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SUPPLEMENTARY MATERIAL

Conformationally Unbiased Macrocyclization Reactions by Ring Closing Metathesis

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General. All reactions were carried out under Ar using Schlenk techniques. **$Cl_2Ru(PCy_3)_2$=CHCH=CPh_2** (**1**) was prepared from 3,3-diphenylcyclopropene according to the literature procedure.[3] **Commercially available reagents**: 10-undecen-1-ol, 5-hexenoic acid, 10-undecenoyl chloride, 5-hexen-1-ol, 4-(N,N-dimethyl)-amino-pyridine (DMAP), (Fluka); 7-octene-1-ol, Pd on charcoal (5%), (Aldrich). **Other substrates**: Racemic 2-methyl-hept-6-en-1-ol (**19**) was prepared from 2-methyl-6-heptenoic acid by reduction with $LiAlH_4$ according to Snider, B. B.; Allentoft, A. J.; Walner, M. B. *Tetrahedron* **1990**, *46*, 8031 - 8042. (*R*)-2-methyl-hept-6-en-1-ol (+)-(**19**) was obtained upon alkylation of (*2S*)-N-propionylbornane-10,2-sultam (**17**)[13] with 1-iodo-5-pentene and subsequent reduction of the resulting product **18**. **CH_2Cl_2** was dried by distillation from CaH_2 and was stored under Ar. **Flash Chromatography:** Merck silica gel 60 (230 - 400 mesh) with n-hexane/ethyl acetate in various proportions as eluent. **Instrumental Analyses:** NMR: Spectra were recorded on a Bruker AC 200 at 200.2 MHz (^1H) and 50.3 MHz (^{13}C) in $CDCl_3$. Chemical shifts are listed downfield in ppm relative to tetramethylsilane. Coupling

constants (J) are given in Hz. IR: Nicolet FT - 7199, wavenumbers in cm^{-1}. MS: Varian CH - 5 (70 eV). HR-MS: Finnigan MAT SSQ 7000 (70 eV). Optical rotation measurements: Jasco DIP - 360 polarimeter in CH_2Cl_2 using a 5 cm path length quartz cell at the temperature stated.

Preparation of Terminally Unsaturated Esters. Representative Procedure. A solution of hex-5-en-1-ol (475 mg, 4.75 mmol) and DMAP (610 mg, 5 mmol) in CH_2Cl_2 (15 mL) was added dropwise to a stirred solution of 10-undecenoyl chloride (810 mg, 4 mmol) in CH_2Cl_2 (20 mL) at 0° C. Stirring was continued for 4 h at room temperature. The reaction mixture was filtered through a short pad of silica, the solvent was evaporated and the product purified by flash chromatography with hexane/ethyl acetate (50:1 → 20:1) as eluent. Ester **3** was obtained as a colorless syrup (1.002 g, 94 %).

Macrocyclization Reactions via Ring Closing Metathesis (RCM). Representative Procedure. A solution of substrate **3** (298 mg, 1.12 mmol) in CH_2Cl_2 (100 mL) and a solution of the ruthenium carbene **1** (50 mg, 0.054 mmol, 5 mol%) in CH_2Cl_2 (100 mL) were simultaneously added dropwise over a period of 24 h to CH_2Cl_2 (50 mL) at room temperature. After stirring for another 6 h, the solvent was removed *in vacuo* and the residue was purified by flash column chromatography with n-hexane/ethyl acetate (100:1) as eluent to afford lactone **4** as a colorless syrup (219 mg, 79 %).

Hydrogenation of Unsaturated Lactones. Representative Procedure. Pd on charcoal (5% w/w, 35 mg) was added to a solution of compound **4** (135 mg, 0.57 mmol) in ethyl acetate (10 mL). The mixture was stirred under H_2 (1 atm) at room temperature for 40 min. The Pd catalyst was filtered off through a short pad of silica

and was washed several times with ethyl acetate. Removal of the solvent *in vacuo* afforded Exaltolide (**2**) in analytically pure form (130 mg, 95 %).

Hex-5-en-1-yl undec-10-enoate (**3**). Colorless syrup. ^{1}H NMR: 1.30 - 1.72 (m, 16H), 1.98 - 2.16 (m, 4H), 2.29 (t, 2H, J = 7.7), 4.07 (t, 2H, J = 6.6), 4.91 - 5.05 (m, 4H), 5.70 - 5.88 (m, 2H). ^{13}C NMR: 25.0, 25.2, 28.1, 28.9, 29.1, 29.1, 29.3, 29.4, 33.3, 33.8, 34.4, 64.1, 114.1, 114.9, 138.3, 139.1, 173.9. IR: 3077, 2976, 2928, 2856, 1738, 1641, 1461, 1441, 1417, 1390, 1354, 1240, 1172, 1116, 993, 910. MS *m/z* (rel. intensity): 266 (M^+, 1), 166 (7), 148 (12), 96 (11), 82 (100).

Pentadec-10-en-15-olide (**4**). Colorless syrup. Ratio of isomers ~ 46 : 54. ^{1}H NMR: 1.30 - 1.49 (m, 10H), 1.54 - 1.72 (m, 4H), 2.00 - 2.10 (m, 4H), 2.29 - 2.37 (m, 2H), 4.07 - 4.18 (m, 2H), 5.28 - 5.45 (m, 2H). ^{13}C NMR: 25.2, 25.4, 26.5, 26.6, 27.1, 27.2, 27.6, 27.9, 28.0, 28.1, 28.2, 28.3, 28.4, 28.4, 29.1, 32.0, 33.9, 34.7, 64.0, 64.1, 129.6, 130.1, 130.4, 131.7, 173.9. IR: 3000, 2928, 2856, 1736, 1461, 1385, 1346, 1252, 1234, 1168, 1152, 1113, 1085, 1024, 969, 719. MS *m/z* (rel. intensity): 238 (M^+, 20), 210 (18), 109 (17), 96 (49), 82 (100), 67 (64), 55 (64). HR-MS *calcd.* for $C_{15}H_{26}O_2$: 238.1933, *found*: 238.1920.

Undec-10-en-1-yl hex-5-enoate (**5**). Colorless syrup. ^{1}H NMR: 1.30 - 1.37 (m, 12H), 1.55 - 1.80 (m, 4H), 1.99 - 2.16 (m, 4H), 2.31 (t, 2H, J = 7.4), 4.06 (t, 2H, J = 6.7), 4.90 - 5.07 (m, 4H), 5.68 - 5.87 (m, 2H). ^{13}C NMR: 24.1, 25.9, 28.7, 28.9, 29.1, 29.2, 29.4, 29.5, 33.1, 33.6, 33.8, 64.4, 114.1, 115.2, 137.6, 139.1, 173.6. IR: 3078, 2928, 2855, 1738, 1641, 1461, 1244, 1171, 993, 911. MS *m/z* (rel. intensity): 266 (M^+, 2), 154 (18), 115 (47), 96 (48), 82 (50), 69 (100), 55 (97).

Pentadec-5-en-15-olide (**6**). Colorless syrup. (*E*) : (*Z*) ~ 77 : 23. ^{1}H NMR: 1.24 - 1.28 (m, 12H), 1.55 - 1.71 (m, 4H), 1.92 - 2.09 (m, 4H), 2.28 (t, 2H, J = 7.2), 4.05 (t, 1.7 H, J = 5.3), 4.08 (t, 0.3 H, J = 5.2), 5.16 - 5.36 (m, 2H). ^{13}C NMR: (*E*)-isomer: 22.5, 25.0, 25.2, 25.9, 26.3, 26.8, 26.9, 27.3, 29.7, 31.0, 31.1, 63.5, 128.5, 131.2, 172.6. (Z)-isomer (resolved signals): 24.4, 24.5, 25.1, 25.2, 25.5, 25.8, 25.9, 26.8, 33.1, 63.3, 127.8, 130.0, 172.7. IR: 3005, 2934, 2850, 1738, 1452, 1350, 1254, 1240, 1170, 969, 714. MS *m/z* (rel. intensity): 238 (M^+, 48), 126 (26), 110 (18), 96 (55), 82 (100), 67 (83). HR-MS *calcd.* for $C_{15}H_{26}O_2$: 238.1933, *found*: 238.1910.

Exaltolide (**2**). Colorless syrup. ^{1}H NMR: 1.32 - 1.45 (m, 20H), 1.57 - 1.70 (m, 4H), 2.33 (t, 2H, J = 7.0), 4.14 (t, 2H, J = 5.8). ^{13}C NMR: 24.9, 25.1, 25.9, 26.0, 26.0, 26.4, 26.7, 26.9, 27.1, 27.2, 27.8, 28.4, 34.4, 63.9, 174.0. IR: 2929, 2858, 1737, 1461, 1349, 1237, 1167, 1108, 1069, 1052, 719. MS *m/z* (rel. intensity): 240 (M^+, 46), 222 (31), 180 (18), 138 (13), 124 (14), 110 (15), 97 (31), 83 (47), 69 (66), 55 (100). HR-MS *calcd.* for $C_{15}H_{28}O_2$: 240.2089, *found*: 240.2080.

10-Undecen-1-yl 10-undecenoate (**8**). Colorless syrup. ^{1}H NMR: 1.30 - 1.41 (m, 24H), 1.55 - 1.65 (m, 4H), 1.98 - 2.08 (m, 4H), 2.28 (t, 2H, J = 7.6), 4.06 (t, 2H, J = 6.7), 4.89 - 5.04 (m, 4H), 5.70 - 5.90 (m, 2H). ^{13}C NMR: 24.6, 25.5, 28.3, 28.5, 28.5, 28.7, 28.7, 28.7, 28.8, 28.9, 29.0, 29.1, 33.4, 34.0, 63.9, 113.7, 113.8, 138.6, 173.4. IR: 3077, 2927, 2855, 1739, 1641, 1465, 1239, 1172, 993, 909, 723. MS *m/z* (rel. intensity): 336 (M^+, 8), 185 (7), 167 (12), 152 (28), 124 (20), 110 (29), 96 (51), 82 (67), 69 (65), 55 (100).

10-Eicosen-20-olide (**9**). Colorless syrup. Ratio of isomers ~ 45 : 55. ^{1}H NMR: 1.23 - 1.45 (m, 22H), 1.58 - 1.68 (m, 4H), 1.98 - 2.03 (m, 4H), 2.31 (t, 2H, J = 6.4), 4.11 (td, 2H, J = 5.6, 1.7), 5.28 - 5.44 (m, 2H). ^{13}C NMR: 25.2, 25.9, 26.2, 26.6, 26.7, 27.7, 28.0, 28.4, 28.5, 28.7, 28.7, 28.8, 29.0, 29.0, 29.1, 29.1, 29.2, 29.4, 29.5, 31.7, 32.0, 34.5, 34.8, 64.0, 64.2, 130.0, 130.1, 130.6, 130.9, 173.9, 174.0. IR: 3001, 2926, 2854, 1737, 1462, 1385, 1348, 1252, 1236, 1175, 1117, 1090, 1066, 1030, 969, 722. MS *m/z* (rel. intensity): 308 (M^+, 32), 290 (11), 124 (18), 110 (23), 96 (74), 82 (100). HR-MS *calcd.* for $C_{20}H_{36}O_2$: 308.2715, *found*: 308.2720.

20-Eicosanolide (**7**). Colorless syrup. ^{1}H NMR: 1.26 - 1.30 (m, 34H), 2.31 (t, 2H, J = 7.0), 4.11 (t, 2H, J = 5.9). ^{13}C NMR (resolved signals): 22.7, 25.1, 26.0, 27.5, 27.6, 27.7, 27.8, 27.9, 28.2, 28.3, 28.4, 28.7, 28.8, 28.9, 29.0, 31.6, 34.7, 64.4, 173.6. IR: 2925, 2854, 1737, 1461, 1351, 1250, 1169, 1112, 808, 722. MS *m/z* (rel. intensity): 310 (M^+, 75), 292 (40), 250 (11), 124 (12), 111 (23), 97 (47), 83 (57), 69 (65), 55 (100). HR-MS *calcd.* for $C_{20}H_{38}O_2$: 310.2872, *found*: 310.2858.

Dec-9-en-2-yl hex-5-enoate (**11**). Colorless syrup; ^{1}H NMR: 1.14 (s, 3H), 1.17 (s, 3H), 1.20 - 1.57 (m, 11H), 1.69 (quint., 2H, J = 7), 1.90 - 2.10 (m, 4H), 2.24 (t, 2H, J = 7), 4.81 - 5.04 (m, 4H), 5.62 - 5.86 (m, 2H). ^{13}C NMR: 173.1, 138.9, 137.7, 115.2, 114.1, 70.7, 35.8, 33.9, 33.7, 33.0, 29.2, 28.9, 28.7, 25.3, 24.1, 19.9. IR: 3080, 2990, 2920, 2860, 1725, 1645, 1380, 1250, 1180, 1130, 990, 910. MS *m/z* (rel. intensity): 252 (M^+, 2), 206 (2), 163 (3), 138 (18), 114 (83), 110 (19), 97 (100), 83 (39), 82 (31), 80 (31), 69 (74), 68 (53), 67 (28), 55 (77), 41 (61).

13-Methyl-tridec-5-en-13-olide (**10**). Colorless syrup; (*E*) : (*Z*) ~ 31 : 69. ^{1}H NMR: 1.19 - 2.46 (m, 22H), 4.88 - 5.07 (m, 1H), 5.30 - 5.41 (m, 2H). ^{13}C NMR: (*Z*)-isomer:

20.7, 23.3, 25.0, 25.0, 25.2, 26.2, 26.6, 27.0, 33.8, 34.7, 69.3, 128.9, 130.9, 173.4. (*E*)-isomer: 20.4, 22.5, 24.3, 26.2, 27.1, 27.4, 31.3, 32.2, 32.6, 34.4, 69.7, 129.3, 132.3, 173.6. IR: 3000, 2930, 2857, 1732, 1653, 1460, 1414, 1374, 1345, 1293, 1246, 1206, 1172, 1132, 1107, 1042, 1022, 971, 877, 806, 719. MS *m/z* (rel. intensity): 224 (M^+, 10), 164 (8), 126 (30), 95 (43), 81 (100), 67 (93), 55 (77).

(+)-(*R*)-2-Methyl-hept-6-en-1-yl oct-7-enoate (+)-(**15**). Colorless syrup. ^{1}H NMR: 0.92 (d, 3H, J = 6.8), 1.02 - 1.52 (m, 8H), 1.56 - 1.83 (m, 3H), 1.99 - 2.10 (m, 4H), 2.31 (t, 2H, J = 7.3), 3.89 (dd, 1H, J = 10.7, 6.6), 3.92 (dd, 1H, J = 10.7, 6.0), 4.91 - 5.05 (m, 4H), 5.70 - 5.90 (m, 2H). ^{13}C NMR: 16.9, 24.9, 26.2, 28.5, 28.6, 32.5, 32.9, 33.6, 33.9, 34.4, 69.1, 114.4, 114.5, 138.7, 138.8, 173.9. IR; 3078, 2932, 2858, 1738, 1641, 1462, 1247, 1172, 994, 911. MS *m/z* (rel. intensity): 252 (M^+, <1), 210 (2), 125 (19), 110 (23), 95 (23), 81 (47), 69 (97), 55 (100). HR-MS *calcd.* for $C_{16}H_{28}O_2$: 252.2089, *found*: 252.2078. $[\alpha]_D^{23}$ = +1.42°, $[\alpha]_{546}^{23}$ = +1.68° (c = 16.5, CH_2Cl_2).

(+)-(*R*)-12-Methyl-tridec-7-en-13-olide (+)-(**16**). Colorless syrup. (*E*) : (Z) ~ 96 : 4,. ^{1}H NMR (*E*-isomer): 0.89 (d, 3H, J = 6.8), 1.18 - 2.11 (m, 15H), 2.30 - 2.37 (m, 2H), 3.81 (dd, 1H, J = 10.8, 9.2), 4.06 (dd, 1H, J = 10.8, 3.5), 5.24 - 5.29 (m, 2H). ^{13}C NMR (*E*-isomer): 15.9, 25.1, 25.3, 26.8, 28.1, 30.2, 31.2, 31.5, 32.3, 34.9, 68.4, 131.5, 131.6, 174.0. IR: 3024, 2929, 2856, 1734, 1461, 1444, 1378, 1341, 1252, 1206, 1168, 1148, 1116, 1007, 970, 737. MS *m/z* (rel. intensity): 224 (M^+, 24), 109 (23), 95 (51), 81 (100), 67 (69). HR-MS *calcd.* for $C_{14}H_{24}O_2$: 224.1776, *found*: 224.1755. $[\alpha]_D^{25}$ = +31.48°, $[\alpha]_{546}^{25}$ = + 32.24° (c = 5.0, CH_2Cl_2).

(+)-(*R*)-12-Methyl-13-tridecanolide (+)-(**12**). Colorless syrup. ^{1}H NMR: 0.92 (d, 3H, J = 6.9), 1.13 - 1.91 (m, 19 H), 2.26 - 2.50 (m, 2H), 3.70 (dd, 1H, J = 10.9, 8.4), 4.20 (dd, 1H, J = 10.9, 3.4). ^{13}C NMR: 16.7, 22.5, 23.7, 24.1, 24.6, 25.6, 25.9, 26.2, 26.3, 30.1, 31.9, 34.2, 68.0, 173.9. IR: 2931, 2861, 1736, 1461, 1447, 1377, 1241, 1150, 1109, 1010, 733. MS *m/z* (rel. intensity): 226 (M^+, 33), 208 (27), 153 (20), 124 (13), 111 (19), 98 (39), 83 (39), 69 (80), 55 (96), 41 (100). HR-MS *calcd.* for $C_{14}H_{26}O_2$: 226.1933, *found*: 226.1920. $[\alpha]_D^{25}$ = + 14.54°, $[\alpha]_{546}^{25}$ = + 17.22° (c = 4.25). ref[12d]: $[\alpha]_D^{25}$ = + 14.7°, $[\alpha]_{546}^{25}$ = + 17.5° (c = 1.4).