Supporting Information

Permanganate oxidation of 1,5,9-trienes: Stereoselective synthesis of tetrahydrofuran-containing fragments

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166.2425
166.1077
166.0328

136.5579
131.5406
124.1868
123.2133

105.4055
105.3456

77.4882
77.0688
76.6494

64.7876
64.6977
60.0398

32.0476
31.9727
31.8679
26.5360
25.6673
25.2031
23.3459
17.5947
16.0820
15.9921
14.1949

(ppm)

166.2875
166.1527
166.1077

136.5878
131.3758
124.2167
122.2847

105.4954
105.4504

77.4582
77.0388
76.6045

64.8025
64.7127
60.0698

39.6560

31.8229
31.7480
26.6558
25.6524
25.2929
17.6396
16.0970
16.0071
14.2098

S14

12c

— 177.1159

— 172.6677

87.2982

85.1415

83.3592

77.4582

77.0239

76.6045

76.1702

— 62.0767

— 35.4174

29.4416

28.4681

28.0787

23.9150

23.8401

— 14.1649

S20

173.0955
177.5680

136.7676
131.5406
124.0969
122.2997
112.0853

77.4282
77.0089
76.5895

29.7112
26.6259
25.8171
25.6823
19.6615
17.6696
16.0670

41.3184
39.6560

S32

Ethyl (2*Z*,6*E*)-3-[(diethoxyphosphoryl)oxy]-7,11-dimethyl-2,6,10-dodecatrienoate (11c).

Following the general procedure for the preparation of *Z*-enol phosphate **11a**, β -keto ester **15** (1 g, 3.75 mmol) afforded **11c** as a yellow oil (1.20 g, 2.97 mmol, 79%). IR ν_{max} (neat) 1721, 1665, 1445, 1281, 1025; ^1H NMR (400 MHz) δ 5.34 (1H, s), 5.11-5.03 (2H, m), 4.25 (4H, quintet, $J = 7.4$ Hz), 4.13 (2H, q, $J = 7.1$ Hz), 2.44 (2H, t, $J = 7.4$ Hz), 2.25 (2H, q, $J = 7.1$ Hz), 2.15-1.92 (4H, m), 1.66 (3H, s), 1.60 (3H, s), 1.58 (3H, s), 1.34 (6H, t, $J = 7.4$ Hz), 1.25 (3H, t, $J = 7.4$ Hz); ^{13}C NMR (100 MHz) 163.9, 161.5, 137.1, 131.6, 124.3, 121.9, 105.5, 64.8 (d, $J = 5.6$ Hz), 60.0, 39.7, 35.4, 26.7, 25.8, 25.0, 17.8, 16.1 (d, $J = 6.7$ Hz), 14.4; MS (CI) m/z (relative intensity) 403 (3, $[\text{M}+\text{H}]^+$); Anal. Calcd for $\text{C}_{20}\text{H}_{35}\text{O}_6\text{P}$: C, 59.70; H, 8.76. Found: C, 59.94; H, 8.87.

Ethyl (2*E*,6*E*)-3-[(diethoxyphosphoryl)oxy]-7,11-dimethyl-2,6,10-dodecatrienate (11d).

Following the general procedure for the preparation of *E*-enol phosphates, β -keto ester **15** (2.00 g, 7.51 mmol) afforded **11d** as a very pale yellow oil (2.30 g, 5.71 mmol, 76%). IR ν_{max} (neat) 1721, 1644, 1281, 1030; ^1H NMR (400 MHz) δ 5.84 (1H, s), 5.16, (1H, t, J = 7.4 Hz), 5.08 (1H, t, J = 5.9 Hz), 4.20 (4H, quintet, J = 7.4 Hz), 4.15 (2H, q, J = 7.1 Hz), 2.83 (2H, t, J = 7.7 Hz), 2.28 (2H, q, J = 7.4 Hz), 2.11-1.92 (4H, m), 1.67 (3H, s), 1.62 (3H, s), 1.37 (6H, t, J = 7.0 Hz), 1.26 (3H, t, J = 7.0 Hz); ^{13}C NMR (100 MHz) 166.4, 166.3, 136.7, 131.5, 124.4, 122.4, 105.6, 64.9 (d, J = 6.7 Hz), 60.2, 39.8, 32.0, 31.9, 26.8, 25.8, 25.4, 17.8, 16.2 (d, J = 6.7 Hz), 14.4; MS (CI) m/z (relative intensity) 425.2 (100, $[\text{M}+\text{Na}]^+$); HRMS Calcd for $\text{C}_{20}\text{H}_{35}\text{PO}_6\text{Na}$: 425.2063. Found: 425.2071 (100, $[\text{M}+\text{Na}]^+$).

Ethyl (2Z,6Z)-3,7,11-trimethyl-2,6,10-dodecatrienoate (12b).

Following the general procedure for the preparation of **12a**, enol phosphate **11b** (800 mg, 1.99 mmol) afforded **12b** as a pale yellow oil (434 mg, 1.64 mmol, 82%). ¹H NMR data were in agreement with the literature,¹⁴ additional data provided. IR ν_{max} (neat) 1716, 1644; ¹³C NMR (100 MHz) 166.4, 160.2, 135.9, 131.6, 124.6, 124.5, 116.4, 59.5, 33.8, 32.0, 26.8, 25.9, 25.5, 23.5, 17.8, 14.5; MS (CI) m/z (relative intensity) 265 (8, [M+H]⁺), 264 (13, [M]⁺), 69 (100).

Ethyl (2Z,6E)-3,7,11-trimethyl-2,6,10-dodecatrienoate (12d).

Following the general procedure for the preparation of **12a**, enol phosphate **11d** (660 mg, 1.64 mmol) afforded **12d** as a colourless oil (420 mg, 1.59 mmol, 97%). ¹H-NMR data were in agreement with the literature,²⁰ additional data provided. IR ν_{max} (neat) 1716, 1650; ¹³C NMR (100 MHz) 166.5, 160.4, 135.9, 131.5, 124.5, 123.7, 116.4, 59.6, 39.8, 33.6, 26.8, 25.8, 25.5, 17.8, 16.1, 14.5; MS (CI) m/z (relative intensity) 265 (5, [M+H]⁺), 264 (12, [M]⁺), 69 (100).

Ethyl (2*S**)-2-hydroxy-2-[(2*R**, 2'*S**, 5*S**)-5'-hydroxy-5'-(1-hydroxy-1-methyl-ethyl)-5,2'-dimethyl-octahydro-[2,2']bifuranyl-5-yl] ethanoate (**16b**).

Following the general procedure for the KMnO_4 oxidation of trienoates, **12b** (360 mg, 1.36 mmol) afforded the crude title lactol **16b** (510 mg crude) as a colourless oil that was used in the next reaction without purification. Selected characterisation data for major hemiacetal epimer: ^{13}C NMR (100 MHz) 173.0, 109.4, 86.4, 84.7, 84.1, 76.2, 73.5, 62.3, 34.7, 33.1, 29.4, 27.6, 25.1, 24.8, 24.0, 22.5, 14.3.

Ethyl (2*S**)-2-hydroxy-2-[(2*R**,2'*S**,5*S**)-2',5-dimethyl-5'-oxo-octahydro-[2,2']bifuranyl-5-yl] ethanoate (**17b**).

To a vigorously stirred suspension of NaIO₄-SiO₂ reagent (6 g) in dry CH₂Cl₂ (20 mL) was added a solution of crude lactol **16b** (510 mg) in dry CH₂Cl₂ (10 mL). The resulting mixture was stirred for 40 min, then the solids were removed by filtration washing with CHCl₃. The resulting solution was concentrated under reduced pressure to give a yellow oil (400 mg). Purification on SiO₂ (35 g) eluting with CH₂Cl₂ / EtOAc (85:15) gave the title lactone **17b** as a colourless oil (0.63 mmol, 180 mg, 46% from **12b**). IR ν_{max} (neat) 3483, 1767, 1737; ¹H NMR (400 MHz) δ 4.26 (2H, q, J = 7.0 Hz), 4.07 (1H, dd, J = 5.9, 9.6 Hz), 4.03 (1H, s), 3.05 (1H, br), 2.79 (1H, ddd, J = 7.4, 10.3, 17.5 Hz), 2.54 (1H, ddd, J = 5.1, 10.3, 17.5 Hz), 2.26-2.40 (2H, m), 1.82-1.99 (2H, m), 1.59-1.80 (2H, m), 1.38 (3H, s), 1.32 (3H, t, J = 7.0 Hz), 1.23 (3H, s); ¹³C NMR (100 MHz) 177.0, 174.0, 87.2, 84.6, 83.2, 76.0, 62.0, 34.2, 29.5, 28.6, 27.1, 23.7, 22.7, 14.1; MS (ES) m/z (relative intensity) 309.1 (49, [M+Na]⁺), 304.1 (100, [M+NH₄]⁺); HRMS (CI) Calcd for C₁₄H₂₃O₆: 287.1495. Found: 287.1484 (92, [M+H]⁺).

Ethyl (2*R**)-2-hydroxy-2-[(2*R**, 2'*R**, 5*S**)-5'-hydroxy-5'-(1-hydroxy-1-methyl-ethyl)-5,2'-dimethyl-octahydro-[2,2']bifuranyl-5-yl] ethanoate (**16c**).

Following the general procedure for the KMnO_4 oxidation of trienoates, **12c** (97 mg, 0.38 mmol) afforded the crude title lactol **16c** (140 mg crude) as a colourless oil that was used in the next reaction without purification. Selected data: ^{13}C NMR (selected signals from crude) (100 MHz) 173.3, 109.5, 86.1, 84.8, 83.2, 76.7, 73.2, 61.2, 36.6, 32.4, 31.7, 27.5, 24.4, 23.9, 23.7, 23.5, 14.1.

Ethyl (2*R**)-2-hydroxy-2-[(2*R**, 2'*R**, 5*S**)-2',5-dimethyl-5'-oxo-octahydro-[2,2']bifuran-5-yl] ethanoate (**17c**).

Following the general procedure for the Pb(OAc)₄ cleavage of lactol **16a**, crude **16c** (110 mg, 0.31 mmol) afforded the title lactone **17c** as a pale yellow oil (37 mg, 0.14 mmol, 46% from **12c**). IR ν_{max} (neat) 3473, 1767, 1731; ¹H NMR (400 MHz) δ 4.28 (1H, dd, *J* = 7.1, 10.8 Hz), 4.23 (1H, dd, *J* = 7.1, 10.8 Hz), 3.99 (1H, s), 3.94 (1H, dd, *J* = 6.7, 8.3 Hz), 2.78-2.89 (1H, m), 2.49 (1H, ddd, *J* = 4.0, 10.5, 17.5 Hz), 2.44 (1H, ddd, *J* = 4.0, 10.5, 12.8 Hz), 2.35 (1H, ddd, *J* = 4.8, 9.0, 12.5 Hz), 1.88-2.14 (3H, m), 1.70 (1H, dt, *J* = 8.3, 12.6 Hz), 1.36 (3H, s), 1.30 (3H, t, *J* = 7.0 Hz), 1.18 (3H, s); ¹³C NMR (100 MHz) 177.9, 172.1, 85.7, 85.0, 84.5, 76.4, 61.6, 35.3, 32.0, 29.5, 26.8, 24.2, 22.4, 14.1; MS (ES) *m/z* (relative intensity) 595.1 (100, [2M+Na]⁺), 309.0 (28, [M+Na]⁺), 304.1 (70, [M+NH₄]⁺); HRMS (CI) Calcd for C₁₄H₂₃O₆: 287.1495. Found: 287.1495 (87, [M+H]⁺).

Ethyl (2*S**)-2-hydroxy-2-[(2*R**, 2'*R**, 5*S**)-5'-hydroxy-5'-(1-hydroxy-1-methyl-ethyl)-5,2'-dimethyl-octahydro-[2,2']bifuranyl-5-yl] ethanoate (**16d**).

Following the general procedure for the KMnO_4 oxidation of trienoates, **12d** (200 mg, 0.76 mmol) afforded the crude title lactol **16d** (240 mg crude) as a colourless oil that was used in the next reaction without purification. ^{13}C NMR (100 MHz) 171.8, 109.7, 85.0, 84.8, 82.9, 77.3, 73.3, 61.5, 33.4, 32.7, 31.9, 28.0, 24.7, 24.5, 24.2, 24.0, 14.3; MS (ES) m/z (relative intensity) 369 (100, $[\text{M}+\text{Na}]^+$).

Ethyl (2*S**)-2-hydroxy-2-[(2*R**, 2'*R**, 5*S**)-5'-hydroxy-5'-(1-hydroxy-1-methyl-ethyl)-5,2'-dimethyl-octahydro-[2,2']bifuranyl-5-yl] ethanoate (**17d**).

Following the general procedure for the Pb(OAc)₄ cleavage of lactol **16a**, crude **16d** (60 mg, from 0.19 mmol of **12d**) afforded the title lactone **17d** (24 mg, 0.09 mmol, 44% from **12d**) as a colourless oil which solidified on standing. Recrystallisation from EtOAc/hexane gave colourless needles suitable for x-ray structural determination. mp 52-55°C; IR ν_{max} (neat) 3483, 1768, 1734; ¹H NMR (400 MHz) δ 4.28 (2H, q, $J = 7.3$ Hz), 4.02 (1H, d, $J = 6.3$ Hz), 3.95 (1H, dd, $J = 7.0, 8.5$ Hz), 3.01 (1H, d, $J = 6.0$ Hz), 2.87 (1H, apparent ddd, $J = 7.2, 9.8, 17.8$ Hz), 2.41-2.52 (2H, m), 2.35 (1H, ddd, $J = 5.0, 8.8, 12.8$ Hz), 1.87-2.07 (3H, m), 1.69 (1H, dt, $J = 8.3, 12.8$ Hz), 1.36 (3H, s), 1.32 (3H, t, $J = 7.0$ Hz), 1.20 (3H, s); ¹³C NMR (100 MHz) 177.6, 173.1, 85.5, 84.7, 84.6, 75.6, 61.9, 34.6, 31.8, 29.5, 26.0, 24.3, 22.0, 14.2; MS (ES) m/z (relative intensity) 325.0 (31, [M+K]⁺), 309.1 (49, [M+Na]⁺), 304.2 (100, [M+NH₄]⁺).