REACTIONS OF 1-SUBSTITUTED 2,4,6-TRINITROBENZENES WITH NUCLEOPHILES

Jaromír KAVÁLEK, Ahmad ASHFAQ* and Vojeslav ŠTĚRBA
Organic Chemistry Department,
Institute of Chemical Technology, 532 10 Pardubice

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Rate constants have been determined of nucleophilic aromatic substitution of 2,4,6-trinitrophenyl methyl ether (*Ia*), 2,4,6-trinitrophenyl ethanoate (*Ic*), 2,4,6-trinitrochlorobenzene (*Ib*), 2,4,6-trinitrodiphenyl ether (*Id*), 2,4,6-trinitro-4'-bromodiphenyl ether (*Ie*), 2,3',4,6-tetranitrodiphenyl ether (*If*), and 2,4,4',6-tetranitrodiphenyl ether (*Ig*) with methoxide, ethanoate, and methyl cyanoethanoate (*II*) anions in methanol. For the compounds *Ia, b* rate and equilibrium constants of addition of the anion $II^{(-)}$ at positions 3 and 5 have been measured, too. In reactions of the compounds *Ia* to *Ig* with ethanoate anion the first (rate-limiting) step produces the phenyl ester *Ic* which reacts with a further ethanoate anion to give 2,4,6-trinitrophenol (*Ih*) and ethanoic anhydride. In reactions of the bromo derivative *Ie* and, to a still larger extent, compound *Id* the methyl derivative *Ia* is formed besides the compound *Ih*.

The reaction of 1-substituted 2,4,6-trinitrobenzenes with nucleophiles proceeds according to Scheme 1 (ref.[1,2]). In the previous communication[1] the reaction of 2,4,6-trinitrophenyl methyl ether with anion of propandioate ester was studied. Rate and equilibrium constants of formation of the mono- and di-adducts and rate of substitution of the methoxy group were measured. The present communication deals with kinetic study of a series of derivatives *Ia* to *Ig* with methoxide anion, ethanoate anion, methanol, and anion $II^{(-)}$ in methanol. The main aim of the present work was determination of the leaving group effect and influence of nucleophile on kinetics and mechanism of the substitution of the leaving group by the nucleophile.

EXPERIMENTAL

Reagents

Methyl 2,4,6-trinitrophenylcyanoethanoate (*Ii*). Solution of 1 g (0·01 mol) methyl cyanoethanoate (*II*) and 2 g (0·008 mol) 2,4,6-trinitrochlorobenzene (*Ib*) in 10 ml methanol was added to solution of 0·3 g compound *II* in 20 ml 1 M $CH_3O^{(-)}$. After two hours the violet solution was neutralized with chloroethanoic acid, and methanol was distilled off under reduced pressure. The residue was diluted with 100 ml benzene, the solution was washed with 0·1M-HCl and water, the benzene

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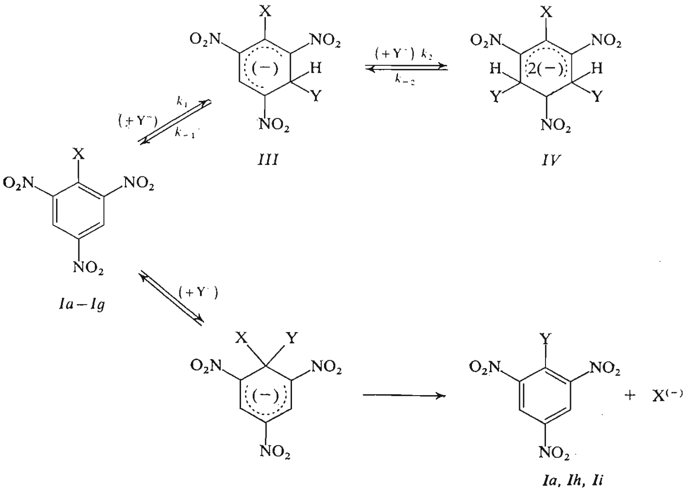
[*] Present address: Punjab University, Lahore, Pakistan.



Scheme 1

layer was separated, dried with sodium sulphate, and benzene was distilled off under reduced pressure. The distillation residue was purified twice by chromatography on a silica gel column with benzene as eluent. After distillation of benzene 2 g (66%) product with m.p. 129·5—131°C was obtained. For $C_{10}H_6N_4O_8$ (310·2) calculated: 38·72% C, 1·95% H, 18·06% N; found: 39·00% C, 2·20% H, 17·73% N. 2,4,6-Trinitrophenyl ethanoate (*Ic*) was prepared from ethanoic anhydride and 2,4,6-trinitrophenol (*V*) by the known procedure[3,4]. 2,4,6-Trinitrodiphenyl ether (*Id*). 2·47 g (0·01 mol) compound *Ib* was dissolved in 10 ml methanol at 40°C and treated with 1·2 g (0·013 mol) phenol dissolved in 10 ml 1M-$CH_3O^{(-)}$. After 2 min 1 ml 1M-HCl was added, and the crystalls separated on cooling were recrystallized from methanol. Yield 2·4 g (80%), m.p. 149—151°C (ref.[5] m.p. 153°C). The same procedure was used for preparation of 2,4,6-trinitro-4′-bromodiphenyl ether (*Ie*) m.p. 143—144°C (ref.[6] m.p. 145°C), 2,3′,4,6-tetranitrodiphenyl ether (*If*) m.p. 169—170°C (ref.[7] m.p. 170°C), and 2,4,4′,6-tetranitrodiphenyl ether (*Ig*) m.p. 159—161°C (ref.[8] 153°C).

Kinetic Measurement

Measurement of formation of the adduct in reactions of the compounds *Ia*, *Ib* with methyl cyanoethanoate anion ($II^{(-)}$) was carried out in methanol at 25°C using a stopped-flow spectrophotometer Durrum. One syringe contained respectively methanolic solution of the compound *Ib* ($6 \cdot 10^{-5}$M) or *Ia* ($1 \cdot 10^{-4}$M) and ester *II* (0·2 or 0·4M). The second syringe contained methanolic methoxide ($8 \cdot 10^{-3}$ to $4 \cdot 10^{-2}$M) and sodium chloride to adjust the ionic strength ($I = 0{\cdot}1$).

The reaction with the chloroderivative *Ib* was measured at 450 nm (λ_{max} of the mono-adduct), the reaction with the compound *Ia* was measured at 540 nm where absorbance of the di-adduct is practically zero, and the mono-adduct only absorbs. The rate constants were calculated from the reaction half-life (read from the screen of the oscilloscope) using equation $k_{obs} = 0{\cdot}69/t_{1/2}$.

Kinetics of the nucleophilic substitution in ethanoate buffers were measured with a spectrophotometer VSU-2P (Zeiss, Jena) in methanol at 25°C with the ionic strength 0·05 adjusted by addition of NaCl. The reaction with ethanoate anion was measured at 360 nm (λ_{max} of the anion of *Ih*), that with the ester *II* was measured at 510 nm (λ_{max} of the anion of *Ii*). 1 cm cell was filled with 2 ml methanolic ethanoate buffer (with the ester *II* in the respective cases), and, after addition of 0·1 ml benzenic solution of the compound *I*, the absorbance increase was measured with time. The rate constants were calculated from the relation $k_{obs} \cdot t = -2{\cdot}3 \log (A_\infty - A_t) + \text{const}$. The rate constants of the reaction with methanol were determined by measurement in methanol at 360 nm.

Measurement of reaction of the compounds *I* with methoxide ion. 1 ml methoxide solution was injected in 10 ml methanolic solution of the compound *I* (10^{-4}M) at 25°C. After a certain time 10 ml ethanoate buffer (0·5M ethanoate) was injected in the reaction solution whereby the alkoxide was neutralized and, at the same time, the substrate was transformed into the compound *V*. After a period corresponding to about 8–10 half-lives of the transformation of the substrate *I*, absorbance of the solution was measured at 360 nm. The rate constants were calculated from the equation $k_{obs} \cdot t = -2{\cdot}3 \log (A_t - A_\infty) + \text{const.}$, where t is the time period between the injections of methoxide and ethanoate buffer.

RESULTS AND DISCUSSION

The rate and equilibrium constants of formation of the mono-adduct *III* in the reaction of *Ia*, *Ib* with the anion of ester *II* were measured by the stopped-flow method. The observed rate constant is defined by the relation $k_{obs} = k_1[II^{(-)}] + k_{-1}$. Concentration of the anion $II^{(-)}$ was calculated from the analytical concentrations of the ester *II* and methoxide anion and from the equilibrium constant $K = 54$ of the reaction (*A*) (ref.[9])

$$II + CH_3O^{(-)} \overset{K}{\rightleftharpoons} II^{(-)} + CH_3OH\,. \qquad (A)$$

In all the cases the dependence of k_{obs} on concentration of the anion was linear. The rate constants determined from the slope value and intercept at *y*-axis are given in Table I. Value of the equilibrium constant K_1 was calculated both as a ratio of the rate constants k_1/k_{-1} and from the absorbance value of the monoadduct *III* itself (found separately at high concentration of the anion $II^{(-)}$) and absorbance of the reaction mixture after 8–10 half-lives and concentration of the ester *II*.

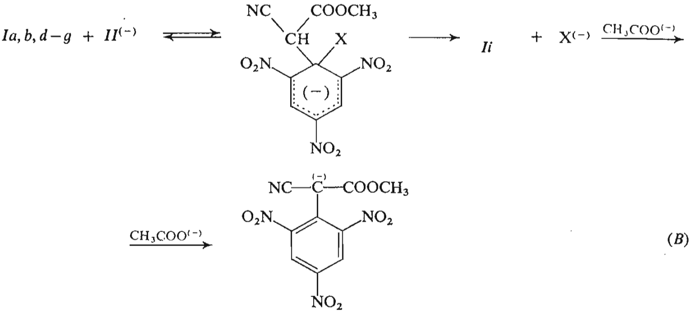
Formation of the di-adduct *IV* is slower by about 2 orders of magnitude, and its rate and equilibrium constants were determined for the compound *Ia* with the use of Eq. (*1*) (ref.[1]).

$$k_{obs} = k_2[II^{(-)}]\,K_1[II^{(-)}]/(1 + K_1[II^{(-)}]) + k_2\,. \qquad (1)$$

These values could not be determined for the derivative *Ib*, because the formation of the di-adduct *IV* is accompanied by simultaneous nucleophilic substitution of chlorine, the both products having similar spectra.

Equilibrium constants of formation of the mono-adduct *III* are higher than those in the reaction of the both substrates *Ia*, *b* with methoxide anion[10,11] by about 2 orders of magnitude.

In ethanoate buffers the anion $II^{(-)}$ concentration is so small that the adducts *III* and *IV* are not formed practically, the substitution (*B*) being the only reaction.



(*B*)

As the compound *Ii* is a much stronger acid than ethanoic acid, the final product is the anion of *Ii*. In all the cases the reaction (*B*) was pseudomonomolecular, the observed rate constants being directly proportional to the ester *II* concentration for the given buffer ratio. At a given concentration of the ester *II* they are directly proportional to the ratio $[CH_3CO_2^{(-)}]/[CH_3CO_2H]$. The reaction rate is given by Eq. (*2*).

TABLE I

Rate and Equilibrium Constants of Addition of Anion $II^{(-)}$ to 3-Position (k_1, 1 mol^{-1} s^{-1} k_{-1}, s^{-1}; K_1, 1 mol^{-1}) and to 3,5-Positions (k_2, k_{-2}, K_2) of the Compounds *Ia, Ib*

Substrate	$k_1 . 10^{-3}$	k_{-1}	K_1	k_2	k_{-2}	K_2
Ib	5·2 ± 0·5	37 ± 3	140 ± 20[a]	—	—	—
Ia	7·6 ± 0·8	72 ± 4	106 ± 16[b]	195 ± 25	0·25 ± 0·03	780 ± 200[c]

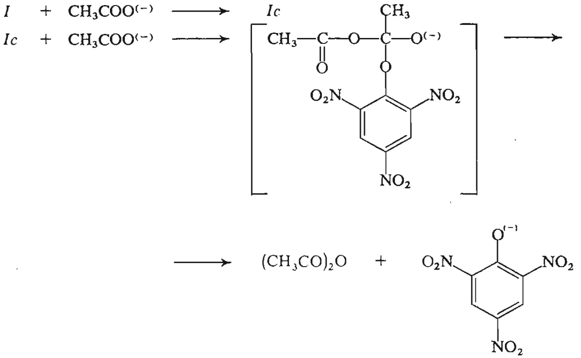
[a,b,c] The *K* values calculated from the absorbances are 145 ± 25, 102 ± 4, 750 ± 100.

$$v = k_{obs}[I] = k[\mathrm{N\overset{(-)}{C}CHCO_2CH_3}]\,[I]$$

$$k_{obs} = k\,.\,K[\mathrm{N\overset{(-)}{C}CHCO_2CH_3}]\,.\,10\ \mathrm{exp}\,.\,\log\frac{[\mathrm{CH_3CO_2^{(-)}}]}{[\mathrm{CH_3CO_2H}]} + \mathrm{p}K_\mathrm{A} - \mathrm{p}K_\mathrm{MeOH} \tag{2}$$

$\mathrm{p}K_\mathrm{A}$ of ethanoic acid is 9·625 (ref.[12]), $\mathrm{p}K_\mathrm{MeOH}$ of methanol is 16·916 (ref.[13]). Values of the rate constants k are given in Table II. The values $\log k$ of the disubstituted diphenyl ethers *Id*–*g* correlate with the respective σ constants, the slope being $\varrho = 0{\cdot}86$. This relatively low ϱ value and the correlation with the Hammett ϱ constant for the 4-nitro derivative *Ig* suggest that the rate-limiting step consists in attack of the substrate *I* by the anion $II^{(-)}$. The rate constants ratio $k_{\mathrm{Ib}} : k_{\mathrm{Ia}}$ equals 18, although the rate constants ratio in the reaction with methoxide ion is almost unity. This fact is probably due to the rate-limiting step consisting in splitting off of methoxy group from the tetrahedral intermediate.

In the reactions of the compounds type *I* with ethanoate anion the practically only product is trinitrophenol *Ih* except for the compounds *Id*, *e* which give about 50 and 20 per cent compound *Ia*, respectively. Formation of the anion of the acid *Ih* can be represented by the sequence (*C*).



(*C*)

In the reaction (*C*) ethanoate anion acts directly as nucleophile. The second step ($Ic + \mathrm{CH_3CO_2^{(-)}}$) is far faster than the first step, and, consequently, the reactions are pseudomonomolecular (except for the compounds *Ig* and *If* for which the time dependence of $\log (A_\infty - A_t)$ is not linear for the first 20 per cent of conversion).

Values of the rate constants are given in Table II. Dependence of log k on σ constants is non-linear, the ϱ constant value being decreased from 4 to 1. For the compounds *If* and *Ig* the rate-limiting step consists in attack of the 1-carbon atom by ethanoate anion, whereas for *Id* decomposition of the tetrahedral intermediate to the ethanoyl derivative *Ic* is rate-limiting.

Reaction of *Ib*, *If* and *Ig* with methoxide anion produces the compound *Ia* as the primary product which reacts further with methoxide anion to give the Meisenheimer complex. The rate constants given in Table II relate to the first reaction step. Attack by methoxide anion is rate-limiting. The rate constant of the reaction with *Ib* is somewhat higher than that obtained for attack of 1-position of the compound *Ia* by methoxide ion ($17{\cdot}3 \text{ l} . \text{mol}^{-1} \text{ s}^{-1}$). The rate constants of the compounds *Ig* and *If* are 7 and 5 times higher, respectively, than that of the compound *Ib*, although chlorine is a better leaving group than 4- or 3-nitrophenoxy group in most cases. A possible explanation is that sterical repulsion (crowding) in the derivatives *If* and *Ig* is lowered by formation of the activated complex whereby the reaction is facilitated.

For the compounds *Ic*, *If* and *Ig* the reaction rate with methanol itself was measured, the respective rate constants being given in Table II. The reactivity ratio of *If* to *Ig* is only twice as large as that of the reaction with methoxide ion. This finding could indicate that attack of the substrate *I* by methanol is rate-limiting in this case, too.

TABLE II

Rate Constants k ($\text{l mol}^{-1} \text{ s}^{-1}$) of Reactions of the Compounds *Ia* to *Ig* with Nucleophiles in Methanol at 25°C

Substrate	k	$10^4 . k$	k	$10^5 . k$
	$NCC^{(-)}HCOOCH_3$	$CH_3COO^{(-)}$	$CH_3O^{(-)}$	CH_3OH
Ia	8·0 ± 1·5	—	17·3[a]	—
Ib	141 ± 6	5·7 ± 0·2	19·8 ± 0·9	—
Ic	—	320 ± 20	—	21 ± 0·6
Id	33·5 ± 1·5	0·6 ± 0·1	—	—
Ie	53 ± 2	4·7 ± 0·2	—	—
If	135 ± 4	40 ± 2	97 ± 6	1·7 ± 0·1
Ig	166 ± 7	53 ± 4	140 ± 12	3·4 ± 0·6

[a] Ref.[14].

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