ASYMMETRIC INDUCTION AND TRIPLET SENSITIZATION IN THE SOLID STATE PHOTOCHEMISTRY OF *ANTI*-9-CARBOXYBENZONORBORNADIENE

by

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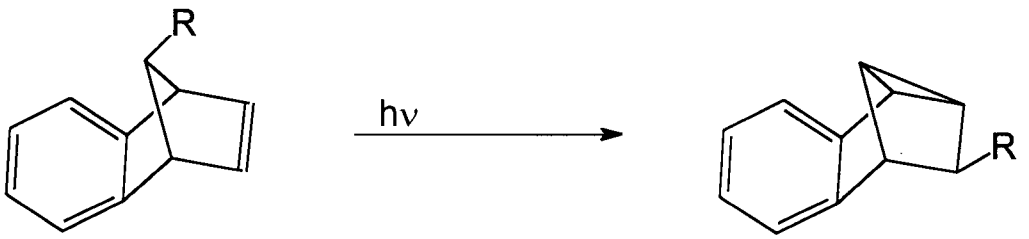
ABSTRACT



19 R = CO_2H
45 R = CO_2CH_3

54 R = CO_2H
53 R = CO_2CH_3

Acid **19** and its methyl ester **45** were prepared, and studies of their photochemical reactivity were made in both the solution phase and solid state. Unexpectedly, both compounds underwent di-π-methane rearrangement to the corresponding undecatrienes **54** and **53** upon direct irradiation in solution. Ester **45** reacted more rapidly in the solid state than in solution, although acid **19** did not react at all in the solid state. Although di-π-methane rearrangement usually occurs only from the excited triplet state in constrained cyclic systems such as these, benzonorbornadiene derivatives **19** and **45** appear capable of undergoing the reaction from either the singlet or triplet excited state.

Although the di-π-methane rearrangement would occur upon direct irradiation, the reaction was much faster when a triplet sensitizer was used. The solution phase reaction could be sensitized with acetone, acetophenone, or benzophenone. Sensitization was also possible in the solid state. Crystals of the complex formed between acid **19** and *p*-acetylpyridine, upon irradiation with

long-wave ultraviolet light that was not absorbed by the acid ($\lambda > 330$ nm), gave rearranged product.

Asymmetric induction could also be carried out. Although acid **19** is achiral, its undecatriene rearrangement product is chiral. Irradiation of crystals of salts formed between acid **19** and commercially available, optically pure, chiral amines gave optically active undecatriene products at low conversions. Enantiomeric excesses as high as 41% were observed. Rearrangement was slow. The most rapid rearrangement occurred for the (-)-ephedrine salt of acid **19**, which reached 31% conversion to product after 6 hours.

Crystals of acid **19** with chiral triplet sensitizer amines were also irradiated. These chiral triplet sensitizer auxiliaries were prepared by coupling natural amino acids to benzyl alcohols and phenols which contained aryl ketone groups. The auxiliaries were isolated as their hydrobromide salts and converted to the free base form immediately before use.

Rearrangement of the salts formed with these chiral triplet sensitizer amines was very rapid. In the solid state, complete conversion to product occurred in less than 1 hour. Enantiomeric excesses (22% - 91%) were generally higher than those obtained upon irradiation of salts prepared with commercially available amines (5.9% - 41%).

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Dedicated to my friends
Christy Gass
Paulette Guindon
Frank Kohler

with thanks

INTRODUCTION

There are several points of view from which a discussion of the work presented in this thesis could be, conceivably, introduced. One obvious starting point would be the development by the Scheffer photochemistry group of the ionic auxiliary method, as an answer to some of the difficulties inherent in carrying out photochemical investigations in the solid state.[1] Another would be the considerable body of research relating to the photochemistry of benzonorbornadiene[2] derivatives[3-28] - and, indeed, upon other substrates which rearrange by the di-π-methane mechanism.[29,30] Yet a third approach might forego any immediate mention of the field of photochemistry, and begin to discuss this project as a contribution to the area of asymmetric synthesis. To complicate matters further, none of these possibilities stands in complete independence of the others. Scheffer and coworkers have published papers which apply the ionic auxiliary method to studies of the di-π-methane rearrangement.[1,31,32] One could point to Louis Pasteur's resolution of tartaric acid via salt formation with chiral amines as the forerunner of the chiral version of the ionic auxiliary method.[33] And so the list goes on. The question of where to begin is problematic for every thesis.

Because of this confusion - or, rather, this wealth of possibilities - the introduction to this thesis should be considered to have three parts. Part one will begin with a brief review of some aspects of solid state photochemistry, the development of the ionic auxiliary method, and the extension of the ionic

auxiliary method to the achievement of both triplet sensitization and asymmetric induction in a single photoreaction - the primary goal of this work. Part two will discuss the di-π-methane rearrangement, particularly that of the benzonorbornadienes, the family to which the compounds studied in this thesis belong. Finally, part three will bring together these two disparate threads, and introduce an additional field of which this work could be considered an extension, that of triplet sensitized asymmetric induction in the solution phase.[34] Hopefully, this approach will clarify rather than befuddle, and will provide a flavour of the interdisciplinary nature of this work - indeed, of almost all scientific endeavours.

1. The Ionic Auxiliary Method.

The field of solid state photochemistry has a long, respectable history. The earliest known organic photoreaction, in fact, occurred in the solid state, Trommsdorf having reported the yellowing and cleavage of crystals of santonin upon exposure to sunlight in 1834.[35] However, particularly throughout the twentieth century, the majority of investigations of photochemical behaviour have been concerned with reactions occurring in the solution phase.

There were reasons for this. The intermolecular and lattice forces operative in solid compounds were neither well-defined nor well-understood, and there was a paucity of methods available by which solid state reactions could be monitored or analyzed. This was an obvious hindrance to developing mechanistic explanations for solid state photoreactions. In more recent years, with, for example, the advent of solid state NMR techniques and the refinement of the discipline of X-ray crystallography, this disadvantage has been somewhat minimized.[36] However, there remain enormous gaps in the understanding of how different molecules interact with one another in crystalline lattices. It is still not possible to predict in which lattice arrangement a new compound will crystallize, although attempts have been made to develop guidelines. In addition, as every chemist who has collaborated with X-ray crystallographers knows, the mere production of crystalline material suited for X-ray analysis can be a daunting - often impossible - task, let alone the prediction of how the molecules will orient themselves within those much longed-for crystals.

Another hindrance to the development of solid state photochemistry concerns bimolecular reactions. It is easy to carry out bimolecular photoreactions in the solution phase. Such reactions as sensitization, quenching, intermolecular electron transfer, and intermolecular cycloaddition have all been thoroughly investigated in solution. The problem with carrying out these reactions in the solid state is that it is very difficult to bring the two different molecules close enough together in order for reaction between them to occur.[1] Manual grinding in a mortar and pestle is generally not sufficient.

Scheffer and coworkers have overcome this particular limitation through use of the ionic auxiliary method.[1] In this method, the substrate under investigation is tethered to a carboxylic acid, and the auxiliary, that which is meant to react with or perturb the reactivity of the substrate, is tethered to an amine. Salts are prepared between the carboxylic acid and the amine and, upon irradiation of crystals of the salt, the two components are held closely enough together in the lattice in order for reaction to take place. Of course, the opposite approach, involving an amine-tethered substrate and acid-tethered auxiliary, is equally valid, and has also been investigated.[31,32,37]

The ionic auxiliary method has shown great utility. Two of the main applications are triplet sensitization and asymmetric induction. Each of these will be introduced separately in the following two sections.

1.1. Ionic Sensitizers.

One bimolecular process that has been facilitated in the solid state through use of the ionic auxiliary method is triplet sensitization. In solution, substrates which show reactivity from their excited triplet states can be made to react in that manner simply by adding to the solution of substrate a molecule that can act as a triplet sensitizer. The sensitizer absorbs the radiation, becomes excited to the first excited singlet state, and then undergoes rapid intersystem crossing to its lowest-lying triplet state. This first triplet state is generally of an energy between that of the singlet ground state and that of the lowest singlet excited state. The triplet excited sensitizer then transfers its triplet energy to the substrate, promoting the substrate to the triplet state, and returning itself to the singlet ground state (Figure 1.1.1).[38] The substrate may then undergo reactions characteristic of its triplet excited state, depending on the particular system under investigation. Many compounds exhibit differing reactivity between their singlet and triplet excited states.

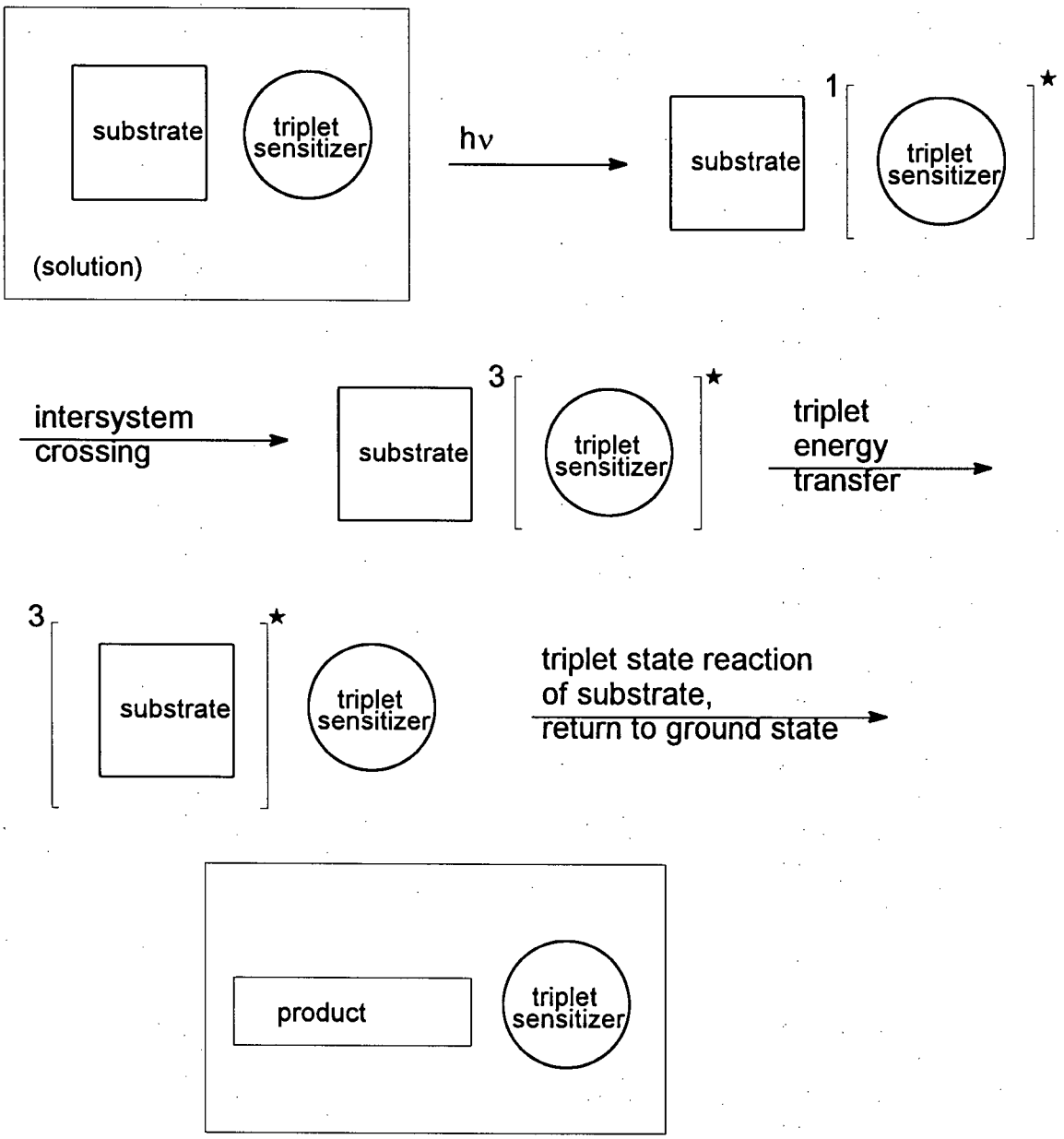


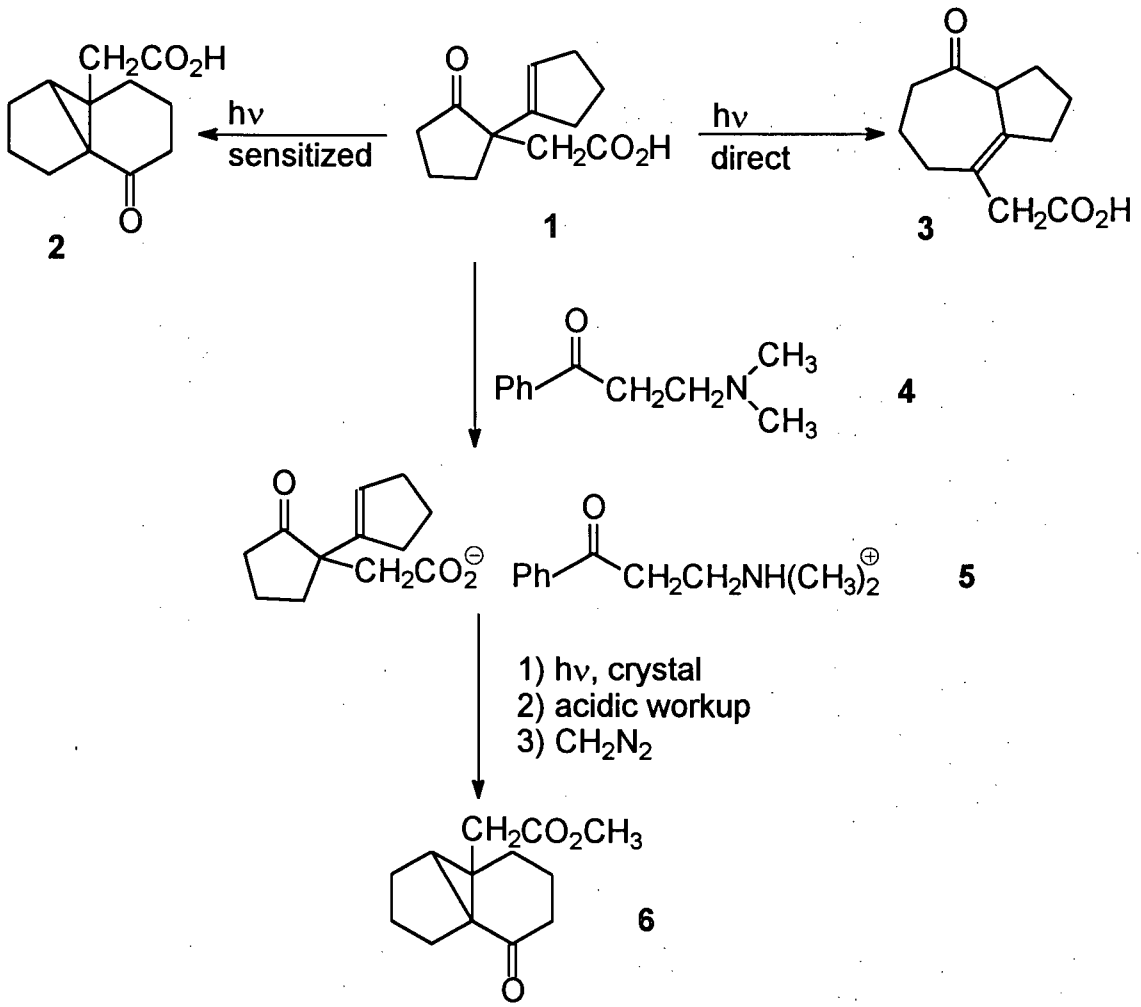
Figure 1.1.1. Triplet sensitization in the solution phase.

An effective triplet sensitizer should have a triplet energy level above that of the substrate, in order for efficient energy transfer to occur. It should also absorb light at a wavelength at which the substrate does not show absorbance. If triplet reactivity is desired, excitation of the substrate to its singlet excited state

by direct irradiation should be avoided. Finally, the sensitizer must be a molecule which undergoes extremely efficient intersystem crossing between its singlet and triplet excited states, with a quantum yield of not much less than 1. Aryl ketones such as acetophenone and benzophenone fulfill these and other requirements, and have seen much use as triplet sensitizers.[30]

There are compounds which undergo rapid and efficient intersystem crossing, and are also reactive from their triplet states. Obviously, these do not make effective triplet sensitizers. If their triplet reactivity is of interest, however, this can be studied without the assistance of a triplet sensitizer. The adamantyl aryl ketones, a subject of extensive investigation by Scheffer and coworkers, are an example of such a family of compounds.[1,39,40]

Spatial proximity of sensitizer to substrate is required in order for triplet sensitization to take place.[38] This is a problem in the solid state; one which can be, happily, overcome by application of the ionic auxiliary method. Salt formation between an acid-linked substrate and an amine-linked sensitizer brings the two moieties close enough together for energy transfer to take place. For example, β,γ-unsaturated ketones rearrange in solution by either the singlet-mediated 1,3-acyl shift reaction, or the triplet-sensitized oxadi-π-methane rearrangement (Scheme 1.1.1).[41] Salt **5** of carboxylic acid **1** with aryl ketone amine **4**, upon irradiation in the solid state, gave the triplet-derived product **6** exclusively.[42]



Scheme 1.1.1. Use of the ionic auxiliary method to carry out triplet sensitization in the solid state.[42]

Conversion of carboxylate-linked substrates to the corresponding methyl esters following irradiation is the workup method of choice within the Scheffer research group. The salt is usually shaken with an organic solvent and aqueous acid to convert the carboxylate back to the acid, and the organic extract is then treated with diazomethane. Analysis of reactions is usually accomplished by GC injection, and it is easier to carry out GC analysis on esters than on acids.

1.2. Ionic Chiral Auxiliaries.

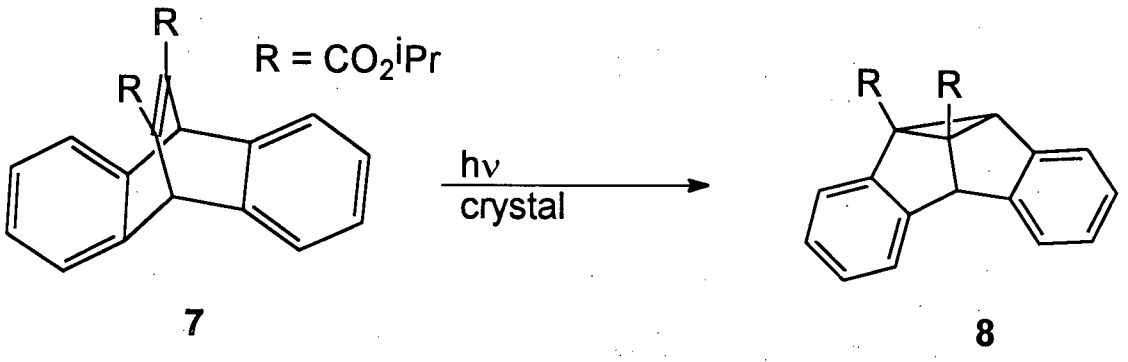
Scheffer and coworkers have carried out a great deal of work involving the application of the ionic auxiliary method to asymmetric induction in the solid state.[1,31,32,37,40] A prelude to this work was their investigation into the area of absolute asymmetric synthesis, which is described below.

1.2.1. Absolute Asymmetric Synthesis.

Absolute asymmetric synthesis has been reviewed recently by Sakamoto.[43] It involves the generation of optically active chiral product from an achiral starting material, without the external intervention of pre-existing optical activity. Generally speaking, reactions that convert achiral starting materials to chiral products will yield racemates, in photochemical as well as in ground state processes. However, there are a few achiral, photochemically reactive molecules which crystallize spontaneously in chiral space groups. Thus, although the substrate is achiral, its crystals are chiral. Irradiation of these chiral crystals often leads to optically active chiral products in high enantiomeric excess.

An example is given below, in Scheme 1.2.1.1.[44] Diester **7** crystallizes in the chiral space group $P2_12_12_1$, and irradiation of single crystals of this compound leads to the chiral dibenzosemibullvalene derivative **8** in greater than

95% enantiomeric excess. Irradiation of **7** in solution, however, gives racemic product.



7 **8**

Scheme 1.2.1.1. An example of an absolute asymmetric synthesis.[44]

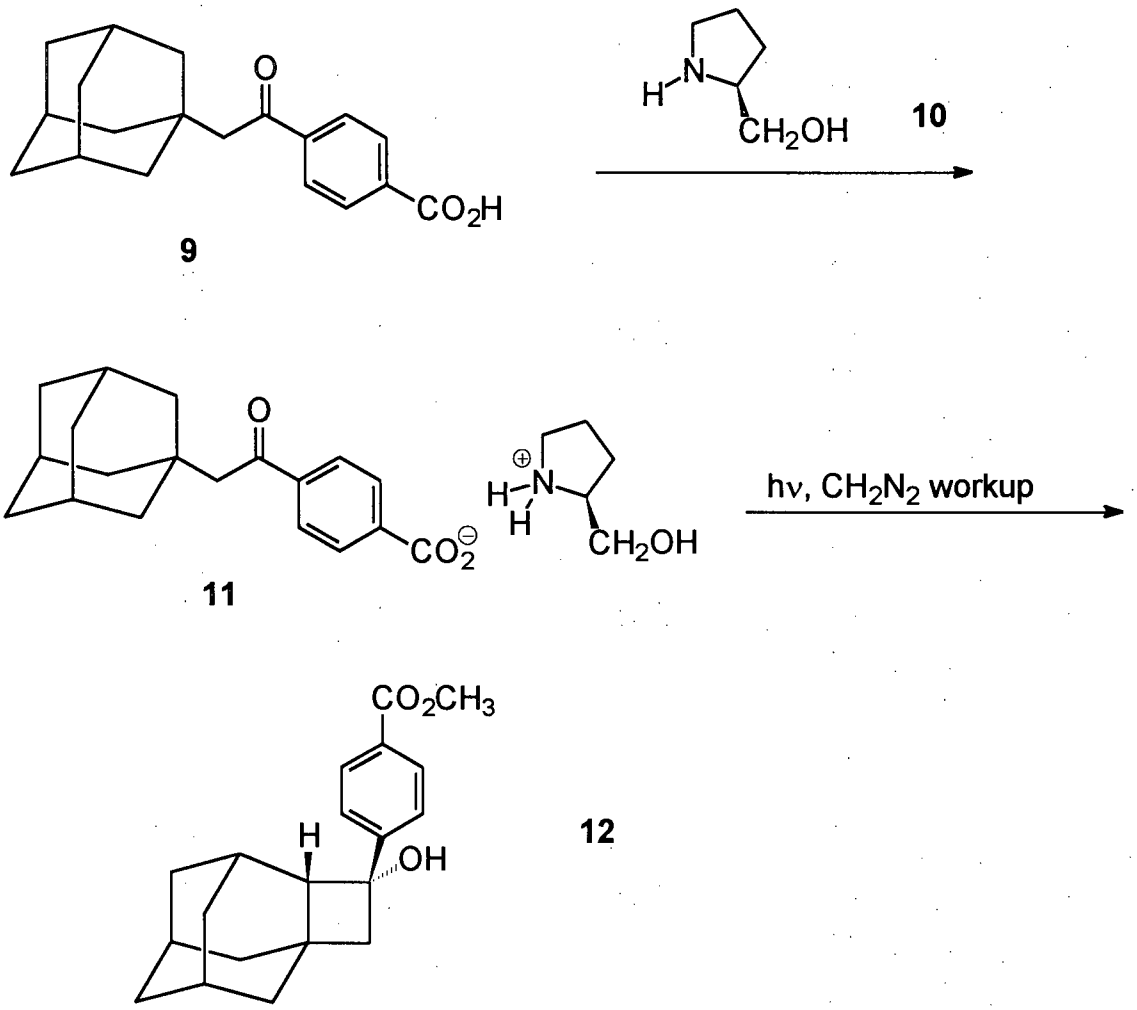
Many absolute asymmetric syntheses have been carried out. The problem with this field, as a method of asymmetric induction, lies in its lack of generality. Few achiral molecules crystallize spontaneously in chiral space groups, and the factors which determine their tendency to do so are not well understood.[45] A more general means of achieving asymmetric induction in the solid state was required.

1.2.2. Chiral Salts of Achiral Substrates.

Although the crystallization of achiral substrates can not be relied upon to yield chiral crystals, the crystallization of enantiomerically pure chiral substrates certainly can. A salt formed between an achiral carboxylic acid and an optically active chiral amine would itself be optically active and chiral, and would of

necessity crystallize in a chiral space group. Irradiation in the solid state of such chiral crystals can thus be anticipated to produce an optically active acid product, which could be freed readily from the amine auxiliary by an acidic workup.

This is indeed the case. Salt **11** of the achiral acid-linked adamantyl phenyl ketone **9** with L-prolinol (**10**) gave, upon irradiation in the crystalline state and diazomethane workup, 97% enantiomeric excess of the dextrorotatory form of cyclobutanol product **12** (Scheme 1.2.2.1).[39] Other systems give similar results. The chiral lattice arrangement necessitated by the presence of the chiral auxiliary induces asymmetry in the reaction mechanism, and causes one of the possible enantiomers to be favoured.



Scheme 1.2.2.1. Asymmetric induction through the ionic auxiliary method.[39]

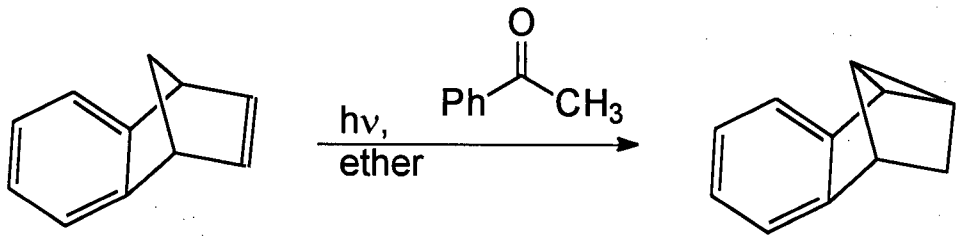
1.3. Sensitized Asymmetric Induction in the Solid State.

Although the utility of the ionic auxiliary method in carrying out both triplet sensitization and asymmetric induction had been demonstrated, no experiments had been carried out in which both effects could be observed at the same time. In fact, to our knowledge, sensitized asymmetric induction in the solid state had never been observed by any research group. There was no reason why the ionic auxiliary method should be incapable of accomplishing this. Surely a chiral auxiliary which incorporated triplet sensitizer functionality could be either found or prepared, and such an auxiliary should be able to induce both sensitization and asymmetry in solid state reactions.

In order to demonstrate this, the substrate chosen had to have four main features. It had to be achiral, and had to react photochemically to give a chiral product. It also had to do so via its excited triplet state. Finally, the substrate had to be amenable to the introduction of a carboxylic acid substituent, without disturbing either its achirality or its triplet energy.

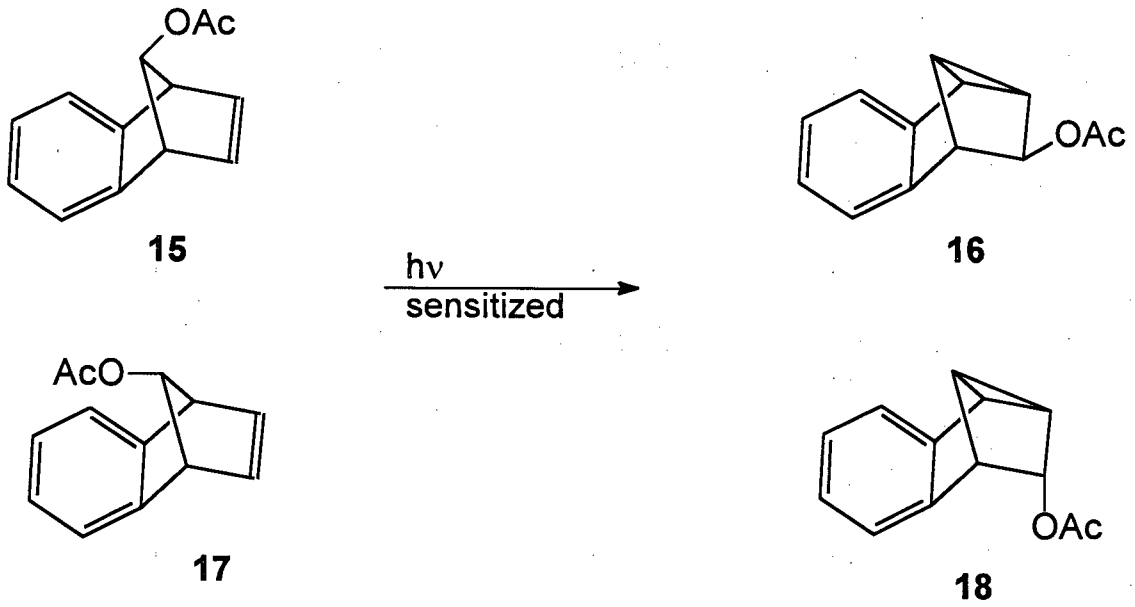
Benzonorbornadienes appeared to be ideal substrates. They have been known since 1966 to rearrange photochemically from their triplet states to the corresponding tetracyclo[5.4.0.$0^{2,4}$.$0^{3,6}$]undeca-1(7),8,10-trienes (Scheme 1.3.1; henceforth, this thesis will refer to the aforementioned family of compounds simply as "undecatrienes", for obvious reasons).[3] Benzonorbornadiene (**13**) is achiral, and its undecatriene rearrangement product (**14**) is chiral. In addition, irradiation of either *anti*- or *syn*-9-substituted benzonorbornadienes has been

shown to give exclusively the *exo*- or *endo*-undecatriene derivative, respectively (Scheme 1.3.2).[6]



13 **14**

Scheme 1.3.1. Triplet sensitized irradiation of benzonorbornadiene (**13**).[3]

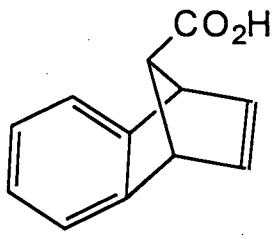


15 **16** **17** **18**

Scheme 1.3.2. Triplet sensitized irradiation of 9-substituted benzonorbornadienes.[6]

We decided to prepare as our photochemical substrate *anti*-9-carboxybenzonorbornadiene (**19**, Figure 1.3.1). This compound meets all the aforementioned requirements, and had been synthesized by Buske and Ford.[46]

Salts would be prepared between acid **19** and optically pure chiral amines possessing triplet sensitizer functionality, and irradiated in the crystalline state, in order to demonstrate - hopefully - that sensitization and asymmetric induction could be achieved at the same time.



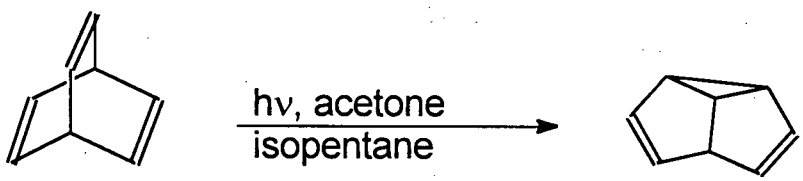
19

Figure 1.3.1. *anti*-9-Carboxybenzonorbornadiene (**19**).

2. The Di-π-methane Rearrangement.

2.1. Discovery and Mechanism.

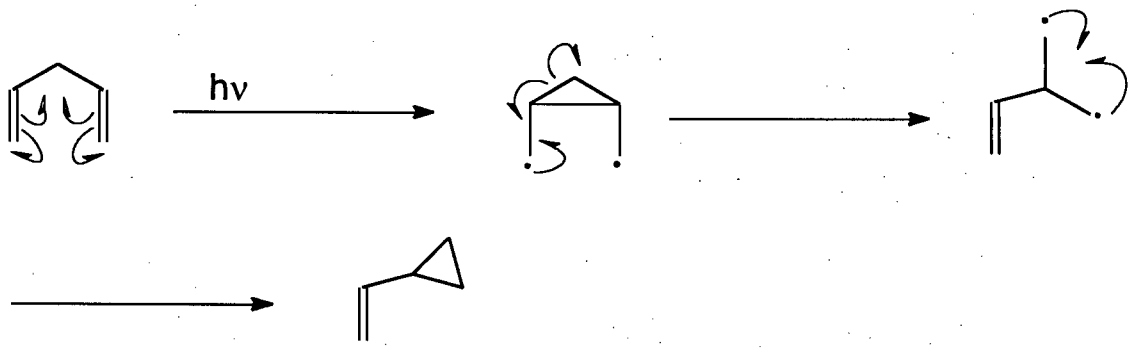
One of the earliest examples of the di-π-methane rearrangement was reported by Zimmerman and coworkers in 1966.[47] Upon acetone-sensitized irradiation, barrelene (**20**) was converted to its isomer semibullvalene (**21**), as illustrated in Scheme 2.1.1. The reaction was later shown to be a general one, which could conceivably take place, via the same mechanism, between any two π-systems separated by an sp^3-hybridized carbon atom.[30] The π-systems do not have to be vinyl groups, or even carbon-only systems. Examples abound in which one of the π-systems is an aryl group, including the benzonorbornadienes described in this work. There are also variations involving C=O or C=N double bonds, the oxa- and aza-di-π-methane rearrangements, respectively.



20 **21**

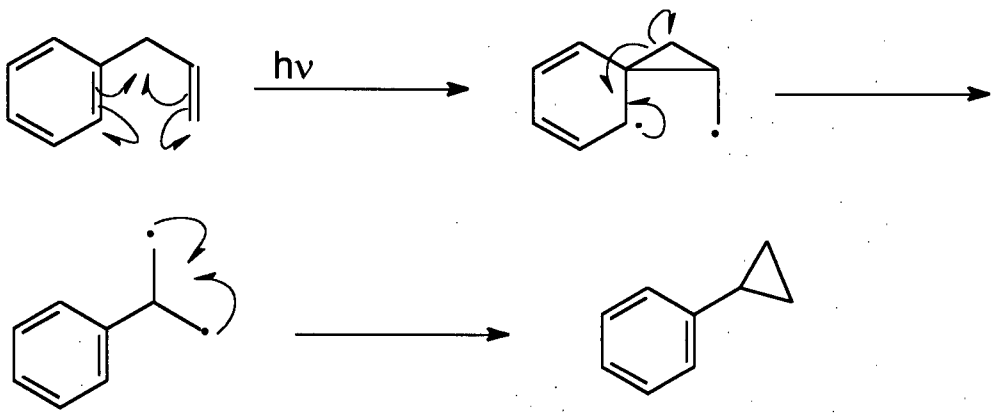
Scheme 2.1.1. Acetone-sensitized photorearrangement of barrelene to semibullvalene.[47]

The basic mechanism is shown below, in Scheme 2.1.2. The first step involves formation of a bridge between the two reacting π bonds, at the carbon atoms adjacent to the sp^3-hybridized centre, resulting in formation of a 1,4-biradical. One of the cyclopropane bonds then cleaves homolytically, to regenerate one of the original π bonds and form a rearranged 1,3-biradical. For systems in which the two cyclopropane bonds leading to rearranged biradical upon cleavage are non-equivalent, cleavage generally occurs to yield the more stable radical intermediate. Finally, biradical closure to the cyclopropane ring in the product occurs.



Scheme 2.1.2. Mechanism of the di-π-methane rearrangement.

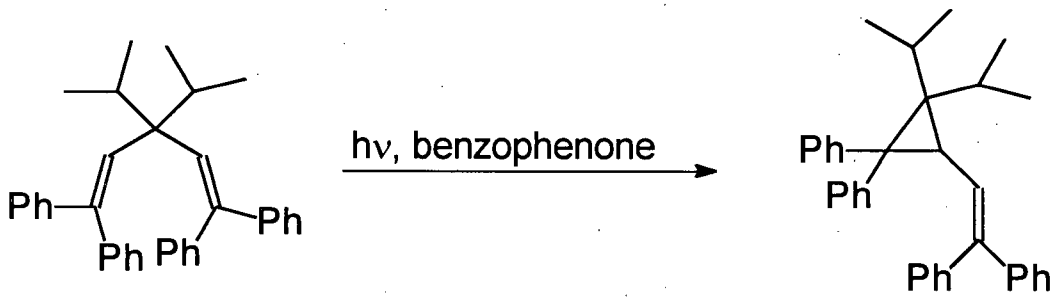
Replacement of one of the vinyl groups by an aromatic ring gives a substrate which will rearrange by the same mechanism, shown in Scheme 2.1.3. When aromatic systems are involved in the initial bridging step, the second step involves cleavage of whichever cyclopropane bond will restore aromaticity. Again, the product derived will contain a cyclopropane ring adjacent to the π-system.



Scheme 2.1.3. Di-π-methane rearrangement involving an aryl group.

The di-π-methane rearrangement can occur from either the singlet or triplet excited state. As a general rule, reactions involving acyclic substrates proceed through the singlet excited state; substrates in which the reacting π-moieties are constrained within a ring rearrange via their triplet excited state. The reason for this is believed to be the extremely facile decay to the ground state for triplet excited π bonds in acyclic systems. Systems in which the π-groups are capable of free rotation about the sp^3-hybridized carbon have a tendency, in the triplet state, to adopt a particular twisted geometry that favours return to the ground state. This return to the ground state tends to occur more rapidly than rearrangement; thus, rearrangement takes place only from the singlet excited state. Cyclic systems, on the other hand, do not show this "free rotor" effect, since they are too constrained to allow adoption of the twisted geometry which favours decay to the ground state; thus, rearrangement of these systems from the triplet state can occur.

Further evidence for this, in addition to observations made regarding whether given compounds react best upon direct or sensitized irradiation, is provided by sterically hindered systems. For example, 3,3-diisopropyl-1,1,5,5-tetraphenyl-1,4-pentadiene (**22**) reacts upon sensitized irradiation (Scheme 2.1.4). The free rotor effect is not viable, due to the hindrance to rotation imposed by the bulky isopropyl groups.

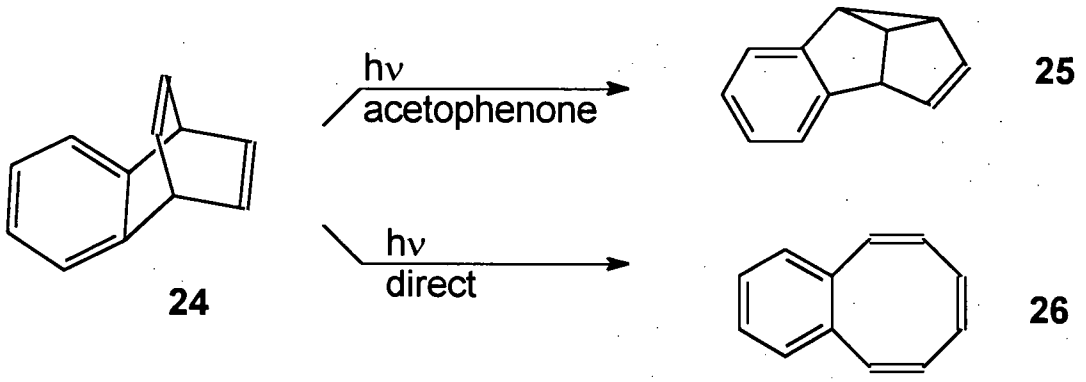


22 **23**

Scheme 2.1.4. Triplet state reactivity of a sterically-encumbered acyclic diene.[30]

The requirement for a triplet sensitizer in cyclic systems is not believed to be due to any inherent inability of the singlet excited state to undergo di-π-methane rearrangement. Many cyclic π-systems can also rearrange via singlet state pericyclic processes, and in many cases these occur too rapidly to allow successful competition from the di-π-methane pathway. For example, although benzobarrelene (**24**) undergoes di-π-methane rearrangement upon triplet

sensitization, direct irradiation leads instead to benzocyclooctatetraene (**26**). This is shown in Scheme 2.1.5.



Scheme 2.1.5. Alternative rearrangement processes for different excited states of benzobarrelene (**24**).[30]

The di-π-methane rearrangement is quite general, and has been studied extensively. A number of reviews have been written, both on mechanistic aspects of the reaction,[29] and on its synthetic utility.[30] Scheffer and coworkers have carried out several research projects involving the di-π-methane rearrangement. Some of these were referred to in Chapter 1; the next section will briefly summarize the investigations carried out on di-π-methane substrates by the Scheffer group before the work presented in this thesis was begun.

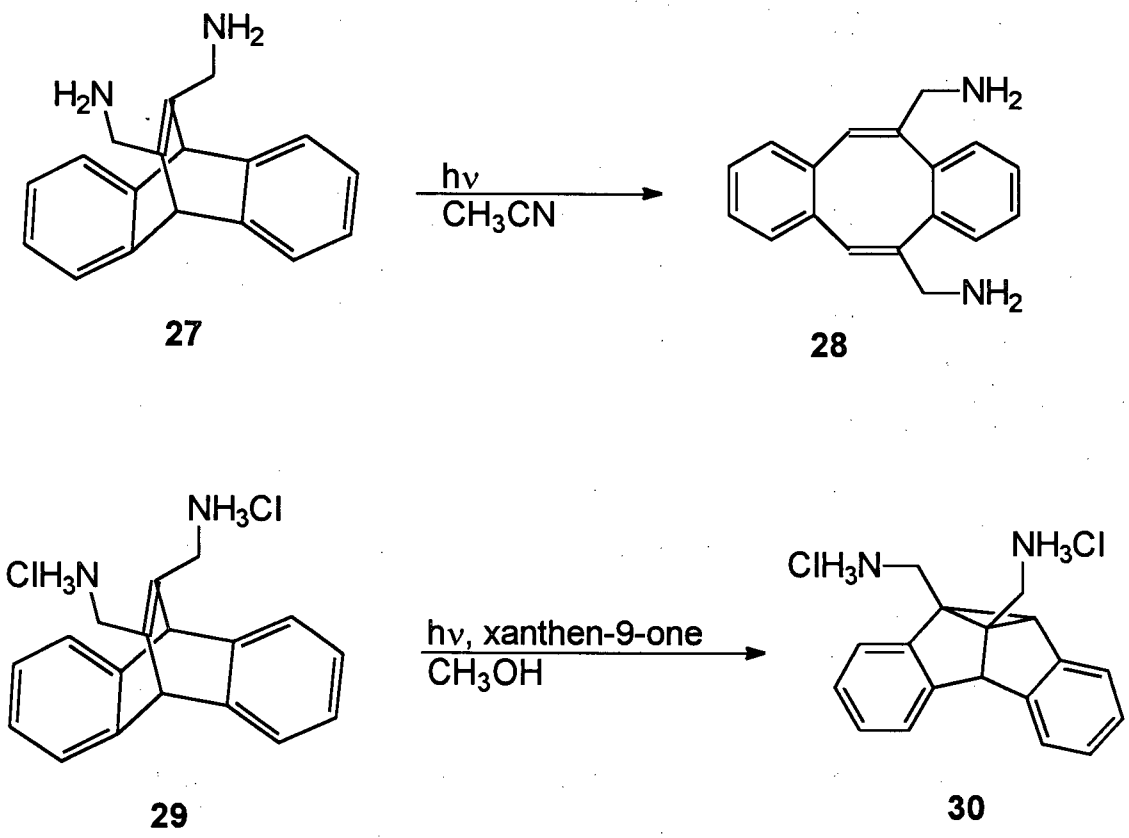
2.2. Di-π-methane Research in the Scheffer Group.

Before the present work was undertaken, di-π-methane research in the Scheffer group had focussed on the solution phase and solid state photochemistry of dibenzobarrelenes. Many of the contributions made in this area have been reviewed by Scheffer and Yang,[48] particularly the work carried out by Scheffer and coworkers on substituent effects. A review by Scheffer and Pokkuluri[36] covers much of the work on molecular crystals of these compounds, and the application of the ionic auxiliary method has also been investigated.[31,32,42,49]

The di-π-methane rearrangement proceeds from the triplet state in these cyclic systems. Dibenzobarrelenes bearing carbonyl substituents on the vinyl bond will, however, react upon direct irradiation. Intersystem crossing from singlet to triplet excited state is a facile process for these compounds, as for the adamantyl aryl ketones mentioned earlier in this thesis.

Dibenzobarrelenes give dibenzocyclooctatetraenes upon reaction from the singlet state, and dibenzosemibullvalenes from the triplet state (Scheme 2.2.1).[49] The triplet state transformation involves conversion of an achiral substrate to chiral product, and it is thus possible to carry out asymmetric induction, which has been done through irradiation of fortuitously chiral substrate crystals,[44,50] and through use of ionic chiral auxiliaries.[31,32] Optically active product has also been obtained by solution phase or solid state irradiation

of dibenzobarrelenes incorporating chiral bridgehead substituents,[51] although of course in these cases the substrates are chiral, and diastereoselectivity rather than enantioselectivity is involved.



Scheme 2.2.1. Direct and sensitized irradiation of dibenzobarrelene derivatives.[49]

Monobenzobarrelenes have also been studied by Scheffer and coworkers,[52] as have β,γ-unsaturated ketones,[1,53] which undergo the

mechanistically equivalent oxa-di-π-methane rearrangement. The majority of projects have, however, involved dibenzobarrelenes.

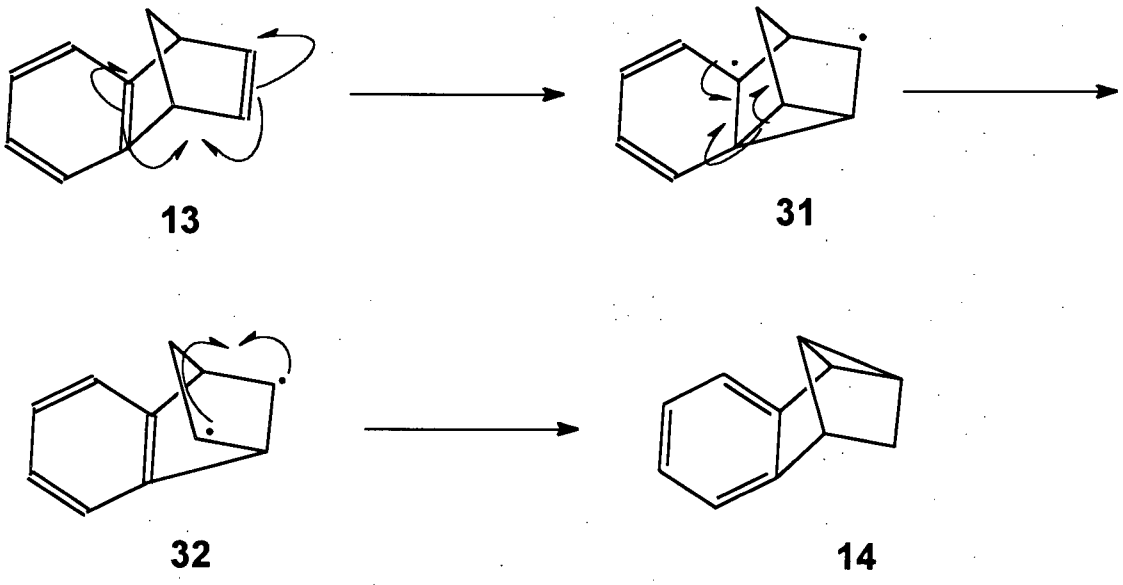
2.3. The Photochemistry of Benzonorbornadiene and its Derivatives.

The photochemistry of benzonorbornadienes was introduced in Chapter 1. Most of the research which elucidated the factors responsible for the regioselectivity of rearrangements of substituted benzonorbornadienes is due to Paquette and coworkers. Paquette published an extensive series of papers[9,12,14-17,19-24] in which he examined benzonorbornadienes substituted in aryl, vinyl, and bridgehead positions.

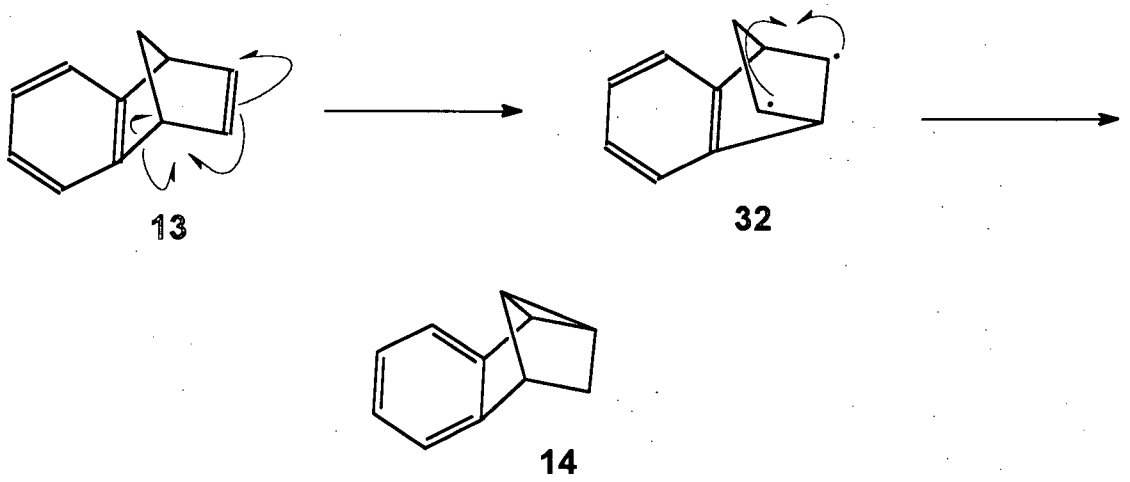
A detailed review of substituent effects is beyond the scope of this work. Generally speaking, directive effects follow the trend of: bridgehead ≈ vinyl >> aryl.[16,17,19,21,23,24] That is, substituents at those positions control the regioselectivity of the rearrangement in that order. Benzonorbornadienes substituted in both aromatic and vinyl positions give product ratios controlled entirely by the directive effect of the vinyl substituent.

One point that does deserve mention concerns the mechanistic detail of the rearrangement. Paquette came to the conclusion that, rather than following the traditional di-π-methane rearrangement as outlined in Section 2.1,

benzonorbornadienes undergo, as the first step in their photorearrangement, a 1,2-aryl shift.[21,22] Compare Schemes 2.3.1 and 2.3.2. In the 1,2-aryl shift mechanism, the initial benzo-vinyl bridging step is bypassed, and biradical **32** is formed directly.



Scheme 2.3.1. Rearrangement of benzonorbornadiene (**13**) via the di-π-methane rearrangement (Zimmerman).



Scheme 2.3.2. Rearrangement of benzonorbornadiene (**13**) via the 1,2-aryl shift mechanism (Paquette).

Paquette has presented considerable evidence in support of this hypothesis, although he does not claim that his evidence rules out the mechanism proposed by Zimmerman. The main points of Paquette's argument are as follows: (1) Bridgehead substituents exert a strong directive effect, consistent with formation of biradical **32** being the product-determining step.[20-22] That is, if biradical **31** is formed, it must be formed reversibly. (2) There is no evidence that biradicals of this sort (**31** or **32**) are formed reversibly, and studies by Adam and coworkers indicate that they are not.[52] (3) The relatively high quantum yields reported by Paquette do not favour energy loss through reversion to starting material as a significant factor in these reactions.[23] (4) Deuterium isotope effects measured for compounds substituted at the bridgehead position are more convincingly explained by the aryl shift mechanism.[20,21] (5) The aryl shift mechanism does not require loss of

aromaticity in the biradical formation step.[21] (6) Compounds such as benzobarrelene (**24**), which could conceivably undergo either vinyl-vinyl or aryl-vinyl bridging, invariably rearrange through the vinyl-vinyl bridging mode.[21] (7) These are not the first systems in which 1,2-aryl migration has been suggested in replacement of a previously-assumed aryl-bridging step. Iwamura and coworkers proposed such a mechanism for the rearrangement of triptycene.[55]

Paquette's proposal should not be regarded as a refutation of Zimmerman's proposed mechanism, a point which Paquette made quite clear.[23] In a review of the di-π-methane rearrangement, Zimmerman himself wrote that proposals of intermediate structures such as **31** and **32** "do not mean to imply that the species depicted along the reaction route necessarily are intermediates and thus correspond to energy minima. Rather these may just be points along the hypersurface leading from excited state of reactant to ground state of product. Each case must therefore be considered separately."[29] Biradicals such as **31** have been proven to exist as intermediates for some di-π-methane rearrangements,[56] but they have not been irrefutably demonstrated for the rearrangements of benzonorbornadienes.

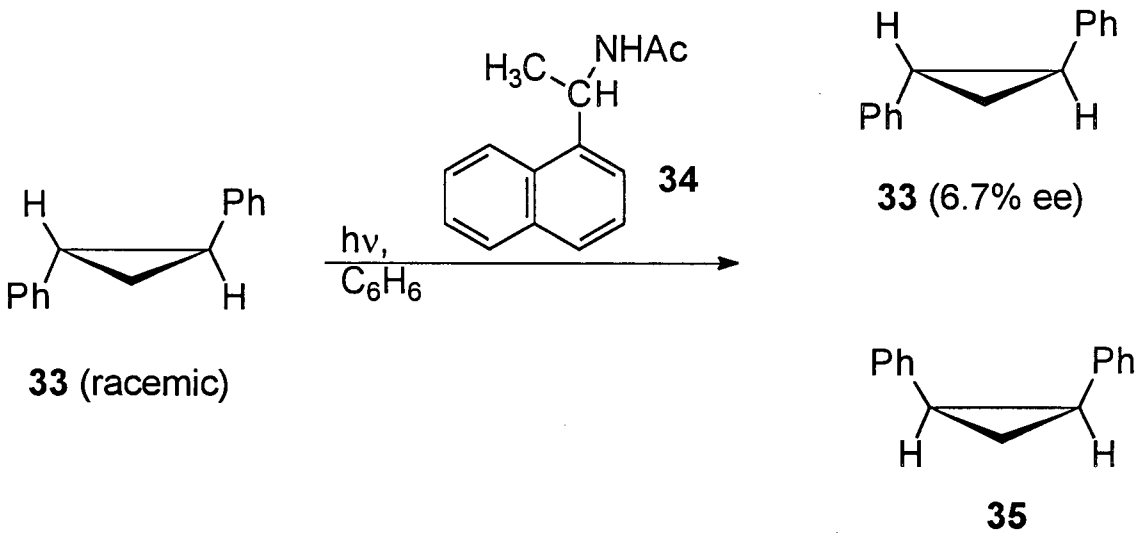
Benzonorbornadienes bearing substituents at the 9-position have received less attention, possibly due to the difficult nature of the syntheses involved. The acid substrate (**19**) chosen for the project described in this thesis had not been investigated photochemically before this work. In addition, no

photochemical studies of benzonorbornadienes had, to date, been performed in the solid state. This project would be the first.

3. Objectives of the Present Research.

3.1. Triplet Sensitized Asymmetric Induction.

As discussed in Chapter 1, sensitized asymmetric induction had never been observed in the solid state. Experiments of this sort have been carried out in the solution phase. The first reported example, by Hammond and Cole,[57] involved singlet sensitization. Irradiation in the solution phase of racemic *trans*-1,2-diphenylcyclopropane (**33**) in the presence of (+)-amide **34** gave a mixture of *cis*- and *trans*-cyclopropanes in which the *trans*-isomer showed enantiomeric excess of 6.7% (Scheme 3.1.1).[58]



Scheme 3.1.1. Sensitized asymmetric induction in the solution phase.[57]

Several similar studies have been carried out, and the field has been reviewed by Inoue.[34] Enantiomeric excesses are usually very low, although Inoue and coworkers have reported values up to 64%.[58] Both singlet and triplet sensitized asymmetric induction have been reported. The energy transfer in these reactions involves collisional quenching of the optically pure chiral sensitizer by the substrate. A racemic or prochiral substrate thus may show selectivity in its approach to the chiral sensitizer, such that one enantiomer or face of the substrate collides in an orientation more favourable for energy transfer, or is capable of a stronger and more long-lived interaction. An exciplex intermediate is often invoked.

Ramamurthy and coworkers have achieved something similar to triplet sensitized asymmetric induction in the photorearrangement of benzonorbornadiene.[28] It is well established that irradiation in the presence of heavy atoms of substrates requiring triplet sensitizers can yield triplet-derived products.[42,53,59] The heavy atom enhances intersystem crossing of the substrate from its single to triplet excited state, through increased spin-orbit coupling. Irradiation of a hexane slurry of Y zeolite included with Tl^+, (+)-ephedrine hydrochloride, and benzonorbornadiene (**13**) gave the undecatriene product (**14**) in 14% enantiomeric excess. In this example, although asymmetric induction was achieved in a triplet state reaction which the substrate would not undergo upon direct irradiation, the two effects observed resulted from two independent species, the thallium ion and the ephedrine hydrochloride.

3.2. Triplet Sensitized Asymmetric Induction of Benzonorbornadiene Derivatives in the Solid State.

In summary, the objectives of the work presented in this thesis were as follows: (1) To investigate the hitherto-unknown photochemistry of benzonorbornadiene derivatives in the solid state. (2) To make use of the ionic auxiliary method to achieve both triplet sensitization and asymmetric induction. (3) To do so by salt formation between *anti*-9-carboxybenzonorbornadiene (**19**) with auxiliaries which would contain both triplet sensitization and asymmetric induction capability in a single unit.

To accomplish these objectives, the first goal was to prepare acid **19**. Its methyl ester would also be prepared, and the reactivity of both compounds upon sensitized solution phase irradiation would be investigated. Although there was no reason to expect otherwise, no experiment had demonstrated that either of these compounds was photoreactive. Direct irradiation of both compounds in the solution phase and solid state would also be carried out, in order to show that photoreaction would not occur in the absence of a triplet sensitizer.

Once these initial studies had been completed, we intended first to determine whether salts formed between acid **19** and known triplet sensitizer amines would give di-π-methane rearrangement product. Having established this, the remainder of the project was expected to involve the design and synthesis of chiral triplet sensitizer bases, salt formation with acid **19**, and irradiation of the salts to discover whether the goals of the project could be

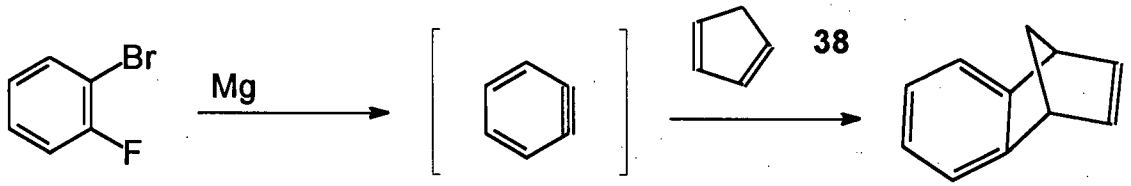
realized. We also hoped to obtain X-ray crystal structures of these salts, and to correlate the information obtained thereby with the irradiation results, in order to gain a better understanding of the factors involved in asymmetric induction and energy transfer in benzonorbornadiene photorearrangements.

RESULTS AND DISCUSSION

4. The Synthesis of *anti*-9-Carboxybenzonorbornadiene (19).

4.1. Synthesis of Benzonorbornadiene (13)

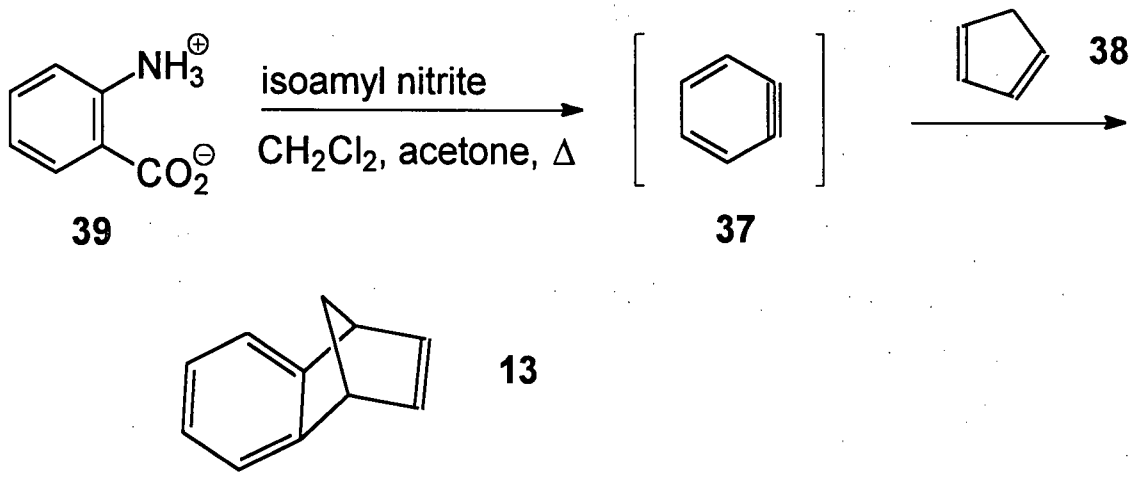
Benzonorbornadiene (**13**) was synthesized according to the procedure used by Wittig and Knauss[60] (Scheme 4.1.1). Cyclopentadiene (CPD, **38**) was added to benzyne (**37**) prepared *in situ* by treatment of 1-bromo-2-fluorobenzene (**36**) with magnesium. Modifications were made to the original Wittig procedure due to difficulties encountered in scaling up the reaction. Originally, a solution of **36** and **38** was added to the magnesium from a dropping funnel. However, we found that this method gave low yield, accompanied by extensive dimerization of CPD. Dicyclopentadiene could not be separated from **13** by distillation, and even chromatographic separation was difficult. This problem was overcome by adding the THF solution of **36** and **38** to the magnesium shavings via a cannula, keeping the reagent solution at -78 °C until it was added. Benzonorbornadiene could be obtained in this way in 82% yield.



36 37 13

Scheme 4.1.1. Preparation of benzonorbornadiene (**13**).

Most of the substituted benzonorbornadienes studied by Paquette were prepared by a different method,[15] outlined for the parent compound in Scheme 4.1.2. This method also involves Diels-Alder addition of benzyne to CPD. We attempted to synthesize **13** in this fashion, but obtained an extremely low yield (2%). Again, dimerization of CPD was the major problem, with the solution of CPD and benzyne precursor being held at or above room temperature for an extended period of time.



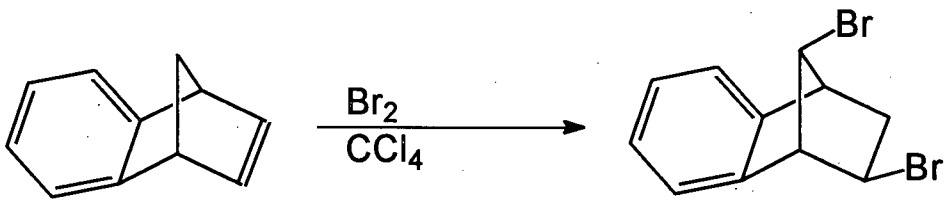
39 37 13

Scheme 4.1.2. Preparation of benzonorbornadiene (**13**) via diazotization of anthranilic acid (**39**).

Benzonorbornadiene smells strongly of ripe mangoes, a fact which spoiled the author's enjoyment of several fruit salads during the days occupied by the synthesis of this compound.

4.2. Synthesis of *exo*-2-*anti*-9-Dibromobenzonorbornene (40).

Bromination of benzonorbornadiene had been performed by Cristol and Nachtiagall,[61] to yield the rearranged dibromide **40** (Scheme 4.2.1). Their procedure was followed.

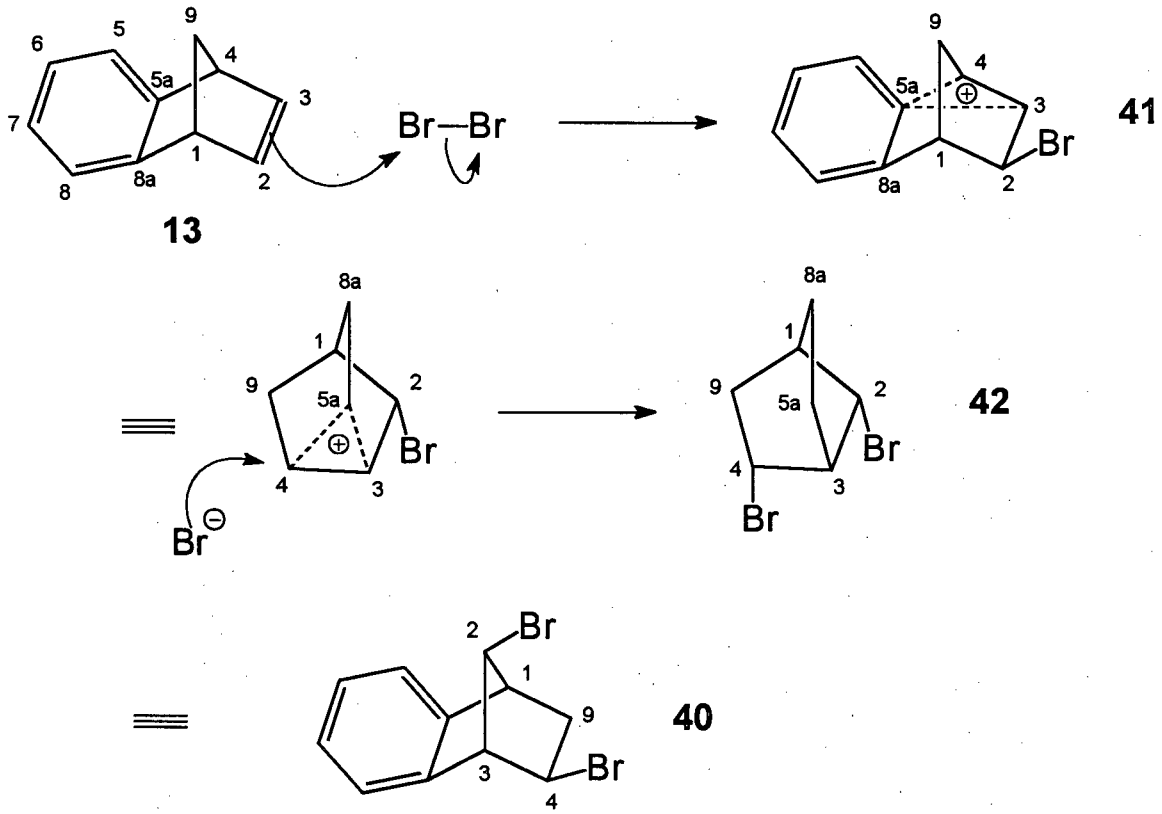


13 **40**

Scheme 4.2.1. Bromination of benzonorbornadiene (**13**).

Bromination of the double bond in **13** occurs with Wagner-Meerwein rearrangement, according to the mechanism shown in Scheme 4.2.2. Electrophilic addition to the double bond gives the nonclassical bridged carbocation intermediate **41**, shown here in two orientations (the aromatic ring, connected at positions 5a and 8a, has been omitted in some of the structures, to simplify the scheme). Nucleophilic attack of bromide ion occurs at the cation site

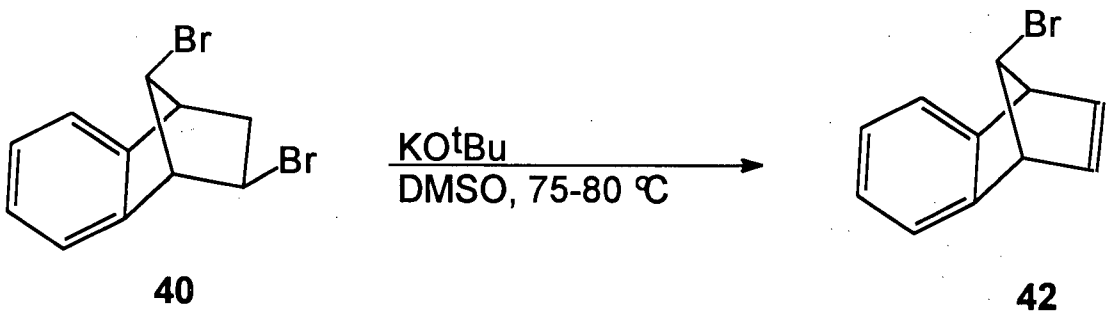
which experiences the least amount of steric hindrance, position 4, at the least shielded face. The upper face of the carbocation is shielded from attack by bridging to the aromatic ring. Thus, the two bromine atoms are added so that they will end up as far away as possible from both the aromatic ring and from each other.



Scheme 4.2.2. Wagner-Meerwein rearrangement upon bromination of benzonorbornadiene (**13**).

4.3. Synthesis of *anti*-9-Bromobenzonorbornadiene (42).

Cristol and Nachtigall[61] accomplished the dehydrobromination of **40** according to Scheme 4.3.1, by treatment of the dibromide in dimethyl sulfoxide (DMSO) with potassium *tert*-butoxide. We had difficulty obtaining reproducible results with this method, often observing either extensive decomposition and production of sticky black tars from which it was difficult to extract product, or unreacted starting material. Wilt and coworkers,[62] who used effectively the same procedure, also reported difficulties.

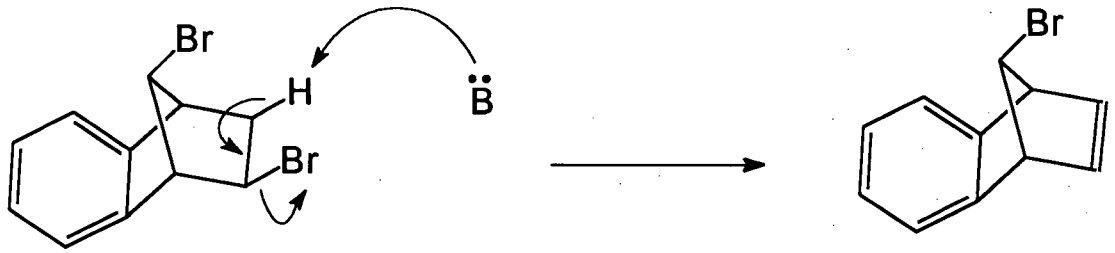


40 **42**

Scheme 4.3.1. Reported synthesis of *anti*-9-bromobenzonorbornadiene (**42**).[61]

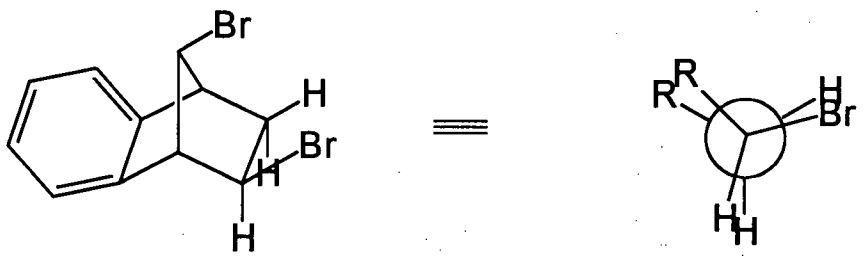
The main problem with this reaction is that the fixed orientation of the substituents at the 2- and 3-positions of norbornyl-type substrates does not favour *trans*-elimination, and an *exo,cis*-elimination pathway - less favourable on stereoelectronic grounds - is followed instead (Scheme 4.3.2).[63] As pictured in

Figure 4.3.1, the 3-*endo* proton, which would have to be removed in order to allow *trans*-elimination, is fixed at an angle of about 60° out of the ideal antiperiplanar arrangement. An *exo,cis*-mechanism involving considerable carbanion character is postulated instead. Such a mechanism seems even more likely for *exo*-benzonorbornadienyl halides than for *exo*-norbornyl halides. Compounds such as **40** experience considerable shielding of the 3-*endo* proton by the aromatic ring, and this should create a significant steric hindrance to the approach of a base.



40 **42**

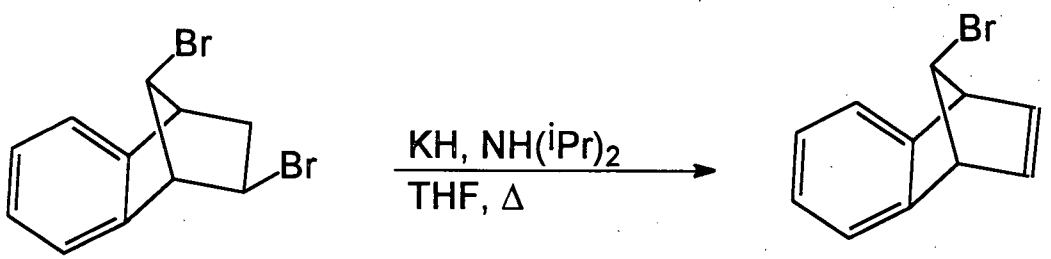
Scheme 4.3.2. *exo,cis*-Elimination of hydrogen bromide from dibromide **40**.



40

Figure 4.3.1. Newman projection of dibromide **40**.

In the event, attempts to dehydrobrominate **40** as shown in Scheme 4.3.1 failed. Many other approaches to monobromide **42** were made, including dehydrobromination with KH / dimethylsulfoxide, LDA in THF, or lithium bromide / lithium carbonate in DMF, as well as dehydration of bromohydrins formed by aqueous treatment of benzonorbornadiene with N-bromosuccinimide.[64] The best and most consistent results were obtained with potassium hydride (KH, 3.4 equivalents) and diisopropylamine (2.7 equivalents) in refluxing THF (Scheme 4.3.3; the ideal concentration of dibromide **40** in the reaction mixture was determined to be 0.17 M). Optimization of this procedure eventually allowed isolation of 95% yield crude product, shown by GC analysis to contain 90% monobromide **42**.



40 **42**

Scheme 4.3.3. Dehydrobromination of **40** with potassium hydride and diisopropylamine.

There are two problems with this procedure. The first is that the reaction conditions tend not to be entirely reproducible. The KH used is obtained as a 35% w/w suspension in mineral oil. The 35% value given was used in

calculating the weight of KH from the bottle required in order to make up the desired amount. However, the KH tends to settle out in the bottle, and the KH / mineral oil suspension actually weighed out was certainly more than 35% KH, although the exact percentage was not known, and probably varied between experiments.

The second problem is that, according to a paper published by Raucher and Koolpe,[65] this procedure should not work. It was initially tried as a misinformed attempt to carry out the dehydrobromination step with potassium diisopropylamide (KDA). However, this procedure is not the correct way to prepare KDA - the reagent is made by addition of potassium *tert*-butoxide to lithium diisopropylamide (LDA) at -78 °C. Apparently, KDA is unstable in THF at 0 °C - and also presumably, by extension, at reflux temperatures.

We do not know why this method works in the dehydrobromination of **40**. One possibility is that the active reagent is an alkoxide species formed by attack of KDA upon THF.[66] The important point, however, is that the method does work, and that it works more effectively than anything else that was attempted.

Cristol and Nachtigall purified monobromide **42** by recrystallization from ethanol;[61] Wilt and coworkers by reduced pressure distillation.[62] We found that recrystallization gave notoriously poor yields. Rather than attempt distillation of a low-melting solid, we attempted to purify the monobromide by sublimation. This worked very well, and pure, white product was obtained. Purification in higher yield, and of larger quantities, could be accomplished by dry flash

chromatography;[67] the product obtained by this method was pale yellow, but it was still of sufficient purity to be used in the next step.

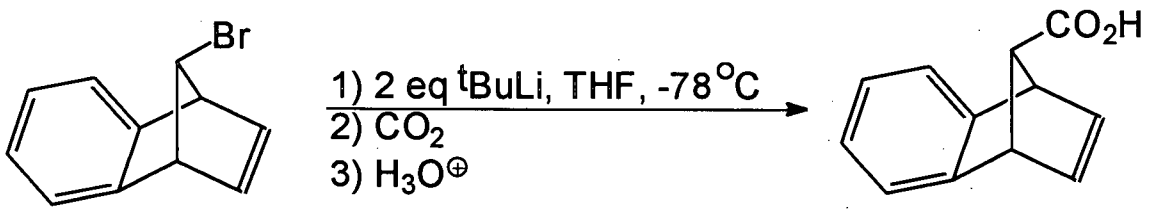
Complete conversion of dibromide **40** to monobromide **42** is esential, because it is almost impossible to remove traces of the dibromide by conventional purification methods.

During the reflux period, the colour of the solution changed from golden brown to reddish purple. This colouration disappeared when the reaction mixture was quenched. Cristol and Nachtigall[60] also noted the appearance of a dark purple colouration during their dehydrobromination step and, while their procedure was somewhat different from the one followed here, familiarity is always comforting.

Care must be taken in attempting to vacuum-dry this compound. It is volatile enough that samples disappeared when left under vacuum overnight.

4.4. Synthesis of *anti*-9-Carboxybenzonorbornadiene (19).

To prepare acid **19**, monobromide **42** was first added to a solution of *tert*-butyllithium in THF, at -78 °C, to form the organolithium derivative of **42**. This was then quenched by addition of dry carbon dioxide gas, and the carboxylate was protonated by addition of aqueous acid (Scheme 4.4.1).



42 **19**

Scheme 4.4.1. Preparation of acid **19** by transmetalation and CO_2 quenching.

Acid **19** had been prepared in a similar manner by Buske and Ford,[46] who prepared the lithium species by treatment of **42** with *sec*-butyllithium, and quenched the reaction mixture by pouring it over crushed dry ice.

Acid **19** was prepared in 74% recrystallized yield. Large crystals suitable for X-ray analysis were readily obtained, and the crystal structure and packing diagram are given in Figures 4.4.1 and 4.4.2, respectively. The crystals were monoclinic, of space group $P2_1/c$. The benzo-vinyl distances (C7-C5 and C12-C4, Figure 4.4.1) were 2.432 and 2.435 Å. The acid was shown to exist as a

dimer, with four molecules to a unit cell, each pair held facing one another through hydrogen-bonding. This appeared to be the dominant intermolecular interaction. The *anti*-orientation of the 9-carboxy group was also confirmed unequivocally by determination of the crystal structure.

The purified acid sublimes upon heating (204.5-205 °C). It does not melt at atmospheric pressure.

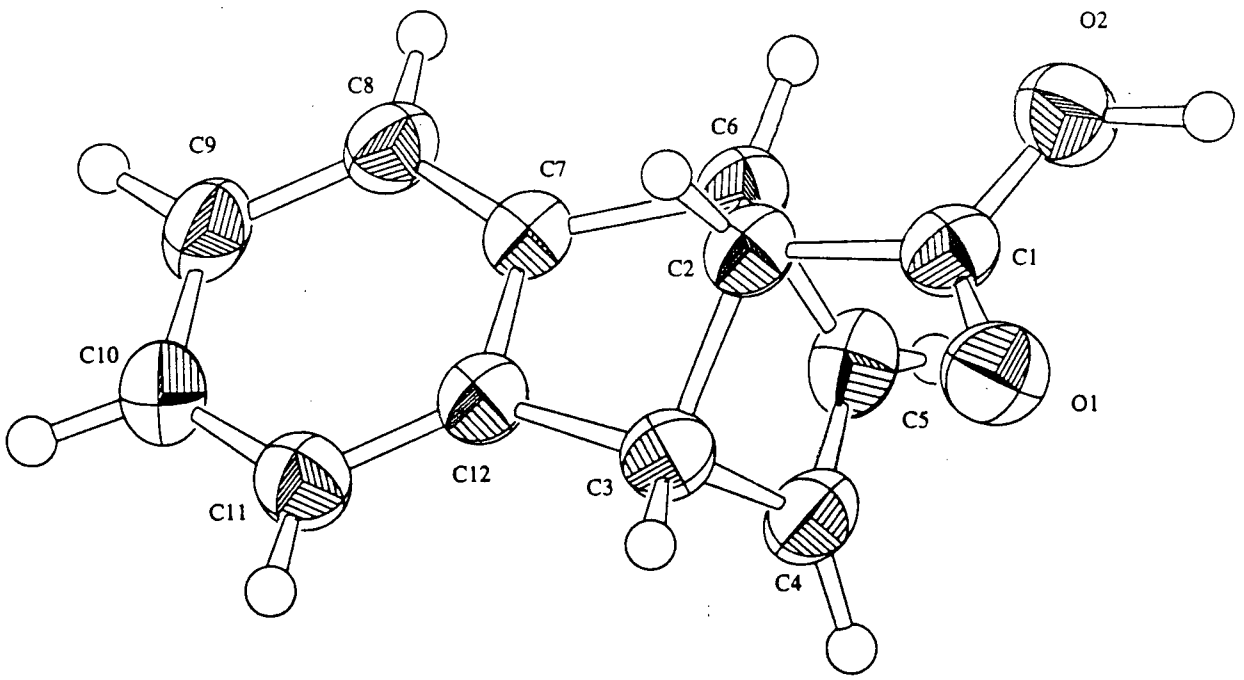


Figure 4.4.1. X-ray crystal structure of acid **19**.

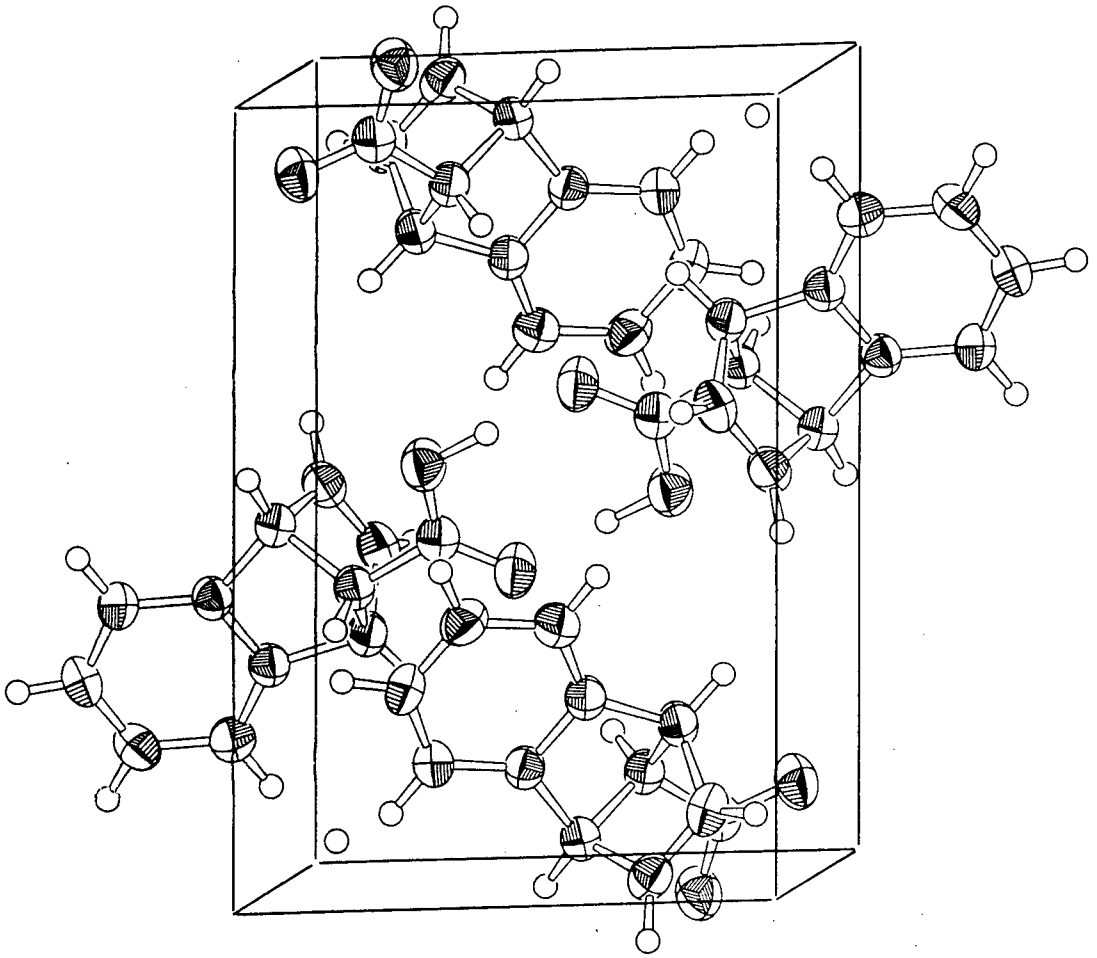
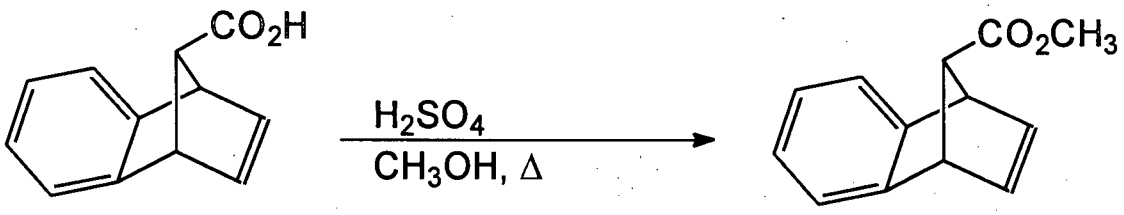


Figure 4.4.2. Packing diagram for acid **19**.

4.5. Synthesis of *anti*-9-Carbomethoxybenzonorbornadiene (45).

The methyl ester of acid **19**, compound **45**, was prepared by sulfuric acid-catalyzed Fischer esterification in refluxing methanol, as described by Buske and Ford (Scheme 4.5.1).[46]



19 **45**

Scheme 4.5.1. Preparation of methyl ester **45**.

Buske and Ford mentioned that a minor amount (1.2%) of an unidentified compound having a similar GC retention time to that of **45** was observed. They also mention that they made no attempt to isolate this compound. Our results confirm their observation. GC analysis consistently showed 1-2% of a minor product, separated by a retention time difference of 0.08 minutes. This minor product could not be removed, although numerous attempts were made. The GC separation could not be significantly improved by variation of the analysis conditions. The presence of this impurity did not affect the elemental analysis results, which would seem to indicate that it is an isomer of **45**. A similar impurity was also present in samples of monobromide **42**. The impurity, for both

monobromide and ester, could only be observed by GC analysis. No other spectral data suggested that either compound was not entirely pure.

One possibility is that the impurity consists of the *syn*-9-isomer. However, as will be pointed out later in this thesis, the irradiation results do not support this hypothesis, since the minor product does not react upon irradiation. Another explanation - which, unfortunately, runs into the same difficulty when the irradiation results are explained - is that the impurity is a 2-carbomethoxy (or 2-bromo) isomer of the major product. Although Cristol and Nachtigall[61] reported dibromide **40** as the sole product of benzonorbornadiene bromination, they observed formation of dichloride mixtures upon chlorination of the same hydrocarbon. The observed products are shown in Figure 4.5.1. If bromination of benzonorbornadiene were to yield a minor amount of dibromide **51**, analogous to dichloride **46**, this compound would be expected to give, by *exo,cis*-elimination, the vinyl bromide **52** (Scheme 4.5.2). This rationale could also be used to explain formation of the *syn*-9-monobromide, by dehydrobromination of a dibromide analogous to **48**. It is quite conceivable that either of these suggested dibromides might not separate from dibromide **40** upon GC analysis.

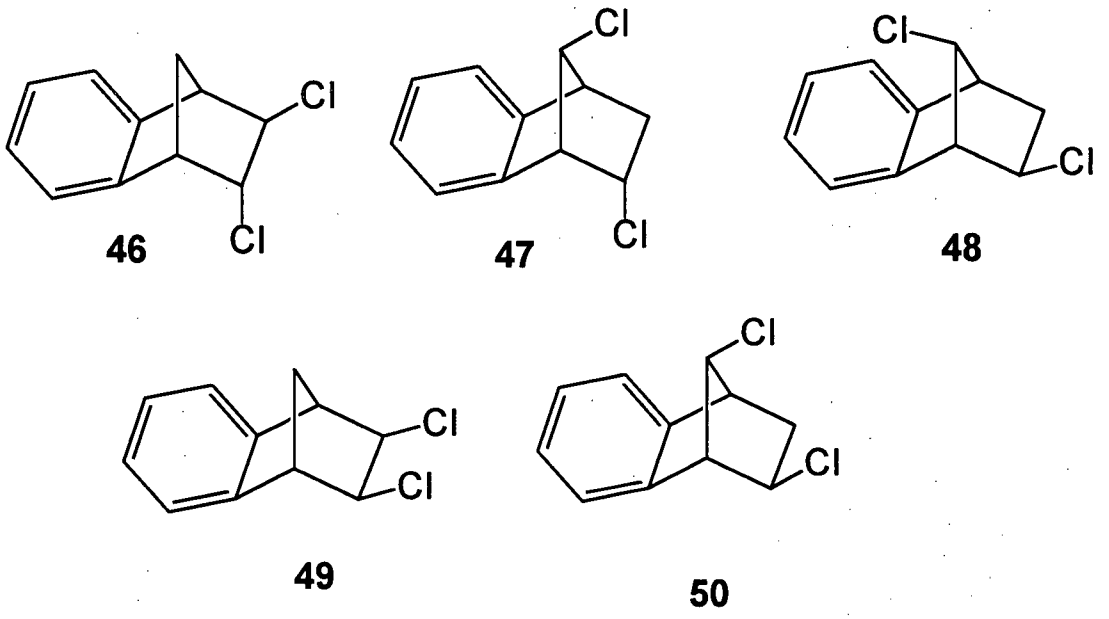
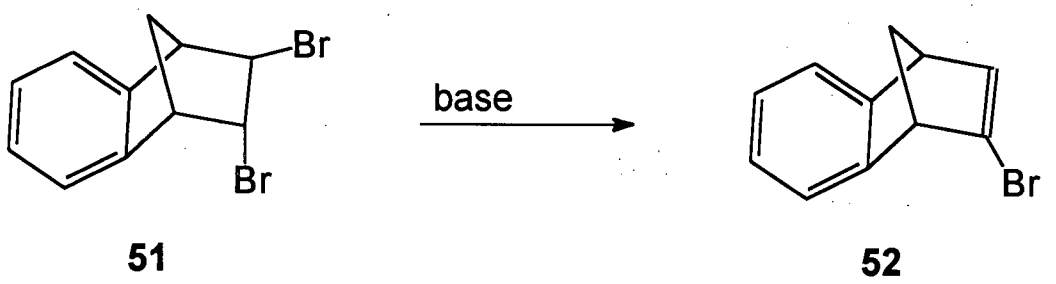


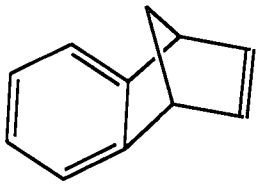
Figure 4.5.1. Various dichloride isomers formed upon chlorination of benzonorbornadiene (**13**).[61]



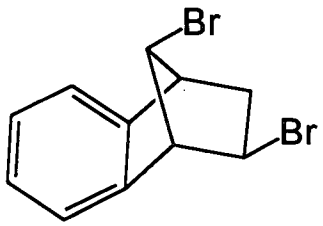
Scheme 4.5.2. Formation of a vinyl bromide (**52**), a possible source of the observed impurity.

4.6. Nomenclature of Benzonorbornadiene and its Derivatives.

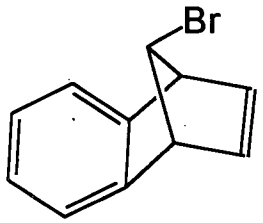
As noted earlier,[2] benzonorbornadiene is not the approved IUPAC name for compound **13**. The correct names for compounds **13**, **40**, **42**, **19**, and **45** are given below, in Figure 4.6.1.[68] The numbering system used in assigning IUPAC names was maintained in the names used in this thesis; thus, the benzonorbornadienes are numbered as methano-bridged dihydronaphthalenes, with the methano bridge carbon assigned the number 9. Both Cristol[61] and Wilt[62] assign the methane bridge position as carbon 7, by analogy with norbornadiene; however, this thesis uses the numbering system followed by Paquette.[9]



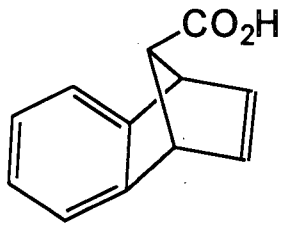
13; 1,4-methano-1,4-dihydronaphthalene



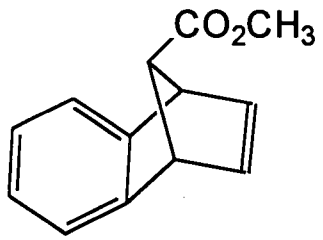
40; *exo*-2-*anti*-9-dibromo-1,4-methano-1,2,3,4-tetrahydronaphthalene



42; *anti*-9-bromo-1,4-methano-1,4-dihydronaphthalene



19; 1,4-methano-1,4-dihydronaphthalene *anti*-9-carboxylic acid



45; methyl 1,4-methano-1,4-dihydronaphthalene *anti*-9-carboxylate

Figure 4.6.1. IUPAC names for benzonorbornadiene and derivatives.

4.7. ^{1}H NMR Analysis of Benzonorbornadiene and its Derivatives.

Cristol and Nachtigall reported ^{1}H NMR data for compounds **13**, **42**, and **19**;[69] Wilt and coworkers report data for compounds **40** and **42**.[62] These analyses were carried out at 60 MHz, and many of the coupling constants are either missing or imprecise. Nonetheless, their work greatly simplified the task of assigning the proton resonances for these compounds. The proton resonances, assignments, and coupling constants are reported in Table 4.7.1.

The values obtained usually agree well with those reported in the literature, and are usually easy to interpret. The aliphatic regions of compounds **42** and **19** were not amenable to simple analysis, and thus the peaks are reported as multiplets. Benzonorbornadiene and its derivatives contain protons which are chemically equivalent but magnetically inequivalent, and this tends to complicate the spectra.

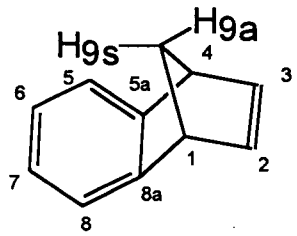
In the spectrum of benzonorbornadiene (**13**), the bridgehead protons appear as a quintet (J = 1.7 Hz). This was observed by Cristol,[69] as was the appearance of a triplet (J = 1.9 Hz) for the olefinic protons. Each bridgehead proton shows vicinal coupling to both 9-protons and to the adjacent olefinic proton, and long-range allylic coupling to the other olefinic proton. All four couplings, coincidentally, are approximately equal in strength. It may seem unusual for 3- and 4-bond couplings to be equivalent in strength; however, the dihedral angle between each bridgehead protons and its vicinal neighbours approaches 90°, and thus the couplings are expected to be small. The same

rationale explains why the olefinic protons appear as a triplet, each coupled about equally to each of the two bridgehead protons. The *syn*-9 proton shows long-range coupling to the olefinic protons; both the *syn* and *anti* protons appear as doublets of triplets, but the *syn*-9 proton resonance also shows considerable broadening.

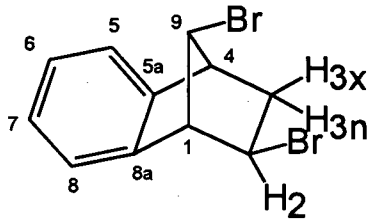
In the spectrum of dibromide **40**, Wilt *et al.* found that H-1 appeared as a doublet, coupled to H-9 (1.5 Hz).[62] We observed a singlet for this proton. Wilt did not observe coupling between H-1 and its vicinal neighbour H-2 - probably due, once again, to the dihedral angle between these protons - or between H-1 and H-4 (expected long-range coupling). H-2 appeared in our spectrum as an eight-line pattern with three distinct splittings, representing couplings to both of the 3-protons (8.1 and 4.5 Hz) and to H-9. This is confirmed by Wilt, as is the splitting pattern we observed for the *endo*-3-proton. For the *exo*-3-proton, Wilt observed a doublet of triplets, with equal couplings to H-4 and H-2, and a larger coupling to the *endo*-3-proton. We observed the same pattern. However, we did not observe a corresponding splitting of the H-4 resonance. The H-4 resonance appeared as a triplet (Wilt reported a doublet of doublets) with J = 1.8 Hz. This corresponds well enough to the splitting of 1.4 Hz observed in the H-9 resonance, but not to the 4.2 Hz coupling unassigned for the *exo*-3 resonance. Finally, although Wilt reported H-9 as a multiplet, we observed a triplet (J = 1.4 Hz), coupled as described previously to H-2 and H-4.

The NMR spectrum of ester **45** was reported by Buske and Ford.[46] The splitting patterns we observed are less well resolved. We observed coupling

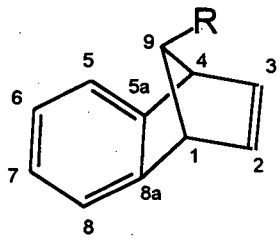
between the bridgehead protons and the adjacent olefinic protons, whereas Buske also found that each bridgehead proton appeared to couple equally to both olefinic protons and to H-9. We also observed an unassignable splitting of 3.5 Hz for the bridgehead resonance. The small long-range coupling (0.35 Hz) observed by Buske between H-9 and the olefinic protons was not resolved. H-9 appeared as a broadened singlet.



13



40



R=Br (**42**)
CO_2H (**19**)
CO_2CH_3 (**45**)

Figure 4.7.1. Accompanying structures for Table 4.7.1 (see below).

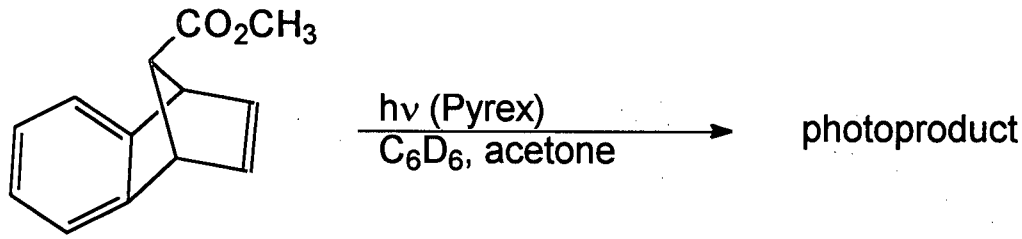
Table 4.7.1. ^{1}H NMR data for benzonorbornadiene (**13**) and its derivatives. For a list of abbreviations, see Experimental, General Procedures (9.1). mt. = multiplicity.

Compound	H-1	H-2	H-3/H-3x	H-3n	H-4	aromatic	aromatic	H-9/H-9s	H-9a
13 (200 MHz, $CDCl_3$) δ (ppm, mt.) J (Hz)	4.03 (t) J = 1.7	6.94 (t) J = 1.9	6.94 (t) J = 1.9	N/A	4.03 (t) J = 1.7	7.38 (dd) J = 5.1 J = 3.1	7.09 (dd) J = 5.1 J = 3.1	2.40 (br dt) $J_{9s,9a}$ = 7.1 $J_{9s,1}$ = 1.5 $J_{9s,2}$ = broadening	2.48 (dt) $J_{9a,9s}$ = 7.1 $J_{9a,1}$ = 1.5
40 (300 MHz, $CDCl_3$) δ (ppm, mt.) J (Hz)	3.74 (s)	3.78 (ddd) $J_{2,3n}$ = 8.1 $J_{2,3x}$ = 4.5 $J_{2,9}$ = 1.4	2.85 (dt) $J_{3x,3n}$ = 13.5 J = 4.2	2.20 (dd) $J_{3n,3x}$ = 13.2 $J_{3n,2}$ = 7.8	3.50 (t) J = 1.8	7.17 (m)	7.17 (m)	4.13 (t) J = 1.4	Br
42 (300 MHz, $CDCl_3$) δ (ppm, mt.) J (Hz)	4.10 (m)	6.74 (m)	6.74 (m)	N/A	4.10 (m)	7.26 (dd) J = 5.3 J = 3.2	7.04 (dd) J = 5.4 J = 3.0	4.40 (m)	Br
19 (200 MHz, d_6-acetone) δ (ppm, mt.) J (Hz)	4.1 (m)	6.7 (m)	6.7 (m)	N/A	4.1 (m)	7.1 (dd) J = 5.2 J = 3.1	6.9 (dd) J = 5.2 J = 3.1	3.2 (m)	CO_2H 10.8 (br s)
45 (400 MHz, C_6D_6) δ (ppm, mt.) J (Hz)	4.07 (dd) J = 3.5 J = 1.7	6.53 (t) J = 1.8	6.53 (t) J = 1.8	N/A	4.07 (dd) J = 3.5 J = 1.7	7.02 (dd) J = 5.2 J = 3.0	6.84 (dd) J = 5.2 J = 3.1	3.10 (br s)	CO_2CH_3 3.28 (s)

5. Photochemical Studies of *anti*-9-Carboxybenzonorbornadiene (19) and *anti*-9-Carbomethoxybenzonorbornadiene (45).

5.1. Initial Investigations.

In order to confirm that the system was photochemically reactive, a Pyrex NMR tube containing a sample of ester **45** in C_6D_6 to which 1 drop of acetone had been added was irradiated (Scheme 5.1.1). The solution was analyzed by gas chromatography during and after irradiation, and the results displayed in Table 5.1.1 were obtained.



45

Scheme 5.1.1. Initial sensitized solution phase irradiation of ester **45**.

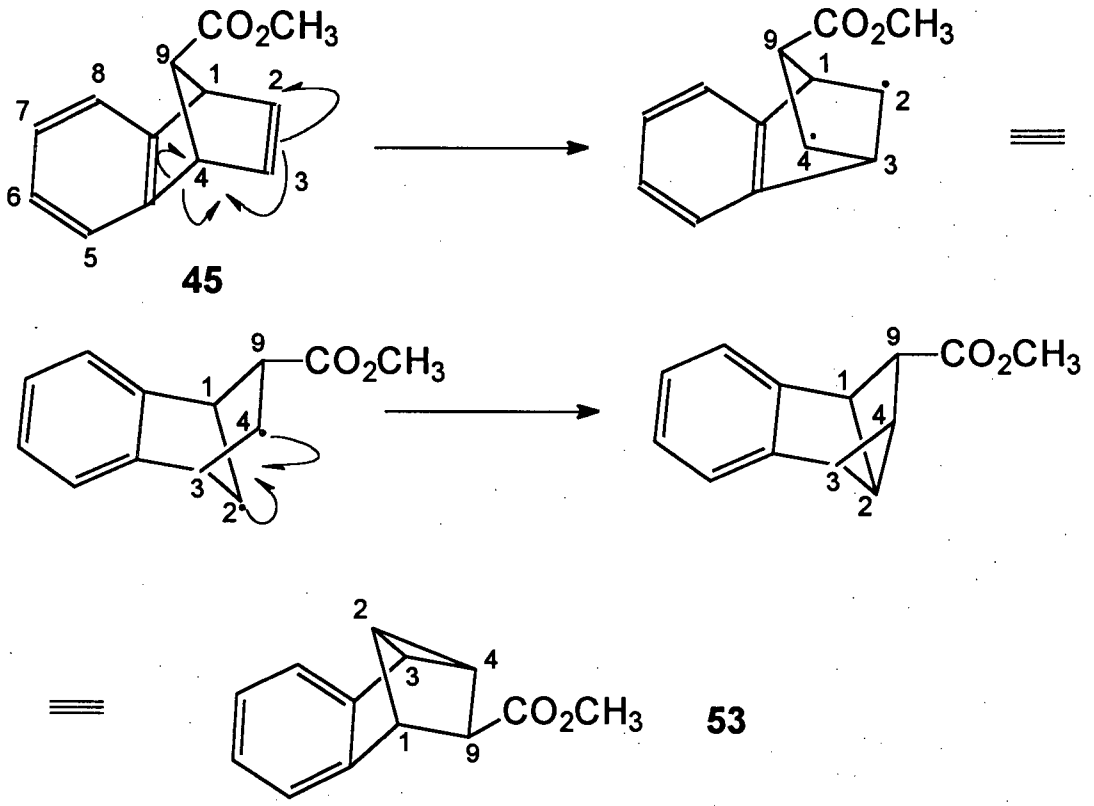
Table 5.1.1. Results of acetone-sensitized irradiation of ester **45**.

Irradiation Time (min)	% Conversion	% Yield of major photoproduct
30	67	100
60	93	79
90	97	72

As shown, irradiation of **45** gives a single photoproduct at relatively high conversion. Small amounts of three other unidentified products were obtained upon extended periods of irradiation.

The use made within this thesis of the term "yield" should be defined at this point. For small-scale photochemical reactions, such as those described in Table 5.1.1, values given for percent conversion and percent yield are reported as measured by GC analysis. The photoreactions were carried out on 5 mg samples, and product mixtures were not isolated or weighed. Conceivably, additional photoproducts not observed by GC analysis could have been formed, and these would not have been detected by the method used here. We assumed that the amounts of such photoproducts would be negligible, and could be omitted from consideration. "Percent conversion" refers to "100% - (area of starting material peak)". "Percent yield" refers to "(area of major photoproduct peak) / (percent conversion)".

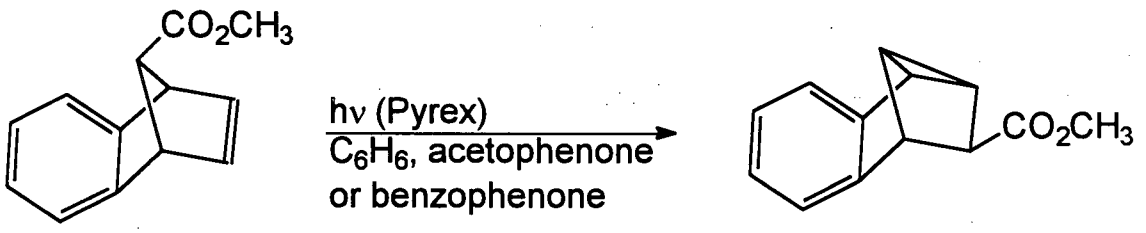
As discussed in Section 1.3, photorearrangement of **45** is expected to yield *exo*-undecatriene derivative **53**. A mechanism leading to this product is shown in Scheme 5.1.2. The initial irradiation experiment here was done on too small a scale to allow purification and characterization of the photoproduct - required, in order to demonstrate convincingly that the expected photoproduct was, in fact, formed.



Scheme 5.1.2. 1,2-aryl shift mechanism leading to expected *exo*-undecatriene **53**.

5.2. Preparation of Photoproduct Samples.

Initially, photoproduct **53** was prepared on a scale that allowed full characterization by sensitized solution phase irradiation of **45**, shown in Scheme 5.2.1. Either acetophenone or benzophenone could be used as the triplet sensitizer. The photoproduct was purified by column chromatography and short-path distillation; characterization by conventional spectoscopic methods (*vide infra*) showed that the isolated photoproduct was indeed compound **53**.

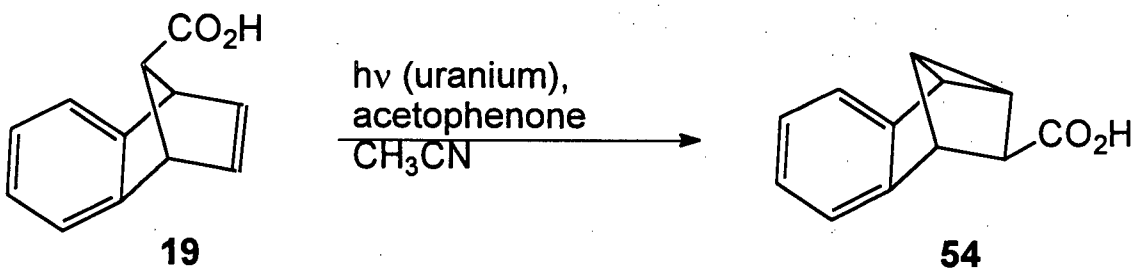


45 **53**

Scheme 5.2.1. Preparative-scale solution phase irradiation of **45**.

Effective removal of the sensitizer ketone was difficult. It could not be completely removed by either chromatography or distillation. Acetophenone is often chosen as the triplet sensitizer in di-π-methane reactions because it can usually be removed by distillation;[30] unfortunately, ester **53** is also quite volatile. The difficulty encountered in removing the sensitizer decreased the yield of **53** considerably.

In order to overcome this problem, the irradiation procedure shown in Scheme 5.2.2 was adopted. Photoproduct **54** could be removed from the acetophenone by extraction into 5% sodium hydroxide as the carboxylate. Once the acid photoproduct had been isolated, it could be converted in quantitative yield to methyl ester **53** by treatment with ethereal diazomethane. This allowed the preparation of sensitizer-free photoproduct in high yield (82%).



19 **54**

Scheme 5.2.2. Preparation of acid photoproduct (**54**).

5.3. NMR Analysis of the Photoproducts.

^{1}H and ^{13}C NMR spectra of photoproducts **53** and **54** were obtained. ^{1}H-^{13}C correlation spectra (HMQC) were also obtained for both photoproducts, and compound **53** was, in addition, subjected to ^{1}H-^{1}H correlation spectroscopy (COSY) and systematic homonuclear decoupling of the aliphatic region. The ^{1}H NMR spectrum of ester photoproduct **53** is shown in Figure 5.3.1. The NMR data for compound **53** is presented in Tables 5.3.1 and 5.3.2, and the data for compound **54** is presented in Table 5.3.3.

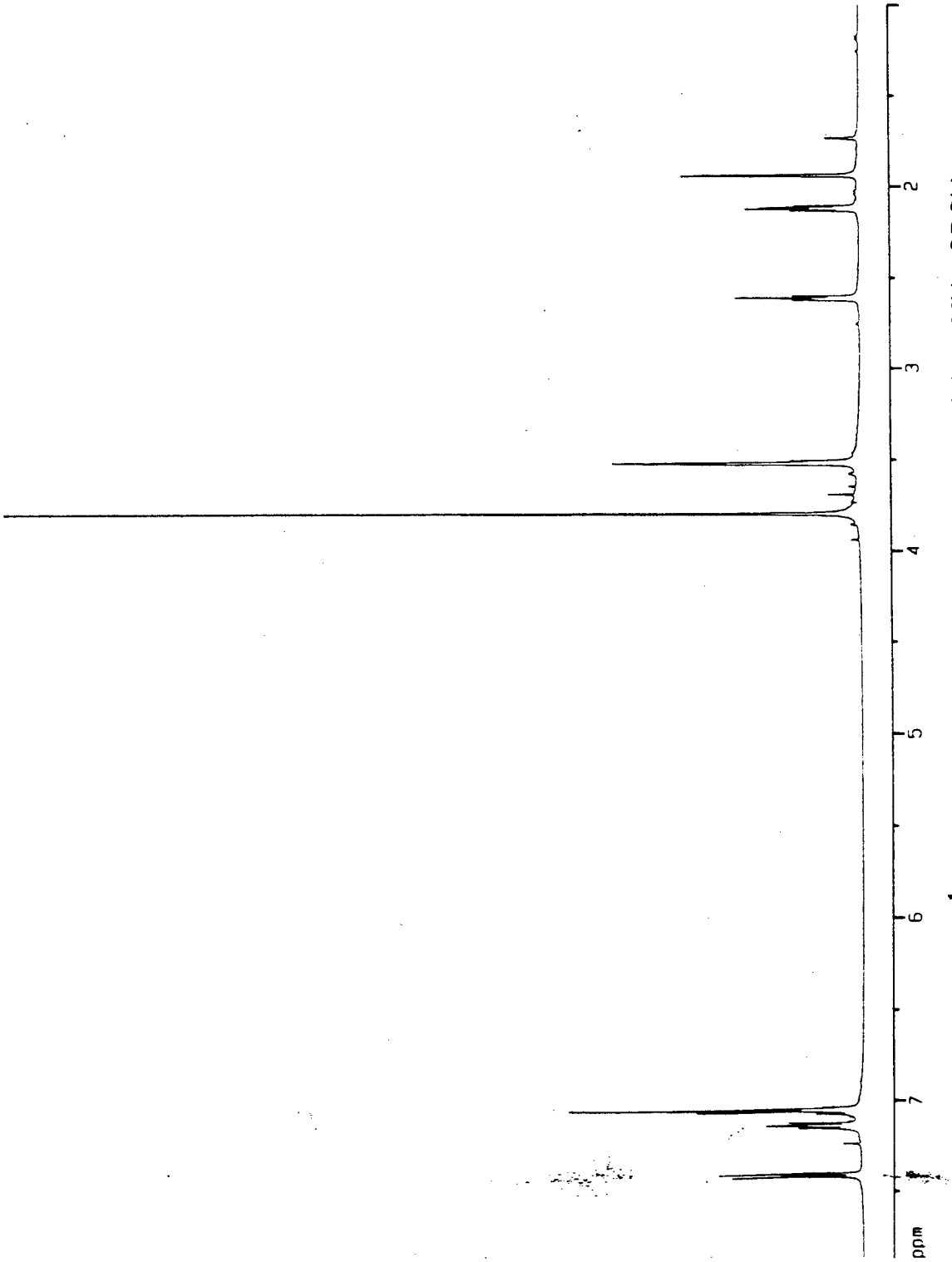
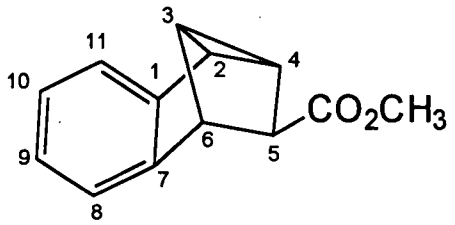


Figure 5.3.1. ^{1}H NMR spectrum of ester photoproduct **53** (500 MHz, $CDCl_3$).

Table 5.3.1. ^{1}H NMR data (500 and 400 MHz, $CDCl_3$) for ester photoproduct **53**.

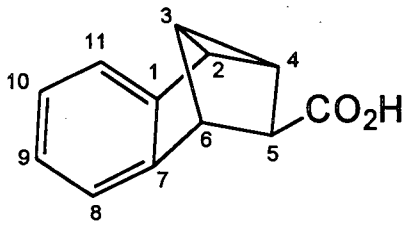


^{1}H NMR (500 MHz) δ ppm (# H, multiplicity, J (Hz))	**Assignment**	**COSY Correlations (400 MHz)**	**Homonuclear Decoupling Correlations (400 MHz)**
7.42 (1, d, 7.4)	H-8 or H-11	m at 7.14	
7.14 (1, m)	H-9 or H-10	m at 7.14, m at 7.06	
7.06 (2, m)	aromatic	m at 7.14	
3.80 (3, s)	OCH_3		
3.51 (2, m)	H-6, H-3	H-2, H-4, H-5	
2.61 (1, m)	H-2	m at 3.51, H-4	m at 3.51, H-4
2.12 (1, m)	H-4	m at 3.51, H-2	m at 3.51, H-2
1.94 (1, m)	H-5	m at 3.51	m at 3.51

Table 5.3.2. ^{13}C NMR (125 MHz, $CDCl_3$) data for ester photoproduct **53** and correlation to the ^1H NMR (500 MHz) spectrum.

Assignment	**^{13}C NMR (125 MHz) δ ppm (APT phase from 75 MHz)**	**HMQC Correlation to ^1H NMR (500 MHz) δ ppm**
C-1	146.49 or 142.79 (+)	
C-2	29.30 (-)	2.61
C-3	45.39 (-)	3.51
C-4	22.07 (-)	2.12
C-5	46.65 (-)	1.94
C-6	47.62 (-)	3.51
C-7	146.49 or 142.79 (+)	
C-8	125.15, 123.17, or 120.50 (-)	7.42, 7.06
C-9	126.33, 125.15, or 120.50 (-)	7.14, 7.06
C-10	126.33, 125.15, or 120.50 (-)	7.14, 7.06
C-11	125.15, 123.17, or 120.50 (-)	7.42, 7.06
$\underline{C}O_2CH_3$	175.98 (+)	
$CO_2\underline{C}H_3$	51.99 (-)	3.80

Table 5.3.3. ^{1}H (500 MHz) and ^{13}C (125 MHz) NMR (CD_3CN) data for acid photoproduct **54**.



^{1}H NMR (500 MHz) δ ppm (# H, multiplicity, J (Hz))	**Proton Assignment**	**HMQC Correlation to ^{13}C NMR (125 MHz) δ ppm**	**Carbon Assignment**
7.44 (1, d, 7.4)	H-8 or H-11	124.14	C-8 or C-11
7.14 (1, ddd, 7.3, 6.0, 2.7)	H-9 or H-10	127.35	C-9 or C-10
7.06 (2, m)	aromatic	126.17, 121.49	aromatic CH
3.49 (1, m)	H-6	48.59	C-6
3.46 (1, m)	H-3	46.32	C-3
2.65 (1, t, 5.0)	H-2	30.08	C-2
2.11 (1, m)	H-4	22.98	C-4
1.77 (1, d, 2.3)	H-5	47.55	C-5

Paquette's investigations into the photochemistry of substituted benzonorbornadienes were very useful in the assignment of the resonances for these two compounds. His group prepared and characterized many undecatrienes, of various substitution patterns.[16]

Assignment of the resonances in the spectra of the two photoproducts is basically the same, and will be discussed only for ester photoproduct **53**, with reference to the data for photoproduct **54** whenever that is useful. The peaks tend to be narrower in the ^{1}H NMR spectrum of **54**, which was determined, for

solubility reasons, in CD_3CN rather than in $CDCl_3$, and the peaks and couplings are therefore better resolved.

The resonance farthest upfield in the ^1H NMR spectrum was assigned to H-5. Although H-5 is adjacent to a carbonyl group, it is shielded by the aromatic ring. The HMQC spectrum correlates this proton to one of the most downfield aliphatic carbons - C-5 would not be expected to show the effect of aromatic shielding to the extent that H-5 would.

Because it is in a benzylic position, H-6 was expected to appear farthest downfield. Further confirmation that this is the correct assignment for the downfield aliphatic resonance is provided by the COSY spectrum, which shows that this is the only proton having a significant coupling interaction to H-5.

Assignment of H-4 was made upon its HMQC correlation to the carbon atom farthest upfield. The 4-position is part of the cyclopropane ring and far from the aromatic ring, so this assignment seems reasonable. Paquette found that C-4 was always the carbon atom farthest upfield.[16]

Assignment of H-2 and H-3 was made by analogy to Paquette's work. Paquette found that, despite the fact that H-2 is in a benzylic position, H-3 always appeared downfield of H-2, usually as part of a multiplet with H-6. Derivatives in which the 3-position had been substituted with a cyano group gave spectra in which the downfield two-proton multiplet had become a one-proton multiplet.

The only coupling interaction observed for H-5 was to H-6, at 2.3 Hz. This low value is due to the dihedral angle between these two protons, which

approaches 90°. Coupling was not observed between H-4 and H-5, in either Paquette's compounds or in ours. The resonance assigned to H-2 appears as a triplet in the spectrum of acid **54**, although a doublet of doublets was expected. Apparently, the coupling constants $J_{2,3}$ and $J_{2,4}$ happen to be identical for compound **54**.

The downfield aromatic peak shows only an *ortho*-coupling of 7.4 Hz. In the spectrum of acid **54**, the peak immediately upfield shows two resolved *ortho*-couplings (7.3 and 6.0 Hz) and a *meta*-coupling (2.7 Hz). This allowed assignment of the two resonances to H-8 or H-11, and H-9 or H-10, respectively; further assignment could not be made.

5.4. Chiral GC Analysis of the Ester Photoproduct (53).

Before asymmetric induction studies were carried out, ester photoproduct **53** was subjected to analysis by chiral GC, in order to determine the operating conditions which gave optimal separation of the two enantiomers. The samples used in these analyses were racemic, having been prepared by solution phase irradiation, in the absence of optical activity.

The optimal conditions are given in the Experimental section (Chapter 9.1). Assignment of the enantiomers as dextrorotatory (+) and levorotatory (-) is described in Chapter 10.3.

5.5. Direct Irradiation.

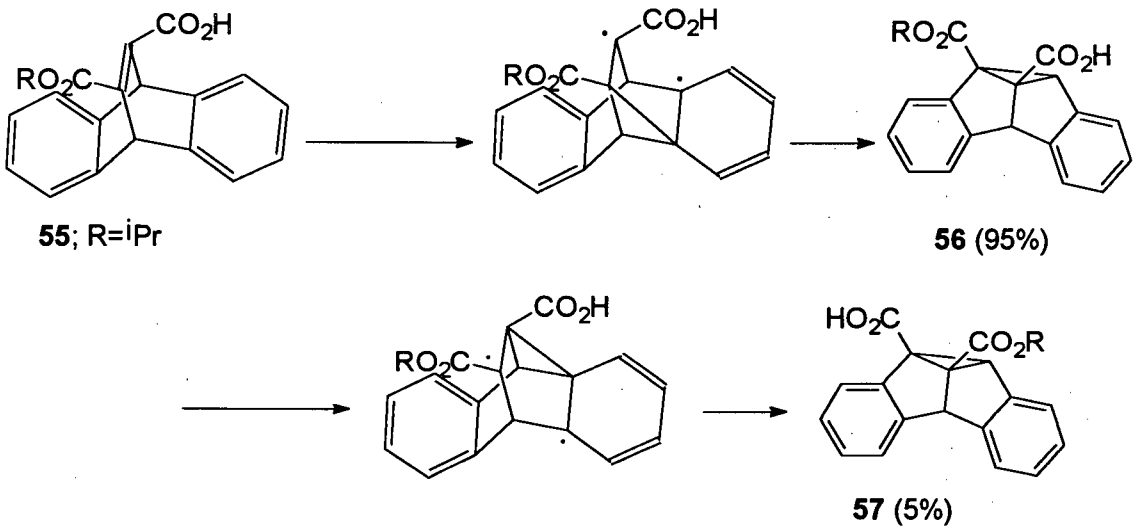
Although there was no reason to expect either acid **19** or ester **45** to react upon direct irradiation, these experiments were nonetheless carried out. Unexpectedly, both compounds are reactive. The results are shown in Table 5.5.1.

Table 5.5.1. Direct irradiation of acid **19** and ester **45**. Samples of the acid were analyzed after conversion to the methyl ester by treatment with diazomethane.

Substrate	Conditions	Filter (λ cutoff, nm)	% Conversion
19	CH_3CN solution, 5h	quartz (200)	39 (17% **53**)
	CH_3CN solution, 6h	Vycor (240)	20 (23% **53**)
	CH_3CN solution, 6h	Pyrex (290)	2.8 (75% **53**)
	solid, 6h	quartz	0
	solid, 5h	Corex (260)	0
	solid, 6h	uranium (330)	0
45	CH_3CN solution, 2h	quartz	50 (6.4% **53**)
	CH_3CN solution, 12h	Pyrex	7.5
	CH_3CN solution, 5h	uranium	0
	solid, 2h	quartz	35
	solid, 6h	Corex	22
	solid, 12h	Pyrex	100 (81% **53**)
	solid, 5h	uranium	0

Neither substrate reacts upon irradiation with uranium-filtered light. This is not surprising; the substrates do not show UV absorption above 300 nm. The extent of reaction is generally greater in a series upon irradiation with light of successively shorter wavelengths. The purity of the photoproduct decreases upon irradiation of the substrate with more energetic light.

Results of solution phase irradiations are comparable for acid and ester. However, the acid does not react at all upon irradiation in the solid state, regardless of the wavelength used. This may be due to the packing arrangement. The acid crystallizes as a dimer, hydrogen-bonded across the unit cell through the carboxy groups of facing molecules (recall Figure 4.4.2). The acid has a very high degree of symmetry, and it also has quite a high sublimation point (204.5-205 °C), both of which would seem to indicate that the molecules in crystals of the acid exist in a very rigid arrangement. The system may be too rigid to allow the motions which would have to take place upon rearrangement. Scheffer and coworkers[70] found that irradiation of dibenzobarrelene mixed acid-ester **55** (Scheme 5.5.1) in the crystalline state led almost exclusively to the product derived from bridging at the vinyl site farthest removed from the carboxy group. Compound **55** was shown by IR to exist exclusively as a hydrogen-bonded dimer in the solid state, and the rationale suggested to explain the observed reactivity was the same as that offered here.

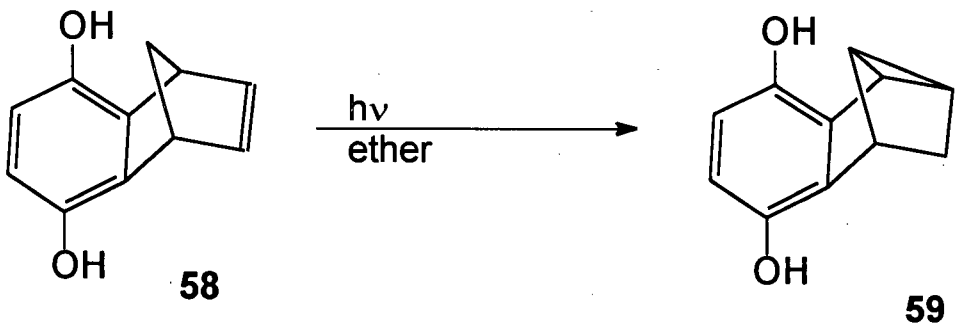


Scheme 5.5.1. Regioselectivity in the solid state photorearrangement of acid-ester **55**.[70]

This is all very well, but it does not explain why either acid **19** or ester **45** reacts at all upon direct irradiation. There is some evidence to suggest that very low yields of rearranged product may be formed upon direct irradiation of benzonorbornadiene derivatives,[5,18] but the extent of conversion to product observed for ester **45** in the solid state is certainly without precedent. On the other hand, this has been, to date, the only investigation of the solid state reactivity of a benzonorbornadiene derivative.

There is precedent for rearrangement upon direct irradiation of certain benzonorbornadienes bearing substituents on the aromatic ring, particularly substituents - such as ketones and nitro groups - which are known to promote intersystem crossing to the triplet state.[7,10,13,14] The reactivity of these compounds is usually explained by postulating enhancement of intersystem crossing by the substituent, although Fuerniss *et al.* proposed that the

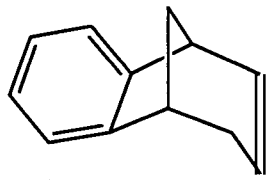
rearrangement of 5,8-dihydroxybenzonorbornadiene (**58**) proceeded through the singlet state (Scheme 5.5.2).[10]



58 **59**

Scheme 5.5.2. Rearrangement of benzonorbornadiene **58** upon direct irradiation.[10]

The best explanation for the observed solid state reactivity of ester **45** seems to be simply that the di-π-methane rearrangement in substituted benzonorbornadienes - at least, in this substituted benzonorbornadiene - can proceed from either the triplet or singlet excited state. Benzonorbornadiene itself is converted slowly to the undecatriene rearrangement product upon direct solution phase irradiation.[18] The homologue of benzonorbornadiene shown in Figure 5.5.2, compound **61**, undergoes di-π-methane rearrangement on either direct or sensitized irradiation, although it is a cyclic compound.[71] The reason given by Zimmerman for the lack of singlet state di-π-methane reactivity observed for cyclic systems is that many of these systems can rearrange instead by electrocyclic processes that are often much faster.[30] If a cyclic system does not have electrocyclic processes that compete effectively, there is no reason for di-π-methane rearrangement not to occur.



61

Figure 5.5.2. Benzo[6,7]bicyclo[3.2.1]octa-2,6-diene (**61**), a homologue of benzonorbornadiene.[71]

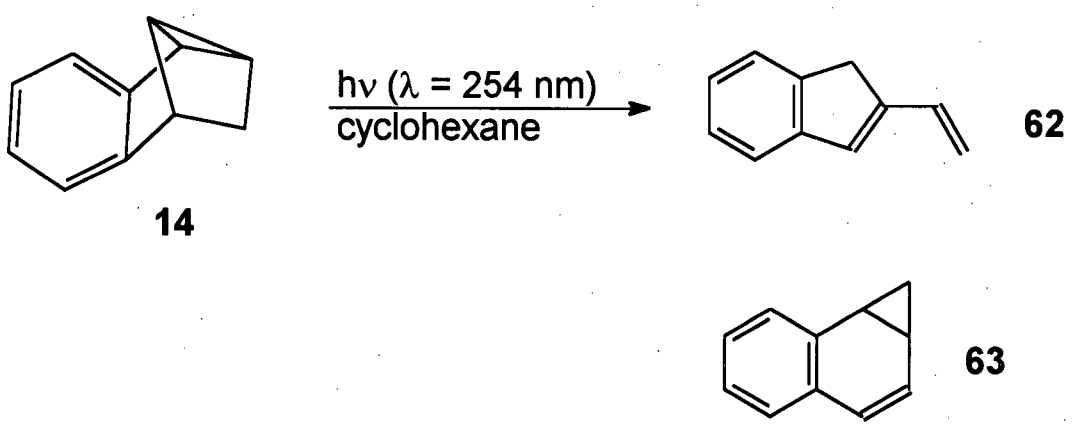
Thus, we conclude that the *anti*-9-substituted benzonorbornadienes studied in this work are capable of undergoing di-π-methane rearrangement from either the singlet or triplet excited state, although rearrangement from the triplet state is much faster (compare the results shown in Table 5.1.1 with those in Table 5.5.1). We are not certain why the reaction is so much faster in the solid state than in solution. Perhaps, in solution, quenching of the singlet excited state occurs through collisional interaction with solvent or other substrate molecules. Or, perhaps intersystem crossing to the triplet is enhanced for some reason in the crystalline state, so that irradiation in the solid state leads to reaction from both the singlet and triplet excited states.

The small impurity peak present in the starting material samples (discussed in Chapter 4.5) did not appear to be reactive. It remained at its initial concentration (1-2%) through all the experiments that were carried out.

5.6. Possible Secondary Photoproducts.

Small amounts of additional products were observed in most experiments (experiments for which the yield of **53** is not reported did not give detectable amounts of these products). These rarely appeared in greater than 15% total yield, and usually the yield was much lower (experiments for which extremely low product yields are reported gave GC traces showing extensive decomposition and many peaks). These additional products, believed to be secondary photoproducts, were not isolated.

Johnson and Davis[18] found that the undecatriene photoproduct of benzonorbornadiene rearrangement (**14**) underwent rapid conversion to a complex mixture of secondary and tertiary photoproducts, upon irradiation at 254 nm. The major products at low conversion were 2-vinylindene (**62**) and benzonorcaradiene (**63**), as shown in Scheme 5.6.1. The reaction was postulated to involve the singlet excited state, since acetone-sensitized irradiation ($\lambda > 300$ nm) was not effective.



Scheme 5.6.1. Direct irradiation of undecatriene **14**.[18]

The secondary photoproducts could not be completely removed from samples of undecatriene **53** prepared in this work. This did not affect elemental analysis results, indicating that these products are isomers of **53**. Irradiation of **53** (Pyrex, CH_3CN solution or thin film) gave samples in which the ratio of these products to compound **53** had been significantly enhanced (Table 5.6.1).

Table 5.6.1. Direct irradiation of photoproduct **53**.

Irradiation Conditions	**Ratio of Secondary Peak to 53**	
	12.83 min	**13.46 min**
starting material	0.043	0.0033
CH_3CN solution, 12h	0.18	0.027
thin film, 12h	0.096	not determined

The only difficulty in considering the extra peaks observed in the GC traces as secondary photoproducts is that they also appear in samples prepared by sensitized irradiation with light of wavelengths above 330 nm. Compound **53** should certainly not absorb strongly at these wavelengths; the ester carbonyl group is not conjugated to the aromatic ring, or even in an orientation from which the two groups can show any strong interaction. The UV spectrum measured for compound **53** does show a small absorbance maximum at 323 nm (ε 53.1), but this is probably due to the inseparable vinylindene or benzonorcaradiene derivatives, which would absorb at longer wavelengths. The secondary products observed in this work may be derived from thermal reaction of **53**, or they may be the product of reaction from the triplet state of **53**. Johnson and Davis[18]

found that **14** is unreactive from its triplet state, but the same is not necessarily true for **53**.

5.7. Extension of Direct Irradiation Results.

Since acid **19** and its derivatives did react upon direct irradiation, it now seemed possible to carry out asymmetric induction with chiral bases that were not capable of functioning as triplet sensitizers. The results of these experiments are described in Chapter 7; Chapter 8 discusses the results obtained from irradiation of salts prepared with chiral triplet sensitizers. The triplet state reaction of benzonorbornadienes is much faster than that observed upon direct irradiation, and we felt that it would still be worthwhile to investigate the sensitized asymmetric induction project originally planned, even though, contrary to our expectations, the substrates did not require a sensitizer in order to react.

Chapter 6 discusses triplet sensitization of the reaction through formation of salts with commercially available amines known to sensitize the di-π-methane rearrangement.

6. Triplet Sensitizer Salts of *anti*-9-Carboxybenzonorbornadiene (19).

As discussed in Section 3.2, as a prelude to planned investigations into sensitization of the photorearrangement by chiral triplet sensitizers, studies were undertaken to demonstrate that sensitization of the symmetric form of the reaction was possible through salt irradiation. Salts of acid **19** with known triplet sensitizer amines were prepared, and irradiated both in the solution phase and in the solid state.

The sensitizers chosen for these experiments are shown in Figure 6.1. Amines **64** and **66** were available in free base from; amine **65** was obtained as its hydrochloride salt and converted to the free base immediately before use by treatment with potassium hydroxide.

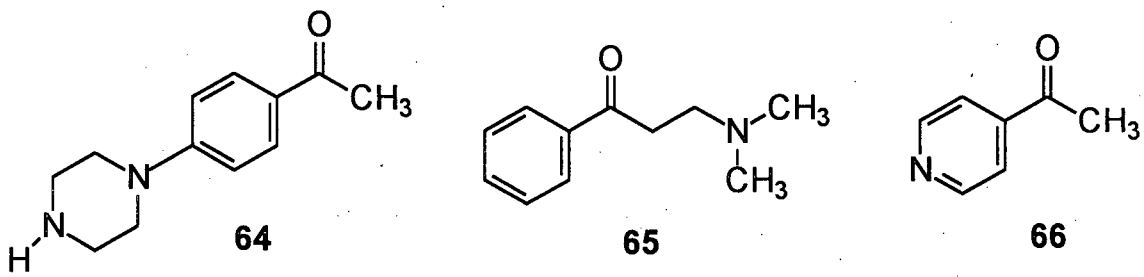


Figure 6.1. Triplet sensitizers used in salt formation with acid **19**.

A salt could not be prepared between acid **19** and amine **65**. This may be because tertiary amines are slightly less basic in solution than primary and

secondary amines, due to the interference of the alkyl groups with effective solvation - and hence, stabilization - of the ammonium ions.[72]

Salt formation between acid **19** and amine **64** gave yellow crystals (salt **67**) which were suitable for X-ray analysis. The X-ray crystal structure and packing diagram are shown in Figures 6.2 and 6.3 respectively. The space group of these monoclinic crystals was $P2_1/a$ (# 14). The unit cell contains four carboxylate ions in the centre, with an ammonium ion on the outside of the square associated with each.

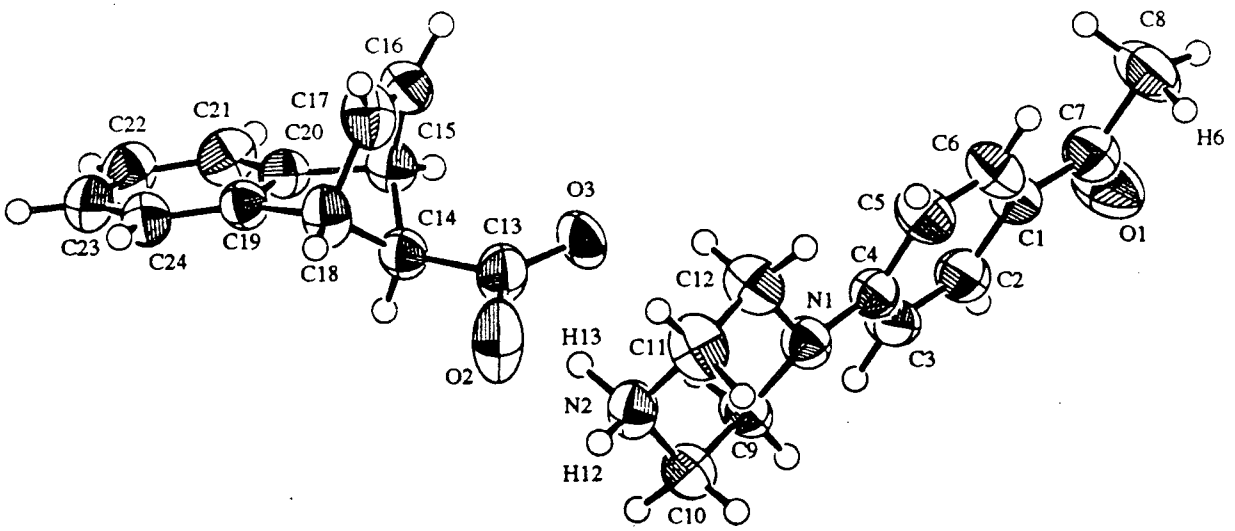


Figure 6.2. X-ray crystal structure obtained for salt **67**.

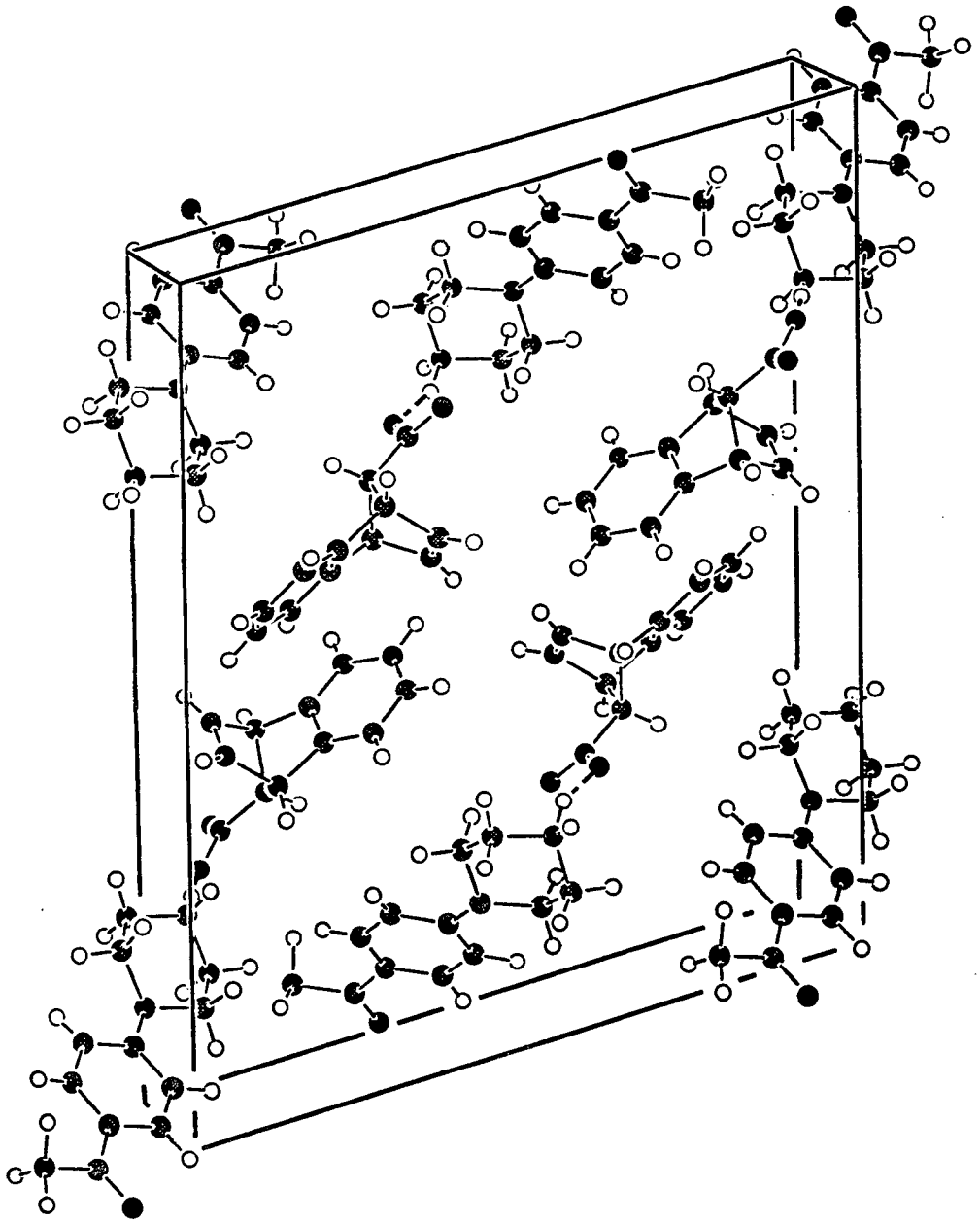


Figure 6.3. Packing arrangement for salt **67**.

Pyridines are even less basic than teriary amines.[72] However, a complex (not a salt), presumably involving hydrogen-bonding between the acid proton and pyridine nitrogen, was formed (complex **68**). To prepare this complex, a large excess of *p*-acetylpyridine had to be used. Elemental analysis did show that the complex formed nonetheless contained the acid and pyridine in a 1:1 ratio. The IR spectrum showed a peak for the acid carbonyl group in this complex at 1696 cm^{-1}, very close to the value obtained for the acid alone (1698 cm^{-1}). The IR spectrum obtained for salt **67** contained peaks at 1599 and 1412 cm^{-1}, typical values for the symmetric and antisymmetric stretching vibrations of a carboxylate group.

Irradiation of salt **67** for up to 6 hours in either CH_3CN solution or the solid state (λ > 330 nm) gave small amounts of unidentified products (< 20% conversion), but no detectable amount of photoproduct **53**. Solution phase irradiation of acid **19** (3:1 benzene / acetonitrile) in the presence of 10 equivalents of amine **64** did not yield compound **53** either.

There are two factors which may contribute to the inability of amine **64** to sensitize the photoreaction. As shown in the packing diagram (Figure 6.3), the aromatic ketone portion of the ammonium ion is not in close proximity to the aromatic ring of the carboxylate. The aromatic rings of the carboxylate ions interact with one another, and appear to be shielded from interaction with the aromatic rings of the ammonium ions by the aliphatic positions of the carboxylates and by the piperazine rings of the ammonium ions.

The second factor is that the triplet energy of this amine may be too low to sensitize the photoreaction of acid **19**. The piperazine ring substituted onto the aromatic ring should considerably decrease the triplet energy of amine **64** with respect to acetophenone. Ethyl benzoate has a triplet energy of 324 kJ/mol, while the triplet energy of ethyl 4-(dimethylamino)benzoate is only 284 kJ/mol.[73] Since the triplet energy of acetophenone is 310 kJ/mol, a similar effect resulting from introduction of a 4'-piperazine group might reduce the triplet energy of amine **64** to 270 kJ/mol. The triplet energy of benzonorbornadiene is estimated at 290 kJ/mol,[5] so it seems quite reasonable that the amine in question would be an ineffective sensitizer of benzonorbornadiene derivatives.

Triplet sensitization does occur in the *p*-acetylpyridine complex (**68**). The irradiation results are shown in Table 6.1.

Table 6.1. Irradiation of the complex (**68**) formed between acid **19** and *p*-acetylpyridine (**66**) ($\lambda > 330$ nm).

Irradiation Conditions	**% Conversion**	**% Yield of 53**
CH_3CN solution, 40 min	13	56
CH_3CN solution, 12h	52	80
solid, 40 min	28	100
solid, 3h	42	100

Triplet sensitization of the acid with *p*-acetylpyridine is less effective than with acetone (E_T = 332 kJ/mol[73]), acetophenone, or benzophenone (E_T = 289 kJ/mol[73]). It does, however, occur, as evidenced by the fact that the results shown are for irradiation with light that the acid does not absorb, and that gives

no conversion to product for either the acid or ester alone. Conversion to photoproduct **53** is cleaner in the solid state than in solution, and is also more rapid. Other studies have also shown that sensitization through irradiation of salts or complexes tends to be more effective in the solid state than in solution.[42] The rationale given is that the proximity of the sensitizer and substrate in the solid state enhances energy transfer with respect to the situation observed in the solution phase. Also, in the solution phase, solvation of the sensitizer and substrate tends to inhibit their interaction with one another. The rate decrease observed here upon going from the solid state to the solution phase was not as significant as it has been for these other studies. However, those studies usually involved irradiation of salts in methanol solution. Solvation of neutral acid and pyridine molecules by acetonitrile would not be expected to be as important a factor in separating the two moieties from each other as it would be for solvation of ions by methanol.

These results demonstrate that it is possible to carry out solid state triplet sensitization of acid **19**, indicating that salt formation with chiral triplet sensitizers should also allow sensitization of the photorearrangement.

7. Asymmetric Induction in the Photochemistry of *anti*-9-Carboxybenzonorbornadiene (19).

7.1 Preparation of Chiral Salts.

Salt or complex formation was attempted between acid **19** and each of the compounds shown in Figure 7.1.1 (names of compounds are given in Table 7.1.1). For those which gave solid, recrystallized products, the yield and crystal morphology are described in Table 7.1.2.

Table 7.1.1. Key to Figure 7.1.1.

Compound Number	Name of Compound
69	(S)-(-)-α-methylbenzylamine
70	(R)-(+)-α-methylbenzylamine
71	(1R,2S)-(-)-norephedrine
72	(1R,2S)-(-)-ephedrine
73	L-(S)-(-)-prolinamide
74	(1S,2S)-(+)-pseudoephedrine
75	L-(S)-(+)-arginine
76	L-(S)-(+)-2-pyrrolidinemethanol
77	(1S)-(-)-2,10-camphorsultam
78	L-(S)-(+)-lysine
79	*trans*-1,2-[4'-(2'-amino-6'-chloropyrimidine)amino]cyclohexane
80	(1S,2S)-(+)-2-amino-1-phenyl-1,3-propanediol

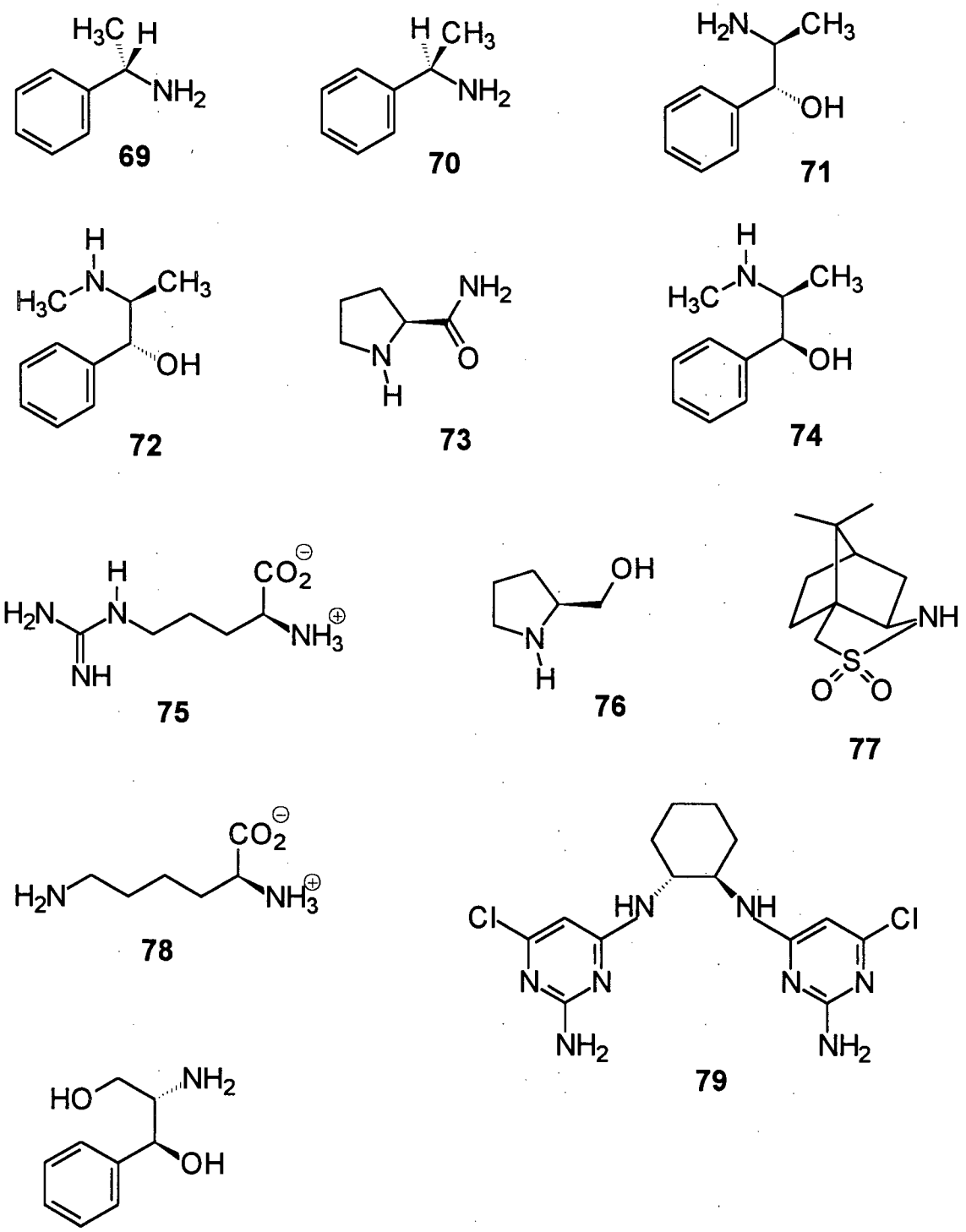


Figure 7.1.1. Chiral compounds for which salt or complex formation with acid **19** was attempted. See Table 7.1.1 for key.

Table 7.1.2. Yield and crystal morphology of chiral salts / complexes prepared.

Chiral Amine (# of Salt)	Percent recrystallized yield (Solvent)	Crystal morphology
69 (**81**)	85 (chloroform)	White powder. Voluminous in solution; shrank considerably upon isolation.
70 (**82**)	66 (chloroform)	Same as enantiomer.
71 (**83**)	70 (acetonitrile)	Tiny white needles.
72 (**84**)	21 (ethyl acetate)	Precipitated in solution as a voluminous mass of large, bluish, translucent crystals. Shrank to a white powder upon isolation.
73 (**85**)	69 (acetonitrile)	Small, iridescent, off-white flakes.
79 (**86**)	35 (acetonitrile)	4:1 acid / base complex (from ^{1}H NMR). Mostly white powder, containing some irregular, transparent, colourless plates.

7.2. Irradiation of Chiral Salts.

All the salts described in Table 7.1.2 gave ester photoproduct **53** upon irradiation with Pyrex-filtered light ($\lambda > 290$ nm) in either the solution phase or solid state. Complex **86** reacted upon irradiation in acetonitrile / methanol solution, but did not react at all in the solid state. The reason for this was not known and was not pursued.

Results of the salt irradiations are given below in Table 7.2.1.

Table 7.2.1. Irradiation results for chiral salts of acid **19** (**81-85**). Unless otherwise indicated, solution phase irradiation was carried out in CH_3CN / CH_3OH.

Salt	Irradiation Conditions	Percent Conversion	Percent Enantiomeric Excess (sign of rotation of product)
81	CH_3CN solution, 12h	2.3	0
	solid, 12h	4.3	5.9 (+)
	solid, 6h	2.7	16 (+)
82	solid, 6h	2.6	13 (-)
83	solution, 12h	17	0
	solid, 12h	34	9.4 (-)
	solid, 6h	7.2	20 (-)
	solid, 3h	2.0	30 (-)
84	solution, 6h	2.7	0
	solid, 6h	31	20 (-)
	solid, 3h	14	16 (-)
	solid, 1h	2.8	9.5 (-)
85	solution, 12h	6.8	0
	solid, 12h	1.5	41 (-)

Solution phase irradiation of these chiral salts gives (after aqueous acid / diazomethane workup) racemic ester photoproduct **53**. This was expected. The chiral environment in these systems is a consequence of the crystal lattice arrangement, which, of course, does not exist in solution. No enantiomeric excess would be expected for the products of photorearrangement in these cases, unless a strong interaction between the carboxylate and ammonium ion occurred in solution. Conversion to product is also slower for each salt in

solution than in the solid state, as was observed previously (Section 5.5) for benzonorbornadiene ester **45**.

Salts **81** and **82** formed between the two enantiomers of α-methylbenzylamine give ester photoproducts of equal and opposite optical rotation upon irradiation in the solid state. This was also to be expected, and demonstrates that the system is well-behaved. The chiral effect exerted by the crystal lattice in each of these salts should be equal and opposite, and mirror-image packing arrangements should exist.

Enantiomeric excesses tend to decrease upon increasing percent conversion. This trend is followed well in salts **81** and **83**. Salt **83** in particular, the norephedrine salt, shows a drastic increase in enantioselectivity for the photorearrangement upon decreasing the percent conversion from 34 to 2. This is a general phenomenon. As photoreaction of a crystal occurs, the lattice arrangement tends to break down. The product ions are not exactly the same shape as the substrate ions, and do not fit perfectly into the substrate lattice sites. Reaction tends to take place more quickly at the surfaces and pre-existing defect sites of crystals, so that the transformation from starting material to product does not occur evenly throughout the sample. Also, since the sample, over the course of the reaction, ceases to be a pure crystalline material, the melting point usually decreases, and the ambient temperature in the box which surrounds the photochemical lamp is often high enough to induce melting, which further degrades the lattice. Since the lattice arrangement itself is specifically responsible for the observed enantioselectivity, it is not surprising that effects

which break down this lattice should contribute to a decrease in the optical activity of the product.

The ephedrine salt (**84**) does not follow this trend. However, the appearance of the crystals was less regular than for any of the other salts. Salt **84** could best be described as a white powder; even in solution, the shape of the crystals was not very desirable. The crystals may have contained more defects than the crystals of the other salts did, decreasing the control that the lattice arrangement could have over the enantioselectivity of photorearrangement.

Unfortunately, no solvent could be found for any of these salts from which X-ray quality crystals could be obtained. All the crystals obtained were very small and fragile. We had hoped that X-ray structure data would provide insight into these systems, perhaps suggesting why the rate of reaction is so different from salt to salt, and why the prolinamide salt **85** gives photoproduct of such high enantiomeric excess compared with, for example, the methylbenzylamine salts (**81** and **82**). An X-ray crystal structure might also have shown why the ephedrine salt (**84**) gives such unpredictable results.

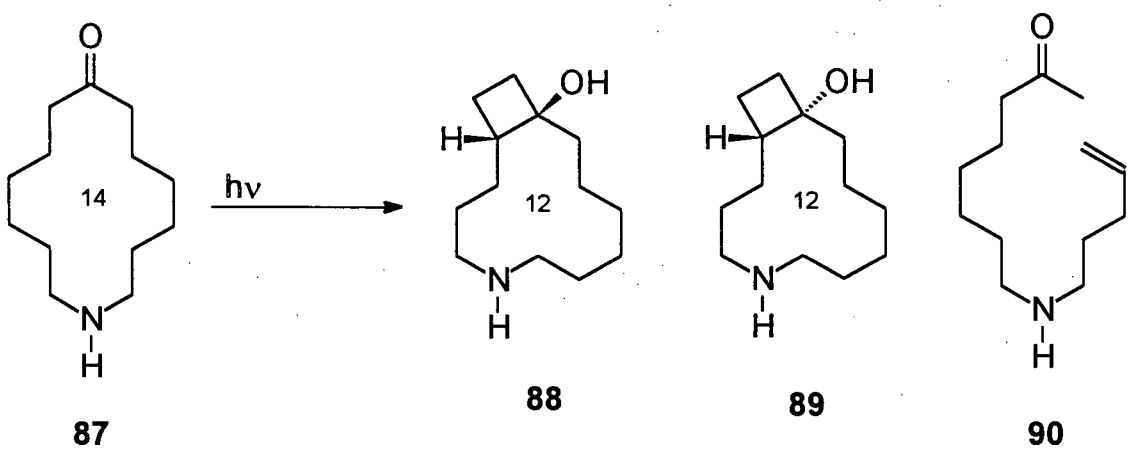
Although the photoreaction does occur upon direct irradiation - none of the ammonium ions present appears to be sensitizing the reaction - rearrangement is quite slow. Reaction times are long, and percent conversion is often very low even after irradiation for 12 hours. Most of the enantiomeric excesses obtained are disappointing. They are generally an improvement on the 14% enantiomeric excess obtained by Pitchumani and Ramamurthy for the irradiation of benzonorbornadiene included in chirally modified zeolites,[27] but are

not markedly better - with the exception of the 41% enantiomeric excess observed for the irradiation of the prolinamide salt (**85**). We were concerned for some time that the rigidity of the substrate we had chosen might make it impossible to obtain very high enantiomeric excesses of product, under any circumstances.

7.3. The Origin of Enantioselectivity in Chiral Crystals.

In the ionic auxiliary method, the chiral crystal lattice induces enantioselectivity by making the transition state leading to one of the two enantiomeric products lower in energy than the other. There are two ways this can occur. In the first, observed by Scheffer and coworkers for irradiation of salts of macrocycle **87** with chiral acids,[37] the chiral auxiliary controls the conformation in which the substrate crystallizes. Compound **87** is quite flexible, and can exist in solution in more than one conformation. Upon irradiation, it undergoes Norrish/Yang type II reaction, to give the products shown in Scheme 7.3.1. The first step after excitation is abstraction of a γ-hydrogen atom to yield a 1,4-biradical, and this is the step that determines which cyclobutanol enantiomer will be formed. In solution, none of the four γ-hydrogens is abstracted more easily than any of the others. However, crystallization of the macrocycle as its (S)-(-)-malate salt fixes it in one conformation, a conformation in which only one of those four hydrogens is close enough to the carbonyl oxygen to be abstracted. Thus, irradiation of this salt in the crystalline state

leads to >98% enantiomeric excess of the *cis*-cyclobutanol (**88**) derived from abstraction of that hydrogen.



87 **88** **89** **90**

Scheme 7.3.1. Products formed in solution upon irradiation of macrocycle **87**.[37]

The other way in which a chiral crystalline environment can induce enantioselectivity - probably that which operates in the work described here - is through steric hindrance. Crystallization of an achiral acid with a chiral, optically pure base causes the carboxylate ions to orient themselves in a particular fashion with respect to one another and to the ammonium ions. This chiral packing arrangement may make one side of carboxylate less hindered than the other. If the difference is significant, and if a considerable degree of motion is required in order to complete the photorearrangement, a steric barrier to formation of the less favoured product may be created. This is basically an extension of the reaction cavity theory developed by Cohen.[74] Cohen suggested

that a reacting molecule in a crystalline environment could be considered to exist in a cavity formed by its neighbouring molecules, and that reactions would be less likely to take place if they required the substrate to adopt a geometry that did not fit within the relatively immobile walls of this cavity.

For example, consider the photorearrangement of *anti*-9-carboxybenzonorbornadiene. Enantioselectivity will depend on which side of the molecule is involved in the product-determining 1,2-aryl shift - a step which should involve a very considerable degree of motion. Imagine that the chiral base with which the acid is crystallized is a cupped human hand. If the salt were to crystallize so that the acid had a hand-shaped base on each side, it should be easier to move the aromatic ring towards the vinyl group in the 1,2-shift on the side which faced the concave palm of the hand. The convex back of the hand would sterically shield the side of the acid which it faced.

The benzonorbornadiene system is quite inflexible, unlike the floppy macrocycle discussed above, and it seems unlikely that the observed enantioselectivity has a conformational origin, with the chiral base causing the acid to crystallize so that one benzo-vinyl distance is shorter than the other. Enantioselectivity through the reaction cavity concept seems much more plausible.

7.4. Irradiation of Chiral Salts at Reduced Temperature.

Because melting often causes a reduction in the enantioselectivity of a photoreaction, due to breakdown of the controlling lattice environment, irradiations are often carried out at reduced temperatures. This can increase the observed enantioselectivity by a considerable degree. Accordingly, salts **81**, **83**, and **84** were irradiated in the solid state, at temperatures from 0 to -20 °C. The results are shown in Table 7.4.1.

Table 7.4.1. Irradiation of salts of acid **19** at low temperatures.

Salt	Irradiation Conditions	Percent Conversion	Percent Enantiomeric Excess (sign of optical rotation)
81	12h (0 °C)	2.9	19 (+)
83	12h (0 °C)	24	4.6 (-)
	6h (0 °C)	2.9	16 (-)
	12h (-10 °C)	2.0	30 (-)
84	6h (0 °C)	7.5	15 (-)
	3h (0 °C)	2.8	14 (-)
	5h (-10 °C)	1.7	9.2 (-)
	12h (-20 °C)	2.3	17 (-)

These results are not really any better than those obtained through irradiation of salts at ambient temperatures, although they are not any worse. Perhaps, at the low conversions to which these salts were irradiated at reduced temperatures, most of the reaction occurs at the surface or at defect sites. This

would be expected to yield poor enantiomeric excesses. However, irradiation of norephedrine salt **83** to 24% conversion gives only 4.6% enantiomeric excess.

8. Design, Synthesis and Application of Chiral Triplet Sensitizer Auxiliaries.

8.1. Choice of Auxiliary.

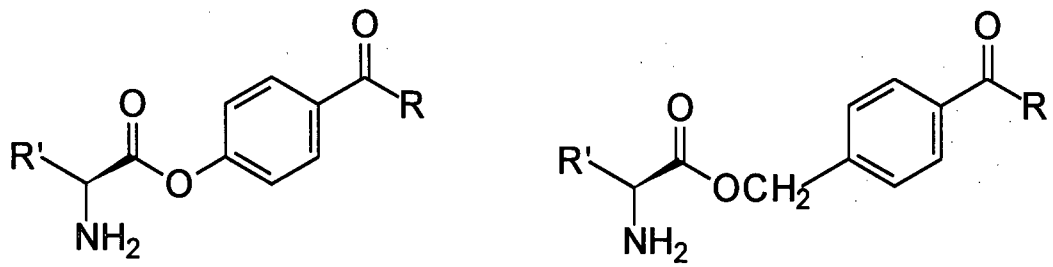
We had shown that the ionic auxiliary method could be used to achieve either triplet sensitization or asymmetric induction in the solid-state photochemistry of *anti*-9-carboxybenzonorbornadiene (**19**). Having accomplished this, we now wished to demonstrate that both processes could be effected in one experiment. Crystalline-state irradiation of salts formed between the acid substrate and chiral bases possessing triplet sensitizer capability should yield optically active product - much more quickly than in the direct irradiation experiments. The photorearrangement should also occur upon exposure to lower-energy ultraviolet light, of wavelengths above 330 nm - wavelengths at which the sensitizer shows absorbance, but at which the substrate does not.

The first step was to design an auxiliary. The ideal compound would, or course, contain a functional group capable of sensitizing the di-π-methane rearrangement of benzonorbornadiene derivatives, in addition to being an optically pure chiral molecule. It would be relatively easy to synthesize and amenable to variation of non-essential functional groups, so that the synthetic protocol established could be used to prepare a wide selection of different

auxiliaries exhibiting similar behaviour. It would also contain an amino functional group, in order to allow salt formation with the acid substrate.

Amino acid derivatives were an obvious choice. Auxiliaries prepared from natural amino acids would be chiral and optically pure. The starting materials would be readily available and inexpensive, and a variety of auxiliaries could be prepared through the same procedure simply by changing the amino acid used. Many amino acids are also available in N-protected forms, which would allow linkage of the acid group to a hydroxyl-tethered triplet sensitizer by ester formation, without interference from the free amino group.

Since we had shown that the photorearrangement could be sensitized by either acetophenone or benzophenone, we chose to use aromatic ketones as the triplet energy transfer motif. An ester linkage would be formed between the desired amino acid, and either a 4-hydroxyphenone or a 4-ketobenzyl alcohol (Figure 8.1.1).



R = CH_3, Ph
R' = functional group of amino acid

Figure 8.1.1. General structures of the proposed chiral triplet sensitizer auxiliaries.

The complementary approach, involving ester linkage of 4-ketobenzoic acids to amino alcohols, was also considered (Figure 8.1.2). An advantage of this method was that the appropriate benzoic acids were commercially available, unlike the benzyl alcohols. However, the selection of amino alcohols was less extensive than the selection of amino acids, it was more difficult to find amino alcohols with readily removable N-protecting groups, and the amino alcohols tended to be more expensive. Thus, the first approach was chosen.

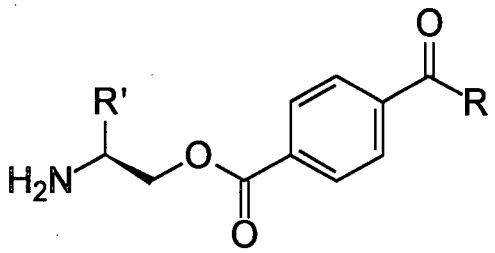
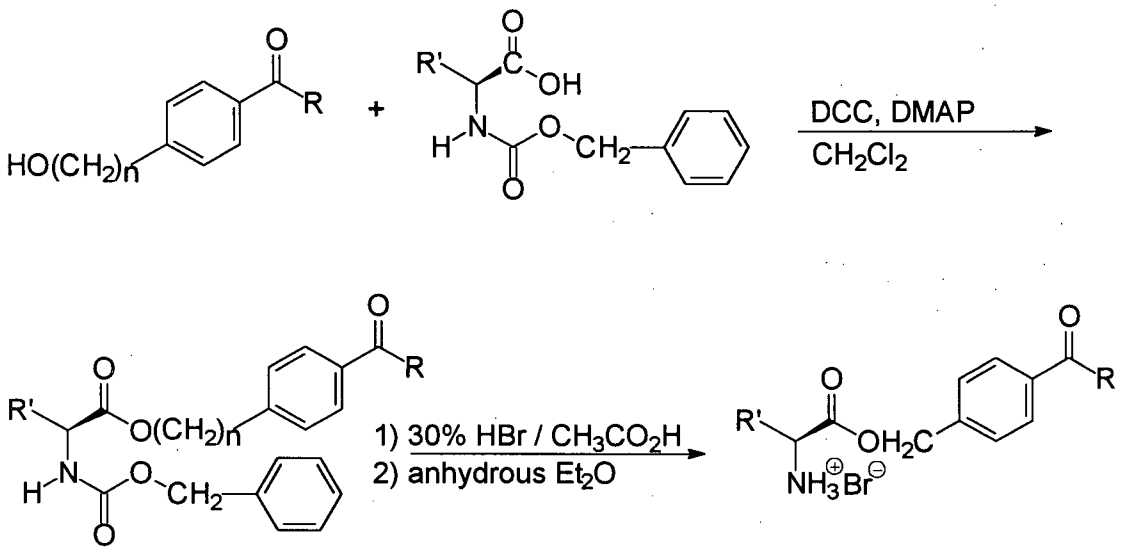


Figure 8.1.2. An alternative design for the chiral sensitizer auxiliaries.

8.2. Synthesis of the Auxiliaries.

The auxiliaries were prepared by a two-step sequence (Scheme 8.2.1). Esterification of the phenol or benzyl alcohol with an N-carbobenzyloxy- (Cbz-)-protected amino acid was followed by deprotection of the amino group with hydrogen bromide in acetic acid. The auxiliaries were isolated and characterized as their hydrobromide salts, because the free α-amino esters were

expected to be less stable. Commercially available α-amino esters are usually sold as the hydrochloride salts.

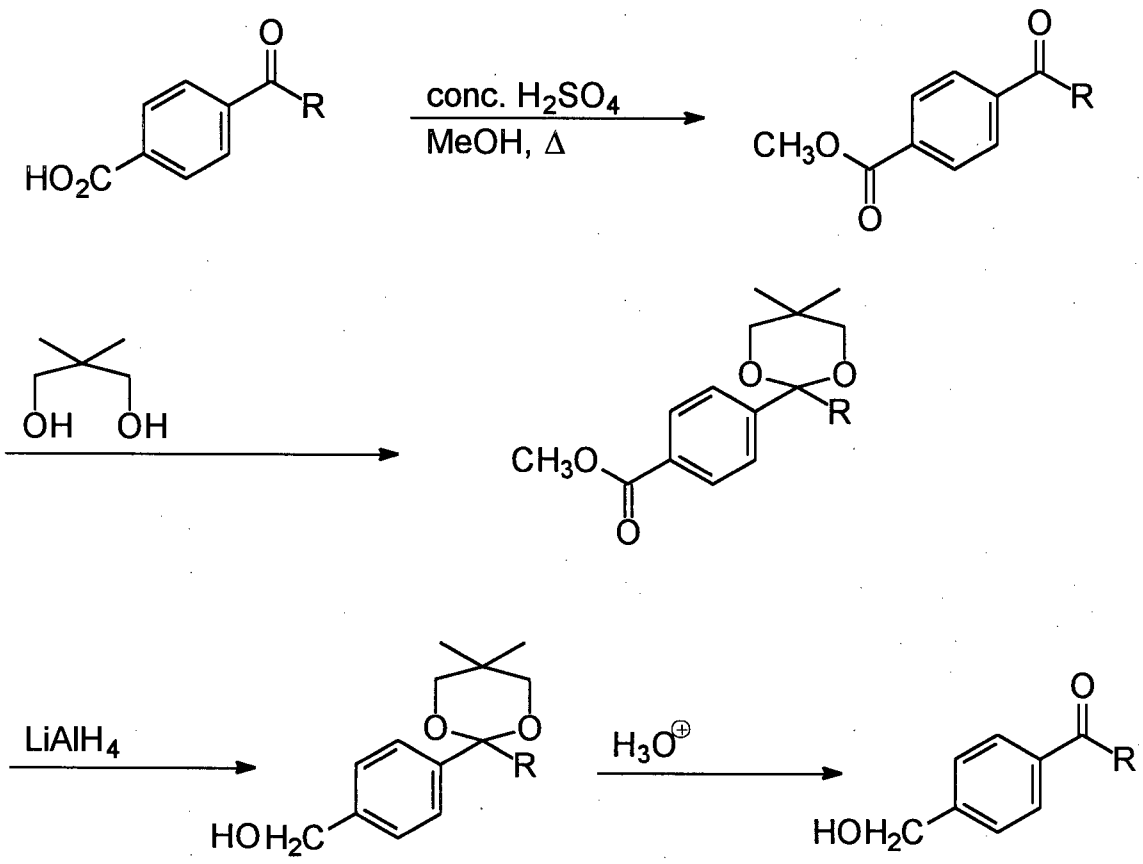


R = CH_3, Ph
R' = functional group of amino acid
n = 0,1

Scheme 8.2.1. Synthesis of auxiliaries as hydrobromide salts.

8.2.1. Synthesis of the Keto Alcohols.

The two keto alcohols used were not commercially available, and were synthesized in four steps from the keto benzoic acids (Scheme 8.2.1.1). Fischer esterification in methanol was followed by protection of the ketone as the neopentylene ketal and reduction of the ester with lithium aluminum hydride. Acidic hydrolysis restored the ketone functionality.

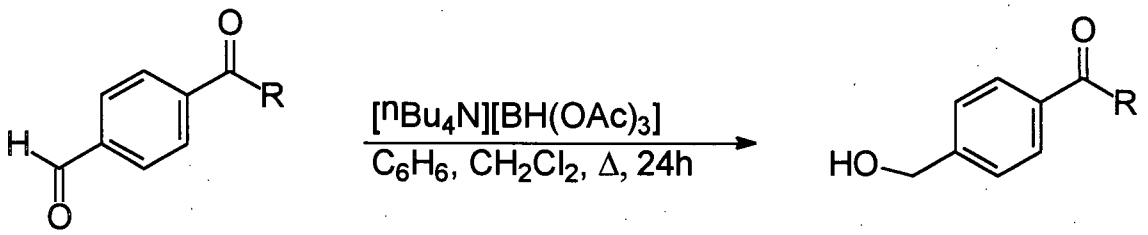


R = CH_3 (**91**), Ph (**92**)

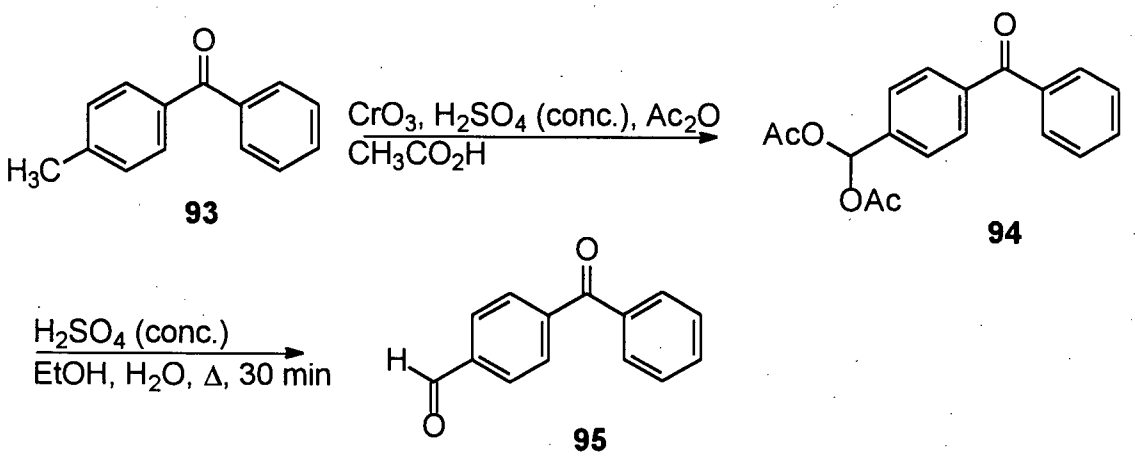
Scheme 8.2.1.1. Preparation of the 4-keto benzyl alcohols (**91** and **92**).

Both benzyl alcohols had been synthesized by Nutaitis and Gribble[75] by chemoselective reduction of the keto aldehydes (Schemes 8.2.1.2, 8.2.1.3, 8.2.1.4). We attempted to prepare 4-benzoylbenzyl alcohol (**92**) by their method. However, we encountered some difficulties in optimizing the synthesis of 4-benzoylbenzaldehyde (**95**) at the comparatively small scale we required (the original reference[76] used 50 g of the starting material). The 4-benzoylbenzyl alcohol prepared by this method also required purification by column

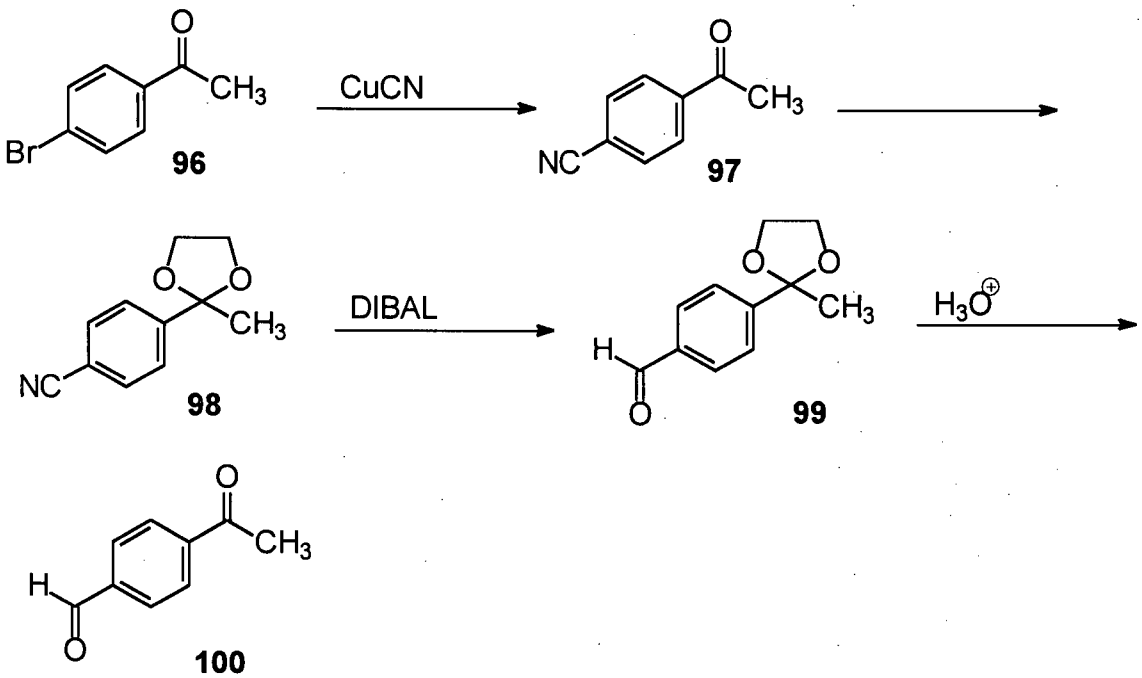
chromatography; this was a distinct disadvantage, as several grams of the benzyl alcohol product were needed. The synthesis delineated in Scheme 8.2.1.1 appeared more promising.



Scheme 8.2.1.2. Preparation of the keto alcohols by selective aldehyde reduction.[75]



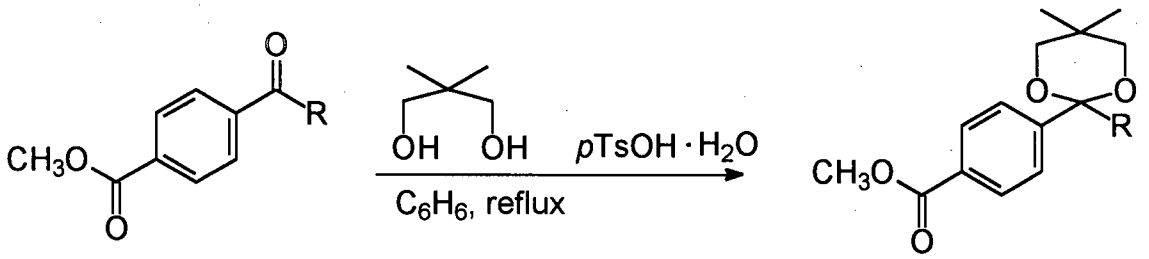
Scheme 8.2.1.3. Synthesis of 4-benzoylbenzaldehyde (**95**).[76]



Scheme 8.2.1.4. Synthesis of 4-acetylbenzaldehyde (**100**) carried out by Nutaitis and Gribble.[75] We did not attempt to prepare this compound.

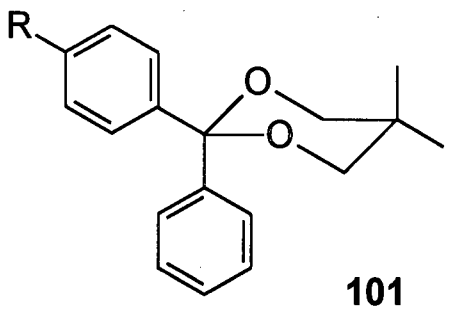
8.2.1.1. Protection of the Ketone.

Following quantitative conversion to the methyl ester, the ketone group was protected with neopentylene glycol in refluxing benzene, using *p*-toluenesulfonic acid as the catalyst (Scheme 8.2.1.1.1). Water was removed azeotropically by condensation in a Dean-Stark trap.

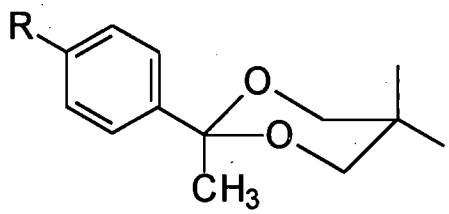


Scheme 8.2.1.1.1. Protection of the ketone.

The 4-acetyl derivative was converted to ketal **102** after 3 hours (sometimes, due to time constraints, it was left for longer time periods). However, complete reaction of the 4-benzoyl compound took 26 hours. Examination of the structures for the two cyclic ketals shows a severe 1,3-diaxial interaction for benzoyl derivative **101**, involving an axial phenyl group (Figure 8.2.1.1.1). The additional steric bulk imposed by the phenyl group would be expected to cause a kinetic barrier to ketal formation, compared to formation of a ketal where this substituent was only a methyl group. Thus, the acetyl compound reacts faster because there is less steric hindrance to its doing so.



101



102

$R = CO_2CH_3$

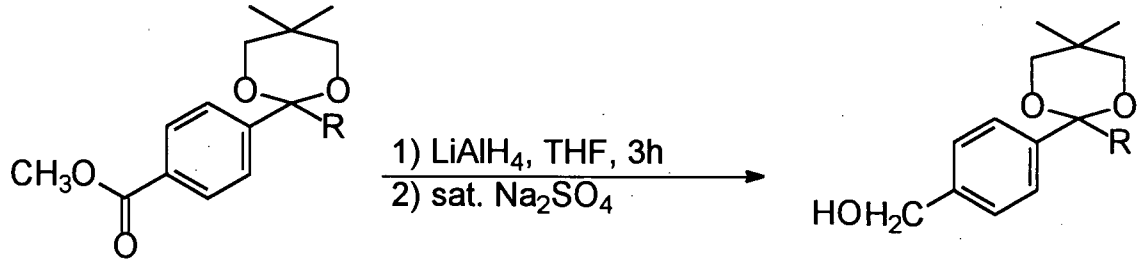
Figure 8.2.1.1.1. Unfavourable interactions involving the axial phenyl group.

Further evidence of this unfavourable diaxial interaction is provided by the ^{1}H NMR spectra of the two ketals. In the spectrum of **101**, the chemical shifts of the geminal methyl groups (0.72, 0.67 ppm) are quite close. Therefore, there is little difference in the chemical environments experienced by the two groups, which indicates that each spends considerable amounts of time in both axial and equatorial environments. The same methyl groups, however, appear at very different shifts in the spectrum of **102** (1.19, 0.20 ppm), indicating that the two groups exist in different environments, one predominantly axial and the other equatorial, and that therefore one of the two groups on the other side of the ring also has a pronounced equatorial bias.

The ketal of the acetyl derivative was recrystallized from ethanol prior to the reduction step; the ketal of the benzyl compound, however, required no intermediate purification.

8.2.1.2. Reduction of the Ester.

The ester was reduced to the primary alcohol with $LiALH_4$ (Scheme 8.2.1.2.1).

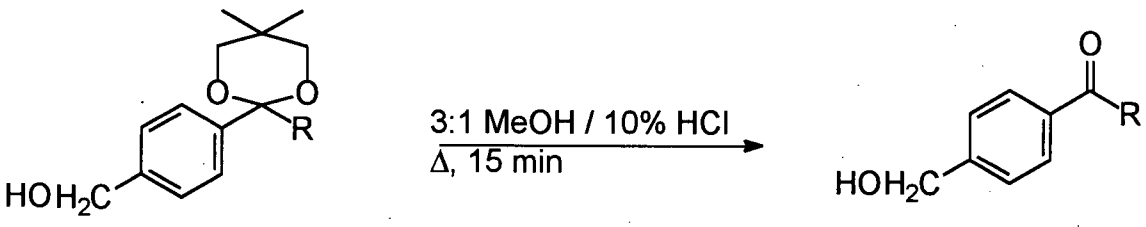


Scheme 8.2.1.2.1. Reduction of the ester.

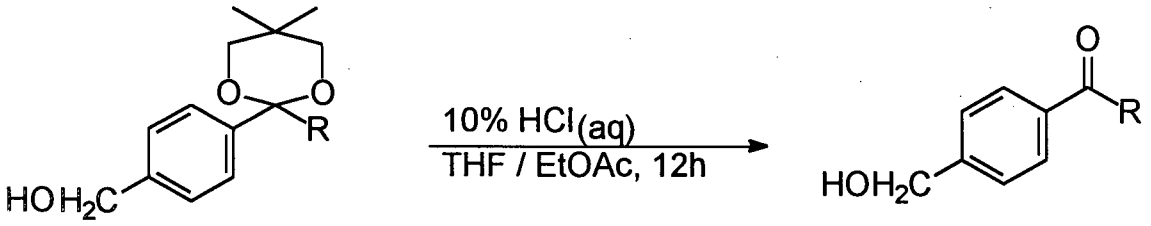
The products of this step were not characterized. They were obtained as viscous oils from which the last traces of solvent could not be readily removed. They were carried on directly to the hydrolysis step without even attempting to calculate product yields.

8.2.1.3. Hydrolysis of the Ketal.

The crude products of the previous step were hydrolyzed by treatment with aqueous acid in refluxing methanol (Scheme 8.2.1.3.1). Complete hydrolysis was rapid. Hydrolysis could also be achieved by addition of aqueous acid to the tetrahydrofuran / ethyl acetate solution obtained after workup of the hydride reduction, followed by stirring overnight at room temperature (Scheme 8.2.1.3.2).



Scheme 8.2.1.3.1. Hydrolysis of the ketal in refluxing solvent.

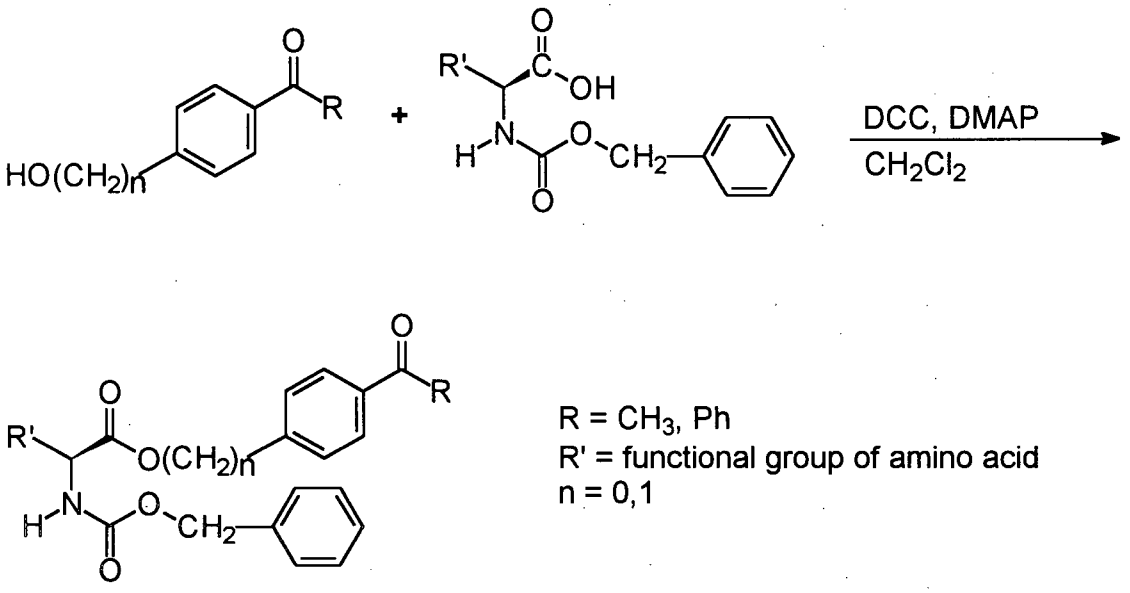


Scheme 8.2.1.3.2. Room temperature hydrolysis of the ketal.

In either case, the keto alcohol product was of sufficient purity to be used in the ester formation step. Neither chromatography nor recrystallization was required. A pure sample of 4-benzoylbenzyl alcohol (**92**) was prepared for analysis by recrystallization from cyclohexane.

8.2.2. Formation of the Ester Linkage.

The esters were formed by addition of the N-carbobenzyloxyamino acid to the appropriate benzyl alcohol or phenol (Scheme 8.2.2.1).[77] Reaction of the acid with dicyclohexylcarbodiimide leads to the acid anhydride. This reacts *in situ* with the dimethylaminopyridine to yield a pyridinium intermediate in which the carbonyl group is activated for nucleophilic attack by the alcohol. Attack by the alcohol yields the desired ester product and regenerates the dimethylaminopyridine catalyst.[78]



Scheme 8.2.2.1. DCC coupling of protected amino acids to the benzyl alcohol or phenol.

The N-protected esters were initially isolated as nonvolatile oils of extremely high viscosity (Table 8.2.2.1). Carbobenzyloxy-L-phenylalanine 4-acetylbenzyl ester (**107**) solidified under vacuum, and solid products could also be obtained for the protected L-valine 4-benzoylbenzyl and L-alanine 4-acetylbenzyl esters (**105** and **106**) through recrystallization from ethanol. The yields for these recrystallizations were usually low; fortunately, recrystallization was only necessary for the preparation of analytically pure material. The HBr deprotection step could be carried out very nicely on unrecrystallized material. Products which would not solidify were characterized as oils, following purification by dry flash chromatography.[67]

Table 8.2.2.1. N-Cbz protected esters.

N-carbobenzyloxy [...] ester	**State**	**Yield**	**Conformational Diastereomers?**
L-proline 4-acetylbenzyl (**103**)	liquid	91%	yes
L-proline 4-benzoylbenzyl (**104**)	liquid	85%	yes
L-valine 4-benzoylbenzyl (**105**)	solid	94% (8.7% recrystallized)	no
L-alanine 4-acetylbenzyl (**106**)	solid	100% (11% recrystallized)	no
L-phenylalanine 4-acetylbenzyl (**107**)	solid	100% (62% recrystallized)	no
L-proline 4-benzoylphenyl (**108**)	liquid	72%	yes
L-valine 4-benzoylphenyl (**109**)	liquid	100%	no

The ^{1}H and ^{13}C NMR spectra of the esters formed with L-proline (**103**, **104**, and **108**) show that these compounds exist as 1:1 mixtures of inseparable conformational diastereomers. This is a result of the somewhat hindered rotation about the C-N bond of the carbamate, due to its partial double bond character (Figure 8.2.2.1). The effect is also present for Cbz-derivatives of the other amino acids (Figure 8.2.2.2); however, for these compounds, structure **A** is considerably more favourable than structure **B**. In structure **B**, steric hindrance would exist between the OCH_2Ph group of the carbamate and the carbonyl group of the ester; thus, the NMR spectra will not show the presence of **B**. In the

proline derivatives, the two isomers related by rotation about the C-N bond are close enough in energy that the presence of both is not at all surprising. A similar situation exists for N,N-dimethylformamide, in which the two methyl groups are shown by ^{1}H and ^{13}C NMR spectroscopy to be non-equivalent.

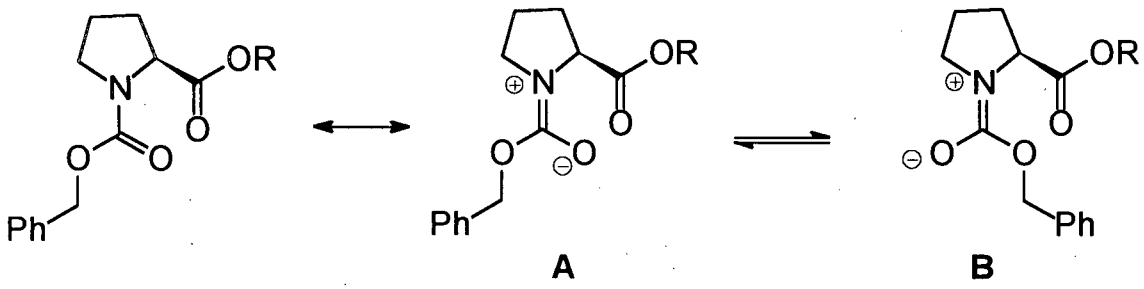


Figure 8.2.2.1. Conformational diastereomers for derivatives of Cbz-L-proline.

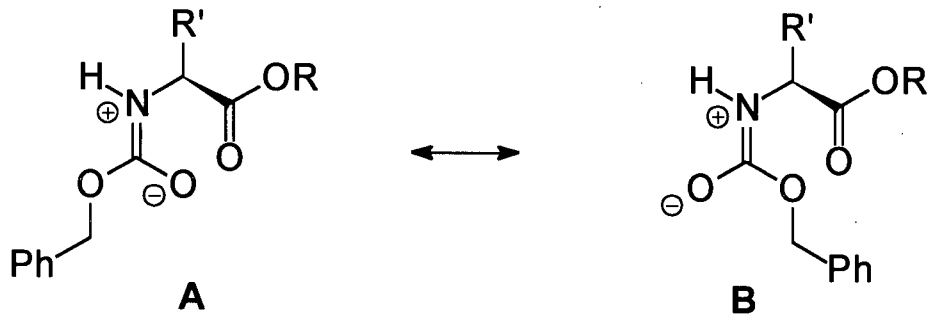
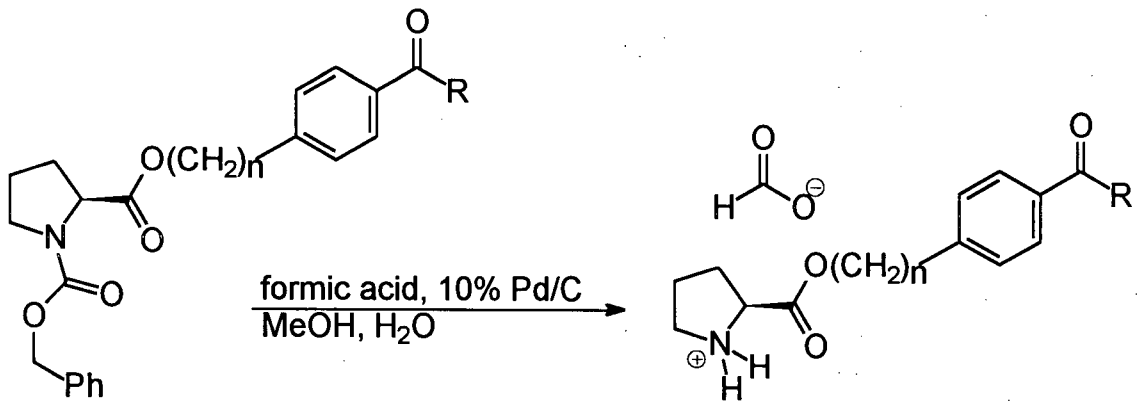


Figure 8.2.2.2. Possible conformational diastereomers for Cbz-derivatives of primary amino acids.

8.2.3. Deprotection of the Amino Group.

8.2.3.1. Deprotection by Catalytic Transfer Hydrogenation.

Deprotection was first attempted by catalytic transfer hydrogenation from formic acid (Scheme 8.2.3.1.1).[79] This method proved unsuccessful. Even after addition of extra formic acid and catalyst, and after extended stirring at reflux temperature, no reaction occurred. The substrates carbobenzyloxy-l-proline 4-benzoylphenyl ester (**108**) and carbobenzyloxy-L-proline 4-acetylbenzyl ester (**103**) were subjected to this treatment.

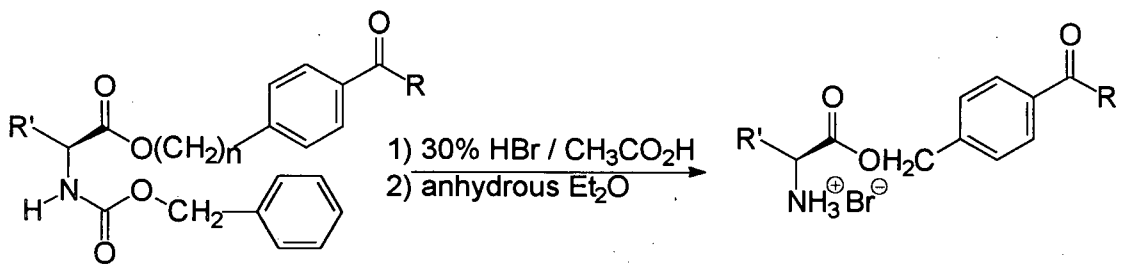


Scheme 8.2.3.1.1. Attempted deprotection of the amino group through catalytic transfer hydrogenation.

Upon reflection, this was probably not the best way to deprotect a Cbz-amino group in the presence of a benzyl ester, since this methodology is frequently used to achieve benzyl ester cleavage. Phenyl ketones are also susceptible to hydrogenation conditions.

8.2.3.2. Deprotection by Hydrogen Bromide in Acetic Acid.

Successful deprotection was acheived with hydrogen bromide (Scheme 8.2.3.2.1).[80] A 30% w/w solution of hydrogen bromide in acetic acid was added to the protected compound, under a nitrogen atmosphere, and stirring and shaking were continued until vigorous carbon dioxide evolution had ceased (15-30 minutes). The hydrobromide was then precipitated by addition of anhydrous diethyl ether and overnight refrigeration. Filtration then yielded solid product, which was triturated repeatedly with portions of anhydrous ether until a free-flowing powder was obtained.



Scheme 8.2.3.2.1. Deprotection of the Cbz-amino esters by HBr.

The hydrobromide salts of L-proline 4-benzoylbenzyl and 4-acetylbenzyl ester (**111** and **110**, respectively) could not be isolated as free-flowing powders through trituration. Hydrobromide **111** could be obtained as a white powder by recrystallization from acetonitrile, but it was still extremely hygroscopic, and a satisfactory elemental analysis could not be obtained. Attempts to recrystallize hydrobromide **110** from a wide variety of solvents were unfruitful. We tried to

isolate this compound as the free base by washing an organic suspension of the hydrobromide salt with 5% sodium carbonate, but this unfortunately caused hydrolysis of the ester bond. The only products obtained were 4-acetylbenzyl alcohol (**91**) and L-proline.

The instability of the ester bond to such a weakly basic solution was surprising. However, the α-ammonium group in the hydrobromide is strongly electron-withdrawing, which would increase the electrophilicity of the ester carbonyl, making it much more susceptible to nucleophilic attack. In the presence of a large amount of water or another nucleophilic solvent, the equilibrium could be pushed towards hydrolysis. A later observation was that NMR samples of the hydrobromide salts - and of other salts involving these ammonium ions - show instability when CD_3OD is used as the solvent. The spectra change slowly over time. This does not occur when aprotic solvents such as CD_3CN and d_6-DMSO are used.

8.3. Preparation of Salts Between *anti*-9-Carboxybenzonorbornadiene and New Chiral Triplet Sensitizers.

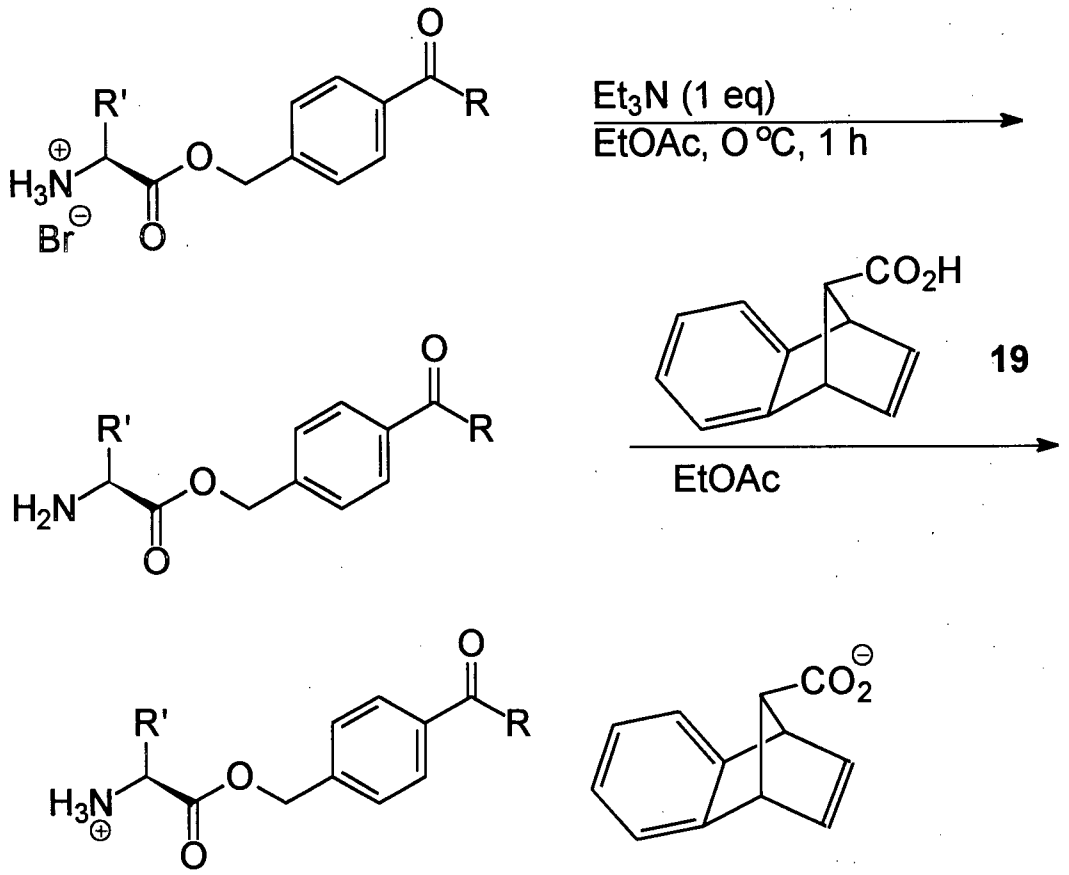
8.3.1. Free Amine Formation Through Deprotonation by Inorganic Bases.

Before the danger inherent in exposing these ammonium ions to protic solvents became apparent, attempts were made to prepare the salt of acid **19**

with the free base form of hydrobromide **111**. The amine was liberated by treatment with either sodium hydroxide or sodium carbonate, and the solution of free amine added to a solution of acid **19**. The solvent used was then removed *in vacuo*, and recrystallization of the crude product was attempted. Not surprisingly, all such attempts, from a wide variety of recrystallization solvents, were unsuccessful.

8.3.2. Free Amine Formation Through Deprotonation by Triethylamine.

Since exposing the ammonium ions to high concentrations of nucleophilic solvent for any length of time seemed to be a bad idea, the free base was prepared immediately before use by stirring a suspension of the hydrobromide in ethyl acetate at 0 °C for one hour, after addition of one equivalent of triethylamine. The white precipitate of triethylammonium hydrobromide was filtered off, and the solution of free amine then added to an ethyl acetate solution of the acid (Scheme 8.3.2.1). Crude salt was isolated by removal of the ethyl acetate, and then recrystallized from acetonitrile. This procedure was used by Ramachandran and Li to prepare the free base form of L-proline 4-benzyl ester from its hydrochloride salt, without racemization,[81] so it seemed likely that it would also work well for the systems under investigation here.



Scheme 8.3.2.1. Preparation of salts between chiral triplet sensitizers and acid **19**.

8.4. Irradiation of the Chiral Triplet Sensitizer Salts.

Results of the salt irradiations with long-wave ultraviolet light are reported in Table 8.4.1.

Table 8.4.1. Irradiation of chiral triplet sensitizer salts.

Amine (# of Salt)	Irradiation Conditions	Percent Conversion	Percent Enantiomeric Excess (sign of optical rotation)
L-valine 4-benzoylbenzyl ester (116)	CH_3CN solution, 1h	83	0
	solid, 1h	100	29 (+)
	30 min	95	31 (+)
	10 min	79	31 (+)
	10 min	67	31 (+)
	8 min	61	30 (+)
	4 min	2.1	22 (+)
	8 min (0 °C)	29	28 (+)
	2h (-20 °C)	84	31 (+)
	30 min (-20 °C)	40	27 (+)
L-phenylalanine 4-acetylbenzyl ester (117)	CH_3CN solution, 20 min[a]	100	0
	solid, 30 min[a]	83	41 (-)
	15 min[a]	93	45 (-)
	5 min[a]	55	47 (-)
	8h (-20 °C)	74	50 (-)
	2h (-20 °C)	19	66 (-)
	30 min (-20 °C)	4.5	70 (-)
L-valine 4-benzoylphenyl ester (118)	CH_3CN / CH_3OH solution, 15 min[a]	14	0
	solid, 30 min[a]	100	81 (-)
	5 min[a]	100	82 (-)
	1 min[a]	58	84 (-)
	4h (-20 °C)	100	91 (-)
	1h (-20 °C)	100	86 (-)

Irradiations were carried out by exposure to uranium-filtered light ($\lambda > 330$ nm), unless otherwise indicated. Conversions and enantiomeric excesses were determined by GC. [(a)] Irradiated at 350 nm.

As was observed for the chiral salts investigated in Chapter 7, irradiation in the solution phase did not lead to any enantiomeric excess in the product formed. This was expected.

The rearrangements described in Table 8.4.1 occur much more rapidly than the unsensitized - presumably singlet state - reactions discussed in Chapter 7. They also occur much more rapidly than upon sensitization with *p*-acetylpyridine in the solid state, which was described in Chapter 6. This made it much easier to carry out a number of these irradiation experiments; compare the maximum irradiation time of 8 hours reported in Table 8.4.1 with the routine 12 hour irradiation times required in Chapter 7. Most of these irradiations took less than 30 minutes. The chiral bases used here are obviously very effective triplet sensitizers, both in solution and in the solid state. They appear to rival acetophenone and benzophenone in their efficacy as triplet sensitizers of solution phase reactions.

Asymmetric induction is also much better with these bases than with those used in Chapter 7. Enantiomeric excesses are generally higher, and remain high even at conversion levels which gave no detectable amount of unreacted starting material. The 91% enantiomeric excess of (-)-**53** obtained at quantitative conversion (-20 °C) of the salt with L-valine 4-benzoylphenyl ester (salt **118**) is particularly striking.

Salt **117** gives a remarkable increase in photoproduct enantiomeric excess upon decreasing the percent conversion and temperature. Salt **118** also shows this trend. Salt **116** does not. This may be an artefact of the irradiation

method used, to some extent. As described in Chapter 10, solid state samples are prepared for irradiation by crushing the crystals - as evenly as possible - between two quartz plates. "As evenly as possible" is the key phrase. It is very difficult to ensure that the layer of crystals between the plates is of a perfectly even thickness, although this is the ideal. Upon irradiation, the thinner layer of crushed crystals around the edges reacts faster than the thicker layer in the middle. Thus, the percent conversion value obtained is an average of the percent conversions for the different regions of the sample, and may not give an accurate picture of how conversion levels affect enantiomeric excesses.

On the other hand, an ideal situation would be one in which the enantioselectivity would not decrease upon increasing conversion, in which the substrate were smoothly converted to product without degradation of the lattice. Examples have been reported of topotactic, or single crystal-to-single crystal, transformations, in which this has been the case.[40] Topotactic rearrangements give a solid solution of product and starting material at all points in the reaction, and proceed with very little change in the overall lattice arrangement. One advantage of these reactions is that they can be monitored by X-ray crystallography at various stages - if single, high-quality crystals of the starting material are obtained - to give an actual picture of the structural changes taking place within the lattice.

Attempts were made to grow large, single crystals of these salts, particularly of salt **118**, which seemed more likely than the others to undergo a topotactic rearrangement. However, large crystals could not be obtained, and

thus X-ray analysis of these salts was not possible. That was unfortunate. X-ray analysis would have been invaluable in attempting to explain why the enantioselectivities observed differed so much from one another. Also, if the tantalizing prospect of observing a topotactic rearrangement for salt **118** had become a reality, the absolute configurations of the enantiomers of photoproduct **53** could have been assigned, by determining the crystal structure of the photoproduct salt.

8.5. Further Applications.

If time had permitted, many more chiral triplet sensitizers of the same general structure could have been prepared, and their effectiveness studied. There are many amino acids, and different auxiliaries could have been prepared by linking each of them to each of the benzyl alcohols, and to 4-hydroxyacetophenone and 4-hydroxybenzophenone. Very minor differences in auxiliary structure can result in a drastic change in the results obtained upon salt formation and irradiation, as shown for the two L-valine auxiliaries. One interesting investigation would be to study whether the enantioselectivity is generally improved for derivatives of a given amino acid by linking the acid to a phenol rather than to a benzyl alcohol, as was observed here. The number of auxiliaries studied here is rather too small to make any conclusions of that sort.

In theory, these auxiliaries could be used in any system which requires triplet sensitization for efficient conversion to photoproduct, and for which the

conversion involves an achiral substrate and chiral product. For example, dibenzobarrelene derivatives, known to undergo sensitization by acetophenone and benzophenone, should be ideal candidates.

The effectiveness of these auxiliaries as solution phase triplet sensitizers also suggests that they might find utility for that purpose. One of the difficulties encountered in preparing large amounts of photoproduct **53** by acetophenone or benzophenone sensitized solution phase irradiation is that it was very tedious to remove the sensitizer from the photoproduct. The auxiliaries studied here could be removed simply by washing with aqueous acid. Of course, there would be no need, in such reactions, for a chiral auxiliary. However, the preparation of a sensitizer between 4-hydroxyacetophenone or 4-hydroxybenzophenone and glycine by the methodology described here would be simple and inexpensive.

EXPERIMENTAL

9. Preparation of Photochemical Substrates.

9.1. General Procedures.

Melting Points (MP)

The melting points were determined on a Fisher-Johns melting point apparatus and are uncorrected.

Elemental Analyses (Anal.)

Elemental analyses were carried out by Mr. Peter Borda, Department of Chemistry, University of British Columbia.

Mass Spectra (MS)

Mass spectrometric analyses were carried out by the B.C. Regional Mass Spectrometry Centre at the University of British Columbia Department of Chemistry. Low and high resolution mass spectra were obtained on a KRATOS MS50 instrument. Desorption chemical ionization (DCI) mass spectra were obtained on a KRATOS MS80 instrument. Fast atom bombardment (FAB) mass spectra were determined on an AEI MS-9 mass spectrometer with xenon bombardment of an alcohol matrix (as indicated in parentheses) of the sample. Liquid secondary ion mass spectra (LSIMS) were determined on a KRATOS

Concept IIHQ hybrid mass spectrometer. Mass to charge ratios (m/e) are given, with relative intensities in parentheses for EI and DCI spectra. Molecular ions are designated as M^+.

Infrared Spectra (IR)

Infrared spectra were taken on a Perkin-Elmer 1710 Fourier transform infrared spectrometer. Absorption maxima are reported in cm^{-1}. Solid samples were prepared by grinding the compound of interest with anhydrous potassium bromide in a mortar and pestle, and pressing the mixture into pellets in an evacuated die (Perkin-Elmer 186-0002) with a laboratory press (Carver, model B) at 17,000 psi. Liquids of low to moderate viscosity were applied neat between two sodium chloride plates. Liquids of high viscosity were analyzed as carbon tetrachloride solutions in a sodium chloride cell.

Ultraviolet Spectra (UV)

Ultraviolet spectra were taken on a Perkin-Elmer Lambda-4B UV/vis spectrometer. Wavelengths for each absorption maximum (λ_{max}) are reported in nanometers (nm), and extinction coefficients (ε (M^{-1} cm^{-1})) are given in parentheses.

Nuclear Magnetic Resonance Spectra (NMR)

Spectra recorded on the Bruker AC-200 were obtained in automation mode. Spectra recorded on other spectrometers were obtained either by the

author, by Marietta Austria or Liane Darge of the University of British Columbia Chemistry Department NMR Services Laboratory, or by Matthew Netherton.

^{1}H NMR

Proton nuclear magnetic resonance spectra (^{1}H NMR) were recorded on the following spectrometers: Bruker AC-200 (200 MHz), Varian XL-300 (300 MHz, Bruker WH-400 (400 MHz) and Bruker AMX 500 (500 MHz). The positions of the signals are given as chemical shifts (δ) in parts per million (ppm) with respect to tetramethylsilane (TMS) at δ 0 ppm; however, the internal reference standard used in each case was the residual proton signal present in the deuterated solvent. Reported chemical shifts are followed in parentheses by the number of protons, the multiplicity of the peak, the coupling constant (J) in Hz, and the atomic assignment. The following abbreviations are used in reference to the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, dt = doublet of triplets, m = multiplet, br = broad. In some cases, in order to verify structures, HMQC (Heteronuclear Multiple Quantum Coherence, ^{1}H - ^{13}C correlation) experiments on the Bruker AMX-500 spectrometer, and COSY (COrrelated SpectroscopY) and homonuclear decoupling experiments on the Bruker WH-400 spectrometer were carried out.

^{13}C NMR

The following spectrometers were used to record the carbon nuclear magnetic resonance spectra (^{13}C NMR): Bruker AC-200 at 50.3 MHz, Varian XL-

300 at 75.4 MHz, Bruker AM-400 at 100.6 MHz, and Bruker AMX-500 at 125.8 MHz. All spectra were determined with broad band proton decoupling. The positions of the signals are given as chemical shifts (δ) in parts per million (ppm) with respect to tetramethylsilane at δ 0 ppm; however, the internal reference standard used in each case was the central transition of the solvent carbon atom. Reported chemical shifts are followed in parentheses by the carbon assignments, which were often made possible by an APT (attached proton test) experiment.

Optical Rotations ($[\alpha]_D^T$)

Optical rotation measurements were carried out on a Perkin-Elmer 241MC polarimeter at the sodium D line (589 nm).

Crystallographic Analysis (X-RAY)

X-ray crystal structures were determined using single-crystal X-ray analysis, on a Rigaku AFC6S 4-circle diffractometer, and drawn with a locally modified version of the ORTEP program at the 50% probability level. Structures were determined by Dr. Brian Patrick and Eugene Cheung under the supervision of Professor James Trotter, in the Chemistry Department of the University of British Columbia.

Chromatography

Chromatographic purifications of compounds were carried out using either standard percolation chromatography, flash chromatography, or dry flash chromatography. Procedures are described in *Experimental Organic Chemistry: Principles and Practice*.[67] Silica gel 60 (230-400 mesh) was used, with the appropriate solvent combination.

Thin Layer Chromatography (t.l.c)

Thin layer chromatography was carried out on pre-coated silica gel plates (E. Merck, 60, 230-400 mesh) with an aluminum backing and fluorescent indicator (F_{254}).

Gas Chromatography (GC)

Gas liquid chromatographic (GC) analysis was carried out on a Hewlett-Packard 5890A gas chromatograph with a flame ionization detector (250 °C), a Hewlett-Packard 3392A integrator, and a 30 m × 0.25 mm fused silica capillary column (HP-5, Hewlett-Packard). Column head pressure was maintained at 14 psi (carrier gas: helium), and the injector temperature was maintained at 250 °C. Chiral GC analysis employed a Hewlett-Packard 5890 Series II gas chromatograph with a flame ionization detector (225 °C), a Hewlett-Packard 3393A integrator, and a 30 m × 0.25 mm fused silica capillary column with a 0.25 μm film thickness (Gamma-DEX™-120, Supelco Inc.). Column head pressure was maintained at 350 kPa (carrier gas: helium), column temperature was

maintained at 120 °C (all runs were isothermal), and the injector temperature was maintained at 220 °C.

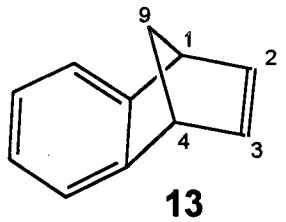
Injection volumes were typically 1-2 μL.

Reagents and Solvents

Unless otherwise specified, reagents were used as supplied by the Aldrich Chemical Company. Solvents were supplied by Fisher Scientific Inc., and deuterated solvents by Cambridge Isotope Laboratories.

9.2. Preparation of *anti*-9-Carboxybenzonorbornadiene (19).

Benzonorbornadiene (13)



13

Benzonorbornadiene was synthesized according to a modification of the procedure reported by Wittig and Knauss.[60] A solution of 1-bromo-2-fluorobenzene (**36**, 13 mL, 20 g, 0.11 mol) and freshly-cracked cyclopentadiene (**38**, 9.4 mL, 7.6 g, 0.11 mol) was prepared in anhydrous tetrahydrofuran (80 mL, distilled from sodium / benzophenone) and held at -78 °C. To initiate the reaction, a 20 mL aliquot of this solution was added in one portion via a cannula, with stirring, to magnesium shavings (3.2 g, 0.13 mol), which had been placed in a flask fitted with a reflux condenser, under a nitrogen atmosphere. When vigorous reflux of this mixture occurred, indicating that the reaction was underway, the remainder of the chilled tetrahydrofuran solution was added dropwise. Stirring was continued for 40 minutes upon completion of the addition.

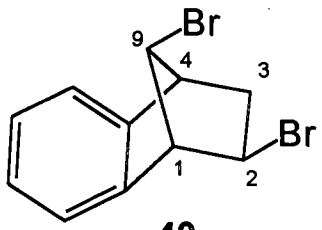
The reaction was quenched by removal of the solvent *in vacuo* and addition of saturated ammonium chloride solution (100 mL) to the residue. The suspension thus obtained was extracted into diethyl ether, and the ethereal solution of crude product was then washed with brine, dried over anhydrous magnesium sulfate, and evaporated to yield benzonorbornadiene (**13**) as a

yellow oil with a distinct aroma of ripe mangoes (12.8 g, 82%). This oil could be used in the next step without further purification; pure product could, however, be obtained by chromatography (hexanes).

IR (thin film, NaCl) ν_{max} : 3067 (alkene C-H), 2983, 2935 (CH_2), 1455 (aromatic C=C), 758 (aromatic C-H) cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$) : δ 7.38 (2H, dd, J = 5.1, 3.1 Hz, aromatic), 7.09 (2H, dd, J = 5.1, 3.1 Hz, aromatic), 6.94 (2H, t, J = 1.9 Hz, H-2,3), 4.03 (2H, quintet, J = 1.7 Hz, H-1,4), 2.48 (1H, dt, $J_{9a,9s}$ = 7.1 Hz, J = 1.5 Hz, *anti* H-9), 2.40 (1H, br dt, $J_{9s,9a}$ = 7.1 Hz, J = 1.5 Hz, *syn* H-9).

exo-2-_anti_-9-Dibromobenzonorbornene (40)



40

According to the procedure outlined by Wilt *et al.*,[62] bromine (3.1 mL, 9.7 g, 60 mmol) in carbon tetrachloride (40 mL) was added dropwise to a solution of benzonorbornadiene (**13**, 7.8 g, 55 mmol) in carbon tetrachloride (65 mL), at 0 °C, in the dark. After the addition had been completed, the ice bath was removed and the reaction mixture allowed to stir for 1 hour. Excess bromine was removed by washing with 10% sodium bisulfite, then with water. Removal of

carbon tetrachloride was accomplished *in vacuo*, and the brown oil thus obtained was purified by dry flash chromatography (80% petroleum ether / 20% dichloromethane) and recrystallization (ethanol). White crystalline product was isolated (7.9 g, 38%).

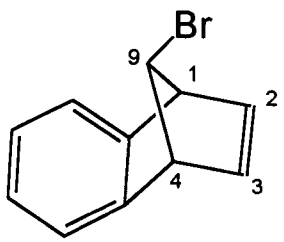
MP : 78.0-78.5 °C (lit.[62] 76-77 °C).

IR (KBr) ν_{max} : 3021 (aromatic C-H), 1459 (aromatic C=C) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$) : δ 7.17 (4H, m, aromatic), 4.13 (1H, t, J = 1.4 Hz, H-9), 3.78 (1H, ddd, $J_{2,3n}$ = 8.1 Hz, $J_{2,3x}$ = 4.5 Hz, $J_{2,9}$ = 1.4 Hz, H-2), 3.74 (1H, s, H-4), 3.50 (1H, t, J = 1.8 Hz, H-1), 2.85 (1H, dt, $J_{3x,3n}$ =13.5 Hz, J = 4.2 Hz, H-3-*exo*), 2.20 (1H, dd, $J_{3n,3x}$ =13.2 Hz, $J_{3n,2}$=7.8 Hz, H-3-*endo*).

^{13}C NMR (75 MHz, $CDCl_3$) : δ 143.51, 142.89 (aromatic C), 127.80, 127.28, 121.77, 121.30 (aromatic CH), 56.42, 55.55, 51.04, 45.11 (aliphatic CH), 36.57 (C-3).

***anti*-9-Bromobenzonorbornadiene (42)**



42

A two-necked flask was fitted with a condenser and flame-dried under a nitrogen atmosphere. Potassium hydride (KH, 14 g of a 35% w/w suspension in mineral oil; 4.9 g, 120 mmol) was placed in the flask and rinsed with anhydrous tetrahydrofuran (3 × 10 mL, distilled from sodium / benzophenone). The KH was then suspended in tetrahydrofuran (110 mL), and diisopropylamine (13.6 mL, 9.8 g, 97 mmol) was added by syringe, with stirring. After 20 minutes, a solution of dibromide **40** (11.0 g, 36 mmol) in tetrahydrofuran (110 mL) was added by syringe. The mixture was then stirred for another 20 minutes, after which it was heated to reflux temperature. A vivid, reddish-purple colour developed. Reflux was continued until GC analysis indicated that conversion to product was complete (4 h).

The reaction was quenched by slow addition of 5% hydrochloric acid to the cooled mixture (0 °C), which caused the colour of the solution to change from purple to golden-brown. Tetrahydrofuran was removed *in vacuo*, and the product was extracted into diethyl ether, washed with water, and dried over anhydrous magnesium sulfate. Evaporation of diethyl ether gave a yellowish-brown solid (7.6 g, 95% yield). This could be used in the next step without further purification; pure product could, however, be obtained as a white solid by sublimation.

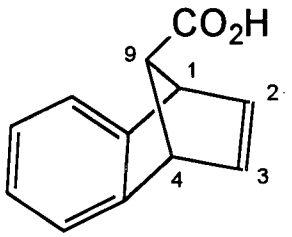
MP : 50.5-52.0 °C (lit.[62] 53-54 °C).

IR (KBr) ν_{max} : 1647 (alkene C=C), 1542, 1508 (aromatic C=C), 777 (aromatic C-H), 724 (C-Br) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$) : δ 7.26 (2H, dd, J = 5.3, 3.2 Hz, aromatic), 7.04 (2H, dd, J = 5.4, 3.0 Hz, aromatic), 6.74 (2H, m, H-2,3), 4.40 (1H, m, H-9), 4.10 (2H, m, H-1,4).

^{13}C NMR (75 MHz, $CDCl_3$) : δ 147.04 (aromatic C), 139.50, 125.61, 122.02 (aromatic and olefinic CH), 74.23 (C-9), 57.27 (C-2,3).

***anti*-9-Carboxybenzonorbornadiene (19)**



19

A modification of the procedure used by Buske and Ford[46] was followed. A solution of *tert*-butyllithium (22 mL of a 1.7 M hexane solution, 37 mmol) in anhydrous tetrahydrofuran (80 mL, distilled from sodium / benzophenone) was prepared at -78 °C under a nitrogen atmosphere. After the solution had been allowed to stir for 5 minutes, a solution of monobromide **42** (3.6 g, 16 mmol) in anhydrous tetrahydrofuran (150 mL) was added by syringe. Stirring was continued for 30 minutes, during which time the solution turned dark forest green, almost black. The organolithium species was quenched by addition of dry carbon dioxide gas, prepared by allowing the vapour produced in a flask of dry ice to pass first over a chloroform / dry ice trap, then through a drying tube of

calcium sulfate. The solution developed a bright fuschia colour during the quenching process, but this colour gradually faded to yellow as the reaction mixture was allowed to warm to room temperature. After the solution had reached ambient room temperature, it was acidified with 5% hydrochloric acid.

The acid was isolated by removal of the tetrahydrofuran *in vacuo*, extraction into diethyl ether, and extraction of the acid from the ethereal solution into 5% sodium hydroxide as the carboxylate. Acidification of the aqueous carboxylate solution with concentrated hydrochloric acid precipitated the acid as a white solid, which, after refrigeration for 1 hour, was collected by suction filtration and dried under vacuum. The crude acid was recrystallized from chloroform to give large, colourless spars (2.26 g, 74%). Crystals suitable for X-ray analysis were readily obtained.

MP : 204.5-205 °C (lit.[46] 198-200 °C).

IR (KBr) ν_{max} : 3013 (alkene C-H), 3000 (acid O-H), 1698 (acid C=O) cm^{-1}.

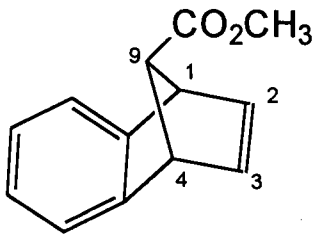
UV (MeOH) λ_{max} : 275 (459), 268 (536), 261 (475), 216 (2730) nm.

^{1}H NMR (200 MHz, acetone-d_6) : δ 10.8 (1H, br s, $CO_2\underline{H}$), 7.1 (2H, dd, J = 5.2, 3.1 Hz, aromatic), 6.9 (2 H, dd, J = 5.2, 3.1 Hz, aromatic), 6.7 (2H, m, H-2,3), 4.1 (2H, m, H-1,4), 3.2 (1H, m, H-9).

^{13}C NMR (75 MHz, CD_3OD) : δ 174.17 (CO_2H), 151.37 (aromatic C), 141.76, 125.72, 122.56 (aromatic and olefinic CH), 82.19 (C-9), 53.17 (C-1,4).

X-RAY : space group $P2_1/c$ (#14), monoclinic, a = 9.795(3) Å, b = 7.988(1) Å, c = 12.197(2) Å, β = 108.27(1)°, V = 906.2(3) $Å^3$, Z = 4, D_{calc} = 1.365 g/cm^3, R = 0.049, R_W = 0.065.

***anti*-9-Carbomethoxybenzonorbornadiene (45)**



45

According to the procedure of Buske and Ford,[46] acid **19** (1.00 g, 5.40 mmol) was refluxed in methanol (100 mL) in the presence of concentrated sulfuric acid (1.25 mL) until conversion to the ester was complete, as indicated by t.l.c. analysis (17 h). The reaction mixture was diluted with cold water (100 mL) and extracted with dichloromethane. The organic extract was then washed successively with 5% sodium hydroxide, water, and saturated sodium chloride, and dried over anhydrous magnesium sulfate. Removal of the dichloromethane gave an off-white product, which was sublimed to yield a white solid (0.804 g, 74%). Pure product could also be obtained by recrystallization from pentane.

MP : 91.5-92.0 °C.

Anal. calculated for $C_{13}H_{12}O_2$: C, 77.98; H, 6.04. Found C, 77.94; H, 5.94.

MS m/e (relative intensity) : 200 (M^+, 30), 168 (100), 141 (88), 115 (41).

IR (KBr) ν_{max} : 3018 (alkene C-H), 1730 (ester C=O), 1235, 1221 (ester C-O), 741 (aromatic C-H) cm^{-1}.

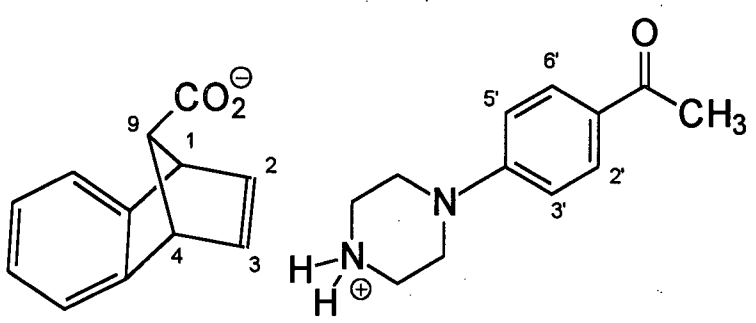
UV (MeOH) : λ_{max} : 275 (330), 268 (405), 217 (2330) nm.

^{1}H NMR (400 MHz, C_6D_6) : δ 7.02 (2H, dd, J = 5.2, 3.0 Hz, aromatic), 6.84 (2H, dd, J = 5.2, 3.1 Hz, aromatic), 6.53 (2H, t, J = 1.8 Hz, H-2,3), 4.07 (2H, dd, J = 3.5, 1.7 Hz, H-1,4), 3.28 (3H, s, CH_3), 3.10 (1H, br s, H-9).

^{13}C NMR (75 MHz, $CDCl_3$) : δ 170.83 (C=O), 149.79 (aromatic C), 140.84, 124.78, 121.70 (aromatic and olefinic CH), 80.56 (bridge CH), 51.85 (bridgehead CH), 51.75 (CH_3).

9.3. Preparation of Triplet Sensitizer Salts of Acid 19.

4'-Piperazinoacetophenone salt of acid 19 (67)



67

A solution of acid **19** (96 mg, 0.50 mmol) was prepared by dissolution in a minumum of diethyl ether. To this was added a second solution of 4'-piperazinoacetophenone (**64**, 110 mg, 0.53 mmol), which had been dissolved in a minimum of boiling diethyl ether. The ether was allowed to evaporate, and the yellow solid obtained was recrystallized from ethyl acetate. Large yellow crystals were obtained (0.11 g, 55%), and a second recrystallization yielded large, yellow spars suitable for X-ray analysis.

MP : 158-165 °C (dec).

Anal. calculated for $C_{24}H_{26}N_2O_3$: C, 73.82; H, 6.71; N, 7.17. Found : C, 73.93; H, 6.81; N, 7.12.

MS +FAB (matrix : thioglycerol) : 205 (ammonium).

MS -LSIMS (matrix : thioglycerol) : 293 (carboxylate + matrix), 185 (carboxylate).

IR (KBr) ν_{max} : 3000 (NH_2^+), 1674 (ketone C=O), 1599, 1412 (carboxylate C=O), 1538 (N-H bending), 737 (aromatic C-H) cm^{-1}.

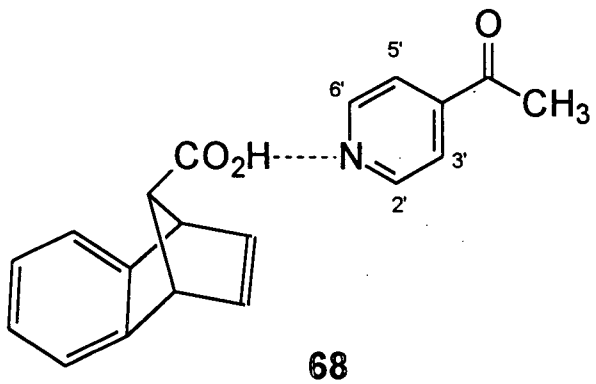
UV (methanol) λ_{max} : 318 (19,000), 233 (7500), 206 (32,000) nm.

^{1}H NMR (400 MHz, $CDCl_3$) : δ 8.79 (2H, s, NH_2^+), 7.86 (2H, d, 8.9 Hz, ammonium H-2',6'), 7.16 (2H, dd, J = 5.0, 3.1 Hz, carboxylate aromatic), 6.90 (2H, dd, J = 5.2, 3.1 Hz, carboxylate aromatic), 6.85 (2H, d, J=8.9 Hz, ammonium H-3',5'), 6.66 (2H, d, J = 1.5 Hz, olefinic), 4.11 (2H, d, J = 1.6 Hz, bridgehead CH), 3.46 (4H, m, ammonium CH_2), 3.26 (1H, s, CH bridge), 3.16 (4H, m, ammonium CH_2), 2.48 (3H, s, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$) : δ 196.43 (ketone C=O), 177.27 (carboxylate C=O), 153.37 (ammonium C-4'), 150.44 (carboxylate aromatic C), 140.77 (carboxylate CH), 130.30 (ammonium C-2',6'), 128.67 (ammonium C-1'), 124.36, 121.31 (carboxylate CH), 114.07 (ammonium C-3',5'), 83.68 (bridge CH), 52.48 (bridgehead CH), 45.80 (CH_2), 43.28 (CH_2), 26.10 (CH_3).

X-RAY : space group $P2_1/a$ (#14), monoclinic, a = 16.875(2) Å, b = 6.0339(5) Å, c = 20.719(3) Å, β = 104.00(1)°, V = 2047.0(4) Å^3, Z = 4, D_{calc} = 1.267 g/cm^3, R = 0.051, R_W = 0.056.

_p_-Acetylpyridine complex with acid 19 (68)



68

To a solution of acid **19** (0.15 g, 0.81 mmol) in diethyl ether (10 mL) was added *p*-acetylpyridine (1.0 mL, 1.1 g, 9.0 mmol). Ether was removed *in vacuo*, and the white solid obtained was rinsed with ether prior to recrystallization. Small, white spars were obtained from acetonitrile (0.076 g, 31%).

MP : 204-205 °C.

Anal. calculated for $C_{19}H_{17}NO_3$: C, 74.25; H, 5.58; N, 4.56. Found C, 73.96; H, 5.60; N, 4.46.

MS +LSIMS (matrix : thioglycerol) : 295 (acid + H + matrix), 187 (acid + H).

IR (KBr) ν_{max} : 3000 (acid O-H), 2822, 2520 (N...H), 1696 (C=O), 1248 (C-O), 821 (aromatic C-H), 757 (aromatic C-H) cm^{-1}.

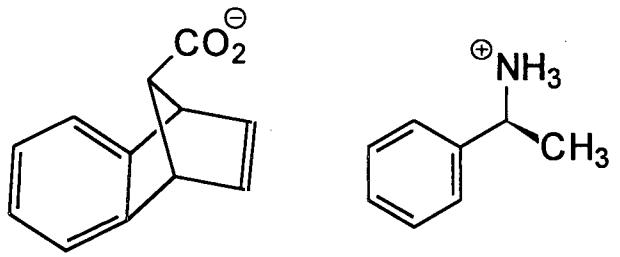
UV (methanol) λ_{max} : 334 (402), 275 (2900), 212 (15,000) nm.

^{1}H NMR (400 MHz, $CDCl_3$) : δ 8.82 (1H, d, J=4.4 Hz, CO_2H), 7.75 (2H, d, J=6.0 Hz, pyridine H-2',6'), 7.23 (4H, m, pyridine H-3',5'; acid aromatic), 6.96 (2H, m, acid aromatic), 6.76 (2H, m, acid olefinic), 4.20 (2H, m, bridgehead CH), 3.36 (1H, t, J = 1.6 Hz, CH bridge), 2.62 (3H, s, CH_3).

^{13}C NMR (75 MHz, CD_3OD) : δ 199.0 (ketone C=O), 174.1 (acid C=O), 151.4 (pyridine C-2',6'), 151.4 (acid aromatic C), 145.0 (pyridine aromatic C), 141.8, 125.7 (acid CH), 123.0 (pyridine C-3',5'), 122.6 (acid CH), 82.2 (bridge CH), 53.2 (bridgehead CH), 26.7 (CH_3).

9.4. Preparation of Chiral Salts of Acid 19.

(S)-(-)-α-Methylbenzylamine salt of acid 19 (81)



81

Acid **19** (0.12 g, 0.63 mmol) and (S)-(-)-α-methylbenzylamine (**69**, 0.081 mL, 0.076 g, 0.63 mmol) were each dissolved in hot chloroform (10 mL), and the two solutions were then combined. After standing overnight, a white powder was collected by suction filtration (0.16 g, 85%).

MP : 175-178 °C (subl, dec).

Anal. calculated for $C_{20}H_{21}NO_2$: C, 78.15; H, 6.89; N 4.56. Found C, 78.35; H, 6.70; N, 4.40.

MS +LSIMS (matrix : thioglycerol) : 122 (ammonium).

MS -LSIMS (matrix : thioglycerol) : 291 (carboxylate + matrix - H_2)

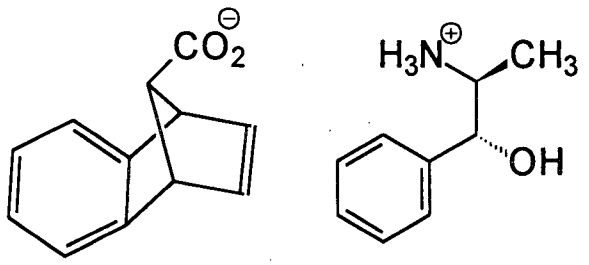
IR (KBr) ν_{max} : 3000 (NH_3^+), 1618 (N-H bending), 1532, 1412 (C=O), 767, 698, 738 (aromatic C-H) cm^{-1}.

UV (methanol) λ_{max} : 276 (468), 268 (575), 262 (563), 256 (553), 216 (3800) nm.

^{1}H NMR (400 MHz, CD_3OD) : δ 7.43 (4H, m, ammonium aromatic), 7.38 (1H, m, ammonium aromatic), 7.06 (2H, dd, J = 5.2, 3.1 Hz, carboxylate aromatic), 6.86 (2H, dd, J = 5.2, 3.1 Hz, carboxylate aromatic), 6.65 (2H, m, olefinic), 4.40 (1H, q, J = 6.7 Hz, CH-N), 4.08 (2H, dd, J = 3.7, 1.8 Hz, bridgehead CH), 3.15 (1H, d, J = 1.4 Hz, CH bridge), 1.60 (3H, d, J=6.8 Hz, CH_3).

^{13}C NMR (75 MHz, CD_3OD) : δ 179.1 (C=O), 152.5 (carboxylate aromatic C), 141.5 (carboxylate CH), 140.4 (ammonium aromatic C), 130.2 (ammonium C-2',6'), 130.0 (ammonium C-4'), 127.6 (ammonium C-3',5'), 125.2 (carboxylate CH), 122.1 (carboxylate CH), 86.8 (bridge CH), 54.1 (bridgehead CH), 52.2 (CH-N), 21.1 (CH_3).

(1R,2S)-(-)-norephedrine salt of acid 19 (83)



83

Acid **19** (0.11 g, 0.59 mmol) and (1R,2S)-(-)-norephedrine (**71**, 0.090 g, 0.60 mmol) were each dissolved in boiling diethyl ether (10 mL). The solutions were then combined, ether was removed *in vacuo*, and the white solid was recrystallized from acetonitrile. Tiny white needles were obtained (0.14 g, 70%).

MP : 155.0-157.5 °C (subl, dec).

Anal. calculated for $C_{21}H_{23}NO_3$: C, 74.75; H, 6.87; N, 4.15. Found C, 74.31; H, 6.80; N, 4.02.

MS +LSIMS (matrix : thioglycerol) : 152 (ammonium), 134 (ammonium - H_2O).

MS -LSIMS (matrix : glycerol + methanol) : 277 (carboxylate + glycerol), 185 (carboxylate).

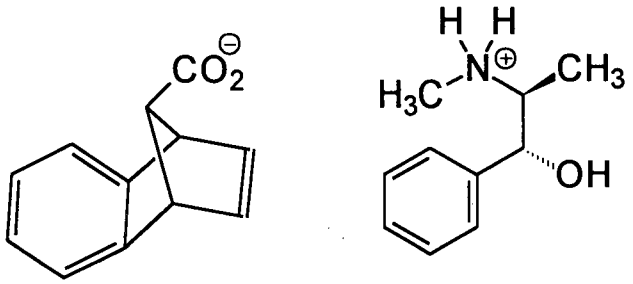
IR (KBr) ν_{max} : 3348 (O-H), 3000 (NH_3^+), 1526, 1424 (C=O), 762, 701, 736 (aromatic C-H) cm^{-1}.

UV (methanol) λ_{max} : 276 (520), 268 (631), 263 (604), 257 (596), 214 (6710) nm.

^{1}H NMR (400 MHz, CD_3OD) : δ 7.39 (5H, m, ammonium aromatic), 7.13 (2H, dd, J = 5.2, 3.1 Hz, carboxylate aromatic), 6.86 (2H, dd, J = 5.2, 3.1 Hz, carboxylate aromatic), 6.65 (2H, t, J = 1.9 Hz, olefinic), 4.92 (1H, d, J=3.5 Hz, CH-O), 4.09 (2H, dd, J = 3.6, 1.8 Hz, CH bridgehead), 3.48 (1H, dq, J = 6.8, 3.5 Hz, CH-N), 3.16 (1H, br t, J = 1.6 Hz, CH bridge), 1.06 (3H, d, J = 6.8 Hz, CH_3).

^{13}C NMR (75 MHz, CD_3OD) : δ 179.1 (C=O), 152.5 (carboxylate aromatic C), 141.7 (ammonium aromatic C), 141.5 (carboxylate CH), 129.5 (ammonium C-4'), 128.9 (ammonium C-2',6'), 127.2 (ammonium C-3',4'), 125.2, 122.1 (carboxylate CH), 86.7 (bridge CH), 73.6 (CH-O), 54.1 (bridgehead CH), 53.6 (CH-N), 12.5 (CH_3).

(1R,2S)-(-)-ephedrine salt of acid 19 (84)



84

Acid **19** (0.13 g, 0.69 mmol) and (1R,2S)-(-)-ephedrine (**72**, 0.11 g, 0.69 mmol) were each dissolved in boiling ethyl acetate (5 mL). The two solutions were combined and brought back to the boiling point, and the total volume increased to 20 mL. The salt precipitated as a voluminous mass of large, transparent crystals, but these shrank considerably when collected by suction filtration, and a white powder was obtained (0.051 g, 21%).

MP : 143-145 °C (subl, dec).

Anal. calculated for $C_{22}H_{25}NO_3$: C, 75.19; H, 7.17; N, 3.99. Found : C, 75.13; H, 7.07; N, 4.17.

MS +LSIMS (matrix : thioglycerol) : 166 (ammonium), 148 (ammonium - H_2O).

MS -LSIMS (matrix : thioglycerol) : 293 (carboxylate + matrix), 185 (carboxylate).

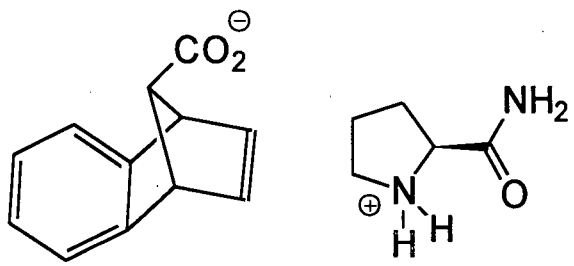
IR (KBr) ν_{max} : 3014 (O-H), 2712 (NH_3^+), 1571, 1387 (C=O), 753, 702, 732 (aromatic C-H) cm^{-1}.

UV (methanol) λ_{max} : 276 (523), 268 (638), 263 (606), 257 (597), 218 (3930) nm.

^{1}H NMR (400 MHz, CD_3OD) : δ 7.39 (4H, m, ammonium aromatic), 7.29 (1H, m, ammonium aromatic), 7.14 (2H, dd, J = 5.1, 3.1 Hz, carboxylate aromatic), 6.86 (2H, dd, J = 5.2, 3.1 Hz, carboxylate aromatic), 6.65 (2H, t, J = 1.8 Hz, olefinic), 5.09 (1H, d, J=3.1 Hz, CH-O), 4.09 (2H, dd, J = 3.6, 1.8 Hz, CH bridgehead), 3.36 (1H, dq, J = 6.7, 3.1 Hz, CH-N), 3.16 (1H, t, J = 1.6 Hz, CH bridge), 2.72 (3H, s, CH_3-N), 1.04 (3H, d, J=6.7 Hz, CH_3-C).

^{13}C NMR (75 MHz, CD_3OD) : δ 179.2 (C=O), 152.5 (carboxylate aromatic C), 141.6 (ammonium aromatic C), 141.5 (carboxylate CH), 129.5 (ammonium C-2',6'), 128.8 (ammonium C-4'), 127.0 (ammonium C-3',5'), 125.2 (carboxylate CH), 122.1 (carboxylate CH), 86.8 (bridge CH), 71.8 (CH-O), 61.4 (CH-N), 54.1 (bridgehead CH), 31.5 (CH_3-N), 10.0 (CH_3-C).

(S)-(-)-Prolinamide salt of acid 19 (85)



85

Acid **19** (0.10 g, 0.54 mmol) and (S)-(-)-prolinamide (**73**, 0.061 g, 0.54 mmol) were each dissolved in methanol (10 mL), and the two solutions combined. The methanol was evaporated, and the solid obtained was

recrystallized from acetonitrile. Small, iridescent, off-white flakes were collected by suction filtration (0.11 g, 69%).

MP : 148-150 °C.

Anal. calculated for $C_{17}H_{20}N_2O_3$: C, 67.98; H, 6.71; N, 9.33. Found C, 67.77; H, 6.68; N, 9.15.

MS +LSIMS (matrix : thioglycerol) : 115 (ammonium).

MS -LSIMS (matrix : thioglycerol) : 293 (carboxylate + matrix), 185 (carboxylate).

IR (KBr) ν_{max} : 3345, 3171 (amide N-H), 1678 (amide C=O), 1569, 1398 (carboxylate C=O), 736 (aromatic C-H) cm^{-1}.

UV (methanol) λ_{max} : 276 (467), 268 (536), 262 (444), 220 (2120), 217 (2050), 215 (2010) nm.

^{1}H NMR (400 MHz, CD_3OD) : δ 7.18 (2H, dd, J = 5.2, 3.1 Hz, aromatic), 6.90 (2H, dd, J = 5.2, 3.1 Hz, aromatic), 6.69 (2H, t, J = 2.0 Hz, olefinic), 4.15 (1H, m, CH-N), 4.12 (2H, dd, 3.6, 1.7 Hz, CH bridgehead), 3.33 (2H, m, CH_2-N), 3.20 (1H, br t, J = 1.4 Hz, CH bridge), 2.39 (1H, m, CH_2-C), 2.00 (3H, m, CH_2-C).

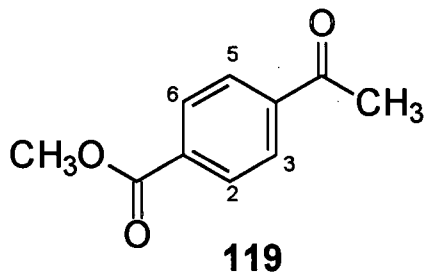
^{13}C NMR (75 MHz, CD_3OD) : δ 178.8 (carboxylate C=O), 173.1 (amide C=O), 152.3 (aromatic C), 141.5, 125.3, 122.2 (carboxylate CH), 86.3 (bridge CH), 60.8 (CH-N), 54.0 (bridgehead CH), 47.2 (CH_2-N), 31.3 (CH_2-C), 25.4 (CH_2-C).

9.5. Preparation of Chiral Triplet Sensitizers.

9.5.1. Preparation of 4-Substituted Benzyl Alcohols.

9.5.1.1. Preparation of 4-Acetylbenzyl Alcohol (91).

Methyl 4-acetylbenzoate (119)



119

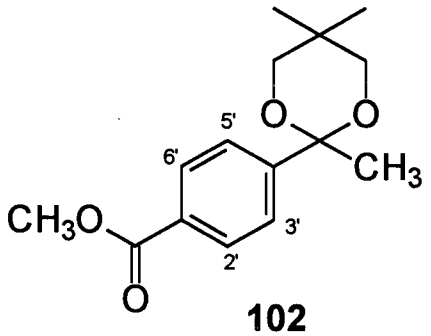
A solution of 4-acetylbenzoic acid (**120**, 1.0 g, 6.1 mmol) and concentrated sulfuric acid (1.25 mL) in methanol (50 mL) was heated at reflux temperature until t.l.c. analysis indicated complete conversion to product (4 h). The reaction mixture was then diluted to 100 mL with cold water and extracted into dichloromethane. The organic extract was washed successively with 5% sodium carbonate and saturated sodium chloride, dried over anhydrous magnesium sulfate, and evaporated to yield product as a pale yellow, iridescent solid (1.0 g, 100%).

MP : 93.5-94.0 °C (lit.[82] 95.0-95.5 °C).

IR (KBr) ν_{max} : 1723 (ester C=O), 1678 (ketone C=O), 1572, 1502 (aromatic C=C), 1284, 1114 (C-O) cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$) : δ 8.09 (2H, d, $J_{2,3}$ = 8.6 Hz, H-2,6), 7.98 (2H, d, $J_{3,2}$ = 8.6 Hz, H-3,5), 3.93 (3H, s, CH_3-O), 2.62 (3H, s, CH_3-C=O).

Methyl 4-acetylbenzoate, neopentylene ketal (102)



102

A solution of ester **119** (9.1 g, 51 mmol), neopentylene glycol (10.6 g, 102 mmol), and *p*-toluenesulfonic acid monohydrate (110 mg) in benzene (110 mL) was heated to reflux in a flask fitted with a condenser and Dean-Stark trap. Heating was continued until complete conversion to product was indicated by t.l.c. analysis (silica, 90% petroleum ether / 10% ethyl acetate). The reaction mixture was then cooled to room temperature and washed with 5% sodium carbonate. The aqueous washing was extracted with diethyl ether, and the combined organic extracts were then washed with water, dried over anhydrous potassium carbonate, and evaporated. Crude product was obtained as a viscous yellow oil, which solidified into a slushy, crystalline mass.

Recrystallization from ethanol gave white crystals with the appearance of pure, driven snow (9.4 g, 70%).

MP : 81.5-82.5 °C.

Anal. calculated for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63. Found C, 68.20; H, 7.62.

MS DCI(+) (ammonia) : m/e (relative intensity) : 265 (M+1, 13), 249 (100), 179 (38), 163 (61), 129 (85), 119 (10), 69 (34), 56 (11), 43 (23).

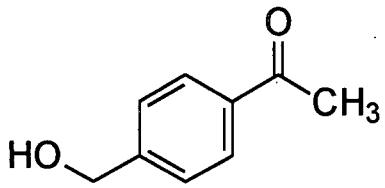
Exact mass calculated for $C_{15}H_{21}O_4$ (methane, M+1) : 265.14398. Found : 265.14356.

IR (KBr) ν_{max} : 2959, 2858 (C-H), 1724 (C=O), 1610, 1575, 1474 (aromatic C=C), 1277, 1185, 1082 (C-O) cm^{-1}.

^{1}H NMR (400 MHz, C_6D_6) : δ 8.17 (2H, dd, $J_{2',3'}$ = 6.7 Hz, $J_{2',6'}$ = 1.8 Hz, H-2',6'), 7.46 (2H, dd, $J_{3',2'}$ = 6.7 Hz, $J_{3',5'}$ = 1.8 Hz, H-3',5'), 3.50 (3H, s, CH_3-O), 3.22 (4H, m, CH_2-O), 1.59 (3H, s, CH_3-C(OR)$_2$Ph), 1.19 (3H, s, eq-C$\underline{H}_3$-C(CH$_2$R)$_2$CH$_3$), 0.20 (3H, s, ax-C$\underline{H}_3$-C(CH$_2$R)$_2$CH$_3$).

^{13}C NMR (100 MHz, C_6D_6) : δ 166.5 (C=O), 147.0 (aromatic C), 130.4 (aromatic CH), 130.3 (aromatic C), 127.2 (aromatic CH), 100.2 ($\underline{C}$-(OR)$_2$(CH$_3$)Ph), 71.8, (CH_2-O), 51.6 (CH_3-O), 32.0 ($\underline{C}H_3$-C(OR)$_2$Ph), 29.8 ($\underline{C}$-(CH$_2$R)$_2$(CH$_3$)$_2$), 22.9 (CH_3), 21.6 (CH_3).

4-Acetylbenzyl alcohol (91)



91

Under a nitrogen atmosphere, a suspension of lithium aluminum hydride (2.7 g, 71 mmol) in anhydrous tetrahydrofuran (300 mL, distilled from sodium / benzophenone) was prepared, and cooled in an ice bath to 0 °C. A solution of ketal **102** (9.4 g, 36 mmol) in tetrahydrofuran (30 mL) was added dropwise, with stirring, via an addition funnel. Upon completion of the addition, the ice bath was removed, and the reaction mixture allowed to stir for 2.5 hours. The reaction was then cooled to 0 °C, and quenched by careful dropwise addition of saturated sodium sulfate (35 mL). The white, crystalline precipitate which formed was removed by suction filtration and discarded, after rinsing several times with ethyl acetate. The tetrahydrofuran and ethyl acetate were then removed *in vacuo*, to yield a faintly yellowish, highly viscous oil.

The oil was not purified. Hydrolysis to the ketone was achieved by dissolving the oil in methanol / hydrochloric acid (300 mL methanol, 100 mL 5% hydrochloric acid), and heating at reflux temperature for 3.5 hours. Methanol was removed *in vacuo*, and the aqueous suspension of product extracted into dichloromethane. The organic extract was washed successively with 5% sodium

bicarbonate, water, and saturated sodium chloride, dried over anhydrous magnesium sulfate, and evaporated to give an off-white solid (4.0 g, 75%).

MP : 53.5-55.0 °C (lit.[75] 51-54 °C).

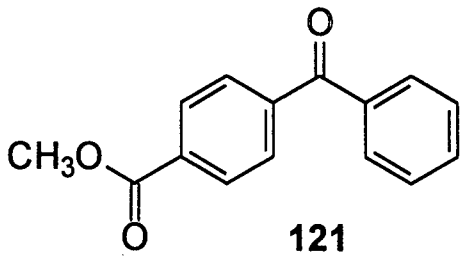
IR (KBr) ν_{max} : 3430 (O-H), 1657 (C=O), 1605, 1569 (aromatic C=C), 1282 (O-H bending), 1049 (C-O), 817 (aromatic C-H) cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$) : δ 7.92 (2H, d, J = 8.3 Hz, aromatic), 7.43 (2H, d, J = 8.4 Hz, aromatic), 4.75 (2H, s, CH_2-O), 2.57 (3H, s, CH_3-C=O), 2.00 (1H, s, OH).

^{13}C NMR (75 MHz, CD_3CN) : δ 198.7 (C=O), 148.5 (aromatic C), 136.9 (aromatic C), 129.2 (aromatic CH), 127.3 (aromatic CH), 64.1 (CH_2-O), 27.0 (CH_3).

9.5.1.2. Preparation of 4-Benzoylbenzyl Alcohol (92).

Methyl 4-benzoylbenzoate (121)



121

A solution of 4-benzoylbenzoic acid (**122**, 3.0 g, 13 mmol) and concentrated sulfuric acid (3.75 mL) in methanol (150 mL) was heated at reflux temperature until t.l.c. analysis (80% petroleum ether / 20% ethyl acetate)

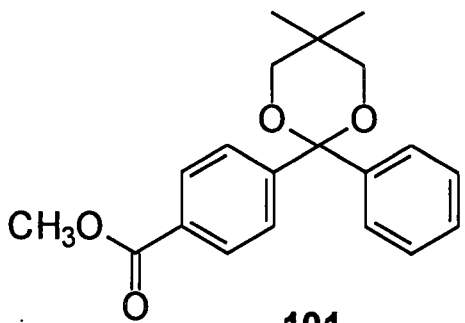
indicated that product formation was complete (3 hours). The reaction mixture was poured into cold water (600 mL), and extracted into dichloromethane. The extracts were washed with 5% sodium carbonate and saturated sodium chloride, dried over anhydrous magnesium sulfate, and evaporated to yield product as a white solid (3.2 g, 100%).

MP : 104.5-106.0 °C (lit.[83] 107 °C).

IR (KBr) ν_{max} : 1718 (ester C=O), 1647 (ketone C=O), 1283, 1108 (C-O) cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$) : δ 8.13 (2H, d, J = 8.1 Hz, aromatic), 7.80 (4H, m, aromatic), 7.61 (1H, tt, J = 7.3, 1.9 Hz, aromatic), 7.48 (2H, m, aromatic), 3.95 (3H, s, CH_3).

Methyl 4-benzoylbenzoate, neopentylene ketal (101)



101

A solution of methyl 4-benzoylbenzoate (**121**, 2.1 g, 8.7 mmol), neopentylene glycol (1.8 g, 17 mmol), and *p*-toluenesulfonic acid (100 mg) in benzene (25 mL) was heated at reflux in a flask fitted with a condenser and

Dean-Stark trap. Reflux was continued until t.l.c. analysis (90% petroleum ether / 10% ethyl acetate) indicated that conversion to product was complete (26 hours). The cooled reaction mixture was washed with 5% sodium carbonate, and the washing was then extracted with diethyl ether. The combined organic extracts were washed with water, dried over anhydrous potassium carbonate, and evaporated to yield a viscous, yellowish oil which solidified to a white, crystalline solid (2.7 g, 93%).

MP : 99.5-101.0 °C.

Anal. calculated for $C_{20}H_{22}O_4$: C, 73.60; H, 6.79. Found C, 73.50; H, 6.83.

MS m/e (relative intensity) : 326 (M^+, 2.1), 249 (80), 191 (93), 181 (23), 163 (72), 105 (100), 77 (42), 69 (75), 42 (24).

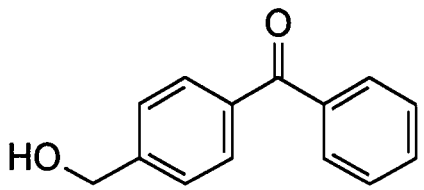
Exact mass calculated for $C_{20}H_{22}O_4$: 326.15179. Found : 326.15085.

IR (KBr) ν_{max} : 2949 (C-H), 1723 (C=O), 1279, 1100, 1020 (C-O), 709 (aromatic C-H) cm^{-1}.

^{1}H NMR (400 MHz, C_6D_6) : δ 8.11 (2H, d, J = 8.7 Hz, aromatic), 7.69 (2H, d, J = 8.7 Hz, aromatic), 7.64 (2H, d, J = 8.7 Hz, aromatic), 7.16 (2H, m, aromatic), 7.03 (1H, m, aromatic), 3.45 (7H, m, CH_2-O and CH_3-O), 0.72 (3H, s, CH_3), 0.67 (3H, s, CH_3).

^{13}C NMR (125 MHz, C_6D_6) : δ 166.4 (C=O), 148.0, 142.4 (aromatic C), 130.0, 128.7 (aromatic CH), 128.3 (aromatic C), 128.1, 126.9, 126.8 (aromatic CH), 100.8 ($\underline{C}$-$(OR)_2(Ar)_2$), 72.0 (CH_2-O), 51.5 (CH_3-O), 30.0 ($\underline{C}$-$(CH_2R)_2(CH_3)_2$), 22.4, 22.3 (CH_3).

4-Benzoylbenzyl alcohol (92)



92

A suspension of lithium aluminum hydride (1.7 g, 45 mmol) in anhydrous tetrahydrofuran (190 mL, distilled from sodium / benzophenone) was prepared under a nitrogen atmosphere and cooled to 0 °C in an ice bath. A solution of protected ester **101** (6.8 g, 21 mmol) in tetrahydrofuran was added dropwise, with stirring, from an addition funnel. Upon completion of the addition, the ice bath was removed, and stirring continued for 2 hours. The reaction was quenched by cooling to 0 °C, and slowly and carefully adding saturated sodium sulfate solution (20 mL). The crystalline white precipitate which formed was removed by suction filtration and discarded, after it was rinsed well with ethyl acetate.

Hydrolysis was accomplished by addition of 5% hydrochloric acid (50 mL) to the tetrahydrofuran / ethyl acetate solution of product, and stirring at room temperature until complete conversion to the deprotected benzyl alcohol was indicated by t.l.c. analysis (80% petroleum ether / 20% acetone) (21 hours). The organic solvents were then removed *in vacuo*, and the product extracted out of the remaining aqueous suspension into dichloromethane. The dichloromethane

solution was washed with 5% sodium bicarbonate, water, and saturated sodium chloride, dried over anhydrous magnesium sulfate, and evaporated. Product was obtained as a viscous, faintly yellowish oil, which solidified upon refrigeration to yield a waxy, white solid (3.4 g, 77%). Pure alcohol for analysis could be obtained by recrystallization from cyclohexane.

MP : 63.5-65.0 °C (lit.[75] 61-64 °C).

Anal. calculated for $C_{14}H_{12}O_2$: C, 79.23; H, 5.70. Found C, 79.31; H, 5.63.

MS m/e (relative intensity) : 212 (M^+, 60), 183 (11), 181 (15), 135 ([M^+-Ph], 100), 107 (21), 105 (92), 89 (22), 77 (75), 51 (23).

Exact mass calculated for $C_{14}H_{12}O_2$: 212.08372. Found : 212.08414.

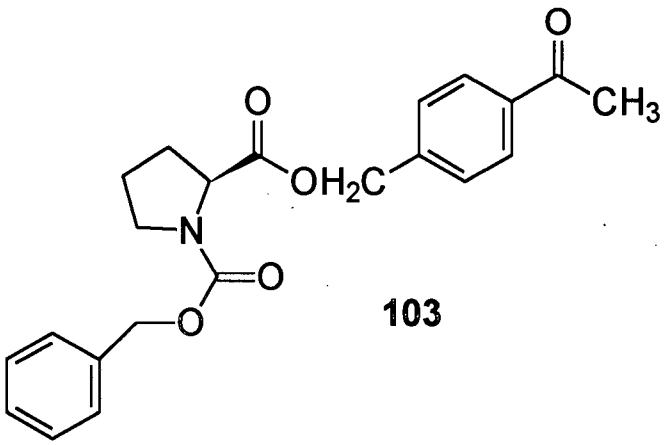
IR (KBr) ν_{max} : 3311 (O-H), 1652 (C=O), 1282 (O-H bending), 1047 (C-O), 730, 705 (aromatic C-H) cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$) : δ 7.77 (4H, m, aromatic), 7.57 (1H, tt, J = 7.2, 1.9 Hz, aromatic), 7.47 (4H, m, aromatic), 4.78 (2H, s, CH_2), 2.01 (1H, s, OH).

^{13}C NMR (75 MHz, $CDCl_3$) : δ 196.59 (C=O), 145.63, 137.51, 136.56 (aromatic C), 132.42, 130.33, 129.96, 128.24, 126.34 (aromatic CH), 64.55 (CH_2-O).

9.5.2. Preparation of Chiral Triplet Sensitizers as Hydrobromide Salts.

Carbobenzyloxy-L-proline 4-acetylbenzyl ester (103)



103

A solution of carbobenzyloxy-L-proline (**123**, 1.7 g, 6.7 mmol), 4-acetylbenzyl alcohol (**91**, 1.0 g, 6.7 mmol), and dimethylaminopyridine (47 mg) in dichloromethane (10 mL) was prepared under a nitrogen atmosphere and cooled to 0 °C. Dicyclohexylcarbodiimide (1.7 g, 8.2 mmol) was then added, and the reaction mixture was stirred for 5 minutes. The ice bath was removed after 5 minutes, and the mixture allowed to stir at room temperature for 3 hours.

The dicyclohexylurea precipitate was removed by suction filtration, and the filtrate evaporated *in vacuo*. The residue was taken up in dichloromethane, re-filtered, and washed successively with 5% hydrochloric acid (2 ×), 5% sodium bicarbonate (until basic), water (until neutral), and saturated sodium chloride (1 ×). The dichloromethane solution was then dried over anhydrous magnesium sulfate, and evaporated to give a slightly cloudy, yellowish oil, which was purified

by dry flash chromatography (80% dichloromethane / 20% ethyl acetate). A cloudy, syrupy, off-white oil was obtained (2.33 g, 91%). NMR analysis showed that the product exists as an inseparable mixture of conformational diastereomers, due to hindered rotation about the carbamate C-N bond.

Anal. calculated for $C_{22}H_{23}NO_5$: C, 69.28; H, 6.08; N, 3.67. Found C, 69.40; H, 6.21; N, 3.80.

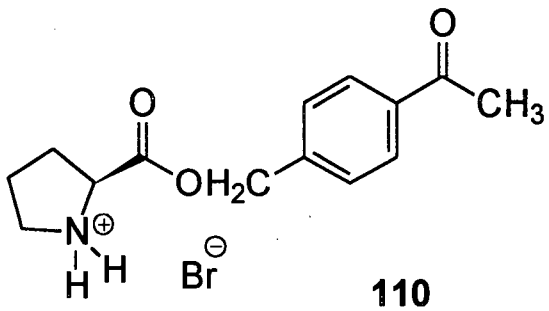
MS m/e (relative intensity) : 381 (M^+, 0.37), 330 (0.41), 275 (0.67), 204 (45), 160 (62), 134 (38), 91 (100).

IR (CCl_4 solution, NaCl) ν_{max} : 1753 (ester C=O), 1712 (2 peaks: carbamate and ketone C=O), 1690 (ketone C=O), 1266, 1165 (C-O) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) : δ 7.87 (1H, d, J = 8.2 Hz, acetophenone ring), 7.80 (1H, d, J = 8.2 Hz, acetophenone ring), 7.20 (7H, m, aromatic), 5.09 (4H, m, CH_2-O), 4.41, 4.35 (1H, dd (2), J = 8.6, 3.2 Hz; 8.6, 3.9 Hz, CH-N), 3.51 (2H, m, CH_2-N), 2.51, 2.50 (3H, s, CH_3-C=O), 2.18 (1H, m, CH_2-C), 1.89 (3H, m, CH_2-C).

^{13}C NMR (75 MHz, $CDCl_3$) : δ 197.5, 197.4 (ketone C=O), 172.3, 172.2 (ester C=O), 154.7, 154.0 (carbamate CO), 140.8, 140.5, 136.60, 136.57, 136.46, 136.30 (aromatic C), 128.43, 128.39, 128.29, 128.23, 127.82, 127.75, 127.65, 127.56, 127.50 (aromatic CH), 66.85, 66.78, 65.73, 65.64 (CH_2-O), 59.09, 58.72 (CH-N), 46.79, 46.29 (CH_2-N), 30.76, 29.73 (CH_2), 26.50 ($\underline{C}H_3$-C=O), 24.19, 23.39 (CH_2).

L-Proline 4-acetylbenzyl ester hydrobromide (110)



110

Ester **103** (2.3 g, 6.0 mmol) was placed in a two-necked round-bottomed flask under a nitrogen atmosphere, and a 32% w/w solution of hydrogen bromide in acetic acid (4.4 mL, 6.0 g, in excess) was added by syringe, with stirring. The mixture immediately turned bright, golden yellow, and evolution of carbon dioxide gas was observed. The reaction was allowed to continue until a marked slackening of carbon dioxide evolution was apparent (15 minutes), after which anhydrous diethyl ether (60 mL) was slowly added. At first, addition of ether induced formation of a white precipitate, which swirled gently and gracefully above a yellow sludge at the bottom of flask. With continued stirring, the white precipitate and yellow sludge coalesced into a dandelion yellow, gummy solid. The mixture was stirred for 15 minutes at room temperature, and then refrigerated for 3 hours. The yellow solid was collected by suction filtration, triturated repeatedly with anhydrous ether, and dried overnight under vacuum.

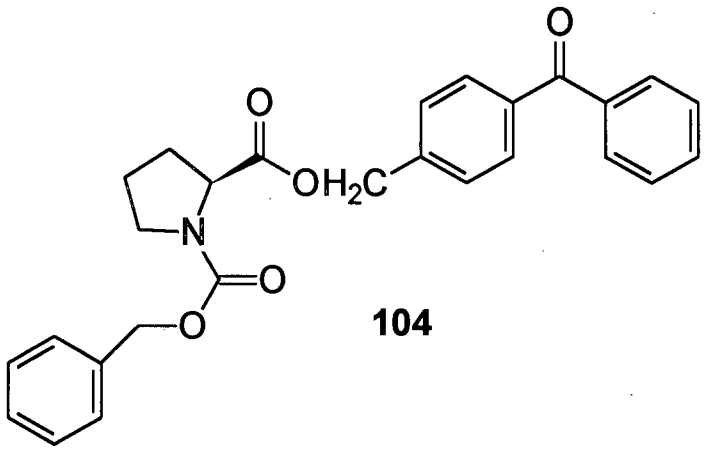
The mustard-yellow powder which was obtained (0.96 g, 49%) could not be completely characterized, apparently due to its extremely hygroscopic nature. It was not possible to obtain a free-flowing powder; the solid obtained was

always gummy, and would become more so upon exposure to atmospheric conditions.

^{1}H NMR (400 MHz, CD_3CN) : δ 10.18 (2H, br s, NH_2^+), 7.96 (2H, d, J = 8.4 Hz, aromatic), 7.53 (2H, d, J = 8.5 Hz, aromatic), 5.29 (2H, s, CH_2-O), 4.50 (1H, m, CH-N), 3.39 (2H, m, CH_2-N), 2.55 (3H, s, CH_3-C=O), 2.39 (1H, m, CH_2), 2.15 (1H, m, CH_2), 2.02 (2H, m, CH_2).

^{13}C NMR (75 MHz, CD_3CN) : δ 198.54 (ketone C=O), 169.69 (ester C=O), 141.02, 138.01 (aromatic C), 129.37, 129.02 (aromatic CH), 68.21 (CH_2-O), 60.14 (CH-N), 46.99 (CH_2-N), 29.16 (CH_2), 27.06 (CH_3), 24.38 (CH_2).

Carbobenzyloxy-L-proline 4-benzoylbenzyl ester (104)



104

A solution of carbobenzyloxy-L-proline (**123**, 1.1 g, 4.4 mmol), 4-benzoylbenzyl alcohol (**92**, 0.94 g, 4.4 mmol) and dimethylaminopyridine (36 mg) in dichloromethane (5 mL) was prepared under a nitrogen atmosphere and

cooled to 0 °C in an ice bath. Dicyclohexylcarbodiimide (0.95 g, 4.6 mmol) was added. The reaction mixture was allowed to stir for 5 minutes before the ice bath was removed, and then allowed to stir at room temperature until complete conversion to product was indicated by t.l.c. analysis (70% dichloromethane / 30% acetone, 2.5 hours).

The white precipitate of dicyclohexylurea was removed by suction filtration, and the filtrate evaporated. The residue was dissolved in fresh dichloromethane and, when it became apparent that no urea remained in the residue and that a second filtration was not required, the dichloromethane solution was washed with 0.5 M hydrochloric acid (2 ×), and saturated sodium bicarbonate (2 ×), dried over anhydrous magnesium sulfate, and evaporated. The viscous, yellowish oil isolated was purified by dry flash chromatography (90% dichloromethane / 10% ethyl acetate). A colourless, viscous oil was obtained (1.65 g, 85%). NMR analysis showed that the product exists as conformational diastereomers, due to hindered rotation about the C-N carbamate bond.

Anal. calculated for $C_{27}H_{25}NO_5$: C, 73.11; H, 5.69; N, 3.16. Found C, 72.85; H, 5.83; N, 3.22.

MS DCI+ (NH_3) m/e (relative intensity) : 444 (M+1, 3.5), 400 (3.4), 204 (66), 196 (100), 160 (95), 91 (81), 43 (m, 0.25).

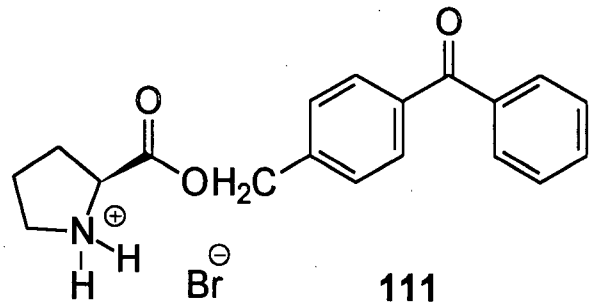
Exact mass calculated for $C_{27}H_{26}NO_5$ (M+1, NH_3 + CH_4) : 444.18109. Found : 444.18195.

IR (CCl_4 solution, NaCl) ν_{max} : 1753 (ester C=O), 1713 (carbamate C=O), 1665 (ketone C=O), 1277, 1165 (C-O), 700 (aromatic C-H) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) : δ 7.8 - 7.2 (14 H, m, aromatic), 5.13 (4H, m, CH_2-O), 4.46, 4.40 (1H, dd (2), J = 8.6, 3.6 Hz, CH-N), 3.55 (2H, m, CH_2-N), 2.24 (1H, m, CH_2), 1.95 (3H, m, CH_2).

^{13}C NMR (75 MHz, $CDCl_3$) : δ 195.83, 195.73 (ketone C=O), 172.23, 172.07 (ester C=O), 154.57, 153.90 (carbamate C=O), 140.04, 139.77, 137.14, 137.08, 136.97, 136.91 (aromatic C), 132.25, 132.21, 130.01, 129.99, 129.68, 128.16, 128.12, 128.03, 127.67, 127.52, 127.42, 127.17, 127.11 (aromatic CH), 66.70, 66.68 (CH_2-O), 65.65, 65.57 (CH_2-O), 59.00, 58.61 (CH-N), 46.68, 46.17 (CH_2-N), 30.63, 29.61 (CH_2), 24.07, 23.26 (CH_2).

L-Proline 4-benzoylbenzyl ester hydrobromide (111)



111

Ester **104** (0.92 g, 2.1 mmol) was placed in a two-necked round-bottomed flask under a nitrogen atmosphere, and a solution of 30% w/w hydrogen bromide in acetic acid (1.5 mL, 2.1 g, in excess) was added by syringe, with stirring. The reaction mixture immediately turned golden yellow, and rapid evolution of carbon

dioxide gas was observed. The reaction was allowed to continue until completion was indicated by the cessation of bubbling, at which point anhydrous diethyl ether (10 mL) was added to precipitate the hydrobromide salt. This crashed out of solution as a cream-coloured powder, which was collected by suction filtration, triturated with ether, dried under vacuum, and recrystallized from acetonitrile to yield product as a white powder (0.056 g, 6.9%).

MP : 107.0-108.5 °C.

MS +LSIMS (matrix : thioglycerol) : 701, 699 (2[$C_{19}H_{20}NO_3$]Br), 619 (2[$C_{19}H_{20}NO_3$]-H), 414, 412 (M+Na), 310 (M-Br).

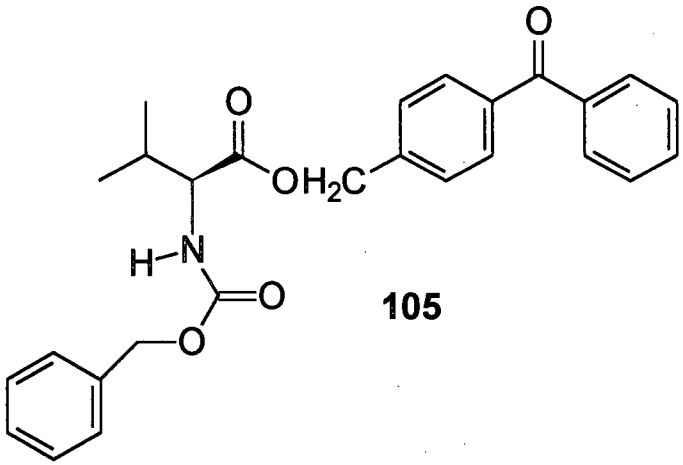
Exact mass calculated for 2[$C_{19}H_{20}NO_3$]Br : 701.20682. Found : 701.20594.

IR (KBr) ν_{max} : 2966 (NH_2^+), 1742 (ester C=O), 1645 (ketone C=O), 1281, 1234 (C-O) cm^{-1}.

^{1}H NMR (400 MHz, CD_3CN) : δ 10.13 (2H, br s, NH_2^+), 7.77 (3H, m, aromatic), 7.67 (1H, tt, J = 7.4, 1.3 Hz, aromatic), 7.55 (5H, m, aromatic), 5.34 (2H, s, CH_2-O), 4.48 (1H, m, CH_2-N), 2.17 (1H, m, CH_2), 2.03 (3H, m, CH_2).

^{13}C NMR (75 MHz, CD_3OD) : δ 197.95 (ketone C=O), 169.97 (ester C=O), 141.18, 138.95, 135.61 (aromatic C), 134.00, 131.34, 130.99, 129.61, 129.27 (aromatic CH), 68.55 (CH_2-O), 60.82 (CH-N), 47.26 (CH_2-N), 29.36 (CH_2), 24.57 (CH_2).

Carbobenzyloxy-L-valine 4-benzoylbenzyl ester (105)



105

A solution of carbobenzyloxy-L-valine (**124**, 1.23 g, 4.90 mmol), 4-benzoylbenzyl alcohol (**92**, 1.04 g, 4.90 mmol), and dimethylaminopyridine (28 mg) in dichloromethane (5 mL) was prepared under a nitrogen atmosphere and cooled in an ice bath to 0 °C. Dicyclohexylcarbodiimide (1.11 g, 5.39 mmol) was added, causing immediate appearance of a white precipitate. The suspension was stirred for 5 minutes at 0 °C, at which point the ice bath was removed, and stirring continued until complete conversion to product was indicated by t.l.c. analysis (90% dichloromethane / 10% ethyl acetate, 1.25 hours). The reaction mixture was subjected to suction filtration to remove the precipitated dicyclohexylurea, and the dichloromethane solution of crude product was then washed successively with 5% hydrochloric acid (2 ×), 5% sodium bicarbonate (2 ×), water, and saturated sodium chloride. It was then dried over anhydrous magnesium sulfate and evaporated, to yield a viscous, cloudy, yellowish oil containing numerous flecks of white precipitate (2.05 g, 94%). This could be

used in the deprotection step with only a quick purification by dry flash chromatography (95% dichloromethane / 5% ethyl acetate); pure product for characterization purposes could, however, be obtained as a white powder by recrystallization from ethanol (0.195 g, 8.9%).

MP : 72-73 °C.

Anal. calculated for $C_{27}H_{27}NO_5 \bullet ½\ C_2H_5OH$: C, 71.78; H, 6.45; N, 2.99. Found C, 72.06; H, 6.18; N, 3.25.

MS DCI+ (NH_3) m/e (relative intensity) : 492 (M+H+C_2H_5OH, 0.39), 446 (M+1, 0.71), 379 (5), 358 (3), 206 (41), 196 (54), 162 (71), 91 (100).

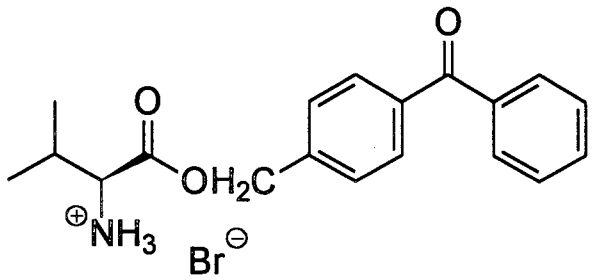
Exact mass calculated for $C_{27}H_{28}NO_5$ (M+1, NH_3+CH_4) : 446.19675. Found : 446.19500.

IR (KBr) ν_{max} : 3369 (N-H), 2971 (C-H), 1713 (2 peaks, ester and carbamate C=O), 1667 (ketone C=O), 1530 (N-H bending)1310, 1283, 1230 (C-O) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) : δ 7.72 (2H, br d, J = 7.6 Hz, aromatic), 7.52 (1H, m, aromatic), 7.40 (4H, m, aromatic), 7.27 (5H, m, aromatic), 5.45 (1H, br d, J=8.8 Hz, N-H), 5.19 (2H, s, CH_2-O), 5.05 (2H, s, CH_2-O), 4.34 (1H, dd, J = 8.9, 4.8 Hz, CH-N), 2.14 (1H, m, C<u>H</u>$(CH_3)_2$), 0.91 (3H, d, J=6.8 Hz, CH_3), 0.83 (3H, d, J=6.9 Hz, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$) : δ 195.91 (ketone C=O), 171.68 (ester C=O), 156.11 (carbamate C=O), 139.62, 137.23, 137.16, 136.03 (aromatic C), 136.36, 130.14, 129.80, 128.31, 128.13, 127.97, 127.89, 127.60 (aromatic CH), 66.82, 65.96 (CH_2-O), 58.94 (CH-N), 31.00 (<u>C</u>H-C$(CH_3)_2$), 18.85 (CH_3), 17.30 (CH_3).

L-Valine 4-benzoylbenzyl ester hydrobromide (112)



112

Ester **105** (2.05 g, 4.60 mmol) was placed in a two-necked round-bottomed flask under a nitrogen atmosphere. A 32% w/w solution of hydrogen bromide in acetic acid (3.5 mL, 4.8 g, in excess) was added by syringe, with stirring. Vigorous carbon dioxide evolution commenced, lasting for 25 minutes. After evolution of carbon dioxide had subsided, anhydrous diethyl ether (50 mL) was added slowly by pipet, with stirring, to precipitate the hydrobromide salt. The suspension produced was refrigerated overnight, and the peach-coloured, somewhat gummy, solid was then collected by suction filtration. Repeated trituration (5 ×) with anhydrous ether gave a free-flowing, finely-divided power with a faint pink colouration (1.31 g, 72%).

MP : 138.5-140.0 °C.

Anal. calculated for $C_{19}H_{22}NO_3Br \bullet ½ H_2O$: C, 56.87; H, 5.78; N, 3.49. Found C, 56.83; H, 5.71; N, 3.69.

MS +LSIMS (matrix : thioglycerol) : 705, 703 (2[$C_{19}H_{22}NO_3$]Br), 623 (2[$C_{19}H_{22}NO_3$]-H), 312 (M-Br).

Exact mass calculated for $2(C_{19}H_{22}NO_3)Br$: 705.23636. Found : 705.23505.

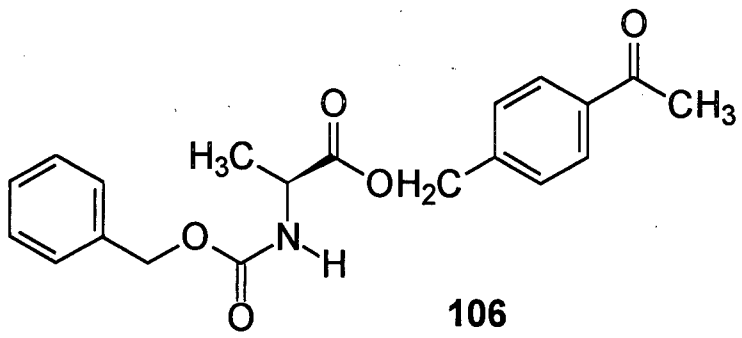
IR (KBr) ν_{max} : 3449 (NH_3^+), 2967 (C-H), 2361 (NH_3^+), 1738 (ester C=O), 1660 (ketone C=O), 1500 (N-H bending), 1281, 1210 (C-O) cm^{-1}.

^{1}H NMR (400 MHz, CD_3CN) : δ 7.90 (3H, br s, NH_3^+), 7.76 (4H, m, aromatic), 7.65 (1H, m, aromatic), 7.59 (2H, br d, J=8.4 Hz, aromatic), 7.53 (2H, br t, J = 7.8 Hz, aromatic), 5.34 (2H, m, CH_2-O), 4.03 (1H, m, CH-N), 2.44 (1H, m, C<u>H</u>$(CH_3)_2$), 1.06 (3H, d, J=7.0 Hz, CH_3), 1.03 (3H, d, J=7.0 Hz, CH_3).

^{13}C NMR (75 MHz, d_6-DMSO) : δ 195.42 (ketone C=O), 168.75 (ester C=O), 139.74, 136.89, 136.85 (aromatic C), 132.87, 129.81, 129.62, 128.67, 128.25 (aromatic CH), 66.47 (CH_2-O), 57.28 (CH-N), 29.47 (<u>C</u>H$(CH_3)_2$), 18.23, 17.64 (CH_3).

$[\alpha]_D^{24}$ (0.018 g/mL DMSO, 24 °C) : +3°.

Carbobenzyloxy-L-alanine 4-acetylbenzyl ester (106)



106

A solution of carbobenzyloxy-L-alanine (**125**, 1.49 g, 6.66 mmol), 4-acetylbenzyl alcohol (**91**, 1.00 g, 6.66 mmol), and dimethylaminopyridine (39 mg)

in dichloromethane (10 mL) was prepared under a nitrogen atmosphere and cooled, with stirring to 0 °C. Dicyclohexylcarbodiimide (1.51 g, 7.32 mmol) was added. A white precipitate formed immediately. The reaction mixture was stirred at 0 °C for 5 minutes; the ice bath was then removed, and the reaction allowed to proceed at room temperature for 1.25 hours. After this time had elapsed, the precipitated dicyclohexylurea was removed by suction filtration, the filtrate was washed successively with 5% hydrochloric acid (2 ×), 5% sodium bicarbonate (2 ×), water, and saturated sodium chloride, dried over anhydrous magnesium sulfate, and evaporated. Product was obtained as a cloudy, yellowish, viscous oil with crystals suspended in it, and solidified upon refrigeration to an ivory-coloured, waxy solid (2.37 g, 100%). Pure product was obtained as a white powder by recrystallization from ethanol.

MP : 67.0-67.5 °C.

Anal. calculated for $C_{20}H_{21}NO_5$: C, 67.59; H, 5.96; N, 3.94. Found C, 67.53; H, 5.89; N, 3.98.

MS DCI+ (NH_3) m/e (relative intensity) : 356 ($[M+1]^+$, 18), 312 ($[M-CO_2]^+$, 13), 134 (93), 91 ($C_7H_7^+$, 100).

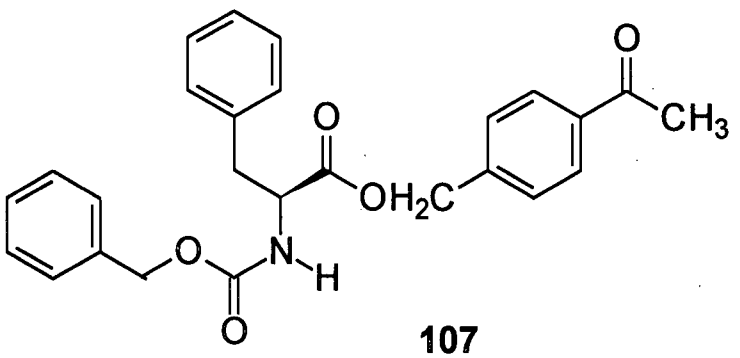
Exact mass calculated for $C_{20}H_{22}NO_5$ (M+1) : 356.14981. Found : 356.14984.

IR (KBr) ν_{max} : 3318 (N-H), 1735 (ester C=O), 1685 (br, ketone and carbamate C=O), 1536 (N-H bending), 1257, 1208, 1174, 1055 (C-O), 836, 756, 699 (aromatic C-H) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) : δ 7.92 (2H, d, J=8.0 Hz, acetophenone aromatic), 7.40 (2H, d, J=7.8 Hz, acetophenone aromatic), 7.32 (5H, m, benzyl aromatic), 5.27 (2H, s, CH_2-O), 5.20 (1H, br s, N-H), 5.09 (2H, s, CH_2-O), 4.44 (1H, m, CH-N), 2.58 (3H, s, CH_3-C=O), 1.42 (3H, d, J=7.2 Hz, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$) : δ 197.56 (ketone C=O), 172.70 (ester C=O), 155.57 (carbamate C=O), 140.45, 136.89, 136.11 (aromatic C), 128.62, 128.50, 128.17, 128.07, 127.79 (aromatic CH), 66.94 (CH_2-O), 66.19 (CH_2-O), 49.64 (CH-N), 26.64 ($\underline{C}H_3$-C=O), 18.51 ($\underline{C}H_3$-CHR).

Carbobenzyloxy-L-phenylalanine 4-acetylbenzyl ester (107)



107

A solution of carbobenzyloxy-L-phenylalanine (**126**, 1.87 g, 6.26 mmol), 4-acetylbenzyl alcohol (**91**, 0.94 g, 6.26 mmol), and dimethylaminopyridine (39 mg) in dichloromethane (10 mL) was prepared under a nitrogen atmosphere and cooled in an ice bath to 0 °C. Dicyclohexylcarbodiimide (1.43 g, 6.93 mmol) was added. A white precipitate appeared immediately. The suspension was stirred

at 0 °C for 5 minutes, after which time the ice bath was removed, and stirring continued for another 2 hours.

The dicyclohexylurea precipitate was removed by suction filtration, and the filtrate washed successively with 5% hydrochloric acid (2 ×), 5% sodium bicarbonate, water, and saturated sodium chloride. The solution was then dried over anhydrous magnesium sulfate and evaporated to yield a viscous, faintly yellowish oil, which crystallized under vacuum. Pure product was obtained as a white powder (1.67 g, 62% yield) by recrystallization from ethanol.

MP : 80-82 °C.

Anal. calculated for $C_{26}H_{25}NO_5 \bullet ½\ C_2H_5OH$: C, 71.35; H, 6.21; N, 3.08. Found C, 71.59; H, 5.82; N, 3.24.

MS DCI+ (NH_3) m/e (relative intensity) : 478 (M+1+C_2H_5OH, 0.83), 432 (M+1, 1.1), 388 (2.6), 280 (34), 133 (28), 91 (100).

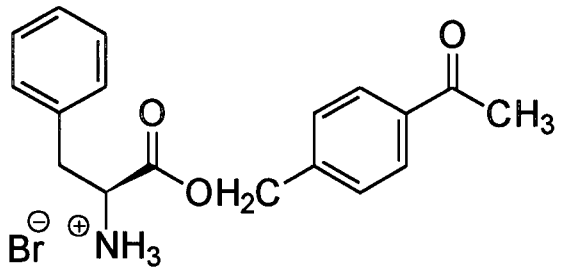
IR (KBr) ν_{max} : 3362 (N-H), 1713 (ester and carbamate C=O), 1677 (ketone C=O), 1531 (N-H bending), 1263, 1037 (C-O), 817, 753, 701 (aromatic C-H) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) : δ 7.91 (2H, d, J = 8.0 Hz, aromatic), 7.31 (7H, m, aromatic), 7.21 (3H, m, aromatic), 7.03 (2H, m, aromatic), 5.18 (1H, m, N-H), 5.15 (2H, s, CH_2-O), 5.08 (2H, s, CH_2-O), 4.70 (1H, m, CH-N), 3.10, 3.09 (1H, s (2), CH_2-Ph), 2.58 (3H, s, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$) : δ 197.55 (ketone C=O), 171.30 (ester C=O), 155.58 (carbamate C=O), 140.12, 136.91, 136.07, 135.39 (aromatic C), 129.20, 128.61,

128.56, 128.49, 128.19, 128.10, 128.06, 127.16 (aromatic CH), 67.00 (CH_2-O), 66.26 (CH_2-O), 54.84 (CH-N), 38.18 (CH_2-Ph), 26.65 (CH_3).

L-Phenylalanine 4-acetylbenzyl ester hydrobromide (114)



114

Ester **107** (1.56 g, 3.62 mmol) was placed in a two-necked, round-bottomed flask under a nitrogen atmosphere. A solution of 30% w/w hydrogen bromide in acetic acid (3.4 mL, 4.6 g, in excess) was added by syringe, with stirring. When it became apparent that the substrate was not dissolving in the reagent solution, and that carbon dioxide evolution was not taking place, an additional 3.4 mL hydrogen bromide solution was added, followed by 5 mL glacial acetic acid. The reaction was left alone for 2 hours, after which time the hydrobromide product was precipitated by addition of anhydrous diethyl ether (40 mL). The suspension was stirred at room temperature for 1.5 hours and refrigerated for 2 days. The hydrobromide salt was then collected by suction filtration and triturated repeatedly with anhydrous ether (5 ×). A white, free-flowing powder was obtained (1.23 g, 90%).

MP : 205-209 °C.

Anal. calculated for $C_{18}H_{20}NO_3Br$: C, 54.56; H, 5.60; N, 3.53. Found C, 55.00; H, 5.20; N, 3.42.

MS +LSIMS (matrix : thioglycerol) : 677, 675 ($2[C_{18}H_{20}NO_3]Br$), 595 ($2[C_{18}H_{20}NO_3]$-1), 399 ($C_{18}H_{20}NO_3Na$-1), 298 ($C_{18}H_{20}NO_3$).

Exact mass calculated for $2(C_{18}H_{20}NO_3)Br$: 677.20506. Found : 677.20425.

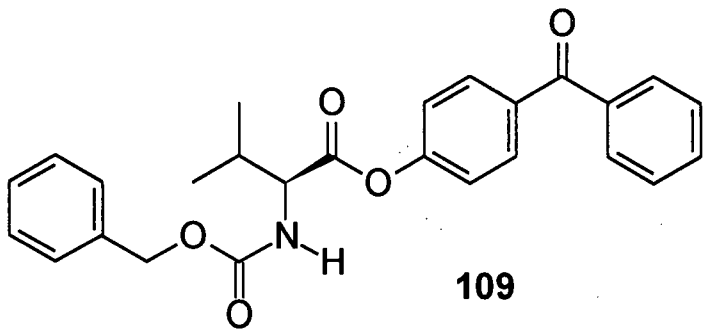
IR (KBr) ν_{max} : 1735 (ester C=O), 1689 (ketone C=O), 1249, 1230 (C-O) cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6) : δ 8.48 (3H, br s, NH_3^+), 7.91 (2H, d, J=8.2 Hz, acetophenone aromatic), 7.36 (2H, d, J=8.2 Hz, acetophenone aromatic), 7.30 (3H, m, benzyl aromatic), 7.22 (2H, m, benzyl aromatic), 5.22 (2H, m, CH_2-O), 4.42 (1H, t, J = 6.9 Hz, CH-N), 3.17 (1H, dd, J = 13.6, 6.3 Hz, CH_2-Ph), 3.08 (1H, dd, J = 14.1, 7.6 Hz, CH_2-Ph), 2.57 (3H, s, CH_3).

^{13}C NMR (75 MHz, DMSO-d_6) : δ 197.64 (ketone C=O), 168.86 (ester C=O), 139.98, 136.53, 134.49 (aromatic C), 129.41, 128.67, 128.25, 128.04, 127.34 (aromatic CH), 66.38 (CH_2-O), 53.19 (CH-N), 36.02 (CH_2-Ph), 26.87 (CH_3).

$[\alpha]_D^{24}$ (0.023 g/mL DMSO, 24 °C) : +15°.

Carbobenzyloxy-L-valine 4-benzoylphenyl ester (109)



109

A solution of carbobenzyloxy-L-valine (**124**, 1.27 g, 5.04 mmol), 4-hydroxybenzophenone (**127**, 1.00 g, 5.04 mmol), and dimethylaminopyridine (51 mg) in dichloromethane (10 mL) was prepared under a nitrogen atmosphere and cooled in an ice bath to 0 °C. Dicyclohexylcarbodiimide (1.15 g, 5.55 mmol) was added. Precipitate formed immediately. Stirring was maintained at 0 °C for 5 minutes, after which time the ice bath was removed and stirring continued for another 4 hours. Suction filtration was used to remove the white precipitate of dicyclohexylurea, and the filtrate was washed successively with 5% hydrochloric acid (2 ×), 5% sodium bicarbonate (2 ×), water, and saturated sodium chloride, dried over anhydrous magnesium sulfate, and evaporated. Product was obtained as a viscous, orange oil, and was purified by dry flash chromatography (90% dichloromethane / 10% ethyl acetate). A viscous, colourless oil with white specks in it was isolated (2.17 g, 100%).

Anal. calculated for $C_{26}H_{25}NO_5$: C, 72.37; H, 5.84; N, 3.25. Found C, 72.13; H, 5.99; N, 3.32.

MS DCI+ (NH_3) m/e (relative intensity) : 432 (M+1, 1.1), 288 (10), 234 (19), 224 (12), 198 (14), 162 (15), 121 (11), 99 (12), 91 (100), 56 (10).

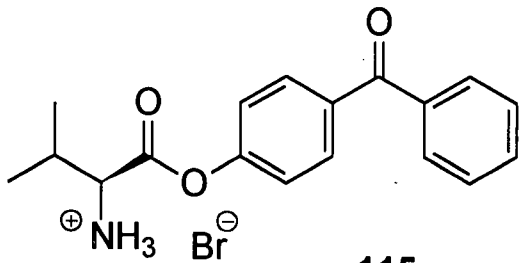
Exact mass calculated for $C_{26}H_{26}NO_5$ (M+1) : 432.18109. Found : 432.18112.

IR (CCl_4 solution, NaCl) ν_{max} : 3442 (N-H), 2969 (aliphatic C-H), 1765 (ester C=O), 1732 (carbamate C=O), 1666 (ketone C=O), 1501 (N-H bending), 1276, 1204, 1164 (C-O) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) : δ 7.83 (2H, d, J=8.4 Hz, aromatic), 7.77 (2H, m, aromatic), 7.58 (1H, tt, J = 7.4, 1.6 Hz, aromatic), 7.47 (2H, m, aromatic), 7.36 (5H, m, benzyl aromatic), 7.18 (2H, d, J=8.2 Hz, aromatic), 5.35 (1H, d, J=8.5 Hz, N-H), 5.13 (2H, s, CH_2-O), 4.55 (1H, dd, J = 8.6, 4.8 Hz, CH-N), 2.36 (1H, m, $C\underline{H}(CH_3)_2$), 1.09 (3H, d, J=6.8 Hz, CH_3), 1.03 (3H, d, J=6.9 Hz, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$) : δ 195.38 (ketone C=O), 170.36 (ester C=O), 153.40 (carbamate C=O), 137.26, 136.00, 135.31 (aromatic C), 132.50, 131.65, 129.90, 128.52, 128.29, 128.23, 128.10, 121.28 (aromatic CH), 67.18 (CH_2-O), 59.19 (CH-N), 31.18 ($\underline{C}H(CH_3)_2$), 19.05, 17.59 (CH_3).

L-Valine 4-benzoylphenyl ester hydrobromide (115)



115

Ester **109** (2.17 g, 5.03 mmol) was placed in a two-necked, round-bottomed flask under a nitrogen atmosphere, and a 30% w/w solution of hydrogen bromide in acetic acid added by syringe, with stirring. The reaction was allowed to proceed until the cessation of carbon dioxide evolution marked complete conversion to product, and anhydrous diethyl ether (50 mL) was then added to precipitate the hydrobromide. The resultant suspension was refrigerated overnight, and the hydrobromide product was then collected by suction filtration and triturated repeatedly and laboriously with anhydrous ether (25 ×), until a fine, free-flowing, off-white powder was obtained (0.93 g, 49%).

MP : 204-206 °C (dec above 180 °C).

MS +LSIMS (matrix : thioglycerol) : 693, 306.

IR (KBr) ν_{max} : 3000 (NH_3^+), 1754 (ester C=O), 1650 (ketone C=O), 1598 (N-H bending), 1287, 1198 (C-O) cm^{-1}.

^{1}H NMR (400 MHz, CD_3OD) : δ 7.89 (2H, m, aromatic), 7.78 (2H, m, aromatic), 7.66 (1H, m, aromatic), 7.54 (2H, m, aromatic), 7.38 (2H, m, aromatic), 4.30 (1H, d, J=9.0 Hz, CH-N), 2.51 (1H, m, C<u>H</u>$(CH_3)_2$), 1.23 (3H, d, J=7.1 Hz, CH_3), 1.22 (3H, d, J=7.0 Hz, CH_3).

^{13}C NMR (75 MHz, DMSO-d_6) : δ 194.73 (ketone C=O), 167.42 (ester C=O), 152.61, 136.77, 135.30 (aromatic C), 132.91, 131.66, 129.64, 128.69, 121.82 (aromatic CH), 57.47 (CH-N), 29.56 (<u>C</u>H$(CH_3)_2$), 18.44, 17.77 (CH_3).

$[\alpha]_D^{22}$ (0.024 g/mL DMSO, 22 °C) : -6.3°.

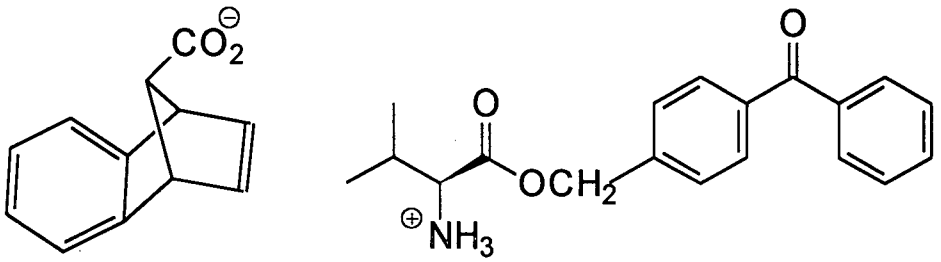
9.5.3. Preparation of Chiral Triplet Sensitizer Salts of Acid 19.

A suspension of the ammonium hydrobromide in ethyl acetate (20 mL) was prepared, and cooled to 0 °C, with stirring. An equimolar amount of triethylamine was added, and the suspension was stirred for 1 hour.[81] The white precipitate of triethylammonium bromide was removed by suction filtration, and the filtrate added to a solution of acid in ethyl acetate (10 mL). Ethyl acetate was removed *in vacuo*, and the crude salt obtained was recrystallized from acetonitrile. Recrystallized product yields and crystal morphologies are described in Table 9.5.3.1.

Table 9.5.3.1. Chiral sensitizer salts of acid **19**.

Auxiliary used (# of Salt)	**Amount of auxiliary used**	**Amount of acid used**	**Yield**	**Crystal morphology**
112 (116)	0.21 g (0.54 mmol)	0.10 g (0.54 mmol)	58%	white powder (resembles laundry detergent)
114 (117)	0.20 g (0.54 mmol)	0.10 g (0.54 mmol)	40%	coarse, off-white powder
115 (118)	0.20 g (0.54 mmol)	0.10 g (0.54 mmol)	52%	very fine, white needles that clump together

Salt of L-valine 4-benzoylbenzyl ester with acid 19 (116)



116

MP : 137.5-139.5 °C.

Anal. calculated for $C_{31}H_{31}NO_5 \bullet ½ H_2O$: C, 73.50; H, 6.37; N, 2.76. Found C, 73.84; H, 6.23; N, 3.04.

MS +LSIMS (matrix : thioglycerol) : 312 (ammonium).

MS -LSIMS (matrix : thioglycerol + methanol) : 185 (carboxylate).

IR (KBr) ν_{max} : 2589 (NH_3^+), 1742 (ester C=O), 1658 (ketone C=O), 1622, 1419 (carboxylate C=O), 1504 (N-H bending), 1284, 1199 (C-O), 760, 734, 703 (aromatic C-H) cm^{-1}.

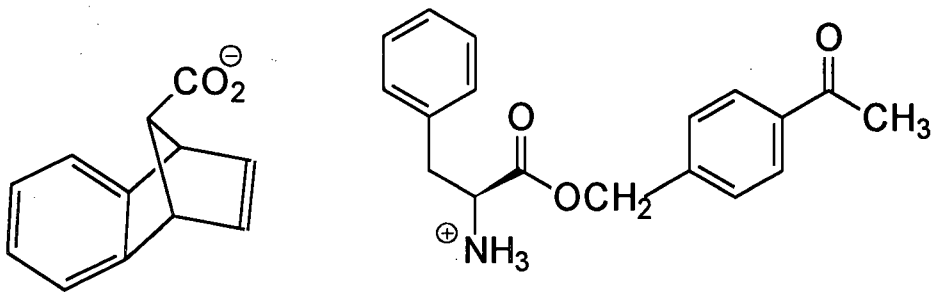
UV (methanol) λ_{max} : 335 (653), 255 (22,500), 210 (29,200) nm.

^{1}H NMR (400 MHz, CD_3OD) : δ 7.74 (4H, m, ammonium aromatic), 7.63 (1H, m, ammonium aromatic), 7.52 (4H, m, ammonium aromatic), 7.17 (2H, dd, J = 5.2, 3.1 Hz, carboxylate aromatic), 6.88 (2H, dd, J = 5.2, 3.1 Hz, carboxylate aromatic), 6.68 (2H, t, J = 1.9 Hz, olefinic), 4.71 (2H, s, CH_2-O), 4.10 (2H, dd, J = 3.7, 1.8 Hz, CH bridgehead), 3.62 (1H, d, J = 4.9 Hz, CH-N), 3.20 (1H, t, J = 1.6

Hz, CH bridge), 2.13 (1H, m, C<u>H</u>$(CH_3)_2$), 1.00 (3H, d, J = 7.0 Hz, CH_3), 0.99 (3H, d, J = 7.0 Hz, CH_3).

^{13}C NMR (75 MHz, DMSO-d_6) : δ 195.42 (ketone C=O), 174.74 (carboxylate C=O), 171.35 (ester C=O), 150.23 (carboxylate aromatic C), 140.92 (ammonium aromatic C), 140.76 (carboxylate CH), 136.95, 136.55 (ammonium aromatic C), 132.77, 129.83, 129.62, 128.61, 127.79 (ammonium aromatic CH), 124.35, 121.49 (carboxylate CH), 81.16 (bridge CH), 64.95 (CH_2-O), 59.41 (CH-N), 51.44 (bridgehead CH), 31.76 (<u>C</u>H$(CH_3)_2$), 19.14, 17.46 (CH_3).

Salt of L-phenylalanine 4-acetylbenzyl ester with acid 19 (117)



117

MP : 111-113 °C.

Anal. calculated for $C_{30}H_{29}NO_5$: C, 74.52; H, 6.04; N, 2.90. Found C, 74.31; H, 5.89; N, 2.77.

MS +LSIMS (matrix : thioglycerol) : 577 (2[ammonium]-H_2O-1), 298 (ammonium).

MS -LSIMS (matrix : glycerol + methanol) : 277 (carboxylate + glycerol), 185 (carboxylate).

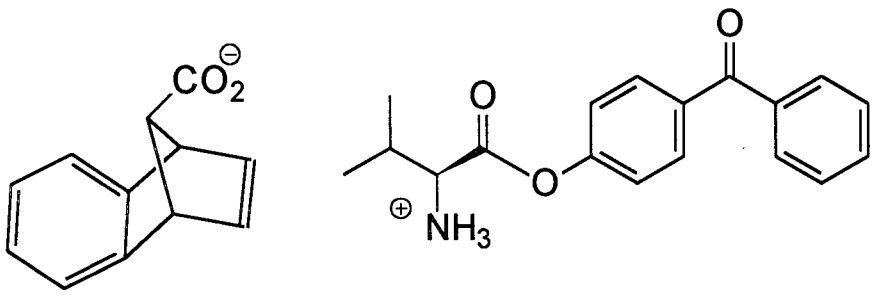
IR (KBr) ν_{max} : 3005, 2888 (NH_3^+), 1747 (ester C=O), 1686 (ketone C=O), 1611, 1490 (N-H bending), 1550, 1417 (carboxylate C=O), 1264, 1220 (C-O), 760, 738, 702 (aromatic C-H) cm^{-1}.

UV (methanol) λ_{max} : 247 (16,100), 210 (28,900) nm.

^{1}H NMR (400 MHz, CD_3OD) : δ 7.96 (2H, dt, J = 7.5, 1.7 Hz, ammonium aromatic), 7.47 (1H, d, J=8.5 Hz, ammonium aromatic), 7.37 (1H, d, 8.4 Hz, ammonium aromatic), 7.34-7.15 (7H, m, aromatic), 6.89 (2H, dd, J = 5.2, 3.1 Hz, carboxylate aromatic), 6.69 (2H, t, J = 1.9 Hz, olefinic), 5.20 (2H, s, CH_2-O), 4.11 (2H, dd, J = 3.7, 1.8 Hz, CH bridgehead), 3.98 (1H, m, CH-N), 3.22 (1H, t, J = 1.6 Hz, CH bridge), 3.05 (2H, m, CH_2-Ph), 2.59 (3H, s, CH_3).

^{13}C NMR (75 MHz, DMSO-d_6) : δ 197.60 (ketone C=O), 174.51 (carboxylate C=O), 171.28 (ester C=O), 150.18 (carboxylate aromatic C), 141.22 (ammonium aromatic C), 140.79 (carboxylate CH), 137.67, 136.29 (ammonium aromatic C), 129.25, 128.28, 128.20, 127.69, 126.73 (ammonium aromatic CH), 124.38, 121.51 (carboxylate CH), 80.99 (bridge CH), 64.89 (CH_2-O), 55.74 (CH-N), 51.40 (bridgehead CH), 40.56 (CH_2-Ph), 26.79 (CH_3).

Salt of L-valine 4-benzoylphenyl ester with acid 19 (118)



118

MP : 143-144 °C.

Anal. calculated for $C_{30}H_{29}NO_5 \bullet ½ H_2O$: C, 73.15; H, 6.14; N, 2.84. Found C, 73.37; H, 6.15; N, 3.00.

MS +LSIMS (matrix : thioglycerol) : 298 (ammonium).

MS -LSIMS (matrix : thioglycerol) : 291 (carboxylate + matrix - H_2).

IR (KBr) ν_{max} : 3000 (NH_3^+), 1764 (ester C=O), 1668 (ketone C=O), 1597, 1421 (carboxylate C=O), 1277, 1193 (C-O), 765, 739, 706 (aromatic C-H) cm^{-1}.

UV (methanol) λ_{max} : 254 (13,900), 210 (27,100) nm.

^{1}H NMR (400 MHz, CD_3OD) : δ 7.87-6.88 (13H, m, aromatic), 6.69 (2H, t, J = 1.8 Hz, olefinic), 4.11 (2H, dd, J = 3.7, 1.9 Hz, CH bridgehead), 3.72 (1H, br s, CH-N), 3.21 (1H, br s, CH bridge), 2.27 (1H, m, C<u>H</u>$(CH_3)_2$), 1.12 (3H, d, J=9.2 Hz, CH_3), 1.10 (3H, d, J=9.2 Hz, CH_3).

^{13}C NMR (75 MHz, d_6-DMSO) : δ 194.41 (ketone C=O), 174.05 (carboxylate C=O), 171.32 (ester C=O), 152.80 (ammonium aromatic C), 150.21 (carboxylate aromatic C), 140.84 (carboxylate CH), 132.58, 131.88, 129.19, 128.44

(ammonium aromatic CH), 124.44, 121.58 (carboxylate CH), 115.35 (ammonium aromatic CH), 80.99 (bridge CH), 59.19 (CH-N), 51.45 (bridgehead CH), 31.13 ($\underline{C}H(CH_3)_2$), 18.74, 17.35 (CH_3).

10. Photochemical Studies.

10.1. General Procedures.

Irradiation Sources

Photochemical irradiations were carried out with either a Hanovia 450 W medium pressure mercury lamp, or a Rayonet Photochemical Chamber Reactor (Model RPR-100). The Hanovia lamp was operated in a water-cooled immersion well, and the light output passed through a glass filter. Various filters were used, depending on the wavelength of light desired; these were: quartz ($\lambda \geq 200$ nm), Vycor ($\lambda \geq 240$ nm), Corex ($\lambda \geq 260$ nm), Pyrex ($\lambda \geq 290$ nm), and uranium ($\lambda \geq 330$ nm). The Rayonet reactor was equipped with 16 low-pressure lamps, which emitted at 3500 Å.

Solution State Irradiation

Spectral-grade solvents (Fisher) were used for irradiations carried out in the solution state. For preparative-scale irradiations, the solution of the substrate in the appropriate solvent was placed in a large photochemical reactor and deoxygenated with nitrogen for 30 minutes, with stirring, prior to reaction. Efficient stirring was maintained throughout the irradiation period. All preparative-scale solution state irradiations were performed with a Hanovia lamp. For irradiations carried out on an analytical scale, the solutions (5-10 mg in 5 mL) were placed in a small quartz reaction tube (5 mL capacity), purged with

nitrogen for 20 minutes prior to reaction, and sealed to exclude air. The tubes were then suspended by copper wire in front of the lamp used. Analytical-scale reactions were not stirred during irradiation.

Solid State Irradiations

Solid samples were prepared by crushing the compound to be irradiated (5-10 mg for analytical-scale experiments) between two quartz plates, fastening the plates together at top and bottom with Scotch™ utility tape, and placing the resulting "crystal sandwich" in a polyethylene bag. The bag was purged with nitrogen, and sealed under a positive pressure of nitrogen with a heat-sealing device. The sealed bag was suspended in front of the lamp with copper wire, at an approximate distance of 5 cm.

To carry out irradiations at reduced temperatures, the bag was placed in a solvent reservoir containing ethanol cooled by a Cryocool immersion cooler (CC-100 II). The temperature was controlled by a Cryotrol from NESLAB Instruments Inc..

For irradiations in which the Hanovia mercury lamp was used, the lamp was turned off halfway through the reported irradiation time to allow the sample to be turned, so that both sides would receive approximately equal amounts of light. In the Rayonet reactor, the sample was suspended in the centre of a ring of bulbs, and therefore both sides of the sample received equal amounts of light.

Analysis of Photochemical Reactions

The photochemical reactions were monitored and analyzed by injection on a gas chromatograph (GC). For solid state samples, the solid material was rinsed off the plates with an appropriate solvent, in order to make GC injection possible. Percent conversions were determined by injection on an HP-5 column, under the following conditions: initial temperature = 120 °C, initial time = 5 minutes, rate = 15 °C / minute, final temperature = 300 °C, final time = 1-10 minutes.

Analysis of Carboxylic Acids and Salts

Carboxylic acids and carboxylate salts were converted to their methyl esters prior to GC analysis, by treatment with ethereal diazomethane. Diazomethane was prepared according to the Aldrich bulletin accompanying commercially available Diazald™. A solution of potassium hydroxide (0.4 g, 7 mmol) in water (0.5 mL) and ethanol (2.0 mL) was placed in a 100 mL distilling flask fitted with a dropping funnel and distillation condenser. Ground glass joints were not used, owing to the danger of explosive decomposition of diazomethane. The potassium hydroxide solution was heated in a water bath to 65 °C, and a solution of Diazald™ (1.7 g, 7.9 mmol) in diethyl ether (16 mL) was added slowly from the dropping funnel. Once this solution had been added, the dropping funnel was rinsed with ether and a second 16 mL aliquot of ether was added slowly to the potassium hydroxide solution, until the distillate produced was colourless. The ethereal solution of diazomethane which distilled over was

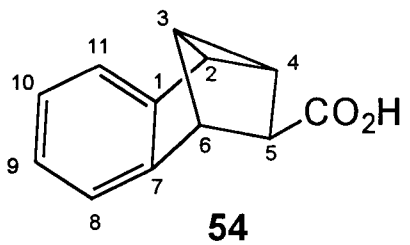
collected in a large sample vial cooled in an ice bath, and the vial was then sealed with parafilm and stored in a freezer until required.

To prepare a sample for GC analysis, ethereal diazomethane was added dropwise via pipet to a solution of the carboxylic acid in an appropriate solvent (usually diethyl ether). Complete conversion to the methyl ester was indicated by the persistence of the characteristic yellow colour of diazomethane. The ester solution was allowed to stand in the fumehood for at least 50 minutes prior to GC injection, to allow evaporation of excess diazomethane.

To analyze analytical-scale irradiations of acid, the irradiation solvent, or the solvent used to rinse the crystals off the plates, was removed *in vacuo*, and the residue re-dissolved in diethyl ether prior to treatment with diazomethane. To analyze irradiated samples of the various salts studied, the residue remaining after removal of the solvent was shaken with diethyl ether and 5% aqueous hydrochloric acid. The aqueous acid protonated the carboxylate, and kept the ammonium ion in protonated form. The acid was then extracted into the ether layer, while the ammonium chloride salt remained in the aqueous layer. Treatment of the ether layer with diazomethane produced the methyl ester.

10.2. Preparation of Photoproduct Samples

exo-tetracyclo[5.4.0.0^{2,4}.0^{3,6}]undeca-1(7),8,10-trien-5-carboxylic acid (54)



54

A stirred solution of *anti*-9-carboxybenzonorbornadiene (**19**, 1.0 g, 5.4 mmol) and acetophenone (0.63 mL, 0.65 g, 5.4 mmol) in acetonitrile was irradiated with uranium-filtered light (λ > 330 nm) until GC analysis of the methyl esters (formed by treatment of reaction mixture samples with ethereal diazomethane) indicated that conversion to product was complete (4.5 hours).

Acetonitrile was removed *in vacuo*, and the residue dissolved in dichloromethane. The acid was extracted as the carboxylate into 5% sodium hydroxide, and the aqueous extract washed with dichloromethane prior to acidification with concentrated hydrochloric acid. The aqueous suspension of acid was then extracted with dichloromethane, and the extract washed with saturated sodium chloride and dried over anhydrous magnesium sulfate. Evaporation of the dichloromethane yielded an off-white powder (0.82 g, 82%). Pure product could be obtained as large, colourless crystals by recrystallization from chloroform.

MP : 126-127 °C.

Anal. calculated for $C_{12}H_{10}O_2$: C, 77.40; H, 5.41. Found C, 77.10; H, 5.44.

MS m/e (relative intensity) : 186 (M^+, 50), 168 (100), 141 (59), 140 (30), 139 (22), 115 (20).

Exact mass calculated for $C_{12}H_{10}O_2$: 186.06808. Found : 186.06847.

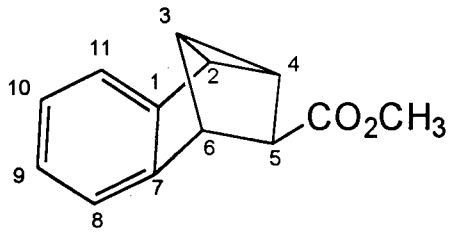
IR (KBr) ν_{max} : 3000 (acid O-H), 1696 (C=O), 759 (aromatic C-H) cm^{-1}.

UV (methanol) λ_{max} : 323 (53.1), 279 (813), 271 (900), 216 (5200) nm.

^{1}H NMR (500 MHz, CD_3CN) : δ 7.44 (1H, d, J=7.36 Hz, H-8 or H-11), 7.14 (1H, ddd, J = 7.3, 6.0, 2.7 Hz, H-9 or H-10), 7.06 (2H, m, aromatic), 3.49 (1H, m, H-6), 3.46 (1H, m, H-3), 2.65 (1H, t, J=5.0 Hz, H-2), 2.11 (1H, m, H-4), 1.77 (1H, d, J=2.3 Hz, H-5).

^{13}C NMR (125 MHz, CD_3CN) : δ 176.98 (C=O), 147.92 (C-1 or C-7), 144.07 (C-1 or C-7), 127.35 (C-9 or C-10), 126.17 (aromatic CH), 124.14 (C-8 or C-11), 121.49 (aromatic CH), 48.59 (C-6), 47.55 (C-5), 46.32 (C-3), 30.08 (C-2), 22.98 (C-4).

Methyl *exo*-tetracyclo[5.4.0.0^{2,4}.0^{3,6}]undeca-1(7),8,10-trien-5-carboxylate (53)



53

Acid photoproduct **54** (0.50 g, 27 mmol) was esterified by treatment of a diethyl ether solution (30 mL) with ethereal diazomethane, until complete conversion to product was indicated by persistence of a yellow colouration. The solution was allowed to stir, uncovered (in a fume hood), until the yellow colour faded. Removal of the ether gave product as a yellowish oil with a sharp, pleasant aroma (0.50 g, 100%). Pure product could be obtained as a colourless oil by chromatography (75% pentane / 25% ethyl acetate) and short-path distillation.

Anal. calculated for $C_{13}H_{12}O_2$: C, 77.98; H, 6.04. Found C, 77.66; H, 5.95.

MS m/e (relative intensity) : 200 (M^+, 12), 168 (100), 141 (62), 140 (32), 139 (21), 115 (26).

Exact mass calculated for $C_{13}H_{12}O_2$: 200.08372. Found : 200.08391.

IR (thin film, NaCl) ν_{max} : 1734 (C=O), 1470 (aromatic C=C), 1269, 1228 (C-O), 753 (aromatic C-H) cm^{-1}.

UV (methanol) λ_{max} : 324 (60), 278 (828), 271 (913), 215 (6310) nm.

^{1}H NMR (500 MHz, $CDCl_3$) : δ 7.42 (1H, d, J=7.4 Hz, H-8 or H-11), 7.14 (1H, m, H-9 or H-10), 7.06 (2H, m, aromatic), 3.80 (3H, s, $OC\underline{H}_3$), 3.51 (2H, m, H-6 and H-3), 2.61 (1H, m, H-2), 2.12 (1H, m, H-4), 1.94 (1H, m, H-5).

^{13}C NMR (125 MHz, $CDCl_3$) : δ 175.98 (C=O), 146.49 (C-1 or C-7), 142.79 (C-1 or C-7), 126.33 (C-9 or C-10), 125.15 (aromatic CH), 123.17 (C-8 or C-11), 120.50 (aromatic CH), 51.99 (OCH_3), 47.62 (C-6), 46.65 (C-5), 45.39 (C-3), 29.30 (C-2), 22.07 (C-4).

10.3. Optical Rotation of the Photoproduct Enantiomers.

A sample of salt **117** between acid **19** and L-phenylalanine 4-acetylbenzyl ester (0.0974 g, 0.201 mmol) was irradiated in the Rayonet reactor, in the solid state, for 2.7 hours. The salt was then washed off the plates with methanol, and the methanol removed *in vacuo*. Extraction of the acid into diethyl ether was accomplished by shaking the residue with ether and 5% aqueous hydrochloric acid, separating the layers, and extracting the aqueous layer a second time with ether. Solid impurities were removed by gravity filtration, and the acid converted to the methyl ester by treatment with ethereal diazomethane. The ester solution was allowed to stand loosely covered in the fumehood overnight, in order to allow the excess diazomethane to evaporate, and the ether was then removed *in vacuo*. A yellow oil was obtained (0.0349 g). The yellow oil was purified by dry flash chromatography (15 g silica, 80% pentane / 20% ethyl acetate) particularly

to remove any chiral impurities that might have been derived from the chiral auxiliary. A faintly yellowish oil (0.0206 g, 51%) was isolated.

The optical rotation was determined at 26 °C, in 2.00 mL of acetone, in a 0.100 dm cell. A value of -0.061° was obtained. Since chiral GC analysis showed that this sample contained an excess of the enantiomer which eluted first, it was possible to assign the first enantiomer as the levorotatory (-) form, and the second enantiomer as the dextrorotatory (+) form.

Chiral GC analysis showed that the (-)-enantiomer was present in 42% enantiomeric excess. Based on this value, the standard optical rotation for the methyl ester photoproduct could be estimated. The $[\alpha]_D$ value calculated for the measured sample was -59°. Thus, the $[\alpha]_D$ value for optically pure levorotatory photoproduct should be about -140°.

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