QUATERNARY SALTS OF N,N-DIMETHYLAMINOETHYL ESTERS OF PIVALIC AND 2-METHYL-3-METHOXYPROPIONIC ACID AND THEIR HYDROLYSIS*
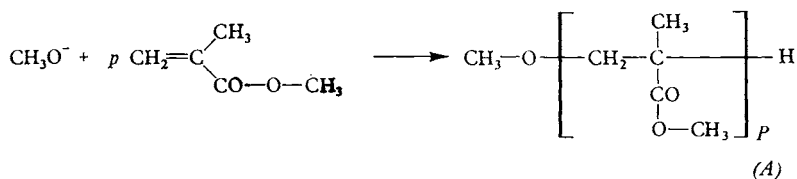
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The synthesis and kinetics of quaternization of model compounds of poly(N,N-dimethylamino-ethyl methacrylate) in water–alcoholic solutions brought about by methyl iodide and the alkaline hydrolysis of products in water have been investigated. N,N-Dimethylaminoethyl pivalate was selected as a model of the structural unit of the reported polymer; N,N-dimethylaminoethyl-2--methyl-3-methoxypropionate was the model of the terminal unit of the anionically prepared polymer.

The kinetics of chemical transformations of polymers in which several polymer effects are operative simultaneously requires modelling of the partial process or of the effect by means of suitable low-molecular weight compounds, if a detailed description is wanted. Such description of the reactions of polymers can be adequately achieved by studying transformations of a number of oligomers, *i.e.* chemically well characterized species which serve as model compounds in the investigation of polymers. Oligomers of the methacrylate series can be prepared as derivatives of oligo(methyl methacrylates) which can be obtained in a mixture by reacting sodium methoxide with the methanolic solution of methyl methacrylate:

$$CH_3O^- + p\ CH_2{=}C\underset{CO{-}O{-}CH_3}{\overset{CH_3}{\big\langle}} \longrightarrow CH_3{-}O{-}\left[{-}CH_2{-}\underset{\underset{O{-}CH_3}{\overset{|}{CO}}}{\overset{\overset{CH_3}{|}}{C}}{-}\right]_P{-}H$$

(A)

A problem then arises how to separate the oligomers according to the degree of polymerization (P) and within the framework of a certain degree of polymerization according to the stereoisomerism of the oligomeric backbone. The first member, where $P = 1$, is a mixture of two enantiomers which — with respect to chemical

transformations — are reaction equivalent; in this case it is sufficient to achieve perfect separation with respect to the degree of polymerization.

In this study we describe the preparation of dimethylaminoethyl esters of pivalic and 2-methyl-3-methoxypropionic acid, the kinetics of their quaternization with methyl iodide in a water–alcoholic mixture and the kinetics of alkaline hydrolysis of quaternized products with aqueous sodium hydroxide. N,N-Dimethylamino-ethyl-2-methyl-3-methoxypropionate is the first member of the oligomeric series and at the same time a model compound of the terminal unit of anionically prepared oligomers or polymers of N,N-dimethyl aminoethyl methacrylate; N,N-dimethyl-aminoethyl pivalate models the structural unit (internal) of the polymer. By means of the simplest compounds, the reactions investigated in this study, *i.e.* quaterniza-tion and alkaline hydrolysis, model the behaviour of polyelectrolytes based on poly (2-methacryloyloxyethyl)trimethyl ammonium salts and their nonquaternary precursors in the synthesis and under demanding conditions of application of the polymers.

By using the reaction between methyl iodide and poly(N,N-dimethylaminoethyl methacrylate), it is possible to prepare strongly dissociated quaternary polyelectro-lytes:

(B)
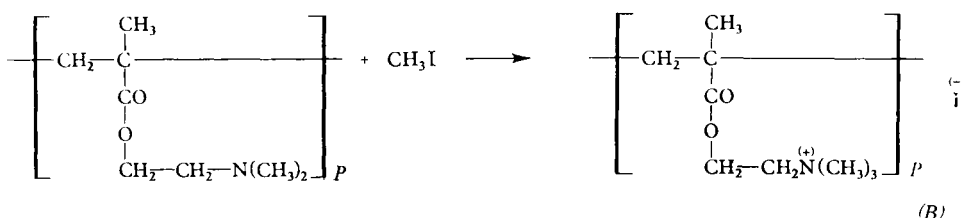
A distinct rise in polarity accompanying the quaternization reaction is also reflected in the solution behaviour of the polymer during the reaction. While the starting polymer (as a base) is not soluble in water, but can very readily be dissolved in ethanol, water is a good solvent for the final product, and ethanol due to its low polarity cannot keep the polymer dissolved in solution. Hence, the reaction carried out in ethanol soon leads to the separation of an incompletely reacted polymer, which renders impossible a kinetic study of the reaction. The use of mixed solvents ethanol–water leads to interesting reaction courses[1], which show some kinetic anomalies depending on the tacticity of the starting polymer and on the composition of the solvent. In solutions with a high content of ethanol (above 57%) the mass rate constant of quaternization reaction of polymers increases from its initially low value, while in mixtures poor in ethanol the same constant decreases from the ori-ginally high value. In solutions containing 57% of ethanol the rate constant is con-version-independent, so that from the kinetic point of view the polymers behave as low-molecular weight compounds. In this study we have therefore investigated the

kinetics of quaternization of the simplest model compounds in a solvent with 57% of ethanol, in order to obtain quantitative data on the reaction course which later on might be used in a comparison with the behaviour of the polymers.

EXPERIMENTAL

Preparation of Compounds

Methyl ester of 2-methyl-3-methoxypropionic acid (I) was prepared by a procedure used in the anionic oligomerization of methyl methacrylate[8] in which the ratio of the components has been adjusted so that predominantly an adduct of methanol and methyl methacrylate is formed: A mixture of methyl methacrylate (187·2 g, 1·870 mol), absolute methanol (58·21 g, 1·82 mol), solution of sodium methoxide in methanol (16·2 g of a 15·5% solution, 0·0465 mol), 2,4,6-tris-(dimethylaminomethyl)phenol (1·5 g, 0·0057 mol) was heated 5 h, *i.e.* until a constant boiling temperature (75·0°C) was reached. After neutralization with dilute hydrochloric acid (1 : 1) the mixture was shaken with water (1 : 1), and the organic phase was separated. Distillation gave 118·3 g (47·9%) of the product, b.p. 146·3°C, n_D^{20} 1·4055, d^{25} 0·97185 g cm^{-3}. The reported[8] values are: b.p. 147°C, n_D^{20} 1·4055. For $C_6H_{12}O_3$ (132·2) calculated: 54·52% C, 9·15% H; found: 54·52% C, 9·39% H.

3-Methoxy-2-methylpropionic acid (II) was prepared by the alkaline hydrolysis of *I*. A mixture of *I* (97·9 g, 0·829 mol) and sodium hydroxide (37·3 g, 0·933 mol) in water (210 g, 11·67 mol) was heated to boil for 8 h. After neutralization with hydrochloric acid (100 g of a 38% solution, 1·03 mol) the mixture was extracted with benzene (3 × 50 ml), the organic phase was separated, the solvent was removed by distillation, and distillation yielded 33·1 g (37·8%) of the product, b.p. 69°C/133·3 Pa, n_D^{20} 1·4198. The reported[9] values are b.p. 83°C/400 Pa and n_D^{20} 1·4192. For $C_5H_{10}O_3$ (118·1) calculated: 50·83% C, 8·53% H: found 50·69% C, 8·23% H.

3-Methoxy-2-methylpropionyl chloride (III). The acid *II* (100 g, 0·847 mol) was added dropwise to boiling thionyl chloride (107 g, 0·9 mol) in nitrogen atmosphere. After the addition the mixture was heated to boil for additional 30 min. Distillation yielded 86·23 g (74·6%) *III*, b.p. 143—143·5°C. For $C_5H_9ClO_3$ (152·6) calculated: 43·97% C, 6·63% H; 25·99% Cl; found: 44·26% C, 6·72% H, 25·44 Cl (argentometrically).

N,N-Dimethylaminoethyl 2-methyl-3-methoxypropionate (IV). Dimethylaminoethanol (Fluka) (35·75 g, 0·4885 mol) was slowly added to *III* (66·72 g, 0·4885 mol). After 30 min triethyl amine (50 g, 0·4941 mol) was added to the mixture. The precipitate of triethylammonium chloride was removed by filtration and dried (65·17 g, 97%). Distillation of the filtrate gave 38·28 g (77·9%) *IV*, b.p. 54—55°C/80 Pa, n_D^{20} 1·4285, d_{25} 0·95186 g cm^{-3}. For $C_9H_{19}NO_3$ (189·3) calculated: 57·11% C, 10·12% H, 7·41% N; found: 57·08% C, 10·19% H, 7·44% N.

2-(3-Methoxy-2-methylpropionyloxyethyl)trimethylammonium iodide (V). Compound *IV* (6·75 g, 0·0357 mol) was dissolved in benzene (50 ml), and methyl iodide (5·82 g, 0·041 mol) was added to the solution. Yellow liquid phase separated from the solution and crystallized after 3 h. Recrystallization from chloroform gave 10·36 g (86·7%) *V*, m.p. 68—69°C. For $C_{10}H_{22}INO_3$ (331·3), calculated: 36·26% C, 6·70% H, 38·32% I, 4·20% N; found: 36·21% C, 6·72% H, 38·19% I, 4·10% N.

N,N-Dimethylaminoethyl pivalate (VI) was prepared from dimethylaminoethanol and pivaloyl chloride[1] (Fluka), and its quaternary salt, 2-pivaloyloxyethyltrimethylammonium chloride (*VII*), was obtained by a reaction between 2-chloroethyl pivalate and trimethyl amine[7].

Quaternization and Hydrolysis

The kinetics of quaternization and alkaline hydrolysis was investigated by means of a modified version of an apparatus described earlier which makes possible an isothermal mixing of solutions of reagents, determination of the total starting volume of the reaction mixture and a highly reproducible constant volume[10,11] sampling. Modification for work with volatile compounds consisted in the use of a larger flask used for adding the solution of methyl iodide which without the sampling head was fixed at the moment of adding to the reactor neck, and in the use of over-pressure (injection syringe) for transferring the reaction mixture into the sampling head fixed at the reactor neck until the components have been mixed together and the starting volume has been read off.
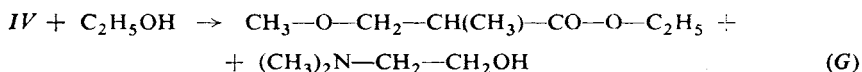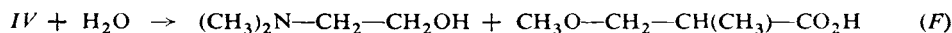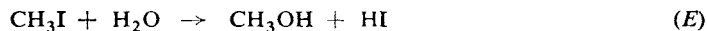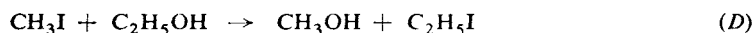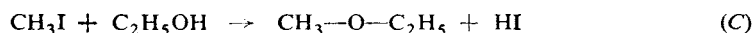
The degree of conversion of the quaternization reaction was determined by the potentio-metric titration of iodide ions formed with a $0 \cdot 1$ M solution of silver nitrate (silver and mercuro-sulfate electrode) after the reaction has been stopped by adding a 50% excess of cooled $0 \cdot 05$ M sulfuric acid to the sample of the reaction mixture.

The degree of conversion of alkaline hydrolysis was determined by the titration of samples in which the reaction had been stopped by adding the reaction mixture to a cooled solution of dilute hydrochloric acid, the amount of which corresponded to the original alkalinity. The acid (II) arising by hydrolysis was titrated with a $0 \cdot 1$ M solution of sodium hydroxide with phenolphthalein as the indicator.

The solvents used were a mixture of ethanol and water with 57 mass % of ethanol in the quaternization reactions and water in the alkaline hydrolysis.

RESULTS AND DISCUSSION

In the first stage of the study we examined the extent of side reactions which might become operative in the study of quaternization. Solvolytic reactions were considered in the investigation, on the one hand, between the alkylating agent (methyl iodide) and components of the solvent, and on the other, between N,N-dimethylaminoethyl 2-methyl-3-methoxypropionate (IV) and the solvents:

$$CH_3I + C_2H_5OH \rightarrow CH_3{-}O{-}C_2H_5 + HI \qquad (C)$$

$$CH_3I + C_2H_5OH \rightarrow CH_3OH + C_2H_5I \qquad (D)$$

$$CH_3I + H_2O \rightarrow CH_3OH + HI \qquad (E)$$

$$IV + H_2O \rightarrow (CH_3)_2N{-}CH_2{-}CH_2OH + CH_3O{-}CH_2{-}CH(CH_3){-}CO_2H \qquad (F)$$

$$IV + C_2H_5OH \rightarrow CH_3{-}O{-}CH_2{-}CH(CH_3){-}CO{-}O{-}C_2H_5 + $$
$$+ (CH_3)_2N{-}CH_2{-}CH_2OH \qquad (G)$$

Gas chromatography has revealed that in the reaction mixture containing methyl iodide and the solvent (57% ethanol, 43% water) at $22 \cdot 1°C$ no methoxyethane had been formed after 50 h, even in traces, and that methyl iodide had reacted to methanol in an amount of $1 \cdot 3\%$ and to hydrogen iodide, in $1 \cdot 5\%$ (titrimetrically). The average conversion $1 \cdot 4\%$ gives the rate constant $7 \cdot 8 \cdot 10^{-8}$ s^{-1}. For methyl iodide in water at, $e.g.$, $59 \cdot 95°C$ the reported hydrolysis constant[3] is $9 \cdot 07 \times 10^{-6}$ s^{-1}. The quaternization reaction rate constant for substrate IV (Table I) at $22 \cdot 1°C$ is $3 \cdot 5 \times 10^{-3}$, so that the solvolytic reaction of methyl iodide is not operative along with the quaternization.

Neither dimethylaminoethanol nor 2-methyl-3-methoxypropionic acid (*II*) was detected at room temperature within 24 h in a reaction mixture composed of the solvent and ester *IV*. This suggests that neither hydrolysis nor transesterification takes place. It was found, moreover, that dimethylaminoethanol is quaternized with methyl iodide virtually at the same rate as ester *IV* ($3 \cdot 5 \times 10^{-3}$ l mol^{-1} s^{-1} at 22·1°C), so that the side reaction *F* would not distort the experimental results.

A comparison between the rate constants of several further derivatives showed that the agreement in the case of dimethylaminoethanol and ester *IV* was not random: along with the reported value for *IV* and dimethylaminoethanol, the value $3 \cdot 33 \times 10^{-3}$ l mol^{-1} s^{-1} at 22·7°C was found for dimethylaminoethyl pivalate. A similar accord was found for *IV* ($1 \cdot 23 \times 10^{-3}$) and for monomeric dimethylaminoethyl methacrylate ($1 \cdot 7 \times 10^{-3}$) (both values at 11°C); the value for dimethylaminoethyl pivalate at 12·5°C was $1 \cdot 33 \times 10^{-3}$ l mol^{-1} s^{-1}.

The validity of the kinetic description was verified by using the equation for a bimolecular second-order reaction of quaternization of both model compounds (*i.e.*, independence of the rate constant of quaternization on concentrations of the starting compounds — Table I). In the case of the quaternization reaction of *IV* the independence of the rate constant of quaternization of ionic strength was checked (an addition of a tenfold and a fifty-fold amount of lithium nitrate with respect to ester *IV* did not virtually affect the rate constant)[1].

The results of kinetic measurements of the quaternization of esters *IV* and of N,N-dimethylaminoethyl pivalate (*VI*), *i.e.* the temperature dependences of the rate constants are summarized in Table II; the values of the activation quantities calculated therefrom are presented in Table III. The latter values, as well as the fact that dimethylaminoethanol is quaternized at the same rate as substrate *IV* and further compounds, indicate that the quaternization reaction is only little dependent on steric conditions (substitution) of the oxygen atom situated in the γ-position with respect to the alkylated nitrogen atom.

Generally, the reaction between methyl iodide and compounds derived from dimethylaminoethanol may be characterized as a hydrophilization reaction which proceeds sufficiently quickly at room or at a slightly elevated temperature and gives products in a quantitative yield also in diluted water–alcoholic solutions. One of the main criteria in the estimation of the suitability of strong base ion exchangers or polyelectrolytes in certain cases are the basicity and stability of the polymer under investigation with respect to the alkaline medium. In the case of polymeric quaternary ammonium bases both these properties depend on the chemical quality of substituents bound to the quaternary nitrogen atom. At elevated temperatures and with the alkali hydroxides in excess quaternary bases derived from the reaction products of chloromethylated styrene (or the copolymer of styrene and divinylbenzene) undergo the Hofmann degradation[2,4-6]. Up to 120°C quaternary polyelectrolytes based on 2-(methacryloyloxyethyl trimethylammonium hydroxide) undergo alkaline hydrolysis as the only degradation reaction in which choline is formed together with structural units of polymethacrylic acid. At temperatures above 140°C, also

products of the Hofmann degradation are formed, along with hydrolytic products[6].

For 2-(3-methoxy-2-methylpropionyloxyethyl)trimethylammonium iodide (*V*), the first member in a series of oligomeric or polymeric products prepared by reacting

TABLE I

Rate constant of quaternization of substrate *IV* with methyl iodide in a water–alcoholic solution (57 mass % ethanol) at 22·1°C

$[CH_3I]_0 \cdot 10^2$	$[IV]_0 \cdot 10^2$	$k \cdot 10^3$
$mol\,l^{-1}$		$1\,mol^{-1}\,s^{-1}$
3·21	18·34	3·33
8·82	8·86	3·50
10·49	9·70	3·67
21·35	5·21	3·50

TABLE II

Dependence of the rate constant of quaternization on temperature for *IV* and *VI*

$T, °C$	$k \cdot 10^3, 1\,mol^{-1}\,s^{-1}$	$T, °C$	$k \cdot 10^3, 1\,mol^{-1}\,s^{-1}$
	IV	34·8	9·17
0·3	0·53		*VI*
11·0	1·23	12·5	1·33
20·0	2·83	22·7	3·17
22·1	3·67	32·1	6·90
30·0	7·33		

TABLE III

Kinetic quantities of quaternization reactions between methyl iodide and substrates *IV* or *VI* in a water–alcoholic solution (57 mass % ethanol)

Quantity	*IV*	*VI*
Frequency factor, $10^8\,1\,mol^{-1}\,s^{-1}$	1·4 ± 0·6	1·8 ± 0·1
Activation energy, $kJ\,mol^{-1}$	60·0 ± 2·0	60·9 ± 0·7
Activation enthalpy, $kJ\,mol^{-1}$	57·5 ± 2·0	58·6 ± 0·6
Activation entropy, $J\,mol^{-1}\,K^{-1}$	−96·6 ± 6·8	−95·2 ± 2·0

with sodium methoxide, the rate of alkaline hydrolysis has been determined. In view of the presence of a quaternary ammonium group bearing a positive charge, it was necessary to measure the dependence of the rate of hydrolysis on the ionic strength of the reaction mixture. Since the total ion concentration remains unchanged in the alkaline hydrolysis, due to an equivalent amount of carboxylate ions formed from the hydroxyl ones, the ionic strength can be regarded as constant in each experiment. No complicating phenomena which should be borne in mind with dimers and higher oligomers occur in the case of the first member investigated in this study which contains only a single ester bond.

In compounds containing several ester groups bearing quaternary ammonium ions in the original molecule the total number of positive ions and counterions in the molecule is $2P$; P is the degree of polymerization. After the dimer has been hydrolyzed to the first degree, a "zwitte-rion" is formed, at least partly, in solutions of low ionic strength; from the formally kinetic point of view this "zwitterion" should be regarded as an electrically neutral molecule, *i.e.*, its further hydrolysis is independent of the ionic strength. Similar, but more complicated relations arise during the hydrolysis of higher oligomers or polymers in which, along with the already described effective decrease in the charge number, the formation of polyelectrolyte complexes may become operative (preferentially with higher members of the series) which may lead as far as to phase separation, and of course to basic changes in the effective concentration of reacting groups.

Table IV presents the rate constants of the alkaline hydrolysis of quaternary ester V as a function of the temperature and ionic strength of reaction mixtures in which the ionic strength has been adjusted by adding sodium iodide. From the linear dependence of the rate constants of hydrolysis V on the square root from the ionic strength at the individual temperatures (T), the rate constants (k) extrapolated to zero ionic strength have been calculated:

T, °C	11·49	17·69	25·79	32·59
k, 1 mol^{-1} s^{-1}	0·450	0·677	0·952	2·62

The basic kinetic quantities (Table V) have been determined from the temperature dependence of these reaction rate values. For the sake of comparison, the same Table contains kinetic quantities reported by us earlier[6,7] for a sterically more hindered model compound, *i.e.*, 2-pivaloyloxyethyltrimethylammonium chloride, the rate constants of which are much lower, in agreement with the larger steric hindrances on the α-carbon atom with respect to the ester carbonyl. For the sterically more demanding pivalate we found a higher activation energy value which is the cause of the steeper rise in the reaction rate with temperature (at 0°C the hydrolysis of V proceeds 8·3 times more quickly than that of pivalate, but at 40°C V reacts only 5·4 times more quickly).

TABLE IV

Dependence of the rate constant of alkaline hydrolysis of substrate V on reaction temperature and ionic strength of the reaction mixture. Aqueous ethanol used as solvent (57 mass % ethanol)

T, °C	I, mol l^{-1}	$\sqrt{I}$	k, l mol^{-1} s^{-1}
32·59	0·008641	0·09296	1·51
32·59	0·02534	0·1592	1·28
32·59	0·04822	0·2196	1·08
32·59	0·1086	0·3296	1·05
25·79	0·009358	0·09674	0·923
25·79	0·01986	0·1409	0·727
25·79	0·04218	0·2054	0·638
25·79	0·1541	0·3926	0·558
17·69	0·008829	0·09396	0·563
17·69	0·02028	0·1424	0·515
17·69	0·06799	0·2607	0·435
17·69	0·1035	0·3217	0·360
11·49	0·008401	0·09166	0·382
11·49	0·04654	0·2157	0·267
11·49	0·08617	0·2935	0·233
11·49	0·1407	0·3751	0·205

TABLE V

Kinetic quantities of alkaline hydrolysis in aqueous solutions calculated for zero ionic strength for substrates V and VII

Quantity	V	VII
Frequency factor, 10^7 l mol^{-1} s^{-1}	2·5 ± 0·2	9·1 ± 0·3
Activation energy, kJ mol^{-1}	42·1 ± 3·1	49·8 ± 1·4
Activation enthalpy, kJ mol^{-1}	39·7 ± 3·8	47·3 ± 1·4
Activation entropy, J mol^{-1} K^{-1}	−112 ± 16	−101·2 ± 1·5

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