Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Supporting Information

A sterically demanding organo-superbase avoids decomposition of a naked trifluoromethyl carbanion directly generated from fluoroform

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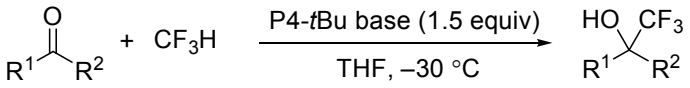
Experimental Section

General Methods:

All reactions were performed in oven-dried glassware under a positive pressure of nitrogen. Solvents were transferred *via* syringe and were introduced into the reaction vessels though a rubber septum. All reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm Merck silica-gel (60-F254). The TLC plates were visualized with UV light and 7% phosphomolybdic acid or $KMnO_4$ in water/heat. Column chromatography was carried out on a column packed with silica-gel 60N spherical neutral size 63-210 μm. The ^{1}H-NMR (300 MHz) and ^{19}F-NMR (282 MHz) spectra for solution in $CDCl_3$ were recorded on a Varian Mercury 300. Chemical shifts (δ) are expressed in ppm downfield from internal TMS or $CDCl_3$. Mass spectra were recorded on a SHIMADZU GCMS-QP5050A.

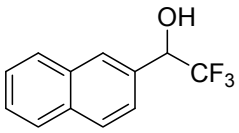
General procedure for the *t*-Bu-P4 base mediated trifluoromethylation.



1 **2**

The Schlenk tube containing carbonyl compound **1** (0.10 mmol) in THF was charged with HCF_3 by cooling in liquid nitrogen under vacuum. This tube was cooled to -30 ˚C, and P4-*t*Bu base (150 μL 1.0 M in hexane, 0.15 mmol, 1.5 equiv) was added. Then, HCF_3 was bubbled for one minute at the same temperature. After being stirred for 2 h, the reaction mixture was quenched with sat. NH_4Cl aq. The aqueous layer was extracted with CH_2Cl_2, and the combined organic layers was washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (*n*-hexane/ethyl acetate = 9/1) to give α-trifluoromethyl alcohol **2**.

2,2,2-Trifluoro-1-(naphthalen-2-yl)ethanol (2a)

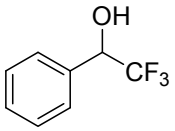


This compound has been previously prepared and characterized.[1]

A reaction of 2-naphthaldehyde **1a** (15.6 mg, 0.10 mmol), P4-*t*Bu base (150 μL 1.0 M in hexane, 0.15 mmol, 1.5 equiv), HCF_3 (excess) in THF (0.5 mL) at -30 ˚C, and a purification by column chromatography on silica gel (*n*-hexane/ethyl acetate = 9/1) to give **2a** (20.0 mg, 88%) as a white solid.

^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.76 (brs, 1H), 5.19 (q, J = 6.6 Hz, 1H), 7.51-7.59 (m, 3H), 7.85-7.95 (m, 4H); ^{19}F NMR ($CDCl_3$, 282 MHz) δ -78.5 (d, J = 5.9 Hz, 3F); MS (EI, *m/z*) 226 (M^+). These assignments matched with those previously published.[1]

2,2,2-Trifluoro-1-phenylethanol (2b)

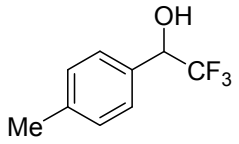


This compound has been previously prepared and characterized.[1,2]

A reaction of benzaldehyde **1b** (10.6 mg, 0.10 mmol), P4-*t*Bu base (150 μL 1.0 M in hexane, 0.15 mmol, 1.5 equiv), HCF_3 (excess) in THF (0.5 mL) at -30 ˚C, and a purification by column chromatography on silica gel (*n*-hexane/ethyl acetate = 9/1) to give **2b** (13.1 mg, 74%) as a colorless oil.

^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.58 (brs, 1H), 5.03 (q, J = 6.6 Hz, 1H), 7.40-7.43 (m, 3H), 7.47-7.48 (m, 2H); ^{19}F NMR ($CDCl_3$, 282 MHz) δ -78.9 (d, J = 5.9 Hz, 3F); MS (EI, *m/z*) 176 (M^+). These assignments matched with those previously published.[1,2]

2,2,2-Trifluoro-1-*p*-tolylethanol (2c)

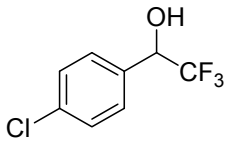


This compound has been previously prepared and characterized.[1,2]

A reaction of 4-methylbenzaldehyde **1c** (12.0 mg, 0.10 mmol), P4-*t*Bu base (150 μL 1.0 M in hexane, 0.15 mmol, 1.5 equiv), HCF_3 (excess) in THF (0.5 mL) at -30 ˚C, and a purification by column chromatography on silica gel (*n*-hexane/ethyl acetate = 9/1) to give **2c** (14.4 mg, 76%) as a white solid.

^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.37 (s, 3H), 2.54 (brs, 1H), 4.98 (m, 1H), 7.22 (d, *J* = 8.1 Hz, 2H), 7.36 (d, *J* = 8.1 Hz, 2H); ^{19}F NMR ($CDCl_3$, 282 MHz) δ -78.9 (d, *J* = 6.6 Hz, 3F); MS (EI, *m/z*) 190 (M^+). These assignments matched with those previously published.[1,2]

1-(4-Chlorophenyl)-2,2,2-trifluoroethanol (2d)

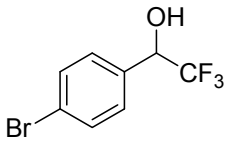


This compound has been previously prepared and characterized.[1,2]

A reaction of 4-chlorobenzaldehyde **1d** (14.1 mg, 0.10 mmol), P4-*t*Bu base (150 μL 1.0 M in hexane, 0.15 mmol, 1.5 equiv), HCF_3 (excess) in THF (0.5 mL) at -30 ˚C, and a purification by column chromatography on silica gel (*n*-hexane/ethyl acetate = 9/1) to give **2d** (18.2 mg, 86%) as a white solid.

^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.82 (brs, 1H), 5.01 (q, *J* = 6.5 Hz, 1H), 7.37-7.44 (m, 4H); ^{19}F NMR ($CDCl_3$, 282 MHz) δ -79.0 (d, *J* = 7.1 Hz, 3F); MS (EI, *m/z*) 210 (M^+). These assignments matched with those previously published.[1,2]

1-(4-Bromophenyl)-2,2,2-trifluoroethanol (2e)

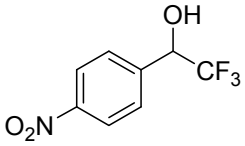


This compound has been previously prepared and characterized.[2]

A reaction of 4-bromobenzaldehyde **1e** (18.5 mg, 0.10 mmol), P4-*t*Bu base (150 μL 1.0 M in hexane, 0.15 mmol, 1.5 equiv), HCF_3 (excess) in THF (0.5 mL) at -30 ˚C, and a purification by column chromatography on silica gel (*n*-hexane/ethyl acetate = 9/1) to give **2e** (20.5 mg, 80%) as a white solid.

^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.73 (brs, 1H), 5.05 (q, *J* = 6.6 Hz, 1H), 7.36 (d, *J* = 8.1 Hz, 2H), 7.55 (d, *J* = 8.4 Hz, 2H); ^{19}F NMR ($CDCl_3$, 282 MHz) δ -79.0 (d, *J* = 6.8 Hz, 3F); MS (EI, *m/z*) 254 (M^+-1), 256 (M^++1). These assignments matched with those previously published.[2]

2,2,2-Trifluoro-1-(4-nitrophenyl)ethanol (2f)

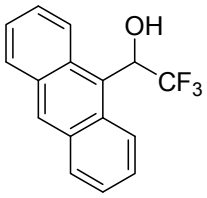


This compound has been previously prepared and characterized.[1]

A reaction of 4-nitrobenzaldehyde **1f** (15.1 mg, 0.10 mmol), P4-*t*Bu base (150 μL 1.0 M in hexane, 0.15 mmol, 1.5 equiv), HCF_3 (excess) in THF (0.5 mL) at -30 ˚C, and a purification by column chromatography on silica gel (*n*-hexane/ethyl acetate = 8/2) to give **2f** (11.5 mg, 52%) as a white solid.

^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.90 (brs, 1H), 5.19 (q, J = 6.4 Hz, 1H), 7.70 (d, J = 8.4 Hz, 2H), 8.28 (d, J = 8.4 Hz, 2H); ^{19}F NMR ($CDCl_3$, 282 MHz) δ -78.7 (d, J = 5.9 Hz, 3F); MS (EI, *m/z*) 221 (M^+). These assignments matched with those previously published.[1]

1-(Anthracen-9-yl)-2,2,2-trifluoroethanol (2g)

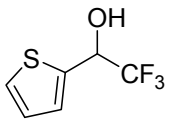


This compound has been previously prepared and characterized.[3]

A reaction of 9-antracene carbaldehyde **1g** (20.6 mg, 0.10 mmol), P4-*t*Bu base (150 μL 1.0 M in hexane, 0.15 mmol, 1.5 equiv), HCF_3 (excess) in THF (0.5 mL) at -30 ˚C, and a purification by column chromatography on silica gel (*n*-hexane/ethyl acetate = 9/1) to give **2g** (20.3 mg, 74%) as a pale yellow solid.

^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.10 (brs, 1H), 6.62 (q, J = 7.9 Hz, 1H), 7.44-7.57 (m, 4H), 8.00 (d, J = 8.1 Hz, 2H), 8.11 (brs, 1H), 8.51 (s, 1H), 8.94 (brs, 1H); ^{19}F NMR ($CDCl_3$, 282 MHz) δ -74.5 (d, J = 7.9 Hz, 3F); MS (EI, *m/z*) 276(M^+). These assignments matched with those previously published.[3]

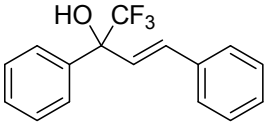
2,2,2-Trifluoro-1-(thiophen-2-yl)ethanol (2h)



This compound has been previously prepared and characterized.[1]

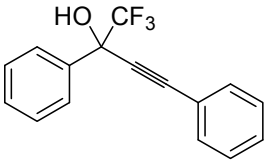
A reaction of 2-thiophenaldehyde **1h** (11.2 mg, 0.10 mmol), P4-*t*Bu base (150 μL 1.0 M in hexane, 0.15 mmol, 1.5 equiv), HCF_3 (excess) in THF (0.5 mL) at -30 ˚C, and a purification by column chromatography on silica gel (*n*-hexane/ethyl acetate = 9/1) to give **2h** (11.9 mg, 65%) as a colorless oil.
^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.66 (brs, 1H), 5.29 (q, *J* = 6.2 Hz, 1H), 7.06 (dd, *J* = 3.8, 5.0 Hz, 1H), 7.21 (d, *J* = 3.6 Hz, 1H), 7.41 (dd, *J* = 1.1, 5.0 Hz); ^{19}F NMR ($CDCl_3$, 282 MHz) δ -79.2 (d, *J* = 5.9 Hz, 3F); MS (EI, *m/z*) 182 (M^+). These assignments matched with those previously published.[1]

(*E*)-1,1,1-Trifluoro-2,4-diphenylbut-3-en-2-ol (2i)



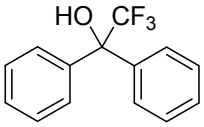
This compound has been previously prepared and characterized.[4]
A reaction of calcone **1i** (20.8 mg, 0.10 mmol), P4-*t*Bu base (150 μL 1.0 M in hexane, 0.15 mmol, 1.5 equiv), HCF_3 (excess) in THF (0.5 mL) at -30 ˚C, and a purification by column chromatography on silica gel (*n*-hexane/ethyl acetate = 95/5) to give **2i** (20.0 mg, 72%) as a pale yellow oil.
^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.75 (s, 1H), 6.72 (d, *J* = 15.9 Hz, 1H), 6.89 (d, *J* = 15.9 Hz, 1H), 7.30-7.44 (m, 8H), 7.65 (d, *J* = 6.3 Hz, 2H); ^{19}F NMR ($CDCl_3$, 282 MHz) δ -79.0 (s, 3F); MS (EI, *m/z*) 278 (M^+). These assignments matched with those previously published.[4]

1,1,1-Trifluoro-2,4-diphenylbut-3-yn-2-ol (2j)



This compound has been previously prepared and characterized.[5]
A reaction of 1,3-diphenylprop-2-yn-1-one **1j** (20.6 mg, 0.10 mmol), P4-*t*Bu base (150 μL 1.0 M in hexane, 0.15 mmol, 1.5 equiv), HCF_3 (excess) in THF (0.5 mL) at -30 ˚C, and a purification by column chromatography on silica gel (*n*-hexane/acetone = 9/1) to give **2j** (25.4 mg, 92%) as a pale yellow oil.
^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.23 (s, 1H), 7.36-7.44 (m, 6H), 7.52-7.55 (m, 2H), 7.81-7.82 (m, 2H); ^{19}F NMR ($CDCl_3$, 282 MHz) δ -80.8 (s, 3F); MS (EI, *m/z*) 276 (M^+). These assignments matched with those previously published.[5]

2,2,2-Trifluoro-1,1-diphenylethanol (2k)

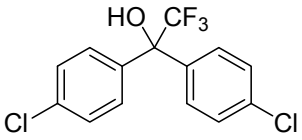


This compound has been previously prepared and characterized.[6]

A reaction of benzophenone **1k** (18.2 mg, 0.10 mmol), P4-*t*Bu base (150 μL 1.0 M in hexane, 0.15 mmol, 1.5 equiv), HCF_3 (excess) in THF (0.5 mL) at -20 ˚C, and a purification by column chromatography on silica gel (*n*-hexane/acetone = 9/1) to give **2k** (23.2 mg, 92%) as a white solid.

^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.93 (s, 1H), 7.34-7.40 (m, 6H), 7.48-7.50 (m, 4H); ^{19}F NMR ($CDCl_3$, 282 MHz) δ -74.8 (s, 3F); MS (EI, *m/z*) 252 (M^+). These assignments matched with those previously published.[6]

1,1-Bis(4-chlorophenyl)-2,2,2-trifluoroethanol (2l)

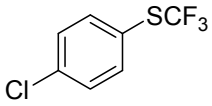


This compound has been previously prepared and characterized.[4]

A reaction of 4,4'-dichlorobenzophenone **1l** (25.1 mg, 0.10 mmol), P4-*t*Bu base (150 μL 1.0 M in hexane, 0.15 mmol, 1.5 equiv), HCF_3 (excess) in THF (0.5 mL) at -20 ˚C, and a purification by column chromatography on silica gel (*n*-hexane/acetone = 9/1) to give **2k** (26.3 mg, 82%) as a pale-yellow oil.

^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.01 (s, 1H), 7.34 (d, J = 8.7 Hz, 4H), 7.41 (d, J = 8.7 Hz, 4H); ^{19}F NMR ($CDCl_3$, 282 MHz) δ -75.1 (s, 3F); MS (EI, *m/z*) 320 (M^+). These assignments matched with those previously published.[4]

(4-Chlorophenyl)(trifluoromethyl)sulfane (5)



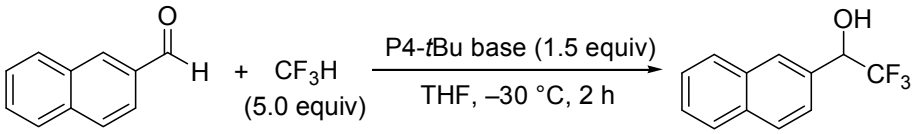
This compound has been previously prepared and characterized.[7]

A reaction of 4,4'-dichlorodiphenyl disulfide **4** (28.7 mg, 0.10 mmol), P4-*t*Bu base (150 μL 1.0 M in hexane, 0.15 mmol, 1.5 equiv), HCF_3 (excess) in THF (0.5 mL) at -10 ˚C, and a purification by column chromatography on silica gel (*n*-hexane) to give **5** (15.7 mg, 74%) as a colorless oil.

^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.41 (d, J = 8.1 Hz, 2H), 7.32 (d, J = 8.4 Hz, 2H); ^{19}F NMR ($CDCl_3$, 282

MHz) δ -43.4 (s, 3F); MS (EI, *m/z*) 212 (M^+). These assignments matched with those previously published.[7]

_t_-Bu-P4 Base mediated trifluoromethylation using 5.0 equiv of HCF_3.



1a **2a**

The Schlenk tube containing 2-naphthaldehyde **1a** (15.6 mg, 0.10 mmol) in THF was cooled to -30˚C, and P4-*t*Bu base (150 μL 1.0 M in hexane, 0.15 mmol, 1.5 equiv) was added. Then, HCF_3 (35.0 mg, 0.50 mmol, 5.0 equiv) was bubbled at the same temperature. After being stirred for 2 h, the reaction mixture was quenched with sat. NH_4Cl aq. The aqueous layer was extracted with CH_2Cl_2, and the combined organic layers was washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (*n*-hexane/ethyl acetate = 9/1) to give **2a** (19.2 mg, 85%) as a white solid.

References:

1) Q. Xu, H. Zhou, X. Geng, P. Chen. *Tetrahedron* **2009**, *65*, 2232.

2) M. Shi, X.-G. Liu, Y.-W. Guo, W. Zhang, *Tetrahedron* **2007**, *63*, 12731.

3) K. H. Yong, J. M. Chong, *Org. Lett.* **2002**, *4*, 4139.

4) G. K. S. Prakash, J. Hu , G. A. Olah, *Org. Lett.*, **2003**, *5*, 3253.

5) V. R. Chintareddy, K. Wadhwa, J. G. Verkade, *J. Org. Chem.* **2011**, *76*, 4482.

6) R. P. Singh, R. L. Kirchmeier, J. M. Shreeve, *Org. Lett.*, **1999**, 1, 1047.

7) A. Harsányi, É. Dorkó, Á. Csapó, T. Bakó, C. Peltz , J. Rábai, *J. Fluorine Chem*. **2011**, *132,* 1241.