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UNIVERSITY OF DURHAM

A Thesis

entitled

Some Aspects of the Cyclopropyl-Allyl Rearrangement

Submitted by

Graham Smale, B.Sc.

(Grey College)

A candidate for the Degree of Doctor of Philosophy

1969

20 JAN 1970
LIBRARY

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The author wishes to express his sincere thanks to Dr. D.T. Clark for his continual help and encouragement during his supervision of this work, and to Professor W.K.R. Musgrave for his interest.

Thanks are also due to the I.C.I. Petrochemical and Polymer Laboratory for measuring the 220 MHz spectra, to many technical and laboratory staff for their help, and to the Science Research Council for a maintenance grant.

G. Smale.

Durham, 1969.

MEMORANDUM

The work described in this thesis was carried out in the University of Durham, between October 1966 and June 1969. This work has not been submitted for any other degree and is the original work of the author except where acknowledged by reference.

Part of this work has been the subject of the following publications:-

D.T. Clark and G. Smale, Chem. Comms., 1969, 15, 868.

D.T. Clark and G. Smale, Chem. Comms., in press.

SUMMARY

Some Aspects of the Cyclopropyl-Allyl Rearrangement

The acetolyses of hydro-, chloro- and phenyl-substituted exo and endo-bicyclo[n.1.0]alkyl chlorides has provided evidence for several cyclopropyl to allyl ring opening modes. These involve either concerted ring opening with ionisation of the leaving group, non-concerted ring opening via a cyclopropyl cation of finite lifetime or the initial formation of a 'semi open' cyclopropyl cation, lying in a potential minimum.

The solvolysis rates and activation parameters for the endo series of compounds (both hydro and phenyl substituted) are entirely consistent with the favoured concerted process. The results for the exo series require a different interpretation. Both the parent ($n = 3,4$) alkyl chlorides are solvolytically inert whilst the $n = 5$ compound rearranges rapidly. This is consistent with the data for the corresponding tosylates, for which a mechanism involving a partially opened cyclopropyl cation has been postulated.

The introduction of a phenyl substituent into the compounds for which this process is energetically unfavourable, ($n = 3,4$), has a large ($10^6 - 10^8$) rate enhancing effect and changes the mechanism to a non-concerted carbonium ion process. For the $n = 5$ isomer, introduction of a phenyl group produces a relatively small rate enhancement and the mechanism does not change.

Solvolysis of the gem-dichloro compounds ($n = 3,4$) again provides good evidence for the concerted mechanism.

CONTENTS

INTRODUCTION

CHAPTER I

I.1. Introduction to Woodward-Hoffmann Orbital Symmetry Rules.

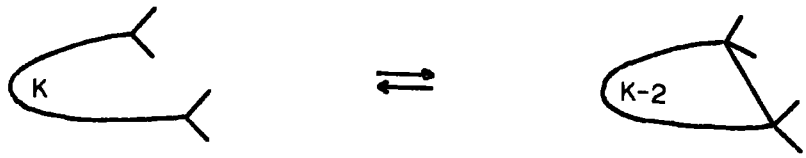
Theoretical chemistry, albeit in its very crudest form has provided a tremendous impetus to organic chemistry over the past 20 years. In the 1950's for example, the predictions of Hückel Theory that carbocyclic ring systems containing $(4n + 2)\pi$-electrons should be aromatic, stimulated a considerable research effort in the synthesis of large carbocyclic rings. More recently (1965), predictions by Woodward and Hoffmann,[1-7] based on Extended Hückel Theory (E.H.T.) have marked an important achievement of Molecular Orbital Theory and have thrown new light upon a large and important class of concerted organic reactions - which in current terminology are designated 'Pericyclic Reactions'. (For leading reviews see Refs. 8, 9, 10, 11).

Within this definition may be included, intramolecular electrocyclic reactions, intermolecular cyclo-addition reactions and sigmatropic rearrangements (see Fig.I.1). A large number of reactions important in organic synthesis fall into these categories - among these the Diels-Alder and Cope reactions and the Claisen Rearrangement. These reactions are either thermally or photochemically induced and often proceed in a highly stereospecific manner.

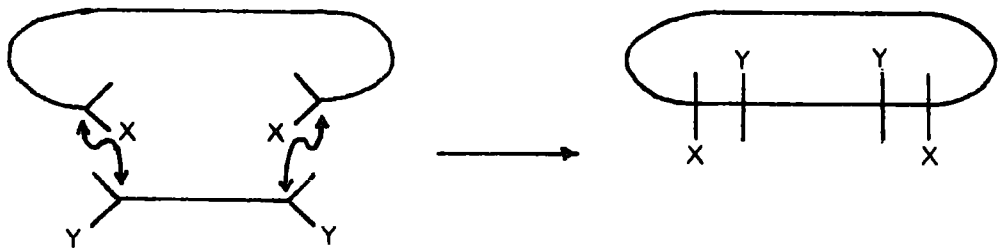
The advent of the Woodward-Hoffmann theory has unified a large body of reactions which were previously categorised under the label 'no mechanism' reactions. The Woodward-Hoffmann theory relies heavily

Fig. I.1.

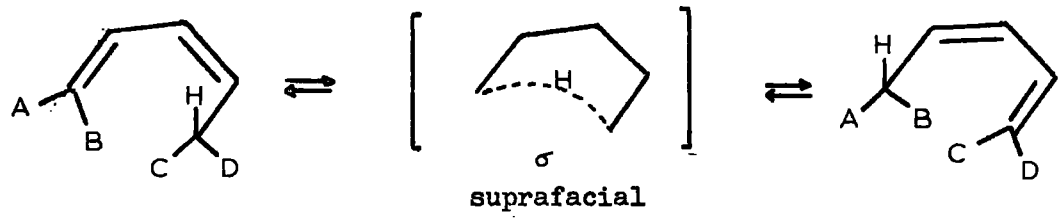
Electrocyclic Reactions.

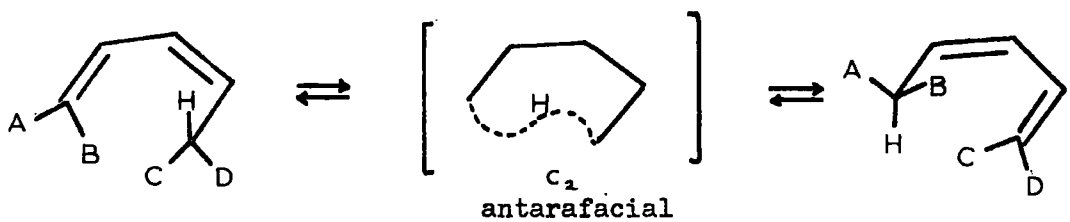


Intermolecular Cycloaddition Reactions.



Sigmatropic Reactions.





upon the results of calculations based upon E.H.T. which is an empirical molecular orbital theory in which both nuclear and electron interactions are not explicitly considered. The interpretation of concerted pathways is in terms of the symmetry properties of the reactant and product energy levels. A similar approach has also been developed by Longuet-Higgins and Abrahamson[12] - utilising the principles of Group Theory to correlate graphically the energy levels of the products and reactants and give a qualitative account of both ground and excited state interactions involved. These problems have been treated theoretically by several workers using variations on the same basic method.[13,14]

A reaction is termed 'symmetry allowed' when it is possible to transform continuously the orbitals of the reactants into those of the products in such a way that the bonding character of the filled orbitals is preserved - thus ensuring the minimum energy path for the reaction. In symmetrical systems it is a relatively simple matter to determine whether a reaction is symmetry allowed, by following the interaction of the participating orbitals along the reaction path and constructing the appropriate correlation diagram. However, for some systems, one of the possible concerted reaction pathways may possess no element of symmetry apart from the identity. In this case the situation is more complex and a detailed examination of the energy level is required in order to follow the orbitals throughout the reaction. In the simple Woodward-Hoffmann treatment, the stereochemical

course of the reaction is determined by the symmetries of the highest occupied molecular orbitals of reactants and products.

An analogy has been drawn between this treatment of electrocyclic reactions and Fukui's frontier orbital theory for substitution in aromatic systems.[15] Both treatments suffer from the same deficiency, namely that only one or two terms in a summation of energy terms are considered.

The work described in this thesis is concerned with the simplest 'electrocyclic' transformation - that of cyclopropyl to allyl cation, hence only the general theory applicable to this type of system (4n or 4n + 2 π-electrons) will be discussed in detail.

I.2. The Stereochemistry of Electrocyclic Reactions.

Woodward and Hoffmann defined an electrocyclic transformation as the formation of a single bond between the termini of a linear conjugated system containing k π-electrons, and the reverse process:-

Fig. I.2.

The geometrical isomerism of the open chain system will be related to the geometry of the cyclised arrangement. Hence in a system terminally substituted by groups A-D, cyclisation might take place in a uniquely disrotatory sense or in a conrotatory fashion. This will necessarily be a highly stereospecific process. (Fig.I.3).

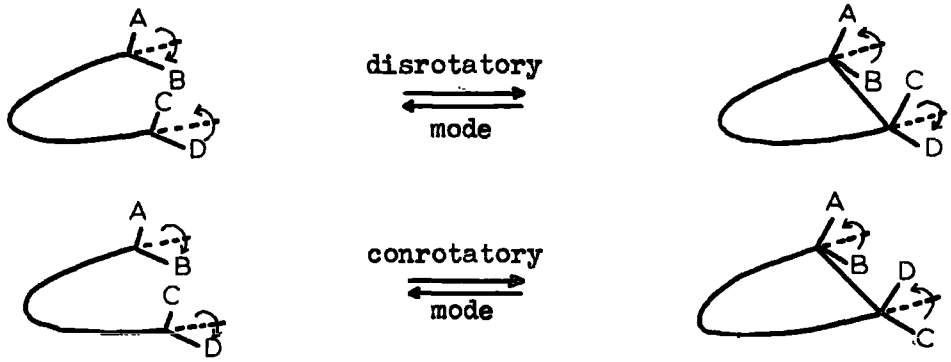


Fig. I.3.

If the stereochemistry is indeed determined by the symmetry of the highest occupied ground-state molecular orbital of the open chain molecule, bonding overlap must occur by interaction of the terminal π-lobes in order that a new σ bond may be formed between the termini. In an open chain system containing $4n$ π-electrons, the above symmetry rule requires that a conrotatory process takes place so that there is no sign inversion in the region of overlap of the terminal lobes. Similarly a $(4n + 2)$ π-electron system requires a disrotatory motion to achieve the same purpose.

Fig. I.4.

$4n$ π-electrons (n = 1) $(4n + 2)$π-electrons (n = 1)

To construct the orbital correlation diagrams it is necessary to consider intermediate configurations in which the terminal groups have been rotated in a disrotatory or conrotatory fashion. In the disrotatory mode, the transition state is characterised by a plane of

symmetry and in the conrotatory mode by a twofold axis of symmetry - whereas the reactants and products possess both symmetry elements.

Since an open chain 4n or (4n + 2) π-electron system is an even alternant, the highest occupied orbital and lowest unoccupied orbital in the Hückel approximation are symmetrically placed with respect to a non-bonding orbital and have the same absolute magnitude for the coefficients of the molecular orbital at each atom.

Promotion of an electron from the highest occupied to the lowest unoccupied orbital therefore involves a change in the symmetry with respect to the orbital coefficients at the terminal atoms. Hence the photochemical reaction proceeds through the corresponding excited state in the opposite sense to the thermally induced reaction.

Many unique and interesting examples of these processes may now be found in the literature thanks mainly to the efforts of chemists probing the validity of the Woodward-Hoffmann Rules.

Of the 4n π-electron systems, the most common example is the interconversion of butadiene and cyclobutene - the thermal isomerisation of cyclobutene clearly being conrotatory.

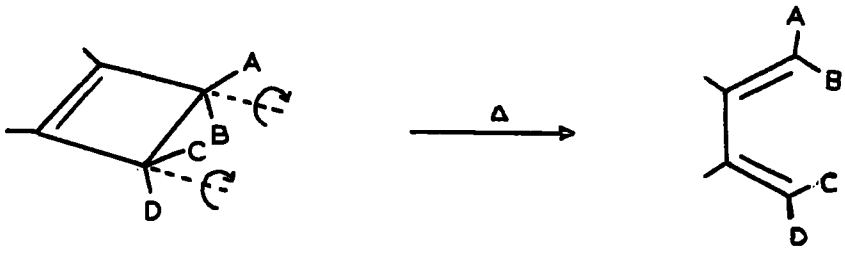


Fig. I.5.

The cyclohexadiene-hexatriene interconversion represents the (4n + 2) electron system (n = 1). Thermally the process is disrotatory although steric demands suggest the reverse process should occur. However the conrotatory process is observed in either direction under photochemical conditions.

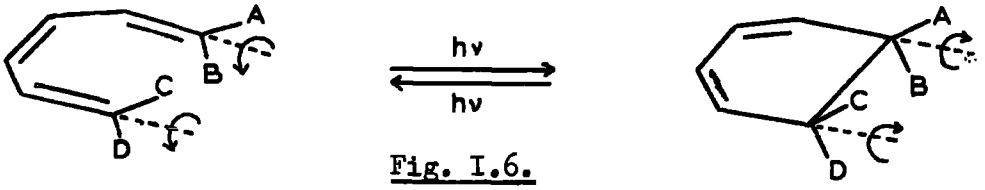


Fig. I.6.

Woodward and Hoffmann also made several predictions for the cyclopropyl-allyl rearrangement (these will be presented in detail later) - and these are shown below.

Predicted G.S. Reactions			Type
Cyclopropyl cation	⟶	allyl cation	Disrotatory
" radical	⟶	allyl radical	Conrotatory
" anion	⟶	allyl anion	Conrotatory

Recently, however, with the increasing power of computing facilities it has been possible for theoretical chemists to attempt more sophisticated Molecular Orbital treatments of such systems.

The original Extended Hückel calculations on which the Woodward-Hoffmann predictions are based have been repeated and extended by Kutzelnigg[16] in the case of the cyclopropyl cation and anion. Although a case can be made for the quantum mechanical validity of E.H.T.

for neutral species, for charged species the arguments become extremely tenuous and detailed conclusions must be viewed with caution.

Modified semi-empirical Pople-Segal CNDO II calculations[17,18] on the same system for the ground and excited state reactions have confirmed the predictions for the anion and cation transformations but suggest that the ground state reaction of the radical proceeds in a disrotatory manner analogous to the cationic case. This is in direct contrast to the original Woodward-Hoffmann prediction. However, these authors now concede that their predictions concerning the radical case may be in error.[19]

These all-valence SCF MO calculations with inclusion of configuration interaction have enabled a detailed analysis of transformations involving particular excited states. This treatment whilst giving a good account of energy differences in ground and excited states does lead to incorrect energy differences between the cyclopropyl and allyl systems due mainly to the nuclear repulsion terms. By modifying the method of calculating this term, the energy difference between the two systems can be made much more realistic. Although this treatment includes all electron and nuclear interactions (and is therefore on a firmer basis than E.H.T.) the method neglects inner shell electrons and since it is in the zero differential overlap approximation, many of the electron repulsion integrals are also neglected.

The stereochemical factors governing the transformation cyclopropyl to allyl can only be unravelled by a non-empirical all electron quantum mechanical treatment. Absolute energy differences involved in this transformation have very recently been calculated in an 'ab initio' treatment using a linear combination of Gaussian type functions as atomic orbitals.[20] In this case a detailed analysis of the energy terms shows that the simple type of relationship presented by Woodward and Hoffmann is not reproduced by the more sophisticated calculations and that the role of the 'inner shell' electrons appears to be more important than has previously been assumed by chemists.

Further 'ab initio' calculations on similar electrocyclic systems would obviously be of considerable interest and would show how much reliance can be placed on a deceptively simple treatment such as that proposed by Woodward and Hoffmann.

CHAPTER II

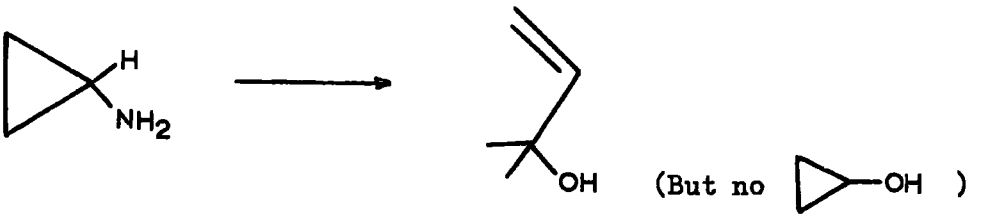
The Cyclopropyl-allyl Rearrangement

II.1. Background.

The cationic reactions of cyclopropyl derivatives are quite unusual, since these compounds are observed to be extraordinarily unreactive in solvolytic reactions and yield rearranged, ring opened products. For example, cyclopropyl tosylate undergoes acetolysis only slowly at a temperature of 175°, to give allyl acetate. This rate is $\sim 2 \times 10^{+5}$ x slower than that for the related cycloalkane, cyclohexyl tosylate. However, despite the large amount of work on the synthesis and reactions of small ring compounds in the last 50 years, plausible explanations for this surprising result have only recently appeared in the literature.

This lack of reactivity has been attributed to a number of factors, including:- 1. The greater electronegativity of the carbon atom in the strained ring. 2. The conjugative delocalisation of the electrons in the carbon-leaving group bond. 3. The increased internal strain in going to a planar Transition State (T.S.).

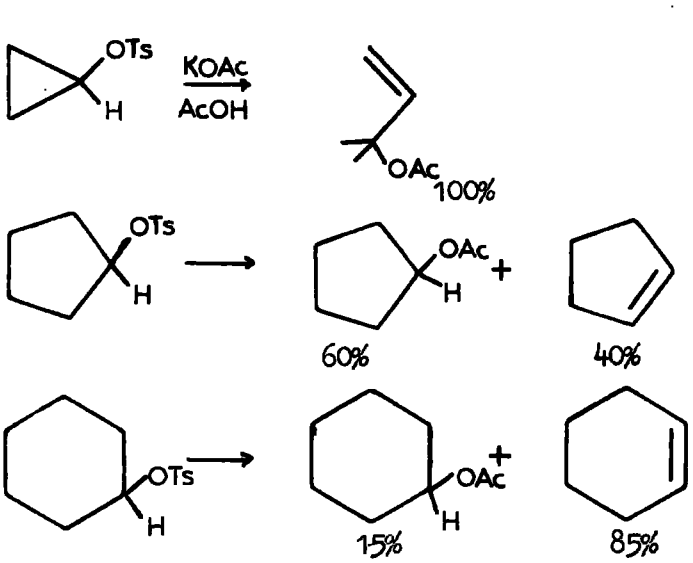
Gustavson,[21] in 1891, noted the relative solvolytic inertness of chlorocyclopropane in alcoholic potassium hydroxide and compared it in reactivity to 1-chloro propene. This behaviour paralleled that observed by Kisher[22] in the nitrous acid deamination of cyclopropylamine, only allyl alcohol, (but no cyclopropanol) was produced.



This was confirmed by later workers.[23] The inference was that the reaction produced a cyclopropyl cation with a great propensity to rearrange.

Similar conclusions were reached from a study of the reaction of nitroso cyclopropyl urea with KOH, again only allyl alcohol could be isolated.[24] However these studies were made with unsubstituted cyclopropyl derivatives, where little information on the mode of reaction can be gained from an examination of the products. It was certainly recognised that the low reactivity of cyclopropyl tosylate made it unlikely that the fairly stable allyl cation was formed directly in the rate determining step.

In 1951, Roberts and Chambers[25] investigated some nucleophilic displacement reactions of a number of cycloalkyl tosylates and chlorides.



	$K_{rel.}$ (60°)	ΔH^{*} (K.cals.)
	2.5×10^{-5}	33.8
	16	27.6
	1	27.4

The solvolytic reactivity sequence in acetic acid, was found to be cyclopentyl ~ cyclobutyl > cyclohexyl >> cyclopropyl. The acetolyses of the five and six-membered ring compounds proceeded normally, first order kinetics being observed and the products being a mixture of acetates and alkenes, quite analogous to those obtained in other carbonium ion reactions of cycloalkyl derivatives.

Cyclopropyl tosylate was found to be extremely unreactive, the sole product being allyl acetate. They proposed that this low reactivity was due to the same factors which operate in phenyl and vinyl tosylates, i.e. the possibility of conjugation between the cyclopropyl residue and the π system of the tosyl group, which should increase the C-OTosyl bond strength. Furthermore, an increase in the S character of the carbon orbital bonding to the tosylate would also strengthen the carbon to leaving-group bond.

In studying cyclopropyl halides, Cromwell and Graff[26] similarly assumed an increase in C-X double bond character, from overlap of halogen p-orbital with the cyclopropane 'bent bonds'.

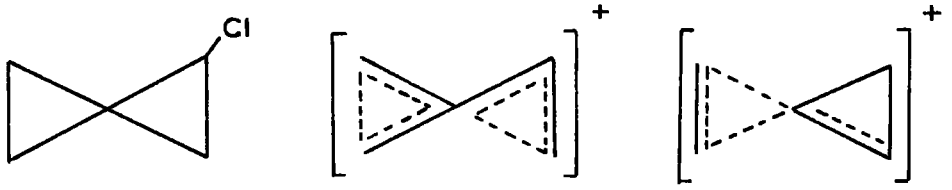
At about the same time Brown[27] studied the hydrolyses of 1-chloro-1-methyl cycloalkanes and concluded that the concept of 'I' strain explained the inertness of cyclopropyl derivatives. ('I' strain is the change in internal strain which results from a change in co-ordination number of a ring atom). The formation of an assumed

trigonal T.S. would involve an increase in energy over and above that which would be involved in the formation of a similar T.S. from an open chain compound.

However, from their work on the electrical effects of cycloalkyl groups,[28] Roberts and Chambers were unconvinced of the superiority of steric over electronic factors in these reactions.

Schleyer[29] suggested that although the T.S. for the formation of cyclopropyl cations could not resemble the fully ring opened allylic cation, the existing evidence showed that cyclopropyl derivatives could undergo assisted type of solvolysis faster than could be predicted solely on the basis of simple angle strain arguments. He proposed a partially opened cyclopropyl cation involving extensive charge delocalisation, for the T.S.

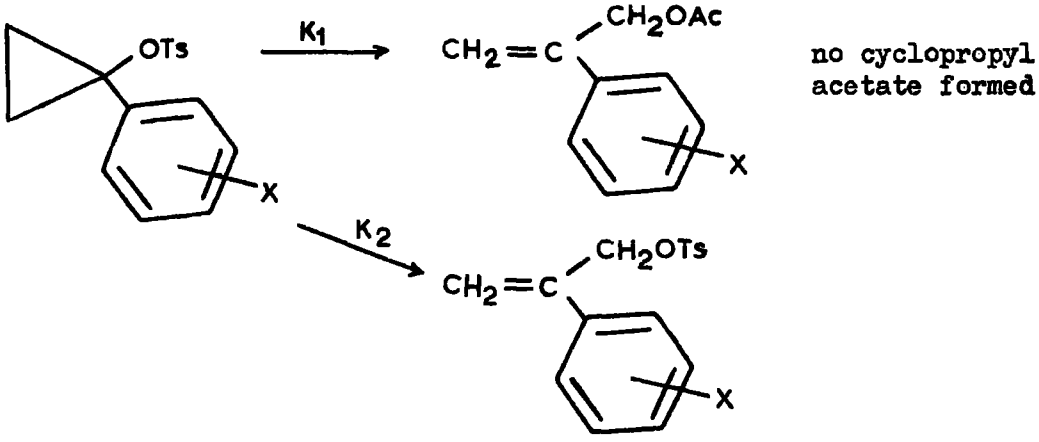
This view was supported by quantitative studies on the solvolysis of 1-halo spiroalkanes.[30] The rate of ethanolysis of chlorospiropentane (I), at 200°, proved to be 4-6 x greater than that of chlorocyclopropane. It was suggested that this was explicable by a T.S. resembling (II) with a small amount of delocalisation into



I II III

the other ring, although homo-allylic structures such as (III) were not ruled out. However, on the basis of such small rate enhancements, this argument is not very compelling.

The first really important study of the stereospecificity of ring opening, was made in 1964 by Depuy and co-workers,[31,32] and preceded Woodward and Hoffmann's communication. They studied the rates of acetolysis of substituted 1- and 2-aryl cyclopropyl tosylates, by following spectrophotometrically the appearance of the styrene chromophore.



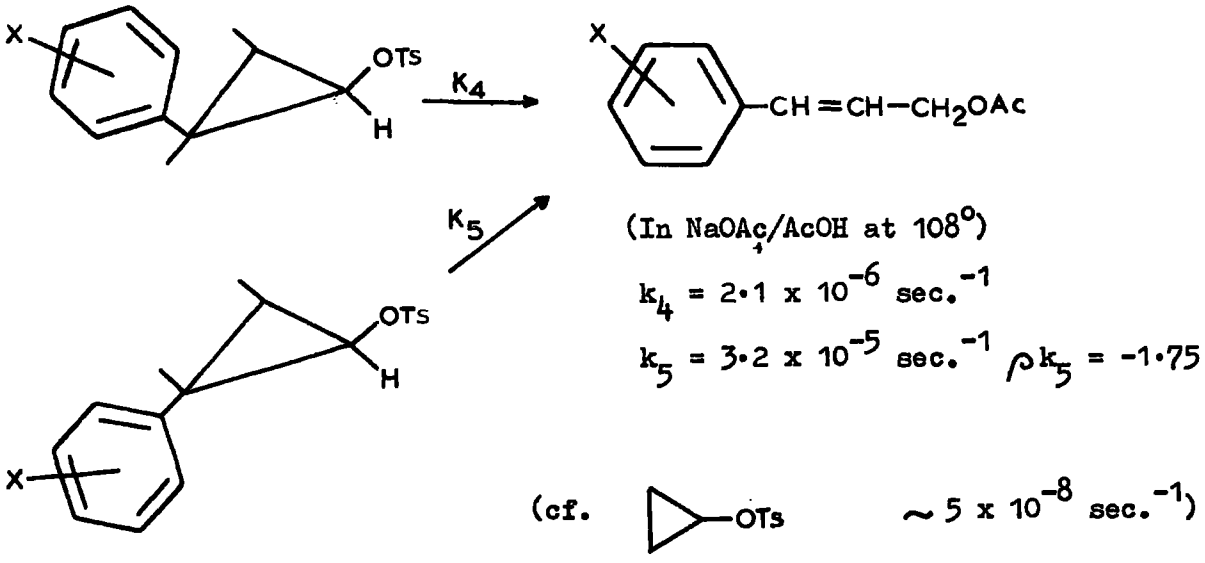
(In NaOAc/AcOH at 108° $k_1 = 1{\cdot}9 \times 10^{-3}$ sec.$^{-1}$ $\rho k_1 = -4{\cdot}31$

$k_2 = 8{\cdot}2 \times 10^{-3}$ sec.$^{-1}$ $\rho k_2 = -3{\cdot}94$

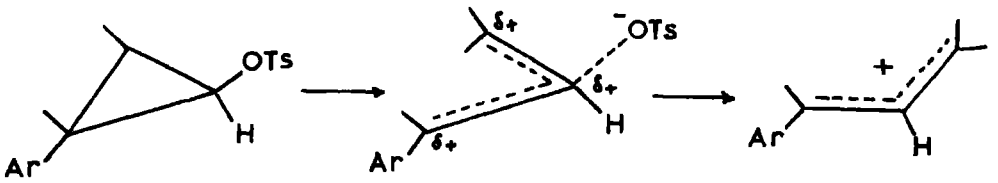
$k_3 = 4{\cdot}0 \times 10^{-4}$ sec.$^{-1}$).

As expected, the 1-aryl cyclopropyl tosylates solvolysed much more rapidly than cyclopropyl tosylate itself. These workers considered

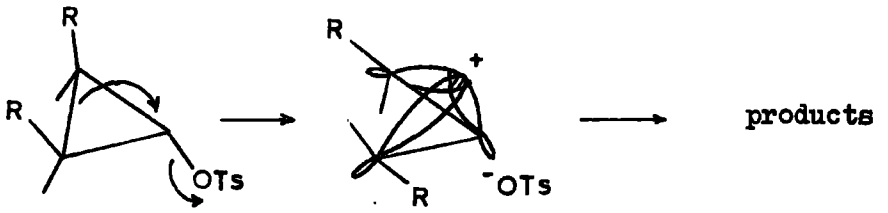
it significant that no 1-phenyl cyclopropyl acetate was isolated, although stable to the reaction conditions. More surprising was the fact that both cis and trans-2-aryl cyclopropyl tosylates solvolysed faster than cyclopropyl tosylate, although the inductive effect ($-I_\sigma$) of the phenyl group might have been expected to decrease the rate if a true cation had been formed. However, this ignores the fact that, as stated previously, the cyclopropyl system and phenyl can be conjugated (cf. the tosylate system).



Again, a thorough search failed to reveal any cyclopropyl acetate. Depuy concluded that the accelerating effect of a 2-aryl substituent and large negative ρ (Rho) values ruled out the formation of a free cyclopropyl cation in the T.S., and proposed a ring opening concerted with solvolysis, so that the aryl group stabilised the positive charge generated on the benzyl carbon in the T.S.



Similarly, a concerted mechanism was assigned to the 1-substituted derivatives. In the light of later work, this assignment is open to question, as will be outlined later. However, the fact that there is a significant rate difference between the cis and trans-2-aryl isomers, is of considerable interest. The transformation of 2-substituted cyclopropyl tosylate through the proposed T.S., into the cinnamyl cation, involves rotation of the aryl group through approximately 90°. Depuy was thus led independently (of Woodward and Hoffmann) to the conclusion that the direction of rotation of the substituents was dependent on the stereochemistry of the leaving group, i.e. as the leaving group moves away, thehydrogenatoms will begin to rotate so as to bring the electrons of the C_2-C_3 bond to the back face of the C_1-OTosyl bond. Thus groups trans to the leaving group have preferred outward rotation and those cis rotate inward. This would account for the slower rate of solvolysis of cis-2-aryl cyclopropyl tosylate than the trans isomer. In the former, the initial product would be the sterically hindered cinnamyl cation.



These observations led directly to theoretical investigations on this problem, which are dealt with in the next section.

II.2. Theoretical Aspects.

The experimental investigations of Depuy were closely followed, in 1965, by the theoretical investigations of Woodward and Hoffmann. According to their principle of conservation of orbital symmetry, they proposed three ring opening modes for the concerted process. In current nomenclature these are disrotatory modes (1) and (2) and conrotatory mode (1). (Fig. II.1).

Using an intermediate geometry with C_1C_2 (C_1C_3) 1·5Å and $C_2\hat{C}_1C_3$ 90°, E.H.T. calculations predicted a disrotatory process in the ground state of the cation and a conrotatory one in the anion and radical. Furthermore, in the cationic case, the disrotatory mode in which the groups cis to the leaving group rotated inwards, was the most favourable (Dis.(2)).

If the cyclopropyl carbonium ion is formed prior to rearrangement, two further modes must be considered, disrotatory (0) and conrotatory (0).

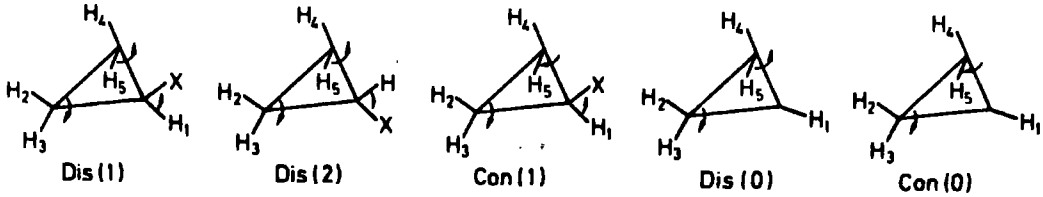


Fig. II.1

(Both semi- and non-empirical calculations[17,20] have shown that the cyclopropyl carbonium ion has a planar configuration about C_1, hence the disrotatory modes become identical).

Fig. II.2 shows the cross section of the envisaged reaction co-ordinates for the dis.(2) mode. The initial rotation is about an axis bisecting the C_1-C_2-C_3 (C_1-C_3-C_2) angles and finishes along the axis of the C_1C_2 (C_1C_3) bonds. Hence a continuous change in axes of rotation, bond angles and bond lengths were assumed for the transformation in both semi- and non-empirical calculations.

(a) Concerted Process.

Woodward and Hoffmann's treatment is solely qualitative, and gives no indication, for example, of how much more energetically favourable the 'correct' disrotatory mode is, compared with the other modes.

The energy differences involved in the three modes of transformation in a concerted process, in the ground and excited states, have been investigated using a semi-empirical SCF MO

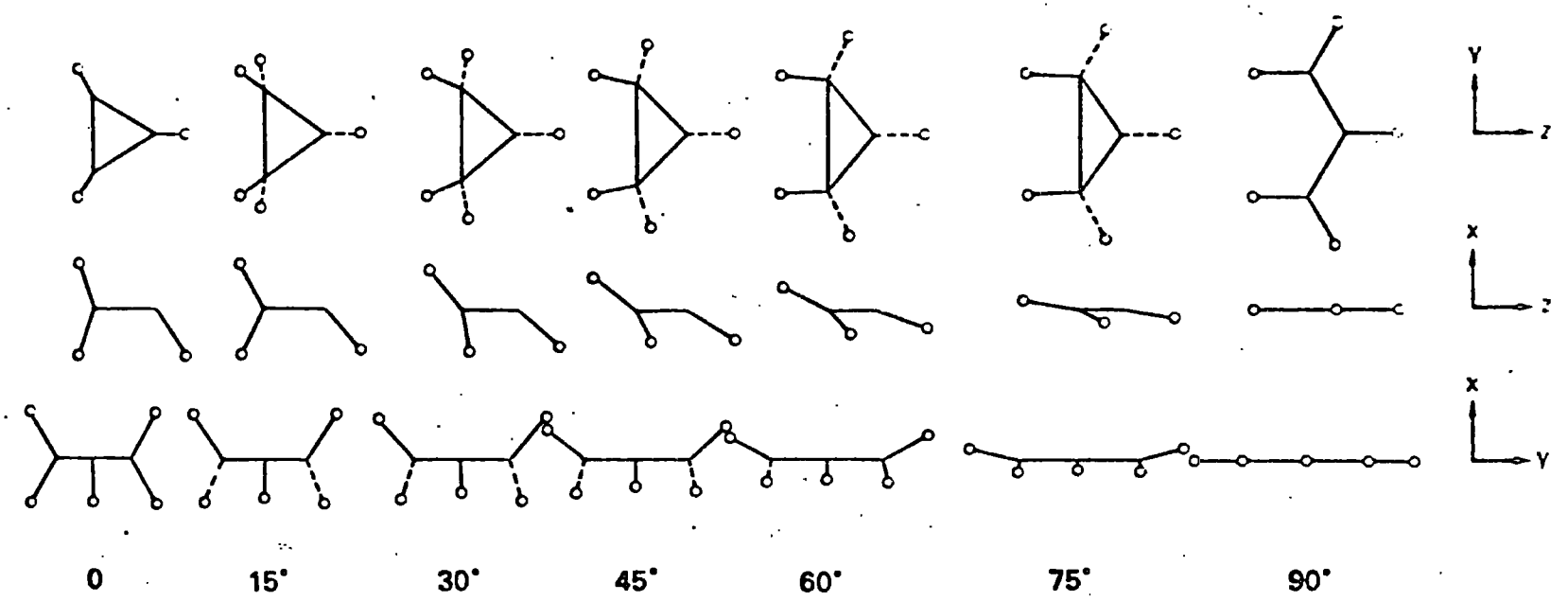


FIG. II.2. Cross Section of the Envisaged Reaction Co-ordinate for Disrotatory Mode 2.

treatment[17] and absolute energy changes by a non-empirical SCF method.[20] For the concerted process, all calculations so far carried out have been on a model where cyclopropyl cation has been formed by adiabatic removal of the leaving group, followed by relaxation to the planar allyl system. The effect of the leaving group has not been explicitly taken into account and it was assumed that the effect would be the same for all modes of transformation. However, the important feature is the energy differences between the modes.

Both semi- and non-empirical calculations have indicated that the 'wrong' mode, dis.(1), is as energetically unfavourable as the con.(1) process. This important result, which was not dealt with in Woodward and Hoffmann's qualitative discussion, has been varified experimentally, as will be seen later.

The dis.(2) mode is favoured over the other two modes by about 1·5 eV (~34 K.cals.) (Fig.II.3a), however, there appears to be no simple explanation for this although the main difference lies in the electronic energy terms. The main energy difference occurs at low angles of rotation ($< 45^{\circ}$) suggesting that the T.S. for the transformation occurs relatively early. This is in agreement with Depuy's results. Atomic charge distributions indicate that the positive charge at C_1 becomes less than that at C_2 or C_3 for angles of rotation $> 45^{\circ}$, whereas the experimental ρ values (~ -2·0) obtained by Depuy[31,32] from the solvolysis of substituted aryl cyclopropyl tosylates, indicated

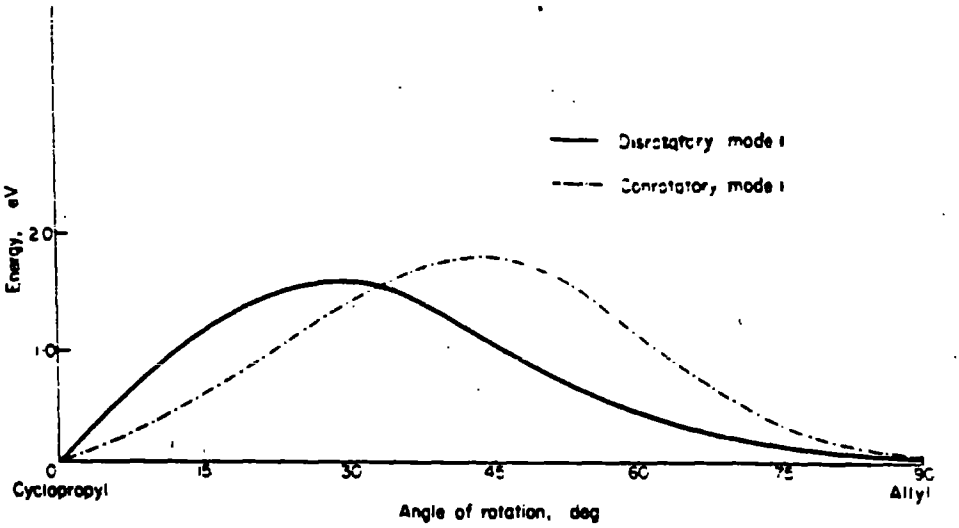


Fig. II.3a. Energy differences vs angle of rotation for disrotatory 1 and conrotatory 1 modes compared with the lowest energy mode. disrotatory mode 2.

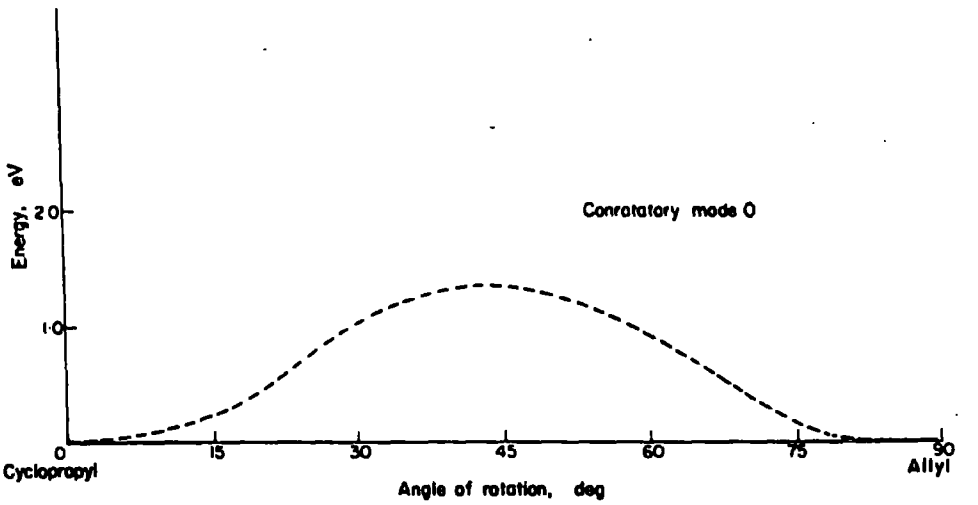


Fig. II.3b. Energy difference vs angle of rotation for conrotatory mode 0 compared with the lowest energy mode disrotatory mode 0.

a larger charge density at C_1 than C_2 or C_3

(b) Non-concerted Process Involving Free Cyclopropyl Cation.

'Ab initio' calculations suggest that a free cyclopropyl cation adopts a planar configuration about C_1. The favoured transformation, dis.(0) involves no activation barrier, whereas the con.(0) mode requires an activation energy of $\sim$ 46 K.cals. This is mainly due to the lower electronic energy for the former.

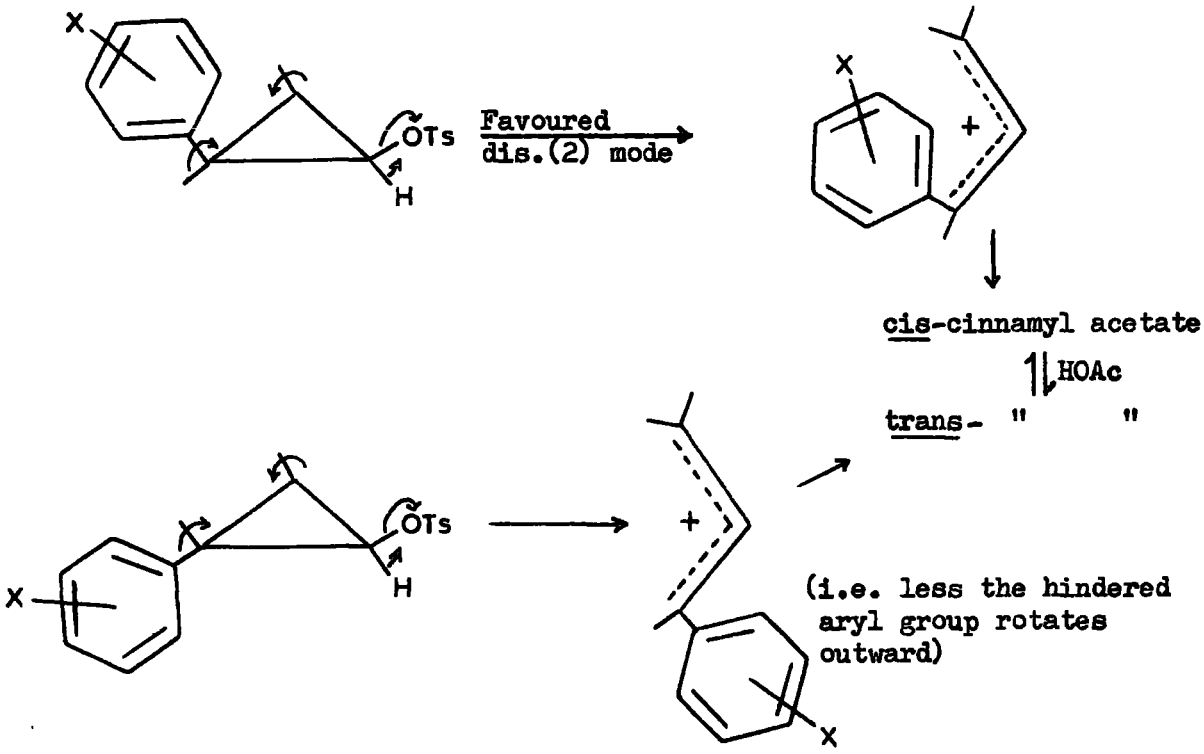
The non empirical treatment demonstrates the weakness of the Woodward-Hoffmann theory, in that a fortuitous balance of factors (undetermined by E.H.T.), contributing to the total energy, give the illusion that the highest occupied molecular orbitals control the course of reaction.

A comparison of the energy terms for the two energetically favoured modes of transformation, dis.(0) and dis.(2) for a planar and bent cyclopropyl cation respectively, show that for small angles of rotation the dis.(0) mode is lower in energy. However, in the dis.(2) mode as H_1 moves toward the plane of the ring, the nuclear energy difference compared with dis.(0) rapidly decreases, and for an angle of rotation of 30° the dis.(2) mode is lower in energy. The transformation of free cyclopropyl to allyl cation must, therefore, involve the initially planar H_1 moving out of plane and returning as allyl is reached.

III.3. Solvolytic Evidence for the Concerted Cyclopropyl-allyl Cation Rearrangement

(a) Monocyclic Systems.

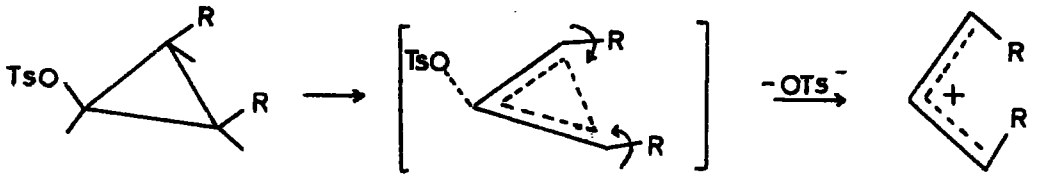
With the Woodward-Hoffmann theory in view, Depuy and co-workers therefore rationalised their rate data for the 2-phenyl cyclopropyl tosylate as follows:-



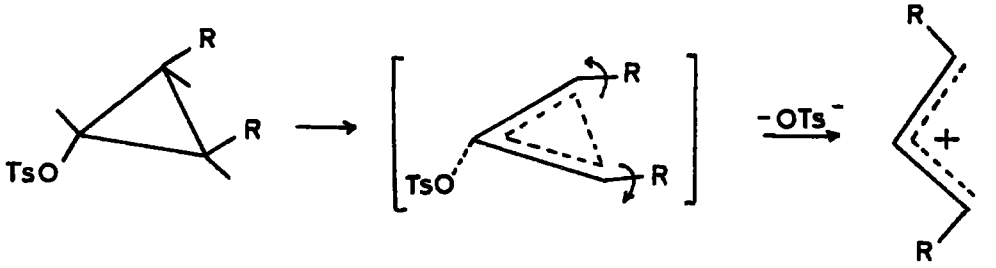
The mode of ring opening should be distinguishable from an examination of the product stereochemistry. However, cis and trans-cinnamyl acetate equilibrate under the reaction conditions, hence the evidence for the ring opening mode rests solely on the small rate difference between the two isomers.

This work was later extended[33] to 2,2-diphenyl and cis and trans-2-phenyl substituted cyclopropyl chlorides using a potentiometric method to determine the chloride ion liberated. The rates at 150° were ~ 20 x slower than the corresponding tosylates, for the cis isomer and ~ 55 x for the trans isomer. The second phenyl group on C_2, as expected increased the rate by a factor of 14 x compared with the cis and 3 x for the trans isomer.

More convincing evidence for the stereochemistry of ring opening has been provided by Schleyer and co-workers, from their investigations on the solvolysis of 2,3-disubstituted cyclopropyl tosylates.[34,35]



cis



trans

The cis isomers (R = Me), should solvolyse more slowly than the trans isomers, since in the former, a dis.(2) mode would lead to a

sterically strained T.S., whereas outward disrotation for the trans isomer should produce some measure of steric acceleration.

The relative rate constants (Table II.1) are consistent with this hypothesis.

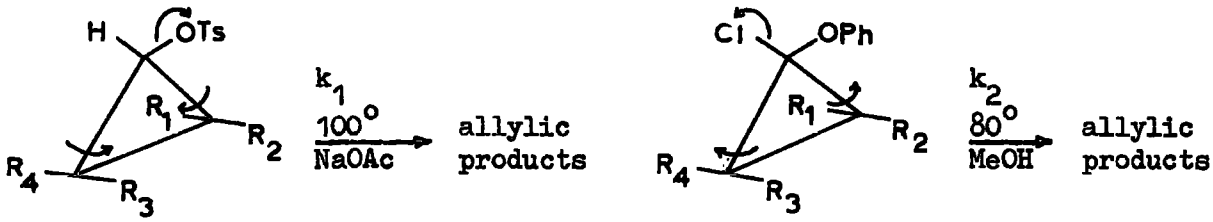


Table II.1

R_1	R_2	R_3	R_4	k_1	k_2
CH_3	CH_3	H	H	67	83
H	CH_3	H	CH_3	62	65
CH_3	H	H	CH_3	1	1
CH_3	CH_3	H	CH_3	35	20
CH_3	CH_3	CH_3	CH_3	10130	1375

Two methyl groups introduced 'cis' have a different effect depending on whether they are endo or exo to the leaving group. In the exo isomer, the rate enhancement is $\sim$1800 due to the electronic

contribution of methyl, however, this is offset by steric factors in the endo case (rate enhancement ~4).

The 2,2-dimethyl and trans-2,3-dimethyl compounds solvolyse at approximately the same rate, since in both cases, one methyl rotates outward and one inward. Introduction of a third and fourth methyl again accelerates the solvolysis, since stabilisation is increased in the T.S., without increasing steric interference.

The corresponding phenoxy-chloro compounds have also been studied and there is a close parallel in relative rates between tosyl and phenoxy-chloro cyclopropanes. This is good evidence that these compounds solvolyse by a dis.(2) mechanism although it is significant that the +M effect of the phenoxy group is apparently unable to stabilise the cyclopropyl cation sufficiently for the reaction to become non-concerted.

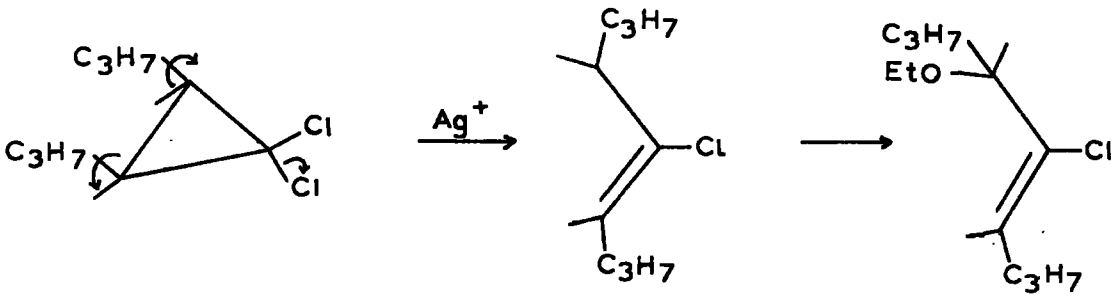
Numerous variations on the type of cyclopropyl substitution have appeared in the literature. The results of the solvolysis of cyclopropyl bromide, substituted in the 2-position by cyclopropyl, vinyl and ethyl groups, are also in general agreement with the above

Table II.2. Activation parameters for 2-substituted cyclopropyl bromides

Substituent	Isomer	$\Delta H^{\ddagger}$ (K.cal.)	$\Delta S^{\ddagger}$ (e.u.)
cyclopropyl	trans	23·9	-7·7
	cis	25·9	-8·8
vinyl	trans	19·9	-25·8
	cis	19·3	-27·6
ethyl	trans	20·6	-22·2
	cis	22·5	-23·1

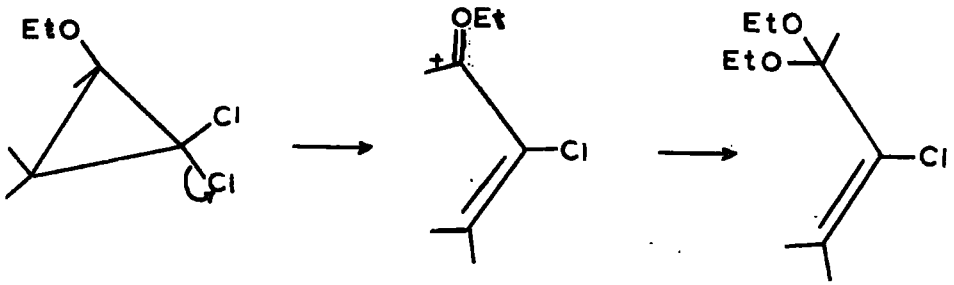
data.[36] The trans isomers solvolyse 11-20 x faster at 130° than the corresponding cis isomers. The large observed rate enhancement (~20 x at 130°) of cyclopropyl over ethyl substituent, implies delocalisation into the cyclopropyl substituent in the T.S. The $\Delta H^{\ddagger}$ value for the ethyl substituent is lower than that for cyclopropyl in both cis and trans isomers, hence the increase in rate is entirely due to the more positive $\Delta S^{\ddagger}$ in the latter system. This has been rationalised by assuming some degree of ring opening of the cyclopropyl substituent in the T.S.

When cis-1,1-dichloro-2,3-dipropyl cyclopropane is solvolysed[37] the chlorine atom cis to hydrogen is lost preferentially, since the trans-chloroether is the only product isolated.

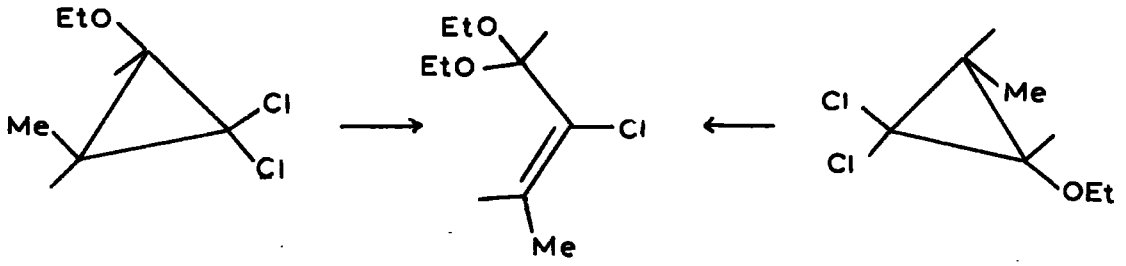


Loss of chlorine cis to alkyl, again would have given a strained T.S. leading to a cis-chloroether.

A 2-ethoxy substituent also strongly enhances the rate of solvolytic ring opening.[38] Thus 1,1-dichloro-2-ethoxy cyclopropane in refluxing ethanol/pyridine, yields the acetal under conditions where the alkyl substituted gem-dihalocyclopropanes are quite stable.

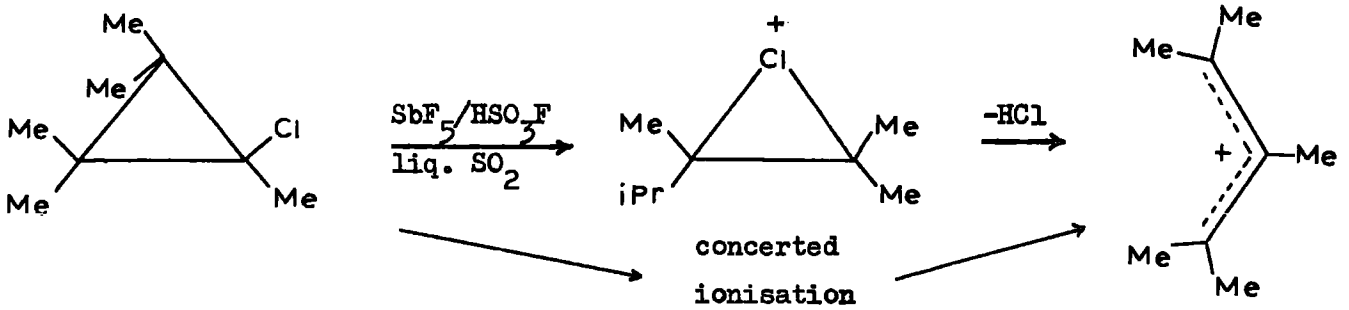


Both cis and trans-1,1-dichloro-2-ethoxy-3-methyl cyclopropane yield solely the trans-acetal. For the cis isomer, this is in accord with the Woodward-Hoffmann rules, since the cis product would require inward disrotation of the substituents.



The stereospecific formation of the trans-acetal from the trans isomer can only be rationalised on steric grounds, since the allyl cation with ethoxy trans to the methyl group should be preferred.

Recently, Olah[39] hoped to determine the timing of the concerted ring opening, by reacting cyclopropyl halides with fluoro-sulphonic acid/antimony pentafluoride in liquid SO_2 (a system which readily ionises alkyl and acyl halides). The rationalisation behind this was presumably that at low temperatures, the cyclopropyl cation would be observable by N.M.R. and its rearrangement to the allyl system could be followed by warming the mixture. Thus, pentamethyl cyclopropyl chloride gave the corresponding allyl cation, which could have been produced by direct, concerted ionisation with ring opening.

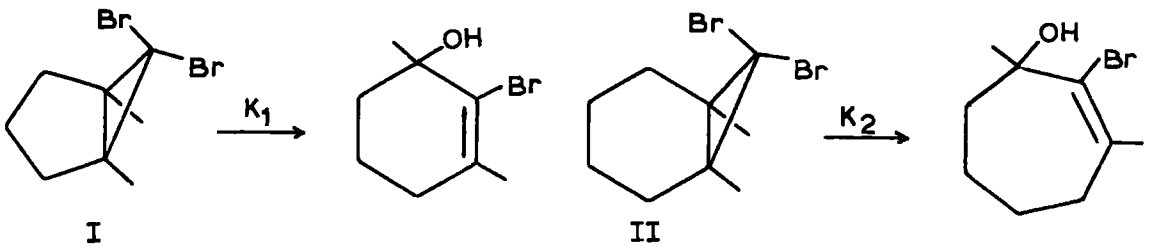


However, an alternative mechanism involving the intermediate trimethyl isopropyl ethylene chloronium ion, followed by loss of HCl, could not be ruled out and thus no definite conclusions could be drawn.

(b) Bicyclic Systems.

Some interesting results supporting the theoretical predictions of a dis.(2) mode for concerted reactions, have resulted from studies (involving both thermal and solvolytic rearrangements), of bicyclic systems containing the cyclopropane ring. These systems provide a severe constraint on certain ring opening modes, through the operation of strain factors.

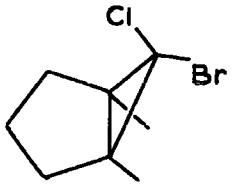
Skell and Sandler,[40] were the first to realize the high degree of stereospecificity involved in the solvolysis of compounds (I) and (II).



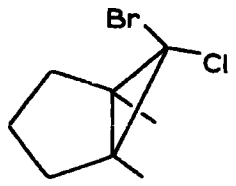
I II

$k_1 > k_2$ by 200 x

They concluded that the driving force for this reaction, in addition to the formation of the allyl cation, was the relief of steric strain in opening the cyclopropane ring. More important however, was their observation that (III) stereospecifically lost chlorine on solvolysis, at the same rate that (IV) lost bromine, to give



III



IV

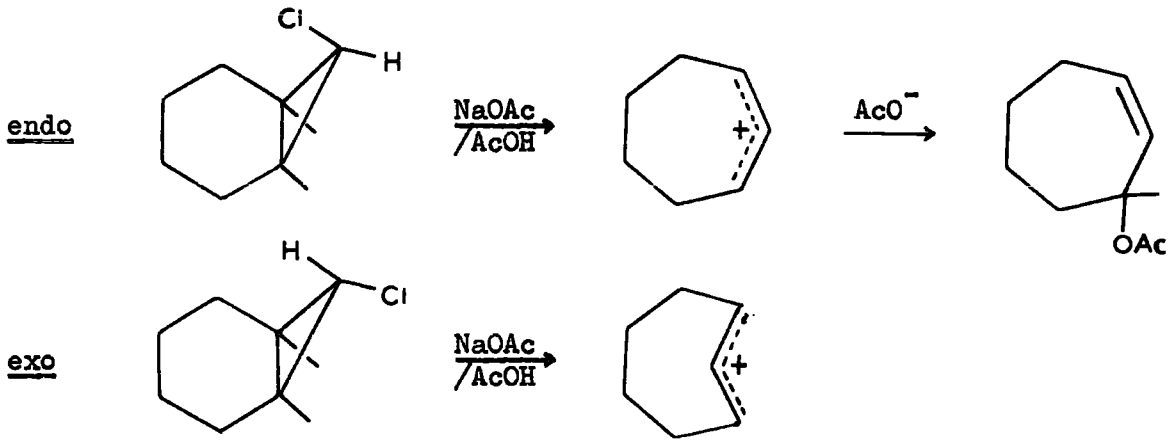
the respective allyl alcohols.

Deamination of 7-aminobicyclo[4.1.0]heptane also gave a cycloalkenyl alcohol,[41] correcting earlier work where the product was wrongly identified as the 7-hydroxy compound.[42]

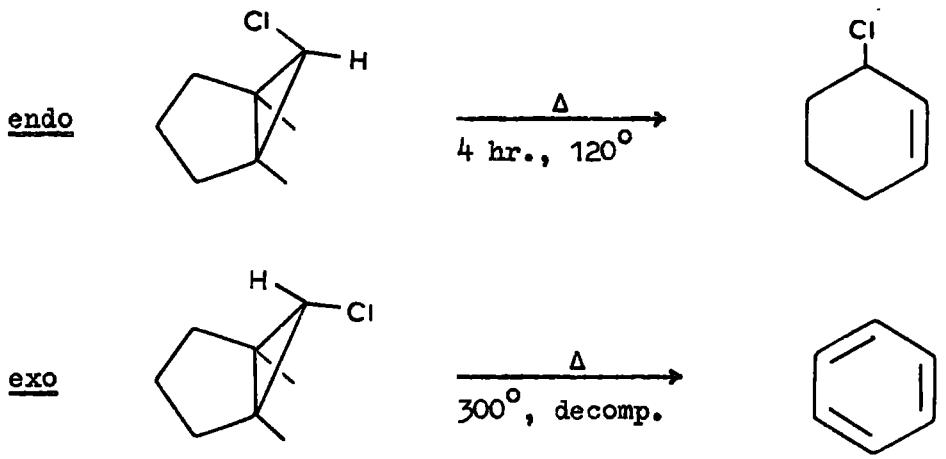
These important results were noted by Depuy,[31] who prepared and solvolysed 1-phenyl, exo-7-tosylbicyclo[4.1.0]heptane. This was found to be very unreactive under conditions where 2-phenyl cyclopropyl tosylate would solvolyse readily. Ring opening in the correct disrotatory manner would produce a trans double bond in a seven-membered ring, a system which is severely strained.

Similarly, exo-7-chlorobicyclo[4.1.0]heptane was unaffected after 2 hrs. at 210° in 2M silver acetate/acetic acid ($k_{125^\circ} < 8 \times 10^{-9}$ sec.$^{-1}$), whereas the endo isomer solvolysed smoothly at 125° to give

the expected cis-cyclohepten-1-yl acetate. (k_{125}^{o} = 1·4 x 10^{-6} $sec.^{-1}$).[43] The exo isomer could go by a dis.(1) mode to give a cis-allyl cation, but calculations show that this is energetically very unfavourable. The experimental results provide strong confirmation of these results.

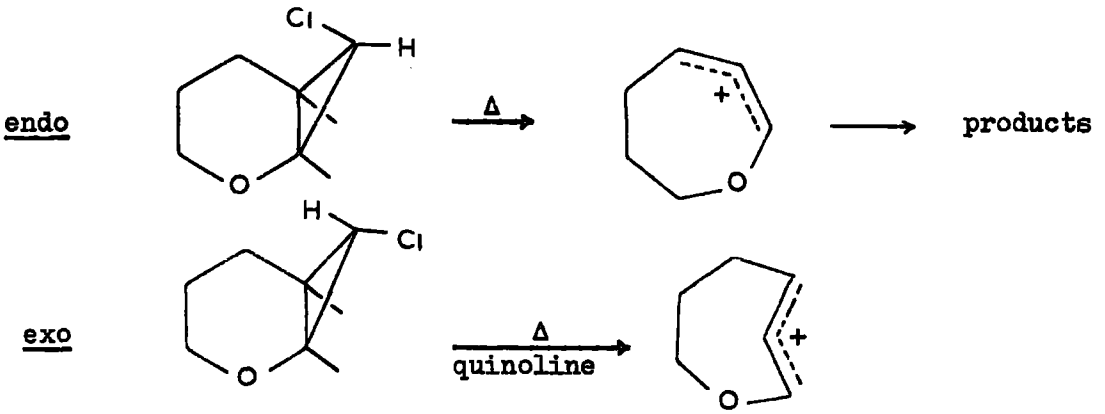


(cf. the pyrolysis of endo and exo-chlorobicyclo[3.1.0]hexanes.[44]).



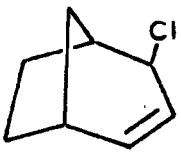
On the basis of these results, a number of anomalies in the literature have been corrected.

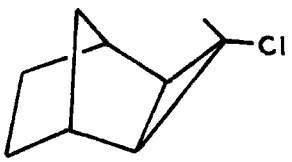
Schweitzer and Parham,[45] prepared the <u>endo</u> and <u>exo</u>-oxanorcaranes, but wrongly assigned the structures on the basis of isomer distribution. One isomer readily rearranges, while the other is stable to heating in quinoline at 175°.



However, the dis.(2) mode of ring opening for the <u>exo</u> isomer should be energetically very unfavourable, and other workers later reversed the assignment.[46a,b]

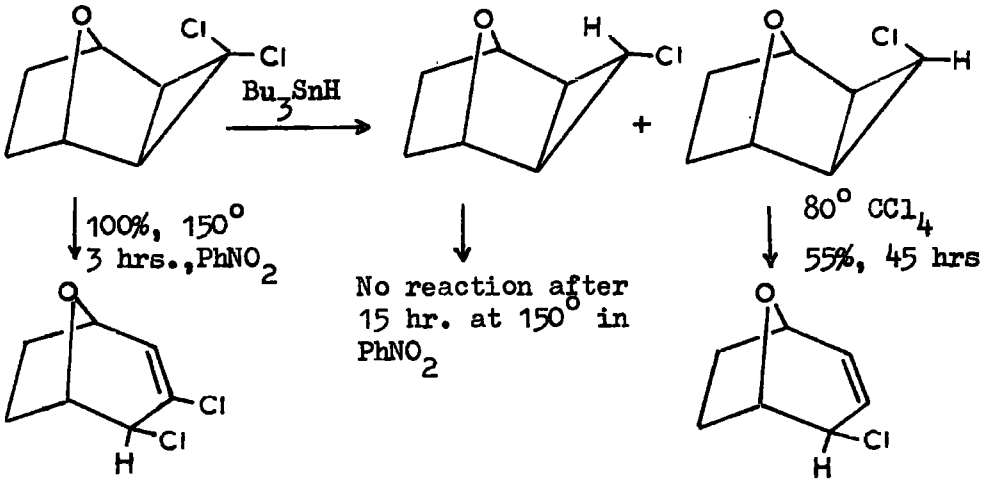
Jefford et al.[47] recently examined the reaction between chlorocarbene and norbornane and reported the formation of four isomeric products. These workers later revised their findings and concluded that only <u>exo</u> addition took place to give <u>syn</u> and <u>anti</u> (II) adducts, but that the <u>syn</u> adduct rearranged under the reaction conditions to give ring opened material.

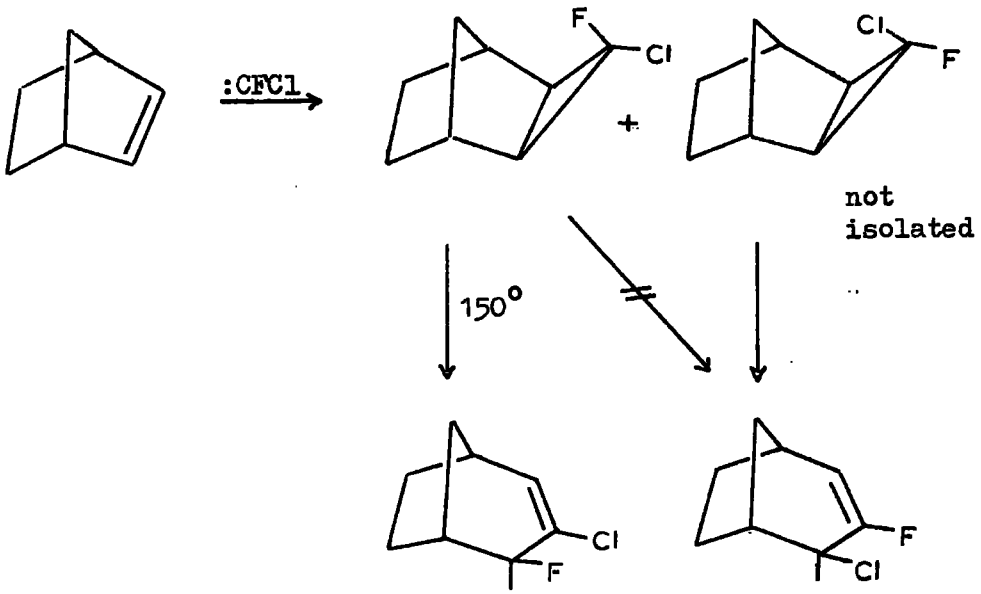




I II

This parallels the behaviour found in other norbornane systems.[49,50]





Perhaps the most thorough and instructive investigations of fused ring systems, has been made by Schöllkopf.[35,51] This involved the acetolysis of exo- and endo-bicyclo[n.1.0]alkyl tosylates. The results for the endo compounds are shown in Table II.3.

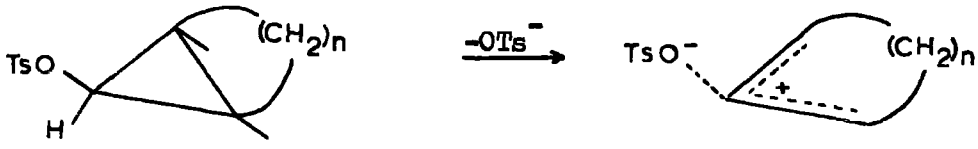


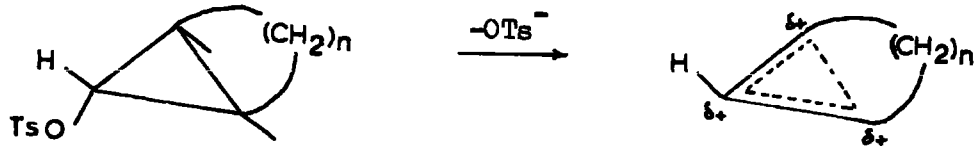
Table II.3.

n	K.rel.*(100°)	Products
3	25000	cis-2-cyclohexen-1-yl acetate
4	62	cis-2-cyclohepten-1-yl acetate
5	3·1	cis-2-cyclo-octen-1-yl acetate
6	3·5	cis-2-cyclononen-1-yl acetate

*Relative to cyclopropyl tosylate

The cyclohexenyl cation, according to models, is relatively strain free, whereas the cycloheptenyl and -octenyl cations exhibit both torsional and transannular strain. This would account for the large rate decrease in going down the series.

More interesting are the results for the exo series where the favoured disrotatory mode is strongly hindered when n is small. Table II.4.



I

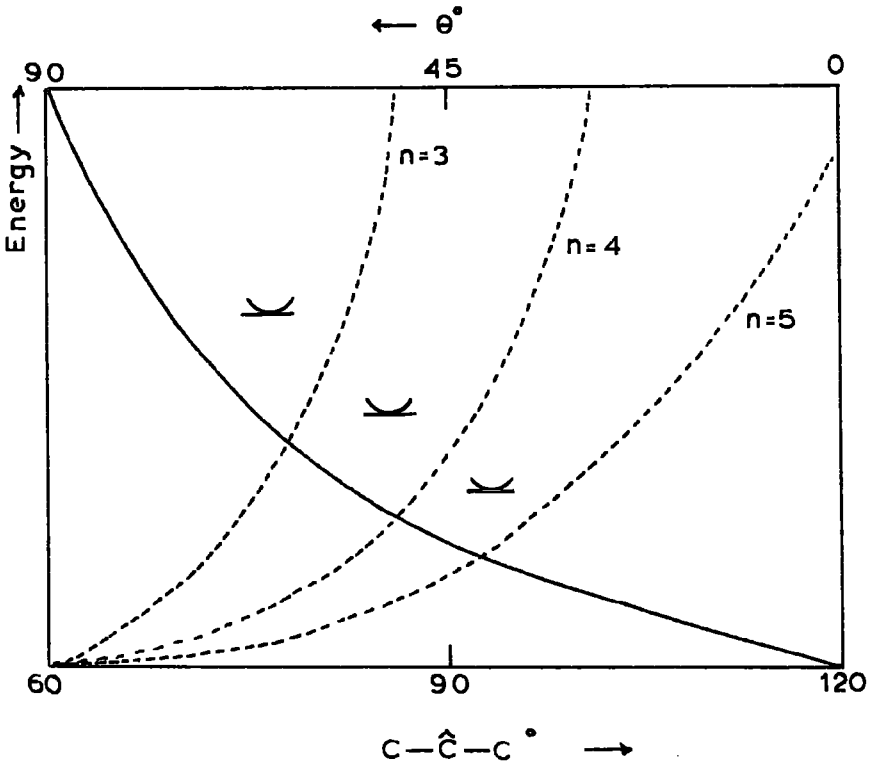
Table II.4.

n	K.rel.*(100°)	Products
3	<< 0·01	-
4	1·7	exo-7-norcaryl acetate, cis-cycloheptyl diacetate (1:1)
5	2500	trans and cis-2-cyclo-octen-1-yl acetate, cis-cyclo-octyl-1,3-diacetate
6	10,000	cis-2-cyclononen-1-yl acetate

The bicyclo[3.1.0]tosylate (n = 3) is extremely inert to solvolysis (90% unchanged after 3 months in NaOAc/AcOH at 150°). Ring opening via a cyclopropyl cation, or by the 'unfavoured' disrotatory mode, dis.(1), requires a larger amount of energy. For n = 4, Schöllkopf proposed that ionisation began in a dis.(2) fashion to give a 'semi open' cation (I), which was intermediate between a cyclopropyl and allyl cation. This species could either react with solvent to produce returned acetate or proceed to the allyl cation. 'Ab initio' quantum

mechanical calculations[20] have shown that there is no activation barrier between the free cyclopropyl and allyl cations, for a disrotatory process. However, the presence of a fused ring introduces strain which increases as the second ring becomes smaller and the sum total gives a 'semi open' cation which lies in a shallow potential minimum (Fig. II.4).

Fig.II.4.



—— π electron energy

----- strain energy

From this position either returned or allylic material could be produced. An energy barrier must thus be surmounted before reaching the substituted allyl cation, which involves a trans double bond in a seven-membered ring. This is supported by the nature of the products isolated and this will be discussed in detail later.

Non-empirical calculations have also shown that for angles of rotation $> 30^{\circ}$, a small out of plane bending of the C_1 hydrogen atom (in such a manner that the reaction appears to be a dis.(2) mode), is energetically favourable.

It can be seen therefore, that there is an overwhelming body of experimental (qualitative and quantitative) and theoretical evidence for a ring opening mechanism concerted with ionisation of the leaving group. A large dispersal of charge around the cyclopropane ring occurs in the T.S. Steric and strain effects also play a part in determining the product stereochemistry and the rate of reaction.

II.4. Evidence for the Free Cyclopropyl Cation.

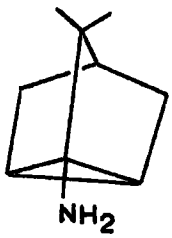
There is relatively little experimental data in the literature for the formation of cyclopropyl cations. The evidence for these is based on either, (or both), of the criteria:-

(a) that the reaction is known to generate carbonium ions, (e.g. nitrous acid deamination) or:-

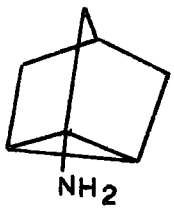
(b) that cyclopropyl derivatives are formed in the reaction and are isolated as products.

(a) From Deamination of Amines.

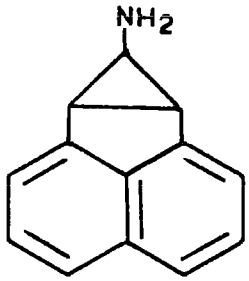
Evidence here is not very strong, and alternative paths have been proposed. Apotricyclylamine (I),[52] 1-amino-nortricyclene (II)[53] and 3-amino-1,2-cyclopropano-acenaphthalene (III),[54] have all been reported to yield unrearranged products on deamination.



I



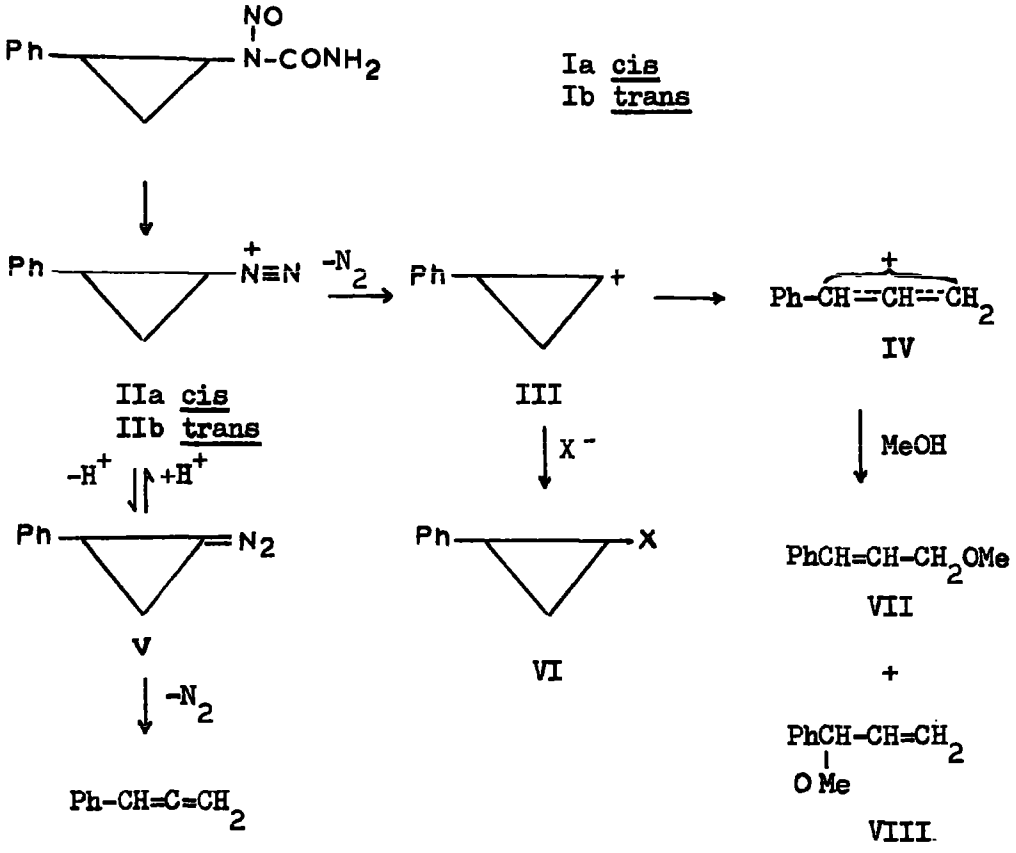
II



III

It was assumed in the reactions of (II) and (III), that the unrearranged product was formed by collapse of a diazonium acetate ion pair directly to the products. Others[55] have found that a free radical path for the decomposition of aliphatic diazonium salts was energetically possible, and might compete with the usual carbonium ion process when the latter was relatively unfavourable (as in fused systems).

A more sophisticated investigation of cyclopropyl deamination reactions, by Kirmse and Schütte[56,57] is outlined below.



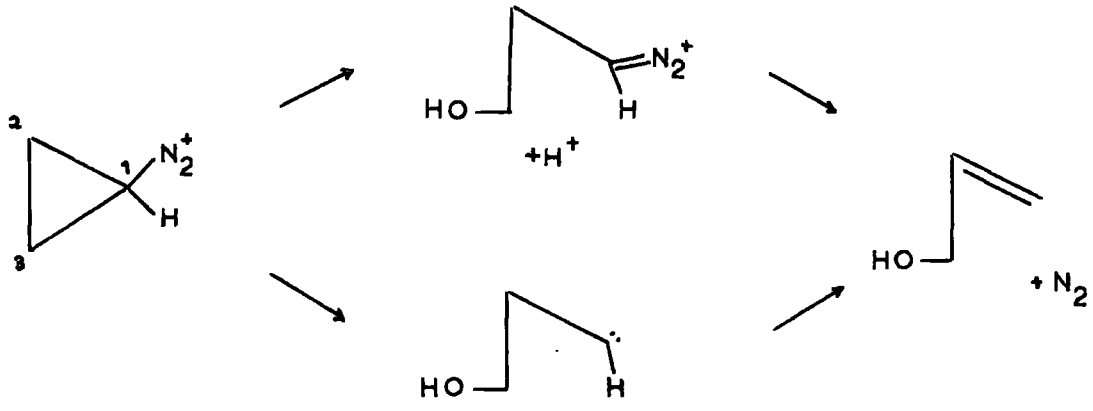
Treatment of N-nitroso-N-2-phenyl cyclopropyl urea with excess sodium formate in MeOD, gave phenyl-allyl-methyl-ethers (VII) and (VIII), with 0·25 g. atom of D/mole. Thus only 25% of (IIa) or (b) underwent cis - trans isomerisation via (V). Both (Ia) and (b) gave mainly trans- (VII), with only a trace of the cis isomer, thus pointing to a common intermediate. Had the reaction been concerted, (Ia) would have given cis- (VII) and (Ib), trans- (VII).

Table II.5.

	Products %					
Starting Material	Phenyl Allene	cis-(VI)	trans-(VI)	trans-(VII) X = OCH_3	cis-(VII)	VIII
Ia	0·1	0·03	0·30	25	0·1	60
Ib	0·1	0·02	0·14	24	0·1	60

Addition of LiBr gave a very small yield (1-2%) of trans-2-phenyl cyclopropyl bromide (cis < 0·05%) by stereospecific trapping of the cation. The same isomer distribution was obtained from both precursors. However, these deamination reactions are extremely exothermic and it is possible that a 'hot' allyl cation is formed which will allow cis - trans isomerisation of VII.

Other, less direct routes, involving C_1-C_2 bond fission, have also been proposed.[62]

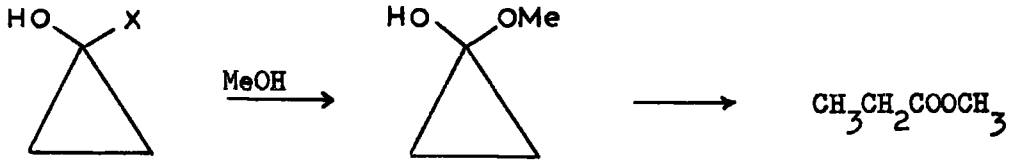


As a consequence, C_1 of cyclopropylamine becomes C_2 or C_3 of allyl alcohol, whereas by the cyclopropyl cation route, it becomes C_2. However, deamination of cyclopropylamine-1-d showed that essentially all the deuterium was concentrated at C_2 in allyl.

(b) Formation of Cyclopropyl Derivatives.

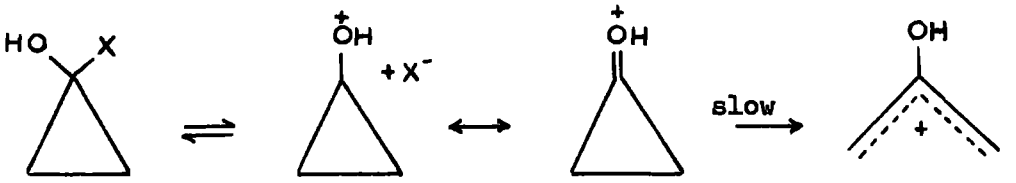
Carbonium ion stabilising groups may be substituted at the C_1 carbon atom to stabilise the cation as it is formed.

The reaction of methanol with substituted hydroxy cyclopropanes gives the corresponding methyl hemiketal of cyclopropanone in 100% yield, which ring opens in the presence of acid to methyl propionate.[58]

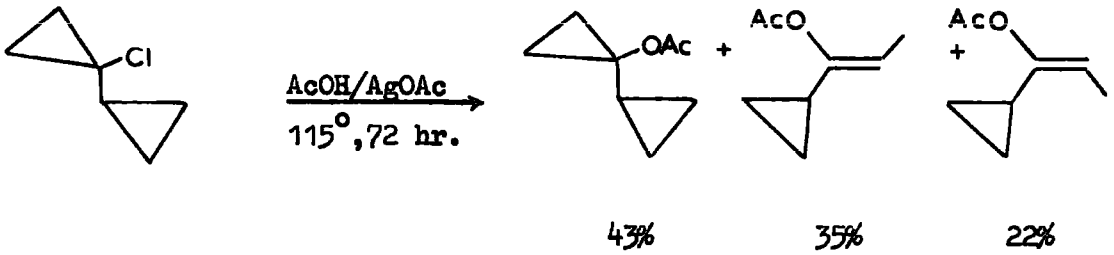


X = OAc,Cl

The activation energy for the formation of the 1-hydroxy cyclopropyl cation appears from this to be quite low. This may be compared with the 1-phenoxy cyclopropanes, previously mentioned, which are thought to solvolyse by a concerted mechanism.[35] A slow ring opening step is proposed with the hydroxy group stabilising the cation by its +M effect.

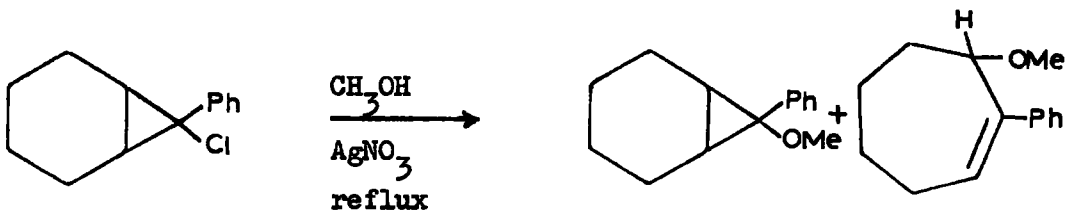


The well known carbonium ion stabilising ability of the cyclopropyl group, has been utilised by Landgrebe and Becker[59,60] to generate the cyclopropyl cation. Solvolysis of 1-chlorobicyclopropyl produced the mixture of products shown.



This was the first solvolysis reaction of a cyclopropyl derivative which did not give <u>solely</u> ring opened products, and this would indicate a large positive charge density on the C_1 carbon atom. The allylic products were shown <u>not</u> to arise from 1-acetoxy bicyclopropyl since this was inert to acid catalysed ring opening. Comparison with the 1-isopropyl substituted chloride gave a 1355 x rate enhancement at 150°, due mainly to charge delocalisation into the cyclopropane ring.

Very recently, the silver ion assisted methanolysis of a <u>mixture</u> of epimeric 7-chloro-7-phenylbicyclo[4.1.0]heptanes has been shown to give a mixture of products.[61]



I

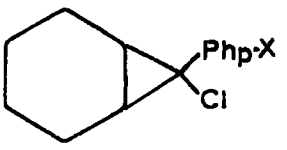
II
<u>endo</u> and <u>exo</u>

III

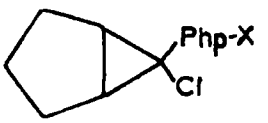
The mixture (I) was reacted at room temperature giving (II) and (III) in 4:1 ratio. The endo isomer of (I), (unreacted at this temperature) was then solvolysed at reflux temperature to give (II) and (III) in the ratio 1:12. The formation of returned material was taken as unambiguous evidence for the formation of the cyclopropyl cation.

II.5. This Work.

The work described in this thesis has been concerned with examples of non-concerted ring openings of bicyclic cyclopropyl derivatives. As has been shown, the advantage of using bicyclic systems, is that one disrotatory mode is sterically very unfavourable, if the second ring fused to the cyclopropyl is small enough. It was thought to be of considerable interest to look at the effect of phenyl substitution on the solvolysis of systems which are known to ring open by a dis.(2) mode and its effect on the 'wrong' isomers of these systems where the favoured dis.(2) concerted process is energetically unfavourable. Both endo and exo isomers of the para-substituted 6-chloro-6-phenyl-bicyclo[3.1.0]hexanes (I) and the 7-chloro-7-phenyl bicyclo[4.1.0]-heptanes(II) were prepared and solvolysed in acetic acid/sodium



II



I

acetate solution.

This system, utilising a relatively poor leaving group in a poor solvolysing medium was chosen in order to increase the demands on the reactant for stabilisation through increased ring opening, thus emphasising the steric and electronic effect of the phenyl group and substituents. For comparison, the endo and exo hydro-chloro and the gem-dichloro compounds have been solvolysed in order to study entropy and enthalpy effects in rate enhancements.

The phenyl- and hydro-chlorobicyclo[5.1.0]octane compounds were also studied, since the 'wrong' isomers in this case may solvolyse via a 'semi open' cyclopropyl cation.

This data is presented in full in the next chapter.

CHAPTER III

Discussion of Experimental

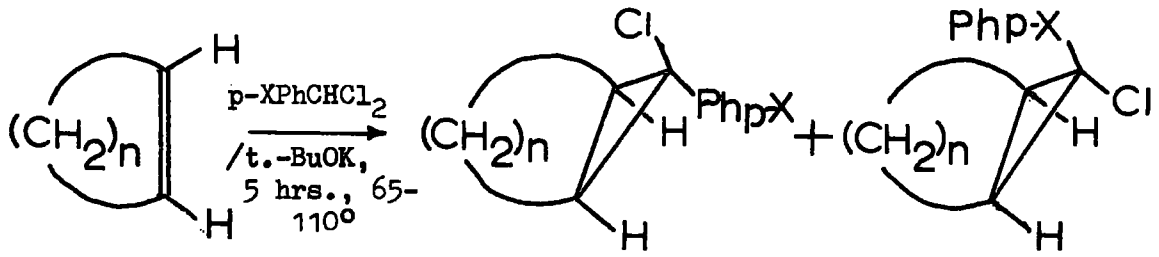
III.1. Introduction.

As mentioned previously, a series of phenyl-substituted bicyclic systems involving the cyclopropane ring were chosen for solvolytic study, in the expectation that a group, such as phenyl, capable of stabilising a positive charge, might produce a cyclopropyl cation of finite lifetime. It has also been proposed that in all probability, Depuy's suggestion[32] that the acetolysis of 1-phenyl cyclopropyl tosylate is a concerted process, is incorrect. It is the purpose of this study to compare the reactions of these substituted compounds with their unsubstituted analogues, for which theoretical evidence for a non concerted dis.(2) mechanism would seem to be fairly conclusive.

The compounds chosen for study are shown in Fig. III.1.

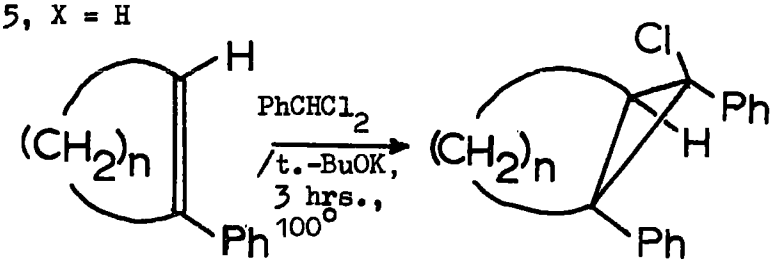
It has not been possible to isolate all of the isomers shown, as some are so reactive that they disappear during the work-up procedure. Although the synthesis of these compounds is relatively straightforward, the major task has been the separation of isomers in a sufficiently pure state and in large enough samples for kinetic determinations. This is particularly the case with the phenyl-substituted compounds, since reactions of benzal chlorides with potassium tert.-butoxide (t.-BuOK) even with excess olefin as solvent, tend to produce a large proportion of high boiling, presumably

Fig.III.1.



n = 3, X = H, Me, Cl, F
n = 4, X = H, Me, Cl, F
n = 5, X = H

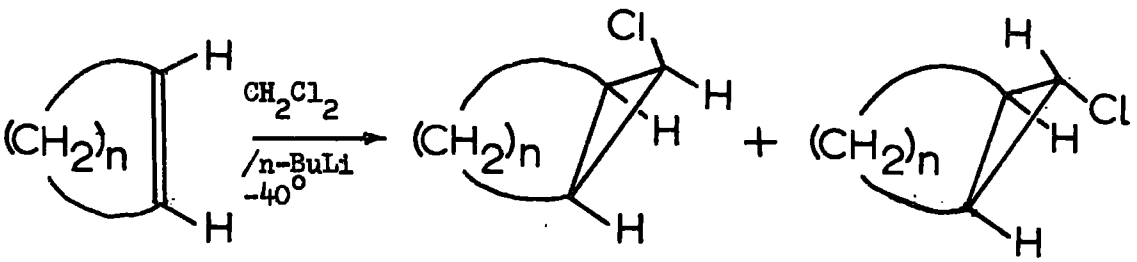
endo-chloro exo-chloro



+ no exo isomer

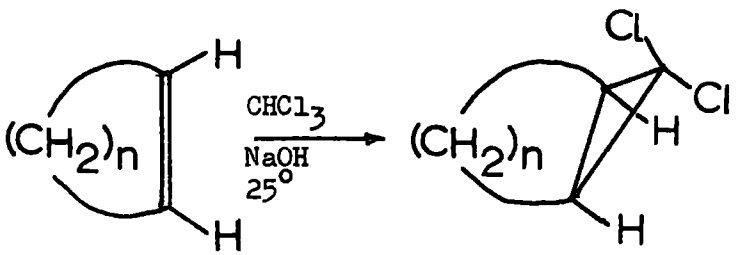
n = 4, X = H

endo-chloro



n = 3, 4, 5

endo-chloro exo-chloro



n = 3, 4

polymeric material, from which it is difficult to extract the mixture of epimers.

Gas-liquid chromatography (g.l.c.) has proved to be completely unsuitable for isomer separation of the phenyl-substituted compounds, since these rearrange or decompose readily under a wide variety of g.l.c. conditions. Thin layer chromatography (t.l.c.) on alumina or silica gel, with various solvent systems gives R_f value differences of 0·1 or less, hence scaling up to thick layer chromatography proved inadequate.

The problem was finally solved by a combination of conventional column chromatography and 'dry column' chromatography.[62] The latter technique is an improved chromatographic method by which separations comparable to those obtainable by t.l.c. can be carried out fairly rapidly on a column on a preparative scale. Details of this method are provided in Chapter IV, Section III.

The phenyl-chloro compounds used for kinetic runs were all solids (except exo-6-chloro-6-phenylbicyclo[3.1.0]hexane) and were isomerically pure. They were all recrystallised or resublimed before use and had sharp melting-points. They were stored in a refrigerator at 0° until use. The exo- and endo-bicyclo[n.1.0]hydro-chloro compounds are all liquids which were separated with some difficulty by g.l.c. The isomers were only resolvable with long retention times

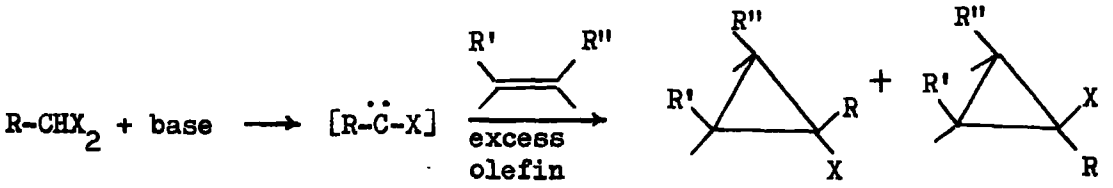
(high temperatures caused decomposition) and small injections ($\sim 100\,\mu l.$). The configurations of all starting materials and products were assigned on the basis of 220 and 100 MHz ^1H N.M.R., with the aid of spin decoupling, and by g.l.c.

III.2. Carbenes as Routes to Substituted Cyclopropanes.

Carbene insertion into a double bond is a very useful synthetic route to a wide variety of heterosubstituted cyclopropanes and has given great momentum to research into small rings.

The original work of Hine[63] on the alkaline hydrolysis of chloroform, for which he postulated a dichlorocarbene intermediate has been extended to include the base catalysed reactions of a number of other halogen substituted compounds in the presence of olefins. In 1954, Doering and Hoffmann[64] obtained 7,7-dichloro-bicyclo[4.1.0]heptane from the reaction of t.-BuOK, chloroform and cyclohexene. This was the first structural evidence for Hines' 'divalent intermediate'.

McElvain and Weyna[65] later employed this general principle to generate phenyl-chloro carbene by the action of t.-BuOK on benzal chloride, the carbene in each case was trapped via addition to ketene acetals. For the general case:-



exo (anti) endo (syn)

However, the production of 1-chloro-1-phenyl cyclopropanes by the butoxide α-elimination method is limited. The reaction does not proceed well at temperatures much below 70°C under simple reaction conditions, precluding the use of butenes as acceptors. In most cases, yields are well below 30-40%.

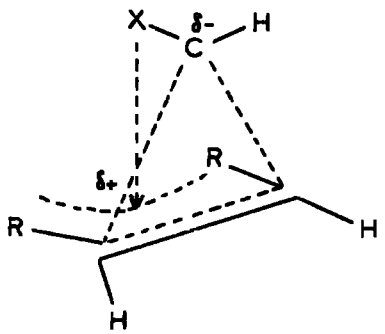
Although, Moss[66] has recently developed an improved method employing methyl-lithium as base, this route was found to be unsuitable for large-scale (~ 4 gm.) preparations required in this work. Reactions of substituted benzal chlorides with n-butyl-lithium as base were unsuccessful.

Stereochemistry. Several attempts have been made to determine the reactivities and stereochemistry of addition of 'carbenes' produced from benzal chlorides,[67] i.e. whether the reaction involves a free carbene as intermediate, or a complexed methylene in which the valency of the methylene carbon is greater than two ('carbenoid').

Rationalisation of the observed stereoselectivities of phenyl-halo carbenes in terms of a unified model of the T.S. has not been very successful. Closs and Coyle[68] have shown that exo/endo ratios

are affected both by the nucleophilicities of the olefin substrate and by the nature of the halide ions present in solution. The concept of a free carbene was discarded in favour of a key intermediate involving α,α-dichlorobenzyl-lithium, which could lose lithium chloride and add to the olefin.

The cyclopropyl compounds prepared during this work have all shown a predominant endo (syn) stereoselectivity. This has also been attributed to attractive forces between the polarisable carbene substituent and the alkyl groups of the substrate.[69]



Opposing this, however, are non-bonded repulsive interactions which will be particularly severe if either the alkyl groups on the olefin or the carbene substituent are unusually large.

III.3. The Preparation and Solvolysis of para-substituted Endo and Exo-7-chloro-7-phenylbicyclo[4.1.0]heptanes (Norcaranes)

(i) Preparation. Substituted phenyl-chloro carbenes, generated by the method of McElvain and Breslow,[65,70] were added to cyclohexene in yields of between 20-35%. It was found that the lower the boiling

point of the olefin employed, the longer was the reaction time required for reasonable yields. The t.-BuOK used was rigorously dried, since tert.-butanol impurity, even in small amounts, drastically reduced yields.

The carbene precursors were prepared by two main routes: (a) by radical chlorination, under u.v. irradiation of the para-substituted toluene, until a weight equivalent to two chlorines had been added, or (b) by the reaction of PCl_5 on the para-substituted aldehyde.

(a) $p\text{-XPhCH}_3 \xrightarrow[Cl_2]{h\nu} p\text{-XPhCHCl}_2 + 2HCl$ X = Cl, F, COOEt

(b) $p\text{-XPhCHO} \xrightarrow{PCl_5} p\text{-XPhCHCl}_2 + POCl_3$ X = Me, NO_2

The para-hydro, -chloro and -fluoro compounds were liquids, and were distilled before use. The others (X = Me, NO_2, COOEt) were solids and were recrystallised before use. All benzal chlorides were stored under dry nitrogen in the dark.

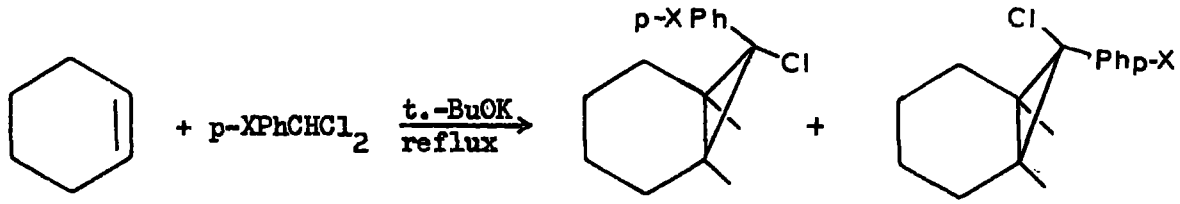
Reaction of para-hydro, -chloro, -fluoro and methyl benzal chlorides with t.-BuOK in excess cyclohexene under reflux, gave the appropriate norcarane compounds, plus polymeric material.

Reaction of $p\text{-NO}_2\text{PhCHCl}_2$ with t.-BuOK under reflux, was extremely vigorous producing only polymeric material. The reaction was repeated at several temperatures down to -78°, however the carbene could not be trapped out, and the only product isolable, in low yield (~3%) was

1,2-dichloro-1,2-di-(p-nitrophenyl)-ethylene, formed by dimerisation of the carbene. Under the same conditions, p-carbethoxy benzal chloride was recovered largely unchanged, plus a small amount of polymeric material.

Attempted para-nitration of 7-chloro-7-phenylnorcarane with $AcOH/HNO_3$ produced solely polymeric material.

Table III.1. shows the isomer ratios observed by g.l.c.



X	exo	endo
H	1	1·5
Cl	5	1
F	1	1·5
Me	1	2·0

Table III.1.

It is not certain whether the unusual exo/endo ratio of the para-chloro compound is due to the stereochemistry of addition, or whether the endo isomer decomposes during the work-up procedure.

All isomers are low-melting white solids soluble in methanol. Previous attempts at separations have only met with partial success.

Hodgkins et al.[71] obtained the isomers of 7-chloro-7-phenylnorcarane in an impure form by g.l.c., with difficulty, on a ditriricinoleate glycol 400 polyethylene column at 130°. Later workers[68] were unsuccessful using g.l.c., but isolated the major (endo) isomer, free of olefin, by column chromatography on alumina. The exo isomer reportedly decomposed under the conditions used.

(ii) Solvolysis and Products.

(a) Endo-chloro Series. The parent compound of this series, 7-chlorobicyclo[4.1.0]heptane has previously been studied,[43] and a concerted dis.(2) mode of ring opening postulated.

Table III.2 gives the rates of reaction and activation parameters for this and the para-substituted phenyl compounds. The endo stereochemistry was readily established by 220 MHz ^{1}H N.M.R. The C_3, C_4 methylene protons are more shielded by the phenyl ring in the exo isomers and hence appear much further upfield than in the endo isomers. (See Chapter VI).

The effects of replacing hydrogen by phenyl is a relatively small rate enhancement. A para-methyl group increases the rate by a factor of 3 and a para-fluorine atom decreases the rate slightly (the para-chloro isomer was not isolated in pure form). This indicates a relatively small electron demand at the reaction centre. The introduction of a bridgehead substituent (R = Ph) has a relatively small rate

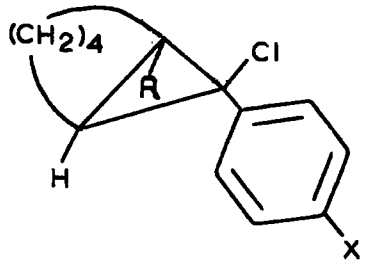


Table III(2). Acetolysis of substituted endo-bicyclo[4.1.0]heptanes

R	X	Temp.(°C)	K(sec.$^{-1}$)	E_A(K.cals.)	$\Delta S^{\neq}$ (e.u.)
endo-7-chloro-bicyclo[4.1.0] heptane		150	$1.479 \times 10^{-5} \pm 0.001$	34.24 ± 0.03	-2.33 ± 0.07
		125	$1.145 \times 10^{-6} \pm 0.002$		
H	H	125	$4.07 \times 10^{-5} \pm 0.02$	30.20 ± 0.07	-5.27 ± 0.17
		100	$3.15 \times 10^{-6} \pm 0.01$		
H	Me	125	$1.37 \times 10^{-4} \pm 0.04$	30.06 ± 0.42	-3.19 ± 1.09
		100	$1.07 \times 10^{-5} \pm 0.03$		
H	F	125	$3.790 \times 10^{-5} \pm 0.003$	30.02 ± 0.06	-5.85 ± 0.14
		100	$2.98 \times 10^{-6} \pm 0.01$		
Phenyl	H	125	$5.40 \times 10^{-4} \pm 0.01$	28.28 ± 0.08	-4.94 ± 0.22
		100	$4.91 \times 10^{-5} \pm 0.03$		

enhancing effect (a factor of 13x). This is in agreement with theoretical predictions[20] which show that in the T.S. for the dis.(2) ring opening, the positive charge is extensively delocalised. Most of the rate enhancement for phenyl substitution appears to come from the enthalpy terms (~4 K.cals), since the entropies are all approximately the same.

The main product for the phenyl substituted compounds is the substituted phenyl-cyclohepta-1,3-diene (Fig. III.2). With the hydrochloro compound only cycloheptenyl acetate is isolated, whereas phenyl substitution enables conjugation of phenyl with the diene system. The structure of the diene was confirmed by its ^{1}H N.M.R. and mass spectrum.

It was not clear at first whether the dienes were formed directly from the allyl cation by loss of a proton, or from ring opened acetate, by loss of acetic acid. An attempted synthesis of 2-phenyl-3-cyclohepten-1-yl acetate (and phenyl-cyclohepta-1,3-diene) to determine whether this was stable to the reaction conditions, is outlined below:-

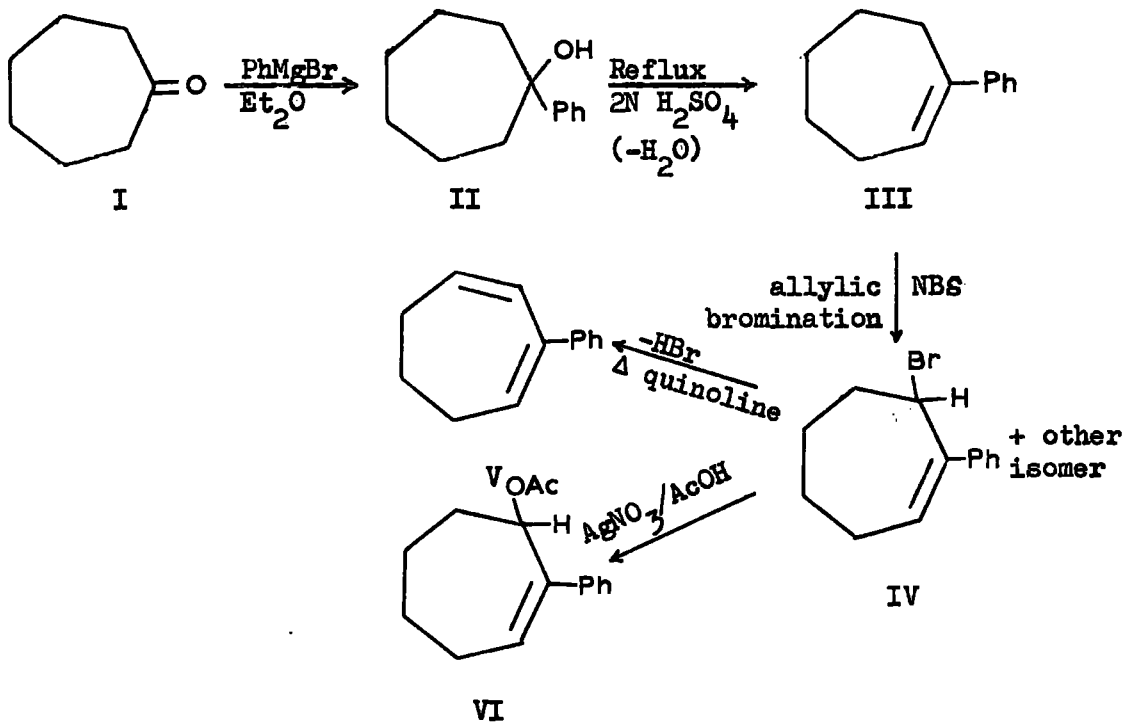
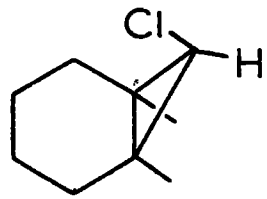
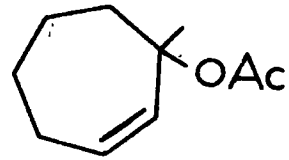


Fig. III.2. Relative rates and acetolysis products of endo-7-chlorobicyclo[4.1.0]heptanes.



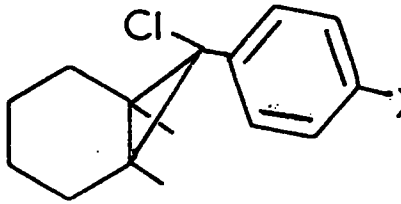
NaOAc/AcOH
125°



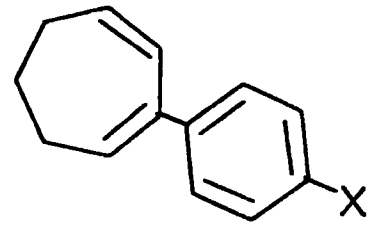
cis-cyclohepten-1-yl acetate

$K_{rel.}^{125°}$

1



NaOAc/AcOH
125°

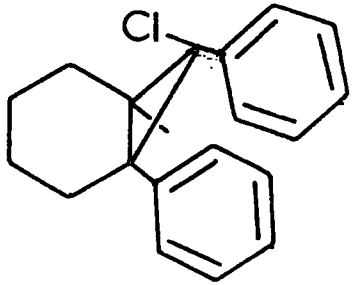


para-subst. cyclohepta-1,3-diene

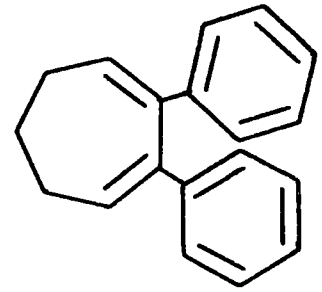
X = H 35·5

X = Me 114·2

X = F 33·1



NaOAc/AcOH
125°

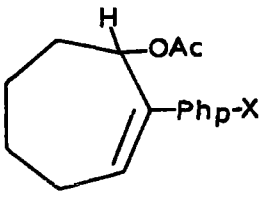


2,3-diphenylcyclohepta-1,3-diene

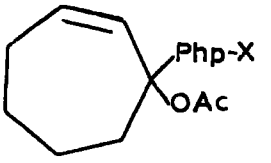
472

Grignard reaction on cycloheptanone (I), gave phenyl-cycloheptanol (II) in 63% yield, followed by dehydration to phenyl-cyclohexene (III) with refluxing 2N sulphuric acid (67%). Allylic bromination with N-bromosuccinimide gave an isomeric mixture of bromides (IV). However, this compound could not be successfully acetolysed or dehydrobrominated, and repeated attempts produced only complex mixtures. Nevertheless, the ^{1}H N.M.R. of phenylcycloheptene served as a useful comparison to that of the product diene.

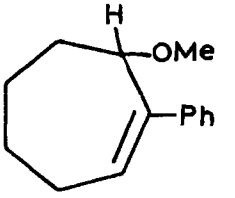
The detection by N.M.R. of small amounts (15-20%) of the acetate (VIII) (X = F), has established that the diene is in equilibrium with



(VII)



(VIII)

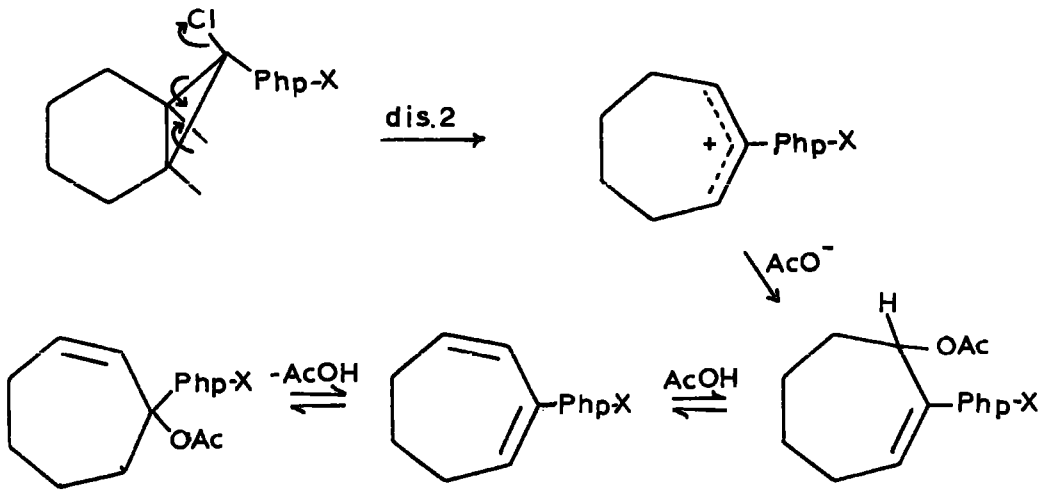


(IX)

ring opened acetate (VII), acetic acid adding across the 1,2-double bond to give the more stable acetate (VIII).

These results may be compared with the products obtained by Ledlie and Nelson[61] from the silver ion assisted methanolysis of 7-chloro-7-phenylbicyclo[4.1.0]heptane. Under less rigorous conditions, (refluxing methanol), these workers isolated the ring opened methoxy compound (IX), 3-methoxy-cycloheptene (and no diene), plus a small amount of a mixture of the two returned methoxy isomers (Ratio 12:1). (See Chapter II, p.42).

This data is entirely consistent with a concerted dis.(2) mechanism:-



(not isolated)

Thus for the particular case of the phenyl compounds where there is a choice of the favoured concerted mode, or the initial formation of a carbonium ion, the <u>former</u> route is favoured.

(b) <u>Exo-chloro Series</u>.

Table III.3 gives the rates and activation parameters for this series.

The hydro-chloro isomer, as expected, is almost completely inert. A sample has been kept at 175° for 1 month without detectable reaction, and this has enabled estimation of an upper limit to the rate constant, (assuming a detectable lower limit of reaction of ~ 0·5%). However in the case of the corresponding tosylate,[51] reaction does proceed to produce returned acetate and ring opened <u>trans</u>-2-cyclohepten-1-yl acetate which adds acetic acid to produce the 1,3-cycloheptyl diacetate.

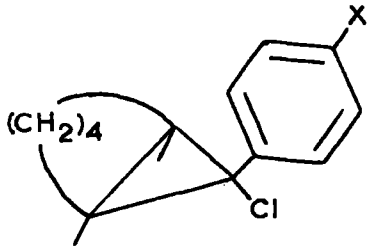
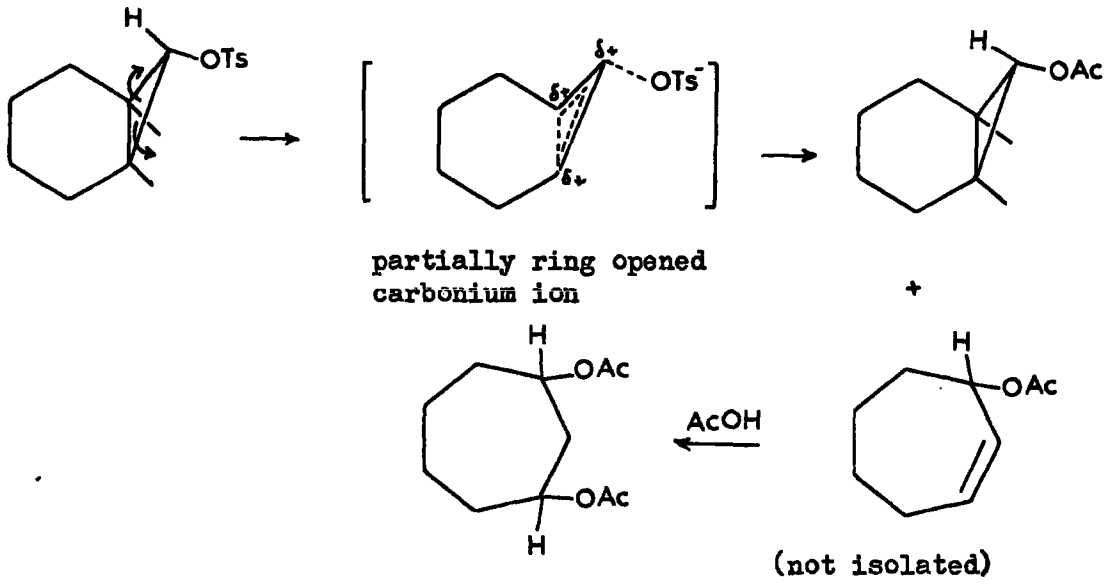


Table III.3. Acetolysis of substituted exo-7-chlorobicyclo[4.1.0]heptanes

X	Temp.(°C)	K(sec.$^{-1}$)	E_A(K.cals.)	$\Delta S^{\ddagger}$(e.u.)
exo-7-chloro-bicyclo[4.1.0] heptane	125	$< 1.0 \times 10^{-10}$ *		
H	125	$1.47 \times 10^{-4} \pm 0.02$	31.68 ± 0.13	1.00 ± 0.35
	100	$1.002 \times 10^{-5} \pm 0.003$		
Cl	125	$6.76 \times 10^{-5} \pm 0.06$	30.78 ± 0.12	-2.81 ± 0.30
	100	$4.98 \times 10^{-6} \pm 0.03$		
F	125	$1.87 \times 10^{-4} \pm 0.01$	29.77 ± 0.12	-3.29 ± 0.30
	100	$1.50 \times 10^{-5} \pm 0.01$		
Me	125	$2.60 \times 10^{-3} \pm 0.50$	28.0 ± 1.5	-2.2 **
	100	$2.40 \times 10^{-4} \pm 0.50$		

* An independent estimate of this figure can be obtained from Depuy's data for the tosylates. Cyclopropyl tosylate solvolyses at about the same rate at 100° as exo-7-tosylbicyclo[4.1.0]heptane. Hausser's estimate[33] of 5.5×10^{-10} sec.$^{-1}$ at 150° for cyclopropyl chloride compares favourably with the value quoted for the bicyclic chloride at 125°.

** It has so far been impossible to obtain an absolutely pure sample of this isomer and these figures are based on a computer fit to the experimental data on samples containing a 5:1 mixture in favour of the endo isomer.

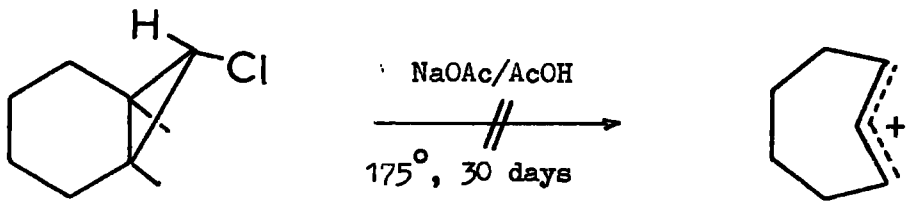


The postulated[35] pathway for this, involves a partially ring opened carbonium ion in a potential minimum, which then adds acetate to produce returned or ring opened acetate. Non empirical calculations[20] indicate that the dis.(1) and con.(1) modes have almost identical activation barriers.

The results for the phenyl-substituted compounds, however, are strikingly different. The ring opened products are the dienes identical to those produced from the concerted ring opening of the corresponding endo isomers (~40%). The remainder of the product comprises a 1:1 mixture of the two internally returned acetates (~60%).

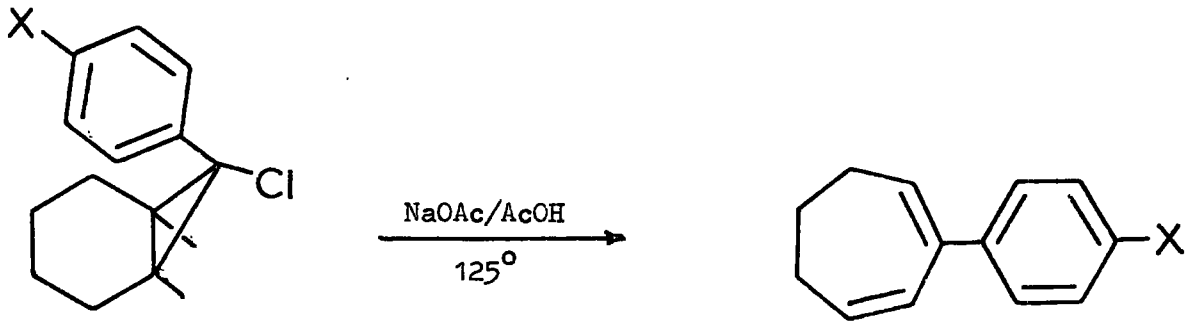
The huge rate enhancements (well over 10^6 x) and the large effect of the substituents present a convincing argument for a non-concerted dis.(0) reaction, with the intermediate formation of a free cyclopropyl

Fig. III.3. Relative rates and acetolysis products of exo-7-chlorobicyclo[4.1.0]heptanes.



K.rel. 125°

1



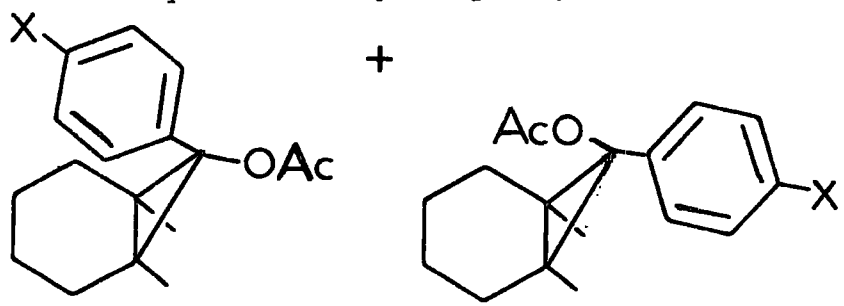
X = H 1·5 x 10^6

X = Cl 0·67 x 10^6

X = Me 26·71 x 10^6

X = F 1·92 x 10^6

para-subst. cyclohepta-1,3-diene



exo : endo

1 : 1

carbonium ion prior to rearrangement. Part of the large observed rate enhancement will be steric in origin since there will be considerable relief of non-bonded interactions in going to the carbonium ion. (Fig. III.4).

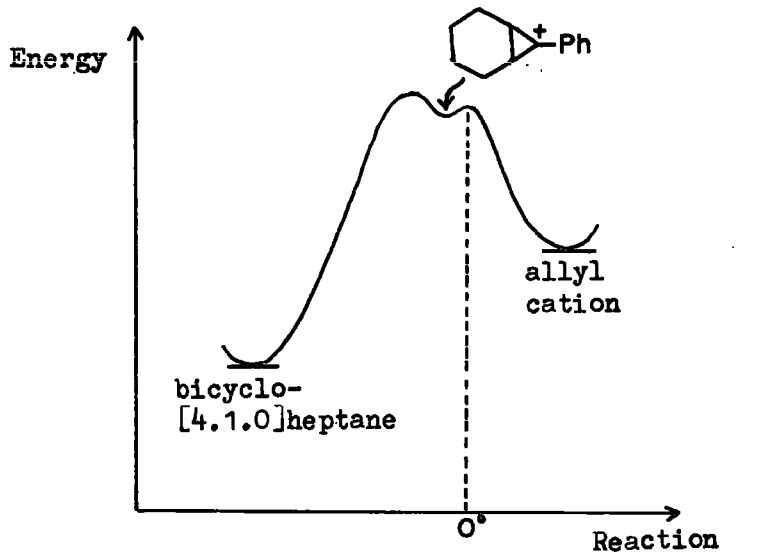


Fig. III.4.

Dreiding models of the carbonium ion show that attack from both sides is hindered, hence the formation of equimolar quantities of the two returned acetates is not unreasonable.

The products obtained from the methanolysis of 7-chloro-7-phenyl-bicyclo[4.1.0]heptane at room temperature,[61] were a mixture of the ring opened ether and the two returned methoxy compounds in 1:3·6 ratio. This was taken as conclusive evidence for a non-concerted dis(O) mechanism. However, the assignment of a non-concerted pathway for the exo-chloro isomer on the evidence of product distribution (from a mixture

of isomers) alone, is not unambiguous and is open to alternative interpretation.

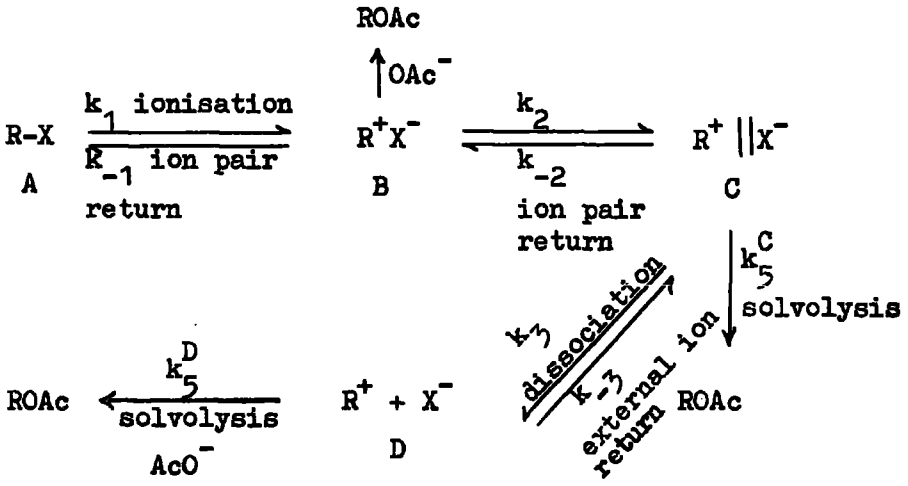
In the absence of other evidence, the formation of returned material might well result from addition of methoxide ion to a 'partially open' cyclopropyl cation of the type proposed by Schöllkopf. 'Ab initio' calculations on this system show quite clearly that the energetic preference for exo addition of a partially opened cation is quite small and hence it is not unreasonable that a mixture of the two ethers be formed with the exo isomer predominating.

The substituent effects are very similar to those obtained by Depuy[31,32] in the solvolysis of 1-phenyl cyclopropyl tosylate and this strongly suggests that this reaction also proceeds via a dis.(O) ring opening. A large rate enhancement over cyclopropyl tosylate was also observed. The fact that cyclopropyl acetates were not formed in this case is not sufficient ground for rejecting the formation of a cyclopropyl cation. The deamination reaction studied by Kirmse and Schütte[56] (see Chapter II), for example, produced returned material which accounted for less than 1% of the total products.

This seems to emphasise that the formation of returned material depends on a number of factors. Foremost among these is the relative nucleophilicity of tosylate, acetate and chloride.

During acetolysis, the cyclopropyl carbonium ions, are almost certainly formed as intimate ion pairs (B) or solvent separated ion pairs

(C), and the stage reached in the reaction will depend both on the nature



of the solvent and the substrate structure.[72] For the case of the phenyl-substituted compounds, in acetic acid (dielectric constant ~6) the ion pairs either rearrange to the allylic cation, or the weakly nucleophilic chloride ion is displaced by the stronger acetate ion, which then collapses to give the acetate or again rearranges to the allylic system.

The exo-phenyl-chloro isomer has been heated to 180° in nitrobenzene and although it rearranges, there appears to be none of the other isomer formed. (Variable temperature ^{1}H N.M.R.).

The cyclopropyl carbonium ion formed, is in a shallow potential minimum and the amount of returned material depends on the activation barrier for rearrangement. The activation energies do not appear to differ greatly between the series. Whereas the exo para-hydro isomer has a higher activation energy than the endo isomer, for the para-fluoro

compounds, the reverse is the case. The entropy values are certainly slightly lower for the endo series, possibly indicating a higher degree of solvation of the positive charge on the cyclopropane ring.

It is significant, however, that a large amount of rearranged tosylate is produced in the acetolysis of 1-phenyl cyclopropyl tosylate, which subsequently undergoes acetolysis in a second step. The ion pair formed with the strongly nucleophilic tosylate anion will either collapse to give returned tosylate or rearrange to products.

III.4. The Preparation and Solvolysis of Para-substituted Exo-6-chloro-6-phenylbicyclo[3.1.0]hexanes

The importance of studying these bicyclo[3.1.0] compounds is that a partially ring opened route for solvolysis in this case, is most unlikely, since even the corresponding tosylate does not solvolyse.[35]

For this series of compounds, only the exo-chloro isomers, which were exceedingly difficult to purify, were isolated. This is not too surprising, since extrapolation of the results for the corresponding [4.1.0] heptanes indicate that the endo isomer would solvolyse extremely readily. The exo stereochemistry was readily established by g.l.c. and by comparison of the ^{1}H N.M.R. shifts with those of the corresponding bicyclo-[4.1.0]heptanes.

The para-fluoro isomer could not be isolated in a crystalline state and N.M.R. showed ~10% decomposition to ring opened allylic

material. However, a measurement of acetolysis rate on an impure sample, enabled estimation of an approximate rate at 100°.

Table III.4 summarises the rates and activation parameters for these isomers and the parent exo hydro-chloro compound. The latter has been kept at 175° for 1 month without detectable solvolysis, thus paralleling the behaviour of the corresponding tosylate. Considerable decomposition (darkening of solution)was observed after ~ 2 weeks, although none of the pyrolysis product (benzene), reported by Baird and Reese[44] could be detected by g.l.c. A lower limit was placed on the rate of solvolysis of the chloride.

The rate enhancements (see Fig. III.5) for the phenyl compounds are of the same order of magnitude ($\sim 10^8$) as those for the exo-bicyclo-[4.1.0]heptanes, as would be expected of the reaction were non-concerted. The products observed are also in accord with this assignment.

These are the substituted phenyl-cyclohexa-1,3-dienes and a mixture of the returned acetates with the endo isomer predominating (> 3:1). The methyl ^{1}H N.M.R. resonance for this isomer appears ~0·15 p.p.m. upfield from that of the endo isomer since the most favourable conformation for the endo acetate group appears (from models) to be above the plane of the phenyl ring, reducing non-bonded interaction with the cyclopentane protons to a minimum.

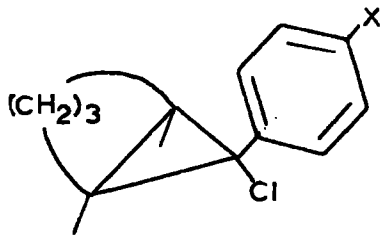


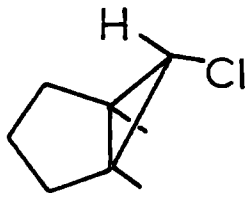
Table III.4.

Acetolysis of substituted exo-bicyclo[3.1.0]hexanes

X	Temp.(°C)	K(sec.$^{-1}$)	E_a(K.cals.)	$\Delta S^{\neq}$(e.u.)
exo-6-chloro-bicyclo[3.1.0] hexane	125	$< 1.0 \times 10^{-12}$ *	-	-
H	125	$1.472 \times 10^{-4} \pm 0.001$	29.74 ± 0.08	-3.87 ± 0.20
	100	$1.185 \times 10^{-5} \pm 0.008$		
Cl	125	$5.98 \times 10^{-5} \pm 0.01$	29.85 ± 0.04	-5.39 ± 0.11
	100	$4.76 \times 10^{-6} \pm 0.01$		
Me	100	$2.600 \times 10^{-4} \pm 0.005$	27.54 ± 0.05	-3.50 ± 0.14
	75	$1.802 \times 10^{-5} \pm 0.008$		
F	100	$\sim 2.5 \times 10^{-5}$	-	-

*This compound is solvolytically inert but will solvolyse more slowly than the corresponding bicyclo[4.1.0]heptane. This value is based on the fact that the bicyclo[3.1.0]tosylate solvolyses ~ 170 x slower than the bicyclo[4.1.0] compound at 100°.[35] Hence at 125° the rate for the chloride will be $\sim 1 \times 10^{-12}$.

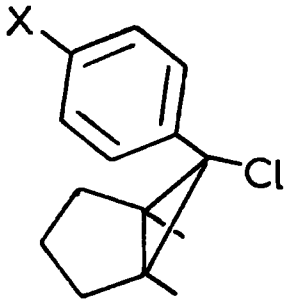
Fig. III.5. Relative rates and acetolysis products of exo-6-chlorobicyclo[3.1.0]hexanes.



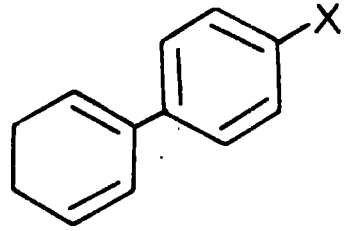
NaOAc/AcOH
175°, 30 days

K.rel. 100°

1



NaOAc/AcOH
100°



para-subst. cyclohexa-1,3-diene

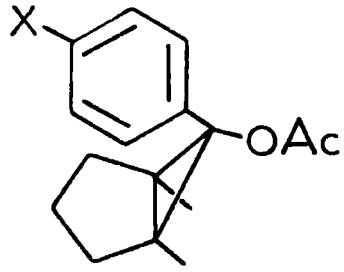
X = H 1·19 x 10^8

X = Cl 4·76 x 10^7

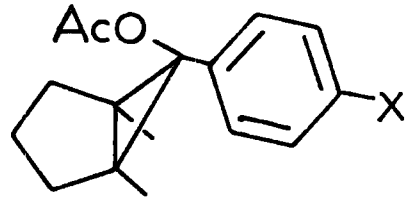
X = Me 2·60 x 10^9

X = F 2·5 x 10^8

+



exo



endo

The N.M.R. spectrum of the diene shows a multiplet in the vinylic region due to the vicinal hydrogens, superimposed on a triplet (also observed in the spectrum of authentic phenyl cyclohexene) due to the proton on C_1.

The substituent effects for this series are similar to those for the exo-bicyclo[4.1.0]heptanes. A para-methyl group reduces the overall activation energy by about 2 K.cals.

The results from these compounds provide firm evidence for the dis.(0) process since, in this case there is no other reaction path which is energetically feasible.

III.5. Comparative Evidence for Concerted Dis.(2), Non-concerted Dis.(0) and Partially Ring Opened Carbonium Ion Mechanisms.

In Section III.3, evidence has been presented that para-substituted exo-7-chloro-7-phenylbicyclo[4.1.0]heptanes undergo a non-concerted ring opening by a dis.(0) mode. Although this evidence is compelling, it is important to completely rule out a mechanism involving an initial dis.(2) ring opening with the formation of a partially ring opened carbonium ion.

Thus, as a comparison, the corresponding bicyclo[3.1.0] and [5.1.0] compounds were studied. The rates of acetolysis of the [5.1.0] compounds investigated are shown in Table III.5. As mentioned previously the importance of studying the [3.1.0] compounds is that for the exo isomer

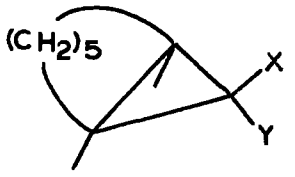


Table III.(5). Acetolysis of substituted endo and exo-bicyclo[5.1.0]octane

X	Y	Temp.(°C)	k(sec.$^{-1}$)	E_A(K.cals.)	$\Delta S^{\neq}$(e.u.)
Cl	Ph	150	$4.77 \times 10^{-5} \pm 0.01$	31.37 ± 0.06	-6.78 ± 0.14
		125	$4.58 \times 10^{-6} \pm 0.02$		
Ph	Cl	150	$4.00 \times 10^{-3} \pm 0.50$	22.40 ± 1.50	-19.0
		125	$7.50 \times 10^{-4} \pm 0.50$		
Cl	H	175	$6.26 \times 10^{-6} \pm 0.02$	34.76 ± 0.13	-7.52 ± 0.30
		150	$6.41 \times 10^{-7} \pm 0.05$		
H	Cl	175	$2.81 \times 10^{-4} \pm 0.01$	28.10 ± 0.09	-14.82 ± 0.20
		150	$4.35 \times 10^{-5} \pm 0.02$		

a 'semi open' mode of ring opening is energetically unfavourable since even the tosyl compound does not ring open.

Considering the endo-bicyclo[5.1.0] compounds, (Table III.6), there is a relatively small rate enhancement on replacing hydrogen by a phenyl group (~104 at 125°). Furthermore, both the endo [5.1.0] isomers solvolyse more slowly than the corresponding [3.1.0] and [4.1.0] compounds, the hydro-chloro compound solvolysing only slowly at 175°.

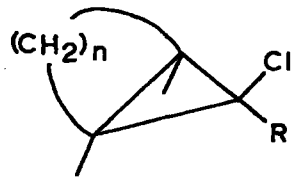
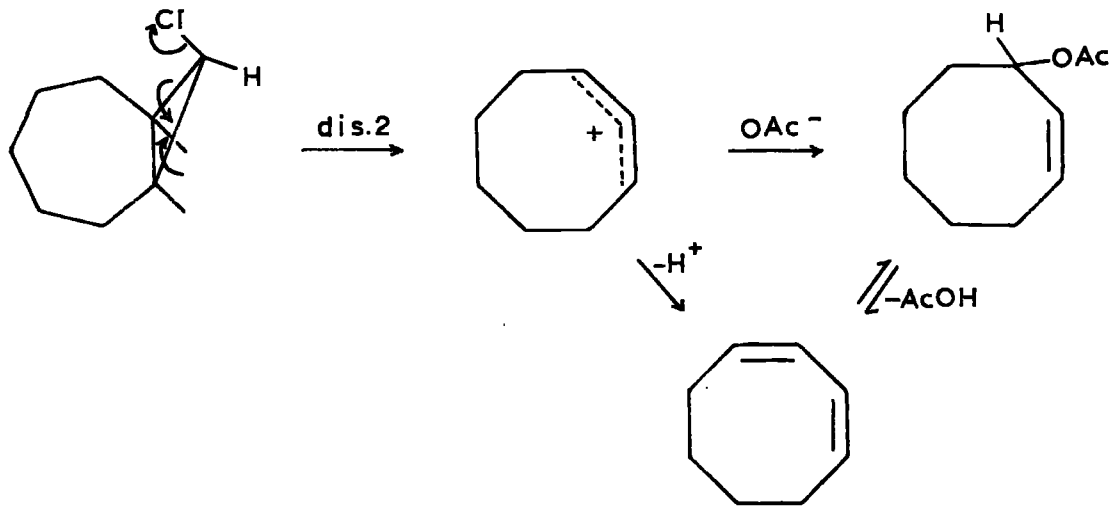


Table III.6.

Acetolysis products and activation parameters for endo-bicyclo[n.1.0]alkyl chlorides

n	R	$k_{rel.}^{125^\circ}$	$k_{rel.}^{100^\circ}$ (tosylates)	E_A K.cal./mole	ΔS^* e.u.	products
3	H	2.59×10^{4}	4.03×10^{2}	25.96 ± 0.06	-2.43 ± 0.19	cis-2-cyclohexen-1-yl acetate
4	H	1	1	34.24 ± 0.03	-2.33 ± 0.07	cis-2-cyclohepten-1-yl acetate
5	H	3.83×10^{-2}	5.0×10^{-2}	34.76 ± 0.13	-7.52 ± 0.30	cis-2-cyclo-octen-1-yl acetate + cyclo-octa-1,3-diene
		$k_{rel.}^{125^\circ}$ (R=Ph/R=H)$_n$				
3	Ph	-		-	-	-
4	Ph	0.36×10^{2}		30.2 ± 0.07	-5.27 ± 0.17	2-phenyl-cyclohepta-1,3-diene
5	Ph	1.04×10^{2}		31.37 ± 0.06	-6.78 ± 0.14	2-phenyl-cyclo-octa-1,3-diene + 3-phenyl-3-cyclo-octen-1-yl acetate

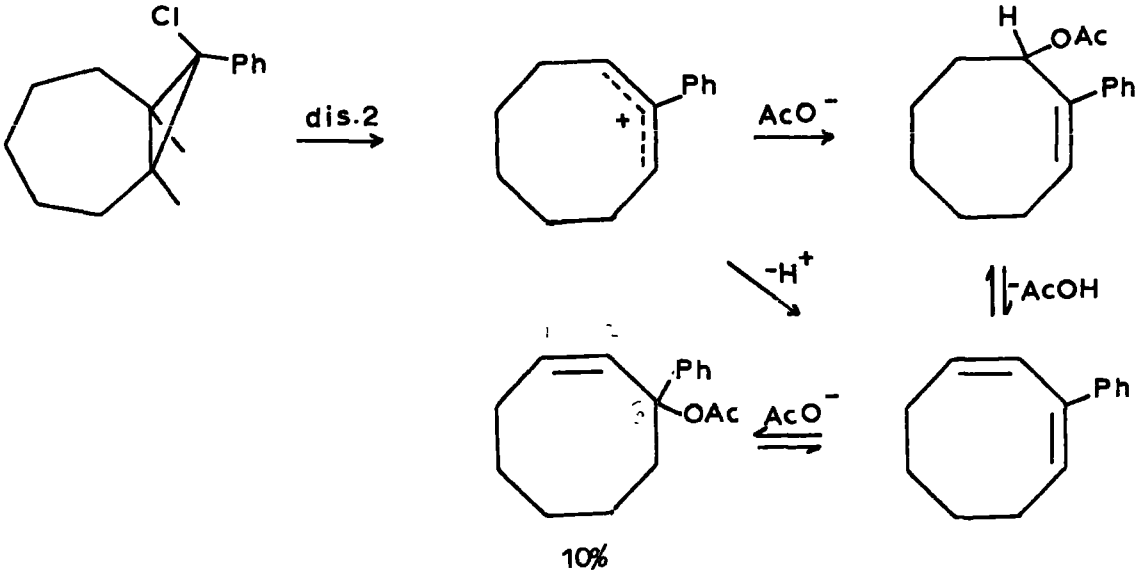
This data parallels that found by Schöllkopf[35,51] for the corresponding tosylates. The decrease in rate with increasing ring size is probably due to an increase in torsional and transannular strain in going to the cation, and this is reflected by the relatively high activation energy (34·76 K.cals.), for the parent compound. The evidence presented by Schöllkopf for the <u>endo</u> [5.1.0] tosylate is consistent with a dis.(2) mode, and the kinetic data and the nature of the products for the phenyl and hydro-chloro compounds suggest a similar process. There is a close similarity, for example, in the entropies of activation through the series and this is good evidence for a dis.(2) mode.



Products of the solvolysis at 150° of the hydro-chloro isomer are <u>cis</u>-2-cyclo-octen-1-yl acetate and cyclo-octa-1,3-diene.

The high proportion of diene is almost certainly a result of the high solvolysis temperature and long reaction time.

Similarly for the phenyl-substituted isomer a large amount of 2-phenyl cyclo-octa-1,3-diene was observed together with the -ene acetate in equilibrium with diene.



10%

3-phenyl-3-cyclo-octen-1-yl acetate 20%

For the exo series of compounds (Table III.7), the effect of replacing hydrogen by phenyl differs markedly both in terms of rate enhancement and product distribution for the [3.1.0] and [4.1.0] compounds on the one hand and the [5.1.0] on the other. For the former, already discussed, the rate enhancements on phenyl substitution and the formation of returned acetates gives good support for the assignment of a dis.(0) mechanism. In contrast with this, the results for the [5.1.0] compounds require a different interpretation. The activation parameters for the exo compounds are remarkably different to the endo series.

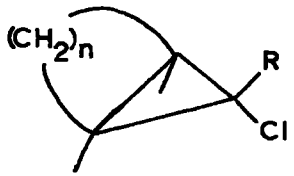


Table III.7. Acetolysis products and activation parameters for exo-bicyclo[n.1.0]alkyl chlorides

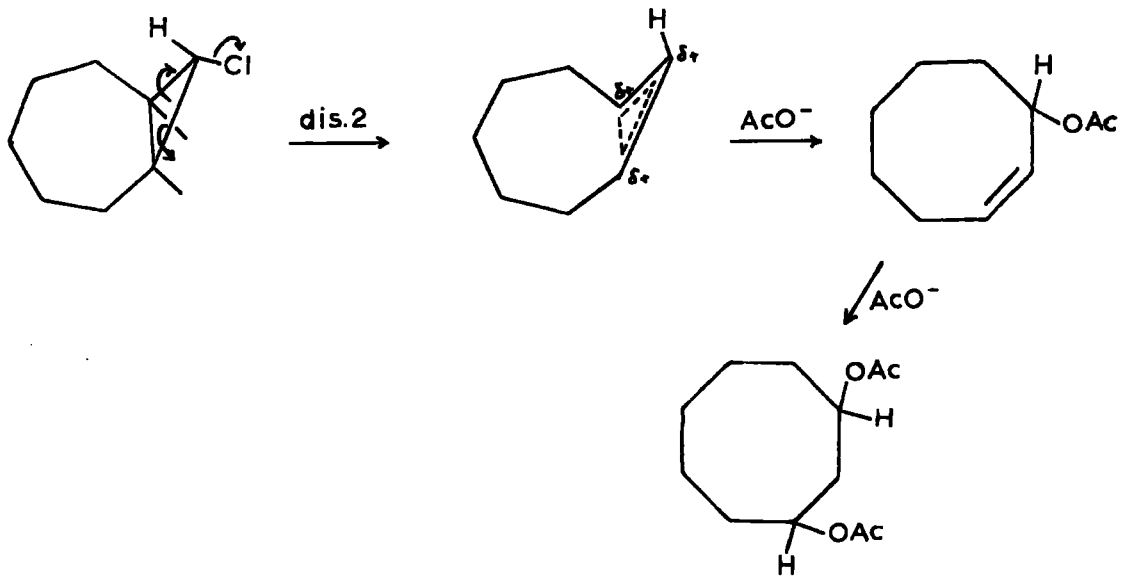
n	R	$k_{rel.}^{125^\circ}$	$k^1_{rel.}$ (tosylates) 100°	E_A K.cal./mole	ΔS e.u.	products
3	H	10^{-2} [a]	10^{-2}	-	-	-
4	H	1 [b]	1	-	-	-
5	H	$5{\cdot}26 \times 10^4$	$1{\cdot}47 \times 10^3$	$28{\cdot}10 \pm 0{\cdot}09$	$-14{\cdot}82 \pm 0{\cdot}20$	cis-2-cyclo-octen-1-yl acetate, cis-cyclo-octyl-1,3-diacetate.
		$k_{rel.}^{125^\circ}$ (R=Ph/R=H)$_n$				
3	Ph	$1{\cdot}5 \times 10^8$		$29{\cdot}74 \pm 0{\cdot}08$	$-3{\cdot}87 \pm 0{\cdot}20$	2-phenyl-cyclohexa-1,3-diene, exo and endo-6-phenyl-6-acetyl bicyclo[3.1.0]hexanes.
4	Ph	$1{\cdot}5 \times 10^6$		$31{\cdot}68 \pm 0{\cdot}13$	$1{\cdot}00 \pm 0{\cdot}35$	2-phenyl-cyclohepta-1,3-diene, exo and endo-7-phenyl-7-acetyl bicyclo[4.1.0]heptanes.
5	Ph	$1{\cdot}43 \times 10^2$		$22{\cdot}40 \pm 1{\cdot}50$	-19·00	2-phenyl-cyclo-octa-1,3-diene, cis-2-phenyl-cyclo-octyl-1,3-diacetate.

[a] Based on b and the results for the corresponding tosylates.

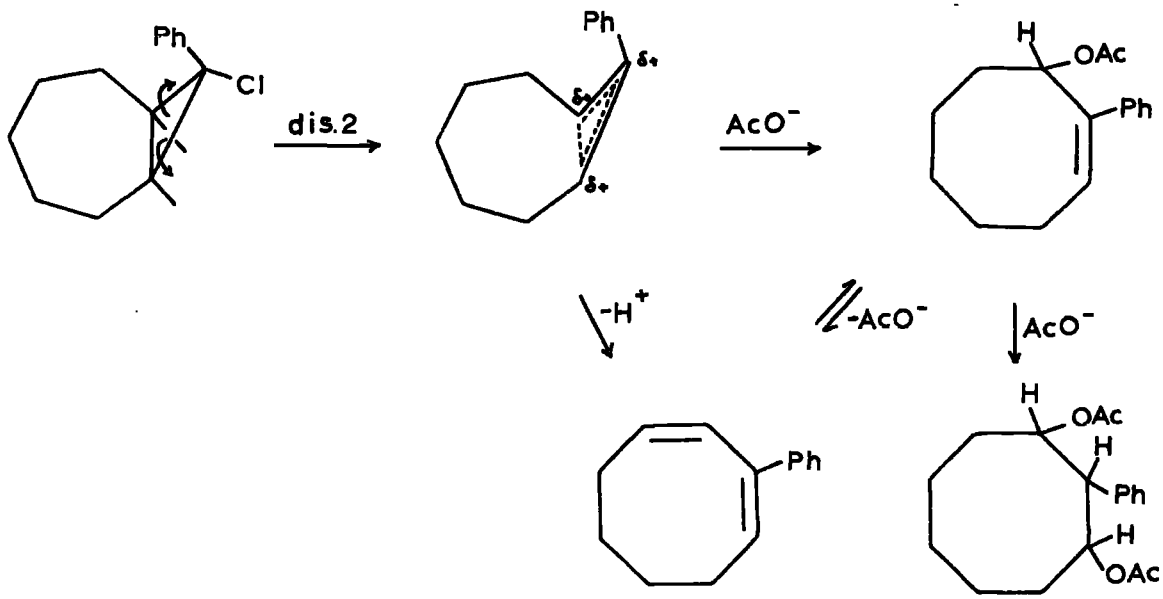
[b] This is an estimated upper limit $k = 1{\cdot}0 \times 10^{-10}$, based on the limit of detectable chloride ion, no solvolysis at 175°C.

The [5.1.0] hydro-chloro isomer has a large rate enhancement over the corresponding [3.1.0] and [4.1.0] compounds, neither of which would solvolyse at 175°. For the tosylate, Schöllkopf[35] proposed a 'semi open' intermediate cation reacting from initial dis.(2) rotation in the 'wrong' direction and the results for the chlorides seem to confirm this hypothesis. The large negative entropy (-14·82 e.u.) is consistent with a highly solvated T.S. in which the positive charge is delocalised around the cyclopropyl ring. The strain involved in proceeding to the T.S. does not appear to be very great as the activation energy (28·10 K.cals.) compares favourably with the <u>endo</u> isomer which ring opens in the 'correct' direction.

The products, <u>cis</u>-2-cyclo-octen-1-yl acetate (35%) and <u>cis</u>-cyclo-octyl-1,3-diacetate (65%) are similar to those isolated by Schöllkopf from acetolysis of the tosylates.



For the phenyl compound, the rate enhancements are of a different order of magnitude, and the products are different than in the bicyclo-[3.1.0] and [4.1.0] cases. There is a relatively small rate enhancement over exo-7-chlorobicyclo[5.1.0]octane which suggests that solvolysis might take place by a partially ring opened intermediate, similar to that already outlined. This is strengthened by the large negative entropies for both the parent and phenyl substituted [5.1.0] compounds.



The results may be summarised as follows. For the endo-bicyclo-[n.1.0]alkyl chlorides solvolysis proceeds by a concerted dis.(2) mechanism and replacement of hydrogen by phenyl gives a relatively small rate enhancement and does not alter the mechanism. For the exo series, when the favoured routes involving a partially ring opened carbonium ion is energetically very unfavourable (n = 3,4), introduction of a

phenyl group alters the mechanism to a dis.(O) process.

However, when n = 5 the parent exo compound solvolysis by a 'semi open' carbonium ion faster than the endo isomer and substitution of phenyl for hydrogen has no effect on the mechanism.

III.6. The Solvolysis and Products of Hydro-chlorobicyclo[n.1.0]-alkanes (n = 3,4,5)

It is of interest to examine the exo and endo isomers of this group, since in the case of the exo compounds a dis.(2) concerted process produces a trans double bond in the ring opened product, a system which will be severely strained when n is small. An increase in rate would be expected as n increases.

Two of these compounds have been studied previously. Cristol and co-workers[43] separated the endo and exo-bicyclo[4.1.0]heptanes by g.l.c., and acetolysed them at one temperature only. They obtained $K^{endo}_{125^0} = 1{\cdot}4 \times 10^{-6}$ sec.$^{-1}$, $K^{exo}_{125^0} < 8 \times 10^{-9}$ sec.$^{-1}$

Endo and exo-6-chlorobicyclo[3.1.0]hexane have not been separated completely by g.l.c. The exo isomer was obtained by distillation of a mixture with quinoline. The thermal rearrangement only of these compounds has been studied.[44]

For the endo group, where a dis.(2) mode is the energetically favoured route, a study of the variation of rate with ring size is useful. Comparison of the data for the endo chlorides with von Schleyers' and Schöllkopf's results for the tosylates, clearly shows

that the differences in rate down the series are almost solely due to activation energy differences. There is an activation energy difference of almost 10 K.cals. between the [3.1.0] and [5.1.0] compounds. As the strain release decreases, so does the rate. Since chloride is a poorer leaving group than tosylate, this means that the T.S. is much nearer the products and hence the rate enhancements for the chlorides are much larger than for the tosylates (Fig. III.6).

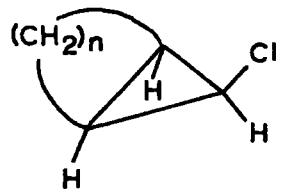
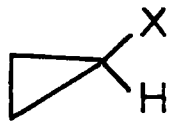
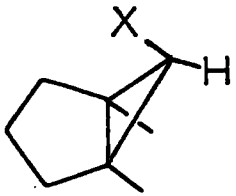
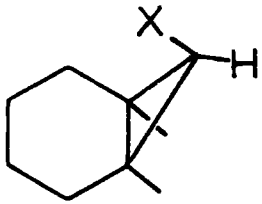
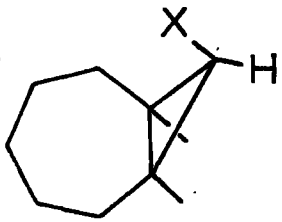


Table III.8. Acetolysis of endo-chlorobicyclo[n.1.0]alkanes

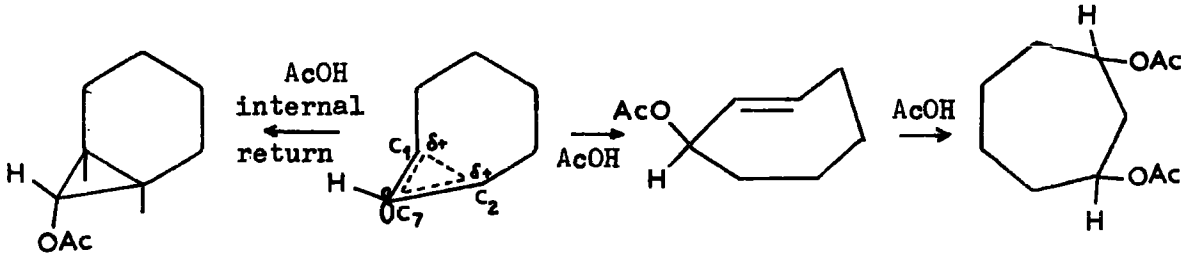
n	Temp.(°C)	K(sec.$^{-1}$)	E_A(K.cals.)	$\Delta S^{\ddagger}$ (e.u.)
3	50	$1.53 \times 10^{-5} \pm 0.01$	25.96 ± 0.06	-2.43 ± 0.19
	75	$2.80 \times 10^{-4} \pm 0.01$		
4	125	$1.145 \times 10^{-6} \pm 0.002$	34.24 ± 0.03	-2.33 ± 0.07
	150	$1.479 \times 10^{-5} \pm 0.001$		
5	150	$6.41 \times 10^{-7} \pm 0.05$	34.76 ± 0.13	-7.52 ± 0.30
	175	$6.26 \times 10^{-6} \pm 0.2$		

For the corresponding exo-chloro isomers (Fig III.7) there is no detectable reaction for n = 3 or 4, since the dis.(2) mode is energetically very unfavourable. However, exo-7-tosylbicyclo[4.1.0]-heptane (n = 4) solvolyses slowly, since tosyl, with better leaving

Fig. III.6. Relative rates and acetolysis products for endo-bicyclo[n.1.0]alkyl chlorides and tosylates

Compound	X = tosyl K.rel. 100°	X = Cl K.rel. 150°	X = tosyl products	X = Cl products
	1	1	allyl acetate	-
	2.5×10^4	10^8	cis-2-cyclohexen-1-yl acetate	cis-2-cyclohexen-1-yl acetate
	62	2.4×10^4	cis-2-cyclohepten-1-yl acetate	cis-2-cyclohepten-1-yl acetate
	3.1	1.1×10^3	cis-2-cyclo-octen-1-yl acetate	cyclo-octa-1,3-diene, 50% cis-2-cyclo-octen-1-yl acetate, 10%

group ability, enables the system to proceed to the 'semi-open' intermediate cation much earlier in the reaction path, than for the chloride, i.e. the charge density increases at C_1 and C_2 and decreases at C_7, as the reaction proceeds to the allylic system.

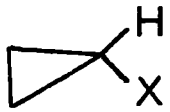
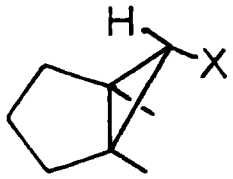
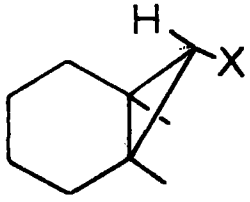
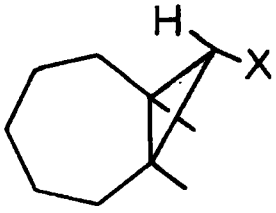


I II not isolated III IV

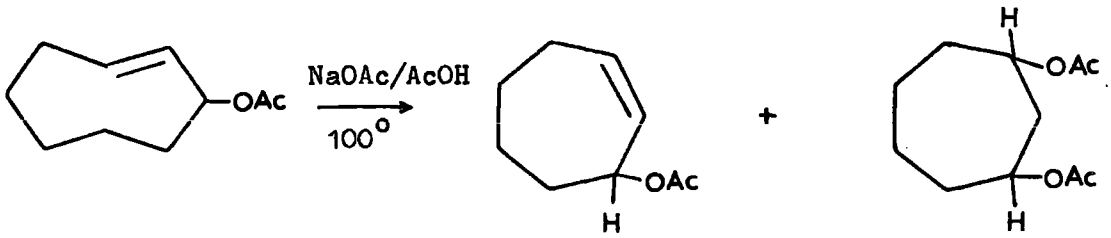
The formation of the products, cis-cycloheptyl-1,3-diacetate IV and exo-7-tosylbicyclo[4.1.0]heptane (II) have been explained[35] in terms of the 'semi open' cation (I), which adds acetic acid at C_1 to give the highly strained trans-2-cyclohepten-1-yl acetate (III) which adds further acetic acid to give the diacetate. Schöllkopf has proposed that the p-orbital on C_7 has some s-character, making it more accessible on the exo side, thus accounting for the high exo stereoselectivity. Both empirical and non-empirical calculations on the cyclopropyl system itself, show that there is some justification for this.

For the exo-bicyclo[5.1.0]tosylate, only monocyclic products are obtained, since presumably as n increases, the T.S. is closer to the allyl than the cyclopropyl system. Whitham[73] has shown that (VI) and

Fig. III.7. Relative rates and acetolysis products for exo-bicyclo[n.1.0]alkyl chlorides and tosylates

	X = Tosyl $K_{rel.}$ (100°)	X = Cl $K_{rel.}$ (150°)	X = Tosyl products	X = Cl products
	1	1	allyl acetate	-
	0·01	1	-	-
	1·7	1	exo-7-norcaranyl acetate cis-cycloheptyl-1,3-diacetate (1:1)	-
	$2·5 \times 10^3$	10^5	trans and cis-2-cyclo-octen-1-yl acetate cis-cyclo-octyl-1,3-diacetate	cis-cyclo-octen-1-yl acetate cis-cyclo-octyl-1,3-diacetate

(VII) may be obtained by treating trans-3-cyclo-octen-1-yl acetate (V) with acetic acid/sodium acetate. This demonstrates that the trans



V VI VII

cis-3-cyclo-octen-1-yl acetate

cis-cyclo-octyl-1,3-diacetate

compound is the precursor of the two isolated products.

The same products are isolated from solvolysis of the exo-chloride, cis-3-cyclo-octen-1-yl acetate (35%) and cis-cyclo-octyl-1,3-diacetate (65%).

III.7. The Solvolysis and Products of Gem-dichlorobicyclo[n.1.0]-alkanes (n = 3,4)

6,6-Dichlorobicyclo[3.1.0]hexane and 7,7-dichlorobicyclo[4.1.0]-heptane were solvolysed to compare the effect of a chlorine substituent on the rate of solvolysis, with those of phenyl and hydrogen substituents, already mentioned.

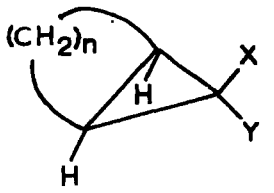


Table III.9. Acetolysis of gem-dichlorobicyclo[n.1.0]alkanes

n	X	Y	$K_{rel.}$ (100°)	E_A (K.cal.)	$\Delta S^{\ddagger}$ (e.u.)
3	Cl	H	1	25·96 ± 0·06	-2·43 ± 0·19
3	H	Cl	$< 2{\cdot}7 \times 10^{-11}$	-	-
3	Cl	Cl*	$2{\cdot}7 \times 10^{-3}$	27·92 ± 0·16	-9·13 ± 0·41
3	Ph	Cl	$3{\cdot}3 \times 10^{-3}$	29·74 ± 0·08	-3·87 ± 0·20
			$K_{rel.}$ (150°)		
4	Cl	H	1	34·24 ± 0·03	-2·33 ± 0·07
4	H	Cl	$6{\cdot}7 \times 10^{-5}$	-	-
4	Cl	Cl**	$2{\cdot}8 \times 10^{-1}$	29·72 ± 0·58	-15·00 ± 1·33
4	Cl	Ph	3·1	30·20 ± 0·07	-5·27 ± 0·17
4	Ph	Cl	$2{\cdot}7 \times 10^{2}$	31·68 ± 0·13	1·00 ± 0·35

* At 125° $K = 1{\cdot}03 \times 10^{-4} \pm 0{\cdot}01$

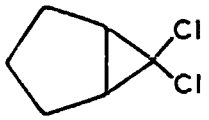
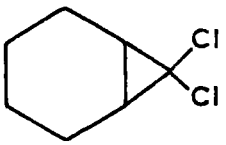
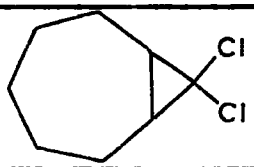
100° $K = 9{\cdot}69 \times 10^{-5} \pm 0{\cdot}10$

** At 175° $K = 3{\cdot}93 \times 10^{-5} \pm 0{\cdot}13$

150° $K = 5{\cdot}44 \times 10^{-6} \pm 0{\cdot}10$

Bergman[74] has studied the thermal and solvolytic rearrangements of the dichlorobicyclo[n.1.0] systems where n = 3, 4 and 5. These results are summarised in Table IV.10.

Table IV.10.

Compound	Heat	Solvolysis 0·1N $AgNO_3$/EtOH
	100% in < 3 hr. at 153-188°. No reaction in 2 hr. at 75° in T.H.F.	100% in several hours at 25°
	Stable for 8 hr. at 196-199°	No reaction for several weeks at 25°
	Stable for 5 hr. at 221-225°	No reaction in several weeks at 25°

Thermal rearrangement of the [3.1.0] compound gave 2,3-dichlorocyclohexene, whilst acetolysis in AcOH/Ac_2O (125°, 15 hrs.) gave 2-chloro-3-cyclohexen-1-yl acetate (47%) and rearranged starting material (19%). It was concluded that the ease of rearrangement of the cyclopentene adduct in contrast to those of cyclohexene and -heptene, was due to additional strain in the former system.

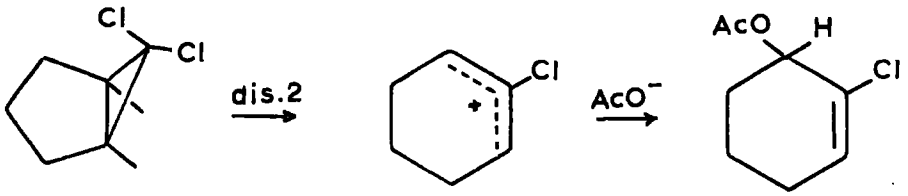
No rearrangement was observed on treating 1,1-dichloro-2-phenyl-, and 2,2-diphenyl-cyclopropanes with 0·1N silver nitrate at room

temperature, and it was assumed that the stability of the intermediate carbonium ion was the important factor.

From Table III.9. it can be seen that the [3.1.0] dichloro compound solvolyses much more slowly than the parent endo-chloro compound, due to the higher activation energy for the former, and faster, by a factor of 10^8 than the exo isomer. It can be inferred from this that initial removal of the exo chlorine by a dis.(2) mode would be energetically very unfavourable. Two paths are possible for solvolysis. Either a concerted dis.(2) ring opening can take place with loss of the endo-chlorine, or the exo-chlorine could be removed in a non-concerted dis.(0) process. In either case, a chlorine atom at C_1, at which there is considerable positive charge development during reaction, should slow down the reaction appreciably.

The fact that the dichloro compound and the exo phenyl-chloro isomer (which goes by a dis.(0) mode) solvolyse at approximately the same rate at 100° and that there is a large rate decrease ($\sim 10^{-3}$) between the endo parent isomer and the dichloro compound, points to a dis.(2) mode of ring opening for the gem dichloro[3.1.0] compound.

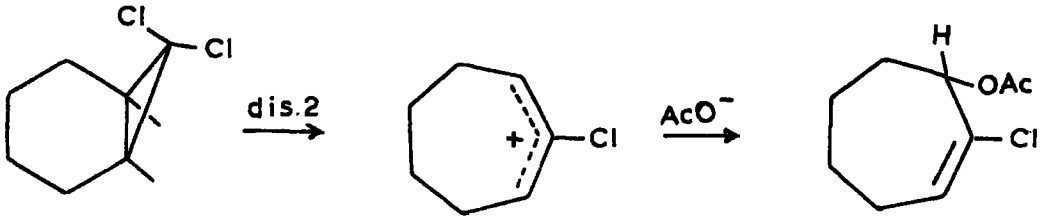
The products are consistent with those observed by Skell and Sandler,[40] who solvolysed the bromo-chloro compounds. These workers also found preferential removal of the endo halogen atom and this also suggests a dis.(2) mode.



2-chloro-3-cyclohexen-1-yl acetate

In comparison, the [4.1.0] compound solvolysed only slowly at 175°. At this temperature the chlorine atom in the vinylic product solvolysed slowly as the product formed. Hence this compound was studied by an initial rates method, where all measurements were taken in the first 15% of reaction, before a significant proportion of solvolysable product had accumulated.

Inspection of Table III.9. again reveals a rate decrease over the hydro and phenyl endo-chloro compounds both of which solvolyse by a dis.(2) mode, and a 10^4 rate enhancement over the exo-hydro isomer. Furthermore, the exo-phenyl compound proceeding via a dis.(0) mechanism has a 300 x rate enhancement. This, together with the similarity of the products and the fact that no returned acetate or diacetate is formed is good evidence for the operation of a dis.(2) mode with preferential loss of the endo chlorine atom.



It also appears that the solvolysis of the dichloro[3.1.0] and [4.1.0] compounds is accompanied by a large negative entropy term, compared with the parent hydro-chloro compounds.

CHAPTER IV

Section I. Experimental for Chapter III

IV.1. Instrumentation.

Infra-red (I.R.) spectra were recorded, using a Grubb-Parsons Spectromaster spectrometer, as contact films (liquids or low melting solids) or as KBr discs (solids). U.V. spectra were recorded using a Unicam S.P.800 spectrophotometer. Molecular weights and precise mass measurements were determined mass spectrometrically using A.E.I. M.S.9 spectrometers. 100 and 220 MHz ^{1}H n.m.r. spectra were recorded using Varian H.A.100 and H.R.220 (I.C.I., Runcorn) spectrometers. Variable temperature ^{1}H n.m.r. spectra were run on a Perkin-Elmer R.10 spectrometer operating at 60 MHz. Analytical scale g.l.c. was performed on a Griffin and George D6 Gas Density Balance Chromatograph (G.D.B.) (nitrogen carrier gas). The response of this machine is proportional to the difference in molecular weight between the compound and the carrier gas.

The column packing was 30% silicone elastomer on celite (Column "O"). Peak areas were measured directly using a Honeywell Integrator.

Preparative scale g.l.c. was carried out on an Aerograph "Autoprep" A.700 instrument (hydrogen carrier gas) employing 20' x 3/8" columns (i) 30% silicone elastomer on celite (Column "O"), (ii) 30% di-n-decylphthalate on celite (Column "A").

Melting points and boiling points are uncorrected.

IV.2. Purification of Reagents.

Commercial cyclopentene, -hexene and -heptene were dried over molecular sieve and distilled before use. Benzal chloride was distilled through a 20 cm. Vigreux column, at 100°/20 mm. Chloroform and methylene chloride were dried over molecular sieve and distilled immediately prior to use.

IV.3. Preparation of Potassium tert.-Butoxide.

This was prepared by a modification of the method of Hodgkins et al.[71] A 4 l. flange head flask fitted with mechanical stirrer and condenser, was charged under dry nitrogen with dry tert.butanol (2 l., distilled from sodium). 100 g. (2·56 mole) of potassium metal on small pieces was added while maintaining a gentle reflux. Finally the mixture was refluxed for 3 hrs. with rapid stirring to ensure complete reaction of the potassium. The excess tert.-butanol was removed by distillation under reduced pressure and the remaining butoxide was dried at 140°, in vacuo, in a drying pistol. The dry solid was ground to a fine white powder and stored under nitrogen.

This was transferred to the weighed reaction vessel via a glass tube, under nitrogen and the quantities of the other reactants were adjusted to this approximate weight.

IV.4. Preparation of Substituted Benzal Chlorides.

(1) p-Chlorobenzal Chloride.[75] Dry chlorine was passed slowly into p-chlorotoluene (53 g., 0·42 mole) in a 500 ml. flask, illuminated by a medium pressure (100 w.) u.v. lamp. The reaction temperature was gradually raised to maintain a steady reflux throughout. The flask was periodically weighed until a weight increase equivalent to the addition of 0·84 mole of chlorine was observed. Distillation through a 20 cm. column packed with glass helices, under reduced pressure yielded p-chlorobenzal chloride (75 g., 92%) as a colourless liquid. B.pt. 105-107°/25 mm. The mass spectrum showed a parent ion at M194 and a peak corresponding to P^+-Cl at M159 (base peak).

(2) p-Fluorobenzal Chloride. Procedure as in (1). 50 g. (0·45 mole) of p-fluorotoluene yielded after distillation, p-fluorobenzal chloride (67 g., 83%), a colourless liquid, B.pt. 83-85°/50 mm. Analytical g.l.c. (Col. '0' 100°) showed ~95% purity. The mass spectrum showed a parent ion at M178 and peaks corresponding to P^+-F at M159, and P^+-Cl (base peak) at M143.

(3) p-Methylbenzal Chloride. This was prepared after the method of Moss.[66] An 85 g. (0·4 mole) sample of phosphorus pentachloride was placed in a 2-neck 500 ml. flask fitted with a dropping funnel and stirrer. The temperature was maintained at 25° by a water bath and the flask was shielded to exclude direct light.

p-Tolualdehyde (50 g., 0·4 mole) was added dropwise, with stirring over 1 hr. and stirring was continued for a further 6 hr. The reaction mixture was then poured over crushed ice (300 g.), thoroughly agitated and the resulting solid rapidly filtered, washed with water and taken up in ether (100 ml.). The ethereal solution was washed with $NaHCO_3$ solution (100 ml.) and water (100 ml.) and dried (Na_2SO_4). Removal of ether under reduced pressure, and recrystallisation of the resulting solid from methanol, gave p-methylbenzal chloride (52 g., 72%) as white crystals, M.pt. 49-50° (Lit.[66] 50-51°). This compound was stored under dry N_2, in the dark. The mass spectrum showed a parent peak M174, and peaks corresponding to P^+-Cl at M139 (base peak) and P^+-2Cl at M104(56%).

(4) <u>p-Nitrobenzal Chloride</u>.[76] p-Nitrobenzaldehyde (30 g., 0·2 mole) (prepared by chromic acid oxidation of p-nitrotoluene[77]) was added slowly to PCl_5 (60 g., 0·3 mole) contained in a 250 ml. flask. The mixture was warmed on a water bath for ½ hr., allowed to cool to room temperature and poured onto ice (100 g.). Filtration of the solidified product, followed by recrystallisation from ethanol, yielded p-nitrobenzal chloride (14 g., 35%) as pale yellow/green crystals, M.pt. 46° (Lit.[76] 46°). The mass spectrum showed a parent ion at M205 and peaks corresponding to P^+-Cl at M170 (base peak) and P^+-2Cl at M135 (41%).

IV.5. Synthesis and Separation of Para-substituted 7-Chloro-7-phenylbicyclo[4.1.0]heptanes

(1) 7-Chloro-7-phenylbicyclo[4.1.0]heptane. Benzal chloride (9 g., 0·055 mole) was added dropwise over 1 hr. to a stirred suspension of potassium tert.-butoxide (t.-BuOK) (11·2 g., 0·10 mole) in dry cyclohexene (33 g., 0·4 mole), contained in a 250 ml. 3-neck flask which had previously been purged with dry nitrogen. Initially a vigorous reaction took place and a gentle reflux was maintained for a further 6 hrs. The black mixture was poured over crushed ice (100 g.), extracted with ether (3 x 20 ml.) and dried (Na_2SO_4). Removal of the ether and distillation through a 10 cm. Vigreux column in vacuo, gave 7-chloro-7-phenylbicyclo[4.1.0]heptane, (4·8 g., 41%), a colourless viscous liquid. B.pt. 91-96°/0·05 mm. (Lit.[71] 170-173°/33 mm.). Analytical g.l.c. (Col. 'O', 125°) indicated a two component mixture, ratio 1:1·5 (exo:endo).

Separation of Isomers (see also Section III). (a) endo 1·0 g. of the isomeric mixture was passed down a 7' x 3/4" column packed with alumina (100-240 mesh, alkaline, Brockmann Activity 1), eluting with 40-60° petroleum ether. The exo isomer partly rearranged on this packing. Recovery of pure isomer ~20%. Sublimation (60°/10^{-2} mm.) gave endo-7-chloro-7-phenylbicyclo[4.1.0]heptane as fine white needles, M.pt. 36·5°. (Found: C, 75·5; H, 6·7; Cl, 17·45; $C_{13}H_{15}Cl$ requires C, 75·6; H, 7·24; Cl, 17·0%).

The mass spectrum showed a parent ion at M206 (32%) and peaks corresponding to P^+-Cl at M171 (25%) and Ph-CCl=CH_2 at M138 (base peak). Metastable peaks for the transitions $157^+ \rightarrow 143^+$, $143^+ \rightarrow 129^+$, $129^+ \rightarrow 115^+$ were visible due to successive loss of methylene groups.

I.R. spectrum No.11. N.M.R. spectrum No.1. The u.v. spectrum showed a medium intensity band at 223 mμ (ϵ_{max} = 7150, cyclohexane).

(b) exo. Pure samples of this isomer were obtained by passing 1·0 g. of the mixture down a 7' x 3/4" column packed with silica gel (50-100 mesh, Brockmann Activity 2), eluting with 40-60° petroleum ether. Recovery of pure isomer ~15%. Sublimation (40°/10^{-2} mm.) yielded exo-7-chloro-7-phenylbicyclo[4.1.0]heptane as colourless crystals, M.pt. 54°. (Found: C, 75·7; H, 7·1; Cl, 16·8%).

The mass spectrum was essentially the same as that of the endo isomer.

I.R. spectrum No.12. N.M.R. spectrum No.2. The u.v. spectrum showed a medium intensity band at 221 mμ (ϵ_{max} = 7550, cyclohexane).

(2) 7-Chloro-7-p-methyl-phenylbicyclo[4.1.0]heptane. Procedure as outlined in (1). 4·3 g. (0·025 mole) of p-methylbenzal chloride dissolved in 15 ml. of cyclohexene was added to 11·2 g. (0·1 mole) of t-BuOK in 20 ml. of cyclohexene (total 33·0 g., 0·4 mole). Distillation through a 10 cm. Vigreux column in vacuo, gave a colourless liquid (2·9 g., 33%). B.pt. 96-98°/0·05 mm. Analytical g.l.c. (Col.'O' 125°) indicated a two component mixture, ratio 1:2. (exo:endo).

Separation of Isomers (a) endo. The major isomer was separated by dry column chromatography using a 30" x $1\frac{1}{2}$" column dry packed with alumina (100-240 mesh, activity 2). Elution of a 1·0 g. sample using 40-60° petroleum ether gave ~15% recovery. Recrystallisation from methanol gave endo-7-chloro-7-p-methyl-phenylbicyclo[4.1.0]heptane, as white needles, M.pt. 37-38°. (Found: C, 75·9; H, 7·60; Cl, 16·4; $C_{14}H_{17}Cl$ requires C, 76·4; H, 7·6; Cl, 16·0%). The mass spectrum showed a parent ion at M220 (38%) and peaks corresponding to P^+-HCl at M184 (base peak) and P^+-Me at M205 (10%). Metastable peaks for the transitions $169^+ \rightarrow 152^+$, $152^+ \rightarrow 139^+$ were visible. I.R. spectra No.13. N.M.R. spectrum No.9.

(b) exo. This isomer partially decomposed even on column packings of activity 3, and consequently was not obtained in isomerically pure form.

(3) 7-Chloro-7-p-chloro-phenylbicyclo[4.1.0]heptane. Procedure as outlined in (1). p-Chlorobenzal chloride, (5·0 g., 0·025 mole) was added dropwise to a stirred suspension of t-BuOK (11·2 g., 0·1 mole) in cyclohexene (33·0 g., 0·4 mole) and refluxed for 8 hrs. Distillation through a 10 cm. Vigreux column, in vacuo, gave a colourless liquid (2·9 g., 27%), B.pt. 105-107°/0·05 mm. Analytical g.l.c. (Col.'O', 140°) indicated a two component mixture, ratio 5:1 (exo:endo).

Separation of Isomers - (a) endo. This was impossible to separate pure from the major isomer because of the high adverse isomer ratio.

(b) exo. 1·0 g. of the distilled mixture was passed down a 30" x 3/4" dry packed alumina column (100-240 mesh, activity 2). Elution with pentane gave 25% recovery of pure material. Sublimation (80°, 10^{-2} mm.) gave exo-7-chloro-7-p-chloro-phenylbicyclo[4.1.0]heptane, as white crystals, M.pt. 70°. (Found: C, 64·8; H, 5·55; Cl, 29·6; $C_{13}H_{14}Cl_2$ requires C, 65·0; H, 5·80; Cl, 29·2%).

The mass spectrum showed a parent ion at M240 (11%) and peaks corresponding to P^+-Cl at M205 (20%) and P^+-2Cl at M170 (base peak). I.R. spectrum No.14. N.M.R. spectrum No.3.

(4) 7-Chloro-7-p-fluoro-phenylbicyclo[4.1.0]heptane. Procedure as outlined in (1). p-Fluorobenzal chloride (4·5 g., 0·025 mole) was added to t-BuOK (11·2 g., 0·1 mole) in cyclohexene (33·0 g., 0·4 mole) and refluxed for 6 hrs. Distillation through a 10 cm. Vigreux column in vacuo gave a pale yellow liquid (1·2 g., 19%), B.pt. 89-90°/ 0·05 mm. Analytical g.l.c. (Col. '0', 140°) indicated a two component mixture ratio 1:1·5 (exo:endo).

Separation of Isomers (a) endo. This was separated on a 7' x 3/8" column packed with alumina (100-240 mesh, activity 2). 1·0 g. eluted with pentane gave 20% recovery. Sublimation, (40°/10^{-2} mm.) gave endo-7-chloro-7-p-fluoro-phenylbicyclo[4.1.0]heptane as white needles,

M.pt. 38° (Found: C, 69·6; H, 5·90; Cl, 15·83; F, 8·66; $C_{13}H_{14}ClF$ requires C, 69·7; H, 6·26; Cl, 15·60; F, 8·50%). The mass spectrum showed a parent ion at M224 (26%) and peaks corresponding to P^+-HCl at M189 (68%). Base peak p-$FPhCH_2^+$ at M109. I.R. spectrum No.15. N.M.R. spectrum No.10.

(b) exo. The same column and packing as described above. A loading of 0·75 g. gave ~15% recovery. Sublimation (50°, 10^{-2} mm.) gave exo-7-chloro-7-p-fluoro-phenylbicyclo[4.1.0]heptane as white crystals, M.pt. 54-55°. (Found: C, 69·90; H, 5·61; Cl, 15·20; F, 8·35%). The mass spectrum was essentially the same as that of the endo isomer. I.R. spectrum No.16. N.M.R. spectrum No.11.

(5) Attempted Preparation of 7-Chloro-7-p-nitro-phenylbicyclo[4.1.0]-heptane

p-Nitrobenzal chloride (5·1 g., 0·025 mole) added to t.-BuOK (11·2 g., 0·1 mole) in cyclohexene (28·0 g., 0·4 mole) at -78°, yielded on work-up 1,2-dichloro-1,2-di-(p-nitrophenyl)-ethylene (0·3 g., 3%), yellow crystals, M.pt. 197-198°. The mass spectrum showed a parent ion at M338 and peaks corresponding to P^+-Cl at M303, P^+-2Cl at M268, and P^+-NO_2Cl_2 at M222.

Starting material (40%) and a considerable amount of tar were also recovered.

IV.6. Synthesis and Separation of para-substituted 6-Chloro-6-phenyl-bicyclo[3.1.0]hexanes

Only the exo isomer was isolated in each case. These reactions produced a large amount of side products of similar retention time, from which it was difficult to separate the desired compound.

(1) 6-Chloro-6-phenylbicyclo[3.1.0]hexane. Procedure as outlined in IV.5(1). Benzal chloride (4·7 g., 0·03 mole) was added to t.-BuOK (11·2 g., 0·1 mole) in cyclopentene (27·2 g., 0·4 mole) and refluxed for 6 hrs. Distillation gave a yellow oil as crude product. This was passed down a 30" x ½" dry alumina column (activity 2) eluting with 40-60° petroleum ether. Distillation in vacuo through a 15 cm. column packed with glass helices, gave exo-6-chloro-6-phenylbicyclo[3.1.0]hexane, as a colourless liquid (1·7 g., 21%), B.pt. $69°/10^{-2}$ mm. Analytical g.l.c. (Col. '0' 100°) showed one component only. (Found: C, 75·08; H, 6·1; Cl, 17·90; $C_{12}H_{13}Cl$ requires C, 75·0; H, 6·80; Cl, 18·20%).

The mass spectrum showed a parent at M192 (32%) and peaks corresponding to P^+-Cl at M157 (27%) and P^+-C_6H_5 at M115 (base peak). I.R. spectrum No.7. N.M.R. spectrum No.12.

(2) 6-Chloro-6-p-methyl-phenylbicyclo[3.1.0]hexane. Procedure as outlined IV.5(1). p-Methyl benzal chloride (4·3 g., 0·025 mole) was added to t.-BuOK (11·2 g., 0·1 mole) in cyclopentene (27·2 g., 0·4 mole) and refluxed for 2 hrs., producing a black tar.

Distillation ($73-74^{\circ}/10^{-2}$ mm.) gave a yellow oil, which was purified by chromatography as outlined above giving a colourless liquid (1·2 g.). This was allowed to stand in a refrigerator for several days at -10°. The resulting crystals were cold filtered and recrystallised from methanol to give white needles of exo-6-chloro-6-p-methyl-phenylbicyclo-[3.1.0]hexane, M.pt. $36-37^{\circ}$. (Found: C, 75·4; H, 7·0; Cl, 16·8. $C_{13}H_{15}Cl$ requires C, 75·7; H, 7·3; Cl, 17·0%). Analytical g.l.c. (Col. '0' 100°) showed one component. The mass spectrum showed a parent ion at M206 (31%) and peaks corresponding to P^{+}-Me at M191 (50%), P^{+}-HCl at M170 (base peak). Metastable peaks due to the transitions $155^{+} \longrightarrow 141^{+}$, and $141^{+} \longrightarrow 127^{+}$ were also visible. I.R. spectrum No.8. N.M.R. spectrum No.14.

(3) 6-Chloro-6-p-chloro-phenylbicyclo[3.1.0]hexane. Procedure as outlined in IV.5(1). p-Chlorobenzal chloride (5·0 g., 0·025 mole) was added to t.-BuOK (11·2 g., 0·1 mole) in cyclopentene (27·2 g., 0·4 mole) and refluxed for 6 hrs. Distillation ($75-80^{\circ}/10^{-2}$ mm.) gave a yellow oil (1·4 g.) which was purified by the same procedure outlined above. Sublimation (45°, 10^{-2} mm.) gave white crystals of exo-6-chloro-6-p-chloro-phenylbicyclo[3.1.0]hexane, M.pt. 41°. (Found: C, 63·8; H, 5·29; Cl, 30·8. $C_{12}H_{12}Cl_2$ requires C, 63·7; H, 5·3; Cl, 31·0%). Analytical g.l.c. (Col. '0' 100°) showed one component only. The mass spectrum showed a parent ion at M226 (72%)

and peaks corresponding to P^+-HCl at M191 (72%) and P^+-$PhCH_2Cl$ at M125 (base peak). A metastable peak due to the transition $153^+ \rightarrow 139^+$ was visible. I.R. spectrum No.9. N.M.R. spectrum No.13.

(4) 6-Chloro-6-p-fluoro-phenylbicyclo[3.1.0]hexane. Procedure as outlined in IV.5(1). p-Fluorobenzal chloride (4·5 g., 0·025 mole) was added to t.-BuOK (11·2 g., 0·1 mole) in cyclopentene (27·2 g., 0·4 mole) and refluxed for 5 hrs. Distillation and purification as in (2) and (3) failed to produce crystalline material. Physical and kinetic measurements were therefore made on the pale yellow oil. B.pt. 80-81°/0·05 mm. The mass spectrum showed a parent ion at M210 (28%) and peaks corresponding to P^+-HCl at M174 (base peak) and $P\text{-}FPhCH_2^+$ at M109 (67%). I.R. spectrum No.10.

IV.7. Synthesis and Separation of 8-Chloro-8-phenylbicyclo[5.1.0]octane.

Procedure as outlined in IV.5(1). Benzal chloride (4·5 g., 0·027 mole) was added to t.-BuOK (11·2 g., 0·1 mole) in cycloheptene (38·4 g., 0·4 mole) and refluxed for 2 hrs. Distillation (110-112°, 0·05 mm.) gave a colourless oil (1·5 g., 24% yield). Preparative scale g.l.c. showed a two component mixture, ratio 1:2 (exo:endo). Separation of Isomers - endo. This was separated on a 7' x 3/4" alumina column (100-240 mesh, activity 1) eluting with a mixture of 80% pentane and 20% CCl_4. Recovery from 1·0 gm. of mixture ~20%. Sublimation

(45°, 10^{-2} mm.) gave 8-chloro-8-phenylbicyclo[5.1.0]octane as white crystals, M.pt. $39-40^{\circ}$. (Found: C, 76·3; H, 7·3; Cl, 15·8; $C_{14}H_{17}Cl$ requires C, 76·4; H, 7·7; Cl, 15·9%).

The mass spectrum showed a parent ion at M220 (15%) and peaks corresponding to P^{+}-HCl at M184 (21%), base peak at M138. Successive loss of ($-CH_2$) then takes place. I.R. spectrum No.18. N.M.R. spectrum No.15.

IV.8. Synthesis and Separation of endo- and exo-chlorobicyclo[n.1.0]-alkanes

The preparations of these compounds are essentially the same, hence a full experimental account is given for the bicyclo[4.1.0] compound only.

(1) 7-Chlorobicyclo[4.1.0]heptane. This was prepared by the method of Closs and Closs.[79] n-Butyl lithium (40 ml. of 2·5 molar solution, 0·1 mole) was added slowly over 60-90 mins. to a rapidly stirred mixture of cyclohexene (33·0 g., 0·4 mole) and methylene chloride (17 g., 0·2 mole) contained in a 1 l. 3 neck flask which had previously been purged with nitrogen. The flask was surrounded by a cooling bath maintained at -35 to -40°. The mixture was then stirred at 0° for 3 hrs. After warming to room temperature, water (100 ml.) was added and the mixture extracted with ether (3 x 30 ml.) and dried (Na_2SO_4). Distillation under reduced pressure through a 20 cm. Vigreux

column gave 7-chlorobicyclo[4.1.0]heptane (3·4 g., 27%), B.pt. 94-97°/ 70 mm. (Found: C, 64·6; H, 8·0; Cl, 27·3; $C_7H_{11}Cl$ requires C, 64·6; H, 8·5; Cl, 26·9%). Analytical g.l.c. (Col. 'O' 100°) indicated a two component mixture, ratio 1:2 (exo:endo).

Separation of Isomers. Preparative scale g.l.c. (Col. 'A' 100°), 150 ml. min.$^{-1}$ of H_2. Retention times 4½ and 5 hrs. for exo and endo isomers respectively. The mass spectrum was essentially the same for both isomers. A parent ion was observed at M130 (20%) and peaks corresponding to P^+-Cl at M95 (53%) and P^+-CH_2Cl at M81 (base peak).

I.R. spectra - endo No.3 N.M.R. spectra - endo No.18

" " exo No.4 " " exo No.19

(2) 6-Chlorobicyclo[3.1.0]hexane. Procedure as outlined in (1). n-Butyl-lithium (40 ml. of 2·5 molar solution, 0·1 mole) was added to cyclopentene (27·2 g., 0·4 mole) and methylene chloride (17 g., 0·2 mole) at -30°. Distillation under reduced pressure through a 20 cm. Vigreux column gave 6-chlorobicyclo[3.1.0]hexane (4·2 g., 18%), B.pt. 86-88°/ 70 mm. (Found: C, 61·6; H, 7·1; Cl, 29·9; C_6H_9Cl requires C, 62·0; H, 7·80; Cl, 30·2%). Analytical g.l.c. (Col. 'O' 80°) indicated a two component mixture, ratio 1:2 (exo:endo).

Separation of Isomers. Preparative scale g.l.c.(Col. 'A' 80°), 150 ml. min.$^{-1}$ H_2. Retention times 3½ and 4 hrs. for exo and endo isomers respectively. Mass spectrum - endo. A parent ion was observed

at M116 (6%) and peaks corresponding to P^+-HCl at M81 (base peak) and P^+-CH_2Cl at M67 (38%). exo. Parent ion at M116 (6%), P^+-Cl at M81 (18%) and P^+-C_4H_9 at M59 (base peak).

I.R. spectra - endo No.1 N.M.R. spectra - endo No.16

" " exo No.2 " " exo No.17

(3) 8-Chlorobicyclo[5.1.0]octane. Procedure as outlined in (1). n-Butyl-lithium (40 ml. of 2·5 ml. of 2·5 molar solution, 0·1 mole) was added to cycloheptene (38·4 g., 0·4 mole) and methylene chloride (17 g., 0·2 mole) at -20° over 2 hrs. Distillation under reduced pressure through a 20 cm. Vigreux column gave 8-chlorobicyclo[5.1.0]octane (2·9 g., 20·1%), B.pt. 105-108°/70 mm. (Found: C, 66·7; H, 6·2; Cl, 23·8; $C_8H_{13}Cl$ requires C, 66·7; H, 9·0; Cl, 24·3%). Analytical g.l.c. indicated a two component mixture ratio 1:3 (exo:endo). Separation of Isomers. Preparative scale g.l.c. (Col. '0' 110°), 150 ml. min.$^{-1}$ H_2. Retention times 6 hrs. and 6 3/4 hrs. for exo and endo isomers respectively. The mass spectrum was essentially the same for both isomers. A parent ion was observed at M144 (26%) and peaks corresponding to P^+-Cl at M109 (26%) and P^+-CH_2Cl at M95 (46%). Base peak at M67 ($C_5H_7^+$).

I.R. spectra - endo No. 5 N.M.R. spectra - endo No. 5

" " exo No. 6 " " exo Nos. 6 and 20

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IV.9. Synthesis of gem-dichlorobicyclo[n.1.0]alkanes.

(1) 7,7-Dichlorobicyclo[4.1.0]heptane. This compound was prepared by the method of Doering and Hoffmann.[64] Chloroform (10 g., 0·085 mole) was added dropwise over 2 hrs. to a stirred suspension of t.-BuOK (7 g., 0·063 mole) in cyclohexene (33 g., 0·4 mole), contained in a 250 cc. 3 neck flask which had previously been purged with nitrogen. The flask was surrounded by a cooling bath maintained at -15 to -20°. The mixture was stirred for a further ½ hr. and was then stored in a refrigerator overnight. Water (50 ml.) was added after warming to room temperature, and the mixture extracted with ether (50 ml.) and dried (Na_2SO_4). Distillation under reduced pressure through a 10 cm. column packed with glass helices gave 7,7-dichlorobicyclo[4.1.0]heptane (5·4 g., 39%), B.pt. 74-75°/10 mm. (lit.[64] 78-79°/15 mm.). The mass spectrum showed a parent ion at M164 (24%) and peaks corresponding to P^+-Cl at M129 (52%). Base peak at M80 ($C_6H_8^+$). I.R. spectrum No.20.

(2) 6,6-Dichlorobicyclo[3.1.0]hexane.[80] Cyclopentene (17·0 g., 0·025 mole), chloroform (29·5 g., 0·25 mole) and anhydrous caustic soda pellets (40 g., 1·0 mole) in 25 cc. of 'diglyme' were stirred for 16 hrs. at 25° in a 250 cc. flask. The mixture was then poured onto crushed ice (100 g.) and the organic layer separated and dried (Na_2SO_4). Distillation under reduced pressure over a 10 cm. column of glass helices gave 6,6-dichlorobicyclo[3.1.0]hexane (4·3 g., 11·5%),

B.pt. 68°/20 mm. (Lit.[80] 69°/20 mm.). The mass spectrum showed a parent ion at M150 (10%) and peaks corresponding to P^+-HCl at M114 (58%) and P^+-2HCl at M79 (base peak). I.R. spectrum No.19.

IV.10. Synthesis of endo-1,7-diphenyl-7-chlorobicyclo[4.1.0]heptane.

Benzal chloride (4·0 g., 0·025 mole) was added dropwise to a stirred mixture of t.-BuOK (11·2 g., 0·1 mole) in phenyl-cyclohexene (31·6 g., 0·2 mole), over 1 hr. at 100°. The mixture was stirred for 3 hrs. after the initial vigorous reaction. Water (50 ml.) was then added and the layers extracted with ether (50 ml.), and dried (Na_2SO_4). The crude product could not be distilled without considerable decomposition. 1·0 g. was passed down a 40" x 1½" dry alumina column (100-240 mesh, activity 2), eluting with pentane. The colourless oil obtained was allowed to stand in a refrigerator at -10° for 3 days. The crystals formed were cold filtered and recrystallised from methanol, giving endo-1,7-diphenyl-7-chlorobicyclo[4.1.0]heptane (0·9 g., 13%) as white crystals, M.pt. 61-62°. (Found: C, 81·1; H, 6·47; Cl, 13·1. $C_{19}H_{19}Cl$ requires C, 80·9; H, 6·7; Cl, 12·4%). Analytical g.l.c. (Col. '0' 130°) showed one peak only (endo isomer).

The mass spectrum showed a parent ion at M282 (~ 0·2%) and peaks corresponding to P^+-HCl at M246 (1%) and a base peak at M91 ($PhCH_2^+$). A metastable for the transition $129^+ \rightarrow 115^+$ was observed. The u.v. spectrum showed a broad bond at 222 mμ (ϵ_{max} = 10,400, cyclohexane). I.R. spectrum No.17. N.M.R. spectrum No.4.

IV.11. The Attempted Synthesis of Phenylcyclohepta-1,3-diene.

(1) Phenylcycloheptanol. Bromobenzene (90·5 g., 0·57 mole) in 200 ml. of dry ether was added dropwise, maintaining a gentle reflux, over 1 hr. to magnesium turnings (15·5 g., 0·65 mole) contained in a 1 l. 3 neck flask which had previously been purged with nitrogen. The mixture was stirred for a further 30 mins. and 56 g. (0·5 mole) of cycloheptanone in 200 cc. of dry benzene were added under reflux over 2 hrs. The mixture was cooled and poured onto crushed ice (750 g.), mixed with conc. H_2SO_4 (25 ml.). After shaking the organic layer was separated and washed with $NaHCO_3$ solution (100 ml.) and water (200 ml.). The benzene was removed on a rotary evaporator and the residue steam distilled to remove excess starting materials. The product was dissolved in ether (100 ml.) and dried (Na_2SO_4). Distillation in vacuo yielded phenylcycloheptanol, a white low melting solid (60 g., 63%), B.pt. 99-100°/10^{-1} mm. (lit.[81] 120-129°/0·8 mm.).

(2) Dehydration of Phenylcycloheptanol. Phenylcycloheptanol (30 g., 0·16 mole) and 2N sulphuric acid (50 ml.) were stirred under reflux for 5 hrs. The mixture was cooled, extracted with ether (50 ml.) and dried (Na_2SO_4). Distillation in vacuo gave phenylcycloheptene, a colourless oil (17 g., 67%), B.pt. 93-94°/1·0 mm. (Lit.[82] 74·5-76·5°/0·3 mm.)

(3) Reaction of Phenylcycloheptene with N-bromo-succinimide. Phenylcycloheptene (14 g., 0·09 mole) and NBS (9 g., 0·05 mole) in 40 ml. dry CCl_4 were placed in a 100 ml. 2 neck flask which had previously been purged with nitrogen. The flask was illuminated by a 100 w. clear bulb. 1 mg. of benzoyl peroxide was added and the flask warmed gently, until a slow evolution of HBr was obtained. When the evolution of gas had ceased the excess olefin was distilled off in vacuo, leaving the crude bromide. This was extracted with ether (40 ml.) and dried (Na_2SO_4). Removal of the ether gave an impure yellow solid, a mixture of the two allylic bromides. The mass spectrum showed a parent ion at M251 (21%) and a peak corresponding to P^+-HBr at M171 (base peak).

(4) Dehydrobromination of Bromo-1-phenylcycloheptenes. This was attempted with a variety of bases (pyridine, t.-BuOK), but the two phenyl-cyclohepta-1,3-dienes could not be detected in the tarry reaction product.

(5) Acetolysis of Bromo-1-phenylcycloheptenes. This was carried out in silver acetate/acetic acid but produced a complex mixture of products from which it proved impossible to separate the desired compound.

Section II

Acetolysis Product Studies

Since only small samples (~1 g.) of the majority of compounds investigated could be obtained in isomerically pure form, the task of product identification was made more difficult. In general, 0·3-0·4 g. of each compound was reacted with a ~0·2 molar excess of NaOAc in acetic acid for 3-5 half-lives (85-95% reaction). Water (2 ml.) was then added, the excess acid neutralised with $NaHCO_3$, extracted with ether (5 ml.) and dried (Na_2SO_4). After removal of ether under reduced pressure, the products were vacuum distilled into a glass ampoule for analysis. Products and their percentage composition in mixtures were determined on the basis of analytical g.l.c., integrated 100 and 220 MHz ^1H N.M.R., and precise mass measurement. These were in remarkably good agreement. Several of the acetate products did not exhibit a parent ion strong enough for mass measurement. However, the majority exhibited peaks at $P^+-CH_2=C=O$ or P^+-CH_3CO which were measured instead.

IV.12. Para-x-substituted 7-Chloro-7-phenylbicyclo[4.1.0]heptanes.

(a) X = H, endo. G.l.c. (Col. '0' 100°) indicated one main peak only. The mass spectrum showed a parent ion at M170 (base peak) and peaks corresponding to P^+-CH_3 at M155 (75%) and then successive loss of methylene groups. Mass measurement: (Found: 170·1092;

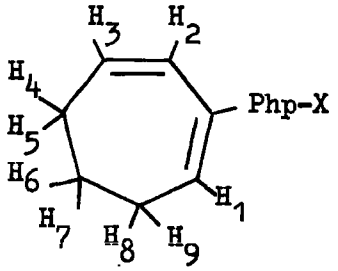
$C_{13}H_{14}$ requires 170·1095). The ^1H N.M.R. corresponded to 2-phenyl-cyclohepta-1,3-diene. The spectrum was similar to that of authentic 1-phenylcycloheptene (figures in brackets). C_1 proton, triplet 4·00 τ J = 6 c.p.s. (4·01 τ, J = 6 c.p.s.). C_2: multiplet 4·16 τ, C_5, C_6, C_7 methylene protons: 7·44 (7·34), 8·03 (8·30), 7·70 (7·74) τ respectively. Phenyl group 2·86 τ (2·84). There was no trace of ring opened acetate as a minor product.

<u>exo</u> - g.l.c. (Col. '0', 100°) indicated 3 components, ratio ~ 1:1:1. The mass spectrum showed a parent ion for the diene (Found: 170·1098). A parent ion was also present for the two returned acetates at M230 (2%) and a peak due to P^+-CH_3CO at M187 (35%). Mass measurement: (Found: 230·1303. $C_{15}H_{18}O_2$ requires 230·1307).

The diene and <u>endo</u> returned acetate were separated by thick layer chromatography on silica gel, using pentane as the mobile phase. The diene spectrum corresponded exactly with that from the solvolysis of the <u>endo</u> chloro isomer. The <u>exo</u> acetate exhibited a sharp singlet at 8·30 τ and a multiplet at 2·78 τ for the phenyl group. The spectrum was otherwise similar to that of other bicyclo[4.1.0] compounds. There were no olefinic resonances present.

The ^1H N.M.R. resonances for the substituted cyclohepta-1,3-dienes are summarised in Table IV.1.

Table IV.1.



P-X	H_1	H_2H_3	H_4H_5	H_6H_7	H_8H_9	Ph
H	4·0, J = 7 c.p.s.	4·16	7·44	8·03	7·70	2·86
Me	4·0, J = 7 c.p.s.	4·16	7·34	8·05	7·74	2·96 p-Me, 7·74
Cl	4·2	4·20	7·36	8·04	7·72	2·80
F	4·0, J = 7 c.p.s.	4·10	7·30	8·06	7·64	2·78-3·10
2,3-diphenyl	3·4, J = 7 c.p.s.	(H_3) 3·4 J = 4 c.p.s.	7·90	7·90	7·90	2·98

(b) X = Me (i) endo. The products were 2-p-methyl-phenyl-cyclohepta-1,3-diene (95%) and 3-p-methyl-phenyl-3-cyclohepten-1-yl acetate. G.l.c. (Col. 'O' 100° showed two components, ratio ~15:1, the minor component was of longer retention time. This ratio was the same for the different samples solvolysed at 125° and 100° respectively.

The mass spectrum showed a parent ion at M184 (base peak) and peaks corresponding to P^+-Me at M169 (70%), P^+-CH_3CH_2 at M155 (metastable) (Mass measurement: Found 184·1254; $C_{14}H_{16}$ requires

184·1252). A small peak observed at M202 was probably due to loss of ketene from ring opened acetate at M244. However this peak was too small to measure accurately. It is likely that acetic acid adds across the diene double bond with the acetate group on C_3. The ^1H N.M.R. showed diene as the sole product.

(ii) exo. Solvolysis was carried out on a 5:1 endo:exo mixture and the products are thus not well defined. G.l.c. showed one major component (diene) and two much smaller ones. The mass spectrum indicated mainly diene, however a small peak at M202 (P^+-CH_2CO) was measured (Found: 202·1349; $C_{14}H_{18}O$ requires 202·1358). It is not conclusive whether this arises from ring opened or returned acetate.

(c) X = Cl (i) exo. Products were a mixture of 2-p-chlorophenylcyclohepta-1,3-diene (~50%) and returned acetate (~50% 1:1 ratio). G.l.c. (Col. 'O' 100°) showed 3 peaks ratio ~ 2:1:1. The mass spectrum showed parent ion for the diene at M204 (base peak) and peaks corresponding to P^+-Cl at M169 (61%). Metastable peaks due to the transitions $154^+ \rightarrow 140^+$ and $140^+ \rightarrow 126^+$ were also observed. The parent ion for the acetates appeared at M264 (weak) and P^+-CH_3CO at M221.

Mass measurements: diene (Found: 204·0707; $C_{13}H_{13}Cl$ requires 204·0706). Acetates: (on P^+-CH_3CO, Found: 221·0740; $C_{13}H_{14}OCl$ requires 221·0734). The ^1H N.M.R. was almost identical with that for (a).

The acetate methyl resonances occurred at 8·12 τ (exo) and 8·25 τ (endo).

(d) X = F (i) endo. The products were 2-p-fluoro-phenyl-cyclohepta-1,3-diene and 3-p-fluoro-phenyl-3-cyclohepten-1-yl acetate, and these were separated by thick layer chromatography on silica gel using pentane as the mobile phase. G.l.c. (Col. 'O' 100°) showed 2 peaks ratio 4:1. The mass spectrum of the diene exhibited a parent ion at M188 (75%) and peaks corresponding to P^+-CH_3 at M174 (base peak). Metastables for the transitions $174^+ \rightarrow 160^+$ and $160^+ \rightarrow 147^+$ were also present.

The ring opened acetate exhibited a peak at M248 (weak) and P^+-CH_2CO at M206. Mass measurements. Diene (Found: 188·1001; $C_{13}H_{13}F$ requires 188·1001). Acetate (on P^+-CH_2CO, Found: 206·1088; $C_{11}H_{15}OF$ requires 206·1107). Integration of the ^1H N.M.R. acetate methyl resonance (8·1 τ) confirmed ~20-25% acetate present. This was identified as the 3-acetate since the C_3 proton normally observed at ~5·0 τ was absent from the spectrum.

(ii) exo. Products were 2-p-fluoro-phenylcyclohepta-1,3-diene (50%) and a mixture of returned acetates (50%), as for exo X = Cl. Mass measurements: diene (Found: 188·1004). Acetate (on P^+-CH_2CO, 206·1100).

IV.13. Endo-1,7-diphenyl-7-chlorobicyclo[4.1.0]heptane.

The sole product was 2,3-diphenylcyclohepta-1,3-diene, which

recrystallised from methanol as pale yellow crystals, M.pt. 93-94° (81% yield) (Found: C, 92·2; H, 7·32. $C_{19}H_{18}$ requires C, 92·7; H, 7·3%).

The u.v. spectrum showed two bands at 246 mμ and 211 mμ (ϵ_{max} = 27600, cyclohexane). There was no fluorescence under u.v. of long or short wavelength. (This may be compared with the 1,4-diphenyl compound,[83] ϵ_{max} = 29500, blue fluorescence under u.v.). The mass spectrum showed a parent ion at M246 (base peak) and peaks corresponding to P^+-nCH_2 at M231 (11%), M217 (14%) and M203 (21%). I.R. spectrum No.23. The ^{1}H N.M.R. spectrum showed the two allylic protons as a triplet at 3·4τ J = 4 c.p.s. and the 6 methylene protons as a sharp singlet at 7·9τ.

IV.14. Para-X-substituted 6-Chloro-6-phenylbicyclo[3.1.0]hexanes.

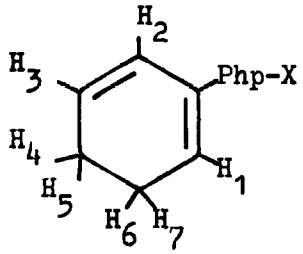
Only the exo isomers were acetolysed.

(a) X = H. The products were 2-phenylcyclohexa-1,3-diene (50%) and returned acetates, endo ~40% and exo ~10%. Analytical g.l.c. (Col. 'O' 80°) showed 2 main peaks, ratio 1:1 with a small shoulder on the longer retained peak. For the diene, the mass spectrum showed a parent ion at M156 (base peak) and peaks corresponding to P^+-nCH_2 at M142, M128 and M114. For the acetates, no parent ion was visible at M216, but a peak at M174 corresponded to P^+-CH_2CO. Mass measurements:

diene (Found: 156·0934; $C_{12}H_{12}$ requires 156·0939). Acetates (on P^+-CH_2CO, Found: 174·1048; $C_{12}H_{14}O$ requires 174·1045).

The ^1H N.M.R. resonances for the substituted cyclohexadienes are summarised in Table IV.2. The acetate methyl groups appeared at 8·18 τ (endo) and 8·04 τ (exo).

Table IV.2.



X	H_1	H_2H_3	H_4H_5	H_6H_7	Ph	P-X
H	3·84	4·18	8·0-8·3	8·0-8·3	2·82	-
Me	3·86	4·20	8·0-8·3	8·0-8·3	2·96	7·71
Cl	3·83	4·20	7·9-8·26	7·9-8·26	2·82	-
F	3·84	4·20	8·0-8·3	8·0-8·3	2·92	-
Phenyl cyclo-hexene	4·00	-	7·6-7·8	7·6-7·8	2·80	-

(b) X = Me. The products were 2-p-methyl-phenylcyclohexa-1,3-diene (50%) and the endo and exo returned acetates (~40% and ~10% respectively). This was confirmed by analytical g.l.c. (Col. '0' 80°)

which showed a two component mixture, ratio ~1:1. The diene mass spectrum exhibited a parent ion at M170 (base peak) and peaks corresponding to P^+-CH_3 at M155 (22%) and $P^+-(CH_2)_nCH_3$ at M141, M127 and M113. For the acetate, no parent ion was visible at M230, but a peak at M188 corresponded to P^+-CH_2CO. Mass measurement: Diene (Found: 170·1095; $C_{13}H_{14}$ requires 170·1095). Acetate (on P^+-CH_2CO; Found: 188·1197; $C_{13}H_{16}O$ requires 188·1201). The ^1H N.M.R. spectrum for the endo acetate exhibited sharp singlets at 8·17 τ (endo acetate Me)and 7·71 τ (para Me). A small amount (~10%) of the exo acetate was observed in the N.M.R. spectrum of the mixture (acetate methyl at 8·02 τ).

(c) X = Cl. The products were 2-p-chloro-phenylcyclohexa-1,3-diene (50%) and the endo and exo returned acetates (~40% and~10% respectively). G.l.c. (Col. 'O' 80°) showed two peaks only, ratio ~1:1. The diene mass spectrum showed a parent ion at M190 (60%) and peaks corresponding to P^+-2H at M188 (base peak) and P^+-nCH_2 at M176, M162 and M148. For the acetate, no parent ion was observed at M250, but a peak at M208 corresponded to P^+-CH_2CO. Mass measurement: Diene (Found: 190·0553; $C_{12}H_{11}Cl$ requires 190·0550). Acetate (on P^+-CH_2CO: Found 208·0650. $C_{12}H_{13}OCl$ requires 208·0655). The ^1H N.M.R. spectrum for the acetate exhibited a sharp singlet at 8·15 τ (endo acetate Me) and a multiplet at 8·04 τ (bridgehead protons). A small amount of the exo acetate gave a small singlet at 8·01 τ.

(d) X = F. The products were 2-p-fluoro-phenylcyclohexa-1,3-diene (50%) and the endo returned acetate (50%). G.l.c. (Col. '0' 80°) showed 2 peaks, ratio ~1:1. The diene mass spectrum showed a parent ion at M174 (base peak) and peaks corresponding to P^+-F at M155 (41%) and successive loss of methylene groups. A weak parent ion for the acetate was observed at M234 and a peak corresponding to P^+-CH_2CO at M192. Mass measurements: Diene (Found: 174·0844; $C_{12}H_{11}F$ requires 174·0845); acetate (Found: 192·0944; $C_{12}H_{13}OF$ requires 192·0950). The ^1H N.M.R. spectrum for the acetate exhibited a sharp singlet (acetate methyl) at 8·17τ. No exo isomer was observed.

IV.15. 6-Chlorobicyclo[3.1.0]hexanes.

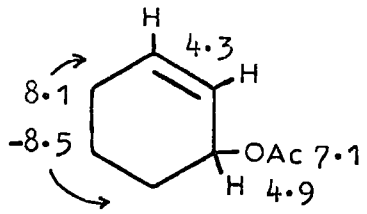
(i) Endo. The products were a mixture of cis-2-cyclohexen-1-yl acetate (90%), and 3-chlorocyclohexene (10%). Analytical g.l.c. (Col. '0' 80°) showed 1 peak only. The mass spectrum of the acetate exhibited a small parent ion at M140 (5%) and peaks corresponding to P^+-CH_2CO at M98 (35%) and P^+-CH_3COO at M81 (base peak). A small parent ion for the chloride appeared at M116. Mass measurement: acetate (Found: 140·0833; $C_8H_{12}O_2$ requires 140·0837).

The ^1H N.M.R. resonances are shown in Fig. IV.1.

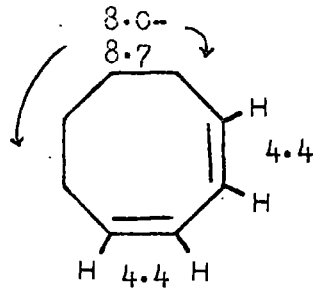
The product % ratio was calculated from the integrated N.M.R. spectrum.

(ii) Exo. This isomer was unreacted after 1 month at 175°. 95% of starting material was recovered.

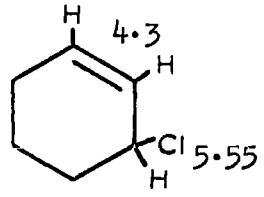
Fig.IV.1.



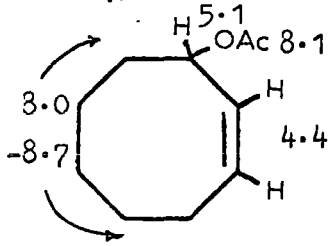
cis-2-cyclohexen-1-yl acetate



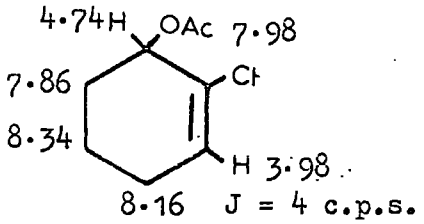
cyclo-octa-1,3-diene



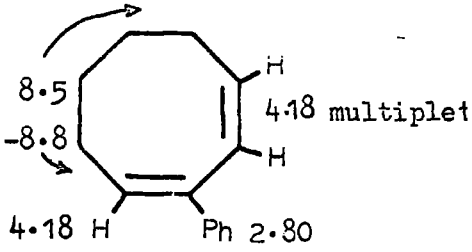
3-chlorocyclohexene



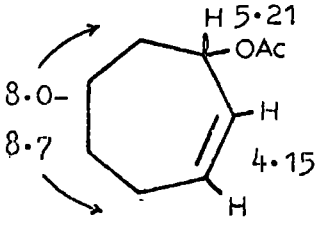
cis-2-cyclo-octen-1-yl acetate



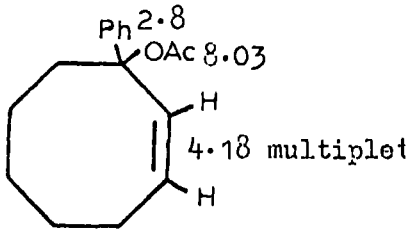
2-chloro-3-cyclohexen-1-yl acetate



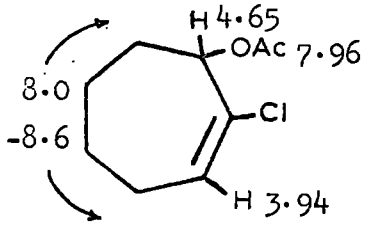
2-phenylcyclo-octa-1,3-diene



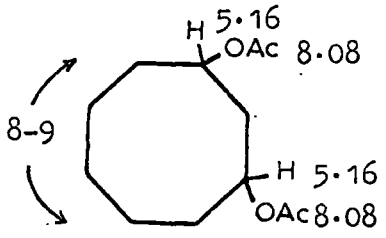
cis-2-cyclohepten-1-yl acetate



3-phenyl-3-cyclo-octen-1-yl acetate



2-chloro-3-cyclohepten-1-yl acetate



cis-cyclo-octyl-1,3-diacetate

IV.16. 7-Chlorobicyclo[4.1.0]heptanes

(i) Endo. The product was cis-2-cyclohepten-1-yl acetate. Analytical g.l.c. (Col. 'O' 100°) showed 1 peak only. The mass spectrum exhibited a very weak parent ion at M154 (~0·5%) and peaks corresponding to P^+-CH_2CO at M112 (2%) and P^+-CH_3COOH at M94 (base peak). Mass measurement: acetate (Found: 154·0991; $C_9H_{14}O_2$ requires 154·0994. The ^1H N.M.R. resonances are outlined in Fig. IV.1.

(ii) Exo. This isomer was unreacted after 1 month at 175° and 90% of starting material was recovered.

IV.17. 8-Chlorobicyclo[5.1.0]octanes

(i) Endo. Analytical g.l.c. (Col. 'O' 125°) showed 3 peaks, ratio ~1:1:0·2. The centre peak corresponded to starting material in retention time (40%). The products were cis-2-cyclo-octen-1-yl acetate (10%) and cyclo-octa-1,3-diene (50%). The acetate mass spectrum exhibited a parent ion at M168 (10%) and a peak corresponding to P^+-CH_2CO at M146 (base peak). The diene parent ion occurred at M108 (base peak). Mass measurements: acetate (Found: 168·1144; $C_{10}H_{16}O_2$ requires 168·1150). Diene (Found: 108·0934; C_8H_{12} requires 108·0939). The ^1H N.M.R. data is summarised in Fig. IV.1.

(ii) Exo. The products were cis-cyclo-octyl-1,3-diacetate (65%) and cis-2-cyclo-octen-1-yl acetate (35%). Analytical g.l.c. (Col. 'O' 140°) showed two peaks ratio 1:2.

The diacetate mass spectrum exhibited a weak parent ion at M228 (5%) and peaks corresponding to P^+-CH_2CO at M186 (11%) and P^+-2CH_2CO at M144 (37%). The monoacetate had a parent ion at M168 (18%) and a peak corresponding to P^+-CH_2CO at M126 (base peak). Mass measurement: diacetate (on P^+-2CH_2CO, Found: 144·1147; $C_8H_{16}O_2$ requires 144·1150). Monoacetate (Found: 168·1151; $C_{10}H_{16}O_2$ requires 168·1150). The ^1H N.M.R. data is summarised in Fig. IV.1.

IV.18. 8-Chloro-8-phenylbicyclo[5.1.0]octanes.

(i) Endo. Analytical g.l.c. (Col. 'O' 140°) showed 3 peaks, ratio ~ 1:3·5:0·5. The middle peak corresponded starting material (70%) in retention time. The products were, 2-phenylcyclo-octa-1,3-diene (20%) and 3-phenyl-3-cyclo-octen-1-yl acetate (10%). The diene mass spectrum had a parent ion at M184 (80%) and peaks corresponding to P^+-CH_3 at M169 (33%) and $P^+-C_2H_5$ at M155 (base peak, metastable). The acetate parent ion occurred at M244 and a peak at M202 corresponded to P^+-CH_2CO (base peak). Mass measurements: Diene (Found: 184·1252; $C_{14}H_{16}$ requires 184·1251). Acetate (on P^+-CH_2CO; Found: 202·1358; $C_{14}H_{18}O$ requires 202·1358). The ^1H N.M.R. data is summarised in Fig.IV.1.

(ii) Exo. This isomer was solvolysed in a mixture with the endo compound and it has not proved possible to determine the % of each product. However, 2-phenylcyclo-octene, 3-phenyl-3-cyclo-octen-1-yl

acetate and 2-phenylcyclo-octyl-1,3-diacetate were all present. Mass measurement diacetate (on Ph^+-CH_2CO. Found: 220·1456; $C_{14}H_{20}O_2$ requires 220·1463). The fact that the diacetate was not observed as a product of the acetolysis of the endo isomer indicates that it originated from the exo compound.

IV.19. 6,6-Dichlorobicyclo[3.1.0]hexane.

The product was 2-chloro-3-cyclohexen-1-yl acetate. Analytical g.l.c. (Col. '0', 80°) showed one peak only. The mass spectrum showed a parent ion at M174 (11%) and peaks corresponding to P^+-Cl at M139 (25%) and P^+-CH_3COOH at M114 (base peak). Mass measurement: (Found: 174·0442; $C_8H_{11}ClO_2$ requires 174·0448). The ^1H N.M.R. data is summarised in Fig.IV.1. I.R. spectrum No.21.

IV.20. 7,7-Dichlorobicyclo[4.1.0]heptane.

The reaction was not taken to completion to avoid solvolysing the second chlorine atom. Analytical g.l.c. (Col. '0' 100°) showed two peaks, ratio ~1:1 the first of which corresponded to starting material). The product was 2-chloro-3-cyclohepten-1-yl acetate. The parent ion of this compound was too weak from mass measurement, however on P^+-Cl (Found: 153·0911; $C_9H_{13}O_2$ requires 153·0915) and on P^+-CH_2CO (Found: 146·0497; $C_7H_{11}O_9$ requires 146·0499). The ^1H N.M.R. data is shown in Fig.IV.1. I.R. spectrum No.22.

Section III

Separation Procedures

IV.21. Dry Column Chromatography.[62] This is an extremely useful technique which is essentially a large scale extension of thin layer chromatography (T.L.C.). The resolution obtained with this procedure is often far better than that obtained from a conventional liquid filled column. Provided the absorbents are suitably deactivated and the same solvent system is used, the conditions for dry column chromatography are directly transferable from those for T.L.C. R_f values and load factors are also approximately the same.

In practise, the absorbents (activity 1) used were deactivated by the addition of water, (3% w/w, activity 2, 6% w/w, activity 3) and equilibrated by rotation on a rotary evaporator for 3-4 hrs. The absorbent was then packed into a suitable column in a dry state, using a mechanical vibrator to ensure even packing and elimination of air pockets. The mixture was then loaded on to the top of the column (solids were dissolved in the minimum of solvent) and allowed to soak into the absorbent completely. The solvent (all hydrocarbon solvents were dried over sodium wire) was run into the top of the column and the rate of elution was controlled by a tap at the bottom. Various fractions were taken, the solvent removed on a rotary evaporator, and then analysed by g.l.c. The pure fractions were then stripped of residual solvent and recrystallised or sublimed. The column size was

determined by the amount of material available and the R_f value of the mixture. Long, thin columns were used in preference to short, wide ones, since with the latter, the compounds tended to move down the column in an uneven band.

Some compounds decomposed immediately when this technique was applied and further deactivation of the column, whilst preventing decomposition, would not effect a separation. Preliminary work on absorbents, deactivation and solvents, was carried out on thin layer plates and then scaled up.

IV.22. Liquid Column Chromatography. This method was used to separate compounds which decomposed on dry columns. Long, narrow columns were employed and 100 ml. fractions were continuously removed. The columns were packed with a slurry of absorbent and solvent, using a mechanical vibrator to eliminate air bubbles.

IV.23. Thick Layer Chromatography. Small-scale separations were carried out using thick layer plates and fluorescent grades of alumina or silica gel. The fluorescence enabled identification and recovery of milligram amounts of colourless products, sufficient for mass spectral and N.M.R. analysis.

CHAPTER V

Kinetic Measurements

V.1. Reagents.

The silver nitrate solutions used were prepared by weighing the appropriate amount of Analar reagent for $^{N}/_{100}$ solution. The exact normality was then determined by titration with standard sodium chloride solution using potassium chromate indicator. The solutions were stored in darkened containers until use, and were regularly standardised.

Solvent acetic acid used was Analar grade (chloride ion content $< 2 \times 10^{-4}\%$), and was used without further purification. Analar grade sodium acetate ($Cl^- < 2 \times 10^{-3}\%$) was also used.

V.2. Procedure for Kinetic Runs.

The chloride ion content of a given solution was determined by a potentiometric method employing a silver wire as the indicator electrode while a glass electrode served as the reference. The e.m.f. between the electrodes was measured with an E.I.L. direct reading pH meter. The end point was indicated by a large change in the e.m.f. produced, for small additions ($\sim 0{\cdot}01$ ml.) of silver nitrate solution. It was found that a sufficiently accurate end point could not be obtained using a titrating solution more dilute than $^{N}/_{100}$.

In a normal procedure, 0·3 - 0·4 g. of the compound under investigation was weighed into a volumetric flask together with $\sim 0{\cdot}2$

molar excess of sodium acetate. Acetic acid was added to a total volume of 80 ml. After shaking, the flask was allowed to stand for several hours at room temperature. 5 ml. (approx.) aliquots of this solution were measured into 15 glass ampoules from a graduated pipette.

The exact weight of compound in each case was calculated in order to give 'infinity' titres of ~10 mls. of $^{N}/_{100}$ silver nitrate.

The sealed ampoules were suspended in a thermostat of conventional design and allowed to equilibrate for at least 10 minutes. The temperature was controlled to $\pm 0{\cdot}1^{\circ}$ by a contact thermometer and relay. (The temperatures quoted were measured with thermometers standardised by the National Physical Laboratory). Two ampoules were removed at the start of the run (t = 0) as 'zero' reading. The next tube was not removed until 15 - 20% reaction had taken place, and the rest were removed at regular intervals over two half-lives. The 'infinity' readings were taken from the last three ampoules after 10 half lives (considerable darkening of the solution was usually observed). The reaction was quenched by rapidly cooling the ampoule in an acetone/'drikold' bath at -78°. The chloride content was then determined by breaking open the ampoule under ~40 ml. of acetic acid in a glass titration cell containing the electrodes. The mixture was rapidly stirred during titration to prevent precipitation of silver chloride on the electrodes, which tended to decrease the sensitivity of the system.

Since only small quantities of compounds were available, only one accurate run was carried out at each temperature. A preliminary run was first carried out using approx. 0·1 g. of compound and six ampoules to give a 'rough' rate of reaction, (usually within ~10% of the accurate run). The accurate determination was then made, removing ampoules at time intervals appropriate to the reaction rate previously determined. The ampoules were stored in a refrigerator until the end of the run, and the contents were all titrated at the same time.

The exo-chlorobicyclo[n.1.0]alkanes (n = 3,4) were heated up to 1 month at 175°. Ampoules were removed at 2 day intervals and titrated. No reaction was observed, assuming a detectable limit of reaction. With an infinity titre of 10 mls., this meant that the addition of 0·05 ml. (~1 drop) of $^{N}/_{100}$ $AgNO_3$ was sufficient to react with all the chloride ion present in solution. A blank determination was also carried out with the same volume of unreacted solution.

V.3. The Measurement of First Order Rates.

The first-order integrated rate coefficients (K_1) were calculated from equation V.1.:-

$$K_1 = \frac{2303}{t} \log_{10} \frac{T_\infty - T_o}{T_\infty - T_t} \qquad \ldots\ldots \text{V.1.}$$

where t is the time in seconds, and T_∞, T_t and T_o are the titres at times of t = infinity, t = t and t = o respectively. The values of K_1 quoted in this thesis are mean values of usually about 10 separate rate determinations.

The standard error (σ) in the mean rate coefficient (K_m) was obtained from equation V.2.

$$\sigma(K_1) = \frac{[\sum(K_1 - K_m)^2]^{\frac{1}{2}}}{n} \qquad \ldots\ldots \text{V.2.}$$

where n was the number of separate determinations of K_1. If any individual values of K_1 differed from the mean by more than $2\frac{1}{2}\ \sigma$ (each), where σ (each) = $n^{\frac{1}{2}}\sigma(K_1)$, these values were rejected and a new mean rate coefficient and $\sigma(K_1)$ were determined. This process was repeated (if necessary) until the individual values of K_1 were within $2\frac{1}{2}\ \sigma$ (each) of the mean value (K_m).

V.4. The Energy of Activation.

The activation energy, E_A, was calculated from values of the rate coefficients (K) at two temperatures and refers to the mean temperature, $(T_a + T_b)/2$:-

$$E_A = \frac{2{\cdot}303\ RT_aT_b}{T_a - T_b} \log_{10}\frac{K_a}{K_b} \qquad \ldots\ldots \text{V.3.}$$

where K_a and K_b are the values of K at the absolute temperatures T_a and T_b respectively. The standard error in E_A was obtained from equation V.4.:-

$$\sigma(E_A) = \frac{RT_aT_b}{T_a - T_b} \left[\left(\frac{\sigma_a}{K_a}\right)^2 + \left(\frac{\sigma_b}{K_b}\right)^2\right]^{\frac{1}{2}} \quad \ldots\ldots \text{V.4.}$$

where σ_a and σ_b are the standard errors in K_a and K_b respectively.

V.5. The Entropy of Activation.

The entropy of activation, ΔS^*, at the temperature $(T_a + T_b/2)$ was calculated from equation V.5.:-

$$\frac{\Delta S^*}{2{\cdot}303R} = \log_{10}K_a - 10{\cdot}7531 - \log_{10}\left(\frac{T_a - T_b}{2}\right) + \frac{E_A}{2{\cdot}303RT_a} \quad \ldots\ldots \text{V.5.}$$

where K_a refers to the temperature T_a, and E_A to $(T_a + T_b)/2$.

The standard error in ΔS^*, $\sigma(\Delta S^*)$, was obtained from the approximation:

$$\sigma(\Delta S^*) \simeq \frac{\sigma(E_A)}{(T_a + T_b)/2} \quad \ldots\ldots \text{V.6.}$$

V.6. Initial Rates Measurements.

It was found, in the case of the acetolysis of 7,7-dichloro-bicyclo[4.1.0]heptane at 175°, that the second chlorine atom started to solvolyse after ring opening to 2-chloro-3-cyclohepten-1-yl acetate, giving inaccurate rate constants for the run.

Consequently, this reaction was studied by an initial rates method, where all the ampoules were removed during the first 15% of reaction, before a large enough concentration of ring opened material had built up. However, it is well known that due to the form of the

first order rate equation, relatively large errors are involved during the early and later stages of a kinetic run. It is usual to take readings between 15% and 80% of reaction. The errors for these runs were thus correspondingly larger than normal.

V.7. Solvolysis of Isomeric Mixtures.

As previously mentioned, the exo isomers of 7-chloro-7-methyl-phenylbicyclo[4.1.0]heptane and 8-chloro-8-phenylbicyclo[5.1.0]octane, rearranged too readily on chromatographic columns to enable separation from the endo isomers. Hence a pure sample of the mixture of isomers was prepared by using alumina sufficiently deactivated to prevent rearrangement. The ratio exo:endo was determined approximately by g.l.c. taking the mean of 10 separate integration determinations. The mixture was then solvolysed, and a large fall-off in rate was observed as the reaction proceeded.

Knowing the accurate rate constant (K_m) for the endo isomer, and the ratio exo:endo, a computer fit was made to the experimental data using the following procedure.

If A and B are the two components of the mixture, during solvolysis there are two reactions occuring simultaneously. Assuming there is no interaction between the components, in the mixture:-

$$K_A = \log_e ({}^a/a-x)/60t \qquad \ldots\ldots \text{V.7.}$$

$$K_B = \log_e ({}^b/b-y)/60t \qquad \ldots\ldots \text{V.8.}$$

where (a + b) is equal to the observed 'infinity' reading for the mixture, and (x + y) is the reading at any time t.

The ratio a/b is known from other measurements. Substitution of a and the known value of K_A into equation V.7. enables calculation of x at time t. From this, y may be calculated and substitution of this and b into equation V.8. gives a value of K_B at time t.

In practice, an estimated value of K_B was used, which was varied over wide limits, to give the minimum standard error between the computed and experimental titres. The value of $^a/_b$ was simultaneously varied between small limits to ensure that the ratio measured by g.l.c. was reasonably accurate. Although the errors involved are somewhat higher than normal, this procedure enabled measurement of rates which would otherwise have been inaccessible. The errors quoted for K_m are estimated from the three values of K_m which gave the minimum standard error.

V.8. Kinetic Plots.

Figs. V.1-5. represent some typical acetolysis runs, as a plot of $\log_{10}(^a/_{a-x})$ v. time (in seconds).

Fig. V.1. Acetolysis of endo-7-chlorobicyclo[4.1.0]heptane at 125 ± 0·1°.

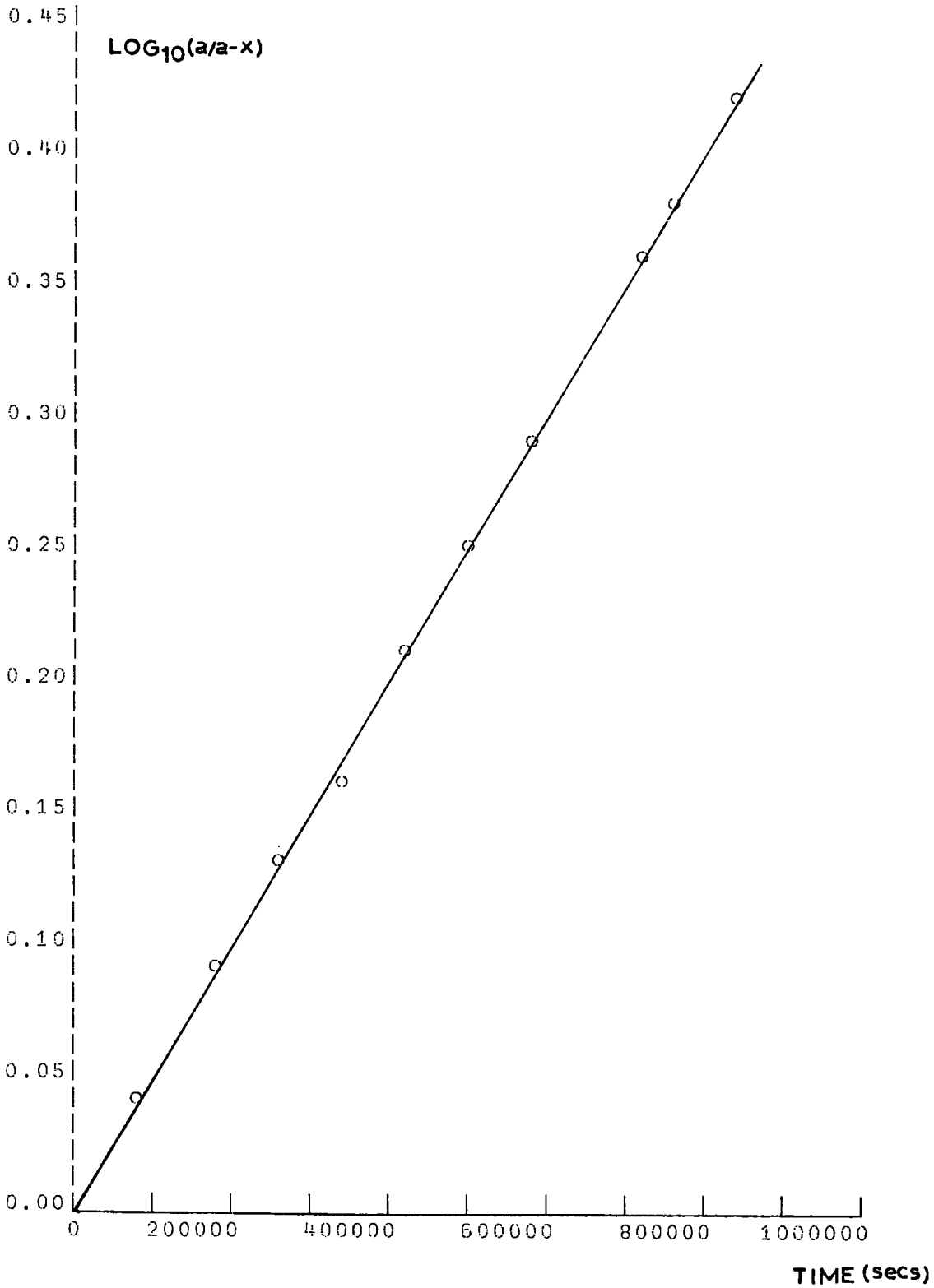


Fig. V.2. Acetolysis of exo-7-chloro-7-p-chloro-phenylbicyclo[4.1.0]-heptane at 100 ± 0.1°

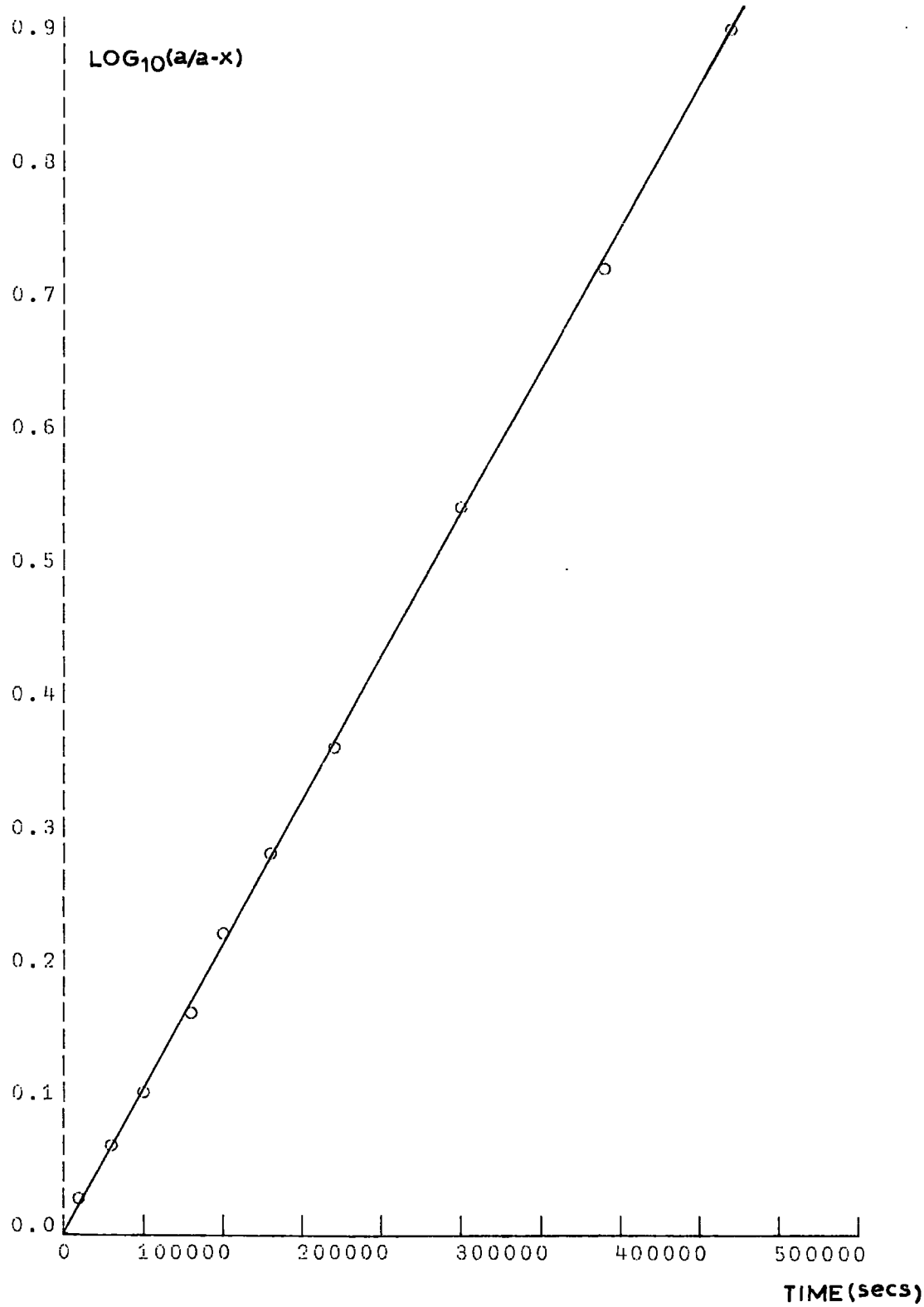


Fig. V.3. Acetolysis of endo-1,7-diphenyl-7-chlorobicyclo[4.1.0]heptane at 125 ± 0·1°

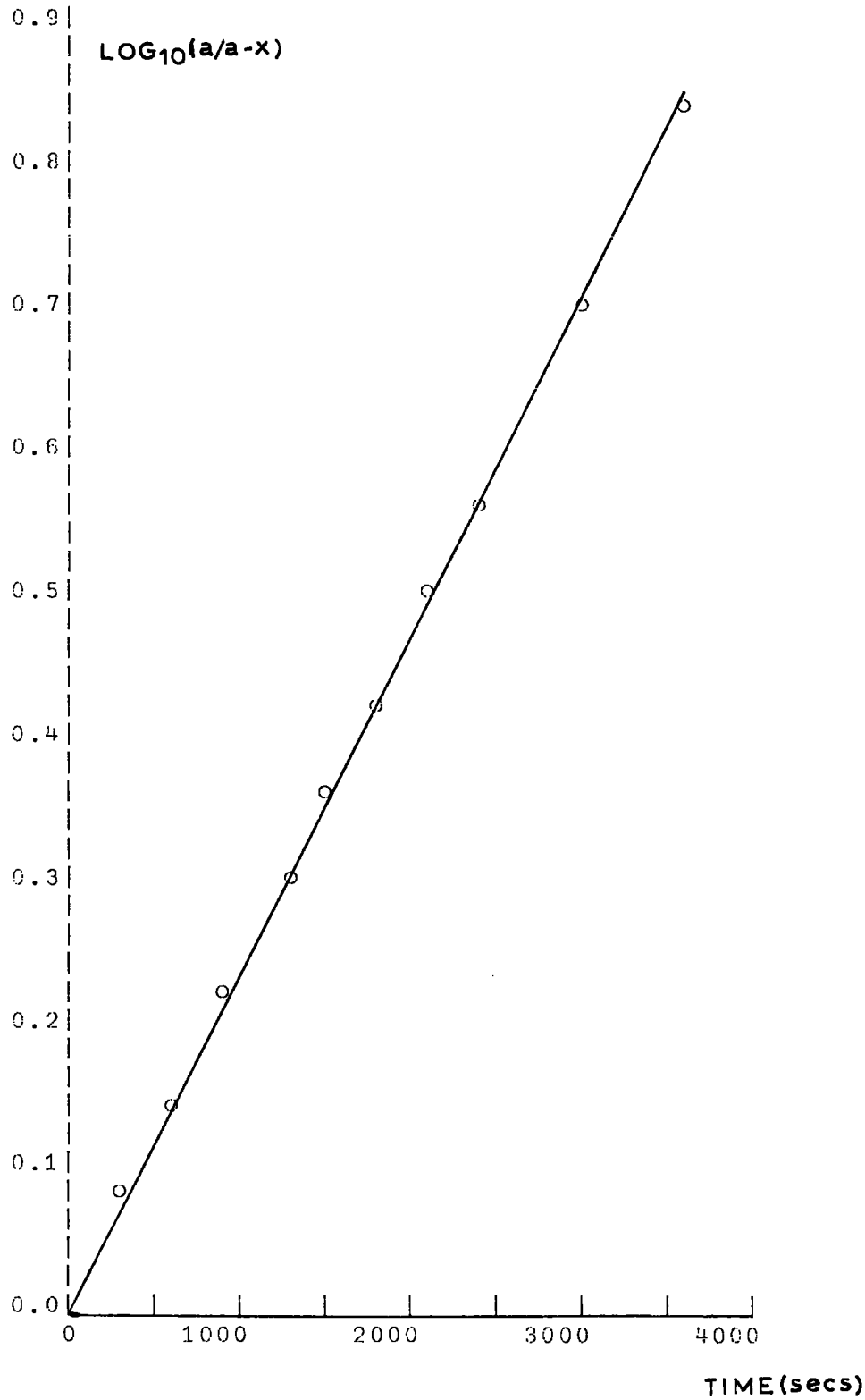


Fig. V.4. Acetolysis of exo-6-chloro-6-p-chloro-phenylbicyclo[3.1.0]-hexane at 125 ± 0·1°

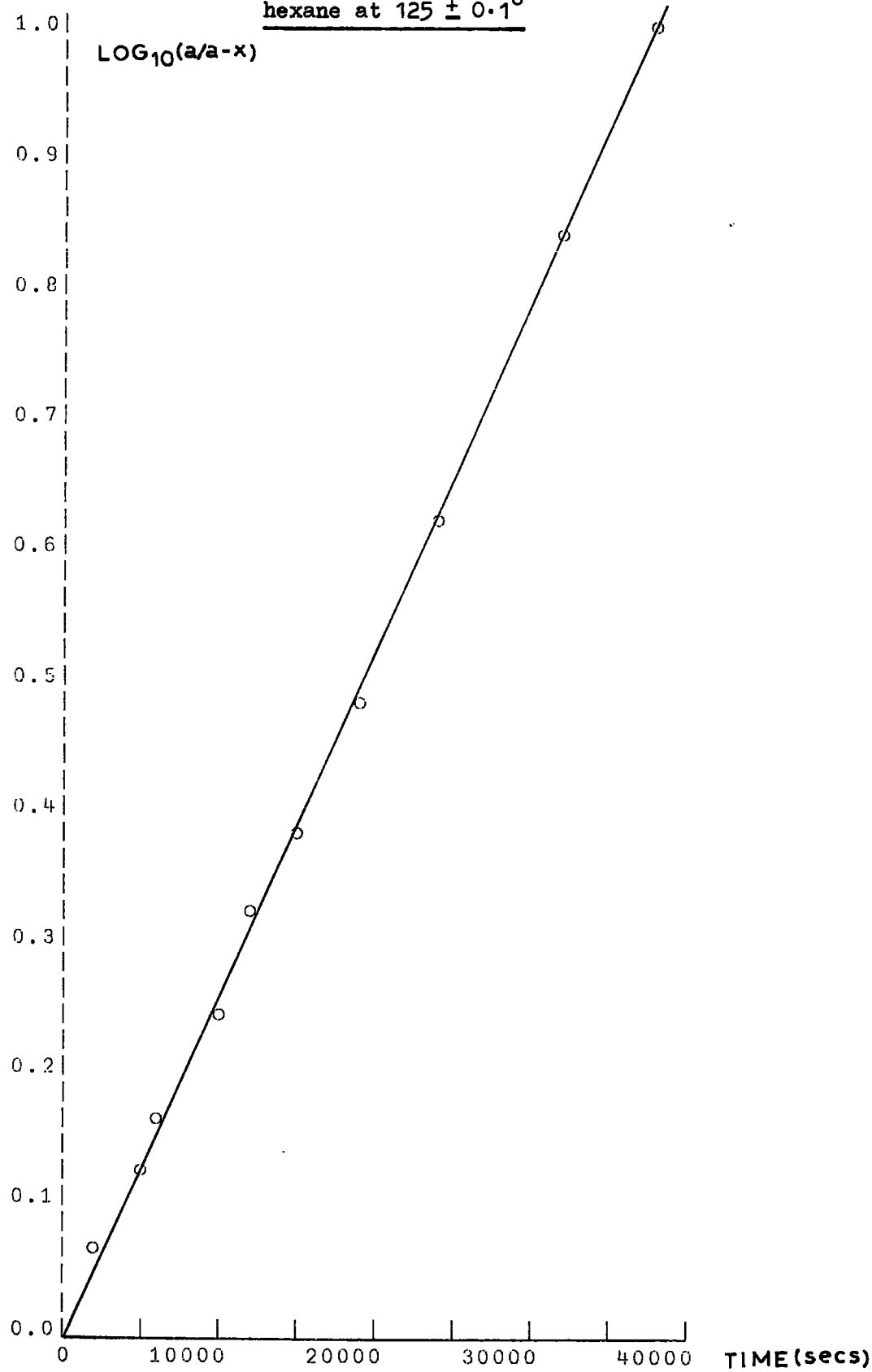
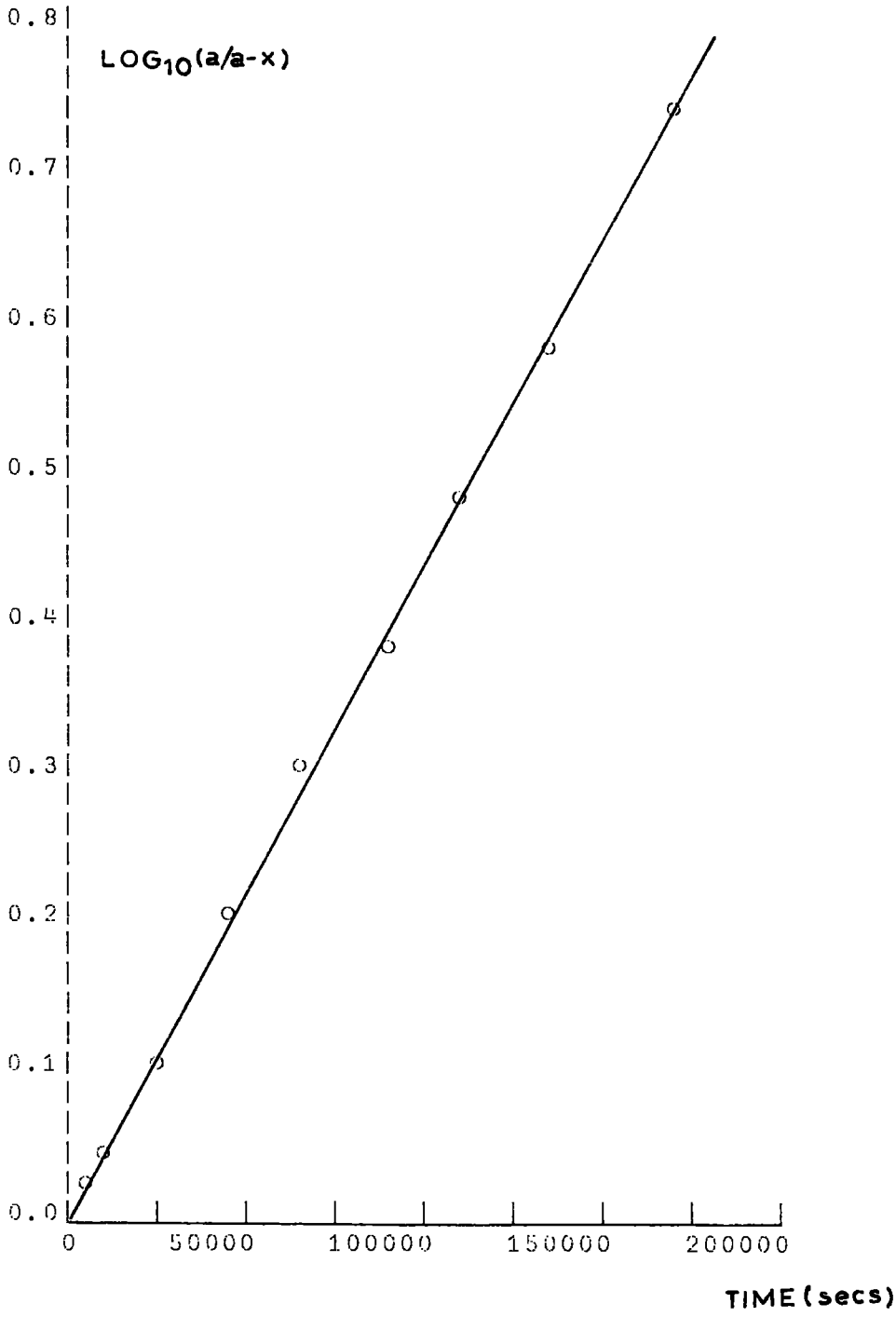


Fig. V.5. Acetolysis of exo-7-chloro-7-phenylbicyclo[4.1.0]heptane at 125 ± 0.1°



CHAPTER VI

^{1}H Nuclear Magnetic Resonance Spectra of some Bicyclo[n.1.0]alkanes.

VI.1. Introduction.

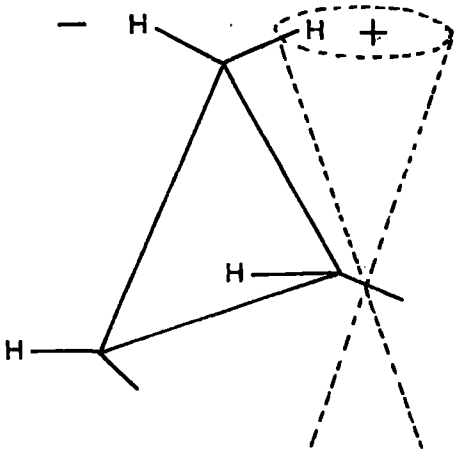
N.M.R. is an extremely useful technique for determining the conformation of cyclopropane rings, and many studies of substituted cyclopropanes have appeared in the literature. However, relatively little work has been carried out on bicyclic cyclopropane systems and much of this has been concerned with the assignment of exo or endo proton resonances only.

The bridgehead and methylene proton resonances of the compounds prepared for kinetic study were unresolved at 60 MHz and it was necessary to run spectra at 100 MHz and sometimes at 220 MHz to enable accurate assignment of peaks. Spin decoupling of exo or endo protons was also carried out to determine the bridgehead proton resonances.

Cyclopropyl protons generally occur at high field strengths due to increased screening by the cyclopropane ring. A methylene group in cyclopropane (9·78 τ) for example is shielded to a much greater extent than the methylene group in propane (8·67 τ).[84] This has been attributed to the greater mobility of the electrons in cyclopropane compared to ordinary saturated compounds which may produce a ring current in the magnetic field. However, it has alternatively been shown that such an effect would be small and that it would actually cause deshielding at the ring proton positions.[85]

Studies have also been made on the effect of ring size on the chemical shift of ring protons. A significant decrease in shielding with decrease in ring size, was found for all compounds except cyclopropanes. The chemical shift difference from the larger ring compounds were explained in terms of the diamagnetic anisotropic effect of the neighbouring C-C bonds in the molecule. However, the shielding observed in cyclopropanes is too large to be explained in the same way.

Measurements of the N.M.R. of substituted cyclopropanes[86,87] have also shown that for many substituents, the cyclopropyl protons cis to the substituent were upfield from those trans to the substituent. A similar situation occurs in bicyclic systems, since the C-C bonds of the larger fused ring may function as substituents. A cyclopropyl proton situated cis or trans will be in the anisotropy region of the C-C bond and will experience shielding or deshielding respectively.[35,88]



In bicyclic compounds, the shielding of H_A (Table VI.1) reaches a maximum with a ten membered fused ring.[89] It has been pointed out however, that models do not show striking differences in the proximity of other methylene groups in the ring, to H_A, sufficient to explain the large upfield shift with ring size.

	Chemical Shift*	
n	H_A	H_B
2	-0·4	-0·7
3	-0·02	-0·21
4	0·04	-0·47
5	-0·02	-0·7
6	0·30	-0·4
7	0·42	-0·4
8	0·48	-0·51
10	0·35	-0·4

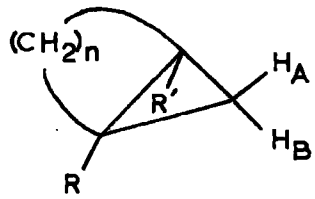


Table VI.1.

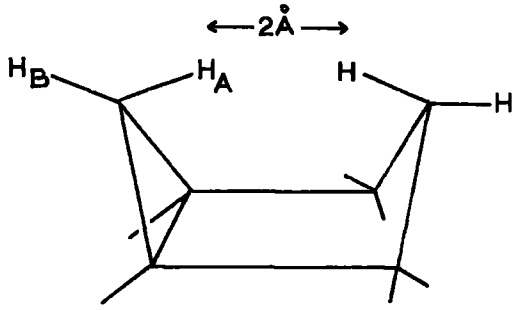
*Relative to T.M.S. internal standard.

Other workers[86] have studied various bicyclic systems substituted at the bridgehead and have found that all of the compounds in which the cis proton (H_A) resonates at a lower field than the trans proton (H_B), have either a bicyclo[3.1.0]pentane nucleus and one R. substituent, or a bicyclo[4.1.0]hexane nucleus with one R. substituent and a hydroxyl group on the fused ring. They concluded that the deshielding of the cis proton is dependent both on the number of substituents and on the size of the ring system. (Table VI.2.).

n	H_A	H_B	R
3	9·70	9·85	Me
4	9·81	9·66	Me
4	10·04	9·37	H
5	9·84	9·84	Me
6	10·10	9·66	Me

Table VI.2.

Calculations of the diamagnetic anisotropic shielding effect of the C-C bonds show that inversion of the cis and trans proton resonances is not expected when the ring size reaches five (n = 3) and that some other interaction must be present in the smaller ring to cause further deshielding of the trans proton. It has been suggested that this additional effect is caused by non-bonded interactions between transannular protons in the boat-shaped conformation of the bicyclo[3.1.0]-hexane molecule.



The methylene protons of the cyclopropane ring in fused systems can be distinguished by their coupling with the bridgehead protons, where $J_{BH} > J_{AH}$ and this is supported by all the evidence in the

literature. When both J_{AH} and J_{BH} can be identified in the spectrum, the most upfield resonance can be unambiguously assigned. (See Table VI.3.).

n	X	Y	$Shift_X$	$Shift_Y$	J(c.p.s.)
3	H	Cl	7·38	-	1·5
3	H	OMe	7·22	-	3·00
4	H	OMe	7·25	-	3·0
4	H	OPh	6·75	-	2·70
3	Cl	H	-	6·72	7·00
3	OMe	H	-	6·95	7·0
4	OMe	H	-	7·1	6·5
4	OPh	H	-	6·48	6·6

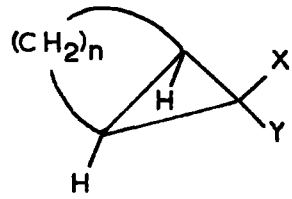


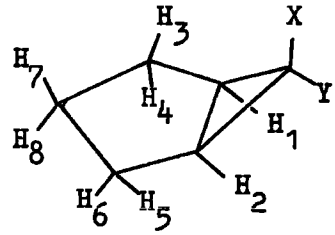
Table VI.3.

VI.2. N.M.R. Spectra of some Bicyclo[3.1.0]hexanes.

The proton resonances assigned for this series are summarised in Table VI.4.

In the hydro-chloro compounds, the trans proton occurs at lower field than the cis proton (both triplets, from coupling with bridgehead protons) by 0·66 p.p.m., in agreement with the literature assignment. (Ref.[44] endo 6·72 τ J = 7 c.p.s., exo 7·38 τ, J = 1·5 c.p.s.). Spin decoupling of the trans proton collapsed the multiplet at 8·4 τ to a single peak (N.M.R. No. 16) and the bridgehead protons were assigned to this resonance. A similar decoupling experiment

Table VI.4.



			CHEMICAL SHIFT* p.p.m.					
N.M.R. No.	X	Y	H_1H_2	H_3H_4 H_5H_6	H_7H_8	Shift X	Shift Y	J c.p.s.
12	Ph	Cl	7·94	8·20	8·84	2·75	-	-
13	pClPh	Cl	7·96	8·22	8·78	2·75	-	-
14	pMePh	Cl	7·98	8·22	8·80	2·78	-	-
-	pFPh	Cl	7·96	8·14	8·74	2·90	-	-
-	Cl	Cl	8·22	7·94	8·06	-	-	-
17	H	Cl	8·46	8·30	8·10 8·20	7·46	-	1·0
16	Cl	H	8·40	8·18	8·05 8·25	-	6·80	7·0

*Centre of signal relative to tetramethyl silane as internal reference. All spectra were recorded in CCl_4 as solvent.

on the cis proton produced less conclusive results, however the bridgehead protons were assigned to the multiplet at 8·46 τ (N.M.R. No.17).

The resonances of the methylene protons were interpreted on the basis of integration ratios and the fact that from models protons H_7 and H_8 were likely to be the least shielded and therefore the furthest downfield.

The phenyl substituted compounds were less straightforward to interpret, since there was no 6-proton coupling with the bridgehead protons. A high field resonance equivalent to two protons was observed in the region 8·8 τ. Models showed that in the exo isomer the protons H_7 and H_8 were considerably shielded by the phenyl ring and this accounted for this high field resonance.

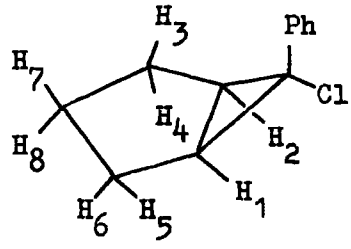
The shielding contribution from the ring current of the phenyl group may be calculated by the method of Bovey and Johnson.[90] These workers used the free electron model of Pauling to calculate the magnetic field around a benzene ring which was rotating rapidly about all axes in a magnetic field. It was assumed that the π-electrons precess in two circular paths, one on each side of the ring, equal in radius to the C-C distance in the benzene ring.

The full tables for calculating shielding values are given in reference 84, p.595. The co-ordinates p and z (measured in ring radii, ≡ 1·39Å) were measured from Dreiding models of the phenyl-

bicyclo[3.1.0]hexane system, with the phenyl ring in the best conformation. The axes employed were the plane of the phenyl ring and a line perpendicular to the ring passing through its centre.

The predicted shielding parameters for the endo and exo isomers are shown in Tables VI.5. and VI.6.

	above plane	Z	in plane	P	Calc. Shift	Obs. Shift
H_1	1·10	0·8	4·60	3·3	0·22	0·56
H_3	1·4	1·0	2·00	1·4	-0·11	0·10
H_4	2·60	1·9	3·20	2·3	-0·09	
H_7	2·20	1·6	0·80	0·6	-3·00	-0·64
H_8	3·40	2·5	2·20	1·6	-0·45	-0·74



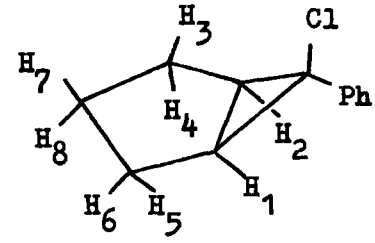
exo

Table VI.5.

In general the bridgehead protons tend to shift downfield for both isomers. However the major difference is for the protons H_7 and H_8 the shift in each case being in a different direction. As shown in the table, for the exo isomer these protons exhibit a large upfield shift.

The predicted shifts for the endo isomer on the other hand, show a small apparent decrease in the applied field. There is no data, however, for the observed shifts, since the endo isomers were not isolated.

	above plane	Z	in plane	P	Calc. Shift
H_1	1·40	1·0	3·00	2·2	0·38
H_3	0·40	0·3	5·00	3·6	0·21
H_4	1·30	1·1	5·40	3·9	0·12
H_7	0·64	0·5	6·00	4·3	0·15
H_8	1·30	1·1	6·40	4·6	0·11



endo

Table VI.6.

From the integration ratios and comparison of the spectra with those of the phenyl-substituted exo-[4.1.0] compounds the bridgehead protons were assigned to the peak at ~ 7·98 τ and the other methylene protons to the multiplet at ~ 8·20 τ.

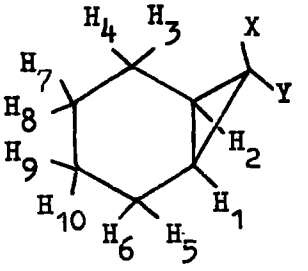
The bridgehead protons for the gem-dichloro compound appear midway between those for the phenyl and hydro-substituted compounds. The multiplet for H_7H_8 appears at higher field than for the other methylene protons, which reverses the assignment for the hydro-chloro isomers.

VI.3. N.M.R. Spectra of Some Bicyclo[4.1.0]heptanes.

The N.M.R. data for these compounds is given in Table VI.6.

For the hydro-chloro compounds, the trans proton again resonates at lower field than the cis proton by 0·50 p.p.m. In the trans isomer, spin decoupling of the 7-proton (triplet) reduces a multiplet

Table VI.7.



			CHEMICAL SHIFT; p.p.m.					
N.M.R. No.	X	Y	H_1H_2	H_3H_4, H_5H_6	H_7H_8, H_9H_{10}	X	Y	J c.p.s.
-	Cl	Cl	8·32	8·74	8·1 -8·3	-	-	-
7	Cl	H	8·95	8·80	8·24 -8·42	-	6·96	8·0
1	Cl	Ph	8·70	8·54	8·00 8·20	-	2·82	-
9	Cl	PhpMe	8·63	8·63	8·16	-	3·00	-
10	Cl	PhpF	8·58	8·58	8·10	-	3·10	-
4	Cl	Ph	H, 7·61 Ph, 3·06	8·42 8·64	7·56 8·10	-	3·06	-
8	H	Cl	8·87	8·80	8·26	7·46	-	5·0
2	Ph	Cl	8·24	8·10 8·24	9·10 9·38	2·70	-	-
3	PhpCl	Cl	8·24	8·10 8·24	8·94 9·33	2·61	-	-
11	PhpF	Cl	8·22	8·22	9·20	2·84	-	-

centred on 8·95 τ to a single peak at 8·88 τ (N.M.R. No. 18). Hence the bridgehead protons were assigned to the resonance at 8·95 τ. Assignment of the bridgehead protons for the cis isomer is more difficult

due to a large number of overlapping peaks. Decoupling of the triplet at 7·46τappears to affect the multiplet at 8·87 τ (N.M.R. No. 19). The 7-proton of the endo chloro isomer, as expected has a larger coupling constant (8 c.p.s.) than that of the exo isomer (5 c.p.s.).

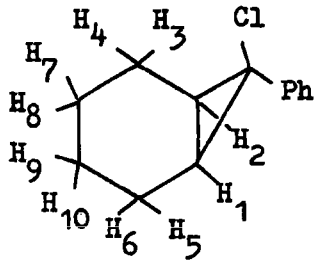
The phenyl-substituted isomers were readily distinguished, since in the exo compounds, the phenyl ring projects from C_7 directly over protons H_7H_8 and H_9H_{10}. These are shifted upfield by ~ 1·1 p.p.m. compared with those in the parent compound. For the endo series as a whole these protons appear in the general region 8·0 - 8·4 τ.

The predicted shifts for the phenyl bicyclo[4.1.0]heptane system were calculated as before. However this is a relatively crude approximation since only one conformation of the cyclohexane ring was considered. In practise the ring will be 'flipping' between the two preferred conformations. The results are collected in Table VI.8. and VI.9.

The bridgehead shifts for both isomers are very small. On the other hand, H_7 and H_9 of the exo isomer again show a large upfield shift, which is not exhibited by the endo isomer. The shifts in the latter case are slightly downfield.

The H_3H_4, H_5H_6 protons occur at 8·4 - 8·8 τ and the exact position seems independent of the nature of the substituting group, Y. These protons also resonate at lower field than those of the exo compounds which occur between 8·1 and 8·24 τ.

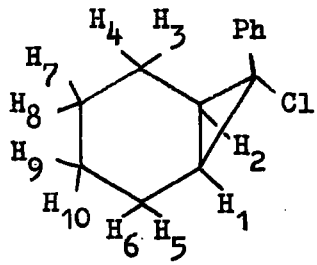
	Above plane	Z	In plane	P	Calc. Shift	Obs. Shift
H_1	0·6	0·4	4·6	3·3	0·27	0·63
H_3	1·4	1·0	2·6	1·9	0·42	0·65
H_4	2·6	1·9	3·4	2·4	0·06	
H_7	1·10	0·8	1·2	1·2	-4·30	-1·1
H_8	3·1	2·2	0·6	0·4	-1·57	
H_9	3·6	2·6	0·6	0·4	-1·01	-1·1
H_{10}	4·2	3·0	2·2	1·6	-0·35	



exo

Table VI.8.

	Above plane	Z	In plane	P	Calc. Shift	Obs. Shift
H_1	1·48	1·1	2·9	2·1	0·3	0·25
H_3	0·2	0·1	4·8	3·5	0·24	0·26
H_4	1·2	1·1	5·2	3·7	0·13	
H_7	0·4	0·3	6·8	4·9	0·15	0·1-
H_8	1·4	1·0	6·6	4·8	0·11	0·2
H_9	1·2	1·1	5·0	3·6	0·14	0·1-
H_{10}	0·6	0·40	6·4	4·6	0·15	0·2



endo

Table VI.9.

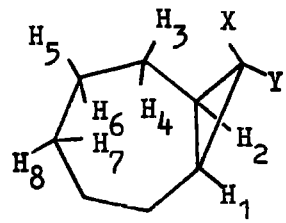
The bridgehead protons of the endo and exo isomers were assigned from integration ratios measured on 220 MHz spectra.

Those of the endo isomers appear at slightly higher field than in the exo series, possibly due to shielding by the phenyl group in the trans position.

The bridgehead protons of the gem-dichloro compound are shifted downfield compared with the parent compounds.

VI.4. N.M.R. Spectra of some Bicyclo[5.1.0]octanes.

The data for the four compounds prepared is summarised in Table VI.10.



			CHEMICAL SHIFT, p.p.m.						
N.M.R. No.	X	Y	H_1H_2	H_3H_4	H_5H_6	H_7H_8	X	Y	J c.p.s.
15	Cl	Ph	8·65	8·56	8·1-8·4	7·9	-	2·81	-
5	Cl	H	8·87	8·65	8·1	8·1	-	6·77	7·0
-	Ph	Cl	8·20	9·20	8·55	8·3	2·80	-	-
6	H	Cl	8·79	8·90	8·20	7·75	7·42	-	3·0

Table VI.10.

As in the case of the [3.1.0] and [4.1.0] hydro-chloro compounds, the trans proton appears at lower field, and has a larger coupling constant than the cis proton. Protons H_7 and H_8 occur at lowest field in both isomers, together with H_5 and H_6.

Spin decoupling of the 8-proton of the endo isomer caused the multiplet at 8·87 τ to collapse to a singlet. For the exo isomer the effect of decoupling the 8-proton was less pronounced since the coupling constant is small (3 c.p.s.). (N.M.R. No.20).

The assignments for the endo phenyl chloro compound are essentially similar to those for the parent compound. For the exo isomer, models show that H_3 and H_4 are most shielded by the phenyl ring and these are shifted upfield by 0·64 p.p.m.

APPENDIX I

KINETIC RESULTS

Run 1: Acetolysis of endo-6-chlorobicyclo[3.1.0]hexane at 75 ± 0·1°

Titrant: 0·0098N

Time (mins.)	Ml. titrant	$\log_{10}(a/a-x)$	$10^4K(sec.^{-1})$
0	1·75	-	-
10	2·92	0·0712	2·731
20	3·98	0·1476	2·832
30	4·80	0·2176	2·783
41	5·55	0·2932	2·745
50	6·13	0·3624	2·782
60	6·72	0·4463	2·854
69	7·09	0·5085	2·828
84	7·61	0·6146	2·809
91	7·82	0·6660	2·809
∞	9·49		

Mean $K_{75}° = 2·797 \times 10^{-4} \pm 0·012$ sec.$^{-1}$

Run 2: Acetolysis of endo-6-chlorobicyclo[3.1.0]hexane at 50 ± 0·1°

Titrant: 0·0098N

Time (mins.)	Ml. titrant	$\log_{10}(a/a-x)$	$10^5K(sec.^{-1})$
0	0·63	-	-
90	1·32	0·0353	1·507
270	2·51	0·1040	1·478
540	4·05	0·2128	1·512
782	5·15	0·3115	1·529
1141	6·37	0·4560	1·534
1354	6·95	0·5463	1·548
1655	7·58	0·6718	1·558
2031	8·14	0·8254	1·560
2588	8·66	1·0429	1·546
∞	9·46		

Mean $K_{50}° = 1·530 \times 10^{-5} \pm 0·009$ sec.$^{-1}$

Run 3: Acetolysis of Endo-7-chlorobicyclo[4.1.0]heptane at 150 ± 0·1°

Titrant: 0·0095N

Time (mins.)	Ml. titrant	$\log_{10}(a/a-x)$	$10^5 K(sec.^{-1})$
0	0·15	-	-
75	0·76	0·0289	1·481
140	1·26	0·0542	1·486
230	1·90	0·0888	1·482
380	2·86	0·1466	1·478
470	3·38	0·1814	1·481
572	2·92	0·2208	1·481
696	4·50	0·2675	1·475
805	4·96	0·3084	1·470
980	5·65	0·3782	1·481
1429	6·94	0·5494	1·475
∞	9·61		

Mean $K_{150}° = 1·479 \times 10^{-5} \pm 0·001$ sec.$^{-1}$

Run 4: Acetolysis of Endo-7-chlorobicyclo[4.1.0]heptane at 125 ± 0·1°

Titrant: 0·0095N

Time (mins.)	Ml. titrant	$\log_{10}(a/a-x)$	$10^6 K(sec.^{-1})$
0	0·26	-	-
1319	1·08	0·0389	1·133
2880	1·98	0·0861	1·147
4325	2·72	0·1292	1·146
5530	3·28	0·1649	1·144
7035	3·90	0·2081	1·135
8265	4·41	0·2473	1·148
9810	4·94	0·2920	1·142
12040	5·64	0·3593	1·145
12790	5·87	0·3839	1·152
14063	6·22	0·4242	1·157
∞	9·82		

Mean $K_{125}° = 1·145 \times 10^{-6} \pm 0·002$ sec.$^{-1}$

Run 5: Acetolysis of Endo-8-chlorobicyclo[5.1.0]octane at 175 ± 0·1°

Titrant: 0·0098N

Time (mins.)	Ml. titrant	$\log_{10}(a/a-x)$	$10^6 K(sec.^{-1})$
0	0·17	-	-
75	0·46	0·0128	6·560
244	1·04	0·0397	6·237
468	1·84	0·0796	6·529
832	2·84	0·1354	6·244
1140	3·62	0·1844	6·209
1473	4·42	0·2413	6·287
1839	5·00	0·2877	6·004
2485	6·21	0·4043	6·244
2947	6·82	0·4776	6·219
3734	7·58	0·5905	6·068
∞	10·14		

Mean $K_{175}^{o} = 6·260 \times 10^{-6} \pm 0·052$ sec.$^{-1}$

Run 6: Acetolysis of Endo-8-chlorobicyclo[5.1.0]octane at 150 ± 0·1°

Titrant: 0·0098N

Time (mins.)	Ml. titrant	$\log_{10}(a/a-x)$	$10^7 K(sec.^{-1})$
0	0·18	-	-
1805	0·80	0·0293	6·232
2880	1·15	0·0468	6·233
4314	1·59	0·0698	6·207
5817	2·05	0·0952	6·281
7468	2·52	0·1228	6·311
9402	2·98	0·1516	6·190
12121	3·63	0·1959	6·205
14805	4·20	0·2389	6·194
20215	5·21	0·3274	6·216
∞	9·68		

Mean $K_{150}^{o} = 6·230 \times 10^{-7} \pm 0·013$

Run 7: Acetolysis of Exo-8-chlorobicyclo[5.1.0]octane at 175 ± 0·1°

Titrant: 0·0098N

Time (mins.)	Ml. titrant	$\log_{10}(a/a-x)$	$10^4 K(sec.^{-1})$
0		-	-
10	2·14	0·0730	2·817
19	3·23	0·1386	2·799
25	3·86	0·1813	2·783
33	4·64	0·2407	2·799
39	5·12	0·2818	2·773
46	5·80	0·3475	2·899
52	6·04	0·3733	2·755
61	6·64	0·4455	2·803
73	7·28	0·5385	2·831
94	8·10	0·6971	2·846
∞	9·96		

Mean $K_{175^\circ} = 2{\cdot}810 \times 10^{-4} \pm 0{\cdot}012$ sec.$^{-1}$

Run 8: Acetolysis of Exo-8-chlorobicyclo[5.1.0]octane at 150 ± 0·1°

Titrant: 0·0098N

Time (mins.)	Ml. titrant	$\log_{10}(a/a-x)$	$10^5 K(sec.^{-1})$
0	0·30	-	-
82	1·68	0·0939	4·393
170	2·86	0·1942	4·384
213	3·37	0·2460	4·431
278	3·96	0·3147	4·344
355	4·55	0·3964	4·285
505	5·48	0·5680	4·316
622	5·98	0·6990	4·313
878	6·66	0·9820	4·292
1484	7·26	1·7051	4·409
∞	7·40		

Mean $K_{150^\circ} = 4{\cdot}352 \times 10^{-5} \pm 0{\cdot}017$ sec.$^{-1}$

Run 9: Acetolysis of Endo-7-chloro-7-phenylbicyclo[4.1.0]heptane at 125 ± 0.1°

Titrant: 0.0089N

Time (mins.)	Ml. titrant	$\log_{10}(a/a-x)$	10^5 K(sec.$^{-1}$)
0	0.28	-	-
35	0.96	0.0371	4.065
75	1.66	0.0789	4.036
131	2.55	0.1386	4.059
190	3.35	0.2003	4.045
245	4.02	0.2597	4.067
300	4.61	0.3197	4.089
375	5.26	0.3972	4.064
435	5.64	0.4498	3.968
525	6.27	0.5541	4.050
635	6.93	0.6995	4.227
∞	8.59		

Mean $K_{125}^{o} = 4.067 \times 10^{-5} \pm 0.019$ sec.$^{-1}$

Run 10. Acetolysis of Endo-7-chloro-7-phenylbicyclo[4.1.0]heptane at 100 ± 0.1°

Titrant: 0.0089N

Time (mins.)	Ml. titrant	$\log_{10}(a/a-x)$	10^6K(sec.$^{-1}$)
0	0.20	-	-
330	0.72	0.0268	3.113
751	1.35	0.0616	3.146
1110	1.84	0.0907	3.136
1503	2.35	0.1233	3.147
1860	2.77	0.1521	3.137
2610	3.57	0.2128	3.129
3240	4.22	0.2693	3.189
3930	4.78	0.3246	3.170
5540	5.90	0.4624	3.203
7210	6.63	0.5835	3.106
∞	8.90		

Mean $K_{100}^{o} = 3.148 \times 10^{-6} \pm 0.009$ sec.$^{-1}$

Run 11: Acetolysis of Exo-7-chloro-7-phenylbicyclo[4.1.0]heptane at 125 ± 0·1°

Titrant: 0·0109N

Time (mins.)	Ml. titrant	$\log_{10}(a/a-x)$	$10^4 K(sec.^{-1})$
0	0·57	-	-
10	1·23	0·0355	1·362
20	1·91	0·0754	1·446
30	2·50	0·1132	1·448
41	3·10	0·1554	1·455
51	3·59	0·1932	1·454
73	4·56	0·2794	1·469
102	5·56	0·3908	1·470
134	6·43	0·5183	1·484
162	7·14	0·6600	1·563
240	8·05	0·9563	1·529
∞	8·98		

Mean $K_{125}^{o} = 1·468 \times 10^{-4} \pm 0·016$ sec.$^{-1}$

Run 12: Acetolysis of Exo-7-chloro-7-phenylbicyclo[4.1.0]heptane at 100 ± 0·1°

Titrant: 0·0109N

Time (mins.)	Ml. titrant	$\log_{10}(a/a-x)$	$10^5 K(sec.^{-1})$
0	0·16	-	-
62	0·48	0·0163	1·007
172	1·03	0·0458	1·021
423	2·10	0·1096	0·994
785	3·41	0·2031	0·993
1122	4·45	0·2951	1·009
1500	5·30	0·3881	0·993
1860	6·01	0·4847	1·000
2254	6·62	0·5893	1·003
2851	7·28	0·7409	0·997
∞	8·86		

Mean $K_{100}^{o} = 1·002 \times 10^{-5} \pm 0·003$ sec.$^{-1}$

Run 13: Acetolysis of Endo-7-chloro-7-p-methyl-phenylbicyclo[4.1.0]-heptane at 125 ± 0.1°

Titrant: 0.0098N

Time (mins.)	Ml. titrant	$\log_{10}(a/a-x)$	$10^4 K(sec.^{-1})$
0	0.24	-	-
15	1.34	0.0642	1.641
25	1.86	0.0981	1.506
35	2.33	6.1313	1.440
50	2.93	0.1777	1.364
65	3.48	0.2251	1.329
80	3.97	0.2722	1.306
100	4.52	0.3319	1.274
120	5.02	0.3944	1.261
150	5.66	0.4903	1.254
180	6.37	0.6295	1.342
∞	8.25		

Mean $K_{125}° = 1.372 \times 10^{-4} \pm 0.037$ sec.$^{-1}$

Run 14: Acetolysis of Endo-7-chloro-7-p-methyl-phenylbicyclo[4.1.0] heptane at 100 ± 0.1°

Titrant: 0.0105N

Time (mins.)	Ml. titrant	$\log_{10}(a/a-x)$	$10^5 K(sec.^{-1})$
0	0.23	-	-
210	1.30	0.0646	1.181
408	2.21	0.1283	1.207
892	3.67	0.2553	1.098
1235	4.47	0.3447	1.071
1532	5.04	0.4219	1.057
1906	5.64	0.5214	1.050
2311	6.11	0.6192	1.028
2719	6.48	0.7156	1.010
3138	6.70	0.7849	0.960
∞	7.97		

Mean $K_{100}° = 1.074 \times 10^{-5} \pm 0.025$ sec.$^{-1}$

Run 15: Acetolysis of Exo-7-chloro-7-p-methyl-phenylbicyclo[4.1.0] heptane at 100 ± 0.1°

Titrant: 0.0098N
Ratio - exo:endo = 0.214:1

Ml. titrant (experimental)	Ml. titrant (computed)
0.80	0.82
1.55	1.54
2.56	2.51
3.14	3.10
3.99	3.99
5.21	5.24
5.97	6.03
6.86	7.01
7.60	7.65
7.97	7.99

$K_{125}^{o} = 2.40 \times 10^{-4} \pm 0.50$ sec.$^{-1}$

Run 16: Acetolysis of Exo-7-chloro-7-p-methyl-phenylbicyclo[4.1.0] heptane at 125 ± 0.1°

Titrant: 0.0098N
Ratio - exo:endo = 0.210:1

Ml. titrant (experimental)	Ml. titrant (computed)
1.12	1.13
1.75	1.79
2.12	2.22
2.78	2.84
3.21	3.32
3.80	3.94
4.83	4.83
5.80	6.03
6.50	6.52
7.67	7.75

$K_{100}^{o} = 2.60 \times 10^{-3} \pm 0.50$ sec.$^{-1}$

Run 17: Acetolysis of Exo-7-chloro-7-p-chloro-phenylbicyclo[4.1.0] heptane at 125 ± 0·1°

Titrant: 0·0095N

Time (mins.)	Ml. titrant	$\log_{10}(a/a-x)$	$10^5 K(sec.^{-1})$
0	0·49	-	-
45	1·74	0·0842	7·184
110	3·06	0·1955	6·820
135	3·48	0·2379	6·762
165	4·01	0·2980	6·931
195	4·34	0·3401	6·693
245	4·93	0·4274	6·695
295	5·41	0·5142	6·689
385	6·04	0·6631	6·610
497	6·57	0·8463	6·535
625	7·00	1·0872	6·676
∞	7·58		

Mean $K_{125}° = 6·759 \times 10^{-5} \pm 0·055$ sec.$^{-1}$

Run 18: Acetolysis of Exo-7-chloro-7-p-chloro-phenylbicyclo[4.1.0] heptane at 100 ± 0·1°

Titrant: 0·0095N

Time (mins.)	Ml. titrant	$\log_{10}(a/a-x)$	$10^6 K(sec.^{-1})$
0	0·18	-	-
160	0·55	0·0210	5·029
450	1·20	6·0604	5·155
790	1·85	0·1039	5·046
1280	2·67	0·1657	4·968
1725	3·38	0·2274	5·059
2185	3·92	0·2810	4·935
2775	4·56	0·3545	4·903
4230	5·77	0·5408	4·906
5640	6·53	0·7188	4·891
7065	7·05	0·9036	4·909
∞	8·03		

Mean $K_{100}° = 4·980 \times 10^{-6} \pm 0·027$ sec.$^{-1}$

Run 19: Acetolysis of Endo-7-chloro-7-p-fluoro-phenylbicyclo[4.1.0]heptane at 125 ± 0.1°

Titrant: 0.0098N

Time ($sec.^{-1}$)	Ml. titrant	$\log_{10}(a/a-x)$	$10^5 K(sec.^{-1})$
0	0.11	-	-
61	1.10	0.0604	3.803
109	1.78	0.1074	3.783
162	2.45	0.1593	3.774
226	3.18	0.2239	3.803
303	3.90	0.2988	3.784
390	4.59	0.3850	3.789
499	5.28	0.4928	3.790
625	5.89	0.6171	3.789
842	6.61	0.8327	3.795
1049	7.03	1.0370	3.793
∞	7.73		

Mean $K_{125}^{o} = 3.790 \times 10^{-5} \pm 0.055\ sec.^{-1}$

Run 20: Acetolysis of Endo-7-chloro-7-p-fluoro-phenylbicyclo[4.1.0]heptane at 100 ± 0.1°

Titrant: 0.0098N

Time ($sec.^{-1}$)	Ml. titrant	$\log_{10}(a/a-x)$	$10^6 K(sec.^{-1})$
0	0.16	-	-
811	1.36	0.0613	2.903
1442	2.20	0.1101	2.930
2261	3.18	0.1749	2.969
2840	3.79	0.2207	2.983
3691	4.51	0.2819	2.931
4863	5.43	0.3752	2.961
5773	6.08	0.4557	3.029
7205	6.82	0.5704	3.038
8683	7.37	0.6808	3.009
10090	7.80	0.7922	3.013
∞	9.27		

Mean $K_{100}^{o} = 2.977 \times 10^{-6} \pm 0.014\ sec.^{-1}$

Run 21: Acetolysis of Exo-7-chloro-7-p-fluoro-phenylbicyclo[4.1.0]-heptane at 125 ± 0·1°

Titrant: 0·0091N

Time (mins.)	Ml. titrant	$\log_{10}(a/a-x)$	$10^4 K(sec.^{-1})$
0	0·25	-	-
10	1·16	0·0050	1·918
20	1·96	0·0993	1·904
30	2·65	0·1468	1·877
40	3·29	0·1960	1·880
50	3·86	0·2451	1·881
65	4·57	0·3153	1·861
82	5·26	0·3964	1·855
95	5·73	0·4618	1·866
135	6·70	0·6394	1·818
172	7·40	0·8364	1·866
∞	8·62		

Mean $K_{125}° = 1·873 \times 10^{-4} \pm 0·008$ sec.$^{-1}$

Run 22: Acetolysis of Exo-7-chloro-7-p-fluoro-phenylbicyclo[4.1.0]-heptane at 100 ± 0·1°

Titrant: 0·0085N

Time (mins.)	Ml. titrant	$\log_{10}(a/a-x)$	$10^5 K(sec.^{-1})$
0	0·57	-	-
180	1·70	0·0684	1·459
272	2·23	0·1047	1·477
505	3·38	0·1956	1·486
770	4·37	6·2927	1·459
990	5·09	0·3801	1·473
1321	6·01	0·5257	1·527
1575	6·41	0·6083	1·482
1903	6·94	0·7494	1·511
2190	7·37	0·9116	1·597
2850	7·77	1·1489	1·547
∞	8·32		

Mean $K_{100}° = 1·502 \times 10^{-5} \pm 0·013$ sec.$^{-1}$

Run 23: Acetolysis of Exo-6-chloro-6-phenylbicyclo[3.1.0]hexane at 125 ± 0.1°

Titrant: 0.0098N

Time (mins.)	Ml. titrant	$\log_{10}(a/a-x)$	$10^4 K(sec.^{-1})$
0	0.26	-	-
20	1.70	0.0766	1.469
30	2.34	0.1155	1.477
40	2.91	0.1533	1.471
50	3.44	0.1917	1.472
60	3.93	0.2305	1.475
80	4.78	0.3074	1.475
100	5.48	0.3829	1.469
120	6.08	0.4599	1.471
140	6.58	0.5366	1.471
160	7.01	0.6154	1.476
∞	9.17		

Mean $K_{125}° = 1.472 \times 10^{-4} \pm 0.001$ sec.$^{-1}$

Run 24: Acetolysis of Exo-6-chloro-6-phenylbicyclo[3.1.0]hexane at 100 ± 0.1°

Titrant: 0.0098N

Time (mins.)	Ml. titrant	$\log_{10}(a/a-x)$	$10^5 K(sec.^{-1})$
0	0.15	-	-
160	1.15	0.0507	1.217
351	2.16	0.1088	1.190
560	3.13	0.1730	1.185
805	4.13	0.2509	1.196
1314	5.69	0.4098	1.197
1515	6.15	0.4705	1.192
1711	6.54	0.5295	1.188
2157	7.26	0.6654	1.184
2748	7.93	0.8470	1.183
3450	8.32	1.0033	1.116
∞	9.22		

Mean $K_{100}° = 1.185 \times 10^{-5} \pm 0.008$ sec.$^{-1}$

Run 25: Acetolysis of Exo-6-chloro-6-p-methyl-phenylbicyclo[3.1.0]-hexane at 100 ± 0.1°

Titrant: 0.0011N

Time (mins.)	Ml. titrant	$\log_{10}(a/a-x)$	$10^4 K(sec.^{-1})$
0	2.62	-	-
15	4.09	0.1020	2.611
21	4.58	0.1422	2.598
30	5.25	0.2039	2.608
48	6.32	0.3252	2.600
81	7.65	0.5475	2.594
93	8.01	0.6342	2.617
112	8.43	0.7636	2.616
130	8.71	0.8779	2.591
146	8.92	0.9890	2.600
158	9.02	1.0540	2.560
∞	9.64		

Mean $K_{100}° = 2.600 \times 10^{-4} \pm 0.005$ sec.$^{-1}$

Run 26: Acetolysis of Exo-6-chloro-6-p-methyl-phenylbicyclo[3.1.0]-hexane at 75 ± 0.1°

Titrant: 0.0011N

Time (mins.)	Ml. titrant	$\log_{10}(a/a-x)$	$10^5 K(sec.^{-1})$
0	0.07	-	-
189	1.79	0.0877	1.782
318	2.82	0.1503	1.814
410	3.43	0.1921	1.798
549	4.19	0.2505	1.751
676	4.94	0.3170	1.800
816	5.68	0.3945	1.855
977	6.21	0.4599	1.807
1273	7.10	0.5984	1.804
1599	7.82	0.7556	1.814
1804	8.13	0.8460	1.800
∞	9.47		

Mean $K_{75}° = 1.802 \times 10^{-5} \pm 0.008$ sec.$^{-1}$

Run 27: Acetolysis of Exo-6-chloro-6-p-chloro-phenylbicyclo[3.1.0]-hexane at 125 ± 0·1°

Titrant: 0·0101N

Time (mins.)	Ml. titrant	$\log_{10}(a/a-x)$	$10^5 K(sec.^{-1})$
0	0·18	-	-
38	1·03	0·0595	6·008
78	1·81	0·1223	6·019
108	2·32	0·1690	6·004
161	3·07	0·2481	5·915
203	3·60	0·3143	5·941
248	4·08	0·3844	5·949
318	4·67	0·4897	5·910
399	5·26	0·6290	6·050
538	5·85	0·8354	5·959
638	6·15	0·9961	5·992
∞	6·82		

Mean $K_{125}° = 5·975 \times 10^{-5} \pm 0·014$ sec.$^{-1}$

Run 28: Acetolysis of Exo-6-chloro-6-p-chloro-phenylbicyclo[3.1.0]-hexane at 100 ± 0·1°

Titrant: 0·0121N

Time (mins.)	Ml. titrant	$\log_{10}(a/a-x)$	$10^6 K(sec.^{-1})$
0	0·14	-	-
437	0·73	0·0547	4·799
1020	1·41	0·1276	4·799
1440	1·84	0·1809	4·821
1868	2·21	0·2327	4·781
2478	2·68	0·3089	4·784
3000	3·00	0·3697	4·730
4155	3·59	0·5106	4·716
5352	4·04	0·6607	4·737
6183	4·25	0·7536	4·678
7103	4·48	0·8852	4·783
∞	5·13		

Mean $K_{100}° = 4·763 \times 10^{-6} \pm 0·014$ sec.$^{-1}$

Run 29: Acetolysis of Exo-6-chloro-6-p-fluoro-phenylbicyclo[3.1.0]-hexane at 100 ± 0.1°

Titrant: 0.0098N

Time (mins.)	Ml. titrant	$\log_{10}(a/a-x)$	K(sec.$^{-1}$)
0	1.47	-	-
39	2.24	0.0523	5.19
96	3.04	0.1149	4.60
169	3.72	0.1762	4.00
271	4.40	0.2472	3.50
441	5.01	0.3228	2.81
808	6.39	0.5669	2.69
1390	7.26	0.8471	2.34
1886	7.64	1.0660	2.19
∞	8.22		

Mean K_{100° = 2.5×10^{-5} *

*This is an approximate value of the rate constant, extrapolated from a graph of K vs. time. The sample was contaminated by ~10% of solvolysable ring opened products produced during the preparation and work-up procedure.

Run 30: Acetolysis of Endo-1,7-diphenyl-7-chlorobicyclo[4.1.0]heptane at 125 ± 0·1°

Titrant: 0·0108N

Time (mins.)	Ml. titrant	$\log_{10}(a/a-x)$	$10^4K(sec.^{-1})$
0	0·30	-	-
5	1·22	0·0711	5·459
10	1·99	0·1412	5·417
15	2·64	0·2106	5·388
21	3·30	0·2947	5·385
25	3·69	0·3533	5·423
30	4·08	0·4210	5·386
35	4·45	0·4968	5·447
40	4·71	0·5593	5·366
50	5·18	0·7018	5·387
60	5·50	0·8350	5·342
∞	6·39		

Mean $K_{125}° = 5·400 \times 10^{-4} \pm 0·011$ sec.$^{-1}$

Run 31: Acetolysis of Endo-1,7-diphenyl-7-chlorobicyclo[4.1.0]heptane at 100 ± 0·1°

Titrant: 0·0108N

Time (mins.)	Ml. titrant	$\log_{10}(a/a-x)$	$10^5K(sec.^{-1})$
0	0·41	-	-
45	1·12	0·0561	4·783
90	1·77	0·1147	4·890
150	2·52	0·1939	4·960
210	3·14	0·2723	4·977
271	3·67	0·3529	4·997
350	4·21	0·4540	4·978
448	4·72	0·5776	4·948
560	5·18	0·7305	5·006
767	5·68	0·9970	4·989
1046	6·00	1·3365	4·904
1596	6·20	1·9228	4·623
∞	6·27		

Mean $K_{100}° = 4·914 \times 10^{-5} \pm 0·030$ sec.$^{-1}$

Run 32: Acetolysis of Endo-8-chloro-8-phenylbicyclo[5.1.0]octane at 150 ± 0·1°

Titrant: 0·0100N

Time (mins.)	Ml. titrant	$\log_{10}(a/a-x)$	$10^5 K(sec.^{-1})$
0	0·10	-	-
60	1·58	0·0747	4·775
95	2·35	0·1193	4·818
130	3·01	0·1615	4·768
180	3·89	0·2251	4·799
223	4·53	0·2780	4·784
261	5·02	0·3234	4·755
315	5·69	0·3943	4·803
396	6·45	0·4917	4·765
482	7·09	0·5952	4·739
847	8·61	1·0372	4·700
∞	9·47		

Mean $K_{150}° = 4·771 \times 10^{-5} \pm 0·010$ sec.$^{-1}$

Run 33: Acetolysis of Endo-8-chloro-8-phenylbicyclo[5.1.0]octane at 125 ± 0·1°

Titrant: 0·0105N

Time (mins.)	Ml. titrant	$\log_{10}(a/a-x)$	$10^6 K(sec.^{-1})$
0	0·11	-	-
300	0·80	0·0349	4·468
1089	2·40	0·1287	4·535
1537	3·17	0·1822	4·550
1991	3·86	0·2365	4·559
2477	4·50	0·2938	4·552
2941	5·06	0·3510	4·580
3766	5·87	0·4498	4·583
4390	6·41	0·5309	4·641
5166	6·90	0·6204	4·609
6475	7·59	0·7895	4·679
∞	9·04		

Mean $K_{125}° = 4·576 \times 10^{-6} \pm 0·018$ sec.$^{-1}$

Run 34: Acetolysis of Exo-8-chloro-8-phenylbicyclo[5.1.0]octane at 150 ± 0.1°

Titrant: 0.0098N

Ml. titrant (experimental)	Ml. titrant (calculated)
0.75	0.78
2.04	1.90
3.20	3.33
3.63	3.74
3.88	4.07
4.51	4.55
5.51	5.44
6.24	6.14
7.15	7.06
7.97	7.78

$K_{150^\circ} = 4.00 \times 10^{-3} \pm 0.50$ sec.$^{-1}$

Run 35: Acetolysis of Exo-8-chloro-8-phenylbicyclo[5.1.0]octane at 125 ± 0.1°

Titrant: 0.0098N

Ml. titrant (experimental)	Ml. titrant (calculated)
1.27	1.22
2.42	2.31
3.06	3.16
3.46	3.68
3.99	4.10
4.68	4.73
6.07	5.85
6.34	6.27
7.19	7.04
7.85	7.80

$K_{125^\circ} = 7.50 \times 10^{-4} \pm 0.50$ sec.$^{-1}$

Run 36: Acetolysis of 6,6-Dichlorobicyclo[3.1.0]hexane at 125 ± 0·1°

Titrant: 0·0089N

Time (mins.)	Ml. titrant	$\log_{10}(a/a-x)$	$10^4 K(sec.^{-1})$
0	0·17	-	-
23	1·51	0·0594	0·991
39	2·41	0·1044	1·028
57	3·20	0·1482	0·998
73	3·97	0·1956	1·028
86	4·53	0·2336	1·042
102	5·31	0·2928	1·102
118	5·65	0·3214	1·045
131	6·05	0·3576	1·048
162	6·82	0·4372	1·036
206	7·64	0·5418	1·009
∞	10·65		

Mean $K_{125}^{o} = 1·033 \times 10^{-4} \pm 0·010$ sec.$^{-1}$

Run 37: Acetolysis of 6,6-Dichlorobicyclo[3.1.0]hexane at 100 ± 0·1°

Titrant: 0·0089N

Time (mins.)	Ml. titrant	$\log_{10}(a/a-x)$	$10^6 K(sec.^{-1})$
0	0·09	-	-
239	1·44	0·0594	0·954
362	2·12	0·0927	0·983
570	2·93	0·1360	0·916
682	3·51	0·1699	0·956
1290	5·80	0·3379	1·005
1512	6·41	0·3963	1·006
1807	7·06	0·4686	0·995
2033	7·49	0·5240	0·989
2767	8·38	0·6676	0·926
3209	8·98	0·8009	0·958
∞	10·65		

Mean $K_{100}^{o} = 9·688 \times 10^{-6} \pm 0·096$ sec.$^{-1}$

Run 38: Acetolysis of 7,7-Dichlorobicyclo[4.1.0]heptane at 175 ± 0.1°

Titrant: 0.0098N

Time (mins.)	Ml. titrant	$\log_{10}(a/a-x)$	$10^5 K(sec.^{-1})$
0	0.21	-	-
5	0.35	0.0067	5.111
10	0.43	0.0105	4.034
15	0.52	0.0149	3.808
20	0.63	0.0203	3.894
25	0.72	0.0248	3.802
32	0.86	0.0318	3.816
40	0.93	0.0354	3.396
49	1.18	0.0484	3.790
61	1.39	0.0596	3.750
73	1.65	0.0739	3.886
∞	9.41		

Mean $K_{175}^{o} = 3.928 \times 10^{-5} \pm 0.134$ sec.$^{-1}$

Run 39: Acetolysis of 7,7-Dichlorobicyclo[4.1.0]heptane at 150 ± 0.1°

Titrant: 0.0091N

Time (mins.)	Ml. titrant	$\log_{10}(a/a-x)$	$10^6 K(sec.^{-1})$
0	0.16	-	-
45	0.28	0.0059	5.005
87	0.41	0.0123	5.433
150	0.57	0.0204	5.216
180	0.64	0.0239	5.109
225	0.77	0.0307	5.234
287	0.94	0.0396	5.301
330	1.12	0.0493	5.737
376	1.21	0.6543	5.538
414	1.40	0.0648	6.011
474	1.53	0.0722	5.850
∞	9.10		

Mean $K_{150}^{o} = 5.444 \times 10^{-6} \pm 0.100$ sec.$^{-1}$

Run 40: Acetolysis of Exo-6-chlorobicyclo[3.1.0]hexane at 175 ± 0·1°

Ampoules were removed and analysed at 2 day intervals for 30 days. Although considerable darkening of the solution took place, especially toward the end of this period, no chloride ion was observed assuming a detection limit of reaction of 0·5%

$$K_{125}^{o} < 1{\cdot}0 \times 10^{-12} \text{ sec.}^{-1}$$

Run 41: Acetolysis of Exo-7-chlorobicyclo[4.1.0]heptane at 175 ± 0·1°

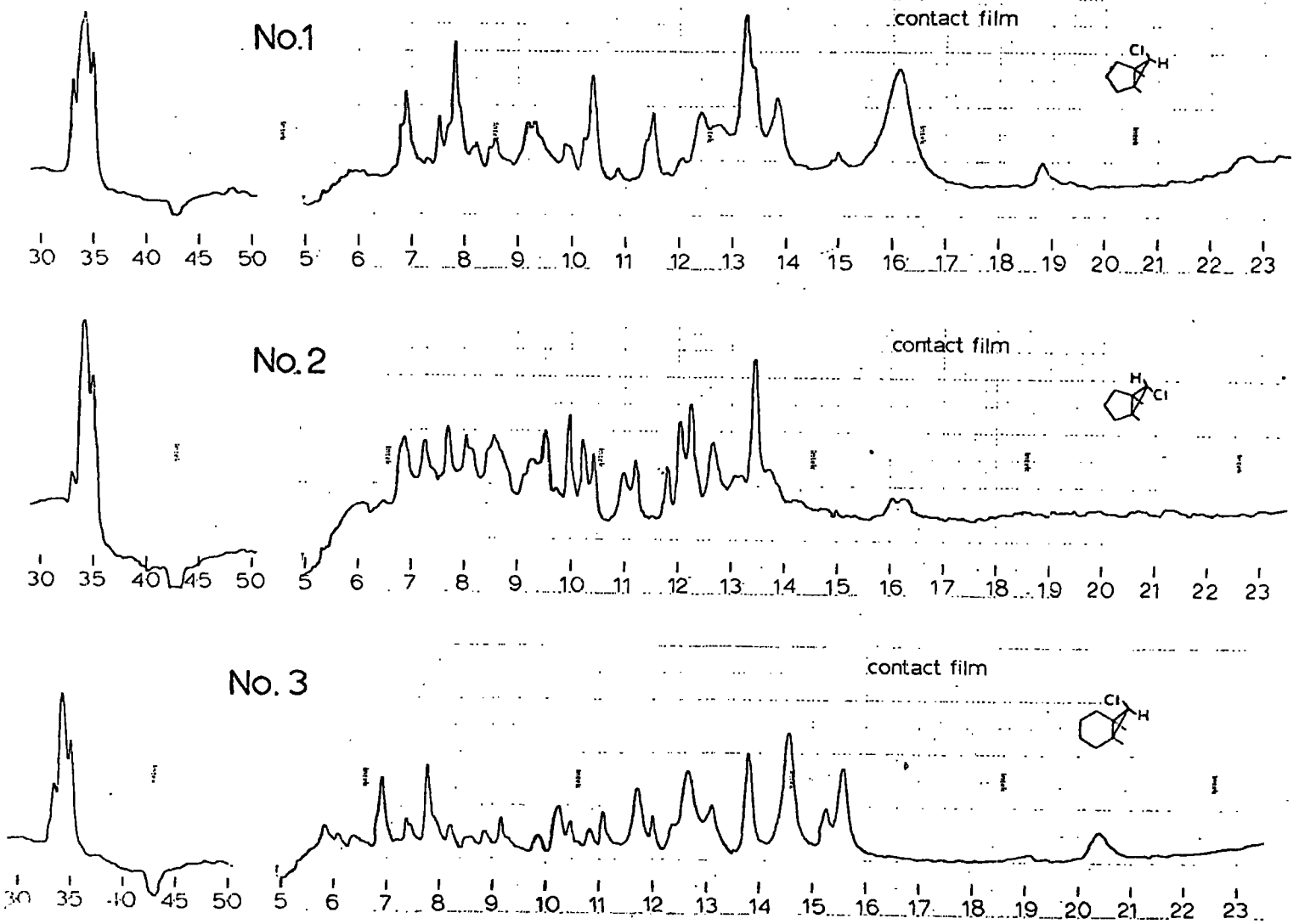
Ampoules were removed and analysed as in Run 40. Again considerable darkening took place but no solvolysis was observed.

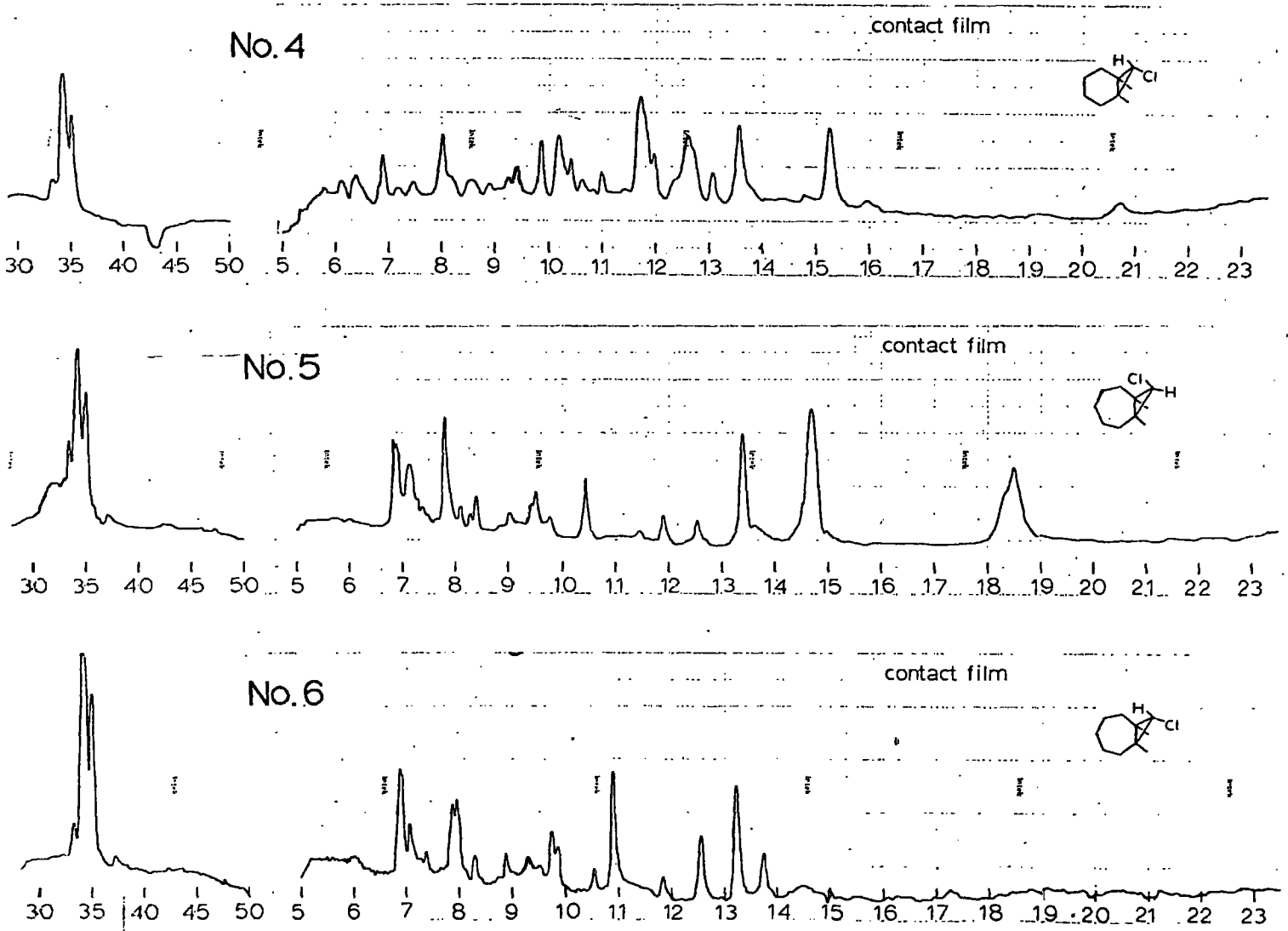
$$K_{125}^{o} < 1{\cdot}0 \times 10^{-10} \text{ sec.}^{-1}$$

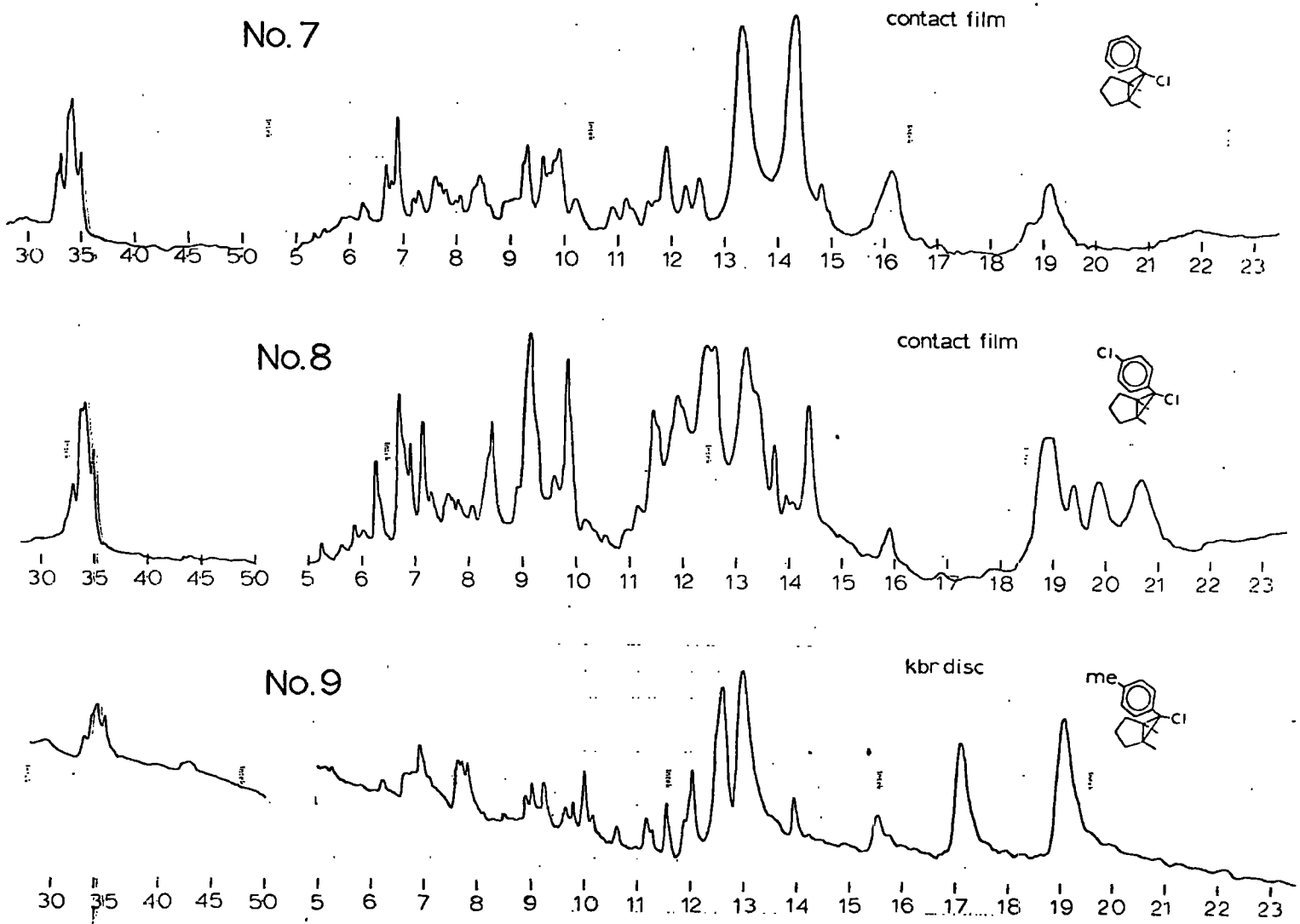
APPENDIX II

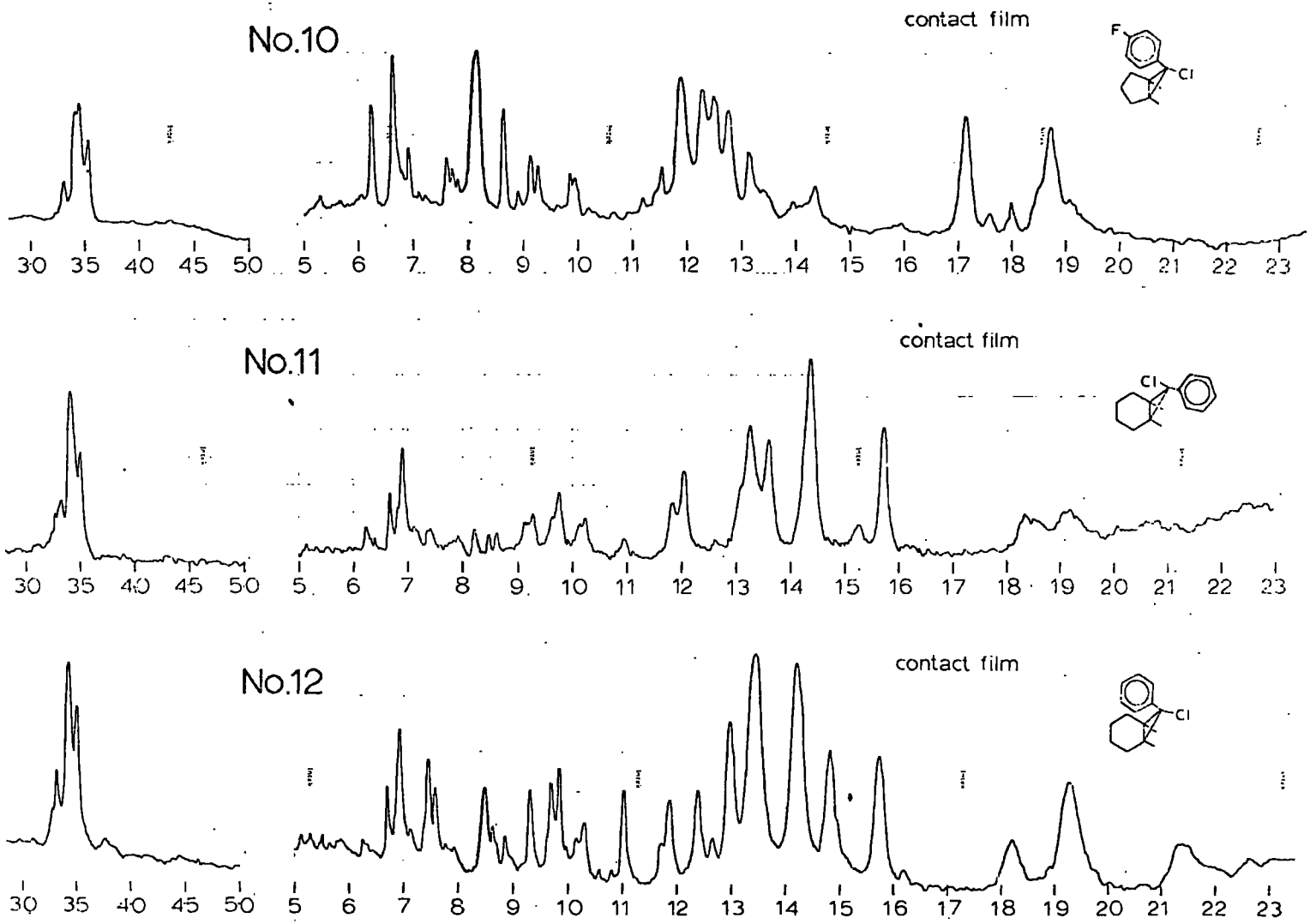
INFRARED SPECTRA

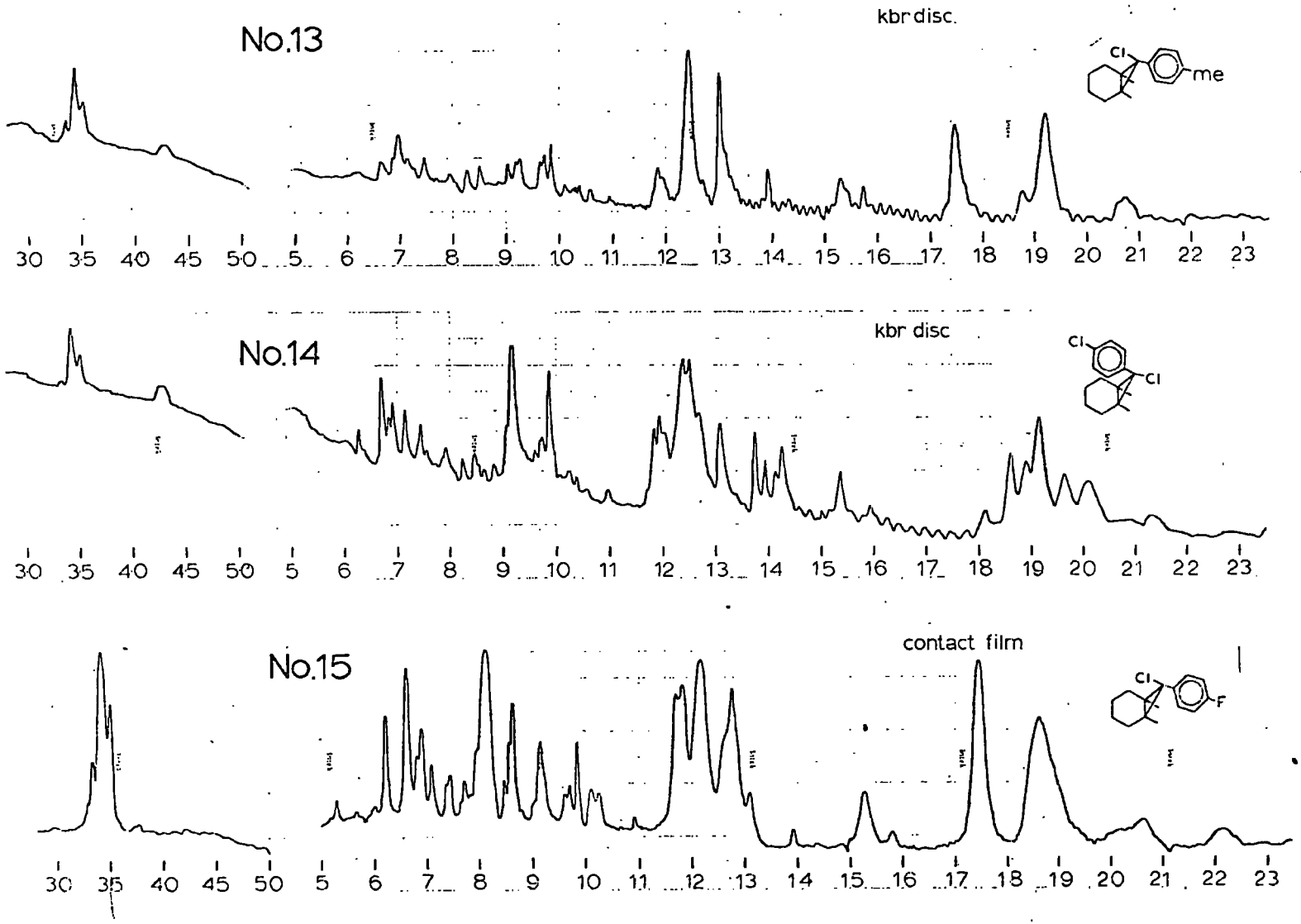
INDEX OF INFRARED SPECTRA


No.1
contact film
Cl
H
30 35 40 45 50
5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23
No.2
contact film
H
Cl
30 35 40 45 50
5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23
No. 3
contact film
Cl
H
30 35 40 45 50
5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23


No.4
contact film
H
Cl
30 35 40 45 50 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23
No.5
contact film
Cl
H
30 35 40 45 50 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23
No.6
contact film
H
Cl
30 35 40 45 50 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23


No. 7
contact film
Cl
30 35 40 45 50 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23
No.8
contact film
Cl
Cl
30 35 40 45 50 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23
No.9
kbr disc
me
Cl
30 35 40 45 50 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23


No.10
contact film
F
Cl
30 35 40 45 50 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23
No.11
contact film
Cl
30 35 40 45 50 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23
No.12
contact film
Cl
30 35 40 45 50 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23


No.13
kbr disc.
Cl
me
30 35 40 45 50 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23
No.14
kbr disc
Cl
Cl
30 35 40 45 50 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23
No.15
contact film
Cl
F
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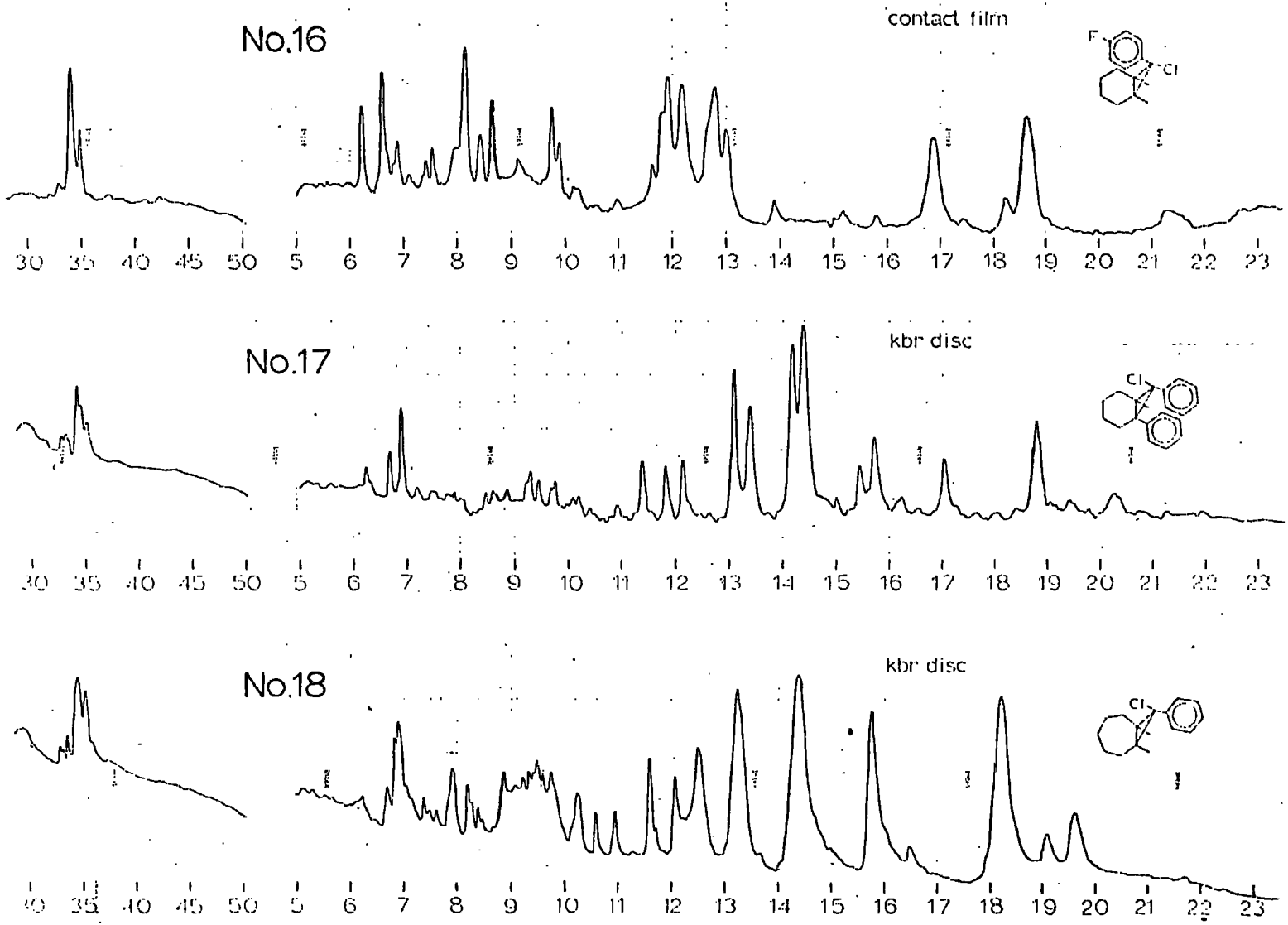
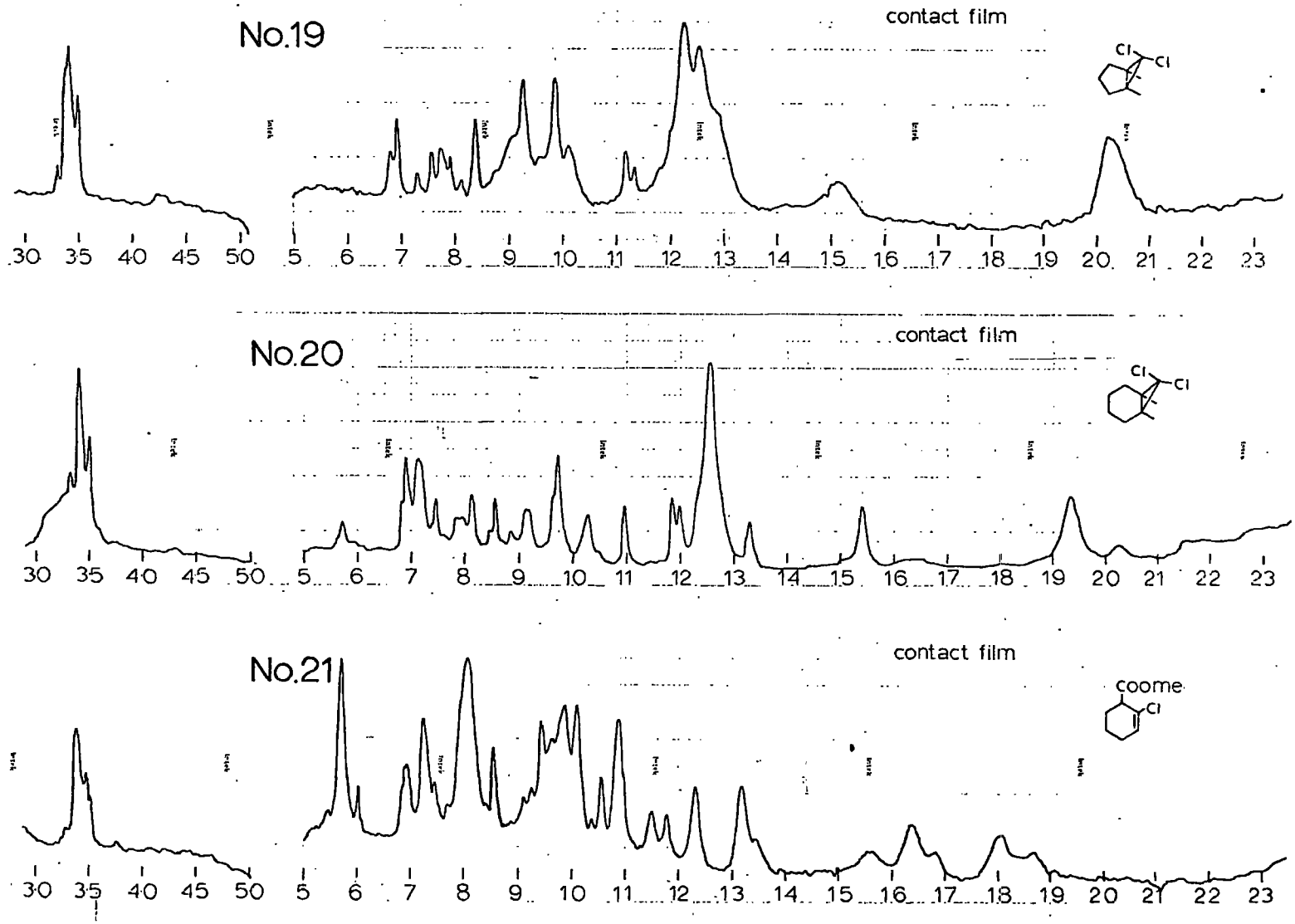
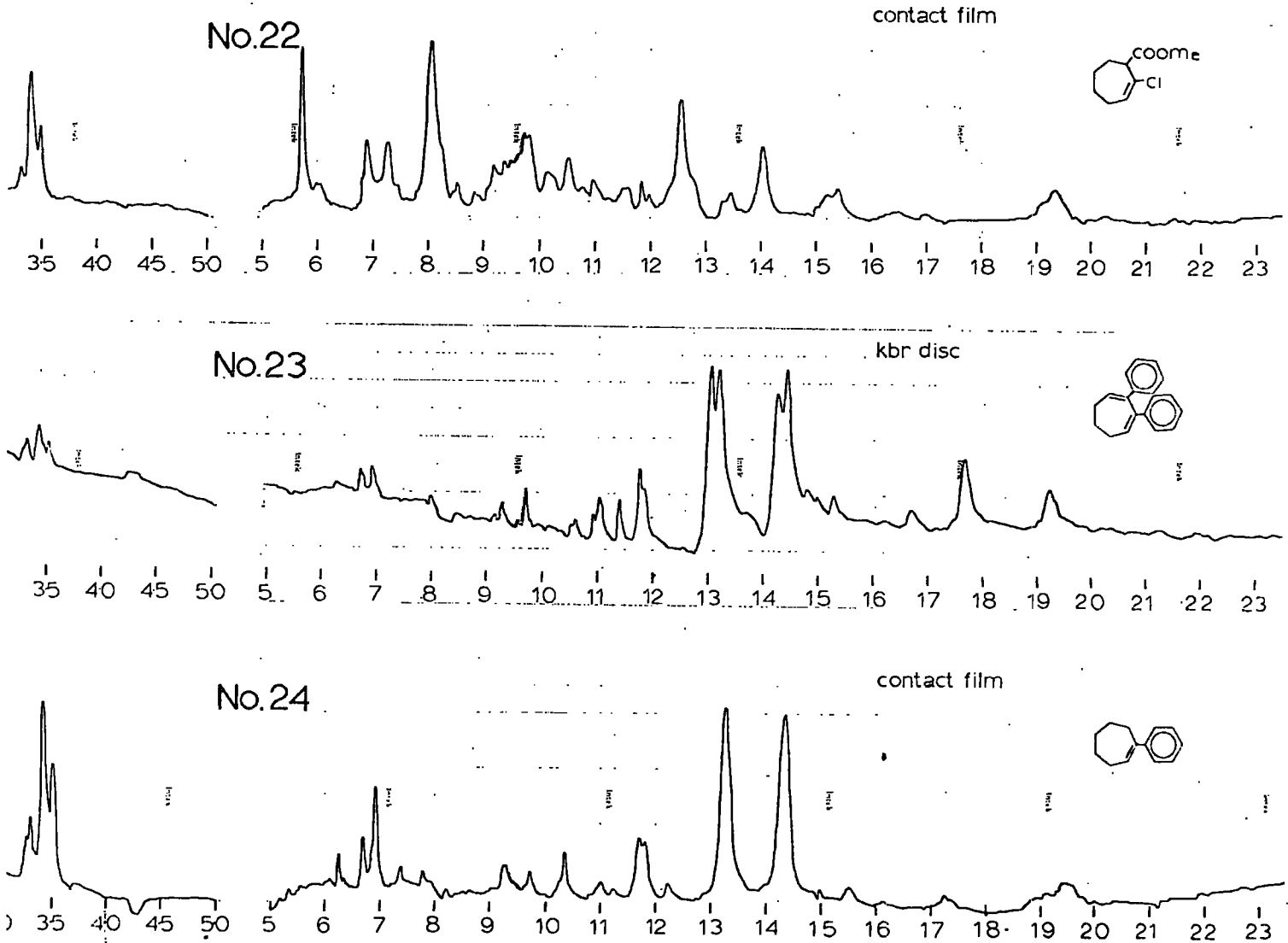

No.16
contact film
F
Cl
30 35 40 45 50 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23
No.17
kbr disc
Cl
30 35 40 45 50 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23
No.18
kbr disc
Cl
30 35 40 45 50 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23

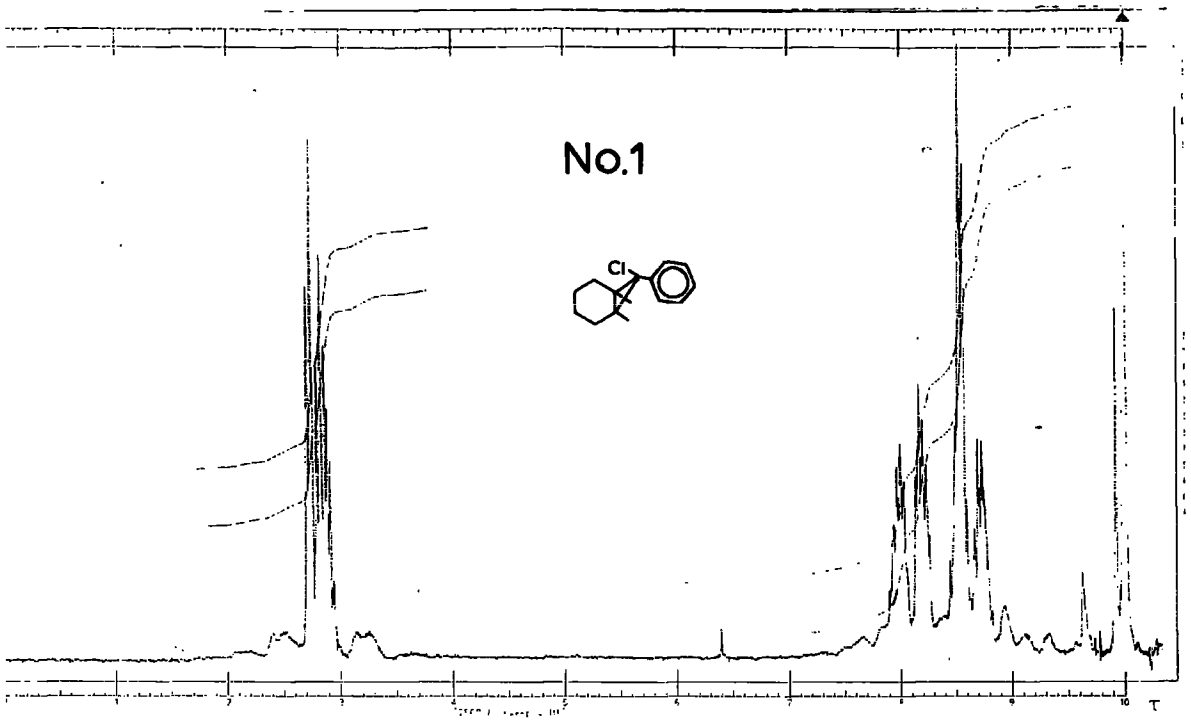

No.19
contact film
Cl
Cl
30 35 40 45 50
5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23
No.20
contact film
Cl
Cl
30 35 40 45 50
5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23
No.21
contact film
coome
Cl
30 35 40 45 50
5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23

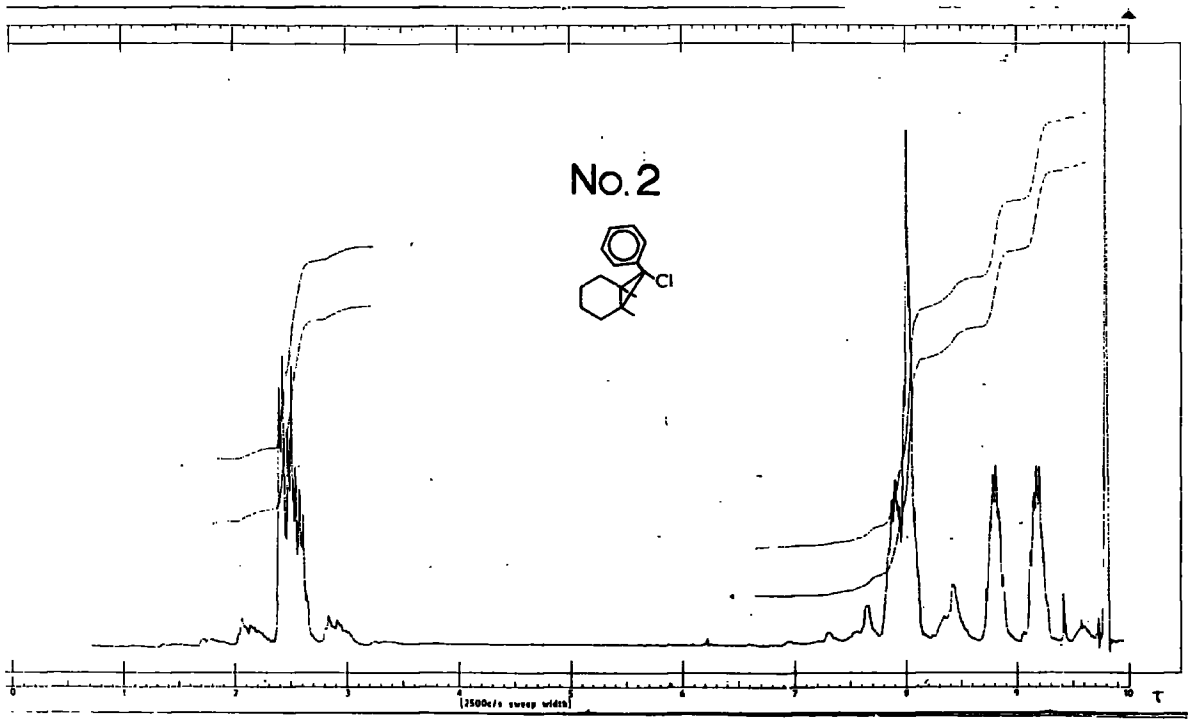

No.22
contact film
coome
Cl
35 40 45 50 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23
No.23
kbr disc
35 40 45 50 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23
No.24
contact film
35 40 45 50 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23

APPENDIX III

^1H N.M.R. SPECTRA

INDEX OF ^{1}H N.M.R. SPECTRA


No.1
Cl
τ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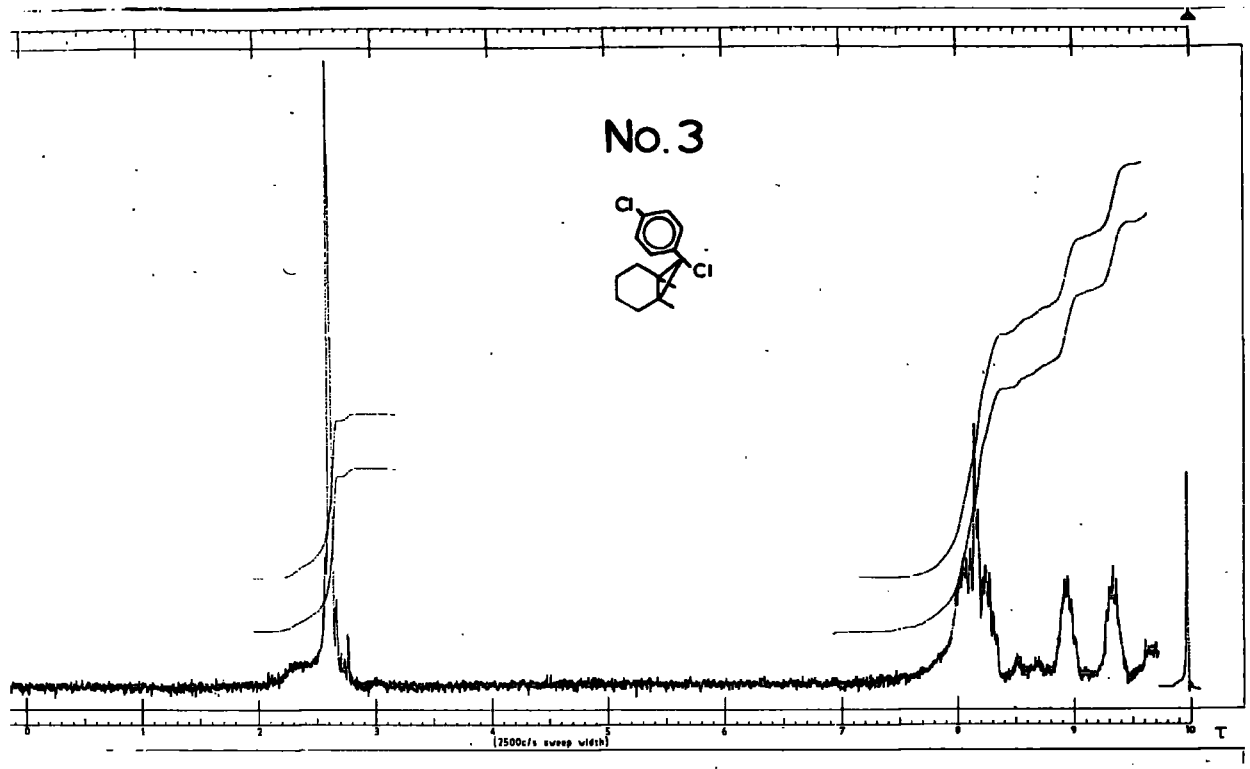
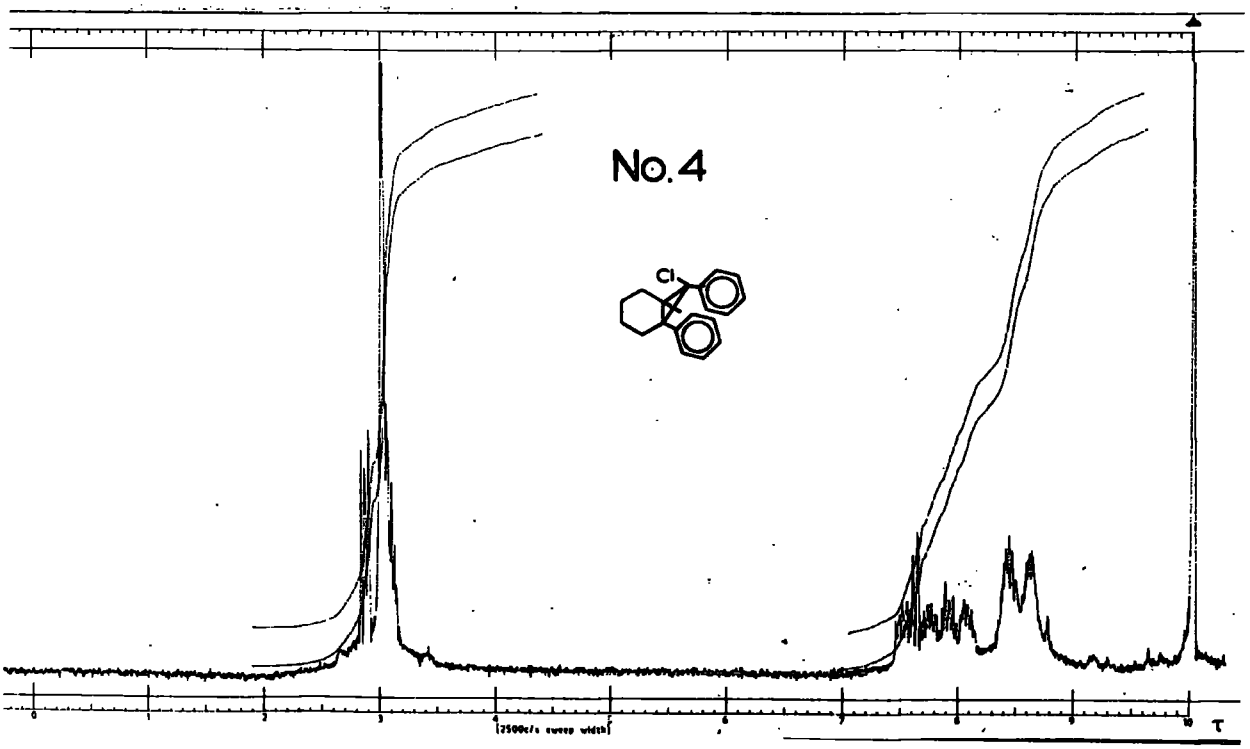
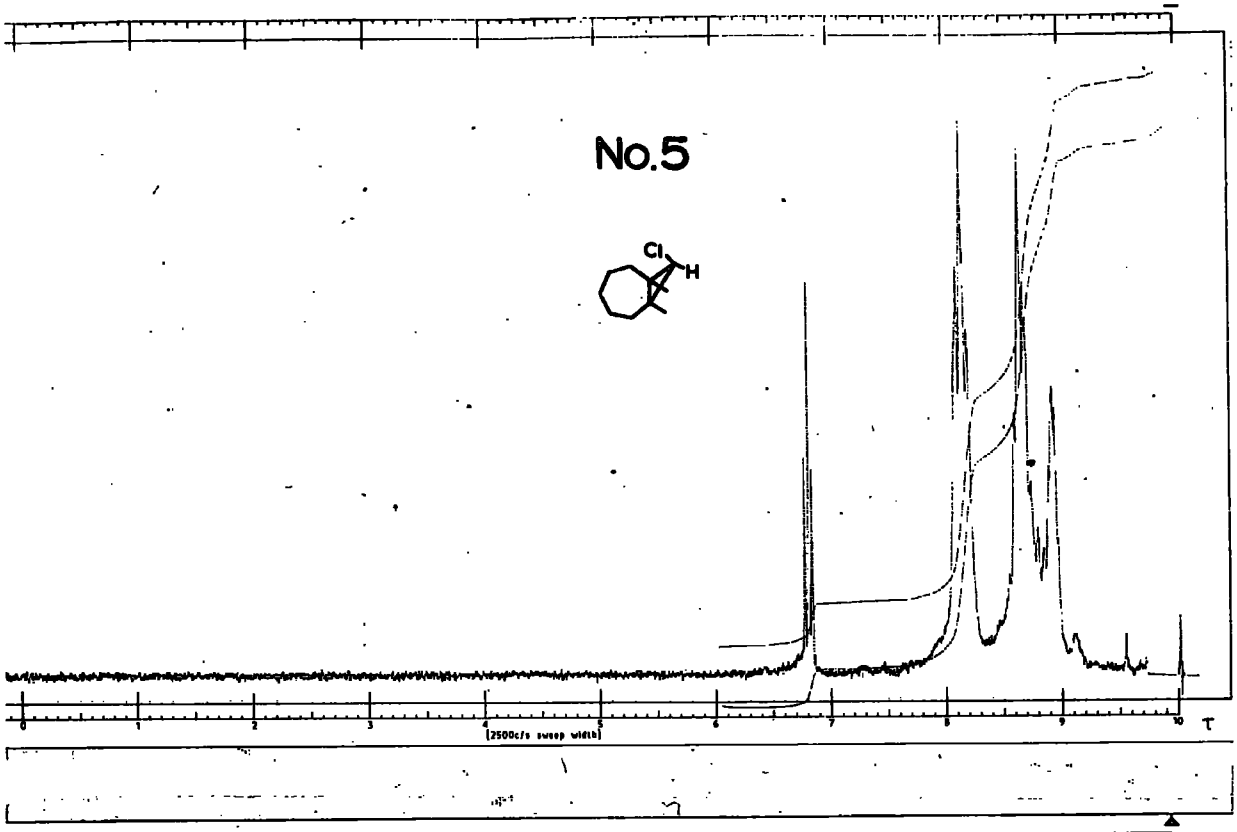
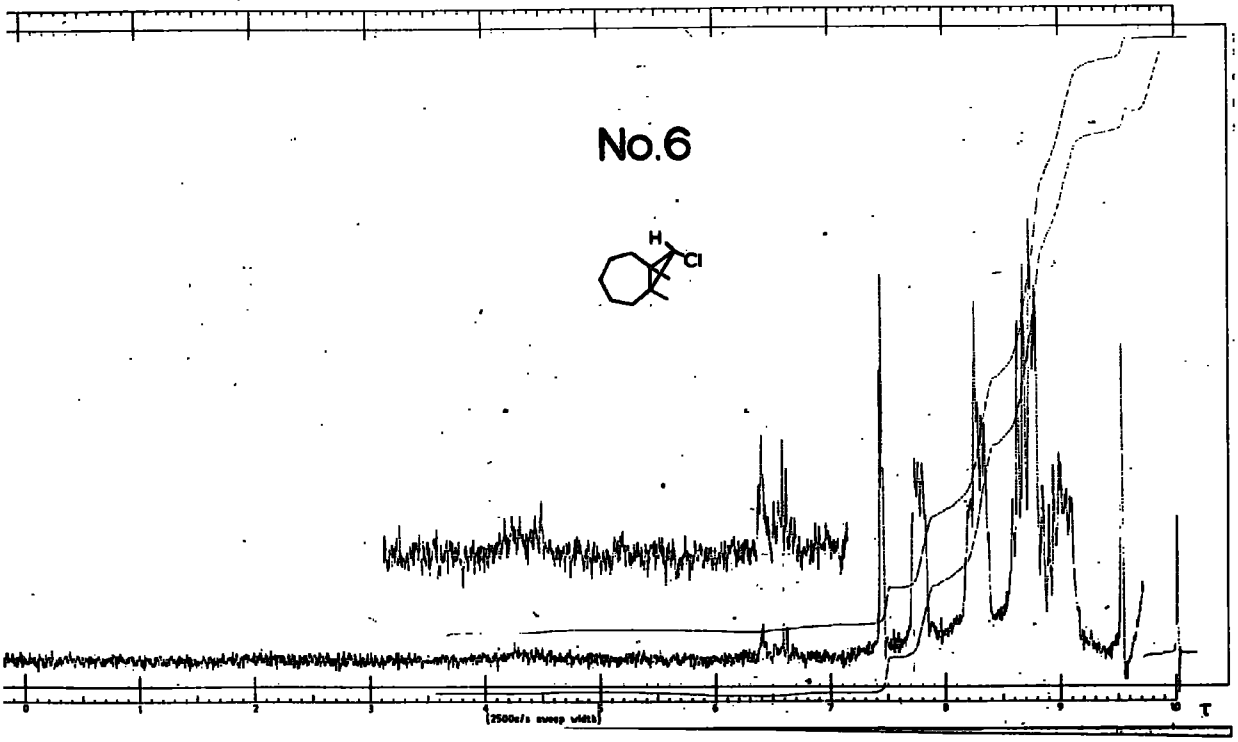
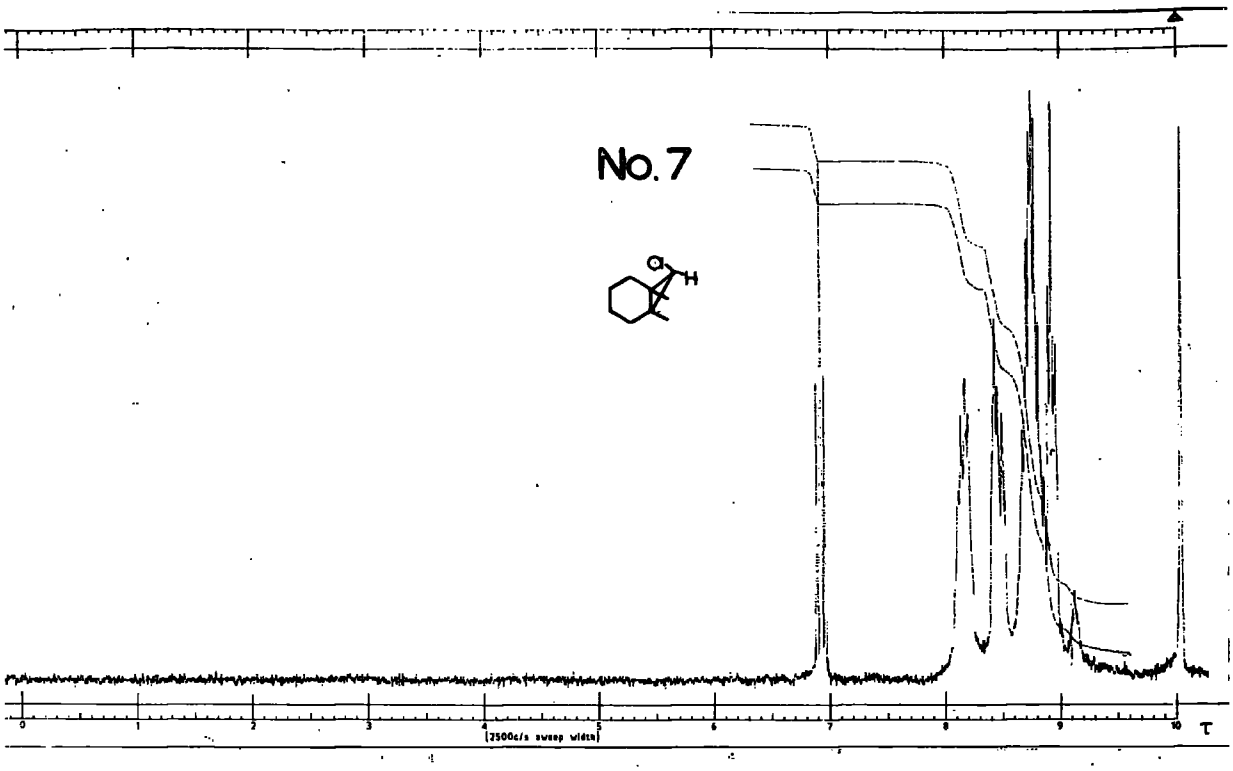
Cl
τ

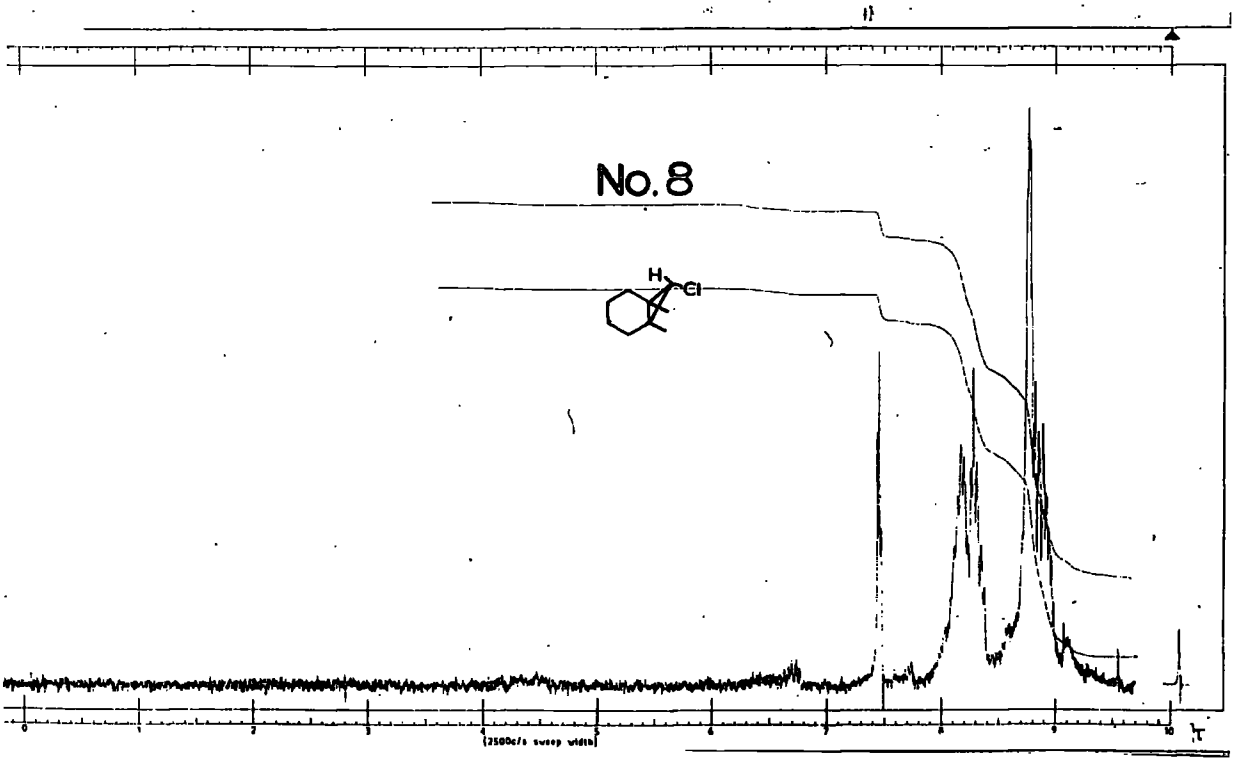

No. 3
Cl
Cl
τ


No. 4
Cl
τ


No.5
Cl
H
0
1
2
3
4
5
6
7
8
9
10
τ
[2500c/s sweep width]


No.6
H
Cl
0
1
2
3
4
5
6
7
8
9
10
τ
[2500c/s sweep width]


No. 7
O
H
0
1
2
3
4
(2500c/s sweep width)
5
6
7
8
9
10
τ


No. 8
H
Cl
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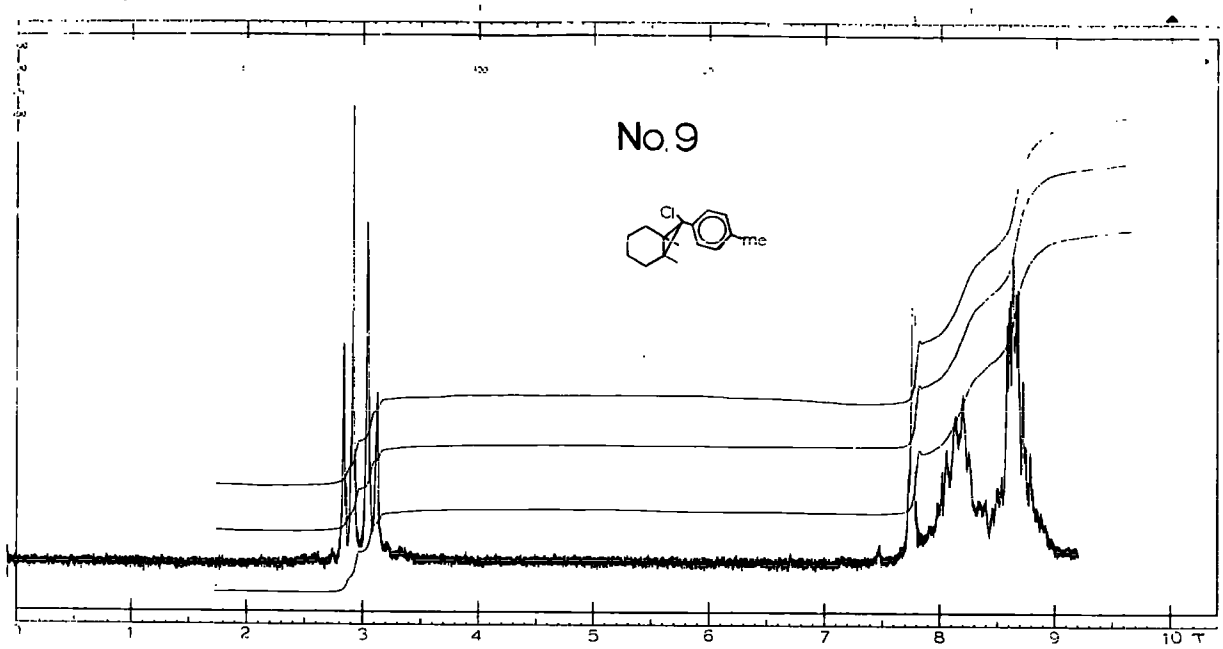
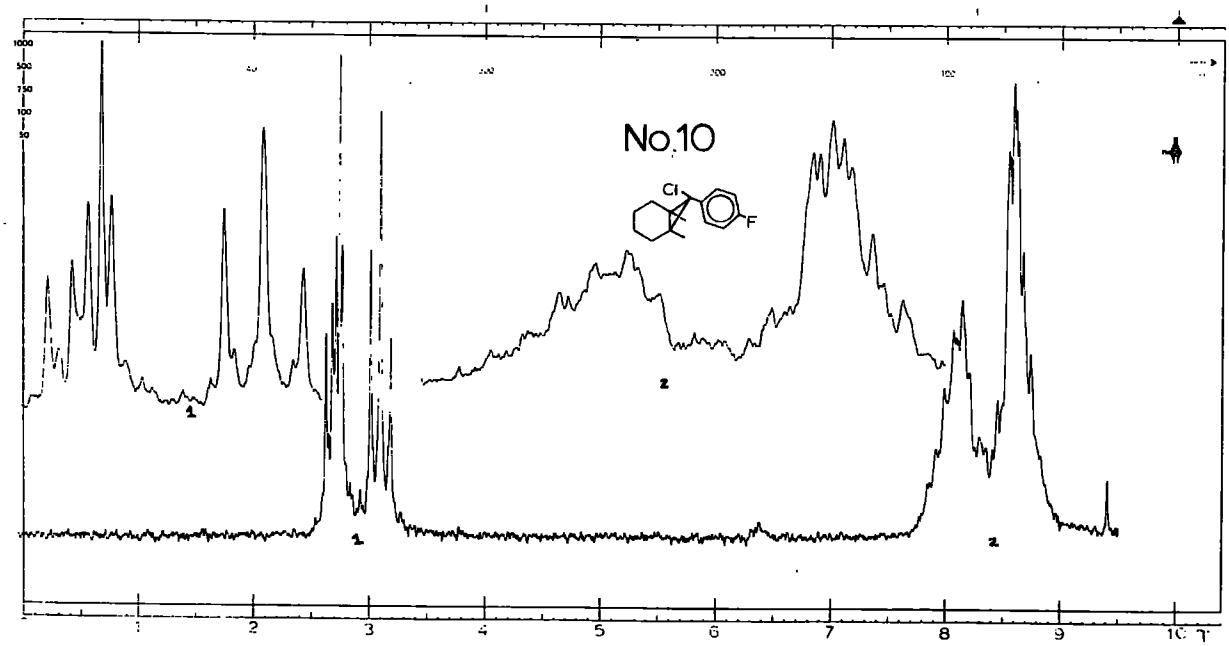
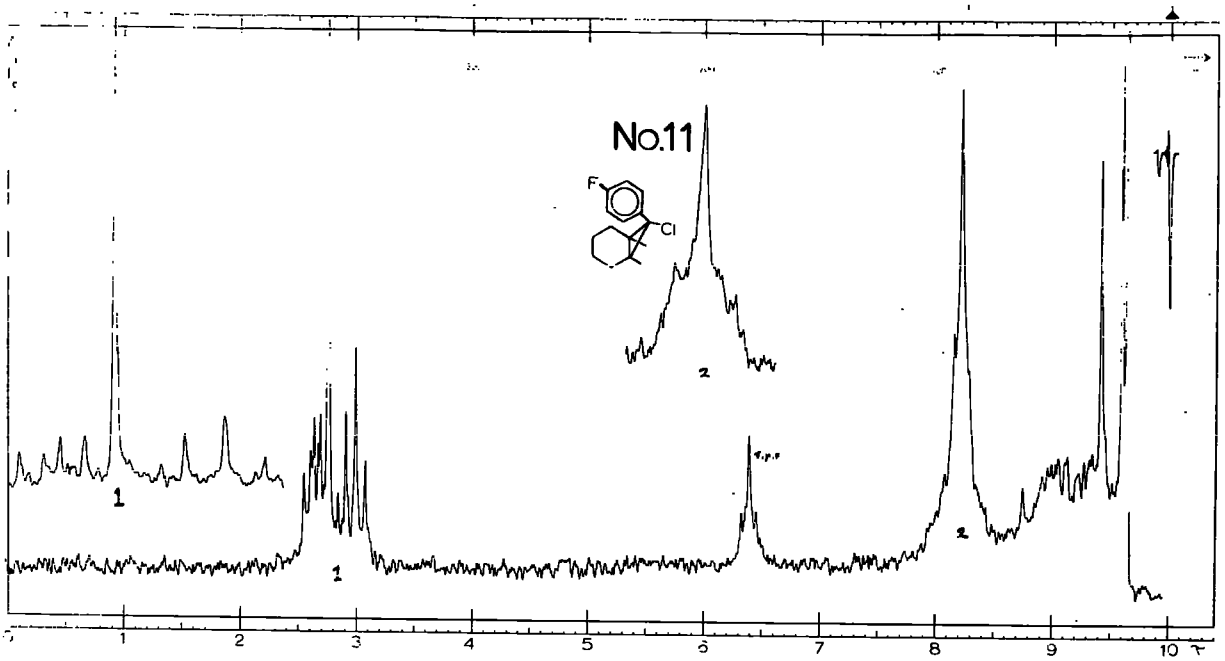
1
2
3
4
(2500c/s sweep width)
5
6
7
8
9
10
τ


No. 9
Cl
me
1 2 3 4 5 6 7 8 9 10 τ


No.10
Cl
F
1
2
1
2
2 3 4 5 6 7 8 9 10 τ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F
Cl
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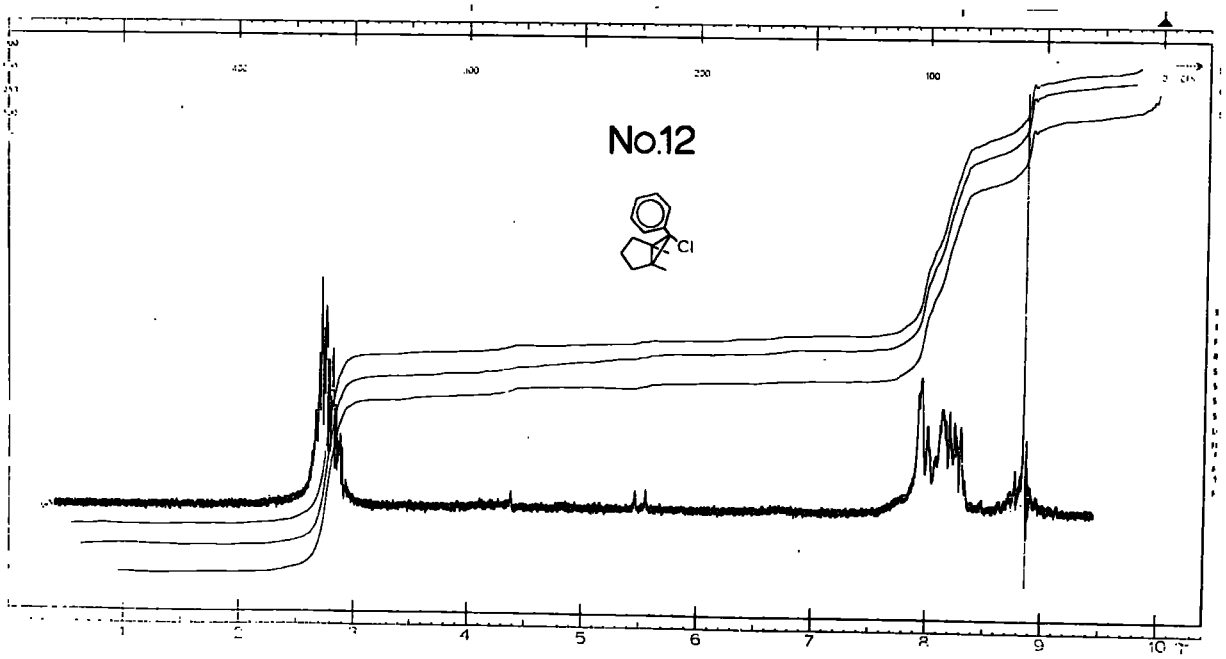
1
2
2
1 2 3 4 5 6 7 8 9 10 τ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Cl
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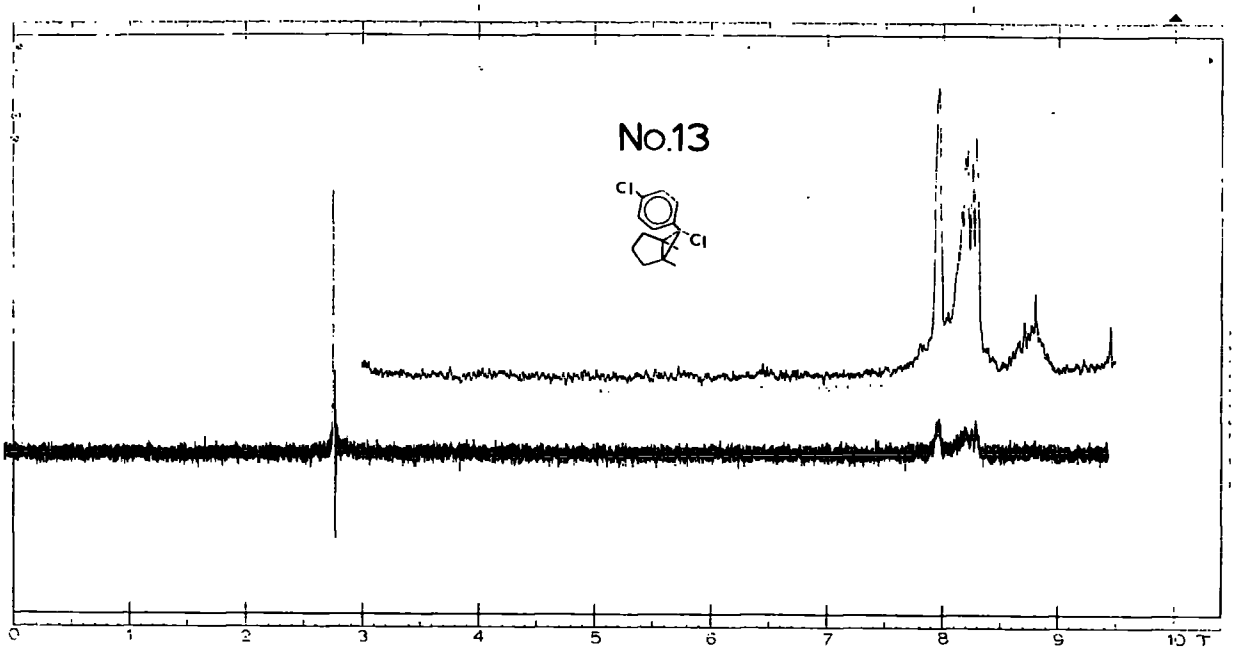
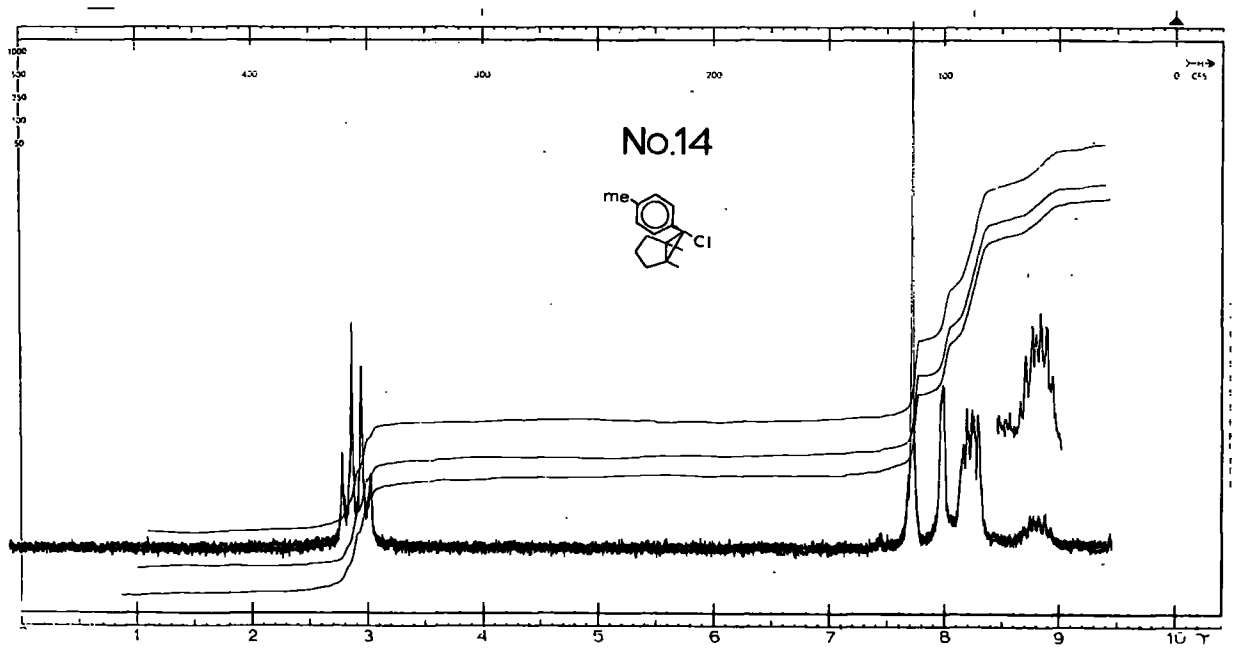
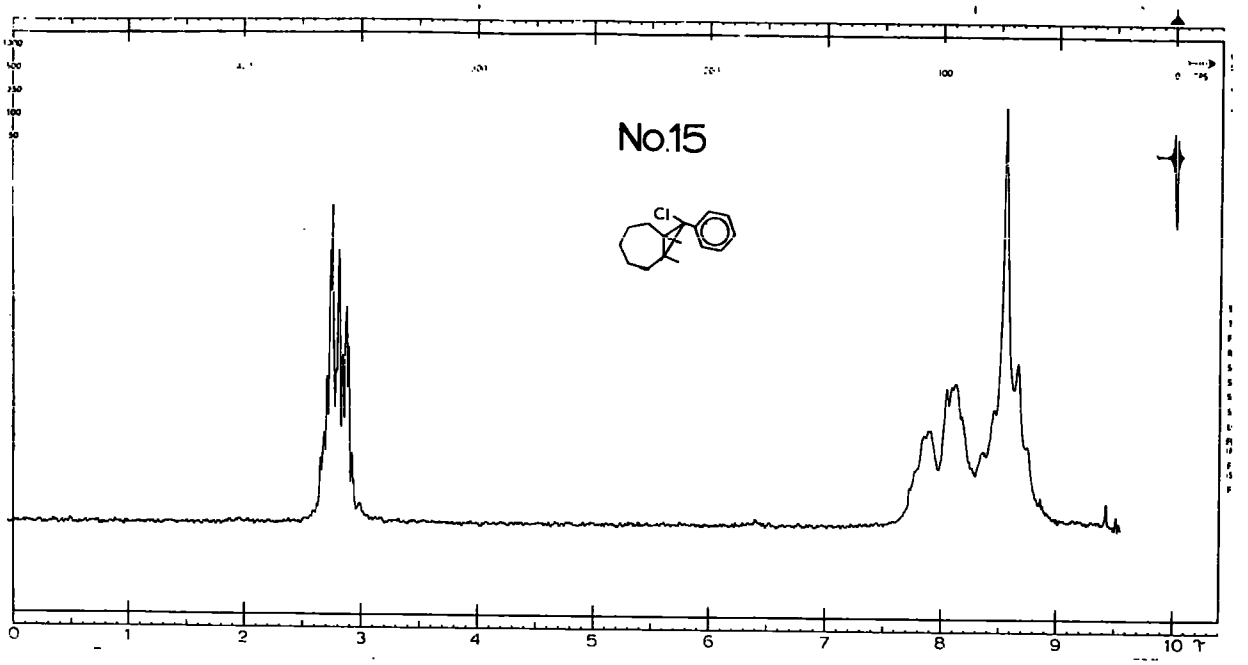

No.13
Cl
Cl
0
1
2
3
4
5
6
7
8
9
10 T


No.14
me
Cl
1
2
3
4
5
6
7
8
9
10 T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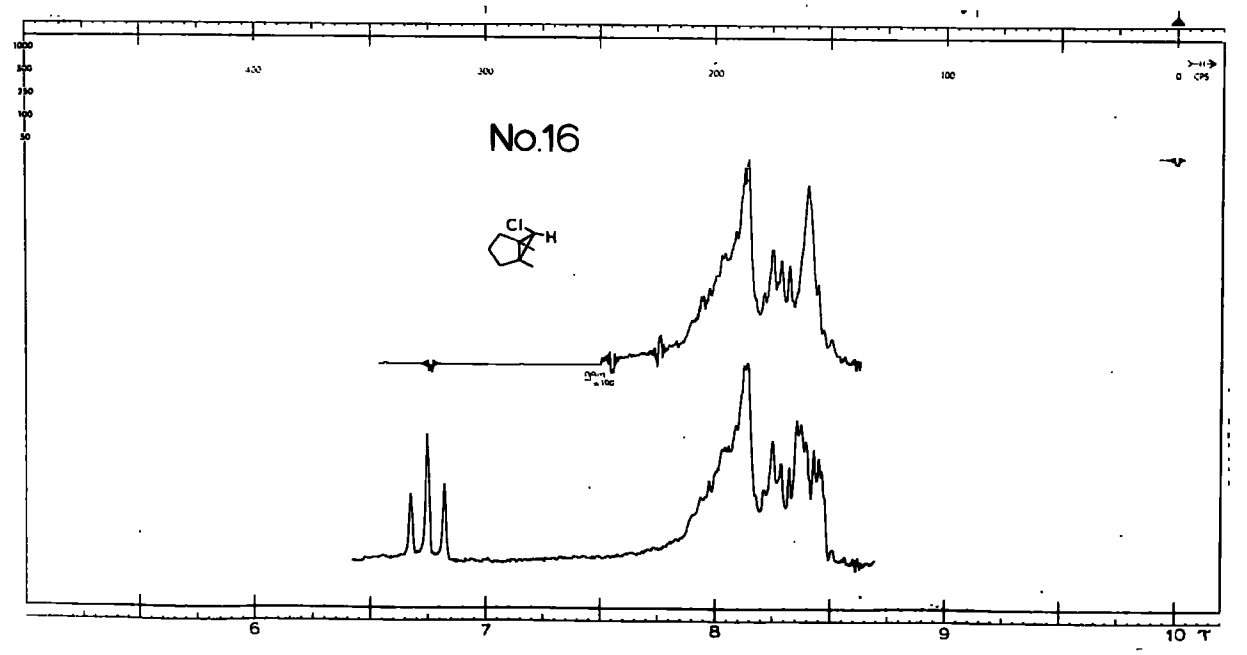
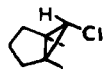
Cl
0
1
2
3
4
5
6
7
8
9
10 τ


No.16
Cl
H
6
7
8
9
10 τ

No.17



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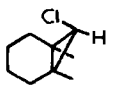
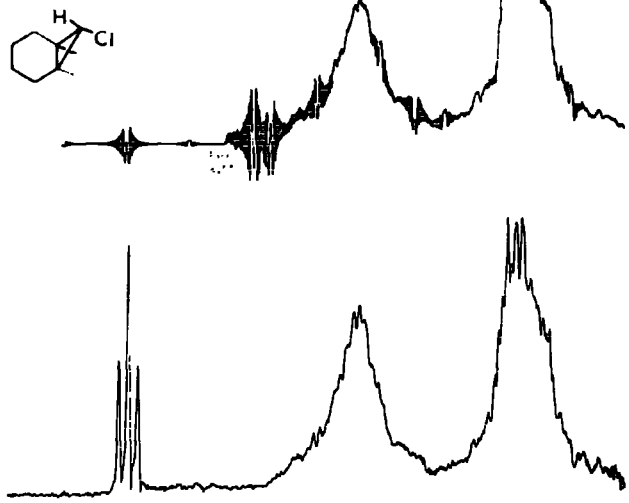
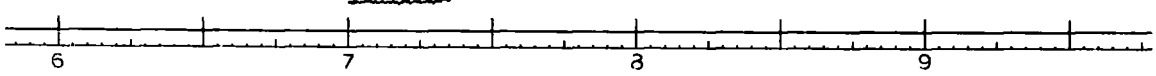
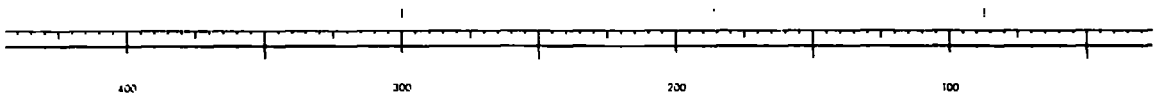


No.19







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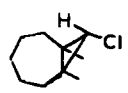

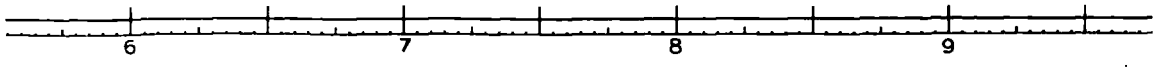

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