S_NH reactions of 3-fluoronitroarenes with chloromethyl sulfone as the method for the construction of 6-fluoro-3-sulfonylindoles

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5-R-6-Fluoro-3-phenylsulfonylindoles were synthesized by the S_NH reaction of 3-fluoronitrobenzenes with chloromethyl phenyl sulfone in DMSO in the presence of KOH with subsequent reduction of the nitro group and intramolecular cyclization of imidates.

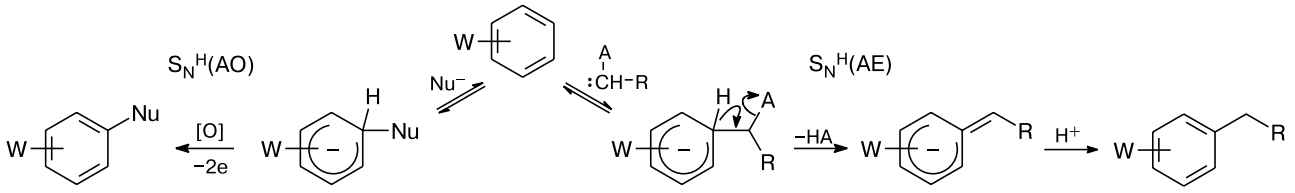
Key words: vicarious nucleophilic substitution of hydrogen, 3,4-difluoronitrobenzene, 4-R-3-fluoronitrobenzenes, 5-R-6-fluoro-3-phenylsulfonylindoles.

Nucleophilic substitution of hydrogen in aromatic systems is an efficient method for the functionalization of arenes and construction of fused heterosystems on their basis.[1] In contrast to the oxidative version of nucleophilic substitution of hydrogen, proceeding with participation of external oxidant according to the "addition—oxidation" scheme S_NH(AO), so called "vicarious" nucleophilic substitution[2—4] follows the "addition—elimination" scheme S_NH(AE) (Scheme 1). In this case, the role of the oxidant, which "removes" a pair of electrons from the intermediate σ^H-adduct, is played by an assisting group A, inserted into the intermediate, which leaves it as the anion. In case of nitroarenes, containing good leaving groups (for example, Cl or F), both versions of the S_NH reactions allow one to retain the halogen atoms, which opens great potentialities for further transformations.

Indole ring is a structural fragment of many drugs, widely used in medicine. Thus, 1-(*p*-chlorobenzoyl)-5-methoxy-2-methylindole-3-acetic acid ("Indometacin") is an active anti-inflammatory medicine,[5] alkaloids vinblastine and vincristine show anti-tumor (cytostatic) effect.[6] Ethyl 6-bromo-4-dimethylaminomethyl-5-hydroxy-1-methyl-(2-phenylthiomethyl)indole-3-carboxylate hydrochloride (medicine "Arbidol") has an inhibiting effect upon influenza viruses of the A and B types (see Ref. 7). Sulfonyl derivatives of indole also have various pharmacological properties. Suffice it to mention that succinate of [3-(2-dimethylamino)ethyl-1*H*-indol-5-yl]-*N*-methylmethanesulfonamide ("Sumatripan") is used for the migraine treatment,[5] *N*-arylsulfonylindolecarboxamides are effective toward the HIV-1 infection,[8] whereas *N*-aryl- and *N*-alkylindolyl sulfones have anti-tumor activity and are the modulators of $5HT_6$-receptors for the treatment of central nervous system diseases.[9—11] Among the fluoro-substituted *N*-sulfonylindoles, compounds having anti-asthmatic and anti-allergic properties are found.[12]

Methods for the synthesis of sulfonyl derivatives of indoles depend on the location of the substituent. Thus, *N*-sulfonylindoles are obtained by *N*-arylsulfonylation of 1*H*-indoles with arylsulfonyl chlorides,[9] 5-sulfonyl-substituted indoles, by the Fischer cyclization of 4-sulfonyl-

Scheme 1



W: electron-withdrawing group (NO_2, NO), **A**: assisting nucleophilic group (Cl, CN, OAr, SAr, *etc.*),
R: electron-withdrawing group (SO_2Ph, SPh, CN, *etc.*)

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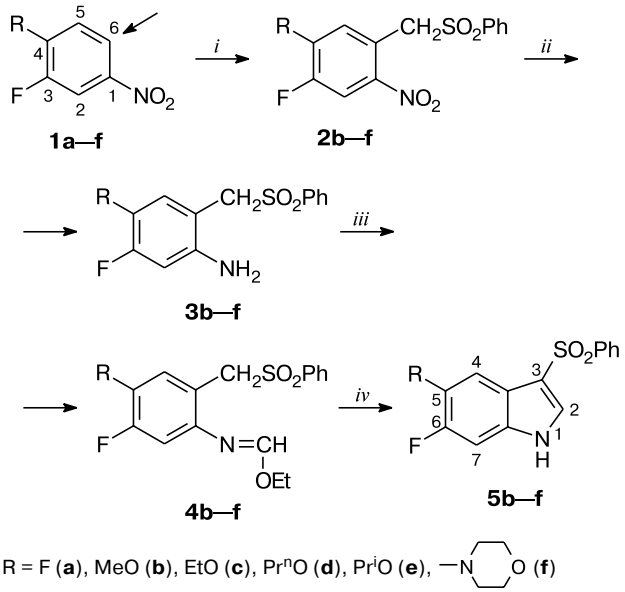
phenylhydrazines.[5] 3-Sulfonyl-1*H*-indole-2-carboxamides were synthesized by the oxidation of 3-arylthio-1*H*-indole-2-carboxamides with 3-chloroperbenzoic acid.[8] The synthesis of 3-sulfonyl-substituted indoles by the cyclization of *o*-substituted arylsulfonylmethylnitrobenzenes, obtained by the substitution of hydrogen in nitro derivatives of arenes upon treatment with vicarious nucleophiles, *viz.*, aryl chloromethyl sulfones,[13,14] is the most promising method. In the literature, there is no data on methods for the synthesis of fluoro-containing 3-sulfonylindoles.

Earlier, we showed that nucleophilic substitution of hydrogen (S_NH) in nitroarenes can be used for the synthesis of fluoro-containing 1,2,4-benzotriazines.[15] In the present work, a possibility of application of the S_NH methodology in nitroarenes as the key step in the synthesis of fluoro-containing 3-sulfonylindoles was studied. 3,4-Difluoronitrobenzene (**1a**) and 4-R-3-fluoronitrobenzenes **1b—f** were chosen as the subjects for the study (Scheme 2). 3,4-Difluoronitrobenzene (**1a**) was obtained by the nitration of *o*-difluorobenzene,[16] whereas 4-R-3-fluoronitrobenzenes **1b—f**, by the reaction of **1a** with the corresponding alcohols or morpholine.[15]

Scheme 2



R = F (**a**), MeO (**b**), EtO (**c**), Pr^nO (**d**), Pr^iO (**e**), —N O (**f**)

Reagents and conditions: *i.* $ClCH_2SO_2Ph$, KOH/DMSO; *ii.* Sn, MeOH, HCl; *iii.* $HC(OEt)_3/H^+$; *iv.* NaOH/DMSO.

Table 1. Reaction conditions, yields, melting points, elemental analysis and ^1H NMR spectroscopy (DMSO-d_6) data of 4-substituted 3-fluoro-6-(phenylsulfonylmethyl)nitrobenzenes **2b—f**

Compound	*T*/°C (τ/h)	Yield (%)	M.p. /°C (R_f)	Found / Calculated (%)			Molecular formula (M)	^1H NMR spectrum δ (*J*/Hz)
				C	H	N		
2b	25 (24)	64	184—185 (0.34)*	51.65 / 51.68	3.41 / 3.71	4.41 / 4.30	$C_{14}H_{12}FNO_5S$ (325.33)	3.80 (s, 3 H, MeO); 5.10 (s, 2 H, CH_2); 7.07 (d, 1 H, H(5), $^4J_{H,F}$ = 8.6); 7.63—7.59 (t, 2 H, Ph); 7.65—7.70 (m, 3 H, Ph); 7.78 (d, 1 H, H(2), $^3J_{H,F}$ = 10.1)
2c	25 (24)	71	132—133 (0.50)*	53.04 / 53.09	4.05 / 4.15	4.11 / 4.13	$C_{15}H_{14}FNO_5S$ (339.35)	1.39 (t, 3 H, MeCH$_2$O); 4.07 (q, 2 H, MeCH$_2$O); 5.10 (s, 2 H, CH_2); 7.09 (d, 1 H, H(5), $^4J_{H,F}$ = 8.2); 7.53—7.59 (t, 2 H, Ph); 7.65—7.73 (m, 3 H, Ph); 7.87 (d, 1 H, H(2), $^3J_{H,F}$ = 11.1)
2d	25 (7)	64	151—152 (0.60)*	54.05 / 54.39	4.31 / 4.56	3.83 / 3.96	$C_{16}H_{16}FNO_5S$ (353.31)	1.02 (t, 3 H, Me(CH$_2$)$_2$O); 1.78, 3.94 (both m, 2 H each, Me(CH$_2$)$_2$O); 5.10 (s, 2 H, CH_2); 7.08 (d, 1 H, H(5), $^4J_{H,F}$ = 8.3); 7.54—7.60 (t, 2 H, Ph); 7.66—7.70 (m, 3 H, Ph); 7.88 (d, 1 H, H(2), $^3J_{H,F}$ = 11.1)
2e	25 (24)	60	106—107 (0.62)*	54.43 / 54.39	4.42 / 4.56	3.89 / 3.96	$C_{16}H_{16}FNO_5S$ (353.31)	1.28, 1.31 (both s, 3 H each, Me$_2$CHO); 4.58 (m, 1 H, Me$_2$CHO); 5.10 (s, 2 H, CH_2); 7.11 (d, 1 H, H(5), $^4J_{H,F}$ = 8.2); 7.52—7.58 (t, 2 H, Ph); 7.64—7.71 (m, 3 H, Ph); 7.8 (d, 1 H, H(2), $^3J_{H,F}$ = 11.3)
2f	25 (3)	70	171—172 (0.88)**	50.54 / 50.60	4.09 / 4.24	6.69 / 6.90	$C_{17}H_{17}FN_2O_5S$ (380.39)	3.11 (m, 4 H, N(CH$_2$)$_2$); 3.72 (m, 4 H, O(CH$_2$)$_2$); 5.09 (s, 2 H, CH_2); 6.76 (d, 1 H, H(5), $^4J_{H,F}$ = 8.8); 7.54—7.60 (t, 2 H, Ph); 7.64—7.71 (m, 3 H, Ph); 7.8 (d, 1 H, H(2), $^3J_{H,F}$ = 13.4)

* Eluent: dichloromethane.

** Eluent: ethyl acetate.

It was found that the reaction of 4-R-3-fluoronitrobenzenes **1b—f** with chloromethyl phenyl sulfone, proceeding in DMSO in the presence of KOH at room temperature, leads to the selective substitution of the H(6) hydrogen atom in *o*-position to nitro group and is finished by the formation of 4-R-3-fluoro-6-(phenylsulfonylmethyl)nitrobenzenes **2b—f** in 60—71% yield (Table 1). The similar reaction of 3,4-difluoronitrobenzene (**1a**) with chloromethyl phenyl sulfone is complicated by the hydrolysis of the C—F bond in *p*-position to the nitro group and the product of vicarious substitution of hydrogen was not isolated in this case. The structures of the synthesized compounds **2b—f** were established on the basis of ^{1}H NMR spectra, elemental analysis data, and mass spectra. The assignments of signals of fluorine atoms in the products formed were made by the analysis of the $^nJ_{H,F}$ spin-spin coupling constant values. In the ^{1}H NMR spectra of compounds **2b—f**, signals of the H(5) protons in the region δ 7.0—7.8 and H(2) protons in the region δ 7.8—7.9 as characteristic doublets with constant values on the fluorine atoms $^4J_{H(5),F(3)}$ = 8.2—8.8 Hz and $^3J_{H(2),F(3)}$ = 10.1—11.4 Hz were observed (see Table 1). The reduction of the nitro group in compounds **2b—f** was performed by metal tin in methanol with hydrochloric acid for 3—7 h, resulting in the corresponding amino-substituted sulfones **3b—f** in 59—71% yield (Table 2). Amines **3b—f** were converted to the corresponding imidates **4b—f** in 54—85% yield by the reflux in triethyl orthoformate in the presence of catalytic amount of acetic acid (Table 3). In the ^{1}H NMR spectra of imidates **4b—f**, the singlet signals of the methyne protons are observed in the region 7.1—7.3 ppm. The base-catalyzed intramolecular cyclization of imidates **4b—f** proceeds under mild conditions at room temperature for 3—4 h to form fluoro-containing 3-sulfonylindoles **5b—f** in 70—80% yield (Table 4). In the ^{1}H NMR spectra of compounds **5b—f**, signals of the H(4) protons (δ 7.30—7.32) and H(7) protons (δ 7.21—7.25) as the doublets with constant values on the fluorine atoms $^4J_{H(4),F(6)}$ = 7.5—8.3 Hz and $^3J_{H(7),F(6)}$ = 10.8—12.3 Hz were observed (see Table 4). Signals of the H(2) methyne protons of the indole ring are in the region 7.48—7.55 ppm, whereas signals of the NH protons resonate as the broad singlet in the region 11.99—12.65 ppm.

Table 2. Reaction conditions, yields, melting points, elemental analysis and ^{1}H NMR spectroscopy (DMSO-d_6) data of 4-substituted 3-fluoro-6-(phenylsulfonylmethyl)anilines **3b—f**

Compound	*T*/°C (τ/h)	Yield (%)	M.p. /°C (R_f)*	Found / Calculated (%)			Molecular formula (M)	^{1}H NMR spectrum δ (*J*/Hz)
				C	H	N		
3b	60—62	71	256—257	56.86 56.93	4.63 4.77	4.69 4.74	$C_{14}H_{14}FNO_3S$ (295.34)	3.52 (s, 3 H, MeO); 4.42 (s, 2 H, CH_2); 4.79 (br.s, 2 H, NH_2); 6.40 (d, 1 H, H(5), $^4J_{H,F}$ = 9.4); 6.50 (d, 1 H, H(2), $^3J_{H,F}$ = 13.6); 7.54—7.60 (t, 2 H, Ph); 7.66—7.79 (m, 3 H, Ph)
3c	60—62 (3)	59	115—116 (0.28)	58.19 58.23	5.17 5.21	4.42 4.52	$C_{15}H_{16}FNO_3S$ (309.37)	1.22 (t, 3 H, $\underline{Me}CH_2O$); 3.71 (q, 2 H, $Me\underline{CH_2}O$); 4.38 (s, 2 H, CH_2); 4.76 (br.s, 2 H, NH_2); 6.40 (d, 1 H, H(5), $^4J_{H,F}$ = 9.0); 6.47 (d, 1 H, H(2), $^3J_{H,F}$ = 13.4); 7.52—7.58 (t, 2 H, Ph); 7.64—7.78 (m, 3 H, Ph)
3d	60—62 (3)	66	84—85 (0.60)	59.27 59.42	5.64 5.60	4.17 4.33	$C_{16}H_{18}FNO_3S$ (323.39)	0.96 (t, 3 H, $\underline{Me}CH_2CH_2O$); 1.62 (q, 2 H, $Me\underline{CH_2}CH_2O$); 3.60 (t, $MeCH_2\underline{CH_2}O$); 3.64 (br.s, 2 H, NH_2); 4.38 (s, 2 H, CH_2); 6.38 (d, 1 H, H(5), $^4J_{H,F}$ = 9.1); 6.48 (d, 1 H, H(2), $^3J_{H,F}$ = 13.1); 7.52—7.58 (t, 2 H, Ph); 7.64—7.78 (m, 3 H, Ph)
3e	60—62 (3)	63	126—127 (0.62)	59.30 59.42	5.52 5.60	4.21 4.33	$C_{16}H_{18}FNO_3S$ (323.39)	1.07, 1.13 (both s, 3 H each, $\underline{Me_2}CHO$); 3.99 (m, 1 H, $Me_2\underline{CH}O$); 4.39 (s, 2 H, CH_2); 4.80 (br.s, 2 H, NH_2); 6.40 (d, 1 H, H(5), $^4J_{H,F}$ = 9.4), 6.46 (d, 1 H, H(2), $^3J_{H,F}$ = 13.2); 7.50—7.51 (t, 2 H, Ph); 7.53—7.78 (m, 3 H, Ph)
3f	60—62 (7)	59	185—186 (0.77)	58.27 58.38	5.46 5.30	7.09 7.03	$C_{17}H_{19}FN_2O_3S$ (350.41)	2.62 (m, 4 H, $N(CH_2)_2$); 3.63 (m, 4 H, $O(CH_2)_2$); 4.34 (br.s, 2 H, NH_2); 4.36 (s, 2 H, CH_2); 6.22 (d, 1 H, H(5), $^4J_{H,F}$ = 9.4); 6.44 (d, 1 H, H(2), $^3J_{H,F}$ = 14.4); 7.50—7.56 (t, 2 H, Ph); 7.63—7.74 (m, 3 H, Ph)

* Eluent: ethyl acetate.

Table 3. Reaction conditions, yields, melting points, elemental analysis and ^{1}H NMR spectroscopy (DMSO-d_6) data of 4-substituted *N*-ethoxymethylene-3-fluoro-6-(phenylsulfonylmethyl)anilines **4b—f**

Compound	*T*/°C (τ/h)	Yield (%)	M.p. /°C (R_f)*	Found / Calculated (%)			Molecular formula (M)	^{1}H NMR spectrum δ (*J*/Hz)
				C	H	N		
4b	145—146 (7)	53	96—98 (0.80)	56.86 56.93	4.63 4.77	4.69 4.74	$C_{17}H_{18}FNO_4S$ (351.14)	1.29 (t, 3 H, MeCH$_2$O); 4.08 (q, 2 H, MeCH$_2$O); 3.79 (s, MeO); 4.50 (s, 2H, CH$_2$); 6.69 (d, 1 H, H(2), $^3J_{H,F}$ = 12.4); 6.97 (d, 1 H, H(5), $^4J_{H,F}$ = 8.9); 7.24 (s, 1 H, CH); 7.45—7.55 (t, 2 H, Ph); 7.61—7.64 (m, 3 H, Ph)
4c	145—146 (3)	85	132—133 (0.70)	59.08 59.16	5.54 5.51	3.78 3.83	$C_{18}H_{20}FNO_4S$ (365.43)	1.28 (t, 3 H, MeCH$_2$O); 4.01 (q, 2 H, MeCH$_2$O); 1.39 (t, 3 H, MeCH$_2$O); 4.06 (q, 2 H, MeCH$_2$O); 4.47 (s, 2 H, CH$_2$); 6.64 (d, 1 H, H(2), $^3J_{H,F}$ =12.3); 6.97 (d, 1 H, H(5), $^4J_{H,F}$ = 9.3); 7.19 (s, 1 H, CH); 7.43—7.51 (t, 2 H, Ph); 7.59—7.65 (m, 3 H, Ph)
4d	145—146 (7)	65	68—69 (0.86)	59.82 60.14	5.72 5.84	3.63 3.69	$C_{19}H_{22}FNO_4S$ (379.45)	1.04 (t, 3 H, MeCH$_2$CH$_2$O); 1.79 (m, 2 H, MeCH$_2$CH$_2$O); 3.91 (t, 3 H, MeCH$_2$CH$_2$O); 1.29 (t, 3 H, MeCH$_2$O); 4.07 (q, 2 H, MeCH$_2$O); 4.49 (s, 2 H, CH$_2$); 6.66 (d, 1 H, H(2), $^3J_{H,F}$ = 11.9); 6.97 (d, 1 H, H(5), $^4J_{H,F}$ = 8.9); 7.22 (s, 1 H, CH); 7.48—7.52 (t, 2 H, Ph); 7.55—7.63 (m, 3 H, Ph)
4e	145—146 (7)	63	104—105 (0.39)	60.28 60.14	5.63 5.84	3.85 3.69	$C_{19}H_{22}FNO_4S$ (379.45)	1.25, 1.29 (both t, 3 H each, Me$_2$CHO); 4.43 (m, 1 H, Me$_2$CHO); 1.31 (t, 3 H, MeCH$_2$O); 4.05 (q, 2 H, MeCH$_2$O); 4.49 (s, 2 H, CH$_2$); 6.65 (d, 1 H, H(2), $^3J_{H,F}$ = 12.2), 7.01 (d, 1 H, H(5), $^4J_{H,F}$ = 8.8); 7.24 (s, 1 H, CH); 7.44—7.54 (t, 2 H, Ph); 7.60—7.63 (m, 3 H, Ph)
4f	145—146 (7)	54	132—133 (0.39)	58.27 58.38	5.46 5.30	7.99 7.03	$C_{20}H_{23}FN_2O_4S$ (406.47)	1.29 (t, 3 H, MeCH$_2$O); 4.09 (q, 2 H, MeCH$_2$O); 2.91 (m, 4 H, N(CH$_2$)$_2$); 3.73 (m, 4 H, O(CH$_2$)$_2$); 4.46 (s, 2 H, CH$_2$); 6.60 (d, 1 H, H(2), $^3J_{H,F}$ =13.2); 6.80 (d, 1 H, H(5), $^4J_{H,F}$ = 9.2); 7.26 (s, 1 H, CH); 7.43—7.49 (t, 2 H, Ph); 7.51—7.63 (m, 3 H, Ph)

* Eluent: ethyl acetate—dichloromethane (1 : 8).

In conclusion, in the present work, the reactions of nucleophilic substitution of hydrogen by vicarious reagent, chloromethyl phenyl sulfone, in the series of fluoro-containing nitroarenes, as well as the synthesis of earlier unknown fluoro-containing 3-phenylsulfonylindoles were accomplished for the first time.

Experimental

^{1}H NMR spectra were recorded on a Bruker WP-250 and Bruker DRX-400 spectrometers (250.13 and 400.13 MHz), Me_4Si was used as the internal standard. Mass spectra were recorded on a Varian MAT-311A instrument, conditions of the recording: accelerating voltage, 3 kV; energy of the ionizing ions, 70 eV; direct inlet of a sample into the source of electrons. Reaction course and purity of the compounds synthesized were monitored by TLC on Silufol UV-254 plates in dichloromethane, ethyl acetate, and in ethyl acetate—dichloromethane (1 : 8). Characteristics of the compounds synthesized are given in Tables 1—4.

Synthesis of 4-R-3-fluoro-6-(phenylsulfonylmethyl)nitrobenzenes 2b—f (general procedure). Potassium hydroxide (9.4 mmol) was added to a stirred solution of 4-R-3-fluoronitrobenzene **1b—f** (1.32 mmol) and chloromethyl phenyl sulfone (1.32 mmol) in DMSO (5 mL). The reaction mixture was stirred at room temperature for 3—24 h, then, acidified with 10% aqueous HCl to pH 3—4. The precipitate formed was filtered off and recrystallized from ethanol.

Synthesis of 4-substituted 3-fluoro-6-(phenylsulfonylmethyl)anilines 3b—f (general procedure). Tin (4.2 mmol) was added to a suspension of 4-substituted 3-fluoro-6-(phenylsulfonylmethyl)nitrobenzene **2b—f** (0.84 mmol) in methanol (3 mL) and concentrated hydrochloric acid (3 mL). The reaction mixture was refluxed for 3—7 h, then, made basic with 10% aq. NaOH to pH 8—9. The precipitate formed was filtered off and recrystallized from ethanol.

Synthesis of 4-substituted *N*-ethoxymethylene-3-fluoro-6-(phenylsulfonylmethyl)anilines 4b—f (general procedure). Acetic

Table 4. Reaction conditions, yields, melting points, elemental analysis, mass and ^{1}H NMR spectroscopy (DMSO-d_6) data of 5-substituted 6-fluoro-3-phenylsulfonylindoles **5b—f**

Compound	*T*/°C (τ/h)	Yield (%)	M.p./°C (R_f)*	Found / Calculated (%)			Molecular formula (M)	MS *m/z* (I_{rel} (%))	^{1}H NMR spectrum δ (*J*/Hz)
				C	H	N			
5b	25 (3)	41	134—135 (0.58)	58.80 / 59.03	3.97 / 3.96	4.59 / 4.59	$C_{15}H_{12}FNO_3S$ (305.17)	305 $[M]^+$ (100), 290 $[M]^+$ (1.76), 228 $[M]^+$ (1.89), 164 $[M]^+$ (13.26)	3.91 (s, 3 H, MeO); 7.25 (d, 1 H, H(7), $^3J_{H,F}$ = 11.5); 7.33 (d, 1 H, H(4), $^4J_{H,F}$ = 8.2); 7.51 (s, 1 H, CH); (7.54—7.55 (t, 2 H, Ph); 7.94—7.97 (m, 3 H, Ph); 12.02 (br.s, 1 H, NH)
5c	25 (3)	82	256—257 (0.58)	58.67 / 60.18	4.28 / 4.42	4.29 / 4.38	$C_{16}H_{14}FNO_3S$ (319.29)	319 $[M]^+$ (100), 290 $[M]^+$ (5.94), 242 $[M]^+$ (2.13), 178 $[M]^+$ (4.59)	1.43 (t, 3 H, $\underline{Me}CH_2O$); 4.11 (q, 2 H, $MeCH_2O$); 7.22 (d, 1 H, H(7), $^3J_{H,F}$ = 10.8); 7.30 (d, 1 H, H(4), $^4J_{H,F}$ = 8.1); 7.48 (s, 1 H, CH); 7.49—7.51 (m, 2 H, Ph); 7.91—7.94 (m, 3 H, Ph); 12.65 (br.s, 1 H, NH)
5d	25 (5)	50	214—215 (0.52)	61.53 / 61.25	5.03 / 4.83	4.34 / 4.20	$C_{17}H_{16}FNO_3S$ (333.39)	333 $[M]^+$ (41.6), 291 $[M + 1]^+$ (100), 214 $[M]^+$ (5.80), 150 $[M]^+$ (27.01)	1.09 (t, 3 H, $\underline{Me}CH_2CH_2O$); 1.83, 4.03 (both t, 2 H each, Me $(\underline{CH_2})_2O$); 7.24 (d, 1 H, H(7), $^3J_{H,F}$ = 10.8); 7.31 (d, 1 H, H(4), $^4J_{H,F}$ = 8.2); 7.52 (s, 1 H, CH); 7.54 (t, 2 H, Ph); 7.93—7.97 (m, 3 H, Ph); 12.65 (br.s, 1 H, NH)
5e	25 (3.5)	52	156—157 (0.70)	59.99 / 61.25	4.88 / 4.83	3.98 / 4.20	$C_{17}H_{16}FNO_3S$ (333.39)	333 $[M]^+$(16.41), 291 $[M]^+$ (100), 214 $[M]^+$ (4.73), 150 $[M]^+$ (19.96)	1.24, 1.34 (both t, 3 H each, $\underline{Me}_2CHO$); 4.54 (m, 1 H, $Me_2\underline{CH}O$); 7.23 (d, 1 H, H(7), $^3J_{H,F}$ = 11.1), 7.31 (d, 1 H, H(4), $^4J_{H,F}$ = 7.5); 7.49 (s, 1 H, CH); 7.53—7.55 (t, 2 H, Ph); 7.93—7.97 (m, 3 H, Ph)
5f	25 (4)	75	275 (0.21)	60.06 / 59.98	4.47 / 4.75	7.46 / 7.77	$C_{18}H_{17}FN_2O_3S$ (360.40)	360 $[M]^+$ (89.45), 345 $[M + 1]^+$ (1.29), 219 $[M]^+$ (3.31)	3.01 (m, 4 H, $N(CH_2)_2$); 3.76 (m, 4 H, $O(CH_2)_2$); 7.20 (d, 1 H, H(7), $^3J_{H,F}$ = 12.3); 7.32 (d, 1 H, H(4), $^4J_{H,F}$ = 8.3); 7.55 (s, 1 H, CH); 7.56—7.60 (m, 2 H, Ph); 7.94—7.96 (m, 3 H, Ph); 11.99 (br.s, 1 H, NH)

* Eluent: ethyl acetate—dichloromethane (1 : 8).

acid (few drops) was added to a solution of 4-substituted 3-fluoro-6-(phenylsulfonylmethyl)aniline **3b—f** (0.3 mmol) in triethyl orthoformate (4 mL). The reaction mixture was refluxed for 7 h and cooled, hexane (5 mL) was added, the precipitate formed was filtered off and recrystallized from hexane—ethyl acetate (3 : 1).

Synthesis of 5-substituted 6-fluoro-3-phenylsulfonylindoles 5b—f (general procedure). Finely powdered NaOH (0.08 g, 2 mmol) was added to a solution of 4-substituted *N*-ethoxymethylene-3-fluoro-6-(phenylsulfonylmethyl)aniline **4b—f** (0.4 mmol) in DMSO (4 mL). The reaction mixture was stirred at room temperature for 3—4 h, then, neutralized with 10% aq. NH_4Cl. The precipitate was filtered off and recrystallized from ethanol—ethyl acetate (2 : 1).

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