Furazans and Furazan Oxides. Part I.[1] Synthesis and Reactions of Some Strained Furazan *N*-Oxides [2]

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Furazan *N*-oxides with a strained ring bridging the 3- and 4-positions are progressively deoxygenated by trialkyl phosphites, forming furazans, which can in some cases be isolated, and dinitriles. Heating in the presence of an acetylene forms bis(nitrile oxide) adducts (isoxazoles), with the more highly-strained types.

It has been known for many years that it is difficult to prepare the furazan or furazan *N*-oxide ring system directly fused to another five-membered ring. In his definitive review,[3] Boyer pointed out that only two examples were known in the furazan *N*-oxide (furoxan) series [(1a) or (1b)[4] and (3) [5]], and one in the furazan series (4).[6] Since then, a few ring-D-fused steroidal furoxans have been reported.[7]

We undertook an investigation into strained furazan *N*-oxides, in order to confirm that ring strain is responsible for their instability, or difficulty of formation, and to ascertain what kind of strain (stretching, bending, or twisting) is effective, and whether it has any influence on the rate of furoxan isomerisation [*e.g.* (1a) ⇌ (1b)]. The present paper describes the first results from this project.

Dihydrocyclopentafurazan N-*Oxides.*—It seemed surprising to us that the examples known at that time (1967) of furoxans fused to a five-membered ring both had an apparent extra source of strain, in the form

[1] Earlier papers on this topic have appeared under the broader heading of '*N*-Oxides and Related Compounds' (see, *e.g.*, Part XXXVI, ref. 15 below).

[2] A preliminary account of some of this work has appeared: M. Altaf-ur-Rahman and A. J. Boulton, *Chem. Comm.*, 1968, 73.

[3] J. H. Boyer, in 'Heterocyclic Compounds,' vol. 7, ed. R. C. Elderfield, Wiley, New York, 1961, p. 462.

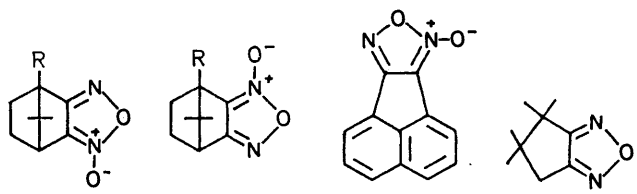
[4] M. O. Forster, *J. Chem. Soc.*, 1903, **83**, 514.

[5] F. M. Rowe and J. S. H. Davies, *J. Chem. Soc.*, 1920, **117**, 1344.

[6] C. K. Ingold and C. W. Shoppee (*J. Chem. Soc.*, 1928, **125**, 365) report compound (4) as having m.p. 209°. We feel that it is improbable that a compound of structure (4) would melt so high; we are currently reinvestigating the problem.

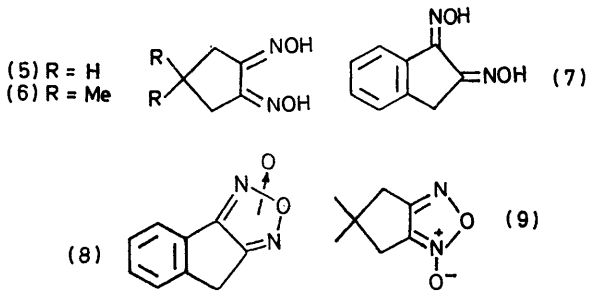
[7] H. Reimann and H. Schneider, *Canad. J. Chem.*, 1968, **46**, 77.

of bridging groups or fused rings. We successfully repeated the earlier preparations,[4,5] in the course of which we found that both compounds (1) and (3) were liable to explode at elevated temperatures. Attempted



(1a)R = Me (1b)R = Me (3) (4)
(2a)R = Br (2b)R = Br

hypochlorite oxidation of cyclopentane-1,2-dione dioxime (5) gave a greenish colour, and a white precipitate, which vigorously decomposed on filtration.[8] Similarly, we were unable to isolate the oxidation product of indane-1,2-dione dioxime (7), although the i.r. spectrum of a $CHCl_3$ extract suggested the presence of the furoxan (8) (strong absorption at *ca.* 1640 cm^{-1}).



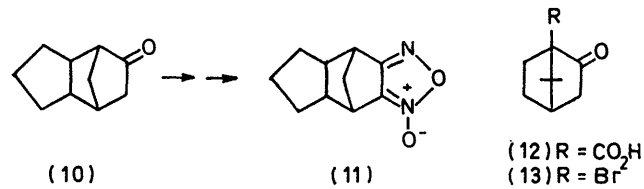
(5) R = H (7)
(6) R = Me

(8) (9)

4,4-Dimethylcyclopentane-1,2-dione, prepared from dimedone *via* 3,3-dimethylglutaric acid following Komppa's synthesis, was converted into the dioxime (6), which with hypochlorite gave a stable furoxan (9). The stabilising effect of the two methyl groups is noteworthy; substitution effects stabilising rings in cases of ring–chain tautomerism have been known for many years.[9]

4,7-*Methanobenzofurazan* N-*Oxides*.—The furoxan (1) (bornenofuroxan) was prepared as described,[4] as a mixture of both isomers (see n.m.r. section). Failure to nitrosate norbornan-2-one prevented our investigation of norbornenofuroxan. The tricyclic ketone (10) was successfully converted into the furoxan (11), which slowly decomposed on storage at room temperature. We were unable to nitrosate 2-oxobornan-10-oic acid (12), but the bromo-ketone (13) gave the furoxan (2).

4,6-*Methanobenzofurazan* N-*Oxides*.—Derivatives of the pinane skeleton were next examined. Molecular models confirm what might intuitively have been supposed: that when the bridging dimethylmethano-group in (1) is shifted one position round the six-membered ring, to give (14) or (15) (R = Me), although the total strain of the system is increased, that applied to the atoms of the furoxan ring is relieved. Conveniently available ketones in this series are 6,6-dimethylnorpinan-2-one (nopinone) (16), pinan-4-one (verbanone) (17), and pinan-3-one (isopinocamphone) (18). Furoxans (14 and 15; R = H and Me) were prepared from the first two of these. Nitrosation (NaOEt–$C_5H_{11}ONO$) of (18) gave no isonitroso-derivative, probably owing to reaction at the tertiary position, followed by ring cleavage.

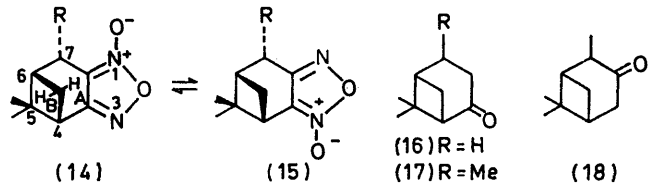


(10) (11) (12)R = CO_2H
(13)R = Br

We attempted to prepare an enamine from (18), in the hope that nitrosation could be thereby effected at the methylene group, but we were unable (*cf.* ref. 10) to isolate any product from the ketone with morpholine, pyrrolidine, piperidine, or dimethylamine, with a variety of catalysts (see Experimental section). Furthermore, initial experiments at nitrosating 1-(4-morpholino)-cyclohexene showed only limited promise.

The tautomeric structures and equilibration of these furoxans [(14) ⇌ (15)] are discussed in the n.m.r. section.

Phosphite Deoxygenation.—Trialkyl phosphites are known to deoxygenate furoxans to furazans.[11] In the hope that this reaction would provide the hitherto



(14) (15) (16)R = H (17)R = Me (18)

unknown furazan from the furoxan (1), we heated (1) under reflux with trimethyl phosphite. The product, however, showed a prominent i.r. band at 2240 cm^{-1}, and was identified as camphoronitrile (19). Furoxan (3) similarly provided naphthalene-1,8-dicarbonitrile, and furoxan (11) the perhydropentalenedicarbonitrile (20). In one experiment, the indenofuroxan (8), prepared in chloroform solution, gave *o*-cyanobenzyl cyanide in 15% yield, but attempts to repeat this failed. No nitrile was formed on phosphite reduction of the di-

[8] J. H. Boyer [3] also reports an unsuccessful attempt to prepare this compound, and the formation of green or blue intermediates during dioxime oxidations (ref. 3, p. 471).

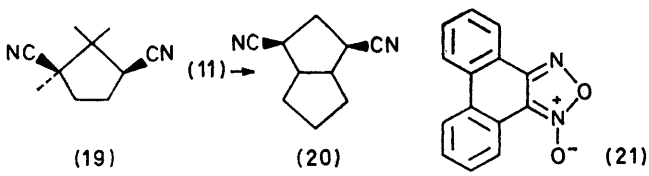
[9] P. R. Jones, *Chem. Rev.*, 1963, **63**, 461.

[10] Y. Chrétien-Bessière and M. Barthélémy, *Compt. rend.*, 1967, **264**, 710; *Bull. Soc. chim. France*, 1969, 2725.

[11] T. Mukaiyama, H. Nambu, and M. Okamoto, *J. Org. Chem.*, 1962, **27**, 3651; C. Grundmann, *Chem. Ber.*, 1964, **97**, 575; A. S. Bailey and J. M. Evans, *Chem. and Ind.*, 1964, 1424.

methylcyclopentafurazan *N*-oxide (9), nor on similar treatment of a chloroform solution of hypochlorite-oxidised dioxime (5). The fate of the furoxan was not determined, in these cases.

The conditions for deoxygenating furoxans (1), (3), and (11) are considerably milder than those usually employed for furazan preparation. Thus, the furoxan (1) was deoxygenated (to the dinitrile) by trimethyl phosphite in benzene solution at 70°, with a half-life for the reaction of *ca.* 30 min. In contrast, phenanthrofuroxan (21) was recovered unchanged after heating under reflux (112°) with trimethyl phosphite after 7 h; triethyl phosphite (at 158°) gave the furazan nearly quantitatively. The reaction with the furoxans (3) and (11) was studied kinetically, following by i.r.



(19) (20) (21)

intensity measurements both furoxan disappearance (band at 1670—1640 cm^{-1}) and cyanide formation (band at *ca.* 2200 cm^{-1}). No intermediate furazan was detected, nor did the initial spectra indicate the formation of a phosphite–furoxan complex. Figure 1 illustrates, for

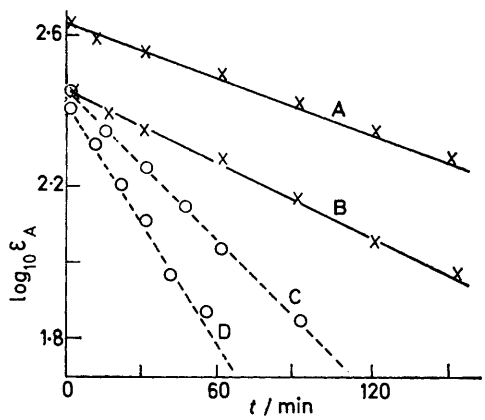


FIGURE 1 Furazan *N*-oxide decomposition by trimethyl phosphite: A, furazan *N*-oxide (11) with 0·33M-phosphite at 40°; B, as A but with 0·435M-phosphite; C, acenaphthofurazan *N*-oxide (3) with 0·17M-phosphite at 68°; D, as C but with 0·26M-phosphite

each compound, the linear dependence of log (furoxan concentration) upon time, for two different phosphite concentrations (in excess; pseudo-first-order kinetics observed), and Figure 2 shows the dependence of first-order rate on phosphite concentration (see Experimental section for details of measurements). The dependence of the rate on phosphite concentration is seen to be of first order; rate-determining ring-opening to dinitrile dioxide, followed by rapid deoxygenation, is therefore excluded.

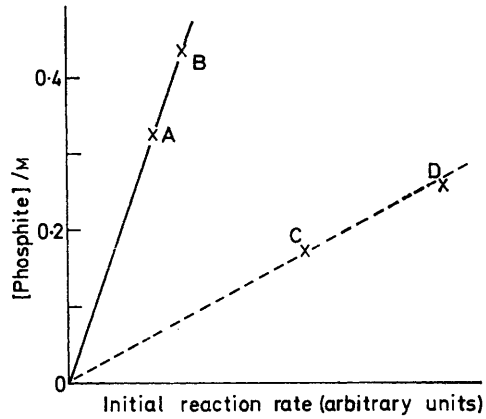
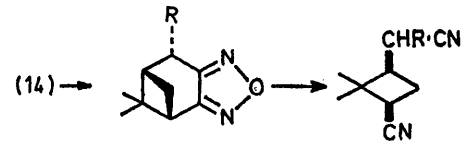


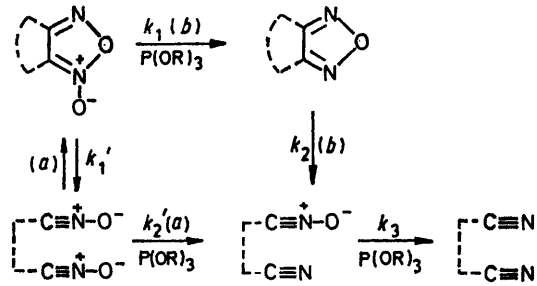
FIGURE 2 Dependence of furazan *N*-oxide decomposition rate on phosphite concentration: AB, furazan *N*-oxide (11) at 40°; CD, furazan *N*-oxide (3) at 68°

The 4,6-methanobenzofurazan *N*-oxides (14; R = H and Me) can be reduced by heating under reflux with



(22) (23)

tri*methyl* phosphite to the furazans (22), which in turn form the dinitriles (23) in triethyl phosphite. Experimental difficulties prevented our measuring the dependence of the rate of dinitrile formation from the furazans on phosphite concentration. Although the final stages are uncertain, therefore, we favour path (*b*) of the Scheme as explaining all the results most satisfactorily. In furoxans (1), (3), and (11), in which the heterocyclic ring C–C bond is subject to the most extension strain, k_3, $k_2 \gg k_1$. In furoxans (14) and (15) $k_3 \gg k_1 > k_2$,



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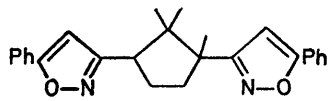
while in unstrained furoxans only the first step (k_1) is observed. Nitrile oxide deoxygenations (k_3) are known to be fast reactions, in general.[12] It is difficult to

[12] C. Grundmann and H.-D. Frommeld, *J. Org. Chem.*, 1965, **30**, 2077.

exclude path (*a*) (rate-determining deoxygenation of an equilibrium dinitrile dioxide intermediate) for the 4,6-methanobenzofurazan *N*-oxides, particularly in view of the results described in the next section, but in the isomeric series it is ruled out by the isolation of the intermediate furazan.

Phenylacetylene Adducts.—The possibility of ring-opening to a dinitrile dioxide was investigated by heating the furoxans (1), (3), (9), and (11) with an excess of phenylacetylene. At 100° in CCl_4, (1) formed a 2 : 1 adduct (24); (11) similarly gave (25) under even milder conditions (55°), but no adduct could be isolated from the acenaphtho- (3) or dimethylcyclopenta-furoxan (9). Other compounds were not investigated. In the absence of phenylacetylene the furoxans (1) and (11) slowly polymerised on heating in CCl_4. An alternative route, an intermediate 1 : 1 adduct between the furoxan and phenylacetylene, opening to give an isoxazole-nitrile oxide, is rendered unlikely by the qualitative similarity of the rates of adduct formation in the presence of phenylacetylene and of polymerisation in its absence.



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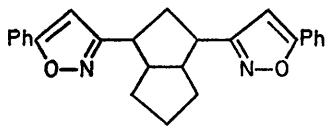
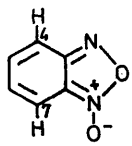


(25)

*N.m.r. Spectra.**—Proton resonance spectra have proved useful in structural assignment in the furoxan series. Previous work has shown chemical shift difference ($\Delta\tau$) of *ca.* 0·25 p.p.m. between 4- and 7-H in the rigid benzofuroxan system (26),[13] while protons attached to methyl groups on the furoxan ring show $\Delta\tau$ 0·17—0·23 p.p.m.[14,15] and α-protons on an ethyl group have $\Delta\tau$ 0·14 p.p.m.[14] [(27) ⇌ (28)]. In every case the proton nearer the *N*-oxide group absorbs at higher field than that next to the unoxidised N(5) of the furazan ring. Because of the consistency in the direction of this shift, we feel that it may be applied with



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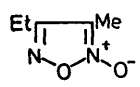

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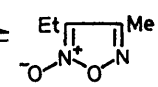
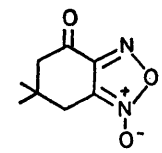


(28)

confidence to the assignments in the rigid systems dealt with in this paper.

The dimethylcyclopentafurazan *N*-oxide (9) showed a six-proton singlet (τ 8·68) and two singlets at τ 7·44 and 7·32. In compounds (29) and (30) (the closest



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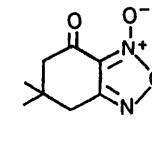

(30)

analogy available) the chemical shifts of the protons adjacent to the heterocyclic rings are τ 7·30 and 7·10, respectively.[16]

The furoxan (1) gave a spectrum which was resolved, in part, by addition of the contact shift reagent tris-(6,6,7,7,8,8,8-heptafluoro-2,2-dimethyloctane-3,5-dionato)europium [Eu(fod)$_3$].[17] In CCl_4 alone, four methyl peaks are found, two (of equal area) at τ 8·64 and 8·67, and two, twice the area of the others, at τ 8·96 and 9·05. There are in addition two overlapping doublets at 7·02 and 7·06, each with J 4 Hz, and a very complex multiplet in the region 7·6—8·6. Addition of Eu(fod)$_3$ separated all the peaks, and also split the more intense methyl absorptions into two, thus showing the furoxan to be an equimolar mixture of isomers (1a) and (1b). The small chemical shift difference between the signal for the bridgehead proton in (1a) and in (1b) (0·04 p.p.m.) is comparable with that in the pinane series (see later).

The bromo-furoxan (2) showed two singlets (τ 8·92 and 8·98), a triplet (1H) at 6·95 (peak separation 3·5 Hz), and a complex multiplet (4H) (7·6—8·8). Further synthetic work is in progress, aimed at solving the remaining problems associated with the spectra in this series.

Both the isomers (14) and (15) of the pinene derivatives (R = Me) were isolated, which greatly assisted structural assignment, both in these cases and in that of the norpinane derivative (R = H). In the latter, only one compound was isolated, which was unchanged on heating. Its n.m.r. spectrum corresponded to that of the more stable of the two homologues (14; R = Me). The change in chemical shifts of 4- and 7-H on isomerisation of (15) to (14) (R = Me), by which the structures are assigned, are in the expected direction, but are rather small (+0·15 for 4-H, −0·04 p.p.m. for 7-H). The 4-methyl (R) group also shifts upfield (+0·10 p.p.m.). Chemical shifts and coupling constants are listed in the Table. Particularly noteworthy, in the spectra of this series, is the large chemical shift difference between the two geminal methyl groups on the four-membered

* In this section, chemical shifts are for solution in CCl_4, unless otherwise stated.

[13] R. K. Harris, A. R. Katritzky, S. Øksne, A. S. Bailey, and W. G. Paterson, *J. Chem. Soc.*, 1963, 197.
[14] F. B. Mallory and A. Cammarata, *J. Amer. Chem. Soc.*, 1966, **88**, 61.
[15] A. J. Boulton, P. Hadjimihalakis, A. R. Katritzky, and A. Majid Hamid, *J. Chem. Soc.* (*C*), 1969, 1901.
[16] J. Ackrell and A. J. Boulton, unpublished work.
[17] R. E. Rondeau and R. E. Sievers, *J. Amer. Chem. Soc.*, 1971, **93**, 1522.

ring, and the even larger difference for the geminal protons opposite (see Figures 3 and 4); in the bornane series the methyl separation was much less. We are assuming that the proximity of the heterocyclic ring leads to a shielding effect; if this is incorrect the assignments for the geminal methyls and protons have to be reversed. There is also ambiguity over the orientation of the methyl group (R) in the compounds (14), (15), and (22) (R = Me). The hydrogenation stage, producing pinan-4-one (17), is expected to leave this methyl group *cis* to the *gem*-dimethylmethylene bridge, and as the subsequent reactions showed no evidence of isomerisation the *cis*-orientation in the products is assumed.

N.m.r. spectra of furazan *N*-oxides and furazans of the pinane series

Chemical shifts (τ values, in CCl_4)

Proton(s)	(14; R = Me)	(15; R = Me)	(22; R = Me)	(14; R = H)	(22; R = H)
4-H	7·0m	7·04m	6·87m	7·02m	6·79m
6-H	7·8m	7·8m	7·75m	7·6m	7·6m
7-$H_{(2)}$	6·89dq	6·74dq	6·71dq	7·25d	6·98d
8-H_A	8·55d	8·55d	8·63d	8·56d	8·65d
8-H_B	7·1m	7·1m	7·09m	7·08m	7·12m
5-Me	8·5s	8·5s	8·52s	8·51s	8·5s
5-Me	9·06s	9·1s	9·27s	9·16s	9·31s
7-Me	8·60d	8·50d	8·54d		

s = Singlet, d = double(t), q = quartet, m = multiplet.

Coupling constants (Hz)

J	(14; R = Me) [a]	(15; R = Me) [a]	(22; R = Me)	(14; R = H) [b]	(22; R = H)
4,6	5·0	5·0	5·0		5·0
6,7	2·5	2·5	2·5	3·0	3·0
4,8B	5·2	5·2	5		5·0
6,8B	5·5	5·5	6·0		6·0
7,7-Me	7·0	7·0	7·5		
8A,8B	−10·3	−10·3	−10·8	−10·5	−10·5

[a] Measured in C_6H_6–CCl_4 (1 : 1); remainder in CCl_4. [b] Incompletely analysed.

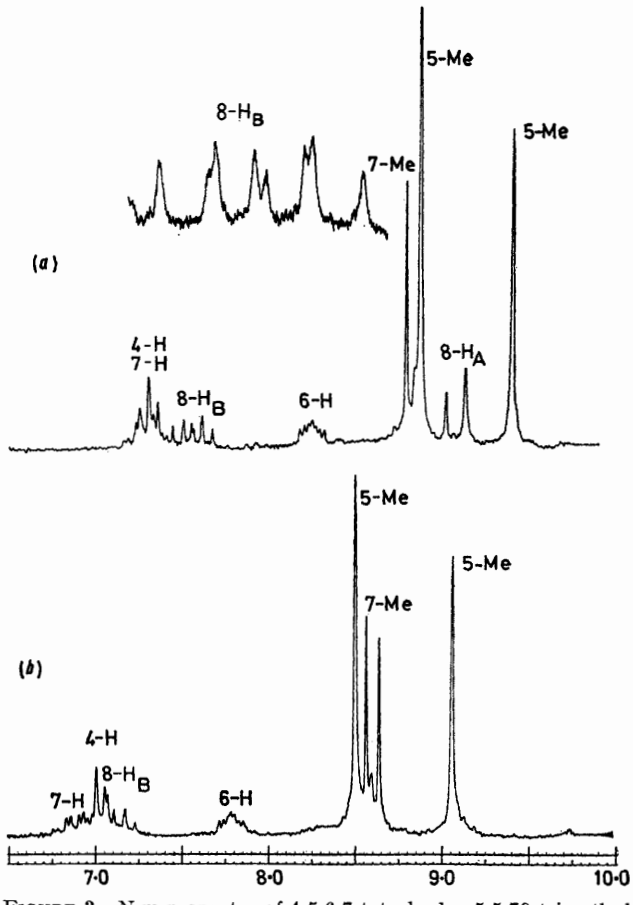

FIGURE 3 N.m.r. spectra of 4,5,6,7-tetrahydro-5,5,7β-trimethyl-4α,6α-methanobenzofurazan 1-oxide (14; R = Me) in (*a*) C_6H_6–CCl_4 (1 : 1) and in (*b*) CCl_4; inset: 8-H_B (10 Hz per scale unit)

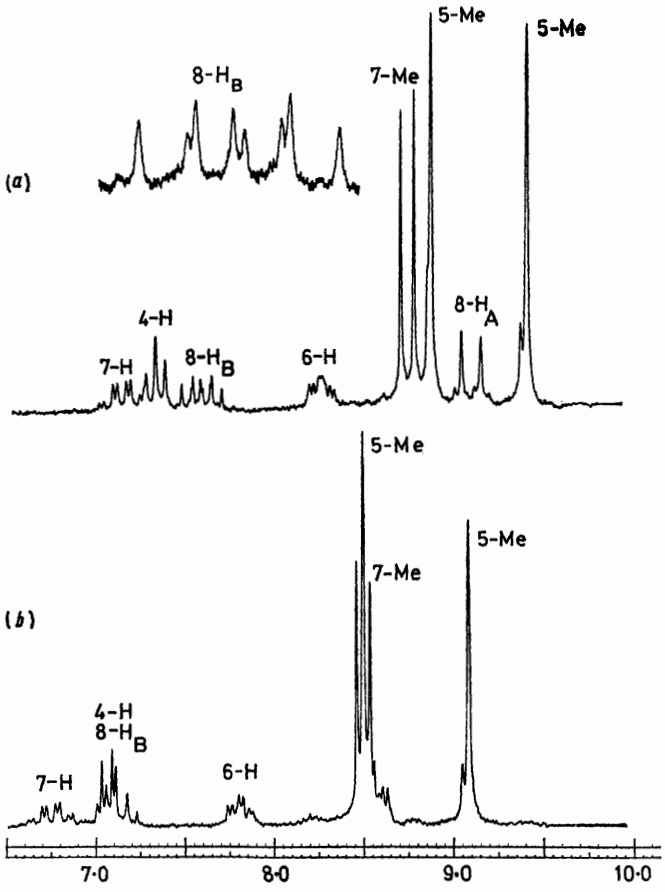

FIGURE 4 N.m.r. spectra of 4,5,6,7-tetrahydro-5,5,7β-trimethyl-4α,6α-methanobenzofurazan 3-oxide (15; R = Me) in (*a*) C_6H_6–CCl_4 (1 : 1) and in (*b*) CCl_4; inset: 8-H_B (10 Hz per scale unit)

The isomerisation of (15) to (14) (R = Me) is apparently contrary to expectation on steric grounds. However, it appears that the bridgehead proton 4-H eclipsing the *N*-oxide group is far more unfavourable a situation than that in (14), where the *N*-oxide bisects the angle between the C–H and C–R bonds. For (15) $\rightleftharpoons$ (14) (R = Me) at 95°, the equilibrium constant is 4 (ΔG^0 4·4 kJ mol^{-1}).

Mass Spectra.—All new compounds described here gave mass spectra in accord with their assigned structures.

Both the nitriles (23) (for which there is precedent [18]) and the furazan (22; R = Me) showed $(P + 1)^+$ peaks considerably more intense than the parent P^+, owing to hydrogen transfer. The nitrile (19) was more normal, with $(P + 1)^+$ *ca.* 50% of P^+. The mode of sample introduction may affect this ratio: the dinitrile (19) is a solid, the others are liquids. The nitriles (23) gave prominent fragments due to cleavage of the four-membered ring, showing peaks from $R^2_2C{:}CHR^1{\cdot}CN^+$, $R^2_2C{:}CH{\cdot}CHR^1{\cdot}CNH^+$, $R^2_2C{:}CH{\cdot}CN^+$, and $R^2_2C{:}CH{\cdot}CNH^+$ (R^1, R^2 = H or Me).

The mass spectra of furoxans usually show the following features: peaks due to loss of N_2O_2 from the parent, and cleavage to nitrile and nitrile oxide fragments.[15,19,20] A $(P - 16)^+$ peak, which usually appears in heterocyclic *N*-oxides,[21] is often weak or absent in furoxans.[19] In the last respect the furoxans of the present paper are typical, with $(P - 16)^+$ peaks insignificant beside $(P - 15)^+$ (—Me) when methyl groups are present, and $(P - 17)^+$ (—OH). A fuller account of the mass spectra of these compounds will be published elsewhere.

General Conclusions.—The objectives outlined in the introduction are still largely unattained. The strain present in the 4,6-methanobenzofurazan *N*-oxide series, while producing anomalous phosphite cleavage of the ring, does not apparently alter the rate of isomerisation, since the conversion (15) ⟶ (14) (R = Me) proceeded at a rate similar to that found in other examples.[14,15] In the more highly strained cases, ring cleavage (of C–C and N–O bonds) probably takes precedence over isomerisation, but firm evidence has still to be obtained.

EXPERIMENTAL

N.m.r. spectra at 100 and 60 MHz were taken with Varian HA 100 and Perkin-Elmer R 12 instruments, respectively. Mass spectra were measured on a Perkin-Elmer–Hitachi RMU 21 spectrometer, with 70 V ionising potential. I.r. spectra, for the concentration determinations in the rate measurements, were run in 0·1 mm NaCl cells, with an equivalent strength of phosphite solution in the compensating beam, on a Perkin-Elmer model 225 grating spectrometer. The peaks measured followed Beer's law, with slight deviation. The reactions were thermostatted to ±0·2° in a water-bath.

Oxidation of Cyclopentane-1,2-dione Dioxime (5).—The dioxime,[22] dissolved in the minimum amount of aqueous 2N-NaOH at 0°, was apparently unchanged on addition of neutral aqueous sodium hypochlorite. Subsequent passage of chlorine produced a small amount of a white precipitate, accompanied by a green-blue colour. The solid decomposed rapidly on the paper during filtration.[8]

Oxidation of Indane-1,2-dione Dioxime (7).—The dioxime (2·5 g), prepared by the method of Bark and Brandon,[23] was oxidised in 1N-sodium hydroxide (25 ml) at 0° with a solution of bromine (4 g) in 2N-sodium hydroxide in the presence of chloroform (50 ml), with continuous shaking. After 0·5 h the organic layer was separated, dried ($MgSO_4$), and heated under reflux for 1 h with trimethyl phosphite (15 ml). The solution was cooled and poured into water, and the excess of phosphite was hydrolysed by addition of a few drops of conc. hydrochloric acid. The organic layer was again separated, and the solvent was removed *in vacuo*. The residue was chromatographed on alumina (Woelm, activity 1), eluting with benzene, to give *o*-cyanobenzyl cyanide (0·3 g, 15%) as pink plates, m.p. 81° (lit.,[24] 81°). Conditions for the reaction are apparently critical, since we were unable to detect any nitrile products in later experiments on phosphite reduction of chloroform, benzene, or carbon tetrachloride extracts of the hypobromite oxidation of the dioxime, despite many attempts to reproduce the conditions above.

5,6-Dihydro-5,5-dimethyl-4H-cyclopentafurazan 1-Oxide (9).—The diketone prepared from diethyl 3,3-dimethylglutarate and diethyl oxalate [25] was converted into the dioxime (6) (40% yield), m.p. 204—205° (decomp.), with hydroxylamine hydrochloride and sodium acetate in aqueous methanol. The crude dioxime (0·25 g) in aqueous 10% NaOH (10 ml) was oxidised by aqueous sodium hypochlorite (10 ml; prepared by passing Cl_2 into aqueous 20% NaOH until neutral). A white precipitate was formed, which was filtered off and crystallised from light petroleum (b.p. 40—60°), giving the *furazan N-oxide* (0·2 g, 80%) as plates, m.p. 68° (Found: C, 54·8; H, 6·6; N, 18·2. $C_7H_{10}N_2O_2$ requires C, 54·6; H, 6·5; N, 18·2%), $\nu_{max.}$ 1665 and 1540 cm^{-1} (furazan), τ (CCl_4) 8·68 (6H), 7·44 (2H), and 7·32 (2H).

Considerable charring occurred on heating the furazan *N*-oxide (9) with phenylacetylene in CCl_4 at 100° (sealed tube). However only starting material was obtained from the residue. Unidentified products (i.r.: no C≡N or furazan bands) were obtained after reflux of (9) with trimethyl phosphite.

Acenaphtho[1,2-c]furazan 1-Oxide (3).—This was prepared according to Rowe and Davies,[5] and isolated as pink needles, m.p. 198—199° (lit.,[5] 199°), the colour of which we were unable to remove completely, although from its variable intensity it was undoubtedly caused by contamination.

4,5,6,7-Tetrahydro-4,8,8-trimethyl-4,7-methanobenzofurazan 1-Oxide (1a and 1b; R = Me).—This was prepared as described,[4] m.p. 143—144° (lit.,[4] 144°).

2-Oxobornan-10-oic Acid (12).—2-Oxobornane-10-sulphonic acid was converted, *via* the acid chloride, into 2-oxobornan-10-oic acid by the method of Bartlett and Knox,[26] m.p. 228° (lit.,[26] 233—234°). An attempt to prepare the isonitroso-derivative of this acid, with pentyl nitrite and potassium t-butoxide (2 mol), failed; only unchanged acid was obtained from the mixture on work-up.

1-Bromo-7,7-dimethylnorbornan-2-one (13).—2-Oxobor-

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nan-10-oic acid (3·2 g) in methanol (40 ml) was titrated (phenolphthalein) with methanolic 5% KOH to neutrality. Aqueous silver nitrate (3·5 g in 10 ml) was then added, with vigorous shaking, and the precipitated white solid was filtered off and dried to give the crude silver salt (5·9 g). This (5 g) was added in small portions to bromine (4 g) in CCl_4 (40 ml) (both dried over P_2O_5 and distilled) at 50°. Carbon dioxide was evolved and silver bromide was precipitated. The mixture was heated at 60° for 15 min, cooled, and filtered. The solution was washed with aqueous sodium hydrogen sulphite, sodium hydrogen carbonate, and water, and then dried ($MgSO_4$). Removal of solvent left the *bromo-ketone* (3·4 g, 50%) as white needles, m.p. 190° (sealed tube; lit.,[27] 192—193°) (from light petroleum) (Found: C, 49·8; H, 5·7. $C_9H_{13}BrO$ requires C, 49·8; H, 6·0%), $\nu_{max.}$ 1755 cm^{-1} (C=O).

1-*Bromo*-7,7-*dimethylnorbornane*-2,3-*dione Dioxime*.—Potassium (6 g) was dissolved in t-butyl alcohol (160 ml) and the foregoing ketone (8 g) was added to the solution, which was stirred for 20 min. Pentyl nitrite (17 g) was added dropwise with cooling, and the solution was stirred for a further 20 min. Then light petroleum (b.p. 40—60°; 250 ml) was added and the mixture was stirred for a further 2·5 h. The mixture was then extracted twice with water and once with 0·05N-NaOH (100 ml). The aqueous extracts were combined, acidified (HCl), and extracted with ether. The ether extracts were dried ($MgSO_4$) and the solvent was removed under reduced pressure, leaving the bromo-isonitroso-ketone as an oil, which was used without purification.

The bromo-isonitroso-ketone was heated to reflux in ethanol (250 ml) and water (100 ml) with hydroxylamine hydrochloride (7 g) and sodium acetate (14 g) for 5 h. An equal volume of water was then added and the mixture was left at 0° overnight. The precipitated white solid was separated by filtration and crystallised from ethanol (charcoal) to give the *dioxime* (3·0 g, 36%) as white prisms, m.p. 175° (decomp.) (Found: C, 41·1; H, 5·0; N, 10·4. $C_9H_{13}BrN_2O_2$ requires C, 41·4; H, 5·0; N, 10·7%).

4-*Bromo*-4,5,6,7-*tetrahydro*-8,8-*dimethyl*-4,7-*methanobenzofurazan* N-*Oxide* (2).—To the above dioxime (1·5 g) in aqueous 10% KOH (10 ml) at 0° was added aqueous 10% potassium hypobromite, also at 0°, until no further precipitate was formed. The solid was filtered off, dried, and recrystallised from light petroleum as small white needles, m.p. 113°, of the *furazan* N-*oxide* (0·4 g, 27%) (Found: C, 41·7; H, 4·6; N, 10·7. $C_9H_{11}BrN_2O_2$ requires C, 41·7; H, 4·3; N, 10·8%), $\nu_{max.}$ 1630 and 1560 cm^{-1} (furazan *N*-oxide).

4,4a,6,7,7a,8-*Hexahydro*-4,8-*methano*-5H-*indeno*[5,6-c]*furazan* 1-*Oxide* (11).—Tricyclo[5,2,1,$0^{2,6}$]decan-8-one * (10) was converted into its isonitroso-derivative, and thence into the *dioxime* (m.p. 177°, decomp.) (Found: C, 61·8; H, 7·1; N, 14·3. $C_{10}H_{14}N_2O_2$ requires C, 61·8; H, 7·1; N, 14·4%) following the method described above for the bromonorbornanone (13). Oxidation of the dioxime was effected by sodium hypochlorite in the usual way, to give the *furazan* N-*oxide* (25% yield overall) as needles, m.p. 62—63° (from light petroleum) (Found: C, 62·4; H, 6·2; N, 14·5. $C_{10}H_{12}N_2O_2$ requires C, 62·5; H, 6·3; N, 14·8%). $\nu_{max.}$ 1670 and 1550 cm^{-1} (furazan *N*-oxide).

The compound is unstable on storage; although its macroscopic appearance was normal, microscopic examination of a one-year-old sample showed considerable deterioration into amorphous matter, which was insoluble in light petroleum and in carbon tetrachloride.

4,5,6,7-*Tetrahydro*-5,5-*dimethyl*-4,6-*methanobenzofurazan* 1-*Oxide* (14; R = H).—Pin-2(10)-ene was converted into 6,6-dimethylnorpinan-2-one (16) by ozonolysis, and the isonitroso-derivative was prepared, following the procedure of Meinwald and Gassman.[28] The isonitroso-compound (10 g) was heated under reflux for 4 h in ethanol–water (1 : 1; 200 ml) with hydroxylamine hydrochloride (11 g) and sodium acetate (22 g). The precipitate, which formed after cooling and addition of water (100 ml), was crystallised from ethanol, giving buff needles of 6,6-*dimethylnorpinane*-2,3-*dione dioxime* (5·5 g, 50%), m.p. 233° (decomp.) (Found: C, 59·2; H, 7·6; N, 15·0. $C_9H_{14}N_2O_2$ requires C, 59·3; H, 7·7; N, 15·3%). The dioxime (4·5 g) was oxidised at 0° in aqueous 10% NaOH by addition of 10% sodium hypochlorite until precipitation ceased. The solid was removed by filtration and crystallised from light petroleum (b.p. 40—60°), giving the *furazan* N-*oxide* (2·25 g, 50%) as white needles, m.p. 58·5° (Found: C, 59·8; H, 6·4; N, 15·4. $C_9H_{12}N_2O_2$ requires C, 60·0; H, 6·6; N, 15·5%), $\nu_{max.}$ 1655 and 1540 cm^{-1} (furazan *N*-oxide) N.m.r. details are given in the Table.

4,5,6,7-*Tetrahydro*-5,5,7β-*trimethyl*-4α,6α-*methanobenzofurazan* N-*Oxide* [(14) ⇌ (15); R = Me].—Pin-2-en-4α-ol (*gem*-dimethyl bridge is considered to be β) (*trans*-verbenol) (16 g), prepared by the method of Whitham [29] was oxidised with manganese dioxide [30] (75 g) in dichloromethane (250 ml). The mixture was filtered and the manganese dioxide washed with dichloromethane. Evaporation of the filtrate gave crude pin-2-en-4-one ($\nu_{max.}$ 1670 and 1615 cm^{-1}) which was taken up in ethanol (100 ml) and stirred in a hydrogen atmosphere with PtO_2 (100 mg). After 2 h the hydrogen uptake ceased. The solution was filtered, the solvent was removed at the pump, and the residue was distilled under reduced pressure to give pinan-4-one (12 g, 75%), b.p. 70° at 3 mmHg (lit.,[31] b.p. 220—225°). Pinan-2-one (17) was converted into its *isonitroso-derivative*,† m.p. 171—172° (decomp.) (Found: C, 66·2; H, 8·1; N, 7·5. $C_{10}H_{15}NO_2$ requires C, 66·3; H, 8·3; N, 7·7%), following the method described above for the bromonorbornanone (13). The isonitroso-derivative (1 g) in methanol (25 ml) was treated with hydroxylamine hydrochloride (1 g) and sodium acetate (1·2 g) in water (5 ml) at room temperature for 12 h. The mixture was then poured onto ice and the precipitated *dioxime* filtered off (900 mg, 85%), m.p. 238—240° (decomp.) (from ethyl acetate) (Found: C, 61·2; H, 8·1; N, 14·0. $C_{10}H_{16}N_2O_2$ requires C, 61·2; H, 8·2; N, 14·0%). Oxidation of the dioxime (1 g) was effected by stirring with ethyl acetate (50 ml) and aqueous potassium ferricyanide solution (100 ml, 10%) containing saturated aqueous sodium carbonate solution (10 ml). After 1 h the organic layer was

* Aldrich Chemical Co. The suppliers were unable to state whether it was the *exo*- or *endo*-isomer.

† (+)-Isonitrosopinan-4-one is well authenticated, but data on the (±)-compound have not appeared in the literature.

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separated, washed with brine, and decolourised with alumina (4 g), eluting with ether. Evaporation of the eluate under reduced pressure gave the *furazan* N-*oxide* (15), flakes (750 mg; 76%), m.p. 73—75° (from light petroleum) (Found: C, 62·0; H, 7·2; N, 14·3. $C_{10}H_{14}N_2O_2$ requires C, 61·8; H, 7·3; N, 14·4%), $\nu_{max.}$ 1640 and 1515 cm^{-1} (furazan *N*-oxide). Isomerisation of (15) (500 mg) was effected by heating under reflux in toluene (5 ml) for 4 h. The mixture was decolourised with alumina (2 g), eluting with ether. The solvent was removed at the pump and the residue was crystallised from light petroleum to give the *furazan* N-*oxide* (14) (300 mg, 60%) as long glistening needles, m.p. 85—87° (Found: C, 62·0; H, 7·3; N, 14·1%), $\nu_{max.}$ 1630 and 1535 cm^{-1} (furazan *N*-oxide).

The equilibrium constant for (14) ⇌ (15) was determined from the integration of the n.m.r. spectrum of a solution of (14) in chlorobenzene which had been heated at 95° until no further change in the spectrum was observed.

Phosphite Reduction.—(*a*) *Quantitative* (*kinetic*). Aliquot portions (*ca.* 0·2 g) of the furazan *N*-oxides (1), (3), and (11) were heated in benzene with a 5—15-fold excess of trimethyl phosphite, in a thermostatted water-bath (±0·2°). Before heating, and at intervals of *ca.* 5 min, samples were withdrawn and their i.r. spectra were scanned over the regions 2300—2100 and 1700—1600 cm^{-1}, with 0·1 mm pathlength NaCl cells, with benzene in the compensating beam. The results are shown in Figures 1 and 2.

(*b*) *Qualitative* (*preparative*). Furazan *N*-oxides (1), (3), (9), and (11) (*ca.* 1 g) were heated under reflux for 3—4 h with trimethyl phosphite (15 ml). The mixture was cooled, poured into water, acidified (conc. HCl; *ca.* 0·2 ml), and left for 12 h. The resulting mixture was extracted with benzene or ether, the extracts were dried ($MgSO_4$), the solvent was removed *in vacuo*, and the residue was recrystallised from light petroleum. Thus were obtained camphoronitrile (19), m.p. 160° (lit.,[32] m.p. 160°) (88%, naphthalene-1,8-dicarbonitrile, m.p. 230—232° (lit.,[33] 232°) (82%), and cis-*octahydropentalene*-1,3-*dicarbonitrile* (20) (50%), m.p. 55° (Found: C, 74·8; H, 7·6; N, 17·6. $C_{10}H_{12}N_2$ requires C, 75·0; H, 7·5; N, 17·5%), $\nu_{max.}$ 2240 and 2230 cm^{-1} (CN). Only a small quantity of an unidentified product was obtained from furazan *N*-oxide (9) in this way.

No nitrile was obtained on hypochlorite oxidation, followed by phosphite reduction, of cyclopentane-1,2-dione dioxime. The results with dioxime (7) are described above.

Phosphite reduction of furazan *N*-oxide (14; R = H and Me) was effected as follows. The furazan *N*-oxide (250 mg) in trimethyl phosphite (2 ml) was heated under reflux for 3 h and the cooled solution was poured into dilute aqueous HCl (25 ml, 3%). When the odour of phosphite had disappeared the solution was extracted with light petroleum (2 × 10 ml) and the extracts were dried. Evaporation of the solvent gave the *furazan* as an oil, which crystallised as long shining needles on cooling a solution in light petroleum to *ca.* −20°. In this manner were obtained 4,5,6,7-*tetrahydro*-5,5-*dimethyl*-4,6-*methanobenzofurazan* (22; R = H) (75%), m.p. 39° (Found: C, 66·1; H, 7·2; N, 17·0. $C_9H_{12}N_2O$ requires C, 65·8; H, 7·4; N, 17·1%); and 4,5,6,7-*tetrahydro*-5,5,7β-*trimethyl*-4α,6α-*methanobenzofurazan* (22; R = Me), oil (70%), m.p. *ca.* 0° (Found: C, 67·6; H, 7·8; N, 15·9. $C_{10}H_{14}N_2O$ requires C, 67·4; H, 7·9; N, 15·7%).

Reduction of the furazan *N*-oxides (14; R = H and Me) (100 mg) to the dinitriles (23; R = H and Me), was was achieved by using more forcing conditions [triethyl phosphite under reflux (2 ml, 4 h)] than those required for reduction to furazan. The work-up procedure involved hydrolysis of the unchanged phosphite, ether extraction (2 × 25 ml), followed by careful chromatography of the crude product on silica gel (10 g) eluting with ether–light petroleum (1 : 2). The dinitriles were distilled by the method of Harding and Kinnel.[34] In this way were obtained as oils: (cis-3-*cyano*-2,2-*dimethylcyclobutyl*)*acetonitrile* (45%) (Found: C, 72·6; H, 8·1; N, 18·9. $C_9H_{12}N_2$ requires C, 72·9; H, 8·2; N, 18·9%) and 2-(cis-3-*cyano*-2,2-*dimethylcyclobutyl*)*propiononitrile* (65%) (Found: C, 74·3; H, 8·7; N, 17·3. $C_{10}H_{14}N_2$ requires C, 74·0; H, 8·7; N, 17·3%).

1,2,2-*Trimethyl*-1,3-*bis*-(5-*phenylisoxazol*-3-*yl*)*cyclopentane* (24).—Heating the furazan *N*-oxide (1) (1 g) with phenylacetylene (1·1 g) in CCl_4 (20 ml) for 12 h in a sealed tube at 100°, followed by removal of the solvent, left an amorphous solid residue which formed stable gels with a wide variety of solvents (C_6H_6, CCl_4, $CHCl_3$, ligroin, Et_2O, EtOH, *etc.*), from which the solvent could be removed by pressing, leaving an amorphous mass. After several days the ethanolic gel formed crystals; subsequently, recrystallisation was effected without difficulty. The *adduct* (24) formed white needles, m.p. 134—135° (from ethanol) (Found: C, 78·1; H, 6·4; N, 7·1. $C_{26}H_{26}N_2O_2$ requires C, 78·3; H, 6·5; N, 7·0%).

1,3-*Bis*-(5-*phenylisoxazol*-3-*yl*)*octahydropentalene* (25).—This was similarly prepared from the furazan *N*-oxide (11) at 55°, over 24 h. Chromatography on alumina (MeOH) gave the *perhydropentalene* (25), which crystallised from light petroleum as needles, m.p. 133—134° [Found: C, 79·1; H, 6·2; N, 7·1%; *M* (mass spec.), 396. $C_{26}H_{24}N_2O_2$ requires C, 78·8; H, 6·1; N, 7·1%; *M*, 396]. Both this and the foregoing product (24) had a prominent i.r. absorption at 3130 cm^{-1}, characteristic of isoxazoles with an unsubstituted ring position.*

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* Although normally described as of 'weak' intensity (S. Califano, F. Piacenti, and G. Speroni, *Spectrochim. Acta*, 1959, **15**, 86; E. Borello, *Gazzetta*, 1959, **89**, 1437), the ν(CH) bands of isoxazoles are nevertheless unusually strong, in comparison with vibrations of this type in other ring systems (A. J. Boulton, unpublished data).