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An efficient preparation of *N*-per- (or poly)fluorophenyl pyrroles and *N*-fluoroalkanesulfonyl pyrroles

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Abstract—Hetero-Diels–Alder reaction of *N*-sulfinyl per- (or poly)fluoroaniline and *N*-sulfinylfluoroalkanesulfonyl amine with 1,3-dienes affords the corresponding cycloadduct 3,6-dihydro-1,2-thiazine-1-oxide which is readily converted to *N*-per- (or poly)fluorophenyl pyrrole and *N*-fluoroalkanesulfonyl pyrrole under mild reaction conditions in good yields.

1. Introduction

Pyrroles are important heterocycles broadly used in materials science[1] and found in naturally occurring and biologically important molecules.[2] Accordingly, substantial attention has been paid to develop efficient methods for the synthesis of pyrroles. Most known methods for the construction of the pyrrole ring proceed via various types of cycloaddition or cycloisomerization of acyclic precursors.[1–3] For example, Gevorgyan[4] reported the Cu-assisted cycloisomerization of alkynyl imines into the pyrrole ring, while Ragaini[5] found that under CO pressure and catalyzed by $(Pd(Phen)_2)(BF_4)_2$ the reaction of 1,3-diene with nitroarenes afforded the oxazines which then eliminated water on heating to give the corresponding *N*-arylpyrroles (Scheme 1).

Moreover, most synthetic methods give the best results for pyrroles bearing one or two substituents in the 2 and 5-position.[6] Recently, we synthesized polyfunctionalized 3-fluoropyrroles from rhodium(II) acetate-catalyzed intramolecular N–H insertion reaction of δ-amino-γ,γ-difluoro-α-diazo-β-ketoesters (Scheme 2).[7]

To the best of our knowledge, there are no convenient methods for the formation of *N*-fluorophenyl pyrroles. The cycloaddition reactions of *N*-sulfinylanilines have attracted major interest since they were first synthesized many years ago.[8–10] The *N*-sulfinylamino group (–N=S=O) is an excellent reagent for (4+2)-cycloadditions with 1,3-dienes[8–10] and some derivatives also undergo (2+2)-cycloadditions with ynamines.[11] These (4+2)-cycloadducts 3,6-dihydro-1,2-thiazine-1-oxides are converted to *N*-arylated pyrroles by base treatment[12] or photolysis.[13]

In this paper, we report an efficient two-step preparation of *N*-per- (or poly) fluorophenyl pyrroles and *N*-fluoroalkanesulfonyl pyrroles: (1) (4+2)-cycloaddition of *N*-sulfinyl per- (or poly)fluoroanilines or *N*-sulfinylfluoroalkanesulfonyl amines with 1,3-dienes. (2) Conversion of the cycloadducts 3,6-dihydro-1,2-thiazine-1-oxides to *N*-per-(or poly)fluorophenyl pyrroles or *N*-fluoroalkane- sulfonyl pyrroles under basic reaction conditions.

2. Results and discussion

N-sulfinyl per- (or poly)fluoroanilines Ar_fNSO **1** or *N*-sulfinylfluoroalkane sulfonyl amines R_fSO_2NSO **2** are easily prepared by refluxing the per- (or poly) fluoroanilines or fluoroalkanesulfonyl amides with an excess of sulfonyl chloride. They are very reactive towards many organic reagents such as aldehydes, alcohols, malonates, carboxylic acids and acid anhydrides, etc. affording the condensation or addition products.[14–16]

The thermal cycloaddition reaction of these new fluorine-containing *N*-sulfinylamines with 1,3-dienes occurred smoothly. For example, stirring of **1** with 2-methyl-1,3-butadiene **3** or 2,3-dimethyl-1,3-butadiene **4** in a sealed tube at 80°C for 8 h gave the six-membered 2-(fluorophenyl)-3,6-dihydro-1,2-thiazine-1-oxides in good yield (>80%) (Scheme 3).

It was observed that the reactions of **1** with **3** gave two isomers **5** and **6**, which could not be separated by column chromatography. According to the proton NMR spectra of

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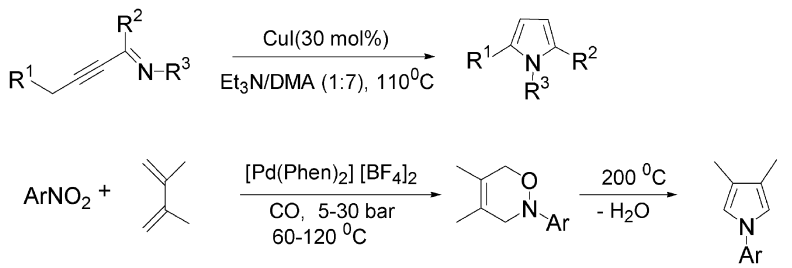
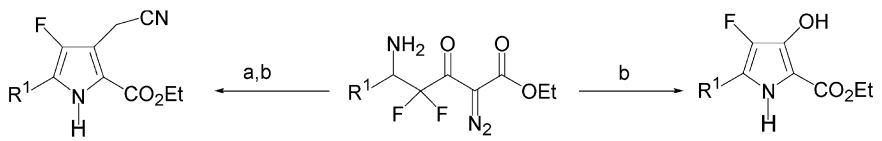
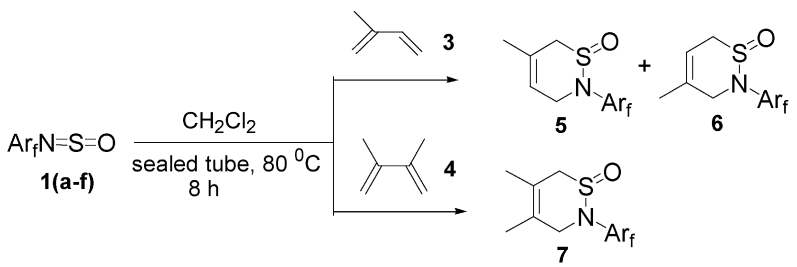


Scheme 1.



Scheme 2. (a) $Ph_3P{=}CHCN$, toluene, 55°C. (b) 1 mol% $Rh_2(OAc)_4$, toluene, reflux.



Scheme 3.

the mixed products, the 5-methyl substituted product **5** was the major product. While **1e** reacted with **3** afforded a mixture of isomers **5e** and **6e** in a ratio of 1:1 (Table 1, entry 5). The ^{1}H NMR spectra of all these cycloproducts **5**, **6** and **7** showed the axial and equatorial protons of two cyclic methylene groups. The axial and equatorial protons appeared as two AB peaks with the 6-CH_2 at the down field. For example, 4,5-dimethyl-2-(4-chloro-tetrafluoro-phenyl)-3,6-dihydro-1,2-thiazine-1-oxide **7b**, $\Delta\nu_{AB}$=311.7 Hz (for 6-CH_2) and 165.6 Hz (for 3-CH_2), the coupling constant of the gem-protons for the 6-CH_2 and 3-CH_2 are 16.8 and 15.6 Hz, respectively. While several literature works did not show clear AB peaks in their ^{1}H NMR spectra and reported as multiplets for the ring methylene groups.[17,18]

Table 1. Cycloaddition of *N*-per- (or poly)fluoroanilines with 1,3-dienes **3** or **4**[a]

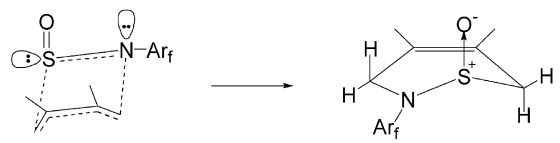
Entry	Reactant **1** (Ar_f)	**3** or **4**	Product and ratio[b]	Yield (%)[c]
1	C_6F_5(**1a**)	**3**	**5a/6a** (4:1)	80
		4	**7a**	83
2	4-ClC_6F_4(**1b**)	**3**	**5b/6b** (7:1)	97
		4	**7b**	99
3	4-HC_6F_4(**1c**)	**3**	**5c/6c** (2:1)	99
		4	**7c**	97
4	2,4-$F_2C_6H_3$(**1d**)	**3**	**5d/6d** (2:1)	88
		4	**7d**	100
5	3,4-$ClFC_6H_3$(**1e**)	**3**	**5e/6e** (1:1)	95
		4	**7e**	93
6	2-FC_6H_4(**1f**)	**3**	**5f/6f** (2:1)	100
		4	**7f**	96

[a] Reaction was carried out in a sealed tube at 80°C using CH_2Cl_2 as a solvent.
[b] The ratio of product **5/6** based on the ^{1}H NMR spectra.
[c] Isolated yield.

The molecular structure of the cylcloproduct **5c** was established by an X-ray crystallographic analysis (Fig. 1).

It is clear that the tetrafluorophenyl group is in the pseudo-equatorial position and the oxygen atom is in the pseudo-axial position. The six-membered ring adopts a more stable chair conformation.[19] An ordered pericyclic reaction transition state is proposed for this Hetero-Diels–Alder reaction and the stereochemistry of the products (Scheme 4).[20]

Under basic reaction conditions compounds **5**, **6** and **7** readily transformed the corresponding *N*-fluorophenyl pyrroles in moderate to excellent yields (Scheme 5). Generally, *N*-perfluorophenyl- or *N*-(4-chloro-tetrafluoro) phenyl-3,6-dihydro-1,2-thiazine-1-oxide gave lower yield (45–66%), while *N*-(monofluoro)phenyl- or *N*-(difluoro)-



Scheme 4.

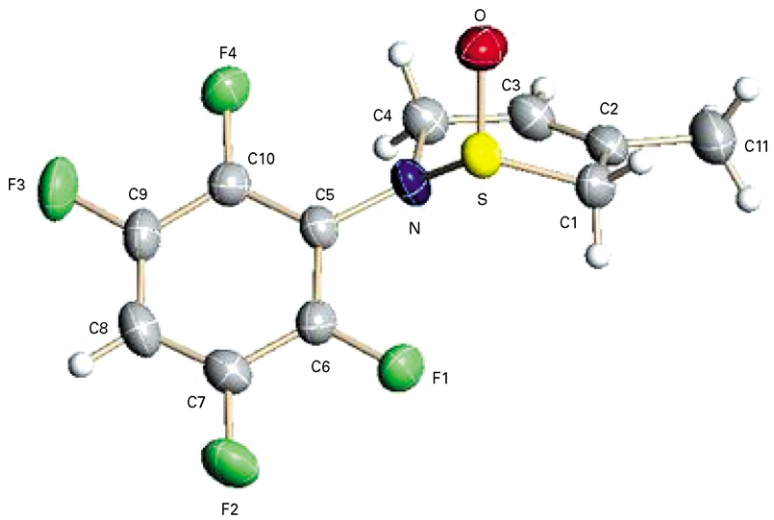
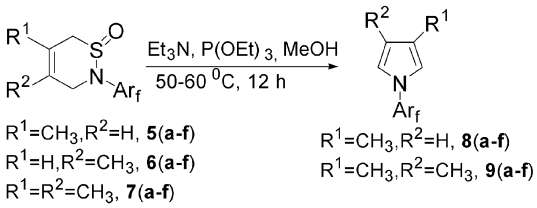


Figure 1. X-Ray crystal structure of **5c**.



Scheme 5.

phenyl-3,6-dihydro-1,2-thiazine-1-oxide gave higher yields (Table 2).

In the process for the formation of pyrroles, Et_3N should either act as a base abstracting the 6-hydrogen or as a nucleophile attracking the sulfur atom and then caused the ring opening followed by the elimination of 'HSOH' to afford *N*-fluoro-phenyl pyrroles (Scheme 6).[17,21]

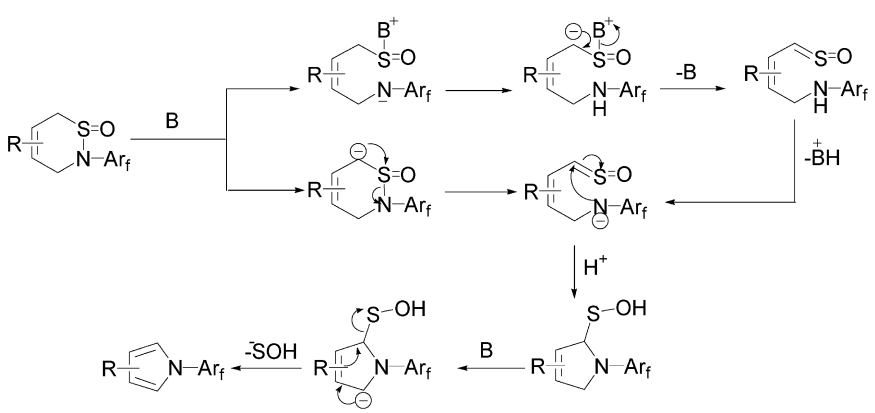
These *N*-fluorophenyl pyrroles are fully characterized spectroscopically and some are further elucidated by X-ray crystallographic analysis. Figure 2 shows the X-ray crystal structure of compound **8a**. The bond lengths of N–C_6, N–C_7 and N–C_{10} are 1.408, 1.378 and 1.381 Å, respectively; all are shorter than normal nitrogen–carbon single bond indicating its conjugated property. However, it was shown that the pentafluorophenyl plane and the pyrrole plane are not coplanar, the angle between the two planes is

Table 2. Preparation of *N*-per (or poly) pyrroles **8** and **9**

Entry	Reactant **5**, **6** or **7**	Reaction condition[a]	Product	Yield (%)[b]
1	**5a**, **6a**	50°C, 8 h	**8a**	55
2	**7a**	50°C, 8 h	**9a**	50
3	**5b**, **6b**	50°C, 12 h	**8b**	66
4	**7b**	50°C, 12 h	**9b**	45
5	**5c**, **6c**	50°C, 12 h	**8c**	57
6	**7c**	50°C, 12 h	**9c**	70
7	**5d**, **6d**	60°C, 24 h	**8d**	67
8	**7d**	60°C, 24 h	**9d**	80
9	**5e**, **6e**	60°C, 24 h	**8e**	64
10	**7e**	60°C, 24 h	**9e**	88
11	**5f**, **6f**	60°C, 24 h	**8f**	71
12	**7f**	60°C, 24 h	**9f**	91

[a] All reactions were carried out in MeOH.
[b] Isolated yield.

49°, it is very similar to *N*-pentafluorophenyl aromatic aldimine $C_6F_5N{=}CHPh$, in which the angle between the phenyl and pentafluorophenyl planes is 49.2°.[17] XRD analysis of compound **8a** showed the existence of the intermolecular hydrogen bonds between the fluorine atom of the pentafluorophenyl and the hydrogen atom of the pyrrole ring, the distance of H···F is 2.496 Å and the angle of C_1–F_1···H is 148.41°. The packing map (Fig. 3) shows that the pentafluorophenyl plane in one molecule is parallel and just overlaps with the pyrrole planes in the other



Scheme 6.

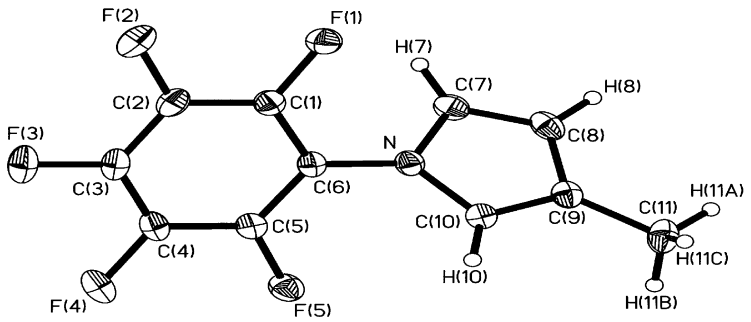


Figure 2. X-Ray crystal structure of **8a**.

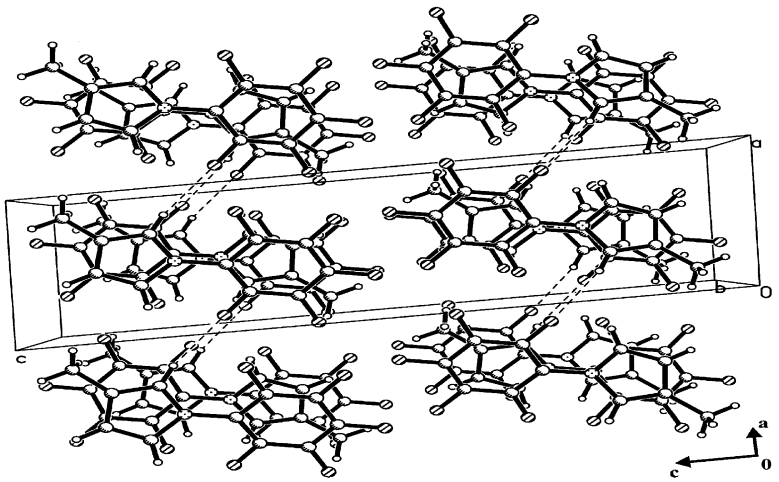


Figure 3. The packing map of **8a**.

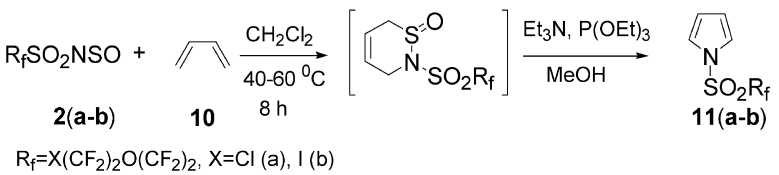
two molecules, the pyrrole plane also lies between the two pentafluorophenyl planes. The distance between the two parallel planes is 3.47 Å. These alternate overlapped molecules suggest some interaction between the π-electron systems. The average volume per non-H atom is 15.2 Å. On the basis of the above fact, it may be concluded that the molecular packing in the cell is very dense.

Under similar reaction conditions, *N*-sulfinylfluoroalkanesulfonyl amines R_fSO_2NSO **2** could also react with 1,3-butadiene **10**. The ^1H NMR spectra of the crude products showed only two unsaturated proton at 5.78 and 5.69 ppm, indicating the cycloaddition products was formed. However, an attempt to purify the product by distillation or column chromatography failed. It was found that during the column chromatography on silica gel the six-membered ring opened to give an inseparable mixture. While fractional column distillation of the crude products gave mainly the corresponding fluoroalkanesulfonyl amides $R_fSO_2NH_2$. The easy decomposition of *N*-fluoroalkanesulfonyl 3,6-dihydro-1,2-thiazine-1-oxides may be attributed to the strong electron-withdrawing ability of R_fSO_2 group. Treatment of the crude products with Et_3N and $P(OEt)_3$ in methanol gave expected *N*-fluoroalkanesulfonyl pyrroles **11** in about 60–65% yield. Products **11** are stable and can be further purified by fractional column distillation (Scheme 7).

In conclusion, we have demonstrated a concise and efficient synthetic route to *N*-fluorophenyl pyrroles or *N*-fluoroalkanesulfonyl pyrroles from readily available starting compounds *N*-sulfinyl fluoroanilines or *N*-sulfinylfluoroalkane sulfonyl amines by two reaction steps. Further chemical transformation of these fluorine-containing pyrroles is under investigation.

3. Experimental

Melting points were measured in Temp-Melt apparatus and were uncorrected. ^1H, ^{13}C and ^{19}F NMR spectra were recorded in $CDCl_3$ on Bruker AM-300 instruments with Me_4Si and $CFCl_3$ (with upfield negative) as the internal and external standards, respectively. IR spectra were obtained with a Nicolet AV-360 spectrophotometer. Low resolution



Scheme 7.

mass spectrum or high resolution mass spectra (HRMS) were obtained on a Finnigan GC–MS 4021 or a Finnigan MAT-8430 instrument using the electron impact ionization technique (70 eV), respectively. Elemental analyses were performed by this Institute. X-Ray crystallographic structure analysis was performed on a Bruker P4 instrument. Dichloromethane was distilled from CaH_2 and reagents were purified before use. *N*-sulfinyl per- (or poly)fluoroanilines and *N*-sulfinylfluoroalkanesulfonyl amines were prepared as previous described.[14,22]

3.1. General procedure for the reaction of *N*-sulfinyl per-(or poly)fluoroanilines (1) with 1,3-dienes (3) or (4)

3.1.1. 2-(4-Chloro-tetrafluorophenyl)-4,5-dimethyl-3,6-dihydro-1,2-thiazine-1-oxide (7b). A solution of *N*-sulfinyl-(4-chloro-tetrafluoro)aniline **1b** (0.49 g, 2.00 mmol) and 2,3-dimethyl-1,3-butadiene **4** (2.5 mmol) in dry CH_2Cl_2 (5.0 mL) was placed in a sealed tube, and stirred at 80°C for 8 h. The solvent was removed in vacuo, the residue was purified on silica gel using ethyl acetate/hexane (v/v, 1:8) as the elutent to give a white solid product **7b**, which was further recrystallized from dichloromethane/hexane (v/v, 1:1) to give the pure product **7b** (0.65 g, 1.98 mmol, 99%) as colorless crystals. Mp: 122–124°C. IR (KBr) cm^{-1}: 2920, 2857, 1496, 1158, 1077. ^1H NMR ($CDCl_3$) δ 1.78 (3H, s, CH_3), 1.84 (3H, s, CH_3), 3.19 (AB, J_{AB}=15.6 Hz, 1H, 3-Ha), 3.42 (AB, J_{AB}=15.9 Hz, 1H, 6-Ha), 3.75 (AB, J_{AB}=16.2 Hz, 1H, 3-H_b), 4.46 (AB, J_{AB}=16.8 Hz, 1H, 6-H_b). ^{19}F NMR ($CDCl_3$) δ −140.42 (2F, d, J=13.8 Hz), −144.77 (2F, d, J=15.5 Hz). ^{13}C NMR ($CDCl_3$) δ 17.0, 19.8, 47.2, 54.8, 104.3, 115.2, 124.3, 125.0, 143.4 (d, $^1J_{C-F}$=167.6 Hz), 146.8 (d, $^1J_{C-F}$=156.9 Hz). MS: *m/z* (%) 327 (M^+, 11), 82 (100). Anal. calcd for $C_{12}H_{10}ClF_4NOS$: C, 43.99; H, 3.08; N, 4.28. Found: C, 43.94; H, 2.98; N, 4.04.

3.1.2. 5-Methyl-2-(pentafluorophenyl)-3,6-dihydro-1,2-thiazine-1-oxide (5a) and 4-methyl-2-(pentafluorophenyl)-3,6-dihydro-1,2-thiazine-1-oxide (6a). Colorless crystals, mp: 65–68°C. IR (KBr) cm^{-1}: 2945, 1520, 1396, 1380, 1185, 1096, 1033, 988. ^1H NMR ($CDCl_3$) δ 1.57 (0.6H, s, 4-CH_3), 1.91 (2.4H, s, 5-CH_3), 3.20 (AB, J_{AB}=16.2 Hz, 1H, 3-Ha), 3.57 (AB, J_{AB}=17.1 Hz, 1H, 6-Ha), 3.71 (AB, J_{AB}=16.2 Hz, 1H, 3-H_b), 4.52 (AB, J_{AB}=17.1 Hz, 1H, 6-H_b), 5.77 (1H, s, 4,5-H). ^{19}F NMR ($CDCl_3$) δ −145.06 (2F, d, J=16.6 Hz), −155.15 (1F, t, J=21.4 Hz), −161.40 (2F, m). MS: *m/z* (%) 297 (M^+, 15), 229 (3), 167 (20), 68 (100), 67 (42), 53 (12). Anal. calcd for $C_{11}H_8F_5NOS$: C, 44.45; H, 2.71; N, 4.71. Found: C, 44.52; H, 2.63; N, 4.57.

3.1.3. 4,5-Dimethyl-2-(pentafluorphenyl)-3,6-dihydro-1,2-thiazine-1-oxide (7a). Colorless crystals, mp: 57–58°C. Lit.[23] 57–58°C.

3.1.4. 5-Methyl-2-(4-chloro-tetrafluorophenyl)-3,6-dihydro-1,2-thiazine-1-oxide (5b) and 4-methyl-2-(4-chloro-tetrafluorophenyl)-3,6-dihydro-1,2-thiazine-1-oxide (6b). Colorless crystals, mp: 134–136°C. IR (KBr) cm^{-1}: 2905, 1482, 1161, 1088. ^1H NMR ($CDCl_3$) δ 1.59 (0.37H, s, 4-CH_3), 1.88 (2.63H, s, 5-CH_3), 3.20 (AB, J_{AB}=16.2 Hz, 1H, 3-Ha), 3.62 (AB, J_{AB}=16.5 Hz, 1H, 6-Ha), 3.71 (AB, J_{AB}=16.2 Hz, 1H, 3-H_b), 4.56 (AB, J_{AB}=16.5 Hz, 1H, 6-H_b), 5.79 (1H, s, 4,5-H). ^{19}F NMR ($CDCl_3$) δ −140.35 (2F, d, J=13.8 Hz), −144.89 (2F, d, J=14.9 Hz). MS: *m/z* (%) 315 (M^++2, 1), 313 (M^+, 2), 185 (2), 183 (6), 68 (100), 67 (36), 53 (12). Anal. calcd for $C_{11}H_8ClF_4NOS$: C, 42.12; H, 2.57; N, 4.46. Found: C, 42.29; H, 2.54; N, 4.34.

3.1.5. 5-Methyl-2-(2,3,5,6-tetrafluorophenyl)-3,6-dihydro-1,2-thiazine-1-oxide (5c) and 4-methyl-2-(2,3,5,6-tetrafluorophenyl)-3,6-dihydro-1,2-thiazine-1-oxide (6c). Colorless crystals, mp: 121–122°C. IR (KBr) cm^{-1}: 3041, 1640, 1503, 1478, 1186, 1154, 1145, 1080. ^1H NMR ($CDCl_3$) δ 1.61 (1H, s, 4-CH_3), 1.92 (2H, s, 5-CH_3), 3.20 (AB, J_{AB}=15.9 Hz, 1H, 3-Ha), 3.63 (AB, J_{AB}=16.8 Hz, 1H, 6-Ha), 3.72 (AB, J_{AB}=15.9 Hz, 1H, 3-H_b), 4.58 (AB, J_{AB}=16.8 Hz, 1H, 6-H_b), 5.79 (1H, s, 4,5-H), 6.98–7.04 (1H, m, Ar). ^{19}F NMR ($CDCl_3$) δ −138.30 (2F, m), −146.07 (2F, m). MS: *m/z* (%) 279 (M^+, 3), 211 (11), 149 (13), 68 (100), 67 (52), 53 (13). Anal. calcd for $C_{11}H_9F_4NOS$: C, 47.31; H, 3.25; N, 5.02. Found: C, 47.30; H, 3.33; N, 4.91.

3.1.6. 4,5-Dimethyl-2-(2,3,5,6-tetrafluorophenyl)-3,6-dihydro-1,2-thiazine-1-oxide (7c). Colorless crystals, mp: 104–106°C. IR (KBr) cm^{-1}: 3025, 2926, 1510–1449, 1194–1037. ^1H NMR ($CDCl_3$) δ 1.78 (3H, s, CH_3), 1.84 (3H, s, CH_3), 3.19 (AB, J_{AB}=15.6 Hz, 1H, 3-Ha), 3.45 (AB, J_{AB}=15.9 Hz, 1H, 6-Ha), 3.75 (AB, J_{AB}=16.2 Hz, 1H, 3-H_b), 4.49 (AB, J_{AB}=15.9 Hz, 1H, 6-H_b), 6.95–7.07 (1H, m, Ar). ^{19}F NMR ($CDCl_3$) δ −138.35 (2F, m), −145.93 (2F, m). MS: *m/z* (%) 293 (M^+, 5), 211 (2), 149 (13), 82 (100), 67 (61). Anal. calcd for $C_{12}H_{11}F_4NOS$: C, 49.16; H, 3.78; N, 4.78. Found: C, 49.11; H, 3.66; N, 4.59.

3.1.7. 5-Methyl-2-(2,4-difluorophenyl)-3,6-dihydro-1,2-thiazine-1-oxide (5d) and 4-methyl-2-(2,4-difluorophenyl)-3,6-dihydro-1,2-thiazine-1-oxide (6d). Yellow oil. IR (KBr) cm^{-1}: 2915, 1598, 1505, 1432, 1296, 1145, 1145, 1084. ^1H NMR ($CDCl_3$) δ 1.84 (1H, s, 4-CH_3), 1.88 (2H, s, 5-CH_3), 3.16 (AB, J_{AB}=16.2 Hz, 1H, 3-Ha), 3.61 (AB, J_{AB}=16.5 Hz, 1H, 6-Ha), 3.72 (AB, J_{AB}=16.2 Hz, 1H, 3-H_b), 4.26 (AB, J_{AB}=16.5 Hz, 1H, 6-H_b), 5.52 (0.33H, s, 5-H), 5.77 (0.66H, s, 4-H), 6.85–6.92 (2H, m, Ar), 7.36–7.75 (1H, m, Ar). ^{19}F NMR ($CDCl_3$) δ −111.14 (1F, m), −117.69 (1F, m). MS: *m/z* (%) 243 (M^+, 12), 175 (26), 113 (24), 68 (100), 67 (41), 53 (14). Anal. calcd for $C_{11}H_{11}F_2NOS$: C, 54.31; H, 4.56; N, 5.76. Found: C, 54.48; H, 4.96; N, 5.63.

3.1.8. 4,5-Dimethyl-2-(2,4-difluorophenyl)-3,6-dihydro-1,2-thiazine-1-oxide (7d). Colorless crystals, mp: 92–94°C. IR (KBr) cm^{-1}: 3033, 2926, 1505, 1438, 1430, 1269, 1220, 1147, 1112, 1076. ^1H NMR ($CDCl_3$) δ 1.77 (3H, s, CH_3), 1.83 (3H, s, CH_3) 3.15 (AB, J_{AB}=16.5 Hz, 1H, 3-Ha), 3.43 (AB, J_{AB}=16.2 Hz, 1H, 6-Ha), 3.74 (AB, J_{AB}=16.2 Hz, 1H, 3-H_b), 4.16 (AB, J_{AB}=15.9 Hz, 1H, 6-H_b), 6.84–6.92 (2H, m, Ar), 7.39–7.47 (1H, m, Ar). ^{19}F NMR($CDCl_3$) δ −111.23 (1F, m), −117.77 (1F, m). MS: *m/z* (%) 257 (M^+, 34), 175 (11), 113 (25), 82 (100), 67 (67). Anal. calcd for $C_{12}H_{13}F_2NOS$: C, 56.02; H, 5.09; N, 5.44. Found: C, 55.99; H, 4.91; N, 5.25.

3.1.9. 5-Methyl-2-(3-chloro-4-fluorophenyl)-3,6-dihydro-1,2-thiazine-1-oxide (5e) and 4-methyl-2-(3-chloro-4-fluorophenyl)-3,6-dihydro-1,2-thiazine-1-oxide (6e). Colorless crystals, mp:104–106°C. IR (KBr) cm^{-1}: 2914,

1504, 1232, 1066. ^{1}H NMR ($CDCl_3$) δ 1.57 (1.5H, s, 4-H), 1.88 (1.5H, s, 5-CH_3), 3.20 (AB, J_{AB}=15.9 Hz, 1H, 3-Ha), 3.49 (AB, J_{AB}=16.8 Hz, 1H, 6-Ha), 3.65 (AB, J_{AB}=15.9 Hz, 1H, 3-H_b), 4.13 (AB, J_{AB}=16.8 Hz, 1H, 6-H_b), 5.53 (0.5H, s, 5-H), 5.79 (0.5H, s, 4-H), 7.07–7.28 (3H, m, Ar). ^{19}F NMR ($CDCl_3$) δ −119.61 (1F, m). MS: *m/z* (%) 261 (M^++2, 9), 259 (M^+, 23), 193 (10), 191 (26), 156 (42), 131 (11), 129 (33), 68 (100), 67 (34), 53 (9). Anal. calcd for $C_{11}H_{11}ClFNOS$: C, 50.87; H, 4.27; N, 5.39. Found: C, 50.89; H, 4.15; N, 5.19.

3.1.10. 4,5-Dimethyl-2-(3-chloro-4-flurophenyl)-3,6-dihydro-1,2-thiazine-1-oxide (7e). Colorless crystals, mp: 174–175°C. IR (KBr) cm^{-1}: 2935, 2903, 1584, 1506, 1238, 1062. ^{1}H NMR ($CDCl_3$) δ 1.81 (3H, s, CH_3), 1.83 (3H, s, CH_3), 3.20 (AB, J_{AB}=16.2 Hz, 1H, 3-Ha), 3.48 (AB, J_{AB}=15.9 Hz, 1H, 6-Ha), 3.68 (AB, J_{AB}=16.2 Hz, 1H, 3-H_b), 4.14 (AB, J_{AB}=15.9 Hz, 1H, 6-H_b), 7.08–7.28 (3H, m, Ar). ^{19}F NMR ($CDCl_3$) δ −119.82 (1F, m). MS: *m/z* (%) 275 (M^++2, 3), 273 (M^+, 7), 212 (2), 210 (6), 131 (5), 129 (14), 82 (100), 67 (52). Anal. calcd for $C_{12}H_{13}ClFNOS$: C, 52.65; H, 4.79; N, 5.12. Found: C, 52.61; H, 4.65; N, 5.02.

3.1.11. 5-Methyl-2-(2-fluorophenyl)-3,6-dihydro-1,2-thiazine-1-oxide (5f) and 4-methyl-2-(2-fluorophenyl)-3,6-dihydro-1,2-thiazine-1-oxide (6f). Yellow oil. IR (KBr) cm^{-1}: 2914, 1498, 1449, 1259, 1084. ^{1}H NMR ($CDCl_3$) δ 1.85 (1H, s, 4-CH_3), 1.88 (2H, s, 5-CH_3), 3.15 (AB, J_{AB}=16.1 Hz, 1H, 3-Ha), 3.67 (AB, J_{AB}=16.2 Hz, 1H, 6-Ha), 3.73 (AB, J_{AB}=16.1 Hz, 1H, 3-H_b), 4.29 (AB, J_{AB}=16.2 Hz, 1H, 6-H_b), 5.52 (0.33H, s, 5-H), 5.78 (0.66H, s, 4-H), 7.07–7.41 (4H, m, Ar). ^{19}F NMR ($CDCl_3$) δ −122.73 (1F, m). MS: *m/z* (%) 225 (M^+, 43), 157 (53), 95 (43), 68 (100), 67 (47), 53 (15). Anal. calcd for $C_{11}H_{12}FNOS$: C, 58.65; H, 5.37; N, 6.22. Found: C, 58.41; H, 5.30; N, 6.17.

3.1.12. 4,5-Dimethyl-2-(2-fluorophenyl)-3,6-dihydro-1,2-thiazine-1-oxide (7f). Colorless crystals, mp: 81–86°C. IR (KBr) cm^{-1}: 2914, 2824, 1609, 1499, 1454, 1440, 1203, 1120, 1075. ^{1}H NMR ($CDCl_3$) δ 1.78 (3H, s, CH_3), 1.83 (3H, s, CH_3), 3.15 (AB, J_{AB}=16.2 Hz, 1H, 3-Ha), 3.48 (AB, J_{AB}=16.2 Hz, 1H, 6-Ha), 3.75 (AB, J_{AB}=16.2 Hz, 1H, 3-H_b), 4.20 (AB, J_{AB}=16.2 Hz, 1H, 6-H_b), 7.07–7.45 (4H, m, Ar). ^{19}F NMR($CDCl_3$) δ −122.82 (1F, m). MS: *m/z* (%) 239 (M^+, 12), 157 (5), 95 (20), 82 (100), 67 (70). Anal. calcd for $C_{12}H_{14}FNOS$: C, 60.23; H, 5.90; N, 5.85. Found: C, 60.23; H, 5.94; N, 5.75.

3.2. General procedure for preparation of *N*-per- (or poly)fluorophenyl pyrroles 8 and 9

The dihydrothiazine oxide **7b** (0.33 g, 1 mmol) was added to a stirring solution containing triethylamine (0.07 mL, 0.05 g, 0.5 mmol), triethyl phosphite (0.26 mL, 0.25 g, 1.5 mmol) and methanol (10 mL). The mixture was stirred at 60°C overnight. Then the reaction solvent was removed in vacuo. The residue was treated with hydrochloric acid (1N, 12 mL) and then was extracted with ether (10 mL×3). The organic layer was washed with water, dried over $MgSO_4$ and concentrated in vacuo. Flash column chromatography on silica gel, eluting with hexane afforded the product, which was further recrystallized from hexane to give the pure product **9b** (0.12 g, 45%) as colorless crystals.

3.2.1. 1-(4-Chloro-tetrafluorophenyl)-3,4-dimethylpyrrole (9b). Colorless crystals, mp: 100–102°C. IR (KBr) cm^{-1}: 3080, 2948, 1537, 1499, 1157, 976. ^{1}H NMR ($CDCl_3$) δ 2.06 (6H, s, CH_3), 6.65 (2H, s, 2,5-H). ^{19}F NMR($CDCl_3$) δ −140.53 (2F, d, *J*=15.5 Hz), −149.14 (2F, d, *J*=14.4 Hz). ^{13}C NMR ($CDCl_3$) δ 10.06, 119.54, 119.62, 119.66, 121.48, 141.44 (d, $^1J_{C-F}$=246.7 Hz), 144.74 (d, $^1J_{C-F}$=248.21 Hz). MS: *m/z* (%) 279 (M^++2, 25), 278 (M^++1, 42), 277 (M^+, 76), 276 (M^+−1, 100), 264 (4), 262 (11), 67 (10). Anal. calcd for $C_{12}H_8ClF_4N$: C, 51.91; H, 2.90; N, 5.04. Found: C, 51.78; H, 2.79; N, 4.89.

3.2.2. 1-(Pentafluorophenyl)-3-methylpyrrole (8a). Colorless crystals, mp: 73–74°C. IR (KBr) cm^{-1}: 3140, 2953, 2932, 1515, 1305, 1242, 1065, 987. ^{1}H NMR ($CDCl_3$) δ 2.17 (3H, s, CH_3), 6.25–6.26 (1H, m, 4-H), 6.65 (1H, s, 2-H), 6.77–6.80 (1H, m, 5-H). ^{19}F NMR ($CDCl_3$) δ: −149.62 (2F, d, *J*=16.9 Hz), −157.54 (1F, t, *J*=17.8 Hz), −161.75 (2F, t, *J*=21.3 Hz). MS: *m/z* (%) 248 (M^++1, 10), 247 (M^+, 87), 246 (M^+−1, 100), 167 (10), 53 (7). Anal. calcd for $C_{11}H_6F_5N$: C, 53.45; H, 2.45; N, 5.67. Found: C, 53.42; H, 2.56; N, 5.58.

3.2.3. 1-(Pentafluorophenyl)-3,4-dimethylpyrrole (9a). Colorless crystals, mp: 91–92°C. Lit.[23] 91–92°C.

3.2.4. 1-(4-Chloro-tetrafluorophenyl)-3-methylpyrrole (8b). Colorless crystals, mp: 59–60°C. IR (KBr) cm^{-1}: 3146, 2930, 1524, 1499, 1154, 975. ^{1}H NMR ($CDCl_3$) δ 2.17 (3H, s, CH_3), 6.25–6.26 (1H, m, 4-H), 6.70 (1H, m, 5-H), 6.82–6.85 (1H, m, 2-H). ^{19}F NMR ($CDCl_3$) δ: −140.61 (2F, d, *J*=15.2 Hz), −149.13 (2F, d, *J*=14.4 Hz). MS: *m/z* (%) 265 (M^++2, 29), 264 (M^++1, 43), 263 (M^+, 91), 262 (M^+−1, 100), 185 (3), 183 (7), 53 (27). Anal. calcd for $C_{11}H_6ClF_4N$: C, 50.12; H, 2.29; N, 5.31. Found: C, 50.22; H, 2.27; N, 5.31.

3.2.5. 1-(2,3,5,6-Tetrafluorophenyl)-3-methylpyrrole (8c). Colorless crystals, mp: 51–52°C. IR (KBr) cm^{-1}: 3099, 2927, 1517, 1174, 1144, 939. ^{1}H NMR ($CDCl_3$) δ 2.16 (3H, s, CH_3), 6.23–6.24 (1H, m, 4-H), 6.70–6.72 (1H, m, 5-H), 6.83–6.86 (1H, m, 2-H), 6.95–7.06 (1H, m, Ar). ^{19}F NMR ($CDCl_3$) δ −138.21 (2F, m), −149.90 (2F, m). MS: *m/z* (%) 230 (M^++1, 10), 229 (M^+, 77), 228 (M^+−1, 100), 149 (9), 53 (8). HRMS (*m/z*) calcd for $C_{11}H_7F_4N$[M^+], 229.0501, found 229.0515.

3.2.6. 1-(2,3,5,6-Tetrafluorophenyl)-3,4-dimethylpyrrole (9c). Colorless crystals, mp: 72–73°C. IR (KBr) cm^{-1}: 3089, 2944, 2927, 1646, 1514, 1174, 1141, 937. ^{1}H NMR ($CDCl_3$) δ 2.07 (6H, s, CH_3), 6.67 (2H, s, 2,5-H), 6.91–7.02 (1H, m, Ar). ^{19}F NMR ($CDCl_3$) δ: −138.38 (2F, m), −150.23 (2F, m). MS: *m/z* (%) 244 (M^++1, 12), 243 (M^+, 91), 242 (M^+−1, 100), 228 (12), 149 (9), 67 (10). Anal. calcd for $C_{12}H_9F_4N$: C, 59.26; H, 3.73; N, 5.76. Found: C, 59.25; H, 3.71; N, 5.61.

3.2.7. 1-(2,4-Difluorophenyl)-3-methylpyrrole (8d). Colorless oil. IR (KBr) cm^{-1}: 3095, 2925, 1522, 1439, 1270, 1144, 971. ^{1}H NMR ($CDCl_3$) δ 2.16 (3H, s, CH_3),

6.17–6.19 (1H, m, 4-H), 6.73–6.74 (1H, m, 5-H), 6.85–7.00 (3H, m, 2-H and Ar), 7.27–7.35 (1H, m, Ar). ^{19}F NMR ($CDCl_3$) δ −112.92 (1F, m), −120.67 (1F, m). MS: *m/z* (%) 194 (M^++1, 10), 193 (M^+, 85), 192 (M^+−1, 100), 113 (14), 53 (11). HRMS (*m/z*) calcd for $C_{11}H_9F_2N$ [M^+-CH_3], 178.0456, found 178.0468.

3.2.8. 1-(2,4-Difluorophenyl)-3,4-dimethylpyrrole (9d). Colorless crystals, mp: 33–34°C. IR (KBr) cm^{-1}: 3084, 2926, 1535, 1516, 1142, 969. ^{1}H NMR ($CDCl_3$) δ 2.06 (6H, s, CH_3), 6.70 (2H, s, 2,5-H), 6.86–6.98 (2H, m, Ar), 7.24–7.31 (1H, m, Ar). ^{19}F NMR ($CDCl_3$) δ −113.72 (1F, m), −120.95 (1F, m). MS: *m/z* (%) 208 (M^++1, 10), 207 (M^+, 79), 206 (M^+−1, 100), 192 (12), 113 (7). Anal. calcd for $C_{12}H_{11}F_2N$: C, 69.55; H, 5.35; N, 6.76. Found: C, 69.77; H, 5.51; N, 6.53.

3.2.9. 1-(3-Chloro-4-fluorophenyl)-3-methylpyrrole (8e). Colorless crystals, mp: 47–48°C. IR (KBr) cm^{-1}: 3117, 2924, 1509, 1262, 1239, 1069. ^{1}H NMR ($CDCl_3$) δ 2.15 (3H, s, CH_3), 6.17–6.18 (1H, m, 4-H), 6.78 (1H, s, 2-H), 6.89–6.91 (1H, m, 5-H), 7.16–7.20 (2H, m, Ar), 7.37–7.40 (1H, m, Ar). ^{19}F NMR ($CDCl_3$) δ −120.35 (1F, m). MS: *m/z* (%) 211 (M^++2, 25), 210 (M^++1, 42), 209 (M^+, 75), 208 (M^+−1, 100), 131 (4), 129 (11), 53 (7). Anal. calcd for $C_{11}H_9ClFN$: C, 63.02; H, 4.33; N, 6.68. Found: C, 62.84; H, 4.28; N, 6.72.

3.2.10. 1-(3-Chloro-4-fluorophenyl)-3,4-dimethylpyrrole (9e). Colorless crystals, mp: 38–40°C. IR (KBr) cm^{-1}: 3095, 2924, 2859, 1531, 1504, 1260, 1216, 1069, 1046. ^{1}H NMR ($CDCl_3$) δ 2.06 (6H, s, CH_3), 6.74 (2H, s, 2,5-H), 7.13–7.16 (2H, m, Ar), 7.33–7.36 (1H, m, Ar). ^{19}F NMR ($CDCl_3$) δ −121.22 (1F, m). MS: *m/z* (%) 225 (M^++2, 24), 224 (M^++1, 42), 223 (M^+, 73), 222 (M^+−1, 100), 208 (9), 131 (4), 129 (11), 67 (7). Anal. calcd for $C_{12}H_{11}ClFN$: C, 64.44; H, 4.96; N, 6.26. Found: C, 64.30; H, 5.12; N, 5.99.

3.2.11. 1-(2-Fluorophenyl)-3-methylpyrrole (8f). Colorless oil. IR (KBr) cm^{-1}: 3071, 2923, 1614, 1515, 1352, 1231. ^{1}H NMR ($CDCl_3$) δ 2.17 (3H, s, CH_3), 6.18–6.19 (1H, m, 4-H), 6.81–6.82 (1H, m, 5-H), 6.93–6.95 (1H, m, 2-H), 7.13–7.21 (3H, m, Ar), 7.31–7.37 (1H, m, Ar). ^{19}F NMR ($CDCl_3$) δ −125.19 (1F, m). MS: *m/z* (%) 176 (M^++1, 11), 175 (M^+, 85), 174 (M^+−1, 100), 95 (13), 53 (11). Anal. calcd for $C_{11}H_{10}FN$: C, 75.41; H, 5.75; N, 7.99. Found: C, 75.07; H, 5.63; N, 8.36.

3.2.12. 1-(2-Fluorophenyl)-3,4-dimethylpyrrole (9f). Colorless oil. IR (KBr) cm^{-1}: 3050, 2924, 1533, 1508, 1400, 1365, 1108, 1053. ^{1}H NMR ($CDCl_3$) δ 2.11 (6H, s, CH_3), 6.82 (2H, s, 2,5-H), 7.16–7.37 (4H, m, Ar). ^{19}F NMR ($CDCl_3$) δ −125.77 (1F, s). MS: *m/z* (%) 190 (M^++1, 11), 189 (M^+, 81), 188 (M^+−1, 100), 174 (12), 95 (14), 67 (9). Anal. calcd for $C_{12}H_{12}FN$: C, 76.17; H, 6.39; N, 7.40. Found: C, 76.00; H, 6.37; N, 7.73.

3.2.13. 1-[(5-Chloro-3-oxa-octafluoropentyl)sulfonyl]-pyrrole (11a). Colorless oil, bp: 76–78°C/266 Pa. IR (KBr) cm^{-1}: 3180, 1590, 1560, 1430, 1310, 1230–1140, 1060. ^{1}H NMR ($CDCl_3$) δ 6.30 (2H, m), 7.00 (2H, m). ^{19}F NMR ($CDCl_3$) δ −74.81 (2F, s, $ClCF_2$), −82.32 (2F, m, CF_2O), −87.34 (2F, m, OCF_2), −117.82 (2F, s, CF_2S). MS: *m/z* (%) 383 (M^++2, 31), 381 (M^+, 58), 137 (16), 135 (52), 130 (5), 116 (100), 114 (27), 87 (8), 85 (27), 66 (75). Anal. calcd for $C_8H_4ClF_8NO_3S$: C, 25.18; H, 1.06; N, 3.67; F, 39.83. Found: C, 25.42; H, 0.98; N, 4.07; F, 39.95.

Table 3. X-Ray data collection and processing parameters for compounds **5c** and **8a**

Compound	**5c** (CCDC 215664)	**8a** (CCDC 215665)
Formula	$C_{11}H_9F_4NOS$	$C_{11}H_6F_5N$
Size (mm)	0.51×0.26×0.24	0.22×0.31×0.27
Space group	*P*-1	*P*2 (1)/*C*
Crystal system	Triclinic	Monoclinic
a (Å)	5.960(0)	6.148(1)
b (Å)	9.612(1)	7.762(1)
c (Å)	10.822(1)	21.141(4)
α (°)	110.630(2)	90.00
β (°)	105.298(2)	94.70(3)
γ (°)	82.126(2)	90.00
V (Å^3)	559.08(12)	1005.5(3)
Z-value	2	4
D_{calc} (g cm^{-3})	1.659	1.633
μ (mm^{-1})	0.330	0.162
T (K)	293(2)	293(2)
2θ range (°)	4–56	4–55
Total reflections	3438	3340
F(000)	284	496
Independent reflections	2483	2294
R_{int}	0.0248	0.0339
$I>2\sigma(I)$	1954	1282
Parameters	199	157
Goodness of fit	0.953	1.014
Final *R* indices ($I>2\sigma(I)$)	0.0401; 0.0901	0.0541; 0.1380
R indices (all data)	0.0502; 0.0939	0.1043; 0.1684

3.2.14. 1-[(5-Iodo-3-oxa-octafluoropentyl)sulfonyl]-pyrrole (11b). Colorless oil. IR (KBr) cm^{-1}: 3153, 1463, 1422, 1336, 1296, 1196–1142, 1060. ^{1}H NMR ($CDCl_3$) δ 6.50 (2H, m), 7.20 (2H, m). ^{19}F NMR ($CDCl_3$) δ −65.25 (2F, m, ICF_2), −81.61 (2F, m, CF_2O), −85.52 (2F, m, OCF_2), −114.89 (2F, s, CF_2S). MS: *m/z* (%) 473 (M^+, 100), 227 (56), 177 (43), 116 (66), 114 (28), 66 (98). Anal. calcd for $C_8H_4F_8INO_3S$: C, 20.31; H, 0.85; N, 2.96. Found: C, 20.28; H, 0.99; N, 3.14.

3.3. X-Ray crystal structure data of compounds (5c) and (8a)

Intensity data were collected at 293(2) K on Bruker P4 diffractometer with graphite monochromator and Mo Kα radiation (λ=0.71073 Å). The structure was solved by direct methods and explained using Fourier techniques. The nonhydrogen atoms were refined anisotropically, hydrogen atoms were included but not refined. The final cycle of full matrix least-squares refinement was based on F^2, respectively. All calculations were performed using SHELXS-97 and SHELXL-97 programs. X-Ray data for compounds **5c** and **8a** are listed in Table 3.

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