Intermediates in Nucleophilic Aromatic Substitution. IV.[1] Kinetic Study of the Interaction of 1,3,5-Trinitrobenzene with the Lyate Ions of Water, Methanol, and Ethanol in the Respective Solvents[2]

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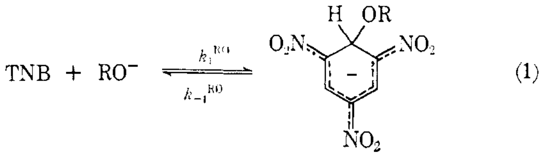
Abstract: The kinetics of reversible Meisenheimer complex (I, IIa, IIb) formation between 1,3,5-trinitrobenzene and the respective lyate ions in water, methanol, and ethanol has been studied by the stopped-flow and the temperature-jump methods. The rate coefficients for complex formation are in the ratio 1:188:918 for OH^-, CH_3O^-, and $C_2H_5O^-$, respectively; the low value for OH^- is intelligible in terms of strong OH^- solvation in the ground state. The rate coefficients of reversion to reactants are in the ratio 1:31:2.9 for the same sequence of bases. The surprisingly low value for OH^- is attributed to intramolecular hydrogen bonding to an *o*-nitro group in the complex I. The kinetic and thermodynamic parameters of the reactions of 1,3,5-trinitrobenzene with CH_3O^- and $C_2H_5O^-$ are compared with literature data on the reactions of 2,4,6-trinitroanisole with the same nucleophiles, to form 1,1 complexes (IVa, IVb) as well as 1,3 complexes (IIIa, IIIb). Complexes from 1,3,5-trinitrobenzene (IIa, IIb), like 1,3 complexes from 2,4,6-trinitroanisole, are formed much faster than the 1,1 complexes, but are like 1,3 complexes thermodynamically less stable than 1,1 complexes. Old explanations of this peculiar reactivity pattern are discussed and a new one based on ground-state resonance stabilization of 2,4,6-trinitroanisole is offered.

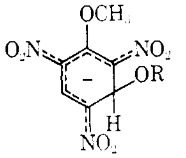
The predominant reaction of 1,3,5-trinitrobenzene, henceforth abbreviated TNB, with a variety of nucleophiles is known to be the formation of a σ complex, often referred to as a Meisenheimer[3] complex, symbolized MC in this paper.[4] The structure of the MC's formed by the action of an alkoxide or hydroxide ion is represented by I, IIa, and IIb in eq 1. Though other interactions between TNB and a variety of nucleophiles to form CT complexes[5] and radical anions,[6,7] or to undergo ring-proton abstraction[8-10] or attack on the nitrogen of one of the nitro groups,[11] have been reported, they all seem to be of minor importance compared to σ-complex formation in the specific systems under current study; thus, they do not need concern us here.



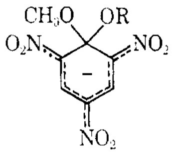
I, R = H
IIa, R = CH_3
IIb, R = C_2H_5

Equilibrium data have been reported on the reactions of TNB with hydroxide,[12] methoxide,[7] and ethoxide[13,4b] ion in the respective solvents. An extensive kinetic study was made only in the ethanol system,[13a] but the complex formed between TNB and ethoxide ion was wrongly interpreted as a CT complex.[13a] A comparison of kinetic data in the three base-solvent systems would appear to be of considerable interest with respect to general reactivity problems in nucleophilic aromatic substitution reactions; our focus is particularly on the rates of nucleofugic leaving group expulsion, *i.e.*, on the rate coefficients k_{-1}^{RO}.[11]

Another interesting comparison is the one between the reactions of methoxide or ethoxide ion with TNB and with 2,4,6-trinitroanisole (TNA), respectively; this may shed some light on the problem of the kinetically controlled 1,3 complex (III) *vs.* the thermodynamically controlled 1,1 complex (IV) formation found by Servis[14] in dimethyl sulfoxide and similar later findings by Fendler, *et al.*,[15] for 1-methoxy-2,4,6-



IIIa, R = CH_3
IIIb, R = C_2H_5



IVa, R = CH_3
IVb, R = C_2H_5

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[1] Part III: C. F. Bernasconi, *J. Org. Chem.*, **35**, 1214 (1970).

[2] Supported in part by a grant from the Petroleum Research Fund administered by the American Chemical Society. Grateful acknowledgment is made to the donors of this fund.

[3] J. Meisenheimer, *Ann.*, 323, 205 (1902).

[4] For recent reviews see: (a) R. Foster and C. A. Fyfe, *Rev. Pure Appl. Chem.*, **16**, 61 (1966); (b) E. Buncel, A. R. Norris, and K. E. Russell, *Quart. Rev. Chem. Soc.*, 22, 123 (1968); (c) P. Buck, *Angew. Chem. Int. Ed. Engl.*, 8, 120 (1969); (d) J. Miller, "Aromatic Nucleophilic Substitution," Elsevier Publishing Co., Amsterdam, 1968; (e) M. R. Crampton, *Advan. Phys. Org. Chem.*, 7, 211 (1969).

[5] G. Briegleb, W. Liptay, and M. Cantner, *Z. Phys. Chem.* (*Frankfurt*), **26**, 55 (1960).

[6] (a) R. E. Miller and W. F. K. Wynne-Jones, *J. Chem. Soc.*, 2375 (1959); (b) R. E. Miller and W. F. K. Wynne-Jones, *Nature*, **186**, 149 (1960).

[7] V. Gold and C. H. Rochester, *J. Chem. Soc.*, 1692 (1964).

[8] R. J. Pollitt and B. C. Saunders, *Proc. Chem. Soc.*, 176 (1962).

[9] E. Buncel and E. A. Symons, *Can. J. Chem.*, **44**, 771 (1966).

[10] M. R. Crampton and V. Gold, *J. Chem. Soc., B*, 498 (1966).

[11] C. F. Bernasconi, *J. Amer. Chem. Soc.*, **92**, 129 (1970).

[12] (a) T. Abe, *Bull. Chem. Soc. Jap.*, 33, 41 (1960); (b) V. Gold and C. H. Rochester, *J. Chem. Soc.*, 1710 (1964).

[13] (a) E. F. Caldin and G. Long, *Proc. Roy. Soc., Ser. A*, **226**, 263 (1955); (b) G. Lambert and R. Schaal, *J. Chim. Phys.*, **59**, 1170 (1962).

[14] (a) K. L. Servis, *J. Amer. Chem. Soc.*, 87, 5495 (1965); (b) *ibid.*, **89**, 1508 (1967).

[15] (a) J. H. Fendler, E. J. Fendler, and C. E. Griffin, *J. Org. Chem.*, 34, 689 (1969); (b) E. J. Fendler, J. H. Fendler, C. E. Griffin, and J. W. Larsen, *ibid.*, 35, 287 (1970).

Table I. Reaction of TNB with OH^- in Water, Stopped-Flow Determinations[a]

[NaOH], *M*	τ_{OH}^{-1} (15°), sec^{-1}	τ_{OH}^{-1} (25°), sec^{-1}	τ_{OH}^{-1} (35°), sec^{-1}
0.02	6.64 ± 0.15		18.6 ± 0.50
0.10	8.40 ± 0.20	13.1 ± 0.30	26.6 ± 0.65
0.20	9.82 ± 0.25	16.0 ± 0.40	37.0 ± 1.0
0.10	11.1 ± 0.27	19.9 ± 0.50	47.0 ± 1.2
0.40	13.0 ± 0.30	23.3 ± 0.55	54.5 ± 1.4
0.50	15.2 ± 0.40	29.8 ± 0.70	65.7 ± 1.8
0.60		31.3 ± 0.80	
k_1 (M^{-1} sec^{-1})	15.8 ± 0.8	37.5 ± 1.8	98.0 ± 5.0
k_{-1} (sec^{-1})	6.8 ± 0.35	9.8 ± 0.5	16.5 ± 0.8
$K = k_1/k_{-1}$ (M^{-1})	2.32 ± 0.24	3.73 ± 0.37	5.94 ± 0.60

[a] $[TNB]_0 = 5 \times 10^{-6}$ or 10^{-5} *M;* total electrolyte concentration maintained at 1.0 *M* by adding appropriate amounts of NaCl.

dinitrocyano- and 1-methoxy-2,4,6-dicyanonitrobenzenes. Both II and III are formed by nucleophilic attack on an unsubstituted carbon and thus the reactions should be very similar.

We wish now to report such a kinetic study.

Results

Reaction of TNB with OH^- in Water. Some preliminary kinetic data on this reaction have been reported in 10% dioxane–90% water as by-products of a temperature-jump study of the interaction between TNB and aliphatic amines.[11] We have now investigated the reaction more thoroughly at three different temperatures in pure water by the stopped-flow method. The results are summarized in Table I. All experiments were conducted with NaOH in large excess over TNB, and at a constant ionic strength of 1.0 *M* by adding appropriate amounts of NaCl. The reciprocal relaxation time (observed first-order rate coefficient for approach to equilibrium) is thus given by eq 2, where k_1^{OH} and k_{-1}^{OH} are as defined in eq 1.

$$1/\tau_{OH} = k_1^{OH}[NaOH] + k_{-1}^{OH} \qquad (2)$$

Plots of τ_{OH}^{-1} *vs.* [NaOH] at 15, 25, and 35° are shown in Figure 1. They are linear as called for by eq 2. k_1^{OH} and k_{-1}^{OH} were determined from slopes and intercepts, respectively, and are reported, along with the equilibrium constants, $K^{OH} = k_1^{OH}/k_{-1}^{OH}$, at the bottom of Table I. From Arrhenius plots (not shown), activation parameters were calculated. Kinetic and thermodynamic data at 25° are summarized in Table IV.

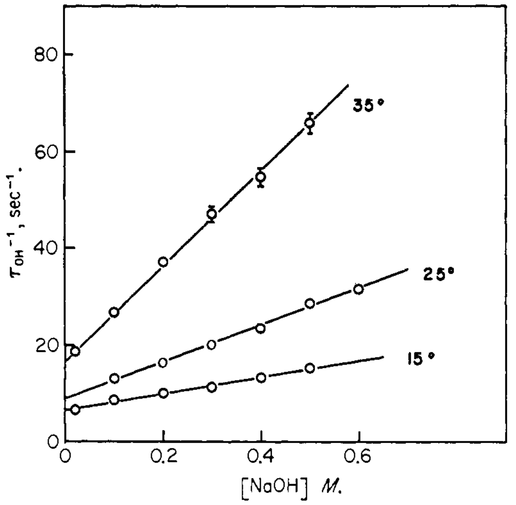

Figure 1. Reaction of TNB with NaOH in water; τ^{-1} as a function of [NaOH] at three temperatures.

Reaction of TNB with CH_3O^- in Methanol. The reaction of TNB with $NaOCH_3$ is rather fast and requires the application of the temperature-jump technique.[16] The kinetics of equilibrium approach was studied with $NaOCH_3$ in large excess over TNB, and at constant electrolyte concentration maintained at 0.2 *M* by adding $NaClO_4$ as needed. The reciprocal relaxation time obeyed eq 3 at the temperatures of 15.1, 25, and 35°, as can be seen from Figure 2. $k_1^{CH_3O}$

$$1/\tau_{CH_3O} = k_1^{CH_3O}[NaOCH_3] + k_{-1}^{CH_3O} \qquad (3)$$

and $k_{-1}^{CH_3O}$, along with K^{CH_3O} calculated from these plots, are included in Table II. Kinetic and thermodynamic parameters at 25° are summarized in Table IV.

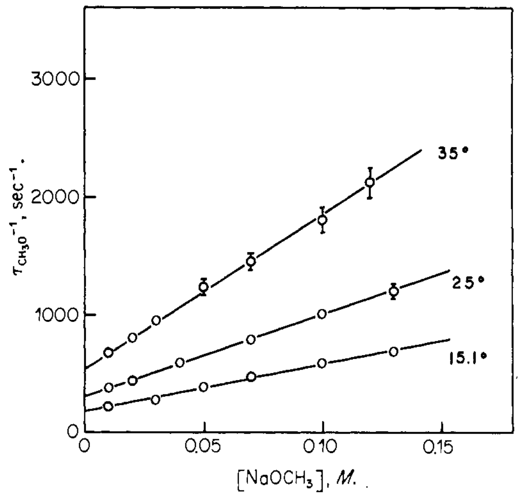

Figure 2. Reaction of TNB with $NaOCH_3$ in methanol; τ^{-1} as a function of $[NaOCH_3]$ at three temperatures.

Reaction of TNB with $C_2H_5O^-$ in Ethanol. Though a rather complete kinetic study has been reported by Caldin and Long,[13a] we have reinvestigated this system, mainly because their activation parameters were very much out of line with the general picture emerging from Table IV (see Discussion), and because k_{-1}^{EtO} had not been measured directly at or near room temperature.

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[16] M. Eigen and L. DeMaeyer, *Tech. Org. Chem.*, **8**, 895 (1963).

Table II. Reaction of TNB with CH_3O^- in Methanol, Temperature-Jump Determinations[a]

$[NaOCH_3]$, M	$\tau_{CH_3O}^{-1}$ (15.1°), sec^{-1}	$\tau_{CH_3O}^{-1}$ (25°), sec^{-1}	$\tau_{CH_3O}^{-1}$ (35°), sec^{-1}
0.01	220 ± 6	372 ± 10	670 ± 20
0.02		431 ± 13	800 ± 25
0.03	277 ± 10		950 ± 35
0.04		599 ± 20	
0.05	390 ± 18		1,230 ± 60
0.07	469 ± 20	781 ± 30	1,450 ± 70
0.10	587 ± 30	1,000 ± 40	1,800 ± 100
0.12			2,120 ± 150
0.13	720 ± 40	1,204 ± 60	
k_1 (M^{-1} sec^{-1})	3,900 ± 250	7,050 ± 400	13,100 ± 700
k_{-1} (sec^{-1})	180 ± 10	305 ± 15	538 ± 30
$K = k_1/k_{-1}$ (M^{-1})	21.7 ± 2.6	23.1 ± 2.6	24.3 ± 2.7

[a] $[TNB]_0 = 8 \times 10^{-5}$ M for experiments at $[NaOCH_3] > 0.03$ M, $[TNB]_0 = 2 \times 10^{-4}$ M for experiments at $[NaOCH_3] \leq 0.03$ M; total electrolyte concentration maintained at 0.2 M by adding appropriate amounts of $NaClO_4$.

This time we conducted our experiments with a large excess of TNB over NaOEt, so that the relaxation time as determined in the stopped-flow spectrometer[17] is given by eq 4. The reason for the rather unorthodox

$$1/\tau_{EtO} = k_1^{EtO}[TNB] + k_{-1}^{EtO} \qquad (4)$$

choice of the excess component was in the necessity to use rather low concentrations of the excess component (10^{-4} to 5×10^{-3} M) in order to get accurate intercepts in Figure 3. At such low concentrations, even very low levels of absorbed atmospheric CO_2 may well alter the actual base concentration in an uncontrolled manner, thus rendering the experimental data inaccurate. When the base is the component at lower concentration, partial neutralization by CO_2 does not affect the results as long as this neutralization is very slow compared to the reaction under study, which was the case here. Traces of the reaction of EtO^- with CO_2 could be observed and interfered slightly with our determinations at the lowest TNB concentrations. A typical oscilloscope picture is shown in Figure 4.[18] These pictures were evaluated by drawing the infinity line as shown in Figure 4 which is equivalent to assuming that the rise due to the side reaction is linear within the short time period covered on the picture. The small error possibly introduced by this procedure has been taken into account in estimating the limits of error.

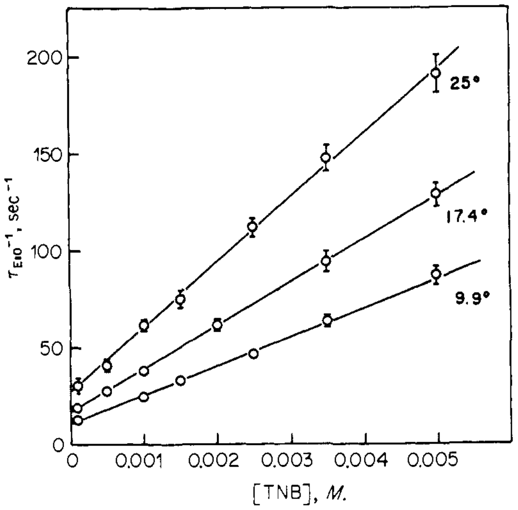

Figure 3. Reaction of TNB with NaOEt in ethanol; τ^{-1} as a function of [TNB] at three temperatures.

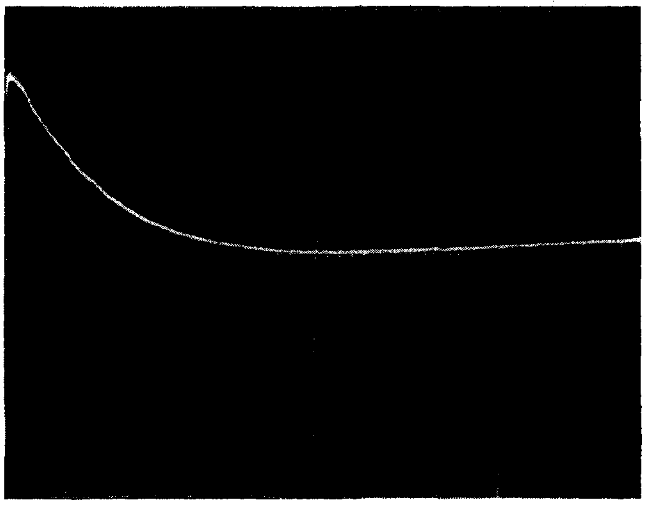

Figure 4. Representative oscilloscope picture of reaction of TNB with NaOEt at low [TNB] ([TNB] = 10^{-4} M, [NaOEt] ≈ 5×10^{-5} M, λ = 450 mμ, 9.9°, 0.05 sec/unit).

From slopes and intercepts in Figure 3, k_1^{EtO} and k_{-1}^{EtO} were calculated at 9.9, 17.4, and 25°; they are reported in Table III. The kinetic and thermodynamic parameters, along with those determined by Caldin and Long,[13a] are summarized in Table IV.

Discussion

Reactions of TNB with OH^-, CH_3O^-, and $C_2H_5O^-$. Equilibrium constants for MC formation between TNB and the three mentioned nucleophiles have been measured previously by various authors. They are included in Table IV. Our equilibrium constants derived from kinetics agree fairly well with those in the methoxide–methanol and hydroxide–water systems but not quite as well in the ethoxide–ethanol system. The reasons for the discrepancies are difficult to assess.

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[17] Some experiments were also made with the temperature-jump apparatus with the same results as for the runs in the stopped-flow machine within experimental error. We found the stopped-flow method more convenient to use however because of the better temperature control and because of some cavitation problems in this solvent.

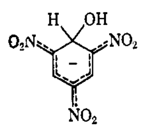
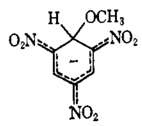
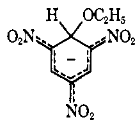
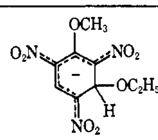
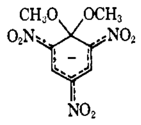
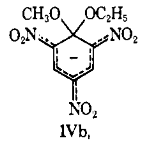
[18] That the gentle rise of the infinity line is actually due to the reaction of CO_2 with EtO^- can be shown by deliberately introducing some more CO_2 into the system, which has the effect of increasing the slope of the rising portion in proportion to the CO_2 added.

Table III. Reaction of TNB with $C_2H_5O^-$ in Ethanol, Stopped-Flow Determinations[a]

$10^3 \times$ [TNB], M	τ_{EtO}^{-1} (9.9°), sec^{-1}	τ_{EtO}^{-1} (17.4), sec^{-1}	τ_{EtO}^{-1} (25°), sec^{-1}
0.10	13.1 ± 1.2	18.8 ± 1.8	30.2 ± 3.0
0.50		27.5 ± 2.0	41.1 ± 3.0
1.0	24.7 ± 2.0	37.6 ± 2.0	61.5 ± 3.0
1.5	33.5 ± 2.0		74.9 ± 3.5
2.0		61.2 ± 3.0	
2.5	46.3 ± 2.0		112 ± 5.0
3.5	63.3 ± 3.0	93.6 ± 4.5	147 ± 7.0
5.0	87.0 ± 4.0	129 ± 6.0	191 ± 9.5
k_1 (M^{-1} sec^{-1})	14,800 ± 750	22,200 ± 1000	33,400 ± 1,700
k_{-1} (sec^{-1})	10.6 ± 1.0	16.9 ± 1.7	27.5 ± 2.7
$K = k_1/k_{-1}$ (M^{-1})	1,400 ± 200	1,310 ± 190	1,210 ± 180

[a] $[NaOC_2H_5] \approx 2.5 \times 10^{-5}$ M.

Table IV. Kinetic and Thermodynamic Parameters of Meisenheimer Complexes at 25°

	 I, in H_2O	 IIa, in CH_3OH	 IIb, in C_2H_5OH	 IIIb, in C_2H_5OH[a]	 IVa, in CH_3OH[b]	 IVb, in C_2H_5OH[a]
k_1 (M^{-1} sec^{-1})	37.5[c]	7,050	33,400 (27,500[d,e])	3690[f]	17.3	20.2[g]
k_{-1} (sec^{-1})	9.8[c]	305	27.5	472[f]	1.04×10^{-3}	Large
$K = k_1/k_{-1}$ (M^{-1})	3.73[c] (2.7[h,i])	23.1 (15.4[j])	1,210 (2,400[d,e]) 1,600,[k] 2,070[l]	7.3[f]	17,000	
pK_a	13.43 (14.40,[m] 13.19[n])	15.58[o] (15.71[p])	15.82[q]			
$\Delta H_1^{\ddagger}$ (kcal mol^{-1})	15.6 ± 0.8	10.2 ± 0.8	8.7 ± 1.0 (11.7 ± 0.1[e])	9.8 ± 0.3	12.9 ± 1.0	12.5 ± 0.2
$\Delta S_1^{\ddagger}$ (eu)	1.1 ± 2.7	−6.7 ± 2.7	−8.6 ± 3.4 (2.2 ± 0.6[e])	−9.3 ± 1.0	−9.4 ± 3.4	−8.4 ± 0.7
$\Delta H_{-1}^{\ddagger}$ (kcal mol^{-1})	7.3 ± 0.8	9.2 ± 0.8	10.4 ± 1.2 (11.4 ± 0.2[e])	13.1 ± 0.3	18.4 ± 1.0	17.5–20.0[s]
$\Delta S_{-1}^{\ddagger}$ (eu)	−29.4 ± 2.7	−16.3 ± 2.7	−16.9 ± 4.0 (−14.3 ± 0.6[e])	−2.3 ± 1.0	−4.8 ± 3.4	
ΔH (kcal mol^{-1})	8.3 ± 1.6	1.0 ± 1.6	−1.4 ± 2.2 (0.3 ± 0.3[e])	−3.3 ± 0.6[t,u]	−5.5 ± 2.0 (−4.86 ± 0.3[t])	−5 to −7.5[s]
ΔS (eu)	30.5 ± 5.4	9.6 ± 5.4	8.3 ± 7.4 (16.5 ± 1.5[e])	−7.5 ± 3.0	−4.6 ± 4.0 (3.0[t])	

[a] J. B. Ainscough and E. F. Caldin, *J. Chem. Soc.*, 2528 (1956). [b] Reference 15a. [c] In 10% dioxane–90% water, $\mu = 0.5$ M, $k_1 = 49.0$ M^{-1} sec^{-1}, $k_{-1} = 9.8$ sec^{-1}, $K = 5.0$ M^{-1} as determined in ref 11. [d] At 20°. [e] Reference 13a. [f] Calculated from thermodynamic parameters determined at very low temperatures by Ainscough and Caldin, footnote *a*. [g] Extrapolated to 25° from $k_1 = 6.36$ M^{-1} sec^{-1} at 10°. [h] Reference 12a. [i] Reference 12b. [j] Reference 7. [k] Reference 13b. [l] Reference 4b. [m] R. Schaal, *J. Chim. Phys.*, **52**, 796 (1955), from acidity function in ethylenediamine–water mixtures. [n] G. Lambert and R. Schaal, *C. R. Acad. Sci., Ser. C*, **225**, 1939 (1962), see Discussion. [o] Using the same pK_a = 16.92 of methanol as in footnote *p*. [p] R. Schaal and G. Lambert, *J. Chim. Phys.*, **59**, 1151 (1962). [q] Using pK_a = 18.9 of ethanol. [r] E. J. King, "Acid-Base Equilibria," The Macmillan Company, New York, N. Y., 1965, p 798. [s] Estimated, assuming a similar or slightly higher value than for CH_3O^- attack in methanol. [t] Calorimetric determination, J. W. Larsen, J. H. Fendler, and E. J. Fendler, *J. Amer. Chem. Soc.*, **91**, 5903 (1969). [u] For what is presumably CH_3O^- attack on the 3 position, $\Delta H = -1.48 \pm 0.5$ kcal mol^{-1} in methanol; see Larsen, *et al.*, footnote *t*.

Gold and Rochester[12b] have criticized Abe's[12a] method of calculating K^{OH} for I, because the intercept of a Benesi–Hildebrand[19] plot is too small and uncertain for an accurate estimate of the extinction coefficient of I and K^{OH}, due to 1:2 complex formation at higher base concentration. Interestingly, by assuming an extinction coefficient of 30,000, they also got a K^{OH} value of 2.7 M^{-1} from the linear portion of a plot of OD *vs.* base concentration.

Our kinetic determination is not affected by 1:2 complex formation nor by slow decomposition reactions of TNB in basic solution and thus can be considered inherently more reliable.

Whereas the agreement between the pK_a value derived from K^{CH_3O} in methanol and the one reported by Schaal and Lambert[20] is close, there exists a big discrepancy of about 1 pK unit between Schaal's[21] and our pK_a value in aqueous solution. However, in a later communication, Lambert and Schaal[22] express some doubts about their value, which could be wrong because of concurrent complex formation of TNB with the ethylenediamine used as a solvent component in their acidity function procedure. They suggest a new pK_a value of 13.19, derived by subtracting 2.52 from the pK_a in methanol; 2.52 is the average difference p$K_a^{CH_3OH}$ − p$K_a^{H_2O}$ for a number of weak acids.

There exists also a notable discrepancy between the thermodynamic parameters determined by Caldin and Long[13a] and the ones found in this study for the ethoxide–ethanol system. The disagreement is especially

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(19) H. A. Benesi and J. H. Hildebrand, *J. Amer. Chem. Soc.*, **71**, 2703 (1949).

(20) See Table IV, footnote *p*.

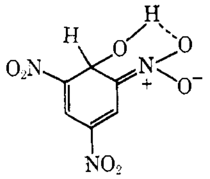
(21) See Table IV, footnote *m*.

(22) See Table IV, footnote *n*.

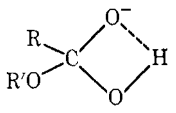
large with respect to $\Delta H_1^{\ddagger}$ and $\Delta S_1^{\ddagger}$, though interestingly the k_1 values at room temperature reported by the two laboratories are very nearly the same. The much higher $\Delta S_1^{\ddagger}$ value of Caldin and Long compared to all the other $\Delta S_1^{\ddagger}$ values for methoxide or ethoxide attack summarized in Table IV led us to suspect an experimental error and to reinvestigate this reaction. Our results fit far better into the general picture emerging from Table IV. Some qualitative temperature-jump experiments also confirmed that the reaction is indeed exothermic by at least 1 kcal mol^{-1} (our value determined from an Arrhenius plot is $\Delta H = -1.4$ kcal mol^{-1}) instead of slightly endothermic as reported by Caldin and Long.

Though our rate and equilibrium data for the three bases OH^-, CH_3O^-, and $C_2H_5O^-$ are not strictly comparable because of different solvents, the solvent effect is likely to be very small for these isoelectric reactions[23] and is not expected to influence the general picture emerging from these results. The relative k_1^{RO} values are in the ratio 1:188:918 for OH^-, CH_3O, and $C_2H_5O^-$, which confirms the general pattern found in other nucleophilic additions or substitutions on aromatic[24] or acyl[25] carbon, in particular for the pair OH^-/CH_3O^-. This *a priori* rather abnormal reactivity pattern when compared with the relative basicities, which are in the ratio 1:0.62:1.80 for OH^-, CH_3O^-, and $C_2H_5O^-$, respectively, in water[26] or 1:0.30:1.27 in 2-propanol,[27] has generally been attributed to greater solvation of OH^- compared to CH_3O^- or $C_2H_5O^-$.[4d,25b,28] The appreciably higher $\Delta S_1^{\ddagger}$ value for k_1^{OH} as compared to $k_1^{CH_3O}$ and k_1^{EtO} seems to support this interpretation.

From the reactivity pattern in the k_1^{RO} values one might have expected that the k_{-1}^{RO} values would be in the reactivity order $k_{-1}^{OH} \gg k_{-1}^{CH_3O} > k_{-1}^{EtO}$. Instead they are in the ratio $k_{-1}^{OH}:k_{-1}^{CH_3O}:k_{-1}^{EtO}$ = 1:31:2.9, which does not correlate with the pK_a values of the solvents either. The much lower than expected value of k_{-1}^{OH} may be attributed to intramolecular hydrogen bonding to one of the *o*-nitro groups in I′, similar to a suggestion by Shain and Kirsch[29] for the intermediate V in the alkaline hydrolysis of esters. The very strongly negative entropy of activation for k_{-1}^{OH} compared to $k_{-1}^{CH_3O}$ or k_{-1}^{EtO} is consistent with such an interpretation: less solvent molecules would be tied up for solvating the nitrogroups in I than in IIa or IIb. The lower than expected rate of decomposition of the MC formed from TNB and *n*-butylamine in 10% dioxane–90% water was recently explained along similar lines.[11]



I′



V

Reactions of TNB and of TNA with CH_3O^- and $C_2H_5O^-$. It is interesting to compare the reactions of TNB with CH_3O^- or $C_2H_5O^-$ with the 1,1 complex (IIIa, IIIb) formations from TNA; kinetic and thermodynamic data from Fendler, *et al.*,[15a,30] and from Ainscough and Caldin[32] (IIIb) on these latter are included in Table IV. Though the stability of IVa is greater by a factor of ~1000 than that of IIa, its rate of formation is about a factor of 400 smaller than for the latter; thus the greater stability of IVa stems entirely from its very slow rate of decomposition, which is nearly a factor of 3×10^5 smaller than $k_{-1}^{CH_3O}$ in the TNB system. A similar situation apparently prevails in ethanol when IIb and IVb are compared, though the information about IVb is not complete. The variation in the k_1 values is seen to be virtually exclusively an enthalpy affair, whereas for k_{-1} it appears to be due both to enthalpy and entropy changes, though also here the enthalpy effects dominate.

In 1956, Ainscough and Caldin[32] reported the observation of a second process taking place in ethanolic sodium ethoxide solutions of TNA, which was faster than the reaction forming IVb. This was attributed to CT-complex formation, an interpretation which later evidence could not support.[4a] It is now generally believed that Ainscough and Caldin's fast reaction was due to 1,3-complex (IIIb) formation.[4a,e,14,15b] This new interpretation is due to Servis,[14] who observed in the nmr a rapid 1,3-complex (IIIa) formation between TNA and CH_3O^- in dimethyl sulfoxide, followed by a slow rearrangement to the more stable 1,1 complex (IVa). Analogous findings have later been reported by Fendler, *et al.*,[15] with 2,4,6-cyanodinitro- or 2,4,6-dicyanonitroanisoles and CH_3O^- in dimethyl sulfoxide.

Ainscough and Caldin's data on the 1,3 complex (IIIb) are included in Table IV. The rate and equilibrium constants given at 25° have been calculated from their thermodynamic parameters determined at much lower temperatures. One can see that IIIb is formed fast but decomposes fast, whereas the more stable 1,1 complex IVb is formed slowly, in agreement with the qualitative nmr observations referred to above[14,15] for methoxide ion attack.

Most recently, a calorimetric determination of $\Delta H = -1.48 \pm 0.5$ kcal mol^{-1} for what is believed[33] to be 1,3-complex (IIIa) formation in methanol has been reported,[33] showing that also in methanol the 1,3 complex (IIIa) is thermodynamically less stable than IVa by about 3 kcal mol^{-1}.

It appears that the fast rate of formation but relatively low thermodynamic stability of 1,3 complexes and of MC's from TNB, which both are formed by nucleophilic attack on an unsubstituted carbon, as opposed to the slow formation of the more stable 1,1 complexes, which involves nucleophilic attack on a

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[23] Preliminary results from our laboratory on a similar study in mixed alcoholic aqueous solvents with high water content show that the rates of the methoxide and ethoxide ion reactions are not significantly affected by the change in solvent.

[24] (a) J. F. Bunnett and G. T. Davis, *J. Amer. Chem. Soc.*, **76**, 3011 (1954); (b) J. Murto, *Acta Chem. Scand.*, **18**, 1024 (1964); (c) E. Tommila and J. Murto, *ibid.*, **16**, 53 (1962); (d) J. Murto, *Ann. Acad. Sci. Fenn., Ser. A2*, No. 117 (1962).

[25] (a) M. L. Bender and W. A. Glasson, *J. Amer. Chem. Soc.*, **81**, 1590 (1959); (b) W. P. Jencks and M. Gilchrist, *ibid.*, **84**, 2910 (1962).

[26] P. Ballinger and F. A. Long, *ibid.*, **82**, 795 (1960).

[27] J. Hine and M. Hine, *ibid.*, **74**, 5266 (1952).

[28] T. C. Bruice and S. J. Benkovic, "Bioörganic Mechanisms," Vol. I, W. A. Benjamin Inc., New York, N. Y., 1966, p 102.

[29] S. A. Shain and J. F. Kirsch, *J. Amer. Chem. Soc.*, **90**, 5848 (1968).

[30] In a previous paper,[31] we listed activation parameters for IIIa formation from various sources. This newest determination by Fendler, *et al.*,[15a] appears to be the most reliable.

[31] C. F. Bernasconi, *J. Amer. Chem. Soc.*, **90**, 4982 (1968).

[32] See Table IV, footnote *a*.

[33] See Larsen, *et al.*, Table IV, footnote *t*.

carbon bearing a methoxy group, are related phenomena and have probably a common origin. This has already been recognized by Crampton and Gold.[34] In an attempt to rationalize these findings, Crampton and Gold,[34] and earlier Gold and Rochester[7] suggested that the 1,1 complex (IVa) is a less strained structure than TNA, but the transition state leading to IVa was sterically more strained than TNA; on the other hand, steric effects should be unimportant in the transition states leading to IIa or IIIa. The higher stability of 1,1 complexes was attributed to release of steric strain from the substrate as well as to the inductive effect of the methoxy group.

Though it seems reasonable that steric strain be smaller in a 1,1 complex compared to the reactant, it is difficult to visualize why this strain should go through a maximum in the transition state.

Fendler, *et al.*,[15a] also criticized this explanation based on steric strain, mainly on the grounds that 1,3 complexes were not observed with 1-methoxy-2,6-dinitrobenzene and 1-methoxy-2,4-dinitronaphthalene; the transition state leading to the 1,3 complex in the case of 1-methoxy-2,6-dinitrobenzene would be expected to be quite strongly favored by steric factors at the expense of the transition state leading to the 1,1 complex.

The problem is perhaps best discussed in terms of the thermodynamic parameters summarized in Table IV. It appears that the differences in the $\Delta H_{-1}^{\ddagger}$ and ΔH values between a situation where the alkoxide ion has attacked an unsubstituted carbon (IIa, IIb, IIIb) and a situation where it has attacked a carbon bearing a methoxy group (IVa, IVb) are probably primarily related to the fact that multiple alkoxy (or fluoro) substitution has a large stabilizing effect on a sp^3 carbon relative to a nonsubstituted or little-substituted sp^3 carbon as well as relative to an equally substituted sp^2 carbon.[35] This would explain the higher stability of 1,1 complexes of TNA compared to 1,3 complexes or TNB complexes. In the transition state the degree of alkoxy substitution is somewhere in between reactant and complex; so is the hybridization of the carbon in question. This should diminish the stabilizing influence of the methoxy group and one expects a lesser effect on $\Delta H_{-1}^{\ddagger}$ (or k_{-1}^{RO}) than on ΔH (or K^{RO}). Though the enthalpy data are somewhat difficult to compare between the TNB and TNA systems, due to considerable differences in the $\Delta S_{-1}^{\ddagger}$ and ΔS values, it is nevertheless clear that on the contrary $\Delta H_{-1}^{\ddagger}$ (or k_{-1}^{RO}) is more affected than ΔH (or K^{RO}) by methoxy substitution ($\Delta H_{-1}^{\ddagger}$(IVa) $-\Delta H_{-1}^{\ddagger}$(IIa) = 9.2 kcal mol^{-1}, ΔH(IIa) $-$ ΔH(IVa) = 6.5 kcal mol^{-1}; ratio of k_{-1}^{RO} values IVa:IIa = 1:3 $\times$ 10^5; ratio of K values IIa:IVa = 1:736). This is most probably due to a considerable ground-state stabilization of TNA through resonance structures like Va and Vb which have the effect of making ΔH less negative than expected on the basis of alkoxy stabilization of the sp^3 carbon in the 1,1 complex alone.

For the same reason, $\Delta H_1^{\ddagger}$ for alkoxide attack on the 1 position in TNA is higher than for attack on TNB, instead of being lower as would be expected from the stabilizing influence on the transition state by higher methoxy substitution and partial sp^3 character of the carbon, or even simply from consideration of the inductive effect of the methoxy group. A well-known example for the rather strong rate-retarding effect of ground-state resonance stabilization involving the methoxy substituent is the hydrolysis of *p*-methoxydiazonium ion compared to the unsubstituted benzenediazonium ion.[36] The unsubstituted diazonium ion is hydrolyzed faster by a factor of >6000 than the methoxy-substituted compound, although the hydrolysis of aryldiazonium ions is generally accelerated by electron-releasing substituents in the aromatic residue.[36]

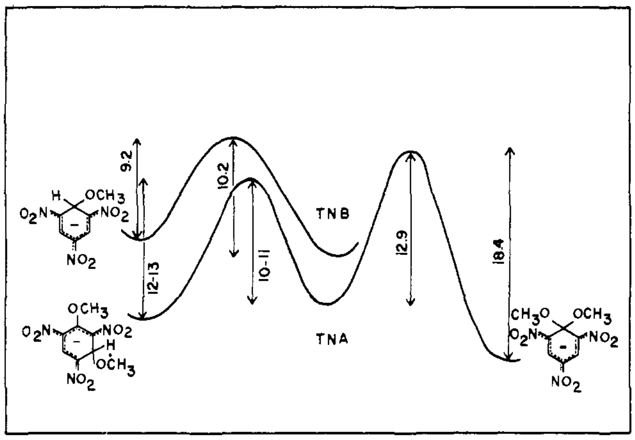
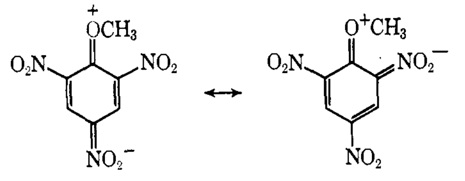
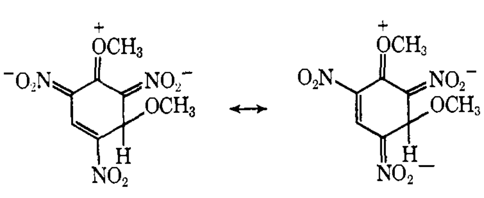


Figure 5. Potential energy diagram for the reactions of methoxide ion with TNA and withTNB in methanol.



Va Vb

In comparison of 1,3 complexes with the 1,1-complex formation from TNA, the situation is different in that both reactions have the same ground-state energy level. From this one might expect the 1,1 complexes to be formed equally fast or faster than the 1,3 complexes, which is in disagreement with the facts. However, the 1,3 complexes can benefit from resonance stabilization involving the methoxy group, too (VIa ↔ VIb), and so does the transition state leading to the 1,3 complex.[37] Thus, ground-state stabilization of TNA



VIa VIb

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[34] M. R. Crampton and V. Gold, *J. Chem. Soc., B*, 893 (1966).

[35] (a) J. Hine, *J. Amer. Chem. Soc.*, **85**, 3239 (1963); (b) J. Hine, L. G. Mahone, and C. L. Liotta, *ibid.*, **89**, 5911 (1967).

[36] M. L. Crossley, R. H. Kienle, and C. H. Benbrook, *ibid.*, **62**, 1400 (1940).

[37] That k_1^{EtO} in the case of IIIb is smaller by a factor of ~10 than in the case of IIb, though perhaps expected to be slightly larger because of the inductive effect of the methoxy substituent, may be seen as an indication that resonance stabilization in the 1,3 complex is not quite as effective as in TNA; two resonance structures (VIa and VIb) involving the methoxy group can be drawn in the former, three (Va and two Vb) for the latter.

will significantly affect only 1,1-complex formation and reduce its rate compared to 1,3 complex—as well as compared to TNB complex formation.

The above rationalizations are consistent with a very recent report by Norris,[38] showing that with cyanide ion in chloroform TNA forms a 1,3 complex which is more stable than the 1,1 complex. When there is no stabilizing effect by double alkoxy substitution on the sp^3 carbon, the 1,1 complex can indeed be expected to become less stable than the 1,3 complex because of the mentioned resonance effects.

Crampton[4e] has drawn a potential energy diagram for the 1,1- and 1,3-complex formation from TNA and CH_3O^- in methanol, assuming that the activation energies for IIIa are about the same as those determined by Ainscough and Caldin[32] for IIIb. It is now interesting to add the energy profile for IIa formation to Crampton's diagram. This is shown in Figure 5. The ground-state resonance stabilization of TNA relative to TNB has been assumed to be 4 kcal mol^{-1}.

It is noteworthy that Miller's[39] method of calculating relative energy levels of initial states, intermediates, and transition states in nucleophilic aromatic substitutions, which has often proved remarkably successful in its predictions,[4d,40] does not give satisfactory results when nucleophilic attack on an unsubstituted carbon is under consideration. This has already been pointed out by Servis[14b] in the case of IIIa, and is again found for IIa in this study. Miller[41] calculated values for $\Delta H_1^{\neq}$ and $\Delta H_{-1}^{\neq}$ of 14.5 and 21.5 kcal mol^{-1} respectively, whereas the experimental values are 10.2 ± 0.8 and 9.2 ± 0.8 kcal mol^{-1}, respectively.

Experimental Section

Materials. 1,3,5-Trinitrobenzene (Eastman White Label) was recrystallized twice from ethanol, mp 123°. Reagent grade methanol and ethanol were used without further purification. Stock solutions of sodium methoxide and of sodium ethoxide were prepared by dissolving sodium metal in the respective solvents under a stream of nitrogen.

Rate Measurements. Stopped-flow determinations were performed on a Durrum[42] stopped-flow spectrometer at 450 mμ. The relaxation times listed in Tables I and III represent average values of 3–4 single determinations. The temperature-jump experiments were carried out on a temperature-jump transient spectrometer from Messanlagen Gmbh.[43] Temperature jumps of 1–1.5° were found adequate for the system under study. Relaxation times were determined at wavelengths between 450 and 530 mμ, depending on the optical density of the solutions. Each reported relaxation time represents the average of at least four relaxation curves.

Acknowledgment. I wish to thank Dr. J. Miller for carrying out the theoretical calculations of the thermodynamic parameters for the reaction of TNB with methoxide ion.

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(38) A. R. Norris, *Can. J. Chem.*, 47, 2895 (1969).

(39) J. Miller, *J. Amer. Chem. Soc.*, 85, 1628 (1963).

(40) D. L. Hill, K. E. Ho, and J. Miller, *J. Chem. Soc., B*, 299 (1966).

(41) Personal communication by J. Miller.

(42) Durrum Instrument Corp., Palo Alto, Calif.

(43) Massanlagen Gmbh., Göttingen, Germany.