Asymmetric Synthesis of Bicyclo[4.3.1] and [3.3.2]decadienes via [6+3] Trimethylenemethane Cycloaddition with Tropones

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Supporting Information

Materials and Methods:

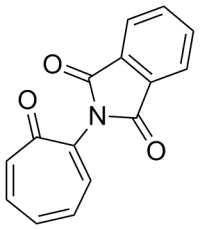
All reactions were carried out under an atmosphere of nitrogen or argon in oven-dried glassware with magnetic stirring, unless otherwise indicated. Reaction solvents were dried using J. C. Meyer's Solvent Purification System passing through activated alumina prior to use. All other reagents were purchase from commercial sources and used without further purification, unless otherwise indicated. Microwave reactions were conducted using a Biotage Initiator 2.0, Model 355302 microwave synthesizer.

Flash Chromatography was performed using SiliCycle SilicaFlash F 60 40-60 μm 60 Å silica gel. Analytical thin-layer chromatography was performed with 0.25 mm coated commercial silica gel plates (E. Merck, DC-Glasfolien, Kieselgel 60 F254) and visualized with UV light and potassium permanganate stain. Melting points were obtained on a Thomas-Hoover apparatus in open capillary tubes and are uncorrected. Proton nuclear magnetic resonance (^{1}H-NMR) data were acquired on a Mercury 400 (400 MHz), a Varian 400 (400 MHz), or on a Varian Unity Inova-500 (500 MHz) spectrometer. Carbon-13 nuclear magnetic resonance (^{13}C-NMR) data were acquired at 100 MHz on a Mercury 400 or at 125 MHz on a Varian Unity Inova 500 spectrometer. Chemical shifts are reported in delta (δ) units, part per million (ppm) relative to deuterochloroform (7.26 ppm for ^{1}H NMR and 77.23 ppm for ^{13}C. Chiral HPLC analyses were performed on a Thermo Separation Products Spectra Series P-100 or P-200 and UV100 (254 nm or 220 nm) using Chiralcel columns (OB-H, OC, OD-H, OJ-H), or Chiralpak column (AD, AS, IA, IB, IC) eluting with the solvent mixtures indicated. Optical rotations were measured on a Jasco DIP-1000 digital polarimeter using 5 cm cells and the sodium D line (589 nm) at ambient temperature in dichloromethane. Infrared (IR) data were recorded as films on potassium bromide (KBr) pellets on a Thermo Scientific Nicolet IR 100 FT-IR spectrometer. High resolution mass spectra were obtained from Stanford University on a Micromass Q-Tof API US Mass Spectrometer using positive electrospray ionization (+ESI). Elemental analysis were conducted by M-H-W Laboratories, Pheonix, Az.

Abbreviations:
Me = methyl
Et = ethyl
EtOAc = ethyl acetate
PE = petroleum ether

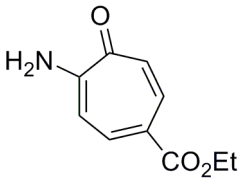
Tropone Syntheses:

The 2, 3, and 4-carboethoxy tropones were synthesized according to literature procedures via cyclopropanation of anisole followed by oxidation of the intermediate cycloheptatrienes.[1] A rhodium catalyzed reaction of Anciaux[2] was used to generate ethyl-4-methoxycyclohepta-2,4,6-triene-1-carboxylate and ethyl-2-methoxycyclohepta-2,4,6-triene-1-carboxylate. The thermal decomposition of ethyl diazoacetate as described by Garst[3] provided the ethyl-3-methoxycyclohepta-2,4,6-triene-1-carboxylation. Oxidation to the requisite tropones followed the procedure of Garst[3] or with molecular bromine.[4] 2-Chlorotropone[5], 2-acetoxytropone[6] and 2-phenyltropone[7] were prepared from tropolone following the procedures of Doering.



2-Phthalimido-2,4,6-cycloheptatrien-1-one **3g**

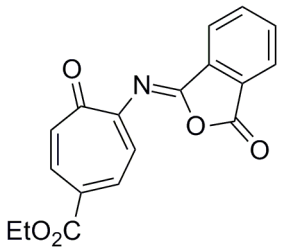
To a solution of 2-aminotropone[6] (0.100 g, 0.826 mmole) and 4-dimethylaminopyridine (0.151 g, 1.24 mmole) in 5 mL CH_2Cl_2 held at room temperature was added phthaloyl dichloride (0.179 mL, 1.24 mmole). The reaction mixture was stirred for 1 h then quenched with saturated $NaHCO_3$ and extracted twice with CH_2Cl_2. The combined fractions were dried over Na_2SO_4, filtered and concentrated. Purification by flash chromatography (CH_2Cl_2/1% MeOH) gave the desired product as a white solid. R_f = 0.4 (50% EtOAc/PE); M.P = 184 °C;^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92-7.89 (band, 2H), 7.78-7.75 (band, 2H), 7.42 (dd, *J* = 8.8, 1.0 Hz, 1H), 7.27-7.22 (band, 2H), 7.13 (m, 1H), 7.07 (dd, *J* = 8.9, <1.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 181.4, 166.8, 141.6, 138.0, 136.3, 136.0, 134.6, 132.2, 131.9, 124.1; IR (film) 1720, 1632, 1589, 1464, 1372, 1278, 1118 cm $^{-1}$; Anal. calc'd for $C_{15}H_9NO_3$: C, 71.71, H, 3.61, N, 5.58. Found: C, 71.88, H, 3.62, N, 5.52.



2-amino-4-carboethoxy-2,4,6-cycloheptatrien-1-one

To a solution of 4-(carboethoxy)-2,4,6-cycloheptatrien-1-one (**3a**) (0.622 g, 3.49 mmole), pyridine (0.564 mL, 6.98 mmole) and 10 mL ethanol (>95%) was added hydroxylamine (0.291 g, 4.20 mmole). The reaction mixture was heated to 45 °C for 4 h. The solvents

were evaporated and the residue purified by column chromatography (40-60% EtOAc/PE) to give 0.311 g (45%) of the aminotropone as a brown solid. m.p. = 155-160 °C, R_f = 0.25 (50% EtOAc/PE). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13-8.08 (band, 2H), 7.15 (d, *J* = 12.4 Hz, 1H), 6.85 (d, *J* = 10.8 Hz, 1H), 4.34 (ddd, *J* = 6.8, 6.8, 6.8 Hz, 2H), 1.38 (dd, *J* = 7.2, 7.2, 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.6, 166.9, 158.7, 139.2, 136.7, 128.8, 124.1, 110.1, 61.5, 14.3; IR (film) 3334, 3277, 3195, 1678, 1603, 1537, 1444, 1354, 1275 cm $^{-1}$.



2-isophthalimido-4-carboethoxy-2,4,6-cycloheptatrien-1-one **3i**

To a solution of 2-amino-4-carboethoxy-2,4,6-cycloheptatrien-1-one (0.125 g, 0.647 mmole), triethylamine (0.451 mL, 3.23 mmole) and 6 mL CH_2Cl_2 held at –20 °C was added phthaloyl dichloride (0.140 mL, 0.971 mmole) in a dropwise fashion. After slowly warming to 0 °C over 20 min, the reaction was quenched with saturated $NaHCO_3$. The organic layer was separated and the aqueous layer extracted twice with CH_2Cl_2. The combined organic fractions were dried over Na_2SO_4, filtered and concentrated under reduced pressure. Purification by column chromatography (30% EtOAc/PE) gave 0.160 (76%) of tropone **3i** as a yellow solid. m.p. = 155-157 °C, R_f = 0.55 (50% EtOAc/Pe). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95-7.90 (band, 3H), 7.73 (ddd, *J* = 7.2, 7.2, 0.8 Hz, 1H), 7.66 (ddd, *J* = 7.6, 7.6, 0.8 Hz, 1H), 7.42 (d, *J* = 7.6 Hz, 1H), 7.21 (d, *J* = 12.4 Hz, 1H), 6.66 (d, *J* = 9.6 Hz, 1H), 4.35 (ddd, *J* = 7.2, 7.2, 7.2 Hz, 2H), 1.38 (dd, *J* = 7.2, 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 165.7, 165.3, 144.0, 138.3, 137.6, 135.1, 131.9, 128.4, 126.1, 125.4, 124.8, 123.0, 106.7, 62.1, 14.2; IR (film) 2990, 1789, 1705, 1624, 1542, 1455, 1345, 1281, 1239, 1210, 1099 cm $^{-1}$; MS (ESI) for $C_{18}H_{13}NO_5$ [M + Ma] calc. 346.0692, found 346.0691.

[6+3] TMM cycloaddition products

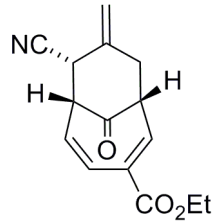
General procedure:

Standard procedure for TMM [6+3] cycloadditions:

A mixture of the tropone (0.200 mmole), $Pd(dba)_2$ (0.0058 g, 0.010 mmole, 5 mole%) and phosphoramidite ligand **L5** (0.020 mmole, 10 mol%) were placed in a flask and purged with argon for 10 min. The solids were dissolved in 0.8 mL (0.25 M) toluene and the reaction mixture was stirred for 5-10 min. After the flask was cooled to 0°C for a further 5 min using an ice bath, the TMM donor **2**[8] (0.074 mL, 0.320 mmole, 1.6 equiv.) was added and the reaction left overnight at 0-4°C under an argon atmosphere. The

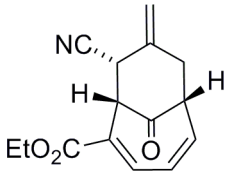
reaction mixture was then passed through a small pad of silica gel and the solvents were evaporated under reduced pressure. Diastereomeric ratios were determined by crude ^{1}H NMR analysis. Purification was achieved using flash chromatography.

Preparation of racemates for chiral HPLC analysis followed the general procedure using a racemic mixture of ligand **L1**.



TMM adduct **4a**

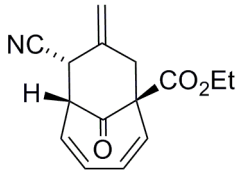
The reaction was run according to the standard conditions using 4-carboethoxy tropone (0.0369 g, 0.225 mmol). The crude mixture was purified by flash column chromatography (20%-30% ethyl acetate/petroleum ether) to yield 0.0405 g (74%) of a slightly yellow solid. An analytical sample was prepared by preparatory thin layer chromatography (5% methanol/methylene chloride). Chiral HPLC using IB column, 30% isopropanol/heptane, 1mL/min, 254nm, elution after 14 (minor) and 18 (major) minutes gave an enantiomeric excess of 99%. R_f = 0.25 (30% EtOAc/PE); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.77 (d, *J* =8.4 Hz, 1H), 6.72 (d, *J* =12.4 Hz, 1H), 5.76 (dd, *J* = 12.2, 7.8 Hz, 1H), 5.51 (s, 1H), 5.26 (s, 1H), 4.23 (m, 2H), 3.83 (d, *J* =5.4 Hz, 1H), 3.70 (m, 1H), 3.59 (m, 1H), 2.75 (dd, *J* = 14.0, 6.4 Hz, 1H), 2.67 (d, *J* =14.0 Hz, 1H), 1.31 (dd, *J* =7.7, 7.7Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 202.7, 166.2, 135.4, 132.9, 129.6, 126.7, 122.8, 119.9, 116.0, 61.9, 54.2, 52.9, 40.9, 39.4, 14.3; IR (film) 2984, 2936, 1715, 1614, 1445, 1368, 1252, 1094, 1052 cm^{-1}; $[\alpha]^{23}_D$ = 102.9° (c 2.3, CH_2Cl_2); mp = 200 °C (decomp); HRMS [M + Na] calc 280.0950, found 280.0954.



TMM adduct **4b**

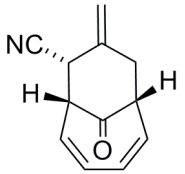
A mixture of 3-carboethoxy tropone (0.037 g, 0.206 mmole), $Pd(dba)_2$ (0.0059 g, 0.010 mmole) and the phosphoramidite ligand **L5** (0.014 g, 0.021 mmole) were placed in a flask and purged with argon for 10 min. The solids were dissolved in 1 mL (0.2 M) toluene and the reaction mixture was stirred for 5-10 min at room temperature. The TMM donor **2** (0.077 mL, 0.330 mmole) was then added and the reaction left overnight at room temperature under an argon atmosphere. The reaction mixture was then passed through a

small pad of silica gel and the solvents were evaporated under reduced pressure. Further purification was achieved using flash chromatography (CH_2Cl_2 – 2% MeOH/CH_2Cl_2) to yield 0.043 g (80%) of the desired product as a white solid. Chiral HPLC using OD column, 25% isopropanol/heptane, 0.8 mL/min, 254nm, elution after 15.8 (minor) and 22.0 (major) minutes gave an enantiomeric excess of 99%. R_f = 0.25 (25% EtOAc/PE); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.26 (d, *J* = 8.4 Hz, 1H), 6.02 (dd, *J* = 11.6, 8.4 Hz, 1H), 5.71 (dd, *J* = 11.6, 7.3 Hz, 1H), 5.62 (s, 1H), 5.19 (s, 1H), 4.49 (dd, *J* = 6.2, 2.9 Hz), 4.26 (m, 2H), 3.84 (m, 1H), 3.54 (m, 1H), 2.74 (dd, *J* = 14.0, 5.4 Hz, 1H), 2.57 (dd, *J* = 14.0, 2.0 Hz, 1H), 1.33 (dd, *J* = 7.0, 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 203.5, 165.7, 136.4, 133.6, 133.1, 124.2, 124.0, 119.9, 115.9, 62.2, 53.9, 51.9, 40.7. 39.5, 14.3; IR (film) 2982, 2246, 1711, 1602, 1446, 1366, 1274, 1219, 1146, 1093, 1048 cm^{-1}; $[\alpha]^{23}_D$ = –136.7° (c 2.5, CH_2Cl_2); mp = 99-101 °C; HRMS [M + Na] calc 280.0950, found 280.9047.



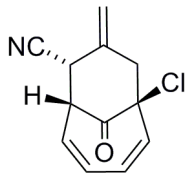
TMM adduct **4c**

The reaction was run under the standard conditions using 2-carboethoxy tropone (0.040 g, 0.225 mmol) and purified by a silica gel flash column (15% ethyl acetate/petroleum ether) yielding 0.045 g (77%) of the desired product as white crystals. Chiral HPLC using IA column, 95:5 heptane/isopropanol, 1mL/min, 254nm, elution after 15.7 (major) and 16.8 (minor) minutes gave an enantiomeric excess of 99%. R_f = 0.30 (20% EtOAc/PE); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.02 (dd, *J* =11.4, 7.7 Hz, 1H), 5.93 (dd, *J* =11.9, 7.9 Hz, 1H), 5.65 (d, *J* = 11.9 Hz, 1H), 5.64 (dd, *J* = 11.3, 6.4 Hz, 1H), 5.54 (bs, 1H), 5.26 (bs, 1H), 4.28 (dq, *J* = 7.2, 0.8 Hz, 2H), 3.94 (d, *J* = 5.6, 1H), 3.69 (dd, *J* = 7.9, 5.6 Hz, 1H), 3.23 (d, *J* = 14.0, 1H), 2.63 (d, *J* = 14.0, 1H), 1.30 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 200.1, 170.0, 132.8, 128.2, 126.5, 124.9, 122.1, 119.9, 115.9, 66.6, 62.5, 53.7, 43.4, 40.7,14.3; IR (film) 3056 (w), 2984 (w), 1739 (s), 1262 (s), 1239 (m), 1048 (w), 909 (m) cm^{-1}; $[\alpha]^{23}_D$ = 175.1°(c 3.5, CH_2Cl_2); mp = 94°C. HRMS $[M+Na]^+$ calc 280.0950, found 280.0946.



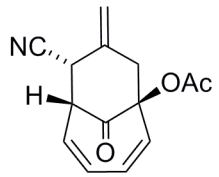
TMM adduct **4d**

A mixture of tropone (0.015 g 0.140 mmole), $Pd(dba)_2$ (0.004 g, 0.007 mmole) and phosphoramidite ligand **L5** (0.0096 g, 0.014 mmole) were placed in a flask and purged with argon for 10 min. The solids were dissolved in 0.56 mL (0.25 M) toluene and the reaction mixture was stirred for 5-10 min at room temperature. The TMM donor (0.050 mL, 0.225 mmole) was then added and the reaction was placed in an oil bath preheated to 45 °C. After heating for 1.5 h under an argon atmosphere, the reaction mixture was then passed through a small pad of silica gel and the solvents were evaporated under reduced pressure. Further purification was achieved using flash chromatography (20% EtOAc/PE) to yield 0.023 g (89%) of a white solid. Chiral HPLC using IC column, 20% ethylacetate/heptane, 1.0 mL/min, 254nm, elution after 8.5 (minor) and 9.0 (major) minutes gave an enantiomeric excess of 99%. R_f = 0.20 (20% EtOAc/PE); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.03 (dd, *J* = 11.5 Hz, 7.7 Hz, 1H), 5.87 (dd, *J* = 11.6 Hz, 7.7 Hz, 1H), 5.60 (dd, *J* = 11.6, 7.8 Hz, 1H), 5.52 (s, 1H), 5.46 (dd, *J* = 11.6, 7.8 Hz, 1H), 5.25 (s, 1H), 3.82 (d, *J* = 5.6 Hz, 1H), 3.63 (m, 1H), 3.43 (m, 1H), 2.68 (dd, *J* = 14.1, 6.5 Hz, 1H), 2.55 (dd, *J* = 14.0, 1.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 204.3, 133.6, 128.5, 126.7, 125.1, 121.4, 119.2, 116.3, 54.2, 53.5, 40.9, 39.9; IR (film) 3030 (w), 2927 (w), 2244 (w), 1725 (vs), 1415 (m), 1314 (w), 1275 (w), 1146 (w), 912 (m), 874 (m), 801 (m), 677 (m) cm^{-1}; $[\alpha]^{23}_D$ = 52.6° (c 1.2, CH_2Cl_2); mp = 126°C; HRMS [M+Na] calc: 208.0738, found 208.0742.



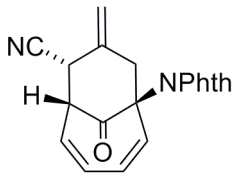
TMM adduct **4e**

The reaction was run according to the general procedure using 2-chlorotropone (0.030 g, 0.213 mmol).The crude material was purified by a flash chromatography (1:1 ether/petroleum ether) resulting in 0.044 g (94%) of slightly yellow solid crystals, from which x-ray quality crystals could be obtained after recrystallization from dichloromethane/heptane. Chiral HPLC using IC column, 20% ethylacetate/heptane, 1 mL/min, 254 nm, 6.7 (minor) and 12 (major) minutes gave an enantiomeric excess of 94%. R_f = 0.25 (50% Et_2O/PE); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.00 (dd, *J* = 11.5, 7.9 Hz, 1H), 5.81 (dd, *J* = 12.0, 7.8 Hz, 1H), 5.72 (m, 1H), 5.60 (s, 1H), 5.56 (d, J=12.0, 1H), 5.34 (s, 1H), 3.89-3.85 (band, 2H), 3.13 (d, *J* = 13.7 Hz, 1H), 2.99 (d, *J* = 13.5, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 195.9, 133.1, 130.5, 130.3, 127.7, 123.5, 123.0, 120.6, 115.4, 52.6, 51.4, 40.7; IR (film) 2920 (m), 2280 (w), 1743 (s), 1440 (m), 1285 (w), 980 (m), 933 (m), 896 (w), 845 (m), 806 (m) cm^{-1}; $[\alpha]^{22}_D$ = 225.9° (c 0.4, CH_2Cl_2); mp = 145°C; HRMS [M+Na] calc: 242.0349, found 242.0353.



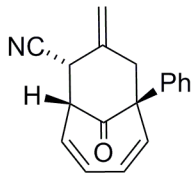
TMM adduct **4f**

The reaction was run following the general procedure using 2-acetoxytropone (0.
030 g, 0.183 mmol). The crude material was purified by flash column chromatography (20% ethyl acetate/petroleum ether) to give 0.040 g (90%) of the desired product as a white solid. Chiral HPLC using IA column, 10:90 isopropanol/heptane, 1 mL/min, 254 nm, 11.3 (minor) and 14.2 (major) minutes gave an enantiomeric excess of 96%. R_f = 0.2 (20% EtOAc/PE); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.00 (dd, *J* = 11.5, 7.9 Hz, 1H), 5.82 (dd, *J* = 12.0, 7.9 Hz, 1H), 5.65 (dd, *J* = 11.5, 7.6 Hz, 1H), 5.50 (d, *J* = 12.0 Hz, 1H), 5.47 (dd, J = 1.7, 1.7 Hz, 1H), 5.31 (dd, *J* = 1.7, 1.7 Hz, 1H), 4.01 (m, 1H), 3.77 (dd, *J* = 7.6, 5.0 Hz, 1H), 3.31 (d, *J* = 13.5 Hz, 1H), 2.70 (d, *J* = 13.5 Hz, 1H), 2.14 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 197.1, 169.9, 133.2, 128.5, 127.6, 123.0, 122.7, 119.7, 115.9, 86.6, 52.3, 44.9, 39.5, 21.5; IR (film) 3032 (w), 2943)w),l 2246 (w), 1742 (m), 1722 (s), 1439 (w), 1369 (w), 1243 (m), 1056 (m), 923 (m) cm^{-1}; $[\alpha]^{23}_D$ = 252.3° (c 0.4, CH_2Cl_2); mp = 153°C; HRMS [M+Na] calc 266.0793, found 266.0796.



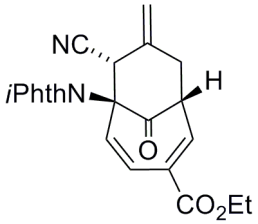
TMM adduct **4g**

The reaction was according to the standard procedure using 2-phthalimido tropone (**3g**) (0.040, 0.159 mmol). Purification of the crude material using flash chromatography (CH_2Cl_2 – 5% MeOH/CH_2Cl_2) gave 0.045 g (85%) of the desired product as a white solid. Chiral HPLC using IA column, 10% isopropanol/heptane, 1 mL/min, 254 nm, 17.8 (minor) and 23.5 (major) minutes gave an enantiomeric excess of 86%. R_f = 0.2 (20% EtOAc/PE); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.85-7.80 (band, 2H), 7.77-7.72 (band, 2H), 6.39 (d, *J* = 12.3 Hz, 1H), 6.07 (dd, *J* = 11.4, 8.0 Hz, 1H), 5.9 (dd, *J* = 12.1, 7.8 Hz, 1H), 5.71 (dd, *J* = 11.3, 8.1 Hz, 1H), 5.59 (dd, *J* = 1.5, 1.5 Hz, 1H), 5.30 (bs, 1H), 4.09 (dd, *J* = 5.5, 1.0 Hz, 1H), 3.96 (d, *J* = 13.5 Hz, 1H), 3.83 (dd, *J* = 8.1, 5.5 Hz, 1H), 2.78 (d, *J* = 13.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 197.3, 133.1, 128.5, 126.3, 122.3, 121.9, 120.3, 116.0, 89.8, 73.6, 52.1, 44.8, 40.0; IR (film) 3473 (w), 2247 (w), 1778 (w), 1716 (s), 1467 (w), 1369 (m), 1325 (w), 1134 (w), 719 (w) cm^{-1}; $[\alpha]^{24}_D$ = 71.6° (c 1.5, CH_2Cl_2); mp = 166°C; HRMS [M+Na] calc 353.0902, found 353.0911.



TMM adduct **4h**

A mixture of 2-phenyl tropone (0.0204 g, 0.112 mmol), $Pd(dba)_2$ (0.0032 g, 0.0056 mmol) and phosphoramidite ligand **L5** (0.0077 g, 0.0112 mmol) was purged with argon for 10 min. The solids were dissolved in 0.45 mL toluene and stirred at room temperature for 5 minutes before TMM donor **2** (0.075 mL, 0.336 mmol) was added and the mixture stirred for 36 h. The crude material was purified using flash chromatography (15% ethyl acetate/petroleum ether) to give 0.014 g of the major diastereomer along with 0.005 g of the minor diastereomer (64% total). Chiral HPLC of the major diastereomer using IA column, 90:10 heptane/isopropanol, 1 mL/min, 254nm, 10.3(minor) and 14(major) minutes, determined an enantiomeric excess of 93%. Analytical data for major diastereomer: R_f = 0.3 (20% EtOAc/PE); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.41-7.26 (band, 5 H), 6.08 (dd, *J* = 11.3, 7.6 Hz, 1H), 5.97 (dd, *J* = 11.8, 7.7 Hz, 1H), 5.77 (dd, *J* = 11.3, 8.5 Hz, 1H), 5.66 (s, 1H), 5.40 (d, *J* = 11.8 Hz, 1H), 5.25 (s, 1H), 3.93 (bd, *J* = 6.4 Hz, 1H), 3.72 (dd, *J* = 8.4, 6.4 Hz, 1H), 3.28 (d, *J* = 13.5 Hz, 1H), 2.81 (d, *J* = 13.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 202.6, 140.3, 134.7, 132.7, 128.5, 128.4, 128.2, 128.0, 124.6, 123.3, 119.2, 116.3, 63.7, 53.6, 44.4, 41.4; IR (film) 3021 (w), 2923 (w), 2240 (w), 1996 (w), 1711 (s), 1495 (w), 1446 (m), 1412 (m), 1298 (w), 1271 (m), 1216 (w), 1145 (m), 906 (m), 810 (m) cm^{-1}; $[\alpha]^{23}_D$ = 252.5° (c 1.4, CH_2Cl_2); mp = 162 °C; HRMS [M+Na] calc: 284.1051, found 284.1052.

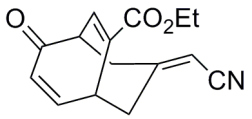


TMM adduct **4i**

Tropone **3i** (0.030 g, 0.0928 mmole), Pd_2dba_3-$CHCl_3$ complex (0.0024 g, 0.00232 mmole) and ligand **L5** (0.0064 g, 0.00928 mmole) were placed in a flask and purged with argon for 5 min. The solids were dissolved in 0.92 ml toluene and the reaction mixture stirred for 10 min. The flask was cooled to 0°C for a further 10 min using an ice bath. TMM donor **2** (0.0330 ml, 0.1485 mmole) was then added and the reaction left overnight at 4°C. The reaction mixture was then passed through silica gel and solvents evaporated. Products were purified by flash chromatography (20-30% EtOAc/PE) giving 20.3 mg of major diastereomer and 9.0 mg of minor diastereomer as clear oils giving a total of 29.3 mg (78%).

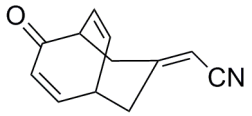
Analysis of major diastereomer: Chiral HPLC using IB column, 35% Ethylacetate/Heptane, elution at 6.7 (minor) and 7.6 (major) mins gave an enantiometric excess of 91%. R_f = 0.3 (30% EtOAc/PE). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 7.6 Hz, 1H), 7.71 (ddd, *J* = 7.6, 7.6, 1.2 Hz, 1H), 7.65 (ddd, *J* = 7.6, 7.6, 1.2 Hz, 1H), 7.27 (d, *J* = 7.6 Hz, 1H), 7.03 (d, *J* = 7.6 Hz, 1H), 6.79 (dd, *J* = 12.4, 1.2 Hz, 1H), 6.01 (d, *J* = 12.4 Hz, 1H), 5.57 (s, 1H), 5.32 (s, 1H), 4.32-4.24 (band, 2H), 4.15-4.08 (m, 1H), 3.86 (bs, 1H), 2.85 (dd, *J* = 14.0, 2.0 Hz, 1H), 2.79 (dd, *J* = 14.0, 5.6 Hz, 1H), 1.35 (dd, *J* = 7.2, 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.7, 166.2, 166.0, 144.2, 136.1, 135.3, 132.4, 132.0, 129.1, 127.3, 126.7, 125.9, 124.4, 123.1, 121.6, 114.6, 92.8, 62.2, 49.7, 41.0, 40.8, 14.4; IR (film) 2984, 1789, 1715, 1666, 1467, 1371, 1281, 1260, 1242, 1099, 1044 cm $^{-1}$; $[\alpha]^{23}_D$ = –24.2 (c 2.0, CH_2Cl_2); MS (ESI) for $C_{23}H_{18}O_{10}$ [M + Na] calc. 402.1216, found 402.1217.
Analysis of minor diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.68-7.59 (band, 2H), 7.16 (dd, *J* = 7.2, 1.0 Hz, 1H), 7.11 (dd, *J* = 8.0, 1.0 Hz, 1H), 6.77 (dd, *J* = 12.4, 1.2 Hz, 1H), 5.83 (d, *J* = 12.0 Hz, 1H), 5.29 (d, *J* = 1.6 Hz, 1H), 5.24 (s, 1H), 4.33-4.24 (band, 2H), 4.12 (dd, *J* = 6.9, 6.9 Hz, 1H), 3.89 (bs, 1H), 3.18 (dd, *J* = 14.3, 6.5 Hz, 1H), 2.73 (d, *J* = 14.3 Hz, 1H), 1.36 (dd, *J* = 7.2, 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.0, 166.2, 166.1, 144.9, 137.1, 135.1, 133.7, 131.7, 128.6, 128.4, 126.8, 125.6, 124.5, 124.3, m123.8, 122.9, 115.1, 92.4. 62.2, 48.6, 40.5, 37.7, 14.4; IR (film) 2924, 2253, 1787, 1712, 1667, 1467, 1369, 1281, 1101, 1070, 1042, 953 cm $^{-1}$; HRMS (ESI) for $C_{23}H_{18}N_2O_5$ [M] calc. 402.1216, found 402.1214.

Cope Rearrangements



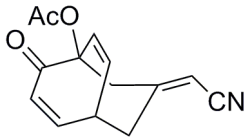
Bicyclo[3.3.2]decadiene **5a**

TMM adduct **4a** (0.0204 g, 0.0793 mmole) was dissolved in 2 mL toluene and heated to 170 °C in a microwave synthesizer for a total of 1.5 hours. The reaction was purified using flash chromatography (30% EtOAc/PE) to give 0.0153 g (75%) of the desired product as a white solid. R_f=0.35 (30% ethyl acetate/petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.26 (dd, *J* = 8.8, 1.8 Hz, 1H), 6.82 (dd, *J* = 11.7, 9.1 Hz, 1H), 6.07 (dd, *J* = 11.7, 1.5 Hz, 1H), 5.28 (dd, *J* = 1.3, 1.3 Hz, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 3.57 (dddd, *J* = 8.7, 7.5, 2.7, 1.6 Hz, 1H), 3.15 (ddd, *J* = 14.0, 6.1, 1.5 Hz, 1H), 2.69 (ddd, *J* = 13.7, 6.1, 1.4 Hz, 1H), 2.55 (ddd, *J* = 13.6, <1.0, <1.0 Hz, 1H), 2.42 (ddd, *J* = 14.1, <1.0, <1.0 Hz, 1H), 1.32 (t, *J* = 7.1Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 194.8, 165.7, 162.3, 147.2, 142.0, 139.5, 133.5, 115.8, 101.7, 61.9, 52.6, 38.8, 36.3, 35.1, 14.4; IR (film) 2983 (w), 2218 (m), 1709 (s), 1653 (s), 1393 (m), 1251 (s), 1161 (w), 1092 (w), 1035 (w), 818 (w), 783 (w) cm^{-1}; $[\alpha]^{23}_D$ = 39.3° (c 1.5, CH_2Cl_2); mp = 150°C; HRMS [M+Na] calc. 280.0950, found 280.0946.



Bicyclo[3.3.2]decadiene **5d**

The unsubstituted TMM adduct **4d** (0.0420 g, 0.227 mmol) was dissolved in 2 mL toluene and reacted in the microwave synthesizer at 170 °C for a total of 3.75 hours. The crude mixture was purified using flash chromatography (20% ethyl acetate/petroleum ether) to give 0.0301 g (72%) of the desired product as white crystals and 0.0064 g starting material (85% brsm). Chiral HPLC using IC column, 80:20 heptane/ethyl acetate, 1mL/min, 254nm, elution after 9 (minor) and 17 (major) minutes showed an enantiomeric excess of 98%ee.
R_f =0.15 (20% EtOAc/PE); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.76 (dd, *J* = 11.8, 8.9 Hz, 1H), 6.49 (ddd, *J* = 9.7, 8.3, 1.3 Hz, 1H), 6.11 (ddd, *J* = 9.7, 8.4, 1.3 Hz, 1H), 6.04 (dd, *J* = 11.7, 1.7 Hz, 1H), 5.26 (dd, *J* = 1.5, 1.5 Hz, 1H), 3.47 (m, 1H), 3.41 (m, 1H), 3.10 (ddd, *J* = 13.6, 5.9, 1.4 Hz, 1H), 2.64 (ddd, *J* = 13.5, 5.9, 1.4 Hz, 1H), 2.50 (m, 1H), 2.46 (ddd, *J* = 13.7, <1.0, <1.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 196.8, 163.7, 147.6, 138.8, 133.4, 130.1, 116.1, 101.1, 53.1, 39.5, 37.7, 35.4; IR (film) 3044 (m), 2950 (m), 2892 (w), 2848 (w), 2218 (s), 1671 (s), 1649 (s), 1618 (m), 1441 (m), 1428 (w), 1401 (m), 1281 (m), 1246 (w), 1208 (m), 1165 (m), 874 (m), 832 (m), 780 (m) cm^{-1}; $[\alpha]^{25}_D$ = –100.1° (c 2.1, CH_2Cl_2); mp = 127 °C. HRMS [M+Na] calc. 208.0738, found 208.0736.



Bicyclo[3.3.2]decadiene **5f**

The 2-acetoxy substituted TMM adduct **4f** (0.0310 g, 0.127 mmole) was dissolved in 2 mL toluene and heated to 170 °C in the microwave synthesizer for a total of 3.5 hours. Purification by flash chromatography (25% ethyl acetate/petroleum ether) gave 0.0222 g (72%) of the desired product as white crystals and 0.0054 g recovered starting material (87% brsm). R_f = 0.1 (20% ethyl acetate/petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.80 (dd, *J* = 11.9, 9.0 Hz, 1H), 6.35 (dd, *J* = 10.7, 8.6 Hz, 1H), 6.18 (d, *J* = 12.0 Hz, 1H), 6.04 (d, *J* = 10.8 Hz, 1H), 5.28 (dd, *J* = 1.5, 1.5 Hz 1H), 3.45 (m, 1H), 3.07 (ddd, *J* = 14.0, 5.7, 1.1 Hz, 1H), 2.80 (ddd, *J* = 12.7, 1.6, 1.6 Hz, 1H), 2.64 (d, *J* = 12.7 Hz, 1H), 2.49 (ddd, *J* = 13.9, <1.0, <1.0 Hz, 1H), 2.15 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.4, 169.5, 159.0, 147.2, 136.3, 132.4, 132.1, 115.6, 103.5, 86.7, 45.7, 36.7, 35.5, 21.3; IR (film) 3059 (w), 2960 (w), 2920 (w), 2225 (m), 1740 (m), 1675 (s), 1626 (w), 1430 (m), 1377 (s), 1247 (s), 1232 (m), 1201 (m), 1068 (m), 1035 (s), 819 (m), 780 (m) cm^{-1}; $[\alpha]^{23}_D$ = –245.6° (c 0.8, CH_2Cl_2) mp = 159-163 °C; HRMS [M+Na] calc. 266.0793, found 266.0790.

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