Pergamon

Tetrahedron Letters 41 (2000) 6959–6963

TETRAHEDRON LETTERS

Reaction of polyfluorinated imines with trifluoromethyltrimethylsilane. Direct synthesis of *N*-(perfluoro-*t*-butyl)amines

Viacheslav A. Petrov*

DuPont Central Research and Development,† Experimental Station, PO Box 80328, Wilmington, DE 19880-0328, USA

Received 29 June 2000; accepted 15 July 2000

Abstract

The reaction of *N*-arylimines of hexafluoroacetone and $CF_3Si(CH_3)_3$ (**1**) in the presence of CsF results in a 48–84% yield formation of $ArN(H)C(CF_3)_3$. The reaction requires an equimolar amount of CsF and rapidly proceeds in solvents such as THF or monoglyme. Interaction of $CF_3N{=}C(CF_3)_2$ with excess of **1** leads to the formation of novel amine $[(CF_3)_3C]_2NH$. Stable salt of this amine is isolated in a reaction of isomeric $CF_3CF_2N{=}CFCF_3$ with an excess of **1** in the presence of CsF. © 2000 Published by Elsevier Science Ltd.

Trifluorotrimethylsilane (**1**) is a powerful trifluoromethylating agent,[1] which has been used (usually under catalysis by fluoride anion) for the introduction of a CF_3 group into a variety of organic substrates, including aldehydes,[2–4] hydrocarbon and polyfluorinated ketones,[5–7] esters,[7] and sulfur-based electrophiles.[3,7,8] However, imines were reported to have a sluggish reactivity towards **1**.[1,9–11] Trifluoromethylation of imines using **1** could be achieved, either under special conditions (in the presence of trimethylsilylimidazole[12]) or by use of substrates with an activated C=N bond, such as nitrones,[9] azirines[10] or perfluoro-2,6-dimethyl-1-azacyclohexene.[13] Imines of polyfluorinated ketones $R_f(R_f')C{=}NR$ (readily available from reaction of polyfluoroketones with either amines[14] or arylisocyanates[15–17]) known to have a C=N bond highly reactive towards nucleophiles[18,19] due to its polarization by two perfluoroalkyl groups.

In this work it is found that *N*-arylimines of hexafluoroacetone (**2a**–**p**) rapidly react with reagent **1** in the presence of equimolar amounts of CsF to give corresponding aryl-*N*-perfluoro-*t*-butyl amines **3a**–**p** in moderate to high yield.

* Corresponding author.

† Publication No. 8089.

0040-4039/00/$ - see front matter © 2000 Published by Elsevier Science Ltd.
PII: S0040-4039(00)01182-5

$$Ar\text{-}N{=}C(CF_3)_2 + CF_3Si(CH_3)_3 + CsF \xrightarrow[1)\ THF\ \ 2)\ H^+]{15\text{-}25^oC,\ 2\text{-}16h} Ar\text{-}N(H)C(CF_3)_3 + FSi(CH_3)_3 \quad (1)$$

1

Starting imine	Ar	Product, yield, %
2a	C_6H_5	**3a** (77)
2b	2-CH_3-C_6H_4	**3b** (49)
2c	4-CH_3-C_6H_4	**3c** (62)
2d	2-CF_3-C_6H_4	**3d** (78)
2e	3-CF_3-C_6H_4	**3e** (74)
2f	4-CF_3-C_6H_4	**3f** (84)
2g	3-Cl-C_6H_4	**3g** (71)
2h	4-CH_3O-C_6H_4	**3h** (48)
2i	4-Br-C_6H_4	**3i** (81)
2j	4-O_2N-C_6H_4	**3j** (79)
2k	2-F-C_6H_4	**3k** (67)
2l	3-F-C_6H_4	**3l** (67)
2m	4-F-C_6H_4	**3m** (73)
2n	2,4-F-C_6H_3	**3n** (75)
2o	3,5-CF_3-C_6H_3	**3o** (69)
2p	4-CF_3-C_6F_4	**3p** (67)

Despite the fact that aryl amines **3** are high boiling point liquids (with the exception of **3j** being a solid), they can be purified by distillation. All ^{19}F NMR spectra of amines **3** contain a signal of $(CF_3)_3C$ fragment around –70 ppm. ^{13}C NMR spectra of compounds **3a**,**b**,**h** contain a resonance around 70 ppm with corresponding splitting pattern ($J_{C-F} = 27$–29 Hz, decet) assigned to the tertiary carbon of *F*-*t*-butyl group (see Table 1). Typically, mass spectra (EI) of amines **3** exhibit a signal of parent ion, along with intense signals corresponding to subsequent loss of CF_3^+, $C_2F_6H^+$ and CF_3CN^+ fragments by molecular ion. IR spectra of amines **3** exhibit a doublet around 3400 and 3450 cm^{-1} assigned to N–H group. The structure of **3j** is firmly established by X-ray diffraction.

The choice of the solvent is crucial for a trifluoromethylation reaction. For example, interaction of **2a** and **1** in CH_3CN solvent proceeds rapidly but an isolated yield of corresponding amine does not exceed 20–25% due to extensive tar formation. However, in solvents such as THF and monoglyme a fast and slightly exothermic reaction rapidly proceeds (20–25°C, 2–3 h) producing amine **3a** in 77% yield. On the other hand, with ether as a solvent the reaction is quite slow and conversion of imine **2a**, even after several days at ambient temperature, does not exceed a few percent. In sharp contrast to trifluoromethylation of carbonyl compounds, often carried out in the presence of a catalytic amount of CsF,[7] the process represented by Eq. (1) requires an equimolar amount of CsF, since the interaction between **1** and **2** results in the formation of cesium salt of corresponding amine **3** (see below), which is converted into a final product during aqueous work-up of the reaction mixture. For example, trifluoromethylation of **2a** in the presence of 10 mol% of CsF results in a 10 to 15% conversion of starting material (THF, 12 h at 25°C), whereas the same reaction carried out in the presence of an equimolar amount of CsF is completed after 2–3 h at ambient temperature. The rate of reaction is sensitive to the nature of substituent in an aromatic ring of imine, and reaction between **1** and imines **2b** and **2h** carrying electron-donating substituents in phenyl ring (Ar = 2-CH_3-C_6H_4- and 4-CH_3O-C_6H_4, respectively) is noticeably slower compared to **2a** and requires 10 to 16 h to achieve complete conversion of starting materials. On the other hand, the reaction of **1** and imines **2d**–**f** (Ar = 2-, 3-

Table 1
Experimental data for amines **3a**–**3p**, **5** and **5a**[a]

Comp. no.	B.P./mmHg (m.p.)	^{19}F NMR	^{1}H NMR	IR (cm^{-1})	Anal.% found (calc) or MS
3a[b]	45–46/12	–68.96	3.85 (1H), 7.00–7.30 (5H)	3403, 3450	F, 54.97 (54.95)
3b[c]	64/20	–69.21	2.33 (3H), 3.78 (1H), 7.08 (1H), 7.20 (3H)	3427, 3478	F, 52.29 (52.58)
3c	64–64.5/18	–68.88	2.18 (3H), 3.75 (1H), 6.90–7.10 (4H)	3403, 3450	C, 39.89 (40.63); H, 2.30 (2.48); F, 51.71 (52.58); N, 4.14 (4.31)
3d	50.5–51/19	–61.37 (3F, m), –69.13 (9F, q, 1.9 Hz)	4.73 (1H), 7.21 (1H), 7.36 (1H), 7.51 (1H), 7.64 (1H)	3477	F, 59.78 (60.13)
3e[d]	65/19	–63.45 (3F), –68.86 (9F)	4.00 (1H), 7.26 (1H), 7.36 (3H)	3395, 3456	F, 60.48 (60.13)
3f	71–72/15	–62.88 (3F), –68.90 (9F)	4.15 (1H), 7.10 (2H), 7.49 (2H)	3405, 3453	C, 34.02 (34.85); H, 1.26 (1.33); F, 60.55 (60.13); N, 3.82 (3.69)
3g	73–74/16	–68.88	3.95 (1H), 6.90–7.30 (4H)	3400, 3433	F, 50.27 (49.48)
3h[e]	63/5	–68.78	3.76 (1H), 3.82 (3H), 6.82 (2H), 7.12 (2H)	3411, 3477	F, 50.00 (50.12)
3i	83–83.5/19	–68.78	3.95 (1H), 7.04 (2H), 7.43 (2H)	3400, 3441	C, 30.56 (30.79); H, 1.46 (1.29); F, 43.58 (43.84); N, 3.53 (3.59)
3j	(83–84)[f]	–68.97	6.61 (1H),[g] 7.41 (2H), 8.22 (2H)	3390[h]	C, 33.74 (33.72); H, 1.49 (1.42); N, 7.79 (7.87)
3k	43.5–44/17	–69.57 (9F), –127.75 (1F)	4.10 (1H), 6.80–7.20 (4H)	3400, 3450	F, 58.83 (57.72)
3l	50–51/18	–68.92 (9F), –112.19 (1F)	3.95 (1H), 6.68 (2H)	3400, 3444	329 (M$^+$, 80%)
3m	56.5–57/18	–68.92 (9F), –116.32 (1F)	3.80 (1H), 6.93 (2H), 7.22 (2H)	3400, 3456	F, 57.65 (57.72)
3n	45–46/15	–69.51 (9F), –112.23 (1F), –120.55 (1F)	3.95 (1H), 6.88 (2H), 7.31 (1H)	3400, 3455	F, 59.95 (60.20)
3o	76/15	–63.90 (6F), –68.97 (9F)	4.25 (1H), 7.48 (2H), 77.60 (1H)	3406, 3456	C, 32.27 (32.23); H, 1.02 (0.90); N, 3.29 (3.13)
3p	76/110	–56.92 (3F), –69.94 (9F), –140.82 (2F), –143.11 (2F)	3.80	3397, 3425	C, 28.97 (29.29); H, 0.27 (0.22); N, 3.41 (3.10)
5[i]	100–101	–69.89	2.89	3454	453 (M$^+$, 3%)
5a[g]	–	–71.49	–		

[a] NMR solvent is $CDCl_3$ unless specified.
[b] ^{13}C NMR {H}: 69.99 (decet, 25 Hz), 121.28 (q, 300 Hz), 125.54, 128.52, 139.38.
[c] ^{13}C NMR {H}: 16.30, 70.30 (decet, 27 Hz), 121.28 (q, 290 Hz), 125.19, 125.34, 130.48, 132.96, 139.38.
[d] See also Ref. 24.
[e] ^{13}C NMR {H}: 54.14, 70.19 (decet, 27 Hz), 113.70, 121.25 (q, 293 Hz), 128.91, 131.52.
[f] Crystallized from hexane.
[g] In deuteroacetone.

and 4-CF_3-C_6H_4-, respectively) is much faster. It is exothermic and rapidly proceeds under mild conditions (10–25°C, 2 h). Trifluoromethylation of imine **2p**[20] proceeds under similar conditions producing perfluorinated amine **3p** in 67% yield.

All attempts to prepare corresponding perfluoro-*t*-butyl amine from $CH_3N{=}C(CF_3)_2$[14] failed, since even under mild conditions in THF as a solvent, exothermic and hard to control reaction leads to rapid darkening of the reaction mixture and extensive tar formation, although perfluorinated imine $CF_3N{=}C(CF_3)_2$ (**4**) (known to exist in equilibrium with isomer containing terminal C=N bond[21]) under similar conditions rapidly reacts with several mols of **1**. The reaction of **4**, **1** and CsF (ratio 1:4:1.1, respectively, 10–25°C, 2–3 h) results in high yield formation of a novel representative of stable perfluorinated secondary amine-bis (*F*-*t*-butyl)-amine (**5**) (Eq. (2)).

$$\underset{\mathbf{4}}{(CF_3)_2C{=}NCF_3} + \mathbf{1} \xrightarrow[\substack{1)\ CsF\\ 2)\ H^+}]{THF} \underset{\mathbf{5},\ 75\%}{[(CF_3)_3C]_2NH} + F\text{-}Si(CH_3)_3 \tag{2}$$

The formation of **5** is a result of multiple sequential nucleophilic trifluoromethylations of imine **4** leading to complete replacement by the CF_3 groups of fluorine substituents in α-position to nitrogen.

Stable salt **5a** is isolated in the reaction of isomeric *F*-3-azapentene-2[22] and excess of reagent **1** after filtration of reaction mixture and removal of solvent (Eq. (3)).

$$CF_3CF_2N{=}CFCF_3 + \mathbf{1} \xrightarrow[THF]{CsF} \underset{\mathbf{5a},\ 95\%}{[(CF_3)_3C]_2\overset{-}{N}\ \overset{+}{Cs}} \tag{3}$$

Compound **5a** is a white solid sparingly soluble in polar organic solvents (acetonitrile, acetone, THF) and stable under normal conditions in the absence of moisture. The structure of **5a** is confirmed by X-ray analysis.

Although the majority of known compounds containing -$C(CF_3)_3$ (with very few exceptions[23,24]) have been prepared utilising the chemistry of highly toxic perfluoroisobutene,[25,26] this methodology cannot be applied for direct synthesis of amines carrying the -$C(CF_3)_3$ group at nitrogen, while described in this work, a reaction of hexafluoroacetone imines with **1** provides a direct and simple route to *N*-perfluoro-*t*-butyl amines.

In a typical experiment, a mixture of 0.05 mol of imine and 0.055 mol of **1** is added dropwise to a stirred mixture of 0.06 mol of dry CsF in 70 ml of THF to keep the temperature between 15 to 25°C. The reaction mixture is agitated at ambient temperature for 2–3 h (12–16 h for **2b** and **2h**), until the complete conversion of imine is achieved (GC), diluted with 150 ml of 10% hydrochloric acid, and extracted with CH_2Cl_2 (2×50 ml). The organic layer is dried over $MgSO_4$, the solvent removed and the residue distilled.

Acknowledgements

The author thanks Dr. Grushin for stimulating discussions, W. Marshall for carrying out X-ray analysis of **3j** and **5a** and R. Smith Jr. for technical support.

References

1. For a review on the application of fluoroalkylsilanes in organic synthesis, see: Prakash, G. K. S.; Yudin, A. K. *Chem. Rev*. **1997**, *97*, 757–786.
2. Ramaiah, P.; Krishnamurti, R.; Prakash, G. K. S. *Org. Synth*. **1995**, *72*, 232–240.
3. Patel, N. R.; Kirchmeier, R. L. *Inorg. Chem*. **1992**, *31*, 2537–2540.
4. Krishnamurti, R.; Bellew, D. R.; Prakash, G. K. S. *J. Org. Chem*. **1991**, *56*, 984–989.
5. Nelson, D. W.; O'Reilly, N. J.; Speier, J.; Gassman, P. G. *J. Org. Chem*. **1994**, *59*, 8157–8171.
6. Kotun, S. P.; Anderson, J. D. O.; DesMarteau, D. D. *J. Org. Chem*. **1992**, *57*, 1124–1131.
7. Singh, R. P.; Cao, G.; Krishnamurti, R.; Kirchmeier, R. L.; Shreeve, J. M. *J. Org. Chem*. **1999**, *64*, 2873–2876.
8. Kolomeitsev, A. A.; Movchun, V. N.; Kondratenko, N. V.; Yagupolski, Yu. L. *Synthesis* **1990**, 1151–1152.
9. Nelson, D. W.; Easly, R. A.; Pintea, B. N. V. *Tetrahedron Lett*. **1999**, *40*, 25–28.
10. Felix, C. P.; Khatimi, N.; Laurent, A. J. *Tetrahedron Lett*. **1994**, *35*, 3303–3304.
11. Petasis, N. A.; Yudin, A. K.; Zavialov, I. A.; Prakash, G. K. S.; Olah, G. A. *Synlett* **1997**, 606–608.
12. Blazejewski, J.-C.; Anselmi, E.; Wilmshurst, M. P. *Tetrahedron Lett*. **1999**, *40*, 5475–5478.
13. Banks, R. E.; Besheesh, M. K.; Lawrence, N. J.; Tovell, D. J. *J. Fluorine Chem*. **1999**, *97*, 79–84.
14. Middleton, W. J.; Krespan C. G. *J. Org. Chem*. **1965**, *30*, 1398–1402.
15. Zeifman, Yu. V.; Gambaryan, N. P.; Knunaynts, I. L. *Dokl. Akad. Nauk SSSR* **1963**, *153*, 1334–1336.
16. Hall, G. E.; Middleton, W. J.; Roberts, J. *J. Am. Chem. Soc*. **1971**, *93*, 4778–4781.
17. Petrov, V. A.; Khasnis, D. D. *Isr. J. Chem*. **1999**, *39*, 147–150.
18. Fokin, A. V.; Kolomiets, A. F.; Vasil'ev, N. V. *Uspekhi Khimii* **1984**, *53*, 398–430.
19. Osipov, S. N.; Kolomiets, A. F.; Fokin, A. V. *Uspekhi Khimii* **1992**, *61*, 1490–1457
20. Petrov, V. A.; Desmarteau, D. D. *J. Fluorine Chem*. **1996**, *77*, 175–181.
21. Kirchmeier, R. L.; Lasouris, U. L.; Shreeve, J. M. *Inorg. Chem*. **1975**, *14*, 592–596.
22. Petrov, V. A.; Belen'kii, G. G.; German, L. S. *Izv. AN USSR. Ser. Khim*. **1985**, 1934–1935.
23. For example, $(CF_3)_3COH$ has been prepared by reaction of **1** and hexafluoroacetone (see Ref. 6); compound **3e** was prepared by ring-opening reaction of corresponding aziridine under action of HF (Ref. 24).
24. Petrov, V. A. *J. Fluorine Chem*. in press.
25. Dyatkin, B. L.; Delaygina, N. I.; Sterlin, S. R. *Uspekhi Khimii* **1976**, *45*, 1205–1221.
26. Zeifman, Yu. V.; Ter-Gabrielayn, E. G.; Gambaryan, N. P.; Knunyants, I. L. *Uspekhi Khimii* **1984**, *53*, 431–461.