

STUDY OF REACTION OF SUBSTITUTED NITROPHENYL ACETATES AND BENZOATES WITH NUCLEOPHILES

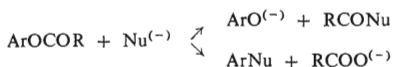
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Reaction of 2-substituted 4,6-dinitrophenyl acetates and benzoates with methoxide, 4-bromophenoxide and acetate anions and with anion of methyl cyanoacetate has been studied in methanol at 25°C, and the respective rate constants have been determined along with the rate constant ratios of nucleophilic attacks at carbonyl carbon (C_{CO}) and C_1 carbon of the aromatic ring (C_{Ar}). Content of the 2-substituted 4,6-dinitrophenols formed by nucleophilic attack at C_{CO} increases in the product with increasing hardness of the nucleophiles in the series methyl cyanoacetate anion < 4-bromophenoxide anion < methoxide anion. The substituents polar effects are decisive for the attack at C_{Ar} , whereas both polar and steric effect operate in the attack at C_{CO} . Methoxide anion attacks the C_{CO} of 2,4-dinitrophenyl ester even faster than the C_{CO} of 2,4,6-trinitrophenyl ester.

Aryl esters of carboxylic acids can be attacked by nucleophiles either at their carbonyl carbon atom C_{CO} or at aromatic carbon atom C_{Ar} carrying the acyloxy group.



In the study¹ of reaction of substituted phenyl acetates and benzoates with O- and N-nucleophiles in aqueous and alcoholic media it was found that the nucleophiles attack exclusively the C_{CO} to give the substituted phenoxide ion. Only methanolysis of 2,4,6-trinitrophenyl benzoate² gave predominantly 1-methoxy-2,4,6-trinitrobenzene as the product of nucleophilic attack at C_{Ar} . Carbanions³ and thiophenolate ion⁴, which belong to soft bases⁵, attack the C_{Ar} relatively more than hard oxygen and nitrogen nucleophiles do. Ratio of the products formed by the attacks at C_{Ar} and C_{CO} increases with increasing σ constant of the substituents present in the benzene ring⁴.

In this work reaction of 2-substituted 4,6-dinitrophenyl acetates *Ia–Ic* and benzoates *IIa–IIc* with methoxide, 4-bromophenoxide, acetate and methyl cyanoacetate anions is studied with the aim of determination of effects of substituents and type of nucleophile on ratio of the products and on the reaction rate constants.

EXPERIMENTAL

The $^1\text{H-NMR}$ spectra were measured with a BS 487 B Tesla apparatus at 80 MHz using hexamethyldisiloxane as internal standard.

The acetates *Ia—Ic* were prepared by 2 to 3 h boiling of the respective phenol with a tenfold molar excess of acetic anhydride and were purified by crystallization from CCl_4 or benzene-hexane mixture. 2,4,6-Trinitrophenyl acetate (*Ia*), m.p. 86—88°C (ref.⁶ 86—87°C); 2-chloro-4,6-dinitrophenyl acetate (*Ib*), m.p. 99—100°C. For $\text{C}_8\text{H}_5\text{ClN}_2\text{O}_6$ (260.6) calculated: 36.87% C, 1.93% H, 10.75% N; found: 36.73% C, 1.97% H, 10.77% N; 2,4-dinitrophenyl acetate (*Ic*), m.p. 70—72°C (ref.⁷ 72°C). The benzoates *Ila—Ilc* were prepared by 3 h boiling of the respective phenols with threefold molar excess of benzoyl chloride and were purified by crystallization from benzene-hexane mixture. 2,4,6-Trinitrophenyl benzoate (*Ila*), m.p. 164—166°C (ref.⁸ 163—164°C); 2-chloro-4,6-dinitrophenyl benzoate (*Ilb*), m.p. 118—120°C. For $\text{C}_{13}\text{H}_7\text{ClN}_2\text{O}_6$ (322.7) calculated: 48.39% C, 2.19% H, 8.68% N; found: 48.70% C, 2.41% H, 8.49% N; 2,4-dinitrophenyl benzoate (*Ilc*), m.p. 133—134°C (ref.⁸ 132—133°C).

Methyl 2-(2-chloro-4,6-dinitrophenyl)-2-cyanoacetate (*IVb*). Solution of 4.7 g (0.02 mol) 1-methoxy-2-chloro-4,6-dinitrobenzene and 3 g (0.03 mol) methyl cyanoacetate in 60 ml methanol was treated with 5.3 ml 4.35M sodium methoxide (0.023 mol). After several minutes standing at room temperature a part of the methanol was distilled off in vacuum, the residue was diluted with 250 ml water and neutralized with 0.1M-HCl. The product was extracted in about 250 ml benzene, the extract was dried with anhydrous sodium sulphate, and the benzene was distilled off in vacuum. The raw product was purified by chromatography on a silica gel column using chloroform as eluent. The chromatographically pure product was crystallized 3 times from CCl_4 -hexane mixture. Yield 3.76 g (62%), m.p. 98—100°C; for $\text{C}_{10}\text{H}_6\text{ClN}_3\text{O}_6$ (299.6) calculated: 40.09% C, 2.02% H, 14.02% N; found: 40.22% C, 2.22% H, 14.04% N. The $^1\text{H-NMR}$ spectrum (CDCl_3 , 24°C): aromatic H $\delta = 8.64$ and $\delta = 8.86$ (a pair of doublets, $J = 2.4$ Hz), $\delta(\text{OCH}_3) = 3.87$. The methine group gives a very broad signal between $\delta = 5.0$ to 5.7 which changes into sharp singlet $\delta(\text{CH}) = 5.89$ on addition of a drop of trifluoroacetic acid. Preparation of methyl 2-(2,4,6-trinitrophenyl)-2-cyanoacetate (*IVa*) and methyl 2-(2,4-dinitrophenyl)-2-cyanoacetate (*IVc*) was described in the previous reports^{9,10}.

Kinetic measurements. The following solutions were used for the kinetic measurements: $5 \cdot 10^{-3}\text{M}$ esters *Ia—Ic* and *Ila—Ilc* in benzene, acetate buffers 5 : 1, 1 : 1 and 1 : 5 (acetate-acetic acid; the sodium acetate concentration was 0.5M in every case), 0.5M 4-bromophenol, 1M methyl cyanoacetate in methanol. The solutions of sodium methoxide were prepared by dilution of 1M stock solution with methanol, and their concentrations were determined titrimetrically. All the kinetic measurements were carried out in methanol at 25°C. Kinetic measurements of reaction with acetate ion: 1 drop of solution of the ester *Ia—Ic* or *Ila—Ilc* was added to 2 ml acetate buffer in tempered quartz cell and the time dependence of absorbance of formed phenol was measured at its λ_{max} (*Ila* 355 nm, *Ilb* 375 nm, *Ilc* 360 nm) using a VSU 2P spectrophotometer (Zeiss, Jena). The rate constants were calculated from Eq. (1).

$$-k_{\text{obs}} \cdot t = 2.303 \log (A_{\infty} - A_t) + \text{const.} \quad (1)$$

The kinetic measurements in bromophenolate buffers were carried out in the same way. The stock solutions of the bromophenolate buffers were prepared by mixing 0.5M 4-bromophenol and 0.1M sodium methoxide and completing the volume with methanol. The reaction kinetics with methoxide ion: one drop of $5 \cdot 10^{-3}\text{M}$ solution of the benzoate *Ilb* was added in 2 ml sodium methoxide solutions. The further procedure was identical with that given above.

The reaction kinetics with methyl cyanoacetate anion: 1M methyl cyanoacetate was added to sodium methoxide solution (final volume 2 ml) followed by 1 drop $5 \cdot 10^{-3}$ M benzoate *Ib*. The time increase of absorbance at λ_{\max} of the anion of the product *IVb* (485 nm) was measured. The rate constants were calculated from Eq. (1).

The reaction kinetics of the compounds *Ia–Ic*, *IIa*, *IIc* with methoxide ion were followed by the stopped-flow technique at 25°C using a Durrum Spectrophotometer model D-110. One syringe contained sodium methoxide solution (concentration $5 \cdot 10^{-3}$ to 10^{-2} M), the other one contained methanolic solution of the ester (concentrations $2 \cdot 10^{-4}$ M *IIa*, 10^{-4} M *Ia*, $5 \cdot 10^{-3}$ M *Ib*, *Ic*, *IIc*). The methanolic ester solutions were prepared immediately before use. The analytical wavelengths were 340 nm (*Ia*, *IIa*) and 365 nm (the other esters). The reaction half-lives were read from the oscilloscope of the spectrophotometer, every experiment was repeated several times. The rate constants were calculated from the relation $k_{\text{obs}} = 0.693/\tau_{1/2}$.

The product ratio *III/IV* and *III/V* was determined with the use of the same solutions as those used in kinetic experiments. Besides that the following solutions were used: $5 \cdot 10^{-3}$ M 2,4-dinitrochlorobenzene, $5 \cdot 10^{-3}$ M 1-methoxy-2,4-dinitrobenzene, $5 \cdot 10^{-3}$ M 1-methoxy-2-chloro-4,6-dinitrobenzene, and $5 \cdot 10^{-3}$ M 1-methoxy-2,4,6-trinitrobenzene in benzene. For the reaction of methoxide ion with the trinitrophenyl esters *Ia*, *IIa* 0.2 ml fresh methanolic solution $5 \cdot 10^{-4}$ M *Ia* (or *IIa*) prepared immediately before the experiment was added to 1.8 ml sodium methoxide solution of $2 \cdot 10^{-3}$ and 10^{-2} M concentration, respectively. After shaking 20 μ l acetic acid was added, and the absorbance *A* was measured at 355 nm in a 1 cm quartz cell (absorbance of the formed compound *Va* was subtracted from the absorbance *A*). Amount of the formed *Va* (in %) was calculated from Eq. (2):

$$\% Va = 100(A_{100} - A)/(A_{100} - A_0). \quad (2)$$

A_0 is the absorbance of the solution measured under the same conditions with the use of the same volume of methanol instead of sodium methoxide. A_{100} is the absorbance of the solution containing acetate buffer instead of methoxide (0.5M sodium acetate, 0.1M acetic acid). The absorbance A_{100} was measured after about 8 half-lives of the reaction with acetate ion (*i.e.* about 300 and 3000 s for *Ia* and *IIa*, respectively).

In the case of reactions with 2-chloro-4,6-dinitrophenyl esters *Ib*, *IIb* 2 ml fresh $5 \cdot 10^{-4}$ M solution *Ib* (or *IIb*) was added to 8 ml $2 \cdot 10^{-3}$ (or 10^{-2})M sodium methoxide. After mixing, 1 ml of this solution was mixed with 1 ml dimethyl sulphoxide in a 1 cm cell, and 50 μ l 1M sodium methoxide was added. The absorbance *A* of this solution was measured at 495 nm. Amount of the formed 1-methoxy-2-chloro-4,6-dinitrobenzene *Vb* (in %) was calculated from Eq. (3):

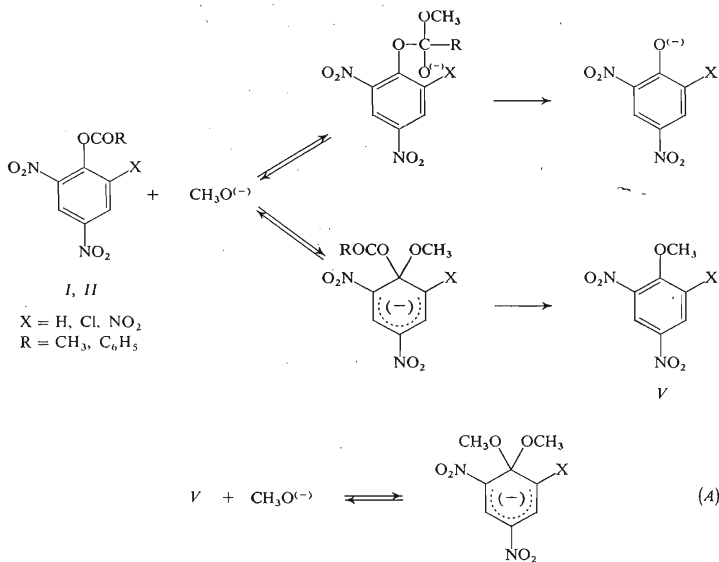
$$\% Vb = 100(A - A_0)/(A_{100} - A_0). \quad (3)$$

The absorbance A_0 was determined by a measurement under the same conditions, the solution of methoxide being, however, replaced by the same volume of methanol. The absorbances A_{100} were determined in the same way using solution *Vb* of the same concentration instead of *Ib* (or *IIb*). Composition of the products after reaction with 4-bromophenoxide ion was determined for the esters *Ib* and *IIb*. 2 ml $5 \cdot 10^{-4}$ M ester solution was added to 8 ml 4-bromophenolate buffer (0.5M 4-bromophenol, 0.05M sodium 4-bromophenoxide). 0.6 ml of this solution was mixed with 1 ml dimethyl sulphoxide and 0.4 ml 1M sodium methoxide in a 1 cm cell, and the absorbance *A* was measured at 495 nm. Amount of the formed compound *Vb* (in %) was calculated from Eq. (3), the measured value *A* being corrected by multiplication by the dilution factor 1.67.

Composition of products after the reaction with methyl cyanoacetate anion was determined for the esters *Ib*, *IIb*, *Ic*, *IIc*. 0.2 ml $5 \cdot 10^{-4}$ M solution of the ester was mixed with 1.8 ml 0.05 to 2 M methyl cyanoacetate in methanol (or mixture methanol–dimethyl sulphoxide containing 20 μ l 1 M sodium methoxide) in a 1 cm cell. The absorbance *A* was measured at 485 nm. The amounts of the formed compounds *IVb* and *IVc* (in %) were calculated from Eq. (3). The values A_0 were determined by the above-given way. For determination of the value A_{100} solutions of *Ib* or *IIb* were replaced by *Vb* of the same concentration (the absorbance A_{100} was measured after about 1200 s), and solutions *Ic* or *IIc* were replaced by solution of 2,4-dinitrochlorobenzene (A_{100} was measured after about 300 s).

RESULTS AND DISCUSSION

Reactions of substituted phenyl acetates and benzoates follow Scheme 1. For the trinitrophenyl esters the equilibrium (*A*) is shifted in favour of the Meisenheimer complex, and, therefore, the reaction mixture had to be acidified with acetic acid so that the ratio $[IIIa]/[Va]$ might be determined. The equilibrium (*A*) can be



SCHEME 1

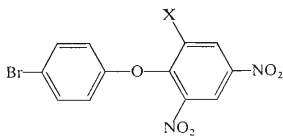
shifted in favour of the Meisenheimer complex by addition of both methoxide and dimethyl sulphoxide, which was made use of for determination of the ratio $[III]/[V]$ in reactions of the esters *Ib*, *Iib*, *Iic*, the formed methoxy derivative *V* being determined spectrophotometrically as the corresponding Meisenheimer complex. In the case of the 2,4-dinitrophenyl acetate *Ic* the amount of the formed methoxy derivative *Vc* is small and was not determined. The found values are given in Table I.

The reactions of the studied esters with methoxide ion are 1. order in both the substrate and methoxide ion in all the cases. With excess methoxide ion the reactions proceeded as pseudomonomolecular. The observed rate constant k_{obs} is a sum of the rate constants of reaction of methoxide ion with carboxylic group (k_{CO}) and with aromatic carbon atom (k_{Ar}).

$$k^{\text{OCH}_3} = k_{\text{obs}}/[\text{CH}_3\text{O}^{(-)}] = k_{\text{Ar}}^{\text{OCH}_3} + k_{\text{CO}}^{\text{OCH}_3} \quad (4)$$

As the both reactions are of the same order, ratio of the rate constants is equal to ratio of concentrations of the products. The found values of rate constants are given in Table I.

Reactions in bromophenolate buffer involve both methoxide and 4-bromophenoxide anions as nucleophiles. Each of the two nucleophiles can react either with carbonyl or with aromatic carbon atoms. In the former case the corresponding phenol is formed, in the latter case the 4-bromophenoxy derivative *VI* is produced which reacts with methoxide ion to give the methoxy derivative *V*.



As the absorbances of the both ethers at the used analytical wavelength are small and almost the same, the reaction does not make itself felt spectroscopically. The observed rate constant k_{obs} increased (for the given ratio of concentrations of the buffer components) linearly with the buffer concentration. The value k_{obs} extrapolated to zero buffer concentration is due to the reaction with methoxide ion. The corresponding value k^{OCH_3} was calculated by dividing the extrapolated k_{obs} by the methoxide ion concentration calculated from $\text{p}K_{\text{a}}$ of 4-bromophenol¹¹ in methanol ($\text{p}K_{\text{a}} = 13.61$), from $\text{p}K_{\text{s}}$ of methanol¹² (16.916) and from the buffer composition. The found values of rate constants (Table II) are in average by 20–25% lower than those found by direct measurement with methoxide ion (Table I). Slopes of the dependence

of k_{obs} on concentration of 4-bromophenoxide ion give the rate constant k^{ArO} of the reaction of 4-bromophenoxide ion with the carboxyl and aromatic carbon atoms in analogy to Eq. (4). Value of the rate constant k^{ArO} decreases with increasing ratio [4-bromophenol]/[4-bromophenoxide ion] (Table II). This decrease of the rate

TABLE I

Rate Constants k^{OCH_3} , $k_{\text{CO}^{\text{OCH}_3}}^{\text{OCH}_3}$, $k_{\text{Ar}^{\text{OCH}_3}}^{\text{OCH}_3}$ ($\text{l mol}^{-1} \text{s}^{-1}$) and Composition of Reaction Products after Reaction of the Esters I and II with Methoxide Anion in Methanol at 25°C

| Ester | k^{OCH_3} | % V | % III | $k_{\text{Ar}^{\text{OCH}_3}}^{\text{OCH}_3}$ | $k_{\text{CO}^{\text{OCH}_3}}^{\text{OCH}_3}$ | A^a |
|-------|--------------------|------------|-------|---|---|-------|
| Ia | 290 | 28 | 72 | 81 | 209 | 7.6 |
| IIa | 125 | 78 | 22 | 97.5 | 27.5 | |
| Ib | 53 | 1.5 | 98.5 | 0.8 | 52 | 10 |
| IIb | 6.4 | 18.5 | 81.5 | 1.2 | 5.2 | |
| Ic | 410 | — | 100 | — | 410 | 5.6 |
| IIc | 73 | ≤ 0.3 | 99.7 | ~ 0.2 | 72.8 | |

^a Ratio of the rate constants $(k_{\text{CO}^{\text{OCH}_3}}^{\text{OCH}_3})_{\text{acetate}} / (k_{\text{CO}^{\text{OCH}_3}}^{\text{OCH}_3})_{\text{benzoate}}$.

TABLE II

Rate Constants ($\text{l mol}^{-1} \text{s}^{-1}$) and Composition of Reaction Mixture after Reaction of the Esters I and II in 4-Bromophenolate Buffers in Methanol at 25°C

| Ester | $k^{\text{ArO}} \cdot 10^2$ | k^{OCH_3} | % V | % III | $k_{\text{Ar}^{\text{ArO}}}^{\text{ArO}} \cdot 10^2$ | $k_{\text{CO}^{\text{ArO}}}^{\text{ArO}} \cdot 10^2$ | A^a |
|-------|-----------------------------|--------------------|-----|--------|--|--|-------|
| Ib | 38.5 ^b | 38.0 ^b | 6.8 | 93.2 | 2.6 ^b | 36 ^b | 8.8 |
| | 43.0 ^c | 40.5 ^c | | | | | |
| IIb | 8.36 ^d | 4.5 ^d | 54 | 46 | 4.8 ^b | 4.1 ^b | |
| | 8.55 ^b | 4.8 ^b | | | | | |
| | 10.6 ^c | 4.8 ^c | | | | | |
| Ic | 225 ^d | 300 ^d | — | 100 | — | 225 ^d | |
| IIc | 34 ^d | 52.5 ^d | | 98—100 | | $\sim 34^d$ | 6.6 |
| | 45 ^b | 60 ^b | | | | | |
| | 54.5 ^c | 55 ^c | | | | | |

^a Ratio of the rate constants $(k_{\text{CO}^{\text{ArO}}}^{\text{ArO}})_{\text{acetate}} / (k_{\text{CO}^{\text{ArO}}}^{\text{ArO}})_{\text{benzoate}}$. ^b The constants obtained by measurements in the buffer [4-bromophenol]/[4-bromophenoxide] = 4 : 1; ^c (3 : 2); ^d (9 : 1).

constant k^{ArO} can be due either to the 4-bromophenol affecting character of the medium (e.g. its dielectric constant) or to specific interaction taking place between bromophenol and bromophenoxide ion whereby its reactivity is lowered.

Composition of the products of the reaction of the esters *Ib* and *IIf* with 4-bromophenoxide ion was determined with the use of the buffer containing 0.5M 4-bromophenol and 0.05M 4-bromophenoxide ion. From the kinetic experiments it followed, that reaction with methoxide ion was negligible under these conditions. The found ratios of the product concentrations $[IIIb]/[Vb]$ are given in Table II.

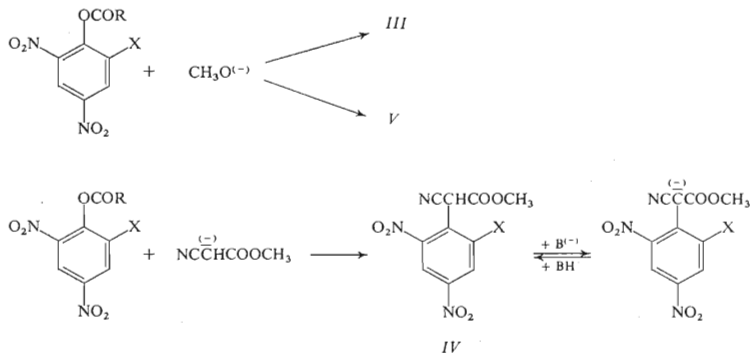
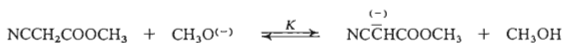
The reaction of the esters *Ia* and *IIf* with methyl cyanoacetate anion at the initial methoxide ion concentration below about $5 \cdot 10^{-4}M$ produces the compound *IVa*. In case of the ester *Ia*, methanolysis to 2,4,6-trinitrophenol took place to a smaller extent. The other esters react with methyl cyanoacetate anion to give both the compound *IV* and the corresponding phenol *III* and methoxy derivative *V* (Table III). The ratio $[IV]/([III] + [V])$ increased with dimethyl sulphoxide concentration, and, in a given medium, it increased practically linearly with methyl cyanoacetate concentration. As the ratio $[NCCHCO_2CH_3]^{(-)}/[CH_3O^{(-)}]$ also increases linearly with methyl cyanoacetate concentration¹⁰, obviously, methyl cyanoacetate anion reacts predominantly or exclusively with aromatic carbon of the esters to give the compound *IV* (Scheme 2), and the concentration ratio $[IV]/([III] + [V])$ is determined by the ratio of the reaction rates of the substrate with methyl cyanoacetate

TABLE III

Concentration Ratio $[IV]/([III] + [V])$ in Products of Reactions of Esters *I* and *II* with Methyl Cyanoacetate Anion in Methanol (*a*) and in Mixtures Dimethyl Sulphoxide-Methanol (by Vol.) 1 : 3 (*b*), 1 : 1 (*c*), 3 : 1 (*d*) at 25°C

| Ester | <i>a</i> | <i>b</i> | <i>c</i> | <i>d</i> |
|------------|-----------|--------------|--------------|-------------|
| <i>Ib</i> | 19 (1M) | — | — | — |
| <i>IIf</i> | 0.45 (1M) | 2.1 (1.5M) | 4.6 (0.5M) | — |
| | — | 1.35 (0.75M) | 1.3 (0.1M) | — |
| | — | 0.4 (0.25M) | 0.63 (0.05M) | — |
| <i>Ic</i> | — | — | 0.16 (1M) | 1.25 (2M) |
| | — | — | — | 0.62 (0.8M) |
| <i>IIf</i> | 0.13 (2M) | — | — | — |

^a The numbers in brackets give concentrations of methyl cyanoacetate.



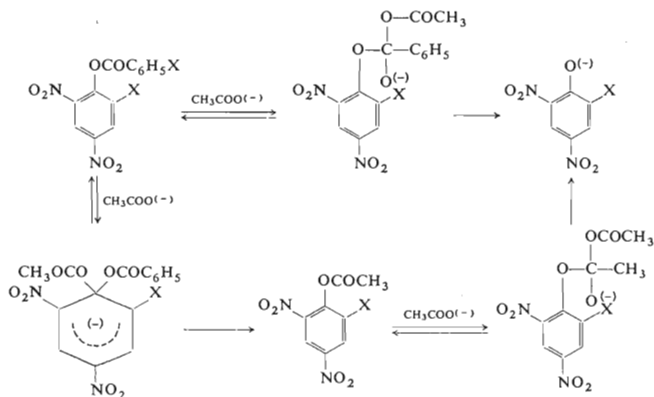
anion and with methoxide anion. Increasing concentration of dimethyl sulphoxide in methanol results in reactivity increase of both methyl cyanoacetate and methoxide anions, the latter being somewhat greater¹⁰. At the same time the ratio $[\text{NC}\overset{(-)}{\text{C}}\text{HCO}_2 \cdot \text{CH}_3]/[\text{CH}_3\text{O}^{(-)}]$ increases, too. From the results it follows that increase of the ratio $[\text{NC}\overset{(-)}{\text{C}}\text{HCO}_2 \cdot \text{CH}_3]/[\text{CH}_3\text{O}^{(-)}]$ is greater than that of the rate constants ratio $k^{\text{OCH}_3}/k^{\text{IV}}$. It means that the influence of dimethyl sulphoxide on the pre-equilibrium is dominant.

The reaction of methyl cyanoacetate anion with the ester *Ib* was followed kinetically. The rate constant k^{IV} of formation of the compound *IV* was calculated from Eq. (5). Although the reaction

$$k^{\text{IV}} = (k_{\text{obs}} - k^{\text{OCH}_3} \cdot [\text{CH}_3\text{O}^{(-)}]) / [\text{NC}\overset{(-)}{\text{C}}\text{HCO}_2 \cdot \text{CH}_3] \quad (5)$$

produces the anion of the compound *IV*, the rate-limiting step consists in formation of the compound *IV*, as the subsequent deprotonation is faster by several orders of magnitude. The found value of the rate constant is $k^{\text{IV}} = 1.90 \pm 0.15 \text{ (l mol}^{-1} \text{ s}^{-1}\text{)}$.

Reactions of the benzoates *Ila–Iic* with acetate anion follow the Scheme 3. The reaction of the acetates *Ia–Ic* with acetate anion takes place at C_{Ar} to give identical compounds, so that the reaction course is simplified. In the both cases the final



SCHEME 3

reaction product is the corresponding phenol *III*. The dependence $\log(A_\infty - A_t)$ vs time was linear in all the cases except for the ester *IIa* where the absorbance increase was slower in the initial phase than it should be according to the 1. order kinetics in the substrate. The time change of the absorbance agrees with the calculated one, if the following values of ratios are used: $(k_{\text{CO}})_{\text{acetate}}/(k_{\text{CO}})_{\text{benzoate}} = 15$, and $k_{\text{CO}}/k_{\text{Ar}} = 7 : 3$ (for the compound *IIa*). In contrast to the other used oxygen nucleophiles (methoxide and bromophenoxide ions) the acetate anion attacks carbonyl group predominantly in all the cases.

In the buffer $[\text{acetate}]/[\text{acetic acid}] = 5$ the dependences of the rate constants k_{obs} on the acetate concentration were linear up to the acetate concentration about 0.2M. At higher concentrations the k_{obs} increased faster than it corresponded to linear dependence. This acceleration is obviously due to the increase in ionic strength which stabilizes the activated complex with respect to the starting compounds. In the buffer $[\text{acetate}]/[\text{acetic acid}] = 0.2$, on the contrary, the increase was slower as compared to linear dependence of k_{obs} vs acetate concentration. This deviation from linear dependence can be explained by the change of medium due to increasing concentration of acetic acid. In the acetate buffer 1 : 1 the both effects are compensated, and the dependence k_{obs} vs $[\text{CH}_3\text{CO}_2^-]$ is linear in the whole range up to 0.5M CH_3CO_2^- . The rate constants k^{AcO} defined by the slope of the linear dependence k_{obs} vs $[\text{CH}_3\text{CO}_2^-]$ are given in Table IV.

Two criteria have been used in the discussion of the factors affecting the reaction course — the rate constant values obtained by direct measurement and the rate constant ratios determined from concentrations of the reaction products. The attack of benzoate carboxylic group by a nucleophile is slower in all the cases by about one order of magnitude than that of the acetate carboxylic group, the leaving groups being the same. On the contrary, the attack of C_{Ar} of the substituted phenyl benzoates is somewhat faster (about 1.5x) than that of the corresponding phenyl acetates. The both effects cause the ratio k_{Ar}/k_{CO} to be always substantially higher (10–20x) with the benzoates than with the corresponding acetates. Amount of phenol in the reaction products increases in the series of the nucleophiles: methyl cyanoacetate anion, 4-bromophenoxide anion, methoxide anion. In the same direction hardness of the bases is increased, too, and this is probably the decisive factor. The substituent X can affect the reaction by its steric and polar effects. The centre C_{Ar} is attacked by nucleophile at an approximately perpendicular direction with respect to the plane of the ring, hence steric effect of the substituent X is relatively small. In the activated complex the leaving group is deviated from the ring plane, which decreases steric interactions between the leaving group and substituent X. Steric effect of X on the nucleophile is opposite to that on the leaving group, thus the resulting sterical effect is small and can be either slightly accelerating or retarding. The polar effect of the substituent X is decisive. In all cases rate constants of nucleophilic attacks at C_{Ar} decrease in the series $X = NO_2 > Cl > H$. Thus *e.g.* the reactions of methoxide ion with the esters *Ia* and *IIa* are faster than those with *Ib* and *IIb*, respectively, by about 2 orders of magnitude.

When the carboxylic group is attacked, steric and polar effects are comparable and their result depends considerably on the nucleophile, too. With acetate ion the fastest reaction is found for 2,4,6-trinitrophenyl derivatives, 2-chloro-4,6-dinitro-

TABLE IV

Rate Constants ($l\ mol^{-1}\ s^{-1}$) of Reactions of Esters *I* and *II* with Acetate Ion in Methanol at 25°C

| Ester | $k^{AcO} \cdot 10^4$ | A^a | Ester | $k^{AcO} \cdot 10^4$ | A^a | Ester | $k^{AcO} \cdot 10^4$ | A^a |
|------------|----------------------|-------|------------|----------------------|-------|------------|----------------------|-------|
| <i>Ia</i> | 320 | 11 | <i>Ib</i> | 12 | 17 | <i>Ic</i> | 14 | 12.7 |
| <i>IIa</i> | 29 | | <i>IIb</i> | 0.7 | | <i>IIc</i> | 1.1 | |

^a Ratio of the rate constants $(k^{AcO})_{acetate}/(k^{AcO})_{benzoate}$.

phenyl derivatives being the slowest. Methoxide and 4-bromophenoxide anions react most rapidly with 2,4-dinitro derivatives. In the latter cases steric effect is so important that 2-nitro group is deactivating as compared with 2-hydrogen.

Ratio of the rate constants k_{Ar}/k_{CO} increases in all the cases in the following series: 2,4-dinitro < 2-chloro-4,6-dinitro < 2,4,6-trinitro. This relation is affected by both steric and polar effects of the substituent X. The polar effect of X affects far more k_{Ar} than k_{CO} , because C_{Ar} is closer to X than C_{CO} is. Bulky substituents (both Cl and NO_2) hinder sterically approach of nucleophiles to C_{CO} , whereas nucleophilic attack of C_{Ar} is sterically affected by them only little.

The activated complex of the attack of C_{Ar} is more polarizable (larger delocalization of electrons) than that of the attack of the carbonyl group. Therefore, addition of dimethyl sulphoxide should increase k_{Ar} more than k_{CO} . The ratio k_{Ar}/k_{CO} is 2.2 times greater in 50% dimethyl sulphoxide than in methanol for the reaction of methoxide ion with the ester *Ib*.

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