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NMR Study of the Intramolecular Nonmutual Exchange of 5-Halobenzofuroxan. II. Mechanism of Ring Opening Reaction[1]

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The tautomerism of 5-chlorobenzofuroxan, 5-bromobenzofuroxan, and 5-iodobenzofuroxan was studied by the proton magnetic resonance (PMR) at 60 MHz. The rate of intramolecular rearrangement between the tautomers was calculated from the PMR line shape, using the density matrix method of intramolecular nonmutual exchange. The activation parameters for the intramolecular rearrangement were found to be $\Delta H^{\ast}=5\sim24$ kcal/mol, $\Delta S^{\ast}=-34\sim+33$ cal/deg·mol. Structure of the transition state is discussed from electronic energies of the system and it was concluded that this reaction proceeds *via* a transition state of *p*-*o*-dinitrosobenzene produced by the electrocyclic ring opening reaction of benzofuroxan.

Keywords——NMR; density matrix method; tautomerism; rearrangement; benzofuroxan; 5-fluorobenzofuroxan; 5-chlorobenzofuroxan; 5-bromobenzofuroxan; 5-iodobenzofuroxan

Introduction

In the preceding work,[1] the rate of tautomerism of 5-fluorobenzofuroxan was studied by proton magnetic resonance (PMR) spectral analysis using the density matrix method of intramolecular nonmutual exchange developed Johnson,[3] and the thermodynamic parameters of intramolecular rearrangement between 5-fluorobenzofuroxan and 6-fluorobenzofuroxan were estimated from the theory of the absolute reaction rate. In the present work, tautomerism of 5-chlorobenzofuroxan, 5-bromobenzofuroxan, and 5-iodobenzofuroxan was studied by the same procedure.

Recently, it was recognized that the most reasonable mechanistic pathway for the tautomerism involves ring opening of frazane oxide to give *o*-dinitrosobenzene as a transient intermediate to afford either Ia and Ib.

From the positive entropies of activation provided by means of nuclear magnetic resonance (NMR) spectral analysis, Mallory, *et al.*[4] showed that the tautomerisms of 4,7-dichlorobenzofuroxan and 5,6-dichlorobenzofuroxan proceed *via* a transition state such as *o*-dinitrosobenzene, and suggested various possibilities for the *o*-dinitrosobenzene structure as shown in Charts 2 and 3.

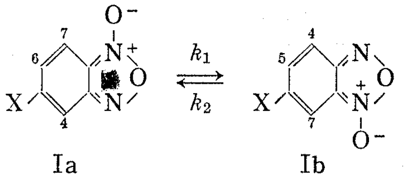

Chart 1

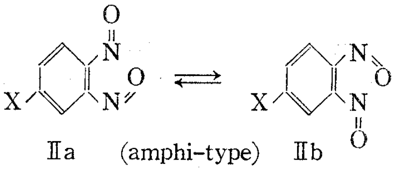

Chart 2

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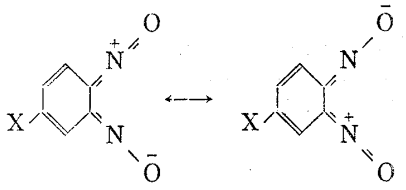
[1] S. Uematsu and Y. Akahori, *Chem. Pharm. Bull.* (Tokyo), **25**, 3261 (1977).

[2] Location: *2-2-1, Oshika, Shizuoka, 422, Japan.*

[3] C.S. Johnson, Jr., *J. Chem. Phys.*, **41**, 3277 (1964); C.S. Johnson, Jr., "Advances in Magnetic Resonance," Vol. 1, ed. by J.S. Waugh, Academic Press, Inc., New York, 1965, p. 1.

[4] F.B. Mallory, S.L. Manatt, and C.S. Wood, *J. Am. Chem. Soc.*, **87**, 5433 (1965).



IIIa (linear type) IIIb

Chart 3

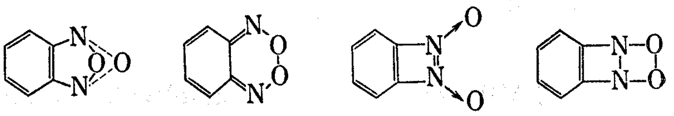


Chart 4

$$\mathrm{Ia} \overset{k_1}{\rightleftarrows} \left[\mathrm{IIIa} \longleftrightarrow \mathrm{IIIb}\right] \underset{k_2}{\rightleftarrows} \mathrm{Ib}$$

Chart 5

Using bond energy arguments, Mallory and Cammarate[5] concluded that other possibilities (Chart 4) were far less likely but no sound evidence has been given for the intermediary *o*-dinitrosobenzene. We excluded the possibility that *o*-dinitrosobenzene ($\mathrm{IIa} \rightleftarrows \mathrm{IIb}$) is the transition state of this reaction, because negative values for the entropy of activation were experimentally obtained for this tautomerism. To interprete the mechanism of this reaction, a model similar to an electrocyclic ring opening reaction of cyclobutene to butadiene[6] is introduced; namely, this tautomerism proceeds *via* a transition state *ϕ-o*-dinitrosobenzene ($\mathrm{IIIa} \leftrightarrow \mathrm{IIIb}$) produced by an electrocyclic ring opening reaction of benzofuroxan.[7] This model is interpreted by means of HMO method and the calculated energies agree with the experimental values. Therefore, it is concluded that the tautomerism of 5-halobenzofuroxan proceeds *via* a transition state of *ϕ-o*-dinitrosobenzene produced by the electrocyclic reaction as shown in Chart 5.

Experimental

5-Halobenzofuroxans were prepared by the method described in our preceding paper[1] and their melting points were agreed with reported values: 5-chlorobenzofuroxan, mp 47—48° (reported,[8] 48°) and 5-bromobenzofuroxan, mp 68° (reported,[8] 69°). 5-Iodobenzofuroxan was prepared by the thermal decomposition of 4-iodo-2-nitrophenylazide and recrystallized from hexane to yellow crystals (48% from 4-iodo-2-nitroaniline[9]), mp 77.5°. *Anal.* Calcd. for $C_6H_3IN_2O_2$: C, 27.51; H, 1.15; N, 10.69; I, 48.44. Found: C, 27.21; H, 1.30; N, 10.81; I, 47.99.

The compounds were sublimed *in vacuo* and sample solutions were prepared as follows: 5-chlorobenzofuroxan (100 mg), 5-bromobenzofuroxan (75 mg), and 5-iodobenzofuroxan (75 mg) were dissolved in 0.5 ml of a mixed solvent ($CDCl_3$: $(CH_3)_2CO = 1:3$), and the solutions were degassed before PMR measurements. The PMR spectra at 60 MHz were obtained on a JNM C60-H (Japan Electron Optics Laboratory, Tokyo), under the experimental condition described in the preceding paper.[1] The spectra were analyzed by means of Pople's method[10] and the density matrix method of intramolecular nonmutual exchange,[11] and the thermodynamic parameters were obtained as in the preceding method.

Results and Discussion

The coupling constants and chemical shifts are listed in Tables I and II. The calculated and experimental spectra are shown in Fig. 1 to 5, Arrhenius plots are given in Fig. 6, and the activation parameters are summarized in Table III.

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[5] F.B. Mallory and A. Cammarate, *J. Am. Chem. Soc.*, **88**, 61 (1966).

[6] R.B. Woodward and R. Hoffmann, *J. Am. Chem. Soc.*, **87**, 395 (1965).

[7] H.E. Simmons and J.F. Bunnett (ed.), "Orbital Symmetry Papers," American Chemical Society, Washington, D.C., 1974, p. 335.

[8] D. Britton and W.E. Noland, *J. Org. Chem.*, **27**, 3218 (1962).

[9] P. Brenans, *Compt. rend.*, **158**, 717 [*C.A.*, **8**, 2147 (1914)].

[10] J.M. Anderson and J.D. Baldeschwieler, *J. Chem. Phys.*, **40**, 3241 (1964).

[11] G. Binsch, *J. Am. Chem. Soc.*, **91**, 1304 (1969); G. Binsch, "Dynamic Nuclear Magnetic Resonance Spectroscopy," ed. by L.M. Jackman and F.A. Cotton, Academic Press, Inc., New York, 1975, p. 59.

Table I. Coupling Constants (Hz) in Substituted Benzofuroxans

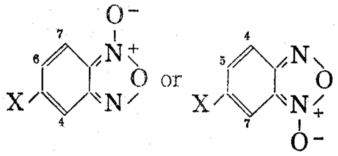	J_{4-5}	J_{4-6}	J_{4-7}	J_{5-7}	J_{6-7}
5-Chloro-	—	1.52	0.85	—	9.23
6-Chloro-	9.45	—	0.83	1.65	—
5-Bromo-	—	1.38	0.78	—	9.41
6-Bromo-	9.47	—	0.87	1.59	—
5-Iodo-	—	1.15	0.86	—	9.22
6-Iodo-	9.74	—	0.91	1.10	—

Table II. Chemical Shifts of Substituted Benzofuroxans[a)]

Substituted benzofuroxan	Chemical shift (Hz) of proton			
	ν_4	ν_5	ν_6	ν_7
5-Chloro-	342.56	—	310.03	325.75
6-Chloro-	339.86	319.21	—	327.87
5-Bromo-	357.24	—	317.99	322.90
6-Bromo-	337.37	327.56	—	341.13
5-Iodo-	371.19	—	326.83	313.08
6-Iodo-	328.09	335.74	—	353.48

a) Chemical shifts were measured from acetone signal (60 MHz).

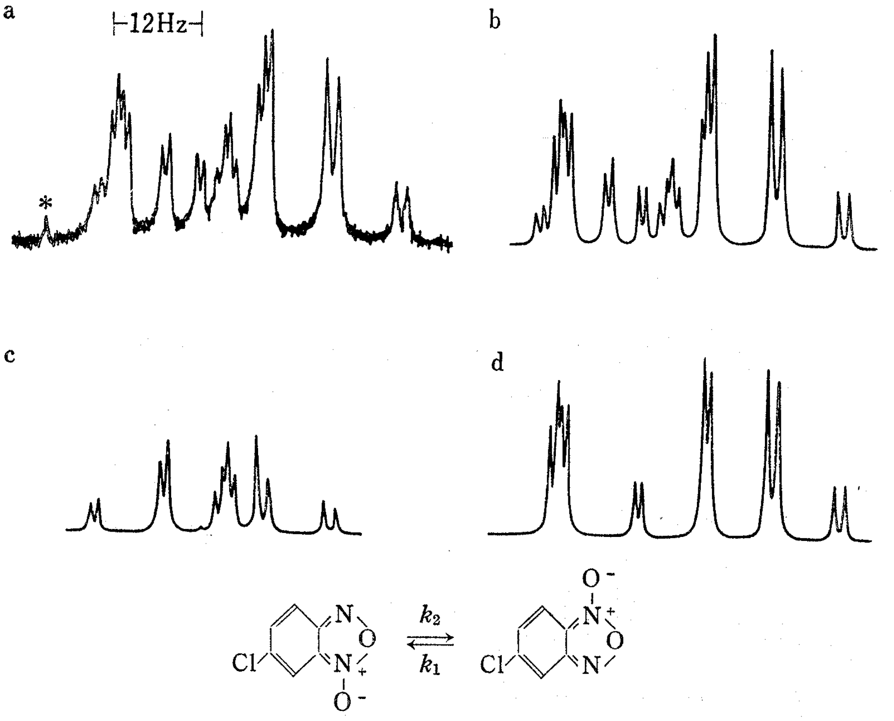

Fig. 1. Experimental and Theoretical Spectra for 5- and 6-Chlorobenzofuroxan

a) Experimental spectrum at 60 MHz and −78°C; b) theoretical spectrum obtained by Pople's model assuming isotropic random field relaxation, superposition of c and d; c) calculated line shape for 6-chlorobenzofuroxan; d) calculated line shape for 5-chlorobenzofuroxan.
*) singlet caused by chloroform in deuterochloroform.

5-Chlorobenzofuroxan (Ia$\rightleftarrows$Ib; X=Cl)

At −78°, the rearrangement is comparatively slow and the spectrum consists of superposition of the spectra of 5-isomer and 6-isomer. The fractional population of 5-isomer is 0.69 and the free-energy difference ΔF between the tautomers is 290 cal/mol, and the activation parameters agree with the results obtained by Boulton, *et al.*[12] using the method of signal coalescence. The spectra in the temperature range from −78° to +30° are analyzed by Pople's method and the density matrix method, and the results are shown in Fig. 1 and 2, respectively.

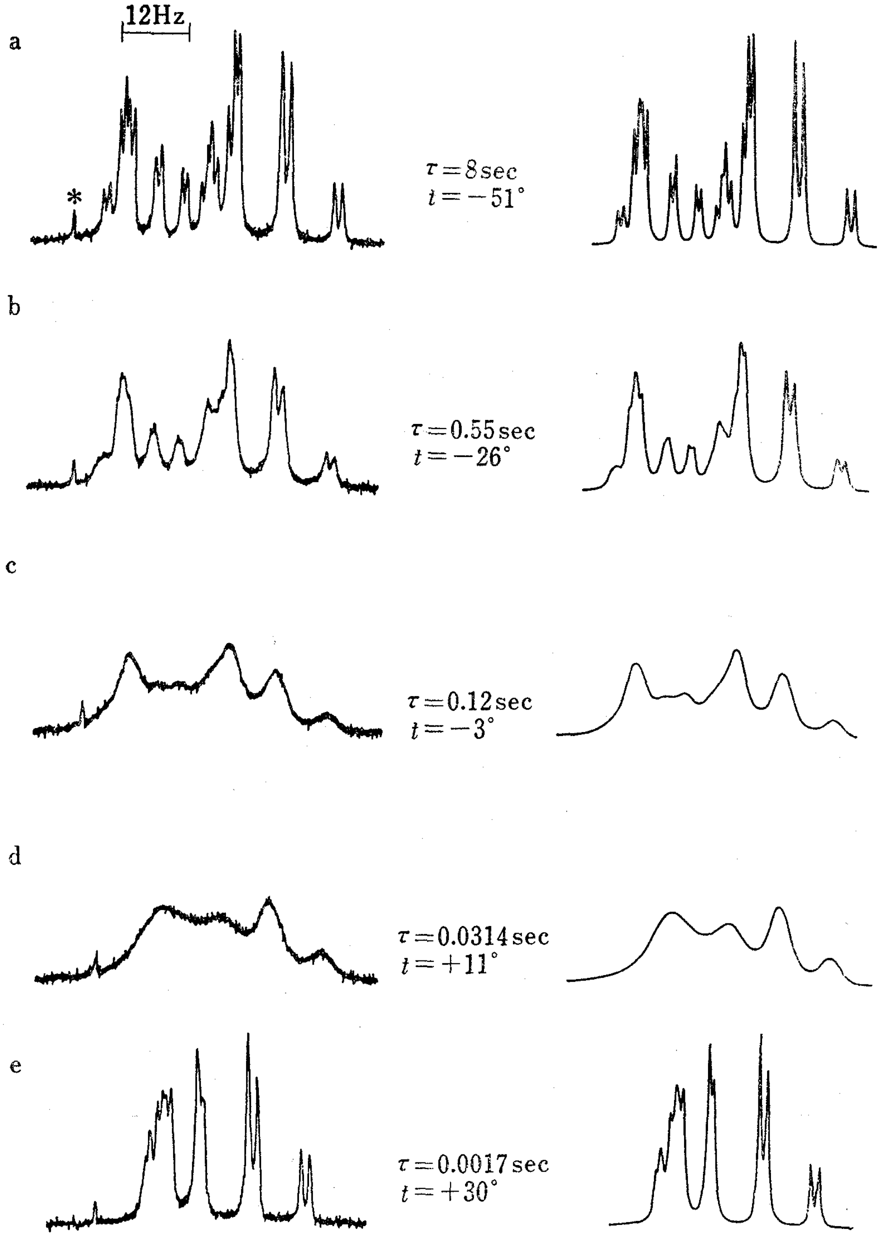

Fig. 2. Experimental and Theoretical Spectra for the Intramolecular Rearrangement between 5- and 6-Chlorobenzofuroxan

Theoretical spectra are calculated by means of the density matrix method.
*) signal of chloroform.

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[12] A.J. Boulton, A.R. Katritzky, M.J. Sewell, and B. Wallis, *J. Chem. Soc.* (*B*), 1967, 914.

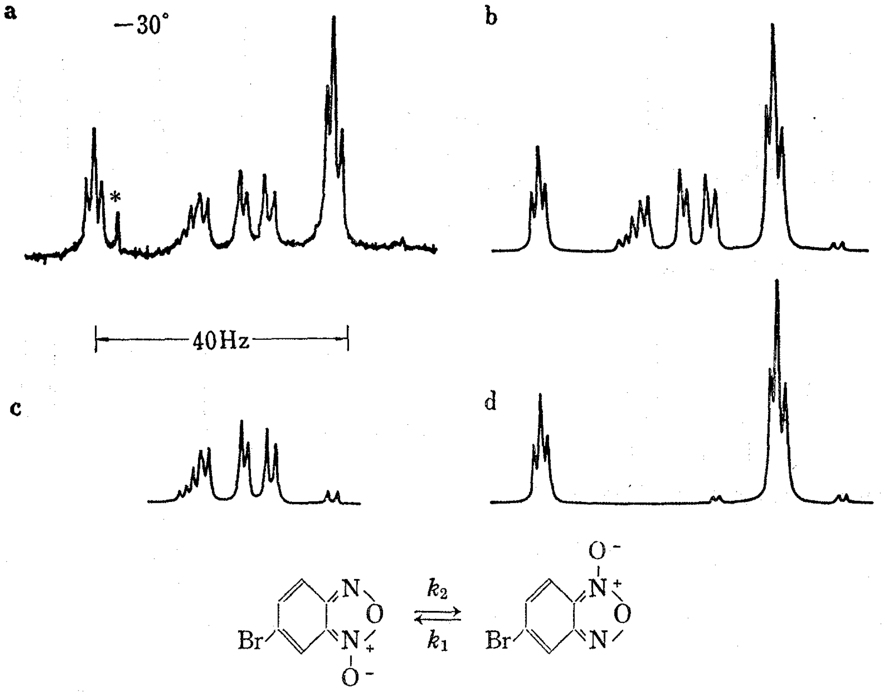


Fig. 3. Experimental and Theoretical Spectra for 5- and 6-Bromobenzofuroxan

a) experimental spectrum at 60 MHz and −30°; b) theoretical spectrum obtained by Pople's model assuming isotropic random field relaxation, superposition of c and d; c) calculated line shape for 6-bromobenzofuroxan; d) calculated line shape for 5-bromobenzofuroxan.
*) signal of chloroform.

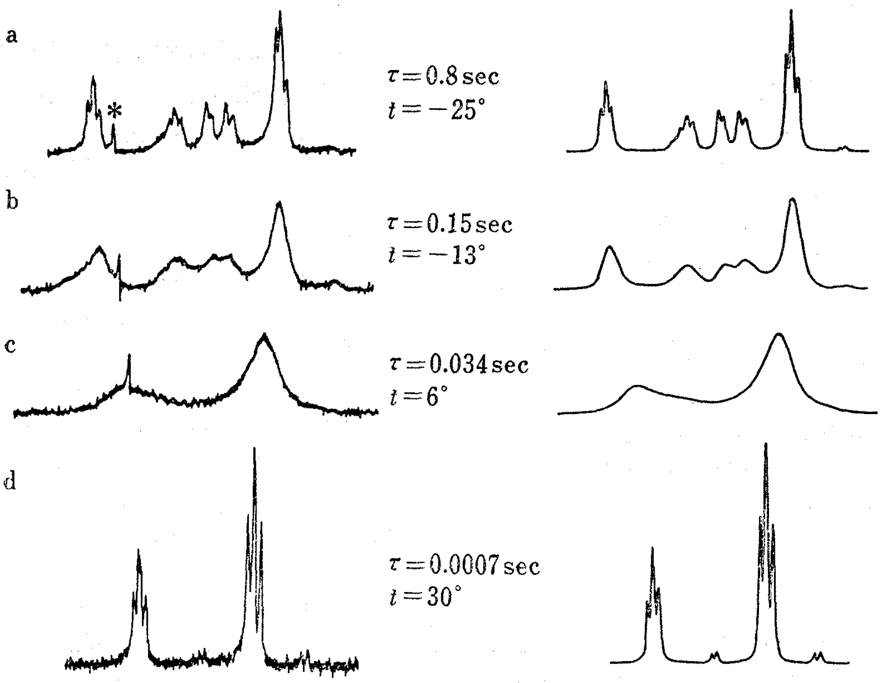


Fig. 4. Experimental and Theoretical Spectra for Intramolecular Rearrangement between 5- and 6-Bromobenzofuroxan

Theoretical spectra are calculated by means of the density matrix method.
*) signal of chloroform.

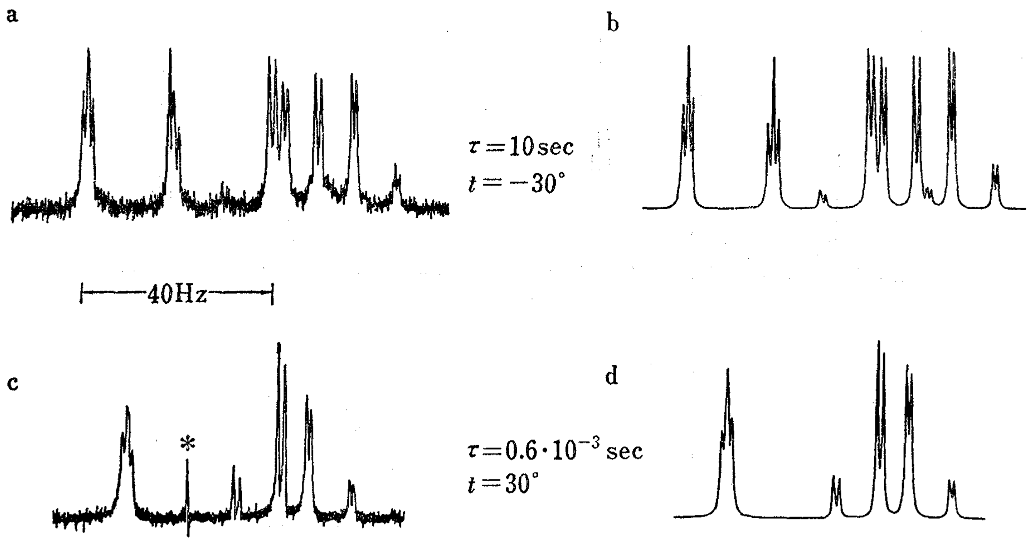


Fig. 5. Experimental and Theoretical Spectra for the Intramolecular Rearrangement between 5- and 6-Iodobenzofuroxan

The theoretical spectra are calculated by means of the density matrix method.
*) signal of chloroform.

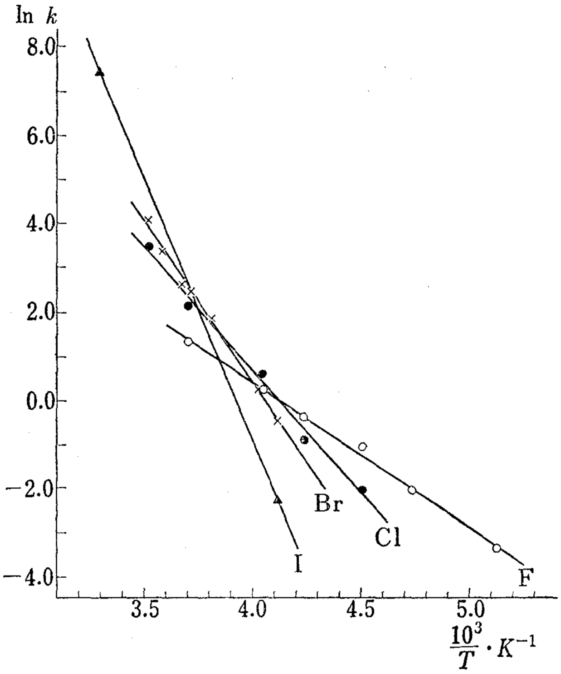


Fig. 6. Arrhenius Plots of the Kinetic Data for 5-Halobenzofuroxan at 60 MHz

—○—: 5-fluoro-, —○—: 5-chloro-,
—×—: 5-bromo-, —▲—: 5-iodo-.

5-Bromobenzofuroxan (Ia$\rightleftarrows$Ib; X=Br)

Fig. 3 illustrates the experimental and theoretical spectra at −30°, and the fractional population of 5-isomer is 0.60 and ΔF is 190 cal/mol. The spectra in the temperature range from −30° to +30° are analyzed in a similar manner as above and the results are shown in Fig. 4.

5-Iodobenzofuroxan (Ia$\rightleftarrows$Ib; X=I)

Experimental and theoretical spectra in the temperature range from −30° to +30° are shown in Fig. 5. The fractional population of 5-isomer is 0.55 at −30°, and ΔF is 100 cal/mol.

From the thermodynamic parameters shown in Table III, four results are derived as follows.

(1) The reaction is the first-order reaction *via* a transition state.

(2) The effect of halogens on the free energy difference, ΔF, decreases in the order of F, Cl, Br, and I.

(3) The enthalpy of activation, $\Delta H^{\ddagger}$, increases in the order of F, Cl, Br, and I.

(4) The entropy of activation, $\Delta S^{\ddagger}$, increases in the order of F, Cl, Br, and I, and the values of the entropy of activation are negative except for iodo derivative.

The fact that remarkable changes of $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ have been found experimentally is consistent with the suggestion that the effect of halogen substituents is due to their influence on the electronic structure transition state rather than on the steric hindrance; this reaction would proceed in an orderly manner since the values of $\Delta S^{\ddagger}$ are negative.

TABLE III. Thermodynamic Quantities for the Intramolecular Rearrangement between 5- and 6-Halobenzofuroxan

Substituted benzofuroxan	E_a kcal/mol	log A	$\Delta H^{\ddagger}$ kcal/mol	$\Delta S^{\ddagger}$ cal/deg. mol	ΔF cal/mol
5-Fluoro-[b]	6.55 ± 0.09	5.89 ± 0.09	6.10 ± 0.09	-33.0 ± 0.4	410
6-Fluoro-[b]	6.14 ± 0.09	5.89 ± 0.09	5.69 ± 0.09	-33.0 ± 0.4	
5-Chloro-	11.13 ± 0.26	10.02 ± 0.23	10.64 ± 0.26	-14.3 ± 1.1	290
6-Chloro-	10.85 ± 0.26	10.02 ± 0.23	10.35 ± 0.26	-14.3 ± 1.1	
5-Bromo-	14.55 ± 0.52	12.90 ± 0.43	14.03 ± 0.52	-1.2 ± 2.0	190
6-Bromo-	14.36 ± 0.52	12.90 ± 0.43	13.84 ± 0.52	-1.2 ± 2.0	
5-Iodo-	23.7	20.3	23.2	32.6	100
6-Iodo-	23.5	20.3	23.0	32.3	

a) The errors are average deviations (assuming only random errors).
b) Reference 1.

In order to interprete these results, two models are presumed. The model A involves *o*-dinitrosobenzene, IIa and IIb, for the transition state as shown in Chart 2. The model B involves the transition state in the form of a resonance hybrid between the linear type IIIa and IIIb as shown in Chart 3, proposing the name *ψ*-*o*-dinitrosobenzene (IIIa↔IIIb) as against the *o*-dinitrosobenzene of amphi-type.

For the model A, these negative values of $\Delta S^{\ddagger}$ tend to rule out the possibility that *o*-dinitrosobenzene is the transition state of this reaction, since it is expected that the formation of *o*-dinitrosobenzene from benzofuroxan would have positive entropies of activation. Consequently the model A is not suitable for the mechanism of this rearrangement reaction.

In order to investigate the model B, a model similar to the conversion of cyclobutene to butadiene[6] is introduced for the electrocyclic ring opening reaction of benzofuroxans to *ψ*-*o*-dinitrosobenzenes. The ring opening can be achieved by breaking the σ-bond N_1–O_2 (Chart 6-a), followed by rehybridization of these atoms, and rotation about N_1–C_9 and O_2–N_3 bonds so as to weaken the interaction (Chart 6-b). In the limit that both atoms rotate through 90°, it forms *sp*-hybride orbitals (Chart 6-c) and a resonance hybride takes place between structures of type IIIa and IIIb, affording the name *ψ*-*o*-dinitrosobenzene. The differ-

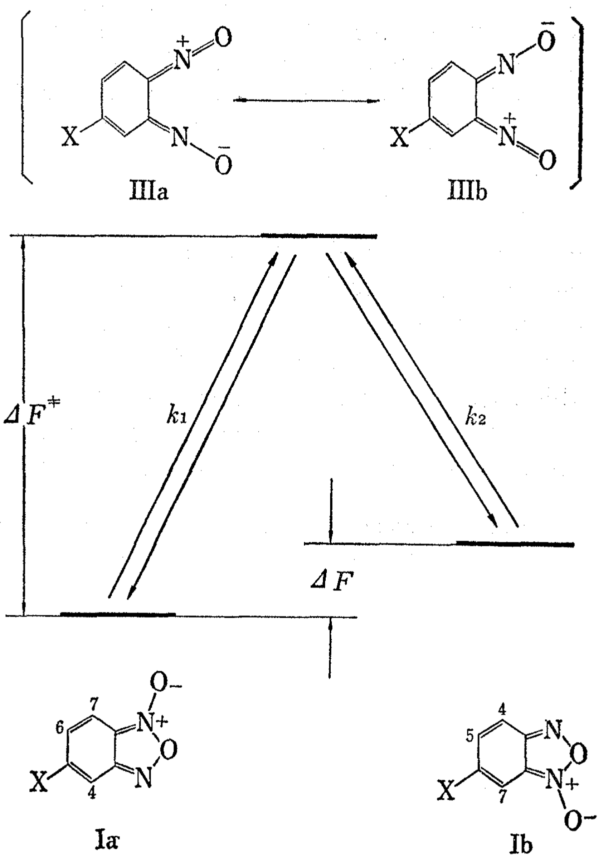


Fig. 7. Energy Diagram of Electrocyclic Ring Opening Model

Resonance hybride occurs between structures of type IIIa and IIIb, proposing the name *ψ*-*o*-dinitrosobenzene, and then reaction process occurs between benzofuroxan and transition state *ψ*-*o*-dinitrosobenzene.

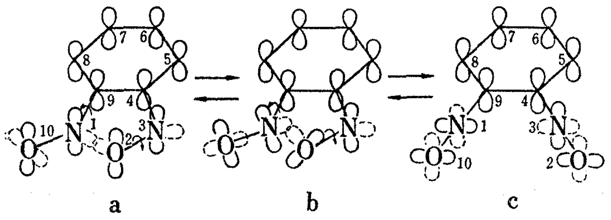


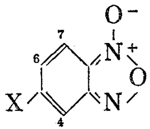
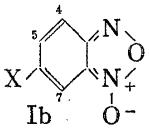
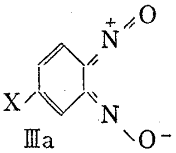
Chart 6

ence between electronic energy of benzofuroxan and that of ψ-o-dinitrosobenzene is approximated by the following equation:

$$\Delta E \simeq (E_{\pi,\psi}+E_{\pi,\mathrm{N_1-O_{10}}}) - (E_{\pi,\mathrm{b}}+E_{\sigma,\mathrm{N_1-O_2}}),$$

where $E_{\pi,\psi}$ is the π-electronic energy of a conjugated system for ψ-o-dinitrosobenzene, $E_{\pi,\mathrm{N_1-O_{10}}}$ is the π-electronic energy of $\mathrm{N_1-O_{10}}$ π-bond for ψ-o-dinitrosobenzene; $E_{\pi,\mathrm{b}}$ and $E_{\sigma,\mathrm{N_1-O_2}}$ are π-electronic energy of conjugated system and σ-electronic energy of $\mathrm{N_1-O_2}$ σ-bond for benzofuroxan, respectively. The conjugated systems for benzofuroxan and ψ-o-dinitrosobenzene consist of 11 p_z orbitals and 14 π-electrons, and these π-electronic energies are calculated with Streitwieser's HMO method,[13] where the auxiliary inductive parameter is $\delta=1/10$ and the π-electronic energies of ψ-o-dinitrosobenzene are approximated by that of structure of type IIIa. $E_{\sigma,\mathrm{N_1-O_2}}$ and $E_{\pi,\mathrm{N_1-O_{10}}}$ are also calculated using $P_\sigma(\mathrm{N})$—$P_\sigma(\mathrm{O})=1.40$ Å, $S_{\mathrm{NO}}=0.28$ and $P_\pi(\mathrm{N})$—$P_\pi(\mathrm{O})=1.14$ Å, $S_{\mathrm{NO}}=0.21$,[14] respectively; the difference between the calculated $E_{\sigma,\mathrm{N_1-O_2}}$ and $E_{\pi,\mathrm{N_1-O_{10}}}$ is 17.6 kcal/mol. The energy level diagram of the model B and the calculated energies are shown in Fig. 7 and Table IV, respectively. As a result, good agreement was obtained between the calculated and experimental energies. The fact[5] that the energies of activation found in benzofuroxans are about 20 kcal/mol less than those found in furoxans is interpreted easily if the model B is used to calculate the energies. From these arguments, it is seen that ψ-o-dinitrosobenzene on the restricted electronic structure is reasonable as a transition state rather than o-dinitrosobenzene.

TABLE IV. π-Electronic Energy and Difference between the Energies[a]

X	α_X	β_{C-X}	 Ia	 Ib	 IIIa	IIIa—Ia −0.44β(kcal/mol)	Ib—Ia (cal/mol)
F	$\alpha+3.0\beta$	0.70β	$14\alpha+25.3491\beta$	$14\alpha+25.3450\beta$	$14\alpha+25.3075\beta$	-0.4818β(19.25)	-0.0041β(164)
Cl	$\alpha+2.0\beta$	0.42β	$14\alpha+23.1851\beta$	$14\alpha+23.1817\beta$	$14\alpha+23.1427\beta$	-0.4824β(19.28)	-0.0034β(134)
Br	$\alpha+1.5\beta$	0.30β	$14\alpha+22.1120\beta$	$14\alpha+22.1093\beta$	$14\alpha+22.0690\beta$	-0.4830β(19.30)	-0.0027β(108)
I	$\alpha+0.8\beta$	0.10β	$14\alpha+20.6122\beta$	$14\alpha+20.6099\beta$	$14\alpha+20.5686\beta$	-0.4836β(19.32)	-0.0023β (92)

a) A. Streitwieser's parameters are used to calculate π-electronic energy of conjugated system, the energies of IIIa are used as approximation of ψ-o-dinitrosobenzens, 0.44β is the difference between the N-O sigma bond energy ($E_{\sigma,\mathrm{N_1-O_2}}$) and the N-O pi bond energy ($E_{\pi,\mathrm{N_1-O_{10}}}$), and the used value of β is −40 kal/mol.

Therefore it may be concluded that this reaction proceeds *via* a transition state of ψ-o-dinitrosobenzene produced by the electrocyclic ring reaction of 5-halobenzofuroxan.

Acknowledgement The authors are indebted to the Computer Center of Shizuoka Prefectural Government for the use of their computer for the present work.

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[13] A. Streitwieser, Jr., "Molecular Orbital Theory for Organic Chemists", John wiley and Sons, Inc., New York, 1961, p. 128.

[14] O. Kikuchi, "Bunshi Kidoho" (Molecular Orbital Method), Kodansha, Tokyo, 1971, p. 143.