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SYNTHESES OF PERFLUOROALKYL N-POLYETHOXYLATED AMIDES

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SUMMARY

Monodisperse perfluoroalkyl N-polyethoxylated amides, $C_nF_{2n+1}CONH(CH_2CH_2O)_mH$, with $n = 6, 7, 8$ and 9 and $m = 2, 3,$ and 4 , are potential nonionic fluorinated surfactants. The syntheses of these compounds are described.

INTRODUCTION

Fluorochemical surfactants in general are used in industry as superwetting agents, antifogging agents, defoamers, print enhancers, floor polishers, and a number of other applications [1]. Nonionic fluorinated surfactants are also used as emulsifiers for perfluorochemical blood substitutes [2]. Many industrial nonionic fluorinated surfactants are mixtures having the general structure



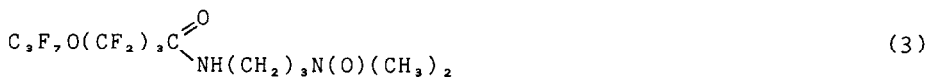
where n and m have a distribution of different values (i.e. the mixtures are polydisperse surfactants). When it is desired to

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use a nonionic fluorinated surfactant to solubilize perfluorocarbons to prepare aqueous emulsions, polydisperse surfactants do not form extremely stable microemulsions [3]. On the other hand, monodisperse surfactants of the type



in which n and m have single values for each compound, are excellent emulsifiers for perfluorocarbons [3]. The enhanced physical stability with such surfactants extends the lifetime of the blood substitute in the circulatory system and improves its storage properties. Another nonionic surfactant which has been used to prepare stable aqueous microemulsions of perfluorocarbons is called XMO-10 [2] and has the structural formula



The syntheses of both 2 and 3 are rather elaborate and the yields are not too high. In order to investigate alternative monodisperse compounds as nonionic fluorinated surfactants, we have devised new methods to synthesize monodisperse perfluoroalkyl N-polyethoxylated amides



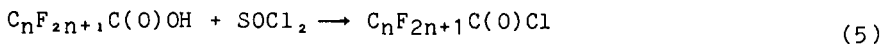
Details of the synthetic steps are given here.

EXPERIMENTAL

Methyl perfluorooctanoate and perfluorononanoic acid were purchased from Columbia Chemicals, Camden, South Carolina.

Perfluorooctanoyl chloride, perfluorooctanoic acid, and perfluorodecanoic acid were purchased from SCM Specialty Chemicals, Gainesville, Florida. Perfluoroheptanoic acid was purchased from Fluka Co., Switzerland. 2-(2-Aminoethoxy)ethanol, 2-bromoethylammonium bromide, diethylene glycol and triethylene glycol were purchased from Aldrich Chemical Company, Milwaukee, Wisconsin.

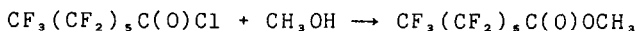
Preparation of Perfluoroacid Chlorides



The acyl chlorides are intermediates of the amides. A typical procedure for preparing the acyl chloride with $n = 6$ is described below. Procedures for preparing compounds with $n = 7$, 8, and 9 are similar. 7.28 gm (0.02 mole) of perfluoroheptanoic acid, 4 gm of thionylchloride (0.034 mole) and 0.1 gm of pyridine (to facilitate initiation of the reaction) were placed in a 50 ml 3-necked round bottom flask provided with a reflux condensor, a drying tube, a stirring bar and a N_2 -inlet. The reaction commenced immediately with an appearance of fumes due to the evolution of HCl. The contents were warmed and brought to a smooth reflux. Refluxing was continued for 2 hrs. The flask was cooled and two layers distinctly separated out. The lower layer of perfluoroheptanoyl chloride was separated and distilled. Traces of excess of thionyl chloride distilling at 76-78°C was discarded. The distillation was continued and the pure fraction distilling out at 110-115°C was collected (6.95 gm, 91%). ^{19}F NMR was consistent with the structure of the product.

Preparation of methyl esters

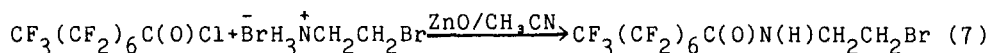
The methyl esters of the perfluoroalkanoic acids are starting materials for preparing amides with $m = 2$. The ester with $n = 7$ (methyl perfluorooctanoate) is commercially available from Columbia Chemicals, Camden, South Carolina. The typical procedure for preparing methyl perfluoroheptanoate is described below. The preparations of other methyl esters are similar.



1.38 gm of methanol (0.04 mole) and 0.1 gm of pyridine (catalytic amount) were placed in a 50 ml 3-necked round bottom flask equipped with a drying tube, a dropping funnel, and a stirring bar. The flask was placed in a trough containing ice and salt mixture. 7.65 gm of perfluoroheptanoyl chloride (0.02 mole) was then added from the dropping funnel such that the temperature did not rise above 10°C. Stirring was continued at 0°-5°C for 4 hrs. Two layers separated out. The lower layer of methylperfluoroheptanoate was separated and dissolved in 100 ml of ether. The ether layer was washed in a separatory funnel with 2x50 ml of 5% NaHCO₃ solution, followed by 2x50 ml of saturated saline solution and finally dried over anhydrous MgSO₄. Distillation of ether in a rotary evaporator afforded a colorless liquid (6.7 gm; 88%). This was then distilled in vacuo 60-65°C/3 mm. Both ¹H & ¹⁹F NMR were consistent with the structure of the product.

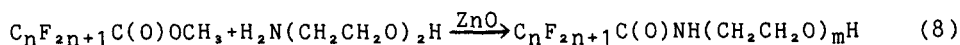
Preparation of N-(2-bromoethyl)perfluoroalkyl amides

N-(2-bromoethyl)perfluoroalkyl amides are starting materials for the N-polyethoxylated amides 4 with $m > 2$. A typical procedure for the synthesis is described in the following:



8.64 gm (0.01 mole) of perfluorooctanoyl chloride, 8 gm (0.03 mole) of 2-bromoethylammonium bromide, 1.6 gm (0.01 mole) of ZnO and 50 ml of CH_3CN were placed in a 100 ml 3-necked round bottom flask provided with a reflux condenser, a drying tube, a stirring bar and a N_2 inlet. The contents were heated and brought to a smooth reflux. Refluxing was continued overnight. The flask was cooled and the acetonitrile was removed in a rotary evaporator. The reaction mixture was diluted with 75 ml of saturated saline solution and extracted with 3x60 ml portions of ether. The ether extract was washed with 3x60 ml portions of 10% NaHCO_3 and finally again with 2x75 ml of saturated saline solution. The ether layer was dried over MgSO_4 and distilled off in a rotary evaporator to afford a colorless white solid (9.6 gm 91%). The procedure for preparing the homolog with $n=6$ is similar. The ^1H and ^{19}F NMR, IR and mass spectra were consistent with the structure of the products.

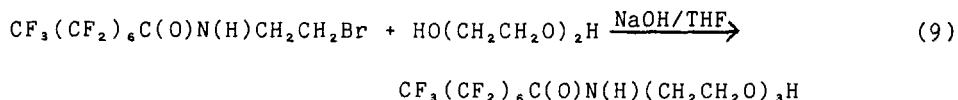
Preparation of N-diethoxylated amides ($m=2$)



0.01 mole (4.28 gm) of methyl perfluorooctanoate or the methyl ester of another perfluoroalkanoic acid, 0.05 mole (1.25 gm) of 2-(2-aminoethoxy)ethanol and 0.01 mole (0.813 gm) of ZnO were placed in a 50 ml 3-necked round bottom flask equipped with a reflux condenser, a N₂ inlet and a stirring bar. The contents were gradually warmed and brought to a gentle reflux. Refluxing was continued overnight. The flask was cooled and the light-brown reaction mixture was diluted with 50 ml of saturated saline solution and extracted with 3x15 ml portions of ether. The ether extract was again washed with 2x50 ml portions of saturated saline solution and finally dried over MgSO₄. Distillation of ether in vacuo afforded a colorless thick liquid which solidifies in the refrigerator (4.3 gm 86%). The thick oily solid was then vacuum distilled (Kugelrohr, 140-150°C/3 mm). ¹H, ¹³C and ¹⁹F NMR spectra were consistent with the structure of the desired product.

Preparation of N-polyethoxylated amides with m = 3 and 4

A typical reaction for this procedure is



15 ml of diethylene glycol (large excess) and 80 mg (2 mmole) of NaOH were placed in a 100 ml 3 necked round bottom flask equipped with a stirring bar, a reflux condenser, a drying tube, and a N₂ inlet. The flask was gradually warmed (temperature inside the flask = 52°C) such that complete dissolution of sodium hydroxide

took place. A solution of 1.04 gm (0.002 mole) of N-(2-bromoethyl)perfluorooctanamide in 10 ml of dry THF was added drop by drop such that the temperature did not rise above 60°C. After complete addition of the amide, heating was continued for another hour. The completion of the reaction can be tested by the neutrality of a pH paper. The flask was cooled and the contents were diluted with 25 ml of saturated saline solution. Tetrahydrofuran was distilled off in a rotary evaporator and the reaction mixture was extracted with 3x50 ml portions of chloroform. The chloroform layer was again washed with 2x40 ml portions of saturated saline solution and finally dried over MgSO₄. Distillation of chloroform in a rotary evaporator afforded a thick liquid which promptly solidified (0.565 gm, 52%). Distillation of the product (Kugelrohr, 145-152°C/3 mm) yielded a colorless white semisolid whose ¹H, ¹⁹F NMR are consistent with the structure of the product.

For m = 4, triethylene glycol was used in place of diethylene glycol. Compounds with n = 6 were prepared in a similar way.

DISCUSSION

The synthesis of monodisperse fluorinated N-polyethoxylated amides having the structure



which is similar to that of 4, was reported by Gartiser et al. [5]. In their method, one of the OH groups in a monodisperse polyethylene glycol is first converted into an amino group in a multi-step synthesis. The polyethoxylated amine is subsequently reacted with an acid in the presence of benzotriazolylxytrisdimethylaminophosphonium hexafluorophosphate ("BOP") and triethylamine. In our synthesis, we found that the reaction of the amine with the methyl ester using ZnO as catalyst proceeded smoothly with high yield (reaction 8). For $n = 7$ and $m = 2$, both starting materials are commercially available, and the synthesis involves only a single step. For $m = 2$, the use of N-(2-bromoethyl)perfluoroalkyl amide as a starting material for the preparation of the ethoxylated amides also worked well.

Simple, high yield syntheses of perfluoroalkyl N-ethoxylated amides have been shown. All together, eight compounds in this series have been prepared as potential fluorosurfactants. These include compounds $n = 6$ and 7 with $m = 2, 3,$ and 4 , and also $n = 8$ and 9 with $m = 2$. All the compounds are completely miscible with water at room temperature. The compound with $n = 7$ and $m = 1$ was also prepared, but it is not soluble in water and probably does not have surfactant properties. Unlike their hydrocarbon analogs, aqueous solutions of the perfluoroalkyl polyethoxylated amides have very high viscosities. For example, a 0.5% (w/v) solution of the compound with $n = 7$ and $m = 2$ has a viscosity of 6.20 cp at 298 K, which is 7 times the viscosity of water. However, the viscosity goes down rapidly in the presence of a nonionic hydrocarbon surfactant. Other physical properties of these compounds, including ternary phase diagrams with water and perfluorodecalin, are being studied.

ACKNOWLEDGEMENT

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REFERENCES

- 1 M.C. Allison, Polym. Paint Colour J. 174 (1984), 446.
- 2 L.C. Clark, Jr., R.E. Moore, D.G. Kinnett and E.I. Incho, Jr. Prog. Clin. Biol. Res., 122 (1983) 169.
- 3 G. Mathis, P. Leempoel, J.-C. Ravey, C. Selve and J.-J. Delpéuch, J. Am. Chem. Soc., 106 (1984) 6162.
- 4 M.-J. Stébé, G. Serratrice and J.-J. Delpéuch, J. Phys. Chem., 89 (1985) 2837.
- 5 T. Gartiser, C. Selve, L. Mansuy, A. Robert and J.-J. Delpéuch, J. Chem. Res. (M), (1984) 2672.