Intermediates in Nucleophilic Aromatic Substitution. VII.[1] Stopped-Flow Temperature-Jump Study of the Transient 1,3-Methoxide Ion Adduct of 2,4,6-Trinitroanisole in Methanol

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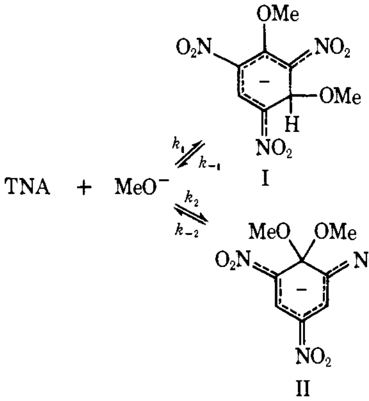
Abstract: By using the stopped-flow temperature-jump technique spectroscopic evidence was found for the 1,3-methoxide ion adduct of 2,4,6-trinitroanisole in methanol which precedes the thermodynamically more stable 1,1 complex (classical Meisenheimer complex). Kinetic and thermodynamic parameters were determined and are compared with previous data on the interaction between 1,3,5-trinitrobenzene and methoxide ion.

Ever since Servis[3] first observed by nmr that in dimethyl sulfoxide (DMSO) formation of the classical Meisenheimer complex (II) from 2,4,6-trinitroanisole (TNA) and methoxide ion is preceded by a much faster attack on the 3 position, considerable attention has been directed toward I and similar isomeric 1,3 complexes (Scheme I). The 1,3 complex (I) though formed faster is thermodynamically less stable than the 1,1 complex (II) and is completely converted to II within a few minutes[3] in DMSO. This conversion is catalyzed by methanol.

Scheme I



Crampton and Gold[4] could still observe the transient species I by nmr in 30 mol % of methanol–70 mol % of DMSO, but not in an equimolar solvent mixture. Fendler, *et al.*,[5] made similar observations with 2,4,6-dinitrocyano- and 2,4,6-nitrodicyanoanisoles.

Terrier, *et al.*,[6] were able to measure the visible absorption spectra of a number of 1,3 complexes in methanol–DMSO mixtures rich in DMSO by a continuous-flow technique. They also reported kinetic data obtained from stopped-flow experiments. Recently they were able to extend such spectral and kinetic studies to DMSO–methanol mixtures with as much as 74.7% methanol by weight in the case of 4-cyano-2,6-dinitroanisole and 42.5% methanol for 4-nitro-2,6-dicyanoanisole.[7]

So far the only indication of 1,3 complex formation in pure methanol has come from a calorimetric study of the interaction of TNA and of 2,4-dicyano-6-nitroanisole with methoxide reported by Larsen, Fendler, *et al.*,[5c,8] Their investigation suggests the formation of a transient intermediate prior to the 1,1 complex formation and it was proposed that it could be the elusive 1,3 complex.

The main obstacle to obtain more direct structural evidence for the 1,3 complex as well as to a kinetic study of its equilibrium reaction with TNA is the interplay of two factors. (1) I and TNA have a much shorter lifetime in pure methanol than in DMSO or DMSO–methanol mixtures. (2) The equilibration between TNA and I is very fast in this solvent. Note that these are two different problems. The lifetime refers to the time I and TNA can be observed before they are essentially irreversibly converted to II ($k_2 \gg k_{-2}$); this conversion is described by the rate eq 1 when the base is present in large excess.

$$-\frac{d([\mathrm{TNA}] + [\mathrm{I}])}{dt} = \frac{k_2[\mathrm{MeO^-}]}{1 + K_1[\mathrm{MeO^-}]}([\mathrm{TNA}] + [\mathrm{I}]) \quad (1)$$

With $k_2 = 17.3\ M^{-1}\ \mathrm{sec}^{-1}$ [5a] and a typical range of base concentrations between 0.05 and 0.5 M one calculates minimum half-lives of about 800 to 80 msec.[9] This is well within the time range of the stopped-flow (SF) technique.

The equilibration between TNA and I, the rate of which depends on k_1 and k_{-1}, is however too fast for the SF method and requires for its measurement a faster technique such as the temperature-jump (TJ) method. Because of the short lifetime of I and TNA, the TJ experiment must be performed very shortly after mixing of TNA with the base. This can be done by combining the two techniques in a stopped-flow temperature-jump (SFTJ) apparatus.

We wish now to report such a SFTJ study.

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

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

[5] (a) J. H. Fendler, E. J. Fendler, and C. E. Griffin, *J. Org. Chem.*, 34, 689 (1969); (b) E. J. Fendler, C. E. Griffin, and J. H. Fendler, *Tetrahedron Lett.*, 5631 (1968); (c) E. J. Fendler, J. H. Fendler, C. E. Griffin, and J. W. Larsen, *J. Org. Chem.*, 35, 287 (1970).

[6] (a) F. Terrier and F. Millot, *C. R. Acad. Sci., Ser. C*, 268, 808 (1969); (b) F. Millot and F. Terrier, *Bull. Soc. Chim. Fr.*, 2694 (1969); F. Terrier and F. Millot, *ibid.*, 1743 (1970).

[7] F. Terrier, C. Dearing, and R. Schaal, paper presented at the 21st Meeting of the Societé de Chimie Physique, 1970.

[8] J. W. Larsen, J. H. Fendler, and E. J. Fendler, *J. Amer. Chem. Soc.*, 91, 5903 (1969).

[9] This is by assuming $K_1[\mathrm{MeO^-}] \ll 1$; if $K_1[\mathrm{MeO^-}]$ becomes comparable to or larger than 1, the half-lives would become correspondingly longer.

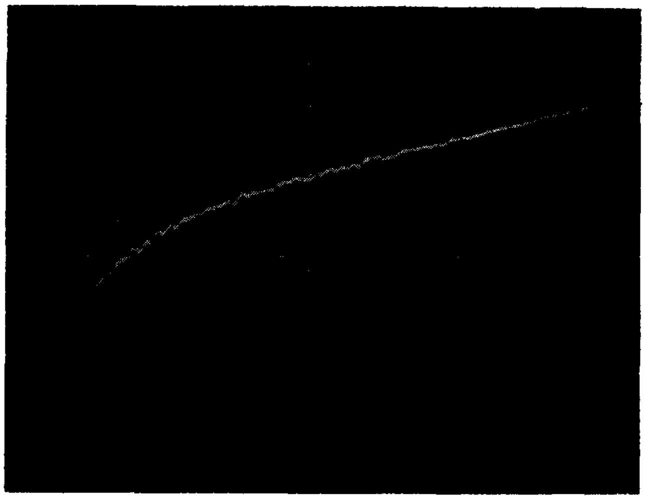


Figure 1. Representative oscilloscope trace at 25°; $[\text{TNA}]_0 = 10^{-4}$ M, $[\text{NaOMe}]_0 = 0.05$ M; 2 msec/horizontal division; delay time = 80 msec; $\lambda = 450$ mμ.

Results and Discussion

When a temperature jump of about 17.5° is applied on a solution of TNA and NaOMe approximately 80 msec after mixing one obtains a trace like the one in Figure 1. The linear portion of the curve corresponds to an OD increase due to the formation of II; the much faster preceding process is attributed to the equilibration between TNA and I. Extrapolation of the linear portion as indicated in Figure 1 gives the infinity line of the preceding exponential. The amplitude of this exponential at $t = 0$ (distance between oscilloscope trace and the infinity line measured on the first vertical graticule line in Figure 1) as a function of wavelength agrees qualitatively[10] with the spectra of typical 1,3 complexes[6,7] and strongly supports our structural assignment.

Relaxation times were determined as function of [NaOMe] with NaOMe in large excess over TNA. They obey eq 2 as shown in Figure 2. Rate coefficients

$$\frac{1}{\tau_1} = k_1[\text{MeO}^-] + k_{-1} \qquad (2)$$

and equilibrium constants determined at three different temperatures are summarized in Table I, whereas thermodynamic parameters are summarized in Table II.

Table I. Reaction of TNA and MeO^- to Form I in Methanol

Temp, °C[a]	k_1, M^{-1} sec^{-1}	k_{-1}, sec^{-1}	$K_1 = k_1/k_{-1}$, M^{-1}
25 ± 1	950 ± 100	350 ± 20	2.71 ± 0.45
37 ± 1	2050 ± 150	650 ± 30	3.16 ± 0.40
46 ± 1	3400 ± 250	890 ± 40	3.82 ± 0.49

[a] Temperature-jump $\Delta T = 17.5 \pm 1°$; the temperatures are those after the jump.

Our findings do not agree very well with those of Larsen, Fendler, *et al.*,[5c,8] based on calorimetry; assuming $K_1 > 10^3$ they calculated $\Delta H_1 = -1.48 \pm 0.5$ kcal/mol. The present study shows that $K_1 \ll 10^3$ and that ΔH is positive. That the process is indeed endothermic is confirmed by the fact that the OD always increases after a temperature jump, indicating an increase in the concentration of I upon increasing the temperature.[11]

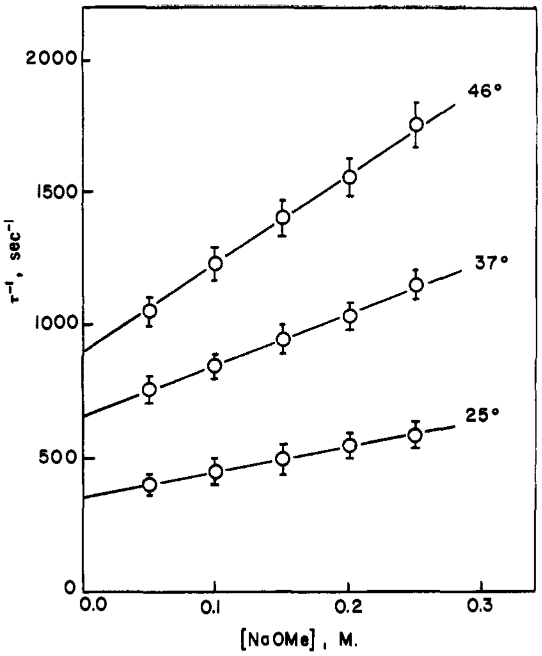
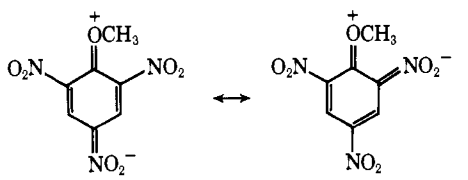


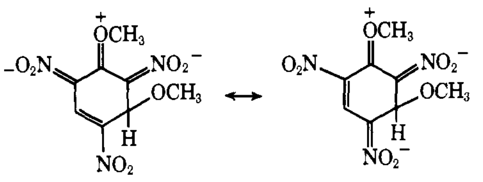
Figure 2. $1/\tau_1$ as function of [NaOMe]; $[\text{TNA}]_0 = 10^{-4}$ M in all runs; ionic strength maintained at 0.5 M by adding NaClO_4.

Table II includes kinetic and thermodynamic parameters on the reactions of TNA with MeO^- to give I and II as well as corresponding data for the reaction of 1,3,5-trinitrobenzene (TNB) with the same base in methanol. It is apparent that there is a great similarity in all parameters for the reaction of TNA to give the 1,3 complex on the one hand and the reaction of TNB on the other, whereas the reaction of TNA to give the 1,1 complex is strikingly different. Thus the former which both involve nucleophilic attack on an unsubstituted carbon as a common feature have relatively low equilibrium constants but high rate coefficients, whereas the latter involving nucleophilic attack on a methoxy-substituted carbon is slow but has a high equilibrium constant for complex formation. Similar things can be said about the activation parameters, the most striking feature being the much higher $\Delta \overset{\leftarrow}{H}^{\ddagger}$ value for II compared to the others. The reasons believed to be responsible for this behavior have been extensively discussed in an earlier report.[12] The main factor was attributed to

TNA



I



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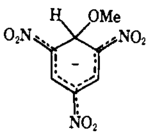
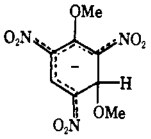
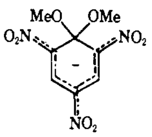
[10] Accurate amplitude evaluations are quite difficult in SFTJ work.

[11] A referee has suggested that the discrepancy could be due to a difference in the salt concentrations in the two studies.

[12] C. F. Bernasconi, *J. Amer. Chem. Soc.*, **92**, 4682 (1970).

Table II. Kinetic and Thermodynamic Parameters of Reactions of TNA and TNB with MeO^- in Methanol at 25°

	 III[a]	 I[b]	 II[c]
$\overrightarrow{k}$ (M^{-1} sec^{-1})	7050	950	17.3
$\overleftarrow{k}$ (sec^{-1})	305	350	1.03 ± 10^{-3}
K (M^{-1})	23.1	2.71	17,000
$\Delta\overrightarrow{H}^{\ddagger}$ (kcal mol^{-1})	10.2 ± 0.8	10.4 ± 1.0	12.9 ± 1.0
$\Delta\overrightarrow{S}^{\ddagger}$ (eu)	-6.7 ± 2.7	-10.8 ± 3.4	-9.4 ± 3.4
$\Delta\overleftarrow{H}^{\ddagger}$ (kcal mol^{-1})	9.2 ± 0.8	8.2 ± 0.5	18.4 ± 1.0
$\Delta\overleftarrow{S}^{\ddagger}$ (eu)	-16.3 ± 2.7	-19.3 ± 1.7	-4.8 ± 3.4
ΔH (kcal mol^{-1})	1.0 ± 1.6	2.2 ± 1.5	-5.5 ± 2.0
ΔS (eu)	9.6 ± 5.4	8.5 ± 5.1	-4.6 ± 4.0[d]

[a] C. F. Bernasconi, *J. Amer. Chem. Soc.*, **92**, 4682 (1970). [b] This work. [c] Reference 5a. [d] Reference 8.

resonance stabilization involving the methoxy group in TNA, in I, and thus also in the transition state leading to I, whereas such resonance stabilization is not possible in TNB or its complex, nor in II and thus probably very little in the transition state leading to II. The consequence is that in proceeding from TNA to II the resonance energy of TNA which is lost in II has to be overcome and this reduces the rate; the reaction to form I is not (or less strongly) slowed down because the resonance stabilization is (at least partially) conserved in I.

The somewhat smaller rate and equilibrium constants for 1,3 complex formation compared to the reaction of TNB might be attributed to the loss of part of the resonance stabilization in going from TNA to I or perhaps more simply to a steric hindrance to coplanarity of the flanking *o*-nitro groups, preventing an optimal resonance interaction.[12a]

Experimental Section

Materials. 2,4,6-Trinitroanisole (Eastman White Label) was recrystallized twice from ethanol, mp 67.5°. Reagent grade methanol and $NaClO_4$ (both Merck) were used without further purification. Stock solutions of sodium methoxide were prepared by dissolving sodium metal (previously washed with methanol) in methanol under a stream of nitrogen.

Rate Measurements. A De Maeyer-Rabl[13] TJ apparatus modified for SFTJ operation by L. B. Veil[14] was used. The relaxation was monitored at 450 mμ except for the study of the amplitudes where wavelength between 400 and 550 mμ at 10-mμ intervals were used. Each reported relaxation time represents the average of at least three relaxation curves such as shown in Figure 1.

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[12a] NOTE ADDED IN PROOF. The recent work of Terrier, *et al.*,[7] has shown that the discrepancy between thermodynamic stability of the 1,3 and 1,1 complexes and their rates of formation becomes very much smaller when the *p*-nitro group in TNA is replaced by a substituent less efficient or unable to withdraw electrons by resonance interaction such as F, Cl, CF_3, whereas the cyano group shows intermediate behavior between the nitro group and these three substituents. This lends further support to our interpretation.

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