Mild Functionalization of Tetraoxane Derivatives via Olefin Metathesis: Compatibility of Ruthenium Alkylidene Catalysts with Peroxides

Anupam Jana and Karol Grela*

Biological and Chemical Research Centre, Department of Chemistry, University of Warsaw, Żwirki i Wigury 101, 02-089 Warsaw, Poland
*K.G.: tel, +48-22-8220211 ext. 420; fax, +48-22-8220211; email: prof.grela@gmail.com

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General information
All reactions were carried out under argon atmosphere in oven-dried glassware with magnetic stirring. Commercially available chemicals were used without further purification. Grubbs II catalyst was purchased from Aldrich (catalogue no 569747), and nitro-Hoveyda-Grubbs catalyst from Stream (catalogue no 44-0758) and TCI (catalogue no N1060). Solvents were distilled prior to use by Solvent Purification System, Mbraun MB-SPS-800. Analytical thin-layer chromatography (TLC) was performed on silica gel 60 with fluorescent indicator UV254 TLC plates. The spots were visualized staining with a solution of vanillin (15 g vanillin, 250 mL EtOH and 2.5 mL H$_2$SO$_4$), followed by heat. Flash column chromatography was performed using silica gel 60 (particle size 0.040–0.063 mm) typically using a n-hexane/ethyl acetate eluent system. FT-IR spectra were recorded with Thermo Scientific™ Nicolet™ iSTM50 FT-IR spectrometer. NMR spectra were measured at room temperature on an Agilent Mercury 400 MHz spectrometer. NMR spectra were calibrated to the solvent residual signals of CDCl$_3$. $^1$H NMR spectra were recorded at 400 MHz. Data are reported as follows: chemical shift, multiplicity (s: singlet, d: doublet, t: triplet, q: quartet, qui: quintuplet, m: multiplet), coupling constant ($J$ in Hz) and integration. $^{13}$C NMR spectra were recorded at 100 MHz using broadband proton decoupling and chemical shifts are reported in ppm using residual solvent peaks as reference. Carbon multiplicities were assigned by DEPT techniques. HOMO decoupled spectra was measured on an Agilent DD2 600 MHz spectrometer. High resolution mass spectra were recorded on a MS (ESI) spectra LCMS-IT TOF Shimadzu. HPLC was performed using chromatograph equipped with WatSIL Si 100/5 µm with hexane/i-PrOH as the eluent.

A usual workup of the reaction mixture consists of extraction with ether or ethyl acetate, washing with water, brine, drying over Na$_2$SO$_4$, and then concentrated under reduced pressure on a rotary evaporator unless specified. Reported yields are based upon isolation following purification by silica gel column chromatography; isolated material were judged to be homogeneous based upon TLC and NMR.
but-3-en-1-yl dispirol[adamantane-2,3'-[1,2,4,5]tetraoxane-6',1''-cyclohexane]-4''-carboxylate (12)

To a stirred solution of carboxylic acid A (600 mg, 1.85 mmol) in 8 ml anhydrous CH$_2$Cl$_2$ was added 11 mg DMAP and alcohol B (272 mg, 3.7 mmol). Then, DCC (771 mg, 3.7 mmol) was added to the reaction mixture at 0°C, which is stirred for 1 h. Then reaction mixture was diluted with ethyl acetate and quenched with sat. NH$_4$Cl solution (2 ml). After usual work up and flash chromatography (2% EA/hex.) pure product (515 mg, 74%) 12 was isolated. Colourless liquid; IR $\nu$ max 2909, 1730, 1449, 1173, 1109, 996, 924 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 5.80-5.73 (m, 1H), 5.12-5.03 (m, 2H), 4.13 (q, $J$ = 6.8 Hz, 2H), 3.14 (s, 1H), 2.88 (s, 1H), 2.40-2.33 (m, 3H), 2.10-1.41 (m, 20H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 174.6, 134.1, 117.4, 110.6, 107.3, 63.5, 41.7, 34.5, 33.2, 30.5, 28.3, 27.2, 24.8, 24.1; ESI-HRMS calcd. For C$_{21}$H$_{30}$O$_6$Na (M+Na$^+$) 401.1938, found 401.1940.

Similarly-

but-3-en-1-yl 7,8,15,16-tetraoxadispiro[5.2.5.26]hexadecane-3-carboxylate (14)

Colourless liquid; Yield: 67%; IR $\nu$ max 2938, 2861, 1445, 1325, 1259, 1731, 1177, 1030, 922, 641 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 5.82-5.71 (m, 1H), 5.12-5.06 (m, 2H), 4.13 (t, $J$ = 6.8 Hz, 2H), 2.86 (s, 1H), 2.45-2.43 (m, 3H), 2.27 (s, 2H), 1.94-1.43 (m, 15H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 174.6, 134.1, 117.4, 108.5, 107.4, 63.5, 41.7, 33.2, 31.9, 30.4, 28.2, 25.5, 24.8, 23.9, 22.1; ESI-HRMS calcd. For C$_{17}$H$_{26}$O$_6$Na (M+Na$^+$) 349.1627, found 349.1619.

but-3-en-1-yl 7,8,16,17-tetraoxadispiro[5.2.6.26]heptadecane-3-carboxylate (15)

Colourless liquid; Yield: 71%; IR $\nu$ max 2932, 2860, 1729, 1446, 1356, 1318, 1255, 1191, 1172, 1009, 988, 920, 736 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 5.79-5.70 (m, 1H), 5.13-5.04 (m, 2H), 4.12 (t, $J$ = 6.8 Hz, 2H), 2.82 (s, 1H), 2.42-2.34 (m, 5H), 1.92-1.56 (m, 17H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 174.6, 134.1, 117.4, 113.3, 106.9, 63.5, 41.7, 36.2, 33.2, 31.1, 30.4, 29.7, 28.3, 24.8, 23.9, 22.7, 22.5; ESI-HRMS calcd. For C$_{18}$H$_{28}$O$_6$Na (M+Na$^+$) 363.1784, found 363.1773; EA (%) calcd. For C$_{18}$H$_{28}$O$_6$, C 63.51, H 8.29, O 28.20, found C 63.44, H 8.24.
General procedure for cross metathesis:

The tetraoxane containing alkene (0.3 mmol) and cross-partner (0.9 mmol) was dissolved in 5 mL dry dichloromethane. The mixture was stirred at 45 °C for 2-4 h in presence nitro-Hoveyda-Grubbs type catalyst 5 (3 mol %). Reaction was monitored by TLC. After completion (TLC), the reaction mixture was concentrated in vacuo. Purification of the residue by column chromatography [EA/hex] afforded the pure product.

5-acetoxypent-3-en-1-yl (1r,3r,5r,7r)-dispiro[adamantane-2,3'-[1,2,4,5]tetraoxane-6',1''-cyclohexane]-4''-carboxylate (13)

Light yellow liquid; yield 90%; IR νmax 2935, 1728, 1449, 1227, 1174, 1090, 996, 925 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 5.76-5.61 (m, 2H), 4.62 (d, J = 6.0 Hz) and 4.51 (dd, J = 0.8, 6.0 Hz)(2H) (E/Z= 8:1), 4.13 (dd, J = 0.8, 6.0 Hz, 2H), 3.14 (s, 1H), 2.89 (s, 1H), 2.41-2.34 (m, 3H), 2.06 (s, 3H), 2.04 – 1.41 (m, 20H); ¹³C NMR (100 MHz, CDCl₃) δ 174.6, 170.9, 131.2, 126.9, 110.7, 107.3, 64.9, 63.3, 41.8, 37.1, 34.4, 33.3, 31.8, 30.3, 28.3, 27.2, 24.8, 24.0, 21.1; ESI-HRMS calcd. For C₂₄H₃₄O₈Na (M+Na⁺) 473.2151, found 473.2151.

5-chloropent-3-en-1-yl (1r,3r,5r,7r)-dispiro[adamantane-2,3'-[1,2,4,5]tetraoxane-6',1''-cyclohexane]-4''-carboxylate (16)

Colourless liquid; yield 87%; IR νmax 2927, 2858, 1732, 1450, 1172, 1103, 1061, 938, 682 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 5.78-5.65 (m, 2H), 4.13 (d, J = 6.8 Hz, 2H), 4.09 (dd, J = 0.8, 8.0 Hz) and 4.03-4.02 (m)(2H) (E/Z= 6:1), 3.15 (s, 1H), 2.89 (s, 1H), 2.41-2.38 (m, 3H), 2.04 – 1.50 (m, 20H); ¹³C NMR (100 MHz, CDCl₃) δ 174.6, 130.9, 128.9, 110.6, 107.2, 63.2, 45.0, 41.7, 37.1, 34.4, 33.3, 31.7, 30.3, 28.3, 27.2, 24.8, 23.9; ESI-HRMS calcd. For C₂₂H₂₃ClO₆Na (M+Na⁺) 449.1701, found 449.1721.
5-cyclohexylpent-3-en-1-yl (1r,3r,5r,7r)-dispiro[adamantane-2,3’-[1,2,4,5]tetraoxane-6’,1’’-cyclohexane]-4’’-carboxylate (17)

Light yellow liquid; yield 87%; IR ν max 2917, 2852, 1730, 1448, 1254, 1129, 1172, 1060, 997, 925 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 5.52-5.46 (m, 1H), 5.39-5.33 (m, 1H), 4.08 (t, J = 6.4 Hz) and 4.06 (t, J = 6.4 Hz) (2H) (E/Z = 4:1), 3.15 (s, 1H), 2.89 (s, 1H), 2.44-2.27 (m, 3H), 2.04-1.40 (m, 27H), 1.38-0.87 (m, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 174.7, 132.4, 126.2, 110.6, 107.3, 64.2, 41.8, 40.8, 38.1, 37.1, 34.4, 33.3, 33.2, 32.2, 30.5, 28.4, 27.2, 26.7, 26.5, 26.4, 24.8, 24.0; ESI-MS calcd. For C₂₈H₄₂O₆Na (M+Na⁺) 497.2879, found 497.2877.

9-((tert-butyldimethylsilyl)oxy)non-3-en-1-yl (1r,3r,5r,7r)-dispiro[adamantane-2,3’-[1,2,4,5]tetraoxane-6’,1’’-cyclohexane]-4’’-carboxylate (18)

(E/Z = 8:1) by HPLC; light yellow liquid; yield 68%; IR ν max 2935, 1716, 1449, 1182, 1089, 1059, 968, 925 682 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 5.52-5.46 (m, 1H), 5.39-5.33 (m, 1H), 4.08 (t, J = 6.4 Hz, 2H), 3.61 (t, J = 6.0 Hz, 2H), 3.15 (s, 1H), 2.89 (s, 1H), 2.41-2.27 (m, 3H), 2.04-1.36 (m, 26H), 0.89 (s, 9H), 0.04 (s, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 174.7, 133.5, 125.3, 110.6, 107.3, 64.2, 63.2, 41.8, 37.1, 34.4, 33.3, 32.5, 32.4, 32.2, 30.3, 28.3, 27.2, 26.1, 25.7, 24.8, 24.0, 18.5, -5.1; ESI-MS calcd. For C₃₁H₅₂O₇SiNa (M+Na⁺) 587.3375, found 587.3383.

5-phenylpent-3-en-1-yl (1r,3r,5r,7r)-dispiro[adamantane-2,3’-[1,2,4,5]tetraoxane-6’,1’’-cyclohexane]-4’’-carboxylate (19)

Colourless liquid; yield 77%; IR ν max 2907, 1722, 1450, 1193, 1177, 1137, 996, 924, 698 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.23-7.01 (m, 5H), 5.63-5.56 (m, 1H), 5.42-5.35 (m, 1H), 4.08-4.03 (m, 2H), 3.35 (d, J = 6.8 Hz) and 3.27 (d, J = 6.8 Hz)(E/Z = 5:1), 3.08 (s, 1H), 2.83 (s, 1H), 2.44-2.25 (m, 3H), 2.04 – 1.50 (m, 20H); ¹³C NMR (100 MHz, CDCl₃) δ 174.7, 140.6, 132.2, 128.6, 128.6, 128.5, 126.8, 126.2, 110.6, 107.3, 63.9, 41.8, 39.2, 37.1, 34.5, 33.3, 32.1, 30.4, 28.3, 27.2, 26.2, 24.8, 24.0; ESI-MS calcd. For C₂₉H₃₆O₃Na (M+Na⁺) 491.2410, found 491.2408.
5-acetoxypent-3-en-1-yl 7,8,15,16-tetraoxadispiro[5.2.59.26]hexadecane-3-carboxylate (20)

Light yellow liquid; yield 89%; IR ν max 2939, 1730, 1449, 1229, 1174, 1058, 943, 735, 518 cm⁻¹; 1H NMR (400 MHz, CDCl₃) δ 5.74-5.62 (m, 2H), 4.62 (d, J = 6.0 Hz) and 4.51 (dd, J = 0.8, 6.0 Hz)(2H) (E/Z = 6:1), 4.12 (t, J = 6.8 Hz, 2H), 2.89 (s, 1H), 2.46-2.31 (m, 3H), 2.22 (s, 2H), 2.07 (s, 3H), 31.8, 30.5, 29.7, 28.3, 25.5, 24.8, 23.9, 22.2, 21.1; ESI-HRMS calcld. For C₂₀H₃₀O₈Na (M+Na⁺) 421.1833, found 421.1839; EA (%) calcld. For C₂₀H₃₀O₈, C 60.29, H 7.59, O 32.12, found C 60.30, H 7.42.

![Chemical structure of 5-acetoxypent-3-en-1-yl 7,8,15,16-tetraoxadispiro[5.2.59.26]hexadecane-3-carboxylate (20)](image)

5-chloropent-3-en-1-yl 7,8,15,16-tetraoxadispiro[5.2.59.26]hexadecane-3-carboxylate (21)

Colourless liquid; yield 89%; IR ν max 2935, 2859, 1731, 1448, 1358, 1160, 1090, 996, 925, 509 cm⁻¹; 1H NMR (400 MHz, CDCl₃) δ 5.76-5.62 (m, 2H), 4.13 (t, J = 6.4 Hz, 2H), 4.62 (d, J = 8.0 Hz) and 4.03-4.01 (m)(2H) (E/Z = 6:1), 2.87 (s, 1H), 2.44-2.37 (m, 3H), 2.27 (s, 2H), 1.94-1.44 (m, 15H); 13C NMR (100 MHz, CDCl₃) δ 174.6, 130.9, 128.9, 108.6, 107.4, 63.2, 45.0, 41.7, 31.9, 31.7, 30.4, 29.7, 28.2, 25.5, 24.8, 23.9, 22.1; ESI-HRMS calcld. For C₁₈H₂₇ClO₆Na (M+H⁺) 397.1387, found 397.1387; EA (%) calcld. For C₁₈H₂₇ClO₆, C 57.67, H 7.26, O 25.61, Cl 9.46, found C 57.63, H 7.11, Cl 9.57.

![Chemical structure of 5-chloropent-3-en-1-yl 7,8,15,16-tetraoxadispiro[5.2.59.26]hexadecane-3-carboxylate (21)](image)

5-acetoxypent-3-en-1-yl 7,8,16,17-tetraoxadispiro[5.2.69.26]heptadecane-3-carboxylate (22)

Light yellow liquid; yield 78%; IR ν max 2933, 2861, 1732, 1446, 1361, 1317, 1229, 1191, 1171, 1067, 1033, 967, 775 cm⁻¹; 1H NMR (400 MHz, CDCl₃) δ 5.74-5.63 (m, 2H), 4.62 (d, J = 6.0 Hz) and 4.51 (dd, J = 0.8, 6.0 Hz)(2H) (E/Z = 6:1), 4.12 (t, J = 6.8 Hz, 2H), 2.83 (s, 1H), 2.46-2.36 (m, 5H), 2.06 (s, 3H), 2.04-1.57 (m, 17H); 13C NMR (100 MHz, CDCl₃) δ 174.6, 130.9, 128.9, 106.9, 107.4, 63.2, 45.0, 41.7, 31.9, 30.4, 29.7, 28.3, 24.8, 23.9, 22.6, 22.5, 21.1; ESI-HRMS calcld. For C₂₁H₃₂O₈Na (M+Na⁺) 435.1989, found 435.2007.

![Chemical structure of 5-acetoxypent-3-en-1-yl 7,8,16,17-tetraoxadispiro[5.2.69.26]heptadecane-3-carboxylate (22)](image)

(E)-5-methoxy-5-oxopent-3-en-1-yl 7,8,16,17-tetraoxadispiro[5.2.69.26]heptadecane-3-carboxylate (23)

Colourless liquid; yield 89%; IR ν max 2933, 2860, 1723, 1457, 1316, 1270, 1191, 1170, 1066, 985, 924, 735 cm⁻¹; 1H NMR (400 MHz, CDCl₃) δ 6.89 (td, J = 6.8, 15.6 Hz, 1H), 5.88 (td, J = 1.6, 15.6 Hz, 1H), 4.18 (t, J = 6.4 Hz, 2H), 3.72 (s, 3H), 2.83 (s, 1H), 2.52 (dq, J = 1.6, 6.4 Hz, 2H), 2.43-2.37 (m, 3H), 1.89-1.46 (m, 17H); 13C NMR (100 MHz, CDCl₃) δ 174.5, 166.7, 144.4, 123.3, 113.3, 106.8, 62.3, 51.7, 41.6,
6-methoxy-6-oxohex-3-en-1-yl 7,8,16,17-tetraoxadispiro[5.2.6.9.26]heptadecane-3-carboxylate (24)

Light yellow liquid; \( E/Z = 13:1 \) by HPLC; yield 55%; IR \( \nu_{\text{max}} \) 2929, 2856, 1735, 1447, 1356, 1317, 1193, 1172, 1063, 997, 925, 775 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 5.52-5.45 (m, 1H), 5.37-5.30 (m, 1H), 4.08 (t, \( J = 6.8 \) Hz, 2H), 3.66 (s, 3H), 2.82 (s, 1H), 2.45-2.26 (m, 6H), 2.05-1.25 (m, 30H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 174.7, 174.4, 133.7, 125.2, 113.3, 106.9, 64.2, 51.6, 41.8, 34.2, 32.7, 32.2, 30.4, 29.6, 29.4, 29.3, 29.2, 29.2, 29.1, 29.0, 27.4, 27.0, 25.1, 24.8, 23.9, 22.6; ESI-HRMS calcd. For C\(_{27}\)H\(_{44}\)O\(_8\)Na (M+Na\(^+\)) 519.2928, found 519.2948.

7-(((13S)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-3-yl)oxy)-7-oxohept-3-en-1-yl (1r,3r,5r,7r)-dispiro[adamantane-2,3'-[1,2,4,5]tetraoxane-6',1''-cyclohexane]-4''-carboxylate (25)

Colourless solid; yield 67%; IR \( \nu_{\text{max}} \) 2933, 2859, 1732, 1493, 1255, 1151, 1060, 997, 912, 730 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.29-7.28 (m and 7.27-2.26 (m) (1H) \( E/Z = 2:1 \), 6.84-6.78 (m, 2H), 5.61-5.47 (m, 2H), 4.10 (t, \( J = 6.8 \) Hz, 2H), 3.14 (s, 1H), 2.92-2.49 (m, 2H), 2.47-2.20 (m, 8H), 2.15-1.47 (m, 30H), 0.91 (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 220.9, 174.6, 171.9, 148.7, 138.7, 137.5, 130.9, 127.2, 126.5, 121.7, 118.8, 110.5, 107.3, 90.1, 80.1, 76.1, 62.0, 48.1, 44.3, 41.7, 38.1, 37.6, 36.0, 34.4, 34.3, 33.3, 32.1, 31.7, 30.3, 29.5, 28.3, 28.1, 27.2, 26.5, 25.9, 24.8, 24.0, 21.7, 14.0; ESI-HRMS calcd. For C\(_{42}\)H\(_{54}\)O\(_9\)Na (M+Na\(^+\)) 725.3660, found 725.3676.
decyl 1-cyclopropyl-7-(1-(7-(((1r,3r,5r,7r)-dispiro[adamantane-2,3'-[1,2,4,5]tetraoxane-6',1''-cyclohexane]-4''-carbonyl)oxy)heptahydro-6'H-pyrrolo[3,4-b]pyridin-6-yl)-6,8-difluoro-4-oxo-1,4-dihydroquinoline-3-carboxylate (27)

To a suspension of the aminoacid 33 (1 g, 2.57 mmol) in chloroform 3 mL and pyridine (406 mg, 5.14 mmol) a solution of 4-penetenoyl chloride (365 mg, 3.08 mmol) in chloroform (2 mL) and the reaction mixture was stirred overnight at room temperature. The solvent was removed in vacuo, the solid residue was suspended in water (15 mL), filtered off with suction and washed with water (10 mL). The crude product was dissolved in hot acetone (15 mL) and left for crystallization. Finally, the mixture was cooled down to about 0 °C, the crystals were collected on the filter, washed with cold acetone and air dried. Yield 820 mg (68 %).

To a stirred solution of amide, product of previous step (200 mg, 0.42 mmol) in 5 mL anhydrous CH$_2$Cl$_2$ was added 52 mg DMAP and 1-decanol (137 mg, 0.85 mmol). EDC (244 mg, 1.27 mmol) was added to the reaction mixture at 0 °C, which was then stirred for 60 h. Then reaction mixture was concentrated and pure ester (190 mg, 73%) was obtained after flash chromatography (90% ethyl acetate-hexane).

The alkene 12 (100 mg, 0.26 mmol) and alkene 26 (56 mg, 0.09 mmol) was dissolved in 2 mL dry DCM. The mixture was refluxed at 45 °C for 12 h in presence nitro-catalyst 5 (3 mg, 5 mol %). Then, another 5 mol % of the catalyst was added and refluxed for another 12 h. Then, DCM was evaporated and product 27 (34 mg, 40%) was purified by column chromatography. ($E/Z = 4:1$) by HPLC; yellow solid; IR $\nu_{\text{max}}$ 2917, 2852, 1730, 1448, 1254, 1129, 1172, 1060, 997, 925 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.75 (s, 1H), 7.82 (d, $J = 9.6$ Hz, 1H), 5.56–5.42 (m, 2H), 5.25 (s, 1H), 4.65–4.55 (m, 1H), 4.17–3.45 (m, 8H), 3.19–2.19 (m, 12H), 2.01–1.13 (m, 27H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 176.2, 174.8, 174.1, 167.9, 153.4, 150.8, 149.5, 132.9, 131.1, 129.3, 127.1, 126.3, 110.7, 108.2, 107.9, 107.2, 63.9, 56.8, 54.6, 50.5, 48.7, 41.8, 41.7, 40.5, 37.5, 37.0, 36.2, 35.5, 34.3, 33.8, 33.3, 32.0, 30.3, 28.3, 27.1, 24.9, 24.6, 23.9, 9.6, 8.9; ESI-HRMS calcd. For C$_{54}$H$_{73}$O$_{10}$N$_3$F$_2$ (M$^+$) 962.5337, found 962.5345.

Compound 28

The alkene 12 (30 mg, 0.08 mmol) was dissolved in 0.5 mL dry dichloromethane. The mixture was stirred at 45 °C for 4 h in presence nitro-Hoveyda-Grubbs type catalyst 5 (1.5 mg, 3 mol %). After completion (TLC), the reaction mixture was concentrated in vacuo. Purification of the residue by column chromatography [3 % EA/hex] afforded the pure product (25 mg, 87%).

($E/Z = 2:1$) by HPLC; Light yellow liquid; yield 87%; IR $\nu_{\text{max}}$ 2914, 2858, 1733, 1450, 1358, 1319, 1168, 1135, 1060, 996, 925, 731 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 5.48-5.45 (m, 2H), 4.08 (q, $J = 6.8$ Hz, 4H), 3.15 (s, 2H), 2.89 (s, 2H), 2.43-2.30 (m, 6H), 2.05–1.41 (m, 40H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 174.6, 128.4, 110.6, 107.3, 63.8, 41.8, 37.1, 34.4, 33.3, 32.2, 30.3, 28.3, 27.2, 24.9, 24.0; ESI-HRMS calcd. For C$_{40}$H$_{56}$O$_{12}$Na (M$^+$Na$^+$) 751.3664, found 751.3700.
hepta-1,6-dien-4-yl (1r,3r,5r,7r)-dispiro[adamantane-2,3’-[1,2,4,5]tetraoxane-6’,1”-cyclohexane]-4”-carboxylate (29)

Synthesized by same procedure described for compound 12. Yield 73%; Colourless liquid; IR ν max 2908, 2858, 1727, 1449, 1361, 1128, 1091, 996, 915, 732 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 5.77-5.67 (m, 2H), 5.01-4.95 (m, 5H), 3.15 (s, 1H), 2.88 (s, 1H), 2.42-2.24 (m, 5H), 2.10-1.59 (m, 20H); ¹³C NMR (100 MHz, CDCl₃) δ 174.1, 133.6, 118.1, 110.6, 107.3, 72.2, 41.9, 38.3, 37.1, 34.4, 33.3, 30.4, 28.3, 27.2, 24.8, 23.9; ESI-HRMS calcd. For C₂₄H₃₄O₆Na (M+Na⁺) 441.2253, found 441.2252; EA (%) calcd. For C₂₄H₃₄O₆, C 68.88, H 8.19, O 22.94. found C 68.77, H 8.03.

cyclopent-3-en-1-yl (1r,3r,5r,7r)-dispiro[adamantane-2,3’-[1,2,4,5]tetraoxane-6’,1”-cyclohexane]-4”-carboxylate (30)

The diene 29 (77 mg, 0.18 mmol) was dissolved in 2 mL DCM and stirred for 1 hour in presence of nitro catalyst (1 mg, 1 mol %). Then, solvent was evaporated and purified by column chromatography (2% EA/hex) to obtain pure product 30 (54 mg, 75%). Colourless liquid; IR ν max 2909, 2859, 1725, 1449, 1254, 1129, 1173, 1060, 927, 682 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 5.72-5.68 (m, 2H), 5.39-5.35 (m, 1H), 3.15 (s, 1H), 2.88 (s, 1H), 2.77-2.69 (m, 2H), 2.40-2.31 (m, 3H), 2.10-1.58 (m, 20H); ¹³C NMR (100 MHz, CDCl₃) δ 174.6, 128.4, 110.6, 107.3, 74.2, 41.8, 39.9, 37.1, 34.5, 33.3, 30.4, 28.4, 27.2, 24.8, 23.9; ESI-HRMS calcd. For C₂₂H₂₆O₆Na (M+Na⁺) 413.1940, found 413.1937.

(1r,3r,5r,7r)-4’-((prop-2-yn-1-ylOxy)methyl)dispiro[adamantane-2,3’-[1,2,4,5]tetraoxane-6’,1”-cyclohexane] (31)

To a stirred solution of LAH (22 mg, 0.57 mmol) in 2 mL diethyl ether, the ester C (100 mg, 0.28 mmol) dissolved in 3 mL ether was added dropwise at 0 °C. The solution was stirred for 1 h. The reaction mixture was quenched by sat. solution of sodium sulphate (1 mL) and stirred for 1 h. The clear solution was separated and evaporated. The product 34 was purified by column chromatography using 20% EA/hexane solution. Yield 75 mg (85%). NaH (16 mg, 60% in mineral oil) was taken in 2-necked round-bottom flask and the oil was washed with n-hexane twice. Compound 34 (80 mg, 0.26 mmol) dissolved in 5 mL of THF was added to suspension of NaH in THF (5 mL). The mixture was refluxed for 1 h. Then propargyl bromide (2 equiv. 0.52 mmol) and 10 mg TBAI were added. The whole mixture was further refluxed for 24 h. Then reaction mixture was cooled to 0 °C
and quenched with sat. NH₄Cl soln. (1 mL). After usual work up, pure compound 31 (45 mg, 50%) was obtained by column chromatography (1% EA/hex). Colourless liquid; IR νmax 2912, 2858, 1733, 1448, 1258, 1093, 1049, 995, 923 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 4.11 (d, J = 2.4 Hz, 2H), 3.36 (s, 2H), 3.15 (s, 2H), 2.41 (t, J = 2.4 Hz, 1H), 2.10 - 1.58 (m, 19H), 1.28 - 1.25 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 110.6, 108.2, 80.0, 74.7, 74.3, 58.4, 37.1, 34.4, 33.3, 33.2, 31.0, 28.7, 27.2, 25.5, 25.0; ESI-HRMS calcd. For C₂₀H₂₈O₅Na (M+Na⁺) 371.1834, found 371.1827.

(1r,3r,5r,7r)-4''-(((2-methylenebut-3-en-1-yl)oxy)methyl)dispiro[adamantane-2,3'[:1,2,4,5]tetraoxane-6',1''-cyclohexane] (32)³

A pressure tube (50 mL) was thoroughly flushed with argon and charged with a solution of an alkyne 31 (80 mg, 0.24 mmol) and the catalyst 5 (2 mol %) in anhydrous CH₂Cl₂ (7 mL). The gaseous ethylene was delivered to the tube. The mixture was stirred under the ethylene gas atmosphere (4 atm) for approximately 3 h in autoclave. Then again 2 mol % catalyst 5 was added and stirred at 4 atm. Pressure for another 1 h. After completion (TLC), the residue was concentrated under reduced pressure and purified by column chromatography (1% EA/hex) to give the product 32 (60 mg, 67%). Light yellow liquid; IR νmax 2915, 2815, 1449, 1256, 1102, 1061, 899 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 6.35 (dd, J = 6.8, 10.8 Hz, 1H), 5.32 - 5.22 (m, 4H), 4.13 (s, 2H), 3.28 - 3.14 (m, 4H), 1.97 - 1.25 (m, 21H); ¹³C NMR (100 MHz, CDCl₃) δ 142.7, 136.7, 117.4, 114.6, 110.5, 108.3, 75.0, 71.0, 37.3, 37.1, 34.4, 33.3, 31.1, 30.2, 28.9, 27.2, 25.7, 25.2; ESI-HRMS calcd. For C₂₂H₃₂O₅Na (M+Na⁺) 399.2147, found 399.2140.

Reference: