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Dimeric Surfactants : First Synthesis of an Asymmetrical Gemini Compound

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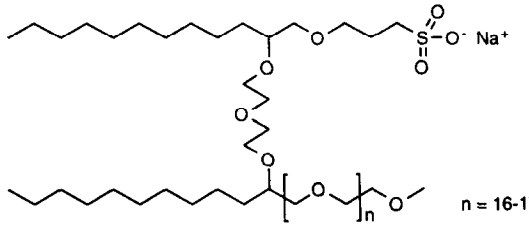
Abstract: The heterodimeric surfactant **1** is synthesized through a 6-step procedure, starting from 1,2-epoxydodecane. The preliminary evaluation of the performances of that asymmetrical gemini representing a new kind of surface-active agents reveals interesting physical properties.

Much attention has been paid to the synthesis and evaluation of "non-conventional" surfactants for the last decade[1-7]. Bolaform-type and gemini-type surfactants have gained special interest because of their unusual aggregation properties[6,8-22]. The name gemini was assigned in 1991 to amphiphilic compounds possessing two surfactant sub-structures (*i.e.* a long hydrophobic chain bearing a hydrophilic group) connected together through a spacer arm[23]. Geminis are about 3 orders of magnitude more efficient at reducing surface tension, and more than 2 orders of magnitude more efficient at forming micelles than are conventional ionic surfactants[13,14]. In addition, they show positive synergistic effects when mixed with other surfactants.

We became highly interested in this new type of amphiphiles because of several potential applications as drug delivery systems, therapeutical agents, catalysts in chemical reactions or detergents for industrial and household applications for example. Here we report the synthesis and preliminary evaluation of the original asymmetrical gemini structure **1** (Fig. 1).



1

- Figure 1 -

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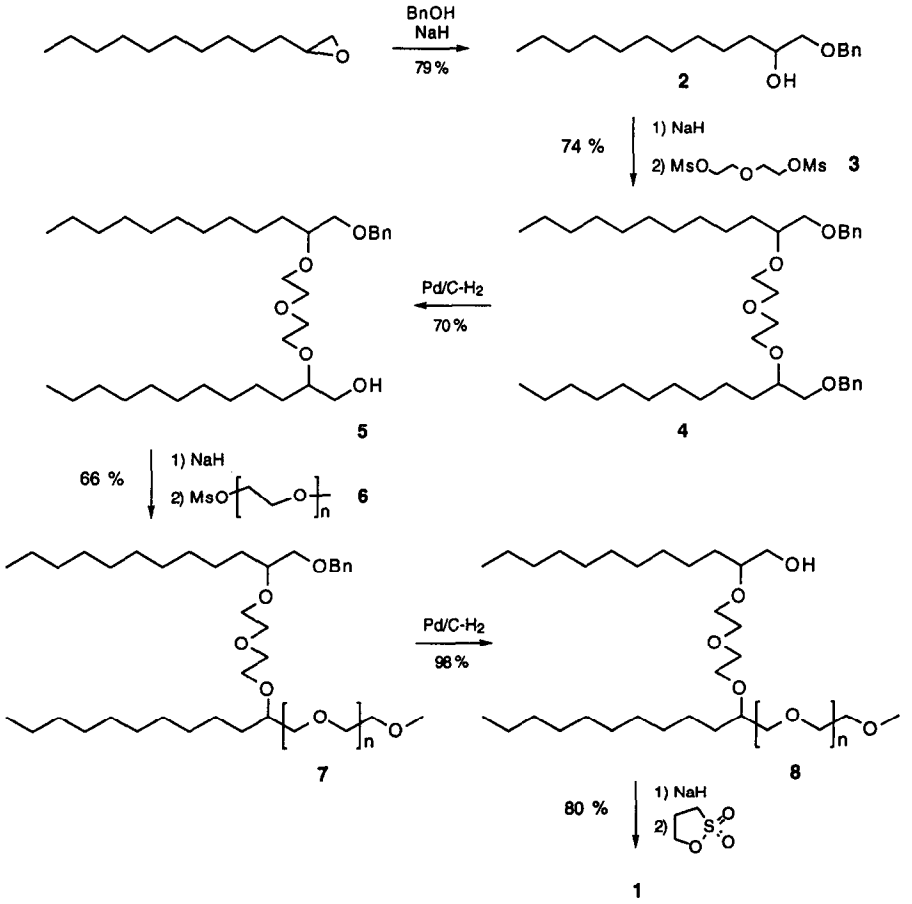
The heterodimeric surfactant has been designed so as to exhibit an original combination of the properties of non-ionic and anionic surfactants. The compound has two identical hydrophobic chains but presents two different hydrophilic head groups: one is a poly(oxyethylene) moiety and the second is a sulfonic acid sodium salt. The two surfactant monomers are connected together by the mean of a flexible hydrophilic poly(oxyethylene) spacer. Though the properties of that new surface-active material are not easy to predict in advance, they are expected to be appreciably different from those obtained by simply mixing the corresponding monomers.

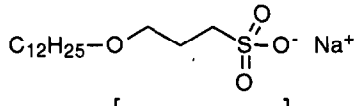
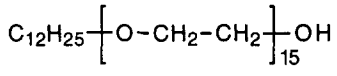
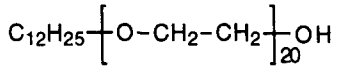
The synthesis of the title compound **1** is achieved following a 6-step procedure, starting from commercially available 1,2-epoxydodecane (Fig. 2). The benzyloxy alcohol **2** is obtained by reaction of the epoxidodecane with benzyl alcohol, in the presence of sodium hydride. The reaction is conducted in benzyl alcohol in order to avoid the formation of side-products resulting from oligomerisation of the starting material. The bis-methanesulfonyl ester of diethylene glycol **3** is then substituted twice by the sodium alkoxide obtained



- Figure 2 -

from **2**, in refluxing anhydrous dioxane. The resulting bis-benzyl ether **4** leads to the monohydroxy compound **5** by partial catalytic hydrogenolysis over Pd/C. The sodium salt of **5** is further condensed with the methanesulfonyl ester of poly(oxyethylene) 750 monomethyl ether **6** to afford the polyether compound **7**. Hydrogenolysis of the later compound over Pd/C and reaction of the subsequent alcohol **8** in refluxing dioxane with 1,3-propane sultone[24,25] in the presence of sodium hydride furnishes the targeted gemini compound **1**[26].

The values measured for critical micelle concentration (cmc) and static surface tension (surface tension at cmc, γcmc) for compound **1** and those reported in the literature for the corresponding monomers or analogue compounds are listed in Table 1. As expected, the gemini compound exhibits a cmc value far below that of the sulfonate and polyether monomers, and even below that of the symmetrical bis-sulfonate gemini[27]. The values for the static surface tension at the cmc are not meaningfully different as far as we can compare them between **1** and the monomers.

Compound	cmc (M)*	γcmc (mN/m)	Reference
1	$1.5\ 10^{-5}$	39.8	-
	$5.0\ 10^{-3}$	38.9	[25]
	$1.2\ 10^{-4}$	-	[28]
	$1.6\ 10^{-4}$	-	[28]

* The cmc values were measured in pure water at 20 °C.

- Table 1 -

We have described the synthesis and preliminary evaluation of a new gemini compound with asymmetrical structure. To our knowledge, the preparation and properties of such heterodimeric surfactant have never been reported till now. Extensive physical characterization of **1** is currently underway and complete results will be published elsewhere.

References

1. Cheng, Y.; Ho, D.M.; Gottlieb, C.R.; Kahne, D.; Bruck, M.A. *J. Am. Chem. Soc.* **1992**, *114*, 7319-7320.
2. Menger, F.M.; Yamasaki, Y. *J. Am. Chem. Soc.* **1993**, *115*, 3840-3841.
3. Menger, F.M.; Whitesell, L.G. *J. Org. Chem.* **1987**, *52*, 3793-3798.

4. Nusselder, J.J.H.; Engberts, J.B.F.N. *J. Am. Chem. Soc.* **1989**, *111*, 5000-5002.
5. Stein, T.M.; Gellman, S.H. *J. Am. Chem. Soc.* **1992**, *114*, 3943-3950.
6. Perez, L.; Torres, J.L.; Manresa, A.; Solans, C.; Infante, M.R. *Langmuir* **1996**, *12*, 5296-5301.
7. Wassermann, H.; Azim, E.; Coudert, G.; Achilefu, S.; Selve, C. *J. Chem. Soc. Perkin Trans II* **1992**, 2043-2047.
8. Zana, R. *Langmuir* **1996**, *12*, 1208-1211.
9. Duivenvoorde, F.L.; Feiters, M.C.; van der Gaast, S.J.; Engberts, J.B.F.N. *Langmuir* **1997**, *13*, 3737-3743.
10. Song, L.D.; Rosen, M.J. *Langmuir* **1996**, *12*, 1149-1153.
11. Sumida, Y.; Masuyama, A.; Oki, T.; Kida, T.; Nakatsuji, Y.; Ikeda, I.; Nojima, M. *Langmuir* **1996**, *12*, 3986-3990.
12. Danino, D.; Talmon, Y.; Zana, R. *J. Colloid Interface Sci.* **1997**, *185*, 84-93.
13. Menger, F.M.; Littau, C.A. *J. Am. Chem. Soc.* **1993**, *115*, 10083-10090.
14. Rosen, M.J. Geminis: A new generation of surfactants. In *Chemtech*, 1993; pp. 30-33.
15. Zana, R.; Talmon, Y. *Nature* **1993**, *362*, 228-230.
16. Alami, E.; Levy, H.; Zana, R.; Skoulios, A. *Langmuir* **1993**, *9*, 940-944.
17. Danino, D.; Talmon, Y.; Zana, R. *Langmuir* **1995**, *11*, 1448-1456.
18. Masuyama, A.; Yokota, M.; Zhu, Y.P.; Kida, T.; Nakatsuji, Y. *J.C.S. Chem. Commun.* **1994**, 1435-1436.
19. Zhu, Y.P.; Masuyama, A.; Kobata, Y.; Nakatsuji, Y.; Okahara, M.; Rosen, M.J. *J. Colloid Interface Sci.* **1993**, *158*, 40-45.
20. Zhu, Y.P.; Masuyama, A.; Okahara, M. *J. Am. Oil Chem. Soc.* **1990**, *67*, 459-466.
21. Dam, T.; Engberts, J.B.F.N.; Karthäuser, J.; Karaborni, S.; van Os, N.M. *Colloids Surf. A* **1996**, *118*, 41-49.
22. Castro, M.J.L.; Kovensky, J.; Fernandez Cirelli, A. *Tetrahedron Lett.* **1997**, *38*, 3995-3998.
23. Menger, F.M.; Littau, C.A. *J. Am. Chem. Soc.* **1991**, *113*, 1451.
24. Carrea, G.; Ottolina, G.; Riva, S. *Helv. Chim. Acta* **1988**, *71*, 762-772.
25. Suga, K.; Miyashige, T.; Takada, T.; Watanabe, S.; Moriyama, M. *Aust. J. Chem.* **1968**, *21*, 2333-2339.
26. Satisfactory analytical data were obtained for all purified compounds. Selected spectroscopic data for **1** (2 diastereomers) are as follows: ^{1}H-NMR ($CDCl_3$, 200 MHz, ppm) d 3.65-3.58 (m, 76H); 3.54-3.49 (m, 6H); 3.42-3.38 (m, 2H) 3.34 (s, 3H); 2.92-2.84 (m, 2H); 2.07-1.99 (m, 2H); 1.43-1.21 (m, 36H); 0.83 (t, J = 6.4 Hz, 6H). ^{13}C-NMR ($CDCl_3$, 50 MHz, ppm) d 79.02 and 78.98; 78.92 and 78.81; 73.27 and 73.22; 73.03 and 73.00; 71.71; 70.63; 70.54; 70.33; 70.20; 69.70; 68.72; 68.36; 68.16; 58.88; 48.25; 31.78; 31.42 and 31.37; 30.98 and 30.85; 29.67; 29.51; 29.22; 25.41 and 25.28; 25.20 and 25.02; 22.55; 13.99. IR (neat, cm^{-1}) n 3502 (b); 2923; 2859; 1458; 1348; 1299; 1245; 1112; 1045.
27. Renouf, P.; Hebrault, D.; Guérin, G.; Desmurs, J.R.; Mioskowski, C.; Lebeau, L. *in preparation.*
28. Harada, T.; Nishikido, N.; Moroi, Y., Matuura, R. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 2592-2597.