A Metathesis Approach to the Synthesis of Polyheterocyclic Structures from Oxanorbornenes

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Acid 3.1: A solution of ester **3** (692 mg, 2.57 mmol) was dissolved in MeOH (50 mL) and water (50 mL), and to this solution LiOH·H₂O (162 mg, 3.85 mmol) was added. The hydrolysis reaction was allowed to stir at room temperature for 18 hours. The MeOH was evaporated, and the aqueous mixture was acidified by the careful addition of c.HCl to achieve pH 4. Following acidification, solid NaCl was added to saturate the aqueous mixture. The product was obtained by extraction with 10% isopropanol/CHCl₃. The combined organic extracts were dried over Na₂SO₄, filtered and concentrated to afford acid **3.1** (656 mg, quant.), used without further purification in subsequent transformations: ¹H NMR (500 MHz, CDCl₃): δ 6.66 (d, *J* = 5.1 Hz, 1H), 6.33 (d, *J* = 5.0 Hz, 1H), 5.63 (d, *J* = 5.2 Hz, 1H), 5.13 (d, *J* = 4.1 Hz, 1H), 4.80 (s, 1H), 3.64 (s, 1H), 2.85 (s, 1H), 1.43 (s, 9H). ¹³C NMR (125 MHz, CDCl₃): δ 171.6, 158.5, 139.2, 132.6, 82.9, 82.4, 78.9, 56.5, 55.5, 28.2; FTIR (thin film): 3600-2400 (br), 3318, 2979, 1707, 1638, 1522, 1456, 1394, 1368, 1297, 1253, 1164, 1058, 1027, 987, 906, 860, 806, 699 cm⁻¹. Exact mass calculated for (C₁₂H₁₇O₅N + Na)⁺ (ESI) 278.1004, found 278.1003.

Allyl ester 4: To a solution of acid **3.1** (172.5 mg, 0.676 mmol) in methanol/water (5mL:1mL) was added 20% Cs₂CO₃ dropwise to until pH 7 was obtained. The reaction mixture was evaporated to dryness and the resulting cesium salt was taken up in DMF (10 mL). Allyl bromide (65 μL, 0.743 mmol) was added and the reaction was left to stir overnight at room temperature under an argon atmosphere. Ethyl acetate was added to the reaction mixture and was washed with water several times, then brine. The organic layer was then dried over sodium sulfate and concentrated *in vacuo* to afford 176 mg of crude product. The crude product was chromatographed using 30% ethyl ether/hexane (*R*_F = 0.30 in 50% EE/Hx) to provide **4** as a white solid (132.8 mg, 66% yield).

mp 74-75°C; [α]_D (CH₂Cl₂) = -112°; IR (film, cm⁻¹): 3345, 2977, 1739, 1714, 1518, 1367, 1277, 1252, 1171, 992; ¹H NMR (500 MHz, CDCl₃) δ: 6.46 (dd, *J* = 1.6 Hz, *J* = 5.8 Hz, 1H), 6.36 (dd, *J* = 1.3 Hz, *J* = 5.8 Hz, 1H), 5.86 (m, 1H), 5.30 (d, *J* = 17.3 Hz, 1H), 5.23 (d, *J* = 10.6 Hz, 1H), 5.12 (d, *J* = 4.7 Hz, 1H), 4.91 (br s, 1H), 4.78 (s, 1H), 4.55 (dd, *J* = 1.2 Hz, *J* = 5.8 Hz, 2H), 4.05 (br s, 1H), 2.73 (m, 1H), 1.44 (s, 9H, Boc); ¹³C NMR (125 MHz, CDCl₃) δ: 170.0, 155.3, 135.5, 135.3, 131.7, 118.6, 85.3, 79.8, 78.6, 65.5, 54.4, 52.3, 28.3; HRMS: Calcd for C₁₅H₂₁NO₅Na: 318.1317. Found: 318.1329.

Bis-allylated metathesis substrate 5: To a solution of allyl ester **4** (1.28 g, 4.33 mmol) and allyl bromide (0.45 mL, 5.20 mmol) in DMF (43 mL) was added NaH (95%, dry) (153 mg, 6.07 mmol). The reaction was stirred for 1.5 hours at room temperature, at which time the mixture was poured into pH 7 buffer and Et₂O. The layers were separated and the aqueous layer was extracted with three portions of Et₂O. The combined organic extracts were washed with brine, dried over Na₂SO₄, filtered and concentrated. Silica gel chromatography (20% Et₂O/petroleum ether) afforded metathesis substrate **5** as a colorless oil (1.04 g, 72%): ¹H NMR (500 MHz, CDCl₃): δ 6.43 (dd, *J* = 1.9, 5.8 Hz, 1H), 6.34 (dd, *J* = 1.3, 5.8 Hz, 1H), 5.82 (ddt, *J* = 5.6, 5.6, 10.5, 17.2 Hz, 2H), 5.26 (ddd, *J* = 1.5, 3.0, 17.2 Hz, 1H), 5.17 (br ddd, *J* = 1.1, 10.5 Hz, 1H), 5.09 (ddd, *J* = 1.7, 3.3, 17.2 Hz, 1H), 5.07-5.04 (m, 2H), 4.81 (br s, 1H), 4.50 (dt, *J* = 1.4, 1.4, 5.6 Hz, 2H), 3.91 (br s, 2H), 2.90 (t, *J* = 4.2 Hz, 1H), 1.39 (s, 9H); ¹³C NMR (125 MHz, CDCl₃): δ 170.7, 155.4, 135.8, 135.6, 135.5, 131.8, 118.2, 115.1, 83.8, 80.0, 78.4, 65.3, 59.1, 47.9, 44.8, 28.2; FTIR (thin film): 2978, 1739, 1694, 1647, 1454, 1366, 1172 cm⁻¹. Exact mass calculated for (C₁₈H₂₅O₅N + Na)⁺ (ESI) 358.1630, found 358.1647.

Tricyclic lactone 9: A solution of metathesis substrate **5** (100 mg, 0.298 mmol) in DCM (600 mL) was degassed by passing a stream of argon through the stirring solution for 20 minutes. The stream of argon was replaced with ethylene, and after 5 minutes, Tricyclohexylphosphine[1,3-bis(2,4,6-trimethylphenyl)-4,5-dihydroimidazol-2-ylidene][benzylidene]ruthenium(IV)dichloride **6** (75 mg, 0.089 mmol) was added and the solution was stirred at room temperature. The conversion of starting material to a spot high in R_f was observed by TLC (50% Et₂O/petroleum ether, KMnO₄ stain) to occur over the course of 45 minutes. At this time, ethylene was allowed to evolve from the reaction mixture, aided by purging of the solution with a stream of argon for 45 minutes. Over this period, the initial new high R_f spot was converted to a lower one, which was still higher than the starting material spot. Following this transformation, the flask was fitted with a reflux condenser and the solution was heated at reflux under an argon atmosphere for a further 2 hours, following the TLC to conversion to another spot of lower R_f than the starting material. The reaction mixture was cooled to room temperature and ethyl vinyl ether (13 mL) was added. This solution was allowed to stir overnight. The reaction mixture was concentrated and the residue was purified by silica gel chromatography (50% Et₂O/petroleum ether) to afford the tricyclic product **9** (46 mg, 50%): ¹H NMR (500 MHz, CDCl₃): δ 6.18 (d, *J* = 10.3 Hz, 1H), 6.14-6.04 (m, 2H), 5.74 (br s, 1H), 5.08 (m, 1H), 4.59 (m, 2H), 4.38 (dd, *J* = 6.5, 12.0 Hz, 1H), 4.20 (dd, *J* = 2.7, 19.0 Hz, 1H), 4.07 (d, *J* = 8.7 Hz, 1H), 3.85 (dd, *J* = 2.7, 19.0 Hz, 1H), 3.57 (t, *J* = 9.7 Hz, 1H), 1.42 (s, 9H); ¹³C NMR (125 MHz, C₆D₆, 70 °C): δ 170.7, 154.5, 137.9, 127.2, 126.6, 125.8, 80.3 (br), 77.1, 77.0, 63.1, 61.2, 52.0, 48.3, 28.4; FTIR (thin film): 2975, 2927, 2850, 1740, 1694, 1645, 1435, 1394, 1368, 1177, 1148 cm⁻¹. Exact mass calculated for (C₁₆H₂₁O₅N + Na)⁺ (ESI) 330.1317, found 330.1309. Fully opened intermediate **7** (rotamers): ¹H NMR (500 MHz, CDCl₃): δ 5.90-5.80 (m, 2H), 5.74 (ddd, *J* = 7.0, 10.4, 17.3 Hz, 1H), 5.71-5.65 (m, 1H), 5.10-5.02 (m, 2H); Six-membered ring closed intermediate **8**: ¹H NMR (500 MHz, CDCl₃): δ 6.10 (d, *J* = 10.3 Hz, 1H), 5.92-5.84 (m, 1H), 5.74 (ddd, *J* = 7.8, 10.2, 17.3 Hz, 1H), 5.68 (d, *J* = 8.5 Hz, 1H), 5.35-5.26 (m, 2H), 5.22-5.16 (m, 2H), 4.82 (dd, *J* = 8.0, 9.8 Hz, 1H), 4.59-4.54 (m, 2H), 4.17 (br d, *J* = 17.3 Hz, 1H), 4.12-4.08 (m, 1H), 4.01 (t, *J* = 10.5 Hz, 1H), 3.76 (dq, *J* = 2.7, 2.7, 18.8 Hz, 1H), 3.45 (dd, *J* = 9.2, 11.5 Hz, 1H), 1.40 (s, 9H); ¹³C NMR (125 MHz, CDCl₃): δ 170.3, 154.2, 134.6, 126.6, 125.9, 118.9, 118.3, 80.9, 77.3, 65.4, 60.0, 50.9, 47.2, 28.3.

Tricyclic amino-lactone 9.1: To a solution of Boc-protected tricycle **9** (46 mg, 0.15 mmol) in DCM (10 mL) at 0 °C was added TFA (10 mL). The solution was allowed to slowly warm to room temperature over the course of 1 hour. Solvent was removed *en vacuo* and the residue was dissolved in DCM (10 mL). 1N aq. KHCO_3 (10 mL) was added and the neutralization step was allowed to stir for 45 minutes. Solid NaCl was added to saturate the aqueous layer, which was then extracted with CHCl_3 three times. The combined organic extracts were dried over Na_2SO_4 , filtered and concentrated to afford the secondary amine **9.1** (31 mg, 99%), which crystallized to afford a sample suitable for X-ray crystallographic analysis: m.pt. 124 °C (dec.) ^1H NMR (500 MHz, CDCl_3): δ 6.20 (ddd, $J = 1.7, 3.6, 10.2$ Hz, 1H), 6.14-6.00 (m, 2H), 5.72 (ddd, $J = 2.5, 5.9, 10.2$ Hz, 1H), 5.16 (dt, $J = 2.6, 2.7, 10.9$ Hz, 1H), 4.57 (dd, $J = 7.8, 12.5$ Hz, 1H), 4.37 (ddd, $J = 1.6, 7.0, 12.7$ Hz, 1H), 3.98-3.94 (m, 1H), 3.75 (ddd, $J = 2.8, 6.1, 17.6$ Hz, 1H), 3.52 (ddd, $J = 2.7, 5.7, 17.6$ Hz, 1H), 3.25 (t, $J = 10.8$ Hz, 1H), 3.13 (dd, $J = 8.8, 10.5$ Hz, 1H), 2.10 (br s, 1H); ^{13}C NMR (125 MHz, CDCl_3): δ 172.2, 140.0, 128.8, 125.48, 125.45, 77.0, 75.3, 62.3, 61.8, 54.1, 47.3; FTIR (thin film): 3320 (br), 2918, 2849, 1724, 1451, 1436, 1394, 1364, 1332, 1254, 1234, 1212, 1171, 1129, 1105, 1084, 1062, 1028, 1006, 957, 912, 793 cm^{-1} . Exact mass calculated for $(\text{C}_{11}\text{H}_{13}\text{O}_3\text{N} + \text{H})^+$ (ESI) 208.0974, found 208.0974.

Allyl carbamate 10: To a solution of ester **3** (231 mg, 0.858 mmol) and allyl bromide (90 μL , 1.01 mmol) in DMF (8.5 mL) was added NaH (95%, dry) (27 mg, 1.05 mmol). Upon completion of the reaction (1.5 hours), the reaction was poured into Et_2O and pH 7 buffer. The aqueous layer was extracted with a further three portions of Et_2O . The combined organic extracts were washed with brine, dried over Na_2SO_4 , filtered and concentrated. The product was purified by silica gel chromatography (20-50% Et_2O /petroleum ether) to afford allyl carbamate **10** as a colorless oil (234 mg, 88%): ^1H NMR (500 MHz, CDCl_3): δ 6.43 (dd, $J = 1.9, 5.8$ Hz, 1H), 6.33 (dd, $J = 1.4, 5.8$ Hz, 1H), 5.82 (dddd, $J = 4.5, 7.4, 9.2, 15.3$ Hz, 1H), 5.10 (dq, $J = 1.7, 1.7, 17.2$ Hz, 1H), 5.06 (dq, $J = 1.7, 1.7, 10.4$ Hz, 1H), 5.05-5.03 (m, 1H), 4.80 (s, 1H), 4.66-4.30 (br s, 1H), 3.95-3.85 (m, 2H), 3.61 (s, 3H), 2.87 (t, $J = 4.2$ Hz, 1H), 1.39 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3): δ 177.2, 160.1, 139.4, 139.1, 139.0, 117.4, 84.1 (br), 80.2, 78.5, 57.9 (br), 50.3, 45.9, 42.8, 25.3; FTIR (thin film): 3083, 3006, 2978, 1744, 1694, 1645, 1436, 1407, 1392, 1366, 1313, 1273, 1245, 1225, 1171, 1093, 1048, 1006, 974, 906, 886, 861, 827, 798 cm^{-1} . Exact mass calculated for $(\text{C}_{16}\text{H}_{23}\text{O}_5\text{N} + \text{H})^+$ (CI) 310.1654, found 310.1660.

Acid 11: To a solution of methyl ester **10** (210 mg, 0.68 mmol) in MeOH (5 mL) and water (5 mL) was added LiOH-H₂O (43 mg, 1.02 mmol). The mixture was stirred for 2 hours until TLC indicated consumption of the ester starting material. Methanol was removed *en vacuo*, and the aqueous mixture was acidified to pH 5 by the addition of c.HCl. Solid NaCl was added to saturation, and the acid product was extracted with three portions of 10% isopropanol/CHCl₃. The organic extracts were dried over Na₂SO₄, filtered and concentrated to afford the crude acid **11**, of sufficient purity to be used in further reactions (200 mg, quant.): ¹H NMR (500 MHz, CDCl₃): δ 6.45 (d, *J* = 5.0 Hz, 1H), 6.28 (d, *J* = 5.0 Hz, 1H), 5.59 (dddd, *J* = 4.8, 7.6, 9.2, 15.5 Hz, 1H), 5.12-5.03 (m, 3H), 4.81 (s, 1H), 4.28 (br d, *J* = 2.6 Hz, 1H), 3.91 (br d, *J* = 4.7 Hz, 2H), 2.73 (s, 1H), 1.40 (s, 9H); ¹³C NMR (125 MHz, CDCl₃): δ 172.4, 158.3, 139.9, 134.8, 133.4, 115.6, 82.4, 80.7, 77.7, 59.0, 55.4, 45.1, 28.1; FTIR (thin film): 3620-2420 (br), 2976, 2932, 1738, 1694, 1625, 1476, 1455, 1411, 1368, 1338, 1314, 1275, 1247, 1228, 1169, 1032, 993, 974, 907, 861 cm⁻¹. Exact mass calculated for (C₁₅H₂₁O₅N + H)⁺ (CI) 296.1498, found 296.1494.

Lactam metathesis substrate 12: To a solution of acid **11** (95 mg, 0.322 mmol) and allyl benzyl amine (52 mg, 0.354 mmol) in DCM (3.2 mL) was added EDCI (68 mg, 0.354 mmol). The reaction mixture was stirred for 14 hours at room temperature. The mixture was diluted with DCM, washed with water, and the aqueous layer extracted again with DCM. The combined organic extracts were washed with brine, dried over Na₂SO₄, filtered and concentrated. The residue was purified by silica gel chromatography (30% Et₂O/petroleum ether) to afford metathesis substrate **12** as a colorless oil (75 mg, 55%) (rotamers): ¹H NMR (500 MHz, CDCl₃): δ 7.34-7.09 (m, 5H), 6.44-6.42 (m, 2H), 5.86 (dddd, *J* = 5.1, 5.1, 10.6, 16.7 Hz, 0.67H), 5.70 (dddd, *J* = 4.7, 5.1, 10.3, 16.8 Hz, 1.33H), 5.23-4.80 (m, 6H), 4.64-4.37 (m, 3H), 4.14-3.72 (m, 4H), 3.00 (t, *J* = 4.1 Hz, 1H), 1.43 (s, 3H), 1.38 (s, 6H); ¹³C NMR (125 MHz, CDCl₃): δ 170.7, 155.4, 137.3, 136.6, 136.2 (br), 135.6, 135.4, 133.7 (br), 133.0, 132.6, 128.9, 128.5, 127.9, 127.6, 127.2, 126.1, 117.2 (br), 117.0, 115.7, 83.3, 80.1, 79.2, 79.1, 60.8, 49.6, 48.7, 48.3, 48.1, 46.4, 46.2, 44.9, 44.8, 28.3, 28.2; FTIR (thin film): 3084, 2978, 2930, 1693, 1650, 1496, 1454, 1404, 1365, 1331, 1271, 1244, 1209, 1170, 11473, 1081, 1051, 991, 924, 888, 861, 827, 774 cm⁻¹. Exact mass calculated for (C₂₅H₃₂O₄N₂ + Na)⁺ (ESI) 425.2440, found 425.2435.

Tricyclic lactam 13: A solution of metathesis substrate **12** (10 mg, 0.0236 mmol) in DCM (47 mL) was degassed by passing a stream of argon through the stirring solution for 20 minutes. The stream of argon was replaced with ethylene, and after 5 minutes, Tricyclohexylphosphine[1,3-bis(2,4,6-trimethylphenyl)-4,5-dihydroimidazol-2-ylidene][benzylidene]ruthenium(IV)dichloride **6** (6 mg, 0.007 mmol) was added. The solution was stirred at room temperature, monitoring the conversion of starting material to a spot high in *R_f* by TLC (50% Et₂O/petroleum ether, KMnO₄ stain). This was complete after 1 hour. Ethylene was allowed to evolve from the mixture, assisted by a stream of argon bubbled through the solution for 2.5 h. The solution was then stirred under an atmosphere of argon for a further 24 h, over which time the initial high *R_f* product was converted to one with an *R_f* similar to but slightly higher than that of the initial

starting material (50% Et₂O/petroleum ether, KMnO₄ stain). Ethyl vinyl ether (0.5 mL) was added to the reaction, and the solution was allowed to stir overnight. The reaction mixture was concentrated and the residue was purified by silica gel chromatography (30% Et₂O/petroleum ether) to afford tricyclic lactam **13** (9 mg, 95%) as a white solid, from which crystals were obtained suitable for X-ray analysis: m.pt. 124°C; [α]_D = -181° (*c* = 1.5 x 10⁻³, MeOH) (rotation = -0.272° in [3 mg/2 mL MeOH]); ¹H NMR (500 MHz, CDCl₃): δ 7.30-7.23 (m, 5H), 6.10 (br d, *J* = 9.8 Hz, 1H), 5.81 (br d, *J* = 10.2 Hz, 1H), 5.73 (br s, 1H), 5.67 (dddd, *J* = 3.1, 7.3, 7.3, 10.3 Hz, 1H), 4.96 (br d, *J* = 10.9 Hz, 1H), 4.90-4.72 (br s, 1H), 4.70 (br d, *J* = 14.5 Hz, 1H), 4.47 (br d, *J* = 13.7 Hz, 1H), 4.26 (br dd, *J* = 2.0, 18.7 Hz, 1H), 4.11-4.07 (br s, 1H), 3.87 (br d, *J* = 18.0 Hz, 2H), 3.70 (t, *J* = 9.7 Hz, 1H), 3.26 (br s, 1H), 1.40 (s, 9H); ¹³C NMR (125 MHz, CDCl₃): δ 175.9, 159.1, 141.3, 137.4, 131.9, 131.5, 131.1, 130.53, 130.48, 129.6, 80.3, 75.6, 61.8, 49.5, 48.8, 46.6, 40.9, 25.4; FTIR (thin film): 3309, 3044, 2975, 2927, 2849, 2249, 1692, 1659, 1650, 1644, 1495, 1476, 1442, 1368, 1347, 1332, 1280, 1231, 1148, 1118, 1080, 1019, 968, 911 cm⁻¹. Exact mass calculated for (C₂₃H₂₈O₄N₂)⁺ (CI) 396.2049, found 396.2059.

Benzyl carbamate 19: To a solution of allyl ester **4** (500 mg, 1.7 mmol) in DMF (17 mL) was added benzyl bromide (0.3 mL, 2.54 mmol) and then NaH (95%, dry) (64 mg, 2.54 mmol). This was stirred for 30 minutes at room temperature. The solution was then poured into Et₂O and saturated aq. NH₄Cl. The aqueous layer was extracted three times with Et₂O, and the combined organic extracts were washed with brine and dried over Na₂SO₄. Following filtration and evaporation of solvent, the residue was purified by silica gel chromatography (15% EtOAc/petroleum ether) to afford benzyl carbamate **19** (510 mg, 78%): ¹H NMR (500 MHz, CDCl₃): δ 7.40-7.10 (m, 5H), 6.50-6.25 (m, 2H), 5.86 (ddt, *J* = 5.7, 5.7, 10.5, 17.2 Hz, 1H), 5.29 (ddd, *J* = 1.4, 2.9, 17.2 Hz, 1H), 5.21 (dd, *J* = 1.0, 10.5 Hz, 1H), 5.10 (d, *J* = 12.3 Hz, 1H), 5.06 – 5.01 (m, 2H), 4.75-4.52 (m, 4H), 2.87 (t, *J* = 4.2 Hz, 1H), 1.38 (br s, 9H); ¹H NMR (500 MHz, C₆D₆, 70 °C): 7.32 (d, *J* = 7.5 Hz, 2H), 7.17 (t, *J* = 7.5 Hz, 2H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.17 (d, *J* = 5.1 Hz, 1H), 5.98 (dddd, *J* = 5.6, 5.6, 10.1, 17.2 Hz, 1H), 5.10 (dd, *J* = 1.4, 17.2 Hz, 1H), 4.98 (dd, *J* = 0.9, 10.1 Hz, 1H), 4.81 (br s, 1H), 4.78 (d, *J* = 4.6 Hz, 1H), 4.69 (d, *J* = 16.5 Hz, 1H), 4.59 (s, 1H), 4.57 (d, *J* = 16.0 Hz, 1H), 4.39-4.34 (m, 2H), 2.86 (t, *J* = 4.2 Hz, 1H), 1.39 (s, 9H); ¹³C NMR (125 MHz, C₆D₆, 70 °C): δ 170.6, 156.1, 140.8, 136.1, 135.7, 132.7, 128.6, 127.0, 126.9, 117.7, 83.9, 80.0, 78.8, 65.1, 60.4, 48.7, 46.5, 28.4; FTIR (thin film): 3005, 2977, 2932, 1738, 1694, 1649, 1496, 1454, 1411, 1392, 1366, 1345, 1313, 1274, 1166, 1121, 1076, 991, 908, 862 cm⁻¹. Exact mass calculated for (C₂₂H₂₇O₅N + Na)⁺ (ESI) 408.1787, found 408.1787.

Benzylamine 15: To a solution of Boc-protected secondary amine **19** (50 mg, 0.13 mmol) in DCM (5 mL) at 0 °C was added TFA (5 mL). The solution was allowed to slowly warm to room temperature over the course of 1 hour. Solvent was removed *en vacuo* and the residue dissolved in DCM (5 mL). 1N aq.

KHCO₃ (5 mL) was added and the neutralization step was allowed to stir for 45 minutes. Solid NaCl was added to saturate the aqueous layer, which was extracted with CHCl₃ three times. The combined organic extracts were dried over Na₂SO₄, filtered and concentrated to afford the secondary amine **15** (21 mg, 56%): ¹H NMR (500 MHz, CDCl₃): δ 7.37-7.21 (m, 5H), 6.39 (dd, *J* = 1.3, 5.9 Hz, 1H), 6.36 (dt, *J* = 1.1, 1.1, 5.8 Hz, 1H), 5.87 (dddd, *J* = 5.8, 5.8, 10.6, 17.2 Hz, 1H), 5.23 (dt, *J* = 1.0, 1.1, 10.4 Hz, 1H), 5.11 (d, *J* = 4.7 Hz, 1H), 4.81 (s, 1H), 4.56-4.51 (m, 2H), 3.87 (m, 2H), 3.18 (d, *J* = 2.9 Hz, 1H), 2.78 (dd, *J* = 3.4, 4.6 Hz, 1H), 1.63 (br s, 1H); ¹³C NMR (125 MHz, CDCl₃): δ 171.0, 139.8, 135.5, 135.4, 131.9, 128.4, 128.0, 127.0, 118.5, 83.6, 78.5, 65.3, 62.2, 52.6, 52.1; FTIR (thin film): 3316, 3084, 3062, 3026, 3006, 2928, 1732, 1647, 604, 1496, 1454, 1364, 1312, 1280, 1193, 1118, 993, 905, 867, 736, 700 cm⁻¹. Exact mass calculated for (C₁₇H₁₉O₃N + H)⁺ (ESI) 286.1443, found 286.1435.

Dimeric tertiary amide 16: Allyl ester **19** (51 mg, 0.132 mmol) was dissolved in DCM (5 mL) and cooled to 0 °C. Following the addition of TFA (5 mL), the reaction was allowed to stir for 1 hour with gradual warming to room temperature. The solvents were removed *en vacuo* and the crude amine salt was reconstituted in DCM (2 mL) and DIPEA (0.115 mL) was added. During this time, the acid **11** (39 mg, 0.132 mmol) was dissolved in DCM (2 mL) and cooled to 0°C. Oxalyl chloride (2.0 M/DCM, 75 μL, 0.145 mmol) was then added, followed by a drop of DMF. The acid chloride formation was allowed to proceed for 1 hour, gradually reaching room temperature. Solvent and excess reagents were removed *en vacuo*. The crude acid chloride was reconstituted in DCM (2 mL) and added to the 0°C solution of the crude amine salt containing DIPEA. The acylation reaction was allowed to stir for 1 hour, with warming to room temperature. The reaction mixture was diluted with DCM, washed with water, 0.1M aq. HCl, another portion of water, and the organic layer was dried over Na₂SO₄. The solution was filtered and concentrated, and the residue was purified by silica gel chromatography (15-40% EtOAc/petroleum ether) to afford dimeric metathesis substrate **16** as a colorless oil (29 mg, 39%): ¹H NMR (500 MHz, CDCl₃): δ 7.50-7.10 (m, 5H), 6.70-2.80 (m, 24H), 1.51, 1.48 (2 singlets, total 9H) rotamers, see attached spectrum; ¹³C NMR (125 MHz, CDCl₃) also rotamers, see attached spectrum: δ 172.3, 171.8, 171.7, 170.6, 170.4, 155.7, 155.3, 138.6, 138.5, 137.2, 136.6, 136.5, 136.4, 136.1, 135.7, 135.4, 135.3, 135.0, 133.0, 132.9, 131.8, 131.3, 129.1, 128.8, 128.6, 128.5, 128.4, 128.3, 128.0, 127.5, 126.7, 126.5, 126.4, 125.2, 119.5, 118.3, 116.0, 115.5, 83.9, 83.6, 83.4, 83.0, 80.7, 80.4, 80.1, 79.5, 79.4, 79.1, 78.5, 78.4, 67.2, 66.5, 65.9, 65.4, 61.5, 60.5, 58.1, 48.1, 48.0, 46.9, 46.9, 46.5, 45.23, 45.19, 45.0, 44.8, 44.6, 28.4, 28.3; FTIR (thin film): 3086, 3004, 2976, 2932, 1733, 1688, 1652, 1558, 1540, 1496, 1454, 1419, 1403, 1365, 1337, 1315, 1293, 1275, 1254, 1198, 1166, 1016, 992, 907, 863, 725, 698 cm⁻¹. Exact mass calculated for (C₃₂H₃₈O₇N₂ + Na)⁺ (ESI) 585.2577, found 585.2584.

Tetracyclic tertiary amide 17: A solution of dimeric metathesis substrate **16** (29 mg, 0.0515 mmol) in DCM (100 mL) was degassed by passing a stream of argon through the stirring solution for 30 minutes. The stream of argon was replaced with ethylene, and after 5 minutes, Tricyclohexylphosphine[1,3-bis(2,4,6-trimethylphenyl)-4,5-dihydroimidazol-2-ylidene][benzylidene]ruthenium(IV)dichloride **6** (13 mg, 0.015 mmol) was added. The solution was stirred at room temperature for 2 hours, at which time the stream of ethylene was replaced with a stream of argon. Ethylene was allowed to evolve from the reaction mixture in this manner over 2 hours, at which time the flask was fitted with a reflux condenser and the solution heated to reflux for 20 hours. Upon cooling to room temperature, ethyl vinyl ether (2.25 mL) was added. The solution was allowed to stir for a further 48 hours. The reaction mixture was concentrated and purified by silica gel chromatography (50% Et₂O/petroleum ether) to afford tetracycle **17** (2 mg, 7%): ¹H NMR (500 MHz, CDCl₃): δ 7.53-7.49 (m, 2H), 7.31-7.24 (m, 3H), 6.15 (dd, *J* = 1.3, 10.6 Hz, 1H), 6.10 (dd, *J* = 0.9, 10.1 Hz, 1H), 6.04 (dddd, *J* = 3.1, 7.0, 7.0, 10.2 Hz, 1H), 5.79-5.70 (m, 1H), 5.68-5.64 (m, 1H), 5.35-5.30 (m, 2H), 5.30-5.26 (m, 2H), 5.09 (d, *J* = 5.5 Hz, 1H), 5.06 (s, 1H), 4.84 (dd, *J* = 4.8, 7.4 Hz, 1H), 4.74-4.70 (m, 1H), 4.66-4.60 (m, 2H), 4.41 (t, *J* = 9.2 Hz, 1H), 4.37-4.24 (m, 4H), 4.14-4.08 (m, 2H), 4.06 (dd, *J* = 4.8, 9.0 Hz, 1H), 3.82 (dq, *J* = 3.2, 3.2, 3.2, 18.6 Hz, 1H), 3.63 (dd, *J* = 8.9, 10.7 Hz, 1H), 1.47 (s, 9H); ¹³C NMR (125 MHz, CDCl₃): δ 172.8, 171.7, 154.3, 137.2, 136.7, 135.6, 135.0, 129.4, 128.5, 128.0, 126.7, 125.5, 124.9, 118.8, 118.5, 81.4, 80.0, 78.3, 77.4, 75.4, 68.6, 61.5, 60.1, 54.6, 51.4, 49.2, 47.2, 28.4; FTIR (thin film): 2954, 2925, 2853, 1732, 1700, 1644, 1472, 1456, 1447, 1419, 1400, 1368, 1348, 1298, 1255, 1236, 1217, 1161, 1117, 1106, 1078, 1043, 996, 930, 914 cm⁻¹. Exact mass calculated for (C₃₂H₃₈O₇N₂ + Na)⁺ (ESI) 585.2577, found 585.2568.

Bicyclic ester 21: A solution of allyl carbamate **10** (195 mg, 0.646 mmol) in DCM (1.0 L) was degassed by passing a stream of argon through the stirring solution for 20 minutes. The stream of argon was replaced with ethylene, and after 5 minutes, Tricyclohexylphosphine[1,3-bis(2,4,6-trimethylphenyl)-4,5-dihydroimidazol-2-ylidene][benzylidene]ruthenium(IV)dichloride **6** (28 mg, 0.032 mmol) was added and the solution was stirred at room temperature for 3 h. Conversion of the starting material to a spot high in *R_f* was evidenced by TLC analysis (50% Et₂O/petroleum ether, KMnO₄ stain). The stream of ethylene was replaced with a stream of argon to purge the solution of ethylene for 2 h, then the solution was stirred under an atmosphere of argon overnight. The reaction was incomplete, so a further portion of catalyst was added (18 mg) and stirring was continued for 5 hours, with argon bubbling through the solution. This served to complete the transformation, at which time the initial high *R_f* product was converted to one with an *R_f* similar to but slightly higher than that of the initial starting material. Ethyl vinyl ether (28 mL) was then added and the solution was allowed to stir overnight. The reaction mixture was concentrated and purified by silica gel chromatography (20% EtOAc/petroleum ether) to afford ester **21** as an oil (191 mg, 98%): ¹H NMR (500 MHz, CDCl₃): δ 6.04 (d, *J* = 10.2 Hz, 1H), 5.68 (ddd, *J* = 7.8, 10.2, 17.6 Hz, 1H), 5.63 (m, 1H), 5.25 (dd, *J* = 1.0, 17.0 Hz, 1H), 5.13 (dd, *J* = 0.7, 10.3 Hz, 1H), 4.76 (dd, *J* = 8.1, 9.8 Hz, 1H), 4.16-4.07 (br m, 1H), 4.06-4.02 (m, 1H), 3.94 (dd, *J* = 10.7, 11.1 Hz, 1H), 3.71 (dq, *J* = 2.8, 2.8, 2.8, 18.7 Hz, 1H), 3.61 (s, 3H), 3.40 (dd, *J* = 9.1, 11.5 Hz, 1H), 1.36 (s, 9H); ¹³C NMR (125 MHz, CDCl₃): δ 171.0, 154.2, 134.6, 126.5, 125.9, 118.7, 80.8, 77.3, 62.2, 60.0, 51.6, 51.0, 47.2, 28.3; FTIR (thin film): 2977, 2952, 2928, 2851, 1741, 1700, 1652, 1646, 1606, 1594, 1558, 1540, 1504, 1473, 1438, 1382, 1366,

1329, 1299, 1236, 1219, 1156, 1120, 1075, 1045, 987, 962, 933, 858, 814, 755 cm^{-1} . Exact mass calculated for $(\text{C}_{16}\text{H}_{23}\text{O}_5\text{N} + \text{Na})^+$ (ESI) 332.1474, found 332.1479.

Bicyclic acid 22: To a solution of bicyclic ester **21** (162 mg, 0.548 mmol) in dioxane (5 mL) and water (5 mL) was added LiOH-H₂O (70 mg, 1.64 mmol) and the solution was stirred at room temperature for 2.5 h. The reaction mixture was poured into saturated aq. NH₄Cl and then c.HCl was added to achieve pH 5. This was then extracted with three portions of EtOAc. The combined organic extracts were washed with water, brine, dried over Na₂SO₄, filtered and concentrated to afford the acid **22** (126 mg, 82%), used crude in further transformations: ¹H NMR (500 MHz, CDCl₃): δ 6.10 (d, J = 10.3 Hz, 1H), 5.79 (ddd, J = 7.6, 10.3, 17.3 Hz, 1H), 5.68 (d, J = 9.7 Hz, 1H), 5.33 (d, J = 17.1 Hz, 1H), 5.17 (d, J = 10.4 Hz, 1H), 4.83 (dd, J = 8.0, 9.7 Hz, 1H), 4.15 (d, J = 18.3 Hz, 1H), 4.12-4.07 (m, 1H), 3.96 (t, J = 10.9 Hz, 1H), 3.75 (dq, J = 2.7, 2.7, 2.7, 18.8 Hz, 1H), 3.38 (dd, J = 9.1, 11.5 Hz, 1H), 1.41 (s, 9H); ¹³C NMR (125 MHz, CDCl₃): δ 175.3, 154.5, 134.2, 126.6, 125.7, 119.0, 80.8, 77.4, 67.0, 60.0, 51.1, 47.2, 28.4; FTIR (thin film): 3386-2900 (br), 2977, 2929, 2905, 1738, 1704, 1644, 1478, 1446, 1369, 1346, 1300, 1249, 1220, 1154, 1118, 1075, 1042, 1001, 985, 968, 929, 912, 857 cm^{-1} . Exact mass calculated for $(\text{C}_{15}\text{H}_{21}\text{O}_5\text{N} + \text{Na})^+$ (ESI) 318.1317, found 318.1332.

Benzylated bicyclic lactone 19.1: A solution of allyl ester **19** (53 mg, 0.137 mmol) in DCM (275 mL) was degassed by passing a stream of argon through the stirring solution for 20 minutes. The stream of argon was replaced with ethylene, and after 5 minutes, Tricyclohexylphosphine[1,3-bis(2,4,6-trimethylphenyl)-4,5-dihydroimidazol-2-ylidene][benzylidene]ruthenium(IV)dichloride **6** (35 mg, 0.041 mmol) was added. The solution was stirred at room temperature for 1 h, at which time the stream of ethylene was replaced with a stream of argon. Ethylene was allowed to evolve in this manner for 2 hours. The flask was then fitted with a reflux condenser and the solution heated to reflux for 4 hours. The solution was cooled to room temperature, and ethyl vinyl ether (5 mL) was added. This solution was allowed to stir overnight. The reaction mixture was concentrated and purified by silica gel chromatography (15-20% EtOAc/petroleum ether) to afford the bicyclic lactone **19.1** (30 mg, 57%): ¹H NMR (500 MHz, CDCl₃): δ 7.27-7.21 (m, 5H), 6.12 (d, J = 10.6 Hz, 1H), 6.04 (ddt, J = 3.0, 6.8, 6.8, 10.2 Hz, 1H), 5.44 (ddd, J = 8.1, 8.1, 17.1 Hz, 1H), 5.20 (br s, 1H), 5.14 (d, J = 17.1 Hz, 1H), 4.94 (d, J = 10.2 Hz, 1H), 4.65 (br s, 1H), 4.50 (br s, 2H), 4.32 (d, J = 13.7 Hz, 1H), 4.36-4.26 (br s, 1H), 4.36-4.26 (dd, J = 7.3, 13.2 Hz, 1H), 4.06-3.80 (br s, 1H), 1.48 (s, 9H); ¹H NMR (500 MHz, C₆D₆, 70 °C): δ 7.30 (d, J = 7.5 Hz, 2H), 7.12 (t, J = 7.5 Hz, 2H), 7.04 (t, J = 7.5 Hz, 1H), 5.94 (d, J = 10.6 Hz, 1H), 5.62 (ddd, J = 6.0, 10.3, 17.0 Hz, 1H), 5.39 (ddt, J = 3.0, 6.6, 6.6, 10.4 Hz, 1H), 5.17 (d, J = 17.0 Hz, 1H), 5.21-5.12 (br m, 1H), 4.84 (d, J = 10.4 Hz, 1H), 4.72 (br s, 2H), 4.48 (d, J = 15.2 Hz, 1H), 4.37 (d, J = 15.2 Hz, 1H), 3.86 (dd, J = 5.7, 13.3 Hz, 1H), 3.90-3.80 (br s, 1H), 3.53 (dd, J = 7.4, 13.3 Hz, 1H), 1.37 (s, 9H); ¹³C

NMR (125 MHz, CDCl_3): δ 171.9, 155.1, 138.3, 136.6, 135.1, 128.4, 128.2, 127.5, 125.2, 118.8, 80.9, 79.7, 75.5, 68.1, 61.4, 54.7, 52.1, 28.5; ^{13}C NMR (125 MHz, C_6D_6 , 70 °C): δ 171.3, 155.4, 139.2, 136.7, 136.5, 128.7, 128.6, 127.6, 125.5, 117.4, 80.5, 80.3, 76.1, 69.0, 60.8, 54.7, 53.0, 28.5; FTIR (thin film): 2976, 2929, 1736, 1688, 1496, 1466, 1455, 1429, 1368, 1320, 1281, 1248, 1163, 1125, 1062, 1042, 1029, 1000, 928, 904, 794, 701, 668 cm^{-1} . Exact mass calculated for $(\text{C}_{22}\text{H}_{27}\text{O}_5\text{N} + \text{H})^+$ (CI) 386.1967, found 386.1950.

Bicyclic benzylamine 20: To a solution of Boc-protected secondary amine **19.1** (10 mg, 0.026 mmol) in DCM (3.5 mL) at 0 °C was added TFA (3 mL). The solution was allowed to slowly warm to room temperature and stirring was continued until TLC analysis indicated complete consumption of starting material (1 hour). The solvent was removed *en vacuo* and the residue dissolved in DCM (3 mL). 1N aq. KHCO_3 (3 mL) was added and the neutralization reaction was allowed to stir for 45 minutes. Solid NaCl was added to saturate the aqueous layer, which was extracted with 10% isopropanol/ CHCl_3 three times. The combined organic extracts were dried over Na_2SO_4 , filtered and concentrated. The residue was purified by silica gel chromatography (66% EtOAc/petroleum ether) to afford the secondary amine **20** (6 mg, 81%): ^1H NMR (500 MHz, CDCl_3): δ 7.34-7.23 (m, 5H), 6.17 (d, J = 10.7 Hz, 1H), 6.11-6.05 (m, 1H), 6.00 (ddd, J = 7.7, 10.2, 17.2 Hz, 1H), 5.35 (ddd, J = 0.9, 1.2, 17.1 Hz, 1H), 5.23 (ddd, J = 0.6, 1.3, 10.3 Hz, 1H), 4.69 (dq, J = 2.4, 2.4, 2.4, 7.2 Hz, 1H), 4.63-4.57 (m, 1H), 4.31 (ddd, J = 0.8, 7.4, 13.7 Hz, 1H), 3.99 (dd, J = 2.2, 5.6 Hz, 1H), 3.95 (dd, J = 5.8, 7.6 Hz, 1H), 3.86 (d, J = 13.1 Hz, 1H), 3.76 (d, J = 13.1 Hz, 1H), 3.20 (dd, J = 2.0, 7.2 Hz, 1H), 1.57 (br s, 1H); ^{13}C NMR (125 MHz, CDCl_3): δ 171.2, 139.8, 136.2, 134.8, 128.5, 128.1, 127.3, 126.2, 118.4, 86.2, 75.3, 66.6, 61.4, 53.9, 52.8; FTIR (thin film): 3316, 3028, 2848, 1732, 1682, 1495, 1471, 1454, 1403, 1384, 1276, 1214, 1171, 1100, 1049, 1027, 994, 933, 794, 740, 699 cm^{-1} . Exact mass calculated for $(\text{C}_{17}\text{H}_{19}\text{O}_3\text{N} + \text{H})^+$ (ESI) 286.1443, found 286.1453.

Tetracyclic tertiary amide 17: To a solution of 2-chloro-1-methyl pyridinium iodide (12 mg, 0.0474 mmol) and TEA (13 μL , 0.095 mmol) in DCM (1.2 mL) at 0 °C was added a solution of acid **22** (10 mg, 0.0339) in DCM (0.35 mL) and then a solution of amine **20** (9.7 mg, 0.0339 mL) in DCM (0.38 mL). This mixture was stirred for 30 minutes at 0 °C, and was then allowed to warm to room temperature and stir for a further 24 hours. The reaction mixture was concentrated and purified by silica gel chromatography (40% EtOAc/petroleum ether) to afford the tetracycle **17** (3.5 mg, 18%, 31% yield based on recovery of amine component): the spectral data matched that of the product obtained from the ring-methathesis of **272**.

Alcohol 25.1: A solution of **21** (92 mg, 0.297 mmol) in dry ethyl ether (4 mL) was added to a solution of lithium aluminum hydride (45 mg, 1.19 mmol) in dry ethyl ether (1 mL) at 0°C under inert atmosphere. After 1 hour, ethyl acetate was added and washed with 0.2 M HCl. The aqueous layer was washed with ethyl acetate. The combined organic layers were washed with brine, dried over sodium sulfate, concentrated *in vacuo*. The crude product was chromatographed using 5:1 hexane:ethyl acetate (R_F = 0.23 in 25% ethyl acetate/hexane) to obtain **25.1** as a colorless film (34.9 mg, 42% yield).

Alternative procedure: To a cooled solution (-78° C) of methyl ester **21** (82 mg, 0.267 mmol) in toluene (2mL) was added DIBAL (1.5 M solution in toluene, 0.89 mL, 1.33 mmol). After 10 minutes, the reaction was quenched with Rochelle's salt and allowed to warm up to room temperature and then was extracted with methylene chloride. The combined organic layers were washed with brine, dried over sodium sulfate, filtered and concentrated *in vacuo*. The crude product was chromatographed using 30% ethyl ether/hexane (R_F = 0.27 in 50% EE/Hex) to obtain **25.1** as a colorless film (47 mg, 62% yield).

$[\alpha]_{25}(\text{CH}_2\text{Cl}_2) = -91^\circ$; IR (film, cm^{-1}): 3455, 2975, 2926, 1697, 1476, 1437, 1367, 1344, 1248, 1161, 1036, 927; ^1H NMR (500 MHz, CDCl_3) δ : 6.13 (dd, $J = 1.5$ Hz, $J = 10.2$ Hz, 1H, H_6), 5.87 (m, 1H, H_1), 5.66 (dddd, $J = 10.1$ Hz, $J = J = J = 2.8$ Hz, 1H, H_{10}), 5.35 (d, $J_{1,8} = 17.1$ Hz, 1H, H_8), 5.23 (d, $J_{1,7} = 10.4$ Hz, 1H, H_7), 4.72 (t, $J = 8.2$ Hz, 1H, H_2), 4.31 (d, $J = 18.4$ Hz, 1H, H_{11}), 4.11 (m, 1H, H_5), 3.78 (m, 2H, H_9 and H_{11}), 3.61 (br s, 2H, H_3 and H_9), 2.94 (t, $J = 9.8$ Hz, 1H, H_4), 1.46 (s, 9H, Boc); ^{13}C NMR (125 MHz, CDCl_3) δ : 155.0, 134.8, 127.7, 125.6, 118.1, 82.0, 81.0, 76.8, 63.7, 62.6, 47.6, 44.7, 28.4; HRMS (CI) Calcd for $\text{C}_{15}\text{H}_{23}\text{NO}_4 + \text{H}$: 282.1705. Found: 282.1697.

Aldehyde 25: To a solution of alcohol **25.1** (153.4 mg, 0.545 mmol) and pyridine (88 μL , 1.09 mmol) in methylene chloride at 0° C was added Dess-Martin reagent (300 mg, 0.709 mmol). After 1 hour, more Dess-Martin reagent (46mg, 0.109 mmol) was added. After another hour, the reaction was warmed to room temperature. The reaction mixture was diluted with ethyl ether after 1 hour and extracted with water, saturated sodium bicarbonate, and sodium thiosulfate. The combined aqueous layers were washed with ethyl ether. The combined ether layers were dried over sodium sulfate and concentrated *in vacuo* to give the crude product. Purification by silica gel chromatography (10-20% ethyl ether/hexane, R_F = 0.48 in 50% EE/Hx) afforded aldehyde **25** as a colorless oil (111 mg, 73% yield).

$[\alpha]_{\text{D}}(\text{CH}_2\text{Cl}_2) = -24^\circ$; IR (film, cm^{-1}): 2977, 2843, 1725, 1693, 1411, 1368, 1345, 1240, 1163, 981, 935. ^1H NMR (500 MHz, CDCl_3) δ : 9.68 (d, $J = 2.7$ Hz, 1H), 6.18 (d, $J = 10.2$ Hz, 1H), 5.74 (m, 2H), 5.37 (d, $J = 17.0$ Hz, 1H), 5.24 (d, $J = 10.3$ Hz, 1H), 4.91 (dd, $J = 7.7$ Hz, $J = 10.2$ Hz, 1H), 4.13 (m, 2H), 3.96 (dt,

$J = 2.8$ Hz, $J = 10.7$ Hz, 1H), 3.83 (m, 1H), 3.50 (dd, $J = 11.1$ Hz, $J = 8.9$ Hz, 1H), 1.42 (s, 9H, Boc); ^{13}C NMR (125 MHz, CDCl_3) δ : 199.5, 154.7, 134.5, 126.8, 125.4, 118.6, 80.8, 77.6, 58.4, 56.0, 46.8, 28.2; HRMS (CI) Calcd for $\text{C}_{15}\text{H}_{21}\text{O}_4\text{N}+\text{H}$: 280.1548. Found: 280.1546.

Bicyclic lactone 24.1: Argon was bubbled through a solution of **4** (200 mg, 0.677 mmol) in methylene chloride (500 mL, 1.4 mM). Ethylene was then bubbled through and the Grubb's catalyst **6** (28 mg, 0.0339 mmol, 0.05 eq) was added. After 45 minutes, the ethylene source was removed, argon was bubbled through, the reaction was heated to reflux for 3 hours. More catalyst was added (10 mg, 0.012 mmol, 0.02 eq) and the reaction was refluxed for an additional hour. After the reaction cooled to room temperature, ethyl vinyl ether was added (3mL) and the reaction was allowed to stir overnight. The reaction mixture was concentrated *in vacuo* and purified by silica gel chromatography (5% EE/ CH_2Cl_2 , $R_F = 0.24$) two times to afford **24.1** as a pale brown film (61.6 mg, 31%).

$[\alpha]_D$ (CH_2Cl_2) = -25°

IR (film, cm^{-1}): 3336, 2979, 1732, 1522, 1404, 1367, 1297, 1244, 1170, 1046, 1024, 932, 868, 795, 732; ^1H NMR (500 MHz, d_8 -toluene, quintet = 2.09, 27°C) δ : 5.86 (m, 2H), 5.34 (m, 1H), 5.18 (d, $J = 17.3$ Hz, 1H), 4.98 (d, $J = 10.3$ Hz, 1H), 4.69 (br s, 1H), 4.33 (br s, 1H), 4.29 (br s, 1H), 4.23 (br s, 1H), 3.72 (br s, 1H), 3.44 (br s, 1H), 1.40 (s, 9H, Boc); ^1H NMR (500 MHz, d_8 -toluene, quintet = 2.09 ppm, 80°C) δ : 5.85 (m, 2H), 5.43 (m, 1H), 5.18 (d, $J = 17.3$ Hz, 1H), 4.97 (d, $J = 10.4$ Hz, 1H), 4.58 (br s, 1H), 4.37 (br s, 1H), 4.24 (br s, 1H), 4.08 (br s, 1H), 3.90 (dd, $J = 6.3$ Hz, $J = 13.6$ Hz, 1H), 3.58 (dd, $J = 7.2$ Hz, $J = 13.6$ Hz, 1H), 3.34 (br s, 1H), 1.40 (s, 9H, Boc); ^{13}C NMR (125 MHz, d_8 -toluene, septet = 20.4 ppm) δ : 171.0, 155.5, 137.4, 136.6, 126.4, 117.3, 83.0, 79.4, 75.8, 61.0, 60.1, 53.2, 28.4; HRMS Calcd for $\text{C}_{15}\text{H}_{21}\text{NO}_5+\text{Na}$: 318.1317. Found: 318.1319.

Primary amine 24.2: To a solution of **24.1** (92.6 mg, 0.314 mmol) in methylene chloride (1 mL) was added TFA (1 mL) at room temperature. After 30 minutes, the reaction was concentrated and then basified with 1N KHCO_3 to pH 8. The aqueous layer was extracted several times with ethyl acetate. The combined ethyl acetate layers were dried over sodium sulfate and concentrated. The amine was then dissolved in methanol and treated with activated charcoal to remove the colored impurities. After filtration through celite, the methanol was removed *in vacuo* to afford amine **24.2** as a yellow oil in quantitative yield.

$[\alpha]_D$ (MeOH) = $+5^\circ$

IR (film, cm^{-1}): 3442, 1680, 1554, 1430, 1204, 1182, 1137, 1023; ^1H NMR (500 MHz, CDCl_3) δ : 6.21 (br d, $J = 10.6$ Hz, 1H), 6.11 (m, 1H), 5.95 (ddd, $J = 7.6$ Hz, $J = 10.3$ Hz, $J = 17.9$ Hz, 1H), 5.40 (ddd, $J = 0.9$ Hz, $J = 1.5$ Hz, $J = 17.2$, 1H), 5.29 (ddd, $J = 0.7$ Hz, $J = 1.5$ Hz, $J = 10.3$ Hz, 1H), 4.85 (dddd, $J = J = J = 2.2$ Hz, $J = 8.6$ Hz, 1H), 4.67 (m, 1H), 4.37 (ddd, $J = 1.2$ Hz, $J = 7.3$ Hz, $J = 13.4$ Hz, 1H), 3.94 (dd, $J =$

4.5 Hz, $J = 6.9$ Hz, 1H), 3.85 (m, 1H), 3.22 (dd, $J = 4.5$ Hz, $J = 8.6$ Hz, 1H), 1.67 (br s, 2H, NH_2); ^{13}C NMR (125 MHz, CDCl_3) δ : 171.4, 136.5, 135.5, 125.9, 119.1, 87.1, 74.6, 61.6, 59.7, 57.4; HRMS Calcd for $\text{C}_{10}\text{H}_{13}\text{NO}_3 + \text{H}$: 196.0974. Found: 196.0983.

Tetracyclic secondary amine 26: Sodium triacetoxyborohydride (50 mg, 0.237 mmol) and glacial acetic acid (4 drops from 22G needle) was added to a solution of aldehyde **25** (47 mg, 0.169 mmol) and amine **24** (as the TFA salt, 52 mg, 0.0169 mmol) in methylene chloride (2 mL). After 24 hours, saturated sodium bicarbonate was added and extracted with ethyl acetate several times. The combined organic extracts were dried over Na_2SO_4 , filtered and concentrated. The crude product was purified by silica gel chromatography (50% EtOAc/Hx) to afford secondary amine **26** (70 mg, 90%) as a pale yellow oil.

$[\alpha]_{\text{D}}$ (MeOH) = -56°

IR (film, cm^{-1}): 3354, 2922, 2852, 1735, 1693, 1436, 1366, 1259, 1169, 1140, 1073, 1053, 992, 928; ^1H NMR (500 MHz, CDCl_3) δ : 6.20 (d, $J = 10.6$ Hz, 1H), 6.11 (m, 2H), 5.98 (m, 2H), 5.70 (m, 1H), 5.33 (m, 2H), 5.23 (t, $J = 11.0$, 2H), 4.70 (m, 3H), 4.34 (m, 2H), 4.11 (d, $J = 10.5$ Hz, 1H), 3.86 (m, 1H), 3.82 (dd, $J = 2.2$ Hz, $J = 5.4$ Hz, 1H), 3.69 (m, 1H), 3.48 (m, 1H), 3.34 (d, $J = 7.9$ Hz, 1H), 2.91 (dd, $J = 4.4$ Hz, $J = 11.5$ Hz, 1H), 2.73 (m, 2H), 1.64 (br s, 1H), 1.46 (s, 9H, Boc); ^{13}C NMR (125 MHz, CDCl_3) δ : 171.4, 153.7, 136.3, 135.5, 134.8, 127.7, 126.1, 126.0, 117.9, 117.8, 85.9, 82.2, 80.1, 77.2, 76.2, 75.3, 67.3, 63.1, 61.4, 53.6, 48.2, 48.0, 44.2, 28.5; HRMS (CI) Calcd for $\text{C}_{25}\text{H}_{34}\text{O}_6\text{N}_2 + \text{H}$: 459.2495, Found: 459.2504.

Tetracyclic tosyl-amine 27: A solution of amine **26** (11 mg, 0.0240 mmol), DMAP (one small crystal), tosyl chloride (6.8 mg, 0.0360, recrystallized from Pet. Ether) and triethylamine (7 μL , 0.048 mmol) in methylene chloride (0.1 mL) was stirred for 48 hours at room temperature. HCl solution (0.2 N) was added and the reaction mixture was extracted with methylene chloride. The combined methylene chloride layers were dried over Na_2SO_4 , filtered, and concentrated *in vacuo*. Purification by silica gel chromatography (25% EtOAc/Hexane) afforded **27** (12.1 mg, 82%) as a clear film.

$[\alpha]_{\text{D}}$ (CH_2Cl_2) = -71°

IR (film, cm^{-1}): 2924, 2853, 1738, 1688, 1598, 1452, 1368, 1345, 1286, 1236, 1162, 1030, 932; ^1H NMR (500 MHz, CDCl_3) δ : 7.72 (d, $J = 8.3$ Hz, 2H), 7.29 (d, $J = 8.3$ Hz, 2H), 6.15-6.09 (m, 3H), 5.98 (ddd, $J = 6.9$ Hz, $J = 10.4$ Hz, $J = 17.1$ Hz, 1H), 5.76 ($J = 7.5$ Hz, $J = 10.3$ Hz, $J = 17.4$ Hz, 1H), 5.65 (m, 1H), 5.33 (m, 1H), 5.24 (d, $J = 10.4$ Hz, 1H), 4.99-4.83 (m, 5H), 4.75 (dd, $J = 7.8$ Hz, 1H), 4.38-4.28 (m, 4H), 4.19 (m, 1H), 4.06 (m, 1H), 3.74 (d, $J = 17.3$ Hz, 1H), 3.52-3.57 (m, 2H), 2.95 (dd, $J = 10.0$ Hz, 2H), 2.42 (s, 3H), 1.43 (s, 9H, Boc); ^{13}C NMR (125 MHz, CDCl_3) δ : 171.0, 154.2, 143.7, 137.1, 135.2, 135.1,

135.0, 129.7, 128.1, 127.9, 126.9, 126.1, 118.7, 118.2, 81.8, 80.3, 77.2, 76.1, 74.8, 65.2, 64.9, 61.2, 51.5, 48.8, 48.4, 41.2, 28.4, 21.5; HRMS (ES) Calcd for $C_{32}H_{40}O_8N_2S+Na$: 635.2403. Found: 635.2403.

Pentacycle 28: Argon was bubbled through a solution of **27** (20 mg, 0.0326 mmol) in benzene (0.5M, 70 mL) for 30 minutes. Grubbs catalyst **6** (3 mg, 0.00353 mmol, 11 mol%) was added and the reaction mixture was heated to 80°C for 3 days while adding 3 mg of catalyst every 24 hours. The reaction was concentrated and diluted with methylene chloride (5 mL). To this solution was added tris(hydroxymethyl)phosphine (15 mg, 0.012 mmol) and triethylamine (0.032 mL, 0.024 mmol) to make the ruthenium catalyst water soluble. This was solution was vigorously stirred for 15 minutes, then stirred with water for an additional 20 minutes. The aqueous layer was washed with methylene chloride, and the combined methylene chloride layers were dried over sodium sulfate, filtered and concentrated. The crude product was subject to silica gel chromatography using 2% ethyl ether/ methylene chloride as the eluent to obtain **28** as a colorless film (5 mg, 26% yield).

R_F = 0.17 in 4% EE/DCM

$[\alpha]_D$ (CH_2Cl_2): -129°

IR (film, cm^{-1}): 2968, 2924, 2854, 1732 (s), 1694 (s), 1454, 1395, 1367, 1341, 1290, 1236, 1161 (s), 1095, 1066, 1000; 1H NMR (500 MHz, $CDCl_3$) δ : 7.70 (d, J = 8.3 Hz, 2H), 7.28 (d, J = 8.0 Hz, 2H), 6.16 (m, 2H), 6.09 (m, 1H), 5.78 (ddd, J = 2.1 Hz, J = 6.6 Hz, J = 11.7 Hz, 1H), 5.72 (ddd, J = 1.2 Hz, J = 5.5 Hz, J = 11.7 Hz, 1H), 5.65 (m, 1H), 5.27 (ddd, J = 1.9 Hz, J = 5.4 Hz, J = 8.1 Hz, 1H), 4.90 (m, 1H), 4.63-4.59 (m, 2H), 4.41 (dd, J = 7.3 Hz, 1H), 4.37-4.28 (m, 4H), 4.19 (dd, J = 4.8 Hz, J = 8.4 Hz, 2H), 3.72 (ddd, J = 3.1 Hz, J = 5.7 Hz, J = 18.5 Hz, 1H), 2.90 (dd, J = 11.0 Hz, J = 15.1 Hz, 1H), 2.77 (dd, J = 9.6 Hz, J = 12.3 Hz, 1H), 2.41 (s, 3H), 1.48 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ : 170.8, 154.2, 143.7, 137.4, 135.4, 133.5, 129.9, 129.6, 129.4, 126.6, 126.0, 125.8, 81.5, 80.7, 78.8, 76.6, 76.4, 72.1, 62.5, 61.3, 53.7, 50.8, 49.5, 48.1, 28.3, 21.5; HRMS (ES) Calcd for $C_{30}H_{36}O_8N_2S+Na$: 607.2090. Found: 607.2109.

Alcohol 29: A solution of **10** (109.5 mg, 0.354 mmol) in dry ethyl ether (1 mL) was added to a solution of lithium aluminum hydride (27 mg, 0.708 mmol) in dry ethyl ether (1 mL) at 0°C under inert atmosphere. After 1 hour, ethyl acetate was added and washed with 0.2 M HCl. Then the aqueous layer was washed with ethyl acetate. The combined organic layers were washed with brine, dried over sodium sulfate, concentrated in vacuo. The product was chromatographed using 4:1:1 hexane:ethyl ether:ethyl acetate (R_F = 0.29 in 2:1:1 hexane: ethyl ether: ethyl acetate) to obtain **29** as a colorless film (82.6 mg, 83% yield).

IR (film, cm^{-1}): 3426, 2977, 2932, 2875, 1688, 1661, 1478, 1455, 1409, 1366, 1335, 1276, 1247, 1169, 1148, 1094, 1029, 928, 906, 845, 768, 725; 1H NMR (500 MHz, $CDCl_3$) δ : 6.40 (dd, J = 1.5 Hz, J = 5.7

Hz, 1H), 6.34 (d, $J = 5.6$, 1H), 5.88 (m, 1H), 5.12 (m, 2H), 4.93 (s, 1H), 4.87 (s, 1H), 3.96 (d, $J = 4.9$ Hz, 2H), 3.78 (s, 1H), 3.59 (d, $J = 7.8$ Hz, 1H), 3.18 (t, $J = 9.2$ Hz, 1H), 2.04 (br s, 1H), 1.44 (s, 9H, Boc); ^{13}C NMR (125 MHz, CDCl_3) δ : 156.9, 135.9, 135.7, 135.2, 115.2, 81.3, 80.7, 78.5, 64.0, 59.8, 49.8, 44.8, 28.3; HRMS Calcd for $\text{C}_{15}\text{H}_{23}\text{O}_4\text{NNa}$: 304.1524, Found: 304.1527.

Primary amine 31: To a solution of allyl ester **4** (29 mg, 0.0981 mmol) in methylene chloride (0.5 mL) was added TFA (0.2 mL). After 30 minutes, the reaction mixture was concentrated *in vacuo* and basified to pH 8 with 1N KHCO_3 . The aqueous layer was extracted with ethyl acetate several times. The combined organic layers were dried over sodium sulfate, filtered, and concentrated *in vacuo* to afford **31** as a colorless oil (19 mg, quant.).

$[\alpha]_D$ (MeOH): -110°

IR (film, cm^{-1}): 3354 (br), 2930, 1732 (s), 1682 (s), 1651, 1427, 1316, 1203, 1134, 1042, 992, 903, 859, 835, 800, 722, 697; ^1H NMR (500 MHz, CDCl_3) δ : 6.44 (d, $J = 5.9$ Hz, 1H), 6.38 (d, $J = 5.9$ Hz, 1H), 5.87 (m, 1H), 5.30 (dd, $J = 1.3$ Hz, $J = 17.2$ Hz, 1H), 5.25 (dd, $J = 1.0$ Hz, $J = 10.4$ Hz, 1H), 5.17 (d, $J = 4.5$ Hz, 1H), 4.83 (s, 1H), 4.56 (d, $J = 5.8$ Hz, 2H), 4.25 (br s, 2H, NH_2), 3.47 (br s, 1H), 2.90 (m, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ : 170.5, 136.2, 135.5, 132.1, 119.3, 85.4, 79.4, 66.1, 55.4, 53.6; HRMS (ES) Calcd for $\text{C}_{10}\text{H}_{13}\text{O}_3\text{N}+\text{Na}$: 196.0974. Found: 196.0980.

Preparation of mixture of 32 and 33: To a solution of alcohol **29** (30 mg, 0.107 mmol) and sodium bicarbonate (45 mg, 0.533 mmol) in methylene chloride (1 mL) was added Dess-Martin periodinane (68 mg, 0.160 mmol). After 1.5 hours, the reaction was allowed to warm to room temperature, where an additional Dess-Martin periodinane (16 mg, 0.038 mmol) was added. The reaction was diluted with ether after 45 minutes and washed with water, saturated sodium bicarbonate solution, and saturated sodium thiosulfate pentahydrate. The combined aqueous layers were washed with ether. The combined ether layers were dried over sodium sulfate, filtered, and concentrated to afford crude aldehyde **30**.

To a solution of amine **31** (21 mg, 0.107 mmol) in methylene chloride was added the crude aldehyde (as a solution in methylene chloride) immediately followed by the addition of sodium triacetoxyborohydride (32 mg, 0.149 mmol). After 24 hours, saturated sodium bicarbonate solution was added and the aqueous layer was washed with ethyl acetate several times. The combined ethyl acetate layers were dried over sodium sulfate, filtered and concentrated *in vacuo*. The crude product that was subjected to silica gel chromatography using 10% Ace/Hx to afford a mixture of 2 inseparable amines **32** and **33** (29.1 mg).

A very small amount of relatively pure **33** was obtained for characterization:
clear film; $[\alpha]_D$ (CH_2Cl_2): -60°

IR (film, cm^{-1}): 3299, 2976, 2930, 1732 (s), 1684 (s), 1454, 1408, 1366, 1334, 1275, 1246, 1171 (s), 993, 905; ^1H NMR (500 MHz, CDCl_3) δ : 6.43 (dd, $J = 1.9$ Hz, $J = 5.8$ Hz, 1H), 6.40 (m, 2H), 6.36 (dd, $J = 1.3$ Hz, $J = 5.8$ Hz, 1H), 5.89 (dddd, $J = J = 5.8$ Hz, $J = 10.6$ Hz, $J = 16.3$ Hz, 1H), 5.31 (dddd, $J = J = J = 1.4$ Hz, $J = 17.2$ Hz, 1H), 5.25 (dd, $J = 1.2$ Hz, $J = 10.5$ Hz, 1H), 5.16 – 5.11 (m, 2H), 5.10 (dd, $J = 1.5$ Hz, $J = 10.3$ Hz, 1H), 4.92 (d, $J = 3.3$ Hz, 1H), 4.81 (s, 1H), 4.74 (br s, 1H), 4.55 (m, 2H), 3.95 (m, 3H), 3.06 (s, 1H), 2.73 (s, 1H), 2.60 (br s, 2H), 2.12 (s, 1H), 1.59 (br s, 1H, NH), 1.45 (s, 9H; HRMS (ES) Calcd for $\text{C}_{25}\text{H}_{34}\text{O}_6\text{N}_2+\text{Na}$: 459.2495. Found: 459.2495.

Sulfonamide 34: Tosyl chloride (19 mg, 0.0989 mmol), DMAP (2 mg), and triethylamine (28 μL , 0.198 mmol) was added to a solution of the mixture of amines (**32** and **33**, 29.1 mg) in methylene chloride (0.2 mL) and stirred for 24 hours at room temperature. The reaction mixture was diluted with methylene chloride and extracted with water. The water layer was extracted with methylene chloride (3 x 5 mL). The combined organic layer was washed with brine, dried over sodium sulfate, filtered, and concentrated *in vacuo*. The crude product was chromatographed using 30% EE/Hx as the eluent to afford the tosylated amine of **32** (7.7 mg) and the desired tosylated amine **34** (23.7 mg, 36% yield over 3 steps beginning with the alcohol) as a clear film.

$R_F = 0.20$ in 50% EE/Hx

$[\alpha]_D$ (CH_2Cl_2): -77°

IR (film, cm^{-1}): 3082, 2976, 2930, 1737, 1683 (s), 1598, 1451, 1407, 1366, 1338, 1273, 1244, 1164 (s), 1101, 1019, 994, 908, 858; ^1H NMR (500 MHz, CDCl_3) δ : 7.61 (d, $J = 8.2$ Hz, 2H), 7.22 (d, $J = 8.0$ Hz, 2H), 6.74 (d, $J = 5.5$ Hz, 1H), 6.45 (m, 2H), 6.25 (dd, $J = 1.1$ Hz, $J = 5.8$ Hz, 1H), 5.89 (m, 1H), 5.76 (m, 1H), 5.24 (dd, $J = 1.3$ Hz, $J = 17.2$ Hz, 1H), 5.22 (dd, $J = 0.8$ Hz, $J = 10.4$, 1H), 5.16 – 5.12 (m, 2H), 5.07 (dd, $J = 1.1$ Hz, $J = 10.3$ Hz, 1H), 4.97 (d, $J = 4.5$ Hz, 1H), 4.86 (s, 1H), 4.75 (s, 1H), 4.43–4.34 (m, 2H), 4.31 (s, 1H), 3.92 (s, 2H), 3.81 (s, 1H), 3.47 (d, $J = 15.2$ Hz, 1H), 3.05 (m, 1H), 2.78 (t, $J = 4.1$ Hz, 1H), 2.38 (s, 3H), 2.33 (s, 1H), 1.43 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3) δ : 169.9, 156.3, 143.3, 136.8, 136.4, 136.3, 135.9, 135.4, 131.5, 129.6, 127.4, 118.6, 115.2, 84.7, 81.8, 80.0, 79.7, 78.8, 65.5, 60.8, 59.6, 47.0, 46.1, 45.8, 44.8, 28.4, 21.4; HRMS (ES) Calcd for $\text{C}_{32}\text{H}_{40}\text{O}_8\text{N}_2\text{S}+\text{Na}$: 635.2403. Found: 635.2420.

Pentacycle 28: Argon was bubbled through a solution of **34** (5 mg, 0.0082 mmol) in methylene chloride (0.5mM, 16 mL) for 30 minutes. Grubbs catalyst **6** (3 mg, 0.00353 mmol, 43 mol%) was added and the reaction mixture was heated to reflux. More Grubbs catalyst (4 mg) was added over 24 hours. (The total amount of catalyst used was 7 mg, 100 mol %.) The reaction was concentrated and diluted with methylene chloride (5 mL). To this solution was added tris(hydroxymethyl)phosphine (30 mg, 0.24 mmol, 29 eq) and triethylamine (0.032 mL, 0.024 mmol). This was solution was vigorously stirred for 15

minutes, then stirred with water for an additional 20 minutes. The aqueous layer was washed with methylene chloride, and the combined methylene chloride layers were dried over sodium sulfate, filtered and concentrated. The crude product was subject to silica gel chromatography using 2-4% ethyl ether/methylene chloride as the eluent to obtain 28 as a colorless film (0.5 mg, 10% yield).

¹H NMR Spectrum of 3

¹H NMR Spectrum of **4**

^{13}C NMR Spectrum of Compound 4.

^{13}C NMR Spectrum of Compound 5.

7

^1H NMR Spectrum of 7

8

^{13}C NMR Spectrum of Compound 8.

¹H NMR Spectrum of **9**

^{13}C NMR Spectrum of Compound 9 (C_6D_6 , 70°C).

^1H NMR Spectrum of 9.1

^{13}C NMR Spectrum of Compound 9.1

X-ray Structure Determination of Compound 9.1.

Compound 265, $C_{11}H_{13}NO_3$, crystallizes in the orthorhombic space group $P2_12_12_1$ (systematic absences $h00$: $h=\text{odd}$, $0k0$: $k=\text{odd}$, and $00l$: $l=\text{odd}$) with $a=5.1635(5)\text{\AA}$, $b=8.5138(9)\text{\AA}$, $c=22.427(2)\text{\AA}$, $V=985.9(2)\text{\AA}^3$, $Z=4$ and $d_{\text{calc}}=1.396\text{ g/cm}^3$. X-ray intensity data were collected on a Rigaku Mercury CCD area detector employing graphite-monochromated Mo- K_α radiation ($\lambda=0.71069\text{ \AA}$) at a temperature of 143°K . Indexing was performed from a series of four 0.5° oscillation images with exposures of 30 seconds per frame. A hemisphere of data was collected using 60 second exposures and a crystal-to-detector distance of 40 mm. A total of 440 images were collected: one sweep was performed using ϕ -scans from -90° to $+90^\circ$ in 0.5° steps at $\omega = 0^\circ$ and $\chi = 0^\circ$ with a detector swing angle of -10° ; a second sweep was done using ω -scans from -20° to $+20^\circ$ in 0.5° steps at $\chi = -90^\circ$ and $\phi = 0^\circ$ with a detector swing angle of -10° . Oscillation images were processed using CrystalClear¹, producing a listing of unaveraged F^2 and $\sigma(F^2)$ values which were then passed to the CrystalStructure² program package for further processing and structure solution on a Dell Pentium III computer. A total of 5213 reflections were measured over the ranges $5.12 \leq 2\theta \leq 50.7^\circ$, $-5 \leq h \leq 4$, $-9 \leq k \leq 7$, $-26 \leq l \leq 23$ yielding 1687 unique reflections ($R_{\text{int}} = 0.0158$). The intensity data were corrected for Lorentz and polarization effects and for absorption, using REQAB³ (minimum and maximum transmission 0.848, 1.000).

The structure was solved by direct methods (SIR97⁴). Refinement was by full-matrix least squares based on F^2 using SHELXL-97⁵. All reflections were used during refinement

(F^2 's that were experimentally negative were replaced by $F^2 = 0$). The weighting scheme used was $w=1/[\sigma^2(F_o^2) + 0.0591P^2 + 0.3089P]$ where $P = (F_o^2 + 2F_c^2)/3$. Non-hydrogen atoms were refined anisotropically and hydrogen atoms were refined using a "riding" model. Refinement converged to $R_1=0.0364$ and $wR_2=0.0981$ for 1645 reflections for which $F > 4\sigma(F)$ and $R_1=0.0373$, $wR_2=0.0992$ and $GOF = 1.073$ for all 1687 unique, non-zero reflections and 136 variables⁶. The maximum Δ/σ in the final cycle of least squares was 0.000 and the two most prominent peaks in the final difference Fourier were +0.457 and -0.460 e/Å³.

Table 1. lists cell information, data collection parameters, and refinement data. Final positional and equivalent isotropic thermal parameters are given in Table 2. Anisotropic thermal parameters are in Table 3. Tables 4. and 5. list bond distances and bond angles. Figure 1. is an ORTEP⁷ representation of the molecule with 30% probability thermal ellipsoids displayed.

Figure 1. ORTEP drawing of the title compound with 30% probability thermal ellipsoids.

^{13}C NMR Spectrum of Compound 10.

^1H NMR Spectrum of 11

^{13}C NMR Spectrum of Compound 11.

^1H NMR Spectrum of Compound 12.

^{13}C NMR Spectrum of Compound 12.

^{13}C NMR Spectrum of Compound 13.

^1H NMR Spectrum of 15

^{13}C NMR Spectrum of Compound 15.

^{13}C NMR Spectrum of Compound 16.

¹H NMR Spectrum of 17

^{13}C NMR Spectrum of Compound 17.

¹H NMR Spectrum of **19**

^1H NMR Spectrum of 19.1

^1H NMR Spectrum of Compound 19.1 (C_6D_6 , 70°C).

^1H NMR Spectrum of Compound 20.

¹³C NMR Spectrum of Compound 20.

¹H NMR Spectrum of 21

^{13}C NMR Spectrum of Compound 21.

¹H NMR Spectrum of **22**

^{13}C NMR Spectrum of Compound 22.

^1H NMR Spectrum of 24.1

^{13}C NMR Spectrum of 24.1

¹H NMR Spectrum of 24.2

^{13}C NMR Spectrum of 24.2

¹H NMR Spectrum of 25

^{13}C NMR Spectrum of 25

^1H NMR Spectrum of 26

^1H NMR Spectrum of 27

^1H NMR Spectrum of 31

¹H NMR Spectrum of 33

¹H NMR Spectrum of 34

^{13}C NMR Spectrum of **34**