, 1 equiv) in dry THF (1 mL) via a cannula. The crude oil obtained was subjected to flash chromatography (10 g TLC grade silica gel, 24:1 then 2:1 petroleum ether–diethyl ether) to afford two fractions which were concentrated under reduced pressure. The first fraction to be eluted was distilled to afford 153 mg (64%) of the title compound as a light yellow oil. The spectral data were identical with those reported above (section 3.3.2.3.1. p 225). The second compound to be eluted afforded 23 mg (10%) of unreacted *S*-(pyridin-2-yl) decanethioate (**210**).

3.3.4.1.2 Synthesis of ((4-Methoxybenzyl)oxy)acetyltrimethylgermane (**180**)

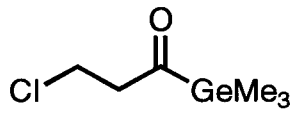


180

Following general procedure 7, to a cold (–78 °C) stirred solution of $Me_3GeCu{\bullet}Me_2S$ (**168**) (0.80 mmol, 1.5 equiv) in dry THF (4.3 mL total) was added a solution of *S*-(pyridin-2-yl) ((4-methoxybenzyl)oxy)ethanethioate (**212**) (156 mg, 0.54 mmol, 1 equiv) in dry THF (1 mL) via a cannula. The crude oil obtained was subjected to flash chromatography (10 g TLC grade silica gel, 17:3 petroleum ether–diethyl ether) and distilled to afford 89 mg (62%) of the

title compound as a light yellow oil. The spectral data were identical with those reported above (section 3.3.2.3.4, p 228).

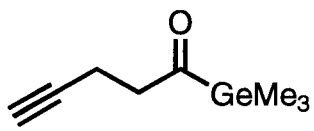
3.3.4.1.3 Synthesis of 3-Chloropropanoyltrimethylgermane (**183**)



183

Following general procedure 7, to a cold (–78 °C) stirred solution of $Me_3GeCu{\bullet}Me_2S$ (**168**) (0.80 mmol, 1.5 equiv) in dry THF (4.3 mL total) was added a solution of *S*-(pyridin-2-yl) 3-chloropropanethioate (**213**) (107 mg, 0.54 mmol, 1 equiv) in dry THF (1 mL) via a cannula. The reaction mixture was stirred at –78 °C for 3 h, then was poured into a stirred aqueous NH_4Cl–NH_4OH solution (pH 8–9, 12 mL). The dried organic extracts were concentrated via distillation at atmospheric pressure. The crude oil obtained was subjected to flash chromatography (10 g TLC grade silica gel, gradient elution from 32:1 to 17:3 petroleum ether–diethyl ether) to afford 26 mg (23%) of the title compound as a light yellow oil. Spectral data were identical with those reported above (section 3.3.2.3.7(a), p 235).

3.3.4.1.4 Attempt at Synthesizing Pent-4-ynoyltrimethylgermane (**185**)



185

A cold (–78 °C) stirred solution of $Me_3GeCu{\bullet}Me_2S$ (**168**) (0.50 mmol, 1 equiv) in dry THF (5 mL total), prepared via the "inverse" addition method (section 3.3.2.2(b), p 223), was transferred via a cannula, to a cold (–78 °C) stirred solution of *S*-(pyridin-2-yl) pent-4-yne-

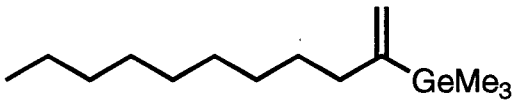
thioate (**211**) (192 mg, 1.00 mmol, 2.00 equiv) in dry THF (5 mL). The flask that initially contained the $Me_3GeCu{\bullet}Me_2S$ (**168**) was rinsed with dry THF (2 × 1 mL), and the rinses were transferred via a cannula to the solution of *S*-(pyridin-2-yl) pent-4-ynethioate (**211**). The reaction mixture was stirred at –78 °C for 3 h, then was poured into a stirred aqueous NH_4Cl–NH_4OH solution (pH 8–9, 10 mL) and diethyl ether (20 mL) was added to the mixture. The heterogeneous mixture was stirred vigorously, open to the atmosphere, until the aqueous layer was deep blue. The yellow precipitate was removed by filtration of the mixture through a plug of glass wool in a funnel. The layers of the filtrate were separated and the aqueous portion was extracted with diethyl ether (2 × 10 mL). The combined organic extracts were washed with water (2 × 5 mL) and brine (5 mL), were dried over anhydrous magnesium sulfate and were filtered and concentrated under reduced pressure. The crude oil thus obtained was subjected to flash chromatography (7.5 g TLC grade silica gel, 32:1 petroleum ether–diethyl ether, then 1:1 petroleum ether–ethyl acetate and finally ethyl acetate) to afford 5 fractions which were concentrated under reduced pressure. The first fraction to be eluted afforded 26 mg of 5-(but-3-yn-1-yl)-4-(bis(trimethylgermyl)methyl)pent-4-eno-5-lactone (**205**). Spectral data were identical with those reported above (3.3.2.3.9(b), p 241). The next two fractions to be eluted afforded only trace amounts of unidentified compounds. The fourth fraction to be eluted afforded 27 mg of 2,2'-disulfanediyldipyridine. The fifth fraction to be eluted afforded 29 mg of a mixture of compounds. ^{1}H NMR spectroscopy analysis suggested that the major component (≈50%) was 4-trimethylgermylpent-4-enamide (**198**). Spectral data were identical with those reported above (3.3.2.3.9, p 241).

3.3.5 SYNTHESIS OF 2-TRIMETHYLGERMYLALK-1-ENES VIA WITTIG OLEFINATION OF ACYLTRIMETHYLGERMANES

3.3.5.1 GENERAL PROCEDURE 8: PREPARATION OF THE 2-TRIMETHYLGERMYLALK-1-ENES

To a stirred suspension of methyltriphenylphosphonium bromide (1.25–2.60 equiv) in dry solvent (0.07–0.2 M) was added a solution of *n*-BuLi in hexanes (1.20–2.50 equiv) via a syringe. The yellow mixture was stirred for 20–30 min, then a solution of the appropriate acyltrimethylgermane (1 equiv) in dry solvent was added, via a cannula, to generate a final concentration 0.04–0.1 M of the acyltrimethylgermane. The reaction mixture was stirred for 15–20 min then was treated with anhydrous methanol (2–3 drops). Petroleum ether or diethyl ether (≈30 mL per mmol of acyltrimethylgermane) was added. The precipitate formed was removed by filtration of the mixture through Celite and the collected material was washed with petroleum ether or diethyl ether (≈20 mL per mmol of acyltrimethylgermane). The filtrate was concentrated under reduced pressure and the crude oil thus acquired was flash chromatographed and the derived oil was distilled to afford the desired 2-trimethylgermylalk-1-ene as a clear colorless oil.

3.3.5.1.1 Synthesis of 2-Trimethylgermylundec-1-ene (**214**)



214

Following general procedure 8, to a cold (0 °C) stirred suspension of methyltriphenylphosphonium bromide (873 mg, 2.44 mmol, 1.25 equiv) in dry THF (15 mL) was added a

solution of *n*-BuLi (1.60 M in hexanes, 1.47 mL, 2.35 mmol, 1.20 equiv). The mixture was stirred at 0 °C for 10 min, then was warmed to rt and was allowed to stir for an additional 20 min. A solution of decanoyltrimethylgermane (**170**) (534 mg, 1.95 mmol, 1 equiv) in dry THF (5 mL) was added via a cannula. The reaction mixture was stirred at rt for 20 min. The crude oil acquired was subjected to flash chromatography (50 g silica gel, 49:1 petroleum ether–diethyl ether) and the derived oil was distilled (80–90 °C/0.1 Torr) to afford 476 mg (90%) of the title compound as a clear colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.48 (d, 1H, J = 2.8 Hz, vinylic proton trans to -Ge(CH_3)$_3$), 5.14 (d, 1H, J = 2.8 Hz, vinylic proton cis to -Ge(CH_3)$_3$), 2.16 (t, 2H, J = 7.6 Hz, -C$\underline{H}_2$C(=CH_2)-), 1.44–1.16 (m, 14H), 0.86 (t, 3H, J = 7.0 Hz, -CH_2C$\underline{H}_3$), 0.19 (s, 9H, -Ge(CH_3)$_3$).

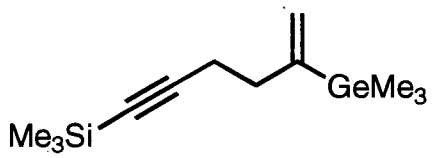
^{13}C NMR (75.4 MHz, $CDCl_3$): δ 154.5 (-$\underline{C}$(=CH_2)-), 121.2 (-C(=$\underline{C}H_2$)-), 37.5, 31.9, 29.64, 29.57, 29.43, 29.37, 29.0, 22.7, 14.1 (-$CH_2\underline{C}H_3$), –1.8 (-Ge(CH_3)$_3$).

IR (film): 3047, 2926, 1604, 1466, 1236, 916, 824, 759, 599 cm^{-1}.

HRMS for $C_{13}H_{27}{}^{74}Ge$ (M – CH_3)$^+$: calcd 257.1325, found 257.1329.

Anal. calcd for $C_{14}H_{30}Ge$: C 62.05, H 11.16; found: C 62.27, H 11.26.

3.3.5.1.2 Synthesis of 2-Trimethylgermyl-6-trimethylsilylhex-5-yn-1-ene (**215**)



215

Following general procedure 8, to a stirred suspension of methyltriphenylphosphonium

bromide (435 mg, 1.22 mmol, 1.63 equiv) in dry benzene (9 mL) at rt was added a solution of *n*-BuLi (1.59 M in hexanes, 0.74 mL, 1.2 mmol, 1.6 equiv). The mixture was stirred at rt for 30 min. A solution of 5-trimethylsilylpent-4-ynoyltrimethylgermane (**114**) (203 mg, 0.75 mmol, 1 equiv) in dry benzene (2 mL) was added via a cannula. The reaction mixture was stirred at rt for 20 min. The crude oil acquired was subjected to flash chromatography (38 g silica gel, petroleum ether) and the derived oil was distilled (135–145 °C/11 Torr) to afford 173 mg (86%) of the title compound as a clear colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.52 (d, 1H, J = 2.0 Hz, vinylic proton trans to -Ge(CH_3)$_3$), 5.21 (d, 1H, J = 2.0 Hz, vinylic proton cis to -Ge(CH_3)$_3$), 2.42–2.27 (m, 4H, -CH_2CH_2-), 0.20 (s, 9H, -Ge(CH_3)$_3$), 0.12 (s, 9H, -Si(CH_3)$_3$).

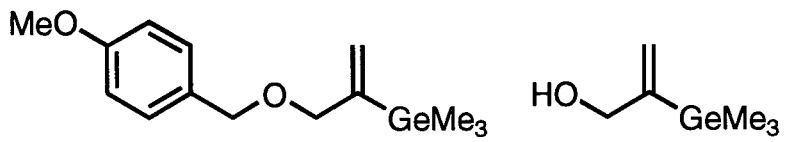
^{13}C NMR (75.4 MHz, $CDCl_3$): δ 152.1 (-$\underline{C}$(=CH_2)-), 122.2 (-C(=$\underline{C}H_2$)-), 107.1 (-C≡$\underline{C}$Si(CH_3)$_3$), 84.7 (-$\underline{C}$≡CSi(CH_3)$_3$), 35.9 (-$\underline{C}H_2$C(=CH_2)-), 19.6 (-$\underline{C}H_2$C≡C-), 0.2 (-Si(CH_3)$_3$), –2.0 (-Ge(CH_3)$_3$).

IR (film): 3050, 2964, 2177, 1609, 1411, 1250, 921, 843, 760, 600 cm^{-1}.

HRMS for $C_{11}H_{21}{}^{74}Ge^{28}Si$ (M – CH_3)$^+$: calcd 255.0624, found 255.0629.

Anal. calcd for $C_{12}H_{24}GeSi$: C 53.58, H 8.99; found: C 53.30, H 8.95.

3.3.5.1.3 Synthesis of 1-((4-Methoxybenzyl)oxy)-2-trimethylgermylprop-2-ene (**216**) and 2-Trimethylgermylprop-2-en-1-ol (**219**)



216 **219**

*a) 1-((4-Methoxybenzyl)oxy)-2-trimethylgermylprop-2-ene (**216**)*

Following general procedure 8, to a cold (0 °C) stirred suspension of methyltriphenylphosphonium bromide (709 mg, 1.98 mmol, 1.25 equiv) in dry THF (10 mL) was added a solution of *n*-BuLi (1.60 M in hexanes, 1.19 mL, 1.90 mmol, 1.20 equiv). The mixture was stirred at 0 °C for 10 min, then was warmed to rt and was allowed to stir for an additional 10 min. A solution of ((4-methoxybenzyl)oxy)acetyltrimethylgermane (**180**) (472 mg, 1.59 mmol, 1 equiv) in dry THF (6 mL) was added via a cannula. The reaction mixture was stirred at rt for 15 min. The crude oil acquired was subjected to flash chromatography (25 g TLC grade silica gel, 23:4 petroleum ether–diethyl ether) and the derived oil was distilled (88–98 °C/0.007 Torr) to afford 429 mg (91%) of 1-((4-methoxybenzyl)oxy)-2-trimethylgermylprop-2-ene (**216**) as a clear colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25 (d, 2H, J = 8.8 Hz), 6.86 (d, 2H, J = 8.8 Hz), 5.74 (dt, 1H, J = 2.6 and 1.4 Hz), 5.32 (dt, 1H, J = 2.6 and 1.4 Hz), 4.40 (s, 2H, -$C_6H_4C\underline{H}_2O$-), 4.11 (t, 2H, J = 1.4 Hz, -$C\underline{H}_2C(=CH_2)$-), 3.79 (s, 3H, -OCH_3), 0.22 (s, 9H, -$Ge(CH_3)_3$).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 159.0, 150.8 (-$\underline{C}(=CH_2)$-), 130.5, 129.2, 122.9 (-$C(=\underline{C}H_2)$-),

113.6, 74.7, 71.6, 55.2 (-OCH_3), -2.0 (-$Ge(CH_3)_3$).

IR (film): 1614, 1515, 1250, 1088, 1039, 824, 602 cm^{-1}.

HRMS for $C_{14}H_{22}{}^{74}GeO_2$: calcd 296.0832, found 296.0838.

Anal. calcd for $C_{14}H_{22}GeO_2$: C 57.02, H 7.52; found: C 56.80, H 7.65.

*b) 2-Trimethylgermylprop-2-en-1-ol (**219**)*

To a stirred solution of 1-((4-methoxybenzyl)oxy)-2-trimethylgermylprop-2-ene (**216**) (52 mg, 18 mmol, 1 equiv) in a CH_2Cl_2–water (18:1, 2.11 mL total) mixture was added DDQ[99] (44 mg, 19 mmol, 1.1 equiv; this reaction was not performed under an atmosphere of argon). The brown–green reaction mixture was stirred at rt for 40 min. The solids were removed by filtration of the mixture through Celite and the collected material was washed with CH_2Cl_2 (5 mL). The filtrate was concentrated under reduced pressure. The crude oil thus acquired was subjected to flash chromatography (5 g TLC grade silica gel, 9:1 CH_2Cl_2–diethyl ether) to afford 23 mg (75%) of 2-trimethylgermylprop-2-en-1-ol (**219**)[127] as a clear colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.73 (d, 1H, J = 2.2 Hz, vinylic proton trans to -$Ge(CH_3)_3$), 5.28 (d, 1H, J = 2.2 Hz, vinylic proton cis to -$Ge(CH_3)_3$), 4.28 (s, 2H, -C$\underline{H}_2$OH), 1.32 (br s, 1H, exchanges with D_2O, -OH), 0.22 (s, 9H, -$Ge(CH_3)_3$).

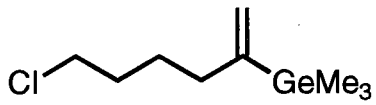
^{13}C NMR (75.4 MHz, $CDCl_3$): δ 153.1 (-$\underline{C}$(=CH_2)-), 120.1 (-C(=$\underline{C}H_2$)-), 66.7 (-CH_2-), –2.2 (-$Ge(CH_3)_3$).

IR (film): 3306, 827 cm^{-1}.

HRMS for $C_5H_{11}{}^{74}GeO$ $(M - CH_3)^+$: calcd 161.0022, found 161.0028.

Anal. calcd for $C_6H_{14}GeO$: C 41.24, H 8.07; found: C 41.30, H 8.13.

3.3.5.1.4 Synthesis of 6-Chloro-2-trimethylgermylhex-1-ene (**217**)



217

Following general procedure 8, to a cold (0 °C) stirred suspension of methyltriphenylphosphonium bromide (625 mg, 1.75 mmol, 1.25 equiv) in dry diethyl ether (25 mL) was added a solution of *n*-BuLi (1.60 M in hexanes, 1.05 mL, 1.68 mmol, 1.20 equiv). The mixture was stirred at 0 °C for 10 min, then was warmed to rt and was allowed to stir for an additional 20 min. After the yellow mixture had been cooled to 0 °C, a solution of 5-chloropentanoyltrimethylgermane (**182**) (332 mg, 1.40 mmol, 1 equiv) in dry diethyl ether (6 mL) was added via a cannula. The reaction mixture was stirred at 0 °C for 15 min. The crude oil acquired was subjected to flash chromatography (38 g silica gel, petroleum ether) and the derived oil was distilled (115–125 °C/9 Torr) to afford 278 mg (84%) of the title compound as a clear colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.50 (d, 1H, J = 2.4 Hz, vinylic proton trans to -Ge(CH_3)$_3$), 5.18 (d, 1H, J = 2.4 Hz, vinylic proton cis to -Ge(CH_3)$_3$), 3.52 (t, 2H, J = 6.8 Hz, -CH_2Cl), 2.20 (t, 2H, J = 7.6 Hz, -C$\underline{H}_2$C(=CH_2)-), 1.76 (quintuplet, 2H, J = 6.8 Hz, -C$\underline{H}_2$$CH_2$Cl), 1.58–1.50 (m, 2H, -C$\underline{H}_2$$CH_2$C(=$CH_2$)-), 0.20 (s, 9H, -Ge($CH_3$)$_3$).

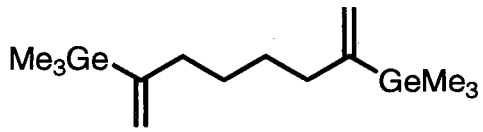
^{13}C NMR (75.4 MHz, $CDCl_3$): δ 153.4 (-$\underline{C}$(=CH_2)-), 121.9 (-C(=$\underline{C}$$H_2$)-), 44.9, 36.5, 32.2, 26.0, –1.9 (-Ge(CH_3)$_3$).

IR (film): 3047, 2943, 1605, 1413, 1236, 918, 825, 599 cm^{-1}.

HRMS for $C_8H_{16}{}^{35}Cl^{74}Ge$ $(M - CH_3)^+$: calcd 221.0152, found 221.0145.

Anal. calcd for $C_9H_{19}ClGe$: C 45.94, H 8.14; found: C 45.90, H 8.24.

3.3.5.1.5 Synthesis of 2,7-bis(Trimethylgermyl)octa-1,7-diene (**218**)



218

Following general procedure 8, to a stirred suspension of methyltriphenylphosphonium bromide (1.17 g, 3.28 mmol, 2.60 equiv) in dry benzene (26 mL) at rt was added a solution of *n*-BuLi (1.59 M in hexanes, 1.98 mL, 3.15 mmol, 2.50 equiv). The mixture was stirred at rt for 30 min. A solution of hexanedioylbis(trimethylgermane) (**184**) (438 mg, 1.26 mmol, 1 equiv) in dry benzene (6 mL) was added via a cannula. The reaction mixture was stirred at rt for 15 min. The crude oil acquired was subjected to flash chromatography (50 g silica gel, petroleum ether) and the derived oil was distilled (70–80 °C/0.3 Torr) to afford 368 mg (85%) of the title compound as a clear colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.49 (d, 2H, J = 2.6 Hz, 2 × vinylic proton trans to -Ge$(CH_3)_3$), 5.15 (d, 2H, J = 2.6 Hz, 2 × vinylic proton cis to -Ge$(CH_3)_3$), 2.18 (m, 4H, 2 × -C$\underline{H}_2$C(=CH_2)-), 1.39 (m, 4H, 2 × -C$\underline{H}_2$$CH_2$C(=$CH_2$)-), 0.19 (s, 18H, 2 × -Ge$(CH_3)_3$).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 154.2 ($\underline{C}$(=CH_2)), 121.4 (C(=$\underline{C}H_2$)), 37.3, 28.7, –1.8 (-Ge$(CH_3)_3$).

IR (film): 3047, 2928, 1605, 1236, 917, 824, 759, 599 cm^{-1}.

HRMS (DCI, isobutane) for $C_{14}H_{31}{}^{72}Ge^{74}Ge$ $(M + 1)^+$: calcd 345.0859, found 345.0867.

Anal. calcd for $C_{14}H_{30}Ge_2$: C 48.94, H 8.80; found: C 49.20, H 8.98.

3.4 CONJUGATE ADDITION OF (TRIMETHYLGERMYL)COPPER(I)–DIMETHYL SULFIDE (168) AND LITHIUM (TRIMETHYLGERMYL)CUPRATES 222–225 TO SELECTED UNSATURATED CARBONYL SYSTEMS

3.4.1 PREPARATION OF THE (TRIMETHYLGERMYL)CUPRATES 222–225

3.4.1.1 PREPARATION OF THE LITHIUM BIS(TRIMETHYLGERMYL)CUPRATE (**222**)

$(Me_3Ge)_2CuLi$
222

A cold (–10 °C) solution of Me_3GeLi (**149**) (1.40 mmol, 1 equiv) in dry THF (0.6 mL), prepared as described above (section 3.3.2.1.1, p 221), was transferred via a cannula to a cold (–78 °C) stirred suspension of $CuBr{\bullet}Me_2S$ (144 mg, 0.70 mmol, 0.50 equiv) in dry THF (9 mL). The flask that initially contained the Me_3GeLi solution was rinsed with dry THF (2 × 1.2 mL) and the rinses were transferred via a cannula to the suspension of $CuBr{\bullet}Me_2S$. The suspension was stirred at –78 °C for 1 h to afford a clear golden solution. The reagent **222** was then ready to use.

3.4.1.2 PREPARATION OF THE LITHIUM (TRIMETHYLGERMYL)CYANOCUPRATE (**223**)

$Me_3GeCu(CN)Li$
223

A cold (–10 °C) solution of Me_3GeLi (**149**) (1.52 mmol, 1 equiv) in dry THF (0.6 mL), prepared as described above (section 3.3.2.1.1, p 221), was transferred via a cannula to a cold (–78 °C) stirred suspension of CuCN (136 mg, 1.52 mmol, 1 equiv) in dry THF (9 mL). The flask that initially contained the Me_3GeLi solution was rinsed with dry THF (2 ×

1.2 mL) and the rinses were transferred via a cannula to the suspension of CuCN. The suspension was stirred at –78 °C for 1 h to afford a yellow opaque solution. The reagent **223** was then ready to use.

3.4.1.3 PREPARATION OF THE DILITHIUM BIS(TRIMETHYLGERMYL)CYANOCUPRATE (**224**)

$(Me_3Ge)_2Cu(CN)Li_2$
224

A cold (–10 °C) solution of Me_3GeLi (**149**) (1.52 mmol, 1 equiv) in dry THF (0.6 mL), prepared as described above (section 3.3.2.1.1, p 221), was transferred via a cannula to a cold (–78 °C) stirred suspension of CuCN (68 mg, 0.76 mmol, 0.50 equiv) in dry THF (9 mL). The flask that initially contained the Me_3GeLi solution was rinsed with dry THF (2 × 1.2 mL) and the rinses were transferred via a cannula to the suspension of CuCN. The suspension was stirred at –78 °C for 1 h to afford a clear colorless solution. The reagent **224** was then ready to use.

3.4.1.4 PREPARATION OF THE DILITHIUM METHYL(TRIMETHYLGERMYL)CYANOCUPRATE (**225**)

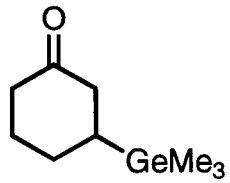
$Me_3Ge(Me)Cu(CN)Li_2$
225

To a cold (–10 °C) stirred solution of Me_3GeLi (**149**) (1.43 mmol, 1 equiv) in dry THF (0.6 mL), prepared as described above (section 3.3.2.1.1, p 221), was added a solution of MeLi (1.37 M in diethyl ether, 1.04 mL, 1.43 mmol, 1 equiv). This solution was transferred via a cannula to a cold (–78 °C) stirred suspension of CuCN (128 mg, 1.43 mmol, 1 equiv) in dry THF (9 mL). The flask that initially contained the Me_3GeLi solution was rinsed with dry THF (2 × 1.2 mL) and the rinses were transferred via a cannula to the

suspension of CuCN. The suspension was stirred at –78 °C for 1 h to afford a clear colorless solution. The reagent **225** was then ready to use.

3.4.2 ADDITION OF (TRIMETHYLGERMYL)COPPER(I)–DIMETHYL SULFIDE (168) AND (TRIMETHYLGERMYL)CUPRATES 222–225 TO CYCLIC ENONES

3.4.2.1 GENERAL PROCEDURE 9: SYNTHESIS OF 3-TRIMETHYLGERMYLCYCLOHEXANONE (229) FROM CYCLOHEX-2-EN-1-ONE (226)



229

To a cold (–78 °C) stirred solution of the appropriate (trimethylgermyl)copper(I) reagent (0.65–1.3 equiv) in dry THF was added a solution of cyclohex-2-en-1-one (**226**) (1 equiv) in dry THF to generate a final concentration of ≈0.08 M of the enone. The resulting mixture was stirred at –78 °C for 0.5 h, then was poured into stirred aqueous NH_4Cl–NH_4OH (pH 8–9, ≈20 mL per mmol of enone) and diethyl ether (≈40 mL per mmol of enone) was added to the mixture. The heterogeneous mixture was stirred vigorously, open to the atmosphere, until the aqueous layer was deep blue. The layers were separated and the aqueous portion was extracted with diethyl ether (2 × ≈10 mL per mmol of enone). The combined organic extracts were washed with water (2 × ≈10 mL per mmol of enone) and brine (≈10 mL per mmol of enone), were dried over anhydrous magnesium sulfate, and then were filtered and concentrated under reduced pressure. The crude oil acquired was subjected to flash chromatography and the resultant oil was distilled (150–160 °C/12 Torr) to afford the title compound as a clear colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.41–2.24 (m, 3H), 2.20–2.10 (m, 2H), 1.86–1.78 (m, 1H), 1.71 (ddddd, 1H, J = 12.8, 12.8, 12.8, 5.0 and 3.8 Hz), 1.46 (dddd, 1H, J = 12.8, 12.8, 12.8 and 3.6 Hz), 1.30 (dddd, 1H, J = 13.6, 12.8, 3.4 and 3.4 Hz), 0.10 (s, 9H, -Ge(CH_3)$_3$).

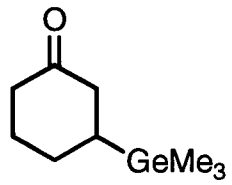
^{13}C NMR (75.4 MHz, $CDCl_3$): δ 212.5 (-CO-), 43.6, 41.9, 29.7, 28.6 (-<u>C</u>H(Ge(CH_3)$_3$)-), 27.0, –4.5 (-Ge(CH_3)$_3$).

IR (film): 1713, 1228, 823, 600 cm^{-1}.

HRMS for $C_9H_{18}{}^{74}GeO$: calcd 216.0569, found 216.0565.

Anal. calcd for $C_9H_{18}GeO$: C 50.32, H 8.45; found: C 50.30, H 8.30.

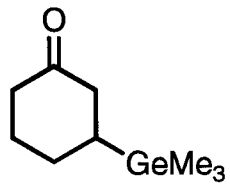
3.4.2.1.1 Preparation of 3-Trimethylgermylcyclohexanone (**229**) Using (Trimethylgermyl)-copper(I)–Dimethyl Sulfide (**168**)



229

Following general procedure 9, to a cold (–78 °C) stirred solution of $Me_3GeCu{\bullet}Me_2S$ (**168**) (1.48 mmol, 1.30 equiv) in dry THF (12.1 mL), prepared as described above (section 3.3.2.2, p 223), was added a solution of cyclohex-2-en-1-one (**226**) (109 mg, 1.14 mmol, 1 equiv) in dry THF (2.5 mL). The black mixture was stirred at –78 °C for 0.5 h. The crude oil acquired was subjected to flash chromatography (13 g silica gel, 9:1 petroleum ether–diethyl ether) and the resultant liquid was distilled to afford 189 mg (77%) of 3-trimethylgermylcyclohexanone (**229**). The spectral data were identical with those reported above.

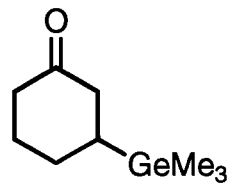
3.4.2.1.2 Preparation of 3-Trimethylgermylcyclohexanone (**229**) Using Lithium Bis-(trimethylgermyl)cuprate (**222**)



229

Following general procedure 9, to a cold (–78 °C) stirred solution of $(Me_3Ge)_2CuLi$ (**222**) (0.70 mmol, 0.65 equiv) in dry THF (12.1 mL), prepared as described above (section 3.4.1.1, p 265), was added a solution of cyclohex-2-en-1-one (**226**) (104 mg, 1.08 mmol, 1 equiv) in dry THF (2.5 mL). The black mixture was stirred at –78 °C for 0.5 h. The crude oil acquired was subjected to flash chromatography (11 g silica gel, 17:3 petroleum ether–diethyl ether) and the derived oil was distilled to afford 198 mg (86%) of 3-trimethylgermyl-cyclohexanone (**229**). The spectral data were identical with those reported above.

3.4.2.1.3 Preparation of 3-Trimethylgermylcyclohexanone (**229**) Using Lithium (Trimethyl-germyl)cyanocuprate (**223**)

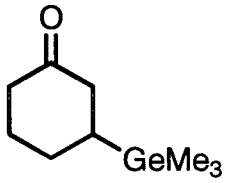


229

Following general procedure 9, to a cold (–78 °C) stirred solution of $Me_3GeCu(CN)Li$ (**223**) (1.52 mmol, 1.30 equiv) in dry THF (12.1 mL), prepared as described above (section 3.4.1.2, p 265), was added a solution of cyclohex-2-en-1-one (**226**) (113 mg, 1.17 mmol, 1

equiv) in dry THF (2.5 mL). The orange mixture was stirred at –78 °C for 0.5 h. The crude oil acquired was subjected to flash chromatography (10 g TLC grade silica gel, 17:3 petroleum ether–diethyl ether) and the resultant oil was distilled to afford 227 mg (90%) of 3-trimethylgermylcyclohexanone (**229**). The spectral data were identical with those reported above.

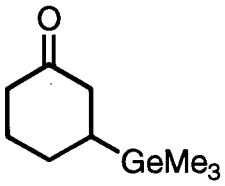
3.4.2.1.4 Preparation of 3-Trimethylgermylcyclohexanone (**229**) Using Dilithium Bis-(trimethylgermyl)cyanocuprate (**224**)



229

Following general procedure 9, to a cold (–78 °C) stirred solution of $(Me_3Ge)_2Cu(CN)Li_2$ (**224**) (0.70 mmol, 0.65 equiv) in dry THF (12.1 mL), prepared as described above (section 3.4.1.3, p 266), was added a solution of cyclohex-2-en-1-one (**226**) (113 mg, 1.17 mmol, 1 equiv) in dry THF (2.5 mL). The orange solution was stirred at –78 °C for 0.5 h. The crude oil acquired was subjected to flash chromatography (14 g silica gel, 17:3 petroleum ether–diethyl ether) and the derived oil was distilled to afford 213 mg (85%) of 3-trimethylgermylcyclohexanone (**229**). The spectral data were identical with those reported above.

3.4.2.1.5 Preparation of 3-Trimethylgermylcyclohexanone (**229**) Using Dilithium Methyl-(trimethylgermyl)cyanocuprate (**225**)

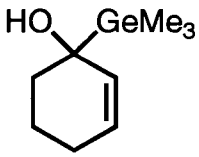


229

Following general procedure 9, to a cold (–78 °C) stirred solution of $Me_3Ge(Me)Cu(CN)Li_2$ (**225**) (1.43 mmol, 1.30 equiv) in dry THF (12.1 mL), prepared as described above (section 3.4.1.4, p 266), was added a solution of cyclohex-2-en-1-one (**226**) (106 mg, 1.10 mmol, 1 equiv) in dry THF (2.5 mL). The clear colorless solution was stirred at –78 °C for 0.5 h. The crude oil acquired was subjected to flash chromatography (13 g silica gel, 17:3 petroleum ether–diethyl ether) and the resultant liquid was distilled to afford 207 mg (87%) of 3-trimethylgermylcyclohexanone (**229**). The spectral data were identical with those reported above.

3.4.2.2 ADDITION OF TRIMETHYLGERMYLLITHIUM (**149**) TO CYCLOHEX-2-EN-1-ONE (**226**)

3.4.2.2.1 Synthesis of 1-Trimethylgermylcyclohex-2-en-1-ol (**230**)



230

A cold (–10 °C) stirred solution of Me_3GeLi (**149**) (2.07 mmol, 1.30 equiv) in dry THF (0.9 mL), prepared as described above (section 3.3.2.1.1, p 221), was transferred via a

cannula to cold (–78 °C) stirred dry THF (16 mL). The flask that initially contained the Me_3GeLi solution was rinsed with dry THF (2 × 1 mL) and the rinses were transferred via a cannula to the cold (–78 °C) stirred dry THF. After the solution had been stirred for 5 min, a solution of cyclohex-2-en-1-one (**226**) (153 mg, 1.59 mmol, 1 equiv) in dry THF (2 mL) was added via a cannula. The reaction mixture was stirred at –78 °C for 5 min, then was poured into a stirred solution of NH_4Cl–NH_4OH (pH 8–9, 20 mL) and diethyl ether (30 mL) was added to the mixture. The layers were separated and the aqueous portion was extracted with ethyl acetate (2 × 10 mL). The combined organic extracts were washed with water (2 × 10 mL) and brine (10 mL), were dried over anhydrous magnesium sulfate, and then were filtered and concentrated under reduced pressure. The crude oil acquired was subjected to flash chromatography (35 g TLC grade silica gel, 49:1 CH_2Cl_2–diethyl ether) to afford two fractions which were concentrated under reduced pressure. The first fraction to be eluted afforded 69 mg (20%) of 3-trimethylgermylcyclohexanone (**229**). The spectral data were identical with those reported above (section 3.4.2.1, p 268). The second fraction to be eluted was distilled (130–140 °C/9 Torr) to afford 202 mg (59%) of 1-trimethylgermylcyclohex-2-en-1-ol (**230**) as a clear colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.75 (ddd, 1H, J = 9.8, 3.8 and 3.0 Hz, -CH=C<u>H</u>CH$_2$-), 5.69 (ddd, 1H, J = 9.8, 1.4 and 1.4 Hz, -C<u>H</u>=CHCH$_2$-), 2.08–1.98 (m, 1H), 1.94–1.72 (m, 3H), 1.68–1.50 (m, 2H), 1.27 (s, 1H, exchanges with D_2O, -OH), 0.17 (s, 9H, -Ge(CH$_3$)$_3$).

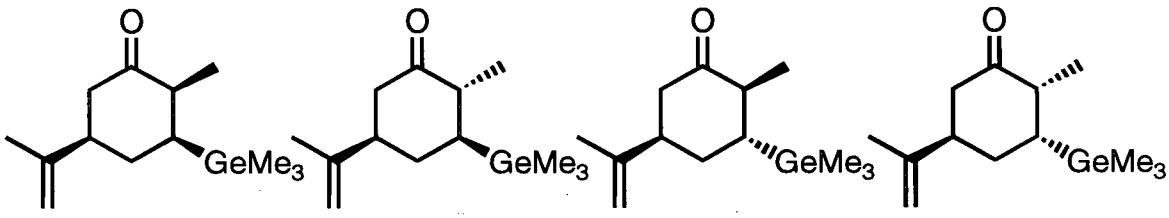
^{13}C NMR (75.4 MHz, $CDCl_3$): δ 131.4 (vinylic carbon), 128.4 (vinylic carbon), 67.7 (tetra-substituted carbon), 34.0, 25.0, 18.3, –4.6 (-Ge(CH$_3$)$_3$).

IR (film): 3435, 3016, 2932, 1234, 823, 737, 602 cm^{-1}.

HRMS for $C_9H_{18}{}^{74}GeO$: calcd 216.0569, found 216.0567.

Anal. calcd for $C_9H_{18}GeO$: C 50.32, H 8.45; found: C 50.36, H 8.52.

3.4.2.3 GENERAL PROCEDURE 10: SYNTHESIS OF (2*R*,3*S*,5*S*)-, (2*S*,3*S*,5*S*)- (2*R*,3*R*,5*S*)- AND (2*S*,3*R*,5*S*)-5-ISOPROPENYL-2-METHYL-3-TRIMETHYLGERMYLCYCLOHEXANONE (**234**)–(**237**) FROM *l*-CARVONE (**227**)



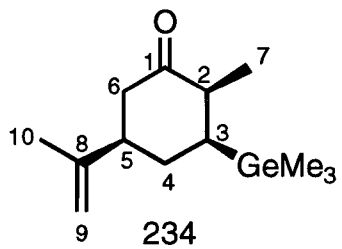
234 **235** **236** **237**

To a cold (–78 °C) stirred solution of the appropriate (trimethylgermyl)copper(I) reagent (1.3 equiv) in dry THF, was added chlorotrimethylsilane (1.3 equiv) via a syringe. After the mixture had been stirred for 5 min, a solution of *l*-carvone (**227**) (1 equiv) in dry THF was added via a cannula. The reaction mixture was stirred at –78 °C for 0.5 h, then was warmed to 0 °C over a 0.5 h period. The mixture was poured into stirred aqueous NH_4Cl–NH_4OH (pH 8–9, ≈20 mL per mmol of enone) and diethyl ether (≈20 mL per mmol of enone) was added to the mixture. The heterogeneous mixture was stirred vigorously, open to the atmosphere, until the aqueous layer was deep blue. The layers were separated and the aqueous portion was extracted with diethyl ether (2 × ≈10 mL per mmol of enone). The combined organic extracts were washed with water (2 × ≈10 mL per mmol of enone) and brine (≈10 mL per mmol of enone), were dried over anhydrous magnesium sulfate, and then were filtered and concentrated under reduced pressure. The crude oil acquired was dissolved

in THF (≈0.07 M; this reaction was not performed under an atmosphere of argon) and 1 M hydrochloric acid (6 drops) was added. After the mixture had been stirred at rt for 1 h, diethyl ether (≈20 mL per mmol of enone) was added, the organic layer was dried over anhydrous magnesium sulfate, and then was filtered and concentrated under reduced pressure. The crude oil obtained was subjected to flash chromatography and the derived oil was distilled to afford a mixture of the four diastereomeric 5(*S*)-isopropenyl-2-methyl-3-trimethylgermylcyclohexanones (**234**)–(**237**) as a clear colorless oil.

3.4.2.3.1 Isolation and Characterization of the Four Diastereomeric 5(*S*)-Isopropenyl-2-methyl-3-trimethylgermylcyclohexanones (**234**)–(**237**)

*a) Isolation and Characterization of (2R,3S,5S)-5-Isopropenyl-2-methyl-3-trimethylgermylcyclohexanone (**234**)*



Two samples (≈100 mg each) of a mixture of the four diastereomeric 5(*S*)-isopropenyl-2-methyl-3-trimethylgermylcyclohexanones were subjected to HPLC (silica Partisil, 10 μm; 22 mm × 250 mm column, 99:1 hexane–ethyl acetate, 9 mL/min, RI detector) individually. These chromatographies resulted in a rough separation to afford three fractions, which were concentrated under reduced pressure. The corresponding fractions of the two samples were pooled, and the isolated amounts are derived from the pooled fractions. The

first fraction to be eluted, fraction ***A*** (retention time 42–52 min), afforded 45 mg of an oil which consisted of a mixture of two components (compounds **237** and **235**). The second fraction to be eluted, fraction ***B*** (retention time 53–62 min) afforded 28 mg of an oil which was mostly one component (compound **236**). The third fraction to be eluted (retention time 65–78 min) afforded 28 mg of (2*R*,3*S*,5*S*)-5-isopropenyl-2-methyl-3-trimethylgermylcyclohexanone (**234**) as a clear colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 4.75 (s, 1H, H-9a), 4.73 (s, 1H, H-9b), 2.55 (qd, 1H, J = 7.2 and 4.0 Hz, H-2), 2.50 (dd, 1H, J = 13.0 and 13.0 Hz, H-6a), 2.42–2.32 (m, 1H, H-5), 2.24 (ddd, 1H, J = 13.0, 1.8 and 1.8 Hz, H-6b), 1.77–1.60 (m, 5H, H-4a, H-4b and -CH_3-10), 1.39 (ddd, 1H, J = 13.4, 4.0 and 3.8 Hz, H-3), 1.12 (d, 3H, J = 7.2 Hz, -CH_3-7), 0.15 (s, 9H, -$Ge(CH_3)_3$).

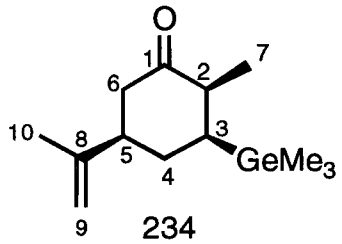
Detailed ^{1}H NMR data, derived from COSY and NOE difference experiments, are given in **Table 23**.

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 215.5 (-CO-), 147.7 (-$\underline{C}$(=CH_2)-), 109.6 (-C(=$\underline{C}H_2$)-), 49.8, 46.3, 42.4 (secondary carbon), 32.2, 26.8 (secondary carbon), 20.5, 14.7, –2.7 (-$Ge(CH_3)_3$).

IR (film): 3083, 2970, 1708, 1645, 1237, 891, 824, 599 cm^{-1}.

HRMS for $C_{13}H_{24}{}^{74}GeO$: calcd 270.1039, found 270.1041.

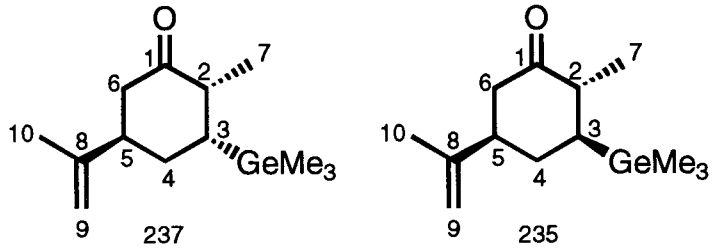
Table 23: ^{1}H NMR Data from ^{1}H–^{1}H Homonuclear Correlation Spectroscopy and Nuclear Overhauser Enhancement Difference Experiments for (2*R*,3*S*,5*S*)-5-Isopropenyl-2-methyl-3-trimethylgermylcyclohexan-1-one (**234**)



Assignments H-x	^{1}H NMR[a] δ ppm (mult, *J* (Hz))	COSY Correlations	Observed NOEs
H-9a	4.75 (s)	-CH_3-10	
H-9b	4.73 (s)	-CH_3-10	
H-2	2.55 (qd, 7.2, 4.0)	H-3, -CH_3-7	
H-6a	2.50 (dd, 13.0, 13.0)	H-5, H-6b	
H-5[b]	2.42–2.32 (m)	H-4a, H-4b, H-6a, H-6b	H-3, H-4b, H-9b
H-6b	2.24 (ddd, 13.0, 1.8, 1.8)	H-4b, H-5, H-6a	
H-4a	1.77–1.66 part of 1.77–1.60 (m)	H-3, H-4b, H-5	
-CH_3-10	1.73 part of 1.77–1.60 (m)	H-9a, H-9b	
H-4b	1.66–1.60 part of 1.77–1.60 (m)	H-3, H-4a, H-5, H-6b	
H-3[b]	1.39 (ddd, 13.4, 4.0, 3.8)	H-2, H-4a, H-4b	H-2, H-5
-CH_3-7[b]	1.12 (d, 7.2)	H-2	H-2, H-6a
-$Ge(CH_3)_3$[b]	0.15 (s)		H-2, H-3, H-4b, -CH_3-7

[a] 400 MHz, $CDCl_3$. [b] Irradiation of this signal generated the corresponding NOEs in the right hand column.

*b) Isolation and Characterization of (2S,3R,5S)- and (2S,3S,5S)-5-Isopropenyl-2-methyl-3-trimethylgermylcyclohexanone (**237**) and (**235**)*



Fraction ***A*** (45 mg) was subjected to reversed phase HPLC (C_{18} μBondapak, 10 μm; 8 mm × 100 mm column, 40:60 to 65:35 acetonitrile–water, 5% step increments/10 min, 1 mL/min, UV-vis detector λ = 254 nm) in four approximately equal portions. The combined first fractions to be eluted (retention time 56 min) were distilled (72–82 °C/0.007 Torr) to afford 23 mg of (2*S*,3*R*,5*S*)-5-isopropenyl-2-methyl-3-trimethylgermylcyclohexanone (**237**).

^{1}H NMR (400 MHz, C_6D_6): δ 4.73 (s, 2H, H-9a and H-9b), 2.43 (ddd, 1H, *J* = 13.6, 4.8 and 2.0 Hz, H-6a), 2.35–2.25 (m, 2H, H-2 and H-5), 2.07 (dd, 1H, *J* = 13.6 and 11.2 Hz, H-6b), 1.82 (dddd, 1H, *J* = 13.6, 5.2, 4.6 and 2.0 Hz, H-4a), 1.56–1.47 (m, 4H, H-4b and -CH_3-10), 1.38 (ddd, 1H, *J* = 6.2, 4.6 and 4.6 Hz, H-3), 1.07 (d, 3H, *J* = 6.2 Hz, -CH_3-7), 0.10 (s, 9H, -$Ge(CH_3)_3$).

Detailed ^{1}H NMR data, derived from COSY and NOE difference experiments, are given in **Table 24**.

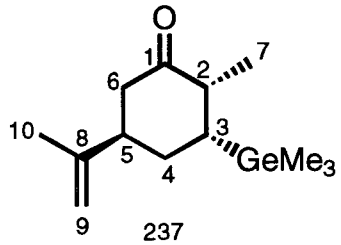
^{13}C NMR (75.4 MHz, $CDCl_3$): δ 212.8 (-CO-), 147.3 (-$\underline{C}$(=CH_2)-), 110.3 (-C(=$\underline{C}H_2$)-), 47.8, 45.4 (secondary carbon), 44.6, 32.4 (secondary carbon), 32.2, 20.9, 14.9, –0.8 (-$Ge(CH_3)_3$).

IR (film): 3075, 2972, 1713, 1646, 1238, 892, 826, 596 cm^{-1}.

HRMS for $C_{13}H_{24}{}^{74}GeO$: calcd 270.1039, found 270.1037.

Anal. calcd for $C_{13}H_{24}GeO$: C 58.06, H 9.00; found: C 58.00, H 9.00.

Table 24: ^{1}H NMR Data from ^{1}H–^{1}H Homonuclear Correlation Spectroscopy and Nuclear Overhauser Enhancement Difference Experiments for (2*S*,3*R*,5*S*)-5-Isopropenyl-2-methyl-3-trimethylgermylcyclohexanone (**237**)



Assignments H-x	^{1}H NMR[a] δ ppm (mult, *J* (Hz))	COSY Correlations	Observed NOEs
H-9a and H-9b	4.73 (s)	-CH_3-10	
H-6a	2.43 (ddd, 13.6, 4.8, 2.0)	H-4a, H-5, H-6b	
H-2 and H-5	2.35–2.25 (m)	H-3, H-4a, H-4b, H-6a, H-6b, -CH_3-7	
H-6b[b]	2.07 (dd, 13.6, 11.2)	H-5, H-6a	H-2, H-6a, H-9, -CH_3-10
H-4a	1.82 (dddd, 13.6, 5.2, 4.6, 2.0)	H-3, H-4b, H-5, H-6a	
H-4b and -CH_3-10	1.56–1.47 (m)	H-3, H-4a, H-5, H-9a, H-9b	
H-3[b]	1.38 (ddd, 6.2, 4.6, 4.6)	H-2, H-4a, H-4b	H-2, H-4a
-CH_3-7[b]	1.07 (d, 6.2)	H-2	H-2, H-3, -$Ge(CH_3)_3$
-$Ge(CH_3)_3$[b]	0.10 (s)		H-3, H-4a, H-5, -CH_3-7

[a] 400 MHz, C_6D_6. [b] Irradiation of this signal generated the corresponding NOEs in the right hand column.

The combined second fractions to be eluted (retention time 59 min) afforded 9.8 mg of (2*S*,3*S*,5*S*)-5-isopropenyl-2-methyl-3-trimethylgermylcyclohexanone (**235**).

^{1}H NMR (400 MHz, C_6D_6): δ 4.69 (d, 1H, *J* = 1.4 Hz, H-9a), 4.64 (d, 1H, *J* = 1.4 Hz, H-9b), 2.48 (ddd, 1H, *J* = 12.4, 3.5 and 2.4 Hz, H-6a), 2.21–2.11 (m, 1H, H-5), 1.97 (dd, 1H, *J* = 13.2 and 12.4 Hz, H-6b), 1.92 (dq, 1H, *J* = 13.2 and 6.6 Hz, H-2), 1.69 (dddd, 1H, *J* = 13.2, 3.2, 3.2 and 2.4 Hz, H-4a), 1.50 (s, 3H, -CH_3-10), 1.22 (ddd, 1H, *J* = 13.2, 13.2 and 11.8 Hz, H-4b), 1.08 (d, 3H, *J* = 6.6 Hz, -CH_3-7), 0.77 (ddd, 1H, *J* = 13.2, 13.2 and 3.2 Hz, H-3), 0.04 (s, 9H, -$Ge(CH_3)_3$).

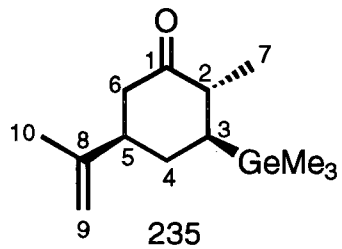
Detailed ^{1}H NMR data, derived from COSY and NOE difference experiments, are given in **Table 25**.

^{13}C NMR (75.4 MHz, C_6D_6): δ 210.4 (-CO-), 147.9 (-$\underline{C}$(=CH_2)-), 109.6 (-C(=$\underline{C}H_2$)-), 49.5, 46.75 (secondary carbon), 46.70, 35.2, 34.0 (secondary carbon), 20.4, 14.7, –2.4 (-$Ge(CH_3)_3$).

IR (film): 3080, 2972, 1713, 1645, 1237, 891, 824, 597 cm^{-1}.

HRMS for $C_{13}H_{24}{}^{74}GeO$: calcd 270.1039, found 270.1043.

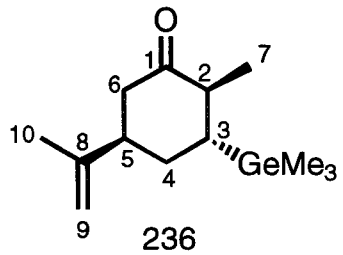
Table 25: ^{1}H NMR Data from ^{1}H–^{1}H Homonuclear Correlation Spectroscopy and Nuclear Overhauser Enhancement Difference Experiments for (2*S*,3*S*,5*S*)-5-Isopropenyl-2-methyl-3-trimethylgermylcyclohexanone (**235**)



Assignments H-x	^{1}H NMR[a] δ ppm (mult, *J* (Hz))	COSY Correlations	Observed NOEs
H-9a	4.69 (d, 1.4)	-CH_3-10	
H-9b	4.64 (d, 1.4)	-CH_3-10	
H-6a	2.48 (ddd, 12.4, 3.5, 2.4)	H-4a, H-5, H-6b	
H-5[b]	2.21–2.11 (m)	H-4a, H-4b, H-6a, H-6b	H-3, H-4a, H-6a, H-9b, -CH_3-10
H-6b	1.97 (dd, 13.2, 12.4)	H-5, H-6a	
H-2	1.92 (dq, 13.2, 6.6)	H-3, -CH_3-7	
H-4a	1.69 (dddd, 13.2, 3.2, 3.2, 2.4)	H-3, H-4b, H-5, H-6a	
-CH_3-10	1.50 (s)	H-9a, H-9b	
H-4b[b]	1.22 (ddd, 13.2, 13.2, 11.8)	H-3, H-4a, H-5	H-2, H-4a, H-6b
-CH_3-7[b]	1.08 (d, 6.6)	H-2	H-2, H-3, neg. H-6b,[c] -$Ge(CH_3)_3$
H-3[b]	0.77 (ddd, 13.2, 13.2, 3.2)	H-2, H-4a, H-4b	H-4a, H-5, -CH_3-7
-$Ge(CH_3)_3$[b]	0.04 (s)		H-2, H-3, H-4a, H-4b, -CH_3-7

[a] 400 MHz, C_6D_6. [b] Irradiation of this signal generated the corresponding NOEs in the right hand column. [c] This signal appeared negative as a result of a possible relay NOE from H-2.

*c) Isolation and Characterization of (2R,3R,5S)-5-Isopropenyl-2-methyl-3-trimethylgermyl-cyclohexanone (**236**)*



Fraction ***B*** (28 mg) from the initial chromatography was resubjected to HPLC under identical conditions (silica Partisil, 10 μm; 22 mm × 250 mm column, 99:1 hexane–ethyl acetate, 9 mL/min, RI detector) and the acquired liquid was distilled (60–70 °C/0.007 Torr) to afford 8.2 mg of (2*R*,3*R*,5*S*)-5-isopropenyl-2-methyl-3-trimethylgermylcyclohexanone (**236**).

^{1}H NMR (400 MHz, C_6D_6): δ 4.94 (s, 1H, H-9a), 4.86 (s, 1H, H-9b), 2.58 (ddd, 1H, *J* = 14.2, 4.4 and 2.0 Hz, H-6a), 2.41–2.34 (m, 1H, H-5), 2.11 (dd, 1H, *J* = 14.2 and 6.0 Hz, H-6b), 2.01 (dq, 1H, *J* = 11.0 and 6.8 Hz, H-2), 1.69 (dddd, 1H, *J* = 13.8, 4.6, 3.6 and 2.0 Hz, H-4a), 1.50 (s, 3H, -CH_3-10), 1.38 (ddd, 1H, *J* = 13.8, 11.0 and 4.6 Hz, H-4b), 1.12 (ddd, 1H, *J* = 11.0, 11.0 and 3.6 Hz, H-3), 1.07 (d, 3H, *J* = 6.8 Hz, -CH_3-7), 0.05 (s, 9H, -$Ge(CH_3)_3$).

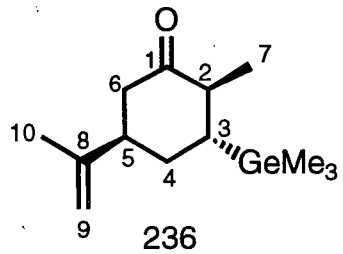
Detailed ^{1}H NMR data, derived from COSY and NOE difference experiments, are given in **Table 26**.

^{13}C NMR (75.4 MHz, C_6D_6): δ 210.8 (-CO-), 146.5 (-$\underline{C}$(=CH_2)-), 112.9 (-C(=$\underline{C}H_2$)-), 47.2, 44.5 (secondary carbon), 44.0, 30.1, 29.9 (secondary carbon), 21.9, 15.6, –2.5 (-$Ge(CH_3)_3$).

IR (film): 3080, 2971, 1708, 1645, 1451, 1237, 986, 824, 597 cm^{-1}.

HRMS for $C_{13}H_{24}{}^{74}GeO$: calcd 270.1039, found 270.1031.

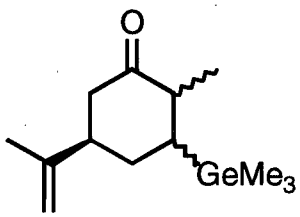
Table 26: ^{1}H NMR Data from ^{1}H–^{1}H Homonuclear Correlation Spectroscopy and Nuclear Overhauser Enhancement Difference Experiments for (2*R*,3*R*,5*S*)-5-Isopropenyl-2-methyl-3-trimethylgermylcyclohexanone (**236**)



Assignments H-x	^{1}H NMR[a] δ ppm (mult, *J* (Hz))	COSY Correlations	Observed NOEs
H-9a[b]	4.94 (s)	-CH_3-10	H-3, H-5, H-6a
H-9b	4.86 (s)	-CH_3-10	
H-6a	2.58 (ddd, 14.2, 4.4, 2.0)	H-4a, H-5, H-6b	
H-5	2.41–2.34 (m)	H-4a, H-4b, H-6a, H-6b	
H-6b	2.11 (dd, 14.2, 6.0)	H-5, H-6a	
H-2	2.01 (dq, 11.0, 6.8)	H-3, -CH_3-7	
H-4a	1.69 (dddd, 13.8, 4.6, 3.6, 2.0)	H-3, H-4b, H-5, H-6a	
-CH_3-10	1.50 (s)	H-9a, H-9b	
H-4b[b]	1.38 (ddd, 13.8, 11.0, 4.6)	H-3, H-4a, H-5	H-2, H-4a, H-5, H-6b
H-3	1.12 (ddd, 11.0, 11.0, 3.6)	H-2, H-4a, H-4b	
-CH_3-7	1.07 (d, 6.8)	H-2	
-$Ge(CH_3)_3$	0.05 (s)		

[a] 400 MHz, C_6D_6. [b] Irradiation of this signal generated the corresponding NOEs in the right hand column.

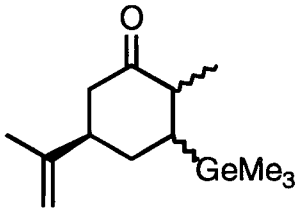
3.4.2.3.2 Preparation of the Diastereomeric Mixture of Four 5(*S*)-Isopropenyl-2-methyl-3-trimethylgermylcyclohexanones (**234**)–(**237**) Using (Trimethylgermyl)copper(I)–Dimethyl Sulfide (**168**)



234–237

Following general procedure 10, to a cold (–78 °C) stirred solution of $Me_3GeCu{\bullet}Me_2S$ (**168**) (1.43 mmol, 1.30 equiv) in dry THF (12.1 mL), prepared as described above (section 3.3.2.2, p 223), was added sequentially chlorotrimethylsilane (155 mg, 1.43 mmol, 1.30 equiv) via a syringe and a solution of *l*-carvone (**227**) (165 mg, 1.10 mmol, 1 equiv) in dry THF (2.5 mL) via a cannula. The crude oil acquired was subjected to flash chromatography (30 g TLC grade silica gel, 9:1 petroleum ether–diethyl ether) and the derived oil was distilled (95–105 °C/0.5 Torr) to afford 243 mg (82%) of the diastereomeric mixture of four 5(*S*)-isopropenyl-2-methyl-3-trimethylgermylcyclohexanones (**234**)–(**237**). ^{1}H NMR spectroscopic analysis indicated a 2.4:1:3.4:1.5 ratio of the 2*S*,3*R*:2*R*,3*R*:2*S*,3*S*:2*R*,3*S* diastereomers.

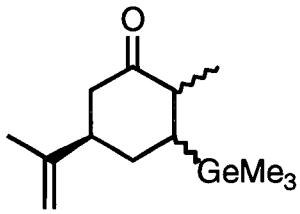
3.4.2.3.3 Preparation of the Diastereomeric Mixture of Four 5(*S*)-Isopropenyl-2-methyl-3-trimethylgermylcyclohexanones (**234**)–(**237**) Using Lithium (Trimethylgermyl)cyanocuprate (**223**)



234–237

Following general procedure 10, to a cold (–78 °C) stirred solution of $Me_3GeCu(CN)Li$ (**223**) (1.39 mmol, 1.30 equiv) in dry THF (12.1 mL), prepared as described above (section 3.4.1.2, p 265), was added sequentially chlorotrimethylsilane (151 mg, 1.39 mmol, 1.30 equiv) via a syringe and a solution of *l*-carvone (**227**) (161 mg, 1.07 mmol, 1 equiv) in dry THF (2.5 mL) via a cannula. The crude oil acquired was subjected to flash chromatography (30 g TLC grade silica gel, 9:1 petroleum ether–diethyl ether) and the derived oil was distilled (100–110 °C/0.1 Torr) to afford 230 mg (80%) of the diastereomeric mixture of four 5(*S*)-isopropenyl-2-methyl-3-trimethylgermylcyclohexanones (**234**)–(**237**). ^{1}H NMR spectroscopic analysis indicated a 2.2:1:3.1:1.3 ratio of the 2*S*,3*R*:2*R*,3*R*:2*S*,3*S*:2*R*,3*S* diastereomers.

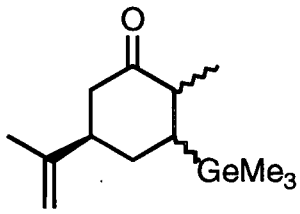
3.4.2.3.4 Preparation of the Diastereomeric Mixture of Four 5(*S*)-Isopropenyl-2-methyl-3-trimethylgermylcyclohexanones (**234**)–(**237**) Using Dilithium Bis(trimethylgermyl)cyano-cuprate (**224**)



234–237

Following general procedure 10, to a cold (–78 °C) stirred solution of $(Me_3Ge)_2Cu(CN)Li_2$ (**224**) (0.69 mmol, 0.65 equiv) in dry THF (12.1 mL), prepared as described above (section 3.4.1.3, p 266), was added sequentially chlorotrimethylsilane (150 mg, 1.38 mmol, 1.30 equiv) via a syringe and a solution of *l*-carvone (**227**) (160 mg, 1.06 mmol, 1 equiv) in dry THF (2.5 mL) via a cannula. The crude oil acquired was subjected to flash chromatography (15 g TLC grade silica gel, 9:1 petroleum ether–diethyl ether) and the resultant oil was distilled (98–108 °C/0.06 Torr) to afford 246 mg (86%) of the diastereomeric mixture of four 5(*S*)-isopropenyl-2-methyl-3-trimethylgermylcyclohexanones (**234**)–(**237**). ^{1}H NMR spectroscopic analysis indicated a 3.9:1:2.5:1.1 ratio of the 2*S*,3*R*:2*R*,3*R*:2*S*,3*S*:2*R*,3*S* diastereomers.

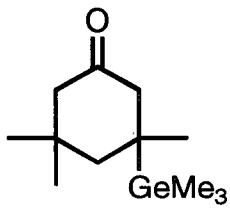
3.4.2.3.5 Preparation of the Diastereomeric Mixture of Four 5(*S*)-Isopropenyl-2-methyl-3-trimethylgermylcyclohexanones (**234**)–(**237**) Using Dilithium Methyl(trimethylgermyl)cyano-cuprate (**225**)



234–237

Following general procedure 10, to a cold (–78 °C) stirred solution of $Me_3Ge(Me)Cu(CN)Li_2$ (**225**) (1.38 mmol, 1.30 equiv) in dry THF (12.1 mL), prepared as described above (section 3.4.1.4, p 266), was added sequentially chlorotrimethylsilane (150 mg, 1.38 mmol, 1.30 equiv) via a syringe and a solution of *l*-carvone (**227**) (160 mg, 1.06 mmol, 1 equiv) in dry THF (2.5 mL) via a cannula. The crude oil acquired was subjected to flash chromatography (15 g TLC grade silica gel, 9:1 petroleum ether–diethyl ether) and the derived oil was distilled (95–105 °C/0.07 Torr) to afford 259 mg (90%) of the diastereomeric mixture of four 5(*S*)-isopropenyl-2-methyl-3-trimethylgermylcyclohexanones (**234**)–(**237**). ^{1}H NMR spectroscopic analysis indicated a 12:3.9:3.1:1 ratio of the 2*S*,3*R*:2*R*,3*R*:2*S*,3*S*:2*R*,3*S* diastereomers.

3.4.2.4 General Procedure 11: Synthesis of 3,5,5-Trimethyl-3-trimethylgermyl-cyclohexanone (**238**) from Isophorone (**228**)



238

To a cold (–78 °C) stirred solution of the appropriate (trimethylgermyl)copper(I) reagent (0.64–1.3 equiv) in dry THF was added a solution of isophorone (**228**) (1 equiv) in dry THF via a cannula to generate a final concentration of ≈0.08 M of the isophorone (**228**). The mixture was stirred at –78 °C, then was warmed to the indicated temperature and was allowed to stir for an additional period of time. The mixture was poured into stirred aqueous NH_4Cl–NH_4OH (pH 8–9, ≈20 mL per mmol of enone) and diethyl ether was added (≈40 mL per mmol of enone) to the mixture. The heterogeneous mixture was stirred vigorously, open to the atmosphere, until the aqueous layer was deep blue. The layers were separated and the aqueous portion was extracted with diethyl ether (2 × ≈10 mL per mmol of enone). The combined organic extracts were washed with water (2 × ≈10 mL per mmol of enone) and brine (≈10 mL per mmol of enone), were dried over anhydrous magnesium sulfate, and then were filtered and concentrated under reduced pressure. The crude oil acquired was subjected to flash chromatography to afford the title compound as a clear colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.35 (d, 1H, J = 13.0 Hz), 2.23 (d, 1H, J = 13.0 Hz), 2.10 (ddd, 1H, J = 13.0, 2.0 and 2.0 Hz), 2.00 (ddd, 1H, 13.0, 2.0 and 2.0 Hz), 1.74 (d, 1H, J = 13.0 Hz), 1.46 (ddd, 1H, J = 13.0, 2.0 and 2.0 Hz), 1.13 (s, 3H), 1.05 (s,

3H), 1.02 (s, 3H), 0.10 (s, 9H, -Ge(CH_3)$_3$).

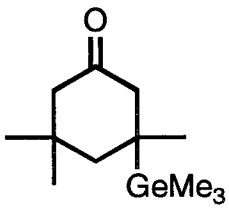
^{13}C NMR (75.4 MHz, $CDCl_3$): δ 213.0 (-CO-), 54.4, 47.8, 44.9, 39.1 (quaternary carbon), 34.2 (-CH_3), 29.1 (-CH_3), 28.4 (quaternary carbon), 22.7 (-CH_3), –5.6 (-Ge(CH_3)$_3$).

IR (film): 1713, 1273, 1238, 823, 597 cm^{-1}.

HRMS for $C_{12}H_{24}{}^{74}GeO$: calcd 258.1039, found 258.1032.

Anal. calcd for $C_{12}H_{24}GeO$: C 56.10, H 9.42; found: C 56.48, H 9.47.

3.4.2.4.1 Preparation of 3,5,5-Trimethyl-3-trimethylgermylcyclohexanone (**238**) Using Dilithium Bis(trimethylgermyl)cyanocuprate (**224**)

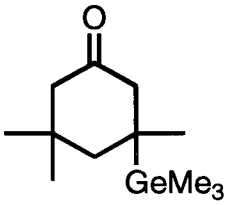


238

Following general procedure 11, to a cold (–78 °C) stirred solution of $(Me_3Ge)_2Cu(CN)Li_2$ (**224**) (0.32 mmol, 0.64 equiv) in dry THF (4.8 mL), prepared as described above (section 3.4.1.3, p 266), was added a solution of isophorone (**228**) (69 mg, 0.50 mmol, 1 equiv) in dry THF (1.5 mL) via a cannula. After the mixture had been stirred at –78 °C for 1 h, dry HMPA (0.23 mL) was added via a syringe. The mixture was allowed to stir for an additional 0.5 h at –78 °C, then it was warmed to 0 °C over a 0.5 h period. The crude oil obtained was subjected to flash chromatography (18 g silica gel, 4:1 then 3:2 petroleum ether–diethyl ether) to afford two fractions, which were concentrated under reduced pressure. The first fraction to be eluted afforded 54 mg (42%) of 3,5,5-trimethyl-3-

trimethylgermylcyclohexanone (**238**) as a clear colorless oil. The spectral data were identical with those reported above. The second fraction to be eluted afforded 30 mg (43%) of unreacted isophorone (**228**).

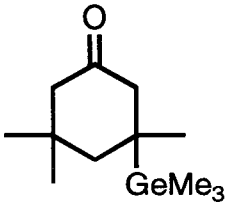
3.4.2.4.2 Preparation of 3,5,5-Trimethyl-3-trimethylgermylcyclohexanone (**238**) Using Dilithium Methyl(trimethylgermyl)cyanocuprate (**225**)



238

Following general procedure 11, to a cold (–78 °C) stirred solution of $Me_3Ge(Me)Cu(CN)Li_2$ (**225**) (0.59 mmol, 1.20 equiv) in dry THF (5 mL), prepared as described above (section 3.4.1.4, p 266), was added a solution of isophorone (**228**) (68 mg, 0.49 mmol, 1 equiv) in dry THF (1.2 mL) via a cannula. The orange mixture was stirred at –78 °C for 1 h, then was warmed to 0 °C over a 45 min period. The crude oil obtained was subjected to flash chromatography (18 g silica gel, 4:1 then 3:2 petroleum ether–diethyl ether) to afford two fractions which were concentrated under reduced pressure. The first fraction to be eluted afforded 42 mg (33%) of 3,5,5-trimethyl-3-trimethylgermylcyclohexanone (**238**) as a clear colorless oil. The spectral data were identical with those reported above. The second fraction to be eluted afforded 25 mg (37%) of unreacted isophorone (**228**).

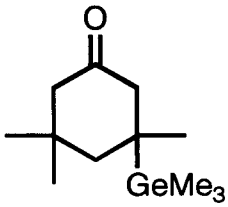
3.4.2.4.3 Preparation of 3,5,5-Trimethyl-3-trimethylgermylcyclohexanone (**238**) Using Dilithium Methyl(trimethylgermyl)cyanocuprate (**225**) and Chlorotrimethylsilane as Additive



238

Following general procedure 11, to a cold (–78 °C) stirred solution of $Me_3Ge(Me)Cu(CN)Li_2$ (**225**) (0.60 mmol, 1.20 equiv) in dry THF (5 mL), prepared as described above (section 3.4.1.4, p 266), was added chlorotrimethylsilane (65 mg, 0.60 mmol, 1.20 equiv) via a syringe. After the mixture had been stirred for 5 min, a solution of isophorone (**228**) (69 mg, 0.50 mmol, 1 equiv) in dry THF (1.2 mL) was added via a cannula. The orange mixture was stirred at –78 °C for 1 h, then was warmed to –30 °C over a 30 min period and was allowed to stir for an additional 1 h. The crude oil obtained was dissolved in THF (5 mL) and 1 M hydrochloric acid (2 drops) was added. The mixture was stirred at rt for 1 h and diethyl ether (5 mL) was added. The mixture was dried over anhydrous magnesium sulfate, and then was filtered and concentrated under reduced pressure. GLC analysis of the crude mixture revealed the presence of ≈20% of unreacted isophorone (**228**). The crude oil acquired was subjected to flash chromatography (10 g silica gel, 4:1 petroleum ether–diethyl ether) to afford 42 mg (33%) of 3,5,5-trimethyl-3-trimethylgermylcyclohexanone (**238**) as a clear colorless oil. The spectral data were identical with those reported above.

3.4.2.4.4 Preparation of 3,5,5-Trimethyl-3-trimethylgermylcyclohexanone (**238**) Using Dilithium Methyl(trimethylgermyl)cyanocuprate (**225**) and Bromotrimethylsilane as Additive

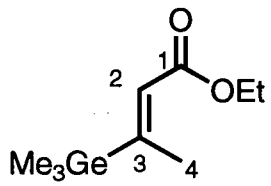


238

Following general procedure 11, to a cold (–78 °C) stirred solution of $Me_3Ge(Me)Cu(CN)Li_2$ (**225**) (1.51 mmol, 1.30 equiv) in dry THF (13.1 mL), prepared as described above (section 3.4.1.4, p 266), was added bromotrimethylsilane (0.70 g, 4.6 mmol, 4.0 equiv) via a cannula. After the mixture had been stirred for 5 min, a solution of isophorone (**228**) (160 mg, 1.16 mmol, 1 equiv) in dry THF (2 mL) was added via a cannula. The red–brown mixture was stirred at –78 °C for 1 h, then was warmed to –15 °C over a 2 h period. The crude oil obtained was dissolved in THF (15 mL) and 1 M hydrochloric acid (6 drops) was added. The mixture was stirred at rt for 1 h and diethyl ether (15 mL) was added. The mixture was dried over anhydrous magnesium sulfate, and then was filtered and concentrated under reduced pressure. The crude oil acquired was subjected to flash chromatography (25 g TLC grade silica gel, 4:1 petroleum ether–diethyl ether) and the derived oil was distilled (86–96 °C/0.05 Torr) to afford 198 mg (66%) of 3,5,5-trimethyl-3-trimethylgermylcyclohexanone (**238**) as a clear colorless oil. The spectral data were identical with those reported above.

3.4.3 ADDITION OF (TRIMETHYLGERMYL)COPPER(I)–DIMETHYL SULFIDE (168) AND (TRIMETHYLGERMYL)CUPRATES TO ACETYLENIC ESTERS

3.4.3.1 GENERAL PROCEDURE 12: SYNTHESIS OF ETHYL (*E*)-3-TRIMETHYLGERMYLBUT-2-ENOATE (**242**) FROM ETHYL BUT-2-YNOATE (**241**)



242

To a cold (–78 °C) stirred solution of the appropriate (trimethylgermyl)copper(I) reagent (0.66–1.32 equiv) in dry THF was added a solution of ethyl but-2-ynoate (**241**) (1 equiv) in dry THF via a cannula. The reaction mixture was stirred at –78 °C for 20–30 min, then acetic acid (1.5–3.9 equiv) was added via a syringe. The thick mixture was stirred for an additional 5 min, then was poured into stirred aqueous NH_4Cl–NH_4OH (pH 8–9, ≈20 mL per mmol of alkynoate) and diethyl ether (≈25 mL per mmol of alkynoate) was added to the mixture. The layers were separated and the aqueous portion was extracted with diethyl ether (2 × ≈10 mL per mmol of alkynoate). The combined organic extracts were washed with water (2 × ≈10 mL per mmol of alkynoate) and brine (2 × ≈10 mL per mmol of alkynoate), were dried over anhydrous magnesium sulfate and then were filtered and concentrated under reduced pressure. The crude oil acquired was subjected to flash chromatography and the derived oil was distilled (110–120 °C/11 Torr) to afford the title compound as a clear colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.95 (q, 1H, J = 1.8 Hz, vinylic proton), 4.14 (q, 2H, J = 7.2 Hz, -C<u>H</u>$_2$CH$_3$), 2.26 (d, 3H, J = 1.8 Hz, vinylic methyl), 1.27 (t, 3H, J = 7.2 Hz, -CH$_2$C<u>H</u>$_3$), 0.23 (s, 9H, -Ge(CH$_3$)$_3$).

Additional ^{1}H NMR data, derived from NOE difference experiments, are given in **Table 27**.

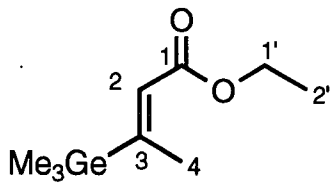
^{13}C NMR (75.4 MHz, $CDCl_3$): δ 165.3 (C=O or C-3), 165.2 (C=O or C-3), 124.8 (C-2), 59.5 (-CH$_2$-), 18.2, 14.3, –3.0 (-Ge(CH$_3$)$_3$).

IR (film): 1718, 1614, 1367, 1340, 1239, 1181, 1117, 1040, 826, 603 cm^{-1}.

HRMS (DCI, NH_3 + CH_4) for $C_9H_{19}{}^{74}GeO_2$ (M + 1)$^+$: calcd 233.0597, found 233.0597.

Anal. calcd for $C_9H_{18}GeO_2$: C 46.83, H 7.86; found: C 47.10, H 7.70.

Table 27: ^{1}H NMR Data from Nuclear Overhauser Enhancement Difference Experiments for Ethyl (*E*)-3-Trimethylgermylbut-2-enoate (**242**)

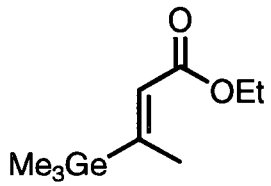


242

Assignments H-x	^{1}H NMR[a] δ ppm (mult, J (Hz))	Observed NOEs
H-2[b]	5.95 (q, 1.8)	-Ge(CH$_3$)$_3$
H-1'[b]	4.14 (q, 7.2)	H-2, -CH$_3$-2'
-CH$_3$-4[b]	2.26 (d, 1.8)	H-1', -Ge(CH$_3$)$_3$
-CH$_3$-2'	1.27 (t, 7.2)	
-Ge(CH$_3$)$_3$[b]	0.23 (s)	H-2, -CH$_3$-4

[a] 400 MHz, $CDCl_3$. [b] Irradiation of this signal generated the corresponding NOEs in the right hand column.

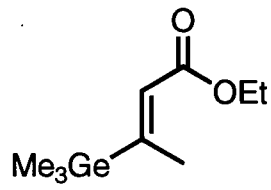
3.4.3.1.1 Preparation of Ethyl (*E*)-3-Trimethylgermylbut-2-enoate (**242**) Using Trimethylgermylcopper(I)–Dimethyl Sulfide (**168**)



242

Following general procedure 12, to a cold (–78 °C) stirred solution of $Me_3GeCu{\bullet}Me_2S$ (**168**) (1.11 mmol, 1.32 equiv) in dry THF (6.5 mL), prepared as described above (section 3.3.2.2, p 223), was added a solution of ethyl but-2-ynoate (**241**) (95 mg, 0.85 mmol, 1 equiv) in dry THF (1 mL) via a cannula. The black mixture was stirred at –78 °C for 30 min, then acetic acid (80 mg, 1.3 mmol, 1.5 equiv) was added via a syringe. The crude oil obtained was subjected to flash chromatography (20 g TLC grade silica gel, 32:1 petroleum ether–diethyl ether) and the derived liquid was distilled to afford 158 mg (81%) of ethyl (*E*)-3-trimethylgermylbut-2-enoate (**242**) as a clear colorless oil. The spectral data were identical with those reported above.

3.4.3.1.2 Preparation of Ethyl (*E*)-3-Trimethylgermylbut-2-enoate (**242**) Using Lithium (Trimethylgermyl)cyanocuprate (**223**)

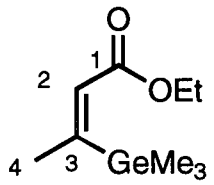


242

Following general procedure 12, to a cold (–78 °C) stirred solution of

$Me_3GeCu(CN)Li$ (**223**) (1.11 mmol, 1.30 equiv) in dry THF (10 mL), prepared as described above (section 3.4.1.2, p 265), was added a solution of ethyl but-2-ynoate (**241**) (97 mg, 0.86 mmol, 1 equiv) in dry THF (1.5 mL) via a cannula. The light orange mixture was stirred at –78 °C for 20 min, then acetic acid (0.20 g, 3.3 mmol, 3.9 equiv) was added via a syringe. The crude oil obtained was subjected to flash chromatography (10 g TLC grade silica gel, 32:1 petroleum ether–diethyl ether) and the derived oil was distilled to afford 180 mg (90%) of ethyl (*E*)-3-trimethylgermylbut-2-enoate (**242**) as a clear colorless oil. The spectral data were identical with those reported above.

3.4.3.2 SYNTHESIS OF ETHYL (*Z*)-3-TRIMETHYLGERMYLBUT-2-ENOATE (**243**) FROM ETHYL BUT-2-YNOATE (**241**) USING DILITHIUM METHYL(TRIMETHYLGERMYL)CYANOCUPRATE (**225**)



243

To a cold (–78 °C) stirred solution of $Me_3Ge(Me)Cu(CN)Li_2$ (**225**) (1.11 mmol, 1.30 equiv) in dry THF (10 mL), prepared as described above (section 3.4.1.4, p 266), was added a solution of ethyl but-2-ynoate (**241**) (96 mg, 0.86 mmol, 1 equiv) in dry THF (1.5 mL) via a cannula. The reaction mixture was stirred at –78 °C for 30 min, then acetic acid (0.13 g, 2.2 mmol, 2.6 equiv) was added via a syringe. The heterogeneous mixture was stirred for an additional 5 min, then was poured into stirred aqueous NH_4Cl–NH_4OH (pH 8–9, 15 mL) and diethyl ether (20 mL) was added to the mixture. The heterogeneous mixture was stirred vigorously, open to the atmosphere, until the aqueous layer was deep blue. The layers were

separated and the aqueous portion was extracted with diethyl ether (2 × 10 mL). The combined organic extracts were washed with water (2 × 10 mL) and brine (2 × 10 mL), were dried over anhydrous magnesium sulfate and then were filtered and concentrated under reduced pressure. The crude oil obtained was subjected to flash chromatography (20 g TLC grade silica gel, 49:1 petroleum ether–diethyl ether) to afford two fractions, which were concentrated under reduced pressure. The first fraction to be eluted afforded 137 mg (69%) of the ethyl (*Z*)-3-trimethylgermylbut-2-enoate (**243**) as a clear colorless oil. An analytically pure sample was obtained by distillation (100–110 °C/10 Torr).

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.28 (q, 1H, J = 1.6 Hz, vinylic proton), 4.13 (q, 2H, J = 7.2 Hz, -C<u>H</u>$_2$CH$_3$), 2.01 (d, 3H, J = 1.6 Hz, vinylic methyl), 1.26 (t, 3H, J = 7.2 Hz, -CH$_2$C<u>H</u>$_3$), 0.29 (s, 9H, -Ge(CH$_3$)$_3$).

Additional ^{1}H NMR data, derived from NOE difference experiments, are given in **Table 28**.

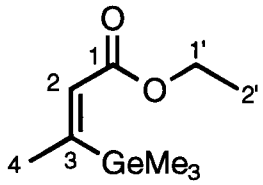
^{13}C NMR (75.4 MHz, $CDCl_3$): δ 166.5 (C=O or C-3), 166.0 (C=O or C-3), 128.4 (C-2), 59.8 (-CH$_2$-), 26.2, 14.3, –0.8 (-Ge(CH$_3$)$_3$).

IR (film): 1718, 1610, 1326, 1196, 1046, 832 cm^{-1}.

HRMS for $C_8H_{15}{}^{74}GeO_2$ (M – CH$_3$)$^+$: calcd 217.0284, found 217.0291.

Anal. calcd for $C_9H_{18}GeO_2$: C 46.83, H 7.86; found: C 46.94, H 7.87.

Table 28: ^{1}H NMR Data from Nuclear Overhauser Enhancement Difference Experiments for Ethyl (*Z*)-3-Trimethylgermylbut-2-enoate (**243**)



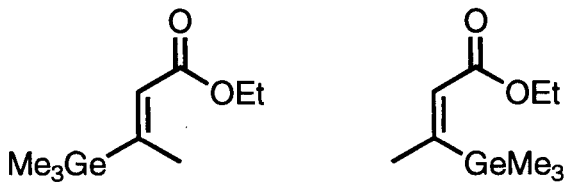
243

Assignments H-x	^{1}H NMR[a] δ ppm (mult, *J* (Hz))	Observed NOEs
H-2[b]	6.28 (q, 1.6)	H-1'
H-1'[b]	4.13 (q, 7.2)	H-2, -CH_3-2'
-CH_3-4[b]	2.01 (d, 1.6)	H-2, -$Ge(CH_3)_3$
-CH_3-2'	1.26 (t, 7.2)	
-$Ge(CH_3)_3$[b]	0.29 (s)	H-1', -CH_3-4

[a] 400 MHz, $CDCl_3$. [b] Irradiation of this signal generated the corresponding NOEs in the right hand column.

The second fraction to be eluted afforded 33 mg (17%) of ethyl (*E*)-3-trimethylgermylbut-2-enoate (**242**) as a clear colorless oil. The spectral data were identical with those reported above (see section 3.4.3.1, p 294).

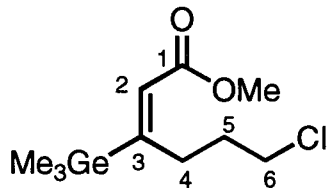
3.4.3.3 SYNTHESIS OF ETHYL (*E*)- AND (*Z*)-3-TRIMETHYLGERMYLBUT-2-ENOATE (**242**) AND (**243**) FROM ETHYL BUT-2-YNOATE (**241**) USING LITHIUM BIS(TRIMETHYLGERMYL)CUPRATE (**222**)



242 **243**

To a cold (–78 °C) stirred solution of $(Me_3Ge)_2CuLi$ (**222**) (0.56 mmol, 0.66 equiv) in dry THF (10 mL), prepared as described above (section 3.4.1.1, p 265), was added a solution of ethyl but-2-ynoate (**241**) (95 mg, 0.85 mmol, 1 equiv) in dry THF (1.5 mL) via a cannula. The light yellow mixture was stirred at –78 °C for 30 min, then acetic acid (80 mg, 1.3 mmol, 1.5 equiv) was added via a syringe. The black mixture was stirred for an additional 5 min, then was poured into stirred aqueous NH_4Cl–NH_4OH (pH 8–9, 15 mL) and diethyl ether (20 mL) was added to the mixture. The layers were separated and the aqueous portion was extracted with diethyl ether (2 × 10 mL). The combined organic extracts were washed with water (2 × 10 mL) and brine (2 × 10 mL), were dried over anhydrous magnesium sulfate and then were filtered and concentrated under reduced pressure. The crude oil obtained was subjected to flash chromatography (10 g TLC grade silica gel, 32:1 petroleum ether–diethyl ether) to afford 176 mg (90%) of a mixture of ethyl (*E*)- and (*Z*)-3-trimethylgermylbut-2-enoate (**242**) and (**243**) (1.7:1, *E*:*Z*) as a clear colorless oil. The spectral data were identical with those reported above (section 3.4.3.1, p 294 and section 3.4.3.2, p 297 respectively).

3.4.3.4 SYNTHESIS OF METHYL (*E*)-6-CHLORO-3-TRIMETHYLGERMYLHEX-2-ENOATE (**248**)



248

To a cold (–78 °C) stirred solution of $Me_3GeCu(CN)Li$ (**223**) (1.24 mmol, 1.30 equiv) in dry THF (11 mL), prepared as described above (section 3.4.1.2, p 265), was added a solution of methyl 6-chlorohex-2-ynoate (**247**)[115] (154 mg, 0.96 mmol, 1 equiv) in dry THF (1.5 mL) via a cannula. The reaction mixture was stirred at –78 °C for 30 min, then acetic acid (90 mg, 1.5 mmol, 1.6 equiv) was added via a syringe. The mixture was stirred for an additional 5 min, then was poured into stirred aqueous NH_4Cl–NH_4OH (pH 8–9, 15 mL) and diethyl ether (20 mL) was added to the mixture. The layers were separated and the aqueous portion was extracted with diethyl ether (2 × 10 mL). The combined organic extracts were washed with water (2 × 10 mL) and brine (10 mL), were dried over anhydrous magnesium sulfate and then were filtered and concentrated under reduced pressure. The crude oil acquired was subjected to flash chromatography (20 g TLC grade gel, 24:1 petroleum ether–diethyl ether) to afford 248 mg (92%) of the title compound as a clear colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.02 (s, 1H, vinylic proton), 3.70 (s, 3H, $-OCH_3$), 3.56 (t, 2H, J = 6.6 Hz, $-CH_2Cl$), 2.86 (t, 2H, J = 8.0 Hz, $-C\underline{H}_2CH_2CH_2Cl$), 1.86 (tt, 2H, J = 8.0 and 6.6 Hz, $-C\underline{H}_2CH_2Cl$), 0.29 (s, 9H, $-Ge(CH_3)_3$).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 168.7 (C=O or C-3), 165.0 (C=O or C-3), 125.5 (C-2), 50.9 ($-OCH_3$), 44.9, 32.1, 29.9, –2.1 ($-Ge(CH_3)_3$).

IR (film): 1718, 1607, 1434, 1347, 1181, 1156, 828, 603 cm^{-1}.

HRMS for $C_9H_{16}{}^{35}Cl^{74}GeO_2$ $(M - CH_3)^+$: calcd 265.0051, found 265.0048.

Anal. calcd for $C_{10}H_{19}ClGeO_2$: C 43.00, H 6.86; found: C 42.98, H 6.68.

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