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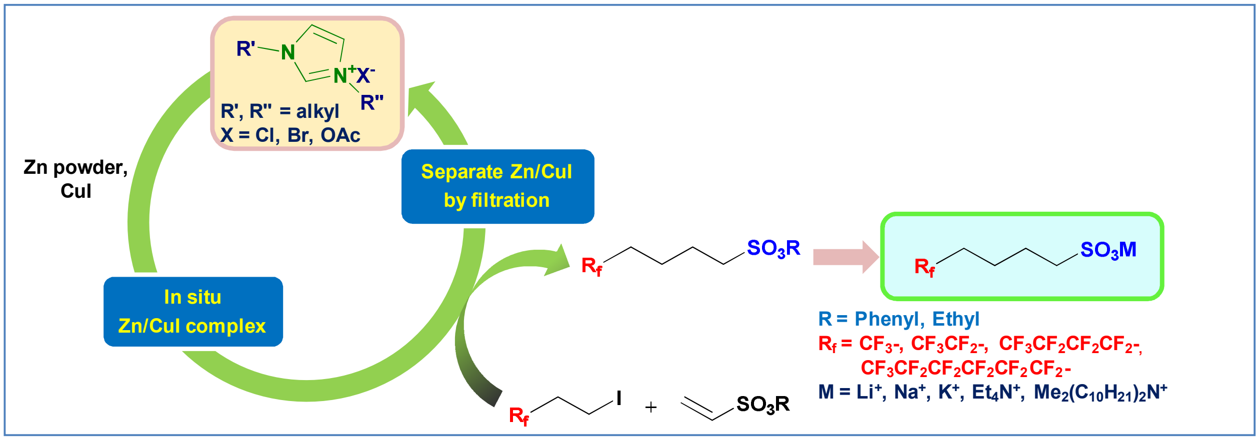
Graphical Abstract

Michael-type addition in imidazolium ionic liquids for the synthesis of bio-degradable and efficient alternatives of perfluorooctanesulfonic acid



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COMMUNICATION

Environmentally benign perfluorooctanesulfonate alternatives using a Zn/CuI mediated Michael-type addition in imidazolium ionic liquids

B. V. D. Vijaykumar,[a] B. Premkumar,[a] Kiwan Jang,[b] Bong-In Choi,[c] J. R. Falck,[d] G. N. Sheldrake[e] and Dong-Soo Shin*[a]

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Design and synthesis of hemi fluorinated perfluorooctanesulfonic acid (PFOS) alternatives was described using a Zn/CuI mediated Michael-type addition reaction in ionic liquids considering environmentally benign reaction conditions as well as products. One of the new potassium sulfonates showed promising surface tension activities when compared to that of PFOS potassium salt.

Perfluoroalkyl substances have been detected worldwide in all kinds of waters and animals etc., but perfluorooctanesulfonic acid (PFOS, **1**) found to be the most rampant compound in humans.[1,2] The man-made PFOS and perfluorooctanoic acid (PFOA) related substances have many applications including surface treatments as they show special properties that comprise heat, chemical and abrasion resistance.[3,4] The fluorinated surfactants show superior surfactant activities when compared to that of hydrogenated ones, particularly due to their lower surface tension as well as low critical micelle concentration (CMC) values. They are used in making commercial stain-repellents, fire fighting foams, paints, leather, paper coatings, photographic emulsifiers, plane hydraulic fluids, pharmaceuticals, electroplating etc.[5] Although, unique properties of PFOS related substances make them important for industrial and consumer applications, their non-degradable emission to the environment turned out to be a serious issue in the aspects of global pollution.[6-8] Even in biological perspective, many derivatives of PFOS are found to be toxic due to their persistent properties that come with strong perfluorinated carbon chain. Thus, in spite of their ubiquitous occurrence and inevitable uses to mankind, PFOS derivatives were noted under the Stockholm Convention on persistent organic pollutants (POPs) since May 2009.

The surface active agents are amphiphilic species composed of both hydrophobic perfluorinated or alkyl chain and hydrophilic group, usually a sulfonic acid group or carboxylic group. Perfluorinated chains can't be degradable under enzymatic or metabolic decomposition conditions and thus they persist for longer periods in the environment. Remarkable degradability of surfactants can be expected if these compounds have considerable degrading points in their structures which undergo enzymatic or chemical transformations to degrade. So alternative PFOS came to spot light to reduce the hazardous effects, being their activities intact. Outrageous threat that admitted according to recent surveys on PFOS related substances,[9,10] industries like 3M company are also active in this field to find alternatives to original surfactants (for instance using C_4-perfluoro chain derivatives).[11] In recent years, research towards biodegradable hemi-fluorinated substances has shown great progress.[12,13] PFOS alternatives have also been prepared by electrochemical perfluorination process, telomerization of vinylidene fluoride or by controlled radical copolymerization of vinylidene fluoride and 3,3,3-trifluoropropene etc.[14] The above methods have some limitations in controlling the process, wastage of solvents or price. Considering these points, we have designed alternative POFS by lessening the number of fluorine atoms in the original one and replacing them with hydrogen atoms so that they can be biodegradable. Thus, we here report the design and synthesis of new class of partially fluorinated sulfonic acid derivatives (Fig. 1) which could be less hazardous and biodegradable surfactants.

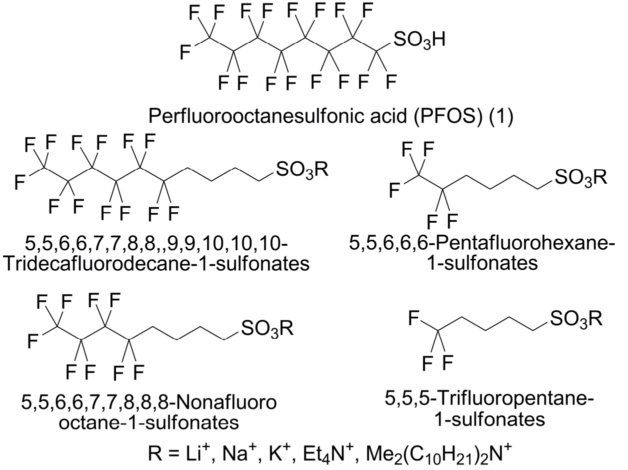


Fig. 1 Structures of PFOS and its designed alternatives.

While coming to the reaction media, ionic liquids play major role in organic synthesis and serve as solvents, co-solvents, catalysts etc., for green and sustainable chemistry.[15-17] In exploring more appropriate and eco-friendly reaction conditions for the synthesis of PFOS alternatives, we have extended one synthetic strategy[18] that involves a conjugate addition reaction of alkyl halides to phenylvinylsulfonate in presence of zinc and copper(I)iodide in ionic liquids. We have generated Zn/CuI complex in various imidazolium based ionic liquids as green solvents for the first time at various temperatures ranging from 0 °C to room temperature. The ionic liquids 1-butyl-3-methylimidazolium chloride ([BMIM]Cl, **I**), 1-ethyl-3-

methylimidazolium acetate ([EMIM]OAc, **II**) and 1-ethyl-3-hydroxyethylimidazolium bromide ([EHEIM]Br, **III**) were used as solvents (Fig. 2) to monitor Michael-type reaction and thus provided us mild and efficient reaction conditions. To conduct the conjugate addition reaction, we have chosen four commercially available partially perfluorinated alkyl halides, 1*H*,1*H*,2*H*,2*H*-perfluorooctyl iodide (**2a**), 1,1,1,2,2,3,3,4,4-nonafluoro-6-iodohexane (**2b**), 1,1,1,2,2-pentafluoro-4-iodobutane (**2c**) and 1,1,1-trifluoro-3-iodopropane (**2d**), which are containing less fluorine content to that of perfluoroalkyl halides.

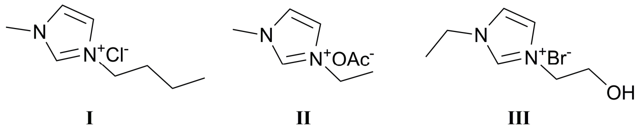
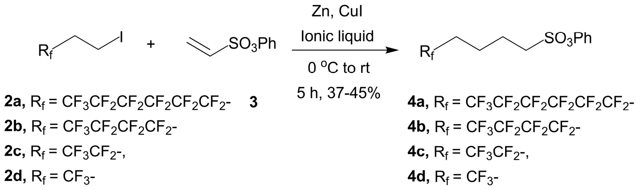


Fig. 2 Structures of ionic liquids **I**, **II** and **III**.

The Michael-type reaction involves *in situ* generation of Zn/CuI complex by slow addition of 0.5 equiv of CuI to 2.5 equiv of Zn dust immersed in ionic liquid at 0 °C (Scheme 1). The reaction mixture was kept for 30 minutes at ambient temperature and then added 1 equiv of phenyl vinylsulfonate (**3**) followed by 1 equiv of alkyl halide (**2**) slowly for 5 min. After 3-4 h at room temperature, the product was extracted into ether repeatedly for 5 times to obtain phenyl sulfonates (**4**). The left over ionic liquid was filtered off under vacuum to separate the Zn/CuI complex. The formation Zn/CuI complex is an exothermic reaction and needs ambient temperatures below 10 °C that can be performed at room temperature for small scale reactions.



Scheme 1 Zn/CuI mediated Michael-type addition in ionic liquids.

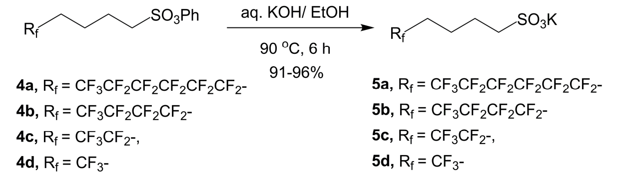
The scope of this reaction to other alkyl halides has been avoided to emphasize our perception on producing biodegradable partially perfluorinated surfactants. This conjugate addition reaction has been successful in protic as well as aprotic ionic liquids, and is a contradiction to previously reported result.[18] Even though, recoverable imidazolium based ionic liquids are considered to be green alternatives to the volatile and flammable organic solvents, they must be handled with utmost care due to their toxicity issues. Ionic liquids provided the suitable environment for the generation Zn/CuI complex, better reactivity of alkyl halides which reduced the reaction times and survived from the formation of homocoupling and other side products. However, we ended up with less yields ranging from 40-45% in the conjugate addition reaction, performed in various ionic liquids even with the mixture of water as shown in Table 1 (Entries 1, 2, 3 & 4). Formamide has found to be the only suitable solvent for this reaction and gave **4b** in 71% yield.[18] Considering this, we have tried the reaction in a mixture of ionic liquid and formamide (Table 1, Entry 5) to obtain no better yields. This result explains the competency of imidazolium ionic liquids over hazardous volatile solvents in generating *in situ* Zn/CuI complex and influence in providing reactive species for the reaction. In spite of moderate yields, this method would promote the research towards eco-friendly reaction conditions and also provided reusability of ionic liquids as solvent with similar product yields.[19]

Table 1 Conjugate addition in various solvents

Entry	Solvent(s)	Temperature/ time	Yield (%)^a
1	[BMIM]Cl	0 °C or r.t., 3 h	45
2	[EMIM]OAc	0 °C or r.t., 4 h	42
3	[EHEIM]Br	0 °C or r.t., 5 h	43
4	[BMIM]Cl/H_2O (3:1)	0 °C to r.t., 4 h	40
5	[BMIM]Cl/formamide (3:1)	0 °C to r.t., 3 h	41

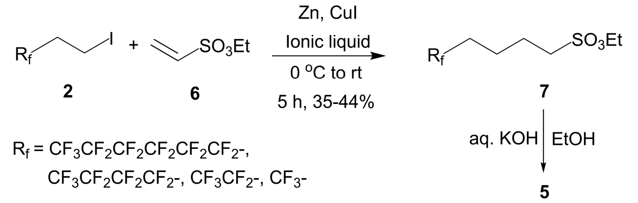
^{a}Isolated yield of **4b**

The mechanism of this reaction is expected to follow a radical type of addition in which the active proton in imidazolium ionic liquid acts as a proton source in presence of Zn/CuI, since the these ionic liquids are active in accelerating many types of radical and carbene promoted reactions that include electron transfer, polymerization etc.[20-22] In the imidazolium ionic liquid with a methyl group at active proton position, reaction did not occur. Besides, commercial Zn-Cu couple failed to give any products in all the solvents used. Pertinent conditions for this reaction are yet to be optimized to improve the yields.



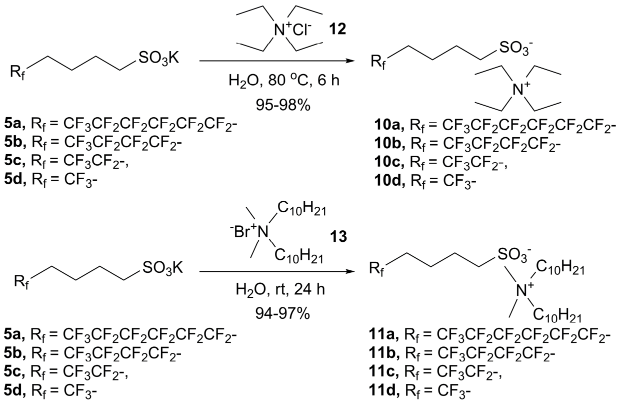
Scheme 2 Base hydrolysis of phenylsulfonates in to **5**.

Further, we have synthesized some important derivatives of new phenylsulfonates (**4**) that are known with PFOS. At first, phenylsulfonates were hydrolyzed with aqueous KOH in ethanol to obtain potassium salts (**5**) as shown in Scheme 2. Removal of phenol from the hydrolysis reaction mixture was nearly successful by following the washing treatments using ether and ethyl acetate but with 5-10% aromatic impurity in the salt. Complete removal of phenol was achieved by successive acid/base treatments of the reaction mixture. To avoid the by-product, phenol in hydrolysing phenylsulfonates and to improve the efficiency of this method on greener side, we have optimized the same reaction by taking ethyl vinylsulfonate (**6**) as starting material as shown in Scheme 3 and achieved ethylsulfonates (**7**). The lithium salts (**8**) and sodium salts (**9**) of sulfonic acids were also synthesized by hydrolysis of corresponding ethylsulfonates (**7**) with LiOH and NaOH respectively.



Scheme 3 Synthesis of **5** from **2** and **6**.

Tetraalkylammonium salts (**10** & **11**) of these sulfonic acids can be prepared by heating their potassium salts with the corresponding ammonium halides (**12** & **13**) in acetonitrile at reflux conditions quantitatively. We have obtained the same results in water at room as well as higher temperatures (Scheme 4).[23] All the compounds prepared were completely characterized by ^{1}H, ^{19}F NMR, IR and Mass spectral data.[19]



Scheme 4 Synthesis of tetraethylammonium sulfonates, **10** and didecyldimethylammonium sulfonates, **11**.

Surface tension measurements of all the potassium sulfonate salts were carried out using Wilhelmy plate tensiometer at room temperature. A collective graph plotted between surface tension and concentration, it is shown in Fig. 3. Surface tension values decreased with the increase in concentration of surfactant as expected. From the graph, it can be revealed that compound **5a** has good surfactant activity compared to that of other potassium salts (**5b, 5c** & **5d**). Surface tension decreased with the increase in chain length as well as fluorine content of the surfactant. The surface tension values from the graph must be correlated according to the fluorine content of individual surfactants. From graph, the critical micelle concentrations (CMCs) of compounds **5a** and **5b** were calculated to be 4681 mg/L and 5561 mg/L respectively at room temperature. The surface tensions of **5a** and **5b** are noted to be 17.7 dyne/cm and 21.8 dyne/cm respectively at their CMCs. These results show superior surfactant behaviour over original PFOS potassium salt (KPFOS) with CMC 4304 mg/L at 80 °C, as the degree of fluorination is related to the CMC.[24,25] The other potassium salts **5c** and **5d** may considered as hydrotropes rather than surfactants at room temperature.

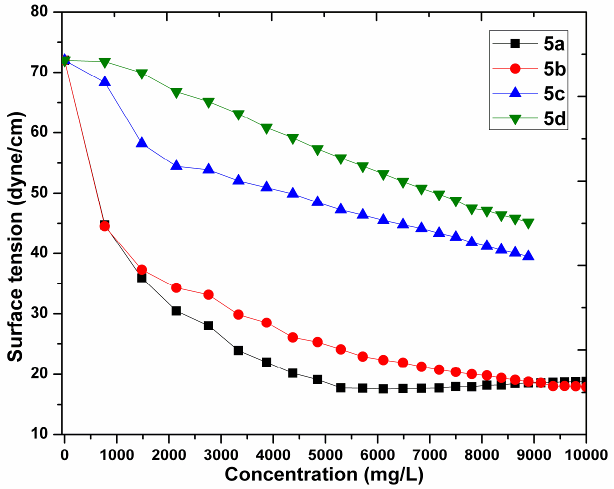


Fig. 3 Surface tension profile of potassium sulfonates (**5a**, **5b**, **5c** and **5d**) in aqueous media at 25 °C.

At first, the results on surface behaviour of **5b** encouraged us to prepare **5a** to find the enhanced activities. Thus, one can observe the efficiency of newly prepared partially perfluorinated surfactants **5a** and **5b** to substitute original PFOS in industrial and chemical applications. The salts of these sulfonic acids anticipate many bio-medicinal applications due to their less perilous effects that come from low fluorine content and also with biodegradable points in their structure. Furthermore, this work persuades research towards the synthesis of partially perfluorinated surfactants as PFOS alternatives for green and sustainable chemistry.

Biodegradability of the surfactants

The biodegradation of our surfactants was determined according to the OECD Test guideline 301 F.[26] This test uses a manometric respirometer to follow the consumption of oxygen during 28 days in a closed flask containing 15 to 50 mg/L of the test substance and inoculums coming from a sewage plant. The percentage of biodegradation is obtained by dividing the resulting biological oxygen demand (BOD) by the theoretical oxygen demand (ThOD) of the test substance. All the potassium salts (**5a,b,c,d**) showed moderate biodegradation but was remained below the 60% level at 28 days, and are not completely biodegradable according to the E.U. directive (Commission Regulation (EC) No. 907/2006 of 20 June 2006).[27] The low level of biodegradation may be due to the non-biodegradability of perfluorocarbon under above mentioned conditions. This left us a clue about the biodegradability of hydrocarbon part of these amphiphilic compounds and also their alkylammonium salts that comprise more percentage of degradable part in their structures. It is also important to note that the biodegradation process of **5a** seems to stop after 14 days, which anticipate the antimicrobial effect of this compound. Finally, all new compounds are more or less biodegradable and can be considered as less toxic, whereas KPFOS was non-biodegradable.[28]

Conclusions

This study demonstrated the design and synthesis of novel hemi-fluorinated sulfonic acid derivatives using a conjugate addition reaction in ionic liquids as key step. *In situ* generation of Zn/CuI complex in various ionic liquids was examined for Michael-type addition reaction for the first time. Using this method, the surfactant derivatives were prepared in only two to three steps. Surface tension behaviour of aqueous solutions of all potassium sulfonates was characterized. These sulfonate derivatives have lower fluorine content when compared to original ones and thus considered as more fluorine efficient. One of the new potassium sulfonates ($C_4F_9CH_2CH_2CH_2CH_2SO_3K$, **5b**) showed promising results in surface tension reduction and biodegradabilities than those of KPFOS. This work illustrates the scope of research towards partially fluorinated environmentally friendly surfactants (PFOS alternatives) particularly by following green methods of preparation.

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Notes and references

[a] *Departments of Chemistry and* [b] *Physics, Changwon National University, Changwon, GN, 641-773, S. Korea; E-mail: dsshin@changwon.ac.kr; Fax: +82-55-213-3439; Tel: +82-55-213-3437*
[c] *Korean Environment Corporation, Gwangju, 506-813, S. Korea*
[d] *Division of Chemistry, Department of Biochemistry, University of Texas Southwestern Medical Center, Dallas, Texas 75390, USA*
[e] *School of Chemistry and Chemical Engineering, David Keir Building, Queen's University Belfast, Belfast BT9 5AG, U.K.*

† Electronic Supplementary Information (ESI) available: [Experimental procedures along with ^{1}H, ^{19}F NMR, IR and Mass spectral data of all new compounds]. See DOI: 10.1039/b000000x/

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