Glyceryl *Bis*ether Sulfates. I: Improved Synthesis

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Sparse literature outlines previous syntheses for glyceryl *bis*ether sulfates, which, while giving rise to the desired molecules, are somewhat cumbersome and suffer from undesired by-product formation. We now report an improved synthesis of the title compounds that results in greater simplicity and reduced by-product formation. An hypothesis is advanced to explain the by-product formation.

KEY WORDS: Centrally located hydrophile, epichlorohydrin, glyceryl *bis*ether sulfate, synthesis.

The surfactant and home products industry carries on an ongoing search for new surfactant structures from which enhanced product performance may be obtained. In the course of such investigations, we have researched surfactant structures that contain a centrally located hydrophilic moiety such as the title compounds, 1,3-*bis*-(alkylethyleneoxy)-propane-2-yl sodium sulfates or glyceryl *bis*ether sulfates (GBES).

The chemical literature (1–8) reveals several synthetic methods to produce GBES and their unsulfated precursor glyceryl *bis*ethoxylates (GBE), and it describes the compounds' physical and spectroscopic properties. However, the known synthetic routes constitute a complex series of reactions and purifications before arriving at the desired compounds. This paper outlines a simple and direct synthetic path that yields GBES and minimizes reaction steps, unwanted impurities and purification steps.

EXPERIMENTAL PROCEDURES

Alcohol ethoxylate samples. The ethoxylated primary linear alcohols used as starting materials for GBES synthesis were of two types, pure homologue and nonpure homologue. Every effort was made to minimize the number of individual compounds used to make the nonpure homolog alcohols, so that each GBES sample would then be as chemically distinct as possible. For example, the $C_5EO_{1.5}$ GBES was derived from an alcohol mixture containing equal parts by weight of C_4-EO_1, C_4-EO_2, C_6-EO_1 and C_6-EO_2 ethoxylated alcohols.

1,3-Bis[*2-(*n-*hexyloxyethoxy)ethoxy*]*propane-2-ol.* A 3-L, three-necked, round-bottom flask, fitted with an addition funnel, mechanical stirrer and an internal thermometer, was charged with diethyleneglycol monohexylether (1000 g, 5.25 moles, 1070 mL) and epichlorohydrin (122 g, 1.31 moles, 103 mL). The reaction mixture was heated to 60°C with vigorous stirring, and sodium hydroxide as a 50% (w/w) solution in water (52.5 g, 1.31 moles NaOH; 105 g, 72 mL 50% solution) was added dropwise over a period of one hour. The reaction was exothermic, and the temperature was maintained at 80–90°C. A white precipitate formed soon after the addition was started. Then, additional sodium hydroxide as a 50% (w/w) solution in water (52.5 g, 1.31 moles NaOH; 105 g, 72 mL 50% solution) was added in one aliquot. After stirring for one more hour at 70–80°C, the reaction was cooled to 40°C and slowly neutralized by the addition of concentrated (37%) HCl (110 mL). Voluminous white precipitate formed. The final pH was carefully adjusted to 6–7.

The crude organic product was decanted away from the separated water and NaCl. This cloudy, slightly yellow, organic product was dried over $MgSO_4$ and filtered to give the clear yellow crude product as a 2:1 ratio (by moles) of diethyleneglycol monohexylether and product 1,3-*bis*-[2-(*n*-hexyloxyethoxy)ethoxy]propane-2-ol (1030 g, 96% of expected mass).

A sample of the crude product mixture (330 g) was placed in a 1-L, round-bottom flask with Teflon boiling chips and a magnetic stir bar, and the flask was fitted with a short-path condenser head. Vacuum distillation removed a small amount of water (5 mL, 25°C at 10 mmHg), followed by the unreacted starting diethyleneglycol monohexylether (163 g, 175 mL, 107%; 130–160°C at 10 mmHg). This left product 1,3-*bis*[2-(*n*-hexyloxyethoxy)-ethoxy]propane-2-ol as a yellow oil (167 g, 95%). The product was estimated to be 95% by weight based on gas chromatography (GC) peak areas, thus giving a 90% overall yield of desired product based on epichlorohydrin. Of the remaining 5% of the isolated product, 3% was starting ethoxylate and 2% was intermediate glycidyl ether. The product was analyzed by GC, GC/mass spectrometry, ^1H nuclear magnetic resonance (NMR), ^{13}C NMR and DEPT ^{13}C NMR. All analyses supported the structure assignment given.

1,3-Bis[*2-(*n-*hexyloxyethoxy)ethoxy*]*propane-2-yl sodium sulfate.* A chlorosulfation apparatus was constructed on a 100-mL scale. In the apparatus, chlorosulfonic acid could be added dropwise as part of a continually flowing (dry) air stream. The stream was routed below the reaction level in the reactor. Thus, the chlorosulfonic acid was quickly dispersed in the reactant alcohol. The reactor was kept at below-atmospheric pressure by means of a water aspirator. Thus, HCl gas produced by the reaction was quickly eliminated. The reaction was stirred vigorously with a mechanical stirrer.

Into the chlorosulfonic acid reactor described above was added 1,3-*bis*[2-(*n*-hexyloxyethoxy)ethoxy]propane-2-ol (30.0 g, 0.0751 moles, formula weight = 399.3 based on hydroxyl number = 140.5), and the addition funnel was charged with chlorosulfonic acid (9.63 g, 0.0826 moles, 5.49 mL). With vigorous stirring, the chlorosulfonic acid was added dropwise over a period of 15 min. Soon after the addition was started, a sharp temperature rise was noted and controlled by means of an ice bath. A yellow color developed over the course of the addition. Once addition was complete, the ice bath was removed, and the reaction was "flushed" of as much HCl as possible by using the air flow and water aspirator. The product sulfonic acid monoester was neutralized with 1.0M NaOH (~100 mL) in a variable-speed blender to pH 9–10 to give an off-white aqueous solution of the desired product 1,3-*bis*[2-(*n*-hexyloxyethoxy)ethoxy]propane-2-yl sodium sulfate (135.7 g, 27.8% active, 97% yield, 87% yield based on epichlorohydrin).

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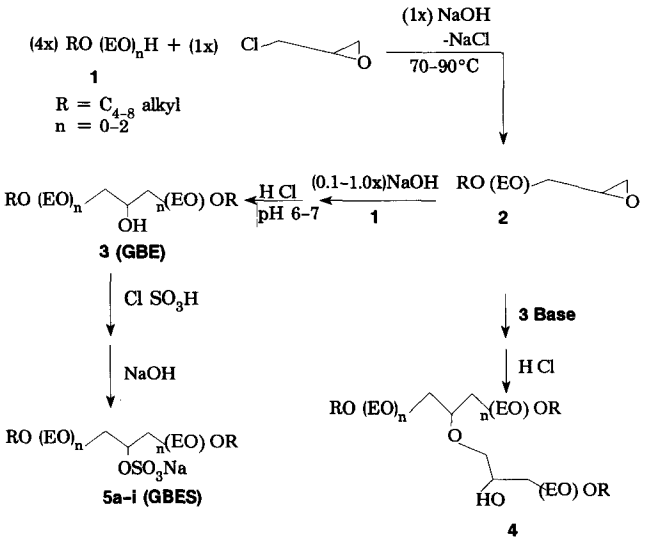
Methylene blue active substance (MBAS). MBAS was measured as in ASTM D-1681 (9).

Oil. Unsulfated alcohol is accounted for as "oil" and was measured by a chromatographic method outlined elsewhere (10).

Inorganic salts. Sodium sulfate and chloride were measured as in ASTM 1570 (9).

Nomenclature. The GBES molecules discussed herein are named for the ethoxylated alcohol from which they were made. For example, C_6EO_2 GBES refers to the compound whose synthesis is described above, 1,3-*bis*[2-(*n*-hexyloxyethoxy)ethoxy]propane-2-yl sodium sulfate. Even though this compound was made from hexyloxyethoxyethanol (C_6EO_2), the total "hydrophobe chain-length" is C_{12}, and the total number of ethyleneoxide (EO) units incorporated is four.



SCHEME 1

RESULTS AND DISCUSSION

A review of the chemical literature revealed only a few references to GBES or their unsulfated precursors GBE. Szymanowsky (1–3), Okahara (4,5) and Ulbrich (6) describe a synthetic route involving reacting epichlorohydrin with an ethoxylate by boron trifluoride catalysis, isolation and purification of the resulting chlorohydrin ether, followed by base-induced epoxidation and condensation between more ethoxylate and the intermediate glycidyl ether. The product was purified by repeated vacuum distillation. This sequence requires multiple steps and purifications and also suffers from potential Lewis acid-catalyzed decomposition of the polyethyleneoxide portion of the ethoxylate with formation of 1,4-dioxane (11).

The two equivalents of ethoxylate were first converted to its alkali metal salt and this was reacted with one equivalent of epichlorohydrin to yield GBE. The product was used without further purification. In our hands, this procedure suffered from slow kinetics and formation of a significant quantity of high-molecular weight by-products, made up mainly of compound 4 in Scheme 1 in which the synthetic route is given for GBES. For example, an attempted synthesis of **3f** by the route outlined in U.S. Patent 4,978,805 (7) required 36 h at 90°C for completion and resulted in formation of approximately 25% of **4f** by GC area. In contrast, synthesis of **3f** by the method described herein was complete in 2 h and resulted in formation of less than 1% of **4f** by GC area.

Finally, it was (8) recommended to first ethoxylate glycerin in the standard base-mediated method, followed by condensation of the ethoxylated glycerin with two equivalents of an alkyl halide to make GBE. This method, however, produces no regiospecificity in the product, which consists of a vast array of compounds; EO and alkyl groups are distributed statistically over the three reactive positions in glycerin.

In an effort to circumvent the above problems with the known synthetic pathways, nine different GBES compounds were produced by the methods detailed in the Experimental Procedure section and outlined in Scheme 1. The reaction sequence eliminates the possible Lewis acid-catalyzed decomposition of the ethoxylate starting material (11), multiple reaction and purification sequences (1–6), long reaction time and major by-product formation (7) and lack of chemical regiospecificity (8). Instead, it employs one quick (2-h) reaction and one purification to make GBE.

Control of the reaction between the ethoxylated alcohol and epichlorohydrin is crucial for the success of this synthetic method. In practice, one charges the reactor with the required amounts of ethoxylate and epichlorohydrin, and NaOH is then added. In this manner, the ethoxylate 1 adds to epichlorohydrin, giving glycidyl ether 2. Then, another equivalent of ethoxylate 1 adds to 2, producing mainly the desired product GBE 3. A small portion of by-product 4 is also made by the undesired reaction between 2 and 3. The GBE is neutralized, decanted and stripped of excess starting ethoxylate and then sulfated to give GBES 5. Although we used chlorosulfonic acid as the sulfating agent, other choices, such as sulfamic acid or sulfur trioxide, would suffice.

Formation of 4 (the main by-product of the literature methods mentioned above) is minimized by using excess ethoxylate relative to epichlorohydrin, by avoiding localized concentrations of alkali during the addition of the first equivalent of NaOH and by adding the alkali to the hot reaction mixture of epichlorohydrin and ethoxylate. Thus, the first equivalent of NaOH is slowly added to the organic reaction mixture as a 50% solution in water under vigorous stirring while the reaction temperature is high enough to promote fast reaction (12). Although definitive proof is not available, a probable explanation for the observed persistent formation of 4 in the absence of the reaction sequence outlined here may lie in the differing reaction rates among 1, 2 and 3. Thus, the rates of the reactions between 1 and epichlorohydrin and between 1 and 2 are probably of similar magnitude, but both are probably substantially slower than the rate of reaction between 2 and 3. This scenario would account for the persistent formation of 4 and would necessitate the above-described measures to minimize the formation of 4. Essentially no multiple adducts of epichlorohydrin were detected. Table 1 lists the analytical data for the GBES samples made by this method.

TABLE 1

Analytical Data for Glyceryl *Bis*ether Sulfates Samples Prepared

Compound	R[a]	n[b]	Pure homologue	Overall yield	% Na_2SO_4	% Oil	% Active
5a	C_4	1	Yes	87	0.81	0.13	16.9
5b	C_5	0.5	No	82	0.65	0.09	19.1
5c	C_5	1.5	No	91	1.29	0.85	14.2
5d	C_6	0	Yes	80	0.69	0.11	21.7
5e	C_6	1	Yes	85	0.25	0.34	18.4
5f	C_6	2	Yes	87	0.61	0.16	27.8
5g	C_7	0.5	No	83	0.68	0.06	17.5
5h	C_7	1.5	No	79	0.62	0.18	26.8
51	C_8	1	No	85	0.57	0.46	22.3

[a]Alcohol chainlength.
[b]The number of ethylene oxide units on each alcohol.

It was also observed that, in single-reaction competitive rate studies, unethoxylated alcohols reacted with epichlorohydrin slower than ethoxylated alcohols. This seems analogous to the well-studied (13) phenomenon where a molecule of fatty alcohol will react slowly with the first molecule of EO during ethoxylation and quickly with subsequent molecules of ethylene oxide.

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REFERENCES

1. Szymanowsky, J., *J. of Chromatogr. 398*:31 (1987).
2. Szymanowsky, J., *Ibid. 409*:29 (1987).
3. Szymanowsky, J., *Coll. Polym. Sci. 266*:765 (1988).
4. Okahara, M., *J. Org. Chem. 48*:1237 (1983).
5. Okahara, M., *Synthesis*:73 (1984).
6. Ulbrich, U., *Collect. Czech. Chem. Comm. 29*:1466 (1964).
7. U.S. Patent 4,978,805.
8. U.S. Patent 5,117,032.
9. *Annual Book of ASTM Standards*, American Society for Testing Materials, Philadelphia, 1993.
10. Sender and Riemersma, *Tenside Surf. Det. 27*:47 (1990).
11. Matheson, K.L., and P.A. Schwab, *Proceedings of 3rd International Surfactants Congress and Exposition*, 1992.
12. Condon, B.D., U.S. Patent applied for, 1994.
13. Geissler, P.R., *J. Am. Oil Chem. Soc. 67*:123 (1990).

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