

Synthesis of Cyclic Type Semi-Fluorinated Disodium Alkanesulfonate

Sridhar Chirumarry, Yohan Ko, Kiwan Jang[†], and Dong-Soo Shin*

Department of Chemistry, Changwon National University, Changwon 51140, Korea.

[†]Department of Physics, Changwon National University, Changwon 51140, Korea.

*E-mail: ds shin@changwon.ac.kr

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ABSTRACT. A new perfluorobutyl substituted cyclic type disodium alkanesulfonate is designed, synthesized and characterized as alternative substance to perfluorooctane sulfonic acid (PFOS, 1), a well-known surfactant. Cyclic type sulfonate was accomplished from commercially available 2,2,3,3,4,4,5,5-octafluoro-1,6-hexanediol in four steps. Bio-degradable perfluorobutyl moiety was introduced from fluorous diol, which is symmetrically substituted amphiphile *via* installation of an intermediate trifluoromethanesulfonyl ester and easily manipulated by double displacement of triflate using potassium malonate and further reduction followed by nucleophilic ring opening are key reactions to get target disodium alkanesulfonate. The efficiency and simplicity in the synthesis of this material offer a new strategy to design PFOS alternatives.

Key words: PFOS alternatives, Cyclic-type sulfonate, Semi-fluorinate surfactants, Gemini surfactant, Surface tension

INTRODUCTION

Surfactants are amphiphilic material that can be greatly reduce the surface tension of water when used in very low concentrations, made up of water soluble (hydrophobic, such as aliphatic, aromatic or mixture of both) and water insoluble or soluble in organic solvent (hydrophobic), and play major role as bactericide, emulsifiers, dispersants, foaming, wetting and cleaning agents.¹⁻³ Depending on the charge present in their hydrophilic head, surfactants are classified into anionic (phosphates, sulfonates, sulfates and carboxylates (soap)), cationic (some form of amines generally quaternary ammonium groups), nonionic (polyethylene glycols) and amphoteric/zwitterionic (alkyl amino acids and acyl ethylene-diamines). Hydrophobic chain generally contain linear or branched hydrocarbon moieties, if it containing fluorocarbons are called fluorosurfactants.⁴ Among the fluorosurfactants manmade perfluoro octane sulfonic acid (PFOS) and its derivatives are proven to be most dependable substrates due to their special physiochemical properties. It has C₈F₁₇ as hydrophobic unit, while sulfonate as hydrophilic unit adds polarity, which is very stable compound that lowers surface tension of water more than that of hydrocarbon surfactant and is used in fire-fighting foam, stain repellents, paints, varnishes, polishes, leather, hydraulic fluids, pharmaceutical, metal plating, semiconductor industry, etc. However, due to chemical and biological stability in the environment and resistance against typical environmental degradation processes, including atmospheric photo-oxidation, direct

photolysis and hydrolysis, they are listed under Annex B of the Stockholm convention on persistent organic pollutants (POPs) in May 2009.⁵ PFOS accumulates to a high degree in humans and animals and caused postnatal deaths according to EPA's assessment and excessive solvation, hypo activity, ataxia, low food consumption, hepatic vacuolization and hypertrophy were found in monkeys when exposed to PFOS.⁶ Therefore, it is necessary to reduce toxicity, hazardous effects and improve biodegradability of PFOS derivatives, which is under progress in recent years. In this regard 3M Company, developed various alternative surfactants that contains shorter C₄-perfluoro chain.⁷ These perfluorobutane based materials are less bio-accumulative, less toxic and sustainable and proven to be potential replacements for eight-carbon homolog PFOS.⁸⁻¹⁰ Instead of linear hydrophobic and monohydrophobic group surfactants, gemini surfactants which contains more than one hydrophobic as well as hydrophilic group shows improved surface properties in solution.¹¹

By considering all the above mentioned structural parameters, previously we have synthesized perfluorobutyl substituted gemini surfactants which showed better CMC values, surface tension profiles and promising biodegradability results.¹² In continuation, present work on assuming gemini structure and bio-degradable shorter fluoroalkyl chain to enable the development of alternatives, we designed the structure of novel sulfonic acid type gemini surfactant having cyclic-type semi-fluoroalkyl group as hydrophobic segment instead of linear fluoroalkyl chain, which is depicted in

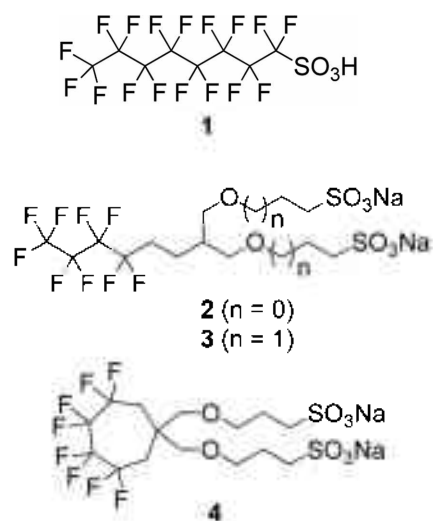


Figure 1. Structure of PFOS and its proposed alternatives.

Fig. 1. For the preparation of PFOS and its derivatives involves electrochemical perfluorination (ECF, which is an electrolytic production method) and telomerization (radical copolymerization) of vinylidene fluoride,¹³ but here in present our work on synthesis of environmentally friendly cyclic-type perfluoroalkyl disulfonates synthesis needed simple route, where introduction of perfluorinated alkyl chain is easily accessible and not cost-effective. Synthesis of target disodium surfactant is achieved from readily available 2,2,3,3,4,4,5,5-octafluoro-1,6-hexanediol in four steps using trifluoromethane-sulfonyl chloride, diethyl malonate and 1,3-propanesultone as other starting materials and involves triflate protection, nucleophilic substitution of dialkylation reaction in presence of sodium hydride as base, ester reduction with lithium aluminium hydride and nucleophilic ring opening of sultones by sodium hydride as base in high yields.

EXPERIMENTAL

All the glassware was dried thoroughly in hot oven and streamed with nitrogen before use. Solvents were dried and purified by conventional methods prior to use. All non-fluorinated starting materials and solvents were obtained from Sigma Aldrich (USA). 2,2,3,3,4,4,5,5-Octafluoro-1,6-hexanediol are purchased from Tokyo Chemical Industries Co. Ltd. (Japan). Melting points were determined on a digital SMP10 capillary melting point apparatus (SRUAT, UK). ¹H NMR (at 400 MHz) and ¹³C NMR (at 100 MHz) spectroscopic data were recorded on an Avance 400 MHz spectrometer (BRUKER, Germany). IR measurements of all the samples were performed on FTIR-6300 Spectrometer (JASCO, Japan). Gas chromatography-mass spectromet-

ric (GC-MS) analyses were carried out with Hewlett-Packard 6890 & 5973 system (AGILENT, USA) and MS spectra were performed on the LCQ Fleet ion trap mass spectrometer (Thermo Fisher Scientific Inc., San Jose, CA) using a Nano spray ion source with a fused-silica emitter (360 × 75 × 30 μm, SilicaTipTM, New Objective) at 2.0 kV capillary voltage, 200 °C capillary temperature, and a syringe flow rate of 0.8 μL/min. The full MS spectra were collected at 150 – 1500 m/z for 30 s with 5 micro scans and 150 maximum injection times (MS).

2,2,3,3,4,4,5,5-Octafluorohexane-1,6-diyl bis(trifluoromethane-sulfonate) (7)

To a solution of diol **6** (500 mg, 1.91 mmol) in dry dichloromethane (20 mL), trifluoromethane-sulfonyl chloride (0.49 mL, 4.68 mmol) was added under nitrogen atmosphere in an ice bath. Triethylamine (1.7 mL, 7.63 mmol) was then added drop wise. A yellow precipitate was observed. The mixture was stirred at room temperature for overnight. The solvent was then removed and the crude compound was dissolved in ethyl acetate (20 mL) and washed twice with water (10 mL). The phases were separated, and the organic phase was washed sequentially with 1 M HCl (20 mL), NaHCO₃ (20 mL), and brine and then dried with MgSO₄ and filtered. The solvent was removed under reduced pressure to yield yellow oil. It was then crystallized from 3:1, hexanes:ethyl acetate to yield **7** as clear crystals (0.94 g, 95%). (M.P. 55–57 °C); ¹H NMR (400 MHz, CDCl₃): δ 4.83 (t, *J* = 12.12 Hz, 4H). ¹³C NMR (100 MHz, CDCl₃): δ 116.89, 68.04 (t, *J* = 28.5 Hz); IR (Neat) ν_{\max} 1417, 1209, 1141, 1020, 830, 613 cm⁻¹; ESI-MS/MS (*m/z*): 549.21 [M+Na]⁺.

(3,3,4,4,5,5,6,6-Octafluorocycloheptane-1,1-diyl) dimethanol (8)

In a 3-neck round bottom flask, potassium hydride (30% in mineral oil, 0.57 g, 4.21 mmol) was washed with pentane. DMF (10 mL) was then added. To this suspension of KH in DMF under vigorous stirring, dimethylmalonate (0.65 mL, 4.21 mmol) was added slowly. After 1 h, compound **7** (0.9 g, 1.76 mmol) was added to the resulting enolate and the reaction was stirred for 12 h. After that, another aliquot of enolate was added, and the reaction was allowed to stir for 24 h longer. The reaction mixture was poured over H₂O (4 mL) and extracted with ether (3 × 5 mL). The combined organic fractions were washed with H₂O (3 × 9 mL) and dried over MgSO₄. The solvent was removed under reduced pressure. The crude cyclic diester product in THF (10 mL) was added dropwise to a stirred solution of LiAlH₄ (80 mg, 5.63 mmol)

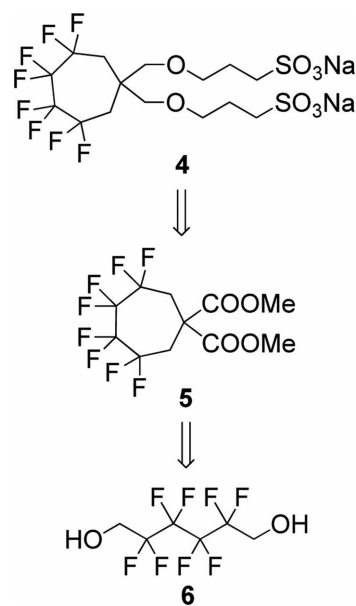
in dry THF (10 mL) under N_2 . After 12 h, at reflux the reaction was cooled to 0 °C and quenched by careful addition of approx. 40% aq. KOH. The precipitated aluminum salts were removed by filtration. The filtrate was concentrated under reduced pressure, then the residual oil redissolved in Et_2O , washed with H_2O , dried (Na_2SO_4) and evaporated in vacuum and purified by column chromatography (hexane:ethyl acetate, 7:3) to get diol **8** (0.15 g, 23%) as a viscous solid. 1H NMR (400 MHz, $CDCl_3$): δ 3.66 (t, $J = 6.316$ Hz, 4H), 1.73–1.61 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 67.21, 27.40; IR (Neat) ν_{max} 3448, 2336, 1682, 1150 cm^{-1} ; GC/MS (m/z): 302 [M].

Sodium 3,3'-(((3,3,4,4,5,5,6,6-octafluorocycloheptane-1,1-diy))bis(methylene))bis(oxy))bis(propane-1-sulfonate) (10)

Diol **8** (0.1 g, 0.33 mmol) pre-dissolved in dry THF (10 mL) solution was added to suspension of sodium hydride (60% in mineral oil, 0.03 g, 0.72 mmol) at 60 °C. Another dry THF solution (5 mL) containing propane sultone (**9**, 0.11 g, 0.82 mmol) was then added to the reaction mixture at the same temperature. After 16 h of stirring under reflux conditions, 20 mL of methanol was added at ambient temperature to deactivate any excess of sodium hydride. After evaporation of the reaction mixture, it was subsequently washed with hexanes (3×10 mL) and ethyl ether (3×10 mL) to remove the oil impurities as well as excess sultone and afforded target compound **6** (0.12 g, 64% yield) as a white solid. 1H NMR (400 MHz, D_2O): δ 3.63–3.47 (m, 4H), 3.39–3.34 (m, 4H), 2.94–2.80 (m, 4H), 1.93–1.67 (m, 8H). ^{13}C NMR (100 MHz, D_2O): δ 71.73, 57.62, 50.72, 30.16, 27.41, 20.73; IR (Neat) ν_{max} 3445, 1642, 1172, 1063 cm^{-1} ; ESI-MS/MS (m/z): 567.07 [M-Na].

RESULTS AND DISCUSSION

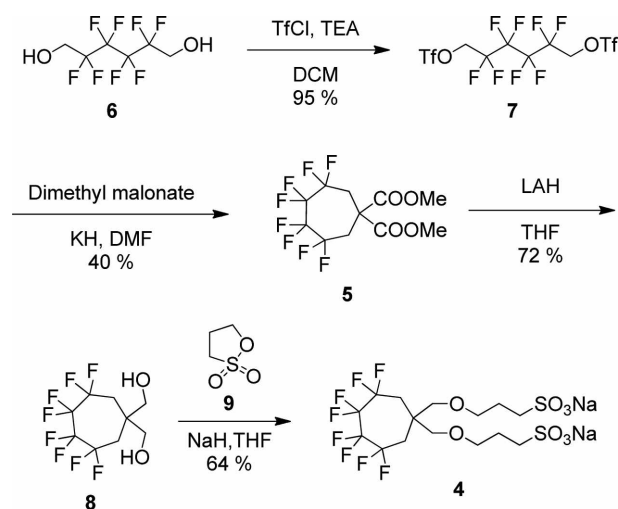
Our group has been engaged in the design and synthesis of various perfluorobutyl substituted sodium alkane sulfonates which are alternatives to PFOS.^{10,12} In continuation of our efforts towards the synthesis of PFOS alternatives, we embarked on the design and synthesis of cyclic type semi-fluorinated disodium sulfonate, another fascinating target. As described earlier, it is evident that the introduction of bio-degradable perfluorobutyl group as hydrophobic chain in surfactant is our foremost priority. With this intention, we used readily available 2,2,3,3,4,4,5,5-octafluoro-1,6-hexanediol as perfluorobutyl source for the construction fluorocarbon surfactant, and utilized metal based reduction and nucleophilic ring opening reactions as key reactions.



Scheme 1. Retrosynthetic analysis of cyclic disodium alkane-sulfonate **4**.

Retrosynthetically, cyclic hemifluorinated dimeric surfactant **4** can be synthesized from commercially available diol **6** in four steps, which is illustrated in *Scheme 1*. The cyclic hemifluorinated bis-sodium sulfonate **4** can be obtained from cyclic diester **5** by using a reduction reaction in presence of lithium aluminum hydride, followed by employing nucleophilic ring opening of propane-1,3-sultone (**9**). The 7 membered rigid fluorous cyclic diester **5**, which in turn can be synthesized from commercially available semi-fluorinated hexane diol **6** by protection reaction with trifluoromethane-sulfonyl chloride to get bis(sulfonic) ester, followed nucleophilic substitution reaction by treatment with sodium malonate in presence of NaH as base.

Our general route to doubly functionalized fluorinated material is sketched in *Scheme 2*. Thus, treatment of semi-fluorinated diol **6** with trifluoromethanesulfonyl chloride in presence of triethylamine in DCM gives an easy access to bis(sulfonic) esters **7** in 95%, which are remarkably stable and easily manipulated building block. The diester **7** was confirmed from 1H NMR, showed triplet at $\delta = 4.83$ ppm ($J = 12.12$ Hz, 4 H) the triflate attached CH_2 group and ^{13}C NMR showed peaks at $\delta = 116.8$ and 68.0 ppm corresponding trifluoro carbon and methylic carbon. Since dehydrofluorination is facile in many fluorinated compounds in the presence of stronger bases, only weakly basic nucleophiles were used here. The selective cyclization by double displacement of triflate group in compound **7** with potassium malonate in dry THF gives flexible seven membered ring



Scheme 2. Synthesis of cyclic disodium alkanesulfonate **4**.

cyclic diester **5** in 40% yield.¹⁴ The complete reduction of cyclic diester **5** in THF with lithium aluminum hydride smoothly afforded diol **8** in 72% yield, without affecting the perfluoroalkyl chain. The ¹H NMR of the diol showed triplet at $\delta = 3.66$ ppm ($J = 6.316$ Hz, 4H) for the corresponding alcohol attached CH₂ group. The IR absorption at $\nu = 3448$ cm⁻¹ clearly indicates hydroxyl functionality. Further, this diol **8** was subjected to the nucleophilic ring opening of sultone **9** in the presence of NaH as base in THF. The propanesultone (**9**) has given corresponding disodium sulfonate **4** in 64% yield, which was confirmed from ¹H and ¹³C NMR, IR and mass spectral data.

CONCLUSION

In summary, we have successfully designed and synthesized novel cyclic type semi-fluorinated disodium alkanesulfonate starting from commercially available 2,2,3,3,4,4,5,5-octafluoro-1,6-hexanediol as fluorocarbon source, which is alternative to non-biodegradable PFOS and its derivatives. The syntheses of cyclic type surfactant involve nucleophilic substitution and nucleophilic ring opening reactions as key steps and used easily accessible 2,2,3,3,4,4,5,5-octafluoro-1,6-hexanediol, trifluoromethane-sulfonyl chloride, dimethyl malonate and propane sultone in four synthetic steps and all steps were robust and low cost with moderate to good yields. All compounds were characterized by ¹H NMR, ¹³C NMR, FTIR and Mass spectroscopy. After successful synthesis of cyclic type gemini surfactant, surface tension behavior studies were under the progress and we are expecting good value of critical micelle concentration due to previously as synthe-

sized linear hemifluorinated disodium alkanesulfonate showed better when compared to that of PFOS. Apart from this, as-synthesized compound is expected to be biodegradable due to having degrading points like ether links, hydrocarbon chain and less perfluoro carbon (C4) chain and would be safer than that of non-biodegradable PFOS.

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