569. *Vibrational Frequency Correlations in Heterocyclic Molecules. Part III.*[1] *Carbonyl Frequencies of Certain Compounds Possessing Fused Six-membered Rings.*

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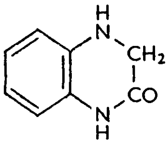
Infrared spectra of tetrahydro-2-oxobenzo-1 : 4-diazine, dihydro-2- and -3-oxobenzomorpholine, dihydro-6-oxo-4 : 5-benz-1 : 3-oxazine, isatoic anhydride, and related bicyclic compounds indicate that they all possess fully ketonic structures. Correlations have been made between ring stability, cyclic C–O–C and exocyclic $>$CO stretching frequencies. Carbonyl frequencies of the benz-1 : 3-oxazines are linearly related to the σ-values of substituent groups and some further evidence has been adduced for transmission through an anilino-group of the effects of substituents in its benzene ring. Substituted isatoic anhydrides possess coupled carbonyl frequencies which maintain a constant separation of 50 cm.$^{-1}$ in spite of asymmetry and substitution factors.

AFTER work on five-membered heterocyclic compounds,[1, 2] the infrared spectra of several six-membered analogues have now been examined. Three main points have been investigated: (*a*) possible tautomeric structures and the associated hydrogen bonds, (*b*) substituent effects in relation to carbonyl frequencies and to the stabilities of these heterocyclic rings, and (*c*) the vibrational coupling of linked carbonyl groups.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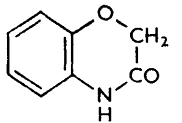
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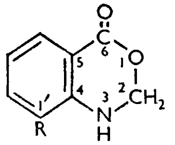
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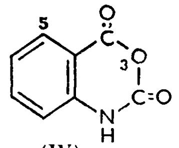
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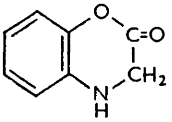
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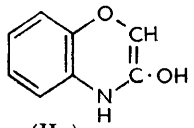
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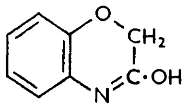
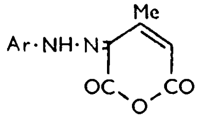

(IIb)


(VI)

(a) *Structures and Hydrogen Bonding.*—In compounds (I)—(V), keto–enol tautomerism is possible in (I), (II), and (V) [as illustrated by (IIa)], and lactam–lactim isomerism can exist in (I), (II), and (IV) [as in (IIb)]. The infrared data in Table 1 indicate that all these compounds exist in the fully ketonic form both in chloroform and in the solid state. This follows from the presence of NH and CO stretching absorption in the 3500—3000 and 1800—1650 cm.$^{-1}$ region respectively, and from the absence of absorption referable to the OH group.[1, 2] Chemical evidence also tends to support the keto-structures. For example, the benzomorpholine (II) forms a number of carbonyl derivatives and with methyl iodide at 135° produces a methyl derivative which is insoluble in dilute acids and alkalis. Isatoic anhydride (IV) may be compared with the phenylhydrazone of β-methyl-γ-oxoglutaconic anhydride (VI). This compound exhibits two carbonyl bands 40 cm.$^{-1}$ apart, together with NH stretching and bending frequencies.[3] Structure (VI) is confirmed by the ultraviolet spectrum. Absence of an enolic hydroxyl group at position 6 is further substantiated by the failure of this compound to form chelate compounds under a variety of conditions. The existence of hydrogen bonding is demonstrated by the broad band between 3300

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[1] Part II, Kellie, O'Sullivan, and Sadler, *J.*, 1956, 3809.
[2] O'Sullivan and Sadler, *J.*, 1956, 2202.
[3] Wiley and Jarboe, *J. Amer. Chem. Soc.*, 1955, **77**, 403.

and 3000 cm.$^{-1}$ present in all but the substituted benz-1 : 3-oxazines (cf. Table 1). Generally the *N*-substituted compounds have lower melting points than the parent substances. Thus dihydro-2-oxobenzomorpholine (II), m. p. 173°, may be compared with its *N*-methyl and *N*-acetyl derivatives, m. p. 59° and 77° respectively. This suggests the presence of intermolecular hydrogen bonding as found in isatin.[2] Table 2 shows a correlation between the melting points of substituted benz-1 : 3-oxazines (III) and the dimensions of the substituent groups. A similar variation has been observed with indigoid dyes and has been explained on the basis of intermolecular hydrogen bonding.[4] *X*-Ray studies have proved the existence of intermolecular association in indigo itself.[5] Now the NH frequencies of the benz-1 : 3-oxazines (Table 2) show that this group is not involved in strong intermolecular hydrogen bonding. The magnitudes of all the quoted substituents, except perhaps chlorine, are enough to preclude such strong associations. However, the correlation of group size with melting point suggests that weak dipolar association may occur, being very weak when the substituent is large. The two groups that can form intramolecular hydrogen bonds produce a slight drop in NH frequency (Table 2).

TABLE 1. *Frequencies (cm.$^{-1}$) for the basic ring structures.*

Compound	(I)	(II)	(III; R = Me)	(IV)	(V)
M. p.	137°	173°	260°	240°	232°
ν(NH) [a]	—	—	3470s	—	—
ν(N–H···O) [a]	3360m 3010m	3130m	—	3270w	3405w 3130m
ν(CO) [a]	1665	1705	1715	1810 1735	1760
ν(CO) [b]	1685	1695	1715	1785 1735	1775
ν(C–O–C) [a]	—	1222s 1052s	1298s 1075s	1260m 1020s	1208s 994m

Ring stability ——— decreases ———►

[a] Frequencies in KBr discs. [b] Frequencies in $CHCl_3$. s = strong, m = medium, w = weak.

(b) *Structural and Substituent Effects on Frequencies.*—A carbonyl group causes an absorption maximum about 30 cm.$^{-1}$ higher in a five-membered than in an analogous six-membered ring structure.[7] This generalisation is supported by the present results. Thus oxindole (1708, 1725 cm.$^{-1}$) may be compared with the amides (I) and (II), phthalide (1750 cm.$^{-1}$) with the lactone (III), and phthalic anhydride (1775, 1789, 1854 cm.$^{-1}$) with

TABLE 2. *Effect of size of substituent* R *on association in dihydro-6-oxo-4 : 5-benz-1 : 3-oxazines* (III).

Subst. R	Cl	Me	NO_2	Br	I	CF_3
M. p.	276°	260°	185°	178°	164°	108°
Group length [a]	3·49	3·54	2·77—4·06 [b]	3·83	4·15	2·46—4·29 [b]
ν(NH) [c]	3470s	3470s	3400s	3480s	3480s	3400s

[a] Distance (A) from the centre of the adjacent ring-carbon atom to the external point of the group, measured in the direction of the C–R axis. Data quoted by Allen and Sutton [6] and by Pauling [6] have been used in obtaining the listed values.

[b] Group lengths are not easy to assess in these cases, but lower and upper bounds are quoted, being obtained respectively by vectorial and arithmetical addition of the appropriate dimensional data. Intramolecular hydrogen bonding is present in both cases. [c] Data from KBr discs.

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[4] Holt and Sadler, "Recent Advances in the Chemistry of Colouring Matters," *Chem. Soc. Special Publ.*, 1956, No. 4, p. 42; Holt, *J. Histochem. Cytochem.*, 1956, **4**, 548; Weinstein and Wyman, *J. Amer. Chem. Soc.*, 1956, **78**, 2387.

[5] von Eller, *Compt. rend.*, 1954, **239**, 975; *Bull. Soc. chim. France*, 1955, **22**, 1433; Gribova, Zhdanov, and Gol'der, *Kristallografiya*, 1956, **1**, 53.

[6] Allen and Sutton, *Acta Cryst.*, 1950, **3**, 46; Pauling, "The Nature of the Chemical Bond," Oxford Univ. Press, 1940.

[7] Bladon, Fabian, Henbest, Koch, and Wood, *J.*, 1951, 2402; Coulson and Moffit, *Phil. Mag.*, 1949, **40**, 1; Förster, *Z. phys. Chem.*, 1939, **43**, *B*, 58.

the anhydride (IV). The wide range of carbonyl frequencies arises from the presence of different carbonyl-containing groups in the rings. The maxima lie in the expected regions for amides, conjugated esters, cyclic anhydrides, and phenyl esters respectively. High frequencies occur when one of the bonds linking the carbonyl group to the rest of the molecule is weak, *i.e.*, in the compounds (I)—(V), the higher the carbonyl frequency, the more reactive the heterocyclic ring. For example, most γ- and δ-amino-acids must be fused or submitted to other dehydration conditions in order to produce lactams, but *o*-aminophenylglycine [8] and *o*-aminophenoxyacetic acid [9] form their lactams (I) and (II) so readily that the free amino-acids have never been isolated. Ring-closure to produce structure (III) is fairly easily effected, this being dependent on the substituent R,[10] but *o*-hydroxyphenylglycine [11] will only produce structure (V) at temperatures above 100°. Stability of the rings should also be reflected in the asymmetric- and symmetric-type stretching frequencies of the cyclic C–O–C group in compounds (III), (IV), and (V). This is supported by the data in Table 1, increase in ring reactivity being paralleled by an increase in CO and a decrease in both C–O–C frequencies. The effect of substituents in the benzene ring on the stability of the heterocyclic ring is demonstrated in Table 4 where again increase in CO frequency occurs with decreases in both C–O–C frequencies. In substituted isatoic anhydrides, the region between 1300 and 830 cm.$^{-1}$ contains very few peaks and the only two that are invariably present are an extremely intense peak near 1025 cm.$^{-1}$ and a medium-to-strong absorption near 1250 cm.$^{-1}$. Therefore these may be assigned as C–O–C bands with reasonable certainty. All the quoted C–O–C frequencies are strong peaks which are absent from the diazine (I).

Compounds (I), (II), (III), and (V) each contain one carbonyl group producing a single carbonyl stretching frequency. Thus effects which cause some cyclic carbonyl compounds, *e.g.*, *cyclo*pentanone,[12] unsaturated γ-lactones,[13] and oxindole [1] to exhibit two maxima in this region are not operative in these six-membered ring systems. Substituent effects have only been investigated for structures (III) and (IV). Carbonyl frequencies of the benz-1 : 3-oxazines (III) are listed with the σ-values of substituents in Table 3. The two properties are correlated excellently. The equation of the regression line for ν is $\nu = 1716 + 21{\cdot}65\sigma$ and the correlation coefficient (r) has the value 0·988. It must be borne in mind, however, that only *meta*-substituents have been studied.

TABLE 3. *σ-Values and* CO *stretching frequencies for substituted dihydro-6-oxo-4 : 5-benz-1 : 3-oxazines* (III).

R	Me	I	Cl	CF$_3$	NO$_2$
σ	−0·069	0·352	0·373	0·415	0·710
ν(CO) [a]	1715	1722	1723	1725	1732

[a] Determined in CHCl$_3$.

(c) *Vibrational Coupling of the Carbonyl Groups in Isatoic Anhydrides* (IV).—In small molecules, coupling frequently occurs between suitably related vibrations of the same frequency causing a band to split into two components, one above and the other below the common frequency. The CO stretching vibrations in some dicarbonyl compounds exhibit this effect. Thus symmetrical acid peroxides, investigated by Davison in the infrared [14] and by Kohlrausch, Pongratz, and Seka in the Raman spectrum,[15] show two peaks about 30 cm.$^{-1}$ apart. Greater proximity of the two carbonyl groups in symmetrical acid

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[8] Plöchl, *Ber.*, 1886, **19**, 6.

[9] Thate, *J. prakt. Chem.*, 1884, **29**, 145.

[10] Sadler and Warren, *J. Amer. Chem. Soc.*, 1956, **78**, 1251.

[11] Vater, *J. prakt. Chem.*, 1884, **29**, 290.

[12] Biquard, *Bull. Soc. chim. France*, 1940, **7**, 894; 1941, **8**, 55, 725.

[13] Dobriner, Katzenellenbogen, and Jones, " Infrared Absorption Spectra of Steroids, An Atlas," Interscience Publ. Co., London, 1953, Chart No. 290.

[14] Davison, *J.*, 1951, 2456.

[15] Kohlrausch, Pongratz, and Seka, *Ber.*, 1933, **66**, 1.

anhydrides usually results in stronger coupling, between 80 and 40 cm.$^{-1}$ separating the two maxima.[16]

This interaction between CO vibrations of in-phase and out-of-phase modes also occurs in substituted isatoic anhydrides. The two very sharp peaks, of approximately equal intensity, are separated by about 50 cm.$^{-1}$, substituents in the benzene ring having little effect on this difference (Table 4). The coupling phenomenon is obscured in some cases with spectra for potassium bromide discs, the intensities being modified and the bands broadened by hydrogen bonding.

In substituted isatins [1, 2] it is possible to correlate carbonyl frequencies with σ-values with reference to both the β- and the α-carbonyl group. In the latter case, the effects are transmitted from the benzene ring to the carbonyl group through the NH group as in substituted oxindoles,[1] acetanilides,[17] and hydroxyiminoacetanilides.[17] The correlations observed with isatins are possible only because vibrational interactions between the carbonyl groups are absent. This is in accordance with the behaviour of other α-diketones; thus diacetyl and benzil both possess a single carbonyl maximum at 1718 and 1681 cm.$^{-1}$ respectively, *i.e.*, in the regions characteristic of monoketonic compounds of related structure.[18] As the introduction of an oxygen atom between the two carbonyl groups results in intense vibrational interaction, a simple correlation between σ-values and frequencies is not to be expected with isatoic anhydrides.

A substituent in either the 6- or the 7-position possesses two σ-values, σ_1 being in virtue of its location with respect to the carbonyl group at position 4 and σ_2 arising from the substituent's position in relation to the NH group.[1, 17] The data in Table 4 show that carbonyl frequencies and σ-values increase roughly together. However, in spite of the presence of some degree of correspondence, no linear relation exist between frequencies and σ-values. Earlier work [17] indicated that a substituent in the benzene ring exerts the same effect on the carbonyl frequencies of Ph·COR and Ph·NH·COR molecules. If this applies to isatoic anhydrides, then carbonyl frequencies should be more closely related to the average substituent constant $\bar{\sigma}$ than to either σ_1 or σ_2 individually. The two characteristic frequencies of the carbonyl group must be close together in order that coupling should occur and, as the separation of the coupled frequencies is both wide and constant throughout the series, it is reasonable to consider the mean frequency $\bar{\nu}$ as representative of the carbonyl

TABLE 4. *σ-Values and* CO *and* C–O–C *stretching frequencies of substituted isatoic anhydrides* (IV).

Subst.	M. p.	σ_1	σ_2	ν_A(CO) [a]	ν_B(CO) [a]	$\Delta\nu$	$\bar{\sigma}$	$\bar{\nu}$	ν(C–O–C) [b]	
5-Me	219°	—	−0·069	1780	1735	45	—	1758	—	—
7-Me	228	−0·170	−0·069	1783	1733	50	−0·120	1758	1278	1035
None	240	0·0	0·0	1785	1735	50	0·0	1760	1260	1020
8-Me	277	−0·069	—	1788	1738	50	—	1763	—	—
6-F	260	0·337	0·062	1788	1738	50	0·200	1763	—	—
7-F	241	0·062	0·337	1789	1737	52	0·200	1763	—	—
7-Cl	260	0·227	0·373	1788	1741	47	0·300	1765	—	—
5-Br	310	—	0·391	1788	1742	46	—	1765	—	—
7-Br	256	0·232	0·391	1788	1741	47	0·312	1765	1250	1027
7-I	272	0·276	0·352	1788	1739	49	0·314	1764	1250	1025
8-I	208	0·352	—	1793	1743	50	—	1768	—	—
8-Cl	232	0·373	—	1796	1748	48	—	1772	—	—
5-CF_3	239	—	0·415	1798	1753	45	—	1776	1220	1030 1005

[a] Data from $CHCl_3$ solutions. [b] Data from KBr discs.
Peaks listed are of strong or medium intensity.

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[16] Thompson, *J.*, 1948, 328; Cooke, *Chem. and Ind.*, 1955, 142.

[17] O'Sullivan and Sadler, *J. Org. Chem.*, 1956, **21**, 1179.

[18] Jones, Humphries, and Dobriner, *J. Amer. Chem. Soc.*, 1950, **72**, 956.

frequencies of the CO–O–CO group. This mean frequency will be close to the individual fundamentals. Comparison of $\bar{\nu}$ and $\bar{\sigma}$ values, where the latter are available, shows that linear dependence exists, the best straight line for ν being $\bar{\nu} = 1760 + 15{\cdot}38\bar{\sigma}$. The existence of this linear relation, with the high correlation coefficient of 0·990, strongly supports the premises that have been outlined.

Isatoic anhydrides in chloroform possess carbonyl bands having approximately equal intensities, whereas considerable differences in intensities usually exist between the pairs of bands with anhydrides, peroxides, and phthalimides. Studies of infrared and Raman intensity are desirable for fuller elucidation of coupling phenomena in complex molecules.

EXPERIMENTAL

Spectra.—Compounds in chloroform were examined with a Perkin-Elmer 21 double-beam recording spectrophotometer. Potassium bromide disc spectra were obtained by using a Baird Associates double-beam recording instrument. Both spectrometers were fitted with rock-salt prisms.

Materials.—M. p.s are in Tables 1—4. Tetrahydro-2-oxobenzo-1 : 4-diazine (I) was prepared from *o*-phenylenediamine by Holley and Holley's method.[19] Dihydro-2-oxobenzomorpholine (II) was obtained from *o*-nitrophenoxyacetic acid.[19, 20] These products were purified by crystallisation from water and aqueous ethanol respectively.

1′-Substituted dihydro-6-oxo-4 : 5-benz-1 : 3-oxazines (III) were obtained from the corresponding anthranilic acids by Villiger's method.[21] All crystallised in white needles from aqueous methanol, as follows: *chloro-* (Found: C, 52·3; H, 3·3. $C_8H_6O_2NCl$ requires C, 52·4: H, 3·1%), *methyl* (Found: C, 66·2; H, 5·5. $C_9H_9O_2N$ requires C, 66·4; H, 5·4%), *iodo-* (Found: C, 34·9; H, 2·2. $C_8H_6O_2NI$ requires C, 35·0; H, 2·5%), *trifluoromethyl* (Found: C, 49·8; H, 2·8. $C_9H_6O_2NF_3$ requires C, 50·2; H, 3·2%), and the *nitro-compound* (Found: C, 49·8; H, 3·1. $C_8H_6O_4N_2$ requires C, 50·0; H, 3·1%).

Substituted isatoic anhydrides (IV) were obtained as white plates by the oxidation of the corresponding isatins [2] with chromic acid in acetic acid.[22] Dihydro-3-oxobenzomorpholine (V) was prepared by Vater's method [11] from *o*-hydroxyphenylglycine.

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[19] Holley and Holley, *J. Amer. Chem. Soc.*, 1952, **74**, 3071.

[20] Minton and Stephen, *J.*, 1922, **121**, 1591.

[21] Villiger, *Ber.*, 1909, **42**, 3529.

[22] Kolbe, *J. prakt. Chem.*, 1884, **30**, 84; Binz and Heuter, *Ber.*, 1915, **48**, 1038; Majime and Kotake, *Ber.*, 1930, **63**, 2237; Panatovic, *J. prakt. Chem.*, 1886, **33**, 58; Rupe and Kersten, *Helv. Chim. Acta*, 1926, **9**, 578; Baker, Schaub, Joseph, McEvoy, and Williams, *J. Org. Chem.*, 1952, **17**, 164.