

THE EFFECT OF THE STRUCTURE OF AROMATIC AMIDES AND ALIPHATIC GLYCOLS ON THE RATE OF A METAL ION-CATALYSED GLYCOLYTIC REACTION*

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The kinetics of lead(II) oxide catalysed and uncatalysed glycolysis of benzamide and eighteen *ortho*-, *meta*- and *para*-substituted benzamides in an excess of aliphatic C₂ to C₅ glycols was determined. Homogeneous metal ion-catalysed reactions were first-order in the amide and half-order in Pb²⁺ ions. Benzamide was converted to the 2-hydroxyethyl ester parallelly by the pseudo-1.5 order catalysed and the pseudo-first order uncatalysed glycolysis reaction; the activation energy of the former reaction was 14.38 ± 0.41 kcal mol⁻¹ and the activation entropy was -44.2 ± 0.9 e.u.. Rate constants of the glycolysis of benzamide decreased with increasing length and branching of the carbon chain of glycols within one order of magnitude. Hammett reaction constant ρ for the catalysed glycolysis of *meta*- and *para*-substituted benzamides with ethylene glycol had a value of 0.48 ± 0.04 ; the logarithms of rate constants for the catalysed glycolysis of *ortho*-substituted benzamides by the same glycol were best correlated with Taft E_s constants ($\delta = 0.53 \pm 0.01$) which indicates that primarily steric effects are operative in this reaction series.

Previous works of this series^{1,2} showed that glycolysis of aromatic and heterocyclic amides with ethylene glycol, proceeding otherwise at a slow rate, can be significantly accelerated in the presence of cadmium(II), lead(II), manganese(II) and tin(II) compounds that are the most efficient catalysts for this reaction³.

In the present communication we report on the structure effects of aromatic amides and aliphatic glycols on the rate of glycolytic reaction that was followed both in the absence and presence of a metal catalyst. Data on the parallel conversion of the amide into the corresponding ester by the catalysed and uncatalysed glycolytic reaction in the presence of a metal catalyst are also reported. The measurements were carried out with the aim to obtain deeper insight into the nature of glycolysis of amides and to get additional data which would render it possible to compare this reaction with the metal ion-catalysed transesterification of aromatic alkyl esters⁴ or glycolysis of aromatic nitriles⁵ with ethylene glycol. These reactions lead also with high selectivity to 2-hydroxyalkyl esters as reaction products.

* Part III in the series Metal Ion-Catalysed Conversion of Amides and Imides into Esters; Part II; This Journal 41, 395 (1976).

EXPERIMENTAL

Chemicals. Benzamide was prepared by a modified procedure to that reported earlier⁶: hydrogen peroxide (30%; 2.1 mol) was added to a stirred mixture of benzonitrile (0.75 mol) and ammonium hydroxide (26%; 0.08 mol) in methanol (300 ml). After 15 h-heating at 50°C, the methanol was distilled off, the solid product was separated by filtration, washed with water and crystallised repeatedly from aqueous ethanol; m.p. 128.0–128.5°C (ref.⁷ m.p. 128°C). *o*-Toluamide, m.p. 141.0–141.5°C (ref.⁶ m.p. 141.5°C) and *p*-toluamide, m.p. 165–166°C (ref.⁷ m.p. 166°C) were prepared by reported procedure⁶ from the corresponding nitriles (Fluka A.G.). *o*-Methoxybenzamide⁸, m.p. 129–130°C (ref.⁸ m.p. 130–131°C), *o*-chlorobenzamide⁹, m.p. 141.0–141.5°C (ref.⁹ m.p. 140–141°C), *o*-bromobenzamide⁸, m.p. 161–162°C (ref.⁸ m.p. 160.5–161.5°C), *m*-toluamide⁶, m.p. 92.0–93.5°C (ref.⁶ m.p. 93.8°C), *m*-trifluoromethylbenzamide, m.p. 126 to 127°C (aq. ethanol) (for C₈H₆F₃NO (189.1) calculated: 50.81% C, 3.20% H, 30.14% F; found: 50.79% C, 3.22% H, 29.78% F), *p*-chlorobenzamide⁷, m.p. 169–170°C (ref.⁷ m.p. 169–171°C) and *p*-bromobenzamide⁸, m.p. 192–193°C (ref.⁸ m.p. 192.0–192.5°C) were obtained by the known procedure from the corresponding acid chlorides. *p*-Nitrobenzamide, m.p. 196–197°C (ref.⁶ m.p. 201.6°C) was prepared by the method reported by Finan and Fathergill for 3,5-dinitrobenzamide¹⁰. *p*-Methoxybenzamide, m.p. 163.0–163.5°C (ref.¹¹ m.p. 160–162°C) was obtained by the reaction of *p*-methoxybenzoic acid (Fluka A.G.) with urea¹¹. All the amides prepared were 98.2–99.2% pure. 2-Hydroxyethyl benzoate, b.p. 146–147°C/9 Torr (ref.¹² b.p. 160–162°C/14 Torr) (for C₉H₁₀O₃ (166.2) calculated: 65.05% C, 6.07% H; found: 65.02% C, 6.19% H), which was used to determine the effect of the initial concentration of the product on the rate of glycolysis, was obtained by the procedure described in the chapter dealing with the product isolation. Aliphatic glycols (commercial products; Fluka A.G.) were purified by vacuum fractionation or crystallisation: ethylene glycol, b.p. 94°C/11 Torr; propylene glycol 87–88°C : 12 Torr; trimethylene glycol 110–111°C/13 Torr; tetramethylene glycol 120–121°C/11 Torr; neopentyl glycol, m.p. 124–125°C (benzene–light petroleum) (ref.¹³ m.p. 126–128°C). Lead(II) oxide (Lachema, Brno) used as a catalyst was of analytical purity grade and was used without further purification. For PbO (223.2) calculated: 92.83% Pb; found: 93.4% Pb. A benzamide–cadmium dichloride complex (C₆H₅CONH₂.CdCl₂) was prepared according to Belladen and Astengo¹⁴. The IR spectra of the pure benzamide and its complex with CdCl₂ were measured in KBr pellets. Both spectra show two absorption bands in the 1700–1600 cm⁻¹ region, usually referred to as “Amide I” ($\nu(\text{C}=\text{O})$) and “Amide II” bands ($\delta(\text{NH}_2)$). In our case the $\nu(\text{C}=\text{O})$ band at about 1660 cm⁻¹ for the pure benzamide (ref.¹⁵ $\nu(\text{C}=\text{O})$ 1658 cm⁻¹) did not change its position in the case of the complex with CdCl₂, while the $\delta(\text{NH}_2)$ band at about 1625 cm⁻¹ for the pure benzamide (this band is not mentioned in the previous work¹⁵) was shifted to about 1605 cm⁻¹ for the complex with CdCl₂. Schwartz and Heyer did not comment a shift by 20 cm⁻¹ of the “Amide II” band to lower frequencies in the IR spectrum of a similar complex of benzamide with titanium tetrachloride, but observed the carbonyl band shift by 26 cm⁻¹ to lower frequency region¹⁵. Nitrogen (Tesla Vrchlábi), used as an inert gas, contained 0.1% (v/v) of oxygen. Melting points were determined with a Kofler hot plate microscope and are uncorrected.

Analytical methods. ¹H-NMR spectra of the new esters were measured on Tesla BS 477 spectrometer (a modified model working at 60 MHz). IR spectra of these compounds were recorded with a double-beam Zeiss (Jena) spectrophotometer, model UR 20 (KBr prisms). The rate of the glycolysis of amides was measured by determining the amount of the ammonia released during the reaction²; the ammonia which was removed from the reactor by a stream of nitrogen was absorbed in 500 ml of 0.1M-H₂SO₄ and the ammonium sulphate content in samples taken at fixed time intervals was determined by amperometric oxidimetry using the hypochlorite method². The amount of the unreacted amide in the reaction mixture was determined by the procedure

described earlier². Material balance of the glycolysis was calculated for the reaction of benzamide with ethylene glycol (the initial molar ratio 1 : 30) catalysed by PbO ($2 \cdot 10^{-3}$ mol kg⁻¹) and carried out at $197 \pm 0.5^\circ\text{C}$. The reaction was stopped after 8 h and the mixture was analysed by gel-permeation chromatography on Kieselgel-60 (Merck) using dioxane as an eluent. According to this analysis, 90% of 2-hydroxyethyl benzoate and 2.0–2.5% of ethylene glycol di-benzoate were formed; the mixture contained further the unreacted benzamide.

Kinetic measurements. The rates of the uncatalysed and catalysed reactions were measured in an apparatus and by the procedure described in the previous work². Measurements were carried out under normal pressure at temperatures ranging from 167 to 197°C and using the amide to glycol initial molar ratio 1 : 30. The effect of the initial concentration of 2-hydroxyethyl benzoate on the rate of the benzamide glycolysis with ethylene glycol was measured at initial concentrations of benzamide 0.4539 mol kg⁻¹, ethylene glycol 13.6170 mol kg⁻¹ and 2-hydroxyethyl benzoate 0.2270 mol kg⁻¹ and 0.6809 mol kg⁻¹. At 0.025–0.050 mol of the amides, a 5 l/h nitrogen flow rate through the reactor and a stirring intensity of 500 rev./min, the reactions took place in the kinetic region. In all experiments the reaction mixtures were homogeneous. Weight changes of the reaction mixtures due to ammonia desorption corresponded for the above amounts of the amides to 0.8–1.0% and were not considered in deriving kinetic equations. Reaction rate was measured at least to 90% conversion of the amides. Each of the reaction constants is an average of two, three or four separate measurements and its value was refined by the least-squares method.

Isolation of the products of the glycolysis of amides with ethylene glycol. The reaction mixture from the kinetic measurement of the rate of the catalysed reaction was cooled to 25°C and freed of the glass scattering (a thin-walled glass ampoule was used to introduce the amide-catalyst mixture into the glycol preheated to the reaction temperature and then scattered by a stirrer). The excess glycol was distilled off under nitrogen in vacuo and the distillation residue was fractionated or crystallised from an appropriate solvent to give the corresponding 2-hydroxyethyl ester, RCO₂(CH₂)₂OH, and glycol diester, (RCO₂CH₂)₂. 2-Hydroxyethyl *m*-nitrobenzoate (22% yield), m.p. 52–53°C (ether) (ref.¹² m.p. 53–55°C). Ethylene glycol di(*m*-nitrobenzoate) (23%), m.p. 136.0–136.5°C (acetone) (ref.¹⁶ m.p. 134°C). 2-Hydroxyethyl *p*-nitrobenzoate (19%), m.p. 77.0–77.5°C (benzene) (ref.¹² m.p. 77–78°C). Ethylene glycol di(*p*-nitrobenzoate) (23%), m.p. 141–142°C (acetone) (ref.¹⁶ m.p. 144°C). 2-Hydroxyethyl *m*-methylbenzoate (27%), b.p. 164–166°C/9 Torr (ref.¹² b.p. 172–175°C/11 Torr). 2-Hydroxyethyl *p*-methylbenzoate (24%), b.p. 130–132°C/1 Torr (ref.¹² b.p. 180–183°C/11 Torr). Ethylene glycol di(*p*-methylbenzoate) (19%), m.p. 118–119°C (cyclohexanol) (ref.¹⁷ m.p. 116–117°C). 2-Hydroxyethyl *p*-chlorobenzoate (20%), m.p. 72–73°C (tetrachloromethane-light petroleum) (ref.¹⁸ m.p. 71.0–71.5°C). Ethylene glycol di(*p*-chlorobenzoate) (24%), m.p. 141.0–141.5°C (aq. N,N-dimethylformamide) (ref.¹⁹ m.p. 140°C). Ethylene glycol di(*p*-bromobenzoate), m.p. 156–157°C (acetone) (ref.¹⁶ m.p. 158°C). Ethylene glycol di(*p*-methoxybenzoate) (35%), m.p. 115.0–115.5°C (glacial acetic acid) (ref.²⁰ m.p. 114°C). All isolated esters gave elemental analyses corresponding to the above structures. Relatively low yields of the esters were due to the product losses during separation of the mixtures of mono- and diesters prepared on a small scale; no attempts were made to optimize the yields.

Characteristics of New Esters

2-Hydroxyethyl *p*-bromobenzoate (16%), m.p. 42.0–43.5°C (ethanol). For C₉H₉BrO₃ (245.1) calculated: 44.10% C, 3.70% H, 32.60% Br; found: 44.13% C, 3.88% H, 32.20% Br. ¹H-NMR spectrum (in CCl₄ with respect to hexamethyldisilane): 4 H (aromatic protons), (m) 8.28, (m)

8.15, (m) 7.70, (m) 7.56 δ p.p.m.; 1 H (hydroxyl proton), 3.31 δ p.p.m.; 4 H (methylene protons), a multiplet centered at 4.12 δ p.p.m. IR spectrum (in CCl_4): $\nu(\text{OH})$ 3400 cm^{-1} ; $\nu(\text{C}=\text{O})$ 1717 cm^{-1} .

Ethylene glycol di(m-methylbenzoate) (30%), m.p. 59.0—59.5°C (aq. ethanol). For $\text{C}_{18}\text{H}_{18}\text{O}_4$ (298.3) calculated: 72.46% C, 6.08% H; found: 72.30% C, 6.27% H. $^1\text{H-NMR}$ spectrum (in CCl_4 with respect to hexamethyldisilane): 8 H (aromatic protons), 8.12, 8.06, 7.62, 7.52 δ p.p.m. (all unresolved doublets); 4 H (methylene protons), (s) 4.89 δ p.p.m.; 6 H (methyl protons), (s) 2.71 δ p.p.m. IR spectrum (in CCl_4): $\nu(\text{C}=\text{O})$ 1736 cm^{-1} .

2-Hydroxyethyl m-trifluoromethylbenzoate (17%), b.p. 112—114°C/0.5 Torr. For $\text{C}_{10}\text{H}_9\text{F}_3\text{O}_3$ (234.2) calculated: 51.28% C, 3.87% H, 24.33% F; found: 51.13% C, 3.63% H, 24.29% F. $^1\text{H-NMR}$ spectrum (in CCl_4 with respect to hexamethyldisilane): 4 H (aromatic protons), an unresolved multiplet centered at 8.03 δ p.p.m.; 1 H (hydroxyl proton), (s) 3.36 δ p.p.m.; 4 H (methylene protons), an unresolved multiplet centered at 4.07 δ p.p.m. IR spectrum (in CCl_4): $\nu(\text{OH})$ 3420 cm^{-1} ; $\nu(\text{C}=\text{O})$ 1740 cm^{-1} .

Ethylene glycol di(m-trifluoromethylbenzoate) (26%), b.p. 152—154°C/0.5 Torr. For $\text{C}_{18}\text{H}_{12}\text{F}_6\text{O}_4$ (406.3) calculated: 53.21% C, 2.98% H; found: 53.20% C, 3.28% H. $^1\text{H-NMR}$ spectrum (in CCl_4 with respect to hexamethyldisilane): 8 H (aromatic protons), (m) 8.62, (m) 8.43, (m) 7.90 and (m) 7.42 δ p.p.m.; 4 H (methylene protons), (s) 4.86 δ p.p.m. IR spectrum (in CCl_4): $\nu(\text{C}=\text{O})$ 1735 cm^{-1} .

RESULTS AND DISCUSSION

Rates of the uncatalysed and lead(II) oxide-catalysed glycolysis of benzamide and a series of *ortho*-, *meta*-, and *para*-substituted benzamides with glycols in excess (the amide to glycol initial molar ratio 1 : 30) under normal pressure were measured within a temperature region of 167 to 197°C and expressed by the rates of ammonia formation. The plot of $\log [A]_0/[A]$ vs time for uncatalysed glycolysis of benzamide (A) with ethylene glycol and for the reaction catalysed by lead(II) oxide gave straight lines (Fig. 1) whose slopes multiplied by a factor of 2.303 gave in both cases pseudo-first order rate constants, k_0 and k_{obs} , respectively; the constant k_0 determined for the uncatalysed glycolysis of benzamide by ethylene glycol at 197°C had a value of $0.0195 \pm 0.0005 \text{ h}^{-1}$ ($r = 0.9986$) and the constant k_{obs} for the same reaction and temperature in the presence of lead(II) oxide ($[\text{PbO}] = 2 \cdot 10^{-3} \text{ mol kg}^{-1}$) equalled to $0.2106 \pm 0.0006 \text{ h}^{-1}$ ($r = 0.9999$).

It is known that glycol esters of carboxylic acids undergo readily a condensation reaction at elevated temperatures in the presence of heavy metals²¹ and this reaction may compete for the same catalyst with the glycolysis of the amide. As it was found, however, by measuring the rate of glycolysis of benzamide at varying initial concentrations of 2-hydroxyethyl benzoate, the kinetics of the glycolysis is not influenced in the studied region by the concentration of this ester (Fig. 1). By this noninhibiting effect the metal ion-catalysed glycolysis of amides differs significantly from the metal ion-catalysed glycolysis of aromatic nitriles whose rate decreases with increasing concentration of the resulting ester²². These facts, an instant removal of ammonia

from the reaction mixture that allowed to neglect the reversible reaction of the ester with ammonia, the low concentration of the amide resulting in only slight volume change and the finding that the glycolytic reaction proceeds, although only to a small extent, also in the absence of the metal catalyst, should be considered; they lead to conclusion that glycolysis of the monoamide by the glycol can be described by kinetic equation (1) where k_c is the pseudo-first order rate constant of the catalytic reaction

$$-d[A]/dt = (k_0 + k_c) [A] \quad (1)$$

calculated by subtracting k_0 from k_{obs} . The validity of this relation up to 90% amide conversion in the presence of various metal catalysts was evidenced in the previous work². The values of rate constants k_{obs} determined for varying concentrations of lead(II) oxide and the respective calculated values of k_c are presented in Table I. The plot of $\log k_c$ vs $\log [PbO]$ for the catalyst concentrations from $5 \cdot 10^{-4}$ to $3 \cdot 10^{-3}$ mol kg⁻¹ showed a straight line. The slope of this line refined by the least squares method confirmed the half order of the glycolytic reaction in lead(II) oxide. Kinetic equation (1) for glycolysis of benzamide with excess ethylene glycol catalysed by lead(II) oxide (B) can be then re-written into Eq. (2) where k is the

$$-d[A]/dt = k_0[A] + k[A] [B]^{1/2} \quad (2)$$

pseudo-1.5 order rate constant for the metal ion-catalysed reaction. The value of constant k which was calculated according to Eq. (3) corresponds at $197 \pm 0.5^\circ C$ to 4.2731 ± 0.0111 kg^{1/2} mol^{-1/2} h⁻¹.

$$k = (k_{obs} - k_0)/[B]^{1/2} \quad (3)$$

FIG. 1
Plot of $\log [A]_0/[A]$ vs Time for Glycolysis of Benzamide (A) with Ethylene Glycol in the Absence of a Catalyst 1, in the Presence of $C_6H_5CONH_2.CdCl_2$ (D) 2 or Lead(II) Oxide 3-5 as Catalysts and at Varying 2-Hydroxyethyl Benzoate (E) Initial Concentrations 4, 5

$[A]_0 = 0.4539$ mol kg⁻¹, $[C_2H_6O_2]_0 = 13.6170$ mol kg⁻¹, $[D] = 2 \cdot 10^{-3}$ mol . kg⁻¹, $[PbO] = 2 \cdot 10^{-3}$ mol kg⁻¹, 4 $[E]_0$: $[A]_0 = 0.5$, 5 $[E]_0/[A]_0 = 1.5$; temperature $197 \pm 0.5^\circ C$.

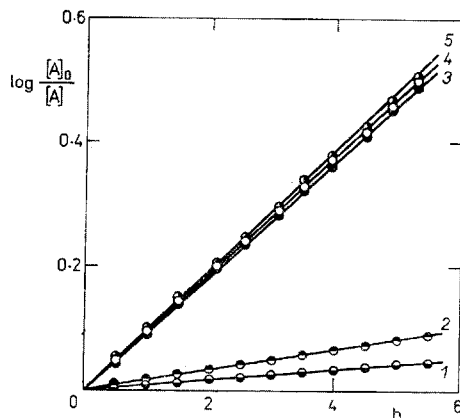


TABLE I

Dependence of Pseudo-First Order Rate Constants k_{obs} and k_c for the Reaction of Benzamide with Ethylene Glycol upon the Concentration of Lead(II) Oxide as Catalyst

$[\text{C}_6\text{H}_5\text{CONH}_2]_0 = 0.4539 \text{ mol kg}^{-1}$; $[\text{C}_2\text{H}_6\text{O}_2]_0 = 13.6170 \text{ mol kg}^{-1}$; temperature $197 \pm \pm 0.5^\circ\text{C}$; rate constants in h^{-1} .

Catalyst conc. mol kg^{-1}	k_{obs}	r^a	k_c
$5 \cdot 10^{-4}$	0.1195 ± 0.0006	0.9996	0.1000
$1 \cdot 10^{-3}$	0.1569 ± 0.0006	0.9997	0.1374
$1.26 \cdot 10^{-3}$	0.1758 ± 0.0006	0.9998	0.1563
$2 \cdot 10^{-3}$	0.2106 ± 0.0006	0.9999	0.1911
$3 \cdot 10^{-3}$	0.2513 ± 0.0006	0.9997	0.2318

^a The correlation coefficient for k_{obs} .

Plotting the values of k_{obs} determined at $197 \pm 0.5^\circ\text{C}$ against the square roots of the lead(II) oxide concentrations ($5 \cdot 10^{-4}$ to $3 \cdot 10^{-3} \text{ mol kg}^{-1}$) yielded a linear dependence (Fig. 2). The constant k calculated from the slope of this dependence had a value of $4.2758 \pm 0.0841 \text{ kg}^{1/2} \text{ mol}^{-1/2} \text{ h}^{-1}$.

Provided that the linear dependence of k_{obs} vs $[\text{PbO}]^{1/2}$ holds also for the region of lead(II) oxide concentrations lower than $5 \cdot 10^{-4} \text{ mol kg}^{-1}$, and that benzamide is transformed in the presence of a metal catalyst by parallel uncatalysed and metal ion-catalysed reactions, then the line in Fig. 2 extrapolated to zero concentration

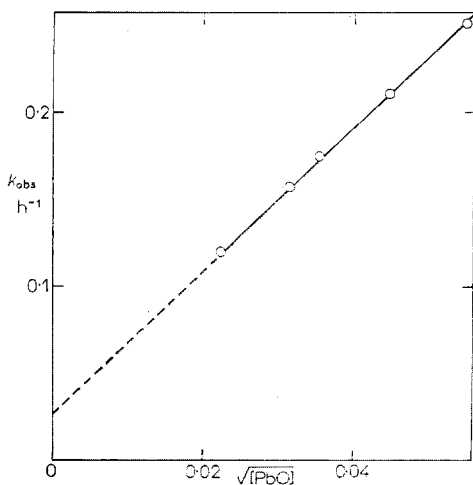


FIG. 2
Linear Dependence of the Pseudo-First Order Rate Constant k_{obs} for Glycolysis of Benzamide with Ethylene Glycol on the Square Root of Concentrations of Lead(II) Oxide as Catalyst

of the catalyst should intersect the ordinate at the point which corresponds to the value of constant k_0 . The constant k_0 calculated from the intercept (Fig. 2) has a value of $0.0218 \pm 0.0030 \text{ h}^{-1}$ ($r = 0.9994$) and differs thus by about 11% from the above-mentioned and independently determined value of k_0 . This fact provides further support for the transformation of the amide by parallel uncatalysed and metal ion-catalysed reactions.

Data on temperature dependence of the pseudo-first order rate constant k_0 and pseudo-1.5 order rate constant k are summarized in Table II. The plot of $\log k$

TABLE II

Temperature Dependence of Pseudo-First Order Rate Constant k_0 for Uncatalysed Glycolysis of Benzamide with Ethylene Glycol and of Pseudo-1.5 Order Rate Constant k for the Lead(II) Oxide-Catalysed Reaction

$[\text{C}_6\text{H}_5\text{CONH}_2]_0 = 0.4539 \text{ mol kg}^{-1}$; $[\text{C}_2\text{H}_6\text{O}_2]_0 = 13.6170 \text{ mol kg}^{-1}$; $[\text{PbO}] = 2 \cdot 10^{-3} \text{ mol kg}^{-1}$.

Temperature K	k_0 h^{-1}	r^a	k $\text{kg}^{1/2} \text{ mol}^{-1/2} \text{ h}^{-1}$
470	0.0195 ± 0.0005	0.9986	4.2731 ± 0.0111
460	0.0150 ± 0.0001	0.9996	3.1707 ± 0.0023
450	0.0100 ± 0.0005	0.9963	2.2025 ± 0.0112
440	0.0064 ± 0.0001	0.9979	1.5049 ± 0.0022

^a The correlation coefficient for k_0 .

TABLE III

Structure Effects of Aliphatic Glycols (C) on the Rate of Glycolysis of Benzamide in the Absence and Presence of Lead(II) Oxide as Catalyst

$[\text{C}_6\text{H}_5\text{CONH}_2]_0 = 0.4539 \text{ mol kg}^{-1}$; $[\text{C}]_0 = 13.6170 \text{ mol kg}^{-1}$; $[\text{PbO}] = 2 \cdot 10^{-3} \text{ mol kg}^{-1}$; temperature $187 \pm 0.5^\circ\text{C}$; the rate constants in h^{-1} .

Glycol	k_0	r^a	k_{obs}	r^b	k_c
Ethylene glycol	0.0150 ± 0.0001	0.9996	0.1568 ± 0.0006	0.9997	0.1418
Trimethylene glycol	0.0110 ± 0.0001	0.9995	0.1307 ± 0.0005	0.9997	0.1197
Tetramethylene glycol	0.0049 ± 0.0001	0.9975	0.1155 ± 0.0008	0.9993	0.1106
Propylene glycol	0.0070 ± 0.0001	0.9980	0.1274 ± 0.0005	0.9998	0.1202
Neopentyl glycol	— ^c	—	0.0895 ± 0.0005	0.9997	0.0895

^a The correlation coefficient for k_0 ; ^b the correlation coefficient for k_{obs} ; ^c the reaction proceeded at an immeasurably slow rate.

against the reciprocal values of the absolute temperature gives a straight line from the slope of which the activation energy, ΔE , of glycolysis of benzamide with ethylene glycol catalysed by lead(II) oxide was calculated; the value of ΔE refined by the least-squares method is $14.38 \pm 0.41 \text{ kcal mol}^{-1}$ ($r = 0.9992$). The rate constant

$$k_{\text{PbO}} = 2.1 \times 10^7 \exp [(-14\,380 \pm 410)/RT] \text{ kg}^{1/2} \text{ mol}^{-1/2} \text{ h}^{-1} \quad (4)$$

k_{PbO} can be thus expressed by Eq. (4). The activation enthalpy, ΔH^\ddagger , and activation entropy, ΔS^\ddagger , were $13.45 \pm 0.41 \text{ kcal mol}^{-1}$ and $-44.2 \pm 0.9 \text{ e.u.}$ (by using the recalculated value of the rate constant k equaling to $1.187 \cdot 10^{-3} \text{ kg}^{1/2} \text{ mol}^{-1/2} \text{ s}^{-1}$), respectively. The value of ΔE found in this work agrees well with the values reported earlier for this reaction catalysed by sodium methoxide² ($14.99 \text{ kcal mol}^{-1}$) and cadmium acetate² ($14.58 \text{ kcal mol}^{-1}$) and does not differ much from the ΔE values determined for hydrolysis of glycinamide ($13.9 \text{ kcal mol}^{-1}$) (ref.²³) and acetamide ($14.3 \text{ kcal mol}^{-1}$) (ref.²⁴) catalysed by cupric ions. The value of ΔS^\ddagger found by us for the reaction under study is comparable with that determined for the amine-catalysed aminolysis of phenyl acetate by methylamine (-45.6 e.u.) (ref.²⁵).

To ascertain the influence of the structure of aliphatic glycols on the course of the glycolysis reaction, the rates of benzamide transformation were also measured in an excess of propylene glycol, trimethylene glycol, tetramethylene glycol and neopentyl glycol (the amide to glycol initial molar ratio 1 : 30). The values of the corresponding pseudo-first order rate constants k_0 , k_{obs} and k_c are recorded in Table III. As it is evident from these data, the rate of both the uncatalysed and lead(II) oxide-catalysed glycolysis of benzamide decreases with increasing length and branching of the glycol carbon chain. Differences in the values of rate constants k_c in the series of catalysed reactions are, however, very small and lie within one order of magnitude. Similarly small differences in the values of constants k_0 were found for the series of uncatalysed reactions, with the exception of the glycolysis of benzamide with neopentyl glycol which proceeded even at 187°C at an immeasurable rate. This small dependence of the reaction rate upon the carbon chain length of glycols distinctly differentiates the glycolysis of benzamide from the metal ion-catalysed glycolysis of aromatic nitriles with aliphatic glycols²². In the latter reaction the rate constants for the glycolysis with ethylene glycol and trimethylene glycol differ by one order of magnitude; when compared to trimethylene glycol, tetramethylene glycol is in turn by one order of magnitude less reactive.

The effect of *ortho*-, *meta*- and *para*-substituents on the aromatic ring of benzamide upon the rate of both uncatalysed and metal ion-catalysed glycolysis with ethylene glycol was determined for the series of 13 benzamide derivatives. Both the uncatalysed and catalysed glycolysis of *meta*- and *para*-substituted benzamides, whose rates were measured up to 90% conversion of the substrate, were first-order in the benzamide derivatives. The values of the corresponding pseudo-first order rate constants

TABLE IV

Pseudo-First Order Rate Constants for Glycolysis of *meta*- and *para*-Substituted Benzamides ($X-C_6H_4CONH_2$) with Ethylene Glycol in the Absence and Presence of Lead(II) Oxide as Catalyst

$[X-C_6H_4CONH_2]_0 = 0.4539 \text{ mol kg}^{-1}$; $[C_2H_6O_2]_0 = 13.6170 \text{ mol kg}^{-1}$; $[PbO] = 2 \cdot 10^{-3} \text{ mol kg}^{-1}$; temperature $197 \pm 0.5^\circ\text{C}$; the rate constants in h^{-1} .

Substituent X	k_0	r^a	k_{obs}	r^b	k_c
<i>p</i> -Nitro	0.0426 ± 0.0008	0.9998	0.4457 ± 0.0013	0.9998	0.4031
<i>m</i> -Nitro	0.0374 ± 0.0001	0.9999	0.4191 ± 0.0014	0.9998	0.3817
<i>m</i> -Trifluoromethyl	0.0282 ± 0.0006	0.9993	0.3247 ± 0.0009	0.9998	0.2965
<i>p</i> -Bromo	0.0240 ± 0.0005	0.9997	0.2656 ± 0.0012	0.9995	0.2416
<i>p</i> -Chloro	0.0244 ± 0.0006	0.9996	0.2594 ± 0.0005	0.9999	0.2350
Hydrogen	0.0195 ± 0.0005	0.9996	0.2106 ± 0.0006	0.9999	0.1911
<i>m</i> -Methyl	0.0169 ± 0.0005	0.9988	0.2000 ± 0.0005	0.9999	0.1831
<i>p</i> -Methyl	0.0164 ± 0.0005	0.9992	0.1790 ± 0.0006	0.9998	0.1626
<i>p</i> -Methoxy	0.0098 ± 0.0005	0.9984	0.1149 ± 0.0005	0.9958	0.1051

^a The correlation coefficient for k_0 ; ^b the correlation coefficient for k_{obs} .

k_0 , k_{obs} and k_c are summarized in Table IV. From comparison of rate constants k_0 for the series of uncatalysed reactions and rate constants k_c for the series of catalysed reactions it follows that their values decrease in the order $p\text{-NO}_2 > m\text{-NO}_2 > m\text{-CF}_3 > p\text{-Br} \approx p\text{-Cl} > \text{H} > m\text{-CH}_3 > p\text{-CH}_3 \gg p\text{-OCH}_3$, indicating the rate-retarding effect of electron-donating substituents. The dependences of $\log k_0$ and k_c on Hammett σ constants (Fig. 3) were linear; an exception was *p*-methoxybenz-

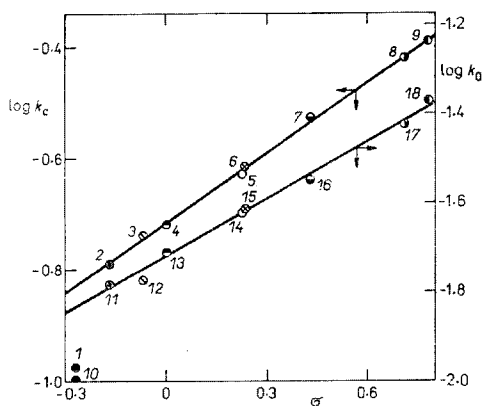


FIG. 3

Hammett Correlation for Glycolysis of *meta*- and *para*-Substituted Benzamides with Ethylene Glycol Catalysed by Lead(II) Oxide 1–9 and for the Uncatalysed Glycolysis Reaction 10–18

1, 10 *p*-OCH₃, 2, 11 *p*-CH₃, 3, 12 *m*-CH₃, 4, 13 H, 5, 14 *p*-Cl, 6, 15 *p*-Br, 7, 16 *m*-CF₃, 8, 17 *m*-NO₂, 9, 18 *p*-NO₂.

amide whose point deviated significantly from the best fit line. The reaction constant ρ_0 for the uncatalysed reaction, calculated without inclusion of *p*-methoxybenzamide, had a value of 0.43 ± 0.03 ($r = 0.9956$) and the analogously calculated reaction constant ρ_c for the reaction catalysed by lead(II) oxide had a value of 0.42 ± 0.01 ($r = 0.9992$). When *p*-methoxybenzamide was included into the Hammett correlation, the constant ρ_0 equaled to 0.50 ± 0.05 ($r = 0.9642$) and the constant ρ_c had a value of 0.48 ± 0.04 ($r = 0.9743$). The Hammett correlation for the uncatalysed glycolysis of *meta*- and *para*-substituted benzamides with ethylene glycol can be expressed by Eq. (5) and the correlation for the lead(II) oxide-catalysed reaction by Eq. (6).

$$\log k_0 = (0.50 \pm 0.05) \sigma - 1.71, \quad (5)$$

$$\log k_c = (0.48 \pm 0.04) \sigma - 0.75. \quad (6)$$

Anomalous behaviour of the *p*-methoxy group in the Hammett correlation (Fig. 3) has been reported also by other authors and explained by a mesomeric *para* interaction with the reaction center²⁶. The low and positive values of reaction constants ρ_0 and ρ_c indicate that both uncatalysed and metal ion-catalysed glycolysis of benzamide and *meta*- and *para*-substituted benzamides is a nucleophilic substitution reaction with the low sensitivity to polar substituent effects. In this connection it is worthy of note that similarly low sensitivity to polar substituent effects was also observed

TABLE V

Pseudo-First Order Rate Constants for Glycolysis of *ortho*-Substituted Benzamides (*o*-X-C₆H₄.CONH₂) with Ethylene Glycol in the Absence and Presence of Lead(II) Oxide as Catalyst
 $[o\text{-X-C}_6\text{H}_4\text{CONH}_2]_0 = 0.4539 \text{ mol kg}^{-1}$; $[\text{C}_2\text{H}_6\text{O}_2]_0 = 13.6170 \text{ mol kg}^{-1}$; $[\text{PbO}] = 2 \cdot 10^{-3} \text{ mol kg}^{-1}$; temperature $197 \pm 0.5^\circ\text{C}$; the rate constants in h^{-1} .

Substituent <i>o</i> -X	k_0	r^a	k_{obs}	r^b	k_c
Nitro	— ^c	—	0.0376 ± 0.0001	0.9999	0.0376
Bromo	0.0082 ± 0.0004	0.9657	0.0933 ± 0.0003	0.9999	0.0851
Chloro	0.0096 ± 0.0003	0.9999	0.1129 ± 0.0003	0.9999	0.1023
Methyl	0.0087 ± 0.0001	0.9992	0.0943 ± 0.0004	0.9998	0.0856
Methoxy	0.0527 ± 0.0001	0.9987	0.2982 ± 0.0008	0.9999	0.2455

^a The correlation coefficient for k_0 ; ^b the correlation coefficient for k_{obs} ; ^c the reaction proceeded at an immeasurably slow rate.

for the acid-catalysed hydrolysis of *meta*- and *para*-substituted benzamides ($\rho = 0.12$) (ref.²⁷).

The kinetics of glycolysis of five *ortho*-substituted benzamides with ethylene glycol was measured in the absence and presence of lead(II) oxide as a catalyst. The uncatalysed and catalysed reactions, which were followed up to 90% conversions of the substrates, were always first-order in the benzamide derivative. The values of the corresponding pseudo-first order rate constants k_0 , k_{obs} and k_c are listed in Table V. From comparison of the values of rate constants k_0 for the series of uncatalysed reactions and of constants k_c for the series of catalysed reactions it follows that the rate of glycolysis of *ortho*-substituted benzamides decreases in the order $OCH_3 > Cl > CH_3 > Br \gg NO_2$; the uncatalysed glycolysis of *o*-nitrobenzamide proceeds at an immeasurable rate. An attempt to correlate the rate constants k_c found for glycolysis of *ortho*-substituted benzamides with Taft σ^* polar substituent constants led to a poor linear correlation which was characterized by the correlation coefficient $r = 0.9053$. The correlation by the two-parameter Taft equation yielded better results ($r = 0.9973$), the δ constant being 0.47 ± 0.00 and ρ^* constant 0.02 ± 0.01 ; the Taft correlation according to this relation could be expressed by Eq. (7).

$$\log k_c = (0.47 \pm 0.00) E_s - (0.02 \pm 0.01) \sigma^* - 1.07. \quad (7)$$

An excellent correlation has been, however, obtained by plotting $\log k_c$ against the E_s steric constant for which the correlation coefficient r was 0.9997. The rate constant δ determined from the slope of the line and refined by the least-squares method had a value of 0.53 ± 0.01 ; hence, the Taft correlation can be best expressed by Eq. (8).

$$\log k_c = (0.53 \pm 0.01) E_s - 1.07. \quad (8)$$

The low value of constant ρ^* in Eq. (7) and the fact that optimal correlation was achieved for the $\log k_c$ vs E_s dependence indicate that polar effects in the metal ion-catalysed glycolysis of *ortho*-substituted benzamides are very small and that primarily steric requirements of the *ortho* substituents play predominant role in this reaction series. This finding is in accordance with the sensitivity to steric effects of aminolysis of esters, the reverse reaction to glycolysis, generally confirmed by the earlier kinetic investigations²⁸. As follows from the positive value of the constant δ , steric effects exert rate-retarding effect upon the glycolytic reaction. It is worthy of note that the value of constant δ found for this reaction is not far from the value of the same constant determined by Reid for acid hydrolysis of *ortho*-substituted benzamides²⁵ ($\delta = 0.81$); as found by Leisten, the rate of the latter reaction also decreases with increasing steric requirements of *ortho* substituents and is independent of their polarity²⁹.

In the study preceding this work it was stated that the ability of a metal compound to form a metal glycolate by the action of a glycol is a *conditio sine qua non* for its catalytic activity in the glycolysis of aromatic carboxamides². In an effort to provide further support for this assumption and to examine the effect of strong acid anion upon the catalytic effectiveness of the metal ion, the rate of glycolysis of benzamide with ethylene glycol was measured in the presence of a stable 1 : 1 complex of benzamide with cadmium dichloride. As follows from Fig. 1, this complex shows very low activity ($k_{\text{obs}} = 0.039 \text{ h}^{-1}$ and $k_c = 0.019 \text{ h}^{-1}$ at $[\text{Cd}^{2+}] = 2 \cdot 10^{-3} \text{ mol kg}^{-1}$ and $197 \pm 0.5^\circ\text{C}$) compared to the relatively high activity of cadmium acetate dihydrate for the identical reaction ($k_c = 0.182 \text{ h}^{-1}$) at nearly the same metal ion concentration ($[\text{Cd}^{2+}] = 1.3 \cdot 10^{-3} \text{ mol kg}^{-1}$) and temperature. The effectiveness of the benzamide-cadmium dichloride complex and cadmium acetate in the glycolytic reaction under study agrees well with that of the acetates and nitrates of cadmium, lead(II), thallium(I) and calcium as catalysts for reesterification of bornyl acetate with methanol. The nitrates of these metals were very little active or fully inactive compared to the corresponding metal acetates³⁰. The high catalytic activity of cadmium salts of weak acids can be accounted for by formation of cadmium glycolates that are effective for glycolysis of amides. On the other hand, cadmium salts of strong inorganic acids, lacking the metal-oxygen bond, provide little or no opportunity for the formation of active metal glycolates. In this connection it warrants mention that *e.g.* tin (II) oxide and tin(II) oxalate (the latter being a salt of a very strong acid but bearing the metal-oxygen bond and being thus able to form tin(II) glycolate, similarly as tin(II) oxide) show the same catalytic activity in the glycolysis of aromatic amides².

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