Supporting Information

2-Chloro-2,2-Difluoroacetophenone: A Non-ODS-Based Difluorocarbene Precursor and Its Use in the Difluoromethylation of Phenol Derivatives

Laijun Zhang, Ji Zheng, and Jinbo Hu*

Key Laboratory of Organofluorine Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Road, Shanghai 200032, China

jinbohu@mail.sioc.ac.cn

Contents

General Information.....	S-2
Characterization data for the isolated compounds 5b , 5c , 5e , 5f , 5g , 5h , 5i , 5j , 5k , 5l , 5m	S-2~S-6
References.....	S-7
¹ H, ¹⁹ F, ¹³ C NMR spectra for compounds 5b , 5c , 5e , 5f , 5g , 5h , 5i , 5j , 5k , 5l , 5m	S-8~S-34

General:

Unless otherwise mentioned, solvents and reagent were purchased from commercial sources and used as received. ^1H , ^{13}C and ^{19}F NMR spectra were recorded on 500 MHz, 400 MHz or 300 MHz NMR spectrometer. ^1H NMR chemical shifts were determined relative to internal $(\text{CH}_3)_4\text{Si}$ (TMS) at δ 0.0 or to the signal of a residual protonated solvent: CDCl_3 δ 7.26. ^{13}C NMR chemical shifts were determined relative to internal TMS at δ 0.0. ^{19}F NMR chemical shifts were determined relative to CFCl_3 at δ 0.0. Mass spectra were obtained on a mass spectrometer. High-resolution mass data were recorded on a high-resolution mass spectrometer in the EI, ESI or MALDI mode.

Characterization data for the isolated compounds:**2-(Difluoromethoxy)naphthalene (5b)**

^1H NMR: δ 7.83 (m, 3H), 7.49 (m, 3H), 7.28 (dd, $J = 9.1, 2.7$ Hz, 1H), 6.63 (t, $J = 73.7$ Hz, 1H). ^{19}F NMR: δ -80.6 (d, $J = 74.4$ Hz, 2F). The characterization data was consistent with the reference [1].

1-(Difluoromethoxy)naphthalene (5c)

Colorless liquid. ^1H NMR: δ 8.18 (t, $J = 5.0$ Hz, 1H), 7.85 (t, $J = 4.4$ Hz, 1H), 7.69 (d, $J =$

8.2 Hz, 1H), 7.54 (t, $J = 4.3$ Hz, 2H), 7.40 (t, $J = 7.5$ Hz, 1H), 7.18 (d, $J = 7.5$ Hz, 1H), 6.65 (t, $J = 73.9$ Hz, 1H). ^{19}F NMR: δ -79.8 (d, $J = 72.5$ Hz, 2F). ^{13}C NMR: δ 147.5, 134.7, 127.8, 126.9, 126.6, 126.5, 125.4, 125.3, 121.6, 116.6 (t, $J = 257.3$ Hz), 113.7. MS (EI, m/z , %): 194 (M^+ , 79.16), 144 (100.00). EA: calcd. for $\text{C}_{11}\text{H}_8\text{F}_2\text{O}$: C, 68.04; H, 4.15; Found: C, 68.18; H, 4.14. IR (film): 3060, 1600, 1582, 1510, 1467, 1375, 1263, 773 cm^{-1} .

4-Chloro-1-(difluoromethoxy)benzene (5e)

^1H NMR: δ 7.33 (d, $J = 8.8$ Hz, 2H), 7.07 (d, $J = 8.8$ Hz, 2H), 6.48 (t, $J = 73.5$ Hz, 1H).

^{19}F NMR: δ -81.2 (d, $J = 73.3$ Hz, 2F). The characterization data was consistent with the reference [2].

2,4-Dichloro-1-(difluoromethoxy)benzene (5f)

^1H NMR: δ 7.46 (d, $J = 2.5$ Hz, 1H), 7.24 (d, $J = 2.3$ Hz, 1H), 7.20 (s, 1H), 6.51 (t, $J = 73.1$ Hz, 1H). ^{19}F NMR: δ -81.7 (d, $J = 71.6$ Hz, 2F). The characterization data was consistent with the reference [3].

4-Bromo-1-(difluoromethoxy)benzene (5g)

^1H NMR: δ 7.48 (d, $J = 8.7$ Hz, 2H), 7.02 (d, $J = 8.7$ Hz, 2H). 6.48 (t, $J = 73.2$ Hz, 1H).

^{19}F NMR: δ -81.2 (d, $J = 73.3$ Hz, 2F). The characterization data was consistent with the reference [4].

1-(Difluoromethoxy)-4-iodobenzene (5h)

^1H NMR: δ 7.69 (d, $J = 9.3$ Hz, 2H), 6.89 (d, $J = 9.5$ Hz, 2H). 6.48 (t, $J = 73.3$ Hz, 1H).

^{19}F NMR: δ -81.2 (d, $J = 73.3$ Hz, 2F). The characterization data was consistent with the reference [4].

1-Bromo-2-(difluoromethoxy)benzene (5i)

^1H NMR: δ 7.62 (d, J = 7.6 Hz, 1H), 7.32 (t, J = 8.3 Hz, 1H), 7.22 (d, J = 8.2 Hz, 1H), 7.11 (t, J = 7.6 Hz, 1H), 6.53 (t, J = 73.5 Hz, 1H). ^{19}F NMR: δ -81.3 (d, J = 73.6 Hz, 2F). The characterization data was consistent with the reference [5].

1-(difluoromethoxy)-2-iodobenzene (5j)

Colorless liquid. ^1H NMR: δ 7.85 (d, J = 7.9 Hz, 1H), 7.35 (t, J = 7.9 Hz, 1H), 7.16 (d, J = 7.9 Hz, 1H), 6.96 (t, J = 7.9 Hz, 1H), 6.52 (t, J = 73.5 Hz, 1H). ^{19}F NMR: δ -80.9 (d, J = 74.3 Hz, 2F). ^{13}C NMR: δ 150.9, 140.1, 129.7, 127.2, 120.3, 116.0 (t, J = 260.8 Hz), 89.1. MS (EI, m/z , %): 270 (M^+ , 100.00). EA: calcd. for $\text{C}_7\text{H}_5\text{F}_2\text{OI}$: C, 31.14; H, 1.87; Found: C, 31.45; H, 1.92. IR (film): 3068, 2992, 1579, 1473, 1442, 1380, 1222, 753 cm^{-1} .

1,3,5-Tribromo-2-(difluoromethoxy)benzene (5k)

White solid. mp: 65-66°C. ^1H NMR: δ 7.74 (s, 2H), 6.59 (t, J = 73.5 Hz, 1H). ^{19}F NMR: δ -80.8 (d, J = 73.9 Hz, 2F). ^{13}C NMR: δ 145.5, 135.6, 120.4, 119.2, 116.2 (t, J = 264.0 Hz). MS (EI, m/z , %): 381(M^+ , 30.37), 332(100.00). EA: calcd. for $\text{C}_7\text{H}_3\text{Br}_3\text{F}_2\text{O}$: C, 22.08; H, 0.79; Found: C, 22.05; H, 0.88. IR (film): 3108, 3069, 1727, 1546, 1445, 1382, 1279, 1064 cm^{-1} .

4-Phenyl-1-(difluoromethoxy)benzene (5l)

White solid. mp: 26-28 °C. ^1H NMR: δ 7.56 (t, J = 8.6 Hz, 4H), 7.44 (t, J = 7.6 Hz, 2H), 7.35 (t, J = 7.6 Hz, 1H), 7.19 (d, J = 8.1 Hz, 2H), 6.54 (t, J = 73.9 Hz, 1H). ^{19}F NMR: δ -80.6 (d, J = 73.0 Hz, 2F). ^{13}C NMR: δ 150.6, 140.1, 138.6, 128.9, 128.5, 127.5, 127.0, 119.9, 116.0 (t, J = 258.3 Hz). MS (EI, m/z, %): 220 (M^+ , 84.72), 170 (100.00). HRMS (EI): calcd. for $\text{C}_{13}\text{H}_{10}\text{F}_2\text{O}$: 220.0700; Found: 220.0704. IR (film): 1609, 1519, 1488, 1386, 1232, 1130, 1047 cm^{-1} .

1-Difluoromethoxy-4-(2'-phenylethenyl)benzene (5m)

White solid. Mp: 95-96 °C. ^1H NMR: δ 7.42 (d, J = 8.0 Hz, 4H), 7.30 (d, J = 7.4 Hz, 2H), 7.19 (t, J = 6.9 Hz, 1H), 7.03 (d, J = 8.5 Hz, 2H), 6.98 (s, 2H), 6.44 (t, J = 73.8 Hz, 1H). ^{19}F NMR: δ -80.670 (d, J = 74.1 Hz, 2F). ^{13}C NMR: δ 150.6, 150.5, 137.1, 134.8, 129.1, 128.731, 127.8, 127.4, 126.5, 119.8, 115.9 (t, J = 258.5 Hz). MS (EI, m/z, %): 246 (M^+ , 100.00). Elemental analysis: calcd. for $\text{C}_{15}\text{H}_{12}\text{F}_2\text{O}$: C, 73.16; H, 4.91; Found: C, 72.84; H, 4.94. IR (film): 3023, 1605, 1509, 1450, 1387, 1241, 1127, 1047 cm^{-1} .

References:

1. Chen, Q.-Y.; Wu, S.-W. *J. Fluorine Chem.* **1989**, *44*, 433.
2. (a) Langlois, B. R. *J. Fluorine Chem.* **1988**, *41*, 247. (b) Rico, I.; Wakselman, C. *Tetrahedron* **1981**, *37*, 4209.
3. Miller, T. *J. Org. Chem.* **1960**, *25*, 2009.
4. Shelyazhenko, S. V.; Fialkov, Y. A.; Yagupol'skii, L. M. *J. Org. Chem. USSR* (Engl. Transl.); **1992**, *28*; 1317; *Zh. Org. Khim.* **1992**; *28*, 1652.
5. (a) Berthel, S. J.; Cheung, A. W.-H.; Thakkar, K. C.; Yun, W. *PCT Int. Appl.* WO 2006050843 (**2006**). (b) Ottosen, E. R.; Horneman, A. M.; Liang, X. *PCT Int. Appl.* WO 2003018535 (**2003**).

NMR spectra for all products

(5b) ¹⁹F NMR