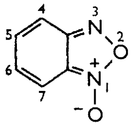
29. *N-Oxides and Related Compounds. Part XIX.* Proton Resonance Spectra and the Structure of Benzofuroxan and its Nitro-derivatives.*

By R. K. Harris, A. R. Katritzky, and S. Øksne, and (in part)
A. S. Bailey and W. G. Paterson.†

A complete interpretation is given for the proton resonance spectra of benzofuroxan and four nitro-derivatives. The temperature-dependence of the spectra enables ΔG^* to be calculated for the tautomeric change of the benzofuroxan heterocyclic ring. Chemical shifts and coupling constants provide information on the electronic structure of benzofuroxans.

Recent proton magnetic resonance spectral evidence has shown that benzofuroxan is 2,1,3-benzo-oxadiazole 1-oxide (I) and disproves the alternative structures (II—IV) which have been proposed (see refs. 1—7). That work has demonstrated that at and below room temperature the benzofuroxan spectrum is unsymmetrical and cannot be that of an A_2B_2 system,[1-3,6,7] but that at elevated temperatures an A_2B_2 pattern is formed, indicating rapid tautomerism.[1,2,4] The subject has been extensively surveyed by Englert.[4] Oxygen-17 resonance experiments are in full agreement.[7a]



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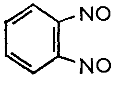

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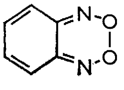

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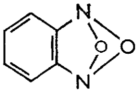

(IV)

We now present a detailed account of our work on nitrobenzofuroxans, which was mentioned in part in our previous note.[1]

Experimental

Compounds were prepared according to the recorded methods cited: benzofuroxan,[8] m. p. 68—69° (lit.,[8] 70—72°); 4-nitro-,[9] m. p. 143—145° (lit.,[9] 143°); 4,6-dinitro-,[9] m. p. 174—175° (lit.,[9] 172°); 5-nitro-,[9] m. p. 68—69° (lit.,[9] 72°); 5,6-dinitro-benzofuroxan,[9] m. p. 175° (lit.,[9] 172°, lit.,[10] 177°).

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* Part XVIII, *J.*, 1961, 43.

† The present results were obtained by the Cambridge workers. Similar room-temperature spectra were obtained in Oxford independently by Bailey and Paterson; they appear as part authors to avoid the proliferation of papers.

[1] Katritzky, Øksne, and Harris, *Chem. and Ind.*, 1961, 990.

[2] Englert, *Z. Naturforsch.*, 1961, **16**b, 413.

[3] Englert, *Z. analyt. Chem.*, 1961, **181**, 447.

[4] Englert, *Z. Electrochem.*, 1961, **65**, 854.

[5] Dischler and Englert, *Z. Naturforsch.*, 1961, **16**a, 1180.

[6] Mallory and Wood, *Proc. Nat. Acad. Sci. U.S.A.*, 1961, **47**, 697.

[7] Bailey and Patterson, personal communication (5th July 1961).

[7a] Diehl, Christ, and Mallory, *Helv. Chim. Acta*, 1962, **45**, 504.

[8] Smith and Boyer, *Org. Synth.*, 1951, **31**, 14.

[9] Drost, *Annalen*, 1899, **307**, 49.

[10] Bailey and Case, *Tetrahedron*, 1958, **3**, 113.

Solutions in acetone were used throughout, except that for 4,6-dinitrobenzofuroxan several solvents were employed. A little tetramethylsilane (TMS) in each solution acted as the internal standard. Measurements were made in Pyrex tubes of 5 mm. outside diameter, and 15 cm. length, sealed under a vacuum (to remove dissolved oxygen).

The spectra were obtained at 40 Mc./sec. with a Varian Associates V 4300B nuclear magnetic resonance spectrometer and 12″ electromagnet with flux stabilisation, sample spinning, and a Varian V 4365 field-homogeneity control unit. " Room temperature " refers to measurements made at 19°. The low-temperature measurements were achieved with a Varian V 4340 variable-temperature probe assembly. Liquid nitrogen was evaporated by means of a small heating-coil in a 20-l. copper Dewar flask, and the cold gas was passed through the probe and insert.

The low temperatures were measured by a copper–constantan thermocouple, one junction of which was placed in the insert about 2 cm. above the radio-frequency receiver coil. A correction of about +1° was made to allow for the fact that the junction could not be placed in the sample. Temperatures quoted are considered accurate to ±2°. Free energies of activation, ΔG^*, are obtained from the Eyring equation at the coalescence temperature, T_c, when

$$\Delta G^* = 2{\cdot}3\mathbf{R}T_c \ln [\sqrt{2}(\mathbf{k}T_c)/\mathbf{h}\pi\delta] = 4{\cdot}59T_c[9{\cdot}97 + \log_{10}(T_c/\delta)],$$

where δ is the chemical shift being averaged, in c./sec. Values of ΔG^* given are probably accurate to ±0·5 kcal./mole, except for benzofuroxan itself, and are measured at the temperatures of coalescence given.

Line positions and splittings were measured by using side-bands of tetramethylsilane generated by a Muirhead-Wigan D 695A decade oscillator and averaging over several traces. Coupling constants are usually accurate to ±0·05 c./sec., internal chemical shifts to ±0·1 c./sec., and chemical shifts from tetramethylsilane to ±0·2 c./sec. The ABC and ABCD spectra were analysed by using the digital computer EDSAC 2, and programmes written by Dr. C. N. Banwell of this laboratory.

RESULTS AND DISCUSSION

Chemical shifts and coupling constants are recorded in Tables 1 and 2, respectively. As the *para*- and *meta*-coupling constants are of comparable magnitude, the assignments of the spectra for Nos. 3, 4, and 5 (Table 1) are initially ambiguous in part (unambiguous values of coupling constants are italicised in Table 2); assignment of chemical shifts is also ambiguous for Nos. 2, 6, 7, and 9. The assignments given for the ambiguous cases have been made by an overall comparison of all the data, and the self-consistency of the pattern thus obtained is their justification.† Proximity to a nitro-group or a heterocyclic ring causes a low-field shift, as found by, *e.g.*, Abraham, Bishop, and Richards,[11] and Looney, Phillips, and Reilly.[12]

TABLE 1.

Chemical shifts * of benzofuroxans.

			Chemical shift (τ) of hydrogen at			
No.	Subst.	Time-averaging	4	5	6	7
1	—	No	2·29	2·49	2·65	2·54
2	—	Yes	2·42	2·58	(2·58)	(2·42)
3	5-Nitro	No	1·27	—	2·02	2·28
4	6-Nitro	No	2·06	1·84	—	1·51
5	5(6)-Nitro †	Yes	1·39	—	1·93	2·17
6	4-Nitro	No	—	1·43	2·41	2·00
7	5,6-Dinitro	No	1·16	—	—	1·26
8	5,6-Dinitro	Yes	1·21	—	—	(1·21)
9	3,6-Dinitro	No	—	0·92	—	0·92

* Corrected for acetone solution at 20°. † Corrected for unequal populations.

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† For the full argument see R. K. Harris, Thesis, Cambridge, 1962.

[11] Abraham, Bishop, and Richards, *Mol. Phys.*, 1960, **3**, 485.

[12] Looney, Phillips, and Reilly, *J. Amer. Chem. Soc.*, 1957, **79**, 6136.

TABLE 2.

Coupling constants (c./sec.) for benzofuroxans (acetone solutions).

Subst.	Time-averaging	*ortho*, across		*meta*, across		*para*, across		
		4,5 or 6,7	5,6	H	NO_2	H, H	H, NO_2	NO_2, NO_2
(Parent)†	Yes	*9·25*	*6·40*	*0·95*	—	*1·05*	—	—
4-Nitro	No	8·93	7·27	*0·81*	—	—	—	—
5-Nitro	No	*9·63*	—	—	1·81	—	0·87	—
6-Nitro	No	*9·82*	—	—	1·97	—	0·89	—
5(6)-Nitro	Yes	*9·82*	—	—	1·91	—	0·84	—
4,6-Dinitro	No	—	—	—	*~1·8*	—	—	—
5,6-Dinitro	No	—	—	—	—	—	—	*0·41*
Benzofurazan †	—	9·34	6·5	0·89	—	1·2	—	—
4-Nitrobenzofurazan	—	9·08	7·33	0·68	—	—	—	—
Naphthalene ‡	—	8·5	7·0	1·4	—	0·7	—	—
o-Nitrobenzene §	—	8·4	8·0	1·4	—	0·1	—	—

Unambiguous values are italicised. † Ref. 5 gives similar values for CH_2Cl_2 solution. ‡ In CCl_4. § Ref. 5.

Spectral Patterns.—At low temperatures, benzofuroxan shows a complex but well-defined ABCD pattern (cf. refs. 3 and 4) which has not previously been interpreted. By using the coupling constants obtained from the high-temperature A_2B_2 pattern in carbon tetrachloride solution,[1] and initial chemical shifts estimated from the data from the other molecules, accurate chemical shifts were obtained when an iterative procedure of comparing calculated and observed spectra was applied; the final values gave a good fit to the experimental spectrum (Fig. 1). Owing to the complexity of the spectrum, it is difficult to obtain an accurate value for ΔG^* for this molecule but, with an average value of *ca.* 8 c./sec. for the chemical shift being averaged by the tautomerism, an estimate of $T_c \approx 5°$ gives $\Delta G^* \approx 15$ kcal./mole. The error in T_c is thought to be not greater than 10°, which introduces an error of less than 1 kcal./mole in ΔG^*.

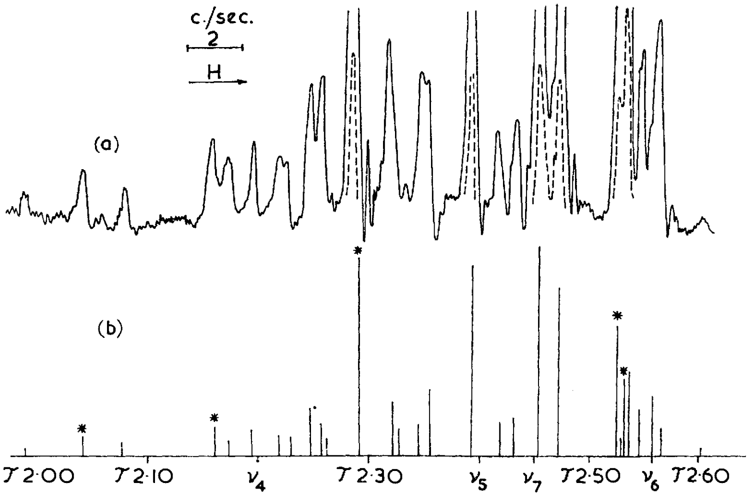
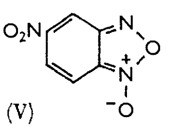


FIG. 1. (a) Benzofuroxan at —42° in acetone. (b) Spectrum calculated from values in Tables 1 and 2. (The asterisks denote superposition of two lines less than 0·1 c./sec. apart.) ν_4, ν_5, etc. give the chemical shifts of the protons at the positions indicated.

At room temperature and above, 5-nitrobenzofuroxan (V) shows a single ABC pattern (Fig. 2), indicating rapid exchange between structures (V) and (VI). At low temperatures (Fig. 3), two separate ABC patterns may be distinguished, which were assigned to the individual 5-nitro- (V) and 6-nitro-benzofuroxan (VI) species. According to the most probable assignment of chemical shifts (see below), relative areas of the bands due to the proton *ortho* to both the nitro-group and the *N*-oxide ring show that the 6-nitro derivative (VI) forms ~70% of the mixture at —31°, *i.e.*, it is more stable than the 5-nitro-analogue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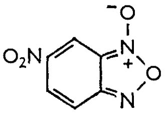
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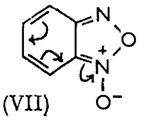
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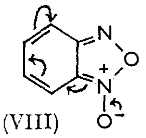
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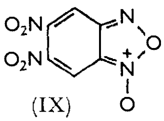
(IX)

(V) by $\Delta G \approx 360$ cal./mole.† The *N*-oxide group of a benzofuroxan both withdraws electrons from the 4- and the 7-position by electronic shifts of type (VII) and makes these available at these positions by shifts of type (VIII). The present results indicate that

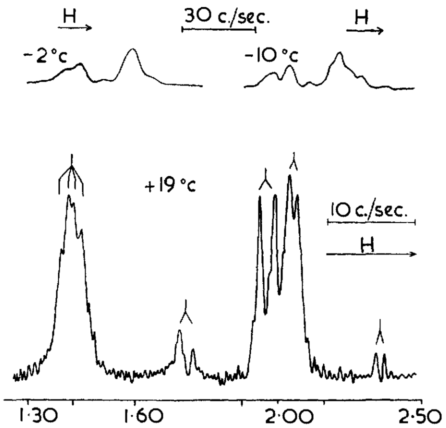

FIG. 2. Single ABC spectrum of rapidly equilibrating 5- and 6-nitrobenzofuroxan.

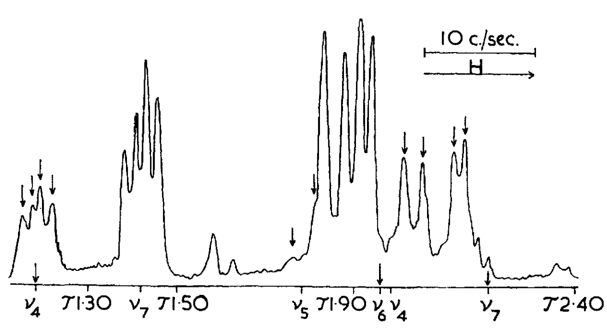

FIG. 3. The two ABC patterns of 5- and 6-nitrobenzofuroxan slowly equilibrating at —31°. The lines and resonance frequencies marked by the arrows arise from the 5-nitro-compound.

these effects largely cancel, but that shifts of type (VIII) are somewhat the more important. The proton *ortho* to both the heterocyclic ring and the nitro-group has a considerable chemical shift to low field of the other two protons, and is coupled to them to a small extent only. Consequently, the system can be treated as an approximate ABX case, and separate coalescence temperatures are observed for the AB and the X parts of the spectrum. These are 273° and 285°K, respectively, giving 13·6 and 14·1 kcal./mole for ΔG^*.

5,6-Dinitrobenzofuroxan (IX) shows a single line (of 1·0 c./sec. half-width) at 20°, but an AB pattern below 0°: the maximum chemical shift observed was 4·04 c./sec. at —50°. The T_c is 278°K, giving ΔG^* 15·0 kcal./mole. Thus the 5- and 6-nitro-groups do not have a large effect on ΔG^*. Englert[4] reports similar results for this molecule, but without resolution sufficient to show the *para*-spin–spin coupling; his estimate of ΔH^* was 10—20 kcal./mole.

4-Nitrobenzofuroxan (X) gives a single ABC pattern (Fig. 4) at temperatures in the range —50° to +160°. This shows that neither of the two possible types of tautomerism (to XI or to XII) is important. The energy of activation for the interconversion (X) $\rightleftharpoons$ (XI) is probably not large, but steric, electrostatic, and mesomeric effects are expected to cause the equilibrium to lie very predominantly on the side of isomer (X). Apparently

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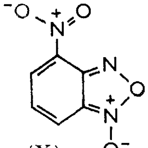
† ΔH could not be measured, but as ΔS is probably small, it should be close to ΔG.

the energy of activation for the process (X) $\rightleftharpoons$ (XII) is >20 kcal./mole, so that time-averaging of the 5- and the 7-proton does not occur.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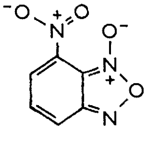
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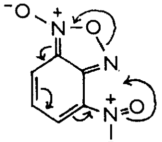
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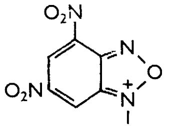
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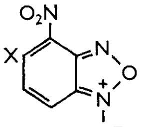
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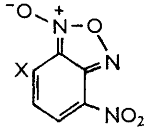
(XV)

These conclusions are supported by the results for 4,6-dinitrobenzofuroxan (XIII). Although this shows a single sharp line (half-width <0·3 c./sec.) in acetone at room temperature, this does not indicate rapid tautomerism of type (X) $\rightleftharpoons$ (XII) (as previously thought [1]) because in other solvents a (single) AB pattern was found (Table 3) which persisted in the temperature range −60° to +180°. The chemical shifts vary with solvent (and temperature) and must be accidentally coincidental for acetone as solvent. It may be estimated that $\Delta G^* > 25$ kcal./mole for the process analogous to (X) $\rightleftharpoons$ (XII). Therefore, it should be possible to isolate suitably substituted derivatives such as (XIV, XV); this has now been achieved, and will be reported separately.[13]

TABLE 3.

4,6-Dinitrobenzofuroxan.

Solvent	Temp. (°C)	Average chemical shift (τ)	δ (c./sec.)	J (c./sec.)
Acetone	20°	0·92	<0·2	—
Dioxan	20	0·93	2·3	1·7
	148	1·12	3·4	1·8
Acetonitrile	20	1·07	3·3	1·8
	104	1·13	5·5	1·9
Dimethyl sulphoxide	20	0·96	9·5	1·9
	108	1·06	2·7	1·7
Melt *	180	0·92	3·3	1·9

* With a little dioxan as an internal standard (τ 6·43).

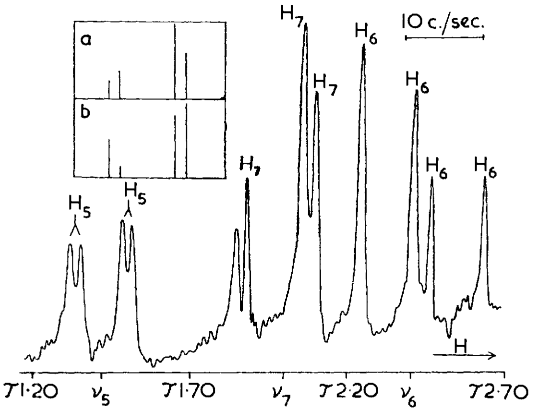

FIG. 4. ABC pattern for 4-nitrobenzofuroxan at 32°. The insets show the relative intensities of the lines due to H_1 (on the same frequency scale as the main Figure) for J_{AB} and J_{BC}, (a) of same sign and (b) of opposite sign. The lines due to H_5 (adjacent to the nitro-group) are broadened, probably by nitrogen quadrupole effects.

Chemical Shifts.—The correlation of chemical shifts with structure is complicated by the variations observed with temperature. For example, the single broad line of 5,6-dinitrobenzofuroxan (IX) at room temperature is at τ 1·21, whereas the centre of the AB spectrum at −50° is at τ 1·00. We have attempted to correct for this by assuming that shifts with temperature are equal for corresponding protons of a pair of tautomers. The

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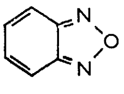
[13] Boulton and Katritzky, *Proc. Chem. Soc.*, 1962, 257.

difference in the chemical shifts between such protons at low temperature is then bracketed about the average value observed at room temperature. A further complication arises with compounds (V) and (VI) because of unequal populations, and corrections to the room temperature values are made on the assumption that the tautomers are present in the ratio 1 : 2. The experiments with compound (XIII) indicate that there are considerable solvent effects, and, since the acetone solutions studied were at different concentrations for different compounds, a dilution error is to be expected, but it is probably small.



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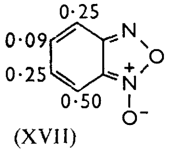

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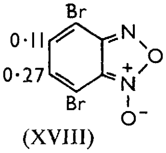

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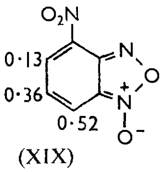

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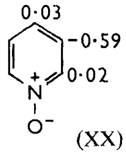

(XX)

[In formulæ (XVII—XX), the numbers indicate shifts to higher field for the *N*-oxide compared with the parent heterocycle.

Effect of the N-*Oxide Oxygen Atom.*—In acetone at room temperature, benzofurazan (XVI) shows an A_2B_2 spectrum with τ 2·04 for the 4,7-protons and τ 2·40 for the 5,6-protons. This indicates that the *N*-oxide oxygen atom in benzofuroxan causes a high-field shift of all the protons: that shown in (XVII) is one of the two possible assignments. The high-field shift is confirmed by Englert and Prinzbach's work[14] on the 4,7-dibromo-compounds (cf. XVIII). Comparison of 4-nitrobenzofurazan (τ 1·30, 2·05, and 1·48) with 4-nitrobenzofuroxan shows that the influence of the *N*-oxide oxygen atom is as in (XIX), which strongly supports the assignments given in (XVII) and (XVIII) and in Table 1.

These assignments are also in agreement with theoretical expectation. The high-field shift indicates that electronic shifts of type (VIII) must be more important than those of type (VII), and these would be expected to give a greater high-field shift at the 4- and the 6- than at the 5-position. The large high-field shift at the 7-position is presumably to be ascribed largely to a molecular anisotropy effect. The magnitude of the electron-donor effect of the *N*-oxide-oxygen atom is surprising: in pyridine 1-oxide it causes only a small high-field shift of the α- and the γ-proton and a considerable low-field shift for the β-proton [approximate figures derived from methyl derivatives[15] are shown in (XX)].

TABLE 4.

Effect on chemical shift ($\Delta\tau$ values) of replacing hydrogen by a nitro-group.

		ortho		*meta*	*para*
Molecule substituted	Position	4—5 or 6—7	5—6	4—6 or 5—7	4—7
Benzofuroxan	4	1·06	—	0·24	0·54
,,	5	1·02	0·63	0·26	—
,,	6	1·03	0·65	0·23	—
4-Nitrobenzofuroxan	6	1·08	0·51	—	—
5-Nitrobenzofuroxan	6	1·02	—	0·11	—
6-Nitrobenzofuroxan	4	0·92	—	—	0·59
,,	5	0·90	—	0·25	—
Benzene	1	0·95		0·27	0·42
Benzofurazan	4	1·10	—	0·35	0·56

Effect of Nitro-groups (Table 4).—The effect of an *o*-nitro-group on the chemical shift is significantly different across the 4,5 and the 6,7-bonds (0·9—1·1 p.p.m.) from that across the 5,6-bond (0·5—0·7 p.p.m.). This indicates that there is partial double-bond fixation

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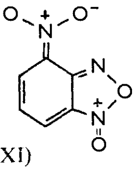
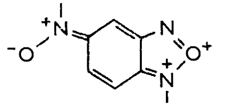
[14] Englert and Prinzbach, *Z. Naturforsch.*, 1962, **17b**, 4.
[15] Katritzky and Lagowski, *J.*, 1961, 43.

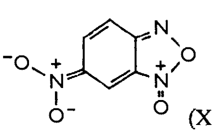
in the benzofuroxan molecule as suggested by Hammick *et al.*[16] The effect of a nitro-group at the *meta-* or *para*-position is less, and is in approximate agreement with the values for nitrobenzene.[17]

Coupling Constants (Table 2).—The *ortho*-coupling constants across the 4,5- or 6,7-bond are significantly larger than those across the 5,6-bonds. A similar inequality is found for benzofurazan and naphthalene.[5] In all these cases the coupling constant across a bond of expected higher order is the greater. It is of interest that, on this criterion, the bond fixation in benzofuroxan and benzofurazan is apparently of comparable extent.

Further small variations of the *ortho*-coupling constants can be correlated with the effect of the nitro-groups. Compared with benzofuroxan itself, contributing structure (XXI) lowers J_{67} and raises J_{56} for 4-nitrogen atom of benzofuroxan. Contributing structures (XXII) and (XXIII) tend to increase J_{67} and J_{45}, respectively, for the 5-nitro- and the 6-nitro-compound; the effect is greater for the latter, as expected.


(XXI)


(XXII)


(XXIII)

For benzofuroxan, the *para*-coupling constant J_{47} is larger than the *meta* J_{46}, which is unusual. The *para*-coupling constants decrease as nitro-groups are successively substituted, as would be expected from the inductive effects of such electronegative substituents.[18] The *meta*-coupling constants increase when across a nitro-group; possibly this is connected with changes in bond angles noted for nitrobenzene by Trotter.[19]

Signs of Coupling Constants.—Proton–proton coupling constants in aromatic systems usually have the same sign.[11,20] The A_2B_2 spectrum of benzofuroxan itself at high temperatures in carbon tetrachloride indicates that this holds in the present series, which is confirmed by finding that the low-temperature spectrum is adequately analysed when the same values of the coupling constants are used, all being taken as positive. The relative intensities of lines in the low- and the high-temperature spectra of 5- and 6-nitrobenzofuroxan show that *meta-* and *para*-coupling constants have the same sign, while a corresponding study of the spectrum of the 5-nitro-derivative shows that the *ortho*-coupling constant across the 5,6 bond has the same sign as the *meta*-value (cf. Fig. 4).

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