6.5 mmol, 12 equiv) of solid KOH. The reaction mixture became hetereogeneous upon heating (oil bath, 55 °C) and was stirred overnight in a closed vessel purged with argon.

The reaction mixture was cooled and extracted with three 10-mL portions of methylene chloride, which were diluted with 30 mL of hexanes prior to drying (Na$_2$SO$_4$) and concentration. The resulting gold oil (97.9 mg, 108% of theoretical yield) was used in the next step without further purification: ^{1}H NMR (CDCl$_3$, 300 MHz, Me$_4$Si = 0.00 ppm) δ 0.85 (s, 9 H), 1.09 (d, 6 H, J = 6.3 Hz), 1.63 (m, 2 H), 2.64 (dq, 2 H, J = 2.3, 6.2 Hz).

The crude piperidine described previously (ca. 0.53 mmol) was added to a dry round-bottom flask and dissolved in 0.5 mL of dry methylene chloride and 0.16 mL (1.15 mmol, 2.2 equiv) of dry triethylamine. The resulting solution was cooled with an ice–acetone bath (−10 °C), and 156 mg (0.715 mmol, 1.3 equiv) of di-*tert*-butyl dicarbonate (Aldrich) was added in a single portion. The reaction was left to stir overnight and warm to room temperature, whereupon saturated aqueous citric acid (1 mL) was added and the reaction mixture diluted with methylene chloride (30 mL). Water (5 mL) was added to wash the organic phase,

followed by brine (5 mL) and drying (Na$_2$SO$_4$) prior to concentration, which afforded 188 mg of crude material.

The desired material was isolated by column chromatography on silica gel (10 g, Aldrich Grade 951), eluting with 5% ether in hexanes initially, followed by 10% ether in hexanes. The desired material demonstrated an R_f of 0.15 (SiO$_2$; 10% ether in hexanes, visualized by *p*-anisaldehyde in ethanol with mild heating), and 57.9 mg (40.4%, based on 80.5% starting material purity over two steps) were obtained as a clear colorless oil: IR (CH$_2$Cl$_2$) 1671 cm^{-1}; ^{1}H NMR (CDCl$_3$, 300 MHz, Me$_4$Si = 0.00 ppm) δ 0.82 (s, 9 H), 1.45 (s, 9 H), 1.19 (d, 6 H, J = 6.7 Hz), 1.95 (m, 2 H), 4.12 (dq, 2 H, J = 7.0 Hz); ^{13}C NMR/DEPT (CDCl$_3$, 75 MHz, CDCl$_3$ = 77.00 ppm) δ C 31.92, 78.77, 155.41, CH 41.61, 47.65, CH$_2$ 30.97, CH$_3$ 24.73, 26.92, 28.55. Anal. Calcd for C$_{16}$H$_{31}$NO$_2$: C, 71.33; H, 11.60; N, 5.20. Found: C, 71.43; H, 11.59; N, 5.16.

Zwitterionic Quaternary Ammonium Alkoxides: Organic Strong Bases

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Stable quaternary ammonium alkoxides, a new type of organic strong base, were obtained from unhindered tertiary alkanolamines and glycidol. At elevated temperatures, the 2-hydroxyethyl derivatives underwent intramolecular rearrangements and deoxyalkylation to form tertiary amine terminated 1,4-poly(3-hydroxyoxetanes). Demethylation was also observed. The 3-hydroxypropyl derivative underwent disproportionation and Hofmann elimination in addition.

Bases play a very important role in organic chemistry as reagents and catalysts. In earlier work, we[1] and others[2] observed the formation of strong bases from reactions of tertiary alkanolamines 1 and epoxides. We have now characterized the addition compounds derived from 1 and glycidol (2) as monomeric and oligomeric zwitterionic quaternary ammonium alkoxides 3 and report their preparation and properties. As potential substitutes for alkali metal alkoxides, they are easily prepared without evolution of hydrogen and their water solubility facilitates separation from organic substrates. Addition compounds have been postulated as intermediates in the amine-catalyzed polymerization of epoxides,[3,4] but only one isolation has been reported.[5] A hexane-insoluble substance obtained from the reaction of 1,2-epoxyoctane with 1a at 75 °C was assigned a quaternary ammonium alkoxide structure on the basis of identification of its thermal decomposition products.

Results and Discussion

Formation of 3 from alkanolamines and glycidol, an exothermic reaction, was readily followed by the appearance of quaternary methyl groups in the ^{1}H NMR spectra and quantified by titration (Table I). Neutralization with HCl enabled isolation and characterization of the major product as the chloride salt (4, x = 1, X = Cl). The balance of products were di- and triglycidyl ethers of 3 (x > 1) in which the ether linkages were predominantly 1,4.[6] No

O-alkylated amines were formed, thus the strong base content measures the percent quaternization and also provides an average value of x.

a: R = R^1 = CH$_3$, n = 2
b: R = CH$_3$, R^1 = CH$_2$CH$_2$OH, n = 2
c: R = R^1 = CH$_3$, n = 3
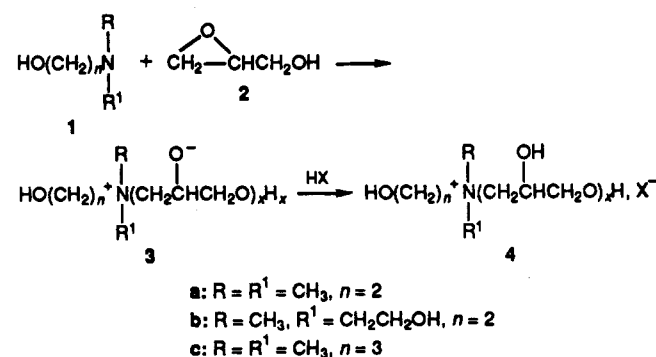
The percent of quaternization was dependent on the structure of the amine. Both increasing the number of 2-hydroxyethyl groups and substitution of 3-hydroxypropyl for 2-hydroxyethyl decreased the percent of quaternization.

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(1) Buriks, R. S.; Lovett, E. G. *J. Org. Chem.* **1987**, *52*, 5247.
(2) McKelvey, J. B.; Benerito, R. R.; Ward, T. L. *Ind. Eng. Chem. Prod. Res. Dev.* **1967**, *6*, 115.
(3) Shechter studied the catalysis of many glycidyl ether reactions. Shechter, L.; Wynstra, J. *Ind. Eng. Chem.* **1956**, *45*, 86.
(4) Vasquez, A.; Matějka, L.; Špaček, P.; Dušek, K. *J. Polym. Sci., Polym. Chem. Ed.* **1990**, *28*, 2305.
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Table I. Parameters and Analytical Data for Quaternary Ammonium Alkoxides 3[a]

amine	g (mol)	glycidol g (mol)	calcd TN	found OH	found BN	% quat[b]	x
DMEA	80.2 (0.90)	33.3 (0.45)	7.93	3.00	4.86	75.7 [c]	1.3
MDEA	107.2 (0.90)	33.3 (0.45)	6.41	1.97	4.30	61.5[d]	1.6
DMPA	92.9 (0.90)	33.3 (0.45)	7.13	2.29	4.78	64.2	1.6
DMPA[e]	47.5 (0.46)	33.3 (0.45)	2.84	1.52	1.37	53.5	1.9

[a] TN, total nitrogen; BN, basic nitrogen; OH, strong base; x, degree of oligomerization. [b] Based on glycidol. [c] 1:1 reaction 73.7% quat; 1:1 reaction in water (50%) 86.9% quat. [d] 1:1 reaction in water (50%) 70.6% quat. [e] 50% in 2-propanol.

Table II. ^{13}C NMR Spectral Data for Quaternary Ammonium Alkoxides 3 (in ppm from External Me$_4$Si in D$_2$O)

assignment	3a	3b	3c
CH$_2$N	69.6, 68.2	67.7, 66.5	69.2, 68.2
CHOH	67.7	67.1	66.0
3-CH$_2$OH	65.8	65.7	64.4
2-CH$_2$OH	56.6	56.4	
MeN +	53.8	51.4	52.8
CH$_2$CH$_2$CH$_2$			30.3
CH$_2$OCH$_2$CH$_2$OH		75.4	75.5
CH$_2$OCH$_2$[a]	73.5, 73.1	73.1	73.5, 72.7
CHOH[a]	71.7	71.7	71.6
3-CH$_2$OH[a]	63.9	63.7	

[a] Minor component, $x = 2$.

Scheme I. Products from 3a and 3b
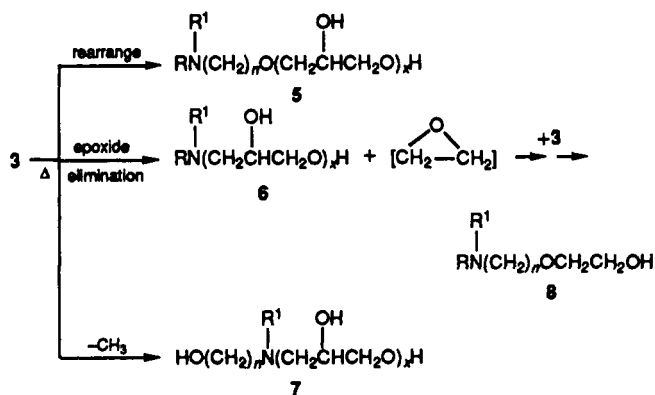

With hindered amines *tert*-butyldiethanolamine and triethanolamine, only traces of 3 were detected.

Solvents also affected the conversion. In water, which supplies a proton and hydroxide ion, oligomerization was suppressed and quaternization of 1a and 1b to form the weaker ammonium hydroxides 4a (X = OH) and 4b (X = OH) rose to 87 and 71%, respectively. In 2-propanol, quaternization of 1c decreased (Table I) and 2% of the glycidol reacted with the solvent to give 2,3-dihydroxypropyl 2-propyl ether (13), confirming the strongly basic character of 3c. By contrast, the percent of quaternization did not change in going from a 2:1 to a 1:1 molar ratio of amine 3a to glycidol, amine as solvent.

These results are interpreted as follows: The alkanolamine nitrogen added to the 1-position of glycidol, creating an oxyanion at the 2-position. In this process, some of the energy provided by release of ring strain in the epoxide was captured by converting a weak base to a strong base. Intramolecular proton transfer from the 3-hydroxyl to the 2-oxyanion suppressed the reverse reaction[7] and stabilized the zwitterion. As the concentration of adduct 3 ($x = 1$) increased, the oxyanions competed with nitrogen for the remaining glycidol to give the oligomeric bases 3 ($x > 1$). Since this is a "living system", addition of more glycidol produces a polymeric base. The absence of O-alkylated derivatives of 1 suggests that intermolecular proton transfer between 3 and 1 was not significant.

We expected the quaternary ammonium alkoxides to be thermally labile because of their basicity, high degree of functionality, and similarity to quaternary ammonium salts whose chemistry is dominated by rearrangements,[8] dealkylation,[9] and Hofmann eliminations[7] to produce uncharged species. The major reactions observed by Tobler[5] were loss of ethylene oxide and intramolecular rear-

rangement to (dimethylamino)ethyl 2-hydroxyoctyl ether and higher homologues. Doumaux[10] found analogous products from the thermal decomposition of tetrakis(2-hydroxyethyl)ammonium hydroxide but preferred an intermolecular pathway. The quaternary ammonium alkoxides 3 were stable at room temperature for months, but on heating at 100 °C for 3–4 h, the alkalinity, viscosity, and percent of quaternization decreased (Table III). The value of x remained the same for 3b and increased slightly for 3a and dramatically for 3c, suggesting disproportion in the latter. NMR spectroscopy (Table IV) indicated the generation of tertiary amines and formation of additional ethers.

Four types of compounds were identified from 3a and 3b by GC-MS on acetyl derivatives (Scheme I and Table V). The rearrangement products of 3a were predominantly (dimethylamino)ethyl ethers of 1,4-poly(3-hydroxyoxetanes) 5a, an assignment supported by a line at 58.4 ppm in the ^{13}C NMR spectrum. A closely related family of (dimethylamino)-1,4-poly(3-hydroxyoxetanes) (6a) arose from loss of ethylene oxide. Multiple components with the same mass were found for both 5a and 6a, indicating isomers. Commercially, 1,4-poly(3-hydroxyoxetanes) have been made by sodium hydroxide catalyzed condensation of glycerol[11] and, recently, Vandenberg[6] obtained branched 1,4-poly(3-hydroxyoxetanes) from KOH-catalyzed polymerization of glycidol and its trimethylsilyl ether. Small amounts of 2-hydroxy-2-(dimethylamino)-ethyl ether (8a) and demethylation products 7a were found. No Hofmann elimination products were detected.

An aqueous solution of 4a (X = OH) was more stable. Heating at 85–98 °C for 24 h resulted in a 14% reduction in quaternization.

Thermolysis of 3b gave 8b, rearrangement products 5b, and the dealkylation products 6b and 7b. The distribution reflected the change in substituents on the amine (Table V).

Substitution of 3-hydroxypropyl for 2-hydroxyethyl produced a dramatic change in chemistry. Thermolysis

(7) Cope, A. C.; Trumball, E. R. *Org. React.* 1960, *11*, 317. In a review of Hofmann elimination reactions, the authors say that products of (2-hydroxyalkyl)ammonium salts are epoxides and tertiary amine.

(8) Dragan [Dragan, S.; Luca, C.; Petrariu, I.; Dima, M. *J. Pol. Sci., Pol. Chem. Ed.* 1980, *18*, 455] and Dutch patent 74,951 (*Chem. Abstr.* 1955, *49*, 14808c) report rearrangements of alkanolammonium salts to ethers.

(9) Leffek, K. T.; Tsao, F. H.-C. *Can. J. Chem.* 1968, *46*, 1215.

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(11) Sandler, S. R.; Berg, F. R. *Polym. Sci. A-1* 1966, *4*, 1253.

Table III. Analyses for Products of Thermal Reactions of 3 after Removal of Excess 1[a]

		mequiv/g					
substrate	recovd 1 mol	calcd TN	found TN	found OH	found BN	x	% convn
DMEA	0.68	4.09	3.67	0.16	4.03	2.0	95
MDEA	0.54	5.21	5.16	0.19	4.99	1.7	94
DMPA	0.81	2.85	2.80	0.68	2.18	5.0	63
DMPA[b]				0.17	2.40	5.0	88

[a] Quantities defined in Table I. [b] 50% in 2-propanol.

Table IV. ^{13}C NMR Spectral Data for Thermal Reaction Products (in ppm from External Me$_4$Si in D$_2$O)

	compound		
assignment	DMEA	MDEA	DMPA
vinyl			135.1
			119.4
CH$_2$OCH$_2$	73.3	73.4	73.6
	72.8	72.9	72.6
	70.0	70.1	70.7
	69.5	69.5	70.0
		65.7	
CHOH	71.6	71.6	71.6
CH$_2$OH	63.7	63.8	63.9
		59.8	
		59.6	
CH$_2$N	58.4	57.5	56.5
		56.5	52.9
MeN	45.4	43.6	45.2
		43.1	45.9
other			27.6[a]
			26.4[a]
minor[b]	89.0	80.7	80.6
	80.1	79.3	76.9
	79.2	77.0	74.9
		75.0	

[a] CH$_2$CH$_2$CH$_2$. [b] Poly-1,2-glycerols and branched glycerols.

Table V. GC–MS Data for Acetate Esters of Thermal Reaction Products

	molecular ions (percent composition)[a]			
x[c]	DMEA	MDEA	DMPA	DMPA[b]
	5a	**5b**	**5c**	**5c**
1	247 (31.2)[d]	319 (31.9)	261 (14.7)	(13.7)
2	363 (12.9)[d]	435 (12.9)	377 (8.7)[d]	(20.0)
3	479 (4.6)[d]	551 (3.3)	493 (3.8)	(8.2)
sum	(48.7)	(48.1)	(27.2)	(41.9)
	6a	**6b**	**6c**	**6c**
1	203 (6.5)	275 (15.7)[d]	203 (5.3)[e]	(0.8)[e]
2	319 (9.1)[d]	391 (19.1)[d]	319 (11.1)	(4.3)
3	435 (10.2)[d]	507 (7.0)	435 (11.8)	(13.8)
4	551 (3.6)[d]		551	(5.5)
sum	(29.4)	(41.8)	(28.2)	(24.4)
	7a	**7b**	**7c**	**7c**
1	275 (3.3)	347 (0.8)	289 (5.0)	(1.2)
2	391 (5.9)	463 (0.6)	405 (5.8)	(3.9)
3	507 (7.7)		521 (0.9)	
sum	(16.9)	(1.4)	(11.7)	(5.1)
	8a	**8b**	**8c**	**8c**
0	133[f] (0.4)	247 (6.5)	100	(0.3)
1			216 (16.9)	(5.9)
2			332 (7.8)[d]	(6.6)
3			448	(2.6)
sum	(0.4)	(6.5)	(24.7)	(15.4)
			10	10
			232 (6.1)	(8.8)
			13	13
			134[f]	(1.9)

[a] Arranged by family. [b] 50% in 2-propanol. [c] Number of glycidol units or degree of oligomerization. [d] More than one isomer. [e] Additional 6c in distillates, 9.3 and 2.0%, respectively. [f] In distillate.

of 3c involved extensive disproportionation to 9c (Scheme II), and was incomplete (Table III). A family of Hofmann elimination products (10c) and the cyclic dimer of glyci-
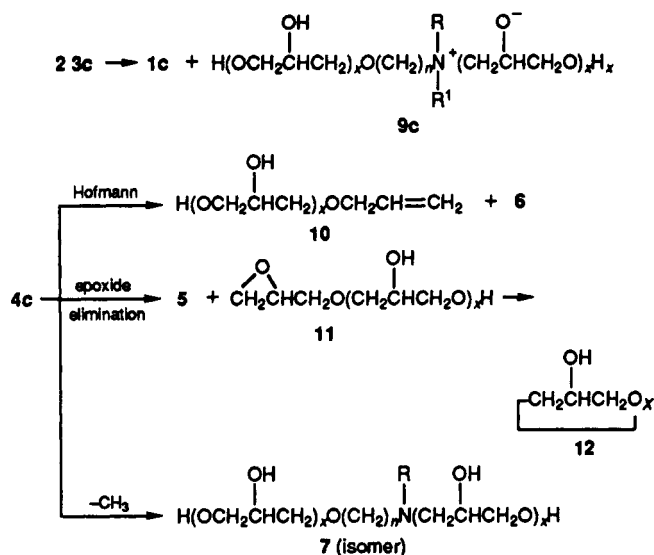
Scheme II. Products from 3c

Table VI. Parameters and Results for Mixed Amine Experiments

component	3a + 3c	3c + 1a	3a + 1c
2-propanol, g	48.2	50.2	32.6
amine	DMPA/DMEA	DMPA	DMEA
g (mol)	14.6 (0.142), 12.6 (0.142)	29.2 (0.284)	17.8 (0.20)
glycidol, g (mol)	21.0 (0.284)	21.9 (0.284)	14.8 (0.20)
portion, g (mol)		all	45.8 (0.137)[a]
amine added		DMEA	DMPA
g (mol)		25.2 (0.284)	14.1 (0.137)
vac dist., g	65.4	100.1	54.9
residue, g	18.5	20.4	135.0
ca.cd TN, mequiv/g	3.25	3.31	3.50
found, TN	3.18	3.11	3.41
found OH	0.64	0.00	0.78
found BN	2.61	3.31	2.71
residual quat, %	19.7	0.00	22.3

[a] Moles of amine in reaction mixture.

dol[12] were identified in addition to 5c, 6c, and 7c. A precursor alkylated on both nitrogen and oxygen, 9c, is required for 10c (x > 1). The remaining compounds can arise from both 3c and 9c.

Thermolysis of 3c prepared in 2-propanol (88% complete) showed a small increase in 5c at the expense of 10c and 6c.

Experiments designed to determine if the formation of 3 was reversible provided some unexpected results. Examination of a mixture of 3a with 1c by ^{13}C NMR spectroscopy revealed no amine exchange.[13] Thermolysis of the mixture gave 5a, 6a, 7a, and, surprisingly, only one product derived from 1c, namely, 7c. No 8 was found.

(12) Cyclic oligomers are usually formed by using Lewis acid catalysts. See: Hiraoka, M. *Crown Compounds, Their Characteristics and Applications*; Elsevier: Amsterdam, 1982; p 30.

(13) Quaternary ammonium salts undergo exchange reactions with ammonia and primary/secondary amines. *Org. React.* 1953, *1*, 138.

Similarly, thermolysis of **3c** with **1a** produced **7a** and a trace of **5a** in addition to **5c, 6c, 7c**, and **10c**. At first glance these results suggested that formation of **3** is irreversible, but a more plausible explanation is that the epoxides regenerated by reversal react faster with oxyanions than with amines, preventing an exchange. Furthermore, the routes to **5** include intramolecular rearrangement and disproportionation but not intermolecular oxyalkylation of a tertiary amine hydroxyl. Compound **7**, the only product derived from reaction of a neutral amine with **3**, cannot arise by simple demethylation. Instead, we propose a four-center reaction involving simultaneous methyl transfer and substitution. Decomposition of **14** to trimethylamine and epoxide[7] ($n = 2$) or allyl alcohol ($n = 3$) provides a driving force.
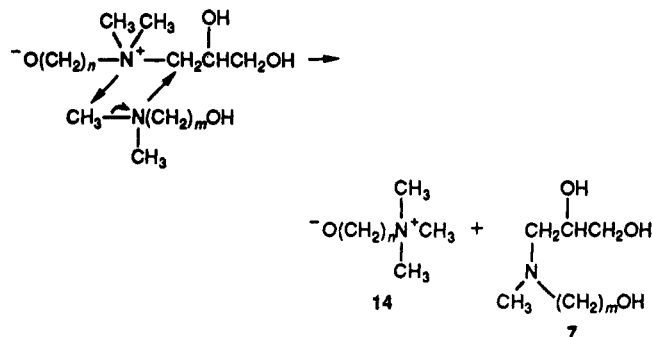
Thermolysis of a mixture of **3a** and **3c** produced a cross product, 3-(dimethylamino)propyl 2-hydroxyethyl ether (**8**, $n = 3$). This result coupled with finding **8** from **3a** and **3b** but not from **3c** or the mixed reactions above suggests that **8** arises from reaction of **3** rather than **1** with ethylene oxide followed by disproportionation.

In conclusion, zwitterionic quaternary ammonium alkoxides are converted to thermodynamically more stable uncharged products by disproportionation, intramolecular rearrangements, and elimination of epoxides or olefins. Demethylation, the only reaction observed between a zwitterion and a neutral amine, was not a simple displacement.

Experimental Section

All commercial chemicals and reagents were used as received except for glycidol, which was vacuum distilled just prior to use.

Bis(2-hydroxyethyl)(2,3-dihydroxypropyl)methylammonium Chloride (3b). Methyldiethanolamine (11.9 g, 0.10 mol), freshly distilled 3-chloro-1,2-propanediol (11.0 g, 0.10 mol), and potassium iodide (0.098 g, 0.00060 mol) were combined and heated at 77–106 °C for 20 h. A 5.0-g sample was chromatographed on 100 g of silica gel (J. T. Baker, 4-μm), using MeOH as solvent, 75-mL fractions, and AgNO$_3$ for detection. Four fractions containing chloride were obtained, 0.3, 1.2, 2.8, and 0.4 g (94%): ^{1}H NMR (D$_2$O) 3.25 (s, 3 H, Me), 3.50–3.85 (d, m, 8 H, CH$_2$N, 3-CH$_2$OH), 4.05 (m, 4 H, 2-CH$_2$OH), 4.29 (p, 1 H, CHOH); ^{13}C NMR (D$_2$O) 51.6 (Me), 56.4 (2-CH$_2$OH), 64.9 (3 CH$_2$OH), 65.9 and 66.5 (CH$_2$N), and 67.2 (CHOH). Anal. Calcd for C$_8$H$_{20}$NO$_4$Cl: C, 41.83; H, 8.78; Cl, 15.43; N, 6.10. Found: C, 41.55; H, 8.28; Cl, 15.88; N, 6.24.

Table VII. GC/MS Data for Mixed Amines Experiments

structure	M$^+$	3a + 3c	3c + 1a	3a + 1c[a]
5a	247	22.8	+[b]	34.3
	363	4.8	1.0	2.6
	479	2.2		
5c	261	8.3	largest[b]	
	377	8.9	20.8	
	551	trace		
6a/6c	203	5.0	3.8	4.4
	319	6.6	4.5	2.9
	435	6.8	6.0	
7a	275	2.3	1.2	8.6
	391	3.3	trace	2.1
	507	7.1		
7c	289	1.5	1.0	6.1
	405	1.6	1.6	
	521	trace		
9	216	0.5	0.5	
	332	0.8	8.5	
8	147[c]	+		
12	134[c]	+	4.2	

[a] Unidentified component of mass 200 (12.8%). [b] Not resolved. Integration from 247 to 261 (36.4). [c] Distillate.

Preparation of Quaternary Ammonium Alkoxides 3. Glycidol was added to the amine at 25–30 °C with cooling supplied by a water bath at 20–25 °C. Below 20 °C, the reaction was extremely slow and above 35 °C, *an uncontrollable exotherm occurred*. Neat 1:1 reactions became unstirrable. The reaction mixture was stirred mechanically at this temperature for 3–4 h or longer. The viscosity increased. Samples were removed for NMR (Table II) and titration (Table I). The sample was added to a known excess of HCl and titrated with sodium hydroxide for remaining acid and tertiary amine. The alkoxide content, which equals the quaternary ammonium content, was calculated from the remaining strong acid.

Thermal Rearrangements. The quaternary ammonium alkoxides were heated at 100 °C for 3–4 h and then vacuum-distilled to remove excess amines, volatile products, and solvents. The residues were analyzed for total nitrogen, basic nitrogen, and alkoxide (Table III). NMR spectra were obtained (Table IV).

Acetylation and GC–MS. Acetic anhydride (a 1 mol excess over the total number of hydroxyl groups in the quaternary ammonium alkoxide) and a portion of the distillation residue were combined. An exothermic reaction ensued. The reaction mixture was heated for 1 h at 100 °C, and then excess acetic anhydride and acetic acid were removed in vacuo. The acetylated product was subjected to chemical ionization GC–MS. The results are given in Tables V and VII. Response factors were assumed to be the same for all compounds.

Mixed Amine Experiments. The quaternary ammonium alkoxides were prepared as described above. The competing alkanolamine was added and the reaction mixture was stirred for several hours, examined by NMR spectroscopy, and subjected to vacuum distillation. The details are given in Table VI. The residues were acetylated and analyzed by GC–MS as described above (Table VII). NMR and GC–MS spectra were obtained on the distillates: ^{13}C NMR (D$_2$O) of **6c**, 70.3 (CHO), 65.5 (C-H$_2$OH), 62.4 (CH$_2$N), 45.9 (Me); **13**, 74.0 (CHO), 71.8 (CHOH), 69.9 (CH$_2$O), 64.0 (CH$_2$OH), 22.4 (Me).