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Synthesis of 5,6-dihydro-2H-thiins and 2,3-dihydro-1,4-oxathiins based on 1-benzylsulfonyl-1,1-dihydropolyfluoroalkan-2-ones

S.V. Yemets*, Yu.P. Bandera, V.M. Timoshenko, Yu.G. Shermolvich

Institute of Organic Chemistry of the National Academy of Sciences of Ukraine, Murmanska Street 5, 02094 Kiev-94, Ukraine

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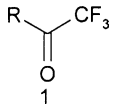
Abstract

1-Benzylsulfonyl-1,1-dihydropolyfluoroalkan-2-ones react with phthalimidosulfenyl chloride or succinimidosulfenyl chloride to form the sulfenylated products on the active methylene group, 1-benzylsulfonyl-1-phthalimido(succinimido)thiopolyfluoroalkan-2-ones. Decomposition of the latter leads to formation of 1-benzylsulfonyl-1-thioxopolyfluoroalkan-2-ones. These compounds easily undergo the hetero Diels–Alder reaction with electron-rich 1,3-dienes as dienophiles and with electron-rich olefins as hetero-1,3-dienes. Polyfluoroalkyl substituted derivatives of six-membered sulfur-containing heterocycles, 5,6-dihydro-2H-thiins and 2,3-dihydro-1,4-oxathiins, are obtained as a result of these reactions.

Keywords: Polyfluoroalkyl ketone; Phthalimidosulfenyl chloride; Succinimidosulfenyl chloride; α-Thioxoketone; Thiin; Oxathiin

1. Introduction

Fluorinated compounds are widely used in synthetic and medical chemistry due to their important physical and chemical properties. In particular, polyfluorinated ketones (**1**) are effective building blocks [1] and bioactive compounds with the properties of enzyme inhibitors [2]. The strong electron-withdrawing character of the polyfluoroalkyl substituent causes increased activity of the carbonyl group of the ketone towards nucleophilic reagents. The ketone can react with the nucleophilic group, which is the active site of an enzyme, and inhibit the last one. Other substituents, R, at the carbonyl group of polyfluoroketones (**1**) have a great influence on the in vivo transport of the compound and on the stability of the adduct of the ketone with the enzyme [3].



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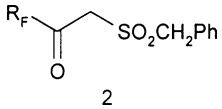
We were interested in the synthesis of the new fluorine containing ketones with heterocyclic substituents based on easily available 1-benzylsulfonyl-1,1-dihydropolyfluoroketones (**2**) [4].



2

It is known, that the activated methylene group of a β-diketone easily transforms into the thiocarbonyl group [5] forming highly reactive α-thioxoketones (**3**). In previous work [5–7], it was demonstrated that different α-thioxoketones reacted as active dienophiles and hetero-1,3-dienes in [4+2]-cycloaddition reactions, giving corresponding thiins (**4**) and 1,4-oxathiins (**5**) (Scheme 1).

We have investigated the reaction of 1,1-dihydropolyfluoroketones (**2**), containing activated methylene groups, with phthalimidosulfenyl chloride or succinimidosulfenyl chloride and have studied properties of the products synthesized.

2. Results and discussion

2.1. Synthesis of 1-benzylsulfonyl-1-imidothiopolyfluoroalkan-2-ones

We have found that polyfluoroalkyl ketone (**2a**) reacts with phthalimidosulfenyl chloride (**6**) at room temperature in chloroform giving a stable crystalline phthalimidothio derivative (**8**). The interaction with succinimidosulfenyl chloride under the same conditions results in the formation

* Corresponding author. Fax: +380-44-573-2693.
E-mail address: sherm@ukrpack.net (S.V. Yemets).

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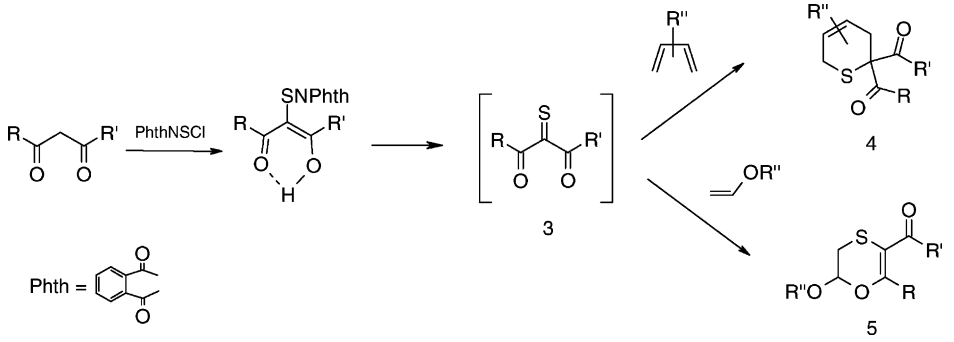
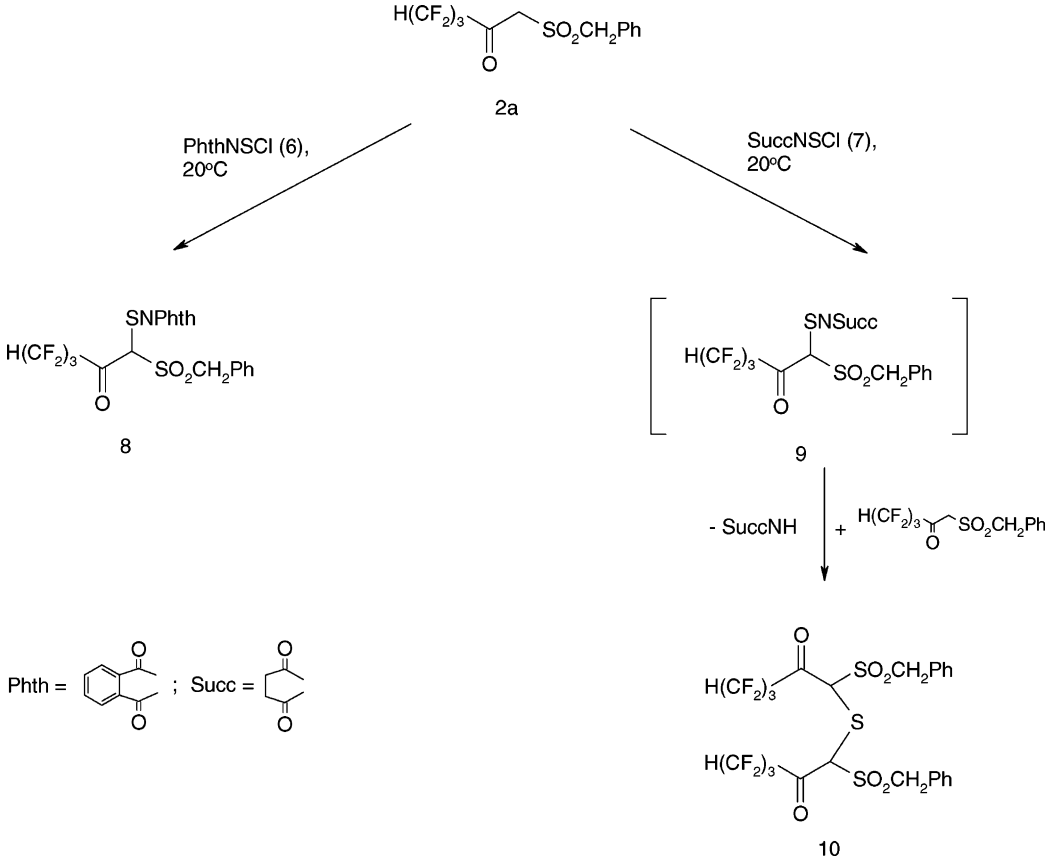


Scheme 1. Generation of α-thioxoketones from ketones.

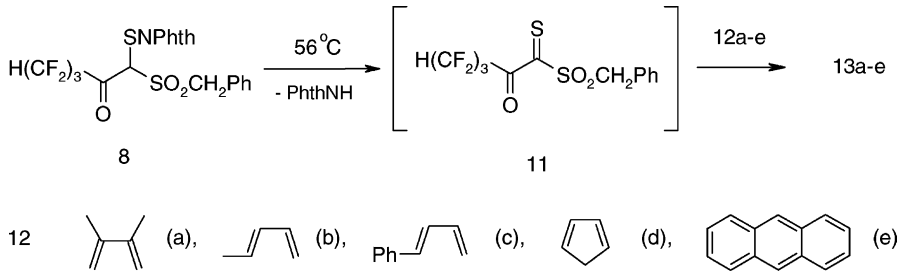
of sulfides (**10**) irrespective of the ratio of the starting reagents. The process probably passes through a step involving the formation of the highly reactive succinimido derivative (**9**), which reacts further with another molecule of the starting ketone with the elimination of succinimide (Scheme 2).

The phthalimido derivative (**8**) as well as the sulfide (**10**) exist both in the solid state and in $CDCl_3$ solution in the keto form. This is confirmed by the presence of absorption bands due to C=O groups at 1730 and 1760 cm^{-1} for compound (**8**) and at 1755 cm^{-1} for compound (**10**) in the IR spectra. The absorption bands of the hydroxyl groups for tautomeric enolic forms and are absent in these IR spectra. Moreover, proton signals of the CHS group at 5.1 ppm for compound (**8**) and at 5.6 ppm for compound (**10**) were formed in the ^1H NMR spectra.

It should be mentioned that the reaction produces only one of the two possible diastereomers of the sulfide (**10**), confirmed by the presence of only one set of signals in the ^{19}F NMR spectrum of the reaction mixture and in the ^1H and ^{19}F NMR spectra of the isolated product. However, isomerization of compound (**10**) takes place over time; after storage of compound (**10**) for 3 months, 40% of the other diastereomer has been observed in the product. In $CDCl_3$ solution, 25% of



Scheme 2. Reaction of 1-benzylsulfonyl-3,3,4,4,5,5-hexafluoropentan-2-one (**2a**) with phthalimidosulfenyl chloride and succinimidosulfenyl chloride.



Scheme 3. Generation of 1-benzylsulfonyl-3,3,4,4,5,5-hexafluoro-1-thioxoalkan-2-one (**11**) and its interaction with 1,3-dienes.

the other isomer appeared in 1 day. The isomerization process probably takes place through enolization of ketone (**10**).

Polyfluoroalkyl ketone (**2b**) is inert towards to phthalimidosulfenyl chloride and succinimidosulfenyl chloride even after prolonged refluxing in chloroform. Such behavior can be explained by the lower acidity of the methylene group in compound (**2b**), due to the lower electron-acceptor nature of the HCF_2CO group compared with the $H(CF_2)_3CO$ group. Compound (**2b**) reacts with phthalimidosulfenyl chloride only in the presence of triethylamine, giving a complicated mixture of unidentified products.

2.2. Generation of 1-benzylsulfonyl-1-thioxopolyfluoroalkan-2-ones and their interaction with 1,3-dienes

Compound (**8**) undergoes complete decomposition with the evolution of phthalimide even at room temperature on dissolving in Me_2SO-d_6. The ^1H NMR spectrum indicates the presence of phthalimide signals at 7.84 ppm (4H, s, Ar) and at 11.34 ppm (1H, s, NH). Phthalimide and unidentified products were formed also under refluxing of phthalimido derivative (**8**) in chloroform.

Decomposition of compound (**8**) in the presence of 1,3-dienes (**12**) (Scheme 3), as trapping reagents for unstable α-thioxoketone (**11**), has allowed a number of new polyfluoroalkyl ketones (**13a–e**) to be obtained, containing the thiin moiety in the α position (Table 1). Reaction proceeds with regioselectivity and diastereoselectivity. Thus, in the case of cyclopenta-1,3-diene the product formed (**13d**) consists of two diastereomers in the ratio 2.4:1. For 1-methylbuta-1,3-diene and 1-phenylbuta-1,3-diene, the formation of two regioisomers is observed, each of which consists of two diastereomers. The ratio of isomers of product (**13b**) is 2.5:2.3:1.4:1 and of product (**13c**) is 3.7:2.1:1.5:1.

However, the pattern of the NMR spectra does not allow definition and assignment of each individual isomer in the mixture. Compounds (**13b–d**) decomposed on attempting to separate oily products by column chromatography on silica gel.

The anthracene derivative (**13e**) can also be utilized to generate thione (**11**). It undergoes a retro Diels–Alder reaction on heating and the compound formed (**11**) reacted with 2,3-dimethylbuta-1,3-diene to give adduct (**13a**) (Scheme 4).

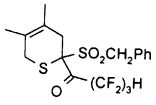
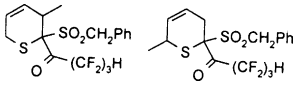
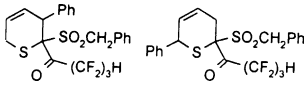
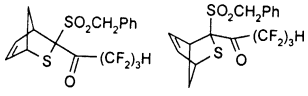
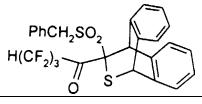
The difluoromethyl ketone bearing the thiin fragment (**13f**) was obtained by reaction of compound (**2b**) with imidosulfenyl chlorides (**6**, **7**) in the presence of triethylamine and 2,3-dimethylbuta-1,3-diene. Obviously, this process also proceeds through the formation of sulfenamide (**14**) and α-thioxoketone (**15**) (Scheme 5).

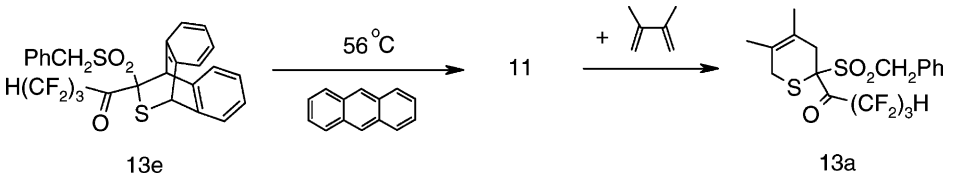
2.3. Interaction of 1-benzylsulfonyl-1-thioxopolyfluoroalkan-2-ones with alkenes

As expected, α-thioxoketone (**11**) appeared to be an active hetero-1,3-diene in a [4+2]-cycloaddition reaction. It was obtained from sulfenamide (**8**) in the presence of styrene or alkylvinyl ethers and this allowed the synthesis of a number of new fluorine containing 1,4-oxathiins (**16–18**) (Scheme 6).

The reaction occurs completely regioselectively as in the case of the reaction of α,α′-dioxothioketones (**3**) [5] and *o*-thioquinones [6] with olefins. We observed only

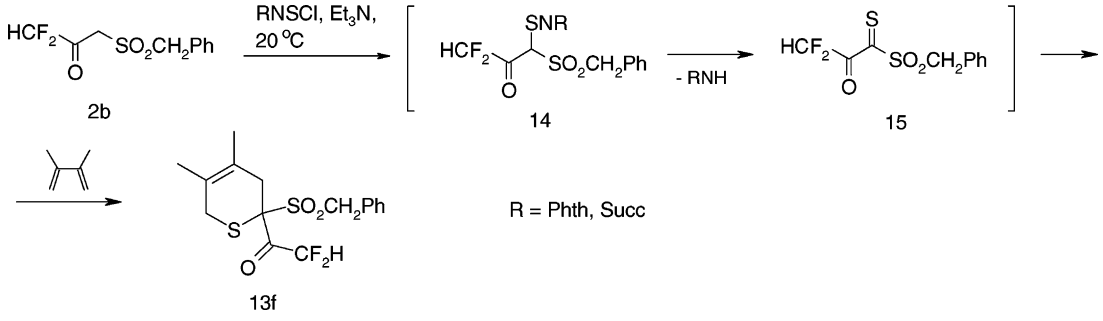
Table 1
5,6-Dihydro-2H-thiins (**13a–e**)

Number	Product
13a	
13b	
13c	
13d	
13e	



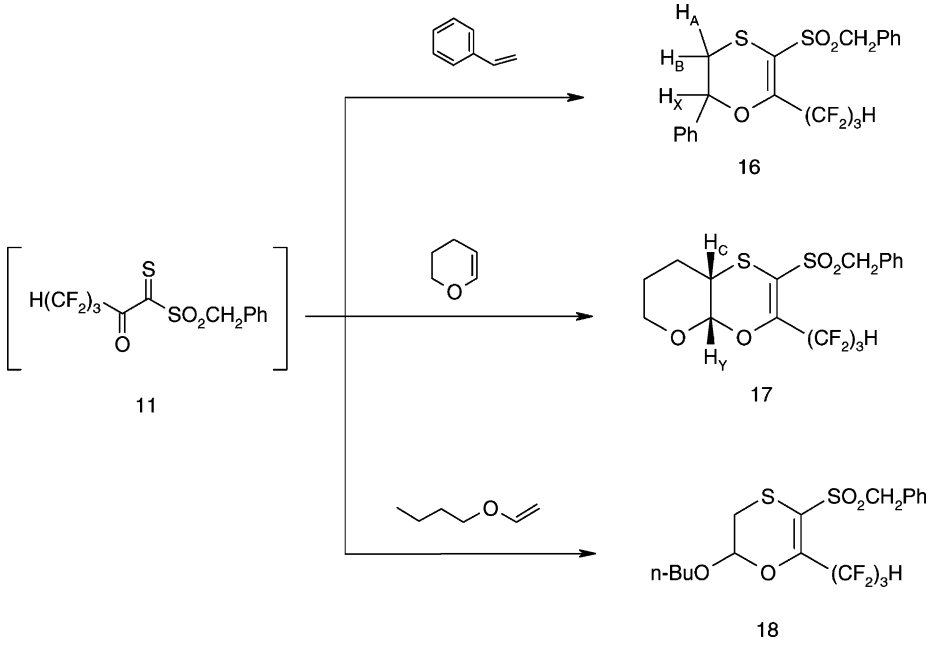
13e 13a

Scheme 4. Decomposition of anthracene derivative (**13e**).



2b 14 15 13f

Scheme 5. Generation of 1-benzylsulfonyl-3,3-difluoro-1-thioxopropan-2-one (**15**) and its interaction with 1,3-diene.



11 16 17 18

Scheme 6. Formation of 2,3-dihydro-1,4-oxathiins.

a single isomer in the ^{1}H and ^{19}F NMR spectra of the crude products (**16–18**). Structures of compounds (**16–18**) are confirmed by NMR spectroscopy data. In particular, signals of an ABX system are present in the ^{1}H NMR spectrum of the oxathiin (**16**) in $CDCl_3$. There are signals of protons of the $C\underline{H}_A\underline{H}_BS$ fragment at 2.81 and 3.06 ppm ($^{2}J_{AB} = 13.7$ Hz, $^{3}J_{AX} = 1.9$ Hz, $^{3}J_{BX} = 8.9$ Hz) and proton of the $C\underline{H}_XO$ fragment at 5.09 ppm ($^{3}J_{AX} = 1.9$ Hz, $^{3}J_{BX} = 8.9$ Hz). In the case of compound (**17**) only one diastereomer has been obtained. The spin-coupling constant $^{3}J_{HH}$ for protons of $SC\underline{H}_C C\underline{H}_Y O_2$ fragment is 2.5 Hz that corresponds to *cis*-connection of pyran and oxathiin rings [5,6].

3. Conclusion

We have shown that 1-benzylsulfonyl-1-thioxopolyfluoroalkan-2-ones can be simply generated from easily available starting materials, 1-benzylsulfonyl-1,1-dihydropolyfluoroalkan-2-ones and phthalimidosulfenyl chloride or succinimidosulfenyl chloride. These reactive intermediates were trapped

with electron-rich 1,3-dienes and alkenes. The new polyfluoroalkyl substituted 5,6-dihydro-2H-thiins and 2,3-dihydro-1,4-oxathiins were obtained as a result of these reactions.

4. Experimental

IR spectra were measured on a UR-10 spectrometer; ^{1}H and ^{19}F NMR spectra were recorded on Varian-VXR (^{1}H NMR: 300 MHz, ^{19}F NMR: 188 MHz) using Me_4Si as internal standard for ^{1}H NMR spectra, and C_6F_6 (−162.9 ppm) as internal standard for ^{19}F NMR spectra.

*4.1. Synthesis of 1-benzylsulfonyl-1-phthalimidothio-3,3,4,4,5,5-hexafluoropentan-2-one (**8**)*

1-Benzylsulfonyl-3,3,4,4,5,5-hexafluoropentan-2-one (**2a**) (23 mmol, 8.01 g) was added to a solution of phthalimidosulfenyl chloride (23 mmol, 4.91 g) in chloroform (30 ml). The mixture was stirred at 20 °C for 2 days. Colorless crystals were filtered off and washed with chloroform (5 ml). The product contains 20 mol% of phtalimide. This crude product was used for further transformations, as further recrystallization from chloroform or benzene did not allow to get out the admixture of phtalimide. Yield of crude product was 9.69 g, 75%.

Colorless crystals, mp 143–145 °C. IR (KBr): ν 1760, 1730 cm^{-1} (C=O); 1340, 1140 cm^{-1} (SO_2). ^{1}H NMR ($CDCl_3$): δ 4.59, 5.47 (2H, CH_2, $^2J_{AB}$ = 13.5 Hz); 5.14 (1H, s, CH); 6.13 (1H, t.t, HCF_2, $^2J_{HF}$ = 51.6 Hz, $^3J_{HF}$ = 5.7 Hz); 7.43 (3H, m, Ph); 7.54 (2H, m, Ph); 7.85, 7.99 (4H, m, PhthN); 20 mol% admixture of phthalimide: 7.77, 7.86 (m, PhthN). ^{19}F NMR ($CDCl_3$): δ −137.94 (2F, d, HCF_2, $^2J_{HF}$ = 51.6 Hz); −130.90 (2F, s, CF_2); −121.74, −119.21 (2F, CF_2, $^2J_{AB}$ = 293.3 Hz).

Anal. Calcd. for $0.8C_{20}H_{13}F_6NO_5S_2 + 0.2C_8H_5NO_2$: C 46.99; H 2.56; N 3.11; S 11.40. Found: C 46.48; H 2.40; N 2.91; S 10.80.

*4.2. Synthesis of bis(1-benzylsulfonyl-3,3,4,4,5,5-hexafluoro-2-oxopentyl)sulfide (**10**)*

A solution of ketone (**2a**) (3.3 mmol, 1.15 g) in chloroform (5 ml) was added to a solution of succinimidosulfenyl chloride (5 mmol, 0.83 g) in chloroform (10 ml). The reaction mixture was stirred at 20 °C for 4 days, washed with water (5 × 50 ml) and organic layer was dried over Na_2SO_4. Chloroform was removed in vacuum (20 mmHg), the residue was treated with diethyl ether (7 ml), an insoluble solid was filtered off and ether solution was evaporated in vacuum (20 mmHg). The yield of crude product was 0.93 g. It was dissolved in diethyl ether (4.5 ml) and admixtures were precipitated by addition of *n*-hexane (6.5 ml). The solution was separated and evaporated. Oily residue was dried in vacuum (0.07 mmHg). The product solidified at storage. Yield 0.54 g, 45%.

Yellowish solid, mp 51–56 °C. IR (film): ν 1755 cm^{-1} (C=O); 1335, 1150 cm^{-1} (SO_2). ^{1}H NMR ($CDCl_3$): δ 4.45, 4.74 (2CH_2, 4H, $^2J_{AB}$ = 13.5 Hz); 5.60 (2H, s, 2CH); 6.08 (2H, t.t, 2HCF_2, $^2J_{HF}$ = 52.2 Hz, $^3J_{HF}$ = 4.8 Hz); 7.45 (10H, m, 2Ph); (25 mol% admixture of other diastereomer was appeared after standing over 1 day in solution: 4.45, 4.84 (2CH_2, $^2J_{AB}$ = 13.2 Hz); 4.90 (s, 2CH); 6.23 (t.t, 2HCF_2, $^2J_{HF}$ = 52.5 Hz, $^3J_{HF}$ = 5.4 Hz)).

^{19}F NMR ($CDCl_3$): δ −137.55 (4F, m, 2HCF_2); −130.45, −130.07 (4F, 2CF_2, $^2J_{AB}$ = 295.2 Hz); −120.92, −120.19 (4F, 2CF_2, $^2J_{AB}$ = 292.9 Hz); (admixture of other diastereomer: −137.83 (m, 2HCF_2); −131.37, −129.43 (2CF_2, $^2J_{AB}$ = 290.7 Hz); −123.69, −119.87 (2CF_2, $^2J_{AB}$ = 282.6Hz)).

Anal. Calcd. for $C_{24}H_{18}F_{12}O_6S_3$: C 39.67; H 2.50; S 13.24. Found: C 39.20; H 2.60; S 12.89.

*4.3. Synthesis of 5,6-dihydro-2H-thiins (**13a–e**) and 2,3-dihydro-1,4-oxathiins (**16–18**) based on sulfenamide (**8**)*

A corresponding diene or alkene (1 mmol) was added to the suspension of compound (**8**) (1 mmol, 0.53 g) in chloroform (7 ml). The mixture was stirred and refluxed for 3 h. After cooling, precipitate of phthalimide was filtered off and chloroform solution was evaporated in vacuum (20 mmHg). The residue was extracted with diethyl ether (3 ml) and filtered from insoluble solid in the case of compounds (**13a–d**, **16–18**). Ether solution was evaporated in vacuum (20 mmHg) and corresponding cycloadduct obtained was dried in vacuum (0.07 mmHg). In the case of compound (**13e**) the residue after evaporation of chloroform was crystallized from benzene.

*4.3.1. 6-Benzylsulfonyl-6-(2,2,3,3,4,4-hexafluorobutyryl)-5,6-dihydro-3,4-dimethyl-2H-thiin (**13a**)*

Yield 0.38 g, 83%. Greenish oil.

^{1}H NMR ($CDCl_3$): δ 1.75 (6H, s, 2CH_3); 2.80, 3.07 (2H, CH_2, $^2J_{AB}$ = 15.4 Hz); 2.99, 3.26 (2H, CH_2, $^2J_{AB}$ = 14.5 Hz); 4.40, 4.58 (2H, $\underline{CH_2}$Ph, $^2J_{AB}$ = 13.2 Hz); 6.12 (1H, t.t, HCF_2, $^2J_{HF}$ = 52.5 Hz, $^3J_{HF}$ = 5.7 Hz); 7.33 (5H, s, Ph). ^{19}F NMR ($CHCl_3$): δ −137.93 (2F, m, HCF_2); −130.89 (2F, m, CF_2); −112.47 (2F, m, CF_2).

Anal. Calcd. for $C_{18}H_{18}F_6O_3S_2$: C 46.95; H 3.94; S 13.93. Found: C 47.00; H 3.81; S 13.60.

*4.3.2. 6-Benzylsulfonyl-6-(2,2,3,3,4,4-hexafluorobutyryl)-5,6-dihydro-2-methyl-2H-thiin, 6-benzylsulfonyl-6-(2,2,3,3,4,4-hexafluorobutyryl)-5,6-dihydro-5-methyl-2H-thiin (**13b**)*

Mixture of isomers. Yield 0.33 g, 73%. Greenish oil.

^{1}H NMR ($CDCl_3$): δ 1.30 (1.05H, d, CH_3, $^3J_{HH}$ = 7.2 Hz); 1.34 (0.97H, d, CH_3, $^3J_{HH}$ = 6.9 Hz); 1.43 (0.42H, d, CH_3, $^3J_{HH}$ = 7.2 Hz); 1.62 (0.57H, d, CH_3, $^3J_{HH}$ = 6.6 Hz); 2.91–3.81 (3H, m, $\underline{CH}$Me, CH_2); 4.31–4.93 (2H, m, $\underline{CH_2}$Ph); 5.82–6.51 (3H, m, CH=CH, HCF_2); 7.39 (5H, m, Ph).

^{19}F NMR ($CHCl_3$): δ −137.96 to−137.41 (2F, m, HCF_2); −133.10 to −128.56 (2F, m, CF_2); −115.38 to −108.80 (2F, m, CF_2).

Anal. Calcd. for $C_{17}H_{16}F_6O_3S_2$: C 45.74; H 3.61; S 14.36. Found: C 45.30; H 3.88; S 14.35.

*4.3.3. 6-Benzylsulfonyl-6-(2,2,3,3,4,4-hexafluorobutyryl)-5,6-dihydro-2-phenyl-2H-thiin, 6-benzylsulfonyl-6-(2,2,3,3,4,4-hexafluorobutyryl)-5,6-dihydro-5-phenyl-2H-thiin (**13c**)*

Mixture of isomers. Yield 0.48 g, 95%. Greenish oil.

^{1}H NMR ($CDCl_3$): δ 2.99–3.44 (2H, m, CH_2); 3.95 (0.15H, m, CHPh); 4.00 (0.12H, m, CHPh); 4.70 (0.29H, m, CHPh); 4.82 (0.44H, m, CHPh); 4.21–5.37 (2H, m, CH_2Ph); 5.70–6.62 (3H, m, CH=CH, HCF_2); 7.43 (10H, m, 2Ph).

^{19}F NMR ($CDCl_3$): δ −138.15 to −137.58 (2F, m, HCF_2); −131.47 to −130.70 (2F, m, CF_2); −114.27 to −112.11 (2F, m, CF_2).

Anal. Calcd. for $C_{22}H_{18}F_6O_3S_2$: C 51.97; H 3.57; S 12.61. Found: C 51.59; H 4.00; S 12.48.

*4.3.4. 6-Benzylsulfonyl-6-(2,2,3,3,4,4-hexafluorobutyryl)-5,6-dihydro-2,5-methylene-2H-thiin (**13d**)*

Yield 0.27 g, 61%. Yellowish oil. IR (film): ν 1720 cm^{-1} (C=O); 1325, 1150 cm^{-1} (SO_2).

^{1}H NMR ($CDCl_3$): δ 1.75, 2.23 (2H, CH_2, $^2J_{AB}$ = 10.2 Hz); 4.27 (1H, s, CH); 4.33 (1H, s, CH); 4.35, 4.65 (2H, CH_2Ph, $^2J_{AB}$ = 13.2 Hz); 5.94 (1H, m, CH=CH); 6.07 (1H, t.t, HCF_2, $^2J_{HF}$ = 52.5 Hz, $^3J_{HF}$ = 5.7 Hz); 6.54 (1H, d.d, CH=CH, $^2J_{HH}$ = 5.4 3.0Hz); 7.33 (5H, m, Ph); 29 mol% admixture of other diastereomer: 1.41, 1.75 (CH_2, $^2J_{AB}$ = 11.1 Hz); 4.13, 4.39 (CH_2Ph, $^2J_{AB}$ = 13.5 Hz); 4.35 (s, CH); 4.52 (s, CH); 6.12 (t.t, HCF_2, $^2J_{HF}$ = 52.2, $^3J_{HF}$ = 5.7 Hz); 6.17 (m, CH=CH); 6.68 (d.d, CH=CH, $^2J_{HH}$ = 5.4 3.0 Hz); 7.33 (m, Ph).

^{19}F NMR ($CHCl_3$): δ −138.18 (2F, m, HCF_2); −130.63 (2F, s, CF_2); −114.05, −112.62 (2F, CF_2, $^2J_{AB}$ = 302.3 Hz); 29 mol% admixture of other diastereomer: −138.18 (m, HCF_2); −129.99 (m, CF_2); −112.67, −112.02 (2F, CF_2, $^2J_{AB}$ = 299.1 Hz).

Anal. Calcd. for $C_{17}H_{14}F_6O_3S_2$: C 45.95; H 3.18; S 14.43. Found: C 45.60; H 3.40; S 14.59.

*4.3.5. 3-Benzylsulfonyl-1,4-o-benzene-3-(2,2,3,3,4,4-hexafluorobutyryl)-3,4-dihydro-1H-2-benzothiin (**13e**)*

Yield 0.55 g, 98%. Colorless crystals, mp 173–175 °C.

^{1}H NMR ($CDCl_3$): δ 2.07, 4.47 (2H, CH_2Ph, $^2J_{AB}$ = 12.7 Hz); 5.44 (1H, s, CH); 5.91 (1H, t.t, HCF_2, $^2J_{HF}$ = 52.2, $^3J_{HF}$ = 5.7 Hz); 6.01 (1H, s, CH); 7.06–7.51 (11H, m, Ar); 7.76–7.90 (2H, m, Ar).

^{19}F NMR ($CDCl_3$): δ −138.32 (2F, m, HCF_2, $^2J_{HF}$ = 52.2); −132.04, −131.24 (2F, m, CF_2, $^2J_{AB}$ = 284.6 Hz); −116.56, −113.49 (2F, m, CF_2, $^2J_{AB}$ = 302.8 Hz).

Anal. Calcd. for $C_{26}H_{18}F_6O_3S_2$: C 56.13; H 3.23; S 11.50. Found: C 56.10; H 3.14; S 11.66.

*4.3.6. 5-Benzylsulfonyl-6-(1,1,2,2,3,3-hexafluoropropyl)-2,3-dihydro-2-phenyl-1,4-oxathiin (**16**)*

Yield 0.32 g, 67%. Colorless crystals, mp 104-106 °C. IR (KBr): ν 1330, 1150 cm^{-1} (SO_2).

^{1}H NMR ($CDCl_3$): δ 2.81, 3.06 (2H, m, SCH_2, AB part of ABX system, $^3J_{AX}$ = 1.9 Hz, $^3J_{BX}$ = 8.9 Hz, $^3J_{AB}$ = 13.7 Hz); 4.51, 4.54 (2H, CH_2Ph, $^2J_{AB}$ = 13.5 Hz); 5.09 (1H, d.d, OCH, X part of ABX system, $^3J_{AX}$ = 1.9 Hz, $^3J_{BX}$ = 8.9 Hz); 6.19 (1H, t.t, HCF_2, $^2J_{HF}$ = 51.9 Hz, $^3J_{HF}$ = 5.5 Hz); 7.27 (2H, m, Ar); 7.41 (8H, m, Ar).

^{19}F NMR ($CHCl_3$): δ −138.95, −137.97 (2F, m, HCF_2, $^2J_{HF}$ = 51.9 Hz, $^2J_{AB}$ = 305.7 Hz); −130.50, −129.17 (2F, CF_2, $^2J_{AB}$ = 278.3 Hz); −110.42, −108.67 (2F, CF_2, $^2J_{AB}$ = 283.8 Hz).

Anal. Calcd. for $C_{20}H_{16}F_6O_3S_2$: C 49.79; H 3.34; S 13.29. Found: C 49.82; H 3.47; S 13.23.

*4.3.7. 9-Benzylsulfonyl-10-(1,1,2,2,3,3-hexafluoropropyl)-2,5,6,7-tetrahydro-4H-pyrano[2,3-b]1,4-oxathiin (**17**)*

Yield 0.30 g, 64%. Colorless crystals, mp 102–105 °C. IR (KBr): ν 1327, 1129 cm^{-1} (SO_2).

^{1}H NMR ($CDCl_3$): δ 1.41–1.87 (4H, m, $2CH_2$); 3.02–3.08 (1H, m, SCH, M part of AMXY system, $^3J_{AM}$ = 2.5 Hz, $^3J_{MX}$ = 4.5 Hz, $^3J_{MY}$ = 12.3 Hz); 3.69–3.85 (2H, m, CH_2); 4.49, 4.50 (2H, CH_2Ph, $^2J_{AB}$ = 14.1 Hz); 5.48 (1H, d, OCHO, A part of AMXY system, $^3J_{AM}$ = 2.5 Hz); 6.27 (1H, t.t, HCF_2, $^2J_{HF}$ = 52.0 Hz, $^3J_{HF}$ = 5.7 Hz); 7.40 (5H, s, Ph).

^{19}F NMR ($CDCl_3$): δ −138.85, −137.99 (2F, m, HCF_2, $^2J_{HF}$ = 52.0 Hz, $^2J_{AB}$ = 304.8 Hz); −130.53, −129.35 (2F, CF_2, $^2J_{AB}$ = 279.8 Hz); −110.65, −108.59 (2F, CF_2, $^2J_{AB}$ = 284.2 Hz).

Anal. Calcd. for $C_{17}H_{16}F_6O_4S_2$: C 44.16; H 3.49; S 13.87. Found: C 44.31; H 3.37; S 13.80.

*4.3.8. 5-Benzylsulfonyl-2-butoxy-6-(1,1,2,2,3,-3-hexafluoropropyl)-2,3-dihydro-1,4-oxathiin (**18**)*

Yield 0.41 g, 85%. Light brown solid, mp 65–66 °C. IR (KBr): ν 1330, 1150 cm^{-1} (SO_2).

^{1}H NMR ($CDCl_3$): δ 0.85 (3H, t, CH_3, $^3J_{HH}$ = 7.3 Hz); 1.29 (2H, m, CH_2); 1.50 (2H, m, CH_2); 2.65 (2H, d, SCH_2, $^3J_{HH}$ = 3.3 Hz); 3.55, 3.79 (2H, m, OCH_2, $^2J_{AB}$ = 9.7 Hz, $^3J_{HH}$ = 6.6 Hz); 4.41 (2H, s, CH_2Ph); 5.32 (1H, t, OCHO, $^3J_{HH}$ = 3.3 Hz); 6.18 (1H, t.t, HCF_2, $^2J_{HF}$ = 51.9 Hz, $^3J_{HF}$ = 5.7 Hz); 7.32 (5H, s, Ph).

^{19}F NMR ($CDCl_3$): δ −138.66 (2F, d, HCF_2, $^2J_{HF}$ = 51.9 Hz); −130.47, −129.52 (2F, CF_2, $^2J_{AB}$ = 280.5 Hz); −109.95, −109.32 (2F, CF_2, $^2J_{AB}$ = 286.8 Hz).

Anal. Calcd. for $C_{18}H_{20}F_6O_4S_2$: C 45.19; H 4.21; S 13.40. Found: C 45.01; H 3.92; S 13.29.

*4.4. Synthesis of thiin (**13e**) based on ketone (**2a**)*

A solution of the ketone (**2a**) (2.9 mmol, 1.01 g) and triethylamine (2.9 mmol, 0.29 g) in chloroform (8 ml) was dropped into a stirred mixture of phthalimidosulfenyl

chloride (2.9 mmol, 0.62 g) and anthracene (2.9 mmol, 0.52 g) in chloroform (7 ml), at 20 °C. The reaction mixture was stirred for a further 5 h at 20 °C. The precipitate of phthalimide was filtered off, chloroform was evaporated in vacuum (20 mmHg), the residue was washed with water (100 ml) and dried. Compound (**13e**) was recrystallized from benzene. Yield 0.81 g, 50%.

*4.5. Reaction of thiin (**13e**) with 2,3-dimethylbuta-1, 3-diene*

A mixture of compound (**13e**) (0.5 mmol, 0.28 g) and 2,3-dimethylbuta-1,3-diene (1 mmol, 0.08 g) in chloroform (7 ml) was refluxed with stirring for 3 h. Chloroform was evaporated in vacuum (20 mmHg) and the residue was extracted with diethyl ether (3 ml). The ether solution was evaporated and residue was dried in vacuum (0.07 mmHg). The yield of compound (**13a**) was 0.15 g, 65%.

Synthesis of 6-benzylsulfonyl-6-(2,2-difluoroacetyl)-5,6-dihydro-3,4-dimethyl-2H-thiin (**13f**) based on ketone (**2b**).

A solution of 1-benzylsulfonyl-3,3-difluoropropan-2-one (**2b**) (2 mmol, 0.50 g) and triethylamine (2 mmol, 0.20 g) in benzene (5 ml) was added to a mixture of phthalimidosulfenyl chloride (2 mmol, 0.43 g) in benzene (5 ml) at 20 °C and stirring. After 30 min, 2,3-dimethylbuta-1,3-diene (4 mmol, 0.33 g) was added to the reaction mixture and stirring was continued for additional 20 h. The solid was filtered and benzene solution was evaporated in vacuum (20 mmHg). The residue was extracted with hot (65 °C) *n*-hexane (3 ml × 3 ml) and after cooling to 20 °C the solution was decanted from precipitated oil. *n*-Hexane was evaporated in vacuum (20 mmHg) and the oil was dried in vacuum (0.07 mmHg).

Yield 0.34 g, 47%. Greenish oil.

^{1}H NMR ($CDCl_3$): δ 1.70 (3H, s, CH_3); 1.75 (3H, s, CH_3); 2.67, 2.97 (2H, CH_2, $^2J_{AB} = 15.9$ Hz); 2.97, 3.22 (2H, CH_2, $^2J_{AB} = 15.6$ Hz); 4.31, 4.39 (2H, $\underline{CH_2}$Ph, $^2J_{AB} = 13.0$ Hz); 6.39 (1H, t, HCF_2, $^2J_{HF} = 52.8$ Hz); 7.32 (5H, s, Ph).

^{19}F NMR ($CDCl_3$): δ −123.86, −122.37 (m, HCF_2, $^2J_{HF} = 52.8$ Hz, $^2J_{AB} = 324.5$ Hz).

Anal. Calcd. for $C_{16}H_{18}F_2O_3S_2$: C 53.32; H 5.03; S 17.79. Found: C 52.93; H 5.09; S 18.02.

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