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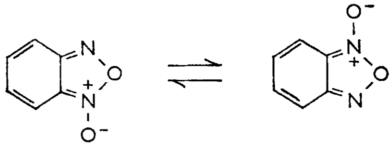
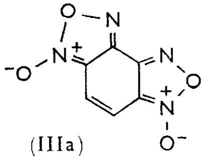
1116. *Heterocyclic Rearrangements. Part IV.*[1] *Furoxano- and Furazano-benzofuroxan*

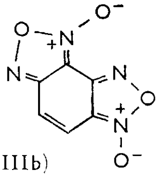
By A. J. Boulton, A. C. Gripper Gray, and A. R. Katritzky

The title compounds are shown to exist in two isomeric forms which undergo rapid interconversion at elevated temperatures. ΔG and ΔG^* values are determined and compared with those of benzofuroxan.

Benzofuroxan has been shown by work from this laboratory,[2] and from elsewhere,[3] to be benzo-2,1,3-oxadiazole 1-oxide, (I) rapidly equilibrating with the 3-oxide (II). We have now studied furoxanobenzofuroxan (III) and furazanobenzofuroxan (IV). The former could exist in three forms (IIIa—c) of which one (IIIc) is expected to be sterically highly improbable and will not be further considered. The latter should exist in two interconvertible forms (IVa, b); in addition there is the possibility of a new type of rearrangement (IVb) ⟶ (V). We now present variable-temperature proton nuclear magnetic resonance (n.m.r.) spectra which provide evidence for the rearrangements (IIIa $\rightleftharpoons$ b) and (IVa $\rightleftharpoons$ b) and allow calculation of equilibrium constants and energies of activation.


(I) (II)


(IIIa)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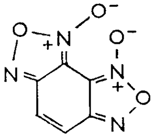
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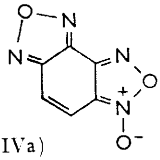
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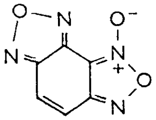
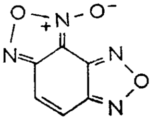

(IVb)


(V)

Preparation of Compounds.—Furoxanobenzofuroxan (III) and furazanobenzofurazan (VI) have been reported [4] as arising by oxidation and dehydration, respectively, of 2,4-dinitrosoresorcinol dioxime. Repetition of this work led to only a very small amount of the bisfuroxan (III), and no bisfurazan (VI); an alternative route was therefore devised, according to the scheme outlined below, which led also to the furazanobenzofuroxan (IV).

5-Chlorobenzofuroxan (VII) (prepared either from 4-chloro-2-nitroaniline or from 5-chloro-2-nitroaniline) was nitrated to give the 4-nitro-derivative (VIII),[5] which on treatment with sodium azide formed the bisfuroxan (III), presumably *via* the intermediate

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[1] Part III, A. J. Boulton, P. B. Ghosh, and A. R. Katritzky, *Angew. Chem.*, 1964, **76**, 816; *Angew. Chem. Internat. Edn.*, 1964, **3**, 693.

[2] R. K. Harris, A. R. Katritzky, S. Øksne, A. S. Bailey, and W. G. Paterson, *J.*, 1963, 197; A. R. Katritzky, S. Øksne, and R. K. Harris, *Chem. and Ind.*, 1961, 990.

[3] *Inter alia*, G. Englert, *Z. Elektrochem.*, 1961, **65**, 854; P. Diehl, H. A. Christ, and F. B. Mallory, *Helv. Chim. Acta*, 1962, **45**, 504.

[4] H. Goldschmidt and J. Strauss, *Ber.*, 1887, **20**, 1607; R. Nietski and W. Geese, *Ber.*, 1899, **32**, 505.

[5] A. J. Boulton and A. R. Katritzky, *Rev. Chim.* (*Acad. R.P.R.*), 1962, **7**, 691.

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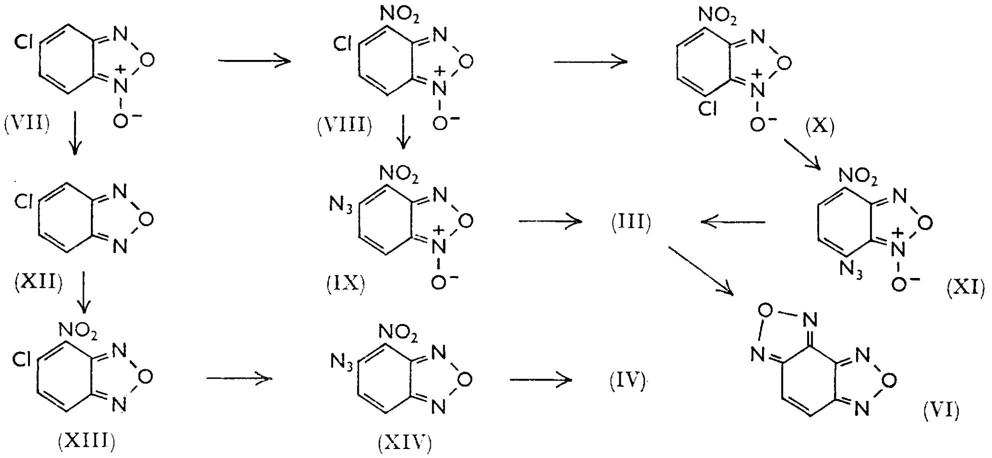
azido-nitro-compound (IX), which was not isolated: nitrogen was evolved from the reaction medium even at 0°. Thermal rearrangement of compound (VIII) into its isomer (X),[5] followed by displacement of chloride by azide, gave an isolable nitroazidobenzofuroxan (XI), which on heating provided the bisfuroxan, probably through the same intermediate (IX) formed from (XI) by another rearrangement of the type (VIII) $\longrightarrow$ (X).

Reduction of the 5-chlorobenzofuroxan to the chlorobenzofurazan (XII), using hydroxylamine,[6] or more conveniently using trimethyl phosphite, followed by nitration, gave 5-chloro-4-nitrobenzofurazan (XIII). The azide (XIV), formed analogously to (IX), was again unstable, the reaction leading directly to the furazanobenzofuroxan (IV).



Usually the crude product fused over a range of about 10° (50—60°), a property which persisted after recrystallisation. On one occasion, however, a product with a higher, sharp melting-point (76—77°) was obtained, and with a somewhat simpler infrared spectrum lacking several of the bands of the lower-melting product. Remelting of the material with the higher melting point occurred at the lower, ill-defined temperature, and recrystallisation also gave the lower-melting product. Sublimation of the 50—60° material gave a solid melting at a still lower temperature, but more sharply (46—47°). Thin-layer chromatography on alumina, in carbon tetrachloride or benzene–light petroleum as solvent, revealed single spots in each case. It thus became apparent that we were dealing with a mixture of the two forms (IVa) and (IVb), which are almost separable at ordinary temperatures, and are rather more stable in the crystalline phase than in solution. This conclusion is entirely compatible with the thermodynamic data obtained from the n.m.r. experiments, which indicate that ΔG^* for interconversion is about 22 kcal./mole (see later). A similar effect might have been expected with the furoxanobenzofuroxan (IIIa $\rightleftharpoons$ IIIb), but this was not observed.

The bisfuroxan (III) was reduced to the bisfurazan (VI) using trimethyl phosphite, after several unsuccessful attempts with hydroxylamine, triphenylphosphine, and alkaline ethanol.

Proton Magnetic Resonance Spectra.—Solutions in acetone, diglyme, and dimethyl sulphoxide were most generally employed, with the addition of a little tetramethylsilane as internal standard. Spectra were measured, with sample spinning, at 34°c using a Perkin-Elmer 40 Mc./sec. permanent-magnet spectrometer, and at other temperatures using a Varian Associates A60 instrument, fitted with a Varian V6040 temperature control and V6031 variable temperature probe, in which the sample is heated by a stream of hot nitrogen. The temperature calibration of the instrument was checked and corrected against the variation in chemical shift between the methylene and hydroxyl protons of a

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[6] T. Zincke and S. Schwarz, *Annalen*, 1899, **307**, 39.

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standard sample of ethylene glycol:[7] temperatures quoted are considered accurate to ±2°. Free energies of activation, ΔG^*, are obtained from the coalescence temperature, T_c, by application of the expression (derived from Eyring's equation):

$$\Delta G^* = \boldsymbol{R}T_c \ln(\sqrt{2}kT_c/h\pi\delta) = 4{\cdot}59T_c\,[9{\cdot}97 + \log_{10}(T_c/\delta)] \qquad (1)$$

where δ is the chemical shift being averaged, in c./sec.

RESULTS AND DISCUSSION

Spectral Patterns.—The room-temperature spectrum of furoxanobenzofuroxan (III) at 40 and at 60 Mc./sec. showed an A_2 singlet and an AB pattern with a small chemical shift between the A and B protons. These types are assigned (Table 1) to (IIIa) and (IIIb), respectively. Integration of spectra measured in acetone (Figure 1) and in dimethyl sulphoxide showed that (IIIb) predominated by a factor of 1·6 : 1; however, in considering the free-energy difference between the forms, the statistical factor of 2 in favour of (IIIb) must be considered. This leads to a small ΔG of 100—150 cal. in favour of (IIIa).

TABLE 1

N.m.r. spectrum of furoxanobenzofuroxan

			AB Spectrum				A
Solvent	Mc./sec.	T	τ_A	τ_B	$\Delta\tau_{AB}$	J_{AB}	τ_A
Acetone	60	27	2·42	2·52	0·10	10·0	2·68
Dimethyl sulphoxide	60	27	2·32	2·42	0·10	10·0	2·61
Diglyme	60	27	2·43	2·54	0·11	—	2·70
Diglyme	60	148	2·73[a]		—	—	—
Dioxan	40	34	2·57[b]		—	9·9	2·75
Acetonitrile	40	34	2·59[b]		—	10·4	2·81
Trifluoroacetic acid	40	34	2·50	2·58	0·075	10·4	2·72
Sulphuric acid	40	34	2·38[b]		—	—	2·54

[a] Time-averaged spectrum (A_2). Mid-point of AB spectrum: central peaks unresolved.

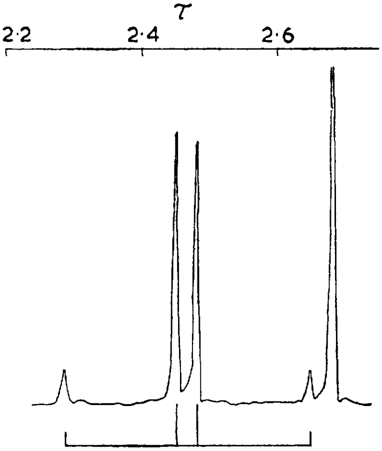

FIGURE 1. N.m.r. spectrum of furoxanobenzofuroxan in acetone at 27°C and 60 Mc./sec.

High-temperature spectra of (III) in dimethyl sulphoxide showed considerable broadening above 100°, and there was some suggestion of coalescence near 140°, but with darkening of the solution and loss of intensity. After heating to 170°, the sample had evidently completely decomposed, as shown by its spectrum after cooling.

Furoxanobenzofuroxan (III) was more stable in diglyme; rapid heating to 180° and

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[7] Method developed by Varian Associates (1962): $T = 188{\cdot}5 - 1{\cdot}660\Delta\nu$ at 60 Mc/sec.

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subsequent cooling gave an unchanged room-temperature spectrum. Spectra taken at various temperatures showed coalescence of the broadened central AB doublet with the A_2 singlet at 137°: in theory there are two coalescence temperatures as the $A_2 - A$ and $A_2 - B$ separations are different. However, these temperatures would be very close to each other. ΔG^* is calculated from equation 1 to be 21·7 ± 0·3 kcal.

TABLE 2

N.m.r. spectra of furazanobenzofuroxan

			AB systems				AB systems			
Solvent	Mc./sec.	T	τ_A	τ_B	$\Delta\tau_{AB}$	J_{AB}	τ_A	τ_B	$\Delta\tau_{AB}$	J_{AB}
Acetone	40	34	2·05	2·15	0·096	9·9	2·18	2·42	0·235	10·0
Dioxan	40	34	2·12	2·22	0·093	9·9	2·26	2·46	0·205	9·9
Dimethyl sulphoxide	60	27	1·97	2·07	0·108	10·1	2·12	2·32	0·207	10·0
Diglyme	60	29	2·06	2·18	0·128	10·1	2·23	2·43	0·207	10·0
Diglyme	60	171	—[a]	—	—	—	2·27	2·47	0·201	9·4

[a] Single AB system.

The room-temperature spectrum of furazanobenzofuroxan (IV) disclosed two overlapping AB spectra (Figure 2). Integration of the spectrum determined in dimethyl sulphoxide showed that isomer (IVa) was favoured over (IVb) by a factor of *ca* 1·2 : 1, *i.e.*, $\Delta G \sim 100$ cal. Heating in dimethyl sulphoxide caused decomposition, but in diglyme a distinct, although still broadened, single AB pattern was obtained at 171° (Figure 3). Above 125°, the lower-field AB pattern is not sufficiently resolved for peaks 2 and 3 to be distinguished, but this broad peak merges with peaks 2 and 3 of the high-field quartet at 141° and 144°, respectively. This gives estimates of $\Delta G^* = 21·8 \pm 2$ and $22·2 \pm 2$ kcal., respectively. The temperature variation of ΔG for the equilibrium (IVa $\rightleftharpoons$ IVb) should be available from (*a*) the variation in area under the two AB patterns in the range 30—100°, and (*b*) comparison of the chemical shifts of the single AB pattern at 170° with those of the two AB patterns at lower temperatures. It appeared that (IVa) predominated over the entire range, but the measurements were not considered sufficiently accurate to allow estimates of ΔH and ΔS to be made.

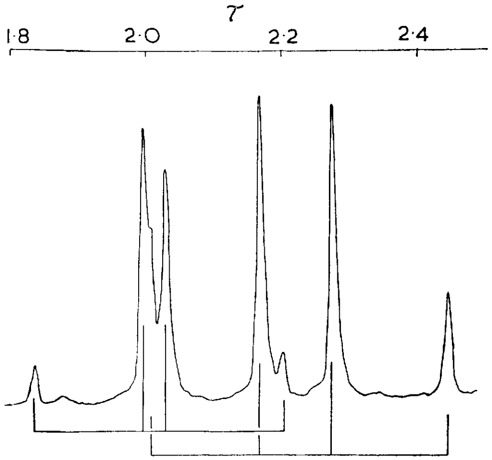

FIGURE 2. N.m.r. spectrum of furazanobenzofuroxan in dimethyl sulphoxide at 27°C and 60 Mc./sec.

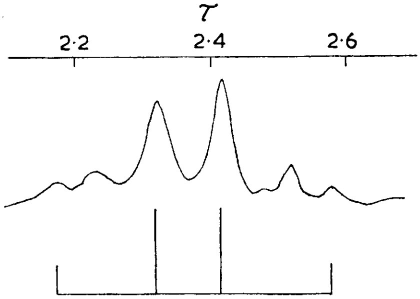

FIGURE 3. N.m.r. spectrum of furazanobenzofuroxan in diglyme at 171°C and 60 Mc./sec. (The peaks at *ca.* 2·22 and 2·52 p.p.m. are spinning sidebands.)

4-Nitro-7-azidobenzofuroxan (XI) gave a single AB pattern; it would be expected to exist essentially completely as (XI).

Energies of Activation.—The ΔG^* values (*ca.* 22 kcal.) for compounds (III) and (IV)

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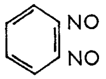
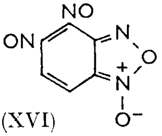
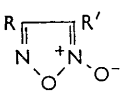
are markedly higher than those (*ca.* 15 kcal.) determined[2,3] for simple benzofuroxans of type (I). Rearrangement of benzofuroxan (I) occurs *via* *o*-dinitrosobenzene (XV), and the resonance energy of the fully-formed benzene ring in (XV) is undoubtedly an important factor in facilitating the rearrangement. Rearrangement of (III) and (IV) will involve intermediates of type (XVI) which do not possess such benzene resonance, and are thus less stable. Simple furoxans (XVII) are still more stable;[8] their rearrangement would have to occur *via* the dinitroso-olefins (XVIII).



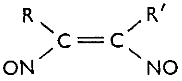
(XV)



(XVI)



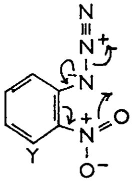
(XVII)

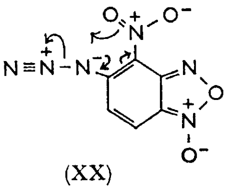


(XVIII)

Similar considerations may explain the spontaneous elimination of nitrogen when 5-chloro-4-nitro-benzofuroxan (VIII) or -benzofurazan (XIII) were treated with sodium azide, even at 0°. Simple *o*-nitrophenylazides decompose readily only above 70° and indeed in our experience several 3-substituted-2-nitroazido-compounds have proved very difficult to decompose satisfactorily. The reaction probably proceeds by the cyclic mechanism (XIX);[9] the adverse effect of Y in (XIX) is felt to be due to steric hindrance to coplanarity. It may now be seen that the loss in benzene resonance energy in forming the transition state (XX) is considerably lower than that to form (XIX).

(XIX)





(XX)

Regarding the energy difference between the isomers (IIIa, b) and (IVa, b), it is of interest that in each case the structure with no oxygen atom between the rings is slightly favoured. This may be due to lone-pair repulsion [greater in (IIIb) and (IVb)] or to differential solvation.

TABLB 3

N.m.r. spectra of benzofuroxan and related compounds in acetone solution

Substituent	Time-averaging	Chemical shift, τ				$J_{4,5}$	$J_{5,6}$	$J_{5,6}$	T (°c)
		4	5	6	7				
None	No	2·29	2·49	2·65	2·54	9·2	6·4	9·2	20[a]
4-Nitro-7-azido	No	—	1·41	2·67	—	—	8·2	—	34
4,5-Furoxano (*sym*)	No	—	—	2·63	2·63	—	—	—	34
4,5-Furoxano (*asym*)	No	—	—	2·37	2·45	—	—	10·2	34
4,5-Furazano	No	—	—	2·18	2·42	—	—	10·0	34
6,7-Furazano	No	2·15	2·05	—	—	9·9	—	—	34
Benzofurazan	—	2·04	2·40	2·40	2·04	9·3	6·5	9·3	20
4,5-Furazanobenzofurazan	—	—	—	1·86	1·86	—	—	—	34

[a] Corrected from −42°.

Chemical Shifts and Coupling Constants (*Table* 3).—In acetone solution, benzene shows a chemical shift of τ 2·69. Annellation of a furazan or a furoxan ring causes shifts to lower field as shown in (XXI) and (XXII).[2] The effects shown in (XXI) and (XXII) must include

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[8] J. V. R. Kaufman and J. P. Picard (*Chem. Rev.*, 1959, **59**, 429) list several pairs of isomers of unsymmetrical furoxans. Interconversion has not been demonstrated to date. [*Added in proof.*—Slow interconversion has now been observed by Mr. A. Majid Hamid in these laboratories.]

[9] T. F. Fagley, J. R. Sutter, and R. L. Oglukian, *J. Amer. Chem. Soc.*, 1956, **78**, 5567; E. Andersen, E. A. Birkhimer, and T. A. Bak, *Acta Chem. Scand.*, 1960, **14**, 1899.

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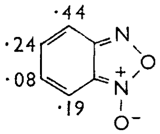
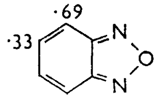
inductive, mesomeric, and anisotropic shifts, together with an upfield shift because the ring current is less in these derivatives than in benzene. There are eight types of nuclear



(XXI)



(XXII)

proton in the species (IIIa, IIIb, IVa, IVb, and VI), and these show chemical shifts in the range 1·86—2·63 τ (Table 3). These chemical shifts are correlated by considering the effects of the two annellated rings as additive, provided 0·15 p.p.m. is added to the result. The discrepancies are then within the range —0·04 to +0·06 [mean 0·00, standard deviation ±0·03]. The correction factor of +0·15 p.p.m. at first sight indicates that the annellation of the second ring has a greater effect on the reduction of ring current than that of the first. However, this is in direct conflict with the fact that the ΔG^* for opening (to the corresponding dinitroso-compound) a furoxan ring of furoxanobenzofuroxan is *greater* than for opening the heterocyclic ring of benzofuroxan itself. Part of this discrepancy may result from mesomeric effects not being transmitted so well in the tricyclic systems as in benzofuroxan.

EXPERIMENTAL

Ultraviolet spectra were measured on a Perkin-Elmer 137UV recording spectrophotometer, with extinction coefficients checked on a Unicam S.P. 500 instrument. Infrared spectra were taken on a Perkin-Elmer 237 spectrometer.

5-*Chlorobenzofuroxan* (VII).—4-Chloro-2-nitroaniline (54·0 g.) was diazotised and treated with excess of sodium azide, yielding 4-chloro-2-nitrophenyl azide (44·2 g., 72%), m. p. 58—59° (decomp.). 5-Chloro-2-nitroaniline (48·1 g.), prepared from ammonia and 2,4-dichloronitrobenzene, was likewise converted into 5-chloro-2-nitrophenyl azide, which was not purified, but decomposed by boiling in glacial acetic acid to give 5-chlorobenzofuroxan (34·5 g., 83%), m. p. 43—44° (lit.,[10] 48°). Decomposition of 4-chloro-2-nitrophenyl azide (44·2 g.) similarly gave the same chlorobenzofuroxan (28·9 g., 76%), m. p. 44—45° from ethanol–water (1 : 1).

5-*Chloro*-4-*nitrobenzofuroxan* (VIII).—5-Chlorobenzofuroxan (10·0 g.) in sulphuric acid (60 ml.) was treated at 0° with nitric acid (*d* 1·5; 4·03 g.) in sulphuric acid (10 ml.) for 15 min. Precipitation with ice–water yielded the crude nitro-product (11·4 g., 90%), m. p. 68—70° from dichloromethane–carbon tetrachloride (1 : 1) (lit.,[5] 78—81°).

4-*Chloro*-7-*nitrobenzofuroxan* (X).—The rearrangement of the 5-chloro-4-nitrobenzofuroxan was effected by boiling 30 min. in acetic acid. Dilution with water and crystallisation of the precipitate from acetic acid gave orange-yellow prisms (1·45 g., 72%), m. p. 137—138° (lit.,[5] 140—141°).

4-*Azido*-7-*nitrobenzofuroxan* (XI).—The chloro-compound (X) (0·5 g.) in acetone–methanol (1 : 1; 1 ml.) was treated with sodium azide (0·15 g.) in acetone–methanol–water (1 : 2 : 2; 1 ml.). After 1 hr. at 20°, the mixture was diluted with water and the precipitated solids crystallised from ethanol, giving dark red crystals (0·4 g., 80%) of the *azido-compound*, m. p. 118—119° (decomp.; decrepitation at 83°) (Found: C, 32·5; H, 1·0; N, 38·05. $C_6H_2N_6O_4$ requires C, 32·4; H, 0·9; N, 37·85%), $\nu_{max.}$ 2130 (N_3), 1635, 1590, 1545, 1525 (NO_2), 1435, 1325 (NO_2), 1285 cm.$^{-1}$, etc.

Furoxanobenzofuroxan (III).—(*a*) *From* 5-*chloro*-4-*nitrobenzofuroxan* (VIII). The 5-chloro-compound (11·1 g.) in acetone–methanol (1 : 1; 20 ml.) was treated with sodium azide (3·36 g.) in acetone–methanol–water (1 : 2 : 2; 25 ml.). When spontaneous effervescence had ceased (1 hr.), precipitation with water and crystallisation of the solids from ethanol gave very pale yellow crystals (5·1 g., 51%) of the furoxanobenzofuroxan, m. p. 94—95° (lit.,[4] 93°). No infrared band in the azide region, but strong bands at 1640, 1590, 1455, 1440, 1015 cm.$^{-1}$, etc., $\lambda_{max.}$ 282 (19,700), 308 (13,800), 322 (12,400), and 346 mμ (ε 5210).

(*b*) *From* 4-*azido*-7-*nitrobenzofuroxan* (XI). The azide (XI) (0·10 g.) was fused and the

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[10] A. G. Green and F. M. Rowe, *J.*, 1913, **103**, 899.

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temperature maintained at 110—115° until decomposition ceased (15 min.). The furoxanobenzofuroxan (0·017 g., 20%) was sublimed from the sticky residue, and identified (m. p., i.r. spectrum) with the product obtained by method (*a*).

5-*Chlorobenzofurazan* (XII).—5-Chlorobenzofuroxan (20·8 g.) and triethyl phosphite (60 g.) in ethanol were refluxed ½ hr. Steam distillation and crystallisation from aqueous ethanol gave damp needles (12·8 g., *ca.* 60%) of the volatile furazan, m. p. of a dried sample 42—44° (lit.,[6] 44°).

5-*Chloro*-4-*nitrobenzofurazan* (XIII).—5-Chlorobenzofurazan (9·3 g.) in sulphuric acid (60 ml.) was nitrated by addition of nitric aid (*d* 1·5; 4·14 g.) in sulphuric acid (9 ml.) at 0°, then warming to 20° for 10 min. Pouring on to ice precipitated the product, which was crystallised from ethanol, giving 5-*chloro*-4-*nitrobenzofurazan* (7·8 g., 65%) as pale yellow plates, m. p. 64—65° (Found: C, 36·2; H, 1·1; N, 20·8. $C_6H_2ClN_3O_3$ requires C, 36·1; H, 1·0; N, 21·05%). The n.m.r. spectrum (acetone solution) showed an AB quartet, with $\tau_A = 1{\cdot}59$, $\tau_B = 2{\cdot}14$, and $J_{AB} = 9{\cdot}5$ c./sec.

Furazanobenzofuroxan (IV).—5-Chloro-4-nitrobenzofuroxan (1·0 g.) in acetone–methanol (1 : 1; 10 ml.) was treated with sodium azide (0·33 g.) in acetone–methanol–water (1 : 2 : 1; 10 ml.) at 20° for 7—8 hr. Dilution with water gave the crude *furazanobenzofuroxan* (0·67 g., 75%) as colourless needles, m. p. 50—60° (from ethanol or benzene), the melting point of which was not improved by repeated crystallisation (Found: C, 40·6; H, 1·1; N, 31·2. $C_6H_2N_4O_3$ requires C, 40·5; H, 1·1; N, 31·5%), $\lambda_{max.}$ 254 (16,100) and 306 mμ (ε 9400), $\nu_{max.}$ 1665, *1635*, 1605, *1555*, 1535, 1445, *1015*, *1000*, 975 cm.$^{-1}$, etc. Italicised bands were weak or absent in the spectrum of a sample (m. p. 76—77%) formed by precipitation by water shortly after the addition of azide to the chloronitrobenzofuroxan. This sample became identical with the lower-melting material after recrystallisation from ethanol, or after melting.

Furazanobenzofurazan (VI).—Furoxanobenzofuroxan (1·0 g.) in methanol (10 ml.) was heated with trimethyl phosphite (5 ml.) for 48 hr. at 120° (sealed tube). Washing with 2N-sulphuric acid and extraction with dichloromethane gave the furazanobenzofurazan (0·44 g., 48%), m. p. 60—61°, from ethanol (lit.,[4] 61°).

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