Available online at www.sciencedirect.com
SCIENCE DIRECT®
Journal of Fluorine Chemistry 123 (2003) 197–205
JOURNAL OF FLUORINE CHEMISTRY
www.elsevier.com/locate/jfluchem

Synthesis and some chemical properties of the 6-arylsulfonyl-6-polyfluoroalkanoyl-5,6-dihydro-2H-thiins—new fluorine-containing ketones

Yu.P. Bandera, S.V. Yemets, V.M. Timoshenko, A.M. Nesterenko, A.N. Chernega, Yu.G. Shermolovich*

Institute of Organic Chemistry of the NAS of Ukraine, Murmanska Street 5, 02094 Kiev 94, Ukraine

Received 18 February 2003; received in revised form 22 April 2003; accepted 29 April 2003

Abstract

1,1-Dihydro-1-tolylsulfonyl polyfluoroalkan-2-ones react with phthalimidosulfenyl chloride to form sulfenylated products on the active methylene group, 1-phthalimidothio-1-tolylsulfonyl polyfluoroalkan-2-ones. Decomposition of the latter leads to formation of 1-thioxo-1-tolylsulfonyl polyfluoroalkan-2-ones. These compounds undergo easily the hetero Diels–Alder reaction with electron-rich 1,3-dienes as dienophiles to give polyfluoroalkanoyl substituted derivatives of 5,6-dihydro-2H-thiins. 6-Arylsulfonyl-6-polyfluoroalkanoyl-5,6-dihydro-2H-thiins obtained react with alkali to give 5,6-dihydro-6-*p*-tolylsulfonyl-2H-thiins and with methanol to give 2-polyfluoroalkanoyl-6H-thiins.

Keywords: Polyfluoroalkyl ketone; α-Thioxoketone; Cycloaddition; Thiin

1. Introduction

Interest in the chemistry of polyfluorinated aliphatic ketones is due to the fact that they can be used, not only as building blocks in organic synthesis [1], but also as enzyme inhibitors [2]. Previously, we described the synthesis of the fluorine-containing ketones of a new type **1a** and **1b** (R = CH_2Ph) with heterocyclic thiin moieties. The reaction occurs through the intermediate formation of 1-thioxopolyfluoroalkan-2-ones (**2a** and **2b**) (R = CH_2Ph) which then react with 1,3-dienes as C=S dienophiles [3] (Scheme 1). In the present work, we studied the synthesis of thiins **1a** and **1b** with arylsulfonyl substituents (R = Ar). The reason of a choice of the arylsulfonyl fragment (R = Ar) as a substituent is that the arylsulfonyl group is a good leaving group, moreover, arylsulfones particularly are often used in desulfonylation processes [4]. For compounds **1a** and **1b** (R = Ar), desulfonylation reactions can lead to the formation of the new heterocycles with exocyclic polyfluoroalkanoyl fragments.

2. Results and discussion

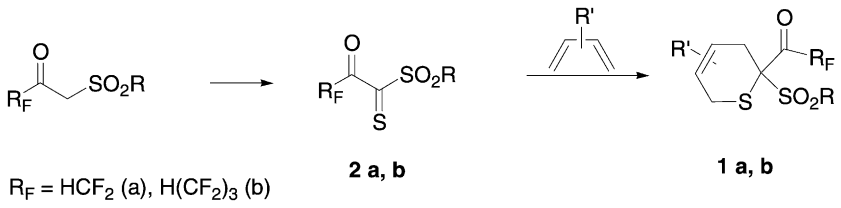
2.1. Synthesis of fluorine-containing heterocyclic ketones

We synthesized new ketones with heterocyclic substituents **3–5** starting from 1,1-dihydro-1-*p*-tolylsulfonyl polyfluoroalkan-2-ones (**6a** and **6b**) following Scheme 2.

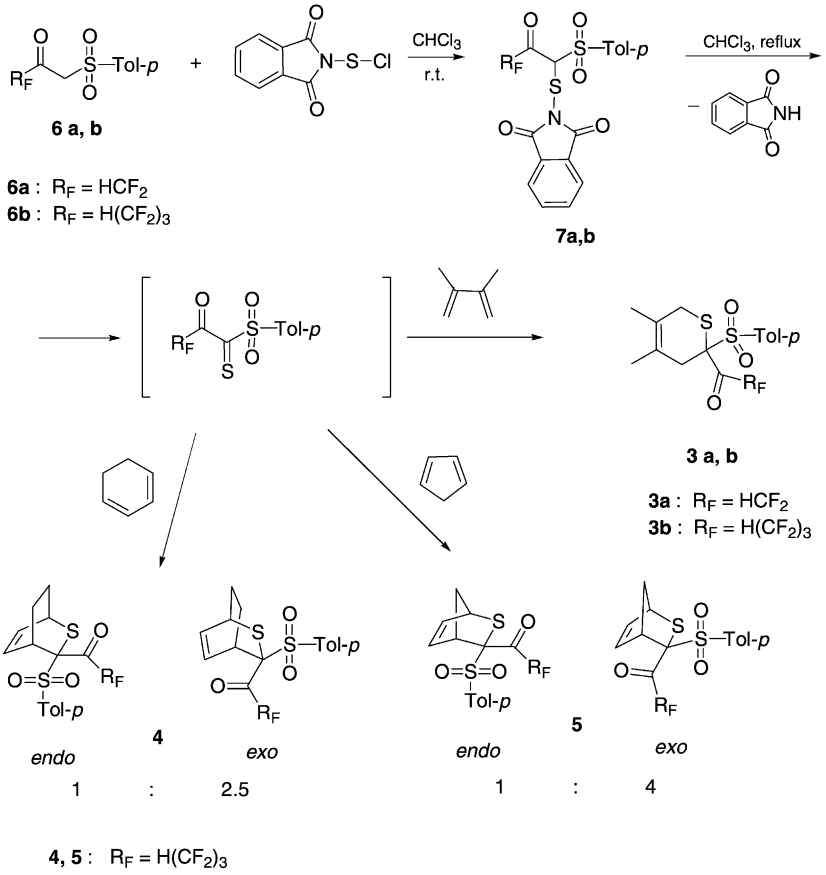
Compounds **3–5** are crystalline. Their composition was proved by elemental analysis and mass-spectrometry and their structure by ^{1}H NMR and ^{19}F NMR data. Compounds **4** and **5** exist as mixtures of *exo*- and *endo*-isomers, testified by the double set of signals in the ^{1}H NMR and ^{19}F NMR spectra. The *exo*/*endo* ratio was 2.5:1 for compounds **4** and 4:1 for compounds **5**, determined by ^{1}H NMR analyses of the crude product mixture. The *exo*-isomer **4** was isolated by the fractional crystallization of the crude mixture from diethyl ether. The molecular structure of this compound was determined by single crystal X-ray diffraction. The perspective view of molecule **4** is shown in Fig. 1, selected geometrical parameters are given in Table 1. It is established that C(=O)$CF_2CF_2CF_2H$ fragment in **4** occupies the *endo*, and SO_2Ar group occupies the *exo* position. Bond lengths and angles in **4** are unexceptional [5,6].

* Corresponding author. Tel.: +38-44-552-8312; fax: +38-44-573-2643.
E-mail address: sherm@bpci.kiev.ua (Yu.G. Shermolovich).

0022-1139/$ – see front matter © 2003 Elsevier Science B.V. All rights reserved.
doi:10.1016/S0022-1139(03)00134-9



Scheme 1.



Scheme 2.

Table 1
Selected bond length (Å) and angles (°) in **4**

S(1)–C(1)	1.822(3)	C(1)S(1)C(5)	96.9(2)
S(1)–C(5)	1.837(4)	S(1)C(1)C(2)	110.4(2)
S(2)–O(1)	1.439(3)	C(1)C(2)C(3)	107.7(3)
S(2)–O(2)	1.437(3)	C(1)C(2)C(7)	112.1(3)
S(2)–C(1)	1.850(4)	C(3)C(2)C(7)	107.7(3)
S(2)–C(8)	1.754(3)	C(2)C(3)C(4)	114.1(4)
C(1)–C(2)	1.571(5)	C(3)C(4)C(5)	113.9(4)
C(2)–C(3)	1.506(6)	S(1)C(5)C(4)	108.1(3)
C(2)–C(7)	1.528(6)	S(1)C(5)C(6)	108.8(3)
C(3)–C(4)	1.393(6)	C(4)C(5)C(6)	110.0(4)
C(4)–C(5)	1.492(7)	C(5)C(6)C(7)	111.2(3)
C(5)–C(6)	1.523(6)	C(2)C(7)C(6)	112.3(3)
C(6)–C(7)	1.481(6)		

2.2. Treatment of 6-arylsulfonyl-6-polyfluoroalkanoyl-5, 6-dihydro-2H-thiins with bases

It could be supposed that formation of carbanion **8** occurred under treatment of compounds **3** with the bases. One of the most probable directions of the transformation of carbanion (**8**) is elimination of the *p*-tolylsulfinate anion (Scheme 3). However, it was found that compounds **3–5** were stable against bases such as tertiary amines; they did not change after boiling in dry triethylamine for 5 h. At the same time, treatment of **3–5** with sodium hydroxide in dioxane leads to the elimination of the polyfluoroalkanoyl substituent with formation of the sodium salt of the corresponding carboxylic acid and thiins **9–11**, rather than

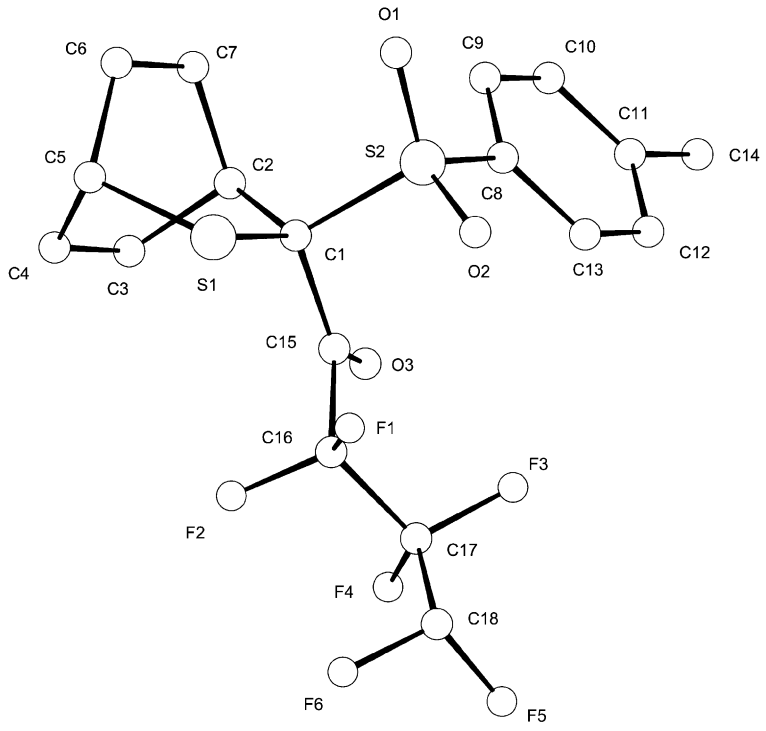
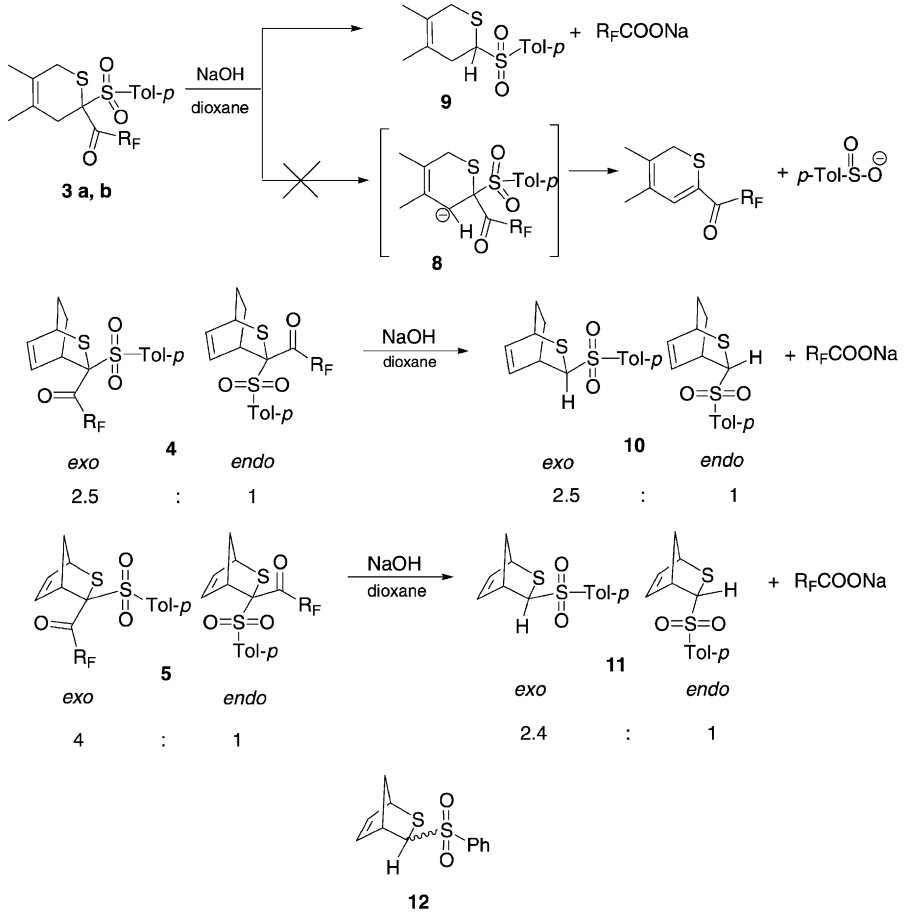


Fig. 1. Perspective view and labeling scheme for molecule **4** (hydrogen atoms are omitted for clarity).



Scheme 3.

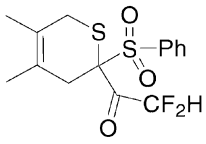
elimination of the *p*-tolylsulfonyl group. Compounds **10** and **11** were formed as a mixture of *exo*/*endo*-isomers. The comparison of the ^{1}H NMR spectrum of compound **11** with the known data [7] for compound **12** led to the conclusion formation of the *exo*-isomer **11** was preferred. This allowed us to propose the preferred formation of the *exo*-isomer of compound **5**.

Haloformic type splitting of compounds **3**–**5** with alkali with the preservation of the *p*-tolylsylfonyl fragment in molecules **9**–**11** was unexpected. Such splitting of fluorine-containing ketones, R_F–C(O)–R, is known and takes place with cleavage of R_F–C bond [8].

2.3. Theoretical calculations of reaction of alkali with 6-arylsulfonyl-6-polyfluoroalkanoyl-5, 6-dihydro-2H-thiins

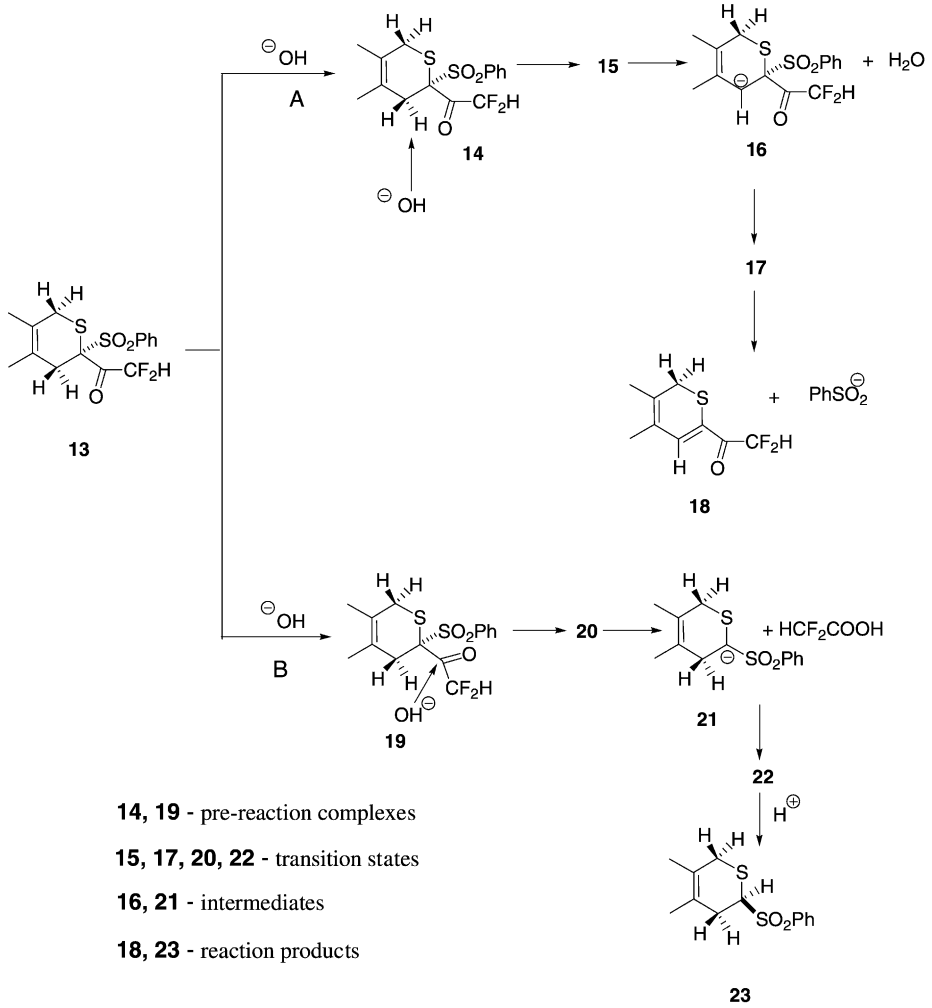
We studied the possible routes of the reaction of alkali with compounds **3**–**5** using the heterocycle **13** as a model by semi-empirical PM3 method (MOPAC 7 version) [9]. The eigenvector following (EF) procedure was used for search of the extreme on the potential energy surface (PES) and transition states (TS) were located by Dewar–Stewart technique [10,11].

The most energetically preferable conformation with $\Delta H^{\circ}_{298} = -581.74$ kJ mol^{-1} was selected as a starting conformation for the initial heterocyclic **13**.



13

We studied two following reaction routes of **13**: an attack of OH^- anion on the hydrogen atom of CH_2 group and on the carbon atom of carbonyl group. Pre-reaction complexes **14** and **19** are formed in both cases by the initial interaction of OH^- anion with heterocyclic **13** (Scheme 4). They differ significantly in structure and in thermodynamic stability (see Table 2). It should be emphasized that complex **19** is more stable than complex **14** due to the notable charge transfer from OH^- in **14**, and it is also evidently preferred by electrostatic factors.



Scheme 4.

Table 2
Formation energies of the states **14–23** in kJ mol^{-1}

State	ΔH°_{298}	E_{act}	$\delta(\Delta H_{reac})$
14	−866.62		
19	−924.04		
15	−848.89	17.73	−108.89
20	−923.18	0.86	−160.21
16	−975.51		
21	−1084.25		
17	−967.06	17.73	−187.43
22	−1059.00	25.25	−16.55
18	−1162.94		
23	−1100.80		

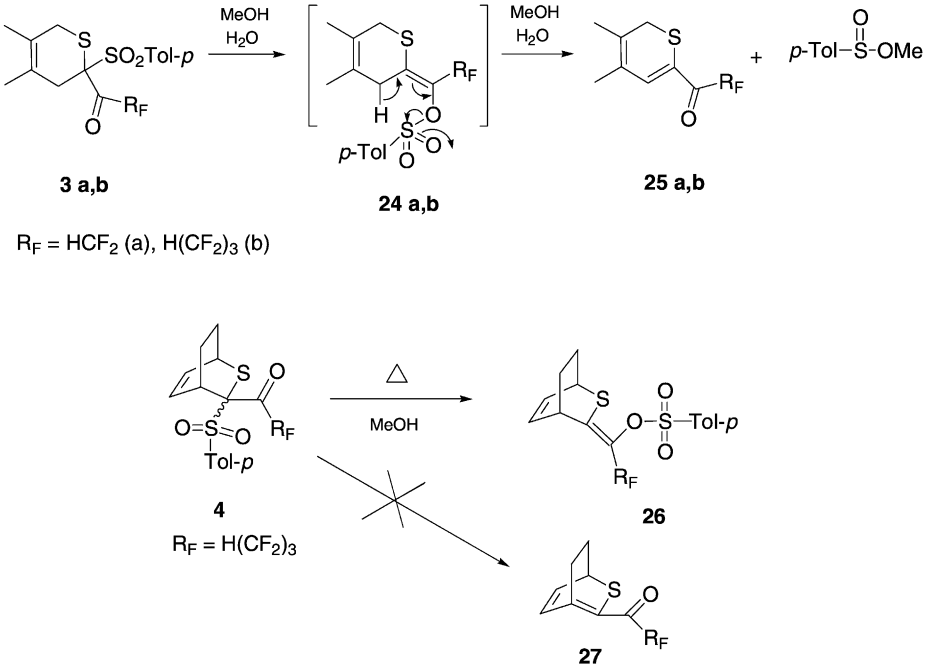
The pre-reaction complexes formed have also different fates. In contrast to the transformation of **14**, which proceeds *via* proton abstraction with E_{act} about 8 kJ mol^{-1}, thus leading to formation of carbanion **16** and water, in the pre-reaction complex **19** the OH^- anion attacks easily (E_{act} = 0.9 kJ mol^{-1}) the carbon of the carbonyl group; the product of addition immediately (i.e. without activation barrier) decomposes into difluoroacetic acid and carbanion **21**.

In accordance with the Hammond principle [12], the transition states **15** and **20** are closely allied structurally to the pre-reaction complexes **14** and **19**, respectively, considering their energetic proximity. Due to comparatively high reaction enthalpies, the processes studied are probably irreversible and the resulting intermediates **16** and **21** after the establishment of thermal equilibriums with the reaction medium must undergo consecutive transformations regardless of the previous stages. Therefore, the transformations of intermediates **16** and **21** result in elimination of the phenylsulfinate anion from **16** and in the abstraction of a proton from the medium to **21**. The progress of these reactions needs only minor activation energies (Table 2), so they should also proceed rapidly.

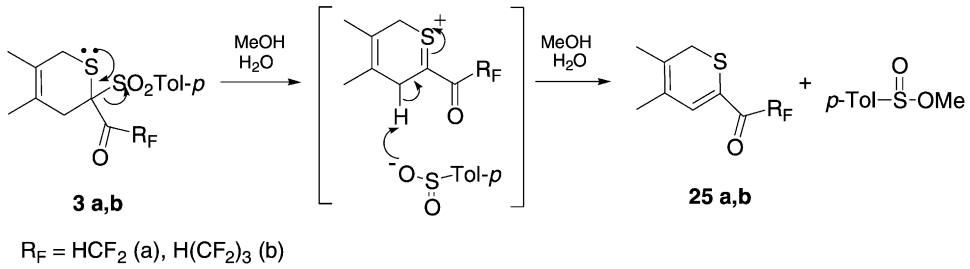
The results of semi-empirical simulation of the reactions demonstrate that the formation of the pre-reactions state **19** is favored over **14**, and that the activation energy for the route leading to the formation of **23** is definitely smaller, being equal to a portion of *kT* at experimental conditions. Hence compound **23** is preferred for the reaction of **13** with alkali. The data presented seem to be a valuable argument for formation of sulfones **9**, **10** and **11** in reactions of **3–5** with alkali.

2.4. Desulfonilation of 6-arylsulfonyl-6-polyfluoroalkanoyl-5,6-dihydro-2H-thiins

The ketones **3** and **4** transform not only under the reaction with alkali, but also when continuously refluxed in methanol (Scheme 5). For example, compound **4** is isomerized into fluorine-containing enol derivative **26**, and compounds **3a** and **3b** give ketones **25a** and **25b** with unsaturated thiin fragment. Evidently that isomerization of **3a** and **3b** into the *O*-sulfonylated enols **24a** and **24b** occurs at the beginning. Intermediates **24a** and **24b** are decomposed under the reaction conditions giving ketones **25a** and **25b** and methyl ether of *p*-toluenesulfonic acid which was also isolated from the reaction mixture. The transformation of the compound **4** stops at enol **26** formation, probably due to steric limitations preventing the formation of the unsaturated ketone **27**.



Scheme 5.



Scheme 6.

On the other hand, alternative mechanism of thins **25a** and **25b** formation can be proposed too (Scheme 6).

3. Conclusion

1-Arylsulfonyl-1-thioxo polyfluoroalkan-2-ones can be readily generated from 1-arylsulfonyl-1-phthalimidothio polyfluoroalkan-2-ones. They were trapped with 1,3-dienes to give 6-arylsulfonyl-6-polyfluoroalkanoyl-5,6-dihydro-2H-thiins. We investigated chemical behavior of the last compounds under treatment with alkali and methanol. These transformations can be used to synthesize 2-polyfluoroalkanoyl-6H-thiins and 6-arylsulfonyl-5,6-dihydro-2H-thiins. Further study of the chemical properties of compounds obtained is under investigation at this laboratory.

4. Experimental

^{1}H NMR and ^{19}F NMR spectra were recorded on the Varian VXR-300 (299.9 MHz for ^{1}H NMR and 282.2 MHz for ^{19}F NMR) using Me_4Si for ^{1}H NMR spectra and C_6F_6 ($\delta = -162.9$) for ^{19}F NMR spectra as internal standards. ES mass-spectra were obtained on AMD-604 at 70 eV. The progress of reactions was monitored by ^{19}F NMR spectroscopy. Column chromatography was performed using silicagel Chemapol L 100/250. The ketones **6a** and **6b** were obtained according to [13].

*4.1. 6-(Difluoroacetyl)-5,6-dihydro-3,4-dimethyl-6-(p-tolylsulfonyl)-2H-thiin (**3a**)*

A solution of sulfone **6a** (1.05 g, 4.23 mmol) and triethylamine (0.43 g, 4.23 mmol) in 10 ml of dry benzene was dropped into a solution of phthalimidosulfenyl chloride (0.9 g, 4.23 mmol) in 25 ml of benzene at stirring and room temperature for 5 min. The mixture was stirred for additional 15 min and solution of 2,3-dimethylbutadiene (0.69 g, 8.4 mmol) in 1 ml of benzene was added. The reaction mixture was stirred for 20 h, precipitate was filtered off and solution was evaporated to dryness in vacuum (20 mmHg). Orange oil obtained was extracted with hot hexane (10 × 10 ml), hexane solution was concentrated in vacuum up to 1/2 of volume and allowed to stay in freezer at −20 °C. The precipitated product was filtered and dried. Yield: 1.1 g (72%). Orange crystals, mp 90–95 °C.

^{1}H NMR: δ 1.68 (6H, s, $2CH_3$); 2.48 (3H, s, CH_3); δ_A 2.45, δ_B 2.71 AB (2H, CH_2, $J_{AB} = 15.1$ Hz); δ_A 3.0, δ_B 3.16 AB (2H, CH_2, $J_{AB} = 15.1$ Hz); 6.6 (1H, t, HCF_2, $J_{HF} = 53.3$ Hz); 7.38 (2H, d, CH_2); 7.71 (2H, d, CH_2). ^{19}F NMR: δ_A −119.89, δ_B −124.02 AB (2F, HCF_2, $^2J_{HF} = 52.8$ Hz, $J_{AB} = 330.0$ Hz). MS (70 eV) *m/z* (%) 360 (2) [M^+], 205 (86) [$M^+ - SO_2Tol$].

Anal. Calcd. for $C_{16}H_{18}F_2O_3S_2$: C 53.32; H 5.03; S 17.79. Found: C 53.25; H 5.04; S 17.64.

*4.2. Synthesis of 5,6-dihydro-2H-thiins (**3b**, **4** and **5**): general procedure*

A mixture of the corresponding diene (20 mmol) and sulfenamide **7** (15 mmol) in 50 ml of dry chloroform was stirred under reflux for 3 h. After cooling the precipitate of phthalimide was filtered off and chloroform solution was evaporated in vacuum (20 mmHg). The residue was extracted with boiling hexane (4 × 25 ml), combined hexane solution was evaporated to half its volume and the precipitated product was filtered and dried.

*4.2.1. 6-(2,2,3,3,4,4-Hexafluorobutyryl)-5,6-dihydro-3,4-dimethyl-6-(p-tolylsulfonyl)-2H-thiin (**3b**)*

Yield 80%. Green crystals, mp 53–55 °C.

^{1}H NMR: δ 1.71 (6H, s, $2CH_3$); 2.48 (3H, s, CH_3); δ_A 2.51, δ_A 3.15 AB (2H, CH_2, $^2J_{AB} = 14.7$ Hz); δ_A 2.86, δ_B 3.08 AB (2H, CH_2, $^2J_{AB} = 14.7$ Hz); 6.13 (1H, tt, HCF_2, $^2J_{HF} = 52.4$ Hz, $^3J_{HF} = 5.9$ Hz); 7.37 (2H, d, Ar); 7.77 (2H, d, Ar). ^{19}F NMR: δ_A −112.3, δ_B −113.11 AB (2F, CF_2, $^2J_{AB} = 299.5$ Hz); −130.81 (2F, m, CF_2); −138.15 (2F, dm, HCF_2, $J_{FH} = 51.9$ Hz).

Anal. Calcd. for $C_{18}H_{18}F_6O_3S_2$: C 46.95; H 3.94; S 13.93. Found: C 47.04; H 4.02; S 13.78.

*4.2.2. 5,6-Dihydro-2,5-ethylene-6-(2,2,3,3,4,4-hexafluorobutyryl)-6-(p-tolylsulfonyl)-2H-thiin (**4**)*

Mixture of isomers (*endo*:*exo*, 1:2.5). Yield 75%. Colorless crystals, mp 104–106 °C. IR 2950 (Alk C–H); 1720 (C=O); 1600 (C=C).

^{1}H NMR (*exo*): δ 1.17–1.30 (1H, m, CH_2); 1.66 (1H, tm, CH_2); 2.15–2.25 (1H, m, CH_2); 2.48 (3H, s, CH_3); 2.6 (1H, tm, CH_2); 3.54 (1H, m, CH); 3.72 (1H, m, CH); 6.06 (1H, dd, CH=CH); 6.08 (1H, tt, HCF_2, $^2J_{HF} = 52.7$ Hz, $^3J_{HF}$ 5.9 Hz); 6.54 (1H, dd, CH=CH); 7.38 (2H, d, Ar); 7.69 (2H, d, Ar). ^{1}H NMR (*endo*): δ 1.32–1.43 (2H, m, CH_2); 1.58 (1H, tm, CH_2); 1.93–2.03 (1H, m, CH_2); 2.47 (3H, s, CH_3); 3.66 (1H, m, CH); 3.83 (1H, m, CH); 6.21 (1H, tt, HCF_2, $^2J_{HF} = 52.3$ Hz, $^3J_{HF} = 5.6$ Hz) 7.34 (2H, d, Ar); 7.63 (2H, d, Ar). ^{19}F NMR: δ_A −112.02, δ_B −113.18 AB (2F, CF_2, $J_{AB} = 302$ Hz); δ_A −130.13, δ_B −131.02 AB (2F, CF_2, $J_{AB} = 288.0$ Hz); −138.20 (2F, dm, HCF_2, $J_{FH} = 55.0$ Hz). MS (70 eV) *m/z* (%) 458 (3) [M^+], 303 (99) [$M^+ - SO_2Tol$].

Anal. Calcd. for $C_{18}H_{16}F_6O_3S_2$: C 47.16; H 3.52; S 13.99. Found: C 47.10; H 3.60; S 13.93.

4.2.3. 5,6-Dihydro-6-(2,2,3,3,4,4-hexafluorobutyryl)-2,5-methylene-6-(p-tolylsulfonyl)-2H-thiin (**5**)

Mixture of isomers (*endo*:*exo*, 1:4). Yield 60%. Colorless oil.

^{1}H NMR: δ 1.39 (1H, d, CH_2, *endo*); 1.68 (1H, m, CH_2, *exo*, *endo*); 2.42 (1H, d, CH_2, *exo*); 2.48 (3H, s, CH_3, *endo*); 2.49 (3H, s, CH_3, *exo*); 3.97 (1H, m, CH, *exo*); 4.24 (1H, m, CH, *exo*, *endo*); 4.35 (1H, m, CH, *endo*); 5.79 (1H, m, CH=CH, *exo*, *endo*); 6.08 (1H, tt, HCF_2, $^2J_{HF} = 51.9$ Hz, *exo*); 6.56 (1H, m, CH=CH, *exo*, *endo*); 7.37 (2H, d, Ar, *endo*); 7.39 (2H, Ar, *exo*); 7.62 (2H, d, Ar, *endo*); 7.69 (2H, Ar, *exo*). ^{19}F NMR: δ_A −112.46, δ_B −114.42 AB (2F, CF_2, $J_{AB} = 302.0$ Hz); δ_A −130.01, δ_A −131.30 AB (2F, CF_2, $J_{AB} = 286.6$ Hz); −138.18 (2F, dm, HCF_2, $J_{FH} = 55.0$ Hz). MS (70 eV) *m/z* (%) 444 (5) [M^+], 289 (99) [$M^+ - SO_2Tol$].

Anal. Calcd. for $C_{17}H_{14}F_6O_3S_2$: C 45.95; H 3.18; S 14.43. Found: C 46.10 H 3.24; S 14.51.

4.3. Synthesis of 3,3,4,4,5,5-hexafluoro-1-(p-tolylsulfonyl)-1-phthalimidothiopentane-2-on (**7b**)

Phtalimidosulfenyl chloride (7.0 g, 32.7 mmol) was added to a solution of sulfone **6b** (8.15 g, 23.4 mol) in 100 ml of dry chloroform and the mixture was stirred at 20 °C for 6 h. Some undissolved material was filtered off and solvent was removed from mother liquor in vacuum (20 mmHg). The residue was treated with 70 ml of diethyl ether to give white crystalline product, which contained 10 mol% of phthalimide and was used for further transformations without additional purification. Yield of crude product was 80%, mp 135–140 °C (decomp.).

^{1}H NMR: δ 2.50 (3H, s, CH_3); 5.24 (1H, s, CH); 6.15 (1H, tt, HCF_2, $^2J_{HF} = 52.0$ Hz, $^3J_{HF} = 5.6$ Hz); 7.55 (2H, d, Ar); 7.82–7.85 (2H, m, Ar); 7.96–7.99 (2H, m, Ar); 8.07 (2H, d, Ar). 10 mol% admixture of phthalimide: 7.77, 7.86 (m, PhthN). ^{19}F NMR: δ_A −119.73, δ_B −120.85 AB (CF_2, 2F, $^2J_{AB} = 296.0$ Hz); δ_A −130.87, δ_B −131.48 AB (CF_2,2F, $^2J_{AB} = 291.0$ Hz); −138.0 (HCF_2, dm, 2F, $J_{FH} = 52.0$ Hz).

Anal. Calcd. for $0.9C_{20}H_{13}F_6NO_5S_2 + 0.1C_8H_5NO_2$: C 46.30; H 2.50; N 2.87; S 11.82. Found: C 45.80; H 2.55; N 3.12; S 11.99.

4.4. Synthesis of 5,6-dihydro-6-(p-tolylsulfonyl)-2H-thiins (**9**, **10** and **11**) from 5,6-dihydro-6-(2,2,3,3,4,4-hexafluorobutyryl)-6-(p-tolylsulfonyl)-2H-thiins (**3a**, **3b**, **4** and **5**): general procedure

Sodium hydroxide (0.36 g, 9 mmol) was added to a solution of appropriate thiins **9**, **10** and **11** (3 mmol) in 20 ml of dioxane–water mixture (5:1). The mixture was stirred at room temperature for 72 h and filtered. Solvents were removed in vacuum (20 mmHg) and residue was treated with 20 ml of diethyl ether. Ether solution was washed with 10 ml of water, dried over $CaCl_2$ and evaporated. Residue was extracted with hot hexane (10 × 10 ml) and hexane solution was concentrated up to 1/3 of volume and cooled. The precipitated product was filtered and dried in vacuum.

4.4.1. 5,6-Dihydro-3,4-dimethyl-6-(p-tolylsulfonyl)-2H-thiin (**9**)

Yield 74%. Colorless crystals, mp 99–103 °C. ^{1}H NMR: δ 1.68 (3H, s, CH_3); 1.72 (3H, s, CH_3); 2.45 (3H, s, CH_3); 2.7 (2H, m, CH_2CH); 2.80 (1H, d, CH_2S); 3.28 (1H, d,CH_2S); 4.08 (1H, t, CHS); 7.34 (2H, d, Ar); 7.82 (2H, d, Ar). MS (70 eV) *m/z* (%) 282 (2) [M^+], 127 (99) [$M^+ - SO_2Tol$].

Anal. Calcd. for $C_{14}H_{18}O_2S_2$: C 59.54; H 6.42; S 22.71. Found: C 60.25; H 6.86; S 22.34.

4.4.2. 5,6-Dihydro-2,5-ethylene-6-(p-tolylsulfonyl)-2H-thiin (**10**)

Mixture of isomers (*endo*:*exo*, 1:2.5). Yield 75%. Colorless crystals, mp 86–88 °C.

^{1}H NMR: δ 1.21 (1H, m, CH_2); 1,71 (1H, dt, CH_2); 2.27 (1H, m, CH_2); 2.61 (1H, m, CH_2); 3.47, 3.58 (1H, m, CH, *endo*, *exo*); 4.12, 4.60 (1H, td, CH, *exo*, *endo*); 6.04, 6.35 (1H, t, CH=CH, *endo*, *exo*); 6.46, 6.60 (1H, t, CH=CH, *endo*, *exo*); 7.34, 7.81 (2H, d, Ar, *exo*, *endo*). MS (70 eV) *m/z* (%) 280 (3) [M^+], 125 (99) [$M^+ - SO_2Tol$].

Anal. Calcd. for $C_{14}H_{16}O_2S_2$: C 59.97; H 5.75; S 22.87. Found: C 60.0; H 5.70; S 22.74.

4.4.3. 5,6-Dihydro-2,5-methylene-6-(p-tolylsulfonyl)-2H-thiin (**11**)

Mixture of isomers (*endo*:*exo*, 1:2.4). Yield 44%. Colorless crystals, mp 40–50 °C. ^{1}H NMR (*exo*): δ_A 1.6, δ_B 2.1 AB (2H, CH_2, $J_{AB} = 9.8$ Hz), 2.45 (3H, s, CH_3), 3.83 (1H, s, CH), 3.97 (1H, s, CH), 4.16 (1H, s, CH), 5.98, 6.47 (2H, dd, CH=CH), 7.35, 7.83 (4H, d, Ar). ^{1}H NMR (*endo*): δ_A 1.62, δ_B 1.72 AB (2H, CH_2, $J_{AB} = 9.4$ Hz), 2.45 (3H, s, CH_3), 3.87 (1H, s, CH), 4.2 (1H, s, CH), 4.98 (1H, d, CH, $^3J_{HH} = 3.5$ Hz), 6.07, 6.49 (2H, dd, CH=CH), 7.34, 7.77 (4H, d, Ar). MS (70 eV) *m/z* (%) 266 (4) [M^+], 111 (100) [$M^+ - SO_2Tol$].

Anal. Calcd. for $C_{13}H_{14}O_2S_2$: C 58.62; H 5.30; S 24.07. Found: C 58.0; H 5.05; S 23.56.

4.5. Synthesis of 2-difluoroacetyl-6H-thiin (**25a**)

Thiin **3a** (10 g, 27.78 mmol) was dissolved in 100 ml of 95% methanol and solution was allowed to stay at room temperature for 72 h. Solvent was evaporated in vacuum (20 mmHg), residue was treated with 150 ml of boiling diethyl ether and solvents was evaporated. Residue was chromatographed over silica gel with mixture of chloroform–hexane (1:1) as eluent. The fraction with R_f 0.53 was collected. After removing of solvents the residue was treated with hexane to give green crystals. Yield 2 g, 35%, mp 52–53 °C. IR (KBr) ν 2920 (Alk C–H); 1690 (C=O); 1630 (C=C).

^{1}H NMR: δ 1.90 (3H, s, CH_3), 1.99 (3H, s, CH_3), 3.25 (2H, s, CH_2), 6.14 (1H, t, HCF_2, $^2J_{HF} = 53.7$ Hz), 7.22 (1H, s, CH=). ^{19}F NMR: $\delta-$ 121.86 (1F, s, HCF_2), −122.04 (1F, s, HCF_2). MS (70 eV) m/z (%) 204 (50) [M^+], 189 (100) [$M^+ - CH_3$].

Anal. Calcd. for $C_9H_{10}F_2OS$: C 52.93; H 4.94; S 15.70. Found: C 52.90; H 5.05; S 15.71.

4.6. Synthesis of 2-(2,2,3,3,4,4-hexafluorobutyryl)-6H-thiin (**25b**)

Thiin **3b** (4.40 mmol) was dissolved in the mixture of 15 ml of benzene and 6 ml of 90% methanol. Solution was kept stirring and heating at 70 °C for 72 h and solvents were evaporated in vacuum (20 mmHg). The residue was extracted with 100 ml of diethyl ether, ether solution was consecutively washed with 100 ml of saturated solution of $NaHCO_3$ and 100 ml of water. After drying over Na_2SO_4 ether was evaporated and residue was chromatographed over silica gel using a mixture chloroform–hexane (1:1) as eluent. The fraction with R_f 0.6 was collected. Green oil. Yield 34%.

^{1}H NMR: δ 1.92 (3H, s, CH_3), 2.01 (3H, s, CH_3), 3.27 (2H, s, CH_2), 6.33 (1H, tt, HCF_2, $^2J_{HF} = 52.6$ Hz, $^3J_{HF} = 5.9$ Hz), 7.33 (1H, s, CH=). ^{19}F NMR: $\delta-$ 113.0 (2F, m, CF_2), −132.41 (2F, m, CF_2), −137.9 (2F, dm, HCF_2).

Anal. Calcd. for $C_{11}H_{10}F_6OS$: C 43.42; H 3.31; S 10.54. Found: C 43.39; H 3.28; S 10.60. MS (70 eV) m/z (%) 304 (47) [M^+], 289 (99) [$M^+ - CH_3$].

4.7. 2,5-Ethylene-6-(2,2,3,3,4,4-hexafluoro-1-p-tolylsulfonatebut-1-ylidene)-5,6-dihydro-2H-thiin (**26**)

A solution of thiin **4** (2.1 g, 4.58 mmol) in 30 ml of 95% methanol was refluxed for 72 h and solvent was evaporated up to 1/2 of volume. Precipitated crystals were filtered, washed with small amount of cold methanol and dried in vacuum.

Yield 0.277 g, 13%. Colorless crystals, mp 94–96 °C. IR (KBr) ν 2970 (Alk C–H); 1620 (C=C). ^{1}H NMR δ 1.57–1.61 (1H, dm, CH_2), 1.72–1.86 (2H, m, CH_2), 2.07–2.17 (1H, m, CH_2), 2.45 (3H, s, CH_3), 3.87 (1H, m, CH), 4.17 (1H, m, CH), 5.91 (1H, tt, HCF_2, $^2J_{HF} = 52.2$ Hz, $^3J_{HF} = 5.7$ Hz), 6.26 (1H, t, CH=), 6.67 (1H, t, CH=), 7.31 (2H, d, Ar), 7.84 (2H, d, Ar). ^{19}F NMR: δ −109.06 (2F, m, CF_2); δ_A −132.43, δ_B −132.97 AB (2F,CF_2, $J_{AB} = 282$ Hz); −138.26 (2F, dm, HCF_2, $J_{FH} = 52$ Hz). MS (70 eV) m/z (%) 458 (2) [M^+].

Anal. Calcd. for $C_{18}H_{16}F_6O_3S_2$: C 47.16; H 3.52; S 13.99. Found: C 47.01; H 3.65; S 14.00.

4.8. X-ray structure determination of thiin **4**

Crystal data: $C_{18}H_{16}F_6O_3S_2$, $M = 458.43$, monoclinic, $a = 21.040(4)$ Å, $b = 9.773(2)$ Å, $c = 20.854(2)$ Å, $\beta = 116.5(1)°$, $V = 3837.5$ Å^3, $Z = 8$, $d = 1.587$ g cm^{-1}, space group $C2/c$, $\mu = 31.85$ cm^{-1}, $F(0\,0\,0) = 1883.9$, crystal size ca. 0.43 mm × 0.46 mm × 0.50 mm. All crystallographic measurements were performed at 18 °C on a CAD-4 Enraf-Nonius diffractometer operating in the ω–2θ scan mode (the ratio of the scanning rates $\omega/2\theta = 1.2$). Intensity data were collected within the range $2° < \theta < 70°$ ($0 < h < 22$, $0 < k < 11$, $-24 < l < 24$) using graphite monochromated Cu Kα radiation ($\lambda = 1.54178$ Å). Intensities of 5005 reflections (3129 unique reflection, $R_{int} = 0.037$) were measured. The data were corrected for Lorentz and polarization effects and the empirical absorption correction based on azimuthal scan data [14] was applied. The structure was solved by direct methods and refined by full-matrix least-squares technique in the anisotropic approximation using the CRYSTALS program package [15]. The 2090 reflections with $I > 3\sigma(I)$ were used in the refinement. All hydrogen atoms were located in the different Fourier maps and included in the final refinement with fixed positional and thermal parameters. Convergence was obtained at $R = 0.051$ and $R_w = 0.058$, GOF = 1.139 (262 refined parameters; observed/variable 8.0; the largest and minimal peaks in the final difference map, 0.40 and −0.43 e Å^{-3}). Chebushev weighting scheme [16] with parameters 2.57, 0.26, 1.88, and −0.25 was used.

Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 200253. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).

Acknowledgements

The authors are grateful to V.M. Bzhezovsky and M.B. Chura for quantum-chemical calculations.

References

[1] J.-P. Begue, D. Bonnet-Delpon, Tetrahhedron 47 (1991) 3207–3258.
[2] M.H. Gelb, J. Am. Chem. Soc. 108 (1986) 3146–3147;

S. Thaisrivongs, D.T. Pals, W.M. Kati, S.R. Turner, L.M. Thomaco, W. Walt, J. Med. Chem. 29 (1986) 2080–2087;
R.J. Cregge, S.L. Durham, R.A. Farretall, J. Med. Chem. 41 (1998) 2461–2480.
[3] S.V. Yemets, Yu.P. Bandera, V.M. Timoshenko, Yu.G. Shermolovich, J. Fluorine Chem. 115 (2002) 175–181.
[4] C. Najera, M. Yus, Tetrahedron 55 (1999) 10547–10558.
[5] H. Fischer, U. Gerbing, K. Treirer, Hofmann J. Chem. Ber. 123 (1990) 725–732.
[6] F.H. Allen, O. Kennard, D.G. Watson, L. Brammer, A.G. Orpen, R. Taylor, J. Chem. Soc. Perkin Trans. II (1987) S1–S19.
[7] E. Vedejs, J.S. Stults, R.J. Wilde, J. Am. Chem. Soc. 110 (1988) 5452–5460.
[8] M. Hojo, Synthesis 12 (1986) 1016–1017.
[9] J.J.P. Stewart, J. Comput.-Aid. Mol. Des. 4 (1) (1990) 1–105.
[10] M.J.S. Dewar, J.J.P. Stewart, J. Chem. Soc. Faraday Trans. II 80 (1984) 227–233.
[11] A. Banerjee, N. Adams, J. Simons, R. Shepard, J. Phys. Chem. 89 (1985) 52–57.
[12] G.S. Hammond, J. Am. Chem. Soc. 77 (1955) 334–338.
[13] Yu.G. Shermolovich, V.M. Timoshenko, V.V. Listvan, L.N. Markovsky, Zhur. Org. Chim. (Russia) 34 (1998) 1167–1171.
[14] A.C.T. North, D.C. Phillips, F.S. Mathews, Acta Crystallogr. A24 (1968) 351–359.
[15] D.J. Watkin, C.K. Prout, J.R. Carruthers, P.W. Betteridge, Crystals Issue 10, Chemical Crystallography Laboratory, University of Oxford, Oxford, 1996.
[16] J.R. Carrythers, D.J. Watkin, Acta Crystallogr. A35 (1979) 698–699.