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INTERCONVERSION OF BENZOFURAZANDIONE MONOXIMES

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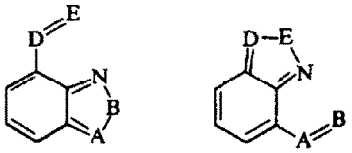
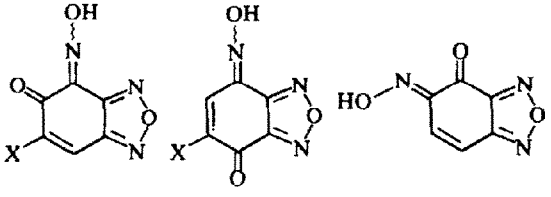
Abstract—The preparation of 5-hydroxy-4-nitroso- and 7-hydroxy-4-nitrosobenzofurazan as well as of their 6-chloro and methyl derivatives is described and the oxime structure of these compounds is established. NMR spectra of benzofurazan-4,5-dione-4-monoxime and benzofurazan-4,7-dione-4-monoxime show evidence for an interconversion, in solution, of two monoximes, the 4,5- and 4,7-derivative prevailing in organic solvents and aqueous alkaline media, respectively. Chloro and methyl derivatives of benzofurazan-4,5- and 4,7-dione-4-monoximes show a similar interconversion in organic solvents.

In previous papers, two of us reported one example of rearrangement in benzofurazan derivatives[1,2] which can be reduced to the generalised Boulton–Katritzky rearrangement A⇆A'.[3]



A A'

In a further investigation, we found other examples, i.e. the rearrangement of 4,5-dioximinobenzofurazan to the 4,7-isomer.[4] In this paper we have extended our studies to a number of monoximes of benzofurazan-4,5- and 4,7-dione (**1–6**), for which tautomeric hydroxy-nitroso forms also are possible.



B **C** **7**

1: X = H **2**: X = H
3: X = Cl **4**: X = Cl
5: X = Me **6**: X = Me

The structure of **1–6** and the possibility of a rearrangement B⇆C were investigated by NMR spectroscopy in a number of organic solvents, and also in alkaline aqueous solution in the case of soluble members.

RESULTS AND DISCUSSION

Products. Borsche and Weber[5] reported that 4 - oximinobenzofurazan - 7 - one (**2**) is formed *via* the corresponding acetyl derivative by dehydration of cyclohexene - 3,4,5,6 - tetraone trioxime with acetic anhydride. The assignment of structure **2** was based on the conversion of the assumed 4 - oximinobenzofurazan - 7 - one into dioxime and the identification of the reduction product of the latter, as 4,7 - diaminobenzofurazan. Repetition of this work led to the discovery that the product described as 4 - oximinobenzofurazan - 7 - one did not correspond to **2**, but to the known 5-oximinobenzofurazan - 4 - one (**7**).[6] The incorrect assignment of structure **2** must have been due to rearrangement which, in the reaction of **7** with hydroxylamine, changed the 4,5-olioxime into the 4,7-isomer.[4]

An alternative route was therefore devised, and compound **2** was prepared by nitrosation of 4 - hydroxybenzofurazan (**8**). In addition to compound **2**, this reaction also yielded 5 - oximinobenzofurazan - 4 - one (**7**); these two products were separated *via* their acetyl derivatives.† Compounds **1**, **3**, **4**, **5** and **6** were prepared in a similar manner; these were the only products in the reaction of nitrous acid with 5 - hydroxy- (**9**), 6 - chloro - 5 - hydroxy- (**10**), 5 - chloro - 4 - hydroxy- (**11**), 5 - hydroxy - 6 - methyl (**12**) and 4 - hydroxy - 5 - methylbenzofurazan (**13**), respectively.

Catalytic hydrogenation of **1** yields 4 - amino - 5 - hydroxybenzofurazan as well as 4 - amino - 7 - hydroxy derivative; **2** similarly gives 4 - amino - 7 - hydroxybenzofurazan together with 4 - amino - 5 - hydroxybenzofurazan (identified by acetylation and comparison with the authentic 4 - acetamido - 7 - hydroxy- and 4 - acetamido - 5 - hydroxyben-

†The structure of acetyl derivatives derived from **2** and **7** have not been investigated.

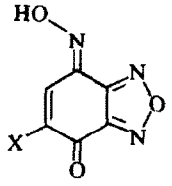
zofurazan 14 and 15[6]). The nature of the reduction products confirms the position occupied by the nitroso (oximino) group in 1 and 2 and shows that these compounds can undergo interconversion in solution.

Structure and rearrangement of 1–6 *in organic solvents.* The NMR data for 1–6 and other related compounds (8–17) in dioxan, dimethyl sulphoxide and pyridine solutions are summarized in Tables 1–3.

The criteria used in the structural assignments for compounds 1–6 are as reported earlier,[7] i.e. comparison with models having a fixed oxime structure, the magnitude of the vicinal coupling constants and the solvent effect.

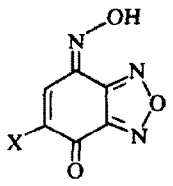
Thus, on the basis of these criteria we concluded that 1 and 2 exist predominantly in the oxime form in the solvents considered [*cf* chemical shifts of 1 and 2 with those of 16 and 17 respectively (Tables 1 and 2); $J_{6,7}$ and $J_{5,6}$ of 1 and 2 with the corresponding values of 8, 9 and 14–17 (Tables 1–3)]. The close analogy between the NMR parameters of 1 and 2 and those of corresponding oximinobenzothiadiazoles[7] supports the structural assignment, since it is known that substitution of endocyclic sulphur by oxygen causes no significant changes.[8,9]

The spectra of 2 show the presence of *syn* (2s) and *anti* (2a) isomers; the spectra of 4 and 6 are interpreted similarly on the basis of the coexistence of two signals due to the two isomers of the oxime form (4a,s; 6a,s).



Cs

2s: X = H
4s: X = Cl
6s: X = Me



Ca

2a: X = H
4a: X = Cl
6a: X = Me

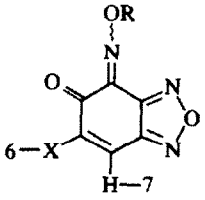
In the absence of suitable models, the assignment of the oxime structure to compounds 3 and 5 (Table 1) was based on the chemical shift of H-7, which, taking into account the effect of substituents, is in good agreement with that of 1; moreover, the solvent shifts for H-7 are similar in 1, 3 and 5. The geometric configuration of the oxime group cannot be established because only one form is detectable in the spectra of these compounds.

Compounds 1 and 2 are interconvertible in solution and this isomerisation is solvent dependent. Thus, in dioxan at 32°, there was no change in the NMR spectrum of 1 for a period of more than 48 h, whereas in DMSO and pyridine the change of 1 to an equilibrium mixture, having roughly the composition 1/2a/2s = 12/70/18, is instantaneous (Table 4). Compound 2 behaves in the same way, and once equilibrium has been reached, it exhibits the same NMR spectrum and isomer ratio as 1.

Addition of triethylamine or water to the dioxan increases the rate of rearrangement, the former to a greater degree than the latter.* The 1⇆2 isomerisation can be followed in dioxan-water, recording the NMR spectrum of these compounds at intervals. Initially, the spectrum of 1 showed, in the "aromatic" region, a single AB pattern, which was joined by two more, the first corresponding to the 2a form, the second to the 2s form; likewise, the two AB patterns arising from the *syn* (2s) and the *anti* (2a) isomers of 2 were joined by another corresponding to the 1 form (Table 4).

Within the limits of experimental accuracy, it can be said that the equilibrium ratio 1/2a/2s was not affected by the solvent. In dioxan-trifluoroacetic acid solutions, interconversion 1⇆2 was not observed even after 100 hr.†

Table 1. Data of NMR spectra at 60 MHz in ppm (τ)



Compounds No	X	R	solv[a]	X-6	H-7	$J_{6,7}$[a]
			Diox	3·35	2·18	10·2
1	H	H	DMSO	3·24	1·97	10·1
			Py	3·18	2·09	10·2
			Diox	3·24	2·20	10·3
16[b]	H	Me	DMSO	3·25	1·97	10·2
			Py	3·20	2·08	10·1
			Diox	—	1·82	—
3	Cl	H	DMSO	—	1·76	—
			Py	—	1·63	—
			Diox	7·90	2·34	1·5
5[c]	Me	H	DMSO	7·87	2·12	1·5
			Py	7·99	2·36	1·5

[a] AB patterns or singlets, unless specified otherwise. Diox. dioxan; DMSO, dimethyl-sulphoxide-d_6; Py, pyridine-d_5. J. in c/s.

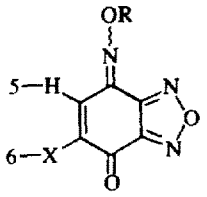
[b] NOMe: diox, obscured by the solvent; DMSO, 5·61; Py, 5·67.

[c] J_{7,CH_3}.

*The spectra in D_2O of 1 and 2 are also recorded; the sparing solubility of compounds in this solvent does not allow the integration of NMR signals. The equilibrium ratio of 1/2a/2s (about 20/80/20) calculated from height of peaks, is about the same as in organic solvents. NMR data in D_2O(τ): 2a 2·24 (H-5), 3·19 (H-6), $J_{5,6}$ = 10·65, 2s 1·96 (H-5), 3·20 (H-6), $J_{5,6}$ = 10·80; 1 3·16 (H-6). 2·01 (H-7), $J_{6,7}$ = 10·20.

†2 undergoes a change in the *anti*/*syn* ratio.

Table 2. Data of NMR spectra at 60 MHz in ppm (τ)[a]

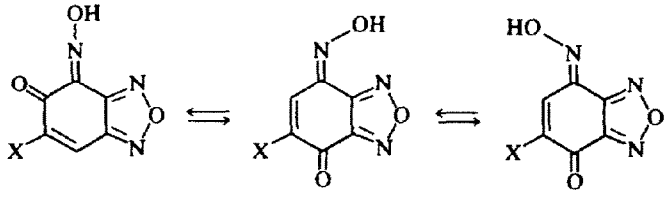


compounds No	X	R	Solv	H-5 s[b]	H-5 a[b]	X-6 s[b]	X-6 a[b]	$J_{5,6}$ s[b]	$J_{5,6}$ a[b]
			Diox	1·97	2·43	3·33	3·33	10·7	10·5
2	H	H	DMSO	1·94	2·23	3·27	3·28	10·9	10·5
			Py	1·71	2·18	3·25	3·25	10·8	10·5
			Diox	2·08	2·48	3·33	3·33	11·0	10·5
17[c]	H	Me	DMSO	2·04	2·32	3·23	3·24	10·8	10·5
			Py	2·10	2·41	3·24	3·24	10·8	10·5
			Diox	1·71	2·11	—	—	—	—
4	Cl	H	DMSO	1·53	1·86	—	—	—	—
			Py	1·42	1·80	—	—	—	—
			Diox	2·13	2·61	7·85	7·88	1·5[d]	1·5[d]
6	Me	H	DMSO	2·07	2·37	7·87	7·90	1·5[d]	1·5[d]
			Py	1·90	2·42	7·86	7·88	1·5[d]	1·5[d]

[a] See footnote *a* to Table 1.
[b] s, *syn*; a, *anti* configuration with respect to H-5.
[c] NOMe. diox, obscured by the solvent; DMSO, 5·73 (*syn*) and 5·65 (*anti*); Py, 5·85 (*syn*) and 5·73 (*anti*).
[d] J_{5,CH_3}.

Compounds **3–6** behave similarly and give an equilibrium mixture of isomers **B**, **Ca** and **Cs** (Scheme 1, Table 5), in about the same ratio as that obtained from **1** and **2**; this indicates that the chloro and methyl substituents have no significant effect on the composition of the isomerisation mixture.

2 in D_2O* (Table 6) are also identical and show the existence of two anions (two AB patterns in a ratio 80/20†) which undergo a rapid interconversion at 100° (the spectrum recorded at various temperatures show coalescence at 50° and a single AB pattern at 100°; subsequent cooling given an unchanged room temperature spectrum).



B **Ca** **Cs**

"X", as in **1–6**

SCHEME 1

Rearrangement of **1–6** *in alkaline media.* When alcoholic solutions of **2**, **4** and **6** are treated with alcoholic potassium hydroxide, salts with the same IR spectra as those obtained from **1**, **3** and **5**, respectively, are obtained.

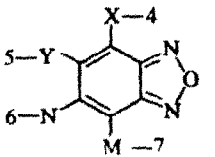
The NMR spectra of the salts derived from **1** and

Acidification of the aqueous solution or of the suspension of the salts derived from **1** or **2** leads to a precipitate consisting exclusively of **1**.‡ The salts derived from **3–6** exibit similar behaviour on acidification.

In order to obtain a more detailed knowledge of the structure of the two anions present in the alkaline solution of **1** or **2**, we have also examined the NMR spectra of the anions (**18**, **20**) of the corresponding oximino-thia-derivatives.[7]

*The salts derived from **3–6** are not sufficiently soluble.
†The same result is obtained with solutions of **1** and **2** in D_2O/K_2CO_3.
‡See Experimental.

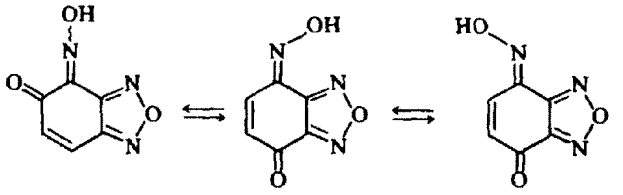
Table 3. Data of NMR spectra at 60 MHz in ppm (τ)[a]



No	Compounds X	Y	N	M	solv[a]	H-4	H-5	H-6	H-7	$J_{5,6}$	$J_{6,7}$	$J_{4,6}$	$J_{5,7}$	$J_{4,7}$
8[b]	OH	H	H	H	Diox	—	3·41	2·71	2·65	7·02	8·90	—	0·71	—
					DMSO	—	3·26	2·55	2·60	7·08	9·37	—	0·94	—
9[b]	H	OH	H	H	Diox	3·18	—	2·89	2·22	—	9·63	2·11	—	0·85
					DMSO	3·07	—	2·72	2·06	—	9·64	2·06	—	0·79
10	H	OH	Cl	H	Diox	2·99	—	—	1·93	—	—	—	—	0·60
					DMSO	2·90	—	—	1·71	—	—	—	—	0·60
11	OH	Cl	H	H	Diox	—	—	2·62[g]	2·62[g]	—	—[g]	—	—	—
					DMSO	—	—	2·48[g]	2·48[g]	—	—[g]	—	—	—
12[c]	H	OH	Me	H	Diox	3·27	—	—	2·43	—	1·50	0·50	—	0·45
					DMSO	3·09	—	—	2·30	—	1·50	0·45	—	0·50
13[d]	OH	Me	H	H	Diox	—	—	2·77[g]	2·77[g]	—	—[g]	—	—	—
					DMSO	—	—	2·65[g]	2·65[g]	—	—[g]	—	—	—
14[e]	NHAc	H	H	OH	Diox	—	1·99	3·47	—	7·80	—	—	—	—
					DMSO	—	2·21	3·32	—	7·95	—	—	—	—
15[f]	NHAc	OH	H	H	Diox	—	—	2·79	2·34	—	9·40	—	—	—
					DMSO	—	—	2·63	2·15	—	9·60	—	—	—

[a] See footnote *a* to Table 1.
[b] ABC pattern, analyzed by LAOCOON 3 computer program, r.m.s. deviation less than 0·06 Hz.
[c] Me: diox, 7·71; DMSO, 7·70. OH: diox, 1·01; DMSO, −1·20. $J_{3,7}$ is referred to J_{7,CH_3}.
[d] Me: diox, 7·75; DMSO, 7·71. $J_{5,6}$ is referred to J_{6,CH_3}.
[e] COMe: diox, 7·83; DMSO, 7·95.
[f] COMe: diox, 7·69; DMSO, 7·62.
[g] A_2 pattern.

Table 4. Equilibration of 4-oximinobenzofurazan-5-one (1) and 4-oximinobenzofurazan-7-one (2a, s)



1 2a 2s

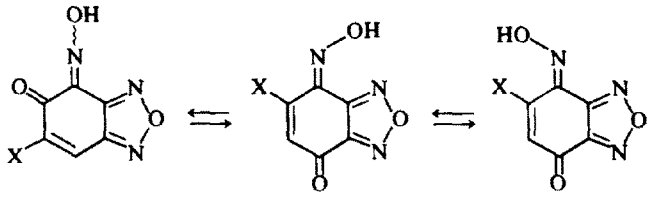
Time hr	Diox/CF_3COOH[a,b]			Diox[a,b]			Diox/H_2O[a,b]			Diox/Et_3N[a,b]			DMSO[a,b]			Py[a,b]		
	1	2a	2s	1	2a	2s	1	2a	2s	1	2a	2s	1	2a	2s	1	2a	2s
0	100	—	—	100	—	—	100	—	—	100	—	—	100	—	—	100	—	—
0·16	100	—	—	100	—	—	100	—	—	13	65	22	12	70	18	14	68	18
0·5	100	—	—	100	—	—	88	12	—	—	—	—	—	—	—	—	—	—
5	100	—	—	100	tr[c]	tr[c]	40	41	19	12	66	22	12	70	18	13	68	19
48	100	—	—	—	—	—	12	66	22	—	—	—	—	—	—	—	—	—
100	100	—	—	84	15	tr[c]	11	68	21	13	67	20	12	70	18	14	69	17
0	—	100		—	100		—	100		—	100		—	100		—	100	
0·16	—	90	10	—	85	15	7	73	20	12	67	21	11	70	19	12	69	19
0·5	—	89	11	—	85	15	9	68	23	—	—	—	—	—	—	—	—	—
5	—	85	15	—	85	15	10	68	22	12	66	22	12	68	20	11	69	20
48	—	75	25	tr[c]	83	17	12	65	23	—	—	—	—	—	—	—	—	—
100	—	73	27	5	77	17	12	65	23	13	66	21	11	69	20	12	70	18

[a] DMSO, dimethylsulphoxide-d_6; Py, pyridine; Diox, dioxan; diox/CF_3COOH, Diox/H_2O, Diox/Et_3N, dioxan with 1% of CF_3COOH, 5% of H_2O, 1% of Et_3N, respectively.

[b] Percentage obtained by integration of NMR spectra; reproducibility of the integral measurements, ±2·5%.

[c] Traces.

Table 5. Equilibrium isomers ratio from monoximes of benzofurazan-4,5 and 4,7-dione (1–6)



B Ca Cs

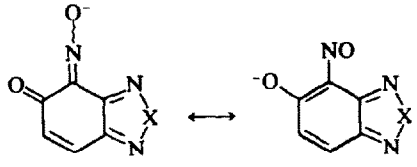
MOX[b]		Isomers ratio											
		DMSO[a]			Py[a]			Diox/Et$_3$N[a]			Diox/H$_2$O[a]		
No	X	B	Ca	Cs	B	Ca	Cs	B	Ca	Cs	B	Ca	Cs
1	H	12	70	18	13	68	19	13	67	20	11	68	21
2	H	11	69	20	12	70	18	13	66	21	12	65	23
3	Cl	12	64	24	15	58	27	23	56	20	22	58	20
4	Cl	15	66	20	16	60	24	20	55	24	17	58	25
5	Me	21	59	20	22	58	20	21	58	21	25	54	21
6	Me	21	58	21	23	54	23	22	55	23	23	52	25

[a] See footnotes *a* and *b* to Table 4.
[b] Starting monoxime.

Table 6. NMR data of 2,1,3-benzo-X-diazole-4,5- and 4,7-dione monoximes in D_2O/K_2CO_3

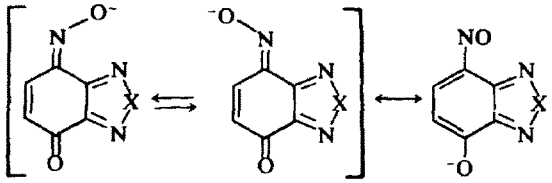
No	Subst	X	H-5	H-6	H-7	$J_{5,6}$[a]	$J_{6,7}$[a]
18a	5-Oximino-4-one	S	—	3·43	2·66	—	10·0
19a	5-Oximino-4-one	O	—	3·22	2·24	—	10·1
20s	4-Oximino-7-one (*syn*)	S	2·14	3·72	—	10·10	—
20a	4-Oximino-7-one (*anti*)	S	2·47	3·79	—	9·80	—
21s	4-Oximino-7-one (*syn*)	O	1·89	3·50	—	9·75	—

[a] J in c/s.



18a: X = S
19a: X = O

18b: X = S
19b: X = O



20a: X = S
21a: X = O

20s: X = S
21s: X = O

20b: X = S
21b: X = O

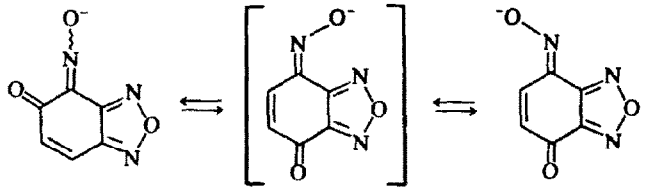
The NMR spectra of **18** and **20** (Table 6) are similar to those of the corresponding neutral molecules[7] (only shielding of H-5, H-6 and H-7 and a slight decrease in $J_{5,6}$ and $J_{6,7}$ is observed and the same *syn*/*anti* ratio as in the neutral molecule is found for **20**. Moreover, no exchange broadening took place on heating to 100°.

These spectral data indicate that the negative charge in anions **18** and **20** is predominantly localised on the oxime oxygen (**18a** and **20a**, s) and that *syn*/*anti* interconversion is undetectable under the experimental conditions reported above.

Making the very reasonable assumptions that also in the anions derived from **1** and **2** the oxime canonical structures prevail (as shown by the high value of the *ortho*-coupling constants), the comparison with the chemical shifts of the thia-derivatives allows us to assign the form prevailing (80%) in the solution of the anions of oxa-

derivatives to the "ortho" structure **19a** (this assignment agrees with the chemical behaviour of the salt); the form present in minor quantity (20%) is assigned to the "para" structure **21**, the isomer **21s** appearing to be more probable.

So, also in aqueous alkali, **1** and **2** are interconvertible and give an equilibrium mixture where the anion of **1** (**19a**) is prevailing*. If **21s** assignment is correct, one could suggests Scheme 2 for the interconversion of anions of benzofurazan - 4,5- and 4,7 - dione - 4 - monoximes.



19a **21a** **21s**

SCHEME 2

We can therefore say that compounds **1–6** give an equilibrium **B⇆C** in organic solvents (displaced towards the *para* form **C**) and that the salts isolated from **4–6** are identical with those isolated from **1–3** and give, on acification, only the *ortho* compounds **B**. Furthermore, the equilibrium **1⇆2** is displaced towards the 4-monoxime of benzofurazan - 4,7 - dione in organic solvents and D_2O and towards the 4-monoxime of benzofurazan - 4,5 - dione in aqueous alkali.

Simple thermodynamic considerations point out that, if an equilibrium exists between two free acids, the weaker acid is the prevailing form, whereas the stronger acid predominates in the anions equilibrium. In our investigation,[7] it was found that the 4-monoxime of benzothiadiazole - 4,5 - dione is a stronger acid than 4-monoxime of benzothiadiazole - 4,7 - dione. If this order of acid strength is also valid for the corresponding oxa-derivatives,† the composition of equilibrium mixture of **1** and **2** in organic solvents, D_2O and aqueous alkali agrees with their acid strength.

EXPERIMENTAL

Light petroleum refers to the fraction of b.p. 30–50°; ligroin to the fraction of b.p. 80–120°.

M.ps. (Buchi–Tottoli apparatus) are uncorrected. NMR spectra were determined on a Jeol C-60HL spectrometer. The chemical shifts are in ppm (τ) from internal TMPS for aqueous solns, and from internal TMS for all other solns. Coupling constants (J) are in c/s (±0·10).

The preparations of **15** and **14** are described in ref's 6 and 2, respectively; those of 4 - oximino - 2,1,3 - benzothiadiazol - 5- and 7-one in Ref 7.

6 - *Chloro* - 5 - *methoxybenzofuroxan* (**22**), was prepared in 80% yield by the sodium hypochlorite oxidation[11] of 4 - chloro - 5 - methoxy - 2 - nitroaniline[12]; m.p. 100–1°, from aqueous EtOH (1:1). (Found: C, 41·86; H, 2·60; N, 13·87. $C_7H_5N_2O_3Cl$ requires: C, 41·92; H, 2·51; N, 13·97%). 5 - *Methoxy* - 6 - *methylbenzofuroxan* (**23**) was obtained in 76% yield in the same manner from 4 - methoxy - 5 - methyl - 2 - nitroaniline[13]; m.p. 118° from EtOH. (Found: C, 53·27; H, 4·50; N, 15·48. $C_8H_8N_2O_3$ requires: C, 53·34; H, 4·47; N, 15·55).

6 - *Chloro* - 5 - *methoxybenzofurazan* (**24**) was obtained in 60% yield by reduction of **22** with hydroxylamine, followed by steam distillation of the alkaline soln of the dioxime;[14] m.p. 119–20°, from n-heptane. (Found C, 45·41; H, 2·82; N, 15·09. $C_7H_5N_2O_2Cl$ requires: C, 45·55; H, 2·73; N, 15·18%.) 5 - *Methoxy* - 6 - *methylbenzofurazan* (**25**) was obtained in 73% yield, in the same manner from **23**; m.p. 123–4°, from n-heptane. (Found: C, 58·51; H, 5·03; N, 16·96. $C_8H_8N_2O_2$ requires: C, 58·54; H, 4·91; N, 17·06%.)

1 - *Azido* - 6 - *chloro* - 5 - *methyl* - 2 - *nitrobenzene* (**26**). A finely divided suspension of 6 - chloro - 5 - methyl - 2 - nitroaniline[15] (1·86 g) in glacial AcOH (18 ml) was diazotised by addition, at 15–20°, to stirred nitrosylsulphuric acid, formed from $NaNO_2$ (0·72 g) and conc H_2SO_4 (8 ml). After the diazotisation was complete, the soln was added dropwise to a stirred soln of sodium azide (0·8 g) in water (10 ml). The ppt obtained was crystallised from light petroleum, to give the azide (1·5 g, 77%), m.p. 62–3°. (Found: C, 39·60; H, 2·42; N, 26·35. $C_7H_5N_4O_2Cl$ requires: C, 39·55; H, 2·37; N, 26·36%.)

4 - *Chloro* - 5 - *methylbenzofuroxan* (**27**). The azide **26** (1·5 g) was heated in ethylene glycol (6 ml) for 1 h at 145–50°. The cooled soln was poured in water and the ppt was collected. It crystallised from EtOH, m.p. 101–2°. (Found: C, 45·51; H, 2·69; N, 15·21. $C_7H_5N_2O_2Cl$ requires: C, 45·55; H, 2·73; N, 15·18%.)

4 - *Chloro* - 5 - *methylbenzofurazan* (**28**). Compound **27** (1·84 g) was heated under reflux for 6 h in anhyd benzene (25 ml) containing trimethyl phosphite (6 ml). The product was steam distilled and crystallised from n-heptane: (1·4 g, 77%), m.p. 94–5°. (Found: C, 49·71; H, 3·02; N, 16·61. $C_7H_5N_2OCl$ requires: C, 49·87; H, 2·99; N, 16·62%.)

4 - *Methoxy* - 5 - *methylbenzofurazan* (**29**). A mixture of **28** (18 g) and 4N NaOMe (270 ml) was heated under reflux for 48 h. After removal of solvent, the residue was diluted with water (500 ml) and filtered. The ppt collected after solubilisation in ether, to remove amorphous material, gave crude 4 - methoxy - 5 - methylbenzofurazan (7 g) in 80–85% purity, there being 20–15% of starting compound **28** present; this mixture was used for the next stage without purification. In addition to crude 4 - methoxy - 5 -

*The insolubility in water of the salts derived from **3–6** does not allow investigation of the equilibria in the corresponding anions.

†The same order of acid strength was observed in hydroxy- or hydroxy-nitrobenzofurazanes and benzothiadiazoles.[10]

methylbenzofurazan, the aqueous alkaline filtrate, acidified with HCl and ether-extracted, gave crude **13** (4.8 g), which was purified by crystallisation from ligroin; m.p. 144–5°. Treatment, during 24 h, of ethereal 4 - hydroxy - 5 - methylbenzofurazan (0·75 g in 50 ml) with an excess of ethereal diazomethane, followed by removal of unreacted diazomethane, washing of ethereal solution with 10% NaOH aq, removal of solvent and sublimation of the residue, gave pure 4 - methoxy - 5 - methylbenzofurazan, m.p. 57–8°. (Found: C, 58·48; H, 4·86; N, 17·11. $C_8H_8N_2O_2$ requires: C, 58·54; H, 4·91; N, 17·06%.)

4 - *Hydroxy* - 5 - *methylbenzofurazan* (**13**). The crude 4 - methoxy - 5 - methylbenzofurazan (10 g) was heated under reflux for 15 min in HBr 48% (200 ml). The ice cooled soln was treated until basic with 10% NaOH and ether-extracted to remove 4 - chloro - 5 - methylbenzofurazan (present in the starting compound). The aqueous alkaline soln acidified with HCl and ether-extracted, gave, after crystallisation of ethereal residue from ligroin, the 4 - hydroxy - 5 - methylbenzofurazan, m.p. 144–5°. (Found: C, 55·92; H, 4·10; N, 18·61. $C_7H_6N_2O_2$ requires: C, 56·00; H, 4·03; N. 18·66%.)

5 - *Chloro* - 4 - *hydroxybenzofurazan* (**11**). The 5 - chloro - 4 - methoxybenzofurazan[16] (10 g) was heated under reflux for 15 min in HBr 48% (800 ml). Cooling then gave the crude hydroxy compound, m.p. 160–70°, which was purified *via* acetyl derivative **30** obtained by treatment, during 2 h at 100°, with Ac_2O. Compound **30** was precipitated and crystallised from light petroleum. m.p. 51–2°. (Found: C, 45·20; H, 2·29; N, 13·13. $C_8H_5N_2O_3Cl$ requires: C, 45·20; H, 2·37; N, 13·17%.) Hydrolysis of 4 - acetoxy - 5 - chlorobenzofurazan (4 g) with dil HCl (1 : 1) (40 ml) during 2 h at 100°, and crystallisation from n-heptane gave pure 5 - chloro - 4 - hydroxybenzofurazan, m.p. 172–3°. (Found: C, 42·21; H, 1·68; N, 16·55. $C_6H_3N_2O_2Cl$ requires: C, 42·26; H, 1·77; N, 16·42%.)

6 - *Chloro* - 5 - *hydroxybenzofurazan* (**10**), was obtained by heating under reflux **24** (5 g) in HBr 48% (200 ml). Cooling then gave 6 - chloro - 5 - hydroxybenzofurazan, m.p. 135–6°, from n-heptane-benzene (5 : 1). (Found: C, 42·19; H, 1·82; N, 16·38. $C_6H_3N_2O_2Cl$ requires: C, 42·26; H, 1·77; N, 16·42%.) In a similar way was obtained 5 - *hydroxy* - 6 - *methylbenzofurazan* (**12**) from **25** (5 g) and HBr 48% (100 ml). Crystallised from ligroin–toluene (1 : 1), m.p. 154–5°. (Found: C, 55·88; H, 4·11; N, 18·67. $C_7H_6N_2O_2$ requires: C, 56·00; H, 4·03; N, 18·66%.)

Benzofurazandione monoximes (**1–6**)

General method. A finely divided suspension of the hydroxy derivative, obtained by acidification, with 2N H_2SO_4 (10 ml), of an alkaline soln of **8–13** (10 mmoles in 25 ml of 0·04 N NaOH), was cooled at 2–3° and aqueous $NaNO_2$ (10 mmoles in 20 ml) was added dropwise with vigorous stirring over 0·5–1 hr. After stirring for 0·5–1 hr, at 2–3°, the mixture was filtered and the ppt was washed with water and dried *in vacuo* over P_2O_5 at room temp. (The chloro-hydroxybenzofurazans reacted only slowly with HNO_2, and longer reaction times were used.) The oximino derivatives **1**, **3–6**, obtained in 75–85% yield, (pure by NMR) were used for spectrophotometric investigation without purification. **1** [from 5 - hydroxybenzofurazan[17] (**9**)]; m.p. 168–9° (dec)*. (Found: C, 43·47; H. 1·77; N, 25·35. $C_6H_3N_3O_3$ requires: C, 43·64; H, 1·83; N, 25·45%.)**3**, (from **10**); m.p. 156–7° (dec). (Found: C, 36·15; H, 0·97; N, 21·03. $C_6H_2N_3O_3Cl$ requires: C, 36·11; H, 1·01; N, 21·06). **4**, (from **11**); m.p. 156–7° (dec). (Found: C, 36·06; H, 1·11; N, 19·9. $C_6H_2N_3O_3Cl$ requires: C, 36·11; H, 1·01; N, 21·06%.) **5**, (from **12**); m.p. 172–4° (dec). (Found: C, 46·81; H, 2·85; N, 23·42. $C_7H_5N_3O_3$ requires: C, 46·93; H, 2·81; N, 23·46%). **6**, (from **13**); m.p. 174–7° (dec). (Found: C, 47·02; H, 2·79; N, 23·51 . $C_7H_5N_3O_3$ requires: C, 46·93; H, 2·81; N, 23·46%). Compound **2**, (from **8**),[17] obtained as a mixture with **7**, was separated in the following manner.

(a) The crude mixture of **2** and **7** (10 g) was dissolved in 30 ml of Ac_2O. On standing ca 15 min at room temp, a ppt separated, which was filtered off (*ca* 1 g), washed with ether and crystallised from benzene, to give the acetyl derivative of **7** (**31**) identical with an authentic sample obtained as in Ref 5; m.p. 142–3° (lit[5]: 142–3°). The Ac_2O filtrate, gradually cooled from 20° to −15°, separated a series of mixtures containing the acetyl derivative of **7** (**31**) and **2** (**32**) progressively enriched in **32**, as the temp decreased. A further fraction of crude **32** was obtained from the residual Ac_2O filtrate, diluted with water and ether-extracted (AcOH removed by washing with $NaHCO_3$). Chromatography of the mixtures containing at least 75% of **32** (NMR estimation), using Merck silica gel and $CHCl_3$-MeOH (100:1) as eluent, gave pure **32**, m.p. 130–1° (from CCl_4). (Found: C, 46·21; H, 2·53; N, 20·21 . $C_8H_5N_3O_4$ requires: C, 46·39; H, 2·43; N, 20·28%). The acetyl derivative **32** (2·4 g) was suspended in MeOH (80 ml) and conc HCl (4 ml) and heated under reflux for 15 min. Removal of solvent from resulting soln, and dilution of residue with water, precipitated the pure 4-*oximinobenzofurazan-7-one* (**2**), m.p. 170–1° (dec). (Found: C, 43·58; H, 1·81; N, 25·39 . $C_6H_3N_3O_3$ requires: C, 43·64; H, 1·83; N, 25·45%).

(b) To the crude mixture of **2** and **7** (16·5 g), dissolved at room temp in 700 ml of EtOH, was added a soln of 4% KOH–EtOH (160 ml). The ppt, filtered and acidified, on suspending in dil HCl (1 : 1), gave **1**, m.p. 168–9° (dec); (alkaline media produce the **2** → **1** rearrangement, *cf* text). The ethanolic alkaline filtrate, cooled at 0°, gave the salt of **7** in about 80% purity; acidification of this salt and crystallisation of resulting product from water, gave pure **7**, m.p. 185–7° (lit[6]: 185–7°).

Benzofurazan - 4,5 - dione - 4 - O - methyloxime (**16**). $AgNO_3$aq (2 g in 10 ml) was added to aqueous K salt of **1** (2 g in 100 ml). The dried Ag salt (2·5 g) was shaken with MeI (2·6 g) in dry ether (100 ml), in a stoppered bottle, for 24 hr. The soln was filtered, the ether removed and the benzofurazan - 4,5 - dione - 4 - O - methyloxime (0·7 g, 42%) was crystallised from n-heptane; m.p. 126–7°. (Found: C, 46·84; H, 2·90; N, 23·39. $C_7H_5N_3O_3$ requires: C, 46·93; H, 2·81; N, 23·46%).

Benzofurazan - 4,7 - dione - 4 - O - methyloxime (**17**). A soln of benzofurazan - 4,7 - dione[2] (1·23 g) and O-methylhydroxylamine hydrochloride (0·68 g) in MeOH (75 ml) was heated under reflux for 3 h. After removal of solvent, the residue was purified by chromatography (using Merck silica gel and ether-light petroleum (1 : 1) as eluent), to give benzofurazan - 4,7 - dione - 4 - O - methyloxime, m.p. 64–5° (from n-heptane). (Found: C, 46·78; H, 2·85; N, 23·41 . $C_7H_5N_3O_3$ requires: C, 46·93; H, 2·81; N, 23·46%).

Hydrogenation of 4 - oximinobenzofurazan - 5- and 7-one (**1, 2**). An ethereal soln of oximino derivative (1·65 g

*M.p. and mixed m.p. of 4 - oximinobenzofurazans - 5- and 7-one are identical or nearly identical, the differences being compatible with the different purity of compounds. This can indicate that a rearrangement occurs also on heating the solid compounds.

in 200 ml) was hydrogenated at room temp and pressure, over 0·5 g of 10% Pd-C. To the ethereal filtrate was added Ac_2O (2 ml) and after standing 10 h at room temp, the solvent was removed and the residue dried *in vacuo* over KOH. **1** and **2** yield a mixture of **15** (65–70%) and **14** (35–30%) (estimated by NMR).

Rearrangement of benzofurazan - 4,7 - diones - 4 - monoximes via potassium salts. To a soln of **2** (1·65 g) in 70 ml of EtOH, was added a soln of 4% KOH–EtOH (10 ml). The blue-green ppt (1·5 g, 75%) was collected and washed with EtOH and ether. An identical salt (by NMR and IR) was obtained, in the same way, from **1**; IR (Nujol mull): 1620s, 1610s, 1540m, 1500s, 1430s, 1400s, 1360m, 1300m, 1260s, 1180w, 1120w, 1050s, 1000s, 880s, 840s cm^{-1}. (Found: C, 35·39; H, 1·10; N, 20·35. $C_6H_2N_3O_3K$ requires: C, 35·46; H, 0·99; N, 20·68%). A finely divided suspension of this salt (2 g) in 10 ml of dil HCl (1:1), gave about 90% of pure **1**; on this basis consitution **19a** can be assigned to this salt. [Acidification of aqueous soln of salt (2 g in 35 ml) with dil HCl, yield about 65% of **1**). On extraction of the aqueous filtrate with ether, further **1** as well as **2** was obtained (it should be noted that **2** can be formed by rearrangement of **1** in water and ether soln)]. In the same way were obtained the rearrangements of **4** and **6** to **3** and **5**, respectively.

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REFERENCES

[1]D. Dal Monte and E. Sandri, *Boll. Sci. Fac. Chim. Ind. Bologna* **26**, 127 (1968)
[2]D. Dal Monte, E. Sandri and S. Pollicino, *Ibid.* **26**, 153 (1968)
[3]A. J. Boulton and A. R. Katritzky, *Rev. Chim. (A.R.P.R.)* **7**, 691 (1962)
[4]A. S. Angeloni, V. Cerè, D. Dal Monte, E. Sandri and G. Scapini, *Tetrahedron* **28**, 303 (1972)
[5]W. Borsche and H. Weber, *Liebigs Ann.* **489**, 270 (1931)
[6]D. Dal Monte, E. Sandri and P. Mazzeracchio, *Boll. Sci. Fac. Chim. Ind. Bologna* **26**, 165 (1968)
[7]A. S. Angeloni, D. Dal Monte, S. Pollicina and G. Scapini, *Tetrahedron*, in press
[8]A. J. Boulton, P. J. Halls and A. R. Katritzky, *Org. Magn. Resonance* **1**, 311 (1969)
[9]N. M. D. Brown and P. Bladon, *Spectrochim. Acta* **24A**, 1869 (1968)
[10]D. Dal Monte, E. Sandri and W. Cerè, *Ann. Chim. Italy* **60**, 801 (1970)
[11]A. G. Green and F. M. Rowe, *J. Chem. Soc.* **101**, 2452 (1912)
[12]I. Molnar, *Helv. Chim. Acta* **46**, 1779 (1963)
[13]R. T. Arnold and J. C. McCool, *J. Am. Chem. Soc.* **64**, 1315 (1942)
[14]T. Zinke and P. Schwarz, *Liebigs Ann.* **307**, 28 (1899)
[15]G. T. Morgan and T. Glover, *J. Chem. Soc.* **119**, 1700 (1921)
[16]F. B. Mallory and S. P. Varimbi, *J. Org. Chem.* **28**, 1656 (1963)
[17]D. Dal Monte and E. Sandri, *Ann. Chim. Italy* **54**, 486 (1964)