Kinetics of the Reactions of Nitro-substituted *N*-Alkylacetanilides with Sodium Methoxide in Methanol[1]

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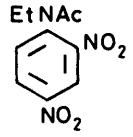
The sodium methoxide-catalysed methanolysis of *N*-ethyl- (**3**) or *N*-methyl-2′,4′,6′-trinitroacetanilide (**4**) is found to proceed with initial formation of a 1,3-disubstituted anionic σ-complex (**II**), which then reverts to the reactant system, relatively slowly giving *N*-alkyl-4-methoxy- (main product) and *N*-alkyl-2′-methoxy-4′,6′-dinitroacetanilides with the amido group unchanged, *via* a 1,4-disubstituted anionic σ-complex (**III**); kinetics and absorption and ^{1}H n.m.r. spectral data are reported.

We have previously reported[2,3] substituent effects in the alkaline hydrolysis of *N*-ethyl- (**1**) and *N*-methyl-2′,4′-dinitroacetanilide (**2**). These hydrolyses proceed by reversible, base-catalysed formation of a tetrahedral intermediate to give *N*-alkyl-2,4-dinitroaniline and acetic acid. Although many reports and reviews on this subject have appeared,[4] there are few papers related to the hydrolysis of acetanilides with a multisubstituted ring. We have found that the sodium methoxide-catalysed methanolysis of *N*-ethyl- (**3**) and *N*-methyl-2′,4′,6′-trinitroacetanilide (**4**) does not proceed normally, but results in ring *C*-substitution by MeO^- at the *para*- (main) or *ortho*-positions.

These results were against our expectation that trinitroacetanilides would undergo normal methanolysis more rapidly than di- or mono-nitroacetanilides because an *N*-alkyltrinitroacetanilide ion is a better leaving group.[2,3] Further, changes in electronic absorption with time showed that the first product is a 1,3-disubstituted anionic σ-complex (**II**) (see Scheme 1; hereafter called the 1,3-complex), which then reverts to the reaction system, giving the products relatively slowly *via* the 1,4-complex (**III**). Thus the reaction path is divided into two distinct stages (hereafter called stages 1 and 2). We report here the kinetics of the base-catalysed substitution of the acetanilides (**3**) and (**4**) in methanol, and discuss the reaction mechanism.



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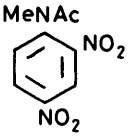

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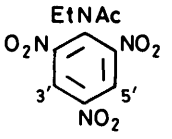

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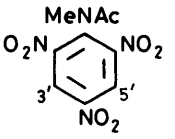


(4)

Experimental

Materials.—N-*Ethyl*-2′,4′,6′-*trinitroacetanilide* (**3**). An aqueous solution of ethylamine (70%; 136 ml; 3 equiv.) was added dropwise to a stirred solution of picryl chloride (12 g, 0.048 mol) in Me_2SO (200 ml) at room temperature. The mixture was then stirred for an additional 4 h, was poured into ice–water (500 ml), neutralized with HCl, and filtered. Recrystallization of the residue from ethanol gave *N*-ethyl-2′,4′,6′-trinitroaniline (3.9 g, 31.5%), m.p. 80.0—80.8 °C (yellow needles); δ (Me_2SO; 60 MHz) 1.4 (3 H, br s, CH_3), 3.2 (2 H, q, CH_2), 8.73 (1 H, br s, NH), and 8.91 (2 H, s, ring H).

A stirred solution of the *N*-ethylaniline (2.5 g, 0.0097 mol) in Ac_2O (61 ml) was heated at 60 °C for 5 h, then poured into ice–water (30 ml) and filtered. The residue was recrystallized from ethanol to give the *anilide* (**3**) (2.6 g, 89.2%), m.p. 135.0—136.5 °C (Found: C, 40.0; H, 3.45; N, 18.6. $C_{10}H_{10}N_4O_7$ requires C, 40.3; H, 3.4; N, 18.8%); δ (Me_2SO; 60 MHz) *ca.* 1.00 (3 H, m, NCH_2CH_3 for *Z*- and *E*-isomers), 1.87 (*E*) and 2.16 (*Z*) (3 H total, each s, $COCH_3$, *E*:*Z* 1.4:1), *ca.* 3.64 (2 H total, m, NCH_2CH_3 for *E*- and *Z*-isomers), and 9.10 (*Z*) and 9.19 (*E*) (2 H total, each s, ring H, *E*:*Z* 1.4:1).

N-*Methyl*-2′,4′,6′-*trinitroacetanilide* (**4**). *N*-Methyl-2,4,6-trinitroaniline was prepared from methylamine and picryl chloride according to the method given for the *N*-ethyl analogue; yield 42%, m.p. 113.0—114.0 °C (lit.,[5] 114 °C).

Compound (**4**) was prepared like compound (**3**); yield 85.0%, m.p. 125.0—125.1 °C (Found: C, 38.2; H, 2.75; N, 19.5. $C_9H_8N_4O_7$ requires C, 38.0; H, 2.8; N, 19.7%); δ (Me_2SO; 60 MHz) 1.80 (*Z*) and 2.21 (*E*) (3 H total, each s, NCH_3, *E*:*Z* 1.9:1), and 9.18 (*Z*) and 9.33 (*E*) (2 H total, each s, ring H, *E*:*Z* 1.9:1).

Preparative Reaction of N-*Methyl*-2′,4′,6′-*trinitroacetanilide* (**4**) *with Sodium Methoxide in Methanol.*—Sodium (0.242 g) was added in portions to methanol (90 ml) at room temperature to give sodium methoxide. Compound (**4**) (3 g) was then added, and the mixture was stirred for 1.5 h at 30 °C, then poured into water (200 ml), and extracted with benzene. The benzene layer was dried ($MgSO_4$) overnight, concentrated under reduced pressure, and set aside for 2—3 days. The crystals formed were filtered off and recrystallized from benzene to give N-*methyl*-4′-*methoxy*-2′,6′-*dinitroacetanilide* (**5**) (1.10 g, 36.8%), m.p. 105.0—106.0 °C (Found: C, 44.45; H, 4.0; N, 15.7. $C_{10}H_{11}N_3O_6$ requires C, 44.6; H, 4.1; N, 15.6%); δ (Me_2SO; 60 MHz) 1.75 (*E*) and 2.11 (*Z*) (3 H total, each s, $COCH_3$, *E*:*Z* 1.4:1), 2.96 (*E*) and 3.25 (*Z*) (3 H total, each s, NCH_3, *E*:*Z* 1.4:1), and 3.98 (*E*) and 3.99 (*Z*) (3 H total, each s, 4-OCH_3).

The filtrate (benzene solution) was subjected to column chromatography (silica gel; benzene) to give three fractions, evaporation of which and recrystallization from methanol gave N-*methyl*-2′-*methoxy*-4′,6′-*dinitroacetanilide* (**6**) (0.47 g, 15.7%), N-*methyl*-2′-*methoxy*-4′,6′-*dinitroaniline* (**7**) (0.01 g, 0.32%), and starting material (**4**) (1.32 g, 41%). Compound (**6**) had m.p. 119.5—120.5 °C (Found: C, 44.5; H, 4.0; N, 15.75. $C_{10}H_{11}N_3O_6$ requires C, 44.6; H, 4.1; N, 15.6%); δ (Me_2SO; 60 MHz) 1.73 (*E*) and 2.17 (*Z*) (3 H total, each s, $COCH_3$, *E*:*Z* 1.3:1), 3.00 (*E*) and 3.30 (*Z*) (3 H total, each s, NCH_3, *E*:*Z* 1.3:1), and 4.09 (*Z*) and

4.10 (*E*) (3 H total, each s, 2′-OCH_3 for *Z*- and *E*-isomers). Compound (**7**) had m.p. 166.0—167.0 °C (Found: C, 34.5; H, 2.5; N, 23.35. $C_7H_6N_4O_6$ requires C, 34.7; H, 2.5; N, 23.1%); δ (Me_2SO; 60 MHz) 2.97 (3 H, d, *J* 2.0 Hz, NCH_3), 3.97 (3 H, s, 2′-OCH_3), 7.93 (1 H, d, *J* 1.5 Hz, 3-H′), and 8.23 (1 H, d, *J* 1.5 Hz, 5-H′).

Preparative Reaction of N-*Ethyl*-2′,4′,6′-*trinitroacetanilide* (**3**) *with Sodium Methoxide in Methanol.*—The reaction was carried out under the conditions given for compound (**4**) except for the reaction time (4 h) to give N-*ethyl*-4′-*methoxy*-2′,6′-*dinitroacetanilide* (**8**) (2.4 g, 84.3%) and N-*ethyl*-2′-*methoxy*-4′,6′-*dinitroacetanilide* (**9**) (0.28 g, 9.8%). Compound (**8**) had m.p. 63.2—64.0 °C (Found: C, 46.8; H, 4.55; N, 14.95. $C_{11}H_{13}N_3O_6$ requires C, 46.6; H, 4.6; N, 14.8%); δ (Me_2SO; 60 MHz) *ca.* 0.90 (3 H, total, m, CH_2CH_3 for *Z*- and *E*-isomers), 1.87 (*E*) and 2.16 (*Z*) (3 H, total, each s, $COCH_3$, *E*:*Z* 4.0:1, *ca.* 3.43 (2 H, m, CH_2CH_3 for *Z*- and *E*-isomers), 4.02 (3 H, s, 4′-OCH_3), and 7.97 (*Z*) and 8.09 (*E*) (2 H total, each s, ring H, *E*:*Z* 4.0:1). Compound (**9**) had m.p. 107.2—108.3 °C (from cooled ethanol) (Found: C, 46.8; H, 4.1; N, 14.7. $C_{11}H_{13}N_3O_6$ requires C, 46.65; H, 4.6; N, 14.8%); δ (Me_2SO; 60 MHz) *ca.* 1.00 (3 H total, m, CH_2CH_3 for *Z*- and *E*-isomers), 1.75 (*E*) and 2.16 (*Z*) (3 H total, each s, $COCH_3$, *E*:*Z* 3.0:1), *ca.* 3.52 (2 H, m, CH_2CH_3 for *Z*- and *E*-isomers), 4.02 (*Z*) and 4.09 (*E*) (3 H, each s, 2′-OCH_3, *E*:*Z* 3.0:1), and *ca.* 8.34 (2 H total, m, ring H).

Rate Measurements.—The rates were measured spectrophotometrically by either conventional (stage 2) or stopped-flow technique (stage 1) at constant ionic strength (0.3M; $NaClO_4$). For the conventional technique, a Hitachi 200—10 spectrophotometer equipped with a thermostatically controlled cell holder (within ±0.02 °C) was employed. The procedure was as follows: appropriate volumes of methanolic solutions of sodium methoxide and sodium perchlorate were combined and diluted quantitatively with methanol; 2.00 ml of the resulting solution was placed in a cuvette which was allowed to come to thermal equilibrium in the cell compartment; 10 μl of a standard solution of substrate (*ca.* 2.07 × 10^{-2} M) was injected and the solution was rapidly mixed, and the decrease in absorbance at the chosen wavelength (420 nm) was followed with time. For the stopped-flow technique, an Ohtsuka Denshi RA-401 stopped-flow spectrophotometric apparatus was employed. The procedure was as follows: appropriate methanolic solutions of substrate [*ca.* (3.0—5.0) × 10^{-4}M] and of sodium methoxide and sodium perchlorate (0.6M) were placed in the two cuvettes and allowed to come to thermal equilibrium in the cell compartment of the apparatus; the increase in absorbance at the chosen wavelength (420 nm) was followed with time.

Results

Absorption Spectra.—Upon addition of an excess of sodium methoxide to a methanolic solution of (**3**), the mixture instantaneously turned red [curve (a) ⟶ (b) in Figure 1]. The colour then faded slowly [curve (b) ⟶ (c) ⟶ (d)]. Curve (b) is attributable to the 1,3-complex (**II**) in view of the results described so far and the ^1H n.m.r. data described in the following section.[6,7]

Several examples of 1,3-complexes of trinitrobenzene derivatives have been reported.[6–17] Almost all the evidence for such species was obtained in mixed solutions containing dimethyl sulphoxide, the present case, in which the absorption spectrum of such a complex was obtained in pure methanol, is unusual. Curve (d) ($\lambda_{max.}$ 323 nm) can be attributed to compound (**IV**), $\lambda_{max.}$(ε) 323 nm (4 400) for (**8**) (R = Et), and 323 nm (2 300) for (**5**) (R = Me). From these results the reaction path can be deduced (Scheme 1): stage 1 [(**I**) + $^-$OMe ⟷ (**II**)] is comparatively fast and stage 2[(**I**) + $^-$OMe ⟶ (**IV**) + NO_2^-] relatively slow. Similar spectral changes were observed for (**4**).

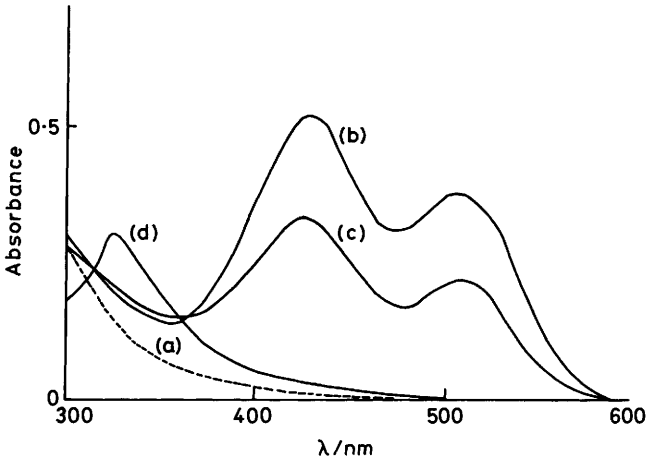
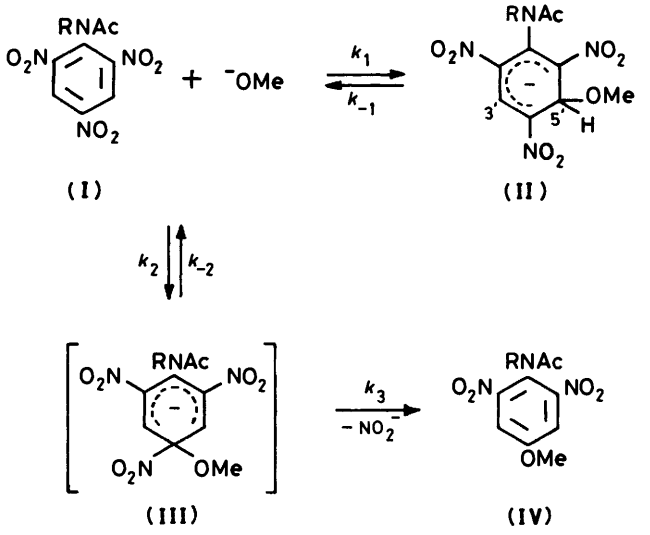


Figure 1. Time-dependent spectral changes for the OMe-catalysed methanolysis of *N*-ethyl-2′,4′,6′-trinitroacetanilide (**3**) (6.22 × 10^{-5}M) at 25 °C ([NaOMe] = 2.34 × 10^{-2}M): (a) (**3**) alone; (b) just after addition of NaOMe; (c) 10 min; (d) 70 min



Scheme 1. R = Et or Me

^1H *N.m.r. Spectra.*—As no clear n.m.r. spectrum of the product of interaction between (**3**) or (**4**) and $^-$OMe was obtained in pure methanol, a 1:1 Me_2SO–MeOH mixture was used. Upon addition of an equivalent of sodium methoxide to (**3**), the singlet signals at δ 9.19 (*E*) and 9.10 (*Z*) [the trinitrophenyl and oxido groups are *trans* and *cis* with respect to the amide C=N bond for the *E* and *Z*-isomers, respectively[18]] were immediately shifted upfield [Figure 2(A) and (B)]: the signals at δ 6.49 (*E*) and 6.20 (*Z*) are attributed to 3′-H of (**II**), which shows the presence of both *E*- and *Z*-isomers even in the 1,3-complex. In addition, signals at δ 8.75 (*E*) and 8.67 (*Z*) are attributed to 5′-H of (**II**). These four signals are doubly split (*J* 1.0 Hz), indicating coupling between 3′-H and 5′-H; further, the developing signal at δ 7.93, attributed to 3′-H and 5′-H of both *E*- and *Z*-isomers of (**IV**), appeared just after addition of sodium methoxide, indicating that the 1,3-complex (**II**) is comparatively unstable. Two hours after addition of sodium methoxide, substitution of the 4′-nitro group by $^-$OMe was complete

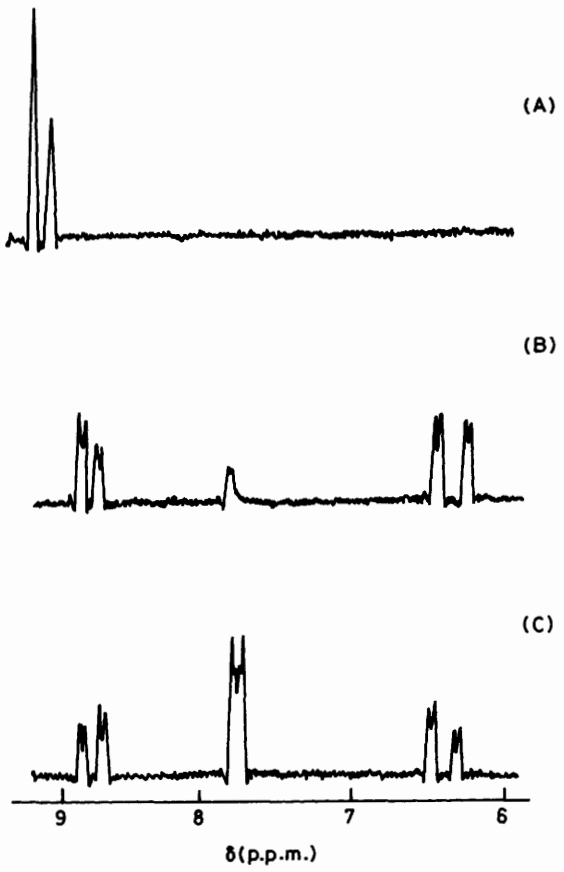


Figure 2. Time-dependence of ^{1}H n.m.r. spectral changes for the $^-$OMe-catalysed methanolysis of *N*-ethyl-2′,4′,6′-trinitroacetanilide (**3**) [(**3**)]:[NaOMe] (1:1) in $(CD_3)_2SO$–MeOH (1:1): (A) (**3**) alone; (B) just after addition of NaOMe; (C) 2 h

[Figure 2(C)]. The n.m.r. results are consistent with the reaction sequence shown in Scheme 1.

Rate Measurements for Stages 1 and 2.—The stage 1 reaction (**I**) $\rightleftharpoons$ (**II**) is much faster than stage 2 (**I**) $\longrightarrow$ (**III**) $\longrightarrow$ (**IV**). In the kinetic treatment of the former, therefore, the latter can be neglected. Stage 1 can thus be dealt with as a pre-equilibrium in the kinetic treatment of stage 2. For the rate of stage 1, the expression (1) is derived. Values of k_1, k_{-1}, and K, therefore, can be obtained from the linear relationship between k_ψ and [$^-$OMe] (Figure 3).

$$k_\psi = k_{-1} + k_1[^-\mathrm{OMe}] \quad (1)$$

$$K = \frac{k_1}{k_{-1}} \quad (2)$$

If $[(\mathbf{I})]_{st}$ (stoicheiometric concentration) = [(**I**)] + [(**II**)], and K is the pre-equilibrium constant for stage 1, the rate constant for stage 2 can be expressed as equation (3). Further,

$$\text{rate} = k_{obs.}[(\mathbf{I})]_{st} = \frac{k_2[^-\mathrm{OMe}][(\mathbf{I})]_{st}}{1 + K[^-\mathrm{OMe}]} \quad (3)$$

$$k_{obs.} = \frac{k_2[^-\mathrm{OMe}]}{1 + K[^-\mathrm{OMe}]} \quad (4)$$

equation (5) can be derived from equation (4).

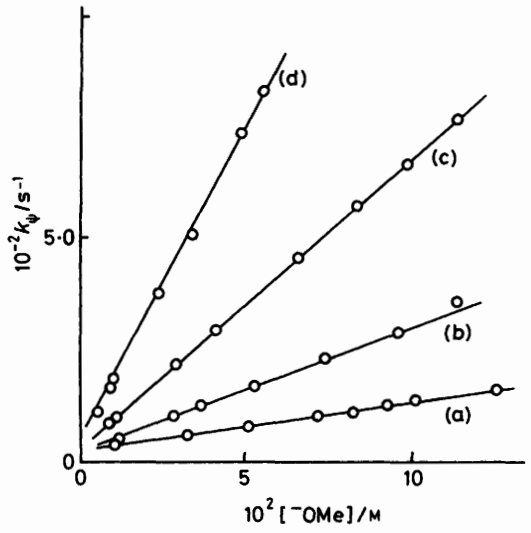


Figure 3. Relationship between k_ψ and [$^-$OMe] for the $^-$OMe-catalysed methanolysis of *N*-methyl-2′,4′,6′-trinitroacetanilide (**4**) (4.01×10^{-4}M): (a) 10 °C; (b) 20 °C; (c) 30 °C; (d) 40 °C

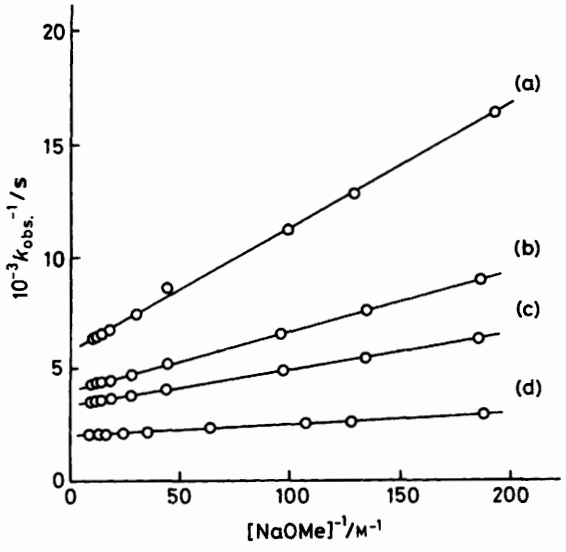


Figure 4. Relationship between $1/k_{obs.}$ and $1/[^-\mathrm{OMe}]$ for the $^-$OMe-catalysed methanolysis of *N*-methyl-2′,4′,6′-trinitroacetanilide (**4**) (5.00×10^{-5}M): (a) 20 °C; (b) 25 °C; (c) 30 °C; (d) 40 °C

$$\frac{1}{k_{obs.}} = \frac{1}{k_2[^-\mathrm{OCH_3}]} + \frac{K}{k_2} \quad (5)$$

From equation (4), a curvilinear relationship between $k_{obs.}$ and [$^-$OMe] (not shown) is expected. In addition, a linear relationship between $1/k_{obs.}$ and $1/[^-\mathrm{OMe}]$ is also expected for stage 2 from equation (5) (Figure 4). The sodium methoxide concentration dependences of the rate constants of stages 1 and 2 for (**3**) are listed in Tables 1 and 2, the relationships (not shown) are similar to those (Figures 3 and 4) for (**4**). The k_2 and K values can be obtained by applying a non-linear least-squares method (Gauss–Newton method) to the results [equation (4)]. These values are summarized in Table 3. The K values obtained from the stage 2 kinetic analysis are 36.9 (extrapolated value), 41.2, 45.9, 51.5, and 63.4 for (**3**), and 50.4 (extrapolated value), 105, 204, and 383 for (**4**) at 10, 20, 30, and 40 °C, respectively.

Table 1. Sodium methoxide concentration dependence of the rate constants (k_ψ) for the alkaline methanolysis of *N*-ethyl-2′,4′,6′-trinitroacetanilide (**3**)[a] (stage 1)

[NaOMe]/M	k_ψ/s^{-1} [b]	[NaOMe]/M	k_ψ/s^{-1} [b]	[NaOMe]/M	k_ψ/s^{-1} [b]
10 °C		20 °C		30 °C	
0.0096	31.3	0.0063	52.3	0.0055	89.0
0.0193	38.9	0.0193	74.6	0.0078	97.3
0.0386	54.0	0.0386	107	0.0105	106
0.0578	69.0	0.0694	160	0.0323	185
0.0694	78.1	0.0781	175	0.0545	264
0.0771	84.1	0.0836	185	0.0783	350
0.0871	91.9	0.0964	207	0.956	411
0.0964	99.1	0.112	234	0.104	441
0.103	104				
40 °C					
0.0054	150				
0.0078	167				
0.0098	181				
0.0135	208				
0.0345	357				
0.0565	514				
0.0783	669				
0.0992	818				

[a] $[(3)]_0 = 9.35 \times 10^{-5}$M; $\mu = 0.3$M ($NaClO_4$); solvent MeOH. [b] Estimated limits of error ±1.2%.

Table 2. Sodium methoxide concentration dependence of the rate constants ($k_{obs.}$) of the alkaline methanolysis of *N*-ethyl-2′,4′,6′-trinitroacetanilide (**3**) (stage 2)[a]

[NaOMe]/M	$k_{obs.}$/s^{-1} [b]	[NaOMe]/M	$k_{obs.}$/s^{-1} [b]	[NaOMe]/M	$k_{obs.}$/s^{-1} [b]
15 °C		20 °C		25 °C	
0.0095	0.63	0.0052	0.69	0.0054	1.25
0.0183	0.98	0.0078	0.96	0.0075	1.61
0.0357	1.38	0.0102	1.16	0.0105	2.05
0.0578	1.65	0.0220	1.87	0.0225	3.20
0.0691	1.74	0.0352	2.33	0.0361	2.92
0.0753	1.79	0.0572	2.76	0.0575	4.56
0.0875	1.86	0.0756	2.98	0.0752	4.88
0.0965	1.90	0.0832	3.05	0.0850	5.01
0.108	1.94	0.102	3.18	0.105	5.21
30 °C		40 °C			
0.0052	2.07	0.0053	5.78		
0.0080	2.86	0.0078	7.61		
0.0095	3.22	0.0093	8.53		
0.0157	4.38	0.0157	11.4		
0.0280	5.79	0.0278	14.6		
0.0410	6.65	0.0410	16.6		
0.0635	7.50	0.0625	18.3		
0.0815	7.91	0.0815	19.2		
0.108	8.31	0.107	20.0		

[a] $[(3)] = 9.12 \times 10^{-5}$M; $\mu = 0.3$M ($NaClO_4$); solvent MeOH. [b] All values are 10^4 $k_{obs.}$; estimated limits of error ±1.0%.

These are in fair agreement with those (Table 3) obtained from the stage 1 kinetic study, indicating the validity of Scheme 2.

Discussion

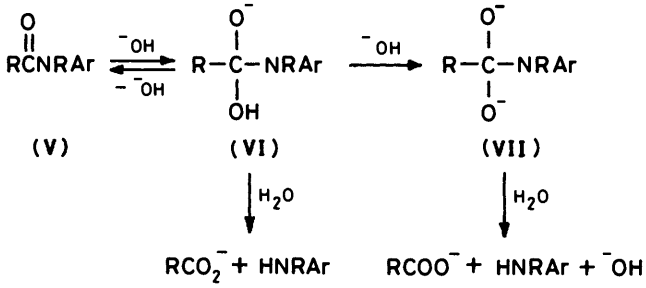
Reaction Mechanism.—It has been reported[2,3] that *N*-alkyl-2′,4′-dinitroacetanilides [(**1**) and (**2**)] are hydrolysed in the presence of sodium hydroxide as shown in Scheme 2, where the formation of (**VI**) is rate-limiting, and the main reaction path is (**V**) + $^-$OH ⇌ (**VI**) + $^-$OH ⇌ (**VII**) + H_2O ⟶ products. Further, it has been found that substituents on the amide nitrogen and at the 2-position of the phenyl moiety reduce the rate of formation of (**VI**) by exerting both inductive and steric effects.[2,3] From these results, it is probably reasonable to ascribe the inability of (**3**) and (**4**) to undergo normal alkaline methanolysis to the presence of nitro groups at the 2- and 6-positions of the phenyl moiety. Even with (**1**) and (**2**), the steric compression due to the 2-nitro group around the carbonyl carbon of (**VI**) is great,[2] so for (**3**) and (**4**) it is no doubt so much greater that the intermediate (**VI**) cannot form.

An isosbestic point can be seen in the spectral changes [Figure 1, curve (b) ⟶ (c) ⟶ (d)], which indicates that the species (**III**) is an unstable intermediate. Its instability is probably due to the presence of nitro groups *meta* to the reaction site.

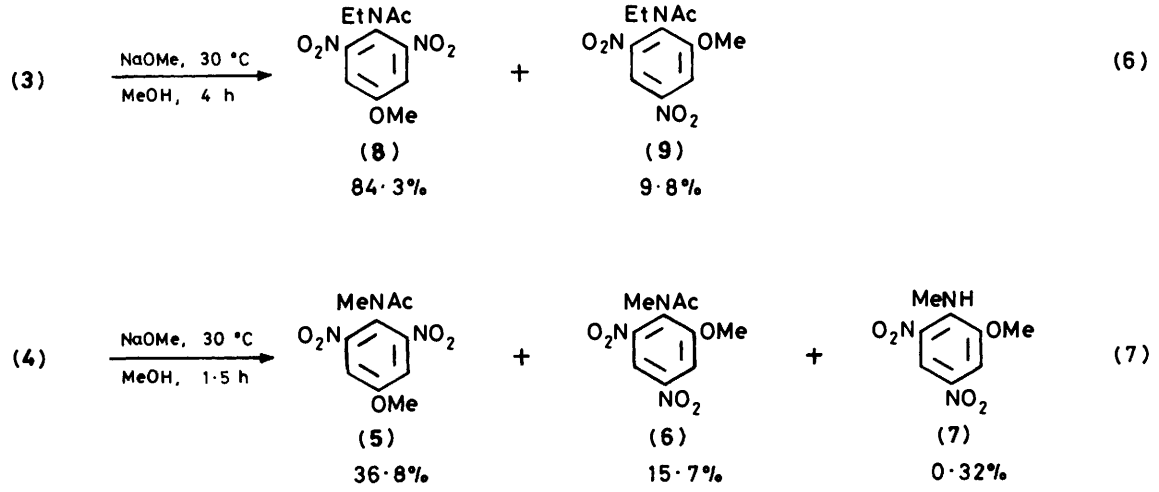
Activation Parameters.—In stage 1 k_1 is larger for (**4**) than for (**3**), depending on $\Delta S^\ddagger$. It is especially interesting that $\Delta S^\ddagger$ for (**4**) is positive, whereas for (**3**) it is negative and small. Results such as these have been reported for aromatic nucleophilic additions

Table 3. Rate constants, and activation and thermodynamic parameters

Stage 1	Temp. (°C)	(**3**)	(**4**)
10^{-3} k_1/dm^3 mol^{-1}s^{-1}	10	0.78 ± 0.00	1.09 ± 0.01
	20	1.72 ± 0.01	2.75 ± 0.01
	30	3.58 ± 0.01	6.45 ± 0.01
	40	7.12 ± 0.00	14.4 ± 0.0
$\Delta H^\ddagger_{293}$/kJ mol^{-1}		51.9 ± 1.3	61.2 ± 0.8
$\Delta S^\ddagger_{293}$/J mol^{-1} K^{-1}		−5.9 ± 1.3	28.9 ± 2.4
$\Delta G^\ddagger_{293}$/kJ mol^{-1}		53.6 ± 0.8	52.3 ± 0.3
k_{-1}/s^{-1}	10	23.9 ± 0.2	21.7 ± 0.7
	20	41.2 ± 0.9	26.2 ± 0.7
	30	69.2 ± 0.9	31.4 ± 0.6
	40	111 ± 0	37.1 ± 0.6
$\Delta H^\ddagger_{293}$/kJ mol^{-1}		35.3 ± 0.6	10.7 ± 0.2
$\Delta S^\ddagger_{293}$/J mol^{-1} K^{-1}		−93.4 ± 2.5	−180 ± 1
$\Delta G^\ddagger_{293}$/kJ mol^{-1}		62.8 ± 0.8	63.6 ± 0.4
K/M^{-1}	10	32.6 ± 0.6	50.4 ± 2.0
	20	41.7 ± 1.1	105 ± 3
	30	51.7 ± 0.7	206 ± 6
	40	64.2 ± 0.0	388 ± 7
ΔH^0_{293}/kJ mol^{-1}		14.1 ± 0.2	47.6 ± 0.4
ΔS^0_{293}/J mol^{-1} K^{-1}		−165 ± 1	−43.5 ± 1.2
ΔG^0_{293}/kJ mol^{-1}		62.7 ± 0.4	60.2 ± 0.4
Stage 2			
10^2 k_2/dm^3 mol^{-1} s^{-1}	15	0.89 ± 0.01	0.95 ± 0.01
	20	1.62 ± 0.00	1.80 ± 0.01
	25	2.89 ± 0.00	3.64 ± 0.02
	30	5.05 ± 0.00	6.14 ± 0.05
	40	14.5 ± 0.0	19.3 ± 0.0
$\Delta H^\ddagger_{293}$/kJ mol^{-1}		81.1 ± 1.6	87.8 ± 2.9
$\Delta S^\ddagger_{293}$/J mol^{-1} K^{-1}		−2.3 ± 9.7	21.8 ± 12.9
$\Delta G^\ddagger_{293}$/kJ mol^{-1}		81.7 ± 3.2	81.4 ± 4.8



Scheme 2. Ar = 2,4-dinitrophenyl



in which an anionic σ-complex is formed.[19–21] On the whole, $\Delta G^{\ddagger}$ values for (3) and (4) differ only a little from each other. Differences between k_1 values have generally been attributed to both solvation and steric effects.[19–21] As shown in the Experimental section, each anilide [(3) and (4)] consists of *E*- and *Z*-isomers. These polarized species can be easily solvated by methanol. On the other hand, interaction between the *N*-alkyl and the nitro groups at the 2′- or 6′-position would be larger if a double bond exists between the amide nitrogen and the carbonyl carbon. As a result, steric interaction would occur even in the ground state. Further, it can be seen from Figure 2 that both *E*- and *Z*-isomers exist even in the 1,3-complex. In the 1,3-complex the nitro group *para* to the reaction site tends to assume coplanarity with the phenyl group through delocalization of the negative charge donated by $^-$OMe. This effect would make interaction between the *N*-alkyl and the nitro groups larger than in the ground state.

Both solvation and steric effects must contribute to the slow formation and a little to the slow decomposition of the 1,3-complex of (3), as compared with (4).

The smaller *K* value for (3) is reflected mainly in the large value for k_{-1}.

The reasoning to account for the formation of the 1,3-complex (stage 1) could apply to formation of the products (stage 2).

Product Analysis.—It is instructive to compare the product analyses for (3) and (4) [equations (6) and (7)]. Although reaction conditions are not the same and rigorous comparison is unreasonable, it is interesting that 2′-alkoxyacetanilides [(9) and (6)] were produced in both cases with a large amount of 2′-substitution relative to 4′-substitution in the case of (4). This result may probably be ascribed to the lesser steric hindrance of the *N*-methyl group. Preliminary experiments did not show that rearrangement reactions [(8) to (9), (9) to (8), (5) to (6), or (6) to (5)] could occur under the conditions given for the product analysis. The k_2 values (Table 3), therefore, could be considered to be the rate constants for 2′- and 4′-substitutions. Compound (7) might be produced from the methanolysis of (6).

Such a replacement reaction as the present one (I) ⟶ (IV) has been found previously in the behaviour of picramide in aqueous sodium hydroxide;[22] in this case an *ortho*-substituted aniline [corresponding to (6) and (9)] was not formed and, in addition, 76% completion was attained in 94 days at 25 °C. This difference in reactivity is presumably due to the nature of the amino groups (amino and amido groups).

Finally it can be concluded that anilides with an alkyl group on the amide nitrogen atom and nitro groups at the 2′-, 4′-, and 6′-positions undergo very little substitution by $^-$OMe at the carbonyl carbon atom, but are easily substituted at the 4′- (mainly) and 2′-positions; this behaviour is very different from the $^-$OMe-catalysed methanolysis of *N*-alkylacetanilides with a nitro group only at the 2′- or 6′-position.[2,3]

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