Supporting Information for

Facile Amide Bond Formation from Carboxylic Acids and Isocyanates

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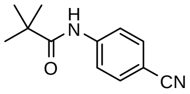
Experimental Part

General Information

Analytical thin layer chromatography (TLC) was performed using Merck TLC 60F-254 plates (0.25 mm), and visualization was accomplished with a PAA stain, which was a mixture of AcOH (2.5 mL), *p*-anisaldehyde (6.5 mL), 95% EtOH (300 mL) and H_2SO_4 (8.5 mL). Optical rotations were measured on a JASCO P-1010 polarimeter. Melting points were determined on a BÜCHI B-540 apparatus. IR-spectra were recorded on a PERKIN ELMER Spectrum 100 spectrophotometer, and ^{1}H and ^{13}C NMR spectra were recorded on a BRUKER UltraShield 300 MHz spectrometer. ^{1}H NMR data are reported as follows: chemical shift in parts par million (ppm) downfield or upfield from tetramethylsilane (0.00), multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet and m = multiplet), coupling constants (Hz) and integration. ^{13}C chemical shifts are reported in ppm downfield or upfield from tetramethylsilane (0.0). High resolution mass spectra were recorded on a WATERS LCT Premier XE mass spectrometer.

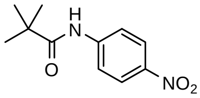
General Procedure for Table 1

Carboxylic acid (0.15 mmol) and *N*,*N*-diisopropylethylamine (35 μL, 0.2 mmol) were dissolved in DMF (1.0 mL) in a 10 mL glass round-bottom flask, and isocyanate (0.1 mmol) was added to the solution in one portion. The reaction mixture was stirred at 25 °C for 2 hours, unless otherwise noted, and then the volatiles were removed under high vacuum. The residue was purified by preparative TLC (Silicagel 60 F254). Pivalic acid, *N*-(9-fluorenylmethoxylcarbonyl)-L-phenylalane, 4-cyanophenyl isocyanate, 4-nitrophenyl isocyanate, 2-bromophenyl isocyanate, 4-bromophenyl isocyanate, benzoyl isocyanate, 4-acetylphenyl isocyanate and 4-trifluoromethylphenyl isocyanate, 3α,12α-dihydroxycholanic acid, and phenyl isocyanate were used as received from the suppliers.



***N*-(4-cyanophenyl) pivalamide** (Entry 1)

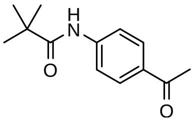
Following the general procedure, pivalic acid (15 mg, 0.15 mmol) and 4-cyanophenylisocyanate (14 mg, 0.10 mmol) were used as substrates. Purification by preparative TLC developed by 99/1 mixture of $CHCl_3$/MeOH gave the corresponding amide (18 mg, 90%). White needles; m. p. = 116.1-117.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71 (d *J* = 8.4 Hz, 2H), 7.66 (br s, 1H), 7.59 (d *J* = 8.4 Hz, 2H), 1.33 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.1, 142.3, 133.1, 119.8, 119.0, 106.8, 39.9, 27.5; ESIHRMS 203.1184 calcd for $C_{12}H_{15}N_2O$ $(M + H)^+$, found 203.1168.



***N*-(4-nitrophenyl) pivalamide** (Entry 2)

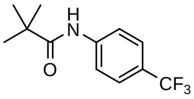
Following the general procedure, pivalic acid (15 mg, 0.15 mmol) and 4-nitrophenylisocyanate (16 mg, 0.10 mmol) were used as substrates. Purification by preparative TLC developed by 99/1 mixture of

$CHCl_3$/MeOH gave the corresponding amide (20 mg, 93%). Yellow needles; m. p. = 154.7-156.4 ^oC; ^1H NMR (300 MHz, $CDCl_3$) δ 8.20 (d *J* = 9.0 Hz, 2H), 7.75 (d *J* = 9.0 Hz, 2H), 7.72 (br s, 1H), 1.35 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.1, 144.0, 143.4, 125.0, 119.3, 40.0, 27.5; ESIHRMS 223.1083 calcd for $C_{11}H_{15}N_2O_3$ $(M + H)^+$, found 223.1062.



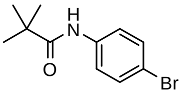
***N*-(4-acetylphenyl) pivalamide** (Entry 3)

Following the general procedure, pivalic acid (15 mg, 0.15 mmol) and 4-acetylphenylisocyanate (19 mg, 0.10 mmol) were used as substrates. Purification by preparative TLC developed by 99/1 mixture of $CHCl_3$/MeOH gave the corresponding amide (19 mg, 88%). White needles; m. p. = 127.0-128.2 ^oC; ^1H NMR (300 MHz, $CDCl_3$) δ 7.93 (d *J* = 9.0 Hz, 2H), 7.67 (d *J* = 9.0 Hz, 2H), 2.58 (s, 3H), 1.34 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.0, 177.0, 142.5, 132.8, 129.6, 119.1, 39.9, 27.5, 26.4; ESIHRMS 220.1338 calcd for $C_{13}H_{18}NO_2$ $(M + H)^+$, found 220.1321.



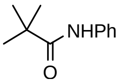
***N*-(4-trifluoromethylphenyl) pivalamide** (Entry 4)

Following the general procedure, pivalic acid (15 mg, 0.15 mmol) and 4-trifluoromethylphenylisocyanate (15 μL, 0.10 mmol) were used as substrates. Purification by preparative TLC developed by 99/1 mixture of $CHCl_3$/MeOH gave the corresponding amide (20 mg, 82%). White needles; m. p. = 154.4-156.6 ^oC; ^1H NMR (300 MHz, $CDCl_3$) δ 7.68 (d *J* = 8.7 Hz, 2H), 7.57 (d *J* = 8.7 Hz, 2H), 7.51 (br s, 1H), 1.34 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.9, 141.1, 126.2 (q *J* = 38 Hz), 125.7, 124.0 (q *J* = 268 Hz), 119.5, 39.8, 27.5; ESIHRMS 244.0949 calcd for $C_{12}H_{13}F_3NO$ $(M – H)^-$, found 244.0942.



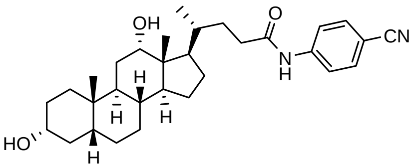
***N*-(4-bromophenyl) pivalamide** (Entry 5)

Following the general procedure, pivalic acid (15 mg, 0.15 mmol) and 4-bromophenylisocyanate (20 mg, 0.10 mmol) were used as substrates. Purification by preparative TLC developed by 99/1 mixture of $CHCl_3$/MeOH gave the corresponding amide (22 mg, 85%). White needles; m. p. = 150.3 -151.8 ^oC; ^1H NMR (300 MHz, $CDCl_3$) δ 7.44 (s, 4H), 7.36 (br s, 1H), 1.32 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.6, 137.1, 131.2, 121.6, 116.7, 39.7, 27.6; ESIHRMS 256.0337 calcd for $C_{11}H_{15}BrNO$ $(M + H)^+$, found 256.0325.



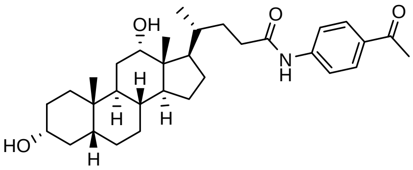
***N*-phenyl pivalamide** (Entry 6)

Following the general procedure, pivalic acid (15 mg, 0.15 mmol) and phenylisocyanate (11 μL, 0.10 mmol) were used as substrates. Purification by preparative TLC developed by 99/1 mixture of $CHCl_3$/MeOH gave the corresponding amide (14 mg, 77%). White needles; m. p. = 130.6-132.0 ^{o}C, lit.[1] 133.1-133.5 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55 (d *J* = 7.5 Hz, 2H), 7.33 (dd *J* = 7.5, 7.5 Hz, 2H), 7.35 (br s, 1H), 7.12 (dd *J* = 7.5, 7.5 Hz, 1H), 1.34 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.6, 138.0, 129.0, 124.2, 120.0, 39.6, 27.6; ESIHRMS 178.1232 calcd for $C_{11}H_{16}NO$ $(M + H)^+$, found 178.1216.



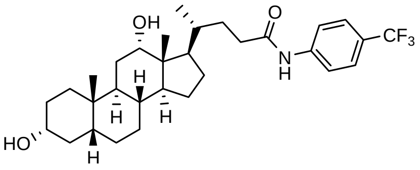
***N*-(4-cyanomethylphenyl) 3α,12α-dihydroxycholanamide** (Entry 7)

Following the general procedure, 3α,12α-dihydroxycholanic acid (59 mg, 0.15 mmol) and 4-cyanophenylisocyanate (14 mg, 0.10 mmol) were used as substrates. Purification by preparative TLC developed by 19/1 mixture of $CHCl_3$/MeOH gave the corresponding amide (42 mg, 85%). White needles; m. p. = 256.8-258.7 ^{o}C; $[\alpha]_D^{23}$ = 36.0 (*c* = 1.67, DMF); ^{1}H NMR (300 MHz, $CDCl_3$ with drops of CD_3OD) δ 9.54 (br s, 0.2H), 7.69 (d *J* = 9.0 Hz, 2H), 7.53 (d *J* = 9.0 Hz, 2H), 3.92 (br s, 1H), 3.60-3.44 (m, 1H), 2.46-2.33 (m, 1H), 2.33-2.18 (m, 1H), 1.89-0.89 (m, 24H), 0.97 (d *J* = 6.0 Hz, 3H), 0.86 (s, 3H), 0.64 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$ with drops of CD_3OD) δ 175.3, 144.5, 134.5, 121.0, 120.9, 120.5, 74.6, 72.8, 49.5, 47.8, 47.8, 43.4, 37.3, 36.6, 36.5, 35.5, 34.9, 34.8, 32.6, 31.2, 29.9, 28.9, 28.5, 27.6, 25.1, 24.4, 18.5, 14.0; ESIHRMS 493.3430 calcd for $C_{31}H_{45}N_2O_3$ $(M + H)^+$, found 493.3454.



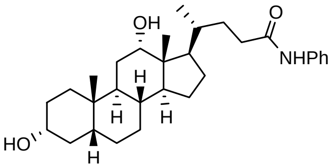
***N*-(4-acetylphenyl) 3α,12α-dihydroxycholanamide** (Entry 8)

Following the general procedure, 3α,12α-dihydroxycholanic acid (59 mg, 0.15 mmol) and 4-acetylphenylisocyanate (19 mg, 0.10 mmol) were used as substrates. Purification by preparative TLC developed by 19/1 mixture of $CHCl_3$/MeOH gave the corresponding amide (44 mg, 86%). White needles; m. p. = 275.4-276.6 ^{o}C; $[\alpha]_D^{25}$ = 35.6 (*c* = 2.12, DMF); ^{1}H NMR (300 MHz, $CDCl_3$ with drops of CD_3OD) δ 9.89 (br s, 0.6H), 7.92 (d *J* = 8.7 Hz, 2H), 7.69 (d *J* = 8.7 Hz, 2H), 3.96 (br s, 1H), 3.64-3.44 (m, 1H), 2.57 (s, 3H), 2.53-2.39 (m, 1H), 2.39-2.22 (m, 1H), 1.98-0.84 (m, 24H), 1.03 (d *J* = 5.7 Hz, 3H), 0.90 (s, 3H), 0.69 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$ with drops of CD_3OD) δ 199.9, 175.6, 145.0, 133.5, 131.0, 120.4, 74.3, 72.7, 49.4, 48.1, 47.7, 43.5, 37.4, 37.3, 36.8, 36.6, 35.5, 35.2, 34.9, 32.9, 31.1, 30.0, 28.9, 28.5, 27.5, 27.3, 25.1, 18.2, 13.9; ESIHRMS 510.3583 calcd for $C_{32}H_{48}NO_4$ $(M + H)^+$, found 510.3550.



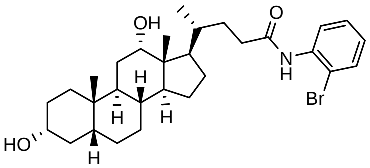
***N*-(4-trifluoromethylphenyl) 3α,12α-dihydroxycholanamide** (Entry 9)

Following the general procedure, 3α,12α-dihydroxycholanic acid (59 mg, 0.15 mmol) and 4-trifluoromethylphenylisocyanate (15 μL, 0.10 mmol) were used as substrates. Purification by preparative TLC developed by 19/1 mixture of $CHCl_3$/MeOH gave the corresponding amide (43 mg, 81%). White needles; m. p. = 250.5-251.2 °C; $[\alpha]_D^{25}$ = 31.4 (*c* = 2.00, DMF); ^{1}H NMR (300 MHz, $CDCl_3$ with drops of CD_3OD) δ 9.31 (br s, 0.2H), 7.66 (d *J* = 8.4 Hz, 2H), 7.50 (d *J* = 8.4 Hz, 2H), 3.92 (br s, 1H), 3.63-3.48 (m, 1H), 2.57 (s, 3H), 2.47-2.33 (m, 1H), 2.33-2.19 (m, 1H), 1.92-0.92 (m, 24H), 0.97 (d *J* = 6.0 Hz, 3H), 0.86 (s, 3H), 0.64 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$ with drops of CD_3OD) δ 175.1, 143.2, 133.1, 127.4,127.3, 127.3, 120.7, 74.6,72.8, 50.1, 49.5, 47.9, 47.8, 43.4, 37.4, 37.3, 36.6, 36.6, 35.5, 34.9, 34.9, 32.7, 31.2, 29.9, 28.9, 28.5, 27.6, 25.1, 24.4, 18.5, 14.0; ESIHRMS 536.3352 calcd for $C_{31}H_{45}F_3NO_3$ $(M + H)^+$, found 536.3323.



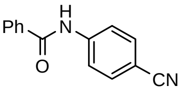
***N*-phenyl 3α,12α-dihydroxycholanamide** (Entry 10)

Following the general procedure, 3α,12α-dihydroxycholanic acid (59 mg, 0.15 mmol) and phenylisocyanate (11 μL, 0.10 mmol) were used as substrates. Purification by preparative TLC developed by 19/1 mixture of $CHCl_3$/MeOH gave the corresponding amide (19 mg, 40%). White foam; $[\alpha]_D^{25}$ = 40.2 (*c* = 2.26, DMF); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 (br s, 1H), 7.56 (d *J* = 7.5 Hz, 2H), 7.31 (dd *J* = 7.5, 7.5 Hz, 2H), 7.09 (dd *J* = 7.5, 7.5 Hz, 1H), 4.01 (br s, 1H), 3.70-3.55 (m, 1H), 2.85 (br s, 2H), 2.50-2.36 (m, 1H), 2.35-2.20 (m, 1H), 1.97-0.96 (m, 24H), 1.01 (d *J* = 5.1 Hz, 3H), 0.92 (s, 3H), 0.69 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.3, 138.3, 128.9, 124.0, 119.8, 73.3, 71.8, 48.1, 46.7, 46.5, 42.1, 36.4, 36.0, 35.3, 35.2, 34.2, 34.0, 33.6, 31.3, 30.6, 28.5, 27.6, 27.2, 26.2, 23.8, 23.2, 17.5, 12.7; ESIHRMS 468.3478 calcd for $C_{30}H_{46}NO_3$ $(M + H)^+$, found 468.3502.



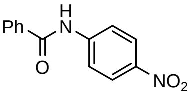
***N*-(2-bromophenyl) 3α,12α-dihydroxycholanamide** (Entry 11)

Following the general procedure, 3α,12α-dihydroxycholanic acid (59 mg, 0.15 mmol) and 2-bromophenylisocyanate (20 mg, 0.10 mmol) were used as substrates. Purification by preparative TLC developed by 19/1 mixture of $CHCl_3$/MeOH gave the corresponding amide (8.7 mg, 16%). Colorless syrup; $[\alpha]_D^{24}$ = 38.0 (*c* = 0.45, DMF); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.36 (br d J = 8.4 Hz, 1H), 7.63 (br s, 1H), 7.55 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.32 (ddd *J* = 8.1, 8.1, 1.5 Hz, 1H), 6.99 (ddd *J* = 8.1, 8.1, 1.5 Hz, 1H), 4.02 (br s, 1H), 3.70-3.55 (m, 1H), 2.60-2.46 (m, 1H), 2.44-2.29 (m, 1H), 2.03-0.98 (m, 24H), 1.06 (d *J* = 6.0 Hz, 3H), 0.93 (s, 3H), 0.71 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 132.2, 128.4, 125.0, 122.0, 121.9, 73.2, 71.8, 48.3, 47.3, 46.5, 42.1, 36.4, 36.1, 35.2, 35.1, 34.8, 34.1, 33.7, 31.4, 30.5, 28.8, 27.5, 27.1, 26.1, 23.7, 23.2, 17.5, 12.8 (2C missed); ESIHRMS 546.2583 calcd for $C_{30}H_{45}BrNO_3$ $(M + H)^+$, found 546.2593.



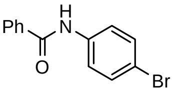
N-(4-cyanophenyl) benzamide (Entry 12)

Following the general procedure, benzoic acid (18 mg, 0.15 mmol) and 4-cyanophenylisocyanate (14 mg, 0.10 mmol) were used as substrates. Purification by preparative TLC developed by 19/1 mixture of $CHCl_3$/MeOH gave the corresponding amide (18 mg, 83%). White needles; m. p. = 164.9-166.0 °C, lit.[2] 164-165 °C; ^{1}H NMR (300 MHz, $CDCl_3$ with drops of CD_3OD) δ 9.42 (br s, 0.2H), 7.86 (d *J* = 7.2 Hz, 2H), 7.83 (d *J* = 9.0 Hz, 2H), 7.58 (d *J* = 9.0 Hz, 2H), 7.52 (dd *J* = 7.2, 7.2 Hz, 1H), 7.44 (dd *J* = 7.2, 7.2 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$ with drops of CD_3OD) δ 167.0, 142.7, 134.2, 133.1, 132.2, 128.6, 127.4, 120.3, 120.2, 119.0; ESIHRMS 221.0720 calcd for $C_{14}H_9N_2O$ $(M - H)^-$, found 221.0713.



N-(4-nitrophenyl) benzamide (Entry 13)

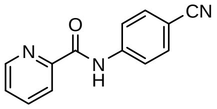
Following the general procedure, benzoic acid (18 mg, 0.15 mmol) and 4-nitrophenylisocyanate (16 mg, 0.10 mmol) were used as substrates. Purification by preparative TLC developed by 19/1 mixture of $CHCl_3$/MeOH gave the corresponding amide (19 mg, 79%). Yellow needles; m. p. = 194.5-197.4 °C; ^{1}H NMR (300 MHz, DMF-d_7) δ 11.08 (br s, 1H), 8.51 (d *J* = 9.3 Hz, 2H), 8.40 (d *J* = 9.3 Hz, 2H), 8.29 (dd *J* = 8.4, 1.2 Hz, 2H), 7.84 (ddd *J* = 8.4, 8.4, 1.2 Hz, 1H), 7.80-7.71 (m, 2H); ^{13}C NMR (75 MHz, DMF-d_7) δ 166.7, 146.2, 143.2, 134.8, 132.4, 128.8, 128.2, 125.0, 120.1; ESIHRMS 241.0619 calcd for $C_{13}H_9N_2O_3$ $(M - H)^-$, found 241.0607.



N-(4-bromophenyl) benzamide (Entry 14)

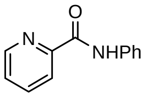
Following the general procedure, benzoic acid (18 mg, 0.15 mmol) and 4-bromophenylisocyanate (20 mg, 0.10 mmol) were used as substrates. Purification by preparative TLC developed by 19/1 mixture of $CHCl_3$/MeOH gave the corresponding amide (20 mg, 75%). White needles; m. p. = 199.0-202.4 °C, lit.[3] 203-204 °C; ^{1}H NMR (300 MHz, $CDCl_3$ with drops of CD_3OD) δ 7.85 (dd *J* = 8.4, 1.5 Hz, 2H), 7.56 (d *J* = 9.0 Hz, 2H), 7.48 (ddd *J* = 8.4, 8.4, 1.2 Hz, 1H), 7.43 (ddd *J* = 8.4, 8.4 Hz, 1H), 7.42 (d *J* = 9.0 Hz, 2H);

^{13}C NMR (75 MHz, $CDCl_3$ with drops of CD_3OD) δ 136.0, 133.3, 133.2, 130.0, 128.7, 123.7, 123.6, 118.4; ESIHRMS 273.9873 calcd for $C_{13}H_9BrNO$ $(M - H)^-$, found 273.9875.



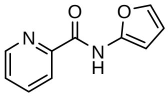
N-(4-cyanophenyl) picolinamide (Entry 15)

Following the general procedure, picolinic acid (18 mg, 0.15 mmol) and 4-cyanophenylisocyanate (14 mg, 0.10 mmol) were used as substrates. Purification by preparative TLC developed by 99/1 mixture of $CHCl_3$/MeOH gave the corresponding amide (20 mg, 90%). White needles; m. p. = 162.8-164.2 ^oC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.26 (br s, 1H), 8.63 (d J = 4.2 Hz, 1H), 8.29 (d J = 7.5 Hz, 1H), 7.94 (ddd J = 7.5, 7.5, 1.2 Hz, 1H), 7.92 (d J = 8.7 Hz, 2H), 7.67 (d J = 8.7 Hz, 2H), 7.54 (ddd J = 7.5, 4.2, 1.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.3 149.0, 148.2, 141.7, 138.0, 133.3, 127.0, 122.6, 119.6, 118.9, 107.2; ESIHRMS 222.0673 calcd for $C_{13}H_8N_3O$ $(M - H)^-$, found 222.0633.



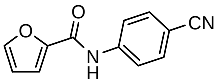
N-4-phenyl picolinamide (Entry 16)

Following the general procedure, picolinic acid (18 mg, 0.15 mmol) and phenylisocyanate (11 μL, 0.10 mmol) were used as substrates. Purification by preparative TLC developed by 99/1 mixture of $CHCl_3$/MeOH gave the corresponding amide (11 mg, 54%). White needles; m. p. = 72.6-74.0 ^oC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.05 (br s, 1H), 8.64 (d J = 4.5 Hz, 1H), 8.33 (d J = 7.8 Hz, 1H), 7.93 (ddd J = 7.8, 7.8, 1.2 Hz, 1H), 7.81 (d J = 7.8 Hz, 2H), 7.50 (ddd J = 7.8, 4.8, 1.2 Hz, 1H), 7.41 (dd J = 7.8, 7.8 Hz, 2H), 7.17 (dd J = 7.8, 7.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.0, 149.8, 148.0, 137.7, 129.1, 126.5, 124.3, 122.4, 119.7; ESIHRMS 199.0871 calcd for $C_{12}H_{11}N_2O$ $(M + H)^+$, found 199.0859.



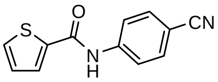
N-(2-furyl) picolinamide (Entry 17)

The reaction was conducted in anhydrous DMF under Ar atmosphere. Following the general procedure, picolinic acid (18 mg, 0.15 mmol) and 2-furylisocyanate (11 mg, 0.10 mmol) were used as substrates. Purification by preparative TLC developed by 99/1 mixture of $CHCl_3$/MeOH gave the corresponding amide (11 mg, 59%). Yellow syrup; ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.31 (br s, 1H), 8.63 (dd J = 4.2 Hz, 0.9 Hz, 1H), 8.28 (d J = 8.1 Hz, 1H), 7.92 (ddd J = 8.1, 8.1, 1.5 Hz, 1H), 7.54 (ddd J = 8.1, 4.5, 1.5 Hz, 1H), 7.14 (dd J = 1.8, 0.9 Hz, 1H), 6.55 (d J = 3.3 Hz, 1H), 6.46 (ddd J = 3.3, 1.8, 0.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.2, 148.8, 148.2, 145.6, 137.7, 135.5, 126.7, 122.4, 111.7, 94.6; ESIHRMS 189.0664 calcd for $C_{10}H_9N_2O_2$ $(M + H)^+$, found 189.0645.



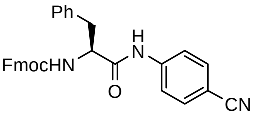
N-(4-cyanophenyl) furamide (Entry 18)

Following the general procedure, 2-furoic acid (17 mg, 0.15 mmol) and 4-cyanophenylisocyanate (14 mg, 0.10 mmol) were used as substrates. Purification by preparative TLC developed by 19/1 mixture of $CHCl_3$/MeOH gave the corresponding amide (17 mg, 90%). White solid; m. p. = 198.8-199.8 ^oC; ^1H NMR (300 MHz, $CDCl_3$ with drops of CD_3OD) δ 8.89 (br s, 0.5H), 7.80 (d J = 11.7 Hz, 2H), 7.61 (d J = 11.7 Hz, 2H), 7.53 (dd J = 1.5, 0.9 Hz, 1H), 7.26 (dd J = 3.6, 0.9 Hz, 1H), 6.55 (dd J = 3.6, 1.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$ with drops of CD_3OD) δ 156.6, 147.0, 145.0, 141.8, 133.2, 120.0, 119.9, 118.8, 116.3, 112.8, 107.0; ESIHRMS 213.0664 calcd for $C_{12}H_9N_2O_2$ (M + H)$^+$, found 213.0661.



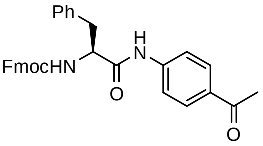
N-(4-cyanophenyl) thiophene-2-carboxamide (Entry 19)

Following the general procedure, thiophene-2-carboxylic acid (19 mg, 0.15 mmol) and 4-cyanophenylisocyanate (14 mg, 0.10 mmol) were used as substrates. Purification by preparative TLC developed by 19/1 mixture of $CHCl_3$/MeOH gave the corresponding amide (19 mg, 82%). White solid; m. p. = 199.4-200.6 ^oC; ^1H NMR (300 MHz, $CDCl_3$ with drops of CD_3OD) δ 7.71 (d J = 8.7 Hz, 2H), 7.70 (dd J = 3.9, 1.2 Hz, 1H), 7.45 (d J = 8.7 Hz, 2H), 7.44 (dd J = 5.1, 1.2 Hz, 1H), 6.96 (dd J = 5.1, 3.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$ with drops of CD_3OD) δ 162.8, 144.3, 140.4, 134.4, 133.3, 130.8, 129.3, 121.9, 121.8, 120.4, 107.8; ESIHRMS 229.0436 calcd for $C_{12}H_9N_2OS$ (M + H)$^+$, found 229.0432.



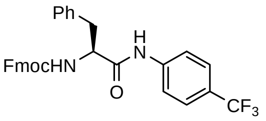
N-(4-cyanophenyl) N^{α}-(9-fluorenylmethoxylcarbonyl)-L-phenylalaninamide (Entry 20)

Following the general procedure, N-(9-fluorenylmethoxylcarbonyl)-L-phenylalanine (58 mg, 0.15 mmol) and 4-cyanophenylisocyanate (14 mg, 0.10 mmol) were used as substrates. Purification by preparative TLC developed by 19/1 mixture of $CHCl_3$/MeOH gave the corresponding amide (40 mg, 82%). White needles; m. p. = 195.2-195.7 ^oC; $[\alpha]_D^{22}$ = 8.7 (c = 0.85, DMF); ^1H NMR (300 MHz, $CDCl_3$) δ 8.27 (br s, 1H), 7.78 (d J = 7.5 Hz, 2H), 7.58-7.38 (m, 8H), 7.35-7.24 (m, 5H), 7.24-7.13 (m, 2H), 5.51 (br s, 1H), 4.57 (br s, 1H), 4.50-4.31 (m, 2H), 4.20 (t J = 6.0 Hz, 1H), 3.14 (d J = 6.0 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.6, 156.5, 143.4, 141.3, 141.2, 135.9, 133.1, 129.2, 128.9, 127.9, 127.4, 127.1, 124.8, 120.1, 119.8, 118.7, 107.5, 67.4, 57.2, 47.0, 38.1; ESIHRMS 488.1974 calcd for $C_{31}H_{26}N_3O_3$ (M + H)$^+$, found 488.1967.



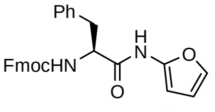
N-(4-acetylphenyl) N^{α}-(9-fluorenylmethoxylcarbonyl)-L-phenylalaninamide (Entry 21)

Following the general procedure, *N*-(9-fluorenylmethoxylcarbonyl)-L-phenylalanine (58 mg, 0.15 mmol) and 4-acetylphenylisocyanate (19 mg, 0.10 mmol) were used as substrates. Purification by preparative TLC developed by 19/1 mixture of $CHCl_3$/MeOH gave the corresponding amide (40 mg, 80%). White needles; m. p. = 207.4-208.3 ^{o}C; $[\alpha]_D^{23}$ = 6.7 (*c* = 1.52, DMF); ^{1}H NMR (300 MHz, $CDCl_3$ with drops of CD_3OD) δ 9.60 (br s, 0.3H), 7.87 (d *J* = 8.7 Hz, 2H), 7.72 (d *J* = 7.5 Hz, 1H), 7.56 (d *J* = 8.7 Hz, 2H), 7.56-7.46 (m, 2H), 7.35 (dd *J* = 7.5, 7.5 Hz, 2H), 7.29-7.11 (m, 7H), 4.51 (t *J* = 6.0 Hz, 1H), 4.37 (dd *J* = 10.2, 7.2 Hz, 1H), 4.27 (dd *J* = 10.2, 6.9 Hz, 1H), 4.13 (dd *J* = 6.9, 6.6 Hz, 1H), 3.12 (dd *J* = 13.5, 6.6 Hz, 1H), 3.00 (dd *J* = 13.5, 6.9 Hz, 1H), 2.54 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$ with drops of CD_3OD) δ 199.6, 187.6, 172.1, 172.1, 145.0, 143.8, 142.6, 137.6, 134.1, 131.0, 130.7, 129.9, 129.1, 128.5, 128.4, 126.4, 126.3, 121.3, 120.9, 120.8, 68.5, 58.2, 48.4, 40.1, 27.6; ESIHRMS 505.2127 calcd for $C_{32}H_{29}N_2O_4$ $(M + H)^+$, found 505.2112.



N-(4-trifluoromethylphenyl) N^{α}-(9-fluorenylmethoxylcarbonyl)-L-phenylalaninamide (Entry 22)

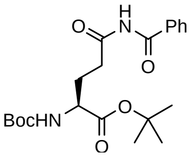
Following the general procedure, *N*-(9-fluorenylmethoxylcarbonyl)-L-phenylalanine (58 mg, 0.15 mmol) and 4-trifluoromethylphenylisocyanate (15 μL, 0.10 mmol) were used as substrates. Purification by preparative TLC developed by 19/1 mixture of $CHCl_3$/MeOH gave the corresponding amide (38 mg, 71%). White needles; m. p. = 230.1-231.7 ^{o}C; $[\alpha]_D^{23}$ = 7.9 (*c* = 1.11, DMF); ^{1}H NMR (300 MHz, $CDCl_3$ with drops of CD_3OD) δ 9.67 (br s, 0.5H), 7.74 (d *J* = 7.5 Hz, 2H), 7.64-7.46 (m, 6H), 7.36 (d *J* = 7.2 Hz, 2H), 7.31-7.12 (m, 7H), 4.50 (t *J* = 6.6 Hz, 1H), 4.38 (dd *J* = 10.5, 7.2 Hz, 1H), 4.26 (dd *J* = 10.5, 6.6 Hz, 1H), 4.24-4.05 (m, 1H), 3.13 (dd *J* = 13.5, 7.2 Hz, 1H), 3.00 (dd *J* = 13.5, 6.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$ with drops of CD_3OD) δ 172.1, 145.0, 145.0, 142.6, 142.3, 137.6, 130.6, 129.9, 129.1, 128.4, 128.4, 127.4, 127.4, 127.3, 127.3, 126.4, 126.3, 121.3, 121.2, 68.4, 58.1, 48.4, 40.1 (1C missed); ESIHRMS 531.1896 calcd for $C_{31}H_{26}F_3N_2O_3$ $(M + H)^+$, found 531.1896.



N-(2-furyl) N^{α}-(9-fluorenylmethoxylcarbonyl)-L-phenylalaninamide (Entry 23)

The reaction was conducted in anhydrous DMF under Ar atmosphere. Following the general procedure, *N*-(9-fluorenylmethoxylcarbonyl)-L-phenylalanine (58 mg, 0.15 mmol) and 2-furylisocyanate (11 mg, 0.10 mmol) were used as substrates. Purification by preparative TLC developed by 19/1 mixture of $CHCl_3$/MeOH gave the corresponding amide (20 mg, 45%). White needles; m. p. = 207.2-209.8 ^{o}C; $[\alpha]_D^{24}$ = 6.7 (*c* = 1.26, DMF); ^{1}H NMR (300 MHz, $CDCl_3$ with drops of CD_3OD) δ 7.72 (d *J* = 7.5 Hz, 1H), 7.51 (dd *J* = 8.4, 8.4 Hz, 2H), 7.41-7.31 (m, 2H), 7.30-7.12 (m, 7H), 7.02 (br s, 1H), 6.33 (dd *J* = 3.0, 2.1 Hz, 1H), 6.24 (d *J* = 3.0 Hz, 1H), 4.49 (d *J* = 6.9 Hz, 1H), 4.35 (dd *J* = 10.5, 6.9 Hz, 1H), 4.25 (dd *J* = 10.5, 6.9

Hz, 1H), 4.12 (dd *J* = 7.8, 6.3 Hz, 1H), 3.12 (dd *J* = 15.5, 6.3 Hz, 1H), 2.96 (dd *J* = 15.5, 7.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$ with drops of CD_3OD) δ 168.5, 156.4, 145.0, 143.6, 141.2, 136.1, 135.6, 129.2, 128.5, 127.7, 127.0, 126.9, 124.9, 119.9, 111.2, 95.5, 67.0, 56.0, 47.0, 38.6 ; ESIHRMS 453.1814 calcd for $C_{28}H_{25}N_2O_4$ (M + H)$^+$, found 453.1826.



N^{δ}-benzoyl O^{β}-*tert*-butyl N^{α}-*tert*-butoxycarbonyl-L-glutaminate (Entry 24)

Following the general procedure, O^{β}-*tert*-butyl *N*-*tert*-butoxycarbonyl-L-glutamic acid (45 mg, 0.15 mmol) and benzoylisocyanate (13 μL, 0.10 mmol) were used as substrates. Purification by preparative TLC developed by by 4/1 mixture of heptane/EtOAc gave the corresponding amide (34 mg, 84%). White solid; m. p. = 85.8-86.5 ^{o}C; $[\alpha]_D^{22}$ = 3.4 (*c* = 2.16, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.46 (br s, 1H), 7.92 (d *J* = 7.5 Hz, 2H), 7.58 (dd *J* = 7.5 ,7.5 Hz, 1H), 7.48 (dd *J* = 7.5, 7.5 Hz, 2H), 5.28 (br d *J* = 7.8 Hz, 1H), 4.26 (dd *J* = 12.0, 7.8 Hz, 1H), 3.17-2.95 (m, 2H), 2.32-2.16 (m, 1H), 2.07-1.90 (m, 1H), 1.47 (s, 9H), 1.42 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.4, 171.5, 165.7, 155.7, 133.1, 132.8, 128.6, 127.9, 82.2, 79.8, 53.3, 33.8, 28.3, 28.0, 27.7; ESIHRMS 407.2182 calcd for $C_{21}H_{31}N_2O_6$ (M + H)$^+$, found 407.2155.

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(2) Inamoto, K.; Shiraishi, M.; Hiroya, K.; Doi, T. *Synthesis* **2010**, 3087-3090.

(3) Lee, C. K.; Yu, J. S.; Ji, Y. R. *J. Heterocyclic Chem.* **2002**, *39*, 1219-1227.