Synthesis of 2-(2-fluorophenyl)-2-methylamino-cyclohexanone as a new ketamine derivative

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Supplementary Material

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1. Spectral data

1.1 Cyclopentyl-(2-fluorophenyl)-ketone (2).

Yield: (90%); light yellow oil. IR (KBr): 2955, 2869, 1679, 1608, 1479, 1451, 1271, 1211, 756 cm^{-1} ; ^1H NMR (250MHz, CDCl_3) δ : 1.6 – 1.72(4H, m), 1.86 – 1.93(4H, m), 3.59 – 3.66(1H, m), 7.06 – 7.23(2H, m), 7.42 - 7.51(1H, m), 7.74 – 7.81(1H, m); ^{13}C NMR (62.90MHz, CDCl_3) δ : 26.09(2 CH_2 , s), 29.27(2 CH_2 , d, $J = 0.64$ Hz), 50.98(CH, d, $J = 5.77$ Hz), 116.42(CH, d, $J = 23.9$ Hz), 124.39(CH, d, $J = 3.45$ Hz), 126.21(quat-C, d, $J = 13.02$ Hz), 130.83(CH, d, $J = 2.89$ Hz), 133.92(CH, d, $J = 8.99$ Hz), 159.40(quat-C, d, $J_{\text{C-F}} = 253.74$ Hz), 201.51(quat-C, C=O) ppm.

1.2 α -bromocyclopentyl-(2-fluorophenyl)-ketone (3)

Yield: (96%); brown oil. ^1H NMR (300MHz, CDCl_3) δ 1.83(2H, m), 2.02(2H, m), 2.37(4H, m), 7.08- 7.21(2H, m), 7.41 - 7.48(1H, m), 7.74 - 7.78(1H, m); ^{13}C NMR (75MHz, CDCl_3) δ 23.22(CH_2 , s), 40.22(CH_2 , s), 73.81(quat-C, s), 116(CH, d, $J = 22\text{Hz}$), 123(CH, d, $J = 3.22\text{Hz}$), 126(quat-C, d, $J = 14.8\text{Hz}$), 130(CH, d, $J = 2.3\text{Hz}$), 132(CH, d, $J = 8.47\text{Hz}$), 159 (quat-C, d, $J_{\text{C-F}} = 250.8\text{Hz}$), 196.37(quat-C, C=O).

1.3 α -hydroxycyclopentyl-(2-fluorophenyl)-N-methylamine (4)

Yield: (81%); shiny crystals. Mp 41.5 – 43.5 $^\circ\text{C}$; IR (KBr): 3297, 2971, 2873, 1656, 996, 765 cm^{-1} ; ^1H NMR (300MHz, CDCl_3) δ : 1.26 – 1.69(5H, m), 1.91 – 2.2(3H, m), 3.03(3H, s), 5.48(1H), 7.03 – 7.27(3H, m), 7.39 – 7.51(1H, m); ^{13}C NMR (75 MHz, CDCl_3) δ : 23.53(CH_2), 23.84(CH_2),

37.8(CH₂), 38.01(CH₂), 39.68(CH₃), 84.08(quat-C), 115.7(CH, d, $J = 24.90$ Hz), 122.16(quat-C, d, $J = 19.62$ Hz), 124.18(CH, d, $J = 2.41$ Hz), 129.12(CH, d, $J = 4.52$ Hz), 130.62(CH, d, $J = 7.54$ Hz), 156.61(quat-C, d, $J_{C-F} = 246.425$ Hz), 171.12(quat-C, C=N) ppm.

1.4 2-(2-fluorophenyl)-2-methylamino-cyclohexanone (5)

Yield: (53%); brown oil. IR (KBr): 3371, 2942, 2863, 1714, 1485, 759 cm⁻¹; ¹H NMR (300MHz, CDCl₃) δ : 1.70 – 1.80(4H, m), 1.93(1H, s), 2.11(3H, s), 2.30 – 2.47(2H, m), 2.55(1H, s), 2.75 – 2.84(1H, m), 7.04(1H, m), 7.17 – 7.22(1H, m), 7.29(1H, m), 7.43(1H, m); ¹³C NMR (75MHz, CDCl₃) δ : 21.95(CH₂), 28.48(CH₂), 29.20(CH₃), 38.18(CH₂), 39.38(CH₂), 68.33(quat-C), 116.13(1CH, d, $J = 23.39$ Hz), 124.24(CH, d, $J = 3.01$ Hz), 126.73(quat-C, d, $J = 12.83$ Hz), 128.83(CH, d, $J = 4.52$ Hz), 129.47(CH, d, $J = 8.30$ Hz), 161(quat-C, d, $J_{C-F} = 246.80$ Hz), 210(quat-C, C=O) ppm.

1.5 (2-fluorophenyl)(1-hydroxycyclopentyl)methanone (6)

Brown oil. IR (KBr): 3480, 2957, 1687, 1611, 1451, 1279, 1219, 753 cm⁻¹; ¹H NMR (300MHz, CDCl₃) δ : 1.79 – 1.92(6H, m), 2.18 – 2.22(2H, m), 2.90(1H), 7.13 – 7.51(4H, m); ¹³C NMR (75 MHz, CDCl₃) δ : 24.75(2CH₂), 39.37(CH₂), 39.40(CH₂), 88.30(quat-C), 116.07(CH, d, $J = 22.5$ Hz), 124(CH, d, $J = 3.22$ Hz), 126(quat-C, d, $J = 16.5$ Hz), 129(CH, d, $J = 3.5$ Hz), 132(CH, d, $J = 8.4$ Hz), 159(quat-C, d, $J_{C-F} = 247.42$ Hz), 206(quat-C, C=O) ppm.

1.6 1-(2-fluorophenyl)-N-methyl-2-oxocyclohexanaminium chloride (7)

Mp 258 – 260 °C .; IR (KBr): 3439, 2975, 2929, 2869, 2663, 1725, 1556, 1491, 1451, 1231, 770 cm^{-1} .; ^1H NMR (300MHz, D_2O) δ : 1.58(2H, m), 1.76 – 1.79(2H, m), 1.94(1H, m), 2.27(3H, s), 2.387 – 2.45(2H, m), 3.11(1H, d, $J = 13.8$ Hz), 7.13 – 7.20(1H, m), 7.32 – 7.34(1H, m) , 7.49(1H, m), 7.62 – 7.64(1H, m).; ^{13}C NMR (75MHz, D_2O) δ : 20.95(CH_2), 26.38(CH_2), 28.67(CH_3), 33.93(CH_2), 38.46(CH_2), 69.43(quat-C), 116.9(CH), 117.12(quat-C, d, $J = 6.792$ Hz), 125.73(CH , d, $J = 2.26$ Hz), 130.15(CH), 133.53(CH , d, $J = 9.057$ Hz), 160.8(quat-C, d, $J = 246.8$ Hz), 209(quat-C, C=O) ppm. MS m/z (percent abundance): 221.2 [M^+] (10%), 193 (45%), 165 (30%), 164 (70%), 109(25%). Anal. calcd. For $\text{C}_{13}\text{H}_{16}\text{FNO} \cdot \text{HCl}$: C, 60.60; H, 6.60; N, 5.43%. Found C, 60.1; H, 6.58; N, 5.41%.

2. Copies of ^1H and ^{13}C NMR spectra

Copy of ^1H -NMR (CDCl_3) spectra for 2

Copy of ^{13}C -NMR (CDCl_3) spectra for 2

Copy of ^1H -NMR (CDCl_3) spectra for 3

Copy of ^{13}C -NMR (CDCl_3) spectra for 3

Copy of ^1H -NMR (CDCl_3) spectra for 4

Copy of ^{13}C -NMR (CDCl_3) spectra for 4

Copy of ^1H -NMR (CDCl_3) spectra for **5**

Copy of ^{13}C -NMR (CDCl_3) spectra for 5

Copy of ^1H -NMR (CDCl_3) spectra for 6

Copy of ^{13}C -NMR (CDCl_3) spectra for 6

Copy of ^1H -NMR (D_2O) spectra for 7

Copy of ^{13}C -NMR (D_2O) spectra for 7

Copy of mass spectra for 7