STERIC EFFECT AT C-7 OF NORBORNENE

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By

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SCOPE AND CONTENTS:

The object of this work was to show unambiguously which face, syn or anti, of the norbornene system is less sterically crowded. This was accomplished by use of thermodynamics and kinetics. These studies have produced the first quantitative measure of the free energy difference between isomers at C-7 caused only by the different steric requirements of the ethano and etheno bridges. In the thermodynamic studies, isomeric mixed ketals were employed. In the course of the stereochemical assignment of these isomers, it was found that a methoxy group has a greater levelling effect on the 7-cation of norbornene than has a p-anisyl group. The knowledge of the sense and approximate magnitude of the steric effect is applied to the reactions of the 7-radical of norbornene to cast light on the nature of this species.

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CHAPTER 1

INTRODUCTION

Bicyclo[2.2.1]hept-2-ene (norbornene) (1) was first prepared from cyclopentadiene and ethylene by Joshel and Butz[1] in 1941. Many papers have been published on this unique molecule and its derivatives, especially in the last two decades. In view of the wealth of accumulated information on the norbornene system, it is surprising that several fundamental questions have not yet been answered. Which face of the norbornene system, syn or anti, is less sterically hindered? That is, does the ethano bridge cause a greater repulsive interaction with a C-7 substituent or an attacking species than does the etheno bridge? What are the magnitudes of such interactions for typical C-7 substituents in terms of the free energy difference between syn and anti isomers? It was the object of this work to answer these questions.

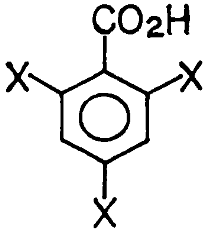
(I)

Many reactions at the C-7 position of norbornene show stereoselectivity[2,3,4,5,6]. In order to explain the syn/anti product distribution both steric and polar factors must be taken into account.

No complete explanation for any reaction at C-7 can be given without a knowledge of the sense and magnitude of the directive effect caused by the different steric requirements of the ethano and etheno bridges. Herein lies the fundamental importance of this work. It has provided the first unambiguous evidence for the sense, and an estimate for the magnitude, of the steric effect. The answers were supplied by a combination of thermodynamic and kinetic studies. There follows a historical review of steric effects and a presentation of the thermodynamic and kinetic equations employed in the solution of the above-mentioned problems.

(1) STERIC EFFECTS

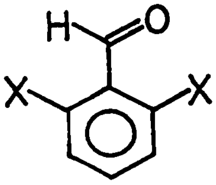
The term "steric hindrance" is generally attributed to Meyer[7], but Kehrmann[8] claims he was first to recognise this effect in chemical systems. Meyer[7] studied the acid catalysed esterification of 2,4,6-substituted benzoic acids (2).



(2)

$X = CH_3, NO_2, Cl, Br$

When both of the ortho positions were substituted, Meyer found that esterification would not proceed. If, however, one ortho substituent was removed, the reaction proceeded easily. These observations were interpreted in terms of steric effects. Goldschmidt[9] made the first attempt to put steric effects on a quantitative basis by studying the rates of acid catalysed esterification for mono-substituted ortho, meta and para benzoic acids. Several substituents were employed. In all cases, Goldschmidt found that the ortho substituted acid reacted more slowly than the meta or para substituted acids. This was again attributed to steric hindrance to reaction. Further studies by various workers on similar systems showed that steric effects were not the only effects operating. It was found that a "steric effect" could be weakened or augmented depending on the reaction type and the positions of the substituents. Davis and Rixon[10] recognised the role of both steric and polar factors in reactions and equilibria. These authors suggested that the steric effect caused by any group may be proportional to its weight (presumably atomic weight). They coined the term "chemical hindrance" as a proportional representation of the steric effects. Science justifiably ignored this term. Reich, Salzmann, and Kawa[11] showed clearly that the "steric hindrance" postulate of Meyer[7] for reactions of ortho-substituted benzene derivatives was a completely inadequate explanation of the data. These authors studied the rates of reaction of di-ortho-substituted aldehydes (3) in the Perkin condensation.



(3)

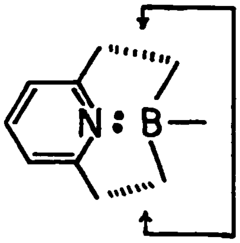
$X = CH_3, NO_2, Cl$

When $X = NO_2$, the rate of condensation was greater than that for X = Cl, and when $X = CH_3$, the reaction did not proceed at all. Such experimental facts were conclusive evidence that these reactions must be dictated by a complex mixture of polar and steric effects. Meyer[7] had looked on steric hindrance as an obstacle to reaction caused by shielding of the reaction site by part of the structure of a branched reagent. While in the early 1900's it was recognised that both steric effects and polar effects were operating in reactions, the next three decades yielded little information on the separation of these effects. A lessening of interest in steric effects resulted, and "steric hindrance" deteriorated into an omnibus term covering a multitude of misunderstood effects. No advance towards further understanding or definition of the steric effect was made until the 1940's. Two new terms gained popularity. "Proximity effect" was an effect attributed to the steric and electronic features of a neighbouring group whose spatial position aided or hindered a reaction. "Ortho effect" described specifically the action of an ortho substituent of a benzenoid system in helping or hindering a reaction. Hughes[12] suggested that the dichotomy of nucleophilic substitution (SN1 and SN2) caused a re-awakening of interest in the steric effect to allow an explanation for a change in mechanism in a series of solvolyses of RBr, where R ranged from methyl to tertiary butyl. Hughes made the interesting point that in these solvolyses steric hindrance to reaction can increase when the major bulk of the group is further from the reaction centre, in direct contradiction to all previous findings.

Having recognised the importance of steric effects in Chemistry, Brown[13] set about "to produce unambiguous evidence upon which the concepts of steric strain and steric hindrance could be founded". Brown's introductory comments in another paper[14] are a reflection of the lack of interest in, and knowledge of, the steric effect. "At that time (1940) the place of steric effects in chemical theory was at a particularly low point and theorists went to extreme lengths to avoid attributing any significant chemical effects to the size and bulk of atoms or groups of atoms." Brown's logical quantitative approach[14] did indeed set the scene and an explosion of information followed on the importance of steric effects in reactions, in equilibria, and in the stability of compounds. Brown's studies on molecular addition compounds, nucleophilic displacements and reactions of highly branched carbon compounds led him to postulate three types of molecular strains, described as "F", "B" and "I" strains. When boron compounds, like BR_3 or BF_3, are added to amine bases, molecular addition compounds result (equation 1).

$$BR_3 + :NR_3 \rightleftarrows R_3B:NR_3 \quad R = H \text{ on alkyl} \qquad [1]$$

An equilibrium is set up, and the equilibrium constant is a reflection of the stability of the complex formed. Brown[14] found that replacing methyl groups by more bulky groups such as isopropyl led to a uniform decrease in the stability of the complex. He suggested that the effect could not be polar and had to be of steric origin. This effect was termed "F" strain, F standing for the "facial" interaction of groups in complex formation, shown below. The facial interaction in the di-ortho substituted pyridines is large.



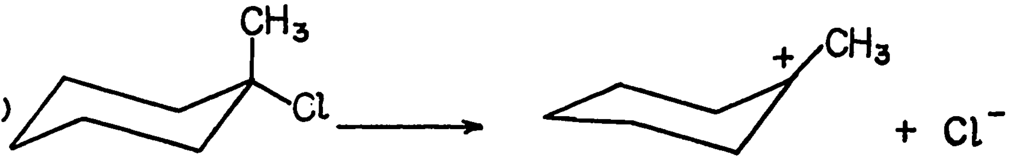
FACIAL STRAIN

"B" strain ("back" strain) is the increase in the steric strain resulting from compression and bond bending within the groups attached to an atom which accompanies the formation of a bond with the atom. "B" strain becomes more important as the group R gets larger. The series of complexes (equation 2) is employed with a common reference acid Z.

$$R_3N: + Z \rightleftarrows R_3N:Z \qquad [2]$$

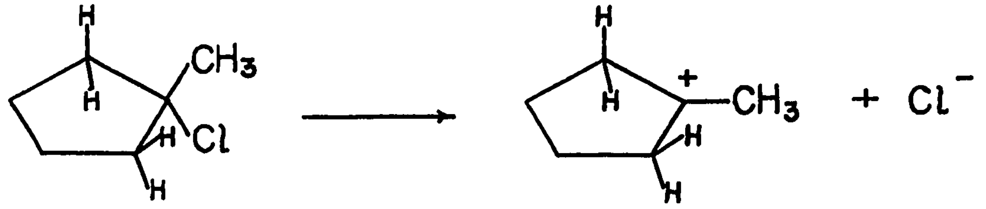
The size of the effect depends on the bulk of the group on the tertiary amine. "I" strain is the increase in internal strain of a cyclic structure resulting from alterations in bond angles and conformations which accompany a change in co-ordination number of a ring atom in the course of a reaction. Brown postulated "I" strain to account for the ionisation rates of 1-chloro-1-methyl cyclohexane and 1-chloro-1-methyl cyclopentane (equations 3 and 4).

(4)



[3]

(5)



[4]

Since the cyclopentane (5) is a planar molecule, there are ten bond-bond interactions. On ionisation, strain is relieved by cutting the number of interactions down to six. The cyclohexane (4) is staggered, but in ionisation it gains bond-bond interaction, hence "I"-strain can account for the fact that (5) ionises much more quickly than does (4).

The first separation of steric and polar effects was attempted by Prévost.[15] He compared the rates of reaction in solvolysis of (6) and (7), and (8) and (9) shown below.

$CH_3{-}CH_2{-}CH_2{-}CH_2{-}Cl$ (6)

$CH_3{-}CHCl{-}CH_2{-}CH_3$ (7)

$CH_3{-}CH{=}CH{-}CH_2Cl$ (8)

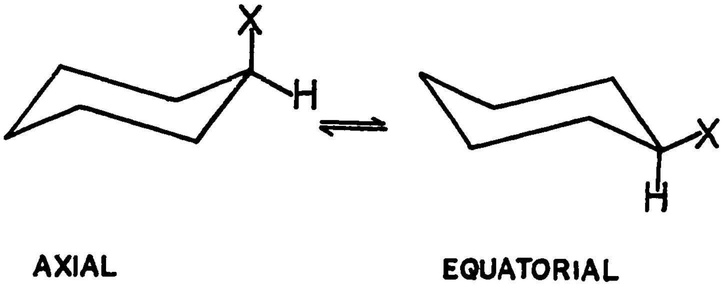
$CH_3{-}CHCl{-}CH{=}CH_2$ (9)

K (rate) was equated to $C \times \frac{M}{S}$, where M is the "mobility" of the Cl^- atom, S is the steric hindrance, and C is a reaction constant. Prévost made the assumption that the "mobility" of the Cl^- atom was the same for the reactions compared. Comparison of the rate values gave the relative steric effects of the systems.

Hill[16] made the first theoretical quantitative evaluation of steric strain. He developed an equation which balanced the Van der Waals repulsion forces and the stretching and bending of bonds to give the minimum potential energy for the molecule. Entropy factors, solvent effects and other polar factors were ignored, but Hill claimed that for simple reactions, such as the addition of boron trifluoride to ammonia, the forces of the type discussed in his paper could give the effects of the type and order of magnitude found experimentally by Brown.[13]

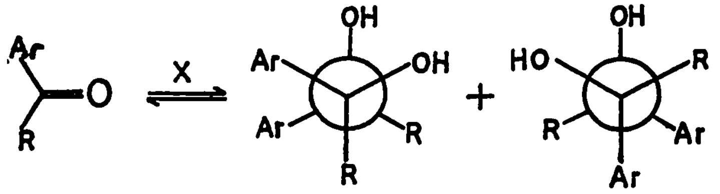
With the introduction of linear free energy relationships by Hammett,[17] the stage was set for the separation of steric and polar effects in reactions. A modification to the Hammett expression by Taft[18] gave an expression which allowed such a separation. This is fully discussed later in this introduction.

Steric effects in equilibria were isolated by determining the equilibrium constant (K) for the equatorial and axial conformers of cyclohexane systems[19] (equation 6).



[6]

The "A" value was defined as the logarithm of the equilibrium constant (K), that is, A is proportional to the free energy difference between the conformations. Steric factors are now known to be responsible for many effects in chemistry. A review of all of these effects is impossible here, so some examples are given under specific headings. In conformational analysis, as noted above, steric effects can cause one conformer to predominate at equilibrium. Felkin[20] showed that several systems, such as the one shown below, show a preference at equilibrium for the meso form (equation 7).

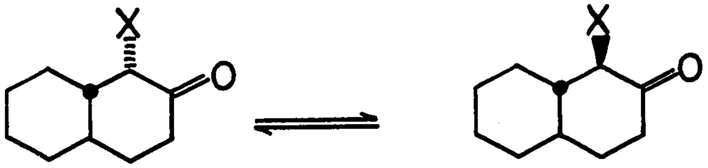


MESO RACEMIC

[7]

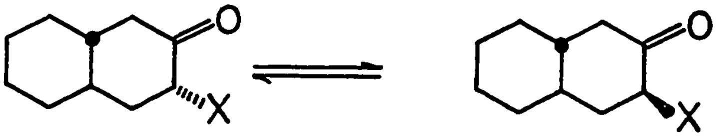
$X = Mg/MgCl_2$

(Presumably Felkin meant the magnesium salts and not the protonated forms were in equilibrium.) Although the equilibrium is heavily on the side of the meso form, there is considerable ambiguity as to whether this is a pure steric effect, since polar effects cannot be ruled out. Few studies on equilibria are free of polar effects, hence one cannot attribute a free energy difference to steric effects in such studies. Casadevall, Mion, and Casadevall[21] cited an example where polar effects were minimised. These authors studied the equilibrium between epimers (10) and (11), and (12) and (13) (equations 8 and 9).



(10) (11)

[8]

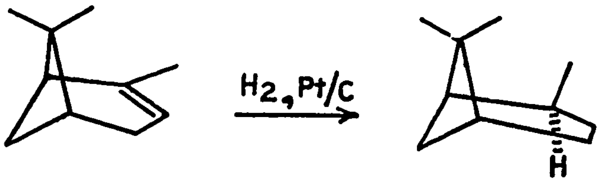


(12) (13)

[9]

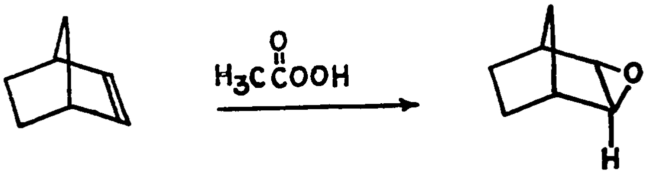
When X is Br or Cl, there is a fairly strong solvent effect on the position of equilibrium. When X is CH_3, there is no solvent effect, and the equatorial isomer is found to be 95% of the equilibrium mixture. This was postulated to be the result of interaction in the axial isomer of the methyl group with the axial hydrogen atoms. (The necessity for solvent-independent equilibria in order to isolate a steric effect is discussed later.)

Steric effects are believed to be responsible for the stereospecific addition of many reagents to certain bicyclic systems. Reduction of α-pinene with hydrogen on a platinum catalyst results in 87% of the exo-methyl compound[22] because of the steric interaction of the bridgehead methyl groups with the surface of the catalyst (equation 10).



[10]

Addition of peracetic acid to norbornene[23] is a completely stereospecific process, producing the exo-epoxide only (equation 11). This must be due to the greater endo hindrance in this case.



[11]

Steric effects manifest themselves in the physical properties of compounds.[24] Changes in vibrational and electronic spectra can be observed on introduction of a bulky group or strain into a molecule. The dipole moments of many aromatic compounds show drastic changes due to steric effects. Even properties such as elasticity of polymers and melting point have been partially attributed to steric effects.[24]

At the present time steric effects are attributed to the repulsive interaction between the electron clouds of adjacent or approaching atoms. The closer the electron clouds (orbitals) come to one another, the higher becomes the potential energy of the system. This energy is referred to as the Van der Waals potential energy. Many attempts have been made to calculate the Van der Waals potential energy function. This is a curve which is the result of a plot of potential energy versus interatomic distance between the two interacting species. For an ideal gas, the calculation of the potential energy function is relatively easy, but for reacting molecules only crude estimates can be made. Doubtlessly in the future there will come solutions to the complex wave-function problems of the present, and with them a more complete understanding of steric effects and strain effects.

THERMODYNAMICS AND EQUILIBRIUM

In this section a short history of the study of equilibrium is given, the basic thermodynamic equations related to equilibrium are presented and the factors which can influence the position of equilibrium for non-ionic isomeric species are discussed.

History of Equilibrium

The early alchemists tended to endow their chemicals with almost human natures, and claimed that reactions occurred when compounds loved each other. As early as 1661, Robert Boyle poured invective on these ideas in "The Sceptical Chymyst". In 1718, Etienne Geoffroy made a systematic study of the order in which acids would displace weaker acids from combination with bases. This order was called "Tables of Affinity". Geoffroy obviously did not recognise that the position of equilibrium is dependent on the concentration of reagents and this was pointed out by Claude Louis Berthollet in 1801. The name "affinity" stuck, however, and described roughly what we now know as the equilibrium constant. Berthollet recognised an equilibrium set-up in the system shown below (equation 12).

$$Na_2CO_3 + CaCl_2 \rightleftarrows CaCO_3 + 2NaCl \qquad [12]$$

He found that the addition of sodium chloride to the system gave back sodium carbonate, and thereby established the first recorded equilibrium. Following equilibrium and kinetic studies by Berthelot and St. Giles,[25] and Wilhelmy, Guldberg and Waage made an enormous contribution to science by recognising that equilibrium is a dynamic and not a static condition, and by deriving a general equation for the equilibrium state. Lindauer[26] sums up the history of equilibrium in the following way:

(a) recognition and acceptance of the influence of the amount of reagent on chemical reactions;

(b) the quantitative formulation of this effect in the Law of Mass Action;

(c) rationalisation of the effect of mass by chemical kinetics and thermodynamics;

(d) refinement of the Law of Mass Action by the addition of activities instead of concentrations; and,

(e) the wide application of chemical thermodynamics to equilibrium situations.

Equations Governing Equilibrium

Consider a simple equilibrium $A + B \rightleftarrows C + D$. According to the Law of Mass Action, the rate of the forward reaction is proportional to the concentrations [A] and [B].

$$\text{i.e., Rate}_{(\text{Forward})} = k_{(\text{Forward})}[A][B] \tag{13}$$

$$\text{Similarly, Rate}_{(\text{Backward})} = k_{(\text{Backward})}[C][D] \tag{14}$$

At equilibrium, however, the rates of Forward (F) and Backward (B) reaction are equal, so,

$$k_F[A][B] = k_B[C][D] \qquad [15]$$

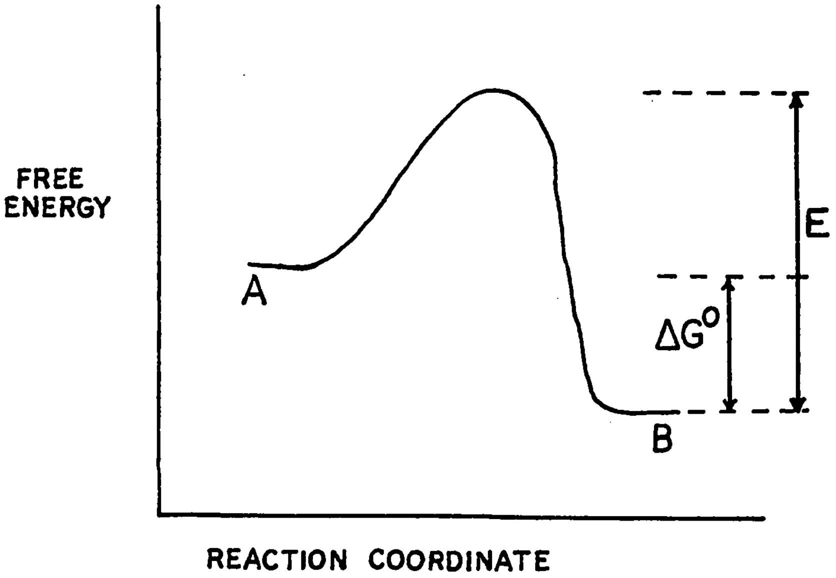
Thus,

$$\frac{k_F}{k_B} = \frac{[C][D]}{[A][B]} = K \qquad [16]$$

The constant K is called the equilibrium constant. For the ketal and imidazolidine systems described under "Results and Discussion" there are but two compounds under study and the equation simplifies to

$$\frac{k_F}{k_B} = \frac{[C]}{[A]} = K \text{ for the equilibrium } A \rightleftarrows C \qquad [17]$$

Consider the energy profile for such an equilibrium



If energy E is supplied and there is no reaction which completely removes either A or B or both, then A and B will equilibrate at the temperature of the reaction. Free energy (G) is a state function, independent of mechanism. The relationship between free energy and equilibrium constant (K) is

$$\Delta G^\circ = -RT\ln K, \qquad [18]$$

where ΔG° is the standard free energy difference between A and B, that is

$$\Delta G^\circ = G^\circ_B - G^\circ_A.$$

Equation [18] is used to calculate ΔG°, knowing the equilibrium constant at temperature T.

Factors Influencing the Position of Equilibrium

Since $\Delta G^\circ = G^\circ_B - G^\circ_A$, the position of equilibrium depends on the relative magnitudes of G°_B and G°_A. These standard free energies can be influenced by pressure, temperature, solvent, steric, polar, and strain factors. The effect of these factors on the position of equilibrium will now be discussed.

Dependence of the Equilibrium Constant on Pressure

The equilibrium constant for the simple equilibrium

$$A \rightleftarrows B$$

is related to the free energy difference by the equation

$$\Delta G^\circ = -RT\ln K \qquad [18]$$

The thermodynamic relationship between the Gibbs' free energy change ΔG and the hydrostatic pressure (P) is

$$V = \left(\frac{\partial G}{\partial P}\right)_T, \text{ where } V = \text{volume.}$$

For a system at equilibrium in a standard state the equation becomes

$$\Delta V^\circ = \left(\frac{\partial \Delta G^\circ}{\partial P}\right)_T \qquad [19]$$

From equations [18] and [19]

$$\left(\frac{\partial \ln K}{\partial P}\right)_T = -\frac{\Delta V^\circ}{RT}$$

The proportion of products at equilibrium, therefore, depends on the volume change which occurs when A is converted to B.

Dependence of the Equilibrium Constant on Temperature

$$-\Delta G^\circ = RT\ln K$$

and

$$\frac{d}{dT}\left(\frac{\Delta G^\circ}{T}\right)_P = -\frac{\Delta H^\circ}{T^2}$$

therefore

$$\left(\frac{d\ln K}{dT}\right)_P = \frac{\Delta H^\circ}{RT^2}$$

A plot of lnK versus $\frac{1}{T}$ gives a slope of $\frac{-\Delta H^\circ}{R}$. ΔH° is assumed to be independent of temperature, hence the equilibrium constant can be estimated by extrapolation for a temperature at which the determination of the equilibrium constant is difficult experimentally.

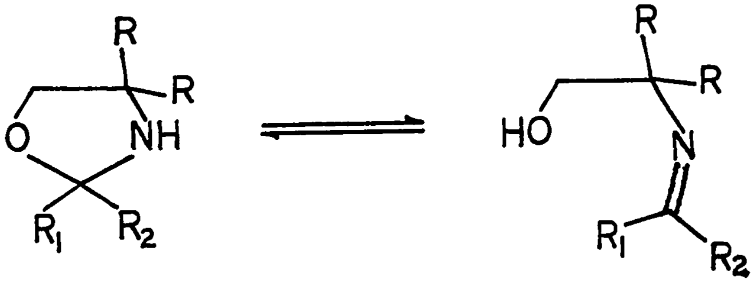
Dependence of the Equilibrium Constant on Solvent

Examples of solvent effects on the equilibria of ionic species are legion and will not be presented here. The discussion will be limited to non-ionic species with a special emphasis on equilibrium between two isomers. A short discussion on the effect of solute-solvent interactions is included.

Early work on the solvent dependence of equilibria was done by Dimroth[27] and Dawson and Leslie.[28] The latter studied the solvent dependence of the equilibrium between potassium iodide and iodine and potassium triiodide (equation 20).

$$KI + I_2 \rightleftarrows KI_3 \qquad [20]$$

Using molecular conductivity measurements, these authors showed that the equilibrium constant showed a fairly large dependence on solvent. Many reports on solvent dependence of keto-enol tautomerisation have been published. Van Uitert, Haas, Fermelius and Douglas[29] showed that for many β-diketones, the enol form is preferred at equilibrium when the polarity of the solvent is low. This result has been verified many times since using different detection techniques.[30,31] Equilibria between the open chain forms and heterocyclic systems show also solvent dependence. One example from the work of Paukstelis and Hammaker[32] is shown below (equation 21).



[21]

R_1 and R_2 varied from H to tertiary butyl. A factor of 18 was reported for the change in the equilibrium constant in going from carbon tetrachloride to dimethyl sulphoxide as solvent. 6-Hydroxycyclodecanone has been shown to be in equilibrium with the hemiketal form[33] (equation 22).

[22]

The keto form was found to be preferred at equilibrium in polar solvents.

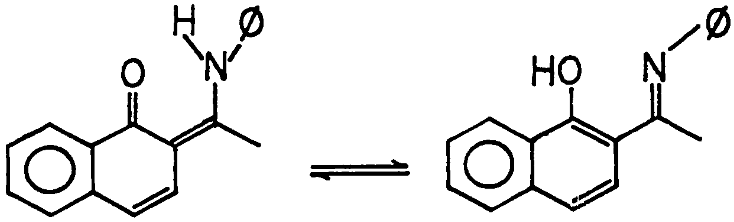
From these data it can be seen that solvent can have a considerable effect on the free energy difference between isomers of non-ionic species. Change of the dielectric constant either by changing solvent[34] or adding an external electric field[35] has been noted to alter ΔG°. Changes in ΔG° with solvent are a result of the tendency of solvent molecules to solvate a solute molecule. The extent of solvation, or clustering of solvent molecules around a solute molecule, depends on the extent of repulsive or attractive interaction between the two. The interactions, for electrically neutral species, can be dipole-dipole or dipole-induced dipole. Solvation can stabilise one molecule A, say, relative to B by lowering its free energy, hence increasing ΔG° and K. Brownstein[36] has shown for a wide variety of equilibria that a linear free energy relationship can be applied (equation 23).

$$\log \frac{K(\text{solvent})}{K(\text{ethanol})} = RS \qquad [23]$$

S is a constant related to the polarity of the solvent and R is a parameter indicating the sensitivity of the system to changes in solvent.

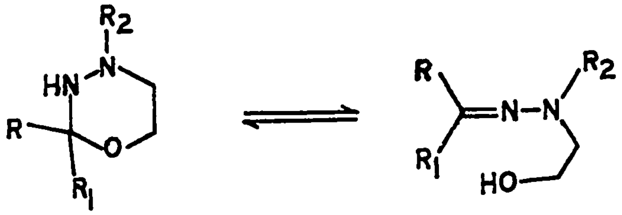
Dependence of the Equilibrium Constant on Polar Effects and Steric/Strain Effects

Few examples are given in the literature in which separation of steric and polar effects on equilibrium constants is unambiguous. Indeed, when a system at equilibrium shows a change in equilibrium constant with change of solvent, then separation of steric and polar effects is not possible. Dudek and Dudek[37] have studied the keto-enol tautomerism for the Schiff's bases of certain ketones (equation 24).



[24]

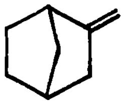
This system showed a strong solvent effect on the position of equilibrium. These authors suggested that steric interaction between the N-phenyl and methyl groups was responsible for making the keto tautomer higher in energy, and hence the enolimine was favoured at equilibrium. The position of equilibrium in this case is obviously the result of a combination of steric and polar effects. Yoffe[38] and his co-workers studied keto-enol tautomerism for α-alkyl acetoacetates. Steric interaction was the reason given for the equilibrium preference for the keto form but once again polar and solvent effects were neglected. Similar conclusions on steric effects in equilibrated systems were drawn by Potekhin and Ioffe[39] who studied the uncatalysed equilibrium shown below (equation 25).



[25]

When R_1 and R are methyl groups, equilibration gives a moderate percentage of the closed form, but if R_1 is methyl and R is either ethyl or tertiary butyl the equilibrium is heavily on the side of the hydrazone. This undoubtedly is partly due to steric interaction, but a polar effect cannot be discounted without conducting a solvent study on the equilibrium.

Relative steric and strain effects in bicyclo[2.2.1]hept-2-ene systems were measured by Maurel, Guisnet and Garin-Place.[40] Isomerisation of 1-methyl bicyclo[2.2.1]hept-2-ene on a cobalt-aluminum catalyst at 250° gave the following percentages of isomers at equilibrium.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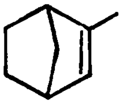
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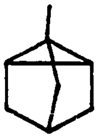
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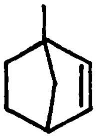
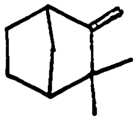
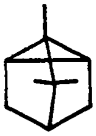

5%

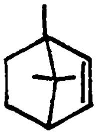
Strain effects in this system tend to favour the double bond being exocyclic. Addition of two methyl groups to the system causes changes in the equilibrium distribution. The equilibrium percentages below doubtlessly reflect a combination of steric and strain effects.



71·5%

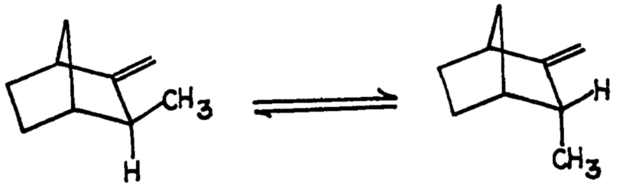


25·5%



3%

Of considerable interest in the system below is the equilibrium distribution between the exo and endo isomers. The exo isomer is preferred by a factor of 66:1, a strong indication that interaction of the endo C-2 methyl with the endo C-5,6 protons is fairly large compared with the interactions of the methyl group with the exo substituents (equation 26).



[26]

In conclusion, it has been demonstrated that the free energy difference between isomers can be measured by measuring the equilibrium constant, and that the free energy difference is dependent on temperature, pressure, solvent, steric and polar effects. The effect of pressure in condensed systems is small; usually hundreds of atmospheres pressure is required to make a reasonable change in the equilibrium constant. Effects, therefore, caused by variation in laboratory pressure are very small and can be ignored. Temperature can be kept constant by using a thermostat. The problem, therefore, in isolating a steric effect, is to remove, or at least, minimise, polar and solvent effects. The manner in which the separation of steric and (all) polar effects was done is fully discussed under "Results and Discussion".

LINEAR FREE ENERGY RELATIONSHIPS AND THEIR APPLICATION TO SEPARATION OF STERIC AND POLAR EFFECTS IN REACTION

The most general free energy relationship known for the effects of substituents on rates or equilibria is the Hammett equation (equation 27).

$$\log k/k_o = \sigma\rho \qquad [27]$$

Sigma (σ) is a substituent constant independent of the nature of the reaction. It is a quantitative measure of the polar effect of a given meta or para substituent relative to a hydrogen atom. Hammett selected the ionisation of substituted benzoic acids for obtaining the constant σ (equation 28),

$$\sigma = \log \frac{K}{K_o} \qquad [28]$$

where K is the ionisation constant of a substituted benzoic acid, and K_o is the ionisation constant of benzoic acid, at 25°. Rho(ρ) is a proportionality constant for the reaction. It is a measure of the sensitivity of reaction series to polar substituents. This basic equation [27] has been modified several times to show different types of free energy relationships, but only the modification by Taft[18] will be considered here. Taft's equation is

$$\log k/k_o = \sigma^* \rho^* \qquad [29]$$

This expression was formulated to evaluate the polar effects of substituents R on the rates of normal hydrolysis of esters, RCOOR'. In this case, σ^* is a substituent constant which depends only on the net polar effect of the substituent R relative to that for R = CH_3. The constant σ^* is starred to denote its different nature and origin from Hammett's σ.

$$\sigma^* \equiv 1/2.48[\log(k/k_o)_{Base} - \log(k/k_o)_{Acid}] \qquad [30]$$

k and k_o are the rate constants for the hydrolysis of esters RCOOR' and CH_3COOR', respectively. The basic assumptions of the above relationship are that

(1) the free energy of activation for these reactions can be treated as independent contributions from steric, resonance and polar effects,

(2) in acidic and alkaline hydrolysis, steric effects and resonance effects are similar for corresponding reactions,

(3) the polar effects of substituents are markedly greater in the alkaline than in the acidic hydrolysis.

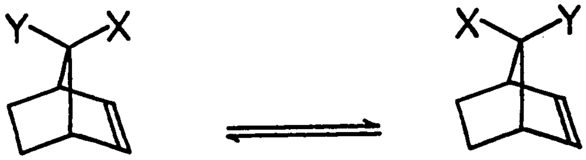
That such assumptions are valid can only be justified by considering the results obtained from use of the equation. For alkaline hydrolysis and transesterification ρ values are in the region of +2.2 to +2.8. For acid catalysed hydrolysis ρ values are in the region of +0.5 to -0.2. Within the experimental error of the latter experiments, the average rho value is zero. Except for certain substituents either conjugated with the carbonyl group or giving changes in interaction with the substrate between reactants and transition state, it may be assumed that the "non polar" $\log(k/k_o)_A$ values are quantitative measures of the steric effects associated with the substituent R (equation 31).

$$\log(k/k_o)_{Acid} = E_S \qquad [31]$$

E_S is the steric parameter giving a quantitative measure of the total steric effect associated with a substituent R relative to the standard, R = CH_3. Results from studies of this type can be summarised as follows. Base catalysed hydrolysis and transesterification reactions are governed primarily by polar effects and the corresponding acid-catalysed reactions are governed primarily by steric effects. These general conclusions will be considered under "Results and Discussion".

RESULTS AND DISCUSSION

As stated in the Introduction, the greatest problem in using equilibrium studies to measure a pure steric effect is in the elimination on minimisation of polar effects. Consider the equilibrium shown below (equation 32).

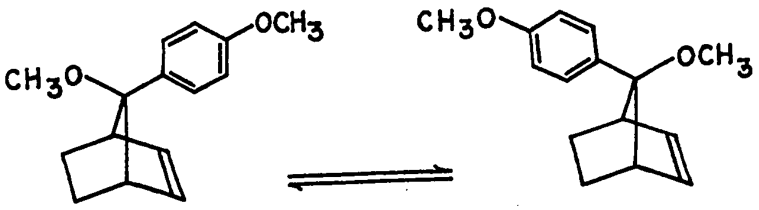


[32]

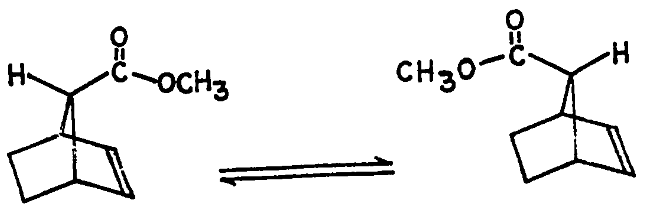
In order to determine the relative steric effects of the ethano and etheno bridges in the above system, substituents X and Y must have the same, or nearly the same, polar characteristics but different bulk. If the substituents are identical in polar characteristics then the resultant dipole moment of the Y-C-X group will lie in the C-1,C-7,C-4 plane. If, however, the substituents X and Y differ only slightly in polar characteristics, the resultant dipole moment will still be fairly close to the C-1,C-7,C-4 plane. Such a unit Y-C-X would balance the polar effects in the molecule and would cause neither isomer to be favoured at equilibrium because of polar factors. A further restraint on the choice of X and Y is that the equilibrium (equation 32) must be feasible within the normal working range of, say, 25-100°. For example, if X were methyl and Y were ethyl, a possible way of equilibrating these species would be the use of a cobalt-aluminium catalyst at high temperatures.[40] This is clearly unsuitable, since the equilibrium constant found for the high temperature may bear no relationship to that in the normal range of temperature. Furthermore, there should be a simple method of measuring the isomer ratio, and an unambiguous criterion for assigning their structures.

Once substituents have been found which will allow the above problems to be overcome, varying the steric requirements of X, keeping Y constant, and equilibrating these systems, should give a series of equilibrium constants which reflect the difference in the steric requirements of X and Y. Assignment of the isomers, coupled with a knowledge of the equilibrium constant, would indicate whether the larger group X prefers to occupy the syn or the anti face at equilibrium.

Two published equilibria of norbornenes with dissimilar substituents at C-7 are shown below (equations 33 and 34).[41a,5]



[33]



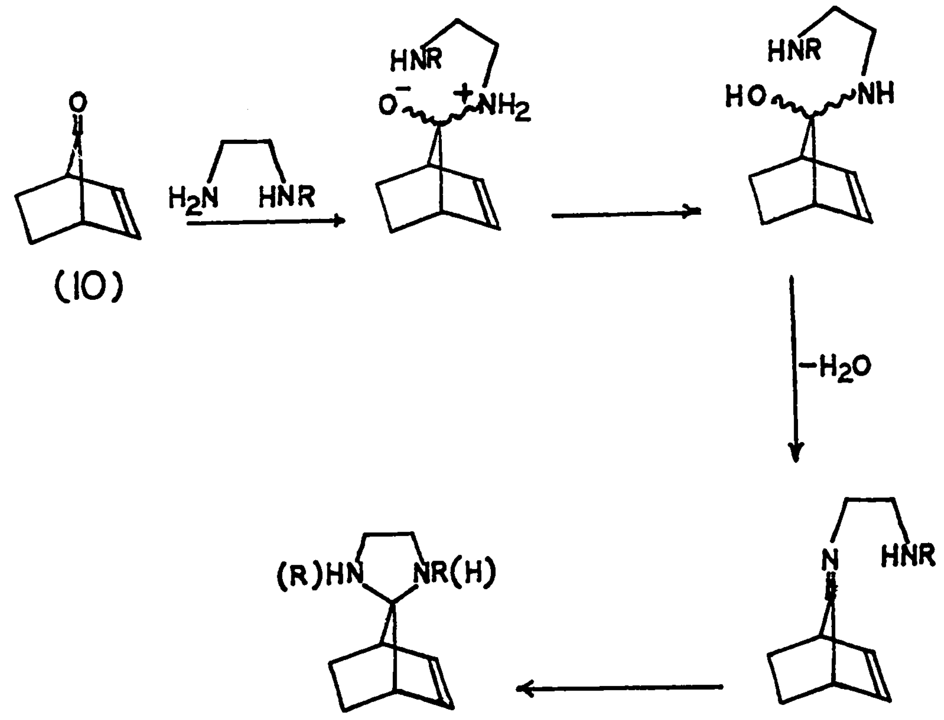
[34]

Sauers' equilibration of the 7-esters[5] (equation 34) showed that the syn isomer was favoured by a factor of 1.22 over the anti isomer. This was attributed to a steric effect. Since a solvent study on the equilibrium has not been done, and since the isomers have substantial dipole moments, the claim that the equilibrium constant is a reflection of a steric effect is unjustifiable. Gassman and Fentiman[41a] found that the p-anisyl group (equation 33) has a strong preference to sit over the syn side (92% syn). The syn isomer, therefore, has a free energy roughly 1700 calories lower than the anti isomer. This is almost definitely not due to steric effects alone.[42]

Two systems were selected to determine the relative steric effects of the two bridges. These employ the same heteroatoms on either side of the bridge to balance polar effects and to facilitate equilibration.

(A) SPIRO IMIDAZOLIDINE SYSTEM

The preparation of the spiro imidazolidines was similar to that employed by Bergmann[43] for imidazolidines of cyclic and acyclic ketones. Bergmann reported that no identifiable product could be obtained from the condensation of cyclopentanone with ethylenediamine, but it was found here that ethylenediamine and its N-alkyl derivatives gave well-defined products with bicyclo[2.2.1]hept-2-en-7-one(10). Norton[44] added various nitrogen containing nucleophiles to (10) and found that the reactions were fast and exothermic. The mechanistic scheme for the formation of these new spiro compounds is shown below. Evidence that the 7-imine is an intermediate will be presented later.



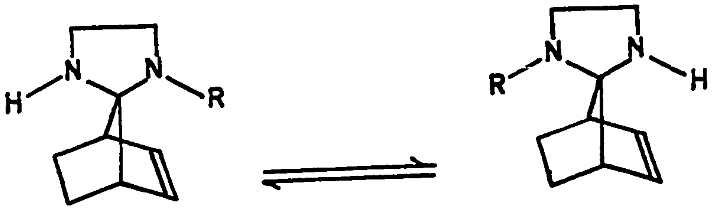
(10)

The products are colourless liquids at room temperature and are unstable to air and water, properties similar to these described by Bergmann.[43] All of the products are unstable in carbon tetrachloride, decomposition being complete in one day in a sealed, degassed tube. In dimethylsulphoxide they have a considerably longer lifetime.

Equilibration of the Imidazolidines

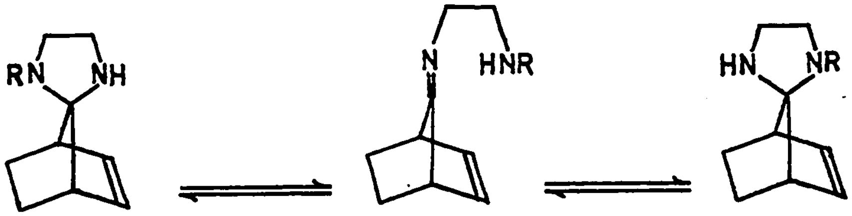
The convention will be adopted that the isomer with the N-alkyl group over the etheno bridge will be called the syn isomer.

Consider the spacial orientation of the N-alkyl group (R) in the imidazolidines. If the nitrogen atom is inverting as expected, the time-averaged position of the alkyl group is over the centre of the etheno bridge in the syn isomer, and over the centre of the ethano bridge in the anti isomer. It was hoped that the almost rigid imidazolidine ring would hold the R group down in this position, thus maximising interaction, and that on equilibration of the isomers (equation 35) one isomer would be favoured.



[35]

Equilibration of the N-methyl and N-ethyl systems (equation 35) gave equilibrium constants close to unity in dimethyl sulphoxide with p-toluenesulphonic acid as catalyst. All equilibration experiments were conducted in an n.m.r. tube, the equilibrium constant being determined by integration of the vinyl triplets corresponding to the syn and anti isomers. For the N-isopropyl, N-t-butyl and N-neopentyl systems, a symmetrical 16-line multiplet appeared at about 3.65τ, in addition to two triplets. Raising the probe temperature from 37° to 75° caused changes in the integrals of all three signals, the integral of the low-field multiplet increasing markedly with temperature, and the integrals of the two triplets correspondingly decreasing. Lowering the temperature back to 37° caused the integrals to return to the values previously noted for this temperature. The three vinyl signals, therefore, are characteristic of three isomers in equilibrium. It is believed that the third isomer is the 7-imine, an intermediate between the two closed forms (equation 36).

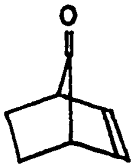


[36]

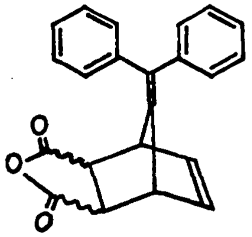
R= ISOPROPYL , NEOPENTYL , TERT.-BUTYL

Justification that the 7-imine is responsible for the 16-line multiplet comes from p.m.r. evidence, i.r. evidence, and thermodynamic evidence, which are discussed in order below.

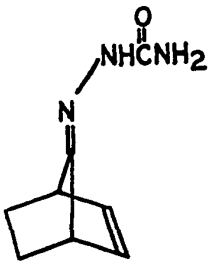
Model compounds (10-12) with sp^2 hybridisation at C-7 are shown below.



(10)



(11)



(12)

For (10) and (11) the p.m.r. vinyl spectrum consists of a triplet, but the semicarbazone (12) exhibits a 16-line multiplet. The chemical shifts of these vinyl protons are 3.50, 3.36 and 3.70τ, respectively. It would appear that changing sp^3 to sp^2 hybridisation at C-7 causes a downfield shift of the vinyl signals. Norbornenes with sp^3 hybridisation at C-7 generally show vinyl triplets at approximately 4.0τ. The 16-line spectrum found in the equilibrium mixtures (equation 36) is centred at 3.65τ in keeping with sp^2 hybridisation at C-7.

Analysis of the 16-line multiplet at 3.65τ (N-Isopropyl System)

As found in other bicyclo [2.2.1]hept-2-ene systems which do not possess an anti-C-7 proton, the vinyl protons couple only to the bridgehead protons.[45] Triple irradiation of the multiplets at 340 Hz and 280 Hz downfield from T.M.S. caused the 16-line multiplet to collapse into an AB-type quartet. No change occurred in the vinyl triplets so selective irradiation of the bridgehead protons of the imine, without irradiation of the bridgehead protons of the two imidazolidines, was achieved. Double irradiation at either 340 Hz or 280 Hz from T.M.S. caused half of the 16-line multiplet to collapse to an asymmetric double doublet, and the other half to collapse to an asymmetric quartet, allowing the coupling constants J-2,1 and J-2,4 to be determined. For all known systems J-2,1 > J-2,4,[45] so the determined coupling constants were assigned on this basis. The coupling pattern is shown in Figure I. The chemical shift difference between the vinyl protons, $|\nu_A-\nu_B|$, is given by

$$|\nu_A-\nu_B| = [(\ell_2-\ell_3)(\ell_1-\ell_4)]^{\frac{1}{2}} = 9.4 \text{ Hz}$$

where ℓ_1, ℓ_2, ℓ_3 and ℓ_4 are the frequencies of the lines of the AB quartet.

The difference in the chemical shift of the C-2,3 protons is another indication that the 7-imine is the third isomer in the equilibrium. The stereochemistry at C-7 dictates that the ethylenediamine chain will be in the C-1,C-7,C-4 plane, thereby rendering the vinyl protons, and the bridgehead protons, magnetically non-equivalent.

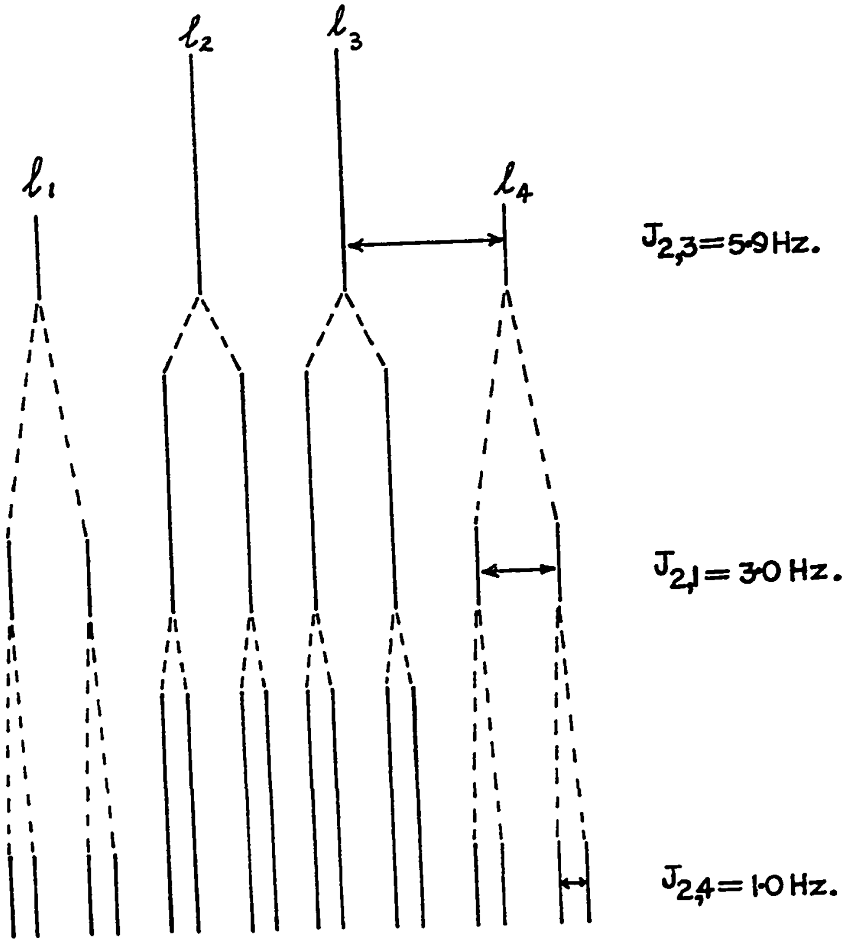


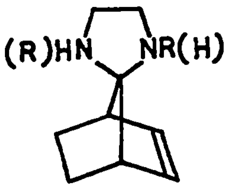
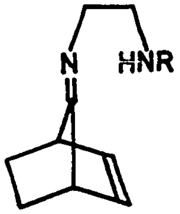
Figure 1. Coupling Pattern for the C-2,3 Protons in the 7-Imine

Infra-red spectra of the N-methyl and N-ethyl imidazolidines do not show a C=N stretching frequency but have strong bending modes in the N-C-N region.[43] The N-isopropyl and N-t-butyl systems show a strong C=N stretching absorption at 1710 cm^{-1}, the high value being attributed to strain at C-7.

The percentages of the imidazolidines and the imine at equilibrium are shown in Table I. It can be seen that the percentage of imine increases dramatically with the size of R. At 37°, the N-t-butyl system has 96% imine, doubtlessly because of a large steric repulsion in the closed form. The N-isopropyl and N-neopentyl systems would be expected to have less steric interaction than the t-butyl in the closed form and, hence, show less imine at equilibrium. The temperature dependence of the equilibrium constant can be explained by the fact that the 7-imine has a much greater entropy than the imidazolidines, and that although strain is imposed at C-7 on forming a double bond, considerable relief of steric interaction occurs on isomerisation to the 7-imine.

In carbon tetrachloride the larger of the vinyl triplets is the downfield one at equilibrium, but in dimethyl sulphoxide the larger triplet is the upfield one. It is believed that this is due to a solvent shift and does not represent the fortuitous but not impossible situation that the equilibrium constants are exactly reversed in the two solvents. Equilibrium constants were found to have the same absolute value in both solvents. The rates of equilibration were fast in dimethyl sulphoxide but very slow in carbon tetrachloride, presumably because of the poor charge-solvating qualities of the latter. An

Table I. Percentages of Imidazolidines and 7-Imine in Equilibrium in Dimethyl Sulphoxide.

R		
METHYL	50 , 50	0
ETHYL	52 , 48	0
NEOPENTYL	34 , 26	40
ISOPROPYL	21 , 12	67
TERT.-BUTYL	*	96

* not measurable because of diffuse signals

unambiguous assignment of the vinyl triplets to the syn and anti compounds has not yet been possible.

(B) MIXED KETAL SYSTEM

Failure to assign the imidazolidines made it imperative that another system be developed containing isomers, the stereochemistry of which could be determined. Ketals and acetals, in equilibrium with the parent ketones and aldehydes, have been used to show steric effects.[46,47] Equilibration of a series of ketones in a 1:1 ratio with triethylorthoformate gave equilibrium constants which showed that increase of the size of the alkyl groups on the ketone caused a large decrease in the extent of ketal formation.[46] Equilibration of straight chain alcohols with aldehydes gave an average of 80% acetal formation, whereas for secondary alcohols the average was 46%. This lowering of the percentage acetal formed was attributed to the increased steric interaction in the acetal on changing from primary to secondary alcohols.[47] Wheeler and Mateos[48] have used the extent of hemiketal formation as a guide to the steric environment of ketones.

The mixed ketal system was derived from the equilibration of 7,7-dimethoxynorbornene, an alcohol ROH, methanol, and a trace of mineral acid (Figure 11). Primary and secondary alcohols were used. Tertiary alcohols dehydrate too readily to be of use and indeed, no tertiary alcohol ketals have been produced in acidic media.

Quenching of the acid by adding strong base stopped equilibration. The four ketals were collected after gas chromatographic separation, the mixed ketals being collected as one unit. The p.m.r. spectra of

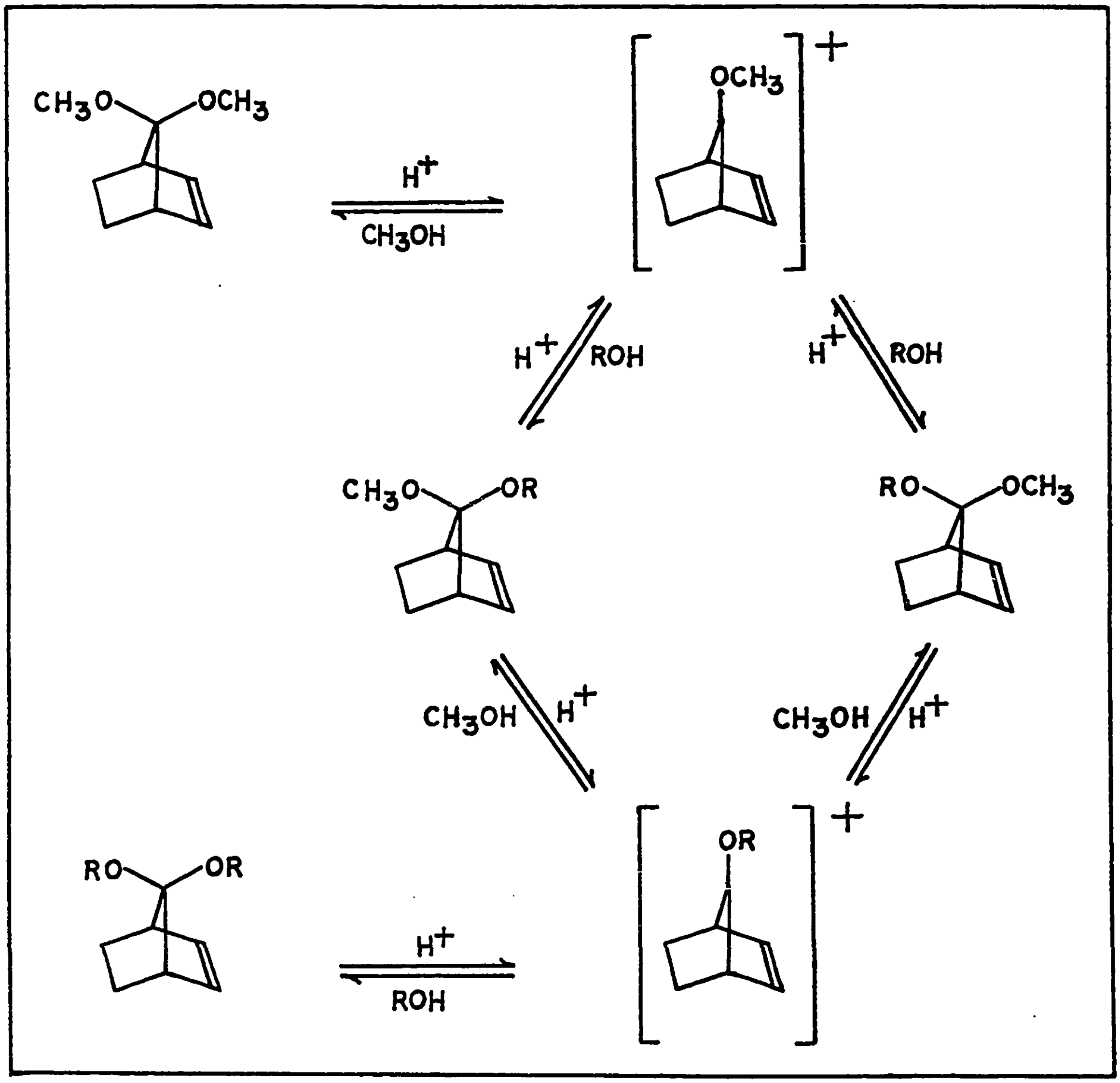


Figure 11. Acid Catalysed Equilibration of 7,7-Dimethoxynorbornene, an Alcohol ROH, and Methanol.

the latter in all cases showed signals at approximately 6.9 and 7.0τ. Integration of the signals, corresponding to syn and anti methoxy groups, gave the equilibrium constant for the system shown below (equation 37).

[37]

The above system meets the conditions (page 25) for determining the relative steric requirements of the ethano and etheno bridges. Alcohols of the type used have dipole moments in the narrow range of 1.66-1.71 D. The dipole moment of the ketal function should lie in, or close to the C-1,C-7,C-4 plane. Since the ketal unit is balanced insofar as polar effects are concerned, the overall dipole moment of the molecule should not cause one isomer to be preferred at equilibrium. The equilibrium constant was found to be independent of solvent, an excellent indication that polar factors had been minimised or eliminated. The equilibrium constant of 1.9 for the isopropyl system at 25° was the same in the neat alcohols mixture and in the same mixtures of the alcohols diluted fivefold with either ether or carbon tetrachloride. Assignment of the mixed ketals will be described later.

The results of the equilibrations using ethanol, 2,2-dimethylpropanol, propan-2-ol, and pentan-2-ol are shown in Table II. The feed ratios were chosen to give a reasonable amount of mixed ketals at equilibrium for collection purposes.

Table II. Percentages of Syn- and Anti-Mixed Ketals in Equilibrium.

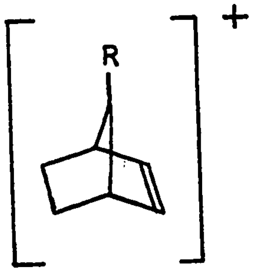
ALCOHOL (ROH)	MIXED KETALS		FEED RATIO ROH/MeOH
	% SYN	% ANTI	
ETHANOL	52	48	2
NEOPENTANOL	57	43	3
ISOPROPANOL	62	38	10
PENTAN-2-OL	64	36	100

"Syn" describes the isomer which has the group OR on the side of the etheno bridge.

Assignment of the mixed Ketals

In the p.m.r. spectra of the mixed ketals there were signals at 6.9τ and 7.0τ, corresponding to the methoxy groups in the two isomers. The downfield signal was, in all cases, larger than the upfield signal, and the ratio of the two gave the equilibrium constant. 7,7-Dimethoxynorbornene, from which the mixed ketals are derived, also shows signals at 6.9τ and 7.0τ. Table V shows the chemical shifts for the remaining protons in the mixed ketals and in 7,7-dimethoxynorbornene (13). It is evident from the similarity in chemical shifts that no large geometric change takes place on formation of the mixed ketals from 13. It is reasonable, therefore, that the signal at 6.9τ in both 13 and in the mixed ketal mixture represents the same methoxy group, syn or anti. The target, therefore, was to assign the methoxy signals of 13 and extrapolate to the mixed ketals.

A survey of the literature on norbornene revealed that a 7-norbornenyl cation (14) is always captured preferentially from the anti side by an external nucleophile.



(14)

Winstein and co-workers,[49a,b] found that the rate of acetolysis of anti-7-norbornenyltosylate was 10'' faster than that of the saturated compound. Since reactions with SN2 mechanisms are virtually unknown for 7-substituted norbornenes, product formation must involve capture of the 7-norbornenyl cation. It was found that the anti-acetate was formed exclusively. Tanida, Tsuji and Irie[50] have shown that 14, R = H, is captured also by water and chloride ion exclusively from the anti side. In his paper on memory effects, Berson[51] reported that the 7-methyl norbornenyl cation was also captured specifically from the anti side. Capture of the 7-p-R-phenyl-7-cation[41a,b] by water was predominantly from the anti side. When R was OCH_3 or $N(CH_3)_2$, capture was preferentially from the anti side giving 92% anti-ol and 8% syn-ol. When R was H on CF_3, the anti alcohol was formed exclusively.

It would appear from these data that increased electron donation by a C-7 substituent to the 7-norbornenyl cation (14) causes a decrease in the stereoselectivity of capture. Based on these findings, the 7-methoxy-7-norbornenyl cation should also be captured preferentially from the anti side, but because a methoxy group is a more powerful stabiliser of positive charge than is a p-anisyl group, it might be anticipated that the stereoselectivity of capture would be lower than that for Gassman's system.[41a,b] Formation and capture of the 7-methoxy norbornenyl cation was done in two ways:

(a) generation of the cation from 7,7-dimethoxynorbornene and aluminium chloride and reduction of the cation by lithium aluminium hydride gave a mixture of the 7-syn and 7-anti methyl ethers in the ratio 5.6:1, respectively. The syn ether was positively identified by the presence of long-range or 'W'-coupling between the anti C-7 proton and the C-2,3 vinyl protons.[45,50] The cation is captured preferentially from the anti side with reduced stereoselectivity, as predicted.

(b) rates of capture of the 7-methoxy-7-norbornenyl cation by deuterated methanol (CD_3OD) from the syn and anti sides were monitored by observing the rate of disappearance of the p.m.r. signals at 6.9 and 7.0τ of 7,7-dimethoxynorbornene (Figure III). The experiment was done using CD_3OD as solvent and p-toluenesulphonic acid as catalyst. The rate of disappearance of the downfield signal was 2.00 ± 0.12 times that of the upfield signal. By analogy with the previous experiment, the downfield signal is attributed to the anti-methoxy group. Lamaty, Malaval, Roque and Geneste[52] have also assigned the upfield signal to the syn methoxy group, although mention was not made of how this assignment was done. In the mixed ketal mixtures, therefore, the downfield signal is also attributed to the anti methoxy group. Since at equilibrium the compound containing the anti methoxy group is the favoured isomer, the larger group -OR in this isomer is sitting on the syn side, and hence the syn side (or the etheno bridge) has a smaller steric requirement than does the ethano bridge.

It can be seen from Table II, page 38, that substantial increase in the bulk of the R group causes only small changes in the equilibrium constant. The steric difference between the etheno and ethano bridges

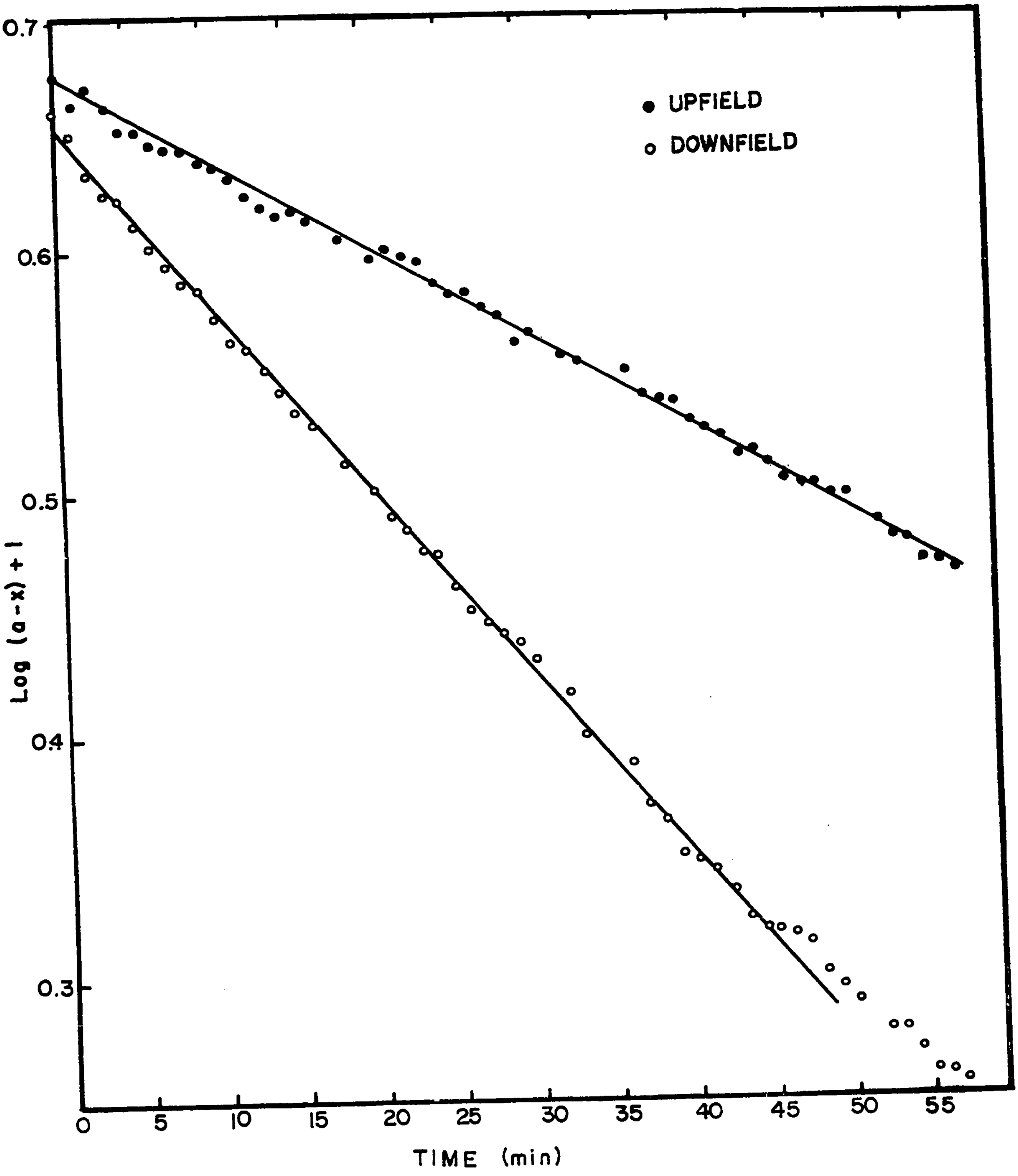
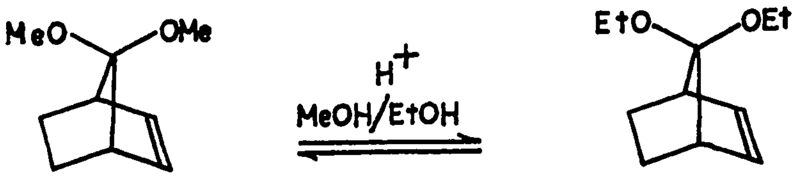


Figure III. Rates of Transketalisation of 7,7-Dimethoxynorbornene in Methanol d_4.

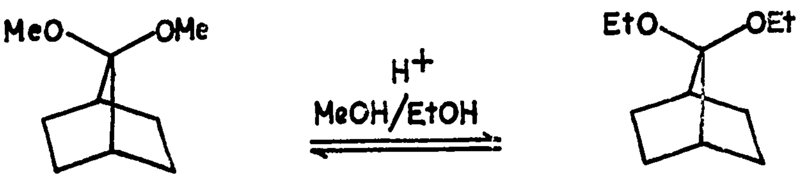
is fairly small; for a group as large as a 2-pentoxy group the mixed ketals have a free energy difference of only 420 calories mole^{-1}.

While, strictly, no comparison can be made between the equilibrium constants of the mixed ketal system and the imidazolidine system, it is of interest to note (Tables I and II) that the results are comparable in magnitude; an indication that both systems are measuring the same effect. It would appear, for both systems, that the magnitude of the equilibrium constant is governed primarily by the bulk of the carbon α to the hetero atom. This has precedent in Lansbury's "β"-effects,[53] studied in the dihydropleiadine system, in which the steric effect comes from the bulk of the substituents on the carbon atom β to the benzene rings. Lansbury[53] warned of the dangers of extrapolating between steric effects in different equilibrated systems, and indeed, there is no correlation between the logarithm of the equilibrium constants found here and either A values or E_s values.

A further thermodynamic probe into the relative steric requirements of the ethano and etheno bridges was conducted. The equilibria shown below were studied in identical solutions (equations 39 and 40).



[39]



[40]

The equilibrium constant is defined as:

$$K_{(eqn)} = \frac{[\text{Dimethoxy}][\text{Ethanol}]^2}{[\text{Diethoxy}][\text{Methanol}]^2}$$

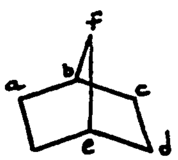
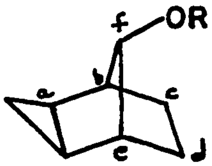
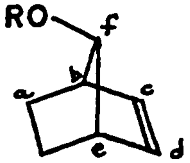
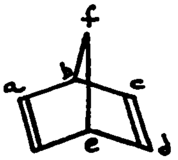
The equilibrium constants were found to be 5.58 ± 0.24 and 8.77 ± 0.33 for 39 and 40, respectively. Clearly, the saturated system prefers the smaller ketal at equilibrium to a greater extent than does the unsaturated system. This again points to the etheno bridge as having a smaller steric requirement than the ethano bridge.

That this effect is due to steric repulsion and not to a geometric change in the carbon framework of the norbornene and norbornane systems can be shown by structure determinations on these skeletons.[55a,b,56] It can be seen from Table III that only very small geometric changes take place on introduction of a double bond into the norbornane skeleton. This is contrary to the suggestion of Bartlett and Giddings[57] who predicted a flattening of the molecule on introduction of a double bond.

Rates of Acid and Base Catalysed Transesterification of the Methyl bicyclo[2.2.1]hept-2-en-7-carboxylate Isomers as a Criterion of Structural Effects in the Norbornene System

As stated in the Introduction, acid catalysed hydrolysis and transesterification reactions are governed primarily by steric effects. If the assumption is made that the 7-esters of norbornene are not an exception to this general rule, then it would be expected that in acid media the transition state for transesterification of the syn ester would be lower in energy than that for the anti ester. The base and acid catalysed transesterification reactions in methanol d_4 are shown

Table III. Geometries of Norbornene and Norbornane Systems.

ANGLE				
abc	107	107	107	104
bcd	103	104	107	108
bfe	95	97	96	96

in Figure IV for the syn isomer.

Since the rates of transesterification were studied by p.m.r. at 35°, it was necessary to determine the free energy difference, $\Delta G°$, between the syn and anti isomers at this temperature. The value of the equilibrium constant K was known to be 1.22 at 65°.[5] Equilibrium constants for the isomerisation (equation 34), measured at 80° and 95° were 1.17 ± 0.03 and 1.14 ± 0.03, respectively. Log K was plotted against $\frac{1}{T}$ for these three temperatures and the resulting straight line was extrapolated to give the equilibrium constant for 35°. From these data $\Delta G°$ at 35° was determined to be 162 ± 15 calories mole^{-1}.

Rates of transesterification for both base and acid catalysed reactions were measured on a mixture of the syn and anti esters in a p.m.r. experiment. The rates of disappearance of the methoxy signals at 6.4τ (anti) and 6.5τ (syn) by methanol d_4 exchange were monitored by comparison with a standard signal. Under the conditions used, isomerisation of the esters did not take place. The ratio of reaction rates was: $\frac{\text{anti}}{\text{syn}} = 1.0 \pm 0.05$ for acid and $\frac{\text{anti}}{\text{syn}} = 1.80 \pm 0.07$ for base (Figures V and VI).

In the base catalysed transesterification, the anti isomer reacts faster than the syn isomer by a factor of 1.8. This can be attributed to repulsion between the π orbitals and the approaching base in the transition state for the syn isomer.

Since the rates for acid-catalysed transesterification of the syn- and anti-7-esters are the same, it follows that the transition state for the syn isomer is lower in free energy than the transition state for the anti isomer by the same amount that the syn ground state is lower than the anti ground state,

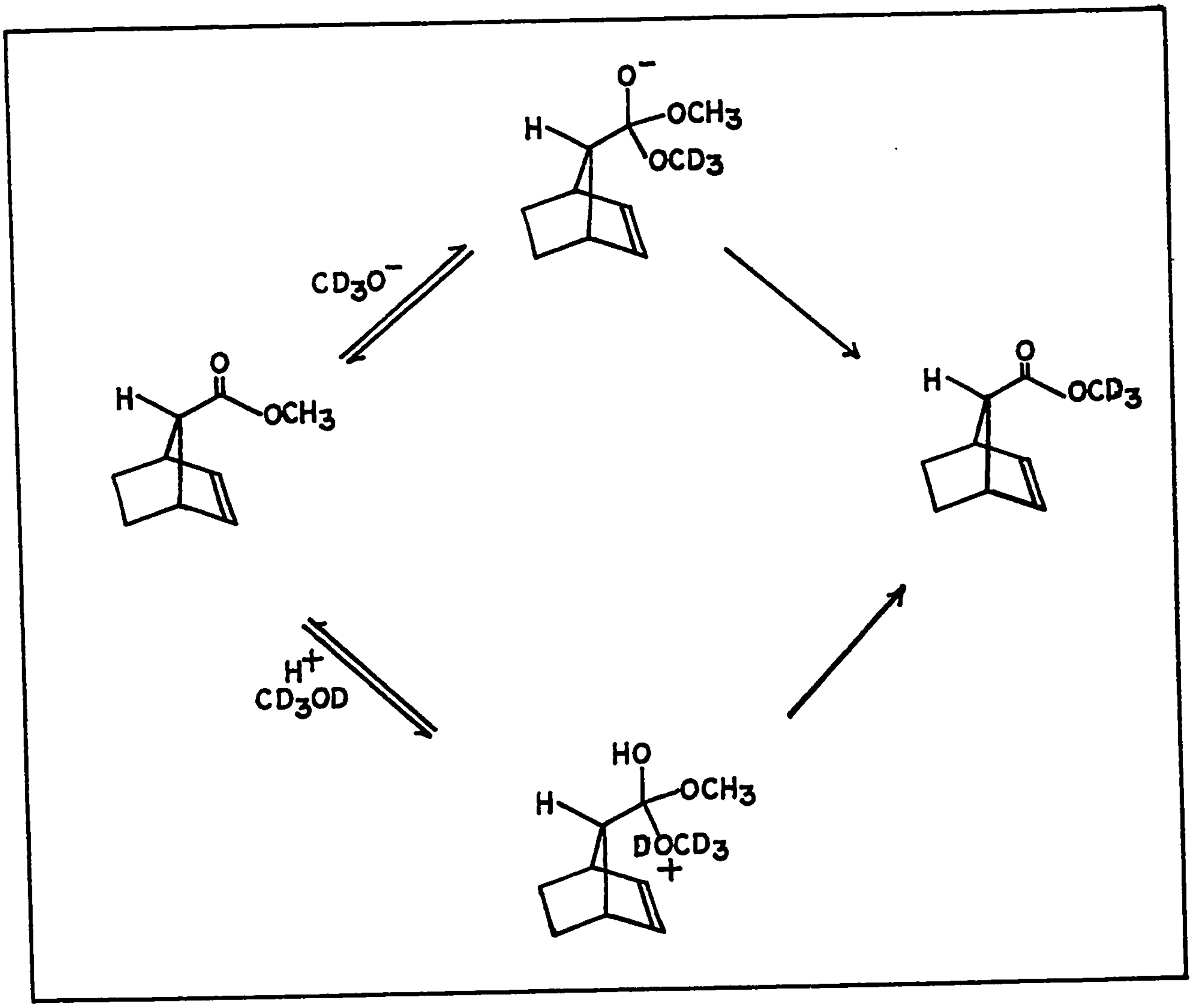


Figure IV. Acid and Base Catalysed Transesterification Reactions of Methylbicyclo[2.2.1]hept-2-en-7-carboxylate.

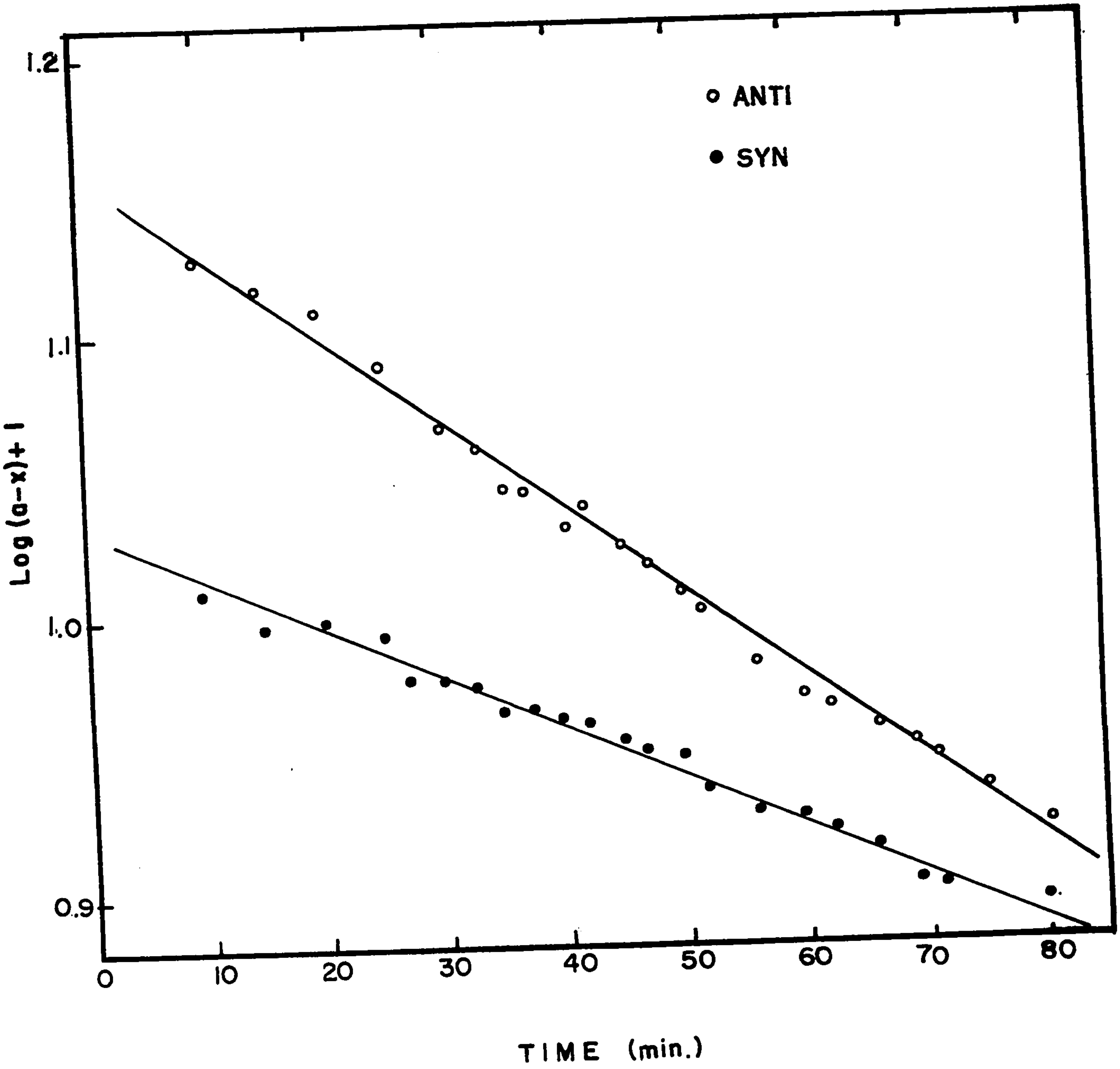


Figure V. Rates of Base Catalysed Transesterification of Methyl bicyclo[2.2.1]-hept-2-en-7-carboxylate.

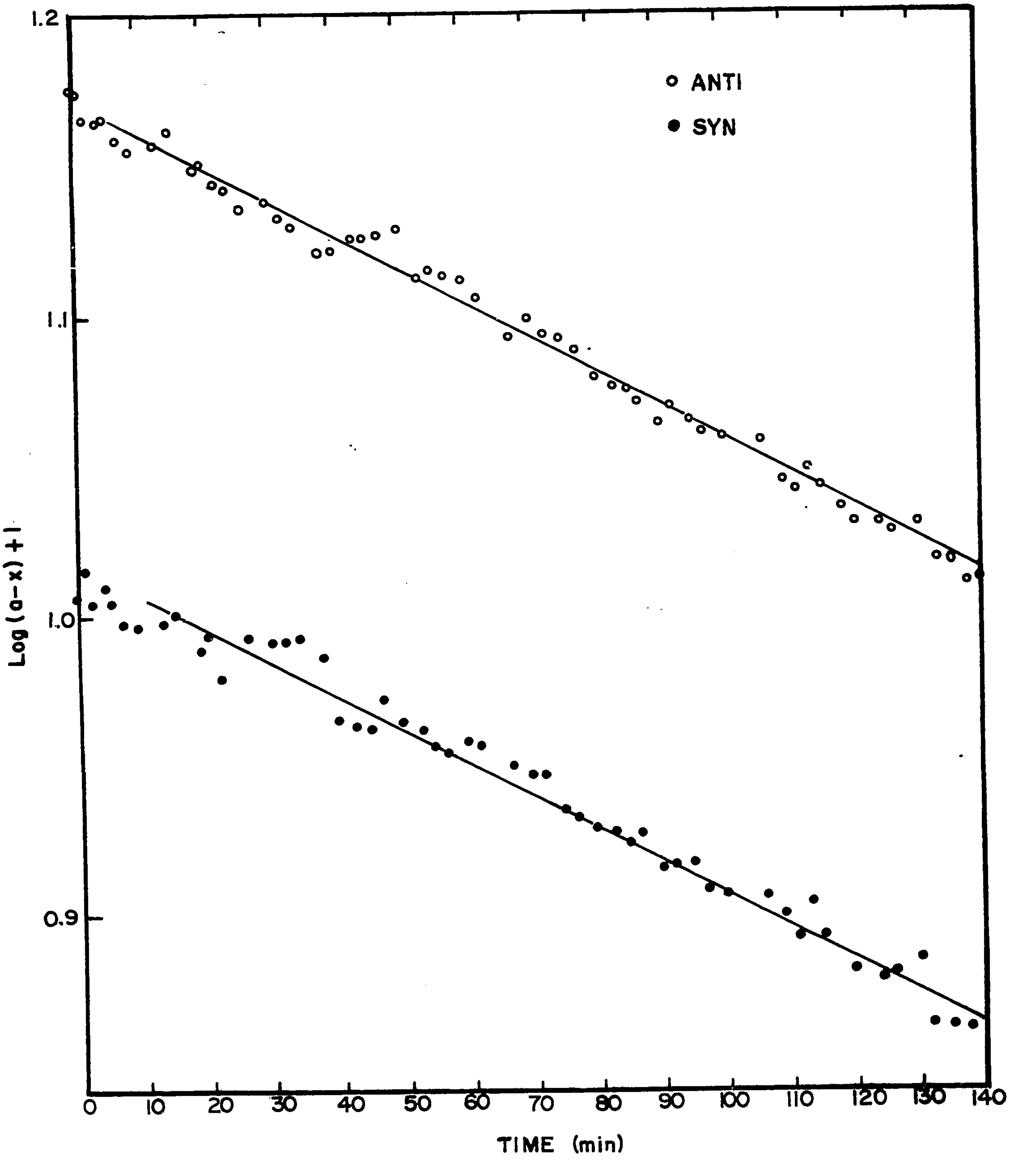


Figure VI. Rates of Acid Catalysed ~~Transesterification~~ Transesterification of ~~Methyl~~ bicyclo[2.2.1]-hept-2-en-7-carboxylate.

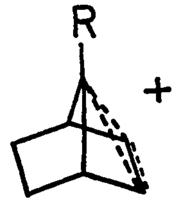
i.e. 162 ± 15 calories mole^{-1}. This result was somewhat surprising. It was expected that the free energy difference for the transition states would be higher than that for the ground states, since the transition states are more bulky than the ground states. A complete explanation of this result is not possible at present. If the syn ester is an exception to the general rule that rho is zero for transesterification, then both steric and polar effects must play a part in determining the relative free energies of both ground and transition states. The free energy difference of 162 cal. mole^{-1} is probably mainly due to a steric effect since both the sense and magnitude of this effect are similar to those found for the mixed ketals, from which polar effects have been removed.

In conclusion, the studies in this work on the mixed ketal system, the symmetrical saturated and unsaturated ketals, and the transesterification, taken collectively, provide unambiguous evidence that the syn side of the norbornene skeleton is less hindered than the anti side. This is in direct contradiction to the suggestion of Brown and co-workers[4,54] that the ethano bridge is less sterically hindering than the etheno bridge. Knowledge of the sense, and of the approximate magnitude, of this steric effect is vital to the explanation of reactions at C-7, especially in cases where stereoselectivity is low, and steric effects may be important. This will be further discussed in connection with certain solvolysis reactions (page 54) and the 7-norbornenyl radical (page 56).

The 7-Norbornenyl Cation and the Levelling Effect

A non-classical 7-norbornenyl cation was first invoked by

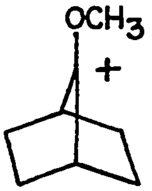
Winstein and co-workers[49a,b] to explain a 10^7 rate ratio for solvolysis of anti- and syn-7-norbornenyl tosylates. This cation has been the subject of much controversy, but it is now generally agreed that the cation can be described as a symmetric delocalised species (16) in which the π-system shares electrons with the empty orbital on C-7.



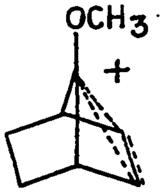
(16)

Structure 16 is reasonable on the basis of rates of reaction,[49a,b] stereochemistry of products,[49a,b,50,51] p.m.r. studies,[58a,b] and theoretical calculations.[59] It was pointed out earlier that the selectivity of capture of a 7-substituted-7-norbornenyl cation shows a strong dependence on the stability of the cation. 7-Norbornenyl cations which bear an electron-withdrawing, or weakly electron-donating, 7-substituent, are captured specifically from the anti side by an external nucleophile. Electron-donating 7-substituents reduce drastically this stereoselectivity. An interesting problem arose from these data. Is it possible to remove completely π-participation from the transition state?

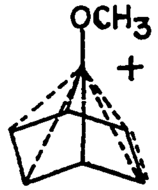
The p.m.r. studies of Winstein, Brookhart and Lustgarten[58b] and the transketalisation study in this work both indicate that π-participation is not completely removed, but is drastically reduced from the case where the 7-substituent is hydrogen or methyl. The former study was a p.m.r. determination of the free energy of activation, $\Delta G^{\ddagger}$, for the isomerisation of the cations (17),(18) and (19).



(17)

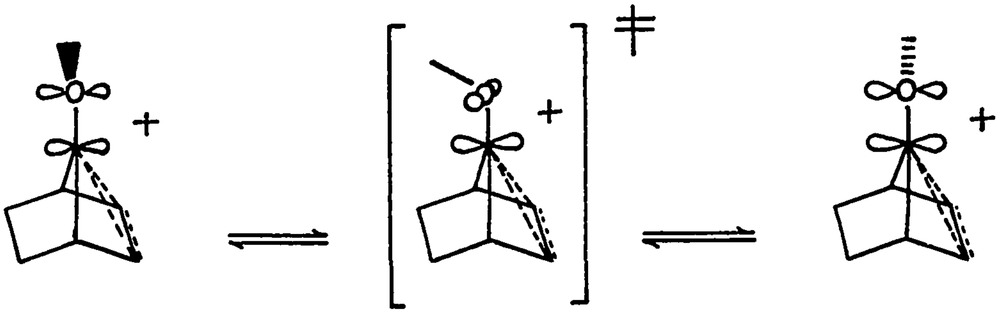


(18)



(19)

In order for p-pπ overlap to occur between C-7 and the oxygen atom, the methyl group must lie in the C-1-C-7,C-4 plane, and is thus closer to one bridgehead proton than the other, rendering the bridgehead protons magnetically non-equivalent. The mechanism of isomerisation is shown below for cation 18 (equation 41)



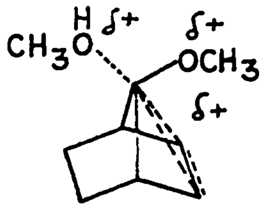
[41]

(20)

In the transition state for isomerisation (20), the p-pπ bonding is lost, or at least, drastically reduced, because of poor bond overlap. The transition state, therefore, gains stabilisation by electron donation from the π-system to C-7. This effect is reflected in the magnitude of $\Delta G^{\ddagger}$ for isomerisation, which was found to be significantly lower for 18 and 19 than for 17. Since the structures of the molecules are fairly similar, this lowering of $\Delta G^{\ddagger}$ for 18 and 19 was attributed to an electronic effect, and can be due only to π-participation in the transition state. The difference in $\Delta G^{\ddagger}$ of about 8 kcal $mole^{-1}$ between cations 17 and 19 virtually eliminates inversion at oxygen[60] as being the mechanism for isomerisation, since inversion must take place in the C-1,C-7,C-4 plane, with retention of p-pπ stabilisation from oxygen in both cations.

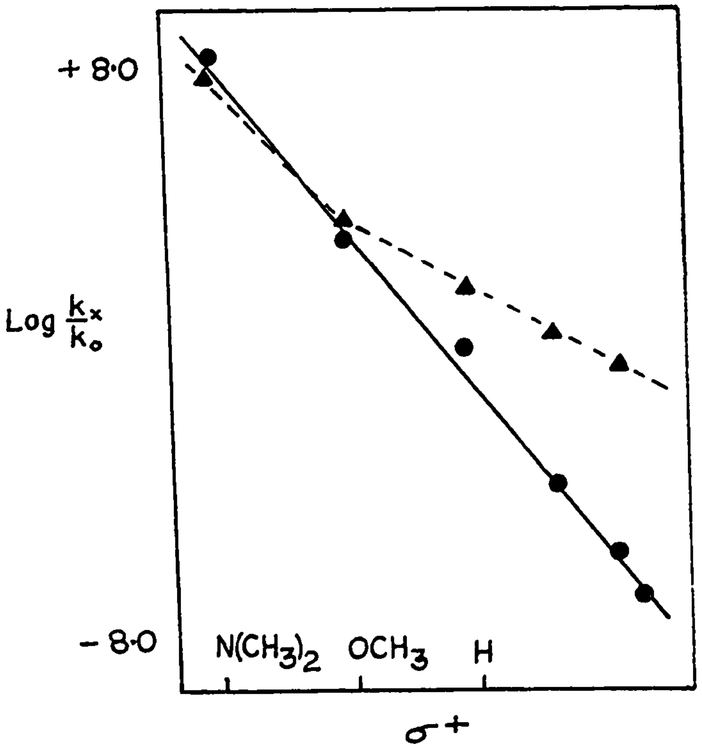
It is worthy of note that although π-participation in the transition state is almost definitely present, the extent of π-participation in the 7-methoxy-7-norbornenyl cation may be very small or zero. The geometry of bond overlap in the transition state favours π-participation, but in the cation itself, the major factor in the stabilisation is undoubtedly the p-pπ overlap between the empty C-7 orbital and the oxygen atom.

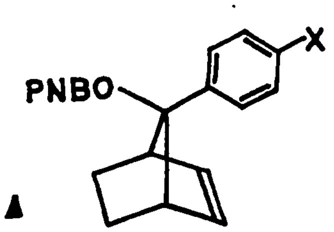
In this present work, it was found that the 7-methoxy-7-norbornenyl cation was captured preferentially from the anti side by a methanol molecule. This system is subject to microscopic reversibility,[71] provided small isotopic effects are ignored. The transition states for isomerisation of the conjugate acids of the ketal are, therefore, identical to the transition states for capture of the intermediate cation by a methanol molecule. The stereoselectivity cannot be due to steric effects and must be due to π-participation in the transition state. The transition state for the transketalisation is, therefore, proposed to be (21).



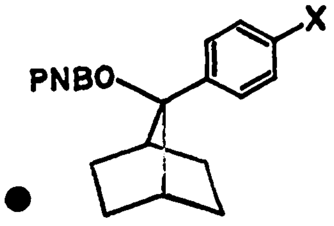
(21)

Gassman and Fentiman[41a,b] have studied the rates of solvolysis in water/dioxane of 7-aryl-7-norbornyl and syn-7-aryl-anti-7-norbornenyl p-nitrobenzoates (22,23). The results are summarised below in a graph of $\log \frac{kx}{ko}$ versus σ^+.





(23)



(22)

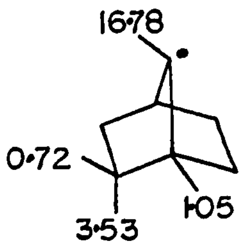
The sharp break in slope for 23 was attributed to what was described as a mechanistic change; that of cessation of π-participation in the transition state.

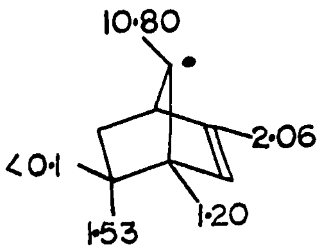
Jaffe[61] has pointed out that when two separate mechanisms can occur, the rho-sigma relationship generally gives a smooth curve, concave upwards, because the two mechanisms generally show different substituent effects. If the above graph for the unsaturated compound 23 is, in fact, a smooth curve, then it would be necessary to postulate that for a fixed group X, the free energy of the transition state for some molecules is dependent only on the group X, while for others it is dependent only on π-participation. Such a postulate is unreasonable. The π-participation would not be expected to discontinue suddenly, but to decrease asymptotically towards zero as the cation-stabilising ability of the aryl group is increased. Evidence for π-participation in substituent-stabilised transition states leading to 7-norbornenyl cations came from the transketalisation study in this work. Even with a powerfully electron-donating group like a 7-methoxy group, the 7-norbornenyl cation shows a stereoselectivity of capture which can be attributed only to π-participation in the transition state. Gassman and Fentiman[41a,b] reported that the 7-p-X-phenyl-7-norbornenyl cation $X = OCH_3$, $N(CH_3)_2$, was captured by water from the anti side with a rate factor of 11.5 over capture from the syn side. Doubtlessly steric effects partly determine this capture ratio, but the relatively high stereoselectivity of capture points to an electronic effect also, i.e., a non-classical transition state. If the transition state for capture is non-classical, that for ionisation of 23, $X = OCH_3$, should also be non-classical. Gassman and Fentiman described the latter system as "just levelled". That is, the p-methoxy substituent was judged just sufficient to erase π-participation in the transition state for ionisation. The basis of this claim was the near equality of the rates of solvolysis for 22 and 23, ($X = OCH_3$ for both); that for 23 being 3.5 fold higher. It is clear from the results of the present work that 3.5 is only a minimum value for the acceleration derived from π-participation. The ground state free energy difference arising out of steric effects should favour ionisation of 22 over 23. Since 23 was found to ionise 3.5 fold faster than 22, the actual enhancement derived from π-participation must be greater than 3.5 fold, and it is not correct to say that the p-anisyl substituent causes complete levelling. Such a qualitative correction for steric effects also accomodates the faster rate of 22 ($X = N(CH_3)_2$) compared to the analogous norbornene. All that is required is that the steric acceleration in 22 is no longer outweighed by the anchimeric assistance in 23. The change of slope in the plot for ionisation of 23 is not accounted for in this way. As stated above, it seems unlikely to the writer that there is, in fact, an abrupt change of mechanism. A complete explanation of these solvolyses is not possible until the free energy difference between the ground states of 22 and 23 is known.

The 7-Norbornenyl Radical

The 7-norbornenyl radical should show characteristics somewhere between those of the 7-norbornenyl cation and the 7-norbornenyl anion. Evidence has already been presented that the 7-cation is non-classical, possibly even with an electron-donating 7-substituent. The 7-anion has been described as a bishomoantiaromatic species.[62] Is the 7-radical a classical or non-classical species? Is a three-centre, three-electron bond formed between the radical at C-7 and the π-electrons? Ohorodnyk and Santry[59] used C.N.D.O. (Complete Neglect of Differential Overlap) approximate self-consistent field calculations to determine the angles for the 7-radical which would minimise the energy of the species. These calculations indicated that the bridge leans towards the π-orbitals, and a non-classical radical was proposed to explain this. Hoffman[63] was much more cautious about making any fixed statement, suggesting that the results of such complex calculations are a function of the information and assumptions fed into them.

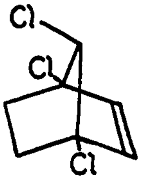
The electron spin resonance spectrum of the 7-radical was determined by Kochi, Bakuzis and Krusic.[64] The most prominent feature of the spectrum was a doublet splitting of 10.80 G due to the hyperfine coupling of the electron with the C-7 proton. Coupling constants to the various protons in the 7-norbornene and 7-norbornane radicals are shown below.



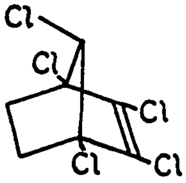


The coupling constant of 10.80 G is very low compared with the value of 23.9 G for the methyl radical. Kochi and co-workers explained this in terms of a bent radical at C-7. It is possible that the low value is due to delocalisation with attendant partial loss of spin density at C-7. These authors claimed that since the C-2,3 splitting in the norbornene radical was roughly the average of the splittings of the exo and endo protons in the norbornane radical, no delocalisation was taking place. The signs of the latter coupling constants have not yet been determined, so the above criterion for a classical or a non-classical radical is ambiguous. Further, if delocalisation does take place in the 7-norbornenyl radical, the bridge should lean over towards the π-system, and as a result the C-2,3 protons would be forced below the C-1,C-2,C-3 plane. In such an event, the coupling of 2.06 G would be a reasonable value, even for a non-classical species.

Sanford[3a] investigated the rates and products for tri-n-butyltin hydride reduction of the compounds shown below (24 and 25).



(24)



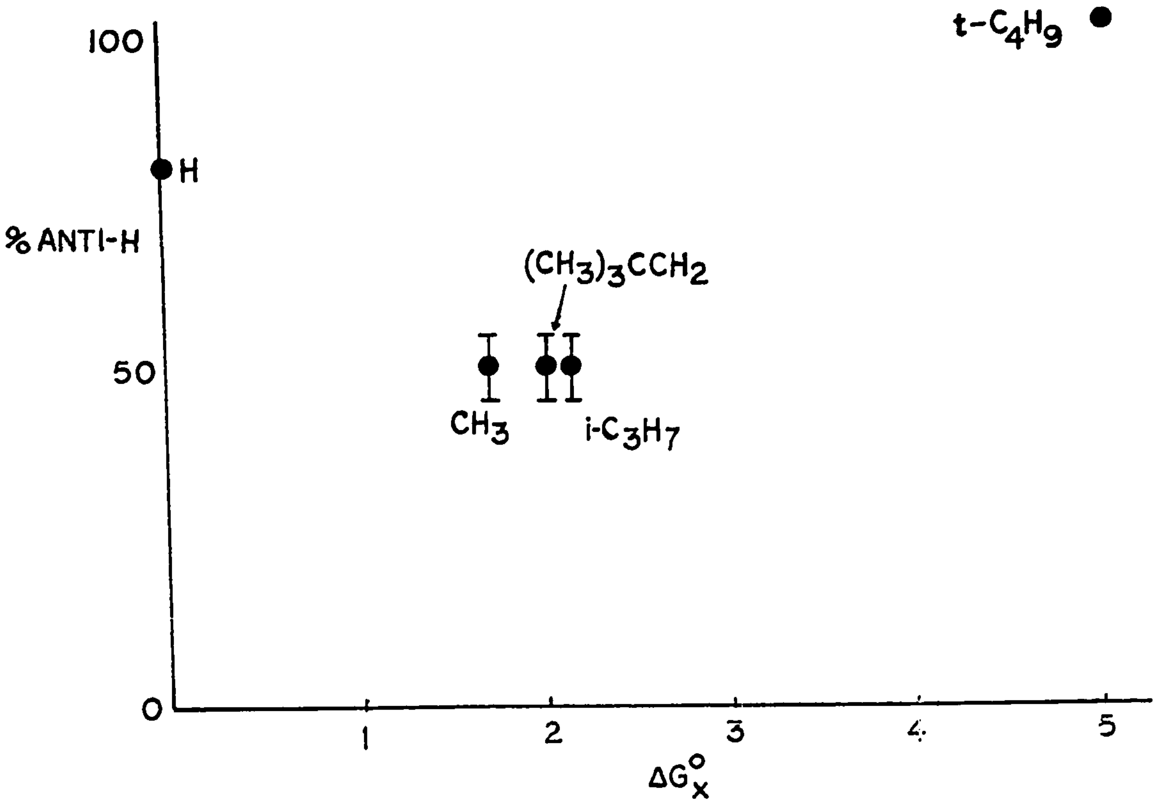
(25)

Both of these reductions gave tricyclic products and rearranged products. Rates, relative to 1,4,7-trichloronorbornane were 15.5 and

260. These large rate enhancements led Sanford to postulate a non-classical transition state.

Russell and Holland,[65] and Cristol and Noreen[66] studied the products of deuterium extraction from tri-n-butyltin deuteride by the 7-norbornenyl radical. A 4:1 preference was found for abstraction by the anti face. Both sets of authors claimed that the stereoselectivity was too small to postulate a non-classical species.

Clark[67] conducted a study of hydrogen abstraction from tri-n-butyltin hydride by various 7-alkyl-7-norbornenyl radicals. The latter author plotted the percentage of anti-H compound formed versus a steric substituent parameter, ΔG°_x.[68]



When X was methyl, isopropyl, n-butyl and neopentyl, abstraction of a hydrogen atom by the radical gave 50 ± 5% of the anti-H compound. When X was either hydrogen or t-butyl, capture by the anti face was preferred with high stereoselectivity. Clearly, the attack ratios do not reflect a smooth variation with the size of the substituent alone, so it is reasonable that the reactions with X = hydrogen and t-butyl are dominated by different effects. Clark's interpretation of the data was that except for X = hydrogen steric effects in the transition state dominated the reaction. The percentage of anti-H compound for X = hydrogen (80%) was explained by postulating a non-classical transition state.

In terms of electron density at C-7, and the demand for stabilisation by delocalisation, the 7-methoxy-7-norbornenyl cation should be a reasonable model for the 7-norbornenyl radical. Although this work has provided good evidence that the transition states leading to the 7-methoxy-7-norbornenyl cation are non-classical, there is no strong evidence indicating that the cation itself should be described as non-classical. In principle, there must be some delocalisation into the π-system for it is unreasonable to expect the interaction to drop other than asymptotically towards zero as the demand for stabilisation drops. Thus, the argument becomes somewhat semantic, depending on whether or not one says an effect "stops" when the limit of detection is reached.

This work has determined that the syn side of the norbornene skeleton is less hindered than the anti side. Attack, therefore, on the 7-norbornenyl radical should be preferred from the syn side if steric effects alone are operating. Experimentally, the reverse is found, attack from the anti side being favoured by a factor of 4 over attack from the syn side. This can only be attributed to an electronic effect. The stereoselectivity, both in sense and in magnitude, is fully consistent with mild participation of the π-orbitals in the transition state. It would be of considerable interest to compare the stereoselectivity of capture of the 7-methoxy-7-norbornenyl radical with that of the 7-methoxy-7-norbornenyl cation. Possibly the stabilisation afforded by the methoxy substituent, together with its relatively low steric requirement, would lead to predominant H-abstraction by the syn face of the radical; a preference that has only been approached thus far with 7-alkyl-7-norbornenyl radicals.[67] Such a result would provide support for assignment of a non-classical structure to the 7-norbornenyl free radical.

EXPERIMENTAL

General

(a) Instruments employed

(i) All proton magnetic resonance (p.m.r.) spectra were run on a Varian HA 100 instrument. All kinetic runs were done on a Varian T-60 instrument. The reference for spectra was tetramethylsilane (T.M.S.), and the solvent carbon tetrachloride unless otherwise stated. Proton magnetic resonance data, unless tabulated, are expressed as: chemical shift (τ), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, sept = septet, m = multiplet), proton integration, assignment, and coupling constant (J,Hz) if important.

(ii) All infra-red spectra were run as thin films on a Perkin-Elmer 337 spectrometer. Spectra were calibrated by reference to the 1601.0 cm^{-1} and 1027.7 cm^{-1} peaks of polystyrene.

(iii) Both preparative and analytical gas-liquid partition chromatography (g.l.p.c.) were carried out on a Varian Aerograph A90-P3 instrument with a thermal conductivity detector. The reasonable assumption was made that the isomers separated had the same thermal conductivity. Dry helium was the only carrier gas used. Quantitative product ratios from g.l.p.c. analyses were obtained by triangulation. In all cases the trace showed a stable base-line.

(iv) The constant temperature baths for the ketal equilibria and the ester isomerisation were filled with water and mineral oil, respectively. The temperature control was a Fisher mercury-contact thermostat which controlled to ±0.2°.

(b) Bicyclo[2.2.1]hept-2-ene, N-methyl ethylenediamine, N-ethyl ethylenediamine and N-isopropyl ethylenediamine were supplied by the Aldrich Chemical Company, Milwaukee, Wisconsin. Methanol d_4 (99.5%) was supplied by Merck Sharp and Dohme of Canada.

7,7-Dimethoxy-1,2,3,4-tetrachlorobicyclo[2.2.1]hept-2-ene

5,5-Dimethoxy-1,2,3,4-tetrachlorocyclopentadiene, prepared by the method of McBee,[69] was placed in a 22 x 3 cm Pyrex tube fitted with a sintered-glass bubbler and a small outlet tube. The bottom (7 cm) was heated in an oil bath at 190°. Ethylene gas was bubbled in for 10 hours, at which time a p.m.r. spectrum indicated 95% reaction. Vacuum distillation produced a slightly yellow viscous liquid, the title compound, b.p. 100-104°/1mm, lit.[70] 72-80°/0.1 mm.

7,7-Dimethoxybicyclo[2.2.1]hept-2-ene

7,7-Dimethoxy-1,2,3,4-tetrachlorobicyclo[2.2.1]hept-2-ene (32 g., 0.11 mole) and t-butanol (90 g, 1.33 mole) were mixed with tetrahydrofuran (550 mℓ) in a 2ℓ three-necked flask fitted with a condenser and a magnetic stirrer. Dry nitrogen was bubbled into the solution for 15 minutes. Sodium (60 g., 2.6 mole) was added as thinly cut plates over 30 minutes, and the reaction was maintained at reflux under nitrogen for 8 hours. The solution was filtered while hot to remove the larger pieces of sodium. To the filtrate was added 100 mℓ of methanol to decompose any remaining sodium before extraction. Careful extraction into petroleum ether, followed by washing with water to remove t-butanol, drying over anhydrous magnesium sulphate, and removal of solvent by evaporation gave an orange liquid. Vacuum distillation of the latter gave the title compound, yield 8.7 g. (52%), b.p. 68-71°/26 mm.

Bicyclo[2.2.1]hept-2-en-7-one

7,7-Dimethoxybicyclo[2.2.1]hept-2-ene (8.5 g.) was added to 1 ℓ of 5% aqueous sulphuric acid. The resulting two-phase system was stirred for 2 hours. Extraction into petroleum ether, followed by drying over anhydrous magnesium sulphate and removal of solvent by evaporation gave 5.5 g., (90%) of bicyclo[2.2.1]hept-2-en-7-one in an almost pure state. Vacuum distillation yielded the product as a colourless liquid, b.p. 70-74°/40 mm., lit.[70] 66-70°/34 mm.

Mixed Ketal Systems -- Equilibration

The following general method applied to all four alcohols (ROH) employed. 7,7-Dimethoxybicyclo[2.2.1]hept-2-ene was added to a mixture of methanol and an alcohol, ROH. To this solution was added a catalytic amount of fuming sulphuric acid. The solution was placed in a dry flask which was stoppered and placed in a constant temperature water-bath at 54 ± 0.2°. When equilibrium was attained, the acid was neutralised by addition of 10 $\overline{N}$ sodium hydroxide which had been heated to 54° in the same bath. The solution was extracted with ether and dried over anhydrous magnesium sulphate. Separation of the components was effected using gas chromatography, 10' x 3/8"

S.E. 30 (10%), at 150°. In all cases, the mixed ketals had similar retention times and were collected as one unit. Integration of the methoxy signals at approximately 6.9τ and 7.0τ in the p.m.r. spectrum gave the equilibrium ratios of the mixed ketals.

The relative g.l.p.c. retention times are shown in Table IV. The isomeric mixed ketals were not separated by the column and are quoted with one retention time. The symmetric ketals of three of the alcohols employed were prepared separately from an acidified solution of the alcohol and bicyclo[2.2.1]hept-2-en-7-one. Identical relative retention times were found for these symmetrical ketals when compared with the relative retention times from the equilibrated systems.

Tables V and VI show p.m.r. chemical shifts for the mixed ketals and the symmetrical ketals, respectively.

Catalytic Hydrogenation of 7,7-Dimethoxybicyclo[2.2.1]hept-2-ene

Palladium on carbon catalyst (200 mg., 5% Pd) was added to a solution of 7,7-dimethoxybicyclo[2.2.1]hept-2-ene (5 g.) in 10 mℓ of methanol. The mixture was stirred under a hydrogen atmosphere until a p.m.r. spectrum indicated that the vinyl signal of the ketal had disappeared. Filtration, followed by evaporation of solvent, gave 7,7-dimethoxybicyclo[2.2.1]heptane, 4.4 g., (87%) as the only product.

Kinetics of Acid-Catalysed Methoxyl Exchange of 7,7-Dimethoxybicyclo[2.2.1]hept-2-ene in Methanol d_4

7,7-Dimethoxybicyclo[2.2.1]hept-2-ene (30 mg.) was added to

Table IV Relative Retention Times for the Ketals*

7-Substituents	Relative Retention Times
$(OCH_3)_2$	1.00
OCH_3, OCH_2CH_3	1.20
$(OCH_2CH_3)_2$	1.35
OCH_3, $OCH(CH_3)_2$	1.56
$(OCH(CH_3)_2)_2$	2.43
OCH_3, $OCH_2C(CH_3)_3$	2.18
$[OCH_2C(CH_3)_3]_2$	4.36
OCH_3, $OCH(CH_3)CH_2CH_2CH_3$	2.61

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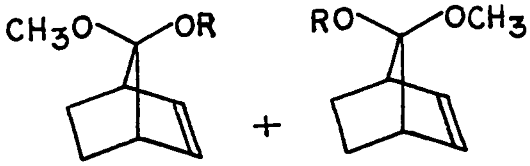
* Isomeric syn and anti mixed ketals were not separated by the column.

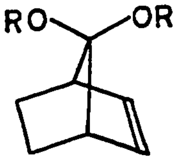
Table V Proton Chemical Shifts for the Mixed Ketals

	C-2,3	C-1,4	EXO C-5,6	ENDO C-5,6	7-OCH_3	
R					ANTI	SYN
CH_3	4.08	7.37	8.21	9.14	6.92	6.99
CH_2CH_3	4.08	7.38	8.21	9.14	6.91	6.98
$CH(CH_3)_2$	4.05	7.39	8.20	9.15	6.86	6.96
$CH_2C(CH_3)_3$	4.10	7.38	8.22	†	6.90	6.98
$CH(CH_3)(CH_2)_2CH_3$	4.08	7.36	8.20	‡	6.86	6.96

† Obscured by protons of the t-butyl group.

‡ Obscured by protons of the 2-pentyl chain.

Table VI Proton Chemical Shifts for the Symmetrical Ketals

 R	C-2,3	C-1,4	EXO C-5,6	ENDO C-5,6	OTHERS
CH_3	4.08	7.37	8.21	9.14	6.92 and 6.99, s, methyl
CH_2CH_3	4.10	7.39	8.20	9.14	8.90 and 8.98, t, methyl 6.63 and 6.73, q, methylene
$HC(CH_3)_2$	4.07	7.41	8.13	9.17	8.89 and 8.97, d, methyl 5.97 and 6.30, sept, methine
$CH_2C(CH_3)_3$	4.07	7.31	8.17	*	9.09 and 9.14, s, methyl 7.00 and 7.12, s, methylene

* Obscured by protons of the t-butyl group.

methanol d_4 (0.35 mℓ) in a clear glass n.m.r. tube. The tube was heated to 35 ± ½° in the probe of the Varian T-60 spectrometer for 20 minutes. p-Toluenesulphonic acid (0.3 mg.) was dissolved in 0.05 mℓ methanol d_4 and the solution was injected into the n.m.r. tube. The tube was well shaken to achieve homogeneity and re-inserted into the probe. The spectrum between 6.7(τ) and 7.0(τ) was scanned at one minute intervals for about 50-60 minutes. The signals seen corresponded to free methanol (6.7τ), and the two ketal methoxy signals at 6.9τ and 7.0τ. The three peak heights were added and the syn and anti peak heights were calculated as a fraction of the total. These fractions gave (a-x), where a is the starting fraction (0.5) and x is the fraction reacted at time t. Log(a-x) was plotted against time and two straight lines resulted. The downfield (6.9τ) signal was found to disappear faster than the upfield (7.0τ) signal by a factor of 2.00 ± 0.12; the average of four runs. The statistical correction for equilibration made by Traylor and Perrin[71] was not employed since the reaction was taken only to 50%.

Reduction of 7,7-Dimethoxybicyclo[2.2.1]hept-2-ene by Aluminium Chloride/Lithium Aluminium Hydride

The procedure was similar to that of Eliel et al.[72] Aluminium chloride (1.3 g., 0.010 mole) was added cautiously to 25 mℓ of dry ether in a 250 mℓ, three-necked, round-bottomed flask fitted with a condenser, pressure-equalising dropping-funnel, and a magnetic stirrer. Lithium aluminium hydride (1.0 g., 0.025 mole) was added as a slurry in 5 mℓ of ether and the mixture was allowed to stand for 30 minutes. 7,7-Dimethoxybicyclo[2.2.1]hept-2-ene (612 mg., 0.004 mole) in 5 mℓ was added dropwise over 15 minutes. The mixture was stirred at room temperature for 1½ hours, when reaction was quenched by the addition of 50 mℓ of 10% aqueous sulphuric acid. Extraction with three 50 mℓ portions of ether, followed by drying over anhydrous magnesium sulphate and removal of solvent by evaporation, yielded 324 mg. (66%) of a mixture of syn- and anti-7-methoxybicyclo[2.2.1]hept-2-ene, and a few percent of another compound. Gas chromatographic analysis of this liquid mixture showed two peaks of relative retention times 1:2 in a ratio of 1:3.6, respectively. (20% D.E.G.S., 5' x ¼'', 110°). Both fractions were collected; p.m.r. spectrum of first component: 4.12, t, 2, C-2,3 vinyl; 6.81, s, 3, C-7 methoxy; 7.00, m, 1, C-7H; 7.42, m, 2, C-1,4 bridgehead; 8.34, m, 2, C-5,6 exo; 9.14, m, 2, C-5,6 endo. A signal at 6.80, s, and others upfield were due to an unidentified compound. Second component: 4.02, m, 2, C-2,3 vinyl, J = 1.0 Hz; 6.60, m, 1, C-7H; 6.79, s, 3, C-7 methoxy; 7.14, m, 2, C-1,4 bridgehead; 8.31, m, 2, C-5,6 exo; 9.00, m, 2, C-5,6 endo. Irradiation of the multiplet at 6.60τ (395 Hz upfield from benzene) caused the vinyl multiplet to collapse to a triplet.

Bicyclo[2.2.1]hept-2-en-7-carboxylic acid

Magnesium (20 g., 0.83 mole) was added to a 1ℓ three-necked flask containing a magnetic stirring bar. The flask was flamed until no more moisture appeared on the necks. A condenser with a drying tube, a pressure-equalising dropping-funnel, and a nitrogen inlet were quickly inserted. When the flask had cooled, ether (600 mℓ) and syn-7-bromobicyclo[2.2.1]hept-2-ene (3 g.) were added. The reaction had an induction period of ½ hour and the Grignard solution was grey in colour. The remainder of the syn-7-bromobicyclo[2.2.1]hept-2-ene (27 g.) was added dropwise over a period of 12-15 hours at room temperature, under an atmosphere of nitrogen. The resulting Grignard solution was added in portions of approximately 15 mℓ in turn into six, 2ℓ conical flasks, each containing 1000 g. of solid carbon dioxide (powdered). The flasks were shaken vigourously and the addition cycle was repeated. Hydrochloric acid (400 mℓ, 2 $\overline{N}$) was added to decompose the resulting complex. The ether layer was extracted three times with 4 $\overline{N}$ sodium hydroxide and the aqueous layer was acidified. Extraction of the crude acids into ether followed by drying over anhydrous magnesium sulphate and evaporation of solvent gave 4.5 g. (19%) of a mixture of the syn and anti isomers of the title compound. The acids were converted into their methyl esters without further purification.

Methyl bicyclo[2.2.1]hept-2-en-7-carboxylate

An ethereal solution of diazomethane was added dropwise to a solution of the above carboxylic acids (8.0 g., mixture) in 100 mℓ ether. Evaporation of the ether yielded a yellow liquid which, on vacuum distillation, gave a mixture of the isomers of the title compound, 6.0 g. (69%), b.p. 90-96°/30 mm, lit.[5] 93-96°/30 mm.

Kinetics of Transesterification of syn- and anti-Methyl bicyclo[2.2.1]-hept-2-en-7-carboxylate in Methanol d_4

(a) Base Catalysed Transesterification

Methyl bicyclo[2.2.1]hept-2-en-7-carboxylate (44 mg. a mixture of syn and anti isomers) was added to methanol d_4 (0.4 mℓ) in an n.m.r. tube. The tube was capped and heated in the probe of the p.m.r. instrument at 35 ± ½° for 30 minutes. Sodium methoxide (10 mg.) was dissolved in 0.1 mℓ of methanol d_4, and 10 μℓ of this solution was injected into the heated n.m.r. tube. Anisole (10 mg.) was added as a standard. The spectrum between 6.2τ and 6.5τ was scanned at two or three minute intervals for approximately 80 minutes. The signals seen corresponded to anisole (6.2τ), anti methoxy (6.4τ) and syn methoxy (6.5τ). The heights of the signals for the syn and anti methoxy groups were calculated as a fraction of the height of the standard signal. These fractions gave $(a-x)_t$, where a and x have the same meaning as in the ketal exchange kinetics (page 65). First order plots of $\log(a-x)_t$ versus time (t) gave straight lines (Figure V) for both syn and anti isomer transesterification with relative slopes 1.8:1, the anti ester reacting more rapidly.

(b) Acid Catalysed Transesterification

The same procedure was used as in the base catalysed transesterification (page 71). Fuming sulphuric acid (98 mg.) was the catalyst. A plot of $\log(a-x)_t$ versus time for the syn- and anti-isomers gave two straight lines with equal slopes (Figure VI).

Equilibration of syn- and anti-Methyl bicyclo[2.2.1]hept-2-en-7-carboxylate

Methyl bicyclo[2.2.1]hept-2-en-7-carboxylate (100 mg., mixture) was added to dry methanol (0.5 mℓ) in a strong glass tube. To this solution was added sodium methoxide (36 mg.). The tube was sealed under vacuum and heated at 80° in a constant temperature bath for 7 days. The tube was dropped into liquid air and then broken open. Analysis by g.l.p.c. showed that the ratio of syn/anti esters was 1.17 ± 0.03. Repetition of the experiment at 95° gave a syn/anti ratio of 1.14 ± 0.03.

N-Methyl Spiro[bicyclo[2.2.1]hept-2-en-7,2'-imidazolidine]

The preparation of the title compound will be described to illustrate the general procedure for the preparation of the N-alkyl imidazolidines (and imines).

To a solution of bicyclo[2.2.1]hept-2-en-7-one (1.08 g., 0.01 mole) in 25 mℓ of benzene, was added N-methyl ethylenediamine (0.89 g., 0.012 mole). The reaction was fast and exothermic. Water was produced and was azeotroped off with benzene, leaving a dark, heavy oil. Vacuum distillation of the latter at 0.1 mm. produced a colourless liquid, the title compound, 1.2 g. (73%). Both isomers were produced, the ratio of these being 1.4:1.

Spiro[bicyclo[2.2.1]hept-2-en-7,2'-imidazolidine]

To a solution of bicyclo[2.2.1]hept-2-en-7-one (0.08 g., 0.01 mole) in 25 mℓ of benzene was added ethylenediamine (0.72 g., 0.012 mole). The solution became red-brown after heating to 40° for 10 minutes. Benzene was removed under reduced pressure at 40° on a rotary evaporator, and the remaining red-brown oil was distilled at 0.1 mm. to yield 0.75 g. (50%) of the title compound; a solid of m.p. 24-25°.

The imidazolidines and their isomeric 7-imines from N-ethyl, N-isopropyl, N-t-butyl and N-neopentyl ethylenediamine were prepared in the following yields: 60%, 60%, 20%, 10%. Table I gives the percentages of the imines and imidazolidines produced.

Spectra

The p.m.r. chemical shifts are shown in Tables VII and VIII. The N-methyl imidazolidines proved to be too unstable to allow separation, so the p.m.r. spectrum for the mixture of isomers is presented (Table VII). For the other imidazolidines, only the chemical shifts of the C-2,3 protons are presented since the equilibrium mixtures give extremely complex p.m.r. spectra in the upfield region (Table VIII).

Equilibration of the N-methyl and N-ethyl imidazolidines was carried out in an n.m.r. tube using a catalytic amount of p-toluenesulphonic acid in dimethyl sulphoxide. The equilibrium isomer ratios were determined by p.m.r. integration of the vinyl triplets.

Infrared Spectra

All the imidazolidine (and imine) systems showed a C-H vinyl stretching absorption at approximately 3060 cm^{-1}. The N-isopropyl and N-t-butyl systems, showed strong C=N absorptions at 1720 cm^{-1} and 1718 cm^{-1}, respectively. The other main absorptions of importance were in the N–C–N and $N{-}CH_2{-}CH_2{-}N$ deformation region but a completely unambiguous assignment of these has not been possible.

N-t-Butylethylenediamine

To a solution of tertiarybutylamine (200 mℓ, 2.0 moles) and

Table VII. Proton Chemical Shifts for the Simple Imidazolidines

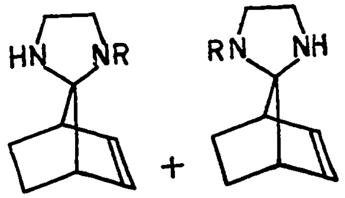
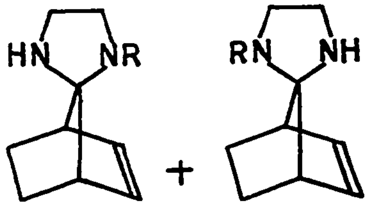
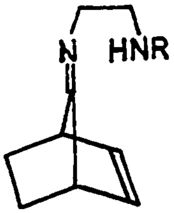
 R	C-2,3	C-1,4	EXO C-5,6	ENDO C-5,6	OTHERS
H	3.98	7.73	8.20	9.19	7.19(m), methylene 8.35 (broad), NH
CH_3	4.04 3.97	7.54 7.65	8.10	9.16	7.18(m), methylene 7.78(s), methyl

Table VIII Chemical Shifts for the C-2,3 Protons in the Equilibrium Mixtures of Imidazolidines and Imines in Dimethyl Sulphoxide

R		
CH_2CH_3	4.00(t), 4.08(t)	(a)
$CH(CH_3)_2$	3.94(t), 4.04(t)	3.67(m)
$CH_2C(CH_3)_3$	3.92(t), 4.06(t)	3.64(m)
$C(CH_3)_3$	(b)	3.65(m)

(a) There was no 7-imine in the N-ethyl system.

(b) Closed form gave diffuse signals which were a small percentage of the total C-2,3 signal.

aziridine (10.4 mℓ, 0.20 mole) was added cautiously hydrochloric acid (1.5 mℓ, 37%) over half an hour. The solution was refluxed for four days, after which time a p.m.r. spectrum indicated that all the aziridine had reacted. The t-butylamine was distilled off leaving a viscous liquid. To the latter was added 2.0 g. of sodium hydroxide pellets and the mixture was extracted with chloroform. The extract was dried over anhydrous magnesium sulphate and the solvent was evaporated. The remaining liquid was distilled to give 5.0 g. (21%) of N-t-butylethylenediamine, b.p. 153-156°, p.m.r. spectrum: 7.40, m, 4, methylene; 8.96, s, 9, t-butyl; 9.08, s, 3, N—H. On shaking with D_2O, the singlet at 9.08τ disappeared.

N-Neopentylethylenediamine

Neopentylamine (8.7 mℓ, 0.067 moles) was mixed with aziridine (2 mℓ, 0.038 moles) in a 25 mℓ round-bottomed flask. A condenser was fitted and hydrochloric acid (0.1 mℓ, 37%) was added down the walls. The solution was stirred at 40° for 2 days before sodium hydroxide pellets (2.0 g.) were added and the material distilled directly under vacuum (14 mm.). N-Neopentylethylenediamine (350 mg.) was produced, p.m.r. spectrum: 7.40, m, 4, methylene; 7.85, s, 3, NH; 9.16, s, 9, t-butyl.

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