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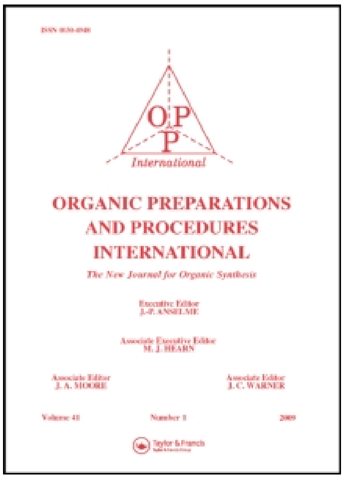

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CONVENIENT DEALKYLATION OF QUATERNARY AMMONIUM SALTS

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CONVENIENT DEALKYLATION OF QUATERNARY AMMONIUM SALTS

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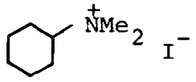
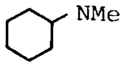
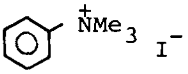
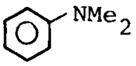
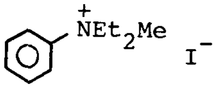
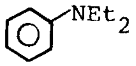
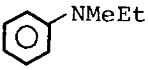
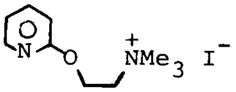
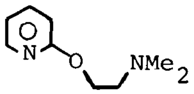
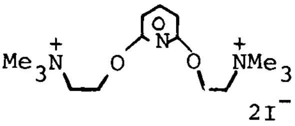
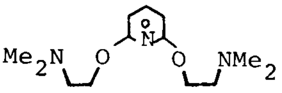
Over the past twenty years, numerous procedures have been devised to dealkylate quaternary ammonium compounds. Dealkylations of quaternary ammonium halides by pyrolysis gave low yields of the corresponding tertiary amines along with decomposition products.[1] The use of reagents with high nucleophilicity[2,3] coupled with lower reaction temperatures, has resulted in less product degradation. In 1950, Kenner and Murray[4] had suggested that demethylation of quaternary ammonium salts occurred by S_N2 attack of hydride ion from $LiAlH_4$. Cope et al.[5] have demonstrated the generality of this reagent for this purpose. Sodium borohydride in polar solvents has been shown to dealkylate ammonium salts smoothly.[2] The use of $Li(C_2H_5)_3BH$ has been reported[6] and high selectivity was demonstrated for removal of a methyl group from $PhN(C_2H_5)(CH_3)_2I$, whereas considerable deethylation was observed with $PhN(C_2H_5)_2(CH_3)I$.[7] We now describe a convenient procedure to dealkylate quaternary compounds using "L-Selectride" [$Li(s\text{-}bu)_3BH$].[8] This procedure can be applied to either pure quaternary ammonium halides or a mixture thereof and thus is demonstrated to be a

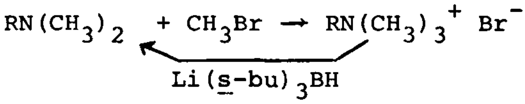
Table 1. Demethylation of Quaternary Ammonium Salts

Compound	Reaction Conditions time(min)	 temp(°C)	Amine	Isolated Yields(%)
$C_{12}H_{25}\overset{+}{N}Me_3Br^-$	60	65	$C_{12}H_{22}NMe_2$	92
	15	25		90
	15	25		93
	45	25		82
				7
	120	65		84
	120	65		68

reliable, essentially quantitative analytical method to afford the corresponding amines.

Table 1 shows the range of quaternary ammonium compounds subjected to this procedure. The reaction is nearly quantitative at 65° or less with short reaction times. Demethylation is favored over deethylation as shown for phenyldiethylmethylammonium iodide. Thus, L-Selectride is slightly more selective to demethylation than lithium triethylborohydride. With hindered ammonium compounds elevated temperatures were used with little or no product degradation.

To evaluate the dealkylation procedure, several samples of commercial dodecyl-, tetradecyl- and hexadecyldimethyl amines[9] were quaternized with methyl bromide in ethanol to give quantitative yields of the methyl quaternary salts. Although the commercial amines contained >95% of a single component, the resultant mixture of ammonium salts was not purified in order to maintain the initial amine distribution (see Experimental). In all cases GLC-MS, analysis showed that dealkylation was highly selective for a methyl group and the amine product mixtures were, within experimental error, identical to the starting amine distribution. (Table 2).



$$\begin{tikzcd}\mathrm{RN(CH_3)_2} + \mathrm{CH_3Br} \arrow[r] & \mathrm{RN(CH_3)_3^+\ Br^-} \arrow[l, bend left, "\mathrm{Li(\underline{s}\text{-}bu)_3BH}"]\end{tikzcd}$$

In order to ascertain the generality of this procedure, commercial quaternary salts were also dealkylated providing a convenient route to the tertiary amines and demonstrating the utility of this procedure, as an analtyical method to determine reactant purity. Experimental values obtained for several selected products are compared with compositions announced by their producers (Table 3). Cetrimide®, $C_{14}H_{19}N(CH_3)_3Br$, was selectively demethylated to give (99.2%) dimethyltetradecylamine, in excellent agreement with reported composition. Bardac®, a mixture of dioctyl-, octyldecyl-, and dioctyldimethylammonium chlorides, was demethylated (>99.5%) to give close agreement with the reported distribution of dialkylmethylamines. Hyamine 3500®, a mixture of alkyldimethylbenzylammonium chlorides, gave products arising from loss of either a methyl or benzyl group; the ratio of demethylation versus debenzylation did not vary appreciably over the wide temperature or time ranges used.

This dealkylation procedure provides a quantitative,

Table 2. Demethylation of Quaternary Salts Derived from Commercial Fatty Amines[a]

Starting Amine Mixture (prior to methylation)					Recovered Amine Mixture (after demethylation)	Reaction Conditions[b]	
R^1	R^2	R^3	%[c]		%[c]	Time (min)	Temp (°C)
C_{10}	CH_3	CH_3	0.3	d	0.1	(1) 60	111
C_{12}	CH_3	CH_3	95.9		93.4	(2) 10	111
C_{14}	CH_3	CH_3	3.0		4.6	(3) 60	65
C_{16}	CH_3	CH_3	0.8		1.9		
C_{12}	CH_3	CH_3	1.2	e	1.1		
C_{14}	CH_3	CH_3	97.0		94.5	(1) 60	111
C_{16}	CH_3	CH_3	1.8		4.0	(2) 60	65
C_{18}	CH_3	CH_3	-		0.4		
C_{12}	CH_3	CH_3	0.1	f	0.3		
C_{14}	CH_3	CH_3	2.2		1.2	60	65
C_{16}	CH_3	CH_3	97.2		95.0		
C_{18}	CH_3	CH_3	0.5		3.5		

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[a] Ethyl Corporation ADMA™ Products. [b] Variation of reaction conditions gave similar product distributions. [c] Product analysis and distribution were ascertained by GLC/MS. [d] Dodecyldimethylation. [e] Tetradecyldimethylation. [f] Hexadecyldimethylation.

general procedure to liberate tertiary amines from their corresponding quaternary salts. Application to the demethylation or debenzylation of simple or complex mixtures of tetraalkylammonium salts has been demonstrated to be a convenient procedure to accurately determine amine distributions.

EXPERIMENTAL

General Comments. Structure and amine distributions analysis were conducted on a Finnigan 4021 Mass Spectrometer (70 eV, 2 sec scan) coupled with a Hewlett-Packard 5710 A gas chromatograph equipped with a flame ionization detector using a 1/4" O.D. (2 mm I.D.) x 15' glass column packed with 10% Carbowax 20 M on 80/100 mesh Gas Chrom Q.

General Procedure for Dealkylation of Quaternary Ammonium Salts - To a stirred suspension of the anhydrous[10] quaternary ammon-

Table 3. Dealkylation of Commercial Alkyl Ammonium Salts.

Reported Composition of Commercial Quats[a]						Recovered Amine Mixture[c] (after dealkylation)				
R^1	R^2	R^3	R^4	%		R^1	R^2	R^3	%[d]	
C_{12}	CH_3	CH_3	CH_3	-		C_{12}	CH_3	CH_3	0.1	
C_{14}	CH_3	CH_3	CH_3	100	d	C_{14}	CH_3	CH_3	99.2	
C_{16}	CH_3	CH_3	CH_3	-		C_{16}	CH_3	CH_3	0.7	
C_8	C_8	CH_3	CH_3	25		C_8	C_8	CH_3	16.5	
C_8	C_{10}	CH_3	CH_3	50	e	C_8	C_{10}	CH_3	47.0	
C_{10}	C_{10}	CH_3	CH_3	25		C_{10}	C_{10}	CH_3	36.5	
C_{12}	CH_3	CH_3	CH_2Ph	60	f	C_{12}	CH_3	CH_3	17.6	52
						C_{12}	CH_3	CH_2Ph	34.4	
C_{14}	CH_3	CH_3	CH_2Ph	40		C_{14}	CH_3	CH_3	21.3	48
						C_{14}	CH_3	CH_2Ph	26.7	
C_{12}	CH_3	CH_3	CH_2Ph	40	g	C_{12}	CH_3	CH_3	14.0	40
						C_{12}	CH_3	CH_2Ph	26.0	
C_{14}	CH_3	CH_3	CH_2Ph	50		C_{14}	CH_3	CH_3	19.5	49.5
						C_{14}	CH_3	CH_2Ph	30.0	
C_{16}	CH_3	CH_3	CH_2Ph	10		C_{16}	CH_3	CH_3	4.1	10.5
						C_{16}	CH_3	CH_2Ph	6.4	

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[a] Composition as stated on chemical sample furnished by industrial source. [b] Various reaction conditions gave similar product distributions. Standard reaction conditions were one hour at 65°C. [c] Product analysis and distribution were ascertained by GLC/MS. [d] Trade name: Cetrimide®, Danochemo, Copenhagen, Denmark. [e] Trade name: Bardac®, Lonza, Inc., Fairlawn, N.J. [f] Trade name: Benzalkonium Chloride®, Danochemo, Copenhagen, Denmark. [g] Trade name: Hyamine 3500®, Rohm and Haas, Co., Philadelphia, PA.

ium salt (2.5 mmol) in dry toluene (25mL), L-Selectride in THF (5mL, 5 mmol) was slowly added under a nitrogen atmosphere. The mixture was stirred at 30° (or temperature stated in the Tables) for 1 hr., then cooled, and aqueous hydrochloric acid (10%, 10mL) was added slowly. After neutralization with aqueous sodium hydroxide (3N), the mixture was dried over anhydrous magnesium sulfate and concentrated *in vacuo* to give the corresponding amine in nearly quantitative yield. GLC analysis of the amine mixtures are given in the Tables. All amine structures were unequivocally proven by spectral comparison with known compounds.

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9. Ethyl Corporation ADMA^{TM} products.
10. Many quaternary ammonium salts ("Quats") are available commercially in aqueous, ethanolic solution, a practical method for pre-drying the sample was necessary. The commercial sample dissolved in excess toluene was refluxed and the protic solvents were removed using a Dean-Stark trap; this procedure was satisfactory for all samples examined. No further drying or sample preparation was required prior to treatment with "L-Selectride".

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