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New synthesis of polyfluoroalkanesulfonylureas

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Abstract

This study describes a new synthesis of F-alkanesulfonyl ureas by reaction of the sodium salt of perfluoroalkane sulfonamide ($R_F = C_4F_9$, C_6F_{13}) with some isocyanates in anhydrous THF. The perfluorinated sulfonylureas are obtained, in one step, from moderate to good yields.

Keywords: F-alkanesulfonyl ureas; Sodium salt of perfluoroalkane sulfonamide; Isocyanates

1. Introduction

The first sulfonylurea VK 57 was tested in 1942 by Marcel Janbon in a hospital in Montpellier France and a few years later, his colleague Auguste Loubatières demonstrated that the compound caused the neoformation of insulin granules in rat beta cells. Since then, the sulfonylureas have been used for the treatment of non insulin-dependent diabetes mellitus (NIDDM) because of their reliable efficiency in many newly diagnosed diabetic patients and their limited side effects and low cost [1–3].

In addition to their biological properties, sulfonylureas are a relatively new class of herbicide used for selective pre and post emergence controls of broad-leaved weeds in croplands. Such molecules are considered of negligible environmental impact because of their low application rates, their very low toxicity towards animals and their short lifetime [4,5].

However, in spite of this important interest related to this family of compounds, there are few examples that describe the synthesis of F-alkanesulfonyl ureas. They involve a reaction of F-alkanesulfonyl isocyanate with amines [6,7] or a Curtius rearrangement of carboximidoyl chlorides [8] or a reaction of *N-bis*-(methylthio)methylene-trifluoromethanesulfonylamide via chloroformamidine intermediate [9].

We describe here a new preparation of perfluoroalkanesulfonyl ureas derivatives starting from salts of sodium of F-alkane sulfonamides with different isocyanates, which is a very effective and new pathway to synthesize these derivatives.

2. Results and discussion

Perfluoroalkanesulfonyl fluorides were prepared from perfluoroalkane iodides, in three steps, in good yields according to a method developed in our laboratory (Scheme 1) [10,11].

The reaction of perfluoroalkane iodide with $Na_2S_2O_4$ in the presence of $Ca(OH)_2$ in a mixture of CH_3CN/H_2O gave the sodium perfluoroalkanesulfinate in good yields. The reaction of perfluoroalkanesulfinate with chlorine in water at 50 °C leads to the formation of perfluoroalkanesulfonyl chloride corresponding in good yields; the product was easily separated by a simple decantation without any purification. The perfluoroalkanesulfonyl fluoride, used in this study, was synthesized from previously prepared perfluoroalkanesulfonyl chloride and a fluorination reagent (NH_4FHF, TEA, H_2O) in CH_2Cl_2 at 30 °C; the product was easily separated by a simple decantation without any purification.

We do not use commercially available perfluoroalkanesulfonyl fluoride, manufactured by electrochemical fluorination of the corresponding alkanesulfonyl fluoride, because of the presence of byproducts [12].

The perfluoroalkanesulfonamides may be synthesized from perfluoroalkanesulfonyl azide intermediates [13,14] or from

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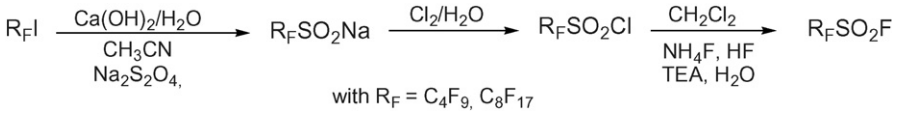
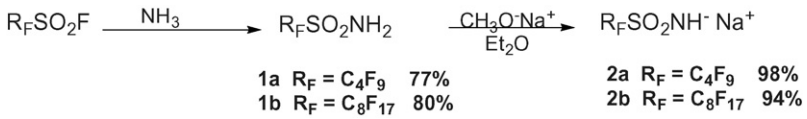


Scheme 1.



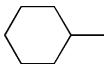
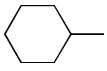
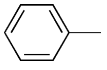
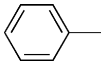
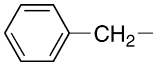
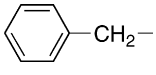
Scheme 2.

perfluoroalkanesulfonyl fluoride by reaction with ammonia, suitable primary or secondary amine [15,16].

In this study, the perfluoroalkanesulfonamides (**1**) were prepared, in good yields, by reaction of perfluoroalkanesulfonyl fluoride which were placed in a dried stainless steel bomb with an excess of ammonia without any solvent at room temperature (Scheme 2). The perfluoroalkanesulfonamides were easily purified by recrystallisation in ethanol/water media.

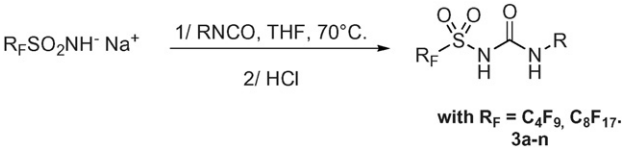
It is interesting to note that the synthesis of perfluoroalkanesulfonamides does not occur by reaction of ammonia with perfluoroalkanesulfonyle chloride as it is the case for the perhydrogenated equivalents. Indeed it had been already shown that perfluoroalkanesufonyle chloride in presence with primary amines lead exclusively perfluoroalkanesulfinates and not to perfluoroalkanesulfonamides [16].

Table 1
Preparation of polyfluoroalkanesulfonyl ureas

Entry	R_F–	R–	Conversion[a] (%)	Yield[b] (%)
3a	C_4F_9		98	83
3b	C_8F_{17}		93	75
3c	C_4F_9		98	79
3d	C_8F_{17}		95	80
3e	C_4F_9		94	79
3f	C_8F_{17}		90	75
3g	C_4F_9	$CH_3(CH_2)_2$–	99	84
3h	C_8F_{17}	$CH_3(CH_2)_2$–	93	62
3i	C_4F_9	$CH_3(CH_2)_5$–	99	79
3j	C_8F_{17}	$CH_3(CH_2)_5$–	94	49
3k	C_4F_9	$(CH_3)_3C$–	99	81
3l	C_8F_{17}	$(CH_3)_3C$–	95	75

[a] The conversions were determined by ^{19}F NMR spectroscopy (Me_2SO) by the relative integration of the functional CF_2 signal of **1** compared with that of the functional CF_2 signal of **3**.

[b] All these compounds were crystallised in a mixture of ethanol/water.



Scheme 3.

Then, the perfluoroalkanesulfonamides underwent a reaction with sodium methylate to give the corresponding sodium sulfonamides in excellent yields in a Et_2O/CH_3OH media (**2** as described in Scheme 2). These compounds were characterized by ^{19}F NMR spectroscopy and HRMS.

It is interesting to note that unlike their hydrogenated counterparts, these sodium sulfonamides have a great stability in particular with respect to the hydrolysis. The electron-attracting effect of the fluorinated chain is responsible for this high stability of these intermediates whatever the length of the F-alkylated chain studied (C_4F_9, C_8F_{17}). However, the stabilizing effect of these F-alkylated chain of sodium perfluoroalkanesulfonamides does not prevent their reaction with highly electrophilic compounds such as isocyanates.

In this context, highly fluorinated sulfonylurea were obtained by the reaction of sodium F-alkane sulfonamide with some commercially available isocyanates in anhydrous THF (**3** as described in Scheme 3). In each case, an excellent conversion of the sodium sulfonamides to sulfonylureas was observed by NMR ^{19}F spectroscopy.

Recrystallisation of these compounds in ethanol/water media gave corresponding sulfonylurea with high purity from moderate to good yields (Table 1).

3. Conclusion

In summary, we have developed a new and efficient method for the synthesis of polyfluoroalkane sulfonylureas starting from sodium sulfonamide salts and alkyl–aryl isocyanate.

The sodium sulfonamides salts were suitable intermediates to synthetize the F-alkane sulfonylureas. The electron-attracting effect of the fluorinated chain is responsible for its high stability of these compounds. Further research will study their biological properties.

4. Experimental

4.1. General

Moisture sensitive reactions were carried out under dry nitrogen. All isocyanate reagents were purchased from Aldrich. Perfluoroalkane iodides were purchased from Elf Atochem. Solvents were distilled from the appropriate drying agents immediately prior to use.

^{1}H, ^{19}F, and ^{13}C NMR spectra were recorded at 300.13 MHz, 282.37 MHz and 75.46 MHz, respectively, with a Brucker Avance 300 spectrometer; chemical shifts are given in δ ppm relative to Me_4Si, CCl_3F, respectively, as internal standards. Coupling constants are given in Hz. IR spectra were obtained using a Nicolet 205 FT-IR instrument (ν cm^{-1}). Mass spectra and HRMS are recorded on a JEOL SX 102 spectrometer. Melting points are recorded at atmospheric pressure unless otherwise stated on a Stuart scientific SMP3 apparatus and were remained without any correction.

4.2. Synthesis of perfluoroalkanesulfonamides **1a** and **1b**

A typical procedure for perfluoroalkanesulfonamides **1a** and **1b** is described. In a 100 mL dried stainless steel bomb, perfluoroalkanesulfonyl fluoride (1 equiv.) was placed with magnetic stirrer, at 25 °C. Then ammonia (3 equiv.) was transferred into the bomb through the vacuum line within 1 h. The excess of ammonia was then removed with a flow of dry N_2. The solid product ($R_FSO_2NHNH_4$ and NH_4F) was acidified with HCl followed by the addition of Et_2O. The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by recrystallisation from EtOH/H_2O (90/10) to give white crystals of the corresponding sulfonamides.

4.2.1. Synthesis of 1,1,2,2,3,3,4,4,4 nonafluoro-n-butanesulfonamide **1a**

25 g of 1,1,2,2,3,3,4,4,4 nonafluoro-*n*-butanesulfonyl fluoride (82.78 mmol) were placed with 0.25 mol of ammonia, then the solid product ($C_4F_9SO_2NHNH_4$ and NH_4F) was acidified with HCl (3 M) (40 mL) followed by addition of Et_2O (50 mL). The product was crystallized from EtOH/H_2O mixture to give pure product (19 g, yield 77%).

mp: 67.5 °C; ^{1}H NMR (300.13 MHz, d_6-acetone): δ 8.2 (m, 2H, SO_2NH_2); ^{19}F NMR (282.37 MHz, d_6-acetone): δ −125.8 (m, 2F, $CF_3C\mathbf{F_2}(CF_2)_2$), −121.0 (m, 2F, $CF_3CF_2C\mathbf{F_2}CF_2$), −113.7 (m, 2F, $CF_3(CF_2)_2C\mathbf{F_2}$), −80.8 (m, 3F, $C\mathbf{F_3}(CF_2)_3$); MS (FAB$^-$, NBA): [M−H$^+$] = 298; HRMS calcd. for $C_4HO_2NF_9S$: 297.9584; found: 297.9572.

4.2.2. Synthesis of 1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8 heptadecafluoro-n-octane sulfonamide **1b**

50 g of 1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8 heptadecafluoro-*n*-octanesulfonyl fluoride (99.6 mmol) were placed with 0.3 mol of ammonia. Then the solid product ($C_8F_{17}SO_2NHNH_4$ and NH_4F) was acidified with HCl (3 M) (80 mL), followed by the addition of Et_2O (100 mL). The product was crystallized from EtOH/H_2O mixture to give pure product (39.8 g, yield 80%).

mp: 154.6 °C. ^{1}H NMR (300.13 MHz, d_6-acetone): δ 8.2 (m, 2H, SO_2NH_2); ^{19}F NMR (282.37 MHz, d_6-acetone): δ −125.8 (m, 2F, $CF_3C\mathbf{F_2}(CF_2)_6$), −122.3 (m, 2F, $CF_3CF_2C\mathbf{F_2}(CF_2)_5$), −121.4 (m, 6F, $CF_3(CF_2)_2(C\mathbf{F_2})_3(CF_2)_2$), −119.9 (m, 2F, $CF_3(CF_2)_5C\mathbf{F_2}CF_2$), −113.5 (m, 2F, $CF_3(CF_2)_6C\mathbf{F_2}$), −80.7 (m, 3F, $C\mathbf{F_3}(CF_2)_7$); MS (FAB$^-$, NBA): [M−H$^+$] = 498; HRMS calcd. for $C_8HO_2NF_{17}S$: 497.9457; found: 497.9455.

4.3. General procedure for the synthesis of sodium perfluoroalkane sulfonamides (**2a**, **2b**)

A solution of perfluoroalkanesulfonamides (1 equiv.), dissolved in anhydrous diethyl ether was added dropwise to a suspension of sodium methylate (95%) in anhydrous methanol (0.9 equiv.). The mixture was refluxed for 3–5 h and then filtered. The filtrate was evaporated in vacuo and the residue was washed three times with diethyl ether to remove the excess of perfluoroalkanesulfonamide and then dried under vacuum.

4.3.1. Synthesis of sodium 1,1,2,2,3,3,4,4,4 nonafluoro-n-butane sulfonamide **2a**

A mixture of 20 g of perfluorobutanesulfonamide **1a** (66.8 mmol) and 3.42 g of sodium methylate (63.37 mmol) dissolved, respectively, in anhydrous diethyl ether (100 mL) and methanol 10 mL was refluxed for 3 h. A 21 g of **2a** were obtained (98%).

^{19}F NMR (282.37 MHz, d_6-acetone): δ −125.8 (m, 2F, $CF_3C\mathbf{F_2}(CF_2)_2$), −121.0 (m, 2F, $CF_3CF_2C\mathbf{F_2}CF_2$), −113.7 (m, 2F, $CF_3(CF_2)_2C\mathbf{F_2}$), −80.8 (m, 3F, $C\mathbf{F_3}(CF_2)_3$); MS (FAB$^-$) *m/z*: 298; HRMS calcd. for $C_4HO_2NF_9S$: 297.9584; found 297.9594.

4.3.2. Synthesis of sodium 1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8 heptadecafluoro-n-octane sulfonamide **2b**

A mixture of 40 g of perfluorooctanesulfonamide **1b** (80.16 mmol) and 4.10 g of sodium methylate (75.94 mmol) dissolved, respectively, in anhydrous diethyl ether (170 mL) and methanol (12 mL) was refluxed for 5 h. A 39.4 g of **2b** were obtained (94%).

^{19}F NMR (282.37 MHz, d_6-acetone): δ −125.9 (m, 2F, $CF_3C\mathbf{F_2}(CF_2)_6$), −122.4 (m, 2F, $CF_3CF_2C\mathbf{F_2}(CF_2)_5$), −121.5 (m, 6F, $CF_3(CF_2)_2(C\mathbf{F_2})_3(CF_2)_2$), −120.0 (m, 2F, $CF_3(CF_2)_5C\mathbf{F_2}CF_2$), −113.5 (m, 2F, $CF_3(CF_2)_6C\mathbf{F_2}$), −80.8 (m, 3F, $C\mathbf{F_3}(CF_2)_7$); MS (FAB$^-$): 498; HRMS calcd. for $C_8HO_2NF_{17}S$: 497.9457; found 497.9423.

4.4. General procedure for the synthesis of perfluoroalkanesulfonyl urea (**3a–g**)

A solution of alkyl/aryl isocyanates (1.1 equiv.) was added dropwise for 5–10 min to a stirred mixture of sodium perfluoroalkanesulfonamide (1 equiv.) in anhydrous THF. The reaction mixture was refluxed for 4–6 h. After cooling, all volatile parts of the mixture were removed in vacuo. The

residue was dissolved in EtOAc and washed with 1 M HCl and water. The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by crystallization from EtOH/H_2O (90/10) to give white crystals of the corresponding sulfonylureas.

4.4.1. Synthesis of N-cyclohexyl, N′-(perfluorobutanesulfonyl urea) ***3a***

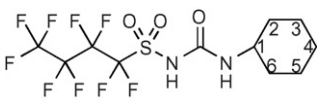
2a (2 g, 6.23 mmol) and cyclohexylisocyanate (0.875 mL, 6.85 mmol) in anhydrous THF (10 mL) were refluxed for 4 h. The crude product was crystallized from EtOH/H_2O mixture to give pure product (2.2 g, yield 83%).

mp: 170.9 °C; IR (KBr): 3361 (ν_{NH}), 1687 ($\nu_{C=O}$), 1195 (ν_{SO_2}), 1142 (ν_{C-F}); ^{1}H NMR (300.13 MHz, d_6-DMSO): δ 1.1 (m, 1H, H_4a), 1.3 (m, 4H, H_3a, H_5a, H_2a, H_6a), 1.5 (m, 1H, H_4e), 1.6 (m, 2H, H_3e and H_5e), 1.7 (m, 2H, H_2e and H_6e), 3.4 (m, 1H, H_1), 7.2 (m, 1H, N**H**), 11.5 (m, 1H, N**H**), with 'e' representing equatorial and 'a' axial; ^{19}F NMR (282.37 MHz, d_6-DMSO): δ −125.8 (m, 2F, $CF_3C\mathbf{F_2}(CF_2)_2$), −121.4 (m, 2F, $CF_3CF_2C\mathbf{F_2}CF_2$), −111.9 (m, 2F, $CF_3(CF_2)_2C\mathbf{F_2}$), −80.6 (m, 3F, $\mathbf{CF_3}(CF_2)_3$); ^{13}C NMR (75.46 MHz, d_6-DMSO): δ 24.1 (**C$_4$**); 24.8 (**C$_3$** and **C$_5$**); 31.7 (**C$_2$** and **C$_6$**); 49.3 (**C$_1$**), 107.8–118.64 (**C$_4$**F_9); 151.2 (**C**=O); MS (FAB$^+$) *m/z*: (M+H$^+$): 425; HRMS calcd. for $C_{11}H_{14}O_3N_2F_9S$: 425.0581; found: 425.0583 (Scheme 4).

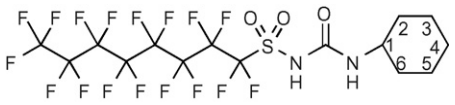
4.4.2. Synthesis of N-cyclohexyl, N′-(perfluorooctanesulfonyl urea) ***3b***

2b (1 g, 1.92 mmol) and cyclohexylisocyanate (0.27 mL, 2.11 mmol) in anhydrous THF (10 mL) were refluxed for 4 h. The crude product was crystallized from EtOH/H_2O mixture to give pure product (0.9 g, yield 75%).

mp: 169.8 °C; IR (KBr): 3365 (ν_{NH}), 1687 ($\nu_{C=O}$), 1203 (ν_{SO_2}), 1149 (ν_{C-F}); ^{1}H NMR (300.13 MHz, d_6-DMSO): δ 1.1 (m, 1H, H_4a); 1.3 (m, 4H, H_3a, H_5a, H_2a, H_6a); 1.5 (m, 1H, H_4e); 1.6 (m, 2H, H_3e and H_5e); 1.7 (m, 2H, H_2e and H_6e); 3.5 (m, 1H, H_1); 7.0 (m, 1H, N**H**); 8.9 (m, 1H, N**H**), with 'e' representing equatorial and 'a' axial; ^{19}F NMR (282.37 MHz, d_6-DMSO): δ −126.3 (m, 2F, $CF_3C\mathbf{F_2}(CF_2)_{6-}$), −122.9 (m, 2F, $CF_3CF_2C\mathbf{F_2}(CF_2)_{5-}$), −122.0 (m, 6F, $CF_3(CF_2)_2(C\mathbf{F_2})_3(CF_2)_2$), −120.6 (m, 2F, $CF_3(CF_2)_5C\mathbf{F_2}CF_2$), −112.0 (m, 2F, $CF_3(CF_2)_6C\mathbf{F_2}$), −80.9 (m, 3F, $\mathbf{CF_3}(CF_2)_7$); ^{13}C NMR (75.46 MHz, d_6-DMSO): δ 24.0 (**C$_4$**); 24.8 (**C$_3$** and **C$_5$**); 31.7 (**C$_2$** and **C$_6$**); 49.2 (**C$_1$**), 106.8–118.1 (**C$_8$**F_{17}); 151.2 (**C**=O); MS (FAB+) *m/z*: (M+H$^+$): 625; HRMS calcd. for $C_{15}H_{14}O_3N_2F_{17}S$: 625.0454; found: 625.0461 (Scheme 5).



Scheme 4.



Scheme 5.

4.4.3. Synthesis of N-phenyl, N′-(perfluorobutanesulfonyl urea) ***3c***

2a (2 g, 6.23 mmol) and phenylisocyanate (0.745 mL, 6.85 mmol) in anhydrous THF (10 mL) were refluxed for 4 h. The product was crystallized from EtOH/H_2O mixture to give pure product (2 g, yield 79%).

mp: 171.3 °C; IR (KBr): 3379 (ν_{NH}), 1621 ($\nu_{C=O}$), 1205 (ν_{SO_2}), 1143 (ν_{C-F}); ^{1}H NMR (300.13 MHz, d_6-DMSO): δ 6.9 (t, J = 7.3, 1H, **H$_{Ar}$**), 7.2 (m, 2H, **H$_{Ar}$**), 7.5 (m, 2H, **H$_{Ar}$**); ^{19}F NMR (282.37 MHz, d_6-DMSO): δ −125.5 (m, 2F, $CF_3C\mathbf{F_2}(CF_2)_2$), −121.2 (m, 2F, $CF_3CF_2C\mathbf{F_2}CF_2$), 112.3 (m, 2F, $CF_3(CF_2)_2C\mathbf{F_2}$), −80.3 (m, 3F, $\mathbf{CF_3}(CF_2)_3$); ^{13}C NMR (75.46 MHz, d_6-DMSO): δ 107–118 (**C$_4$**F_9), 118.1 (2 **C$_{Ar}$**), 121.3 (**C$_{Ar}$**), 128.3 (2 **C$_{Ar}$**), 139.7 (**C$_{Ar}$**); 152.5 (**C**O); MS (FAB$^-$) *m/z*: (M−H$^+$): 417; HRMS calcd. for $C_{11}H_6O_3N_2F_9S$: 416.9955; found: 416.9939.

4.4.4. Synthesis of N-phenyl, N′-(perfluorooctanesulfonyl urea) ***3d***

2b (4 g, 7.68 mmol) and phenylisocyanate (0.92 mL, 8.44 mmol) in anhydrous THF (20 mL) were refluxed for 6 h. The product was crystallized from EtOH/H_2O mixture to give pure product (3.8 g, yield 80%).

mp: 254.9 °C; IR (KBr): 3379 (ν_{NH}), 1621 ($\nu_{C=O}$), 1205 (ν_{SO_2}), 1149 (ν_{C-F}); ^{1}H NMR (300.13 MHz, d_6-DMSO): δ 6.8 (t, J = 7.2, 1H, **H$_{Ar}$**), 7.2 (m, 2H, **H$_{Ar}$**), 7.5 (m, 2H, **H$_{Ar}$**), 7.8 (m, 2H, N**H**, N**H**); ^{19}F NMR (282.37 MHz, d_6-DMSO): δ −125.8 (m, 2F, $CF_3C\mathbf{F_2}(CF_2)_6$), −122.5 (m, 2F, $CF_3CF_2C\mathbf{F_2}(CF_2)_5$), −121.7 (m, 6F, $CF_3(CF_2)_2(C\mathbf{F_2})_3(CF_2)_2$), −120.3 (m, 2F, $CF_3(CF_2)_5C\mathbf{F_2}CF_2$), −112.4 (m, 2F, $CF_3(CF_2)_6C\mathbf{F_2}$), −80.3 (m, 3F, $\mathbf{CF_3}(CF_2)_7$); ^{13}C NMR (75.46 MHz, d_6-DMSO): δ 106.5–117.9 (**C$_8$**F_{17}), 117.4 (2 **C$_{Ar}$**), 120.2 (**C$_{Ar}$**), 127.6 (2 **C$_{Ar}$**), 140.7 (**C$_{Ar}$**), 156.4 (**C**O); MS (FAB$^-$) *m/z*: (M−H$^+$): 617; HRMS calcd. for $C_{15}H_6O_3N_2F_{17}S$: 616.9828; found: 616.9829.

4.4.5. Synthesis of N-benzyl, N′-(perfluorobutanesulfonyl urea) ***3e***

2a (1.5 g, 4.67 mmol) and benzylisocyanate (0.745 mL, 5.14 mmol) in anhydrous THF (10 mL) were refluxed for 4 h. The product was crystallized from EtOH/H_2O mixture to give pure product (2 g, yield 79%).

mp: 171.3 °C; IR (KBr): 3336 (ν_{NH}), 1690 ($\nu_{C=O}$), 1208 (ν_{SO_2}), 1141 (ν_{C-F}); ^{1}H NMR (300.13 MHz, d_6-DMSO): δ 4.3 (s, 2H, NC**H$_2$**), 7.2 (m, 3H, **H$_{Ar}$**), 7.3 (m, 2H, **H$_{Ar}$**), 10 (m, 2H, N**H**); ^{19}F NMR (282.37 MHz, d_6-DMSO): δ −125.64 (m, 2F, $CF_3C\mathbf{F_2}(CF_2)_2$), −121.23 (m, 2F, $CF_3CF_2C\mathbf{F_2}CF_2$), 111.86 (m, 2F, $CF_3(CF_2)_2C\mathbf{F_2}$), −80.34 (m, 3F, $\mathbf{CF_3}(CF_2)_3$); ^{13}C NMR (75.46 MHz, d_6-DMSO): δ 43.6 (**C**H_2), 107–118 (**C$_4$**F_9), 126.9 (**C$_{Ar}$**), 126.9 (2 **C$_{Ar}$**), 128.2 (2 **C$_{Ar}$**), 138.8 (**C$_{Ar}$**), 152 (**C**O); MS (FAB$^+$) *m/z*: (M+H$^+$): 433; HRMS calcd. for $C_{12}H_{10}O_3N_2F_9S$: 433.0268; found: 433.0264.

4.4.6. Synthesis of N-benzyl, N′-(perfluorooctanesulfonyl urea) ***3f***

2b (4 g, 7.68 mmol) and benzylisocyanate (0.92 mL, 8.44 mmol) in anhydrous THF (20 mL) were refluxed for 6 h. The product was crystallized from EtOH/H_2O mixture to give pure product (3.64 g, yield 75%).

mp: 182.2 °C; IR (KBr): 3336 (ν_{NH}), 1687 ($\nu_{C=O}$), 1203 (ν_{SO_2}), 1151 (ν_{C-F}); ^{1}H NMR (300.13 MHz, d_6-DMSO): δ 4.3 (s, 2H, NC**H$_2$**), 7.2 (m, 3H, **H$_{Ar}$**), 7.3 (m, 2H, **H$_{Ar}$**), 7.7 (m, 2H, N**H**, N**H**); ^{19}F NMR (282.37 MHz, d_6-DMSO): δ −125.7 (m, 2F, $CF_3C\mathbf{F_2}(CF_2)_6$), −122.4 (m, 2F, CF_3CF_2–$C\mathbf{F_2}(CF_2)_5$), −121.6 (m, 6F, $CF_3(CF_2)_2(C\mathbf{F_2})_3(CF_2)_2$), −120.2 (m, 2F, $CF_3(CF_2)_5C\mathbf{F_2}CF_2$), −111.8 (m, 2F, $CF_3(CF_2)_6C\mathbf{F_2}$), −80.2 (m, 3F, $C\mathbf{F_3}(CF_2)_7$); ^{13}C NMR (75.46 MHz, d_6-DMSO): δ 43.6 (**C**H$_2$), 107.2–118 (**C$_8$**F$_{17}$), 126.81 (**C$_{Ar}$**), 126.9 (2 **C$_{Ar}$**), 128.2 (2 **C$_{Ar}$**), 138.9 (**C$_{Ar}$**), 153.1 (**C**O); MS (FAB$^+$) *m/z*: (M+H$^+$): 633; HRMS calcd. for $C_{16}H_{10}O_3N_2F_{17}S$: 633.0141; found: 633.0121.

4.4.7. Synthesis of N-propyl, N′-(perfluorobutanesulfonyl urea) 3g

2a (2 g, 6.23 mmol) and *n*-propylisocyanate (0.64 mL, 6.85 mmol) in anhydrous THF (10 mL) were refluxed for 4 h. The product was crystallized from EtOH/H_2O mixture to give pure product (2 g, yield 84%).

mp: 162.5 °C; IR (KBr): 3351 (ν_{NH}), 1693 ($\nu_{C=O}$), 1202 (ν_{SO_2}), 1154 (ν_{C-F}); ^{1}H NMR (300.13 MHz, d_6-DMSO): δ 0.8 (t, J = 7.4, 3H, C**H$_3$**), 1.4 (m, 2H, C**H$_2$**CH$_3$), 3.05 (t, J = 7, 2H, NHC**H$_2$**CH$_2$–), 7.5 (m, 1H, N**H**), 11.7 (m, 1H, N**H**); ^{19}F NMR (282.37 MHz, d_6-DMSO): δ −125.7 (m, 2F, $CF_3C\mathbf{F_2}(CF_2)_2$), −121.3 (m, 2F, $CF_3CF_2C\mathbf{F_2}CF_2$), −112.1 (m, 2F, $CF_3(CF_2)_2C\mathbf{F_2}$), −80.4 (m, 3F, $C\mathbf{F_3}(CF_2)_3$); ^{13}C NMR (75.46 MHz, d_6-DMSO): δ 10.8 (**C**H$_3$), 22.0 (**C**H$_2$CH$_3$), 41.9 (**C**H$_2$CH$_2$), 107–119 (**C$_4$**F$_9$), 153.0 (**C**O); MS (FAB+) *m/z*: (M+H$^+$): 385; HRMS calcd. for $C_8H_{10}O_3N_2F_9S$: 385.0268; found: 385.0268.

4.4.8. Synthesis of N-propyl, N′-(perfluorooctanesulfonyl urea) 3h

2b (1 g, 1.92 mmol) and *n*-propylisocyanate (0.2 mL, 2.11 mmol) in anhydrous THF (20 mL) were refluxed for 6 h. The product was crystallized from EtOH/H_2O mixture to give pure product (0.7 g, yield 62%).

mp: 150.8 °C; IR (KBr): 3351 (ν_{NH}), 1688 ($\nu_{C=O}$), 1202 (ν_{SO_2}), 1142 (ν_{C-F}); ^{1}H NMR (300.13 MHz, d_6-DMSO): δ 0.8 (t, J = 7.4, 3H, C**H$_3$**), 1.4 (m, 2H, C**H$_2$**CH$_3$), 3 (t, J = 6.9, 2H, NHC**H$_2$**CH$_2$), 5.9 (m, 1H, N**H**), 7.2 (m, 1H, N**H**); ^{19}F NMR (282.37 MHz, d_6-DMSO): δ −125.9 (m, 2F, $CF_3C\mathbf{F_2}(CF_2)_6$), −122.6 (m, 2F, $CF_3CF_2C\mathbf{F_2}(CF_2)_5$), −121.7 (m, 6F, $CF_3(CF_2)_2(C\mathbf{F_2})_3(CF_2)_2$), −120.3 (m, 2F, $CF_3(CF_2)_5C\mathbf{F_2}CF_2$), −112 (m, 2F, $CF_3(CF_2)_6C\mathbf{F_2}$), −80.3 (m, 3F, $C\mathbf{F_3}(CF_2)_7$); ^{13}C NMR (75.46 MHz, d_6-DMSO): δ 10.5 (**C**H$_3$), 21.9 (**C**H$_2$CH$_3$), 41.8 (**C**H$_2$CH$_2$), 107.5–117.9 (**C$_8$**F$_{17}$), 152.7 (**C**O); MS (FAB+) *m/z*: (M+H$^+$): 585; HRMS calcd. for $C_{12}H_{10}O_3N_2F_{17}S$: 585.0141; found: 585.0126.

4.4.9. Synthesis of N-hexyl, N′-(perfluorobutanesulfonyl urea) 3i

2a (2 g, 6.23 mmol) and *n*-hexylisocyanate (0.99 mL, 6.85 mmol) in anhydrous THF (10 mL) were refluxed for 4 h. The product was crystallized from EtOH/H_2O mixture to give pure product (2.1 g, yield 79%).

mp: 134.9 °C; IR (KBr): 3340 (ν_{NH}), 1690 ($\nu_{C=O}$), 1206 (ν_{SO_2}), 1137 (ν_{C-F}); ^{1}H NMR (300.13 MHz, d_6-DMSO): δ 0.8 (t, J = 6.6, 3H, C**H$_3$**), 1.2 (m, 6H, $(CH_2)_2(C\mathbf{H_2})_3CH_3$), 1.4 (m, 2H, $CH_2C\mathbf{H_2}(CH_2)_3CH_3$), 3.1 (m, 2H, C**H$_2$**(CH$_2$)$_4CH_3$), 7.2 (m, 1H, N**H**), 11.5 (m, 1H, N**H**); ^{19}F NMR (282.37 MHz, d_6-DMSO): δ −125.8 (m, 2F, $CF_3C\mathbf{F_2}(CF_2)_2$), −121.4 (m, 2F, $CF_3CF_2C\mathbf{F_2}CF_2$), 112.1 (m, 2F, $CF_3(CF_2)_2C\mathbf{F_2}$), −80.5 (m, 3F, $C\mathbf{F_3}(CF_2)_3$); ^{13}C NMR (75.46 MHz, d_6-DMSO): δ 13.7 (**C**H$_3$), 21.9 (**C**H$_2$CH$_3$), 25.6 (**C**H$_2$(CH$_2$)$_2$CH$_3$), 28.7 (**C**H$_2$CH$_2$CH$_3$), 30.8 (NCH$_2$**C**H$_2$), 40.1 (N**C**H$_2$), 107–119 (**C$_4$**F$_9$), 153.10 (**C**O); MS (FAB$^+$) *m/z*: (M+H$^+$): 427; HRMS calcd. for $C_{11}H_{16}O_3N_2F_9S$: 427.0738; found: 427.0734.

4.4.10. Synthesis of N-hexyl, N′-(perfluorooctanesulfonyl urea) 3j

2b (4 g, 7.68 mmol) and *n*-hexylisocyanate (1.22 mL, 8.44 mmol) in anhydrous THF (20 mL) were refluxed for 6 h. The product was crystallized from EtOH/H_2O mixture to give pure product (2.36 g, yield 49%).

mp: 157.9 °C; IR (KBr): 3358 (ν_{NH}), 1686 ($\nu_{C=O}$), 1220 (ν_{SO_2}), 1150 (ν_{C-F}); ^{1}H NMR (300.13 MHz, d_6-DMSO): δ 0.8 (t, J = 6.6, 3H, C**H$_3$**), 1.2 (m, 6H, $(CH_2)_2(C\mathbf{H_2})_3CH_3$), 1.4 (m, 2H, $CH_2C\mathbf{H_2}(CH_2)_3CH_3$), 3.1 (m, 2H, C**H$_2$**(CH$_2$)$_4CH_3$), 5.2 (m, 1H, N**H**), 7 (m, 1H, N**H**); ^{19}F NMR (282.37 MHz, d_6-DMSO): δ −125.8 (m, 2F, $CF_3C\mathbf{F_2}(CF_2)_6$), −122.5 (m, 2F, $CF_3CF_2C\mathbf{F_2}(CF_2)_5$), −121.5 (m, 6F, $CF_3(CF_2)_2(C\mathbf{F_2})_3(CF_2)_2$), −120.2 (m, 2F, $CF_3(CF_2)_5C\mathbf{F_2}CF_2$), −112 (m, 2F, $CF_3(CF_2)_6C\mathbf{F_2}$), −80.2 (m, 3F, $C\mathbf{F_3}(CF_2)_7$); ^{13}C NMR (75.46 MHz, d_6-DMSO): δ 13.7 (**C**H$_3$), 21.9 (**C**H$_2$CH$_3$), 25.7 (**C**H$_2$(CH$_2$)$_2$CH$_3$), 28.8 (**C**H$_2$CH$_2$CH$_3$), 30.8 (NCH$_2$**C**H$_2$), 40.1 (N**C**H$_2$–), 106–122 (**C$_8$**F$_{17}$), 153.1 (**C**O); MS (FAB+) *m/z*: (M+H$^+$): 627; HRMS calcd. for $C_{15}H_{16}O_3N_2F_{17}S$: 627.0610; found: 627.0618.

4.4.11. Synthesis of N-tertbutyl, N′-(perfluorobutanesulfonyl urea) 3k

2a (1 g, 3.11 mmol) and tertbutyl isocyanate (0.39 mL, 3.42 mmol) in anhydrous THF (5 mL) were refluxed for 4 h. The product was crystallized from EtOH/H_2O mixture to give pure product (1 g, yield 81%).

mp: 104.8 °C; IR (KBr): 3396 (ν_{NH}), 1698 ($\nu_{C=O}$), 1188 (ν_{SO_2}), 1139 (ν_{C-F}); ^{1}H NMR (300.13 MHz, d_6-DMSO): δ 1.25 (s, 9H, $(C\mathbf{H_3})_3$), 6.8 (m, 1H, N**H**), 8.7 (m, 1H, N**H**); ^{19}F NMR (282.37 MHz, d_6-DMSO): δ −125.9 (m, 2F, $CF_3C\mathbf{F_2}(CF_2)_2$), −121.5 (m, 2F, $CF_3CF_2C\mathbf{F_2}CF_2$), −111.8 (m, 2F, $CF_3(CF_2)_2C\mathbf{F_2}$), −80.6 (m, 3F, $C\mathbf{F_3}(CF_2)_3$); NMR ^{13}C (75.46 MHz, d_6-DMSO): δ 27.9 (**C**H$_3$)$_3$, 50.9 (**C**(CH$_3$)$_3$), 107–119 (**C$_4$**F$_9$), 149.2 (**C**=O); MS (FAB+) *m/z*: (M+H$^+$): 399; HRMS calcd. for $C_9H_{12}O_3N_2F_9S$: 399.0425; found: 399.0428.

4.4.12. Synthesis of N-tertbutyl, N′-(perfluorooctanesulfonyl urea) 3l

2b (4 g, 7.68 mmol) and tertbutylisocyanate (0.96 mL, 8.44 mmol) in anhydrous THF (20 mL) were refluxed for 6 h. The product was crystallized from EtOH/H_2O mixture to give pure product (3.4 g, yield 75%).

mp: 119 °C; IR (KBr): 3396 (ν_{NH}), 1704 ($\nu_{C=O}$), 1204 (ν_{SO_2}), 1151 (ν_{C-F}); ^{1}H NMR (300.13 MHz, d_6-DMSO): δ 1.2 (s, 9H, $(C\mathbf{H_3})_3$), 6.7 (m, 1H, N**H**), 8.9 (m, 1H, N**H**); ^{19}F NMR (282.37 MHz, d_6-DMSO): δ −126.6 (m, 2F, $CF_3C\mathbf{F_2}(CF_2)_6$),

−123.1(m, 2F, $CF_3CF_2C\mathbf{F_2}(CF_2)_5$), −122.2 (m, 6F, $CF_3(CF_2)_2(C\mathbf{F_2})_3(CF_2)_2$), −120.7 (m, 2F, $CF_3(CF_2)_5C\mathbf{F_2}CF_2$), −112 (m, 2F, $CF_3(CF_2)_6C\mathbf{F_2}$), −81.3 (m, 3F, $\mathbf{CF_3}(CF_2)_7$); ^{13}C NMR (75.46 MHz, d_6-DMSO): δ 27.7 ($\mathbf{C}H_3)_\mathbf{3}$, 50.8 ($\mathbf{C}(CH_3)_3$), 106–122 ($\mathbf{C}_8F_{17}$), 149.3 ($\mathbf{C}$=O); MS (FAB+) *m*/*z*: ($M+H^+$): 599; HRMS calcd. for $C_{13}H_{12}O_3N_2F_{17}S$: 599.0297; found: 599.0314.

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