Pergamon
Tetrahedron Letters 41 (2000) 3069–3072
TETRAHEDRON
LETTERS

Synthetic uses of thioesters of trifluoromethylated acids. Part 2: Reactions with alkenes

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Received 29 January 2000; accepted 22 February 2000

Abstract

The photolysis of trifluoromethanethiosulfonates (CF_3SO_2SR) or trifluorothioacetates (CF_3COSR) in the presence of alkenes provides (trifluoromethyl)alkanes or β-sulfanyl (trifluoromethyl)alkanes. The formation of these compounds can be controlled by the nature and the ratio of the reactants. © 2000 Published by Elsevier Science Ltd. All rights reserved.

Keywords: trifluoromethanethiosulfonates; trifluorothioacetates; photolysis; (trifluoromethyl)alkanes.

The steadily growing interest for fluorinated compounds and, especially, trifluoromethylated products, requires new methods to introduce directly the CF_3 moiety.[1] Among all the presently available strategies,[2] radical trifluoromethylation constitutes the most versatile tool.

We recently described the synthesis[3,4] and the photolytic behavior[4] of thioesters of trifluoroacetic (CF_3COSR) or triflic (CF_3SO_2SR) acids and reported that, under UV irradiation, they generate trifluoromethyl radicals which can be trapped by disulfides to yield trifluoromethyl sulfides.

We have now extended this reaction to alkenes as trapping substrates in order to obtain trifluoromethylated alkanes. The procedure is typically the same as that for disulfides.[5] The results are summarized in Table 1.

In all cases phenyl trifluoromethanethiosulfonate (**1**) led to a mixture of products resulting from a formal addition of CF_3-SR (compounds **4**) and products resulting from a formal hydrotrifluoromethylation (compounds **5**) whereas trifluorothioacetates (**2**) generally delivered **4** only. The high regioselectivity of these reactions must be noticed since, in all cases, the $^{\cdot}CF_3$ radical reacted on the less hindered carbon of the double bond. Such a sensitivity to steric factors explains that best results were obtained from terminal olefins (Table 1, entries 5–9). The different behaviors of **1** and **2** can be rationalized through the mechanism proposed in Scheme 1.

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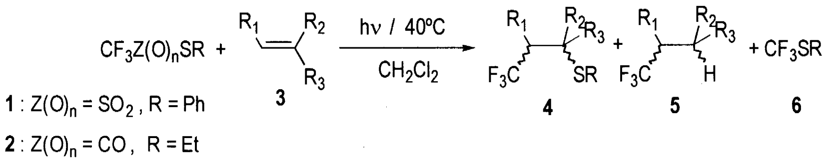
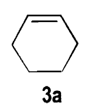
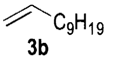
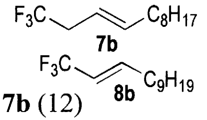
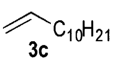
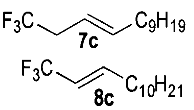
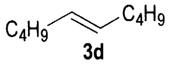
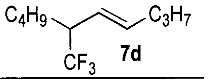
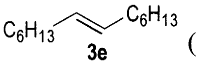
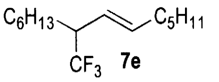
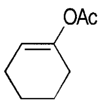
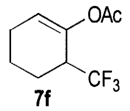
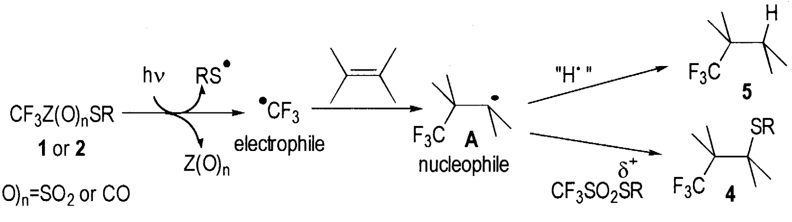
PII: S0040-4039(00)00337-3

Table 1
Photolysis of **1** or **2** in presence of alkenes (**3**)



N°	**1** or **2** (eq.)	**3** (eq.)		$4^{a,b}$ (%)	$5^{a,b}$ (%)	$6^{a,c}$ (%)	Other products ^{a} (%)
1	**1** (1)	 **3a**	(1)	13 (2 dia 99/1)	26	3	
2	**1** (2)		(1)	40 (2 dia 75/25)	25	9	
3	**1** (1)		(2)	8^c	50^c	2	
4	**2** (1.4)		(1)	0	38	12	
5	**1** (1)	 **3b**	(1)	11	36	0	**7b** (12)  **7b** **8b**
6	**1** (2)		(1)	49	33	8	
7	**1** (3)		(1)	46	30	14	
8	**1** (1)		(2)	9^c	40^c	2	**8b** (16) + **7b** (12)
9	**2** (1.6)	 **3c**	(1)	7	36	21	**7c** + **8c** (6)  **7c** **8c**
10	**1** (2)	 **3d**	(1)	26 (2 dia 54/46)	37	11	**7d** (23)  **7d**
11	**2** (1.8)	 **3e**	(1)	0	39	22	**7e** (4)  **7e**
12	**2** (1.4)	 **3f**	(1)	0	26	23	**7f** (3)  **7f**

[a] Determined by ^{19}F NMR analysis *vs.* an internal standard ($PhOCF_3$)
[b] Yields *vs.* **3**, in general
[c] Yields *vs.* **1** or **2**



Scheme 1. Principle of the trifluoromethylation

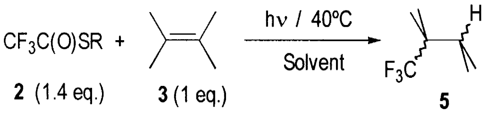
After addition of the electrophilic $^{\cdot}CF_3$ radical onto the substrate, a new carbon-centered radical **A** is formed. However, radical **A** has a weak nucleophilic character[6] which needs to react with a highly electrophilic sulfur atom to deliver **4**. We recently demonstrated that trifluoromethanethiosulfonates are very electrophilic sulfenylating agents because of the high electron-withdrawing character of the CF_3SO_2 moiety,[7] whereas trifluorothioacetates are not.[8]

Thus, **4** can only result from the reaction of **A** with **1**. In the other cases, **A** abstracted a hydrogen atom from the medium and delivered **5**.

Such a mechanism is consistent with the fact that the formation of **4** increased when an excess of CF_3SO_2SR (versus alkene) was used (Table 1, entries 1, 2 and 5–7). On the contrary, an excess of olefin (versus **1** or **2**) led to an increased yield of **5** (Table 1, entries 1, 3 and 5, 8). This means that **5** resulted predominantly from the abstraction of an allylic hydrogen of the substrate by radical **A**.

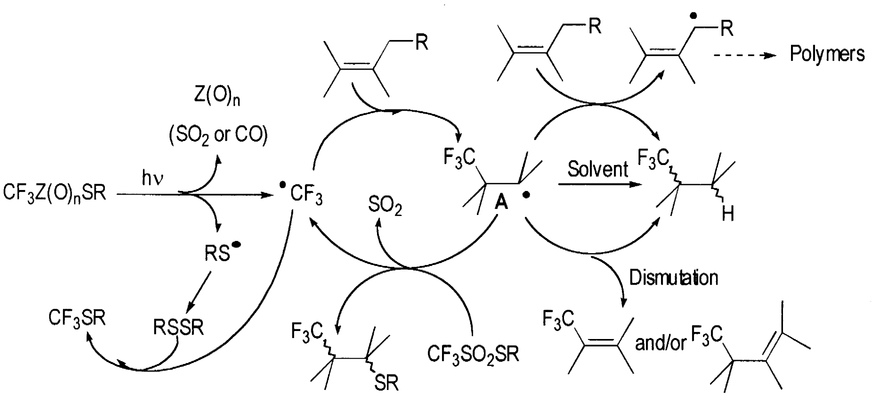
In order to determine if the solvent is also able to transfer hydrogen atoms to **A**, we repeated some reactions in a perhalogenated solvent (Table 2).

Table 2
Photolysis in different solvents



3	Solvent	**5** (%)
3c	CH_2Cl_2	36
	$CFCl_2CF_2Cl$	33
3e	CH_2Cl_2	39
	$CFCl_2CF_2Cl$	33

These experiments showed that the solvent did not provide hydrogen atoms to **A** in a significant way since almost the same amount of **5** was obtained in $CFCl_2CF_2Cl$ and CH_2Cl_2. The dismutation of radical **A** can also be considered as a minor route to **5** since, in some cases, trifluoromethylated olefins (**7** and **8**) were formed as by-products but usually in a far lesser amount than trifluoromethylated alkanes **5**. The different routes to **5** are reported in Scheme 2.



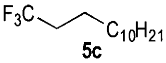
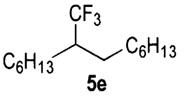
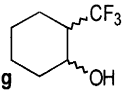
Scheme 2. General mechanism

Trifluoromethylated sulfides (CF_3SR (**6**)) were also formed, as shown in Table 1. These compounds resulted from the reaction of $^{\cdot}CF_3$ with the disulfide produced by dimerization of $RS^{\cdot}$ radicals as described in Part 1 of this study.[4]

The complete mechanism of the photolytic process is summarized in Scheme 2.

After reaction of **2** with the various alkenes, the mixtures of saturated products **5** and unsaturated ones (**7**+**8**) can be reduced to yield selectively a single compound as illustrated in Table 3. Thus, 2-trifluoromethylcyclohexanol (**9g**) can be prepared from cyclohexanone (via **3f**), in three steps only (enolisation, photolysis, reduction).

Table 3
Hydrogenation of the mixture of **5**, **7** and **8**

5+**7**+**8** mixture	[H]	**5** (%)
5c+**7c**+**8c**	H_2 (2 bar) Pd/C AcOH	 **5c** (46%)
5e+**7e**	H_2 (2 bar) Pd/C AcOH	 **5e** (41%)
5f+**7f**	LiAlH$_4$ Et$_2$O	**9g**  (100%)

In conclusion, this strategy could be an effective new method for the synthesis of trifluoromethylated alkanes or β-sulfanyl (trifluoromethyl)alkanes, even if, at the moment, it seems difficult to exceed a 50% yield. It can be noticed that, because of their sulfanyl moiety, the latter compounds can undergo further functionalization and constitute useful synthetic tools which are under study in our laboratory. On the other hand, hydrotrifluoromethylation of alkenes with trifluorothioacetates can constitute a valuable transformation of unsaturated organic substrates since we have demonstrated that the crude photolysis mixtures can be reduced to a single product.

References

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4. Billard, T.; Roques, N.; Langlois, B. R. *J. Org. Chem.* **1999**, *64*, 3813–3820.
5. Thioesters and alkenes, dissolved in 20 mL of dichloromethane, were introduced in a quartz cylindrical flask (plane faces in vertical position), fitted with a vertical reflux condenser. Air was blown off from this solution with nitrogen. Then, the stirred reaction mixture was illuminated by a mercury vapor lamp (Phillips HPK125, 125 W), through the plane walls of the reactor.
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8. Roques, N. Ph.D. Dissertation, University Claude Bernard-Lyon I, Villeurbanne (France), 1996.
9. Compounds **5b**–**e**, **9g** and **4b** were characterized from isolated compounds. For example: **4b**: ^{1}H: 7.24–7.62 (massif, 5H), 3.33 (m, 1H), 2.2–2.5 (massif, 2H), 1.27 (massif, 16H), 0.88 (t, J=6 Hz, 3H). ^{13}C: 133.71, 132.68, 129.14, 127.62, 126.13 (q, J=278 Hz) 42.44 (q, J=2.5 Hz), 39.17 (q, J=27.4 Hz), 33.81 (q, J=1 Hz), 31.91, 29.54, 29.45, 29.32, 29.28, 26.36, 22.72, 14.13. ^{19}F: −63.95 (t, J=11.5 Hz). Compound **5b**: ^{1}H: 2.03 (m, 2H), 1.55 (m, 2H), 1.26 (m, 16H), 0.88 (t, J=6.4 Hz, 3H). ^{13}C: 127.42 (q, J=277 Hz), 33.88 (q, J=28 Hz), 32.07, 29.78, 29.71, 29.51, 29.34, 28.87, 22.83, 21.99 (q, J=2 Hz), 14.16. ^{19}F: −66.9 (t, J=11.3 Hz). The others compounds **4** and **5** were identified by ^{19}F NMR and mass spectrum. By-products **7** and **8** were identified by ^{19}F NMR, mass spectrum and by analogy with the literature (Brookes, C. J.; Coe, P. L.; Pedler, A. E.; Tatlow, J. C. *J. Chem. Soc., Perkin Trans. 1* **1978**, 202–209.