Pergamon

Tetrahedron Letters 43 (2002) 5809–5812

TETRAHEDRON
LETTERS

Fluorinated ketene dithioacetals. Part 9: Synthesis and some chemical properties of new fluorinated 3*H*-1,2-dithiole-3-thiones

Vadim M. Timoshenko,[a,b,*] Jean-Philippe Bouillon,[a] Yuriy G. Shermolovich[b] and Charles Portella[a,*]

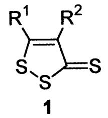
[a]*Laboratoire 'Réactions Sélectives et Applications', Associé au CNRS (UMR 6519), Université de Reims, Faculté des Sciences, B.P. 1039, 51687 Reims Cedex 2, France*
[b]*Institute of Organic Chemistry, NAS of Ukraine, Murmanskaya 5, Kiev-94, 02094, Ukraine*

Received 28 May 2002; revised 14 June 2002; accepted 17 June 2002

Abstract—4-Fluoro-5-perfluoroalkyl-3*H*-1,2-dithiole-3-thiones were prepared by heating the corresponding ketene dithioacetals with magnesium bromide and elemental sulfur. They reacted as dienophiles and 1,3-dipoles in cycloaddition reactions to give new fluorinated organosulfur compounds. © 2002 Elsevier Science Ltd. All rights reserved.

3*H*-1,2-Dithiole-3-thiones **1** have attracted significant attention due to their wide spectrum of biological activity. Derivatives of this class were reported to display antioxidant, chemotherapeutic and radioprotective properties.[1] Dithiolethiones appear to be one of the most promising types of potential chemopreventive agents based on their efficacy in a wide variety of tumour models.[2] Some of their representatives have been developed for clinical applications. In particular, Tritio anetole ($R^1 = p$-$MeOC_6H_4$, $R^2 = H$) (Fig. 1) has been extensively used as a choleretic and sialogogue,[3] Oltipraz® ($R^1 = $ 2-pyrazinyl, $R^2 = Me$) as a chemopreventive agent[4] and as an inhibitor of HIV-1 virus replication.[5]

Apart from bioactive properties, 1,2-dithiole-3-thiones are also interesting from the material chemistry viewpoint. They have been used as precursors for the preparation of vinylogues of tetrathiafulvalene with increased dimensionality or nonlinear optical (NLO) properties,[6] as π-donor moiety for obtaining photoconductive materials, which can be used as electron transport materials for hologram recording.[7]



1

Figure 1.

Due to the great variety of applications, development of convenient methods for synthesising dithiolethiones and expanding their structure diversity remains a subject of active research. The simplest and commonly employed method for the preparation of 1,2-dithiole-3-thiones is thiation of 3-oxoesters with P_4S_{10} or Lawesson's reagent, first giving poor to fair yields,[8] but recently improved.[9] The dithiolethione ring system was also prepared by treatment of β-oxothioic acid or its K-salt, resulting from condensation of CS_2 with ketones, with polysulfanes[10] or hexamethyldisilathiane.[11]

Among the wide variety of 3*H*-1,2-dithiole-3-thiones which have been synthesised, several examples are known with fluoro- or polyfluoroalkyl substituents. 5-Polyfluoroalkyl substituted dithioles **1** ($R^1 = HCF_2$, HCF_2CF_2, $R^2 = H$, Cl, Br) were synthesised from the corresponding esters of β-ketoacids by treatment with P_4S_{10} in the presence of elemental sulfur in poor to moderate yields.[12] Compounds **1** ($R^1 = H$, $R^2 = F$, CF_3) were prepared by reaction of 2-fluoropropene or 2-(trifluoromethyl)propene with elemental sulfur in gas phase at 500°C with 46% yields.[13]

In this communication we wish to report a simple and efficient route to new fluorine containing 3*H*-1,2-dithiole-3-thiones, starting from perfluoroketene dithioacetals, and some of their chemical properties.

Keywords: ketene dithioacetals; dithioles; fluorine and compounds; cycloaddition; Diels-Alder reactions; thiocarbonyl compounds.

* Corresponding authors. Fax: +33 326913166; e-mail: charles.portella@univ-reims.fr

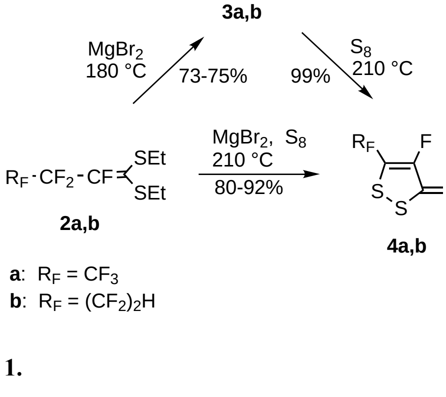
PII: S0040-4039(02)01179-6

We recently reported the preparation of β-bromo-β-trifluoromethyl dithiocrotonic ester **3a** by heating of perfluoroketene diethylthioacetal **2a** with $MgBr_2$.[14] Heating at 240°C for 4 min induced the formation of a minor amount (5%) of a side-product which had lost the Et group. After 5 min heating at this temperature, this compound became the unique isolable product. According to full analytical and spectrometrical studies, it proved to be 4-fluoro-5-trifluoromethyl-3*H*-1,2-dithiole-3-thione **4a** (Scheme 1). These observations prompted us to investigate this reaction in more detail.

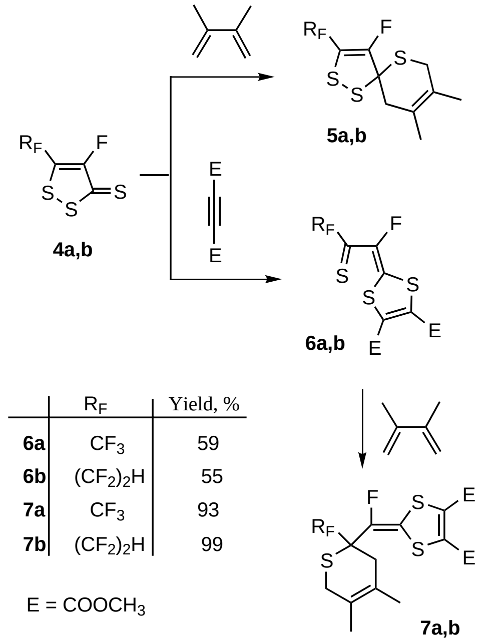
Control of the conversion of **2a** into the crotonic derivative **3a** was observed to be easier by lowering the reaction temperature to 180°C. Assuming that the thermal decomposition of the dithioester **3a** released the elemental sulfur necessary to afford the thermodynamic product **4a**, a mixture of pure **3a** and elemental sulfur was heated at 210°C and gave dithiolethione **4a** in almost quantitative yield. Conveniently, excellent yield of **4a** (92%) was obtained in a one-pot procedure by direct heating of a mixture of **2a**, magnesium bromide and elemental sulfur. Similarly, the higher homologue **4b** was prepared in 80% yield from the corresponding ketene dithioacetal **2b**, showing the generality of this transformation.[15]

Having a good method for the preparation of dithiolethiones **4**, it was interesting to investigate their chemical properties. As far as they can be considered as cyclic analogues of polyfluoroalkyl dithiocarboxylates, which are good dienophiles,[16] and taking into account that 1,2-dithiole-3-thiones can act as 1,3-dipoles,[17] we examined cycloaddition reactions of compounds **4** with 2,3-dimethylbutadiene (DMB) and dimethyl acetylenedicarboxylate (DMAD).

Compounds **4** react slowly with DMB at 30°C in diethyl ether to give cycloadducts **5** (Scheme 2). According to ^{19}F NMR monitoring, **4** was totally and cleanly converted within 48 h into **5** (>90% in the crude reaction mixture). Unfortunately, **5** is too unstable to be purified by silica gel chromatography. Nevertheless cycloadducts **5a**,**b** have been unambiguously identified by NMR spectrometry.[18] In ^{13}C NMR spectra, the appearance of a quaternary carbon atom signal at 70 ppm ($^2J_{CF}=22$ Hz) and the disappearance of signal for C=S carbon at 198 ppm ($^2J_{CF}=28$ Hz) confirmed the cycloaddition on C=S double bond. ^1H NMR spectra displayed two AB systems for CH_2 groups due to asymmetric carbon atom.



Scheme 1.



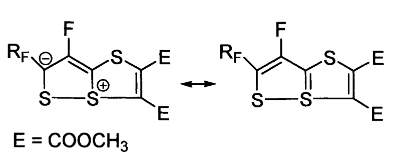
	R_F	Yield, %
6a	CF_3	59
6b	$(CF_2)_2H$	55
7a	CF_3	93
7b	$(CF_2)_2H$	99

E = $COOCH_3$

Scheme 2.

As 1,3-dipole, compounds **4** reacted effectively at room temperature in dichloromethane with DMAD for 3–5 h, giving thioketone derivatives **6** as dark red crystals in 55–59% isolated yields.[19] Here too, compounds **6** partially decomposed during purification by column chromatography (petroleum ether/CH_2Cl_2, 1:1). It was also observed that their solutions became colourless in standing on light for 2–3 days.

Unusual ^{13}C NMR features of compound **6** deserves some comment. The C=S carbon usually appears at >200 ppm; on the other hand, the CS_2 carbon signal is expected in the 125–130 ppm region.[20] The spectra of compounds **6** exhibit an important upfield shifts for C=S carbon (175.0 ppm for **6a**; 177.6 ppm for **6b**) and downfield shift for CS_2 carbon (149.7 ppm for **6a**; 150.0 ppm for **6b**). This phenomenon can be explained taking into account the highly conjugated character of **6**, and the charge distribution according to the canonical forms described in Scheme 3.[21]



E = $COOCH_3$

Scheme 3.

The presence of the thiocarbonyl group in compounds **6** was confirmed by cycloaddition reactions with 1,3-diene. Treatment of **6** with DMB in diethyl ether at room temperature for 1 h afforded 1:1 cycloadducts **7** in almost quantitative yields (Scheme 2). The initial dark red colour of reaction mixture turned to yellow as observed for usual cycloaddition reactions of this type. The products **7** displayed in ^{1}H NMR spectra[22] two AB systems for CH_2 groups. The appearance in ^{13}C NMR spectra of quaternary atoms at 52.6 ppm (quartet of doublets for **7a**) and 52.7 ppm (doublet of triplets for **7b**) with coupling constants $^2J(C\text{-}CF_3)$ and $^2J(C\text{-}CF)$ between 23 and 28 Hz as well as disappearance of C=S carbon signal of starting **6** clearly showed cycloaddition to thiocarbonyl group. The CS_2 carbon (122 ppm) has recovered a normal chemical shift.[20]

In conclusion, we have described a new application of perfluoroketene dithioacetals, which are effectively converted to new fluorinated 3*H*-1,2-dithiole-3-thiones. These compounds react as dienophiles with 2,3-dimethylbutadiene. As 1,3-dipoles, they react with dimethyl acetylenedicarboxylate providing a new fluorinated thioketone derivatives, chemical properties of which are currently under investigation.

Acknowledgements

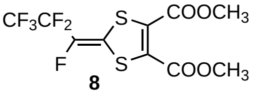
V.T. is grateful to CNRS for an associate position. H. Baillia is thanked for NMR spectra.

References

1. (a) Kensler, T. W.; Groopman, J. D.; Roebuck, B. D.; Curphey, T. J. *ACS Symp. Ser.* **1994**, *546*, 154–163; (b) Maxiutenko, Yu. Y.; Libby, A. H.; Joyner, H. H.; Curphey, T. J.; MacMillan, D. L.; Kensler, T. W.; Roebuck, B. D. *Carcinogenesis* **1998**, *19*, 1609–1615; (c) Oteino, M. A.; Kensler, T. W.; Guyton, K. Z. *Free Radical Biol. Med.* **2000**, *28*, 944–952; (d) Begleiter, A.; Lange, L. *Int. J. Oncol.* **2002**, *20*, 835–838.
2. Smith, A. W.; Arif, J. M.; Gupta, R. C. *Int. J. Cancer* **2001**, *91*, 132–136.
3. Drukarch, B.; Schepens, E.; Stoof, J. C.; Langeveld, C. H. *Eur. J. Pharmacol.* **1997**, *329*, 259–262.
4. Kwak, M.-K.; Egner, P. A.; Dolan, P. M.; Ramos-Gomez, M.; Groopman, J. D.; Itoh, K.; Yamamoto, M.; Kensler, T. W. *Mut. Res.* **2001**, *480–481*, 305–315.
5. For a review, see: Prochaska, H. J.; Chavan, S. J.; Baron, P.; Polsky, B. *J. Cell. Biochem.* **1995**, 117–125.
6. (a) Frere, P.; Belyasmine, A.; Gouriou, Y.; Jubault, M.; Gorgues, A.; Duguay, G.; Wood, S.; Reynolds, C. D.; Bryce, M. R. *Bull. Soc. Chim. Fr.* **1995**, *132*, 975–984; (b) Nguyen, T.-T.; Gouriou, Y.; Salle, M.; Frere, P.; Jubault, M.; Gorgues, A.; Toupet, L.; Riou, A. *Bull. Soc. Chim. Fr.* **1996**, *133*, 301–308.
7. (a) Mysyk, D. D.; Perepichka, I. F.; Perepichka, D. F.; Bryce, M. R.; Popov, A. F.; Goldenberg, L. M.; Moore, A. J. *J. Org. Chem.* **1999**, *64*, 6937–6950; (b) Perepichka, D. F.; Perepichka, I. F.; Bryce, M. R.; Moore, A. J.; Sokolov, N. I. *Synth. Met.* **2001**, *121*, 1487–1488.
8. For reviews, see: (a) Pedersen, C. T. *Adv. Heterocycl. Chem.* **1982**, *31*, 63–113; (b) Pedersen, C. T. *Sulfur Rep.* **1995**, *16*, 173–221.
9. (a) Curphey, T. J. *Tetrahedron Lett.* **2000**, *41*, 9963–9966; (b) Curphey, T. J. *Tetrahedron Lett.* **2002**, *43*, 371–373; (c) Aimar, M. L.; Kreiker, J.; de Rossi, R. H. *Tetrahedron Lett.* **2002**, *43*, 1947–1949.
10. Curphey, T. J. *Tetrahedron Lett.* **1993**, *34*, 3703–3706.
11. Curphey, T. J. *Tetrahedron Lett.* **2000**, *41*, 6977–6980.
12. (a) Bobrov, M. B.; Saloutin, V. I.; Pashkevich, K. I. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1986**, *4*, 879–884; (b) Pashkevich, K. I.; Saloutin, V. I.; Bobrov, M. B. *Sulfur Lett.* **1987**, *6*, 93–98; (c) Krokhalev, V. M.; Saloutin, V. I.; Pashkevich, K. I. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1987**, *10*, 2266–2272.
13. Hodgson, R. L.; Smutny, E. J. 4-Substituted trithiones from sulfur and 2-substituted propenes or propanes. US Pat. 3,394,146 (1968); *Chem. Abstr. 69*, 67362n.
14. Bouillon, J.-P.; Shermolovich, Yu. G.; Portella, C. *Tetrahedron Lett.* **2001**, *42*, 2133–2135.
15. Typical procedure: preparation of 4-fluoro-5-trifluoromethyl-3*H*-1,2-dithiole-3-thiones **4a**. Flask containing the mixture of ketene dithioacetal **2a** (1.0 g, 3.52 mmol), anhydrous magnesium bromide (0.68 g, 3.70 mmol) and fine powdered elemental sulfur (0.12 g, 3.75 mmol) was placed in oil bath preheated to 210°C and kept at this temperature for 5 min. The flask was fitted with small distillation adopter and product was quickly sublimated in vacuum (0.3 mbar). The product was washed out from adopter with diethyl ether and solvent was evaporated in vacuum to give pure (according with GC-MS and NMR data) red crystals of dithiolethione **4a**. Yield 92%; mp 88–90°C; ^{19}F NMR ($CDCl_3$) δ (ppm/CCl_3F): −59.51 (d, 3F, $^4J_{FF}=11.4$ Hz, CF_3), −104.34 (q, 1F, $^4J_{FF}=11.4$ Hz, CF); ^{13}C NMR ($CDCl_3$) δ (ppm): 119.90 (qd, $J_{CF}=274.7$, $^3J_{CF}=3.9$ Hz, CF_3), 136.93 (qd, $^2J_{CF}=39.4$, $^2J_{CF}=20.7$ Hz, C_5), 156.15 (dq, $J_{CF}=276.1$, $^3J_{CF}=2.9$ Hz, CF), 198.21 (d, $^2J_{CF}=27.6$ Hz, C=S); IR (KBr) ν (cm^{-1}): 1368, 1271, 1257, 1170, 1037, 690, 510; GC-MS (*m*/*e*): 220 (M^+, 100%), 144 (M^+-CS_2), 100 (M^+-CS_2-CS). Anal. calcd for $C_4F_4S_3$: C, 21.82; S, 43.68. Found: C, 21.84; S, 43.27%. Compound **4b**: yield 80%, red crystals; mp 68–70°C; ^{1}H NMR ($CDCl_3$) δ (ppm): 6.10 (tm, $^2J_{HF}=53.0$ Hz, HCF_2); ^{19}F NMR ($CDCl_3$) δ (ppm/CCl_3F): −105.64 (pentet, 1F, $^4J_{FF}=9.5$ Hz, CF), −110.64 (m, 2F, CF_2), −134.23 (dm, 2F, $^2J_{FH}=53.5$ Hz, CF_2H); ^{13}C NMR ($CDCl_3$) δ (ppm): 108.83 (ttd, $J_{CF}=253.6$, $^2J_{CF}=38.6$, $^4J_{CF}=2.1$ Hz, HCF_2), 112.86 (ttd, $J_{CF}=254.6$, $^2J_{CF}=31.1$, $^3J_{CF}=4.3$ Hz, CF_2), 137.81 (td, $^2J_{CF}=29.6$, $^2J_{CF}=21.1$ Hz, C_5), 156.38 (dt, $J_{CF}=272.9$, $^3J_{CF}=4.3$ Hz, CF), 198.38 (d, $^2J_{CF}=27.9$ Hz, C=S); IR (KBr) ν (cm^{-1}): 1393, 1350, 1250, 1102, 1028, 952; GC-MS (*m*/*e*): 252 (M^+, 100%), 201 (M^+-HCF_2), 176 (M^+-CS_2), 157, 137, 119.
16. For some cycloaddition reactions of polyfluoroalkyl dithiocarboxylates, see: (a) Ref. 14; (b) Shermolovich, Yu. G.; Slusarenko, Ye. I.; Timoshenko, V. M.; Rozhenko, A. B.; Markovski, L. N. *J. Fluorine Chem.* **1991**, *55*, 329–333; (c) Portella, C.; Shermolovich, Yu. G.; Tschenn, O. *Bull. Soc. Chim. Fr.* **1997**, *134*, 697–702.
17. (a) McKinnon, D. M. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R.; Rees, C. W., Eds; Pergamon Press: Oxford, 1984; Vol. 6, Chapter 4.31; (b) Rees, C.

W.; Rakitin, O. A.; Marcos, C. F.; Torroba, T. *J. Org. Chem.* **1999**, *64*, 4376–4380 and References cited therein.

18. Selected data for cycloadducts **5a**,**b**. Compound **5a**: yellow crystals; mp 76–78°C; ^{1}H NMR (CDCl$_3$) δ (ppm): 1.92 (s, 3H, CH$_3$), 1.99 (s, 3H, CH$_3$), 2.80 (*AB*, 2H, $J_{AB}=15.8$ Hz, CH$_2$), 3.26 (*AB*, 2H, $J_{AB}=15.4$ Hz, CH$_2$); ^{19}F NMR (CDCl$_3$) δ (ppm/CCl$_3$F): −59.82 (d, 3F, $^4J_{FF}=15.5$ Hz, CF$_3$), −112.90 (q, 1F, $^4J_{FF}=15.5$ Hz, CF); ^{13}C NMR (CDCl$_3$) δ (ppm): 19.08 (s, CH$_3$), 20.57 (s, CH$_3$), 32.36 (s, CH$_2$), 41.39 (s, CH$_2$), 69.90 (d, $^2J_{CF}=21.5$ Hz, C$_{quaternary}$), 110.83 (qd, $^2J_{CF}=37.6$, $^2J_{CF}=18.8$ Hz, C$_5$), 120.12 (qd, $J_{CF}=272.4$, $^3J_{CF}=3.2$ Hz, CF$_3$), 125.85 (s, *C*-CH$_3$), 125.99 (s, *C*-CH$_3$), 156.35 (dq, $J_{CF}=299.8$, $^3J_{CF}=3.7$ Hz, CF); GC-MS (*m*/*e*): 270 (M^+–S), 269 (M^+–HS), 268 (M^+–H$_2$S), 253 (M^+–H$_2$S–CH$_3$, 100%). Compound **5b**: ^{1}H NMR (CDCl$_3$) δ (ppm): 1.79 (s, 6H, CH$_3$), 2.84 (*AB*, 2H, $J_{AB}=16.5$ Hz, CH$_2$), 3.26 (*AB*, 2H, $J_{AB}=15.5$ Hz, CH$_2$), 5.93 (tm, 1H, $^2J_{HF}=53.4$ Hz, HCF$_2$); ^{19}F NMR (CDCl$_3$) δ (ppm/CCl$_3$F): −111.36 (m, 2F, CF$_2$), −114.31 (m, 1F, CF), −135.75 (ddq, 2F, $^2J_{FH}=53.4$, $^3J_{FF}=19.0$, $^5J_{FF}=6.9$ Hz, HCF$_2$); ^{13}C NMR (CDCl$_3$) δ (ppm): 19.15 (s, CH$_3$), 20.62 (s, CH$_3$), 32.44 (s, CH$_2$), 41.56 (s, CH$_2$), 70.18 (d, $^2J_{CF}=22.1$ Hz, C$_{quaternary}$), 105.45 (m, =*C*-CF$_2$), 109.20 (tm, $J_{CF}=252.8$ Hz, HCF$_2$), 113.67 (m, CF$_2$), 125.78 (s, *C*-CH$_3$), 126.08 (s, *C*-CH$_3$), 156.36 (d, $J_{CF}=297.8$ Hz, CF).
19. Selected data for compounds **6a**,**b**. Compound **6a**: yield 59%, dark red crystals; R_f 0.5 (petroleum ether/CH$_2$Cl$_2$, 1:1); mp 102–104°C; ^{1}H NMR (CDCl$_3$) δ (ppm): 3.97 (s, 6H, 2×CH$_3$); ^{19}F NMR (CDCl$_3$) δ (ppm/CCl$_3$F): −64.85 (d, 3F, $^4J_{FF}=18.1$ Hz, CF$_3$), −102.35 (q, 1F, $^4J_{FF}=18.1$ Hz, CF); ^{13}C NMR (CDCl$_3$) δ (ppm): 54.18 (s, CH$_3$), 54.35 (s, CH$_3$), 118.79 (qd, $J_{CF}=278.3$, $^3J_{CF}=3.2$ Hz, CF$_3$), 132.75 (s, *C*-C=O), 135.32 (s, *C*-C=O), 149.73 (d, $^2J_{CF}=29.0$ Hz, CS$_2$), 150.96 (d, $J_{CF}=250.4$ Hz, CF), 158.63 (s, C=O), 159.31 (d, $^5J_{CF}=1.8$ Hz, C=O), 175.01 (qd, $^2J_{CF}=36.3$, $^2J_{CF}=13.4$ Hz, C=S); IR (KBr) ν (cm^{-1}): 1748 (C=O), 1711 (C=O), 1581, 1465, 1439, 1393, 1301, 1238, 1191, 1135, 1079; GC-MS (*m*/*e*): 362 (M^+), 303 (M^+–COOCH$_3$), 293 (M^+–CF$_3$), 220 (M^+–DMAD, 100%). Compound **6b**: yield 55%, dark red crystals; R_f 0.4 (petroleum ether/CH$_2$Cl$_2$, 1:1); mp 70–72°C; ^{1}H NMR (CDCl$_3$) δ (ppm): 3.94 (s, 6H, 2×CH$_3$), 6.23 (tt, 1H, $^2J_{HF}=53.1$, $^3J_{HF}=5.1$ Hz, HCF$_2$); ^{19}F NMR (CDCl$_3$) δ (ppm/CCl$_3$F): −101.41 (tt, 1F, $^4J_{FF}=25.0$, $^5J_{FF}=6.9$ Hz, CF), −111.77 (dtd, 2F, $^4J_{FF}=25.0$, $^3J_{FF}=8.6$, $^3J_{FH}=5.1$ Hz, CF$_2$), −136.00 (dq, 2F, $^2J_{FH}=53.1$, $^3J_{FF}=8.6$ Hz, HCF$_2$); ^{13}C NMR (CDCl$_3$) δ (ppm): 54.09 (s, CH$_3$), 54.27 (s, CH$_3$), 109.41 (ttd, $J_{CF}=252.5$, $^2J_{CF}=34.4$, $^4J_{CF}=3.8$ Hz, HCF$_2$), 112.53 (ttd, $J_{CF}=255.7$, $^2J_{CF}=26.9$, $^3J_{CF}=4.8$ Hz, CF$_2$), 132.49 (s, *C*-C=O), 135.20 (d, $^4J_{CF}=2.7$ Hz, *C*-C=O), 150.03 (d, $^2J_{CF}=29.5$ Hz, CS$_2$), 151.22 (d, $J_{CF}=249.3$ Hz, CF), 158.54 (s, C=O), 159.25 (d, $^5J_{CF}=2.7$ Hz, C=O), 177.57 (td, $^2J_{CF}=26.9$, $^2J_{CF}=12.9$ Hz, C=S); IR (KBr) ν (cm^{-1}): 2963, 1734 (C=O), 1715 (C=O), 1570, 1460, 1438, 1298, 1276, 1233, 1187, 1112, 1088, 1057; GC-MS (*m*/*e*): 394 (M^+), 293 (M^+–HCF$_2$CF$_2$), 252 (M^+–DMAD, 100%).
20. For example, signals of carbon of CS$_2$ moiety for the starting ketene dithioacetals **2** were observed at 126.4–126.6 ppm and the chemical shift for CS$_2$ carbons for the model compound **8** (unpublished result) is at 128.6 ppm.



8

21. For examples of the intramolecular S···S 1,5-bonding interactions in the related unfluorinated series, see Ref. 6a.
22. Selected data for cycloadducts **7a**,**b**. Compound **7a**: yield 93%, yellow slowly crystallised oil; R_f 0.6 (petroleum ether/ether, 1:1); ^{1}H NMR (CDCl$_3$) δ (ppm): 1.68 (s, 3H, CH$_3$), 1.73 (s, 3H, CH$_3$), 2.62 (*AB*, 2H, $J_{AB}=16.6$ Hz, CH$_2$), 3.09 (*AB*, 2H, $J_{AB}=16.7$ Hz, CH$_2$), 3.80 (s, OCH$_3$), 3.81 (s, OCH$_3$); ^{19}F NMR (CDCl$_3$) δ (ppm/CCl$_3$F): −73.89 (d, 3F, $^4J_{FF}=2.8$ Hz, CF$_3$), −97.53 (q, 1F, $^4J_{FF}=2.8$ Hz, CF); ^{13}C NMR (CDCl$_3$) δ (ppm): 19.09 (s, CH$_3$), 20.11 (s, CH$_3$), 30.94 (s, CH$_2$), 33.20 (d, $^3J_{CF}=5.9$ Hz, CH$_2$), 52.57 (qd, $^2J_{CF}=28.4$, $^2J_{CF}=23.9$ Hz, C$_{quaternary}$), 53.34 (s, OCH$_3$), 53.40 (s, OCH$_3$), 122.37 (d, $^2J_{CF}=35.6$ Hz, CS$_2$), 122.69 (s, *C*-CH$_3$), 124.14 (s, *C*-CH$_3$), 125.71 (qd, $J_{CF}=285.2$, $^3J_{CF}=4.0$ Hz, CF$_3$), 129.82 (d, $^4J_{CF}=4.2$ Hz, *C*-C=O), 133.00 (s, *C*-C=O), 138.30 (d, $J_{CF}=254.3$ Hz, CF), 160.00 (d, $^5J_{CF}=2.5$ Hz, C=O), 160.01 (s, C=O); GC-MS (*m*/*e*): 444 (M^+), 362 (M^+–DMB), 220 (M^+–DMB–DMAD, 100%). Compound **7b**: yield 99%, yellow oil; R_f 0.5 (petroleum ether/CH$_2$Cl$_2$, 1:1); ^{1}H NMR (CDCl$_3$) δ (ppm): 1.70 (s, 3H, CH$_3$), 1.75 (s, 3H, CH$_3$), 2.66 (*AB*, 2H, $J_{AB}=17.2$ Hz, CH$_2$), 3.11 (*AB*, 2H, $J_{AB}=17.0$ Hz, CH$_2$), 3.83 (s, OCH$_3$), 3.84 (s, OCH$_3$); 5.91 (tt, 1H, $^2J_{HF}=52.5$, $^3J_{HF}=5.4$ Hz, HCF$_2$); ^{19}F NMR (CDCl$_3$) δ (ppm/CCl$_3$F): −95.28 (s, 1F, CF), −119.83 (*AB*, $J_{AB}=267.5$ Hz, CF$_2$), −133.68 (*AB* ddt, $J_{AB}=301.1$, $^2J_{FH}=52.5$, $^3J_{FF}=7.0$, $^5J_{FF}=3.0$ Hz, HCF$_2$); ^{13}C NMR (CDCl$_3$) δ (ppm): 19.13 (s, CH$_3$), 20.20 (s, CH$_3$), 30.90 (s, CH$_2$), 33.02 (m, CH$_2$), 52.74 (dt, $^2J_{CF}=24.0$, $^2J_{CF}=23.0$ Hz, C$_{quaternary}$), 53.37 (s, OCH$_3$), 53.43 (s, OCH$_3$), 109.29 (tt, $J_{CF}=253.5$, $^2J_{CF}=33.6$ Hz, HCF$_2$), 116.35 (ttd, $J_{CF}=261.0$, $^2J_{CF}=25.0$, $^3J_{CF}=3.8$ Hz, CF$_2$), 122.37 (s, *C*-CH$_3$), 122.60 (d, $^2J_{CF}=35.5$ Hz, CS$_2$), 124.29 (s, *C*-CH$_3$), 129.79 (d, $^4J_{CF}=4.3$ Hz, *C*-C=O), 133.04 (s, *C*-C=O), 138.54 (dtt, $J_{CF}=253.4$, $^3J_{CF}=1.4$, $^4J_{CF}=0.9$ Hz, CF), 159.96 (s, C=O), 160.02 (s, C=O); MS (*m*/*e*): 476 (M$^+$, 100), 445 (M^+–OCH$_3$), 394 (M^+–DMB), 375 (M^+–HCF$_2$CF$_2$), 293 (M^+–DMB– HCF$_2$CF$_2$).