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SHORT COMMUNICATIONS

Reaction of 1*H*,1*H*,ω*H*-Perfluoroalkyl Sulfones with α-Phenylglycine Methyl Ester

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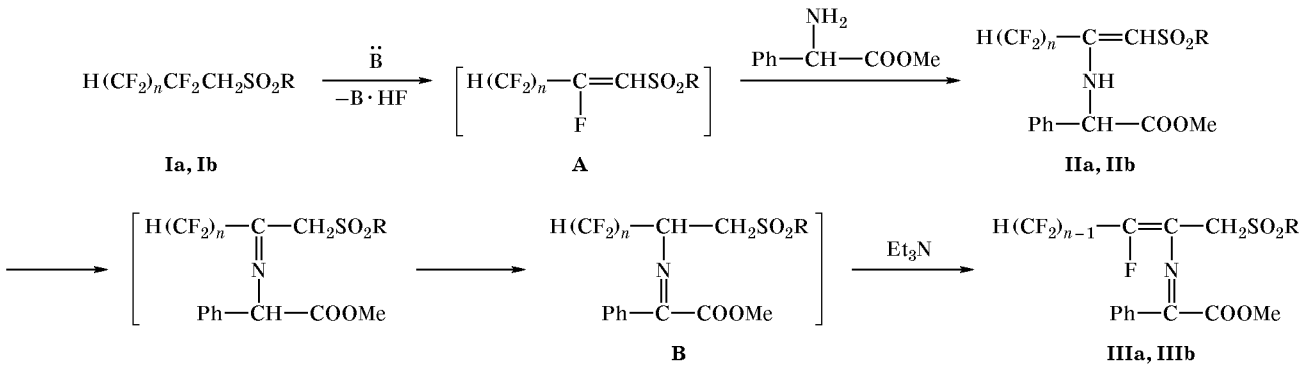
We previously reported on some properties of 1*H*,1*H*,ω*H*-perfluoroalkyl sulfones **I** which are new synthons used in the preparation of fluorinated enamines and ketones [1], pyrazoles [2], and triazoles [3]. The present communication describes reactions of **I** with phenylglycine methyl ester on heating in benzene in the presence or even in the absence of triethylamine. The first stage of the reaction is dehydrofluorination to vinyl fluorides **A** which undergo further transformations (Scheme 1). Monitoring of the reaction course by ^{19}F NMR spectroscopy showed that the rate of these transformations and the structure of final products are determined by two factors: the length of the carbon chain in the polyfluoroalkyl substituent and the presence or absence of triethylamine in the reaction mixture. The reaction of sulfone **Ia** with 3 equiv of phenylglycine methyl ester (which also acts as a dehydrofluorinating agent) leads to formation of enamine **IIa** as a mixture of *cis* and *trans* isomers. When the reaction was carried in the presence of a stronger base, triethylamine, and the reaction time was increased, a series of prototropic isomerizations of compound **IIa** occurred to give fluoroolefin **IIIa** (via elimination of HF in the final stage). Initially, in the ^{19}F NMR spectrum of the reaction mixture signals from the CF_2 group appeared as an *AB* system at δ –125.7 ppm, $^2J_{F,H}$ = 55.8, $^3J_{F,H}$ = 13.0, J_{AB} = 280.8 Hz, which may be assigned to intermediate **B** having an asymmetric carbon atom which is linked to CF_2H group. After 48 h, these signals disappeared from the spectrum, and only those belonging to product **IIIa** were observed.

In the reaction of sulfone **Ib** with phenylglycine methyl ester compound **IIIb** is formed even in the absence of triethylamine. The optimal reactant ratio sulfone **Ib**:phenylglycine methyl ester was 1:4. In this case, the yield of **IIIb** was 90%. We failed to isolate intermediate enamine **IIb**, for it very readily undergoes dehydrofluorination.

Compound **IIIb** is readily hydrolyzed on addition of water or during chromatographic purification on

Scheme 1.



B = Et_3N, $PhCH(NH_2)COOMe$; n = 1 (**a**), 3 (**b**); R = $PhCH_2$.

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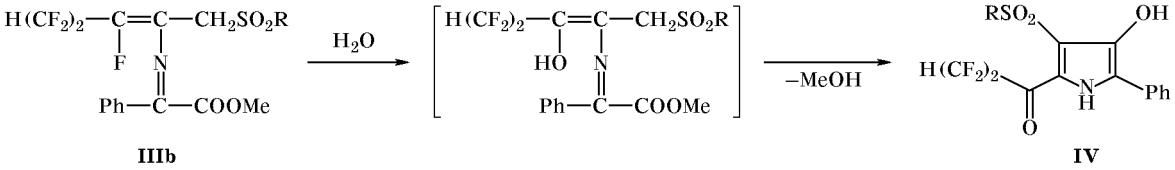
Scheme 2.



R = $PhCH_2$.

silica gel. The hydrolysis is accompanied by cyclization to 2-polyfluoroacylpyrrole **IV** (Scheme 2). It should be noted that the heterocyclization is necessarily preceded by hydrolysis, for fluoroolefin **IIIa** is not hydrolyzed under analogous conditions, and no heterocyclization occurs.

Methyl (1-benzylsulfonyl-2-difluoromethylvinylamino)phenylacetate (IIa). A solution of 6 mmol of phenylglycine methyl ester in 5 ml of benzene was added to a suspension of 2 mmol of sulfone **Ia** in 15 ml of benzene, and the mixture was heated for 1 h at 70°C. The solution was washed with water, dried over Na_2SO_4, and evaporated. The residue was treated with hexane to isolate 87% of enamine **IIa** as a mixture of isomers at a ratio of 4:1. The major isomer was isolated by slow recrystallization of the isomer mixture from hexane. ^{1}H NMR spectrum, δ, ppm: 3.74 s (3H, OCH_3), 4.03 (2H, CH_2, *AB* system, J_{AB} = 13.8 Hz), 4.60 s (1H, CH=), 4.77 d (1H, C**H**NH, $^3J_{H,H}$ = 5.4 Hz), 6.30 br.s (1H, NH), 6.71 t (1H, HCF_2, $^2J_{H,F}$ = 53.6 Hz), 6.96 m (2H, H_{arom}) 7.20–7.38 m (5H, H_{arom}), 7.41–7.48 m (3H, H_{arom}). ^{19}F NMR spectrum, δ_F, ppm: δ_A –121.34 and δ_B –121.99, *AB* system (2F, HCF_2, J_{AB} = 306.8, $^2J_{H,F}$ = 53.6 Hz). Found, %: N 3.47; S 8.21. $C_{19}H_{19}F_2NO_4S$. Calculated, %: N 3.54; S 8.11. Minor isomer: ^{19}F NMR spectrum, δ_F, ppm: δ_A –116.82 and δ_B –119.30, *AB* system (2F, HCF_2, J_{AB} = 304.5, $^2J_{H,F}$ = 54.2 Hz).

Methyl (1-benzylsulfonylmethyl-2-fluorovinylamino)phenylacetate (IIIa) was synthesized by a similar procedure from 2 mmol of sulfone **Ia**, 1 mmol of phenylglycine methyl ester, and 3 mmol of triethylamine (reaction time 48 h). The mixture was evaporated, and the residue was recrystallized from hexane. Yield 52%. mp 88–89°C. ^{1}H NMR spectrum, δ, ppm: 3.97 s (3H, OCH_3), 3.98 m (2H, CH_2), 4.04 s (2H, CH_2Ph), 6.82 d (1H, HCF, $J_{H,F}$ = 79.5 Hz), 6.96 d (2H, H_{arom}), 7.30–7.42 m (5H, H_{arom}), 7.43–7.60 m (3H, H_{arom}), 7.81 m (2H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 51.05 s (OCH_3); 52.70 s (CH_2); 60.08 s (CH_2Ph); 127.82, 127.95, 128.53, 129.03, 129.11, 129.16, 131.15, 132.75, 132.86 s (C_{arom}, =C–N); 140.94 d (=CF, $J_{C,F}$ = 269.4 Hz); 161.32 d (C=N, $^4J_{C,F}$ = 2.9 Hz); 165.04 s (C=O). ^{19}F NMR spectrum, δ_F, ppm: –142.57 d (2F, HCF, $^2J_{H,F}$ = 79.5 Hz). Found, %: N 3.68; S 8.62. $C_{19}H_{18}FNO_4S$. Calculated, %: N 3.73; S 8.54.

Methyl (1-benzylsulfonylmethyl-2,3,3,4,4-pentafluoro-1-butenylamino)phenylacetate (IIIb) was synthesized as described above for compound **IIa** from 2 mmol of sulfone **Ib** and 8 mmol of phenylglycine methyl ester (reaction time 1 h). The solution was evaporated, and the residue was reprecipitated with pentane from carbon tetrachloride. Red–orange oily liquid. Yield 90%. ^{1}H NMR spectrum, δ, ppm: 3.91 s (3H, OCH_3), 4.01 m (2H, CH_2), 4.42 s (2H, CH_2Ph), 5.97 t.t (1H, HCF_2, $^2J_{H,F}$ = 50.1, $^3J_{H,F}$ = 5.2 Hz), 7.20–7.30 m (5H, H_{arom}), 7.51 t (2H, H_{arom}), 7.61 t (1H, H_{arom}), 7.83 d (2H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 52.61 s (OCH_3); 53.18 s (CH_2); 60.15 s (CH_2Ph); 108.78 t.t (HCF_2, $J_{C,F}$ = 253.1, $^2J_{C,F}$ = 36.7 Hz); 111.65 t.m (HCF_2CF_2, $J_{C,F}$ = 253.2 Hz); 127.24, 128.78, 128.85, 128.97, 130.71, 130.85, 131.01, 132.52, 133.21 s (C_{arom}, =C–N); 135.70 d.t (=CF, $J_{C,F}$ = 251.2, $J_{C,F}$ = 30.4 Hz); 162.83 s (C=O); 163.86 d.m (C=N, $J_{C,F}$ = 2.7 Hz). ^{19}F NMR spectrum, δ_F, ppm: –118.51 m (2F, CF_2), –136.92 d.m (2F, HCF_2, $^2J_{H,F}$ = 50.1 Hz), –146.62 m (1F, F–C=). Mass spectrum, *m*/*z* (I_{rel}, %): 475 (2) $[M]^+$, 320 (29) $[M - PhCH_2SO_2]^+$, 91 (100) $[PhCH_2]^+$. Found, %: N 2.86; S 6.90. *M* 475. $C_{21}H_{18}F_5NO_4S$. Calculated, %: N 2.95; S 6.74. *M* 475.44.

3-Benzylsulfonyl-4-hydroxy-5-phenyl-2-(2,2,3,3-tetrafluoropropionyl-1*H*-pyrrole (IV). *a*. Water, 10 ml, was added to 0.15 g of compound **IIIb**, and the mixture was left to stand at room temperature until it solidified (~4 days). The precipitate was filtered off, dried, and recrystallized from pentane–ether (7:3). Yield 0.08 g (57%).

b. Compound **IIIb**, 0.35 g, was subjected to column chromatography on silica gel using methanol–chloroform (2:8) as eluent. Yield 0.2 g (62%). mp 140–142°C. ^{1}H NMR spectrum, δ, ppm: 4.84 s (2H, CH_2Ph), 6.35 t.t (1H, HCF_2, $^2J_{H,F}$ = 52.5, $^3J_{H,F}$ = 5.4 Hz), 7.28–7.34 m (5H, H_{arom}), 7.38–

7.52 m (3H, H_{arom}), 7.66 m (2H, H_{arom}), 8.69 s (1H, NH), 9.56 br.s (1H, OH). ^{13}C NMR spectrum, δ_C, ppm: 61.77 s (CH_2Ph); 108.95 t.t (HCF_2, $J_{C,F}$ = 252.0, $^2J_{C,F}$ = 31.3 Hz); 111.60 t.t (HCF_2CF_2, $J_{C,F}$ = 263.0, $^2J_{C,F}$ = 28.0 Hz); 113.95, 120.16, 124.83, 125.91, 127.35, 127.54, 128.95, 129.33, 129.45, 129.70, 130.94, 147.09 s (C_{arom}); 171.33 t (C=O, $^2J_{C,F}$ = 26.4 Hz). ^{19}F NMR spectrum, δ_F, ppm: –120.38 m (2F, CF_2), –139.53 d.m (2F, HCF_2, $^2J_{H,F}$ = 52.5 Hz). Mass spectrum, *m*/*z* (I_{rel}, %): 441 (16) $[M]^+$, 333 (30), 91 (100) $[PhCH_2]^+$. Found, %: N 3.15; S 7.30. *M* 441. $C_{20}H_{15}F_4NO_4S$. Calculated, %: N 3.17; S 7.26. *M* 441.40.

The ^1H, ^{13}C (solvent $CDCl_3$) and ^{19}F NMR spectra (benzene) were recorded on a Varian VXR-300 spectrometer at 299.9, 75.4, and 282.2 MHz, respectively. The ^1H and ^{13}C chemical shifts were measured relative to the solvent signals ($CDCl_3$, δ 7.26, δ_C 77.16 ppm), and ^{19}F chemical shifts were measured relative to hexafluorobenzene (δ_F –162.9 ppm) as internal reference. The mass spectra were run on an MKh-1321 instrument.

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