Pergamon

SCIENCE DIRECT®

Tetrahedron Letters 44 (2003) 8127–8130

TETRAHEDRON LETTERS

A convenient one-step synthesis of fluoroethylidene derivatives

D. Chevrie,[a] T. Lequeux,[a,*] J. P. Demoute[b] and S. Pazenok[b,*]

[a]*Laboratoire de Chimie Moléculaire et Thioorganique, Université de Caen-ENSICaen, UMR CNRS 6507, 6 Boulevard du Maréchal Juin, 14050 Caen cedex, France*

[b]*Bayer CropScience GmbH, Industriepark Hoechst, G 837, D-65926 Frankfurt am Main, Germany*

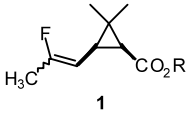
Received 21 July 2003; revised 26 August 2003; accepted 4 September 2003

Dedicated to Professor D. Naumann University of Cologne on the occasion of his 60th birthday

Abstract—A convenient one-step synthesis of *gem*-monofluoroalkylolefins starting from aldehydes or ketones was developed. This method comprises the utilisation of 2-(1-fluoroethyl)sulfonyl-1,3-benzothiazole according to Julia's procedure and opens a new opportunity for the synthesis of fluoroalkylidene derivatives.

The introduction of fluorine atoms into organic molecules is a very useful approach for the modification of biological activity. Compounds containing a single fluorine atom attached to a double bond are of great interest due to their biological properties. Previously, we have shown that replacement of one of the methyl groups in esters of *cis*-chrysanthemic acid by one fluorine atom increases the insecticidal activity (Fig. 1).[1]

The most common method for the synthesis of alkenes containing an [(Alk)CF=] moiety is the reaction of an aldehyde or ketone with fluorinated Horner–Wadworth–Emmons (HWE) reagents like Ph_3P=CHF or $(EtO)_2(O)PCHFCOOEt$.[2] A major limitation of this approach is the difficulty in accessing the phosphorane which requires a monofluorohalomethane or ethane, such as CH_2FI or AlkCHFBr which are either not available commercially or are very expensive, or in the case of the phosphonate, further modification of carboalkoxy group.[3,4] Another method is the use of fluoromethylsulfonylbenzene $PhSO_2CH_2F$ for the olefination, comprising for example the reaction of phenylsulfonylfluoromethyllithium with a carbonyl compound to form α-fluoro-β-hydroxyphenylsulfonyl derivatives.[5] Further dehydration with CH_3SO_2Cl followed by reductive desulfonylation leads to the olefins. The same complex and multistep procedure has been used for olefination with $PhSOCHFCH_3$.[6a] Numerous efforts have been made in order to develop alternative methods and to circumvent these drawbacks.[5,6]

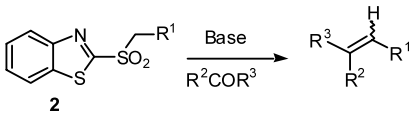


1

Figure 1.

In 1993 Julia and co-workers[7] described a one-step olefination procedure as a convenient alternative to the HWE reaction. According to this novel method benzothiazole sulfones **2** react with aldehydes or ketones, to afford alkenes (Scheme 1). Since the publication by Julia, a number of synthetic applications of this reaction have been reported in the literature.[8]

In the course of our search for an improved synthesis of compound **1**, which initially was prepared via bromofluorination/reduction of 4,7,7-trimethyl-3-oxabicyclo-[4.1.0]-hept-4-en-2-one,[9] we decided to prepare the corresponding fluorine-containing analogues of the Julia reagent and to explore their reactivity towards aldehydes and ketones.



2

Scheme 1.

* Corresponding authors. Tel.: +33-231452854; fax: +33-231452877; e-mail: lequeux@ismra.fr

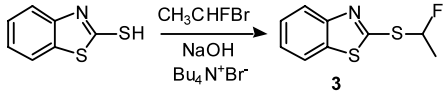
0040-4039/$ - see front matter © 2003 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2003.09.027

For the synthesis of a benzothiazole containing a 2-fluoroethylsulfonyl group we investigated three different synthetic pathways: the direct alkylation of 2-mercaptobenzothiazole with halofluoroalkane, the electrophilic fluorination of 2-ethylsulfanyl or sulfonylbenzothiazole and the Halex reaction from 2-chloroethylsulfanylbenzothiazole.

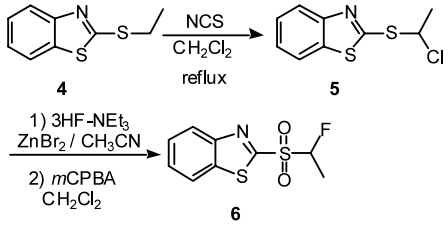
In the first approach the alkylation of 2-mercaptobenzothiazole with 1-bromo-1-fluoroethane was successfully performed under phase transfer catalyst conditions,[10] using an excess of the bromofluoroalkane without solvent (Scheme 2). After 4 h at room temperature, the alkylation was complete and 2-(1-fluoroethylthio)benzothiazole **3** was obtained i n 74% yield.

Due to the high cost of 1-bromo-1-fluoroethane and the need to use it in large excess (10 equiv.), we tested the direct fluorination of 2-ethylsulfanylbenzothiazole as an alternative route. We found that the electrophilic fluorination of **4** with F-TEDA (Selectfluor™) in the presence of triethylamine,[11] afforded the expected sulfide **3** after overnight stirring at room temperature. However, **3** was isolated in low yield (30–35%) due to the competitive formation of 2-ethylsulfinylbenzothiazole as by-product. All attempts to introduce one fluorine atom by treating the corresponding 2-ethylsulfonylbenzothiazole with *N*-fluorobenzenesulfonimide[12] led to a mixture of various fluorinated products.

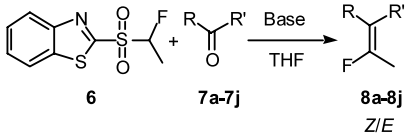
Fortunately, the introduction of one fluorine atom through a Halex reaction of the chlorosulfide **5** was successful (Scheme 3). We found that 2-ethylsulfanylbenzothiazole **4** easily reacted with *N*-chlorosuccinimide to give 2-(1-chloroethylsulfanyl)benzothiazole **5**. The monochlorosulfide was found to be too unstable to be purified via distillation or crystallisation, and was used without any further purification. The fluorination of the sulfide **5** was achieved using $3HF–NEt_3$ (Franz reagent[13]) in the presence of $ZnBr_2$ in CH_3CN solution.[14] The crude fluorosulfide **3** was then oxidised using either *m*CPBA in dichloromethane at room temperature or H_2O_2 in acetic acid. After 24 h, fluorosulfone **6** was obtained as a pale yellow crystalline product in 75% overall yield which could be directly used in the Julia reaction (Scheme 3).[15] We noticed that the chlorination of **4** proceeded with formation of a side product (10%), which contained one additional chlorine atom on the aromatic ring. As shown later, this did not affect the reactivity of the final sulfone **6**.



Scheme 2.



Scheme 3.



Scheme 4.

The olefination of carbonyl compounds with sulfone **6** was performed according to the Julia procedure in THF solution in the presence of a strong base (Scheme 4). The results obtained are presented in Table 1.[16]

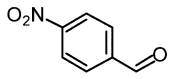
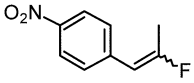
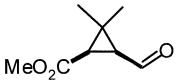
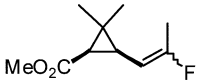
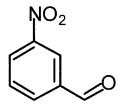
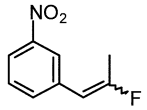
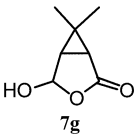
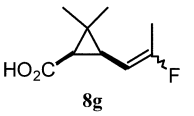
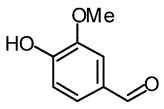
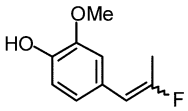
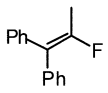
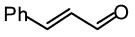
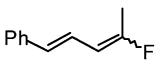
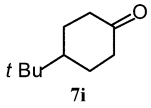
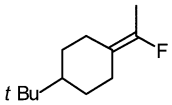
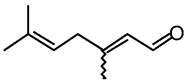
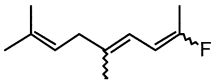
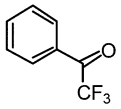
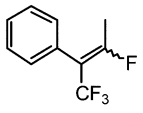
When NaHMDS was used as base at −78°C (method A),[16] the olefination of aldehydes **7a**–**g** proceeded smoothly and afforded the fluoroethylidene derivatives **8a**–**g** in 48–88% yields. In this case the mixture was stirred for 2 h at −78°C and slowly warmed to −10°C over 30 min, before quenching. Surprisingly, it was possible to use the cheaper *t*BuOK (method B)[16] instead of NaHMDS and to perform olefination at −15°C. Under these conditions we obtained the alkenes in good yield, but with a low *E*/*Z* selectivity (2/3 to 1/1). All attempts to improve the *E*/*Z* ratio by using other bases (KHMDS, LiHMDS) or by changing the solvent (toluene) or the temperature were unsuccessful. Ketones were found to be less reactive than aldehydes. When non-enolizible ketones **7h** or **7j** were reacted with sulfone **6** and *t*BuOK at −15°C, alkenes were isolated in lower yields (5–15%) and no product was detected from cyclic ketone **7i**. However, by using NaHMDS at −78°C (method A),[16] the corresponding monofluoroolefins **8h**–**j** were obtained in one step and isolated in 49–69% yields (Table 1).

In conclusion, we report a simple and convenient one-step procedure for the preparation of fluoroalkylidene derivatives from aldehydes and ketones. The method allows the preparation of a variety of fluoroalkenes bearing different functional groups. The process is also easy to control and scale up.[17]

Acknowledgements

We are grateful to Professor S. Z. Zard (Ecole Polytechnique, Palaiseau, France) for helpful discussions.

Table 1. Olefination of aldehydes and ketones from fluorosulfone **6**

RCOR'	Product	Yield % (Method)[16]	*Z/E*[a]	RCOR'	Product	Yield % (Method)[16]	*Z/E*[a]
 **7a**	 **8a**	**88%** (Method B)	39/61	 **7f**	 **8f**	**80%** (Method B)	(55/45)
 **7b**	 **8b**	**86%** (Method B)	37/63	 **7g**	 **8g**	**82%**[b] (Method B)	45/55
 **7c**	 **8c**	**48%**[b] (Method B)	51/49	 **7h**	 **8h**	**49%** (Method A)	-
 **7d**	 **8d**	**55%** (Method B)	38/62	 **7i**	 **8i**	**69%** (Method A)	-
 **7e**	 **8e**	**71%** (Method B) **74%** (Method A)	48/52	 **7j**	 **8j**	**45%** (Method A)	(n.d)

[a] Based on the $^3J_{HF}$ value.

[b]Experiments run in the presence of 2.2 eq. of base.

References

1. Demoute, J. P.; Adams, A.; Demassey, J.; Babin, D. Patent WO 9,932,426, 1999; *Chem. Abstr.* **1999**, *131*, 73815.
2. (a) Burton, D. J.; Yang, Z.; Qiu, W. *Chem. Rev.* **1996**, *96*, 1641–1715 and references cited therein; (b) Xu, Z.; Desmarteau, D. D. *J. Chem. Soc., Perkin Trans. 1* **1992**, 313–315; (c) Etemad-Moghadam, G.; Seyden-Penne, J. *Bull. Soc. Chim. Fr.* **1985**, 448–454; (d) McCarthy, J. R.; Huber, E. W.; Le, T.; Laskovic, M.; Matthews, D. P. *Tetrahedron* **1996**, *52*, 45–58; (e) Veenstra, S. J.; Hauseer, K.; Felber, P. *Bioorg. Med. Chem. Lett.* **1997**, *7*, 351–354.
3. Burton, D. J.; Greenlimb, P. E. *J. Org. Chem.* **1975**, *40*, 2796–2801.
4. Blackburn, G. M.; Parratt, M. *J. Chem. Soc., Chem. Commun.* **1983**, 886–888.
5. (a) McCarthy, J. R.; Matthews, D. P.; Edwards, M. L.; Stemerick, D. M.; Jarvi, E. T. *Tetrahedron Lett.* **1990**, *31*, 5449–5452; (b) Moore, W. R.; Schatzman, G. L.; Jarvi, E. T.; Gross, R. S.; McCarthy, J. R. *J. Am. Chem. Soc.* **1992**, *114*, 360–361.
6. (a) Satoh, T.; Itoh, N.; Onda, K.; Kitoh, Y.; Yamakawa, K. *Tetrahedron Lett.* **1992**, *33*, 1483–1484; (b) McCarthy, J. R.; Matthews, D. P.; Stemerick, D. M.; Huber, E. W.; Bey, P.; Lippert, B. J.; Snyder, R. D.; Sunkara, P. S. *J. Am. Chem. Soc.* **1991**, *113*, 7439–7440; (c) Welch, J. T.; Lin, J. *Tetrahedron* **1996**, *52*, 291–304; (d) Yoshida, M.; Hara, S.; Fukuhara, T.; Yoneda, N. *Tetrahedron Lett.* **2000**, *41*, 3887–3890; (e) Chen, C.; Wilcoxen, K.; Strack, N.; McCarthy, J. R. *Tetrahedron Lett.* **1999**, *40*, 827–830; (f) Allmendinger, T.; Furet, P.; Hungerbûhler, E. *Tetrahedron Lett.* **1990**, *31*, 7297–7300.
7. (a) Baudin, J. B.; Hareau, G.; Julia, S. A.; Lorne, R.; Ruel, O. *Bull. Soc. Chim. Fr.* **1993**, *130*, 856–878; (b) Baudin, J. B.; Hareau, G.; Julia, S. A.; Ruel, O. *Tetrahedron Lett.* **1991**, *32*, 1175–1178; (c) Baudin, J. B.; Hareau, G.; Julia, S. A.; Ruel, O. *Bull. Soc. Chim. Fr.* **1993**, *130*, 336–357.
8. For example see: (a) Bellingham, R.; Jarowicki, K.; Kocienski, P.; Martin, V. *Synthesis* **1996**, 285–296; (b) Smith, N. D.; Kocienski, P.; Street, S. D. *Synthesis* **1996**, 652–666; (c) Hilpert, H.; Wirz, B. *Tetrahedron* **2001**, *57*, 681–694; (d) Charrette, A. B.; Lebel, H. *J. Am. Chem. Soc.* **1996**, *118*, 10327–10328; (e) Blakemore, P. R. *J. Chem. Soc., Perkin Trans. 1* **2002**, 2563–2585.
9. Demoute, J. P.; Hömberger, G.; Pazenok, S.; Babin, D. Patent WO 0,134,592, 2001; *Chem. Abstr.* **2001**, *134*, 366801.
10. Goralski, C. T.; Burk, G. A. *J. Org. Chem.* **1977**, *42*, 3094–3096.
11. Lal, G. S. *J. Org. Chem.* **1993**, *58*, 2791–2796.
12. Taylor, S. D.; Kotoris, C. C.; Hum, G. *Tetrahedron* **1999**, *55*, 12431–12477.
13. Franz, R. *J. Fluorine Chem.* **1980**, *15*, 423–434.
14. (a) Jouen, C.; Lemaître, S.; Lequeux, T.; Pommelet, J.-C. *Tetrahedron* **1998**, *54*, 10801–10810; (b) Lequeux, T.; Lebouc, F.; Lopin, C.; Yang, H.; Gouhier, G.; Piettre, S. *Org. Lett.* **2001**, *3*, 185–188; (c) Gouault, S.; Pommelet, J. C.; Lequeux, T. *Synlett* **2002**, 996–998.

15. **Experimental**:

*(a) 2-(1-Chloroethylsulfanyl)benzothiazole **5***: A solution of 2-(1-ethylsulfanyl)benzothiazole **4** (2 g, 10.24 mmol) in 30 ml CH_2Cl_2 was heated to 45°C and then *N*-chlorosuccinimide (2.05 g, 15.36 mmol) was added in one portion. The mixture was stirred for 2 h at 45°C and then cooled, washed with water and dried over $MgSO_4$. The solvent was removed under reduced pressure to give the title product as an oil (2.38 g) which was used for the fluorination without any purification. ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.06 (d, $^3J_{HH}=6.7$ Hz, 3H, CH_3), 6.15 (q, $^3J_{HH}=6.7$ Hz, 1H, CHCl), 7.38 (t, $^3J_{HH}=7.5$ Hz, 1H, CH), 7.49 (t, $^3J_{HH}=7.5$ Hz, 1H, CH), 7.83 (d, $^3J_{HH}=7.5$ Hz, 1H, CH), 8.00 (d, $^3J_{HH}=7.5$ Hz, 1H, CH).

*(b) 2-(1-Fluoroethylsulfanyl)benzothiazole **3***: A mixture of 2-(1-chloroethylsulfanyl)benzothiazole **5** (1.96 g, 8.53 mmol), anhydrous zinc bromide (2.5 g, 11.1 mmol) and triethylamine trihydrofluoride (5.56 mL, 34.12 mmol) in acetonitrile (30 mL), was stirred at 70°C for 6 h. The mixture was cooled, dissolved in ethyl acetate washed with water and dried over $MgSO_4$. The solvent was removed in vacuum to give the crude title product which was used without purification (91% purity). ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.88 (dd, $^3J_{HH}=6.5$ Hz, $^3J_{HF}=20.3$ Hz, 3H, CH_3), 6.71 (dq, $^3J_{HH}=6.5$ Hz, $^2J_{HF}=53.8$ Hz, 1H, CHF), 7.38 (t, $^3J_{HH}=7.5$ Hz, 1H, CH), 7.48 (t, $^3J_{HH}=7.5$ Hz, 1H, CH), 7.83 (d, $^3J_{HH}=7.5$ Hz, 1H, CH), 7.99 (d, $^3J_{HH}=7.5$ Hz, 1H, CH); ^{19}F NMR (235 MHz, $CDCl_3/CFCl_3$): δ −142.45 (dq, $^3J_{HF}=20.3$ Hz, $^2J_{HF}=53.8$ Hz, 1F, CHF).

*(c) 2-(1-Fluoroethylsulfonyl)benzothiazole **6***: Crude 2-(1-fluoroethylsulfanyl)benzothiazole **3** was dissolved in CH_2Cl_2 and *m*-chloroperbenzoic acid (2.5 equiv.) was added to this solution. The mixture was stirred overnight at room temperature, and then washed with 1 M sodium hydroxide solution and dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was recrystallized from methanol to give the title product **6** (1.55 g, 75%) (mp 75–78°C). ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.92 (dd, $^3J_{HF}=23.2$ Hz, $^3J_{HH}=6.5$ Hz, 3H, CH_3), 5.84 (dq, $^2J_{HF}=47.9$ Hz, $^3J_{HH}=6.5$ Hz, 1H, CHF), 7.50–7.65 (m, 2H), 8.05 (d, $^3J_{HH}=8.0$ Hz, 1H), 8.27 (d, $^3J_{HH}=7.6$ Hz, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 12.01 (d, $^2J_{CF}=20.2$ Hz, CH_3), 99.35 (d, $^1J_{CF}=219.9$ Hz, CF), 122.27, 125.71, 127.79, 128.35 (CH), 137.40, 152.79, 162.00; ^{19}F NMR (235 MHz, $CDCl_3/CFCl_3$): δ −172.0 (dq, $^3J_{HF}=23.2$ Hz, $^2J_{HF}=47.9$ Hz, 1F, CHF); MS (EI, 70 eV): *m*/*z* (%) 245 (7), 136 (52), 108 (100), 91 (19), 47 (18); HMRS (EI) calcd for $C_9H_8FNO_2S_2$ (M^+): 244.998. Found: 245.005.

16. **General procedure for the olefination of aldehydes or ketones**:

Method A: To a THF solution of 2-(1-fluoroethylsulfonyl)benzothiazole **6** (1 equiv.) and the appropriate carbonyl compound (1.05 equiv.) a 1 M solution of sodium bis(trimethlysilyl)amide (1.1 equiv.) in THF was added slowly at −78°C. The mixture was stirred for 2 h at −78°C and then allowed to warm up to room temperature and then quenched with water. The aqueous layer was extracted with ethyl acetate and dried over $MgSO_4$. After solvent evaporation the crude product was purified via recrystallization or column chromatography.

Method B: To a cold THF solution (−17°C) of 2-(1-fluoroethylsulfonyl)benzothiazole **6** (1 equiv.) and the appropriate carbonyl compound (1.05 equiv.) a solution of *t*BuOK (1.1 equiv.) in THF was slowly added. The resulting solution was stirred for 30 min and then quenched by addition of aqueous ammonium chloride solution. The reaction was worked-up in a similar manner to that described for method A.

*Methyl (1R-cis)-3-[(E/Z)-2-fluoro-1-propenyl]-2,2-dimethylcyclopropane-1-carboxylate **8f***: Following method B, from a solution of methyl ester **7f** (668 mg, 4.28 mmol), sulfone **6** (1 g, 4.08 mmol) in THF (10 mL) and a solution of *t*BuOK (502 mg, 4.48 mmol) in THF (5 mL), a mixture of alkenes **8f** (607 mg; 80%) (*E*/*Z* ratio: 45/55) was obtained after purification of the crude oil by flash column chromatography (petroleum ether/ethyl acetate: 95/5). ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.19–1.21 (m, 12H, CH_3 (*E*,*Z*)), 1.62–1.70 (m, 3H, H_3,H_1(*E*), H_1(*Z*)), 1.91 (d, $^3J_{HF}=16.8$ Hz, 3H, CH_3 (*Z*)), 1.92 (d, $^3J_{HF}=17.3$ Hz, 3H, CH_3 (*E*)), 2.12 (t, $^3J_{HH}=9.3$ Hz, 1H, H_3 (*Z*)), 3.60 (s, 6H, CO_2Me (*Z*,*E*)), 4.91 (dd, $^3J_{HF}=36.7$ Hz, $^3J_{HH}=9.6$ Hz, 1H, CH (*Z*)), 5.35 (dd, $^3J_{HF}=20.7$ Hz, $^3J_{HH}=8.2$ Hz, 1H, CH (*E*)); ^{19}F NMR (235 MHz, $CDCl_3/CFCl_3$): δ −92.5 (dq, $^3J_{HF}=20.7$ Hz, $^3J_{HF}=17.3$ Hz, *E* isomer), −103.2 (dq, $^3J_{HF}=36.7$ Hz, $^3J_{HF}=16.8$ Hz, *Z* isomer). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 4.1 (d, $^2J_{CF}$ 32.6, CH_3 (*E*)), 14.5, 14.6 (s, CH_3), 17.9 (d, $^2J_{CF}=30.1$ Hz, CH_3 (*Z*)), 28.2, 28.3 (s, C_1), 28.5, 28.6 (s, CH_3), 29.5 (d, $^3J_{CF}=12.6$ Hz, C_3 (*Z*)), 30.4 (d, $^3J_{CF}=9.6$ Hz, C_3 (*E*)), 51.0, 51.1 (s, OCH_3), 99.5 (d, $^2J_{CF}=11$ Hz, CH (*E*)), 100.6 (d, $^2J_{CF}=28$ Hz, CH (*Z*)), 158.2 (d, $^1J_{CF}=249.7$, CF), 171.1 (s, CO), 171.5 (s, CO); MS (EI, 70 eV): *m*/*z* (%) 186 (22), 156 (89), 152 (7), 141 (33), 139 (100), 113 (15), 111 (45), 93 (6); HMRS (EI) calcd for $C_{10}H_{15}FO_2$ (M^+): 186.106. Found: 186.099.

17. Pazenok, S.; Demoute, J. P.; Zard, S.; Lequeux, T. Patent WO 0,240,459, 2002; *Chem. Abstr.* **2002**, *136*, 386131.