SUPPLEMENTARY INFORMATION:

TiF₄-Catalyzed Direct Amidation of Carboxylic Acids and Amino Acids with Amines

Abdulkhaliq A. Alawaed and P. Veeraraghavan Ramachandran*

[†] Herbert C. Brown Center for Borane Research, Department of Chemistry, Purdue University, West Lafayette, Indiana 47907, United States

E-mail: <u>chandran@purdue.edu</u>

Contents:

General information	S2
General Procedure for the preparation of secondary and tertiary amides	S2
Characterization of secondary and tertiary amides	3-S17
References	7-S19
NMR spectra of secondary and tertiary amides)-S83

Page

General Information

The solvents, carboxylic acids, as well as the amines used to prepare the amides, were purchased from Sigma-Aldrich or Oakwood Chemical. The TiF₄ and toluene were used as received. (*Precaution:* avoid skin contact with TiF_4).

The structures of the product amides were confirmed with nuclear magnetic resonance (NMR) spectroscopy and measured in δ values in parts per million (ppm). The ¹H, ¹³C, and ¹⁹F NMR spectra of the reduction products were recorded on a Bruker 400 MHz spectrometer and Varian INOVA 300 MHz NMR at ambient temperature. The ¹H spectra were calibrated against the residual solvent peak of CDCl₃ (δ = 7.26 ppm) as an internal standard. The ¹³C NMR spectra were reported at 101 MHz or 75 MHz and calibrated using CDCl₃ (δ = 77.0 ppm) as an internal standard. The coupling constants (*J*) were given in hertz (Hz), and the signal multiplicities were described for the NMR data as s = singlet, d = doublet, t = triplet, dd = doublet of doublets, dt = doublet of triplets, qd = quartet of doublets, q = quartet, quint and p = pentet, m = multiplet, and br = broad.. The ¹⁹F NMR spectra were recorded at 376 MHz or and calibrated using CFCl₃ (δ = 0 ppm) as the external standard. Optical rotation was measured on Rudolph autopol III S2 polarimeter and for concentration [c] given in g / 100 mL.

General Procedure for the preparation of secondary and tertiary amides.

In a 25 ml round bottom flask with sealed side arm containing a magnetic stir bar was added TiF₄ (0.1 mmol, 0.1 eq.). Toluene (3 mL) was then added to the flask, followed by addition carboxylic acid (1.1 mmol, 1.0 eq.) in one portion. Amine (1 mmol, 1 eq.) was added to the mixture. A reflux condenser was attached to the flask, and the reaction mixture was brought to reflux, using an oil bath, and monitored by TLC. After completion (~24 hours) the reaction mixture was quenched with 1 N HCl (3 mL) and transferred to a separatory funnel and extracted with

dichloromethane (DCM) $(3 \times 2 \text{ mL})$. The organic layer was washed with 3M sodium hydroxide solution (2 mL). The organic layer was dried with sodium sulfate, filtered through cotton, and concentrated under aspirator vacuum using a rotary evaporator. The reaction residue was diluted with methanol (3mL) and condensed via rotary evaporation to remove toluene solvent. Any remaining traces of solvent were removed by subjecting the solution to high vacuum for 30 min.

Characterization of secondary and tertiary amides.



N-benzylbenzamide (3aa); The compound was prepared as described in the general procedure (white solid, mass = 202 mg, 96% yield); ¹H NMR (400 MHz, CDCl₃) δ 7.79 (d, *J* = 8.3 Hz, 2H), 7.52 – 7.46 (m, 1H), 7.44 – 7.39 (m, 2H), 7.36 – 7.25 (m, 5H), 6.53 (s, 1H), 4.63 (d, *J* = 5.7 Hz, 2H). ¹³C{H} NMR (101 MHz, CDCl₃) δ 167.3, 138.1, 134.3, 131.4, 128.7, 128.5, 127.8, 127.5, 126.9, 44.0.

Compound characterization is in accordance with previous reports.¹



N-benzyl-2-iodobenzamide (3ba); The compound was prepared as described in the general procedure (mass = 233 mg, 69% yield); ¹H NMR (400 MHz, CDCl₃) δ 7.84 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.41 – 7.27 (m, 7H), 7.08 (td, *J* = 7.6, 2.0 Hz, 1H), 6.10 (s, 1H), 4.62 (d, *J* = 5.7 Hz, 2H). ¹³C{H} NMR (101 MHz, CDCl₃) δ 169.1, 142.0, 139.8, 137.5, 131.1, 128.7, 128.2, 128.1, 127.6, 92.4, 44.1.

Compound characterization is in accordance with previous reports.²



N-benzyl-3-fluorobenzamide (3ca); The compound was prepared as described in the general procedure (off-white solid, mass = 226 mg, 99% yield); ¹H NMR (400 MHz, CDCl₃) δ 7.55 – 7.49 (m, 2H), 7.44 – 7.28 (m, 6H), 7.19 (tdd, *J* = 8.3, 2.6, 1.0 Hz, 1H), 6.45 (s, 1H), 4.63 (d, *J* = 5.6 Hz, 2H). ¹³C{H} NMR (101 MHz, CDCl₃) δ 166.0, 162.7 (d, *J* = 248.0 Hz, 1C)163.9, 161.4, 137.8, 136.6 (d, *J* c-F = 6.7 Hz, 1C), 130.2 (d, *J* c-F = 8.1 Hz, 1C), 130.1, 128.8, 127.8, 127.8, 127.7, 122.3, 118.5 (d, *J* c-F = 21.3 Hz, 1C), 114.3 (d, *J* c-F = 23.0 Hz, 1C), 44.2. ¹⁹F NMR (376 MHz, CDCl₃) δ -113.2. (td, *J*c-F = 8.9, 5.6 Hz).

Compound characterization is in accordance with previous reports.^{1,3}



N-benzyl-4-iodobenzamide (3da); The compound was prepared as described in the general procedure (yellow solid, mass = 320 mg, 95% yield); ¹H NMR (400 MHz, CDCl₃) δ 7.77 (d, *J* = 8.5 Hz, 2H), 7.51 (d, *J* = 8.5 Hz, 2H), 7.38 – 7.28 (m, 5H), 6.38 (s, 1H), 4.62 (d, *J* = 5.6 Hz, 2H). ¹³C{H} NMR (101 MHz, CDCl₃) δ 166.4, 137.7, 128.8, 128.5, 127.9, 127.7, 98.4, 44.1. Compound characterization is in accordance with previous reports.¹



N-benzyl-4-(trifluoromethyl)benzamide (3ea); The compound was prepared as described in the general procedure (white solid, mass = 276 mg, 99% yield); ¹H NMR (400 MHz, CDCl₃) δ 7.9 (d, *J* = 8.1 Hz, 2H), 7.7 (d, *J* = 8.0 Hz, 2H), 7.4 – 7.2 (m, 5H), 6.6 (s, 1H), 4.6 (d, *J* = 5.6 Hz, 2H).(400 MHz, CDCl₃) δ 7.89 (d, *J* = 8.0 Hz, 2H), 7.68 (d, *J* = 8.0 Hz, 2H), 7.40 – 7.28 (m, 5H), 6.50 (s, 1H), 4.65 (d, *J* = 5.7 Hz, 2H).¹³C NMR {H} (101 MHz, CDCl₃) δ 166.01, 137.64, 137.54, 133.51, 133.4 (q, *JC*-*F* = 31 Hz, 1C), 128.77, 127.83, 127.72, 127.37, 125.5 (q, *JC*-*F* = 3.5 Hz, 1C), 44.20. ¹³C{H} NMR (101 MHz, CDCl₃) δ 166.0, 137.6, 128.8, 127.9, 127.7, 127.3, 125.6 (q, *J* = 3.9 Hz), 44.2.¹⁹F NMR (376 MHz, CDCl₃) δ -64.5. Compound characterization is in accordance with previous reports.^{1,4}



N-Benzyl-2-methylbenzamide (3fa); The compound was prepared as described in the general procedure (yellow solid, mass = 213 mg, 95% yield); ¹**H** NMR (400 MHz, CDCl₃) δ 7.39 – 7.32 (m, 5H), 7.34 – 7.26 (m, 2H), 7.24 – 7.13 (m, 2H), 6.17 (s, 1H), 4.60 (d, *J* = 5.8 Hz, 2H), 2.45 (s, 3H). ¹³C{H} NMR (101 MHz, CDCl₃) δ 169.9, 138.1, 136.1, 130.9, 129.8, 128.7, 127.7, 127.5, 126.6, 125.6, 43.8, 19.7.

Compound characterization is in accordance with previous reports.⁵



N-benzyl-2-methoxybenzamide (3ga); The compound was prepared as described in the general procedure (colorless oil, mass = 185 mg, 76% yield); ¹H NMR (400 MHz, CDCl₃) δ 8.26 (dd, *J* = 7.8, 1.8 Hz, 1H), 8.19 (s, 1H), 7.50 – 7.41 (m, 1H), 7.40 – 7.30 (m, 4H), 7.31 – 7.25 (m, 1H), 7.10 (t, *J* = 7.6 Hz, 1H), 6.97 (d, *J* = 8.3 Hz, 1H), 4.70 (d, *J* = 5.7 Hz, 1H), 3.92 (s, 1H). ¹³C{H} NMR (101 MHz, CDCl₃) δ 165.2, 157.4, 138.7, 132.7, 132.4, 128.5, 127.4, 127.1, 121.3, 111.2, 55.8, 43.7.

Compound characterization is in accordance with previous reports.⁵



N-Benzyl-3-methoxybenzamide (3ha); The compound was prepared as described in the general procedure (colorless oil, mass = 226 mg, 94% yield); ¹H NMR (400 MHz, CDCl₃) δ 7.43 – 7.26 (m, 8H), 7.03 (ddd, J = 7.7, 2.6, 1.5 Hz, 1H), 6.41 (s, 1H), 4.64 (d, J = 5.7 Hz, 2H), 3.84 (s, 3H). ¹³C{H} NMR (101 MHz, CDCl₃) δ 167.1, 161.3, 159.8, 138.0, 135.8, 129.5, 128.7, 127.8, 127.6, 118.5, 117.7, 112.3, 55.4, 44.1.

Compound characterization is in accordance with previous reports.⁶



N-benzyl-4-methylbenzamide (3ia); The compound was prepared as described in the general procedure (white solid, mass = 179 mg, 80% yield); ¹H NMR (400 MHz, CDCl₃) δ 7.69 (d, *J* = 8.3 Hz, 2H), 7.39 – 7.26 (m, 5H), 7.22 (d, *J* = 7.9 Hz, 2H), 6.39 (s, 1H), 4.64 (d, *J* = 5.7 Hz, 2H), 2.39 (s, 3H). ¹³C{H} NMR (101 MHz, CDCl₃) δ 167.2, 141.9, 138.2, 131.4, 129.1, 128.7, 127.8, 127.5, 126.8, 44.0, 21.3.

Compound characterization is in accordance with previous reports.¹



N-benzyl-4-methoxybenzamide (3ja); The compound was prepared as described in the general procedure (white solid , mass = 239 mg, 99% yield); ¹H NMR (400 MHz, CDCl₃) δ 7.76 (d, *J* = 8.8 Hz, 2H), 7.37 – 7.25 (m, 5H), 6.91 (d, *J* = 8.8 Hz, 2H), 6.38 (s, 1H), 4.62 (d, *J* = 5.7 Hz, 2H), 3.84 (s, 3H). ¹³C{H} NMR (101 MHz, CDCl₃) δ 166.8, 162.1, 138.3, 128.7, 127.8, 127.5, 126.6, 113.7, 77.2, 76.9, 76.6, 55.3, 44.0.

Compound characterization is in accordance with previous reports.¹



N-benzylcinnamamide (3ka); The compound was prepared as described in the general procedure (white solid, mass = 235mg, 99% yield); ¹H NMR (400 MHz, CDCl₃) δ 7.67 (d, *J* = 15.6 Hz, 1H), 7.49 – 7.45 (m, 2H), 7.36 – 7.27 (m, 8H), 6.44 (d, *J* = 15.6 Hz, 1H), 6.18 (s, 1H), 4.55 (d, *J* = 5.8 Hz, 2H). ¹³C{H} NMR (101 MHz, CDCl₃) δ 165.7, 141.3, 138.1, 134.7, 129.6, 128.7, 128.6, 127.8, 127.7, 127.5, 120.4, 43.8.

Compound characterization is in accordance with previous reports.¹



N-benzylnicotinamide (3la); The compound was prepared as described in the general procedure (white solid, mass = 193 mg, 91% yield); ¹H NMR (300 MHz, CDCl₃) δ 8.8 (d, *J* = 1.4 Hz, 1H), 8.4 (dd, *J* = 4.9, 1.7 Hz, 1H), 8.1 - 7.9 (m, 2H), 7.2 - 7.1 (m, 6H), 4.4 (d, *J* = 5.7 Hz, 2H). ¹³C{H}

NMR (75 MHz, CDCl₃) δ 164.7, 150.7, 147.1, 137.0, 134.3, 129.1, 127.6, 126.7, 126.4, 122.4, 42.9.

Compound characterization is in accordance with previous reports.¹



N-(**pyridin-2-ylmethyl**)**benzamide(3ab);** The compound was prepared as described in the general procedure (brown oil, mass = 197 mg, 93% yield); ¹H NMR (300 MHz, CDCl₃) δ 8.5 (d, J = 5.0 Hz, 1H), 7.8 (dd, J = 8.2, 1.5 Hz, 2H), 7.6 (td, J = 7.7, 1.8 Hz, 2H), 7.5 – 7.3 (m, 3H), 7.3 (d, J = 7.9 Hz, 1H), 7.1 (dd, J = 7.2, 5.8 Hz, 1H), 4.7 (d, J = 4.9 Hz, 2H). ¹³C{H} NMR (75 MHz, CDCl₃) δ 167.5, 156.3, 149.0, 136.9, 134.3, 131.5, 128.5, 127.1, 122.4, 122.2, 44.8. Compound characterization is in accordance with previous reports.⁶



N-cyclohexylbenzamide (3ac); The compound was prepared as described in the general procedure (white solid, mass = 183 mg, 90% yield); ¹H NMR (400 MHz, CDCl₃) δ 7.8 – 7.7 (m, 2H), 7.5 – 7.4 (m, 1H), 7.4 – 7.4 (m, 2H), 6.1 (s, 1H), 4.0 – 3.9 (m, 1H), 2.1 – 2.0 (m, 2H), 1.7 (dt, J = 13.2, 4.0 Hz, 2H), 1.7 – 1.6 (m, 1H), 1.5 – 1.4 (m, 2H), 1.3 – 1.2 (m, 3H). ¹³C{H} NMR (101 MHz, CDCl₃) δ 166.5, 135.0, 131.1, 128.4, 126.7, 48.6, 33.1, 25.5, 24.8. Compound characterization is in accordance with previous reports.¹



N-Benzoylmorpholine (3ad); The compound was prepared as described in the general procedure (yellow solid, mass = 181 mg, 95% yield); ¹H NMR (400 MHz, CDCl₃) δ 7.38 (s, 5H), 3.76 – 3.33 (m, 8H). ¹³C{H} NMR (101 MHz, CDCl₃) δ 170.3, 135.2, 129.8, 128.5, 127.0, 66.8, 48.1, 42.5. Compound characterization is in accordance with previous reports.⁷



N-(3-Fluorobenzoyl)morpholine (3cd); The compound was prepared as described in the general procedure (yellow oil, mass = 205 mg, 98% yield); ¹H NMR (400 MHz, CDCl₃) δ 7.42 – 7.35 (m, 1H), 7.17 (dt, *J* = 7.6, 1.2 Hz, 1H), 7.15 – 7.09 (m, 2H), 3.83 – 3.36 (m, 8H). ¹³C{H} NMR (101 MHz, CDCl₃) ¹³C {H}NMR (75 MHz, CDCl₃) δ 167.9 (d, *J*c-F = 2.0 Hz, 1C), 161.5 (d, *J* = 248.5 Hz, 1C), 136.3 (d, *J*c-F = 6.9 Hz, 1C), 129.4 (d, *J*c-F = 8.0 Hz, 1C), 121.7 (d, *J*c-F = 3.2 Hz, 1C), 115.9 (d, *J*c-F = 21.0 Hz, 1C), 113.4 (d, *J* c-F = 22.9 Hz, 1C), 65.78, 47.12, 41.64.8 168.9, 163.7, 161.2, 137.2 (d, *J* = 6.7 Hz), 130.3 (d, *J* = 7.8 Hz), 122.6 (d, *J* = 3.0 Hz), 116.8 (d,

J = 21.0 Hz), 114.3 (d, J = 22.9 Hz), 66.7, 48.1, 42.5. ¹⁹F NMR (376 MHz, CDCl₃) δ -113.0 (td, $J_{C-F} = 8.7, 5.5$ Hz)..

Compound characterization is in accordance with previous reports.⁸98



N-(4-Trifluoromethylbenzoyl)morpholine (3ed); The compound was prepared as described in the general procedure (yellow solid, mass = 256 mg, 99% yield); ¹H NMR (300 MHz, CDCl₃) δ 7.6 (d, J = 8.1 Hz, 2H), 7.4 (d, J = 8.0 Hz, 2H), 3.7 – 3.2 (m, 8H).¹H NMR (400 MHz, CDCl₃) δ 7.68 (d, J = 7.9 Hz, 2H), 7.52 (d, J = 7.9 Hz, 2H), 3.82 – 3.39 (m, 8H).¹³C {H} NMR (75 MHz, CDCl₃) δ 167.90, 137.95, 130.8 (q, $J_{C-F} = 32.8$ Hz, 1C), 126.50, 124.7 (q, $J_{C-F} = 3.8$ Hz, 1C), 124.51, 120.89, 117.28, 65.75, 47.07, 41.56.¹³C{H} NMR (101 MHz, CDCl₃) δ 168.8, 138.8, 131.9, 127.4, 125.6 (q, J = 3.5 Hz), 66.7, 48.0, 42.5. ¹⁹F NMR (376 MHz, CDCl₃) δ -64.5 (t, J = 10.7 Hz).-64.4, -64.47, -64.51.

Compound characterization is in accordance with previous reports.^{7, 10}



N-(2-Methoxybenzoyl)morpholine (3gd); The compound was prepared as described in the general procedure (orange liquid, mass = 135 mg, 61% yield); ¹H NMR (400 MHz, CDCl₃) δ 7.35 (td, *J* = 7.4, 1.8 Hz, 1H), 7.28 – 7.21 (m, 1H), 6.99 (td, *J* = 7.4, 0.9 Hz, 1H), 6.91 (d, *J* = 8.4 Hz, 1H), 3.80 (d, *J* = 28.4 Hz, 7H), 3.67 – 3.54 (m, 2H), 3.32 – 3.17 (m, 2H). ¹³C{H} NMR (101 MHz, CDCl₃) δ 167.8, 155.2, 130.5, 128.0, 125.2, 120.9, 110.8, 66.9, 66.8, 55.4, 47.2, 42.0. Compound characterization is in accordance with previous reports.⁷



N-(3-Methoxybenzoyl)morpholine (3hd); The compound was prepared as described in the general procedure (yellow oil, mass = 212 mg, 96% yield); ¹H NMR (400 MHz, CDCl₃) δ 7.34 – 7.26 (m, 1H), 6.98 – 6.90 (m, 3H), 3.81 (s, 3H), 3.79 – 3.49 (m, 8H). ¹³C{H} NMR (101 MHz, CDCl₃) δ 170.1, 159.6, 136.5, 129.6, 119.0, 115.5, 112.4, 66.8, 55.3, 48.1, 42.5. Compound characterization is in accordance with previous reports.⁷



N-(4-Methoxybenzoyl)morpholine (3jd); The compound was prepared as described in the general procedure (colorless oil, mass = 199 mg, 90% yield); ¹H NMR (400 MHz, CDCl₃) δ 7.37

(d, J = 8.7 Hz, 2H), 6.90 (d, J = 8.8 Hz, 2H), 3.82 (s, 3H), 3.74 – 3.51 (m, 8H). ¹³C{H} NMR (101 MHz, CDCl₃) δ 170.3, 160.8, 129.1, 127.2, 113.7, 66.8, 55.3. Compound characterization is in accordance with previous reports.⁷

N-phenylbenzamide (3ae); The compound was prepared as described in the general procedure (white solid, mass = 187 mg, 95% yield); ¹H NMR (400 MHz, CDCl₃) δ 7.9 (d, *J* = 7.6 Hz, 2H), 7.6 (d, *J* = 7.5 Hz, 2H), 7.6 – 7.5 (m, 1H), 7.5 (t, *J* = 6.8 Hz, 2H), 7.4 (t, *J* = 7.6 Hz, 2H), 7.2 (t, *J* = 7.4 Hz, 1H). ¹³C{H} NMR (101 MHz, CDCl₃) δ 165.6, 137.8, 134.9, 131.8, 129.0, 128.7, 126.9, 124.5, 120.1.

Compound characterization is in accordance with previous reports.¹



3-Fluoro-*N***-phenylbenzamide (3ce);** The compound was prepared as described in the general procedure (yellow solid, mass = 184 mg, 86% yield); ¹**H** NMR (400 MHz, CDCl₃) δ 7.93 (s, 1H), 7.65 – 7.58 (m, 3H), 7.57 (dt, *J* = 9.3, 2.2 Hz, 1H), 7.43 (td, *J* = 8.0, 5.6 Hz, 1H), 7.36 (t, *J* = 8.0 Hz, 2H), 7.23 (td, *J* = 7.8, 1.6 Hz, 1H), 7.16 (t, *J* = 7.4 Hz, 1H). ¹³C{**H**} NMR (101 MHz, CDCl₃) δ 164.2 (d, *J*_{C-F} = 45.7 Hz, 1C), 161.5, 137.5, 137.1 (d, *J*_{C-F} = 5.8 Hz, 1C), 130.3 (d, *J*_{C-F} = 7.9 Hz, 1C), 129.0, 124.8, 122.4 (d, *J*_{C-F} = 2.5 Hz, 1C), 120.3, 118.8 (d, *J*_{C-F} = 21.1 Hz, 1C), 114.4 (d, *J*_{C-F} = 23.0 Hz, 1C). ¹⁹F NMR (376 MHz, CDCl₃) δ -112.8 .(td, *J*_{C-F} = 8.6, 5.3 Hz). Compound characterization is in accordance with previous reports.¹¹



4-Methoxy-*N***-phenylbenzamide (3je);** The compound was prepared as described in the general procedure (yellow solid, mass = 212 mg, 93% yield); ¹H NMR (400 MHz, CDCl₃) δ 7.84 (d, *J* = 8.9 Hz, 2H), 7.77 (s, 1H), 7.63 (d, *J* = 7.3 Hz, 2H), 7.40 – 7.32 (m, 2H), 7.14 (t, *J* = 7.4 Hz, 1H), 6.97 (d, *J* = 8.8 Hz, 2H), 3.87 (s, 3H). ¹³C{H} NMR (101 MHz, CDCl₃) δ 165.1, 162.4, 138.0, 129.0, 128.8, 127.1, 124.2, 120.0, 113.9, 55.4.

Compound characterization is in accordance with previous reports.¹²



N-(3-bromophenyl)benzamide (3af); The compound was prepared as described in the general procedure (gray solid, mass = 212mg, 77% yield); ¹H NMR (300 MHz, CDCl₃) δ 8.0 (s, 1H), 7.8 (s, 1H), 7.8 (d, *J* = 7.2 Hz, 2H), 7.5 (t, *J* = 7.4 Hz, 2H), 7.4 (t, *J* = 7.4 Hz, 2H), 7.2 - 7.2 (m, 1H),

7.1 (t, J = 8.0 Hz, 1H). ¹³C{H} NMR (75 MHz, CDCl₃) δ 164.9, 138.2, 133.4, 131.1, 129.3, 127.8, 126.5, 126.0, 122.2, 121.6, 117.7.

Compound characterization is in accordance with previous reports.¹²

N-(4-Methoxyphenyl)benzamide (3ag); The compound was prepared as described in the general procedure (green solid, mass = 190 mg, 83% yield); ¹H NMR (400 MHz, CDCl₃) δ 7.9 (d, *J* = 7.0 Hz, 2H), 7.8 (s, 1H), 7.6 – 7.5 (m, 3H), 7.5 (t, *J* = 7.3 Hz, 2H), 6.9 (d, *J* = 9.0 Hz, 2H), 3.8 (s, 3H). ¹³C{H} NMR (101 MHz, CDCl₃) δ 165.5, 156.5, 135.0, 131.6, 130.9, 128.6, 126.9, 122.0, 114.2, 55.4.

Compound characterization is in accordance with previous reports.⁷



4-amino-5-chloro-N-(2-(diethylamino)ethyl)-2-methoxybenzamide (3mh); The compound was prepared as described in the general procedure (brown solid, mass = 203mg, 68% yield); ¹**H NMR** (300 MHz, CDCl₃) δ 8.1 (s, 1H), 8.0 (s, 1H), 6.2 (s, 1H), 4.3 (s, 2H), 3.8 (s, 3H), 2.6 (dq, J = 14.1, 6.3 Hz, 6H), 1.0 (t, J = 7.1 Hz, 6H). ¹³C **{H} NMR** (75 MHz, CDCl₃) δ 164.4, 157.6, 146.5, 133.0, 111.5, 108.9, 97.9, 55.9, 51.6, 46.8, 37.4, 11.9.

Compound characterization is in accordance with previous reports.¹

N-Benzylformamide (5aa); The compound was prepared as described in the general procedure (white solid, mass = 133 mg, 99% yield); ¹H NMR (400 MHz, CDCl₃) δ 8.20 (s, 1H), 7.35 – 7.23 (m, 5H), 6.18 (s, 1H), 4.44 (d, J = 5.9 Hz, 2H). ¹³C{H} NMR (101 MHz, CDCl₃) δ 161.0, 137.5, 128.7, 127.7, 127.6, 42.0.

Compound characterization is in accordance with previous reports.¹³

N-benzylacetamide (5ba); The compound was prepared as described in the general procedure (white solid, mass = 148 mg, 99% yield); ¹H NMR (400 MHz, CDCl₃) δ 7.37 – 7.23 (m, 5H), 5.83 (s, 1H), 4.42 (d, *J* = 5.7 Hz, 2H), 2.01 (s, 3H). ¹³C{H} NMR (101 MHz, CDCl₃) δ 169.8, 138.1, 128.6, 127.8, 127.5, 43.7, 23.2.

Compound characterization is in accordance with previous reports.¹



N-benzyl-2,2-dichloroacetamide (5ca); The compound was prepared as described in the general procedure (white solid, mass = 185 mg, 85% yield); ¹H NMR (400 MHz, CDCl₃) δ 7.4 – 7.3 (m, 5H), 7.0 (s, 1H), 6.0 (s, 1H), 4.5 (d, *J* = 5.8 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 164.1, 136.7, 128.8, 127.9, 127.6, 66.3, 44.1. ¹³C{H} NMR (101 MHz, CDCl₃) δ 164.1, 136.7, 128.8, 127.9, 127.6, 66.3, 44.1.

Compound characterization is in accordance with previous reports.¹⁴

N-benzyl-2,2,2-trifluoroacetamide (5da); The compound was prepared as described in the general procedure (pale solid, mass = 114 mg, 56% yield); ¹H NMR (400 MHz, CDCl₃) δ 7.4 – 7.2 (m, 5H), 6.8 (s, 1H), 4.5 (d, *J* = 5.8 Hz, 2H). ¹³C{H} NMR (101 MHz, CDCl₃) δ 157.2(q, *J* c-F = 36.5 Hz, 1C), 156.9, 135.8, 128.9, 128.21, 128.17, 127.9, 115.8 (q, *J*c-F = 286.8 Hz, 1C)120.1, 117.2, 114.4, 43.8. ¹⁹F NMR (376 MHz, CDCl₃) δ -77.3.

Compound characterization is in accordance with previous reports.¹³



N-benzyl-2-cyanoacetamide (5ea); The compound was prepared as described in the general procedure (white solid, mass = 151 mg, 87% yield); ¹H NMR (300 MHz, CDCl₃) δ 7.3 – 7.2 (m, 5H), 6.5 (s, 1H), 4.4 (s, 2H), 3.3 (s, 2H). ¹³C{H} NMR (75 MHz, CDCl₃) δ 159.8, 135.8, 127.9, 127.01, 126.9, 113.6, 43.4, 24.8.

Compound characterization is in accordance with previous reports.¹⁵



N-Benzyl-3,3,3-trifluoropropanamide (5fa); The compound was prepared as described in the general procedure (white solid, mass = 210 mg, 97% yield); ¹**H** NMR (400 MHz, CDCl₃) δ 7.4 – 7.3 (m, 5H), 6.2 (s, 1H), 4.5 (d, *J* = 4.3 Hz, 2H), 3.1 (q, *J* = 10.0 Hz, 2H). ¹³C{H} NMR (101 MHz, CDCl₃) δ 162.4, 137.2, 128.7, 127.7, 125.3, 43.9, 41.6 (q, *J*_{C-F} = 29.4 Hz, 1C), ¹⁹F NMR (376 MHz, CDCl₃) δ -64.4 (t, *J*_{C-F} = 10.6 Hz, 1C).

Compound characterization is in accordance with previous reports.^{16, 17}

N-benzylhexanamide (5ga); The compound was prepared as described in the general procedure (yellow solid, mass = 203mg, 99% yield); ¹H NMR (400 MHz, CDCl₃) δ 7.36 – 7.22 (m, 5H), 5.90 (s, 1H), 4.41 (d, *J* = 5.8 Hz, 2H), 2.19 (t, *J* = 7.6 Hz, 2H), 1.65 (q, *J* = 7.4 Hz, 2H), 1.36 – 1.25 (m, 4H), 0.94 – 0.84 (m, 3H). ¹³C{H} NMR (101 MHz, CDCl₃) δ 172.9, 138.4, 128.6, 127.7, 127.3, 43.4, 36.6, 31.4, 25.4, 22.3, 13.8.

Compound characterization is in accordance with previous reports.¹



N-benzylcyclohexanecarboxamide (5ha); The compound was prepared as described in the general procedure (yellow solid, mass = 214mg, 99% yield); ¹**H** NMR (400 MHz, CDCl₃) δ 7.37 – 7.23 (m, 5H), 5.72 (s, 1H), 4.43 (d, *J* = 5.7 Hz, 2H), 2.11 (tt, *J* = 11.8, 3.5 Hz, 1H), 1.93 – 1.85 (m, 2H), 1.84 – 1.74 (m, 2H), 1.70 – 1.63 (m, 1H), 1.46 (qd, *J* = 12.1, 3.2 Hz, 2H), 1.34 – 1.14 (m, 3H). ¹³C{H} NMR (101 MHz, CDCl₃) δ 175.8, 138.5, 128.6, 127.6, 127.3, 45.5, 43.3, 29.6, 25.6. Compound characterization is in accordance with previous reports.¹



(3r,5r,7r)-*N*-benzyladamantane-1-carboxamide (5ia); The compound was prepared as described in the general procedure (white solid, mass = 223 mg, 83% yield); ¹H NMR (400 MHz, CDCl₃) δ 7.37 – 7.29 (m, 2H), 7.31 – 7.22 (m, 3H), 5.86 (s, 1H), 4.44 (d, *J* = 5.6 Hz, 2H), 2.04 (s, 3H), 1.89 (d, *J* = 3.2 Hz, 6H), 1.78 – 1.67 (m, 6H). ¹³C{H} NMR (101 MHz, CDCl₃) δ 177.7, 138.6, 128.6, 127.6, 127.3, 43.2, 40.6, 39.2, 36.4, 28.0.

Compound characterization is in accordance with previous reports.¹⁴



N-benzyl-2-phenylacetamide (5ja); The compound was prepared as described in the general procedure (white solid, mass = 211 mg, 94% yield); ¹H NMR (400 MHz, CDCl₃) δ 7.39 – 7.22 (m, 8H), 7.21 – 7.14 (m, 2H), 5.73 (s, 1H), 4.41 (d, *J* = 5.8 Hz, 2H), 3.62 (s, 2H). ¹³C{H} NMR (101 MHz, CDCl₃) δ 170.7, 138.0, 134.7, 129.4, 129.0, 128.6, 127.4, 127.3, 43.8, 43.5. Compound characterization is in accordance with previous reports.¹



N-benzyl-2-(naphthalen-1-yl)acetamide (5ka); The compound was prepared as described in the general procedure (white solid, mass = 272 mg, 99% yield); ¹**H NMR** (400 MHz, CDCl₃) δ 8.04 – 7.97 (m, 1H), 7.88 (dd, J = 7.0, 2.5 Hz, 1H), 7.82 (dd, J = 7.8, 2.6 Hz, 1H), 7.60 – 7.48 (m, 2H), 7.48 – 7.39 (m, 2H), 7.18 (dd, J = 5.1, 1.9 Hz, 3H), 7.00 (dd, J = 7.0, 2.6 Hz, 2H), 5.59 (s, 1H), 4.35 (d, J = 5.9 Hz, 2H), 4.09 (s, 2H). ¹³C{H} **NMR** (101 MHz, CDCl₃) δ 170.7, 138.0, 133.9, 132.0, 130.9, 128.7, 128.5, 128.4, 128.3, 127.1, 126.7, 126.2, 125.5, 123.8, 43.3, 41.8. Compound characterization is in accordance with previous reports.¹



N-benzyl-2-(4-isobutylphenyl)propenamide (5la); The compound was prepared as described in the general procedure (white solid, mass = 290 mg, 98% yield); ¹H NMR (400 MHz, CDCl₃) δ 7.3 – 7.2 (m, 5H), 7.1 – 7.1 (m, 4H), 4.4 (s, 2H), 3.6 (q, *J* = 7.2 Hz, 1H), 2.5 (d, *J* = 7.2 Hz, 2H), 1.9 (dq, *J* = 13.8, 6.8 Hz, 1H), 1.5 (d, *J* = 7.2 Hz, 3H), 0.9 (d, *J* = 6.6 Hz, 6H). ¹³C{H} NMR (101 MHz, CDCl₃) δ 174.2, 140.6, 138.5, 138.3, 129.5, 128.5, 127.3, 127.2, 46.6, 44.9, 43.2, 30.1, 22.3, 18.4.

Compound characterization is in accordance with previous reports.¹



N-benzyl-2-hydroxy-2-phenylacetamide (5ma); The compound was prepared as described in the general procedure (orange solid, mass = 156 mg, 65% yield); ¹H NMR (400 MHz, CDCl₃) δ 7.41 – 7.25 (m, 8H), 7.20 – 7.14 (m, 2H), 6.56 (s, 1H), 5.04 (s, 1H), 4.42 (t, *J* = 6.0 Hz, 2H). ¹³C{H} NMR (101 MHz, CDCl₃) δ 172.0, 139.3, 137.6, 128.8, 128.6, 128.6, 127.5, 126.7, 74.1, 43.4. Compound characterization is in accordance with previous reports.¹⁸



N-benzyl-2-phenoxyacetamide (5na); The compound was prepared as described in the general procedure (yellow solid, mass = 239 mg, 99% yield); ¹H NMR (400 MHz, CDCl₃) δ 7.37 – 7.26 (m, 7H), 7.02–7.00 (m, 1H), 6.91 (dd, *J* = 8.8, 1.1 Hz, 2H), 4.56 (d, *J* = 1.8 Hz, 2H), 4.55 (s, 2H). ¹³C{H} NMR (101 MHz, CDCl₃) δ 168.1, 157.0, 137.7, 129.7, 128.7, 127.6, 127.5, 122.1, 114.6, 67.25, 42.88.

Compound characterization is in accordance with previous reports.¹



N-benzylpentadecanamide (50a); The compound was prepared as described in the general procedure (white solid, mass = 310 mg, 93% yield); ¹H NMR (300 MHz, CDCl₃) δ 7.3 – 7.2 (m, 5H), 5.7 (s, 1H), 4.4 (d, J = 5.7 Hz, 2H), 2.2 – 2.1 (m, 2H), 1.6 (p, J = 7.4 Hz, 2H), 1.2 (s, 22H), 0.81 (t, J = 7.5 Hz, 3H). ¹³C{H} NMR (75 MHz, CDCl₃) δ 171.9, 137.4, 127.7, 126.8, 126.5, 42.6, 35.8, 30.9, 28.6, 28.5, 28.3, 24.8, 21.7, 13.1.

Compound characterization is in accordance with previous reports.¹⁹



N-benzyl-10-undecenamide (5pa); The compound was prepared as described in the general procedure (white solid, mass = 236 mg, 86% yield); ¹H NMR (300 MHz, CDCl₃) δ 7.4 – 7.2 (m, 5H), 5.9 – 5.7 (m, 1H), 5.0 – 4.9 (m, 2H), 4.4 (s, 2H), 3.5 (s, 1H), 2.2 (t, *J* = 7.6 Hz, 2H), 2.0 (q, *J* = 6.4 Hz, 2H), 1.6 (q, *J* = 7.3 Hz, 2H), 1.3 (s, 10H). ¹³C{H} NMR (75 MHz, CDCl₃) δ 173.0, 139.2, 138.4, 128.7, 127.8, 127.5, 114.2 43.4, 36.8, 33.8, 29.3, 29.1, 28.9, 25.8. Compound characterization is in accordance with previous reports.¹



N-benzylundec-10-ynamide (5qa); The compound was prepared as described in the general procedure (white solid, mass = 255mg, 94% yield); ¹H NMR (300 MHz, CDCl₃) δ 7.2 – 7.2 (m, 5H), 4.4 (s, 2H), 2.1 (dt, *J* = 9.6, 7.2 Hz, 4H), 1.9 (t, *J* = 2.6 Hz, 1H), 1.6 (t, *J* = 7.5 Hz, 2H), 1.4 (q, *J* = 7.2 Hz, 2H), 1.2 (s, 8H). ¹³C{H} NMR (75 MHz, CDCl₃) δ 171.8, 137.4, 127.7, 126.8, 126.5, 83.7, 76.4, 76.2, 76.0, 75.6, 67.1, 42.4, 35.7, 28.2, 27.9, 27.6, 27.4, 24.7, 17.3. Compound characterization is in accordance with previous reports.²⁰



ethyl 6-(benzylamino)-6-oxohexanoate (5ra); The compound was prepared as described in the general procedure (pale solid, mass = 229 mg, 88% yield); ¹H NMR (300 MHz, CDCl₃) δ 7.3 – 7.1 (m, 5H), 6.2 (s, 1H), 4.3 (d, J = 5.8 Hz, 2H), 4.0 (q, J = 7.1 Hz, 2H), 2.3 – 2.2 (m, 2H), 2.2 – 2.1 (m, 2H), 1.6 – 1.5 (m, 4H), 1.2 (t, J = 7.1 Hz, 3H). ¹³C{H} NMR (75 MHz, CDCl₃) δ 172.5, 171.5, 137.4, 127.6, 126.7, 126.4, 59.3, 42.5, 35.1, 32.9, 24.1, 23.4, 13.2. HRMS (ESI) m/z: [M+H] calculated for C₁₅H₂₂NO₃⁺: 264.1599, found 264.1594.



N-Hexanoylmorpholine (5gd); The compound was prepared as described in the general procedure (yellow oil, mass = 168 mg, 91% yield); ¹H NMR (400 MHz, CDCl₃) δ 3.65 (t, *J* = 4.8 Hz, 4H), 3.63 – 3.56 (m, 2H), 3.48 – 3.41 (m, 2H), 2.28 (t, *J*=3.6, 2H), 1.63 (q, *J* = 7.7 Hz, 2H), 1.36 – 1.28 (m, 4H), 0.89 (t, *J* = 3.5 Hz, 3H). ¹³C{H} NMR (101 MHz, CDCl₃) δ 171.8, 66.9, 66.6, 46.0, 41.8, 33.0, 31.5, 24.8, 22.4, 13.8.

Compound characterization is in accordance with previous reports.²¹



1-Morpholino-2-phenylethan-1-one (5jd); The compound was prepared as described in the general procedure (white soild, mass = 201 mg, 98% yield); ¹**H** NMR (400 MHz, CDCl₃) δ 7.31 (t, *J* = 7.2 Hz, 2H), 7.28 – 7.19 (m, 3H), 3.72 (s, 2H), 3.63 (s, 4H), 3.50 – 3.43 (m, 2H), 3.45 – 3.37 (m, 2H). ¹³C{H} NMR (101 MHz, CDCl₃) δ 169.5, 134.7, 128.7, 128.4, 126.8, 66.7, 66.3, 46.4, 42.0, 40.7.

Compound characterization is in accordance with previous reports.¹⁴



N-benzyl-*N*-methyl-2-phenylacetamide (5ji); The compound was prepared as described in the general procedure (pale oil, mass = 69 mg, 29% yield); ¹H NMR (300 MHz, CDCl₃, mixture of two rotamers 1.4/1) δ (Major rotamer) 7.3 – 7.0 (m, 10H), 4.53 (s, 2H), 3.7 (s, 2H), 3.7 (s, 0H), 2.81 (s, 3H). (Minor rotamer) 7.3 – 7.0 (m, 10H), 4.44 (s, 2H), 3.67 (s, 2H), 2.87 (s, 3H). ¹³C NMR **{H}** (75 MHz, CDCl₃) δ 170.4, 170.1, 136.3, 135.5, 134.1, 133.9, 127.9, 127.80, 127.76, 127.7, 127.5, 127.0, 126.6, 126.3, 125.80, 125.75, 125.4, 52.6, 49.9, 40.2, 39.8, 34.2, 33.0. Compound characterization is in accordance with previous reports.



N-phenylpentadecanamide (50e); The compound was prepared as described in the general procedure (white solid, mass = 188 mg, 60% yield); ¹H NMR (300 MHz, CDCl₃) δ 7.4 (d, *J* = 7.5 Hz, 2H), 7.3 – 7.2 (m, 2H), 7.0 (t, *J* = 7.4 Hz, 1H), 2.3 (t, *J* = 7.5 Hz, 2H), 1.7 – 1.6 (m, 2H), 1.2 (s, 22H), 0.80 (t, *J* = 7.5 Hz, 3H). ¹³C{H} NMR (75 MHz, CDCl₃) δ 170.5, 137.0, 127.9, 123.1, 118.7, 36.8, 30.9, 28.6, 28.6, 28.5, 28.4, 28.3, 24.6, 21.7, 13.1.

Compound characterization is in accordance with previous reports.¹⁹

n-C₅H₁₁

N-Phenylhexanamide (5ge); The compound was prepared as described in the general procedure (yellow solid, mass = 149 mg, 78% yield); ¹**H NMR** (400 MHz, CDCl₃) δ 7.52 (d, *J* = 8.5 Hz, 2H), 7.30 (t, *J* = 8.0 Hz, 2H), 7.09 (t, *J* = 7.4 Hz, 1H), 2.34 (t, *J* = 7.6 Hz, 2H), 1.73 (q, *J* = 7.6 Hz, 2H), 1.38 – 1.31 (m, 4H), 0.91 (t, *J* = 3.5 Hz, 3H). ¹³C{**H**} **NMR** (101 MHz, CDCl₃) δ 171.4, 137.92, 128.9, 124.0, 119.7, 37.7, 31.3, 25.2, 22.3, 13.8.

Compound characterization is in accordance with previous reports.²¹

3,3,3-Trifluoro-N-phenylpropanamide (5fe); The compound was prepared as described in the general procedure (white solid, mass = 196 mg, 97% yield); ¹**H** NMR (400 MHz, CDCl₃) δ 7.6 (s, 1H), 7.5 (d, *J* = 7.2 Hz, 2H), 7.3 (t, *J* = 7.8 Hz, 2H), 7.2 (t, *J* = 7.4 Hz, 1H), 3.2 (q, *J* = 10.4 Hz, 2H). ¹³C{H} NMR (101 MHz, CDCl₃) δ 160.8, 136.7, 129.0, 125.3, 120.4, 42.5 (q, *J*_{C-F} = 29.3 Hz, 1C). ¹⁹**F** NMR (376 MHz, CDCl₃) δ -64.4 (t, *J*_{C-F} = 10.4 Hz)... Compound characterization is in accordance with previous reports.¹⁶



2, *N*-diphenylacetamide (5je); The compound was prepared as described in the general procedure (white solid, mass = 173 mg, 82% yield); ¹H NMR (400 MHz, CDCl₃) δ 7.45-7.37 (m, 4H), 7.36-7.31(m, 3H), 7.32 – 7.23 (m, 2H), 7.17 (s, 1H), 7.08 (t, *J* = 7.2 Hz, 1H), 3.73 (s, 2H). ¹³C{H} NMR (101 MHz, CDCl₃) δ 169.0, 137.5, 134.3, 129.5, 129.2, 128.9, 127.6, 124.4, 119.7, 44.8. Compound characterization is in accordance with previous reports.¹⁸



N-(3-bromophenyl)-2-phenylacetamide (5jf); The compound was prepared as described in the general procedure (gray solid, mass = 274mg, 94% yield); ¹H NMR (300 MHz, CDCl₃) δ 7.6 (s, 1H), 7.6 (t, J = 2.1 Hz, 1H), 7.3 – 7.2 (m, 6H), 7.1 (d, J = 8.5 Hz, 1H), 7.0 (t, J = 8.0 Hz, 1H), 3.6 (s, 2H). ¹³C{H} NMR (75 MHz, CDCl₃) δ 168.6, 137.9, 133.1, 129.2, 128.4, 128.1, 126.6, 126.3, 121.8, 121.4, 117.4, 43.5.

Compound characterization is in accordance with previous reports.²²



N-(4-Methoxy-phenyl)-2-phenyl-acetamide (5jg); The compound was prepared as described in the general procedure (white solid, mass = 239 mg, 99% yield); ¹H NMR (400 MHz, CDCl₃) δ 7.4 – 7.4 (m, 2H), 7.4 – 7.3 (m, 5H), 7.1 (s, 1H), 6.8 (d, *J* = 9.1 Hz, 2H), 3.8 (s, 3H), 3.7 (s, 2H). ¹³C{H} NMR (101 MHz, CDCl₃) δ 168.9, 156.4, 134.5, 130.6, 129.4, 129.1, 127.5, 121.7, 114.0, 55.4, 44.6.

Compound characterization is in accordance with previous reports.²²



2-Phenyl-N-((R)-1-phenylethyl)acetamide (5jj); The compound was prepared as described in the general procedure (yellow solid, mass = 36 mg, 57% yield); ¹H NMR (300 MHz, CDCl₃) δ 7.3 -7.1 (m, 10H), 5.5 (s, 1H), 5.1 -5.0 (p, J = 6.9 Hz, 1H), 3.5 (s, 2H), 1.3 (d, J = 6.9 Hz, 3H). ¹³C NMR {H} (75 MHz, CDCl₃) δ 169.0, 142.0, 133.9, 128.4, 128.0, 127.6, 126.3, 126.3, 124.9, 47.7, 42.9, 20.8. $[\alpha]_D$ +3.4 (c = 1.0, CHCl₃).

Compound characterization is in accordance with previous reports.²³



(9H-fluoren-9-yl)methyl (2-(benzylamino)-2-oxoethyl)carbamate (7aa); The compound was prepared as described in the general procedure (white solid, mass = 241 mg, 62% yield); ¹H NMR (300 MHz, CDCl₃) δ 7.7 (d, J = 7.2 Hz, 2H), 7.5 (d, J = 7.4 Hz, 2H), 7.3 (t, J = 7.3 Hz, 2H), 7.3 – 7.1 (m, 8H), 6.3 (s, 1H), 5.5 (s, 1H), 4.3 (dd, J = 11.4, 6.3 Hz, 4H), 4.1 (t, J = 6.9 Hz, 1H), 3.8 (d, J = 5.6 Hz, 2H). ¹³C{H} NMR (75 MHz, CDCl₃) δ 167.7, 155.6, 142.6, 140.3, 136.6, 127.7, 126.75, 126.68, 126.6, 126.1, 124.0, 119.0, 66.1, 46.0, 43.5, 42.5.

Compound characterization is in accordance with previous reports.²⁴



tert-butyl (2-(benzylamino)-2-oxoethyl)carbamate (7ba); The compound was prepared as described in the general procedure (yellow solid, mass = 231 mg, 88% yield); ¹H NMR (300 MHz, $CDCl_3$) δ 7.2 – 7.1 (m, 5H), 6.9 (s, 1H), 5.5 (t, J = 5.8 Hz, 1H), 4.3 (d, J = 5.8 Hz, 2H), 3.7 (d, J = 5.8 Hz, 2H), 5.7 Hz, 2H), 1.3 (s, 9H). ¹³C{H} NMR (75 MHz, CDCl₃) δ 168.6, 155.2, 137.0, 127.6, 126.6, 126.4, 79.1, 43.3, 42.3, 27.2.

Compound characterization is in accordance with previous reports.¹



ethyl (((9H-fluoren-9-yl)methoxy)carbonyl)glycyl-L-phenylalaninate (7ak); The compound was prepared as described in the general procedure (yellow solid, mass = 470 mg, 99% yield); ¹H **NMR** (400 MHz, CDCl₃) δ 7.8 (d, J = 7.6 Hz, 2H), 7.6 (d, J = 7.6 Hz, 2H), 7.4 (t, J = 7.4 Hz, 2H), 7.3 (t, J = 7.5 Hz, 2H), 7.2 (dd, J = 14.0, 7.2 Hz, 3H), 7.1 (d, J = 7.2 Hz, 2H), 6.8 (s, 1H), 5.8 (t, J = 7.5 Hz, 2H), 6.8 (t, J = 7.5 Hz, 2H), 7.5 Hz, 2H, 7.5 Hz, 7. = 5.7 Hz, 1H), 4.9 - 4.8 (m, 1H), 4.4 (d, J = 7.6 Hz, 2H), 4.2 (t, J = 7.2 Hz, 1H), 4.1 (q, J = 7.2Hz, 2H), 3.9 (t, J = 5.7 Hz, 2H), 3.2 – 3.0 (m, 2H), 1.3 – 1.2 (m, 3H). ¹³C{H} NMR (101 MHz,

CDCl₃) δ 171.3, 168.7, 156.5, 143.7, 141.2, 135.7, 129.2, 128.4, 127.7, 127.0, 125.0, 119.9, 67.2, 61.5, 53.2, 47.0, 44.3, 37.84, 14.0.

Compound characterization is in accordance with previous reports.²⁵



ethyl (tert-butoxycarbonyl)glycyl-L-phenylalaninate (7bk); The compound was prepared as described in the general procedure (yellow oil, mass = 348 mg, 99% yield); ¹H NMR (300 MHz, CDCl₃) δ 7.2 – 7.1 (m, 3H), 7.1 – 7.0 (m, 2H), 6.8 (s, 1H), 5.4 (t, *J* = 5.9 Hz, 1H), 4.8 (q, *J* = 6.1 Hz, 1H), 4.0 (q, *J* = 7.2 Hz, 2H), 3.8 – 3.6 (m, 2H), 3.0 (dd, *J* = 6.1, 3.0 Hz, 2H), 1.4 (s, 9H), 1.1 (t, *J* = 7.1 Hz, 3H). ¹³C{H} NMR (75 MHz, CDCl₃) δ 170.40, 168.4, 155.0, 134.8, 128.3, 127.5, 126.0, 79.0, 60.5, 52.2, 43.1, 36.9, 27.3, 13.0.

Compound characterization is in accordance with previous reports.²⁶



Boc-gly-gly-L-phenylalaninate (7ck); The compound was prepared as described in the general procedure (yellow solid, mass = 256 mg, 63% yield); ¹H NMR (400 MHz, CDCl₃) δ 7.3 – 7.2 (m, 3H), 7.1 (d, *J* = 6.6 Hz, 2H), 5.5 (s, 1H), 4.8 (q, *J* = 6.4 Hz, 1H), 4.1 (q, *J* = 7.1 Hz, 2H), 4.0 – 3.8 (m, 2H), 3.8 (d, *J* = 5.7 Hz, 2H), 3.1 (qd, *J* = 13.9, 6.5 Hz, 2H), 1.4 (s, 9H), 1.2 (t, *J* = 7.1 Hz, 3H). ¹³C{H} NMR (101 MHz, CDCl₃) δ 171.4, 170.1, 168.6, 156.0, 135.8, 129.2, 128.4, 127.0, 80.0, 61.4, 53.4, 44.0, 42.7, 37.8, 28.2, 13.9. HRMS (ESI) m/z: [M+H] calculated for C₂₀H₃₀N₃O₆⁺: 408.2134, found 408..21282128.

References

(1) Ramachandran, P. V.; Hamann, H. J. Ammonia-borane as a Catalyst for the Direct Amidation of Carboxylic Acids. *Org. Lett.* **2021**, *23* (8), 2938-2942.

(2) Yao, B.; Jaccoud, C.; Wang, Q.; Zhu, J. Synergistic effect of palladium and copper catalysts: catalytic cyclizative dimerization of ortho-(1-alkynyl)benzamides leading to axially chiral 1,3-butadienes. *Chem. Eur. J.* **2012**, *18* (19), 5864-5868.

(3) Wang, W.-Q.; Yuan, Y.; Miao, Y.; Yu, B.-Y.; Wang, H.-J.; Wang, Z.-Q.; Sang, W.; Chen, C.; Verpoort, F. Well-defined N-heterocyclic carbene/ruthenium complexes for the alcohol amidation with amines: The dual role of cesium carbonate and improved activities applying an added ligand. *Appl Organometal Chem.* **2020**, *34* (2), e5323.

(4) Feng, C.-L.; Yin, G.-B.; Yan, B.; Chen, J.-Q.; Ji, M. FeCl2·4H2O catalyzed ritter reaction with nitriles and halohydrocarbons. *Chemical Papers* **2019**, *73* (2), 345-353.

(5) Sawant, D. N.; Bagal, D. B.; Ogawa, S.; Selvam, K.; Saito, S. Diboron-Catalyzed Dehydrative Amidation of Aromatic Carboxylic Acids with Amines. *Org. Lett.* **2018**, *20* (15), 4397-4400.

(6) Kerdphon, S.; Quan, X.; Parihar, V. S.; Andersson, P. G. C–N Coupling of Amides with Alcohols Catalyzed by N-Heterocyclic Carbene–Phosphine Iridium Complexes. *J. Org. Chem.* **2015**, *80* (22), 11529-11537.

(7) Su, J.; Mo, J.-N.; Chen, X.; Umanzor, A.; Zhang, Z.; Houk, K. N.; Zhao, J. Generation of Oxyphosphonium Ions by Photoredox/Cobaloxime Catalysis for Scalable Amide and Peptide Synthesis in Batch and Continuous-Flow. *Angew. Chem. Int. Ed.* 2022, *61* (5), e202112668.
(8) Papp, M.; Szabó, P.; Srankó, D.; Sáfrán, G.; Kollár, L.; Skoda-Földes, R. Mono- and double carbonylation of aryl iodides with amine nucleophiles in the presence of recyclable palladium catalysts immobilised on a supported dicationic ionic liquid phase. *RSC Adv.* 2017, *7* (70), 44587-44597, 10.1039/C7RA04680D.

(9) Bolduc, T. G.; Lee, C.; Chappell, W. P.; Sammis, G. M. Thionyl Fluoride-Mediated One-Pot Substitutions and Reductions of Carboxylic Acids. *J. Org. Chem.* 2022, *87* (11), 7308-7318.
(10) Ramkumar, R.; Chandrasekaran, S. Catalyst-Free, Metal-Free, and Chemoselective Transamidation of Activated Secondary Amides. *Synthesis* 2019, *51* (04), 921-932.

(11) Bousfield, T. W.; Pearce, K. P. R.; Nyamini, S. B.; Angelis-Dimakis, A.; Camp, J. E. Synthesis of amides from acid chlorides and amines in the bio-based solvent CyreneTM. *Green Chem.* **2019**, *21* (13), 3675-3681, 10.1039/C9GC01180C.

(12) Xiong, N.; Dong, Y.; Xu, B.; Li, Y.; Zeng, R. Mild Amide Synthesis Using Nitrobenzene under Neutral Conditions. *Org. Lett.* **2022**, *24* (26), 4766-4771.

(13) Ramachandran, P. V.; Hamann, H. J.; Choudhary, S. Amine-boranes as Dual-Purpose Reagents for Direct Amidation of Carboxylic Acids. *Org. Lett.* **2020**, *22* (21), 8593-8597.

(14) Lundberg, H.; Tinnis, F.; Adolfsson, H. Titanium(IV) Isopropoxide as an Efficient Catalyst for Direct Amidation of Nonactivated Carboxylic Acids. *Synlett.* **2012**, *23* (15), 2201-2204.

(15) Gao, G.; Li, Z. Metal-free synthesis of ketonitriles via C–F bond cleavage. *New J. Chem.* **2023**, *47* (13), 6171-6175, 10.1039/D2NJ06338G.

(16) Du, X.; Zhang, W.-M.; Zhang, X.-G.; Tu, H.-Y. Palladium-Catalyzed Selective C-F Bond Cleavage of Trifluoropropanamides Leading to (Z)-N-α-Fluorovinylindoles. *Adv. Synth.Catal.* **2022**, *364* (15), 2546-2550.

(17) Sato, K.; Yuki, T.; Yamaguchi, R.; Hamano, T.; Tarui, A.; Omote, M.; Kumadaki, I.; Ando, A. Mechanistic Studies on α -Trifluoromethylation of Ketones via Silyl Enol Ethers and Its Application to Other Carbonyl Compounds. *J. Org. Chem.* **2009**, *74* (10), 3815-3819.

(18) Chaudhari, P. S.; Salim, S. D.; Sawant, R. V.; Akamanchi, K. G. Sulfated tungstate: a new solid heterogeneous catalyst for amide synthesis. *Green Chem.* **2010**, *12* (10), 1707-1710, 10.1039/C0GC00053A.

(19) Zhang, G.; Gao, B.; Huang, H. Palladium-Catalyzed Hydroaminocarbonylation of Alkenes with Amines: A Strategy to Overcome the Basicity Barrier Imparted by Aliphatic Amines. *Angew. Chem. Int. Ed.* **2015**, *54* (26), 7657-7661.

(20) Lamar, A. A.; Liebeskind, L. S. Carboxyl activation via silylthioesterification: one-pot, twostep amidation of carboxylic acids catalyzed by non-metal ammonium salts. *Tetrahedron Lett.* **2015**, *56* (44), 6034-6037. (21) Kar, S.; Xie, Y.; Zhou, Q. Q.; Diskin-Posner, Y.; Ben-David, Y.; Milstein, D. Near-Ambient-Temperature Dehydrogenative Synthesis of the Amide Bond: Mechanistic Insight and Applications. *ACS Catal.* **2021**, *11* (12), 7383-7393.

(22) Zhou, J.; Paladino, M.; Hall, D. G. Direct Boronic Acid Promoted Amidation of Carboxylic Acids with Poorly Nucleophilic Amines. *Eur. J. Org. Chem.* **2022**, *2022* (41), e202201050.

(23) Dam, J. H.; Osztrovszky, G.; Nordstrøm, L. U.; Madsen, R. Amide Synthesis from Alcohols and Amines Catalyzed by Ruthenium N-Heterocyclic Carbene Complexes. *Chem.Eur. J.* **2010**, *16* (23), 6820-6827.

(24) Suzuki, A.; Takagi, K.; Sato, K.; Wada, T. Synthesis of thioamides from thiocarboxylic acids using phosphonium-type condensing reagents. *Tetrahedron Lett.* **2021**, *75*, 153179.

(25) Wang, P.; Danishefsky, S. J. Promising General Solution to the Problem of Ligating Peptides and Glycopeptides. J. Am. Chem. Soc. **2010**, 132 (47), 17045-17051.

(26) Wang, S.-M.; Zhao, C.; Zhang, X.; Qin, H.-L. Clickable coupling of carboxylic acids and amines at room temperature mediated by SO2F2: a significant breakthrough for the construction of amides and peptide linkages. *Org. Biomol. Chem.* **2019**, *17* (16), 4087-4101, 10.1039/C9OB00699K.

NMR spectra of secondary and tertiary amides






































¹⁹F NMR (376 MHz, CDCl₃) *N*-(4-Trifluoromethylbenzoyl)morpholine (**3ed**)

















¹H NMR (400 MHz, CDCl₃) *N*-(4-Methoxyphenyl)benzamide (**3ag**)



¹H NMR (300 MHz, CDCl₃) 4-amino-5-chloro-N-(2-(diethylamino)ethyl)-2-methoxybenzamide (**3mh**)



















S55

























S66











S71






¹⁹F NMR (376 MHz, CDCl₃) 3,3,3-Trifluoro-*N*-phenylpropanamide (5fe)























