

KINETICS AND MECHANISM OF THE REACTION OF AROMATIC CARBOXYLIC ACIDS WITH ETHYLENE OXIDE IN PROTIC AND APROTIC DIPOLAR SOLVENTS IN THE PRESENCE OF TERTIARY AMINES*

J. MÁLEK and P. ŠILHAVÝ

*Institute of Chemical Process Fundamentals,
Czechoslovak Academy of Sciences, 165 02 Prague 6-Suchdol*

Received December 4th, 1974

Aromatic carboxylic acids react with ethylene oxide in the presence of tertiary amines as catalysts both in protic and in aprotic solvents to give the corresponding 2-hydroxyethyl esters by the amine- and acid-catalysed parallel reactions. In protic solvents, the acid-catalysed reaction is first-order in both the acid and ethylene oxide and its rate correlates with the acid strength by Brønsted equation with the α_1 constant corresponding to a value of 0.62. The parallel amine-catalysed reaction of the acids with $pK_a \geq 3.99$ is in these solvents first-order in both ethylene oxide and the amine, and the Brønsted α_2 constant has a value of 0.34. In the amine-catalysed reaction of the acids with $pK_a < 3.99 > 3.18$ there is a change in the nature of the rate-determining step; the reaction of the acids with $pK_a \leq 3.18$ proceeds solely with the acid participating in the rate-determining step of the amine-catalysed reaction which is first-order in the acid, ethylene oxide, and tertiary amine. Of the two parallel reactions occurring in protic solvents, the amine-catalysed one has the higher activation energy and by about 6 to 7 orders of magnitude higher values of the preexponential factor. In aprotic dipolar solvents the acid-catalysed reaction is first-order in both the acid and ethylene oxide, and the Brønsted constant α'_1 has a value of 0.96. The amine-catalysed reaction is in this case first-order in the acid, ethylene oxide, and tertiary amine, and its kinetics does not change with the acid strength of carboxylic acids; the Brønsted constant α'_2 has a value of 0.60. The Hammett reaction constants ρ_1 , ρ_2 , ρ'_1 and ρ'_2 have the same values as the respective α_1 , α_2 , α'_1 and α'_2 constants.

The previous work of this series was concerned with the kinetics and mechanism of reactions of acetic acid, monochloro- and dichloroacetic acids with ethylene oxide catalysed with tertiary amines and carried out in alcohols as solvents¹. In the work it was suggested that under the conditions used ethylene oxide is consumed by both the acid-catalysed and parallel tert-amine-catalysed bimolecular nucleophilic substitution reactions. The reactions of ethylene oxide were accompanied by side reactions which especially in the case of the chloro-substituted acids led to formation of considerable amounts of by-products. This circumstance left some doubt concerning the validity of the kinetic dependences obtained for the whole region of conversions of the carboxylic acids. The results reported in the above-mentioned study allowed also to draw only qualitative conclusions about the relationship between the rate of the ethylene oxide reaction with carboxylic

* Part III in the series Reactions of Carboxylic Acids with Ethylene Oxide; Part II: This Journal 34, 3098 (1969).

acids and the acid strength. To our knowledge, kinetics of reactions of carboxylic acids with alkylene oxides catalysed with tertiary amines in aprotic dipolar solvents have not up to now been studied; the question about the validity of reported kinetic dependences also for reactions effected in solvents of this type has not therefore been answered.

In the present work we report on the kinetics of the reaction of aromatic carboxylic acids with ethylene oxide in the presence of tertiary amines. The kinetics was measured in a closed system at pressures ranging from 600 to 1070 Torr and temperatures lower than 100°C. Ethylene oxide was subjected to the reaction with benzoic acid (pK_a 4.21) (ref.²) and relatively stronger 2,4-dichlorophenoxyacetic acid (pK_a 3.18) (ref.³) in *n*-butanol as a protic solvent and in nitrobenzene as an aprotic dipolar solvent. By using *meta*- and *para*-substituted benzoic acids, we attempted to correlate rates of their conversion to the corresponding 2-hydroxyethyl esters in both solvents with the structure and strength of the acids by Hammett and Brønsted equations, respectively.

EXPERIMENTAL

Compounds Used

Benzoic acid (Lachema, Brno) was of 99.9% purity, as found by acid number determination, m.p. 122°C (ref.⁴ records m.p. 122.4°C). 2,4-Dichlorophenoxyacetic acid was prepared by repeated crystallisation of the sodium salt (Spolek pro chemickou a hutní výrobu, Ústí n/L.) from water with the addition of activated carbon, followed by acidification with dilute hydrochloric acid to pH 2. The precipitated acid was washed with water until negative test on chloride ions; the COOH content: 100.3%; m.p. 138–139°C (ref.⁵ records m.p. 138°C). Substituted benzoic acids were commercial products (Fluka A.G., Buchs). *p*-Toluylic acid, purum, was recrystallised from ethanol; the COOH content: 99.8%, m.p. 180°C (ref.⁴ records m.p. 179–180°C). *p*-Chlorobenzoic acid, *puriss.*, the COOH content: 99.9%; m.p. 241–242°C (ref.⁴ records m.p. 241.5°C). *p*-Nitrobenzoic acid, *puriss.*, the COOH content: 99.8%; m.p. 241°C (ref.⁴ records m.p. 242°C). *m*-Nitrobenzoic acid, *puriss.*, the COOH content: 99.8%, m.p. 140.0–140.5°C (ref.⁴ records m.p. 140 to 141°C). *m*-Bromobenzoic acid, *puriss.*, the COOH content: 99.8%, m.p. 155°C (ref.⁴ records m.p. 155°C). *p*-Methoxybenzoic acid, *puriss.*, the COOH content: 100.1%, m.p. 184–185°C (ref.⁴ records m.p. 185°C). Pyridine (Fluka A.G.) of reagent grade purity was dried over ground potassium hydroxide for several days, then over metallic sodium and rectified under nitrogen; the fraction used had b.p. 114°C/754 Torr (b.p.⁴ 115.5°C/760 Torr), n_D^{20} 1.5102 (reported⁴ 1.5095). Tri-*n*-butylamine (Fluka A.G.) of reagent grade purity was purified in a similar fashion as was pyridine; b.p. 89°C/10 Torr (ref.⁴ records b.p. 216–217°C), n_D^{20} 1.4300 (ref.⁶ records n_D^{20} 1.4297). *N,N*-Dimethylcyclohexylamine was prepared by distillation of the crude base (Výzkumný ústav organických syntéz, Rybitví) through a 20 TP column; by treating the fraction boiling at 156–161°C/745 Torr with *p*-toluenesulphochloride it was freed of the secondary amine⁷ and a distillation over sodium through a 20 TP column under nitrogen afforded a fraction with b.p. 159.1°C/754 Torr (recorded⁸ b.p. 160–161°C), n_D^{20} 1.4535. The tertiary amines were stored under nitrogen. *n*-Butanol (Spolana, Neratovice) of reagent grade purity was distilled through a column filled with activated 4A molecular sieve and the fraction boiling at 116.4°C/733 Torr (ref.⁴ records b.p. 117.5°C/760 Torr) was collected; n_D^{20} 1.3996 (recorded⁴ n_D^{20} 1.3992). Nitrobenzene (Lachema, Brno), pure, was dried over ground potassium hydroxide for several

days and distilled through a 20 TP column; the fraction collected had b.p. 100°C/140 Torr (ref.⁴ records b.p. 210·8°C/760 Torr), n_D^{20} 1·5498 (ref.⁴ gives n_D^{20} 1·5562). Ethylene oxide (Montecatini-Edison, Italy); 99%, by gas chromatography, contained acetylene \leq 0·05%, acetaldehyde $<$ 0·05% and other impurities (H_2O and CO_2) in amounts less than 1 per cent.

Analytical Methods

The solubility and concentration of ethylene oxide in the solvents and reaction mixtures were for given reaction conditions determined by manometrical measurement of the Henry-Dalton constant⁹ with an apparatus described in the paragraph dealing with kinetic measurements and by the calculation according to the Henry-Dalton law. The same apparatus was also used to measure manometrically the consumption of ethylene oxide during the reaction. The measurements were accurate within $\pm 1\%$.

Concentration of acetaldehyde in ethylene oxide was determined by gas chromatographic analysis¹⁰ with a Chrom I instrument at 23°C; silicone elastomer (30%) on Chromosorb W was used as a stationary phase, with hydrogen as a carrier gas (40 ml/min).

Concentration of carbon dioxide in ethylene oxide was determined by gas chromatography with a chromatograph equipped with a thermal conductivity detector (Vývojové dílny ČSAV, Prague) using 5% poly(ethylene glycol) (m.wt. 1000) on ground unglazed tiles as a stationary phase and argon as a carrier gas (temperature 23°C).

Concentration of a carboxylic acid in the reaction mixture. The sample (1–2 ml) was diluted with 5 ml of ethanol, mixed with 3 ml of pyridine in an atmosphere of nitrogen and titrated with 1M-KOH on phenolphthalein as indicator.

Concentration of tertiary amines in reaction mixtures was determined by the procedure reported earlier¹.

Selectivity of the reaction of individual carboxylic acids with ethylene oxide was checked by titrimetric determination of the unreacted acid in samples of the reaction mixture and by comparing the acid consumption with the amount of the ethylene oxide consumed. Final reaction mixtures were analysed similarly at the end of each kinetic run. In addition to this, the absence of side products was checked by gas chromatographic analyses of the samples of final reaction mixtures with a Pye-Argon chromatograph (20% poly(ethylene glycol) on Chromosorb W, the argon flow rate 60 ml/min, the oven temperature being 160–190°C).

Apparatus

The amounts of absorbed ethylene oxide or of the ethylene oxide consumed during the reaction were measured manometrically with a glass static apparatus¹¹. The apparatus, which was connected to a cylinder containing ethylene oxide (1·2–1·5 at), consisted of ethylene oxide reservoirs (3 l-, 2 l-, and 1 l-round bottom flasks) and of the reaction flask (500 ml) that was equipped with a reflux condenser, a narrow glass tube reaching to the bottom of the flask and serving for removal of samples of the reaction mixture in the course of the reaction, and a thermostated jacket; the reaction flask was placed on a laboratory shaker with a swing length of 7·5 cm and 40–120 swings per min. The pressure of ethylene oxide in the reservoir part of the apparatus and in the reaction flask were read with open manometers; the pressure in the reaction flask was always lower than that in the reservoirs and was kept at a constant value.

Kinetic Measurements

The known amounts of the carboxylic acid (10–30 g), tertiary amine as a catalyst, and n-butanol or nitrobenzene (200–250 ml) as a solvent were introduced into the reaction flask which was then evacuated to 30 Torr and filled with nitrogen. The reaction mixture containing the carboxylic acid in 0.25–3.45 mol kg⁻¹ concentration was warmed up to the reaction temperature in 20 min, the pressure in the flask was reduced to 250 Torr and after stabilization of the reaction temperature (70–90 ± 0.1°C) the flask was connected to the ethylene oxide reservoir. The amount of the ethylene oxide absorbed in the homogeneous reaction mixture at a given temperature was calculated from the known volume of that reservoir part of the apparatus connected to the reaction flask and from the pressure decrease. In the initial phase, the reaction mixture was saturated with ethylene oxide which reacted with the amine and the acid to give the catalytic complex; this was completed in 5 min and then the pressure in the reaction system was stabilized at a constant value that was kept during the whole kinetic run. Kinetic measurements were carried out at pressures ranging from 600 to 1070 Torr, which corresponds to the 0.4–1.1 mol kg⁻¹ ethylene oxide concentration in the reaction mixture. Parallel tests showed that the amount of ethylene oxide consumed by the reaction with the acid and with the amine in first 5 min is negligible, and the reaction time and the consumption of ethylene oxide during the reaction were calculated from this very moment. By an independent measurement it was also proved that the rate by which ethylene oxide dissolves in the reaction mixture is under the reaction conditions employed several times faster than the rate of its consumption by the reaction, and at 40–120 swings per min it was also independent of the intensity of mixing. The reaction rate did not therefore depend on the mass transfer on the liquid–gas phase boundary and kinetic measurements were therefore performed in the kinetic region. By determining the “free carboxyl” concentration in the reaction mixture at varying degrees of conversions of the acids it was found that at the amine concentrations equal to or higher than 0.02 mol kg⁻¹ the acid consumption agrees within experimental error (±1%) with equimolar amounts of the ethylene oxide consumed; also gas chromatographic analysis showed that under these conditions the corresponding 2-hydroxyethyl ester is formed as a sole product. Kinetic measurements were therefore carried out at 0.02–0.15 mol kg⁻¹ concentration of the amines; hence, the time dependence of the consumption of carboxylic acids could be readily determined by following manometrically ethylene oxide consumption; the increase of its consumption with time corresponded to the time-concentration dependence of 2-hydroxyethyl ester formation. Preliminary experiments showed that the total disappearance of the carboxyl anion from the reaction mixture is accompanied by an immediate increase in basicity and also by immediate formation of side products. Kinetic measurements were therefore performed to 95% conversion of carboxylic acids. At the above-mentioned concentrations of the reactants the reaction was accompanied only by 3–5% change of the volume of the reaction mixture; this change was not therefore considered in deriving kinetic equations. Deviations of experimental points from regression lines that are characterized by the correlation coefficient (*r*) are given by the standard deviations (*s*). All concentration data are expressed in mol per 1 kg of the reaction mixture.

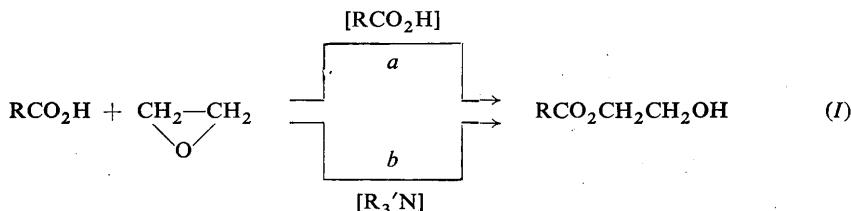
Isolation of Products

The reaction mixture was freed of the solvent by vacuum distillation, in the case of nitrobenzene by steam-distillation; the distillation residue was dissolved in dichloromethane, the solution washed successively with hydrochloric acid (1 : 1), 20% sodium hydrogen carbonate solution, and water until it was neutral, and then it was dried over anhydrous magnesium sulphate. The pure esters were obtained in 90–95% yields by vacuum distillation or crystallisation. 2-Hydroxyethyl benzoate: b.p. 146–148°C/9 Torr (recorded¹² b.p. 160–162°C/14 Torr); m.p. 40.5–41.5°C

(recorded¹³ m.p. 37–38°C). For C₉H₁₀O₃ (166.2) calculated: 65.05% C, 6.07% H; found: 64.70% C, 6.16% H. 2-Hydroxyethyl 2,4-dichlorophenoxyacetate: b.p. 155–157°C/0.5 Torr (recorded¹⁴ b.p. 177–180°C/1.5 Torr). For C₁₀H₁₀O₄Cl₂ (265.1) calculated: 45.30% C, 3.80% H, 26.74% Cl; found: 45.01% C, 3.89% H, 26.8% Cl. 2-Hydroxyethyl 4-hydroxybenzoate. In the presence of tertiary amine as a catalyst, the 4-hydroxy group does not react with ethylene oxide and the only product formed is the corresponding 2-hydroxyethyl ester. The crude ester was recrystallised from n-butanol; m.p. 137–140°C (recorded¹⁵ m.p. 136–140°C). Melting points are uncorrected.

RESULTS AND DISCUSSION

The reaction of benzoic acid with ethylene oxide in n-butanol as a solvent and in the presence of N,N-dimethylcyclohexylamine as a catalyst, which was followed to 92% conversion of the acid, is highly selective, giving the 2-hydroxyethyl ester as a sole product. The time dependence of the overall consumption of ethylene oxide and of the simultaneous formation of the ester (Fig. 1) cannot be, however, described for the whole region of the acid conversion by kinetics of simple order. The reaction proceeds thus via complex mechanism and it was assumed that benzoic acid, similarly as acetic acid¹, undergoes two parallel, the acid-catalysed (*a*) and tertiary amine-catalysed (*b*) reactions, as depicted in Eq. (1). The time dependence of the benzoic acid conversion could be then described by the kinetic equation (1) where A denotes



benzoic acid, B ethylene oxide, C the tertiary amine (N,N-dimethylcyclohexylamine), k_{11} is the rate constant of the acid catalysed reaction (*Ia*), and k_{12} is the rate constant of the tert-amine-catalysed reaction (*Ib*) in protic solvent (n-butanol).

$$r_1 = -d[A]/dt = -d[B]/dt = r_{11} + r_{12} = k_{11}[A][B] + k_{12}[B][C]. \quad (1)$$

The rate constants were determined from the time dependence of the ethylene oxide consumption by the method of initial reaction rates. This method is sufficiently accurate, since in this case the ethylene oxide consumption is linearly dependent on time up to 50% acid conversion (Fig. 1). At the experimental arrangement used ethylene oxide concentration in the reaction mixture was kept constant during the reaction and Eq. (1) can be therefore rewritten for the initial rate r_1^0 to the form (2). This form is suitable for graphical determination of the reaction order in benzoic acid, ethylene

oxide, and the tertiary amine. The linear dependence of r_1^0 on the amine concentration (Fig. 2) shows that the amine-catalysed reaction

$$\begin{aligned} r_1^0 &= -d[A]_0/dt = -d[B]/dt = r_{11}^0 + r_{12}^0 = k_{11}[A]_0[B] + k_{12}[B][C] = \\ &= k'_{11} + k'_{12}[C] \end{aligned} \quad (2)$$

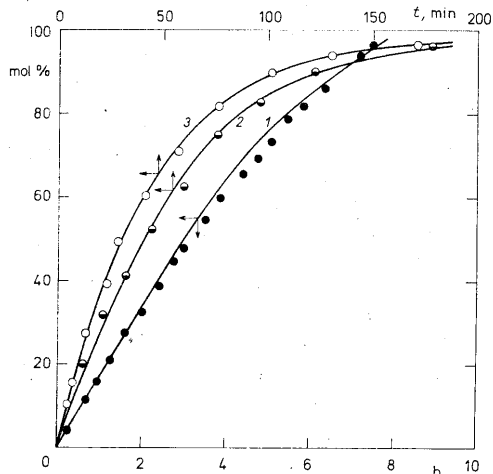


FIG. 1

Time Dependence of Conversion of Benzoic Acid 1 and 2,4-Dichlorophenoxyacetic Acid 2 in *n*-Butanol and of Benzoic Acid in Nitrobenzene 3 to 2-Hydroxyethyl Esters by Reaction with Ethylene Oxide in the Presence of Pyridine

1 $[C_6H_5CO_2H]_0 = 2.302 \text{ mol kg}^{-1}$, $[C_2H_4O] = 0.782 \text{ mol kg}^{-1}$, $[C_5H_5N] = 0.056 \text{ mol kg}^{-1}$, points denote experimental data and the curve represents the calculated time-concentration dependence; 2 $[2,4-Cl_2C_6H_3.OCH_2CO_2H]_0 = 0.8477 \text{ mol kg}^{-1}$, $[C_2H_4O] = 0.782 \text{ mol kg}^{-1}$, $[C_5H_5N] = 0.0592 \text{ mol kg}^{-1}$, points denote experimental data and the curve represents the calculated time-concentration dependence; 3 $[C_6H_5CO_2H]_0 = 2.179 \text{ mol kg}^{-1}$, $[C_2H_4O] = 0.685 \text{ mol kg}^{-1}$, $[C_5H_5N] = 0.0887 \text{ mol kg}^{-1}$; temperature $85 \pm 0.1^\circ\text{C}$.

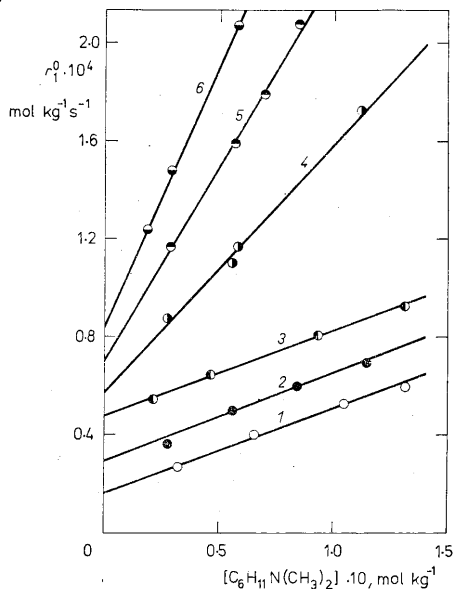


FIG. 2

Dependence of the Initial Rate r_1^0 of the Reaction of Ethylene Oxide with Benzoic Acid in *n*-Butanol on the Initial Acid Concentration and *N,N*-Dimethylcyclohexylamine Concentration and on Temperature

1 $[C_6H_5CO_2H]_0 = 1.26 \text{ mol kg}^{-1}$, $[C_2H_4O] = 1.275 \text{ mol kg}^{-1}$, temperature $70 \pm 0.1^\circ\text{C}$; 2 $[C_6H_5CO_2H]_0 = 2.18 \text{ mol kg}^{-1}$, $[C_2H_4O] = 1.275 \text{ mol kg}^{-1}$, temperature $70 \pm 0.1^\circ\text{C}$; 3 $[C_6H_5CO_2H]_0 = 3.45 \text{ mol kg}^{-1}$, $[C_2H_4O] = 1.275 \text{ mol kg}^{-1}$, temperature $70 \pm 0.1^\circ\text{C}$; 4 $[C_6H_5CO_2H]_0 = 2.18 \text{ mol kg}^{-1}$, $[C_2H_4O] = 0.782 \text{ mol kg}^{-1}$, temperature $85 \pm 0.1^\circ\text{C}$; 5 $[C_6H_5CO_2H]_0 = 2.18 \text{ mol kg}^{-1}$, $[C_2H_4O] = 0.754 \text{ mol kg}^{-1}$, temperature $90 \pm 0.1^\circ\text{C}$; 6 $[C_6H_5CO_2H]_0 = 2.18 \text{ mol kg}^{-1}$, $[C_2H_4O] = 0.630 \text{ mol kg}^{-1}$, temperature $95 \pm 0.1^\circ\text{C}$.

(*Ib*) proceeding at the rate r_{12} (Eq. (1)) is first-order in the amine catalyst. The parallel lines 1–3 in Fig. 2 demonstrate that the same change in concentration of the catalyst results in the same change of r_1^0 , irrespective of the initial acid concentration. Similarly to acetic acid¹ ($\text{p}K_a$ 4.76) (ref.¹⁶) it can be deduced from this fact that the molecule of benzoic acid, with the similar value of dissociation constant ($\text{p}K_a$ 4.21), does not participate in the rate-determining step of the parallel, amine-catalysed reaction (*Ib*).

Initial reaction rates (r_{11}^0) of the parallel reaction (*Ia*) catalysed by the undissociated acid, which are expressed by the values of r_1^0 at the zero concentration of the tertiary amine (Fig. 2), increase linearly with increasing initial concentration of the acid (Fig. 3). The acid-catalysed parallel reaction (*Ia*), that proceeds at the rate r_{11} (Eq. (1)), is therefore first-order in benzoic acid. As the initial reaction rate r_1^0 depends linearly on the ethylene oxide concentration (Fig. 4, line 1), both reactions (*Ia*) and (*Ib*) are of the first-order in ethylene oxide. The zero order of the reaction (*Ib*) and the first order of the parallel reaction (*Ia*) in benzoic acid explain why in *n*-butanol and in the presence of a tertiary amine the time dependence of the overall consumption of ethylene oxide and that of formation of the ester did not obey a simple rate law for the whole region of benzoic acid conversions.

Final verification of the validity of these relationships was made by converting Eq. (2) into Eq. (3) and by comparing

$$[A] = \{[(k_{11}[A]_0 [B] + k_{12}[B] [C]) \exp(-k_{11}t[B])] - k_{12}[B] [C]\} / k_{11}[B] \quad (3)$$

the calculated time-concentration dependence of benzoic acid conversion with the experimental values (Fig. 1). The agreement obtained between these data (the standard deviation $s = 0.021$, maximum relative error = 5.6%) confirmed that the kinetic equation (1) describes with acceptable accuracy the esterification of benzoic acid to 2-hydroxyethyl ester in *n*-butanol and in the presence of a tertiary amine at least to 92% conversion. The values of activation energies and of second-order rate constants k_{11} and k_{12} of both parallel reactions (*Ia*) and (*Ib*), which were calculated from the linear dependence of $\log r_1^0$ on $1/T$, are presented in Table I.

For ascertaining the effect of the carboxylic acid strength on the course of the reaction we studied kinetics of the reaction of ethylene oxide with 2,4-dichlorophenoxyacetic acid in *n*-butanol and in the presence of tertiary amines as catalysts up to 85% conversion of the acid (Fig. 1). Similarly as in the case of benzoic acid, also this reaction (Eq. (1); $R = 2,4\text{-Cl}_2\text{C}_6\text{H}_3\text{OCH}_2\text{-}$, $R_3\text{N} = \text{pyridine or tri-}n\text{-butylamine}$) was highly selective, giving 2-hydroxyethyl 2,4-dichlorophenoxyacetate as a sole product. By contrast to benzoic acid, the time dependence of consumption of the relatively stronger 2,4-dichlorophenoxyacetic acid ($\text{p}K_a$ 3.18) shows first-order behaviour throughout the whole region of conversions (Fig. 5). The reaction is also first-order

in ethylene oxide (Fig. 4, line 2). As it is obvious from the dependence of the pseudo-first order rate constant k_2 on the catalyst concentration (Fig. 6), also in this case the acid is converted to the corresponding ester by both the tertiary amine-catalysed reaction (*Ib*) and by the parallel, acid-catalysed reaction (*Ia*); the rate constant k_{21} of the latter can be read from the intercepts. The observed overall first order of the reaction with respect to the acid may be, however, valid only providing that both parallel reactions (*Ia*) and (*Ib*) are contrary to the relatively weaker benzoic acid — of the first order in 2,4-dichlorophenoxyacetic acid. The time dependence of its overall conversion can be then described by the kinetic equation (4), where A is 2,4-dichlorophenoxyacetic acid, C is a tertiary amine (pyridine), k_{21} is the rate constant of the acid-catalysed reaction (*Ia*), and

$$r_2 = -d[A]/dt = -d[B]/dt = r_{21} + r_{22} = k_{21}[A][B] + k_{22}[A][B][C] \quad (4)$$

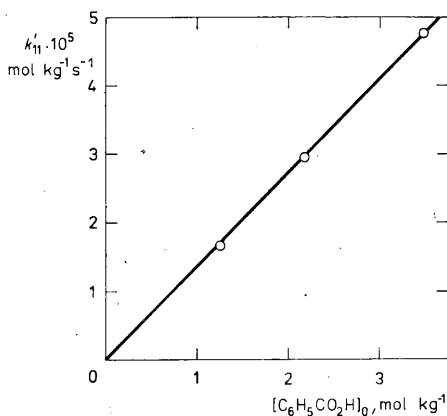


FIG. 3

Dependence of the Rate Constant k'_{11} on the Initial Acid Concentration in the Reaction of Benzoic Acid with Ethylene Oxide in *n*-Butanol and in the Presence of *N,N*-Dimethylcyclohexylamine

$[C_2H_4O] = 1.26 \text{ mol kg}^{-1}$, temperature $70 \pm 0.1^\circ\text{C}$.

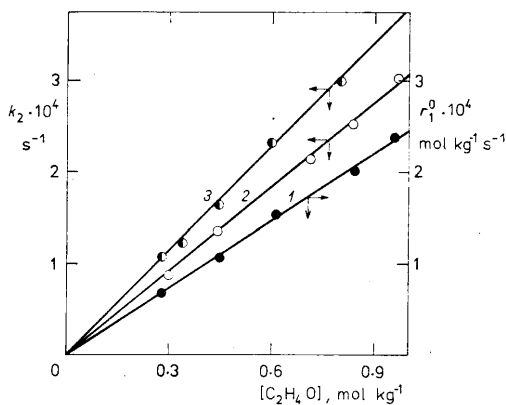


FIG. 4

The Dependence on Ethylene Oxide Concentration of the Initial Rate r_1^0 of the Reaction of Ethylene Oxide with Benzoic Acid in *n*-Butanol 1 and of the Pseudo-first Order Rate Constants k_2 for the Reaction of Ethylene Oxide with 2,4-Dichlorophenoxyacetic Acid in *n*-Butanol 2 and with Benzoic Acid in Nitrobenzene 3 in the Presence of Tertiary Amines

1 $[C_6H_5CO_2H]_0 = 2.18 \text{ mol kg}^{-1}$, $[C_6H_{11}N(CH_3)_2] = 0.113 \text{ mol kg}^{-1}$, $80 \pm 0.1^\circ\text{C}$; 2 $[2,4\text{-Cl}_2C_6H_3OCH_2CO_2H]_0 = 0.896 \text{ mol kg}^{-1}$, $[C_5H_5N] = 0.1163 \text{ mol kg}^{-1}$, $80 \pm 0.1^\circ\text{C}$; 3 $[C_6H_5CO_2H]_0 = 2.18 \text{ mol kg}^{-1}$, $[C_5H_5N] = 0.0573 \text{ mol kg}^{-1}$, $85 \pm 0.1^\circ\text{C}$.

TABLE I
 Activation Energies E and Preexponential Factors k_{ij}^0 of Parallel, Acid- and Tertiary Amine-Catalysed Reactions of Benzoic Acid and 2,4-Dichlorophenoxybenzoic Acid with Ethylene Oxide in *n*-Butanol

Reaction	E kcal mol ⁻¹	r_E	k_{ij}^0
$C_6H_5CO_2H + C_2H_4O^a$	17.8 ± 0.9	0.9974	$k_{11}^0 = 2.3 \cdot 10^6 \text{ kg mol}^{-1} \text{ s}^{-1}$
$C_6H_5CO_2H + C_2H_4O^b$	24.8 ± 0.9	0.9988	$k_{12}^0 = 1.7 \cdot 10^{12} \text{ kg mol}^{-1} \text{ s}^{-1}$
$2,4\text{-Cl}_2C_6H_3OCH_2CO_2H + C_2H_4O^a$	14.1 ± 1.1	0.9971	$k_{21}^0 = 1.1 \cdot 10^5 \text{ kg mol}^{-1} \text{ s}^{-1}$
$2,4\text{-Cl}_2C_6H_3OCH_2CO_2H + C_2H_4O^c$	25.5 ± 0.8	0.9995	$k_{22}^0 = 6.0 \cdot 10^{12} \text{ kg}^2 \text{ mol}^{-2} \text{ s}^{-1}$

^a The acid-catalysed reaction; ^b *N,N*-dimethylcyclohexylamine-catalysed reaction; ^c pyridine-catalysed reaction.

k_{22} is the rate constant of the tertiary amine-catalysed parallel reaction (Ib). At a constant concentration of the amine and ethylene oxide during the course of the reaction, Eq. (4) can be rewritten to Eq. (5). This relation has been

$$r_2 = -d[A]/dt = -d[B]/dt = (k'_{21} + k'_{22})[A] = k_2[A] \quad (5)$$

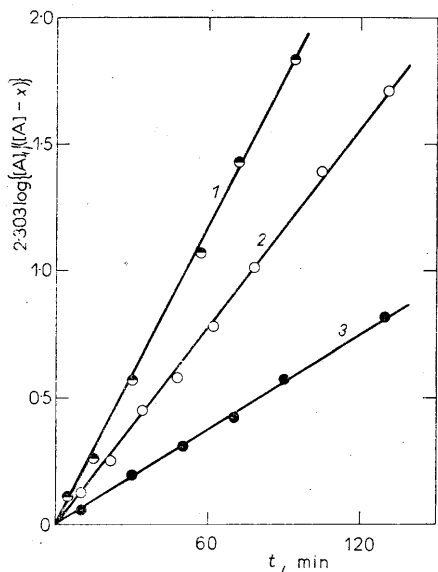


FIG. 5

Reaction of Ethylene Oxide with 2,4-Dichlorophenoxyacetic Acid in *n*-Butanol Catalysed by Pyridine 1 and Tri-*n*-butylamine 2 and with Benzoic Acid in Nitrobenzene in the Presence of Pyridine 3

$[2,4\text{-Cl}_2\text{C}_6\text{H}_3\text{OCH}_2\text{CO}_2\text{H}]_0 = 2.18 \text{ mol} \cdot \text{kg}^{-1}$; $[\text{C}_6\text{H}_5\text{CO}_2\text{H}]_0 = 0.517 \text{ mol} \cdot \text{kg}^{-1}$; temperature $85 \pm 0.1^\circ\text{C}$; 1 $[\text{C}_5\text{H}_5\text{N}] = 0.0581 \text{ mol} \cdot \text{kg}^{-1}$, $[\text{C}_2\text{H}_4\text{O}] = 0.782 \text{ mol} \cdot \text{kg}^{-1}$; 2 $[(n\text{-C}_4\text{H}_9)_3\text{N}] = 0.0581 \text{ mol} \cdot \text{kg}^{-1}$, $[\text{C}_2\text{H}_4\text{O}] = 0.782 \text{ mol} \cdot \text{kg}^{-1}$; 3 $[\text{C}_5\text{H}_5\text{N}] = 0.0735 \text{ mol} \cdot \text{kg}^{-1}$, $[\text{C}_2\text{H}_4\text{O}] = 0.685 \text{ mol} \cdot \text{kg}^{-1}$.

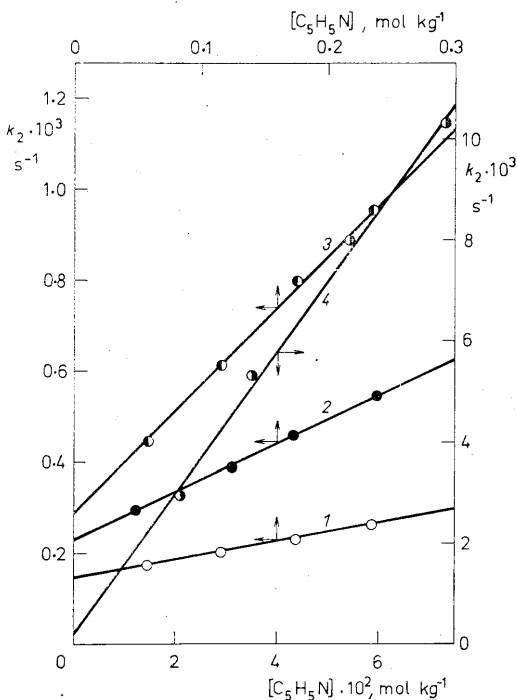


FIG. 6

Dependence of the Pseudo-first Order Rate Constants k_2 for the Reaction of 2,4-Dichlorophenoxyacetic Acid 1, 2, 3 with Ethylene Oxide in *n*-Butanol on Temperature and Pyridine Concentration and for the Reaction of Benzoic Acid 4 in Nitrobenzene on Pyridine Concentration

$[2,4\text{-Cl}_2\text{C}_6\text{H}_3\text{OCH}_2\text{CO}_2\text{H}]_0 = 0.889 \text{ mol} \cdot \text{kg}^{-1}$, $[\text{C}_6\text{H}_5\text{CO}_2\text{H}]_0 = 0.517 \text{ mol} \cdot \text{kg}^{-1}$; 1 $[\text{C}_2\text{H}_4\text{O}] = 1.26 \text{ mol} \cdot \text{kg}^{-1}$, $70 \pm 0.1^\circ\text{C}$; 2 $[\text{C}_2\text{H}_4\text{O}] = 0.782 \text{ mol} \cdot \text{kg}^{-1}$, $85 \pm 0.1^\circ\text{C}$; 3 $[\text{C}_2\text{H}_4\text{O}] = 0.630 \text{ mol} \cdot \text{kg}^{-1}$, $95 \pm 0.1^\circ\text{C}$; 4 $[\text{C}_2\text{H}_4\text{O}] = 0.685 \text{ mol} \cdot \text{kg}^{-1}$, $85 \pm 0.1^\circ\text{C}$.

used to derive the above-mentioned kinetic parameters of the reaction. To confirm their validity, Eq. (5) was converted to Eq. (6)

$$[A] = [A]_0 \exp(k'_{21} + k'_{22})t, \quad (6)$$

where $k'_{21} = k_{21}[B]$ and $k'_{22} = k_{22}[B][C]$. The calculated time-concentration dependence of the 2,4-dichlorophenoxyacetic acid conversion (Fig. 1, curve 2) was compared with experimental values (Fig. 1, points on curve 2). The agreement between experimental and calculated data ($s = 0.012$) shows that Eq. (4) describes very well the time dependence of the conversion of 2,4-dichlorophenoxyacetic acid to the 2-hydroxyethyl ester by its reaction with ethylene oxide in *n*-butanol and in the presence of tertiary amines at least to 85% conversion. The reaction rate is not too dependent on the basicity of the catalyst. As follows from Fig. 5, the rate constant k_2 (Eq. (5)) of the reaction of 2,4-dichlorophenoxyacetic acid in the presence of pyridine (pK_a 5.17) (ref.¹⁷) is about 1.5 times higher ($k_2 = 3.25 \cdot 10^{-4} \text{ s}^{-1}$) than the k_2 constant for the reaction carried out in the presence of the significantly more basic tri-*n*-butylamine (pK_a 10.89) (ref.¹⁸) ($k_2 = 2.17 \cdot 10^{-4} \text{ s}^{-1}$), under otherwise identical reaction conditions. The fact that the parallel, tertiary amine-catalysed reaction is in this case also first-order in the acid cannot be rationalized by the mechanism proposed earlier for the conversion of weak and strong carboxylic acids in protic solvents and in the presence of tertiary amines^{1,9}.

The activation energies, E , calculated from the Arrhenius equation and the values of the preexponential factors k_{21}^0 and k_{22}^0 for both parallel reactions (Eq. (4)) are presented in Table I. There is remarkable similarity between E , k_{11}^0 and k_{21}^0 for both benzoic acid and 2,4-dichlorophenoxyacetic acid-catalysed parallel reactions (*Ia*) (the first terms on the right hand side of Eqs (1) and (4)), as well as E , k_{12}^0 and k_{22}^0 for both tertiary amine-catalysed parallel reactions (*Ib*) (the second terms on the right hand side of Eqs (1) and (4)). Contingent effect that could be exerted by different basicity of *N,N*-dimethylcyclohexylamine relative to pyridine (both used as catalysts) is less than the error in determination of the activation parameters.

The linear dependence of the initial reaction rate r_0^1 of the reaction of *meta*- and *para*-substituted benzoic acids with ethylene oxide in *n*-butanol on the concentration of the catalyst pyridine showed that the extent to which the acid-catalysed parallel reaction (*Ia*) contributes to the overall formation of the 2-hydroxyethyl esters increases with increasing acid strength of the acid. The reaction (*Ia*) is first-order both in the acid and in ethylene oxide. The values of the second-order rate constants k_{11} of the reaction (*Ia*) catalysed by the corresponding acid and of the constants k_{12} of the parallel reaction (*Ib*) catalysed by the amine (Eq. (1); A stands for substituted benzoic acid and C stands for pyridine), which were determined from this relation, are given in Table II. Correlation of $\log k_{11}$ by Brønsted equation gave linear dependence

TABLE II

Values of the Rate Constants k_{11} and k_{12} for the Reaction of Substituted Benzoic Acids ($X-C_6H_4CO_2H$) with Ethylene Oxide in the Presence of Pyridine in *n*-Butanol and of the Constants k_{21} and k_{22} for the Reaction in Nitrobenzene
 $[X-C_6H_4CO_2H]_0 = 0.517 \text{ mol kg}^{-1}$; $[B] = 0.685 \text{ mol kg}^{-1}$ [C_5H_5N] = $0.026-0.14 \text{ mol kg}^{-1}$; temperature $85 \pm 0.1^\circ C$.

No	Carboxylic acid	pK_a^a	Reaction in <i>n</i> -butanol		Reaction in nitrobenzene	
			$k_{11} \cdot 10^3$ $\text{kg mol}^{-1} \text{ s}^{-1}$	$k_{12} \cdot 10^3$ $\text{kg mol}^{-1} \text{ s}^{-1}$	$k_{21} \cdot 10^6$ $\text{kg mol}^{-1} \text{ s}^{-1}$	$k_{22} \cdot 10^3$ $\text{kg}^2 \text{ mol}^{-2} \text{ s}^{-1}$
1	<i>p</i> -H ₃ CC ₆ H ₄ CO ₂ H	4.34	0.031 ± 0.000	0.563 ± 0.007	—	—
2	C ₆ H ₅ CO ₂ H	4.21	0.039 ± 0.001	0.602 ± 0.008	0.066 ± 0.017	0.035 ± 0.001
3	<i>p</i> -ClC ₆ H ₄ CO ₂ H	3.99	0.054 ± 0.001	0.677 ± 0.012	0.105 ± 0.026	0.047 ± 0.002
4	<i>m</i> -BrC ₆ H ₄ CO ₂ H	3.81	0.067 ± 0.001	— ^b	0.178 ± 0.039	0.059 ± 0.001
5	<i>m</i> -O ₂ NC ₆ H ₄ CO ₂ H	3.45	—	—	0.308 ± 0.071	0.092 ± 0.004
6	<i>p</i> -O ₂ NC ₆ H ₄ CO ₂ H	3.44	0.119 ± 0.002	— ^b	0.394 ± 0.083	0.101 ± 0.003

^a Ref.¹⁹; ^b values of the constant k_{12} for the reaction of *p*-nitrobenzoic acid ($0.997 \cdot 10^{-3} \text{ kg mol}^{-1} \text{ s}^{-1}$) and *m*-bromobenzoic acid ($0.748 \cdot 10^{-3} \text{ kg mol}^{-1} \text{ s}^{-1}$) calculated also from Eq. (I) are not included in the table because of the nonlinear Brønsted plot in the region < 3.99 to $> 3.18 \text{ p}K_a$.

for all the acids studied for the acid-catalysed reaction (*Ia*) (Fig. 7). The Brønsted constant α_1 had a value of 0.62 ($r = 0.9997$; $s = 0.008$). In this case the same value had also the Hammett reaction constant ρ_1 . The value of the constant G_1 of Brønsted equation equaled to $1.5 \cdot 10^{-2}$ ($s = 0.02 \cdot 10^{-2}$). On the other hand, nonlinear Brønsted plot, and implicitly also nonlinear Hammett plot, resulting from the dependence of $\log k_{12}$ on pK_a for the amine-catalysed parallel reaction (*Ib*) established that, under the reaction conditions employed, kinetic equations (1) and (4) describe precisely the course of the reactions of ethylene oxide with carboxylic acids of $pK_a \geq 3.99$ and ≤ 3.2 , respectively. The Brønsted constant α_2 and the Hammett reaction constant ρ_2 for the amine-catalysed reaction (*Ib*) in protic medium, which have a value of 0.34 ($r = 0.9999$), are valid only for the acids with $pK_a \geq 4.34$ and ≥ 3.99 . The reaction of these acids is first-order in ethylene oxide and in tertiary amine. From the nonlinear Brønsted plot between pK_a 3.99 and 3.2 it can be concluded that in this region there is change in the nature of the rate-determining step of the reaction. In addition to the mechanism depicted by equation (III) (Scheme 1) (ref.¹), with increasing acid strength of the acid in this region a mechanism is operative involving the participation of the acid in the rate-determining step of the amine-catalysed reaction (*Ib*) (Scheme 1, equation (V)). Based on these facts, the Brønsted plot for both parallel reactions (*Ia*) and (*Ib*) of individual acids could have been with the same justification obtained from the respective rate constants k_{21} and k_{22} of Eq. (4). However, even the strongest acid used, *p*-nitrobenzoic acid, does not react in protic medium by the amine-catalysed reaction (*Ib*) which would be of the first order. This indicates

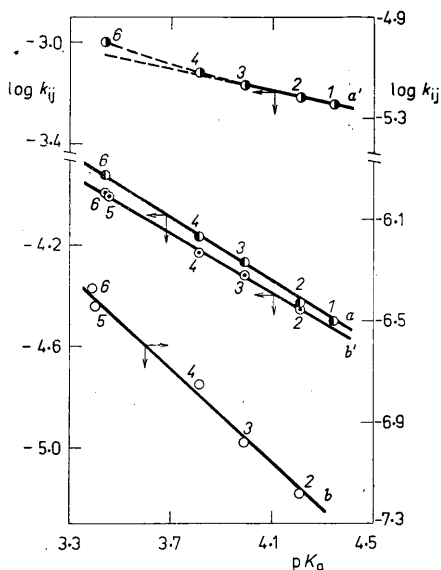
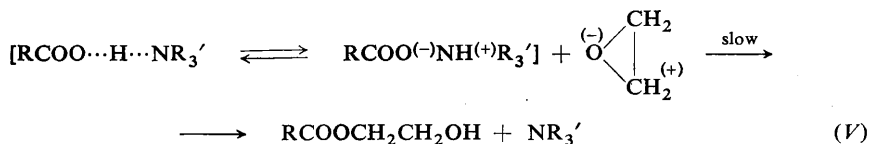
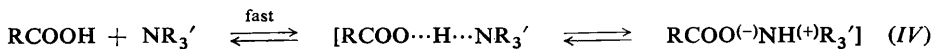
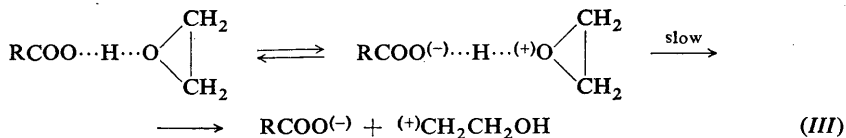
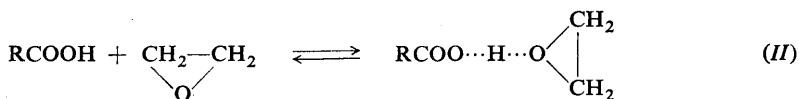


FIG. 7
Brønsted Plot of Logarithms of the Rate Constants k_{11} , k_{12} , k_{21} , and k_{22} versus pK_a of *meta*- and *para*-Substituted Benzoic Acids (for Compounds 1—6 see Table II) for Their Reactions with Ethylene Oxide Catalysed by the Acid (*a*), and Pyridine (*a'*) in *n*-Butanol and for the Reaction Catalysed by the Acid (*b*) and Pyridine (*b'*) in Nitrobenzene

that here also the mechanism assuming the absence of the acid in the rate-determining step of the amine-catalysed reaction (*Ib*) (Scheme 1, equation (III)) plays a certain role. On the other hand, very good agreement between experimental and calculated values for the overall time-concentration dependence for 2,4-dichlorophenoxyacetic acid (pK_a 3.18) confirms the validity of Eq. (4) for the whole region of conversions of this acid and thus also of other carboxylic acids with the same or higher pK_a value. This dependence could not be, however, included into the Brønsted plot owing to different dimension of k_{22} . The amine-catalysed reaction of the carboxylic acids with pK_a in the above mentioned region is then first-order in the acid, ethylene oxide, and tertiary amine. The above kinetic relations may change under different reaction conditions. Thus, for example, terephthalic acid (pK_a^1 3.54, pK_a^2 4.46) (ref.²⁰) reacts with ethylene oxide according to the zero-order kinetics in the acid, due to sparse solubility of the acid in protic solvent, and the first-order kinetics in both ethylene oxide and the amine⁹.

The only product formed by the reaction of benzoic acid with ethylene oxide in nitrobenzene, a typical aprotic dipolar solvent, and in the presence of tertiary amines as catalysts is 2-hydroxyethyl benzoate. In this medium the reaction proceeds much faster than in protic solvents (Fig. 4), in agreement with the known rate-accelerating effect of aprotic dipolar solvents in S_N2 reactions²¹. The overall formation of the ester is first-order in the acid (Fig. 5), ethylene oxide (Fig. 4), and tertiary amine (Fig. 6). The straight line representing the linear dependence of the rate constant on the tertiary amine concentration does not pass through the origin (Fig. 6). As the overall formation of the ester is of the first order in the acid, time dependence of its con-



SCHEME 1

version can be described by Eq. (4) (A denotes benzoic acid). The acid-catalysed reaction (Ia) of benzoic acid in nitrobenzene is therefore first-order in the acid and ethylene oxide, and the amine-catalysed parallel reaction (Ib) is first-order in the acid, ethylene oxide, and tertiary amine. The value of the rate constant k_2 (Eq. (5)) for the reaction effected in the presence of weakly basic pyridine is only slightly higher ($2.14 \cdot 10^{-4} \text{ s}^{-1}$) than that for the reaction catalysed with tri-*n*-butylamine, *i.e.* the compound which is by about five orders of magnitude more basic ($1.50 \cdot 10^{-4} \text{ s}^{-1}$) (using otherwise identical reaction conditions: $[A]_0 = 2.1 \text{ mol kg}^{-1}$; $[B] = 0.705 \text{ mol kg}^{-1}$; $[R'_3N] = 0.0581 \text{ mol kg}^{-1}$; $t = 85^\circ\text{C}$). In contrast to *n*-butanol, in nitrobenzene as a solvent benzoic acid is nearly exclusively converted to the ester *via* the amine-catalysed reaction (Ib). The values of rate constant k_{21} and k_{22} for the reactions of substituted benzoic acids with ethylene oxide in nitrobenzene in the presence of a tertiary amine are summarized in Table II. The linear plot of $\log k_{21}$ against $\text{p}K_a$ of these acids (Fig. 7) according to Brønsted equation gives the constant α'_1 equaling to 0.96 ($r = 0.9957$, $s = 0.06$); the constant G'_1 had a value of $8.2 \cdot 10^{-4}$ ($s = 0.5 \cdot 10^{-4}$). The linear Brønsted plot was also obtained for the amine-catalysed parallel reaction ($\log k_{22}$ vs $\text{p}K_a$) (Fig. 7), the constant α'_1 equaling to 0.60 ($r = 0.9999$, $s = 0.006$) and the constant G'_2 having a value of $1.12 \cdot 10^{-2}$ ($s = 0.01 \cdot 10^{-2}$). The same values as for α'_1 and α'_2 constants were obtained for Hammett reaction constants ρ'_1 and ρ'_2 , respectively, for the acid- and amine-catalysed parallel reactions in nitrobenzene. It is worthy of note that essentially the same values of constants α'_1 and α'_2 were reported by Lebedev and Guskov²² for the acid- (0.95) and potassium hydroxide-catalysed parallel reactions of aromatic carboxylic acids with ethylene oxide in the same solvent. The tertiary amine- and potassium hydroxide-catalysed reactions of the acids with ethylene oxide in this dipolar aprotic solvent differ only in the values of G'_1 and G'_2 constants.

The results of kinetic measurements lead to the following conclusions. Aromatic carboxylic acids react with ethylene oxide in the presence of tertiary amines as catalysts and in protic or aprotic dipolar solvents to give 2-hydroxyethyl esters *via* the tertiary amine-catalysed reaction and partially also *via* the parallel reaction catalysed by the corresponding undissociated acid. The overall rate of acid conversion increases with increasing acid strength of a given acid and is higher in aprotic dipolar solvent than in protic medium. In contrast to the amine-catalysed reaction, the kinetics of the acid-catalysed reaction is independent of the acid strength and the polarity of reaction medium. In protic solvents, the acid-catalysed reaction is always first-order in both the acid and ethylene oxide, irrespective of the acid strength; the Brønsted constant α_1 has a value of 0.62. The kinetics of the parallel, amine-catalysed reaction in protic solvent depends on the acid strength of a given acid; the reaction of the acids with $\text{p}K_a \geq 4.34$ to ≥ 3.99 is first-order in both ethylene oxide and tertiary amine and proceeds thus without participation of the acid in the rate-determining step. Logarithms of the rate constants can be correlated with the acid strength in

this pK_a region by the Brønsted equation, whose constant α_2 has a value of 0.34. In the case of the acids with pK_a between 3.99 and 3.2, the nature of the rate-determining step is changed, which is manifested by nonlinear Brønsted plot in this region.

Proportionally to the increasing strength of the acid, the reaction involving participation of the acid in the amine-catalysed parallel reaction becomes increasingly more important. When pK_a of the acids is less than or equal to 3.18, the amine-catalysed reaction proceeds solely with the participation of the acid. This reaction is first-order in the acid, ethylene oxide, and the amine. In aprotic dipolar solvent the acid-catalysed reaction is strongly suppressed and the acids are converted to 2-hydroxyethyl esters nearly exclusively *via* the parallel, amine-catalysed reaction. The acid-catalysed reaction shows in this medium first-order kinetics in both the acid and ethylene oxide, and the Brønsted constant α'_1 has a value of 0.96. Irrespective of the acid strength of a given acid, the amine-catalysed reaction proceeds in this medium solely with the participation of the acid in the rate-determining step and is first-order in the acid, ethylene oxide and tertiary amine; the corresponding Brønsted constant α'_2 has a value of 0.60. The values of α_1 , α_2 , α'_1 , and α'_2 constants determined from the dependences of logarithms of the rate constants k_{11} , k_{12} , k_{21} , and k_{22} , respectively, on pK_a of *meta*- and *para*-substituted benzoic acids are in this case identical with the values of the corresponding Hammett reaction constants ρ_1 , ρ_2 , ρ'_1 , and ρ'_2 , respectively. Their positive values are in agreement with the increase of the reaction rate with increasing electron-attracting ability of the *meta* and *para* substituents on aromatic ring and with the nucleophilic character of the reaction. Summarizing these results, it seems that the conversion of carboxylic acids by the acid catalysed parallel reaction and taking place without their participation in the rate-determining step of the amine-catalysed reaction can be most likely depicted by equations (II) and (III) (Scheme 1). On the other hand, the conversion of the acids taking place with participation of the undissociated acid in the rate-determining step of the amine-catalysed reaction seems to be best described by equations (IV) and (V) (Scheme 1).

REFERENCES

1. Hetflejš J., Mareš F., Bažant V.: This Journal 34, 3098 (1969).
2. Briegleb G., Bieber A.: Z. Elektrochem. 55, 250 (1951).
3. Pasto D. J., Kent R.: J. Org. Chem. 30, 2684 (1965).
4. Hodgman Ch. J.: *Handbook of Chemistry and Physics*, 47th Edition; Chemical Rubber Publishing Co., Cleveland 1966–1967.
5. Sanders H. J., Prescott R. F.: Ind. Eng. Chem. 51, 974 (1959).
6. Vogel A. I.: J. Chem. Soc. 1948, 1825.
7. Jureček M.: *Organická analýza*, p. 557. Přírodovědecké nakladatelství, Prague 1950.
8. Skita A., Blatt A. H.: *Organic Synthesis*, Vol. I., p. 550. Wiley, London 1961.
9. Mareš F., Hetflejš J., Bažant V.: This Journal 34, 3086 (1969).
10. Mokeeva R. T., Tsarfin A.: Zavod. Lab. 31, 1053 (1965).
11. Schneider P.: Chem. Prům. 19, 318 (1969).

12. Robinson B.: J. Chem. Soc. 1963, 2417.
13. Fischer E.: Chem. Ber. 53, 1638 (1920).
14. Newman M. S., Fones W., Renoll M.: J. Amer. Chem. Soc. 69, 718 (1947).
15. Negoro K., Saeki Y.: Kogyo Kagaku Zasshi 59, 205 (1956).
16. Harned H. S., Ehlers R. W.: J. Amer. Chem. Soc. 55, 65 (1933).
17. Brown H. C., Mihm X. R.: J. Amer. Chem. Soc. 78, 1723 (1956).
18. Hall H. K. Jr.: J. Amer. Chem. Soc. 79, 5441 (1957).
19. Cavill C. W. K., Gibson N. A., Nyholm R. S.: J. Chem. Soc. 1949, 2466.
20. Meites L.: *Handbook of Analytical Chemistry*, 1st Edition. McGraw-Hill, New York 1963.
21. Parker A. J.: Quart. Rev. Chem. Soc. 16, 163 (1962).
22. Lebedev N. N., Guskov K. A.: Kinet. Katal. 5, 787 (1964).

Translated by J. Hetflejš.