Journal of Fluorine Chemistry 132 (2011) 783–791

Contents lists available at ScienceDirect

Journal of Fluorine Chemistry

journal homepage: www.elsevier.com/locate/fluor

New data on the reaction of hexafluorothioacetone with styrenes

Viacheslav A. Petrov [a,*], Will Marshall [b]

[a] DuPont Central Research and Development, Experimental Station, PO Box 80500, Wilmington, DE 19880-0500, United States[1]
[b] DuPont Corporate Center for Analytical Sciences, Experimental Station, PO Box 80500, Wilmington, DE 19880-0500, United States

ARTICLE INFO

Article history:
Received 23 February 2011
Received in revised form 28 March 2011
Accepted 29 March 2011
Available online 5 April 2011

Keywords:
Hexafluorothioacetone
Cyclic dimer of hexafluorothioacetone
Reaction with styrenes
Diels–Alder reaction

ABSTRACT

Hexafluorothioacetone, generated *in situ* from its cyclic dimer (**1**) in the presence of CsF catalyst was shown to react with styrene or 4-alkyl-styrenes (alkyl = c-hexyl, Me, t-Bu) forming the corresponding 2:1 Diels–Alder cycloadducts as major products. All cycloadducts were isolated, and the structure of two of them was established by single crystal X-ray diffraction. While 2-vinylnaphthalene, 4-CF_3- and 4-Cl-styrenes in the presence of CsF catalyst react with **1** producing the corresponding 1:1 Diels–Alder cycloadducts, 4-alkoxy styrenes were found to produce preferentially the corresponding thietanes. The reaction of styrenes with **1** was also found to be sensitive to the source of fluoride ion and the solvent.

1. Introduction

The reaction of hexafluorothioacetone (HFTA) with styrenes was discovered by Middleton in 1965 [1]. Monomeric HFTA was reported to react with styrene, 4-MeO-styrene and 1,1-diphenylethylene to give non-aromatic 2:1 Diels–Alder adducts.

Styrene in this reaction acts as 1,3-diene (for such transformation of styrenes see Ref. [2]), forming 1,3-cyclohexadiene intermediate, which undergoes second Diels–Alder reaction with HFTA forming 2:1 nonromantic cycloadduct [1].

On the other hand, hexafluorothioketene which has very similar reactivity, was reported to react with styrene, 1,1-diphenylethylene and 4-MeO-styrene giving the corresponding *thietanes* [3].

In 1972, the Ishikawa research group reported that readily available [4] cyclic dimer of HFTA [2,2,4,4-tetrakis-(trifluoromethyl)dithietane, **1**] can be used as a convenient source of HFTA [5–7], since in the presence of fluoride ion it exists in equilibrium with HFTA. For example, the reaction of **1** with styrene in the presence of KF catalyst was reported to produce a mixture of two isomeric 2:1 Diels–Alder adducts [8], identical to material prepared by Middleton [1].

Unfortunately, the limited amount of spectroscopic information for the products of the reaction of HFTA or **1** with styrenes does not allow a solid conclusion to be drawn about either the regiochemistry of cycloaddition of HFTA with styrene or the structure of products. These facts, combined with obvious contradictions in the reactivity of HFTA and $(CF_3)_2C{=}C{=}S$ towards styrenes, prompted us to revisit the reaction of HFTA with styrenes in order to clarify the structure of cycloadducts, the regiochemistry of cycloaddition, and the mechanism of the process. Since monomeric HFTA is not readily available and is difficult to handle, it was decided to use the reaction of **1** with fluoride ion for *in situ* generation of HFTA, since this system was previously used for the synthesis of a variety of HFTA-based sulfur-containing heterocycles [5,6,9–12].

2. Results and discussion

2.1. Reaction of styrenes with 1

All initial attempts to reproduce the reaction of **1** with styrene (**2a**) under reported conditions (KF, dry DMF, 25 °C, 2 days, yield of 2:1 Diels–Alder cycloadducts—24% [8]) were unsuccessful. The synthesis [8] was found to be impractical, due to low conversions under reported conditions (~4% styrene conversion after 2 days at 25 °C). The replacement of KF catalyst by more active CsF resulted only in slightly higher conversion (~6%, 2 days at 25 °C, NMR).

We found however, that cycloadduct **3a** can be prepared and isolated in acceptable yield if the reaction was carried out at elevated temperature. Heating the mixture of **1** (10–15 mol%

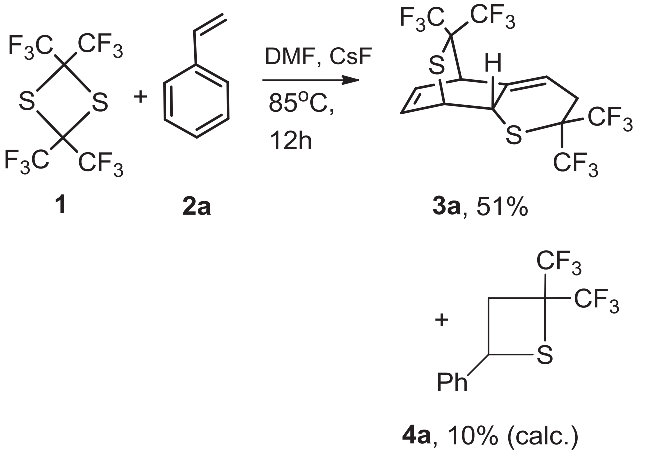
---

* Corresponding author. Tel.: +1 3026951958.
E-mail address: viacheslav.a.petrov@usa.dupont.com (V.A. Petrov).

[1] Publication No. 2010-237.

0022-1139/$ – see front matter © 2011 Elsevier B.V. All rights reserved.
doi:10.1016/j.jfluchem.2011.03.024

excess), styrene (**2a**) and CsF in DMF solvent resulted in the formation of cycloadduct **3a** isolated in 51% yield (Eq. (1)):



(1)

Detailed NMR analysis of the crude reaction mixture revealed the presence of a byproduct formed in this reaction, which was identified as thietane **4a** (NMR and GC/MS).

It should be also pointed out that the formation of compound **3a** is a highly regioselective process, leading to only one (out of eight possible) regioisomer. The structure of isolated 2:1 Diels–Alder adduct **3a** was established by single crystal X-ray diffraction, and it was shown that **3a** is the sterically least-hindered isomer: both sulfur substituents are located on the same side of the cyclohexene ring, in *trans*-position and the C-3 hydrogen occupies an *exo*-position (see Fig. 1).

The same synthetic protocol was applied for the reaction of **1** with styrenes **2b**–**d**, which carried an alkyl substituent in the *para*-position. Similar to **2a**, these styrenes react with **1**, to give Diels–Alder cycloadducts **3b**–**d** as major products, along with smaller amounts of the corresponding thietanes **4b**–**d** (Eq. (2)). The corresponding cycloadducts **3b**–**d** were isolated in 44–63% yield and fully characterized. In the case of styrenes **2c** and **2d**, the corresponding fractions enriched by 30–60 wt.% of thietanes **4c** and **4d** were also obtained and both compounds were fully characterized by NMR spectroscopy and MS-spectrometry (see Tables 1 and 2).

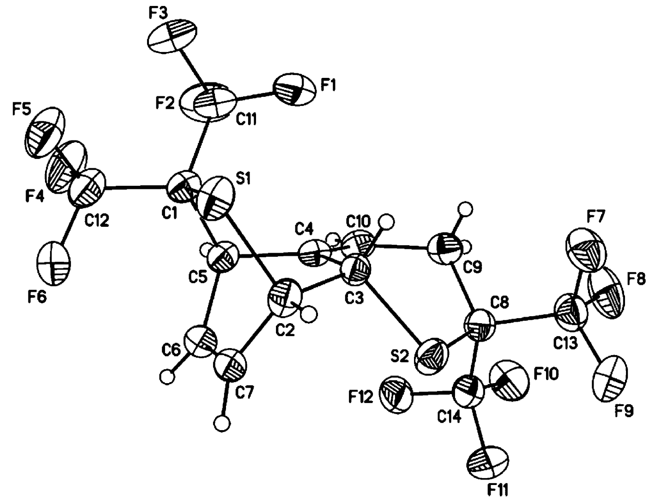
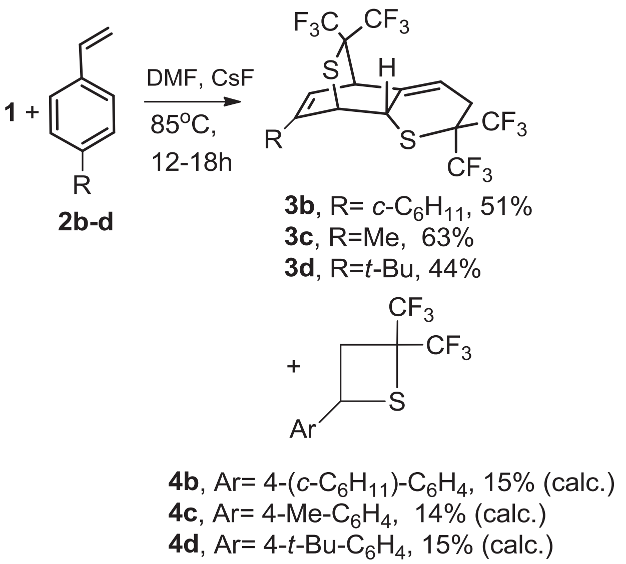


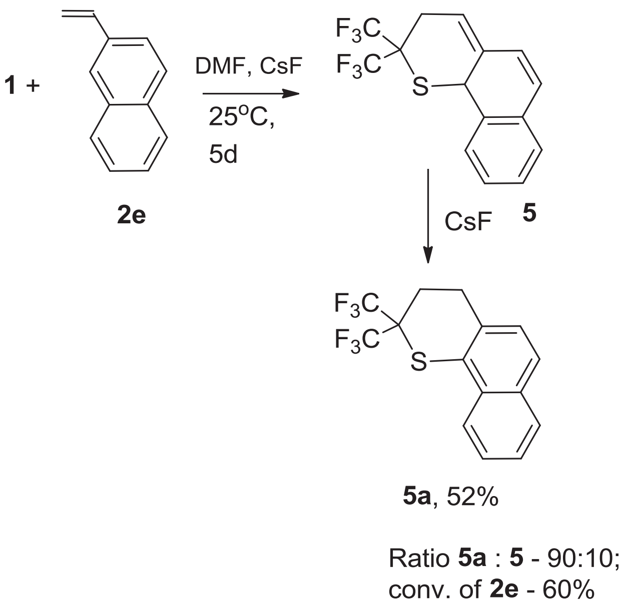
Fig. 1. Structure of adduct **3a**. Thermal ellipsoids are drawn to the 50% probability level.



(2)

Once again, the cycloaddition process leading to products **3b**–**d** was highly regioselective, leading in each case to exclusive formation of one isomer. According a single crystal X-ray diffraction compound **3b** (Fig. 2) has a structure similar to the structure of **3a**.

2-Vinylnaphthalene (**2e**) exhibited different reactivity towards **1**. It was more active in reaction with **1**, but the reaction led to selective formation of 1:1 cycloadduct **5a**, along with small amount of isomeric **5** (Eq. (3)):



(3)

The compound **5a** was purified by crystallization and high regioselectivity of the cycloaddition process was confirmed by single crystal X-ray diffraction. Indeed **5a** (see Fig. 3), forms as a single isomer in which sulfur is connected to C-1 of naphthalene system. No spectroscopic evidence indicating either the formation of other regioisomers or 2:1 Diels–Alder adducts was found in this reaction.

The outcome of the reaction was found to depend strongly on the source of fluoride ion. When it was carried out using less nucleophilic $Bu_4N^+F^- \cdot H_2O$, **5a** was not detected in the crude reaction mixture (NMR) and compound **5** (Eq. (4)) was the only

Table 1
Ratio of reagents, reaction conditions and yields of products for the reaction of 1 with styrenes **2a–l**.

Entry no.	Styrene (ratio **1:2**, mmol), solvent (mL)	Cat. (g)	Temp. (°C)	Time (h)	Products (ratio)[a]	Isolated products (yield, %)	M.p. (°C)[b] (b.p./mm Hg)	MS (*m/z*)
1	**2a** (35:25), DMF (20)	CsF (0.3)	85	12	**3a**, **4a** (90:10)	**3a** (51)	132–133	**3a**, 468 (M^+, $C_{14}H_8F_{12}S_2^+$) **4a**, 286 (M^+, $C_{11}H_8F_6S^+$)
2	**2b** (35:25), DMF (15)	CsF (0.5)	85	16	**3b**, **4b** (85:15)	**3b** (51)	113–114	**3b**, 550 (M^+, $C_{20}H_{18}F_{12}S_2^+$) **4b**, 368 (M^+, $C_{17}H_{18}F_6S^+$)
3	**2c** (23:22), DMF (20)	CsF (0.2)	85	8 h	**3c**, **4c** (86:14)	**3c** (63) **4c**[c] (12, calc.)	65–66	**3c**, 467 ($[M-CH_3]^+$, $C_{14}H_7F_{12}S_2^+$) **4c**, 300 (M^+, $C_{12}H_{10}F_6S^+$)
3	**2d** (25:22), DMF (35)	CsF (0.2)	85	8 h	**3d**, **4d** (85:15)	**3d** (44) **4d**[c] (14, calc.)	61–62	**3d**, 341 ($M-C_3F_6SH$, $C_{15}H_{16}F_6S^+$) **4d**, 342 (M^+, $C_{15}H_{16}F_6S^+$)
4	**2e** (12:11), DMF (15)	CsF (0.2)	25	5d	**5**, **5a**[d] (10:90)	**5a** (52)	81–82	**5a**, 336 M^+, $C_{15}H_{10}F_6S^+$)
5	**2e** (12:11), DMF (15)	$Bu_4N^+F^-\cdot H_2O$ (0.2)	(1) 85, (2) 25	8 h, 2 days	**5**[e]	**5** (40)	121–122	**5**, 336 M^+, $C_{15}H_{10}F_6S^+$)
6	**2f** (18:10), DMF (15)	CsF (0.3)	85	4d	**6**, **7** (15:85)	**7** (43)	51–52	**7,** 354 (M^+, $C_{12}H_7F_9S^+$)
7	**2f** (18:10), DMF (15)	$Bu_4N^+F^-\cdot H_2O$ (0.2)	85	5d	**6**[f]	**6** (30)	(92–95/3)	**6,** 354 (M^+, $C_{12}H_7F_9S^+$)
8	**2g** (20:10) DMF (15)	CsF (1.5)	85	40 h	**6a**, **7a**[g] (59:41)	**7a** (13), **6a** (19calc.)	**7a**, 66–68	**7a,** 320 (M^+, $C_{11}H_7ClF_6S^+$)
9	**2g** (20:15), DMF (15)	$Bu_4N^+F^-\cdot H_2O$ (0.2)	85	20 h	**3e**, **4e**[h] (37:63)	**3e** (53 calc.), **4e** (19% calc.)	–	**4e,** 320 (M^+, $C_{11}H_7ClF_6S^+$)
10	**2h** (27:17), DMF (15)	CsF (0.3)	85	10	**6b**, **4f**, **3f** (57:27:13)	**6b** (19)[i]		**6b**, 304 (M^+, $C_{11}H_7F_7S^+$) **4f,** 304 (M^+, $C_{11}H_7F_7S^+$)
11	**2i** (25:20), DMF (15)	CsF (0.3)	80	8 h	**3g**, **4g** (10:90)	**4g**[j] (60)	**4g** (100/1.4)	**4g**, 316 (M^+, $C_{12}H_{10}F_6OS^+$)
12	**2i** (25:20), DMF (15)	$Bu_4N^+F^-\cdot H_2O$ (0.3)	25	7d	**3g**, **4g** (95:5)	–	–	–
13	**2i** (25:20), THF (15)	$Bu_4N^+F^-\cdot H_2O$ (0.3)	25	18d	**3g**, **4g** (50:50)	–	–	–
14	**2j** (22:20), DMF (25)	$Bu_4N^+F^-\cdot H_2O$ (0.3)	25	2d	**4h**[k]	**4h**[k] (60)	**4h** (87–90/07)	330 (M^+, $C_{13}H_{12}F_6OS^+$)
15	**2k** (22:20), DMF (25)	$Bu_4N^+F^-\cdot H_2O$ (0.3)	25	8d	**4i**[l]	**4i**[l] (68)	**4i** (91–92/07)	358 (M^+, $C_{15}H_{16}F_6OS^+$)
16	**2l**[m] (22:20), DMF (25)	$Bu_4N^+F^-\cdot H_2O$ (0.3)	25[k]	8 h	**4j**[n] (91:9)	**4j**[n] (60)	**4j** (108–111/07)	346 (M^+, $C_{13}H_{12}F_6O_2S^+$)

[a] Ratio in crude product; the rest were starting materials.
[b] Crystallized from hexane, purity >98%.
[c] Was not isolated; characterized in reaction mixture.
[d] Conversion of styrene 60%.
[e] Conversion of styrene 50%.
[f] Conversion of styrene 30%.
[g] Conversion of styrene 50%.
[h] Conversion of styrene 60%.
[i] Conversion of styrene 80%; isolated by column chromatography, purity 94% (6% of **4f**).
[j] Purity 96% (4% of 2:1 Diels–Alder adduct).
[k] Mixture of thietane and 2:1 Diels–Alder adduct (ratio 87:13); purity of isolated thietane 96% (4% of 2:1 Diels–Alder adduct).
[l] Mixture of thietane and 2:1 Diels–Alder adduct (ratio 91:9); purity of isolated thietane 96% (4% of 2:1 Diels–Alder adduct).
[m] Addition of **2l** was exothermic.
[n] Mixture of thietane and 2:1 Diels–Alder adduct (ratio 87:13); purity of isolated thietane 94% (6% of 2:1 Diels–Alder adduct).

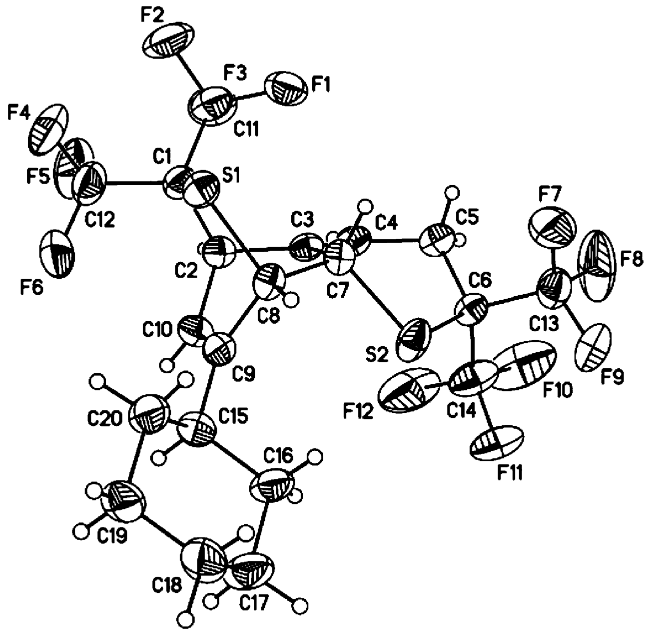


Fig. 2. Structure of adduct **3b**. Thermal ellipsoids are drawn to the 50% probability level.

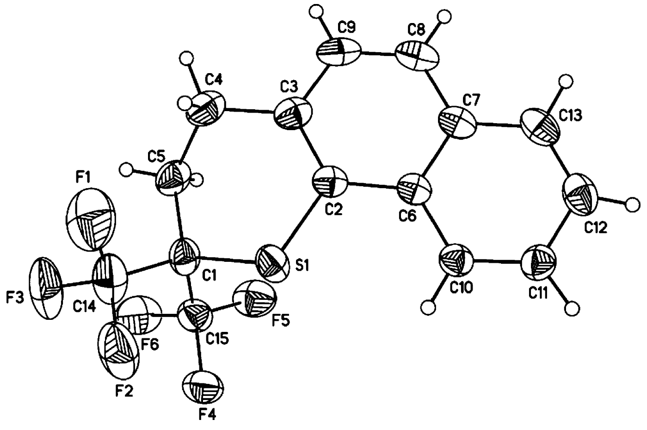


Fig. 3. Structure of **5a**. Thermal ellipsoids are drawn to the 50% probability level. Disordered sulfur position omitted for clarity.

Table 2
NMR data for new compounds[a].

Compound no.	^{1}H NMR (δ, ppm, J, Hz)	^{19}F NMR (δ, ppm, J, Hz)	^{13}C NMR (δ, ppm, J, Hz)
3a	2.21(1H, d, 15.4), 2.96(1H, dd, 15.4, 8.1), 3.86(1H, d, 6.6), 4.06(1H, s), 4.12(1H, d, 6.1), 5.92(1H, d, 7.8), 6.33(1H, t, 6.4), 6.58(1H, t, 7.7)	−64.95(3F, q, 11.7), −66.99(3F, qd, 11.7, 2.4), −69.67(3F, q, 10.1), −71.36(3F, q, 10.1)	26.12, 38.42, 40.71, 43.07, 62.32(sept, 26.0), 63.76(sept, 25.0), 121.15, 123.53(q, 286.0), 123.92(q, 286.0), 123.98(q, 284.0), 124.26(q, 282.0), 128.92, 132.23, 137.67
3b	1.30(2H, m), 1.78(1H, d, 13.6), 1.86(2H, m), 1.96(1H, d, 13.6), 2.17(1H, t, 12.1), 2.27(1H, d, 15.8), 3.00(1H, dd, 15.8, 8.2), 3.81(1H, s), 4.10(1H, s), 4.15(1H, d, 7.3), 5.90(2H, m)	−64.72(3F, q, 11.2), −66.62(3F, qd, 11.2, 2.5), −69.53(3F, q, 10.2), −71.18(3F, q, 10.2)	25.76, 25.98, 26.03, 26.13, 30.56, 31.29, 41.04, 41.61, 42.84, 42.85, 61.56(sept, 26.0), 64.56(sept, 25.5), 119.47, 119.63, 123.73(q, 288.0), 123.99(q, 284.0), 124.00(q, 288.0), 124.40(q, 282.0), 138.55, 149.86(q, 2.5)
3c	1.95(3H, s), 2.18(1H, d, 15.6), 2.94(1H, dd, 15.6, 8.2), 3.54(1H, m), 4.03(2H), 5.87(2H, t, 8.2)	−64.95(3F, q, 11.5), −67.12(3F, qd, 11.5, 2.5), −69.62(3F, q, 10.4), −71.27(3F, q, 10.4)	20.48, 25.64, 41.54, 42.79, 43.04, 61.49(sept, 28.0), 64.54(sept, 26.0), 119.80, 121.79 123.63(q, 285.0), 123.95(q, 286.0), 124.32(q, 282.0), 138.59, 141.57(q, 2.0)
3d	1.13(9H, s), 2.18(1H, d, 15.9), 2.73(1H, dd, 15.9, 8.0), 3.94(1H, m), 4.05(1H, m), 4.09(1H, d, 7.3) 5.84(1H, dm, 7.9), 5.91(1H, dm, 8.1),	−64.68(3F, q, 11.9), −66.71(3F, qd, 11.9, 2.6), −69.81(3F, q, 10.1), −71.34(3F, q, 10.1)	25.58, 28.29, 34.69, 49.22, 41.98, 42.64, 61.29(sept, 26.7), 64.39(sept, 25.4), 119.18, 119.50, 123.78(q, 284.0), 124.00(q, 283.0), 124.43(q, 281.0), 138.34, 152.46(q, 2.0)
3e	2.19(1H, d, 15.4), 2.97(1H, dd, 15.4, 8.0), 3.80(1H, s), 4.02(1H, s), 4.18(1H, d, 7.0), 5.94(1H, m), 6.18(1H, dm, 7.4)	−64.76(3F, q, 10.1), −67.36(3F, qd, 10.1, 2.2), −69.61(3F, q, 10.1), −71.70(3F, q, 10.1)	
3f	2.22(1H, d, 15.4), 2.92(1H, dd, 15.4, 8.0), 3.76(1H, d, 11.2), 3.99(1H, s), 4.23(1H, dd, 7.9, 2.5), 5.57(1H, m), 5.95(1H, m)	−64.53(3F, q, 11.5), −67.00(3F, qt, 11.5, 2.1), −69.57(3F, q, 10.0), −71.13(3F, q, 10.0), −101.34(1F, m)	
3g[b,c]	2.13(1H, d, 15.5), 2.88(1H, dd, 15.5, 8.0), 3.76(3H, s), 3.89(1H, s), 4.07(1H, dd, 7.8), 4.86(1H, dm, 7.6) 5.76(1H, dm, 7.6)	−64.76(3F, q, 11.2), −66.51(3F, qd, 11.2, 2.0), −69.57(3F, q, 9.9), −71.17(3F, q, 9.9)	
3h[d,e]	1.25(3H, t, 7.1), 2.12(1H, d, 15.0), 2.86(1H, dd, 15.0, 8.0), 3.51(1H, m), 3.73(2H, q, 7.1), 3.89(1H, m), 4.05(1H, dd, 7.8), 4.80(1H, dm, 7.6) 5.70(1H, dm, 7.4)	−64.78(3F, q, 11.6), −66.55(3F, qd, 11.6, 2.1), −69.59(3F, q, 10.2), −71.18(3F, q, 10.2)	
4a[e]	3.35(2H, AB quart.), 4.86(1H, t, 8.4) 7.20–7.40(5H)	−73.18(3F, q, 9.7), −74.39(3F, q, 9.7)	
4b[e]	1.30–3.0(10H), 3.31(2H, AB quart.), 4.82(1H, t, 8.4) 7.20–7.40(4H)	−73.14(3F, q, 9.9), −74.36(3F, q, 9.9)	
4c[e]	1.95(3H, s), 3.32(2H, AB quart.), 4.83(1H, t, 8.4) 7.19(2H, d, 7.3), 7.31(2H, d, 7.3)	−73.16(3F, q, 9.7), −74.37(3F, q, 9.7)	
4d	1.31(9H, s), 3.33(2H, A:B quart.), 4.84(1H, t, 8.3), 7.41(2H, d), 7.48(2H, d)	−73.15(3F, q, 9.8), −74.36(3F, q, 9.8)	
4e	3.84(2H, A:B quart.), 4.84(1H, t, 8.4), 7.32(2H), 7.44(2H)	73.23(3F, q, 9.6), −74.42(3F, q, 9.6)	
4f	3.32(2H, A:B quart.), 4.84(1H, t, 8.4), 7.07(2H), 7.51(2H)	−73.20(3F, q, 9.6), −74.39(3F, q, 9.6) −112.74(1F, m)	
4g	3.25(2H, A:B quart.), 3.74(3H, s), 4.75(1H, t, 8.7), 6.84(2H, d), 7.38(2H, d)	−73.11(3F, q, 9.7), −74.34(3F, q, 9.7)	
4h	1.35(3H, t, 7.0), 3.25(2H, A:B quart.), 3.96(2H, q, 7.0), 4.74(1H, t, 8.1), 6.82(2H, d), 7.36(2H, d)	−73.10(3F, q, 9.6), −74.33(3F, q, 9.6)	
4i[f]	1.28(9H, s), 3.26(2H, A:B quart.), 3.96(2H, q, 7.0), 4.75(1H, t, 8.1), 6.92(2H, d), 7.34(2H, d)	−73.12(3F, q, 9.9), −74.33(3F, q, 9.9)	
4j	3.32(2H, A:B quart.), 3.88(3H, s), 3.92(3H, s), 4.80(1H, t, 8.0), 6.83(1H, d), 7.01(1Hdd) 7.15(1H, d)	−73.20(3F, q, 10.2), −74.36(3F, q, 10.2)	36.95, 36.56, 46.88(sept, 31.9), 55.15, 114.26, 123.74(q, 280), 125.34(q, 278), 128.96, 132.62, 159.96
5	2.21(1H, d, 15.6), 3.31(1H, dd, 15.6, 8.0), 5.01(1H, s), 4.06(1H, s), 6.03(1H, t, 6.0), 6.40(1H, d), 6.46(1H, d), 7.18(1H, d) 7.27(2H, m), 7.56(1H, d)	−69.53(3F, q, 9.8), −70.58 (3F, q, 9.8)	
5a	2.38(2H, t, 6.1), 3.04(2H, t, 6.1), 7.31(1H, d), 7.51(1H, t), 7.57(1H, t), 7.71(1Hd), 7.84(1H, d), 8.24(1H, d)	−71.12(s)	27.13, 40.31, 57.36(sept, 27.2), 121.76, 123.81(q, 283), 123.94, 126.95, 127.87, 128.28, 128.76, 129.41, 130.40, 133.01, 141.37
6	2.30(2H, t, 6.3), 2.94(2H, t, 6.3), 7.36(1H, m), 7.77(1H, m), 7.88(1H, m)	−63.14(3F, s), −70.09(6F, s)	
6a	2.27(2H, t, 5.6), 2.84(2H, t, 5.6), 7.13(1H, m), 7.27(1H, m), 7.33(1H, m)	−71.28(s)	
6b	2.28(2H, m), 2.84(2H, t, 6.10, 6.91(1H, m), 7.07(1H, m), 7.16(1H, m)	−72.29(s), −114.13(m)	
7	3.00(2H, t, 5.8), 3.27(2H, t, 5.8), 7.38(1H), 7.62(1H), 8.04(1H)	−62.89(3F, s), −67.28(6F, s)	23.88, 32.12, 58.74(sept, 26.8), 122.40, 124.10(q, 284), 124.55, 124.77, 126.36(m), 131.72, 142.45
7a	2.96(2H, t, 5.8), 3.17(2H, t, 5.8), 7.18(1H), 7.25(1H), 7.76(1H)	−67.25(s)	24.15, 32.60, 56.77(sept, 28.1), 124.12(q, 286), 125.29, 129.35(sept, 3.2), 129.92, 132.15, 132.78, 136.83

[a] In $CDCl_3$ solvent.

[b] Reported values: −3.97(3F, q, 10), −2.66(3F, q, 10), −0.966(3F, q, 11), −0.98; (3F, q, 11) ppm ($FCCl_2CCl_2F$, external standard).

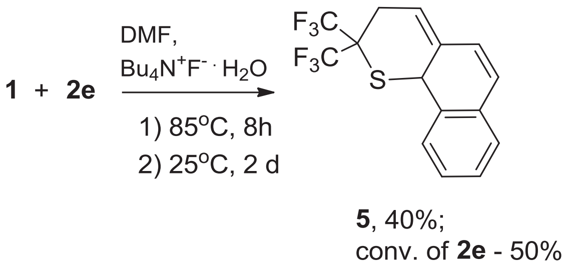
[c] In the product isolated from the reaction carried out in the presence of $Bu_4N^+F^{\bullet-}\cdot H_2O$, a second set of signals corresponding to isomer of **3g** was present: δ = −63.51(q, 10.2 Hz), −64.71(q, 11.7 Hz), −66.41(qd, 11.7, 2.3 Hz), −67.14(q, 10.3 Hz) ppm.

[d] In the product isolated in the reaction carried out in the presence of $Bu_4N^+F^{\bullet-}\cdot H_2O$, a second set of signals corresponding to isomer of **3h** was present: δ = −63.39(3F, q, 10.8 Hz), −64.75(3F, q, 11.7 Hz), −66.44(3F, qd, 11.7, 2.8 Hz), −67.16(3F, q, 10.8 Hz) ppm.

[e] Characterized by NMR in the crude reaction mixture.

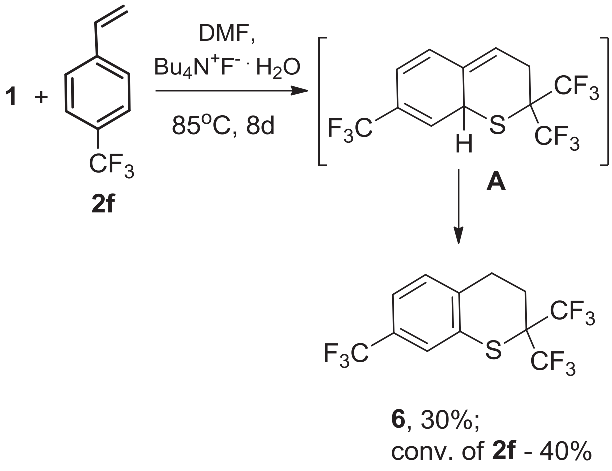
[f] 2:1 Diels–Alder adduct ^{1}H NMR: 1.31(9H, s), 2.12(1H, d, 15.2), 2.86(1H, dd, 15.2, 8.0), 3.37(1H, s) 3.87(1H, s), 3.99(1H, d, 8.0), 4.88(1H, dm, 8.0), 5.73(1H, s) ppm; ^{19}F NMR: −64.78(3F, q, 11.6), −66.55(3F, qt, 11.5, 1.8), −69.59(3F, q, 10.5), −71.80(3F, q, 10.5) ppm.

product, despite the fact that this reaction was carried out at elevated temperature:



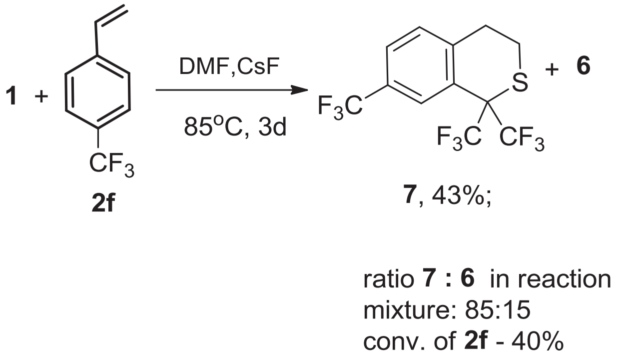
(4)

The introduction of an electron withdrawing substituent in the *para*-position of styrene slows down significantly the Diels–Alder reaction. The typical conversion of styrenes did not exceed 30–60%, even after prolonged heating. For example, the reaction of 4-CF_3-styrene (**2f**) with **1** resulted in selective formation of the 1:1 Diels–Alder cycloadduct **6** (Eq. (5)):



(5)

The absence of intermediate **A** in the reaction mixture may be attributed to increased acidity of the proton in α-position to sulfur, which accelerates the base catalyzed isomerization of **A** into **6**. The replacement of $Bu_4N^+F^-{\cdot}H_2O$ by more active CsF results in a different outcome, leading unexpectedly to the predominant formation of isomer **7**:



(6)

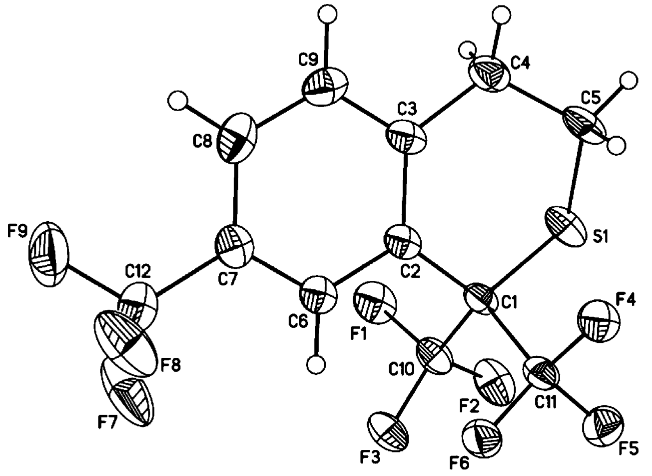
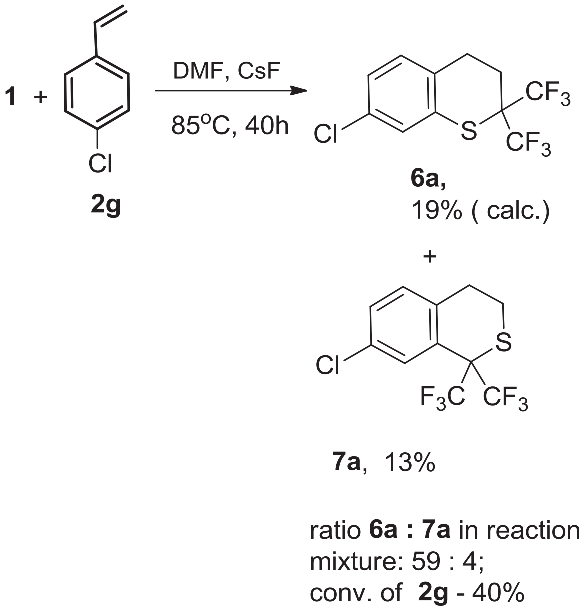


Fig. 4. Structure of **7**. Thermal ellipsoids are drawn to the 30% probability level. Disordered fluorine positions omitted for clarity.

Pure compound **7** was isolated from the reaction mixture by column chromatography and its structure was confirmed by single crystal X-ray diffraction data (Fig. 4).

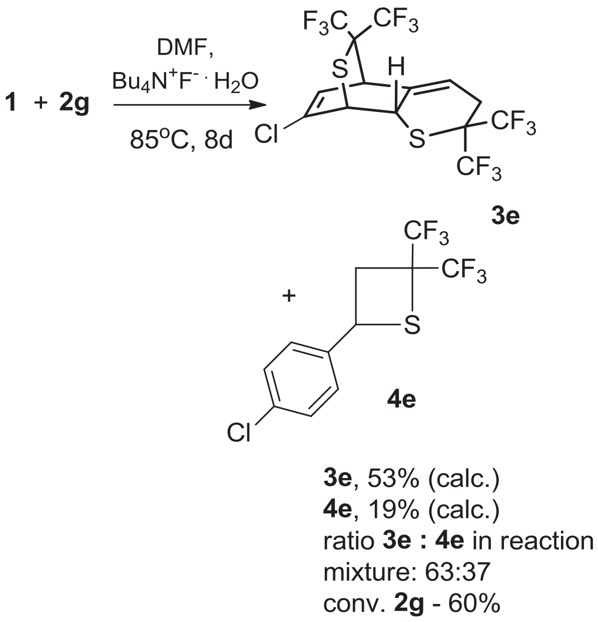
4-Chlorostyrene (**2g**) has similar reactivity and reacts with **1** in the presence of CsF catalyst slowly (55% conversion after 40 h at 85 °C), to produce a mixture of isomers **6a** and **7a** (calc. yield 39 and 19% respectively):



(7)

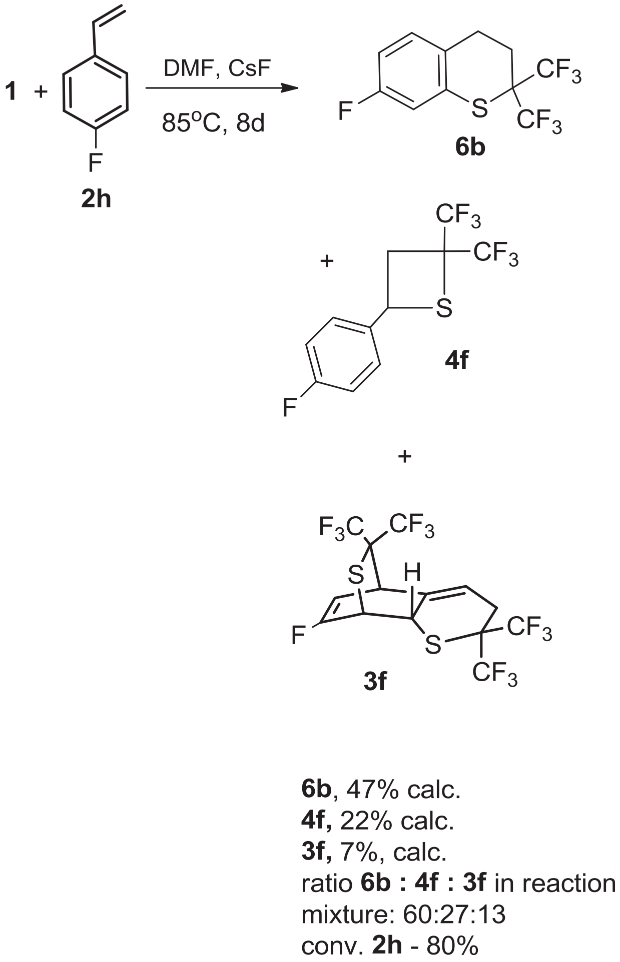
Compound **7a** was isolated from the reaction mixture in 13% yield and its structure was confirmed by single crystal X-ray diffraction.

The effect of the catalyst was also very pronounced in this reaction. When carried out in the presence of $Bu_4N^+F^-{\cdot}H_2O$ catalyst, **3e** and **4e** were the principal products (Eq. (8)) although, the formation of either **6a** or **7a** was not observed under reaction conditions (NMR):



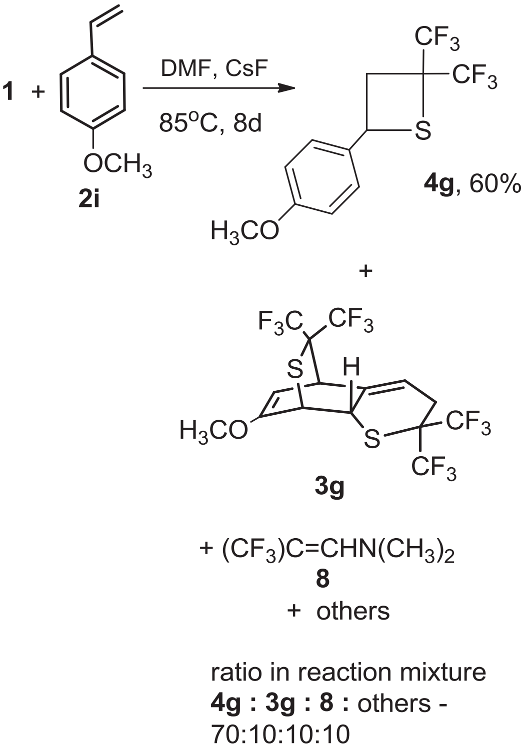
(8)

The reaction 4-fluorostyrene (**2h**) and **1** catalyzed by CsF produced a mixture of compounds **6b**, **4f** and **3f** in ratio 60:27:13 (Eq. (9)):



(9)

The introduction of an alkoxy group in the *para*-position not only increased the reactivity of styrene towards **1**, but it also significantly altered the distribution of reaction products. For example, 4-methoxy styrene (**2i**) rapidly reacts with **1** at elevated temperature (CsF, 8 h, 85 °C) with formation of the *thietane* **4g** as a principal product (Eq. (10)). The reaction mixture also contained a small amount of 2:1 Diels–Alder adduct **3g**, $(CF_3)_2C{=}CHN(CH_3)_2$ (**8**, see discussion below) and two unidentified products (ratio in the reaction mixture 70:10:10:10, respectively):



(10)

The thietane **4g** was isolated in 60% yield and its structure was confirmed by single crystal X-ray diffraction (Fig. 5).

Due to its higher reactivity, the reaction of **2i** with **1** can be carried out at ambient temperature (Eq. (11)) in the presence of $Bu_4N^+F^-{\cdot}H_2O$ catalyst. It produces the thietane **4g**, along with adduct **3g** and another material, the formation of which was not observed at elevated temperature (additional set of signals in ^{19}F NMR spectrum: $\delta = -63.51$(q, 10.2 Hz), -64.71(q, 11.7 Hz), -66.41(qd, 11.7, 2.3 Hz), -67.14(q, 10.3 Hz) ppm, ratio 1:1:1:1). Based on data of NMR spectroscopy and GC/MS spectrometry it was established that new material was an isomer of **3g**, although its exact structure was not determined.

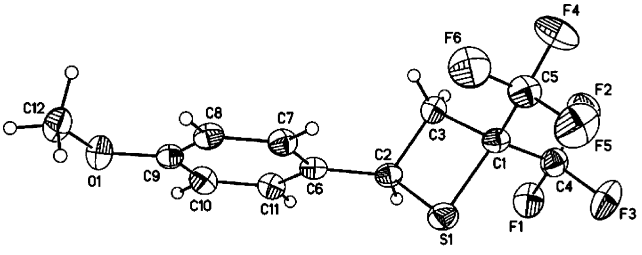
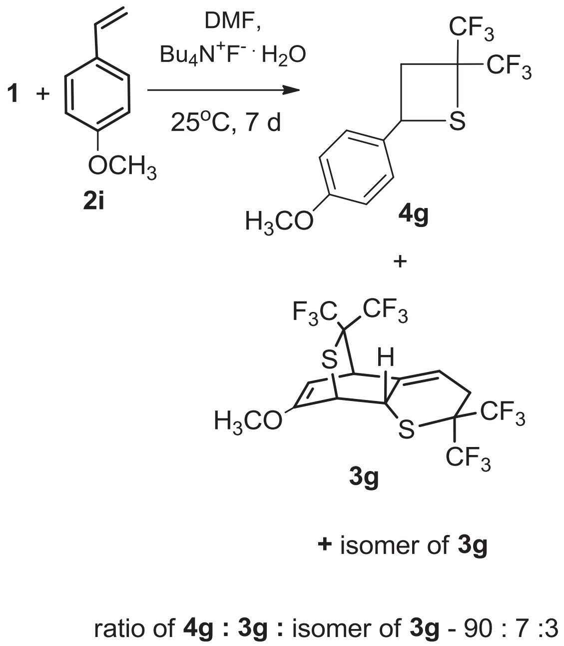


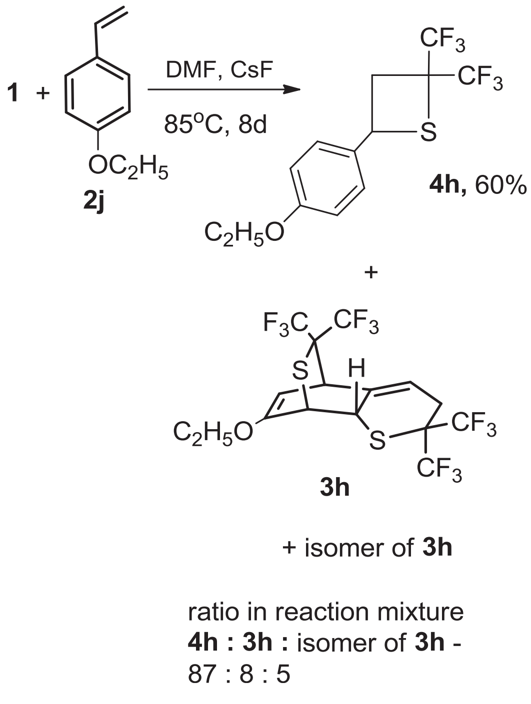
Fig. 5. Structure of **4g**. Thermal ellipsoids are drawn to the 30% probability level.



(11)

It should be also pointed out that the polarity of the solvent had a remarkable effect on the ratio of **4g** and **3g**. For example, the reaction of **2i** and **1** carried out in less polar THF (18 days at 25 °C) resulted in a four fold increase of 2:1 Diels–Alder cycloadduct **3g** and the formation of 1:1 mixture of thietane **4g** and **3g** (the isomer of **3g** was not detected in the reaction mixture, NMR).

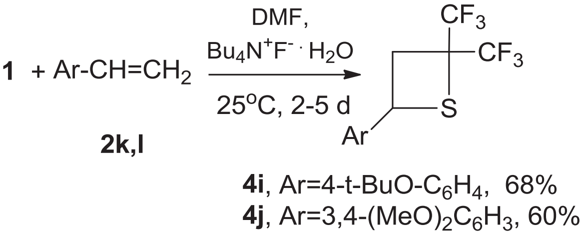
The formation of a second isomer of 2:1 Diels–Alder cycloadduct was also observed in the reaction of styrene **2j** (Eq. (12)). Similar to the reaction of **2i** in DMF, ^{19}F NMR spectrum of the crude reaction mixture along with signals of two principal products **4h** and **3h**, had an additional set of four signals shifted *upfield* relative to signals of **3h** (δ = −63.39(3F, q, 10.8 Hz), −64.75(3F, q, 11.7 Hz), −66.44(3F, qd, 11.7, 2.8 Hz), −67.16(3F, q, 10.8 Hz) ppm, integration 1:1:1:1):



(12)

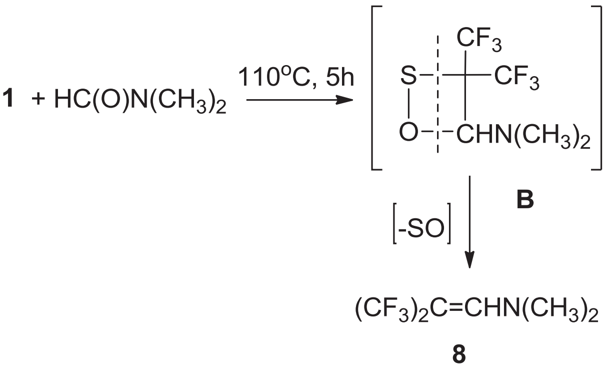
The isomeric material was found to be thermally liable, since after isolation of **4h** by distillation, the NMR analysis of the residue revealed the presence of compound **3h** only, while all signals of the isomeric product had disappeared. Limited thermal stability may also explain the absence of isomeric 2:1 cycloadducts in reactions of styrenes **2a–d** and **2i**, since all these reactions were carried out at elevated temperature.

The reactions of other 4-alkoxy styrenes [RO = OBu-t (**2k**) and 3,5-OMe (**2l**)] with **1** were also relatively slow (2–5 days) at ambient temperature. All reactions carried out in DMF solvent produced a mixture of the corresponding thietanes **4i** or **4j** as two major products (Eq. (13)), along with 10–15% of the corresponding Diels–Alder cycloadducts structurally similar to **3h** (NMR), which were not isolated. Thietanes **4i** and **4j** isolated by distillation (purity 95–97%, see Table 1, entries 15–16) were fully characterized by NMR spectroscopy and MS spectrometry:



(13)

As were mentioned above, all reactions of **1** with styrenes at elevated temperature are accompanied by the formation of a detectable amount of $(CF_3)_2C{=}CHN(CH_3)_2$ (**8**) [13,14] and some nonfluorinated high molecular weight by-products, derived from polymerization of styrenes. Although both processes are relatively slow even at elevated temperature, the formation of byproducts complicates the isolation and lowers the yields of desirable products. As demonstrated in a separate experiment, compound **8** derives from the reaction of **1** with DMF: heating the solution of **1** in DMF led to clean formation of **8** (30% yield after 5 h at 110 °C), identified in the reaction mixture by NMR spectroscopy:



(14)

The formation of **8** was previously observed in the reaction of perfluoroisobutene and DMF [13,14]. A possible mechanism explaining the formation of **8** involves the unstable [2 + 2] cycloadduct **B** (see Eq. (14)) as an intermediate, which further undergoes decomposition. The formation of **8** in the absence of added fluoride ion suggests that at elevated temperature DMF can act as a base, causing the dissociation of **1** with the formation of HFTA. Although the reaction of **1** with DMF is slow even at 110 °C, it is advisable to use an excess of **1** in all reactions carried out in DMF at elevated temperature.

2.2. NMR spectroscopy

Despite the fact that compounds **3a** and **3g** were prepared a long time ago, only limited spectroscopic information is available [1]. Since the identification of reaction products in the present study relied heavily on NMR of the reaction mixtures, the peculiarities of the NMR spectra of new materials need to be discussed. In ^{19}F and ^{1}H spectra the resonances exhibited by major products (Diels–Alder adducts **3a–h**, thietanes **4a–j** and benzothianes **5**, **5a**, **6**, **6a–b** and **7**, **7a**) were well separated and appeared in certain regions. Isolation of representatives of the major types of products combined with structural assignment carried out for compounds **3a**, **3b**, **5a**, **4g**, **7** and **7a** by a single crystal X-ray diffraction (see Figs. 1–5) assured correct identification of the major products.

Due to a loss of aromaticity, the ^{1}H NMR spectra of compounds **3a–h** do not exhibit any resonances in the aromatic region, but instead the spectra of all materials contain two (or three in case of **3a**) resonances of vinyl protons between 4.0 and 5.9 ppm, along with the resonances of magnetically nonequivalent protons of –CH$_2$ group (AB quartet, J_{A-B} = 15–16 Hz) between 2.0 and 3.0 ppm. The resonance of the upfield proton appears as a doublet of doublets with an additional coupling constant (J = 7.8–8.2 Hz, probably to vinyl proton located in same heterocycle). ^{19}F NMR spectra of **3a–g** typically exhibit four separate resonances of CF$_3$ groups of equal intensity. Two upfield signals (quartets at $\delta = \sim -65$ and ~ -67 ppm) were assigned to trifluoromethyls connected to the carbon of the bridge and two more shielded resonances ($\delta = -69.5$ and -72.0 ppm) to trifluoromethyls of unsaturated thiane ring.

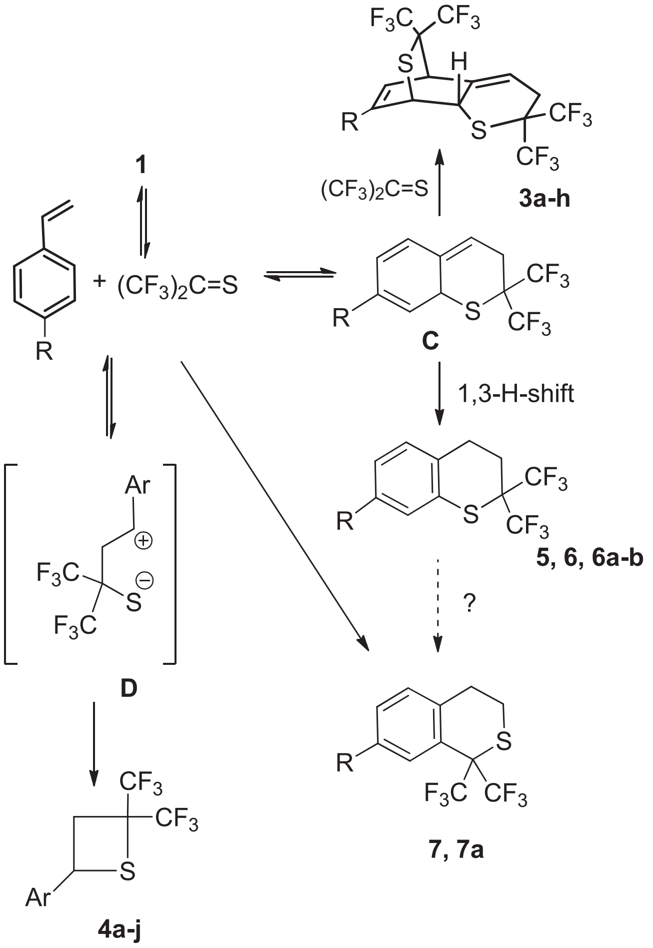
The parameters of ^{19}F NMR spectra of thietanes **4a–j** are similar to those reported for 4-alkoxy-2,2-bis(trifluoromethyl)thietanes [6,10], although in ^{19}F spectra the resonances of CF$_3$ groups are well separated and appear as two quartets at $\delta = \sim -73$ and ~ -74 ppm (J = 9–11 Hz).

In ^{19}F NMR spectra of compounds **5a**, **6**, **6a–b**, **7**, **7a** the resonance of trifluoromethyl groups appear as a singlet. In compounds **7** and **7a** (containing C(CF$_3$)$_2$ group connected directly to aryl group) the resonance is shifted upfield and appear in the range ($\delta = -67$ to -69 ppm *vs.* the corresponding resonances in **5a**, **6**, **6a–b** $\delta = -70$ to -71 ppm) probable due to steric deshielding. In ^{1}H NMR spectra, the resonances of both CH$_2$ groups in **7** and **7a** shifted downfield, relative to the corresponding signals in **5a**, **6**, **6a–b**.

2.3. Mechanistic considerations

The rather complicated mechanism of the fluoride ion catalyzed reaction of styrenes **2** with **1** is depicted in Scheme 1. HFTA (generated by reaction of F$^-$ with **1**) reacts with styrene to form the Diels–Alder adduct **C**. It is likely that this step is reversible, since similar reaction of $(CF_3)_2C{=}C(CN)_2$ and styrenes [16] (originally reported by Middleton [15], but later reinvestigated in great details by Brueckner and Huisgen [16,17]) was demonstrated to be reversible. Under the reaction conditions intermediate **C** can:

(a) react irreversibly with a second mole of styrene to form 2:1 cycloadduct (**3a–h**) – this process is favored by σ – electron donors, such as alkyl groups, but suppressed by electron withdrawing substituents, such as CF$_3$;
(b) undergo retro Diels–Alder process, giving back styrene and HFTA; these two can recombine forming zwitter ion **D**, which further is converted into thietane **4** through irreversible cyclization. Simultaneous formation adducts **3a–g** and thietanes **4a–j** in most cases is indicative that these two are competitive processes, having comparable rates;
(c) undergo 1,3-proton shift to give benzothianes **5a**, **6**, **6a–b**. Electron withdrawing substituents in *para*-position of phenyl group facilitate this process by enhancing the acidity of the proton in α-position to sulfur.



Scheme 1.

The mechanism of further isomerization of **6** and **6a** into **7** and **7a** is not entirely clear. A possible mechanism may involve retro Diels–Alder reaction of intermediate **C** to give styrene and HFTA and "reversed cycloaddition to give compounds **7** and **7a**, but this mechanism does not explain the fact that this process was observed only in the presence of dry CsF (but not for $Bu_4N^+F^-{\cdot}H_2O$) catalyst. At this point existing experimental data are not sufficient to rule out a direct conversion of compounds **6** and **6a** into **7** or **7a** either.

The observed effect of the substituent on the phenyl ring is consistent with the proposed mechanism (Scheme 1). Indeed, the introduction of *p*-donors (especially RO–, and to some extent –F or –Cl substituents) in the *para*-position of the phenyl ring should lead to the stabilization of the zwitter ion **D**, favoring the formation of the thietane product. Even more pronounced trend was observed for the reaction of $(CF_3)_2C{=}C(CN)_2$: while the Diels–Alder products were isolated in the case of 4-R-styrenes (R = H, Cl, Br, F), the exclusive formation corresponding 2 + 2 cycloadducts was observed in the reaction of 4-alkoxy styrenes with $(CF_3)_2C{=}C(CN)_2$ [16,17].

In case of the reaction of HFTA with styrenes alkyl substituents in *para*-position can contribute to some extent to the stabilization of zwitter-ion **D** (facilitating the formation of thietanes **4b–d** byproducts), but strong electron acceptors significantly destabilize the zwitter ion **D**, which can completely shut down the channel of the reaction involving formation of **D** and the formation of the corresponding thietanes.

High sensitivity of the reaction of 4-MeO-styrene and **1** (see discussion in Section 2.1, entries 12, 13, Table 1) is also consistent with the formation of highly polar intermediate in this process. Indeed, when the reaction was carried out in more polar DMF, it led to preferential formation of thietane **4g** (rather than the Diels–Alder adduct **3g**), which probably is the result of better stabilization of polar zwitter-ion **D**, favoring the formation of thietane, rather than the corresponding Diels–Alder adduct.

3. Conclusion

In this study it was demonstrated that the outcome of fluoride ion catalyzed reaction of *para*-substituted styrenes with **1** depends strongly on the structure of the styrene, the nature of the catalyst and polarity of solvent. Major types of products formed in this process were isolated, fully characterized and their structure was established by a single crystal X-ray diffraction.

4. Experimental

^{1}H NMR and ^{19}F NMR spectra were recorded on a Bruker DRX-500 (499.87 MHz) instrument using $CFCl_3$ or TMS as an internal standards. Unless stated otherwise, $CDCl_3$ was used as a lock solvent. GC and GC/MS analyses were carried out on a HP-6890 instrument, using HP FFAP capillary column and either TCD (GC) and mass selective (GS/MS) detectors, respectively. $Bu_4N^+F^-\cdot H_2O$, dry DMF and dry THF (Aldrich), styrenes **2a–l** were obtained from commercial sources and used without further purification. CsF (Aldrich) was dried at 100–120 °C under dynamic vacuum for 4–8 h and was stored in the glove box. Since $Bu_4N^+F^-\cdot H_2O$ readily absorbs water it was also stored and handled inside of the dry box. Compound **1** was prepared according modified procedure using CsF as a catalyst [10]. Due to a high ratio of sulfur to fluorine, elemental analysis were not attempted for new materials and the purity of all isolated compounds established by GC and NMR spectroscopy was at least 97%.

4.1. Crystallography

X-ray data for **3a**, **3b**, **5a**, **4g**, **7** and **7a** were collected at −100 °C using a Bruker 1K CCD system equipped with a sealed tube molybdenum source and a graphite monochromator. The structures were solved and refined using the Shelxtl [18] software package, refinement by full-matrix least squares on F^2, scattering factors from Int. Tab. Vol. C Tables 4.2.6.8 and 6.1.1.4. Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC #799785–799790. 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).

4.2. Reaction of 1 with styrenes (typical procedure)

A mixture of 12–35 mmol of **1** (∼10–15 mol% excess), 10–30 mmol of the corresponding styrene, 0.1–0.5 g of the catalyst and 15–50 mL of dry DMF was agitated at 25–85 °C for period of time specified in Table 1. The reaction mixture was diluted with 200–300 mL of water, extracted by hexane (50 mL ×3), combined organics was washed by water (100 mL ×2), dried over $MgSO_4$ and hexane was removed under reduced pressure. Crude product was isolated either by distillation (compounds **6a**, **4g**, and **4h**) or column chromatography (Silicagel 60, eluent hexane/ethyl acetate 9:1) and crystallization from hexane. Reaction conditions, ratio of reagents, yields, melting (boiling) points and data of mass-spectrometry for products are given in Table 1. ^{1}H, ^{13}C, ^{19}F NMR data are can be found in Table 2.

Acknowledgements

Authors are grateful to Dr. C. Junk for helpful discussion and suggestions and Timothy Bentz for technical support.

References

[1] W.J. Middleton, J. Org. Chem. 30 (1965) 1390.
[2] T. Wagner-Jauregg, Synthesis (1980) 769.
[3] M.S. Raasch, J. Org. Chem. 35 (1970) 3470.
[4] D.C. England, J. Org. Chem. 46 (1981) 153.
[5] T. Kitazume, N. Ishikawa, Chem. Lett. 3 (1973) 267.
[6] T. Kitazume, T. Otaka, R. Takei, N. Ishikawa, Bull. Chem. Soc. Jpn. 49 (1976) 2491.
[7] V.A. Petrov, ACS Symp. Ser. 1003 (2009) 105.
[8] T. Kitazume, N. Ishikawa, Bull. Chem. Soc. Jpn. 46 (1973) 3285.
[9] V. Petrov, W. Marshall, J. Fluorine Chem. 128 (2007) 729.
[10] V.A. Petrov, W. Marshall, J. Fluorine Chem. 131 (2010) 1144.
[11] V.A. Petrov, C.G. Krespan, W. Marshall, J. Fluorine Chem. 126 (2005) 1332.
[12] S.A. Postovoi, I.M. Vol'pin, N.I. Delyagina, M.V. Galakhov, Y.V. Zeifman, L.S. German, Izv. Akad. Nauk SSSR, Ser. Khim. (1989) 1380.
[13] Y.A. Cheburkov, I.L. Knunyants, Izv. Akad. Nauk SSSR, Ser. Khim. (1967) 346.
[14] Y.A. Cheburkov, N. Mukhamadaliev, Y.E. Aronov, I.L. Knunyants, Izv. Akad. Nauk SSSR, Ser. Khim. (1965) 1478.
[15] W.J. Middleton, J. Org. Chem. 30 (1965) 1402.
[16] R. Brueckner, R. Huisgen, Tetrahedron Lett. 31 (1990) 7133.
[17] R. Brueckner, R. Huisgen, J. Schmid, Tetrahedron Lett. 31 (1990) 7129.
[18] G. Sheldrick, SHELXTL Sofware Suite, v. 6.0, Bruker Axes Corp., Madison, WI, 1996