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Stereoselective Addition of CF_3SiMe_3 on Azirines. Synthesis of (E)-Aziridines

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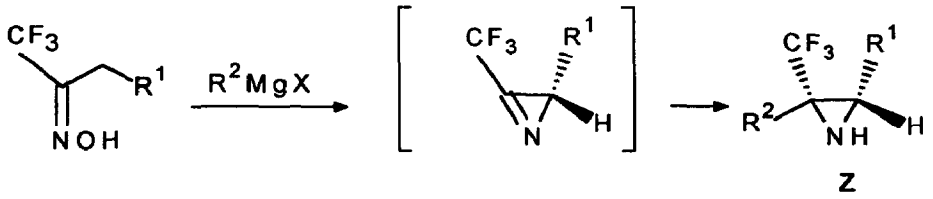
Key words *: Trifluoromethyltrimethylsilane ; azirines ; stereoselective addition.*

Abstract *: The original use of CF_3SiMe_3 on a carbon nitrogen double bond is described. Azirines provide* **(E)-aziridines.**

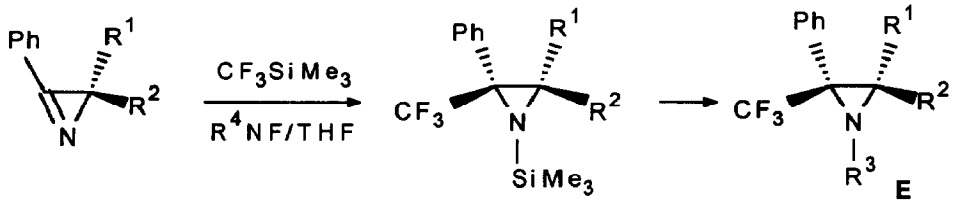
A number of antiviral, antitumor and antifungal agents have been developed in which fluorine substitution has been a key to their biological activity[1,2]. Moreover it is well known that compounds containing the aziridine ring have profound effect on living cells[3a]. So trifluoromethylaziridines are able to have a biological interest. Trifluoromethylaziridines described in the literature are obtained from triazolines or oxazolidines[4]. Recently we tried to synthesise trifluoromethylaziridines from Grignard reagents and trifluoromethyloximes[5] (scheme 1). But this reaction is not general[6] ; when it works, the **Z stereoisomer** is formed.



Scheme 1

So we tried to find another strategy. Recently Prakash and Olah[7] reported a very efficient nucleophilic trifluoromethylation reaction for carbonyl compounds using trifluoromethyltrimethylsilane. This reagent was found to react with many organic compounds, but attempts to add CF_3SiMe_3 to imines under a variety of conditions failed[2]. Prakash considers that "the much weaker N-Si bond-as compared with the O-Si- does not provide sufficient driving force to push the reaction in the forward direction". Indeed when we tried to add CF_3SiMe_3 to n-propylbenzaldimine in different conditions, the reaction failed.

As the carbon nitrogen double bond of an azirine is more reactive towards nucleophilic addition than an imine function[3b], we decided to prepare some azirines and to study the addition of CF_3SiMe_3 in different conditions (scheme 2). The reaction works well and only the **(E)-aziridine** is obtained. Yields are not optimised (table). Extension of this methodology to other substrates is under investigation in order to define to scope of this synthesis.



1 $R^1 > R^2$ 2 3 R^3:H ; 4 R^3:COPh

Scheme 2

Table : **Trifluoromethylaziridines 3 from 1**

	1a R^1: Me ; R^2: H	**1b** R^1=R^2 : Me	**1c** R^1: Ph ; R^2: H	**1d** R^1: CO_2Me ; R^2: H
R_4NF	Et_4NF [a]	Bu_4NF [b]	Et_4NF [a]	Bu_4NF [a]
yield %	**3a** 51	**3b** 41	**3c** 86	**3d** 67

[a] catalytic ; [b] stoechiometric .

Experimental part - example 3c. Trifluoromethyltrimethylsilane (330 mg, 2.32 mmol) was added to a solution of azirine **1c** (300 mg, 1.55 mmol) in THF (1.6 ml) (t°: -4°C). Then Et_4NF (60 mg, 0.32 mmol) was added to the mixture which is stirred for 15 h at room temperature. After a classical work up, the solvents (THF and Et_2O) were removed under reduced pressure and the residue (360 mg) was purified by crystallisation (hexane) and 350 mg (1.33 mmol) of **(E)-3c** was recovered.

Selected spectroscopic data[a]

3a. IR : 3320-3280, 1200-1130 ; NMR ^1H (60 MHz) . 0.88 (d, 3H, J=6.0), 2,65 (q, 1H, J=6.0), 7.43 (m, 5H). NMR ^{19}F (188 MHz) :-72.94 (s). **4a** m.p. (°C) : 63-64[b,c]. Found C 66.75, H 4.49, N 4.60 for $C_{17}H_{14}F_3NO$ C 66.88, H 4.62, N 4.59.

3b. NMR ^1H (60 MHz) : 0.9 (s, 3H), 1.57 (s, 3H), 7.3-7.8 (m, 5H). NMR ^{19}F (56,4 MHz) : -64.83 (s). **4b** m.p. (°C) : 119-121[b,c]. Found C 67.69, H 5 25, N 4.31 for $C_{18}H_{16}F_3NO$: C 67.70, H 5.05, N 4.39.

3c. IR : 3440-3320,1180-1120. NMR ^1H (200 Hz) : 2.1 (1H), 3.82 (s, 1H), 7.1 (m, 10H). NMR ^{13}C (75.4 MHz) : 40.9, 48.46 ($^2J_{CF}$=33.42), 127.36, 127.50, 127.80, 127.89, 128.50 ($^1J_{CF}$=279.0), 128.53, 130.04, 130.60. NMR ^{19}F (56.4 MHz) · -73 0. m p. (°C) 62-63[b]. Found C 68 38, H 4.83, N 5.43 for $C_{15}H_{12}F_3N$ C 68.43, H 4.59, N 5.32.

3d. IR : 3400-3360, 1735, 1220, 1120. NMR ^1H (300 MHz) : 2.1 (1H), 3.27 (1H), 3.60 (s, 3H), 7.39 (5H). NMR ^{13}C (75.4 MHz) : 37.92, 47 70 ($^2J_{CF}$=37.9), 52.95, 123.37 ($^1J_{CF}$=276.8), 128 68, 129.36, 129.84, 129.97, 167.92. NMR^{19}F (56 4 MHz) : -75.0. MS m/z : 244, 214, 186, 185, 77, 59.

[a] NMR : solvent $CDCl_3$; ^1H, ^{13}C δ (TMS) ; ^{19}F δ ($CFCl_3$) ; J Hz. [b] this compound gave satisfactory ions identification by high resolution mass spectrometry [c] NMR ^1H, ^{13}C, ^{19}F data are in agreement with the proposed structure.

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