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Syntheses of Fluorine-Containing Enamines, Ketenedithioacetals, and Acetylene Sulfoxides from 1-Alkythio-3,3-difluoropropynes-1*

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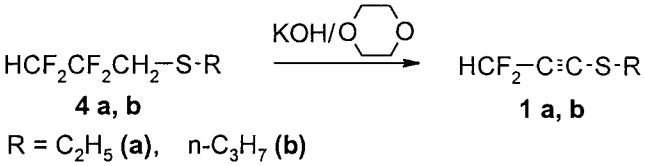
ABSTRACT: *Convenient methods of synthesis of fluorocontaining N,N-dimethylenamines by the reactions of 1,1-dihydrotetrafluoropropyl sulfides with KOH in dimethylformamide and of fluoro-containing 1,4-dienes by the cycloaddition reactions of 1-(alkylsulfinyl)-difluoropropynes with dimethylbutadiene or cyclopentadiene are described.* © 2000 John Wiley & Sons, Inc. Heteroatom Chem 11:383–386, 2000

INTRODUCTION

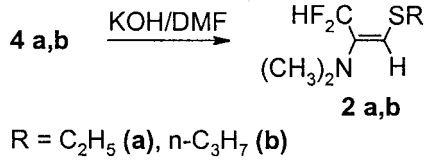
Recently we have reported [1,2] on syntheses and some properties of the representatives of a new type of acetylenes: 1-alkylthio-polyfluoroalkynes-1 (**1**). The influence of polyfluoroalkyl and thioalkyl substituents results in regioselective reactions of the compounds (**1**) with dialkylamines and thiols, with formation only of products in which the dialkylamino- or alkylthio group is located at the carbon atom of the acetylene connected with the polyfluoroalkyl substituent [1,2], whereas the addition of dialkylamines and thiols to polyfluoroalkynes-1 ($Alk_FC{\equiv}CH$) results only in formation of polyfluoroalkylvinylamines ($Alk_FCH{=}CH\text{-}NR_2$) [3] and sulfides ($Alk_FCH{=}CH\text{-}SR$) [4]. Continuing our research on compounds (**1**), we have studied the chemical properties of their enamine (**2**) and sulfoxide derivatives (**3**).

RESULTS AND DISCUSSION

Acetylenes **1** are formed by the action of KOH on 1,1-dihydropolyfluoroalkyl sulfides **4** in dioxane in the presence of 18-crown-6 [2].



We have found that the reaction of sulfides **4a,b** with KOH in dimethylformamide leads to the formation of enamines **2a,b** with yields of 85–95%, this being a preparatively convenient method for the synthesis of fluoro-containing enamines.



The reaction represents a kinetically controllable process and proceeds with formation of only one of two possible geometrical isomers, to which the ex-

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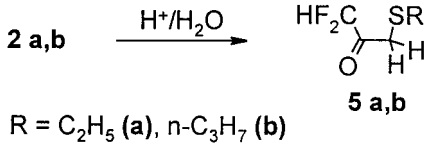
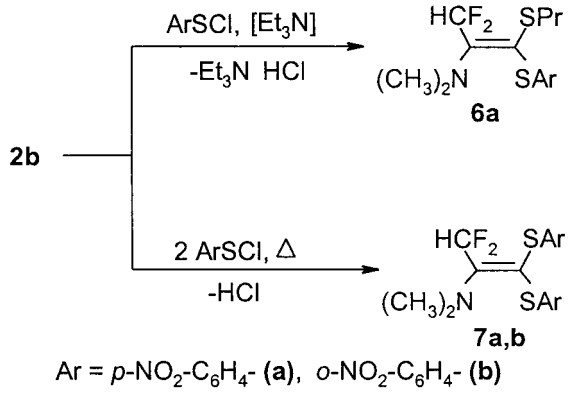
*1-(Alkylthio)-polyfluoroalkynes-1 II; Communication I, see Ref. [1].

istence of only one set of signals in the ^{19}F NMR spectra of the reaction mixtures testify. The formation of the thermodynamically more stable isomers of the enamines **2a,b** occurs only by heating them to 100°C in the process of distillation in vacuum. In each of these cases in the ^{1}H and ^{19}F NMR spectra of the compounds **2a,b,** the new signals of the isomers formed by heating were observed in addition to the signals of the originally formed isomers. The ratio of integrated intensities of initial and new signals is 1:3. This ratio changes in favor of the new isomers at longer heating at 100°C; however, attempts to reach complete isomerization of enamines **2a,b** failed because the long heating resulted in their decomposition. Because only their isomerization is observed through heating of the enamines, and no other type of conversion is noted, the results of a study of the hydrolysis of the enamines **2a,b** or mixture of their isomers are confirmed. In both cases, the formation of ketones **5a,b** is observed.

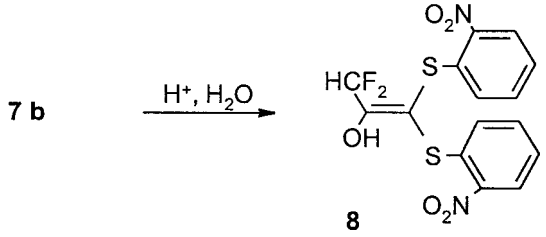


We used enamine **2b** for the synthesis of fluorocontaining ketendithioacetals **6,7**.

Compound **6a** is formed by the reaction of enamine **2b** with *p*-nitrophenylsulfenyl chloride in the presence of triethylamine, and compounds **7a,b** by heating of enamine **2b** with two moles of *p*- or *o*-nitrophenylsulfenyl chloride.

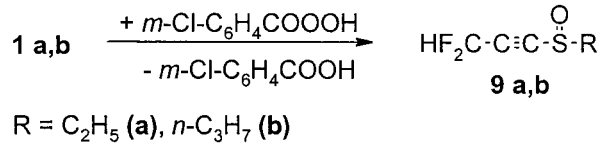


Compounds **6,7a,b** are representatives of a new type of α-substituted fluorocontaining ketenedithioacetals [5], which can be used in syntheses. The acidic hydrolysis of compound **7b**, for example, results in formation of the dithioacetal of difluoropyruvic aldehyde **8**, which, according to the data of ^{1}H NMR and of IR spectroscopy, exists in a solution of deuteroacetone and in the crystal state only in the enolic form.



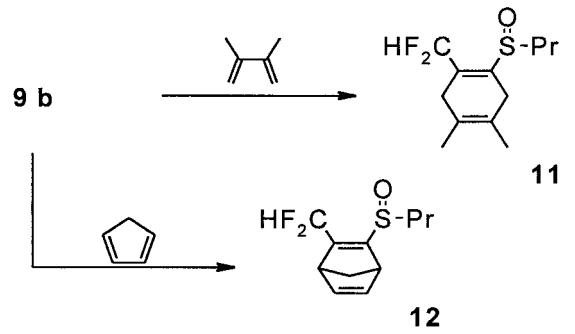
It is known that acetylenes containing electron-withdrawing substituents are capable of entering into 2 + 4 cycloaddition reactions with dienes [6]. The difference in behavior, compared with that of acetylenesulfides **1a,b**, is that they do not react with dimethylbutadiene even with long periods of heating. To increase activity of the acetylene systems **1**, synthesized by us, in reactions of cycloaddition, we have studied the preparation of 1-alkylsulfinyl-3,3-difluoropropynes-1 **9**. It is necessary to note that fluorocontaining acetylene sulfoxides **9** and acetylene sulfones **10** are not presently described in the literature.

In reference [7] it was stated, that the compound 10 (R_F = CF_3) is unstable and cannot be isolated in a pure form.



We have now found that sulfides **1a,b** can react with *m*-chloroperbenzoic acid with formation of sulfoxides **9a,b**.

Compounds **9a,b** are thermally stable, light yellow liquids that can be distilled in vacuum. The oxidation of sulfur essentially raises the activity of acetylenes **9** in reactions of cycloaddition with dienes. The reactions with dimethylbutadiene and cyclopentadiene proceed at room temperature and result in the formation of the difluoromethyl-containing derivatives of 1,4-cyclohexadiene **11** and norbornadiene **12**.



Due to the presence of the sulfur atom, the protons of the CH_2 groups in compounds **11** and **12** become diastereotopic, and their signals in ^1H NMR spectra represent an AB-system (see Experimental section).

EXPERIMENTAL

Melting points were measured on a Nagema melting-point apparatus and are uncorrected. ^1H and ^{19}F NMR spectra were recorded on a Varian VXR (300 MHz) spectrometer as solutions in $CDCl_3$ with GMDS and C_6F_6 as internal standards.

Sulfide **4a** is described in Ref. [1]. The sulfide **4b** is obtained by the method described in Ref.[1]. Yield 80%, b.p. = 145–147°C, ^1H NMR, δ 0.94 (3H, t, $^3J_{HH}$ = 7.2 Hz, CH_3), 1.57 (2H, sextet, $^3J_{HH}$ = 7.2 Hz, CH_2), 2.57 (2H, t, $^3J_{HH}$ = 7.2 Hz, CH_2), 2.95 (2H, t, $^3J_{HF}$ = 15.9 Hz, CH_2), 5.93 (1H, tt, $^2J_{HF}$ = 53.7 Hz, $^3J_{HF}$ = 4.0 Hz, CF_2 H); ^{19}F NMR, δ −138.16 (2F, d, $^2J_{FH}$ = 53.7 Hz, CF_2H), −116.18 (2F, t, $^3J_{FH}$ = 16.5 Hz, CF_2); found: S, 16.75%. $C_6H_{10}F_4S$ requires: S, 16.85%.

1-(Ethylithio)-difluoropropyne (**1a**) is described in Ref. [1]. 1-(Propylthio)-difluoropropyne (**1b**) is obtained by the method described in Ref. [1]. Yield 80%, b.p. = 26–28°C (0.04 mm Hg), ^1H NMR, δ 0.96 (3H, t, $^3J_{HH}$ = 7.2 Hz, CH_3), 1.60 (2H, sextet, $^3J_{HH}$ = 7.2 Hz, CH_2), 2,61 (2H, t, $^3J_{HH}$ = 7.2 Hz, CH_2), 6.01 (1H, t, $^2J_{HF}$ = 55.2 Hz, CF_2H); ^{19}F NMR, δ −103.20 (2F, d, $^2J_{FH}$ = 55.2 Hz, CF_2H);

1-(Alkylthio)-2-N,N-dimethyl-3,3-difluoropropenes **2a,b**

To a suspension of 0.03 mol of finely dispersed KOH in 100 mL of DMF, 0.01 mol of the sulfide **4a,b** was added. The mixture was stirred at room temperature for 24 hours and then it was poured into 150 mL of water, extracted by CH_2Cl_2 (3 × 100 mL), dried over Na_2SO_4 and distilled in vacuum. 1-(Etylthio)-2-*N,N*-dimethyl-3,3-difluoropropene-1 (**2a**). Yield 85%, b.p. = 16–33°C (0.04 mm Hg). ^{19}F NMR, δ −111.83* (thermodynamically more stable isomer), −117.68 (2F, d, $^2J_{FH}$ = 56.4 Hz, CF_2H); found: C, 46.3%; H, 7.31%; N, 7.80%; S, 17.58%. $C_7H_{13}F_2NS$ requires: C, 46.39%; H, 7.23%; N, 7.73%; S, 17.69%. 1-(*n*-Propylthio)-2-*N,N*-dimethyl-3,3-difluoropropene-1 (**2b**). Yield 87%, b.p. = 27–58°C (0.04 mm Hg). ^1H NMR, δ 0.72 (3H, m, CH_3), 1.34 (2H, m, CH_2), 2.20 (2H, m, CH_2), 2.39, 2.53* (6H, s, $N(CH_3)_2$), 4.82, 5.51* (1H, tm, $^2J_{FH}$ = 55.2 Hz, CF_2H); ^{19}F NMR, δ −112.20*, 117.99 (2F, d, $^2J_{FH}$ = 56.4 Hz); found: C, 49.00%; H, 7.65%; N, 7.23%; S, 16.48%. $C_8H_{15}F_2NS$ requires: C, 49.20%; H, 7.74%; N, 7.18%; S, 16.41%.

The ketones **5a,b** were obtained by a method similar to that given in Ref. [2] and had the same analytical and spectral data.

1-(Propylthio)-1-(4-nitrophenylthio)-2-N,N-dimethyl-3,3-difluoropropene-1 (**6**)

To a solution of 0.01 mol of enamine **2b** and 0.01 mol of triethylamine in 10 mL of benzene, 0.01 mol of *p*-nitrophenylsulfenyl chloride was added. The mixture was stirred at room temperature for 3 hours. The precipitate of $Et_3N^+HCl^-$ was separated, and the solvent was evaporated from the filtrate. A viscous liquid that resulted was distilled in vacuum. Yield 74%, b.p. = 53–55°C (0.04 mm Hg). ^1H NMR, δ 0.78 (3H, t, $^3J_{HH}$ = 7.2 Hz, CH_3), 1.40 (2H, sextet, $^3J_{HH}$ = 7.2 Hz, CH_2), 2.47 (2H, t, $^3J_{HH}$ = 7.2 Hz, CH_2), 2.61, 2.81* (6H, s, $N(CH_3)_2$), 7.20 (1H, tm, $^2J_{FH}$ = 52.7 Hz, CF_2H), 6.93, 6.98* (2H, d, $^3J_{HH}$ = 9.0 Hz, CH_{Ar}), 7.79*, 7.80 (2H, d, $^3J_{HH}$ = 9.0 Hz, CH_{Ar}); ^{19}F NMR, δ −112.24, 114.15 (2F, d, $^2J_{FH}$ = 53.9 Hz, CF_2H); found: C, 44.35%; H, 5.40%; N, 8.43%; S, 19.73%. $C_{14}H_{18}F_2N_2O_2S_2$ requires: C, 44.43%; H, 5.59%; N, 8.64%; S, 19.77%.

1,1-Bis(arylthio)-2-N,N-dimethyl-3,3-difluoropropenes **7a,b**

A mixture of 0.01 mol of enamine **2b** and 0.01 mol of arylsulfenyl chloride in 10 mL of benzene was refluxed for 3 hours. The solvent was evaporated in vacuum, and the solid residue was washed with hexane. 1,1-Bis(4-nitrophenylthio)-2-*N,N*-dimethyl-3,3-difluoropropene (**7a**). Yield 77%, m.p. = 123–125°C. ^1H NMR, δ 2.57 (6H, s, $N(CH_3)_2$), 6.67 (2H, d, $^3J_{HH}$ = 9.0 Hz, CH_{Ar}), 6.84 (2H, d, $^3J_{HH}$ = 9.0 Hz, CH_{Ar}), 7.13 (1H, d, $^2J_{HF}$ = 53.1 Hz, CF_2H), 7.73 (2H, d, $^3J_{HH}$ = 9.0 Hz, CH_{Ar}), 7.74 (2H, d, $^3J_{HH}$ = 9.0 Hz, CH_{Ar}); ^{19}F NMR, δ −114.93 (2F, d, $^2J_{HF}$ = 50.4 Hz, CF_2H); found: C, 44.12%; H, 3.53%; N, 9.93%; S, 15.59%. $C_{17}H_{15}F_2N_3O_4S_2$ requires: C, 44.66%; H, 3.75%; N, 10.44%; S, 15.87%. 1,1-Bis(2-nitrophenylthio)-2-*N,N*-dimethyl-3,3-difluoropropene (**7b**). Yield 84%, m.p. = 179–180°C. ^1H NMR, δ 2.44 (6H, s, $N(CH_3)_2$), 6.35 (2H, t, $^3J_{HH}$ = 7.2 Hz, CH_{Ar}), 6.74 (2H, t, $^3J_{HH}$ =

7.4 Hz, CH_{Ar}), 7.02 (1H, t, $^2J_{HF}$ = 52.7 Hz, CF_2H), 7.30 (2H, d, $^3J_{HH}$ = 8.3 Hz, CH_{Ar}), 7.60 (2H, dd, $^3J_{HH}$ = 8.3 Hz, CH_{Ar}); ^{19}F NMR, δ − 114.52 (2F, d, $^2J_{HF}$ = 54.1 Hz, CF_2H); found: C, 44.31%; H, 3.55%; N, 10.93%; S, 15.79%. $C_{17}H_{15}F_2N_3O_4S_2$ requires: C, 44.66%; H, 3.75%; N, 10.44%; S, 15.87%.

1,1-Bis(*2-nitrophenylthio*)*-3,3-difluoropropene-2-ol* (**8**)

A solution of 0.01 mol of enamine **7b** and 2 mL of HCl (35%) in 25 mL of methanol was heated for 2 hours at 50°C. The solvents were evaporated in vacuum, and the residue was purified by crystallization from benzene. Yield 95%, m.p. = 121–123°C. ^{1}H NMR, δ 3.50(1H, s, OH), 7.16 (1H, t, $^2J_{HF}$ = 53.1 Hz, CF_2H), 7.43 (2H, t, $^3J_{HH}$ = 8.3 Hz, CH_{Ar}), 7.55 (2H, t, $^3J_{HH}$ = 8.3 Hz, CH_{Ar}), 7.74 (2H, quintet, $^3J_{HH}$ = 8.1 Hz, CH_{Ar}), 8.16 (2H, t, $^3J_{HH}$ = 8.3 Hz, CH_{Ar}); ^{19}F NMR; δ −119.78 (2F, d, $^2J_{HF}$ = 54.1 Hz, CF_2H); found: C, 45.31%; H, 2.57%; N, 7.53%; S, 15.73%. $C_{15}H_{10}F_2N_2O_5S_2$ requires: C, 45.00%; H, 2.52%; N, 7.00%; S, 16.02%.

1-(*Alkylsulfinyl*)*-difluoropropynes* **9a,b**

To a solution of 0.01 mol of acetylene **1a, b** in 50 mL of $CHCl_3$, a solution of 0.015 mol of mCPBA in $CHCl_3$ was added at 0–5°C. The mixture was stirred for 12 hours at room temperature, evaporated to 1/3 of its volume, and cooled to −15°C. The *m*-chlorobenzoic acid was filtered off, and the filtrate was distilled in vacuum. 1-(Etylsulfenyl)-difluoropropyne (**9a**). Yield 91%, b.p. = 53–55°C (0.04 mm Hg). ^{1}H NMR, δ 1.05 (3H, t, $^3J_{HH}$ = 7.2 Hz, CH_3), 2.88 (2H, m, CH_2), 5.78 (1H, t, $^2J_{HF}$ = 53.2 Hz, CF_2H); ^{19}F NMR, δ −110.48 (2F, d, $^2J_{FH}$ = 54.1 Hz, CF_2H). 1-(*N*-propylsulfinyl)-difluropropyne (**9b**). Yield 93%, b.p. = 72°C (0.04 mm Hg). ^{1}H NMR, δ 0.59 (3H, t, $^3J_{HH}$ = 7.2 Hz, CH_3), 1.38 (2H, m, CH_2), 2.38 (2H, m, CH_2), 5.74 (1H, t, $^2J_{HF}$ = 53.2 Hz, CF_2H); ^{19}F NMR, δ −111.94 (2F, d, $^2J_{FH}$ = 53.8 Hz, CF_2H); found: C, 43.43%; H, 4.54%; S, 19.71%. $C_6H_8F_2OS$ requires: C, 43.36%; H, 4.85%; S, 19.29%.

1-(*n-Propylsulfinyl*)*-2-difluromethyl-4,5-dimethylcyclohexa-1,4-diene* (**11**)

To a solution of 0.01 mol of sulfinylacetylene **9b** in 5 mL of $CHCl_3$, 0.015 mol of 2,3-dimethyl-1,3-butadiene was added. The mixture was stirred for 24 hours at room temperature. The solvent was evaporated in vacuum, and the residue was purified by crystallization from hexane. Yield 53%, m.p. = 82–84°C. ^{1}H NMR, δ 1.01 (3H, t, $^3J_{HH}$ = 7.2 Hz, CH_3), 1.73 (6H, s, CH_3), 1.77 (2H, m, CH_2), 2.51 (2H, s, $CH_{2\ cycl.}$), 3.20 [2H, m, $CH_2S(O)$], 3.37 (2H, s, $CH_{2\ cycl.}$), 7.60 (1H, tm, $^2J_{HF}$ = 53.2 Hz, CF_2H); ^{19}F NMR, δ −115.31 (1F, dd, $^1J_{FF}$ = 304 Hz, $^2J_{FH}$ = 54.0 Hz, CF_2H), −122.12 (1F, dd, $^1J_{FF}$ = 304 Hz, $^2J_{FH}$ = 54.0 Hz, CF_2H); found: C, 57.87%; H, 6.94%; S, 13.48%. $C_{12}H_{18}F_2OS$ requires: C, 58.03%; H, 7.30%; S, 12.91%.

2-(*n-Propylsulfinyl*)*-3-difluromethylnorbornadiene* (**12**)

To a solution of 0.01 mol of sulfinylacetylene **9b** in 5 mL of $CHCl_3$, 0.02 mol of cyclopentadiene was added. The mixture was stirred for 24 hours at room temperature. The solvent was evaporated in vacuum, and the residue was purified by crystallization from hexane. Yield 69%, m.p. = 47–49°C. ^{1}H NMR, δ 1.03 (3H, m, CH_3), 1.78 (2H, m, CH_2), 2.12 (1H, m, CH), 2.27 (1H, m, CH), 3.23 [2H, m, $CH_2S(O)$], 4.07 (2H, m, $CH_{2\ cycl.}$), 6.78 (2H, m, CH=), 7.11 (1H, tm, $^2J_{HF}$ = 53.2 Hz, CF_2H); ^{19}F NMR, δ −117.35 (1F, dd, $^1J_{FF}$ = 301 Hz, $^2J_{FH}$ = 53.0 Hz, CF_2H), −121.21 (1F, dd, $^1J_{FF}$ = 301 Hz, $^2J_{FH}$ = 53.0 Hz, CF_2H); found: C, 57.07%; H, 6.37%; S, 13.48%. $C_{11}H_{14}F_2OS$ requires: C, 56.87%; H, 6.07%; S, 13.80%.

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