

180. *Vibrational Frequency Correlations in Heterocyclic Molecules. Part V.<sup>1</sup> The Infrared Spectra of Some Enolic Structures Related to Oxindole and Isatin.*

By D. G. O'SULLIVAN and P. W. SADLER.

Chemical properties and infrared spectra indicate that *N*-methyloxindole-3-aldehyde possesses a hydroxymethylene structure at position 3. This enolic form exists in the solid and in solution because of the formation of strong resonance-stabilised intramolecular hydrogen bonds of the type well known with aliphatic diketones.

Substituted 4 : 5 : 6 : 7-tetrahydro-*N*-phenylisatins also exist as the 3-enols, stabilised by (i) hydrogen bonding and (ii) extension of conjugation. The carbonyl frequencies respond to changes in the Hammett  $\sigma$  values of aromatic ring substituents in the usual way, the substituent effect being transmitted, although to a reduced extent, through the tertiary nitrogen atom. The substituent effect on the stretching frequencies of those carbonyl groups involved in hydrogen bonding is greater than on unbonded carbonyl groups. Comments are made on other features of the spectra of these compounds and their ethers, anils, and oximes.

The spectrum of indole-3-aldehyde indicates that its carbonyl group has a low bond order and suggests hydrogen-bonded association of a mainly dipolar character.

SUMMATION of bond energies<sup>2</sup> shows that a simple keto-structure is more stable than the enol by about 18 kcal. mole<sup>-1</sup> for ketones and 15 kcal. mole<sup>-1</sup> for aldehydes, and an amide is more stable than the imino-alcohol by about 10 kcal. mole<sup>-1</sup>. Many other factors can arise, particularly in cyclic systems, which may invalidate a simple application of these results. Nevertheless, of the large number of non-phenolic cyclic compounds which could exhibit these types of tautomerism and which have been studied,<sup>3</sup> most have been shown to exist in the ketonic form in the pure state and in solution. It is likely, however, that in solution the compounds exist in equilibrium with minute proportions of the enol. The small variation of  $\Delta F (=RT \ln\{[\text{keto}]/[\text{enol}]\})$  with change in the relative concentrations in solution implies that an energy difference of only 6 kcal. mole<sup>-1</sup> between the two forms will raise the [keto]/[enol] ratio to over 99%, *i.e.*, the enol present will probably be undetectable. The solution may still, however, exhibit enolic reactions if (a) these reactions are rapid, (b) tautomeric equilibrium is rapidly attained, and (c) the keto-form is in itself inert towards the reagents. Where a substance readily undergoes both ketonic and enolic reactions, purely chemical evidence is probably inconclusive. These remarks apply also to amide-imidol tautomerism.

In compounds where enolic forms are favoured, such as phenols and  $\beta$ -diketones, additional features are recognised as exerting a dominant influence on the structure.<sup>4</sup> Thus carbonyl compounds exist almost exclusively in the keto-form unless features such as hydrogen bonding, steric hindrance, or the possible extension of conjugation stabilise the alternative form. After a brief treatment of indole-3-aldehyde, this paper deals with a spectroscopic study of two sets of cyclic compounds which possess chemical properties suggesting the preponderance of enolic tautomers.

<sup>1</sup> Part IV, Holt, Kellie, O'Sullivan, and Sadler, *J.*, 1958, 1217.

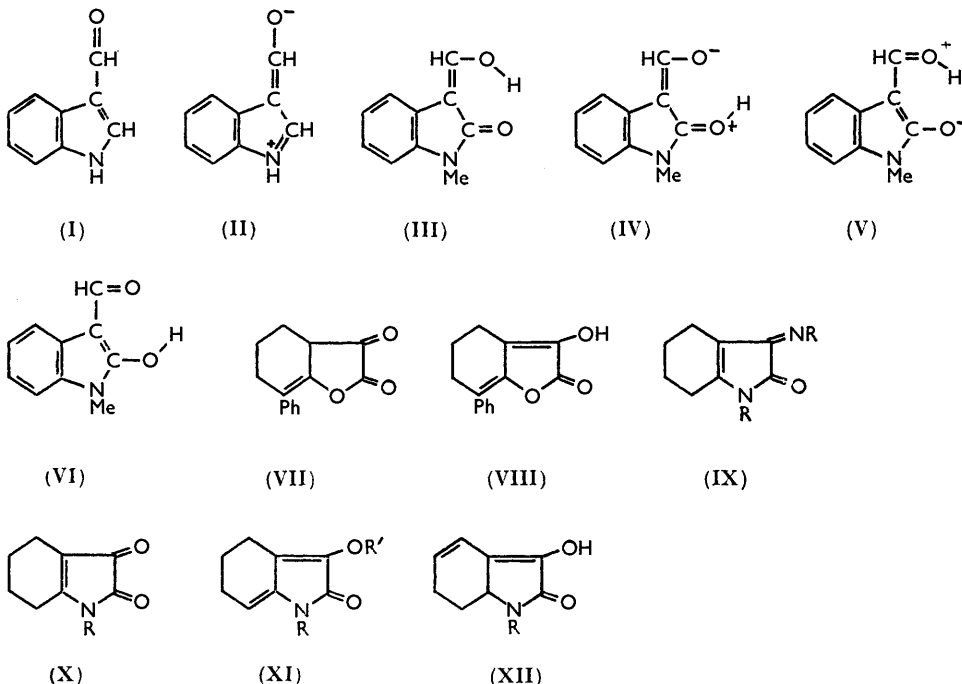
<sup>2</sup> Branch and Calvin, "The Theory of Organic Chemistry," Prentice-Hall, New York, 1946.

<sup>3</sup> Culbertson, Decius, and Christensen, *J. Amer. Chem. Soc.*, 1952, **74**, 4834; Brown and Short, *J.*, 1953, 331; Sensi and Gallo, *Ann. Chim. (Italy)*, 1954, **44**, 232; Brown, Hoerger, and Mason, *J.*, 1955, 211; Gibson, Kynaston, and Lindsey, *ibid.*, p. 4340; O'Sullivan and Sadler, *J.*, 1956, 2202; Kellie, O'Sullivan, and Sadler, *J.*, 1957, 3809; Mason, *ibid.*, pp. 4874, 5010.

<sup>4</sup> Thomson, *Quart. Reviews*, 1956, **10**, 27.

## RESULTS AND DISCUSSION

*Indole-3-aldehyde.*—In potassium bromide discs and in chloroform this compound shows an NH stretching frequency as a broad band between 3120 and 2900  $\text{cm}^{-1}$ . No band is present at a higher frequency. As indole possesses maxima between 3491 and 3447  $\text{cm}^{-1}$  in various solvents, and only very weak maxima near 3340  $\text{cm}^{-1}$  due to hydrogen-bonded association,<sup>9</sup> it is clear that the NH bond in indole-3-aldehyde is involved in fairly strong hydrogen bonding. The carbonyl stretching frequency occurring at 1631  $\text{cm}^{-1}$  in the solid and 1655  $\text{cm}^{-1}$  in chloroform suggests that this group possesses a low bond order. These results show that the dipolar form (II) makes a large contribution to the structure of indole-3-aldehyde and dipolar association occurs so that, in the solid, structures (I) and (II) are the main contributions to each unit in an extensive hydrogen-bonded polymer. Thus a definite aldehydic structure exists, but the carbonyl group possesses a much reduced bond order. The concomitant proximity of a hydrogen atom in the polymer enables the compound to possess enolic properties in addition to its aldehydic properties. Enolic properties result when the N-H bond is split, and the aldehydic properties when the H...O link is broken. The possible alternative that hydrogen bonding occurs between an aldehydic and an enolic molecule may be excluded on the following grounds: (a) the absence of



a free, or very weakly associated, NH stretching frequency,<sup>9</sup> (b) the absence of a hydrogen-bonded OH stretching frequency, and (c) the very low value for the CO stretching frequency.<sup>10</sup>

<sup>5</sup> Van Order and Lindwall, *J. Org. Chem.*, 1945, **10**, 128.

<sup>6</sup> W. König, *J. pr. Chem.*, 1911, **84**, 194.

<sup>7</sup> Angeli and Marchetti, *Atti R. Accad. Lincei*, 1907, **16**, 381; Angeli and Allesandri, *ibid.*, 1914, **23**, 93.

<sup>8</sup> Sumpter and Miller, "Heterocyclic Compounds with Indole and Carbazole Systems," Interscience, New York, 1954, p. 42.

<sup>9</sup> Fuson, Josien, Powell, and Utterbach, *J. Chem. Phys.*, 1952, **20**, 145.

<sup>10</sup> Rasmussen, Tunncliff, and Brattain, *J. Amer. Chem. Soc.*, 1949, **71**, 1068.

*N-Methyloxindole-3-aldehyde*.—Although oxindole-3-aldehyde and its 1-methyl derivative form typical carbonylic derivatives (*e.g.*, oximes,<sup>11</sup> semicarbazones,<sup>12</sup> and aldimines<sup>13</sup>), yet the ferric chloride test for OH is positive and acetyl, benzoyl, and benzenesulphonyl derivatives are readily formed.<sup>12,14</sup> Under different conditions a variety of methyl

TABLE 1. Frequencies in spectra of compounds in potassium bromide discs.

Compound		4000—1425 cm. <sup>-1</sup> region								
		3120s†	2900s†	1631s	1615w	1577w	1519m	1445s		
A,	Indole-3-aldehyde						1498m			
B,	Indole-3-aldoxime	3400—2700s†		1641s			1508w		1462s	
							1493w			
C,	1-Methyloxindole-3-aldehyde	3100—2850m†	1680s	1633s	1611s	1555m	1470s			
		2600—2400s†								
D,	1-Methyloxindole-3-aldoxime	3400m	2905m	1696m	1646m	1611s	1577s	1492m	1437m	
								1474m		
E,	Isatin $\alpha$ -oxime	3400—3000 m†	1716m	1641m	1614s			1483m	1466m	
F,	Isatin $\beta$ -oxime	3200—2600s†	1712s	1662m	1621s				1465s	
4 : 5 : 6 : 7-Tetrahydroisatins										
G,	1-Phenyl-	3210s	2910s	1670s	1650s	1596m		1503s	1451w	
									1433w	
H,	1-( <i>m</i> -Chlorophenyl)-	3170s	2900w	1669s	1652s	1595m		1522w	1433m	
								1484m		
I,	Methyl ether* of 1-phenyl-		2915w	1705s	1652m	1599m		1499s	1460m	
					1639s				1434m	
J,	<i>m</i> -Chloroanil* of 1-( <i>m</i> -chlorophenyl)-			1688s	1640s	1598s	1579s	1525s	1432s	
								1483s		
K,	Oxime* of 1-phenyl-	3300s	2915w	1705s	1646w	1600m		1518s	1447s	
L,	1-Benzyl-	3225s	2920w	1678s	1660s	1590w		1501w	1448m	
									1430m	
M,	Oxime* of 1-benzyl-	3300s	2915m	1674s	1659s			1528w	1458m	
								1498w		
Compound		1425—900 cm. <sup>-1</sup> region								
		1394s	1338m	1300m	1248s	1152m	1127s	1086m	1008w	
A,										
B,	1418s	1343s		1238s		1133s	1099s	1009w		
									930s	
C,	1381s	1344w	1276m	1233s	1190m	1164w	1123s	1110s	1027w	
D,	1390m	1348m	1270m	1240m		1149w	1128m	1094s	1044m	
								1073w	985w	
E,		1329m		1225w		1144w			1027w	
F,	1391w	1349s	1301w	1220m	1195m		1100w	1030s		
G,	1409s	1341w	1313s	1247s	1191m	1168m	1071w	1050w	983m	
H,	1408s	1311s	1300m	1248m	1186m	1169m	1073w	1047w	1002w	
									986m	
I,	1409s	1336m	1291s	1260w	1194s	1160s	1123m	1076w	1054w	
	1376m			1248s	1178m				1020s	
J,	1408s	1345w	1285w	1260w	1178m	1154w		1088w	1051w	
		1328m	1273w	1230w				1073w	997w	
K,		1318m		1240w	1196s			1073w	1059w	
								1039w	990w	
L,	1410s	1368m	1342m	1239m	1198w	1151w	1137w	1081w	1058w	
		1352m	1316s		1179w				1019m	
M,	1401s	1366m	1287w	1233w		1141w	1119w	1091w	1035w	
									968m	
									950s	
									928w	
									913w	

\* At position 3. † Broad band.

derivatives may be obtained.<sup>14,15</sup> In the present study the 1-methyl compound<sup>16</sup> has been selected for scrutiny to avoid the possibility of tautomerism involving the NH group. Spectral features are given in Table 1.

<sup>11</sup> Friedlander and Kielbasinski, *Ber.*, 1911, **44**, 3098.

<sup>12</sup> Fischer and Smeykal, *Ber.*, 1923, **56**, 2368.

<sup>13</sup> Kalb and Berrer, *Ber.*, 1924, **57**, 2105.

<sup>14</sup> Horner, *Annalen*, 1941, **548**, 117; Gränacher and Mahal, *Helv. Chim. Acta*, 1923, **6**, 467.

<sup>15</sup> Julian, Pikel, and Boggess, *J. Amer. Chem. Soc.*, 1934, **56**, 1797.

<sup>16</sup> Julian, Meyer, and Printy in "Heterocyclic Compounds" (ed. Elderfield), John Wiley, New York, 1952, Vol. III, p. 153.

Absence of any absorption above  $3100\text{ cm}^{-1}$  either in the solid or in solution in chloroform or carbon tetrachloride shows the absence of a free OH group, but the broad band of considerable intensity between  $2600$  and  $2400\text{ cm}^{-1}$  shows the presence of very strong hydrogen bonding which is only explicable on the assumption that resonance-stabilised intramolecular hydrogen bonding, as found in aliphatic  $\beta$ -diketones and  $\beta$ -keto-esters,<sup>10,17</sup> is present. The unperturbed forms of this conjugated chelate compound are represented by structures (III)—(VI). As the molecule is not a symmetrical diketone, an unequal contribution is to be expected from structures of type (III) and (VI), but it is likely that all four structures make a substantial contribution to the resonance system, as undue predominance of one form would weaken the hydrogen bonding and would not therefore produce the band at  $2600$ — $2400\text{ cm}^{-1}$ . Bands at  $1680\text{ cm}^{-1}$  and  $1633\text{ cm}^{-1}$  are produced essentially by stretching vibrations of C=O and C=C bonds, but vibrational interactions may occur in this system and distinct assignments may not be possible.

The oxime exhibits an OH stretching frequency at  $3400\text{ cm}^{-1}$  and a carbonyl frequency at  $1696\text{ cm}^{-1}$ , both of which are unchanged in solution. It therefore possesses the expected structure but has a much weaker intramolecular hydrogen bond than the parent compound. Considerable similarity exists between the spectrum of 1-methyloxindole-3-aldoxime and 1-methylisatin  $\beta$ -oxime, and this similarity also extends to isatin  $\beta$ -oxime itself (Table 1). The skeletons are undoubtedly the same and provisional assignments of the aldoxime frequencies at  $1240$  and  $1044\text{ cm}^{-1}$  to N—O—H bending and N—OH stretching modes are possible. Table 1 shows that very marked differences exist between the spectra of these compounds and that of isatin  $\alpha$ -oxime.

*Reduced Isatins.*—Condensation of 2-phenylcyclohexanone with dimethyl oxalate gives a lactone<sup>18</sup> which has been shown unequivocally to have structure (VII) or (VIII). The very pronounced enolic properties and the clearly enhanced conjugation make it likely that (VIII) is the structure adopted in most circumstances. *cyclo*Hexanone itself condenses with dimethyl oxalate to give a substituted glyoxylic ester which reacts with amines to form anils of structure (IX).<sup>19</sup> Acid hydrolysis of the anils produces *N*-substituted 4 : 5 : 6 : 7-tetrahydroisatins which, Horwitz<sup>19</sup> suggests, consist of tautomeric mixtures of keto- and enol forms. Although phenylhydrazones are formed at position 3 and condensations occur with *o*-phenylenediamine to give quinoxalines, the compounds readily undergo methylation at the 3-position, and form other enolic derivatives with equal ease. Formulae (X) and (XI; R' = H) represent the most probable structures for these compounds, (XII) being the only other possibility. Two hydrogen atoms would have to migrate to different positions in structure (XII) to produce ketonic functions at position 3. Therefore, this structure is most unlikely. The existence of lactones (VIII) shows that the type of conjugated ring system in structure (XI) is stable and the close analogy in the reactivities of the two sets of compounds<sup>18,19</sup> strongly suggests the presence of similar ring systems. Also, if R is a substituted phenyl group, more extensive conjugation is possible in (XI) than in (XII). Infrared studies were designed to discover which structure was adopted in the solid and in non-polar solvents and to study the extent to which substituent effects could be transmitted in this system.

Structure (X), possessing no OH or NH bonds, should show no absorption at wavelengths greater than  $2000\text{ cm}^{-1}$  except for CH stretching frequencies near  $3000$ — $2900\text{ cm}^{-1}$  and possibly for weak overtone frequencies, the strongest of which should be the first carbonyl stretching harmonic near  $3400\text{ cm}^{-1}$ . Table 1 shows that a strong and, for this region in the spectrum, very sharp band is present at  $3210\text{ cm}^{-1}$  in the solid, which can only be a hydrogen-bonded OH stretching frequency. This maximum becomes a much broader absorption at about the same frequency in chloroform, whilst in carbon tetrachloride two sharp bands appear, one near  $3490\text{ cm}^{-1}$  and the second near  $3200\text{ cm}^{-1}$ . These bands

<sup>17</sup> Rasmussen and Brattain, *J. Amer. Chem. Soc.*, 1949, **71**, 1073; Hunsberger, *ibid.*, 1950, **72**, 5626.

<sup>18</sup> Bachmann, Fujimoto, and Wick, *ibid.*, p. 1995.

<sup>19</sup> Horwitz, *ibid.*, 1953, **75**, 4060.

are present with all the substituted tetrahydro-*N*-phenylisatins but are completely absent from the spectra of the anils (IX) and the methyl ethers (XI; R' = Me), neither of which can contain hydroxyl groups. The bands near 3200 cm.<sup>-1</sup> are produced by simple hydrogen bonding of reasonable strength and undoubtedly arise from C=O...HO linkages which might be of inter- or intra-molecular type. The high m. p.s of the reduced isatins compared with those of their methyl ethers suggest that intermolecular hydrogen-bonded dimers exist in the solid, whilst the broad absorption in chloroform suggests the presence of both dimer and monomer. The sharper absorption peak occurring between 3200 and 3180 cm.<sup>-1</sup> in carbon tetrachloride is probably produced by OH groups engaged in intra-molecular bonding. The sharp maximum near 3490 cm.<sup>-1</sup> in carbon tetrachloride could be due to OH groups involved in weak hydrogen bonding<sup>17</sup> when such dimers as exist would be formed by hydroxyl association, leaving free ketone groups in the 2-positions. Alternatively, dimers could possess CO...HO bonds of such reduced strength that the CO groups are virtually unaffected and the OH frequencies only slightly depressed. Carbonyl stretching frequencies fully support these suggestions. The only absorption shown by the methyl ethers is a weak CH stretching frequency near 2915 cm.<sup>-1</sup>. With the anils even this absorption is very weak indeed.

*Carbonyl Frequencies.*—The methyl ethers, each of which contains one carbonyl group which cannot be involved in hydrogen bonding, possess sharp maxima at about the same frequency both in the solid and in carbon tetrachloride (Table 2). This also applies to the anils (Table 2) but the molecular environment of the carbonyl group in the anils is very different from that in the ethers. Extended conjugation of the carbonyl group in the anils results in a lowering of its frequency. The reduced isatins themselves possess single carbonyl stretching frequencies in the solid and in chloroform. Their spectra at frequencies above 3000 cm.<sup>-1</sup> suggest that these are stretching frequencies of carbonyl groups involved in hydrogen bonding, and this is strongly supported by the carbonyl frequencies in carbon tetrachloride. Two carbonyl maxima are given in this solvent (Table 2), one slightly above the frequency for the corresponding methyl ether and the other at a frequency slightly above the chloroform maximum. An equilibrium clearly exists, in carbon tetrachloride, between molecules in which the carbonyl group is either unbonded or very weakly bonded and those in which it is involved in quite strong hydrogen bonding. An alternative possibility, that the two frequencies arise from the existence of at least some of the 3-oxo-form, may be discounted from the position of these frequencies, the presence and position of the two OH stretching frequencies, and from the way in which the frequencies vary with the character and position of benzene ring substituents. Thus one concludes that, in the solid, the compound exists as an enol with the OH group fairly strongly hydrogen bonded to the carbonyl group of the adjacent molecule to form a dimer linked by two CO...HO bonds. In chloroform the main solute components are probably a mixture of monomer and dimer, the former possessing intra- and the latter inter-molecular CO...HO bonds of about equal strengths, whilst in carbon tetrachloride the main components are dimers possessing either OH...OH bonds and free carbonyl groups or very weak CO...HO bonds and monomers containing intramolecular CO...HO bonds.\*

*Substituent Effects on Carbonyl Frequencies.*—(a) *Methyl ethers.* Seven of these derivatives of tetrahydro-1-phenylisatin, possessing benzene-ring substituents with Hammett  $\sigma$  values<sup>20</sup> lying over a range of nearly one unit, were examined spectroscopically. Table 2 shows that substituents exert an effect on the carbonyl stretching frequencies  $\nu$  in carbon tetrachloride. As usual, the relation between  $\nu$  and  $\sigma$  is linear, the equation of the regression line for  $\nu$  being  $\nu = 1702.9 + 6.04\sigma$ , and the correlation coefficient  $r$  is 0.980. The substituent effect clearly gets transmitted through the nitrogen atom, but comparison with other compounds shows that it is reduced in magnitude by approximately 50%.

\* The views expressed in this and the preceding paragraph have been modified to take account of a criticism kindly made by a Referee.

<sup>20</sup> Hammett, "Physical Organic Chemistry," McGraw-Hill, New York, 1940, p. 188; Jaffé, *Chem. Rev.*, 1953, **53**, 191.

(b) *Enols*. The upper carbonyl stretching frequency shown by the enols in carbon tetrachloride is not only near that of their methyl ethers, but substituents have quantitatively about the same effect on both these sets of frequencies. This confirms that the carbonyl frequency in the enols is produced by the  $\alpha$ -carbonyl group not markedly affected by hydrogen bonding. The equation of the regression line for the frequencies is  $\nu = 1709.4 + 6.16\sigma$  and the correlation coefficient is 0.963.

The lower carbonyl stretching frequency in carbon tetrachloride is probably produced by the  $\alpha$ -carbonyl group involved in intramolecular hydrogen bonding. Frequencies increase in a linear fashion with the  $\sigma$  values of substituents, the effect being about twice the effect on the upper frequencies. The regression line for the  $\nu$  values is  $\nu = 1689.3 + 14.17\sigma$  and the correlation coefficient is 0.936. Frequencies of the carbonyl band in chloroform lie slightly below those in carbon tetrachloride and also arise from hydrogen-bonded carbonyl groups. Here the regression line for the frequencies is  $\nu = 1683.9 + 17.83\sigma$ , and the correlation coefficient 0.963. Where the maxima in chloroform cover a range of values, the central frequency is recorded in Table 2 and is used in computing the regression line and correlation coefficient. Solid-state infrared spectra are similar to those in chloroform. It is clear from Table 3 that in all these cases substituent effects are greater on a strongly

TABLE 2. Carbonyl stretching frequencies of substituted 4 : 5 : 6 : 7-tetrahydro-1-phenylisatins and related compounds.

Subst.	$\sigma$ Value	Frequencies (cm. <sup>-1</sup> ) of compounds				
		Enol in CHCl <sub>3</sub>	Enol in CCl <sub>4</sub> Band II	Enol in CCl <sub>4</sub> Band I	Methyl ether in CCl <sub>4</sub>	Anil in CHCl <sub>3</sub>
<i>p</i> -NMe <sub>2</sub> .....	-0.6	—	—	—	—	1677
<i>p</i> -MeO .....	-0.268	1678 *	1685 *	1708	1701	1682 *
<i>p</i> -Me .....	-0.170	1683 *	1690	1709	1702	1682
<i>m</i> -Me .....	-0.069	—	—	—	—	1684
None .....	0.0	1684	1689	1709	1703	—
<i>m</i> -MeO .....	0.115	1684	1689	1709	1703	1686
<i>p</i> -Cl .....	0.227	1687	1691	1711	1705	1688
<i>m</i> -Cl .....	0.373	1693	1694	1712	1705	1690
<i>m</i> -NO <sub>2</sub> .....	0.710	1696	1701	1714	1707	1695

\* Central frequency is quoted for a maximum extending over about 4 cm.<sup>-1</sup>. Where blanks occur in these columns the frequencies have not been measured. All bands quoted are intense.

TABLE 3. Effect of hydrogen bonding, involving the carbonyl group, on the slope  $d\nu(\text{CO})/d\sigma$  for substituted 4 : 5 : 6 : 7-tetrahydro-1-phenylisatins and substituted benzoic acids.

Subst.	$\sigma$ Value	Carbonyl stretching frequencies (cm. <sup>-1</sup> )				
		Enol in CCl <sub>4</sub> Band I	BzOH in CCl <sub>4</sub> * (monomer)	Enol in CCl <sub>4</sub> Band II	BzOH in MeOH * (monomer)	BzOH in CCl <sub>4</sub> * (dimer)
<i>p</i> -NH <sub>2</sub> ...	-0.660	—	—	—	1690	—
<i>p</i> -MeO ...	-0.268	1709	1737	1685	1695	1691
<i>p</i> -Me ...	-0.170	1709	1739	1690	1700	1693
None ...	0.0	1709	1743	1689	1705	1693
<i>m</i> -MeO	0.115	1709	—	1689	—	—
<i>p</i> -Br ...	0.232	—	—	—	1710	—
<i>p</i> -Cl .....	0.227	1711	1746	1691	1713	1699
<i>m</i> -Cl ...	0.373	1712	1746	1694	1715	1701
<i>m</i> -NO <sub>2</sub> ...	0.710	1714	1750	1701	1723	1705

\* Estimates of the accuracy of these frequency measurements varying from  $\pm 1$  to  $\pm 5$  cm.<sup>-1</sup> have also been reported.<sup>23</sup>

hydrogen-bonded carbonyl group than on a free group or on one involved in very weak hydrogen bonding. Other examples have been noted of a larger substituent effect on groups involved in hydrogen bonding than on similar unbonded groups (cf., *e.g.*, acetanilide with acetophenone or benzophenone<sup>21</sup>). A striking example is also evident in the values given

<sup>21</sup> O'Sullivan and Sadler, *J. Org. Chem.*, 1956, **21**, 1179.

<sup>22</sup> Flett, *Trans. Faraday Soc.*, 1948, **44**, 767.

by Flett<sup>22</sup> of the effect of substituents on the carbonyl frequencies of carboxylic acids in carbon tetrachloride and methanol.

Change of solvent from carbon tetrachloride to methanol produces the following two effects on the carbonyl frequencies of benzoic acid monomers: (i) all frequencies are reduced, showing that hydrogen-bonded association occurs between the carbonyl group and methanol, and (ii) the displacement of frequencies by substituents is notably enhanced, strongly suggesting that the substituent effect is greater in carbonyl groups involved in this type of hydrogen bonding. This is, however, a matter of some complexity, as smaller substituent effects are exerted on the very strongly hydrogen-bonded carbonyl group of

TABLE 4.  $\sigma$  Values and some lower-frequency bands of substituted 4 : 5 : 6 : 7-tetrahydro-1-phenylisatins in potassium bromide discs.

Subst.	$\sigma$ Value	Frequencies (cm. <sup>-1</sup> )				
<i>p</i> -Me .....	-0.170	1613	1518	1409	1193	686
None .....	0.0	1596	1503	1409	1191	692
<i>p</i> -Cl .....	0.227	1595w	1497	1414	1186	693w
<i>m</i> -Cl .....	0.373	1595	1484	1410	1186	719
<i>m</i> -NO <sub>2</sub> .....	0.710	1586w	1484	1418	1180	727

Bands are of medium or high intensity apart from the exceptions noted in the Table.

the benzoic acid dimer. The symmetry of the dimer molecules does not, in itself, account for the observed phenomena. Although the bond order of the carbonyl group in the dimer is lower than in the hydrogen-bonded monomer, equal contributions of the two principal unperturbed structures result in less polarisation of the carbonyl group than is present in the associated monomer.

A linear correlation also exists between the carbonyl frequencies of the anils and the  $\sigma$  values of their substituents. The regression line for the frequencies is  $\nu = 1685.0 + 13.60\sigma$  and the correlation coefficient is 0.997. Here the large displacements are produced by the sum of two components, the effect transmitted through the tertiary nitrogen atom as in the methyl ethers, and an additional effect arising from the substituent in the second benzene ring and being transmitted through the N=C linkage. As hydrogen bonding cannot occur in these molecules no complications can arise from this cause. Consequently, it can be assumed that substituent effects on carbonyl frequencies are readily transmitted through an N=C linkage. However, the differences in structure between the methyl ether or enol and the anil prevent any quantitative assessment of the transmissive power of this group in the anils. These studies clearly show that hydrogen bonding can confuse the study, by infrared spectra, of the ability of groupings to transmit substituent effects, and imply that such comparative studies should involve parallel series of compounds in which hydrogen bonding cannot occur and should, as far as possible, utilise non-polar solvents.

*Lower Frequencies of Reduced Isatins and Their Derivatives.*—Direct evidence for the existence of a cyclic conjugated diene-ketonic system is not readily disentangled. Carbonyl frequencies of conjugated carbonyls in six-membered rings lie in the 1680—1660 cm.<sup>-1</sup> region.<sup>23</sup> If the carbonyl group is exocyclic to a five-membered ring<sup>24</sup> this frequency range is raised by about 30 cm.<sup>-1</sup> to the higher carbonyl frequencies of the reduced isatins. Thus the magnitudes of the carbonyl frequencies themselves are consistent with the proposed structures.

Analysis of ethylenic frequencies of conjugated systems in some cases provides information on the structural and stereochemical arrangement of the double bonds.<sup>23,25</sup> Un-

<sup>23</sup> Blout, Fields, and Karplus, *J. Amer. Chem. Soc.*, 1948, **70**, 194; Jones, Humphries, and Dobriner, *ibid.*, 1949, **71**, 241.

<sup>24</sup> Förster, *Z. phys. Chem.*, 1939, **43**, B, 58; Coulson and Moffit, *Phil. Mag.*, 1949, **40**, 1; Bladon, Fabian, Henbest, Koch, and Wood, *J.*, 1951, 2402; O'Sullivan and Sadler, *J.*, 1957, 2916.

<sup>25</sup> Rasmussen and Brattain, *J. Chem. Phys.*, 1947, **15**, 120; Jones, Humphries, Packard, and Dobriner, *J. Amer. Chem. Soc.*, 1950, **72**, 86; Freeman, *ibid.*, 1953, **75**, 1859; Lunde and Zechmeister, *ibid.*, 1955, **77**, 1647; Sheppard and Simpson, *Quart. Reviews*, 1952, **6**, 1; Henbest, Meakins, and Wood, *J.*, 1954, 800; Allan, Meakins, and Whiting, *J.*, 1955, 1874; Henbest, Meakins, Nicholls, and Wilson, *J.*, 1957, 997.

fortunately, no known structures sufficiently similar to the present ones have been examined. Consequently, these frequencies cannot be used to confirm structure (XI), or to unravel a stereochemical pattern. However, a number of general comments are possible on the lower frequencies. Apart from the methyl symmetrical bending and methyl rocking frequencies at 1376 and 1178  $\text{cm}^{-1}$  respectively, the C-O-C asymmetrical and symmetrical stretching frequencies at 1123 and 1020  $\text{cm}^{-1}$ , and an unexplained additional C=C stretching frequency at 1639  $\text{cm}^{-1}$ , great similarity exists between the spectra of the methyl ethers and enols. Support that this gives to the evidence that these possess similar structures is weakened, however, because both the anils and the oximes possess many spectral features in common with the ethers and enols.

Bands near 1650, 1600, and 1500  $\text{cm}^{-1}$  are C=C stretching frequencies arising partly in the unsaturated and partly in the aromatic ring systems. Aromatic ring CH bonding frequencies occur near 770  $\text{cm}^{-1}$  and bands characteristic of different types of benzene-ring substitution patterns occur between 880 and 780  $\text{cm}^{-1}$  in the substituted reduced isatins.

Out-of-plane ethylenic CH deformation probably gives rise to the medium-intensity band near 990  $\text{cm}^{-1}$  in the substituted tetrahydroisatins and in their methyl ethers. The band present at 997  $\text{cm}^{-1}$  in the anil (Table 1), which cannot of course be an ethylenic CH frequency, is of much lower intensity. The band that occurs between 1460 and 1430  $\text{cm}^{-1}$  in all the reduced isatins and their methyl ethers arises from  $\text{CH}_2$  deformations in the reduced ring,<sup>26</sup> and the band near 1410  $\text{cm}^{-1}$  might also arise from this cause as conjugation with carbonyl groups can produce a depression of this magnitude.<sup>27</sup>

Table 4 provides evidence of variation of some lower frequencies with the  $\sigma$  values of substituents. Thus the bands near 1600, 1500, and 1190  $\text{cm}^{-1}$  possess frequencies that decrease with increase of  $\sigma$  values and the frequencies of bands near 1415 and 700  $\text{cm}^{-1}$  increase with  $\sigma$  values. Only a few compounds have been included and disc spectra are not as reliable as solution spectra, but the possible existence of these correlations supports the premise that considerable conjugation exists throughout the system. Thus, to a limited extent, the lower frequencies support the enolic character of the reduced isatins and the stabilisation of the enol form by hydrogen bonding and extension of conjugation. It has been proved in at least two cases<sup>28</sup> that steric factors can stabilise enolic forms, and it is conceivable that the stabilities of the reduced ring systems may be a significant factor in this case also.

Spectra of the oximes (Table 1) are similar to those of the reduced isatins and do not include certain characteristic features of the spectra of isatin  $\beta$ -oximes,<sup>29</sup> such as the very intense band near 1020  $\text{cm}^{-1}$ .

#### EXPERIMENTAL

*Spectra.*—Compounds were examined under identical conditions for each medium. The instrument used was a Perkin-Elmer 21 double-beam recording spectrometer fitted with a rock-salt prism.

*1-Methyloxindole-3-aldehyde.*—Prepared by the method of Friedlander and Kielbasinski,<sup>11</sup> this compound formed yellow plates, m. p. 186°. Its oxime<sup>11</sup> formed deep red plates, m. p. 203°.

*1-Aryl-4 : 5 : 6 : 7-tetrahydroisatin 3-Imines (IX)* (see Table 5).—Ethyl 2-oxocyclohexylglyoxylate (0.5 mol.) and the substituted aromatic amine (2 mol.) were heated in methanol under reflux for 3 hr. After cooling, the product was filtered off and washed with methanol. Further material was obtained by adding water to the filtrate, cooling, and then allowing the liquor to crystallise. With *m*-nitroaniline, heating was with propan-2-ol and for 12 hr.

The unsubstituted compound and the *p*-methoxy- and the *p*-chloro-compound were purified by crystallisation from methanol, the *m*-nitro-compound from *n*-butanol, and the remaining compounds of this class from ethanol.

<sup>26</sup> Jones and Cole, *J. Amer. Chem. Soc.*, 1952, **74**, 5648; Jones, Cole, and Nolin, *ibid.*, p. 5662.

<sup>27</sup> Francis, *J. Chem. Phys.*, 1951, **19**, 942.

<sup>28</sup> Fuson, Corse, and McKeever, *J. Amer. Chem. Soc.*, 1940, **62**, 3250; Kohler, Tishler, and Potter, *ibid.*, 1935, **57**, 2517.

<sup>29</sup> O'Sullivan and Sadler, *J. Org. Chem.*, 1957, **22**, 283.



1-*Aryl-4 : 5 : 6 : 7-tetrahydroisatins* (XI; R' = H) (see Table 5, ii).—The anil (8 g.) was suspended in a mixture of propan-2-ol (60 ml.) and concentrated hydrochloric acid (25 ml.) and heated under reflux for 3 hr. After concentration of the product *in vacuo*, the residue was crystallised from aqueous ethanol except for the *m*-methoxy- and the *m*-nitro-compound. With

TABLE 5. *Reduced isatins and derivatives.*

Subst. R	M. p.	Appearance	Yield (%)	Found (%)		Formula	Required (%)	
				C	H		C	H
(i) <i>Imines</i> (IX)								
Phenyl- <sup>19</sup>	193°	Yellow prisms	58	—	—	—	—	—
<i>p</i> -Tolyl-	211	Yellow prisms	71	80.0	6.8	C <sub>22</sub> H <sub>23</sub> ON <sub>2</sub>	80.0	6.7
<i>m</i> -Tolyl-	160	Pale yellow plates	38	79.8	6.8	C <sub>22</sub> H <sub>23</sub> ON <sub>2</sub>	80.0	6.7
<i>p</i> -Methoxyphenyl-	173	Yellow plates	60	73.3	6.1	C <sub>22</sub> H <sub>22</sub> O <sub>3</sub> N <sub>2</sub>	72.9	6.1
<i>m</i> -Methoxyphenyl-	148	Pale yellow plates	51	72.9	6.5	C <sub>22</sub> H <sub>22</sub> O <sub>3</sub> N <sub>2</sub>	72.9	6.1
<i>p</i> -Chlorophenyl- ...	200	Pale yellow needles	46	64.4	4.4	C <sub>20</sub> H <sub>16</sub> ON <sub>2</sub> Cl <sub>2</sub>	64.7	4.3
<i>m</i> -Chlorophenyl- ...	171	Pale yellow needles	64	64.4	4.3	C <sub>20</sub> H <sub>16</sub> ON <sub>2</sub> Cl <sub>2</sub>	64.7	4.3
<i>m</i> -Nitrophenyl- ...	219	Deep yellow needles	69	61.3	4.1	C <sub>20</sub> H <sub>16</sub> O <sub>5</sub> N <sub>4</sub>	61.2	4.1
<i>p</i> -Dimethylamino-phenyl-	263	Bronze needles	35	73.9	7.0	C <sub>24</sub> H <sub>28</sub> ON <sub>4</sub>	74.2	7.2
Benzyl- <sup>19</sup>	123	White needles	63	—	—	—	—	—
(ii) <i>Reduced isatins</i> (XI; R' = H).								
Phenyl- <sup>19</sup>	186°	Pale yellow prisms	60	—	—	—	—	—
<i>p</i> -Tolyl- <sup>19</sup>	195	White prisms	66	—	—	—	—	—
<i>p</i> -Methoxyphenyl-	211	White needles	57	70.2	6.0	C <sub>16</sub> H <sub>15</sub> O <sub>3</sub> N	70.0	5.8
<i>m</i> -Methoxyphenyl-	145	Cream plates	47	70.2	5.9	C <sub>15</sub> H <sub>15</sub> O <sub>3</sub> N	70.0	5.8
<i>p</i> -Chlorophenyl- ...	184	White plates	63	64.0	4.7	C <sub>14</sub> H <sub>13</sub> O <sub>2</sub> NCl	64.2	4.6
<i>m</i> -Chlorophenyl- ...	159	Buff needles	20	63.8	4.8	C <sub>14</sub> H <sub>13</sub> O <sub>2</sub> NCl	64.2	4.6
<i>m</i> -Nitrophenyl- ...	188	Yellow needles	40	61.7	4.0	C <sub>14</sub> H <sub>13</sub> O <sub>4</sub> N <sub>2</sub>	61.8	4.4
Benzyl- <sup>19</sup>	172	White needles	60	—	—	—	—	—
(iii) <i>3-Methoxy-compounds</i> (XI; R' = Me)								
Phenyl- <sup>19</sup>	86°	Yellow needles	—	—	—	—	—	—
<i>p</i> -Tolyl- <sup>19</sup>	87	Yellow plates	—	75.6	6.5	C <sub>16</sub> H <sub>17</sub> O <sub>2</sub> N	75.3	6.7
<i>p</i> -Methoxyphenyl-	110	Cream plates	—	70.6	6.3	C <sub>16</sub> H <sub>17</sub> O <sub>3</sub> N	70.9	6.3
<i>m</i> -Methoxyphenyl-	—	Oil	—	70.6	6.2	C <sub>16</sub> H <sub>17</sub> O <sub>3</sub> N	70.9	6.3
<i>p</i> -Chlorophenyl- ...	—	Oil	—	65.7	5.1	C <sub>15</sub> H <sub>14</sub> O <sub>2</sub> NCl	65.4	5.1
<i>m</i> -Chlorophenyl- ...	168	White needles	—	65.2	5.0	C <sub>15</sub> H <sub>14</sub> O <sub>2</sub> NCl	65.4	5.1
<i>m</i> -Nitrophenyl- ...	80	Yellow plates	—	63.3	4.7	C <sub>15</sub> H <sub>14</sub> O <sub>4</sub> N <sub>2</sub>	63.0	4.9

the former, the residue was extracted with boiling light petroleum (b. p. 100—120°) and the extracts were concentrated; the product that separated was recrystallised from light petroleum. The *m*-nitro-compound (8 g.) was heated under reflux for 6 hr. with *n*-butanol (60 ml.) and concentrated hydrochloric acid (25 ml.). After concentration of the product under reduced pressure, the solid was crystallised from aqueous methanol.

*3-Methoxy-derivatives* (XI; R' = Me) (see Table 5, iii).—Diazomethane in ether was added to the tetrahydroisatin in the minimum quantity of acetone at 0°. The mixture was kept at 0° for 3 hr. and then at room temperature overnight. Excess of diazomethane was removed by distillation, and the residue was concentrated to a small volume and then allowed to evaporate to dryness at room temperature. The residual oil was crystallised from light petroleum (b. p. 40—60°).

*Oximes of Reduced Isatins.*—These were obtained from the parent compounds in the usual way and, after drying at 110°, they were found by analysis to be monohydrates. *4 : 5 : 6 : 7-Tetrahydro-1-phenylisatin 3-oxime* was obtained as pale yellow needles, m. p. 144° (Found: C, 64.7; H, 6.2. C<sub>14</sub>H<sub>16</sub>O<sub>3</sub>N<sub>2</sub> requires C, 64.6; H, 6.2%). *1-Benzyl-4 : 5 : 6 : 7-tetrahydroisatin 3-oxime* formed yellow needles, m. p. 175° (Found: C, 65.5; H, 6.5. C<sub>15</sub>H<sub>18</sub>O<sub>3</sub>N<sub>2</sub> requires C, 65.7; H, 6.6%).

The authors thank Miss M. Pitman and Mr. R. Parkin for assistance with the preparative work and the spectroscopic measurements, respectively, and the Department of Scientific and Industrial Research for a special grant which helped to defray the cost of this research.