Supporting Information 1 (Experimental):

A Modular Approach to Prepare Enantioenriched Cyclobutanes: Synthesis of (+)-Rumphellaone A

Jordan C. Beck‡, Caitlin R. Lacker,‡ Lauren M. Chapman, and Sarah E. Reisman*

The Warren and Katharine Schlinger Laboratory of Chemistry and Chemical Engineering

Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, California 91125

**reisman@caltech.edu*

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1. Materials and Methods

Unless otherwise stated, reactions were performed under a nitrogen atmosphere using freshly dried solvents. Methylene chloride (CH_2Cl_2), diethyl ether (Et_2O), tetrahydrofuran (THF), 1,4-dioxane, *tert*-butyl methyl ether (TBME), and toluene (PhMe) were dried by passing through activated alumina columns. Methanol (MeOH) was distilled over calcium hydride. Acetonitrile (MeCN), *tert*-butanol (*t*-BuOH), anhydrous *N,N*-dimethylformamide (DMF), anhydrous *N,N*-dimethylacetamide (DMA), chloroform ($CHCl_3$), and absolute ethanol (EtOH) were used as received from Fisher Scientific. Methyl vinyl ketone was dried over K_2CO_3 and $CaCl_2$ and then distilled immediately prior to use. K_2HPO_4 was flame-dried under vacuum and dried at 0.200 Torr overnight and stored in a dessicator. Aryl iodides were purchased from Sigma-Aldrich or Combi-Blocks or prepared according to literature procedures. $NiBr_2$•dme and $NiCl_2$•dme were purchased from Strem and stored in a N_2-filled glovebox. Zinc dust and $Pd(OAc)_2$ were purchased from Strem and stored in a dessicator. $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ was purchased from Oakwood chemicals and used as received. $Pd(PPh_3)_4$ and Cs_2CO_3 were purchased from Sigma-Aldrich and stored in a N_2-filled glovebox. All other commercially obtained reagents were purchased from Sigma-Aldrich and used as received unless specifically indicated. Photochemical reactions were conducted using either Kessil A160WE blue LED lamps positioned 3–6 cm from the reactions using a computer fan to keep the reactions at ambient temperature, or 12W blue LED strips lining a beaker wrapped in aluminum foil . Yields of arylation reactions reported are an average of two runs. All reactions were monitored by thin-layer chromatography using EMD/Merck silica gel 60 F254 pre-coated plates (0.25 mm). Silica gel and basic alumina column chromatography was performed as described by Still et al. (W. C. Still, M. Kahn, A. Mitra, *J. Org. Chem*. **1978**, *43*, 2923.) using silica gel (particle size 0.032–0.063) purchased from Silicycle and aluminum oxide (activated, basic, Brockmann I, 58 Å pore size, powder) purchased from Sigma-Aldrich. ^1H and ^{13}C NMR were recorded on a Varian Inova 500 (at 500 MHz and 125 MHz respectively) or a Bruker Avance III HD with Prodigy cyroprobe (at 400 MHz and 101 MHz respectively). ^{19}F NMR spectra were recorded on a Varian Inova 400 (at 376 MHz). NMR data is reported relative to internal chloroform (^1H, $\delta = 7.26$, ^{13}C, $\delta = 77.2$) or to internal methanol (^1H, $\delta = 3.31$, ^{13}C, $\delta = 49.0$) and $PhCF_3$ (^{19}F, $\delta = -63.7$). Data for ^1H NMR spectra are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Multiplicity and qualifier abbreviations are as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. IR spectra were recorded on a Perkin

Elmer Paragon 1000 spectrometer and are reported in frequency of absorption (cm^{-1}). HRMS were acquired using either an Agilent 6200 Series TOF with an Agilent G1978A Multimode source in electrospray ionization (ESI), atmospheric pressure chemical ionization (APCI), or mixed (MM) ionization mode. Specific optical rotations were recorded on a Jasco P-2000 polarimeter using a 100 mm cell.

Abbreviations used: Et_2O – diethyl ether; CH_2Cl_2 – methylene chloride; PhMe – toluene; EtOAc – ethyl acetate; THF – tetrahydrofuran; *t*-BuOH – *tert*-butanol; $CHCl_3$ – chloroform; MeCN – acetonitrile; DMF – *N,N*-dimethylformamide; DMA – *N,N*-dimethylacetamide; dtbbpy – 4,4'-di*tert*butylbipyridine; dme – 1,2-dimethoxyethane; TBME – *tert*-butyl methyl ether; ABNO – 9-azabicyclo[3.3.1]nonane *N*-oxyl.

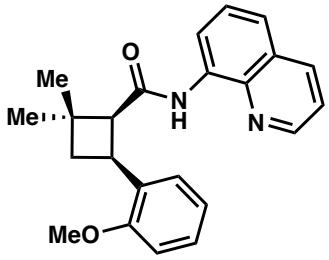
2. C_{sp}^3–H arylation

a. General Procedure

On the bench-top, a 2-dram vial equipped with a stir bar was charged with $Pd(OAc)_2$ (15 mol %, 0.03 mmol), Ag_2CO_3 (1 equiv, 0.2 mmol), cyclobutamide (**4**) (1 equiv, 0.2 mmol), and aryl iodide (2 equiv, 0.4 mmol). TBME (0.2 M, 1 mL) was added to the vial, then the vial was sealed with a Teflon cap and electrical tape and submerged in an oil bath at 90 °C. After approximately 5 minutes for aryl iodide substrates and 30 minutes for heteroaryl iodide substrates, the olive-green mixture became black. The reaction mixture was stirred at 90 °C additional 16 hours, at which point the vial is allowed to cool to room temperature over 15 minutes. The black reaction mixture was diluted with CH_2Cl_2 and filtered over a pad of 20 grams of tightly packed celite. The celite plug was eluted with an additional 100 mL of CH_2Cl_2. Following this, the resultant orange solution was concentrated *in vacuo* and subsequently purified by silica gel column chromatography to give the arylated cyclobutane products. (Note: some substrates required purification with basic alumina as the stationary phase).

d. Characterization of Arylation Products

9a



Prepared from cyclobutamide **4** (1 equiv, 50.8 mg, 0.2 mmol) and 2-iodoanisole (2 equiv, 93.6 mg, 0.4 mmol). The crude residue was purified by column chromatography (10 → 15 → 20% EtOAc/Hexanes) to give a colorless foam.

Run 1: (54.4 mg, 75%), Run 2: (61.2 mg, 84%)

R_f = 0.48 (silica gel, 30% EtOAc/Hex, UV, *p*-anisaldehyde).

$[\alpha]_D^{25}$ = +84.8° (c = 3.3, $CHCl_3$).

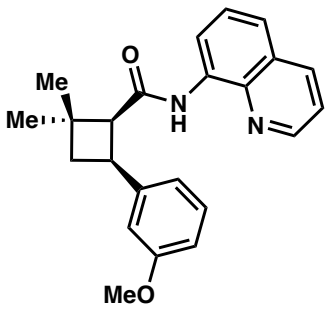
^{1}H NMR (400 MHz, $CDCl_3$): δ 9.57 (s, 1H), 8.77 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.60 (dd, *J* = 4.9, 4.2 Hz, 1H), 8.10 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.44 – 7.36 (m, 3H), 7.24 (dt, *J* = 7.4, 1.5 Hz, 1H), 7.09 (dddd, *J* = 8.2, 7.4, 1.8, 0.8 Hz, 1H), 6.96 (tdd, *J* = 7.5, 1.1, 0.4 Hz, 1H), 6.61 (dd, *J* = 8.1, 1.1 Hz, 1H), 4.09 – 3.95 (m, 1H), 3.62 (s, 3H), 3.46 (ddd, *J* = 8.6, 2.9, 0.8 Hz, 1H), 2.74 (t, *J* = 10.8 Hz, 1H), 2.13 (ddd, *J* = 10.4, 8.4, 2.9 Hz, 1H), 1.53 (s, 3H), 1.22 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 171.13, 157.19, 147.90, 138.41, 136.31, 134.88, 130.18, 127.92, 127.66, 127.54, 127.00, 121.45, 120.75, 120.43, 116.27, 109.43, 58.05, 55.05, 37.10, 35.89, 32.81, 30.33, 25.14.

FTIR (NaCl, thin film, cm^{-1}): 3366, 2952, 5927, 2863, 2361, 1685, 1523, 1485, 1464, 1424, 1324, 1241, 1161, 1132, 1161, 1029, 826, 792, 751.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{23}H_{25}N_2O_2$ $[M+H]^+$: 361.1911; found: 361.1925.

9b



Prepared from cyclobutamide **4** (1 equiv, 50.8 mg, 0.2 mmol) and 3-iodoanisole (2 equiv, 93.6 mg, 0.4 mmol). The crude residue was purified by column chromatography (10 → 15 → 20% EtOAc/Hexanes) to give a white solid.

Run 1: (59.0 mg, 82%), Run 2: (58.3 mg, 81%)

R_f = 0.36 (silica gel, 20% EtOAc/Hex, UV, *p*-anisaldehyde).

$[\alpha]_D^{25}$ = +61.6° (c = 0.4, $CHCl_3$).

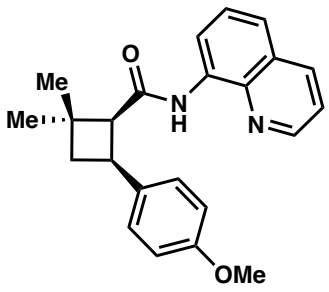
^{1}H NMR (400 MHz, $CDCl_3$): δ 9.62 (s, 1H), 8.75 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.64 (p, *J* = 4.3 Hz, 1H), 8.11 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.45 – 7.38 (m, 3H), 7.13 (t, *J* = 7.9 Hz, 1H), 6.82 (ddt, *J* = 7.6, 1.8, 1.0 Hz, 1H), 6.77 (dt, *J* = 2.7, 1.3 Hz, 1H), 6.63 (ddt, *J* = 8.2, 2.6, 0.9 Hz, 1H), 4.03 (dtd, *J* = 11.0, 8.6, 1.1 Hz, 1H), 3.67 (s, 3H), 3.39 (ddd, *J* = 8.7, 2.9, 0.8 Hz, 1H), 2.76 (t, *J* = 10.7 Hz, 1H), 2.16 (ddd, *J* = 10.4, 8.5, 3.0 Hz, 1H), 1.51 (s, 3H), 1.22 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 170.5, 159.5, 148.0, 143.7, 138.4, 136.4, 134.6, 129.1, 127.9, 127.5, 121.5, 121.2, 119.1, 116.5, 112.3, 111.3, 57.7, 55.1, 37.8, 36.0, 35.8, 30.2, 25.1.

FTIR (NaCl, thin film, cm^{-1}): 3357, 2952, 2925, 1684, 1600, 1582, 1521, 1485, 1424, 1386, 1323, 1259, 1160, 1049, 878, 826, 790, 756, 694.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{23}H_{25}N_2O_2$ $[M+H]^+$: 361.1911; found: 361.1915.

9c



Prepared from cyclobutamide **4** (1 equiv, 50.8 mg, 0.2 mmol) and 4-iodoanisole (2 equiv, 93.6 mg, 0.4 mmol). The crude residue was purified by column chromatography (10 → 15% EtOAc/Hexanes) to give a white, amorphous solid.

Run 1: (47.7 mg, 66%), Run 2: (51.2 mg, 71%)

R_f = 0.23 (silica gel, 20% EtOAc/Hex, UV, *p*-anisaldehyde).

$[\alpha]_D^{25}$ = +59.8° (c = 1.3, $CHCl_3$).

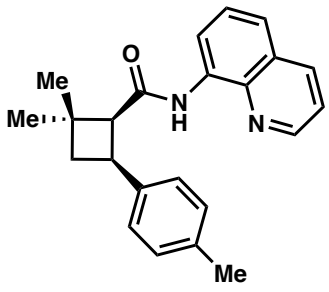
^{1}H NMR (400 MHz, $CDCl_3$): δ 9.58 (s, 1H), 8.75 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.63 (p, *J* = 4.4 Hz, 1H), 8.10 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.45 – 7.38 (m, 3H), 7.20 – 7.13 (m, 2H), 6.80 – 6.73 (m, 2H), 4.00 (q, *J* = 11.1, 8.6 Hz, 1H), 3.70 (s, 3H), 3.34 (ddd, *J* = 8.7, 3.0, 0.8 Hz, 1H), 2.75 (t, *J* = 10.8 Hz, 1H), 2.13 (ddd, *J* = 10.4, 8.6, 3.0 Hz, 1H), 1.51 (s, 3H), 1.23 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 170.6, 157.7, 148.0, 138.4, 136.4, 134.6, 133.7, 127.9, 127.5, 121.5, 121.1, 116.5, 113.6, 57.7, 55.3, 37.9, 35.7, 35.5, 30.2, 25.2.

FTIR (NaCl, thin film, cm^{-1}): 2926, 2361, 1685, 1523, 1485, 1288, 1324, 1247, 1160, 1038, 826, 772.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{23}H_{25}N_2O_2$ $[M+H]^+$: 361.1911; found: 361.1921.

9d



Prepared from cyclobutamide **4** (1 equiv, 50.8 mg, 0.2 mmol) and 4-iodotoluene (2 equiv, 87.2 mg, 0.4 mmol). The crude residue was purified by column chromatography (10 → 15 → 20% EtOAc/Hexanes) to give a white, amorphous solid.

Run 1: (54.1 mg, 79%), Run 2: (55.9 mg, 81%)

R_f = 0.29 (silica gel, 20% EtOAc/Hex, UV, *p*-anisaldehyde).

$[\alpha]_D^{25}$ = +54.2° (c = 2.0, $CHCl_3$).

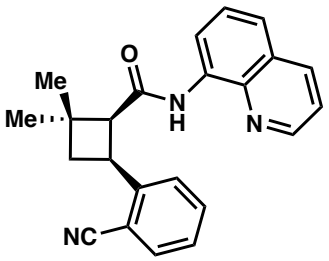
^{1}H NMR (400 MHz, $CDCl_3$): δ 9.60 (s, 1H), 8.76 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.65 (h, *J* = 4.2 Hz, 1H), 8.11 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.50 – 7.36 (m, 3H), 7.14 (d, *J* = 7.8 Hz, 2H), 7.02 (d, *J* = 7.4 Hz, 2H), 4.01 (td, *J* = 10.8, 8.1 Hz, 1H), 3.37 (ddd, *J* = 8.7, 2.9, 0.8 Hz, 1H), 2.76 (t, *J* = 10.8 Hz, 1H), 2.24 (s, 3H), 2.14 (ddd, *J* = 10.4, 8.6, 2.9 Hz, 1H), 1.51 (s, 3H), 1.22 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 170.6, 148.0, 138.7, 138.4, 136.4, 135.0, 134.7, 128.9, 127.9, 127.5, 126.7, 121.5, 121.1, 116.5, 57.7, 37.8, 35.8, 35.7, 30.2, 25.2, 21.2.

FTIR (NaCl, thin film, cm^{-1}): 3360, 2924, 2359, 1686, 1522 1485, 1424, 1386, 1324, 1160, 826, 792.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{23}H_{25}N_2O$ $[M+H]^+$: 345.1961; found: 345.1971.

9e



Prepared from cyclobutamide **4** (1 equiv, 50.8 mg, 0.2 mmol) and 2-iodobenzonitrile (2 equiv, 91.8 mg, 0.4 mmol). The crude residue was purified by column chromatography (10 → 15% EtOAc/Hexanes) to give a pale, yellow foam.

Run 1: (57.6 mg, 81%), Run 2: (64.7 mg, 91%)

R_f = 0.55 (silica gel, 30% EtOAc/Hex, UV, *p*-anisaldehyde).

$[\alpha]_D^{25}$ = –24.4° (c = 5.4, $CHCl_3$).

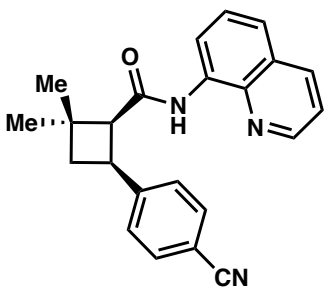
^{1}H NMR (400 MHz, $CDCl_3$): δ 9.76 (s, 1H), 8.81 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.53 (dd, *J* = 7.4, 1.7 Hz, 1H), 8.10 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.56 (td, *J* = 8.0, 7.6, 1.2 Hz, 1H), 7.51 – 7.35 (m, 5H), 7.21 (tdd, *J* = 7.6, 1.3, 0.7 Hz, 1H), 4.21 (dt, *J* = 11.1, 8.3, 7.8 Hz, 1H), 3.74 (ddd, *J* = 8.3, 3.0, 0.8 Hz, 1H), 2.87 (t, *J* = 10.7 Hz, 1H), 2.16 (ddd, *J* = 10.4, 8.3, 3.1 Hz, 1H), 1.57 (s, 3H), 1.20 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 170.0, 148.3, 146.9, 138.5, 136.3, 134.5, 132.6, 128.1, 127.9, 127.2, 126.3, 121.7, 121.4, 118.8, 116.3, 110.6, 57.7, 36.6, 36.1, 35.2, 29.8, 25.1.

FTIR (NaCl, thin film, cm^{-1}): 3353, 2954, 2361, 2222, 1683, 1523, 1485, 1424, 1388, 1323, 1260, 1161, 826, 791, 755, 668.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{23}H_{21}N_3O$ $[M+H]^+$: 356.1757; found: 356.1773.

9f



Prepared from cyclobutamide **4** (1 equiv, 50.8 mg, 0.2 mmol) and 4-iodobenzonitrile (2 equiv, 91.8 mg, 0.4 mmol). The crude residue was purified by column chromatography (10 → 15 → 20 →25 % EtOAc/Hexanes) to give a pale, yellow foam.

Run 1: (50.5 mg, 71%), Run 2: (53.3 mg, 75%)

R_f = 0.32 (silica gel, 30% EtOAc/Hex, UV, *p*-anisaldehyde).

$[\alpha]_D^{25}$ = +102.7° (c = 5.1, $CHCl_3$).

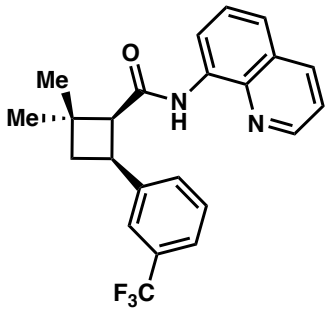
^{1}H NMR (400 MHz, $CDCl_3$): δ 9.66 (s, 1H), 8.79 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.56 (dd, *J* = 7.2, 1.8 Hz, 1H), 8.14 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.50 (dt, *J* = 8.3, 1.8 Hz, 2H), 7.49 – 7.37 (m, 3H), 7.33 – 7.24 (m, 2H), 4.02 (dt, *J* = 10.8, 8.3 Hz, 1H), 3.43 (ddd, *J* = 8.5, 3.0, 0.8 Hz, 1H), 2.77 (t, *J* = 10.7 Hz, 1H), 2.18 (ddd, *J* = 10.4, 8.5, 3.0 Hz, 1H), 1.53 (s, 3H), 1.20 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 169.9, 148.4, 148.2, 138.3, 136.5, 134.2, 131.9, 128.0, 127.5, 127.3, 121.7, 121.6, 119.5, 116.5, 109.3, 57.7, 37.5, 36.1, 36.0, 29.9, 25.0.

FTIR (NaCl, thin film, cm^{-1}): 3353, 2954, 2930, 2361, 2226, 1684, 1608, 1524, 1486, 1424, 1288, 1323, 1161, 826, 792, 755, 668.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{23}H_{22}N_3O$ $[M+H]^+$: 356.1757; found: 356.1752.

9g



Prepared from cyclobutamide **4** (1 equiv, 50.8 mg, 0.2 mmol) and 3-iodotrifluorotoluene (2 equiv, 109.1 mg, 0.4 mmol). The crude residue was purified by column chromatography (10% EtOAc/Hexanes) to give a colorless oil.

Run 1: (67.7 mg, 85%), Run 2: (62.9 mg, 79%)

$\mathbf{R}_f$ = 0.23 (silica gel, 20% EtOAc/Hex, UV, *p*-anisaldehyde).

$[\alpha]_D^{25}$ = +47.3° (c = 3.3, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.63 (s, 1H), 8.77 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.57 (dd, *J* = 6.6, 2.4 Hz, 1H), 8.12 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.50 – 7.36 (m, 5H), 7.39 – 7.26 (m, 2H), 4.05 (dt, *J* = 11.0, 8.7 Hz, 1H), 3.42 (ddd, *J* = 8.6, 3.0, 0.8 Hz, 1H), 2.80 (t, *J* = 10.8 Hz, 1H), 2.20 (ddd, *J* = 10.4, 8.5, 3.0 Hz, 1H), 1.53 (s, 3H), 1.23 (s, 3H).

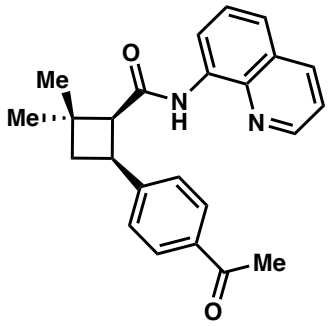
^{13}C NMR (101 MHz, $CDCl_3$): δ 170.2, 148.2, 143.2, 138.5, 136.6, 134.5, 130.4 (q, J_{C-F} = 32 Hz), 130.3, 128.5, 128.1, 127.6, 125.9, 123.7 (q, J_{C-F} = 3.7 Hz), 123.2, 122.8 (q, J_{C-F} = 3.8 Hz), 121.7, 121.5, 116.6, 57.8, 37.8, 36.1, 36.0, 30.2, 30.0, 25.2.

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.50.

FTIR (NaCl, thin film, cm^{-1}): 3355, 2931, 2360, 1684, 1523, 1486, 1425, 1388, 1324, 1162, 1122, 1072, 901, 826, 793, 756, 701, 659.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{23}H_{22}F_3N_2O$ $[M+H]^+$: 399.1679; found: 399.1679.

9h



Prepared from cyclobutamide **4** (1 equiv, 50.8 mg, 0.2 mmol) and 4-iodoacetophenone (2 equiv, 98.7 mg, 0.4 mmol). The crude residue was purified by column chromatography (20% EtOAc/Hexanes) to give a white, amorphous solid.

Run 1: (57.3 mg, 77%), Run 2: (56.6 mg, 76%)

$\mathbf{R}_f$ = 0.41 (silica gel, 40% EtOAc/Hex, UV, *p*-anisaldehyde).

$[\alpha]_D^{25}$ = +95.0° (c = 3.0, $CHCl_3$).

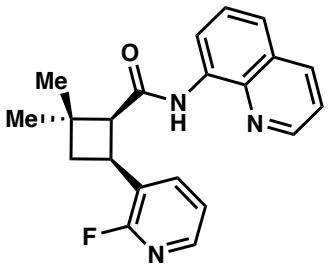
^{1}H NMR (400 MHz, $CDCl_3$): δ 9.73 (s, 1H), 8.85 (dd, *J* = 4.3, 1.7 Hz, 1H), 8.66 (dd, *J* = 7.1, 1.8 Hz, 1H), 8.20 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.94 – 7.87 (m, 2H), 7.51 (dd, *J* = 8.5, 4.1 Hz, 2H), 7.48 (q, *J* = 9.2, 8.2, 8.2 Hz, 1H), 7.39 – 7.33 (m, 2H), 4.12 (td, *J* = 11.3, 9.7, 8.4 Hz, 1H), 3.51 (ddd, *J* = 8.6, 2.9, 0.8 Hz, 1H), 2.88 (t, *J* = 10.7 Hz, 1H), 2.58 (s, 3H), 2.26 (ddd, *J* = 10.3, 8.5, 3.0 Hz, 1H), 1.61 (s, 3H), 1.29 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 198.1, 170.1, 148.5, 148.1, 138.4, 136.5, 134.8, 134.4, 128.4, 128.0, 127.5, 126.7, 121.6, 121.4, 116.5, 57.8, 37.7, 36.1, 36.0, 30.0, 26.7, 25.1.

FTIR (NaCl, thin film, cm^{-1}): 3354, 2954, 2928, 2866, 1678, 1606, 1523, 1485, 1424, 1387, 1323, 1267, 1161, 956, 826, 792, 754, 657.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{24}H_{25}N_2O_2$ $[M+H]^+$: 373.1911; found: 373.1900.

9i



Prepared from cyclobutamide **4** (1 equiv, 50.8 mg, 0.2 mmol) and 2-fluoro-3-iodopyridine (2 equiv, 89.2 mg, 0.4 mmol). The crude residue was purified by column chromatography using silica gel basified with 4 mL of aqueous ammonium hydroxide (10% EtOAc/2% Et_3N/88% hexanes → 15% EtOAc/2% Et_3N/83% hexanes → 20% EtOAc/2% Et_3N/78% hexanes → 35% EtOAc/2% Et_3N/63% hexanes) to give a white foam.

Run 1: (56.1 mg, 80%), Run 2: (56.4 mg, 81%)

$\mathbf{R}_f$ = 0.22 (silica gel, 20% EtOAc/Hex, UV, p-Anisaldehyde).

$[\alpha]_D^{25}$ = +60.8° (c = 0.415, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.66 (s, 1H), 8.77 (dd, *J* = 4.3, 1.7 Hz, 1H), 8.54 (dd, *J* = 7.0, 2.1 Hz, 1H), 8.09 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.96 (ddt, *J* = 4.9, 2.0, 1.0 Hz, 1H), 7.72 (ddq, *J* = 9.9, 7.5, 1.2, 0.7 Hz, 1H), 7.45 – 7.34 (m, 3H), 7.15 (ddd, *J* = 7.1, 4.9, 1.9 Hz, 1H), 3.99 (dtd, *J* = 11.0, 8.6,

1.1 Hz, 1H), 3.44 (ddt, J = 8.4, 2.5, 1.3 Hz, 1H), 2.76 (t, J = 10.7 Hz, 1H), 2.11 (ddd, J = 10.4, 8.4, 3.0 Hz, 1H), 1.53 (s, 3H), 1.19 (s, 3H).

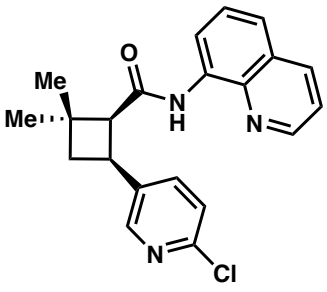
^{13}C NMR (101 MHz, $CDCl_3$): δ 170.2, 161.5 (d, J_{C-F} = 237 Hz), 148.2, 144.6 (d, J_{C-F} = 14.7 Hz), 139.3 (d, J_{C-F} = 6.1 Hz), 138.4, 136.3, 134.4, 127.9, 127.3, 124.2 (d, J_{C-F} = 31.2 Hz), 121.6, 121.4, 121.3 (d, J_{C-F} = 4.0 Hz), 116.4, 57.0, 36.4 (d, J_{C-F} = 14.8 Hz), 30.8, 30.7, 29.8, 25.0.

^{19}F NMR (376 MHz, $CDCl_3$): δ -71.52 (d, J = 10.1 Hz).

FTIR (NaCl, thin film, cm^{-1}): 3355, 3058, 2954, 2930, 2866, 1682, 1605, 1577, 1524, 1486, 1431, 1388, 1372, 1324, 1261, 1240, 1162, 1132, 1112, 826, 793, 758.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{21}H_{21}FN_3O$ $[M+H]^+$: 350.1663; found: 350.1659.

9j



Prepared from cyclobutamide **4** (1 equiv, 50.8 mg, 0.2 mmol) and 5-iodo-2-chloropyridine (2 equiv, 95.8 mg, 0.4 mmol). The crude residue was purified by column chromatography using basic alumina as the stationary phase (0 → 1% MeOH/CH_2Cl_2) to give a colorless foam.

Run 1: (50.6 mg, 69%), Run 2: (49.7 mg, 68%)

R_f = 0.24 (silica gel, 40% EtOAc/Hex, UV).

$[\alpha]_D^{25}$ = +81.1° (c = 4.3, $CHCl_3$).

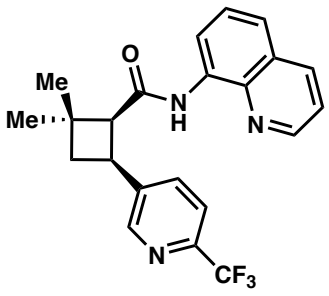
^{1}H NMR (500 MHz, $CDCl_3$): δ 9.64 (s, 1H), 8.76 (dd, J = 4.2, 1.7 Hz, 1H), 8.58 (dd, J = 6.8, 2.2 Hz, 1H), 8.22 (dt, J = 2.6, 0.8 Hz, 1H), 8.11 (dd, J = 8.3, 1.7 Hz, 1H), 7.56 (ddd, J = 8.2, 2.5, 0.9 Hz, 1H), 7.46 – 7.38 (m, 3H), 7.17 (d, J = 8.2 Hz, 1H), 3.96 (q, J = 11.0, 8.5 Hz, 1H), 3.38 (ddd, J = 8.5, 3.0, 0.8 Hz, 1H), 2.76 (t, J = 10.7 Hz, 1H), 2.15 (ddd, J = 10.4, 8.5, 3.0 Hz, 1H), 1.52 (s, 3H), 1.22 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 169.8, 148.8, 148.5, 148.1, 138.3, 137.7, 136.5, 136.3, 134.2, 127.9, 127.4, 123.5, 121.7, 121.6, 116.5, 57.4, 37.4, 36.3, 33.3, 29.8, 29.8, 25.0.

FTIR (NaCl, thin film, cm^{-1}): 3350, 2954, 1682, 1524, 1485, 1460, 1424, 1386, 1324, 1260, 1162, 1133, 1104, 826, 792, 755, 666.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{21}H_{21}ClN_3O$ $[M+H]^+$: 366.1368; found: 366.1370.

9k



Prepared from cyclobutamide **4** (1 equiv, 50.8 mg, 0.2 mmol) and 5-iodo-2-trifluoromethylpyridine (2 equiv, 95.8 mg, 0.4 mmol). The crude residue was purified by column chromatography using silica gel basified with 5 mL of aqueous ammonium hydroxide (5% EtOAc/2% Et_3N/93% hexanes → 10% EtOAc/2% Et_3N/88% hexanes → 15% EtOAc/2% Et_3N/83% hexanes → 20% EtOAc/2% Et_3N/78% hexanes) to give a pale, yellow foam.

Run 1: (71.6 mg, 90%), Run 2: (68.2 mg, 85%)

R_f = 0.19 (silica gel, 20% EtOAc/Hex, UV).

$[\alpha]_D^{25}$ = +67.7° (c = 4.2, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.61 (s, 1H), 8.69 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.52 – 8.41 (m, 2H), 8.04 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.70 – 7.62 (m, 1H), 7.46 (dd, *J* = 8.1, 0.7 Hz, 1H), 7.41 – 7.28 (m, 3H), 3.95 (q, *J* = 11.0, 8.5 Hz, 1H), 3.37 (ddd, *J* = 8.4, 2.9, 0.9 Hz, 1H), 2.73 (t, *J* = 10.7 Hz, 1H), 2.12 (ddd, *J* = 10.4, 8.5, 3.0 Hz, 1H).

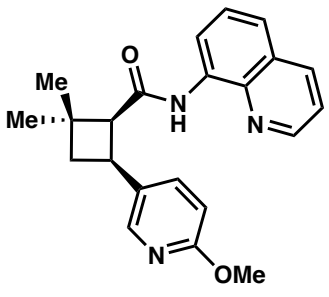
^{13}C NMR (101 MHz, $CDCl_3$): δ 169.7, 148.8, 148.2, 145.5 (q, J_{C-F} = 35 Hz), 141.2, 138.3, 136.5, 135.7, 134.1, 128.0, 127.4, 123.2, 121.7, 120.5, 119.9, 119.9, 119.8, 119.8, 116.5, 57.4, 37.3, 36.5, 33.7, 29.8, 25.0.

^{19}F NMR (282 MHz, $CDCl_3$): δ -68.6.

FTIR (NaCl, thin film, cm^{-1}): 3351, 2957, 1682, 1524, 1486, 1425, 1387, 1340, 1261, 1164, 1134, 1088, 1030, 826, 792, 756, 667.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{22}H_{21}F_3N_3O$ $[M+H]^+$: 400.1631; found: 400.1621.

9l



Prepared from cyclobutamide **4** (1 equiv, 50.8 mg, 0.2 mmol) and 5-iodo-2-methoxypyridine (2 equiv, 94.0 mg, 0.4 mmol). The crude residue was purified by column chromatography using silica gel basified with 4 mL of aqueous ammonium hydroxide (10% EtOAc/2% Et_3N/88% hexanes → 15% EtOAc/2% Et_3N/83% hexanes → 20% EtOAc/2% Et_3N/78% hexanes → 30% EtOAc/2% Et_3N/68% hexanes) to give a white solid.

Run 1: (34.9 mg, 48%), Run 2: (36.1 mg, 50%)

R_f = 0.14 (silica gel, 20% EtOAc/Hex, UV, *p*-anisaldehyde).

$[\alpha]_D^{25}$ = +61.1° (c = 0.415, $CHCl_3$).

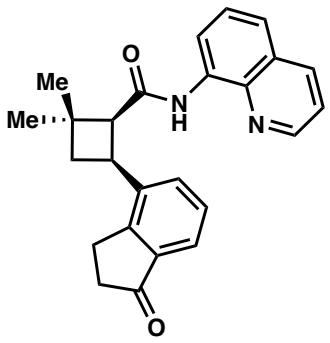
^{1}H NMR (400 MHz, $CDCl_3$): δ 9.60 (s, 1H), 8.76 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.62 (dd, *J* = 5.3, 3.7 Hz, 1H), 8.12 (dd, *J* = 8.3, 1.7 Hz, 1H), 8.01 (dt, *J* = 2.5, 0.9 Hz, 1H), 7.54 (ddd, *J* = 8.6, 2.5, 0.7 Hz, 1H), 7.46 – 7.39 (m, 3H), 6.61 (dd, *J* = 8.6, 0.7 Hz, 1H), 3.96 (qd, *J* = 11.0, 8.6, 1.1 Hz, 1H), 3.84 (s, 3H), 3.33 (ddd, *J* = 8.7, 2.9, 0.8 Hz, 1H), 2.76 (t, *J* = 10.8 Hz, 1H), 2.14 (ddd, *J* = 10.4, 8.6, 3.0 Hz, 1H), 1.51 (s, 3H), 1.23 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 170.3, 162.7, 148.1, 145.3, 138.4, 138.0, 136.4, 134.5, 129.6, 128.0, 127.5, 121.6, 121.4, 116.5, 110.1, 57.6, 53.4, 37.7, 36.1, 33.4, 30.1, 25.1.

FTIR (NaCl, thin film, cm^{-1}): 3352, 2922, 2850, 2351, 1682, 1606, 1574, 1523, 1494, 1486, 1424, 1385, 1324, 1285, 1259, 1160, 1132, 1032, 826, 792, 756.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{22}H_{24}N_3O_2$ $[M+H]^+$: 362.1863; found: 362.1856

9m



Prepared from cyclobutamide **4** (1 equiv, 50.8 mg, 0.2 mmol) and 4-iodo-1-indanone (2 equiv, 103.5 mg, 0.4 mmol). The crude residue was purified by column chromatography (30% EtOAc/Hexanes) to give a pale, yellow foam.

Run 1: (43.4 mg, 56%), Run 2: (39.7 mg, 52%)

R_f = 0.32 (silica gel, 40% EtOAc/Hex, UV, *p*-anisaldehyde).

$[\alpha]_D^{25}$ = +2.0° (c = 5.0, $CHCl_3$).

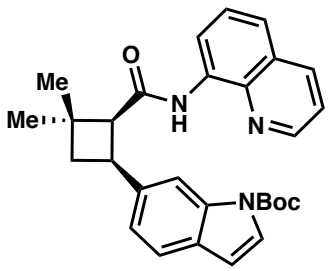
^{1}H NMR (400 MHz, $CDCl_3$): δ 9.57 (s, 1H), 8.74 (dd, *J* = 4.3, 1.7 Hz, 1H), 8.54 (dd, *J* = 7.1, 2.0 Hz, 1H), 8.10 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.56 (ddt, *J* = 17.3, 7.6, 1.1 Hz, 2H), 7.46 – 7.33 (m, 4H), 4.07 (dt, *J* = 11.2, 8.4 Hz, 1H), 3.47 (ddd, *J* = 8.4, 3.0, 0.9 Hz, 1H), 3.10 (ddd, *J* = 17.1, 7.8, 3.8 Hz, 1H), 2.98 (ddd, *J* = 17.1, 7.6, 3.9 Hz, 1H), 2.92 (t, *J* = 10.8 Hz, 1H), 2.57 (dddd, *J* = 32.0, 19.4, 7.8, 3.7 Hz, 2H), 2.18 (ddd, *J* = 10.5, 8.4, 3.1 Hz, 1H), 1.58 (s, 3H), 1.23 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 207.3, 170.1, 153.3, 148.1, 139.5, 138.3, 136.8, 136.5, 134.2, 132.9, 127.9, 127.5, 127.4, 121.6, 121.5, 121.4, 116.6, 57.2, 37.0, 36.5, 36.2, 34.1, 30.1, 25.2, 25.1.

FTIR (NaCl, thin film, cm^{-1}): 3353, 3012, 2954, 2927, 2866, 2359, 1709, 1587, 1523, 1485, 1425, 1386, 1324, 1265, 1162, 1055, 827, 790, 754, 666.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{25}H_{25}N_2O_2$ $[M+H]^+$: 385.1911; found: 385.1921.

9n



Prepared from cyclobutamide **4** (1 equiv, 50.8 mg, 0.2 mmol) and 6-iodo-N-Boc-indole (2 equiv, 137 mg, 0.4 mmol). The crude residue was purified by column chromatography (10% → 15% EtOAc/hexanes) to give a colorless foam.

Run 1: (56.1 mg, 60%), Run 2: (62.8 mg, 67%)

R_f = 0.36 (silica gel, 20% EtOAc/Hex, UV, *p*-anisaldehyde).

$[\alpha]_D^{25}$ = +114.7° (c = 5.7, $CHCl_3$).

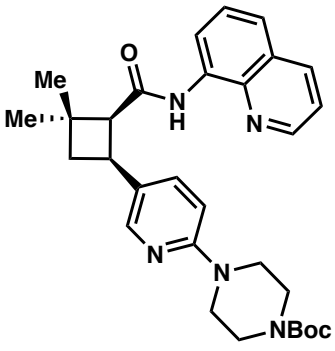
^{1}H NMR (400 MHz, $CDCl_3$): δ 9.64 (s, 1H), 8.65 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.60 (dd, *J* = 6.3, 2.8 Hz, 1H), 8.08 (dd, *J* = 8.3, 1.7 Hz, 1H), 8.03 (s, 1H), 7.47 (d, *J* = 3.7 Hz, 1H), 7.43 – 7.32 (m, 4H), 7.09 (dt, *J* = 8.1, 1.1 Hz, 1H), 6.44 (dd, *J* = 3.7, 0.8 Hz, 1H), 4.19 (dt, *J* = 10.9, 8.6 Hz, 1H), 3.44 (dd, *J* = 8.7, 2.9 Hz, 1H), 2.85 (t, *J* = 10.7 Hz, 1H), 2.25 (ddd, *J* = 10.3, 8.6, 3.0 Hz, 1H), 1.61 (s, 9H), 1.54 (s, 3H), 1.23 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 170.6, 150.0, 147.9, 138.6, 138.4, 136.3, 135.5, 134.7, 128.7, 127.9, 127.5, 125.3, 121.6, 121.5, 121.1, 120.5, 116.5, 113.4, 107.4, 83.4, 57.9, 38.2, 36.4, 35.9, 30.2, 28.3, 25.3.

FTIR (NaCl, thin film, cm^{-1}): 3358, 3008, 2954, 2929, 2866, 1730, 1686, 1618, 1578, 1523, 1485, 1424, 1386, 1370, 1338, 1253, 1214, 1151, 117, 1077, 1022, 826, 816, 756.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{29}H_{32}N_3O_3$ $[M+H]^+$: 470.2438; found: 470.2449.

9o



Prepared from cyclobutamide **4** (1 equiv, 50.8 mg, 0.2 mmol) and 4-(5-iodopyrin-2-yl)piperazine-1-carboxylic acid *tert*-butyl ester (2 equiv, 156 mg, 0.4 mmol). The crude residue was purified by column chromatography using silica gel basified with 5 mL of aqueous ammonium hydroxide (20% EtOAc/2% Et_3N/78% hexanes → 30% EtOAc/2% Et_3N/68% hexanes → 40% EtOAc/2% Et_3N/58% hexanes) to give a pale, yellow foam.

Run 1: (79.9 mg, 77%), Run 2: (84.6 mg, 82%)

R_f = 0.27 (silica gel, 40% EtOAc/Hex, UV, *p*-anisaldehyde).

$[\alpha]_D^{25}$ = +69.2° (c = 5.1, $CHCl_3$).

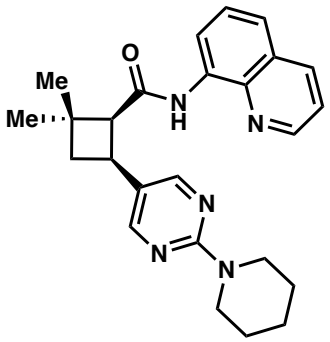
^{1}H NMR (500 MHz, $CDCl_3$): δ 9.58 (s, 1H), 8.74 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.62 (p, *J* = 4.4 Hz, 1H), 8.10 (dd, *J* = 8.2, 1.7 Hz, 1H), 8.06 (dt, *J* = 2.5, 0.8 Hz, 1H), 7.50 (ddd, *J* = 8.7, 2.5, 0.7 Hz, 1H), 7.46 – 7.37 (m, 3H), 6.53 (dd, *J* = 8.8, 0.8 Hz, 1H), 3.93 (dt, *J* = 11.0, 8.6 Hz, 1H), 3.45 (dd, *J* = 6.6, 3.5 Hz, 4H), 3.39 (dd, *J* = 6.3, 3.6 Hz, 4H), 3.30 (dd, *J* = 8.4, 2.9 Hz, 1H), 2.74 (t, *J* = 10.8 Hz, 1H), 2.10 (ddd, *J* = 10.4, 8.5, 2.9 Hz, 1H), 1.51 (s, 4H), 1.47 (s, 9H), 1.24 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 170.4, 158.0, 154.9, 148.0, 146.8, 138.4, 137.0, 136.4, 134.5, 127.9, 127.4, 126.4, 121.6, 121.2, 116.4, 106.9, 79.9, 57.7, 45.5, 37.6, 35.9, 33.5, 30.1, 28.5, 25.1.

FTIR (NaCl, thin film, cm^{-1}): 3357, 3007, 2973, 2928, 2864, 2360, 1686, 1605, 1560, 1524, 1486, 1424, 1391, 1324, 1241, 1166, 1129, 1084, 1000, 934, 864, 826, 792, 756, 686, 666.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{30}H_{38}N_5O_3$ $[M+H]^+$: 516.2969; found: 516.2955.

9p



Prepared from cyclobutamide **4** (1 equiv, 50.8 mg, 0.2 mmol) and 5-iodo-2-(1-piperidinyl)pyrimidine (2 equiv, 116 mg, 0.4 mmol). The crude residue was purified by column chromatography using silica gel basified with 5 mL of aqueous ammonium hydroxide (10% EtOAc/2% Et_3N/88% hexanes → 20% EtOAc/2% Et_3N/78% hexanes → 30% EtOAc/2% Et_3N/68% hexanes) to give a pale yellow foam.

Run 1: (63.0 mg, 76%), Run 2: (60.6 mg, 73%)

R_f = 0.44 (silica gel, 40% EtOAc/Hex, UV).

$[\alpha]_D^{25}$ = +83.3° (c = 3.1, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.59 (s, 1H), 8.74 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.67 (dd, *J* = 6.6, 2.4 Hz, 1H), 8.25 (s, 2H), 8.10 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.47 – 7.42 (m, 2H), 7.40 (dd, *J* = 8.2, 4.2 Hz, 2H), 3.81 (dt, *J* = 11.0, 8.6 Hz, 1H), 3.67 (dd, *J* = 6.2, 4.9 Hz, 4H), 3.27 (dd, *J* = 8.6, 2.9 Hz, 1H), 2.74 (t, *J* = 10.8 Hz, 1H), 2.07 (ddd, *J* = 10.6, 8.5, 2.9 Hz, 1H), 1.60 (p, *J* = 5.5 Hz, 2H), 1.52 (qd, *J* = 5.6, 5.1, 2.3 Hz, 4H), 1.49 (s, 3H), 1.24 (s, 3H).

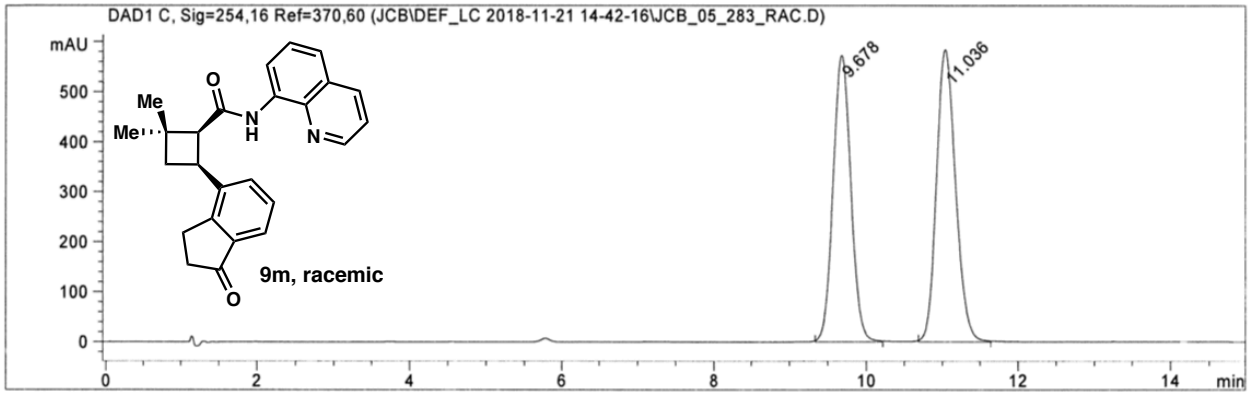
^{13}C NMR (101 MHz, $CDCl_3$): δ 170.2, 160.8, 157.1, 148.1, 138.4, 136.4, 134.5, 127.9, 127.5, 121.6, 121.3, 120.8, 116.5, 57.4, 45.0, 37.3, 36.1, 31.8, 30.0, 25.8, 25.1, 25.0.

FTIR (NaCl, thin film, cm^{-1}): 3355, 2031, 2853, 1682, 1603, 1524, 1485, 1462, 1447, 1366, 1324, 1274, 1256, 1160, 1025, 946, 826, 792, 754.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{25}H_{30}N_5O$ $[M+H]^+$: 416.2445; found: 416.2440.

Proof of Enantiopurity

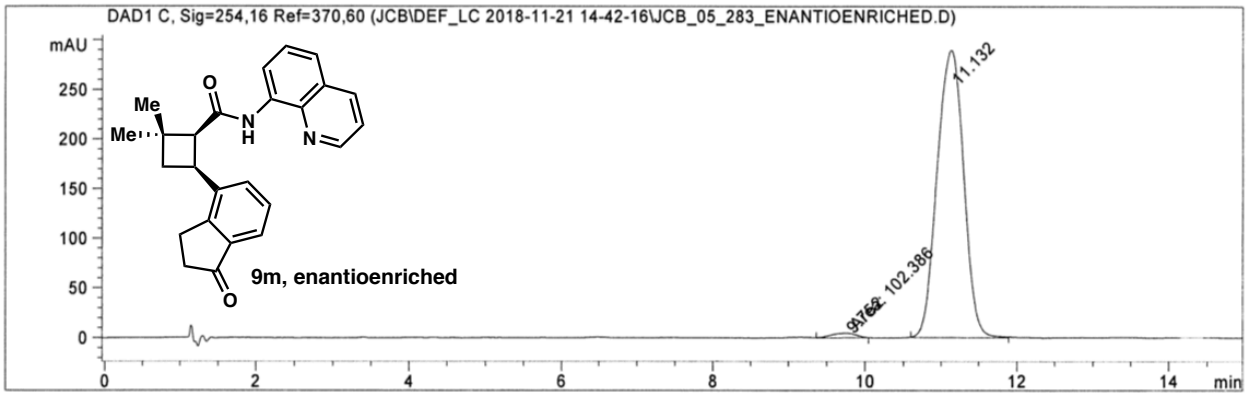
9m, racemic sample. Chiral SFC: (OD-H, 2.5 mL/min, 20% IPA in CO_2, λ = 254 nm): t_R(minor) = 9.7 min, t_R(major) = 11.1 min.



Signal 1: DAD1 C, Sig=254,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.678	BB	0.2468	9170.02637	572.63605	47.0183
2	11.036	BB	0.2746	1.03331e4	583.59204	52.9817
Totals :				1.95031e4	1156.22809	

9m, enantioenriched sample. Chiral SFC: (OD-H, 2.5 mL/min, 20% IPA in CO_2, λ = 254 nm): t_R(minor) = 9.7 min, t_R(major) = 11.1 min.

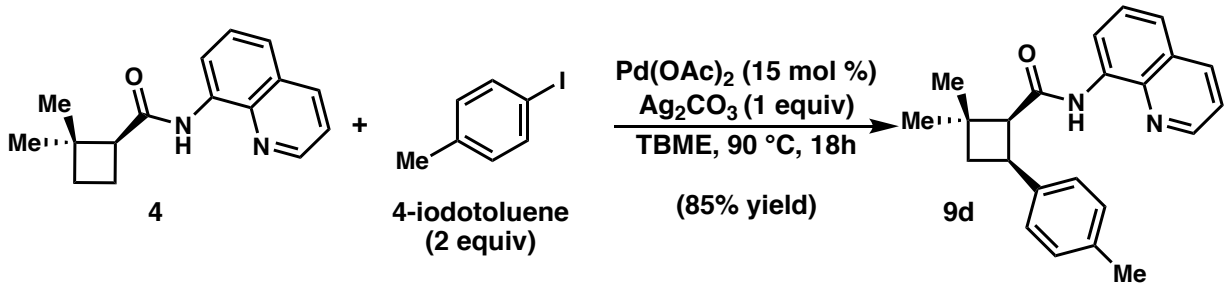


Signal 1: DAD1 C, Sig=254,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.752	MM	0.3621	102.38605	4.71307	1.4187
2	11.132	BB	0.3991	7114.58105	289.14011	98.5813
Totals :				7216.96710	293.85318	

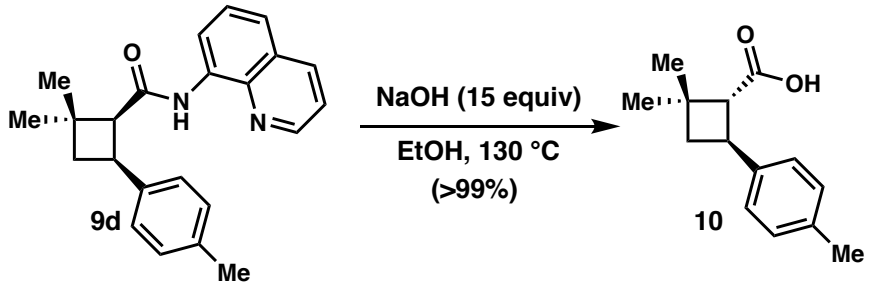
3. Carboxylic Acid Derivatization

Large-scale synthesis of 9d



A 48 mL pressure flask was charged with cyclobutamide **4** (608 mg, 2.39 mmol, 1.00 equiv), Ag_2CO_3 (659 mg, 2.39 mmol, 1.00 equiv), and $Pd(OAc)_2$ (80.5 mg, 0.358 mmol, 15 mol%) followed by 4-iodotoluene (1.04 g, 4.78 mmol, 2.00 equiv). The solids were suspended in TBME (12 mL, 0.2 M). The vessel was sealed, placed in a pre-heated oil bath (90 ºC), and allowed to stir for 18 h. The reaction mixture was cooled to room temperature, diluted with CH_2Cl_2, and filtered through a 40 g celite plug with approx. 150 mL CH_2Cl_2. The solvent was removed *in vacuo*, and the crude oil was purified by silica gel flash chromatography (10 → 15% EtOAc/hexanes) to afford **9d** as a white solid (700. mg, 85% yield).

Hydrolysis: preparation of 10[1]



A 48 mL pressure flask was charged with *cis*-cyclobutamide **9d** (693 mg, 2.01 mmol, 1.00 equiv), sodium hydroxide (1.21 g, 30.2 mmol, 15 equiv), and absolute ethanol (8.5 mL, 0.24 M). The flask was sealed and placed in a pre-heated oil bath (130 ºC) and stirred for 18 h. The reaction mixture was cooled to room temperature, and the solvent was removed *in vacuo*. The crude residue was diluted with 1 M aq HCl (38 mL) and EtOAc (38 mL). The organic and aqueous layers were separated, and the organic layer was washed with 1 M HCl (2 x 38 mL). The organic layer was

dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude reddish solid was purified by silica gel flash chromatography (15 → 20% EtOAc/hexanes) to afford **10** as an off-white solid (443 mg, >99% yield).

R_f = 0.31 (silica gel, 20% EtOAc/Hexanes, *p*-anisaldehyde)

$[\alpha]_D^{25}$ = +123.6° (c = 0.28, $CHCl_3$).

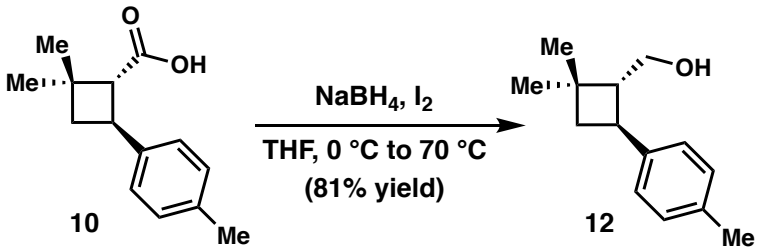
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.13 (d, *J* = 1.1 Hz, 4H), 3.74 (q, *J* = 9.8 Hz, 1H), 2.91 (dd, *J* = 10.0, 0.8 Hz, 1H), 2.32 (s, 3H), 2.11 (ddd, *J* = 10.9, 8.9, 0.9 Hz, 1H), 1.95 (t, *J* = 10.5 Hz, 1H), 1.29 (s, 3H), 1.25 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 178.8, 140.7, 135.9, 129.2, 126.6, 55.2, 39.4, 36.6, 35.1, 30.6, 23.6, 21.2.

FTIR (NaCl, thin film, cm^{-1}): 3021, 2957, 2927, 2867, 2731, 2647,1699, 1516, 1464, 1421 1370, 1281, 1238, 1162 1118, 937, 806, 716.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{14}H_{22}NO_2$ $[M+NH_4]^+$: 236.1645; found: 236.1645.

Reduction to form alcohol 12



A 2-dram vial containing a stir bar was charged with **10** (87 mg, 0.400 mmol, 1.00 equiv) and $NaBH_4$ (37.8 mg, 1.00 mmol, 2.5 equiv). The vial was then evacuated and backfilled with N_2 three times. THF (3.0 mL) was added and the reaction mixture was cooled to 0 °C. I_2 (121.8 mg, 0.480 mmol, 1.2 equiv) was then added as a solution in THF (1 mL) dropwise. The vial was then sealed with a Teflon-lined cap, placed in a pre-heated oil bath (70 ºC), and allowed to stir overnight. Once the reaction was complete, the reaction was cooled to room temperature and quenched with MeOH until bubbling stopped and the reaction mixture turned clear. The reaction mixture was then concentrated, then treated with 20% KOH (4 mL) and allowed to stir for 5 h at room temperature. The aqueous layer was then extracted with EtOAc (6 x 5 mL). The combined

organic layers were dried over Na_2SO_4 and concentrated to afford **12** (82.2 mg, quant yield) as a white solid which was carried forward without further purification.

R_f = 0.38 (silica gel, 20% EtOAc/Hexanes, UV, *p*-anisaldehyde)

$[\alpha]_D^{25}$ = +57.0° (c = 0.42, $CHCl_3$).

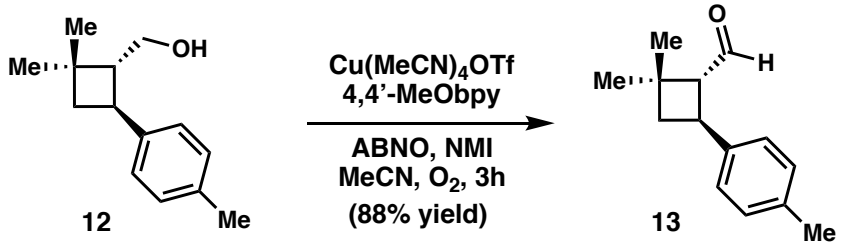
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.18 – 7.08 (m, 4H), 3.75 (qd, *J* = 11.0, 7.2 Hz, 2H), 3.06 (q, *J* = 9.5 Hz, 1H), 2.34 (s, 3H), 2.28 (dddd, *J* = 9.4, 8.3, 6.1, 0.7 Hz, 1H), 2.05 (ddd, *J* = 10.8, 8.7, 0.8 Hz, 1H), 1.82 (t, *J* = 10.3 Hz, 1H), 1.21 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 141.9, 135.6, 129.1, 126.7, 63.6, 53.9, 40.6, 37.6, 33.7, 31.4, 22.5, 21.1.

FTIR (NaCl, thin film, cm^{-1}): 3248, 2954, 2926, 2896, 2864, 1896, 1514, 1453, 1413, 1379, 1368, 1326, 1260, 1218, 1190, 1110, 1092, 1033, 1013, 812, 772.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{14}H_{24}NO$ $[M+NH_4]^+$: 222.1852; found: 222.1846.

Stahl oxidation to form aldehyde 13[2]



12 (0.400 mmol, 1.00 equiv) was dissolved in 1.2 mL MeCN in a 20 mL scintillation vial. In a separate vial $Cu(MeCN)_4OTf$ (7.5 mg, 0.02 mmol, 0.05 equiv) and 4,4'-MeObpy (4.3 mg, 0.02 mmol, 0.05 equiv)) were dissolved in 0.4 mL MeCN and allowed to stir until the solution turned an opaque blue. To this vial was added a solution of ABNO (0.6 mg, 0.004 mmol, 0.01 equiv) and *N*-methylimidazole (3.3 mg, 0.04 mmol, 0.10 equiv) in 0.4 mL MeCN. Once the catalyst solution turned green, it was added to the reaction mixuture and allowed to stir open to air. After 3 h and 6 h, additional portions of catalyst ($Cu(MeCN)_4OTf$ (7.5 mg, 0.02 mmol, 0.05 equiv), 4,4'-MeObpy (4.3 mg, 0.02 mmol, 0.05 equiv) ABNO (0.6 mg, 0.004 mmol, 0.01 equiv), and *N*-methylimidazole (3.3 mg, 0.04 mmol, 0.10 equiv) dissolved in 0.8 mL MeCN) were added. After the addition at 6 h, the reaction vessel was sealed with a rubber septum and the reaction mixture was sparged with $O_{2(g)}$ and allowed to stir under an O_2 atmosphere for an additional 15.5 h. When the reaction was judged to be done by TLC, the reaction mixture was filtered over a short

silica plug, eluting with 20% EtOAc/hexanes, and the resulting solution was concentrated *in vacuo* to give **13** as a brown oil (71.1 mg, 87% yield).

R_f = 0.69 (silica gel, 20% EtOAc/Hexanes, UV, *p*-anisaldehyde)

$[\alpha]_D^{25}$ = +62.9° (c = 1.66, $CHCl_3$).

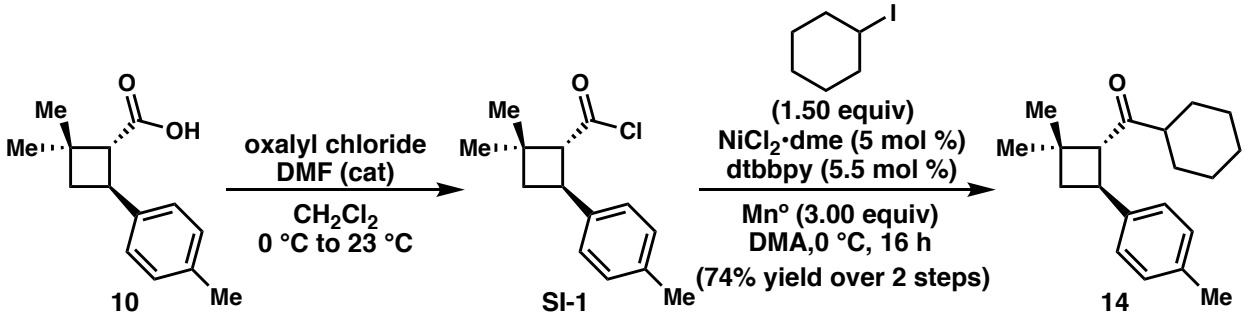
^{1}H NMR (400 MHz, $CDCl_3$): δ 9.86 (d, *J* = 1.6 Hz, 1H), 7.21 – 7.01 (m, 5H), 3.88 (q, *J* = 9.6 Hz, 1H), 2.97 (ddd, *J* = 9.7, 1.7, 0.9 Hz, 1H), 2.34 (s, 3H), 2.12 (ddt, *J* = 10.5, 8.9, 0.8 Hz, 1H), 2.02 (t, *J* = 10.5 Hz, 1H), 1.36 (s, 3H), 1.26 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 203.0, 140.8, 135.8, 129.1, 129.1, 126.5, 126.5, 62.5, 39.9, 37.5, 33.0, 31.3, 24.0, 23.6, 21.1, 21.1.

FTIR (NaCl, thin film, cm^{-1}): 3248, 2954, 2926, 2896, 2864, 1896, 1514, 1453, 1413, 1379, 1368, 1326, 1260, 1218, 1190, 1110, 1092, 1033, 1013, 812, 772.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{14}H_{22}NO$ $[M+NH_4]^+$: 220.1696; found: 220.1691.

Acid chloride formation and Suzuki coupling: preparation of ketone 14[3]



A 1-dram vial containing a stir bar was charged with carboxylic acid **10** (87.3 mg, 0.400 mmol, 1 equiv). The vial was sealed with a septum vial cap and tape and was evacuated and backfilled with N_2 three times. CH_2Cl_2 (0.8 mL, 0.5 M) and 1-2 drops DMF were added, and the reaction mixture was cooled to 0 °C. Oxalyl chloride (0.050 mL, 0.560 mmol, 1.4 equiv) was then added dropwise. Once the addition was complete, the reaction was allowed to stir at room temperature for 1 h, at which point the solvent was removed *in vacuo* to afford acid chloride **SI-1** as a crude oil. **SI-1** was taken forward without further purification.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.16 – 7.06 (m, 4H), 3.79 (q, *J* = 9.7 Hz, 1H), 3.29 (dd, *J* = 9.8, 0.9 Hz, 1H), 2.33 (s, 3H), 2.11 (ddd, *J* = 10.9, 9.1, 1.0 Hz, 1H), 2.01 – 1.88 (m, 1H), 1.41 (s, 3H), 1.31 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 173.3, 139.2, 136.5, 129.4, 126.5, 66.1, 39.0, 37.0, 30.0, 23.2, 21.2.

A flame-dried 1-dram vial containing a 2-dram stir bar (tested before to ensure it would stir) was charged with $NiCl_2$•dme (4.4 mg, 0.020 mmol, 0.05 equiv), dtbbpy (5.9 mg, 0.022 mmol, 0.055 equiv), and Mn° powder (65.9 mg, 1.20 mmol, 3.00 equiv). The vial was sealed with a septa and tape and evacuated and backfilled with N_2 three times. 0.6 mL DMA was then added, and the reaction mixture was stirred vigorously (~1300 rpm) for about 30 min. The mixture should be a dark black color. The reaction mixture was then cooled to 0 °C in an ice bath. Iodocyclohexane (0.078 mL, 0.600 mmol, 1.50 equiv) was then added, followed by freshly prepared acid chloride **SI-1** (94.7 mg, 0.400 mmol, 1.0 equiv) dissolved in 0.8 mL DMA. The sealed vial was then placed in a cryocool set to 0 °C and allowed to stir for 16 h. The reaction mixture was then quenched with 1.0 mL H_2O and extracted with CH_2Cl_2 (4 x 2.0 mL). The combined organic layers were filtered through a Na_2SO_4 plug and concentrated *in vacuo*. The resulting crude oil was purified by silica gel flash chromatography (0 → 5% EtOAc/hexanes) to afford **14** as a pale yellow, clear oil (84.6 mg, 74% yield over 2 steps).

R_f = 0.76 (silica gel, 20% EtOAc/Hexanes, UV, *p*-anisaldehyde)

$[\alpha]_D^{25}$ = +17.1° (c = 2.247, $CHCl_3$).

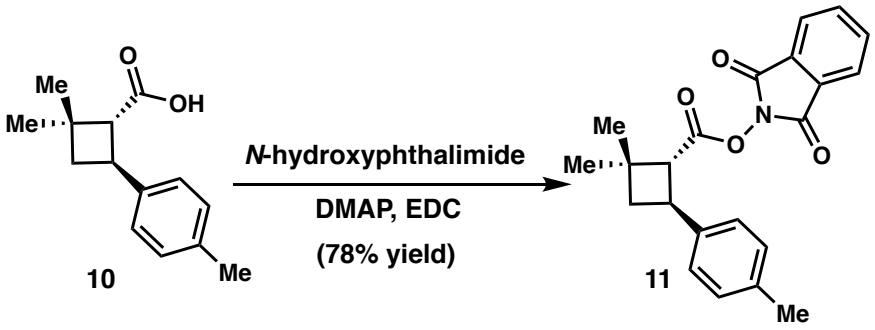
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.11 – 7.05 (m, 2H), 7.02 (d, *J* = 8.0 Hz, 2H), 3.85 (q, *J* = 9.6 Hz, 1H), 3.13 (dd, *J* = 9.6, 0.8 Hz, 1H), 2.31 (s, 3H), 2.21 (tt, *J* = 11.3, 3.3 Hz, 1H), 2.02 (ddd, *J* = 10.6, 8.8, 0.8 Hz, 1H), 1.92 (t, *J* = 10.5 Hz, 1H), 1.88 – 1.62 (m, 3H), 1.44 (tdd, *J* = 13.0, 11.4, 3.6 Hz, 1H), 1.34 (s, 3H), 1.31 – 1.11 (m, 4H), 1.06 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 212.7, 141.7, 135.5, 129.1, 126.5, 60.9, 50.8, 39.1, 37.4, 33.2, 31.3, 29.6, 26.9, 26.3, 26.0, 25.5, 24.0, 21.1.

FTIR (NaCl, thin film, cm^{-1}): 3380, 3048, 3020, 2929, 2855, 1894, 1698, 1515, 1449, 1370, 1331, 1288, 1244, 1183, 1145, 1066, 1021m 994, 952, 892, 829, 805, 759.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{20}H_{32}NO$ $[M+NH_4]^+$: 302.2478; found: 302.2470.

Preparation of NHP ester 11



A 20 mL vial was charged with carboxylic acid **10** (208.9 mg, 0.957 mmol, 1.00 equiv), *N*-hydroxyphthalimide (156.1 mg, 0.957 mmol, 1.00 equiv), and 4-dimethylaminopyridine (11.7 mg, 0.096 mmol, 0.10 equiv). The vial was sealed with a rubber septum and evacuated and backfilled with N_2 three times. The solids were dissolved in CH_2Cl_2 (4 mL), and then EDC (201.8 mg, 1.05 mmol, 1.10 equiv) was added as a slurry in CH_2Cl_2 (1.3 mL). The reaction mixture was allowed to stir for 23 hours at room temperature. The reaction mixture was then transferred to a flask containing EtOAc (50 mL), and the resulting solids were removed by filtration. The filtrate was concentrated *in vacuo* and the crude oil was purified by silica gel flash chromatography (15 → 40% EtOAc/hexanes) to afford **11** as a white solid (272.8 mg, 78% yield).

R_f = 0.46 (silica gel, 20% EtOAc/Hexanes, UV, *p*-anisaldehyde)

$[\alpha]_D^{25}$ = +100.5° (c = 0.42, $CHCl_3$).

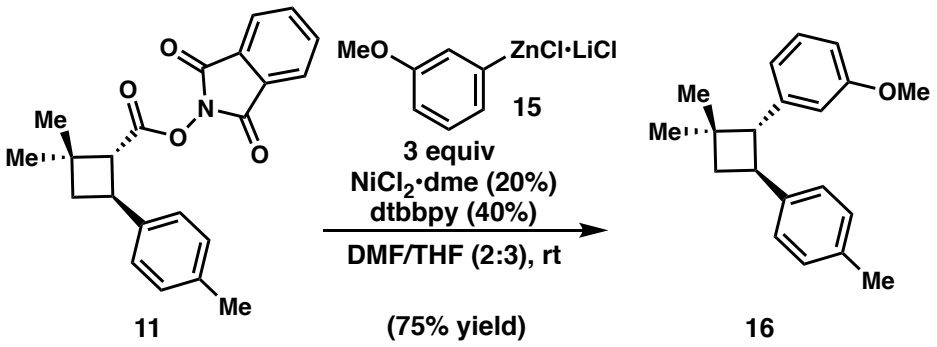
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 – 7.83 (m, 2H), 7.83 – 7.73 (m, 2H), 7.14 (s, 4H), 3.87 (q, *J* = 9.8 Hz, 1H), 3.21 (dd, *J* = 9.9, 0.9 Hz, 1H), 2.33 (s, 3H), 2.20 (ddd, *J* = 10.8, 8.9, 0.9 Hz, 1H), 2.08 (t, *J* = 10.5 Hz, 1H), 1.42 (s, 3H), 1.39 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 168.9, 162.2, 139.7, 136.3, 134.8, 129.3, 129.1, 126.5, 124.0, 52.5, 39.6, 37.5, 35.3, 30.5, 23.7, 21.2.

FTIR (NaCl, thin film, cm^{-1}): 3520, 3022, 2959, 2927, 2868, 1808, 1794, 1745, 1615, 1516, 1467, 1368, 1274, 1186, 1132, 1081, 1016, 972, 878, 811, 786, 696.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{22}H_{21}NO_4$ $[M+NH_4]^+$: 381.1809; found: 381.1814.

Negishi coupling to form diaryl cyclobutane 16[4]



A 25 mL round bottom flask was charged with **11** (109 mg, 0.300 mmol, 1.00 equiv), $NiCl_2$•dme (13.2 mg, 0.060 mmol, 0.20 equiv), and dtbbpy (32.2 mg, 0.120 mmol, 0.40 equiv). The flask was sealed with a septum and then evacuated and backfilled with argon three times. DMF was then added (3.2 mL), forming a green solution. Freshly prepared aryl zinc reagent **15** (4.8 mL, 0.90 mmol, 3.0 equiv, 0.19 M in THF) was then added and the solution turned red. The reaction was allowed to stir for 18 h, at which point the reaction was quenched with 1 M HCl (10 mL) and diluted with EtOAc (10 mL). The organic and aqueous layers were separated, and the organic layer was washed with water (10 mL) and brine (10 mL). The organic layer was dried with $MgSO_4$, filtered, and concentrated *in vacuo* to afford a red oil. The crude material was then purified by silica gel flash chromatography (2.5 → 25% PhMe/hexanes) to afford **16** as a clear oil (63 mg, 75% yield).

R_f = 0.77 (silica gel, 20% EtOAc/Hexanes, UV, *p*-anisaldehyde)

$[\alpha]_D^{25}$ = +195° (c = 0.42, $CHCl_3$).

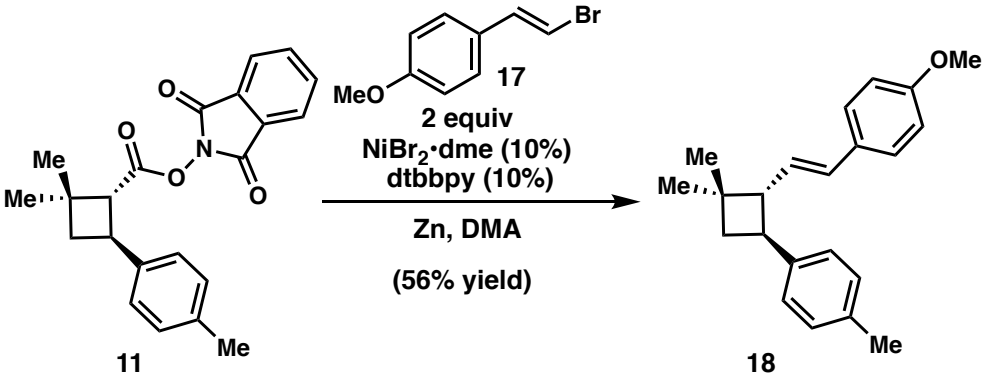
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26 – 7.17 (m, 1H), 7.14 (d, *J* = 8.0 Hz, 2H), 7.08 (d, *J* = 7.9 Hz, 2H), 6.81 (ddt, *J* = 7.6, 1.7, 0.9 Hz, 1H), 6.80 – 6.71 (m, 2H), 3.79 (s, 3H), 3.32 (d, *J* = 10.4 Hz, 1H), 2.30 (s, 3H), 2.16 (ddd, *J* = 10.3, 8.5, 0.7 Hz, 1H), 1.90 (t, *J* = 10.1 Hz, 1H), 1.28 (s, 3H), 0.88 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 159.6, 142.8, 142.1, 135.5, 129.1, 129.0, 126.6, 120.0, 113.6, 111.0, 56.7, 55.2, 40.2, 37.4, 37.2, 30.9, 23.3, 21.1.

FTIR (NaCl, thin film, cm^{-1}): 3014, 2947, 2859, 1596, 1514, 1490, 1458, 1428, 1371, 1318, 1292, 1252, 1166, 1040, 832, 808, 797, 694.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{15}H_{25}O_3$ $[M+H]^+$: 281.1900; found: 281.1899.

Reductive coupling of NHP ester 11 and vinyl bromide 17: preparation of 18[5]



A 1-dram vial containing a 2-dram stir bar was charged with NHP ester **11** (75.7 mg, 0.208 mmol, 1.00 equiv) and vinyl bromide **17** (63.9 mg, 0.300 mmol, 1.50 equiv). A separate ½-dram vial containing a stir bar was charged with dtbbpy (5.4 mg, 0.020 mmol, 0.10 equiv). Both vials were brought into a N_2 filled glovebox. The vial containing dtbbpy was charged with $NiBr_2$•dme (6.2 mg, 0.020 mmol, 0.10 equiv) and DMA (0.200 mL, 1.0 M) and allowed to stir for 10 minutes. The vial containing **11** and **17** was charged with Zn powder (25.4 mg, 0.400 mmol, 2.00 equiv). Once the catalyst solution prestir was complete, the catalyst solution was added to the reaction vial via pipette. The vial was then sealed with a Teflon-lined cap, removed from the glovebox, placed in a pre-heated oil bath (28 °C), and allowed to stir for 15 h. Once the reaction was complete, the reaction mixture was diluted with Et_2O and passed through a short silica plug, eluting with Et_2O. The material was concentrated onto celite *in vacuo*, and the resulting powder was purified by silica gel flash chromatography (0 → 30% PhMe/hexanes) to afford **18** as a white solid (34.1 mg, 56% yield).

R_f = 0.71 (silica gel, 20% EtOAc/Hexanes, UV, *p*-anisaldehyde)

$[\alpha]_D^{25}$ = +238° (c = 1.66, $CHCl_3$).

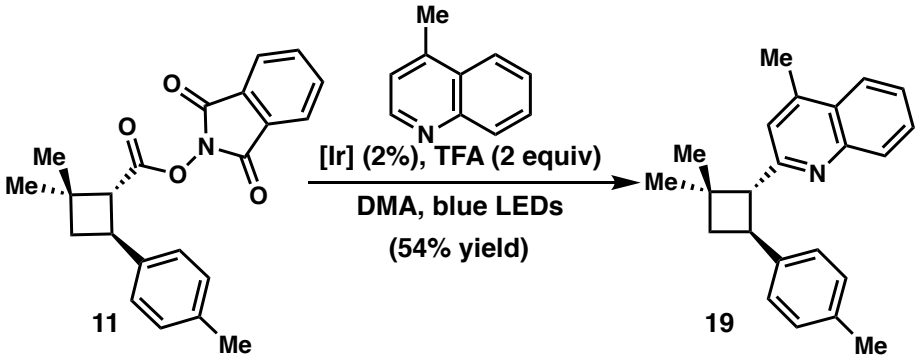
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 – 7.28 (m, 2H), 7.15 (d, *J* = 8.1 Hz, 2H), 7.11 (d, *J* = 8.0 Hz, 2H), 6.89 – 6.83 (m, 2H), 6.34 (d, *J* = 15.8 Hz, 1H), 6.22 (dd, *J* = 15.8, 7.8 Hz, 1H), 3.81 (s, 3H), 3.41 (q, J = 9.5 Hz, 1H), 2.73 (ddt, *J* = 9.5, 7.7, 0.9 Hz, 1H), 2.33 (s, 3H), 2.11 (ddd, *J* = 10.7, 8.5, 0.8 Hz, 1H), 1.87 (t, *J* = 10.3 Hz, 1H), 1.18 (s, 3H), 1.16 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 158.9, 142.3, 135.3, 130.7, 130.0, 129.0, 128.1, 127.3, 126.6, 114.0, 55.9, 55.4, 40.0, 39.6, 36.9, 30.4, 23.6, 21.2.

FTIR (NaCl, thin film, cm^{-1}): 2999, 2951, 2921, 2860, 1607, 1511, 1462, 1370, 1249, 1174, 1106, 1036, 966, 806.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{22}H_{27}O$ $[M+H]^+$: 307.2056; found: 307.2062.

Decarboxylative quinolinylation: preparation of 19[6]



A flame-dried 20dram vial was charged with NHP ester **11** (72.7, mg, 0.200 mmol, 1.00 equiv) and Ir[dF(CF_3)ppy]$_2$(dtbbpy)PF_6 (4.5 mg, 0.004 mmol, 0.02 equiv). The vial was evacuated and backfilled with Ar three times. DMA (2.0 mL, 0.1 M) and lepidine (43.0 mg, 0.300 mmol, 1.50 equiv) were then added, and the reaction mixture was cooled to 0 °C and sparged with Ar 10 minutes. The reaction vial was removed from the ice bath, trifluoroacetic acid (30.6 μL, 0.400 mmol, 2.00 equiv) was added, and the reaction mixture was allowed to stir in front of a 34W blue LED lamp (~3 cm from the lamp). The reaction was monitored by TLC (20% EtOAc/hexanes). Once the reaction was complete (~4 h), the reaction was quenched with 1 mL NEt_3 and 2 mL H_2O. The aqueous layer was extracted with EtOAc (3 mL x 4), and the combined organics were washed with 1 M LiCl. The organic layer was then dried with Na_2SO_4, filtered, and concentrated onto celite *in vacuo*, and the resulting powder was purified by silica gel flash chromatography (0 → 5% EtOAc/hexanes) to afford **19** as a yellow solid (34.1 mg, 54% yield).

R_f = 0.76 (silica gel, 20% EtOAc/Hexanes, UV, *p*-anisaldehyde)

$[\alpha]_D^{25}$ = +305° (c = 1.47, $CHCl_3$).

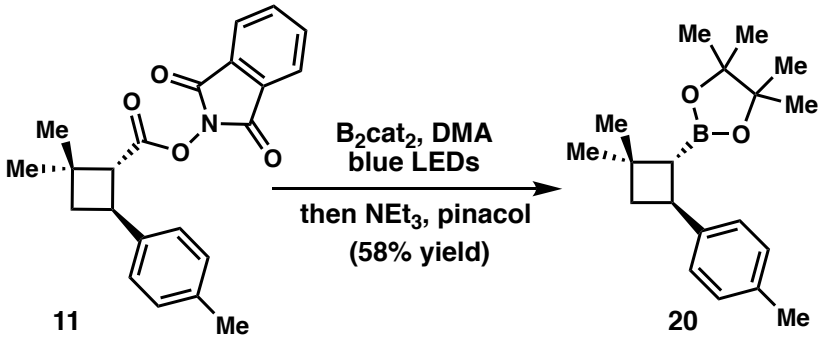
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09 (d, *J* = 8.4 Hz, 1H), 7.95 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.67 (ddd, *J* = 8.3, 6.7, 1.4 Hz, 1H), 7.50 (ddd, *J* = 8.1, 6.8, 1.3 Hz, 1H), 7.21 (d, *J* = 7.9 Hz, 2H), 7.08 (d, *J* = 8.1 Hz, 3H), 4.39 (q, *J* = 9.7 Hz, 1H), 3.52 (d, *J* = 10.1 Hz, 1H), 2.67 (s, 3H), 2.30 (s, 3H), 2.20 (dd, *J* = 10.4, 8.8 Hz, 1H), 2.04 (t, *J* = 10.3 Hz, 1H), 1.39 (s, 3H), 0.89 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.6, 148.0, 143.4, 142.6, 135.2, 130.2, 129.0, 128.9, 128.8, 128.7, 127.1, 126.9, 126.8, 125.4, 123.7, 121.7, 59.1, 39.7, 37.9, 35.4, 31.2, 23.7, 21.1, 18.9.

FTIR (NaCl, thin film, cm^{-1}): 3428, 3950, 2925, 2360, 1603, 1558, 1514, 1446, 1379, 1260, 1176, 1162, 1034, 809, 756.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{23}H_{26}N$ $[M+H]^+$: 316.2060; found: 316.2063.

Decarboxylative borylation of NHP ester 11 to form borylate 20[7]



A flame-dried 2-dram vial was charged with NHP ester **11** (72.7, mg, 0.200 mmol, 1.00 equiv) and B_2cat_2 (59.5 mg, 0.250 mmol, 1.25 equiv). The vial was evacuated and backfilled with Ar three times. DMA (2.0 mL, 0.1 M) was then added, and the reaction mixture was cooled to 0 °C and sparged with Ar for 10 minutes. The reaction vial was removed from the ice bath and suspended inside a large beaker lined with 12W blue LED strips and covered with foil. After 21 h, pinacol (94.5 mg, 0.800 mmol, 4.00 equiv) was added as a solution in NEt_3 (700 μL, 5.04 mmol, 25.2 equiv). After 2 h, the reaction was quenched with H_2O, saturated aqueous NH_4Cl, and EtOAc. The organic and aqueous layers were separated, and the aqueous layer was extracted with EtOAc (2 mL x 3). The combined organics were then dried with Na_2SO_4, filtered, and concentrated onto celite *in vacuo*, and the resulting powder was purified by silica gel flash chromatography (0 → 5% EtOAc/hexanes) to afford **20** as a white solid (35.1 mg, 58% yield).

R_f = 0.81 (silica gel, 20% EtOAc/Hexanes, UV, *p*-anisaldehyde)

$[\alpha]_D^{25}$ = +77.5° (c = 1.47, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.09 (s, 4H), 3.53 (td, *J* = 10.2, 8.2 Hz, 1H), 2.31 (s, 3H), 2.13 (ddd, *J* = 10.6, 8.2, 0.8 Hz, 1H), 2.02 (t, *J* = 10.3 Hz, 1H), 1.68 (d, *J* = 10.5 Hz, 1H), 1.26 (s, 6H), 1.24 (d, *J* = 1.1 Hz, 9H), 1.16 (s, 3H).

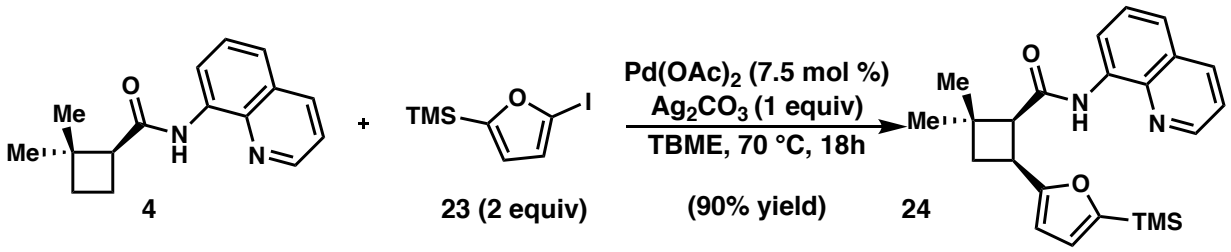
^{13}C NMR (101 MHz, $CDCl_3$): δ 144.1, 134.9, 128.9, 126.3, 83.2, 42.9, 34.3, 34.0, 32.4, 26.6, 25.3, 24.9, 21.1. (Note: the resonance from the carbon attached to the boron was not visible).

FTIR (NaCl, thin film, cm^{-1}): 3444, 2980, 2922, 2946, 2862, 2728, 1898, 1652, 1514, 1462, 1414, 1380, 1363, 1345, 1329, 1275, 1237, 1143, 1112, 1080, 1020, 967, 854, 809, 730.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{19}H_{29}BO_2Na$ $[M+Na]^+$: 323.2158; found: 323.2174.

4. Synthesis of (+)-rumphellaone A

Large-Scale C-H Activation Procedure for the Preparation of 24



A 48 mL pressure flask was charged with cyclobutamide **4** (400 mg, 1.57 mmol, 1.00 equiv), Ag_2CO_3 (434 mg, 1.57 mmol, 1.00 equiv), and $Pd(OAc)_2$ (26.5 mg, 0.118 mmol, 7.5 mol %) followed by TMS-iodofuran **23** (834 mg, 3.15 mmol, 2.00 equiv). The mixture was then suspended in TBME (8.0 mL, 0.2 M). The vessel was sealed under ambient conditions and placed in a pre-heated oil bath (70 ºC). After about 10 minutes, the olive-green mixture becomes black, and the reaction mixture is stirred for an additional 18 h. The reaction mixture was then concentrated, diluted with toluene (3 mL), and loaded directly onto a silica gel column (0 → 20% EtOAc/hexanes) to afford **24** as a clear yellow oil (556 mg, 90% yield).

R_f = 0.56 (silica gel, 20% EtOAc/Hex, UV, *p*-anisaldehyde).

$[\alpha]_D^{25}$ = –57.2° (c = 1.22, $CHCl_3$).

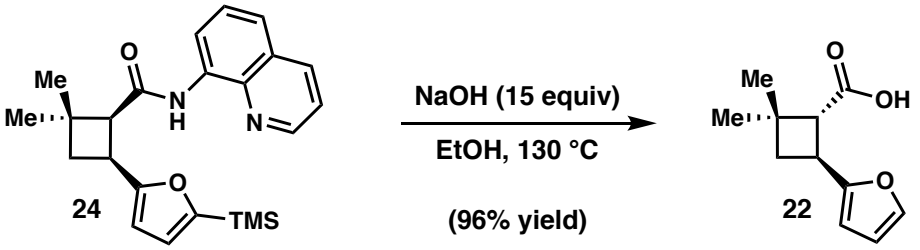
^{1}H NMR (400 MHz, $CDCl_3$): δ 9.61 (s, 1H), 8.77 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.68 (dd, *J* = 6.7, 2.3 Hz, 1H), 8.11 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.48 – 7.39 (m, 3H), 6.48 (d, *J* = 3.1 Hz, 1H), 6.23 (dd, *J* = 3.2, 1.1 Hz, 1H), 4.07 – 3.94 (m, 1H), 3.34 (ddd, *J* = 9.0, 2.2, 0.8 Hz, 1H), 2.61 – 2.50 (m, 1H), 2.19 (ddd, *J* = 11.0, 8.9, 2.3 Hz, 1H), 1.45 (s, 3H), 1.32 (s, 3H), -0.08 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 170.1, 160.1, 158.7, 148.0, 138.5, 136.3, 134.8, 127.9, 127.6, 127.5, 121.5, 121.2, 121.1, 120.5, 120.5, 116.5, 106.8, 55.8, 38.1, 36.6, 32.3, 30.9, 30.7, 30.7, 24.9, –1.8.

FTIR (NaCl, thin film, cm^{-1}): 3360, 3109, 3049, 2954, 2866, 2613, 1944, 1878, 1687, 1595, 1578, 1522, 1485, 1424, 1385, 1324, 1249, 1161, 1131, 1009, 924, 842, 791, 757.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{23}H_{29}N_2O_2Si$ $[M+H]^+$: 392.1993; found: 393.1990.

Hydrolysis: Preparation of 22[1]



A 15 mL pressure flask was charged with *cis*-cyclobutamide **24** (532 mg, 1.36 mmol, 1.00 equiv), sodium hydroxide (813 mg, 20.33 mmol, 15 equiv), and absolute ethanol (5.7 mL, 0.24 M). The flask was sealed and placed in a pre-heated oil bath (130 ºC) and stirred for 18 h. The solvent was then concentrated *in vacuo*, and the crude residue was diluted with 1 M HCl (20 mL) and EtOAc (20 mL). The organic layer was separated and washed with 1 M HCl (2 x 20 mL). At this point, the aqueous layers should be yellow, and the organic layer should be faint brown. The combined aqueous layers were extracted with EtOAc (25 mL), and the second organic layer was washed with 1 M HCl (25 mL) until it was free of 8-aminoquinoline as indicated by TLC (usually 1-2 times). The organic layers were combined, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude reddish solid was purified by silica gel flash chromatography (20 → 40 % EtOAc/hexanes) to afford **22** as an off-white solid (250 mg, 96 % yield).

R_f = 0.5 (silica gel, 30% EtOAc/Hex, *p*-anisaldehyde).

$[\alpha]_D^{25}$ = +133.0° (c = 0.85, $CHCl_3$).

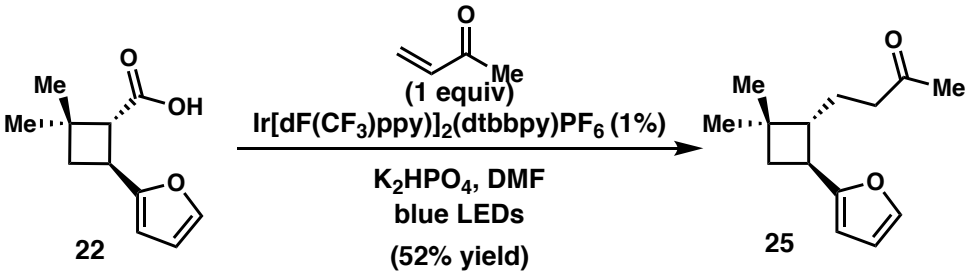
^{1}H NMR (400 MHz, $CHCl_3$): δ 7.32 (dd, *J* = 1.9, 0.9 Hz, 1H), 6.28 (dd, *J* = 3.2, 1.8 Hz, 1H), 6.05 (dt, *J* = 3.2, 0.8 Hz, 1H), 3.72 (q, *J* = 9.5 Hz, 1H), 3.11 – 3.02 (m, 1H), 2.12 – 1.95 (m, 2H), 1.30 (s, 3H), 1.19 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 178.3, 156.6, 141.5, 110.3, 105.0, 53.2, 38.3, 36.8, 30.4, 29.2, 23.4.

FTIR (NaCl, thin film, cm^{-1}): 3119, 2993, 2956, 2869, 1722, 1682, 1604, 1506, 1461, 1411, 1390, 1371, 1276, 1224, 1208, 1175, 1161, 1104, 1067, 1008, 946, 918, 884, 850, 804, 743, 730, 695.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{11}H_{15}O_3$ $[M+H]^+$: 195.1016; found: 195.1019.

Decarboxylative Michael addition: preparation of methyl ketone 25[8]



A 100 mL flame-dried round bottom flask was charged with carboxylic acid **22** (342 mg, 1.76 mmol, 1.00 equiv), $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (19.7 mg, 0.0176 mmol, 0.01 equiv), and K_2HPO_4 (368 mg, 1.76 mmol, 1.00 equiv). The flask was evacuated and backfilled with N_2 three times. DMF (17.6 mL, 0.1 M) and freshly distilled methyl vinyl ketone (144 μL, 1.76 mmol, 1. equiv) were then added, and the reaction mixture was sparged with Ar for 5 minutes. The reaction flask was placed about 5 cm from a 34W blue LED lamp and was allowed to stir at room temperature under N_2. After 42 h, the reaction was quenched with sat aq $NaHCO_3$ and extracted with EtOAc (75 mL x 3). The combined organics were then dried with $MgSO_4$, filtered, and concentrated *in vacuo* to afford the product as a crude oil, which was then purified by silica gel flash chromatography (3 → 10% EtOAc/hexanes) to afford **25** as a white solid (201 mg, 52% yield).

R_f = 0.79 (silica gel, 20% EtOAc/Hexanes, UV, *p*-anisaldehyde)

$[\alpha]_D^{25}$ = +57.8° (c = 1.07, $CHCl_3$).

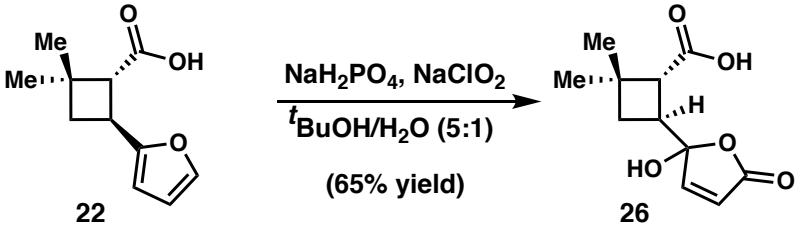
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30 (dd, *J* = 1.8, 0.9 Hz, 1H), 6.27 (dd, *J* = 3.1, 1.9 Hz, 1H), 5.97 (dt, *J* = 3.2, 0.7 Hz, 1H), 2.97 (td, *J* = 9.6, 8.5 Hz, 1H), 2.41 – 2.21 (m, 2H), 2.09 – 1.97 (m, 4H), 1.93 (ddd, *J* = 10.7, 8.5, 0.7 Hz, 1H), 1.88 – 1.79 (m, 1H), 1.74 – 1.59 (m, 2H), 1.11 (s, 3H), 1.08 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 209.1, 158.9, 140.9, 110.3, 104.0, 50.4, 41.5, 39.0, 34.6, 34.3, 30.6, 30.1, 24.2, 22.3.

FTIR (NaCl, thin film, cm^{-1}): 3114, 2953, 2933, 2863, 1717, 1593, 1506, 1451, 1411, 1368, 1360, 1235, 1159, 1150, 1009, 799, 729.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{14}H_{20}O_2Na$ $[M+Na]^+$: 243.1356; found: 243.1359.

Preparation of 26[9]



A 50 mL round bottom flask was charged with carboxylic acid **22 (**200 mg, 1.03 mmol, 1.00 equiv) and was evacuated and backfilled with N_2 three times. 5:1 ^{t}BuOH/H_2O (5.2 mL, 0.2 M) was added. Once the starting material was fully dissolved, NaH_2PO_4•H_2O (213 mg, 1.54 mmol, 1.50 equiv) was added in one portion, followed by $NaClO_2$ (349 mg, 3.09 mmol, 3.00 equiv, 80%). The suspension turned bright yellow within the first 10-15 minutes. The reaction mixture was allowed to stir 2-3 hours, at which point the yellow color dissipated and no more starting material was observed by TLC. The reaction mixture was concentrated *in vacuo*, and the resulting solids were solubilized with a mixture of EtOAc and minimal H_2O. This crude mixture was concentrated onto 4 g SiO_2. The powder was applied to a silica gel column and purified by flash silica gel chromatography (0 → 5% MeOH/CH_2Cl_2, followed by flushing with 50% MeOH/CH_2Cl_2) to afford **26** as a white solid (151 mg, 65% yield, 93% pure by QNMR).

R_f = 0.20 (silica gel, 10% MeOH/CH_2Cl_2, UV, *p*-anisaldehyde)

$[\alpha]_D^{25}$ +62.6° (c = 0.22, MeOH).

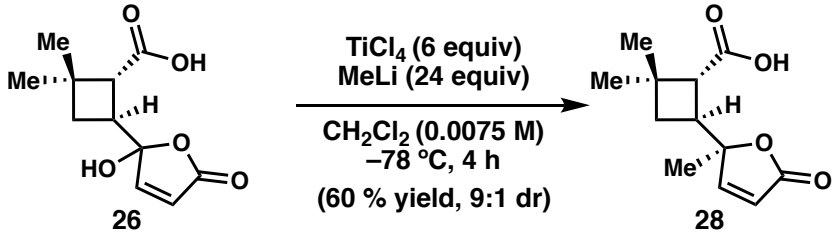
^{1}H NMR (400 MHz, MeOD-*d*$_4$): δ 7.27 (d, *J* = 5.9 Hz, 1H), 6.12 (d, *J* = 5.8 Hz, 1H), 2.92 (q, *J* = 9.4 Hz, 1H), 2.72 (d, *J* = 9.6 Hz, 1H), 1.80 (t, *J* = 10.3 Hz, 1H), 1.70 (dd, *J* = 11.0, 9.0 Hz, 1H), 1.20 (s, 3H), 1.10 (s, 3H).

^{13}C NMR (101 MHz, MeOD-*d*$_4$): δ 175.7, 172.9, 155.7, 123.6, 51.5, 49.5, 37.8, 37.1, 36.9, 36.2, 33.7, 30.4, 30.3, 24.1, 23.7.

FTIR (NaCl, thin film, cm^{-1}): 3098, 2960, 2871, 1726, 1416, 1373, 1280, 1255, 1187, 1160, 1114, 1032, 1007, 935, 852, 829, 713.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{11}H_{16}O_5$ $[M+H]^+$: 227.0919; found: 227.0922.

$Ti(CH_3)_4$ Conditions for Methylation: Preparation of 28



A 50 mL round bottom flask was flame-dried under vacuum and then back-filled with N_2. The flask was charged with CH_2Cl_2 (5 mL) and cooled to –78 ºC, at which point, $TiCl_4$ (142 µL, 1.33 mmol, 6.00 equiv) was added. The flask was then charged with MeLi (1.5 M in Et_2O; 4.00 mL, 5.30 mmol, ~24 equiv) dropwise via syringe, until the color of the solution changed from dark brown, to bright orange, and finally to dark green. The resulting solution was stirred for 1h at –78 ºC. A flame-dried 50 mL pear-shaped (pointed) flask was charged with **26** (49.0 mg, 0.217 mmol, 1.00 equiv) and then evacuated and backfilled with N_2 three times. The substrate was dissolved in CH_2Cl_2 (23 mL) and sonicated to dissolve any particulates. The solution was cooled to –78 ºC, then added to the reaction flask via a slow cannula transfer. If the addition proceeds too quickly or the solution of starting material is not sufficiently cooled, the reaction will favor the undesired diastereomer. The flask containing **26** was rinsed with 2 mL CH_2Cl_2 to complete the transfer. The resulting mixture was allowed to stir at –78 ºC. After 4 h the reaction was quenched with 1 M HCl (20 mL), allowed to warm to 23 °C, and stirred for 30 minutes during which time the aqueous layer became blue/green. The organic and aqueous layers were separated, and the aqueous layer was extracted with EtOAc (20 mL x 4), dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude residue was purified by silica gel flash chromatography (0 → 10% MeOH/CH_2Cl_2) to afford **28** white solid (29 mg, 9:1 dr, 60% yield)

R_f = 0.43 (silica gel, 10% MeOH/CH_2Cl_2, UV, *p*-anisaldehyde)

$[\alpha]_D^{25}$ = +43.0° (c = 0.46, $CHCl_3$).

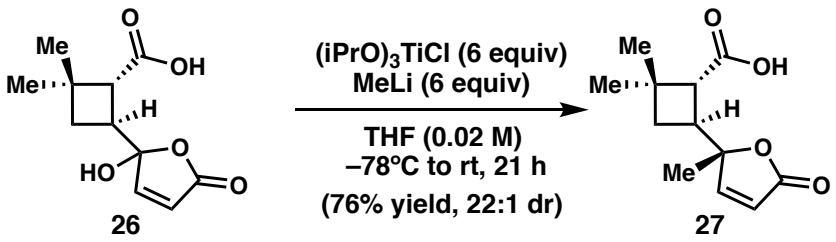
^{1}H NMR (400 MHz, $CDCl_3$): 7.23 (d, *J* = 5.6 Hz, 1H), 6.01 (d, *J* = 5.6 Hz, 1H), 3.48 (s, 1H), 2.99 (dd, *J* = 9.4, 0.8 Hz, 1H), 2.92 – 2.78 (m, 1H), 1.46 – 1.41 (m, 1H), 1.39 (s, 3H), 1.35 (dd, *J* = 11.1, 9.9 Hz, 1H), 1.20 (s, 3H), 1.10 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 178.3, 172.9, 172.8, 158.8, 121.1, 88.5, 49.1, 47.1, 36.4, 35.6, 35.5, 32.1, 29.9, 23.8, 21.7.

FTIR (NaCl, thin film, cm^{-1}): 3087, 2958, 2869, 1737, 1600, 1463, 1453, 1403, 1380, 1372, 1305, 1280, 1266, 1218, 1183, 1163, 1136, 1093, 1037, 961, 924, 880, 852, 824, 728, 711, 658.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{12}H_{20}NO_4$ $[M+NH_4]^+$: 242.1387; found: 242.1394.

$(O^iPr)_3TiCH_3$ Conditions for Methylation: Preparation of 26[10]



A flame-dried 50 mL round bottom flask was backfilled with N_2 and charged with THF (5 mL). The flask was cooled to –78 °C and (*i*-PrO)$_3$TiCl (1 M solution in hexanes; 1.33 mL, 1.33 mmol, 6.00 equiv) was added. MeLi (1.6 M solution in ether; 0.83 mL, 1.33 mmol, 6.00 equiv) was then added dropwise. This mixture was allowed to stir at –78 °C for 1 h. **26** (50 mg, 0.221 mmol, 1.00 equiv) was then added as a solution in THF (5.5 mL). The reaction mixture was slowly warmed to 23 °C over 21h. The reaction was then carefully quenched with 1 M HCl (11 mL) and stirred vigorously for 30 min. The organic and aqueous layers were then separated, and the aqueous layer was extracted with EtOAc (12 mL x 4). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude reaction mixture was purified by silica gel flash chromatography (0 → 4% MeOH/CH_2Cl_2) to afford **27** (37.5 mg, 76% yield, 22:1 dr)

R_f = 0.43 (silica gel, 10% MeOH/CH_2Cl_2, UV, *p*-anisaldehyde)

$[\alpha]_D^{25}$ = +120.4° (c = 1.20, $CHCl_3$).

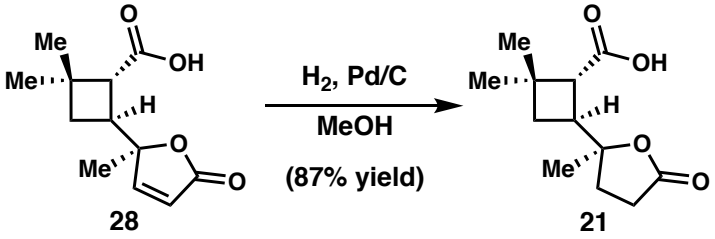
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.29 (d, *J* = 5.6 Hz, 1H), 5.97 (d, *J* = 5.6 Hz, 1H), 2.79 (td, *J* = 9.9, 8.9 Hz, 1H), 2.39 (dd, *J* = 9.8, 0.8 Hz, 1H), 1.93 (t, *J* = 10.4 Hz, 1H), 1.78 (ddd, *J* = 10.8, 8.9, 1.0 Hz, 1H), 1.39 (s, 3H), 1.21 (s, 3H), 1.11 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 177.4, 172.9, 159.5, 120.5, 88.4, 46.9, 36.8, 35.5, 33.5, 29.9, 23.6, 21.6.

FTIR (NaCl, thin film, cm^{-1}): 3091, 2936, 2958, 1869, 1741, 1702, 1464, 1454, 1417, 1371, 1282, 1247, 1208, 1166, 1119, 1090, 1051, 956, 912, 820, 727, 661.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{12}H_{20}NO_4$ $[M+NH_4]^+$: 242.1387; found: 242.1390.

Hydrogenation of methylated products: preparation of 21 and SI-2



A 2-dram vial was charged with lactone **28** (29 mg, 0.129 mmol, 1.00 equiv) and Pd/C (10% by weight, 47 mg, 0.044 mmol, 0.34 equiv). The vial was then evacuated and backfilled with N_2 three times. The solids were suspended in MeOH (1.4 mL, 0.095 M), and the reaction mixture was sparged with a balloon of H_2 for 20 minutes at 0°C, at which point the balloon was replaced with a fresh balloon, and the reaction was allowed to warm to room temperature. The reaction mixture was then stirred for 7 h under an atmosphere of H_2. Once the reaction was complete, the reaction mixture was sparged with argon for 20 minutes, diluted with EtOAc (15 mL), and filtered through celite, and concentrated *in vacuo*. The crude residue was then purified by silica gel flash chromatography (5% MeOH/CH_2Cl_2) to afford **21** (25 mg, 88% yield) as a white solid.

R_f = 0.44 (silica gel, 10% MeOH/CH_2Cl_2, *p*-anisaldehyde)

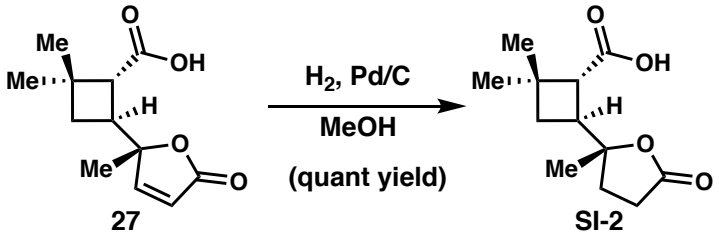
$[\alpha]_D^{25}$ = +76.3° (c = 0.72, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.91 (d, *J* = 9.7 Hz, 1H), 2.72 (t, *J* = 9.5 Hz, 1H), 2.70 – 2.59 (m, 1H), 2.53 (ddd, *J* = 18.2, 9.6, 5.0 Hz, 1H), 2.04 – 1.86 (m, 2H), 1.67 (s, 1H), 1.65 (s, 1H), 1.30 (s, 3H), 1.22 (s, 3H), 1.11 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 178.4, 177.1, 86.3, 86.3, 48.7, 39.1, 35.3, 32.6, 30.9, 29.9, 29.3, 24.0, 23.7.

FTIR (NaCl, thin film, cm^{-1}): 2958, 2934, 2869, 1773, 1736, 1702, 1459, 1420, 1382, 1369, 1283, 1248, 1166, 1142, 1077, 940, 914, 802, 646.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{12}H_{22}NO_4$ $[M+NH_4]^+$: 244.1543; found: 244.1541.



27 (31.0 mg, 0.138 mmol, 1.00 equiv) was subjected to analogous conditions to afford **SI-2** (32.2 mg, quant yield), which was taken forward without further purification.

$\mathbf{R_f}$ = 0.44 (silica gel, 10% MeOH/CH_2Cl_2, *p*-Anisaldehyde)

$\mathbf{[\alpha]_D^{25}}$ = +51.2° (c = 0.53, $CHCl_3$).

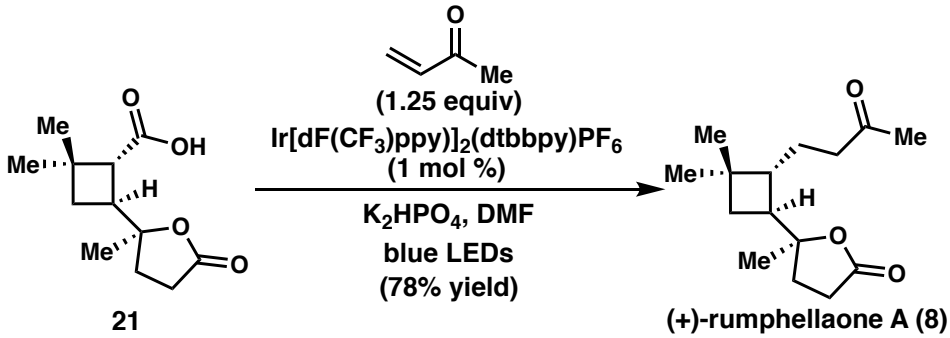
^{1}H NMR (400 MHz, $CDCl_3$): δ 2.78 – 2.56 (m, 3H), 2.50 (ddd, *J* = 18.1, 9.9, 4.9 Hz, 1H), 2.17 – 2.06 (m, 1H), 1.91 (ddd, *J* = 13.1, 10.0, 4.9 Hz, 1H), 1.81 (td, *J* = 9.8, 1.2 Hz, 1H), 1.71 (dd, *J* = 10.8, 8.0 Hz, 1H), 1.29 (s, 3H), 1.21 (s, 3H), 1.11 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 178.4, 177.2, 86.5, 48.1, 39.2, 35.5, 33.6, 30.9, 29.9, 29.3, 23.9, 23.7.

FTIR (NaCl, thin film, cm^{-1}): 2958, 2869, 1770, 1738, 1732, 1704, 1699, 1463, 1422, 1383, 1369, 1283, 1245, 1222, 1165, 1138, 1075, 1002, 965, 941, 914, 802, 757, 711, 648.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{12}H_{22}NO_4$ $[M+NH_4]^+$: 244.1543; found: 244.1537.

Radical decarboxylative coupling to afford (+)-rumphellaone A (8) and *epi*-C8-rumphellaone A (29) [8]



To a 2 dram vial charged with saturated lactone **21** (16 mg, 0.0707 mmol, 1.00 equiv) was added Ir[dF(CF_3)ppy]$_2$(dtbbpy)PF_6 (0.8 mg, 0.0007 mmol, 0.01 equiv) and K_2HPO_4 (14.8 mg, 0.0849 mmol, 1.20 equiv). The reaction vessel was evacuated and backfilled with N_2 three times. DMF (0.71 mL, 0.1 M) was then added, and the reaction mixture was cooled to 0 °C and sparged

with argon for 15 minutes. Freshly distilled methyl vinyl ketone (7.2 μL, 0.0884 mmol, 1.25 equiv) was then added, and the reaction vessel was placed between two 34W blue LEDs (~5-6 cm away from each lamp) and stirred for 24 h with a small fan to keep the reactions at 23 ºC. Once complete, the reaction was diluted with sat. aq. $NaHCO_3$ (0.8 mL) and EtOAc (0.8 mL). The layers were separated, and the aqueous layer was extracted with EtOAc (4 x 1 mL). The combined organic layers were washed with 1 M LiCl (5 mL). The organic layer was then dried over Na_2SO_4, filtered, and concentrated *in vacuo.* The crude material was purified by silica gel flash chromatography (20 → 40% EtOAc/hexanes) to afford pure (+)-rumphellaone A (**8**) (15 mg, 78% yield) as a yellow solid.

R_f = 0.27 (silica gel, 40% EtOAc/Hexanes, UV, *p*-anisaldehyde)

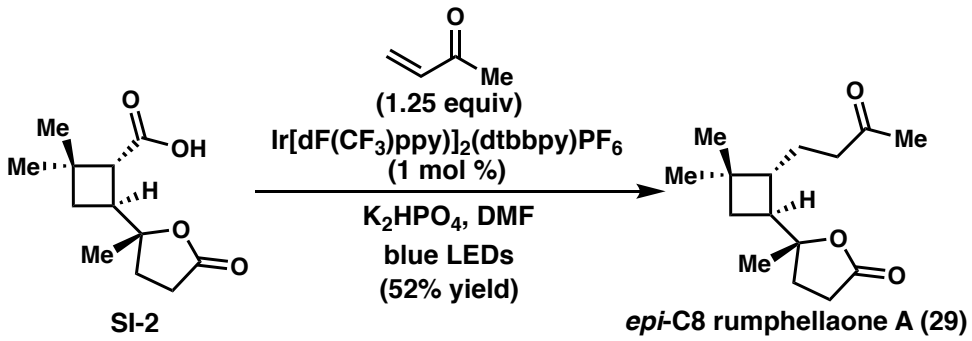
$[\alpha]_D^{25}$ = +43.4° (c = 0.35, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.63 (ddd, *J* =18.1, 10.0, 8.9 Hz, 1H), 2.53 (ddd, *J* = 18.1, 10.0, 5.0 Hz, 1H), 2.36 (t, *J* = 7.9 Hz, 2H), 2.12 (s, 3H), 2.09 – 2.02 (m, 2H), 2.03 – 1.97 (m, 1H), 1.90 (ddd, *J* = 10.2, 9.6, 5.3 Hz, 2H), 1.88 – 1.81 (m, 1H), 1.69 – 1.61 (m, 2H), 1.57 (ddd, *J* = 10.8, 8.6, 0.8 Hz, 1H), 1.42 (t, *J* = 10.3 Hz, 1H), 1.31 (s, 3H), 1.06 (s, 3H), 1.03 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 208.8, 177.1, 87.4, 44.6, 44.4, 42.1, 33.7, 33.1, 31.1, 30.8, 30.1, 29.3, 25.2, 25.0, 22.6.

FTIR (NaCl, thin film, cm^{-1}): 2953, 2929, 2865, 1770, 1715, 1455, 1366, 1250, 1162, 1124, 1077, 938, 803, 645.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{15}H_{25}O_3$ $[M+H]^+$: 253.1798; found: 253.1799.



SI-2 (15.0 mg, 0.066 mmol, 1.00 equiv) was subjected to an analogous procedure to afford *epi*-C8-rumphellaone A (**29**) (8.1 mg, 52% yield) as a white solid.

R_f = 0.33 (silica gel, 40% EtOAc/Hexanes, UV, *p*-anisaldehyde)

$[\alpha]_D^{25}$ = +38.5° (c = 0.41, $CHCl_3$).

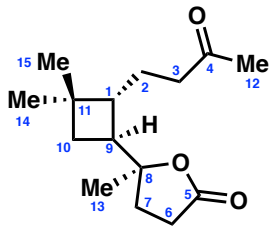
^{1}H NMR (400 MHz, $CDCl_3$): δ 2.63 – 2.56 (m, 2H), 2.39 (dd, *J* = 8.6, 6.6 Hz, 2H), 2.13 (s, 3H), 2.10 – 1.96 (m, 2H), 1.90 (ddd, *J* = 13.0, 8.8, 7.2 Hz, 1H), 1.78 (tdd, *J* = 9.2, 6.6, 0.8 Hz, 1H), 1.71 – 1.57 (m, 3H), 1.51 (t, *J* = 10.4 Hz, 1H), 1.29 (s, 3H), 1.06 (s, 3H), 1.03 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 208.7, 177.1, 87.3, 44.6, 44.1, 41.9, 34.5, 33.4, 31.6, 31.1, 30.2, 29.3, 25.0, 24.0, 22.6.

FTIR (NaCl, thin film, cm^{-1}): 2952, 2932, 2865, 1769, 1715, 1455, 1422, 1365, 1234, 1169, 1155, 1075, 963, 939, 801, 647.

HRMS (ESI-TOF, *m/z*): calc'd for $C_{15}H_{25}O_3$ $[M+H]^+$: 253.1798; found: 253.1799.

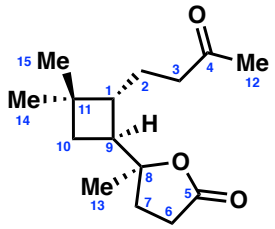
Comparison of ^{1}H NMR spectroscopic data for natural and synthetic (+)-rumphellaone A (8) (carbon numbering as reported by Sung et al.[11])



(+)-rumphellaone A (8)

Carbon Number	**Natural (+)-rumphellaone A** ^{1}H 400 MHz, $CDCl_3$	**Synthetic (+)-rumphellaone A** ^{1}H 400 MHz, $CDCl_3$
1	1.91 (ddd, *J* = 10.0, 9.2, 5.6 Hz, 2H)	1.90 (ddd, *J* = 10.2, 9.6, 5.3 Hz, 2H)
2	1.67 (m, 2H)	1.65 (m, 2H)
3	2.37 (t, *J* = 8.0 Hz, 2H)	2.36 (t, *J* = 7.9 Hz, 2H)
6α	2.63 (ddd, *J* = 18.0, 9.6, 8.8 Hz, 1H)	2.63 (ddd, *J* =18.1, 10.0, 8.9 Hz, 1H)
6β	2.54 (ddd, *J* = 18.0, 10.0, 4.8 Hz, 1H)	2.53 (ddd, *J* = 18.1, 10.0, 5.0 Hz, 1H)
7α	1.84 (m, 1H)	1.84 (m, 1H)
7β	2.01 (m, 1H)	2.01 (m, 1H)
9	2.06 (ddd, 10.4, 10.0, 10.0 Hz, 2H)	2.06 (m, 2H)
10α	1.57 (dd, *J* = 10.0, 10.0 Hz, 1H)	1.57 (ddd, *J* = 10.8, 8.6, 0.8 Hz, 1H)
10β	1.42 (dd, *J* = 10.4, 10.0 Hz, 1H))	1.42 (t, *J* = 10.3 Hz, 1H)
12	2.13 (s, 3H)	2.12 (s, 3H)
13	1.31 (s, 3H)	1.31 (s, 3H)
14	1.03 (s, 3H)	1.03 (s, 3H)
15	1.07 (s, 3H)	1.06 (s, 3H)

Comparison of ^{13}C NMR spectroscopic data for natural and synthetic (+)-rumphellaone A (8).



(+)-rumphellaone A (8)

Carbon Number	**Natural (+)-rumphellaone A** ^{13}C 100 MHz, $CDCl_3$	**Synthetic (+)-rumphellaone A** ^{13}C 101 MHz, $CDCl_3$	**Δ**
1	44.5	44.6	0.1
2	25.1	25.2	0.1
3	42.0	42.1	0.1
4	208.6	208.8	0.2
5	177.0	177.1	0.1
6	29.2	29.3	0.1
7	30.6	30.8	0.2
8	87.2	87.4	0.2
9	44.3	44.4	0.1
10	33.6	33.7	0.1
11	33.0	33.1	0.1
12	29.9	30.1	0.2
13	24.9	25.0	0.1
14	22.5	22.6	0.1
15	30.9	31.1	0.2

5. References

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