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Synthesis of 3-*F*-alkyl-2-methoxy-3-phenylthiopropenals

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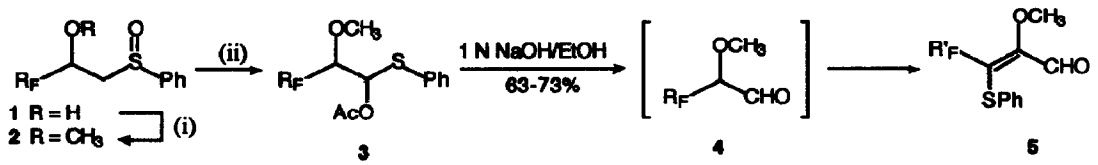
Abstract: *The synthesis of 3-F-alkyl-2-methoxy-3-phenylthiopropenals has been realised by basic hydrolysis of acetylated sulfides of the type R_F-CH(OCH$_3$)-CH(OAc)-S-Ph. A reaction suite is proposed to explain the formation of these aldehydes which may prove useful precursors in synthesis of F-alkylated heterocyclic compounds.*

Polyfluorinated aldehydes may be prepared by several reactions.[1-4] Synthesis of the polyfluorinated α,β-unsaturated aldehydes are much less reported.[5,6] In this work, a convenient route to 3-*F*-alkyl-2-methoxy-3-phenylthiopropenals, described for the first time is given. The basic hydrolysis of the simple acetoxylated sulfides, obtained from homologous sulfoxides via Pummerer reaction, is a good way for aldehydes synthesis.[7-9] When the same process is applied to *F*-alkylated sulfoxides **2** (protected form of **1**), the corresponding acetoxylated sulfides **3** are obtained[10] but, as shown in scheme 1, the basic hydrolysis[11] of the latters yields unsatured aldehydes **5** instead of the homologous satureted ones **4** (table 1).



(i) CH_3I/Ag_2O/DMF, r. t. 6 h, (83-92%); (ii) Ac_2O/NaOAc/DMF, (89-94%).

Scheme 1

Table 1: Compounds **5a-c** prepared

3	R_F	5	R'_F	Yield[a] (%)	bp (°C/Torr)	Ratio[b] (E/Z)
a	C_4F_9	**a**	C_3F_7	63	55/0.8	81/19
b	C_6F_{13}	**b**	C_5F_{11}	71	71/0.4	82/18
c	C_8F_{17}	**c**	C_7F_{15}	73	111/0.5	68/32

[a]Yield of isolated product; [b]based on ^1H and ^{19}F NMR.

The structures of synthesized compounds are determined from the spectroscopic and elemental analysis data.[12]

In this series, the observed hydrogen fluoride elimination with a fluorine atom belonging to an *F*-alkyl substituent has been reported for the aldehydes R_F-CH_2-CHO.[6]

Compounds **5** are obtained as (*E*/*Z*)-isomeric mixtures for which attempt of column chromatography separation have failed.

Stereochemical assignment of isomers is based on: (i) chemical shift of 1-CF_2 which is deshielded when aldehyde function and *F*-alkyl group are on the same side of the unsaturation (minor (*Z*)-isomer) and shielded ($|\Delta\delta| \approx 8$ ppm) for the other case[13,14] (major (*E*)-isomer), (ii) chemical shift of the methoxy group which is more shielded ($|\Delta\delta| = 0.43$ ppm) for the (*Z*)-isomer (magnetic anisotropy effect of aromatic ring[15]), (iii) multiplicity of the aldehydic proton signal which appears as a singlet for (*E*)-isomer and as a triplet for (*Z*)-isomer which allows the required spacial proximity for long-range fluorine-proton coupling (J = 2 Hz) between 1-CF_2 fluorines and formyl proton.[16]

The ratios of these isomers are estimated either by ^{19}F and ^{1}H NMR on the base of the integrated intensities of peaks of 1-CF_2 and CH_3O groups.

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11. General procedure for **5a-c**: an aqueous 1 N NaOH solution (6 mL) was added under N_2 and during 15 min to a stirred solution of sulfide **3a-c** (2 mmol) in ethanol (15 mL) cooled at 0 °C. Stirring was continued for 24 h at r.t. Thus the mixture was poured into a water/ice mixture (50 mL) and extracted with EtOAc (3x50 mL). The organic layer was washed with brine (2x10 mL) and dried (Na_2SO_4).The solvent was removed under reduced pressure and the residue was distilled under vacuum.
12. Physical data for novel compounds are presented below. ^{19}F NMR spectra were in agreement with the structures of these compounds.
    Compound ***5a***. IR (film) 1700, 1636 cm^{-1}; anal. Calc. for $C_{13}H_9F_7O_2S$: C 43.10, H 2.50, F 36.71, S 8.85; found: C 42.80, H 2.35, F 36.50, S 8.57. (*E*)-**5a** ^{1}H NMR (80 MHz, $CDCl_3$) δ 10.06 (s, 1 H, CHO), 7.33 (m, 5 H, H_{arom}), 3.86 (s, 3 H, CH_3); MS (EI) m/z (%) 362 ($M^{+\cdot}$, 25.1), 333 (M-CHO, 0.8), 110 (100.0). (*Z*)-**5a** ^{1}H NMR (80 MHz, $CDCl_3$) δ 9.67 (t, 1 H, J = 2 Hz, CHO), 7.33 (m, 5 H, H_{arom}), 3.43 (s, 3 H, CH_3); MS (EI) m/z (%) 362 ($M^{+\cdot}$, 25.0), 333 (M-CHO, 3.3), 110 (100.0). *Compound* ***5b***. IR (film) 1701, 1636 cm^{-1}; anal. Calc. for $C_{15}H_9F_{11}O_2S$: C 38.98, H 1.96, F 45.20, S 6.94; found: C 38.88, H 1.75, F 44.98, S 6.63. (*E*)-**5b** ^{1}H NMR (80 MHz, $CDCl_3$) δ 10.15 (s, 1 H, CHO), 7.42 (m, 5 H, H_{arom}), 4.00 (s, 3 H, CH_3); MS (EI) m/z (%) 462 ($M^{+\cdot}$, 26.6), 433 (M-CHO, 2.0), 110 (100.0). (*Z*)-**5b** ^{1}H NMR (80 MHz, $CDCl_3$) δ 9.70 (t, 1 H, J = 2 Hz, CHO), 7.42 (m, 5 H, H_{arom}), 3.51 (s, 3 H, CH_3); MS (EI) m/z (%) 462 ($M^{+\cdot}$, 26.7), 433(M-CHO, 2.2), 110 (100.0). *Compound* ***5c***. IR (film) 1700, 1636 cm^{-1}; anal. Calc. for $C_{17}H_9F_{15}O_2S$: C 36.32, H 1.61, F 50.68, S 5.70; found: C 35.93, H 1.41, F 50.49, S 5.43. (*E*)-**5c** ^{1}H NMR (80 MHz, $CDCl_3$) δ 10.10 (s, 1 H, CHO), 7.36 (m, 5 H, H_{arom}), 3.96 (s, 3 H, CH_3); MS (EI) m/z (%) 562 ($M^{+\cdot}$, 6.6), 533(M-CHO, 0.5), 110 (100.0). (*Z*)-**5c** ^{1}H NMR (80 MHz, $CDCl_3$) δ 9.73 (t, 1 H, J = 2 Hz, CHO), 7.36 (m, 5 H, H_{arom}), 3.53 (s, 3 H, CH_3); MS (EI) m/z (%) 562 ($M^{+\cdot}$, 7.6), 533 (M-CHO, 3.7), 110 (100.0).
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