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PART I
THE CONFORMATIONAL ANALYSIS OF TRIMETHYLENE SULFITES

PART II
TRANSANNULAR EFFECTS IN A MEDIUM-SIZED RING

BY

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A Dissertation
Submitted to the Faculty of Graduate Studies through the Department of Chemistry in Partial Fulfillment of the Requirements for the Degree of Doctor of Philosophy at the University of Windsor

Windsor, Ontario
1971

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To my parents
PART I

The considerable controversy in the recent literature prompted this study of alkyl substituted six-membered cyclic trimethylene sulfites. Like trimethylene sulfite, the more stable isomers prefer the chair form with axial $\text{S}=0$, e.g. 4-methyl-, 4,6-dimethyl-, 5,5-dimethyl- and 5-t-butyltrimethylene sulfites. However, increased steric interactions between syn-axial methyl groups and the exocyclic oxygen atom lead to the adoption of non-chair forms such as in the 4-methyl-, racemic 4,6-dimethyl-, 4,4,6-trimethyl- and 4,4,6,6-tetramethyltrimethylene sulfites and to the preference of the alternative chair form with equatorial $\text{S}=0$ for the meso-4,6-dimethyltrimethylene sulfite of higher dipole moment (5.4D).

The axial preference of the $\text{S}=0$ bond from chemical equilibration was estimated to be about 2 kcal/mole with a significant solvent variation. Further, the 5-t-butyl group cannot constrain the ring to a chair form with equatorial $\text{S}=0$ and equatorial t-butyl, instead this molecule probably exists as a mixture of the other chair form (both groups axial) and non-chair forms.

Vapour phase osmometry measurements showed these sulfites to be highly associated in solution even down to the 10 mM level (trimethylene sulfite was mainly dimer in carbon tetrachloride over a large concentration range). This result necessitates caution in any inferences drawn on these sulfites from solution studies (ir, nmr, etc.).
Recent interpretations of ultrasonic relaxation results on these sulfites in terms of a chair-chair anancomeric equilibrium were reinterpreted with due regard to the influence of the vicinal unshared electron pairs on the sulfur and oxygen atoms. Although no barrier was found for the sulfites reported here, a barrier to ring reversal of 8.2 ± 0.2 kcal/mole was found for 5,5-dimethyltrimethylene sulfate.

The above data provide the basis for a coherent system in which trimethylene sulfites have high barriers to chair-chair interconversion, low energy non-chair barriers and conformations, and a strong preference for the axial S=O.

PART II

5,5-Diphenylcyclononyl tosylate was solvolyzed in acetic and trifluoroacetic acid, and the corresponding amine deaminated in acetic acid. The major products were separated and identified. No transannular phenyl or hydride migration was found in the deamination or acetolysis reactions, the only olefin products isolated being the 5,5- and 6,6-diphenylcyclononenes. The trifluoroacetolysis olefin products were those expected from transannular hydride migration: 1,2-diphenyl-, 2,3-diphenyl-, and 3,3-diphenylcyclononene. However, the olefins were found to isomerize under the trifluoroacetolysis conditions so that these olefins may be secondary products.

No transannular phenyl migration products were found, which was verified to the 1% level by the synthesis of the expected transannular product, 1,5-(1,6-)diphenylcyclononene. The lack of any migration in the deamination reaction indicates that in the substituted nine-membered ring this reaction is no more conducive to transannular rearrangements than the corresponding tosylate acetolysis reaction.

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PART II

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Conformational analysis, which now ranks among the most important branches of stereochemistry, probably had its start in 1950 with the classic paper by Barton in which some fundamental relationships between the conformations and chemical reactivity of certain molecules were pointed out. The fundamental tenet of conformational analysis as suggested by Barton and Cookson is that the chemical and physical properties of organic molecules depend not only on their gross structure and stereochemistry but also on the conformations they adopt. The intense work stimulated by these suggestions and the availability of such powerful tools as gas liquid chromatography (glc) and nuclear magnetic resonance (nmr) has led to a reasonable understanding of the behaviour of alicyclic compounds and for background material there are several texts on the subject.  

Recently more attention has been directed toward the conformational analysis of heterocyclic systems, which not only display many points in common with those of alicyclic systems but also provide many interesting and instructive points of difference.

The overall similarities between heterocyclic and alicyclic conformational analyses are important. In general, six-membered heterocyclic compounds, like cyclohexane derivatives, prefer chair conformations with equatorial substituents (for interesting abnormalities see reference 6),
at least in the crystalline state. For example, piperidine,\textsuperscript{7} piperazine,\textsuperscript{8} N,N'-dimethyl and N,N'-dichloropiperazine\textsuperscript{8,9} have chair conformations of geometry closely analogous to that of cyclohexane. \textsuperscript{1,3}Dioxane,\textsuperscript{5,10,11} 1,4-dioxane,\textsuperscript{8,12,13} 1,3-dithiane,\textsuperscript{14} 1,4-dithiane\textsuperscript{4,13,15,16} 1,3,5-trioxane,\textsuperscript{16-18} 1,3,5-trithiane,\textsuperscript{13,16} 1,4-thioxane,\textsuperscript{19} and their derivatives all have chair conformations.\textsuperscript{20-22} Even the highly hetero-substituted dimeric cyclohexane peroxide,\textsuperscript{23} as well as tetramethyl-hexahydrotetrazine,\textsuperscript{24} prefer the heterocyclic ring in the chair form (solid state).

These similarities however should not hide the striking differences that exist between the forces controlling alicyclic and heterocyclic conformations. Five obvious differences need to be considered.\textsuperscript{5} First, torsional interactions along heteroatom-carbon bonds differ from those along carbon-carbon bonds. Secondly, non-bonded interactions are different in heterocyclic and alicyclic systems. Thirdly, the presence of heteroatoms increases the importance of dipolar interactions. Fourthly, the force constants for bond-angle deformation of heteroatoms are different from those of carbon and, finally, internal hydrogen bonding with the heteroatoms can influence the preferred conformations.

The result of these effects is that abnormalities also occur in heterocyclic systems. Some well documented examples are given below in their preferred conformations: \textsuperscript{1,2,26}pentamethyl-1,4-phenyl-1,4-piperidinol (I),\textsuperscript{25} cis-1,4-dithiane-1,4-dioxide (II),\textsuperscript{26,27} and more recently duplodithiocetone (III).\textsuperscript{28}

\[ \text{\begin{tikzpicture} [scale=0.5] % Diagram code here \end{tikzpicture}} \]
Originally, under the influence of Lewis' octet theory, dative links were assumed throughout for the nature of oxy-bonds in oxy-acids of phosphorus, sulfur, chlorine, and likewise for their organic derivatives. Employing molecular refractions, refraction coefficients, and parachor values, it was concluded that there was no indications for assuming a covalent double bond in organic sulfites. Similar conclusions were reached as regards the nature of oxy-bonds in sulfoxides and sulfones. This formulation is no longer favoured. Conclusive experimental data about bond distance, bond energy, and dipole moment indicate that the sulfur-oxygen link is a nearly covalent double bond in which 3d-orbitals on sulfur must play an important role. Although sulfites have not been considered in particular, the general validity of this conclusion seems hardly questionable. Evidence for a covalent double bond in sulfites was also presented by Simon and Kriegsmann from infrared and Raman spectroscopic studies. It appears now to be quite firmly established that the sulfur-oxygen bond in sulfoxides, sulfones, and thionyl halides is a p^2-pd hybrid double bond, with an electric moment corresponding to a charge separation on the atoms of about one-third of an electron in the sense S=O. It is well known that the configuration about the sulfur atom in molecules of the type OSX_2 is pyramidal. Thus, electron diffraction studies have shown thionyl chloride to be pyramidal, with Cl-S-Cl and O-S-Cl angles of 114° and 106°, respectively. The sulfite ion may be thought of as being derived from thionyl chloride by replacement of the two chlorine atoms by oxygen anions. Indeed, the sulfite ion is known to be pyramidal with C_{3v} symmetry both in the crystalline state and as a free ion in aqueous solution. The pyramidal grouping, unlike a planar
configuration about the sulfur, gives rise to isomerism in certain organic molecules, such as the two isomers of 1,4-dithiane-1,4-dioxide (II) mentioned previously, and the resolution of asymmetric sulfoxides into optical isomers.  

The first evidence in organic chemistry for the existence of neutral molecules in which a coordination of three groups of atoms around a central atom is non-coplanar was the isolation of optical isomers in sulfinic esters and sulfoxides. The stability of these compounds towards racemisation indicated that the central sulfur atom is linked to oxygen and carbon by three covalent bonds, without rapid inversion occurring of the pyramidal configuration.

From analogy with the above systems, we should expect alkyl sulfites to have a pyramidal structure about the sulfur atom, since the R-O radicals should behave as typical monovalent groups; hence suitable sulfites should show isomerism.

Although Voss and Blanke suggested in 1931 that coordination of oxygen atoms around the central sulfur atom in a sulfite group might be non-coplanar, analogous to the configuration of sulfoxides and sulfinic esters, this was confirmed by experiment only some twenty years later. In 1952, Herzig and Ehrenstein isolated two isomers of the cyclic sulfite of 3α-chloro-5,19-dihydroxyetiocholanic acid ethyl ester. The existence of isomeric forms could only be explained by assuming asymmetry in the sulfite group, as this would enable the exocyclic S=O bond to take two configurationally different positions relative to the steroid skeleton. A case of isomerism in a simple cyclic compound was discovered a few years later by de la Mare, Klyne, and coworkers who were able to isolate two isomers of 5-chlorotrimethylene sulfite, shown below with the
numbering system used for trimethylene sulfite (TMS):

\[
\begin{array}{c}
\text{H} \\
\text{Cl} \\
\text{O} \\
\text{S=O} \\
\text{O} \\
\end{array}
\]

Similar isomers were obtained for a five-membered ring. VanWoerden in 1963 compiled a list of five- and six-membered cyclic sulfites that had been made with the surprising observation that cis-trans isomerism similar to the cases mentioned had not been noticed for any of these compounds. Hence, he proceeded to study various 5-substituted trimethylene sulfites, together with the parent compound, and was able to isolate three additional pairs of isomers. These new examples, together with the cases reported previously and those reported herein, constitute a firm chemical proof for the pyramidal sulfite group. Additional evidence has been supplied by recent physico-chemical studies, such as X-ray and nmr, the latter showing the nonequivalence of the ring protons due to the asymmetry of the sulfur atom in ethylene sulfite, 5,5-dimethyltrimethylene sulfite, trimethylene sulfite, and three isomers of 4,6-dimethyltrimethylene sulfite, whereas in the corresponding sulfates they are equivalent. Although these results prove the pyramidal structure of the sulfite group in organic molecules, it still leaves unanswered the stability of the SO₃ grouping, the ring conformation, and the orientation of the exocyclic oxygen atom. De la Mare and coworkers assumed a chair with S=0 equatorial bond, discarding the boat form because of strong dipolar effects in the 2-chloro isomers. Arbouzov and Samitov reported the first nmr spectrum of a six-membered cyclic sulfite, 5,5-dimethyltrimethylene sulfite, and tried to explain the chemical shifts of the axial
and equatorial groups through bond anisotropy calculations, assuming a rigid chair with equatorial $S=0$. Lauterbur and coworkers\textsuperscript{50} isolated the first isomers of a trimethylene sulfite substituted in the 4- and 6-positions, 4,6-dimethyltrimethylene sulfite, and reported their infrared (ir) and nmr spectra. Again, however, on infrared data alone they assigned their single racemic isomer a chair form with equatorial $S=0$, one of the two meso isomers a chair form with equatorial $S=0$ because of 1,3-diaxial interactions, and the other a twist (flexible) form (to explain its anomalous band at 1230 cm\textsuperscript{-1} rather than the usual 1190 cm\textsuperscript{-1} hitherto reported for sulfites). Arbouzov and Samitov in 1963 again reported\textsuperscript{48} the nmr spectra of trimethylene sulfite and 5,5-dimethyltrimethylene sulfite with anisotropy calculations. Although in these calculations the structure with $S=0$ axial gave better results and was not contradicted by the van der Waal radii, they still assumed that the exocyclic $S=0$ preferred the equatorial position.

Unfortunately, the one method that could solve the problem unambiguously, namely dipole moments, was further confusing the issue. Arbouzov\textsuperscript{52} in 1960 had calculated the following dipole moments for trimethylene sulfite:

\[
\begin{array}{cccc}
\text{4.9 D} & \text{1.8 D} & \text{5.1 D} & \text{1.0 D}
\end{array}
\]

The experimental value was 3.60 D (debyes), which was interpreted as a mixture of the two possible chair forms. From a study of solvent effects on the dipole moment and $\nu_{SO}$ stretching frequency (little effect), together with the nmr spectra of trimethylene sulfite and two pairs of 5-substituted isomers, VanWoerden and coworkers\textsuperscript{44} concluded that neither trimethylene sulfite (TMS) nor the isomers with lower dipole moments of
the two pairs (5-nitro-5-methyl and 5-t-butyl TMS) were chair mixtures; instead they decided upon a rigid chair with axial $S=0$ ($1190 \text{ cm}^{-1}$) since the stretching frequency for axial bonds tends to be lower than for the corresponding equatorial bond. Hence the $1230 \text{ cm}^{-1}$ was assigned to the equatorial $S=0$. In the nmr, each equatorial hydrogen was more shielded than its geminal axial counterpart, contrary to cyclohexane.

Samitov and Aminova$^{49}$ restudied the bond anisotropies of cyclic sulfites and found an error in the paper$^{34}$ of Pritchard and Lauterbur, concluding from their own calculations on 5,5-dimethyl TMS that (a) the most acceptable values are for axial $S=0$ with both axial methylene and methyl protons downfield relative to their equatorial counterparts, and (b) in such a structure the van der Waal radii are not prohibitive.

Grubbs and Lee$^{53}$ called Hellier's conclusion$^{44}$ of axial $S=0$ "surprising" and chose to draw theirs equatorial, but stated correctly that further work was needed to resolve the conformational uncertainty in six-membered cyclic sulfites.

The first definitive study of organic sulfites to appear was the thesis of VanWoerden$^{45}$ in 1964. The author limited himself to TMS and various 5-substituted derivatives. In addition to extensive alkaline rates of hydrolysis, infrared and dipole moment data in numerous solvents was also given. However, the most interesting point was a reevaluation of the dipole moment calculations taking into account a significant contribution from the sulfur lone pair. This gave a value of 3.5 D for TMS in the chair form with axial $S=0$, in excellent agreement with the experimental value (3.5 D). Also, the calculated and experimental values agreed well in the remaining sulfites shown to be rigid by their solvent independence in the ir and dipole moment work. Those isomers

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displaying solvent dependency were considered mixtures of equilibrating forms, notably the lower melting and less stable isomer II of 5-t-butyl TMS. Hence TMS and related compounds prefer an axial S=O bond and a t-butyl group on C-5 is not sufficient to hold the molecule entirely in a chair conformation with equatorial S=O, if at all. VanWoerden also reassigned the structures of the three isomers of 4,6-dimethyl TMS isolated by Lauterbur, Pritchard and Vollmer; the more stable meso isomer now with an axial S=O bond and equatorial methyl groups, the second meso isomer a mixture of equilibrating forms (the chair form with all groups equatorial probably predominating). He neglected to comment upon the third (racemic) isomer however. From ir data he estimated a $-\Delta G$ value of 4.5 ± 1.5 kcal/mole for the S=O group in favour of the axial position, with an extremely large solvent effect ($\approx 2$ kcal/mole) by polar solvents on the polar conformation (S=O equatorial). He also discussed the factors which may cause the molecules to seek a conformation with axial S=O discarding hydrogen bonding, resonance interactions between the sulfur and the endocyclic oxygens, and concluding that the 'preference' of the S=O bond for an axial orientation might merely reflect a "reluctance of the lone-pair of electrons on the sulfur to take up this orientation, such a constellation being energetically unprofitable."

Edmundson in 1965 concluded from the large chemical shift difference of 1.3 ppm between the methylene protons of 5,5-dimethyl TMS that the S=O bond must be axial in order to shift the axial protons upfield to such a large extent, contrary to Hellier's and Samitov's conclusion that these axial protons were downfield compared to the equatorial protons. Samitov reemphasized this unusual fact in TMS and 5,5-dimethyl TMS, using calculated nmr spectra, anisotropy calculations, and the similarity of chemical shifts with the necessarily axial protons in
4,6-dimethyl TMS (meso isomer I).\(^{50}\) He also pointed out that this same anomaly was true for the C-5 protons (but not the C-4 or C-6) in 1,3-dioxane. At this same time Overberger and coworkers\(^{55}\) studied the high temperature effects on 5,5-dimethyl TMS and the racemic isomer of 4,6-dimethyl TMS, finding no change in the nmr in the former, but some change in the latter in both the nmr and ir spectra. They concluded that the racemic compound was a conformational mixture of chair forms at room temperature with the S=O axial conformation predominating, but this form decreasing with increasing temperature. In addition they reported, like Pritchard et al.\(^{50}\) that heating the less stable meso isomer II to 200° for 15 minutes converted it almost completely into the more stable meso isomer I, which itself was entirely stable (indicating \(-\Delta G \geq 4.4\) kcal/mole). This stability of the SO\(_2\) group to inversion had previously been pointed out by VanWoerden\(^{45}\) by the isolation of stable isomers, which rarely isomerized upon distillation, crystallization, or prolonged storage. From infrared frequencies and the sulfite ion geometry a barrier of about 100 kcal/mole was estimated for this inversion.

In view of all these inconclusive and conflicting results, in 1965 we undertook an ir, nmr, and dipole moment study of TMS, 5-t-butyl TMS, and trimethylene sulfites with increasing methyl substitution on the 4- and 6-positions, with the belief that some or all of these compounds might prefer non-chair (twist) forms, a conclusion which might well explain many apparent discrepancies.\(^{56}\) The possibility also existed of isolating and identifying a sulfite isomer with the chair structure and equatorial S=O, rather than the preferred axial. This would allow a study of the properties of this bond, such as its dipole moment and \(\Delta G\) value, as was accomplished.\(^{57}\) Further, by employing low temperature nmr, it was hoped
to learn more about those compounds thought to exist in conformational equilibria such as the less stable isomer II of 5-t-butyl TMS, which most think is a mixture of chair forms (the $\Delta G$ for the equilibrium $I \rightleftrarrows II$ for these isomers was found to be 1.50 kcal/mole and nearly solvent independent). Arbuzov and coworkers had come to the same conclusion of twist forms for TMS and 5,5-dimethyl TMS on the basis of dipole moments alone (3.3 D for twist forms) almost at this same time. However, since then an X-ray analysis of TMS, and later of 5,5-dichloro TMS, showed these compounds to be in the chair conformation in the solid state with the $S=O$ bond pointing in the axial direction (this has been confirmed for TMS in the gas phase also even more recently by electron diffraction). Shortly afterwards Hellier presented his nmr results for the cyclic sulfites studied by VanWoerden. He chose a rigid chair with axial $S=O$ for TMS as the nmr fit this structure quite well with normal coupling constants, and with axial protons downfield compared to their equatorial geminal counterparts. Also, no change was seen up to $100^\circ$ in the J values, although there was a slight lessening of the chemical shift differences. The calculated spectra fit very well also. The same was true for the more stable isomer I of 5-t-butyl TMS, except that the nmr was run from 20-200$^\circ$ at 25 MHz. For the less stable isomer II of this compound a mixture of flexible forms was proposed, based on the single vicinal J value of 5.5 Hz found. Furthermore, the differences in the chemical shifts for the methylene protons adjacent to the oxygen atoms are the same only for this compound, unlike TMS, 5,5-dimethyl TMS, and 5,5-diethyl TMS. His anisotropy calculations only ruled out boat forms compared to chair forms, not being able to distinguish between axial or equatorial $S=O$ chair forms.

Later in 1967 VanWoerden published the results of his dipole moment
studies on TMS and some 5-substituted derivatives. By means of a simple geometric procedure he was able to show both the magnitude and direction of the sulfite group dipole, the only plausible interpretation being that the S=O bond occupies an axial position for those compounds in rigid chair conformations:

\[ \text{The group moment } \mu \text{ had a most probable value of 2.5 D, so that the following partial bond moments (except for a constant } \Delta \text{) were deduced:} \]

\[
\begin{align*}
S=O & : 2.7 \pm \Delta \\
S-O & : 0 \pm \Delta \\
lone pair & : 1.0 \pm \Delta
\end{align*}
\]

These values provided a consistent description in terms of additive partial moments for the dipole moments of cyclic sulfites, thionyl chloride, and related compounds. The $-\Delta G$ value for the S=O bond was reestimated to be $3.5 \pm 1$ kcal/mole using the nmr bandwidth technique.

Further work on sulfites has appeared much more recently. Wucherpfennig from a study of ir, nmr, and dipole moments has concluded that 5,5-dimethyl TMS and the meso 4,6-dimethyl TMS isomer of lower dipole moment have the chair form with axial S=O, while the other meso isomer of 4,6-dimethyl TMS has a chair form with equatorial S=O and the remaining (racemic) isomer exists as a mixture of twist and perhaps chair forms. From ir and nmr data Cazaux and Maroni concluded that for the analogous racemic 4,6-diisopropyl TMS the favoured conformation is the twist. Lack and Tarasoff proposed from cryoscopic molecular weight data that the second 4,6-dimethyl TMS meso isomer (higher dipole moment) may in fact be a cyclic
12-membered dimer. Using ultrasonic techniques, Wyn-Jones and coworkers decided\textsuperscript{66,67} that these sulfites were anancomeric equilibria of inverting chair conformations. Rowland has found\textsuperscript{68} that certain constrained sulfites in fact adopt the boat conformation, while finally, Samitov and others have discussed\textsuperscript{69} some possible reasons for the axial preference of the $S=0$ in sulfites and sulfoxides.

These results will now be considered along with our own and a conclusion drawn that fits all the data and explains many of the outstanding discrepancies.
Chapter 11

RESULTS AND DISCUSSION

1. Dipole moments

Six-membered ring sulfites can in principle exist in two chair and a variety of non-chair (flexible) forms:

\[
\begin{align*}
\text{O} & \quad \text{S} = \quad \text{O} \\
\text{O} & \quad \text{S} = \quad \text{O} \\
\text{O} & \quad \text{S} = \quad \text{O} \\
\text{O} & \quad \text{S} = \quad \text{O}
\end{align*}
\]

In the case of an equilibrium mixture of conformations, the experimental dipole moment will be an average, in the case of two forms given by

\[
\mu^2 = x_1\mu_1^2 + x_2\mu_2^2
\]

where \( x_1 \) and \( x_2 \) are the mole fractions of components 1 and 2. The usual experimental test for the presence of an equilibrium mixture is the use of different solvents. If the various conformations have different dipole moments, a change in the solvent dielectric should bring about a shift in the equilibrium and hence in \( \mu^2 \). Benzene, which because of its high polarisability favours the more polar forms, and carbon tetrachloride have been found quite satisfactory for this purpose. \( ^{18,45,70} \) Small changes up to 0.1 debye are common for even known compounds and are not considered significant. However, considerably larger changes can be taken as evidence of equilibrium shifts. \( ^{18,45,63} \)

A series of 4-, 5-, and 6-substituted sulfites were synthesized and their dipole moments measured in various solvents (Table 1).

The values in parentheses were obtained by van Woerden or Wucherpfennig. \( ^{63} \)
<table>
<thead>
<tr>
<th>Compound</th>
<th>Substituents&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Dipole Moment (Debye)</th>
<th>( \mu_{\text{C}_6\text{H}<em>6} - \mu</em>{\text{CCl}_4} )</th>
<th>( \mu_{\text{C}_6\text{H}<em>6} - \mu</em>{\text{C}<em>6\text{F}</em>{12}} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>insoluble</td>
<td>3.34(3.46)&lt;sup&gt;b,c&lt;/sup&gt;</td>
<td>(3.52)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>(.06)</td>
</tr>
<tr>
<td>2</td>
<td>( R_2 = \text{CH}_3 )</td>
<td>3.35</td>
<td>3.41</td>
<td>.06</td>
</tr>
<tr>
<td>3</td>
<td>( R_4 = \text{CH}_3 )</td>
<td>4.66</td>
<td>4.75</td>
<td>.09</td>
</tr>
<tr>
<td>4</td>
<td>( R_2 = R_6 = \text{CH}_3 )</td>
<td>3.44</td>
<td>3.51(3.55)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>3.60</td>
</tr>
<tr>
<td>5</td>
<td>( R_2 = R_5 = \text{CH}_3 )</td>
<td>3.97</td>
<td>3.93(3.88)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>3.93</td>
</tr>
<tr>
<td>6</td>
<td>( R_1 = R_5 = \text{CH}_3 )</td>
<td>insoluble</td>
<td>5.31(5.22)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>5.37</td>
</tr>
<tr>
<td>7</td>
<td>( R_1 = R_2 = R_6 = \text{CH}_3 )</td>
<td>3.91</td>
<td>3.86</td>
<td>-.05</td>
</tr>
<tr>
<td>8</td>
<td>( R_1 = R_2 = R_5 = \text{CH}_3 )</td>
<td>4.53</td>
<td>4.71</td>
<td>.18</td>
</tr>
<tr>
<td>9</td>
<td>( R_1 = R_2 = R_5 = R_6 = \text{CH}_3 )</td>
<td>4.22</td>
<td>4.30</td>
<td>.08</td>
</tr>
<tr>
<td>10</td>
<td>( R_3 = R_4 = \text{CH}_3 )</td>
<td>3.38</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>( R_3 = \text{t-butyl} )</td>
<td>3.50</td>
<td>3.54(3.61)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>3.60(3.66)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>12</td>
<td>( R_4 = \text{t-butyl} )</td>
<td>3.54</td>
<td>3.63(3.76)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>3.90(4.00)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> all R's not specified = H  
<sup>b</sup> from ref. 58a  
<sup>c</sup> from ref. 63
and the agreement is quite satisfactory, considering the different methods of calculation (see experimental). These dipole moments permit important conclusions on conformation to be made.

Several of these sulfites have dipole moments corresponding at least approximately to a chair form with axial S=0 (compounds 1, 2, 4, 10 and 11). Van Woerden from his study of 5-substituted trimethylene sulfites has calculated a value of 3.4 debyes for compound 1 and 3.5 debyes for compound 11. The only compound with a moment clearly corresponding to a chair with equatorial S=0 is the 4,6-dimethyl compound 6. Van Woerden has estimated a dipole moment of 5.0 to 5.2 debyes for this compound in this form, as has Wucherpfennig. Thus compound 6 has been assigned this conformation with equatorial S=0. It is interesting to note that Lack at first concluded that this molecule was the cyclic 12-membered dimer based on cryoscopic molecular weight data, but now agrees with our assignment (see nmr section). The 4-methyl and 4,4,6-trimethyl isomers of higher dipole moments, compounds 3 and 8, must also have large amounts of this form (S=0 equatorial) if they exist as equilibria of chair forms, or otherwise non-chair forms with quite similar geometry at the sulfite end of the molecule.

The variation of dipole moment with solvent for compounds in the chair form with axial S=0 are of the order of 0.1 debye, the estimated experimental accuracy. Compound 8 has a slightly larger variation and may be said to be borderline. However, the variation of the 5-t-butyl compound 12 has been confirmed by measurement in two additional solvents, cyclohexane and dioxane. The difference in these two solvents is 0.61 debye which is well outside the experimental error and almost four times that of the corresponding change (0.16 debye) for the other 5-t-butyl

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isomer, compound 11. This is the behaviour expected for molecules existing as interconverting conformations with different dipole moments, the conformation of higher moment being favoured in the more polar solvent. 58, 63

None of the other compounds studied show enough variation of dipole moment with solvent to implicate a conformational equilibrium with certainty.

The tetramethyl compound 2 has a dipole moment of intermediate value which is constant and it therefore seems likely that this compound exists in a non-chair form almost exclusively. Compounds 5 (racemic 4,6-dimethyl) and 7 (4,4,6-trimethyl) have similar moments near 3.9 debyes which implies either a non-chair form 63 or a distortion of the chair with axial S=0.

Since all of these molecules have axial methyl – axial S=0 interactions and in the case of the tetramethyl compound 2 an additional axial methyl – axial methyl interaction, it is perhaps not surprising that they have similar dipole moments and hence conformations, yet different from those compounds without these interactions. However, it is not possible on the basis of dipole moments alone to decide between distorted chair and non-chair alternatives.

Nevertheless, the general constancy of the dipole moments in various solvents (with the exception of 12) even for compounds whose moments deviate considerably from the values expected for chair forms makes it highly unlikely that any of these compounds exist as equilibrium mixtures of conformations with large differences in dipole moment. Hence, with the possible exception of compound 12, none of these compounds exist as equilibrium mixtures of two chair conformations. If equilibria do exist, they probably involve chair and non-chair forms with similar moments or are anomeric 66 in all the solvents employed (obviously not the case for compound 12). The former conclusion will be seen to best fit all the data,
and this same conclusion has been drawn already for the racemic 4,6-
dimethyl compound 5.*

11. Nuclear Magnetic Resonance Spectra

The 60 MHz nmr spectra are given for trimethylene sulfite (TMS),
compound 2, neat (NMR-1), in 50% w/v benzene (NMR-2), and 10% dimethyl-
sulfoxide-\(d_6\) (NMR-3). From the latter, the following parameters were
obtained:

<table>
<thead>
<tr>
<th>Substituent</th>
<th>(\tau)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(H_{4a} = H_{6a})</td>
<td>5.21</td>
</tr>
<tr>
<td>(H_{4e} = H_{6e})</td>
<td>6.03</td>
</tr>
<tr>
<td>(H_{5a})</td>
<td>7.60</td>
</tr>
<tr>
<td>(H_{5e})</td>
<td>8.30</td>
</tr>
</tbody>
</table>

These agree quite well with those found by Hellier\(^6^2\) and Wucherpfennig,\(^6^3\)
and are consistent with a rigid chair structure. Note that as in the case
of protons in the 5-position of 1,3-dioxanes, all axial protons appear
downfield from their geminal equatorial counterparts, unlike cyclohexane
or the 4- and 6-positions in 1,3-dioxane.\(^1^0,5^4\) The axial downfield position
of protons has also been found to be true in cyclic phosphite analogues.\(^7^3\)
The above coupling constants are virtually solvent (deuteriochloroform,
acetone-d$_6$, benzene, pyridine, dimethylsulfoxide-d$_6$, carbon tetrachloride) and temperature (-90° in acetone-d$_6$ to +165° neat and in nitrobenzene) independent, indicating a single stable conformation or an anancomeric equilibrium in all the solvents and temperature range studied.

The similarity of the 4-methyl derivative 2 to compound 1 is readily apparent from examination of its nmr spectrum (NMR-4 and 5). The following were obtained in carbon tetrachloride:

<table>
<thead>
<tr>
<th>Substituent</th>
<th>$r$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$H_{6a}$</td>
<td>5.12</td>
</tr>
<tr>
<td>$H_{6a}$</td>
<td>6.20</td>
</tr>
<tr>
<td>$H_{6e}$</td>
<td>8.70</td>
</tr>
<tr>
<td>$H_{5a}$</td>
<td>7.90</td>
</tr>
<tr>
<td>$H_{5e}$</td>
<td>8.37</td>
</tr>
<tr>
<td>6a6e</td>
<td>11.5</td>
</tr>
<tr>
<td>4a5a 6a5a</td>
<td>11.5</td>
</tr>
<tr>
<td>5a5e</td>
<td>14.0</td>
</tr>
<tr>
<td>4a5e 6a5e</td>
<td>3.0</td>
</tr>
<tr>
<td>5a6e</td>
<td>4.5</td>
</tr>
<tr>
<td>5e6e</td>
<td>2.5</td>
</tr>
<tr>
<td>4aCH$_3$(4e)</td>
<td>6.5</td>
</tr>
</tbody>
</table>

Notice that in benzene (NMR-5), the equatorial proton $H_{5e}$ is shifted upfield consistently more than its geminal axial counterpart, so much so that part is obscured under the methyl group and the remainder is upfield of it. These similarities in chemical shifts (see also Table 3, p 29), coupling constants, and (vide infra) benzene shifts all point to similar geometries, as indicated before by their dipole moments.
The above is also true in the case of the 4,6-dimethyl compound. The chemical shift (NMR-6) of the protons next to the oxygen come around 5.1 for an axial proton, with the S=O bond axial. However, the methyl groups must now shield the axial methylene proton causing the methylene protons to become accidentally degenerate in chemical shift in carbon tetrachloride. Association (vide infra) may also play an important part in this, as shown by the spectrum in dimethylsulfoxide-d$_6$ (NMR-7), where association should be slight. A first order spectrum is still not obtained; however Lack has been able to do so using a 100 MHz instrument. At 60 MHz we obtained the following:

<table>
<thead>
<tr>
<th>Substituent</th>
<th>$\tau$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\text{H}_4a = \text{H}_6a$</td>
<td>4.93</td>
</tr>
<tr>
<td>$\text{H}_5a$</td>
<td>8.30</td>
</tr>
<tr>
<td>$\text{H}_5e$</td>
<td>8.05</td>
</tr>
<tr>
<td>$\text{CH}_3(4e) = \text{CH}_3(6e)$</td>
<td>8.73</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>$J$</th>
<th>Hz</th>
</tr>
</thead>
<tbody>
<tr>
<td>$4a \text{CH}_3(4e) = 6a \text{CH}_3(6e)$</td>
<td>6.5</td>
</tr>
<tr>
<td>$4a5a = 6a5a$</td>
<td>10.8</td>
</tr>
<tr>
<td>$4a5e = 6a5e$</td>
<td>3.3</td>
</tr>
<tr>
<td>$5a5e$</td>
<td>14.4</td>
</tr>
</tbody>
</table>

It is interesting to note also that the axial methylene proton is now at higher field in dimethylsulfoxide-d$_6$, indicating a strong shielding by the methyl group. The methine multiplet is quite symmetrical, has the expected total width of 33.8 Hz, and is unchanged with solvent.

No change was observed in acetone-d$_6$ down to -10° C, and only a slight change in the methylene multiplet in nitrobenzene up to 168°, none in the rest of the spectrum. This may be caused by the chemical
shift degeneracy changing slightly with temperature, or association changes as indicated by the slight changes with solvent mentioned above.

The 5,5-dimethyl compound 10 also has a temperature (-130°C in 1:1 ethyl bromide-d$_5$ - methylene chloride-d$_2$ to room temperature) and solvent independent spectrum, except that the chemical shift difference between the methylene protons decreases with decreasing temperature (62 Hz at room temp in acetone-d$_6$ but 57 Hz at -95°C). This will be discussed later. The chemical shifts in carbon tetrachloride (NMR-8) of the 4 and 6 methylene protons are shifted upfield about 0.2 by the geminal methyl groups but the values agree well with the previous compounds for axial and equatorial protons (S=0 axial), 5.1 and 6.3 respectively. $J_{\text{gem}} = 10.8$ Hz and the upfield equatorial methylene protons are coupled with each other ('$W$' path) with $4J = 1.2$ Hz. The upfield methyl singlet is narrower than its geminal counterpart ($W^* = 1.4$ vs 2.2 Hz) and hence should be the equatorial, which is usually narrower.$^{75a}$

The 5-t-butyl compound 11 is the last that the dipole moments indicated should have a rigid chair form with axial S=0. Hellier found$^{62}$ a temperature independent spectrum (20 to 200°C neat and in nitrobenzene). We found no change in the usual solvents employed (carbon tetrachloride, dimethylsulfoxide-d$_6$, deuteriochloroform, acetonitrile-d$_3$, acetone-d$_6$) and obtained in dimethylsulfoxide-d$_6$ (NMR-9):
The chemical shifts (Table 3) are in the range expected, with the axial methine shifted slightly upfield as was the case with compound 2. It is interesting to note also that unlike the 5,5-dimethyl compound 10, both $H_{4a}$ and $H_{4e}$ are split into triplets by a $J = 1.2$ Hz. If as before the equatorial (W) protons are coupling with each other, then the axial protons are now probably doing likewise by their proximity.

For the dimethyl compound 6, we find that the nmr spectra are consistent with the chair conformation, $S=O$ equatorial. Unfortunately, in carbon tetrachloride (NMR-10), the C-5 methylene signals overlap considerably. However in dimethylsulfoxide-d$_6$ they are well enough separated to permit first order analysis (NMR-11):

<table>
<thead>
<tr>
<th>Substituent</th>
<th>$\tau$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$H_{4a} = H_{6a}$</td>
<td>5.33</td>
</tr>
<tr>
<td>$H_{5a}$</td>
<td>8.38</td>
</tr>
<tr>
<td>$H_{5e}$</td>
<td>8.12</td>
</tr>
<tr>
<td>$CH_3(4e) = CH_3(6e)$</td>
<td>8.68</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>$J$</th>
<th>Hz</th>
</tr>
</thead>
<tbody>
<tr>
<td>$4aCH_3(4e) = 6aCH_3(6e)$</td>
<td>6.5</td>
</tr>
<tr>
<td>$4a5a = 6a5a$</td>
<td>10.8</td>
</tr>
<tr>
<td>$4a5e = 6a5e$</td>
<td>3.0</td>
</tr>
<tr>
<td>$5a5e$</td>
<td>14.5</td>
</tr>
</tbody>
</table>
As with compound \( \text{4} \) before, this is caused by an upfield shift in the C-5 axial proton relative to its equatorial counterpart in going from carbon tetrachloride to dimethylsulfoxide-d\(_6\) so that they are actually reversed in these solvents (axial downfield in carbon tetrachloride but upfield in dimethylsulfoxide-d\(_6\)). The C-4 and C-6 signals are virtually unchanged however. Benzene behaves like dimethylsulfoxide-d\(_6\) but all protons are shifted upfield considerably in this solvent. These results could at least in part be due to strong solute association in carbon tetrachloride.

Upon comparison of the chemical shifts of the C-4 and C-6 axial protons and the equatorial methyl groups of compounds \( \text{4} \) and \( \text{6} \), we find that the methines are virtually identical (band width 33.2 for \( \text{6} \) vs 33.8 Hz for \( \text{4} \)) but on going from axial to equatorial S=0 the axial methine is shifted upfield \(-0.4\nu\) while the equatorial methyl groups are only slightly affected. Again no change was detected in acetone-d\(_6\) down to \(-98^\circ\).

From the dipole moments we predicted that compounds \( \text{3} \) and \( \text{8} \) should have large amounts of this equatorial S=0 form or a non-chair form with the same geometry at the heteroatom end. Unfortunately the \( \text{4} \)-methyl isomer of higher dipole moment, compound \( \text{3} \), has a very complex and non first order spectrum (NMR-12 and 13), so that not very much information can be obtained at 60 MHz. However, there are some interesting points. The downfield protons adjacent to the oxygen atoms now overlap at about 5.6\( \nu\) in carbon tetrachloride (cf. 5.5\( \nu\) for compound \( \text{6} \)) and are shifted approximately equally in benzene. The methylene protons overlap at around 8.2\( \nu\) in this same solvent with a band width of only 21 Hz although a part may be obscured by the methyl group. This seems to be the case as benzene causes these two protons to separate with the methyl group still obscuring part of the spectrum. There is no significant change in acetone-d\(_6\) down to \(-82^\circ\).
The additional methyl groups in the 4,4,6-trimethyl compound \( \tilde{8} \) simplify the spectrum somewhat (NMR-14). The methine proton comes at about 5.5\( \tau \), the same as in compound \( \tilde{6} \) (indicating a quite similar \( S=0 \) geometry). However, the axial methylene proton is downfield at 7.5\( \tau \), as in compound \( \tilde{1} \). In more polar solvents these two methylene protons come closer together (axial 8.1\( \tau \) and equatorial 8.3\( \tau \) in dimethylsulfoxide-\( d_6 \)). Furthermore, the methine signal is now solvent dependent as shown by the expanded spectra (NMR-15, 16, and 17). The outermost doublets serve as a good probe for the \( J_{4a5e} \) coupling; the coupling constant (\( J \)) values obtained in the different solvents are listed in Table 2:

![Chemical structure](image)

**Table 2**

<table>
<thead>
<tr>
<th>Solvent</th>
<th>( J_{5a5e} )</th>
<th>( J_{4a5a} )</th>
<th>( J_{4a5e} )</th>
<th>( J_{4aCH_3} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>carbon tetrachloride</td>
<td>14.4</td>
<td>11.8</td>
<td>3.2</td>
<td>6.5</td>
</tr>
<tr>
<td>nitrobenzene (room temp)</td>
<td>14.8</td>
<td>11.4</td>
<td>3.5</td>
<td>6.6</td>
</tr>
<tr>
<td>(87°)</td>
<td>15.0</td>
<td>11.6</td>
<td>3.6</td>
<td>6.8</td>
</tr>
<tr>
<td>methylene chloride-( d_2 )</td>
<td>14.8</td>
<td>11.6</td>
<td>3.2</td>
<td>6.6</td>
</tr>
<tr>
<td>acetone-( d_6 )</td>
<td>14.8</td>
<td>c</td>
<td>4.6</td>
<td>6.8</td>
</tr>
<tr>
<td>acetonitrile-( d_3 )</td>
<td>14.8</td>
<td>c</td>
<td>4.4</td>
<td>6.6</td>
</tr>
<tr>
<td>dimethylsulfoxide-( d_6 )</td>
<td>15.8</td>
<td>14.6</td>
<td>1.5</td>
<td>6.8</td>
</tr>
<tr>
<td>dimethylformamide</td>
<td>16.8</td>
<td>14.9</td>
<td>2.0</td>
<td>6.6</td>
</tr>
</tbody>
</table>

- a concentration around 15% w/v
- b in Hz (±0.2)
- c obscured by solvent

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Little change was noted upon heating to 87° in nitrobenzene. Unfortunately the compound decomposed at higher temperature or upon heating in dimethysulfoxide-d₆. In the table the first three solvents gave virtually identical spectra, as did the next two, and the last two, indicating three solvent classes. Hence, although the dipole moment change with solvent was borderline (0.18 debye from cyclohexane to benzene) the nmr changes with solvent indicate that this compound exists in either a mixture of chair and non-chair forms or of a non-chair form exclusively. Either choice could give dipole moments within the range found. As the necessarily axial methyl group should disfavour the chair form, the latter possibility is not surprising and for reasons we shall see later is more than likely the case. In such a form (non-chair), small changes in geometry could easily bring about large changes in couplings with concomitant small changes in dipole moment.

For the 4,6-dimethyl isomer, compound ⁵, an intermediate and constant value of 3.9 debyes was found, which is within the range (3.7 to 4.5 debyes) expected for a twist form with quasi-axial S=0. This is again substantiated in the nmr. Although the spectrum is rather complex in carbon tetrachloride, the methine protons appear at 5.03 and 5.67, decoupling showing the low field methine coupled to the high field methyl doublet and the high field methine to the lower methyl doublet. In dimethysulfoxide-d₆ (NMR-18), the C-5 protons are equivalent producing a simple spectrum with the following values:

<table>
<thead>
<tr>
<th>Substituent</th>
<th>τ</th>
</tr>
</thead>
<tbody>
<tr>
<td>H₆ₐ</td>
<td>5.03</td>
</tr>
<tr>
<td>H₄ₑ</td>
<td>5.41</td>
</tr>
<tr>
<td>CH₃(₄ₑ)</td>
<td>8.50</td>
</tr>
<tr>
<td>CH₃(₆ₑ)</td>
<td>8.65</td>
</tr>
<tr>
<td>H₅ₐ = H₅ₑ</td>
<td>8.00</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>J</th>
<th>Hz</th>
</tr>
</thead>
<tbody>
<tr>
<td>4αCH(<em>\text{J}(4a) = 6αCH(</em>\text{J}(6e)</td>
<td>6.6</td>
</tr>
<tr>
<td>4ε5ε = 4ε5α</td>
<td>5.7</td>
</tr>
<tr>
<td>6α5α = 6α5ε</td>
<td>6.8</td>
</tr>
</tbody>
</table>

In this molecule the methine signals are much closer together - 5.1 and 5.4 Hz; also, as reported previously,\(^5^5\) the methyl and to a lesser extent the methylene proton separations are temperature dependent, the latter becoming a sharp triplet around 64° and the former moving closer together with increasing temperature (methyl separation at -105° was 15 Hz in acetone-\(d_6\), 12 Hz at room temperature in this solvent as well as neat, while neat at 168° 8 Hz). However, unlike the results\(^5^5\) of Overberger, above 64° the sharp methylene triplet again became more complex until by 168° it was similar to its room temperature spectrum. These small changes in chemical shift with temperature are common in these sulfite molecules and has previously been pointed out in the case of compound \(^{10}\) where the change is in the opposite direction. The sulfate derivative of compound \(^{12}\) which is already inverting rapidly at room temperature has two singlets which also move together slightly with an increase in temperature (199 Hz separation in acetone-\(d_6\) at room temperature but 209 Hz at -106°). The less stable 5-t-butyl isomer, compound \(^{12}\), behaves like compound \(^{6}\), the methylene separation decreasing with decreasing temperature (27 Hz at -82° in acetone-\(d_6\) while 32 Hz at room temperature). These results can be explained by conformational changes, association phenomena (either solute-solute and/or solute-solvent), or viscosity effects. The danger in interpreting small nmr chemical shift changes arising from temperature or solvent changes as evidence for the former (conformational changes) has recently been strongly emphasized by Lasslo.\(^7^6\) In view of the strong
association tendencies of these sulfite molecules (discussed later), this second explanation seems the most probable. No other significant change in compound 5 was noted down to -105° in acetone-d₆.

The nmr parameters of compound 5, the racemic isomer of intermediate dipole moment, can be interpreted as either a chair-chair equilibrium as was done or by the existence of non-chair (twist) form(s) as the dipole moments indicate and as we shall see later is more in accord with barriers in rings containing adjacent vicinal unshared electron pairs. Cazaux and Maroni have reached a similar conclusion for a series of racemic 4,6-disubstituted sulfites, as has also Wucherpfennig for this compound. Considering the axial S=O - axial methyl interaction in both the possible chair forms this result is perhaps not surprising.

The 4,4,6-trimethyl compound 7 has this same interaction and the same solvent independent dipole moment. The spectrum is again complex in carbon tetrachloride with part of the methylene protons obscured by the methyl groups. However, the methine absorption occurs at 4.9τ which is similar to the axial proton of compound 5 (5.0τ), the axial methyl at 8.3τ (8.4τ for 5), and the equatorial methyl groups at 8.7τ (8.65τ for 5). As with compound 5, in dimethylsulfoxide-d₆ (NMR-19) a very simple spectrum was obtained with the methylene protons again equivalent:

<table>
<thead>
<tr>
<th>Substituent</th>
<th>τ</th>
</tr>
</thead>
<tbody>
<tr>
<td>H₄a</td>
<td>4.85</td>
</tr>
<tr>
<td>CH₃(4e)</td>
<td>8.30</td>
</tr>
<tr>
<td>CH₃(6a) = CH₃(6e)</td>
<td>8.68</td>
</tr>
<tr>
<td>H₅a = H₅e</td>
<td>8.04</td>
</tr>
<tr>
<td>4aCH₃(4e)</td>
<td>6.5</td>
</tr>
<tr>
<td>4a5a = 4a5e</td>
<td>6.6</td>
</tr>
</tbody>
</table>
The striking similarities between these two compounds lead to the same two alternatives for both. The first, however, of a chair-chair equilibrium is not very likely because of the expected large axial methyl - axial methyl interaction in the chair form with equatorial S=0 required by this explanation. A non-chair (twist) form or forms is certainly the better choice, the moreso as these should not necessitate any large dipole moment change with solvent (as is the case with a chair-chair equilibrium).

Addition of one further methyl group to give compound \(9\) raises the dipole moment to \(4.3\) debyes. Now even in dimethylsulfoxide-\(d_6\) the methylene protons are not equivalent (NMR-20) but rather have a large \(J_{\text{gem}} = 15.3\) Hz. The methyl groups are equivalent in this solvent but not in carbon tetrachloride or benzene. This extra methyl group should cause sufficient distortion in a chair structure to render this form highly unlikely. A non-chair form is consistent with the nmr and dipole moment data; hence this molecule is probably in a non-chair form with a higher dipole moment than compounds \(5\) or \(7\).

The last compound is \(12\), the less stable 5-t-butyl isomer, and the only one whose dipole moment changes significantly with solvent. However, in the nmr, a solvent and temperature (-99° to room temperature in acetone-\(d_6\)) independent spectrum was obtained (NMR-21), and the values obtained in carbon tetrachloride are listed below:

<table>
<thead>
<tr>
<th>Substituent</th>
<th>(\tau)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(H_{4a} = H_{6a})</td>
<td>5.28</td>
</tr>
<tr>
<td>(H_{4e} = H_{6e})</td>
<td>6.09</td>
</tr>
<tr>
<td>(H_{5e})</td>
<td>8.38</td>
</tr>
<tr>
<td>t-butyl</td>
<td>8.94</td>
</tr>
</tbody>
</table>

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Although this compound has been assumed to be a mixture of chair forms, mainly because of its dipole moment variation with solvent, such a conclusion is unwarranted as it neglects the possibility of the existence of non-chair forms. Rather, the lack of variability of the single coupling constant as well as its magnitude (5.3 Hz) point either to a mixture of non-chair forms with near equal couplings but different dipole moments, or to a mixture of non-chair and chair forms (which should have different dipole moments including the chair with axial t-butyl (\(\Delta G_{25} = 1.5 \text{ kcal/mole} \)). This latter possibility would better explain the dipole moment variation and recently Bentrude has come to a similar conclusion for the corresponding 5-t-butyl phosphite analogue. Eliel found the same solvent independence for J in the less stable 2-methyl-5-t-butyl-1,3-dioxane isomer although the couplings were consistent with the predominance of a chair form with axial t-butyl. The greater preference of this chair form in the dioxane case may be due to a greater preference of the 2-methyl group (\(\Delta G_{25} = 4.1 \text{ kcal/mole} \)) for a chair rather than a non-chair form compared to an axial S=0 (i.e. chair non-chair energy differences may be much smaller in sulfites than in 2-substituted 1,3-dioxanes).

<table>
<thead>
<tr>
<th>J</th>
<th>Hz</th>
</tr>
</thead>
<tbody>
<tr>
<td>4a4e</td>
<td>6a6e</td>
</tr>
<tr>
<td>4a5e</td>
<td>4e5e = 6a5e = 6e5e</td>
</tr>
</tbody>
</table>

**Benzene Solvent Shifts**

The benzene induced solvent shifts relative to carbon tetrachloride are given in Table 3 (total data listed in Appendix I). Since it has been pointed out that for consistent results in solvent effects, dilute solutions where maximum complexing occurs must be used, the preferred
TABLE 3 - Benzene Solvent Shifts

<table>
<thead>
<tr>
<th>Compound</th>
<th>R₁</th>
<th>R₂</th>
<th>R₃</th>
<th>R₄</th>
<th>R₅</th>
<th>R₆</th>
<th>CC₄</th>
<th>Δ</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5.12</td>
<td>0.45</td>
</tr>
<tr>
<td>2 R₂=CH₃</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5.12</td>
<td>0.47</td>
</tr>
<tr>
<td># 3 R₁=CH₃</td>
<td>8.60</td>
<td>0.49</td>
<td>5.6</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>4 R₂=R₆=CH₃</td>
<td>5.06</td>
<td>0.24</td>
<td>8.73</td>
<td>0.48</td>
<td>8.27</td>
<td>0.65</td>
<td>c</td>
<td>c</td>
</tr>
<tr>
<td>5 R₂=R₅=CH₃</td>
<td>5.03</td>
<td>0.28</td>
<td>8.42</td>
<td>0.35</td>
<td>5.65</td>
<td>0.63</td>
<td>8.02</td>
<td>0.71</td>
</tr>
<tr>
<td># 6 R₁=R₅=CH₃</td>
<td>8.61</td>
<td>0.47</td>
<td>5.46</td>
<td>0.84</td>
<td>8.46</td>
<td>0.87</td>
<td>8.25</td>
<td>0.37</td>
</tr>
<tr>
<td>7 R₁=R₂=R₆=CH₃</td>
<td>8.30</td>
<td>0.82</td>
<td>4.93</td>
<td>0.17</td>
<td>8.72</td>
<td>0.38</td>
<td>8.68</td>
<td>0.46</td>
</tr>
<tr>
<td># 8 R₁=R₂=R₅=CH₃</td>
<td>8.58</td>
<td>0.42</td>
<td>8.53</td>
<td>0.32</td>
<td>5.48</td>
<td>0.63</td>
<td>8.27</td>
<td>0.88</td>
</tr>
<tr>
<td>9 R₁=R₅=R₆=CH₃</td>
<td>8.36</td>
<td>0.29</td>
<td>8.43</td>
<td>0.47</td>
<td>7.12</td>
<td>0.47</td>
<td>7.96</td>
<td>0.82</td>
</tr>
<tr>
<td>10 R₃=CH₃</td>
<td>5.33</td>
<td>0.36</td>
<td>6.60</td>
<td>0.61</td>
<td>8.67</td>
<td>0.47</td>
<td>9.13</td>
<td>0.79</td>
</tr>
<tr>
<td>11 R₃=t-butyl</td>
<td>5.34</td>
<td>0.13</td>
<td>6.22</td>
<td>0.38</td>
<td>7.91</td>
<td>0.35</td>
<td>9.03</td>
<td>0.60</td>
</tr>
<tr>
<td>12 R₄=t-butyl</td>
<td>5.28</td>
<td>0.40</td>
<td>6.09</td>
<td>0.49</td>
<td>8.94</td>
<td>0.47</td>
<td>8.38</td>
<td>0.67</td>
</tr>
</tbody>
</table>

a R = H unless otherwise specified
b Δ = τ CC₄(20%) - τ Benzene(∞ dilution)
c if left blank, R₅ = R₁, R₆ = R₂, and R₃ = R₄
# isomer of higher dipole moment (Forms other than chair with axial S=O predominant)
Figure 1. Determination of benzene ASIS values for 5-t-butyltrimethylene sulfite (11) at infinite dilution (zero concentration). The 100% value is the chemical shift in 20% $\text{CCl}_4$ solution.
Figure 2. Determination of benzene ASIS values for 1,4,6-trimethylene sulfite (8) at infinite dilution (zero concentration). The values are for two separate determinations.
method is to do a concentration study and extrapolate the shifts to infinite dilution. This produced some interesting results; for some sulfite isomers, straight lines were obtained (e.g. compound 11, Figure 1), while others gave quite noticeable curvature in either direction (e.g. compound 8, Figure 2). The extrapolated values at zero concentration (infinite dilution) were quite reproducible (generally \( \pm 3 \) Hz) and clearly demonstrate the danger of merely measuring these shifts at a single concentration. Although carbon tetrachloride is the recommended "inert" reference solvent for such studies, some values were obtained using dimethylsulfoxide-\( \delta_6 \) (Appendix ii) for comparison after the persistent association of these sulfites was discovered (vide infra).

The following points and conclusions can be made:

(a) The aromatic solvent-induced shifts (ASIS)\(^{76}\) are almost always larger for the C-5 substituents than for the C-4 and C-6 ones (even for the methyl groups in compound 10 and the t-butyl of compound 11) except for compound 2 where the axial methyl has an extremely large shift. This would indicate that the benzene approaches this end of the molecule, the positive end of the dipole, as is now generally considered to be the case.\(^{76,82,83}\) In fact, a model for the benzene-solute collision complex in which the resultant dipole moment of the sulfite lies perpendicular to the plane of the benzene ring in many cases gives shifts that agree at least qualitatively with those predicted using the benzene shielding values calculated previously.\(^{84}\) The complex for compound 1 is depicted below:
(b) The ASIS of the equatorial C-5 substituent (R_3 in all compounds except 3, 6, and 8 in which R_4 is the equatorial) is in most cases larger than its axial counterpart. Compounds 4 and 5 have about equal benzene shifts, while 7 is the one exception. If only those compounds shown to exist in chair forms are considered, this would indicate that for them the equatorial substituent is closer to the centre of the benzene ring.

(c) Compounds 1, 2, and 10, which were assigned chair forms have virtually the same ASIS values. However the values for compound 11 are considerably smaller, indicating that the equatorial t-butyl group is blocking the benzene from approaching as close as in the case of the other three compounds.

(d) Generally the axial group at C-4 and C-6 has a smaller ASIS than its equatorial counterpart, as would be expected in the proposed complex.

(e) Compounds likely having non-chair forms (5, 7, 8, and 9) generally display unusual ASIS behaviour. The C-5 methylene protons of compounds 5 and 7 have equal ASIS values in dimethylsulfoxide-d_6; in compounds 2 and 8 the relative magnitudes of the shifts for these protons are reversed in this solvent (i.e. axial ASIS is now greater than the equatorial ASIS). In dimethylsulfoxide-d_6 compound 8 also has the unique property of near equal ASIS values for its axial (R_2) and equatorial (R_1) methyl groups. Compound 9 has a very large difference (17) between the R_3 and R_4 ASIS values which is equalled only by that of compound 6 (vide infra).

(f) The ASIS value for the axial hydrogen atoms is large in compound 6 but small in compound 4, while the equatorial methyl groups are about equally shifted. Furthermore, the difference in the ASIS values of R_3 and R_4 is now much larger (the more so in dimethylsulfoxide-d_6), the equatorial (R_3 in compound 5, R_4 in compound 6) having the larger ASIS. All this indicates that the benzene molecule is now on "top" of the sulfite 6 as shown below.
(g) The use of dimethylsulfoxide-d$_6$ instead of carbon tetrachloride produces generally the same trends but for the exceptions already noted. Usually going from carbon tetrachloride to dimethylsulfoxide-d$_6$ causes an upfield shift in the C-5 substituent which tends to decrease the separation between the axial and equatorial substituents (so much that in compounds 4 and 6 the order is reversed - axial upfield relative to the equatorial). These changes could be caused by solvent effects on conformational geometry or equilibria (as is more than likely the case in some compounds, notably 7 and 8) or by increased solute-solute association in carbon tetrachloride relative to dimethylsulfoxide-d$_6$, with the larger effect on the C-5 substituents pointing to a 'head to tail' type dipole association (large anisotropy of the S=O group expected to affect these positions to a much greater extent).

111. **Infrared Spectra (ir)**

From a study of the S=O bond stretching region (about 1150 to 1250 cm$^{-1}$) for the sulfite compounds 1 to 12 (IR-1 to 12) in 5% (w/v) carbon tetrachloride and acetonitrile, solvents of considerably different polarity ($\varepsilon = 2$ vs 38), it can be seen that:

(a) No significant change occurs from one solvent to the other for those compounds designated as chair forms with axial S=O (compounds 1, 3, 4, 10 and 11).
The following infrared spectra of the 1150-1250 cm\(^{-1}\) regions were recorded in 5% (w/w) solutions of carbon tetrachloride (left hand spectra) and acetonitrile (right hand spectra) for the compounds indicated:

IR-1  trimethylene sulfite (1)

IR-2  4-methyltrimethylene sulfite (2)

IR-3  4-methyltrimethylene sulfite (3)

IR-4  4,6-dimethyltrimethylene sulfite (4)

IR-5  4,6-dimethyltrimethylene sulfite (5), racemic

IR-6  4,6-dimethyltrimethylene sulfite (6)

IR-7  4,4,6-trimethyltrimethylene sulfite (7)

IR-8  4,4,6-trimethyltrimethylene sulfite (8)
IR-9 4,4,6,6-tetramethyltrimethylene sulfite (9)

IR-10 5,5-dimethyltrimethylene sulfite (10)

IR-11 5-t-butyltrimethylene sulfite (11)

IR-12 5-t-butyltrimethylene sulfite (12)
(b) Those compounds which the dipole moment data indicated should have significant amounts of equatorial $S=O$ (either chair or non-chair), compounds 2, 6, and 8, have a strong band at the higher frequency (around $1230 \text{ cm}^{-1}$) which is usually the most intense band (especially in acetonitrile).

(c) The compounds which by nmr and dipole moment studies were concluded to exist mainly in non-chair forms (compounds 5, 7, and 9) have new bands in the $1200$ to $1210 \text{ cm}^{-1}$ region that change only slightly with solvent.

(d) The 5-t-butyl compound 12 which had a large dipole moment variation with solvent also varies considerably in the infrared (IR-12).

Additional solvent and temperature effects were carried out on these sulfites and the results are listed in Appendix iii. The absorbance ratios given are those of the higher band in question relative to the main band around $1190 \text{ cm}^{-1}$ (arbitrarily assigned a value of 1), assuming equal extinction coefficients. Although this data is very rough, it does tend to reinforce the conclusions pointed out above. Generally, the use of a solvent of high dielectric constant, a neat sample, or higher temperature increased the ratio in favour of the higher ($1230 \text{ cm}^{-1}$) band (compound 4 is an exception while compound 2 remains virtually unchanged). These changes could be taken as indicative of changes in conformational equilibria, although not necessarily chair chair which has usually been assumed.$^{59a}$ However, in view of the strong sulfite association found (next section), such conclusions must be considered as speculative until the effect of association in the infrared is determined.

IV. Association by Vapour Phase Osmometry

Because of the novel suggestion$^{65}$ that compound 6 may have the dimeric form below (rather than monomeric), based on a cryoscopic molecular weight
of 312 +12 (even though no peak at m/e = 300 could be found in the mass spectrum), it was decided to undertake a brief survey of the apparent molecular weight ($M^*$) of the sulfites by vapour phase osmometry.

While we found no evidence for this dimeric 12-membered cyclic structure, we did discover that the compound in question (compound 6) and several other trimethylene sulfites are appreciably associated in solution. Although most of the data is limited to the determination of $M^*$ at one concentration, certain trends are readily apparent from Table 4. Where more than one determination was made, the value reported in this table is the average, with all the data recorded in appendix IV.

From the table, the following observations can be made:

1. Association is greatest for the unsubstituted compound, and can involve higher aggregates than dimers.

2. The orientation of the S=0 bond has little effect on association (e.g. compounds 4 and 6).

# This result would be surprising if this indeed were the structure, since cyclic sulfites ordinarily yield molecular ions of significant intensity (about 1% of base peak). The alleged rapid thermal conversion of compound 6 to 4 cannot explain the lack of an ion at m/e = 300, since sulfites carefully purified to remove all traces of acid do not, in fact, isomerize thermally (see section V). Further, the mass spectra of these two isomers are significantly different, a result incompatible with a fast thermal conversion of compound 6 to 4 in the spectrometer.
TABLE 4 - Sulfite (Osmometric) Molecular Weights ($\frac{M^*}{M}$)$^a$

![Diagram of sulfite structure]

<table>
<thead>
<tr>
<th>Compound$^b$</th>
<th>Cyclohexane</th>
<th>Dioxane</th>
<th>CCl$_4$</th>
<th>Benzene</th>
<th>Acetonitrile</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5.38</td>
<td>1.57</td>
<td>2.18$^c$</td>
<td>1.55</td>
<td>1.21</td>
</tr>
<tr>
<td>2 R$_2$ = CH$_3$</td>
<td>3.08</td>
<td>-</td>
<td>1.71</td>
<td>1.30</td>
<td>1.17</td>
</tr>
<tr>
<td># 3 R$_1$ = CH$_3$</td>
<td>2.24</td>
<td>1.69</td>
<td>1.69</td>
<td>1.28</td>
<td>1.07</td>
</tr>
<tr>
<td>4 R$_2$ = R$_6$ = CH$_3$</td>
<td>1.99</td>
<td>1.25</td>
<td>1.43</td>
<td>1.22</td>
<td>1.00</td>
</tr>
<tr>
<td>5 R$_2$ = R$_5$ = CH$_3$</td>
<td>1.85</td>
<td>1.22</td>
<td>1.43</td>
<td>1.21</td>
<td>1.09</td>
</tr>
<tr>
<td># 6 R$_1$ = R$_5$ = CH$_3$</td>
<td>1.53</td>
<td>1.17</td>
<td>1.25</td>
<td>1.24</td>
<td>1.00</td>
</tr>
<tr>
<td>7 R$_1$ = R$_2$ = R$_6$ = CH$_3$</td>
<td>1.53</td>
<td>-</td>
<td>1.34</td>
<td>1.21</td>
<td>1.03</td>
</tr>
<tr>
<td># 8 R$_1$ = R$_2$ = R$_5$ = CH$_3$</td>
<td>1.47</td>
<td>-</td>
<td>1.28</td>
<td>1.22</td>
<td>1.05</td>
</tr>
<tr>
<td>9 R$_1$ = R$_2$ = R$_5$ = R$_6$ = CH$_3$</td>
<td>1.23</td>
<td>-</td>
<td>1.33</td>
<td>1.31</td>
<td>1.12</td>
</tr>
<tr>
<td>10 R$_3$ = R$_4$ = CH$_3$</td>
<td>2.00</td>
<td>-</td>
<td>1.59</td>
<td>1.19</td>
<td>1.30</td>
</tr>
<tr>
<td>11 R$_3$ = t-butyl</td>
<td>1.10</td>
<td>1.04</td>
<td>1.13</td>
<td>1.04</td>
<td>1.05</td>
</tr>
<tr>
<td>12 R$_4$ = t-butyl</td>
<td>1.08</td>
<td>1.04</td>
<td>1.13</td>
<td>1.04</td>
<td>1.08</td>
</tr>
</tbody>
</table>

$a$ ratio of apparent molecular weight to theoretical  
$b$ R = H unless otherwise specified  
$c$ value taken from Figure 3  
# isomers of higher dipole moments (forms other than chair with axial S=O predominant)
(3) A 5-t-butyl group virtually destroys any association (e.g. compounds 11 and 12), while 5,5-dimethyl groups do not. Axial methyl groups in the 4 and 6 positions also hinder association, whereas equatorial methyls do not (cf. compound 2 vs 7).

(4) Compounds that have been assigned non-chair forms also have relatively less association (e.g. compounds 5 and 9).

(5) Association decreases in more polar solvents until almost nil in acetonitrile.

All the above are consistent with the formation of a head-to-tail type of dimer:

\[
\begin{align*}
\text{(Mn)} & \quad \text{(Mm)} \\
\text{(Md)} & \quad \text{(Mm)} \\
\end{align*}
\]

which would continue to 'stack up' to give higher polymers. In this dimer it is necessary to tilt the individual sulfites as shown such that their individual dipoles lie nearly at right angles, in order to explain the lack of effect of association in the dipole moment work. This is because the experimentally determined dipole moment (\(\mu_{\text{exp}}\)) varies as the square root of the molecular weight used in its calculation (see Experimental for further discussion and references). Hence, if the measurement was actually performed on dimers, the resultant dipole moment for this dimeric species (\(\mu_D\)) would be \(\sqrt{2} \mu_{\text{exp}}\). The dipole moment then of the individual monomers (\(\mu_M\)) in this dimeric species depends on the way in which they align with each other:

\[
\frac{\mu_D}{2} = \frac{\mu_{\text{exp}}}{\sqrt{2}} , \quad \mu_M = \mu_M , \quad \frac{\mu_D}{\sqrt{2}} = \mu_{\text{exp}}
\]
Consequently the monomer dipole moment ($\mu_M$) calculated on the basis of pure dimer formation can vary from zero to the original $\mu_{\text{exp}}$ determined on the basis of monomer only, depending on the dimer geometry as shown above; only in the case where the angle between the two monomer dipoles is about 90° is the resultant monomer dipole moment ($\mu_M$) independent of the presence and the degree of association.

Since the degree of association changes from one solvent to another, association (unless of the 90° type) should produce non-linear plots of dielectric constant - weight fraction and solvent dependent dipole moments. No cases of the former were found (e.g. Figure 4 in the Experimental) and only one case of the latter (compound 12). Similar results would also be expected unless the degree of association remained constant throughout the concentration range used in the dipole moment determinations (typically about 2 to 0.5 grams of sulfite per 100 ml of solvent). Although a concentration study on trimethylene sulfite in carbon tetrachloride (Figure 3) indicates that the concentration range used in the dipole moment study (about 40 to 160 mM) may in fact not be large enough to change significantly the degree of association (which would explain the absence of non-linearity in the dielectric constant - weight fraction plots), a change of solvent often brings about a marked variation in the degree of association while the resultant dipole moments remain essentially constant with solvent (e.g. compounds 1, 2, 3, 5 and 10). Thus, this unusual lack of dipole moment variation in solvents shown by molecular weight data to change considerably the degree of association can be rationalized by dimer (or higher) formation with near 90° geometry.

One other form of association which should also not affect significantly the resultant dipole moment as it has this same relative (90°)
geometry, although it does not explain as well all the above-mentioned trends (1 to 5), is the following:

This type of structure has previously been proposed for some sulfoxide dimers, and may also be involved here to some extent, particularly in those cases involving higher degrees of association such as compound 1 in cyclohexane.

For solutions of trimethylene sulfite (1) in carbon tetrachloride, the apparent molecular weight ($M^*$) was determined at several concentrations and a plot made of $M^*$ versus concentration (mM). From the plot (Figure 3), it is apparent that dimer formation persists to remarkably low concentration;

![Diagram showing molecular structure and plot](image)

Figure 3. Plot of the ratio ($M^*/ M$) of the apparent ($M^*$) to true ($M$) molecular weight against molar concentration for solutions in carbon tetrachloride. Error limits are ± 4%.
the dashed line at 5 mM represents the concentration where intermolecular
association is usually considered negligible in infrared studies. Recently Eglinton and Kovacs reported molecular weight data (osmometric) which demonstrated unusually persistent association in some systems where H-bonding could occur. Several points for one of their most strongly associated molecules (stearic acid) are included in the figure for comparison. It can be seen that trimethylene sulfite is even more strongly associated even though it has no such possible H-bonding. Strong dipole-dipole interactions have been implicated for molecules with large dipole moments, but not at such low concentrations. Further, preliminary work on ethylene sulfite and carbonate (appendix iv) indicate that they may be even more strongly associated.

V. Chemical Equilibration

Previous estimates of the energy difference between the axial S=0 and equatorial S=0 in the chair form have ranged from $4.5 \pm 1.5 \text{kcal/mole}$ to $2-2.5 \text{kcal/mole}$. Although chemical equilibration is regarded as one of the least equivocal methods of determining conformational free energies, little has appeared on sulfites. Table 5 below contains some

<table>
<thead>
<tr>
<th>Compound</th>
<th>Solvent</th>
<th>Time (weeks)</th>
<th>Response Ratio</th>
<th>Area Ratio</th>
<th>K $-\Delta G^\circ$ (kcal/mole)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 and 6</td>
<td>CCl$_4$</td>
<td>2</td>
<td>0.952±0.021</td>
<td>87.82±12.13</td>
<td>83.6±13.4 2.62±0.10</td>
</tr>
<tr>
<td></td>
<td>CCl$_4$</td>
<td>2</td>
<td>0.806±0.050</td>
<td>109.6±18.38</td>
<td>88.3±20.3 2.66±0.14</td>
</tr>
<tr>
<td></td>
<td>CH$_2$CN</td>
<td>10</td>
<td>0.969±0.013</td>
<td>18.26±3.63</td>
<td>17.7±3.8 1.70±0.13</td>
</tr>
<tr>
<td></td>
<td>ether·HCl</td>
<td>2</td>
<td>0.969±0.013</td>
<td>16.53±2.17</td>
<td>16.02±2.53 1.64±0.10</td>
</tr>
<tr>
<td>2 and 3</td>
<td>CH$_2$CN</td>
<td>6</td>
<td>0.831±0.057</td>
<td>21.37±4.29</td>
<td>17.8±4.8 1.70±0.16</td>
</tr>
</tbody>
</table>

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additional equilibration data. The two 4,6-dimethyl compounds 4 and 6 were employed since compound 6 is the only clear cut case of a sulfite in a chair form with equatorial S=0. Compounds 2 and 3 were also equilibrated, although the conformation of compound 3 is less certain.

The lower $\Delta G$ value determined in acetonitrile would ordinarily be attributed to some solvent effect. However, the presence of an unknown and possibly unequal amount of self-association in the one molar solutions of compounds 4 and 6 could influence the value of $\Delta G$ in carbon tetrachloride as well. Peculiarly enough, the two $\Delta G$ values in acetonitrile are the same even though the dipole moment of compound 3 makes its conformation doubtful. Further studies on these conformational energies and related association studies are necessary. For the present, a value of 2 (± 0.5) kcal/mole seems to be the best estimate for the preference of the S=0 for the axial position in the chair form.

It should also be noted that the reported thermal isomerization of these sulfites (e.g. compounds 4 and 6) was found to occur only in the presence of acid contamination. Sulfites such as compound 6 or 8 carefully purified by gas liquid chromatography (glc) were stable up to 200°, but isomerized readily (compound 6 to 4 and 8 to 7) with a trace of acid, even at room temperature (see Experimental). Lack has informed us of similar findings after a reinvestigation of her results reported before her knowledge of this fact.

VI. Sulfate Studies

For reasons given in the next section, it was concluded that trimethylene sulfates should have inversion barriers amenable to nmr analysis. After finding a satisfactory solvent mixture, a barrier of 8.1 ± 0.2 kcal/mole based on the coalescence temperature (-107°) of the methylene quartet or
was found for 5,5-dimethyltrimethylene sulfate (NMR-22). This barrier
was virtually unchanged in a solvent mixture of 1:1 ethyl bromide-d$_5$ -
methylene chloride-d$_2$, 1:1 m-fluorotoluene - methylene chloride-d$_2$, or
1:5 toluene-d$_8$ - methylene chloride-d$_2$.

Extensive nmr work was also carried out on 5-t-butyltrimethylene
sulfate in various solvents and solvent mixtures from -121 to +180°. No
coalescences were found nor significant changes with temperature. However,
large changes were obtained from one solvent to another. Low dielectric
solvents such as benzene or toluene gave a first order spectrum consistent
with a rigid chair with equatorial t-butyl (NMR-23). High dielectric
solvents such as acetone-d$_6$ or methanol-d$_4$ gave a simplified spectrum
(doubled and quintet, $J = 8.1$ Hz) consistent with an averaging due to rapid
inversion between chair and non-chair forms (NMR-24). Other solvents such
as deuteriochloform, methylene chloride-d$_2$, or nitrobenzene gave non-first
order spectra consistent with conformational mixtures (NMR-25). These
results can be accommodated by a conformational mixture of chair forms
(t-butyl equatorial) and non-chair forms, the latter favoured in high
dielectric solvents and the former in low dielectric solvents, assuming
a significant effect of solvent on the equilibrium. Further work is
necessary before this interpretation can be considered adequate.

V11. Ultrasonic Absorption Reinterpretation

Recently some trimethylene sulfites and sulfates$^{66,67,93,94}$ were
found to undergo ultrasonic absorption with subsequent relaxation, which
in all cases was attributed to a perturbation of a chair-chair anancomeric
equilibrium in these compounds. Since this interpretation necessitates a
surprisingly low ring inversion barrier (vide infra), and since ultrasonic
measurement cannot itself lead to any conformational assignments\textsuperscript{94} (in fact, earlier interpretations in this area have on occasion betrayed a lack of understanding of conformational analysis\textsuperscript{95}), it was decided to see if another interpretation would fit better all the known data. This reevaluation is particularly necessary when one considers the ultrasonic values in terms of other known systems.

First, let us consider the ultrasonic enthalpy differences $\Delta H^\circ$ (Table 6) assigned to the two chair forms for a number of cyclic sulfites. Based on the experimental energy differences in closely related six-membered ring systems, values were obtained by an estimation of the various interactions in each chair conformation, and the molecules are listed in Table 6 in order of increasing estimated energy difference between the two chair forms. Although these values must be taken as only approximate, they should have at least qualitative significance. The differences range from about 2 to 10 kcal/mole which corresponds to a factor of around $10^5$ in the equilibrium constant $K$ at room temperature,\# while the ultrasonic values are nearly constant at about 1.3 kcal/mole, corresponding to an equilibrium constant of less than $10^1$. In fact the ultrasonic technique is only sensitive to a minimum of 1-2\% ($K = 10^2$).\textsuperscript{66} The serious disagreement between these two approaches to chair-chair energy differences can be even more readily seen in the case of the 4,6-dimethyl compound $\overset{\circ}{\sim}$ and its isomer, compound $\overset{\dagger}{\sim}$. The experimentally determined free energy difference between axial and equatorial $\overset{\circ}{S}=0$ (2.0 ± 0.5 kcal/mole) is by itself larger than the ultrasonic $\Delta H^\circ$ (≤1.2 kcal/mole) which must include not only this energy difference but also the energy of a 1,3-diaxial methyl interaction. That is to say, accepting even roughly the ultrasonic values requires that

\# Entropy effects are too small to affect this argument significantly.
<table>
<thead>
<tr>
<th>Compound $^a$</th>
<th>$S=0$ axial</th>
<th>Estimated interactions in chair forms</th>
<th>$S=0$ equatorial</th>
<th>Difference</th>
<th>$\Delta H^0$ ultrasonic</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0</td>
<td>2.0$^b$</td>
<td>2.0</td>
<td>1.3</td>
<td></td>
</tr>
<tr>
<td>10 $R_2=R_4=CH_3$</td>
<td></td>
<td>5-$Me_{ax}$</td>
<td>2.0$^b$ + $Me_{ax}$</td>
<td>2.0</td>
<td>1.5</td>
</tr>
<tr>
<td>13 $R_3=CH_3, R_4=NO_2$</td>
<td>0</td>
<td>2.0$^b$ + 0.7$^c$ + 0.5$^c$</td>
<td>3.2</td>
<td>none</td>
<td></td>
</tr>
<tr>
<td>2 $R_2=CH_3$</td>
<td>0</td>
<td>2.0$^b$ + (1.7 - 2.9)$^d$</td>
<td>3.7 - 4.9</td>
<td>$\leq$ 1.2</td>
<td></td>
</tr>
<tr>
<td>7 $R_1=R_2=R_6=CH_3$</td>
<td>4-$Me_{ax}$ (1.6)$^f$</td>
<td>2.0$^b$ + (5.4 - 8.9)$^e$</td>
<td>5.8 - 9.3</td>
<td>none</td>
<td></td>
</tr>
<tr>
<td>4 $R_2=R_6=CH_3$</td>
<td>0</td>
<td>2.0$^b$ + (5.4 - 8.9)$^e$</td>
<td>7.4 - 10.9</td>
<td>$\leq$ 1.2</td>
<td></td>
</tr>
<tr>
<td>14 $R_2=R_3=R_6$</td>
<td>0</td>
<td>2.0$^b$ + (5.4 - 8.9)$^e$ + 0.7$^c$</td>
<td>8.1 - 11.6</td>
<td>$\leq$ 1.2</td>
<td></td>
</tr>
</tbody>
</table>

$^a$ $R = H$ unless otherwise specified

$^b$ this is a $\Delta G$ value (this work and ref. 91), but entropy considerations are not large enough to be important to this comparison

$^c$ from ref. 59

$^d$ lower value for 1,3-dithiane, higher for dioxane (E. L. Eliel, J. Amer. Chem. Soc., 91, 2708 (1969))

$^e$ lower value for cyclohexane, higher for dioxane and 1,3-dithiane (E. L. Eliel, ibid, 2705 (1969))

$^f$ estimate from the sulfate value in ref. 93
the structure A (S=0 equatorial) below for compound \( \bar{4} \) be as or more stable than the structure for compound \( \bar{6} \), which would be very surprising indeed:

\[
\begin{align*}
\text{A} & \quad \text{B} \\
\text{(ultrasonic ?)} & \quad \text{isomerization} \\
\text{Compound 6}
\end{align*}
\]

The above demonstrates the unreliability of enthalpy measurements by the ultrasonic technique, which are based on certain assumptions (namely \( \Delta H \gg \frac{\Delta V}{V} \cdot \frac{C_p}{\theta} \)) which may not be correct.#

A further discrepancy in Table 6 is the fact that the nitro compound \( \bar{1} \) and the sulfite \( \bar{7} \) unexplainedly failed to give an ultrasonic relaxation.

Even more peculiar is the fact that the six-membered ring compounds below which have two chair forms of equal energy have been observed to give a relaxation (barrier about 5 kcal/mole).67

\[
\begin{align*}
\text{O} & \quad \text{C}_2\text{H}_5 \\
\text{O} & \quad \text{C}_2\text{H}_5
\end{align*}
\]

Here the relaxation cannot be caused by a chair-chair equilibrium and hence it has been attributed to chair-boat interconversion. Further evidence has

# Wyn-Jones has informed us that \( \Delta V/V \) may well be around 5% which would invalidate this assumption and hence lead to erroneous estimates of \( \Delta H^0 \). Whether this could lead to deviations in this value of the magnitude indicated in Table 6 is open to question, however.
come from the spirodioxane barriers determined by nmr. For example, the 5,5-dimethyl derivative (shown below) has a $\Delta G^\ddagger = 8.3$ kcal/mole.

The above discrepancies between the nmr and ultrasonic results in the 1,3-dioxanes is also true in the case of the inversion barriers for trimethylene sulfates. A barrier of 4.6 kcal/mole (room temperature) was reported for 4-methyltrimethylene sulfate (less stable to more stable). After taking into account entropy contributions and the 1.75 kcal/mole added for the $\Delta G^\circ$ of a 4-methyl (axial) group, we obtain a $\Delta G^\ddagger \approx 7.5$ kcal/mole at $-107^\circ$, while the lower value determined by nmr for 5,5-dimethyltrimethylene sulfate at this temperature is $8.1 \pm 0.2$ kcal/mole to which 0.8 kcal/mole must be added for the unfavourable axial 5-methyl group, to give 8.9 kcal/mole for the nmr barrier to ring inversion. This discrepancy of at least 1.4 kcal/mole is too large to be accounted for by the combined error limits.

Furthermore, the acoustical workers' inherent assumption that the axial methyl - axial S=O interaction is not sufficient to cause serious distortion and/or non-chair forms is highly questionable when one considers the following:

(a) Compound 5 without doubt involves non-chair forms.

(b) Compound 7 from its dipole moment value alone must have severe distortion even if the chair form only is considered.

(c) Compound 3 also shows little preference for the axial methyl and axial S=O chair.

(d) Analogous 2 - 4 diaxial interactions in substituted 1,3-dioxanes are large and give rise to non-chair forms.
Thus it appears that in the sulfate case, as in the dioxane, the ultrasonic results may well be for a chair/non-chair equilibrium. Herein may lie the solution to the dilemma of finding a reasonable conformational change to which the ultrasonic relaxation data for the sulfites may be assigned, rather than the highly unlikely chair/chair equilibrium.

It is suggested\(^9\) that the trimethylene sulfites which have been shown by ultrasonic measurements to exist as conformational equilibria have non-chair conformations with energies comparable to the preferred chair form (and perhaps even lower). Compounds not giving an ultrasonic result are limited to a single chair or non-chair conformation. Compound 2 and possibly 7 are examples of the latter while compound 1 in Table 6 may be an example of the former. The existence of some cyclic sulfites derived from 1,3-dihydroxycholestanones in the boat form with both axial and equatorial S=O has already been demonstrated.\(^6\)

While the sulfite energy differences measured by ultrasonic absorption are anomalous in terms of chair/chair interconversion, their accompanying barriers (in addition to the 1,3-dioxane and sulfate barriers already mentioned) are even more difficult to understand in these terms.

Sulfite barriers of 3.5 to 5.5 kcal/mole (\(\Delta H^+\), less stable to more stable)\(^#\) are typical of the ultrasonic data.\(^6\) These values are about half the chair/chair barriers for cyclohexane (13.1 kcal/mole for methylcyclohexane\(^6\)) and may be the lowest recorded for saturated six-membered ring systems. The only comparable chair/chair barrier is that for 1,4-disila-1,1,4,4-tetramethylcyclohexane (less than 6 kcal/mole\(^1\)), which

\[\text{\# Although the } \Delta H^0 \text{ values are suspect, their maximum is fixed at about 2.5 kcal/mole by the acoustical detection limit of 1-2\% minor isomer, giving } \Delta H^+ \text{ a maximum of 6-8 kcal/mole for sulfites by ultrasonic absorption.}\]
can easily be understood in terms of the four low Si-C barriers (about 1.6 kcal/mole) in this ring. In the next section we will show that such low barriers for cyclic sulfites which contain five pairs of vicinal unshared electron pairs conflict drastically with the barriers found in similar compounds containing this structural feature.

V111. Vicinal Unshared Electron Pairs, Polar Bonds, and Barriers to Rotation

According to the calculations of Hendrickson, and more recently of Harris and Spragg, the major contributing factor to ring inversion barriers is torsional strain. Other contributing factors include steric interactions and ring distortion. It is now generally agreed that the energetically lowest pathway for ring inversion in cyclohexane is a half-chair or 'cyclohexene-like' transition state and that the incipient motion continues to the metastable boat conformation, which can partially alleviate some of its strain by distorting itself to a twist boat. However, regardless of the nature of the transition state, the fact that the major contributor to the ring inversion barrier is torsional strain, allows the barrier in cyclic molecules to be estimated at least qualitatively from torsional barriers in suitable acyclic analogues (i.e. the barrier of 10.3 kcal/mole in cyclohexane should be related to the 3.4 kcal/mole rotational barrier about the carbon-carbon bond in propane for example). Hence, a ring containing single bonds with higher barriers to rotation would be expected to have a higher barrier to ring inversion. The expectation of a higher or lower barrier relative to cyclohexane then rests on the choice of suitable acyclic rotational barriers. Wyn-Jones chose propane, dimethyl ether, and dimethyl sulfide (3.20, 2.73 and 2.13 kcal/mole respectively) to rationalize his much lower sulfite barriers to inversion found by his ultrasonic technique. This we believe is an
extremely poor choice, because of the peculiarly high barriers usually found about single bonds between atoms with unshared electron pairs. Unfortunately, the rotational barrier for probably the best analogue, dimethyl sulfite, has not been recorded yet. However, the rotational barriers around single bonds between atoms possessing unshared electron pairs have been measured\textsuperscript{105,107-110} and calculated\textsuperscript{111-115} for a large variety of compounds.

These barriers are generally of the order of 10 kcal/mole, a value seldom reached by the most hindered ethane derivatives lacking vicinal electron pairs. Although the magnitude of the contribution by the vicinal non-bonded electron pair interactions to these barriers is still controversial\textsuperscript{28,107,108,110,111,115,116} relative to other possible contributions, the basic facts, summed up in two simple rules by Wolfe and co-workers,\textsuperscript{115} still remain:

"Rule (1): electron pair - electron pair, electron pair - polar bond or polar bond - polar bond interactions cause a significant increase in rotation-inversion barriers of atoms bearing these substituents;

Rule (2): when electron pairs or polar bonds are placed or generated on adjacent pyramidal atoms, syn or anti periplanar orientations are disfavoured energetically with respect to that structure which contains the maximum number of gauche interactions."

There is also abundant evidence that one or more bonds of this sort increase the barrier to ring inversion\textsuperscript{73,116} in spite of the reduction in rotation barrier for neighbouring bonds where only one atom has unshared electron pairs, as the following data illustrate. Notice that most rings containing non-adjacent heteroatoms show barriers of the same order as cyclohexane,\textsuperscript{96} except for substitution of an SO or SO\textsubscript{2} unit for CH\textsubscript{2} which
causes a substantial increase in the barrier:

Series 1\#: (Ref. 87, 103, 104, 116-119)

\[
\begin{array}{cccc}
10.3 & X=O; \ E_a=10.7 \\
& X=NH; \ E_a=14.5 \\
& X=S; \ E_a=11.6 \\
& X=SO; \ E_a=14.2 \\
& X=SO_2; \ E_a=14.9 \\
\end{array}
\]

Series 2: (Ref. 100 and 116)

\[
\begin{array}{cccc}
11.2 & X=O; \ 14.6 & X=O; \ 15.0 & 12.9 \\
& X=S; \ 13.4 & X=S; \ 16.0 \\
\end{array}
\]

Series 3: (Ref. 118 and 120)

\[
\begin{array}{cccc}
& -65^\circ & -43^\circ & -8^\circ \\
barrier & 10.3 & 11.6 & 13.2 \\
\end{array}
\]

\# All barriers are $\Delta G^\#$ (kcal/mole) unless otherwise specified.
Similar effects occur in five- and seven-membered rings.\textsuperscript{120}

The broad applicability of Rule 2 which describes the static (thermo-dynamic) properties of these systems, does not appear to have been noted previously, but the effect of this rule upon stable conformations and upon intrinsic reactivities of diastereotopic groups or atoms is profound.\textsuperscript{115,121} Rule 2 also applies to the $\alpha$- sulphinylcarbanion,\textsuperscript{122} the $\alpha$- sulphonylcarbanion,\textsuperscript{123} and the $\alpha$- sulphhydrylcarbanion,\textsuperscript{124} but there is an exception, which will be discussed later. However, before applying this rule to predict the relative stabilities of the axial or equatorial orientation of the S=O, it is necessary to know which of the two (an electron pair or polar bond) takes precedence. This can be obtained from the computed graph of the total conformational energy of the $\alpha$- sulphinylcarbanion as a function of rotation about the C=S bond\textsuperscript{122} (Figure 4). Here it is seen that the energy minima correspond to structures with the lone pair on carbon gauche to both the S=O and S lone pair or gauche to the lone pair and anti periplanar to the S=O, while maxima occur when the carbon lone pair is either syn or anti periplanar to the sulphur lone pair. Hence anti periplanar lone pairs are less favourable than an anti periplanar lone pair - S=O bond by a large amount, which explains the large axial preference of the S=O in the sulfites.

This axial preference might be ascribed to the well known "anomeric effect"\textsuperscript{125} which carbohydrate chemists refer to as the tendency of an electronegative substituent (halogen, sulphur, oxygen) at the anomeric centre (C-1) of a pyranose ring to exhibit a greater preference for the axial orientation over the equatorial conformation than it does in cyclo-hexane. This apparent exception to rule 2, also called the "Edward-Lemieux effect"\textsuperscript{114} (as well as the "rabbit ear" effect\textsuperscript{126}), corresponds to destabilization of a conformation which places a polar bond between two electron pairs.
This effect is usually explained in terms of repulsions among non-bonding electron pairs of substituent and ring heteroatom(s);\textsuperscript{87,96} but a more recent explanation\textsuperscript{73,115} rules out these "dipole-dipole" repulsive rabbit-ear interactions between non-bonded electron pairs as the main cause, explaining it by the way in which the nuclear-nuclear and electron-electron repulsive and nuclear-electron attractive interactions of the bonded electron pairs are balanced with each other (i.e. interactions between the polar bonds are most important in explaining the Edward-Lemieux effect). This same balance of interactions between the bonded electron pairs also is the origin of the barriers.

One might ask why the chair/chair barrier in the sulfate case is not higher by rule 1 also. A comparison of the calculated barrier heights in the $\alpha$- sulphonyl,\textsuperscript{123} $\alpha$- sulphinyl,\textsuperscript{122} and $\alpha$- sulphhydrylcarbanions\textsuperscript{124} (5 : 12.8 : 18.8 kcal/mole respectively) provides an explanation while again emphasizing the large barrier increases relative to cyclohexane brought about by adjacent electron lone pairs, whatever the cause.

Considering these results, it seems that for trimethylene sulfites (with unshared electron pairs on three adjacent atoms) the choice between a high ($\geq$17 kcal/mole) and a low ($<8$ kcal/mole) barrier to ring inversion can be made with some confidence. The only conclusion compatible with these arguments is that the barrier to ring inversion is high and further that interactions of vicinal electron pairs and/or polar bonds are the major cause of this barrier as well as the other conformational properties such as the strong axial preference of the S=O bond.

The possibility that p-d type bonding between the sulfur atom and the endocyclic oxygen atoms might be the cause of this strong axial preference of the S=O bond has also been considered,\textsuperscript{69} but any significant contribution
by the sulfur d-orbitals was not found by Wolfe and co-workers in their calculations. 115

**Two-Fold rotational barriers and conformer energy minima.**

A very interesting characteristic of the calculated rotational barriers for bonds with vicinal unshared electron pairs was pointed out by Wolfe also, namely that only two maxima and minima occur (unlike cyclohexane which has three of each). This is readily seen in Figure 4 which contains the total energy curves for 360° rotation about the C-S bonds in hydrogen methyl sulfoxide and its carbanion, as well as the corresponding curve for ethane (see reference 115 for further related molecules). The CH₃SHO molecule has an ethane-like barrier except that its three maxima and minima are shifted about 20° to the right, while its carbanion has two of these maxima and the minimum between them (θ = 80 to 200°) replaced by a much larger maximum (θ = 130°), as well as a few other smaller shifts. Furthermore, the curve for the carbanion shows energies of 4.4, 12.8 and 0 kcal/mole for the conformations corresponding to the preferred staggered ethane conformations. Hence, the staggered conformation of the perfect chair form in cyclohexane may correspond in the case of molecules with two fold barriers to rotation to an energy minimum, or it may in fact correspond to the highest energy on the rotation curve or any intermediate value. The arbitrary assignment of the chair form as the preferred conformation in six-membered rings containing one or more bonds with vicinal unshared electron pairs then may be quite erroneous, when one takes into consideration that the conformational preference for the chair over non-chair forms in cyclohexane should be equated with the preference of the staggered over the eclipsed conformation in ethane.

In addition, it would appear that, because of the increased height
Figure 4. Variation of the total energy of ethane, hydrogen methyl sulfoxide and its carbanion as a function of rotation about the C-C or C-S bond ($\theta$).
and therefore importance of these two fold barriers, the chair preference should decrease relative to the non-chair form with the introduction of one or more bonds of this type. In fact, one well documented case for the twist form preference in a molecule of this type is 3,3,6,6-tetramethyl-1,2,3,5-tetrathiane \(^{28,116}\) (duplodithioacetone) where the twist form is preferred by 0.5 to 1 kcal/mole. The small entropy difference between the chair and twist forms of this molecule may reflect the reduced flexibility of non-chair forms in these systems.

The current view that trimethylene sulfite prefers the chair form may well be correct. However, the possibility of relatively low energy non-chair forms seems to be strong. This work, including the reinterpretation of the ultrasonic data of Wyn-Jones, and the nmr work of Cazaux and Maroni referred to earlier may be cited in support of this position. It is also extremely interesting to find that these same conclusions are being drawn in recent work\(^{73,75b,127}\) on the phosphorous analogues of sulfites viz., polar bond prefers axial position strongly, twist forms implicated in the less stable 5-t-butyl trans isomers (cf. compound \(\underline{12}\))\(^{73}\) and high ring inversion barriers.

Further, it seems likely that steric interactions are capable of changing relative energy levels of sulfite conformations drastically. For example, non-chair forms probably predominate in compound \(\underline{2}\). A greatly simplified means of visualizing these results is to consider the sulfite molecule as two separate halves, one consisting of the carbon atoms and possessing the usual cyclohexane-like properties such as non-rigidity, the other being the rigid heteroatom end possessing those properties characteristic of systems with adjacent lone pairs and polar bonds \(\underline{i.e.}\) rules 1 and 2. The low ultrasonic barriers (about half that of cyclohexane
would then be due to changes mainly in the carbon end\textsuperscript{5b} (chair to non-chair) and are too low to be seen by nmr. The rigidity of the other end would explain the dipole moment results and be the main cause of the high barriers to overall chair/chair ring inversion. Steric interactions created by increased substitutions at C-4 and C-6 should then lower non-chair energy levels relative to chair and eventually even cause the S=0 to take up the equatorial position (as found in compound \textsuperscript{6}). The possibility of non-chair forms of different dipole moments in equilibrium with the chair\textsuperscript{73} with 5-t-butyl and S=0 both axial would then explain the behaviour of the dipole moments of compounds like \textsuperscript{12}.

1X. Summary and Conclusions.

As was too often done in the past, recent analyses of six-membered heterocyclic ring conformations continue to assume cyclohexane-like properties although many of these assumptions have been found not to hold.\textsuperscript{73} For this reason a recent interpretation of ultrasonic absorption data on various trimethylene sulfites resulted in a number of contradictions with the results for sulfites from other methods and conformational studies on other molecules in which the importance of unshared electron pairs on adjacent atoms has been well documented.

Because of the importance of the electron lone pairs on sulfur and oxygen in these molecules, the above ultrasonic results were reinterpreted together with other new data on the sulfites and sulfates. The result for trimethylene sulfites is a system with a high barrier to chair/chair interconversion, low energy non-chair barriers and conformations, and a strong preference for axial S=0. This result does not conflict with any previously reported facts nor any found in the course of this study, and the ultrasonic technique becomes an important probe for non-chair to chair transitions in these systems.
NMR-1  Neat trimethylene sulfite (1). Reference signal is tetramethylsilane.

NMR-2  Solution (50% w/v) of trimethylene sulfite (1) in benzene.

NMR-3  Solution (10%) of trimethylene sulfite (1) in dimethylsulfoxide-d₆.

NMR-4  Solution (20%) of 4-methyltrimethylene sulfite (2) in carbon tetrachloride. Upper portion was recorded at higher gain.

NMR-5  Solution (10%) of 4-methyltrimethylene sulfite (2) in benzene. Upper portion was recorded at higher gain.

NMR-6  Solution (10%) of 4,6-dimethyltrimethylene sulfite (4) in carbon tetrachloride. The low field methylene portion was expanded by a factor of five.
Solution (20%) of 4,6-dimethyltrimethylene sulfite (4) in dimethylsulfoxide-d$_6$. Upper portions are five-fold expansions of the smaller signals.

Solution (20%) of 5,5-dimethyltrimethylene sulfite (10) in carbon tetrachloride.

Solution (10%) of 5-t-butyltrimethylene sulfite (11) in dimethylsulfoxide-d$_6$. Upper portions are five-fold expansions of the smaller signals.

Solution (20%) of 4,6-dimethyltrimethylene sulfite (6) in carbon tetrachloride. Upper portions were recorded at higher gain.

Solution (10%) of 4,6-dimethyltrimethylene sulfite (6) in dimethylsulfoxide-d$_6$. Upper portions are five-fold expansions of the smaller signals.

Solution (10%) of 4-methyltrimethylene sulfite (3) of higher dipole moment in dimethylsulfoxide-d$_6$. Upper portions are five-fold expansions.
NMR-13 Solution (10%) of 4-methyltrimethylene sulfite (3) in benzene. Upper portion is five-fold expansion of low field methylene group.

NMR-14 Solution (10%) of 4,4,6-trimethyltrimethylene sulfite (8) in carbon tetrachloride. Upper portions are five-fold expansions of the smaller signals. The spectrum resulting from decoupling the methyl (9) is also shown.

NMR-15 Five-fold expansion of low field methylene portion of 4,4,6-trimethyltrimethylene sulfite (8) in 10% methylene chloride-d₂.

NMR-16 Five-fold expansion of low field methylene portion of 4,4,6-trimethyltrimethylene sulfite (8) in 10% acetonitrile-d₃.

NMR-17 Five-fold expansion of low field methylene portion of 4,4,6-trimethyltrimethylene sulfite (8) in 10% dimethylformamide.

NMR-18 Solution (10%) of 4,6-dimethyltrimethylene sulfite (5) in dimethylsulfoxide-d₆. Upper portion is a five-fold expansion of the low field methylene group.
NMR-19 Solution (10%) of 4,4,6-trimethyltrimethylene sulfite (7) in dimethylsulfoxide-\textit{d}_6. Upper portion was recorded at higher gain.

NMR-20 Solution (10%) of 4,4,6,6-tetramethyltrimethylene sulfite (9) in dimethylsulfoxide-\textit{d}_6. Upper portion is a five-fold expansion of the low field signal.

NMR-21 Solution (25%) of 5-t-butyltrimethylene sulfite (12) in benzene. Upper portions recorded at higher gain.

NMR-22 Solution (10%) of 5,5-dimethyltrimethylene sulfate in equal volumes of methylene chloride-\textit{d}_2 and ethyl bromide-\textit{d}_5. The signals at and below coalescence were also recorded.

NMR-23 Solution (10%) of 5-t-butyltrimethylene sulfite in benzene-\textit{d}_6. Upper portions are five-fold expansions.

NMR-24 Solution (10%) of 5-t-butyltrimethylene sulfite in acetone-\textit{d}_6. Upper portion was expanded five times. Part was obscured by solvent.
NMR-25  Solution (10%) of 5-t-butyltrimethylene sulfate in methylene chloride-$d_2$. Upper portions were expanded five-fold.
Chapter 111
EXPERIMENTAL

a Syntheses

Sulfites

A number of methods exist for the production of sulfites, but by far the best and simplest for cyclic sulfites is the reaction of thionyl chloride with the corresponding diol. The dimethyl sulfite ester interchange is known to give numerous side products, but was tested to see if higher yields of the less stable isomers could be obtained. However, yields of the less stable isomers were poorer than those from the pyridine-thionylchloride method, together with the usual large amount of side products. For example, in the preparation of the two isomers of 5-t-butyl trimethylene sulfites, compounds 11 and 12, a ratio of 73:27 was obtained in favour of the more stable isomer (compound 11) in methylene chloride with dimethyl sulfite, while in benzene with pyridine and thionyl chloride this was decreased to a 60:40 ratio. The following procedure for 4-methyl trimethylene sulfite, compound 2, will serve as an example of this method:

To 45 g (0.50 mole) of 1,3-butanediol dissolved in 300 ml benzene (dried over sodium) and 150 ml dry pyridine was added dropwise with external cooling (ice) and stirring 44 ml of thionyl chloride (0.61 mole) in 100 ml dry benzene over a period of three hours. The pyridine hydrochloride salt was filtered, the benzene solution neutralized by washing with saturated sodium bicarbonate solution (caution, emulsion), followed by 100 ml of 0.1 N hydrochloric acid, and finally 100 ml of water. The benzene layer was dried with magnesium sulfate (or potassium carbonate), filtered, and concentrated on a rotary evaporator heating up to about 50°, then the sulfites collected from the gas chromatograph.
All sulfites were prepared in this manner except for trimethylene sulfite, compound 1, itself, which was prepared either in diethyl ether or carbon tetrachloride without pyridine,\(^4\) and tetramethyl compound 9, which required the following modified procedure because of the ease of dehydration of the di-tertiary diol:

After freezing in liquid nitrogen 17.2 g (0.14 mole) of 2,4-dimethyl-2,4-pentanediol in 100 ml dry pyridine, 30 g (0.24 mole) of thionyl chloride in 100 ml more pyridine was added slowly in about one-fifth portions, allowing the mixture to thaw with shaking then refreezing between additions. After complete addition (20 min), the solution was allowed to warm to room temperature with occasional shaking, then left standing overnight. The brown product was dissolved in 500 ml of water, extracted with six 150 ml portions of ether, then dried over potassium carbonate with some added decolorizing charcoal. The ether solution was filtered, concentrated on the rotary evaporator, and vacuum distilled collecting the fraction boiling around 95° at 0.25 mm (40% yield). The pure sulfite was then collected from the gas chromatograph.

\[
\text{Anal. Calcd for } C_{14}H_{22}O_5S : C, 47.17; H, 7.92; O, 26.93; S, 17.99.
\]

\[
\text{Found : C, 47.27; H, 7.97; O, 26.81; S, 17.78.}
\]

All diols were commercially available except two, 5-t-butylpropane-1,3-diol and 2,4-dimethyl-2,4-pentanediol. These were prepared as follows:

**5-t-butylpropane-1,3-diol**

The method of Boldt and Schulz\(^1\) with diethyl malonate and a Lewis acid plus t-butyl chloride was attempted unsuccessfully numerous times (boron trifluoride-etherate and aluminum chloride used). Also, VanWoerden's method\(^1\) with sodium ethoxide (14 days) gave poor results, while with sodium hydride none of the desired product was obtained. Hence the two step
method of Widequist was used. Ethyl isopropylidene was first prepared by
the procedure of Cope:

A mixture of 1 kg (6.25 moles) of ethyl malonate, 540 g (9.3 moles)
of acetone, 800 g (7.8 moles) of acetic anhydride and 120 g of freshly
fused zinc chloride was heated under reflux at 110° for 24 hrs. The mixture
was cooled, 800 ml of benzene added, and the solution extracted with four
500 ml portions of water, which was in turn extracted with two 100 ml
portions of benzene. The benzene fractions were combined, washed once with
60 ml of water, and concentrated on the rotary evaporator. The residue
was distilled through a Vigreux column to remove unreacted diethyl malonate
(about 400 ml). The pale yellow residue was 81% product (by glc) and
amounted to 445 g (35% yield). This crude isopropylidene malonate was used
without further purification.

The above product in 550 ml of anhydrous ethyl ether was added with
cooling to a solution of methyl magnesium iodide prepared from 75 g of
magnesium turnings in 400 ml anhydrous ether to which 500 g of iodomethane
in 370 ml ether was slowly added with cooling. After the addition (1 hr),
the solution was heated at a vigorous reflux for 10 min, then cooled. Ice
water was added until frothing ceased, the resulting solid dissolved in
dilute sulfuric acid, filtered, and the water layer extracted four times
with ether. The ether extracts were combined, concentrated on the rotary
evaporator and the residue distilled. The yield of ethyl t-butyl malonate
(bp 98 - 102° at 9 mm) was 405 g.

This ester (150 ml), dissolved in 250 ml anhydrous ether, was added
dropwise with stirring to 30 g lithium aluminum hydride in 850 ml ether
contained in a 2 l flask equipped with condenser. Later an additional 100
ml of ether was added to facilitate stirring. After complete addition
(2 hrs), 250 ml of water was slowly added over a period of an hour with
good stirring. The mixture was filtered through a sintered glass filter, the granular solid dissolved in cold 20% sulfuric acid (1 l) and extracted with six 200 ml portions of ether. The combined ether solution was dried over magnesium sulfate, filtered, concentrated on the rotary evaporator, and the residue recrystallized from petroleum ether (30 - 60°). The yield of diol, mp 54-56°, was 45 g for an overall yield of about 15% (for an alternate procedure, see reference 10).

2,4-dimethyl-2,4-pentanediol

The method of Esafov\textsuperscript{133} was used. To 24.4 g (1 mole) of magnesium turnings in 100 ml dry ether was added slowly with cooling and stirring 62.2 ml (1 mole) iodomethane in 300 ml anhydrous ether. After complete addition (5 hrs), the solution was warmed to room temperature and 58.1 g (0.50 mole) diacetone alcohol dissolved in 100 ml dry ether slowly added with cooling over a period of 3 hrs. The solution was then left stirring overnight, decomposed with excess water (100 ml), and dissolved in 100 ml of 1:3 acetic acid. The ether layer was separated, the aqueous layer saturated with salt and extracted with five 100 ml portions of ether. The combined ether fractions were then neutralized with two 75 ml portions of saturated sodium carbonate solution, washed with 100 ml saturated brine, 50 ml more sodium carbonate solution since still acidic, followed by 50 ml brine, and then dried over potassium carbonate. After filtration, the ether was removed and the residue distilled, collecting the diol (55% yield) which boiled from 66-67° at 3 mm, \( n^D_{24} = 1.4326 \).

The sulfites were collected on one of two gas chromatographs, depending on the amount of sample desired. The first was an F & M 720 using an 8ft x 0.25in 10% LAC 728 (Diethylene Glycol Succinate) on 60-80 mesh Diatoport W
with a helium flow rate of 60 cc/min and a temperature range of 110 to 150°.
The second was a Varian 712 Autoprep with a 14 or 19 ft x 0.378 in 20% LAC
728 on 40-60 mesh Chromosorb W with a nitrogen flow rate of 60 or 100 cc/min
and a temperature range of 125 to 160°. Analytical determinations were
performed on the 720 with a 5½ ft x 0.25 in 10% LAC 728 column, 60 cc helium/
min at 90-150°, and in all cases the isomers were greater than 99% pure.

The following additional physical data and information will be helpful:

TMS (1):
bp 62-64° at 11 mm, nD = 1.4517

4-MethylTMS (2) and (3):

\[
\text{Anal. Caled for } C_4H_8O_2S : C, 35.25; H, 5.92; O, 35.25; S, 23.55.
\]

<table>
<thead>
<tr>
<th></th>
<th>C</th>
<th>H</th>
<th>O</th>
<th>S</th>
</tr>
</thead>
<tbody>
<tr>
<td>(2)</td>
<td>35.27</td>
<td>6.17</td>
<td>35.37</td>
<td>23.90</td>
</tr>
<tr>
<td>(3)</td>
<td>35.30</td>
<td>5.93</td>
<td>35.00</td>
<td>23.43</td>
</tr>
</tbody>
</table>

5-t-ButylTMS:
compound 11: mp 44-45°, which was recrystallized virtually pure
isomerically from petroleum ether.

compound 12: mp 37-38°, thermally stable (glc) except in presence of acids.

4,6-DimethylTMS (4), (5) and (6):
In pyridine the isomer ratios were 13:54:33 in the order of elution,
4, 5, then 6. Compound 6, mp 44.5-45.5°, was sometimes hard to collect in
large quantities. However, it was found that enriched 6 was left in the
residue after the other two isomers were distilled around 74-84° at 11 mm,
which greatly speeded its collection by glc.

4,4,6-TrimethylTMS (7) and (8):
From the pyridine method compounds 7 and 8 were obtained in a ratio
of 4:1. Compound 8 could be concentrated by distilling isomer 7 around 28°
at 0.75 mm. Then compound 8 was obtained pure by recrystallization of the residue from petroleum ether to give large prismatic crystals, mp 38-39°.

Anal. Calcd for C₆H₁₂O₃S : C, 43.90; H, 7.37; O, 29.21; S, 19.52.

Found (7) : C, 45.07; H, 7.44; O, 28.37; S, 19.44.

(8) : C, 43.98; H, 7.49; O, 29.36; S, 19.30.

Sulfates

5,5-Dimethyltrimethylene Sulfate

To 32 g of calcium permanganate (Alfa) dissolved in 40 ml glacial acetic acid and 800 ml water was added dropwise after cooling in ice 10 g of the sulfite (compound 10) with stirring over a period of 2 hrs. The solution was neutralized with potassium bicarbonate, decolorized with sodium bisulfite, and extracted with potassium carbonate solution. The ether layer was filtered and concentrated on the rotary evaporator. The solid sulfate, mp 79.5-80.5°, was recrystallized twice from ether and gave 6.64 g (60%).

5-t-Butyltrimethylene Sulfate

Calcium permanganate (9 g) in 9 ml of water was added dropwise to a cooled solution of 40 ml glacial acetic acid, 15 ml water, and 5 g of 5-t-butylTMS (compound 11) until there was a permanent pink colour (1 hr).

The mixture was then added to a cold solution of 50 g sodium carbonate in 100 ml of water, the resulting solution neutralized (colourless) with sodium bisulfite, diluted to 500 ml with water, and extracted with six 100 ml portions of ether. After working up as the sulfate above, there remained 5.45 g (35%) of a white solid, mp 137-138°.

Physical Measurements

Melting points were determined with a Fisher-Johns Apparatus and are reproducible results were difficult to obtain for this compound even on the same sample. This is the best series obtained.
uncorrected. The infrared spectra were recorded on a Beckman IR-10 and the nmr spectra on a JEOLCO JNM C60S or C60HL instrument. Solutions are weight volume percentages unless otherwise specified. All solvents employed were spectrograde, and nmr chemical shifts are relative to internal tetramethylsilane. Elemental analyses were performed by Midwest Microlab, Inc., Indianapolis, Indiana, and thermochemical molecular weights (vapour phase osmometry) by Schwarzkopf Microanalytical Laboratory, New York.

c Dipole Moments

Dipole moments were calculated according to the method of Guggenheim from dielectric constants determined with a Wissenschaftlich-Technische Werkstatten (Germany) Dipolemeter DM01 at 20°. Solvents were commercial spectrograde chemicals dried over Linde molecular sieve type 4A (washed with ethanol and activated). The determination equation has the form:

\[ \mu^2 = \frac{27 kT}{4 N_1} \cdot \frac{1}{d_1 (\epsilon_1 + 2)^2} \cdot (a_\epsilon - a_n) \cdot M_2 \]

where
- \( k = \) Boltzmann constant = \( 1.381 \times 10^{-16} \) erg/deg
- \( N_1 = \) Lohschmidt's Number = \( 6.023 \times 10^{-23} \) mol\(^{-1}\)
- \( d_1 = \) solvent density
- \( \epsilon_1 = \) solvent dielectric constant
- \( a_\epsilon = \) slope of the plot of \( \epsilon_{12} - \epsilon_1 \) versus \( W_2 \)
- \( \epsilon_{12} = \) solution dielectric constant
- \( W_2 = \frac{m_2}{(m_1 + m_2)} \)
- \( m_1 = \) weight of solvent
- \( m_2 = \) weight of solute

# For pertinent references as well as a critical discussion of dipole moment methods see reference 135.
and $a_n$ = slope of the plot of $(n_{12}^2 - n_1^2)$ versus $W_2$

$n_{12}$ = solution refractive index
$n_1$ = solvent refractive index
$M_2$ = solute molecular weight

At 20° C the first term is a constant = $1.433 \times 10^{-37}$

This equation can only be used if the plots of $a_S$ and $a_n$ are straight lines, and concentrations which give the solution a dielectric constant ($\epsilon_{12}$) about 0.2 above that of the solvent should be the maximum. Straight lines were obtained in all cases, and $a_n$ was found to be negligible with the sulfites. The procedure was as follows:³⁶

The sulfite (0.3 to 0.6 g) was weighed ($W_1$) into a 25 ml volumetric flask and made up to the mark with solvent and reweighed ($W_1 + W_2$). The dipole cell was filled with this solution, allowed to equilibrate for 10 min (7 min for dioxane), and the instrument reading(s) taken and corrected for non-linearity with the graph provided by the manufacturer. ($\epsilon_{12}$ was then calculated by subtraction of the solvent $S$ from this corrected reading and multiplying the result by the appropriate instrument constant $\Delta \epsilon/\Delta S$, determined before with standards). The solution was retrieved, then 15 or 20 ml ($W_2$ now equal to 0.6 or 0.8 the previous value) was pipetted into a second 25 ml volumetric flask, made up to the mark and reweighed. After rinsing thoroughly the cell with spectrograde acetone and drying with high-pure nitrogen, a second reading was taken with this diluted solution. This was continued until $\Delta(\epsilon_{12} - \epsilon_1)$ was about 0.01. A plot of $\epsilon_{12} - \epsilon_1$ versus the weight fraction $W_2$ was made (and $n_{12}^2 - n_1^2$ also if necessary) to check linearity, the actual slope was obtained from a least squares line calculated on an IBM 1620.
The following standards were used:

<table>
<thead>
<tr>
<th>Solvent</th>
<th>( n_D^{20} )</th>
<th>( S )</th>
<th>( \epsilon )</th>
<th>( d_1^{20} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>carbon tetrachloride</td>
<td>1.4603</td>
<td>997.3</td>
<td>2.2363</td>
<td>1.595</td>
</tr>
<tr>
<td>cyclohexane</td>
<td>1.4251</td>
<td>474.1</td>
<td>2.0228</td>
<td>0.7785</td>
</tr>
<tr>
<td>benzene</td>
<td>1.5011</td>
<td>1112.7</td>
<td>2.2825</td>
<td>0.8790</td>
</tr>
<tr>
<td>p-dioxane</td>
<td>1.4220</td>
<td>923.7</td>
<td>2.218</td>
<td>1.0336</td>
</tr>
</tbody>
</table>

A plot of \( \epsilon \) versus \( S \) gave a straight line with \( \frac{\Delta \epsilon}{\Delta S} = 4.075 \times 10^{-4} \).

The following sample calculation for 4,6-dimethylTMS, compound 6, in benzene is typical:

<table>
<thead>
<tr>
<th>Reading</th>
<th>( S_{\text{solution}} )</th>
<th>( S_{\text{solvent}} )</th>
<th>( \epsilon_{12} - \epsilon_1 ) (( = \Delta S \times 10^{-4} ))</th>
<th>( W_2 \times 10^3 )</th>
<th>( n_D^{20} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1632.9</td>
<td>1112.7</td>
<td>0.2120</td>
<td>9.827</td>
<td>1.5006</td>
</tr>
<tr>
<td>2</td>
<td>1422.2</td>
<td>&quot;</td>
<td>0.1261</td>
<td>5.892</td>
<td>&quot;</td>
</tr>
<tr>
<td>3</td>
<td>1300.0</td>
<td>&quot;</td>
<td>0.0763</td>
<td>3.536</td>
<td>&quot;</td>
</tr>
<tr>
<td>4</td>
<td>1258.6</td>
<td>&quot;</td>
<td>0.0595</td>
<td>2.840</td>
<td>&quot;</td>
</tr>
<tr>
<td>5</td>
<td>1235.2</td>
<td>&quot;</td>
<td>0.0499</td>
<td>2.276</td>
<td>&quot;</td>
</tr>
<tr>
<td>6</td>
<td>1189.4</td>
<td>&quot;</td>
<td>0.0313</td>
<td>1.362</td>
<td>&quot;</td>
</tr>
</tbody>
</table>

The plot of \( \epsilon_{12} - \epsilon_1 \) versus \( W_2 \times 10^3 \) is given in Figure 5. Substituting the slope (\( a_\epsilon \)) of this plot (21.44 from computer least squares) in the above equation, together with the other constants gives:

\[
\mu^2 = 1.443 \times 10^{-37} \cdot \frac{1}{0.8790(2.2825 + 2)^2} \cdot (21.44 - 0) \cdot 150.21
\]

\[
= 1.443 \times 10^{-37} \cdot 9.3178 \cdot 21.44 \text{ (dyne-cm}^4)\]
Figure 5. Plot of the difference in dielectric constant ($\varepsilon_{12} - \varepsilon_1$) versus weight fraction ($w_2 \times 10^3$) in determination of the dipole moment for 4,6-dimethyltrimethylene sulfite (6).
Hence \( \mu = 5.37 \times 10^{-18} \) (dyne·cm)
\[ = 5.37 \text{ debye} \quad (1 \text{ debye} = 10^{-18} \text{ dyne·cm}) \]

As a further check on the agreement of this method with the literature, two non sulfite compounds were also determined — nitrobenzene and 1,2-dichloroethane with the results listed below:

<table>
<thead>
<tr>
<th>Compound</th>
<th>Solvent</th>
<th>Dipole moment (debyes)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Found</td>
</tr>
<tr>
<td>nitrobenzene</td>
<td>cyclohexane</td>
<td>3.97 (20°)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4.04 (25°)</td>
</tr>
<tr>
<td>1,2-dichloroethane</td>
<td>cyclohexane</td>
<td>1.39 (20°)</td>
</tr>
</tbody>
</table>

Furthermore, reproducibility was checked on several sulfite isomers and was found to be generally within 0.1 debye (e.g. TMS in carbon tetrachloride gave values of 3.31 and 3.37 debyes). Hence this is the estimated error limit, and generally the values in Table 1 agree with those of other workers within this limit.

**d Benzene Solvent Shifts**

Benzene solvent shifts at infinite dilution were obtained by determining the shift values of the sulfites made up at a known weight-volume percentage (e.g. 50-60%), then diluting this sample to one half by the addition of a volume of solvent equal to that of the resultant sample and solvent volumes. This was repeated until the solutions were too dilute to obtain good spectra (about 3%), and a graph made and extrapolated to zero percent solute. These values were then subtracted from those obtained either in 20% carbon tetrachloride solution to give the benzene solvent shift.
at infinite dilution or from the values obtained in 10% dimethylsulfoxide-d₆ to give the values recorded in appendix ii. There was no significant concentration dependence in these solvents for these ranges (10 to 20%). In most cases straight lines were obtained in the above plot and when extended to 100% solute concentration the values here agreed well with those obtained in the carbon tetrachloride solution (20%), as shown in Figure 1. However, in many cases these lines were found to curve in the dilute range, as shown in Figure 2. Reproducibility was checked and found to be within about 2 Hz. Hence the values for the solvent shifts at infinite dilution - $\Delta (CCl₄ - \phi)$ are estimated to be within ± 3 Hz.

It should be noted that in the dilution procedure a density of one for the solute was assumed. Calculations have shown that changing this value only tilts the curve around the value at zero concentration and does not change this extrapolated value.

e Equilibrations

The results in Table 7 were obtained on isomerically pure sulfites previously collected and checked by glc. The acid equilibrations were carried out in magnetically stirred sealed vials at room temperature. The solutions were 1M in sulfite with 100 µl of boron trifluoride-etherate added per 3 ml of solution, except for the set carried out in anhydrous diethyl ether saturated with dry hydrochloric acid. A minimum of two samples were used, one initially on each side of the final equilibrium composition. These samples were neutralized with solid potassium carbonate after equilibrium had been achieved, filtered, and analyzed by glc on a 6ft x 0.25in 10% Carbowax 20M column on 60-80 mesh Poropak S at 160° and a helium flow rate of 60 cc/min. The second carbon tetrachloride sample batch of compounds ₅ and ₆ used an 8ft x 0.50in 10% Carbowax 20M on 60-80 mesh Chromosorb W.
preparatory column to increase sample size, but the results were not as good. Response ratios were determined on synthetic mixture of the sulfites under identical chromatographic conditions. The results and error limits were calculated in an identical manner to that of Eliel.\textsuperscript{138}

The reported thermal interconversion\textsuperscript{55,65} of sulfites was found\textsuperscript{72} to occur only in the presence of acid as catalyst, e.g. the 4,6-dimethyl sulfite was carefully purified by glc was stable at up to 200\textdegree{} for at least an hour, but was converted rapidly to its isomer even at room temperature when treated with a small amount of anhydrous hydrogen chloride. Similar results were obtained for compounds \(\text{2} \), \(\text{8} \) and \(\text{12} \).

\textbf{f Ring Inversion in Sulfates}

The 5,5-dimethyltrimethylene sulfate was run in a 5\% (w/v) solution of 1:1 methylene chloride-\textsubscript{d\textsubscript{2}} - ethyl bromide-\textsubscript{d\textsubscript{2}} on the C60HL instrument. The barrier found was unchanged using a solvent mixture of 1:1 m-fluorotoluene - methylene chloride-\textsubscript{d\textsubscript{2}} or 1:5 toluene-\textsubscript{d\textsubscript{8}} - methylene chloride-\textsubscript{d\textsubscript{2}}. The low temperature unit was calibrated with a thermocouple placed inside a spinning sample tube containing the same solvent mixture used in the calculation. Temperature variation by height of the thermocouple was no more than one degree and altogether the temperature is estimated accurate to at least \(\pm 2\degree{}\).

Spectra were recorded down to -137\degree{} but there was little further change below -119\degree{}. The following parameters were obtained:

\[
\begin{array}{lll}
\text{Methylene protons} & \text{Methyl protons} \\
T_c & -107 \pm 2\degree{} & -109 \pm 2\degree{} \\
\delta_{AB} & 24.5 \pm 0.1 \text{ Hz} & 22.0 \pm 0.1 \text{ Hz} \\
J_{AB} & 10.5 \pm 0.1 \text{ Hz} & - \\
\end{array}
\]

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The rate constant at coalescence can be estimated from

\[ k_{\text{coal}} = \pi \sqrt{\left( \nu_A - \nu_B \right)^2 + 6 J_{AB}^2} / \sqrt{2} \]

and for this system was found to be 78.95 sec\(^{-1}\) based on the methylene protons and 48.87 based on the methyl protons. The activation energy can then be estimated from the Eyring equation:

\[ k = K(k_B T/h) \exp \left( -\Delta G^\ddagger / RT \right) \]

Assuming \( K = 1 \), values of \(-\Delta G^\ddagger\) at -107° of 8.1 ± 0.2 kcal/mole based on the methylene protons, and 8.4 ± 0.2 kcal/mole at -109° based on the methyl coalescence were obtained.
References

15. (a) H. J. Dothie, Acta Cryst., 6, 804 (1953); (b) R. E. Marsh, ibid., 8, 91 (1955).
33. (a) H. P. Koch and W. E. Moffitt, Trans. Faraday Soc., 47, 8 (1951);
74. Prof. R. E. Lack, Univ. of Sydney, Australia, private communication.
77. (a) L. Cazaux and P. Maroni, private communication; (b) idem., presented at the Fifty-first Conference of the Chemical Institute of Canada, University of British Columbia, Vancouver, June, 1968.
95. Reference 4, p 185.

128. (a) P. Boldt and L. Schulz, Naturwissenschaften, 51, 288 (1964); (b) idem., Chem. Abs., 63, 16221e.


Appendix i

List of chemical shifts ($\tau$) versus concentration (w/v %) in benzene.

TMS (1):

<table>
<thead>
<tr>
<th>Conc.</th>
<th>$R_1$</th>
<th>$R_5$</th>
<th>$R_2$</th>
<th>$R_6$</th>
<th>$R_4$</th>
<th>$R_3$</th>
</tr>
</thead>
<tbody>
<tr>
<td>30</td>
<td>5.42</td>
<td>a</td>
<td>6.76</td>
<td>a</td>
<td>8.07</td>
<td>9.25</td>
</tr>
<tr>
<td>20</td>
<td>5.48</td>
<td></td>
<td>6.85</td>
<td></td>
<td>8.17</td>
<td>9.39</td>
</tr>
<tr>
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<td>5.51</td>
<td></td>
<td>6.85</td>
<td></td>
<td>8.25</td>
<td>9.49</td>
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<tr>
<td>5</td>
<td>5.54</td>
<td></td>
<td>6.95</td>
<td></td>
<td>8.30</td>
<td>9.56</td>
</tr>
<tr>
<td>0$^b$</td>
<td>5.57</td>
<td></td>
<td>7.00</td>
<td></td>
<td>8.35</td>
<td>9.60</td>
</tr>
</tbody>
</table>

4-MethylTMS (2):

<table>
<thead>
<tr>
<th>Conc.</th>
<th>$R_1$</th>
<th>$R_5$</th>
<th>$R_2(CH_3)$</th>
<th>$R_6$</th>
<th>$R_4$</th>
<th>$R_3$</th>
</tr>
</thead>
<tbody>
<tr>
<td>57</td>
<td>5.41</td>
<td>6.58</td>
<td>9.03</td>
<td>c</td>
<td>8.27</td>
<td>8.85</td>
</tr>
<tr>
<td>28.5</td>
<td>5.47</td>
<td>6.73</td>
<td>9.13</td>
<td></td>
<td>8.41</td>
<td>9.00</td>
</tr>
<tr>
<td>14.2</td>
<td>5.50</td>
<td>6.82</td>
<td>9.20</td>
<td></td>
<td>8.50</td>
<td>9.15</td>
</tr>
<tr>
<td>7.1</td>
<td>5.54</td>
<td>6.88</td>
<td>9.24</td>
<td></td>
<td>8.56</td>
<td>9.27</td>
</tr>
<tr>
<td>3.6</td>
<td>5.57</td>
<td>6.93</td>
<td>9.27</td>
<td></td>
<td>8.59</td>
<td>9.29</td>
</tr>
<tr>
<td>0$^b$</td>
<td>5.59</td>
<td>7.00</td>
<td>9.29</td>
<td></td>
<td>8.63</td>
<td>9.33</td>
</tr>
</tbody>
</table>

# 4-MethylTMS (3):

<table>
<thead>
<tr>
<th>Conc.</th>
<th>$R_1(CH_3)$</th>
<th>$R_5$</th>
<th>$R_2$</th>
<th>$R_6$</th>
<th>$R_4$</th>
<th>$R_3$</th>
</tr>
</thead>
<tbody>
<tr>
<td>59.5</td>
<td>8.85</td>
<td>c</td>
<td>c</td>
<td>c</td>
<td>c</td>
<td>c</td>
</tr>
<tr>
<td>29.8</td>
<td>8.95</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14.9</td>
<td>9.01</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.9</td>
<td>9.05</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.9</td>
<td>9.07</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0$^b$</td>
<td>9.09</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

a if left blank, $R_4 = R_5$, $R_2 = R_6$, and $R_3 = R_4$

b extrapolation to infinite dilution

c unable to determine

# isomers of higher dipole moment ($S=0$ equatorial)
### 4,6-DimethylTMS (4):

<table>
<thead>
<tr>
<th>Conc.</th>
<th>$R_1$</th>
<th>$R_2$</th>
<th>$R_2(CH_3)$</th>
<th>$R_6(CH_3)$</th>
<th>$R_4$</th>
<th>$R_3$</th>
</tr>
</thead>
<tbody>
<tr>
<td>32.9</td>
<td>5.22</td>
<td>9.05</td>
<td>8.75</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16.5</td>
<td>5.27</td>
<td>9.13</td>
<td>8.83</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8.2</td>
<td>5.28</td>
<td>9.18</td>
<td>8.88</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0$^b$</td>
<td>5.30</td>
<td>9.21</td>
<td>8.92</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### 4,6-DimethylTMS (5):

<table>
<thead>
<tr>
<th>Conc.</th>
<th>$R_1$</th>
<th>$R_2(CH_3)$</th>
<th>$R_2(CH_3)$</th>
<th>$R_6$</th>
<th>$R_4$</th>
<th>$R_3$</th>
</tr>
</thead>
<tbody>
<tr>
<td>33.7</td>
<td>5.25</td>
<td>8.70</td>
<td>9.00</td>
<td>6.02</td>
<td>8.50</td>
<td></td>
</tr>
<tr>
<td>16.9</td>
<td>5.27</td>
<td>8.73</td>
<td>9.05</td>
<td>6.13</td>
<td>8.61</td>
<td></td>
</tr>
<tr>
<td>8.4</td>
<td>5.30</td>
<td>8.75</td>
<td>9.13</td>
<td>6.21</td>
<td>8.68</td>
<td></td>
</tr>
<tr>
<td>0$^b$</td>
<td>5.31</td>
<td>8.77</td>
<td>9.17</td>
<td>6.28</td>
<td>8.73</td>
<td></td>
</tr>
</tbody>
</table>

### # 4,6-DimethylTMS (6):

<table>
<thead>
<tr>
<th>Conc.</th>
<th>$R_2$</th>
<th>$R_6$</th>
<th>$R_4(CH_3)$</th>
<th>$R_5(CH_3)$</th>
<th>$R_3$</th>
<th>$R_4$</th>
</tr>
</thead>
<tbody>
<tr>
<td>26.6</td>
<td>6.00</td>
<td>8.98</td>
<td>8.53</td>
<td>c</td>
<td></td>
<td></td>
</tr>
<tr>
<td>13.3</td>
<td>6.13</td>
<td>9.02</td>
<td>8.58</td>
<td>9.15</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.7</td>
<td>6.23</td>
<td>9.06</td>
<td>8.60</td>
<td>9.24</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0$^b$</td>
<td>6.30</td>
<td>9.08</td>
<td>8.62</td>
<td>9.33</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### 4,4,6-TrimethylTMS (7):

<table>
<thead>
<tr>
<th>Conc.</th>
<th>$R_1$</th>
<th>$R_5(CH_3)$</th>
<th>$R_2(CH_3)$</th>
<th>$R_6(CH_3)$</th>
<th>$R_4$</th>
<th>$R_3$</th>
</tr>
</thead>
<tbody>
<tr>
<td>48</td>
<td>5.04</td>
<td>8.73</td>
<td>8.95</td>
<td>8.95</td>
<td>8.35</td>
<td>8.44</td>
</tr>
<tr>
<td>24</td>
<td>5.07</td>
<td>8.93</td>
<td>9.04</td>
<td>9.02</td>
<td>8.45</td>
<td>8.48</td>
</tr>
<tr>
<td>12</td>
<td>5.09</td>
<td>9.02</td>
<td>9.10</td>
<td>9.09</td>
<td>8.52</td>
<td>8.50</td>
</tr>
<tr>
<td>6</td>
<td>5.10</td>
<td>9.05</td>
<td>9.10</td>
<td>9.08</td>
<td>8.52</td>
<td>8.50</td>
</tr>
<tr>
<td>3</td>
<td>5.10</td>
<td>9.10</td>
<td>9.13</td>
<td>9.09</td>
<td>8.54</td>
<td>8.52</td>
</tr>
<tr>
<td>0$^b$</td>
<td>5.10</td>
<td>9.12</td>
<td>9.14</td>
<td>9.10</td>
<td>8.56</td>
<td>8.52</td>
</tr>
</tbody>
</table>

### # 4,4,6-TrimethylTMS (8):

Refer to Figure 2

---

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### 4,4,6,6-TetramethylTMS (9):

<table>
<thead>
<tr>
<th>Conc.</th>
<th>(R_1(CH_3))</th>
<th>(R_5(CH_3))</th>
<th>(R_2(CH_3))</th>
<th>(R_6(CH_3))</th>
<th>(R_4)</th>
<th>(R_3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>45.3</td>
<td>8.58</td>
<td>8.75</td>
<td>7.53</td>
<td>8.43</td>
<td></td>
<td></td>
</tr>
<tr>
<td>22.6</td>
<td>8.60</td>
<td>8.81</td>
<td>7.55</td>
<td>8.56</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11.3</td>
<td>8.64</td>
<td>8.87</td>
<td>7.56</td>
<td>8.69</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.6</td>
<td>8.65</td>
<td>8.89</td>
<td>7.56</td>
<td>8.73</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.8</td>
<td>8.61</td>
<td>8.89</td>
<td>7.59</td>
<td>8.75</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0(^b)</td>
<td>8.65</td>
<td>8.90</td>
<td>7.59</td>
<td>8.78</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### 5,5-DimethylTMS (10):

<table>
<thead>
<tr>
<th>Conc.</th>
<th>(R_1)</th>
<th>(R_5)</th>
<th>(R_2)</th>
<th>(R_6)</th>
<th>(R_4(CH_3))</th>
<th>(R_3(CH_3))</th>
</tr>
</thead>
<tbody>
<tr>
<td>36.4</td>
<td>5.63</td>
<td>6.98</td>
<td>9.00</td>
<td>9.65</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18.2</td>
<td>5.67</td>
<td>7.11</td>
<td>9.10</td>
<td>9.80</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9.1</td>
<td>5.67</td>
<td>7.17</td>
<td>9.12</td>
<td>9.87</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.5</td>
<td>5.66</td>
<td>7.18</td>
<td>9.10</td>
<td>9.89</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0(^b)</td>
<td>5.69</td>
<td>7.21</td>
<td>9.14</td>
<td>9.92</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### 5-t-ButylTMS (11):

Refer to Figure 1

### 5-t-ButylTMS (12):

<table>
<thead>
<tr>
<th>Conc.</th>
<th>(R_1)</th>
<th>(R_5)</th>
<th>(R_2)</th>
<th>(R_6)</th>
<th>(R_3)</th>
<th>(R_4(t\text{-butyl}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>26.8</td>
<td>5.61</td>
<td>6.42</td>
<td>8.82</td>
<td>9.30</td>
<td></td>
<td></td>
</tr>
<tr>
<td>13.4</td>
<td>5.64</td>
<td>6.51</td>
<td>8.93</td>
<td>9.38</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.7</td>
<td>5.64</td>
<td>6.53</td>
<td>9.00</td>
<td>9.39</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.4</td>
<td>5.65</td>
<td>6.55</td>
<td>9.02</td>
<td>9.39</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0(^b)</td>
<td>5.68</td>
<td>6.58</td>
<td>9.05</td>
<td>9.41</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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Appendix ii - Benzene Solvent Shifts Relative to Dimethylsulfoxide (DMSO)

<table>
<thead>
<tr>
<th>Compound</th>
<th>DMSO $\Delta^b$</th>
<th>DMSO $\Delta^b$</th>
<th>DMSO $\Delta^b$</th>
<th>DMSO $\Delta^b$</th>
<th>DMSO $\Delta^b$</th>
<th>DMSO $\Delta^b$</th>
<th>DMSO $\Delta^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5.21 0.37</td>
<td>c</td>
<td>c</td>
<td>6.03 0.97</td>
<td>c</td>
<td>c</td>
<td>7.60 0.75</td>
</tr>
<tr>
<td>4 R_2=R_6=CH_3</td>
<td>4.93 0.37</td>
<td></td>
<td></td>
<td>8.73 0.48</td>
<td>8.30 0.53</td>
<td></td>
<td>8.05 0.53</td>
</tr>
<tr>
<td>5 R_2=R_5=CH_3</td>
<td>5.03 0.28</td>
<td>8.50 0.27</td>
<td>8.65 0.52</td>
<td>5.41 0.87</td>
<td>8.00 0.73</td>
<td></td>
<td>c</td>
</tr>
<tr>
<td># 6 R_1=R_5=CH_3</td>
<td>8.68 0.54</td>
<td></td>
<td></td>
<td>5.33 0.97</td>
<td>8.12 1.21</td>
<td></td>
<td>8.38 0.24</td>
</tr>
<tr>
<td>7 R_1=R_2=R_6=CH_3</td>
<td>8.30 0.82</td>
<td>4.85 0.25</td>
<td>8.68 0.42</td>
<td>8.68 0.46</td>
<td>8.04 0.52</td>
<td>8.04 0.48</td>
<td></td>
</tr>
<tr>
<td># 8 R_1=R_2=R_5=CH_3</td>
<td>8.63 0.37</td>
<td></td>
<td></td>
<td>8.46 0.39</td>
<td>5.25 0.86</td>
<td>8.33 0.82</td>
<td>8.10 1.00</td>
</tr>
<tr>
<td>9 R_1=R_2=R_5=R_6=CH_3</td>
<td>8.50 0.15</td>
<td></td>
<td></td>
<td>8.50 0.40</td>
<td>7.53 0.08</td>
<td>7.72 1.06</td>
<td></td>
</tr>
<tr>
<td>10 R_3=R_4=CH_3</td>
<td>5.47 0.22</td>
<td></td>
<td></td>
<td>6.37 0.84</td>
<td>8.78 0.36</td>
<td>9.14 0.78</td>
<td></td>
</tr>
<tr>
<td>11 R_2 = t-butyl</td>
<td>5.35 0.12</td>
<td></td>
<td></td>
<td>6.00 0.60</td>
<td>7.85 0.41</td>
<td>9.10 0.53</td>
<td></td>
</tr>
</tbody>
</table>

\( \Delta = \tau_{\text{DMSO}(10\%)} - \tau_{\text{Benzene(solvolog dilution)}} \)

a R = H unless otherwise specified

b if left blank, R_2 = R_1, R_6 = R_2, and R_3 = R_4

# isomer of higher dipole moment (forms other than chair with axial S=O predominant)
<table>
<thead>
<tr>
<th>Compound</th>
<th>Major S=O (cm⁻¹)</th>
<th>Conditions</th>
<th>Ratio</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1228, 1190</td>
<td>CCl₄ (2.5%)</td>
<td>0.13:1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1228, 1183</td>
<td>CH₃CN (2.5%)</td>
<td>0.25:1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1229, 1210, 1190</td>
<td>CS₂ (2.5%)</td>
<td>0.12:0.15:1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1227, 1198</td>
<td>CDCl₃ (5%)</td>
<td>0.23:1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1230, 1183</td>
<td>neat @ R.T.</td>
<td>0.35:1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1228, 1187</td>
<td>neat @ 148°</td>
<td>0.49:1</td>
<td>shoulder @ 1210</td>
</tr>
<tr>
<td>2</td>
<td>1242, 1220, 1188</td>
<td>CCl₄ (5%)</td>
<td>0.10:0.08:1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1240, 1220, 1186</td>
<td>CS₂ (5%)</td>
<td>0.12:0.10:1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1240, 1220, 1182</td>
<td>CH₃CN (5%)</td>
<td>0.12:0.10:1</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>1232, 1190</td>
<td>CCl₄ (7.5%)</td>
<td>1.9:1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1235, 1189</td>
<td>CS₂ (5%)</td>
<td>1.8:1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1223, 1182</td>
<td>CDCl₃ (5%)</td>
<td>3.5:1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1222, 1180</td>
<td>CH₃CN (5%)</td>
<td>7.6:1</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>1220, 1190</td>
<td>CCl₄ (2.5%)</td>
<td>0.12:1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1225, 1180</td>
<td>CDCl₃ (5%)</td>
<td>0.12:1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1225, 1182</td>
<td>CH₃CN (5%)</td>
<td>0.07:1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1220, 1186</td>
<td>C₆H₆ (5%)</td>
<td>0.07:1</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>1237, 1215, 1191</td>
<td>CCl₄ (2.5%)</td>
<td>0.11:0.25:1</td>
<td>no significant change with temperature in neat sample</td>
</tr>
<tr>
<td></td>
<td>1233, 1210, 1189</td>
<td>CS₂ (5%)</td>
<td>0.10:0.28:1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1235, 1215, 1200, 1182</td>
<td>CH₃CN (5%)</td>
<td>0.10:0.33:0.52:1</td>
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</table>
### Appendix iii - Continued

<table>
<thead>
<tr>
<th>Compound</th>
<th>Major $S=0$ (cm$^{-1}$)</th>
<th>Conditions</th>
<th>Ratio</th>
<th>Remarks</th>
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<tbody>
<tr>
<td>6</td>
<td>1230, 1186</td>
<td>CCl$_4$ (5%)</td>
<td>9.4:1</td>
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<td></td>
<td>1232, 1185</td>
<td>CS$_2$ (2.5%)</td>
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<td></td>
<td>1220, 1180</td>
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<td>23:1</td>
<td>1180 very weak shoulder</td>
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<td></td>
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<tr>
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<tr>
<td></td>
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<td>0.13:1</td>
<td>shoulder @ 1210</td>
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<tr>
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<td>1239, 1191</td>
<td>neat @ 140$^\circ$</td>
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<tr>
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<td>1229, 1196-86</td>
<td>CCl$_4$ (5%)</td>
<td>0.39:1</td>
<td>1196-86 doublet</td>
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<tr>
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<td>1226, 1175</td>
<td>CDCl$_3$ (10%)</td>
<td>0.74:1</td>
<td>shoulders @ 1200 and 1190</td>
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<tr>
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<tr>
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<td>neat @ 138$^\circ$</td>
<td>0.91:1</td>
<td>very broad bands</td>
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<td>0.26:0.22:1</td>
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<td>1210 weak, 1192 shoulder</td>
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<td></td>
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<td>CS$_2$ @ +30$^\circ$</td>
<td>0.36:1</td>
<td>1195-85 doublet</td>
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**Appendix IV - Sulfite (Osmometric) Molecular Weights ($M^*/M$)**

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<tr>
<th>Compound</th>
<th>Cyclohexane</th>
<th>Dioxane</th>
<th>$CCl_4$</th>
<th>$C_6H_6$</th>
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<td>1</td>
<td>5.28 (1.04)$^b$</td>
<td>1.57 (1.66)</td>
<td>(see Fig 3)</td>
<td>1.55 (1.98)</td>
<td>1.21 (1.45)</td>
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<td>5.43 (0.99)</td>
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<td>5.42 (0.29)</td>
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<tr>
<td>2</td>
<td>3.00 (1.16)</td>
<td>-</td>
<td>1.71 (1.03)</td>
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<td>1.47 (1.59)</td>
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<td>1.08 (1.16)</td>
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<td>C₆H₆</td>
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<td>---------</td>
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<tr>
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<td>1.33 (0.31)</td>
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<td>1.27 (0.66)</td>
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<td>1.04 (0.68)</td>
<td>1.13 (0.41)</td>
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<td>Ethylene sulfite</td>
<td>-</td>
<td>-</td>
<td>5.13 (0.084)</td>
<td>-</td>
<td>1.21 (1.85)</td>
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<td>4.90 (0.32)</td>
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<td>4.87 (1.00)</td>
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<td></td>
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<td>4.37 (3.22)</td>
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<tr>
<td>Ethylene carbonate</td>
<td>-</td>
<td>-</td>
<td>14.3 (0.56)</td>
<td>-</td>
<td>1.03 (0.77)</td>
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<td></td>
<td></td>
<td>1.03 (1.09)</td>
</tr>
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</table>

a ratio of apparent molecular weight to theoretical
b concentration (weight %) in brackets
INTRODUCTION

Medium ring compounds (those that are eight to eleven-membered) exhibit unique physical and chemical properties because of their intrinsic steric interference between non-adjacent atoms (termed I-strain by Brown). The main contributors to the total I-strain are valence angle deviations of the ring atoms (Baeyer strain) and the strong intramolecular non-bonding (van der Waal) interactions which are a result of the ring geometry. These latter non-bonding interactions include both repulsions between adjacent atoms or orbitals attached to ring members (Pitzer strain) and interactions in more remote positions (e.g. 3,4,5) which produce the transannular strain typical of medium ring compounds.

This inherent proximity of atoms across the ring which is responsible for the transannular strain can also lead to unexpected transannular reactions at positions that are inert in alicyclic compounds. If this transannular interaction leads to the migration of an atom or group across the ring, it can be classified as a transannular rearrangement. Many interesting examples of this proximity effect deal with the behaviour of carbonium ions in medium sized rings, since the reaction conditions for formation of these carbonium ions are the same which favour rearrangements in other (acyclic) systems as well. Consequently, solvolyses and nucleophilic substitution reactions generally are the reactions which most often have demonstrated these transannular effects.

The migratory aptitude of a group, which is the ability of a substituent group or atom to migrate to the positive centre, directs attention to the migratory group itself. While this is indeed important,
both external (e.g., solvent and catalyst) and internal (carbonium ion structure) factors can be equally or more important. Internal factors controlling group migration may be listed as:

(i) starting material conformation and configuration;
(ii) the configuration, conformation, and steric compression at the migration origin of the unrearranged carbonium ion;
(iii) eclipsing effects in the transition state of the rearrangement step;
(iv) the electron density at the migration origin and terminus;
(v) the intrinsic migratory aptitude of the group.

In general, aryl groups are most mobile, then hydrogen and finally alkyl groups. This is consistent with the requirement that the group should be able to accommodate much of the positive charge of the carbonium ion.\textsuperscript{3} 1,2-Shifts of all three groups in the above order are well known. However, although transannular hydride shifts are well documented in medium sized rings,\textsuperscript{2,3,4} there are no reported cases of alkyl migrations and only one case of phenyl.\textsuperscript{5} The latter involved a 1,5-phenyl transannular migration in 5,5-diphenylcyclooctyl tosylate to give 1,5-diphenylcyclooctene to the extent of one per cent in trifluoroacetic acid. Only one other case of transannular phenyl migration in solvolysis has been reported\textsuperscript{6} which was for the special case of the epimeric exo-3,3-diphenyltricyclo [3.2.1.0\textsubscript{2,4}] oct-8-yl tosylate which underwent transannular phenyl participation as shown below (one isomer only),
followed by or coupled with disrotary opening of the cyclopropyl ring. This allows the phenyl migration to occur stereospecifically across the six-membered ring to displace the anti-tosylate function. A similar type of transannular displacement occurred\textsuperscript{7} in the base catalyzed elimination reaction of 4,4-diphenylcyclohexyl tosylate which gave as much as 21\% 1,4-diphenylcyclohexene. Similarly \textit{cis}-4-methyl-4-phenylcyclohexyl tosylate also gave 19\% of the transannular product:

\[
\begin{array}{c}
\text{Me} \quad \text{Ph} \quad \text{H} \\
\text{t-BuO}^- \\
t-BuOH \\
\end{array}
\xrightarrow{\text{decalin}}
\begin{array}{c}
\text{Ph} \\
\text{CH}_3 \\
\text{t-BuO}^- \\
\end{array}
\]

A merged elimination ($E_2$) and intramolecular displacement ($S_{N1}$) process was postulated for this elimination-rearrangement reaction. The rearrangement failed to occur during solvolysis (acetolysis or formolysis) or during deamination of the corresponding amine.

The occurrence of 1,5-hydride migration in the reaction of cyclooctyl derivatives has been well documented.\textsuperscript{8} For example, solvolysis of 1,2,2,8,8-pentadeuterocyclooctyl brosylate showed 53\% 1,5-hydride migration in acetic acid, with almost no 1,3-hydride shift. \textit{cis}-5-Methylcyclooctyl tosylate gave 90\% 1,5-hydride migration (no methyl), while the \textit{trans} isomer with its unfavourable stereochemistry for 1,5-hydride migration gave only 9\% of 1,5-rearranged products. The corresponding \textit{cis}- and \textit{trans}-5-t-butylcyclooctyl tosylates gave 99 and 12\% 1,5-rearranged products respectively.

The medium sized cycloalkanes are flexible and can undergo conformational changes that place a given hydrogen atom in a number of different environments. However, a larger substituent such as
phenyl imposes certain conformational restrictions which may make trans-annular participation highly probable, because the aryl group and reaction centre are held together in suitable relative orientation, or may rule it out completely if the attainment of the prerequisite stereochemistry is not possible. In the case of a geminal pair of substituents the available positions may be further restricted to those which are unfavourable for proximity effects and transannular shifts, so that at first transannular phenyl migration in these medium rings was not considered likely.\textsuperscript{2} The discovery of phenyl migration in the 5,5-diphenylcyclooctyl system demonstrated that this was not correct, while at the same time showing the effect of the medium. In general, as the solvent becomes relatively less nucleophilic (trifluoroacetic acid is less nucleophilic than acetic or formic acid) the amount of transannular rearrangement increases.\textsuperscript{4,5}

From a comparison\textsuperscript{9} of the relative strain energies of the medium-sized ring cycloalkanes relative to cyclohexane set at 0.0 kcal/mole (Figure 1), the cyclononyl system appeared to be an excellent one to

![Figure 1. Ring strain energies $\Delta H^0$ compared to cyclohexane (set at 0.0 kcal/mole).](image-url)
Because of its higher I-strain, more pronounced transannular effects might result. Acetolysis of both 5,5-diphenyl and 5,5-dimethylcyclononyl tosylate\textsuperscript{10,11} have been reported and no products from transannular migration were obtained. However, the limited means of product identification employed in the above cases (neither gas chromatography nor nuclear magnetic resonance) meant that products present to the extent of a few per cent could easily have been missed. It was decided to repeat the above work on the 5,5-diphenylcyclononyl tosylate in acetic acid as well as in the less nucleophilic trifluoroacetic acid.

Furthermore, it is well known that skeletal rearrangements and hydride shifts usually occur to a greater extent in deamination reactions than in solvolysis.\textsuperscript{12-16} Although there is still some controversy over the explanation of the cause(s) of this difference between solvolysis and deamination, it is probably related to the relative activation energies ($E_{\text{act}}$) for loss of nitrogen from the diazonium ion ($E_{\text{act}} \approx 3-5$ kcal/mole) compared to the solvolysis activation energy ($E_{\text{act}} \approx 25-30$ kcal/mole). The deamination reaction is also strongly exothermic while the solvolysis reaction is highly endothermic.\textsuperscript{15} Since the activation energy is lower in the deamination reaction, differences in the $E_{\text{act}}$ between competing modes of reaction are smaller and the rates of competing reactions become more similar, i.e. there is lower discrimination in deamination so that rearrangements that are unimportant in solvolysis may become significant in deamination. Application of the Hammond Postulate to the two reactions leads\textsuperscript{12} to the conclusion that the transition state for the exothermic deamination reaction should resemble the starting diazonium ion pair (bonds to solvent should be weak and long), while that for the endothermic solvolysis should
resemble the first intermediate in the reaction (bonds to solvent relatively strong, while the carbon to leaving group bond is weak and long).

All the above indicates that the carbonium ion from deamination is different from that usually encountered in solvolysis and the idea of a high-energy vibrationally excited or 'hot' carbonium ion has been proposed,\textsuperscript{12,13} and more recently\textsuperscript{15} the term 'free cation' as opposed to the 'encumbered cation' produced in the endothermic solvolysis reaction. These endothermic processes require solvent participation so that cation intermediates are always relaxed with respect to their neighbouring ions and dipoles, i.e. the cations are encumbered by these anions and dipoles at the transition state and at all other stages. In contrast, in the exothermic deamination reactions which can proceed without this encumbrance, the cation is generated from the diazonium ion in a solvent cavity aligned to solvate the diazonium ion. Relaxation to produce an encumbered cation involves realignment of the neighbouring solvent dipoles and/or near anions. Intramolecular changes around the free cation prior to this relaxation accounts for the difference between the deamination and solvolysis results.

The free cation from deamination may have a lifetime which is rather less than the period of rotation about the carbon-carbon bonds in the cation.\textsuperscript{14} The consequences of this phenomenon, usually referred to as 'ground-state control',\textsuperscript{12,14} is manifested in the following observations:

(a) Equatorial amine gives the corresponding substitution product in good yield, while elimination occurs to a small extent only.

(b) For axial amine, elimination is the preferred reaction, with
small amounts of both axial (retained configuration) and equatorial (inverted configuration) substitution products.

These results are well documented in the isomeric 5-t-butylcyclohexyl amines:

Free long-lived carbonium ions cannot be involved since the two isomers would then yield the same ion (and products). One explanation\(^\text{15}\) involves the alignment of the developing p-orbital with the \(\beta\)-carbon-hydrogen bonds. Since such alignment is necessary for migration or elimination to occur and exists only in the case of the axial amine, it is not surprising that the axial conformer should give rise to more elimination, while in the equatorial isomer substitution is the preferred reaction path (greater amount from equatorial position since axial approach is sterically hindered). Another explanation involving a bridged carbonium ion species has been advanced\(^\text{16}\) but as yet has not been experimentally verified.

However, an alternate explanation and one which must be considered in solvents of low polarity such as acetic acid is the ion pair hypothesis.\(^\text{12,14,17}\) In the case of the 5-t-butylcyclohexylamine isomers, in the time interval between the loss of nitrogen and the attack of solvent molecules on the \(\beta\)-hydrogen, the counterion can maintain a difference between the isomeric species. The position of the counterion determines the structure of the reacting species and the modes of
decomposition. Delocalization of the cation charge would place an appreciable positive charge on the $\beta$-axial hydrogens, and attack by any Lewis base in the solvent cage should be sufficient for olefin formation. To put this another way, in solvents of such low polarity as acetic acid, no free carbonium ions are involved but rather either an encumbered carbonium ion (this encumbrance is a consequence of the unique spatial relationship of the counterion or leaving group), or a diazonium ion which gives products or rearranged intermediates concurrent with loss of nitrogen. The only difference between the encumbered carbonium ion and diazonium ion pathways is a matter of timing with regard to nitrogen departure. In the former case the carbon-nitrogen bond is broken, leaving a full positive charge on the carbon whereas in the latter, product and intermediate forming reactions occur prior to complete breakage of the carbon-nitrogen bond.

In addition, it has recently been noted that partitioning of the carbonium ions in solvolysis reactions with $E_1$ mechanism may vary with the nature of the leaving group. It appears that a substantial portion of proton removal from the $\beta$-carbon is executed by the counterion (e.g. tosylate). Therefore the more basic the displaced group and the less basic the solvent the larger will be the ratio of elimination to substitution products. Herein may lie the explanation of the usual larger occurrence of acetate esters (substitution product) as the chief products from deamination in acetic acid as compared to solvolysis products.

In view of the above considerable differences between deamination and solvolysis reactions (in particular the 'ground-state control' and different leaving group effects) it was decided to carry out a deamination
reaction on the 5,5-diphenylcyclononyl system also, to see what effect these differences would have, particularly since no previous deamination reactions have been performed on such geminally substituted medium ring compounds.
RESULTS

Acetolysis of 5,5-Diphenylcyclononyl Tosylate

5,5-Diphenylcyclononyl tosylate was prepared from diphenyl methane in about five per cent overall yield by the route shown (Scheme I):

Scheme I

\[
\begin{align*}
\text{Ph}_2\text{CH}_2 & \quad \xrightarrow{1. \text{KNH}_2, \text{NH}_2} (\text{twice}) \quad \text{Ph}_2\text{C(OCH}_2\text{CH}_2\text{CH}_2\text{OEt})_2 \\
\text{BrCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{I} & \quad \xrightarrow{2. \text{BrCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{I}} \quad \text{Ph}_2\text{C(OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CN})_2 \\
\text{Ph}_2\text{C(OCH}_2\text{CH}_2\text{CH}_2\text{OEt})_2 & \quad \xrightarrow{\text{Na}, \text{xylene, } \Delta} \quad \text{Ph}_2\text{C(OCH}_2\text{CH}_2\text{CH}_2\text{CN})_2 \\
\text{Ph}_2\text{C(OCH}_2\text{CH}_2\text{CH}_2\text{OEt})_2 & \quad \xrightarrow{1. \text{LAH}} \quad \text{Ph}_2\text{C(OCH}_2\text{CH}_2\text{CH}_2\text{CN})_2 \\
\end{align*}
\]

The tosylate (1.8 g) was solvolyzed in anhydrous glacial acetic acid at 35° for 12 half-lives (36 hrs) according to the procedure of Blomquist.\textsuperscript{10} The product was reduced with lithium aluminum hydride and subjected to column chromatography followed by gas liquid chromatography (glc). The best separation was obtained on a silicone gum nitrile (XE-60) column and the acetolysis results are shown in Figure 2. The two small peaks

Figure 2. Products of the 5,5-diphenylcyclononyl tosylate solvolysis in acetic acid from XE-60 column. Compound (not found) was eluted at the point indicated.
(unnumbered) before \( 7 \) constituted less than 0.1% of the total product, while the two peaks following \( 7 \) were each less than a per cent; hence none of these were identified. Compound \( 7 \) (16%) was collected and shown by infrared (ir) and nuclear magnetic resonance (nmr) spectra to be identical with 5,5-diphenylcyclononanol. Authentic transannular rearrangement product 1,5- and/or 1,6-diphenylcyclononene (8) was synthesized (Scheme II) and was eluted at the point indicated (time scale approximate). From a synthetic mixture, it was determined that 1% of this rearranged compound could be detected. The first (largest) peak (68% of total product) was found to be a 56:44 mixture (by nmr) of

Scheme II

\[
\begin{align*}
PhCH=CHCOOEt & \xrightarrow{\text{NaOEt}} PhCH(CH_2COOEt)CH(COOEt) \xrightarrow{\Delta} HBr \\
PhCH(CH_2COOH) & \xrightarrow{1. \text{MeOH, } \text{H}_2\text{SO}_4} PhCH(CH_2CH-CN) \xrightarrow{2. \text{MeOH, } \text{H}_2\text{SO}_4} HBr \\
PhCH(CH_2COOMe) & \xrightarrow{1-4 \text{above}} PhCH(CH_2CH-CN) \xrightarrow{1-2 \text{above}} \\
PhCH(CH_2CH-CN) & \xrightarrow{\text{Na, xylene, } \Delta} \\
& \xrightarrow{1. \text{PhLi}} 8 \\
& \xrightarrow{2. \text{I}_2, \Delta} 
\end{align*}
\]

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a cis and trans isomeric olefin 1a and 1b. The cis isomer alone was obtained when this mixture was heated under reflux in glacial acetic acid or upon glc collection from an acid contaminated Carbowax 20M column. The cis isomer also only was obtained from deamination (vide infra). Compound 2 (15%) was an olefin, but only the cis isomer was obtained. From their spectral characteristics, these compounds were identified as cis- and trans-5,5-diphenylcyclonene (1a) and (1b), and cis-6,6-diphenylcyclonennone (2).

Trifluoroacetolysis of 5,5-Diphenylcyclononyl Tosylate

5,5-Diphenylcyclononyl tosylate (4 g) was solvolyzed in trifluoroacetic acid 0.3M in sodium trifluoroacetate at 5° for 23 hours, and the product was reduced and analyzed in the same way as the acetolysis product. The glc result is given in Figure 3. Peaks that are unnumbered were less than a per cent each and thus were not identified. Authentic compound 8 was eluted at the point shown but was not detected in the product mixture (1% of synthetic mixture detectable). Compounds 5 and 6 had similar retention times to 1 and 2, but were not identical to them.
Compounds 3 and 4 present to the extent of 47% and 17% respectively, were identified as the trans and cis isomers of 1,2-diphenylcyclononene on the basis of their spectral data.

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Compound 5 (7% of total product) was identified as 2,3-diphenylcyclononene by comparison of its spectral features with 2,3-diphenylcyclohexene, 20 1,5-(1,6-)diphenylcyclononene (8), and 2,3-diphenylcyclooctene. 5 Compound 6 constituted 15% of the product and was identified as 3,3-diphenylcyclononene also on the basis of its spectral characteristics.

Deamination of 5,5-Diphenylcyclononylamine

5,5-Diphenylcyclononylamine was prepared from the tosylate via displacement with azide, followed by lithium aluminum hydride reduction, and purification was accomplished by means of the picrate then regeneration from an ion exchange resin. Deamination could not be achieved in trifluoroacetic acid and hence was carried out in refluxing glacial acetic acid (130°) with 1.1 equivalents of isoamyl nitrite. 21 The product was chromatographed without reduction and gave 37% olefin, 46% acetate, and 17% alcohol (percentages are based on moles, unless specified by weight). The olefin fraction consisted of a 62:38 mixture of the cis isomers only of 5,5- and 6,6-diphenylcyclononenes 1a and 2, with no trace of any other (to the 1% level). The acetate fraction was identified

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as 5,5-diphenylcyclononyl acetate by comparison of its ir, nmr, and melting point (undepressed when mixed) with authentic sample. The alcohol fraction was not analyzed further.

Olefin Stability Tests

Because of the known addition of both acetic acid$^{22}$ and trifluoroacetic acid$^{5,23}$ to olefins, the effect of these solvents on a known mixture of olefins (near equal amounts of 1a and 1b plus 9% of 2) and on 1,5-(1,6$^\text{a}$)diphenylcyclononene (8) was studied under the various reaction conditions. Although the olefins were not very soluble in trifluoroacetic acid, under conditions identical to the trifluoroacetolysis, 27% of 8 and 8% of 4 were obtained, the remainder being the starting olefin (54% 1 and 11% 2). Only a very small amount of trifluoroacetate was detected in the infrared (1780 cm$^{-1}$). None of compound 8 was detected in the mixture after the trifluoroacetic acid test. The detection of any 5 or 6 was not possible because of the presence of the unrearranged starting olefins which would obscure them. Under acetolysis conditions, 17% of the acetate was obtained from the mixture of olefins 1 and 2; whereas the olefin 8 gave about 35% acetate under deamination conditions. Furthermore, under these deamination conditions, 1b was converted entirely into 1a.
DISCUSSION

Product Identification

Since compounds 1 - 6 were identified on the basis of their spectral data alone, some further comments are warranted. All compound molecular weights were checked by mass spectrometry.

The spectral characteristics of compounds 1 and 2 were compared with those of the two similar olefins, 5,5- and 4,4-diphenylcyclooctene (compounds 9 and 10 respectively), obtained by Cope.\textsuperscript{5}

\[ \text{Ph} \quad \text{Ph} \]

\[ \text{9} \]

\[ \text{Ph} \quad \text{Ph} \]

\[ \text{10} \]

These compounds exhibited ultraviolet (uv) and nmr spectra similar to 1 and 2: several weak maxima below 300 mp, \( \lambda = 200-400 \), and the following nmr (deuteriochloroform) data: 9, 2.8(s,10), 4.4(m,2), 7.7(m,8), 8.6(m,2); 10, 2.82(s,10), 4.5(m,2), 7.08(d,2,\( J = 8 \) Hz), 8.1(centre of complex band, 8).

The choice of 1a versus 2 (5,5- or 6,6-diphenyl) rather than vice versa was made for three reasons:

(i) In the nmr spectrum of 9, the high field methylene multiplets are much more symmetrical than those of 1a (see Figure 4).

(ii) The bulk of the high field multiplet in Figure 4(a) is at higher field than that of 4(b) (8.8 vs. 8.5) which indicates that these four methylene protons are farther away from the electron withdrawing gem-diphenyl and C=O groups in (a) relative to (b). This would occur in the case of the 5,5-diphenylcyclononene 1a. This
argument neglects the effects of long range shielding however.

(iii) From Dreiding molecular models, it can be seen that for 5,5-
diphenylcyclononene both the cis and trans isomers are relatively
flexible, whereas in the corresponding 6,6-diphenyl case movement of
the C=C part of the ring is severely restricted in the trans isomer by
the transannular gem-diphenyl group (in the 5,5-diphenyl case, this
movement is hindered only by the transannular methylene group). This
restriction should tend to make the trans-6,6-diphenyl olefin relatively
less stable than the trans-5,5-diphenyl olefin (although both trans
isomers are highly strained compared to their cis counterparts) which
may account for its not being detected.

However, it must be admitted (for symmetry reasons also) that the
olefinic protons in the symmetric 6,6-diphenyl olefin 2 would be expected
to be equivalent unlike those in 1a, whereas in fact the reverse was
found. Decoupling of the methylene protons near 7.7τ gave in the case
of 1a and 1b singlets for the olefinic protons, while in the case of 2,
two doublets ($J = 11$ Hz) separated by 17 Hz ($\delta = 28$ Hz). This olefinic non-equivalence can be explained by the existence of mainly in an asymmetric conformation, but unfortunately the same explanation may apply to the case of the methylene protons. Thus, the possibility that these two assignments for compounds 1 and 2 may be reversed does exist. Other assignments, in particular those involving phenyl migration, are ruled out by the other data (vide infra).

Compound 5 (like 3, 4, and 8) displayed in its infrared spectrum multiple weak bands in the 1600-1560 cm$^{-1}$ region and a large increase in ultraviolet intensity (cf. 2,3-diphenylcyclooctene$^5$ which had a maximum at 236 m$\mu$, log $\varepsilon = 3.83$), both of which indicate conjugation of the double bond with an aromatic ring.$^{24}$

Compound 6 displayed no such conjugation and was the most difficult to identify. However, the proposed structure most consistent with the data for this compound is 3,3-diphenylcyclononene (6). The olefinic protons must then be shielded strongly by the gem-diphenyl groups and hence shifted upfield considerably. Unfortunately there have not been any other reported examples of cyclic olefins with geminal diphenyl substitution in the 3-position with which to compare this effect.

Compounds 3 and 4 present to the extent of 47% and 17% respectively were identified as the trans and cis isomers of 1,2-diphenylcyclononene from the lack of olefinic protons in their nmr spectra and the large increase in ultraviolet absorption for these compounds. The choice of 3 as the trans isomer was based on the criterion that the trans-diphenyl isomer usually has the stronger ultraviolet absorption (e.g. the stilbenes) and is the more stable compound (amount of $\frac{3}{4}$).
Significance of Results

In such a large ring as the cyclononyl, there are a great many possible transannular migrations, especially when one considers that more than one combination of migrations can lead to the same product as well. Some of the possible olefinic products that could result from various phenyl migrations are given in Scheme III. In the absence of any transannular phenyl or hydride migration, only two products are expected, namely 5,5- and 6,6-diphenylcyclononene. This expectation was confirmed in both the acetolysis and deamination reactions on 5,5-diphenylcyclononyl tosylate indicating that such substitution prohibits transannular phenyl as well as hydride migration (which is known to occur during acetolysis of the unsubstituted tosylate\textsuperscript{4,22,25}). It appears that the large geminal phenyl groups are restricted to conformations unfavourable for proximity effects and transannular phenyl shifts, as indicated by the slight reduction in the rate of acetolysis of the 5,5-disubstituted tosylate relative to that of the unsubstituted compound.\textsuperscript{10}

However, in the trifluoroacetolysis of 5,5-diphenylcyclononyl tosylate, the case is not as clear cut. The products found can be derived by a 1,4- and/or 1,6-hydride migration, followed by proton loss (to give 6) or a 1,2-phenyl migration followed by proton loss (to give 3 - 6). The possibility of a series of 1,2-hydride shifts also exists. Although only about a third of the 5,5-diphenyl olefin mixture reacted to give the 1,2-phenyl migration products 3 and 4 in the olefin isomerization test reaction (5 and 6 would be obscured by the starting olefins and hence their presence is unknown), it is difficult to draw a conclusion from the results concerning the amount
of isomerization that would occur during the solvolysis, since in this
case the olefin would be present, at least initially, in a homogeneous
solution, while the olefin isomerization test was heterogeneous through­
out. The same inconclusive results were obtained for the analogous
5,5-diphenylcyclooctene case when the olefins were tested in trifluoro­
acetic acid.5

The possibility that any rearranged 1,5-(1,6-)diphenyl olefin \( \sim \)
formed in the reaction might preferentially add acetic acid and hence go
undetected in the olefin fraction was also checked. Although this olefin
gave more acetate under the deamination conditions than the 5,5-diphenyl­
cyclononene test mixture gave under the solvolysis conditions (35\% vs. 17\%),
this difference should not be large enough for the olefin \( \sim \) to go
undetected. Further, no rearrangements other than cis-trans isomerization
were found to occur in acetic acid. The absence of any trans-5,5-
diphenylcyclononene \( \sim \) in the deamination product might indicate the
presence of a different mechanism of elimination in the case of the amine
leaving group (e.g. cis elimination)17 compared to that of the tosylate
which gave nearly a 50:50 mixture of the cis and trans isomers. But, the
latter olefin mixture under the deamination conditions (refluxing glacial
acetic acid) isomerized entirely to the cis isomer, which precludes any
conclusion in this regard (cf. the cyclodecylamine results, reference
16, p 674).

The choice of a protic medium for deamination with alkyl nitrite
was made on the basis21 that this is the most efficient medium for
olefin production and in addition gives rise to the largest amount of
rearranged olefins. Under these conditions it has been shown21 that
the reaction occurred through a diazonium species (i.e. carbenic

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decomposition of intermediate diazoalkane does not occur). Attempts to use trifluoroacetic acid and alkyl nitrite failed to give any olefin but instead an unidentified salt was obtained. It appears that diazotization at such high acidity is too slow to occur. Diazotization in this same acid was attempted with sodium nitrite but gave extensive (at least 50%) ring nitration, possibly as a result of the abundant dinitrogen tetroxide formed in this medium. A new synthesis of alkyl nitrates has recently been reported under similar conditions to these. Consequently these attempts were abandoned and the more common glacial acetic acid used.

In this solvent, the amount of olefin obtained was 37%, while 46% of acetate and 17% alcohol resulted. This large increase in the amount of substitution product relative to that obtained in solvolysis is common for deamination in glacial acetic acid (in fact acetate esters are usually the main products) and this has been discussed in the introduction.
SUMMARY AND CONCLUSIONS

5,5-Diphenylcyclononyl tosylate was solvolyzed in acetic and trifluoroacetic acids, and the corresponding amine deaminated in glacial acetic acid. The major products were separated and identified. No transannular phenyl nor hydride migration was found, although the possibility of the latter in trifluoroacetolysis still remains. The lack of phenyl rearrangement in the deamination indicates that, in the case of substituted nine-membered ring compounds, such reaction conditions are no more conducive to transannular rearrangements than the corresponding tosylate solvolyses. However, the acetic acid - alkyl nitrite reaction appears to be an efficient medium for olefin formation without additional side reactions in medium ring compounds.

SUGGESTIONS FOR FURTHER RESEARCH

In view of the considerable amount of transannular phenyl migration\(^7\) (21%) on treatment of 4,4'-diphenylcyclohexyl tosylate with sodium t-butoxide in refluxing dimethylsulfoxide (even though the reaction fails in the absence of base, i.e. in solvolysis and deamination), it would be interesting to test the 5,5-diphenylcyclononyl tosylate under identical conditions. The geometry of the nine-membered ring may be even more suitable for the proposed merged elimination (\(E_2\)) and intramolecular displacement (\(S_{N1}\)) process. If rearrangement was found to occur in this base catalyzed elimination-rearrangement reaction, further work on the effect of ring size might then be warranted.
EXPERIMENTAL

All melting points were taken on a Fisher-Johns apparatus and are uncorrected. Infrared spectra were obtained on a Beckman IR-12 usually in 10% (w/w) carbon tetrachloride solution. Nuclear magnetic resonance spectra were recorded on a Jeolco JNM-C60HL instrument also in 10% (w/v) carbon tetrachloride solution and shifts are in \( \tau \) units relative to tetramethylsilane. Small samples were accumulated on a Jeolco JRA-1 spectrum accumulator. The mass spectra were obtained from Morgan Schaeffer Corp., Montreal. Gas liquid chromatography analyses were carried out on an F and M Model 720 Gas Chromatograph utilizing one of the following columns: A, 10ft x 0.25in XE-60 (Silicone gum nitrile); B, 6ft x 0.25in QF-1; C, 6ft x 0.25in Carbowax 20M, all 10% on 60-80 mesh Chromosorb W. Olefin retention times generally ranged from 30 to 60 min on these columns, and area measurements were made by planimeter. Except as noted the drying agent was magnesium sulfate and solvents were removed under reduced pressure on a rotary evaporator. Liquid column chromatography was performed on a 350 x 25 mm column with fritted filter using Fisher certified neutral alumina, Brockman Activity 1 (80-200 mesh). Yields were determined by fraction weights and glc analysis.

2-Hydroxy-6,6-Diphenylcyclononanone (11) - This compound was prepared by the method of Blomquist with the higher sodium-ester molar ratio recommended. Yields of 35-45% crude acyloin were usual, but this was always contaminated with about equal amounts of an ester (1740 cm\(^{-1}\)) and hydrocarbon. All attempts at purification (recrystallization and
chromatography) were unsuccessful, hence purification was left to the ketone step.

5,5-Diphenylcyclononanone (12) - The crude acyloin 11 was reduced with zinc and hydrochloric acid in glacial acetic acid according to the procedure reported. Attempts with refluxing hydroiodic acid gave poor results. The resulting ketone was difficult to purify by recrystallization because of the large amount of impurities. The method chosen for purification for ease and optimum yield of pure ketone was a combination of column chromatography (alumina) and recrystallization at -20° from cyclohexane. The impure ketone was placed on alumina (about 50:1 w/w) and first washed with petroleum ether (30-60°) to remove the usual 20-30% hydrocarbon impurity, followed by methylene chloride until a slow moving dark band was about to be eluted to give 30-40% ketone. The dark band consisted mainly of the ester (1740 cm⁻¹) impurity. The ketone fraction still contained a small amount of impurity (1740 cm⁻¹) but after recrystallization from a small amount of cyclohexane the ketone 12 was obtained pure, mp 113.5-116° (ir, 1704 cm⁻¹, C=O). Overall yield of pure ketone for the acyloin condensation and reduction step was generally 10-15%.

  Found: C, 86.04; H, 8.42; O, 5.75.

5,5-Diphenylcyclononanone oxime (13) - The oxime was prepared from the ketone 12 by the standard pyridine method and was recrystallized from an ether-hexane mixture. This oxime proved to be very difficult to recrystallize and gave poor yields, especially when impure ketone 12.
was used; hence this was not a good method for purification of the ketone by regeneration from the oxime (purified oxime did however give pure ketone upon ceric ammonium nitrate oxidation).\(^3\) Twice recrystallized and dried oxime had mp 175-177\(^\circ\) and gave a satisfactory analysis.

\textbf{Anal.} Calcd for C\(^{21}\)H\(^{25}\)NO: C, 82.04; H, 8.20; N, 4.56.

\textbf{Found:} C, 82.24; H, 8.43; N, 4.55.

\textit{5,5-Diphenylcyclononanol (7)} - The pure ketone 12 (4 g) was dissolved in 100 ml anhydrous ether and added slowly to 1.6 g lithium aluminum hydride in an equivalent amount of dry ether. The solution was heated at reflux overnight with magnetic stirring, excess hydride decomposed by the slow addition of 1.5 ml of water, 1.5 ml of 15\% sodium hydroxide solution, then 4.5 ml more water. The granular solid was filtered, the ether filtrate dried over sodium sulfate and concentrated leaving 3.8 g of a low melting semi-solid which could not be recrystallized.

\textbf{Anal.} Calcd for C\(^{21}\)H\(^{26}\)O: C, 85.76; H, 8.90; O, 5.43.

\textbf{Found:} C, 86.03; H, 8.96; O, 5.73.

\textit{5,5-Diphenylcyclononyl acetate (14)} - This compound was obtained in about 75\% overall yield from the ketone 12 by the reported method,\(^1\) but had mp 101-102\(^\circ\) (reported 96-98\(^\circ\)). The ir spectrum had an acetate band at 1735 cm\(^{-1}\) and the following nmr: 2.81(s,10), 5.0(m,1), 7.65(m,4), 8.05(s,3), 8.0-9.0(m,10).

\textit{5,5-Diphenylcyclononyl tosylate (15)} - The method of Brown and Ham\(^1\) was used and a yield of 90\% based on the alcohol was common, mp 102-104\(^\circ\). This compound was relatively unstable and consequently was never heated above 30\(^\circ\) nor kept for long periods of time. ir: 1360, 1170(d), 1090 and 885(brl) cm\(^{-1}\); nmr(deuteriochloroform): 2.50(quartet,4,J = 8 Hz),

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Acetolysis of 5,5-diphenylcyclononyl tosylate (15) - The tosylate (1.3 g) was dissolved in 108 ml anhydrous acetic acid\textsuperscript{10} and stirred at 35° for 36 hrs (12 half-lives). The solvolysis product was quenched with 300 ml cold water and extracted with four 50 ml portions of ether. The combined ether portions were then washed with five 50 ml portions of water, two 40 ml portions of saturated sodium bicarbonate solution and dried. After filtering and removing the ether there remained 1.16 g of an amber viscous liquid. This was dissolved in 50 ml anhydrous ether, 100 mg lithium aluminum hydride added, and the mixture stirred for 3 hrs. Water (0.5 ml) was added dropwise, followed by magnesium sulfate (1-2 g). The mixture was stirred for an hr, filtered, and the ether removed leaving 1.03 g of a colourless oil. This was subjected to column chromatography on 70 g alumina using first petroleum ether (30-60°) as eluent. Seventeen (60 ml) fractions were collected and combined to give 804 mg of a white solid (Fraction 1). The eluent was then changed to ether followed by methylene chloride for another 20 fractions each, but gave a combined total of only 39 mg of white solid (Fraction 2). Finally three methanol fractions were collected, combined, and the solvent removed. The residue was dissolved in methylene chloride, filtered, and concentrated in order to remove any column residue to give 191 mg brown oil (Fraction 3). The total amount recovered from the column was 1.03 g.

The three fractions were analyzed by glc on column B (175°, 1/min, 60 cc helium/min) and gave identical results to that shown in Figure 2. Fraction 1 consisted only of compounds 1 and 2 (80:20), while the second fraction contained a small amount of 2 in addition to 1 and 2.
Fraction 3 consisted mainly of compound 7 and the other small unidentified compounds (total \(\approx 1\%\)). The overall distribution was 1 (68\%), 2 (15\%), and 7 (16\%). Sufficient quantities of 1, 2, and 7 were collected by glc (column A) for spectral examination. Fraction 1 after one recrystallization from petroleum ether (30-60°) had mp 84-88° but after a second recrystallization 92-94°, which by glc still contained about 9% of 2. The compound 1 collected was shown by nmr to be a 56:44 mixture of 1a and 1b, and fortuitously the recrystallized Fraction 1 gave only 1a when subjected to gas chromatography on an old (acid contaminated) column C (205°, 50 cc helium/min). The nmr of 1b was hence obtained by subtraction of the portion due to 1a. Compound 7 was shown by comparison of the ir, nmr, and glc retention times to be identical to 5,5-diphenylcyclononanol. The pertinent data is listed below:

1a : ir (CCl₄, \(\text{cm}^{-1}\)) 3088, 3058, 3010, 2930, 2858, 1653(w), 1600, 1580(w), 1490, 1472, 1440, 1025(d), 725, 700; nmr (CCl₄, \(\tau\)) 2.82(s,10), 4.32(near t,2,\(J = 6\) Hz), 7.5-9.1(m,12).

1b : ir (in addition to those of 1a) 992(s); nmr (CCl₄, \(\tau\)) 2.87(s,10), 4.65(m,2), 7.5-9.2(m,12);

uv (56:44 mixture of 1a and 1b in cyclohexane, \(\text{mp}\)) 270(log \(\epsilon = 2.65\)), 266sh(2.67), 263(2.75), 259(2.78), 254(2.79), 249(2.78), 244(2.75), 218inf(4.14); m/e 276(P), 277(P+1, 23.2%), and the following additional prominent peaks: 193(B), 180, 179, 178, 167, 165, 117, 91, 41.

2 : ir (CCl₄, \(\text{cm}^{-1}\)) 3090, 3060, 3010, 2935, 2860(d), 1650(w), 1598, 1580(w), 1495, 1480, 1442, 1030, 700; nmr (CCl₄, \(\tau\)) 2.83(s,10), 4.0-5.0(m,2), 7.4-8.9(m,12); uv (cyclohexane, \(\text{mp}\)) 270(log \(\epsilon = 2.79\)), 265sh(2.82), 263(2.88), 259(2.90), 254(2.90), 249(2.88), 244(2.84),
219\text{inf}(4.52); m/e 276(P), 277(P+1, 23.2%), and the following additional prominent peaks: 205, 193, 181, 180(B), 179, 178, 167, 165, 129, 115, 103, 91, 77, 41.

**Trifluoroacetolysis of 5,5'-diphenylcyclononyl tosylate (15)** - The tosylate (4 g) was added to 35 ml trifluoroacetic acid (Eastman highest purity) containing 1.43 g (0.3 molar) sodium trifluoroacetate and the mixture was stirred at 5° for 23 hrs. An aliquot taken after 18 hrs showed virtually no tosylate in the infrared spectrum. The mixture was poured cautiously into 500 ml cold saturated sodium bicarbonate solution and extracted with five 50 ml portions of ether. The combined ether portions were washed twice with 25 ml of water, dried, filtered, and concentrated to give 2.16 g of a brown oil (small 1780 cm\(^{-1}\), trifluoroacetate). This was dissolved in 150 ml dry ether, 0.15 g lithium aluminum hydride added, and the mixture stirred magnetically for a half hour. After the dropwise addition of one ml of water, the solution was stirred for another 30 min, a few grams of magnesium sulfate were added, the mixture filtered through celite, and the solvent removed to give 1.9 g of an amber oil. This was chromatographed on 70 g alumina beginning with pentane as eluent. The first five 100 ml fractions were combined to give 1.03 g of a yellow oil (Fraction I), which by glc (Figure 3) on column A (180°, 17 min, 60 cc helium/min) consisted of 3, 4, 5 and 6 (65:24:3:8). Over the next ten 100 ml fractions methylene chloride was added gradually up to 5% by volume and these fractions combined to give 0.31 g yellow oil (Fraction II), which by glc consisted mainly of the same four compounds in the ratio 30:10:20:37 and the few other peaks (all <1%) shown in the figure. The eluent was then changed to 10:1 ether-methanol and four 100 ml fractions collected, which combined
gave 0.36 g of a brown oil (Fraction III); by glc this consisted of mainly 5 and 6 (7 and 17% respectively) and 45% 7 (same retention time as 5,5'-diphenylcyclononanol). The total recovery was 1.70 g with the following composition: 3 (47%), 4 (17%), 5 (7%), 7 (9%), with the remainder totalling a maximum of 5% (all individually less than 1%). None of compound 8 was detected, while a synthetic mixture of 1% 8 in Fraction II was eluted at the point indicated in Figure 3. Sufficient quantities of compounds 3 to 6 were collected for spectral analysis:

3 : ir (CCl₄, cm⁻¹) 3080, 3060, 3020, 2930, 2855, 1598, 1572(w), 1489, 1474, 1443(d), 1072, 1021, 702; nmr (CCl₄, δ) 2.99(s,10), 7.34(m,4), 8.33(br s,10); uv (cyclohexane, με) 246sh(ε = 3.97); m/e 276(P), 277(P+1, 23.4%), and the following prominent peaks: 115, 105, 91(B), 77.

4 : ir (CCl₄, cm⁻¹) 3084, 3062, 3026, 2925, 2845, 1600, 1585(w), 1575(w), 1492, 1467, 1446, 1032, 703; nmr (CCl₄, δ) 2.78(s,10), 7.81(m,4), 8.52(br s,10); uv (cyclohexane, με) 245sh(ε = 3.68).

5 : ir (CCl₄, cm⁻¹) 3082, 3060, 3024, 2929, 2857, 1599, 1584(w), 1574(w), 1493, 1476, 1450, 1075, 1032, 702; nmr (CCl₄, δ) 2.87(s and 3.00m(10), 4.21(t,1,J = 8.6 Hz), 5.78(m,1), 7.53(m,2), 8.29(br s,10); uv (cyclohexane, με) 238sh(ε = 3.74); m/e 276(P), 277(P+1, 23.1%), and the following additional prominent peaks: 205, 129, 117, 115, 91(B).

6 : ir (CCl₄, cm⁻¹) 3085, 3065, 3030, 2925, 2855, 1600, 1495, 1477, 1452(t), 1370, 1072, 1030(d), 702; nmr (CCl₄, δ) 2.75(s,10), 6.15(d,1,J = 10 Hz), 6.70(m,1), 7.7sh and 8.32br s(12); uv (cyclohexane, με) 274(ε = 3.09), 267(3.11), 260(3.06), 254(2.97), 224inf(4.09); m/e 276(P), 277(P+1, 23.4%), and the following
additional prominent peaks: 205, 192, 179, 115, 91(B).

5,5-Diphenylcyclononylamine (16) - Hydrogenation of the oxime 13 in methanol over 5% rhodium-on-alumina\(^\text{30}\) was extremely slow, while reduction with lithium aluminum hydride gave mainly a secondary amine probably by oxime rearrangement.\(^\text{31}\) Hence the following method was used: to 6.2 g tosylate 15 dissolved in 120 ml dry dimethylsulfoxide was added 1.7 g sodium azide. The solution was stirred magnetically for five days at room temperature, poured into 250 ml cold water, and extracted with four 50 ml portions of ether. The combined ether portions were washed in turn with four 25 ml portions of water, dried over sodium sulfate, filtered, and concentrated to give 3.5 g of azide (ir \(2100\ \text{cm}^{-1}\)) . This was dissolved in 150 ml dry tetrahydrofuran, 2.0 g lithium aluminum hydride added and the mixture heated to reflux for two hrs, then left stirring overnight. After the dropwise addition of two ml of water, two ml of 15% sodium hydroxide was added, followed by six more ml of water. The resulting solid was filtered and the filtrate dried with sodium sulfate. After removal of solvent there remained 3.6 g of a colourless viscous oil. This was dissolved in 40 ml 95% ethanol and 80 ml of a saturated ethanolic picric acid solution added. The solution was heated to reflux, left overnight, and the picrate filtered and dried (dec 236-238\(^{\circ}\)).

**Anal.** Calcd for \(\text{C}_{27}\text{H}_{30}\text{N}_{4}\text{O}_{7}\) : C, 62.06; H, 5.79; N, 10.72.

Found : C, 62.15; H, 5.72; N, 10.60.

The picrate was dissolved in 400 ml of 5% sodium hydroxide solution (heated) and the amine extracted with three 100 ml portions of ether. The ether fractions were combined and washed with a small
portion of 5% sodium hydroxide solution, then passed through about 50 g Rexyn 201, followed with 200 ml of ether. The ether solution was dried with sodium sulfate, filtered, and concentrated. The pure amine was finally dried under reduced pressure at 100° in a drying tube to give 1.45 g white solid, mp 95-96°, which turned brown on exposure to air. The overall yield was 38%; ir (CCl₄, cm⁻¹) 3320; nmr (CCl₄, δ) 2.73(s,10), 6.3(m,1), 7.4-9.5(m,16).

Found : C, 85.73; H, 8.99.

The acetamide was prepared in similar manner to the acetate 14 but was recrystallized from ethyl acetate-cyclohexane, mp 233-235°; ir (KBr, cm⁻¹) 3280, 2940, 1640, 1560, 1490, 1450, 750, 705; m/e 335(P), 276, 206, 205, 193, 168, 167, 166, 140, 129, 127, 117, 115, 114, 100, 91(B), 70, 60, 57, 56, 44, 43.

Anal. Calcd for C₂₉H₂₉NO : C, 82.34; H, 8.71; N, 4.17.
Found : C, 82.30; H, 8.49; N, 4.39.

Deamination of 5,5-diphenylcyclononylamine (16) - An attempt with sodium nitrite and trifluoroacetic acid gave large amounts of aromatic nitration (ir, strong 1525 and 1350 cm⁻¹), possibly from the dinitrogen tetroxide produced. Substitution of isoamyl nitrite gave an unknown solid, mp 190-195°, with a large increase in weight and no olefin even after an hour at reflux. Hence glacial acetic acid was used; amine (0.54 g) was dissolved in 10 ml glacial acetic acid in a 25 ml two-neck flask equipped with a septum and condenser with calcium chloride drying tube. Using a syringe 290 µl (1.1 equivalents) of freshly distilled isoamyl nitrite (Eastman practical) was added and the solution heated at reflux (bath 130°) with magnetic stirring for 5 hrs, then cooled and

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left stirring overnight. The solution was poured into 25 ml cold water, extracted with three 25 ml portions of ether, which in turn were combined and washed with two portions of water and saturated sodium bicarbonate solution, then dried. After filtration and ether removal there remained 0.8 g of a brown viscous oil (ir, strong 1735 cm⁻¹). This was chromato-

graphed on 40 g alumina, beginning with petroleum ether (30-60°). Eight 70 ml fractions gave 0.17 g of amber product which by glc (column A) and nmr was shown to be a 62:38 mixture of compounds 1a and 2. While slowly increasing the amount of methylene chloride up to 50%, fifteen additional fractions were collected to give 0.25 g of an amber oil, which was identical by ir and nmr (mixed with authentic) to 5,5-
diphenylcyclononyl acetate 14 (decomposed under glc conditions). Recrystallization from petroleum ether (30-60°) gave a white solid, mp 98-100°, unchanged with added 14. Five more 70 ml fractions were collected with pure methylene chloride and gave 0.1 g brown oil which by ir and nmr was shown to be a near 50:50 mixture (80:20 by weight) of 5,5-diphenylcyclononanol 2 and isoamyl alcohol. Hence, the overall yield was 0.50 g which consisted of 37% olefin, 46% acetate, and 17% alcohol.

5-Phenylazelanitrile (17) - This compound was synthesized by the method of Cope and Kinnel,32 using the reported dimethylsulfoxide method of nitrile synthesis rather than refluxing ethanol.

Dimethyl 5-phenylazelate (18) - The dinitrile 17 (23 g) was hydrolyzed by heating at reflux for 16 hrs in 200 ml concentrated hydrochloric acid. The cooled solution was made basic with 15% sodium hydroxide, extracted with several portions of ether, then acidified to pH 2 and extracted
with more ether portions. The combined ether fractions were dried, filtered, and concentrated leaving 25 g of an amber liquid. This was dissolved in 175 ml methanol, 10 ml concentrated sulfuric acid added, and the mixture heated at reflux for 6 hrs. The cooled solution was poured into 250 ml cold water, extracted with three 150 ml portions of ether, which were combined, washed with two 100 ml portions of saturated brine, and dried. The solution was filtered and the solvent removed. The residue was distilled, collecting the fraction boiling from 185-191° at 2.5mm (n_D^23 = 1.4950). The yield of ester was 21.4 g (67% from dinitrile 17).

2-Hydroxy-6-phenylcyclononanone (19) - The same procedure of acyloin ring closure as that used for the diphenyl compound 11 was employed with 15.8 g of the diester 18. The acyloin was collected in the fraction boiling from 149-158° at about 0.2mm, and gave 2.6 g of a viscous liquid which had characteristic infrared bands at 3480 and 1704 cm⁻¹.

5-Phenylcyclononanone (20) - The 2.6 g of acyloin 19 were reduced by the same procedure used for reduction of the acyloin 11, and the resulting 2 g of impure ketone subjected to column chromatography on 50 g alumina, starting with petroleum ether as eluent. This gave about 0.4 g of a hydrocarbon material, after which the eluent was changed gradually to pure methylene chloride and the fractions combined until a slow moving dark band was about to be eluted, giving 0.6 g of a brown liquid which had a strong 1704 and weak 1735 cm⁻¹ band in the infrared spectrum. The dark band displayed a strong hydroxyl absorption as well as the 1735 cm⁻¹ band. The ketone was purified by glc collection from an 8ft x 0.50in 10% XE-60 on 60-80 mesh Chromosorb W column (230°, 60 cc...
helium/min) and had a retention time of about 18 min. In total 0.34 g of the ketone was collected; ir(CCl₄, cm⁻¹) 1704; nmr (CCl₄, t) 2.79(s,5), 7.57(m,5), 8.20(m,10).

**Anal.** Calcd for C₁₅H₂₀O : C, 83.28; H, 9.32.

**Found :** C, 82.98; H, 9.23.

1,5-(1,6-)Diphenylcyclononene (8) - To a solution of phenyl lithium prepared from 0.8 g each of bromobenzene and lithium wire (high sodium content) in 10 ml dry ether, the 0.3 g of ketone 20 in 5 ml dry ether was added slowly. The solution was heated at reflux for an hr, cooled and stirred for two more hrs, then 15 ml water added. The aqueous layer was separated, extracted twice with 15 ml of ether, and the combined organic phases dried over sodium sulfate. After filtration and solvent removal there remained 0.5 g of a brown oil (ir, strong OH), which was dissolved in 100 ml dry benzene containing a few crystals of iodine. The solution was heated at reflux for 26 hrs with a 25 ml capacity Dean-Stark water trap, then cooled and washed with 10 ml of saturated sodium thiosulfate solution, two 5 ml water portions, and dried over sodium sulfate. After solvent removal there remained 0.4 g brown liquid. This was subjected to glc analysis on an 8ft x 0.50in 10% SE-30 on 60-80 mesh Chromosorb W column (225°, 60 cc helium/min). The olefin had a retention time of about 40 min and was collected in sufficient quantity to permit spectral analysis:

**Anal.** Calcd for C₂₁H₂₄ : C, 91.25; H, 8.75.

**Found :** C, 90.98; H, 8.73.

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Olefin stability tests - To 1.8 ml trifluoroacetic acid containing 70 mg (0.3 molar) sodium trifluoroacetate and 80 mg p-toluenesulfonic acid (1 equivalent) was added 100 mg of the twice recrystallized olefin from Fraction 1 of the acetolysis product (which consisted of about equal amounts of 1a and 1b and 9% 2). This was stirred magnetically in a sealed vial for 23 hrs at 5° (heterogeneous throughout), poured into 15 ml saturated sodium bicarbonate solution, extracted with ether, the ether layers washed with water and dried over sodium sulfate. After filtration and solvent removal, the residue (ir, small 1780 cm⁻¹) was shown by glc to consist of 27% 3, 8% 4, 54% 1a (no trans 1b in ir), and 11% 2. Small amounts of 5 and 6 would have been obscured under the last two peaks and hence could not be detected.

After heating at 35°50 mg of the same olefin mixture used above in 1 ml of glacial acetic acid containing 35 mg (1 equivalent) p-toluenesulfonic acid for 35 hrs, the solution was worked up in analogous manner to that of the acetolysis product. By ir and nmr comparison of a mixture of known concentration, the product was estimated to contain 18% (23% by weight) of the acetate 14.

About 20 mg of the olefin 8 was dissolved in 0.5 ml glacial acetic acid with 19 µl isoamyl nitrite, and the solution heated at reflux (130°) for 5 hrs, then left stirring overnight. After identical work up as that of the deamination product, the residue (ir, strong 1740 cm⁻¹, acetate) was estimated by nmr to be about 35% of the mixture.

Treatment of a 42 mg sample of the same olefin mixture used in the trifluoroacetolysis test (about 50:50 1a and 1b) in the same manner as the olefin 8 above resulted in complete isomerization of 1b to 1a (no 1b detectable by ir nor nmr), with the formation of only a small amount of acetate.
REFERENCES

16. L. Friedman, ibid., p 655.
17. (a) T. Cohen and A. R. Daniewski, J. Amer. Chem. Soc., 91, 533 (1969); (b) M. Cocivera and S. Winstein, ibid., 85, 1702 (1963); (c) T. Cohen
and E. Jankowski, ibid., 86, 4217 (1964).


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