THERMAL REARRANGEMENTS OF

cis-2-ALKYLCYCLOPROPANECARBOXYLATES

AND METHYL 2- AND 3-PENTENOATES

by

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A THESIS SUBMITTED IN PARTIAL FULFILMENT OF

THE REQUIREMENTS FOR THE DEGREE OF

DOCTOR OF PHILOSOPHY

in the Department of

CHEMISTRY

We accept this thesis as conforming to the

required standard

THE UNIVERSITY OF BRITISH COLUMBIA

August, 1967

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ABSTRACT

Seven alkyl substituted methyl cyclopropanecarboxylates having an alkyl group on C-2 cis to the ester group have been found to rearrange thermally to their corresponding γ,δ-unsaturated esters at temperatures ranging from 240° to 300°. The corresponding trans isomers are unaffected under identical reaction conditions. It is proposed that the rearrangement takes place by an intramolecular 1,5-hydrogen transfer via a six-membered cyclic transition state. The kinetics for these reactions have been studied and show first-order plots which are linear to 70% reaction. The heat of activation ($\Delta H^{\ddagger}$) was found to be between 25 to 38 kcal/mole and the entropy of activation ($\Delta S^{\ddagger}$) was found to be between -8 and -37 eu. from measurements made over a 20° range. This and other information fully support a cyclic hydrogen transfer mechanism.

Four methyl cis-2-pentenoates have been found to undergo both geometric and positional thermal isomerizations to yield equilibrium mixtures of 2- and 3-pentenoates at temperatures ranging from 240° to 300°. The 3-pentenoates produced from the corresponding trans-2-pentenoates were found to be formed via the cis-2-pentenoates. Studies using β-isopropyl acrylate and methacrylate showed that the rate of positional isomerization was much

faster than that of geometric isomerization. For these systems it was therefore possible to study the kinetics of the positional isomerism in the absence of competing geometric isomerization. The kinetic data provided first-order plots. The heat of activation ($\Delta H^{\ddagger}$) was found to be between 18 and 38 kcal/mole and the entropy of activation ($\Delta S^{\ddagger}$) was found to be between -8 to -50 eu. An intramolecular 1,5-hydrogen transfer mechanism involving a six-membered cyclic transition state similar to that for the cyclopropane series is indicated and is suggested to be the general mechanism for conversion of α,β-unsaturated esters to β,γ-unsaturated esters.

The series of 2-alkylcyclopropanes have been prepared by the decomposition of the corresponding pyrazolines. Some of these pyrazolines have been newly synthesized for this work and include methyl 3,5,5-trimethyl-3-carbomethoxy-Δ^1-pyrazoline, methyl 5,5-dimethyl-3-carbomethoxy-Δ^1-pyrazoline and 3,5-dimethyl-3-cyano-Δ^1-pyrazoline. The decomposition of pyrazolines also yielded some of the α,β-unsaturated esters required for this research. Several, however, have also been synthesized by the modified Wittig reaction.

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ACKNOWLEDGEMENT

The author wishes to express his sincere appreciation to Dr. D. E. McGreer for his constant interest and encouragement during the course of this research and the preparation of this thesis.

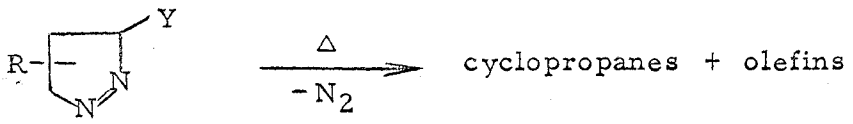
Thanks are extended to Dr. R. E. Pincock who read and commented on this thesis.

The author is indebted to Mrs. A. Brewster, Miss C. Burfitt and Mr. R. Burton for the N.M.R. spectra, to Dr. A Bernhardt, Mrs. C. Jenkins and Mr. P. Borda for the micro-analyses.

Financial assistance from the National Research Council and the University of British Columbia is gratefully acknowledged.

I. INTRODUCTION

Recently a considerable amount of work has been done in this laboratory concerning the pyrolysis of Δ^1-pyrazolines (1-7). This reaction has long been considered as a convenient synthetic method for the preparation of cyclopropane derivatives, and of α,β- and β,γ-unsaturated olefins (8). However, our main interest in the pyrolysis of



R = H, alkyl

Y = CO_2R, COR, CN

Δ^1-pyrazolines has been to investigate the mechanism of ring opening and product formation. In order to accomplish this, the exact stereochemistry of not only Δ^1-pyrazolines but also the products of pyrolysis has had to be determined. During the course of this investigation, difficulties were encountered in the assignment of stereochemistry to the cyclopropane derivatives and α,β-unsaturated olefins. For example, nuclear magnetic resonance and infrared data indicate the presence of a cyclopropane ring in both cis- and trans-1,2-dimethyl-1-acetylcyclopropane (1 and 2)* but their stereochemistry cannot be determined with certainty (9). Most methods that have successfully identified the stereo-

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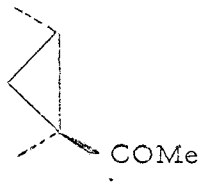
* All the drawn structures show carbon-carbon bonds; each corner representing a carbon and the required hydrogen or hydrogens attached to it are implied.



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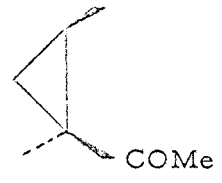
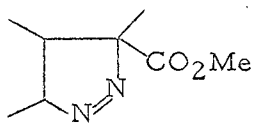


2

chemistry of isomeric pairs make use of comparisions of the properties of the two isomers. It is thus more difficult if only one of the two isomers is available; for example, the exact stereochemistry of one isomer of methyl 2, 3-dimethyl-2-pentenoate (3) obtained from the pyrolysis of 3, 4, 5-trimethyl-3-carbomethoxy-Δ^1-pyrazoline (4) could not be determined on the basis of the data available (6) but was determined by comparison when the second isomer was later obtained (7).



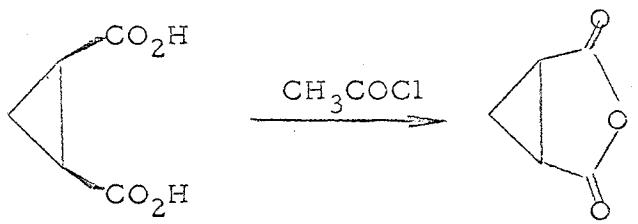
$\xrightarrow{\Delta}$ $C_2H_5(CH_3)C{=}C(CH_3)CO_2Me$ + etc.

4 3

Various chemical and physical methods have been reported for the determination of the stereochemistry of cyclopropanes and α,β-unsaturated olefins. These methods will be discussed first, for the cyclopropanes and later for the α,β-unsaturated olefins.

In 1890, Buchner (10) assigned the stereochemistry to the two

cyclopropane-1-2-dicarboxylic acids on the basis that on heating or by treatment with acetyl chloride, the cis isomer (5) gave cyclopropane-anhydride (7) whereas the trans isomer (6) remained unchanged.



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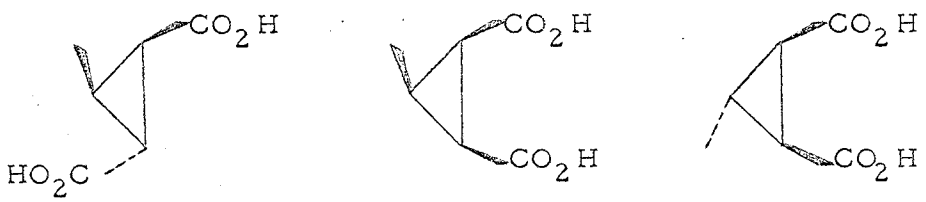
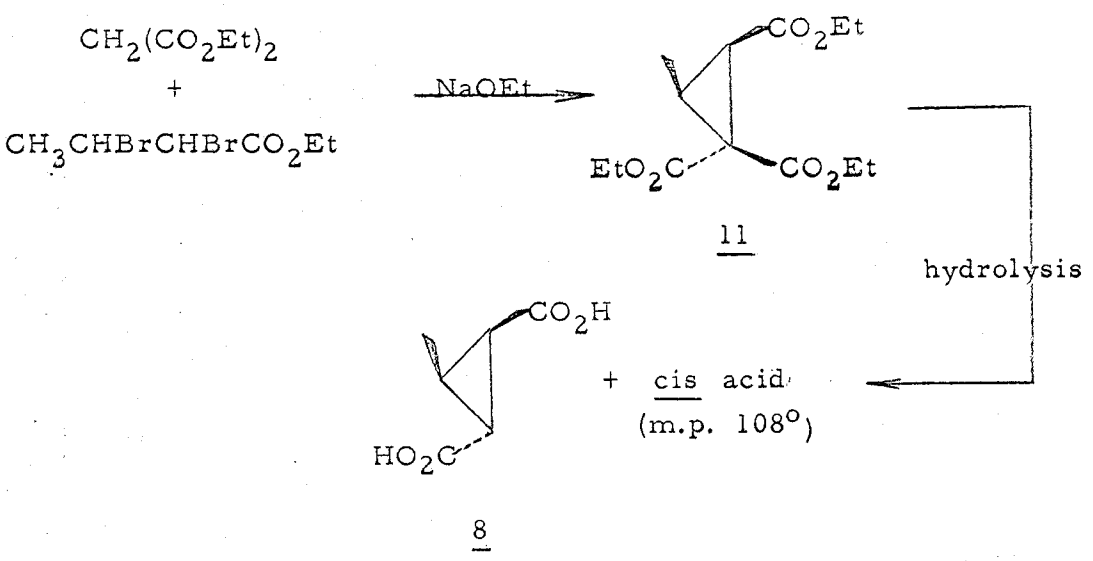
This method was also used for the assignment of structure for the trans isomer (8) of 3-methylcyclopropane-1,2-dicarboxylic acid (11-13). The two cis isomers (9 and 10) with melting points of 132° and 108° both formed anhydrides. Only one of these two cis acids, the



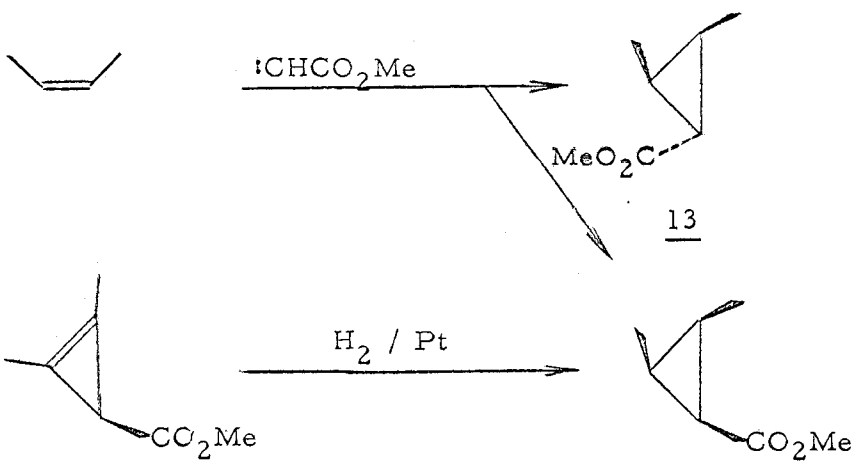
8 9 10

one melting at 108°, was formed together with the trans isomer (8) in the reaction of ethyl 2,3-dibromobutanoate with diethyl malonate followed by complete hydrolysis (11). With the assumptions that the dibromide was formed by trans addition to methyl trans-crotonate and that S_N2 displacement of both bromines takes place on ring closure, then 11 would be the intermediate (14) and only acids with trans and



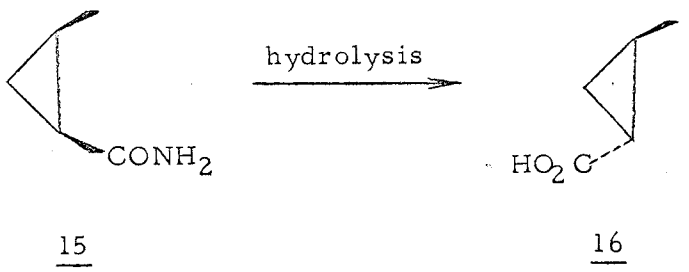
(cis)-cis configuration would result (11). Thus the cis isomer with melting point 108° was assigned the structure (cis)-cis-3-methylcyclopropane-1, 2-dicarboxylic acid (9) and the other with melting point 132° was assigned the structure (trans)-cis-3-methylcyclopropane-1, 2-dicarboxylic acid (10).

Structural distinction between the two methyl cis-2, 3-dimethylcyclopropane-1-carboxylates (12 and 13) obtained by stereospecific addition of carbomethoxycarbene to cis-butehe (15) was accomplished by the application of the principle of surface hindrance in catalytic hydrogenation (16). Addition of hydrogen being from the catalyst surface to the underside of the absorbed olefin in cis addition, the geometry of adsorption controls the stereochemistry of the product. In the case of methyl 1, 2-dimethylcyclopropene-3-carboxylate (14), the favored configuration of adsorption leaves the methyl carboxylate group trans to the catalyst surface and leads to an all cis product, i.e., methyl cis-



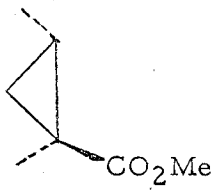
2, 3-dimethylcyclopropane-cis-1-carboxylate (12), thus 12 was differentiated from 13.

Another way to distinguish isomeric cyclopropanecarboxylic acids is to apply certain chemical reactions to convert the cis isomer to the more stable trans isomer. There are two methods for the inversion, one is by treating the cis acid with thionyl chloride (17) and the other is to hydrolyze the nitrile or amide of the cis acid with ethanolic potassium hydroxide (18). For example, cis-2-methylcyclopropanecarboxamide (15) was converted by hydrolysis to the trans-2-methylcyclopropane-



carboxylic acid (16) (19). Under the base conditions the anion at the α-C is presumably formed permitting inversion which on equilibration gives the more stable trans form.

Competitive saponification of isomeric esters of cyclopropane-carboxylic acids has also been useful for structural distinction. The rate of saponification of methyl cis-1, 2-dimethylcyclopropane-1-carboxylate (17) is found to be faster than its trans isomer (18) presumably due to the fact that the ester moiety of cis isomer (17) is less hindered sterically (20).



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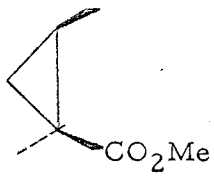

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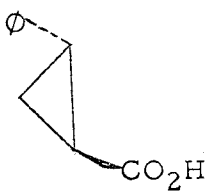
The use of spectroscopic methods for the determination of stereochemistry of cyclopropane derivatives has been limited to nuclear magnetic resonance. This is mainly due to the lack of useful information from infrared and ultraviolet adsorptions of cyclopropane derivatives. Recently, a considerable attention has been devoted to the infrared study of cyclopropane compounds (21 and references therein) but the purpose was limited to the detection of the cyclopropane ring in molecules. Farkas and coworkers (22) and Veldstra (23) attempted to assign geometric configuration to 2-phenylcyclopropane-

carboxylic acids and their 3-alkyl substituted analogues with little success. The differences in ultraviolet curves for these isomeric pairs of acids have been found to be relatively small, e.g., trans-2-phenylcyclopropanecarboxylic acid (19) absorbs at longer wavelength (by 6.5 mμ) then its cis isomer (20). These spectral measurement may be regarded



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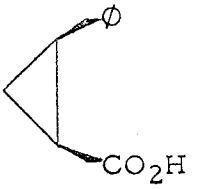
log ε = 2.56
λmax = 266.5 mμ



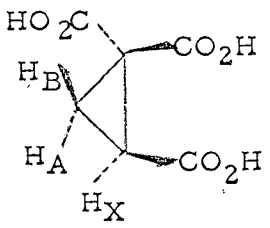
20

log ε = 2.33
λmax = 260 mμ

as useful only if spectra of both isomers are available.

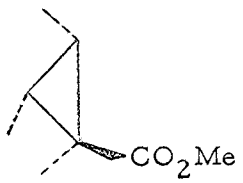
Nuclear magnetic resonance spectroscopy has been used widely in recent years for the structural determination of substituted cyclopropanes. The coupling constants and chemical shifts of a large numbers of substituted cyclopropanes have been determined recently (24-27). There are several important findings which can be used to determine the geometry of substituted cyclopropanes. The first of these is that the cis vicinal proton-proton coupling constant is greater than the trans in cyclopropanes (23-24). The second is that both cis and trans coupling constants are relatively insensitive to the nature of substituents, their values are between +8.0 to +11.2 c.p.s. and +5.2 to +8.0 c.p.s. for cis and trans protons respectively. And the third is that the chemical

shifts are strongly influenced by the nature of the substituents on the ring, especially, magnetically anisotropic species, such as a phenyl or a carbonyl group. The spectrum of cyclopropane-1, 1, 2-tricarboxylic acid (21) showed a large cis (H_A-H_X) coupling constant of 9.33 c.p.s. and a smaller trans (H_B-H_X) of 6.55 c.p.s. The chemical shifts of H_A and H_B are 7.70 τ and 7.58 τ respec-



21

tively. The reason that H_B appears at lower field than H_A is because there are two carboxylic group cis to H_B whereas there is only one cis to H_A and consequently, H_B is more deshielded by the anisotropy of the carboxyl group. Recently, McGreer and coworkers (6) assigned configuration to methyl cis,cis- and cis,trans-1,2,3-trimethyl-1-cyclopropanecarboxylate (22 and 23) based on symmetry consideration and the anisotropic influence on chemical shifts. In 22, there is a plane of



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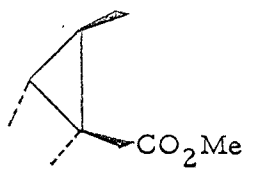
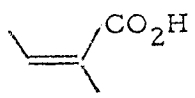


23

symmetry with respect to C-2 and C-3, thus the C-2 and C-3 methyls are equivalent and appear as a doublet at 9.07 τ which is split by a ring proton at 8.59 τ. On the other hand, the C-2 and C-3 methyls in 23 are non-equivalent because the former is cis to the carbomethoxy group whereas the latter is trans to the same and as a result, the C-2 methyl shows a doublet at 8.91 τ and the C-3 methyl shows a doublet at 8.94 τ. The 8.91 τ peak is split by a ring hydrogen trans to the carbomethoxy group at 9.37 τ. The 8.94 τ peak is split by the hydrogen cis to the carbomethoxy group at 8.61 τ. Clearly this chemical shift is markedly affected by the anisotropy of the carbomethoxy group but that of the cis ring methyl is not. This is in contrast to observations on the α,β-unsaturated carbonyl derivatives described below.

Methods for the structural determination of α,β-unsaturated olefins have rarely been studied. Sudborough and Davies (28) studied the rates of esterification of angelic (24) and tiglic (25) acids and



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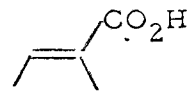

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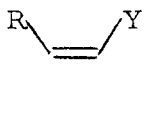
found that the former is esterified slower due to the steric effect of the methyl cis to the carboxylic group.

Infrared spectroscopy is very useful for configurational analysis of α,β-unsaturated olefins. For the isomeric disubstituted

olefins (29), 26 shows two bands, one at 1415 cm^{-1} due to C=H in-plane bending and the other at 730-675 cm^{-1} due to C-H out-of-plane bending. On the other hand 27 shows only one band at 965 cm^{-1} due to C-H out-of-plane bending. For systems that are tri- or tetra-substi-



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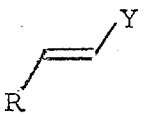
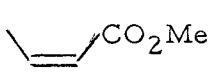


27

R = alkyl, aryl
Y = CO_2H, CO_2R
COR, CN

tuted, the use of infrared spectroscopy is limited because there are no infrared bands which can be reliably correlated with configurations.

During the past few years the application of nuclear magnetic resonance spectroscopy to the assignment of configurations of α,β-unsaturated olefins has proven very successful. This method can determine the configuration of not only mono- and di- but also tri- and tetra-substituted olefins. The most important information is that any cis β-vinyl proton or proton on the first carbon of an alkyl group attached to the β-carbon cis to a diamagnetic anisotropic group, such as a carbonyl group, will be deshielded with respect to the trans arrangement (30). The proton-proton coupling constants for vinyl protons across the double bond are especially valuable for the isomeric vicinal disubstituted olefins because the cis coupling constant has been found to be smaller than the trans coupling constant (31-33). For example, the coupling constants (HC=CH) for methyl cis- and trans-crotonate (28 and 29)



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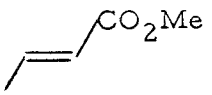
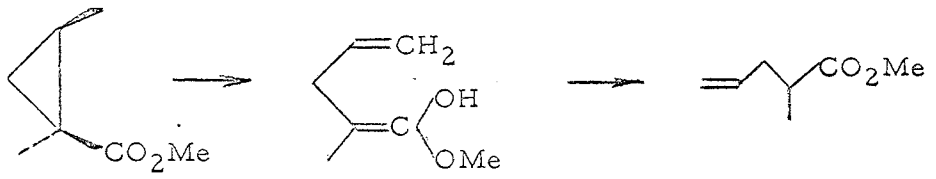


29

are 11.4 c.p.s. and 15.5 c.p.s. respectively, as determined by the ABX_3 treatment of Waugh and Fessenden (33) and by first-order perturbation theory analysis (31). The C-3 methyl appears at lower field by 0.26 τ units for the cis isomer whereas its C-3 hydrogen appears at higher field by 0.62 τ units than those of the trans isomer. These effects are due to the anisotropic effect of the carbomethoxy group.

Judging from the example described above, it is possible but sometimes risky to determine the structure with certainty if only one of the isomers is present. Both isomers are required for comparison purposes. The presence of both isomers will then render it possible for the determination of the structure with certainty. However, it is of value to search for another method which can serve the same purpose when only one of the isomers is present.

Recently, we have observed (34) a novel reaction in which a cis-2-alkylcyclopropanecarboxylate, e.g. 18, rearranges thermally to give exclusively a γ,δ-unsaturated ester (31) whereas the trans isomer (17) remains unchanged under identical reaction conditions. A mechanism proposed for this thermal rearrangement was that it involves an allylic



18 30 31

enol intermediate 30. This proposed intermediate is analogous to the allylic enol intermediate proposed for the photoisomerization of crotonaldehyde to 3-buten-1-al (35) and of α,β-unsaturated ketones to β,γ-unsaturated ketones (36). During the course of this research, other laboratories have investigated variations of this reaction and these are presented in the discussion.

This thermal rearrangement of cis-2-alkylcyclopropanecarboxylates is potentially valuable for structural determination not only of cyclopropane derivatives but also of α,β-unsaturated olefins. It is the purpose of this research to investigate the stereochemical aspect of this rearrangement reaction and to extend it to the α,β-unsaturated esters in the hope that a convenient and accurate method of configurational analysis can be found for these compounds.

II. DISCUSSION

II-I PREPARATION WORK

Compounds synthesized

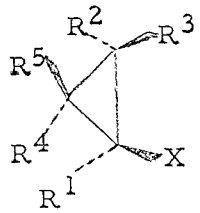
For the present study, a series of 2-alkylcyclopropanes with an electron withdrawing group such as carbomethoxy, acetyl or cyano at C-1 and a series of substituted cis- and trans-unsaturated esters were required. These cyclopropanes can be prepared by the decomposition of the corresponding pyrazolines. The unsaturated esters can also be prepared by this method, however, the yields of some of them are low and another synthetic method was found necessary. We have adapted the modified Wittig reaction for this purpose. These synthetic methods will be discussed below. In Table I and Table II are listed the 2-alkylcyclopropanes and α,β-unsaturated esters respectively, prepared for the present study.

Pyrazoline method

The use of pyrazolines as the starting material for the preparation of 2-alkylcyclopropanes and α,β-unsaturated esters was based on the experience encountered in our laboratory with such compounds. It has been shown (37-39) that pyrazolines can easily be prepared by the addition of a diazoalkane to an olefin which is activated by an electron withdrawing group such as carbomethoxy, acetyl or cyano. The addition product is a Δ^1-pyrazoline which usually rearranges to

TABLE I

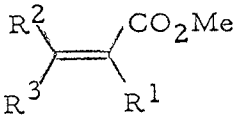
2-Alkylcyclopropanes



Cyclopropane	X	R^1	R^2	R^3	R^4	R^5	Reference
32	CO_2Me	Me	Me	Me	H	H	this work
33	CO_2Me	Me	H	Et	H	H	7
34	CO_2Me	Me	Et	H	H	H	7
35	CO_2Me	H	Me	Me	H	H	this work
18	CO_2Me	Me	H	Me	H	H	3
17	CO_2Me	Me	Me	H	H	H	3
36	CO_2Me	H	H	Me	Me	H	3
37	CO_2Me	H	H	Me	H	H	2
16	CO_2Me	H	Me	H	H	H	2
38	CO_2Me	Me	H	Me	Me	H	6
39	CO_2Me	Me	Me	H	Me	H	6
2	COMe	Me	H	Me	H	H	5
40	CN	Me	H	Me	H	H	this work
41	CN	Me	Me	H	H	H	this work

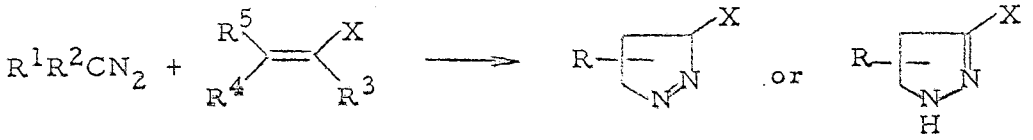
TABLE II

α,β-Unsaturated esters



α,β-Unsaturated ester	R^1	R^2	R^3	method* or reference
42	Me	i-Pr	H	W.
43	Me	H	i-Pr	W. and P.
44	H	i-Pr	H	W.
45	H	H	i-Pr	W. and P.
46	Me	Et	H	W.
47	Me	H	Et	W.
48	H	Et	H	P. (2)
49	H	H	Et	W.

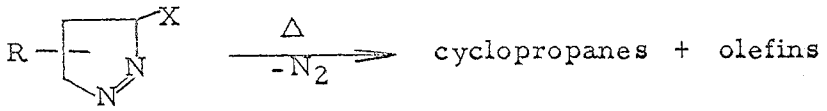
* W = modified Wittig reaction, P = pyrazoline method.



R = H, alkyl

X = CO_2R, COR, CN

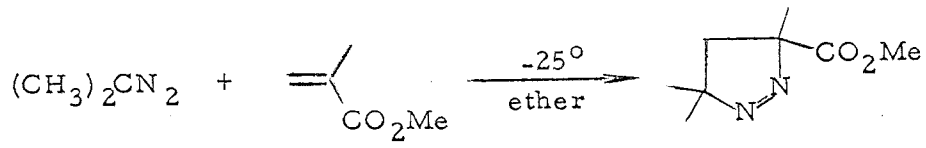
the more stable form, Δ^2-pyrazoline if R^3 is a hydrogen. These pyrazolines, when decomposed, give a product mixture consisting of cyclopropanes and olefins following the loss of nitrogen (1-7, 40-46).



All of the 2-alkylcyclopropanes listed in Table I have been prepared from their corresponding Δ^1- or Δ^2-pyrazoline by either thermal or photochemical decomposition. All of the required pyrazolines have been prepared previously in this laboratory except the following, 3,5,5-trimethyl-3-carbomethoxy—Δ^1-pyrazoline (50), 5,5-dimethyl-3-carbomethoxy—Δ^1- and Δ^2-pyrazoline (53 and 54) and 3,5-dimethyl-3-cyano—Δ^1-pyrazoline (55), and their preparation and decomposition are discussed below.

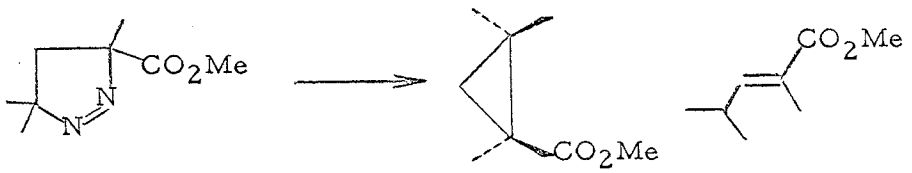
3,5,5-Trimethyl-3-carbomethoxy—Δ^1-pyrazoline (50) was prepared by the addition of methyl methacrylate to an ethereal solution of diazo-isopropane at -25° which was prepared, in situ, by oxidizing

acetone hydrazone with silver oxide (47). The pyrazoline structure was



50

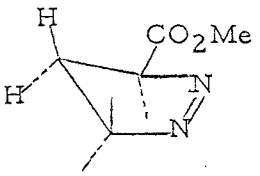
readily characterized by N. M. R. which shows the ester methyl at 6.27 τ and the non-equivalent C-5 methyls at 8.60 τ and 8.64 τ. The two hydrogens at C-4 show an AB system (48) with a pair of doublets at 8.03 τ and 8.79 τ, $J_{gem} \simeq 13.1$ c.p.s. This Δ^1-pyrazoline when decomposed by heating on a steam bath gave a product mixture consisting of methyl 1, 2, 2-trimethylcyclopropane-1-carboxylate (32) and methyl trans-2, 4-dimethyl-2-pentenoate (43) in the ratio of 84:16. The exclusive formation of the trans olefin (43) suggests that only one hydrogen on C-4 is in



50 32 43

a position to migrate and by analogy with the mechanism suggested by McGreer, et. al. (6, 7) it would be the hydrogen trans to the ester group as in the conformation 51. It is not clear at this time why that hydrogen should be in the preferred position for migration since a methyl group would be expected to be larger than a carbomethoxy group and thus the

alternative conformation 52 would be expected to be favored.



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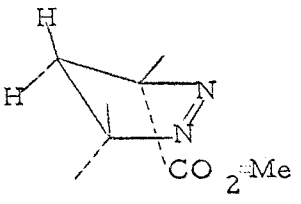
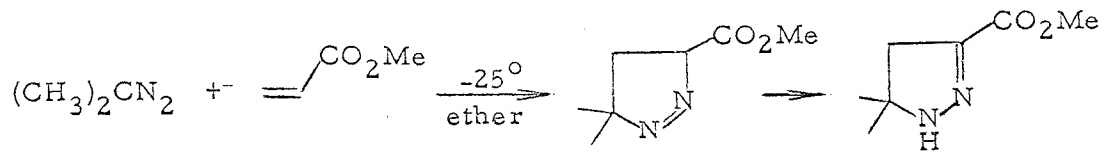


52

The structure of methyl 1, 2, 2-trimethylcyclopropane-1-carboxylate (32) was determined by its N. M. R. spectrum which shows three singlets at 9.01 τ, 8.87 τ and 8.74 τ for the ring methyls. The two geminal hydrogens on C-3 form an AB system (48) and show a pair of doublet at 9.74 τ and 8.58 τ with $J_{gem} \simeq 4.6$ c.p.s.

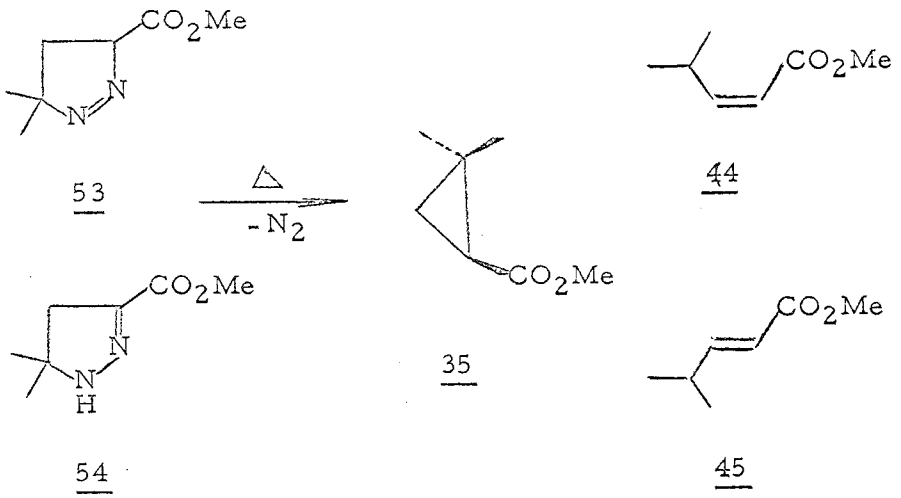
The stereochemistry of methyl trans-2, 4-dimethyl-2-pentenoate (43) can be distinguished from its cis isomer (42) prepared by the method of modified Wittig reaction (discussed later) on the basis of their N. M. R. spectra. The C-3 hydrogen of the cis isomer appears at higher field (0.87 τ) than that of trans isomer because the latter is deshielded (49) by the anisotropic carbomethoxy group, which is cis to it. On the other hand, the C-4 methine hydrogen of the cis isomer is at lower field (0.61 τ) than that of the trans isomer as it is deshielded by the carbomethoxy group.

5,5-Dimethyl-3-carbomethoxy-Δ^1-pyrazoline (53) was prepared by reacting methyl acrylate with diazo-isopropane , in situ, at -25°. This Δ^1-pyrazoline is capable of rearranging to the more stable conjugated



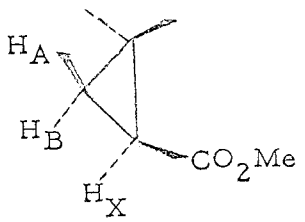
53 54

Δ^2-pyrazoline (54) as stated earlier and it was found that rearrangement occurred partially before the product was isolated from the reaction mixture. Attempted separation of these isomers by distillation gave a lower boiling fraction consisting of both isomers and a higher boiling fraction of pure Δ^2-pyrazoline (54) as indicated by N. M. R. analyses. The N. M. R. spectra of the two isomers are quite different because the Δ^2 isomer is symmetric with respect to the plane of the ring while the Δ^1 isomer is not. The preferred conformation of the Δ^1 isomer is an envelope with the carbomethoxy group at C-3 in a pseudo equatorial position (6). As a result the methyls on C-5 and the hydrogens on C-4 are non-equivalent, the former appear at 8.15 τ and 8.33 τ and the latter at 6.71 τ and 7.49 τ. On the other hand, the C-5 methyls as well as the C-4 hydrogens on the Δ^2 isomer are equivalent due to symmetry and as a result, the methyls show a singlet at 8.72 τ and the hydrogens show a singlet at 7.36 τ. Furthermore, the Δ^2 isomer has a hydrogen attached to the N-1 which appears at 3.16 τ. A mixture consisting of both Δ^1 and Δ^2 isomers (53 and 54) was pyrolyzed at 100-170° and gave a product mixture of methyl 2, 2-dimethylcyclopropane-1-carboxy-



late (35), methyl cis- and trans-4-methyl-2-pentenoate (44 and 45) in a ratio of 26:4:70.

The structure of methyl 2,2-dimethylcyclopropane-1-carboxylate (35) is indicated partly by its N. M. R. spectrum and partly due to the fact that it is the only logical cyclopropane product derived from the pyrazoline. Its N. M. R. spectrum shows two singlets at 8.81 τ and 8.86 τ for the methyls on C-2. The three hydrogens on C-1 and C-2 form an ABX system (48) and show three pairs of doublets at 8.50 τ (H_X), 9.0 τ (H_A, resolved at 100 Mc in benzene) and 9.21 τ (H_B). The



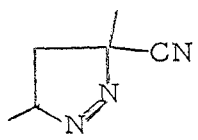
35

proton-proton coupling constants are $J_{gem} \simeq 4.0$ c.p.s., $J_{cis} \simeq 8.1$ c.p.s. and $J_{trans} \simeq 5.1$ c.p.s. These values are in good agreement with that

of 2,2-dimethylcyclopropane-1-carboxylic acid (the acid form of 35) as determined by Patel, et. al. (24).

The stereochemistry of methyl cis- and trans-4-methyl-2-pentenoate (44 and 45) are assigned on the basis of N. M. R. and I. R. analyses. The trans isomer shows an I. R. band at 990 cm^{-1} typical of trans vicinal vinylic hydrogens whereas the cis isomer shows a vinyl C-H in-plane bending band at 1417 cm^{-1} (29). The cis isomer shows a smaller proton-proton coupling constant for the vinyl protons across the double bond than the trans isomer (31, 32), e.g., 11.4 c.p.s. for the cis isomer and 15.8 c.p.s. for the trans isomer. Nuclear magnetic resonance analyses also show that the C-3 hydrogen of the trans isomer is at lower field (3.14 τ) than that of the cis isomer (4.03 τ) due to deshielding by the anisotropy of the ester group (49).

3,5-Dimethyl-3-cyano-Δ^1-pyrazoline (55) was prepared by the addition of methacrylonitrile to diazoethane in ether at 0°. The N. M. R. spectrum (Figure 1) of the product shows it has the same general fea-



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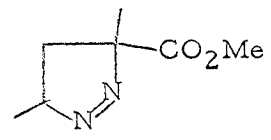


56

tures as that of the analogous 3,5-dimethyl-3-carbomethoxy-Δ^1-pyrazoline (56) (3) and that it is a mixture of cis and trans isomers (C-3 and

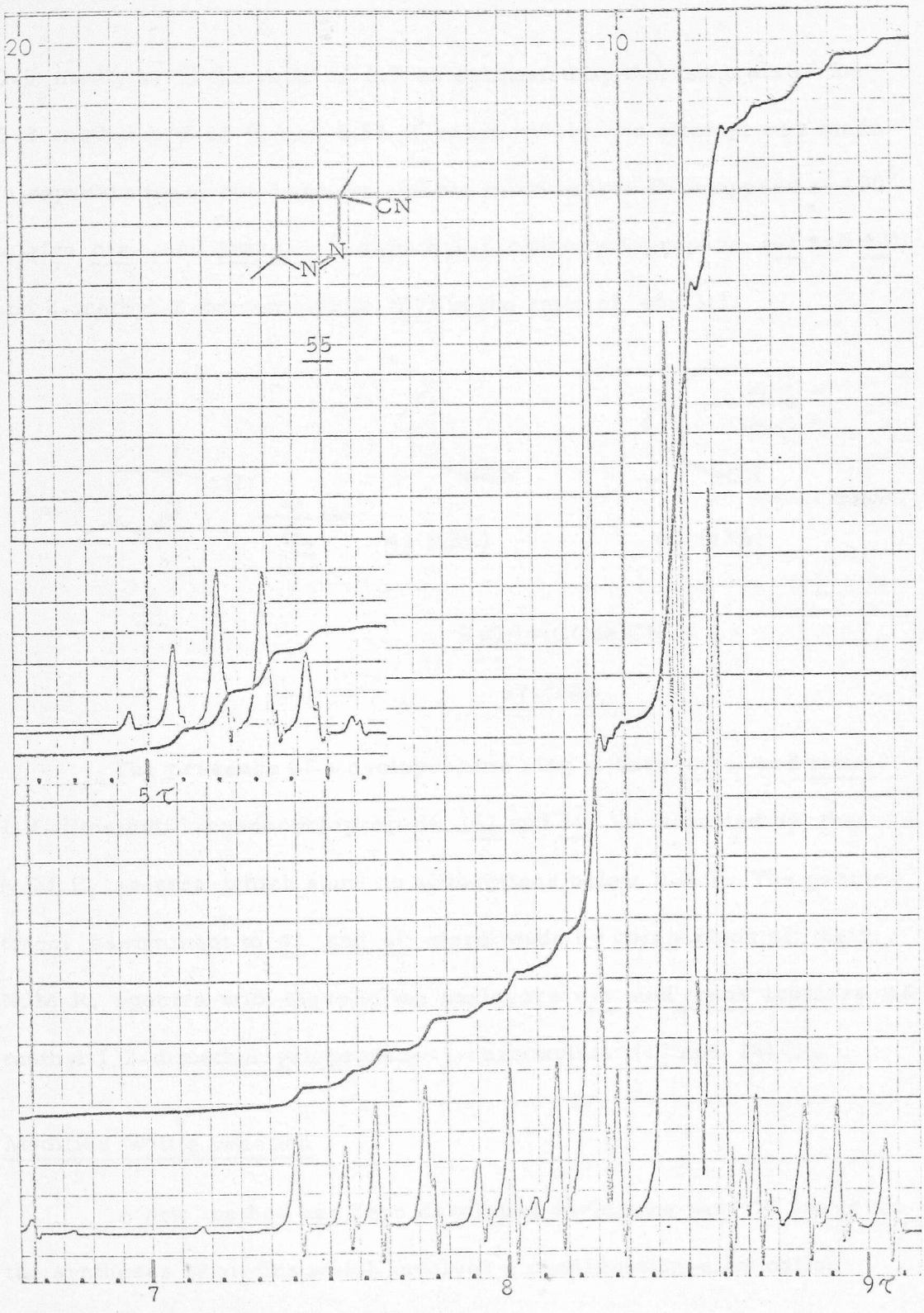
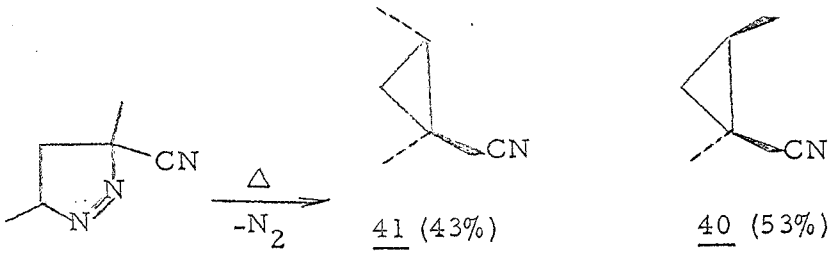


FIGURE I-N. M. R. spectrum of 3,5-dimethyl-3-cyano-Δ^1-pyrazoline (55)

C-5 methyls) in the ratio of 6:7 as estimated by the integrals of the C-3 methyl at 8.21 τ and 8.51 τ respectively. No attempt was made to separate these two isomers and the mixture was decomposed at 100° to give cis- and trans-1,2-dimethyl-1-cyanocyclopropane (41 and 40) and 2-methyl-2-pentenonitrile (57) in the ratio of 44:53:3.



55

41 (43%)

40 (53%)

EtCH=C(Me)CN

57 (3%)

The presence of a cyclopropane ring in both cis- and trans-1,2-dimethyl-1-cyanocyclopropane (41 and 40) is indicated by their N.M.R. spectra which show no absorptions below 8.0 τ. The geometrical assignment to 41 and 40 were made by comparison of their N.M.R. spectra with those of the analogous cis and trans isomers of methyl 1,2-dimethylcyclopropane-1-carboxylate (17 and 18) (3).

Modified Wittig reaction

A new method has been developed during the past 15 years for the syntheses of olefins which involves a condensation-elimination between a phosphonium ylid (58) and an aldehyde or ketone to form an olefin and a phosphine oxide. This reaction has been named the Wittig

$$R_3P{=}CR'_2 + R''_2CO \longrightarrow R'_2C{=}CR''_2 + R_3PO$$

58

reaction (50-62) after Professor G. Wittig for his observation that methylene triphenyl phosphorane reacted with benzophenone to give diphenyl ethylene (59) and triphenyl phosphine oxide, and his subsequent contributions to this olefin synthesis (51;52). Recently, a modified

$$\phi_3P{=}CH_2 + \phi_2CO \xrightarrow{\text{ether}} \phi_2C{=}CH_2 + \phi_3PO$$

59

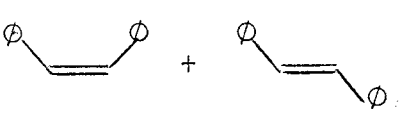
Wittig reaction has been developed in which a carbonyl compound is reacted with a phosphinoxy carbanion (60, Z = R)(63-65) or a phosphonate carbanion (61, Z = OR)(40) instead of a phosphonium ylid to afford an olefin.

$$Z_2\overset{O}{\overset{\|}{P}}\text{-}\bar{C}R_2 + R'_2CO \longrightarrow R_2C{=}CR'_2 + Z_2\overset{O}{\overset{\|}{P}}\text{-}\bar{O}$$

60 (Z = R)
61 (Z = OR)

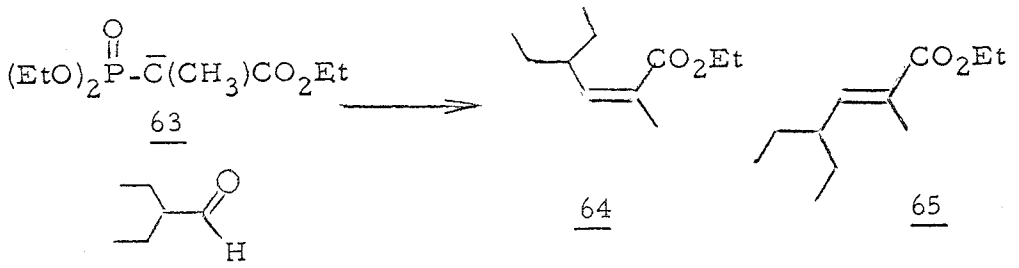
The reaction of phosphorous ylids with carbonyl compounds can give rise to cis and trans olefins and usually the trans olefins predominate. The first observation of this possibility was the formation of stilbenes from the reaction of benzylidene triphenyl phosphorane (62) and benzaldehyde which gave a cis:trans ratio of 3:7 (51). Occasionally,

$$\phi_3P{=}CH\phi + \phi CHO \longrightarrow$$



62

the cis isomers predominate (67-69), e.g., the reaction of triethyl α-phosphonopropionate carbanion (63) and α-ethylbutyraldehyde gave ethyl cis- and trans-2-methyl-4-ethyl-2-hexenoate (64 and 65) in the ratio of 75:25 (69). In general, the olefin formation by the Wittig reaction



or its modified reaction is intrinsically a stereo-nonselective reaction. There are various factors such as the structure of the reactants, the effects of the salts present, nature of solvent, temperature of reaction and the solubility of the ylid and reaction intermediate, which could affect the steric course of the reaction and thus the ratio of cis and trans olefins. These factors will not be discussed here since they have been reviewed recently (60-62,70) and they are out of the scope of this thesis.

Recently Kinstle (69) prepared a series of α,β-unsaturated esters by the reaction of aldehydes with phosphonate carbanions and the results showed predominantly the cis isomers. This led us to apply this modified Wittig reaction to synthesize a series of methyl 2-pentenoates (listed in Table II, p. 14) that are required for the present research. The results (Table III) differ from that of Kinstle (69) in two aspects, firstly, the olefins obtained under similar reaction con-

TABLE III

Product compositions for the modified Wittig reaction

$$(RO)_2\overset{O}{\overset{\|}{P}}\underset{66}{CR'CO_2Me} + R''CHO \longrightarrow R''CH=CR'CO_2Me$$

R'	R''	R	α,β-unsaturated esters	
			cis	trans
CH_3	i-C_3H_7	C_2H_5	72	28
CH_3	i-C_3H_7	CH_3	70	30 *
H	i-C_3H_7	C_2H_5	4	96
H	i-C_3H_7	CH_3	31	69
CH_3	C_2H_5	C_2H_5	13	87
CH_3	C_2H_5	CH_3	38	62
H	C_2H_5	C_2H_5	4	96

* Kinstle's result, see ref. 69.

ditions to those used by Kinstle were predominantly trans isomers except for methyl 2,4-dimethyl-2-pentenoate in which case the cis isomer (42) predominanted. Secondly, when dimethyl phosphonate (66, R = Me) was used instead of diethylphosphonate anion (66, R = Et), the yield of cis olefins increased greatly. For example, the yield of methyl cis-4-methyl-2-pentenoate (44) increased from 4% to 31%. Further study of this reaction might find an interesting relation between the structure of the phosphonate and the stereochemistry of the product.

II-2 THERMAL REARRANGEMENT OF CYCLOPROPANES

Thermal rearrangement of cyclopropanes and identification of products

A series of cyclopropanes with a C-1 carbomethoxy, acetyl or cyano group and a C-2 alkyl group had been prepared as described earlier and are listed in Table I (p.14). Some of these are geometrical isomers having the C-2 alkyl group and the C-1 functional group in either the *cis* or *trans* relationship. All of these cyclopropanes were subjected to thermal rearrangement reaction conditions at temperatures ranging from 240° to 300°. A half gram sample of the cyclopropanes in a standard N. M. R. sample tube was sealed at a pressure of 1 mm. Hg. or less and heated in a tube furnace at the desired temperature. The thermal rearrangement reactions were followed by N. M. R. analyses to observe any changes as they occurred. The product mixture was then analysed by vapor phase chromatography and the components separated and identified as discussed later.

Two facts were observed from the thermal rearrangement reactions of the cyclopropanes, The first is that cyclopropanes with a C-2 alkyl group *cis* to the C-1 carbonyl group rearranged to γ,δ-unsaturated esters or ketones exclusively whereas their corresponding *trans* isomers remained unchanged under identical reaction conditions. The second is that if the C-1 carbonyl group in the cyclopropanes was replaced by a cyano group, no change was observed to the molecule even where it was *cis* to the C-2 alkyl group.

The γ,δ-unsaturated esters and ketone obtained from the thermal rearrangement of cyclopropanes (Figure 2) have been identified and their physical data determined. The identifications are based on elemental micro-analyses and spectroscopic analyses (N. M. R. and I. R.). The latter will be discussed as follows.

Thermal rearrangement of methyl 1, 2, 2-trimethylcyclopropane-1-carboxylate (32) at 280° for 10 hours yielded methyl 2, 4-dimethyl-4-pentenoate (67) with less than 2% 32 remaining. The N. M. R. spectrum of 67 shows two singlets at 8.31 τ and 6.41 τ due to the methyl on C-4 and the ester methyl respectively. The C-2 methyl showed a doublet at 8.91 τ ($J \simeq 6.5$ c.p.s.) since it was split by the hydrogen on C-2 which appeared, together with the C-2 methylene hydrogens, as a set of multiplets at the region 7.20 τ to 8.10 τ. The terminal methylene hydrogens showed a broad singlet at 5.31 τ.

Two γ,δ-unsaturated esters together with trace amount of methyl trans-1-methyl-2-ethylcyclopropane-1-carboxylate (33) (methyl and ethyl groups trans) were obtained when 33 was heated at 280° for 18 hours. They are methyl cis- and trans-2-methyl-4-hexenoate (68 and 69). Vapor phase chromatographic analysis shows that 68 and 69 were formed in the ratio of 1:4.7. Their N. M. R. spectra (60 Mc and 100 Mc) show the skeletal structure of methyl 2-methyl-4-hexenoate but cannot determine their cis-trans geometry due to the similarity and complexity of the multiplets for the vinyl hydrogens (Table IV). However, the geometry

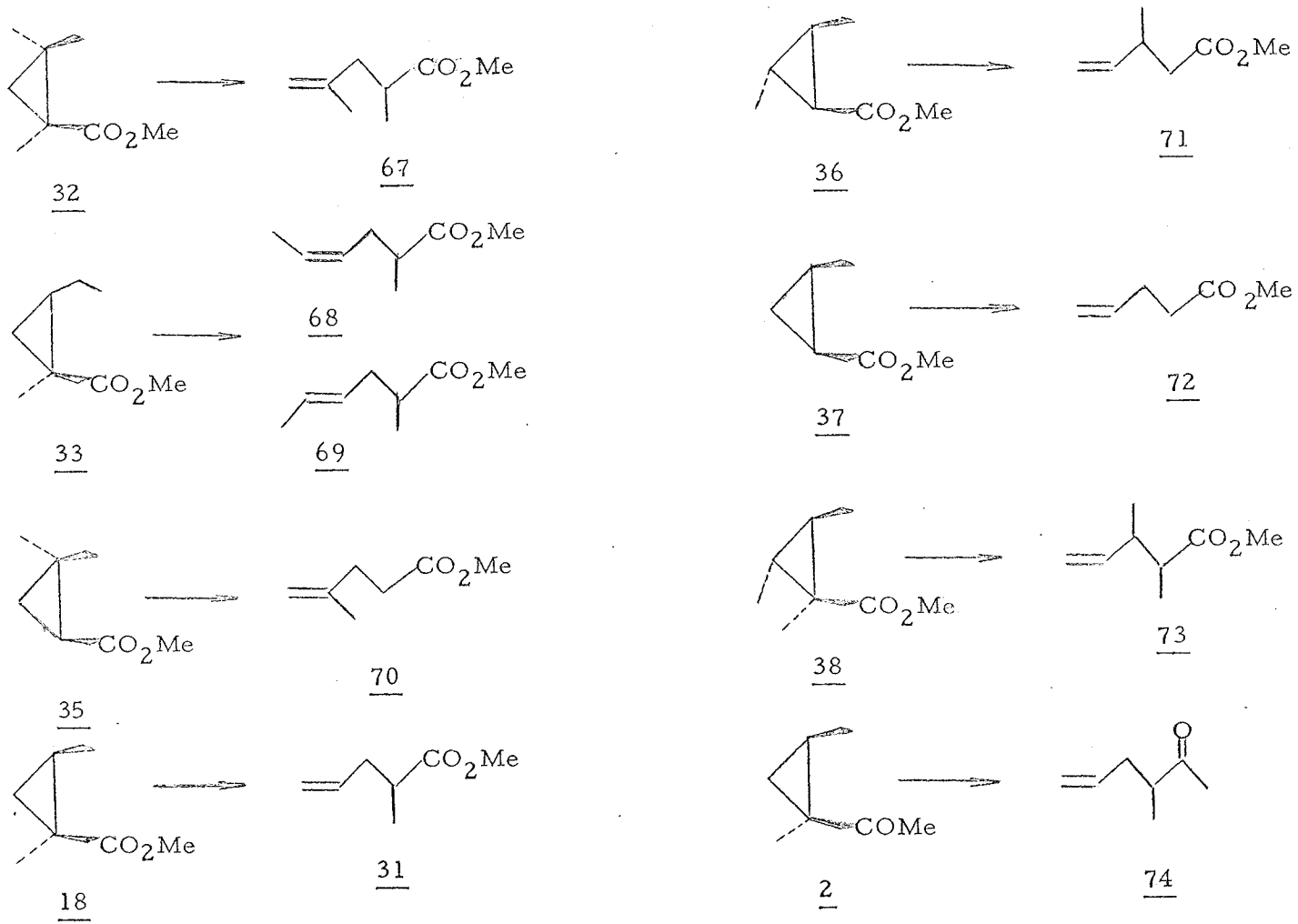


FIGURE 2 -- Products of the thermal rearrangement of cis-2-alkylcyclopropanes

TABLE IV

N. M. R. data of methyl cis- and trans-2-methyl-4-hexenoate (68 and 69)

	cis (68)	trans (69)
ester methyl	6.40 τ, singlet	6.41 τ, singlet
C-2 methyl	8.88 τ, doublet $J \simeq 6.3$ c.p.s.	8.96 τ, doublet $J \simeq 6.5$ c.p.s.
vinyl methyl	8.39 τ, doublet $J \simeq 5.7$ c.p.s.	8.36 τ, doublet $J \simeq 4.7$ c.p.s.
C-2 and C-3 hydrogens	7.35 - 8.05 τ multiplet	7.50 - 8.10 τ multiplet
vinyl hydrogens	4.25 - 4.95 τ multiplet	4.50 - 5.00 τ multiplet

of 68 and 69 can be distinguished by I. R. analyses on the basis that the trans isomer (69) showed a C-H out-of- plane bending band at 973 cm^{-1} (29). Furthermore, a consideration of the stereochemistry of the thermal rearrangement reaction indicates that the trans isomer would be formed predominantly (this will be discussed later).

Methyl 2, 2-dimethylcyclopropane-1-carboxylate (35) rearranged on heating at 258° for 50 hours (95% completed) to methyl 4-methyl-4-pentenoate (70) which was readily identified by its N. M. R. spectrum. It shows four peaks, all singlets, at 8.25 τ, 7.64 τ, 6.35 τ and 5.26 τ with integrals corresponding to 3, 4, 3 and 2 hydrogens respectively. The peaks at 8.25 τ and 6.35 τ are due to the vinyl methyl and ester methyl respectively. The low field singlet at 5.26 τ is due to the terminal methylene hydrogens. The C-2 and C-3 methylene hydrogens showed

a singlet at 7.64 τ which indicates that these hydrogens are equivalent.

Methyl 2-methyl-4-pentenoate (31) was obtained in 99% yield when methyl trans-1, 2-dimethylcyclopropane-1-carboxylate (18) was heated at 300° for 18 hours. Its N. M. R. spectrum shows a singlet at 6.49 τ due to the ester methyl. The C-2 methyl showed a doublet at 8.97 τ ($J \simeq 6.5$ c.p.s.) as it was split by the C-2 methine hydrogen which appeared with the C-3 methylene hydrogens as a set of multiplets in the region of 7.35 τ to 8.10 τ. The terminal methylene hydrogens showed two sets of multiplets centred at 5.05 τ and 5.26 τ whereas the C-4 vinyl hydrogen showed another multiplet at 4.15 τ to 4.85 τ.

Methyl trans-2, 3-dimethylcyclopropane-1-carboxylate (36) rearranged thermally to methyl 3-methyl-4-pentenoate (71). After heating 36 at 258° for 50 hours, the reaction mixture contained 10% of unchanged 36 and 90% of 71. The N. M. R. spectrum of 71 shows a singlet at 6.41 τ due to the ester methyl, a doublet at 8.79 τ ($J \simeq 6.3$ c.p.s.) due to the C-3 methyl which was split by the C-3 methine hydrogen at 7.35 τ (complex multiplet). The two non-equivalent C-2 methylene hydrogens were both split by the C-3 methine hydrogen into doublets at 7.79 τ ($J \simeq 8.6$ c.p.s.) and 7.76 τ ($J \simeq 5.8$ c.p.s.), the lower field line of each doublet coincide and thus a total of three lines resulted. There were also three sets of multiplets centred at 5.18 τ, 4.95 τ and 4.22 τ due to the two terminal methylene hydrogens and the C-4 vinyl hydrogen respectively.

Methyl 4-pentenoate (72) was obtained from the thermal rearrangement of methyl cis-2-methylcyclopropane-1-carboxylate (37). Its N. M. R. spectrum shows three singlets at 7.67 τ, 7.62 τ and 6.45 τ attributed to the C-2 methylene hydrogens, the C-3 methylene hydrogens and the ester methyl. The two terminal hydrogens showed two sets of multiplets at 5.08 τ and 4.84 τ whereas the vinyl hydrogen at C-4 showed a multiplet at 4.09 τ.

Methyl cis,trans-1, 2, 3-trimethylcyclopropane-1-carboxylate (38) rearranged thermally to methyl 2, 3-dimethyl-4-pentenoate (73). The reaction mixture contained 95% of 73 and 5% of 38 after 12 hours at 280°. Its N. M. R. spectrum shows a singlet at 6.38 τ due to the ester methyl. The C-2 and C-3 methine hydrogens showed a multiplet centred at 7.64 τ. The C-2 methyl which was split by the C-2 hydrogen showed a doublet at 9.01 τ ($J \simeq 6.6$ c.p.s.) and the C-3 methyl which was split by the C-3 hydrogen also showed a doublet at 8.94 τ ($J \simeq 6.7$ c.p.s.). Three sets of multiplets at $\left\{\begin{matrix} 5.14\ \tau, \\ 4.92\ \tau \end{matrix}\right.$ and 4.31 τ were assigned to the two terminal hydrogens and the C-4 vinyl hydrogens respectively.

3-Methyl-5-hexen-2-one (74) was obtained from the thermal rearrangement of trans-1, 2-dimethyl-1-acetylcyclopropane (2). The structure of 74 had been reported earlier (5).

Kinetic studies

The rates of thermal rearrangement of the cyclopropanes to their corresponding γ,δ-unsaturated compounds have been studied. The general method of rate determination was to prepare a number of samples sealed in 4 mm x120 mm tubes. These were placed in the furnace and came to thermal equilibrium in less than 15 minutes. The temperature of the furnace was maintained to $\pm 0.5^{\circ}C$. Samples were removed at varying intervals cooled and analysed by V. P. C. for the γ,δ-unsaturated product in relation to the unreacted cyclopropane compound. There was no evidence for polymerization or decomposition of the reactants or products and thus the mole fraction as determined by integration of the peak areas could be used in the rate equation. The accuracy of these measurements depends on the accuracy of the integration (disc integration was used) and the relative response by the detector to the isomeric samples. These results gave excellent first order kinetics with no induction period. The rate expression used was the following,

$$k = \frac{2.303}{t} \log \frac{a_o}{a_o - x}$$

where a_o is the initial mole fraction of the starting cyclopropane, and x is the mole fraction of the γ,δ-unsaturated compound formed in time interval t. A plot of the quantity $\log (a_o/a_o - x)$ versus t will result in a straight line for a first-order reaction. The slope m of the line obtained multiplied by 2.303 will be equal to the rate constant k,

$$k = 2.303 \times m$$

The half-life $t_{1/2}$ of the reaction was calculated by the following equation (71),

$$t_{1/2} = \frac{2.303 \log 2}{k} = \frac{\log 2}{m}$$

The results of the kinetic studies are tabulated in Table V, and some typical first-order rate plots are shown in Figures 3, 4 and 5.

The heats of activation $\Delta H^{\ddagger}$ and the entropies of activation $\Delta S^{\ddagger}$ were calculated by the following formula (72),

$$k = \frac{k_B T}{h} e^{-\Delta H^{\ddagger}/RT} e^{\Delta S^{\ddagger}/R}$$

where k_B is the Boltzmann constant, and h is Planck's constant. The logarithm form of this equation is

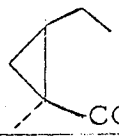
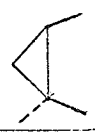
$$\log \frac{k}{T} = 10.319 - \frac{1}{T}\left(\frac{\Delta H^{\ddagger}}{4.574}\right) + \frac{\Delta S^{\ddagger}}{4.574}$$

and a plot of log (k/T) vs. 1/T gave a straight line whose slope multiplied by 4.574 gave $\Delta H^{\ddagger}$. Substituting this $\Delta H^{\ddagger}$ back to the above equation gave $\Delta S^{\ddagger}$. Some of these plots (log k/T vs. 1/T) are shown in Figures 6, 7 and 8.

A word should be said concerning the accuracy of the rate constants obtained. The errors of measurement of time, the mole fraction of the starting cyclopropane and of the γ,δ-unsaturated olefin

TABLE V

Kinetic results of the thermal rearrangement of cyclopropanes

Cyclopropane	run no.	temp. (°C)	$k \times 10^{-5}$ (sec^{-1})	$t_{1/2}$ (h)	$\Delta H^{\neq}$ [1] (kcal)	$\Delta S^{\neq}$ [1] eu
 32	46	240.4	2.21	8.72		
	29	252.0	5.35	3.60	37.5	- 7.8
CO_2Me	18	259.4	8.53	2.26		
 33	16	259.4	1.53	12.62*		
	44	272.2	3.25	5.93	33.9	- 18.1
CO_2Me	37	283.7	6.50	2.96		
 35	13	259.4	1.27	15.16		
	43	272.2	2.95	6.53	36.1	- 14.2
CO_2Me	38	283.7	5.92	3.25		
 18	17	259.4	1.18	16.30		
	45	272.2	2.41	8.00	30.2	- 25.4
CO_2Me	39	283.7	4.31	4.47		
 36	14	259.4	0.68	28.46		
	52	272.2	1.37	14.11	32.5	- 22.0
CO_2Me	48	283.7	2.68	7.19		
	40	297.4	5.46	3.53		
 37	19	259.4	0.61	31.39		
	20	272.2	1.45	13.24		
	47	283.7	2.98	6.46	35.9	- 16.0
CO_2Me	41	297.4	6.29	3.06		
 38	15	259.4	0.43	45.00		
	22	272.2	0.85	22.68		
	28	283.7	1.35	14.31	25.2	- 36.7
	49	283.7	1.26	15.33		
CO_2Me	42	297.4	2.23	8.65		

* For the formation of the trans olefin (69), the rate constant and the half-life were 1.26 and 15.31 respectively.

[1] The estimated maximum errors in $\Delta H^{\neq}$ and $\Delta S^{\neq}$ are ±10%.

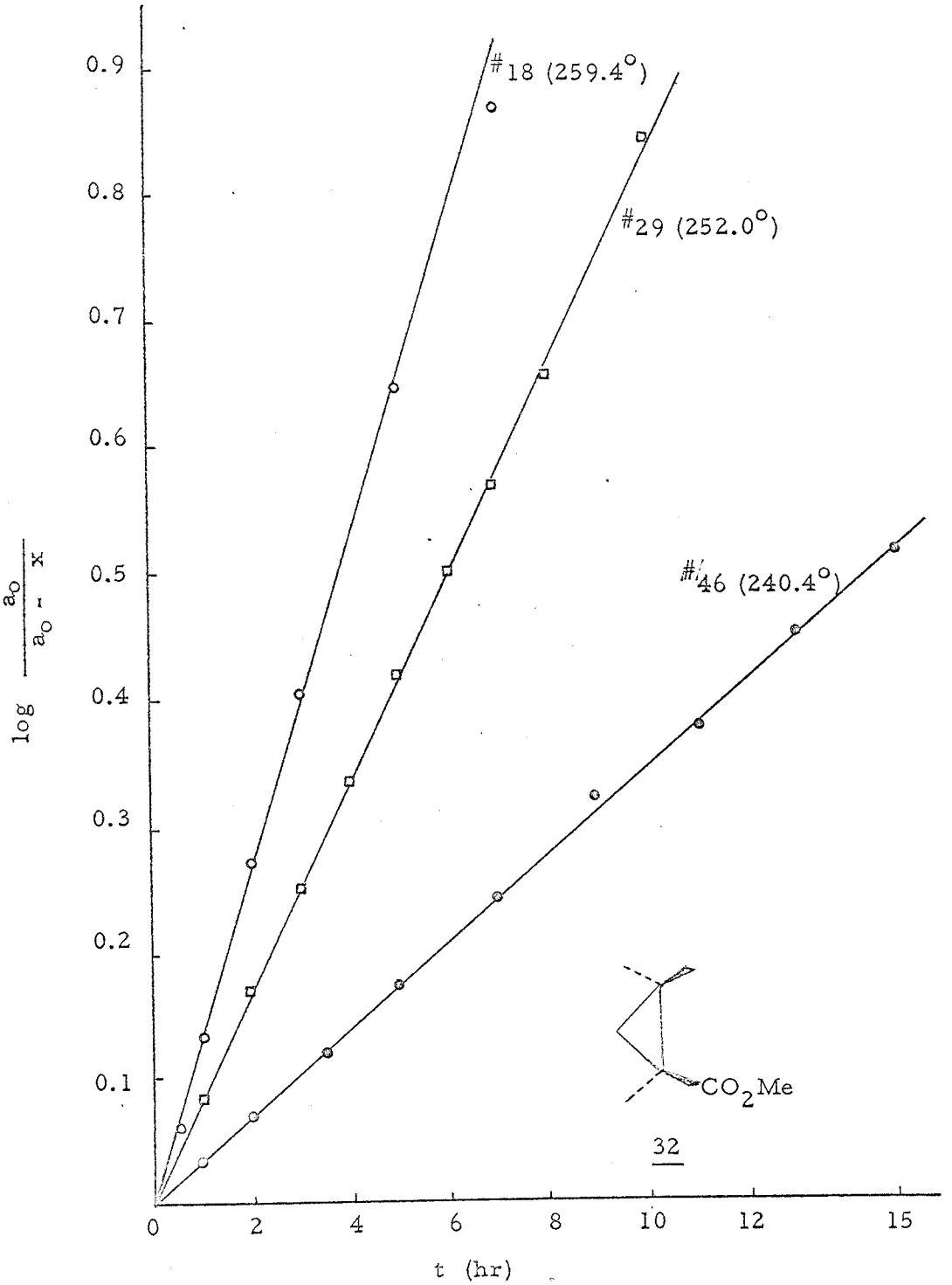


FIGURE 3 - First-order rate plots for the thermal rearrangement of 32

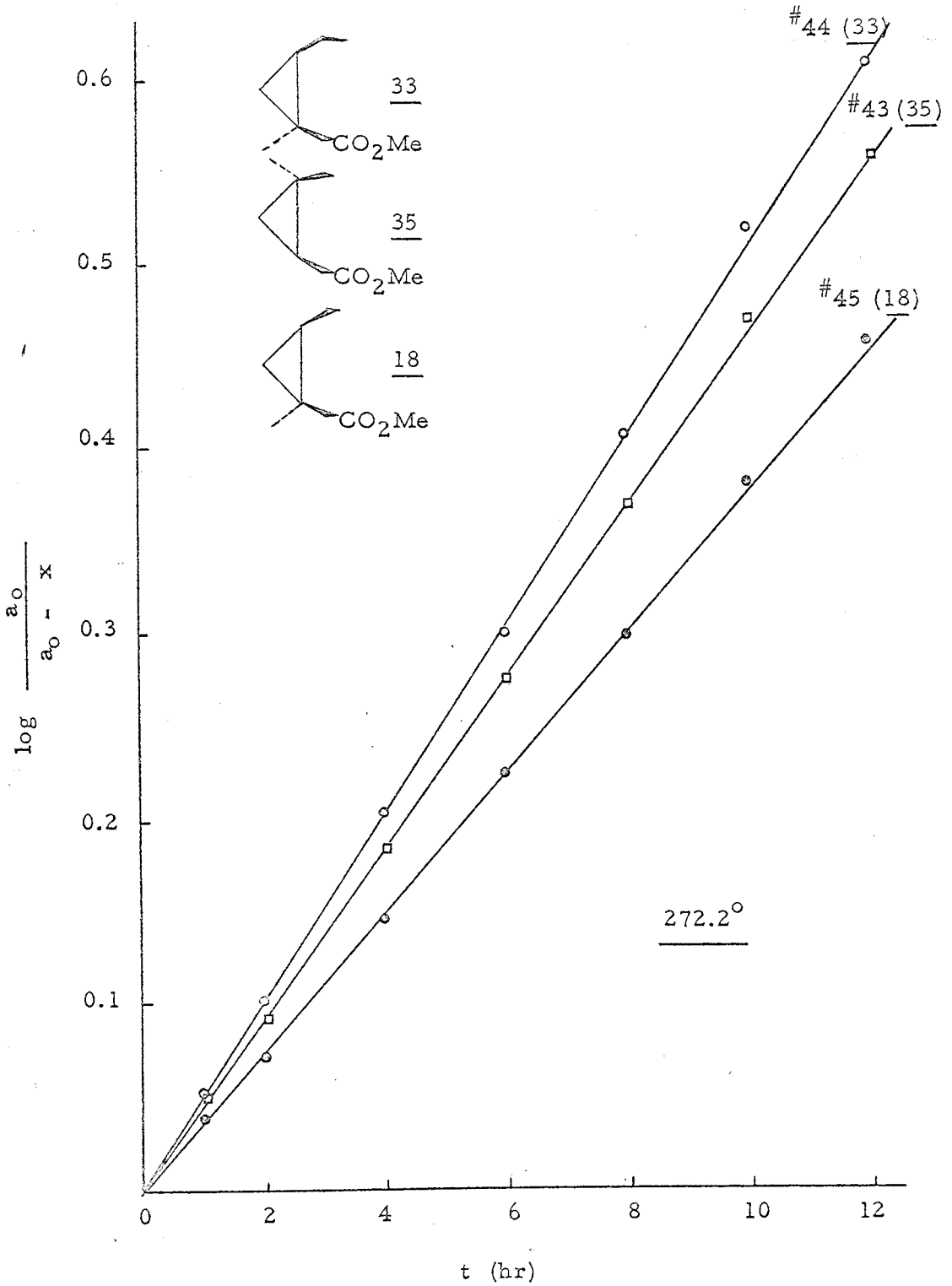


FIGURE 4 - First-order rate plots for the thermal rearrangement of 18, 33 and 35

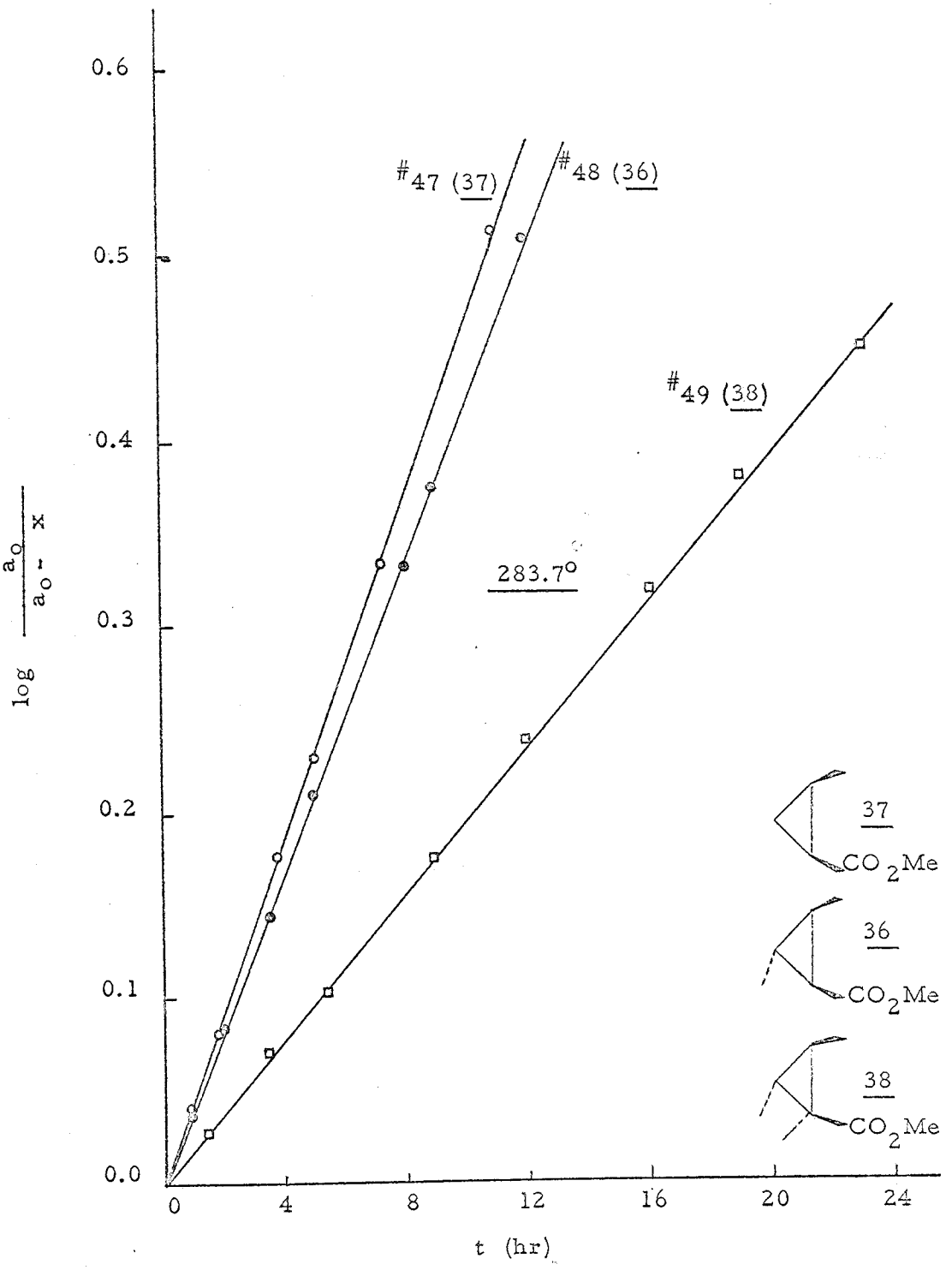


FIGURE 5 - First-order rate plots for the thermal rearrangement of 36, 37 and 38

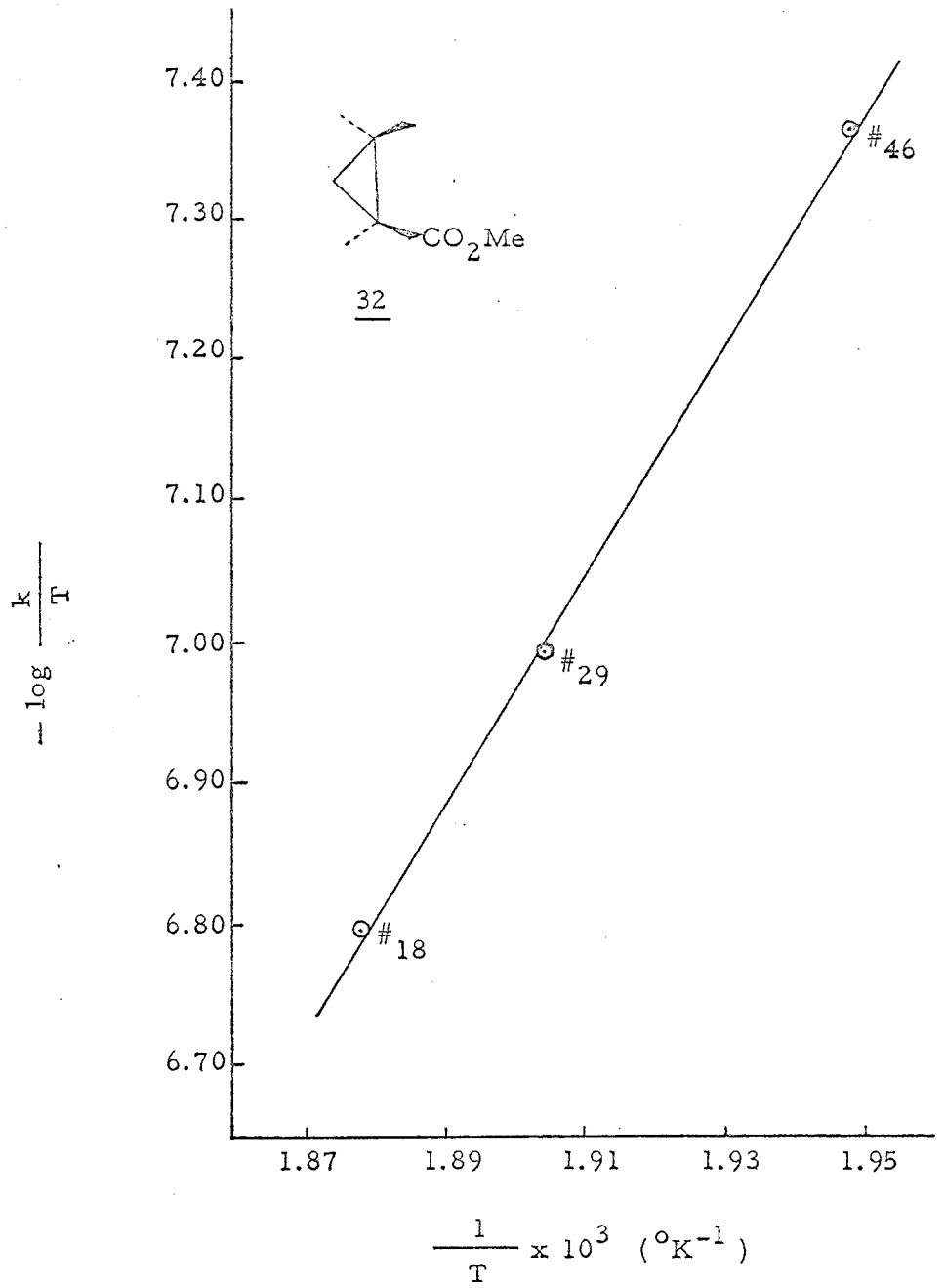


FIGURE 6 - Activation plot for the thermal rearrangement of 32

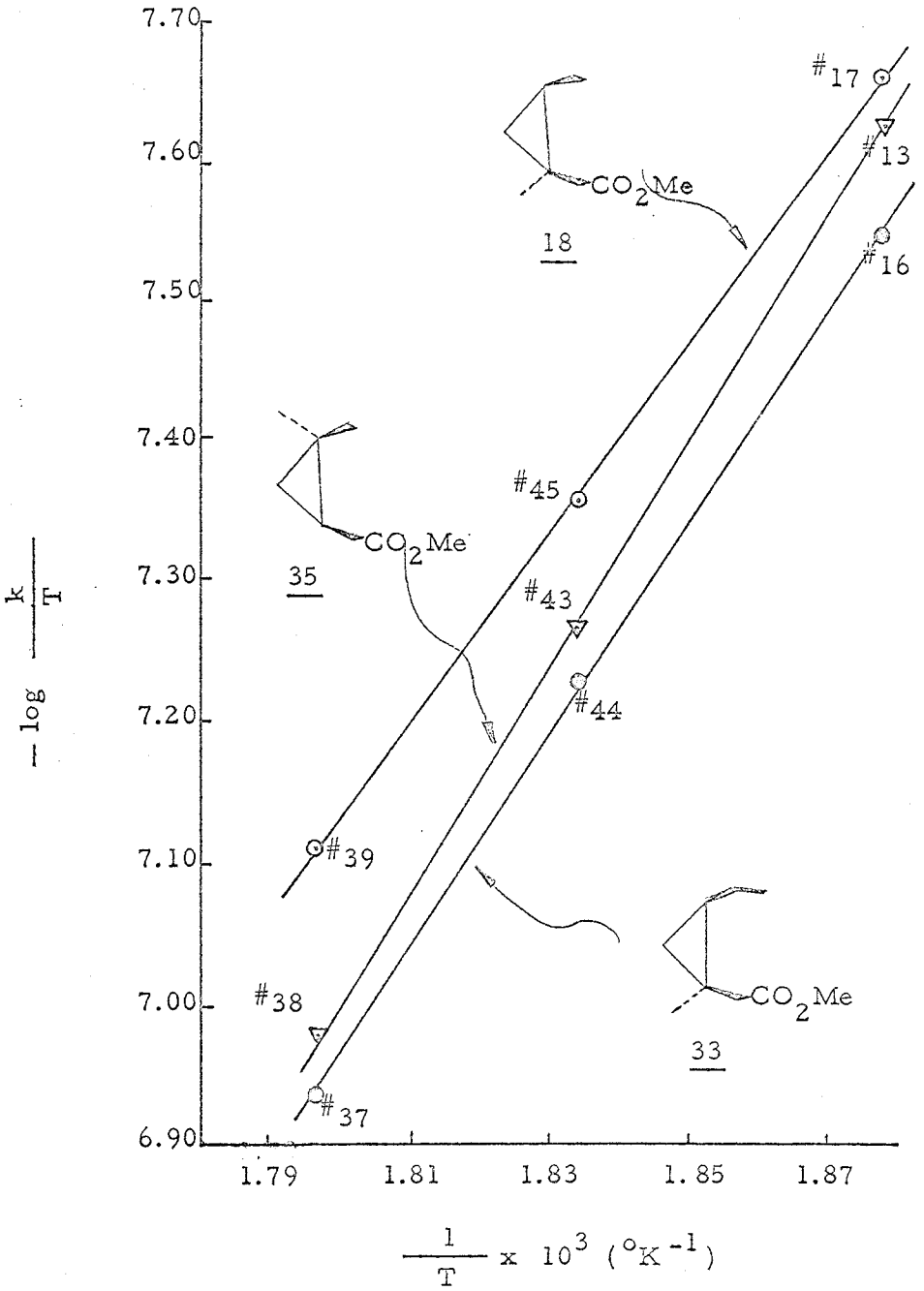


FIGURE 7 - Activation plots for the thermal rearrangement of 18, 33 and 35

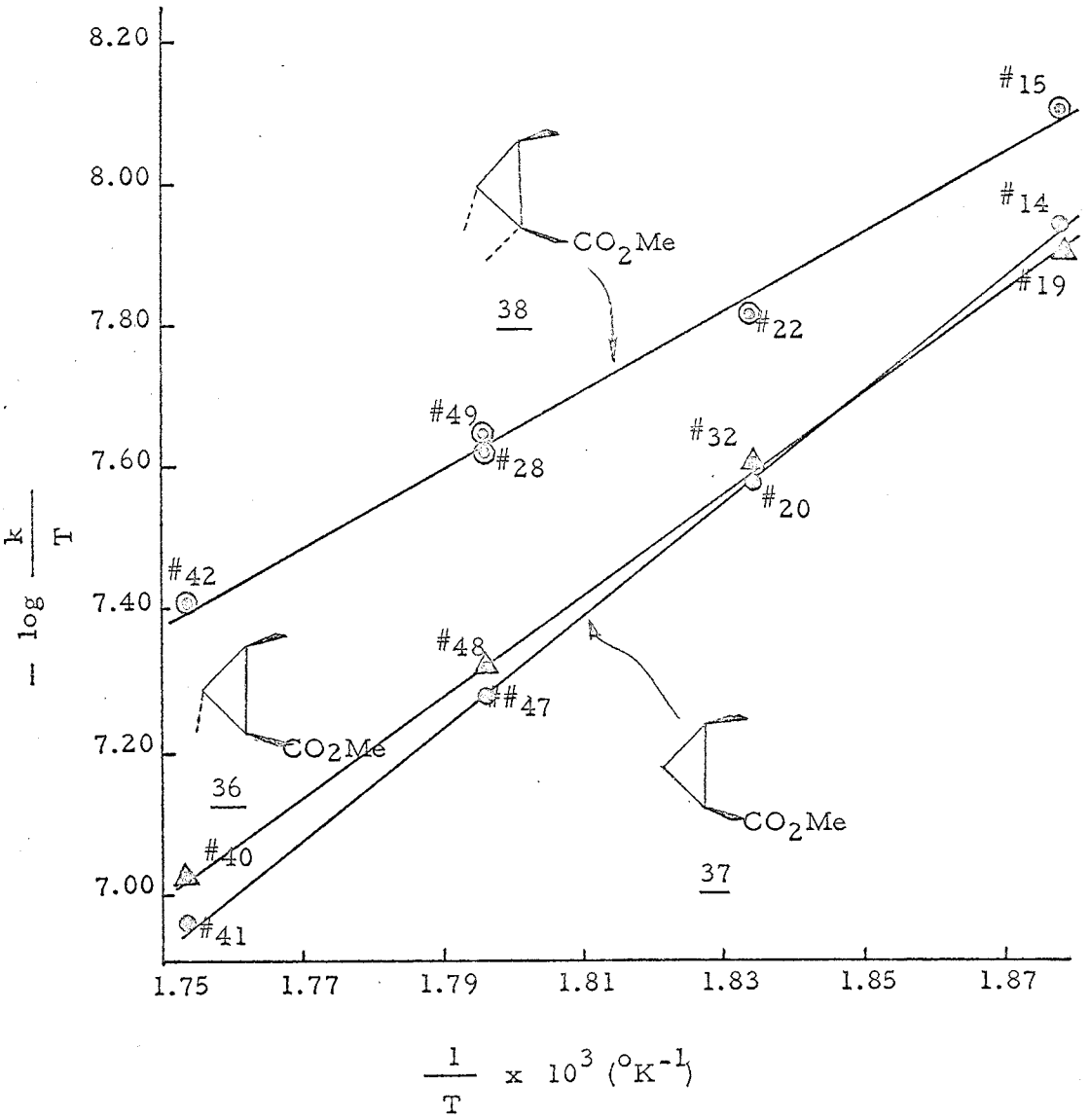
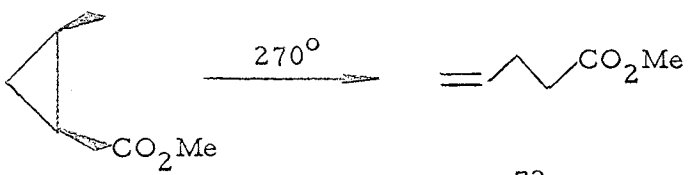


FIGURE 8 - Activation plots for the thermal rearrangement of 36, 37 and 38

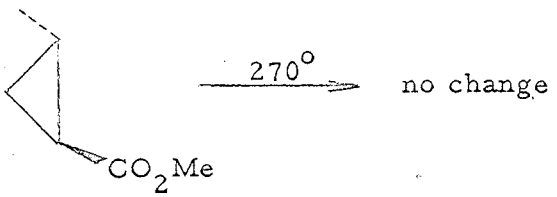
are very small ($< 1\%$). The biggest error is the temperature of the reaction. The temperature of the reaction furnace was kept to within $\pm 0.5^{\circ}$ or better. From the Arrhenius equation this temperature variation corresponds to an error of approximately $\pm 5\%$ in the rate constant (100).

Discussion of results

The results of the thermal rearrangement reactions on the series of 2-alkyl-1-cyano-, 1-acetyl- and 1-carbomethoxycyclopropanes show two significant facts. Firstly, all cis-2-alkyl-1-acetyl and 1-carbomethoxycyclopropanes rearranged exclusively to their corresponding γ,δ-unsaturated ketones and esters (Figure 2) in quantitative yield, whereas their trans isomers remained unchanged under identical reaction conditions. For example, methyl cis-2-methyl-1-cyclopropanecarboxylate (37) yielded methyl 4-pentenoate (72) when heated at 270° while the trans isomer (16) showed no sign of change. Secondly, when the C-1

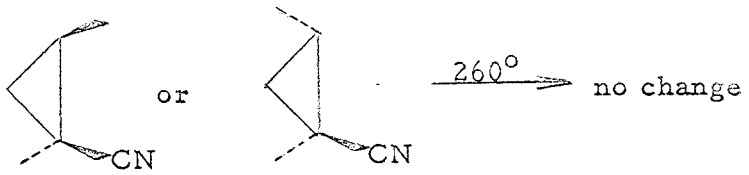


37 72



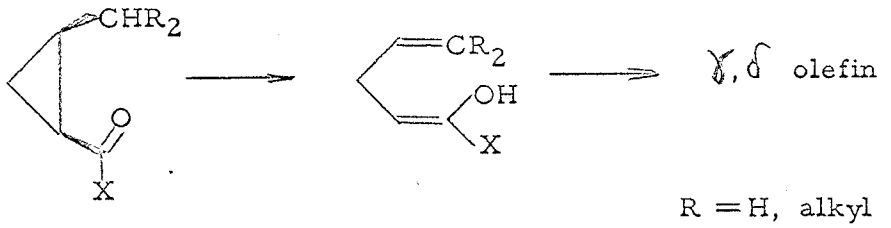
16

carbonyl group in the cyclopropane molecule was replaced by a cyano group, no observable change occurred even if it was cis to the C-2 alkyl group. Thus both cis- and trans-1,2-dimethyl-1-cyanocyclopropane (41 and 40) remained unchanged after being heated at 260° for 17 hours.



40 41

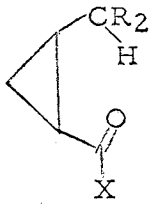
The mechanism for the thermal rearrangement of cis-2-alkyl-1-acetyl and 1-carbomethoxycyclopropanes to the γ,δ-unsaturated ketones and esters had been proposed by McGreer, et al. (34) to involve an allyic enol intermediate 76. The results of the present studies of the



75 76

thermal rearrangement reactions suggest that this intermediate arises via a six-membered cyclic transition state 77 by an intramolecular 1,5-hydrogen transfer of a hydrogen from the C-2 alkyl to the oxygen in the C-1 carbonyl concerted with opening of the cyclopropane ring at

C-1 and C-2. This is possible only if the C-2 alkyl and the C-1 carbonyl



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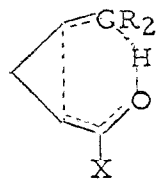

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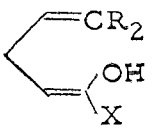
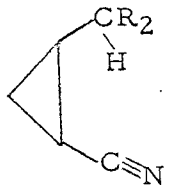


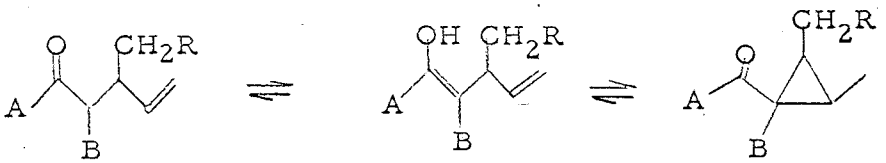
76

are cis to each other; whereas it would not be possible with the two groups in trans geometry. The cyclic transition state is also suggested by the fact that the nitriles do not react. The C–C≡N group is linear and not able to bring the nucleophilic nitrogen into close proximity to the hydrogen of the C-2 methyl.

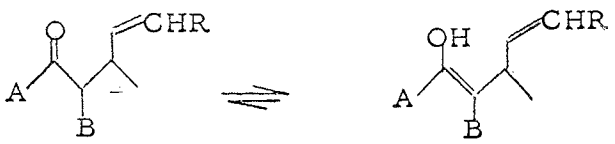


78

During the course of this research, Roberts, et al. (73-75) have reported a four-step reversible thermal isomerization of one homoallylic carbonyl compound 79 to another 83 via the allylic enols 80 and 82 and the cyclopropyl carbonyl compound 81. They also demonstrated the whole reversible sequence, 79 ⇌ 83, by deuterium tracer experiments and thus showed that reversible intramolecular hydrogen transfers are thermally induced between aliphatic allylic ends and the



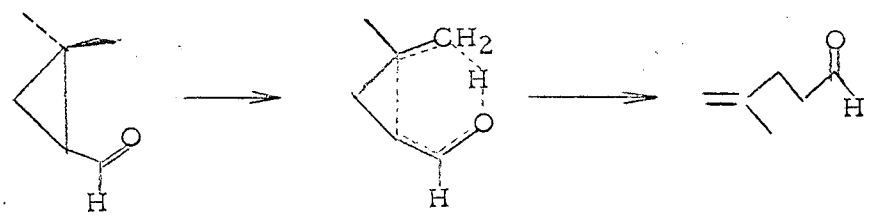
79 80 81



A = H, R, Ar, OR
B = H, R, AR, COR, COAr, CO_2R

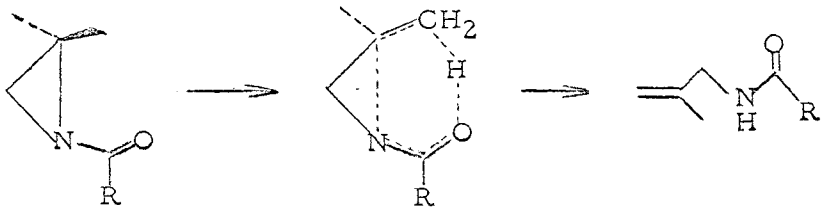
83 82

cyclopropyl carbonyl system. There are several other reactions that probably occur via similar intramolecular 1,5-hydrogen shifts that have been reported in the recent literature. The thermal rearrangement of 2,2-dimethylcyclopropanealdehyde (84) to 4-methyl-4-pentenal (86) has been reported by Ohloff (77) to occur via transition state 85. Fanta and



84 85 86

co-workers reported the transition state 88 for the thermal isomerization of acylaziridines (87) to give unsaturated amides (89) Another closely related reaction is the thermal rearrangement of cis-1-methyl-

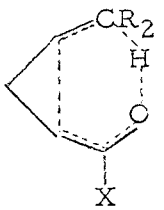


87 88 89

2-vinylcyclopropane (90) to cis-1,4-hexadiene (91) for which an intramolecular 1,5-hydrogen transfer has also been proposed (80). This differs from the others in that a carbon-carbon double bond is involved

90 91

in the hydrogen transfer instead of a carbon-oxygen double bond. The proposed transition states for these reactions are similar to the six-membered cyclic transition state 77 suggested earlier for the thermal rearrangement of cyclopropanes.



77

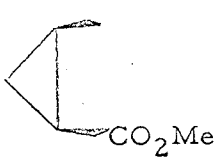
A cyclic transition state, such as 77, would have significantly less freedom of motion than the initial state. A reaction which involves such a cyclic transition state would be expected to show a very large negative entropy of activation (76). This is indeed the case for our kinetic studies of the thermal rearrangement reactions of cis-2-alkyl-cyclopropane-1-carboxylates (Table V) gave very large negative entropies of activation, e.g., -8 e.u. to -37 e.u. These values are in good agreement with those reported by Ellis and Frey (80) for the thermal rearrangement of 90 to 91 (~ -11.6 e.u.) where a cyclic transition state is proposed, and by Roberts et al. (75) for the thermal rearrangement of 2,2-dimethyl-1-acetylcyclopropane (95) to 5-methyl-5-hexen-2-one (96) (~ -10 e.u.) where an allylic enol intermediate is in-

95 96

dicated. Ellis and Frey also suggested that there is considerable contribution to the stabilization of the transition state by allylic delocalisation energy. This is indicated by the low activation energy, i.e., 31 kcal/mole, obtained for the reaction 90 → 91. In comparison, the activation energy for the thermal rearrangement of vinylcyclopropane to cyclopentene, where a cyclic transition state is probably not involved, was found to be about 50 kcal/mole (97). In the present work we have found heats of

activation for the thermal rearrangement of cis-2-alkylcyclopropane-1-carboxylates to be 25 to 38 kcal/mole as anticipated if the rearrangement proceeds via a cyclic transition state.

An additional observation is apparent from the kinetic studies of the thermal rearrangement of the cis-2-alkylcyclopropanes to their corresponding γ,δ-unsaturated olefins. The rates of rearrangement have been found to be affected by the number of substituents on the three ring carbon atoms. Since the bond breakage always occured on the C(1)-C(2) bond, hence, it is possible to explain the differences in rates of rearrangement in terms of steric effect upon the bond dissociation energy. It is known that the dissociation of the carbon-carbon single bond in ethane decreases with the addition of aliphatic as well as aryl substituents (95, 96). Suppose we consider the unsubstituted cyclopropane as a 1,2-disubstituted ethane, then the addition of substituents to the C-1 and C-2 of the cyclopropane would reduce the bond dissociation energy of the C(1)-C(2) bond and thus increase the rate of rearrangement. For example, the rate of thermal rearrangement increases in the order of 1,2-disubstituted (37), 1,1,2- and 1,2,2-trisubstituted (18, 33 and 35) and the 1,1,2,2-tetrasubstituted (32) cyclopropanes.



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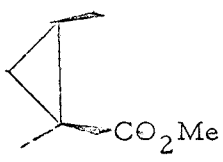

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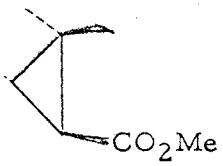

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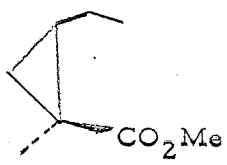

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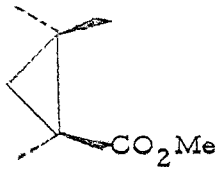
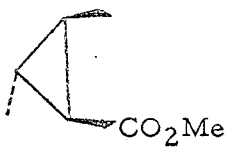


32

On the other hand, when substituent is then added to C-3, it is possible that the effect of substituents on C-1 and C-2 in reducing the bond strength is reduced due to bond weakening in the C(1)-C(3) and C(2)-C(3) bonds. This would account for the slower rates of thermal rearrangement for the 1, 2, 3-trisubstituted (36) and 1, 1, 2, 3-tetrasubstituted (38) cyclopropanes. Alternatively, the substituent on C-3 might affect the ease with which the carbonyl group on C-1 and the methyl group on C-2 approach the transition state geometry.



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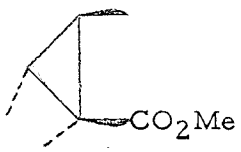
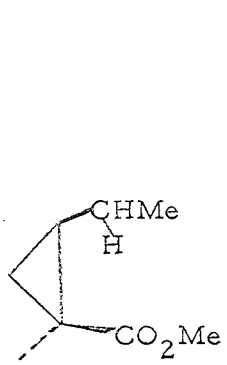


38

One of the cis-2-alkylcyclopropanes studied has a C-2 ethyl cis to the C-1 carbonyl, and this is methyl trans-1-methyl-2-ethylcyclopropane-1-carboxylate (33). There are two hydrogens which can transfer to the carbonyl oxygen to form two isomeric γ,δ-unsaturated olefins, namely, methyl cis-2-methyl-4-pentenoate (68) and methyl trans-2-methyl-4-pentenoate (69). However, they are not formed in equal amounts

but in the ratio of 1:4.7 in favor of 69. A consideration of Dreiding models of the transition states 92 and 93 shows that 93 is favored, since 92 requires eclipsing of the methyl group (on the C-2 ethyl) and the C-3 ring hydrogens whereas 93 does not.



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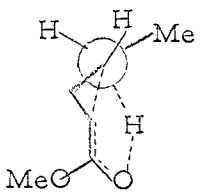

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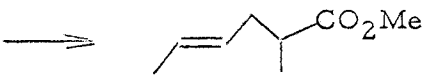

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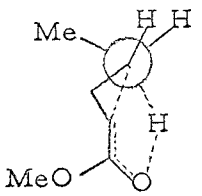

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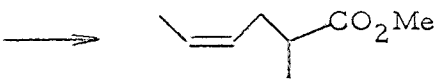

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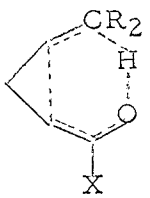
It is of interest to compare the rate of formation of the trans product (69) from 33 with that for the formation of 31 from 18. The



77

stereochemistry of 33 is quite similar to that of 18 except that the hydrogen for migration is secondary in the case of 33, and is primary in the case of 18. The rate of formation of 69 ($t_{1/2}$ at 259.4° is 15.31 hrs.)

is about three times faster than the rate of formation of 31 ($t_{1/2}$ at 259.4° is 48.9 hrs. per hydrogen*). Thus a faster rate of reaction is obtained for migration of a secondary hydrogen than a primary hydrogen as would be expected if bond breaking of the C-H bond were important in the transition state, such as 77, as proposed.

To sum up, a series of 2-alkylcyclopropanes have been prepared. Those with a C-1 carbonyl group cis to a C-2 alkyl group were found to rearrange to their corresponding γ,δ-unsaturated olefins when heated at temperatures ranging from 240° to 300°. All others were found thermally stable. The thermal rearrangement reactions were clearly unimolecular. These results suggest that the rearrangement reactions proceed by an intramolecular 1,5-hydrogen transfer via a six-membered transition state 77. This is supported by the large negative entropies of activation and low heats of activation obtained from the kinetic studies.

By way of conclusion, this thermal rearrangement reaction of a cis-2-alkylcyclopropane to a γ,δ-unsaturated olefin should be of value in solving the stereochemistry of isomeric cyclopropanes. In contrast to those methods described in the introduction section of this thesis, the above method does not require the presence of both isomers. McGreer et al., has employed this method successfully in distinguishing the stereochemistry of a number of cyclopropanes. One example is that the

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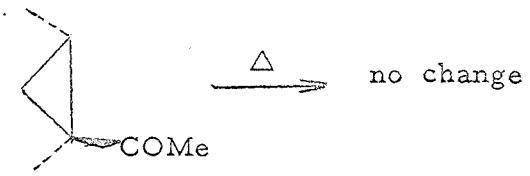
* Corrected for the statistically faster rate due to the three available hydrogens.

stereochemical assignment to cis- and trans-1,2-dimethyl-1-acetyl-cyclopropane (1 and 2) is made on the basis that 2 rearranges thermally to 3-methyl-5-hexen-2-one (74) whereas 1 does not (5). Similarly,

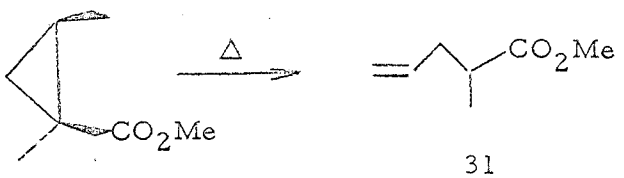
74

2



1

the structure of methyl trans-1,2-dimethylcyclopropane-1-carboxylate (18) is confirmed by the fact that it rearranges thermally to give methyl 2-methyl-4-hexenoate (31) (34).



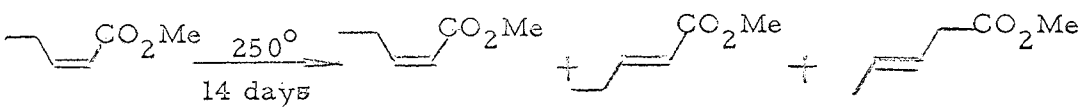
31

18

II-3 THERMAL ISOMERIZATION OF OLEFINS

Thermal isomerization of olefins and identification of products

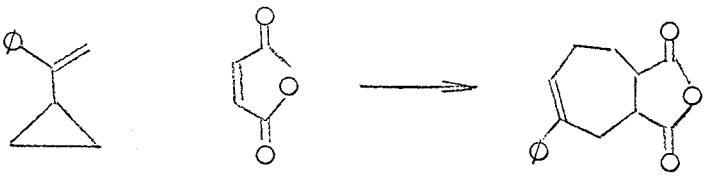
The isomerization of unsaturated acids, esters, ketones and nitriles to yield equilibrium mixtures has been studied under a variety of conditions. Rinehart et al. (69, 81) have used sodium glycolate in ethylene glycol as catalyst, and Linstead et al. (98) simply heated the acids in "pure" state at their boiling points. This isomerization is also possible thermally at temperatures near 300° with or without iodine catalyst, and yields a mixture of α,β- and β,γ-unsaturated esters. McGreer et al. (2) reported the thermal isomerization of methyl cis-2-pentenoate (48) in a sealed tube at 250° for two weeks to give a mixture consisting of 7% of 48, 48% of methyl trans-2-pentenoate (49) and 45% of methyl trans-3-pentenoate (94). Having demonstrated a six-membered cyclic



48 48 (7%) 49 (48%) 94 (45%)

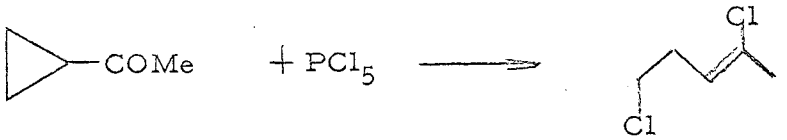
transition state for the intramolecular 1,5-hydrogen transfer in the thermal rearrangement of the cyclopropane series, we now wished to test whether the formation of β,γ products might be a result of a similar cyclic hydrogen transfer possible from the cis α,β-unsaturated ester but not from the trans. There is some precedent for there are many reactions which have analogies in the cyclopropane and olefin series where

the cyclopropane ring is placed in a position equivalent to the double bons, Sarel and Breuer (82) showed that α-cyclopropylstyrene (97) undergoes Diels Alder reaction with maleic anhydride to give 4-phenylcyclohept-4-ene-1,2-dicarboxylic anhydride (98). This is an illustration of



97 98

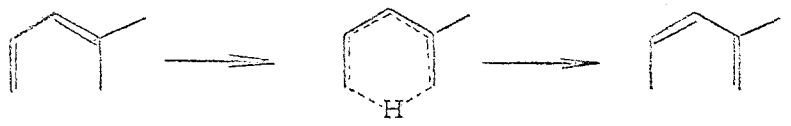
the type of behavior which suggests that cyclopropanes have some similarity to double bond in their chemistry. Similarly, the reaction of acetylcyclopropane (99) and phosphorous pentachloride to yield 2,5-dichloro-2-pentene (100) in dicates that the cyclopropane ring acts like a



99 100

double bond in a straight chain compound so that a normal dichloride is initially formed which then rearranges to give 100 (83).

A closely related isomerization reaction is the thermal interconversion of cis-4-methyl-1,3-pentadiene (104) to cis-2-methyl-1,3-pentadiene (106) (99). The reaction involves the overall 1,5-hydrogen transfer with concomitant migration of both carbon-carbon double bonds via a six-membered cyclic transition state, 105. This shows that 1,5-



104 105 106

hydrogen transfer is possible in analogous compounds such as α,β-unsaturated esters provided that they have the correct geometry. Butler et al. (94) in a study of the thermal isomerization of methyl cis-crotonate to methyl trans-crotonate has already noted no evidence that the small amout of β,γ isomer formed was formed preferentially from the cis than the trans. This system is not however ideal due to the low equilibrium value of the β,γ isomer and studies were therefore directed towards the esters with ethyl and isopropyl groups on the β-carbon which at equilibria give more of the β,γ isomer (2, 69, 81).

From the previous study four isomeric pairs of α,β-unsaturated esters were available as has been described earlier and these are listed in Table II (p. 14). These esters were isomerized thermally at temperatures ranging from 240° to 300°. Results show that after each of these α,β-unsaturated esters was isomerized, the product mixture usually consisted of, the initial ester, its geometric isomer and the corresponding β,γ isomer. These β,γ-unsaturated esters were prepared and isolated from the thermal isomerization of their cis isomers. (Figure 9). They were characterized by elemental microanalyses and spectral (N. M. R. and I. R.) analyses and the latter are discussed below.

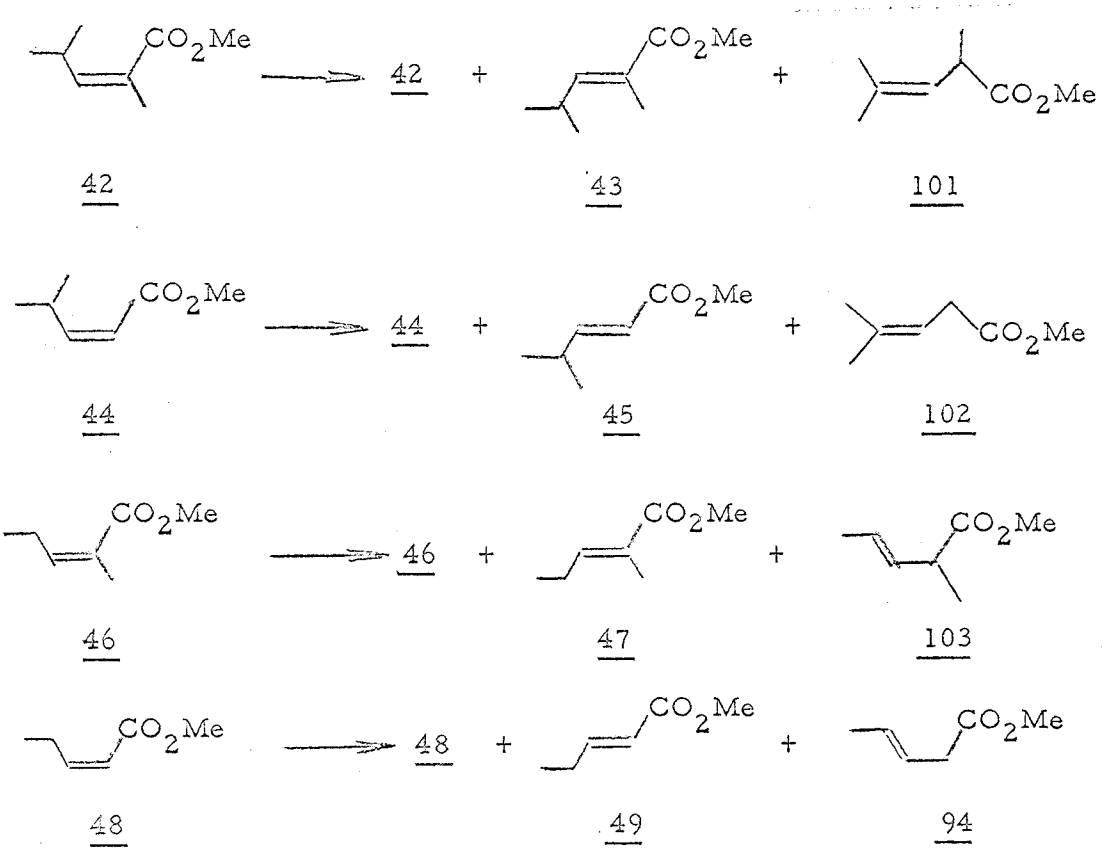


FIGURE 9 -- Products from the thermal isomerization of cis-2-pentenoates

Methyl 2, 4-dimethyl-3-pentenoate (101) was characterized by its N. M. R. spectrum. It shows a singlet at 6.38 τ due to the ester methyl, a doublet at 8.84 τ ($J \simeq 7.1$ c.p.s.) due to the C-2 methyl which being split by the C-2 methine hydrogen which in turn, appeared as a multiplet at 6.76 τ. The C-4 methyls showed two doublets at 8.34 τ and 8.28 τ ($J \simeq 1.4$ c.p.s. for both) probably split by the C-3 olefinic hydrogen which appeared as a multiplet at 4.89 τ.

Methyl 4-methyl-3-pentenoate (102) showed a N. M. R. peak at 6.40 τ due to the ester methyl. Two slightly broadened singlets at 8.26 τ

and 8.37 τ are assigned to the C-4 methyls. The C-2 methylene hydrogens showed a broad doublet at 7.08 τ ($J \simeq 7.2$ c.p.s.) and the C-3 olefinic hydrogen showed a multiplet at 4.75 τ.

Methyl trans-2-methyl-3-pentenoate (103) was assigned the trans geometry on the basis that it showed an I. R. band at 971 cm^{-1} due to the two olefinic hydrogens vibrate in opposite direction (29). The N. M. R. spectrum of 103 shows two doublets one at 8.81 τ ($J \simeq 7.1$ c.p.s.) due to the C-2 methyl which was split by the C-2 methine hydrogen at 7.0 τ (multiplet), the other at 8.31 τ ($J \simeq 4.6$ c.p.s.) due to the C-4 methyl which was split by the C-4 vinyl hydrogen. The latter and the C-3 vinyl hydrogen showed a multiplet centred at 4.51 τ.

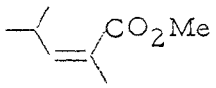
The compound methyl 3-pentenoate (94) had been characterized previously (2).

The data for the thermal isomerization reactions of the methyl 2- and 3-pentenoates at various temperatures and durations are listed in Tables VI, VII, VIII and IX. In these tables, the data for the equilibrium studies are also included. They show the following results which are common to all esters studied.

The cis α,β isomers thermally isomerized to give the trans α,β isomers and the β,γ isomers. The relative rates of formation were faster for the β,γ isomers than the trans α,β isomers. As a result, the relative amounts of the β,γ isomers built up to maxium values

TABLE VI

Thermal rearrangement of methyl 2,4-dimethyl-2- and 3-pentenoates



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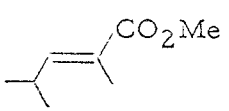

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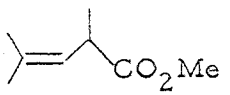


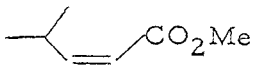
101

Initial olefin	run no.	time (hr.)	temp. (°C)	cis-α,β	trans-α,β	β,γ
cis-α,β	35	30	283.7°	28.3	2.0	69.7
cis-α,β	51	17	297.4°	17.3	1.5	81.2
cis-α,β	59	83	297.4°	9.6	4.2	86.2
cis-α,β	59	151	297.4°	8.6	6.7	84.7
77% cis-α,β & 23% trans-α,β	64	290	297.4°	7.7	28.7	63.6
	64	353*	297.4°	7.9	28.6	63.5
trans-α,β	59	83	297.4°	2.8	74.8	22.4
trans-α,β	59	151	297.4°	2.4	69.6	27.0
trans-α,β	59	174	297.4°	3.7	68.0	28.3
β,γ	36	36	283.7°	2.3	--	97.7
β,γ	36	86	283.7°	5.1	--	94.9
β,γ	36	155	283.7°	6.5	--	93.5
β,γ	59	83	297.4°	6.7	--	93.3
β,γ	59	151	297.4°	7.7	0.5	91.8

* Equilibrium attained -- 7.9% cis-α,β, 28.6% trans-α,β and 63.5% β,γ.

TABLE VII

Thermal rearrangement of methyl 4-methyl-2- and 3-pentenoates



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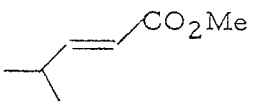

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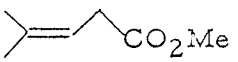


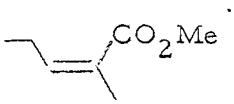
102

Initial olefin	run no.	time (hr.)	temp. (°C)	cis-α,β	trans-α,β	β,γ
cis-α,β	56	7	259.4°	15.7	4.8	79.5
cis-α,β	63	4	297.4°	1.9	2..3	95.8
cis-α,β	63	6	297.4°	1.7	4.0	94.3
cis-α,β	63	24	297.4°	1.8	4.7	93.5
cis-α,β	63	40	297.4°	1.7	7.3	91.4
75% cis-α,β &	65	211*	297.4°	1.5	17.9	80.6
25% trans-α,β	65	290*	297.4°	1.5	17.7	80.8
cis-α,β	66	259*	297.4°	1.5	17.7	80.8
cis-α,β	66	336*	297.4°	1.5	17.6	80.9
trans-α,β	66	259*	297.4°	1.5	17.8	80.7
trans-α,β	66	336*	297.4°	1.5	17.8	80.7
trans-α,β	63	4	297.4°	--	91.6	8.4
trans-α,β	63	6	297.4°	--	90.0	10.0
trans-α,β	63	24	297.4°	--	82.1	17.9
trans-α,β	63	40	297.4°	trace	78.1	21.9
β,γ	63	4	297.4°	1.8	2,1	96.1
β,γ	63	40	297.4°	1.5	9.3	89.2
β,γ (10% )	63	4	297.4°	1.7	2.6	95.7

* Equilibrium attained -- 1.5% cis-α,β , 17.7% trans-α,β and 80.8% β,γ .

TABLE VIII

Thermal rearrangement of methyl 2-methyl-2- and 3-pentenoates



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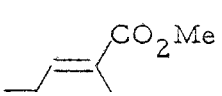

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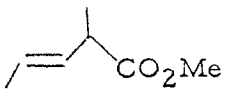


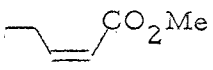
103

Initial olefin	run no.	time (hr.)	temp. (°C)	cis-α,β	trans-α,β	β,γ
cis-α,β	50	4	297.4°	81.9	7.7	10.4
cis-α,β	50	6	297.4°	73.1	10.5	16.4
cis-α,β	50	10	297.4°	62.0	14.8	23.2
cis-α,β	50	21	297.4°	41.8	21.7	36.5
cis-α,β	58	83	297.4°	18.5	39.7	41.8
cis-α,β	58	174*	297.4°	16.2	45.9	37.9
cis-α,β	58	200*	297.4°	16.3	45.8	37.9
trans-α,β	58	83	297.4°	10.3	67.4	22.3
trans-α,β	58	151	297.4°	11.6	61.8	26.6
trans-α,β	58	174	297.4°	12.6	58.8	28.6

* Equilibrium attained -- 16.2% cis-α,β, 45.9% trans-α,β and 37.9% β,γ.

TABLE IX

Thermal rearrangement of methyl 2- and 3-pentenoates



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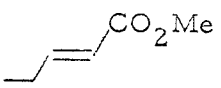

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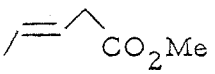

94

Initial olefin	run no.	time (hr.)	temp. (°C)	cis-α,β	trans-α,β	β,γ
cis-α,β	8	5	259.4°	86.4	1.8	11.8
cis-α,β	8	22	259.4°	46.4	6.0	47.4
cis-α,β	8	61	259.4°	13.7	12.4	73.9
cis-α,β	*	336	250°	7	48	45
trans-α,β	*	336	250°	7	47	46
trans-α,β	10	17	259.4°	1.5	89.5	9.0
trans-α,β	10	26	259.4°	2.2	81.1	16.7
trans-α,β	10	64	259.4°	3.9	61.3	34.8
β,γ	10	17	259.4°	9.2	11.7	79.0
β,γ	10	26	259.4°	8.6	16.0	75.4
β,γ	10	41	259.4°	8.0	26.8	65.2
β,γ	10	64	259.4°	7.7	31.1	61.2

* See reference 2, equilibrium attained -- 7% cis-α,β, 48% trans-α,β and 45% β,γ.

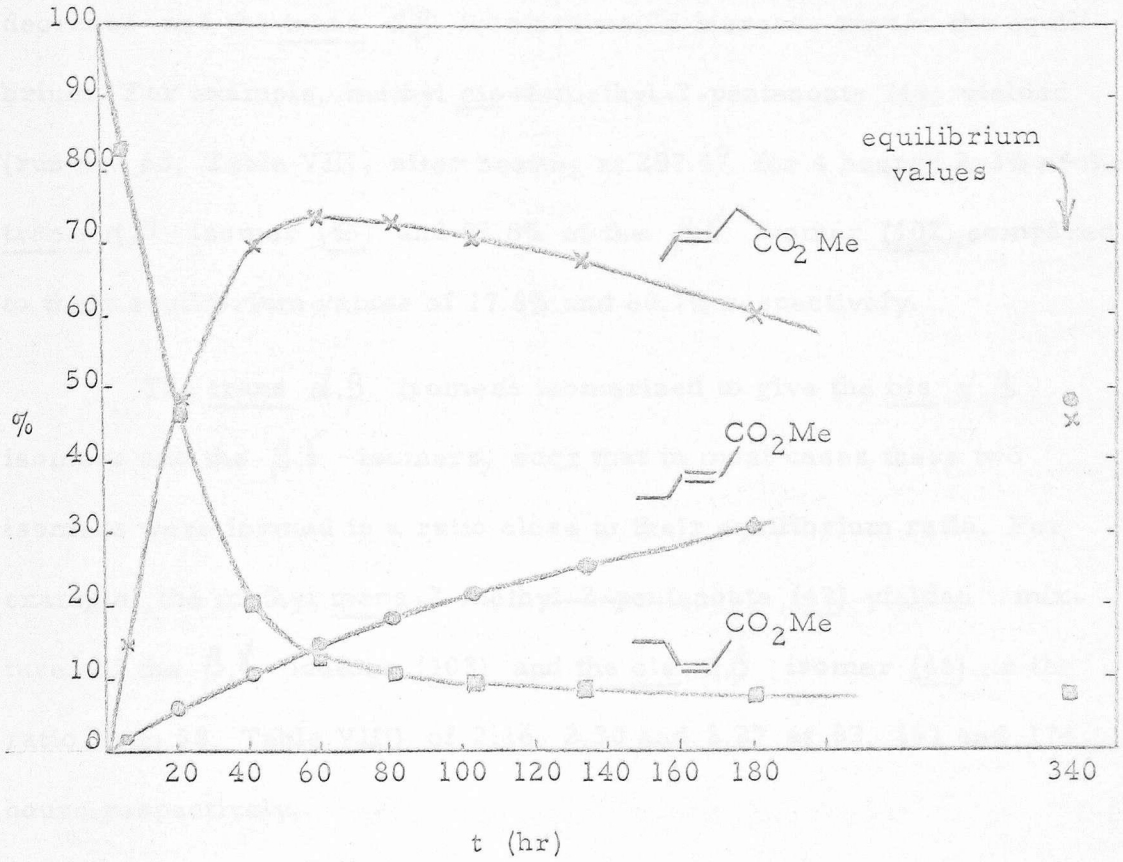

FIGURE 10 - Equilibration of methyl 2- and 3-pentenoates

(Figure 10) which were above their equilibrium values whereas the relative amounts of the trans α,β isomers were always below their equilibrium values. After reaching a maxium, the β,γ isomers would decrease and the trans α,β isomers would increase toward the equilibrium. For example, methyl cis-4-methyl-2-pentenoate (44) yielded (run no. 63, Table VII), after heating at 297.4° for 4 hours, 2.3% of the trans α,β isomer (45) and 95.8% of the β,γ isomer (102) compared to their equilibrium values of 17.8% and 80.7% respectively.

The trans α,β isomers isomerized to give the cis α,β isomers and the β,γ isomers, such that in most cases these two isomers were formed in a ratio close to their equilibrium ratio. For example, the methyl trans-2-methyl-2-pentenoate (47) yielded mixtures of the β,γ isomer (103) and the cis α,β isomer (46) in the ratio (run 58, Table VIII) of 2.16, 2.30 and 2.27 at 83, 151 and 174 hours respectively.

The β,γ isomers isomerized to give the cis α,β and trans α,β isomers in unpredictable proportion initially. As the heating was prolonged, the cis α,β isomers reached the equilibrium proportion relative to the β,γ isomers first. In the case of methyl 2,4-dimethyl-3-pentenoate (101), only the cis α,β isomer (42) was formed in the initial stages of the reaction (run no. 36 & 59, Table VI) and the ratio of 42/101 had almost reached its equilibrium value before traces of the trans α,β isomer (43) began to form.

From the data shown in the tables, it can be seen that the relative rates of isomerization reactions of the cis α,β isomers were much faster than the trans α,β isomers and the β,γ isomers. For example, after 4 hours at 297.4° (run no. 63, Table VII) over 99% of methyl cis-4-methyl-2-pentenoate (44) had isomerized, whereas only 10% and 20% of the trans α,β isomer (45) and the β,γ isomer (102) respectively had isomerized (the figures of percentage quoted here had been corrected after taking into account the equilibrium values of the three isomers).

Studies were carried out to determine the distribution of the three isomers at equilibrium. For each olefin system, all three isomers had been used individually as the initial olefin from which the point of equilibrium was reached. In some cases when either the trans α,β isomer or the β,γ isomer was used, equilibrium could not be reached due to the slow rate of isomerization. Higher temperatures could not be used to overcome this as extensive pyrolysis of the compounds into lower fragments took place at temperatures above 325°. To overcome this difficulty, mixtures of the isomers at close to equilibrium composition were used and equilibrium was considered reached when two or more runs of different time intervals gave essentially the same proportion of isomers.

Kinetic studies

Results of the thermal isomerization reactions discussed in the previous section indicate that the cis α,β isomers isomerized to the β,γ isomers faster than to the trans α,β isomers. In the case of methyl cis-2,4-dimethyl-2-pentenoate (42), the relative rates of formation for the β,γ isomer was so much faster than that for the trans α,β isomer that the ratio of β,γ /trans α,β was 54:1 after 90%* of 42 had isomerized (run no. 51, Table VI). This is also true for methyl cis-4-methyl-2-pentenoate (44) which isomerized to the β,γ isomer and the trans α,β isomer in the ratio of 41:1 after 99%* of 44 had isomerized (run no. 63, Table VII). These data indicate in a qualitative way that the isomerization of the cis α,β isomer to the β,γ isomer might be followed kinetically independent of the cis α,β to trans $\alpha\beta$ or trans α,β to β,γ isomerization paths. Consequently, the kinetics of thermal isomerization reactions of these two cis-2-pentenoates (42 and 44) to their corresponding 3-pentenoates (101 and 102) were studied at various temperatures. The kinetic data obtained gave good straight lines when plotted using the first-order rate law.

The rate constants (k) and half-lives ($t_{1/2}$) of these thermal isomerization reactions were calculated from first-order rate plots of log $a_o/(a_o-x)$ versus time t (Figures 11 and 12). Their heat of activa-

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* Corrected after taking into account the equilibrium value of the cis α,β isomer.

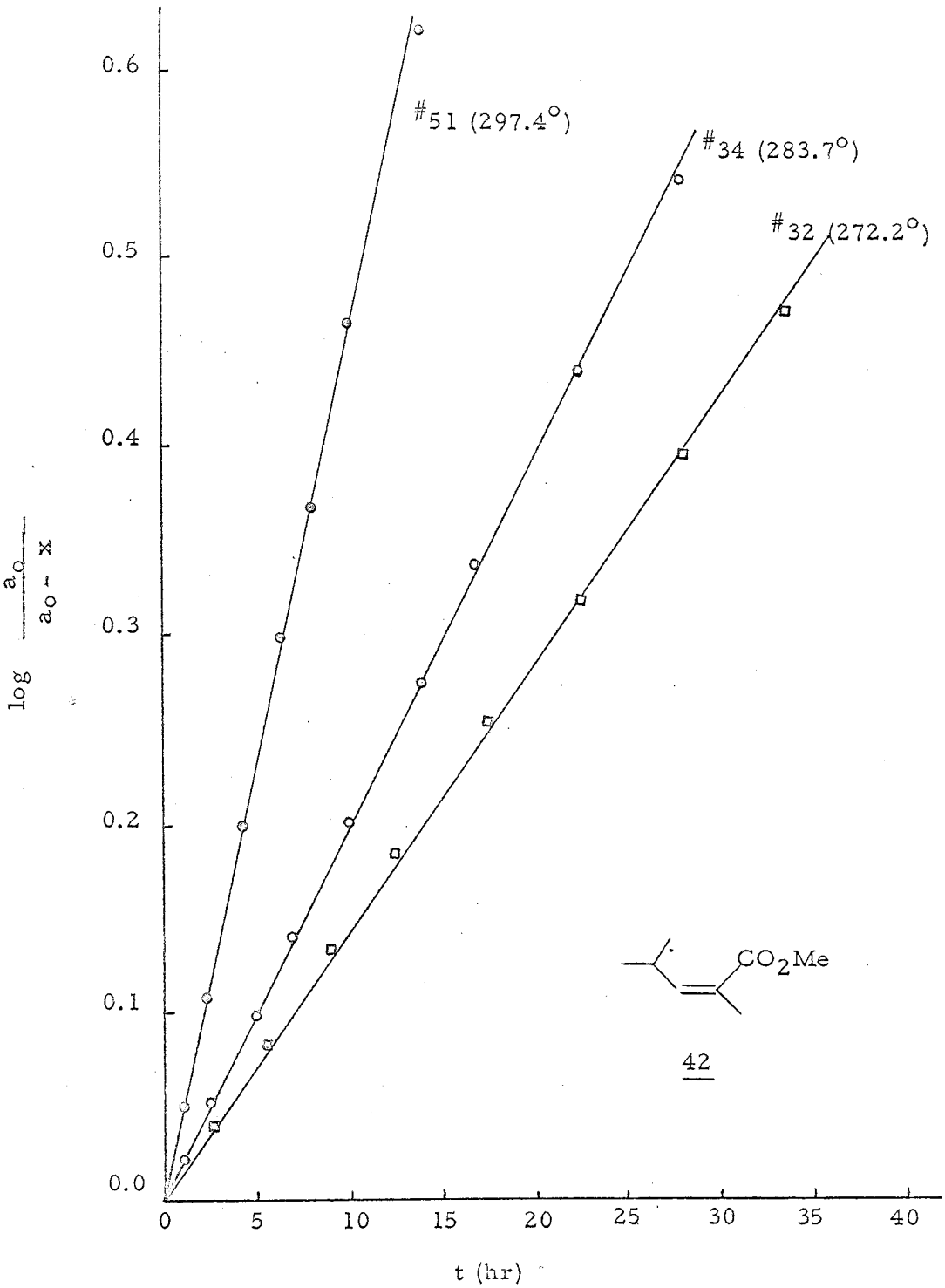


FIGURE 11 - First-order rate plots for the thermal isomerization of 42

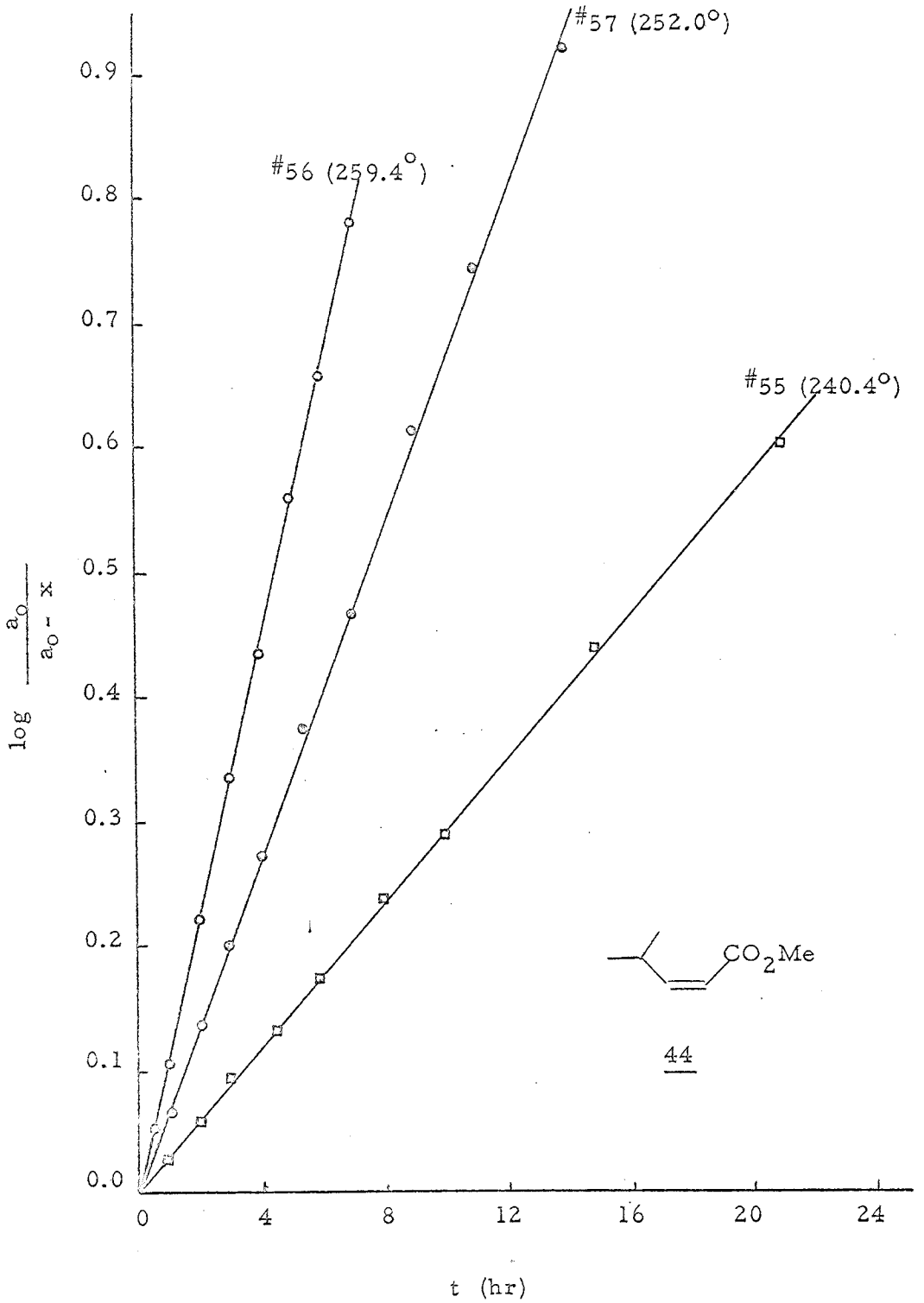


FIGURE 12 - First-order rate plots for the thermal isomerization of 44

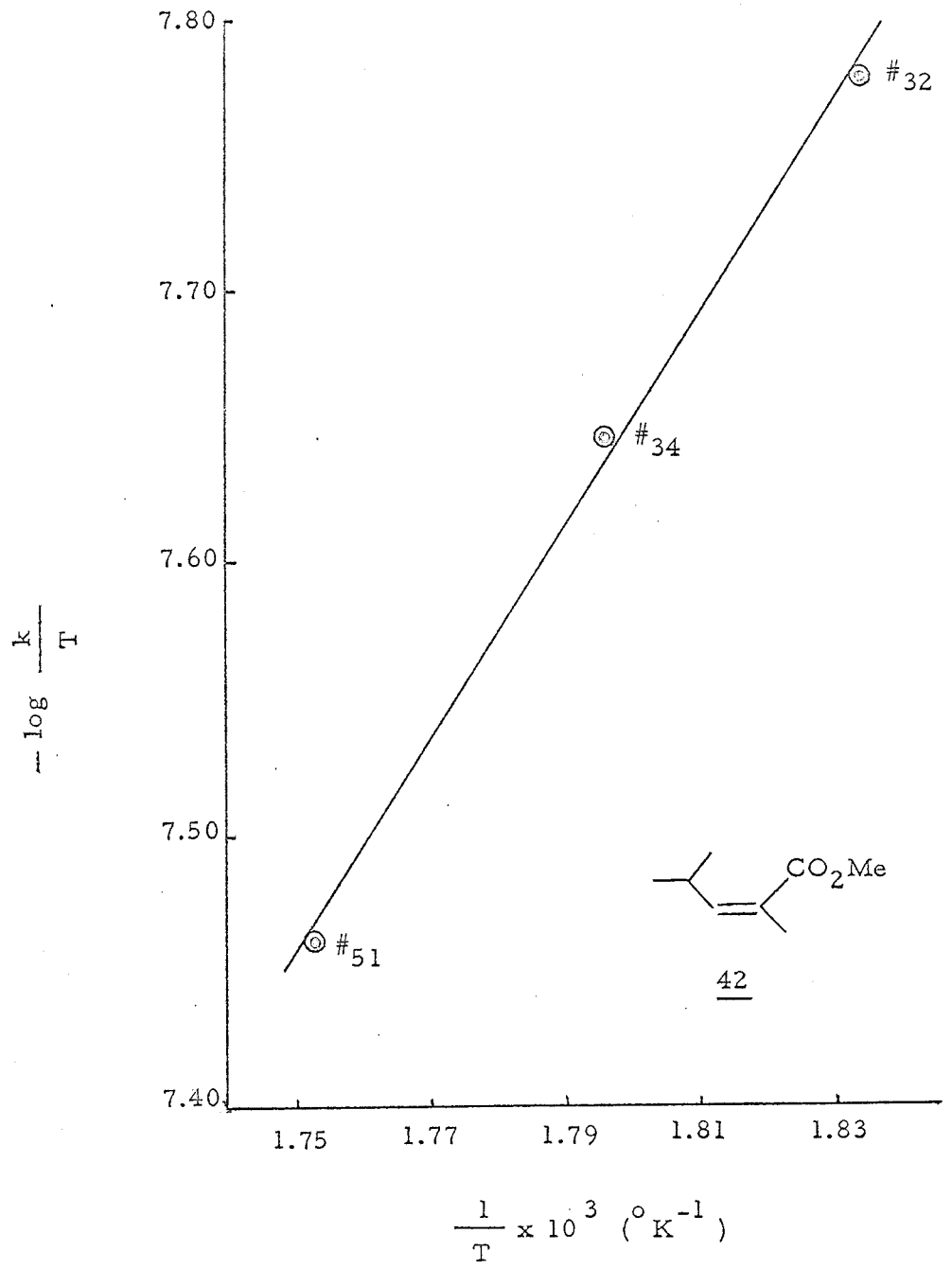


FIGURE 13 - Activation plot for the thermal isomerization of 42

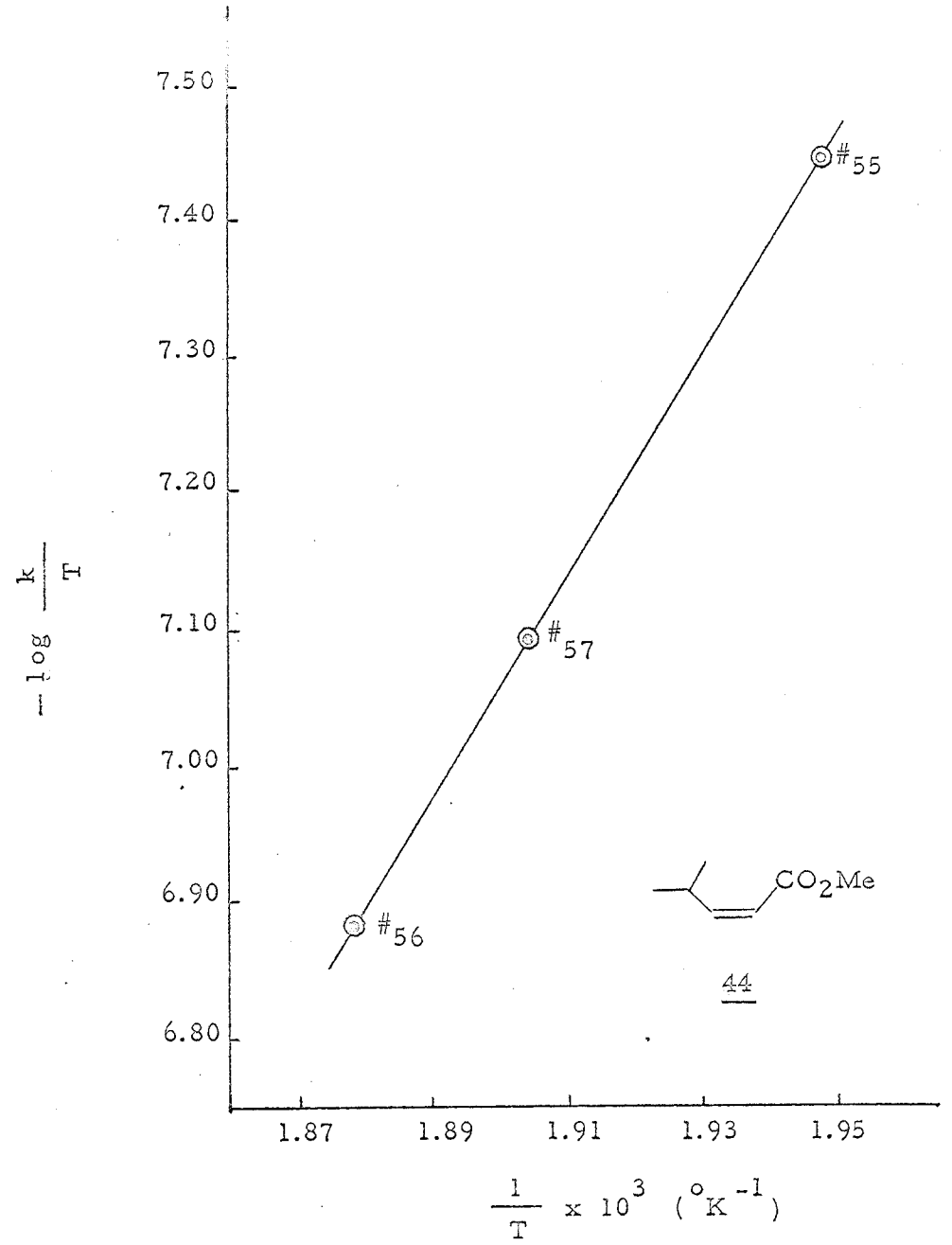
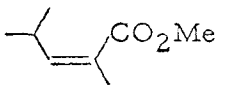


FIGURE 14 - Activation plot for the thermal isomerization of 44

TABLE X

Kinetic data of the thermal isomerization of methyl cis-2,4-dimethyl-2-pentenoate (42)



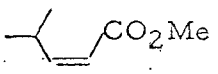
42

Run no.	temp. (°C)	k x 10^{-5} (sec^{-1})	$t_{1/2}$ (hr^{-1})	$\Delta H^{\ddagger}$ ($\frac{kcal}{mole}$)	$\Delta S^{\ddagger}$ (e.u.) at 272.2°
32	272.2°	0.91	21.1		
33	272.2°	0.90	21.3		
34	283.7°	1.26	15.3	17.9[1]	-49.9[1]
35	283.7°	1.28	15.1		
51	297.4°	2.98 *	6.5		

* After taking into account the equilibrium values of the three isomers, this k becomes 3.021 (1.4% diff.). See Appendix for calculation.

TABLE XI

Kinetic data of the thermal isomerization of methyl cis-4-methyl-2-pentenoate (44)



44

Run no.	temp. (°C)	k x 10^{-5} (sec^{-1})	$t_{1/2}$ (hr^{-1})	$\Delta H^{\ddagger}$ ($\frac{kcal}{mole}$)	$\Delta S^{\ddagger}$ (e.u.) at 259.4°
55	240.4°	1.86	10.4		
57	252.0°	4.28	4.5	37.5[1]	- 8.2[1]
56	259.4°	7.06 *	2.7		

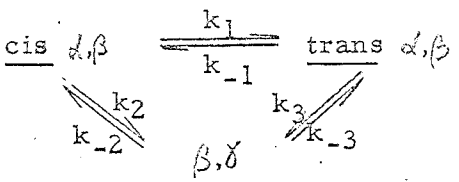
* After taking into account the equilibrium values of the three isomers, this k becomes 7.222 (2.2% diff.). See Appendix for calculation.

[1] The estimated maximum errors in $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ are ±10%.

tion ($\Delta H^{\ddagger}$) and entropies of activation ($\Delta S^{\ddagger}$) were calculated from plots of log k/T versus 1/T (Figures 13 and 14). These kinetic results are listed in Tables X and XI.

Discussion of results

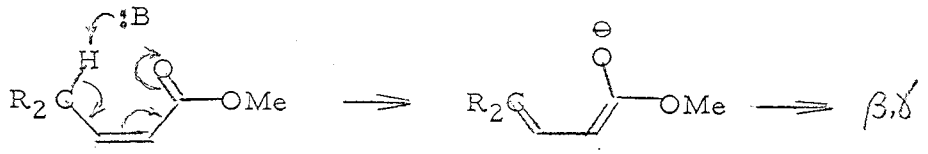
Let us now consider the mechanism for the thermal isomerization of the unsaturated esters. There are six different steps to be considered as shown below. Results of the thermal isomerization and kinetic



studies indicate that the cis α,β isomers isomerized to the β,γ isomers (k_2) faster than to the trans α,β isomers (k_1) for the systems with a β-isopropyl group and that all other steps are very slow.

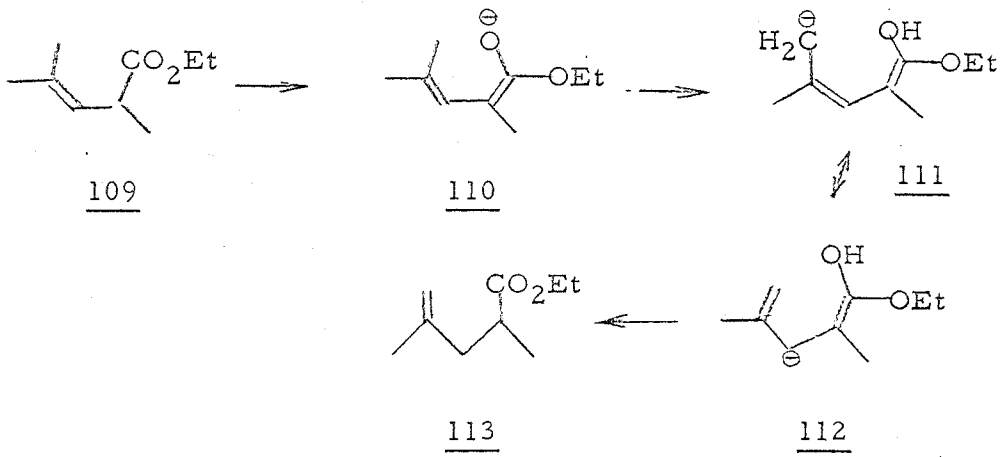
We can consider three mechanisms in which a cis α,β-unsaturated ester can isomerize to its corresponding β,γ isomer. These are the base catalysed isomerization, the free radical rearrangement and the intramolecular 1,5-hydrogen transfer via a six-membered cyclic transition state.

The base catalysed isomerization (84) involves the formation of an enolate ion of the cis α,β-unsaturated ester, 108, by proton abstraction by the base. This enolate ion (108) would then rearrange to give



107 108

the β,γ isomer. Since a base is directly involved in the isomerization, its presence would be expected to strongly affect the rate of isomerization. This was not observed on our kinetic studies for with the addition of 10% pyridine into a sample, there was no significant change in the rate of isomerization of the β,γ isomer (Table VII, run no. 63). We further note that Kinstle reported (69) a γ,δ isomer, 113, as a major product at equilibrium for the base catalysed isomerization of ethyl cis-2,4-dimethyl-2-pentenoate using sodium glycolate in ethylene glycol at 195° and suggested that 113 is formed from the β,γ isomer (109). The



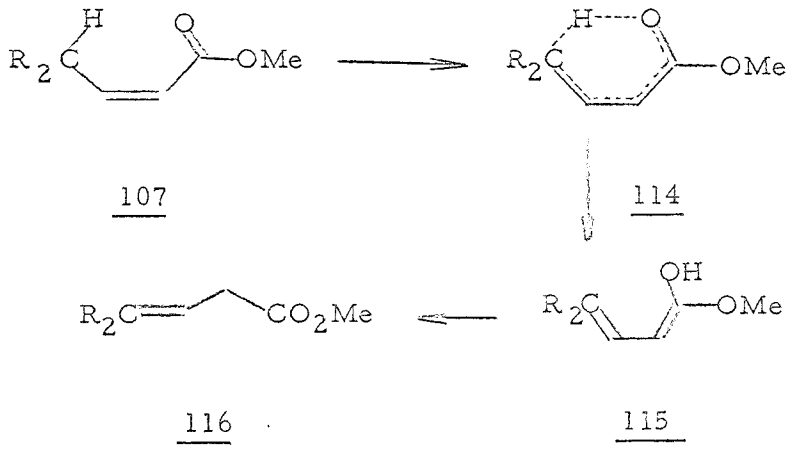
109 110 111 112 113

mechanism proposed involves the formation of an enolate ion of the β,γ isomer, 110, followed by proton abstraction by oxygen to form an allylic carbanion 111, which then gives the γ,δ isomer (113). There is no in-

dication of the formation of γ,δ isomers in the present studies although these were looked for even at long reaction times. We thus conclude that base catalysis mechanism is not important in our system.

If the isomerization took place by a free radical mechanism, one would expect the following results. Firstly, the rate of isomerization would be affected by the presence of oxygen since it is a free radical inhibitor (93). Secondly, both the cis and the trans α,β isomers would give the β,γ isomer at comparable rates and the β,γ isomer would give both the cis and the trans α,β isomers at comparable rates since the mechanism to either would be expected to require similar activation energies. All these points are in constrast with our observations which have found the rate independent of the presence of oxygen, the conversion of the cis α,β isomer to the β,γ isomer faster than that of the trans α,β to the β,γ isomer (runs 35 and 59, Table VI) and the conversion of the β,γ isomer to the cis α,β isomer faster than the β,γ isomer to the trans α,β isomer (run 36, Table VI). We therefore conclude that a free radical mechanism is not important.

A cyclic mechanism similar to that discussed earlier for the thermal rearrangement of methyl cis-2-alkylcyclopropane-1-carboxylates does seem to satisfactorily explain the results of the thermal isomerization of α,β-unsaturated esters. The six-membered cyclic transition state, 114, is shown below, and would lead to the enol 115. such a hydrogen transfer can only take place if the alkyl group bearing



107 114

116 115

the hydrogen to be transferred and the carboxylate group are cis to each other. Therefore, only the cis α,β-unsaturated esters can isomerize to the β,γ isomers, and vice versa. The enolene type intermediate although not expected to be stable would be expected to be accessable in a pre-equilibrium steps for the β,γ to cis α,β isomerization (75). In our data the cis orientation is clearly necessary for the β-isopropyl acrylates and is indicated in the β-ethyl acrylates. This data is, illustrated graphically in Figure 10 (p. 61) to show the fast built up of β,γ isomer from the cis α,β isomer. No such distinction was found for the β-methyl series (94) in the gas phase. It is significant however that for all of these systems β,γ isomers appear in the final equilibrium mixture. Isomerization of a γ,δ olefin at 297° shows cis to trans interconversion but no chain isomerization. Finally the large negative entropies of activation in the β-isopropyl series is fully in line with the proposal of a cyclic transition state for the isomerization reactions.

The 1,5-hydrogen transfer mechanism discussed above provides

for the formation of β,γ isomers but not for γ,δ isomers. In at least one case noted above if a path for formation of the γ,δ isomer were available then it should appear in appreciable quantities at equilibrium. This was not observed.

It has been discussed above that the 1,5-hydrogen transfer reaction in the α,β-unsaturated esters requires a cis relationship between the β-alkyl substituent and the ester carbonyl group. The nature of the β-alkyl substituent affects the relative importance of the 1,5-hydrogen transfer reaction, i.e., the isomerizations of cis α,β to β,γ and the cis α,β to trans α,β. The rate of the isomerization of the cis α,β to β,γ appears to increase with the change in β-alkyl substituent from methyl to ethyl to isopropyl. For the cyclic 1,5-hydrogen transfer, a tertiary hydrogen might be expected to be most readily transferred since a secondary hydrogen has been observed in the first section of this thesis to be more readily transferred than a primary hydrogen.

At the same time the cis α,β to trans α,β isomerization appears to become slower as the β-alkyl substituent is changed from methyl to ethyl to isopropyl. It is possible that in the cis α,β to trans α,β isomerization the hybridization of the carbons changed from sp^2 to sp^3, and as the size of β-alkyl is increased, this reaction is sterically inhibited. Thus the rate of the cis α,β to trans α,β isomerization is reduced and as a result, the isomerization of cis α,β to β,γ is observed as an isolated step.

To conclude, it has been shown that cis α,β-unsaturated esters can be isomerized thermally to their β,γ isomers. The isomerization reaction proceeds by an intramolecular 1,5-hydrogen transfer via a six-membered cyclic transition state, 114. Although this step has been

114

demonstrated in detail only for compounds with a β-isopropyl group, it is anticipated to be important for the thermal equilibration of unsaturated esters, ketones and aldehydes.

III. EXPERIMENTAL

General statement

All boiling points are uncorrected and most of them were determined by the micro inverted capillary method. Refractive indices were determined at temperatures ranging from 20° to 27° using an Abbe Refractometer.

Infrared spectra were measured with a Perkin-Elmer Model 21DB spectrometer fitted with sodium chloride optics. Samples were dissolved in carbon tetrachloride in 5 - 10% solution. Most infrared bands are calibrated using the 1603 cm^{-1} band of the polyethylene film as standard.

Nuclear magnetic resonance spectra were recorded on a Varian Associates A-60 spectrometer and/or on a Varian Associates HA-100 spectrometer by Mrs. A. Brewster, Miss C. Burfitt and Mr. R. Burton of this department. The double resonance spectra were measured on the HA-100. Samples were dissolved in carbon tetrachloride to 20% solution by volume unless otherwise stated. Tetramethyl silane was used as internal standard.

The vapor phase chromatography unit used was an Aerograph Model A-90-P equipped with a thermal conductivity detector.

The elemental microanalyses were performed by Dr. A. Bernhardt and by Mrs. C. Jenkins and Mr. P. Borda of this department.

Preparation of methyl 1, 2, 2-trimethyl-1-cyclopropanecarboxylate (32)

Acetone azine: 75 g (1.5 moles) of hydrazine hydrate (99-100%) was added slowly to 176 g (3 moles) of acetone at 0°. The mixture was then heated in a steam bath for 5 hrs, cooled to room temperature, 50 g of anhydrous potassium carbonate was added to aid separation of water. This treatment was repeated with 20 g portions until the product was dry. The organic fraction was fractionally distilled to give 135 g (80%) of a colorless liquid, b. p. 132-3°, n_D^{25} 1.4514 (lit. (85), b. p. 129-32°, n_D^{20} 1.4533).

Acetone hydrazone: a mixture of 135 g (1.2 moles) of acetone azine and 60 g (1.2 moles) of hydrazine hydrate was heated at 110° for 17 hrs. It was then repeatedly treated with 20 g portions of anhydrous potassium carbonate until dry. Fractional distillation gave 145 g (84%) of a colorless liquid, b. p. 120-2° (lit. (86), b. p. 115-20°).

3, 5, 5-Trimethyl-3-carbomethoxy-Δ^1-pyrazoline (50): a mixture of 58 g (0.25 mole) of silver oxide and 300 ml of anhydrous ether was cooled to -60°, to this were added simultaneously 18 g (0.25 mole) of acetone hydrazone and 15 g (0.15 mole) of methyl methacrylate with stirring over a period of 10 minutes (2-diazopropane prepared in situ (47)).. The resulting mixture was first allowed to warm up to -25° and was kept stirring at that temperature for 60 minutes, then warmed to room temperature. The black precipitate was filtered, the ether flash evaporated. The residue was fractionally distilled to give 15 g of 50,

b. p. 55-6° at 0.1 mm.

Anal. Calcd. for $C_8H_{14}O_2N$: C, 56.47; H, 8.23; N, 16.47. Found: C, 56.30; H, 8.13; N, 16.35.

The N. M. R. spectrum of 50 shows the following peaks, the C-5 methyls at 8.64 τ and 8.60 τ (both singlet), the C-4 hydrogens at 8.79 τ and 8.03 τ (both doublet, $J \simeq 13.1$ c.p.s.), the C-3 methyl at 8.46 τ (singlet) and the ester methyl at 6.27 τ (singlet).

Liquid phase pyrolysis of 12.5 g of 3,5,5-trimethyl-3-carbomethoxy-Δ^1-pyrazoline (50) at 90-100° gave 9.5 g (91%) of a colorless liquid boiling up to 165°. Vapor phase chromatographic separation using a 20' x 3/8" dinonylphthalate column at 158° with helium flow rate of 85 ml per min gave two components, A and B in the ratio of 83.8% to 16.2%, retention time of 14.6 and 22.3 min respectively.

Component A: b. p. 148.5°, n_D^{25} 1.4280, was assigned the structure of methyl 1,2,2-trimethyl-1-cyclopropanecarboxylate (32) on the basis of its N. M. R. spectrum (20% by volume in benzene) which shows three singlets at 9.01 τ, 8.87 τ and 8.74 τ for the three ring methyls, another singlet at 6.57 τ for the ester methyl, two doublets at 9.74 τ and 8.58 τ ($J_{gem} \simeq 4.6$ c.p.s.) for the AB system for the C-3 hydrogens. When carbon tetrachloride was used as solvent for the N. M. R. spectrum, the low field doublet appeared hidden under the low field singlet which now appeared at 8.71 τ.

Anal. Calcd. for $C_8H_{14}O_2$: C, 67.57; H, 9.93. Found: C, 67.69; H, 9.88.

A. splittings of methyls on C-4 and hydrogen on C-4

B. the multiplet due to the hydrogen on C-4 is reduced to a doublet with some further long range splitting when the methyls on C-4 are irradiated

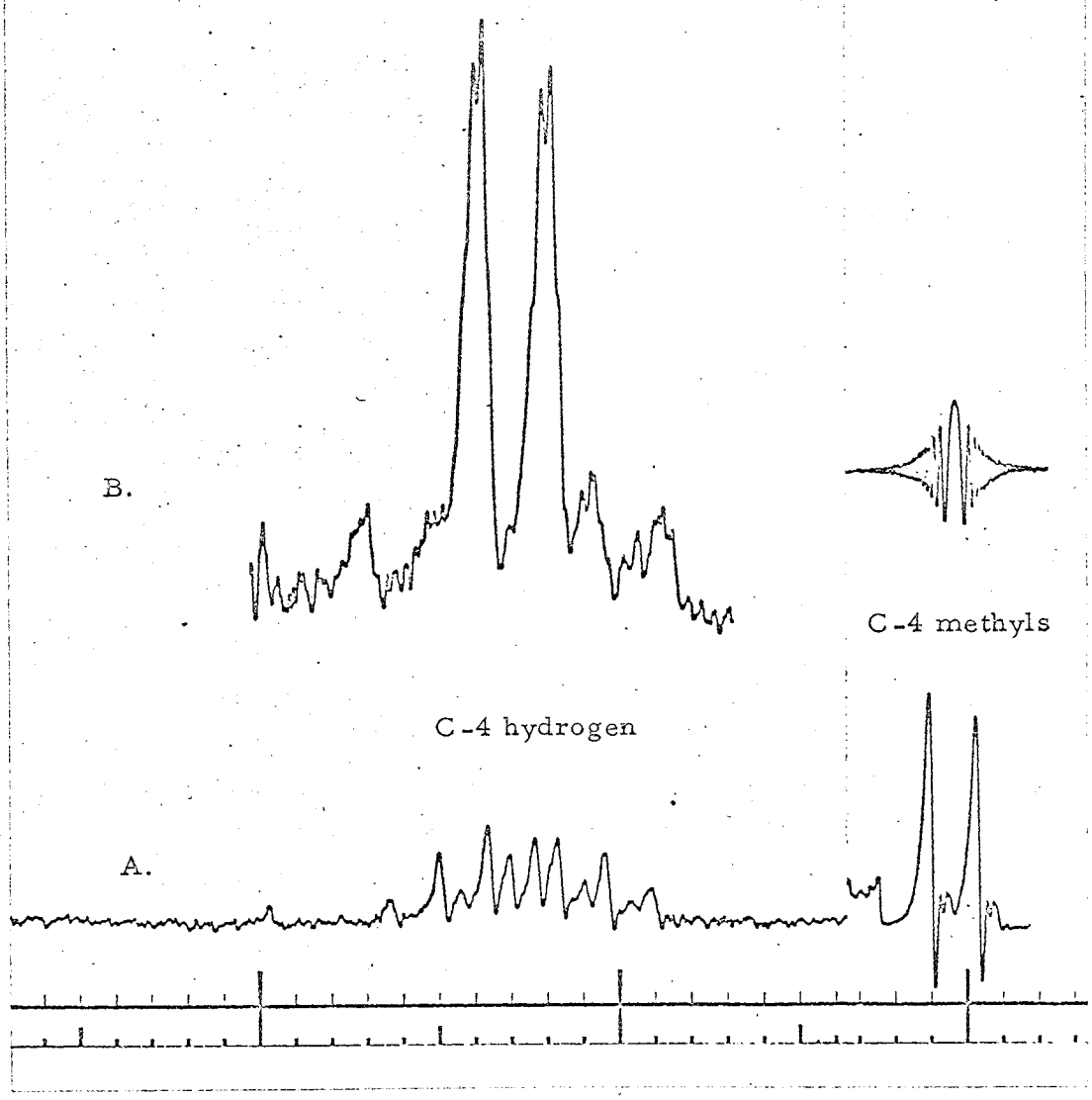


FIGURE 15 - Double resonance N.M.R. spectrum of 43

Component B: b. p. 164.5°, n_D^{25} 1.4366 (lit. (90), b. p. 49-50° at 10 mm, n_D^{20} 1.4384), it showed I. R. and N. M. R. bands characteristic of methyl trans-2, 4-dimethyl-2-pentenoate (43). The I. R. spectrum shows bands at 1714 cm^{-1} and 1649 cm^{-1} for the conjugated carbonyl and double bond stretching vibrations respectively. The N. M. R. spectrum shows peaks at 8.98 τ (doublet, $J \simeq 6.7$ c.p.s.) for the C-4 methyls, 8.20 τ (doublet, $J_{1,3} \simeq 1.4$ c.p.s.) for the C-2 methyl, 6.33 τ (singlet) for the ester methyl, 3.51 τ (2 quartets, $J_{1,2} \simeq 9.6$ c.p.s., $J_{1,3} \simeq 1.4$ c.p.s.) for the olefinic hydrogen and 7.36 τ (multiplet) for the C-4 hydrogen. The multiplicity of the 7.36 τ multiplet was reduced when the 8.98 τ doublet was irradiated employing the double resonance technique (87) at 100 Mc (Figure 15).

Anal. Calcd. for $C_8H_{14}O_2$: C, 67.57; H, 9.93. Found: C, 67.85; H, 9.71.

Preparation of methyl 2, 2-dimethyl-1-cyclopropanecarboxylate (35)

5, 5-Dimethyl-3-carbomethoxy- Δ^1-pyrazoline (53) and Δ^2-pyrazoline (54): 116 g (0.5 mole) of silver oxide in 500 ml of anhydrous ether was reacted with 36 g (0.5 mole) of acetone hydrazone and 43 g (0.5 mole) of methyl acrylate as described in the preparation of 50 above except that the mixture was kept at -25° for 30 min. Fractional distillation gave 31 g of a colorless liquid, b. p. 85-97° at 0.1 mm, which was shown by N. M. R. to be a mixture of the Δ^1- and Δ^2-pyrazolines. Subsequent distillation gave a fraction, b. p. 96-7° at 0.1 mm,

of pure Δ^2-pyrazoline (54). The N. M. R. spectrum of 54 shows the C-5 methyls at 8.72 τ (singlet), the C-4 hydrogens at 7.36 τ (singlet), the ester methyl at 6.27 τ (singlet) and the N-1 hydrogen at 3.16 τ (broad). Through a comparison of the spectrum of the pure Δ^2-pyrazoline (54) and that of the Δ^1- and Δ^2-pyrazoline mixture, the following peaks were assigned to the Δ^1-pyrazoline (53), the C-5 methyls at 8.33 τ and 8.15 τ (both singlet), the C-4 hydrogens at 7.49 τ and 6.71 τ (both multiplets), the ester methyl at 6.37 τ (singlet) and the C-3 hydrogen at 5.41 τ (broad). Pyrolysis of 31 g of the mixed pyrazolines (53 and 54) at 100-170° yielded 24 g (94%) of a colorless liquid boiling up to 150°. This was separated by V. P. C. using a 20' x 3/8" dinonylphthalate column at 165° with helium flow rate of 85 ml per min to give components C and D in the ratio of 3:7 with retention time of 11.0 and 16.2 min respectively.

Component C: this was found to be a mixture of methyl 2, 2-dimethyl-1-cyclopropanecarboxylate (35) and methyl cis-4-methyl-2-pentenoate (44) in the ratio of approximately 85:15 (or 23% and 4% respectively of the total product from pyrolysis) as indicated by N. M. R. analysis. 35 showed N. M. R. peaks at 8.86 τ and 8.81 τ (both singlet) for the methyls on C-2, 6.37 τ (singlet) for the ester methyl, 8.50 τ (pair of doublet) for the C-1 hydrogen, 9.0 τ (pair of doublet, 100 Mc in benzene) for the C-3 hydrogen trans to the C-1 hydrogen and 9.21 τ (pair of doublet) for the C-3 hydrogen cis to the C-1 hydrogen. The C-1 and C-2 hydrogens form an ABX coupling system with $J_{gem} \simeq 4.0$ c.p.s.,

$J_{cis} \simeq 8.1$ c.p.s. and $J_{trans} \simeq 5.1$ c.p.s. Methyl cis-4-methyl-2-pentenoate (44) showed N. M. R. peaks at 8.99 τ (doublet, $J \simeq 6.6$ c.p.s.) for the C-4 methyls, 6.36 τ (singlet) for the ester methyl, 4.43 τ (doublet, $J_{cis} \simeq 11.4$ c.p.s.) for the C-2 olefinic hydrogen and 4.03 τ (2 doublets, $J_{cis} \simeq 11.4$ c.p.s., $J_{1,2} \simeq 9.2$ c.p.s.) for the C-3 olefinic hydrogen. Attempts to separate 35 and 44 were unsuccessful.*

Component D: b. p. 150°, n_D^{22} 1.4298, was characterized by N. M. R. and I. R. spectral anaylses to be methyl trans-4-methyl-2-pentenoate (45). Three I. R. bands at 1723 cm^{-1}, 1657 cm^{-1} and 990 cm^{-1} are consistent with the structure assigned. Its N. M. R. spectrum shows peaks at 8.91 τ (doublet, $J \simeq 6.7$ c.p.s.) for the C-4 methyls, 6.34 τ (singlet) for the ester methyl, 4.32 τ (2 doublets, $J_{trans} \simeq 15.8$ c.p.s., $J_{1,3} \simeq 1.4$ c.p.s.) for the C-2 olefinic hydrogen, 3.14 τ (2 doublets, $J_{trans} \simeq 15.8$ c.p.s., $J_{1,2} \simeq 6.5$ c.p.s.) for the C-3 olefinic hydrogen and 7.54 τ (multiplet) for the C-4 hydrogen.

Anal. Calcd. for $C_7H_{12}O_2$: C, 65.49; H, 9.45. Found: C, 65.39; H, 9.44.

Preparation of cis- and trans-1, 2-dimethyl-1-cyanocyclopropane (41&40)

3, 5-Dimethyl-3-cyano-Δ^1-pyrazoline (55): 12 g of methacrylonitrile was added in 5 min to an ethereal solution of diazoethane (from 40 g of N-nitrosoethylurea) (88) at 0° and the resulting solution was left stirring for 30 min. Flash evaporation of the ether gave 20 g of crude 55.

* Anal. Calcd. for $C_7H_{12}O_2$ (mixture of 35 and 44): C, 65.49; H, 9.45. Found: C, 65.37; H, 9.62.

The N.M.R. spectrum (Figure 1, p. 21) of the crude 55 showed it to be a mixture of the cis and trans isomers (the C-3 methyl and the C-5 methyl) with peaks similar to those of an analogous mixture of cis- and trans-3,5-dimethyl-3-carbomethoxy-Δ^1-pyrazoline (3). Ten grams of the crude 55 was pyrolysed at a temperature of 100° and separation by V.P.C. using a 20'x3/8" dinonylphthalate column at 145° with helium flow rate of 85 ml per min gave three components, E, F and G in the ratio of 52.6%, 44.4% and 3.0% with retention times of 13.6, 17.5 and 20.0 min respectively.

Component E: b.p. 137.5°, n_D^{26} 1.4179, it was assigned the structure of trans-1,2-dimethyl-1-cyanocyclopropane (40). It showed an I.R. (Perkin-Elmer Model 137) band at 2242 cm^{-1} characteristic of the C≡N stretching vibration. The N.M.R. spectrum of 40 showed the C-1 methyl at 8.65 τ (singlet), the C-2 methyl at 8.70 τ (doublet, J≃5.6 c.p.s.) and the three ring hydrogens in the region 8.80 τ to 9.30 τ (multiplet).

Anal. Calcd. for C_6H_9N: C, 75.74; H, 9.54; N, 14.72. Found: C, 75.82; H, 9.67; N, 14.92.

Component F: b.p. 149°, n_D^{26} 1.4238, it was assigned the structure cis-1,2-dimethyl-1-cyanocyclopropane (41). Its N.M.R. spectrum shows the C-1 methyl at 8.69 τ (singlet), the C-2 methyl at 8.75 τ (doublet, J≃8.5 c.p.s.), one of the ring hydrogens at 9.60 τ (multiplet) and the remaining hydrogens at the region 8.50 τ to 9.00 τ (multiplet) which is under the 8.69 τ and 8.75 τ signals and thus not resolved.

Anal. Calcd. for C_6H_9N: C, 75.74; H, 9.54; N, 14.72. Found: C, 75.72; H, 9.80; N, 14.82.

Component G: b.p. 155°, n_D^{26} 1.4326, it was assigned the structure of 2-methyl-2-pentenonitrile (57). Its I.R. spectrum (Perkin Elmer Model 137) shows C≡N stretching vibration at 2208 cm^{-1}. The N.M.R. spectrum of 57 shows peaks at 8.95 τ (triplet, J≃7.4 c.p.s.) for the C-4 methyl, 8.14 τ (broad) for the C-2 methyl, 7.80 τ (quintet) for the C-4 methylene hydrogens and 3.74 τ (multiplet) for the C-3 olefinic hydrogen.

Anal. Calcd. for C_6H_9N: C, 75.74; H, 9.54; N, 14.72. Found: C, 75.56; H, 9.71; N, 14.58.

Preparation of methyl cis- and trans-2,4-dimethyl-2-pentenoate (42 &43)

(C)-methyl-(P)-diethyl-α-phosphonopropionate: a mixture of 66 g (0.4 mole) of triethylphosphite and 34 g (0.2 mole) of methyl α-bromopropionate was heated in a 500 ml two necked round bottom flask equipped with a thermometer and a condenser which was connected to a dry ice-acetone trap. Ethyl bromide began to form and condensed at the trap when the reaction temperature reached 120° and ceased at 170°. The resulting solution was distilled to give 42 g (93%) of a colorless liquid, b.p. 62-5° at 0.15 mm. Its N.M.R. spectrum shows the C-2 methyl at 8.68 τ (pair of doublets, J≃7.2 c.p.s., J_{H-P}≃17.8 c.p.s.), the C-2 hydrogen at 6.94 τ (pair of quartets, J≃7.2 c.p.s., J_{H-P}≃23.5 c.p.s.), the (C)-ester methyl at 6.31 τ (singlet), the methyl on the (P)-ethyl at

8.72 τ (triplet, $J \simeq 7.1$ c.p.s.) and the methylene hydrogens of the (P)-ethyl at 5.89 τ (pair of quartets, $J \simeq 7.1$ c.p.s., $J_{H-P} \simeq 8.5$ c.p.s.)

Two hundred millilitres of glyme (distilled from sodium hydride) in a 1-liter three necked round bottom flask equipped with a dropping funnel, a stirrer and a thermometer was cooled to 0°, 11 g (0.19 mole) of sodium hydride (49% dispersion in oil) was added and stirred. To this suspension maintained at 15-20° was added dropwise with stirring in one hr 42.5 g (0.19 mole) of (C)-methyl-(P)-diethyl-α-phosphonopropionate, after the addition, it was kept stirring for 1 hr at 15° followed by 5 min at 35°, then it was cooled to 15°. To this was added in 15 min 14.5 g (0.19 mole) of isobutyraldehyde with vigorous stirring. The resulting mixture was heated to reflux for 20 min, cooled to room temperature, diluted with 300 g of ice, extracted with 5 portions of 100 ml of ether. The combined ethereal solution was washed three times with 250 ml of water, dried with anhydrous sodium sulfate. Flash evaporation of ether gave 23 g (83%) of a colorless liquid which when analyzed by V. P. C. using a 10'x 1/4" dinonylphthalate column at 166° with helium flow of 35 ml per min gave 55.8% methyl cis-2, 4-dimethyl-2-pentenoate (42), 16.2% ethyl ester of 42, 21.6% of methyl trans-2, 4-dimethyl-2-pentenoate (43) and 6.4% ethyl ester of 43 with retention times 15.5, 21.2, 24.2 and 32.6 min respectively. The ethyl esters can be converted to their respective methyl esters by the following procedure. Three and a half grams of the above product in 10 ml of 30% potassium hydroxide solution

was heated with constant stirring until only one layer was resulted (1 hr), evaporated to dryness on a steam bath, diluted with 20 ml of water, cooled to 0°, acidified with concentrated hydrochloric acid on Congo Red. Extracted 3 times with 25 ml portions of ether, the combined extract was dried with anhydrous sodium sulfate, and treated with diazomethane in ether, flash evaporation gave 3.4 g (99%) of a colorless liquid which consisted of 71.2% of 42 and 28.8% of 43.

Methyl cis-2,4-dimethyl-2-pentenoate (42): b.p. 149.5°, n_D^{25} 1.4308 (lit. (90), b.p. 58-9° at 23 mm, n_D^{20} 1.4328). It showed I.R. bands at 1772 cm^{-1} and 1646 cm^{-1} for the conjugated carbonyl and double bond stretching vibrations respectively. The N.M.R. spectrum shows peaks at 9.04 τ (doublet, $J \simeq 6.7$ c.p.s.) for the C-4 methyls, 8.18 τ (doublet, $J_{1,3} \simeq 1.4$ c.p.s.) for the C-2 methyl, 6.32 τ (singlet) for theester methyl, 4.38 τ (pair of quartets, $J_{1,2} \simeq 9.6$ c.p.s., $J_{1,3} \simeq$ 1.4 c.p.s.) for the C-3 olefinic hydrogen and 6.75 τ (multiplet) for the C-4 hydrogen.

Anal. Calcd for $C_8H_{14}O$: C, 67.57; H, 9.93. Found: C, 67.38; H, 10.00.

Methyl trans-2,4-dimethyl-2-pentenoate (43): the physical data, elemental analysis and spectral assignments have been given earlier (p. 80).

Preparation of methyl cis- and trans-4-methyl-2-pentenoate (44 and 45)

Trimethyl phosphonoacetate: a mixture of 77 g (0.5 mole) of bromoacetate and 87 g (0.7 mole) of trimethyl phosphite was heated from

80° to 160° as described earlier for the preparation of (C)-methyl-(P)-diethyl-α-phosphonopropionate. Fractional distillation yielded 73 g (80%) of a colorless liquid, b. p. 85-6° at 0.08 mm.

Anal. Calcd for $C_5H_{11}O_5P$: C, 32.97; H, 6.09. Found: C, 32.63; H, 6.37.

The N. M. R. spectrum of trimethyl phosphonoacetate shows the (P)-ester methyls at 6.25 τ (doublet, $J_{H-P} \simeq 11.1$ c.p.s.), the methylene hydrogens at 7.07 τ (doublet, $J_{H-P} \simeq 21.7$ c.p.s.) and the (C)-ester methyl at 6.28 τ (singlet). The latter showed a doublet ($J_{H-P} \simeq 0.6$ c.p.s.) on expanded 100 Mc N. M. R. spectrum.

Twenty-two grams (0.3 mole) of isobutyraldehyde was reacted with 54.6 g (0.3 mole) of trimethyl phosphonoacetate, 14.4 g (0.3 mole) of sodium hydride in 300 ml of glyme according to the procedure described above for the preparation of 42 and 43 with minor change. After the addition of isobutyraldehyde, the mixture was kept stirring for 20 min at 20° instead of under reflux. The yield was 17.6 g (46%) consisting of 30.8% of methyl cis-4-methyl-2-pentenoate (44) and 69.2% of methyl trans-4-methyl-2-pentenoate (45) as shown by V. P. C. The mixture was distilled with a spinning band column to give 5.2 g 44, b. p. 138-40° and 9.2 g 45, b. p. 148-50°.

Methyl cis-4-methyl-2-pentenoate (44): b. p. 140°, n_D^{22} 1.4225. It showed I. R. bands at 1723 cm^{-1} and 1650 cm^{-1} and 1417 cm^{-1}. The N. M. R. spectral data have been reparted earlier in this thesis (p. 82).

Anal. Cacld. for $C_7H_{12}O_2$: C, 65.59; H, 9.44. Found: C, 65.60; H, 9.56.

Methyl trans-4-methyl-2-pentenoate (45): all physical data, elemental analysis and spectral data have been presented earlier in this thesis (p. 82).

A similar reaction using (C)-methyl-(P)-diethylphosphonoacetate, whose preparation is given below, in 0.1 mole scale yielded 7 g (53%) of a mixture consisting of 4% of cis isomers (44 and ethyl ester of 44) and 96% of trans isomers (45 and ethyl ester of 45). The ratio of methyl esters to ethyl esters was approximately 32:68. (C)-methyl-(P)-diethylphosphonoacetate was prepared according to the method used for the preparation of trimethyl phosphonoacetate. A mixture of 51 g (0.33 mole) of methyl bromoacetate and 85 g (0.5 mole) of triethyl phosphite was heated from 95-170° and worked up, to yield 61 g (88%) of (C)-methyl-(P)-diethylphosphonoacetate, b. p. 71-3° at 0.1 mm (89). Its N. M. R. spectrum shows peaks at 6.30 τ (singlet) for the (C)-ester methyl, 6.96 τ (doublet, $J_{H-P} \simeq 21.9$ c.p.s.) for the C-2 methylene hydrogens, 5.88 τ (pair of quartets, $J \simeq 7.1$ c.p.s., $J_{H-P} \simeq 8.4$ c.p.s.) for the methylene hydrogens of the ester ethyl and 8.71 τ (triplet, $J \simeq 7.1$ c.p.s.) for the methyl of the ester ethyl.

Preparation of methyl cis- and trans-2-methyl-2-pentenoate (46 and 47)

Trimethyl α-phosphonopropionate: this was prepared according to the method for the preparation of trimethyl phosphonoacetate. Thus, from

75 g (0.6 mole) of trimethyl phosphite and 67 g (0.4 mole) of methyl α-bromopropionate at reaction temperature 95-150°, 25 g (53% based on the methyl α-bromopropionate used) of trimethyl α-phosphonopropionate, b.p. 82-4° at 0.1 mm, was obtained. It showed N.M.R. peaks at 8.65 τ (pair of doublets, $J \simeq 7.2$ c.p.s., $J_{H-P} \simeq 17.9$ c.p.s.) for the C-3 methyl, 7.02 τ (multiplet) for the C-2 hydrogen, 6.29 τ (singlet) for the (C)-ester methyl and 6.28 τ (doublet, $J_{H-P} \simeq 11.0$ c.p.s.) for the (P)-ester methyls.

According to the procedure described above for the preparation of 44 and 45, 24.5 g (0.125 mole) of trimethyl α-phosphonopropionate, 7.5 g (0.125 mole) of propionaldehyde and 6 g (0.125 mole) of sodium hydride in 150 ml of glyme gave 5 g (56%) of colorless liquid, b.p. 130-55°. It was analysed by V.P.C. using a 10' by 1/4" dinonylphthalate column at 170°, with helium flow of 35 ml per min to give 38% of methyl cis-2-methyl-2-pentenoate (46) and 62% of methyl trans-2-methyl-2-pentenoate (47). Both 46 and 47 had been characterized by their N.M.R. and I.R. spectral analyses. They were identical to those reported earlier (3).

A second preparation using (C)-methyl-(P)-diethyl-α-phosphonopropionate yielded 12 g (73%) of a mixture consisting of 13% cis esters (46 and ethyl ester of 46) and 87% of trans esters (47 and ethyl ester of 47). The ratio of methyl esters to ethyl esters was 72:28.

Preparation of cis- and trans-2-pentenoate (48 and 49)

According to the procedure described above for the preparation

of 44 and 45, 8.7 g (0.15 mole) of propionaldehyde, 31.5 g (0.15 mole) of (C)-methyl-(P)-diethyl-phosphonoacetate and 7.2 g (0.15 mole) of sodium hydride in 150 ml of glyme gave 6.5 g (43%) liquid. Vapor phase chromatographic analysis (10'x 1/4" dinonylphthalate column at 168°, helium flow of 35 ml per min) of the product gave 4% of cis esters (48 and ethyl ester of 48) and 96% of trans esters (49 and ethyl ester of 49). The ratio of methyl esters to ethyl esters was 79:21. Both 48 and 49 had been characterized by comparing their I.R. and N.M.R. spectra to those reported previously (2).

Thermal rearrangement of methyl 1,2,2-trimethyl-1-cyclopropane-carboxylate (32) at 280°

A sample of 500 μl of 32 in a sealed N.M.R. tube was heated at 280° for 10 hr. The product was analyzed by V.P.C. (10'x 1/4" didecylphthalate column at 150° with helium flow rate of 40 ml per min) to give the starting material (less than 2%) and methyl 2,4-dimethyl-4-pentenoate (67) at 12.2 and 13.8 min respectively.

Methyl 2,4-dimethyl-4-pentenoate (67): b.p. 155°, n_D^{24} 1.4228 (lit. (91), b.p. 51° at 12 mm, n_D^{20} 1.4270). It showed N.M.R. peaks at 8.91 τ (doublet, J≃6.5 c.p.s.) for the C-2 methyl, 8.31 τ (broad) for the C-4 methyl, 6.41 τ (singlet) for the ester methyl, 5.31 τ (broad) for the C-5 terminal methylene hydrogens and at the region of 7.20 τ to 8.10 τ (multiplet) for the C-2 and C-3 hydrogens.

Anal. Calcd. for $C_8H_{14}O_2$: C, 67.57; H, 9.93. Found: C, 67.42; H, 10.14.

Thermal rearrangement of methyl trans-1-methyl-2-ethyl-1-cyclopropanecarboxylate (33) at 280°

A sample of 0.5 ml of 33 in a sealed N. M. R. tube was heated at 280° for 18 hr. Analysis by V. P. C. using a 20'x1/4" diethylene glycol succinate column at 153° with helium flow rate of 35 ml per min gave a trace amount of 33, 17.5% of methyl cis-2-methyl-4-hexenoate (68) and 82.5% of methyl trans-2-methyl-4-hexenoate (69) with retention times of 18.5, 23.1 and 26.1 min respectively.

Methyl cis-2-methyl-4-hexenoate (68): b. p. 164.5°, n_D^{26} 1.4261. It showed a carbonyl band at 1737 cm^{-1}. The N. M. R. spectrum shows the C-2 methyl at 8.88 τ (doublet, J≃6.3 c.p.s.), the C-5 methyl at 8.39 τ (doublet, J≃5.7 c.p.s.), the ester methyl at 6.40 τ (singlet), the C-2 and C-3 hydrogens at 7.35 τ to 8.05 τ (multiplet) and the olefinic hydrogens at 4.25 τ to 4.95 τ (multiplet).

Anal. Calcd. for $C_8H_{12}O_2$: C, 67.57; H, 9.93. Found: C, 67.33; H, 9.97.

Methyl trans-2-methyl-4-hexenoate (69): b. p. 161°, n_D^{26} 1.4225. It showed two I. R. bands at 1736 cm^{-1} and 973 cm^{-1} due to the carbonyl and C-H out-of-plane stretching vibrations respectively. The N. M. R. spectrum shows the C-2 methyl at 8.96 τ (doublet, J≃6.5 c.p.s.), the C-5 methyl at 8.36 τ (doublet, J≃4.7 c.p.s.) the ester methyl at 6.41 τ (singlet), the C-2 and C-3 hydrogens at 7.50 τ to 8.10 τ (multiplet) and the olefinic hydrogens at 4.50 τ to 5.00 τ (multiplet).

Anal. Calcd. for $C_8H_{12}O_2$: C, 67.57; H, 9.93. Found: C, 67.36; H, 10.00.

Thermal rearrangement of methyl 2,2-dimethyl-1-cyclopropane-carboxylate (35) at 258°

A sample (0.5 ml) consisting of 85% of 35 and 15% of methyl cis-4-methyl-2-pentenoate (44) in a sealed N. M. R. tube was heated at 258° for 50 hr . Product analysis by V. P. C. using a 20'x3/8" dinonylphthalate column at 155° with helium flow of 85 ml per min showed three peaks at 14.7, 18.9 and 23.3 min respectively. The first peak was the starting material (<5%), the second and the third peaks with a ratio of ~85:15 were characterized to be methyl 4-methyl-4-pentenoate (70) and methyl 4-methyl-3-pentenoate (102).

Methyl 4-methyl-4-pentenoate (70): b. p. 149°, n_D^{23} 1.4230. Its N. M. R. spectrum shows four singlets at 8.25 τ (broad) for the C-4 methyl, 7.64 τ for the C-2 and C-3 methylene hydrogens, 6.35 τ for the ester methyl and 5.20 τ (broad) for the C-5 terminal methylene hydrogens.

Anal. Calcd. for $C_7H_{12}O_2$: C, 65.49; H, 9.45. Found: C, 65.67; H, 9.53.

Methyl 4-methyl-3-pentenoate (102): its N. M. R. spectrum is identical to that isolated from the thermal isomerization of methyl cis-4-methyl-2-pentenoate (44) as discussed later (p.100).

Thermal rearrangement of methyl trans-1,2-dimethyl-1-cyclopropane-carboxylate (18) at 300°

A sample of 0.5 ml of 18 in a sealed N. M. R. tube was heated at 300° for 18 hr. Product analysis by V. P. C. using a 10'x1/4" dinonylphthalate column at 140° with helium flow of 35 ml per min showed that 18 had rearranged almost quantitatively to methyl 2-methyl-4-pentenoate (31) (99%).

Methyl 2-methyl-4-pentenoate (31): b. p. 137.5°, n_D^{22} 1.4156. It showed N. M. R. peaks at 6.49 τ (singlet) for the ester methyl, 8.97 τ (doublet, J≅6.5 c.p.s.) for the C-2 methyl, 7.35 τ to 8.10 τ (multiplet) for the C-2 and C-3 hydrogens, 5.05 τ and 5.26 τ (both multiplet) for the terminal hydrogens and 4.15 τ to 4.85 τ (multiplet) for the C-4 olefinic hydrogen.

Anal. Calcd. for $C_7H_{12}O_2$: C, 65.49; H, 9.45. Found: C, 65.68; H, 9.57.

Thermal rearrangement of methyl trans-2,3-dimethyl-1-cyclopropane-carboxylate (36) at 258°

Three hundred microliters of 36 was heated at 258° for 50 hr in a sealed N. M. R. tube. Vapor phase chromatography of product using a 10'x1/4" dinonylphthalate column at 150° with helium flow of 35 ml per min gave methyl 3-methyl-4-pentenoate (71) and unchanged 36 in a ratio of 90:10 with retention times of 12.5 and 14.4 min respectively.

Methyl 3-methyl-4-pentenoate (71): b. p. 137.5°, n_D^{24} 1.4152.

Its N. M. R. spectrum shows the C-3 methyl at 8.97 τ (doublet, J≅5.3 c.p.s.), the ester methyl at 6.41 τ (singlet), the C-2 methylene hydrogens one at 7.79 τ (doublet, J≅8.6 c.p.s.) and the other at 7.76 τ (doublet, J≅5.8 c.p.s.), the C-3 hydrogen at 7.35 τ (multiplet) and the three olefinic hydrogens at 5.18 τ, 4.95 τ and 4.22 τ (all multiplets).

Anal. Calcd. for $C_7H_{12}O_2$: C, 65.49; H, 9.45. Found: C, 65.58; H, 9.45.

Thermal rearrangement of methyl cis-2-methyl-1-cyclopropane-carboxylate (37) at 294°

A sample (2 ml) containing 28.2% of 37 and 71.8% of methyl trans-2-methyl-1-cyclopropanecarboxylate (16) (100 Mc N. M. R. spectrum of the high field region of this mixture is shown in Figure 16A) in a sealed tube was heated at 294° for 18 hr to give two components H and J in the ratio of ~1:3. They were separated by V. P. C. using a 10'x1/4" Ucon polar column at 92° with helium flow at 50 ml per min with retention times of 16.8 and 19.7 min respectively.

Component H: b. p. 125.5°, n_D^{22} 1.4148. It was assigned the structure of methyl 4-pentenoate (72) on the basis of its N. M. R. spectrum which shows three singlets at 7.67 τ, 7.62 τ and 6.45 τ and three sets of multiplets at 5.08 τ, 4.84 τ and 4.09 τ.

Anal. Calcd. for $C_6H_{10}O_2$: C, 63.11; H, 8.84. Found: C, 62.90; H, 8.81.

Component J: b. p. 130.5°, n_D^{25} 1.4195. It was assigned the

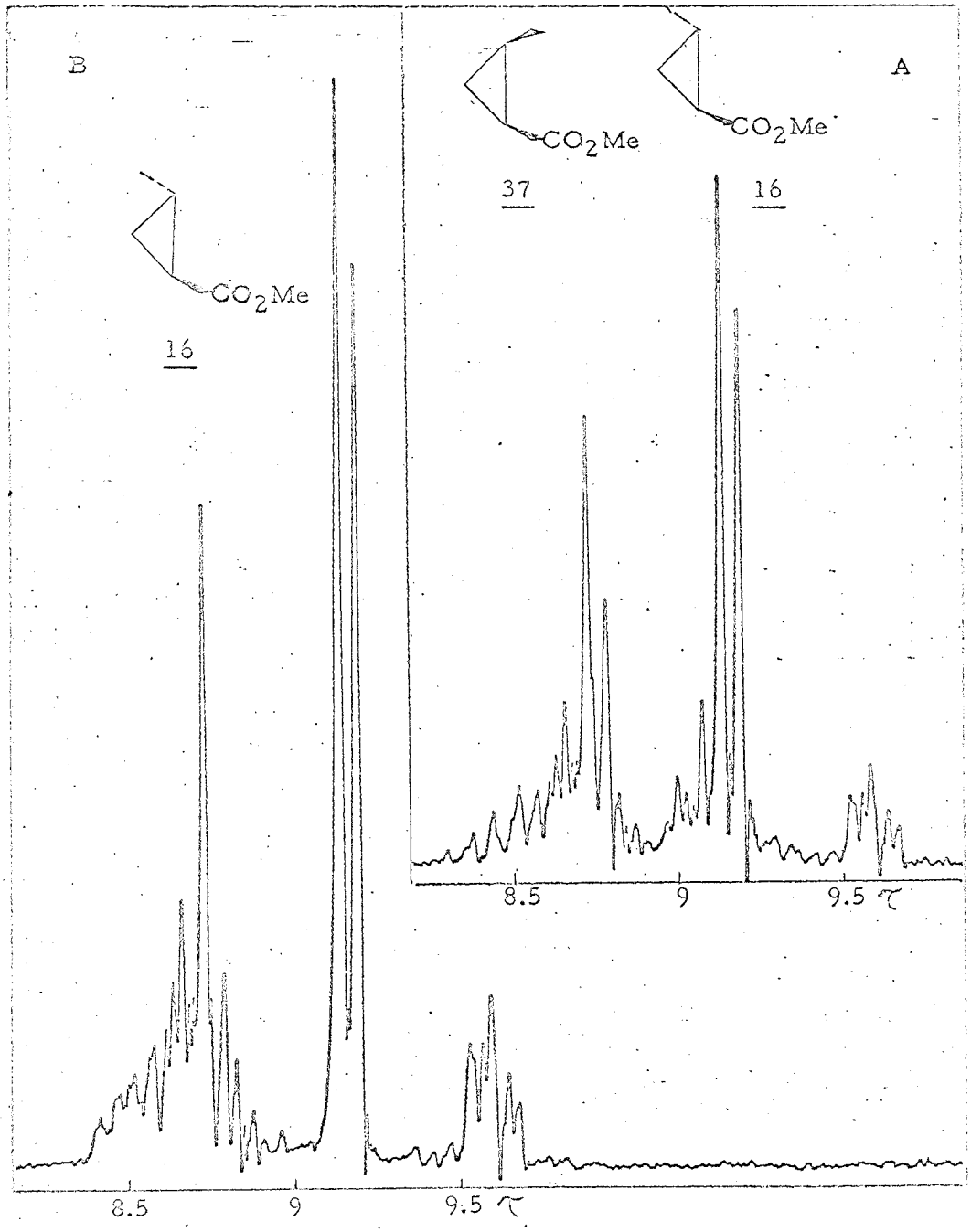


FIGURE 16-A. 100 Mc N. M. R. spectrum of mixture of 37 and 16

B. 100 Mc N. M. R. spectrum of 16

structure of methyl trans-2-methyl-1-cyclopropanecarboxylate (16) on the basis that it did not rearrange on heating (5 hr at 294°). The 100 Mc N. M. R. spectrum of the high field region of 16 is shown in Figure 16B.

Anal. Calcd. for $C_6H_{10}O_2$: C, 63.11; H, 8.84. Found: C, 63.40; H, 8.62.

Thermal rearrangement of methyl cis, trans-1,2,3-trimethyl-1-cyclopropanecarboxylate (38) at 280°

Six hundred microliters of 38 in a sealed N. M. R. tube was heated at 280° for 12 hr. Product analysis by V. P. C. using a 20' x 3/8" didecylphthalate column at 168° with helium flow at 85 ml per min gave 5% unchanged 38 and 95% of methyl 2,3-dimethyl-4-pentenoate (73) with retention times of 25,7 and 24.0 min respectively.

Methyl 2,3-dimethyl-4-pentenoate (73): b.p. 151.5°, n_D^{23} 1.4212. The N. M. R. spectrum shows peaks at 9.01 τ (doublet, J≃6.6 c.p.s.) for the C-2 methyl, 8.94 τ (doublet, J≃6.7 c.p.s.) for the C-3 methyl, 7.64 τ (multiplet) for the C-2 and C-3 methine hydrogens, 6.38 τ (singlet) for the ester methyl, 5.14 τ, 4.92 τ and 4.31 τ (all multiplets) for the three olefinic hydrogens.

Anal. Calcd. for $C_8H_{14}O_2$: C, 67.57; H, 9.93. Found: C, 67.47; H, 9.91.

Attempted thermal rearrangement of methyl trans-2-alkyl-1-cyclopropanecarboxylates

Samples of several methyl trans-2-alkyl-1-cyclopropanecarboxylates, in sealed N. M. R. tubes, were heated at temperatures above 250° and V. P. C. and N. M. R. analyses showed no rearrangement occurred. These methyl trans-2-alkyl-1-cyclopropanecarboxylates are listed below with temperature of reaction and the length of heating in brackets: methyl cis-1-methyl-2-ethyl-1-cyclopropanecarboxylate (34) (280°, 18 hr), methyl cis-1,2-dimethyl-1-cyclopropanecarboxylate (17) (300°, 18 hr), methyl trans-2-methyl-1-cyclopropanecarboxylate (16) (294°, 23 hr) and methyl cis,cis-1,2,3-trimethyl-1-cyclopropanecarboxylate (39) (280°, 12 hr).

Attempted thermal rearrangement of cis- and trans-1,2-dimethyl--1-cyanocyclopropane (41 and 40) at 258°

Samples of 41 and 40 in sealed N. M. R. tubes were heated at 258° for 17 hr. No rearrangement occurred to either compound as indicated by both V. P. C. and N. M. R. analyses.

Kinetic studies of the thermal rearrangement of cyclopropanes

The kinetics of the thermal rearrangement of methyl cis-2-alkyl-1-cyclopropanecarboxylates to their corresponding γ,δ-unsaturated esters had been studied at various temperatures ranging from 240° to 300°. For each kinetic run, 10 to 15 samples were heated at a desired temperature in sealed tubes. The samples, 7 ml each were placed in pyrex tubes, 120 mm x 4 mm O. D. (the volume of each tube was approximately

0.5 ml) and sealed at atmospheric pressure. They were removed at various time intervals and quenched by cooling with ice water and analysed by V. P. C. All kinetic runs were followed to at least 70% completion. They gave good first-order kinetics and rate constants were obtained from first-order plots. The heats of activation and entropies of activation were obtained by graphical presentation of the temperature dependence of rate constant (see text). The results are summarized in Table V (p. 34).

The furnace used for the heating of the samples was a vertical cylindrical induction furnace. Sample tubes were placed inside the metal cylinder which was heated to the desired temperature by the heating coil around it. The electrical input to the heating coil was controlled by an input controller (Temcometer, trade name of the thermo Electric Co.). The temperature inside the furnace was maintained to $\pm 0.5^{\circ}$ of the desired temperature which was observed by a thermomter placed in the same level as the sample tubes. The thermometer, 400 mm length, -10° to $+400^{\circ}$ range with 1° subdivision, had been corrected, from 240° to 340°, against a standard thermometer (Fisher 2C4131, National Bureau of Standard Calibrated).

The chromatographic unit used was an Aerograph Model A-90-P with thermal conductivity detector. The columns and analysis conditions were different for each of the cyclopropane-γ,δ-olefin system as has been noted earlier under the thermal rearrangement of cyclopropanes.

Chromatograms were recorded on a Honeywell Model Electronik 15 graphic recorder and were converted to digital data by peak area determination using a disc chart integrator. The response of the detector to the cyclopropanes and their γ,δ-olefins had been determined by analyzing 1:1 and/or 2:1 mixtures of the two species and was found to be accurate to less than ±1%.

All samples of cyclopropanes and γ,δ-olefins used for the kinetic studies and the determination of the response of the detector had been purified by V. P. C. to better than 99.9% purity.

Preparation of methyl 2,4-dimethyl-3-pentenoate (101)

A sample of 2 ml of methyl cis-2,4-dimethyl-2-pentenoate (42) in a sealed tube (220 mm x 6 mm I. D.) was heated at 281° for 5 days. Vapor phase chromatography (10' x 1/4" dinonylphthalate column at 160° with helium flow of 35 ml per min) analysis showed that 90% of 42 isomerized to 101.

Methyl 2,4-dimethyl-3-pentenoate (101): b. p. 159.5°, n_D^{27} 1.4280. The N. M. R. spectrum shows the C-2 methyl at 8.84 τ (doublet, J ≃ 7.1 c.p.s.), the C-4 methyls at 8.34 τ and 8.28 τ (both doublet, J ≃ 1.4 c.p.s.), the ester methyl at 6.38 τ (singlet), the C-2 methine hydrogen at 6.76 τ (multiplet) and the C-3 olefin hydrogen at 4.89 τ (multiplet).

Anal. Calcd. for $C_8H_{14}O_2$: C, 67.57; H, 9.93. Found: C, 67.74; H, 9.92.

Preparation of methyl 4-methyl-3-pentenoate (102)

A sample of 1 ml of methyl cis-4-methyl-2-pentenoate (44) in a sealed tube was heated at 294° for 3 hr. Vapor phase chromatography (10' x 1/4" dinonylphthalate column at 160°, helium flow of 35 ml per min) of the product showed more than 97% of 44 isomerized to 102.

Methyl 4-methyl-3-pentenoate (102): b. p. 153.5°, n_D^{22} 1.4298 (lit. (91), b.p. 145-8° at 640 mm, n_D^{25} 1.4302). It showed N. M. R. peaks at 8.37 τ and 8.26 τ (both broad) for the C-4 methyls, 6.40 τ (singlet) for the ester methyl, 7.08 τ (doublet, J ≃ 7.2 c.p.s.) for the C-2 methylene hydrogens and 4.75 τ (multiplet) for the C-3 olefin hydrogen.

Anal. Calcd. for $C_7H_{12}O_2$: C, 65.59; H, 9.44. Found: C, 65.49; H, 9.55.

Preparation of methyl trans-2-methyl-3-pentenoate (103)

One milliliter of methyl cis-2-methyl-2-pentenoate (46) in a sealed tube was heated at 294° for 85 hr. Product analysis by V. P. C. using a 10' x 1/4" dinonylphthalate column at 152° with helium flow at 35 ml per min gave 18% of the starting olefin 46, 40% of methyl trans-2-methyl-pentenoate (47) and 42% of 103.

Methyl trans-2-methyl-3-pentenoate (103): b. p. 140°, n_D^{23} 1.4217 (lit. (3), b.p. 139, n_D^{23} 1.4229). The I. R. bands at 1734 cm^{-1} and 971 cm^{-1} are consistent with the structure of 103. The N. M. R. spectrum showed the C-2 methyl at 8.31 τ (doublet with fine splitting), the ester methyl at 6.39 τ (singlet), the C-2 methine hydrogen at 7.00 τ

(multiplet) and the olefinic hydrogens at 4.51 τ (multiplet).

Anal. Calcd. for $C_7H_{12}O_2$: C, 65.59; H, 9.44. Found: C, 65.77; H, 9.68.

Preparation of methyl trans-3-pentenoate (94)

A sample of 500 μl of methyl cis-2-pentenoate (48) in a sealed tube was heated at 270° for 50 hr. Analysis by V.P.C. using a 20' x 3/8" dinonylphthalate column at 150° with helium flow of 50 ml per min gave 48, methyl trans-2-pentenoate (49) and 94 in the ratio of 8:40:52.

Methyl trans-3-pentenoate (94): b.p. 131°, n_D^{24} 1.4196 (lit. (2), b.p. 136°, n_D^{21} 1.4220). The N.M.R. spectrum of 94 is identical to that reprted by McGreer et.al. (2).

Thermal isomerization, equilibration and kinetic studies of olefins

The apparatus, general procedure and composition analysis were similar to those employed for the cyclopropanes as described earlier in this thesis. Equilibration was considered reached when the percent composition remained constant for a considerable length of time. First-order kinetics was observed for the isomerization of methyl cis-4-methyl-2-pentenoate (44) and methyl cis-2,4-dimethyl-2-pentenoate (42) to methyl 4-methyl-3-pentenoate (102) and methyl 2,4-dimethyl-3-pentenoate (101) respectively. Their rate constants, heats of activation and entropies of activation were determined as discussed in the text.

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APPENDIX

The rate constants reported in Table X and XI for the thermal isomerization of cis α,β-unsaturated esters to their β,γ isomers were determined by disregarding all other slow steps (see text). Such a method shows slight deviation from the value obtained through calculation by taking into account all the possible steps. The thermal isomerization can be represented as follows;

$$T \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} C \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} \beta$$

where T = trans α,β isomer, C = cis α,β isomer and β = β,γ isomer. The rate equation for the formation of β,γ isomer is

$$d\beta/dt = k_2 C - k_{-2}\beta$$

or, letting $C = 1 - \beta - T = 1 - \beta$ (T is small) and $\frac{k_2}{k_{-2}} = 53.9$ (ratio of β,γ isomer to cis α,β isomer at equilibrium for the system 44 and 102)

$$d\beta/dt = k_2\left(1 - \frac{54.9}{53.9}\beta\right)$$

On integration it gives

$$k_2 = -2.303 \times \frac{53.9}{54.9} \log \frac{1}{1 - \frac{54.9}{53.9}\beta}$$

Therefore for the thermal isomerization of 44 to 102, k_2 is found to be 7.222×10^{-5} sec^{-1} (run 56), and for 42 to 101, k_2 equals to 3.021×10^{-5} sec^{-1} (run 51). The deviations are only 2.2% and 1.4% respectively, which are within experimental errors.