Supporting Information

Practical Synthesis of Unsymmetrical Ureas from Isopropenyl Carbamates

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General Methods. Melting points are uncorrected. Nuclear Magnetic Resonance (NMR) spectra were recorded in CDCl₃ or dms_o-d₆ using on a 400 MHz or a 500 MHz spectrometer. Spectra were referenced to residual CDCl₃ (7.26 ppm for ¹H ; 77.0 ppm for ¹³C) or dms_o-d₆ (2.50 ppm for ¹H; 39.50 ppm for ¹³C). High resolution Mass Spectrometry (HRMS) analyses were performed by positive electrospray ionization. All reagents were purchased from chemical suppliers and used without any further purification. Yields were determined by mass recovery of the crude ureas. Purities were established by HPLC area%. In the case of HPLC area% purities <98%, the purity was determined by ¹H NMR. ¹H NMR purities were recorded using dimethyl fumarate as internal standard. Ureas **1**, ¹**25**, ¹**28**, ²**29** ³ and **32-35** ⁴⁻⁵ are known compounds.

(5-*t*-Butyl-2-*p*-tolyl-2*H*-pyrazol-3-yl)-carbamic acid isopropenyl ester (6). Sodium hydroxide pellets (1.17 g, 28.4 mmol, 2.5 equiv.) were dissolved in water (9 mL) and the mixture was cooled to 5 °C. Ethyl acetate (20 mL) and the hydrochloride of amine **2** (3 g, 11.3 mmol) were added while keeping the temperature below 5 °C. The mixture was stirred at 0-5 °C till it became a clear solution. Isopropenyl chloroformate (1.73 mL, 15.8 mmol, 1.4 equiv.) was added dropwise over 15 minutes while keeping the temperature below 10 °C. The reaction mixture was then stirred at room temperature for 3 hours. The layers were separated. The organic layer was washed with brine (10 mL), dried over MgSO₄ and concentrated to 10 mL. Heptane (20 mL) was added. The solution was concentrated to 10 mL and cooled to 2-5 °C overnight. The precipitate was filtered, washed twice with 10 mL heptane and dried under high vacuum to give a white solid in 73% yield (2.6 g). m.p. 91-93 °C; ¹H NMR (CDCl₃, 400 MHz) δ 7.34 (d, *J* = 8.3 Hz, 2 H), 7.31 (d, *J* = 7.9, 2 H), 6.84 (br s, 1 H), 6.42 (br s, 1 H), 4.75 (br s, 1 H), 4.71 (s, 1 H), 2.41 (s, 3 H), 1.95 (br s, 3 H), 1.35 (s, 9 H); ¹³C NMR (CDCl₃, 100 MHz) δ 162.2, 152.4, 150.0, 138.3, 135.4, 130.3, 124.9, 102.2, 93.7, 32.4, 30.3, 21.1, 19.5.

Phenyl-carbamic acid isopropenyl ester (9). Sodium hydroxide pellets (6.44 g, 161.0 mmol, 1.5 equiv.) were dissolved in water (80 mL) and the mixture was cooled to 5 °C. Ethyl acetate (180 mL) and aniline (9.8 mL, 107.4 mmol) were added while keeping the temperature below 5 °C. Isopropenyl

chloroformate (16.43 mL, 150.3 mmol, 1.4 equiv.) was added dropwise over 15 minutes while keeping the temperature below 10 °C. The reaction mixture was then stirred at room temperature for 30 minutes. The layers were separated. The organic layer was washed with brine (100 mL), dried over MgSO₄ and concentrated to 80 mL. Heptane (150 mL) was added. The solution was concentrated to 80 mL and cooled to 2-5 °C overnight. The precipitate was filtered, washed twice with 100 mL heptane and dried under high vacuum to give a solid in 38% yield (5.0 g). ¹H NMR (CDCl₃, 400 MHz) δ 7.32 (m, 2 H), 7.23 (m, 1 H), 7.01 (m, 2 H), 6.69 (br s, 1 H), 4.72 (s, 1 H), 4.68 (s, 1 H), 1.93 (s, 3 H); ¹³C NMR (CDCl₃, 100 MHz) δ 152.5, 139.0, 129.1, 125.7, 124.7, 123.8, 102.0, 19.7.

(3,5-Dichloro-phenyl)-carbamic acid isopropenyl ester (10). Sodium hydroxide pellets (741 mg, 18.4 mmol, 1.5 equiv.) were dissolved in water (8 mL) and the mixture was cooled to 5 °C. Ethyl acetate (18 mL) and 3,5-dichloroaniline (2 g, 12.3 mmol) were added while keeping the temperature below 5 °C. Isopropenyl chloroformate (1.35 mL, 17.2 mmol, 1.4 equiv.) was added dropwise over 15 minutes while keeping the temperature below 10 °C. The reaction mixture was then stirred at room temperature for 30 minutes. The layers were separated. The organic layer was washed with brine (10 mL), dried over MgSO₄ and concentrated to 10 mL. Heptane (20 mL) was added. The solution was concentrated to 10 mL and cooled to 2-5 °C overnight. The precipitate was filtered, washed twice with 10 mL heptane and dried under high vacuum to give a solid in 57% yield (1.7 g). ¹H NMR (CDCl₃, 400 MHz) δ 7.50 (br s, 1 H), 7.38 (m, 2 H), 7.02 (m, 1 H), 4.82 (s, 1 H), 4.75 (s, 1 H), 1.97 (s, 3 H); ¹³C NMR (CDCl₃, 100 MHz) δ 152.2, 151.2, 139.4, 135.1, 123.5, 117.1, 102.5, 19.4.

Pyridin-3-yl-carbamic acid isopropenyl ester (11) 3-Aminopyridine (10.0 g, 100.5 mmol) was dissolved in THF (150 mL). *N*-methylmorpholine (13.8 mL, 126.2 mmol, 1.2 equiv.) was added in one portion and the solution cooled to 0-5 °C with an ice/water bath. Isopropenyl chloroformate (14.0 mL, 126.2 mmol, 1.2 equiv.) was added over 30 minutes leading to a yellow suspension. Once the addition was complete, the suspension was stirred at room temperature for 4 hours. The reaction mixture was diluted with water (100 mL) and EtOAc (150 mL) and the aqueous layer was drained. The organic layer

was washed with half-saturated brine (100 mL) and concentrated to a red oil. Purification by flash chromatography using EtOAc afforded a light yellow solid in 60 % yield (10.6 g). ^1H NMR (CDCl_3 , 500 MHz) δ 8.93 (br s, 1H), 8.64 (s, 1H), 8.34 (d, $J = 3.5$, 1 H), 8.19 (br s, 1H), 7.32 (dd, $J = 6.6$, 3.9, 1 H), 4.81 (s, 1 H), 4.74 (s, 1 H), 2.00 (s, 3 H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 151.04, 149.94, 142.56, 139.00, 134.16, 123.98, 122.30, 100.39, 18.11.

General Procedure for the Synthesis of Unsymmetrical Ureas. A solution of carbamate (2 mmol) and amine (2 mmol, 1 equiv.) in 4 mL THF was heated to 55 °C. *N*-Methylpyrrolidine (21 μL , 0.2 mmol, 0.1 equiv.) was added. The reaction mixture was stirred at 55 °C for 30 minutes and cooled down to room temperature. Concentration under vacuum afforded the crude product.

***N*-(5-*tert*-Butyl-2-*p*-tolyl-2*H*-pyrazol-3-yl)-*N'*-(1-naphthyl)urea (1).**¹ The general procedure was followed using isopropenyl carbamate 6 (627 mg, 2 mmol) and 1-aminonaphthalene (287 mg, 2 mmol, 1 equiv.). The crude product was isolated in 97% yield (774 mg). HPLC: 94.0 area%; ^1H NMR purity: 94.0 - 94.5%; m.p. 100-106 °C; ^1H NMR (CDCl_3 , 400 MHz) δ 7.82 (d, $J = 8.2$ Hz, 1 H), 7.70-7.65 (m, 2 H), 7.50-7.43 (m, 2 H), 7.40 (br s, 1 H), 7.35-7.30 (m, 2 H), 7.15-7.10 (m, 3 H), 6.98 (d, $J = 8.1$ Hz, 2 H), 6.39 (s, 1 H), 2.23 (s, 3 H), 1.32 (s, 9 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 162.2, 153.2, 137.6, 136.2, 135.2, 134.2, 132.0, 129.9, 129.8, 128.4, 126.5, 126.2, 125.5, 124.5, 124.3, 122.1, 121.3, 95.6, 32.3, 30.2, 20.9; HRMS calcd for $\text{C}_{25}\text{H}_{27}\text{N}_4\text{O}$ ($M + \text{H}$). 399.2179, found 399.2192.

***N*-(5-*tert*-Butyl-2-*p*-tolyl-2*H*-pyrazol-3-yl)-*N'*-cyclohexylurea (21).** The general procedure was followed using isopropenyl carbamate 6 (627 mg, 2 mmol) and cyclohexylamine (229 μL , 2 mmol, 1 equiv.). The reaction mixture was stirred at room temperature for 4 hours. The crude product was isolated in quantitative yield (708 mg). HPLC: 99.2 area%; m.p. 209-210 °C; ^1H NMR (CDCl_3 , 400 MHz) δ 7.19 (d, $J = 8.3$ Hz, 2 H), 7.08 (d, $J = 8.2$ Hz, 2 H), 6.92 (s, 1 H), 6.16 (s, 1 H), 5.59 (d, $J = 7.7$ Hz, 1 H), 3.45-3.35 (m, 1 H), 2.26 (s, 3 H), 1.80-1.70 (m, 2 H), 1.65-1.50 (m, 3 H), 1.27 (s, 9 H), 1.30-1.20 (m, 2 H), 1.15-1.05 (m, 1 H), 1.05-0.90 (m, 2 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 162.1, 154.1, 137.2, 136.8, 135.8, 129.7, 124.3, 95.5, 48.8, 33.2, 32.3, 30.2, 25.4, 24.6, 20.9; HRMS calcd for

C₂₁H₃₁N₄O (M + H) 355.2492, found 355.2502; Anal. calcd for C₂₁H₃₀N₄O C, 71.15; H, 8.53; N, 15.80, found C, 71.10; H, 8.48; N, 15.74.

2-[3-(5-*tert*-Butyl-2-*p*-tolyl-2*H*-pyrazol-3-yl)-ureido]-3-methyl-butyric acid methyl ester (22). The general procedure was followed using isopropenyl carbamate **6** (627 mg, 2 mmol), *L*-valine methyl ester hydrochloride (335 mg, 2 mmol, 1 equiv.) and *N*-methylpyrrolidine (230 μ L, 2.2 mmol, 1.1 equiv.). The reaction mixture was stirred at 55 °C for 30 minutes, cooled down to room temperature, diluted with CH₂Cl₂, washed with water, dried over MgSO₄, filtered, and concentrated to give the crude product as a white crystalline solid in 95% yield (733 mg). HPLC: 99.2 area%; m.p. 189-190 °C; ¹H NMR (CDCl₃, 400 MHz) δ 7.32 (d, *J* = 8.3 Hz, 2 H), 7.18 (d, *J* = 8.2 Hz, 2 H), 6.96 (s, 1 H), 6.30 (s, 1 H), 5.93 (d, *J* = 8.9 Hz, 1 H), 4.35 (dd, *J* = 9.0, 4.7 Hz, 1 H), 3.60 (s, 3 H), 2.33 (s, 3 H), 2.10-2.00 (m, 1 H), 1.32 (s, 9 H), 0.86 (d, *J* = 6.8 Hz, 3 H), 0.76 (d, *J* = 6.8 Hz, 3 H); ¹³C NMR (CDCl₃, 100 MHz) δ 173.5, 162.1, 154.5, 137.5, 136.2, 135.6, 129.8, 124.5, 96.2, 57.8, 52.1, 32.3, 31.1, 30.2, 21.0, 18.9, 17.4; HRMS calcd for C₂₁H₃₁N₄O₃ (M + H) 387.2390, found 387.2393; Anal. calcd for C₂₁H₃₀N₄O₃ C, 65.26; H, 7.82; N, 14.50; found: C, 65.22; H, 7.89; N, 14.43; [α]_D²² +17.9° (*c* 0.23, CHCl₃).

***N*-(5-*tert*-Butyl-2-*p*-tolyl-2*H*-pyrazol-3-yl)-*N*',*N*'-(pentamethylene)urea (23).** The general procedure was followed using isopropenyl carbamate **6** (627 mg, 2 mmol) and piperidine (198 μ L, 2 mmol, 1 equiv.). The reaction mixture was stirred at room temperature for 2 hours. The crude product was isolated in 99% yield (673 mg). HPLC: 99.9 area%; m.p. 159-160 °C; ¹H NMR (CDCl₃, 400 MHz) δ 7.31 (d, *J* = 8.3 Hz, 2 H), 7.22 (d, *J* = 8.2 Hz, 2 H), 6.58 (s, 1 H), 6.35 (s, 1 H), 3.26 (t, *J* = 5.4 Hz, 4 H), 2.35 (s, 3 H), 1.60-1.55 (m, 2 H), 1.50-1.45 (m, 4 H), 1.31 (s, 9 H); ¹³C NMR (CDCl₃, 100 MHz) δ 162.0, 153.1, 137.4, 137.0, 135.9, 130.0, 124.3, 94.5, 45.2, 32.2, 30.2, 25.4, 24.1, 21.0; HRMS calcd for C₂₀H₂₉N₄O (M + H). 341.2335, found 341.2342; Anal. calcd for C₂₀H₂₈N₄O C, 70.56; H, 8.29; N, 16.46, found: C, 70.49; H, 8.24; N, 16.43.

***N*-(5-*tert*-Butyl-2-*p*-tolyl-2*H*-pyrazol-3-yl)-*N*',*N*'-(3-oxapentamethylene)urea (24).** The general procedure was followed using isopropenyl carbamate **6** (627 mg, 2 mmol) and morpholine (174 μ L, 2

mmol, 1 equiv.). The crude product was isolated in 92% yield (630 mg). HPLC: 99.7 area%; m.p. 178-180 °C; ¹H NMR (CDCl₃, 400 MHz) δ 7.29 (d, *J* = 8.3 Hz, 2 H), 7.21 (d, *J* = 8.3 Hz, 2 H), 6.75 (s, 1 H), 6.27 (s, 1 H), 3.58 (t, *J* = 4.8 Hz, 4 H), 3.25 (t, *J* = 4.8 Hz, 4 H), 2.36 (s, 3 H), 1.32 (s, 9 H); ¹³C NMR (CDCl₃, 100 MHz) δ 161.7, 154.0, 137.2, 136.3, 136.0, 129.7, 123.9, 96.5, 66.1, 44.0, 32.2, 30.2, 20.9; HRMS calcd for C₁₉H₂₇N₄O₂ (M + H) 343.2128, found 343.2132.

***N*-(5-*tert*-Butyl-2-*p*-tolyl-2*H*-pyrazol-3-yl)-*N'*-phenylurea (25).**¹ The general procedure was followed using isopropenyl carbamate **6** (627 mg, 2 mmol) and aniline (182 μL, 2 mmol, 1 equiv.). The reaction mixture was stirred at 55 °C for 3 hours. The crude product was isolated in 98% yield (681 mg). HPLC: 99.1 area%; m.p. 92-95 °C; ¹H NMR (CDCl₃, 400 MHz) δ 8.05 (s, 1 H), 7.20-7.15 (m, 1 H), 7.15-7.10 (m, 2 H), 7.10-7.00 (m, 2 H), 7.00-6.95 (m, 2 H), 6.95-6.90 (m, 1 H), 6.90-6.85 (m, 2 H), 6.21 (s, 1 H), 2.11 (s, 3 H), 1.13 (s, 9 H); ¹³C NMR (CDCl₃, 100 MHz) δ 162.4, 152.3, 138.0, 137.8, 136.6, 135.0, 129.9, 128.9, 124.6, 123.6, 119.7, 95.5, 32.3, 30.2, 20.9; HRMS calcd for C₂₁H₂₅N₄O (M + H) 349.2022, found 349.2023.

***N*-(5-*tert*-Butyl-2-*p*-tolyl-2*H*-pyrazol-3-yl)-*N'*-methyl-*N'*-phenylurea (26).** The general procedure was followed using isopropenyl carbamate **6** (627 mg, 2 mmol) and *N*-methylaniline (217 μL, 2 mmol, 1 equiv.). The reaction mixture was stirred at 55 °C for 3 hours. The crude product was isolated in quantitative yield (724 mg). HPLC: 99.2 area%; m.p. 109-111 °C; ¹H NMR (CDCl₃, 400 MHz) δ 7.35-7.25 (m, 3 H), 7.15-7.10 (m, 2 H), 7.05-6.95 (m, 4 H), 6.48 (s, 1 H), 6.46 (s, 1 H), 3.29 (s, 3 H), 2.31 (s, 3 H), 1.32 (s, 9 H); ¹³C NMR (CDCl₃, 100 MHz) δ 162.1, 152.4, 141.9, 137.2, 1367.0, 135.2, 130.2, 129.8, 128.0, 127.2, 124.1, 92.2, 36.9, 32.5, 30.2, 20.9; HRMS calcd for C₂₂H₂₇N₄O (M + H) 363.2179, found 363.2171; Anal. calcd for C₂₂H₂₆N₄O C, 72.90; H, 7.23; N, 15.46, found: C, 72.53; H, 7.24; N, 15.15.

***N*-(5-*tert*-Butyl-2-*p*-tolyl-2*H*-pyrazol-3-yl)-*N'*-(pyridine-4-yl)urea (27).** The general procedure was followed using isopropenyl carbamate **6** (627 mg, 2 mmol) and 4-aminopyridine (189 mg, 2 mmol, 1 equiv.) The crude product was isolated in 98% yield (751 mg). HPLC: 87.8 area%; ¹H NMR purity:

91%; ^1H NMR (CDCl_3 , 400 MHz) δ 9.84 (br s, 1 H), 8.05 (d, $J = 6.3$ Hz, 2 H), 7.89 (br s, 1 H), 7.19 (d, $J = 6.4$ Hz, 2 H), 7.02 (d, $J = 8.2$ Hz, 2 H), 6.93 (d, $J = 8.2$ Hz, 2 H), 6.46 (s, 1 H), 2.20 (s, 3 H), 1.29 (s, 9 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 162.6, 150.7, 149.4, 147.0, 138.5, 136.7, 134.8, 129.9, 125.2, 112.6, 93.9, 32.4, 30.3, 21.0; HRMS calcd for $\text{C}_{20}\text{H}_{24}\text{N}_5\text{O}$ ($\text{M} + \text{H}$) 350.1975, found 350.1978.

***N*-phenyl-*N'*-(3-oxapentamethylene)urea (28).**² The general procedure was followed using phenyl-carbamic acid isopropenyl ester (355 mg, 2 mmol) and morpholine (175 μL , 2 mmol, 1 equiv.) in 4 mL of ethyl acetate. The reaction mixture was stirred at 77 $^\circ\text{C}$ for 18 hours. The crude product was isolated in 99% yield (410 mg). HPLC: 97.4 area%; ^1H NMR purity: 97%; m.p. 156-158 $^\circ\text{C}$ (lit.² 157-159 $^\circ\text{C}$); ^1H NMR (CDCl_3 , 400 MHz): δ 7.27 (m, 2H), 7.22 (m, 2H), 6.97 (t, $J = 7.2$ Hz, 1H), 6.58 (br s, 1H), 3.62 (t, $J = 4.9$ Hz, 4H), 3.38 (t, $J = 4.9$ Hz, 4H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 155.2, 138.7, 128.9, 123.4, 120.3, 119.9, 66.4, 44.2; HRMS calcd for $\text{C}_{11}\text{H}_{15}\text{N}_2\text{O}_2$ ($\text{M} + \text{H}$) 207.1128, found 207.1132.

***N*-benzyl-*N'*-phenylurea (29).**³ The general procedure was followed using phenyl-carbamic acid isopropenyl ester (355 mg, 2 mmol) and benzylamine (219 μL , 2 mmol, 1 equiv.) in 4 mL toluene. The reaction mixture was stirred at reflux for 18 hours. The crude product was isolated in 99% yield (448 mg). HPLC: 100 area%; m.p. 170-171 $^\circ\text{C}$ (lit.³ 171-172 $^\circ\text{C}$); ^1H NMR ($\text{DMSO}-d_6$, 400 MHz): δ 8.56 (s, 1H), 7.41 (m, 3 H), 7.32 (m, 4H), 7.23 (m, 3H), 6.89 (t, $J = 7.3$ Hz, 1H), 6.62 (t, $J = 5.8$ Hz, 1H), 4.30 (d, $J = 5.9$ Hz, 2H); ^{13}C NMR ($\text{DMSO}-d_6$, 100 MHz): δ 155.2, 140.4, 140.3, 128.6, 128.3, 127.1, 126.7, 121.0, 117.6, 42.7; HRMS calcd for $\text{C}_{14}\text{H}_{15}\text{N}_2\text{O}$ ($\text{M} + \text{H}$) 227.1178, found 227.1181.

***N*-benzyl-*N'*-(3,5-dichlorophenyl)urea (30).** The general procedure was followed using (3,5-dichlorophenyl)-carbamic acid isopropenyl ester (492 mg, 2 mmol) and benzylamine (219 μL , 2 mmol, 1 equiv.). The reaction mixture was stirred at 55 $^\circ\text{C}$ for 21 hours. The crude product was isolated in quantitative yield (600 mg). HPLC: 98.3 area%; m.p. 187-189 $^\circ\text{C}$; ^1H NMR (CDCl_3 , 400 MHz): δ 8.22 (br s, 1H), 7.31 (d, $J = 1.9$ Hz, 2H), 7.24 (m, 4H), 7.17 (m, 1H), 6.83 (t, $J = 1.8$ Hz, 1H), 5.50-4.50

(br s, 1 H), 4.32 (s, 2H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 155.2, 142.0, 139.2, 134.7, 128.5, 127.5, 121.2, 116.2, 43.7; HRMS calcd for $\text{C}_{14}\text{H}_{13}\text{N}_2\text{OCl}_2$ ($\text{M} + \text{H}$) 295.0399, found 295.0392.

***N*-(3,5-dichlorophenyl)-*N'*-(1-indanyl)urea (31).** The general procedure was followed using (3,5-dichlorophenyl)-carbamic acid isopropenyl ester (492 mg, 2 mmol) and 1-aminoindane (220 μL , 2 mmol, 1 equiv.). The reaction mixture was stirred at 55 $^\circ\text{C}$ for 45 hours. The crude product was isolated in 98% yield (532 mg). HPLC: 96.8 area%; ^1H NMR purity: 96%; m.p. 245-248 $^\circ\text{C}$; ^1H NMR ($\text{DMSO}-d_6$, 400 MHz): δ 8.80 (s, 1 H), 7.51 (d, $J = 1.8$ Hz, 2H), 7.29-7.20 (m, 4H), 7.09 (t, $J = 1.8$ Hz, 1H), 6.78 (d, $J = 8.1$ Hz, 1H), 5.17 (q, $J = 7.8$ Hz, 1H), 2.92 (m, 1H), 2.81 (m, 1H), 2.44 (m, 1H), 1.81 (m, 1H); ^{13}C NMR ($\text{DMSO}-d_6$, 100 MHz): δ 154.6, 144.0, 142.9, 142.8, 134.0, 127.5, 126.4, 124.6, 123.8, 120.1, 115.7, 54.5, 33.5, 29.6; HRMS calcd for $\text{C}_{16}\text{H}_{15}\text{N}_2\text{OCl}_2$ ($\text{M} + \text{H}$) 321.0555, found 321.0549.

***N*-Butyl-*N'*-(pyrid-3-yl)urea (32).**⁴ The general procedure was followed using pyridin-3-yl-carbamic acid isopropenyl ester (363 mg, 2 mmol), *n*-butylamine (238 μL , 2.3 mmol, 1.2 equiv) and *N*-methylpyrrolidine (42 μL , 0.4 mmol, 0.2 equiv.). The reaction mixture was stirred at 55 $^\circ\text{C}$ for 12 hours. HPLC: 98.7 area%. The solvent was evaporated to give an orange oil that was stirred with heptane (4 mL) to afford a tan solid. The solid was filtered off and washed with heptane (8 mL). Drying under vacuum afforded the product as a tan solid in 96% yield (371 mg). HPLC: 99.7 area%; ^1H NMR ($\text{DMSO}-d_6$, 500 MHz): δ 8.56 (s, 1 H), 8.53 (s, 1 H), 8.10 (d, $J = 3.6$, 1 H), 7.88 (d, $J = 7.8$, 1 H), 7.24 (dd, $J = 7.3$, 4.8, 1 H), 6.25 (s, 1 H), 3.12-3.08 (m, 2 H), 1.45-1.40 (m, 2 H), 1.35-1.28 (m, 2 H), 0.90 (t, $J = 7.2$, 3 H); ^{13}C NMR ($\text{DMSO}-d_6$, 125 MHz): δ 153.1, 140.0, 137.5, 135.2, 122.3, 121.4, 36.8, 29.8, 17.8, 11.6; Anal. calcd for $\text{C}_{10}\text{H}_{15}\text{N}_3\text{O}$ C, 62.15; H, 7.82; N, 21.74, found C, 61.86; H, 7.65; N, 21.46.

***N*-cyclohexyl-*N'*-(pyrid-3-yl)urea (33).**⁴ The general procedure was followed using pyridin-3-yl-carbamic acid isopropenyl ester (363 mg, 2 mmol) and cyclohexylamine (252 μL , 2.2 mmol, 1.1 equiv.). The reaction mixture was stirred at 55 $^\circ\text{C}$ for 12 hours. HPLC: 98.8 area%. The reaction was diluted with ether (20 mL) and washed with water (10 mL) and brine (10 mL). The organic layer was

concentrated to a red oil. Drying under vacuum afforded the product as a tan solid in 94% yield (414 mg). HPLC: 99.6 area%; ^1H NMR (CDCl_3 , 500 MHz): δ 8.64 (s, 1 H), 8.50 (s, 1 H), 8.12 (d, $J = 4.4$, 1 H), 7.92 (d, $J = 8.3$, 1 H), 7.19 (dd, $J = 8.3$, 4.8, 1 H), 6.01 (d, $J = 7.7$, 1 H), 3.66-3.59 (m, 1 H), 1.91-1.89 (m, 2 H), 1.67-1.64 (m, 2 H), 1.57-1.53 (m, 1 H), 1.32-1.24 (m, 2 H), 1.18-1.06 (m, 3 H); ^{13}C NMR (CDCl_3 , 125 MHz): δ 153.7, 140.0, 137.6, 135.7, 125.2, 122.4, 47.1, 31.7, 23.7, 23.0.

***N*-(3-oxapentamethylene)-*N'*-(pyrid-3-yl)urea (34).**⁵ The general procedure was followed using pyridin-3-yl-carbamic acid isopropenyl ester (363 mg, 2 mmol), morpholine (192 μL , 2.1 mmol, 1.05 equiv.) and *N*-methylpyrrolidine (42 μL , 0.4 mmol, 0.2 equiv.). The reaction mixture was stirred at 55 $^\circ\text{C}$ for 24 hours. HPLC: 98.4 area%. This crude solid was stirred with 3 mL of 10/1 Heptane/THF to afford a tan solid after filtration and drying under high vacuum in 92% yield (383 mg). HPLC: 99.8 area%; ^1H NMR ($\text{DMSO}-d_6$, 500 MHz): δ 8.71 (s, 1 H), 8.66 (d, $J = 2.2$, 1 H), 8.16 (d, $J = 4.3$, 1 H), 7.89 (d, $J = 8.3$, 1 H), 7.27 (dd, $J = 8.3$, 4.6, 1 H), 3.63 (t, $J = 4.7$, 4 H), 3.46 (t, $J = 4.7$, 4 H); ^{13}C NMR ($\text{DMSO}-d_6$, 125 MHz): δ 154.3, 142.2, 140.8, 136.4, 125.8, 122.5, 65.3, 43.5.

***N*-Phenyl-*N'*-(pyrid-3-yl)urea (35).**⁴ The general procedure was followed using pyridin-3-yl-carbamic acid isopropenyl ester (363 mg, 2 mmol), aniline (182 μL , 2 mmol, 1 equiv.) and *N*-methylpyrrolidine (42 μL , 0.4 mmol, 0.2 equiv.). The reaction mixture was stirred at 55 $^\circ\text{C}$ for 18 hours and cooled down. A solid precipitated at room temperature. Heptane (4 mL) was added and the suspension stirred at room temperature for 2 hours. The solid was filtered off and washed with heptane (8 mL) to afford the product as a light tan solid in 92% yield (394 mg). HPLC: 99.1 area%; ^1H NMR ($\text{DMSO}-d_6$, 500 MHz): δ 8.84 (s, 1 H), 8.79 (s, 1 H), 8.62 (d, $J = 2.4$, 1 H), 8.20 (dd, $J = 4.6$, 1.3, 1 H), 7.95 (dq, $J = 8.3$, 2.4, 1.5, 1 H), 7.48 (d, $J = 7.6$, 2 H), 7.34-7.27 (m, 3 H), 6.99 (t, $J = 7.4$, 1 H); ^{13}C NMR ($\text{DMSO}-d_6$, 125 MHz): δ 151.6, 141.9, 139.2, 138.5, 135.5, 127.8, 124.2, 122.6, 121.1, 117.5; Anal. calcd for $\text{C}_{12}\text{H}_{11}\text{N}_3\text{O}$ C, 67.59; H, 5.20; N, 19.71, found C, 67.30; H, 5.13; N, 19.47.

References.

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F2 - Acquisition Parameters
 Date_ 20040901
 Time 10.24
 INSTRUM spect
 PROBD 5 mm QNP 1H/13
 PULPROG zg30
 TD 65536
 SOLVENT CDCl3
 NS 16
 DS 0
 SWH 8278.146 Hz
 FIDRES 0.126314 Hz
 AQ 3.9584243 sec
 RG 203.2
 DW 60.400 usec
 DE 6.00 usec
 TE 297.2 K
 D1 1.50000000 sec
 MCREST 0.00000000 sec
 MCWRR 0.01500000 sec

===== CHANNEL f1 =====
 NUC1 1H
 P1 12.75 usec
 PL1 -4.00 dB
 SFO1 400.1324710 MHz

F2 - Processing parameters
 SI 32768
 SF 400.1300000 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00

F2 - Acquisition Parameters
 Date_ 20040902
 Time 3.05
 INSTRUM spect
 PROBHD 5 mm BBO BB-1H
 PULPROG zgpg30
 TD 65536
 SOLVENT CDCl3
 NS 20480
 DS 4
 SWH 23980.814 Hz
 FIDRES 0.365918 Hz
 AQ 1.3664756 sec
 RG 16384
 DW 20.850 usec
 DE 6.00 usec
 TE 295.2 K
 D1 0.50000000 sec
 d11 0.03000000 sec
 MCREST 0.00000000 sec
 MCWRK 0.01500000 sec

===== CHANNEL f1 =====
 NUC1 13C
 P1 8.10 usec
 PL1 -3.00 dB
 SFO1 100.6731249 MHz

===== CHANNEL f2 =====
 CPDPRG2 waltz16
 NUC2 1H
 PCPD2 100.00 usec
 PL2 -2.00 dB
 PL12 18.86 dB
 PL13 18.86 dB
 SFO2 400.3316013 MHz

F2 - Processing parameters
 SI 32768
 SF 100.6630649 MHz
 WDW EM
 SSB 0
 LB 3.00 Hz
 GB 0
 PC 1.40

F2 - Acquisition Parameters
 Date_ 20040913
 Time 16.14
 INSTRUM spect
 PROBHD 5 mm QNP 1H/13
 PULPROG zg30
 TD 65536
 SOLVENT CDCl3
 NS 16
 DS 0
 SWH 8278.146 Hz
 FIDRES 0.126314 Hz
 AQ 3.9584243 sec
 RG 35.9
 DW 60.400 usec
 DE 6.00 usec
 TE 298.2 K
 D1 1.50000000 sec
 MCREST 0.00000000 sec
 MCWRR 0.01500000 sec

===== CHANNEL f1 =====
 NUCL 1H
 P1 12.75 usec
 PL1 -4.00 dB
 SFO1 400.1324710 MHz

F2 - Processing parameters
 SI 32768
 SF 400.1300086 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00

F2 - Acquisition Parameters
 Date_ 20040923
 Time 9.44
 INSTRUM spect
 PROBD 5 mm QNP 1H/13
 PULPROG zg30
 TD 65536
 FIDRES 0.126314 Hz
 AQ 3.9584243 sec
 RG 80.6
 DW 60.400 usec
 DE 6.00 usec
 TE 297.2 K
 D1 1.50000000 sec
 MCREST 0.00000000 sec
 MCWRK 0.01500000 sec

===== CHANNEL f1 =====
 NUC1 1H
 P1 12.75 usec
 PL1 -4.00 dB
 SFO1 400.1324710 MHz

F2 - Processing parameters
 SI 32768
 SF 400.1300094 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00

F2 - Acquisition Parameters
 Date_ 20040913
 Time 16.06
 INSTRUM spect
 PROBHD 5 mm QNP 1H/13
 PULPROG zg30
 TD 65536
 SOLVENT CDCl3
 NS 16
 DS 0
 SWH 8278.146 Hz
 FIDRES 0.126314 Hz
 AQ 3.9584243 sec
 RG 45.3
 DW 60.400 usec
 DE 6.00 usec
 TE 298.2 K
 D1 1.50000000 sec
 MCREST 0.00000000 sec
 MCWRR 0.01500000 sec

===== CHANNEL f1 =====
 NUCL 1H
 P1 12.75 usec
 PL1 -4.00 dB
 SFO1 400.1324710 MHz

F2 - Processing parameters
 SI 32768
 SF 400.1300096 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00

F2 - Acquisition Parameters

Date_ 20040927

Time 9.29

INSTRUM spect

PROBHD 5 mm BBO BB-1H

PULPROG zg30

TD 32768

SOLVENT CDCl3

NS 16

DS 0

SWH 8278.146 Hz

FIDRES 0.252629 Hz

AQ 1.9792372 sec

RG 25.4

DW 60.400 usec

DE 6.00 usec

TE 295.2 K

DL 1.50000000 sec

MCREST 0.00000000 sec

MCWRK 0.01500000 sec

===== CHANNEL f1 =====

NUC1 1H

P1 9.06 usec

PL1 -2.00 dB

SFO1 400.3332026 MHz

F2 - Processing parameters

SI 32768

SF 400.3300000 MHz

WDW EM

SSB 0

LB 0.30 Hz

GB 0

PC 1.00

F2 - Acquisition Parameters
 Date_ 20040927
 Time 9.20
 INSTRUM spect
 PROBHD 5 mm BBO BB-1H
 PULPROG zg30
 TD 32768
 SOLVENT CDCl3
 NS 16
 DS 0
 SWH 8278.146 Hz
 FIDRES 0.252629 Hz
 AQ 1.9792372 sec
 RG 50.8
 DW 60.400 usec
 DE 6.00 usec
 TE 295.2 K
 D1 1.50000000 sec
 MCREST 0.00000000 sec
 MCWRR 0.01500000 sec

===== CHANNEL f1 =====
 NUC1 1H
 P1 9.06 usec
 PL1 -2.00 dB
 SFO1 400.3332026 MHz

F2 - Processing parameters
 SI 32768
 SF 400.3300395 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00

F2 - Acquisition Parameters
 Date_ 20041019
 time 17.52
 INSTRUM spect
 PROBD 5 mm BBO BB-1H
 PULPROG zg30
 TD 32768
 SOLVENT CDCl3
 NS 16
 DS 0
 SWH 8278.146 Hz
 FIDRES 0.252629 Hz
 AQ 1.9792372 sec
 RG 28.5
 DW 60.400 usec
 DE 6.00 usec
 TE 296.2 K
 D1 1.50000000 sec
 MCREST 0.00000000 sec
 MCWRK 0.01500000 sec

==== CHANNEL f1 =====
 NUC1 1H
 P1 9.06 usec
 PL1 -2.00 dB
 SFO1 400.3332026 MHz

F2 - Processing parameters
 SI 32768
 SF 400.3300000 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00

F2 - Acquisition Parameters
 Date_ 20041019
 Time 15.50
 INSTRUM spect
 PROBD 5 mm QNP 1H/13
 PULPROG zg30
 TD 65536
 FIDRES 0.126314 Hz
 AQ 3.9584243 sec
 RG 90.5
 DW 60.400 usec
 DE 6.00 usec
 TE 298.2 K
 D1 1.50000000 sec
 MCREST 0.00000000 sec
 MCWRK 0.01500000 sec

===== CHANNEL f1 =====
 NUC1 1H
 P1 12.00 usec
 PL1 0.00 dB
 SFO1 400.1324710 MHz

F2 - Processing parameters
 SI 32768
 SF 400.1300089 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00

F2 - Acquisition Parameters
 Date_ 20041102
 Time 17.14
 INSTRUM spect
 PROBHD 5 mm BBO BB-1H
 PULPROG zg30
 TD 32768
 SOLVENT CDCl3
 NS 32
 DS 0
 SMH 8278.146 Hz
 FIDRES 0.252629 Hz
 AQ 1.9792372 sec
 RG 114
 DW 60.400 usec
 DE 6.00 usec
 TE 296.2 K
 D1 1.50000000 sec
 MCREST 0.00000000 sec
 MCWRK 0.01500000 sec

==== CHANNEL f1 =====
 NUC1 1H
 P1 9.06 usec
 PL1 -2.00 dB
 SFO1 400.3332026 MHz

F2 - Processing parameters
 SI 32768
 SF 400.3300350 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00

F2 - Acquisition Parameters
 Date_ 20041102
 Time 20.07
 INSTRUM spect
 PROBHD 5 mm BBO BB-1H
 PULPROG zgpg30
 TD 65536
 SOLVENT CDCl3
 NS 1024
 DS 4
 SMH 23980.814 Hz
 FIDRES 0.365918 Hz
 AQ 1.3664756 sec
 RG 8192
 DW 20.850 usec
 DE 6.00 usec
 TE 296.2 K
 D1 0.50000000 sec
 d11 0.03000000 sec
 MCREST 0.00000000 sec
 MCWRK 0.01500000 sec

===== CHANNEL f1 =====
 NUC1 13C
 P1 8.10 usec
 PL1 -3.00 dB
 SFO1 100.6731249 MHz

===== CHANNEL f2 =====
 CPDPRG2 waltz16
 NUC2 1H
 PCPD2 100.00 usec
 PL2 -2.00 dB
 PL12 18.86 dB
 PL13 18.86 dB
 SFO2 400.3316013 MHz

F2 - Processing parameters
 SI 32768
 SF 100.6630590 MHz
 WDM EM
 SSB 0
 LB 3.00 Hz
 GB 0
 PC 1.40

F2 - Acquisition Parameters
 Date_ 20041104
 Time 9.57
 INSTRUM spect
 PROBHD 5 mm BBO BB-1H
 PULPROG zg30
 TD 32768
 SOLVENT DMSO
 NS 16
 DS 0
 SWH 8278.146 Hz
 FIDRES 0.252629 Hz
 AQ 1.9792372 sec
 RG 143.7
 DW 60.400 usec
 DE 6.00 usec
 TE 296.2 K
 D1 1.50000000 sec
 MCREST 0.00000000 sec
 MCWRR 0.01500000 sec

===== CHANNEL f1 =====
 NUC1 1H
 P1 9.06 usec
 PL1 -2.00 dB
 SFO1 400.3332026 MHz

F2 - Processing Parameters
 SI 32768
 SF 400.3300000 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00

F2 - Acquisition Parameters

Date_ 20041103

Time 19.00

INSTRUM spect

PROBHD 5 mm BBO BB-1H

PULPROG zgpg30

TD 65536

SOLVENT DMSO

NS 1024

DS 4

SWH 23980.814 Hz

FIDRES 0.365918 Hz

AQ 1.3664756 sec

RG 4597.6

DW 20.850 usec

DE 6.00 usec

TE 297.2 K

DI 0.5000000 sec

d11 0.0300000 sec

MCREST 0.0000000 sec

MCWRK 0.01500000 sec

===== CHANNEL f1 =====

NUC1 13C

P1 8.10 usec

PL1 -3.00 dB

SFO1 100.6731249 MHz

===== CHANNEL f2 =====

CPDPRG2 waltz16

NUC2 1H

PCPD2 100.00 usec

PL2 -2.00 dB

PL12 18.86 dB

PL13 18.86 dB

SFO2 400.3316013 MHz

F2 - Processing Parameters

SI 32768

SF 100.6631093 MHz

WDW EM

SSB 0

LB 3.00 Hz

GB 0

PC 1.40

F2 - Acquisition Parameters
 Date_ 20041101
 Time 18.45
 INSTRUM spect
 PROBHD 5 mm BBO BB-1H
 PULPROG zg30
 TD 32768
 SOLVENT CDCl3
 NS 32
 DS 0
 SMH 8278.146 Hz
 FIDRES 0.252629 Hz
 AQ 1.9792372 sec
 RG 287.4
 DW 60.400 usec
 DE 6.00 usec
 TE 296.2 K
 D1 1.50000000 sec
 MCREST 0.00000000 sec
 MCWRK 0.01500000 sec

==== CHANNEL f1 =====
 NUC1 1H
 P1 9.06 usec
 PL1 -2.00 dB
 SFO1 400.3332026 MHz
 F2 - Processing parameters
 SI 32768
 SF 400.3300206 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00

F2 - Acquisition Parameters
 Date_ 20041101
 Time 19.37
 INSTRUM spect
 PROBHD 5 mm BBO BB-1H
 PULPROG zgpg30
 TD 65536
 SOLVENT CDCl3
 NS 1024
 DS 4
 SWH 23980.814 Hz
 FIDRES 0.365918 Hz
 AO 1.3664756 sec
 RG 8192
 DW 20.850 usec
 DE 6.00 usec
 TE 296.2 K
 D1 0.50000000 sec
 d11 0.03000000 sec
 MCREST 0.00000000 sec
 MCWRR 0.01500000 sec

===== CHANNEL f1 =====
 NUC1 13C
 P1 8.10 usec
 PL1 -3.00 dB
 SFO1 100.6731249 MHz

===== CHANNEL f2 =====
 CPDPRG2 waltz16
 NUC2 1H
 PCPD2 100.00 usec
 PL2 -2.00 dB
 PL12 18.86 dB
 PL13 18.86 dB
 SFO2 400.3316013 MHz

F2 - Processing parameters
 SI 32768
 SF 100.6630590 MHz
 WDW EM
 SSB 0
 LB 3.00 Hz
 GB 0
 PC 1.40

F2 - Acquisition Parameters
 Date_ 20041103
 Time 17.14
 INSTRUM spect
 PROBD 5 mm BBO BB-1H
 PULPROG zg30
 TD 32768
 SOLVENT DMSO
 NS 32
 DS 0
 SWH 8278.146 Hz
 FIDRES 0.252629 Hz
 AQ 1.9792372 sec
 RG 161.3
 DW 60.400 usec
 DE 6.00 usec
 TE 297.2 K
 DL 1.50000000 sec
 MCREST 0.00000000 sec
 MCWRK 0.01500000 sec

===== CHANNEL f1 =====
 NUC1 1H
 P1 9.06 usec
 PL1 -2.00 dB
 SFO1 400.3332026 MHz

F2 - Processing parameters
 SI 32768
 SF 400.3300000 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00

F2 - Acquisition Parameters
 Date_ 20041103
 Time 19.42
 INSTRUM spect
 PROBD 5 mm BBO BB-1H
 PULPROG zgpg30
 TD 65536
 SOLVENT DMSO
 NS 1024
 DS 4
 SWH 23980.814 Hz
 FIDRES 0.365918 Hz
 AQ 1.3664736 sec
 RG 4597.6
 DW 20.850 usec
 DE 6.00 usec
 TE 297.2 K
 D1 0.5000000 sec
 d11 0.0300000 sec
 MCREST 0.0000000 sec
 MCWRK 0.0150000 sec

===== CHANNEL f1 =====
 NUC1 13C
 P1 8.10 usec
 PL1 -3.00 dB
 SFO1 100.6731249 MHz

===== CHANNEL f2 =====
 CPDPRG2 waltz16
 NUC2 1H
 PCPD2 100.00 usec
 PL2 -2.00 dB
 PL12 18.86 dB
 PL13 18.86 dB
 SFO2 400.3316013 MHz

F2 - Processing Parameters
 SI 32768
 SF 100.6631093 MHz
 WDWN EM
 SSB 0
 LB 3.00 Hz
 GB 0
 PC 1.40

¹H NMR (DMSO-d₆, 500 MHz)

^{13}C NMR (DMSO- d_6 , 125 MHz)

^1H NMR (CDCl_3 , 500 MHz)

^{13}C NMR (CDCl_3 , 125 MHz)

¹H NMR (DMSO-d₆, 500 MHz)

^{13}C NMR (DMSO- d_6 , 125 MHz)

¹H NMR (DMSO-d₆, 500 MHz)

^{13}C NMR (DMSO- d_6 , 125 MHz)