DEGRADATION OF PIVALAMIDOALKYL-TRIMETHYLAMMONIUM HYDROXIDES

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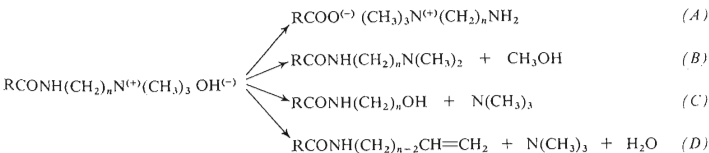ω-Pivalamidoalkyl-trimethylammonium hydroxides $(CH_3)_3CCONH(CH_2)_nN^+(CH_3)_3OH^-$ (*I*, $n = 2, 3, 4$) were degraded in an aqueous solution having a concentration of 1·1 mol/kg at 70 and 120°C for 0·5—70 h. These compounds undergo hydrolysis under the above conditions; moreover, at *n* equal to 2 and 4 consecutive reactions take place, that is, alkylation of the primary amino group with the alkyl groups of the quaternary ammonium group. The Hofmann degradation of *I* does not occur to any considerable extent.

In an attempt to develop new types of strongly basic anion exchangers possessing an increased thermal stability, we have already studied[1,2] the preparation and degradation of linear polymethacrylates and of the respective low-molecular weight models — pivalates, of a general formula $RCOO(CH_2)_nN^+(CH_3)_3OH^-$, where $n = 2, 4, 6$. It was found on this occasion that in many cases the ester bond did not hold out in the alkaline solution of a quaternary ammonium base. We therefore concentrated on amides, which are well known to be more resistant to alkaline hydrolysis. This paper reports the preparation of model amides of the type $RCONH-(CH_2)_nN^+(CH_3)_3OH^-$ (*I*: R = $(CH_3)_3C$—; *Ia*: $n = 1$; *Ib*: $n = 2$; *Ic*: $n = 3$; *Id*: $n = 4$; *II*: R = $(CH_3)_2CH$—, $n = 3$) and the degradation of *Ib−d* in aqueous solutions at elevated temperatures. *I* and *II* were prepared by employing the known methods, that is, by reacting the respective diamine with acyl chloride and by following quaternization.

Attempts to prepare the lowest homolog *Ia* have failed. Already iodide proved to be unstable in this case: only tetramethylammonium iodide could be isolated in an attempt of recrystallization. The tendency exhibited by the iodide corresponding to *Ia* to get rid of the positive charge on the nitrogen atom is obviously so strong, that it reacts even with a weaker nucleophilic agent — the iodide ion (the products being N-(iodomethyl)pivalamide and trimethylamine), and of course the more so with a strong nucleophilic agent — trimethylamine, giving rise to N-(dimethyl-aminomethyl)pivalamide and tetramethylammonium iodide. $(CH_3)_3N^+CH_2N^+(CH_3)_32I^-$ decomposes[3] to tetramethylammonium iodide in a similar way. In the available literature we have not found any description or characterization of quaternary derivatives of geminal diamines of the type $R'CONHCH_2N^+R''_3$ (R′, R″ alkyls), with the exception of a single case[4], *i.e.*, 1-(tri-chloroacetamidomethyl)-1-methylpiperidinium iodide. It may be assumed, therefore, that the respective hydroxide, *Ia*, would be rather an unstable compound.

N,N-Disubstituted amides analogous to *I* could not be prepared in a simple manner. Thus, attempt at the preparation of an analog of *Ib via* N,N-bis(2-chloroethyl)pivalamide has completely failed. In the reaction of pivaloyl chloride with bis(2-chloroethyl)amine the IR spectra have revealed in the reaction mixture a gradual decrease in the content of the tertiary amide ($1630-1640$ cm^{-1}) with a simultaneous increase in the absorption of the ester group (1730 to 1735 cm^{-1}); a similar reaction with diethanolamine was carried out in order to compare the IR spectra. Obviously, this phenomenon is another case of the known rearrangement[5] of N,N-bis(2-chloroethyl)amides leading to 2-[(2-chloroethyl)amino]ethyl esters. We also gave up attempts at the preparation of an analog of *Ic* because of the insignificant yields of the synthesis of bis(3-dimethylaminopropyl)amine *via* the respective sulphonamide.

Quaternary ammonium bases of the type *I* can be transformed in an aqueous solution *via* the alkaline hydrolysis of the amide (reaction (A)) and the degradation of the quaternary ammonium base by nucleophilic substitution (reaction (B), (C)) or *via* elimination (reaction (D)). If one bears in mind also the possible consecutive reactions, a varied number of compounds may arise as a result, a complete quantitative analysis of which under the variable conditions of transformation would obviously be too demanding. We therefore concentrated only on the determination of the key components, which indicate the extent of the assumed main reactions $(A)-(D)$. These are the following: $(CH_3)_3CCOO^-$ (determines the extent of hydrolysis), the loss of strong basicity (gives the overall extent of hydrolysis and the extent of degradation of the quaternary ammonium base), the content of trimethylamine, methanol (the sum of the two determines the extent of degradation), and the content of the primary amino group (gives the extent of hydrolysis). Only a qualitative determination was carried out in the case of the other products.

$$RCOO^{(-)} \; (CH_3)_3N^{(+)}(CH_2)_n NH_2 \qquad (A)$$

$$RCONH(CH_2)_n N(CH_3)_2 \; + \; CH_3OH \qquad (B)$$

$$RCONH(CH_2)_n N^{(+)}(CH_3)_3 \; OH^{(-)} \qquad RCONH(CH_2)_n OH \; + \; N(CH_3)_3 \qquad (C)$$

$$RCONH(CH_2)_{n-2}CH{=}CH_2 \; + \; N(CH_3)_3 \; + \; H_2O \qquad (D)$$

Acidimetric titration in water seemed to be best suited for the determination of the carboxylate content in the degradation mixtures (in an aqueous — alcoholic medium the carboxylates are titrated together with amines). Since with some diamines a low titration exponent is found for the second amino group (*e.g.*, 2-dimethylaminoethylamine has p$T_1 = 7.9$, p$T_2 = 4.5$), which could coincide with the titration exponent of the carboxylates, the content of the latter was also determined independently by fixing all amines and ammonium bases on a strongly acid cation exchanger and by alkalimetric titration of the eluate containing a free carboxylic acid.

The degree of hydrolysis can be determined indirectly also by determining the total basicity by acidimetric titration, since the total basicity always increases in the hydrolysis of *I*. (Here, the total basicity means the sum of all species that can be acidimetrically titrated, *i.e.* the quatern-

ary ammonium base, amines and pivalates.) The total basicity of the degradation mixtures was determined by acidimetric titration in water and in aqueous methanol. If the extent of hydrolysis, and thus the content of carboxylates are small, there will be no distinct inflexion on the titration curve in water, which will give lower values of the total basicity. On the other hand, in the titration in aqueous methanol the carboxylates are titrated along with the amines, and the error is thus eliminated. The determination of the degree of hydrolysis from the total basicity of the reaction mixture served also for control purposes; the degree of hydrolysis thus determined roughly agreed with the hydrolytic conversion obtained by the above methods, which means that there was no loss of trimethylamine in the manipulations with the degradation mixture.

The determination of quaternary ammonium bases in the presence of amines is generally regarded as easy if acidimetric titration is used. We have proved, however, that at concentrations of 0.01—0.001N the quaternary ammonium bases are potentiometrically titrated in water along with common amines, with an exception for amines the basicity of which has been weakened (e.g. in $H_2N(CH_2)_3N^+(CH_3)_3OH^-$ by the proximity of a positive charge). Both kinds of bases — strong and weak — can be readily distinguished at the given concentrations by potentiometric titration in aqueous methanol and aqueous dimethyl sulphoxide; at the same time, however, the strong base thus found is usually lower by as much as 10% than the real one. Aqueous ethanol cannot be employed for this purpose: pure quaternary ammonium bases — both low-molecular and high-molecular weight ones, as well as NaOH, at a concentration of 10^{-3}N and free from carbonates, exhibit during the titration with hydrochloric acid in aqueous ethanol a transition corresponding to a weak base, in addition to that corresponding to a strong base.

The determination of trimethylamine in the complex degradation mixture was rather problematic. In the gel permeation chromatography[6] (Spheron 300/THF) and in the liquid–liquid chromatography[7] trimethylamine yields broad waves, similarly to other amines, and obviously due to sorption on the polymeric material. Paper chromatography with the detection by means of the Dragendorff reagent is rather unreliable for quantitative purposes. We eventually chose the removal of volatile amines from the alkalized degradation mixture, absorption in dilute hydrochloric acid and gas chromatographic determination using an internal standard. However, the results thus obtained must be regarded as semiquantitative only.

Model bases $Ib-d$ were degraded in an aqueous solution ($c = 1.1$ mval/g) at 70° and 120°C for $0.5-70$ h. The analytical data thus obtained on the content of pivalate and of the primary amino group, on the loss of the strong base, on the total basicity and on the trimethylamine content in the degradation mixtures were related to the initial content of the degraded base and used for calculating conversions as functions of the reaction time. The following can be said a priori about the course of the conversion curves: If the conversion curves obtained from the content of pivalate and of the primary amino group, from the loss of the OH^- group and from the total basicity are identical, then only a simple hydrolysis occurs, without consecutive reactions. If a curve deviates from the group of identical conversion curves, this indicates yet another reaction, e.g.: a) the curve of the OH^- loss deviated towards higher values indicates degradation of the quaternary ammonium base or some other reaction with the participation of the hydroxyl ions; b) the curve of the NH_2 content deviated towards lower values indicates a consecutive reaction of NH_2 (e.g. reaction with the quaternary ammonium group, i.e. alkylation of the NH_2 group); c) the curve of the pivalate content deviated towards lower values indicates a consecutive reaction

of pivalate (*e.g.* ester formation). Although some determinations are subjected to a considerable error (especially quaternary ammonium bases), conclusions may be drawn already from the shape of the conversion curves. With the model compounds *Ic, Id* at 70°C and with *Ic* at 120°C, virtually only hydrolysis takes place (reaction (*A*)); in the other cases hydrolysis was followed by a reaction of ω-amino-alkyltrimethylammonium pivalate with simultaneous disappearance of the quaternary ammonium base (Figs 1, 2).

We could not find any mention in the literature about the kinetics of the alkaline hydrolysis of N-alkyl amides bearing a quaternary ammonium group on the alkyl group. By analogy with ω-trimethylammonioalkyl pivalates[1,2] and other amides[8], one may expect that for the alkaline hydrolysis of model compounds *Ia* simple kinetic equation of 2nd order with the same concentrations of the starting com-

FIG. 1

Degradation of $(CH_3)_3CCONH(CH_2)_nN^+\text{-}(CH_3)_3OH^-$ at 70°C, Dependence of Conversions on Reaction Time

Reaction for: *a*) *n* = 2, *b*) *n* = 3, *c*) *n* = 4. Determination of conversion from: ○ pivalate content (alkalimetrically after the cation exchanger), ◕ pivalate content (acidimetrically), ◑ total basicity (acidimetrically), ◐ content of the primary amino group (spectrophotometrically), ◑ trimethylamine content (gas chromatography), ● 3-dimethylaminopropylamine content (gas chromatography), ⊗ loss of strong basicity (acidimetrically).
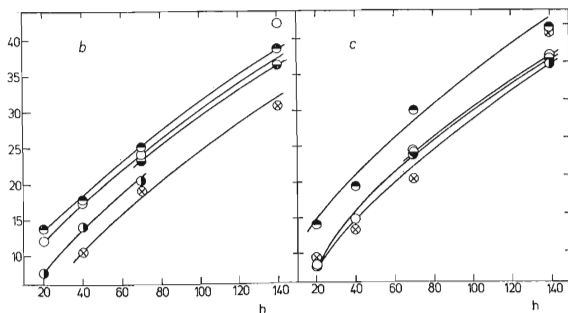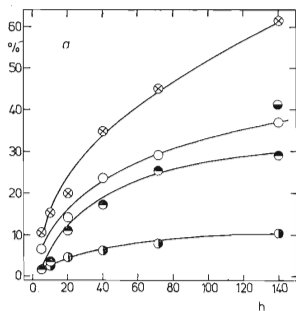
ponent will be valid. This equation has been rearranged to become $kt = x/a(a - x) =$ $= (1/dc^2) \cdot cm/(cw - m)$, where a and c are the concentrations of the base (mol/l and mmol/g, resp.) at $t = 0$, x and m resp. are the concentration (mol/l) and the amount (mmol) of pivalate at a time t, w is the amount of solution of the degraded base (g), d is the specific weight of the solution of the degraded base (g/ml). The $A = cm/(cw - m)$ values were correlated with t by using the least squares method; if consecutive reactions took place to any considerable extent, only a few initial experimental points were used (Fig. 3). In all cases the correlation coefficients were $r \geqq 0.99$, except the degradation of Ib, where $r = 0.98$. The equation thus rearranged is satisfied by Ic and Id at 70°C and Ic at 120°C within the whole range of the reaction times, while Ib at 70°C and Ib and Id at 120°C only in the initial stages (Fig. 3). These plots enable the ratio of the hydrolysis rate constants to be determined:
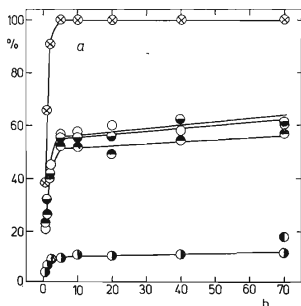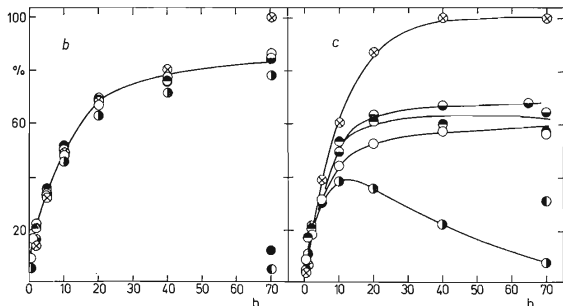

Fig. 2

Degradation of $(CH_3)_3CCONH(CH_2)_nN^+$-$(CH_3)_3OH^-$ at 120°C, Dependence of Conversions on Reaction Time

Reaction for: *a*) $n = 2$, *b*) $n = 3$, *c*) $n = 4$. Meaning of symbols *cf.* Fig. 1.

$k_{n=2} : k_{n=3} : k_{n=4} = 1\cdot91 : 1\cdot18 : 1$ at 70°C, and $3\cdot11 : 1\cdot05 : 1$ at 120°C. Such order is in agreement with the expected inductive effect of the positive charge of the ammonium nitrogen on the rate of the alkaline hydrolysis. From these rate data the activation energy of hydrolysis could be estimated $(E_a$ in kcal/mol K): $19\cdot1$ for Ib, $15\cdot9$ for Ic, and $16\cdot5$ for Id.

In the above cases the hydrolysis is obviously accompanied to a great extent by another reaction of the quaternary ammonium base, which owing to the OH^- consumed makes the hydrolysis slow down and then cease. In addition, in the case of Ib and Id the consecutive reaction of ω-aminoalkyltrimethylammonium pivalate on the primary amino group takes place. Obviously, the reaction causing the OH^- ions to be consumed is not the degradation of the quaternary ammonium base (reactions (B), (C), (D)), but the neutralization of the ammonium cation (NH_2^+) formed by an intermolecular (reactions (E), (F)) or an intramolecular (reactions (G), (H)) nucleophilic attack of the primary amino group on the α-carbon atom with respect to the quaternary ammonium group:
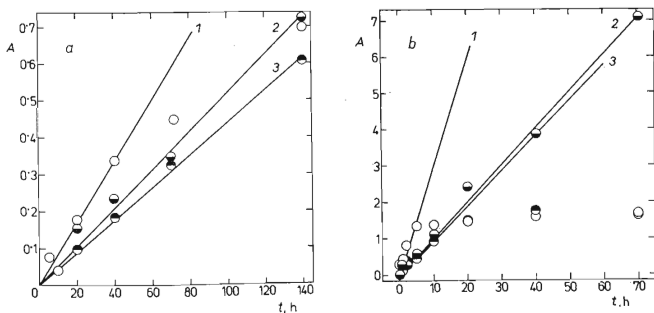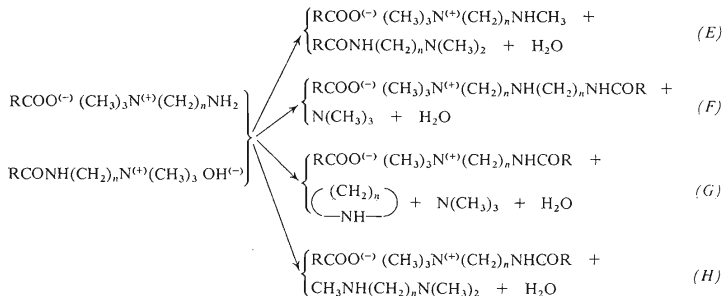

FIG. 3

Degradation of $(CH_3)_3CCONH(CH_2)_nN^+(CH_3)_3OH^-$, Plot for 2nd Order Reaction for Hydrolysis (cf. text)

Temperature (°C): a) 70, b) 120. Curves: 1 $n = 2$, 2 $n = 3$, 3 $n = 4$.

$$\begin{cases} \text{RCOO}^{(-)} (CH_3)_3 N^{(+)}(CH_2)_n NHCH_3 \ + \\ \text{RCONH}(CH_2)_n N(CH_3)_2 \ + \ H_2O \end{cases} \quad (E)$$

$$\begin{cases} \text{RCOO}^{(-)} (CH_3)_3 N^{(+)}(CH_2)_n NH(CH_2)_n NHCOR \ + \\ N(CH_3)_3 \ + \ H_2O \end{cases} \quad (F)$$

$$\text{RCOO}^{(-)} (CH_3)_3 N^{(+)}(CH_2)_n NH_2$$

$$\text{RCONH}(CH_2)_n N^{(+)}(CH_3)_3 \ OH^{(-)}$$

$$\begin{cases} \text{RCOO}^{(-)} (CH_3)_3 N^{(+)}(CH_2)_n NHCOR \ + \\ \left(\begin{matrix} (CH_2)_n \\ -NH- \end{matrix}\right) \ + \ N(CH_3)_3 \ + \ H_2O \end{cases} \quad (G)$$

$$\begin{cases} \text{RCOO}^{(-)} (CH_3)_3 N^{(+)}(CH_2)_n NHCOR \ + \\ CH_3 NH(CH_2)_n N(CH_3)_2 \ + \ H_2O \end{cases} \quad (H)$$

This hypothesis is supported by the fact that the conversion curves for the loss of OH^- and for the content of NH_2 are roughly equidistant from the hydrolytic curves (Figs 1a, 2a,c), *i.e.* that OH^- and NH_2 disappear from the reaction mixture in equivalent amounts. Moreover, if the OH^- consuming reaction was the degradation of the quaternary ammonium base due to OH^- (reactions (B), (C), (D)), it would be difficult to find a plausible explanation why Ic is virtually not degraded at all in this manner. The exceptional tendency of Ib, Id to be degraded by an attack by NH_2 rather favours the intramolecular attack (reactions (G), (H)), facilitated by the formation of a five-membered ring in the transition state:

This is also corroborated by the formation of a comparatively large quantity of trimethylamine (Fig. 2c) and pyrrolidine from Id. After the degradation of the model compounds Ic, d (but not Ib), diamines $(CH_3)_2 N(CH_2)_n NH_2$ were detected in the reaction mixtures. These products obviously are not due to the degradation of the respective base according to (B) followed by hydrolysis, because in no case was it possible to prove methanol by the gas chromatographic method; their formation could be explained by intermolecular transalkylation (analogy of reactions (E), (F)):

$$2 (CH_3)_3 N^+ (CH_2)_n NH_2 \ \xrightarrow{\ OH^-\ } \ (CH_3)_2 N(CH_2)_n NH_2 \ + \ (CH_3)_3 N^+ (CH_2)_n NHCH_3 \ + \ + \ H_2O \quad (J)$$
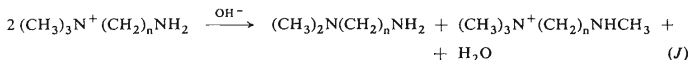
The behaviour of Ib in the degradation differs in many respects from its homologs. Isolation

of the insoluble product containing carboxylic groups should be added to the characteristics mentioned above, but the structure and formation of this product have not been studied in greater detail.

It was found that the model amides *I* were indeed more resistant towards hydrolysis than similar esters[2]. In spite of this, however, the main drawback of the amide quaternary ammonium bases of type *I* as potential models of strongly basic anion exchangers consists in their relatively easy hydrolyzability. Hydrolysis leads to the decay of the quaternary ammonium base and generates the primary amino group. The latter, which is perhaps an even more active nucleophilic agent than the OH^- group, can later on degrade another molecule of the quaternary ammonium base, and the ammonium ion ($—NH_2^+—$) formed in the reaction may in turn irreversibly abstract the OH^- ion from yet another molecule of the base (*cf.* reactions (*E*)-(*H*)). Thus, one act of hydrolysis causes the decay of up to two exchange groups; this is what makes the hydrolysis of the amide quaternary ammonium bases so harmful and undesirable. A suitable way out in such case would be suppression of the undesirable hydrolysis by choosing structures more resistant towards it. Only then could differences in the resistance of various structural types of the quaternary ammonium bases towards degradation become apparent. However, judging by the pivalates–poly(methacrylates)[1,2] relation one may expect that poly(methacrylamides) would be more resistant to the hydrolysis than similar pivalamides.

EXPERIMENTAL

Chemicals

2-Dimethylaminoethylamine pure (Fluka), 3-dimethylaminopropylamine pure (Fluka). 4-Dimethylaminobutylamine was prepared in a 60% yield from the respective nitrile by reduction with sodium in butanol[9]; b.p. 75—76°C/6 kPa. NMR (CDCl$_3$, HMDS): 8·56 (m), CCH_2CH_2C; 8·37 (s), NH_2; 7·77 (s), $(CH_3)_2N$; 7·69 (m), CH_2N; 7·30 (t) CH_2N. 4-Dimethylaminobutyronitrile, b.p. 81—82·3°C/3·1 kPa was prepared in 85% yield by an exchange reaction between 3-dimethylaminopropyl chloride and NaCN in dimethyl sulphoxide similarly to ref.[10]; the product was isolated from the aqueous solution by continuous extraction with ether. Pivaloyl chloride was prepared from pure pivalic acid (Fluka) and benzoyl chloride[11]; pivalamide was obtained from pivaloyl chloride and gaseous ammonia[12]. 3-Dimethylaminopropyl chloride, b.p. 55 to 56·5°C/6·7 kPa was prepared from hydrochloride (Chemopharma, Ústí n.L.) by treating with aqueous NaOH and extraction with ether.

Model Compounds

N-(ω-*Dimethylaminoalkyl*)amides RCONH(CH$_2$)$_n$N(CH$_3$)$_2$. An ether solutions of acyl chloride was added dropwise to an ether solution of (CH$_3$)$_2$N(CH$_2$)$_n$NH$_2$ (molar ratio 1 : 2·5) with external cooling so that the temperature of the reaction mixture did not exceed 5—10°C. After stirring for one hour the mixture was left to stand for 24 h. Various procedures were used in the further course: *a*) diamine hydrochloride precipitated from the solution was removed by filtration, and the filtrate was treated further by distillation; *b*) the reaction mixture was evaporated

in vacuo to dryness, the residue was stirred with benzene, diamine hydrochloride was sucked off, and the filtrate was further distilled; c) the reaction mixture was shaken with water, the aqueous solution was alkalized with sodium hydroxide, extracted with ether, and the ether extract was distilled. Purity of the products was in all cases higher than 99% (gas chromatographically, 15% cyanoethylated silicone rubber GE XE-60 on Chromosorb W 80/100 mesh at 130°C). The properties of the products for n = 2—4 are listed in Table I.

N-(ω-*Trimethylammoniumalkyl*)*amide iodides* $RCONH(CH_2)_nN^+(CH_3)_3I^-$. Freshly distilled methyl iodide was added dropwise to a solution of $RCONH(CH_2)_nN(CH_3)_2$ in absolute ether (molar ratio 1 : 1·1—1·2). The raw product was recrystallized from the mixture benzene–isopropyl alcohol. The properties of the products, for *n* = 2—4, *i.e.* of iodides corresponding to the bases *Ib—d* and *II*, are given in Table II.

N-(*Dimethylaminomethyl*)*pivalamide*. 10 ml of 40% aqueous formaldehyde (0·13 mol) was added with stirring to 6 g pivalamide (0·059 mol) in 35 ml of ethanol; after 10 min, 12·5 ml of 34% aqueous dimethylamine (0·09 mol) was added to the mixture. Stirring continued 1 h at room temperature and 0·5 h at 65°C. Volatile compounds were removed by distillation *in vacuo* at 50°C, the rest was diluted with benzene, and 2·5 g of pivalamide was filtered off. The filtrate yielded after distillation 2·5 g of the raw product, b.p. 90—100°C/27 Pa, m.p. 60—65°C (benzene––hexane). For $C_8H_{18}N_2O$ (158·2), calculated: 17·70% N; found: 16·95% N. NMR (CDCl₃, HMDS): 8·79 (s), $(CH_3)_3$; 7·76 (s) $N(CH_3)_2$; 6·01 (d) CH_2; 3·87 (s, broad) CONH. The NMR analysis and elemental analysis make it clear that the product contains some 20% of unreacted pivalamide (both compounds cannot be separated by gas chromatography on Carbowax 20M or on poly(ethyleneglycol adipate). The raw product was transformed into N-(trimethylammonio-methyl)pivalamide iodide with a 50% excess of methyl iodide in ether (quaternization is

TABLE I
N-(ω-Dimethylaminoalkyl)amides $RCONH(CH_2)_nN(CH_3)_2$

R	*n*	Formula	Calculated/Found			B.p., °C/kPa (isolation[a])	Yield %
			% C	% H	% N		
t-Bu	2	$C_9H_{20}N_2O$	62·75	11·70	16·26	90—95/0·7—0·8	93
			63·00	12·08	15·91	(a)	
t-Bu[b]	3	$C_{10}H_{22}N_2O$	64·47	11·90	15·04	105—110/0·5	80
			63·98	12·10	14·29	(b)	
t-Bu	4	$C_{11}H_{24}N_2O$	65·95	12·08	13·98	120—125/0·7	95
			65·30	11·97	13·31	(c)	
i-Pr[c]	3	$C_9H_{20}N_2O$	62·75	11·70	16·26	124—126/0·5	90
			61·63	12·03	16·06	(c)	

[a] Procedures *cf.* Experimental. [b] NMR (CDCl₃, HMDS): 8·85 (s) $(CH_3)_3C$; 7·79 (s) $(CH_3)_2N$; 8·37 (m) CCH_2C; 7·60 (t) CH_2N; 6·71 (q) $\underline{CH_2}NH$; 2·27 (s) CONH. [c] NMR (CDCl₃, HMDS): 8·92 (s), 8·85 (s), $(\underline{CH_3})_2CH$; 8·37 (m) CCH_2C; 7·80 (s) $(CH_3)_2N$; 7·80 (m) CH; 7·64 (t) CH_2N; 6·70 (m) $\underline{CH_2}NH$.

slow). The yield of the raw product is practically quantitative, but it cannot be purified by crystallization (*cf.* further). M.p. 147—153°C. For $C_9H_{21}IN_2O$ (300·2) calculated: 36·01% C, 7·05% H, 42·27% I; found: 37·26% C, 7·53% H, 40·35% I. NMR (D_2O, DSS): 8·82 (s), 8·75 (s), 8·74 (s) $C(CH_3)_3$; 7·08 (s), 6·97) s), 6·87 (s) $N^+(CH_3)_3$; 5·39 (m) CH_2. The IR spectrum is similar to that of $(CH_3)_3CCONH(CH_2)_2N^+(CH_3)_3I^-$. In an attempt at recrystallization (from acetonitrile or the mixture benzene–isopropyl alcohol) it is decomposed with formation of tetramethylammonium iodide, which was identified by the melting point, by determining iodide and nitrogen, and by comparison of the NMR and IR spectra with those of the authentic sample.

3-Aminopropyltrimethylammonium iodide. The compound was prepared by two procedures. *a*) Methyl iodide was added dropwise to a benzene solution of 3-dimethylaminopropylamine with cooling (molar ratio 1 : 0·95), the precipitate was filtered off and washed with benzene. It can be seen from the NMR spectrum of the raw product that methylation takes place also on the primary amino group. On drying over P_2O_5 and recrystallization from the mixture benzene–isopropyl alcohol, m.p. was 167—169°C. For $C_6H_{17}IN_2$ (344·1), calculated: 29·52% C, 7·02% H; found: 29·87% C, 7·25% H. NMR (D_2O, DSS): 8·08 (m) CCH_2C; 7·30 (t) CH_2N; 6·88 (s) $(CH_3)_3N^+$; 6·62 (t) CH_2N^+. Titration with 0·1N-HCl and 0·1N-AgNO$_3$ revealed an equivalent ratio iodide : amine = 1·09 : 1. *b*) 3-Acetamidopropyl-trimethylammonium iodide[13] [m.p. 113—115°C (EtOH–ether); NMR (D_2O, DSS): 7·98 (s, m) CH_3CO, CCH_2C; 6·86 (s) CH_3N^+; 6·65 (m) CH_2NH, CH_2N^+] was hydrolyzed by boiling 2·5 h with conc. hydrochloric acid; evaporation several times *in vacuo* with water yielded $H_2N(CH_3)_3N^+(CH_3)_3I^- \cdot HCl$, a hygroscopic crystalline product which can be recrystallized from the mixture ethanol–ether.

The aqueous solutions of the base prepared by passing an aqueous solution of chloride-iodide through the anion exchanger in the OH^- form is not stable; at room temperature the content of the strong bases in this solution spontaneously decreases.

TABLE II

N-(ω-Trimethylammonioalkyl)amides $RCONH(CH_2)_nN^+(CH_3)_3I^-$

R	n	Summary formula	Calc./Found % I	M.p., °C	Yield %	NMR[c] (multiplicity)		
						R	$(CH_3)_3N^+$	$(CH_2)_n$
t-Bu	2	$C_{10}H_{23}IN_2O$	40·04 40·96[a] 41·10[b]	154—5·5	93	8·83 (s)	6·81 (s)	5·3 (m)
t-Bu	3	$C_{11}H_{25}IN_2O$	38·66 38·45[b]	185—6·5	—	8·82 (s)	6·84 (s)	7·96 (m) 6·68 (m)
t-Bu	4	$C_{12}H_{27}IN_2O$	37·08 37·60[a]	154·5—6	74	8·84 (s)	6·90 (s)	8·36 (m) 6·76 (m)
i-Pr	3	$C_{10}H_{23}IN_2O$	40·39 40·85[a]	126·5—7	79	8·94 (s) 8·87 (s) 7·50 (m)	6·88 (s)	8·00 (m) 6·72 (m)

[a] Iodometrically. [b] Argentometrically (potentiometrically). [c] In D_2O, DSS.

N,N-*Bis*(*3-dimethylaminopropyl*)*benzenesulphonamide* was prepared from benzenesulphonamide and 3-dimethylaminopropyl chloride (molar ratio 1 : 2) similarly to ref.[14] *via* a 17·5 h reaction in boiling dimethylformamide. The raw product was purified by extraction of an ether solution with 10% aqueous NaOH. Yield: 10%. For $C_{16}H_{29}N_3O_2S$ (327·5), calculated: 12·83% N; found 12·59% N. NMR (CDCl₃, HMDS): 8·29 (m), CCH₂C; 7·85 (s) CH₃N; 7·75 (m) CH₂NMe₂; 6·83 (t) SO₂NCH₂; 2·49 (m) arom.H.

Bis(*3-dimethylaminopropyl*)*amine* was prepared by splitting N,N-bis(3-dimethylaminopropyl)-sulphonamide with chlorosulphonic acid similarly to ref.[15]; hydrolysis with boiling 25% HCl (40 h) was unsuccessful. After ClSO₃H had been distilled off *in vacuo*, the reaction mixture was heated 1·5 g with an excess of 50% aqueous NaOH to 100°C and extracted with ether. B.p. of the product 105—110°C/3·7 kPa (ref.[16] gives 91—92°C/3·2 kPa), content 98·2% (GLC), NMR (CDCl₃, HMDS): 8·35 (m) CCH₂C; 7·79 (s) CH₃N; 7·69 (t) CH₂N; 7·37 (t) CH₂N.

Degradation of Quaternary Ammonium Bases

0·1—0·2M aqueous solution of quaternary iodide was passed through a column of the anion exchanger Wofatit SBW in the OH⁻ form and the eluate was collected under nitrogen. (The eluate was checked for the absence of iodide with AgNO₃.) An aqueous solution of the base was concentrated at 35°C *in vacuo* to an approximate concentration of the strong base of 1·1 mval/g and stored under nitrogen; the solutions contained up to three equivalent per cent of carbonates. The contents were determined by titration with 0·1M-HCl in water and in aqueous methanol. Each time a definite amount of solution containing 0·3—0·5 mval of the base was weighed into stainless steel autoclaves, the latter were filled with nitrogen, closed and heated in a silicone oil bath to 70 and 120°C ($\pm$0·3°C). After degradation the autoclave was cooled to −10 to −15°C, the contents were quantitatively transferred into a 10 ml volumetric flask and filled with degassed distilled water up to the mark. After the degradation of *Ib* at 120°C the reaction mixture contained a brown flaky precipitate which was isolated on acidifying with hydrochloric acid in a maximum yield of 5 weight % of the starting base (after a 70 h reaction time). The precipitate is insoluble in water and ethanol. Found: C 72·64, 73·41%; H 7·21, 7·30%; N 1·21, 1·21%; Cl 1·57%. IR: bonded OH or NH (3400 cm⁻¹), COOH (1720 cm⁻¹).

Analytical Methods

Apparatus. The melting points were determined with the Boetius block. The NMR spectra were recorded with a JEOL PS-100 apparatus at 100 MHz with hexamethyldisiloxane (HMDS) and sodium 3-trimethylsilylpropanesulphonate (DSS) as the internal standard; chemical shifts were expressed on ppm in the τ scale. The infrared spectra were recorded with Perkin-Elmer 621 and 457 apparatuses. The UV spectra were measured with a Cary 14 apparatus. Acidobasic titrations were performed with an automatic titration apparatus Radiometer TTTIc using an automatic burette ABU 12, a recording device SBR 2c, a G 202C glass electrode and a saturated calomel electrode.

Determination of pivalate and of the strong and total basicities. Each time 1 ml of the stock solution was titrated with 0·1M-HCl in water (in order to determine pivalate and the total basicity, in the case of *Ic* also the strong basicity) and in aqueous methanol (to determine the strong and total basicities). Another 1 ml aliquot was passed through a column of Ostion KS in the H⁺ form and the eluate was titrated with 0·1M-NaOH (for the determination of pivalate).

Spectrophotometric determination of the primary amine group (ref.[17,18]). A mixture of 1 ml of borax buffer solution (pH 8·4), 1 ml of 20 times diluted stock solution and 1 ml of freshly

prepared 0·1% aqueous solution of sodium trinitrobenzenesulphonate was heated in an indirect light to 40°C for 2 h. 1 ml of c. 1M-HCl was added, and absorption in the range 330—350 nm was measured against a blank test. $\varepsilon = 1\cdot4 \cdot 10^4$ cm^{-1} mol^{-1} was used in the calculations[18].

Gas chromatographic determination. After 70 h degradation at 120°C carried out as described above, an excess (c. 300% of the initial basicity) of 2·5M-HCl was added, and attempts were made to detect methanol in this mixture by the gas chromatographic method (Porapak Q). The acidic solution was further alkalized with an excess of KOH; volatile amines were removed into dilute HCl by a stream of nitrogen at room temperature during one hour. The absorption solution was evaporated to dryness *in vacuo*, and 1 ml of methanol, 1 ml of 10% NaOH and a weighed amount of a standard triethylamine solution were added to the residue. In the solution thus obtained, trimethylamine was determined by gas chromatography (10% polyoxiran 600 on Cellite 60/80 mesh deactivated with 5% of sodium metanilate) by using the method of internal standard (triethylamine) and calibration. Preliminary experiments showed that the recovery of trimethylamine in expulsion with nitrogen was 90%. The alkaline solution, from which trimethylamine had been removed, was acidified with HCl, evaporated *in vacuo* to dryness, dissolved in a minimum amount of water, alkalized and extracted with 1 ml of ether. A search for amines — 2-dimethylaminoethylamine, 3-dimethylaminopropylamine, 4-dimethylaminobutylamine and pyrrolidine was carried out in the ether solution using gas chromatography (the same system as for trimethylamine). Attempts were made to detect methyl pivalate (cyanoethylated silicone rubber GE XE-60) in the stock solution (*cf.* Determination of pivalate). Neither methanol nor methyl pivalate could be detected, the respective diamines were found after degradation of the models *Ic, Id,* but not in the case of *Ib.*

Paper chromatography. The descending method on a Whatman 4 chromatographic paper was employed. After the degradation of *Id* at 120°C, pyrrolidine was detected in the reaction mixture after having been transformed into N-(3,5-dinitrobenzoyl)pyrrolidine (system formamide/benzene–cyclohexane 2 : 1, detection with *p*-dimethylaminobenzaldehyde after the reduction with SnCl$_2$) (ref.[19]).

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