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entitled

# "SPECTROSCOPIC EXAMINATION OF ORGANIC MOLECULES"

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by

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## TO MY PARENTS

This work, probably the only concrete evidence I can give them of all that they have done for me.

# CONTENTS

# PREFACE

The research work reported in this thesis deals mainly with hydrogen bonding in various classes of organic compounds. It has always been the author's intention to extend his knowledge and experience in this field to biological situations where the hydrogen bond appears to be all important. Lack of time, however, precluded any experimental approach. In the introductory section, therefore, the author should like to depart from tradition and deal with the importance of the hydrogen bond in biological systems. This decision receives support since the excellent review of hydrogen bonding by TICHY[1] tackles the subject of intramolecular hydrogen bonding in non-biological systems in a very comprehensive manner.

# INTRODUCTION

"The most fruitful application of H bridge theory will be to a better understanding of complicated organic substances."

HUGGINS, J.Org.Chem.,1,405 (1936).

## Deoxyribonucleic Acid (DNA), Ribonucleic Acid (RNA), and Related Bio-polymers.

Nucleic acids are long chain molecules of high molecular weight in which five-membered rings of the sugars deoxyribose, or ribose, are joined by phosphate ester links. Each of the sugars has attached to it a purine or pyrimidine type base, which can be of four different types (Figure 1). In DNA these are adenine, guanine, thymine and cytosine; in RNA adenine, guanine, cytosine and uracil.

Both DNA and RNA appear to possess a secondary structure by virtue of the fact that the purine and pyrimidine bases can undergo hydrogen bonding with each other. In the case of DNA, this secondary structure takes the form of a long highly ordered helix composed of two strands held together by hydrogen bonds between the bases.[2-4] The model looks like a spiral staircase, in which the bases form the steps and the phosphate ester chains provide the banisters (Figure 2). These intermolecular hydrogen bonds are not made indiscriminately, but are restricted to specific pairs of bases, the adenine (A) always being bonded to thymine (T) and the guanine (G) to cytosine (C) (Figure 3).

It is nearly six years since the first integrated argument was presented that RNA molecules possess secondary structure, in the form of helical regions embedded within a single polynucleotide chain.[5] The secondary structure of RNA arises from intramolecular interactions. It takes the form of DNA-like helical regions, arising from hairpin turns of the polynucleotide chain. The base pairs in the helical regions are only A-U and G-C. Maximal formation of the A-U and G-C pairs occurs because non-bonded residues can loop out of a helical region, so that the properly bonded, complementary bases fall into place (Figure 4).[6]

## Conformation of DNA in Solution

It is now firmly established that this secondary structure of the DNA molecule plays an important role in reproduction in the living cell (aqueous medium), by an "unzipping" of the double helix to form two separate daughter strands which acquire a newly synthesised strand of the correct base sequence to reform two new double helical structures.

The biochemist has studied this destruction of the secondary structure by a variety of techniques such as titration,[7-10] ultraviolet spectroscopy,[11,12] biological activity,[13] and macromolecular analysis (light scattering, viscosity, and flow dichroism).[14,15] These denaturation studies are often quoted as providing additional evidence for the hydrogen bond stabilization of the secondary structure of DNA.[7,10] STURTEVANT et al.,[16] however, conclude that the conventional WATSON-CRICK model in which hydrogen bonds are the sole source of stability is probably not completely correct. This is not really surprising if note is taken of the fact that the long intermolecular hydrogen bonds postulated for the base-pairing scheme would be expected to be weak. If these N-H····N and N-H····O bonds indeed have lengths

of nearly 3·0 Å assigned to them, they would be expected to be weaker than the O-H····N, O-H····O, and N-H····O hydrogen bonds formed between the bases and water in the random coil configuration, and would be much weaker than the strong water-water hydrogen bonds in liquid water. Thus something else must account for the stability of the double helix in aqueous medium. FALK et al.[17] have employed infrared spectroscopy in a study of the hydration of DNA. There are three molecular subgroups in DNA (the heterocyclic bases, deoxyribose, and the diesterified phosphate groups) which provide sites where water molecules can be adsorbed. The five possible hydration sites, indicated in Figure 5, may, of course, contain more than one water molecule and conversely one water molecule may be attached to more than one site. These authors conclude that water adsorbs on the sites provided by the $PO_2^- Na^+$ (area 1) of the DNA backbone between relative humidity (r.h.) 0 to 65%. The P-O-C (area 2) and C-O-C (area 3) oxygens also become hydrated below 65% r.h. Above 65% r.h. the C=O groups and ring nitrogens (area 4) become hydrated. The hydration process is complete by about 80% r.h. and further hydration occurs with swelling. At 80% r.h., therefore, all the hydration sites of the DNA molecule are filled, and the conditions for the stability of an ordered helix are still satisfied. What then causes the "unzipping" of the DNA helix in aqueous medium? Is the known stability of DNA strengthened by solvent effects? These questions and many others might well be answered by considering smaller bio-polymers under similar conditions.

Recently SUTOR[18] has remarked that the structure of DNA has to be constructed with CH····O(phosphate) contacts of 2·88 Å.[19] She has summarized the literature and reports that many heterocyclic examples which appear to exhibit this close contact phenomenon contain a purine or pyrimidine skeleton. She concludes "it is tempting to speculate as to wheather the CH····O hydrogen bonds play as an important a part in the structure of biological molecules

as the others kinds of hydrogen bonds do." These arguments, however, apply to conformation in the solid state and need not necessaryily apply to the conformation of such molecules in aqueous medium.

## Conformation of RNA in Solution

A great deal of interest has been aroused by problems associated with the structure and function of RNA. It is believed to take a fundamental role in protein synthesis, such as helping to determine the sequence of amino acids in the protein undergoing synthesis. Is the hydrogen bond an essential part in the mechanism? The RNA macromolecules vary in conformation depending on such conditions as the ionic strength, temperature, and other parameters.[20]

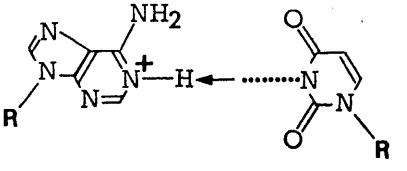
The biologists and biochemists have turned to the association of synthetic bio-polymers and oligonucleotides for guidance on conformation with function.

## Bio-polymers and Oligonucleotides

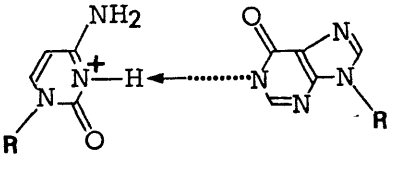
Infrared spectroscopy can be of considerable help when studying hydrogen bonding in inert solvents such as carbon tetrachloride. When dealing with nucleosides, nucleotides, etc., however, we are compelled to use aqueous media from the solubility point of view as well as that of having the system as close as possible to that in the living cell. This means that the normal approach of determining whether hydrogen bonding occurs or not is almost impossible since the water absorptions will mask the hydroxyl and amino fundamental stretching vibrations.

KYOGOKU et al.[21] claimed that when they mixed in aqueous solution equal proportions of adenosine and uridine a complex crystal was

obtained. A hydrogen bonded complex between 1-methylthymine and 9-methyladenine has already been demonstrated in the solid state by the X-ray method (Figure 6).[22] The infrared spectrum of the mixed crystal of adenosine and uridine showed a strong band in the infrared at 1700 cm.$^{-1}$ which was not observed for the two nucleosides by themselves. These authors[21] attributed this new band to a structure resulting from a proton transfer from the uracil to the adenine residue such as:



This pairing is said to involve a $\pi$-electron localization in the C=N bonds of the adenine residue, giving rise to the new band at 1700 cm.$^{-1}$. A similar situation was observed between cytidine and guanosine:



Here, then, is perhaps an infrared criterion for the base pairing scheme in nucleic acid structures. Indeed a number of experimental facts have been recorded which show that the 1710 cm.$^{-1}$ band is certainly characteristic of the secondary structure of nucleic acids.[23,24] The question to be asked, however, is what scheme in the secondary structure is responsible for the appearance of the 1710 cm.$^{-1}$ band.[25] If proton transfer in nucleic acids does occur, then this would put the interchain attractive forces of nucleic acids on a different basis from those generally accepted. The electrostatic attraction by proton transfer would almost certainly account for an important part of the molecular stabilization.

Does hydrogen bonding hold together the polynucleotide chains? The importance of hydrophobic forces in biological macromolecules may well be another factor in stabilization.

LIPSETT et al.[26] have continued with these studies by observing complex formation between long-chain polynucleotides and oligonucleotides. They attempted to evaluate the relative bond stabilities of the different base pairs in DNA [(A-T),(G-C)] and RNA [(A-U),(G-C)]. They took as models the association of polyuridylic acid and adenine oligonucleotides. Polyuridylic acid associates with members of the three series, pApA.....pA, ApAp.....A, and ApAp.....Ap, larger then the trinucleotide to form three-stranded 2:1 complexes in 0·001 M $MgCl_2$ and two-stranded 1:1 complexes in 0·1 M NaCl. The relative strengths of the component bonds in such complexes were determined by measuring the thermal stability of the complexes, eg. the temperature at which they are half-dissociated ($T_m$).[27] In all three series the dissociation temperatures, $T_m$, were quite similar and increased with increasing oligonucleotide chain length. Polyuridylic acid forms complexes with pApApApU, pApApApApU, and pApApApAUp which are less stable then the corresponding oligonucleotides without the terminal uridine residue. These unbonded "tails" of uridylate at the end of each oligonucleotide are bent sufficiently out of position so as not to block a position on the polyuridylic acid chain (Figure 7).

The synthetic polynucleotides have aroused considerable interest because of their close relation to the naturally occuring nucleic acids. Both the natural and synthetic polymers are capable of taking up more than one secondary structure, and a great deal of attention has been focussed on these structural changes. In suitable environments many polynucleotides are capable of forming elongated, helical molecules in which successive groups have a fixed position relative to each other. LANGRIDGE and RICH[28] have

reported an X-ray diffraction study of the helical form of polycytidylic acid. According to these authors the stable helix form of polycytidylic acid is hemi-protonated (Figure 8). They go on to say that in contrast to polyadenylic acid[29] the additional proton which is added to stabilize the polycytidylic acid helix is involved directly in hydrogen bonding, while in polyadenylic acid, the contribution which the added proton makes to form the helix is predominantly electrostatic in character. The helical structures assumed by these polynucleotides are very similar in nature to those adopted by another group of biological important molecules, the proteins and polypeptides, where inter-amide hydrogen bonds are responsible for the secondary helical structure (Figure 9). KLOTZ and FRANZEN[30] have studied the association of N-methylacetamide in aqueous solution using the first overtone vibrations of the N-H fundamental stretching vibration. Their results with this model system for proteins and polypeptides lead them to believe that interpeptide hydrogen bonds cannot contribute significantly to the stabilization of macromolecular organization. Here again other forces must be involved besides the hydrogen bond (cf. DNA and RNA).

To continue with the association of the polynucleotides, MILES and FRAZIER [31] have recently studied the helix strandedness in the polyadenylic-polyuridylic acid complex by infrared spectroscopy (solutions in $D_2O$). Their measurements and conclusions are based on the fact that different complexes have different spectra in the region 1600-1800 $cm.^{-1}$, resulting from hydrogen bonding between bases and protonation of the pyrimidine ring. The different polynucleotides have the following spectral bands:

| | $\nu$ | $\varepsilon^a$ | $\nu$ | $\varepsilon^a$ | $\nu$ | $\varepsilon^a$ | $\nu$ | $\varepsilon^a$ |
|---|---|---|---|---|---|---|---|---|
| Poly A | | | | | | | 1628 | 1057 |
| Poly U | 1692 | 710 | 1657 | 1230 | | | | |
| Poly (A+U) | 1691 | 436 | 1672 | 544 | | | 1631 | 398 |
| Poly (A+2U) | 1696 | 567 | 1677 | 378 | 1657 | 599 | | |

In this way one can differentiate between poly (A+U) and poly (A+2U). Thus infrared spectroscopy provides a useful and convenient method of analysis. However, the X-ray method is still of primary importance in determining the type of helix taken up by polynucleotides.[32-34]

Infrared demonstration of two- and three strand helix formation between poly C and guanosine mononucleotides and oligonucleotides has been reported recently.[35] The infrared frequencies associated with the various complexes are summarized in Table 1.

It seems reasonable, therefore, that the use of infrared spectroscopy in a study of these complexes will not involve traditional measurements on $\nu$(OH) and $\nu$(NH) in inert solvents, but rather the changes involved when proton transfer and hydrogen bonding alter the vibrations associated with the carbonyl and ring vibrations of the purine and pyrimidine bases. Admittedly, there are many questions still to be answered concerning the mode of action of biological molecules and, in particular, the importance of the hydrogen bond in nature. A systematic study of the complex formation of nucleosides and nucleotides might well reveal the importance and function of the hydrogen bond. The fact that two elongated polymeric species wrap around each other (in solution) to form a two-stranded helical molecule, i.e. poly (A+U), must infer a very high degree of specificity in the molecular structure of the two polymers. So far studies have been restricted to simple systems similar to those described above. Perhaps much more valuable information might be gained by looking at systems with various bases specifically employed along the polymer chain and seeing if the association is maintained or partially destroyed. THACH and DOTY[36] have recently described the enzymatic synthesis of tri- and tetra-nucleotides of defined base sequence. These compounds might well provide a valuable link in a systematic study

of base pairing. One way or the other it is only by a long and detailed analysis that molecules such as DNA are likely to reveal "what makes them tick".

TABLE 1*

Absorption Maxima in $cm.^{-1}$

| Material† | Band Assignments | | | | |
|---|---|---|---|---|---|
| | Protonated cytosine ring vibration | Guanine carbonyl vibration | Cytosine carbonyl vibration | Unprotonated cytosine ring vibration | Guanine ring vibration |
| 5'-dGMP + poly C : two-stranded helix | - | 1682 | 1652 | 1622 | 1581<br>1586 |
| 5'-dGMP + 2poly C : three-stranded helix | 1707 | 1687 | 1656[a] | 1623 | 1582<br>1565 |
| GpGpGp + poly C ; two-stranded helix | - | 1679 | 1650 | 1621 | 1581<br>1561 |
| GpG + 2poly C : three-stranded helix | 1707 | 1684 | 1655[a] | - | 1580<br>1568 |

* Values taken from ref. 35.
† 5'-dGMP, deoxyguanosine-5'-phosphate.
Poly C, polycytidylic acid.
GpGpGp, guanylyl-(3',5')-guanylyl-(3',5')-guanosine-3'-phosphate.
GpG, guanylyl-(3',5')-guanosine.
a Predominantly $\nu(C{=}O)$ in both protonated and unprotonated cytosines.

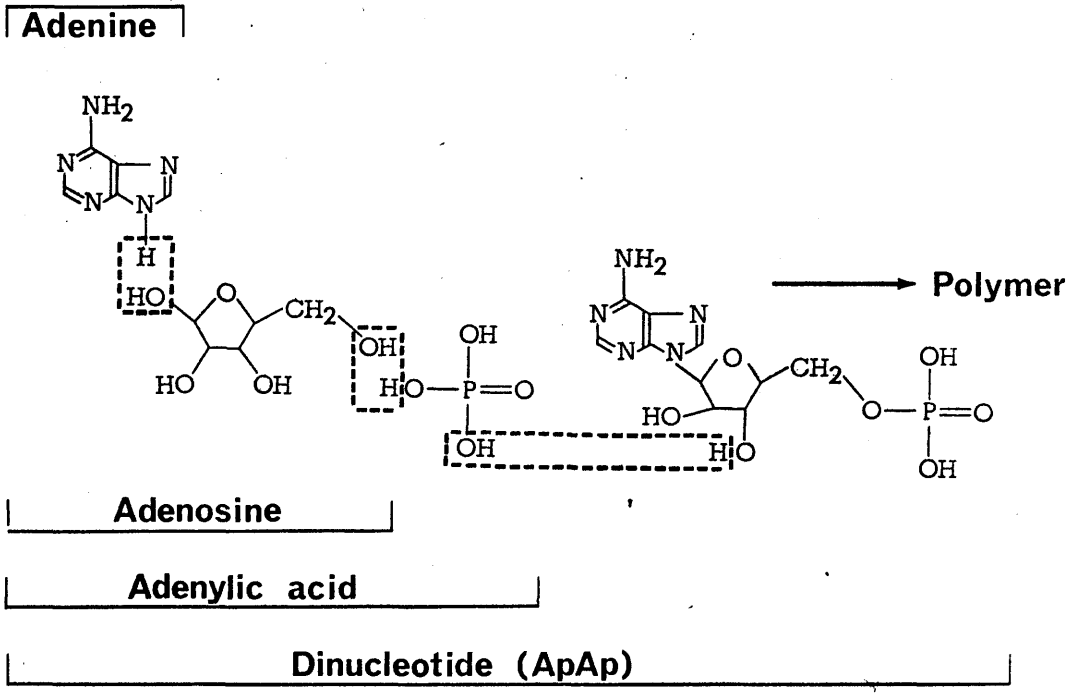



FIGURE 1. Nucleic acids (3 stages). RNA shown. DNA lacks the hydroxyl group in the sugar ring at position 2'.

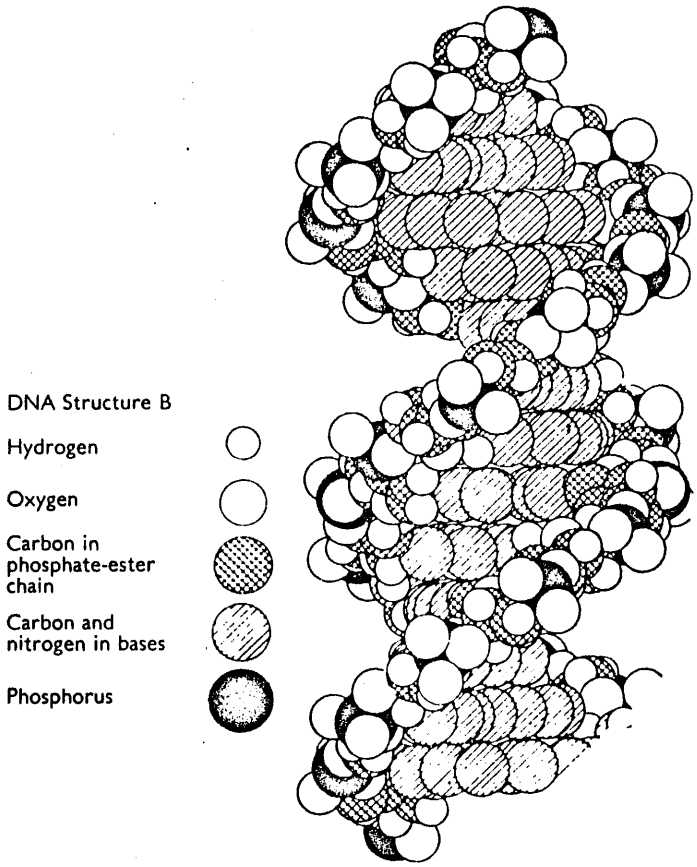



**FIGURE 2.** **Double helix configuration of DNA. (Reproduced from an original drawing by Prof. M.H.F. Wilkens F.R.S.).**

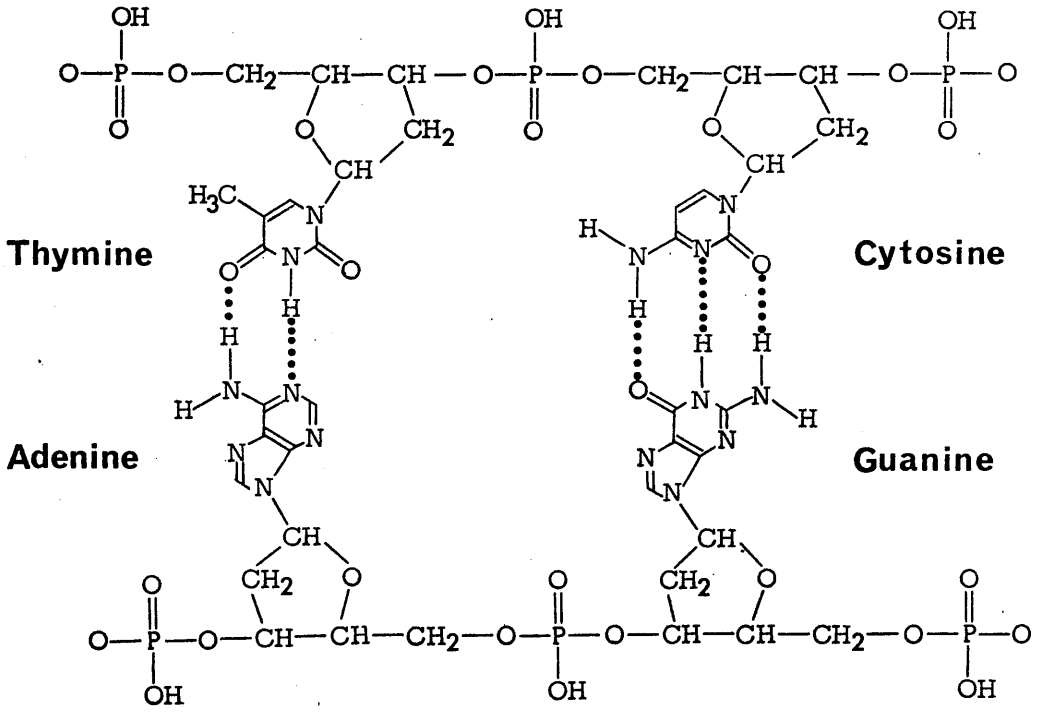



**FIGURE 3.** **Base pairing scheme in the double helical structure of DNA.**

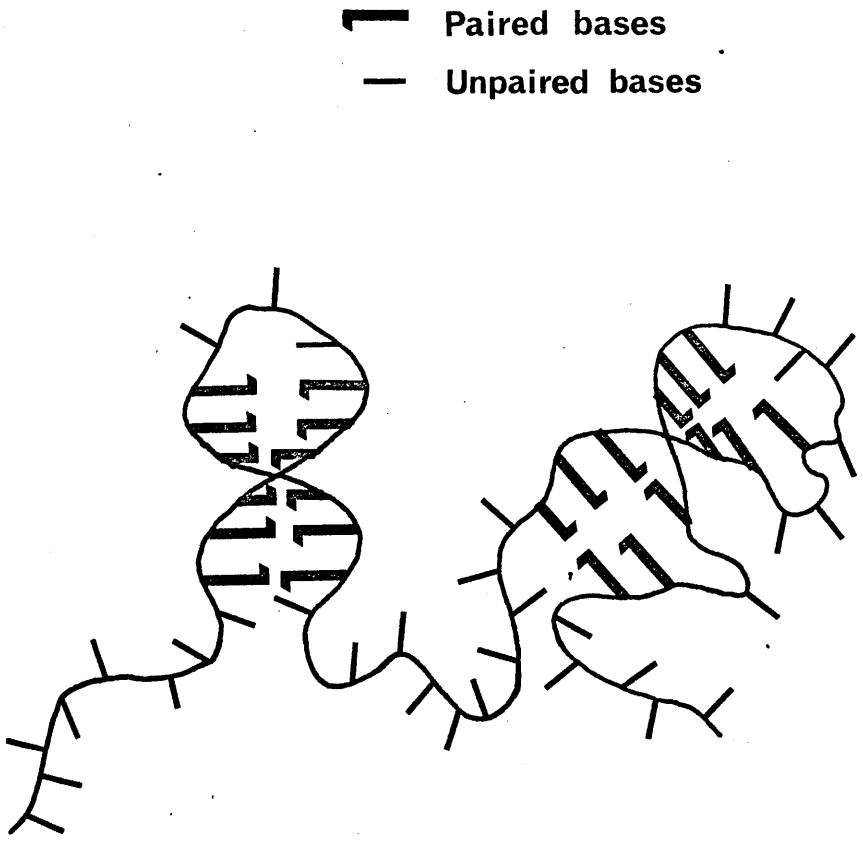



FIGURE 4. A schematic diagram of the secondary structure of RNA.

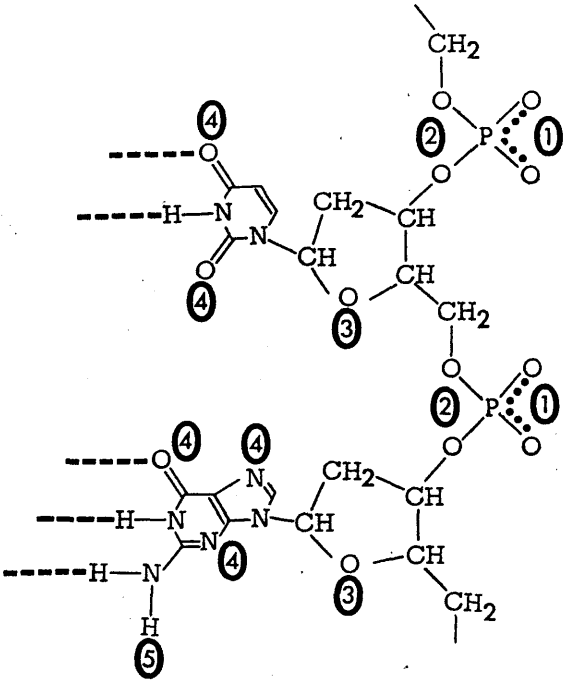
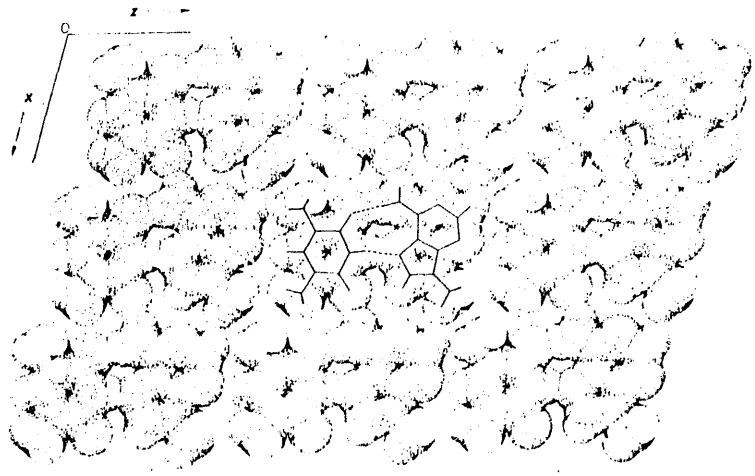
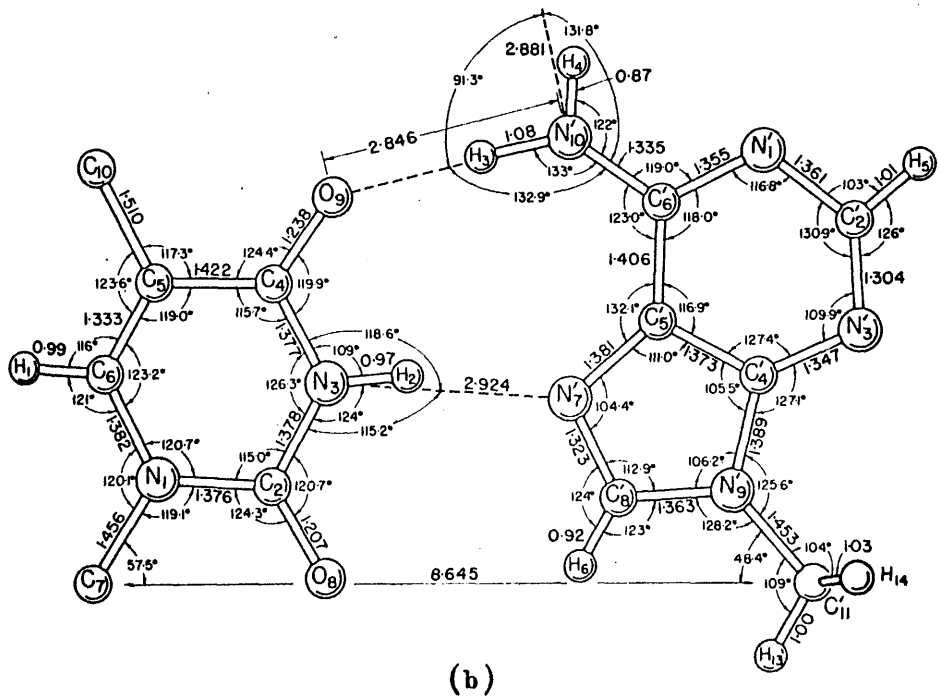


FIGURE 5. A schematic drawing of one strand of DNA containing thymine and guanine bases indicating sites for possible water adsorption. (Redrawn from ref. 17).



(a)




(b)

**FIGURE 6.** Hydrogen bonded complex between 1-methylthymine and 9-methyladenine. (a) packing of the base pairs in a layer parallel to (010). (b) the molecular dimensions of the base pair. (Reproduced from ref. 22).

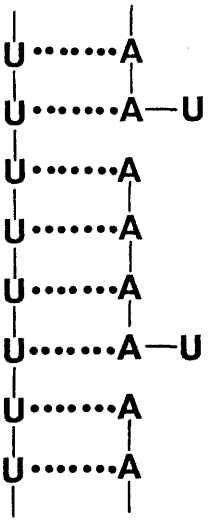



FIGURE 7. Two-stranded complex involving polyuridylic acid and pApApApAU. The non-matching uridylic acid residue of pApApApAU does not occupy a position in the helix. (Redrawn from ref. 26).

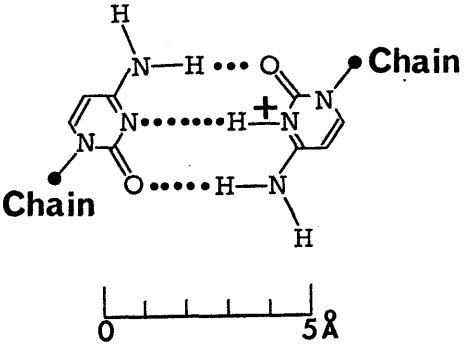



**FIGURE 8.** Proposed hydrogen bonding between cytosine bases in polycytidylic acid. The cytosine on the right has an additional proton, as indicated by the + sign. However, the positive charge is probably distributed over the pyrimidine ring. It is likely that alternate bases along a given polymer chain will tend to be prontonated. (Redrawn from ref. 28).

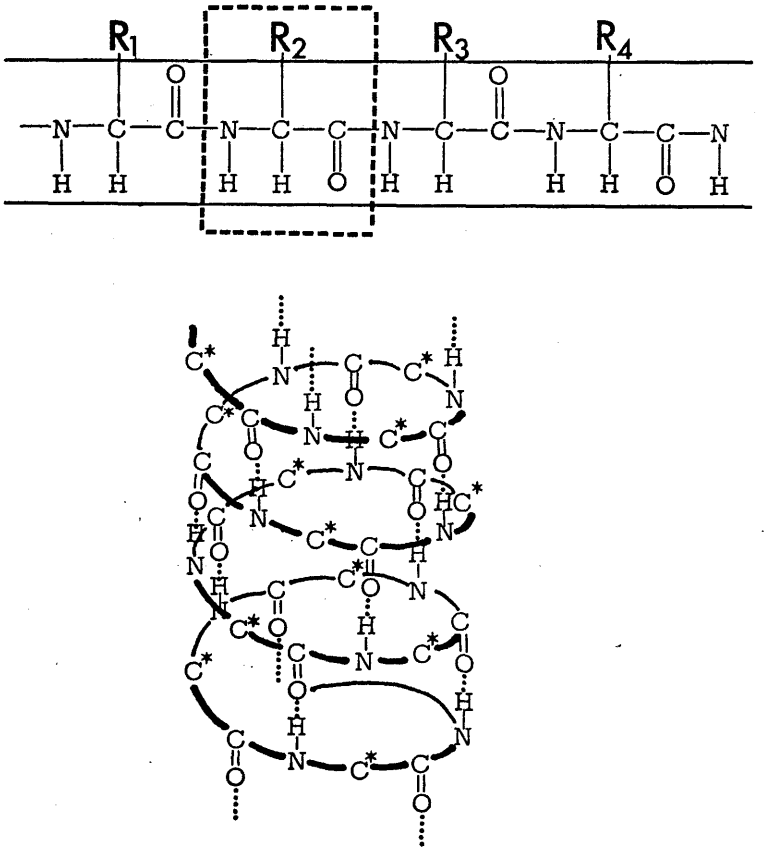
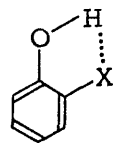



**FIGURE 9.** Schematic diagram of the secondary structure of a polypeptide adopted through inter-amide hydrogen bonds.

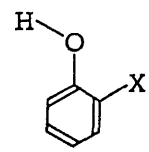
# HYDROGEN BONDING IN PHENOLS

## HISTORICAL

The first case of intramolecular hydrogen bonding to be studied spectroscopically was that of the 2-halophenols. PAULING[37] interpreteted the appearance of two hydroxyl stretching frequencies to an equilibrium between possible "cis" and "trans" forms,




"cis"




"trans"

the high frequency band resulting from the "trans" form, while the lower bonded frequency band was due to the intramolecularly hydrogen bonded "cis" form. In recent times BAKER[38] has re-investigated a series of halophenols and his results can be summarized as follows:

| Halogen | $\Delta\nu$(OH) cm.$^{-1}$ | $\varepsilon_b/\varepsilon_f$ |
|---|---|---|
| F | 20 | - |
| Cl | 58 | 0.56 |
| Br | 74 | 0.38 |
| I | 93 | 0.14 |

$\Delta\nu$ = $\nu$(OH) free - $\nu$(OH) bonded.

He observed that the concentration of the bonded "cis" form decreases on going from fluorine to iodine ( from $\varepsilon_b/\varepsilon_f$ values ). Another group of workers,[39] however, has also made a study of

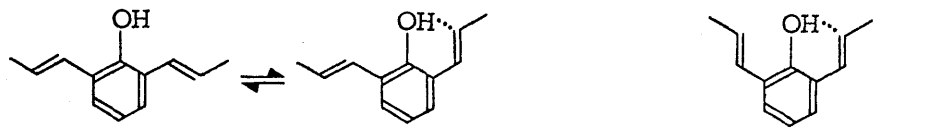
2-halophenols and their results suggest that the order of strength of the intramolecular hydrogen bonds formed is F > I > Br > Cl.

BROWN et al.[40] have made a study of the buttressing effect of alkyl groups on the 3- and 6-position in 2-bromophenols. In the case of 2,4-dibromophenol and 2,4-dibromo-6-methylphenol the bonded frequency is 3528 $cm.^{-1}$. Introduction of a 6-t-butyl group into such a system shifts the frequency of the bonded band to 3509 $cm.^{-1}$. Further substitution in the 3-position by a methyl group causes the frequency to shift to 3500 $cm.^{-1}$. In this study, therefore, noticeable buttressing effects occur only when bulky alkyl groups like t-butyl are introduced next to the hydroxyl, thereby enforcing the hydroxyl group to point towards the adjacent bromine atom in the 2-position. A similar situation has been observed in a study of 2-nitrophenols.[41]

An interesting contribution to conformational analysis of phenolic compounds emerged from a study of 2-aminophenol and 2-dimethylaminophenol by BAKER and SHULGIN.[41] The spectrum of 2-aminophenol showed only a single free hydroxyl absorption, while that of 2-dimethylaminophenol exhibited a single broad bonded absorption ($\Delta\nu$=245 $cm.^{-1}$). In the case of 2-aminophenol the free electron pair orbital is perpendicular to the aromatic nucleus, a situation which is very unfavourable for hydrogen bonding. Introduction of methyl groups on the nitrogen atom, however, brings about steric interactions and the methyl groups take up skew arrangements with respect to the phenyl ring. This situation now brings the electron lone pair on the nitrogen into a position suitable for intramolecular hydrogen bonding.

OKI et al.[42] have studied restricted rotation in 2-propenyl-phenols. The spectrum of 2,6-dipropenylphenol exhibits two hydroxyl stretching frequencies (3603 and 3546 $cm.^{-1}$) indicating

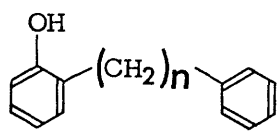
freedom of rotation of the trans-propenyl groups. The spectrum of the corresponding 3,5-dimethyl-2,6-dipropenylphenol, however, exhibits only a bonded hydroxyl band (3526 cm.$^{-1}$) suggesting that



3603 3546 3526 cm.$^{-1}$

the methyl groups in the 3- and 5-position effectively hinder free rotation of the propenyl groups and enforce an intramolecular hydrogen bonded conformation.

In the case of 2-(phenylalkyl)phenols OKI et al.[43] found that for phenyl group devoid of any electron releasing or attracting

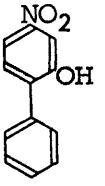


| | $\Delta\nu$ |
|---|---|
| n = 0 | 42 |
| = 1 | 51 |
| = 2 | 61 |
| = 3 | - |

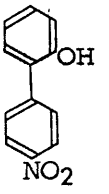
substituents, intramolecular interaction is limited to those ortho-phenylalkylphenols with not more than two separating methylene groups, i.e. n=0, 1, 2.

WULF, LIDDEL and HENDRICKS[44] were the first to note split absorption of the hydroxyl stretch first overtones in 2-hydroxydiphenyl. OKI et al.[45] demonstrated that the interaction must be of the OH$\cdots\pi$ type by studying the effect of a para-nitro group on the acidity of the phenolic hydroxyl in 2-hydroxy-4-nitrodiphenyl and on the basicity of the non-phenolic ring in 2-hydroxy-4'-nitrodiphenyl. The expected enhancement and suppression of the intrabonded forms were observed.

$\nu_f$ = 3597
$\nu_b$ = 3554
$A_b/A_f$ = 13




$\nu_f$ = 3601
$\nu_b$ = 3579
$A_b/A_f$ = 1




In 2,2'-dihydroxydiphenyl two bonded $\nu$(OH) absorptions are observed ($\Delta\nu$=43 and 103 cm.$^{-1}$).[46] The OH····$\pi$ interaction accounts for the band with $\Delta\nu$(OH)=43 cm.$^{-1}$. The other bonded form is an OH····OH interaction. This latter bonded form occurs to a much lesser extent than the OH····$\pi$; the conformation responsible may provide some degree of strain although the $\Delta\nu$ value is greater.

# INTRODUCTION

Conformational analysis of fairly rigid molecules such as those of the steroids and triterpenoids is well established, but comparatively little attention has been given to the stereochemistry of more flexible systems and of molecular aggregates in solution. In the present study two main types of flexible phenolic compounds have been examined, namely, the polynuclear novolaks and o-hydroxy-depsides.

The availability[47] of a number of polynuclear phenols of the novolak type (flexible molecules, in which the phenolic nuclei are linked by methylene bridges) has enabled a study of their hydroxyl stretching absorptions under conditions of high resolution. These molecules assume well-defined intramolecularly hydrogen bonded conformations both as monomers and, in certain cases, as intermolecularly hydrogen bonded dimers.

As an extension of the study of conformational analysis of flexible systems the infrared spectra of o-hydroxy-depsides and related compounds have been studied to determine the extent of the interaction of the hydroxyl group with the ester linkage. A reaction of value in determining the structure of gallotannins is methanolysis[48] whereby these o-hydroxy-depsides are split at the ester linkage by methanol at neutral pH. This section of the work was undertaken in collaboration with Prof. R.D. Haworth and Dr. E. Haslam of the Department of Chemistry, University of Sheffield.

The experimental approach[49] distinguishes non-bonded from bonded hydroxyl groupings by comparing the lowered hydroxyl stretching absorption frequency of the latter with the non-bonded

value of about 3600 $cm.^{-1}$. Further, hydroxyl absorptions frequencies due to intermolecular hydrogen bonds differ from those pertaining to the intramolecular type in being dependent on concentration, and the number of non-bonded hydroxyl groupings may be inferred from the intensity of the 3600 band relative to the intensity of the same band in simple phenols.[50] Certain stereochemical requirements have to be met by conformations for which reasonably strong ($\nu_{OH}$ ca. 3300 $cm.^{-1}$) hydrogen bonds involving phenolic hydroxyls are postulated: approximate co-planarity of the C-O-H bond with the benzene ring;[50] an O····O distance of approximately 2·7 Å; and the hydrogen atom must lie somewhere near a line joining the two oxygens. [The exact positioning is not certain. The lone pairs on the receptor oxygen probably induce a pseudo-tetrahedral disposition with respect to the latter, though there is likely to be more trigonal character in phenolic bonding than that of alcohols owing to electron delocalization involving the aromatic nucleus.] The weaker, OH····benzene ring, type of hydrogen bond is unlikely to compete, except in unusual steric situations.

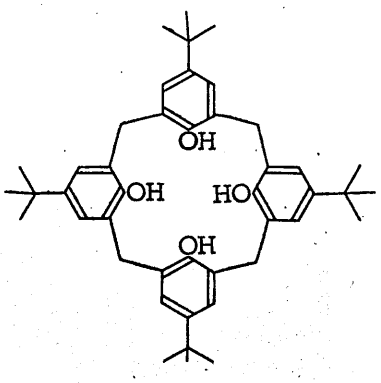
# RESULTS and DISCUSSION

The results are presented in three parts - first of all, the general survey of the polynuclear novolaks leading on to a detailed study of a series of alkyl substituted dinuclear novolaks and finally the work on the pyrocatechol monoesters and related compounds.

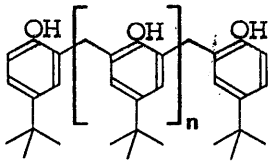
## Polynuclear Novolaks

The cyclic tetranuclear novolak (1) represents, perhaps, the simplest case of those listed in Table 2 and illustrated in Figure 10. From an examination of the Dreiding model, it would appear that the most stable conformation should be that having a closed ring of hydrogen bonds, with each of the hydrogen atoms between two oxygen atoms as indicated diagrammatically (C in Figure 11). The absorption data are in complete accord as the only hydroxyl absorption in dilute carbon tetrachloride solution is the broad, intense, symmetrical band near 3200 $cm.^{-1}$ (Figure 10a) which was concentration independent over the range examined ( since a closely similar band was observed in the solid state, the crystal may well consist of an array of such basin-shaped molecules). Most interestingly, the acyclic tetra-, penta- and hexa-nuclear novolaks (2, n=2, 3, and 4) absorb in a similar manner and it would seem, therefore, that in solution these molecules exist as the 'cyclic' intramolecularly hydrogen bonded monomers D, F and G, respectively (Figure 11). The similarity in absorption pattern of the cyclic (1) and acyclic (2,n=2) tetra-nuclear novolak is illustrated in Figure 10a. The increased width and asymmetry of the band of the latter compound is probably a result of the increased mobility of the molecular backbone. Dimeric association at the low concentrations examined is conceivable but unlikely in view of the ease with which the models of the monomers can be induced to

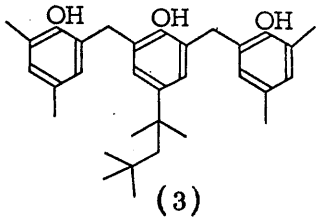
take up the conformations illustrated (Figures 11 and 12).



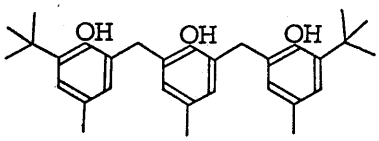

(1)




(2, n=0-4)




(3)




(4)

Unlike the preceding compounds, the di- and tr-nuclear novolaks (2,n=0 and 1) show concentration dependent absorptions implying the existence of self-association even at very low concentrations. This behaviour (Table 2 and Figure 10b,c) is almost certainly due to monomer-dimer equilibria and arises from the inability of the di- and tri-nuclear monomers (A and B, respectively in Figure 11) to form closed rings of hydrogen bonds in the manner already discussed for the monomers of the tetra-, penta- and hexa-nuclear compounds (D, F and G, respectively). Examination of Dreiding models suggests that relatively unstrained closed rings of hydrogen bonds are possible for the di- and tri-nuclears dimers, the former species (E) being closely analogous to the tetranuclear compound (D), and the latter (H) to the hexanuclear compound (G). Although both E and H apparently persist to very low concentrations (about 1 mM), the trinuclear dimer (H) seems the more strongly associated on the grounds of both $\nu_{max}$ and the relative intensities of the monomer and dimer

bands. The measurement of molecular weight in solution at these concentrations would have helped considerably, but unfortunately no further supplies of the novolaks for which dimerization is posulated were available.

The effect of ortho-substitution of the terminal rings of the trinuclear novolak has been examined. As anticipated, introduction of the methyl groupings (compound 3, Figure 10b,c) greatly reduced dimer formation, while no dimer at all could be detected in fairly concentrated solution of the di-t-butyl compound (4). Models of the type H dimer of compound (3) show pronounced interaction between the ortho methyls and it is conceivable that other cyclic conformations (for example, I and J), where some of the benzene rings are orientated in opposing senses and the methyl groups are directed away from each other, may be more stable.

The absorptions ascribed to the monomers (species B) of the three trinuclear novolaks merit some comment. First, the trend in the free hydroxyl frequencies: no ortho substitution 3596, ortho methyl 3606 and ortho t-butyl 3622 $cm.^{-1}$. The values for the corresponding cis-conformations (OH directed towards the alkyl grouping) of single ortho-alkyl substituted phenols[50-53] are 3612, 3621 and 3647 $cm.^{-1}$, respectively. [The ortho methyl value given is that for 2,6-dimethylphenol since only a single unresolved band at 3613 $cm.^{-1}$ is observed for 2-methylphenol itself.] The lower values of the novolak monomers undoubtedly register the electronic effect[54] of the intramolecular hydrogen bond on the terminal hydroxyl. The same effect can be detected in the data given by COGGESHALL[55] and GODDU.[56] Secondly, the broad bands assigned to the intramolecular bonded hydroxyls show some sign of sub-structure and indeed, frequency differences might be expected between the two hydroxyl groups involved. KUHN and BOWMAN[57] sought an indication of such behaviour in their somewhat parallel study of simple acyclic triols.

It is interesting to compare the hydrogen bonding shifts, $\Delta\nu$, for the monomers of the series of novolaks (2,n=0,1,2,3, and 4) given in Table 3. The considerable increase in $\Delta\nu$ on going from (2,n=1) to (2,n=2) must certainly reflect the increased effectiveness resulting from the formation of the cyclic system (D) of hydrogen bonds. The simple addition of a fourth oxygen to the first three would otherwise be of little consequence. Numerous workers[49-51,57] have discussed the nature of the association equilibria present in solutions of alcohols and of phenols. Both cyclic (for example, K) and acyclic (for example, L) hydrogen bonded species have been proposed. In the case of phenol itself the bands at 3485 and 3350 $cm.^{-1}$ (Table 2) are generally held to be due to dimers (L) and trimers, respectively, and on steric grounds it seems likely that the latter might well be cyclic (K). On the other hand, the hydroxyl region of a concentrated (2·5 M) solution of phenol in carbon tetrachloride closely resembles that of a very dilute solution (Figure 10c) of a trinuclear novolak where the acyclic monomer predominates, and it is tempting to propose that the phenol trimer is also acyclic. This argument is unsatisfactory, however, as the novolaks are more closely analgous to the ortho alkyl substituted phenols for which different values for $\nu_{OH}$[dimer] and $\nu_{OH}$[trimer] are quoted.[50,53] In fact, the $\Delta\nu$ values for phenol are dimer, (equivalent to species A, Table 3) 126 $cm.^{-1}$ and trimer 261 $cm.^{-1}$. The relatively large increase from 126 to 261 $cm.^{-1}$ is a strong indication that the band centred at 3350 $cm.^{-1}$ is mainly due to cyclic trimer. Acyclic trimer or higher polymers may well be present, but a cyclic tetramer could not be a major contributor.

TABLE 2

Hydroxyl Stretching Frequencies, $\nu$(OH) in Carbon Tetrachloride

| Compound | Results at two different concentrations | | | | | | | | | | Assignments | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Conc. (mM) | Cell path (mm) | $\nu$ ($cm^{-1}$) | $\Delta\nu^{a}_{1/2}$ ($cm^{-1}$) | $\epsilon^{a}$ | Conc. (mM) | Cell path (mm) | $\nu$ ($cm^{-1}$) | $\Delta\nu^{a}_{1/2}$ ($cm^{-1}$) | $\epsilon^{a}$ | Hydrogen bonding | Hydroxyls involved | Species Fig. 11 |
| 1 | 0·27 | 20 | 3,200 | (190) | 670 | Concentration independent | | | | | Intra | 4 | C |
| 2, n=2 | 0·32 | 20 | 3,215 | (280) | 440 | Concentration independent | | | | | Intra | 4 | D |
| n=3 | 0·30 | 20 | 3,200 | (280) | 610 | Concentration independent | | | | | Intra | 5 | F |
| n=4 | 0·20 | 20 | 3,190 | (280) | 650 | Concentration independent | | | | | Intra | 6 | G |
| n=0 | 25·80 | 0·5 | 3,606 | 26 | 60 | 0·7 | 20 | 3,606 | 28 | 155 | Free | 1) | A |
| | | | 3,470 | sh | - | | | 3,470 | (110) | 110 | Intra | 1) | |
| | | | 3,260 | (260) | 175 | | | 3,250 | - | 65 | Inter | 4 | E |
| n=1 | Sat. Soln. | 0·5 | | | | 0·49 | 20 | 3,596 | 36 | 80 | Free | 1) | B |
| | | | | | | | | 3,394 | - | 110 | Intra | 2) | |
| | | | 3,220 | br | - | | | 3,220 | (230) | 290 | Inter | 6 | H |
| 3 | 16·20 | 0·5 | 3,606 | 40 | 110 | 0·47 | 20 | 3,606 | 28 | 120 | Free | 1) | |
| | | | 3,520 | sh | - | | | 3,520 | sh | - | | ) | B |
| | | | 3,390 | - | 220 | | | 3,400 | (180) | 200 | Intra | 2) | |
| | | | 3,220 | - | 160 | | | | | | Inter | 6 | H |
| 4 | 15·50 | 0·5 | 3,622 | 25 | 165 | Concentration independent | | | | | Free | 1) | |
| | | | 3,520 | sh | - | | | | | | | ) | B |
| | | | 3,350 | (190) | 240 | | | | | | Intra | 2) | |
| Phenol | 2,500 | 0·05 | 3,611 | 19 | - | 100 | 0·51 | 3,611 | 19 | - | Free | 1) | L |
| | | | | | | | | 3,485 | - | - | Inter | 1) | |
| | | | 3,350 | (280) | - | | | | | | Inter | 3 | K(?) |

Values in parentheses are approximate; - not measured; sh. shoulder, br, broad band.

TABLE 3.

$\Delta\nu$ Values for the Novolaks 2, n = 0, 1, 2, 3, and 4.

| n | 0 | 1 | 2 | 3 | 4 |
|---|---|---|---|---|---|
| Species assigned (Figure 11) | A | B | D | F | G |
| No. of hydroxyls involved | 2 | 3 | 4 | 5 | 6 |
| $\Delta\nu$ cm.$^{-1}$ | 141 | 217 | 397 | 411 | 421 |

$\Delta\nu = \nu_{OH}[\text{non-bonded}] - \nu_{OH}[\text{bonded}]$.
$= 3611 - \nu_{OH}[\text{bonded}]$.

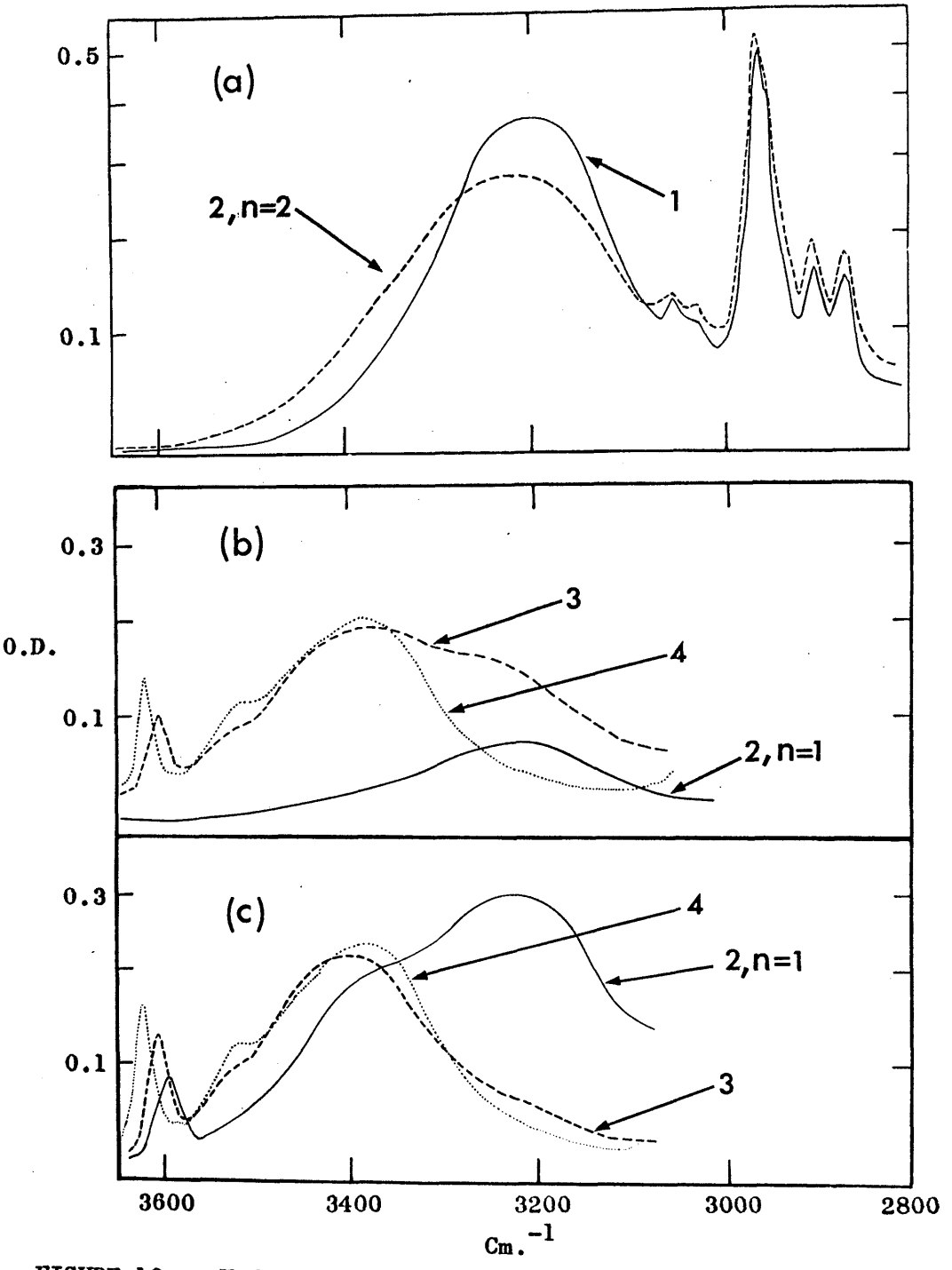



FIGURE 10. Hydroxyl stretching absorptions in carbon tetrachloride of the novolaks 1, 2 (n=1 and 2), 3, and 4. Concentrations: (a) ca. 0.3 mM; (b) ca. 15 mM except for 2 (n=1) saturated solution; and (c) ca. 0.5 mM. Cell paths: (a) 20 mm.; (b) 0.5 mm.; and (c) 20 mm.

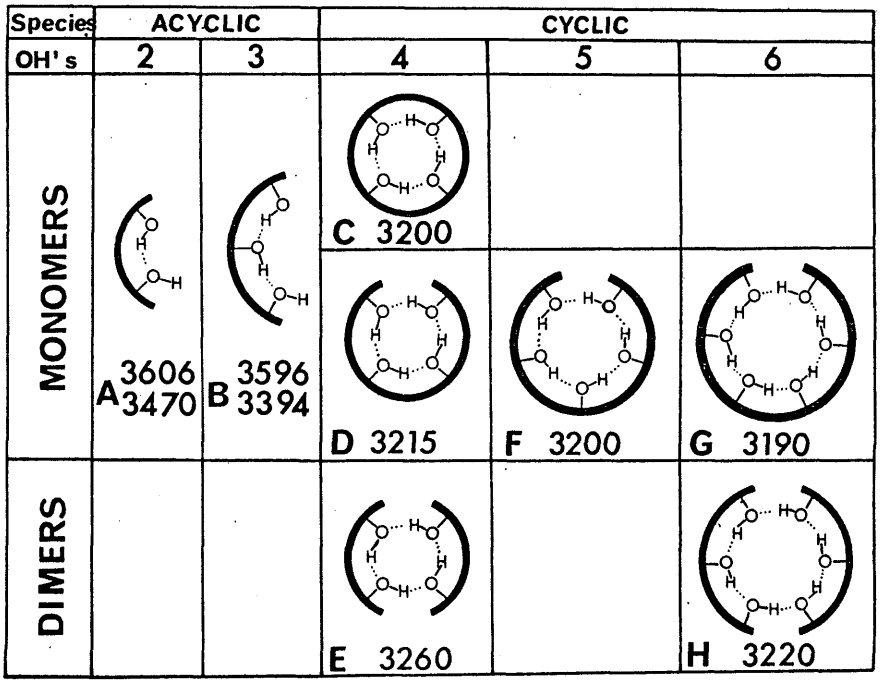
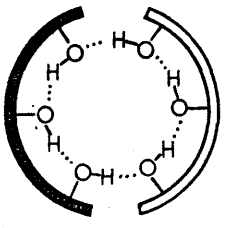
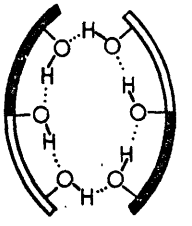



FIGURE 11. Summary of assignments for the novolaks (1) and (2, n=0-4). Values quoted are the frequency measurements in $cm.^{-1}$.



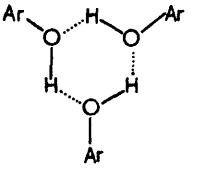
I



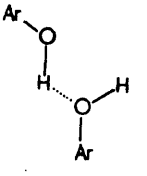
J

▮ Indicates the C-H bonds of the methylene groups directed upwards.

▯ Indicates the C-H bonds of the methylene groups directed downwards.



K



L

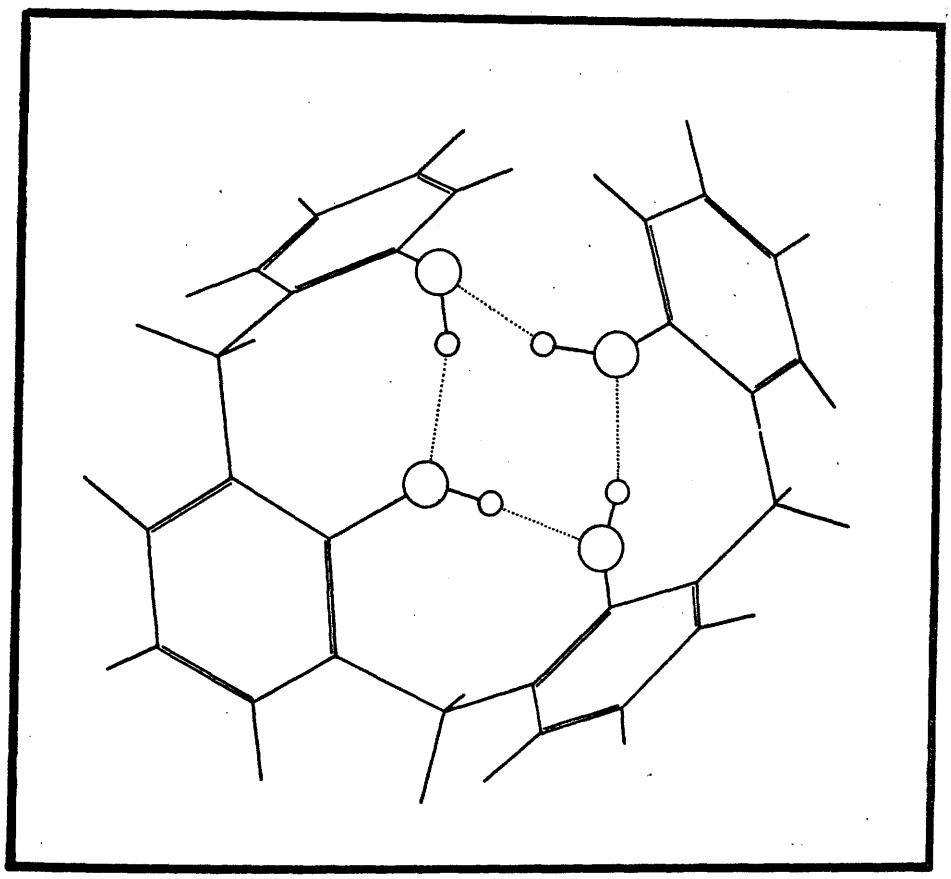
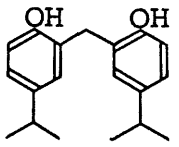


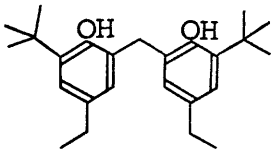
FIGURE 12. Planar projection of the Dreiding molecular model of the postulated conformation (D) of the acyclic tetranuclear novolak (2, n=2). The large and small circles indicate the oxygen and hydrogen atoms of the hydroxyl groups respectively. The dotted lines indicate hydrogen bonds. The para-t-butyl groups have been omitted.

## Alkyl Substituted Dinuclear Novolaks

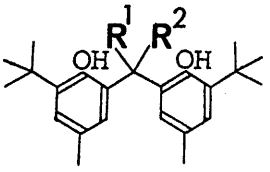
COGGESHALL[55] and, later GODDU[56] have examined the hydroxyl stretching region of a number of alkyl substituted dinuclear novolaks (bis-phenylol alkanes) related to (2, n=0) but the concentration and frequency ranges covered were narrow and these workers did not elucidate the monomer-dimer relationships established in the previous section on polynuclear novolaks. However, it is clear from COGGESHALL'S data for an ortho-di-t-butyl substituted novolak that dimeric association is absent in quite concentrated (0·5 M) solutions in carbon tetrachloride (cf. 2, n=0). The cis and trans forms postulated by COGGESHALL[55] to explain the non-bonded and bonded hydroxyl absorptions are now unnecessary, but the peculiar effect reported[55,56] for the dinuclear novolaks substituted on the central aliphatic carbon requires elucidation.




(5)




(6)




(7)

a, $R^1=R^2=H$; b, $R^1=H$, $R^2=CH_3$; c, $R^1=H$, $R^2$=cyclohexyl; d, $R^1=H$, $R^2$=phenyl; e, $R^1=R^2=CH_3$; f, $R^1=CH_3$, $R^2$=Et.

Four alkyl substituted dinuclear novolaks (5, 6, 7b and 7e) have been compared. Compound (5) is representative of the type of dinuclear novolak already discussed in the previous section of this thesis when it was found that in the absence of ortho substituents OH····OH intra-bonding is dominant at low concentrations, but is superceded by dimerisation (involving a complete ring of four hydrogen bonded hydroxyls) at higher concentrations. The ortho-di-

substituted dinuclear novolak (6) exemplifies the type of heavily hindered phenol for which intermolecular association is difficult, and which permits an assessment of the competing intramolecular situations. In the isomeric, but more heavily hindered dinuclear novolak (7e), this latter situation is further emphasised. The degree of substitution of novolak (7b) is of intermediate extent.

Compound (5) [Table 4, Figure 13] shows the presence of three hydroxyl absorptions in $CCl_4$. Following the previous results the band at 3476 $cm.^{-1}$ is assigned to an intramolecular OH····OH hydrogen bond; the appearance of an unhindered hydroxyl group at 3611 $cm.^{-1}$ ($\varepsilon^a$ approximately equivalent to that for one phenolic OH group) adds support to this assignment. The broad, concentration dependent, band at 3300 $cm.^{-1}$ is assigned to the closed ring of hydrogen bonds which results from dimeric association in the manner already discussed. In chloroform solution where some interaction with the solvent is to be expected the absorption bands (Table 4, Figure 13) broaden and decrease in frequency and the amount of interbonding is reduced.

Compound (6) [Table 4, Figure 13] has a more complex spectrum, though introduction of the ortho-di-t-butyl groups prevents self-association. The shoulder at 3450 $cm.^{-1}$ (in $CCl_4$) is assigned to the intramolecular OH····OH bond (cf. compound 5, 3476 $cm.^{-1}$). Support for this assignment is adduced from the presence of the absorption at 3639 $cm.^{-1}$ (in $CCl_4$), which is characteristic of a hindered free hydroxyl group where the OH group is directed towards a t-butyl group ($\varepsilon^a$ equivalent to approximately half that for one free hydroxyl[50]). The sharper band at 3516 $cm.^{-1}$ is assigned to an intramolecular OH····benzene ring (OH····$\pi$ type) hydrogen bond. OKI and IWAMURA[58] have already shown that this sort of bonding situation pertains in ortho-hydroxydiphenylmethane (o-benzylphenol), where (in $CCl_4$) the OH····$\pi$ bond absorbs at 3560 $cm.^{-1}$

with $\Delta\nu_{\frac{1}{2}}^{a} \approx 56$ cm.$^{-1}$. The unsubstituted phenyl ring is formally more free to rotate than the corresponding heavily substituted benzene ring of compound (6), but the band is about the same width.

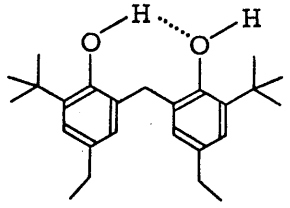
Several conformers may be in equilibrium. Thus for $CCl_4$, the following conformations might be present:-

6(i) A conformer involving an intramolecular OH····OH hydrogen bond (3450 cm.$^{-1}$) with the 'free' hydroxyl group (3639 cm.$^{-1}$) directed towards the ortho-t-butyl group.

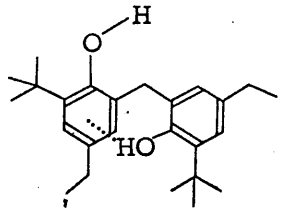
6(ii) A conformer involving an intramolecular OH····π hydrogen bond (3516 cm.$^{-1}$) with the other hydroxyl group free, but not necessarily directed towards the ortho-t-butyl group (this would explain the slight shoulder at 3620 cm.$^{-1}$).

6(iii) A conformer involving two similar intramolecular OH····π bonds (3516 cm.$^{-1}$).

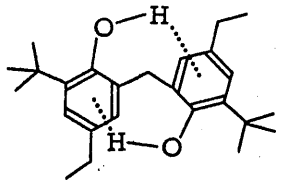
6(iv) A conformer with both hydroxyls free (3639 cm.$^{-1}$ and 3620sh cm.$^{-1}$).



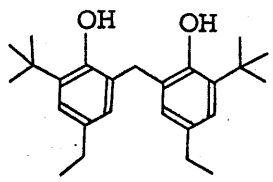
6(i)



6(ii)



6(iii)



6(iv)

The conformer(s) involving the intramolecular OH····π type of hydrogen bond is favoured in $CCl_4$ (according to $\varepsilon^a$ values). In n-hexane solution, however, this conformation is more favoured as can be seen by the increased intensity of the band at 3517 $cm.^{-1}$ (Figure 13) at the expense of the other absorption bands. It is interesting that the frequency of this band is practically the same in all three solvents (Table 4). This fact gives support to conformer 6(iii) since the π-bonded hydroxyl groups in this conformation would be relatively inacessible to solvent molecules. This trend of solvent behaviour might be anticipated on the grounds that non-polar solvents will favour conformations in which alkyl groups are directed towards the solvent cage and polar groups such as hydroxyls are directed into the interior of the molecule. The reverse situation would apply in polar solvents such as $CHCl_3$ and the exposed OH····OH arrangement could be directly solvated by chloroform molecules. In summary, therefore, the intramolecular OH····π hydrogen bonded conformation(s) of 6 is strongly favoured in n-hexane, but is less favoured in $CCl_4$ and especially $CHCl_3$, but the exact constitution of the equilibrium mixture remains in doubt.

Compound (7b) [Table 4, Figure 13] exhibits only two hydroxyl absorptions in n-hexane, $CCl_4$ and $CHCl_3$. The high frequency band, which must correspond to a free hydroxyl directed towards an ortho-alkyl group[50], falls in frequency but increases in intensity on going from n-hexane through $CCl_4$ to $CHCl_3$. The second band is assigned to an intramolecular OH····π hydrogen bond of the type already discussed for compound (6), though the band is shifted to a slightly lower frequency. The intensity data require that the dominant conformer in n-hexane and $CCl_4$ is the doubly OH····π hydrogen bonded system [cf. 6(iii)]. The free hydroxyl absorption must arise from conformer(s) corresponding to 6(ii) and 6(iv).

Finally, compound (7e), the most heavily substituted of the four novolaks studied in this section, has a single intense $\nu_{OH}$ absorption (Table 4, Figure 13). The bulky ortho alkyl substituents prevent intermolecular association at all concentration levels as was fully confirmed by molecular weight estimation in $CCl_4$. The molecular weight (vapour pressure method) was found to be 367 ± 5 (theoretical 368). The single narrow absorption band at 3484 $cm.^{-1}$ indicates that both hydroxyls must be similarly hydrogen bonded intramolecularly to the adjacent benzene rings [cf. 6(iii)]. The only other possiblity would be the arrangement, already suggested by COGGESHALL[55] for these compounds, which involves paired hydroxyls, $\overset{\text{O-H}}{\underset{\text{H-O}}{\cdot\cdot}}$. However, such an association would seem to have no precedent and is, in any case, sterically impossible without twisting the OH bonds out of the plane of the benzene rings. The narrowness of the absorption band [40] at 3484 $cm.^{-1}$, as observed in all solvents, implies a rigid[58] well-defined complex. The only conformation which would seem to fit the data is illustrated in Figure 14. Methyl substitution of the central aliphatic carbon (6→7b→7e) evidently interferes sterically with the formation of the OH····OH intramolecular hydrogen bond. Examination of the Dreiding model of (7e) shows that one of these methyl groups rotates into the line of the OH····OH intra bond as the O·····O distance nears 2·7 Å. On the other hand, these bridge methyls are quite distant in the OH····π bonded conformer (Figure 14).

Some data for novolaks of type (7) [including (7b) and (7e) discussed above] have been recorded by COGGESHALL[55] and later GODDU[56] (Table 5). In view of the present results the bonded band in each case can be assigned to an OH····π intramolecular hydrogen bond. From the data in Table 5 it would seem that a single bulky substituent such as cyclohexyl (7c) is sufficient to enforce complete OH····π bonding.

Literature data (in $CCl_4$) for three OH····π intramolecularly bonded compounds[58,59] and data for compounds (7b) and (7e) are presented in Table 6. A reference point is provided by WEST[60] for phenol in benzene as solvent (3564 $cm.^{-1}$; the bonding shift, $\Delta\nu$ = 47 $cm.^{-1}$). The absorption characteristics displayed by compound (7e) - the bonding shift ($\Delta\nu$ = 163 $cm.^{-1}$), the half-band width ($\Delta\nu^a_{\frac{1}{2}}$ = 22 $cm.^{-1}$), and the integrated absorption intensity ($A \times 10^{-4}$ = 9.8) - can only be explained by a particularly well-defined and relatively strongly bonded conformation (Figure 14) with a very limited range of internal movement. It is especially interesting that the total integrated absorption intensities, $A \times 10^{-4}$, per hydroxyl for (7b) and (7e) are respectively 3 and 4 times that observed for the other compounds.

To test the stability of this rigid conformation adopted by compound (7e) all four novolaks (5, 6, 7b and 7e) have been examined in basic solvents. In diethyl ether (Table 7) compounds (5), (6) and (7b) exhibited very broad bands centred around 3350 $cm.^{-1}$ as expected for $OH\cdots O(Et)_2$ intermolecular association, though in the case of compound (7b) the 3484 $cm.^{-1}$ band remained to some extent. Compound (7e), however, showed only the sharp intense band at 3483 $cm.^{-1}$, demonstrating that the intramolecularly hydrogen bonded conformation (Figure 14) is undisturbed in solution in diethyl ether. Again, when compounds (7b) and (7e) were examined in pyridine, which is a much more basic solvent than diethyl ether, compound (7b) exhibited a very broad band as expected for $OH\cdots NC_5H_5$, i.e. OH····π conformation broken, while compound (7e) still showed a band at 3482 $cm.^{-1}$. It is quite remarkable that the intra-bonded conformation is undisturbed in a solvent which is such a good acceptor for hydrogen bonding, and it is the introduction of the second methyl group which seems to be important. However, the increased half-band width ($\Delta\nu^a_{\frac{1}{2}}$ = 65 $cm.^{-1}$) for (7e) as compared with that in ether ($\Delta\nu^a_{\frac{1}{2}}$ = 24 $cm.^{-1}$) can be explained by some slight degree of interaction with neighbouring pyridine molecules.

The spectra of (7e) in the solid state (KCl disc) and in solution ($CCl_4$) were virtually superposable over the regions examined [(3650-1600 cm.$^{-1}$) and (1500-1000 cm.$^{-1}$)]. Compounds (5) and (6), however, exhibited marked differences, especially in the fingerprint region (new bands and differences in relative intensities). The conformation of (7e) in the crystal is therefore presumed to be the same as that assigned from the solution data (Figure 14).

An attempt has been made, with only limited success, to find further evidence bearing on the conformation adopted by compound (7e) by examining the molecule in other ways (n.m.r., u.v., and g.l.c.). Since this rigid conformation involving two intramolecular OH$\cdots\pi$ hydrogen bonds exists at all concentrations examined (0·1 M to 0·3 mM in $CCl_4$) it was possible to determine the chemical shift of the hydroxylic proton in this conformation by the n.m.r. technique. It was found to be a single sharp, concentration independent, signal at 5·1 tau. Addition of $D_2O$ caused this signal to disappear slowly over a peroid of a few minutes. [It is difficult to draw comparisions with other OH$\cdots\pi$ intra-bonded molecules since they usually require to be recorded at very low levels of concentration to ensure no interbonding present]. There were no marked differences in the u.v. spectra for compound (7e) and other phenols under consideration recorded in cyclohexane paralleling the infrared measurements in n-hexane. Phenols exhibit a high intensity band around 270 m$\mu$ which is assigned to a $\pi \rightarrow \pi^*$ transition. Both 2,6-di-t-butyl-4-methylphenol and compound (5) have twin peaks in this region - 278 and 284 m$\mu$ ($\varepsilon$=2000) and 280 and 285 m$\mu$ ($\varepsilon$=4650), respectively. On the other hand, however, compounds (6) and (7e) each have a single flat-topped peak - 285 m$\mu$ ($\varepsilon$=4650) and 284 m$\mu$ ($\varepsilon$=5100), respectively. COGGESHALL[55], however, has found marked variations in the degree of ionization of the different novolaks in solvents containing dissolved base.

Compound (6) ionizes readily whereas compound (7e) undergoes very little ionization [i.e. less acidic then (6)]. This information is in keeping with the conformation assigned to compound (7e) (Figure 14) where the hydroxyls are protected by steric congestion. The comparative shielding from the environment experienced by the phenolic groups in compound (7e) is further illustrated by the g.l.c. data reported in Table 8. Compound (6), which is isomeric with (7e) but possessing much more exposed phenolic hydroxyls, shows a more than three-fold increase in retention time on changing from the non-polar hydrocarbon phase (Apiezon L) to the highly polar polyester phase (phenyldiethanolamine succinate). By contrast, compound (7e) under the same conditions has the same retention time on both phases: such behaviour is in keeping with inhibition of hydrogen bonding between the phenolic hydroxyls of the solute molecules and the basic sites of the polar phase.

The alkyl substituted bis-phenylol alkanes (5, 6, 7b and 7e) illustrate in rather a clear way how progressively increasing steric congestion can affect the conformations of molecules and their ability to associate intermolecularly with other molecules of the same type or with those of the solvent. Thus:-

(a) The lightly substituted bis-phenylol alkane (5) associates tenaciously to form a ring of four hydrogen bonds (3200 $cm.^{-1}$ in $CCl_4$). In very dilute solution the conformation of the monomer involves a fairly strong OH····OH intramolecular hydrogen bond (3476 $cm.^{-1}$ in $CCl_4$).

(b) Introduction of twin bulky ortho alkyl substituents (6) prevents self-association but not association with basic solvent molecules, such as ether or pyridine. In solvents such as n-hexane, carbon tetrachloride and chloroform the monomer is present as more than one conformer and these involve OH····$\pi$ intra-bonds as well as OH···OH. The least polar solvents (n-hexane > $CCl_4$ > $CHCl_3$) favour the conformers having OH····$\pi$ bonds.

(c) A single methyl substituent (7b) on the central aliphatic carbon greatly increases the dominance of the conformer(s) involving OH····π intra-bonds but the hydroxyls are still capable of association with basic solvents. One remarkable feature is the conformational control exercised by the solvent. In n-hexane compound (7b) must be almost entirely in the completely bonded OH····π conformation [cf. 6(iii)]; in $CHCl_3$ the proportion of conformer(s) with a free hydroxyl is greatly increased at the expense of the OH····π intra-bonded conformation; in $CCl_4$ the effect is intermediate.

(d) Introduction of the final methyl substituent (7e) forces the molecule to adopt a single very restricted conformation (Figure 14) having two identical OH····π intramolecular hydrogen bonds (3484 $cm.^{-1}$ in $CCl_4$). The hydroxyls are buried within the molecule and their stretching frequencies, ν(OH), are almost unaffected by even strongly basic solvents.

Finally, the spectrum of (7e) in the solid state shows the same well-defined ν(OH) absorption at 3484 $cm.^{-1}$ as in solution and the conformation in the crystal is therefore presumed to be the same as that observed in solution. Support for these findings concerning the "narcissistic" conformation of compound (7e) could come from an X-ray analysis of a suitable heavy atom derivative. Such a spiral conformation is formally capable of optical resolution provided the strength of the two intramolecular hydrogen bonds is sufficient to maintain the conformation under the conditions employed in the attempted resolution. Should this prove to be the case, this molecule, or a suitable derivative, would be the first example of optical activity where asymmetry is largely maintained by intramolecular hydrogen bonding.

TABLE 4.

Hydroxyl Stretching Absorptions of Compounds (5, 6, 7b and 7e).

| Compound | n-hexane | | | $CCl_4$ | | | $CHCl_3$ | | | Assignments |
|---|---|---|---|---|---|---|---|---|---|---|
| | $\nu$ | $\Delta\nu_{\frac{1}{2}}^{a}$ | $\varepsilon^{a}$ | $\nu$ | $\Delta\nu_{\frac{1}{2}}^{a}$ | $\varepsilon^{a}$ | $\nu$ | $\Delta\nu_{\frac{1}{2}}^{a}$ | $\varepsilon^{a}$ | |
| 5 | Insoluble | | | 3611 | 26 | 170 | 3600 | 40 | 190 | 'Free' |
| | | | | 3476 | 100 | 125 | 3450 | br | 140 | OH····OH intra |
| | | | | 3300 | br | - | | | | OH····OH inter |
| 6 | 3647 | - | 85 | 3639 | 32 | 100 | 3631 | 32 | 165 | 'Free' hindered |
| | 3620 | sh | - | 3620 | sh | - | | | | Free |
| | 3517 | 38[b] | 330 | 3516 | 58[b] | 210 | 3515 | - | 85 | OH····π intra |
| | 3470 | sh | 100 | 3450 | sh | - | 3440 | - | 85 | OH····OH intra |
| 7b | 3647 | - | 25 | 3634 | - | 40 | 3626 | 18 | 100 | Free hindered |
| | 3500 | 36 | 665 | 3499 | 50 | 385 | 3500 | 82 | 245 | OH····π intra |
| 7e | 3483 | 15 | 1650 | 3484 | 22 | 1000 | 3486 | 40 | 630 | OH····π intra |

All absorptions were found to be concentration independent over the range studied except those for compound (5). Concentrations and cell paths are given in Figure 13.
- Not measured.
sh Shoulder.
br Broad band.
b Half-band width measured by reflection of undisturbed wing.

TABLE 5.

Literature Data[55,56] Recorded for Hydroxyl Stretching Absorptions of Compounds of Type (7).

| Compound | $R^1$ | $R^2$ | $\nu$(OH) absorptions in $CCl_4$ | | $\frac{\varepsilon_b \times 100}{\varepsilon_f + \varepsilon_b}$ | Ref. |
|---|---|---|---|---|---|---|
| | | | $\nu$(OH) free | $\nu$(OH) bonded† | | |
| 7a | H | H | 3636 | 3500 | 69.7 | 55 |
| 7b | H | $CH_3$ | 3636 | 3500 | 81.7 | 55 |
| 7c | H | cyclohexyl | | 3480 | 100 | 55 |
| 7d | H | phenyl | 3636 | 3500 | 92.3 | 55 |
| 7e | $CH_3$ | $CH_3$ | | 3480 | 100 | 55,56 |
| 7f | $CH_3$ | $C_2H_5$ | | 3480 | 100 | 55 |

† Assigned to OH····π in the present work.

TABLE 6.

Summary of Hydroxyl Stretching Absorptions and Integrated Absorption Intensities for Various Phenols in $CCl_4$.

| Compound | $\nu$ | $\Delta\nu_{\frac{1}{2}}^{a}$ | $\varepsilon^{a}$ | $\Delta\nu^{\dagger}$ | A x $10^{-4}$ | Assignment |
|---|---|---|---|---|---|---|
| p-cresol | 3612 | 17 | 200 | - | 1.25 | Free |
| o-hydroxydiphenyl | 3607 | 18 | 25 | - | 0.18 | Free |
| | 3565 | 17 | 200 | 46 | 1.17 | OH····π intra |
| 2,2'-dihydroxy-diphenyl | 3599 | 18 | 55 | - | 0.30 | Free |
| | 3554 | 19 | 390 | 57 | 2.28 | OH····π intra |
| o-hydroxydiphenyl-methane* | 3611 | 17 | | - | 0.87 | Free |
| | 3560 | 56 | | 51 | 0.80 | OH····π intra |
| 7b | 3634 | - | 40 | - | 0.25 | Free |
| | 3499 | 50 | 385 | 148 | 6.90 | OH····π intra |
| 7e | 3484 | 22 | 1000 | 163 | 9.80 | OH····π intra |

All samples examined in 2 cm. cells (ca. 0.01 M). Areas calculated according to RAMSAY'S method[61].

† $\Delta\nu = \nu$(OH) free - $\nu$(OH) bonded. The value for $\nu$(OH) free has been taken as 3611 $cm.^{-1}$ except for 7b and 7e where the value of 2,6-di-t-butylphenol (3647 $cm.^{-1}$) has been adopted.

* Results taken from ref. 58. In this reference OKI and IWAMURA quote a value of 0.20 and 1.28 for A x $10^{-4}$ for the free and bonded hydroxyl absorptions of o-hydroxydiphenyl respectively.

TABLE 7.

Hydroxyl Stretching Absorptions for Compounds (5, 6, 7b and 7e) in Diethyl Ether and Pyridine.

| Solvent | Compound | Molarity | $\nu$ | $\Delta\nu_{\frac{1}{2}}^{a}$ | $\varepsilon^{a}$ | Assignment |
|---|---|---|---|---|---|---|
| Diethyl ether | 5 | 0.13 | (3350) | br | - | OH····O(Et)$_2$ |
| | 6 | 0.10 | (3350) | br | - | OH····O(Et)$_2$ |
| | 7b | 0.05 | 3484 | - | 160* | OH····$\pi$ intra |
| | | | (3300) | br | - | OH····O(Et)$_2$ |
| | 7e | 0.04 | 3483 | 24 | 1070 | OH····$\pi$ intra |
| Pyridine | 7b | 0.04 | (3200) | br | - | OH····NC$_5$H$_5$ |
| | 7e | 0.06 | 3482† | 65 | 800 | OH····$\pi$ intra |

Cell thickness 0.5 mm. Values in parenthesis are approximate.
* Apparent peak height used without substraction of contribution from overlapping 3300 cm.$^{-1}$ band.
† There is extensive broadening at the base of the peak which may correspond to a little intermolecular association.

TABLE 8.

Retention Times for Compounds (6) and (7e).

| Column Conditions | Compound | $R_t$ mins. |
|---|---|---|
| 0.5 % Apiezon L at 175° and 30 ml./min. | n-Docosane ($C_{22}$) | 7.8 |
| | 6 | 20.3 |
| | 7e | 9.05 |
| 2 % Phenyldiethanolamine Succimate at 175° and 20 ml./min. | n-Octacosane ($C_{28}$) | 14.05 |
| | 6 | 72.50 |
| | 7e | 9.05 |

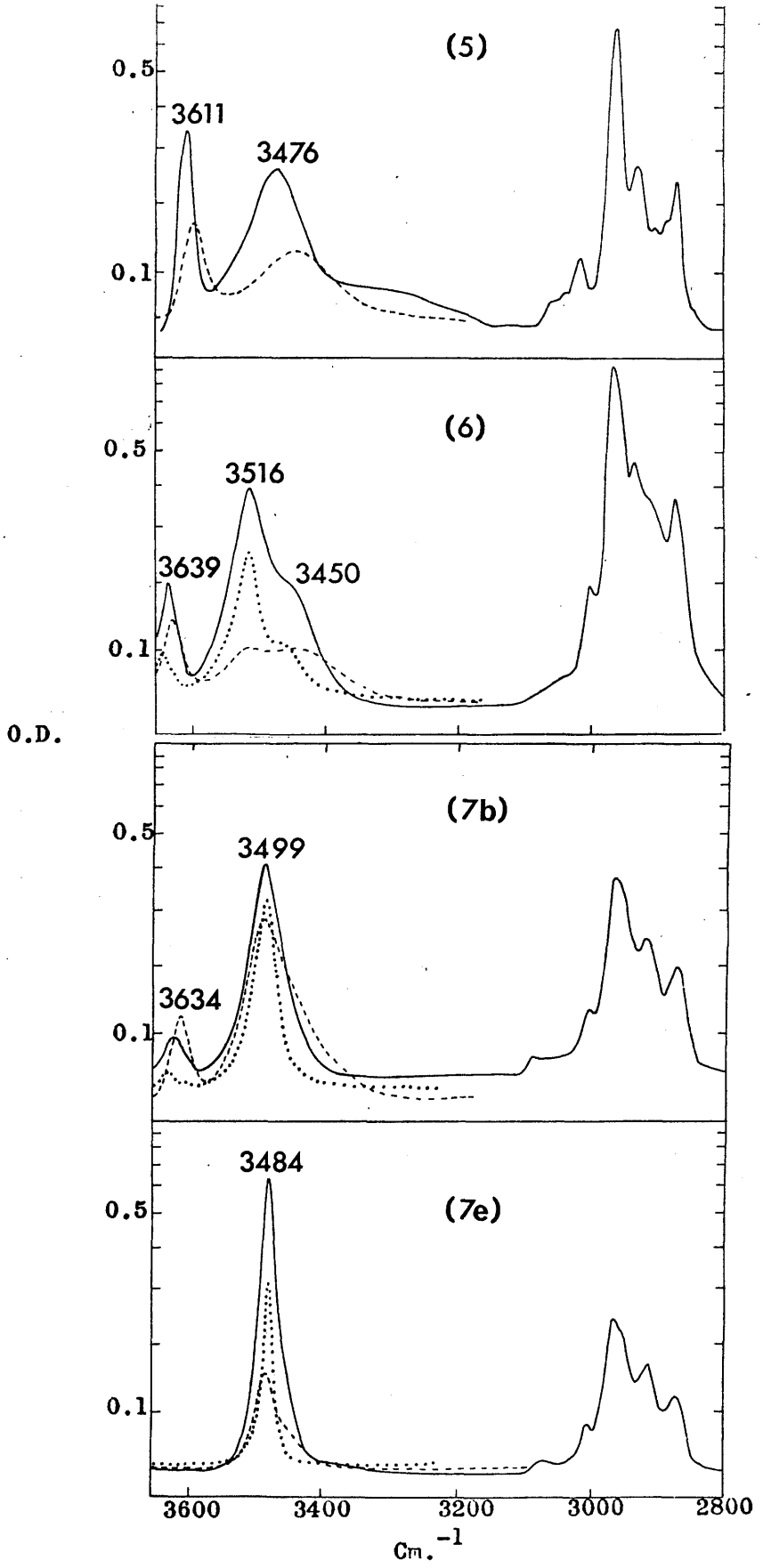



FIGURE 13. Hydroxyl stretching absorptions for solutions of compounds (5, 6, 7b and 7e) in n-hexane (·····), carbon tetrachloride (———), and chloroform (- - - - -). Frequency values quoted are for $CCl_4$. Cell paths: n-hexane and $CHCl_3$, 0.5 mm; $CCl_4$, 2 cm. Concentrations: n-hexane, ca. 5 mM, $CCl_4$, 1 mM, $CHCl_3$, 3 mM.

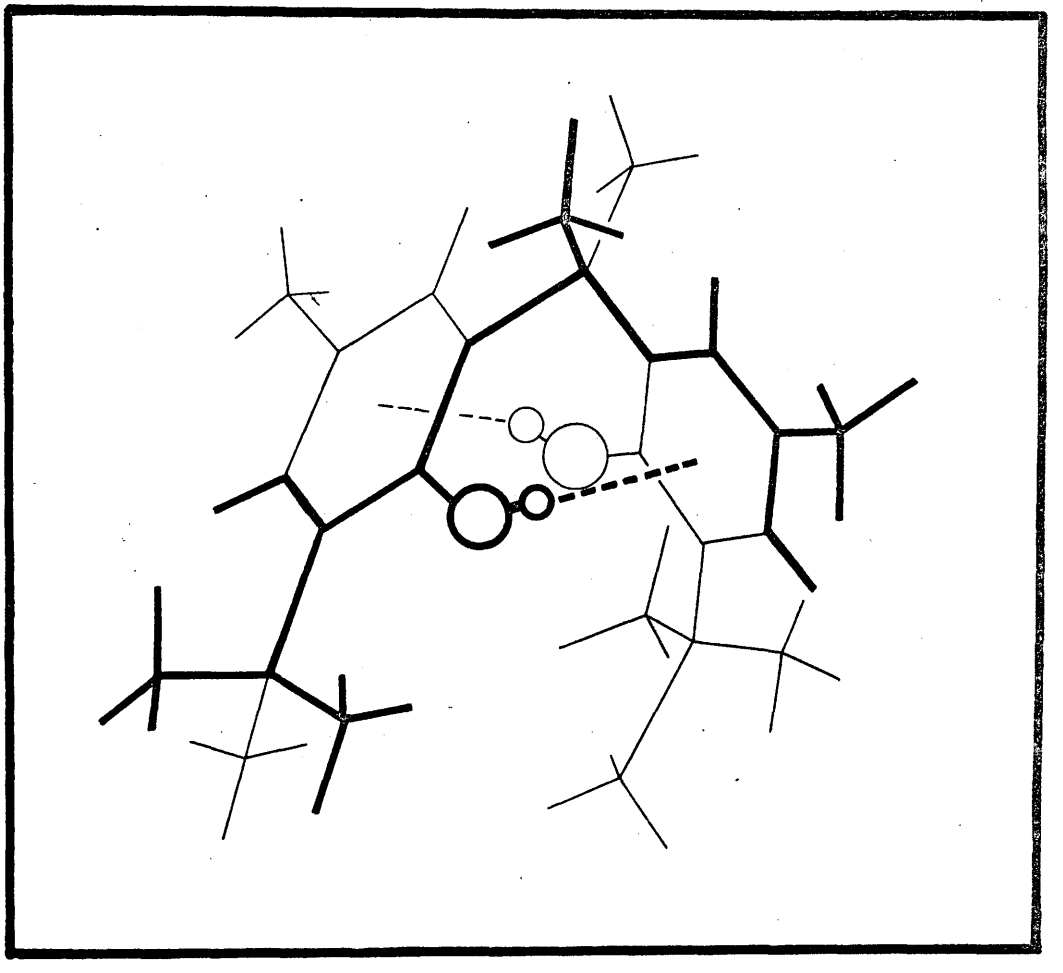
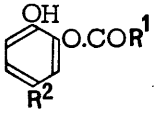


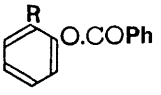
FIGURE 14. Planar projection of the Dreiding molecular model of the single conformation assigned to compound (7e). The large and small circles indicate the oxygen and hydrogen atoms of the hydroxyl groups respectively. The dotted lines indicate the hydrogen bonds. The front edge of the molecule is depicted by heavy lines.

Pyrocatechol Monoesters and Related Compounds

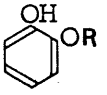
The infrared spectra of various o-hydroxy-depsides of the type (8) and related compounds (9 and 10) in several solvents have been examined in an attempt to determine the extent of interaction of the o-hydroxy group with the ester linkage.




(8)

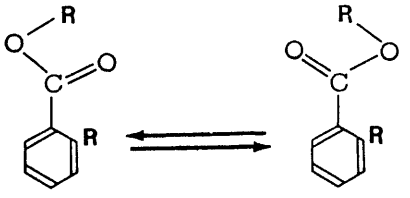



(9)




(10)

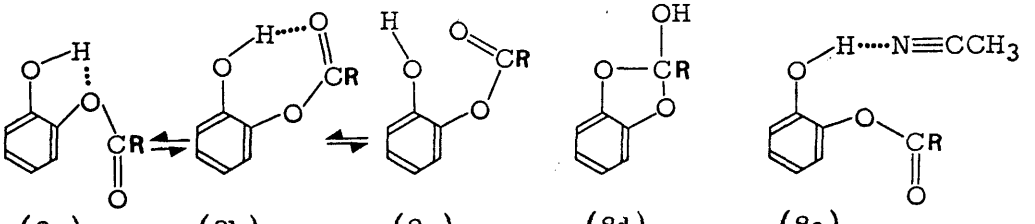
The effect of ortho-substitution in phenyl benzoate by groups other than hydroxyl was first examined (type 9, Table 9) and, in general, a small increase in the carbonyl stretching frequency, $\nu(C{=}O)$ (in $CCl_4$), was noted; the observed shifts could not, however, be correlated with the corresponding Taft $\sigma^*$ values[62] of the substituent groups. There was no indication of split bands of the type encountered in the ortho-substituted benzoate series, where they have been attributed to conformational isomers (11a, 11b).[63] One compound, guaiacol benzoate (9, R=OMe),




(11a) (11b)

was examined in several solvents and the carbonyl absorption (Table 10) showed the expected[63] fall with increasing solvent polarity. In chloroform there was evidence of slight splitting which could be explained in terms of the existence of more than one conformation of the ester molecule or, more precisely, of its solvated complex with chloroform molecules.

In contrast to the above results, two distinct carbonyl bands were observed with the introduction of a hydroxyl group into the ortho-position of a phenyl ester. The results for compounds of this type (8) are listed in Table 11, and illustrated in Figure 15. At low concentrations in carbon tetrachloride where any intermolecular associations, other than with the solvent molecules, have been eliminated, the effect is concentration independent and is readily explicable in terms of two intramolecularly hydrogen bonded species (e.g. 8a and 8b). Species (8a), for which the carbonyl absorption is slightly displaced to a higher frequency relative to those of the reference compounds (Table 9; 9,R=H and OMe), is analogous to that suggested by HENBEST and LOVELL[64] in a study of the acetates of cis-3,5-dihydroxy-steroids, and to the five-membered hydrogen bonded conformation of pyrocatechol[65] and of other pyrocatechol derivatives discussed below. Species (8b) exemplifies the seven-membered ring type of intramolecular hydrogen bond: carbonyl and hydroxyl absorptions are both markedly lowered but the breadth of the latter



| | (8a) | (8b) | (8c) | (8d) | (8e) | |
|---|---|---|---|---|---|---|
| $\nu_{OH}$ | 3590 | 3380 | 3607 | 3600? | 3365 | cm.$^{-1}$ |
| $\nu_{CO}$ | 1753 | 1712 | 1750 | | 1745 | cm.$^{-1}$ |

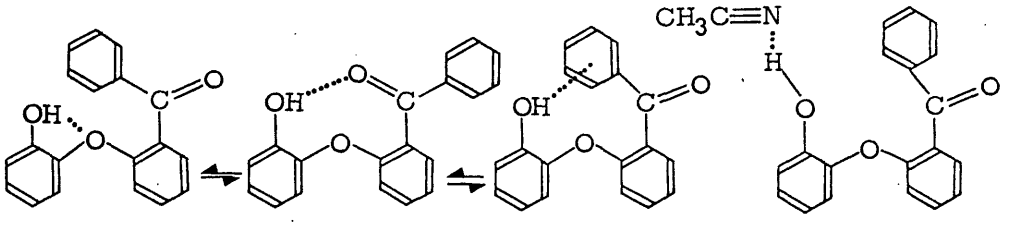
suggests considerable molecular flexibility. The ester grouping cannot be planar in this conformation. The shoulder at ca. 3607 cm.$^{-1}$ indicates the presence of a small proportion of a conformation bearing a free hydroxyl group, for example (8c), though species (8d) would also explain this absorption.

Similar conclusions can be drawn for the other two compounds shown in Table 11. For the protocatechuate derivative (8; $R^1$=Ph, $R^2$=$CO_2Me$) the methoxycarbonyl group accounts for a part of the carbonyl absorption at 1726 $cm.^{-1}$. There is a higher proportion of the lower frequency carbonyl band in the O-acetate (8; $R^1$=Me, $R^2$=H): this might be ascribed to the greater basicity of the acetate than of the benzoate carbonyl, though the changed proportions do not seem to be reflected in the hydroxyl region.

These assignments are supported by measurements for the benzoate (8; $R^1$=Ph, $R^2$=H) at different temperatures (Table 12) and in solvents of varying polarity (Table 13). In tetrachloroethylene increase in temperature results in the expected increase in the ratio (R) of the intensities of the high frequency bands [already ascribed to the less strongly bonded form (8a)] to the low frequency bands. The solvents shifts for the carbonyl group showed a rough parallel with those of the model compounds (Table 10) except for the behaviour in acetonitrile where the intermolecularly bonded species (8e) undoubtedly predominates (cf. the solvent shifts for benzophenone and phenol listed in Tables 16 and 15, respectively, and the ensuing discussion). The intramolecularly bonded species (8a and 8b) persist in chloroform solution and it may be noted, in accordance with other experience,[63] that the solvent shift of the intrabonded carbonyl (that of 8b) is relatively small.

Results for some related compounds of type (10) are given in Tables 14-16 and illustrated in Figures 16 and 17. 2-o-Hydroxyphenoxybenzophenone is of special interest as here there are at least three, and possibly four, electron-rich sites for intramolecular bonding by the phenolic hydroxyl group. The absorptions have been assigned to the three conformations (12a, 12b and 12c) by comparison with the results in Figure 16 and Table 14, and in the literature.[49] The conformations (12a and 12b) are analogous to (8a and 8b), though

the predominant one, (12b), involves a hydrogen bond closing a 9-membered rather than a 7-membered ring. It is often assumed that



| | (12a) | (12b) | (12c) | (12d) | |
|---|---|---|---|---|---|
| $\nu_{OH}$ | 3561 | 3274 | 3531 | 3364 | cm.$^{-1}$ |
| $\nu_{CO}$ | 1670 | 1657 | 1670 | 1667 | cm.$^{-1}$ |

intramolecular hydrogen bonding closes only 5- or 6-membered rings; such bonding is certainly common but there can be little doubt that formal ring size is not the most important criterion for successful intramolecular hydrogen bonding. The molecule must be free to adopt a conformation in which the hydroxyl group and the basic centre are favourably placed with respect to both distance and orientation from one another. The proportion of molecules in this form will, of course, depend on many factors, for example, the number of alternative conformations and their energy content, the nature of the solvent, and the temperature of the solution. Systems involving relatively rigid units such as the benzene ring are often fairly restricted as to the number of distinct conformations they can adopt. In such cases, conformers (e.g. 12b) may be detectable which involve intramolecular hydrogen bonds between centres at first sight widely separated.

The behaviour (Figure 17 and Tables 15 and 16) of compound (12) in various solvents is much like that already described for the benzoate (8; $R^1$=Ph, $R^2$=H). The intramolecular hydrogen bonds are

broken (only partially with 12) in acetonitrile, but not in chloroform, as can be seen from the comparative values provided for phenol and benzophenone. The carbonyl band of 2-o-hydroxy-phenoxybenzophenone (12) at 1650 $cm.^{-1}$ (in acetonitrile) is assigned to the intra-bonded conformer (12b) in equilibrium with (12d).

The conformational equilibria revealed in this work must play some part in determining the reactivity of the compounds concerned. It is particularly interesting that the infrared method permits some evaluation, admittedly very qualitatively, of the change in the proportions of the various conformers with change of solvent and of temperature. Further studies with a greater variety of substances and solvents would be of value; thus measurements in methanolic solution should show the effect of solvent on the carbonyl absorption of o-hydroxy-depsides of type (8) and lead to an understanding of the easy methanolysis. Recently HANSEN[66] has reported the kinetics of alkaline hydrolysis of catechol monoacetate (in methanol). The hydrolysis of catechol monoacetate ($pK_a' = 8.56$) was found to be 500 times faster than expected from a consideration of the inductive and resonance effects. This author attributes the fast rate of hydrolysis to intramolecular hydrogen bonding between the phenolic hydroxyl and the ester oxygen facilitating cleavage between the ester oxygen and the carbonyl function.

TABLE 9.

Carbonyl Absorptions of Some ortho-Substituted Phenylbenzoates (9) in $CCl_4$.

| R | $\nu$(C=O) | $\Delta\nu_{\frac{1}{2}}^{a}$ | $\varepsilon^{a}$ |
|---|---|---|---|
| H | 1746 | 13 | 665 |
| Me | 1746* | 14 | 690 |
| Cl | 1753 | 14 | 730 |
| Br | 1751 | 11 | 760 |
| OMe | 1748 | 14 | 655 |
| $NO_2$ | 1756 | 14 | 720 |

Solutions ca. 1.5 mM in 5 mm. cells.
* Asymmetric peak.

TABLE 10.

Carbonyl Absorptions of Guaiacol Benzoate (9; R=OMe) in Various Solvents.

| Solvent | $\nu$(C=O) | $\Delta\nu_{\frac{1}{2}}^{a}$ | $\varepsilon^{a}$ |
|---|---|---|---|
| n-hexane | 1754 | 10 | 820 |
| $CCl_4$ | 1748 | 14 | 655 |
| $CHCl_3$ | (1740*) | 26 | 430 |
| $CH_3.CN$ | 1740* | 17 | 530 |

Solutions ca. 30 mM examined in 0.51 mm cells, except for n-hexane (15 mM in 0.51 mm cell).
Values in parenthesis are approximate.
* Asymmetric peak.

TABLE 11.

Hydroxyl and Carbonyl Absorptions of Some ortho-Hydroxy phenyl Esters (8) in $CCl_4$.

| Compound (8) | $R^1$ | $R^2$ | $\nu_{OH}$ | $\Delta\nu^a_{\frac{1}{2}}$ | $\varepsilon^a$ | $\nu_{CO}$ | $\Delta\nu^a_{\frac{1}{2}}$ | $\varepsilon^a$ |
|---|---|---|---|---|---|---|---|---|
| O-Benzoyl-pyrocatechol | Ph | H | 3607 | sh | - | 1753 | 17 | 460 |
| | | | 3590* | 24 | 85 | 1712* | 22 | 165 |
| | | | (3380) | (240) | 25 | | | |
| O-Acetyl-pyrocatechol† | Me | H | 3606 | sh | - | 1778 | 20 | 240 |
| | | | 3585* | 23 | 95 | 1736 | 16 | 230 |
| | | | (3410) | (220) | 25 | | | |
| Me 3-O-Benzoyl-protocatechuate‡ | Ph | $CO_2Me$ | 3598 | sh | - | 1755* | 15 | m |
| | | | 3577* | 25 | m | 1726* | 15 | s |
| | | | (3350) | (290) | w | 1712 | sh | - |

Cell paths for the hydroxyl and carbonyl region were 5 cm. and 2 cm. respectively, and solutions were ca. 0.3 mM. Measurements were made at several molarities and the absorptions above found to be concentration independent.

* Asymmetric peak.

† Ph acetate: $\nu(CO)_1$ (in $CCl_4$) 1768* $cm.^{-1}$, $\Delta\nu^a_{\frac{1}{2}}$ 13 $cm.^{-1}$, $\varepsilon^a$ 560 $l.mole^{-1}cm.^{-1}$.

‡ Me benzoate: $\nu(CO)_1$ (in $CCl_4$) 1730 $cm.^{-1}$, $\Delta\nu^a_{\frac{1}{2}}$ 11 $cm.^{-1}$, $\varepsilon^a$ 900 $l.mole^{-1}cm.^{-1}$.

For other symbols see Tables 9 and 10.

TABLE 12.

Hydroxyl and Carbonyl Absorptions of O-Benzoylpyrocatechol (8; $R^1$=Ph, $R^2$=H) in $C_2Cl_4$ at Various Temperatures.

| Temp. | $\nu_{OH}$ | $\Delta\nu^a_{\frac{1}{2}}$ | $\varepsilon^a$ | R | $\nu_{CO}$ | $\Delta\nu^a_{\frac{1}{2}}$ | $\varepsilon^a$ | R |
|---|---|---|---|---|---|---|---|---|
| 26° | 3606 | sh | - | | 1754 | 14 | 470 | |
| | 3587 | 23 | 60 | 3.0 | 1711* | 19 | 180 | 2.6 |
| | (3395) | (235) | 20 | | | | | |
| 50° | 3604 | sh | - | | 1754 | 14 | 435 | |
| | 3587 | 23 | 60 | 4.0 | 1712* | 20 | 160 | 2.7 |
| | (3385) | (235) | 15 | | | | | |
| 80° | 3611 | sh | - | | 1754 | 14 | 405 | |
| | 3589 | 23 | 55 | 5.5 | 1713* | 20 | 130 | 3.1 |
| | (3385) | (250) | 10 | | | | | |

Hydroxyl frequencies determined for ca. 10 mM solutions in 3 mm. cells. Carbonyl frequencies determined for ca. 5 mM solutions in 3 mm. cells. R = $\varepsilon^a$(high frequency band)/$\varepsilon^a$(low frequency band).
For symbols see Tables 9-11.

TABLE 13.

Hydroxyl and Carbonyl Absorptions of 1-O-Benzoylpyrocatechol (8; $R^1$ = Ph, $R^2$ = H) in Various Solvents.

| Solvent | $\nu_{OH}$ | $\Delta\nu_{\frac{1}{2}}^{a}$ | $\varepsilon^{a}$ | $\nu_{CO}$ | $\Delta\nu_{\frac{1}{2}}^{a}$ | $\varepsilon^{a}$ |
|---|---|---|---|---|---|---|
| n-hexane | - | - | - | 1757 | 11 | s |
| | | | | 1715* | 14 | w |
| $CCl_4$ | 3607 | sh | - | 1753 | 17 | 460 |
| | 3590 | 24 | 85 | 1712* | 22 | 165 |
| | (3380) | (240) | 25 | | | |
| $CHCl_3$ | 3583* | 37 | 65 | 1746* | 22 | 385 |
| | (3420) | (245) | 10 | 1710* | (30) | 100 |
| $CH_3CN$ | 3365* | (180) | 105 | 1745 | 21 | 515 |

Solutions ca. 25 mM, except for n-hexane (saturated solution), in 0.5 mm. cell.
For symbols see Tables 9-11.

TABLE 14.

Hydroxyl Absorptions of Guaiacol and Related Compounds (10) in $CCl_4$.

| Compound | $\nu_{OH}$ | $\Delta\nu_{\frac{1}{2}}^{a}$ | $\varepsilon^{a}$ | Assignments |
|---|---|---|---|---|
| 12 | 3561 | 28 | 30 | Intra OH····O |
| | 3531 | 56 | 20 | Intra OH····π |
| | 3274 | 208 | 135 | Intra OH····O=C |
| o-HO.$C_6H_4$.O.$C_6H_4$.$CH_2$Ph-o | 3559* | 26 | 120 | Intra OH····O |
| | 3516* | 32 | 85 | Intra OH····π |
| 10; R=Ph | 3562 | 22 | 180 | Intra OH····O |
| 10; R=Me | 3558 | 24 | 185 | Intra OH····O |

Solutions ca. 1.5 mM examined in 2 cm. Cells.
For other symbols see Tables 9-11.

TABLE 15.

Hydroxyl Absorptions of 2-o-Hydroxyphenoxybenzophenone (12) and Phenol in Various Solvents.

| Solvent | 2-o-Hydroxyphenoxybenzophenone $\nu_{OH}$ | $\Delta\nu_{\frac{1}{2}}^{a}$ | $\varepsilon^{a}$ | $\Delta\nu$ | Phenol $\nu_{OH}$ | $\Delta\nu_{\frac{1}{2}}^{a}$ | $\varepsilon^{a}$ | $\Delta\nu$ |
|---|---|---|---|---|---|---|---|---|
| n-hexane | 3570 | - | w | | 3621 | 14 | - | 0 |
| | 3538 | - | s | | | | | |
| | 3286* | 145 | s | 0 | | | | |
| $CCl_4$ | 3561* | 28 | 30 | | 3612 | 17 | 205 | 9 |
| | 3531* | 56 | 20 | | | | | |
| | 3274* | 208 | 135 | 12 | | | | |
| $CHCl_3$ | 3552* | 36 | 40 | | 3599 | 32 | 150 | 22 |
| | 3240* | 250 | 100 | 46 | | | | |
| $CH_3CN$ | 3364* | 160 | 115 | -78 | 3413 | 140 | 175 | 208 |

Concentrations and cell thicknesses: for 2-o-hydroxyphenoxybenzophenone in n-hexane saturated, 0.5 mm., in $CCl_4$ 1.6 mM, 20 mm., in $CHCl_3$ 20 mM, 2 mm., and in $CH_3CN$ 20 mM, 0.5 mm.; for phenol in n-hexane saturated, 0.5 mm., in $CCl_4$ 5 mM, 5 mm., in $CHCl_3$ 50 mM, 0.5 mm., and in $CH_3CN$ 50 mM, 0.5 mm. Solvent shift values, $\Delta\nu = \nu(\text{n-hexane}) - \nu(\text{solvent})$ in $cm.^{-1}$. For symbols see Tables 9-11.

TABLE 16.

Carbonyl Absorptions of 2-o-Hydroxyphenoxybenzophenone (12) and Benzophenone in Various Solvents.

| Solvent | 2-o-Hydroxyphenoxy-benzophenone | | | | Benzophenone | | | |
|---|---|---|---|---|---|---|---|---|
| | $\nu_{CO}$ | $\Delta\nu_{\frac{1}{2}}^{a}$ | $\varepsilon^{a}$ | $\Delta\nu$ | $\nu_{CO}$ | $\Delta\nu_{\frac{1}{2}}^{a}$ | $\varepsilon^{a}$ | $\Delta\nu$ |
| n-hexane | 1670 | sh | - | 0 | 1671 | 8 | 695 | 0 |
| | 1660 | 9 | - | 0 | | | | |
| $CCl_4$ | 1667 | sh | - | 3 | 1666 | 10 | 595 | 5 |
| | 1657 | 11 | 690 | 3 | | | | |
| $CHCl_3$ | - | sh | - | - | 1658 | 18 | 490 | 13 |
| | 1651* | 18 | 500 | 9 | | | | |
| $CH_3CN$ | 1667* | 19 | 300 | 3 | 1661 | 10 | 550 | 10 |
| | 1650* | 14 | 250 | 10 | | | | |

Concentrations and cell thicknesses: for 2-o-hydroxyphenoxybenzophenone in n-hexane saturated, 0.5 mm., in $CCl_4$ 1.6 mM, 5 mm., in $CHCl_3$, 20 mM, 0.5 mm., and in $CH_3CN$ 20 mM, 0.5 mm.
For symbols see Tables 9-11.

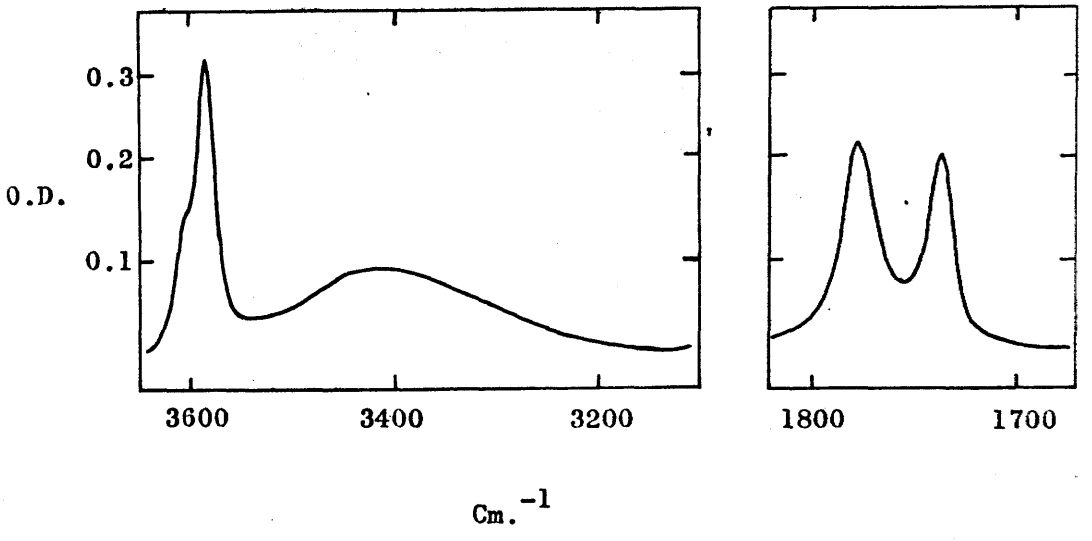



FIGURE 15. Hydroxyl and carbonyl stretching absorptions of O-acetylpyrocatechol (8; $R^1$=Me, $R^2$=H) in carbon tetrachloride solution (1.65 mM) examined in 2 cm. and 0.5 cm. cells, respectively.

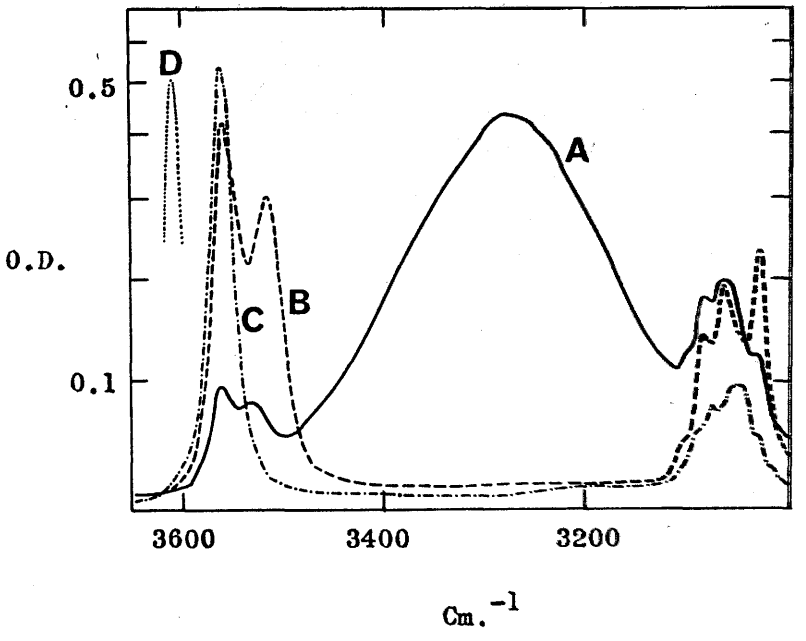



FIGURE 16. Hydroxyl stretching absorptions of phenol and of certain derivatives of pyrocatechol in carbon tetrachloride.
(A) 2-o-Hydroxyphenoxybenzophenone (12); (B) o-(o-benzylphenoxy)phenol; (C) o-phenoxyphenol; and (D) phenol. Solutions (ca. 1.5 mM) examined in 2 cm. cells.

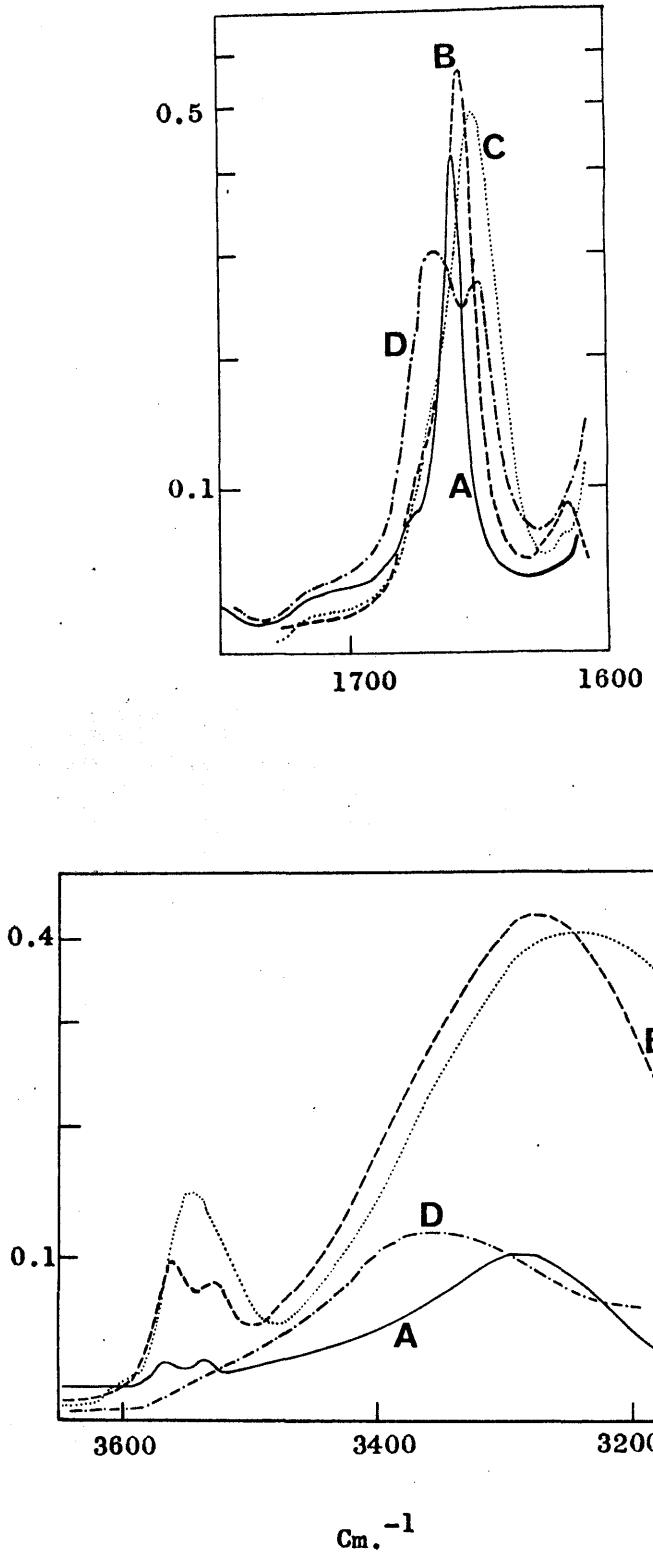



FIGURE 17. Hydroxyl and carbonyl stretching absorptions of 2-o-hydroxyphenoxybenzophenone (12) in various solvents.
(A) n-Hexane; (B) carbon tetrachloride; (C) chloroform; and (D) acetonitrile.
Concentrations and cell thicknesses are given in Tables 15 and 16.

# INFRARED STUDIES OF TERPENOID COMPOUNDS

## INTRODUCTION

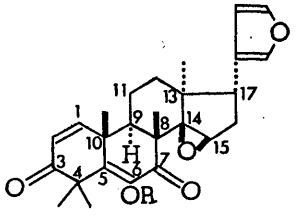
A great deal of attention and research in this department is devoted to natural product chemistry with particular emphasis on the terpene family. The presence or absence of intramolecular hydrogen bonding in natural products can frequently be inferred from an examination of the hydroxyl stretching frequencies obtained with ditule solutions in inert solvents.[67] Such information can have considerable diagnostic value but there are few instances in the literature where spectral data refer to molecules of precisely known stereochemistry, The complete structure of the degraded $C_{26}$ triterpene cedrelone[68] and the diterpenoid lactone rosololactone[69] have been determined by the X-ray crystallographic method, and the present work deals with spectra-structure correlations for these compounds and related members. The study of cedrelone and related compounds was carried out in collaboration with Dr. S.G. McGeachin who specially prepared and purified the compounds for the infrared study. In the case of the study of rosololactone and related diterpenoid lactones the compounds were isolated and purified by Drs. A.I. Scott and D.S. Young.

In addition, a group of sesquiterpenoid lactones have been studied in an attempt to resolve the reason for the complexity observed in the carbonyl stretching region. The lactones studied were provided by Drs. K.H. Overton, R.P.M. Bond and J.D. Connolly.

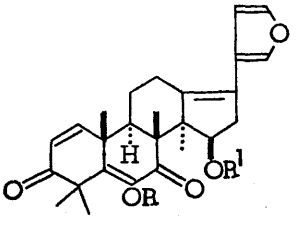
# RESULTS and DISCUSSION

## Cedrelone and Related Compounds

The results are detailed in Tables 17 and 18 and summarized in Table 19. One important structural feature of cedrelone and its close relatives (13) is that ring C is held in the boat conformation. Other related compounds (14) have the more favoured chair conformation in ring C and are referred to as isocedrelones.



(13)



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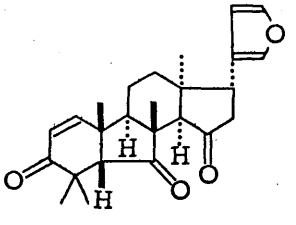
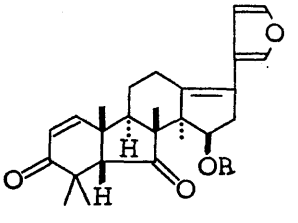
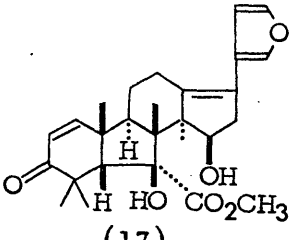


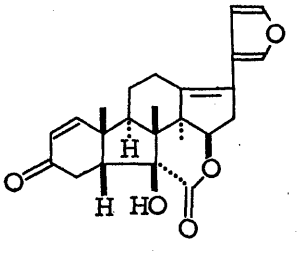
(15)



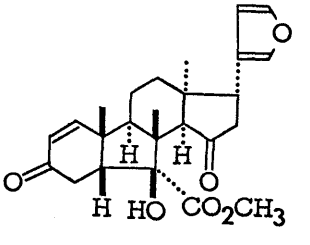
(16)



(17)



(18)



(19)

In both cedrelone methyl ether (13; R=Me) and cedrelone acetate (13; R=Ac) the presence of a conjugated enone system in ring A and in ring B is characterized by a single, intense, symmetrical absorption at ca. 1700 cm.$^{-1}$ (in $CCl_4$; Table 17). The high extinction coefficient of this absorption accords with the presence of two carbonyl groupings. Introduction of an epoxide grouping at positions 1 and 2 as in 1,2-epoxy-cedrelone acetate (13; R=Ac, 1,2-epoxy) splits the carbonyl absorption into two well-defined bands; the higher frequency band at 1722 cm.$^{-1}$(in $CCl_4$; Table 17) is attributed to the carbonyl adjacent to the epoxide group in ring A, and the lower frequency absorption at 1708 cm.$^{-1}$(in $CCl_4$) is assigned to the ring B carbonyl. Saturation of the double bond in ring A (13; R=Ac, 1,2-dihydro- and hexahydro-) slightly reduces the absorption frequencies of both carbonyl groups as compared with those observed for the 1,2-epoxy-compound.[70] Even so, the ring A carbonyl frequency for the 1,2-dihydro-compound is somewhat higher (1714 cm.$^{-1}$ in $CHCl_3$), than that previously described for a 4,4-dimethyl-3-oxo-5α-system.[71] LEHN, LEVISALLES, and OURISSON[72] conclude that ring A in such systems exists as a deformed chair - a decision reached after taking into account the interactions between 1,3-diaxial methyl groups. The X-ray analysis[68] of cedrelone iodoacetate, however, revealed that ring A possessed a boat-like conformation rather than the alternative half-chair; the former presumably minimizes the non-bonded interactions between the 4-methyl groups and the bulky 6-substituent. The same argument should apply to cedrelone and its simple derivatives whether the particular molecule is in a crystal lattice or is surrounded by relatively inert solvent molecules. There is no marked change in the carbonyl absorptions (Table 17) on passing from carbon tetrachloride to chloroform solution, only the expected lowering in frequency (by 5-10 cm.$^{-1}$) and the increased breadth of the band.[73] Preferential solvation of the α-epoxy-group may explain the unusually small shifts recorded for the two compounds having this grouping.

In the spectrum of cedrelone itself (13;R=H) there are two peaks in the carbonyl region (1695 and 1678 cm.$^{-1}$ in $CCl_4$; Table 17) and one band in the hydroxyl region (3417 cm.$^{-1}$ in $CCl_4$; Table 18). The data for dihydrocedrelone (13; R=H, 1,2-dihydro;Figure 18) reveal that the higher band, that at 1695 cm.$^{-1}$, in the spectrum of cedrelone is to be attributed to the ring A carbonyl. Incidentally, this absorption moves about 9 cm.$^{-1}$ to lower frequency when ring B is five-membered, presumably as a result of bond-angle changes at the A/B ring junction.

The carbonyl and hydroxyl absorptions of the diosphenol system in cedrelone and derivatives are typically both low in frequency and insensitive to solvation.[73] A planar projection of a Dreiding model of dihydrocedrelone (13; R=H, 1,2-dihydro) is illustrated in Figure 19. The intramolecular diosphenol hydrogen bond is in the form of a planar ring with an O····O distance of ca. 2.8 Å and the angle subtended at the carbonyl oxygen atom by the proton of the hydroxyl group is 80°. This is a particularly well-defined conformation and the intra-bonded $\nu$(OH) absorption is unusually narrow.[40]

Attention is now focussed on the isocedrelones (14) which have the more favoured chair conformation in ring C. In the case of isocedrelone diacetate (14; R=$R^1$=Ac) the enone systems in rings A and B are characterized by a very strong absorption at 1698 cm.$^{-1}$ (in $CCl_4$; Table 17). Replacement of one of the acetate groupings by a hydroxyl group (14; R=Ac, $R^1$=H, 1,2-dihydro) causes the formation of a seven-membered hydrogen bond involving the ring B carbonyl (shift to 1672 cm.$^{-1}$ in $CCl_4$) and the ring D hydroxyl (Tables 17 and 18; Figure 18). When both acetate groupings are replaced by hydroxyls, as in dihydroisocedrelone (14; R=$R^1$=H, 1,2-dihydro), the ring B carbonyl absorption appears to shift to much lower frequency (1623 cm.$^{-1}$ in $CCl_4$) and two hydroxyl

absorptions are observed at 3415 and 3466 cm.$^{-1}$ (*Figure 18*), and hence both hydroxyl groups require to be intramolecularly bonded to the carbonyl function in ring B. This is illustrated in the planar projection of the Dreiding model shown in *Figure 19*. The planar five-membered ring hydrogen bond of the diosphenol group exists as it does in dihydrocedrelone (13; R=H, 1,2-dihydro; Figure 19), but the seven-membered ring formed by the intramolecular hydrogen bond involving the ring D hydroxyl must be twisted. Measurements with the model give an O····O distance for this latter hydrogen bond of ca. 2·8 Å, the dihedral angle formed by the bonds linking $C_{(17)}$, $C_{(15)}$, and $O_{(4)}$ as 45°, and the angle made by the O-H bond with the line joining the two oxygen centres as 15°. Once again the stereochemistry must be favourable to hydrogen-bond formation, although the breadth of the absorption band is much greater than that of the diosphenol system, suggesting a greater degree of conformational freedom.[58] However, the ring B carbonyl is actually at a slightly lower value when bonded singly by the ring D hydroxyl rather than by the diosphenol hydroxyl itself (e.g. 14: R=Ac, $R^1$=H, and 13; R=H, respectively; a more closely matched pair of compounds was not available). An interesting and related example of a hydrogen bond closing a seven-membered ring has been provided by WALL et al.[74]: the compound is a steroid derivative, 3β-acetoxy-4'-hydroxy-2'-methyl-16,17-butano-5α-androsta-1',3',16-trien-12-one, and the oxygen atoms of the phenolic hydroxyl and the cyclohexanone-type carbonyl are held by the rigid framework. The hydrogen bond is quite strong [ν(OH) = 3235 cm.$^{-1}$ and ν(CO) = 1685 cm.$^{-1}$ in $CS_2$] in spite of the enforced aplanarity of the carbon-oxygen bonds.

Also illustrated in Figure 18 are the results obtained with bromoform solutions (broken lines). These measurements support the view that the strong band at 1623 cm.$^{-1}$ (in $CCl_4$) exhibited by dihydroisocedrelone (14; R=$R^1$=H, i,2-dihydro) corresponds to the carbonyl (ring B) which is hydrogen bonded by both hydroxyls.

If the bands at 1658 and 1623 cm.$^{-1}$ has been mutally involved in Fermi resonance or vibrational coupling, then change of solvent would have altered their relative intensities.[75] The band of medium strength at 1658 cm.$^{-1}$ ( in $CCl_4$) is assigned to a double-bond stretching vibration (see below).

Absorption data have been obtained for solutions of hexahydrocedrelone (13; R=H, hexahydro) and of isocedrelone acetate (14; R=Ac, $R^1$=H) in carbon tetrachloride-diethyl ether solvent mixtures (up to 50% ether by volume). No marked changes were observed in the intensity, breadth, or position of the hydroxyl and carbonyl absorptions. Diethyl ether normally behaves as a Lewis base,[76] but it is evident that the intramolecular bonded hydroxyls in these particular molecules are not readily accessible; in compound (13; R=H, hexahydro) the methyl groups on position 4 lie very close to the diosphenol hydroxyl and may well prevent approach of the solvent molecules while in both compounds the intramolecular hydrogen bonds confer some degree of solvent insensitivity. Even so, some indications of intermolecular hydrogen bond formation could be discerned at the higher ether concentrations; thus, there was a new, very broad and low frequency absorption in the hydroxyl region and there was some reduction in the intensity of the intra-bonded carbonyl of ring B relative to that of the ring A carbonyl.

Contraction of ring B to a five-membered system, as in compound (15), raises the carbonyl stretching frequency to 1758 cm.$^{-1}$ ( in $CCl_4$), but introduction of a hydroxyl into ring D, as in compound (16; R=H; Table 17 and Figure 20), gives rise to another seven-membered intramolecular hydrogen bond and $\nu$(CO) falls to 1718 cm.$^{-1}$ with $\nu$(OH) at 3470 cm.$^{-1}$ (all in $CCl_4$).

Several different intramolecular hydrogen bonds are possible in compound (17; Tables 17 and 18, and Figure 20). The tentative

conclusion is that the ring B hydroxyl is bonded to the carbonyl of the ester grouping while the ring D hydroxyl is "free". Similarly it is concluded that compound (18; Tables 17 and 18, and Figure 20) shows the presence of a five-membered intramolecular hydrogen bond between the hydroxyl group and carbonyl of the lactone ring.

In summary, the values quoted in Tables 17 and 18 and summarized in Table 19 illustrate the constancy of both $\nu$(CO) and $\nu$(OH) when certain intramolecular situations are held relatively constant. Similarly, certain minor changes in molecular structure produce consistent changes in $\nu$(CO) and $\nu$(OH), in so far as overlapping permits accurate assignment of bands. Two types of intramolecular hydrogen bond provide the chief interest: the planar five-membered diosphenol system, and the twisted seven-membered system. In both cases, the small solvation shifts may be due to the inability of the solvent molecules such as chloroform and diethyl ether to approach the acceptor sites. The small, but definite, upward shift ($CCl_4$ to $CHCl_3$) of the diosphenol hydroxyl frequency is especially intriguing as the shift is normally downward for a phenolic hydroxyl, for example.[76]

The assignments for the stretching absorptions of the carbon-carbon double bonds, $\nu$(C=C), are less complete than those of the carbonyl and hydroxyl groups (Table 18). The $\Delta^{1,2}$ absorption has not been located and it is presumed to be of low intensity; the ring A enone system is known[77] to be non-planar. By contrast, the absorption due to $\Delta^{5,6}$-diosphenol double bond is quite prominent (medium strength, where a carbonyl is termed strong) and is at about 1627 ($\varepsilon$ ca. 150), 1612 ($\varepsilon$ ca. 100), and 1622 $cm.^{-1}$ for the cedrelone diosphenol itself, the acetate, and the methyl ether, respectively. The same absorption is harder to locate in the isocedrelone series where is an additional double bond in the 13,17 position. The

medium-strength absorptions near 1637 cm.$^{-1}$ in the ring B and D diacetate is presumably due, in part, to the 5,6-double bond, but in the free hydroxy-compounds the 7-ketone carbonyl absorption moves into this region and definitive assignments are not feasible. Conceivably, the band near 1658 cm.$^{-1}$ could represent the $\Delta^{13,17}$ bond, with the $\Delta^{5,6}$ absorption hidden within the strong carbonyl band at 1623 cm.$^{-1}$.

TABLE 17

Carbonyl Absorptions of Cedrelone and Related Compounds

| Compound No: | R | $R^1$ | Additional Structural Features | Ring A Carbonyl | | | | | | Ring B Carbonyl | | | | | | Additional carbonyl bands | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | $CCl_4$ | | | $CHCl_3$ | | | $CCl_4$ | | | $CHCl_3$ | | | $CCl_4$ | | | $CHCl_3$ | | | |
| | | | | $\nu$ | $\Delta\nu_{\frac{1}{2}}$a | $\epsilon^a$ | $\nu$ | $\Delta\nu_{\frac{1}{2}}$a | $\epsilon^a$ | $\nu$ | $\Delta\nu_{\frac{1}{2}}$a | $\epsilon^a$ | $\nu$ | $\Delta\nu_{\frac{1}{2}}$a | $\epsilon^a$ | $\nu$ | $\Delta\nu_{\frac{1}{2}}$a | $\epsilon^a$ | $\nu$ | $\Delta\nu_{\frac{1}{2}}$a | $\epsilon^a$ | Species |
| 13 | Me | | | 1696† | 11 | 1290 | 1692† | 20 | 940 | 1696† | 11 | 1290 | 1692† | 20 | 940 | | | | | | | |
| | Ac | | | 1701† | 18 | 870 | - | - | - | 1701† | 18 | 870 | - | - | - | 1770 | 12 | 500 | - | - | - | enol OAc |
| | Ac | | 1,2-Epoxy | 1722b | 10 | 620 | 1721b | 13 | 320 | 1708 | 10 | 680 | 1705b | 20 | 340 | 1770 | 14 | 460 | 1763 | 22 | 230 | enol OAc |
| | Ac | | 1,2-dihydro | 1720b | 11 | 630 | 1714sh | 19 | 520 | 1705b | 12 | 740 | 1702 | 18 | 655 | 1770 | 14 | 550 | 1764 | 17 | 500 | enol OAc |
| | Ac | | 1,2,20,21,22,23-hexahydro | 1720b | 10 | 600 | 1714sh | 16 | 520 | 1705b | 12 | 750 | 1701b | 22 | 625 | 1770 | 14 | 515 | 1763 | 17 | 440 | enol OAc |
| | H | | | 1695b | 20 | 540 | 1685sh | - | - | 1678b | 15 | 570 | 1678b | 18 | 770 | | | | | | | |
| | H | | 1,2-epoxy | 1723 | 11 | 585 | 1719 | 20 | 465 | 1681 | 13 | 535 | 1681 | 19 | 450 | | | | | | | |
| | H | | 1,2-dihydro | 1718 | 10 | 665 | 1713 | 17 | 465 | 1678 | 13 | 550 | 1677 | 18 | 440 | | | | | | | |
| | H | | 1,2,20,21,22,23-hexahydro | 1717 | 9 | 645 | 1712 | 17 | 440 | 1678 | 12 | 565 | 1676 | 19 | 420 | | | | | | | |
| 14 | Ac | Ac | | 1698†a | 13 | 1060 | 1694†a | 19 | 705 | 1698†a | 13 | 1060 | 1694†a | 19 | 705 | 1766 | 15 | 670 | 1759a | 25 | 490 | enol OAc |
| | | | | | | | | | | | | | | | | 1743 | 17 | 560 | 1729 | 35 | 420 | OAc($C_{(15)}$) |
| | Ac | Ac | 23-acetyl | 1699†b | 10 | 1120 | 1693†b | 14 | 750 | 1699†b | 10 | 1120 | 1693†b | 14 | 750 | 1767 | 15 | 680 | 1760a | 20 | 430 | enol OAc |
| | | | | | | | | | | | | | | | | 1743b | 18 | 560 | 1729 | 33 | 395 | OAc($C_{(15)}$) |
| | | | | | | | | | | | | | | | | 1688sh | 10 | 740 | 1683 | - | - | Ac($C_{(23)}$) |
| | Ac | Ac | 21-acetyl | 1697†b | 14 | 1330 | 1688† | 26 | 920 | 1697†b | 14 | 1330 | 1688† | 26 | 920 | 1767 | 14 | 610 | 1760a | 20 | 350 | enol OAc |
| | | | | | | | | | | | | | | | | 1744 | 19 | 490 | 1730 | 29 | 290 | OAc($C_{(15)}$) |
| | | | | | | | | | | | | | | | | 1692sh | - | - | 1688† | 26 | 920 | Ac($C_{(21)}$) |
| | Ac | H | | 1699 | 15 | - | 1695b | 18 | 475 | 1672 | 20 | - | 1667b | 22 | 460 | 1771 | 15 | - | 1764 | 18 | 470 | enol OAc |
| | Ac | H | 1,2-dihydro | 1721 | 12 | - | 1714 | 20 | 490 | 1672 | 15 | - | 1665 | 22 | 350 | 1772 | 15 | - | 1764 | 24 | 560 | enol OAc |
| | H | H | | 1699a | - | - | 1685ab | 22 | 320 | 1622 | - | - | 1619a | 25 | 340 | | | | | | | |
| | H | H | 1,2-dihydro | 1718 | 11 | 560 | 1713 | 17 | 420 | 1623b | 11 | 540 | 1620 | 17 | 450 | | | | | | | |
| 15 | | | | 1692 | 16 | - | 1683 | 22 | 480 | 1758† | 11 | - | 1751† | 16 | 750 | 1758† | 11 | - | 1751† | 16 | 750 | Ring D CO |
| 16 | | | 15-keto | - | - | - | 1683 | 21 | 525 | - | - | - | 1755† | 14 | 800 | - | - | - | 1755† | 14 | 800 | Ring D CO |
| | H | | | 1691 | 14 | 670 | 1683 | 23 | 495 | 1718b | 17 | 385 | 1714b | 26 | 290 | | | | | | | |
| | Ac | | | 1690 | 15 | 620 | 1682 | 25 | 470 | 1742† | 23 | 725 | 1738† | 31 | 655 | 1742† | 23 | 725 | 1738† | 31 | 655 | OAc($C_{(15)}$) |
| 17 | | | | 1688b | 14 | - | 1677b | 22 | 620 | | | | | | | 1705b | 15 | - | 1703b | 21 | 425 | Ester CO |
| 18 | | | | 1686 | 12 | 470 | 1677 | 20 | 520 | | | | | | | 1753 | 15 | 450 | 1743 | 25 | 445 | Lactone CO |
| 19 | | | | 1690 | 18 | - | 1683 | 21 | - | | | | | | | 1742† | 16 | - | 1735† | 22 | - | Ester CO |
| | | | | | | | | | | | | | | | | 1742† | 16 | - | 1735† | 22 | - | Ring D CO |

Molarities generally in the range 1 to 20mM, but some solutions were saturated and of unknown concentration.

$\nu$ and $\Delta\nu_{\frac{1}{2}}$a are in $cm^{-1}$. Cell paths: for $CCl_4$ 5mm, $CHCl_3$ 0.51mm - Not measured.

†Two or more bands superimposed at this frequency, only one set of data ($\nu_{max}$, $\Delta_{\frac{1}{2}}$a, $\epsilon^a$) is quoted and correlations based on these values are more tentative, since the contributions of the individual stretching absorptions cannot be observed. a Asymmetric band. b $\Delta_{\frac{1}{2}}$a calculated by using the undisturbed wing of asymmetric bands. sh Shoulder, $\Delta_{\frac{1}{2}}$a calculated as in b.

TABLE 18

Hydroxyl and Carbon-Carbon Double Bond Absorptions of Cedrelone and Related Compounds

| Compound No: | R | $R^1$ | Additional Structural Features | Ring B hydroxyl | | | | | | Ring D hydroxyl | | | | | | Carbon-carbon double bonds | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | $CCl_4$ | | | $CHCl_3$ | | | $CCl_4$ | | | $CHCl_3$ | | | $CCl_4$ | | | $CHCl_3$ | | |
| | | | | $\nu$ | $\Delta\nu_{\frac{1}{2}}$ a | $\epsilon$ a | $\nu$ | $\Delta\nu_{\frac{1}{2}}$ a | $\epsilon$ a | $\nu$ | $\Delta\nu_{\frac{1}{2}}$ a | $\epsilon$ a | $\nu$ | $\Delta\nu_{\frac{1}{2}}$ a | $\epsilon$ a | $\nu$ | $\Delta\nu_{\frac{1}{2}}$ a | $\epsilon$ a | $\nu$ | $\Delta\nu_{\frac{1}{2}}$ a | $\epsilon$ a |
| 13 | Me | | | | | | | | | | | | | | | (1654) | sh | vw | | | |
| | | | | | | | | | | | | | | | | (1621) | sh | vw | 1622 | - | vw |
| | Ac | | 1,2-epoxy | | | | | | | | | | | | | (1617) | - | - | 1615 | (17) | (50) |
| | Ac | | 1,2-dihydro | | | | | | | | | | | | | (1615) | - | - | 1612 | (16) | (130) |
| | Ac | | 1,2,20,21,22,23,hexahydro | | | | | | | | | | | | | 1623 | (25) | w | 1610 | (15) | (95) |
| | H | | | 3417 | 41 | 115 | 3425 | 64 | 90 | | | | | | | 1629 | (13) | (145) | 1627 | (19) | (180) |
| | H | | 1,2-epoxy | 3418 | 38 | 120 | 3428 | 58 | 95 | | | | | | | 1629 | (13) | (140) | 1630 | (18) | (150) |
| | H | | 1,2-dihydro | 3418 | 39 | 125 | 3430 | 64 | 90 | | | | | | | 1627 | (10) | (160) | 1626 | (15) | (170) |
| | H | | 1,2,20,21,22,23-hexahydro | 3420 | 38 | 120 | 3430 | 60 | 85 | | | | | | | 1626 | (10) | (150) | 1624 | (13) | (180) |
| 14 | Ac | Ac | | | | | | | | | | | | | | 1638 | (20) | (115) | 1637 | (28) | (115) |
| | Ac | Ac | 23-acetyl | | | | | | | | | | | | | 1639 | (18) | (125) | 1638 | (22) | (120) |
| | Ac | Ac | 21-acetyl | | | | | | | | | | | | | 1639 | - | (100) | 1638 | - | (60) |
| | Ac | H | | | | | | | | 3460 | (120) | - | 3415 | 195 | 95 | 1630 | - | w | 1630 | (20) | (225) |
| | Ac | H | 1,2-dihydro | | | | | | | 3450 | (120) | - | 3410 | br | - | | | | 1628 | (24) | (210) |
| | H | H | | 3413b | 56 | - | 3418†a | 115 | 145 | 3475b | 98 | - | 3418†a | 115 | 145 | 1658 | - | - | 1659 | - | (145) |
| | H | H | 1,2-dihydro | 3415b | 50 | 190 | 3418† | 105 | 200 | 3466b | 80 | 130 | 3418† | 105 | 200 | 1658 | 11 | 200 | 1658 | 15 | 135 |
| 16 | H | | | | | | | | | 3470 | 76 | 110 | 3440 | 126 | 80 | | | | 1631 | - | - |
| 17 | | | | 3530 | 29 | - | 3525b | 58 | 80 | 3602 | 28 | - | 3604a | 52 | 95 | | | | | | |
| 18 | | | | 3595 | 16 | 110 | 3593 | 20 | 100 | | | | | | | 1629 | - | - | | | |
| 19 | | | | 3546a | 85 | - | 3520 | 100 | - | | | | | | | | | | | | |

Values in parenthesis are approximate. For symbols see Table 17. Cell paths, $\nu$(OH): for $CCl_4$ 2mm, $CHCl_3$ 2mm, $\nu$(C=C): for $CCl_4$ 5mm, $CHCl_3$ 0.51mm. Dilutions were made but no change was encountered.

TABLE 19.

Assignments for Stretching Absorptions due to Carbonyl and Hydroxyl Functions.

| Grouping | Average Values | |
|---|---|---|
| | $\nu$ cm.$^{-1}$ | $\Delta\nu$* cm.$^{-1}$ |
| 3-Ketone in ring A | 1720 | 6 |
| 3-Ketone in ring A, 1,2-epoxide | 1722 | 2 |
| 3-Ketone in ring A, $\Delta^{1,2}$ and six-membered ring B | 1698 | 9 |
| 3-Ketone in ring A, $\Delta^{1,2}$ and five-membered ring B | 1689 | 9 |
| 7-Ketone of diosphenol | 1679 | 1 |
| 7-Ketone of diosphenol and bonding by 15-hydroxyl | 1622 | 3 |
| 7-Ketone of diosphenol methyl ether | 1696 | 4 |
| 7-Ketone of diosphenol acetate, cedrelones | 1704 | 3 |
| 7-Ketone of diosphenol acetate, isocedrelones | 1698 | 5 |
| 7-Ketone of diosphenol acetate, and bonding by 15-hydroxyl | 1672 | 6 |
| 6-Acetate of diosphenol acetates, ring B | 1769 | 7 |
| 15-Acetate, ring D | 1743 | 14 |
| 6-Hydroxy of diosphenol in ring B | 3416 | -8 |
| 15-Hydroxyl in ring D, bonding to 7-ketone | 3460 | 45 |

All data drawn from Tables 17 and 18.

* $\Delta\nu = \nu_{CCl_4} - \nu_{CHCl_3}$. Typical variation amongst $\nu$(CO) values $\pm$ 3 cm.$^{-1}$.

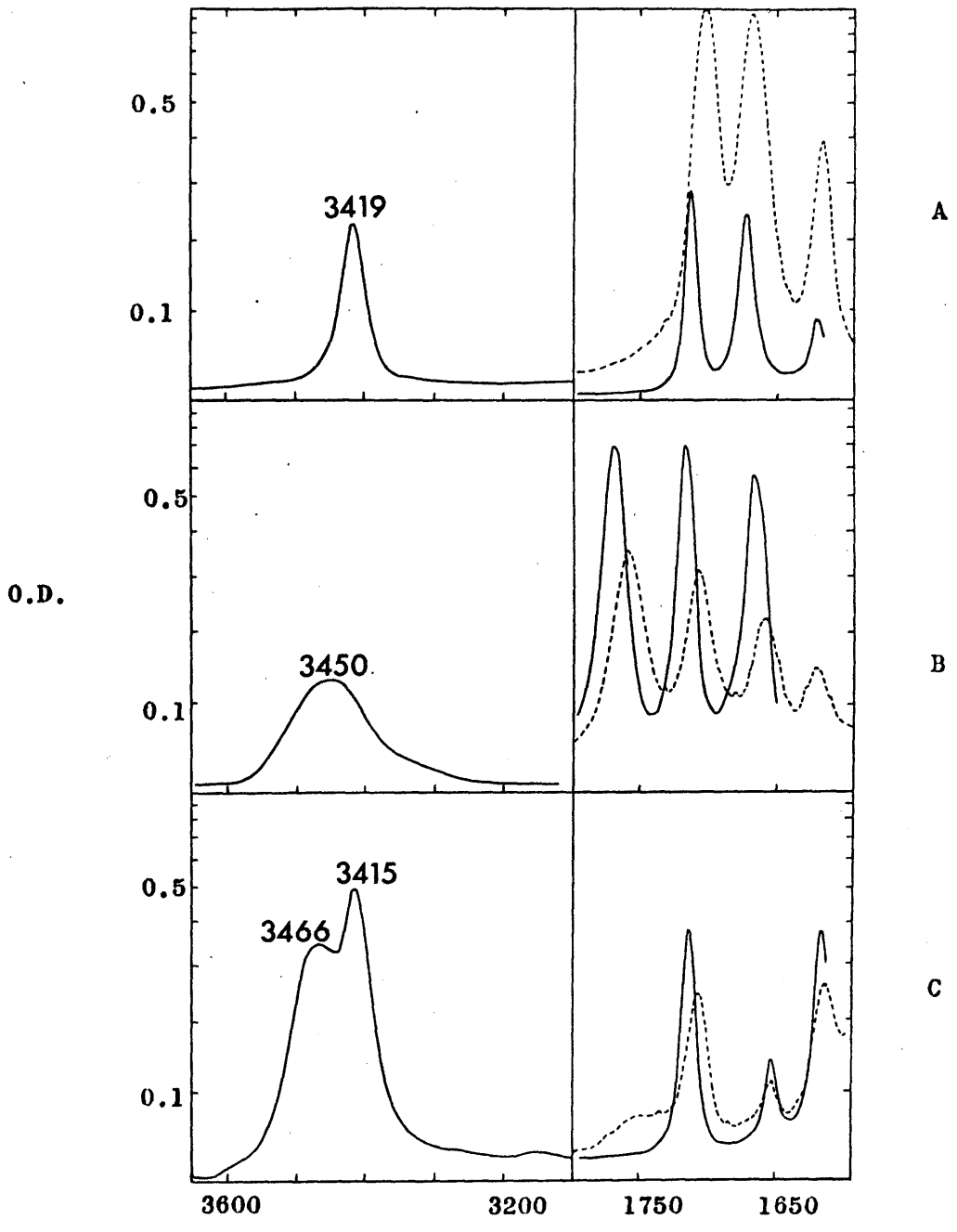



**FIGURE 18.** Absorptions in the hydroxyl and carbonyl stretching regions. A, Dihydrocedrelone (13; R=H, 1,2-dihydro); B, dihydroisocedrelone acetate (14; R=Ac, $R^1$=H, 1,2-dihydro); and C, dihydroisocedrelone (14; R=$R^1$=H, 1,2-dihydro) in carbon tetrachloride (full line) and bromoform (broken line). Solutions in carbon tetrachloride in 2 cm. (hydroxyl) and 5 mm. (carbonyl) cells; bromoform, 0.47 mm. cells. Concentrations: for compounds (13; R=H, 12-dihydro) and (14; R=$R^1$=H, 1,2-dihydro) in carbon tetrachloride, 1.5 and 1.3 mM respectively while the rest were saturated solutions.

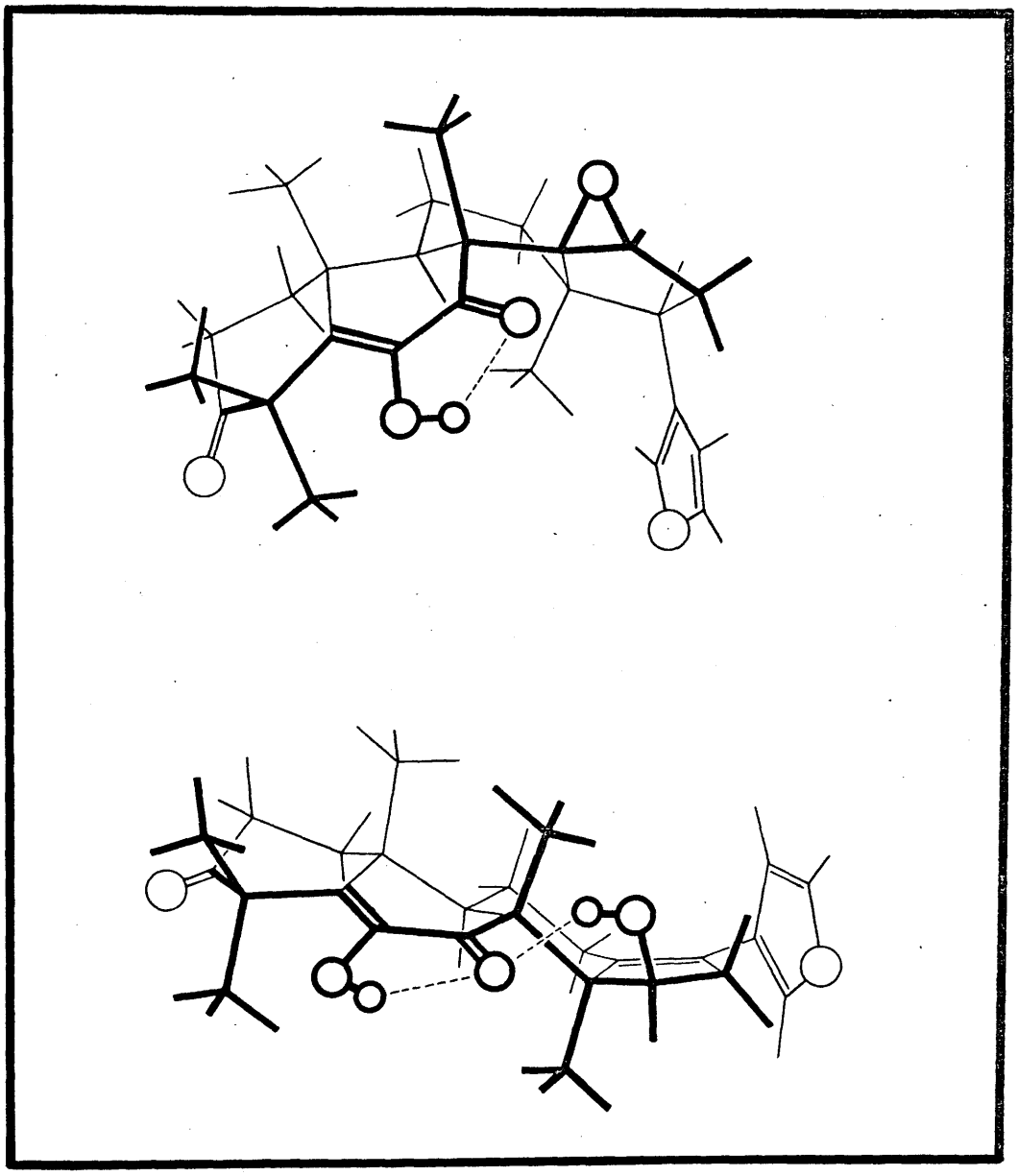


FIGURE 19. Projections of Dreiding molecular models of compounds (13; R=H, 1,2-dihydro) and (14; R=$R^1$=H, 1,2-dihydro). Thickened lines indicate nearest side of the molecule and dotted lines the hydrogen bonds.

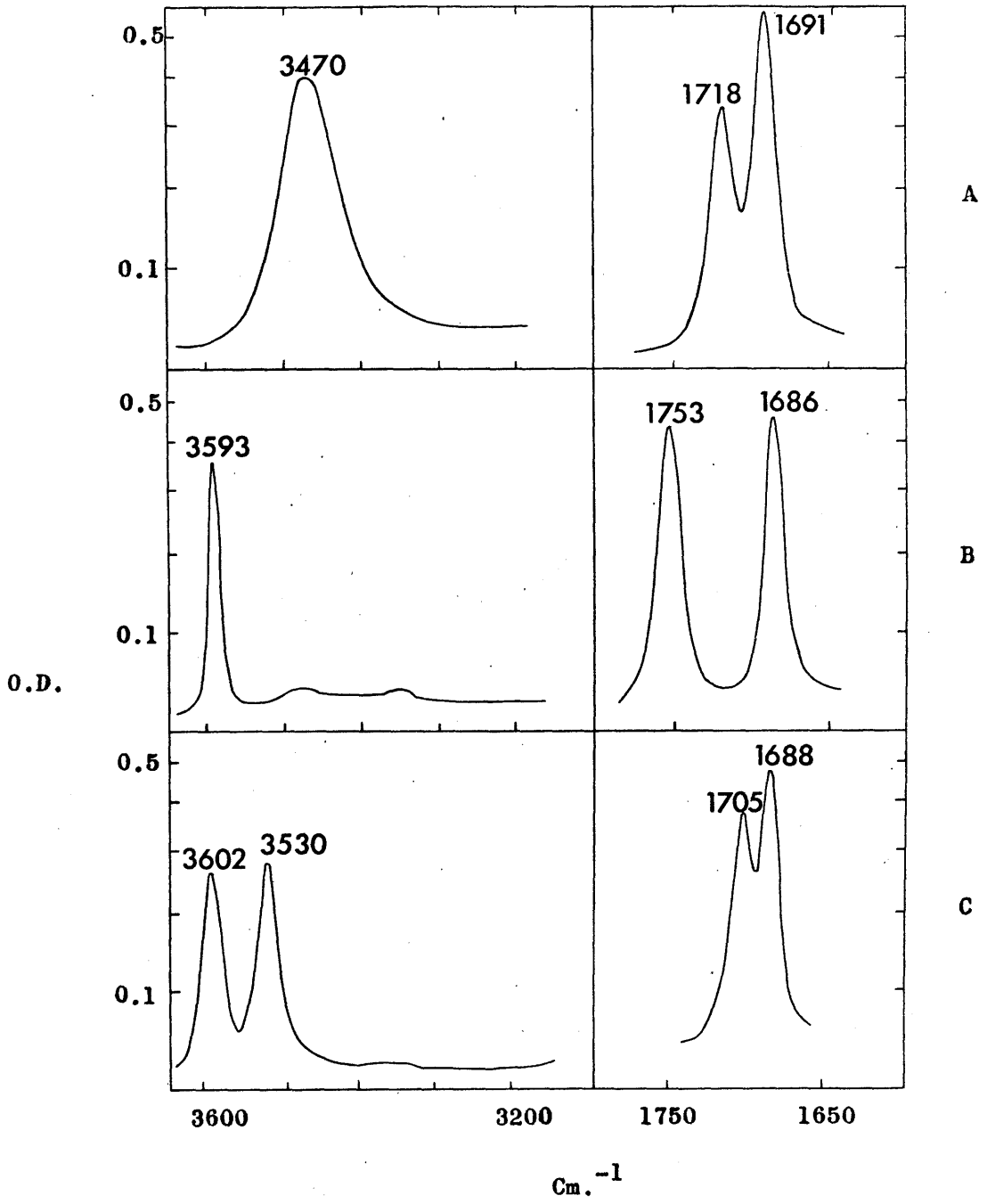
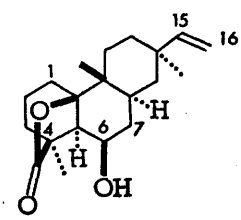


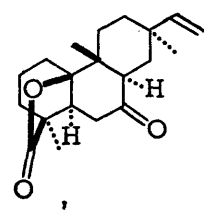

FIGURE 20. Absorptions in the hydroxyl and carbonyl stretching regions. A, The norketone (16; R=H); B, isocedrelone acid lactone (18); and C, methyl isocedrelonate (17). Solutions in carbon tetrachloride in 2 cm. (hydroxyl) and 5 mm. (carbonyl) cells. Concentrations for compounds (16; R=H), (18) and (17) were 1.67, 1.72, and saturated respectively.

Rosololactone and Related Compounds

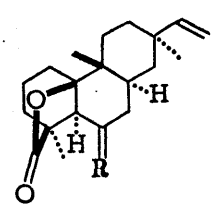
The results are summarized in Table 20. In all four diterpenoid lactones, rosololactone (20), rosenonolactone (21), rosonolactone (22a), and 9-deoxyrosenonolactone (22b) the presence of a $\gamma$-lactone system in ring A is characterised by an intense symmetrical absorptions at ca. 1780 cm.$^{-1}$ (in $CCl_4$, Table 20). The extinction coefficients accord with the presence of one such lactone grouping per molecule. It is interesting to note that these absorptions are all sharp ($\Delta\nu_{\frac{1}{2}}^{a}$ ca. 16 cm.$^{-1}$) in contrast to the $\gamma$-lactones discussed in the following section i.e. no Fermi resonance involved. The ketonic grouping at $C_7$ as in rosenonolactone (21) absorbs at 1719 cm.$^{-1}$ (in $CCl_4$). Introduction of the ketonic carbonyl grouping at $C_6$, however, as in rosonolactone (22a) increases the frequency of absorption to 1727 cm.$^{-1}$. This increase of 8 cm.$^{-1}$ may well be a result of dipole interaction of a carbonyl grouping at $C_6$ whereas the carbonyl group at $C_7$ in unable to participate in an interaction of this kind.




(20)




(21)




(22) a, R=O
b, R=$H_2$

In the spectra of rosololactone (20) and dihydro-rosololactone there is no evidence for the presence of any intramolecular hydrogen bonding involving the hydroxyl group, and the lactonic carbonyl or ester oxygen, in spite of the fact that both groupings lie on the same side of the ring junction A/B. Although the OH····O=C distance of 2.8 Å is favourable no intramolecular hydrogen bond is formed. This situation must reflect the unsuitability of the p-orbitals of both the carbonyl and the alkyl oxygen with respect to the s-orbital of the proton of the hydroxyl group. This lack of intramolecular hydrogen bonding although, on first sight, the arrangement seems favourable indicates that the stereochemistry of such an arrangement is the most important factor in deciding whether or not bonding occurs.

It is frequently assumed that intermolecular hydrogen bonding is absent at concentrations as low as 0.01-0.001 M, except in special cases such as the carboxylic acids, oximes and dimedone derivatives.[78] Recently, however, this class of phenomenon has been extended to include such compounds as cyclohexane-1,3-diols,[79] steroidal hydroxy-esters,[80] labdane-8α,15-diol,[81] novolaks (a section of this thesis), 3-acetyl-5-hydroxybenzo[b]-thiophen,[82] and 5β-B-nor-cholestan-3α,6α-diol.[83] In the present work intermolecular association of rosololactone molecules is also unusually persistent. Progressive dilution from 20 mM to 0.2 mM clearly shows (Figure 21) absorbance at 3535 $cm.^{-1}$ (in $CCl_4$) due to an intermolecular hydrogen bond (band is concentration dependent). The lactonic carbonyl absorption at 1778 $cm.^{-1}$ also shows the presence of intermolecular hydrogen bonding by the appearance of the shoulder at 1757 $cm.^{-1}$. There is, therefore, intermolecular hydrogen bonding between the hydroxyl of one molecule and the carbonyl of another. The question of the nature of this associated species is an important one. The concentration range employed in this study has been such as to ensure that a monomer-dimer equilibrium is in operation. This postulation might well be invalid if, for example, the assocaiated tetramer were more stable than the dimeric species. For the purpose

of this dicussion only the dimeric species is considered to be present. Is it an open or closed dimer? To enable an assestment of this problem the measurement of apparent molecular weight of various solutions of rosololactone (20) in carbon tetracloride have been correlated with their ν(OH) absorptions. This correlation of apparent molecular weight and ν(OH) absorptions will give a clue to the nature of the dimeric species existing in dilute solution. From the molecular weight measurements the percentage of monomer to dimer (open and closed) can be determined. A second set of results for this equilibrium can also be calculated from the intensities of the ν(OH) free absorption figures. The resulting inequality between the two sets derived from these two different sources should be a measure of the equilibrium between open and closed dimer. The results are summarized in Table 21. There is, in fact, an equilibrium between the open and closed dimeric species. The molecular arrangement for such an associated species to exist at such low levels of concentration must be highly specific (energy and stereochemistry). The values in Table 21 illustrated that the open dimer is more favoured than the closed.

If this dimeric equilibrium exists in very dilute solution then the same dimer might be present in the solid state. The solid state spectrum (Figure 22) of rosololactone (20) shows a single ν(OH) bonded absorption at 3523 $cm.^{-1}$ and two distinct carbonyl absorptions at 1763 and 1710 $cm.^{-1}$. The appearance of a single fairly sharp bonded ν(OH) absorption means that all the hydroxyls appear to be similarly intermolecularly hydrogen bonded. The carbonyl absorption at high frequency (1763 $cm.^{-1}$) could correspond to unassociated lactonic carbonyl groups and the shoulder on the low frequency side of the band to dimeric association. The carbonyl absorption at 1710 $cm.^{-1}$, however, is extremely low for a bonded carbonyl group. This large shift from the free position would seem to infer that the carbonyl is bonded to two hydroxyl groups [cf. cedrelone twin hydrogen bond case]. This interpretation

seems to be the most feasible. On the other hand the explanation may well lie in Fermi resonance effects. Examination of rosololactone (20) as a nujol mull still showed the presence of two distinct carbonyl bands (1763 and 1710 $cm.^{-1}$) eliminating the possibilty of a chemical change in the preparation of the KCl disc under high pressure.

In carbon tetrachloride solution both dihydro-rosololactone and dibromo-rosololactone exhibit the same dimeric equilibrium established for the parent compound, rosololactone (20). Their solid state spectra, howevr, are quite different in appearance from that of the parent compound. Dihydro-rosololactone exhibits a single bonded hydroxyl absorption at 3511 $am.^{-1}$ and a carbonyl absorption at 1751 $cm.^{-1}$ with a shoulder at 1768 $cm.^{-1}$. In this case the hydroxyl of one molecule might be bonding to the carbonyl of another while the hydroxyl of the latter bonds to the carbonyl of a third molecule and so on, or a closed dimer might the major species. In the case of dibromo-rosololactone the solid state $\nu$(OH) bonded absorption appears as a very broad band centred around 3400 $cm.^{-1}$, with a broad carbonyl band at ca. 1760 $cm.^{-1}$. The X-ray examination of the packing adopted by the molecules shows the presence of OH····Br hydrogen bonds.[84] The infrared evidence is in keeping with this picture.

Finally, examination of the 1000-1200 $cm.^{-1}$ reveals that there is considerably overlap of the $\nu$(C-O) and $\gamma$(CH) absorptions of molecules with double bonds in the 15,16-position [cf. lactone disccussion above].

TABLE 20.

Absorptions of Rosololactone (20) and Related Compounds

| No. | Compound | $CCl_4$ | | | | | | Solid state* | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Hydroxyl | | | Carbonyl | | | Hydroxyl | | Carbonyl | |
| | | $\nu$ | $\Delta\nu_{\frac{1}{2}}^{a}$ | $\varepsilon^{a}$ | $\nu$ | $\Delta\nu_{\frac{1}{2}}^{a}$ | $\varepsilon^{a}$ | $\nu$ | $\Delta\nu_{\frac{1}{2}}^{a}$ | $\nu$ | $\Delta\nu_{\frac{1}{2}}^{a}$ |
| 20 | Rosololactone | 3633 | 12 | 120 | 1778 | 16 | 910 | 3523 | 80 | 1763 | 16 |
| | | (3535)† | br | 15 | | | | | | 1710 | 16 |
| | 15,16-dihydro-rosololactone | 3633 | 12 | 120 | 1778 | 16 | 940 | 3511 | 70 | 1768 | sh |
| | | (3535)† | br | 15 | | | | | | 1740 | - |
| | 15,16-dibromo-rosololactone | 3632 | - | - | | | | 3400 | br | 1766 | sh |
| | | (3530)† | - | - | | | | | | 1750 | - |
| 21 | Rosenonolactone | | | | 1780 | 15 | 880 | | | | |
| | | | | | 1719 | 12 | 500 | | | | |
| | 15,16-dihydro-rosenonolactone | | | | 1780 | 16 | 890 | | | | |
| | | | | | 1719 | 12 | 550 | | | | |
| 22a | 15,16-dihydro-rosonolactone | | | | 1788 | 15 | 1000 | | | | |
| | | | | | 1712 | 12 | 410 | | | | |
| 22b | 9-deoxyrosenonolactone | | | | 1774 | 19 | 845 | | | | |
| | 15,16-dihydro-9-deoxyrosenonolactone | | | | 1773 | 18 | 860 | | | | |

Values in parenthesis are approximate.
Concentrations: $CCl_4$, ca. 2.0 mM examined in 2 cms. cells [$\nu$(OH)] and 5 mm. cells [$\nu$(CO)].
- Not measured.
† Concentration dependent band.
* Prepared as KCl discs. For the nujol mull of rosololactone the following bands were observed, 3521 (50), 1763 (10) and 1710 (12) $cm.^{-1}$.

TABLE 21.

Correlation of Molecular Weight with $\varepsilon^a$ Values for Free Hydroxyl Absorptions of Rosololactone (20).

| Conc. mg/ml. $CCl_4$ | M.W. Measurements | | | Infrared Measurements | | | | |
|---|---|---|---|---|---|---|---|---|
| | M.W. Obs.† | % Calc. Monomer | % Calc. Dimer | $\varepsilon^a$ Calc.* Free | $\varepsilon^a$ Obs. Free | $\varepsilon^a$ Open Dimer | % Open Dimer | % Closed Dimer |
| 4.4 | 488±5 | 46 | 64 | 56 | 80 | 24 | 38 | 26 |
| 1.8 | 417±5 | 69 | 31 | 86 | 105 | 19 | 30 | 1 |
| 0.34 | 340 | 93 | 7 | 116 | 120 | 4 | 6.4 | 0.6 |

† Measurements conducted above 5 mM concentration level are accurate to within ±5. Below this limit the errors will be slightly higher.

* Calculated from percentage monomer derived from molecular weight study assuming 100% monomer has $\varepsilon^a$ value of 125 at infinite dilution.

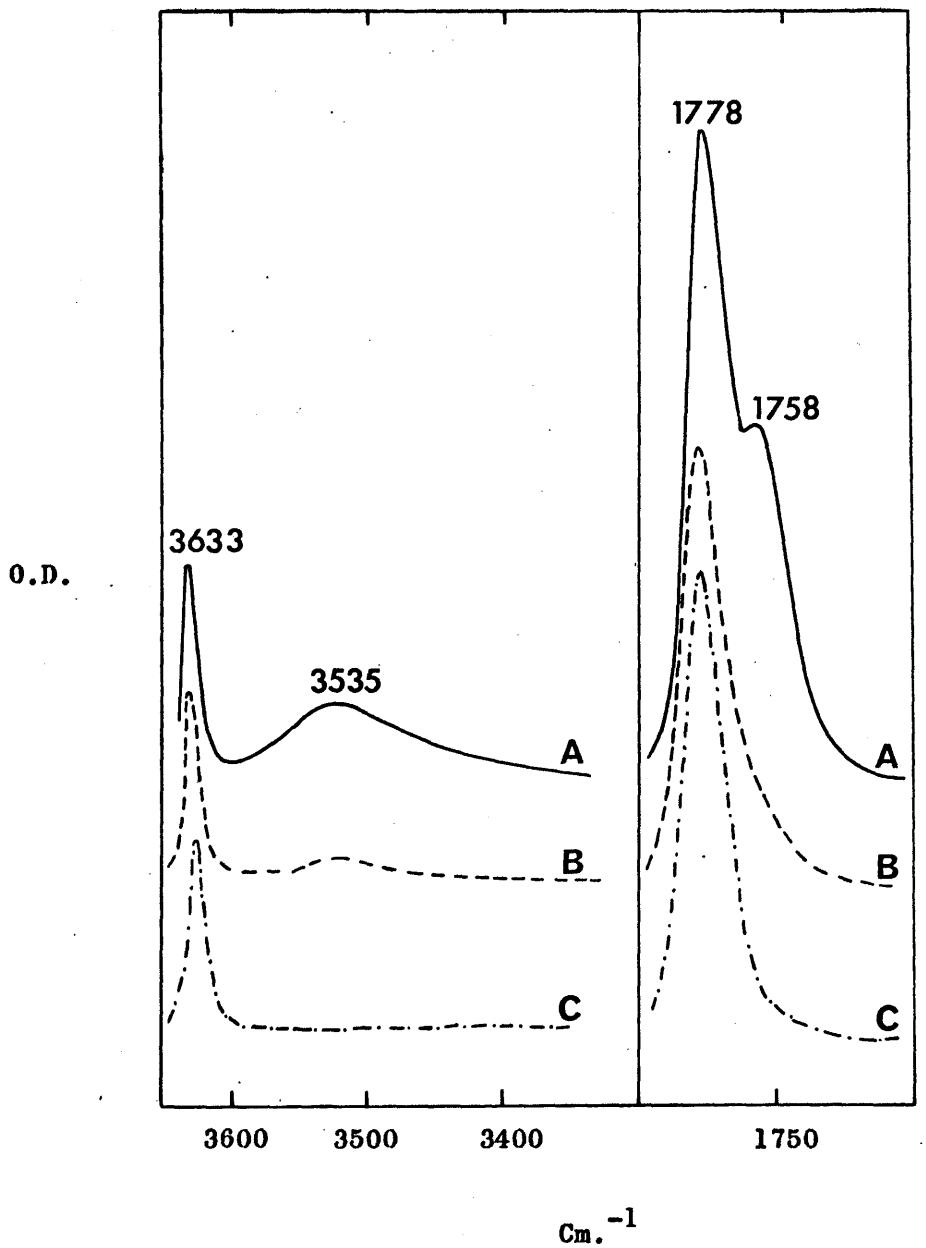



FIGURE 21. Absorptions in the hydroxyls and carbonyl stretching regions for rosololactone (20): A, 20 mM in 0.5 mm. cells [ν(OH) and ν(CO)]; B, 2 mM in 5 mm. cells [ν(OH)] and 2 mm. cells [ν(CO)]; C, 0.2 mM in 5 cm. cells [ν(OH)] and 2 cm. cells [ν(CO)].

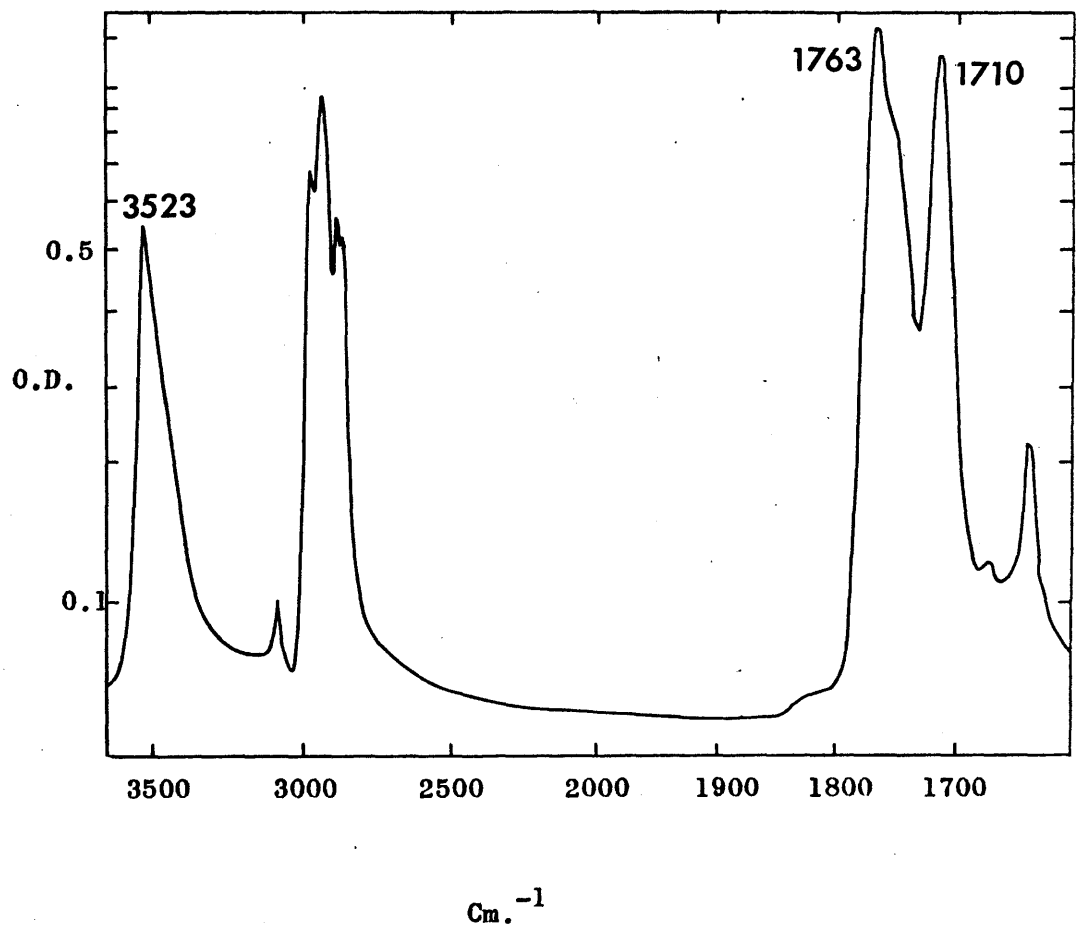
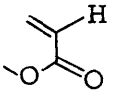



FIGURE 22. Infrared spectrum of rosololactone (20), ca. 1 mg in 300 mgs. potassium chloride.

γ-Lactones

Lactones containing the basic system (A) almost invariably exhibit carbonyl absorptions of complex shape,[75] and Fermi resonance[85] involving the carbonyl stretching frequency and

(A) 

first overtone of the γ(CH) of the α-hydrogen has been postulated by JONES and his colleagues.[75] The relative intensities of the observed pairs of bands are dramatically solvent-dependent and the frequencies show much smaller and more irregular solvent shifts[86] than do those of normal carbonyl groups.[87]

The availability[88] of a number of sesquiterpenoid lactones has permitted a study of the carbonyl absorptions under conditions of high resolution, and it has become evident that the complexity is not confined to the system (A), but is also displayed, though to a lesser degree, by saturated five-ring lactones. Again, the relative intensities of the various peaks and shoulders are solvent-dependent and solution in the more polar or more powerful hydrogen bonding solvents is accompanied by a shift of the absorption centre to lower frequency.

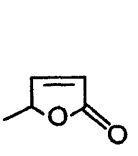
The present work examines the solvent-dependence of the absorptions occurring in the ν(C=O) region between 1700 and 1800 $cm.^{-1}$. The results, in general, support and extend the literature findings.[75] In the lactones examined (23-34), these absorptions are complex and also markedly solvent-sensitive (Figure 23). Bifurcate bands in the carbonyl region of compounds containing a single carbonyl function can have their origin in conformational equilibria,[86] solvent-solute interactions,[89] hot transitions,[90] Fermi resonance or vibrational coupling. Other explanations

such as intermolecular hydrogen bonding through enolic forms and by methylene groups[91] are at variance with normal experience. An attempt has been made to establish the origin of the irregularly shaped bands and these attempts, involving the effects of solvent, temperature and of an additional solute, are discussed below. Some more general points are dealt with first.

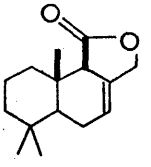
The lactones show the simplest carbonyl bands in n-hexane solution, and if the approximate peak positions are compared over the limited range of compounds examined, one can conclude that it is not possible to distinguish saturated γ-lactones from their αβ-unsaturated counterparts by simple inspection of the peak maximum. However, it is true that in the present series the saturated lactones lie in the range 1806 to 1787 cm.$^{-1}$ while the αβ-unsaturated compounds absorb between 1791 and 1773 cm.$^{-1}$. This partial overlap is, of course, the result of the competing effects of conjugation and strain.[92] Where direct comparision is possible between αβ-unsaturated five-ring lactones and the corresponding di-hydro-compound then, the latter does absorb slightly to higher frequency, but stereochemical differences can also produce significant frequency shifts, as for example, between lactones (29) and (30). It is more difficult to compare the different lactones in carbon tetrachloride and chloroform because of the more irregular shapes, or even the splitting, of the bands in the latter solvent. However, if an approximate estimate of the position of the band centre is made then, it is found that the shifts, n-hexane to chloroform, range from 18 to 36 cm.$^{-1}$, with the smaller shifts being encountered with lactones (25), (26) and (29), where there might be some grounds for assuming a steric inhibition to solvation.

Inspection of Figure 23 reveals that the general pattern is such that some lactones show several shoulders, or even distinct bands, in the carbonyl region and that these vary in intensity with

change of solvent as the main carbonyl absorption moves through the region. However, the overall intensity, as measured by the approximate band area, over the carbonyl region is much the same in the three solvents, no matter how split up the band. Only the pair of $\alpha\beta$-unsaturated lactones (23 and 32) bearing an $\alpha$-hydrogen show marked splitting in all three solvents. The other unsaturated lactones (26, 27, and 28) show much smoother band contours rather like those of the saturated lactones (24, 25, 29, 31, 33, and 34).



(23)



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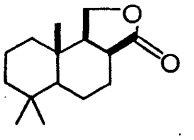

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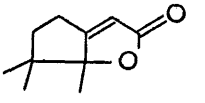

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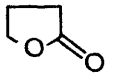

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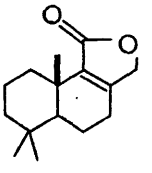

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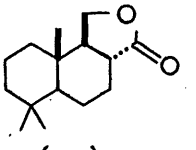

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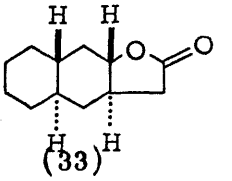

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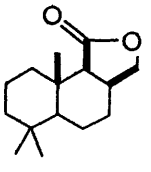

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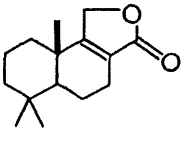

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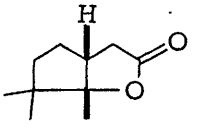

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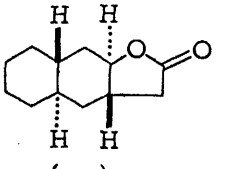


(34)

Campholenolactone (32) exhibits the phenomenon most markedly, thus there is a shift of the main absorption band from 1786 cm.$^{-1}$ in the n-hexane to around 1750 cm.$^{-1}$ in chloroform. This direction of shift is characteristic of that found for the stretching absorption of an $X^{\delta+}=O^{\delta-}$ dipole, and is attributed to an intermolecular association of the type,[89] $X^{\delta+}=O^{\delta-}\cdots HCCl_3$. It is conceivable that more than one band could result from the presence of several solute-solvent species, but this seems unlikely in view of the complexity shown in carbon tetrachloride, for which specifically orientated complexes seem unreasonable. At this juncture, one might

assign the absorption at 1786 cm.$^{-1}$ (in n-hexane) to the stretching absorption of the C=O bond. However, the band at lower frequency (1758 cm.$^{-1}$ in n-hexane and 1759 cm.$^{-1}$ in $CCl_4$) increases in intensity at the expense of the higher frequency band, and it is evident that the true position for $\nu$(CO) cannot be determined by simple inspection. This transference of intensity in the 1700 to 1800 cm.$^{-1}$ region is further illustrated in Figure 24. The remainder of the spectrum is practically unaltered by change of solvent indicating that a solvent-sensitive conformational equilibrium is not present, since different conformers normally have several different absorption bands. There is, however, a band at 881 cm.$^{-1}$ (in n-hexane), $\Delta\nu^{a}_{\frac{1}{2}} \approx 8$ cm.$^{-1}$, $\varepsilon^{a} \approx 190$, which progressively increases in frequency as the polarity of the solvent is increased. This absorption band is in the region expected for the out-of-plane deformation vibration of the $\alpha$-hydrogen attached to the double bond and it is assumed that this is the correct assignment. Indeed JONES and his collaborators have already suggested[75] that Fermi resonance with the first overtone, $2\gamma$(CH), of this vibration might be responsible for the bifurcate absorption reported for the carbonyl regions of other lactones of type (A). The data reported in this thesis accords well with their findings, thus, in the case of campholenolactone (32), the main band in the carbonyl region decreases in frequency as the polarity of the solvent is increased, while the band assigned to the $\gamma$(CH) of the $\alpha$-hydrogen increases in frequency; in the absence of Fermi resonance, the first overtone of $2\gamma$(CH) would be expected to lie near 1762, 1768 and 1788 cm.$^{-1}$ in n-hexane, $CCl_4$, and $CHCl_3$, respectively. If it is assumed that, for a solution of campholenolactone (32) in n-hexane, the intense band at 1786 cm.$^{-1}$ and the small peak at 1758 cm.$^{-1}$ represent largely unperturbed $\nu$(CO) and $2\gamma$(CH) absorptions, respectively, then normal solvent-shifts of the former would bring it to about 1776 cm.$^{-1}$ in $CCl_4$ and 1756 cm.$^{-1}$ in $CHCl_3$. Fermi resonance would then be maximal in $CCl_4$ where the two interacting frequencies are closest - ca. 1776 and 1778 cm.$^{-1}$. Decreased interaction would

be expected in chloroform where the two frequencies would again be well separated, though now in the reverse order. Hence, in the case of campholenolactone (32), Fermi resonance between $\nu$(CO) and $2\gamma$(CH) could account reasonably well for the observed solvent-dependence of the absorptions in the carbonyl region. Solvation undoubtedly does affect the $\alpha$-hydrogen in some specific way as indicated by the upward shift of the band assigned to $\gamma$(CH) in the i.r. but also by the downfield shift of the signal due to this proton in the n.m.r. When going from n-hexane to $CCl_4$ to $CHCl_3$ only the triplet dure to this proton was seen to move appreiably, thus: $\tau$(n-hexane) = 4.42, $\tau$ ($CCl_4$) = 4.37, $\tau$ ($CHCl_3$) = 4.26.

Fermi resonance with $2\gamma$(CH) can only be part of the answer, for $\beta$-angelica lactone shows more complex absorption still and the lactones which do not possess $\alpha$-olefinic hydrogens also exhibit irregular or partially split bands. However, there is no uniform behaviour in the saturated lactones and some (e.g. 28 and 29) have fairly sharp single peaks in all three solvents. A simple saturated $\gamma$-lactone can have a high $\nu$(CO) frequency and a very high apparent intensity (peak height) where the band is sharp, e.g. (33), $\nu$(CO) = 1805 cm.$^{-1}$ and $\varepsilon^a$ = 1310, in n-hexane. In any case, a single conformer should give a sharp carbonyl band in the absence of Fermi resonance, but there is the complicating factor that enhanced resonance could occur if the geometry of this single conformer happened to be favourable. Other overtones and combinations must be involved if Fermi resonance is indeed the correct explanation, but there seems little hope of locating the relevant fundamentals. The strong absorptions in the 1300-900 cm.$^{-1}$ region, which are ascribed to $\nu$(C-O) modes, are possibilities, but it was impossible to correlate their frequencies with those in the carbonyl region. Each lactone displays several strong bands ($\varepsilon^a$, 150-500) but the region of strongest absorption are often quite different. Thus, for lactones (27) and (28) the strongest

bands are clustered around 1000 cm.$^{-1}$, for (31)and (32) they are near 1240, 1100 and 950 cm.$^{-1}$, and for (24) there is only one intense band near 1250 cm.$^{-1}$, with weaker absorptions near 1030 cm.$^{-1}$. Changes in ring strain, steric interactions, and bond hybridization presumably engender the wide variations encountered within this region. Incidentally, these strong, sharp absorptions, when they appear as low as 900 cm.$^{-1}$ in the spectrum of a $\gamma$-lactone, are readily confused with $\gamma$(CH) absorptions for doubly-bonded carbon.

Further information has been sought by submitting two of the lactones to a measurement at elevated temperatures and in the presence of a second solute. The absorptions in the $\nu$(CO) regions of solutions (ca. 0.4 M) of $\beta$-angelica lactone (23) and campholenolactone (32) in tetrachloroethylene have been examined at 30° and 75°. No clearly defined changes were observed apart from the expected slight reduction in peak height at the higher temperature and no definite conclusions may be drawn though these results could be taken as negative evidence in favour of the Fermi resonance explanation. Addition of p-cresol to a solution of a lactone in n-hexane brings about specific solvation of the lactone group by the p-cresol molecules. The association (Figure 25) is of the type $MeC_6H_5OH\cdots O{=}C$, as evinced by the low values for $\nu$(OH) and the 'carbonyl band' - in the case of campholenolactone (32) ca. 3420 and 1744 cm.$^{-1}$, respectively. The shifting of the equilibrium towards the complex with increasing p-cresol concentration is apparent from the data in Figure 25 and there is clearly a general resemblance between the carbonyl region observed for a p-cresol-lactone complex and that for the lactone alone in the chloroform solution. This is in keeping with the results for solution spectra of inter-alia cyclohexanones[89,93] and sulphoxides (see later section) Although it would seem that the equilibrium has not been displaced as far as complete complex formation the bands show fine structure indicative of Fermi resonance. In the hydroxyl region, competing self-association

of the p-cresol gives rise to cresol dimer, and trimer or polymer absorptions near 3500 and 3200 cm.$^{-1}$ respectively; at the 0.064 M p-cresol concentration there may be some complex formation of the type, ArOH····OH(Ar)····O=C.

In $CCl_4$, $\gamma$(CH) for campholenolactone (32) is assigned to the band at 884 cm.$^{-1}$ (Figure 24). Introduction of p-cresol into the solution brings about the appearance of a shoulder at 890 cm.$^{-1}$ which is accordingly attributed to the $\gamma$(CH) for the cresol-lactone complex. Here, and in the case of chloroform solvation, the effect is probably brought about by the shift of the $\pi$ electrons of the double bond which would accompany donation of electron density by the carbonyl group to the phenolic proton.

In summary, carbonyl absorptions of complex shape seem to be fairly common of $\gamma$-lactones, whether they possess $\alpha\beta$-unsaturation or not. Fine structure is especially prominent in those $\alpha\beta$-unsaturated lactones which bear an $\alpha$-hydrogen and here Fermi resonance with $2\gamma$(CH) probably supplies part of the explanation. The problem merits further study, particularly by isotopic substitution and by the solvation complex approach.

TABLE 22.

**Absorptions in the Carbonyl Stretching Region of the Lactones (23-34) in Various Solvents.**

| No. | Compound | n-hexane | | | $CCl_4$ | | | $CHCl_3$ | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | $\nu$ | $\Delta\nu_{\frac{1}{2}}^{a}$ | $\varepsilon^{a}$ | $\nu$ | $\Delta\nu_{\frac{1}{2}}^{a}$ | $\varepsilon^{a}$ | $\nu$ | $\Delta\nu_{\frac{1}{2}}^{a}$ | $\varepsilon^{a}$ |
| 23 | β-Angelica lactone | 1800 | sh | 200 | 1802 | sh | 100 | 1804 | - | w |
| | | 1791 | 13 | 1120 | 1783 | 15 | 840 | 1784 | 22 | 230 |
| | | 1762 | - | 140 | 1765 | 11 | 445 | 1759 | 15 | 845 |
| | | | | | | | | 1741 | 12 | 325 |
| 24 | γ-Butrolactone | 1801 | 16 | 500 | 1796 | sh | 415 | 1793 | sh | - |
| | | 1787 | sh | - | 1784 | 11 | 570 | 1774 | 19 | 630 |
| 25 | Dihydrodrimenin | 1798 | sh | - | 1797 | sh | - | 1770 | 26 | 480 |
| | | 1787 | 11 | 880 | 1779 | 13 | 800 | 1760 | | 500 |
| | | | | | 1758 | sh | - | | | |
| 26 | Drimenin | 1789 | 14 | 595 | 1781 | 15 | 705 | 1771 | 19 | 630 |
| | | 1772 | sh | 170 | | | | | | |
| 27 | Isodrimenin | 1773 | 10 | 730 | 1766 | 14 | 1095 | 1751 | sh | 500 |
| | | | | | | | | 1741 | 28 | 670 |
| 28 | Confertifolin | 1771 | 7 | 1000 | 1769 | 14 | 1235 | 1750 | 27 | 930 |
| 29 | Cis-dihydro-confertifolin | 1791 | 9 | 1000 | 1779 | 13 | 925 | 1772 | 22 | 685 |
| 30 | Trans-dihydro-confertifolin | 1801 | 12 | 900 | 1792 | 15 | 680 | 1782 | sh | 420 |
| | | | | | 1778 | sh | - | 1770 | 27 | 620 |
| 31 | Dihydro-camphol-enolactone | 1791 | 11 | 870 | 1783 | 26 | 600 | 1757 | 27 | 650 |
| | | | | | 1775 | | | | | |
| 32 | Campholeno-lactone | 1786 | 9 | 1300 | 1783 | 18 | 760 | 1782 | 23 | 180 |
| | | 1758 | - | 190 | 1759 | 14 | 575 | 1752 | sh | - |
| | | | | | | | | 1744 | 24 | 700 |
| 33 | | 1805 | 9 | 1310 | 1797 | 21 | 820 | 1777 | 27 | 530 |
| | | | | | 1787 | sh | 610 | 1766 | sh | 370 |
| 34 | | 1806 | 8 | 1370 | 1796 | 23 | 800 | 1780 | 28 | 560 |
| | | | | | 1786 | sh | 520 | 1772 | | 520 |

Solutions ca. 10 mM run in 0.5 mm. cells.

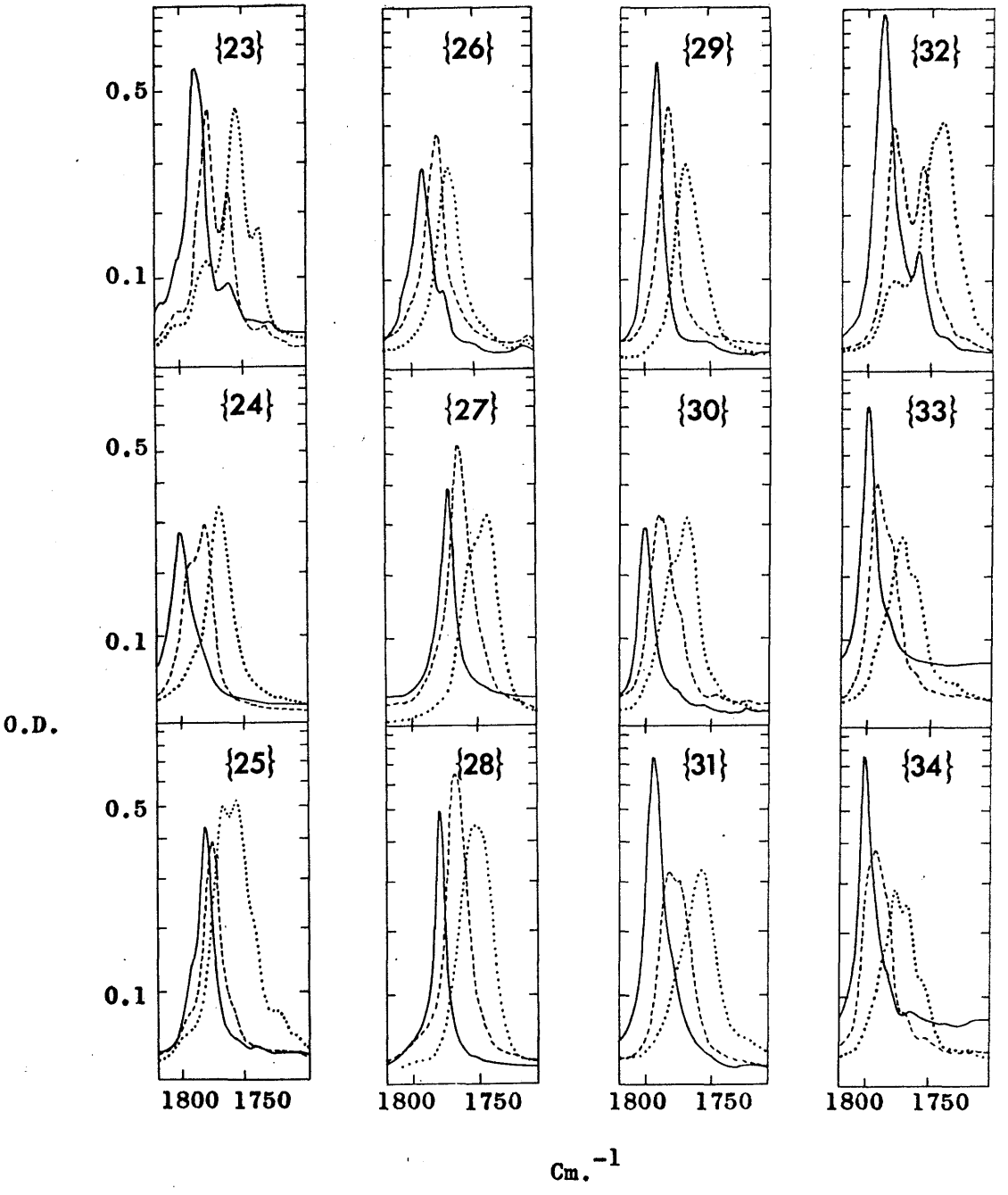



FIGURE 23. Absorptions in the carbonyl stretching region of the lactones (23-34) in n-hexane (————), carbon tetrachloride (- - - - - -), and chloroform (.....). Solutions ca. 10 mM examined in 0.5 mm. cells.

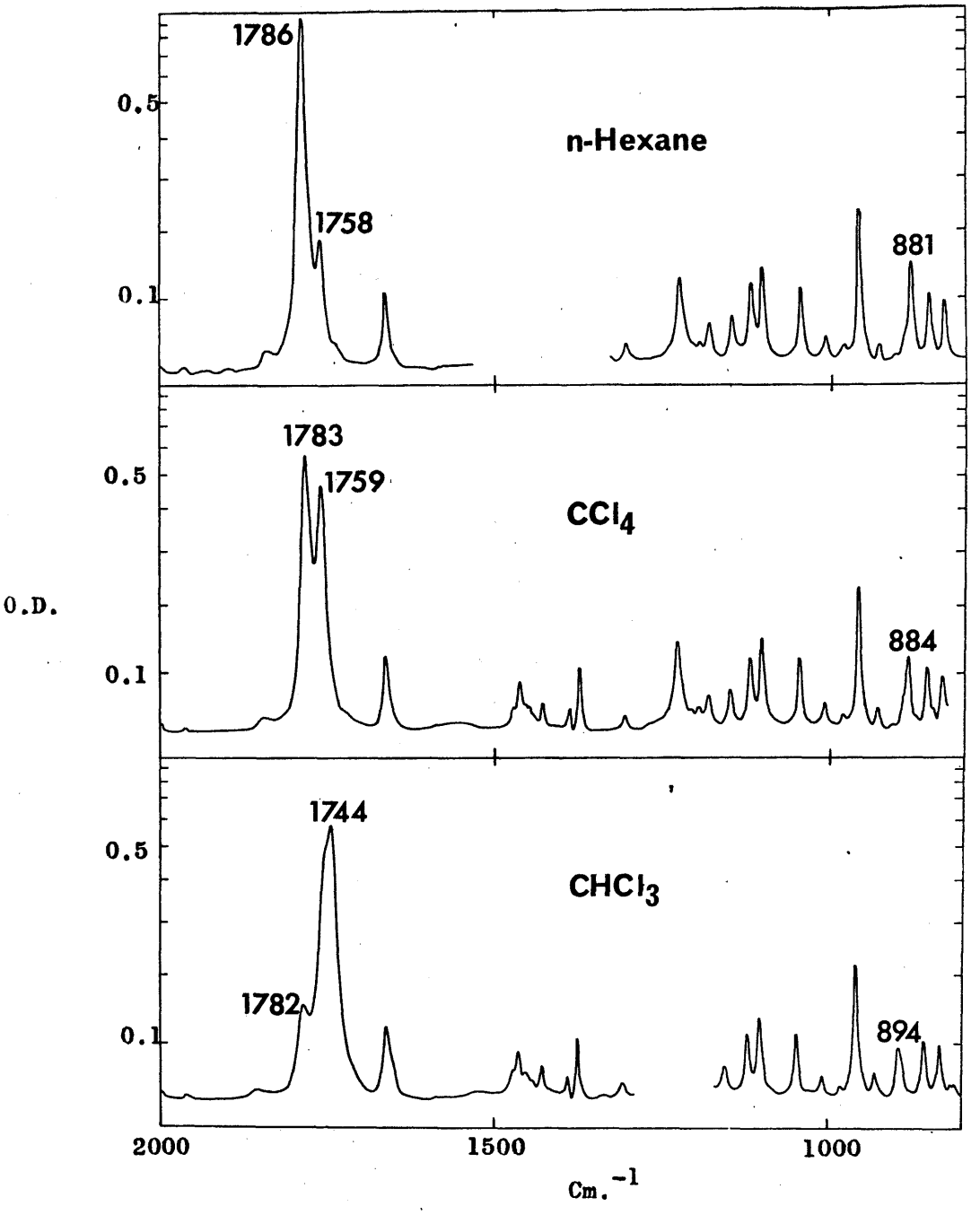
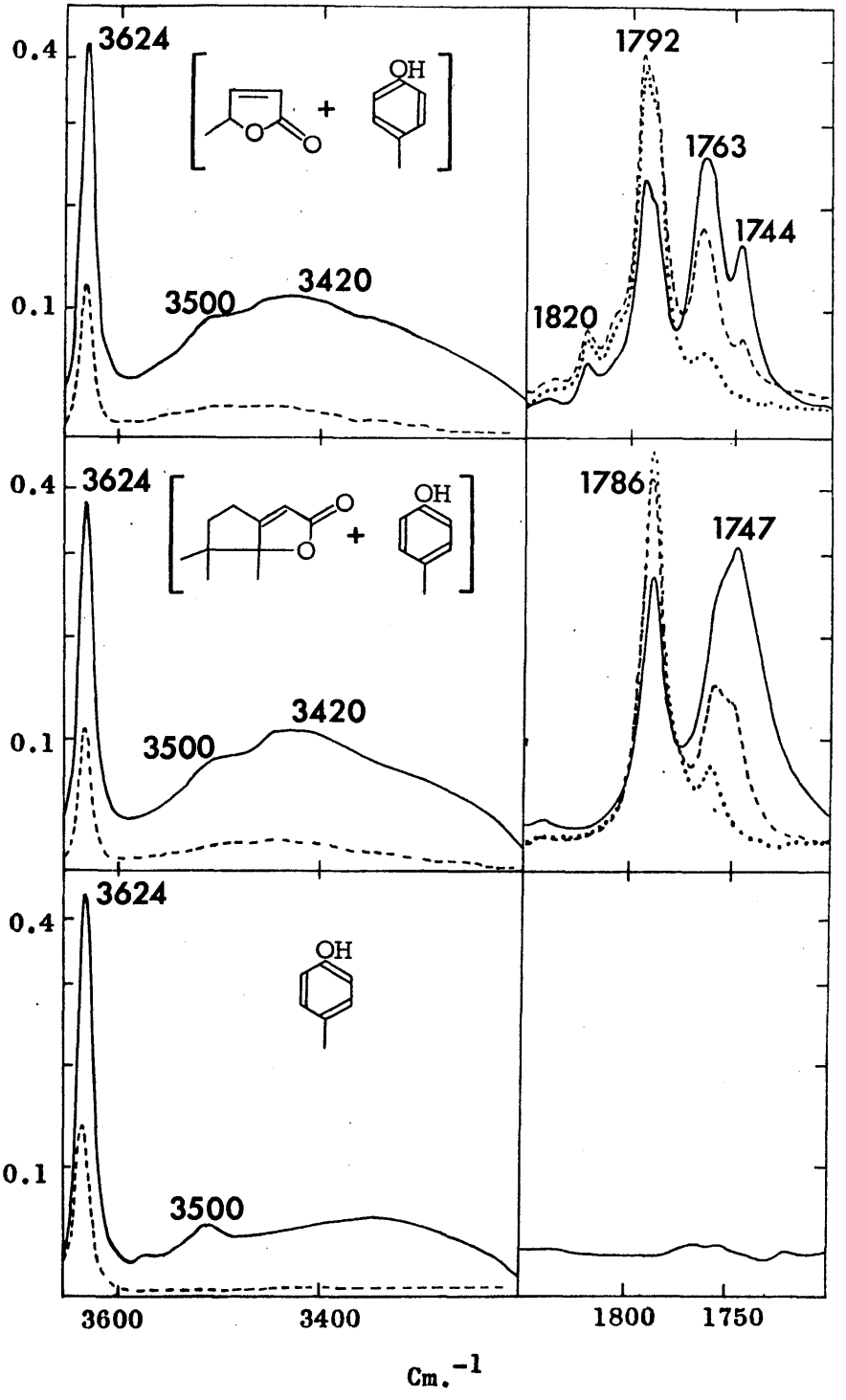



FIGURE 24. The spectrum of campholenolactone (32) recorded over the range 800-2000 cm.$^{-1}$ for ca. 0.05 M solutions (0.1 mm. cells) in n-hexane, carbon tetrachloride, and chloroform.




O.D.

**FIGURE 25.** Absorptions in the hydroxyl and carbonyl stretching regions for solutions (ca. 0.015 M) of β-angelica lactone (23) and campholenolactone (32) in n-hexane alone (·····), and in mixtures of n-hexane and p-cresol (- - - - - -, 0.016 M; and ————, 0.064 M). Absorptions are also recorded for n-hexane solutions of p-cresol (————, 0.064 M; and - - - - -, 0.016 M). All measurements in 0.5 mm. cells.

# INFRARED STUDIES WITH SULPHOXIDES

## INTRODUCTION

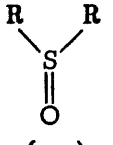
The stretching vibration, $\nu(S{=}O)$, of the sulphoxide grouping in simple alkyl and aryl sulphoxides is well known to occur near 1050 $cm.^{-1}$.[92] Even though this is a region of the spectrum rich in skeletal and other modes with which $\nu(S{=}O)$ might couple, this latter vibration is reputedly insensitive to substitution,[92] the reason given being that the sulphoxide grouping is approximately tetrahedral.[94]

The present work examines the solvent dependence of the sulphoxide stretching absorption in a series of simple sulphoxides - the monosulphoxides. As an extension of this work a series of disulphoxides has been examined since in a thian oxide system the S=O group might either be equatorially or axially orientated and a difference in frequency of the $\nu(S{=}O)$ might be anticipated on analogy with the behaviour of the stretching vibrations $\nu(C{-}O)$, $\nu(C{-}D)$ and $\nu(C{-}Halogen)$.[95] All the compounds studied were synthesised and purified by Dr. D.T. Gibson.

# RESULTS and DISCUSSION

## Monosulphoxides

BELLAMY et al.[96] have already demonstrated that the stretching vibration of the S=O link of the sulphoxides exhibits a solvent dependence which parallels that of the carbonyl link, in accordance with the polar nature of the $S^{\delta+}=O^{\delta-}$ bond. The present work examines the solvent dependence of the absorptions occurring in the $\nu$(S=O) region between 1100 and 1000 cm.$^{-1}$. The results, in general, support and extend the literature findings,[96-98] but in several instances they illustrate the application of the solvent-shift procedure to the assignment of the sulphoxide stretching absorption.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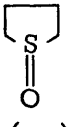
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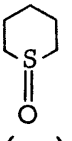
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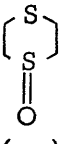

(38)

[a, R=Me; b, R=Et; c, R=i-Pr; d, R=t-Bu; e, R=Ph].

In the sulphoxides examined (35-38) the bands near 1050 cm.$^{-1}$ are the strongest in the spectrum, though in the case of diphenyl sulphoxide (35e) the absorption is matched in intensity by the C-H deformation modes (ca. 700 cm.$^{-1}$) of the aromatic ring hydrogens. The $\nu$(S=O) assignment is unambiguous for dimethyl sulphoxide (35a) and agrees with the value of 1085 cm.$^{-1}$ (n-hexane) reported by BELLAMY et al.[96] SALONEN[99] has already made use of infrared and Raman spectroscopy in a detailed study of the assignments of both the fundamental and combination absorptions for dimethyl sulphoxide. In the case of diethyl sulphoxide (35b),

however, there are several bands in the expected region, and their solvent behaviour (Table 24, Figure 26B) is peculiar. The higher sulphoxides (35c-e, 36, and 37) show similarly complex absorption patterns (Figure 26).

The occurrence of several strong bands in the sulphoxide stretching region of the spectra of compounds containing a single sulphoxide function is likely to be caused by dipole-dipole interaction, solvent-solute interaction, "hot" transitions, conformational equilibria, vibrational coupling or Fermi resonance. To establish the origin of the complex patterns observed a detailed study was made of the effect of solvent, concentration, and temperature. The results (Table 24, Figures 26C, 27 and 28) obtained for di-isopropyl sulphoxide (35c), a representative member of the sulphoxide series, are discussed in detail.

On going to chloroform solution there is a marked shift of the main absorption band from 1067 $cm.^{-1}$ (n-hexane) to 1047 $cm.^{-1}$. This behaviour is typical of that normally associated with the fundamental stretching absorption of an $X^{\delta+}=O^{\delta-}$ dipole, such as that of the carbonyl grouping, and is attributed to an intermolecular association of the type $X{=}O\cdots HCCl_3$.[89,97,98] At this juncture, it might seem reasonable to assign the absorption at 1067 $cm.^{-1}$ (n-hexane) to the fundamental stretching absorption of the S=O bond. However, the band at lower frequency (1019 $cm.^{-1}$ in n-hexane and 1012 in chloroform) increases in intensity (n-hexane to chloroform) at the expense of the higher frequency band, and it is evident that the true position of the $\nu(S{=}O)$ absorption cannot be determined by simple inspection. This transference of intensity in the 1100 to 1000 $cm.^{-1}$ region is further illustrated in Figure 27. The remainder of the spectrum is unaltered by change of solvent, indicating that a solvent-sensitive conformational equilibrium is not present, since different conformers usually have several different absorption bands. The effect of temperature on the absorption bands

in the $\nu(S{=}O)$ region of di-isopropyl sulphoxide (35c) was twofold (Figure 28). With increasing temperature the intensities of both bands decreased and the half-band widths increased, but the ratio of the areas of the two bands remained constant. This behaviour would seem to exclude the "hot" transition explanation [cf. KRAIHANZEL and WEST[90]] as well as any form of conformational equilibrium. Measurements carried out in a very polar solvent such as acetonitrile (Table 24) illustrate the shift of the higher frequency band while the lower absorption band remains at almost exactly the same frequency as that observed in n-hexane. This behaviour is the reverse of that expected for conformational isomers where, not only would both absorption bands have been shifted to lower frequency, but also the band at higher frequency would have gained intensity.[63]

It would seem reasonable to conclude that vibrational coupling or Fermi resonance involving the $\nu(S{=}O)$ mode originates the complex absorption behaviour of the sulphoxides studied. For this reason no single value for the position of the $\nu(S{=}O)$ is immediately obvious for any of these compounds with perhaps the exception of dimethyl sulphoxide (35a) and tetramethylene sulphoxide (36). Recently DE LA MARE et al.[100] have assigned certain bands between 1100 and 1000 $cm.^{-1}$ to the $\nu(S{=}O)$ modes of the isomeric 1,4-dithian-1,4-dioxides. The spectra were recorded for the solid state, and these workers do, in fact, comment on the presence of more than one strong band in the expected region, and remark that the spectra either exhibit crystal field effects or involve ring-stretching vibrations. Solution data are more instructive (see discussion of disulphoxides). Fermi resonance has already been established between the $\nu(S{=}O)$ and an aromatic absorption band near 1090 $cm.^{-1}$ in diphenyl sulphoxide.[101] From the results reported in this thesis a similar additional interaction would appear to exist with the aromatic vibration at 1022 $cm.^{-1}$. In the case of the aliphatic sulphoxides, however, the absorption bands which are involved in

the vibrational coupling or the Fermi resonance with $\nu(S{=}O)$ are of less obvious origin. OTTING and NEUGEBAUER[102] in their study of sulphoxides reported two bands near 480 $cm.^{-1}$ which they ascribed to the bending vibration of the S-O bond. It is conceivable that Fermi resonance is taking place between $\nu(S{=}O)$ and a combination band or the first overtone of the S-O bending vibration, $2\delta(SO)$. On the other hand, in dimethyl sulphoxide the band around 1016 $cm.^{-1}$ (Figure 26A), which has been assigned to the rocking vibration of the methyl groups, $\rho(S\text{-}CH_3)$, by HORROCKS and COTTON[103], may be involved in vibrational coupling.[104]

An attempt has been made (Table 25) to arrive at a rough estimate of the "true" position [therein termed $\nu(S{=}O)^*$] of the fundamental stretching vibration of the S=O bond (i.e. as if it were unaffected by coupling or Fermi resonance) by calculating the mid-point for the intensity distribution (area under the recorded curve) between 1100 and 1000 $cm.^{-1}$. This calculation is based on the tentative assumption that nearly all the intensity in the 1100 to 1000 $cm.^{-1}$ region is derived from $\nu(S{=}O)$ whether as a single band (uncoupled) or distributed as several bands (coupled or involved in Fermi resonance). In all three solvents there is a fairly consistent decrease in the value of $\nu(S{=}O)^*$ as the bulk of alkyl substitution increases (i.e. increasing inductive effect, +I) from dimethyl to di-t-butyl sulphoxide (Ia-d). This is perhaps an indication that this mathematically contrived value, $\nu(S{=}O)^*$, has some significance. There is also a marked increase in frequency of this $\nu(S{=}O)^*$ on going from tetramethylene (36) to pentamethylene (37) sulphoxide [cf. ref. 98]. This increase, which is to be compared with the decrease experienced for $\nu(CO)$ in the analogous situation could arise from the change in C-S-O interbond angles in moving from a five-membered ring to a six. The general trend in solvent-shift values [$\Delta\nu_{1-2}$ and $\Delta\nu_{1-3}$] seems to hold good with the exception of compound (37), the anomalous behaviour of which may reflect the

presence of an additional absorption band, most likely a ring breathing vibration, in the region 1100 to 1000 cm.$^{-1}$ which is interfering with the area calculation. This approach would seem to provide a more logical presentation for a system involving several bands, one of which would normally be assigned to a given mode of vibration.

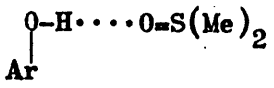
Figure 29 illustrates the close similarity between the solid and liquid state spectra of the two sulphoxides (35b, 35d) and those obtained for the same compounds in chloroform solution. This similarity presumably derives from an accidental correspondence in effective polarity and it demonstrates that solid state or liquid film data cannot be used for precise location of the $\nu$(S=O) absorption.[105] It is conceivable that in some cases association may occur between the acidic hydrogens ($\alpha$ to the S=O linkage) and the S=O linkages of neighbouring sulphoxide molecules.

Dimethyl sulphoxide is fully miscible with water and this property is undoubtedly due to the ability of the sulphoxide grouping to act as a proton acceptor in hydrogen bonding.[99] BARNARD et al.[106] showed that in chloroform solution sulphoxides form stronger intermolecular hydrogen bonds with methanol than do the corresponding sulphones. Sulphoxides and related compounds have recently been used as anti-oxidants[107,108] in the retardation of the autoxidation of squalene and, in this particular case, a hydrogen bonded complex[109] is postulated. This ability of the sulphoxide grouping to act as a powerful basic site for intermolecular hydrogen bonding is illustrated in Figure 30. The addition of water to dimethyl sulphoxide results in the $\nu$(S=O) shifting to a lower frequency while a new band appears at 1650 cm.$^{-1}$. This latter vibration is attributed to the O-H deformation modes of the associated water molecules. The shift of the $\nu$(S=O) absorption represents the solvent shift [$\Delta\nu = \nu(S{=}O)_{\text{n-hexane}} - \nu(S{=}O)_{\text{water}}$] for water as solvent.

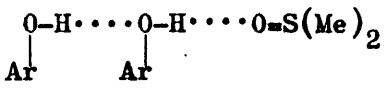
COTTON et al.[110] and FRANCIS and COTTON[111] in their study of sulphoxides as ligands have reported that the acceptor is the oxygen atom in the majority of the metal complexes studied. In such cases $\nu(S=O)$ shifted to lower frequencies. DRAGO and MEEK[104] have reported discrepancies in the assignments for dimethyl sulphoxide complexes, and they suggest that vibrational coupling is responsible.

As already discussed, chloroform has the ability to hydrogen bond with the oxygen atom of the sulphoxide grouping. This type of solvation can be extended to stronger acids, for example p-cresol, as shown by the results which follow [cf. ref. 97], but, there is one major difference: only a very small amount of p-cresol instead of pure chloroform, is needed to complex sulphoxide molecules dissolved in n-hexane. It is interesting that the same band pattern in the 1100 to 1000 $cm.^{-1}$ region is maintained although the association is clearly much stronger, a fact that lends further support to the arguments advanced in the preceding section. Figure 31A shows the sulphoxide absorption of dimethyl sulphoxide in n-hexane containing various amounts of p-cresol. In the pure hydrocarbon solvent dimethyl sulphoxide exhibits a single band at 1085 $cm.^{-1}$, but the addition of p-cresol (0.023M) causes a new one to appear at 1058 $cm.^{-1}$, while the intensity of the original band decreases. In the hydroxyl stretching region new absorption appears at 3288 $cm.^{-1}$. This behaviour indicates the existence of an equilibrium system involving two species, presumably free sulphoxide and a hydrogen bonded complex (39) of dimethyl sulphoxide and p-cresol. When the p-cresol concentration is increased to 0.092 M the original band at 1085 $cm.^{-1}$ has disappeared and yet another new broad band near 1042 $cm.^{-1}$ has appeared, while the band at 1016 $cm.^{-1}$ has also increased in intensity. At this concentration of p-cresol, however, two absorption bands resulting from self-association (Figure 31C) of the p-cresol molecules are observed. [In a previous study of hydrogen bonding in phenols the bands at ca. 3500 and 3390 $cm.^{-1}$ were assigned the dimeric

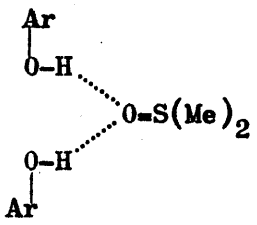
and trimeric associated species.] Hence, in dimethyl sulphoxide solutions containing this particular concentration of p-cresol, a competitive system involving variously associated species results. The results obtained at low p-cresol concentration indicate that the species (39) is present. However, at the higher concentration an additional species is indicated by the appearance of the broad



(39)



(40)



(41)

absorptions near 1040 and 3370 cm.$^{-1}$. An exactly similar situation has been reported by WHETSEL and KAGARISE[89] in their study of the complexes formed by acetone or cyclohexanone with p-cresol. They attributed the appearance of the two new bands in the carbonyl region to 1:1 and 1:2 complexes of the ketones with p-cresol [for acetone complexes, $\Delta\nu$(CO) ca. 10 and 16 cm.$^{-1}$ respectively]. The evidence in the present work would similarly support 1:1 and 1:2 complexes of dimethyl sulphoxide with p-cresol, but the observed $\nu$(OH) would favour a 1:2 complex of the type (40) rather than of the other type (41). WHETSEL and KAGARISE[89] postulated both these structures for the phenol-ketone association, but $\nu$(OH) values were not reported in their study. The results in the $\nu$(OH) region, however, suggest that the absorption band at 3288 cm.$^{-1}$ is to be assigned to the 1:1 cresol-sulphoxide complex (39), while the other absorption band

(ca. 3370 $cm.^{-1}$) at higher p-cresol concentration is to be attributed to the 1:2 complex (40).

An exactly similar study (Figure 31B) was carried out using di-t-butyl sulphoxide (35d) and the behaviour is analogous to that of dimethyl sulphoxide. The greater shift in the $\nu$(OH) region, however, indicates that di-t-butyl sulphoxide is a better donor in spite of steric hindrance, presumably as a result of the greater inductive effect, +I, of the t-butyl groups.

Sulphoxides are much more effective hydrogen bonding acceptors (Lewis bases) than the corresponding ketones, as can be seen from the data (Table 26) for dimethyl sulphoxide and acetone. The shifts, $\Delta\nu$(OH) and $\Delta\nu$(X=O), on complex formation are much greater for the former, as is the ratio of complex to unassociated solute (indicated by the ratio of abasorbancies). BISCARINI et al.[112] have carried out similar experiments with the sulphone group, i.e. $-SO_2-$, as proton acceptor in hydrogen bonding with phenol in carbon tetrachloride. These workers record a $\Delta\nu$(OH) value of 145 $cm.^{-1}$ for the dimethyl sulphone-phenol complex. The corresponding shift (in n-hexane) for the dimethyl sulphoxide-p-cresol complex is 336 (Table 26) showing sulphoxides are much better and more effective hydrogen bond acceptors than the corresponding sulphones. GRAMSTAD[113] examined the hydrogen bonding between sulphoxides and phenol. Although he quotes $\nu$(S=O) values for the various sulphoxides studied, he makes no comment of the band pattern and the possibility of Fermi resonance or some associated phenomenon. His assignments and conclusions, however, parallel our results and his assignments of absorption bands to the $\nu$(S=O) are consistent with the results from the present study.

TABLE 23.

Bands in the $\nu(S{=}O)$ Region (1100-1000 $cm.^{-1}$) for Various Simple Sulphoxides (35-38).

| No. | Compound | Chloroform | | | Solid state or liquid film (L) | |
|---|---|---|---|---|---|---|
| | | $\nu$ | $\Delta\nu_{\frac{1}{2}}$[a] | $\varepsilon$[a] | $\nu$ | $\Delta\nu_{\frac{1}{2}}$[a] |
| 35a | Dimethyl sulphoxide | 1055* | 24 | 310 | (1057)*(L) | (50) |
| | | 1033 | sh | - | | |
| | | 1013 | (11) | (95) | | |
| 35b | Diethyl sulphoxide | 1054 | - | 150 | 1057* | - |
| | | 1041 | - | 135 | 1037 | sh |
| | | 1020 | - | 240 | 1018 | - |
| 35c | Di-isopropyl-sulphoxide | 1047 | 14 | 195 | 1057 | - |
| | | 1012 | 13 | 315 | 1018 | - |
| 35d | Di-t-butyl sulphoxide | 1097[a] | 7 | 140 | 1096[a] | - |
| | | 1026 | (16) | 185 | 1034 | - |
| | | 1012 | 13 | 305 | 1016 | 13 |
| 35e | Diphenyl sulphoxide | 1090 | 9 | 250 | 1087 | - |
| | | 1040 | 18 | 285 | 1037 | - |
| | | 1022 | 5 | 195 | 1023 | - |
| 36 | Tetramethylene sulphoxide | 1092 | 15 | 60 | 1094 | - |
| | | 1020 | 9 | 330 | 1024 | 24 |
| 37 | Pentamethylene sulphoxide | 1068 | 11 | 115 | 1070 | 15 |
| | | 1029 | 16 | 315 | 1035 | 21 |
| 38 | 1,4-Dithian monoxide | 1044 | 26 | 300 | 1019 | (25) |
| | | 1034 | sh | 240 | | |

The strongest bands observed for each compound are underlined.
Values in parenthesis are approximate.
sh Shoulder.
- Not measured.
* Asymmetric peak.
† Solutions were ca. 0.25 M in 0.5 mm. cells.
a Ascribed to sulphone impurity.

TABLE 24

Solvent Dependence of $\nu$(S=O) for Various Sulphoxides

| Solvent | 35a $Me_2SO$ | | | 35b $Et_2SO$ | | | 35c $(iso\text{-}Pr)_2SO$ | | | 35d $(t\text{-}Bu)_2SO$ | | | 35e $Ph_2SO$ | | | 36 $(CH_2)_4SO$ | | | 37 $(CH_2)_5SO$ | | | 38 | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | $\nu$ | $\Delta\nu_{a/2}$ | $\varepsilon^a$ | $\nu$ | $\Delta\nu_{a/2}$ | $\varepsilon^a$ | $\nu$ | $\Delta\nu_{a/2}$ | $\varepsilon^a$ | $\nu$ | $\Delta\nu_{a/2}$ | $\varepsilon^a$ | $\nu$ | $\Delta\nu_{a/2}$ | $\varepsilon^a$ | $\nu$ | $\Delta\nu_{a/2}$ | $\varepsilon^a$ | $\nu$ | $\Delta\nu_{a/2}$ | $\varepsilon^a$ | $\nu$ | $\Delta\nu_{a/2}$ | $\varepsilon^a$ |
| Hexane | 1085 | 14 | 210 | 1075 | 17 | 210 | 1067 | 7 | 420 | 1105† | 6 | 145 | 1096 | 10 | 325 | 1095 | 16 | 110 | 1078 | 10 | 310 | 1066 | 7 | - |
| | | | | 1026* | - | - | 1019 | 8 | 140 | 1050 | 7 | 480 | 1056 | 7 | 310 | 1043 | 12 | 260 | 1059 | (12) | 90 | | | |
| | | | | | | | | | | 1019 | (11) | 65 | 1022 | 5 | 80 | | | | 1041 | 7 | 135 | | | |
| $C_2Cl_4$ | 1075 | 17 | 280 | 1069 | 24 | - | | | | | | | 1095 | 9 | 260 | | | | | | | 1060 | 13 | - |
| | | | | 1026* | - | - | | | | | | | 1053 | 7 | 300 | | | | | | | | | |
| | | | | | | | | | | | | | 1022 | 4 | 85 | | | | | | | | | |
| $CCl_4$ | 1072 | 16 | 420 | 1066 | 25 | - | 1058 | 11 | 355 | 1102† | 5 | 165 | 1093 | 8 | 340 | 1094 | 15 | 100 | 1073 | 9 | 285 | 1057 | 14 | 545 |
| | | | | 1025* | - | - | 1018 | 8 | 255 | 1039 | 13 | 335 | 1052 | 8 | 420 | 1036 | 13 | 355 | 1053 | (10) | 175 | | | |
| | | | | | | | | | | 1019 | (8) | 110 | 1022 | 4 | 95 | | | | 1038 | 7 | 245 | | | |
| $CS_2$ | 1071 | 12 | 480 | 1066 | 20 | - | | | | | | | 1093 | 8 | 360 | | | | | | | 1056 | 9 | 510 |
| | | | | 1024* | - | - | | | | | | | 1051 | 6 | 495 | | | | | | | | | |
| | | | | | | | | | | | | | 1022 | 4 | 120 | | | | | | | | | |
| $CH_3CN$ | 1061 | (13) | - | 1059* | - | - | | | | | | | 1091 | 7 | - | | | | | | | (1050) | - | - |
| | | | | 1022* | - | - | | | | | | | 1047 | (7) | - | | | | | | | | | |
| | | | | | | | | | | | | | 1022 | - | - | | | | | | | | | |
| Pyridine | (1060) | 6 | - | (1059)* | - | - | | | | | | | 1091 | - | - | | | | | | | 1049 | (17) | - |
| | | | | (1020)* | - | - | | | | | | | 1047 | - | - | | | | | | | | | |
| $CHCl_3$ | 1055* | 24 | 310 | 1054* | - | 150 | 1047 | 15 | 195 | 1097† | 7 | 140 | 1090 | 9 | 250 | 1092 | 15 | 60 | 1068* | 11 | 115 | 1044 | 26 | 300 |
| | | | | 1020* | - | 240 | 1012 | 13 | 315 | 1026 | (16) | 185 | 1040 | 18 | 285 | 1020 | 19 | 330 | 1029 | 16 | 315 | 1034 | sh | 240 |
| | | | | | | | | | | 1012 | 13 | 305 | 1022 | 5 | 195 | | | | | | | | | |

*Asymmetric peak

†Ascribed to sulphone impurity

Solutions were ca. 0.25 M examined in 0.5mm cells except for $CH_3CN$ (0.05mm) and pyridine (0.1mm), and with the exception of compound 38 which was run in $CCl_4$ and $CS_2$ in 2mm cells.

TABLE 25.

Calculated Mid-point†, $\Delta(S{=}O)^*$, of Band Absorption Pattern Between 1100 and 1000 cm.$^{-1}$.

| No. | Compound | $\nu(SO)^*$ | | | Shifts | |
|---|---|---|---|---|---|---|
| | | $\nu_1$ n-hexane | $\nu_2$ $CCl_4$ | $\nu_3$ $CHCl_3$ | $\Delta\nu_{1-2}$ | $\Delta\nu_{1-3}$ |
| 35a | Dimethyl sulphoxide | 1081 | 1068 | 1048 | 13 | 33 |
| 35b | Diethyl sulphoxide | 1068 | 1055 | 1030 | 13 | 38 |
| 35c | Di-isopropyl-sulphoxide | 1063 | 1051 | 1021 | 12 | 42 |
| 35d | Di-t-butyl sulphoxide | 1048 | 1038 | 1015 | 10 | 33 |
| 36 | Tetramethylene sulphoxide | 1049 | 1033 | 1020 | 16 | 29 |
| 37 | Pentamethylene sulphoxide | 1072 | 1045 | 1033 | 27 | 39 |

† Areas were calculated by Simpson's Rule, $\nu(S{=}O)^*$ corresponding to the frequency at which the area on the high frequency side is equal to that on the low frequency side.
$\Delta\nu_{1-2} = \nu_1 - \nu_2$. $\Delta\nu_{1-3} = \nu_1 - \nu_3$.

TABLE 26.

**Assignments for Hydrogen Bonded Complexes in n-Hexane Solution.**

| Assignments | p-cresol and $(CH_3)_2SO$* | | | p-cresol and $(CH_3)_2CO$ | | |
|---|---|---|---|---|---|---|
| | $\Delta\nu$(SO) | $\Delta\nu$(OH) | $\frac{D_{complex}}{D_{free}}$ | $\Delta\nu$(CO) | $\Delta\nu$(OH) | $\frac{D_{complex}}{D_{free}}$ |
| 1:1 complex | 27 | 336 | 0.12 | 10 | 224 | 0.05 |
| 1:2 complex | 40 | 258 | 1.0 | 16 | 134 | 0.3 |

* Solutions of acetone and dimethyl sulphoxide were ca. 0.025 M.
† $\Delta\nu$(OH) given for band assigned to $\nu_2$:

$$ArOH\cdots\overset{\nu_2}{\underset{\displaystyle Ar}{O}}H\cdots\overset{\nu_1}{O}{=}X(CH_3)_2$$

where X = C or S.
The p-cresol concentrations for the measurements referring to the 1:1 and 1:2 complexes were 0.023 M and 0.09 M respectively.
$\Delta\nu$ $cm.^{-1}$ values refer to $\nu_{free} - \nu_{bonded}$.
$D_{complex}$ and $D_{free}$ refer to the observed absorbancies.

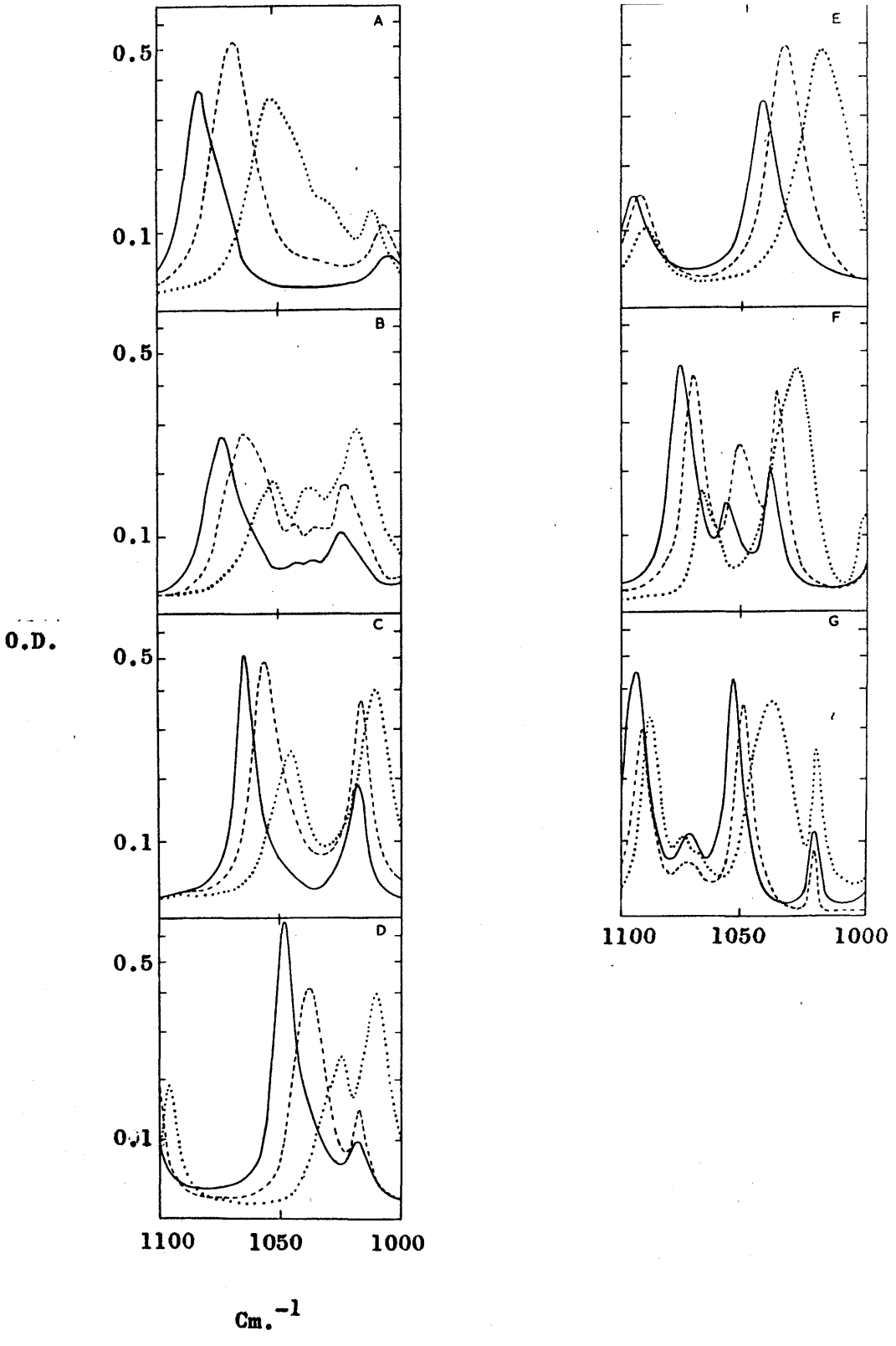



FIGURE 26. Absorptions in the S=O stretching region of seven sulphoxides in n-hexane (———), carbon tetrachloride (- - - - - -), and chloroform (·····). (A) $Me_2SO$; (B) $Et_2SO$; (C) iso-$Pr_2SO$; (D) t-$Bu_2SO$; (E) $(CH_2)_4SO$; (F) $(CH_2)_5SO$ and (G) $Ph_2SO$. Solutions (ca. 0.25 M) examined in 0.5 mm cells.

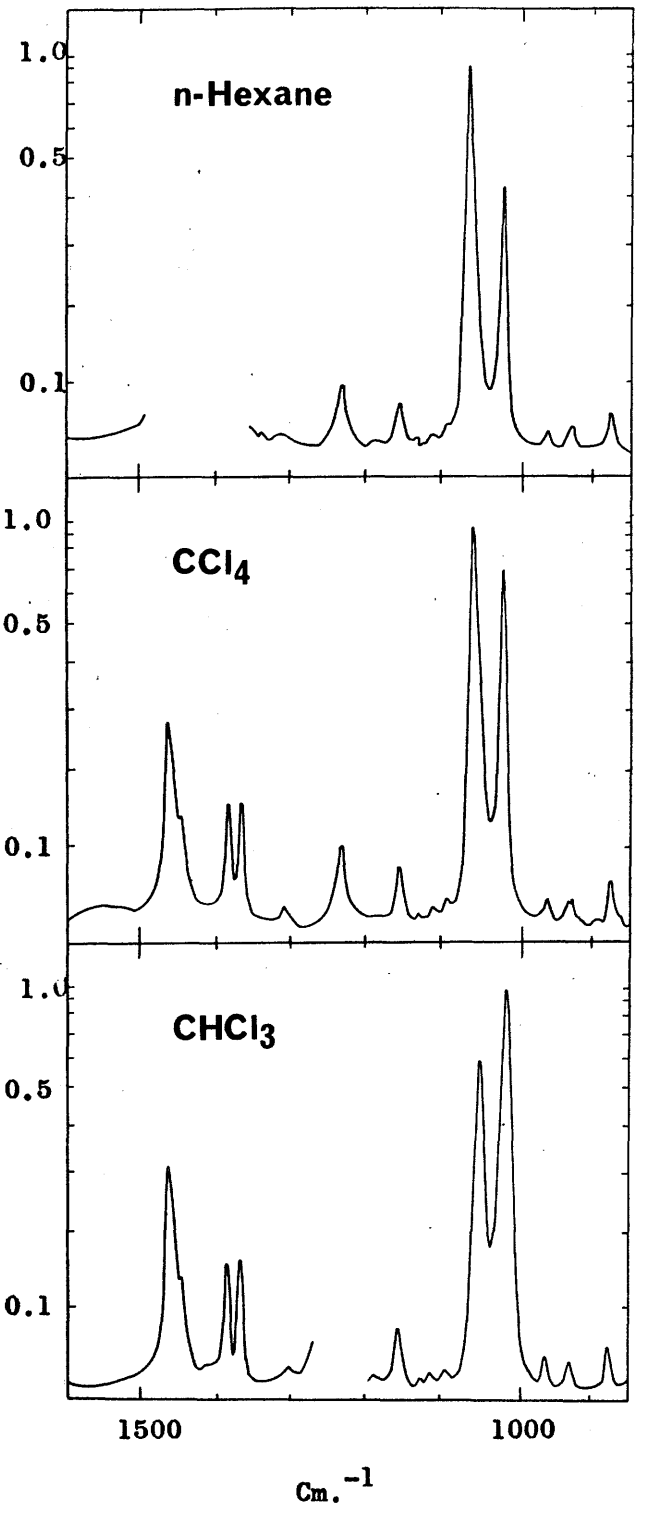



FIGURE 27. The spectrum of di-isopropyl sulphoxide recorded over the range 850-1600 cm.$^{-1}$ for ca. 0.23 M solutions (0.1 mm cells) in n-hexane, carbon tetrachloride, and chloroform.

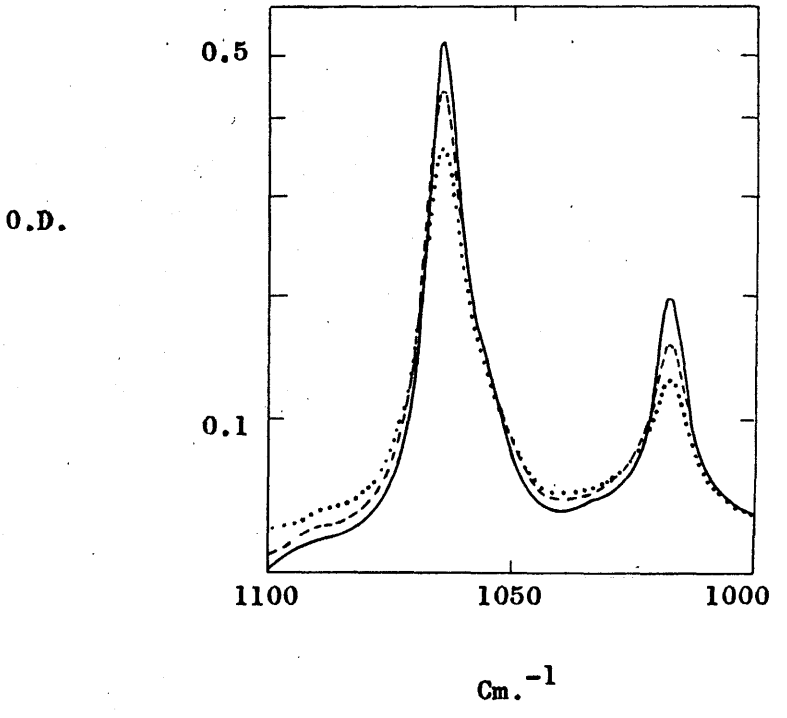



FIGURE 28. Absorptions in the S=O stretching region recorded for a 0.039 M solution of di-isopropyl sulphoxide in n-hexane at 27°(————), 51°(- - - - -) and 68° (·····).

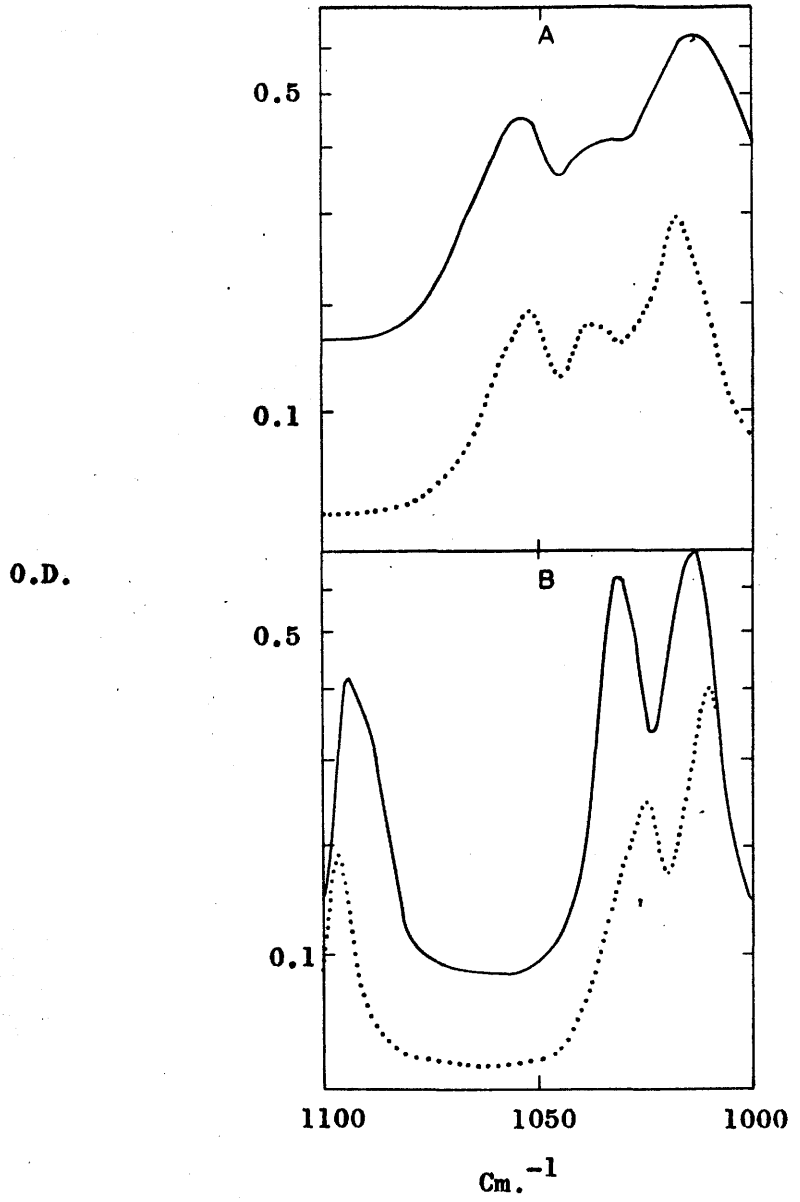



FIGURE 29. Absorption in the S=O stretching region of (A) diethyl sulphoxide and (B) di-t-butyl sulphoxide. Pure compound (————, liquid film and mull in Nujol, respectively) and as ca. 0.25 M solution in chloroform (·····, 0.5 mm. cells).

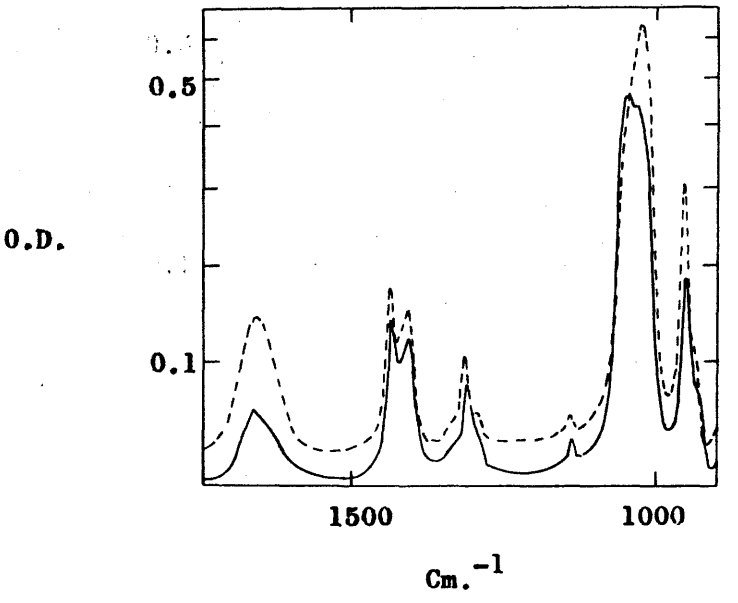



FIGURE 30. Effect of added water on the spectrum of dimethyl sulphoxide. Liquid films containing small quantity (————) and larger quantity ( ------- ) of water.

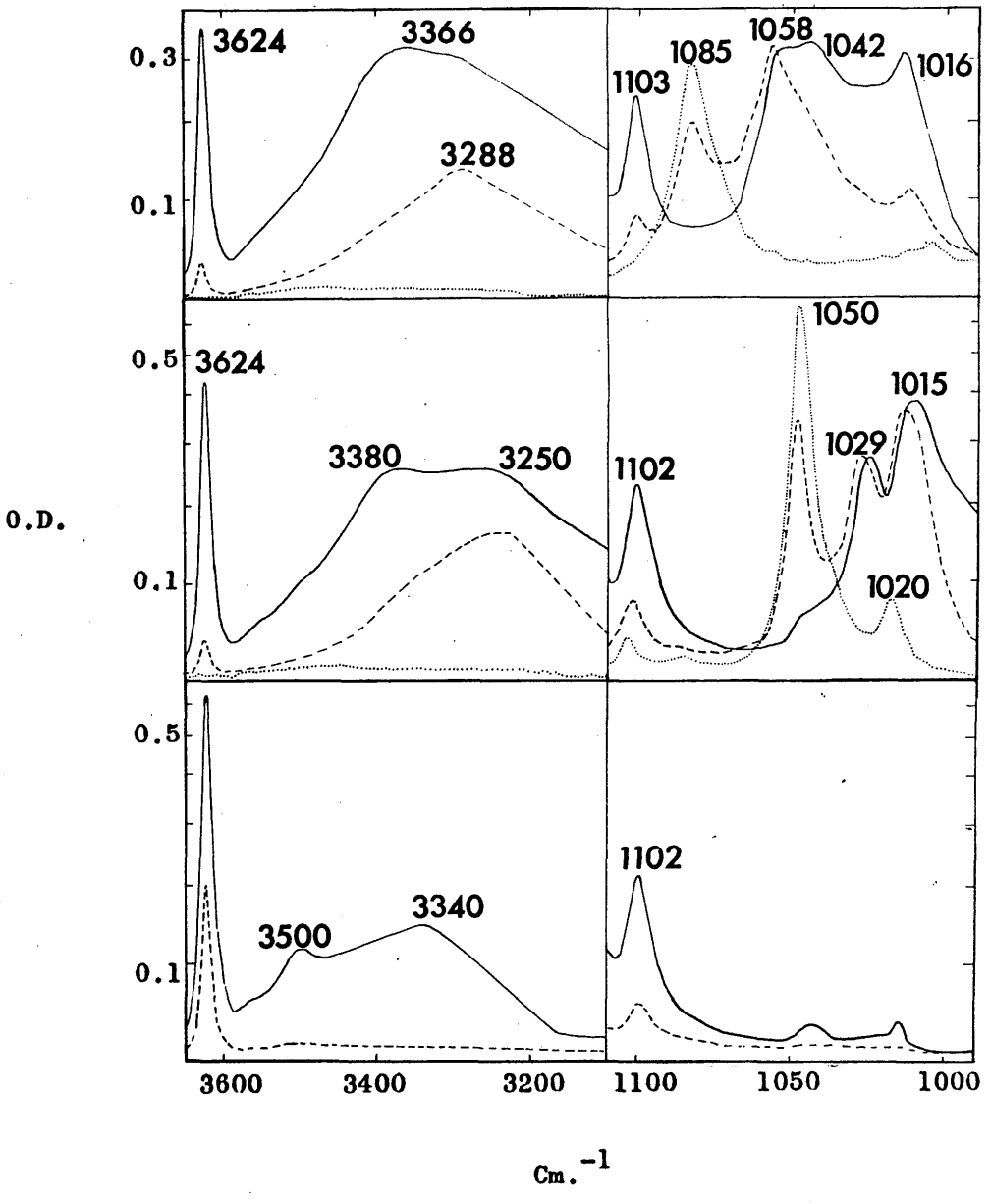
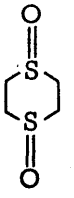



FIGURE 31. Absorptions in the O-H and S=O stretching regions for solutions (ca. 0.025 M) of (A) dimethyl sulphoxide and (B) di-t-butyl sulphoxide in n-hexane alone (·····), and in mixtures of n-hexane and p-cresol (- - - -, 0.023 M; and ————, 0.092 M). Absorptions are also recorded for n-hexane solutions of p-cresol (- - - -, 0.023 M; and ————, 0.092 M). All measurements in 0.5 mm. cells.

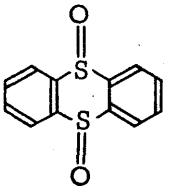
## Disulphoxides

### 1,4-Dithian-dioxides (42)

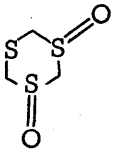
Two isomers, cis and trans, of structure (42) are possible. They were first obtained by BELL and BENNETT[114], who suggested that the more water-soluble compound, designated $\alpha$, was the trans-isomer. In a rcent X-ray study SHEARER[115] has confirmed this suggestion and has shown that in the crystal the molecule has the chair conformation with the S=O groups diaxially orientated (42b). The cis- or $\beta$-isomer has also been examined[116] by the X-ray method and found to have the chair conformation (42a) in which one S=O bond is axial and the other equatorial.



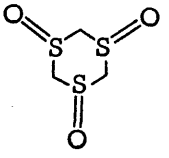
(42)



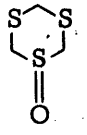
(43)



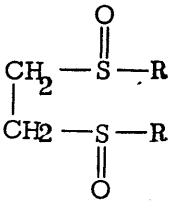
(44)



(45)



(46)



(47)

[a, R=$CH_3$; b, R=Et; c, R=PH; d, R=p-toyl].

In the present work it had been hoped that the infrared solvent-shift method[117a] might be employed in the elucidation of the conformation(s) of these two isomers when in solution. In each case boat forms are feasible but are adjudged unlikely in view of the unfavourable interactions which normally de-stabilize boat as against chair forms. Accordingly only the chair forms are discussed. However, the dioxides proved to be insufficiently soluble in every solvent examined, with the sole exception of chloroform. The results are given in Table 27 and are interpreted below.

The trans-isomer ($\alpha$). Two chair conformations (42b and 42c) of this molecule are possible, but the comparative narrowness of the single $\nu$(SO) absorption (Figure 32A) is suggestive of the predominance of one conformation in chloroform solution and it seems reasonable to assume that this should be that found in the crystal (42b). Indeed the spectral records are similar. The tentative assignment is therefore made:- $\nu$(SO) [in $CHCl_3$] axial ca. 1036 $cm.^{-1}$.

The cis-isomer ($\beta$). There is only one chair conformation (42a) possible and the broad absorption (in $CHCl_3$) centred on 1055 (Figure 32B) must incorporate contributions from both the axially and equatorially directed sulphoxide groups. If the assignment for the trans-isomer has been made correctly then these contributions might be $\nu$(SO) axial ca. 1040 and $\nu$(SO) equatorial ca. 1070 $cm.^{-1}$. The solid state spectrum (Figure 32B), however, which is that of the same conformation, shows the main absorption in this region shifted somewhat to lower frequencies and split into several bands. DE LA MARE et al.[100] in their recent parallel investigation of the dithian dioxides, based their conclusions on spectra determined for the solid state, but the chloroform solution data presently reported have greater validity. Solid state spectra often reflect the effect of intermolecular interactions in the crystal, partial orientation of the crystallites etc. Discrepancies between the solid state spectra herein reported and those detailed by DE LA MARE et al.[100] would seem to have their origin in the presence of sulphone impurities. Certain close approaches are to be seen in the unit cells of both isomers, for example, according to SHEARER[115], in the crystal of the trans-isomer (conformer 42b), "the shortest van der Waals contacts are 3.34, 3.35 and 3.39 Å between the oxygen atom of one molecule and the carbon atoms of adjacent molecules". The hydrogen atoms lie more or less along these contacts and C-H····O=S hydrogen bonds may represent part of the crystal forces reflected by the high melting points, involatility and insolubility of these compounds.

The insolubility of these compounds unfortunately precluded measurements of their dipole moments[118] and of their ultraviolet light absorption.[117b,c] Lack of a full solvent study did not permit the establishment or exclusion of Fermi resonance or vibrational coupling involving the ν(SO).

Thianthrene dioxides (43)

Both stereoisomeric forms of thianthrene dioxide (43) are known. HOSOYA and WOOD[119] using the X-ray method, have shown that in the crystalline state, the trans-isomer has the boat conformation (43c), one S=O group being boat-axial and the other boat equatorial, which is the only stable arrangement possible with normal bond angles and bond lengths. The cis-isomer, for which two conformations (43a and 43b) are possible, exists as the latter one, the cis-anti (43b), in the solid state[119] and both S=O groups are boat-equatorial. The molecule is butterfly-shaped with the two S=O groups more or less coplanar with the adjacent aromatic hydrogens. TAYLOR[120] in his re-interpretation of the data of BERGMANN and TSCHUDNOWSKY[121], considered that the dipole moments [cf. ref. 122] of the cis- and trans-isomers in benzene solution (found 1.7 and 4.2 D respectively) were consistent with the conformations (43b) and (43c).

The infrared results (Table 28, Figure 33) in the present work show interesting differences between the two isomers in band pattern and solvent shift behaviour. In the case of the trans-isomer, where only one conformation (43c) is possible, the band pattern (Figure 33B) is quite complex and changes markedly with the solvent employed. Since a conformational effect can be completely excluded Fermi resonance or coupling, possibly involving aromatic absorptions or ν(C-S) modes, must be invoked. The band at 1059 $cm.^{-1}$ (in $CCl_4$) and 1044 $cm.^{-1}$ (in $CHCl_3$) is ascribed to an axial S=O grouping since this is exposed to solvation (large solvent-shift and broad band)

whereas the equatorial S=O grouping should be protected from solvation by the adjacent aromatic hydrogens (small solvent-shifts and narrow band). Accordingly the $\nu$(SO) absorption of this equatorial S=O group is identified as the high-intensity band at 1080 cm.$^{-1}$ (in $CCl_4$) and 1075 cm.$^{-1}$ (in $CHCl_3$).

In the case of the cis-isomer two conformations are feasible (43a) and (43b), in which both S=O groups are axial or equatorial, respectively. If the S=O groupings were both axial (43a) then by analogy with the trans-isomer, a single strong band at 1060 cm.$^{-1}$ (in $CCl_4$) exhibiting marked solvent shifts should be expected. The appearance of a very strong, fairly solvent-insensitive band at 1095 cm.$^{-1}$ (in $CCl_4$) and 1088 cm.$^{-1}$ (in $CHCl_3$) is in keeping with the protected, equatorial-directed S=O groups of conformation (43b). Some support for this suggestion can be adduced from the data given in Table 28 for benzophenone and anthraquinone and from a similar study of diphenyl sulphoxide. In both diphenyl sulphoxide and benzophenone the oxygen atoms are fairly accessible to solvent molecules and considerable solvent-shifts results. However, the oxygen atoms of cis-thianthrene dioxide (43b) and anthraquinone are alike in having a much more shielded environment and solvent-shifts are only small. The cis-isomer, therefore, exists as conformer (43b) in all the solvents studied, including benzene for which there are supporting dipole moment data.[120,121] It is reluctantly concluded that BOESEKEN and VAN DER MEULEN'S[123] picturesque description of a rapid equilibrium between conformers (43a) and (43b), "It is probable that the molecule is flexible and that it moves like a bird in flight, continuously making an angle of 120$^{o}$ with its wings", is invalid. ARONEY et al.[124] have revived the age-old suggestion that the thianthren molecule itself is not ridid in solution but is capable of "flapping" about a line joining the sulphur atoms since the energy barrier for inversion through the planar form is relatively low (6-7 kcal/mole).[125]

On this basis they conclude that the oxides might also be non-rigid molecules. TAYLOR'S[120] inability to isolate two forms of the cis-dioxide (43) is taken by them as supporting evidence that the system oscillates between the two possible forms i.e. cis-dioxide isolated has an average conformation. The present infrared measurements, however, have demonstrated that the cis-dioxide has a definite fixed conformation (43b) with the two S=O bonds equatorial rather than axial (43a). ARONEY et al.[124], however, interpret their data (apparent polarities and electric birefringences) examined in benzene solution at 25° in terms of the average conformation resulting from a "flapping" about the line joining the sulphur atoms. Their treatment and conclusions regarding thianthren itself appear to be valid, but, "the lower symmetry of the β-dioxide does not allow us to locate with precision the principal semi-axis or the resultant dipole moment, so that analogous calculations for this molecule would be highly speculative".

In the trans-isomer the postulated Fermi resonance of the 1059 $cm^{-1}$ (in $CCl_4$) band with that at ca. 1030 $cm.^{-1}$, masks the true solvent-shift experienced by the ν(SO) absorption of the axial S=O group. For this reason a ν(SO)* area calculation was performed as described for the monosulphoxides, revealing that the ν(SO)* was 1054 and 1034 $cm.^{-1}$ in carbon tetrachloride and chloroform respectively. Hence the estimate for the shift ($CCl_4$ to $CHCl_3$) of the unperturbed S=O stretching absorption of the axial sulphoxide group is 20 $cm.^{-1}$, as compared with a value of 15 $cm.^{-1}$ based on the single 1059 $cm.^{-1}$ band.

Although the environment of the aromatic hydrogens differs in (43b) and (43c), the absorptions due to the C-H bending and stretching modes are almost idential. [For cis- and trans-thianthrene dioxide: ν(CH) in $CCl_4$ = 3066 vw $cm.^{-1}$, γ(CH) in $CS_2$ = 762 s, 754 m, 731 w $cm.^{-1}$. Anthraquinone, by contrast, has ν(CH) = 3074 vw $cm.^{-1}$, γ(CH) = 837 s, 708 s $cm.^{-1}$].

In summary, these infrared measurements on the cis- and trans-isomers of dithian dioxide and thianthrene dioxide are consistent with these compounds maintaining the same conformation in solution as has been found for the crystalline state by X-ray crystallography. Furthermore, it would seem that the $\nu$(SO) falls in with other $\nu$(X-Y) in that the value for an equatorially oriented group is higher than that for an axial one.

Miscellaneous sulphoxides (44-46, and 47a-d).

Two isomers, cis and trans, of structure (44) are possible.[114] Solution measurements other than in chloroform were not feasible owing to marked insolubility, but the chloroform solution spectra of both isomers are very similar (Table 27). There is, in fact, only one conformation for the trans-isomer (44c) while there are two possible chair conformations for the cis-isomer (44a) and (44b). The similarity in the spectra may arise from an equilibrium between (44a) and (44b) giving approximately as many axial S=O groups as equatorial ones, but firm conclusions seem unjustifiable.

Solutions of the $\alpha$ and $\beta$ isomers[114] of the compound type (47) have idential spectra over the region 1100-1000 cm.$^{-1}$ but there are slight differences in the solid state spectra. This is to be anticipated, since the two S=O groups would be expected to behave more or less independently in solution where free rotation is nominally possible. In view of the limited data presently available no attempt has been made to discuss the configuration and conformation of the compounds (44) and (46).

TABLE 27.

Bands in the $\nu$(SO) Region (1100-1000 cm.$^{-1}$) for Various Disulphoxides (42-46).

| No. | Compound | Isomer | Chloroform | | | Solid state | |
|---|---|---|---|---|---|---|---|
| | | | $\nu$ | $\Delta\nu_{\frac{1}{2}}$[a] | $\varepsilon$[a] | $\nu$ | $\Delta\nu_{\frac{1}{2}}$[a] |
| 42 | 1,4-Dithian-1,4-dioxide | cis | **1055** | 24 | 610 | 1049 | - |
| | | | | | | **1035** | 26 |
| | | | | | | 1026 | |
| | | | | | | 1019 | |
| | | trans | **1036** | 15 | 760 | **1023** | 15 |
| | | | | | | 1015 | |
| 43 | Thianthrene dioxide | cis | **1088** | 11 | 875 | **1088** | 10 |
| | | | 1028 | 5 | 550 | 1078 | - |
| | | trans | 1095 | - | 165 | 1092 | - |
| | | | **1075** | 16 | 310 | **1074** | 8 |
| | | | 1044 | 16 | 400 | 1038 | 8 |
| | | | 1030 | 18 | 320 | 1028 | - |
| | | | 1024 | | 300 | 1025 | - |
| 44 | 1,3,5-Trithian-1,3-dioxide* | | 1071 | sh | - | 1050 | 50 |
| | | | **1048** | - | - | **1042** | |
| 45 | 1,3,5-Trithian-1,3,5-dioxide* | | | | | 1053[a] | 45 |
| 46 | 1,3,5-Trithian monoxide | | 1065 | sh | - | (**1040**) | - |
| | | | **1045** | 25 | 360 | | |
| 47a | Dimethyl dithioethane dioxide* | | 1055 | sh | - | 1037 | - |
| | | | **1045** | 26 | 420 | **1017**[a] | - |
| 47b | Diethyl dithioethane dioxide* | | **1045**[a] | 37 | 365 | **1040** | - |
| | | | 1035 | sh | - | 1017 | - |
| | | | 1026 | sh | - | | |
| | | | 1023 | sh | - | | |
| 47c | Diphenyl dithioethane dioxide* | | 1086 | - | - | 1090 | - |
| | | | 1071 | - | - | 1068 | - |
| | | | **1044** | 20 | 565 | **1035** | - |
| | | | | | | 1017 | - |
| 47d | Di-p-toyl dithioethane dioxide* | | 1084 | - | - | 1084 | - |
| | | | **1043** | 22 | 545 | **1040** | - |
| | | | 1018 | - | - | 1018 | - |

The strongest bands observed for each compound are underlined; all except very weak bands or inflections have been reported in this Table. Values in parenthesis are approximate.

* The infrared spectra of both isomers are almost idential in the region (1100-1000 cm.$^{-1}$) and only one set of values is quoted.

a Asymmetric peak.

sh Shoulder.

- Not measured.

TABLE 28

Solvent Dependence of $\nu$(SO) and $\nu$(CO)

| Solvent | cis-Thianthrene dioxide (43)* | | | trans-Thianthrene dioxide (43)* | | | $Ph_2CO$ | | | Anthraquinone | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | $\nu$ | $\Delta\nu_{a/2}$ | $\varepsilon^a$ | $\nu$ | $\Delta\nu_{a/2}$ | $\varepsilon^a$ | $\nu$ | $\Delta\nu_{a/2}$ | $\varepsilon^a$ | $\nu$ | $\Delta\nu_{a/2}$ | $\varepsilon^a$ |
| Hexane | Sparingly soluble | | | Sparingly soluble | | | 1671 | 8 | 695 | 1682 | 6 | - |
| $C_2Cl_4$ | 1096 | 8 | - | 1082 | - | - | 1666 | 10 | 755 | 1679 | 5 | 1900 |
| | | | | 1062 | - | - | | | | | | |
| $CCl_4$ | 1095 | 7 | - | 1080 | 7 | - | 1666 | 10 | 600 | 1679 | 6 | 1550 |
| | | | | 1059 | 13 | | | | | | | |
| $CS_2$ | 1093 | 6 | 1350 | 1080 | 6 | - | 1663 | 8 | 745 | 1677 | 5 | - |
| | | | | 1058 | 7 | - | | | | | | |
| $CH_3CN$ | (1090) | - | - | (1078) | - | - | | | | | | |
| | | | | (1050) | - | - | | | | | | |
| Pyridine | 1091 | (9) | - | 1078 | 9 | - | | | | | | |
| | | | | 1050 | 12 | - | | | | | | |
| $CHCl_3$ | 1088 | 11 | 875 | 1074 | 16 | 400 | 1658 | 18 | 490 | 1676 | 10 | 1150 |
| | | | | 1044[a] | 16 | 310 | | | | | | |
| Benzene | 1093 | 7 | 1100 | 1093 | - | w | | | | | | |
| | | | | 1080 | 5 | s | | | | | | |

* Only selected bands in the $\nu$(SO) region (cf. text)
s Strong
w Weak
Cell paths: 0·05mm except for $CCl_4$ (2mm); $CS_2$ (2mm); and $CHCl_3$ (0·5mm)

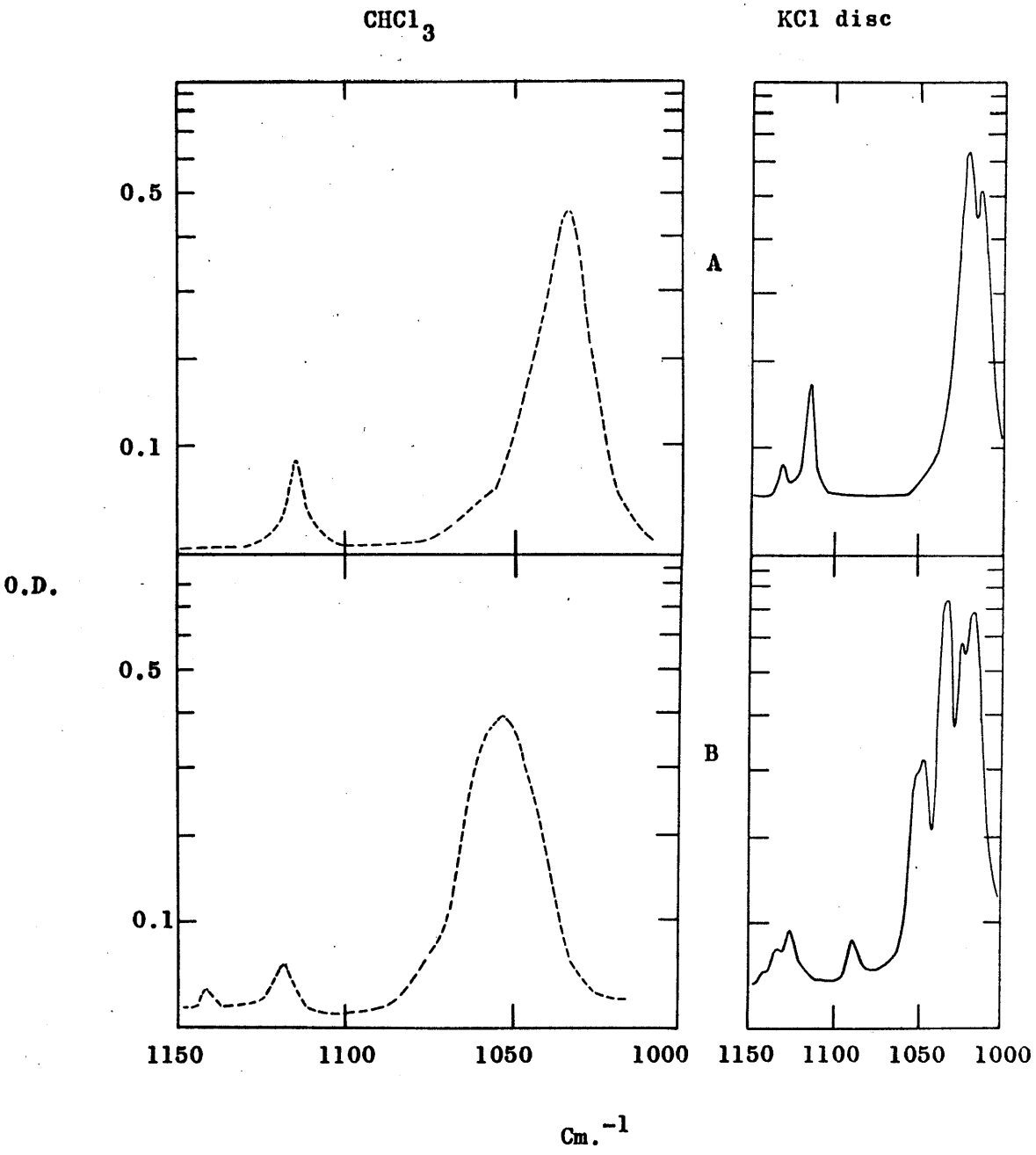



FIGURE 32. Absorptions in the S=O stretching region of the stereoisomeric 1,4-dithian dioxides (42); A, trans-isomer and B, cis-isomer. Spectra of chloroform solutions (ca. 0.012 M) in 0.5 mm cells on the left, and of solid state suspensions in KCl (0.5 mgs. in 300 mgs.) on the right.

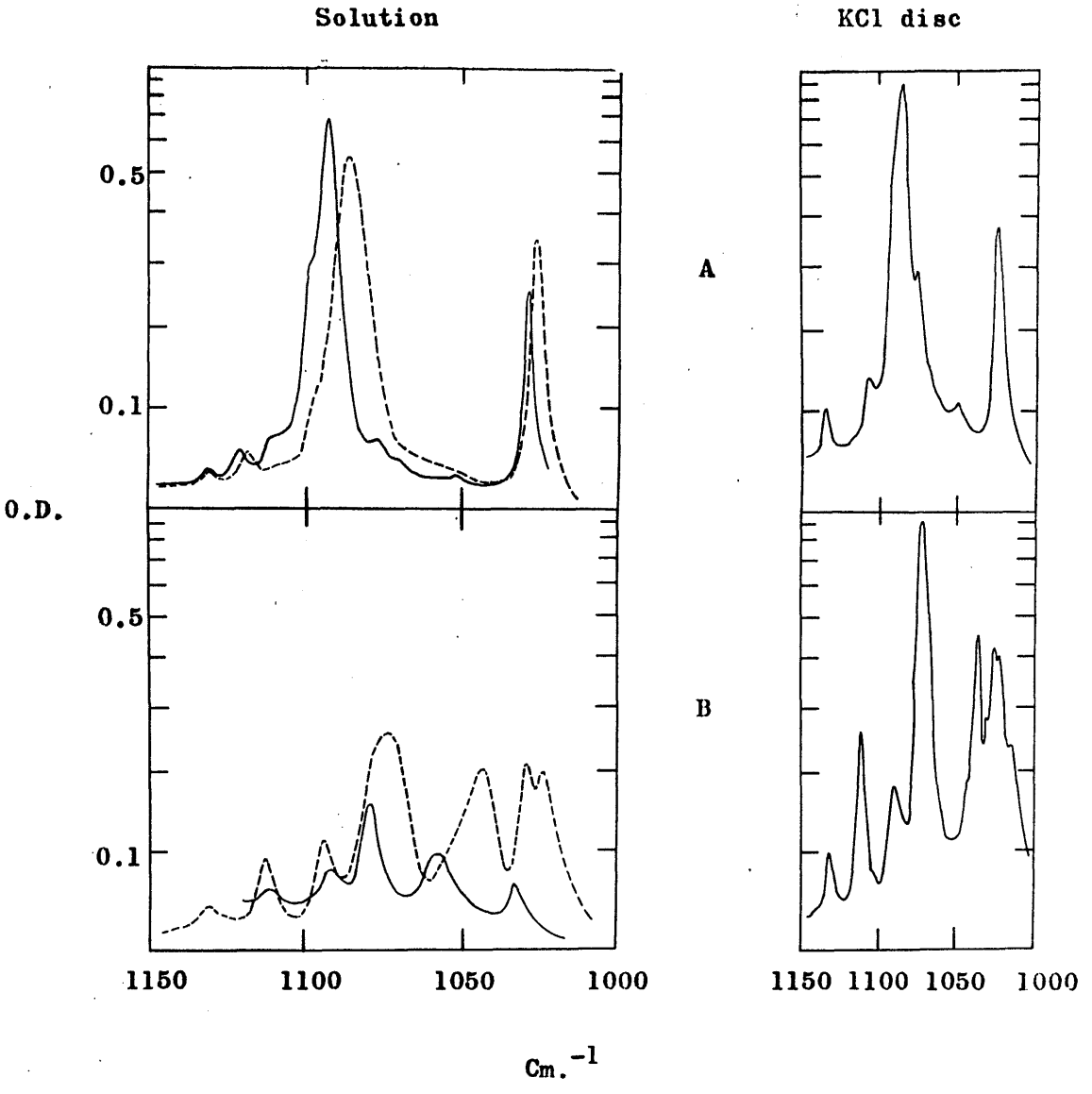
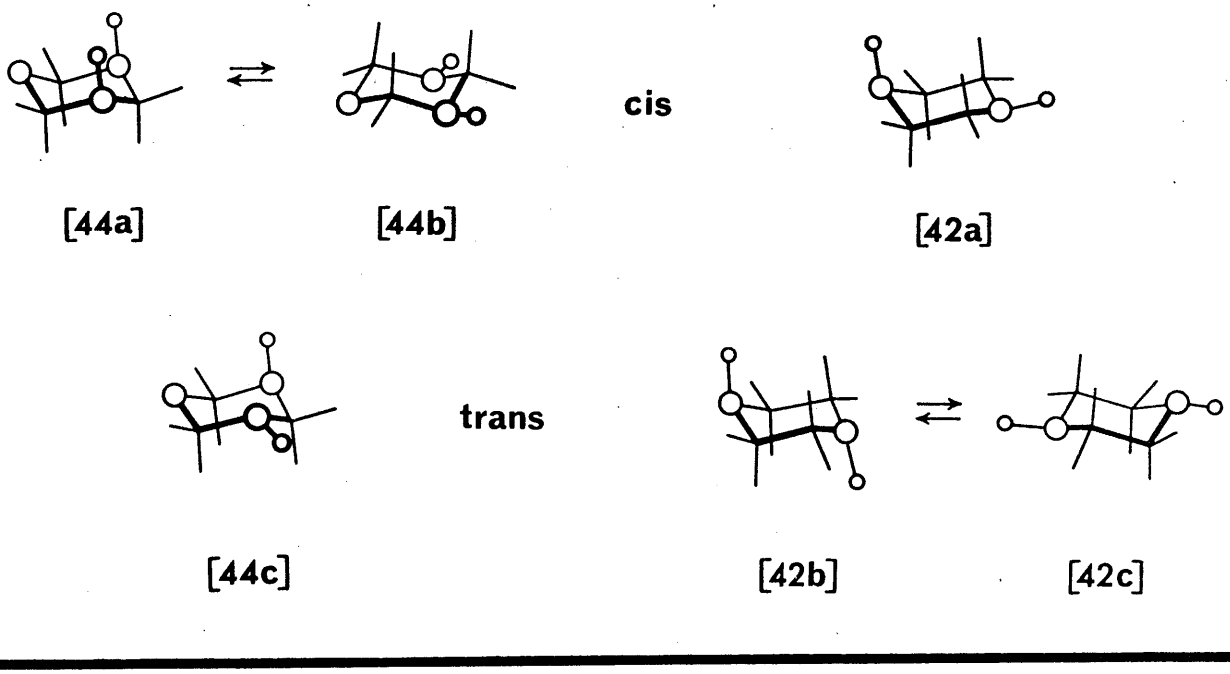
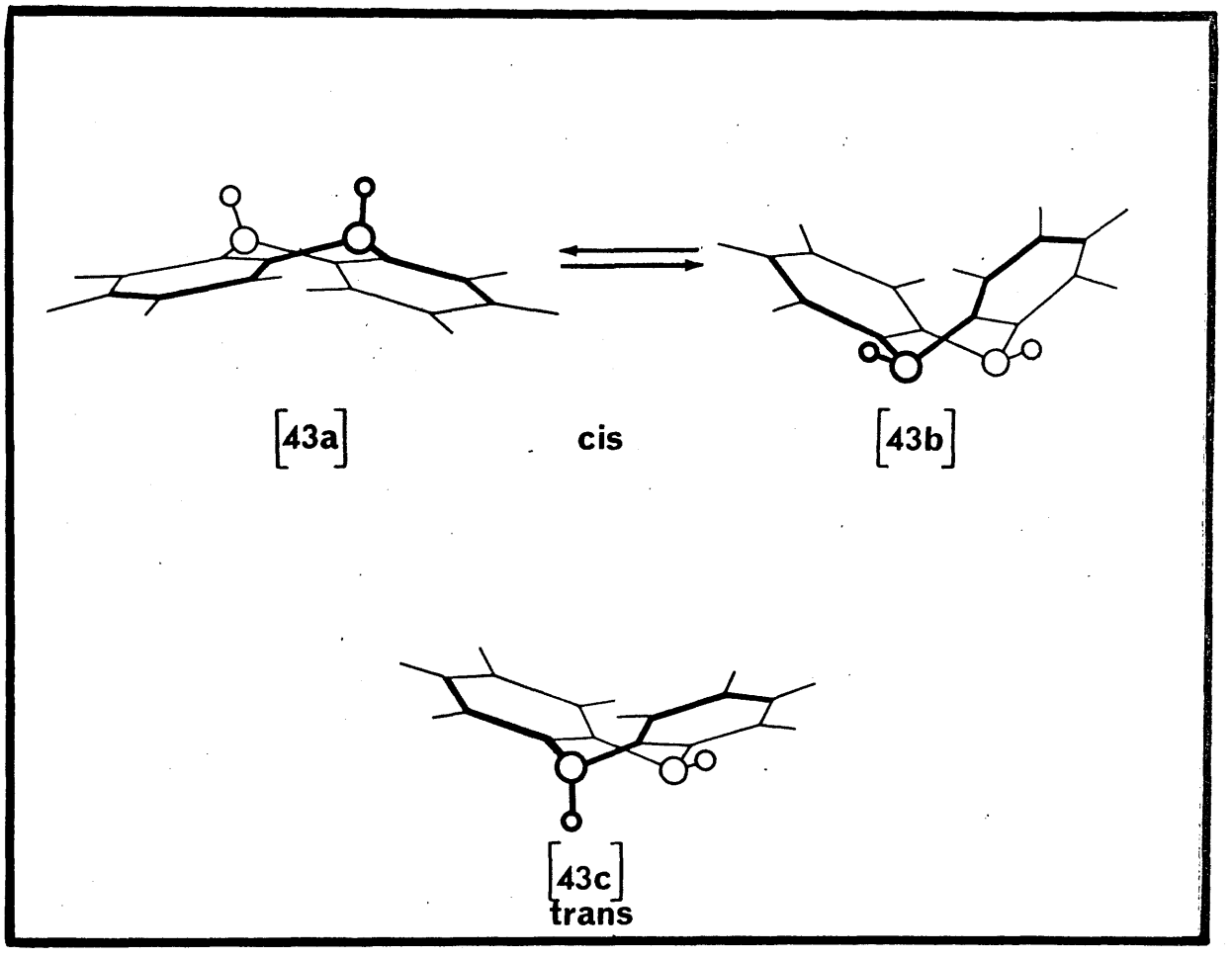



FIGURE 33. Absorptions in the S=O stretching region of the stereoisomeric thianthrene dioxides (43); A, cis-isomer and B, trans-isomer. Solution spectra (————, $CCl_4$ and - - - - -, $CHCl_3$) on the left, and of solid state suspensions in KCl (0.5 mg. in 300 mg.) on the right. Cell paths: $CCl_4$ (saturated solution), 2 mm.; $CHCl_3$ (ca. 0.012 M), 0.5 mm.


cis
trans
[44a]
[44b]
[42a]
[44c]
[42b]
[42c]


[43a]
cis
[43b]
[43c]
trans

# EXPERIMENTAL

## Compounds

### Hydrogen Bonding in Phenols

Compounds (1) and (2) were kindly supplied by Prof. A. ZINKE[47] of the Institute for Organic and Pharmaceutical Chemistry, Graz, Austria : (3) by Mr. A.R. PHILPOTTS, Dr. H.C. BAILEY, and Mr. P.A. JENKINS of the Distillers Co. : (5), (6) and (7e) by Dr. R.F. GODDU[56] of the Hercules Powder Co. : (7b) by Dr. N.D. COGGESHALL[55] of the Gulf Research and Development Co. : (12) and o-phenoxyphenol by Dr. J.D. LOUDON[126] : o-$\alpha$-phenylbenzyloxyphenol, b.p. 164-166°/ 1 mm., $n_D^{21} = 1.6116$ was obtained by hydrogenation of (12) in ethanol over 10% palladised charcoal [Found: C, 82.5; H, 6.3. $C_{19}H_{16}O_2$ requires C, 82.5; H, 5.9%]. The remaining compounds were of commercial origin and purified by distillation or crystallisation, dried and checked by thin-layer chromatography before use. The pyrocatechol monoesters were synthesised and purified by Prof. R.D. HAWORTH, Dr. E. HASLAM and Mr. R. BIGGINS of the Department of Chemistry, University of Sheffield.

### Infrared Studies of Terpenoid Compounds

The preparation and purification of cedrelone and related compounds (13-19) was undertaken by Dr. S.G. McGEACHIN.[127]

The isolation and purification of rosololactone and related compounds (20-22) was carried out by Prof. A.I. SCOTT and Dr. D.S. YOUNG.[69]

$\beta$-Angelica lactone (23) and $\gamma$-butyrolactone (24) were obtained commercially and purified by distillation. Compounds (33) and (34) were kindly supplied by Prof. W.S. JOHNSON.[128] The remaining lactones were provided by Drs. K.H. OVERTON, R.P.M. BOND, and J.D. CONNOLLY.[88]

Infrared Studies with Sulphoxides

Samples of dithian, trithian and related oxides were supplied by [the late] Prof. G.M. BENNETT, F.R.S.[114] The remaining sulphoxides were synthesised and purified by Dr. D.T. GIBSON.

## Solvents

n-Hexane (spectroscopic grade), carbon tetrachloride (AnalaR), and carbon disulphide (AnalaR) were used without further purification. Chloroform (AnalaR) was freed from ethanol by two successive passages through blue silica gel immediately before use. Diethyl ether was dried over sodium wire. Acetonitrile was purified by prolonged treatments with potassium hydroxide, calcium chloride, and phosphorus pentoxide, followed by distillation. Pyridine was redistilled twice from potassium hydroxide immediately before use. For the ether-carbon tetrachloride mixtures, solvents were measured out weight for weight. These mixed solvents were used as soon as possible after preparation. Tetrachloroethylene was purified by passage through chromatographic silica gel. Freshly sublimed p-cresol was used and precautions taken to avoid adsorption of moisture.

## Measurements

### Infrared

Spectra were recorded linearly in $cm.^{-1}$ as percentage transmission with a Unicam SP. 100 double-beam infrared spectrophotometer equipped with an SP. 130 sodium chloride prism-grating double monochromator [3000 lines per inch (2150-3650 $cm.^{-1}$) and 1500 lines per inch (650-2150 $cm.^{-1}$)] operated under vacuum. The calibration was checked against the spectrum of water vapour after each group of measurements. The hydroxyl and carbonyl absorptions were scanned at 4.6 and 8.0 $cm.^{-1}$ per min., respectively. Frequency measurements for the "free" and intrabonded hydroxyl and carbonyl

bands are believed to be accurate to ± 1 $cm.^{-1}$. The linearity of the percentage transmission scale was checked by SHREWSBURY'S procedure[129], and the intensities were measured on bands of not less than 10% transmission. The theoretical spectral slit-width, computed from tables supplied by Unicam Instruments Ltd., was 5.5 $cm.^{-1}$ at 3600 $cm.^{-1}$, 4.5 $cm.^{-1}$ at 3350 $cm.^{-1}$, and 3.4 $cm.^{-1}$ at 1700 $cm.^{-1}$. Unless specified otherwise, peaks were symmetrical; the apparent half-band widths, $\Delta\nu_{\frac{1}{2}}^{a}$, are quoted to the nearest integer; where necessary they were determined by reflection of the undisturbed wings of the unsymmetrical bands. Intensities are given as apparent extinction coefficients, $\varepsilon^{a}$, ($l.mole^{-1}cm.^{-1}$) rounded to the nearest 5 units and measured from a solvent-solvent base-line superimposed on the record of the spectrum of the solution (determined with solvent in the reference beam).

Nuclear Magnetic Resonance

Spectra were determined on the Perkin-Elmer Model R 10 Nuclear Magnetic Resonance Spectrometer using tetramethylsilane (TMS) as internal standard.

Ultraviolet

Spectra were obtained using a Unicam SP. 800B Spectrophotometer.

Molecular Weight

Molecular weights in dilute carbon tetrachloride were determined with a Mechrolab Vapour Pressure Osmometer Model 301A precalibrated with benzil in carbon tetrachloride.

Gas Chromatography

Results were obtained on a Pye "Argon Chromatograph" using 46" x 1/5" columns.

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7. "Hydrogen Bonding in Phenols. Part II. The Alkyl Substituted Bis-phenylol Alkanes (Dinuclear Novolaks)", T. CAIRNS and G. EGLINTON, J. Chem. Soc., in press.

8. "Infrared Studies of Terpenoid Compounds. Part III. Rosololactone and Related Diterpenoid Lactones from Trichothecium roseum Link", T. CAIRNS, G. EGLINTON, D.S. YOUNG, and A.I. SCOTT, J. Chem. Soc., in preparation.

# ADDITIONAL PUBLICATIONS

The following publications derive from the author's participation in, and his enthusiasm for, the teaching of applied spectroscopy to the undergraduate and graduate students of the Department of Chemistry, University of Glasgow.

1. "Spectroscopic Problems in Organic Chemistry", T. CAIRNS, Heyden & Son Ltd., London(1964).

2. "Spectroscopy in Education", T. CAIRNS, Perkin-Elmer Instrument News, 15, 2, 5(1964).

3. "Spectroscopic Techniques in Organic Chemistry", A.J. BAKER and T. CAIRNS, Education in Chemistry, 2, 87(1965).

4. "Spectroscopic Techniques in Organic Chemistry", A.J. BAKER and T. CAIRNS, Heyden & Son Ltd., London(1965).