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COMMUNICATIONS

Direct Gas Chromatographic Analysis of Long-Chain Alcohols and Alkyltrimethylammonium Bromides

Keyphrases Alkyltrimethylammonium bromides—analysis
Alcohols, long chain—analysis TLC—analysis GLC—analysis

Sir:

Quaternary ammonium compounds have numerous industrial applications [for example, see Schwartz *et al.* (1)]. In pharmacy, alkyltrimethylammonium halides are important both for their antibacterial action, which may be linked to their micellar properties (2-4), and when used in combination with long-chain fatty alcohols to form mixed emulsifiers (5-8). We are studying the self-bodying action of mixed emulsifiers, including those of the alkyltrimethylammonium bromide-long-chain alcohol type (5, 6).

Commercial alkyltrimethylammonium bromides, including cetrimide BP, and alcohols, such as cetostearyl alcohol BP, are mixtures of homologs, and it is desirable to have a simple, direct method of analysis suitable for all materials.

Link and Morrisette (9) described the analysis of long-chain alcohols by GLC, using a nonpolar substrate on a solid support treated with alkali. However, there is some controversy over the analysis of quaternary

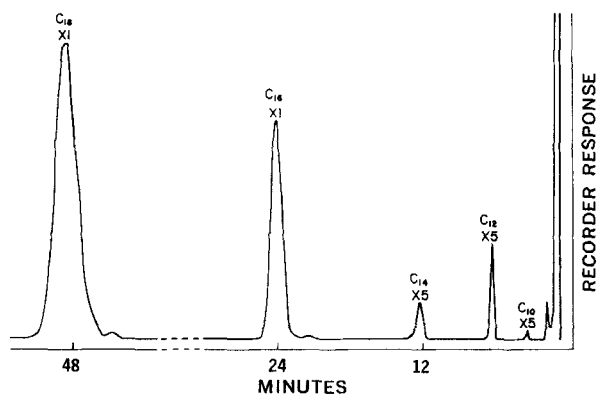


Figure 1—Chromatogram of cetostearyl alcohol BP.

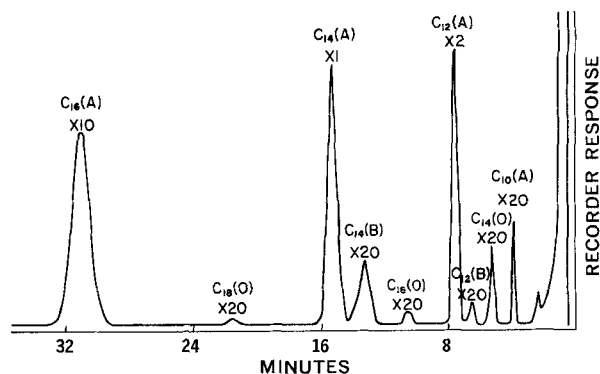


Figure 2—Chromatogram of cetrimide BP. Key: (A) = tertiary amine; (O) = olefin; and (B) = alkyl bromide. For certain peaks, detector sensitivity increased by the factor shown.

compounds in alkaline conditions. Metcalfe (10) used a similar column to analyze long-chain quaternary compounds; under the conditions described, the corresponding tertiary amines were produced. Analysis of these provided a measure of the total homolog composition of the original mixture. No peak had a retention time that corresponded to any of the postulated higher olefins which would result from a Hofmann degradation.

Laycock and Mulley (11) were unable to reproduce Metcalfe's (10) experiments, and thus they modified the column and analyzed quaternary ammonium compounds in the form of the hydroxides. Under their conditions, each compound decomposed quantitatively into a mixture of tertiary amine and olefin.

Neither paper reported checks on the original quaternary compounds for tertiary amine content which, if present, would make the analyses inaccurate.

We have investigated the homolog composition of a series of alcohols and alkyltrimethylammonium bromides using a similar column to that described by Metcalfe (10). A Perkin-Elmer F.11 chromatograph with flame-ionization detector was used. The column was stainless steel, 2 m. long, 0.3175 cm. (0.125 in.) o.d., packed with acid-washed Chromosorb W (60-80 mesh) coated with 10% w/w potassium hydroxide. The flow rate of the carrier gas, nitrogen, was 25 ml./min. The injection and column temperature for 4% w/v solutions of the alcohols dissolved in *n*-heptane were 225-230

Table I—Analysis of Long-Chain Alcohols by GLC^a

Constituents Present	Commercial Long-Chain Alcohols					Retention Time, min.
	Cetostearyl Alcohol BP	Dodecanol	Tetradecanol	Hexadecanol	Octadecanol	
Decanol	(0.2)	(0.4)	—	—	—	3.4
Dodecanol	1.3	99.2	0.5	0.5	0.5	6.3
Tetradecanol	0.5	(0.2)	99.0	0.7	1.4	12.3
Impurity	(0.4)	—	(0.2)	(0.3)	—	—
Hexadecanol	24.7	(0.4)	(0.3)	98.0	0.6	24.3
Impurity	(0.4)	—	(0.1)	0.6	0.5	—
Octadecanol	72.8	—	—	—	97.5	49.3

^a The figures in parentheses are estimated values.

Table II—Analysis of Alkyltrimethylammonium Bromides by GLC^a

Constituents Present	Commercial Alkyltrimethylammonium Bromides						Retention Time ^b , min.
	Cetrimide BP (I.C.I.)	Cetrimide BP (Compass)	Dodecyltrimethylammonium Bromide	Tetradecyltrimethylammonium Bromide	Hexadecyltrimethylammonium Bromide	Octadecyltrimethylammonium Bromide	
Decyltrimethylammonium bromide	(0.4)	0.5	0.6	—	—	—	3.9
1-Bromododecane	(0.1)	0.3	1.3	—	—	—	7.2
Dodecyltrimethylammonium bromide	19.9	21.9	94.6	2.0	1.5	1.5	7.6, 2.7
1-Bromotetradecane	0.7	1.6	—	0.9	—	—	14.4
Tetradecyltrimethylammonium bromide	68.5	68.4	2.3	92.5	1.9	1.9	15.6, 5.5
1-Bromohexadecane	(0.2)	(0.2)	—	(0.1)	1.5	—	29.6
Hexadecyltrimethylammonium bromide	9.9	8.0	0.5	4.0	91.5	2.4	30.6, 11.3
1-Bromooctadecane	—	—	—	—	—	1.6	55
Octadecyltrimethylammonium bromide	—	—	—	—	3.0	91.2	58.9, 22
Eicosyltrimethylammonium bromide	—	—	—	—	(0.7)	1.5	110

^a The figures in parentheses are estimated values. ^b Retention times for quaternaries are those of tertiary amine and olefin, respectively.

and 240°, respectively. For the alkyltrimethylammonium bromides dissolved in isopropyl alcohol (4% w/v), they were 265–270 and 232°, respectively. Sample sizes varied from 0.5–2 μl., and during runs the detector sensitivity was varied to estimate small traces of impurity. The peak areas were measured by electronic integration on a Digital Integrator type IE 165A¹. Narrow sharp peaks were obtained for both types of compound (Figs. 1 and 2).

The response of the flame-ionization detector is essentially proportional to the carbon content of the compound being analyzed. An approximate correction, C, for the flame-ionization response has been suggested (12, 13). This converts the response per gram of material to response per gram of carbon:

$$C = \frac{\text{molecular weight of material}}{\text{number of carbon atoms} \times 12} \quad (\text{Eq. 1})$$

Each peak area was multiplied by this correction factor, and the percentage of each component was determined by the internal normalization method; that is, each corrected peak area was expressed as a percentage of the total corrected peak area. The results for cetostearyl alcohol² and other long-chain alcohols³ are shown in

Table I. These results are the mean of at least two analyses, and in general repetitive runs differed by less than 1%. There were trace unidentified impurities before the main C₁₆ and C₁₈ peaks.

The main peaks for all the alkyltrimethylammonium bromides⁴ had the retention times of corresponding tertiary amines, although traces of corresponding olefins were detected (less than 2% total in every analysis). Thus, the main reaction was the decomposition of quaternary ammonium compound to tertiary amine and alkyl halide, as reported by Metcalfe (10). However, the alternative method of decomposition in alkaline conditions, the Hofmann degradation to tertiary amine and olefin did occur, but to a lesser extent. The peak areas were corrected for carbon content, and impurities before the main peaks were identified as corresponding alkyl bromides, using standards of the authentic materials⁵.

⁴ Cetrimide BP, a commercial mixture of alkyltrimethylammonium bromides, I.C.I., Macclesfield, Cheshire, England, and Compass Chemicals Ltd., London, England. The alkyltrimethylammonium bromides: dodecyltrimethylammonium bromide, tetradecyltrimethylammonium bromide, hexadecyltrimethylammonium bromide, and octadecyltrimethylammonium bromide, Schuchardt München, Munich 8, Germany; nominal purities: dodecyltrimethylammonium bromide, tetradecyltrimethylammonium bromide, octadecyltrimethylammonium bromide, 95%; hexadecyltrimethylammonium bromide, 98–99%.

⁵ 1-Bromododecane, B.D.H. Chemicals Ltd., Poole, England; 1-bromotetradecane, Ralf N. Emanuel Ltd., Alperton, England; and 1-bromohexadecane, Hopkins and Williams Ltd., Chadwell Heath, England.

¹ Gas Chromatograph Ltd., Maidenhead, England.

² Cetostearyl alcohol BP, Loveridge Ltd., Southampton, England.

³ Dodecanol, puriss. grade, and tetradecanol, purum grade, Fluka, Buchs S. G., Switzerland. Hexadecanol and octadecanol, nominal purities 99%, B.D.H. Chemicals Ltd., Poole, England.

Octahedral Hybridization of Hydrogenic Orbitals in Molecular Orbital and Ligand Field Calculations

Keyphrases □ Hydrogenic orbitals—octahedral hybridization □ Molecular orbital, ligand field calculations—octahedral hybridization of hydrogenic orbitals

Sir:

Various quantum chemical methods have been applied to the correlation of theoretical indexes of drug and biochemical activity with experimentally determined quantities (1). Among these are molecular orbital theory and ligand field theory. The applications of these treatments to any molecular system containing hexacoordinate atoms (*e.g.*, transition metal ions in metalloenzymes) necessarily entails knowledge of a set of six d^2sp^3 hybrid orbitals, composed of linear combinations of the hydrogenic s , p , and d orbitals, to describe the bonding situation and to provide the appropriate orbitals for the calculation of π -electron energies, charge densities, and other indexes of molecular reactivity (2). The construction of d^2sp^3 hybrid orbitals was originally discussed by Pauling (3). The set of d^2sp^3 hybrids given by Pauling is:

$$\psi_1 = \frac{1}{\sqrt{6}}s + \frac{1}{\sqrt{2}}p_z + \frac{1}{\sqrt{3}}d_z \quad (\text{Eq. 1})$$

$$\psi_2 = \frac{1}{\sqrt{6}}s - \frac{1}{\sqrt{2}}p_z + \frac{1}{\sqrt{3}}d_z \quad (\text{Eq. 2})$$

$$\psi_3 = \frac{1}{\sqrt{6}}s + \frac{1}{\sqrt{12}}d_x + \frac{1}{2}d_z + \frac{1}{\sqrt{2}}p_x \quad (\text{Eq. 3})$$

$$\psi_4 = \frac{1}{\sqrt{6}}s + \frac{1}{\sqrt{12}}d_x + \frac{1}{2}d_z - \frac{1}{\sqrt{2}}p_x \quad (\text{Eq. 4})$$

$$\psi_5 = \frac{1}{\sqrt{6}}s + \frac{1}{\sqrt{12}}d_x - \frac{1}{2}d_z + \frac{1}{\sqrt{2}}p_y \quad (\text{Eq. 5})$$

$$\psi_6 = \frac{1}{\sqrt{6}}s + \frac{1}{\sqrt{12}}d_x - \frac{1}{2}d_z - \frac{1}{\sqrt{2}}p_y \quad (\text{Eq. 6})$$

where ψ_1 – ψ_6 are the d^2sp^3 hybrids and s , p_x , p_y , p_z , and d_z are hydrogenic orbitals. Necessary and sufficient conditions for the set ψ_1 – ψ_6 to form a complete set of d^2sp^3 orbitals are that the orbitals are equivalent (*i.e.*, they each contain probability density of s , p , and d character in the ratio of 1:3:2), they are normalized (*i.e.*, $\int \psi_i \psi_i dT = 1$, where dT is the volume element in space), and they are orthogonal to one another (*i.e.*, $\int \psi_i \psi_j dT = 0$). Upon examination of the atomic orbital coefficients, it can be seen that the hybrid orbitals fulfill the required conditions of equivalence and normalization but do not form an orthogonal set. For example, the integral of the product of ψ_1 and ψ_4 is not zero but rather $1/3$.

The alkyltrimethylammonium bromides were checked for tertiary amine content using TLC. The 20 × 20-cm. glass plates were coated with a 0.25-mm. thickness of aluminum oxide G, using a Desega spreader, and were air dried. For spotting, pure tertiary amines⁶ were diluted with ethanol, and the alkyltrimethylammonium bromides were dissolved in water. The dilutions were calculated so that the weight of tertiary amine deposited from a calibrated capillary tube was approximately 0.1% of the weight of quaternary surfactant deposited. The developing solvent was a mixture of acetone and water (100:5), and Dragendorff's reagent was used to color the quaternaries and the tertiary amines orange. The more polar quaternaries were strongly adsorbed onto the substrate and thus moved only a short distance from the point of application. It was estimated that there was less than 0.2% tertiary amine in each quaternary compound examined. These quantities would not significantly alter the analyses based on GLC.

The results for the alkyltrimethylammonium bromides are shown in Table II; they are the mean of at least two analyses, and repetitive runs in general differed by less than 1%.

These results have been used to confirm the validity of Shinoda's equation (14) for predicting the CMC of mixtures of quaternary ammonium surfactants containing up to seven components (15). They have also been used to investigate the mechanism of the self-bodying action of mixed emulsifiers of the type alkyltrimethylammonium bromides–cetostearyl alcohol (5, 6).

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⁶ Dimethylaminododecane, dimethylaminotetradecane, and dimethylaminoctadecane, Fluka, Buchs S. G., Switzerland.