# Supplementary Information

# Direct esterification of amides by the dimethylsulfate-mediated activation of amide C–N bonds

**Contents**



## Supplementary Note 1

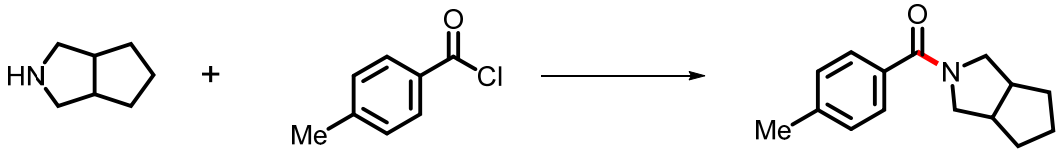
## General Information

All glassware was thoroughly oven-dried. Chemicals and solvents were either purchased from commercial suppliers or purified by standard techniques. Thin-layer chromatography plates were visualized by exposure to ultraviolet light and/or staining with ninhydrin hydrate followed by heating on a hot plate. Flash chromatography was carried out using silica gel (200−300 mesh). $^{1}$H NMR and $^{13}$C NMR spectra were recorded on a Brucker 400 Hz, 500 Hz, or 600 Hz instrument. Data for $^{1}$H NMR was presented as the chemical shift in ppm, and multiplicities were denoted as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. Data for $^{13}$C NMR were reported as chemical shift. The ESI mass spectra were determined on a Thermo Fisher FINNIGAN LTQ instrument. All high-resolution mass spectra (HRMS) results were obtained on an Agilent 1290-6545 UHPLC-QTOF LC/MS spectrometer or Thermo Scientific Orbitrap Exploris GC/MS spectrometer. Thin-layer chromatography (TLC) inspections were performed on silica gel plates (GF-254). All commercially available chemicals and solvents were directly used without further purification unless otherwise noted.

## Experimental section

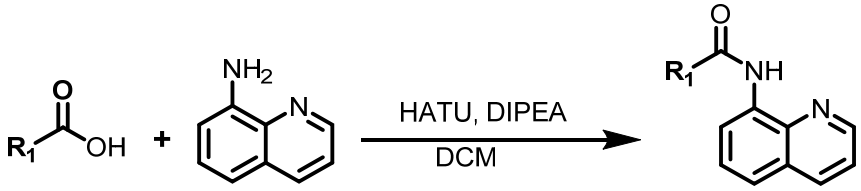
## Synthesis of

## (hexahydrocyclopenta[c]pyrrol-2(1H)-yl)(p-tolyl)-methanone 1hc



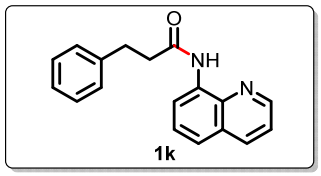

To a solution of octahydrocyclopenta[c]pyrrole (111 mg, 1.0 mmol, 1.0 equiv.) in dicholoromethane (5.0 mL) was slowly added 4-methylbenzoyl chloride (186 mg, 1.2 mmol, 1.2 equiv.) followed by triethylamine (152 mg, 1.5 mmol, 1.5 equiv.) at 0 °C. After complete addition, the reaction was allowed to stir continuously until all the starting material was consumed completely (monitored by TLC, approx. 3-5 h). After completion, the reaction mixture was quenched with water and extracted with dichloromethane. The combined organic layer was washed with brine solution, dried over $Na_2SO_4$. The product was purified by column chromatography on silica gel to afford pure compound **1hc** (202 mg, 88% yield) as a colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.38 (d, $J$ = 8.1 Hz, 2H), 7.19 (d, $J$ = 7.9 Hz, 2H), 3.84 (s, 1H), 3.71 – 3.40 (m, 2H), 3.22 (s, 1H), 2.66 (d, $J$ = 15.6 Hz, 2H), 2.37 (s, 3H), 1.94 – 1.67 (m, 3H), 1.67 – 1.45 (m, 2H), 1.35 (s, 1H). $^{13}$C{$^1$H}NMR (100 MHz, $CDCl_3$) $\delta$ 169.63, 139.79, 134.21, 128.82, 127.22, 55.36, 51.83, 43.82, 41.91, 32.32, 31.72, 25.60, 21.38. HRMS (EI): calcd for $C_{15}H_{19}NO$: 229.1467, found: 229.1465.

## General procedure for preparation of 8-aminoquinoline amide substrates



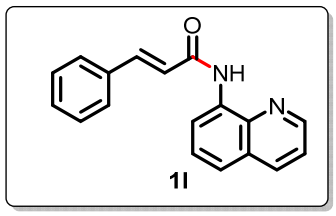

To a mixture of substituted carboxylic acids (1 mmol, 1.0 equiv) in dichloromethane (5 mL) was added 8-aminoquinoline (1.0 mmol, 1.0 equiv), HATU (1.0 mmol, 1.0 equiv) and followed by DIPEA (1.5 mmol, 1.5 equiv). After complete addition, the reaction was allowed to stir continuously until all the starting material was consumed completely (monitored by TLC, approx. 2-5 h). After completion, the reaction mixture was quenched with water and extracted with dichloromethane. The combined organic layer was washed with brine solution, dried over $Na_2SO_4$. The product was purified by column chromatography on silica gel to afford pure compounds.

**3-phenyl-N-(quinolin-8-yl)propanamide**



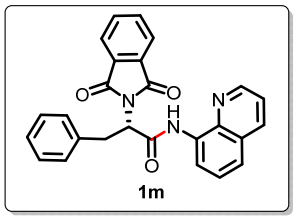

Following the general procedure compound **1k** was obtained from 3-phenylpropanoic acid (150 mg, 1.0 mmol). The crude product was purified by silica-gel column chromatography (DCM/MeOH = 100/1 to 30/1) to afford the title compound **1k**[1] (248 mg, 90%) as a white solid; m.p. 64–66 °C. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 10.01 (s, 1H), 8.91 (dd, $J$ = 7.5, 1.1 Hz, 1H), 8.82 (dd, $J$ = 4.2, 1.5 Hz, 1H), 8.16 (dd, $J$ = 8.3, 1.5 Hz, 1H), 7.82 (d, $J$ = 15.6 Hz, 1H), 7.64 – 7.49 (m, 4H), 7.48 – 7.35 (m, 4H), 6.79 (d, $J$ = 15.6 Hz, 1H). $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 170.74, 148.11, 140.81, 138.33, 136.36, 134.47, 128.58, 128.43, 127.94, 127.44, 126.26, 121.60, 121.46, 116.49, 39.74, 31.50. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{18}H_{17}N_2O$ 277.1136, found: 277.1134.

**N-(quinolin-8-yl)cinnamamide**



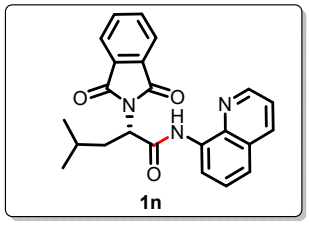

Following the general procedure compound **1l** was obtained from cinnamic acid (148 mg, 1.0 mmol). The crude product was purified by silica-gel column chromatography (DCM/MeOH = 100/1 to 30/1) to afford the title compound **1l**[2] (250 mg, 91%) as a white solid; m.p. 110-113 °C. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 10.01 (s, 1H), 8.91 (dd, $J$ = 7.5, 1.1 Hz, 1H), 8.82 (dd, $J$ = 4.2, 1.5 Hz, 1H), 8.16 (dd, $J$ = 8.3, 1.5 Hz, 1H), 7.82 (d, $J$ = 15.6 Hz, 1H), 7.64 – 7.49 (m, 4H), 7.48 – 7.35 (m, 4H), 6.79 (d, $J$ = 15.6 Hz, 1H). $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 164.15, 148.13, 142.11, 138.41, 136.51, 134.83, 134.65, 129.93, 128.89, 128.07, 128.00, 127.54, 121.69, 121.68, 121.58, 116.93. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{18}H_{15}N_2O$ 275.1179, found: 275.1176.

**(S)-2-(1,3-dioxoisoindolin-2-yl)-3-phenyl-N-(quinolin-8-yl)propanamide**




Following the general procedure compound **1m** was obtained from (S)-2-(1,3-dioxoisoindolin-2-yl)-3-phenylpropanoic acid (295 mg, 1.0 mmol). The crude product was purified by silica-gel column chromatography (DCM/MeOH = 100/1 to 30/1) to afford the title compound **1m**[3] (358 mg, 85%) as a white solid; m.p. 122 – 123 °C. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 10.25 (s, 1H), 8.66 (dd, $J$ = 6.4, 2.5 Hz, 1H), 8.53 (dd, $J$ = 4.2, 1.6 Hz, 1H), 8.04 (dd, $J$ = 8.3, 1.6 Hz, 1H), 7.74 (dd, $J$ = 5.5, 3.1 Hz, 2H), 7.63 (dd, $J$ = 5.5, 3.1 Hz, 2H), 7.49 – 7.38 (m, 2H), 7.31 (dd, $J$ = 8.3, 4.2 Hz, 1H), 7.22 – 7.06 (m, 5H), 5.38 (dd, $J$ = 9.8, 6.9 Hz, 1H), 3.78 – 3.69 (m, 2H). $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 166.85, 165.38, 147.24, 137.43, 135.69, 135.22, 133.14, 132.82, 130.60, 127.98, 127.66, 126.80, 126.27, 125.92, 122.51, 120.96, 120.58, 115.74, 55.20, 33.71. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{26}H_{20}N_3O_3$ 422.1499, found: 422.145.

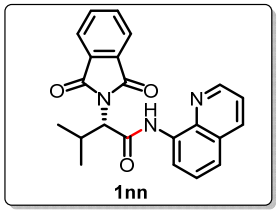
**(S)-2-(1,3-dioxoisoindolin-2-yl)-4-methyl-N-(quinolin-8-yl)pentanamide**




Following the general procedure compound **1n** was obtained from

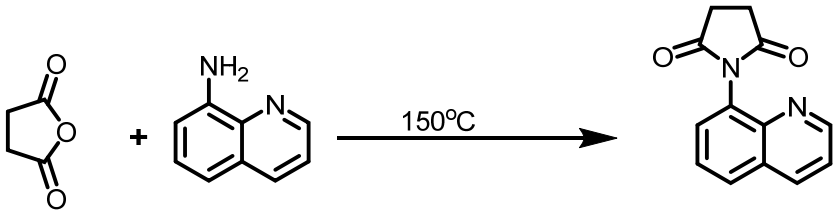
(S)-2-(1,3-dioxoisoindolin-2-yl)-4-methylpentanoic acid (261 mg, 1.0 mmol). The crude product was purified by silica-gel column chromatography (DCM/MeOH = 100/1 to 30/1) to afford the title compound **1n**[4] (340 mg, 88%) as a white solid; m.p. 103 – 106 °C. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 10.37 (s, 1H), 8.82 – 8.68 (m, 2H), 8.17 (dd, $J$ = 8.3, 1.6 Hz, 1H), 7.93 (dd, $J$ = 5.5, 3.1 Hz, 2H), 7.79 (dd, $J$ = 5.5, 3.1 Hz, 2H), 7.59 – 7.50 (m, 2H), 7.45 (dd, $J$ = 8.3, 4.3 Hz, 1H), 5.26 (dd, $J$ = 11.3, 5.0 Hz, 1H), 2.68 (ddd, $J$ = 13.9, 11.4, 4.3 Hz, 1H), 2.20 – 2.08 (m, 1H), 1.67 – 1.58 (m, 1H), 1.07 (dd, $J$ = 10.7, 6.6 Hz, 6H). $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 168.17, 167.39, 148.27, 138.42, 136.44, 134.21, 133.93, 131.92, 127.90, 127.38, 123.61, 121.90, 121.60, 116.88, 53.66, 37.42, 25.59, 23.25, 21.32. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{23}H_{22}N_3O_3$ 388.1656, found: 388.1654.

**(S)-2-(1,3-dioxoisoindolin-2-yl)-3-methyl-N-(quinolin-8-yl)butanamide**



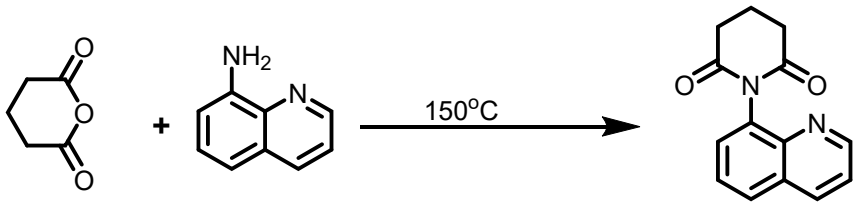

Following the general procedure compound **1nn** was obtained from (S)-2-(1,3-dioxoisoindolin-2-yl)-3-methylbutanoic acid (247 mg, 1.0 mmol). The crude product was purified by silica-gel column chromatography (DCM/MeOH = 100/1 to 30/1) to afford the title compound **1nn**[3] (317g, 85%) as a white solid; m.p. 112 – 114 °C. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 10.58 (s, 1H), 8.93 – 8.68 (m, 2H), 8.13 (dd, $J$ = 8.3, 1.6 Hz, 1H), 7.89 (dd, $J$ = 5.4, 3.1 Hz, 2H), 7.73 (dd, $J$ = 5.5, 3.0 Hz, 2H), 7.58 – 7.36 (m, 3H), 4.70 (d, $J$ = 10.8 Hz, 1H), 3.36 – 3.11 (m, 1H), 1.23 (d, $J$ = 6.6 Hz, 3H), 1.00 (d, $J$ = 6.6 Hz, 3H).$^{13}$C {$^1$H}NMR (100 MHz, $CDCl_3$) $\delta$ 168.14, 166.84, 148.53, 138.72, 136.19, 134.27, 131.63, 127.91, 127.25, 123.66, 121.98, 121.63, 117.00, 77.37, 77.06, 76.74, 63.22, 27.34, 20.48, 19.62. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{22}H_{20}N_3O_3$ 374.1499, found: 374.1496.

**1-(quinolin-8-yl)pyrrolidine-2,5-dione**



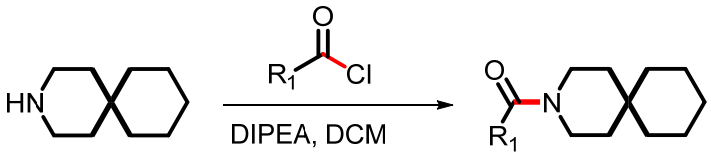

Succinic anhydride (118 mg, 1.18 mmol) and 8-aminoquinoline 5 (190 mg, 1.30 mmol) were dissolved in tetrahydrofuran (5 mL). The solvent was removed in vacuo and the residue was heated at 150 °C for 5 hours. The crude product was purified by silica-gel column chromatography (DCM/MeOH = 150/1 to 50/1) to afford the title compound **1of**[5] (253 mg, 95%) as an off-white solid; m.p. 186-188 °C. 1 H NMR (400 MHz, $CDCl_3$) $\delta$ 8.88 (dd, $J$ = 1.6 Hz, J = 4.2 Hz, 1 H), 8.20 (dd, $J$ = 1.6 Hz, J = 8.3 Hz, 1 H), 7.93 (dd, $J$ = 2.1 Hz, J = 7.4 Hz, 1 H), 7.66 – 7.60 (m, 2 H), 7.46 – 7.42 (m, 1 H), 3.20 – 2.91 (m, 4 H). $^{13}$C{$^1$H}NMR (100 MHz, $CDCl_3$) $\delta$ 176.90, 150.99, 143.47, 136.24, 130.15, 129.78, 129.46, 129.28, 126.14, 122.02, 28.95. HRMS (EI): calcd for $C_{13}H_{10}N_2O_2$: 226.0742, found: 226.0740

**1-(quinolin-8-yl)piperidine-2,6-dione**



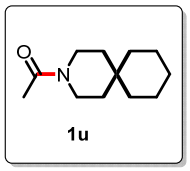

Glutaric anhydride (135 mg, 1.18 mmol) and 8-aminoquinoline 5 (190 mg, 1.30 mmol) were dissolved in tetrahydrofuran (5 mL). The solvent was removed in vacuo and the residue was heated at 150 °C for 5 hours. The crude product was purified by silica-gel column chromatography (DCM/MeOH = 150/1 to 50/1) to afford the title compound **1og**[6] (260 mg, 92%) as a foamy solid. $^{1}$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.84 (dd, $J$ = 4.1, 1.4 Hz, 1H), 8.19 (d, $J$ = 8.1 Hz, 1H), 7.89 (dd, $J$ = 8.1, 1.1 Hz, 1H), 7.67 – 7.51 (m, 2H), 7.41 (dd, $J$ = 8.2, 4.1 Hz, 1H), 2.99 (dd, $J$ = 15.1, 7.0 Hz, 2H), 2.88 (ddd, $J$ = 17.2, 7.6, 4.9 Hz, 2H), 2.31 (dd, $J$ = 7.9, 5.6 Hz, 1H), 2.24 – 2.09 (m, 1H). $^{13}$C{$^{1}$H}NMR (100 MHz, $CDCl_3$) $\delta$ 173.03, 150.77, 143.70, 136.45, 136.32, 133.48, 129.79, 129.22, 129.08, 126.18, 121.69, 33.06, 17.45.
HRMS (EI): calcd for $C_{14}H_{12}N_2O_2$: 240.2620, found: 240.2617.

## General procedure for preparation of 3-Azaspiro[5.5]undecane amide substrates



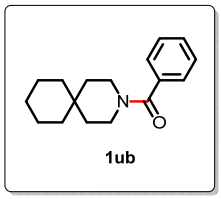

To a solution of 3-azaspiro[5.5]undecane (2.0 mmol, 1.0 equiv.) in dicholoromethane (5.0 mL) was slowly added respective acid chlorides (2.4 mmol, 1.2 equiv.) followed by triethylamine (3.0 mmol, 1.5 equiv.) at 0 ℃. After complete addition, the reaction was allowed to stir continuously until all the starting material was consumed completely (monitored by TLC, approx. 3-5 h). After completion, the reaction mixture was quenched with water and extracted with dichloromethane. The combined organic layer was washed with brine solution, dried over $Na_2SO_4$. The product was purified by column chromatography on silica gel to afford pure compounds.

**1-(3-Azaspiro[5.5]undecan-3-yl)ethan-1-one**



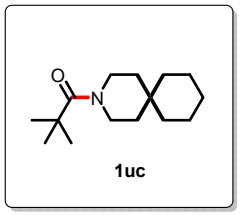

Following the general procedure compound **1u** was obtained from 3-azaspiro[5.5]undecane (306 mg, 2.0 mmol). The crude product was purified by silica-gel column chromatography (EA/PE = 10/1 to 4/1) to afford the title compound **1u** (277 mg, 80%) as a colorless oil;. $^{1}$H NMR (400 MHz, $CDCl_3$) $\delta$ 3.63 – 3.47 (m, 2H), 3.45 – 3.29 (m, 2H), 2.08 (s, 3H), 1.52 – 1.30 (m, 14H). $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$) $\delta$ 168.86, 42.37, 37.36, 36.11, 31.27, 26.64, 21.51, 21.39. HRMS (EI): calcd for $C_{12}H_{21}NO$: 195.1623, found: 195.1621.

**Phenyl(3-azaspiro[5.5]undecan-3-yl)methanone**



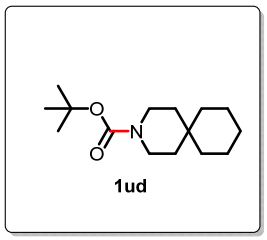

Following the general procedure compound **1ub** was obtained from 3-azaspiro[5.5]undecane (306 mg, 2.0 mmol). The crude product was purified by silica-gel column chromatography (EA/PE = 10/1 to 4/1) to afford the title compound **1ub** (437 mg, 85%) as a foamy solid. $^{1}$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.09 (d, $J$ = 8.9 Hz, 2H), 6.90 – 6.79 (m, 2H), 6.78 (s, 1H), 4.15 (q, $J$ = 7.1 Hz, 2H), 3.79 (s, 3H), 1.33 (t, $J$ = 7.1 Hz, 3H). $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$) $\delta$ 170.29, 136.53, 129.35, 128.39, 126.84, 36.22, 31.57, 26.67, 21.42. HRMS (EI): calcd for $C_{17}H_{33}NO$: 257.178, found: 257.176.

**2,2-Dimethyl-1-(3-azaspiro[5.5]undecan-3-yl)propan-1-one**



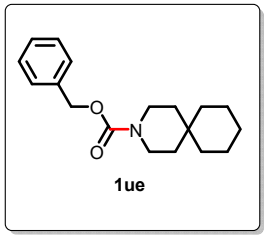

Following the general procedure compound **1uc** was obtained from 3-azaspiro[5.5]undecane (306 mg, 2.0 mmol). The crude product was purified by silica-gel column chromatography (EA/PE = 10/1 to 4/1) to afford the title compound **1uc** (394 mg, 83%) as a foamy solid. $^{1}$H NMR (400 MHz, $CDCl_3$) $\delta$ 3.61 – 3.47 (m, 4H), 1.40 (dd, $J$ = 14.9, 9.0 Hz, 14H), 1.27 (s, 9H). $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$) $\delta$ 176.16, 41.02, 38.65, 36.50, 36.39, 31.42, 28.46, 26.71, 21.46. HRMS (EI): calcd for $C_{15}H_{27}NO$: 237.2093, found: 237.2090.

**Tert-butyl 3-azaspiro[5.5]undecane-3-carboxylate**




Following the general procedure compound **1ud** was obtained from 3-azaspiro[5.5]undecane (306 mg, 2.0 mmol). The crude product was purified by silica-gel column chromatography (EA/PE = 10/1 to 4/1) to afford the title compound **1ud** (428 mg, 89%) as a colorless oil;. $^{1}$H NMR (400 MHz, $CDCl_3$) $\delta$ 3.44 – 3.27 (m, 4H), 1.50 – 1.30 (m, 23H). $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$) $\delta$ 155.05, 79.03, 39.40, 36.12, 31.06, 28.46, 26.73, 21.39. HRMS (EI): calcd for $C_{15}H_{27}NO_2$: 253.2042, found: 253.2040.

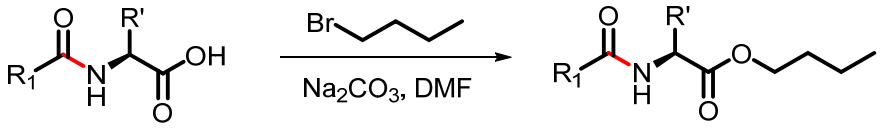
**Benzyl 3-azaspiro[5.5]undecane-3-carboxylate**




Following the general procedure compound **1ue** was obtained from 3-azaspiro[5.5]undecane (306 mg, 2.0 mmol). The crude product was purified by silica-gel column chromatography

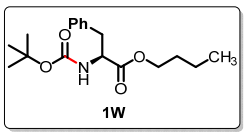
(EA/PE = 10/1 to 4/1) to afford the title compound **1ue** (436 mg, 89%) as a colorless oil;. $^{1}$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.43 – 7.20 (m, 5H), 5.12 (s, 2H), 3.50 – 3.37 (m, 4H), 1.51 – 1.26 (m, 14H). $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$) $\delta$ 155.46, 137.08, 128.46, 127.80, 66.88, 39.73, 36.10, 31.11, 26.71, 21.40. HRMS (EI): calcd for $C_{18}H_{25}NO_2$: 287.1885, found: 287.1882.

## General procedure for preparation of amino acids derivative with protective group substrates



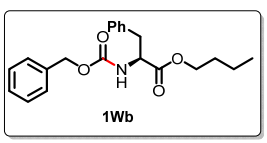

To a solution of amino acids (1.0 equiv.) derivatives in DMF (0.2 M) was added $Na_2CO_3$ (1.0 equiv.), n-bromobutane (1.2 equiv.) and heated for 2−3h at 65℃ in a sealed vial under an atmosphere of $N_2$ (monitored by TLC). Then the mixture was cooled to room temperature, quenched water, extracted with ethyl acetate, and washed with brine. The organic phase was dried over anhydrous $Na_2SO_4$ and concentrated. The residue was purified by column chromatography on silica gel to give pure products.

**Butyl (tert-butoxycarbonyl)-L-phenylalaninate**




Following the general procedure compound **1w** was obtained from (tert-butoxycarbonyl)-L-phenylalanine (265 mg, 1.0 mmol). The crude product was purified by silica-gel column chromatography (EA/PE = 6/1 to 2/1) to afford the title compound **1w**[7] (290 mg, 91%) as a foamy solid. $^{1}$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.33 – 7.25 (m, 3H), 7.16 (d, $J$ = 6.9 Hz, 2H), 5.00 (d, $J$ = 7.6 Hz, 1H), 4.59 (d, $J$ = 7.4 Hz, 1H), 4.17 – 4.11 (m, 2H), 3.10 (t, $J$ = 6.9 Hz, 2H), 1.63 – 1.55 (m, 2H), 1.44 (s, 9H), 1.29 (dd, $J$ = 14.2, 7.0 Hz, 2H), 0.94 (t, $J$ = 7.4 Hz, 3H). $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$) $\delta$ 171.97, 155.08, 136.12, 129.34, 128.49, 126.95, 79.82, 65.20, 54.48, 38.47, 30.51, 28.30, 19.04, 13.64.
HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{18}H_{28}NO_4$ 322.2013, found: 322.2011.

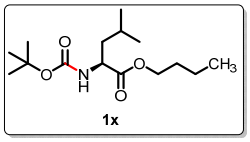
**Butyl ((benzyloxy)carbonyl)-L-phenylalaninate**




Following the general procedure compound **1wb** was obtained from ((benzyloxy)carbonyl)-L-phenylalanine (300 mg, 1.0 mmol). The crude product was purified by silica-gel column

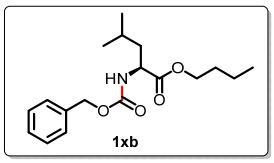
chromatography (EA/PE = 6/1 to 2/1) to afford the title compound **1wb**[8] (327 mg, 92%) as a foamy solid. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.42 – 7.19 (m, 8H), 7.17 – 7.04 (m, 2H), 5.24 (d, $J$ = 8.0 Hz, 1H), 5.09 (s, 2H), 4.65 (dd, $J$ = 14.0, 6.0 Hz, 1H), 4.20 – 4.00 (m, 2H), 3.10 (t, $J$ = 6.1 Hz, 2H), 1.56 (dd, $J$ = 14.5, 7.0 Hz, 2H), 1.31 (dd, $J$ = 15.0, 7.4 Hz, 2H), 0.91 (t, $J$ = 7.4 Hz, 3H). $^{13}$C{$^1$H}NMR (100 MHz, $CDCl_3$) $\delta$ 171.61, 155.63, 136.32, 135.80, 129.33, 128.58, 128.54, 128.19, 128.10, 127.10, 66.95, 65.39, 54.88, 38.36, 30.48, 19.05, 13.66. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{21}H_{26}NO_4$ 356.1856, found: 356.1852.

**Butyl (tert-butoxycarbonyl)-L-leucinate**



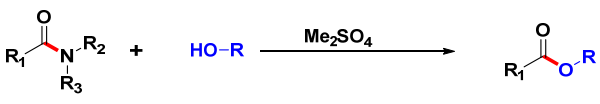

Following the general procedure compound **1x** was obtained from (tert-butoxycarbonyl)-L-leucine (231 mg, 1.0 mmol). The crude product was purified by silica-gel column chromatography (EA/PE = 6/1 to 2/1) to afford the title compound **1x** (256 mg, 90%) as a foamy solid. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.88 (d, $J$ = 7.7 Hz, 1H), 4.30 (d, $J$ = 5.4 Hz, 1H), 4.12 (td, $J$ = 6.7, 2.8 Hz, 2H), 1.71 (dd, $J$ = 14.1, 6.6 Hz, 1H), 1.62 (dt, $J$ = 8.5, 6.7 Hz, 3H), 1.53 – 1.47 (m, 1H), 1.44 (s, 9H), 1.40 – 1.33 (m, 2H), 0.96 – 0.93 (m, 9H). $^{13}$C{$^1$H}NMR (100 MHz, $CDCl_3$) $\delta$ 173.45, 155.17, 79.67, 65.04, 52.17, 41.98, 30.59, 28.33, 24.81, 22.81, 22.00, 19.08, 13.67. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{15}H_{30}NO_4$ 288.2169, found: 288.2165.

**Butyl ((benzyloxy)carbonyl)-L-leucinate**




Following the general procedure compound **1xb** was obtained from ((benzyloxy)carbonyl)-L-leucine (265 mg, 1.0 mmol). The crude product was purified by silica-gel column chromatography (EA/PE = 6/1 to 2/1) to afford the title compound **1xb**[8] (282 mg, 88%) as a foamy solid. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.38 – 7.30 (m, 5H), 5.13 (d, $J$ = 13.1 Hz, 3H), 4.38 (dd, $J$ = 14.0, 8.7 Hz, 1H), 4.13 (t, $J$ = 6.6 Hz, 2H), 1.74 – 1.58 (m, 4H), 1.55 – 1.47 (m, 1H), 1.38 (dd, $J$ = 14.9, 7.4 Hz, 2H), 0.94 (q, $J$ = 6.7 Hz, 9H). $^{13}$C{$^1$H}NMR (100 MHz, $CDCl_3$) $\delta$ 173.20, 155.94, 136.31, 128.53, 128.17, 128.09, 66.97, 65.22, 52.61, 41.98, 30.55, 24.78, 22.80, 21.95, 19.07, 13.67.
HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{18}H_{28}NO_4$ 322.2013, found: 322.2010.

## General procedure for amide esterification

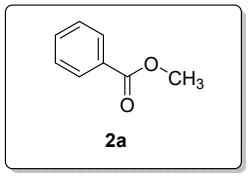



1 2

To a solution of amide **1** (1.0 equiv) in alcohols (0.2 M) was added dimethyl sulfate (1.0 equiv), and heated for 8−24h at 65−120℃ in a sealed vial under an atmosphere of $N_2$

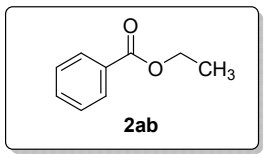
(monitored by TLC). The resulting mixture concentrated in vacuo to give residues. Then the residues were dissolved in ethyl acetate (30 V) and washed with brine, dried over $Na_2SO_4$, filtered, and concentrated in vacuo. The crude product was purified by silica-gel column chromatography to give ester product **2.**

**Methyl benzoate**[9]



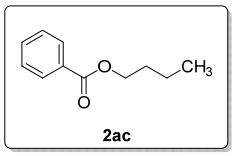

Colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.03 (dd, $J$ = 8.3, 1.2 Hz, 2H), 7.52 (t, $J$ = 7.4 Hz, 1H), 7.41 (t, $J$ = 7.7 Hz, 2H), 3.89 (s, 3H). $^{13}$C{$^1$H}NMR (100 MHz, $CDCl_3$) $\delta$ 167.03, 132.87, 130.18, 129.55, 128.33, 52.01. HRMS (EI): m/z [M] calcd for $C_8H_8O_2$ 136.0524, found: 136.0522.

**Ethyl benzoate**[10]



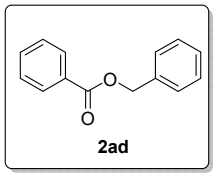

Colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.05 (dt, $J$ = 8.5, 1.6 Hz, 2H), 7.60 – 7.50 (m, 1H), 7.49 – 7.36 (m, 2H), 4.38 (q, $J$ = 7.1 Hz, 2H), 1.39 (t, $J$ = 7.1 Hz, 3H). $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 166.64, 132.80, 130.52, 129.54, 128.32, 60.95, 14.34. HRMS (EI): m/z [M] calcd for $C_9H_{10}O_2$ 150.0681, found: 150.0678.

**Butyl benzoate**[10]



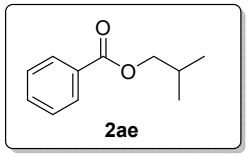

Colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.13 – 7.95 (m, 2H), 7.61 – 7.51 (m, 1H), 7.49 – 7.38 (m, 2H), 4.33 (t, $J$ = 6.6 Hz, 2H), 1.76 (dt, $J$ = 14.5, 6.7 Hz, 2H), 1.58 – 1.40 (m, 2H), 0.98 (t, $J$ = 7.4 Hz, 3H). $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 166.71, 132.79, 130.56, 129.54, 128.32, 64.84, 30.80, 19.29, 13.77. HRMS (EI): m/z [M] calcd for $C_{11}H_{14}O_2$ 178.0994, found: 178.0992.

**Benzyl benzoate**[11]




Colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.16 – 8.01 (m, 2H), 7.65 – 7.50 (m, 1H), 7.49 – 7.29 (m, 7H), 5.37 (s, 2H). $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 166.46, 136.10, 133.05, 130.18, 129.73, 128.62, 128.40, 128.26, 128.19, 66.71. HRMS (EI): m/z [M] calcd for $C_{14}H_{12}O_2$ 212.0837, found: 212.0835.

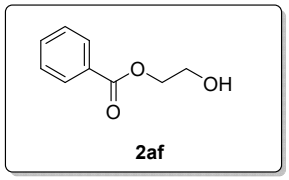
**Isobutyl benzoate**[12]




Colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.11 – 8.00 (m, 2H), 7.61 – 7.51 (m, 1H), 7.51 – 7.36 (m, 2H), 4.11 (d, $J$ = 6.6 Hz, 2H), 2.09 (dt, $J$ = 13.4, 6.7 Hz, 1H), 1.03 (d, $J$ = 6.7 Hz, 6H). $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 166.65, 132.82, 130.55, 129.55, 128.34, 71.02, 27.93, 19.21. HRMS (EI): m/z [M] calcd

for $C_{11}H_{14}O_2$ 178.0994, found: 178.0991.

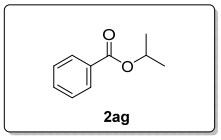
**2-hydroxyethyl benzoate**[13]



2af

Colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.05 (dd, $J$ = 5.2, 3.3 Hz, 2H), 7.65 – 7.49 (m, 1H), 7.44 (dd, $J$ = 10.7, 4.7 Hz, 2H), 4.50 – 4.39 (m, 2H), 4.04 – 3.88 (m, 2H), 2.29 (brs, 1H). $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 166.99, 133.19, 129.87, 129.69, 128.42, 66.67, 61.37. HRMS (EI): m/z [M] calcd for $C_9H_{10}O_3$ 166.0630, found: 166.0628.

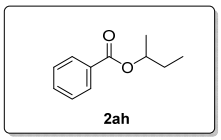
**Isopropyl benzoate**[10]



2ag

Colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.04 (dd, $J$ = 5.2, 3.4 Hz, 2H), 7.63 – 7.49 (m, 1H), 7.42 (dd, $J$ = 10.6, 4.6 Hz, 2H), 5.26 (dt, $J$ = 12.5, 6.3 Hz, 1H), 1.37 (d, $J$ = 6.3 Hz, 6H). $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 166.12, 132.69, 130.93, 129.51, 128.26, 68.33, 21.96. HRMS (EI): m/z [M] calcd for $C_{10}H_{12}O_3$ 164.0837, found: 164.0835.

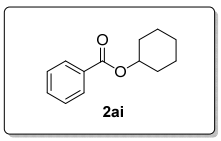
**Sec-butyl benzoate**[14]



2ah

Colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.04 (dd, $J$ = 5.2, 3.3 Hz, 2H), 7.62 – 7.48 (m, 1H), 7.48 – 7.35 (m, 2H), 5.10 (dd, $J$ = 12.5, 6.3 Hz, 1H), 1.83 – 1.57 (m, 2H), 1.34 (d, $J$ = 6.3 Hz, 3H), 0.98 (t, $J$ = 7.5 Hz, 3H). $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 166.25, 132.68, 130.95, 129.51, 128.28, 72.85, 28.97, 19.57, 9.74. HRMS (EI): m/z [M] calcd for $C_{11}H_{14}O_2$ 178.0994, found: 178.0993.

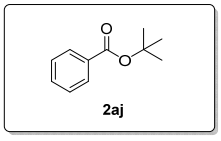
**Cyclohexyl benzoate**[15]



2ai

Colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.11 – 7.99 (m, 2H), 7.54 (dd, $J$ = 10.5, 4.3 Hz, 1H), 7.43 (t, $J$ = 7.6 Hz, 2H), 5.12 – 4.92 (m, 1H), 2.04 – 1.87 (m, 2H), 1.85 – 1.72 (m, 2H), 1.59 (ddd, $J$ = 12.6, 8.1, 3.4 Hz, 3H), 1.42 (ddd, $J$ = 31.0, 9.5, 3.1 Hz, 3H). $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 166.00, 132.67, 131.05, 129.54, 128.26, 73.03, 31.65, 25.50, 23.67. HRMS (EI): m/z [M] calcd for $C_{13}H_{16}O_2$ 204.1150, found: 204.1148.

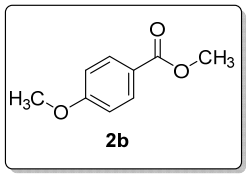
**Tert-butyl benzoate**[10]



2aj

Colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.99 (dd, $J$ = 5.2, 3.3 Hz, 2H), 7.51 (dd, $J$ = 5.0, 3.7 Hz, 1H), 7.46 – 7.37 (m, 2H), 1.60 (s, 9H). $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 165.79, 132.40, 132.04, 129.41, 128.17, 80.96, 28.21. HRMS (EI): m/z [M] calcd for $C_{11}H_{14}O_2$ 178.0994, found: 178.0992.

**Methyl 4-methoxybenzoate**[10]

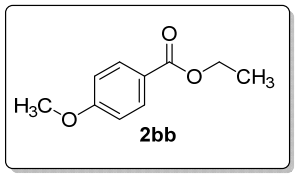


2b

Colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) δ 8.05 – 7.93 (m, 2H), 7.01 – 6.81 (m, 2H), 3.88 (s, 3H), 3.85 (s, 3H). $^{13}$C{$^1$H}NMR

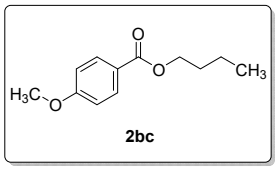
(100 MHz, $CDCl_3$) δ 166.85, 163.34, 131.58, 122.63, 113.60, 55.40, 51.83. HRMS (EI): m/z [M] calcd for $C_9H_{10}O_3$ 166.0630, found: 166.0627.

**Ethyl 4-methoxybenzoate**[16]



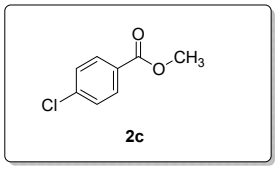

Colorless oil; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.10 – 7.92 (m, 2H), 7.01 – 6.82 (m, 2H), 4.35 (q, $J$ = 7.1 Hz, 2H), 3.85 (s, 3H), 1.38 (t, $J$ = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) $\delta$ 166.40, 163.26, 131.54, 122.98, 113.55, 60.63, 55.41, 14.39. HRMS (EI): m/z [M] calcd for $C_{10}H_{12}O_3$ 180.0786, found: 180.0785.

**Butyl 4-methoxybenzoate**[17]




Colorless oil; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.07 – 7.93 (m, 2H), 7.00 – 6.83 (m, 2H), 4.29 (t, $J$ = 6.6 Hz, 2H), 3.85 (s, 3H), 1.74 (dt, $J$ = 14.6, 6.7 Hz, 2H), 1.47 (dd, $J$ = 15.0, 7.5 Hz, 2H), 0.98 (t, $J$ = 7.4 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) $\delta$ 166.46, 163.25, 131.54, 123.00, 113.56, 64.53, 55.41, 30.85, 19.31, 13.79. HRMS (EI): m/z [M] calcd for $C_{12}H_{16}O_3$ 208.1099, found: 208.1096.

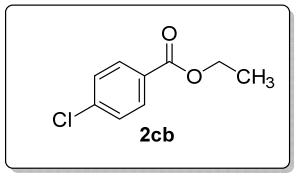
**Methyl 4-chlorobenzoate**[10]




Colorless oil; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.09 (d, $J$ = 8.9 Hz, 2H), 6.90 – 6.79 (m, 2H), 6.78 (s, 1H), 4.15 (q, $J$ = 7.1 Hz, 2H), 3.79 (s, 3H), 1.33 (t, $J$ = 7.1 Hz, 3H). $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$) δ 156.35, 155.88, 131.09, 122.72, 114.14, 62.98, 55.50, 14.44.

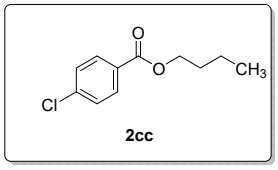
HRMS (EI): m/z [M] calcd for $C_8H_7ClO_2$ 170.0135, found: 170.0133.

**Ethyl 4-chlorobenzoate**[18]




Colorless oil; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.06 – 7.90 (m, 2H), 7.49 – 7.33 (m, 2H), 4.37 (q, $J$ = 7.1 Hz, 2H), 1.39 (t, $J$ = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) $\delta$ 165.75, 139.24, 130.94, 128.96, 128.65, 61.21, 14.29. HRMS (EI): m/z [M] calcd for $C_9H_9ClO_2$ 184.0291, found: 184.0290.

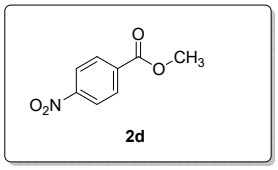
**Butyl 4-chlorobenzoate**[19]




Colorless oil; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.05 – 7.89 (m, 2H), 7.51 – 7.34 (m, 2H), 4.32 (t, $J$ = 6.6 Hz, 2H), 1.75 (dt, $J$ = 14.6, 6.7 Hz, 2H), 1.47 (dd, $J$ = 15.0, 7.5 Hz, 2H), 0.98 (t, $J$ = 7.4 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) $\delta$ 165.82, 139.24, 130.94, 128.99, 128.67, 65.10, 30.74, 19.26, 13.75.

HRMS (EI): m/z [M] calcd for $C_{11}H_{13}ClO_2$ 212.0604, found: 212.0601.

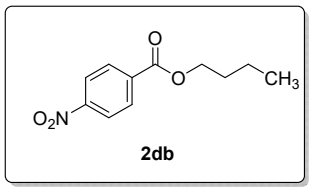
**Methyl 4-nitrobenzoate**[20]




As a foamy solid; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.30 (d, $J$ =

8.9 Hz, 2H), 8.22 (d, $J$ = 8.9 Hz, 2H), 3.99 (s, 3H). $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$) $\delta$ 165.19, 150.57, 135.51, 130.73, 123.57, 52.85.
HRMS (EI): m/z [M] calcd for $C_8H_7NO_4$ 181.0375, found: 181.0373.

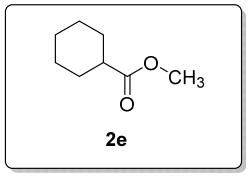
**Butyl 4-nitrobenzoate**[17]



2db

As a foamy solid; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.29 (d, $J$ = 9.0 Hz, 2H), 8.21 (d, $J$ = 9.0 Hz, 2H), 4.38 (t, $J$ = 6.6 Hz, 2H), 1.77 (dd, $J$ = 14.8, 6.9 Hz, 2H), 1.54 – 1.43 (m, 2H), 0.99 (t, $J$ = 7.4 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) $\delta$ 164.78, 150.50, 135.90, 130.67, 123.53, 65.84, 30.65, 19.23, 13.73. HRMS (EI): m/z [M] calcd for $C_{11}H_{13}NO_4$ 223.0845, found: 223.0841.

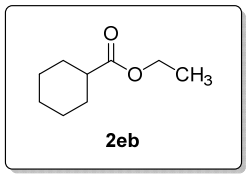
**Methyl cyclohexanecarboxylate**[10]



2e

Colorless oil; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 3.66 (s, 3H), 2.30 (ddd, $J$ = 11.3, 7.6, 3.6 Hz, 1H), 1.90 (dd, $J$ = 13.0, 2.6 Hz, 2H), 1.81 – 1.69 (m, 2H), 1.68 – 1.57 (m, 1H), 1.43 (td, $J$ = 11.7, 5.8 Hz, 2H), 1.35 – 1.13 (m, 3H). $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$) $\delta$ 176.58, 51.43, 43.11, 29.02, 25.75, 25.45.
HRMS (EI): m/z [M] calcd for $C_8H_{14}O_2$ 142.0994, found: 142.0992.

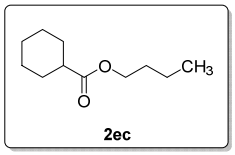
**Ethyl cyclohexanecarboxylate**[21]



2eb

Colorless oil; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 4.11 (q, $J$ = 7.1 Hz, 2H), 2.28 (tt, $J$ = 11.3, 3.6 Hz, 1H), 1.90 (dd, $J$ = 13.0, 2.5 Hz, 2H), 1.81 – 1.69 (m, 2H), 1.69 – 1.57 (m, 1H), 1.53 – 1.37 (m, 2H), 1.35 – 1.15 (m, 6H). $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$) $\delta$ 176.15, 60.01, 43.24, 29.02, 25.78, 25.46, 14.23.
HRMS (EI): m/z [M] calcd for $C_9H_{16}O_2$ 156.1150, found: 156.1147.

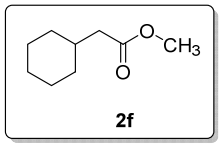
**Butyl cyclohexanecarboxylate**[22]



2ec

Colorless oil; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 4.06 (t, $J$ = 6.6 Hz, 2H), 2.36 – 2.20 (m, 1H), 1.90 (d, $J$ = 12.9 Hz, 2H), 1.79 – 1.71 (m, 2H), 1.61 (dd, $J$ = 14.2, 7.4 Hz, 3H), 1.48 – 1.32 (m, 4H), 1.32 – 1.20 (m, 3H), 0.93 (t, $J$ = 7.4 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) $\delta$ 176.23, 63.95, 43.29, 30.74, 29.05, 25.79, 25.47, 19.16, 13.72. HRMS (EI): m/z [M] calcd for $C_{11}H_{14}O_2$ 184.1463, found: 184.1460.

**Methyl 2-cyclohexylacetate**[23]

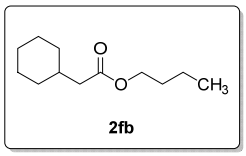


2f

Colorless oil; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 3.66 (s, 3H), 2.19 (d, $J$ = 7.0 Hz, 2H), 1.84 – 1.57 (m, 6H), 1.40 – 1.06 (m, 3H), 1.05 – 0.85 (m, 2H). $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$) $\delta$ 173.61, 51.33, 41.98, 34.89, 33.03, 26.14, 26.02. HRMS (EI): m/z [M] calcd for

$C_9H_{16}O_2$ 156.1150, found: 56.1149.

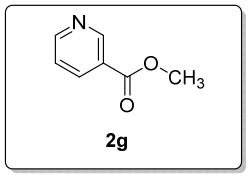
**Butyl 2-cyclohexylacetate**



2fb

Colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.06 (t, $J$ = 6.7 Hz, 2H), 2.17 (d, $J$ = 7.0 Hz, 2H), 1.82 – 1.58 (m, 8H), 1.43 – 1.09 (m, 5H), 0.94 (dd, $J$ = 9.7, 5.0 Hz, 5H). $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 173.29, 64.01, 42.27, 34.95, 33.03, 30.73, 26.17, 26.04, 19.17, 13.70. HRMS (EI): m/z [M] calcd for $C_{12}H_{16}O_2$ 198.1620, found: 198.1616.

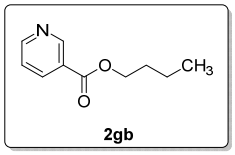
**Methyl nicotinate**[24]



2g

As a foamy solid; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 9.23 (d, $J$ = 0.6 Hz, 1H), 8.90 – 8.66 (m, 1H), 8.43 – 8.20 (m, 1H), 7.40 (dt, $J$ = 8.0, 4.1 Hz, 1H), 3.97 (d, $J$ = 4.5 Hz, 3H). $^{13}$C{$^1$H}NMR (100 MHz, $CDCl_3$) $\delta$ 165.71, 153.41, 150.89, 136.99, 126.00, 123.26, 52.38. HRMS (EI): m/z [M] calcd for $C_7H_7NO_2$ 137.0477, found: 137.0475.

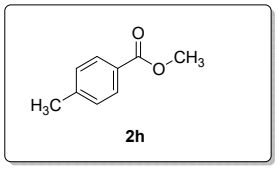
**Butyl nicotinate**[22]



2gb

Colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 9.23 (d, $J$ = 1.6 Hz, 1H), 8.78 (dd, $J$ = 4.8, 1.7 Hz, 1H), 8.30 (dt, $J$ = 7.9, 1.9 Hz, 1H), 7.40 (ddd, $J$ = 7.9, 4.9, 0.6 Hz, 1H), 4.37 (t, $J$ = 6.6 Hz, 2H), 1.78 (dt, $J$ = 14.5, 6.7 Hz, 2H), 1.57 – 1.40 (m, 2H), 0.99 (t, $J$ = 7.4 Hz, 3H). $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 165.31, 153.27, 150.86, 137.03, 126.38, 123.26, 65.30, 30.67, 19.21, 13.71. HRMS (EI): m/z [M] calcd for $C_{11}H_{14}O_2$ 179.0946, found: 179.0943.

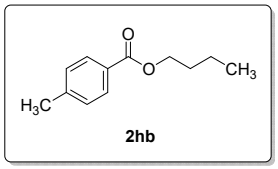
**Methyl 4-methylbenzoate**[10]



2h

As a foamy solid; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ .93 (d, $J$ = 8.2 Hz, 2H), 7.23 (d, $J$ = 8.3 Hz, 2H), 3.89 (s, 3H), 2.40 (s, 3H). $^{13}$C{$^1$H}NMR (100 MHz, $CDCl_3$) $\delta$ 167.18, 143.55, 129.60, 129.08, 127.45, 77.37, 77.05, 76.73, 51.93, 21.64. HRMS (EI): m/z [M] calcd for $C_9H_{10}O_2$ 150.0681, found: 150.0680.

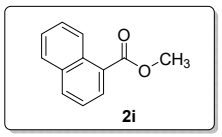
**Butyl 4-methylbenzoate**[25]



2hb

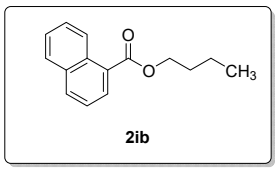
Colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.93 (d, $J$ = 8.2 Hz, 2H), 7.31 – 7.17 (m, 2H), 4.31 (t, $J$ = 6.6 Hz, 2H), 2.40 (s, 3H), 1.74 (dd, $J$ = 14.8, 6.9 Hz, 2H), 1.48 (dd, $J$ = 15.0, 7.5 Hz, 2H), 0.98 (t, $J$ = 7.4 Hz, 3H). $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 166.78, 143.40, 129.57, 129.03, 127.83, 64.65, 30.82, 21.64, 19.30, 13.78. HRMS (EI): m/z [M] calcd for $C_{12}H_{16}O_2$ 192.1150, found: 192.1147.

**Methyl 1-naphthoate**[10]



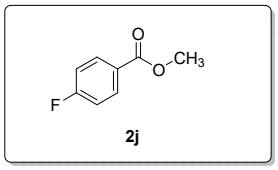

As a foamy solid; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.91 (d, $J$ = 8.0 Hz, 1H), 8.18 (d, $J$ = 8.0 Hz, 1H), 8.01 (d, $J$ = 8.0 Hz, 1H), 7.87 (d, $J$ = 8.0 Hz, 1H), 7.64−7.58 (m, 1H), 7.56− 7.45 (m, 2H), 3.99 (s, 3H). $^{13}$C{$^1$H}NMR (100 MHz, $CDCl_3$) $\delta$ 167.29, 135.53, 132.51, 131.09, 129.38, 128.26, 128.17, 127.78, 127.41, 126.66, 125.25, 52.27. HRMS (EI): m/z [M] calcd for $C_{12}H_{10}O_2$ 186.0681, found: 150.0678.

**Butyl 1-naphthoate**[25]



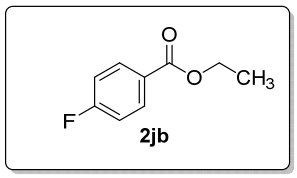

Colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.60 (s, 1H), 8.07 (dd, $J$ = 8.6, 1.7 Hz, 1H), 7.96 (d, $J$ = 8.0 Hz, 1H), 7.88 (d, $J$ = 8.6 Hz, 2H), 7.56 (dtd, $J$ = 16.1, 6.9, 1.3 Hz, 2H), 4.39 (t, $J$ = 6.6 Hz, 2H), 1.81 (dt, $J$ = 14.5, 6.7 Hz, 2H), 1.52 (dt, $J$ = 16.6, 7.5 Hz, 2H), 1.01 (t, $J$ = 7.4 Hz, 3H). $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 166.87, 135.50, 132.53, 130.94, 129.36, 128.16, 128.10, 127.81, 127.77, 126.60, 125.28, 65.01, 30.86, 19.34, 13.81. HRMS (EI): m/z [M] calcd for $C_{15}H_{16}O_2$ 228.1150, found: 228.1148.

**Methyl 4-fluorobenzoate**[10]



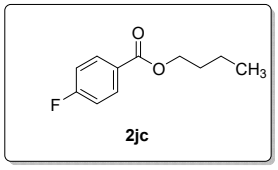

As a foamy solid; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.16 – 7.94 (m, 2H), 7.13 (t, $J$ = 8.7 Hz, 2H), 3.94 (s, 3H). $^{13}$C{$^1$H}NMR (100 MHz, $CDCl_3$) $\delta$ 166.14, 165.76 (d, $J$ = 253.7 Hz), 132.11 (d, $J$ = 9.2 Hz), 126.43 (d, $J$ = 3.0 Hz), 115.50 (d, $J$ = 22.0 Hz), 52.17. HRMS (EI): m/z [M] calcd for $C_8H_7FO_2$ 154.0430, found: 154.0428.

**Ethyl 4-fluorobenzoate**[26]



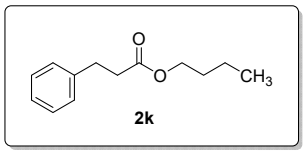

Colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.13 – 8.01 (m, 2H), 7.17 – 7.02 (m, 2H), 4.38 (q, $J$ = 7.1 Hz, 2H), 1.40 (t, $J$ = 7.1 Hz, 3H). $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 165.68 (d, $J$ = 253.5 Hz), 165.61, 132.04 (d, $J$ = 9.4 Hz), 126.76 (d, $J$ = 3.0 Hz), 115.39 (d, $J$ = 22.0 Hz), 61.05, 14.27. HRMS (EI): m/z [M] calcd for $C_9H_9FO_2$ 168.0587, found: 168.0585.

**Butyl 4-fluorobenzoate**[27]



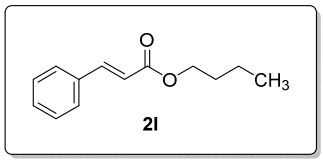

Colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.15 – 7.98 (m, 2H), 7.10 (t, $J$ = 8.7 Hz, 2H), 4.32 (t, $J$ = 6.6 Hz, 2H), 1.74 (dd, $J$ = 14.8, 6.8 Hz, 2H), 1.47 (dd, $J$ = 15.0, 7.5 Hz, 2H), 0.98 (t, $J$ = 7.4 Hz, 3H). $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 165.69 (d, $J$ = 253.3 Hz), 165.57, 132.04 (d, $J$ = 9.4 Hz), 126.77 (d, $J$ = 3.0 Hz), 115.42 (d, $J$ = 21.9 Hz), 64.96, 30.76, 19.26, 13.73. HRMS (EI): m/z [M] calcd for $C_{11}H_{13}FO_2$ 196.0900, found: 196.0897.

**Butyl 3-phenylpropanoate**[28]



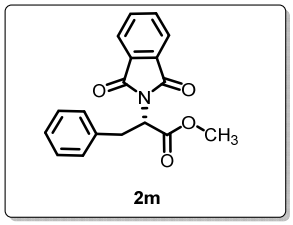

Colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.37 – 7.18 (m, 5H), 4.10 (t, $J$ = 6.7 Hz, 2H), 2.98 (t, $J$ = 7.8 Hz, 2H), 2.65 (t, $J$ = 7.8 Hz, 2H), 1.61 (dt, $J$ = 14.6, 6.8 Hz, 2H), 1.37 (dd, $J$ = 15.0, 7.5 Hz, 2H), 0.94 (t, $J$ = 7.4 Hz, 3H). $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 173.04, 140.60, 128.49, 128.31, 126.24, 64.37, 35.96, 31.03, 30.67, 19.12, 13.72. HRMS (EI): m/z [M] calcd for $C_{13}H_{18}O_2$ 206.1307, found: 206.1305.

**Butyl cinnamate**[29]



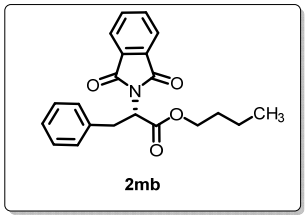

As a white solid; m.p. 140–143 °C. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.68 (d, $J$ = 16.0 Hz, 1H), 7.53 (dd, $J$ = 6.8, 2.8 Hz, 2H), 7.42 – 7.32 (m, 3H), 6.44 (d, $J$ = 16.0 Hz, 1H), 4.21 (t, $J$ = 6.7 Hz, 2H), 1.70 (dt, $J$ = 14.6, 6.8 Hz, 2H), 1.51 – 1.37 (m, 2H), 0.97 (t, $J$ = 7.4 Hz, 3H). $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 167.13, 144.57, 134.50, 130.22, 128.89, 128.07, 118.32, 64.46, 30.80, 19.22, 13.78. HRMS (EI): m/z [M] calcd for $C_{13}H_{16}O_2$ 204.1150, found: 204.1146.

**Methyl (S)-2-(1,3-dioxoisoindolin-2-yl)-3-phenylpropanoate**[30]



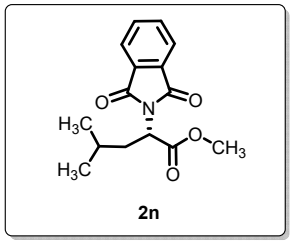

As a white solid; m.p. 115–118 °C. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.77 (dt, $J$ = 7.0, 3.5 Hz, 2H), 7.73 – 7.63 (m, 2H), 7.24 – 7.06 (m, 5H), 5.16 (dd, $J$ = 11.2, 5.3 Hz, 1H), 3.78 (s, 3H), 3.57 (qd, $J$ = 14.3, 8.3 Hz, 2H). $^{13}$C{$^1$H}NMR (100 MHz, $CDCl_3$) $\delta$ 169.36, 167.44, 136.71, 134.09, 131.59, 128.84, 128.56, 126.85, 123.47, 53.27, 52.90, 34.66. HRMS (EI): m/z [M] calcd for $C_{18}H_{15}NO_4$ 309.1001, found: 309.1000.

**Butyl (S)-2-(1,3-dioxoisoindolin-2-yl)-3-phenylpropanoate**




As a foamy solid; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.77 (td, $J$ = 5.2, 2.0 Hz, 2H), 7.69 (td, $J$ = 5.2, 2.0 Hz, 2H), 7.27 – 7.00 (m, 5H), 5.15 (dd, $J$ = 11.1, 5.4 Hz, 1H), 4.19 (td, $J$ = 6.6, 1.5 Hz, 2H), 3.57 (qd, $J$ = 14.3, 8.3 Hz, 2H), 1.67 – 1.53 (m, 2H), 1.31 (dd, $J$ = 15.0, 7.5 Hz, 2H), 0.88 (t, $J$ = 7.4 Hz, 3H). $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 168.91, 167.52, 136.85, 134.07, 131.63, 128.85, 128.55, 126.81, 123.43, 65.87, 53.46, 34.67, 30.46, 19.01, 13.61. HRMS (EI): m/z [M] calcd for $C_{21}H_{21}NO_4$ 351.1471, found: 351.1470.

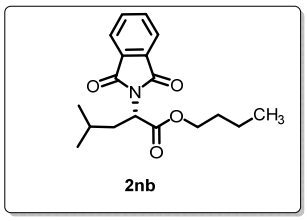
**Methyl (S)-2-(1,3-dioxoisoindolin-2-yl)-4-methylpentanoate**[31]




As a foamy solid; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.87 (dd, $J$ = 5.4, 3.1 Hz, 2H), 7.75 (dd, $J$ = 5.5, 3.0 Hz, 2H), 4.96 (dd, $J$ = 11.5, 4.4 Hz, 1H), 3.73 (s, 3H), 2.38 – 2.29 (m, 1H), 2.00 –

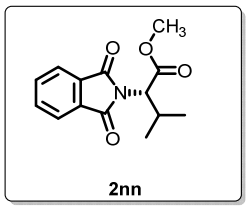
1.94 (m, 1H), 1.55 – 1.42 (m, 1H), 0.94 (dd, $J$ = 10.8, 6.6 Hz, 6H). $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$) $\delta$ 170.28, 167.75, 134.17, 131.87, 123.53, 52.72, 50.64, 37.29, 25.08, 23.16, 21.03. HRMS (EI): m/z [M] calcd for $C_{15}H_{17}NO_4$ 275.1158, found: 275.1156.

**Butyl (S)-2-(1,3-dioxoisoindolin-2-yl)-4-methylpentanoate**




Colorless oil; $^{1}H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.87 (dd, $J$ = 5.5, 3.0 Hz, 2H), 7.74 (dd, $J$ = 5.5, 3.0 Hz, 2H), 4.94 (dd, $J$ = 11.6, 4.4 Hz, 1H), 4.13 (td, $J$ = 6.7, 1.5 Hz, 2H), 2.37 – 2.30 (m, 1H), 1.99 – 1.92 (m, 1H), 1.60 – 1.53 (m, 2H), 1.53 – 1.49 (m, 1H), 1.30 (dt, $J$ = 15.0, 7.4 Hz, 2H), 0.94 (dd, $J$ = 9.9, 6.6 Hz, 6H), 0.86 (t, $J$ = 7.4 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) $\delta$ 169.85, 167.83, 134.14, 131.88, 123.48, 65.65, 50.84, 37.26, 30.46, 25.13, 23.19, 21.05, 18.99, 13.60. HRMS (EI): m/z [M] calcd for $C_{18}H_{23}NO_4$ 317.1627, found: 317.1624.

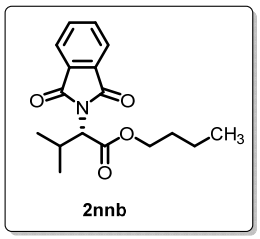
**Methyl (S)-2-(1,3-dioxoisoindolin-2-yl)-3-methylbutanoate**[31]




As a foamy solid; $^{1}H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.88 (dd, $J$ = 5.4, 3.1 Hz, 2H), 7.75 (dd, $J$ = 5.5, 3.1 Hz, 2H), 4.58 (d, $J$ = 8.3 Hz, 1H), 3.71 (s, 3H), 2.87 – 2.67 (m, 1H), 1.15 (d, $J$ = 6.7 Hz, 3H), 0.91 (d, $J$ = 6.8 Hz, 3H). $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$) δ 169.32, 167.77, 134.20, 131.74, 123.58, 57.56, 52.42, 28.57, 20.94, 19.39.

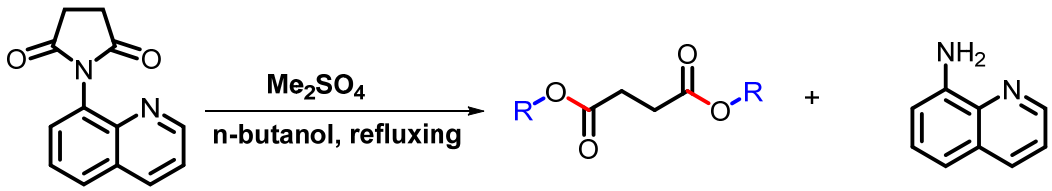
HRMS (EI): m/z [M] calcd for $C_{14}H_{15}NO_4$ 261.1001, found: 261.1000.

**Butyl (S)-2-(1,3-dioxoisoindolin-2-yl)-3-methylbutanoate**




Colorless oil; $^{1}H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.87 (dd, $J$ = 5.5, 3.1 Hz, 2H), 7.75 (dd, $J$ = 5.5, 3.0 Hz, 2H), 4.57 (d, $J$ = 8.3 Hz, 1H), 4.13 (td, $J$ = 6.7, 2.5 Hz, 2H), 2.90 – 2.66 (m, 1H), 1.56 (ddt, $J$ = 13.8, 8.9, 7.1 Hz, 2H), 1.28 (dt, $J$ = 15.0, 7.4 Hz, 2H), 1.16 (d, $J$ = 6.7 Hz, 3H), 0.92 (d, $J$ = 6.8 Hz, 3H), 0.85 (t, $J$ = 7.4 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) $\delta$ 168.90, 167.83, 134.17, 131.75, 123.51, 65.33, 57.82, 30.41, 28.54, 21.00, 19.50, 19.02, 13.56. HRMS (EI): m/z [M] calcd for $C_{17}H_{21}NO_4$ 304.1471, found: 304.1470.

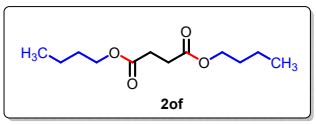
**Dibutyl succinate and 8-aminoquinoline**




**1of** **2of (R = *n*Bu)** **3o**

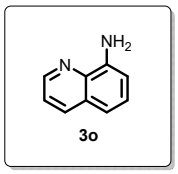
To a solution of amide **1of** (226 mg, 1mmol, 1.0 equiv) in n-butanol (5 mL) was

added dimethyl sulfate (252 mg, 2mmol, 2.0 equiv), and heated for 24h at 120°C in a sealed vial under an atmosphere of $N_2$ (monitored by TLC). The resulting mixture concentrated in vacuo to give residues. Then the residues were dissolved in ethyl acetate (30 V) and washed with sodium bicarbonate saturated solution, brine, dried over $Na_2SO_4$, filtered, and concentrated in vacuo. The crude product was purified by silica-gel column chromatography (5% EtOAc in *n*-hexane as the eluent) to give ester product **2of**[25] (207 mg, 90% yield); and silica-gel column chromatography (15% EtOAc in *n*-hexane as the eluent) to afford 8-aminoquinoline 3**o**[33] (126 mg, 88% yield).



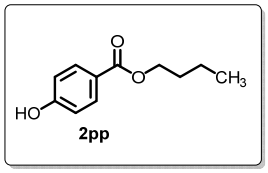
2of

Colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.09 (t, $J$ = 6.7 Hz, 4H), 2.62 (s, 4H), 1.61 (dt, $J$ = 14.7, 6.8 Hz, 4H), 1.38 (dd, $J$ = 15.0, 7.5 Hz, 4H), 0.93 (t, $J$ = 7.4 Hz, 6H). $^{13}$C{$^1$H}NMR (100 MHz, $CDCl_3$) $\delta$ 172.34, 64.54, 30.60, 29.17, 19.07, 13.65.
HRMS (EI): m/z [M] calcd for $C_{12}H_{22}O_4$ 230.1518, found: 230.1516.



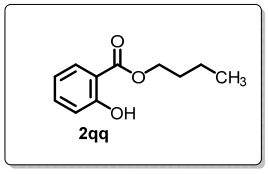
3o

Brown solid; m.p. 63–65 °C. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.79 (dd, $J$ = 4.2, 1.6 Hz, 1H), 8.10 (dd, $J$ = 8.3, 1.6 Hz, 1H), 7.45 – 7.33 (m, 2H), 7.18 (dd, $J$ = 8.1, 0.8 Hz, 1H), 6.96 (dd, $J$ = 7.5, 1.0 Hz, 1H), 4.98 (brs, 2H). $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 147.42, 143.96, 138.41, 136.04, 128.88, 127.41, 121.35, 116.05, 110.07. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_9H_9N_2$ 145.0760, found: 145.0758.



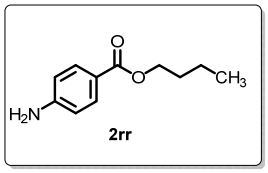
2pp

Colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.95 (d, $J$ = 8.7 Hz, 2H), 7.15 (s, 1H), 6.91 (d, $J$ = 8.7 Hz, 2H), 4.31 (t, $J$ = 6.6 Hz, 2H), 1.85 – 1.64 (m, 12H), 1.47 (dd, $J$ = 15.0, 7.5 Hz, 2H), 0.97 (t, $J$ = 7.4 Hz, 3H). $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 167.46, 160.64, 131.95, 122.26, 115.36, 65.02, 30.76, 19.28, 13.77. HRMS (ESI): m/z $[M - H]^-$ calcd for $C_{11}H_{13}O_3$ 193.0870, found: 193.0864.

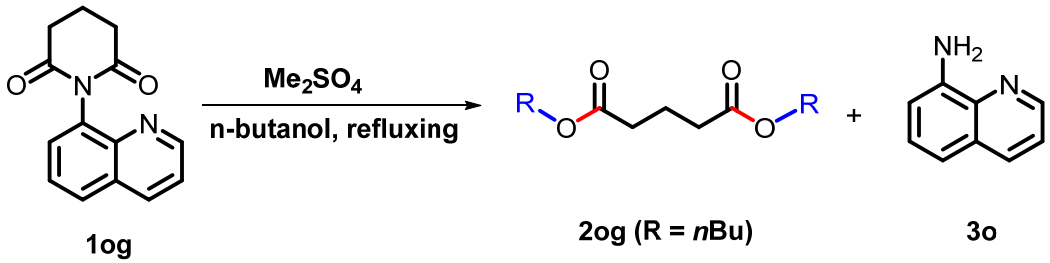


2qq

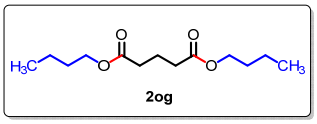
Colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) 10.85 (s, 1H), 7.85 (dd, $J$ = 8.0, 1.7 Hz, 1H), 7.56 – 7.37 (m, 1H), 6.98 (dd, $J$ = 8.4, 0.8 Hz, 1H), 6.94 – 6.76 (m, 1H), 4.36 (t, $J$ = 6.6 Hz, 2H), 1.77 (dt, $J$ = 14.5, 6.6 Hz, 2H), 1.61 – 1.31 (m, 2H), 0.99 (t, $J$ = 7.4 Hz, 3H).$^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 170.27, 161.66, 135.58, 129.88, 119.10, 117.57, 112.66, 65.23, 30.61, 19.22, 13.74. HRMS (ESI): m/z $[M - H]^-$ calcd for $C_{11}H_{13}O_3$ 193.0870, found: 193.0867.




White solid; m.p. 56–58 °C. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.98 – 7.70 (m, 2H), 6.82 – 6.51 (m, 2H), 4.26 (t, $J$ = 6.6 Hz, 2H), 4.19 – 3.90 (brs, 2H), 1.72 (dt, $J$ = 14.5, 6.6 Hz, 2H), 1.47 (dt, $J$ = 14.9, 7.4 Hz, 2H), 0.97 (t, $J$ = 7.4 Hz, 3H). $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 166.79, 150.66, 131.56, 120.19, 113.85, 77.38, 77.06, 76.74, 64.24, 30.91, 19.33, 13.82. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{11}H_{15}NO_2$ 193.1103, found: 193.1098.**Dibutyl glutarate**



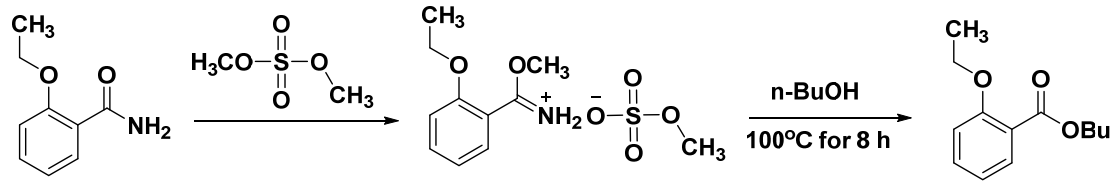

To a solution of amide **1og** (230 mg, 1mmol, 1.0 equiv) in n-butanol (5 mL) was added dimethyl sulfate (252 mg, 2mmol, 2.0 equiv), and heated for 24h at 120°C in a sealed vial under an atmosphere of $N_2$ (monitored by TLC). The resulting mixture concentrated in vacuo to give residues. Then the residues were dissolved in ethyl acetate (30 V) and washed with sodium bicarbonate saturated solution, brine, dried over $Na_2SO_4$, filtered, and concentrated in vacuo. The crude product was purified by silica-gel column chromatography (5% EtOAc in *n*-hexane as the eluent) to give ester product **2og**[32] (227 mg, 93% yield); and silica-gel column chromatography (15% EtOAc in *n*-hexane as the eluent) to afford 8-aminoquinoline (122 mg, 85% yield).




Colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.08 (t, $J$ = 6.7 Hz, 4H), 2.37 (t, $J$ = 7.4 Hz, 4H), 2.01 – 1.88 (m, 2H), 1.61 (dt, $J$ = 14.7, 6.8 Hz, 4H), 1.38 (dd, $J$ = 15.1, 7.5 Hz, 4H), 0.94 (t, $J$ = 7.4 Hz, 6H). $^{13}$C{$^1$H}NMR (100 MHz, $CDCl_3$) $\delta$ 172.94, 64.21, 33.28, 30.62, 20.19, 19.08, 13.62.
HRMS (EI): m/z [M] calcd for $C_{13}H_{24}O_4$ 244.1675, found: 244.1673.

## Synthesis of n-butyl 2-ethoxybenzoate

### Method A




1z INT-1z 2z

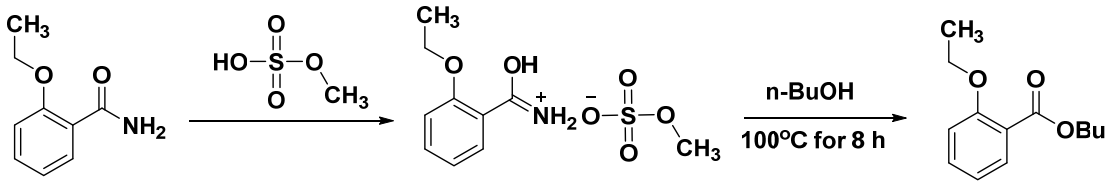
Methyl 2- ethoxybenzimidate Methyl Hydrogen Sulfate (**INT-1z**).

To a 10 mL flask were charged **1z** (1.0g, 5.58 mmol) and dimethyl sulfate (2.11 g, 16.73 mmol). A clear solution formed when the temperature was raised to 70 °C, and the mixture was heated for an additional 8 h. The stirred reaction mixture was cooled to ambient temperature (15−20 °C), and methyl tert-butyl ether (4 mL) was added over 5 min. After an additional stirring for 1h, the resulting precipitate was collected by filtration, and the filter cake was washed with MTBE (0.50 mL × 3) and dried invacuum at 40 °C, giving **INT-1z** (1.40 g, 82%) as a white solid with slightly hygroscopic properties. $^{1}$H NMR (500 MHz, chloroform-d): $\delta$ 12.08 (s, 1H), 10.24 (s, 1H), 8.04 (dd, $J$ = 8.1, 1.5 Hz, 1H), 7.82 – 7.62 (m, 1H), 7.18 (dd, $J$ = 13.7, 8.1 Hz, 2H), 4.49 (s, 3H), 4.40 (q, $J$ = 7.0 Hz, 2H), 3.80 (s, 3H), 1.62 (t, $J$ = 7.0 Hz, 3H). $^{13}$C{$^{1}$H}NMR (125 MHz, $CDCl_3$) $\delta$ 169.99, 159.46, 138.21, 131.49, 121.81, 113.24, 111.65, 66.35, 60.01, 54.89, 14.48. HRMS (ESI): m/z [M – ($^{-}OSO_3Me$)]$^{+}$ calcd for $C_{10}H_{14}NO_2^{+}$ 180.1019, found: 180.1016. Elem. Anal. Calcd for $C_{11}H_{17}NO_6S$: C, 45.35; H, 5.88; N, 4.81; S, 11.01. Found: C, 45.43; H, 5.85; N, 4.87; S, 11.10.

A solution of **INT-1z** (291 mg, 1mmol, 1.0 equiv) in n-butanol (3 mL) was heated for 8 h at 100℃ in a sealed vial under an atmosphere of $N_2$ (monitored by TLC). The resulting mixture concentrated in vacuo to give residues. Then the residues were dissolved in ethyl acetate (30 mL) and washed with sodium bicarbonate saturated solution, brine, dried over $Na_2SO_4$, filtered, and concentrated in vacuo. The crude product was purified by silica-gel column chromatography (5% EtOAc in *n*-hexane as the eluent) to give ester product **2z** (227 mg, 93% yield), as a colorless oil; $^{1}$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.77 (dd, $J$ = 8.0, 1.8 Hz, 1H), 7.51 – 7.33 (m, 1H), 6.96 (t, $J$ = 7.3 Hz, 2H), 4.31 (t, $J$ = 6.6 Hz, 2H), 4.11 (q, $J$ = 7.0 Hz, 2H), 1.74 (dt, $J$ = 14.5, 6.6 Hz, 2H), 1.56 – 1.38 (m, 5H), 0.97 (t, $J$ = 7.4 Hz, 3H). $^{13}$C{$^{1}$H}NMR (100 MHz, $CDCl_3$) $\delta$ 166.76, 158.42, 133.12, 131.51, 121.01, 120.06, 113.25, 64.67, 64.52, 30.80, 19.28, 14.75, 13.73.

HRMS (EI): m/z [M] calcd for $C_{13}H_{18}O_3$ 222.1256, found: 222.1253.

**Method B**




1z INT-3z 2z

2- ethoxybenzimidate Methyl Hydrogen Sulfate (**INT-3z**).

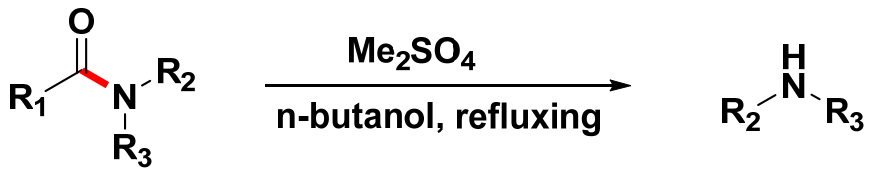
To a solution of amide **1z** (165 mg, 1 mmol) 5 mL of methanol was added methyl hydrogen sulfate (336 mg, 3 mmol), and then heating for 15 min. The resultant solutions were air cooled to room temperature and allowed in open vial for slow evaporation. Solid was obtained within two days.

$^1$H NMR (400 MHz, $CD_3OD$) $\delta$ 7.96 (dd, $J$ = 7.8, 1.8 Hz, 1H), 7.56 – 7.41 (m, 1H), 7.13 (d, $J$ = 8.2 Hz, 1H), 7.09 – 6.96 (m, 1H), 4.24 (q, $J$ = 7.0 Hz, 2H), 3.68 (s, 3H), 1.49 (t, $J$ = 7.0 Hz, 3H). $^{13}$C{$^1$H}NMR (100 MHz, $CD_3OD$) $\delta$ 168.98, 157.42, 133.32, 131.06, 120.74, 120.43, 112.55, 64.57, 53.72, 13.58. HRMS (ESI): m/z [M – ($^-$$OSO_3Me$)]$^+$ calcd for $C_9H_{12}NO_2^+$ 166.0863, found: 166.0855. Elem. Anal. Calcd for $C_{10}H_{15}NO_6S$: C, 43.32; H, 5.45; N, 5.05; S, 11.56. Found: C, 43.25; H, 5.48; N, 5.09; S, 11.64.

n-Butyl 2-ethoxybenzoate.

A solution of **INT-3z** (277 mg, 1mmol, 1.0 equiv) in n-butanol (3 mL) was heated for 8 h at 100℃ in a sealed vial under an atmosphere of $N_2$ (monitored by TLC). The resulting mixture concentrated in vacuo to give residues. Then the residues were dissolved in ethyl acetate (30 mL) and washed with sodium bicarbonate saturated solution, brine, dried over $Na_2SO_4$, filtered, and concentrated in vacuo. The crude product was purified by silica-gel column chromatography (5% EtOAc in *n*-hexane as the eluent) to give ester product **2z** (218 mg, 88% yield), as a colorless oil;

## General procedure for cleavage of acyl protective group on amines with dimethyl sulphate

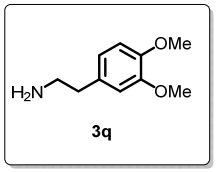



1 3

To a solution of amide **1** (1.0 equiv) in n-butanol (0.2 M) was added dimethyl sulfate (1.0 equiv), and heated for 8h at 120℃ in a sealed vial under an atmosphere of $N_2$ (monitored by TLC). The resulting mixture concentrated in vacuo to give residues. Then the residues were dissolved in ethyl acetate (30 V) and washed with sodium bicarbonate saturated solution, brine, dried over $Na_2SO_4$, filtered, and concentrated in

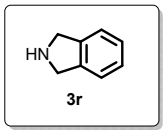
vacuo. The crude product was purified by silica-gel column chromatography to give amine product **3.**

**2-(3,4-Dimethoxyphenyl)ethan-1-amine**[33]



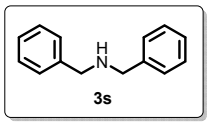

Brown solid; m.p. 153–155 °C. $^{1}$H NMR (400 MHz, $CDCl_3$) $\delta$ 6.77 (d, $J$ = 7.8 Hz, 1H), 6.72 – 6.67 (m, 2H), 3.83 (s, 3H), 3.81 (s, 3H), 2.89 (d, $J$ = 6.8 Hz, 2H), 2.65 (s, 2H), 1.18 (s, 2H). $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) $\delta$ 148.92, 147.45, 132.46, 120.71, 112.08, 111.34, 55.91, 55.81, 43.65, 39.63. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{10}H_{16}NO_2$ 182.1176, found: 182.1175.

**Isoindoline**[34]



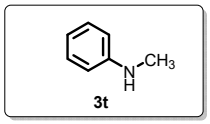

Colorless oil; $^{1}$H NMR (400 MHz, $CD_3OD$) $\delta$ 7.59 – 7.22 (m, 4H), 4.63 (s, 4H). $^{13}$C{$^{1}$H} NMR (100 MHz, $CD_3OD$) $\delta$ 134.16, 128.52, 122.65, 50.54. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_8H_{10}N$ 120.0808, found: 182.1175.

**Dibenzylamine**[35]



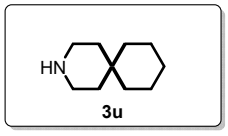

Colorless oil; $^{1}$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.38 – 7.21 (m, 10H), 3.81 (s, 4H), 1.74 (s, 1H). $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) $\delta$ 140.28, 128.43, 128.19, 126.99, 53.16. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{14}H_{16}N$ 198.1277, found: 192.1275.

**N-Methylaniline**[36]



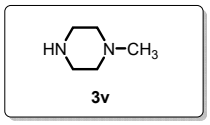

Colorless oil; $^{1}$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.23 – 7.14 (m, 2H), 6.71 (t, $J$ = 7.3 Hz, 1H), 6.61 (dd, $J$ = 8.5, 0.8 Hz, 2H), 2.83 (s, 3H). $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) $\delta$ 149.34, 129.23, 117.29, 112.45, 30.77. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_7H_{10}N$ 108.0808, found: 108.0805.

**3-Azaspiro[5.5]undecane**



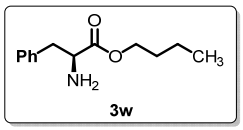

As a foamy solid; $^{1}$H NMR (400 MHz, $CD_3OD$) $\delta$ 3.21 – 3.12 (m, 4H), 1.75 – 1.66 (m, 4H), 1.57 – 1. 44 (m, 10H). $^{13}$C{$^{1}$H} NMR (100 MHz, $CD_3OD$) $\delta$ 39.68, 35.33, 32.39, 29.98, 26.05, 20.82. HRMS (ESI): HRMS (EI): m/z [M] calcd for $C_{10}H_{19}N$ 153.1517, found: 153.1514.

**1-Methylpiperazine**[37]



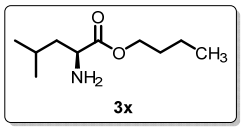

Colorless oil; $^{1}$H NMR (400 MHz, $CDCl_3$) $\delta$ 2.60 (dd, $J$ = 8.6, 4.3 Hz, 4H), 2.08 (s, 3H), 2.05 – 1.86 (m, 4H), 1.71 (s, 1H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) $\delta$ 56.10, 46.44, 45.75. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_5H_{13}N_2$ 101.1073, found: 101.1070.

**Butyl L-phenylalaninate**[38]



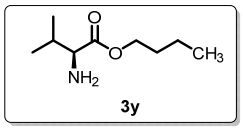

Colorless oil; $^{1}$H NMR (400 MHz, $CD_3OD$) $\delta$ 7.45 – 7.21 (m, 5H), 4.29 (t, $J$ = 7.0 Hz, 1H), 4.17 (t, $J$ = 6.5 Hz, 2H), 3.26 – 3.13 (m, 2H), 1.68 – 1.43 (m, 2H), 1.29 (dd, $J$ = 15.1, 7.5 Hz, 2H), 0.90 (t, $J$ = 7.4 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CD_3OD$) $\delta$ 170.33, 135.40, 130.48, 130.19, 128.99, 67.46, 55.28, 37.59, 31.46, 19.98, 13.99. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{13}H_{20}NO_2$ 222.1489, found: 222.1487.

**Butyl L-leucinate**



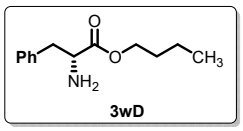

Colorless oil; $^{1}$H NMR (400 MHz, $CD_3OD$) $\delta$ 4.26 (t, $J$ = 6.5 Hz, 2H), 4.01 (t, $J$ = 6.8 Hz, 1H), 1.87 – 1.61 (m, 5H), 1.43 (dd, $J$ = 15.1, 7.5 Hz, 2H), 1.08 – 0.86 (m, 9H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) $\delta$ 171.21, 67.41, 52.59, 40.80, 31.59, 25.70, 22.53, 22.51, 20.09, 13.99. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{10}H_{22}NO_2$ 188.1645, found: 188.1643.

**Butyl L-valinate**



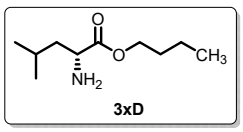

Colorless oil; $^{1}$H NMR (400 MHz, $CD_3OD$) $\delta$ 4.29 (td, $J$ = 6.6, 2.6 Hz, 2H), 3.94 (d, $J$ = 4.6 Hz, 1H), 2.39 – 2.23 (m, 1H), 1.71 (dt, $J$ = 8.7, 6.7 Hz, 2H), 1.56 – 1.35 (m, 2H), 1.10 (dd, $J$ = 7.0, 3.5 Hz, 6H), 0.99 (t, $J$ = 7.4 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CD_3OD$) $\delta$ 170.10, 67.28, 59.47, 31.66, 31.02, 20.12, 18.36, 18.23, 13.91. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_9H_{20}NO_2$ 174.1489, found: 188. 174.1486.

**Butyl D-phenylalaninate**




Colorless oil; $^{1}$H NMR (400 MHz, $CD_3OD$) $\delta$ 7.49 – 7.21 (m, 1H), 4.31 (t, $J$ = 7.0 Hz, 1H), 4.19 (t, $J$ = 6.5 Hz, 1H), 3.29 – 3.13 (m, 1H), 1.66 – 1.49 (m, 1H), 1.30 (dd, $J$ = 15.1, 7.5 Hz, 1H), 0.92 (t, $J$ = 7.4 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CD_3OD$) $\delta$ 171.17, 67.36, 52.54, 40.76, 31.54, 25.65, 22.48, 22.46, 20.04, 13.94.HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{13}H_{20}NO_2$ 222.1489, found: 222.1488.

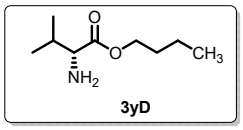
**Butyl D-leucinate**




Colorless oil; $^{1}$H NMR (400 MHz, $CD_3OD$) $\delta$ 4.26 (t, $J$ = 6.5 Hz, 2H), 4.01 (t, $J$ = 6.8 Hz, 1H), 1.87 – 1.61(m, 5H), 1.49 – 1.39 (m, 2H), 1.16 – 0.79 (m, 9H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) $\delta$ 171.21, 67.41, 52.59, 40.80, 31.59, 25.70, 22.53, 22.51, 20.09,

13.99. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{10}H_{22}NO_2$ 188.1645, found: 188.1642.

**Butyl D-valinate**




Colorless oil; $^1$H NMR (400 MHz, $CD_3OD$) $\delta$ 4.27 (td, $J$ = 6.6, 2.6 Hz, 2H), 3.92 (d, $J$ = 4.6 Hz, 1H), 2.43 – 2.15 (m, 1H), 1.68 (dt, $J$ = 8.7, 6.7 Hz, 1H), 1.53 – 1.30 (m, 2H), 1.07 (dd, $J$ = 7.0, 3.5 Hz, 6H), 0.97 (t, $J$ = 7.4 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CD_3OD$) $\delta$ 170.13, 67.31, 59.50, 31.69, 31.05, 20.15, 18.39, 18.26, 13.95. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_9H_{20}NO_2$ 174.1489, found: 188. 174.1488.

## Computational details

Density functional theory (DFT) calculations were performed with Gaussian16[39] package. Geometry optimizations were carried out using the M06-2X functional[40] and 6-31G(d) basis set[41] in solution (1-butanol, ε=17.332) by the continuum method PCM[42]. Frequency analysis was performed at the same level under standard conditions to either a minimum (i.e., no imaginary frequency) or a transition state (i.e., only one imaginary frequency) and to obtain thermodynamic energy corrections. Intrinsic reaction coordinate (IRC) calculations[43] were conducted to verify that all transition state structures connected the corresponding reactants and products. Single-point calculations with the M06-2X/6-311++G(d,p) level of theory[44] and SMD[45] solvent model were performed using the geometries obtained at optimization step. The free energies presented in this work represent M06-2X/6-311++G(d,p) calculated single-point energies with M06-2X/6-31G(d) calculated thermodynamic corrections, denoted as $\Delta G_{sol}$(M06-2X SMD/6-311++G(d,p) // M06-2X PCM/6-31G(d)) or simply as $\Delta G_{sol}$ for the sake of clarity.

## DFT Calculations

### Energy values for the reported species and imaginary frequencies for the transition states

### Optimized cartesian coordinates of the calculated structures

**1a+$Me_2SO_4$**

| | | | |
|---|---|---|---|
| C | -4.64759000 | -1.42448500 | 0.84004300 |
| C | -3.38086800 | -0.86463000 | 0.96432200 |
| C | -2.96173300 | 0.13002100 | 0.07804900 |
| C | -3.81195500 | 0.54308700 | -0.95127300 |
| C | -5.07703700 | -0.02406000 | -1.07950000 |
| C | -5.49809600 | -1.00288200 | -0.18147200 |
| H | -4.97192200 | -2.19029100 | 1.53735700 |
| H | -2.70111100 | -1.18539800 | 1.74684600 |
| H | -3.48454900 | 1.28305000 | -1.67600300 |
| H | -5.73037900 | 0.29371700 | -1.88558200 |
| H | -6.48574900 | -1.44183000 | -0.28194200 |
| C | -1.58450100 | 0.69330600 | 0.26997600 |
| O | -0.70646100 | 0.05139000 | 0.84995200 |
| N | -1.35739900 | 1.92839100 | -0.22296100 |
| H | -2.14014300 | 2.49080400 | -0.52315800 |

| | | | |
|---|---|---|---|
| C | -0.06681400 | 2.56979300 | -0.04882300 |
| H | -0.06865800 | 3.51081400 | -0.59797500 |
| H | 0.13628700 | 2.77012800 | 1.00908900 |
| H | 0.72836600 | 1.92827700 | -0.43733300 |
| S | 3.56979800 | -0.27511500 | -0.35458900 |
| O | 4.96204100 | -0.53656700 | -0.60480200 |
| O | 2.93033600 | 0.91926500 | -0.86242400 |
| O | 2.80446900 | -1.56421400 | -0.87348400 |
| O | 3.33463500 | -0.36367800 | 1.21489100 |
| C | 1.37287000 | -1.58910200 | -0.65802100 |
| C | 2.43749700 | 0.59897100 | 1.83293700 |
| H | 1.02136700 | -2.45665300 | -1.21182400 |
| H | 1.16121800 | -1.69886900 | 0.40635700 |
| H | 0.91935400 | -0.67427300 | -1.04108400 |
| H | 2.48505000 | 0.35822900 | 2.89305000 |
| H | 2.80403100 | 1.60969200 | 1.65339600 |
| H | 1.42104800 | 0.47602600 | 1.45247000 |

## TS-1

| | | | |
|---|---|---|---|
| C | 4.87305300 | 0.95337700 | -1.08860700 |
| C | 5.47029800 | 1.12494200 | 0.15906600 |
| C | 4.82705600 | 0.67226400 | 1.30964100 |
| C | 3.59464900 | 0.03455300 | 1.21494600 |
| C | 2.99865000 | -0.14698200 | -0.03723000 |
| C | 3.63551500 | 0.32773900 | -1.18694000 |
| C | 1.67850000 | -0.81941500 | -0.20734900 |
| O | 1.01481400 | -0.60450400 | -1.25636800 |
| O | -2.70746200 | 0.35455200 | -1.24626600 |
| S | -3.54765100 | 0.01493800 | -0.04080900 |
| O | -4.79503700 | -0.64516100 | -0.38423400 |
| O | -2.73742500 | -0.59645400 | 1.01554100 |
| O | -4.03404800 | 1.45627900 | 0.51358900 |
| C | -2.97766100 | 2.33660000 | 0.91625300 |
| H | 5.36987500 | 1.31004600 | -1.98471600 |
| H | 6.43361300 | 1.61873400 | 0.23647200 |
| H | 5.28069600 | 0.82154900 | 2.28364200 |
| H | 3.09519600 | -0.27961500 | 2.12683100 |
| H | 3.15322300 | 0.19419500 | -2.14897700 |
| H | -3.46490200 | 3.25002900 | 1.25359400 |
| H | -2.40562800 | 1.89110900 | 1.73354600 |
| H | -2.32379000 | 2.55293700 | 0.06713200 |
| C | -0.83430700 | -0.17932200 | -1.19868900 |
| H | -0.80260200 | 0.02753200 | -0.13995900 |
| H | -1.11849300 | -1.15676800 | -1.54941700 |
| H | -0.64094900 | 0.60557200 | -1.91104700 |
| C | 0.08996400 | -2.51012700 | 0.62369000 |
| H | 0.00212700 | -2.84441900 | -0.41229900 |
| H | -0.82670600 | -1.99624900 | 0.92388700 |
| H | 0.24478900 | -3.37698800 | 1.26468000 |
| N | 1.26122900 | -1.64660000 | 0.74465500 |
| H | 1.87632200 | -1.80993300 | 1.53022500 |

## INT-1

| | | | |
|---|---|---|---|
| C | 5.20737600 | -1.29638400 | -0.01886100 |
| C | 5.97023600 | -0.13113000 | 0.04998600 |
| C | 5.35127200 | 1.11844200 | 0.06900600 |
| C | 3.96583500 | 1.20737500 | 0.02878500 |
| C | 3.20019400 | 0.03630500 | -0.02776300 |
| C | 3.82143600 | -1.21742800 | -0.06370300 |
| C | 1.73080000 | 0.09635700 | -0.05709500 |
| O | 1.14684800 | -0.89414900 | -0.66325900 |
| N | 1.09221300 | 1.09628900 | 0.49302500 |
| C | -0.30381000 | 1.51228500 | 0.28137000 |
| C | -0.19374400 | -1.33838400 | -0.31356000 |
| H | 5.69256100 | -2.26606300 | -0.03630100 |
| H | 7.05294700 | -0.19613400 | 0.08146800 |
| H | 5.94780400 | 2.02325100 | 0.10320900 |
| H | 3.49202400 | 2.18419800 | 0.00255900 |
| H | 3.21609400 | -2.11557500 | -0.11411400 |
| H | 1.66765100 | 1.72113800 | 1.04756300 |
| H | -0.36412500 | 2.55726500 | 0.57899300 |
| H | -0.55258700 | 1.42624400 | -0.77602000 |
| H | -1.00186000 | 0.91394300 | 0.86931700 |
| H | -0.21218500 | -2.38371900 | -0.61280900 |
| H | -0.34585700 | -1.24137100 | 0.76028600 |
| H | -0.94557200 | -0.76720400 | -0.85512700 |
| S | -3.75814400 | -0.26276500 | 0.46263900 |
| O | -4.43977800 | -1.42535900 | -0.11872000 |
| O | -4.66133700 | 0.76437500 | 0.99526600 |
| O | -2.61884200 | -0.59017800 | 1.33202400 |
| O | -2.98180300 | 0.45925200 | -0.80263500 |
| C | -3.84546600 | 0.87833000 | -1.85788900 |
| H | -3.21129900 | 1.36449800 | -2.59945700 |
| H | -4.34813000 | 0.01610600 | -2.30423000 |
| H | -4.58812400 | 1.58751300 | -1.48181500 |

## 1-BuOH

| | | | |
|---|---|---|---|
| C | 1.31007700 | 0.47287500 | 0.00000900 |

| | | | |
|---|---|---|---|
| H | 1.33472600 | 1.12358300 | 0.88680800 |
| H | 1.33473300 | 1.12358100 | -0.88679100 |
| O | 2.40924400 | -0.42520900 | 0.00001400 |
| C | 0.03046100 | -0.34321800 | 0.00000500 |
| H | 0.03021600 | -0.99697400 | 0.88142500 |
| H | 0.03023800 | -0.99699600 | -0.88139900 |
| C | -1.22123700 | 0.53163000 | -0.00002200 |
| H | -1.20517100 | 1.18877800 | -0.87878900 |
| H | -1.20518300 | 1.18881700 | 0.87871600 |
| C | -2.50530700 | -0.29410600 | -0.00001200 |
| H | -2.55327700 | -0.93832800 | 0.88417600 |
| H | -3.39279900 | 0.34496600 | -0.00003800 |
| H | -2.55326000 | -0.93837600 | -0.88416500 |
| H | 3.22186600 | 0.09954100 | 0.00006200 |

## TS-2

| | | | |
|---|---|---|---|
| C | 5.60132700 | 0.62261900 | 1.07237300 |
| C | 6.44650700 | 0.10273600 | 0.09256300 |
| C | 5.92671900 | -0.67320200 | -0.94215500 |
| C | 4.55952800 | -0.92115700 | -1.00722100 |
| C | 3.70990900 | -0.38982900 | -0.03212600 |
| C | 4.23558100 | 0.37082400 | 1.01589800 |
| C | 2.24028900 | -0.62418300 | -0.05422700 |
| O | 1.61159200 | -0.62582400 | 1.03772400 |
| N | 1.65477900 | -0.82095500 | -1.23085400 |
| C | 0.29422100 | -1.32036700 | -1.41537400 |
| C | -0.07516100 | 0.20158200 | 1.22862800 |
| H | 6.00748800 | 1.22221200 | 1.88019700 |
| H | 7.51345800 | 0.29577300 | 0.13982000 |
| H | 6.58641400 | -1.09371600 | -1.69361600 |
| H | 4.16842400 | -1.55624500 | -1.79678900 |
| H | 3.56417500 | 0.76175900 | 1.77294100 |
| H | 2.21848300 | -0.68470100 | -2.06007100 |
| H | 0.25791900 | -1.87805800 | -2.35003700 |
| H | 0.03795900 | -1.99291500 | -0.59542800 |
| H | -0.44148800 | -0.51392000 | -1.46007000 |
| H | 0.23142500 | 0.50275800 | 2.21784600 |
| H | 0.11518500 | 0.85610900 | 0.38987300 |
| H | -0.60657400 | -0.72720000 | 1.08524800 |
| S | -3.13137500 | -1.68338500 | -0.52788000 |
| O | -4.50943400 | -2.08091000 | -0.24602500 |
| O | -2.50045200 | -2.30506500 | -1.68772200 |
| O | -2.92257600 | -0.20956300 | -0.46798700 |
| O | -2.22936500 | -2.26933800 | 0.71404100 |
| C | -2.80212100 | -2.10975200 | 2.01682800 |
| H | -2.06072000 | -2.49651900 | 2.71586400 |
| H | -2.99182400 | -1.05365800 | 2.23421100 |
| H | -3.73003200 | -2.67865300 | 2.09428200 |
| C | -1.79415300 | 2.47569300 | 1.36332800 |
| H | -2.64834200 | 2.87510700 | 1.92134200 |
| H | -0.87956000 | 2.84832300 | 1.83733600 |
| O | -1.78249600 | 1.05146300 | 1.53105100 |
| C | -1.86657100 | 2.89558500 | -0.09667300 |
| H | -2.76731000 | 2.46295000 | -0.54996100 |
| H | -1.00929700 | 2.48642600 | -0.64770400 |
| C | -1.88884600 | 4.41651900 | -0.24385100 |
| H | -0.98770600 | 4.83925400 | 0.21757500 |
| H | -2.74346000 | 4.82048800 | 0.31276200 |
| C | -1.97343800 | 4.85153300 | -1.70456800 |
| H | -2.88114100 | 4.45968600 | -2.17476000 |
| H | -1.98957700 | 5.94113800 | -1.79446000 |
| H | -1.11506000 | 4.47822100 | -2.27263800 |
| H | -2.35119300 | 0.62851900 | 0.82910600 |

## $BuOCH_3$

| | | | |
|---|---|---|---|
| C | -0.71362300 | 0.37855500 | -0.00000700 |
| H | -0.77800600 | 1.03074700 | -0.88722700 |
| H | -0.77804300 | 1.03070200 | 0.88724200 |
| O | -1.78142900 | -0.54375400 | -0.00005300 |
| C | 0.59764900 | -0.38508300 | 0.00000200 |
| H | 0.62587700 | -1.03751900 | -0.88163200 |
| H | 0.62583300 | -1.03757100 | 0.88159900 |
| C | 1.81049000 | 0.54309700 | 0.00006000 |
| H | 1.76647700 | 1.19871600 | 0.87894200 |
| H | 1.76651500 | 1.19877600 | -0.87878000 |
| C | 3.12816700 | -0.22786500 | 0.00006200 |
| H | 3.20340500 | -0.86930500 | -0.88426400 |
| H | 3.98754400 | 0.44856000 | 0.00010600 |
| H | 3.20336400 | -0.86936900 | 0.88434500 |
| C | -3.03201200 | 0.10149700 | -0.00006600 |
| H | -3.15631100 | 0.73322700 | -0.89134100 |
| H | -3.80289500 | -0.67130800 | -0.00011000 |
| H | -3.15635700 | 0.73317200 | 0.89124200 |

## INT-2

| | | | |
|---|---|---|---|
| C | 3.56922200 | -1.70569200 | -0.07896000 |
| C | 4.57586000 | -0.95733700 | 0.53086400 |
| C | 4.39259500 | 0.40385600 | 0.76810700 |

| | | | |
|---|---|---|---|
| C | 3.19815700 | 1.01853400 | 0.40520500 |
| C | 2.18802600 | 0.26699600 | -0.20120500 |
| C | 2.37808100 | -1.09407200 | -0.45257100 |
| C | 0.89158600 | 0.86818500 | -0.61104600 |
| O | 0.28167700 | 0.41368100 | -1.61031300 |
| N | 0.42159900 | 1.88527200 | 0.10837500 |
| C | -0.77280100 | 2.64071200 | -0.23993300 |
| H | 3.71390900 | -2.76526500 | -0.26234100 |
| H | 5.50743300 | -1.43502500 | 0.81738200 |
| H | 5.18190000 | 0.98884200 | 1.22828900 |
| H | 3.07249900 | 2.08576800 | 0.56486800 |
| H | 1.57886800 | -1.65663000 | -0.92308400 |
| H | 0.90114300 | 2.12327800 | 0.96681600 |
| H | -0.93582900 | 2.56118000 | -1.31513100 |
| H | -1.64721900 | 2.25686700 | 0.29102700 |
| H | -0.61629900 | 3.68641800 | 0.02533200 |
| S | -2.19563800 | -0.92249700 | 0.06560200 |
| O | -3.23970500 | -1.91240800 | -0.07969900 |
| O | -0.88249300 | -1.30441500 | 0.53875300 |
| O | -2.08914400 | -0.11819200 | -1.26165400 |
| O | -2.68880300 | 0.18658900 | 1.11257900 |
| C | -4.01593200 | 0.70651900 | 0.89307000 |
| H | -4.16149300 | 1.45409600 | 1.67012600 |
| H | -4.07520200 | 1.16911100 | -0.09491800 |
| H | -4.74880200 | -0.09542700 | 0.98862500 |
| H | -1.07290400 | 0.18160100 | -1.44374900 |

## INT-3

| | | | |
|---|---|---|---|
| C | 2.29785600 | -2.14621700 | 0.21959100 |
| C | 3.68983600 | -2.10003600 | 0.15636700 |
| C | 4.34980100 | -0.87662700 | 0.04508200 |
| C | 3.61934000 | 0.30353600 | -0.00532900 |
| C | 2.22115300 | 0.25166700 | 0.04457000 |
| C | 1.55419000 | -0.97367500 | 0.16359900 |
| C | 1.46674300 | 1.50906800 | -0.02446100 |
| O | 2.13161200 | 2.58524400 | 0.32973700 |
| N | 0.22877400 | 1.56731900 | -0.40753000 |
| C | -0.56265800 | 2.79520300 | -0.44759200 |
| H | 1.78650900 | -3.09730400 | 0.32120500 |
| H | 4.26327100 | -3.02040500 | 0.19992100 |
| H | 5.43274700 | -0.84218000 | -0.00220600 |
| H | 4.12218100 | 1.26008900 | -0.09425900 |
| H | 0.47178600 | -1.02565000 | 0.24288800 |
| H | -0.25170800 | 0.70861500 | -0.75318700 |
| H | -1.57306500 | 2.51163300 | -0.73374100 |
| H | -0.59699500 | 3.26060100 | 0.54099900 |
| H | -0.15646300 | 3.49255600 | -1.18566300 |
| S | -2.34350300 | -0.83504600 | -0.31594300 |
| O | -3.60084100 | -1.36442600 | -0.83954300 |
| O | -1.72168300 | -1.63759200 | 0.74353900 |
| O | -1.38975000 | -0.39380600 | -1.36199700 |
| O | -2.69591100 | 0.60954500 | 0.37179700 |
| C | -3.57570200 | 0.53051700 | 1.49678500 |
| H | -3.73915100 | 1.55608700 | 1.82578200 |
| H | -4.52580800 | 0.07743100 | 1.20163400 |
| H | -3.11423100 | -0.05253700 | 2.29756000 |
| H | 1.62478600 | 3.40822600 | 0.20692900 |

## TS-3

| | | | |
|---|---|---|---|
| C | -3.21542000 | -1.61731700 | -0.68781700 |
| C | -2.22580900 | -0.83277900 | -0.10564600 |
| C | -2.38299300 | 0.55339000 | -0.03515700 |
| C | -3.54523500 | 1.14424200 | -0.52668200 |
| C | -4.53460600 | 0.35508600 | -1.11138100 |
| C | -4.37002200 | -1.02404000 | -1.19748800 |
| C | -1.31717000 | 1.41015500 | 0.62022400 |
| N | -1.21711200 | 1.16276700 | 1.99290000 |
| O | 0.00883000 | 1.00132300 | -0.10366700 |
| O | -1.45126100 | 2.75710800 | 0.41094000 |
| C | 0.97206000 | 2.03714200 | -0.43534800 |
| C | 2.30802800 | 1.38388300 | -0.73093800 |
| C | 3.34070800 | 2.41651800 | -1.18226100 |
| C | 4.69228000 | 1.76883900 | -1.47220700 |
| H | -3.08149300 | -2.69315800 | -0.74287400 |
| H | -1.33236100 | -1.30811400 | 0.28937200 |
| H | -3.69459600 | 2.21567800 | -0.43937600 |
| H | -5.43617300 | 0.82254300 | -1.49353500 |
| H | -5.14087600 | -1.63684500 | -1.65348700 |
| H | -1.28848500 | 0.17021400 | 2.19377200 |
| H | 0.49755000 | 0.07849500 | 0.45964000 |
| H | 0.59204000 | 2.56623600 | -1.31329500 |
| H | 1.04658400 | 2.74295000 | 0.39512200 |
| H | 2.67087100 | 0.86299100 | 0.16253400 |
| H | 2.17976800 | 0.62110600 | -1.50875500 |
| H | 2.97496000 | 2.93124100 | -2.07912500 |
| H | 3.45478400 | 3.18206500 | -0.40505900 |
| H | 5.42855600 | 2.51190400 | -1.79028400 |
| H | 5.08085500 | 1.26542300 | -0.58111800 |

| | | | |
|---|---|---|---|
| H | 4.60176700 | 1.01975000 | -2.26546100 |
| C | -0.11945500 | 1.80049100 | 2.71687000 |
| H | -0.25834800 | 1.61300800 | 3.78220700 |
| H | 0.86754300 | 1.41979000 | 2.42238300 |
| H | -0.15813800 | 2.87820000 | 2.54941400 |
| S | 1.56565600 | -2.08702900 | 0.60616700 |
| O | 2.74570100 | -1.72411300 | -0.16123600 |
| O | 1.68799900 | -3.08698200 | 1.64515800 |
| O | 0.85492400 | -0.85128100 | 1.16745800 |
| O | 0.49235900 | -2.71070900 | -0.42722300 |
| C | 0.42998900 | -2.08992100 | -1.72337300 |
| H | -0.38193900 | -2.59501400 | -2.24442100 |
| H | 0.19718900 | -1.02448200 | -1.63086400 |
| H | 1.37486400 | -2.22899500 | -2.24994300 |
| H | -1.62816100 | 2.92120300 | -0.53003200 |

## INT-4

| | | | |
|---|---|---|---|
| C | -2.89874500 | -1.53275600 | -1.80737100 |
| C | -2.00706400 | -0.72600900 | -1.09981100 |
| C | -2.48523800 | 0.12924800 | -0.10740200 |
| C | -3.85639600 | 0.18296200 | 0.16288700 |
| C | -4.74094100 | -0.62098200 | -0.54712500 |
| C | -4.26214200 | -1.48364800 | -1.53360800 |
| C | -1.57327900 | 1.06427500 | 0.67629200 |
| N | -1.85396800 | 0.96636800 | 2.07119200 |
| O | -0.20646900 | 0.67180800 | 0.34852200 |
| O | -1.75360600 | 2.39596200 | 0.31334800 |
| C | 0.86167800 | 1.63695500 | 0.34233300 |
| C | 1.39955300 | 1.79222300 | -1.06828100 |
| C | 2.67471400 | 2.63170900 | -1.09783200 |
| C | 3.20951600 | 2.81706700 | -2.51545200 |
| H | -2.52065000 | -2.20133100 | -2.57442400 |
| H | -0.94590500 | -0.76927900 | -1.32033500 |
| H | -4.21657000 | 0.85747400 | 0.93308700 |
| H | -5.80381400 | -0.57523700 | -0.33164600 |
| H | -4.95191200 | -2.11359100 | -2.08666200 |
| H | -1.91836400 | -0.01412700 | 2.33059400 |
| H | 0.28112500 | -0.66139300 | 0.81766400 |
| H | 0.50162900 | 2.58677300 | 0.74078100 |
| H | 1.63834800 | 1.25135000 | 1.01370000 |
| H | 1.59956200 | 0.79499300 | -1.47879200 |
| H | 0.62716700 | 2.25312700 | -1.69860500 |
| H | 2.48206200 | 3.61159100 | -0.64280200 |
| H | 3.43608200 | 2.14230300 | -0.47656600 |
| H | 4.12730700 | 3.41154800 | -2.52125400 |
| H | 3.43063300 | 1.84857100 | -2.97579400 |
| H | 2.47314400 | 3.32625500 | -3.14583100 |
| C | -0.94358400 | 1.68301500 | 2.95975500 |
| H | -1.31638400 | 1.59310500 | 3.98161800 |
| H | 0.08743600 | 1.30294900 | 2.93216600 |
| H | -0.93790500 | 2.74141300 | 2.69096800 |
| S | 1.78448600 | -2.00588100 | 0.05275800 |
| O | 2.29376900 | -3.28380200 | 0.48920600 |
| O | 1.26483600 | -1.83232100 | -1.28420600 |
| O | 0.74087800 | -1.53699300 | 1.12324100 |
| O | 2.93329200 | -0.90059500 | 0.17747100 |
| C | 3.67732300 | -0.90090000 | 1.41525500 |
| H | 4.36858900 | -0.06514900 | 1.32982800 |
| H | 2.99804400 | -0.74874000 | 2.25716400 |
| H | 4.21862000 | -1.84153100 | 1.52018200 |
| H | -1.74621000 | 2.44702500 | -0.65601500 |

## INT-5

| | | | |
|---|---|---|---|
| C | 4.90766300 | 1.13547500 | 0.15534000 |
| C | 3.51600600 | 1.08105000 | 0.17697600 |
| C | 2.86139100 | -0.06609600 | -0.27144200 |
| C | 3.59710100 | -1.15596000 | -0.73954700 |
| C | 4.98754000 | -1.09682700 | -0.75760800 |
| C | 5.64387900 | 0.04825500 | -0.30987700 |
| C | 1.34939800 | -0.16686900 | -0.22222200 |
| N | 0.97603700 | -0.94873700 | 1.08313900 |
| O | 0.81949600 | 1.09533500 | -0.11023700 |
| O | 0.90085500 | -0.92803200 | -1.26022900 |
| C | -0.60728100 | 1.22047400 | -0.17733700 |
| C | -0.94999800 | 2.69046800 | -0.05072700 |
| C | -2.45731700 | 2.92041900 | -0.15335500 |
| C | -2.82553900 | 4.39260900 | 0.00987400 |
| H | 5.41535800 | 2.03024000 | 0.50052900 |
| H | 2.93653400 | 1.92674900 | 0.53072200 |
| H | 3.07997700 | -2.03840300 | -1.10335500 |
| H | 5.55742500 | -1.94321000 | -1.12681800 |
| H | 6.72815900 | 0.09376800 | -0.32635600 |
| H | -0.03450600 | -1.23270400 | 1.06430600 |
| H | -0.96974900 | 0.81595600 | -1.12939000 |
| H | -1.07334600 | 0.65202500 | 0.63730800 |
| H | -0.57689700 | 3.06395900 | 0.91108800 |
| H | -0.42871700 | 3.24715700 | -0.83864000 |
| H | -2.81066400 | 2.55539100 | -1.12651600 |

| | | | |
|---|---|---|---|
| H | -2.96946800 | 2.31839000 | 0.60755900 |
| H | -3.90523000 | 4.54435900 | -0.07330500 |
| H | -2.50643800 | 4.76709100 | 0.98806200 |
| H | -2.33820700 | 5.00354700 | -0.75705700 |
| C | 1.22723500 | -0.22069200 | 2.35280900 |
| H | 0.92832600 | -0.86328400 | 3.17951000 |
| H | 2.28707300 | 0.02132300 | 2.42217000 |
| H | 0.63307200 | 0.69171800 | 2.34901000 |
| H | 1.51345400 | -1.82160400 | 1.06361400 |
| S | -2.49524400 | -1.76399400 | 0.12853100 |
| O | -3.45997100 | -2.85536900 | 0.13612400 |
| O | -1.68691500 | -1.62806800 | 1.35926000 |
| O | -1.66925400 | -1.70123100 | -1.10044600 |
| O | -3.34142500 | -0.37788900 | 0.15109700 |
| C | -4.18622000 | -0.17196400 | -0.98831500 |
| H | -4.72771600 | 0.75257600 | -0.79238400 |
| H | -3.58009300 | -0.06996300 | -1.89227000 |
| H | -4.88785900 | -1.00319900 | -1.09329300 |
| H | -0.06429100 | -1.14682700 | -1.18492400 |

## TS-4

| | | | |
|---|---|---|---|
| C | 4.92533500 | 1.05179300 | -0.16928000 |
| C | 3.53651200 | 1.07607300 | -0.23546300 |
| C | 2.83864600 | -0.11082000 | -0.47632000 |
| C | 3.52362500 | -1.31624900 | -0.65095900 |
| C | 4.91142700 | -1.33200200 | -0.58276400 |
| C | 5.61137600 | -0.14958100 | -0.34225400 |
| C | 1.36486100 | -0.10895300 | -0.54400100 |
| N | 1.10167000 | -0.49840600 | 1.85872900 |
| O | 0.80733100 | 1.06320200 | -0.45369400 |
| O | 0.76682700 | -1.16303300 | -0.89639500 |
| C | -0.63373800 | 1.15826700 | -0.39374500 |
| C | -0.99072500 | 2.62209300 | -0.26092500 |
| C | -2.50644300 | 2.81835500 | -0.23754400 |
| C | -2.88725700 | 4.28670500 | -0.06921100 |
| H | 5.47229600 | 1.97008300 | 0.01592200 |
| H | 2.99302500 | 2.00555300 | -0.10578700 |
| H | 2.96424000 | -2.22694700 | -0.83506600 |
| H | 5.44793600 | -2.26523800 | -0.71699000 |
| H | 6.69536300 | -0.16477900 | -0.28977400 |
| H | 0.18908700 | -0.91753300 | 2.03520200 |
| H | -1.05440200 | 0.72210400 | -1.30494100 |
| H | -0.96366700 | 0.57507100 | 0.47280800 |
| H | -0.54455800 | 3.02127900 | 0.65793200 |
| H | -0.55430300 | 3.17469900 | -1.10126400 |
| H | -2.93213600 | 2.42991700 | -1.17163900 |
| H | -2.93915300 | 2.22141500 | 0.57437100 |
| H | -3.97285800 | 4.41613500 | -0.06302100 |
| H | -2.49416200 | 4.68511900 | 0.87171400 |
| H | -2.47906500 | 4.89132900 | -0.88565700 |
| C | 1.27269900 | 0.73938900 | 2.61314900 |
| H | 1.23503700 | 0.61501400 | 3.70283900 |
| H | 2.23669000 | 1.18770300 | 2.35161900 |
| H | 0.48893200 | 1.44648500 | 2.32440000 |
| H | 1.80253700 | -1.18234900 | 2.13637400 |
| S | -2.45160000 | -1.80702700 | 0.18424600 |
| O | -3.38331800 | -2.91731600 | 0.08026100 |
| O | -1.69054700 | -1.66885800 | 1.41958000 |
| O | -1.57390600 | -1.71470600 | -1.04475100 |
| O | -3.31627800 | -0.43971700 | 0.14446600 |
| C | -4.19581300 | -0.30317000 | -0.98168900 |
| H | -4.72436900 | 0.63650200 | -0.82849300 |
| H | -3.61651100 | -0.26389900 | -1.90805700 |
| H | -4.90260500 | -1.13492000 | -1.00924100 |
| H | -0.33734900 | -1.30943600 | -0.89198600 |

## [$MeNH_3$] $MeSO_4$

| | | | |
|---|---|---|---|
| N | 2.46555100 | -0.90460800 | -0.20055300 |
| H | 1.64436200 | -1.06743200 | 0.42044600 |
| C | 3.25083900 | 0.24697600 | 0.31947600 |
| H | 3.61731600 | -0.00036500 | 1.31351400 |
| H | 4.08062700 | 0.44596000 | -0.35526700 |
| H | 2.57939800 | 1.10252300 | 0.36095000 |
| H | 3.02587200 | -1.75399400 | -0.29463400 |
| S | -0.53781200 | 0.38100600 | -0.03572600 |
| O | 0.36529600 | 0.57756500 | -1.18059000 |
| O | -1.20842200 | 1.58310500 | 0.45448800 |
| O | -1.69459200 | -0.56486100 | -0.68121100 |
| O | 0.07991500 | -0.43535400 | 1.03965300 |
| C | -2.74294400 | -0.92276200 | 0.22493500 |
| H | -3.42702100 | -1.55300500 | -0.34188700 |
| H | -2.33612600 | -1.47961100 | 1.07314200 |
| H | -3.26134000 | -0.02753900 | 0.57679100 |
| H | 2.03810400 | -0.65930600 | -1.10276200 |

## 3ac

| | | | |
|---|---|---|---|
| C | -4.13259100 | 0.37810700 | 0.00039700 |
| C | -2.88470600 | 0.99086200 | 0.00021000 |

| | | | |
|---|---|---|---|
| C | -1.72579300 | 0.21147500 | -0.00014100 |
| C | -1.81560700 | -1.18274500 | -0.00029300 |
| C | -3.06646700 | -1.79224100 | -0.00010600 |
| C | -4.22322300 | -1.01371800 | 0.00023900 |
| H | -5.03359900 | 0.98286300 | 0.00066500 |
| H | -2.79011500 | 2.07180700 | 0.00032600 |
| H | -0.91083100 | -1.78029400 | -0.00056100 |
| H | -3.13936800 | -2.87496600 | -0.00022900 |
| H | -5.19750200 | -1.49258200 | 0.00038500 |
| C | -0.41195600 | 0.91673300 | -0.00034900 |
| O | -0.28799300 | 2.12295200 | 0.00004300 |
| C | 1.92832200 | 0.68166500 | -0.00023200 |
| H | 2.02061400 | 1.31899100 | -0.88574200 |
| H | 2.02032800 | 1.31910600 | 0.88522100 |
| O | 0.62658900 | 0.07399200 | -0.00041300 |
| C | 2.95654500 | -0.43069400 | -0.00000400 |
| H | 2.80068000 | -1.06327400 | -0.88227600 |
| H | 2.80044900 | -1.06312800 | 0.88233200 |
| C | 4.38170400 | 0.12052900 | 0.00013700 |
| H | 4.52359400 | 0.76138600 | 0.87920700 |
| H | 4.52382200 | 0.76123700 | -0.87900600 |
| C | 5.42659500 | -0.99237000 | 0.00036700 |
| H | 5.31744700 | -1.62846600 | -0.88413400 |
| H | 6.44155300 | -0.58553100 | 0.00046200 |
| H | 5.31722000 | -1.62831200 | 0.88495100 |

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