

# KINETICS OF FORMATION OF $\beta$ -HYDROXYETHYLPYRIDINIUM BENZOATE IN THE REACTION OF PYRIDINE WITH ETHYLENE OXIDE AND BENZOIC ACID IN PROTIC MEDIUM\*

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Received April 30th, 1976

Kinetics of the reaction of pyridine with ethylene oxide and benzoic acid within the time interval limited by a total conversion of pyridine into  $\beta$ -hydroxyethylpyridinium benzoate has been determined. The course of this irreversible reaction in *n*-butanol as a solvent was followed by permeation chromatography on Sephadex LH-20 gel, using acetate buffer as an eluent. The reaction was first order in pyridine, ethylene oxide and benzoic acid and its rate depended upon strength of the acid. Formation of  $\beta$ -hydroxyethylpyridinium benzoate, which catalyzes the subsequent nucleophilic substitution reaction of benzoic acid with ethylene oxide to produce  $\beta$ -hydroxyethyl benzoate, is characterized by relatively low activation enthalpy and highly negative activation entropy. Mechanism of formation of the quaternary salt is discussed.

Base-catalysed selective reaction of carboxylic acids with 1,2-alkylene oxides leading to corresponding  $\beta$ -hydroxyalkyl esters is still the object of considerable interest, both from the synthetic and theoretical points of view. A number of mechanisms were considered in order to account for the participation of tertiary amines as catalysts on the opening of the oxirane ring in these reactions.

For the tertiary amine catalysed reaction of substituted benzoic acids with phenyl glycidyl ether in xylene solutions Sakai and coworkers<sup>1</sup> have proposed formation of a hydrogen-bonded complex (A—H $\cdots$ B) which reacted with phenyl glycidyl ether through the four-centered cyclic addition complex, (A—H $\cdots$ B $\cdots$ C) (identical with the transition state species), to produce finally the corresponding ether-ester. This mechanism has been accepted also by other authors<sup>2-4</sup> for analogous, tertiary amine catalysed reactions of phenyl glycidyl ethers in nonpolar solvents and in nitrobenzene. A hydrogen-bonded complex, ion pairs (A $\cdots$ B $\cdots$ H), free ions (A $^-$  and B $^+$ H) or a cyclic addition complex have been postulated as intermediates in the pyridine catalysed reaction of benzoic acid with phenyl glycidyl ether in nonpolar and aprotic dipolar media<sup>5</sup>. According to another work<sup>6</sup>, free ions, ion pairs and a hydrogen-bonded complex, all participate in the above-mentioned reaction. A different mechanism has been proposed by Eastham and coworkers<sup>7,8</sup> for the reaction of strong inorganic and organic sulphonic acids with ethylene oxide taking place in the presence of tertiary amines in aqueous or pyridine solutions; it involved formation of the quaternary salt (R<sub>3</sub>NCH<sub>2</sub>CH<sub>2</sub>OH) $^+A^-$  and attack of the oxirane ring by the

\* Part V in the series Reactions of Carboxylic Acids with Ethylene Oxide; Part IV: This Journal 41, 101 (1976).

so formed acid anion. The existence of quarternary salts of this type has been evidenced both analytically<sup>9</sup> and synthetically<sup>10,11</sup>. The mechanism proposed by Eastham has been accepted for reactions of carboxylic acids with 1,2-alkylene oxides catalysed by tertiary amines<sup>9,12</sup>; also kinetics of the reaction of aromatic carboxylic acids with  $pK_a \geq 3.2$  with ethylene oxide in a protic medium and in the presence of tertiary amines<sup>13</sup>, arsines, phosphines, and stibines<sup>14</sup> as catalysts studied by us was in accordance with this mechanism.

In an effort to clarify the role of tertiary amines in the reaction of carboxylic acids with 1,2-alkylene oxides we have made a series of rate measurements in a pyridine-ethylene oxide-benzoic acid reaction system using *n*-butanol as a solvent. Conversion of the carboxylic acid into its  $\beta$ -hydroxyethyl ester by the action of ethylene oxide and tertiary amines has been studied by us in detail in a previous work<sup>13</sup>. In the present communication we have centered on the reactions which proceed in the time interval limited by the first contact of ethylene oxide with a pyridine-benzoic acid mixture and by a total conversion of pyridine into the presumed  $\beta$ -hydroxyethylpyridinium benzoate. The most suitable method which enabled us to follow quantitatively formation of this quarternary salt proved to be gel permeation chromatography. Ion-exchange separation method has been used to isolate the quarternary salt from the reaction mixture. To our knowledge, there are no data in the literature on time-concentration dependences for conversion of a tertiary amine, an 1,2-alkylene oxide and a carboxylic acid into the corresponding  $\beta$ -hydroxyalkylammonium salt. We have decided, therefore, to determine the kinetics of formation of  $\beta$ -hydroxyethylpyridinium benzoate and to compare it with kinetic laws by which the subsequent transformation of the acid into its  $\beta$ -hydroxyethyl ester is governed. The measurements were carried out in a closed system at total pressures varying from 780 to 1065 Torr.

## EXPERIMENTAL

Benzoic acid (99.9%) (Lachema, Brno), *m*-nitrobenzoic acid (99.8%) (Fluka A.G., Buchs) and acetic acid, all analytically pure chemicals, were used without further purification. Pyridine (pure) (Fluka A.G., Buchs) was successively dried over crushed potassium hydroxide for several days and by metallic sodium and rectified under nitrogen; the fraction used had b.p. 114°C/747 Torr;  $n_D^{20}$  1.5100.  $\beta$ -Hydroxyethyl benzoate<sup>13</sup>, b.p. 146–148°C/9 Torr, and  $\beta$ -hydroxyethyl *m*-nitrobenzoate<sup>15</sup>, m.p. 52–53°C, which were used as standards in gel permeation chromatography, were prepared by the known procedures. Ethylene oxide (Montecatini-Edison, Italy, 99% by gas chromatography), contained  $\leq 0.05\%$  of acetylene,  $< 0.05\%$  of acetaldehyde and other impurities ( $H_2O$  and  $CO_2$ ) in amounts less than 1%. *n*-Butanol (purum) (Spolana, Neratovice) was distilled through a column packed with an activated 4A molecular sieve and the fraction boiling at 116.5°C/743 Torr was collected;  $n_D^{20}$  1.3995. Sodium acetate trihydrate (Lachema, Brno) was used without further purification. Sephadex LH 20 gel (25–100 $\mu$ ) was purchased from Pharmacia Fine Chemicals AB, Uppsala, Sweden. Acetate buffer with pH 4.95, which was used as an eluent in gel permeation chromatography, had ionic strength  $I = 0.0353$ . A strongly acidic cation exchanger Dowex 50W, 450–100 mesh (Fluka A.G.) was allowed to swell in water

and then it was placed into a  $20 \times 0.7$  cm column; before its use for the isolation of  $\beta$ -hydroxyethylpyridinium chloride the column was washed with 250 ml of 1M-HCl and then with water to neutral reaction.

*Spectral measurements.*  $^1\text{H-NMR}$  spectra were recorded with Tesla BS 477 (80 MHz) instrument (a modified model). IR spectra were measured with Zeiss, Model UR 20 (Jena) spectrophotometer and UV spectra with Beckman DK-2A (330–200 nm) spectrophotometer.

### Gel Permeation Chromatography

Chromatographic measurements were carried out with the use of an apparatus described in a previous work<sup>16</sup> which was equipped with one stainless steel column of 0.8 cm in diameter packed<sup>17</sup> with Sephadex LH-20 gel to a total height of 120 cm. The eluent was degassed acetate buffer (acetic acid–sodium acetate trihydrate) with pH 4.95. After equilibration of the column packing with the eluent for 8 h, samples (2–7  $\mu\text{l}$ ) of the reaction mixture (without further dilution) or standards (solutions in *n*-butanol) were injected into the column by means of a Hamilton microsyringe. The effluent was monitored continuously with a double-beam differential UV analyser (50  $\mu\text{l}$  cells) measuring the absorbance at 254 nm (Development Workshops, Czechoslovak Academy of Sciences, Prague). The analyser was connected to TZ21S linear recorder (Laboratorní přístroje, Prague). Elution volumes,  $V_e$ , which were measured by a siphon integral flow meter and expressed in ml were reproducible to  $\pm 2\%$ ; all solutes were eluted as symmetrical peaks. The measurements were performed at room temperature and at a flow rate of 0.864 ml per min. One analysis of the reaction mixture required approximately 120 min. The presence of benzoic acid, pyridine,  $\beta$ -hydroxyethyl benzoate, and  $\beta$ -hydroxyethyl *m*-nitrobenzoate in reaction mixtures was confirmed by comparison of the elution volumes read from the corresponding peak maxima with the elution volumes of authentic compounds. Under conditions of chromatographic measurements and in the presence of free pyridine, formation of  $\beta$ -hydroxyethylpyridinium benzoate and  $\beta$ -hydroxyethylpyridinium *m*-nitrobenzoate was demonstrated in chromatograms by appearance of a peak of  $\beta$ -hydroxyethylpyridinium cation already at the very beginning of the reaction, without any change in the peaks of benzoic acid or *m*-nitrobenzoic acid. For identification of  $\beta$ -hydroxyethylpyridinium cation or  $\beta$ -hydroxyethylpyridinium benzoate and  $\beta$ -hydroxyethylpyridinium *m*-nitrobenzoate we used  $\beta$ -hydroxyethylpyridinium chloride which was isolated by the procedure described later. Values of  $V_e$  determined for individual compounds were:  $\beta$ -hydroxyethylpyridinium benzoate,  $\beta$ -hydroxyethylpyridinium *m*-nitrobenzoate, and  $\beta$ -hydroxyethylpyridinium chloride, 40.0 ml; pyridine, 54.0 ml; benzoic acid, 78.3 ml;  $\beta$ -hydroxyethyl benzoate, 126.4 ml; *m*-nitrobenzoic acid, 98.1 ml;  $\beta$ -hydroxyethyl *m*-nitrobenzoate, 127.5 ml. Relations of concentration of the solutes in the samples to the corresponding areas of peaks were read from linear calibration graphs.

### Isolation of $\beta$ -Hydroxyethylpyridinium Chloride

Ethylene oxide was introduced into a solution of 5 g (40 mmol) of benzoic acid and 0.5 g (6.3 mmol) of pyridine in 25 ml of *n*-butanol at 80°C, and the course of the reaction was followed by gel permeation chromatography. The reaction was stopped after 66 min when all the pyridine had reacted; the reaction mixture was freed of the excess ethylene oxide by repeated evacuation, cooled to room temperature, diluted with 500 ml of water, and the homogeneous solution formed was fed into a column packed with Dowex 50 W cation exchanger at a flow rate of 0.5 ml/min. The column was then washed with 200 ml of water; the aqueous eluate contained only benzoic acid, its  $\beta$ -hydroxyethyl ester, and *n*-butanol. The subsequent elution of the pyridine derivative

with 1M-HCl was monitored by gel permeation chromatography. The eluate from the column was freed of water and free hydrochloric acid by evaporation at 40–45°C/12 Torr; a pale yellow viscous residue crystallized on cooling. After successive drying over solid NaOH and P<sub>2</sub>O<sub>5</sub>, 0.73 g (72%) of needle-like, strongly hygroscopic crystals of β-hydroxyethylpyridinium chloride was obtained; m.p. 116.5–117.5°C (uncorrected). For C<sub>7</sub>H<sub>10</sub>ClNO (159.6) calculated: 52.67% C, 6.31% H; found: 52.65% C, 6.36% H. <sup>1</sup>H-NMR spectrum (in D<sub>2</sub>O on using 2,2-dimethyl-2-silapentane sodium sulphinate as a reference) showed in addition to γ-protons also usual multiplets of α- and β-protons of the pyridine grouping and two triplets of CH<sub>2</sub> groups. In the solvent used the low-field triplet overlapped with signals of HDO and OH protons; both triplets were centered at δ 6.25 and 5.56 ppm (recalculated to tetramethylsilane as a reference). IR spectrum (KBr discs) of analytically pure sample exhibited a strong broad OH absorption band near to 3400 cm<sup>-1</sup>. UV spectrum (H<sub>2</sub>O): ν<sub>max</sub> 33448 (ε 4336), 39370 (i) (ε 3955), 38610 (ε 4761) and 37879 (sh) cm<sup>-1</sup> (ε 3523M<sup>-1</sup> cm<sup>-1</sup>).

It should be noted that the attempt to prepare β-hydroxyethylpyridinium benzoate by a procedure analogous to that described in a recent work<sup>11</sup> for similar quarternary salts has failed; instead of the crystalline product, a dark brown, very viscous oil was obtained which did not solidify even after standing over P<sub>2</sub>O<sub>5</sub> for several months.

#### Kinetic Measurements

Rates of the reaction of pyridine with ethylene oxide in the presence of benzoic or *m*-nitrobenzoic acid in *n*-butanol were measured with the use of the apparatus described earlier<sup>13</sup>; only a straight glass tube reaching to the bottom of the reaction vessel and serving for sample removal was replaced by a hypodermic syringe equipped with a needle reaching through a silicone rubber septum below the level of the reaction mixture. The reaction flask (500 ml) which contained known amounts of pyridine (2 g; 0.253 mol kg<sup>-1</sup>), benzoic acid (5–20 g; 0.4094–1.638 mol kg<sup>-1</sup>) or *m*-nitrobenzoic acid (1.4 g; 0.3348 mol kg<sup>-1</sup>) in *n*-butanol (78–93 g) was placed into a thermostat, evacuated to 30 Torr, filled with nitrogen and flushed several times with nitrogen. The mixture was warmed up to the reaction temperature (20 min) under stirring and the pressure in the reaction flask was decreased to 250 Torr; after stabilization of the reaction temperature (60 to 90 ± 0.1°C), the flask was connected to ethylene oxide reservoir and the homogeneous reaction mixture was saturated with ethylene oxide. The amount of ethylene oxide dissolved at a given temperature was determined by the known procedure<sup>12,13</sup>. Kinetic measurements were carried out at total pressures varying from 780 to 1065 Torr which correspond to concentrations of 0.595–1.510 mol kg<sup>-1</sup> of ethylene oxide. Parallel experiments have shown that under the given experimental conditions the reacting solution had been saturated with ethylene oxide during 1–2 min; the rate of ethylene oxide absorption was thus many times greater compared to its consumption in the reaction and was also independent on the speed of mixing at 40–120 rev. per min. The reaction took place, therefore, in the kinetic region. The rate of the formation of the quarternary salt was calculated starting from the moment of the first contact of ethylene oxide with the solution of pyridine and the carboxylic acid in *n*-butanol; the reaction was monitored by gel permeation chromatography. Volume changes of the reaction mixture were not considered in deriving the kinetic equations. Deviations of experimental points from regression lines (correlation coefficients (*r*) given) are expressed by standard deviations (*s*). All concentration data are given in moles per 1 kg of the reaction mixture.

## RESULTS AND DISCUSSION

Gel permeation chromatography of a mixture of pyridine and benzoic acid in *n*-butanol on Sephadex LH-20 gel shows two well resolved peaks (Fig. 1a, peaks 1 and 2) of both compounds when acetate buffer is used as an eluent (pH 4.95). If the solution of pyridine and benzoic acid is brought into contact with ethylene oxide at 80°C, another peak appears immediately (Fig. 1b, peak 3) which corresponds to the expected  $\beta$ -hydroxyethylpyridinium benzoate. The area of peak 3 increases with time together with the decreasing area of the peak corresponding to pyridine and it attains maximum at the moment when all the pyridine had reacted (66 min). When the reaction mixture

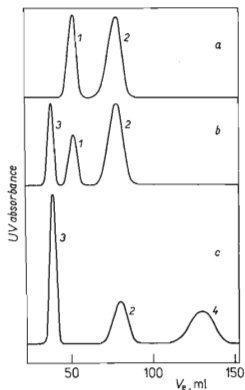


FIG. 1

Gel Chromatogram of Separation of Pyridine 1, Benzoic Acid 2,  $\beta$ -Hydroxyethylpyridinium Benzoate 3, and  $\beta$ -Hydroxyethyl Benzoate 4 in the Reaction of Pyridine with Ethylene Oxide and Benzoic Acid in *n*-Butanol

$t$ , min: a 0, b 3, c 66;  $[C_5H_5N]_0$  0.253 mol kg<sup>-1</sup>;  $[C_6H_5CO_2H]_0$  1.6380 mol kg<sup>-1</sup>;  $[C_2H_4O]_0$  1.020 mol kg<sup>-1</sup>; temperature 80  $\pm$  0.1°C.

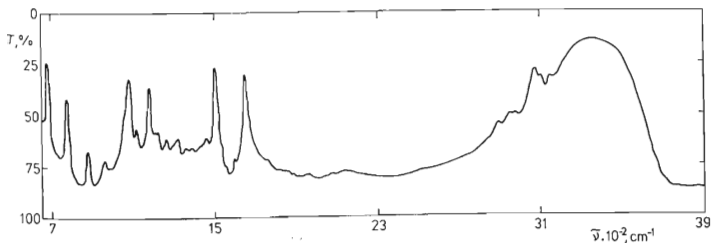


FIG. 2

IR Absorption Spectrum of Crystalline  $\beta$ -Hydroxyethylpyridinium Chloride (KBr Discs)

so formed was subjected to separation on Dowex 50 W cation exchanger, the aqueous eluate contained only benzoic acid, *n*-butanol, and  $\beta$ -hydroxyethyl benzoate; on the other hand, subsequent elution of the cation exchanger with hydrochloric acid followed by work-up of the eluate yielded pure  $\beta$ -hydroxyethylpyridinium chloride (72%) whose structure was unambiguously determined by elemental analysis, NMR and IR spectra (Fig. 2). UV spectrum of the chloride is shown in Fig. 3. The  $V_e$  value (40.0 ml) of this quarternary salt is identical with that found for the product of the reaction of pyridine with ethylene oxide and benzoic acid in excess (Fig. 1b, peak 3). Under conditions of chromatographic analysis where  $\beta$ -hydroxyethylpyridinium benzoate and  $\beta$ -hydroxyethylpyridinium chloride exist in ionic forms, peak 3 in Figs 1b and 1c represents  $\beta$ -hydroxyethylpyridinium cation. This fact is in accordance with the practically unchanged concentration of benzoic acid in the reaction mixture up to the moment when the amount of the quarternary salt so accumulated is sufficient to catalyze effectively the subsequent esterification reaction (after 7 min, the reaction mixture contained only 0.3% of 2-hydroxyethyl benzoate; 70% conversion of pyridine corresponded to formation of 1.5% of the ester). An identical picture has been obtained in the reaction of pyridine with ethylene oxide and an excess of *m*-nitrobenzoic acid; the peak with the smallest elution volume, which appeared on the chromatogram at the very beginning of the reaction, shows the  $V_e$  value equaling to 40.0 ml, in agreement with the above results. It can be thus taken as proved that the quarternary salt which is formed at the beginning of the reaction of pyridine with ethylene oxide and excess benzoic acid or *m*-nitrobenzoic acid is  $\beta$ -hydroxyethylpyridinium benzoate or  $\beta$ -hydroxyethylpyridinium *m*-nitrobenzoate. Judging from the unchanged area of peak 3, the concentrations of these quarternary salts remain constant during the subsequent conversion of benzoic acid into  $\beta$ -hydroxyethyl ben-

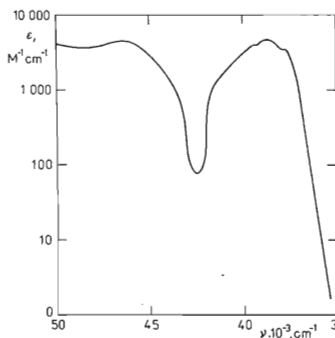


FIG. 3  
UV Absorption Spectrum of an Aqueous Solution ( $6.83 \cdot 10^{-4} M$ ) of  $\beta$ -Hydroxyethylpyridinium Chloride

zoate (Fig. 1c, peak 4) or of *m*-nitrobenzoic acid into  $\beta$ -hydroxyethyl *m*-nitrobenzoate. From these results it can be concluded that the quarternary base or quarternary salts of this type are actual catalysts for the subsequent nucleophilic substitution reaction of carboxylic acids with 1,2-alkylene oxides leading to  $\beta$ -hydroxyalkyl carboxylates. The  $pK_b$  values of these quarternary bases differ much less from one another (unless steric effects play a significant role) than the  $pK_b$ 's of the corresponding tertiary amines<sup>10</sup>. Both these facts explain the little dependence of the rate of formation of  $\beta$ -hydroxyalkyl carboxylates on  $pK_b$  of used tertiary amines<sup>9,12,13</sup>. In all probability; quarternary salts  $(R_3MCH_2CH_2OH)^{(+)}RCOO^{(-)}$ , where M is P, As or Sb, act also as catalysts for the reaction of carboxylic acids with ethylene oxide in the presence of tertiary phosphines, arsines and stibines<sup>14</sup>. In the case of tertiary arsines and stibines, the formation rate of corresponding quarternary salts is, however, so low that it affects directly the kinetics of the formation of 2-hydroxyethyl esters<sup>14</sup>; the absence of an induction period in reactions in which solutions of preacted arsines and stibines have been used<sup>14</sup> gives support to these conclusions.

Kinetics was measured of the formation of  $\beta$ -hydroxyethylpyridinium benzoate in the reaction of pyridine (A) with ethylene oxide (B) and an excess of benzoic acid (C) proceeding within the time interval which was limited, on the one hand, by the first contact of ethylene oxide with a solution of pyridine and the carboxylic acid in *n*-butanol, and on the other hand, by the complete consumption of pyridine. The measurements were carried out at varying initial concentrations of ethylene oxide (a constant partial pressure of ethylene oxide throughout the whole reaction) and benzoic acid (Fig. 4). The reactions were monitored by gel permeation chromatography. By plotting the term  $2.303 \log [A]_0/[A]$  versus time, a linear dependence has been obtained which indicated that pyridine is consumed in the reaction according

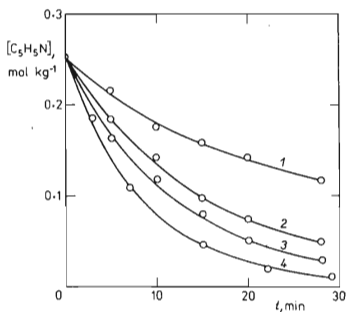


FIG. 4

Conversion of Pyridine in its Reaction with Ethylene Oxide and Benzoic Acid in *n*-Butanol in Dependence upon Time and Initial Concentration of Benzoic Acid

$[C_6H_5CO_2H]_0$ : 1 0.4094 mol kg<sup>-1</sup>, 2 0.8189 mol kg<sup>-1</sup>, 3 1.2280 mol kg<sup>-1</sup>, 4 1.6380 mol kg<sup>-1</sup>;  $[C_5H_5N]_0$  0.2530 mol kg<sup>-1</sup>;  $[C_2H_4O]_0$  1.020 mol kg<sup>-1</sup>; temperature 80  $\pm$  0.1°C.

to first-order kinetics. Time dependence of pyridine consumption can be thus expressed by simple equation (1). This dependence is obeyed through at least 95%

$$-d[A]/dt = k_1[A] \quad (1)$$

conversion of pyridine. As it is obvious from Fig. 4, the rate of pyridine consumption increases with increasing initial concentration of benzoic acid. The dependence of the term  $2.303 \log [A]_0/[A]$  upon time, which was determined at constant initial concentrations of pyridine and ethylene oxide and at varying initial concentrations of benzoic acid, yielded straight lines whose slopes correspond to pseudo-first order rate constants  $k_1$ . The values of these rate constants refined by the least-squares treatment are presented in Table I, along with the values of the corresponding correlation coefficients ( $r$ ). The linear dependence of constants  $k_1$  upon initial concentrations of benzoic acid (Fig. 5) confirmed that the formation of  $\beta$ -hydroxyethylpyridinium benzoate is first order in benzoic acid. The rate of pyridine consumption increased also with increasing initial concentration of ethylene oxide. When the values of the term  $2.303 \log [A]_0/[A]$  for a constant initial concentration of pyridine and benzoic acid at varying initial concentrations of ethylene oxide were plotted against time, linear dependences have been obtained in all cases. The values of pseudo-first order rate constants  $k_2$  obtained from the slopes of these straight lines and refined by the least-squares calculations are summarized in Table I. From the linear dependence of the constants  $k_2$  on the initial concentration of ethylene oxide it follows (Fig. 5) that the formation of  $\beta$ -hydroxyethylpyridinium benzoate ( $D$ ) is also first order in ethylene oxide. Time changes in the concentration of this quatern-

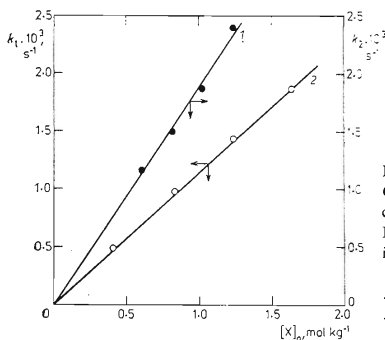


FIG. 5

Dependence of Pseudo-First Order Rate Constants  $k_1$  and  $k_2$  upon Initial Concentrations  $[X]_0$  of Ethylene Oxide 1 and Benzoic Acid 2 in the Reaction with Pyridine in *n*-Butanol

1  $[C_6H_5CO_2H]_0$  1.6380 mol kg<sup>-1</sup>; 2  $[C_2H_4.O]_0$  1.020 mol kg<sup>-1</sup>;  $[C_5H_5N]_0$  0.2430 mol . kg<sup>-1</sup>; temperature 80 ± 0.1°C.



ary salt can be thus expressed by Eq. (2). The third-order rate constant  $k_3$  has been

$$d[D]/dt = k_3[A][B][C] \quad (2)$$

calculated for 80°C according to Eqs (3) and (4)

$$k_3 = k_1/[B]_0[C]_0 \quad (3)$$

$$k_3 = k_2/[B]_0[C]_0 \quad (4)$$

and after the least-squares refinement it had the values  $(1.148 \pm 0.024) \cdot 10^{-3} \text{ kg}^2 \cdot \text{mol}^{-2} \text{ s}^{-1}$  (Eq. (3)) and  $(1.152 \pm 0.035) \cdot 10^{-3} \text{ kg}^2 \text{ mol}^{-2} \text{ s}^{-1}$  (Eq. (4)). Good agreement between these two values confirms that the formation of  $\beta$ -hydroxyethylpyridinium benzoate in protic solvents obeys third-order rate law.

The effect of the acid strength on the rate of pyridine consumption, and hence on the rate of formation of the quaternary salt, is documented by two examples, *i.e.* by comparison of the conversion of pyridine ( $[C_5H_5N]_0 : 0.253 \text{ mol kg}^{-1}$ ) in the reaction with ethylene oxide ( $[C_2H_4O]_0 : 1.020 \text{ mol kg}^{-1}$ ) and benzoic acid ( $pK_a 4.21$ ) and in an analogous reaction with *m*-nitrobenzoic acid ( $pK_a 3.45$ ) ( $[C_6H_5CO_2H]_0 = [m-O_2NC_6H_4CO_2H]_0 = 0.3348 \text{ mol kg}^{-1}$ ; data for this initial concentration of benzoic acid were extrapolated from the relation of  $k_1$  vs  $[C_6H_5CO_2H]_0$ ): during the first 5 min at 80°C, 61.4% of pyridine reacted in the presence of *m*-nitrobenzoic acid by contrast to 10.7% of pyridine consumption in the reaction with benzoic acid.

TABLE I

Values of Pseudo-First Order Rate Constants  $k_1$  and  $k_2$  for the Formation of  $\beta$ -Hydroxyethylpyridinium Benzoate in Relation to Initial Concentrations of Benzoic Acid and Ethylene Oxide

$[C_5H_5N]_0 = 0.253 \text{ mol kg}^{-1}$ ; temperature  $80 \pm 0.1^\circ\text{C}$ ; the concentrations are given in  $\text{mol kg}^{-1}$  and the rate constants in  $\text{s}^{-1}$ .

$[C_6H_5CO_2H]_0$	$[C_2H_4O]_0$	$10^6 \cdot k_1$	$r(k_1)$	$10^6 \cdot k_2$	$r(k_2)$
1.6380	1.020	$1\ 865 \pm 34$	0.9975	—	—
1.2280	1.020	$1\ 430 \pm 20$	0.9980	—	—
0.8189	1.020	$976 \pm 14$	0.9979	—	—
0.4094	1.020	$486 \pm 20$	0.9871	—	—
1.6380	1.240	—	—	$2\ 399 \pm 82$	0.9848
1.6380	1.020	—	—	$1\ 865 \pm 35$	0.9975
1.6380	0.810	—	—	$1\ 494 \pm 25$	0.9971
1.6380	0.595	—	—	$1\ 153 \pm 27$	0.9942

Gel permeation chromatography made possible to follow the time decrease in pyridine concentration simultaneously with the time increase in  $\beta$ -hydroxyethyl benzoate concentration. The fact that in the time interval limited by 70% conversion of pyridine into  $\beta$ -hydroxyethylpyridinium benzoate only 1.5% of  $\beta$ -hydroxyethyl benzoate were formed (for conditions see Fig. 1) speaks for the substantially lower rate of subsequent transformation of benzoic acid into its ester in this phase of the esterification reaction. No products which could be formed by interaction of *n*-butanol as solvent with ethylene oxide or with the carboxylic acid were found in the resulting reaction mixture.

TABLE II

Temperature Dependence of Third-Order Rate Constants  $k_3$  for the Formation of  $\beta$ -Hydroxyethylpyridinium Benzoate in the Reaction of Pyridine with Ethylene Oxide and Benzoic Acid

$[\text{C}_5\text{H}_5\text{N}]_0 = 0.253 \text{ mol kg}^{-1}$ ;  $[\text{C}_6\text{H}_5\text{CO}_2\text{H}]_0 = 1.6380 \text{ mol kg}^{-1}$ ;  $[\text{C}_2\text{H}_4\text{O}]_0$ : 333 K: 1.510  $\text{mol kg}^{-1}$ ; 343 K: 1.275  $\text{mol kg}^{-1}$ ; 353 K: 1.020  $\text{mol kg}^{-1}$ ; 363 K: 0.754  $\text{mol kg}^{-1}$ ; the rate constants  $k_3$  are given in  $\text{kg}^2 \text{ mol}^{-2} \text{ s}^{-1}$ .

	$K$	$10^6 \cdot k_3$	$r(k_3)$		$K$	$10^6 \cdot k_3$	$r(k_3)$
	333	$410 \pm 12$	0.9941		353	$1\,148 \pm 24$	0.9975
	343	$649 \pm 11$	0.9976		363	$2\,042 \pm 35$	0.9970

TABLE III

Values of Activation Parameters for the Formation of  $\beta$ -Hydroxyethylpyridinium Benzoate (D) by the Reaction of Pyridine (A) with Ethylene Oxide (B) and Benzoic Acid (C) in *n*-Butanol and for the Acid- and Base-Catalysed Transformations of Benzoic Acid with Ethylene Oxide into 2-Hydroxyethyl Benzoate in *n*-Butanol in the Presence of *N,N*-Dimethylcyclohexylamine

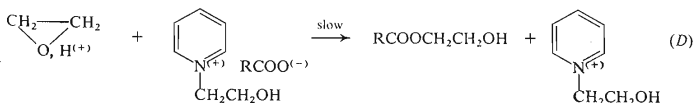
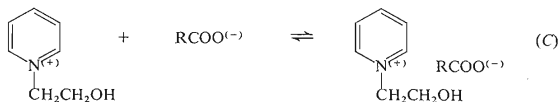
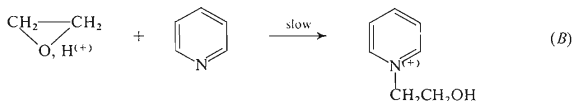
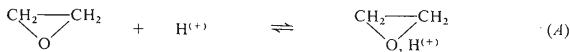
Reaction	$\Delta E$ $\text{kcal mol}^{-1}$	$r(E)$	$\Delta H^\ddagger$ $\text{kcal mol}^{-1}$	$A^a$	$\Delta S^\ddagger$ e.u.
$A + B + C \rightarrow D$	$12.9 \pm 0.8$	0.9963	$12.2 \pm 0.9$	$1.1 \cdot 10^5 \text{ kg}^2 \text{ mol}^{-2} \text{ s}^{-1}$	$-39.5 \pm 2.3$
$C + B \rightarrow E^b$	$17.8 \pm 0.9^c$	0.9973 <sup>c</sup>	$17.2 \pm 0.9^d$	$2.3 \cdot 10^6 \text{ kg mol}^{-1} \text{ s}^{-1c}$	$-31.6 \pm 2.6^d$
$C + B \rightarrow E^e$	$24.8 \pm 0.9^e$	0.9988 <sup>e</sup>	$24.2 \pm 0.9^d$	$1.7 \cdot 10^{12} \text{ kg mol}^{-1} \text{ s}^{-1c}$	$-4.6 \pm 0.6^d$

<sup>a</sup> Preexponential factor; <sup>b</sup> acid-catalysed reaction; <sup>c</sup> data taken from ref.<sup>13</sup>; <sup>d</sup> data calculated from corresponding parameters taken from ref.<sup>13</sup>; <sup>e</sup> base-catalysed reaction.

Variation of the third-order rate constant  $k_3$  with temperature was determined in the range from 60 to 90°C (Table II). The activation energy computed from the linear dependence of  $\log k_3$  on  $T^{-1}$  had a value of  $12.9 \pm 0.8$  kcal mol $^{-1}$  and the formation of  $\beta$ -hydroxyethylpyridinium benzoate can therefore be described by general equation (5).

$$k_3 = 1.1 \cdot 10^5 \exp(-12900 \pm 800/RT) \text{ kg}^2 \text{ mol}^{-2} \text{ s}^{-1} \quad (5)$$

In Table III are presented the values of activation parameters for the quarternary salt formation and for the subsequent acid- and base-catalysed reactions of benzoic acid with ethylene oxide<sup>13</sup> leading to  $\beta$ -hydroxyethyl benzoate. From comparison of activation energies or enthalpies for the above three reactions it follows that transition state is energetically most favoured in the formation of  $\beta$ -hydroxyethylpyridinium benzoate. Highly negative activation entropy is typical for this reaction, indicating an ordered and polar transition state structure in the rate-determining step of the reaction. A similarity of preexponential factors as well as of activation entropies for the formation of quarternary salt and for the acid-catalysed reaction of benzoic acid with ethylene oxide is also remarkable. These parameters contrast significantly with the values of the same activation parameters computed for the base-catalysed reaction of the acid with ethylene oxide. Comparably low negative activation entropy



SCHEME 1

of the latter reaction is consistent with a significant decrease in order in the formation of the transition state. Experimental results so far available do not allow to draw definite conclusions about mechanism of the formation of  $\beta$ -hydroxyethylpyridinium carboxylates by the reaction of pyridine with ethylene oxide and a carboxylic acid in an anhydrous protic solvent. Nevertheless, the third order of the reaction found experimentally, the absence of by-products, the formation of small amounts of  $\beta$ -hydroxyethyl benzoate, the qualitatively determined dependence of the rate of pyridine consumption on the strength of a carboxylic acid, the similarity between activation parameters for the formation of quarternary salt and the acid-catalysed reaction of the acid with ethylene oxide, and the recent study by Wylde and coworkers<sup>18</sup> on the mechanism of the ring opening of alkene oxides by acids, all seem to indicate that the formation of  $\beta$ -hydroxyethylpyridinium carboxylate could be depicted by a sequence of reactions (A)–(C) shown in Scheme 1. The rate-determining step of the formation of quarternary salt is then the nucleophilic substitution reaction (B). As it was proved experimentally, the formation of the ester according to Eq. (D) is kinetically unimportant in the initial phase of the reaction and becomes increasingly important with increasing pyridine conversion. The mechanism depicted in Scheme 1 (Equations (A)–(C) differs from our earlier concept<sup>14</sup> on account of the dependence of the rate of pyridine consumption upon acid strength which was found qualitatively in the present work. The results of kinetic measurements made so far do not exclude the possibility of other paths which would explain the formation of quarternary salts of this type. According to another, kinetically undistinguishable mechanism, the reaction could start by the formation of a molecular complex, ion pairs or free ions of the tertiary base and the carboxylic acid which would be able to attack oxirane ring in the next step. Further experimental data are needed to make unambiguous decision between these mechanistic alternatives.

*The authors thank Dr R. Řeřicha, Dr J. Schraml, and Dr Z. Šir of this Institute for IR, NMR, and UV spectrum measurements.*

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Translated by J. Hetflejš.