Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics


# Conformational Preferences of Furan- and Thiophene-based Arylamides: A Combined Computational and Experimental Study

Jhenny F. Galan, Chi Ngong Tang, Shubhashis Chakrabarty, Zhiwei Liu, Guillermo Moyna and Vojislava Pophristic

**Synthesis and Characterization**: Amides **3** and **4** were prepared from the corresponding acid chlorides and methylamine following standard Shotten-Bauman conditions. Briefly, a 40 wt % aqueous solution of methylamine (20 mL) was added to the chlorides (500 mg) at 0 ºC, and the resulting mixtures allowed to stir at room temperature for 24 h. The solutions were then acidified to pH ~2 with 6 M HCl and extracted with ethyl acetate (3 × 20 mL). The combined organic extracts were then washed with water (1 × 20 mL) and dried over anhydrous $MgSO_4$. The solvent was then removed under reduced pressure to yield the final products. High resolution mass spectra were recorded on Thermo Scientific Exactive Orbitrap mass spectrometer, using Atmospheric Solids Analysis Probe (ASAP) technique.

*N*-methylfuran-2-carboxamide **3**: Obtained as a white solid with 27% yield. M.p.: 57-59 ºC. $^1$H NMR (400 MHz, $CDCl_3$): δ= 2.96 (d, 3H, *J* = 5.0 Hz), 6.33 (bs, 1H), 6.46 (ddd, 1H, *J* = 3.5, 1.7 Hz), 7.08 (dddd, 1H, *J* = 3.5, 0.8 Hz), 7.39 ppm (ddd, 1H, *J* = 1.7, 0.8 Hz). $^{13}$C NMR (100 MHz, $CDCl_3$): δ= 26.2, 112.4, 114.2, 144.1, 148.5, 159.5 ppm. $^1$H NMR (400 MHz, $CD_3OH$): δ= 2.88 (d, 3H, *J* = 4.8 Hz), 8.34 (bs, 1H), 6.55 (ddd, 1H, *J* = 3.5, 1.8 Hz), 7.06 (dddd, 1H, *J* = 3.5, 0.8 Hz), 7.62 ppm (ddd, 1H, *J* = 1.8, 0.8 Hz). $^1$H NMR (400 MHz, $H_2O$/DMSO-$d_6$):δ= 2.79 (d, 3H, *J* = 4.8 Hz), 8.21 (bs, 1H), 6.50 (ddd, 1H, *J* = 3.6, 1.8 Hz), 7.01 (dddd, 1H, *J* = 3.6, 0.8 Hz), 7.55 ppm (ddd, 1H, *J* = 1.8, 0.8 Hz). MS: *m/z* = 126.0648 $[M+H]^+$.

*N*-methylthiophene-2-carboxamide **4**: Obtained as a pale yellow solid with 22% yield. M.p.: 110-112 ºC, $^1$H NMR (400 MHz, $CDCl_3$): δ= 2.96 (d, 3H, *J* = 4.9 Hz), 6.25 (bs, 1H), 7.03 (ddd, 1H, J = 5.0, 3.7 Hz), 7.42 (ddd, 1H, J = 5.0, 1.1 Hz), 7.49 ppm (dd, 1H, *J* = 3.7, 1.1 Hz). $^{13}$C NMR (100 MHz, $CDCl_3$): δ= 27.1, 128.0, 128.3, 130.1, 139.4, 163.2 ppm. $^1$H NMR (400 MHz, $CD_3OH$): δ= 2.88 (d, 3H, *J* = 4.7 Hz), 8.37 (bs, 1H), 7.09 (ddd, 1H, J = 5.0, 3.8 Hz), 7.61 (ddd, 1H, J = 5.0, 1.2 Hz), 7.62 ppm (ddd, 1H, *J* = 3.8, 1.2 Hz). $^1$H NMR (400 MHz, $H_2O$/DMSO-$d_6$): δ= 2.75 (d, 3H, *J* = 4.7 Hz), 8.13 (bs, 1H), 7.02 (ddd, 1H, J = 5.0, 3.8 Hz), 7.47 (ddd, 1H, J = 5.0, 1.1 Hz), 7.54 ppm (ddd, 1H, *J* = 3.8, 1.1 Hz). MS: *m/z* = 142.0319 $[M+H]^+$.