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Fluorinated ketene dithioacetals. Part 7: New β-halo perfluorodithiocrotonic acid esters from perfluoroketene dithioacetals

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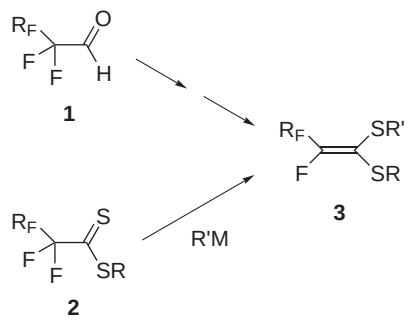
Abstract—Esters of β-bromo or β-chloro perfluorodithiocrotonic acid were prepared from corresponding ketenedithioacetal with anhydrous magnesium halides. These new polyfluorinated dithiocarboxylates are good dienophiles reacting selectively via the C=S bond.

Perfluoroketene dithioacetals **3** are versatile building blocks owing to the easy nucleophilic substitution of the vinylic fluoride and to the masked carboxylic function.[1–6] Although these compounds are usually prepared from perfluoroaldehydes **1**,[4] we reported recently a new method for the synthesis of symmetrical, as well as unsymmetrical, **3** from thiophilic reaction of organolithium or -magnesium reagents with perfluoroalkane dithiocarboxylates **2** (Scheme 1).[7] During this investigation, we observed a particular behavior of the reaction with alkyl magnesium bromide: good yields of **3** were reached only if the magnesium salts produced during the reaction were removed before distillation. Hence a thermal reaction between perfluoroketene dithioacetals **3** and magnesium halides seemed to occur, which deserved further investigation. The present paper reports the results of the study of the thermal reaction of 1,1-bis(ethylsulfanyl)perfluorobut-1-ene **4** with magnesium halides, as well as some chemical transformations of the new products obtained.



Scheme 1.

Compound **4**,[4] on heating with magnesium bromide for 4 min at 240–250°C, was converted into the ethyl β-bromo-F-dithiocrotonate **5a**[8,9] in 74% isolated yield (Scheme 2). Compound **5a** was obtained as a mixture of stereomers ($Z/E \sim 35/65$), which ratio was determined by ^{19}F NMR, taking into account the *cis* and *trans* $^4J_{FF}$ coupling constants.[9,10] A similar reaction occurred with magnesium chloride, leading to the corresponding β-chloro dithiocrotonate **5b**[8,9] (59%, $Z/E \sim 41/59$) except that the thiol ester **6** (26%, $Z/E \sim 95/5$) was obtained as a by-product (Scheme 2). The latter is a hydrolysis by-product which can be explained by some traces of water in magnesium chloride (obtained by dehydration of $MgCl_2$, $6H_2O$).

To the best of our knowledge, compounds **5a**,**b** are the first representatives of β-halo perfluorodithiocarboxylates. A tentative mechanism of the **4**→**5** conversion is depicted in Scheme 3, where coordination of magnesium with the sulfur atom favors the nucleophilic displacement of the ethyl group. The resulting magnesium salt **7** easily loses the β-fluoride to give the intermediate perfluorodithiocrotonate **8**. The last halogen exchange could be explained by the formation of the thermodynamically more stable magnesium fluoride.[11]

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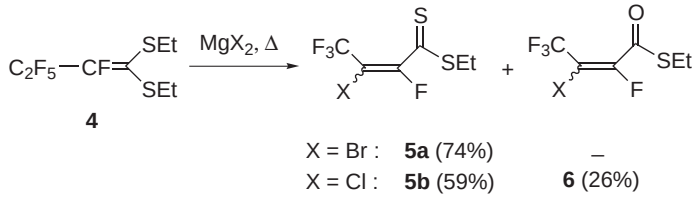
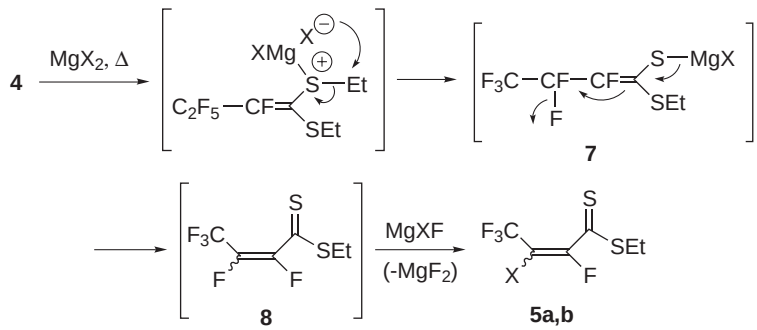
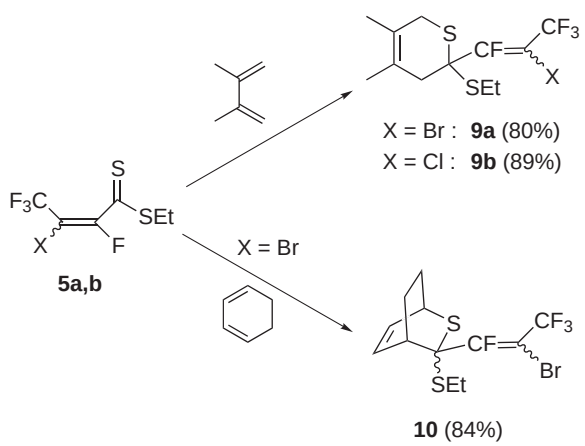


Scheme 2. [8]



Scheme 3.

It was interesting to investigate the ability of such conjugated dithioesters to react as heterodienes or dienophiles. Moreover, either of the two double bonds may be considered as a dienophilic site. Saturated perfluorodithiocarboxylates are excellent 'C=S' dienophiles,[12] whereas α-phosphono-α,β-unsaturated dithioesters are 'C=C' dienophiles.[13] Non-fluorinated dithiocrotonates, unstable compounds, have both heterodiene and C=C dienophile character, giving dimeric compounds.[14] We first attempted a reaction between **5a** and ethyl vinyl ether, considering **5a** as an electron poor heterodiene. No reaction occurred after 2 h in refluxing benzene. On the other hand, compounds **5a**,**b** reacted smoothly with 2,3-dimethyl-1,3-butadiene and cyclohexadiene, giving exclusively the [4+2] cycloadducts **9a**,**b** and **10** from the thiocarbonyl double bond (Scheme 4). High yields were obtained after stirring the reactants for 1 day at room temperature, without solvent. The adducts **9a**,**b**[15,16] were isolated as a mixture of stereomers, with an E/Z ratio similar to the one of the starting dithioesters. Reaction of **5a** with cyclohexadiene gave a complex mixture of stereomers, owing to the presence of four stereogenic centers. From this mixture, three major isomers (31/28/41) of **10**[15,17] were isolated by preparative TLC on silica gel.



Scheme 4. [15]

Therefore, the dithiocrotonates **5a**,**b** behave as all dithioesters bearing a strong electron-withdrawing group such as saturated perfluoroalkyl[12] or phosphonyl[18] groups, giving specifically dihydrothiopyran type adducts.

In summary, we disclose a clean and fast thermal reaction of perfluoroketene dithioacetal **4** with magnesium halides which leads to a new class of β-halo perfluorodithiocrotonic esters **5a**,**b**. These new α,β-unsaturated dithioesters are stable and are excellent dienophiles reacting selectively via the thiocarbonyl group to give cycloadducts **9a**,**b** and **10**. The dithioesters **5a**,**b** are also expected to exhibit an electrophilic reactivity, which is currently under investigation.

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8. *General procedure for the synthesis of **5a**,**b** and **6***: The ketenedithioacetal **4** (2.84 g, 0.010 mol) was added to anhydrous magnesium halide (0.011 mol, 1.1 equiv.) and the resulting mixture was stirred for 4 min at 240–250°C. After cooling at room temperature, the residue was distilled in vacuo to give the corresponding dithioesters **5a**,**b** (red liquids, bp 30–35°C/0.03 mbar for **5a**, bp 40–45°C/0.05 mbar for **5b**) and thiol ester **6**. Compounds **5a**,**b** were additionally purified by column chromatography on silica gel (petroleum ether).
9. *Selected data for compounds **5a**,**b** and **6***. Oils. Compound **5a**: mixture of isomers *E*/*Z* (65/35). ^{19}F NMR ($CDCl_3$) δ (ppm/$CFCl_3$): *E* isomer: −59.9 (d, 3F, $^4J_{FF}=7.6$ Hz), −65.3 (q, 1F, $^4J_{FF}=7.6$ Hz); *Z* isomer: −60.8 (d, 3F, $^4J_{FF}=22.9$ Hz), −73.6 (q, 1F, $^4J_{FF}=22.9$ Hz). ^{1}H NMR ($CDCl_3$) δ (ppm): *E* isomer: 1.43 (t, 3H, $^3J_{HH}=7.6$ Hz), 3.36 (q, 2H, $^3J_{HH}=7.6$ Hz); *Z* isomer: 1.40 (t, 3H, $^3J_{HH}=7.6$ Hz), 3.35 (q, 2H, $^3J_{HH}=7.6$ Hz). ^{13}C NMR ($CDCl_3$) δ (ppm): *E* isomer: 11.4 (CH_3), 31.1 (CH_2), 95.7 (qd, $^2J_{CF}=40.4$, 34.4 Hz, CBr), 120.3 (qd, $^1J_{CF}=270.7$, $^3J_{CF}=10.8$ Hz, CF_3), 158.1 (dq, $^1J_{CF}=272.7$, $^3J_{CF}=3.0$ Hz, CF), 212.2 (d, $^2J_{CF}=25.6$ Hz, CS); *Z* isomer: 11.5 (CH_3), 30.6 (CH_2), 94.4 (qd, $^2J_{CF}=40.3$, 27.6 Hz, CBr), 155.1 (dq, $^1J_{CF}=286.5$, $^3J_{CF}=2.0$ Hz, CF), 213.4 (d, $^2J_{CF}=25.6$ Hz, CS). IR (film, cm^{-1}): 1655. GC–MS (*m*/*e*): 297 (M^+), 295, 217 (100), 191. Compound **5b**: Mixture of isomers *E*/*Z* (59/41). ^{19}F NMR ($CDCl_3$) δ (ppm/$CFCl_3$): *E* isomer: −62.3 (d, 3F, $^4J_{FF}=7.6$ Hz), −75.4 (q, 1F, $^4J_{FF}=7.6$ Hz); *Z* isomer: −63.2 (d, 3F, $^4J_{FF}=22.9$ Hz), −84.2 (q, 1F, $^4J_{FF}=22.9$ Hz). Compound **6**: Mixture of isomers *Z*/*E* (95/5). ^{19}F NMR ($CDCl_3$) δ (ppm/$CFCl_3$): *Z* isomer: −63.9 (d, 3F, $^4J_{FF}=22.9$ Hz), −111.5 (q, ^{1}F, $^4J_{FF}=22.9$ Hz); *E* isomer: −61.0 (d, 3F, $^4J_{FF}=7.6$ Hz), −100.3 (q, 1F, $^4J_{FF}=7.6$ Hz). ^{1}H NMR ($CDCl_3$) δ (ppm): *Z* isomer: 1.35 (t, 3H, $^3J_{HH}=7.3$ Hz), 3.05 (q, 2H, $^3J_{HH}=7.3$ Hz). ^{13}C NMR ($CDCl_3$) δ (ppm): *Z* isomer: 13.8 (CH_3), 23.6 (d, $^4J_{CF}=2.9$ Hz, CH_2), 112.4 (qd, $^2J_{CF}=42.3$, 12.8 Hz, CCl), 119.8 (q, $^1J_{CF}=276.6$ Hz, CF_3), 151.6 (d, $^1J_{CF}=282.5$ Hz, CF), 183.7 (d, $^2J_{CF}=36.4$ Hz, CO). IR (film, cm^{-1}): 1683, 1627. GC–MS (*m*/*e*): 238, 236 (M^+), 208, 175 (100), 69.
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15. *General procedure for the [4+2] cycloaddition reactions of **5a**,**b***: The 2,3-dimethyl-1,3-butadiene or cyclo-1,3-hexadiene (0.012 mol, 1.2 equiv.) was added at room temperature to the dithioesters **5a** or **5b** (0.010 mol, 1.0 equiv.) and the resulting mixture was stirred for 24 h at room temperature. The excess diene was evaporated in vacuo (20 mbar) and the residue was purified by column chromatography on silica gel (petroleum ether/AcOEt 99/1) for cycloadducts **9a**,**b** or by preparative TLC on silica gel (petroleum ether) for compound **10**.
16. *Selected data for cycloadducts **9a**,**b***. Oils. Compound **9a**: Mixture of isomers *E*/*Z* (65/35). ^{19}F NMR ($CDCl_3$) δ (ppm/$CFCl_3$): *E* isomer: −54.2 (d, 3F, $^4J_{FF}=7.6$ Hz), −57.8 (q, 1F, $^4J_{FF}=7.6$ Hz); *Z* isomer: −59.3 (d, 3F, $^4J_{FF}=26.7$ Hz), −77.7 (q, 1F, $^4J_{FF}=26.7$ Hz). ^{1}H NMR ($CDCl_3$) δ (ppm): *E* isomer: 1.29 (t, 3H, $^3J_{HH}=7.3$ Hz), 1.72 (s, 3H), 1.76 (s, 3H), 2.73 (q, 2H, $^3J_{HH}=7.2$ Hz), 2.6–2.8 (m, 1H), 2.91 (d, 1H, $^2J_{HH}=16.4$ Hz), 3.07 (d, 1H, $^2J_{HH}=16.8$ Hz), 3.21 (d, 1H, $^2J_{HH}=16.8$ Hz). ^{13}C NMR ($CDCl_3$) δ (ppm): *E* isomer: 13.6 (CH_3), 19.0 (CH_3), 20.0 (CH_3), 25.4 (CH_2), 31.8 (CH_2), 42.3 (d, $^3J_{CF}=2.0$ Hz, CH_2), 56.6 (d, $^2J_{CF}=24.5$ Hz, C_4), 98.2 (m, CBr), 120.5 (qd, $^1J_{CF}=269.0$, $^3J_{CF}=11.7$ Hz, CF_3), 123.8 (C_4), 125.6 (C_4), 166.6 (dq, $^1J_{CF}=274.6$, $^3J_{CF}=3.5$ Hz, CF); *Z* isomer: 13.8 (CH_3), 25.3 (CH_2), 29.7 (CH_2), 41.6 (d, $^3J_{CF}=6.9$ Hz, CH_2), 125.3 (C_4), 163.0 (dm, $^1J_{CF}=$ 284.5 Hz, CF). IR (film, cm^{-1}): 1623. GC–MS (*m*/*e*): 378 (M^+), 319, 317, 303 (100), 301. Compound **9b**: Mixture of isomers *E*/*Z* (59/41). ^{19}F NMR ($CDCl_3$) δ (ppm/$CFCl_3$): *E* isomer: −56.9 (d, 3F, $^4J_{FF}=11.4$ Hz), −70.9 (q, 1F, $^4J_{FF}=11.4$ Hz); *Z* isomer: −61.9 (d, 3F, $^4J_{FF}=22.9$ Hz), −89.7 (q, 1F, $^4J_{FF}=22.9$ Hz).
17. *Selected data for cycloadducts **10***. Oil. Mixture of isomers: 31/28/41. First isomer: ^{19}F NMR ($CDCl_3$) δ (ppm/$CFCl_3$): −55.3 (d, 3F, $^4J_{FF}=11.4$ Hz), −59.5 (q, 1F, $^4J_{FF}=11.4$ Hz). Second isomer: ^{19}F NMR ($CDCl_3$) δ (ppm/$CFCl_3$): −59.5 (d, 3F, $^4J_{FF}=24.8$ Hz), −69.4 (q, 1F, $^4J_{FF}=24.8$ Hz). ^{1}H NMR ($CDCl_3$) δ (ppm): 1.26 (t, 3H, $^3J_{HH}=7.6$ Hz), 1.6–1.7 (m, 2H), 2.1–2.2 (m, 1H), 2.4–2.5 (m, 1H), 2.6–2.8 (m, 2H), 3.40 (m, 1H), 3.51 (m, 1H), 6.36 (m, 1H), 6.69 (dd, 1H, $^3J_{HH}=7.6$, 7.3 Hz). ^{13}C NMR ($CDCl_3$) δ (ppm): 13.5 (CH_3), 18.8 (CH_2), 25.6 (CH_2), 29.0 (CH_2), 35.4 (d, $^3J_{CF}=7.8$ Hz, CH), 37.6 (CH), 63.9 (d, $^2J_{CF}=20.5$ Hz, C_4), 98.3 (m, CBr), 120.9 (qm, $^1J_{CF}=$ 271.9 Hz, CF_3), 132.3 (CH), 136.8 (CH), 166.0 (dm, $^1J_{CF}=291.4$ Hz, CF). IR (film, cm^{-1}): 1635. GC–MS (*m*/*e*): 297 (M^+–Br), 236, 216 (100), 190. Third isomer: ^{19}F NMR ($CDCl_3$) δ (ppm/$CFCl_3$): −59.2 (d, 3F, $^4J_{FF}=$ 22.9 Hz), −76.0 (q, 1F, $^4J_{FF}=22.9$ Hz).
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