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Stereoselective synthesis of 3-[(perfluoroprop-1-en-2-yl)bicyclo[2.2.1]-hept-5-en-2-yl]sulfanes

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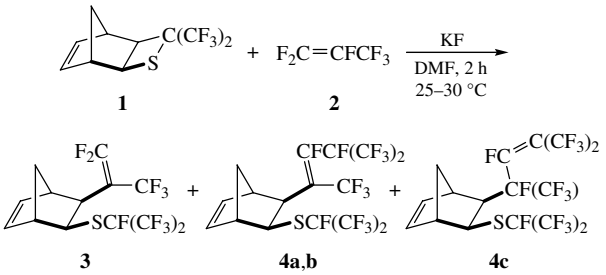
A new synthesis of 3-[(perfluoroprop-1-en-2-yl)bicyclo[2.2.1]hept-5-en-2-yl]sulfanes was developed based on the selective ring opening reaction of *exo*-3-thia-4,4-bis(perfluoroalkyl)tricyclo[4.2.1.$0^{2,5}$]non-7-ene by carbon and nitrogen nucleophiles.

Recently, we reported the stereoselective preparation of *exo*-4,4-bis(perfluoroalkyl)tricyclo[4.2.1.$0^{2,5}$]non-7-ene derivatives through the cycloaddition of quadricyclane to polyfluorinated ketones,[1] imines,[2] olefins[3] and thiocarbonyl compounds, including the high-yield synthesis of *exo*-3-thia-4,4-bis(trifluoromethyl)-tricyclo[4.2.$0^{2,5}$]non-7-ene **1**.[4] The presence of two powerful electron-withdrawing substituents in the –S–C$(CF_3)_2$– moiety results in generation of a substantial positive charge on sulfur and makes possible an attack of nucleophiles on the sulfur atom, for example, in hexafluorothioacetone[5] and 4-alkoxy-2,2-bis(trifluoromethyl)thiethanes.[6,7] Here, the ability of sulfur in **1** to react with carbon and nitrogen nucleophiles was used for the stereoselective synthesis of polyfluorinated norbornenes. Since compound **1** is known to exist as an *exo* isomer, one can expect that ring opening reactions involving C–S bond cleavage may result in the formation of corresponding norbornenes containing both substituents in the *exo* position.

Compound **1** is surprisingly stable to the action of a hard nucleophile (fluoride anion): unchanged **1** was recovered after treatment with CsF at an elevated temperature (DMF, 70 °C, 8 h). On the other hand, an exothermic reaction was observed when hexafluoropropene **2** was added to a mixture of **1** and a dry KF catalyst, resulting in moderate yield formation of ring opening product **3**,[4] along with a smaller amount of **4a–c** (Scheme 1).

A mixture of isomers **4a–c** (yield, 76%; **4a**:**4b**:**4c** ratio of 60:43:6) was isolated in a catalysed reaction of **1** with an excess of **2**. The structures of *trans* and *cis* isomers were assigned to compounds **4a** and **4b**, respectively, based on ^{19}F NMR spectra. Compound **4c** is believed to form as a result of well-known double bond migration under the action of F^-, and its structure is consistent with ^{19}F NMR and GC-MS data. The formation of **3** is a reversible process, since the treatment of this material with CsF (DMF, 25 °C, 2 h) resulted in the formation of an equimolar mixture of **1** and **4a**,**b**. This result can be explained

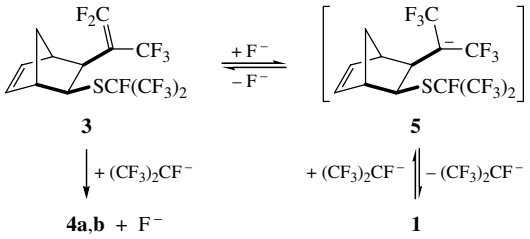


1 **2** **3** **4a**,**b** **4c**

ratio **3**:**4a**–**c**, 90:10
yield of **3**, 65%

Scheme 1

based on the mechanism involving the generation of anion **5** by an attack of the fluoride anion on the fluorinated double bond of **3**, followed by its intramolecular cyclization through the attack of carbanion **5** on positively charged sulfur with the formation of **1** (Scheme 2). Liberated in this process $(CF_3)_2CF^-$ is consumed by reaction with **3** to give isomers **4a**,**b** and the fluoride anion.

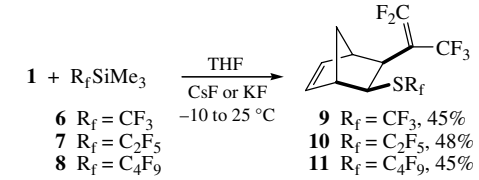


3 **5**

4a,**b** + F^- **1**

Scheme 2

The treatment of **1** with perfluoroalkyl(trimethyl)silanes **6**[8,9]–**8**[10] in the presence of a CsF or KF catalyst also results in the ring opening reaction leading to compounds **9**–**11** (Scheme 3) isolated in moderate yields due to the formation of by-products similar to **4a**–**c**.



Scheme 3

The typical purity of **9**–**11** (isolated after vacuum distillation) was ~95–98% and all attempts to improve the selectivity of this reaction by varying the solvent, temperature and catalyst failed.

Surprisingly, the reaction of **1** with alkyllithium derivatives at a low temperature is highly selective. Both MeLi and Bu^nLi rapidly react with **1** yielding compounds **12** and **13**, respectively (Scheme 4). The addition of alkyllithium in hexane to a solution of **1** in dry THF at –75 °C was followed by the quenching of cold (–70 °C) reaction mixture by 10% HCl, extraction by CH_2Cl_2, drying, and vacuum distillation of the product after the removal of the solvent.

Even hindered LDA gave compound **14** isolated in 68% yield. The interaction of less nucleophilic C_2F_5Li (generated *in situ* from C_2F_5I and Bu^nLi) was slow at –70 °C. However, after warming the reaction mixture to ambient temperature (~4 h), compound **10** (99.6% purity) was isolated in 85% yield. Note that an attempt to prepare compound **11** using *n*-C_4F_9Li under similar conditions failed, probably, due to a significantly lower stability of *n*-C_4F_9Li. Compound **1** reacts with Grignard reagents under mild conditions forming the corresponding ring opening products in high yields (Scheme 5).

The exothermic reaction rapidly proceeded in dry THF at 0–5 °C producing selectively compounds **15**–**17**. Less nucleophilic ethynylmagnesium bromide reacted with **1** significantly slower (20 h, 25 °C), producing ethynylsulfane **18** in 57% yield. This reaction was not as selective, and isolated **18** (~95% purity) was contaminated by other by-products. Despite the fact that reliable elemental analysis was not obtained for new materials due to high content and ratio of fluorine and sulfur, the proposed structures of **9**–**18** are in good agreement with ^1H, ^{13}C, ^{19}F NMR, IR and mass-spectrometric data.† The chemical shifts in the ^{19}F NMR spectra of compounds **3**, **9**–**18** (resonances at –60, –72 and –78 ppm, with relative intensities 3:1:1, respectively) are in good agreement with reported for $CF_2=C(CF_3)–CH_2CH(OR)SR$.[6] Broadening of fluorine resonances in ^{19}F NMR (and certain signals in ^{13}C NMR) spectra of **3**, **9**–**18** at ambient

† For **9**: bp 84–85 (19 Torr); purity 96%. IR (KCl, liq., ν/cm^{-1}): 1738, 1717 (sh, C=C). ^1H NMR ($CDCl_3$) δ: 1.74 (d, 1H, H_d, $J_{7c–7d}$ 9.75 Hz), 1.79 (dq, 1H, H_c, $J_{7c–7d}$ 9.75 Hz, $J_{H(7c)–F_a}$ 3.7 Hz), 2.72 [br. t, 1H, H(2), $J_{2–3}$ 8.47 Hz, $J_{H(2)–F_b}$ 6.4 Hz], 3.00 (s, 1H), 3.19 [m, 1H, H(1), $J_{4–7c}$ 1.0 Hz], 3.43 [dd, 1H, H(3), $J_{2–3}$ 8.47 Hz], 6.15 [dd, 1H, H(5), $J_{5–6}$ 5.75 Hz], 6.36 [dd, 1H, H(6), $J_{5–6}$ 5.75 Hz]. ^{19}F NMR (CD_2Cl_2, –50 °C) δ: –41.04 (s, 3F), –61.10 (dd, 3F, *J* 16.6 and 11.1 Hz), –70.64 (qd, 1F, *J* 16.6 and 6.4 Hz), –77.82 (m, 1F, *J* 16.4, 11.1 and 3.7 Hz). MS, *m*/*z*: 324 ([M]$^+$, $C_{11}H_8F_8S^+$).

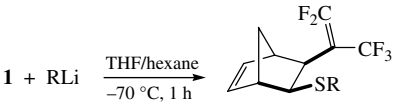
For **10**: to the solution of C_2F_5Li (generated by the reaction of 23 g C_2F_5I with 20 ml of a 1.6 M solution of BuLi in hexane) the solution of 8.2 g of **1** in 10 ml of THF was added slowly at –73 to –70 °C and the reaction mixture was warmed slowly (~5 h) to 25 °C, stirred overnight, quenched by 10% HCl (500 ml); water layer was extracted by CH_2Cl_2 (3×50 ml), organic phase was washed by water (2×300 ml), dried over $MgSO_4$, solvent was removed under vacuum and the residue was distilled under reduced pressure to give **10** (9.5 g, 85%), bp 50–51 °C (0.44 Torr); purity 99.8%. IR (KCl, liq., ν/cm^{-1}): 1739, 1713 (sh, C=C). ^1H NMR ($CDCl_3$) δ: 1.82 (m, 2H), 2.77 (br. t, 1H, *J* ~ 8.5 Hz), 3.04 (s, 1H), 3.19 (s, 1H), 3.51 (dt, 1H, *J* 8.2 Hz), 6.18 (dd, 1H, *J* 5.8 and 3.1 Hz), 6.38 (dd, 1H, *J* 5.8 and 3.4 Hz). ^{19}F NMR ($CDCl_3$) δ: –61.40 (br. s, 3F), –72.49 (br. s, 1F), –78.22 (br. s, 1F), –84.76 (br. t, 3F, *J* 3.4 Hz), –90.63 (br. d, 1F, *J* 238.0 Hz), –93.37 (br. d, 1F, *J* 238.0 Hz). $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ: 40.49, 44.42 (br. s), 45.39 (d, *J* 6.8 Hz), 46.26 (m), 50.87, 88.07 (br., $\Delta\nu_{1/2}$ 60 Hz), 118.90 (qt, *J* 286.0 and 36.8 Hz), 121.71 (td, *J* 287.0 and 40.0 Hz), 135.49, 140.83, 156.71 (t, *J* 302 Hz). MS, *m*/*z*: 255 ([M – C_2F_5]$^+$, $C_{10}H_8F_5S^+$).

For **12**: bp 59–60 °C (0.55 Torr); purity 99.9% (GC). IR (KCl, liq., ν/cm^{-1}): 1740, 1718 (sh, C=C). ^1H NMR ($CDCl_3$) δ: 1.65 (d, 1H, *J* 9.5 Hz), 1.99 (dd, 1H, *J* 9.5 and 4.4 Hz), 2.22 (s, 3H), 2.60 (br. t, 1H, *J* ~ 8.0 Hz), 2.86 (dd, 1H, *J* 8.2 and 1.8 Hz), 2.88 (s, 1H), (s, 2H), 3.10 (s, 1H), 6.15 (dd, 1H, *J* 5.8 and 3.1 Hz), 6.37 (dd, 1H, *J* 5.8 and 3.4 Hz). ^{19}F NMR ($CDCl_3$): –60.84 (br. s, 3F), –72.56 (br. s, 1F), –79.14 (br. s, 1F). $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ: 15.69, 40.84 (br. s), 45.16 (br. s), 45.80 (d, *J* 7.8 Hz), 47.87, 51.11 (t, *J* 2.9 Hz), 54.73, 88.88 (br., $\Delta\nu_{1/2}$ 90 Hz), 123.83 (qdd, *J* 272.3, 14.5 and 4.8 Hz), 135.79, 140.03, 156.71 (t, *J* 296.5 Hz). MS, *m*/*z*: 270 ([M]$^+$, $C_{11}H_{11}F_5S^+$), 204 ([M – C_5H_6]$^+$, $C_6H_5F_5S^+$, 100%).

For **14**: bp 144–146 (0.5 Torr), purity 99.7%. IR (KCl, liq., ν/cm^{-1}): 1739, 1712 (sh, C=C). ^1H NMR ($CDCl_3$) δ: 1.15 (d, 12H, *J* 6.4 Hz), 1.55 (d, 1H, *J* 9.2 Hz), 2.02 (dd, 1H, *J* 4.3 and 9.2 Hz), 2.43 (m, 1H, *J* ~ 8.0 Hz), 2.85 (d, 1H, *J* 8.0 Hz), 2.87 (s, 1H), (s, 2H), 3.15 (s, 1H), 3.25 (sept, 1H, *J* 6.4 Hz), 6.10 (dd, 1H, *J* 5.8 and 3.1 Hz), 6.27 (dd, 1H, *J* 5.8 and 3.4 Hz). ^{19}F NMR ($CDCl_3$) δ: –62.71 (br. s, 3F), –74.46 (br. s, 1F), –81.66 (br. s, 1F). $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ: 22.96 (br.), 39.17, 45.20 (d, *J* 7.8 Hz), 45.60 (br. s), 47.50, 52.20 (br.), 54.73, 58.41 (br. s), 89.00 (br.), 123.54 (qd, *J* 272 and 15.5 Hz), 136.20, 139.77, 155.91 (t, *J* 302.3 Hz). MS, *m*/*z*: 340 ([M – Me]$^+$, $C_{15}H_{19}F_5NS^+$).

For **17**: bp 63–64 (0.5 Torr); purity 99.8%. IR (KCl, liq., ν/cm^{-1}): 1740, 1718 (sh), 1585 (C=C). ^1H NMR ($CDCl_3$) δ: 1.65 (d, 1H, *J* 9.5 Hz), 1.91 (dd, 1H, *J* 9.5 and 4.0 Hz), 2.64 (br. t, 1H, *J* ~ 7 Hz), 2.98 (s, 1H), 3.05 (s, 1H), 3.18 (dd, 1H, *J* 8.3 and 1.8 Hz), 5.24 (d, 1H, *J* 16.8 Hz), 5.26 (d, 1H, *J* 10.1 Hz), 6.16 (dd, 1H, *J* 5.5 and 3.1 Hz), 6.36 (dd, 1H, *J* 5.5 and 3.1 Hz), 6.38 (dd, 1H, *J* 16.8 and 10.1 Hz). ^{19}F NMR ($CDCl_3$) δ: –60.84 (br. s, 3F), –72.08 (br. s, 1F), –78.78 (br. s, 1F). $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ: 40.54 (d, *J* 2.9 Hz), 45.39 (br. s), 46.17 (d, *J* 6.8 Hz), 48.97 (m), 88.74 (br., $\Delta\nu_{1/2}$ 70 Hz), 112.66, 123.83 (qdd, *J* 272.2, 14.5 and 4.8 Hz), 132.36, 135.88, 140.48, 156.93 (t, *J* 297 Hz). MS, *m*/*z*: 282, 283 ([M]$^+$, $C_{12}H_{11}F_4S^+$).

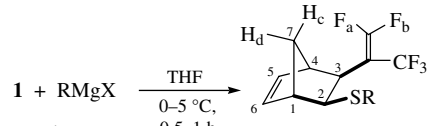
For **18**: bp 85–86 (0.8 Torr); purity 95%. IR (KCl, liq., ν/cm^{-1}): 3305, 2044 (C≡C), 1738, 1713 (sh). ^1H NMR ($CDCl_3$) δ: 1.68 (d, 1H, *J* 9.8 Hz), 2.02 (dd, 1H, *J* 9.8 and 4.0 Hz), 2.59 (br. t, 1H, *J* ~ 8 Hz), 2.87 (s, 1H), 3.01 (s, 1H), 3.32 (s, 1H), 3.35 (dd, 1H, *J* 8.5 and 1.8 Hz), 6.18 (dd, 1H, *J* 5.8 and 3.1 Hz), 6.39 (dd, 1H, *J* 5.8 and 3.4 Hz). ^{19}F NMR ($CDCl_3$) δ: –60.88 (br. s, 3F), –70.01 (br. s, 1F), –77.52 (br. s, 1F). $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ: 40.10 (d, *J* 3.9 Hz), 45.62 (d, *J* 7.8 Hz), 45.77 (br. s), 48.48, 52.071 (t, *J* 2.9 Hz), 73.76, 83.33, 87.82 (br., $\Delta\nu_{1/2}$ 70 Hz), 123.50 (qdd, *J* 273.2, 14.5 and 4.8 Hz), 135.80, 140.96, 157.00 (t, *J* 299.4 Hz). MS, *m*/*z*: 280, 281 ([M]$^+$, $C_{12}H_9F_5S^+$).



10 R = C_2F_5, 85%
12 R = Me, 88%
13 R = Bu^n, 86%
14 R = NPr^i_2, 68%

Scheme 4

temperature is the result of restricted rotation around the C–C bond connecting pentafluoropropenyl and norbornene fragments. Indeed, all resonances in ^{19}F NMR spectra of compounds **3** and **9**, acquired at –50 °C were resolved and observed values of chemical shifts and coupling constants were in good agreement with reported for $CF_2=C(CF_3)CH_2CH(OR)SR$.[6] The *exo*-orientation of both substituents at C(2) and C(3) of the norbornene fragment is defined by the geometry of **1** and also consistent with the presence of substantial coupling constant $^3J_{H\text{-}2\text{–}H\text{-}3}$ 8.0–8.5 Hz; W-coupling constant $^4J_{H\text{-}3\text{–}F_b}$ 6–8 Hz and through-space constant $^6J_{H_c\text{–}F_a}$ 4 Hz observed in compounds **3**, **9**–**18** (see Scheme 5).



R = Ph, X = Br
R = Pr^i, X = Cl
R = CH=CH_2, X = Br

15 R = Ph, 77%
16 R = Pr^i, 84%
17 R = CH=CH_2, 80%

Scheme 5

In conclusion, it was demonstrated that *exo*-3-thia-4,4-bis-(trifluoromethyl)tricyclo[4.2.1.$0^{2,5}$]non-7-ene can be converted with high degree of stereoselectivity into *exo*-3-[(perfluoroprop-1-en-2-yl)bicyclo[2.2.1]hept-5-en-2-yl]-*exo*-sulfanes as a result of ring opening reaction under the action of carbon and nitrogen nucleophilic reagents.

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