

General. Unless otherwise noted, all reactions performed in organic solvents were conducted under an atmosphere of argon with oven dried glassware using standard syringe and septa technique. Analytical thin layer chromatography (TLC) was performed using Whatman silica gel HF₂₅₄ plates or Selecto Scientific alumina B F₂₅₄ plates and UV light, 12- molybdophosphoric acid (PMA stain), or potassium permanganate (KMnO₄ stain) for analysis of the developed plates. Flash column chromatography (FCC) was performed using silica gel 60 (230-400 mesh) or Brockmann I alumina gel (150 mesh). ¹H-NMR spectra were recorded on a Bruker 500 MHz spectrometer in CDCl₃ or C₆D₆ and the chemical shifts were reported in parts per million (ppm) relative to the residue of the solvent, i.e. CD(H)Cl₃ at 7.27 ppm or C₆D(H)₆ at 7.16 ppm. ¹³C-NMR spectra were recorded on a Bruker 125 MHz spectrometer in CDCl₃ or C₆D₆ and the chemical shifts were reported in parts per million (ppm) relative to the solvent peak, i.e. CDCl₃ at 77.23 ppm or C₆D₆ at 128.39 ppm. High resolution mass spectra (HRMS) were obtained on an Ultima Micromass Q-TOF Mass Spectrometer at the Mass Spectrometry Laboratory of Hunter college, CUNY.

General procedure for cross metathesis

A solution of olefin A (1.0 eq.) and olefin B (3.0 eq.) in anhydrous CH₂Cl₂ (0.02M) was degassed under N₂ for 30 min. Grubbs 2nd generation catalyst (10-12 mol%) was then added and refluxed under N₂ for 2-3 hrs. When reaction is complete, the reaction mixture was cooled to r.t. and was quenched by adding few drops of DMSO. The solvent was evaporated under reduced pressure and purified by FCC using Pet./ EtOAc

Synthesis of 29 via Wittig olefination

To a flask containing phosphonium salt **18** (1.82g, 3.00 mmol, *ca.* E/Z=4:1) suspended in THF (20 mL) at -78 °C was dropwisely added sodium hexamethyldisilylamide (NaHMDS) (6.0mL, 0.6 M in toluene). The mixture was warmed up to room temperature for 30 min, cooled back to -78 °C and was dropwisely added aldehyde **11** (1.17 g, 9.0 mmol in 10 mL THF). After 30 min at -78 °C, the reaction mixture was warmed up to room temperature for 1 h. The reaction was dilute with Et₂O, quenched with saturated NH₄Cl solution. The mixture was extracted with Et₂O (3 x 100 mL) and the combined organic phase was washed with brine, water, dried with Na₂SO₄, filtered, concentrated *in vacuo* and purified by FCC to afford the diene **29** (0.758 g, 76%). (*ca.* E/Z= 4:1 as in **18**, newly formed double is pure Z). R_f = 0.44 (1.5:8.5 EtOAc /pet. ether).

General procedure for iodoetherification

To a stirred solution of olefin (1.0 eq.) and freshly activated molecular sieves (4A^o) in anhydrous CH₂Cl₂ (0.008M) at r.t. was added IDCP (2.0 eq.) and stirring continued for 15 min. The reaction was then poured into sat. aq. solution of sod. thiosulfate and extracted with ether. The combined extracts was washed successively with water and brine and dried over Na₂SO₄. The solvent was evaporated under reduced pressure and purified by FCC using Pet. Ether/EtOAc.

General procedure for spiroketalization

AgOTf (4.0 eq.) was added to a stirred solution of cyclization product (1.0 eq.) and 2,4,6 Collidine (4-5 eq) in anhydrous CH₂Cl₂ (0.005M) at r.t.. When the reaction is complete (approx. 15 min.) reaction mixture was poured into sat. aq. solution of sod. thiosulfate and extracted with EtOAc. The combined extracts was washed successively with water and brine and dried over Na₂SO₄. The solvent was evaporated under reduced pressure and purified by FCC using Pet.Ether/ EtOAc.

Physical data for iodoetherification precursors

The iodoetherification precursors were obtained as inseparable mixtures of E/Z alkenes. ¹H-NMR and ¹³C-NMR spectral charts for these compounds are provided in the appendix. The HRMS data is listed below.

19

HRMS [M+H] calcd. for C₂₂H₃₅O₅ 379.2479, found 379.2479.

21

HRMS [M+H] calcd. for C₃₁H₅₅O₆Si 551.3762, found 551.3762

23

HRMS [M+Na] calcd. for C₃₁H₅₅O₆SiNa 573.3581, found 573.3577

24

HRMS [M+Na] calcd. for C₃₇H₅₈O₆SiNa 649.3894, found 649.3901

25

HRMS [M+Na] calcd. for C₂₆H₃₈O₈Si 501.2458, found 501.2469

26

HRMS [M+Na] calcd. for C₃₁H₄₆O₁₀Na 601.2983, found 601.2983

28

HRMS [M+Na] calcd. for C₃₅H₄₄O₆Na 583.3030, found 583.3034

30

HRMS [M+Na] calcd. for C₂₂H₃₂O₅Na 399.2141, found 399.2142

Physical data for iodoetherification products and deprotected alcohol derivatives

The iodoetherification products and their deprotected alcohol derivatives were obtained as inseparable mixtures of diastereomeric iodo-cyclic ethers. ¹H-NMR and ¹³C-NMR spectral charts for these compounds are provided in the appendix. The HRMS data is listed below.

31

HRMS [M+Na] calcd. for C₂₂H₃₃IO₅Na 527.1264, found 527.1268

32

HRMS [M+H] calcd. for $C_{31}H_{54}IO_6$ 677.2728, found 677.2727

33

HRMS [M+H] calcd. for $C_{31}H_{54}IO_6$ 677.2728, found 677.2732

34

HRMS [M+Na] calcd. for $C_{37}H_{57}IO_6Si$ 775.2861, found 775.2858

35

HRMS [M+H] calcd. for $C_{31}H_{44}IO_6$ 639.2177, found 639.2177

36

HRMS [M+Na] calcd. for $C_{26}H_{37}IO_8Na$ 627.1425, found 627.1422

37

HRMS [M+Na] calcd. for $C_{25}H_{35}IO_7Na$ 585.1319, found 585.1325

38

HRMS [M+Na] calcd. for $C_{31}H_{45}IO_{10}Na$ 727.1947, found 727.1948

39

HRMS [M+Na] calcd. for $C_{29}H_{43}IO_9Na$ 685.1844, found 685.1843

42

HRMS [M+Na] calcd. for $C_{22}H_{31}IO_5Na$ 525.1108, found 525.1108

Physical data for spiroketal products and bis-THF 47

1H -NMR and ^{13}C -NMR spectral charts for these compounds are provided in the appendix.

43a

1H NMR 500 MHz ($CDCl_3$) 1.25 (s, 9H), 1.5 (m, 1H), 1.7-2.2 (m, 9H), 3.55 (m, 2H), 4.07 (dd, J = 11.0, 5.3 Hz, 1H), 4.15 (dd, J = 11.0, 6.3 Hz, 1H), 4.2 (m, 1H), 4.25 (m, 1H), 4.6 (m, 2H), 7.25 (m, 2H), 7.3 (m, 3H). ^{13}C NMR 125 MHz ($CDCl_3$) 27.2, 27.6, 30.3, 34.4, 35.6, 35.8, 38.8, 67.7, 73.0, 75.4, 76.7, 77.2, 114.9, 127.5, 127.6, 128.3, 128.4, 138.6, 178.4. HRMS [M+H] calcd. for $C_{22}H_{33}O_5$ 377.2332, found 377.2319. R_f = 0.5 (4:1 Pet. Ether/EtOAc)

43b

1H NMR 500 MHz ($CDCl_3$) 1.7 (m, 1H), 1.85 (m, 2H), 1.95-2.12 (m, 6H), 2.18 (m, 1H), 3.6 (2H), 4.06 (dd, J = 11.5, 4.9 Hz, 1H), 4.11 (dd, J = 11.5, 4.55 Hz, 1H), 4.2 (m, 1H), 4.3 (m, 1H), 4.5 (m, 2H), 7.25 (2H), 7.3 (m, 3H). ^{13}C NMR 125 MHz ($CDCl_3$) 26.7, 27.2, 30.7, 34.5, 35.7, 37.4, 38.8, 66.0, 67.7, 72.9, 75.3, 77.2, 115.0, 127.5, 127.6, 128.3, 138.7, 178.4.

HRMS [M+H] calcd. for C₂₂H₃₃O₅ 377.2332, found 377.2319. R_f = 0.45 (4:1 Pet. Ether/ EtOAc)

44a

¹H NMR 500 MHz (C₆D₆) 1.05 (m, 21H), 1.37-1.47 (m, 3H), 1.5 (m, 1H), 1.67 (m, 2H), 1.73 (m, 2H), 1.8 (m, 1H), 1.88 (dd, *J* = 14.8, 3.8 Hz, 1H), 1.9-2.0 (m, 4H), 2.08 (s, 3H), 3.5 (t, *J* = 6.7 Hz, 2H), 3.6 (dd, *J* = 9.6, 6.3 Hz, 1H), 3.8 (dd, *J* = 9.6, 6.4 Hz, 1H), 4.08 (m, 1H), 4.22 (m, 1H), 4.5 (s, 2H), 5.08 (bt, *J* = 3.0 Hz, 1H), 7.35 (m, 5H). ¹³C NMR 125 MHz (C₆D₆) 12.0, 17.9, 21.0, 22.6, 27.1, 30.3, 35.0, 35.8, 36.1, 39.2, 64.9, 67.3, 68.6, 70.2, 72.7, 81.8, 105.2, 126.7- 128.2, 139.3, 169.9. HRMS [M+Na] calcd. for C₃₂H₅₄O₅NaSi 571.3425, found 571.3424. R_f = 0.6 (4:1 Pet. Ether/ EtOAc)

44b

¹H NMR 500 MHz (C₆D₆) 1.1 (m, 21H), 1.45 (m, 3H), 1.7 (m, 6H), 1.8 (s, 3H), 1.95 (m, 1H), 2.07 (dd, *J* = 11.2, 5.08 Hz, 1H), 2.2 (m, 2H), 2.3 (m, 1H), 3.3 (t, *J* = 6.2 Hz, 2H), 3.65 (m, 2H), 3.73 (m, 1H), 4.34 (s, 2H), 4.37 (m, 1H), 5.26 (m, 1H), 7.27 (m, 3H), 7.4 (m, 2H). ¹³C NMR 125 MHz (C₆D₆) 12.1, 18.0, 20.6, 22.8, 26.4, 29.9, 34.8, 35.0, 35.8, 36.1, 38.2, 66.0, 68.0, 70.0, 70.2, 72.7, 78.8, 106.8, 126.8-128.3, 139.3, 169.0. HRMS [M+Na] calcd. for C₃₂H₅₄O₅NaSi 571.3425, found 571.3424. R_f = 0.7 (4:1 Pet. Ether/ EtOAc)

45a

¹H NMR 500 MHz (CDCl₃) 1.2 (m, 21H), 1.3 (qt, *J* = 11.6 Hz, 1H), 1.4 (m, 1H), 1.5 (m, 1H), 1.56 (m, 2H), 1.8 (m, 3H), 1.95 (m, 1H), 2.1 (s, 3H), 2.2 (ddd, *J* = 11.9, 4.7, 1.6 Hz, 1H), 3.5 (t, *J* = 6.3 Hz, 1H), 3.77 (dd, *J* = 9.4, 7.6 Hz, 1H), 3.9 (m, 1H), 4.1 ((dd, *J* = 9.4, 5.5 Hz, 1H), 4.3 (m, 1H), 4.5 (m, 2H), 5.6 (m, 1H), 7.1 (t, *J* = 7.4 Hz, 1H), 7.2 (t, *J* = 7.4 Hz, 2H), 7.3 (d, *J* = 7.4 Hz, 2H). ¹³C NMR 125 MHz (C₆D₆) 12.0, 18.0, 21.3, 22.4, 27.5, 29.9, 35.8, 37.0, 38.5, 39.3, 67.6, 68.2, 68.8, 70.3, 72.9, 81.4, 106.5, 127.5, 127.6, 128.3, 138.7, 170.3. HRMS [M+Na] calcd. for C₃₂H₅₄O₅NaSi 571.3425, found 571.3427. R_f = 0.7 (8.5:5 Pet. Ether/ EtOAc)

45b

¹H NMR 500 MHz (C₆D₆) 1.1 (m, 21H), 1.22 (m, 1H), 1.3 (m, 1H), 1.55 (m, 6H), 1.7 (s, 3H), 1.8 (m, 2H), 1.9 (m, 1H), 1.95 (m, 1H), 2.0 (t, *J* = 12 Hz, 1H), 2.2 (m, 1H), 3.1 (m, 1H), 3.3 (t, *J* = 6.0 Hz, 2H), 3.6 (m, 2H), 4.3 (m, 3H), 4.9 (m, 1H), 7.1 (m, 3H), 7.3 (bd, *J* = 7.0 Hz, 2H). ¹³C NMR 125 MHz (CDCl₃) 11.9, 17.9, 21.3, 22.3, 26.2, 29.6, 29.7, 32.2, 35.7, 37.1, 40.0, 65.2, 69.3, 70.3, 70.5, 72.9, 79.0, 107.5, 127.5, 127.6, 128.3, 138.7, 170.5. HRMS [M+H] calcd. for C₃₂H₅₅O₅Si 549.3605, found 549.3606. R_f = 0.6 (8.5:5 Pet. Ether/ EtOAc)

47

¹H NMR 500 MHz (CDCl₃) 1.2 (s, 9H), 1.4 (m, 2H), 1.6 (m, 1H), 1.9 (m, 6H), 2.05 (m, 1H), 3.55 (m, 2H), 3.75 (m, 1H), 3.9 (m, 1H), 3.95 (m, 1H), 4.1 (m, 4H), 4.55 (m, 4H), 7.27 (m, 10H). ¹³C NMR 125 MHz (CDCl₃) 27.2, 27.6, 31.7, 31.8, 32.2, 35.9, 38.8, 67.0, 68.0, 70.2, 71.1, 77.2, 73.0, 74.6, 77.2, 80.4, 127.4-128.5, 138.5, 138.8, 178.3. HRMS [M+Na] calcd. for C₃₁H₄₂O₆Na 533.2873, found 533.2870. R_f = 0.7 (6.5:3.5 Pet. Ether/ EtOAc)

48a

¹H NMR 500 MHz (C₆D₆) 1.0 (s, 3H), 1.3 (m, 1H), 1.5 (s, 3H), 1.7 (m, 3H), 1.8-2.1 (m, 5H), 2.25 (m, 1H), 2.98 (s, 3H), 3.5 (t, *J* = 6.1 Hz, 2H), 4.2 (d, *J* = 10.5 Hz, 1H), 4.26 (m, 1H), 4.28 (s, 2H), 4.38 (m, 1H), 4.6 (d, *J* = 6.0 Hz, 1H), 5.0 (d, *J* = 6.0 Hz, 1H), 5.04 (s, 1H), 7.12 (m, 1H), 7.18 (m, 2H), 7.3 (t, *J* = 7.5 Hz, 1H). ¹³C NMR 125 MHz (C₆D₆) 24.5, 26.4, 27.9, 30.5, 34.0, 34.5, 36.5, 54.1, 67.5, 72.7, 75.5, 77.7, 82.6, 85.5, 89.0, 109.7, 111.8, 115.4, 127.5-128.3, 139.1. HRMS [M+Na] calcd. for C₂₄H₃₄O₇Na 457.2196, found 457.2202 R_f = 0.7 (4:1 Pet. Ether/ EtOAc)

48b

¹H NMR 500 MHz (C₆D₆) 1.1 (s, 3H), 1.5 (s, 3H), 1.62 (m, 2H), 1.75 (m, 1H), 1.82 (m, 1H), 1.95 (m, 4H), 2.15 (m, 1H), 2.25 (m, 1H), 3.05 (s, 3H), 3.62 (m, 2H), 4.05 (m, 1H), 4.22 (m, 1H), 4.35 (s, 2H), 4.55 (d, *J* = 10.1 Hz, 1H), 4.65 (d, *J* = 6.0 Hz, 1H), 5.05 (d, *J* = 6.0 Hz, 1H), 5.06 (s, 1H), 7.1 (t, *J* = 8.0 Hz, 1H), 7.18 (m, 2H), 7.32 (d, *J* = 8.0 Hz, 1H). ¹³C NMR 125 MHz (C₆D₆) 27.4, 26.4, 29.0, 31.0, 35.3, 35.7, 37.8, 54.2, 67.8, 72.6, 77.3, 79.1, 82.8, 85.6, 90.8, 109.7, 111.8, 114.8, 127.2-128.4, 139.7. . HRMS [M+Na] calcd. for C₂₄H₃₄O₇Na 457.2196, found 457.2202. R_f = 0.6 (4:1 Pet. Ether/ EtOAc)

49a

¹H NMR 500 MHz (C₆D₆) 1.18 (m, 4H), 1.25(s, 9H), 1.48 (m, 4H), 1.6 (m, 2H), 1.85 (m, 1H), 2.0 (dd, *J* = 12.1, 7.7 Hz, 1H), 2.07 (m, 1H), 2.2 (m, 1H), 2.98 (s, 3H), 3.9 (m, 1H), 4.0 (dd, *J* = 10.8, 2.3 Hz, 1H), 4.1 (m, 1H), 4.3 (m, 2H), 4.4 (d, *J* = 9.9 Hz, 1H), 4.95 (d, *J* = 6.0 Hz, 1H), 5.02 (s, 1H), 7.2 (m, 3H), 7.3 (d, *J* = 8.0 Hz, 2H). ¹³C NMR 125 MHz (C₆D₆) 24.9, 26.8, 27.7, 28.4, 33.9, 38.9, 40.3, 54.8, 67.4, 70.0, 72.7, 80.7, 83.3, 86.0, 90.7, 107.6, 110.5, 112.4, 127.5-128.6, 139.8, 177.9. HRMS [M+Na] calcd. for C₂₉H₄₂O₉Na 557.2721, found 557.2722. R_f = 0.8 (4:1 Pet. Ether/ EtOAc)

49b

¹H NMR 500 MHz (C₆D₆) 1.25 (m, 5H), 1.5 (s, 3H), 1.66 (m, 2H), 1.85-1.95 (m, 3H), 2.05 (m, 1H), 3.0 (s, 3H), 3.2 (m, 1H), 3.3 (m, 1H), 4.06 (dd, *J* = 11.3, 4.1 Hz, 1H), 4.2 (m, 1H), 4.25-4.35 (m, 3H), 4.5 (d, *J* = 6.0 Hz, 1H), 4.95 (d, *J* = 6.0 Hz, 1H), 5.05 (s, 1H), 7.18 (m, 3H), 7.28 (d, *J* = 7.8 Hz, 2H).). ¹³C NMR 125 MHz (C₆D₆) 24.4, 26.3, 27.0, 27.4, 31.5, 33.7, 38.5, 40.6, 54.5, 66.5, 69.1, 69.3, 72.7, 77.8, 82.5, 85.5, 88.7, 107.6, 109.9, 111.8, 127.5-128.3, 139.0, 177.2. HRMS [M+Na] calcd. for C₂₉H₄₂O₉Na 557.2721, found 557.2722. R_f = 0.7 (4:1 Pet. Ether/ EtOAc)

50a

¹H NMR (500 MHz, CDCl₃) δ 1.50-1.47 (m, 1H), 1.71-1.58 (ovrlp m, 4H), 1.92-1.80 (ovrlp m, 3H), 2.03-1.98 (m, 1H), 2.10-2.06 (m, 2H), 2.27-3.24 (dd, *J* = 5.0, 12.5 Hz, 1H), 3.62-3.59 (ovrlp m, 2H), 3.68-3.66 (dd, *J* = 1.7, 10.7 Hz, 1H), 3.80-3.75 (ovrlp m, 2H), 3.92-3.88 (ddd, *J* = 1.8, 4.1, 9.9 Hz, 1H), 4.08-4.05 (m, 1H), 4.71-4.52 (m, 5H), 4.95-4.93 (d, *J* = 11.1 Hz, 1H), 7.38-7.27 (m, 15H); ¹³C NMR (125 MHz, CDCl₃) δ 20.2, 25.1, 35.3, 35.9, 36.1, 40.4, 62.3, 69.2, 71.8, 72.1, 73.3, 75.0, 78.4, 79.0, 107.1, 107.2, 127.4, 127.5, 127.6, 127.7, 127.8, 128.0, 128.3, 128.4, 138.4, 138.6, 138.7, ESIHRMS (M+Na)⁺ calculated for C₃₄H₄₀O₆Na 567.2717, found 567.2723. R_f = 0.3 (4:1 Pet. Ether/ EtOAc)

50b

¹H NMR (500 MHz, CDCl₃) δ 1.83-1.76 (ovrlp m, 3H), 1.95-1.90 (m, 1H), 2.08-2.06 (m, 1H), 2.15-2.11 (m, 1H), 2.21-2.18 (m, 1H), 2.33-2.29 (m, 1H), 3.68-3.66 (m, 2H), 3.74-3.72 (m, 1H), 3.86-3.84 (ovrlp m, 2H), 3.98 (m, 1H), 4.00 (m, 1H), 4.70-4.54 (m, 5H), 4.93-4.91 (d, *J* = 11.1 Hz, 1H), 7.38-7.07 (m, 15H); ¹³C NMR (125 MHz, CDCl₃) δ 20.0, 25.1, 35.1, 36.7, 37.3, 40.6, 62.8, 69.1, 71.8, 73.3, 73.4, 75.0, 78.4, 78.8, 107.4, 107.6, 121.8, 127.5, 127.6, 127.7, 127.8, 128.0, 128.1, 128.3, 128.4, 138.8; ESIHRMS (M+Na)⁺ calculated for C₃₄H₄₀O₆Na 567.2717, found 567.2723. R_f = 0.2 (4:1 Pet. Ether/ EtOAc)

51a/b

¹H NMR (CDCl₃) δ 1.20 (s, 9 H, major), 1.21 (s, 9H, minor), 1.66-1.77 (m, 2H), 1.88-1.95 (m, 2H), 2.02-2.13 (m 5H), 2.32 (tdd, *J*=2.9, 4.3, 17.3 Hz, 1H), 2.40 (qd, *J*=3.0, 17.3 Hz, 1H), 2.53 (tdd, *J*=2.5, 4.0, 17.6 Hz, 1H), 3.89-4.05 (m, 2H), 4.07-4.13 (m, 2H), 4.21 (dd, *J*=6.1, 11.1 Hz, 1H), 4.29 (dd, *J*=7.3, 10.8 Hz, 1H), 4.43 (br. 1H), 5.67-5.73 (m, 2H), 5.84-5.94 (m, 2H). ¹³C NMR (CDCl₃) δ 23.8 (major), 24.0 (minor), 27.3 (major), 27.4 (minor), 33.0 (major), 33.3 (minor), 36.5 (minor), 37.4 (major), 38.0 (major + minor), 65.8, 66.6, 67.8, 67.9, 68.1, 71.4, 105.0 (major), 105.1 (minor), 124.6, 124.7, 124.9, 125.4, 178.5 (major + minor). HRMS [M+Na] calcd. for C₁₄H₂₂O₄ Na 277.1410, found 277.1413. R_f = 0.4 (85:15 Pet. Ether/ EtOAc).