2-acetoxy-1,3-indandione [AID, mp 96 °C (lit.[19] mp 97 °C)].

Preparation of HDT. A solution of 1 g (1 mmol) of NY and 0.25 g (2.5 mmol) of BNAH in 30 mL of methanol was allowed to stand under an atmosphere of nitrogen at room temperature for 15 h, and then 5 mL of petroleum ether was added to the solution. The solution was cooled at 0 °C, and 0.5 g (60%) of HDT [mp 242 °C (lit.[9] mp 243 °C)] was obtained.

Reduction of AT by BNAH. A solution of 1.07 g (5 mmol) of BNAH and 1.61 g (5 mmol) of AT was allowed to stand under an atmosphere of nitrogen at room temperature for 4 h and produced a precipitate immediately. After the mixture was stirred for 4 h, the precipitate was filtered off and dried in vacuo to give 0.8 g of $A^{\cdot}$-Py^{+}, and 0.5 g of D [mp 213 °C (lit.[17] mp 212 °C)] was isolated from the filtrate.

Reduction of HDT by BNAH. A solution of 1.07 g (5 mmol) of BNAH and 1.61 g (5 mmol) of HDT was allowed to stand under an atmosphere of nitrogen at room temperature for 7 h and produced a dark purple solution. After the methanol was evaporated in vacuo, 30 mL of acetic anhydride and 1 mL of pyridine were added to the residue, and the reaction mixture was allowed to stand at room temperature for 10 h. After unreacted acetic anhydride and pyridine were removed under reduce pressure, the residue was washed with methylene chloride three times. From the organic layer 1.4 g (70%) of AID was obtained, and 1 g of $BNA^{+}Cl^{-}$ was isolated by dissolving the insoluble solid in aqueous hydrochloric acid.

Reduction of *p*-Benzoquinone by $A^{\cdot}$-Py^{+}. A solution of 3.3 g (10 mmol) of $A^{\cdot}$-Py^{+} and 0.5 g (5 mmol) of *p*-benzoquinone in 100 mL of ethanol and 2 mL of hydrochloric acid (37%) was allowed to stand under an atmosphere of nitrogen at room temperature for 7 h. After the ethanol was evaporated in vacuo, the reaction mixture was dissolved in water (150 mL), and the solution was extracted with ether five times. From the organic layer 0.5 g (90%) of hydroquinone was obtained, and 2.3 g (90%) of $BNA^{+}Cl^{-}$ and 1.1 g (70%) of A were isolated from the aqueous solution.

Reduction of Benzyl Viologen by $A^{\cdot}$-Py^{+}. A solution of 1.6 g (5 mmol) of $A^{\cdot}$-Py^{+} and 2 g (5 mmol) of benzyl viologen in 100 mL of ethanol and 2 mL of hydrochloric acid (37%) was allowed to stand under an atmosphere of nitrogen at room temperature and produced viologen cation radical (dark green solution, λ_{max} 605 nm in ethanol) immediately. The dark green solution was changed to a yellow solution by bubbling air into the reaction mixture. After the ethanol was removed in vacuo, the residue was recrystallized from ethanol to give 0.47 g (60%) of $BNA^{+}Cl^{-}$, and A (0.4 g, 60%) was isolated from the filtrate.

Reduction of LA by $A^{\cdot}$-Py^{+}. A solution of 6.6 g (20 mmol) of $A^{\cdot}$-Py^{+} and LA in 100 mL of ethanol and 2 mL of hydrochloric acid (37%) was allowed to stand under an atmosphere of nitrogen at room temperature for 15 h. After the ethanol was removed in vacuo, 20 mL of acetic anhydride and 1 mL of pyridine were added to the reaction mixture, and the solution was allowed to stand at room temperature for 10 h. After unreacted acetic anhydride and pyridine were removed under reduced pressure, the residue was dissolved in water, and the solution was extracted with chloroform three times. After the chloroform was removed, the residue was distilled in vacuo to obtain 1.7 g (60%) of diacetylated lipoic acid: bp 202–205 °C (0.07 mmHg); IR (NaCl) 1680 ($C(O)CH_3$), 1740 cm^{-1} (COOH); NMR ($CDCl_3$) δ 1.5–1.8 (m, 8 H, $-(CH_2)_4-$), 1.5–1.8 (m, 2 H, CH_2), 2.33 (s, 6 H, $COCH_3$), 3.00 (t, SCH_2), 3.6 (m, 1 H, SCH), 10.7 (s, 1 H, OH). Anal. Calcd for $C_{12}H_{20}S_2O_4$: C, 49.31; H, 6.90; S, 21.89. Found: C, 49.20; H, 7.01; S, 21.80. $BNA^{+}Cl^{-}$ (2.4 g, 80%) and A (1.9 g, 60%) were also obtained from the aqueous solution.

Reduction of LA by BNAH in the Presence of Catalytic Amounts of Vicinal Tricarbonyl Compounds. Typical Procedure. To a solution of 2.2 g (10 mmol) of BNAH and 2.5 g (12 mmol) of LA in 100 mL of ethanol was added 0.16 g (1 mmol) of A. The reaction mixture was allowed to stand under an atmosphere of nitrogen at room temperature for 60 h. After the ethanol was removed in vacuo, 30 mL of acetic anhydride and 1 mL of pyridine were added to the residue, and the reaction mixture was allowed to stand at room temperature for 10 h. After unreacted acetic anhydride and pyridine were removed in vacuo, the residue was distilled to yield 1.5 g (70%) of diacetylated LA. $BNA^{+}Cl^{-}$ (1.5 g, 60%) was isolated from the residue. The reduction of LA by BNAH in the presence of catalytic amounts of AT, NY, or HDT was also carried out in a similar way. The reaction was stopped after the complete consumption of BNAH was checked spectrophotometrically.

Registry No. A, 50-71-5; BNAH, 952-92-1; $A^{\cdot}$-Py^{+}, 73636-25-6; $BNA^{+}Cl^{-}$, 5096-13-9; NY, 485-47-2; AID, 73636-26-7; HDT, 5103-42-4; AT, 76-24-4; *p*-benzoquinone, 106-51-4; benzyl viologen, 13096-46-3; LA, 62-46-4; diacetylated lipoic acid, 71288-69-2.

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Concurrent Methoxide Ion Attack at the 5- and 7-Carbons of 4-Nitrobenzofurazan and 4-Nitrobenzofuroxan. A Kinetic Study in Methanol

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In methanolic solution, methoxide ions attack both the 5- and 7-carbons of 4-nitrobenzofurazan (**5**) and 4-nitrobenzofuroxan (**8**) to give the Meisenheimer-type complexes **6**, **9** and **7**, **10**. The kinetics of the interactions have been studied by the stopped-flow method. The formation of the 5-methoxyl adducts **6** and **9** is found to always precede that of the thermodynamically more stable 7-methoxyl isomers **7** and **10**. The results indicate that the para-like 4-nitro group is more efficient than the furazan and the furoxan rings in delocalizing the negative charge in **7** and **10**. The kinetic and thermodynamic parameters $\Delta H°$, $\Delta S°$, $\Delta H^{\ddagger}$, and $\Delta S^{\ddagger}$ for the various reactions have been determined. It appears that only a large positive entropy change, $\Delta S°$ (about +80 J mol^{-1} K^{-1}), is responsible for both the formation and the greater stability of the 7-methoxyl complexes **7** and **10** as compared to that of their 5-methoxyl analogues. Stabilization of **7** and **10** by association of the 4-nitro group with the potassium counterion is suggested.

Nitrobenzofurazans and nitrobenzofuroxans have been shown to be potent in vitro inhibitors of nucleic acid synthesis in lymphocites.[2-5] It was suggested that a possible mode of action of these derivatives at the cellular

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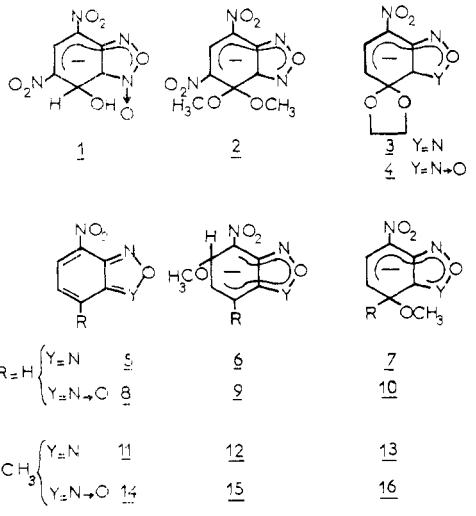
level was formation of Meisenheimer-type complexes with essential cellular SH and/or amino groups. This proposal has heightened interest in the characterization of stable adducts derived from these classes of compounds. Thus, there is now convincing structural evidence, mainly from NMR studies, that a number of mononitro- and dinitrobenzofurazans and -benzofuroxans react with nucleophiles to give stable Meisenheimer complexes.[6-12] For the elucidation of the factors governing the formation and stabilities of these complexes, it was necessary to derive kinetic and thermodynamic parameters relating to their formation and decomposition. In this context, we have recently reported a comprehensive quantitative analysis of the formation and decomposition of the dinitro adducts **1** and **2** [9,13] and the mononitro adducts **3** and **4**.[12] We now report kinetic and thermodynamic data for the reactions of methoxide ion with 4-nitrobenzofurazan (**5**) and 4-nitrobenzofuroxan (**8**) in methanol. Compounds **5** and **8** have been shown by NMR to yield concurrently the isomeric complexes **6**, **7** and **9**, **10**, respectively.[10]



Results

The interactions of methoxide ion with 4-nitrobenzofurazan (**5**) (λ_{max} = 320 nm) and 4-nitrobenzofuroxan (**8**) (λ_{max} = 403 nm) were investigated at 20 °C in the concentration range of 2×10^{-5}–0.1 M potassium methoxide in methanol. Whereas the stable adducts **7** (λ_{max} = 330 nm) and **10** (λ_{max} = 340 nm) are directly formed at the lowest base concentrations, the oscilloscope pictures taken in a stopped-flow apparatus show that their appearance

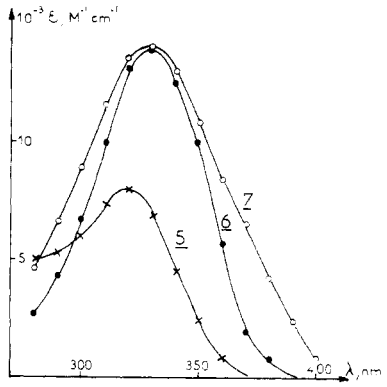


Figure 1. Absorption spectra of 4-nitrobenzofurazan (**5**) and its 5- and 7-methoxyl adducts **6** and **7** in methanol.

is preceded by the much faster formation of a thermodynamically less stable species at base concentrations greater than about 2×10^{-4} M. In view of previous NMR results in methanol–Me_2SO mixtures rich in Me_2SO,[10] there was little doubt that these species were the adducts **6** and **9**, respectively, which arise from concurrent methoxide ion attack at the unsubstituted 5-carbon ortho to the nitro group of **5** and **8**. The absorption spectra of **6** and **7** are shown in Figure 1. As can be seen both of the adducts have a very similar absorption around their maxima. The same is true for the adducts **9** and **10**.

7-Methoxyl Adducts 7 and 10. Direct formation of **7** and **10** according to eq 1 was followed at methoxide ion concentrations less than about 2×10^{-4} M where the formation of the less stable isomers **6** and **9** may be safely neglected. The buffer solutions were the same as those used in previous studies,[14] and no sensitive buffer dependence of the rates was observed under our experimental conditions (ionic strength I = 0.01 M, total buffer concentrations $<4 \times 10^{-2}$ M). On the basis of eq 1, the rates

$$\mathbf{5}\ (\text{or } \mathbf{8}) + CH_3O^- \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} \mathbf{7}\ (\text{or } \mathbf{10}) \quad (1)$$

$$k_2^{obsd} = k_{-2} + k_2[CH_3O^-] \quad (2)$$

must obey eq 2 where k_2^{obsd} is the observed first-order rate constant for the approach to equilibrium, k_2, the second order-rate constant for the formation of **7** and **10**, and k_{-2} the first-order rate constant for the decomposition of these adducts. As expected, plots (Figure 2)[15] of k_2^{obsd} vs. the base concentration were linear, allowing a determination of the k_2 and k_{-2} values from slopes and intercepts. The equilibrium constants K_2 for the formation of **7** and **10** were calculated from $K_2 = k_2/k_{-2}$. We thus obtain at 20 °C k_2 = 3.8 M^{-1} s^{-1}, $k_{-2} = 1.3 \times 10^{-3}$ s^{-1}, and K_2 = 2920 M^{-1} for **7** and k_2 = 17.6 M^{-1} s^{-1}, $k_{-2} = 2.2 \times 10^{-3}$ s^{-1}, and K_2 = 8000 M^{-1} for **10**. Some of the experimental values of k_2^{obsd} for the 4-nitrobenzofuroxan system are given in Table I.

5-Methoxyl Adducts 6 and 9. In less dilute potassium methoxide solutions (5×10^{-4}–0.1 M), the formation of **6** and **9** always preceded that of **7** and **10**. Equation 3 de-

$$\mathbf{5}\ (\text{or } \mathbf{8}) + CH_3O^- \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathbf{6}\ (\text{or } \mathbf{9}) \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} \mathbf{7}\ (\text{or } \mathbf{10}) \quad (3)$$

$$k_1^{obsd} = k_{-1} + k_1[CH_3O^-] \quad (4)$$

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Table I. First-Order Rate Constants k_1^{obsd}, k_2^{obsd}, and $k_2'^{obsd}$ for the Reaction of Methoxide Ion with 4-Nitrobenzofuroxan in Methanol at 20 °C

$[CH_3O^-]$, M	k_1^{obsd}, s^{-1}	$10^3 k_2^{obsd}$, s^{-1}	$10^3 k_2'^{obsd}$, s^{-1}	$10^3(k_2'^{obsd} - k_{-2})$, s^{-1}	$1/k_2'^{obsd} - k_{-2}$, s	$1/[CH_3O^-]$, M^{-1}
2.09×10^{-5} [a,e]		2.68				
3.16×10^{-5} [a,e]		2.68				
5.9×10^{-5} [b,e]		3.32				
1.17×10^{-4} [b,e]		4.19				
1.62×10^{-4} [c,e]		5.21				
2.4×10^{-4} [c,e]		6.20		4	250	4150
3.4×10^{-4} [c,e]			8.4	6.2	161	2940
4.7×10^{-4} [c,e]			8.8	6.6	152	2130
6.3×10^{-4} [d,e]			11.6	9.4	106	1590
8.15×10^{-4} [c,e]			11.9	9.7	103	1230
8.35×10^{-4} [d,e]	3.24		13.7	11.5	87	1200
1.05×10^{-3} [c,e]	3.34		14.9	12.7	79	950
1.82×10^{-3} [d,e]			23.7	21.5	46.5	550
2×10^{-3} [d,e]	3.84		23	20.8	48	500
4×10^{-3} [d,e]	8.05		29	26.8	37.5	250
6×10^{-3} [d,e]	10.21					
8×10^{-3} [d,e]	13.46		31	28.8	34.72	125
0.01 [d,e]	18.23		33	30.8	32.45	100
0.02 [d,f]	30.1		35.6			
0.04 [d,f]	62.7		40			
0.06 [d,f]	88		42			
0.1 [d,f]	145		40, 40.7			

[a] *p*-Cyanophenol buffer. [b] *o*-Bromophenol buffer. [c] *p*-Chlorophenol buffer. [d] Potassium methoxide solution. [e] I = 0.01 M. [f] Ionic strength not constant.

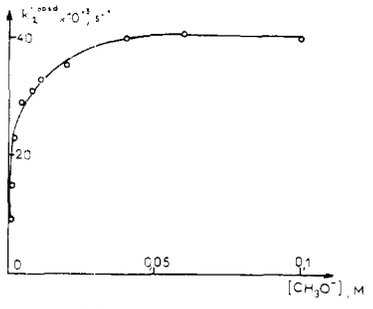


Figure 4. Plot of $k_2'^{obsd}$ against methoxide ion concentration for the appearance of the adduct **10** in methanol (t = 20 °C).

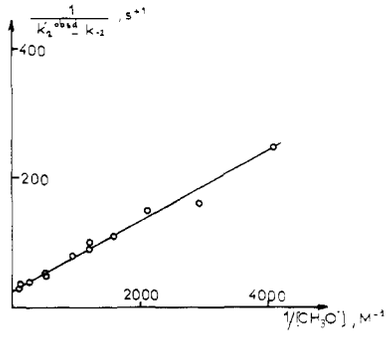


Figure 5. Inversion plot according to eq 6 for the appearance of the adduct **10** in methanol: $[CH_3O^-]$ in the range 2.4×10^{-4}–0.01 M; I = 0.01 M; t = 20 °C.

scribes the interaction which then consisted of two well-separated steps. For the first step which is the fast equilibration between **5** and **6** (or **8** and **9**), the observed first-order rate constant k_1^{obsd} is given by eq 4. Values of the rate constants of formation and decomposition, k_1 and k_{-1} for **6** and **9**, were easily obtained from linear plots (Figure 3)[15] of k_1^{obsd} vs. $[CH_3O^-]$. We thus obtain at 20 °C k_1 = 845 M^{-1} s^{-1}, k_{-1} = 5.2 s^{-1}, and K_1 = 163 M^{-1} for **6** and k_1 = 1420 M^{-1} s^{-1}, k_{-1} = 3 s^{-1}, and K_1 = 475 M^{-1} for **9** ($K_1 = k_1/k_{-1}$).

The second step is the slower equilibrium formation of the stable complexes **7** and **10** from the parent molecules which are considered to be in instantaneous equilibrium with the initially formed isomers **6** and **9**. As expected, the observed first-order rate constant $k_2'^{obsd}$ associated with this process depended curvilinearly on the base concentration according to eq 5 and approached a plateau at the

$$k_2'^{obsd} = k_{-2} + \frac{k_2[CH_3O^-]}{1 + K_1[CH_3O^-]} \quad (5)$$

$$\frac{1}{k_2'^{obsd} - k_{-2}} = \frac{1}{k_2[CH_3O^-]} + \frac{K_1}{k_2} \quad (6)$$

highest base concentrations (Figure 4). Rewriting eq 5 in the form of eq 6 allows a new determination of k_2 and K_1 by combining slopes and intercepts of plots of $1/(k_2'^{obsd} - k_{-2})$ vs. $1/[CH_3O^-]$ which were linear (Figure 5). We thus obtain k_2 = 3.70 M^{-1} s^{-1} and K_1 = 145 M^{-1} for 4-nitrobenzofurazan and k_2 = 18.7 M^{-1} s^{-1} and K_1 = 468 M^{-1} for 4-nitrobenzofuroxan. These values compare well with our earlier determinations. Experimental values of k_1^{obsd} and $k_2'^{obsd}$ are given in Table I for 4-nitrobenzofuroxan.

Measurements at Other Temperatures. The interactions were also studied at 10, 30, and 40 °C in dilute potassium methoxide solutions under the conditions of eq 3. Whereas the k_1 and k_{-1} values were deduced, as previously, from linear plots of k_1^{obsd} vs. $[CH_3O^-]$, the rate constants k_2 for **7** and **10** were obtained by using the $k_2'^{obsd}$ values measured at $[CH_3O^-] > 10^{-2}$ M. At these base concentrations, the k_{-2} values could be safely neglected compared to the $k_2'^{obsd}$ values, allowing a determination of k_2 from the slopes of linear plots (Figure 6)[15] of $k_2'^{obsd}(1 + K_1[CH_3O])$ vs. $[CH_3O^-]$ (eq 7). The k_2 values thus

$$k_2'^{obsd}(1 + K_1[CH_3O^-]) = k_2[CH_3O^-] \quad (7)$$

obtained at 20 °C (k_2 = 3.9 M^{-1} s^{-1} for **7**, k_2 = 19.4 M^{-1} s^{-1} for **10**) again agree reasonably well with those previously determined.

For the benzofurazan system, the final equilibrium optical densities were measured at 330 nm where the two adducts **6** and **7** have similar absorptions (Figure 1). Since the conversion of **6** into **7** is not complete (the ratio K_2/K_1 is equal to about 18 at 20 °C), these measurements provided the value of an apparent equilibrium constant K

Table II. Kinetic and Equilibrium Data for the Formation and Decomposition of the Furazanic Meisenheimer Complexes 6 and 7 in Methanol at Different Temperatures

	complex 6			complex 7		
temp, °C	k_1, M^{-1} s^{-1}	k_{-1}, s^{-1}	K_1, M^{-1}	k_2, M^{-1} s^{-1}	k_{-2}, s^{-1}	K_2, M^{-1}
10	500	2.6	192[a]			
20	845	5.2	163,[a] 145[b]	3.8,[c] 3.7,[d] 3.9[e]	1.3×10^{-3} [c]	2920,[c] 2850
30				8.85[e]	3×10^{-3} [g]	2950[f]
32	1730	14.6	119.3[a]			
40.4	2700	25	108[a]	18.2[e]	6×10^{-3} [g]	3030[f]

[a] Calculated from k_1/k_{-1}. [b] Calculated from the intercept of the linear plot of $1/(k_2'^{obsd} - k_{-2})$ vs. $1/[CH_3O^-]$. [c] From measurements in buffer solutions. [d] From the slope of the linear plot of $1/(k_2'^{obsd} - k_{-2})$ vs. $1/[CH_3O^-]$. [e] From the slopes of linear plots of $k_2'^{obsd}(1 + K_1[CH_3O^-])$ vs. $[CH_3O^-]$. [f] From spectrophotometric measurements as discussed in the Results section. [g] Calculated from k_2/K_2.

Table III. Kinetic and Equilibrium Data for the Formation and Decomposition of the Furoxanic Meisenheimer Complexes 9 and 10 in Methanol at Different Temperatures

	complex 9			complex 10		
temp, °C	k_1, M^{-1} s^{-1}	k_{-1}, s^{-1}	K_1, M^{-1}	k_2, M^{-1} s^{-1}	k_{-2}, s^{-1}	K_2, M^{-1}
10	725	1.5	485[a]	9.9[e]		
20	1420	3	475,[a] 468[b]	17.6,[c] 18.7,[d] 19.4[e]	2.2×10^{-3} [c]	8000[c]
30	2600	6.5	400[a]	40[e]		

[a] Calculated from k_1/k_{-1}. [b] Calculated from the intercept of the linear plot of $1/(k_2'^{obsd} - k_{-2})$ vs. $1/[CH_3O^-]$. [c] From measurements in buffer solutions. [d] From the slope of the plot of $1/(k_2'^{obsd} - k_{-2})$ vs. $1/[CH_3O^-]$. [e] From the slope of linear plots of $k_2'^{obsd}(1 + K_1[CH_3O^-])$ vs. $[CH_3O^-]$.

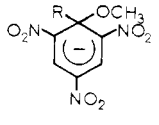
Table IV. Kinetic and Thermodynamic Parameters for the Formation and Decomposition of Complexes 6, 7, 9, and 10 at 25 °C

	6	7	9	10
k_f, M^{-1} s^{-1}	1200	0	1950	28.5
k_r, s^{-1}	8.5	2.04×10^{-3}	4.57	$\simeq 3.35 \times 10^{-3}$ [b]
K, M^{-1}	141	2940	427	$\simeq 8500$[a]
$\Delta H_f^{\ddagger}$, kJ mol^{-1}	38.9	56.0	43.5	45.5
$\Delta S_f^{\ddagger}$, J mol^{-1} K^{-1}	−54.3	−46.8	−38.45	−63.5
$\Delta H_r^{\ddagger}$, kJ mol^{-1}	53.3	52.4	49.5	<45.5[d]
$\Delta S_r^{\ddagger}$, J mol^{-1} K^{-1}	−47.2	−120	−66	$\simeq -145$
ΔH°, kJ mol^{-1}	−14.4	3.6	−6	slightly > 0[c]
ΔS°, J mol^{-1} K^{-1}	−7.1	73.2	27.55	$\simeq 80$[f]
ΔG°, kJ mol^{-1}	−12.3	−18.2	−14.2	−22.6[e]

[a] Estimated from spectrophotometric measurements between 5×10^{-4} and 10^{-3} M. [b] Estimated from $k_r = k_f/K$. [c] Experimental observation. [d] Deduced from $\Delta H_r^{\ddagger} = \Delta H_f^{\ddagger} - \Delta H^{\circ}$. [e] Estimated from $\Delta G^{\circ} = -RT \log K$. [f] Estimated from $\Delta S^{\circ} = \Delta H^{\circ} - \Delta G^{\circ}/T$.

equal to the sum $K_1 + K_2$. By use of the K_1 values kinetically determined, the K_2 values were calculated. As can be seen in Table II, increasing the temperature decreases K_1 and slightly increases K_2. This is in agreement with NMR observations that the detection of **6** is favored at low temperatures.[10] Due to the higher stability of **9** and **10**, similar spectrophotometric measurements could not be performed with accuracy for the benzofuroxan system. Such measurements would have required buffer solutions which have not yet been calibrated over the desired pH range at 10 and 30 °C in methanol. Careful experiments between 5×10^{-4} and 10^{-3} M methoxide revealed, however, that the effect of increasing the temperature is to slightly favor the formation of **10**. As found for **7**, the enthalpy change ΔH_2° associated with this reaction would be slightly greater than zero, in agreement with NMR observations in Me_2SO.[10]

Tables II and III summarize the rate coefficients and equilibrium constants determined at the different temperatures studied for the benzofurazan and benzofuroxan systems, respectively. The derived thermodynamic and kinetic parameters for the formation and decomposition of **6**, **7**, **9**, and **10** are given in Table IV. Table V allows a comparison of the rate and equilibrium constants obtained for these adducts with similar data recently published for the mononitro adducts **12**, **13**, **15**, and **16** derived from 4-nitro-7-methoxybenzofurazan (**11**) and benzofuroxan **14**.[8a,17a] The data for the trinitrobenzene adducts **17** and **18** are also included.[16]



17 R = H

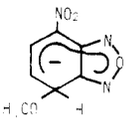
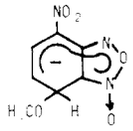
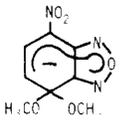
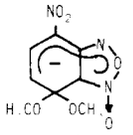
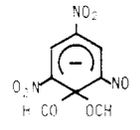
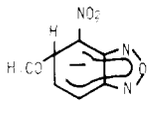
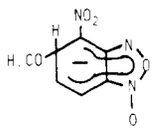
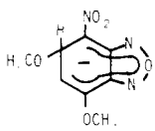
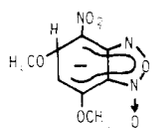
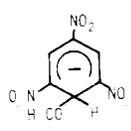
18 R = OCH_3

Discussion

Stability of the Furazan and Furoxan Complexes. Table V shows that in methanol the stability of both the 5-methoxyl complexes **6** and **9** and the 7-methoxyl complexes **7** and **10** is greater than that of the methoxytrinitrobenzene complex **17** which is frequently used as a model for comparison of reactions involving monomethoxyl adducts: the ratios K^6/K^{17}, K^9/K^{17}, K^7/K^{17}, and K^{10}/K^{17} are equal to 8, 21, 130, and 360, respectively. These results emphasize the stability of furazan and furoxan Meisenheimer-type complexes which is a consequence of the very strong electron-withdrawing character of the furazan and furoxan rings. We note that the stability differences are

(16) (a) C. F. Bernasconi, *J. Am. Chem. Soc.*, **92**, 4682 (1970); (b) *ibid.*, **93**, 6975 (1971).
(17) (a) G. Ah-Kow, *C. R. Hebd. Seances Acad. Sci., Ser. C*, **287**, 231 (1978); (b) F. Terrier and G. Ah-Kow, unpublished results.

Table V. Rate and Equilibrium Parameters for some Meisenheimer Complexes in Methanol at 20 °C

	 7 [a]	 10 [a]	 13 [b]	 16 [b]	 18 [c]
k_f, M^{-1} s^{-1}	3.8	17.6	7.56	12.02	11.8
k_r, s^{-1}	1.3×10^{-3}	2.2×10^{-3}	3.55×10^{-3}	2.29×10^{-3}	6.05×10^{-4}
K, M^{-1}	2920	8000	2135	5250	19500
	 6 [a]	 9 [a]	 12 [b]	 15 [b]	 17 [c]
k_f, M^{-1} s^{-1}	845	1420	347	348	5150
k_r, s^{-1}	5.2	3	9.2	5	231
K, M^{-1}	163	475	37.7	69.6	22.3

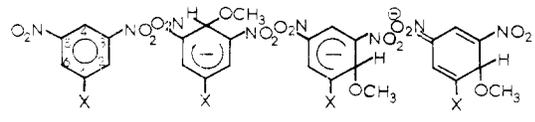
[a] This work. [b] Reference 17a. [c] Values calculated at 20 °C from data in ref 16.

all in favor of the annelated complexes. In previous studies, the trinitrobenzene adducts were always found to be slightly more stable than their annelated analogues; for example, the spiro complexes **3** and **4** are 1.7- and 4.6-fold less stable than their trinitrobenzene analogue in water.[12] Similarly, the *gem*-dimethoxyl complexes **13** and **16** are 9- and 4-fold less stable than the complex **18** in methanol.[16]

As can be seen, **6** and **9** have similar rates of formation and decomposition, as do **7** and **10**, and therefore similar stabilities. That both the ratios K^9/K^6 and K^{10}/K^7 are equal to about 3 shows that the furoxan moiety is in this instance somewhat more efficient than the furazan one in stabilizing the adducts. A similar situation is encountered in comparing the complexes **3** and **4**[17a] as well as the complexes **12** and **15**, **13** and **16**, in methanol: [15] the ratios K^4/K^3, K^{15}/K^{12}, and K^{16}/K^{13} are equal to 1.74, 1.84, and 2.45, respectively. In contrast, the furazan complex **3** is 2.7-fold more stable than its furoxan analogue **4** in water.[12] Differences in the solvation of the *N*-oxide group in water and methanol might explain the observed differences in the overall electron-withdrawing effects of the furoxan and furazan rings.

5-Methoxyl vs. 7-Methoxyl Adduct Formation. Because methoxide ion attack occurs respectively 200- and 70-fold faster at the 5-carbon than at the 7-carbon of both **5** and **8**, the formation of the 5-methoxyl complexes **6** and **9** is initially favored. However, the 7-methoxyl isomers **7** and **10**, which decompose much more slowly than **6** and **9** (the ratios k_r^6/k_r^7 and k_r^9/k_r^{10} are equal to 4160 and 3160, respectively),[18] are thermodynamically more stable products. Both the ratios K^{10}/K^9 and K^7/K^6 are about 20. As a result, about 5% of **6** and **9** is still present in the solutions at final equilibrium.

The situation qualitatively resembles that encountered in the interaction of methoxide ion with 1-substituted 3,5-dinitrobenzenes, **19**.[18-21] In this case, the 4-methoxyl

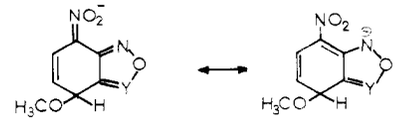


19 20 21 22

(18) In the text and tables, a subscript f or r indicates the forward and reverse directions.

complexes **20** are formed under kinetic control but isomerize rapidly to the 2-methoxyl complexes **21**. The greater stability of the latter has been explained in terms of an extensive delocalization of the negative charge by the nitro group para to their sp^3 carbon (resonance structure **22**).[19] The high efficiency of a para nitro group in delocalizing electrons by resonance interaction is now recognized to be a factor of overwhelming importance in determining the stability of benzene Meisenheimer adducts.[14,22,23]

In the present work, the most stable complexes **7** and **10** are also those formed by attack at the nucleophile para to the nitro group in **5** and **8**. This result suggests that the 4-nitro group is more efficient than the condensed furazan and furoxan rings in delocalizing the negative charge of complexes **7** and **10**; i.e., the resonance structure **23a** would



23a Y=N, Y=N→O 23b

be much more favored than the resonance structure **23b**. Todesco et al. have previously pointed out that the furazan and furoxan rings have a much stronger inductive effect but have less capacity for resonance than a nitro group.[8,24] That a large portion of the negative charge of **7** and **10** is localized on the oxygen atoms of the 4-nitro group is in agreement with an X-ray crystallographic study of the methoxide complex **24**.[25] In this 4,6-dinitro complex, the C_4–N_2 bond is significantly shorter (1.39 Å) than the C_6–N_1 bond (1.44 Å) whereas the C_5–C_6 bond length (1.37 Å) is

(19) (a) F. Millot and F. Terrier, *Bull. Soc. Chim. Fr.*, 1823 (1974); (b) R. Schaal, F. Terrier, J. C. Halle, and A. P. Chatrousse, *Tetrahedron Lett.*, 1393 (1970); (c) A. P. Chatrousse and F. Terrier, *Bull. Soc. Chim. Fr.*, 4549 (1972).

(20) M. R. Crampton and H. A. Khan, *J. Chem. Soc., Perkin Trans. 2*, 733 (1972).

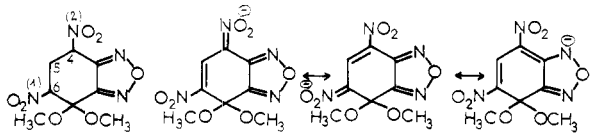
(21) C. A. Fyfe, M. Cocivera, and S. M. H. Damji, *J. Am. Chem. Soc.*, **97**, 5707 (1975).

(22) M. J. Strauss, *Chem. Rev.*, **70**, 667 (1970).

(23) F. Terrier, F. Millot, and R. Schaal, *J. Chem. Soc., Perkin Trans. 2*, 1192 (1972).

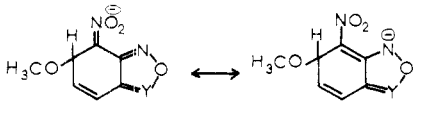
(24) D. Dalmonte, E. Sandri, L. DiNunno, S. Florio, and P. E. Todesco, *J. Chem. Soc. B*, 2209 (1971).

(25) (a) G. G. Messmer and G. J. Palenik, *Chem. Commun.*, 470 (1969); (b) *Acta Crystallogr., Sect. B*, **27**, 314 (1971).



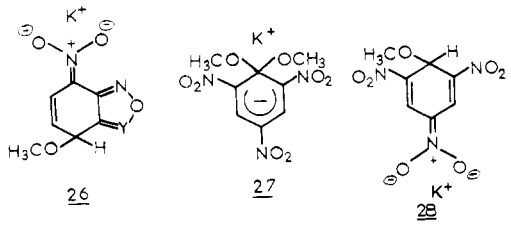
24 24a 24b 24c

close to that of a usual C–C double bond. These features which are similar to those found for the trinitro complex **18**[22,26,27] are consistent with a structure in which the resonance contributor **24a** is much more important than those (**24b**, **24c**) which have a single C_4–N_2 bond. The situation is certainly the same in **7** and **10** which have only a nitro group at the 4-position. Recent evidence[17a,28] that benzofurazan and benzofuroxan adducts with a NO_2 group in the para position of their sp^3 carbon have a much higher tendency (about 10^2-fold) than the trinitrobenzene adducts to form nitronic acids in an acidic medium in water and methanol also supports this conclusion. In contrast, both resonance structures **25a** and **25b** would contribute to the stability of the 5-methoxyl complexes **6** and **9** which do not have a nitro group in the para position of their sp^3 carbon.



25a Y = N, N→O 25b

A comparison of the activation and thermodynamic parameters for the formation and decomposition of the 5- and 7-methoxyl complexes is instructive (Table IV). The formation of **6** and **9** is exothermic whereas that of the more stable complexes **7** and **10** is endothermic. As a result, it is only large positive entropy changes, $\Delta S°$, which ensure both the formation and the greater stability of the 7-methoxyl complexes: $\Delta S_7° = 73.2$ J mol^{-1} K^{-1}, $\Delta S_{10}° = 80$ J mol^{-1} K^{-1}. Of interest is the fact that these positive $\Delta S°$ values essentially reflect the $\Delta S_r^{\ddagger}$ values which are much more negative for **7** and **10** than for **6** and **9** ($\Delta S_{6,r}^{\ddagger} = -47.2$ J mol^{-1} K^{-1}; $\Delta S_{9,r}^{\ddagger} = -66$ J mol^{-1} K^{-1}; $\Delta S_{7,r}^{\ddagger} = -120$ J mol^{-1} K^{-1}; $\Delta S_{10,r}^{\ddagger} = -145$ J mol^{-1} K^{-1}). An explanation of this result, which suggests a much lower solvation requirement of the former complexes, might be in terms of some stabilization of **7** and **10** by association of the potassium counterion with the para-like 4-nitro group as shown in **26**. Although such a stabilization must lower

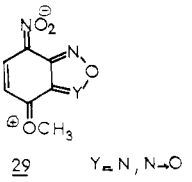


26 27 28

to some extent the entropy of these complexes due to the increase in their orderliness, one can expect this effect to be more than largely canceled by the gain in entropy associated with the desolvation of K^+ and the absence of solvation at the oxygen atoms of their NO_2 group.

While stabilization of benzene Meisenheimer complexes by association with cations is a well-known fact in methanol,[29] it has been observed for *gem*-dimethoxyl adducts such as **18** but not for monomethoxyl adducts such as **17**. On this basis, Crampton has suggested that ion pairs such as **27** where the cation is held by a cage effect by the two oxygen atoms of two methoxyl groups are much more stable than ion pairs such as **28** where the cation is associated with the oxygen atoms of the NO_2 group. However, despite the failure to observe **28**, we feel that the formulation of **26** is not unreasonable since one can expect the localization of the negative charge of the 4-nitro group of **7** and **10** to increase the stability of this ion pair the same way as it increases the tendency of adducts to protonate in acidic medium. Convincing evidence for the existence of **26** could evidently come from measurements of the effect of changing the counterion on the stability of **7** and **10**, with experimental conditions analogous to those described in the benzene series. Indeed, we have been unable to perform such reliable measurements. This is mainly because the values of the equilibrium constants for formation of **7** and **10** are high, so that buffer solutions are required to follow accurately the equilibrium formation of these complexes. In addition, as previously mentioned, the initially formed isomers **6** and **9** are probably present to some extent at final equilibrium. We are presently looking for a more suitable system to check the existence of associations such as **26**.

7-Methoxyl vs. 7,7-Dimethoxyl Complex Formation. The methoxyl group in polynitro-substituted anisoles such 2,4,6-trinitroanisole (TNA) is sterically crowded. The greater stability of the *gem*-dimethoxyl trinitrobenzene complex **18** relative to its monomethoxyl analogue **17** is largely due to the relief of steric strain which occurs on going from TNA to **18**.[22] There is no comparable steric strain around the methoxyl group of 7-methoxy-4-nitrobenzofurazan and -benzofuroxan and, therefore, no relief of steric strain upon the formation of the 7,7-dimethoxyl complexes **13** and **16**. Because of this, stabilities of the same order of magnitude must be expected for the annelated methoxyl and dimethoxyl complexes **7** and **13** on the one hand and **10** and **16** on the other hand. That **7** and **10** are slightly more stable than **13** and **16** (the ratios K^7/K^{13} and K^{10}/K^{16} are equal to 1.36 and 1.5, respectively) is probably due to a greater ground-state stabilization of 7-methoxy-4-nitrobenzofurazan and -benzofuroxan through a resonance structure such as **29** involving the methoxyl



29 Y = N, N→O

group. Such a stabilization has been proven to be effective in methoxyl compounds such as TNA having a nitro group in the para position.[16,30] The somewhat higher stability of the 5-methoxyl complexes **6** and **9** relative to their analogues **12** and **15** may be interpreted in the same way.

Experimental Section

Materials. 4-Nitrobenzofurazan (**5**) and 4-nitrobenzofuroxan (**8**) were prepared and purified as previously described:[31,32] **5**, mp

(26) R. Destro, C. Grammacioli, and M. Simonetta, *Acta Crystallogr.*, **24**, 1369 (1968).
(27) H. Ueda, N. Sakabe, J. Tanaka, and A. Furusaki, *Bull. Chem. Soc. Jpn.*, **41**, 2866 (1968).
(28) F. Terrier and G. Ah-Kow, paper presented at the 4th IUPAC International Symposium on Physical Organic Chemistry, York, England, Sept 4–8, 1978.
(29) (a) M. R. Crampton and H. A. Khan, *J. Chem. Soc., Perkin Trans. 2*, 2286 (1972); (b) M. R. Crampton, B. Gibson, and F. W. Gilmore, *ibid.*, 91 (1979), and references therein.
(30) F. Terrier, A. P. Chatrousse, and R. Schaal, *J. Org. Chem.*, **37**, 3010 (1972).
(31) R. J. Gaughran, J. P. Picard, and J. V. R. Kaufman, *J. Am. Chem. Soc.*, **76**, 2233 (1954).

93 °C (lit.[2,31] mp 93 °C); 8, mp 143 °C (lit.[2,32] mp 143 °C). Methanol and methanolic potassium methoxide solutions were prepared as previously described.[14] The various buffers used for the rate measurements were purified according to classical methods.

Rate and pH Measurements. Stopped-flow determinations were performed on a Durrum stopped-flow spectrophotometer, the cell compartment of which was maintained to ±0.5 °C. Other kinetic measurements were made by using a Beckman Acta III spectrophotometer. All kinetic runs were carried out under pseudo-first-order conditions with a substrate concentration in the range 5×10^{-5}–10^{-4} M. Rate constants are accurate to ±3%. The ionic strength of the potassium methoxide solutions with $[CH_3O^-] < 10^{-2}$ M was kept constant at 0.01 M by adding KBr as necessary.

(32) P. Drost, *Justus Liebigs Ann. Chem.*, **307**, 49 (1899).

The pH of buffered solutions at 20 °C was measured according to a method previously reported by using an hydrogen electrode.[14] The pH values so obtained are relative to the standard state in methanol. The $[CH_3O^-]$ concentration of these solutions (I = 0.01 M) was calculated by solving eq 8 where K_s is the autoprotolysis

$$[CH_3O^-] = K_s/a_{H^+}\gamma_{\pm} \quad (8)$$

constant and $\gamma_{\pm}$ the mean activity coefficient at I = 0.01 M ($K_s = 10^{-16.86}$; $\gamma_{\pm}$ = 0.66 at t = 20 °C).[14]

Registry No. **5**, 16322-19-3; **6**, 73466-75-8; **7**, 59344-28-4; **8**, 18771-85-2; **9**, 59344-30-8; **10**, 59344-31-9, 865-33-8.

Supplementary Material Available: Figures 2, 3, and 6 showing the plots of k_2^{obsd}, k_1^{obsd}, and $k_2'^{obsd}(1 + K_1[CH_3O^-])$, respectively, vs. the methoxide ion concentration for the appearance of the adducts **9** or **10** (3 pages). Ordering information is given on any current masthead page.

Carbon-13 and Proton Nuclear Magnetic Resonance Chemical Shift Assignments in Imides and β-Diketone Enolates[1]

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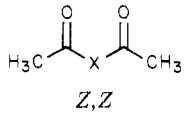
Department of Chemistry, Wayne State University, Detroit, Michigan 48202

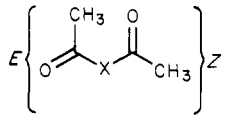
Received September 17, 1979

The low-temperature ^1H and ^{13}C NMR spectra of the imides diacetamide and *N*-acetylpropionamide and the enolate anions 2,4-pentanedionate (acetylacetonate) and 2,4-hexanedionate (propionylacetonate) are presented. Under the conditions used, torsion about C–N and C–C partial double bonds is slow on the NMR time scale, and in the symmetrical compounds three different kinds of acetyl methyl and acetyl carbonyl (in ^{13}C NMR spectra) resonances can be observed: the single resonances from *Z,Z* diastereomers and pairs of resonances from diastereotopic acetyl groups in the *E,Z* (and *Z,E*) diastereomers. The spectra of the unsymmetrical compounds which have two diastereomeric forms (*E,Z* and *Z,E*) were used to complete chemical shift assignments for the diastereotopic groups in the symmetrical compounds which have only a single *E,Z* form. The relation between these assignments and those in amides and simple enolates is discussed.

The *E,Z* forms of diacetamide (**1**) and the isoelectronic enolate anion acetylacetonate (**2**) exhibit large chemical



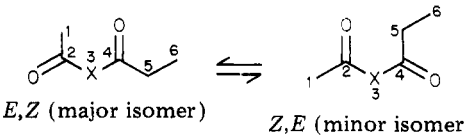
Z,Z



E,Z

1, X = NH
2, X = CH^-

shift differences between diastereotopic carbonyl and/or methyl groups in their ^1H and ^{13}C NMR spectra.[2-4] Assignments of resonances to the *Z,Z* and *E,Z* diastereomers of these and other symmetrical imides and β-diketone enolates can be made on symmetry grounds, since the *E,Z* forms exhibit pairs of resonances for diastereotopic acyl groups while the *Z,Z* diastereomers exhibit only a single resonance for the homotopic acyl groups.[3-5] However, it is not possible, on the basis of the spectra of the symmetrical compounds alone, to assign the pairs of resonances in the *E,Z* diastereomers to the diastereotopic *E* and *Z* acyl groups. This paper describes an approach, using the unsymmetrical homologues of **1** and **2**, viz., *N*-acetylpropionamide (**3**) and propionylacetonate (**4**), to make these assignments and provides information about the effects of neighboring acyl groups on ^1H and ^{13}C NMR chemical shifts which may be useful in making assignments in other compounds.



E,Z (major isomer) *Z,E* (minor isomer)

3, X = NH
4, X = CH^-

It might have been supposed that the magnetic an-

(1) (a) This paper can be considered part of two series: "NMR Studies of Enolate Anions. 7." and "Stereochemistry of Trivalent Nitrogen Compounds. 37." For previous papers in these series see: "NMR Studies of Enolate Anions. 6." (Raban, M.; Haritos, D. P. *J. Am. Chem. Soc.* **1979**, *101*, 5178) and "Stereochemistry of Trivalent Nitrogen Compounds. 36." (Raban, M.; Lauderback, S. K. *J. Org. Chem.*, in press). (b) We thank the National Science Foundation and the National Institute of General Medical Sciences for support of this work. (c) A portion of this paper was abstracted from a thesis submitted by D.H. in partial fulfillment of the requirements of the M.S. degree, Wayne State University.

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