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THE TAUTOMERISM OF HETEROAROMATIC COMPOUNDS WITH FIVE-MEMBERED RINGS—VIII[1]

HYDROXY-OXADIAZOLES OR OXADIAZOLONES

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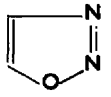
Abstract—The constitution is discussed of the various compounds described in conflicting literature claims as phenyl-hydroxy-oxadiazoles, and authentic specimens of several of the isomers are described. Spectroscopic measurements and p*K* values show that 3-hydroxy-1,2,4- and -1,2,5-oxadiazoles exist predominately in the hydroxy-form, whereas 2-hydroxy-1,3,4- and 5-hydroxy-1,2,4-oxidiazoles occur mainly as the corresponding oxadiazolinones. These results are related to the general pattern of tautomeric behaviour in the hydroxy–azole series.

THE object of this series is to determine the structure of tautomeric or potentially tautomeric azoles, thus to help rationalize their reactions. This paper is concerned with hydroxy–oxadiazoles and –oxadiazolinones. Such derivatives are known in three of the four oxadiazole series (I–IV), but not for the 1,2,3-isomers (I), of which very few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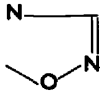
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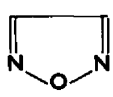
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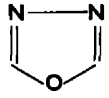
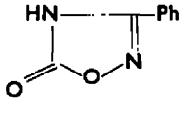
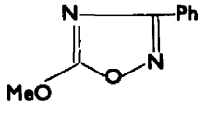
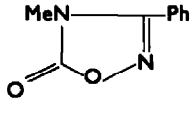

IV

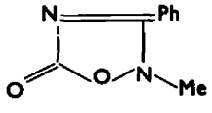
derivatives are known. The tautomeric structure of these compounds has been little discussed previously. For the 1,2,4-oxadiazoles (II) and the furazans (III) there has been much discussion of the constitution of the hydroxy-derivatives. For an involved review of this confused field see Ref.[2]

Preparation of compounds


V


VI


VII


VIII

3-Phenyl-1,2,4-oxadiazolin-5-one (V) was obtained from benzamidoxime and ethyl chloroformate.[3] Ponzio[4] methylated V with dimethyl sulphate to a derivative m.p.

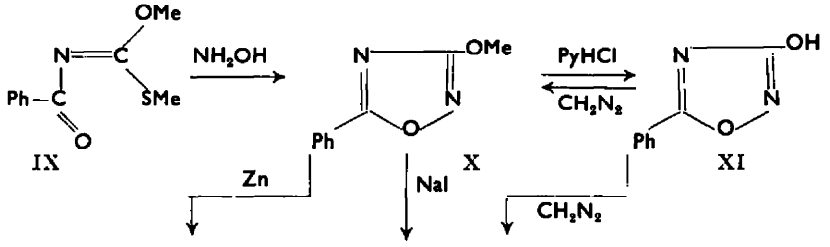
[1] Part VII. A. J. Boulton, A. R. Katritzky, A. Majid Hamid and S. Øksne, *Tetrahedron* **20**, 2835 (1964).

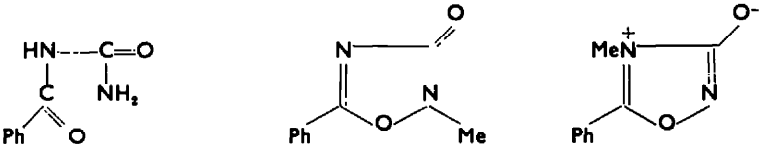
[2] J. H. Boyer in R. C. Elderfield, *Heterocyclic Compounds* Vol. 7; pp. 499–503. J. Wiley, New York (1961).

[3] E. Falck, *Ber. Dtsch. Chem. Ges.* **18**, 2468 (1885).

[4] G. Ponzio, *Gazz. Ital.* **53**, 511 (1923).

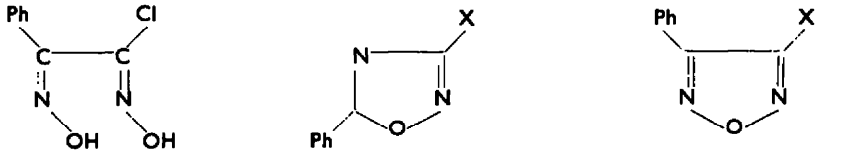
116°. Gompper[5] used diazomethane, and showed that the product, m.p. 119°, was an N-methyl derivative (VII or VIII), by the presence of a strong carbonyl band in the IR spectrum. In our hands, this reaction gave the N-methyl compound, m.p. 118°, together with the methoxy compound (VI; no νC=O), m.p. 37–38°. The same N-methyl derivative was obtained with methyl iodide–sodium methoxide: it is probably the 4-methyl isomer (VII), but attempts to synthesize VII unambiguously failed.





We prepared 3-methoxy-5-phenyl-1,2,4-oxadiazole (X) by Yang and Johnson's route,[6] although their experimental conditions were somewhat modified. Benzoyl chloride was converted to benzoyl thiocyanate, which with methanol gave the carbamate, converted to the imino-thiolcarbonate (IX) by methyl iodide. The structure of X had been proved by reduction to benzoyl urea (XII),[6] but X had not previously been demethylated. From X we prepared 3-hydroxy-5-phenyl-1,2,4-oxadiazole (XI), m.p. 201–203° with pyridine hydrochloride; it was reconverted to the methoxy-compound (X) by diazomethane. The methoxy compound was rearranged to the N-methyl derivative (XIII) by sodium iodide in acetonylacetone (cf[7]); some of the N-methyl derivative was also found in the diazomethane reaction. The possibility that the N-methyl derivative might be the zwitterion (XIIIa) rather than XIII was excluded by hydrolysis to N-benzoyl-N'-methylurea, the structure of which was proved by NMR.

The preparation of 3-hydroxy-5-phenyl-1,2,4-oxadiazole (XI) m.p. 175°, has been



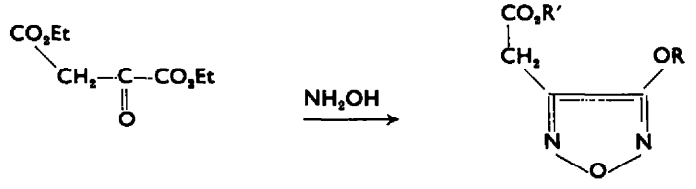
previously claimed by Ponzio[8] by phosphorus pentachloride treatment of phenylchloroglyoxime (XIV) which he stated yielded 3-chloro-5-phenyl-1,2,4-oxadiazole (XV), converted by sodium alkoxides to ethers which were hydrolysed to a product, m.p.

[5] R. Gompper, *Chem. Ber.* **93**, 208 (1960).
[6] S. T. Yang and T. B. Johnson, *J. Amer. Chem. Soc.* **54**, 2066 (1932).
[7] T. L. V. Ulbricht, *J. Chem. Soc.* 3345–8 (1961).

175–176°. This product may well have been 3-hydroxy-4-phenyl-1,2,5-oxadiazole (XVI, X = OH); however, we have been unable to obtain any crystalline product from this reaction sequence.

Ponzio reported[8] that phosphorus oxychloride reacted with phenylchloroglyoxime (XIV) to yield an intermediate chloro compound which was hydrolysed to a hydroxy derivative of m.p. 202°. This he described as the furazan (XVI, X = OH). Silver oxide and alkyl halide converted this into methoxy, m.p. 58–59°, and ethoxy analogues m.p. 47–48°. These m.p.s correspond closely to those found by Yang and Johnson[6] and by us for the compounds of the 5-phenyl-1,2,4-oxadiazole series. However, we failed to isolate crystalline products for the reactions described by Ponzio.[8]

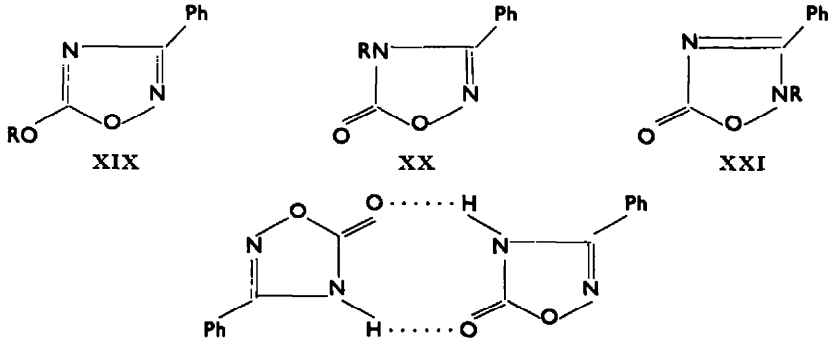
3-Hydroxy-4-phenyl-1,2,5-oxadiazole (XVI, X = OH) has also been claimed by Wieland and Semper[9] as the product, m.p. 110–111° of alkali followed by immediate acidification on phenylfuroxan and further by Gastaldi[10] as the product, m.p. 177°, of the alkaline treatment of di- and tri-acetates of phenylhydroxyglyoxime. We have not tried to repeat any of this work; we consider that one of these claims is more reliable than that of Ponzio referred to in the preceding paragraph.



XVII XVIII

Sodio oxalacetic ester was converted to 3-hydroxyfurazan-4-acetic acid (XVIII, R = R′ = H) by a modification of the method (XVII → XVIII) of Hantszch and Urbahn.[11] The acid was esterified (to XVIII, R′ = Me, R = H) by methanolic hydrogen chloride and converted to the methoxy-ester (XVIII, R′ = R = Me) by diazomethane. Attempts to prepare the N methyl-derivative failed.

Tautomeric structure in the 3-phenyl-1,2,4-oxadiazolin-5-one series



XIX XX XXI

XXII

[8] G. Ponzio, *Gazz. Ital.* **62**, 1025 (1932).
[9] H. Wieland and L. Semper, *Liebigs Ann* **358**, 36 (1908).
[10] C. Gastaldi, *Gazz. Ital.* **55**, 201 (1925).
[11] A. Hantzsch and J. Urbahn, *Ber. Dtsch. Chem. Ges.* **28**, 762 (1895).

Infra-red Spectra. In dilute solution in carbon tetrachloride, 3-phenyl-1,2,4-oxadiazolin-5-one shows a band at 3480 cm^{-1}, the molecular extinction of which creases with dilution. The data indicate a monomer-dimer equilibrium. The dimer almost certainly has the structure XXII. The monomer certainly exists in the NH-form (as shown by the frequency 3480 cm^{-1}), i.e. as XX or XXI and not as XIX.

More concentrated solutions of the tautomeric compound in chloroform, and nujol mulls, show a broad H-bonded NH peak at ca. 3130 cm^{-1}. These spectra resemble clearly those of the N–methyl derivative, and differ from those of the O–Methyl derivative (XIX, R = Me) (Table 1). This shows that in chloroform solution and in the solid state the potentially tautomeric compound exists in the NH-form corresponding to the N–methyl derivative.

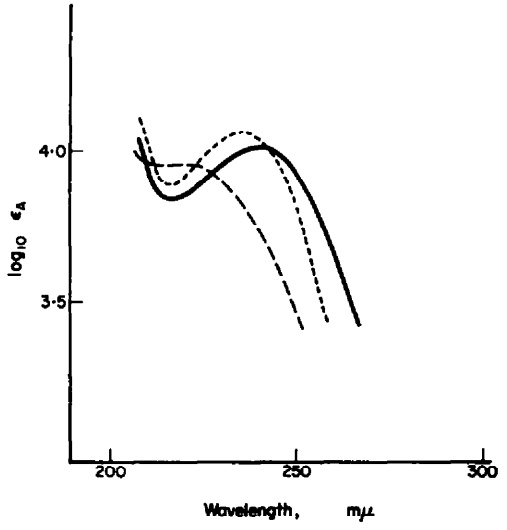
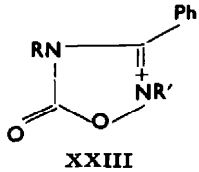
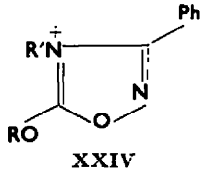


FIG. 1. Ultra-violet spectra of ——— 3-phenyl-1,2,4-oxadiazolin-5-one and its – – – – N–methyl and · · · · · · · O–methyl derivative.
Neutral species in aqueous buffers.

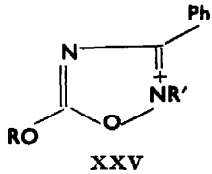
Ultra-violet spectra and basicities (Table 2). The spectra of the neutral species are shown in Fig. 1. The spectra of the potentially tautomeric compound differs from that of the N–methyl derivative, but is fairly close to that of the methoxy-compound (XIX, R = Me). However, the IR results discussed above make it unlikely that this resemblance is more than a coincidence: changing from nonpolar to polar media normally tends to increase the proportion of NH-form, as this has the greatest degree of charge separation (see e.g. Ref[12]). The results probably indicate that there exists in aqueous solution an appreciable proportion of that NH-form which does *not* correspond to the fixed NMe-form.



XXIII



XXIV



XXV

[12] A. R. Katritzky and F. W. Maine, *Tetrahedron* **20**, 299 (1964).

The spectra of the mono-cations in strong sulphuric acid are shown in Fig. 2. Consideration is here complicated by the possibility of three types of mono-cationic species (XXIII–XXV), and by the general similarity of the spectra. If the potentially tautomeric compound formed a cation by protonation at oxygen to yield XXIV or XXV (R = R′ = H), the same type of cation would be formed by the methoxy-derivative, and K_T can be calculated as antilog ($pK_{OMe} - pK_{NH}$) = ca. 5. This would indicate that the tautomeric compound existed to some 17% in the OH form.

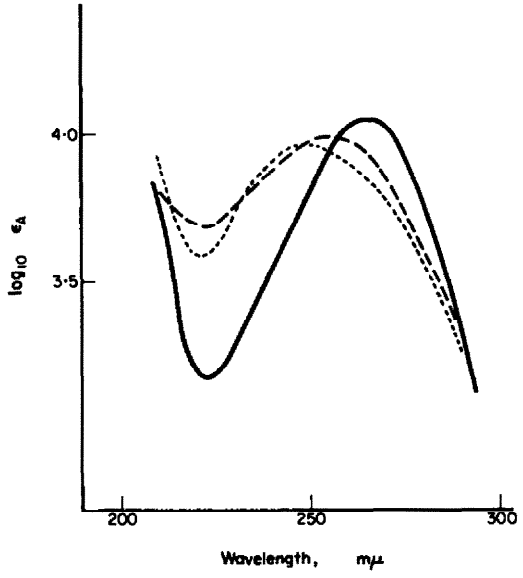
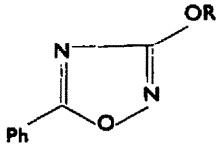


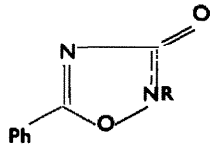
FIG. 2. Ultra-violet spectra of ——— 3-phenyl-1,2,4-oxadiazolin-5-one and - - - - N-methyl and ····· O-methyl derivative cations in sulphuric acid.

The conclusion reached in the last paragraph is unlikely, in view of the IR results and suggests that the potentially tautomeric compound protonates on nitrogen to give cation XXIII (R = R′ = H). Now an estimate of the tautomeric constant for the isomerization (XX ⇌ XXI, R = H) can be made as antilog ($pK_{NMe} - pK_{NH}$), i.e. $K_T \simeq 10$.

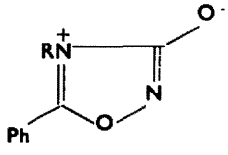
Tautomeric structure in the 5-phenyl-1,2,4-oxadiazolin-3-one series



XXVI



XXVII



XXVIII

The position is here at first sight less complicated with only two forms (XXVI and XXVII) to consider. However, zwitterion forms of type XXVIII must not be entirely ruled out.

TABLE 1. INFRA-RED SPECTRA OF 3-PHENYLOXADIAZOLIN-5-ONE AND ITS METHYL DERIVATIVES

Compound		νC=O		Azole ring		Ph-ring		Azolone ring		Ph-ring		Azole ring			
		cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A
Parent	*a*	1792*	250	1610	25	1599	45	1569	95	—		1465	280	—	
		1763	1300												
	b	1769	vs	1610	m	1600	m	1565	m	1520	m	1474	m	1350	w
N-Methyl	*a*	1775	800	1610	55	1595	60	1561	60	1506	35	1459	200	1321	150
		1735	55												
O-Methyl	*a*	—		1617	850	1590	200	—		1496	90	1448	125	1385	740
				1610*	550					1480*	55			1326	130
		cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A
Parent	*a*	—		—		1026		1002		995		949		887	
	b	1260	m	1111	w	1030	w	1005	w	996	m	949	s	891	s
N-Methyl	*a*	1232	m	1125	m	1064	m	1027	m	—		969	s	883	m
														875	m
O-Methyl	*a*	—		1125	w	1052	m	1025	m	992	m	958	w	890	s
												927	w		

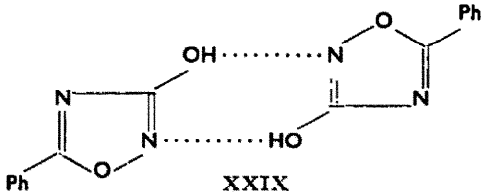
[a] 0·2 M solution in chloroform in 0·1 mm cell.
[b] Nujol mull.
* shoulder.

TABLE 2. ULTRA-VIOLET ABSORPTION MAXIMA

No.	1,2,4-Oxadiazole	Free base[a] λ_{max} mμ	Free base[a] ε_A (× 10^{-4})	Conjugate acid[b] λ_{max} mμ	Conjugate acid[b] ε_A (× 10^{-4})	p*Ka*	λ[c] mμ
1	3-Hydroxy-5-phenyl	252	1·26	281	1·67	−4·2 ± 0·2	250, 260, 280
2	3-Methoxy-5-phenyl	255	1·63	277	1·94	−4·3 ± 0·1	250, 280
3	2-N-Methyl-5-phenyl-1,2,4-oxadiazolin-3-one	250	1·86	290	1·92	−4·35 ± 0·2	250, 290
4	3-Phenyl-5-hydroxy	240	1·02	267	1·38	−6·8 ± 0·2	230, 270
5	3-Phenyl-5-methoxy	237	1·15	251	1·13	−6·1 ± 0·2	230, 235, 255, 260
6	-N-Methyl-3-phenyl 1,2,4-oxadiazolin-5-one	222	0·91	258	1·17	−6·6 ± 0·3	225, 250, 255

[a] Nos. 1 and 4 in 0·11 N H_2SO_4, others in water.
[b] Nos. 1, 2, 5 in 33 N H_2SO_4, others in 36 N H_2SO_4.
[c] Wavelengths used for p*Ka* determinations.

Infra-red spectra (Table 3). In dilute solution in carbon tetrachloride the non-bonded hydroxyl band of 3-hydroxy-5-phenyl-1,2,4-oxadiazole can be seen at 3580 cm^{-1}: its intensity increases with dilution and the data again indicate dimer formation. The structural units in the dimer (and/or polymers) are XXIX, as is demonstrated by the striking resemblance of the IR spectra of mulls and concentrated solutions of the potential tautomer to those of the O–methyl analogue, and the large differences from those of the N–methyl derivative. Minor bands in the chloroform solution suggest that 5–10% of the NH-form may coexist with the OH-form under these conditions.



XXIX

Ultra-violet spectra (Table 2) of the neutral species of the tautomeric compound and its fixed analogues were too similar for aqueous solutions to permit conclusions as to structure. UV spectra of cationic species were also similar, indicating the formation of a cation of the same type.

Basicity measurements (Table 2) indicate that in aqueous solution the oxo- and hydroxy-form are of comparable stability. Thus the tautomerism of 3-hydroxy-5-phenyl-1,2,4-oxadiazole clearly resembles that of 3-hydroxy-5-phenylisoxazole.[1]

Tautomeric structure in the 1,2,5-oxadiazolin-3-one series

The IR spectrum of methyl 3-methoxyfurazan-4-acetate (XVIII, R = R′ = Me) is similar (Table 4) to that of 3-hydroxyfurazan-4-acetate (XVIII, R = H, R′ = Me) suggesting that the latter compound exists in the 3-hydroxy form (just as do the analogous 3-hydroxy-1,2,5-thiadiazoles[12a]). Nevertheless, the IR spectrum of 3-hydroxyfurazan-4-acetate, in contrast to its O-methyl derivative, shows two concentration dependent carbonyl stretching modes. In very dilute solution (0·0001 molar) in carbon tetrachloride the band at ca 1750 cm^{-1} is considerably less intense

TABLE 3. INFRA-RED SPECTRA OF 3-HYDROXY-5-PHENYL-1,2,4-OXADIAZOLE AND ITS METHYL DERIVATIVES

Compound		νC=O cm⁻¹	ε_A	Azole ring cm⁻¹	ε_A	Ph ring cm⁻¹	ε_A	Azole ring cm⁻¹	ε_A	Ph ring cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A
Parent	*a*	1730	50	1638*	120	1604	180	1577	230	1508*	90	1466*	320	—		1313	w	1297	w
				1620	220			1555	150			1455	380						
	b	1665	w	1621	vs	1590*	m	1560	ms	1504	m	1470	vs	1357	s				
O-Methyl	*c*	—		1623	420	1599	380	1574	950	1525*	80	1456	360	1380	1700	1323*	w	—	
						1590*	320	1561*	880			1439	190						
N-Methyl	*c*	1724	680	1613	680	1598	300	1576	680	1496	95	1456	200	1369	220	—		1299	m
												1409	25						

		cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A
Parent	*b*	1275	m	1185	m	1130	m	1098	w	1070	w	1040	w	1027	w	1001	w	975	w	925	w
O-Methyl	*c*	1276	s	1197	m	1116	w	—		1071	m	1049	s	1023	m	987	s	963	m	932	w
				1177	m															915	m
N-Methyl	*c*	1290	m	1170	w	—		—		1075	w	1044	w	1021	w	998	m	—		936	m
				1152	m																

[a] 0·2 M solution in chloroform in 0·1 mm cell.
[b] nujol mulls.
[c] where extinction coefficient is given, the measurement refers to chloroform solution, otherwise to a nujol mull.
* shoulder.

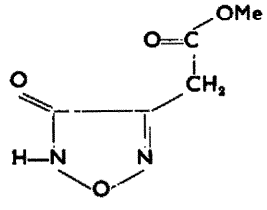
TABLE 4. INFRA-RED SPECTRA OF 1,2,5-OXADIAZOLES

Substituents	Phase	νC=O		Ring		Ring				Me of ester		Me of OMe		βNH(?)	
		cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A
3-Methoxy-4-methoxy-carbonylmethyl	$CHCl_3$	1747	400	1601	230	1548*	120	1540	210	1468	450	1456	100	—	
3-Hydroxy-4-methoxy-carbonylmethyl	$CHCl_3$	1747	230	1613	110	1565	40			1463	85	—			
		1713	260	1603	100	1551	45								
	nujol	1730	vs	1615	s	1565*	m	1555	s	1466*	m	—		1455	s
3-Hydroxy-4-carboxymethyl	nujol	1725	vs	1620	s	1570	s			—		—		1424	s

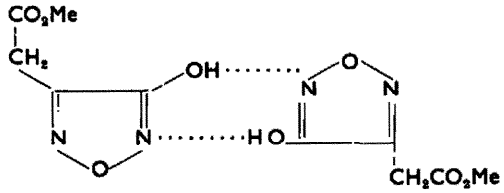
Substituents	Me of ester		Me of OMe		(?) CH_2		Ring		—COO—						Ring		OMe	
	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A
3-Methoxy-4-methoxy-carbonylmethyl	1445	140	1425	150	1412	70	1350	170	1267	180	(1209	vs)	1160	80	1023	150	997	200
3-Hydroxy-4-methoxy-carbonylmethyl	1447	155	—		1409	45	1363	160	($CHCl_3$)		($CHCl_3$)		1162	75	1010	55	995	85
	1443*	s	—		1413	s	1365	s	1255	s	1213	s	1176	s	1019	m	990	s
3-Hydroxy-4-carboxymethyl	—		—		1424	s	1354	m	1316	w	1223	s	1194	m	1024	s	948	m
									1265	s								

* shoulder.

than the band at 1708 cm^{-1}, but its intensity increases with concentration and in 0·005 molar solution it has a larger extinction coefficient than the latter band. This concentration dependence indicates that neither of the bands arises from the ring carbonyl of the oxadiazolinone form (XXX)

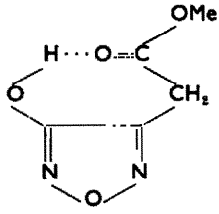


XXX

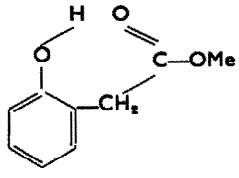


XXXI

However, the variation in intensity would not result from a simple monomer-dimer equilibrium as separate distinct carbonyl frequencies would not be expected and, furthermore, the intensity of the non bonded ν OH peak at ca. 3556 cm^{-1} does not change relative to the H-bonded ν OH peak at ca. 3260 cm^{-1} at the solution is diluted. We assign the 1750 cm^{-1} band to the carbonyl stretching mode in both the dimer (XXXI) and the free monomer and the 1708 cm^{-1} band to that in the intramolecularly H-bonded form of the monomer (XXXII). Confirmation of this assignment comes from the spectrum of methyl *o*-hydroxyphenylacetate (XXXIII).



XXXII

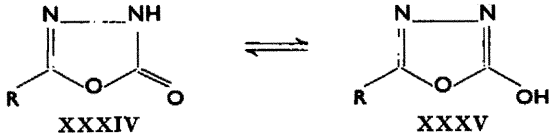


XXXIII

We find only a small non bonded hydroxyl peak at 3610 cm^{-1}, a relatively intense H-bonded hydroxyl band at ca. 3340 cm^{-1} and an intense peak at 1760 cm^{-1} with a shoulder at ca. 1735 cm^{-1}. As this spectrum is almost independent of concentration and since the carbonyl stretching mode in methyl phenylacetate appears[12b] at 1740 cm^{-1}, the band at 1760 cm^{-1} can be assigned to an intramolecularly H-bonded carbonyl group.

Tautomeric structure in the 1,3,4-*oxadiazolin*-2-*one series*

We have investigated no compounds in this series, but literature work[13] indicates that the oxo-form (XXXIV) is preferred in the equilibrium (XXXIV ⇌ XXXV).



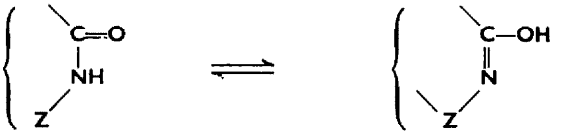
XXXIV XXXV

GENERAL CONCLUSIONS

The balance of evidence indicates that 3-hydroxy-1,2,4- and 1,2,5-oxadiazoles

[12a] J. M. Ross and W. C. Smith, *J. Amer. Chem. Soc.* **86**, 2861 (1964).
[12b] R. R. Hampton and J. E. Newell, *Anal. Chem.* **21**, 914 (1949).

exist predominately in the hydroxy-form, whereas 2-hydroxy-1,3,4- (vide Ref[13]) and 5-hydroxy-1,2,4-oxadiazoles occur mainly as the corresponding oxadiazolinones. These results provide further evidence for the generalization that the equilibrium (XXXVI ⇌ XXXVII) lies far to the left in heteroaromatic systems unless *Z* is an electronegative atom carrying a lone electron pair, e.g. O, NR, or S.



XXXVI XXXVII

EXPERIMENTAL

3-Phenyl-1,2,4-oxadiazolin-5-one. Redistilled ethyl chloroformate (2·4 g) was slowly added to benzamidoxime (2·7 g) in pyridine (5 cc) at 0°. The whole was then heated 30 min at 100°. Water then precipitated O-ethoxycarbonylbenzamidoxime (2·9 g, 73%), which on heating at 140° gave the oxadiazolinone (1·7 g, 51% overall), m.p. 203–205° (lit,[8] m.p. 197°) after recrystallization from EtOH. (Found: C, 59·2; H, 3·6; N, 17·3; $C_9H_8N_2O_2$ requires: C, 59·2; H, 3·7; N, 17·3%.)

Methylation of 3-phenyl-1,2,4-oxadiazolin-5-one. Ethereal diazomethane was added to the oxadiazolinone (2·4 g) suspended in ether (17 cc) until the yellow colour persisted. The whole was then evaporated and the product extracted with pet. ether (3 × 5 cc, b.p. 60–80°). The undissolved N-methyl derivative crystallized from EtOH as needles (1·7 g, 65%), m.p. 118–119° (lit.,[5] m.p. 118°). Evaporation of the pet. ether extracts and triple sublimation of the residue gave *5-methoxy-3-phenyl-1,2,4-oxadiazole* (0·4 g, 15%) as prisms, m.p. 36–37·5°. (Found: C, 61·7; H, 4·8; N, 15·6; $C_9H_8N_2O_2$ requires: C, 61·4; H, 4·5; N, 15·9%.)

O-Methyl N-Benzoylthiocarbamate. Benzoyl chloride (300 g) toluene (50 cc) and dry, powdered KCNS (210 g) were refluxed for 30 min. After cooling, solid was filtered off and the filtrate refluxed for 5 min with MeOH (300 cc). On cooling, the carbamate separated: it was recrystallized from 50% MeOH and then had m.p. 96·5–97·5° (lit.,[14] m.p. 97°) (160 g, 40%).

Dimethyl N-benzoyliminomonothiolcarbonate. The above thiocarbamate (49 g) was stood 1 day with MeI (35·6 g) in methanolic MeONa (from 6 g Na and 250 cc of MeOH). Addition of water gave the product (30 g, 60%), m.p. 36–38° raised by recrystallization from pet. ether (b.p. 60–80°) to 39–41° (lit.,[15] m.p. 43°).

3-Methoxy-5-phenyl-1,2,4-oxadiazole. Dimethyl N-benzoyliminomonothiolcarbonate (10·5 g) in 95% EtOH (10 cc) was mixed with methanolic hydroxylamine (from 4·0 g hydroxylamine hydrochloride and 3·2 g KOH in 30 cc MeOH). After 24 hr at room temp and 12 hr at −15°, the methoxy compound (4·4 g, 50%) separated, m.p. 54–56°, raised by sublimation to 57–59° (lit.,[6] m.p. 54–56°). (Found: C, 61·6; H, 4·5; N, 15·8; calc. for $C_9H_8N_2O_2$: C, 61·4; H, 4·5; N, 15·9%.)

5-Phenyl-1,2,4-oxadiazolin-3-one. The above methoxy compound (0·7 g) and anhydrous pyridine hydrochloride (7 g) were heated at 155–160° for 30 min under N_2. The cooled product on treatment with water left as a residue the *oxadiazolin-3-one* (0·42 g, 65%), sublimed as micro crystals m.p. 201–203°. (Found: C, 59·2; H, 3·9; N, 17·0; $C_8H_6N_2O_2$ requires: C, 59·2; H, 3·7; N, 17·3%.)

2-Methyl-5-phenyl-1,2,4-oxadiazolin-5-one. 3-methoxy-5-phenyl-1,2,4-oxadiazole (0·59 g) and anhydrous NaI (1·5 g) were heated in redistilled acetonylacetone (5 cc) at 100° for 10 hr. Evaporation at 100°/15 mm followed by treatment with water gave the *oxadiazolinone* (0·24 g, 42%) which separated from pet. ether (b.p. 60–80°) as prisms m.p. 118·5–120°. (Found: C, 60·9; H, 4·6; N, 15·8; $C_9H_8N_2O_2$ requires: C, 61·4; H, 4·5; N, 15·9%.)

The oxadiazolinone (0·12 g) was stirred with Zn dust (0·12 g) in water (3·7 cc) and acetic acid (1·3 cc) at 100° for 4 hr. The whole was cooled, basified with Na_2CO_3, and extracted with chloroform

[13] W. R. Sherman, *J. Org. Chem.* **26**, 88 (1961); H. L. Yale, K. A. Loses, F. M. Perry and J. Bernstein, *J. Amer. Chem. Soc.* **76**, 2208 (1954); C. Ainsworth, *Ibid.* **78**, 4474 (1956).

[14] H. L. Wheeler and T. B. Johnson, *Amer. Chem. J.* **24**, 201 (1900).

[15] T. B. Johnson and G. A. Menge, *Amer. Chem. J.* **32**, 364 (1904).

to give N-benzoyl-N'-methylurea (0·6 g, 50%) m.p. 168·5–170° (lit.,[10] m.p. 170–171°) after recrystallization from aqueous EtOH. The NMR spectra in benzene showed the methyl group as a doublet centred at τ 7·52 with a splitting of 5 c/s.

Methylation of 5-phenyl-1,2,4-oxadiazolin-3-one. The oxadiazolinone (0·25 g) was taken up in an ether–MeOH mixture (10 cc 1:1) and an excess of etherial diazomethane added. After evaporation an oily solid remained. Sublimation of this yielded two fractions, firstly the methoxy derivative (0·16 g, 60%), m.p. 49–52° and secondly the N-methyl derivative (0·06 g, 22%), m.p. 108–111°. The compounds were identified by their IR spectra.

3-Hydroxyfurazan-4-acetic acid. The sodio derivative of diethyl oxalylacetate (140 g) was added to aqueous hydroxylamine (from 94 g of hydroxylamine hydrochloride and 71 g Na_2CO_3 in 275 cc water). NaOH (67 g) in water (50 cc) was next added, the solution shaken 4 days at 20°, and the whole stirred for 2 days at 90°. The mixture was cooled to below 5° and acidified to pH 1 with 10 N H_2SO_4 (ca. 350 cc). The solution was ether-extracted (2 × 500 cc, 6 × 250 cc) and the dried (Na_2SO_4) extracts evaporated to give the crude acid (55 g, 60%). Two sublimations of the product gave the acid (39 g) m.p. 154–156° (lit.,[11] m.p. 154–158°).

Methyl 3-methoxyfurazan-4-acetate. The above acid (5·0 g) in peroxide-free ether (200 cc) was treated with excess ethereal diazomethane. After stirring 24 hr at 20°, ether was evaporated and the residue (5·4 g, 90%) distilled twice to give the *ester* as an oil, b.p. 68–69°/0·09 mm. (Found: C, 42·1; H, 4·4; N, 16·0; $C_6H_8N_2O_4$ requires: C, 41·9; H, 4·7; N, 16·3%.)

Methyl 3-hydroxyfurazan-4-acetate. The acid (4·0 g) was refluxed 20 hr with MeOH (200 cc) saturated with dry HCl. Evaporation, treatment of the residue with $NaHCO_3$ aq to pH 1, and chloroform extraction of the mixture gave the *ester* (2·7 g, 60%) which after two sublimations formed prisms m.p. 56–57°. (Found: C, 38·4; H, 4·1; N, 17·4; $C_5H_6N_2O_4$ requires: C, 38·0; H, 3·8; N, 17·7%.)

Acknowledgement—This work was carried out during the tenure (by B. W.) of a D.S.I.R. Research Studentship.

[10] A. E. Dixon, *J. Chem. Soc.* **75**, 375 (1899).