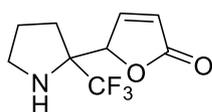


Diastereoselective vinylogous Mannich reaction of perfluoroalkylated cyclic imines with 2-trimethylsilyloxyfuran

Olga I. Shmatova and Valentine G. Nenajdenko

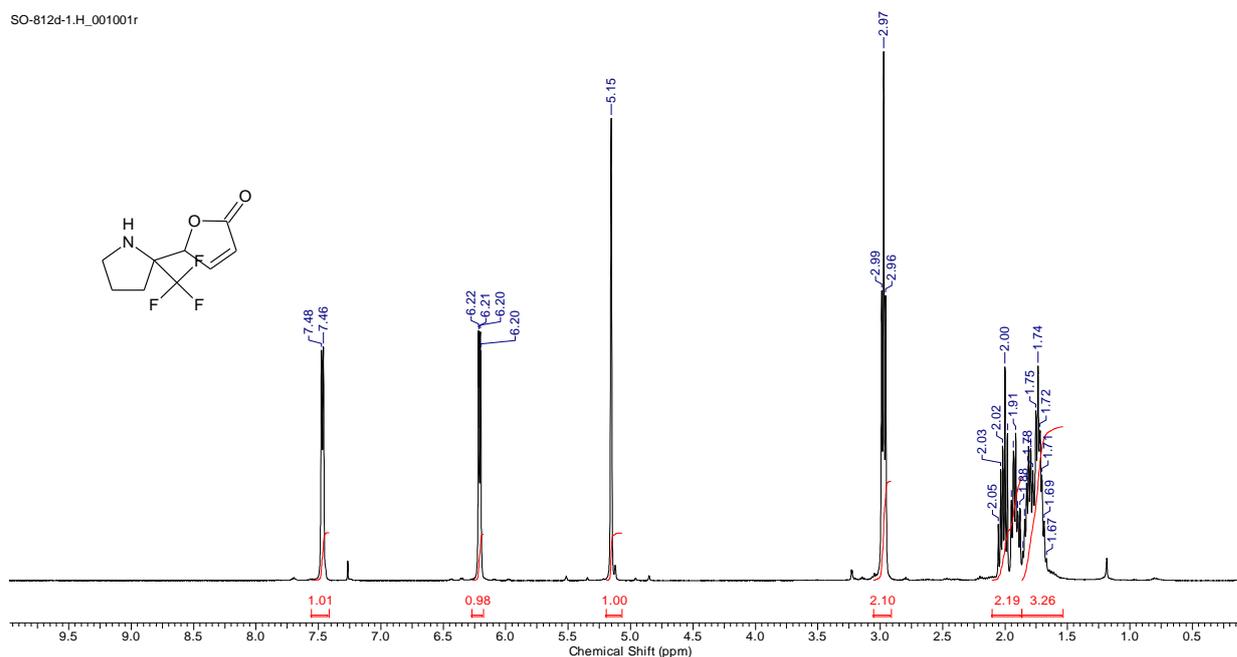
General method. Starting cyclic ketamine **1a-d** (1 mmol) and 2-trimethylsilyloxyfuran **2** (0.2 g, 1.28 mmol) were dissolved in dry dichloromethane (2 ml), and copper(II) trifluoromethanesulfonate (0.018 g, 0.05 mmol) was added. The mixture was kept at room temperature from 1 to 5 days (TLC control). The solvent was evaporated and the product was purified by column chromatography (hexane/ethyl acetate).

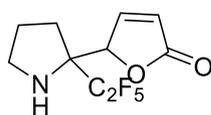
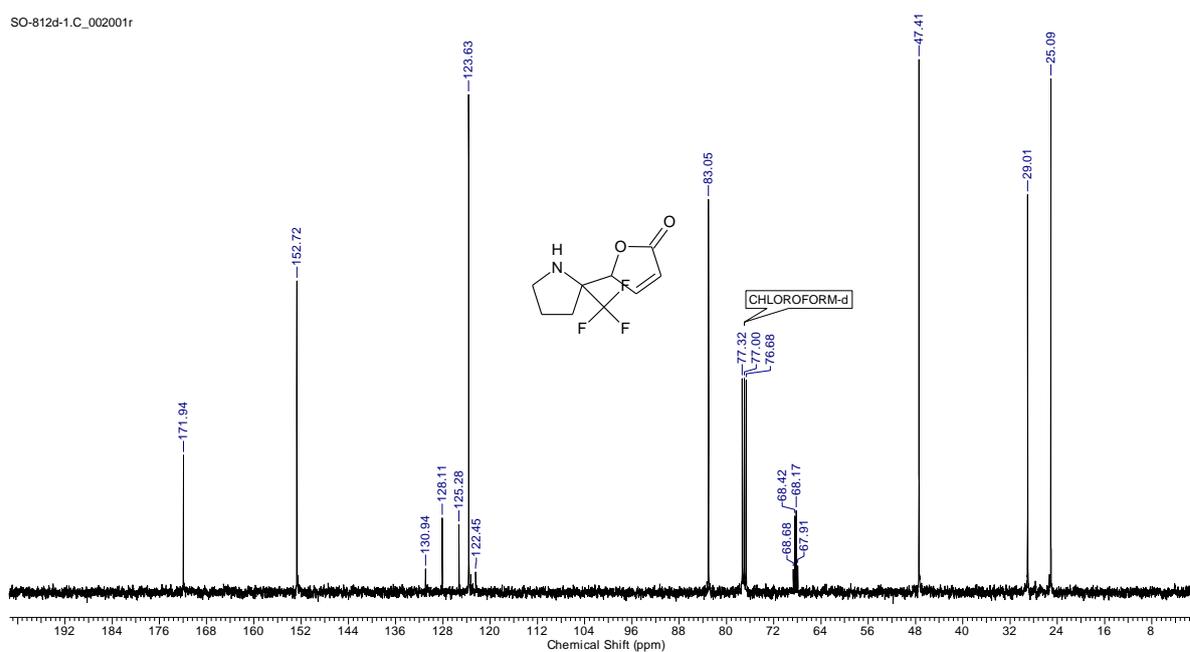


5-[2-(Trifluoromethyl)pyrrolidin-2-yl]furan-2(5H)-one **3a**, ^{19}F NMR yield

100%, after purification 85%, yellow oil. ^1H NMR (400 MHz, CDCl_3): δ 1.67-1.86 (3H, m), 1.88-1.95 (1H, m), 1.98-2.05 (1H, m), 2.97 (2H, t, $J = 6.4$ Hz), 5.15 (1H, t, $J = 1.7$ Hz), 6.20 (1H, dd, $J = 5.7$ Hz, $J = 1.7$ Hz), 7.47 (1H, d, $J = 5.7$ Hz). ^{13}C NMR (100 MHz, CDCl_3): δ 25.1, 29.0 ($\text{CH}_2\text{-C}_q$), 47.4 ($\text{CH}_2\text{-N}$), 68.3 (q, $J_{\text{CF}} = 25.8$ Hz, C-CF_3), 83.1 (CH), 123.6 (C=), 126.7 (q, $J_{\text{CF}} = 284.9$ Hz, CF_3), 152.7 (C=), 171.9 (CO). ^{19}F NMR (376.50 MHz, CDCl_3): δ -76.4 (3F, s, CF_3). IR (ATR, ZnSe): 3372 (bs, NH), 3336 (bs, NH), 1796 (CO), 1755 (CO), 1159, 1091 cm^{-1} . HRMS (ESI): calcd. for $\text{C}_9\text{H}_{11}\text{F}_3\text{NO}_2^+$ [$\text{M}+\text{H}$] $^+$ 222.0737, found 222.0739.

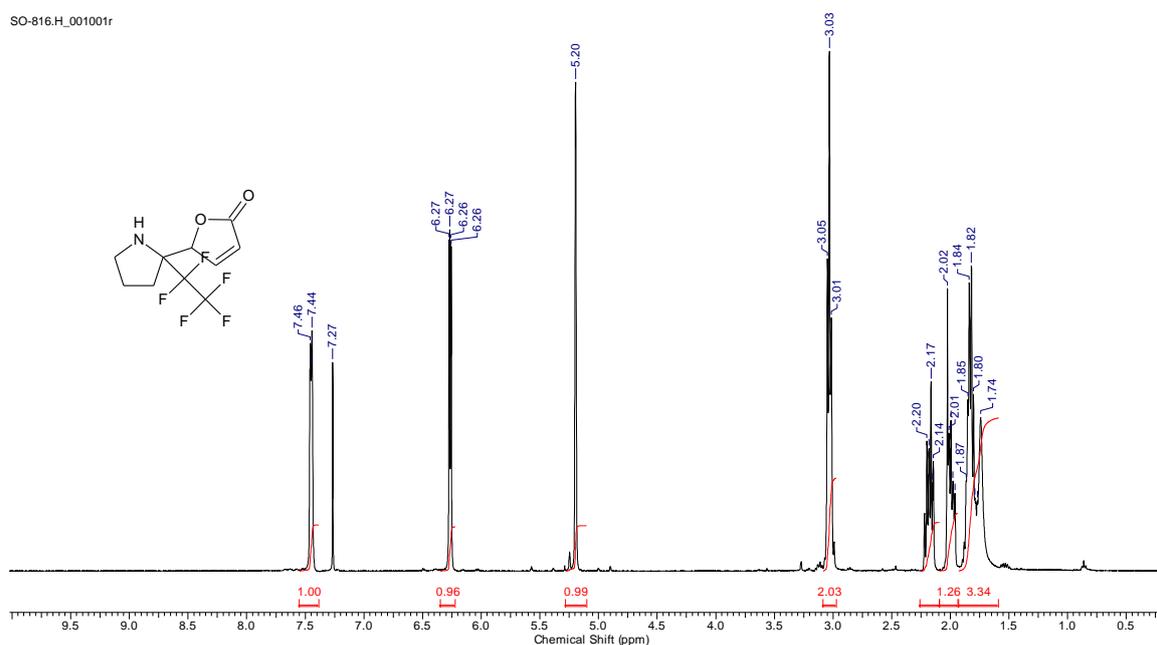
SO-812d-1.H_001001r

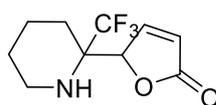
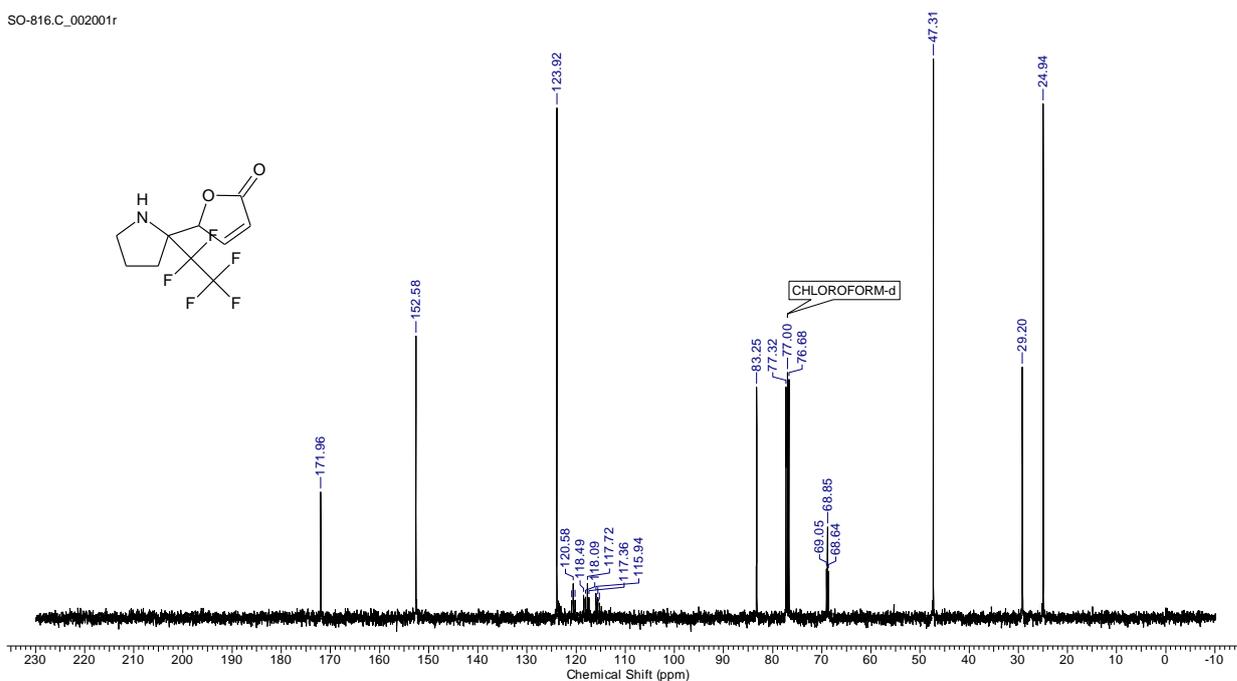




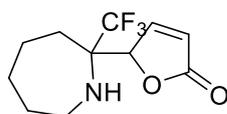
5-[2-(Pentafluoroethyl)pyrrolidin-2-yl]furan-2(5H)-one **3b**, yield 66%, yellow

oil. ^1H NMR (400 MHz, CDCl_3): δ 1.74-1.87 (3H, m incl. 1.74 (1H, bs, NH)), 1.96-2.02 (1H, m), 2.14-2.22 (1H, m), 3.03 (2H, t, $J = 6.6$ Hz), 5.20 (1H, s), 6.27 (1H, dd, $J = 5.8$, $J = 1.9$ Hz), 7.44-7.46 (1H, m). ^{13}C NMR (100 MHz, CDCl_3): δ 24.9, 29.2 ($\text{CH}_2\text{-C}_q$), 47.3 ($\text{CH}_2\text{-N}$), 68.9 (t, $J_{\text{CF}} = 20.3$ Hz, C-CF_3), 83.3, 115.2-120.9 (m, C_2F_5), 123.9 ($\text{C}=\text{}$), 152.6 ($\text{C}=\text{}$), 172.0 (CO). ^{19}F NMR (376.50 MHz, CDCl_3): δ -79.0 (3F, s, CF_3), -117.9 (1F, d, $J = 277.6$ Hz), -120.3 (1F, d, $J = 277.6$ Hz). IR (ATR, ZnSe): 3370 (bs, NH), 1796 (CO), 1762 (CO), 1210, 1163, 1116 cm^{-1} . HRMS (ESI): calcd. for $\text{C}_{10}\text{H}_{11}\text{F}_5\text{NO}_2^+$ $[\text{M}+\text{H}]^+$ 272.0704, found 272.0698.



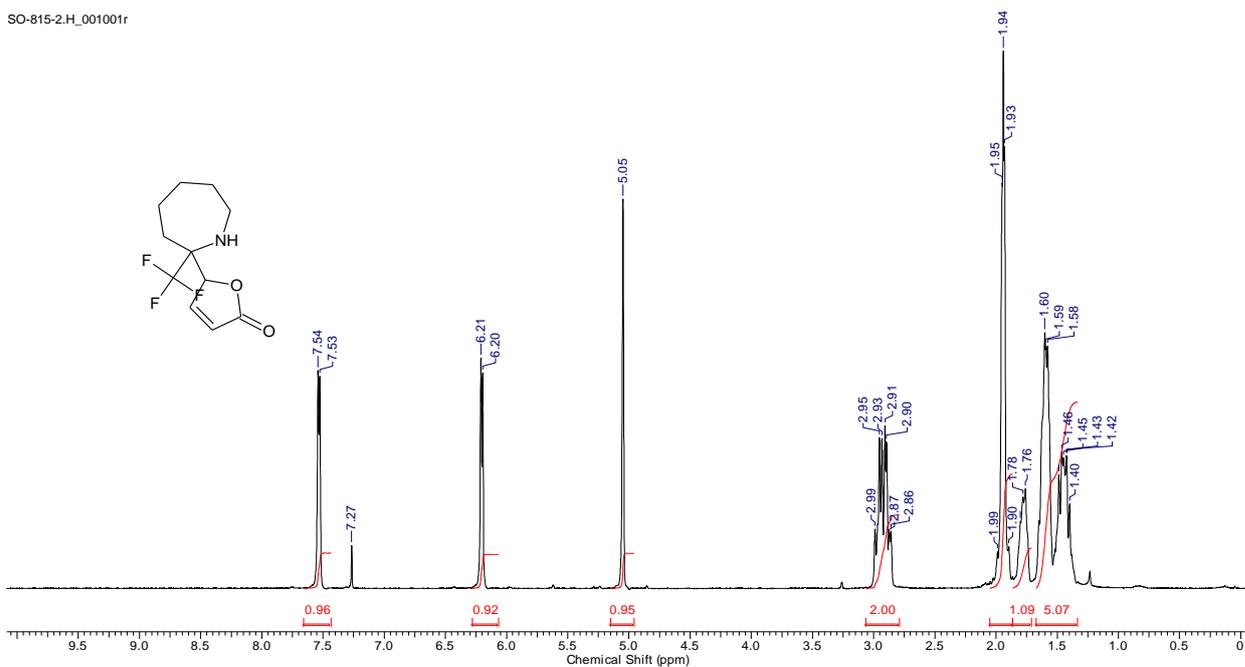


3c, yield 55%, yellow oil. ^1H NMR (400 MHz, CDCl_3): δ 1.49-1.91 (6H, m), 2.14 (1H, bs, NH), 2.85-2.98 (2H, m), 5.18 (1H, t, $J = 1.9$ Hz), 6.15 (1H, dd, $J = 5.8$ Hz, $J = 2.2$ Hz), 7.50-7.52 (1H, m). ^{13}C NMR (100 MHz, CDCl_3): δ 19.4, 24.0, 24.6 ($\text{CH}_2\text{-C}_q$), 40.9 ($\text{CH}_2\text{-N}$), 60.5 (q, $J_{\text{CF}} = 23.6$ Hz, C-CF_3), 82.9 (CH), 122.4 (C=), 126.7 (q, $J_{\text{CF}} = 290.4$ Hz, CF_3), 152.8 (C=), 171.9 (CO). ^{19}F NMR (376.50 MHz, CDCl_3): δ -73.9 (3F, s, CF_3). HRMS (ESI): calcd. for $\text{C}_{10}\text{H}_{13}\text{F}_3\text{NO}_2^+$ $[\text{M}+\text{H}]^+$ 236.0893, found 236.0897.



3d, yield 89%, yellowish oil. ^1H NMR (400 MHz, CDCl_3): δ 1.40-1.65 (5H, m), 1.76-1.80 (1H, m), 1.90-1.99 (3H, m), 2.86-2.99 (2H, m), 5.05 (1H, s), 6.21 (1H, d, $J = 5.7$ Hz), 7.54 (1H, d, $J = 5.7$ Hz). ^{13}C NMR (100 MHz, CDCl_3): δ 23.6, 39.9, 30.8, 33.0 ($\text{CH}_2\text{-C}_q$), 43.7 ($\text{CH}_2\text{-N}$), 65.2 (q, $J_{\text{CF}} = 23.2$ Hz, C-CF_3), 84.9 (CH), 122.7 (C=), 127.2 (q, $J_{\text{CF}} = 290.3$ Hz, CF_3), 152.9 (C=), 172.0 (CO). ^{19}F NMR (376.50 MHz, CDCl_3): δ -75.6 (3F, s, CF_3). IR (ATR, ZnSe): 3386 (bs, NH), 1755 (CO), 1132, 1100 cm^{-1} . HRMS (ESI): calcd. for $\text{C}_{11}\text{H}_{15}\text{F}_3\text{NO}_2^+$ $[\text{M}+\text{H}]^+$ 250.1049, found 250.1056.

SO-815-2.H_001001r



SO-815-2.C_002001r

