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Journal of Fluorine Chemistry 126 (2005) 491–498
JOURNAL OF FLUORINE CHEMISTRY
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Some studies on nucleophilic trifluoromethylation using the shelf-stable trifluoromethylacetophenone-*N*, *N*-dimethyltrimethylsilylamine adduct

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Received 22 September 2004; received in revised form 5 November 2004; accepted 15 November 2004
Available online 7 January 2005

Dedicated with respect and friendship to Professor Dick Chambers, FRS, on the occasion of his 70th birthday.

Abstract

The simple thermal addition product of *N*,*N*-dimethyltrimethylsilylamine with 2,2,2-trifluoroacetophenone provides a shelf-stable reagent for nucleophilic trifluoromethylation of both the carbonyl and the imine group.

Keywords: Nucleophilic trifluoromethylation; Trifluoromethyl carbinols; Aldehydes; Ketones; Imines

1. Introduction

The substitution of a hydrogen atom for fluorine has such a dramatic effect on the physical and biological properties of compounds that considerable research effort is invested into new and improved methods for the introduction of perfluoroalkyl units into such systems. In particular, the enhanced lipophilicity combined with the powerful electron withdrawing capability and small steric requirements at enzyme receptor sites of the trifluoromethyl group guarantees its incorporation into a multitude of highly desirable target molecules for use throughout the pharmaceutical and agrochemical industries, as well as material sciences [1]. A current method for incorporation of the trifluoromethyl moiety is fluoride-induced nucleophilic trifluoromethylation using Ruppert's reagent, trifluoromethyl trimethylsilane [2], due to its efficiency, versatility and mild reaction conditions [3]. The trifluoromethyl anion, per se, is of course extremely unstable, readily liberating difluorocarbene and fluoride anion, unless the formal carbanionic charge can be sufficiently stabilized either by a transition metal such as Cu(I), or, as in Ruppert's reagent, through a weak metalloid sigma bond, such as in the C–Si ''ate'' complex. Perfluoroalkylsilanes are known to be stable, non-toxic and easily handled, but still able to undergo nucleophilic activation of the silicon centre under reaction conditions to liberate the trifluoromethyl moiety. The only significant drawback as far as Ruppert's reagent is concerned is the preparation, which usually involves the use of either bromo- or iodotrifluoromethane, and both of these reagents are now prohibited for ecological reasons. In view of this situation, we therefore embarked on a study with the objective of preparing new reagents for anionic trifluoromethylation.

We now wish to report, in full detail [4], our studies on the preparation and reactivity of the trifluoromethylacetophenone-*N*,*N*-dimethyltrimethylsilylamine adduct as a prototypical shelf-stable reagent for such transformations.

In the first instance, we were aware that considerable literature precedent is available to illustrate the fact that tetrahedral oxyanionic intermediates bearing a trifluoromethyl substituent, undergo expulsion of the trifluoromethyl anion, as exemplified by Normant and coworkers [5] during the deprotonation of fluoroform with potassium dimsylate in

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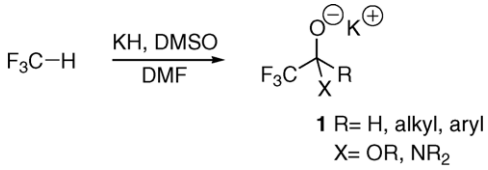
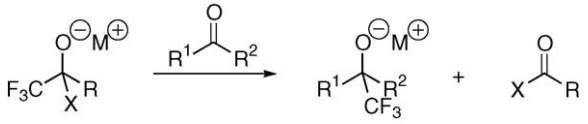
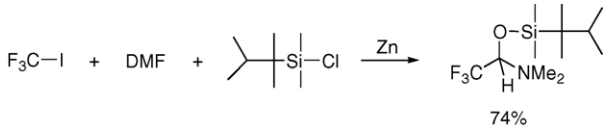
doi:10.1016/j.jfluchem.2004.11.010



Scheme 1.



Scheme 2.

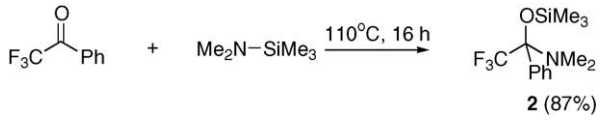


Scheme 3.

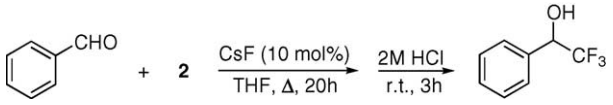
DMF (Scheme 1). The trifluoromethyl anion is thus effectively trapped by the DMF to form the gem-aminoalcoholate **1** (R = H, X = NMe_2, M = K), thereby avoiding carbene degradation products. This stabilised form of the trifluoromethyl anion may then function as a nucleophile and attack a carbonyl group (ketone or aldehyde electrophile) (Scheme 2) to produce the corresponding carbinol.

Shono et al. [6] observed similar results using an electrogenerated base of pyrrolidone, again in DMF, as did Troupel and coworkers [7] using the electrogenerated base of iodobenzene. Indeed, hemiaminolates similar to **1** were isolated by Lang [8] in 1988 by carrying out a silicon-induced addition of fluorine containing organozinc reagents to DMF (Scheme 3).

Mispelaere and Roques [9] have also synthesised the simple addition product of trifluoroacetaldehyde and a secondary amine to make similar hemiaminolates. In a very elegant series of studies, Roques et al. and Langlois et al. [10] have subsequently synthesised a number of these trifluoromethylating agents from fluoroform or hemiaminals of trifluoroacetaldehyde. However, both fluoroform and trifluoroacetaldehyde suffer the drawback of being gases (fluoroform bp −84 °C) and consequently become more difficult to handle in the laboratory. Prakash et al. [11] has explored the use of trifluoromethyl sulfides, sulfoxides and sulfones. In the event, our own study pursued a conceptually similar approach in as much as we sought to develop a simple and experimentally convenient reagent based around such tetrahedral intermediates.



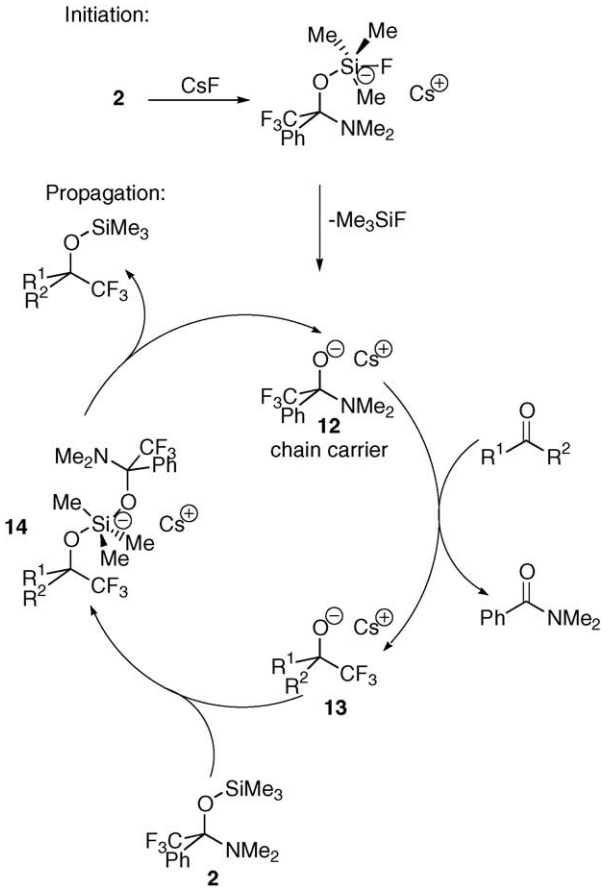
Scheme 4.



Scheme 5.

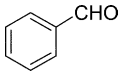
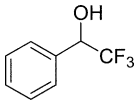
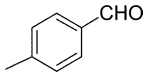
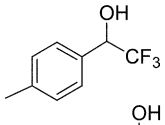
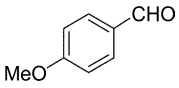
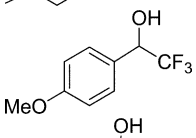
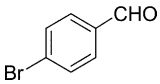
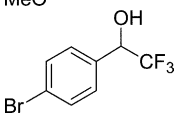
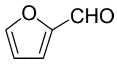
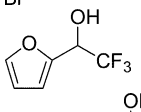
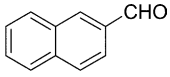
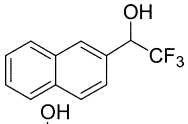
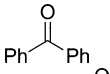
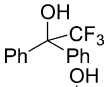
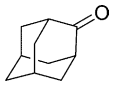
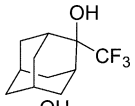
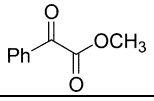
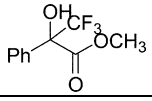
2. Results and discussion

Our attention was especially attracted to an intriguing paper by Abel and Crow [12], who demonstrated that perhalogenoketones, including hexafluoroacetone, were able to insert into the silicon–nitrogen bond of certain aminosilanes to afford isolable tetrahedral compounds of the desired structure. In the same year Itoh et al. [13] also demonstrated the insertion of chloral into *N*,*N*-dimethytrimethylsilylamine. In consequence, we therefore elected to



Scheme 6.

Table 1
Reaction of **2** (2 equiv.) with aldehydes and ketones with caesium fluoride (10 mol%) as the preferred initiator

Entry	Substrate		Product	% Yield[a]
1		3		89 (2)
2		4		69 (16)
3		5		71 (29)
4		6		82 (6)
5		7		73 (26)
6		8		75
7		9		92[b]
8		10		87 (13)
9[c]		11		41 (16)

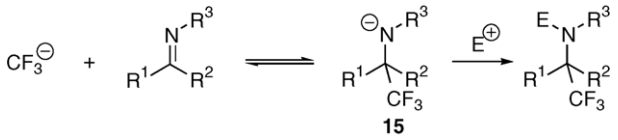
[a] Isolated yields: the numbers in parentheses indicate the yield of the recovered substrate. All products gave data identical to those found in the literature.
[b] Product was isolated as the TMS ether after acidic work up.
[c] Substrate heated to 110 °C in NMP.

examine the analogous reaction of *N*,*N*-dimethytrimethylsilylamine with trifluoroacetophenone under simple thermal conditions. To our delight, this simple reaction furnished the stable reagent **2** in excellent yield (Scheme 4).

As summarised in Scheme 5 and Table 1 a number of trifluoromethylcarbinols, derived from a simple series of non-enolisable aldehydes and ketones, were readily prepared when reacted with two equivalents of reagent **2** in the presence of caesium fluoride (10 mol%) as the preferred initiator in THF. The isolated yields shown are comparable with existing literature methods.

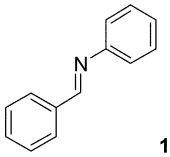
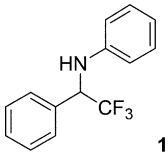
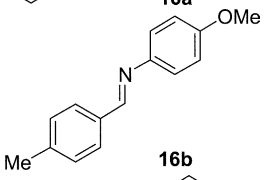
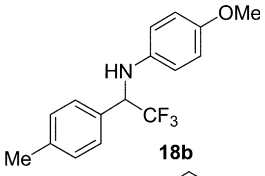
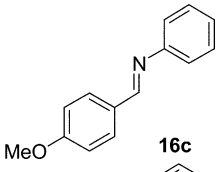
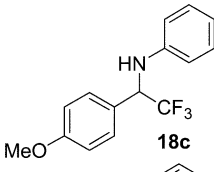
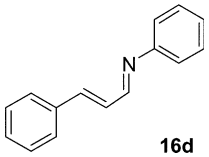
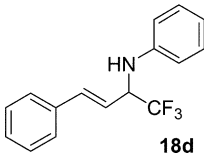
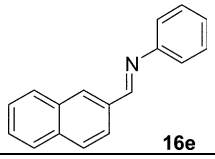
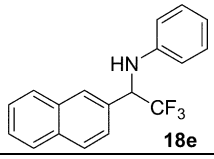
From a mechanistic perspective, the present sequence presumably has many parallels with that postulated for the Ruppert reagent [15]. As shown in Scheme 6 however, the essential difference resides in the propagation sequence when reaction of the product caesium alkoxide **13** with reagent **2** generates an ''ate'' complex **14** whose breakdown to liberate the observed product trimethylsilyl ether must, in contrast to the Ruppert reagent, involve cleavage of a silicon–oxygen bond. Liberation of the chain carrier **12** is therefore inherently more demanding in energy terms than in the case of trifluoromethyltrimethylsilane, albeit that the formation of an amide carbonyl group offsets this to some extent.

Our attention was then directed towards the reactivity of reagent **2** with the inherently less electrophilic imine functional group, which, until the pioneering work of Blazejewski et al. [16] had been considered to be unreactive towards imines with Ruppert's reagent. The formation of a relatively weak silicon–nitrogen bond at the imine nitrogen, as opposed to the stronger silicon–oxygen bond, has also been considered to disfavour propagation of the catalytic cycle and the unstable intermediate **15** (Scheme 7) may therefore revert back to starting material. Blazejewski sought to overcome this problem through the introduction of a suitable electrophile, which could trap the unstable intermediate **15**. Although attempts using chlorotrimethylsilane,



Scheme 7.

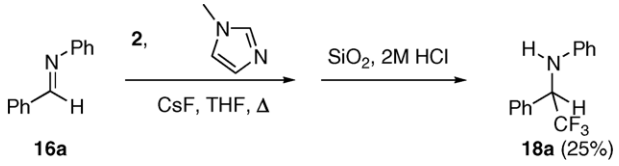
Table 2
Reaction of **2** (3 equiv.) with imines using caesium fluoride (10 mol.%) as the preferred initiator

Entry	Substrate	Product	% Yield[a]
1	 **16a**	 **18a**	60 (55)
2	 **16b**	 **18b**	54
3	 **16c**	 **18c**	33
4	 **16d**	 **18d**	16 (19)
5	 **16e**	 **18e**	44 (57)

[a] Isolated Yields. The numbers in parentheses indicate the yields obtained in the current literature [16].

pentafluorobenzyl bromide and *N*-trimethylsilylacetamide failed, *N*-trimethylsilylimidazole proved to be much more effective in terms of sustaining the catalytic cycle and pushing the reaction equilibrium to the right (Scheme 7). In this way, moderate yields of trifluoromethylated amines were prepared from non-enolisable aromatic imines.

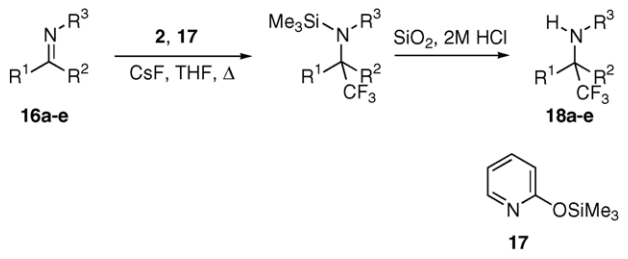
It was therefore of interest to examine the use of *N*-trimethylsilylimidazole in conjunction with reagent **2**. Accordingly, in a preliminary experiment with **16a**, a modified Blazejewski protocol was adapted, wherein caesium fluoride (10 mol%) was used for initial cleavage of the silicon–oxygen bond, and the mixture, instead of stirring at room temperature, was heated at reflux in THF (Scheme 8). After 20 h, hydrolysis of the silicon–nitrogen bond was carried out with silica gel and dilute HCl. Encouragingly, ^{1}H NMR analysis showed a 25% conversion to the monotrifluoromethylated amine product.



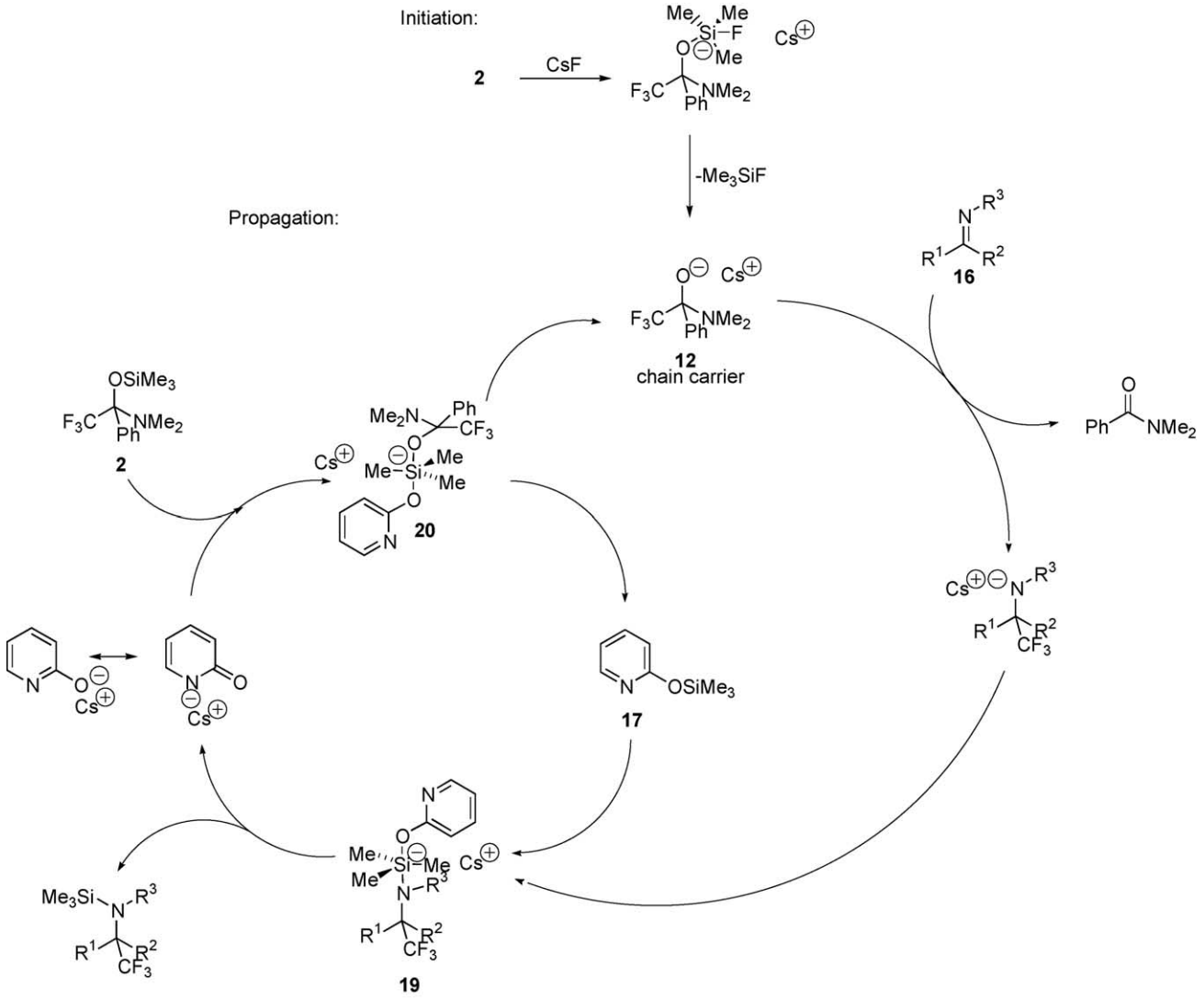
Scheme 8.

In an effort to increase the effectiveness of the silicon relay concept, we decided to examine the use of 2-trimethylsiloxypyridine **17** (Scheme 9) as an alternative to *N*-trimethylsilylimidazole. The results for a series of imines using reagents **2** and **17** in conjunction with caesium fluoride as initiator are shown in Table 2.

The selection of 2-trimethylsiloxypyridine **17** as the silicon transfer reagent was based on the idea that a dual advantage could be taken of the anionic pyridone unit, both as a leaving group with some amide character, and also as a pyridine alkoxide nucleophile for reaction with reagent **2** to liberate the key chain carrier and regenerate **17**. These ideas are encapsulated in Scheme 10, which also shows the two possible "ate" complexes **19** and **20** generated during the cycle.



Scheme 9.



Scheme 10.

3. Conclusion

In summary, the simple and experimentally convenient thermal addition of *N*,*N*-dimethyltrimethylsilylamine to trifluoroacetophenone provides a shelf-stable reagent which has proven to be useful for nucleophilic trifluoromethylation of non-enolisable carbonyl groups. Moreover, the same reagent, in conjunction with 2-trimethylsiloxy pyridine, as a potentially versatile additive for silicon relay under anionic conditions, has also allowed us to demonstrate that addition to simple aromatic imine derivatives is possible.

4. Experimental

4.1. General

All chemicals were of reagent grade or were purified by standard methods before use. THF was purified by distillation from sodium benzophenone ketyl under nitrogen. Melting points were determined using a Reichert hot stage and are uncorrected. Infrared spectra were recorded using NaCl solution cells on a Perkin-Elmer FT-IR 1605 instrument. ^{1}H, ^{13}C, and ^{19}F NMR spectra were measured on a Bruker AMX-300 spectrometer and are referenced to the residual solvent peak ($CFCl_3$ for ^{19}F) in $CDCl_3$.

4.2. Preparative procedures

4.2.1. *N,N*-Dimethyl-(1-phenyl-2,2,2-trifluoroethoxytrimethylsilyl)-amine (**2**)

N,*N*-Dimethylaminotrimethylsilane (5 ml, 0.031 mol) and trifluoroacetophenone (4.34 ml, 0.031 mol) were added to a round bottom flask equipped with a reflux condenser. The neat mixture was heated in an oil bath at 110 °C for 16 h under a nitrogen atmosphere. The product was distilled between 117 and 118 °C/18 mmHg to give a clear oil (7.93 g, 87% yield). IR (film): ν 2958, 2846, 2799, 1255,

1163, 1050; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.20 (9H, s, Si-$(CH_3)_3$), 2.29 (3H, s, N-CH_3), 2.30 (3H, s, N-CH_3), 7.35 (3H, m), 7.58 (2H, m); ^{19}F NMR (282 MHz, $CDCl_3$): δ −71.3; ^{13}C NMR (75 MHz, $CDCl_3$): δ 1.7 (Si-$(CH_3)_3$), 39.9 (N-$(CH_3)_2$), 93.1 (q, ^2J = 28.5 Hz, C-CF_3), 124.2 (q, ^1J = 292 Hz, CF_3), 127.5, 127.8, 128.5, 139.2; Anal. Calcd for $C_{13}H_{20}F_3NOSi$: C, 53.6; H, 6.9; N, 4.8. Found: C, 53.5; H, 7.1; N, 4.8.

4.2.2. Typical experimental procedure for the trifluoromethylation of ketones and aldehydes

Dry, distilled THF (5 ml) was added to a round bottom flask equipped with a reflux condenser, containing pre-dried caesium fluoride (15 mg, 0.098 mmol). Benzaldehyde (100 μl, 0.98 mmol) was then added, followed by **2** (466 μl, 1.97 mmol), and the mixture was heated to reflux for 20 h. Hydrochloric acid (2 M, 1 ml) was then added and stirring was continued for 3 h. The mixture was diluted with diethyl ether, washed with water (3 × 5 ml), sat. brine (5 ml), dried with $MgSO_4$, and the solvent removed in vacuo. The crude product was purified by flash chromatography on silica gel using diethyl ether-hexane (1:9) to give the product as a yellow oil (139 mg, 89%).

*4.2.2.1. 1-Phenyl-2,2,2-trifluoroethanol (**3**).* Spectral properties (^{1}H, ^{13}C, ^{19}F NMR and MS) were identical to those reported in the literature [14a].

*4.2.2.2. 4′-Methyl-1-phenyl-2,2,2-trifluoroethanol (**4**).* Spectral properties (^{1}H, ^{13}C, ^{19}F NMR and MS) were identical to those reported in the literature [14b].

*4.2.2.3. 4′-Methoxy-1-phenyl-2,2,2-trifluoroethanol (**5**).* Spectral properties (^{1}H, ^{13}C, ^{19}F NMR and MS) were identical to those reported in the literature [5b].

*4.2.2.4. 4′-Bromo-1-phenyl-2,2,2-trifluoroethanol (**6**).* mp: 50–52 °C; IR (film): ν 3405, 1595, 1492, 1406, 1267, 1173, 1131, 1077, 1013; ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.02 (1H, br s, OH), 4.94 (1H, q, ^3J = 6.6 Hz, $CHCF_3$), 7.32 (2H, d, ^3J = 8.6 Hz, aromatic), 7.52 (2H, d, ^3J = 8.6 Hz, aromatic); ^{19}F NMR (282 MHz, $CDCl_3$): δ −78.9; ^{13}C NMR (75 MHz, $CDCl_3$): δ 72.0 (q, ^2J = 32 Hz, $CHCF_3$), 123.6, 123.8 (q, ^1J = 282 Hz, CF_3), 129.0, 129.0, 131.7, 131.7, 132.6; MSFAB *m/z* (rel. int.): 256^{81}Br $[M + 1]^+$ (43%). 254^{79}Br $[M + 1]^+$ (44%), 239^{81}Br $[M + 1(–OH)]^+$ (93%), 237^{79}Br $[M + 1(–OH)]^+$ (90%).

*4.2.2.5. 1-(2-Furyl)-2,2,2-trifluoroethanol (**7**).* Spectral properties (^{1}H, ^{13}C, ^{19}F NMR and MS) were identical to those reported in the literature [14c].

*4.2.2.6. 1-(2-Naphthyl)-2,2,2-trifluoroethanol (**8**).* Spectral properties (^{1}H, ^{13}C, ^{19}F NMR and MS) were identical to those reported in the literature [11b].

*4.2.2.7. 1,1-Diphenyl-1-[(trimethylsilyl)oxy]-2,2,2-trifluoroethane (**9**).* Spectral properties (^{1}H, ^{13}C, ^{19}F NMR and MS) were identical to those reported in the literature [14a].

*4.2.2.8. 2-(Trifluoromethyl)-2-adamantanol (**10**).* Spectral properties (^{1}H, ^{13}C, ^{19}F NMR and MS) were identical to those reported in the literature [14a].

*4.2.2.9. 2-Hydroxy-2-phenyl-3,3,3-trifluoro-2-propanoic acid, methyl ester (**11**).* Spectral properties (^{1}H, ^{13}C, ^{19}F NMR and MS) were identical to those reported in the literature [14c].

4.2.3. Typical experimental procedure for the formation of imines

Equimolar amounts of aldehyde and amine were mixed together neat with heating, while a stream of air was blown over the flask to remove water. Products were recrystallized from methanol (Table 3).

4.2.4. 2-Trimethylsiloxy-pyridine (**17**) [17]

To 2-hydroxypyridine (10.0 g, 0.105 mmol) in toluene (25 ml) with triethylamine (16.0 ml, 0.116 mmol) at reflux, was added chlorotrimethylsilane (13.0 ml, 0.105 mmol) dropwise. The resulting mixture was heated at reflux for 30 min. The white precipitate was filtered off and the mother liquor was reduced in vacuo to give a crude oil. The product was distilled under reduced pressure at 80 °C/18 mmHg to give a clear oil which was stored in a schlenk tube due to instability (12.3 g, 70%).

4.2.5. Typical experimental procedure for the trifluoromethylation of imines

Dry, distilled THF (10 ml) was added to a round bottom flask equipped with a reflux condenser, containing pre-dried caesium fluoride (17 mg, 0.111 mmol) and benzylidene-phenyl-amine (200 mg, 1.11 mmol). 2-Trimethylsilyloxy-pyridine (554 mg, 3.31 mmol) was added via syringe, followed by **2** (785 μl, 2.84 mmol). The resulting mixture

Table 3
Comparison of literature melting points for imines

Entry	Imine	mp (°C)	Literature mp (°C)
1	**16a** R^1 = Ph, R^2 = H, R^3 = Ph	53	53–54 [18a]
2	**16b** R^1 = 4-MeC_6H_4, R^2 = H, R^3 = 4-$MeOC_6H_4$	87.5	85.5–86 [18b]
3	**16c** R^1 = 4-$MeOC_6H_4$, R^2 = H, R^3 = Ph	63.5–64.5	63 [18c]
4	**16d** R^1 = PhCH=CH, R^2 = H, R^3 = Ph	107–109	114 [18a]
5	**16e** R^1 = 2-naphthyl, R^2 = H, R^3 = Ph	114.5–116	115 [18a]

was heated at reflux for 20 h. The dark brown mixture was cooled and SiO_2 gel was added (1 g) with 1 M HCl (20 drops). This was stirred for 3 h, and the mixture was then filtered and the solvent removed in vacuo. The crude product was chromatographed on silica gel using 5% diethyl ether in petroleum spirit (40–60).

*4.2.5.1. Phenyl-(1-phenyl-2,2,2-trifluoroethyl)-amine (**18a**).* 60%; IR (film): ν 3416, 1604, 1504, 1250, 1175, 1123; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.30 (1H, br s, NH), 4.95 (1H, q, ^3J = 7.3 Hz, $CHCF_3$), 6.67 (2H, d, ^3J = 8.2 Hz, aromatic), 6.83 (1H, t, ^3J = 7.3 Hz, aromatic), 7.19 (2H, m, aromatic), 7.39–7.50 (5H, m, aromatic); ^{19}F NMR (282 MHz, $CDCl_3$); δ −74.5; ^{13}C NMR (75 MHz, $CDCl_3$): δ 60.5 (q, ^2J = 30 Hz, $CHCF_3$), 114, 119.2, 125.1 (q, ^1J = 282 Hz, CF_3), 127.8, 128.8, 129.0, 129.2, 133.9, 145.4; MSEI 70 eV, *m/z* (rel. int.) 251 $[M]^+$ (100%), 182 $[M\text{-}CF_3]^+$ (53%); HRMS calcd for $C_{14}H_{12}F_3N$: 251.0922; obsd: 251.0918.

*4.2.5.2. (4-Methoxy-phenyl)-(1-p-tolyl-2,2,2-trifluoroethyl)-amine (**18b**).* 54%; IR ($CHCl_3$): ν 3374, 1695, 1600, 1515; ^{1}H NMR (300 MHz $CDCl_3$): δ 2.33 (3H, s, CH_3), 3.70 (3H, s, OCH_3), 3.70 (1H, br s, NH), 4.76 (1H, q, ^3J = 7.3 Hz, $CHCF_3$), 6.59 (2H, d, ^3J = 8.8 Hz, aromatic), 6.72 (2H, d, ^3J = 9.0 Hz, aromatic), 7.18 (2H, d, ^3J = 8.0 Hz, aromatic), 7.32 (2H, d, ^3J = 8.2 Hz, aromatic); ^{19}F NMR (282 MHz, $CDCl_3$): δ −74.6; ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.1 (CH_3), 57.6 (OCH_3), 61.5 (q, ^2J = 29 Hz, $CHCF_3$), 114.7, 115.8, 127.7, 128.4 (q, ^1J = 271 Hz, CF_3), 129.5, 138.9, 153.3; MSEI 70 eV, *m/z* (rel. int.): 295 $[M]^+$ (100%), 226 $[M\text{-}CF_3]^+$ (82%); HRMS calcd for $C_{16}H_{16}F_3NO$: 295.1184; obsd: 295.1178.

*4.2.5.3. Phenyl-[1-(4-methoxy-phenyl)-2,2,2-trifluoroethyl]-amine (**18c**).* 33%; IR ($CHCl_3$): ν 3406, 1605, 1515, 1250, 1173, 1123; ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.69 (3H, s, OCH_3), 4.17 (1H, br s, NH), 4.76 (1H, q, ^3J = 7.2 Hz, $CHCF_3$), 6.54 (2H, d, ^3J = 8.6 Hz, aromatic), 6.67 (1H, t, ^3J = 7.4 Hz, aromatic), 6.8 (2H, d, ^3J = 6.6 Hz, aromatic), 7.05 (2H, dd, ^3J = 7.4 Hz, ^3J = 6.6 Hz, aromatic), 7.27 (2H, d, ^3J = 8.6 Hz, aromatic); ^{19}F NMR (282 MHz, $CDCl_3$): δ −74.7; ^{13}C NMR (75 MHz, $CDCl_3$): δ 54.2 (OCH_3), 59.1 (q, ^2J = 30 Hz, $CHCF_3$), 113.0, 113.3, 118.2, 124.2 (q, ^1J = 282 Hz, CF_3), 127.6, 128.1, 128.3, 144.6, 159.1; MSEI 70 eV, *m/z* (rel. int.): 281 $[M]^+$ (68%), 212 $[M\text{-}CF_3]$ (100%); HRMS calcd for $C_{15}H_{14}F_3NO$: 281.1027; obsd: 281.1027.

*4.2.5.4. Phenyl-(1-cinnamyl-2,2,2-trifluoroethyl)-amine (**18d**).* 16%; IR ($CHCl_3$): ν 3029, 1603, 1506, 1250, 1171, 1122; ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.95 (1H, br s, NH) 4.611 (H, m, $CHCF_3$), 6.19 (1H, dd, ^3J = 6.2 Hz, ^3J = 15.9 Hz, CH-$CHCF_3$), 6.72 (2H, d, ^3J = 8.5 Hz, aromatic), 6.81 (2H, m, aromatic), 7.19–7.39 (7H, m, aromatic + allylic); ^{19}F NMR (282 MHz, $CDCl_3$): δ −75.8; ^{13}C NMR (75 MHz, $CDCl_3$): δ 58.1 (q, ^2J = 30 Hz, $CHCF_3$), 2x 113.8, 119.2, 120.7, 125.1 (q, ^1J = 281 Hz, CF_3), 2x 126.7, 127.8, 128.4, 2x 128.6, 2x 129.4, 135.5, 145.5; MSEI 70 eV, *m/z* (rel. int.): 277 $[M]^+$ (78%), 208 $[M\text{-}CF_3]^+$ (100%); HRMS calcd for $C_{16}H_{14}F_3N$: 277.1078; obsd: 277.1094.

*4.2.5.5. Phenyl-(1-naphthalen-2′-yl-2,2,2-trifluoroethyl)-amine (**18e**).* 44%; mp: 71–73 °C; IR ($CHCl_3$): ν 3412, 1603, 1504; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.45 (1H, br d, ^3J = 6.7 Hz, NH), 5.11 (1H, dq, J_{HF} = 7.2 Hz, J_{HH} = 6.7 Hz, $CHCF_3$), 6.71 (2H, d, ^3J = 8.5 Hz, aromatic), 6.79 (1H, t, ^3J = 7.3 Hz, aromatic), 7.18 (2H, t, ^3J = 6.5 Hz, aromatic), 7.50–7.53 (2H, m, aromatic), 7.55 (1H, d, ^3J = 8.5 Hz, aromatic), 7.84–7.90 (3H, m, aromatic), 7.97 (1H, s, aromatic); ^{19}F NMR (282 MHz, $CDCl_3$): δ −74.0; ^{13}C NMR (75 MHz, $CDCl_3$): δ 60.7 (q, ^2J = 30 Hz, $CHCF_3$), 2x 113.9, 119.2, 124.8, 125.1 (q, ^1J = 282 Hz, CF_3), 126.4, 126.6, 2x 127.8, 128.0, 128.7, 2x 129.2, 131.3, 133.0, 133.4, 145.4; MSEI 70 eV, *m/z* (rel. int.): 301 $[M]^+$ (50%), 232 $[M\text{-}CF_3]$ (100%); HRMS calcd for $C_{18}H_{14}F_3N$: 301.1078; obsd: 301.1076.

Acknowledgements

The support of this work by Zeneca Plc (Syngenta) from their Strategic Research Fund (SRF 281, 1997–1999) is gratefully acknowledged. We thank Dr S. Lee (AstraZeneca, Macclesfield) and Dr R. Salmon (Syngenta, Bracknell) in particular for their helpful comments and fruitful discussion.

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