PYROLYSIS OF A TETRAMETHYLBICYCLO[1.1.0]BUTANE

A THESIS

PRESENTED FOR THE DEGREE

OF

MASTER OF SCIENCE

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by

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Department of Organic Chemistry

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CONTENTS

(i)

Statement.

The work described in this thesis incorporates

no material previously submitted for a degree

in any University, except where due reference

has been made.

(C.F.BURRIDGE)

(ii)

Publications.

Some of the work described in this thesis has been
published in the following paper:-

Methyl 2,2,4,4-tetramethylbicyclo[1.1.0]butane-1-
carboxylate.

Burridge, C.F., and Hamon, D.P.G., Chem.Comm.,
1968, 4, 206.

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(iii)

Acknowledgements.

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Summary.

The vapour phase pyrolysis of methyl 2,2,4,4-tetramethylbicyclo[1.1.0]butane-1-carboxylate has been investigated. The major pyrolysis products have been characterised and possible mechanisms for their formation suggested.

Attempts to prepare 1,3-dibromo-1,2,2,4,4-pentamethylcyclobutane for possible intramolecular cyclisation to 1,2,2,4,4-pentamethylbicyclo[1.1.0]butane have been unsuccessful.

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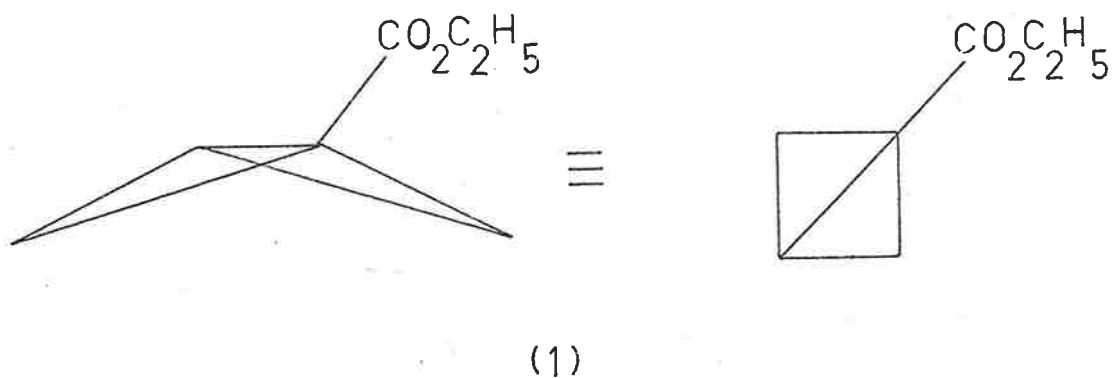
PART I

THE PYROLYSIS OF

METHYL 2,2,4,4-TETRAMETHYLBICYCLO[1.1.0]BUTANE-1-CARBOXYLATE.

Introduction.

The report by Wiberg and Cuila[1] of the first authentic bicyclo[1.1.0]butane derivative, namely ethyl bicyclo[1.1.0]butane-1-carboxylate (1), has stimulated interest in the synthesis and chemistry of these highly strained molecules.*

$$CO_2C_2H_5 \equiv CO_2C_2H_5$$

(1)

One aspect of particular interest has been centred upon the mechanism or mechanisms of the thermal rearrangements of bicyclo[1.1.0] butane and its derivatives. A question which has often been asked concerning bicyclo[1.1.0]butanes is, "what are the relative bond dissociation energies of the central and side bonds?"[2]

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* For excellent discussions regarding the synthesis, structure, and properties of bicyclo[1.1.0]butane and some of its derivatives see reviews by Wiberg and co-workers[2,3] and Pomerantz and Abrahamson.[4]

Molecular orbital studies indicate that the central carbon-carbon bond

is   stronger than the peripheral* bonds, but it is difficult to

make an a priori argument concerning this question. A possible way in

which to gain information about this problem is to examine the thermal

rearrangements of bicyclo[1.1.0]butane and its derivatives. The thermal

rearrangement of bicyclo[1.1.0]butane itself occurs at temperatures

in the vicinity of 200° and gives only butadiene.[2] The latter may be

formed by one or all of three pathways: (1) in a concerted fashion

[Scheme 1, eqn. (a)], (2) one involving a cyclopropylmethyl diradical

[Scheme 1, eqn. (b)], or (3) one involving cyclobutene as an inter-

mediate [Scheme 1, eqn. (c)].

If the reaction is a concerted one [Scheme 1, eqn. (a)], it

may proceed in any one of six ways. Firstly the ring opening may lead

to either a cis- or trans-butadiene (Scheme 2). Secondly, for each of
    processes,
these/three different modes of ring opening can be envisaged. Scheme

3 shows the situation for a symmetrically substituted bicyclo[1.1.0]

butane (2) opening to a trans-butadiene. Firstly, rotation may occur

so that both exo-groups (R) rotate toward the bonds being broken

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* If the bicyclo[1.1.0]butane system is considered as two

equilateral triangles having one common edge,[4] the four remaining

sides of these triangles form the peripheral bonds.

Scheme 1.

cis or trans ------- (a)

cis or trans ------ (b)

H transfer

H transfer ------- (c)

cis or trans

Scheme 2.

cis
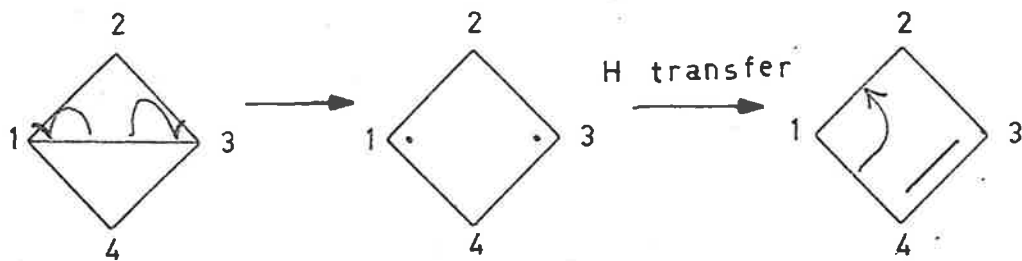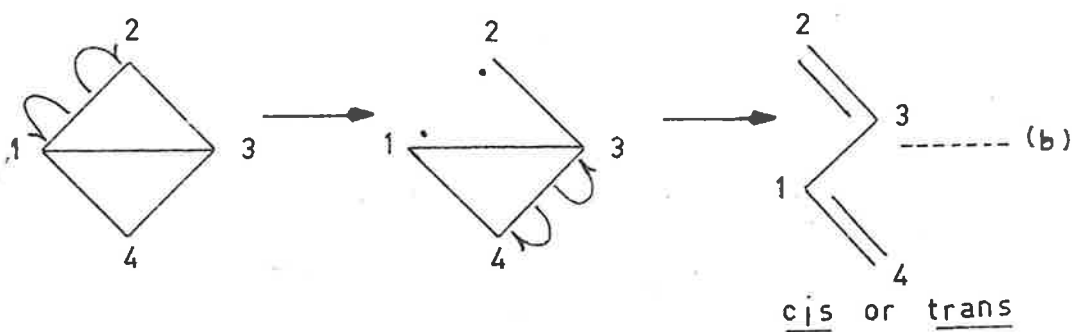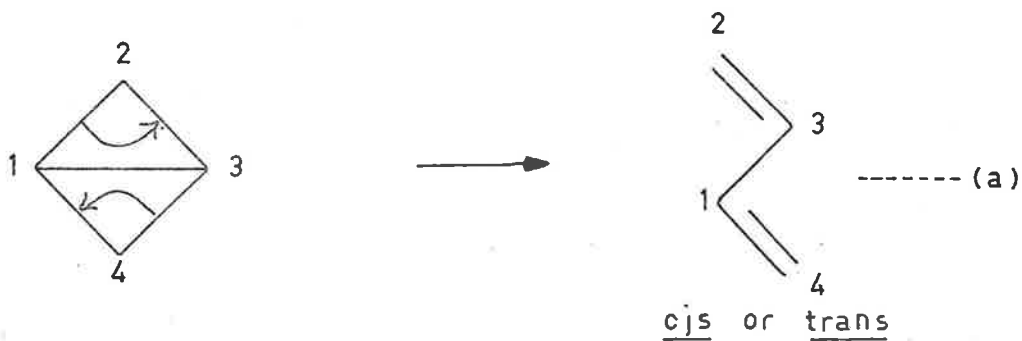
trans
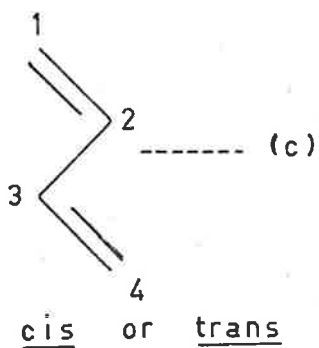
* $\nearrow\!\!\!\!\!+\!\!\!+$ indicates a bond being broken.
**   indicates movement of groups for Schemes 2 and 3.

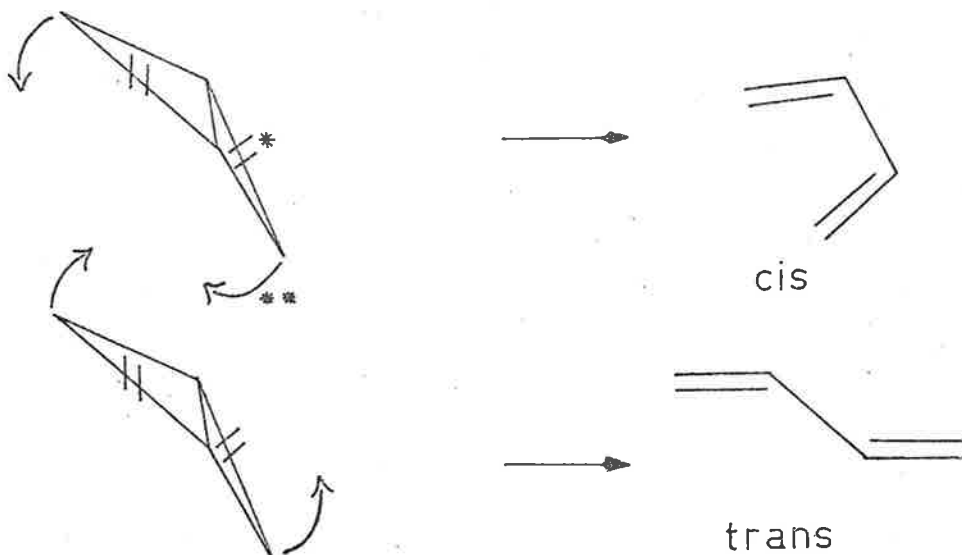(Scheme 3; mode A); secondly, rotation may occur so that both exo-groups move away from the bonds being broken (Scheme 3, mode B); and thirdly, one exo-group may move toward and the other away from the bonds being broken (Scheme 3, mode C). Corresponding modes can be drawn for the opening of substituted bicyclo[1.1.0]butanes to the corresponding cis-butadiene derivative.

One of the most important advances in the understanding of ring opening and ring closure reactions has been the rules put forward by Woodward and Hoffmann.[5] On application of these rules to the ring opening of the bicyclo[1.1.0]butane system, it can be seen that in a concerted reaction to s-trans-butadiene mode A corresponds to a quasi-conrotatory[6] opening of both rings, whilst mode B requires a quasi-disrotatory opening of both rings. In mode C one ring is

Scheme 3.
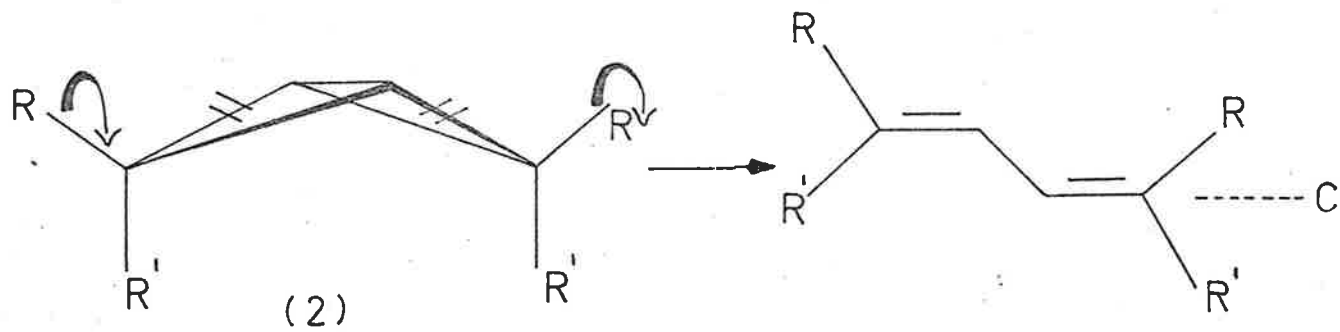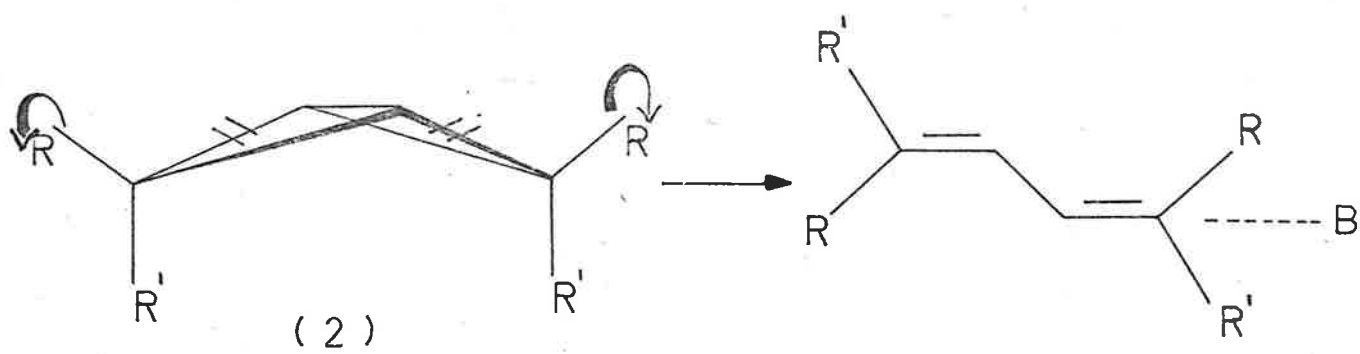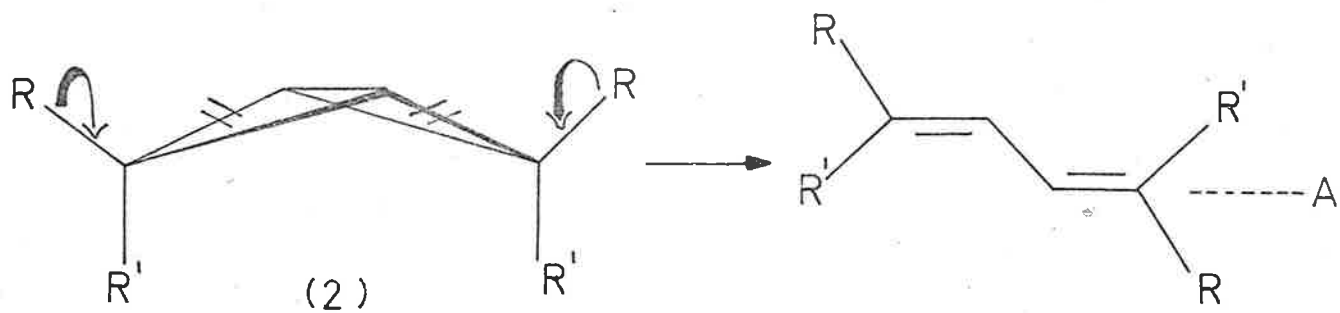
opened in a disrotatory fashion and the other in a conrotatory fashion. For modes A and B conservation of orbital symmetry requires high energy transition states. Thus on the basis of the Woodward-Hoffmann rules[7] a thermal opening via these modes is expected to be energetically unfavourable. By contrast correlation diagrams with symmetry orbitals cannot be constructed for mode C.[7] However on the basis of molecular orbital calculations Wiberg has predicted that for a concerted ring opening mode C will be energetically favourable but modes A and B will not.[3]

In order to gain experimental information about the mode of ring opening of bicyclo[1.1.0]butanes Closs and Pfeffer[6] studied the vapour phase pyrolyses of some methyl substituted bicyclo[1.1.0] butanes. Their results are summarised in Scheme 4, the major pyrolysis products only being shown in each case. Closs and Pfeffer considered two possible interpretations of their experimental findings: (1) that the ring opening process is a concerted one, in which case the predominantly formed dienes are those expected from opening via an unsymmetrical mode (i.e. corresponding to mode C of Scheme 3) as predicted,[3,7] and (2), that the results are consistent with a non-concerted ring opening [corresponding to Scheme 1, eqn. (b)]. However this/process could only operate if it is assumed that the intermediate cyclopropylmethyl diradicals resulting from the opening of the dimethylbicyclo[1.1.0]butanes (3) and (4) collapse into the
latter

Scheme 4.
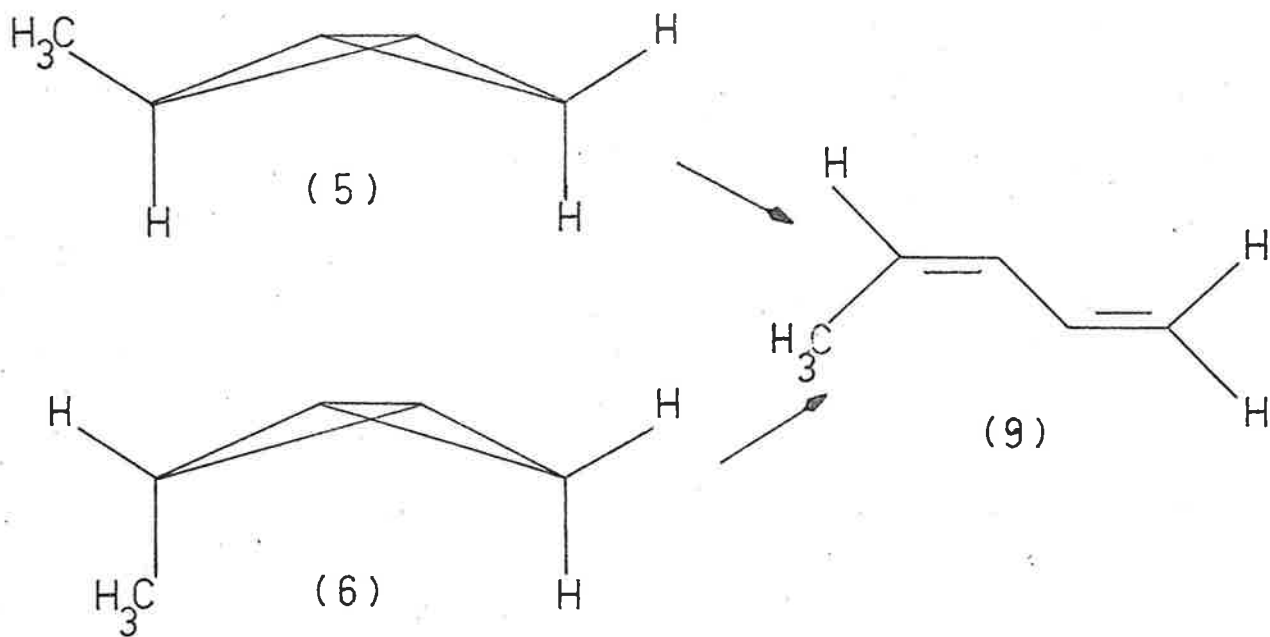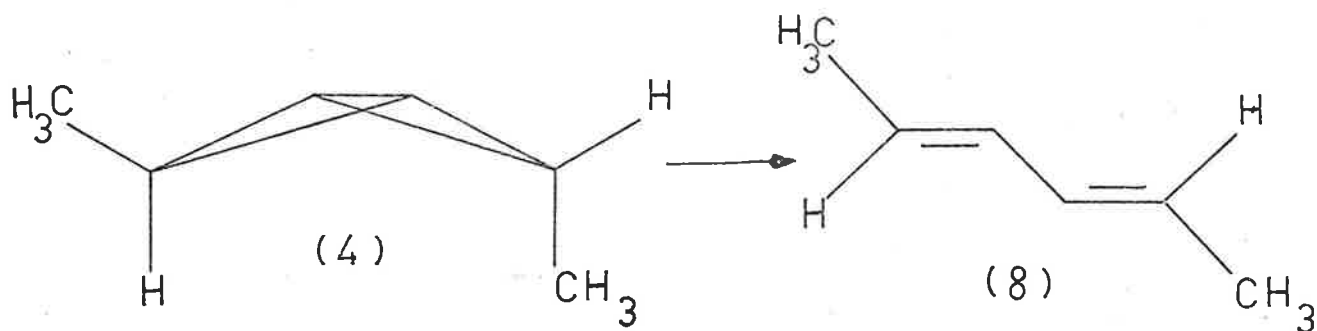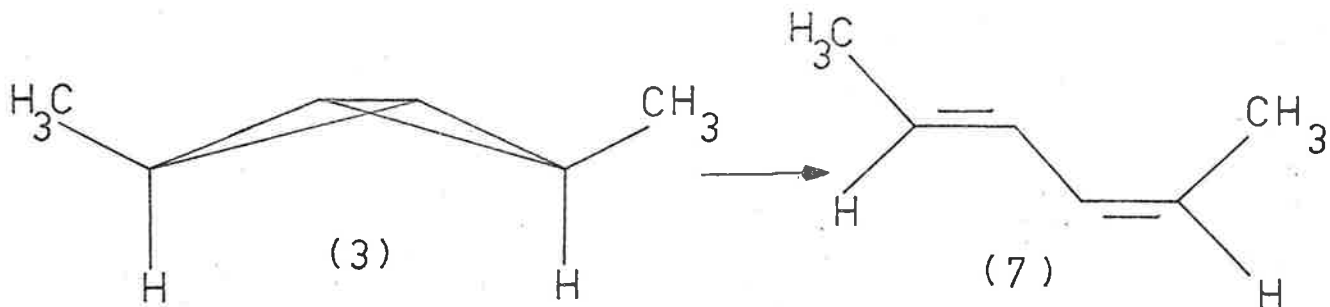
dienes (7) and (8) respectively before rotamer equilibrium is achieved, while the intermediate diradicals derived from the monomethyl derivatives (5) and (b) are required to have a longer lifetime to account for the observed equilibration to (9). The authors considered that the concerted process accommodated their results more satisfactorily.

It is significant also that on the basis of their results Closs and Pfeffer were able to effectively eliminate the third mechanism for the ring opening of bicyclo[1.1.0]butanes, viz. rearrangement to cyclobutene followed by ring opening* to butadiene [Scheme 1, eqn. (c)]. The authors found that the overall stereochemical course of this process corresponds to either of modes A or B, but not C of Scheme 3. Thus on the basis of the Woodward-Hoffmann rules ring opening via a cyclobutene intermediate will not be energetically favourable,[7] although molecular orbital calculations[3] do not rule out the possibility of isomerisation occurring via this pathway. This conclusion (that isomerisation occurring via a cyclobutene intermediate will not be energetically favourable) is supported by a great deal of experimental evidence.[8-12]

However, despite these considerations, the possibility that special substitution patterns may bring to light reactions occurring by any one of the pathways which are not allowed on the basis of the

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*   Expected to be conrotatory on the basis of the Woodward-Hoffmann rules.[7]

Woodward-Hoffmann rules,[5] and other theoretical considerations,[3,4] cannot be dismissed. For example, the observed thermal equilibration of the <u>exo</u>,<u>exo</u> form of the highly substituted bicyclo[1.1.0]butane (10) to its <u>endo</u>,<u>endo</u> form (11).[13] (Scheme 5.)

<u>Scheme 5.</u>

(10)
<u>exo</u>, <u>exo</u>

(10a)

(11)
<u>endo</u>, <u>endo</u>

* Ph denotes
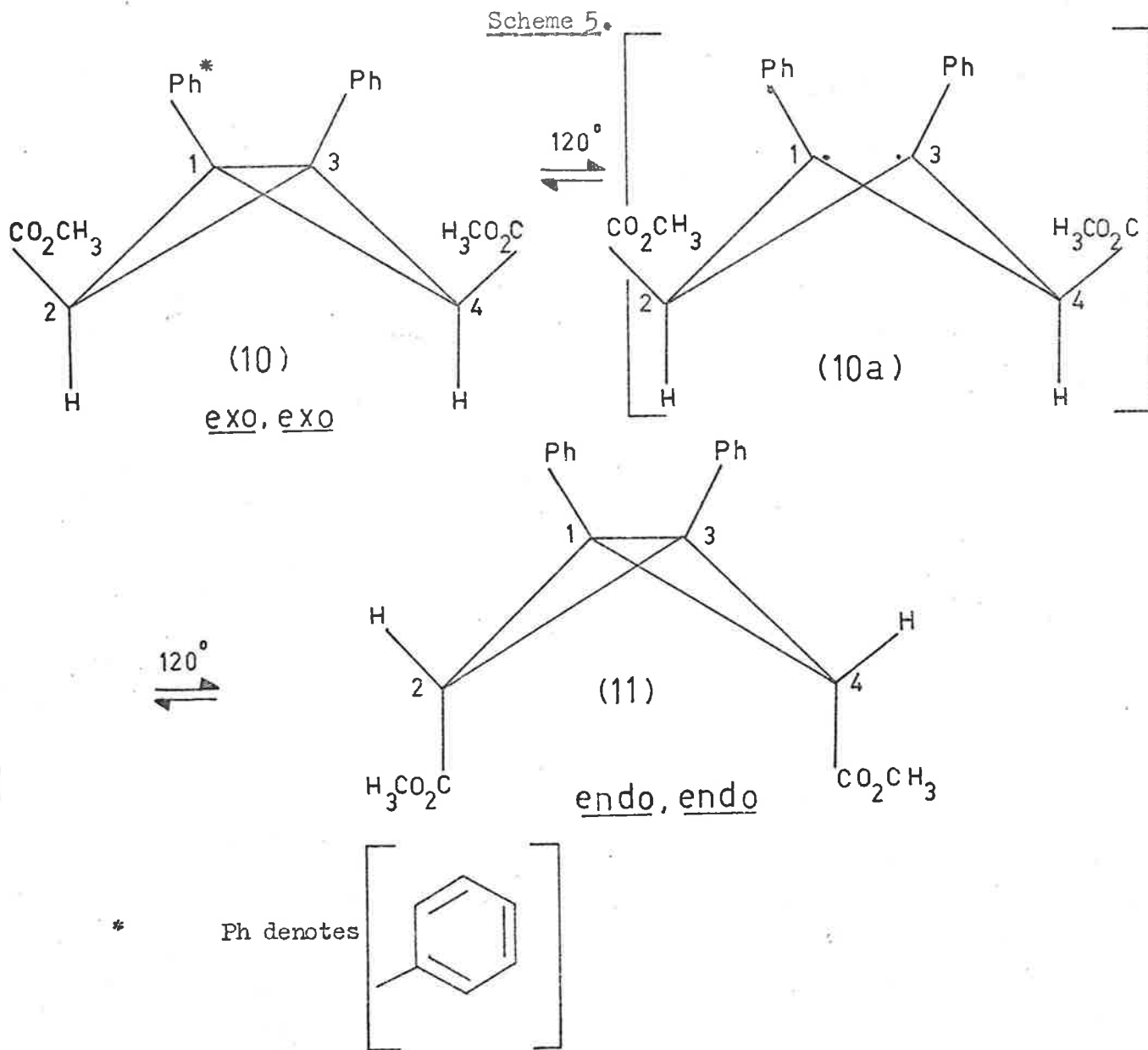
This thermal isomerisation can only readily be envisaged as occurring by the breakage and reconstruction of the central 1,3-bond, a possible intermediate in the isomerisation being the diradical (10a). Despite this experimental fact theoretical considerations,[3,4,5] (based on models of unsubstituted bicyclo[1.1.0]butanes), indicate that it would be a most unlikely process.

Since the substituted bicyclo[1.1.0]butane derivative (12) was available from previous work[14] it was hoped that a study of the vapour phase pyrolysis of this compound would provide additional information about the mechanism or mechanisms of the thermal rearrangements of compounds belonging to the bicyclo[1.1.0]butane series.

(12)
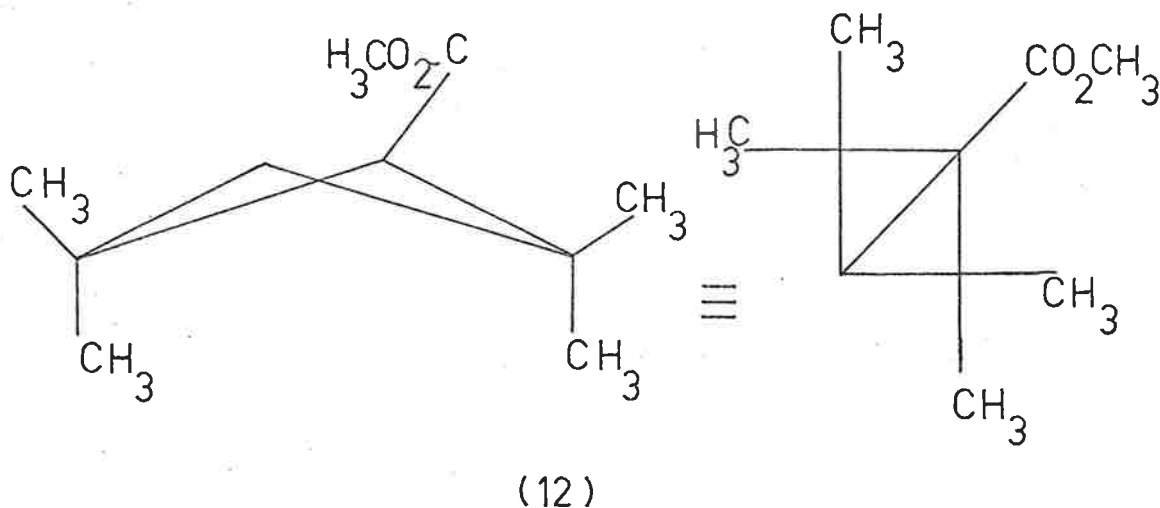
Discussion.

(a)   Synthesis of methyl 2,2,4,4-tetramethylbicyclo[1.1.0]butane-
1-carboxylate (12).

Although the bicyclo[1.1.0]butane derivative (12) had been
prepared previously[14] as shown in Scheme 6, route (a), it was decided
to reinvestigate the reaction sequence involved in its preparation
in an attempt to improve the overall yield. Most of the steps except
the oxidation of the primary alcohol (17) to its corresponding acid
(18), proceeded in satisfactory yields. Under the reaction condi-
tions[15] two products, the expected acid (18) and a second (13) thought
to be the ester[16] of unchanged alcohol (17) and the acid (18), were

(13)
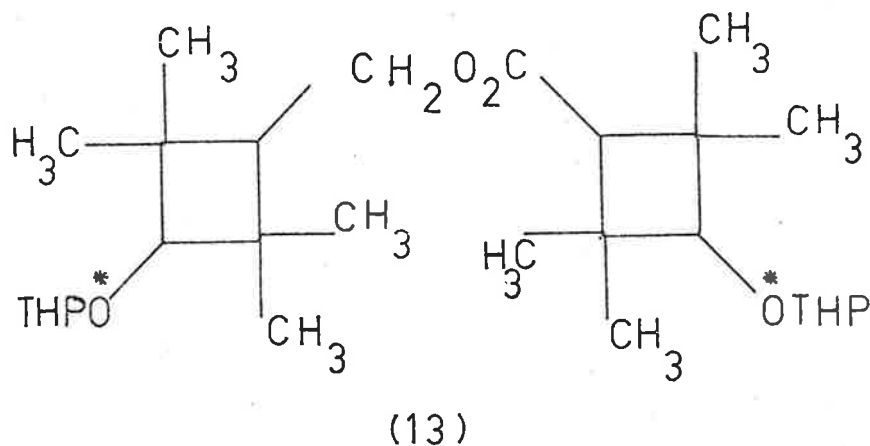
*   This denotes the tetrahydropyranyloxy moiety.
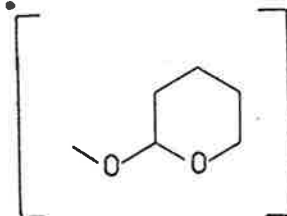
obtained.* It was decided to carry out the oxidation step under a number of different conditions in an attempt to improve the yield of the desired acid.

Using Jones' reagent[18] as the oxidant a series of oxidations with increasing dilution of the alcohol (17), (down to a .05% solution in the solvent acetone), were carried out. However no substantial reduction in the yield of unwanted ester (13) was observed. Similarly, oxidations carried out according to the method of Sarett[19] (chromium trioxide and pyridine), and a method described by Snatzke,[20] (viz. chromium trioxide, N,N-dimethylformamide, and a few drops of conc. sulphuric acid) gave approximately the same proportions of acid and ester as had been observed previously.[16]

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* An analogous product (13a) was observed by Sinclair[17] on attempting the oxidation of (14), which is the dioxalane analogue of the alcohol (17).
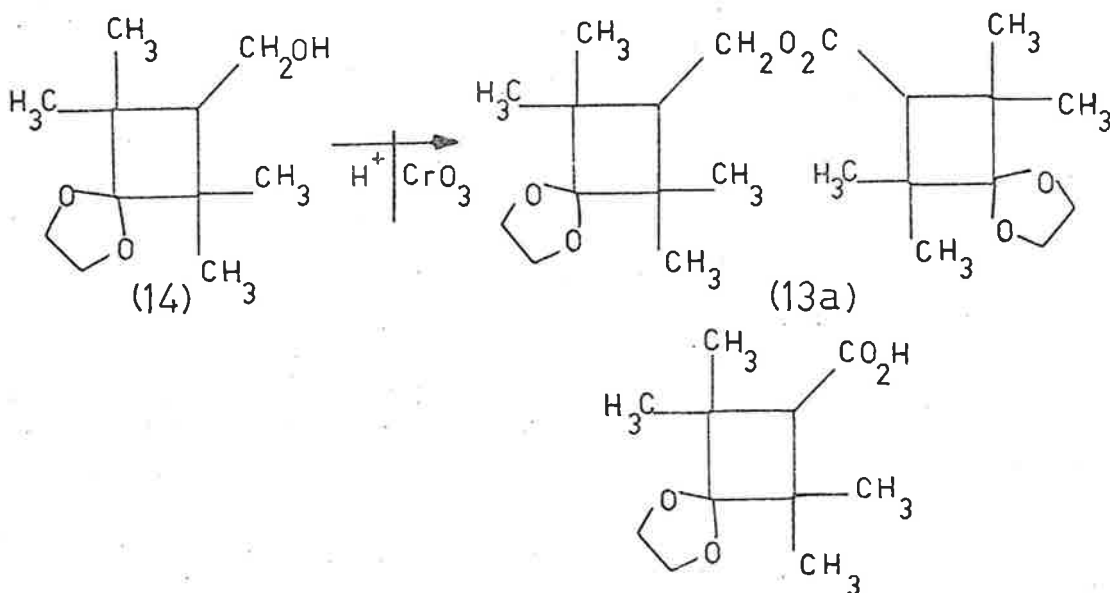
Since the yield of acid (18) could not be improved, a second sequence (Scheme 6, route [b]) eliminating this step was devised.

The enol ether (21) was obtained after a number of unsuccessful attempts using the procedure described previously,[21] viz. phenyl lithium and methoxymethyltriphenylphosphonium chloride to generate the desired phosphorane. A single modification was the dissolution of the ketone (15) in anhydrous hexane* rather than anhydrous ether which was the solvent previously employed. In general a low yield of product (20-50%) was obtained together with unchanged starting material. Improved yields were obtained when the phosphorane was generated by the addition of sodium hydride powder to a stirred suspension of the phosphonium salt in ether, containing a catalytic amount of dimethyl-sulphoxide. However the third method, viz. generation of the required phosphorane by the addition of butyl lithium in hexane to a stirred suspension of the phosphonium salt in hexane** gave the highest yields and was by far the most convenient.

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*   All solvents used in this Wittig reaction were deoxygenated (see Experimental).

**   It did appear that this particular phosphorane was more stable in hexane than in ether.

Scheme 6.

(a)

$$Ph_3P = CH_2$$

(15) $\xrightarrow{Ph_3P=CH_2}$ (16) $\xrightarrow[(2)H_2O_2]{(1) B_2H_6}$

(17) $\xrightarrow{CrO_3 \mid H^+}$ (18) $\xrightarrow{CH_2N_2}$

(19) $\xrightarrow[pyr.]{p-TsCl}$ (20) $\xrightarrow{NaH}$

(12)
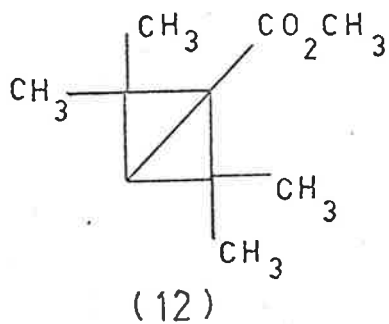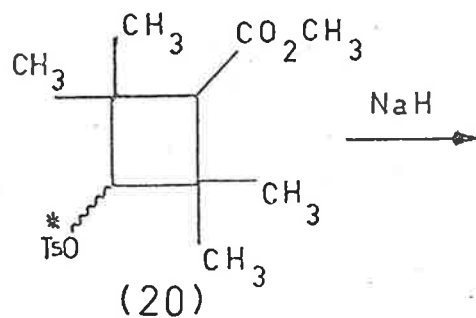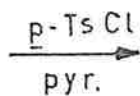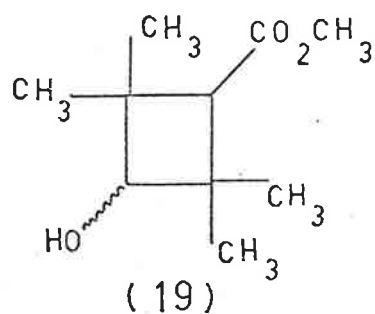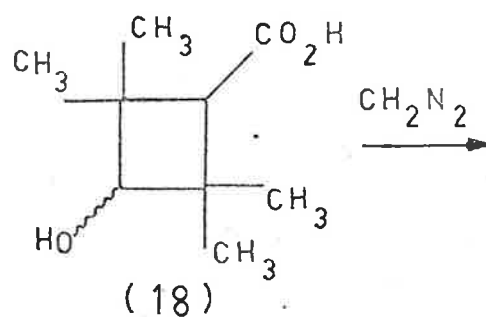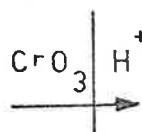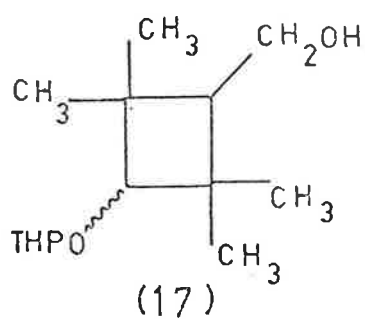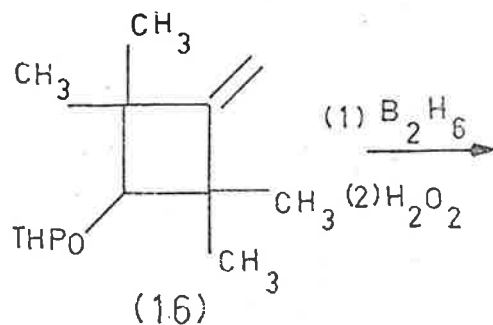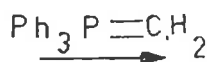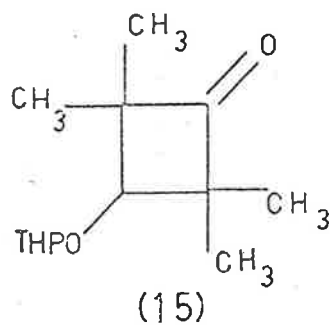
* OTS denotes the p-toluenesulphonyloxy moiety.

Scheme 6.

(b)

(15)   (21)
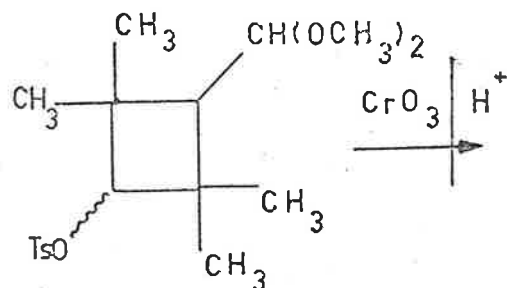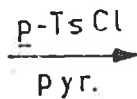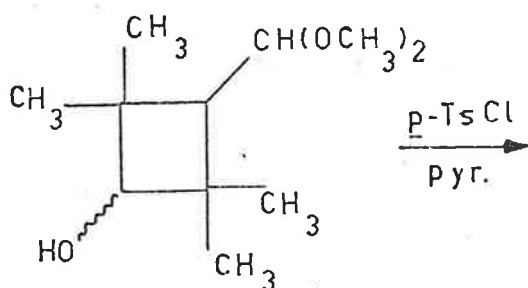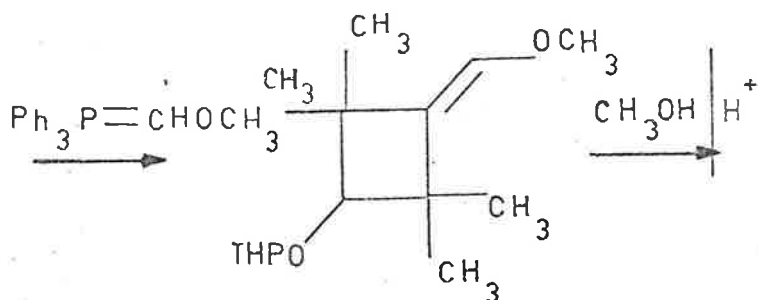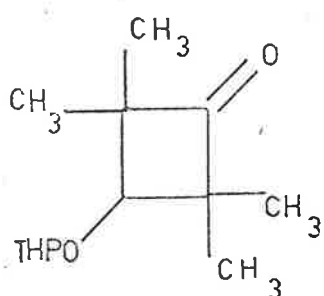
(24)   (25)
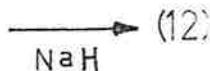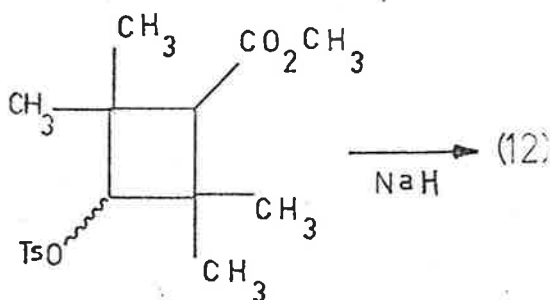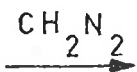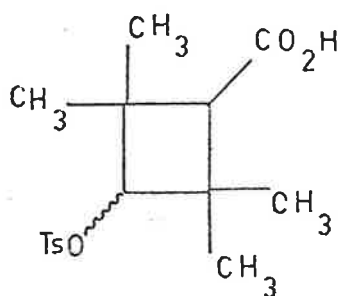
(26)   (20)

‿‿‿‿ Indicates a mixture of isomers.

The structure of the enol ether (21) was confirmed by infrared, n.m.r. (Table 1) and analytical data. The infrared spectrum showed bands at 3040 and 1690 cm^{-1} and strong bands in the 1130-1190 cm^{-1} region characteristic of enol ether and tetrahydropyranylether groups respectively.

(21)
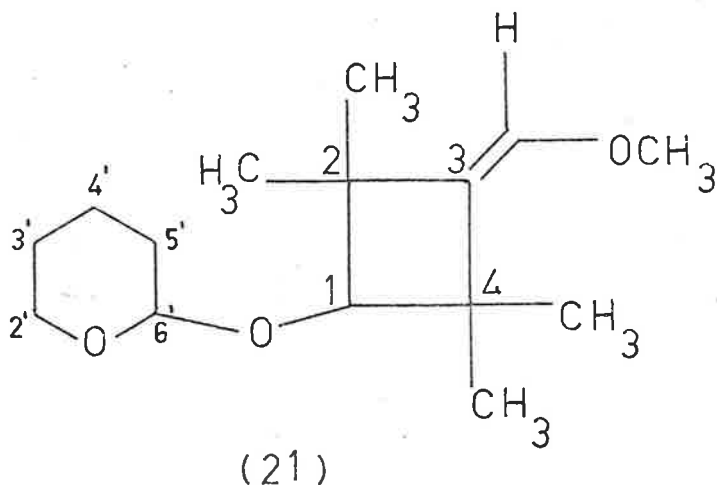
The n.m.r. spectrum of this enol ether provides an interesting example of chirality in an alkylidene cyclobutane derivative. It has been observed that alkylidenecycloalkane derivatives of the general structure shown (fig. 1) are chiral about an axis.[22] This type of chirality has recently been demonstrated[23] in a system when N = 1. The alcohol derivative (A) [fig. 2 (a)] conforms to the structure shown in fig. 1 (N = 1) and should therefore exist in enantiomorphic forms. Introduction of an asymmetric carbon atom during the formation of derivatives of this alcohol will give rise to a mixture of dia-stereoisomers which should in principle be distinguishable by physical

Table 1.

n.m.r. spectrum of (21).

δ (p.p.m.)	Appearance	Proton[*] Count	Assignment
1.02–1.28	multiplet	12	methyl protons at C_2C_4
1.37–1.83	multiplet	6	C_3', C_4', C_5' methylene protons
3.42	singlet	3	methoxyl protons
3.17–4.0	multiplet	2	C_2' methylene protons
3.52	singlet	1	C_1 proton
4.40	broad absorption	1	C_6' proton
5.60	singlet	1	vinyl proton

[*]   Unless otherwise stated the word "proton", refers to the bonded hydrogen nucleus and not to the charged species "H^+".
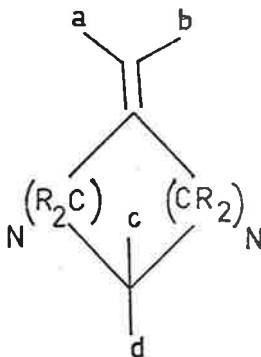
fig. 1.

methods. The tetrahydropyranyloxy derivative (B) [fig. 2 (b)] has an asymmetric carbon atom and has been shown to exist as a mixture of diastereoisomers, i.e. in the n.m.r. spectrum of the alcohol (A), the region in which the saturated methyl groups resonate contains four singlets of equal intensity [fig. 2 (a)]. In the spectrum of the derivative (B) [fig. 2 (b)] however, this region contains seven signals, one of which is broadened and is made up of two signals of almost identical chemical shift. There are thus eight signals confirming the presence of diastereoisomers.

The tetrahydropyranyloxy derivative (21) also conforms to the structure shown in fig. 1 (N = 1), and since it has an asymmetric centre will be expected to exist as a mixture of diastereoisomers. In the n.m.r. spectrum of this compound [fig. 2 (c)] the region in which the saturated methyl groups resonate is made up of six signals, four of almost equal intensity and of the remaining two, one shows a marked increase in intensity due to the superimposition of two signals of identical chemical shift, the other is broadened indicating the presence of two signals of almost identical shift, i.e. eight lines are present; clear evidence that diastereoisomers are present.

It was anticipated that acid hydrolysis of the enol ether (21) would also cleave the tetrahydropyranyl moiety to give the hydroxy-aldehyde (22). However hydrolysis under the conditions described by Ireland and Mander[24] resulted in mixtures of the hydroxy-aldehyde (22)
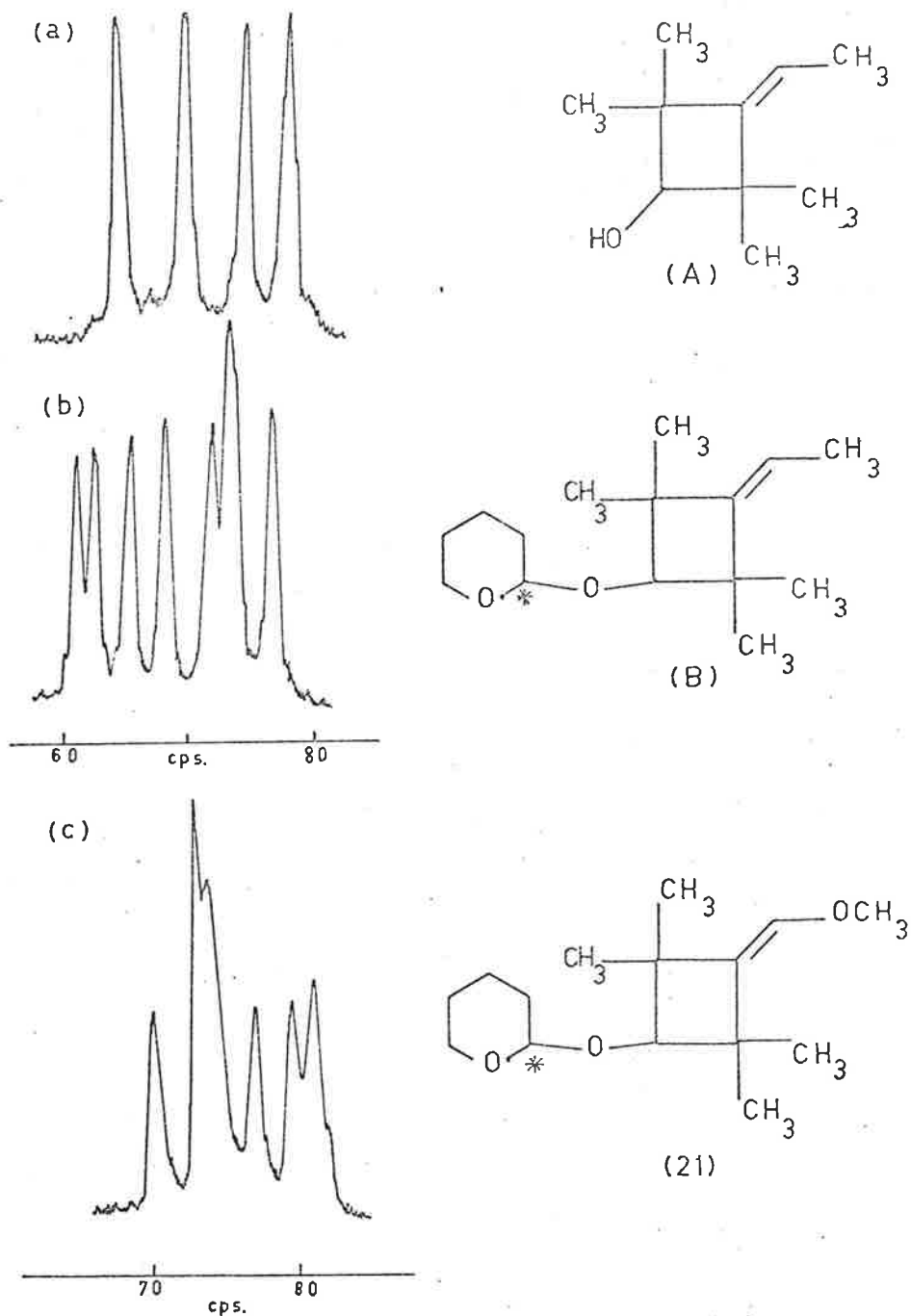
Fig. 2. Absorptions of saturated methyl groups in the n.m.r. spectra of compounds (A), (B) (reproduced from a paper by Hamon[16]), and (21) at 60 Mc/sec.

* Denotes an asymmetric centre.

and its corresponding tetrahydropyranylether. Evidence for this was provided from infrared and n.m.r. spectra. Longer reaction times under the same hydrolysis conditions resulted in decreased yields of the aldehyde (22) apparently due to polymerisation.
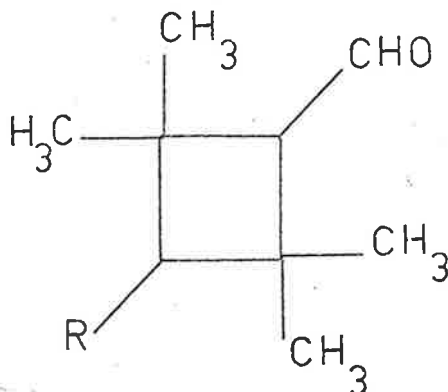
(22) R = OH

(23) R = OTs

In contrast the hydrolysis of the enol ether (21) to the dimethylacetal (24) proceeded readily and in high yield and appeared to be the method of choice.

The structure of the acetal (24) was confirmed by infrared and n.m.r. spectra (Table 2). The infrared spectrum showed a hydroxylic absorption at 3420 cm^{-1}.

As has been observed previously[25] in cyclobutane systems related to (24) the n.m.r. data provide evidence for cis- and trans-isomerism. In the absence of isomerism the resonance due to H_A would be expected to appear as a doublet (split by H_C), but since H_A can
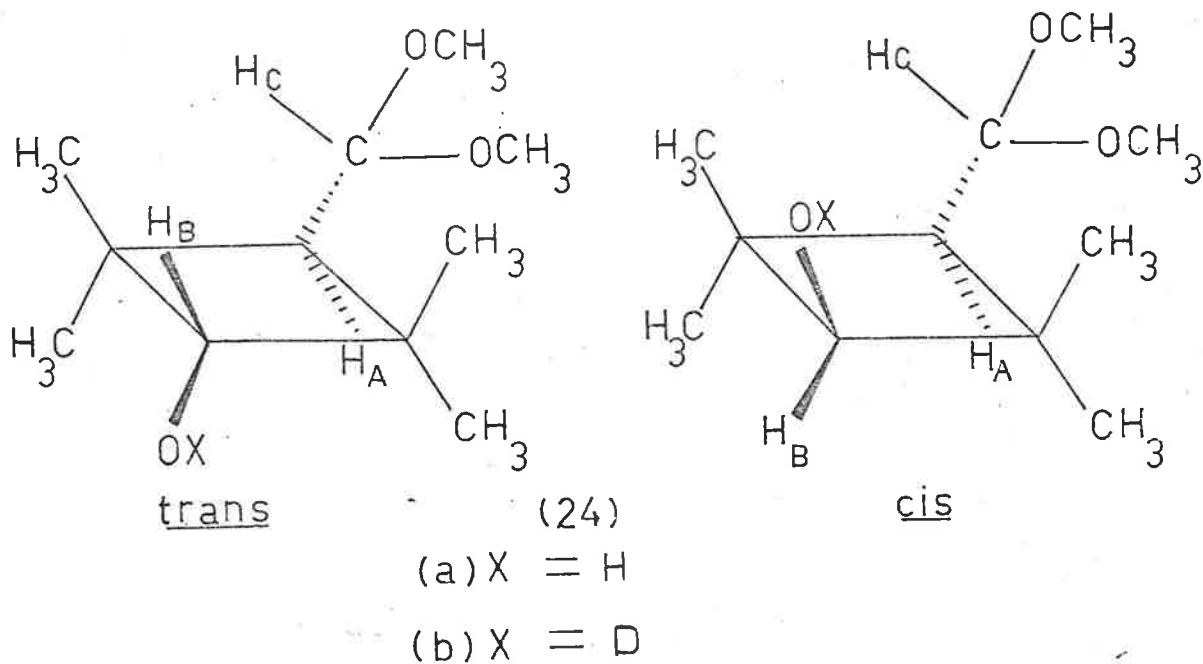
fig. 3

Table 2.

n.m.r. spectrum of (24).

δ (p.p.m.)	Appearance	Proton Count	Assignment
1:02,1.13,1.21,1.26	singlets	12	methyl groups at C_2, C_4
1.98	broad absorption	1	H_A
3.19	singlet	6	methoxyl protons
3.32-3.58	multiplet	2	hydroxyl proton and H_B
4.30	broad absorption	1	H_C

exist in two environments cis and trans to H_B (fig. 3) two doublets
are expected. Since the two doublets due to H_A occur in approximately
the same region they overlap and the nett result is a broad absorption.
For the same reason the resonance due to H_C appears as a broad absorp-
tion, and in the spectrum of the deuterated alcohol [fig. 3 (b)] two
signals rather than one are observed for H_B.

The acetal proved stable to chromatography on neutral alumina,
but tended to convert to the aldehyde (22) when chromatographed on
silica gel. The acetal was found to polymerise slowly on standing
and on attempted distillation (60°/.1 mm). Attempted purification
by preparative vapour phase chromatography also resulted in polymerisa-
tion. Because of its apparent instability the acetal was characterised
as its p-toluenesulphonyloxy derivative (25).

The best yields for the conversion of (24) to (25) were
obtained using a freshly chromatographed sample of the acetal (24),
and nine to ten days appeared to be the optimum reaction time. Any
attempts to increase the rate of the reaction by gentle warming,
resulted in charring and decreased yields. The p-toluenesulphonyloxy
derivative (25) was unstable to chromatography on silica gel [presumably
due to partial conversion to its corresponding aldehyde (23)], but
stable to chromatography on neutral alumina. However it proved
considerably more stable than the parent hydroxy compound (24), and
could be stored indefinitely. Its structure was confirmed by infrared

and n.m.r. spectra (Table 3), and analytical data. The infrared spectrum showed aromatic bands 3020 and 1600 cm^{-1} and sharp bands at 1195 and 1185 cm^{-1} characteristic of a p-toluenesulphonyloxy derivative.
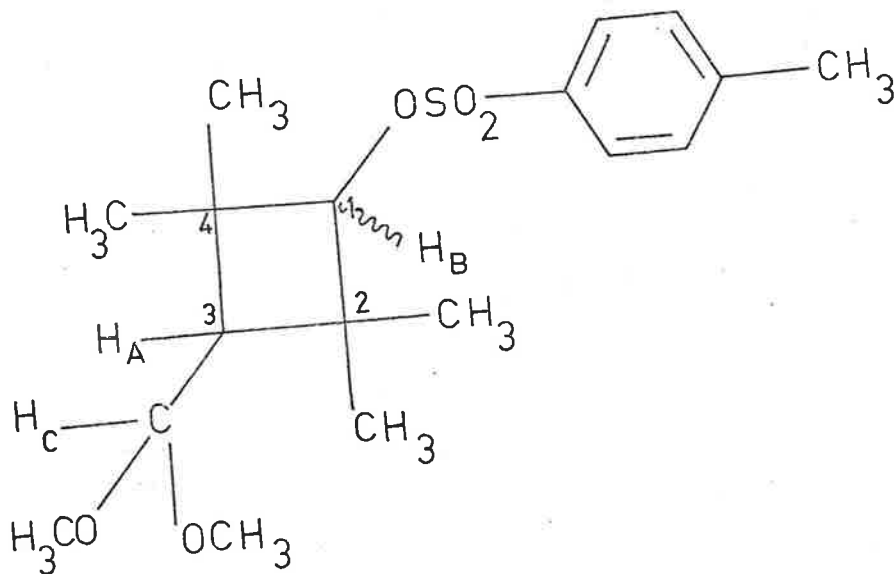
(25)

It is interesting to observe that although the derivative (25) is expected to exist as a mixture of cis- and trans-isomers there is no evidence from the n.m.r. spectrum [see Discussion of n.m.r. spectrum of (24)], to indicate that both isomers are present.*

---

* This does not appear to have been due to fractional crystallisation of one isomer during purification, since this lack of differentiation has been observed in both the n.m.r. spectrum of the mother liquors and of the purified product.

Table 3.

n.m.r. spectrum of (25).

δ (p.p.m.)	Appearance	Proton Count	Assignment
.91, 1.20	2 singlets	12	methyl protons
1.63	doublet (J = 10 c.p.s.)	1	H_A
2.41	singlet	3	aromatic methyl group
3.23	singlet	6	methoxyl protons
4.04	singlet	1	H_B
4.36	doublet (J = 10 c.p.s.)	1	H_C
7.75, 7.30	AB quartet (J = 8 c.p.s.)	4	aromatic protons

The acid (26) was obtained from the p-toluenesulphonyloxy derivative (25) upon treatment with an excess of Jones' reagent.[18]* Its structure was confirmed by infrared and n.m.r. spectra, and analytical data.

The acid (26) was converted in almost quantitative yield to its corresponding methyl ester on treatment with an excess of diazo-methane.[26] The spectral and physical properties of the compound

---

* The Jones' reagent is believed to act as a hydrolysing medium for the dimethylacetal (25) converting it to its corresponding aldehyde (23) which is subsequently oxidised to the acid (26).

prepared in this way were found to be identical to those of the ester (20) obtained previously.[27]

The bicyclo[1.1.0]butane (12) was prepared as described previously,[28] with minor modifications. It was found that the reaction time could be reduced to 16 hr (originally 48 hr) without appreciable decrease in the yield of (12).

Impurities previously observed, viz. involatile solids and 1,2-dimethoxyethane were effectively removed (see Experimental). An analytically pure sample of the bicyclo[1.1.0]butane was obtained from preparative vapour phase chromatography.

C^{13}-H coupling constant of the bridgehead* proton of the bicyclo-[1.1.0]butane derivative (12).

(12)

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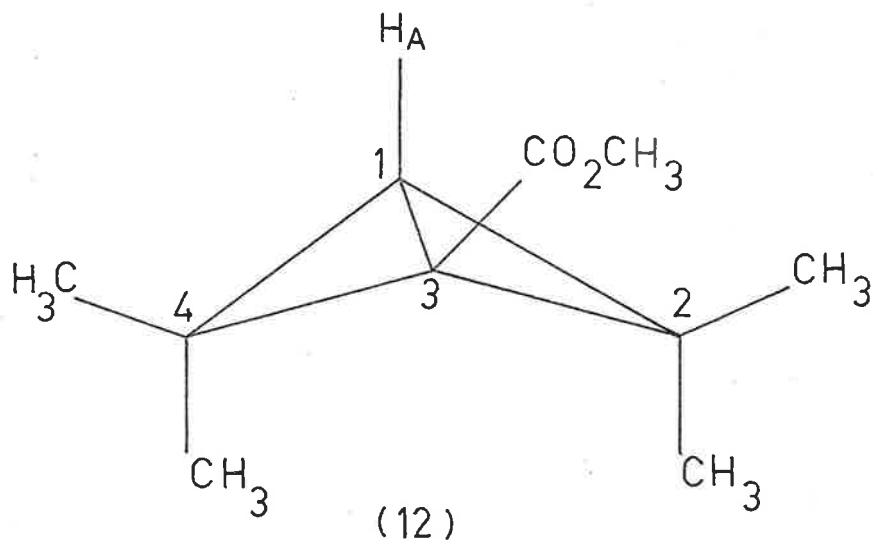
*   The two "bridgehead" positions occur at C_1 and C_3 of the bicyclo[1.1.0]butane system.

Muller and Pritchard[29] have suggested that the proton-carbon[13] spin coupling constant might be used as a direct measure of the amount of s-orbital character in the bonds. Subsequently other authors,[30] have pointed out that this criterion is not entirely satisfactory for all systems, but it is thought nevertheless to provide a rough guide to the amount of s-orbital character in particular bonds. The C^{13}-H spin coupling constant for the bridgehead proton H_A, of the bicyclo-[1.1.0]butane (12) has been found to be J = 191 cps. This is in good agreement with values obtained from other bicyclo[1.1.0]butane derivatives.[2,31]

Using the reported[29] relationship;

$$J \ C^{13}\text{-H} = 500 \ s_H^2$$

J = coupling constant for bridgehead proton

$$s_H^2 = \frac{J \ C^{13}\text{-H}}{500}$$

s_H = s character of C-H bond.

$$= 38.3\%$$

Comparison with the percentage s character for sp^2 (33%) and sp (50%) hybridised systems this value indicates that this bridgehead bond might be expected to behave essentially as a "double bond", a prediction which is borne out by experimental observation.[2,4]

(b)   <u>Pyrolysis of methyl 2,2,4,4-tetramethylbicyclo[1.1.0]butane-</u>
     <u>1-carboxylate (12)</u>.

The vapour phase pyrolyses of (12) were carried out in a quartz* vessel at temperatures in the region of 150°. In all cases three major products were observed (Scheme 7). All were isomeric with the parent bicyclo[1.1.0]butane (12). Separation was achieved by preparative vapour phase chromatography.

Scheme 7.
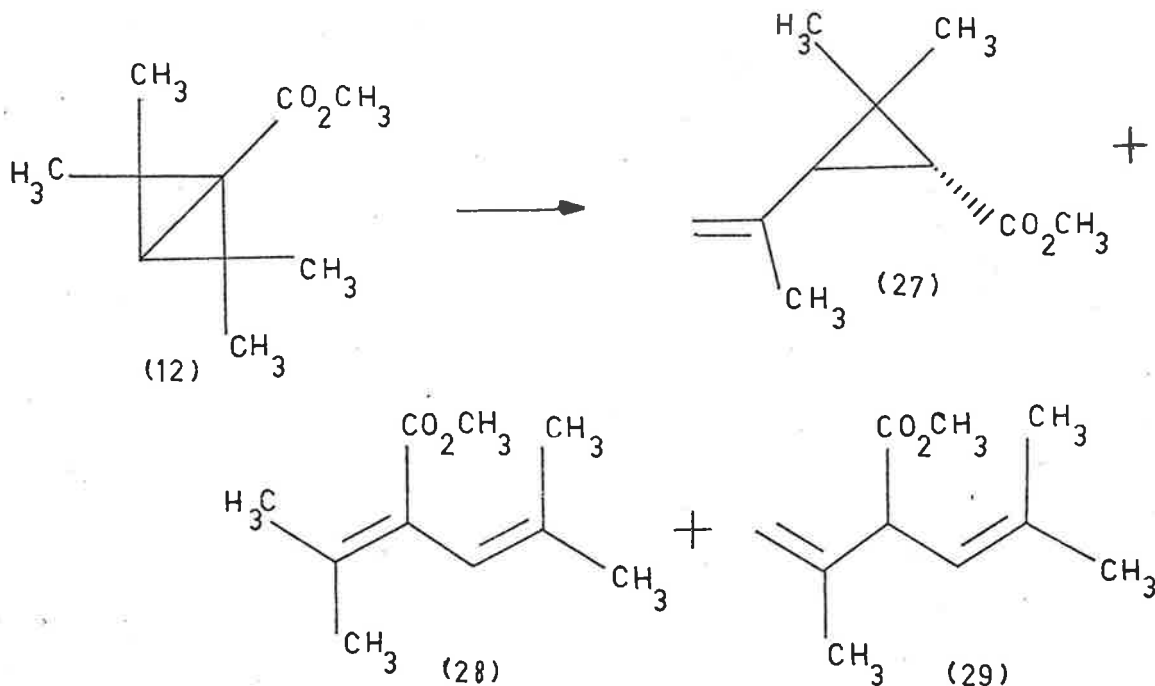
The isomer of shortest retention time was identified as methyl <u>trans</u>-2,α-methylvinyl-1,1-dimethylcyclopropane-3-carboxylate** (27). Assignment of structure was based mainly upon the n.m.r.

_____

*   To eliminate possible surface effects.

**   α- with respect to the cyclopropyl group.

spectrum (Table 4) of the compound. Infrared and analytical data were also consistent with the assigned structure. The infrared spectrum showed strong absorptions at 1725 and 1230 cm^{-1}, indicating an ester function.

Table 4.

n.m.r. spectrum of (27).

δ (p.p.m.)	Appearance	Proton Count	Assignment
1.00, 1.22	singlets	6	methyl groups A and B
1.51, 1.83	AB quartet (J = 6 c.p.s.)	2	H_B, H_A
1.72	singlet	3	CH_3 C
3.56	singlet	3	methoxyl protons
4.54, 4.74	broad singlets	2	H_C, H_D

The n.m.r. spectrum indicated the presence of two methyl groups at a tertiary position at δ1.00 and 1.22. The resonances occurring at δ1.51 and 1.83 were assigned to the protons H_B and H_A respectively [fig. 4(a)]. The doublet centred at δ1.83 shows broadening and fine structure, [fig. 4(a)]. Assignment of this doublet to the proton H_A is based on the expectation that it would be coupled (J = 0-3 c.p.s.)[32] to the methylene protons H_C and H_D. Spin-spin decoupling of these methylene protons resulted in a sharpening of this doublet [fig. 4(b)],

(b)

(H$_A$)1·83   (H$_B$)1·51

6 cps.   6 cps.

2·0   1·7   1·5

ACH$_3$ CH$_3$ B

H$_A$ CO$_2$CH$_3$

H$_C$

H$_D$ H$_B$

CH$_3$ C

(27)

(a)

2·0   1·7   1·5
p. p. m.
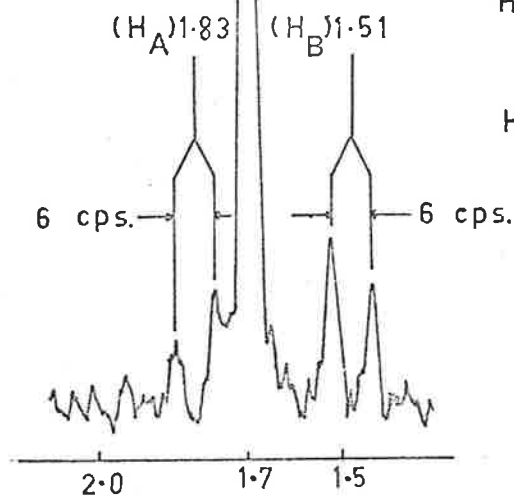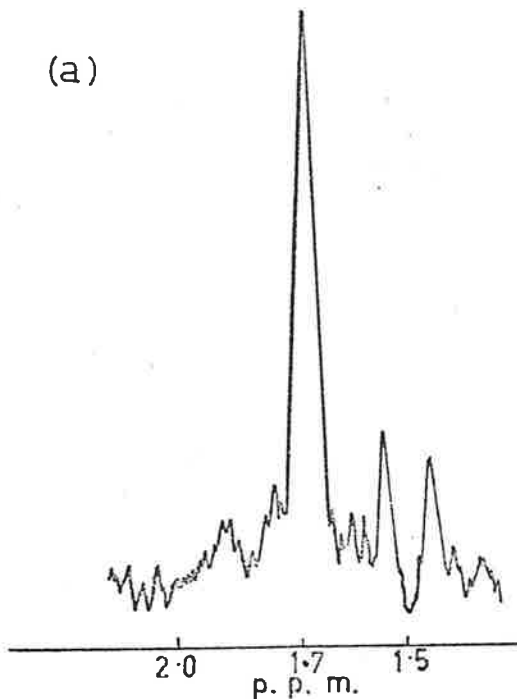
Fig. 4. Spin decoupling of proton H$_A$ by irradiation of methylene

protons H$_C$ and H$_D$

and of the signal due to the methyl group C. Similarly spin-spin decoupling of the proton H_A resulted in some sharpening of the two peaks assigned to the methylene protons H_C and H_D. These however show fine splitting after decoupling due to long-range coupling with the methyl group C. This evidence confirms the assignment of the proton H_A.

Karplus[33] has expressed the coupling constant between protons H_1 and H_2 in the fragment $\overset{H_1}{\diagdown} \overset{H_2}{\diagup}$ as a squared cosine function of the angle between the two hydrogens. A consideration of electron diffraction results of Hassel and Viervoll[34] yield 0° and about 147° for the dihedral angle between the cis-vicinal and trans-vicinal protons of the cyclopropane ring. From the Karplus equation[33] values of 8.2 and 6.4 c.p.s. for the cis-vicinal and trans-vicinal coupling constants respectively, are obtained. These values are roughly in accord with experimental observation.[35] Hutton and Schaefer[36] have reported the n.m.r. spectra of the cis- and trans-chrysanthemumic ethyl esters (A) and (B).
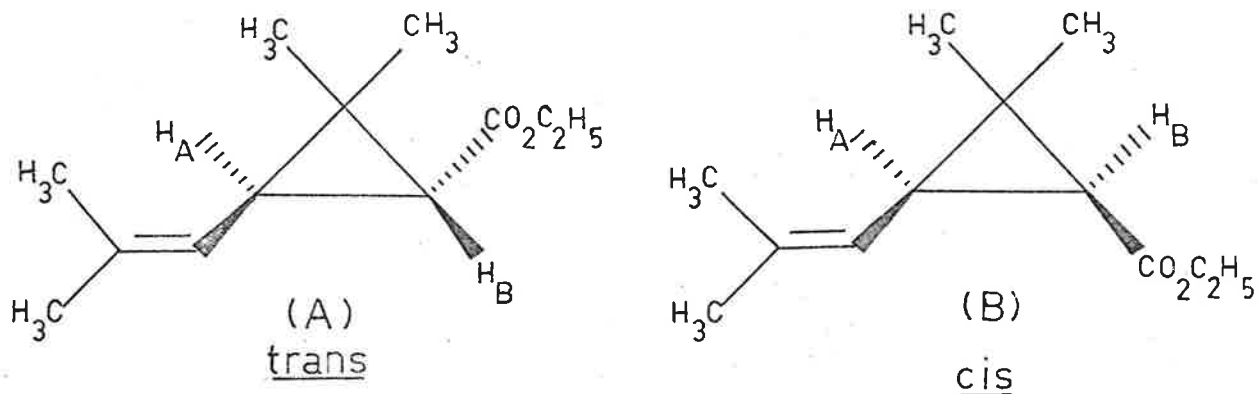
(A) trans

(B) cis

For the protons H_A and H_B they report

$$J_{AB} \quad \underline{trans} = 5.4 \text{ c.p.s.}$$

$$J_{AB} \quad \underline{cis} \quad = 8.7 \text{ c.p.s.}$$

For the cyclopropane derivative (27) the coupling constants for the protons H_A and H_B are observed to be 6 c.p.s. On the basis of the above data and on consideration of the similarities in structure between compounds (A) and (27) the stereochemistry of the latter can, with a fair amount of certainty, be assigned to the trans-configuration.

The second isomer of intermediate retention time was identified as methyl 2,5-dimethylhexa-1,4-diene-3-carboxylate (28). Assignment of structure was again based mainly upon the n.m.r. spectrum (Table 5) of the compound. Infrared and analytical data were consistent with the assigned structure.
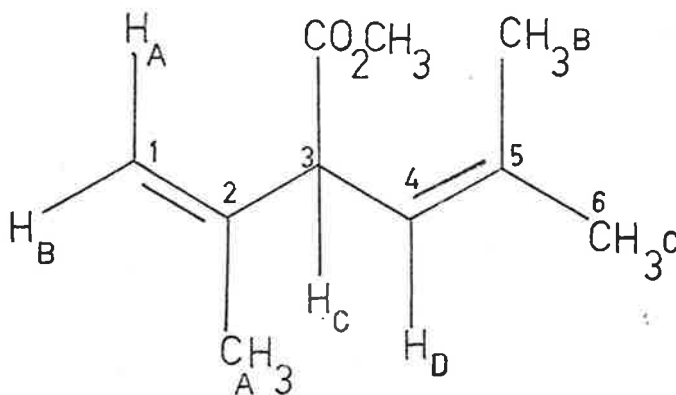
(28)

The infrared spectrum displayed strong absorptions at 1735
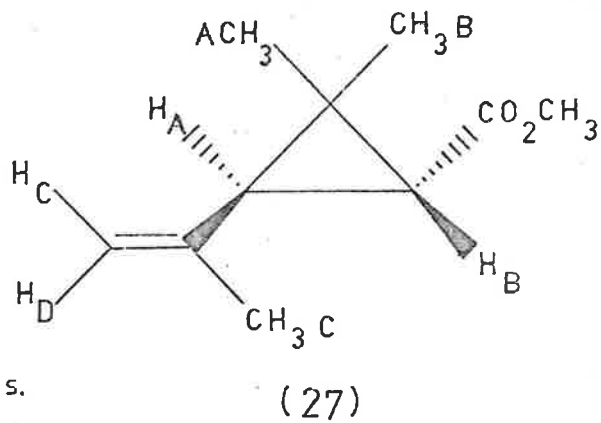and 1230 cm^{-1} indicating an ester function. The resonances occurring
in the region of δ1.59-1.83 were assigned to the methyl groups A, B,
and C. All three peaks show some fine splitting. This is expected
from the allylic coupling between protons H_A, H_B, and H_D (J = 0-3
c.p.s.).[35] Without further study involving the relevant protons

Table 5.

n.m.r. spectrum of (28).

δ (p.p.m.)	Appearance	Proton Count	Assignment
1.61, 1.73, 1.80	singlets	9	methyls A, B, and C
3.63	singlet	3	methoxyl protons
3.78	broad doublet (J = 9 c.p.s.)	1	H_C
4.08	broad singlet	2	H_A, H_B
5.37	broad doublet (J = 9 c.p.s.)	1	H_D

(viz. spin-spin decoupling studies), it would not be possible to assign
the resonance to any one of the three methyl groups.

On the basis of structure (28) the protons H_C and H_D will be
expected to occur as broad doublets as this is observed, J_{CD} being
9 c.p.s.

The observed broadening of the signal assigned to H_D is due

to allylic coupling[35] to the methyl groups B and C whilst long range
coupling to the methyl group A and allylic coupling[32] to the methylene
protons H_A and H_B result in broadening of the signal assigned to the
proton H_C.

The third isomer, of longest retention time, was identified
as methyl 2,5-dimethylhexa-2,4-diene-3-carboxylate (29). Assignment
of this structure was again based mainly upon the n.m.r. spectrum
(Table 6) of the compound.

The infrared spectrum displayed strong bands at 1725 and
1230 cm^{-1} indicating an ester function.

The four resonances in the region of $\delta 1.50$–1.93 each propor-
tional to three protons in area, were assigned to the vinylic methyl
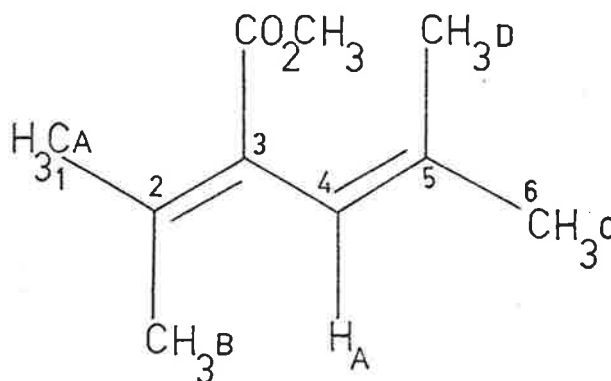
(29)

Table 6.

n.m.r. spectrum of (29)

δ (p.p.m.)	Appearance	Proton Count	Assignment
1.50, 1.70, 1.73, 1.93	singlets with fine splitting	12	methyl groups A, B, C, and D.
3.56	singlet	3	methoxyl protons
5.62	broad absorption	1	H_A

groups A, B, C, and D, the observed fine splitting being due to allylic coupling (J = 0-3 c.p.s.)[32,35] of the methyl groups C and D to the proton H_A, and to homoallylic coupling (J = 1-1.5 c.p.s.)[32] of the methyl groups A and B to the proton H_A. The signal occurring at $\delta 1.93$ can be assigned to the methyl group D since this group has the closest spacial orientation* to the carbomethoxyl group, and is therefore expected to be deshielded with respect to methyls A, B, and C.

However since the coupling constants observed for all four signals are of approximately the same order (between 1 and 1.5 c.p.s.),**

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*   On consideration of models of (29).

**   Not unexpected for systems of this type.[32]

the remaining three signals cannot, with any real certainty, be assigned to any one methyl group.

The three pyrolysis products gave prominent parent molecular ions at m/e 168 confirming that they were isomeric with the parent bicyclo[1.1.0]butane (12). All four compounds [(12), and (27) - (29)] showed an essentially similar fragmentation pattern.

(c)   Discussion of pyrolysis and products.

The pyrolyses of a number of sterically less crowded bicyclo-[1.1.0]butane derivatives have been reported.[2,6,9,12,37,38]   These were all carried out in the vapour phase, in glass or in quartz vessels at temperatures ranging from $150-350^{\circ}$. The major products obtained in these cases were conjugated dienes.

Initially the pyrolyses of (12) were carried out in a quartz vessel which had been normally cleaned. Under these conditions the three products (27), (28), and (29), (Scheme 7) were formed in an approximate ratio of 66:27:7, in that order. Frey[39] and other workers[2,9,11] have observed the extreme sensitivity of bicyclo[1.1.0]butane and its derivatives to acid. (Bicyclo[1.1.0]butane itself will undergo hydration in 0.0001N sulphuric acid at room temperature.)[2] In view of this, it was not inconceivable that under the pyrolysis conditions the bicyclo[1.1.0]butane (12) could have undergone an acid catalysed decomposition on the walls of the pyrolytic vessel. In an attempt to exclude this possibility the pyrolytic procedure was repeated in

a quartz vessel which had been treated with base.* A mixture of the same three products was again obtained but the relative amount of isomer (29) in the reaction product was greatly increased.

When pyrolyses were carried out in the presence of a trace of anhydrous hydrochloric acid, compounds (27; 68%) and (28; 32%) were the only products. Pyrolyses were also carried out in the presence of a small amount of triethylamine. Under these conditions a mixture of the unchanged bicyclo[1.1.0]butane derivative (12; 56%) and isomer (29; 44%) was obtained after 50 minutes (the normal reaction time). Pyrolysis for 3 hr in the presence of triethylamine gave isomer (29) as the only product.

These results strongly suggest that isomers (27) and (28) are products of an acid catalysed breakdown of the bicyclo[1.1.0]butane (12), and that the third isomer (29) may be the true pyrolysis product. Indeed on the basis of the Woodward-Hoffmann rules for electrocyclic reactions[5,6] and other theoretical considerations,[3,4] isomer (29) is the expected product of a thermal ring opening of the bicyclo[1.1.0] butane (12).

The question of the mode of formation of isomers (27) and (28) will now be considered in more detail.

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* The vessel was immersed in triethylamine (24 hr), and dried for 24 hr at 120°.

A mongst the products of the pyrolysis of exo,endo-2,4-dimethyl-
bicyclo[1.1.0]butane Closs and Pfeffer[6] detected, in low yield (less
than 3%), the presence of trans-1-methyl-2-vinylcyclopropane (37), and
cis-1,4-hexadiene (38), a known rearrangement product of cis-1-methyl-
2-vinylcyclopropane.[40]

minor products
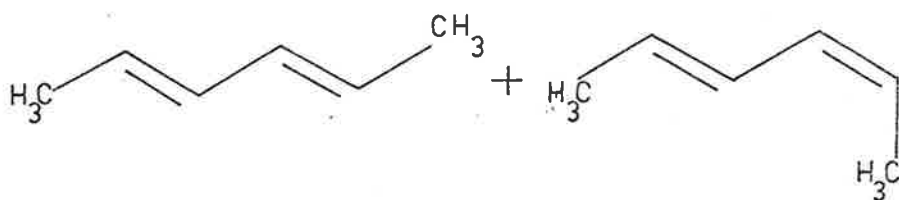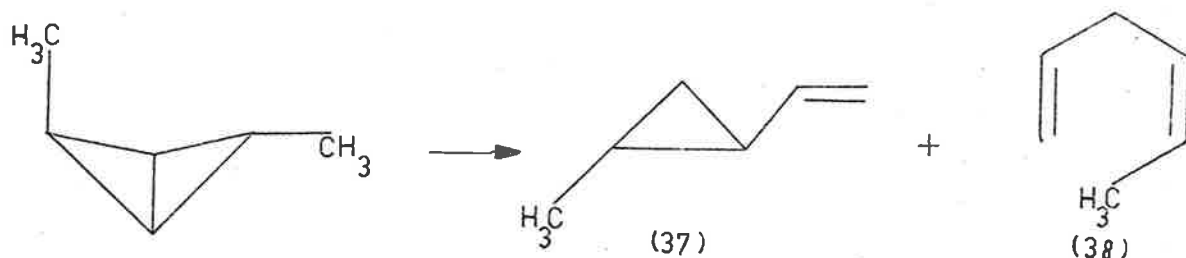
major products

Although not discussed by Closs and Pfeffer the origin of
these two minor products is clearly similar to that of isomers (27)
and (28).

All the reported reactions of bicyclo[1.1.0]butane derivatives
with acid[2,12,38] were carried out in solution, and the products may
not necessarily reflect those which would be formed in the vapour
phase or under anhydrous conditions. Blanchard and Cairncross[38] have

carried out the acid induced hydration of the bicyclo[1.1.0]butane

(30) (Scheme 8), to the single isomer of the cyclobutane derivative

(31), and conclude that the reaction must involve initial protonation*

at C_1 from the side opposite, (that is _trans_ to) the nitrile group

followed by hydration of the carbonium ion formed at C_3.

Scheme 8.

(30)

(31)
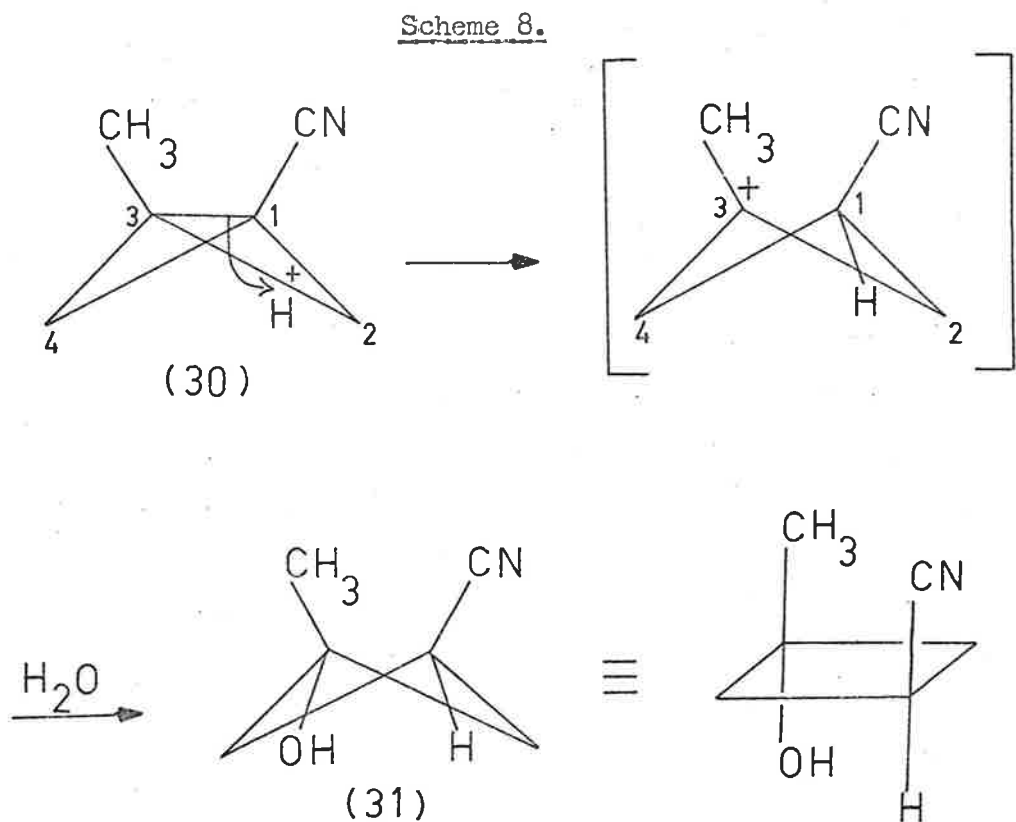
This observation is in accord with results obtained by other

workers in this field.[41]

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*   Refers to the charged species H^+, for the purposes of

         discussion of the pyrolysis.

Based on the above consideration, reaction of the bicyclo-
$[1.1.0]$butane (12) with acid will involve initial protonation at C_1
on the side opposite the carbomethoxyl group, followed by rearrange-
ment of the carbonium ion (32) formed at C_3 to give the highly

Scheme 9.
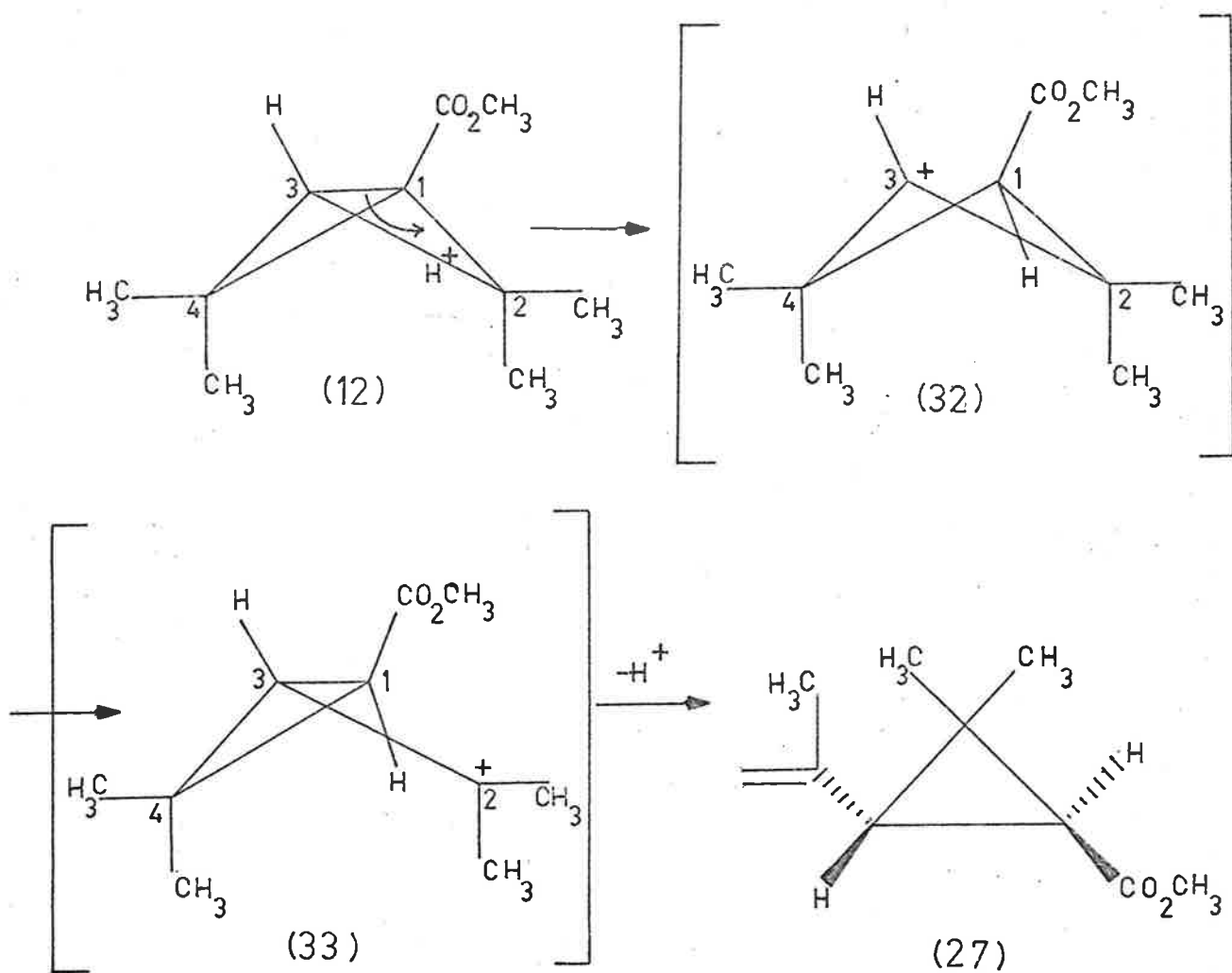
stabilised cyclopropylcarbinyl cation*[42] (33) (Scheme 9).

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*   Other workers have provided evidence for an intermediate "bicyclobutonium ion"[43] in reactions of this type but a consideration of the relative stabilities of the cyclopropylcarbinyl cation (33) with respect to the other contributing structures (32) and (35) indicates that the contribution of these latter ions will be so small as to be negligible. Thus for the present work the possibility of the contribution of an intermediate bicyclobutonium ion of the type (36) is considered unlikely.
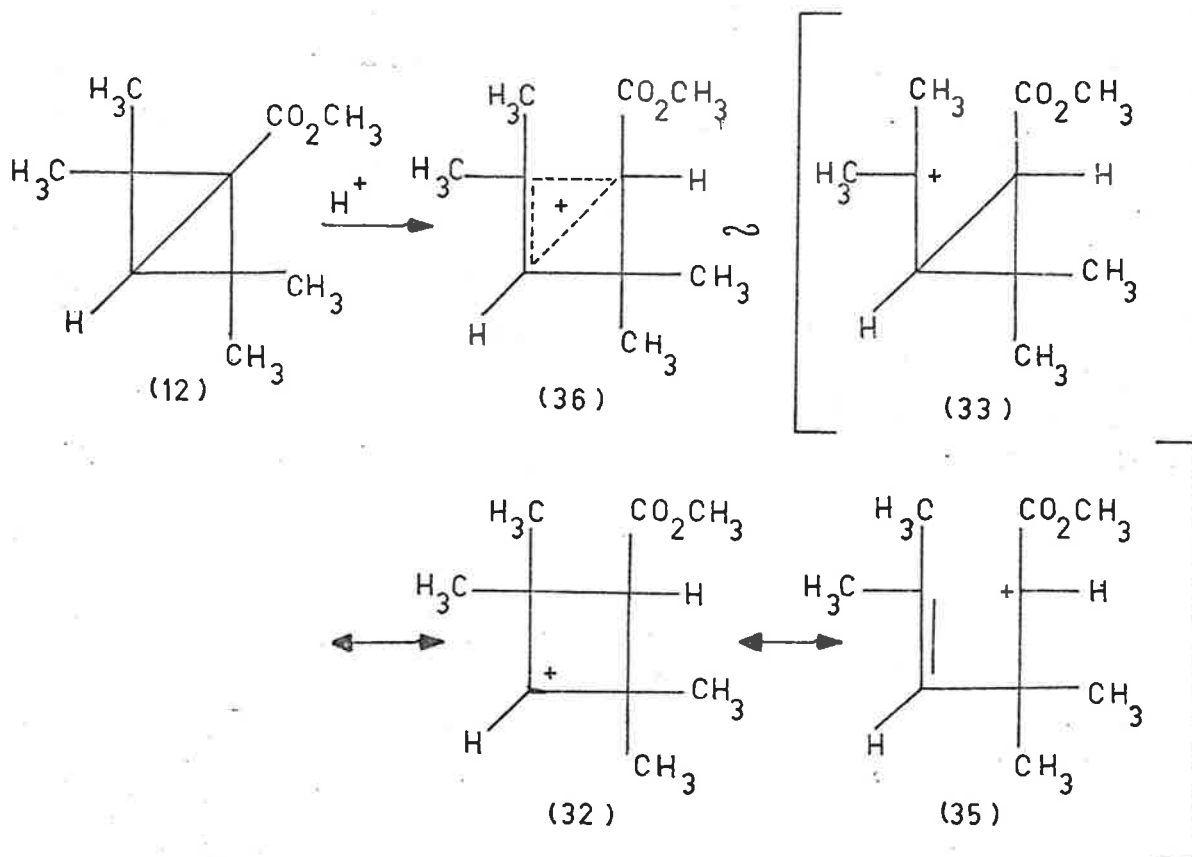
Loss of a proton from cation (33) would be expected to lead to methyl trans-2,α-methylvinyl-1,1-dimethylcyclopropane-3-carboxylate - that is isomer (27). Thus the formation of this isomer from an acid induced breakdown of (12) can readily be explained. However the presence of isomer (28) cannot be rationalised in this way.

There are two possibilities to be considered: (1) that isomer (28) has arisen from an hitherto unknown pathway, or (2) that it is a result of some further breakdown of either (27) or (29). A sample of (29) when resubjected to the pyrolytic conditions did not undergo appreciable decomposition. However when a sample of the cyclopropane derivative (27) was resubjected to the pyrolytic conditions[*] approximately 74% was recovered unchanged, together with 26% of isomer (28). It did appear that (28) had in fact resulted from a thermally induced ring opening of the cyclopropane derivative (27).

An inherent thermal instability of certain vinylcyclopropane derivatives has been well documented.[40,44-46] Ellis and Frey[44] have reported the isomerisation of cis-1-methyl-2-vinylcyclopropane (37) to cis-1,4-hexadiene (38) at temperatures greater than 160° (Scheme 10). They postulate that the isomerisation probably proceeds through the seven-membered ring intermediate (39), and involves a 1-5 hydrogen shift with migration of a double bond. Cleavage of the bond between C_1 and C_2

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[*]   In a quartz vessel which had been treated with base (see Experimental p. 78).

is apparently assisted by electron delocalisation in the allyl residue,[45] so that rearrangement may occur at temperatures much lower than those normally required to cleave a cyclopropane ring.[45-47]

Scheme 10.

(37)　　　　　　　(39)

(38).
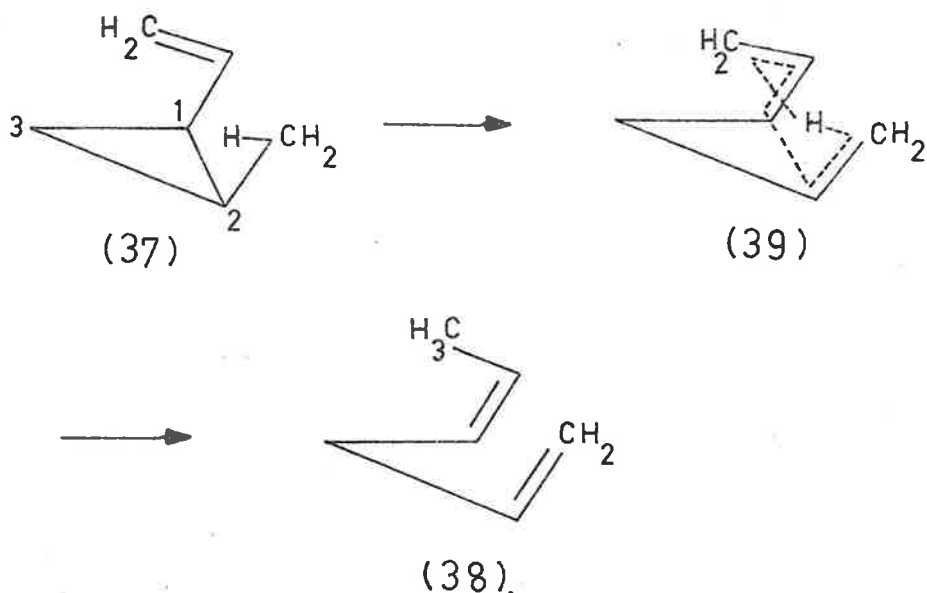
On consideration of the Woodward-Hoffmann rules for sigmatropic reactions,[48] it follows that if the conversion of (37) to (38) is a concerted one the favoured hydrogen atom shift will involve a suprafacial* [1,5]migration. This type of transfer reaction, termed a homo[1,5]sigmatropic shift, is very well documented.[49]

Similarly Vogel and workers[46] have observed isomerisations

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*　　In a suprafacial process the transferred atom or group is associated at all times with the same face of the π -system.

occurring at unexpectedly low temperatures in their studies of the
Cope rearrangement of 1,2-divinylcyclopropanes.

Since the pyrolysis of the bicyclo[1.1.0]butane derivative
(12) was carried out at temperatures of the same order as those
required to isomerise cis-1-methyl-2-vinylcyclopropane (37) (Scheme
10), it is not unlikely that under the pyrolysis conditions the cyclo-
propane derivative (27) might undergo a similar isomerisation to give
the 1,4-hexadiene (28) (Scheme 11).

Scheme 11.

(27)

(28)
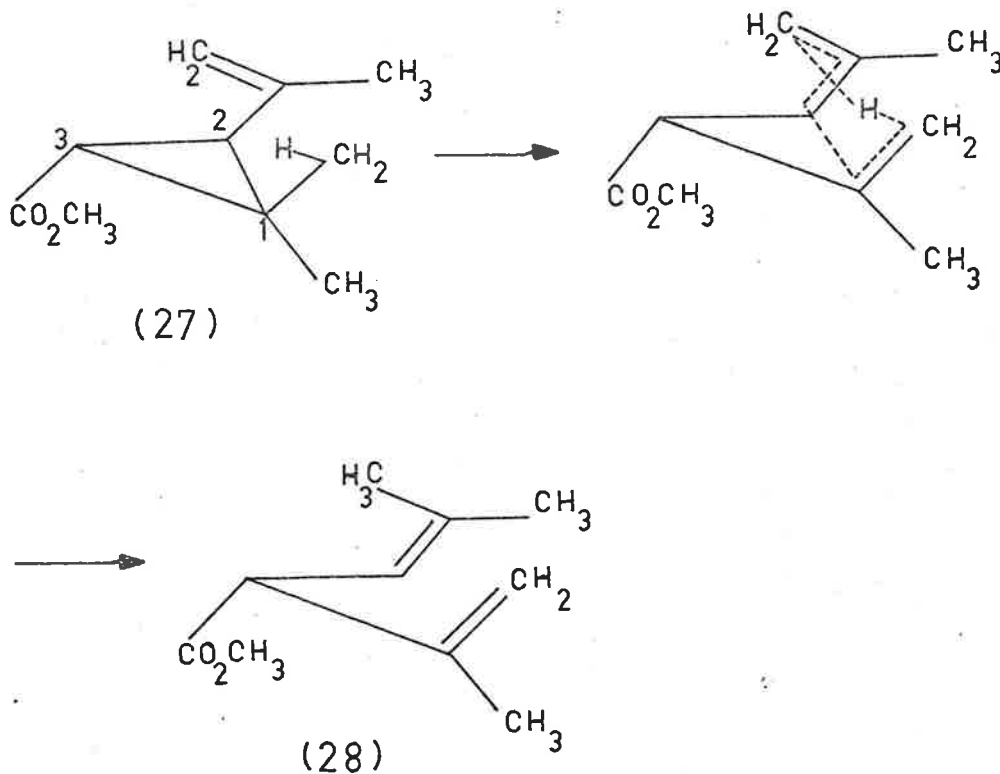
Thus the formation of isomers (27) and (28) as products
of the   breakdown of the bicyclo[1.1.0]butane derivative (12) can
readily be explained.

Consider now the formation of the third isomer (29), believed
to be the true pyrolysis product. Scheme 12 shows the products expected
from the three possible modes of thermal ring opening[*] of the bicyclo-
[1.1.0]butane derivative (12).[2,3,6] A comparison of the observed and
expected products allows two conclusions to be made: (1) rearrangement
of (12) via a cyclobutene intermediate [Scheme 12,eqn (c)] seems unlikely,
and (2) the diene (29) may have arisen from the parent bicyclo[1.1.0]
butane derivative (12) by one or both of the two remaining pathways,
i.e. from a concerted ring opening [Scheme 12,eqn (a)] or from a non-
concerted two step process [Scheme 12,eqn (b)]. These conclusions are
in accord with the results obtained by the majority of workers in this
field.[2,3,4,6,9,12,38]

The diene (29) may also have arisen from an acid or base
catalysed isomerisation of its unconjugated analogue (28).[**] However
there is no evidence from the results of the various pyrolyses to
indicate that an isomerisation of this type was occurring. For

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*   See Scheme 1, Introduction.

**   The conjugated diene (29) might be expected to have greater
stability relative to its unconjugated analogue (28).

Scheme 12.

(12) → (29) ....(a)

(12) → (29) ....(b)
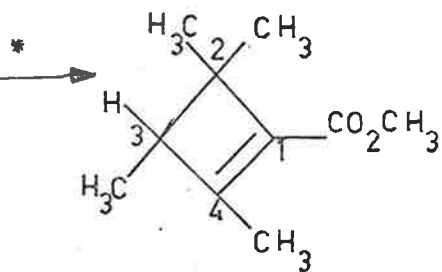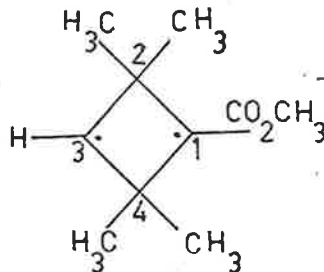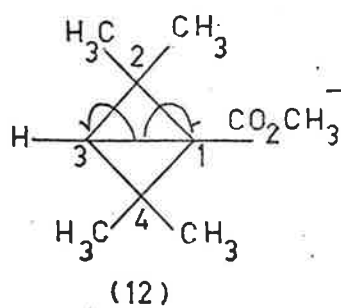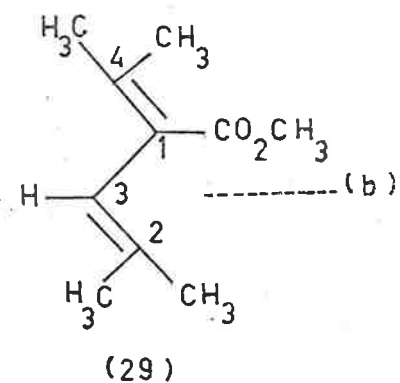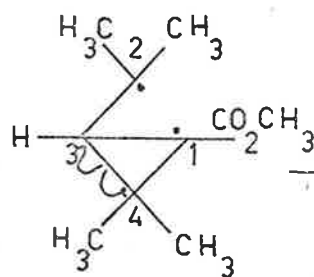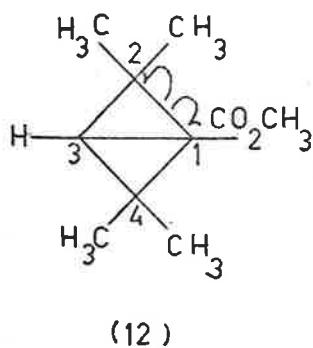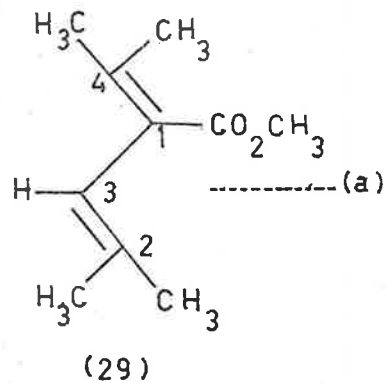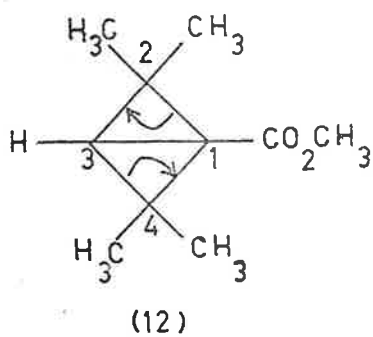
(12) → Ring opened products
(nature dependent upon
whether a H- or a CH$_3$-
shift occurs) ....(c)

*   CH$_3$ -   transfer

completeness, a study of the behaviour of (28) under the pyrolysis conditions would be desirable, but in the absence of sufficient material a study of this nature could not be undertaken.

A preliminary study of the addition of anhydrous hydrogen chloride at room temperature to a solution of the bicyclo[1.1.0]butane (12) in anhydrous carbon tetrachloride was carried out. Vapour phase chromatographic analysis of the solution after one hour indicated that isomers (27; 80%) and (28; 20%) only were present. The n.m.r. spectrum of a reaction mixture similar to that above, but kept at 40°, was taken after intervals of one hour and 17 hours. Signals consistent with the presence of (27) and (28) could be detected but it was not possible to determine the relative amounts of the two isomers with any accuracy. No signals consistent with the presence of isomer (29) were observed.

The occurrence at room temperature of appreciable amounts of isomer (28) in the above reaction mixtures is not consistent with a temperature dependent conversion of (27) to (28), since (27) has been found to be stable to vapour phase chromatography at temperatures in the region of 100°.* Thus it would appear that conversion of (27) to (28) is acid catalysed under these conditions. [Presumably the conversion is achieved by protonation of the methylene group of (27)

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* The temperature region at which the product analyses were carried out.

followed by ring opening to give the 1,4-hexadiene (28, Scheme 13).]

Scheme 13.

(27)   (28)
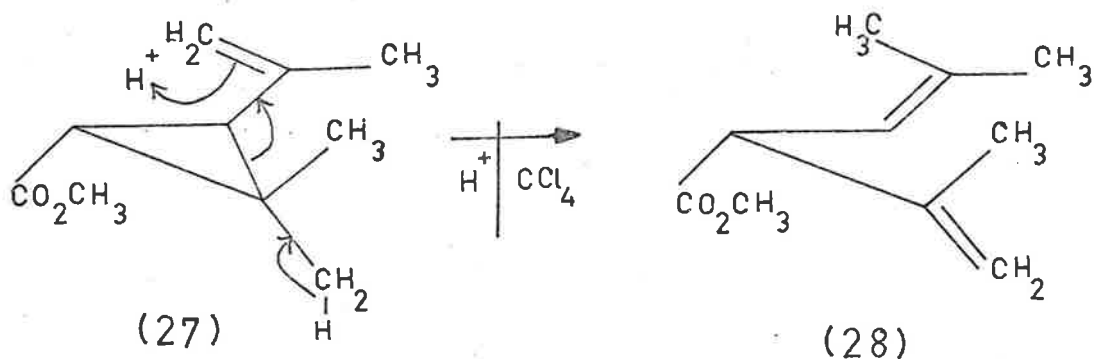
Obviously a more complete study of the properties of isomer (27) is necessary before any other conclusions regarding its conversion to (28) can be made.

A preliminary attempt has been made to prepare the cyclopropane derivative (27). The reaction sequence envisaged is briefly shown in Scheme 14.

Addition of 2-diazopropane to dimethyl fumarate gave the expected pyrazoline (40), which was converted to the cyclopropane derivative (41)[83] on treatment with copper powder. Due to lack of time, conversion of this cyclopropane derivative to isomer (27) was not attempted.

Scheme 14.
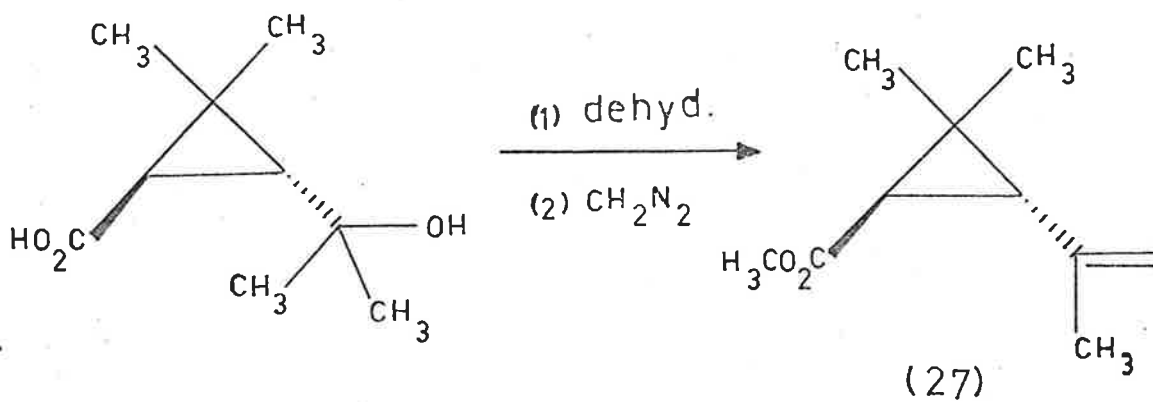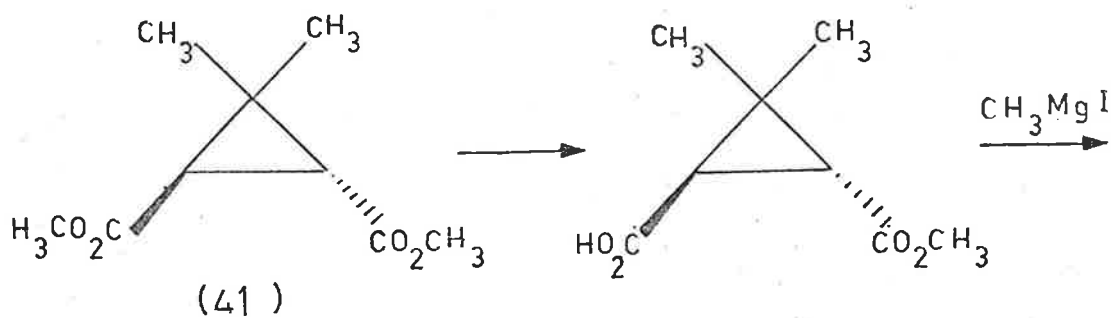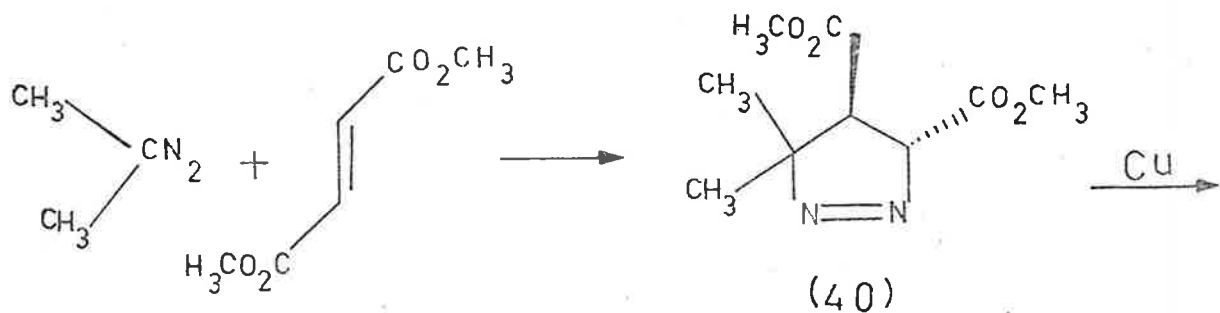
(d)   <u>Added after the initial submission of the thesis.</u>

After the submission of this work the acid catalysed conver-
sion of the bicyclo[1.1.0]butane derivative (42) to the vinylcyclo-
propane (43) was reported[50] (Scheme 15). The analogy between this
acid catalysed ring opening and the conversion of the bicyclo[1.1.0]
butane (12) to the vinylcyclopropane derivative (27) can clearly be
seen and further substantiates the proposal that the latter process
is also an acid catalysed one.

Scheme 15.

(42)   (43)
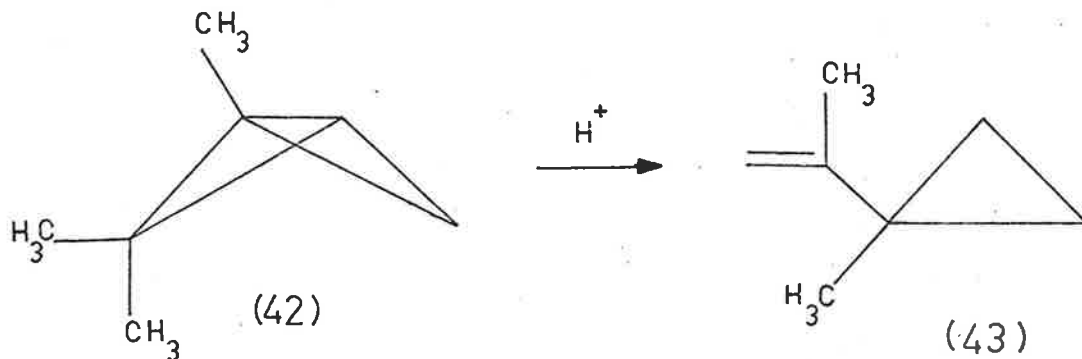
PART II

SYNTHETIC APPROACHES TO

1,2,2,4,4-PENTAMETHYLBICYCLO[1.1.0]BUTANE.

Introduction.

Concurrently with the studies on the pyrolysis of the bicyclo[1.1.0]butane derivative (12) it was anticipated that studies of the thermal rearrangements of other bicyclo[1.1.0]butane analogues would provide a greater understanding of the mechanism or mechanisms of these rearrangements.

During the course of the pyrolytic work on the abovementioned bicyclo[1.1.0]butane, (12), two new analogues were reported.[51,52] One of these was hexamethylbicyclo[1.1.0]butane (45),[51] which was obtained from 1,3-dibromohexamethylcyclobutane (44) by an intramolecular Wurtz reaction[53] (Scheme 16).

Scheme 16.

(44)

(45)
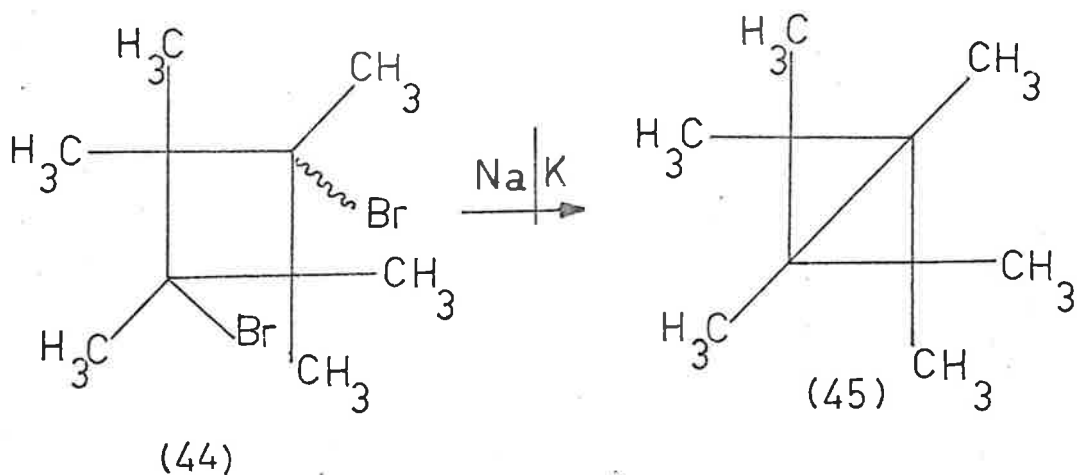
The second analogue, pentamethylbicyclo[1.1.0]butane (47)[52] was obtained by the intramolecular displacement of an alkoxide ion (Scheme 17).

Scheme 17.

(46)   (47)
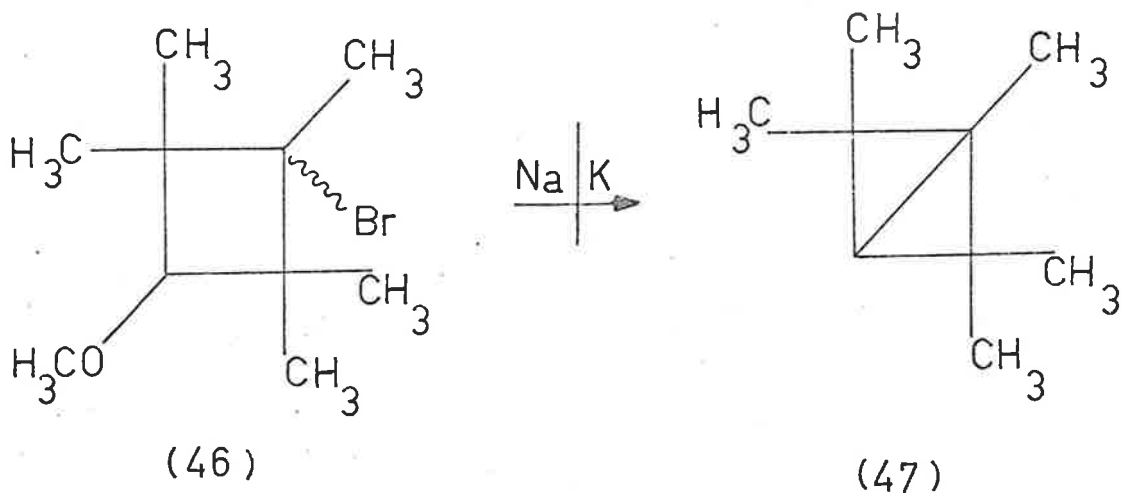
Hamon experienced difficulties in the purification of the bicyclo[1.1.0]butane derivative (47), (mainly due to decomposition during the purification process). It was anticipated that preparation of (47) by an intramolecular Wurtz reaction as described by Hamon for the hexamethyl analogue (45)[51] would overcome some, if not all, of these difficulties.

Discussion.

(a)   Attempted synthesis of 1,3-dibromo-1,2,2,4,4-pentamethyl-
cyclobutane (48).

A suitable intermediate for cyclisation to the pentamethyl-
bicyclo[1.1.0]butane (47) would appear to be the 1,3-dibromide (48).

(48)
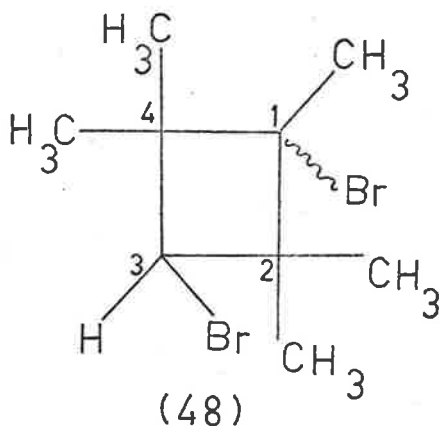
The first synthetic route envisaged towards the preparation
of the intermediate is outlined in Scheme 18. This involved SN_2
displacement by bromide ion of the p-toluenesulphonyloxy group of
compound (49)* followed by addition of liquid hydrogen bromide** to
the resultant bromo derivative (50) to give the desired dibromide (48).

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*   Kindly supplied by Dr. D.P.G. Hamon.

**   This reaction had been carried out on systems closely
        related to (50).[51,52]

Scheme 18.
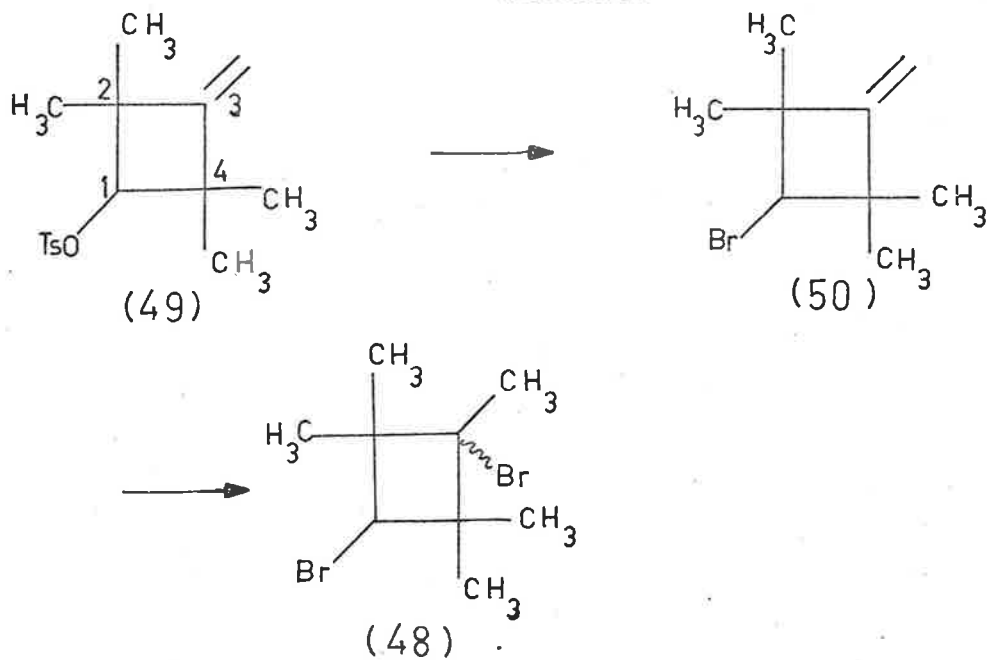
Positions 1 and 3 of the tetrasubstituted cyclobutane ring have been observed to be highly unreactive towards SN_2 displacement.[54] This is not unexpected in view of the large steric crowding of the methyl groups at positions 2 and 4. Accordingly the attempted preparations of (50) were carried out under conditions which would facilitate SN_2 displacements from highly hindered positions.[55,56] However preliminary attempts to prepare (50) from the p-toluene-sulphonyloxy derivative (49) were not successful, starting material being recovered unchanged in all cases.

Although the reactions which were carried out by no means constituted a thorough investigation of the displacement reaction, further study was discontinued at this stage in favour of an alternative synthetic approach to the desired dibromide intermediate (48). This

Scheme 19.

(51)

(52)

(53)

(54)

(55)

(56)
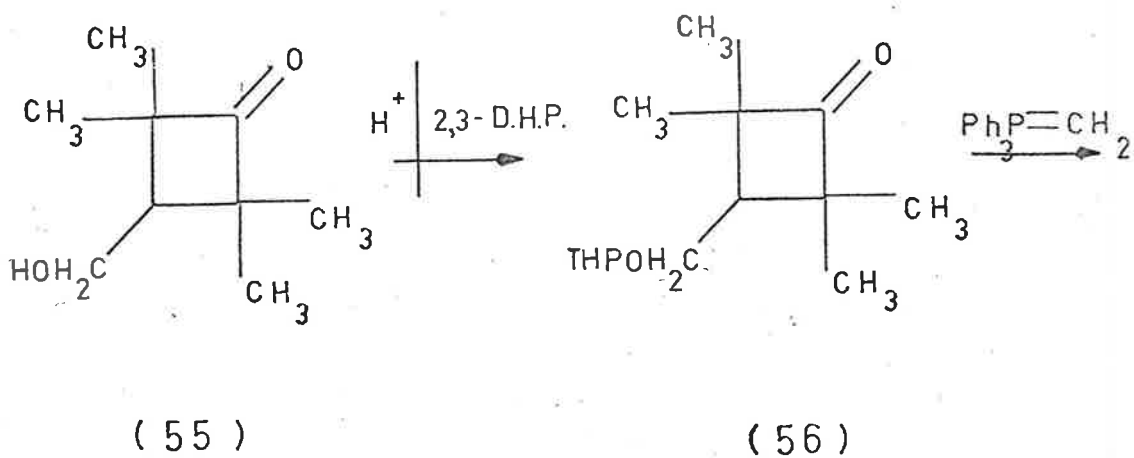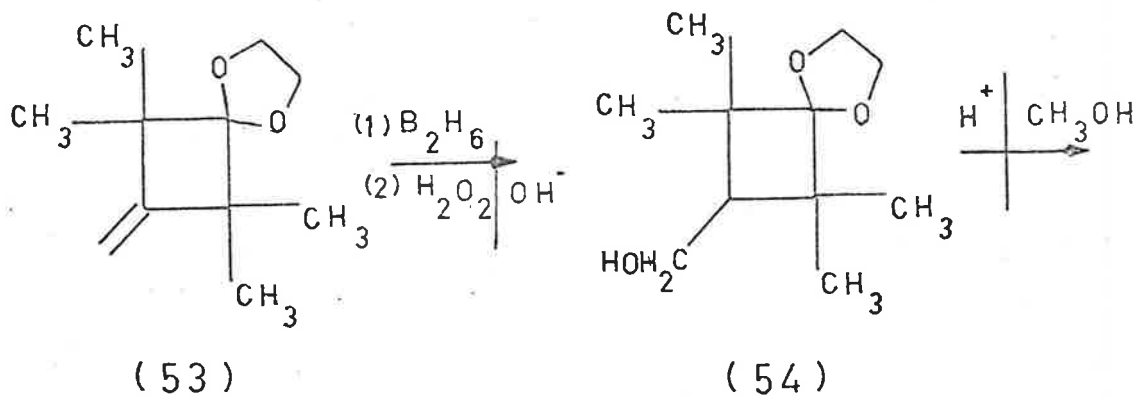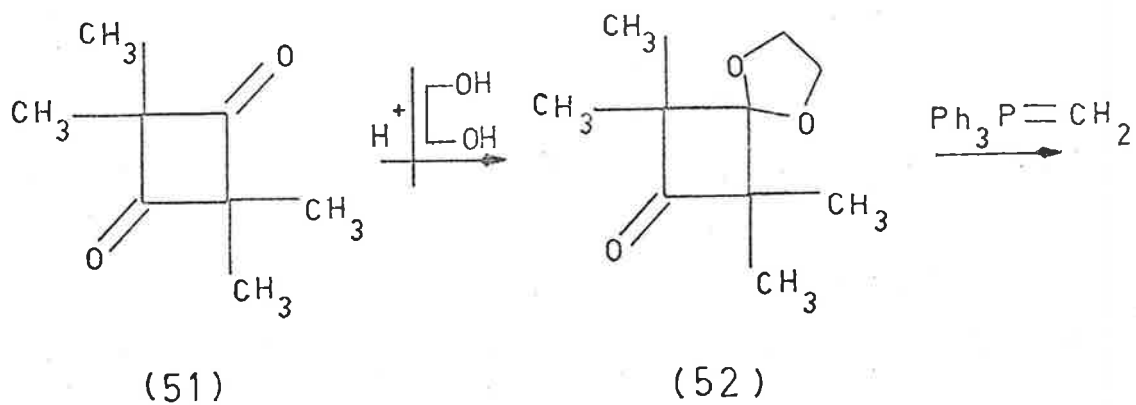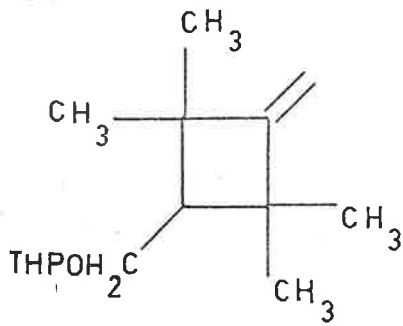
(57)
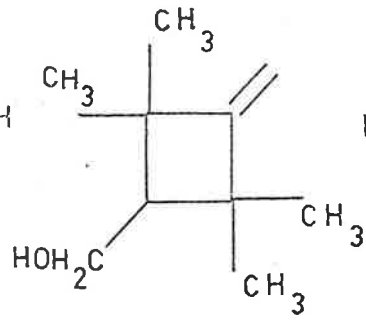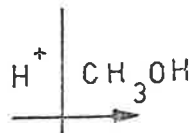
(58)
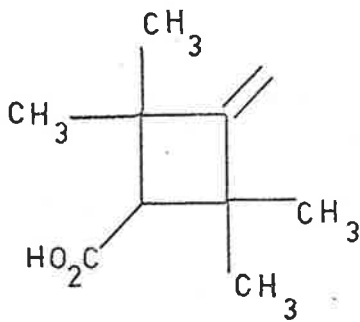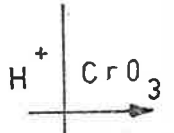
(59)
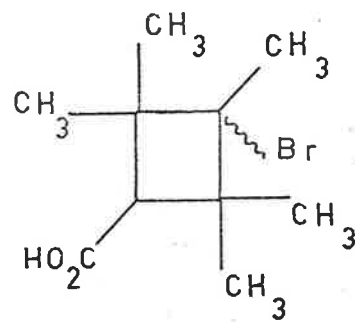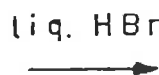
(60)
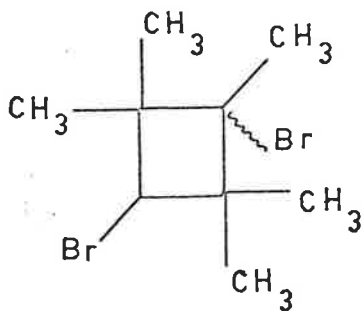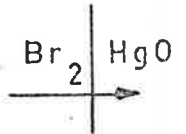
(48)

new approach is outlined in Scheme 19. All of the steps with the exception of the final reaction, were either known reactions[57,58] or had previously been carried out on closely related systems.[14,51,52]

The dioxalane (52) was prepared in 39% yield according to the method of Engen.[59] The procedure used for the preparation of the methylene compound (53) was modified from a method described by Ireland and Mander.[60] Filtration through a short alumina column gave an essentially pure product in high yield (93%).

Engen[59] has reported the preparation of this compound in considerably lower yield (59%) using sodium hydride and dimethyl-sulphoxide to generate the appropriate phosphorane.

Following the hydroboration procedure described by Sinclair,[58] the methylene compound was converted to the alcohol (54) (see Scheme 19). Vapour phase chromatographic analysis of the crude reaction product indicated less than 4% impurity.

Engen[57] has reported the hydrolysis of a dioxalane related to (54) on treatment with refluxing acetic acid for 2 hr. It was found however that the dioxalane (54) was converted smoothly and in high yield to its corresponding ketone (55) on warming with dilute (0.6N) methanolic hydrochloric acid. The infrared, n.m.r., and analytical data were consistent with the structure expected.

The primary alcohol (55) was readily converted to the tetra-hydropyranylether (56) on treatment with an excess of 2,3-dihydropyran containing a trace of acid. The hydroxyl group was protected in this

way to prevent the possible formation of phosphate esters[61] in the subsequent Wittig reaction.

Infrared, n.m.r., (Table 7), and analytical data were consistent with the structure expected. The infrared spectrum displayed a carbonyl absorption at 1785 cm^{-1} and the strong bands in the 1130–960 cm^{-1} region characteristic of cyclobutanones and tetrahydropyranylethers respectively.

Table 7.

n.m.r. spectrum of (56). (See fig. 5, p.58.)

δ (p.p.m.)	Appearance	Proton Count	Assignment
1.06,1.13,1.25	three singlets	12	methyl protons
1.43–1.67	multiplet	6	C_3',C_4',C_5' protons
2.10	triplet J_{AX} = 8.2 c.p.s.; J_{BX} = 7.9 c.p.s.	1	H_X
3.10–4.05	multiplet	2	C_2' protons
3.44, 3.88	two overlapping quartets J_{AB} =-10.1 c.p.s.	2	H_A, H_B
4.45	broad absorption	1	C_6' proton

The presence of the tetrahydropyranyl moiety gives rise to an interesting splitting pattern/region in the in which the protons H_A and H_B are expected to resonate.

In the spectrum of the primary alcohol (55) [fig. 5 (a)] the protons H_A and H_B occur as a doublet (split by H_X, J = 8 c.p.s.). However for the tetrahydropyranyloxy derivative (56) [fig. 5 (b)] the carbon atom to which the protons H_A and H_B are attached is connected via an oxygen bridge to an asymmetric centre. The derivative (56) can be considered to have the general formula $R_2H_XC.CH_AH_B.O.CABC$. In none of the possible conformers of this molecule can H_A and H_B have exactly the same magnetic environment, i.e. they are magnetically non-equivalent.

The term "intrinsic asymmetry"[62] is reserved for this example of magnetic non-equivalence of two nuclei, and the protons H_A and H_B are said to be "diastereotopic".[63] The protons H_A, H_B, and H_X form an ABX system.[64,65] The AB portion of the spectrum of (56) is seen as two overlapping quartets [fig. 5 (b)]* and since all eight peaks can be observed, the value of J_{AB} can be read directly from the spectrum.[65,66] This is found to be J_{AB} =-10.1 c.p.s. Fig. 6 shows a schematic representation of the AB and X regions of the spectrum of (56). The chemical shifts of the protons H_A and H_B are calculated[67] to be $\delta 3.44$ and $\delta 3.88$ respectively. The signals assigned to the proton H_X are seen as a triplet [figs. 5(b) and 6], the values of

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*   These quartets are superimposed over the broad absorption characteristic of the C_2' methylene group of the tetrahydropyranyl moiety.

fig. 5

```
        |234.5|  |225.0|        |206.0| |196.0|              |125.5|
  ***

  |242.5      232.8           214.3        204.0          133.5      117.5
              c.p.s.                                            c.p.s.

         H      and  H                                          H
          A          B                                          X
```
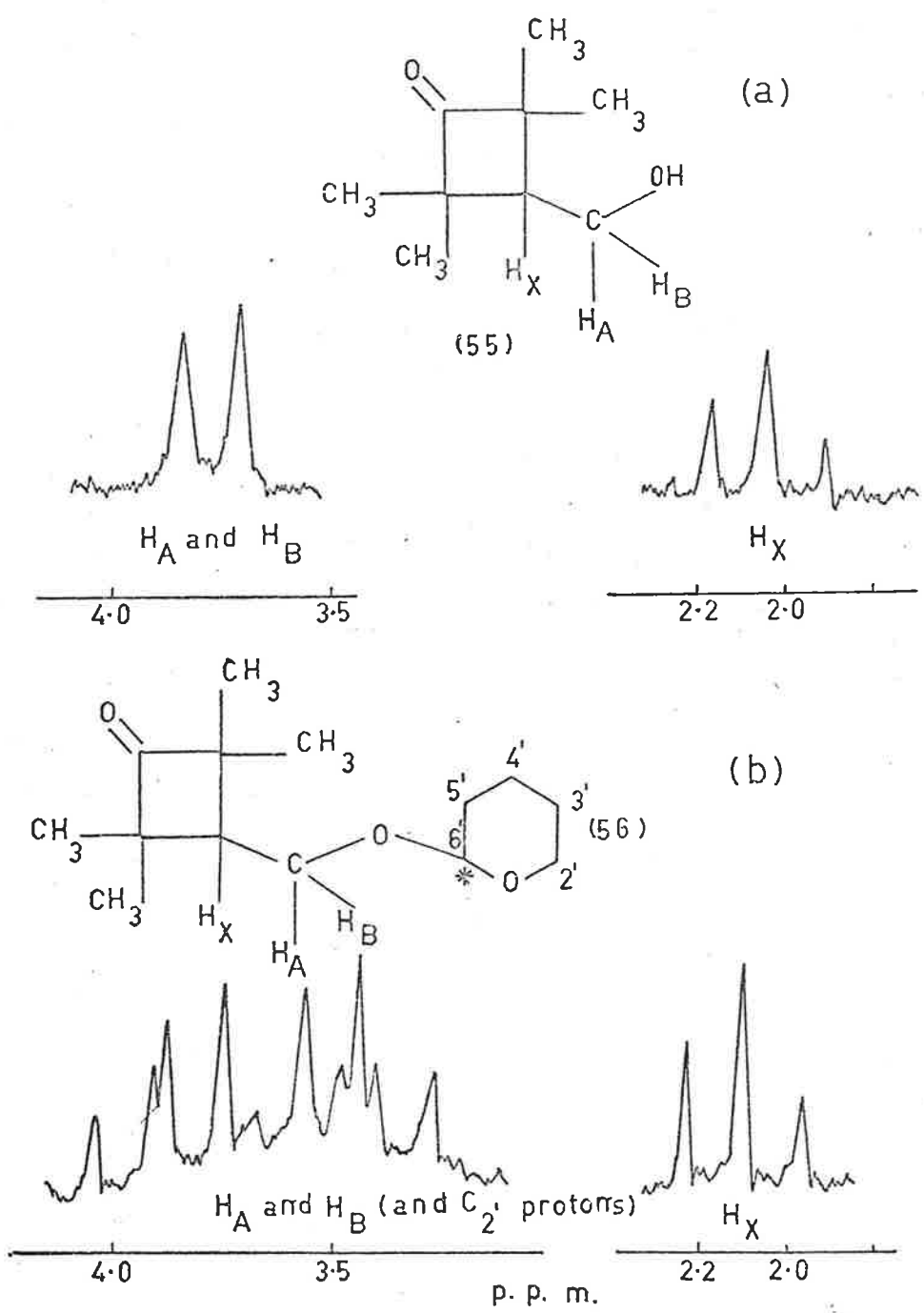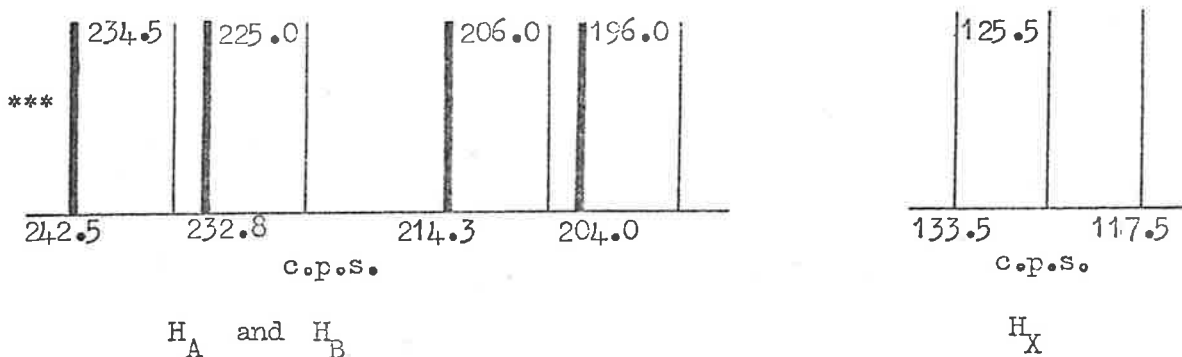
fig. 6

J_{AX}, J_{BX}, and the chemical shift of the proton H_X being calculated[67] to be 8.2 c.p.s., 7.9 c.p.s., and $\delta 2.10$ respectively.*

It is also interesting to note that in the saturated methyl region of the spectrum (56) three signals in an approximate ratio of 2:1:1, and not the initially expected two of approximately equal intensities,** are observed. Since the two protons H_A and H_B

-----

* The assistance of Dr. T.M. Spotswood in the analysis of this spectrum and of the spectrum of (57) is very gratefully acknowledged.

** Two signals due to pseudo-axial and pseudo-equatorial methyl groups respectively, e.g. spectra of (55), (58), and (59).

*** Signifies identification of the two quartets.

(56)
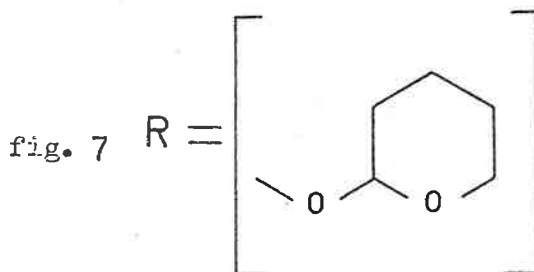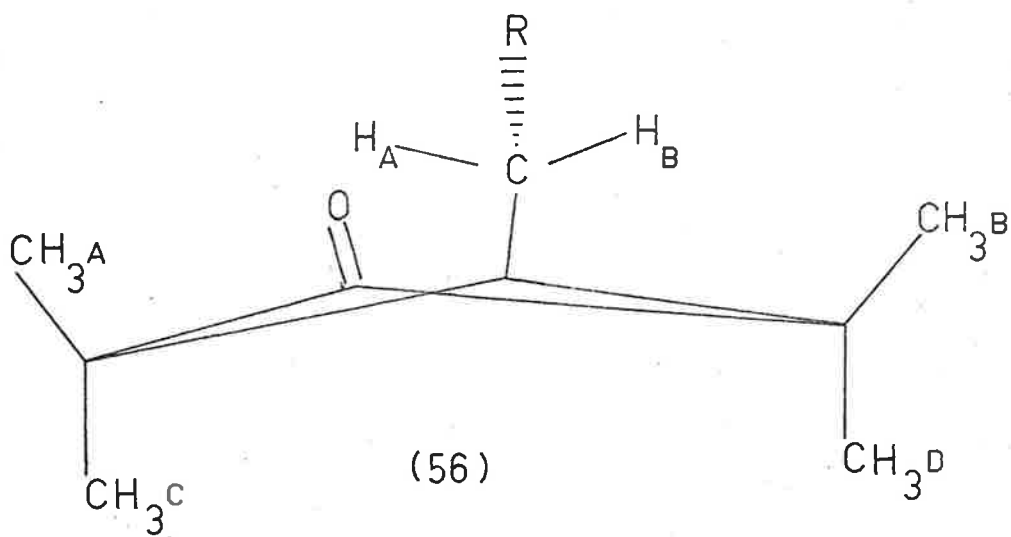
fig. 7

are magnetically non-equivalent, the two methyl groups A and B which
are closest in spacial orientation to these protons (fig. 7) now exist
in two different environments so that a separate signal is seen for
each group. The more distant methyl groups C and D are affected by
the magnetic non-equivalence of the protons H_A and H_B to a lesser
extent so that one signal only is seen for these two groups.

These effects are also exhibited by the methylene derivative
(57).

The methylene compound (57) was obtained in high yield (94%)
by the addition of methylenetriphenylphosphorane[60] to the ketone (56).
The structure of (57) was confirmed by infrared, n.m.r., and analytical

data. The methylene compound (57) was converted smoothly and in almost quantitative yield to the primary alcohol (58) which was in turn treated with Jones' reagent[18] to give the acid (59). The structures of these two latter derivatives were confirmed by infrared, n.m.r., and analytical data.

The bromo-acid (60) was prepared according to a method described by Hamon,[51,52] viz. dissolution of the acid (59) in liquid hydrogen bromide at -78°. The product was found to be relatively unstable undergoing dehydrobromination upon column or vapour phase chromatography. A slow decomposition (presumably initiated by dehydrobromination), was observed on standing at room temperature; at 0°, however it was relatively stable. Stable to sublimation ($60^{\circ}/.1$ mm) the acid was obtained in a relatively pure state by this process. Its structure was confirmed by infrared, n.m.r., (Table 8),
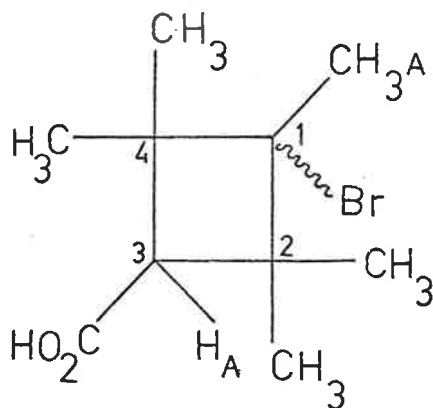
(60)

and analytical data. The infrared spectrum showed absorptions charac-
teristic of an acid, viz. a broad absorption centred around 3000 cm^{-1},
and a carbonyl absorption at 1700 cm^{-1}.

Table 8.

n.m.r. spectrum of (60).

δ (p.p.m.)	Appearance	Proton Count	Assignment
1.12,1.21,1.45	singlets	12	C_2, C_4 methyl groups
1.85	singlet	3	CH_{3A}
2.59, 2.85	singlets	1	H_A
11.26-11.52	broad absorption	1	acid proton

Were only one of the two possible isomers of (60) present, the
resonance observed for the proton H_A would be expected to be a singlet.
The fact that two signals of approximately equal intensities occur in
the general region where the proton H_A would be expected to resonate
indicates that both isomers of (60) are present in approximately equal
amounts. This effect is also exhibited by the cyclobutane derivatives
(17), (24), (26), and (20).

(b)   Modified Hunsdiecker reactions.

The Cristol-Firth[69] modification of the Hunsdiecker reaction
is well known as a convenient method for the bromodecarboxylation of
organic acids. Using this method, Sinclair[58] has recently achieved

the bromodecarboxylation of two cyclobutane derivatives related to
(60), viz. the keto-acid (61) and its corresponding ethyleneglycol
ketal (see Scheme 20).

The bromo-acid (60) was treated according to the method des-
cribed by Sinclair. Benzene* was used as the solvent since the acid
(60) was found to be insoluble in refluxing carbon tetrachloride.

Scheme 20.

(61)   (62)

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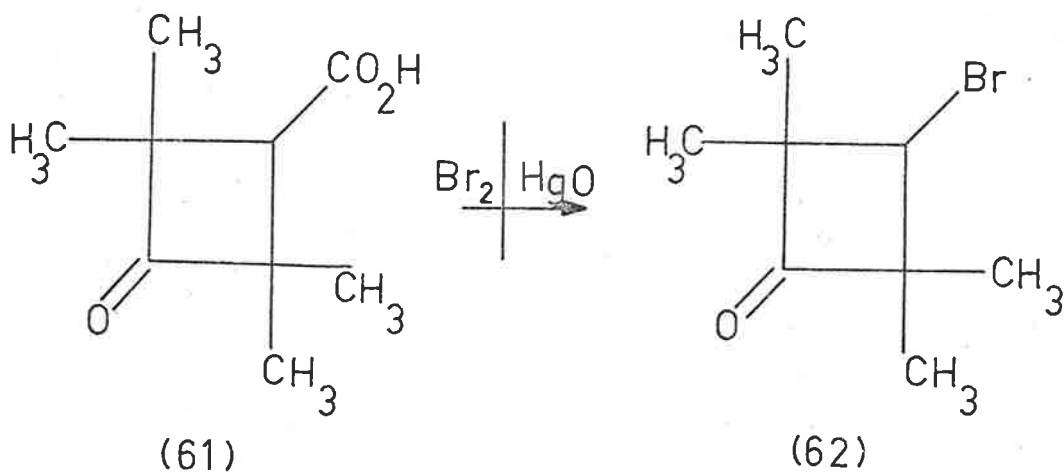
*   Although benzene does not seem to have been used as a solvent
for this reaction, the use of solvents other than carbon tetra-
chloride, viz. dichloroethane[69] and bromobenzene,[70] has been
reported.

The reaction was attempted a number of times but without success. In all cases a large number of apparently unstable products were obtained. Attempted separation of the major components by preparative plate and preparative vapour phase chromatography resulted in decomposition, dark-coloured mixtures being obtained. Similar unstable products were obtained when the reaction was attempted in benzene at room temperature. In both cases no evidence was found for the presence of the required dibromide (48).

Because of the instability of the bromo-acid (60) - (it was thought that the large steric size of bromine atom* at position 1 of the cyclobutane ring might be a factor causing the reaction to the unknown products observed), it was decided to attempt the modified Hunsdiecker reaction upon an analogue of (60) with smaller steric requirements, viz. the hydroxy-acid (64) (Scheme 21).

The acid (64) was prepared by oxidation of the alcohol (55) to its corresponding acid (63), which was in turn treated with an excess of methylmagnesium iodide. The structures of the acids (63) and (64) were confirmed by infrared, n.m.r., and analytical data. As expected the acid (64) was found to be considerably more stable than its bromo-analogue (60).

---

*   Severe interactions between the adjacent methyl groups would be expected.

Scheme 21.

(55)　　CrO₃ / H⁺　　(63)　　CH₃MgI

(64)　　Br₂ / HgO　　(65)　　dehyd.

(50)　　liq. HBr　　(48)
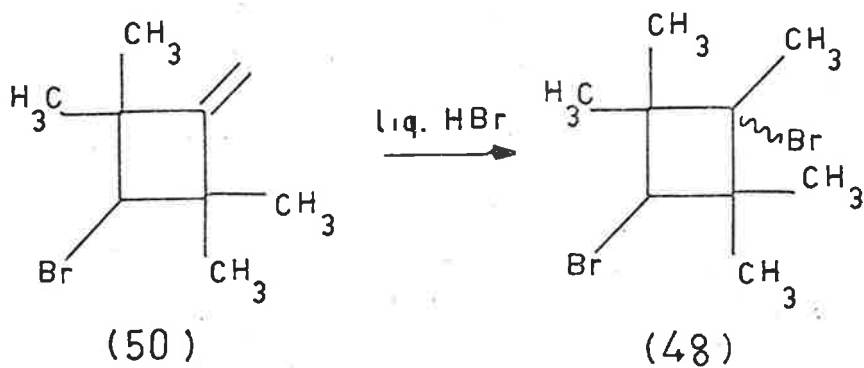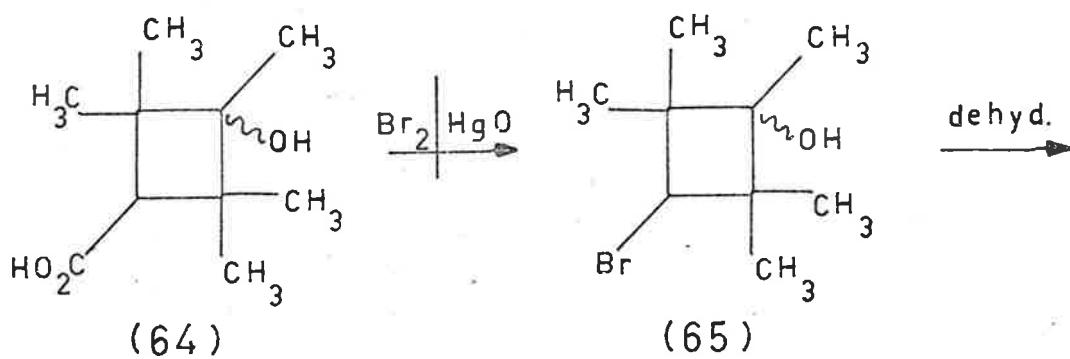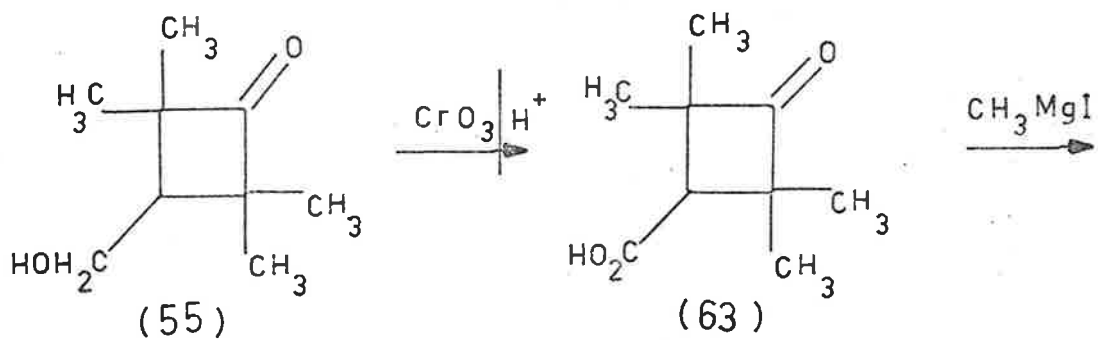
The modified Hunsdiecker reaction on the acid (64), was attempted in benzene initially at 80° and then at room temperature. As before mixtures of unstable compounds which decomposed during purification [as described for (60)], were obtained.

The above reaction was also carried out using the methylene-acid (59).

Treatment of this acid under modified Hunsdiecker conditions[69] would be expected to give one or both of two possible products, viz., the bromide (50) resulting from bromodecarboxylation of (59) and the tribromide (66) resulting from both bromodecarboxylation and bromination of the methylene group of (59, Scheme 22). Treatment of the

Scheme 22.

(59)

(66)
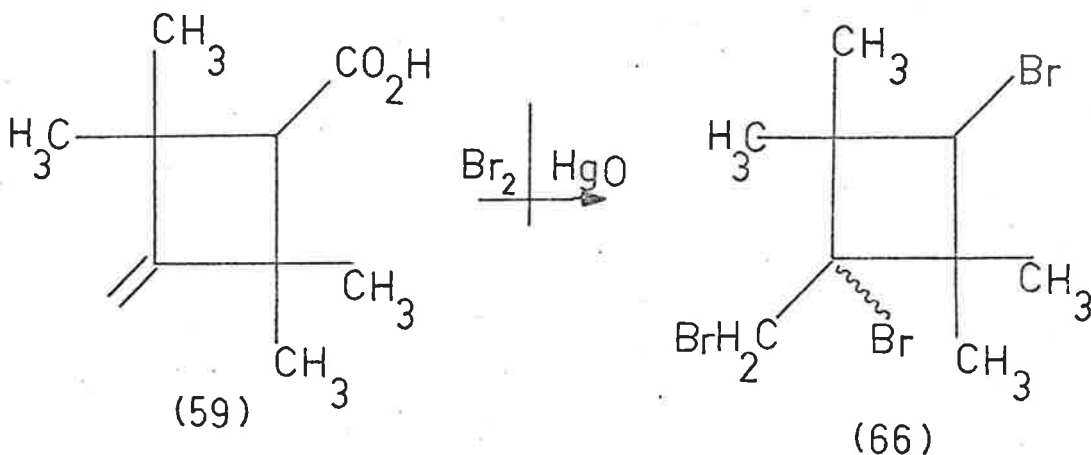
latter product (66) with a suitable debrominating reagent,[71] (viz. chromous sulphate)[72] would be expected to yield the bromide (50) which could then be treated with hydrogen bromide[51,52] to yield the desired dibromide (48) (see Scheme 21).

* The acid (64) was found to be insoluble in refluxing carbon tetrachloride

However on carrying out the modified Hunsdiecker reaction upon the acid (59) unstable products which decomposed on attempted purification were again obtained.

Using a method described by Kochi[73] (viz., lithium chloride and lead tetraacetate in refluxing benzene) a preliminary attempt was made to effect the chlorodecarboxylation of the acids (60) and (59). Scheme 23 shows the expected product in each case.

Scheme 23.
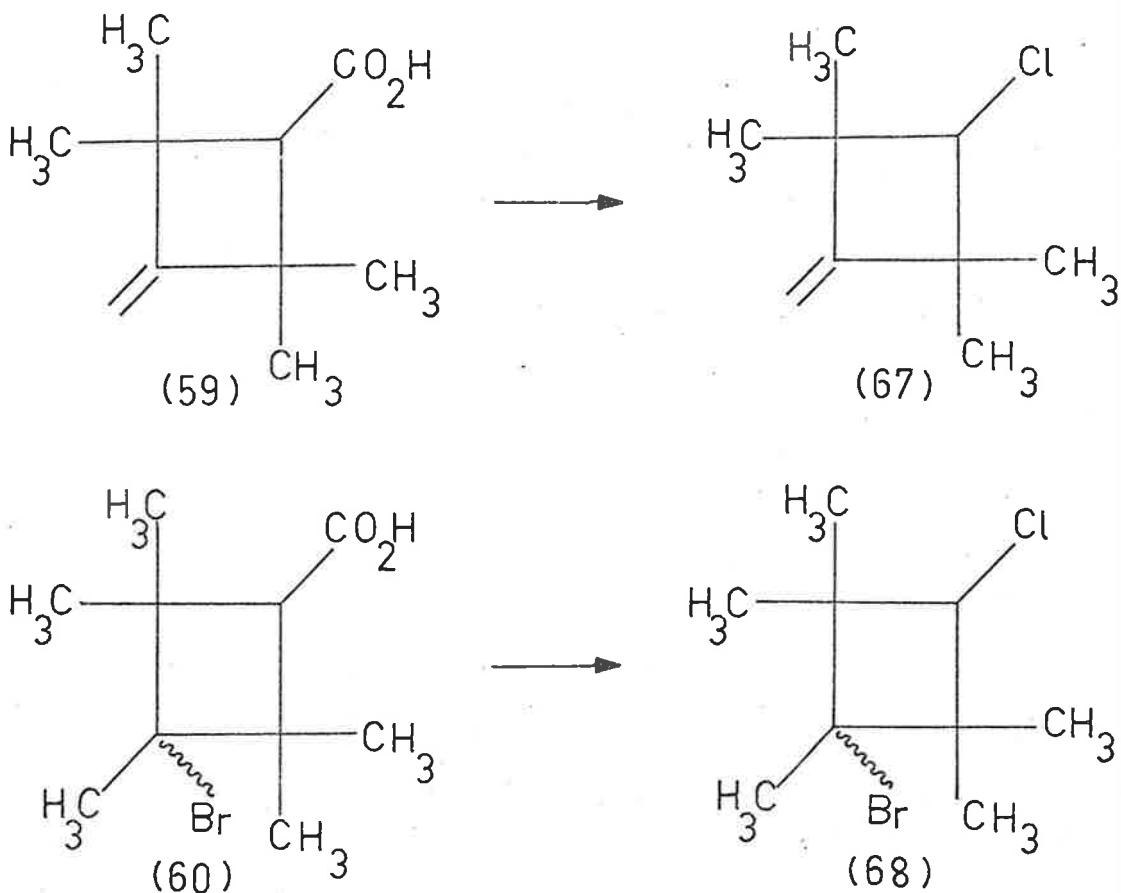
However when this reaction was attempted using the acid (60) unstable products which decomposed on attempted purification were

observed. Preliminary analysis (by t.l.c. and infrared spectrum) of
the product obtained when (59) was treated under the conditions des-
cribed by Kochi[73] indicated that a number of compounds were present.
Absorptions at 1780 and 1740 cm^{-1} in the infrared spectrum of the
reaction product were suggestive of a γ -lactone and an ester group.
Amongst the reaction products may well be compounds similar to the
acetoxy lactone (70) obtained by Moriarty on treatment of endo-5-
carboxy-bicyclo[2,2,1]hept-2-ene (69) with lead tetraacetate and lithium
chloride (Scheme 24).

Scheme 24.
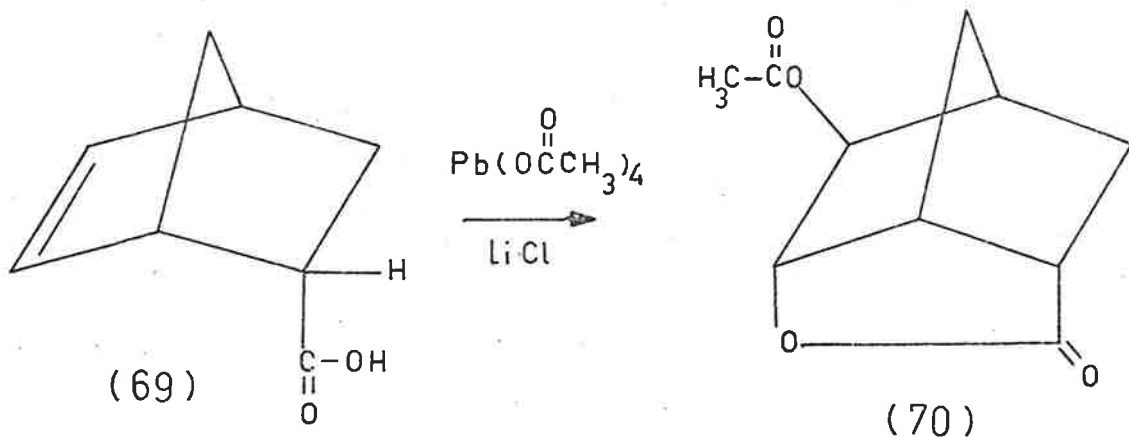
However due to lack of time this reaction was not investigated
further.

EXPERIMENTAL

General Procedure.

Melting points were determined using a Kofler hot stage and are uncorrected.

Microanalyses were carried out by the Australian Microanalytical Service, Melbourne.

Organic extracts were dried over calcium chloride unless otherwise stated.

The chromatographic grades of silica gel were Crosfield Sorbisil SG 60 and Kieselgel G. The preparative plate (p.p.c.) and thin-layer (t.l.c.) chromatography were carried out using the following solvent system unless otherwise stated: ether/light petroleum 1:1 and the position of the components detected with berberin hydrochloride (0.5% in methanol). Alumina was dried to activity I by heating for 3 hr at 400°.

Spectroscopic Determinations.

Infrared spectra were determined with Perkin-Elmer 237 and 337 Grating Spectrophotometers and a Unicam SP200 spectrophotometer.

Mass spectra were recorded using a Hitachi Perkin-Elmer RMU-6D spectrometer, fitted with a double focussing device.

Nuclear magnetic resonance spectra were recorded with Varian DP 60 and T 60 spectrometers at 60 Mc/s and chemical shifts were measured relative to tetramethylsilane as the internal standard.

Solvents.

Diethyl ether was dried over calcium chloride, distilled from calcium hydride, and stored over sodium wire. When "super dry" was required, ether (from sodium) was distilled from lithium aluminium hydride.

Tetrahydrofuran, diglyme, 1,2-dimethoxyethane, benzene, and hexane were distilled from calcium hydride and stored over sodium wire.

Tertiary butanol, dimethylsulphoxide, and N,N-dimethylformamide were distilled from, and stored over, calcium hydride.

Acetone was distilled from potassium permanganate, dried over calcium chloride, and distilled.

Petroleum ether $(30-40^{\circ})$ and $(40-60^{\circ})$ was dried over calcium chloride and distilled.

All other solvents were dried and distilled as necessary.

Vapour Phase Chromatography.

Routine purity checks and quantitative determinations were carried out using Perkin-Elmer 880 and 881 instruments; the latter was equipped with a Perkin-Elmer 194B printing integrator. Both employed flame ionisation detectors, and nitrogen was used as the carrier gas. Preparative separations were achieved with an Aerograph A700 or A705 instrument, using flame ionisation detectors and nitrogen as the carrier gas. For the quantitative analyses the ratio of peak areas was found by the "cut and weigh" technique, and also by using the integrator.

Work Described in Part I.

Oxidations of 1-hydroxymethyl-2,2,4,4-tetramethylcyclobutyltetrahydro-
pyranylether (17).

(a)   Oxidations using Jones' Reagent.[18]

A series of preliminary reactions were carried out with
modifications to the procedure described previously,[15] viz. addition
of Jones' reagent[18] to a solution of the primary alcohol (17) in
acetone. Reactions using concentrations of 10%, 5%, 1%, and .05%* of
the alcohol (17) in acetone were carried out. The products were
identified by infrared and t.l.c. by comparison with authentic samples.[15]
In all cases an approximately 1:1 mixture of acid (18) and ester (13)
was observed. The spectral characteristics (infrared, n.m.r., and mass
spectrum/(13) were found to be identical to those of the compound ob-
served previously.[16]

(b)   Oxidations by the method of Sarett.[19]

The primary alcohol (17), (200 mg, .90 mmole) in pyridine
(2 ml) was mixed thoroughly with "Sarett's[19] reagent" (2.0 mmoles)
in pyridine (3 ml) and allowed to stand in a stoppered vessel for
21 hrs. [This represents a 4% solution of the alcohol (17).] The

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*   Previously[15] a concentration of 15% alcohol (17) in acetone
was used.

products were identified by infrared and t.l.c. by comparison with authentic samples[10] of acid (18) and ester (13). Reactions using concentrations of 1% and .05% alcohol (17) in pyridine were also carried out. In all cases an approximately equal amount by weight of (18) and (13) was obtained.

(c)   Oxidations using a method described by Snatzke.[20]

The primary alcohol (17), (100 mg, .45 mmole) was dissolved in N,N-dimethylformamide (80 ml) and chromium trioxide (100 mg, 1.0 mmole) slowly added. [This represents a 1.2% solution of the alcohol (17).] Concentrated sulphuric acid (2 drops) was added and the mixture allowed to stand for 16 hr at room temperature. The products were identified by infrared and t.l.c. by comparison with authentic samples of acid (18) and ester (13). Once again an approximately equal amount by weight of (18) and (13) was obtained. A small amount of starting alcohol (17) was also obtained.

Preparation of 3-methoxymethylene-2,2,4,4-tetramethylcyclobutyl-tetrahydropyranyl ether (21).

Butyllithium (7.0ml) (Fluka 20-25% in hexane, approx. 21 mmole) was added with stirring to 250 ml anhydrous hexane in a 500 ml two-necked flask in an atmosphere of nitrogen. The flask was evacuated and flushed with nitrogen several times to ensure that the solvent was largely free of oxygen. The solution was cooled to 0° and methoxy-

methyltriphenylphosphonium chloride (m.p. 192-194°; lit.[75] 191-193°),
(10 g, 30 mmole) was added with stirring. A deep orange colour
developed almost immediately. The solution was allowed to stir for
$1\frac{1}{2}$ hr at 0° when the ketone (15), (4.0 g, 16 mmole) dissolved in 2 ml
of anhydrous hexane was added. The solution was allowed to stir over-
night during which time the temperature rose to 25°. Work-up was
modified from a method of Ireland and Mander.[60] The reaction mixture
was extracted with two 50 ml portions of 70% aqueous methanol and the
methanol washings extracted twice with further 50 ml portions of hexane.
The combined hexane extracts were washed with water and dried. Evapora-
tion of the solvent gave an oil (3.80 g) which was chromatographed on
200 g alumina. Elution with hexane (400 ml) gave a colourless liquid
(3.0 g, 75%), b.p. 145-150° (12 mm). ν_{max} (film) 3040, 1690 ($=\!\!\!\!<^{OMe}$),
1120, 1080, 1040, 1015 cm^{-1} (tetrahydropyranylether). The n.m.r.
spectrum (carbon tetrachloride) showed the following absorptions,
δ1.02-1.28 (multiplet 12H), δ1.37-1.83 (multiplet 6H), δ3.42 (singlet
3H), δ3.17-4.0 (multiplet 2H), δ3.52 (singlet 1H), δ4.40 (triplet 3H),
and δ5.60 (singlet 1H). (Found: C, 71.1; H, 10.1. Calc. for
$C_{15}H_{26}O_3$; C, 70.8; H, 10.3%). Elution with 10% ether in hexane
(200 ml) gave an oil (500 mg). The infrared spectrum was identical
with that of (15).

Attempted Preparation of 3-Carboxaldehydo-2,2,4,4-tetramethylcyclo-
butan-1-ol (22). - The enol ether (21), (200 mg, .8 mmole) was

dissolved in 20 ml of ether previously saturated with 70% perchloric

acid. The solution was kept at room temperature for 8 min, poured

into an excess of saturated sodium bicarbonate solution, and extracted

with ether (60 ml). The ether extract was dried and the solvent

removed in vacuo to yield an oil (150 mg). ν_{max} (film) 3420 (O-H),

1710 (aldehyde C=0), 1120, 1080, 1040, and 1015 cm^{-1} (tetrahydro-

pyranylether). The n.m.r. spectrum (deuterochloroform) showed the

following absorptions:- $\delta 1.20$ (multiplet, methyl groups), $\delta 1.60$

(multiplet, C_3', C_4', C_5' methylene protons of tetrahydropyranylether),

$\delta 3.10$-4.00 (multiplet, C_2' methylene protons of tetrahydropyranyl-

ether), $\delta 3.50$ (multiplet, hydroxyl proton), $\delta 4.40$ (broad absorption,

methine proton of tetrahydropyranylether), and $\delta 9.70$ (multiplet),

aldehyde proton. The above procedure was repeated increasing the

reaction time from 8 min to 1 hr at room temperature. A dark viscous

liquid which was filtered through celite (50 g) was obtained on work-

up as described above. Elution with ether (200 ml) gave a yellow

oil (100 mg) which had identical spectral characteristics to those

of the product obtained in the preceding experiment.

Preparation of 3-dimethoxymethyl-1,2,2,4,4-tetramethylcyclobutan-
1-ol (24). - The enol ether (21) (1.5 g, 6.8 mmole) was dissolved

in methanol (20 ml) and two drops of concentrated hydrochloric acid added. The mixture was allowed to stand for $1\frac{1}{2}$ hr when all enol ether (21) had disappeared (by t.l.c.). Ether (25 ml) was added followed by 30 ml saturated sodium bicarbonate solution. Following this, the mixture was extracted with three 20 ml portions of ether. The combined ether extracts were washed with water (25 ml) and dried. Evaporation of the solvent in vacuo gave an oil (1.1 g, 91% crude yield), which was chromatographed on alumina (100 g). Elution with 60% ether in hexane (400 ml) yielded a colourless oil (850 mg, 71%), b.p. 65-70°/.05 mm. ν_{max} 3430 (OH), 1200, 1150, 1070 cm^{-1} (CH$<^{OMe}_{OMe}$). The n.m.r. spectrum (deuterochloroform) showed the following absorptions: $\delta 1.02-1.26$ (multiplet 12H), $\delta 1.98$ (multiplet 1H), $\delta 3.19$ (singlet 6H), $\delta 3.32-3.58$ (multiplet 2H), and $\delta 4.30$ (multiplet 1H). Analytical figures were not obtained because of difficulties experienced in the purification of this compound.

Preparation of 3-dimethoxymethyl-2,2,4,4-tetramethylcyclobutyl-1-tosylate (25). - The hydroxy-acetal (24) (1.0 g, 50 mmole) freshly prepared and chromatographed, was dissolved in 5 ml of anhydrous pyridine and p-toluenesulphonylchloride (2.9 g, 15 mmole) (freshly recrystallised[76]) was added. The mixture was warmed to dissolve the p-toluenesulphonylchloride, and allowed to stand in a closed vessel at room temperature for nine days. Water (10 ml) was added, and the mixture allowed to stand for half an hour. Ether (20 ml) was added

and the aqueous layer extracted three times with 20 ml portions of ether. The combined ether extracts were washed with three 20 ml portions of 1N sodium hydroxide, with water (20 ml), and dried. Evaporation of the solvent _in vacuo_ gave a solid (1.8 g) which contained traces of pyridine. This was chromatographed on alumina (100 g). Elution with 40% ether in light petroleum yielded a white solid (1.3 g, 85%), m.p. 94-96°. An analytical sample was prepared by recrystallisation from ether/light petroleum. ν_{max} 3020, 1600, 1180, 1170 (OTs), 1200, 1070 (CH$\begin{smallmatrix}OMe\\OMe\end{smallmatrix}$). The n.m.r. spectrum (deutero-chloroform) showed the following absorptions:- δ.85, 1.05 (singlets 12H), δ1.63 (doublet 1H, J = 10 c.p.s.), δ2.41 (singlet 3H), δ3.23 (singlet 6H), δ4.04 (singlet 1H), δ4.36 (doublet 1H, J = 10 c.p.s.), and δ7.30, 7.75 (A B quartet, J = 8 c.p.s.). (Found: C, 60.9; H, 7.8; S, 9.0. Calc. for $C_{18}H_{28}O_5S$; C, 60.7; H, 7.9; S, 9.0%).

Preparation of 3-carboxy-2,2,4,4-tetramethylcyclobutyl-1-tosylate (26). - To a cooled (0°C) solution of (25) (1.0 g, 2.8 mmole) in acetone (50 ml) was added dropwise with stirring a solution of chromium trioxide in sulphuric acid (Jones' reagent,[18] 2.8 ml, 11.2 mmole), over 60 min. The solution was concentrated to 25 ml _in vacuo_, diluted with water (50 ml), and extracted with three 50 ml portions of ether. The combined ether extracts were washed with water (25 ml) and dried. Evaporation of the solvent _in vacuo_ yielded a solid (1.0 g) which was chromatographed on silica gel (60 g). Elution

with 30% ether in light petroleum (200 ml) yielded a white solid (850 mg, 87%), m.p. 150-160° decomp. An analytical sample was prepared by recrystallisation from ether/light petroleum. ν_{max} (chloroform) 3600-2400 (acid O-H), 1710 (acid C=O), 1600, 1180, 1170, and 855 cm^{-1} (OTs). The n.m.r. spectrum (deuterochloroform) showed the following absorptions: $\delta 0.96$, 1.05, 1.16, 1.23 (singlets 12H, methyl protons), $\delta 2.45$ (singlet 3H, aromatic methyl group), $\delta 2.73$ (broad singlet, 1H, proton at C_3 of cyclobutane ring), $\delta 4.05$ (broad singlet 1H, proton at C_1 of cyclobutane ring), $\delta 7.25$, 7.70 (AB quartet 4H, J = 8 c.p.s., aromatic protons), and $\delta 11.41-11.52$ (broad absorption 1H, acid proton). (Found: C, 58.5; H, 6.9; S, 9.7. Calc. for $C_{16}H_{22}O_5S$; C, 58.9; H, 6.8; S, 9.9%).

Preparation of 3-carbomethoxy-2,2,4,4-tetramethylcyclobutyl-1-tosylate.[27] (20). - This compound was prepared by the addition of an excess of diazomethane[26] (an ethereal solution prepared by the addition of N-nitrosomethylurea to a stirred mixture of 50% aqueous potassium hydroxide and ether (60 ml) at 0°: the ether layer was separated and dried over potassium hydroxide), to a cold (0°) stirred solution of (26) (800 mg, 2.3 mmole) in ether (20 ml). The solution was allowed to stand at 0° for 5 hr. Evaporation of the solvent gave a solid (800 mg) which was chromatographed on silica gel (50 g). Elution with 15% ether in light petroleum gave a white solid (780 mg, 98%), m.p. 74-81°. Spectral characteristics were identical to those

of the ester (20) obtained previously.[27] When admixed with an authentic sample of (20) no depression in m.p. was observed.

Preparation of methyl 2,2,4,4-tetramethylbicyclo[1.1.0]butane-1-carboxylate (12).[77] - The procedure used was modified to that described previously.[27] An excess of sodium hydride powder* was added to a stirred solution of (20) (100 mg, .33 mmole),/in anhydrous 1,2-dimethoxyethane in an atmosphere of nitrogen. The mixture was allowed to stir for 16 hr at 40° when light petroleum (b.p. 30-40°) (15 ml) was added and the mixture filtered in vacuo through a celite pad. Water (15 ml) was added, the filtrate washed with six 10 ml portions of water, and dried. Evaporation of the solvent gave a yellow liquid (37 mg, 75% crude yield). A sample was purified for analysis by preparative vapour phase chromatography (5' 20% S.E. 52 column at 110° and 60 ml/min). Spectral characteristics were identical with those of the bicyclo[1.1.0]butane (12).[27] Prepared in this way the product was free of 1,2-dimethoxyethane[77] and involatile material. (Found: C, 71.0; H, 9.5. Calc. for $C_{10}H_{16}O_2$; C, 71.4; H, 9.6%).

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* The sodium hydride mineral oil dispersion was repeatedly washed with hexane, refluxed in hexane (50 ml) for 3 hr and dried (.16 mm) for 48 hr.

Pyrolyses of methyl 2,2,4,4-tetramethylbicyclo[1.1.0]butane-1-
carboxylate (12).[77] - The following procedure is typical: (12)
(20-100 mg, .13 - .66 mmole), freshly prepared reaction product,*
was placed in a 250 ml quartz flask, which had either been untreated
or base treated.** A trace of anhydrous hydrochloric acid gas
(generated from a "Kipps" apparatus and then dried) or triethylamine
(1 drop) was introduced at this stage if required. The flask was then
immersed in liquid nitrogen and evacuated (.1 mm),*** immersed in an
oil bath at 150° for varying lengths of time (see Table 9), allowed
to cool, and the contents dissolved in carbon tetrachloride (.4 ml).
The n.m.r. spectrum of the reaction product was then determined, and
gas phase chromatography was used to calculate the proportions of the
major products (greater than 5%) obtained. The identities of the
products were confirmed by the "spiking on" technique employing two
columns of different polarities, viz. 5' 15% S.E. 52, and 10' 5%
F.F.A.P. columns, at 80-110° and 30 ml/min. Varying proportions of

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* The n.m.r. spectrum indicated that the reaction product was
substantially pure.

** The vessel was allowed to stand in the presence of base
(triethylamine) for 24 hr and dried (120°) for 24 hr.

*** Except in the cases where anhydrous hydrochloric acid gas
had been introduced.

three major products were observed in all runs. These were isolated for identification and comparison by preparative vapour phase chromatography (12' 20% carbowax column at 109° and 100 ml/min). The products in order of increasing retention times were:

(a)   Methyl trans-2,α-methylvinyl-1,1-dimethylcyclopropane-3-carboxylate (27) (retention time 7.8 min). The following spectral characteristics were observed: ν_{max} (film) 1725 and 1210 cm^{-1}. The n.m.r. spectrum (carbon tetrachloride) showed the following absorptions: $\delta1.00$ (singlet 3H), $\delta1.22$ (singlet 3H), $\delta1.51$, 1.83 (AB quartet, J = 6 c.p.s., 2H), $\delta1.72$ (singlet 3H), $\delta3.56$ (singlet 3H), $\delta4.54$, 4.74 (broad singlets 2H). Irradiation 175 c.p.s. downfield* from the quartet at $\delta1.44$-1.88, caused these resonances to be sharpened. Similarly, irradiation 175 c.p.s. upfield from the doublet at $\delta4.54$, 4.74 caused these resonances to be sharpened. The mass spectrum showed an m/e 168; requires m/e 168. (Found: C, 71.2; H, 9.7. Calc. for $C_{10}H_{16}O_2$; C, 71.4; H, 9.6%).

(b)   Methyl 2,5-dimethylhexa-1,4-diene-3-carboxylate (28) (retention time 11.2 min). The following spectral characteristics were observed. ν_{max} (film) 1725 and 1210 cm^{-1}. The n.m.r. spectrum (carbon tetrachloride) showed the following absorptions: $\delta1.59$-1.83 (multiplet 9H),

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*   Away from the peak due to the internal standard, tetramethylsilane.

δ3.63 (singlet 3H), δ3.70, 3.87 (broad doublet, J = 9 c.p.s., 1H),

δ4.08 (broad singlet 2H), δ5.27, 5.42 (broad doublet, J = 9 c.p.s., 1H).

The mass spectrum showed an m/e 168; requires m/e 168. (Found: C,

71.0; H, 9.7. Calc. for $C_{10}H_{16}O_2$; C, 71.4; H, 9.6%).

(c)   Methyl 2,5-dimethylhexa-2,4-diene-3-carboxylate (29) (reten-

tion time 13.8 min). The following spectral characteristics were

observed: ν_{max} (film) 1725 and 1215 cm^{-1}. The n.m.r. spectrum

(carbon tetrachloride) showed the following absorptions: δ1.50

(doublet J = 1.0 c.p.s., 3H), δ1.70 (doublet, J = 1.0 c.p.s., 3H),

δ1.73 (doublet, J = 1.5 c.p.s., 3H), δ1.93 (doublet, J = 1.5 c.p.s.,

3H); δ3.56 (singlet 3H), δ5.62 (broad singlet 1H). The mass spec-

trum showed an m/e 168; requires m/e 168.

Pyrolyses of methyl 2,2,4,4-tetramethylbicyclo[1.1.0]butane-1-
carboxylate at 150°.

Table 9.

Reaction Time (min)	Modifications	Relative % of Products.			
		(12)	(27)	(28)	(29)
50	—	—	66	27	7
50	apparatus base treated	—	38	16	46
50	apparatus base treated triethylamine added	56	—	—	44
180	apparatus base treated triethylamine added	—	—	—	95
50	apparatus base treated hydrochloric acid (gas) added.	—	68	32	—

Pyrolysis of methyl trans-2,α-methylvinyl-1,1-dimethylcyclopropane-
3-carboxylate (27).

A purified sample of the derivative (27) (20 mg, .13 mmole)
was heated at 150° for 50 min in a base-treated quartz vessel. The
n.m.r. spectrum (carbon tetrachloride) of the product was consistent
with a mixture of (27) [δ1.08, 1.20 (singlets, methyl protons), δ1.80
(singlet, vinylic methyl group), and δ4.62, 4.88 (broad singlets, vinylic
methylene protons)] and (28) [δ1.61, 1.73, 1.80 (singlets, vinylic methyl
groups)]. The product was analysed by vapour phase chromatography
(10' 5% F.F.A.P. and 5' 15% S.E.52 columns at 90° and 30 ml/min). The
major products were shown to be the cyclopropane (27; 74%) and the
1,4-hexadiene (28; 26%) derivatives.

Treatment of methyl 2,2,4,4-tetramethylbicyclo[1.1.0]butane-1-
carboxylate (12) with acid at room temperature. — The bicyclo-
[1.1.0]butane (12) (20 mg, .13 mmole) was dissolved in carbon tetra-
chloride (0.4 ml) and a catalytic amount of anhydrous hydrogen
chloride (generated from a "Kipps" apparatus and then dried), bubbled
through the solution. After $\frac{1}{2}$ hr the n.m.r. spectrum of this solution
indicated the presence of unchanged starting material (12) [δ1.24, 1.30
(singlets, methyl groups)] and isomer (27) [δ1.08, 1.20 (singlets,
methyl protons), δ1.80 (singlet, vinylic methyl group), and δ4.62
4.88 (broad singlets, vinylic methylene protons)]. After 1 hr, signals
consistent with the presence of isomer (27) (as above) and also isomer

(28) [δ1.61, 1.73, 1.80 (singlets, vinylic methyl groups)] were discernible. No signals consistent with the presence of (12) were observed. After 17 hr a similar spectrum to that obtained after 1 hr was observed. Vapour phase chromatographic analysis (10' 5% F.F.A.P. and 5' 15% S.E.52 columns at 90° and 30 ml/min) of the reaction mixture after 1 hr indicated the presence of (27; 80%) and (28; 20%).

Preparation of dimethyl 3,3-dimethyl-1-pyrazoline-trans-4,5-dicarboxylate (40).

Dimethyl fumarate (1.0 g, 9 mmole) was dissolved in ether (50 ml) and added to an ethereal solution of freshly distilled 2-diazopropane[78] (2 molar excess, calculated on the basis of a 20% yield of the 2-diazopropane) at 0°. The solution was allowed to stand at 0° for 12 hr after which time the pink colouration (due to the presence of 2-diazopropane) was slowly discharged. Evaporation of the solvent yielded a yellow oil (1.6 g, 95%) which slowly crystallised on standing and exhibited the following spectral characteristics. ν_{max} (film) 3349 (N-H), 1740 (ester C=O), and 1580 cm^{-1} (C=N). The n.m.r. spectrum (deuterochloroform) showed the following absorptions: δ1.30, 1.50 (singlets 6H, methyl groups), δ2.17 (broad singlet 1H, methine proton of pyrazoline ring), δ3.70, 3.77 (singlets 6H, methoxyl protons), and δ5.14 (multiplet 1H, amine proton).

Preparation of dimethyl 2,2-dimethylcyclopropane-trans-1,3-dicarboxy-
late*(41).

The pyrazoline (40) (1.0 g, 5.6 mmole) was heated with copper
powder (.7 g, 12 mmole)[79] at 150° until evolution of nitrogen had
ceased. The black oily liquid which was obtained was dissolved in
ether (10 ml) and filtered through celite (100 g). Elution with
ether (200 ml) gave a yellow oil (0.4 g, 50%) which had the following
spectral characteristics. ν_{max} (film) 3025 (weak, C-H stretching of
the cyclopropane ring) and 1730 cm^{-1} (ester C=O). The n.m.r.
spectrum (deuterochloroform) showed the following absorptions:
δ1.11, 1.19 (singlets 6H, methyl protons), δ1.60, 1.71 (AB quartet
J = 6 c.p.s., 2H, methine protons of cyclopropane ring), and δ3.65
(singlet 6H, methoxyl protons). These spectral characteristics were
found to be identical with those of the reported dimethyl 2,2-dimethyl-
cyclopropane-trans-1,3-dicarboxylate [80,81]

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* The preparation of compounds (40) and (41) has been
reported[83] by this method, but no experimental details
were given.

Work described in Part II.

Attempted displacement of the p-toluenesulphonyloxy function of 3-methylene-2,2,4,4-tetramethylcyclobutyl-1-tosylate (49).

In a typical run the p-toluenesulphonate ester (49) (100 mg, .4 mmole) was dissolved in anhydrous acetone* or dimethylsulphoxide, sodium bromide, or sodium iodide (both 2 x molar excess) added, and the solution allowed to reflux for 24 hr. Water (2 ml) was added and the solution extracted with two, 2 ml portions of chloroform. The combined chloroform layers were washed with water (5 ml) and dried. The infrared spectra (CHCl$_3$) of the products were substantially similar to that of an authentic sample of the p-toluenesulphonate ester[54] (49).

Preparation of 2,2,4,4-tetramethylcyclobutanone-dioxalane[59] (52).

This compound was prepared by the method described by Engen.[59] The diketone (51) was refluxed with ethylene glycol in toluene, the three products (51), (52), and the bisdioxalane,[59] were separated and this latter product was hydrolysed (toluene, water, and p-toluene-sulphonic acid) back to the dioxalane (52); 38%, b.p. 84-90°/5 mm, m.p. 56-59° (lit.[59] b.p. 84-87°/5 mm, m.p. 56-57°).

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* The reactions with acetone were carried out in a sealed tube at 150°.

Preparation of 2,2,4,4-tetramethylmethylenecyclobutane-dioxalane[59] (53).

The methyltriphenylphosphonium iodide used was prepared by addition of an excess of methyl iodide to a solution of triphenyl-phosphine in benzene at $0°$. The mixture was allowed to stand over-night, filtered, recrystallised from chloroform/ethyl acetate, filtered, and dried (16 mm) for 48 hr., m.p. 179-180° (lit.[82] 179-180°). The experimental procedure was modified from a method of Ireland and Mander.[60] Anhydrous ether (1000 ml) was added to a solution of potassium tertiary butoxide in tertiary butanol (prepared by dissolving potassium metal [18 g, 450 mmole) in 800 ml of anhydrous tertiary butanol) in an atmosphere of nitrogen. Methyltriphenyl-phosphonium iodide (182 g, 450 mmole) was added with stirring. The mixture became bright yellow after about 5 min and was allowed to stir for a further 5 hr. The dioxalane (52) (72 g, 390 mmole) was then added and the solution allowed to stir for a further 19 hr. Work-up as described by Ireland and Mander[60] gave a solid (67 g, 93%), b.p. 76-79°/5 mm (lit.[49] 75-80°/5 mm).

Vapour phase chromatographic analysis of the crude reaction mixture (5' 15% S.E. 52 column at 80° and 30 ml/min) indicated less than 1% impurity. The spectral characteristics of the compound (53) obtained in this way were identical to those of the compound reported by Engen.[59]

Preparation of 3-hydroxymethyl-2,2,4,4-tetramethylcyclobutane-dioxa-
lane (54).

This compound was prepared according to a method described by
Sinclair;[58] had m.p. 76-79° (lit.[59] 79-80°). Vapour phase chroma-
tographic analysis of the crude reaction product (5' 15% S.E. 52
column at 110° and 30 ml/min) indicated less than 4% impurity.

The spectral characteristics of the compound obtained in this
way were identical to those of an authentic sample of (54).[58]

Preparation of 3-hydroxymethyl-2,2,4,4-tetramethylcyclobutanone (55).

The product (54) (10 g, 50 mmole) was dissolved in methanol
(175 ml) and 2N aqueous hydrochloric acid (75 ml) was added. The
solution was refluxed for 1 hr, cooled, and sodium bicarbonate added
until effervescence had ceased, and the solution was alkaline.
Ether (100 ml) was added and the organic phase separated. The aqueous
phase was extracted with two 100 ml portions of ether and the combined
ether extracts washed with water (50 ml) and dried over anhydrous
magnesium sulphate. Evaporation of the solvent in vacuo gave a solid
which was recrystallised from ether/light petroleum to give white
crystals (7.5 g, 96%), m.p. 55-56°. A sample was prepared for analysis
by sublimation (50°/.1 mm); ν_{max} (chloroform) 3620, 3460 (O-H) and
1760 cm^{-1} (C=O). The n.m.r. spectrum (carbon tetrachloride) showed
the following absorptions: δ1.12, 1.21 (singlets 12H, methyl protons),

$\delta 1.90$-2.17 (triplet 1H, J = 8 c.p.s., methine proton), $\delta 2.60$-3.00 (broad absorption 1H, hydroxyl proton), $\delta 3.70$, 3.83 (doublet 2H, J = 8 c.ps., methylene protons of primary alcohol group). (Found: C, 68.9; H, 10.3. Calc. for $C_9H_{16}O_2$; C, 69.2; H, 10.3%).

Preparation of 3-tetrahydropyranyloxymethyl-2,2,4,4-tetramethyl-cyclobutanone (56).

The product (55) (6.0 g, 39 mmole) was dissolved in 2,3-dihydropyran (11.4 g, 117 mmole freshly distilled from potassium hydroxide pellets), a crystal of p-toluenesulphonic acid added and the solution stirred at room temperature for 1 hr. Saturated aqueous sodium bicarbonate solution (60 ml) was then added and the solution extracted with ether (400 ml). The ether extracts were washed with water and dried. Removal of the solvent in vacuo gave an oil (8.7 g) which was chromatographed on silica gel (300 g). Elution with 10% ether in light petroleum (500 ml) gave a colourless oil (8.5 g, 98%). An analytical sample was prepared by evaporative distillation (87°/.1 mm). ν_{max} (film) 1785 (C=O), 1075, 1050, 1030, 990 cm^{-1} (tetrahydropyranylether). The n.m.r. spectrum (carbon tetrachloride) showed the following absorptions: $\delta 1.06$, 1.13, 1.25 (three singlets 12H), $\delta 1.32$-1.71 (multiplet 6H), $\delta 2.10$ (triplet 1H, J_{AX} = 8.2 c.p.s.,; J_{BX} = 7.9 c.p.s.), $\delta 3.10$-4.05 (multiplet 2H), $\delta 3.44$, 3.88 (two overlapping quartets 2H), J_{AB} = -10.1 c.p.s.), and

$\delta 4.49$ (broad absorption 1H). (Found: C, 70.4; H, 10.1. Calc. for $C_{14}H_{24}O_3$; C, 70.0; H, 10.1%).

Preparation of 1-methylene-3-tetrahydropyranyloxymethyl-2,2,4,4-tetramethylcyclobutane (57).

This was prepared from the ketone (52) (8 g, 33 mmole) by the method described for the preparation of the dioxalane (53), using (3.2 g, 66 mmole) potassium metal in tertiary butanol (80 ml), 250 ml of anhydrous ether, and (23 g, 50 mmole) of the phosphonium salt. An oil (8.5 g), which was chromatographed on silica gel (200 g), was obtained. Elution with 10% ether in light petroleum (200 ml) gave a colourless oil (7.3 g, 94%). An analytical sample was prepared by evaporative distillation (b.p. 72-77°/.1 mm). ν_{max} (film) 3025 (weak, =C-H of double bond), 1670 (sharp, C=C), 1075, 1050, 1030, 990, (tetrahydropyranylether), and 885 cm^{-1} (=CH$_2$ bend). The n.m.r. spectrum (carbon tetrachloride) showed the following absorptions: $\delta 1.07$, 1.14, 1.25 (three singlets 12H, methyl protons), $\delta 1.43-1.67$ (multiplet 6H, methylene protons of tetrahydropyranylether moiety), $\delta 2.02$ (triplet 1H, J_{AX} = 8.1 c.p.s., J_{BX} = 7.8 c.p.s., C_3 proton of cyclobutane ring), $\delta 3.12-3.98$ (multiplet 2H, methylene protons of tetrahydropyranylether group), $\delta 3.30$, 8.76 (two overlapping quartets 2H, J_{AB} = -9.8 c.p.s., methylene protons adjacent to the tetrahydropyranyloxy group), $\delta 4.45$ (broad absorption 1H, methine proton of tetrahydrohydropyranyloxy

group), and $\delta 4.62$ (singlet 2H, vinylic methylene protons). (Found:
C, 76.0; H, 10.7. Calc. for $C_{15}H_{26}O_2$; C, 75.6; H, 11.0%).

Preparation of 3-hydroxymethyl-1-methylene-2,2,4,4-tetramethylcyclo-butane (58).

The compound (57) (7.0 g, 29 mmole) was dissolved in methanol
(50 ml) and concentrated hydrochloric acid (4 drops) added. The
solution was allowed to stand at room temperature for 1 hr when all
of the starting material (57) had disappeared (by t.l.c.). Ether
(50 ml) was added, followed by 50 ml saturated aqueous sodium
bicarbonate solution. The organic phase was separated and the
aqueous phase extracted with two 50 ml portions of ether. The com-
bined ether extracts were washed with water (50 ml) and dried over
anhydrous magnesium sulphate. Evaporation of the solvent in vacuo
gave a solid which was recrystallised from light petroleum to give
white crystals (4.4 g, 98%) m.p. 69-71°. An analytical sample was
prepared by sublimation (40°/2 mm). ν_{max} (chloroform) 3620, 3445
(O-H), 3030 (weak, =C-H of double bond), 1660 (C=C), and 880 cm^{-1}
(=CH$_2$ bend). The n.m.r. spectrum (carbon tetrachloride) showed the
following absorptions: $\delta 1.08$, 1.17 (singlets 12H, methyl protons),
$\delta 1.93$ (triplet 1H, J = 8 c.p.s., methine proton), $\delta 2.52$ (broad
singlet 1H, hydroxyl proton), $\delta 3.69$ (doublet 2H, J = 8 c.p.s.,
methylene protons of primary alcohol group), and $\delta 4.62$ (sharp singlet

2H, vinylic methylene protons). (Found: C, 78.0; H, 11.8. Calc.
for $C_{10}H_{18}O$; C, 77.9; H, 11.8%).

Preparation of 1-methylene-2,2,4,4-tetramethylcyclobutane-3-carboxylate (59).

This compound was prepared from the alcohol (58) (4.0 g, 26
mmole) by addition of Jones' Reagent[18] (14.5 ml, 60 mmole), using the
procedure previously described for the preparation of the acid (26).
The crude reaction product (4.1 g) was chromatographed on silica gel
(200 g). Elution with 15% ether in light petroleum (400 ml) gave
white crystals (3.9 g, 91%), m.p. 96-97°. An analytical sample was
prepared by evaporative distillation (190-195°/.05 mm). ν_{max} (chloro-
form) 3600-2380 (broad acid O-H), 1700 (acid C=O), 1660 (C=C), 880
($=CH_2$ bend) cm^{-1}. The n.m.r. spectrum (carbon tetrachloride) showed
the following absorptions: $\delta1.24$, 1.30 (singlets 12H, methyl protons),
$\delta2.68$ (singlet 1H, methine proton), $\delta4.70$ (singlet 2H, vinylic
methylene protons), and $\delta9.21$-9.39 (broad absorption 1H, acid proton).
(Found: C, 71.2; H, 9.6. Calc. for $C_{10}H_{16}O_2$; C, 71.3; H, 9.6%).

Preparation of 1-bromo-1,2,2,4,4-pentamethylcyclobutane-3-carboxylate (60).

The method for the addition of hydrogen bromide to the acid
(54) was adapted from that described by Hamon.[51,52] The acid (59)

(100 mg, .8 mmole) was placed in a two-necked 50 ml flask, fitted with a dry-ice condenser and a calcium chloride drying tube. An excess of hydrogen bromide (Matheson) was distilled into the flask which had been cooled to -78° in an acetone/dry-ice bath. After standing for 2 hr at -78° the flask was removed and allowed to stand at room temperature for a further 3 hr when all of the hydrogen bromide had evaporated. Ether (15 ml) and water (10 ml) was added, the organic phase separated, extracted with two 5 ml portions of ether, and the combined ether extracts dried. Evaporation of the solvent _in vacuo_ gave a solid which was recrystallised from ether/ light petroleum and further purified by sublimation $(62^{\circ}/.1 \text{ mm})$. White crystals (130 mg, 70%), m.p. $136-141^{\circ}$ were obtained. ν_{max} (chloroform) 3600-2400 (broad acid O-H) and 1700 cm^{-1} (acid C=O). The n.m.r. spectrum (carbon tetrachloride) showed the following absorptions: $\delta 1.12$, 1.21, 1.45, 1.85 (sharp singlets), $\delta 2.05$ (broad singlet) total integration 15H, $\delta 2.59$, 2.85 (broad singlets 1H), and $\delta 11.26-11.52$ (broad absorption 1H, acid proton). (Found: C, 48.2; H, 6.7; Br, 32.0. Calc. for $C_{10}H_{17}O_2Br$; C, 48.2; H, 6.9; Br, 32.1%).

Attempted bromodecarboxylation of (60) using the Cristol-Firth[69] modification of the Hunsdiecker reaction.

In a typical run the bromo-acid (55) (100 mg, 0.4 mmole) and red mercuric oxide (100 mg, .4 mmole) in carbon tetrachloride or

benzene (10 ml) were refluxed with stirring in the absence of light, in an atmosphere of nitrogen in a flask fitted with a water separator. After approximately 20 min a solution of bromine in carbon tetra-chloride or benzene* (5.2 ml, .6 mmole) was added dropwise such that the mixture continued to reflux and the mixture was refluxed with stirring for a further 2 hr when no acid (60) could be detected (by t.l.c.). The mixture was cooled and filtered under reduced pressure through a celite pad, which was then washed with chloroform (50 ml). The combined filtrates were evaporated to give a dark brown oil (45 mg). ν_{max} (film) 1805 and 1710 cm^{-1}. Analytical vapour phase chromatography (5' 15% S.E. 52 at 90° and 30 ml/min) indicated at least five major components. After repeated chromatography (p.p.c.) a relatively stable fraction (17 mg) was obtained. The following spectral characteristics were observed. ν_{max} (film) 1805 cm^{-1}. The n.m.r. spectrum (deutero-chloroform) showed the following absorptions: $\delta 1.09-1.52$ (multiplet), $\delta 1.52-2.20$ (multiplet).

The above reaction was attempted at room temperature using benzene as solvent. A mixture of (60) (100 mg, .4 mmole), red mercuric oxide (100 mg, .4 mmole), and a solution of bromine in anhydrous benzene (70 ml, .8 mmole), in anhydrous benzene (25 ml) was stirred vigorously at room temperature for 90 min, in the absence of light, and in an atmosphere of nitrogen. At this stage no starting acid (60)

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*   freshly purified.

could be detected (by t.l.c.) and analytical vapour phase chroma-
tography (5' 15% S.E. 52 at 90° and 30 ml/min) indicated at least five
major products. Filtration and evaporation of the solvent as des-
cribed for the preceding experiment gave a yellow oil which darkened
rapidly on standing. ν_{max} (film) 1805 and 1710 cm^{-1}. Attempted
separation of the products by preparative vapour phase chromatography
(5' 20% S.E. 52 and 12' 20% carbowax at 90° and 100 ml/min) gave
largely decomposition products, dark oils of similar spectral composi-
tion to the crude reaction product, viz. ν_{max} (CHCl$_3$) 1805 and 1710
cm^{-1}.

Preparation of 2,2,4,4-tetramethylcyclobutanone-3-carboxylate (63).

This was prepared from the alcohol (55) (4.0 mg, 26 mmole)
by addition of Jones' Reagent[18] (14.5 ml, 60 mmole) using the
procedure previously described for the preparation of the acid (26).
The crude reaction product (4.0 g) was chromatographed on silica gel
(200 g). Elution with 30% ether in light petroleum (400 ml) gave white
crystals (3.9 g, 90%), m.p. 93°. An analytical sample was prepared
by sublimation (55°/.1 mm). ν_{max} (chloroform) 3600-2360 (broad acid
O-H), 1783 (cyclobutane C=O), and 1700 cm^{-1} (acid C=O). The n.m.r.
spectrum (carbon tetrachloride/deuterochloroform) showed the following
absorptions: δ1.31, 1.36 (singlets 12H methyl protons), δ2.82 (singlet
1H, methine proton), and δ11.55 (broad singlet 1H, acid proton). (Found:
C, 63.6; H, 8.3. Calc. for $C_9H_{14}O_3$; C, 63.5; H, 8.3%).

Preparation of 1-hydroxy-1,2,2,4,4-pentamethylcyclobutane-1-carboxylate (64).

The acid (63) (3.0 g, 27.5 mmole) in anhydrous ether (10 ml) was added to an ethereal solution of methylmagnesium iodide (4 x excess, prepared from the addition of methyl iodide [20.0 g, 138 mmole] to dry magnesium turnings [2.1 g, 110 mmole] in anhydrous ether [50 ml], in an atmosphere of nitrogen). A dense white precipitate was immediately formed. The mixture was stirred at room temperature for 5 min and carefully poured into ice-cold water (200 ml). The aqueous layer was acidified with concentrated hydrochloric acid extracted with three 100 ml portions of ether, washed with water (50 ml), and dried. Evaporation of the solvent in vacuo gave a solid (3.3 g) which was chromatographed on silica gel (200 g). Elution with 50% ether in light petroleum (500 ml) gave white crystals (3.0 g, 93%), m.p. 130-134°. An analytical sample was obtained by sublimation (90°/.1 mm). ν_{max} (chloroform) 3600-2300 (broad acid O-H), and 1700 cm^{-1} (acid C=O). The n.m.r. spectrum (deuterochloroform) showed the following absorptions: δ1.11, 1.16, 1.23 (broad singlets 15H, methyl protons), δ2.38 (singlet 1H, methine proton), δ7.72 (broad absorption 2H, hydroxyl and acid protons). (Found: C, 64.3; H, 9.7. Calc. for $C_{10}H_{18}O_3$; C, 64.5; H, 9.7%).

Attempted Preparation of 3-bromo-1,2,2,4,4-pentamethylcyclobutan-1-ol (65) via the modified Hunsdiecker[69] reaction.

In a 50 ml two-necked flask fitted with a dropping funnel and a Dean and Stark water separator, a mixture of the acid (64) (300 mg, 1.6 mmole) and red mercuric oxide (420 mg, 1.6 mmole) in benzene (50 ml) was heated with vigorous stirring, in an atmosphere of nitrogen and in the absence of light. The mixture was allowed to reflux for 20 min when a solution of bromine in benzene* (17 ml, 2.0 mmole) was added dropwise so that the mixture continued to reflux. Analytical vapour phase chromatography (5' 15% S.E. 52 at 110° and 30 ml/min) 1 hr after addition of the bromine indicated that no starting acid (64) remained. At least four major products were observed. The reaction mixture was allowed to cool and then filtered under reduced pressure through a celite pad. The celite pad was washed with chloroform (50 ml) and the combined filtrates were evaporated to give a yellow oil (100 mg) which darkened rapidly on standing in air. ν_{max} (film) 1780 (medium) and 1700 cm^{-1} (medium). Attempted separation of the products by preparative vapour phase chromatography (5' 20% S.E. 52 and 12' 20% carbowax columns at 85° and 100 ml/min) gave largely decomposition products; viz. dark oils of similar spectral composition to that of the crude reaction mixture. $[\nu_{max}$ (film) 1780 and 1700 cm$^{-1}.]$

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* freshly purified.

The above reaction was repeated at room temperature - a mixture of (64) (300 mg, 1.6 mmole), red mercuric oxide (420 mg, 1.6 mmole), and a solution of bromine in anhydrous benzene* (17.0 ml, 2.0 mmole) in anhydrous benzene (50 ml) was stirred vigorously at room temperature for 90 min, in an atmosphere of nitrogen, when vapour phase chromatographic analysis (5' 15% S.E. 52 column at 110° and 30 ml/min) indicated that all the starting acid (64) had been consumed. The same mixture of products as had been obtained in the preceding experiment was again observed. Work-up as described for the preceding experiment gave a yellow oil which darkened on standing in air. The infrared spectrum was identical to that of the product obtained from the preceding experiment.

Attempted bromodecarboxylation of (59) using the method described in the preceding experiment.

A mixture of (59), (270 mg, 1.6 mmole), red mercuric oxide (420 mg, 1.6 mmole), and a solution of bromine in anhydrous benzene* (170.0 ml, 2.0 mmole), in anhydrous benzene (50 ml) was stirred vigorously at room temperature for 90 min when vapour phase chromatographic analysis (5' 15% S.E. 52 column at 110° and 30 ml/min) indicated that all the starting acid had reacted. At least five major products were observed. Work-up as described for the preceding experiment gave a yellow oil which darkened standing in air. ν_{max} (film)

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*   freshly purified.

1780, 1750, 1700, and 1230 cm^{-1}. Attempted purification of this product (p.p.c.) gave dark oils of similar composition to that of the crude reaction mixture.

Attempted chlorodecarboxylation of the acid (60) using a method described by Kochi.[73]

To a solution of the acid (60) (150 mg, 0.6 mmole) in degassed benzene* (8 ml) was added anhydrous lithium chloride* (30 mg, .7 mmole) in an atmosphere of nitrogen. Lead tetraacetate** (310 mg, .70 mmole) was added with stirring, and the mixture allowed to stir for 48 hr at 80°. After cooling the mixture, 10% aqueous acetic acid (5 ml) was added, and the mixture extracted with three 10 ml portions of 10% aqueous sodium hydroxide. The organic phase was separated, washed with water (10 ml), and dried over anhydrous magnesium sulphate. Evaporation of the solvent gave a yellow oil which darkened rapidly on standing or on exposure to air. v_{max} 1780, 1760, and 1220 cm^{-1}. Thin-layer chromatography indicated at least five different products. Attempted purification of this product (p.p.c.) resulted in dark oils of similar composition to that of the crude reaction mixture.

The alkaline aqueous layer was acidified with concentrated hydrochloric acid, and extracted with three 10 ml portions of ether.

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*   Kindly supplied by R.C. Cross.

**   Freshly purified and kindly supplied by D.C. Skingle.

The combined ether extracts were washed with water and dried over anhydrous magnesium sulphate. On evaporation of the solvent no appreciable amount of residue could be detected.

Attempted chlorodecarboxylation of the acid (59) using the method described in the preceding experiment. - [(100 mg, .6 mmole) of the acid was used.]

Work-up as described for the preceding experiment gave from the alkali insoluble fraction, a yellow oil (60 mg). ν_{max} (film) 1780, 1740, and 1200 cm^{-1}. Thin-layer chromatography indicated at least four products. From the alkali soluble fraction, a solid (20 mg), the infrared spectrum of which was identical to that of the starting acid (59) was obtained.

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