Alkylation of Ethanolamines: An Approach to a Novel Class of Functional Surfactants

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Abstract: Some monomeric and dimeric surfactants with functional head groups have been synthesized from di- and triethanolamine synthons. The treatment of alkyl bromide with triethanolamine resulted in simultaneous N-alkylation and O-alkylation products. However, with diethanolamine, N-alkylated products were obtained, which were further used to synthesize various double-tailed surfactants and gemini surfactants.

Keywords: Functional surfactants, gemini surfactants, Menschutkin reaction, triethanolamine

INTRODUCTION

In the studies of cationic surfactants, alkyl trimethylammonium ions are of significant importance because of the balanced point charge in the head group, which helps in the formation of organized assemblies in both aqueous and nonaqueous systems. The additional advantage in the use of these oniums is the ease of the synthesis, which does not need a complicated sequence of reaction and follow-up processes.[1]

Incorporation of functionalities in these head groups can add sophistication to organizations and also add applicability to the corresponding surfactants.[2,3] Ethanolamines, a class of compounds with enormous applications in chemical research on quaternization can easily produce such functional head groups.

Triethanolamine (TEA) finds wide applications in the manufacturing of household detergents and polishes, agricultural herbicides, pharmaceutical ointments, petroleum demulsifiers, synthetic resins, plasticizers, adhesives, and sealants. It is also used in the preparation of fluids used with water as lubricants[4] and also as anticorrosion reagents.[5,6] A mixture of TEA and a fatty acid in deionized water, under vigorous stirring, affords a machining fluid, which can be applied in speeding machines to ensure a clean machined surface.[7]

In the pioneering work of gemini surfactants (GSs), a class of surfactants known to exhibit properties such as lesser critical micelle concentration (cmc), greater efficiency in lowering the surface tension of water and the interfacial tension between water and oil, and better solubility in water than conventional monomeric surfactants, TEA ions are the basic structural units.[8] GSs can be used to transfer pharmacological agents into drug-carrying vesicles.[9–12] Recently, many studies concerning the practical use of gemini molecules appeared in the literature, showing that speculative interests were followed by practical applications, due to their unusual properties[13]: (i) lesser cmc and lesser C_{20} (the concentration at which a reduction of the surface tension of 20 mN/m is attained) values, (ii) better adsorption behavior at both the air/water and the solid/water interfaces with respect to their monomers, and (iii) tendency to form micelles of different shapes and dimensions (i.e., spherical, rodlike, threadlike, vesicles), even at low concentration, when compared with similar normal surfactants. Geminis are used as promising surfactants in industrial detergents and have shown efficiency in skin care products, antibacterial products, metal-encapped porphyrazine and vesicle formation, construction of high-porosity materials, antipollution protocols, analytical separations, nanoscale technology, biotechnology, enhanced oil recovery, and paint additives.[14] These are also used in the synthesis of new mesoporous zeolites for catalytic and adsorption applications.[15] The use of transfection agents is necessary to overcome difficulties associated with transferring high-molecular-weight, negatively charged species across the (predominantly) negatively charged cell membrane. This is generally accomplished through encapsulation of DNA, for example, in cationic liposomes. The GSs are good candidates to act as transfection agents because they are effective at low concentrations, thus diminishing any toxic effect, and they possess structural characteristics suitable for transfection of DNA. In particular,

through simple synthetic modifications, these compounds afford opportunities to tailor their structure for improving transfection efficiencies that are not available with traditional surfactant or lipid systems.[16–21]

Despite voluminous work in the field of cationic surfactants containing an ammonium head group, the information regarding synthesis of ethanolamine-based surfactants is limited.[22] The nucleophilicity of amine and hydroxyl functions make the synthesis complicated. Herein we have reported the synthesis of some TEA-based monomeric surfactants with single and double alkyl hydrophobic tails and some novel diethanolamine-based GSs having variation in hydrophobic chain length and spacer length.

RESULTS AND DISCUSSION

The reaction achieved our objectives in getting quaternary ammonium ion from a tertiary base stem with the Menschutkin reaction. Anticipating an easy approach for obtaining hexadecyl triethanolammonium bromide, hexadecyl bromide was treated with TEA neat under reflux condition and at the boiling temperature of alkyl bromide in a sealed tube. The solid white mass obtained from the mixture of the two liquids, in each case, exhibits a single spot in thin-layer chromatography (TLC). The compound was found to be ionic and shows foaming behavior in
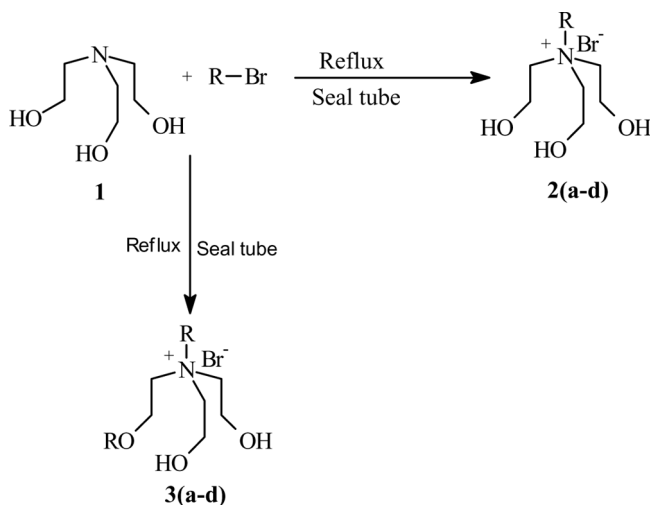
Scheme 1. a, $R = C_6H_{13}$; b, $R = C_8H_{17}$; c, $R = C_{10}H_{21}$; and d, $R = C_{16}H_{33}$.
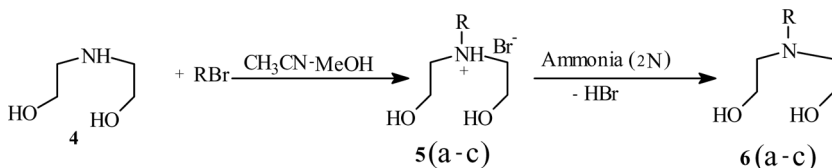
Scheme 2. R = a, $C_{16}H_{33}$; b, $C_{14}H_{29}$; and c, $C_{10}H_{21}$.

aqueous medium. Neither the mass spectra nor the NMR spectral data correspond to the expected product (**2d**). The infrared (IR) spectral data with a strong C–O stretching frequency near $1000 \, cm^{-1}$ in each case and the significant decrease in nitrogen content in the molecule, when compared to that in anticipated product, impelled us to propose an O-alkylation along with N-alkylation during the reaction, affording N-alkyl O-alkyl triethanolammonium bromide (**3d**) (Scheme 1). To see the generality of this process, hexyl, octyl, and decyl bromides were treated with TEA, and similar results were obtained. However, on treatment of hexadecyl bromide with diethanolamine (**4**), hexadecyldimethylammonium bromide was obtained (**5a**), which on treatment with alkali resulted in the corresponding tertiary amine (**6a**) (Scheme 2). In a subsequent reaction, bromoethanol was treated with **6a** to obtain a white mass, which exhibited all spectral characteristics of hexadecyltriethanolammonium bromide. The synthesis of the same compound was also achieved by the treatment of hexadecyl amine with bromoethanol in the presence of alkali, a procedure followed by Mitra et al. (Scheme 3).[22]

The formation of **3a–d** may be attributed to an intermolecular proton-transfer mechanism operating between two molecules of TEA. The transfer may lead to the formation of an ion pair containing a TEA ion and diethanolaminoethoxide (Scheme 4). In the presence of alkyl bromide, the latter ion will give rise to both O- and N-alkylation, and the former will be inert toward alkylation at N center.

The basicity difference of TEA and diethanolamine steers alkylation to different sites. TEA, being more basic in nature, is capable of existing
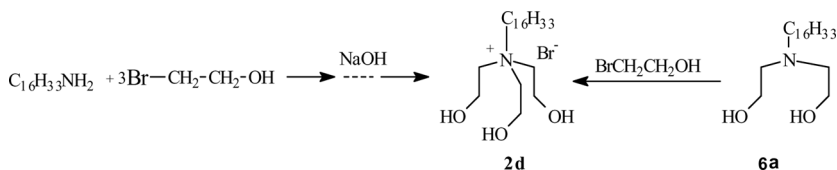
***Scheme 3.*** Formation of hexadecyltriethanolammonium bromide.
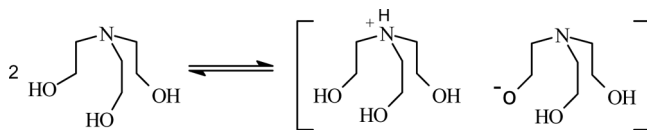
Scheme 4. Ion pair formation of triethanolamine.

in the ion pair form, and both O- and N-sites are alkylated, whereas diethanolamine is alkylated only at nitrogen center.

The N-alkylated products from diethanolamine have been used as the synthon components of some novel tertiary amines. The quaternary diethanolammonium bromides, on treatment with alkali, resulted in alkyldiethanolamines. These bases with decyl, tetradecyl, and hexadecyl chains produce foams in water upon shaking. These compounds also form a condensed monolayer on water surface.

The tertiary bases (**6a–c**) further provide scope of synthesizing some double-tailed surfactants. On Menschutkin reaction with alkyl bromides, the bases afforded quaternary compounds (**7a–g**) (Scheme 5). A $C_{16}C_{10}$ double-tailed quaternary diethanolammonium compound (**7c**) could be obtained by treating C_{16} tertiary base with C_{10} alkyl bromide and separately by treating C_{10} tertiary base with C_{16} alkyl bromide. The products in both the cases have superimposed spectral characteristics, and the melting points are the same. These compounds also produce foam in water and can form a condensed monolayer on water surface. Among the synthesized double-tailed ethanolammonium salts, the $C_{16}C_6$ diethanolammonium bromide (**7a**) is soluble in water in hot conditions but reappears up on cooling.

The tertiary bases (**6a–c**) were used as the synthon components for the synthesis of some GSs (**8a–g**). With dibromoalkanes, the tertiary bases undergo Menschutkin reaction to afford cationic functional GSs, where the cationic onium ions are separated by flexible spacers
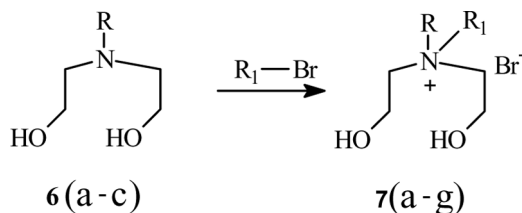
Scheme 5. a, $R = C_{16}H_{33}$, $R_1 = C_6H_{13}$; b, $R = C_{16}H_{33}$, $R_1 = C_8H_{17}$; c, $R = C_{16}H_{33}$, $R_1 = C_{10}H_{21}$; d, $R = C_{16}H_{33}$, $R_1 = C_{14}H_{29}$; e, $R = C_{16}H_{33}$, $R_1 = C_{16}H_{33}$; f, $R = C_{10}H_{21}$, $R_1 = C_{10}H_{21}$; and g, $R = C_{10}H_{21}$, $R_1 = C_{16}H_{33}$.
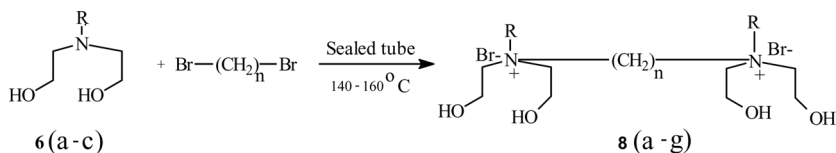
Scheme 6. a, $R = C_{16}H_{33}$, $n = 2$; b, $R = C_{16}H_{33}$, $n = 3$; c, $R = C_{16}H_{33}$, $n = 4$; d, $R = C_{16}H_{33}$, $n = 5$; e, $R = C_{14}H_{29}$, $n = 6$; f, $R = C_{16}H_{33}$, $n = 4$; g, $R = C_{10}H_{21}$, $n = 4$.

(Scheme 6). When the spacers are small, there is a decrease in hydrophobicity, leading to water solubility. The GSs with hexadecyl alkyl chains and $n = 2$ (**6a**) and $n = 3$ (**6b**) spacers are water soluble, whereas the GS with $n = 4$ (**6c**) spacer is soluble in hot water, and they aggregate beyond concentration range 3×10^{-4} to 5.6×10^{-4} M forming, probably, micelles. The critical concentration, termed cmc, is found to be much less than the cmc of CTAB. The GS with $n = 6$ (**6d**) spacer, however, is water insoluble.

Thus a novel class of functional surfactants and the corresponding GSs have been strategically synthesized to open up a new horizon in the area of surfactant systems.

EXPERIMENTAL

Diethanolamine, TEA, alkyl bromides, and dibromoalkanes are of Sisco research-grade (India) and have been used without further purification. Methanol, ethanol, acetonitrile, ethylacetate, cetyl amine, and bromoethanol (Merck, India) were purified by distillation before use.

Synthesis of N-Hexadecyltriethanolammonium Bromide (2)

A mixture of bromoethanol (0.081 mol) and *n*-hexadecyl amine (0.027 mol) in 3:1 molar ratio was refluxed for 24 h followed by dropwise addition of 2.7 M NaOH on a water bath. The reaction mixture was extracted with chloroform, and the organic layer was dried over anhydrous sodium sulfate. Chloroform was removed by evaporation in air, and the solid mass thus obtained was desiccated. The mass was recrystallized from methanol/ethylacetate solvent to obtain a white compound: yield 40%; mp 115°C; ^{1}H NMR (400 MHz, CDCl$_3$): δ/ppm = 0.88 (t, 3H), 1.25–1.34 (br, m, 26H), 1.83 (br, 2H), 3.18–3.23 (br, 2H), 3.35–3.49 (br, 6H), 4.08 (br, 6H). CHN clculated: C, 58.15%; H,

10.57%; N, 3.08%. Found: C, 58.13%; H, 10.64%; N, 3.08%. MS m/z calcd.: 374.62; found: 374.2.

Synthesis of N-Hexadecyldiethanolammonium Bromide (5a)

A mixture of diethanolamine (6.6 mM) and hexadecyl bromide (0.0066 mol) in 1:1 ratio in 20 mL methanol–acetonitrile solvent mixture (30:70) was refluxed for 48 h on a water bath. The solvent was evaporated on a water bath followed by cooling up to 5°C to obtain a milky white mass. It was washed with ether several times to remove any trace of the hexadecyl bromide and recrystallized from methanol/ethyl acetate mixed solvent to obtain a white crystalline product (5a): yield 90%; mp 85°C; ^{1}H NMR (400 MHz, CDCl$_3$): δ/ppm = 0.88 (t, 3H), 1.18–1.35 (br, m, 26H), 1.81 (br, 2H), 3.54 (br, 2H), 3.67 (br, 4H), 4.03 (br, 4H), 8.77 (br, s). CHN calculated: C, 58.52; 10.80; N, 3.41. Found: C, 58.66; H, 11.03; N, 3.30. Mass (m/z): calc.: 330; found: 330.

By following this procedure, 5b was synthesized (reflux time: 44 h, yield 90%, mp 62–65°C). The same procedure was also followed for the synthesis of 5c (reflux time: 50 h, yield 76%, mp 27–32°C). Compound 5b was crystallized from methanol/ethyl acetate.

Synthesis of N-Hexadecyldiethanolamine (6a)

Hexadecyldiethanolammonium bromide (5a: 0.005 mol) was dissolved in 30 mL water followed by addition of 30 ml 2 N ammonia. The solution was transferred to a separating funnel and was extracted with 20-mL portions ether three to four times. The ethereal layers were collected, evaporated to dryness in air, and kept in the desiccator to obtain the desired tertiary amine (6a) in solid state; yield 70%; mp 49–51°C; IR: 3301.70 (-OH), 2920.95 (-CH), 2851.91 (-CH), 1043.90 (-CO), 876.96 (-C-C), 721.77 (-C-C) cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ/ppm = 0.88 (t, 3H), 1.26 (bs, 28H), 2.52 (m, 2H), 2.66 (t, 4H), 3.6 (t, 4H); mass (m/z): 329.57 (calc.); (M$^+$ + 1) 330.6; (M$^+$ −1) 328.8 (found).

Following the same procedure, tetradecyldiethanolamine (6b) and decyldiethanolamine (6c) were synthesized from diethanolamine and corresponding alkyl bromides respectively.

Compound 6b: Yield 75%; waxy solid; IR: 3333.87 (-OH), 2923.98 (-CH), 2853.52 (-CH), 1367.21 (-CN), 1045 (-CO), 877.44 (-C-C), 721.08 (-C-C) cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ/ppm = 0.88 (t, 3H), 1.25 (bs, 22H), 1.45 (m, 2H), 2.52 (t, 2H), 2.65 (t, 4H), 3.61 (t, 4H).

Compound 6c: Yield 70%; waxy solid; IR: 3333.98 (-OH), 2925.57 (-CH), 2854.59 (-CH), 1044.41 (-CO), 876.86 (-C-C), 722.34 (-C-C) cm^{-1};

^{1}H NMR (400 MHz, CDCl$_3$): δ/ppm = 0.88 (t, 3H), 1.26 (bs, 14H), 1.47 (m, 2H), 2.55 (t, 2H), 2.68 (t, 4H), 3.63 (t, 4H).

Synthesis of Hexadecylhexyldiethanolamonium Bromide (7a)

A mixture of hexadecyldiethanolamine (**6a**: 0.0036 mol) and hexyl bromide (0.0036 mol) was heated neat in an oil bath in a sealed tube in 1:1 molar ratio at 140–150°C for 53 h. A dark solid was obtained, which was washed with ether several times until the product became white. The product was crystallized from 1:1 methanol–ethylacetate mixture to obtain hexadecylhexyldiethanolammonium bromide (**7a**); yield 42%; mp 137°C; IR = 3333.67 (OH), 2924.5 (CH), 2852.3 (CH), 1372.58 (CN), 1305.71 (CN), 1075.46 (CO), 875.4 (C-C) cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ/ppm = 0.88 (6H), 1.2–1.39 (32H), 1.89 (4H), 2.88–2.97 (4H), 3.21–3.46 (4H), 4.09 (2H), 4.5 (2H); mass (m/z): 414.73 (calc.), 414.60 (found).

The same procedure was adopted for the synthesis of hexadecyloctyl-diethanolammonium bromide (**7b**) and hexadecyldecyldiethanol ammonium bromide (**7c**). TLC: **7a**, ethyl acetate—single spot; **7b**, no suitable eluent; **7c**, 1:1 mixture of methanol and ethyl acetate—single spot.

Compound **7b**: Reaction time 89 h; yield 35%; mp 185°C; ^{1}H NMR (400 MHz, CDCl$_3$): δ/ppm = 0.88 (6H), 1.25–1.33 (36H), 1.92 (4H), 2.95 (4H), 3.48 (4H), 3.98 (2H), 4.37 (2H).

Compound **7c**: Reaction time 76 h; yield 35%; mp 180°C; ^{1}H NMR (400 MHz, CDCl$_3$): δ/ppm = 0.88 (6H), 1.2–1.33 (40H), 1.92 (4H), 2.93–3.01 (4H), 3.5 (4H), 3.98 (2H), 4.35 (2H).

Synthesis of GSs from Hexadecyldiethanolamine and Dibromoethane (8a)

A mixture of hexadecyldiethanolamine (**6a**: 0.0015 mol) and 1,2-dibromo ethane (0.00075 mol) was heated neat in an oil bath in a sealed tube in a 2:1 molar ratio at 140°C for 30 h. A brownish black solid was obtained, which was washed with ether several times to remove unreacted hexade-cyldiethanolamine and dibromo ethane. A solid white mass was obtained, which was recrystallized from methanol/ethyl acetate (**8a**); yield 32%; mp 60°C; IR: 3329.73 (-OH), 2919.26 (-CH), 2851.55 (-CH), 1074.43 (-CO), 722.25 (-C-C) cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ/ppm = 0.88 (6H), 1.26–1.34 (56H), 1.82 (4H), 3.2–3.5 (8H), 3.6–3.9 (4H), 4.0–4.23 (8H).

By using this procedure, the GSs (**8b–g**) have been synthesized with suitable alkyl bromides and dibromo alkanes.

Compound **8b**: Reflux time: 57 h; yield 20%; mp 128°C; IR: 3369.07 (-OH), 2919.53 (-CH), 2851.76 (-CH), 1111.91 (-CO), 723.80 (-C-C) cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ/ppm = 0.88 (6H), 1.255 (56H), 1.34 (2H), 1.85 (4H), 2.95 (8H), 3.5 (4Ha), 4.0 (4Hb), 4.5 (4H).

Compound **8c**: Reflux time: 28 h; yield 30%; mp 222–224°C; IR: 3331.48 (-OH), 2920.19 (-OH), 2851.76 (-OH), 1075.60 (-CO), 721.94 (-C-C) cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ/ppm = 0.86 (6H), 1.24–1.67 (60H), 3.43 (8H), 3.56 (8H), 3.81 (8H).

Compound **8d**: Reflux time: 56 h; yield 18%; mp 143°C.

Compound **8e**: Reflux time: 50 h; yield 40%; mp 152–155°C; IR: 3438.50 (-OH), 2919.90 (-CH), 1111.88 (-CO), 1261.69 (-CN), 723.80 (-C-C) cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ/ppm = 0.88 (6H), 1.25 (56H), 1.32 (8H), 1.93 (4H), 2.95 (8H), 3.5 (4Ha), 4.0 (4Hb), 4.3 (4H).

Compound **8f**: Reflux time: 54 h; yield 72%; mp 145–148°C; IR: 3392.73 (-OH), 2919.56 (-CH), 2851.77 (-CH), 1111.77 (-CO), 867.90 (-C-C), 723.58 (-C-C) cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ/ppm = 0.88 (6H), 1.25 (44H), 1.31 (8H), 1.94 (4H), 2.92–2.99 (8H), 3.5 (4H), 4.0 (4H), 4.37 (4H).

Compound **8g**: Reflux time: 96 h; yield 70%; mp 136–139°C; IR: 3389.58 (-OH), 2924.14 (-CH), 2854.12 (-CH), 1370.08 (-CN), 1114 (-CO), 871.79 (-C-C), 723.58 (-C-C) cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ/ppm = 0.88 (6H), 1.25 (28H), 1.34 (8H), 1.95 (4H), 2.9–2.98 (8H), 3.48 (4H), 4.0 (4H), 4.38 (4H).

ACKNOWLEDGMENT

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