Formal Total Synthesis of (±)-α– and β–Cedrene. Construction of the Tricyclic Carbon Skeleton Using a Highly Efficient Intramolecular Khand Annulation

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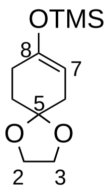
SUPPORTING INFORMATION

General

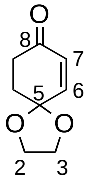
Dry tetrahydrofuran (THF) and diethyl ether (Et$_2$O) were obtained by distilling commercial solvents from sodium benzophenone ketyl and dichloromethane (CH$_2$Cl$_2$) was distilled from calcium hydride. Light petroleum refers to the fraction of b.p. 30-40 ˚C and was distilled prior to use. All organometallic complexes were stored under nitrogen at, or below, -20 ˚C and all reactions were performed under a nitrogen atmosphere unless otherwise stated. ^{1}H and ^{13}C NMR were run on a Bruker WM 250 and a Bruker WM 400 in CDCl$_3$ solutions. Chemical shifts are reported in parts per million downfield relative to tetramethylsilane (δ0.00); coupling constants are reported in hertz. Infrared spectra were obtained on a Mattson 1000 or Nicolet Impact 400D FTIR spectrometer in CH$_2$Cl$_2$ solutions or as films. High resolution mass spectrometry was performed on a JEOL Instruments JMS-AX505HA mass spectrometer system or a Finnigan MAT 900XLT high resolution double focussing mass spectrometer. Mass spectral data is reported as *m/z*.



8-((Trimethylsilyl)oxy)-1,4-dioxaspiro[4.5]dec-7-ene 3

A solution of trimethylsilyl trifluoromethanesulfonate (1.86 g, 1.52 ml, 8.39 mmol) in dichloromethane (20 ml) was added over a 10 min period to a stirred solution of 1,4-dioxaspiro[4.5]decan-8-one **2** (1.19 g, 7.63 mmol) and triethylamine (2.30 g, 3.30 ml, 22.9 mmol) in dichloromethane (70 ml) at -5˚C. The mixture was stirred for 15 min before the reaction was quenched by the addition of saturated aqueous sodium hydrogen carbonate solution (5 ml) then water (35 ml). The organic phase was separated, dried, and evaporated under reduced pressure to leave a crude residue, which was extracted with light petroleum (3 × 20 ml). The light petroleum extracts were combined and filtered through a pad of silica using light petroleum as the eluent. The filtrate was evaporated under reduced pressure to give *8-((trimethylsilyl)oxy)-1,4-dioxaspiro[4.5]dec-7-ene* **3** (1.67 g, 95%) as a colourless oil. υ_{max} (film)/cm^{-1} 1664 (C=C); ^{1}H NMR (400 MHz, CDCl$_3$): δ 0.19 (9H, s, (CH$_3$)$_3$Si), 1.81 (2H, t, *J* 6.6, C^{10}-H), 2.20 (2H, m, C^9-H), 2.26 (2H, m, C^6-H), 3.97 (4H, m, C^{2,3}-H) and 4.73 (1H, m, C^7-H); ^{13}C NMR (100

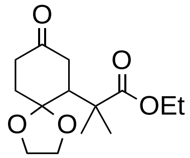
MHz, $CDCl_3$): δ 0.5 ($(CH_3)_3Si$), 28.7, 31.3, 34.1, 64.6 ($C^{2,3}$), 100.8 (C^7), 107.9 (C^5) and 150.0 (C^8); HRMS (EI) *m/z* Calc. for $C_{11}H_{20}O_3Si$ (M^+): 228.1182. Found: 228.1181.



1,4-Dioxaspiro[4.5]dec-6-en-8-one 4

Palladium(II) acetate (1.03 g, 4.60 mmol) was added to a solution of 8-((trimethylsilyl)oxy)-1,4-dioxaspiro[4.5]dec-7-ene **3** (1.00 g, 4.39 mmol) in acetonitrile (70 ml) and the mixture was stirred for 24 h at 25˚C. The solvent was then evaporated under reduced pressure and the black residue was filtered through a pad of silica using dichloromethane as the eluent. The filtrate was washed with saturated aqueous sodium hydrogen carbonate solution (50 ml) to remove traces of acetic acid. The organic phase was dried and evaporated under reduced pressure to give *1,4-dioxaspiro[4.5]dec-6-en-8-one* **4** (0.62 g, 92%) as a pale yellow oil. Found: C, 62.31; H, 6.35. $C_8H_{10}O_3$ requires C, 62.30; H, 6.50%; υ_{max} (film)/cm^{-1} 1683 (C=O); ^1H NMR (400 MHz, $CDCl_3$): δ 2.20 (2H, t, *J* 6.5, C^{10}-H), 2.63 (2H, t, *J* 6.5, C^9-H), 4.05 (4H, m, $C^{2,3}$-H), 6.00 (1H, d, *J* 10.2, C^7-H) and 6.61 (1H, d, *J* 10.2, C^6-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 33.0, 35.4, 65.2 ($C^{2,3}$), 104.1 (C^5), 130.6 (C^7), 146.6 (C^6) and 198.8 (C^8); HRMS (EI) *m/z* Calc. for $C_8H_{11}O_3$ (M^++1): 155.0708. Found: 155.0710.

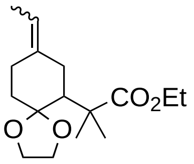
Compound **4** was also prepared by the following method:
A solution of palladium(II) acetate (36.0 mg, 0.16 mmol) and 1,2-*bis*-(diphenylphosphino)ethane (58.0 mg, 0.14 mmol) in acetonitrile (50 ml) was heated to reflux before diallyl carbonate (0.64 g, 4.51 mmol) and 8-((trimethylsilyl)oxy)-1,4-dioxaspiro[4.5]dec-7-ene **3** (0.74 g, 3.24 mmol) were added. The mixture was heated under reflux for a further 40 h. The solvent was then evaporated under reduced pressure to leave a crude residue, which was purified by filtration through a pad of silica using 50% diethyl ether in light petroleum as the eluent. The filtrate was then evaporated under reduced pressure to give *1,4-dioxaspiro[4.5]dec-6-en-8-one* **4** (0.41 g, 82%) as a pale yellow oil. Analytical data were as given above.



Ethyl 2-(1,4-dioxaspiro[4.5]decan-8-on-6-yl)-2-methylpropanoate 5

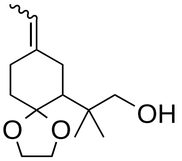
Ytterbium(III) trifluoromethanesulfonate trihydrate (0.06 g, 0.09 mmol) was added to a stirred solution of 1,4-dioxaspiro[4.5]dec-6-en-8-one **4** (0.14 g, 0.91 mmol) and 1-ethoxy-1-((trimethylsilyl)oxy)-2-methylpropene (0.23 g, 1.43 mmol) in dichloromethane (20 ml) at 25˚C. The mixture was stirred for 24 h before it was filtered through a pad of silica using diethyl ether as the eluent. The filtrate was evaporated under reduced pressure to leave a crude residue, which was purified by column chromatography on silica using a 10-50% diethyl ether in light petroleum gradient as the eluent to give *ethyl 2-(1,4-dioxaspiro[4.5]decan-8-on-6-yl)-2-*

methylpropanoate **5** (0.20 g, 81%) as a pale yellow oil. υ_{max} (film)/cm^{-1} 1721 (C=O) and 1689 (C=O);); ^{1}H NMR (400 MHz, CDCl$_3$): δ 1.10 (3H, s, CH$_3$C), 1.13 (3H, s, CH$_3$C), 1.24 (3H, t, *J* 7.1, C*H*$_3$CH$_2$), 1.74 (1H, app dt, *J* 13.5 and 5.5), 1.99 (1H, m), 2.36 (1H, m), 2.48 (1H, m), 2.58 (2H, t, *J* 13.5), 2.71 (1H, dd, *J* 13.5 and 3.9) and 3.91-4.14 (6H, overlapping m, CH$_3$C*H*$_2$, OCH$_2$CH$_2$O); ^{13}C NMR (100 MHz, CDCl$_3$): δ 14.3, 19.5, 27.1, 33.5, 38.3, 39.9, 42.6, 48.8, 60.4 (CH$_3$*C*H$_2$), 63.6 (OCH$_2$), 64.8 (OCH$_2$), 109.6 (OCO), 177.6 (OC=O) and 210.2 (C=O);); HRMS (EI) *m/z* Calc. for $C_{14}H_{22}O_5$ (M$^+$): 270.14672. Found: 270.14603.



Ethyl 2-((*E*)/(*Z*)-8-ethylidene-1,4-dioxaspiro[4.5]decan-6-yl)-2-methylpropanoate 6a/6b

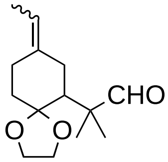
A solution of *n*-butyllithium in hexanes (2.5 M, 4.90 ml, 12.2 mmol) was added over a 5 min period to a stirred solution of ethyltriphenylphosphonium bromide (4.40 g, 11.8 mmol) in tetrahydrofuran (170 ml) at 0˚C. The resultant orange solution was stirred for 5 min then a solution of ethyl 2-(1,4-dioxaspiro[4.5]decan-8-on-6-yl)-2-methylpropanoate **5** (2.60 g, 9.63 mmol) in tetrahydrofuran (30 ml) was added. The mixture was stirred for a further 2 h before the solvent was evaporated under reduced pressure and replaced by hexanes, causing precipitation of triphenylphosphine oxide. This precipitate was removed by filtration through a pad of silica using 10% diethyl ether in light petroleum as the eluent. The filtrate was evaporated under reduced pressure to leave a residue, which was purified by filtration through a second pad of silica using 10% diethyl ether in light petroleum as the eluent to give *ethyl 2-(8-ethylidene-1,4-dioxaspiro[4.5]decan-6-yl)-2-methylpropanoate* **6** (2.50 g, 92%) as a pale yellow oil containing both (*E*)- and (*Z*)-isomers in a ratio of 1:2. υ_{max} (film)/cm^{-1} 1736 (C=O) and 1450 (C=C); ^{1}H NMR (400 MHz, CDCl$_3$): δ 1.16-1.36 (12H, overlapping m), 1.60 (2H, m), 1.79 (1H, m), 1.96 (1H, m), 2.08-2.28 (2H, overlapping m), 2.51 + 2.65 (total of 1H, both m), 3.79-4.14 (6H, overlapping m, CH$_3$C*H*$_2$, OCH$_2$CH$_2$O) and 5.21 (1H, m, =C*H*CH$_3$); ^{13}C NMR (100 MHz, CDCl$_3$): δ 13.3, 13.5, 14.6, 20.3, 25.1, 25.8, 27.8, 27.9, 33.9, 34.8, 35.8, 36.9, 42.9, 43.1, 51.2, 51.8, 60.4 (CH$_3$*C*H$_2$), 60.5 (CH$_3$*C*H$_2$), 63.6 (O*C*H$_2$CH$_2$O), 64.6 (OCH$_2$*C*H$_2$O), 111.6 (OCO), 111.7 (OCO), 117.2 (=*C*HCH$_3$), 117.6 (=C*H*CH$_3$), 137.8 (*C*=CH), 137.9 (*C*=CH), 178.8 (OC=O) and 178.9 (OC=O); HRMS (EI) *m/z* Calc. for $C_{16}H_{26}O_4$ (M$^+$): 282.18311. Found: 282.18408.



(*E*)/(*Z*)-8-Ethylidene-6-(2-methylpropan-1-ol-2-yl)-1,4-dioxaspiro[4.5]decane

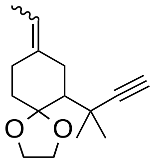
Lithium aluminium hydride (0.30 g, 7.81 mmol) was added to a stirred solution of ethyl 2-((*E*)/(*Z*)-8-ethylidene-1,4-dioxaspiro[4.5]decan-6-yl)-2-methylpropanoate **6a/6b** (2.20 g, 7.80 mmol) in diethyl ether (100 ml) at

0˚C and the mixture was stirred for a further 1 h. The reaction was quenched by the addition of water (0.3 ml) then 10% aqueous sodium hydroxide solution (0.3 ml) and lastly another portion of water (0.9 ml). This resulted in a white granular precipitate, which was removed by filtration through a pad of kieselguhr that was washed thoroughly with diethyl ether. The filtrate was evaporated under reduced pressure to give *8-ethylidene-6-(2-methylpropan-1-ol-2-yl)-1,4-dioxaspiro[4.5]decane* (1.86 g, 99%) as colourless oil containing both (*E*)- and (*Z*)-isomers in a ratio of 1:2. υ_{max} (film)/cm^{-1} 3489 (O-H), and 1440 (C=C); ^{1}H NMR (400 MHz, CDCl$_3$): δ 0.83 + 0.87 (3H, 2 x s, 2 x CH$_3$C), 1.01 + 1.05 (3H, 2 x s, 2 x CH$_3$C), 1.31 (1H, dt, *J* 13.4 and 4.8), 1.57 (3H, m), 1.69 (1H, dd, *J* 13.4 and 4.8), 1.83-2.24 (4H, overlapping m), 2.44 + 2.66 (1H, both m), 3.08 (1H, m), 3.38 (1H, m), 3.55 (1H, m), 3.88-4.22 (4H, overlapping m, OCH$_2$CH$_2$O) and 5.16 (1H, m, =C*H*CH$_3$); ^{13}C NMR (100 MHz, CDCl$_3$): δ 12.8, 13.1, 22.0, 22.1, 24.6, 27.3, 27.5, 33.3, 35.3, 36.1, 36.4, 38.4, 38.6, 47.8, 48.4, 63.0 (O*C*H$_2$CH$_2$O), 63.4 (OCH$_2$*C*H$_2$O), 71.8 (CH$_2$OH), 112.9 (OCO), 116.2 (=*C*HCH$_3$), 116.5 (=*C*HCH$_3$), 137.8 (*C*=CH) and 138.0 (*C*=CH); HRMS (EI) *m/z* Calc. for C$_{14}$H$_{24}$O$_3$ (M$^+$): 240.17254. Found: 240.17255.



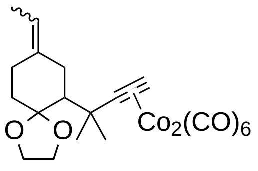
(*E*)/(*Z*)-8-Ethylidene-6-(2-methylpropanal-2-yl)-1,4-dioxaspiro[4.5]decane 7a/7b

The Dess-Martin periodinane (3.26 g, 7.69 mmol) was added to a stirred solution of (*E*)/(*Z*)-8-ethylidene-6-(2-methylpropan-1-ol-2-yl)-1,4-dioxaspiro[4.5]decane (1.50 g, 6.25 mmol) in 10% acetonitrile in dichloromethane (70 ml) at 25˚C. The mixture was stirred for 1 h before the reaction was quenched by the addition of aqueous sodium thiosulfate solution (8.5 g in 20 ml) and saturated aqueous sodium hydrogen carbonate solution (50 ml). This two phase mixture was stirred vigorously for 30 min before the organic phase was separated, dried, and evaporated under reduced pressure to leave a crude residue, which was purified by filtration through a pad of silica using 20% diethyl ether in light petroleum as the eluent. Evaporation of the solvent under reduced pressure gave *8-ethylidene-6-(2-methylpropanal-2-yl)-1,4-dioxaspiro[4.5]decane* **7** (1.44 g, 97%) as a pale yellow oil containing both (*E*)- and (*Z*)-isomers in a ratio of 1:2. υ_{max} (film)/cm^{-1} 2819 (aldehyde C-H), 2710 (aldehyde C-H) and 1727 (C=O); ^{1}H NMR (400 MHz, CDCl$_3$): δ 0.99 + 1.03 (6H, 2 x (2 x s), 2 x (2 x CH$_3$C)), 1.31 (1H, m, (CH$_3$)$_2$CC*H*), 1.59 (3H, m, (=CHC*H*$_3$), 1.81 (1H, m), 1.91 (1H, m), 2.08 (1H, m), 2.22 (2H, m), 2.54 + 2.67 (1H, 2 x m), 3.62 (1H, q, *J* 7.1, OCH$_2$CH$_2$O), 3.86 (3H, m, OCH$_2$CH$_2$O), 5.24 (1H, m, (=C*H*CH$_3$) and 9.31 + 9.32 (1H, 2 x s, O=CH); ^{13}C NMR (100 MHz, CDCl$_3$): δ 13.0, 13.2, 16.2, 23.4, 23.5, 24.6, 25.2, 33.4, 34.2, 35.4, 36.4, 46.9, 47.0, 50.5, 51.1, 63.1 (O*C*H$_2$CH$_2$O), 63.7 (OCH$_2$*C*H$_2$O), 111.0 (OCO), 111.1 (OCO), 117.2 (=*C*HCH$_3$), 117.6 (=*C*HCH$_3$), 136.9 (*C*=CH), 137.1 (*C*=CH), 202.4 (O=CH) and 202.6 (O=CH); HRMS (EI) *m/z* Calc. for C$_{14}$H$_{22}$O$_3$ (M$^+$): 238.15689. Found: 238.15734.



(*E*)/(*Z*)-8-Ethylidene-6-(3-methylbut-1-yn-3-yl]-1,4-dioxaspiro[4.5]decane

Potassium carbonate (1.30 g, 9.42 mmol) was added to a stirred solution of (*E*)/(*Z*)-8-ethylidene-6-(2-methylpropanal-2-yl)-1,4-dioxaspiro[4.5]decane **7a/7b** (1.50 g, 6.30 mmol) and dimethyl (1-diazo-2-oxopropyl)phosphonate (1.82 g, 9.48 mmol) in methanol (40 ml) at 25˚C. The mixture was stirred for 5 d and further portions (5 × 0.5 eq.) of both potassium carbonate (5 × 0.43 g) and dimethyl (1-diazo-2-oxopropyl)phosphonate (5 × 0.60 g) were added to the reaction mixture at regular intervals over this time period. The solvent was evaporated under reduced pressure and the residue was partitioned between diethyl ether (50 ml) and water (50 ml). The organic phase was separated and the aqueous phase was extracted with another portion of diethyl ether (50 ml). The combined organic phase was dried, filtered, and evaporated under reduced pressure to leave a crude residue, which was purified by column chromatography on silica using 10% diethyl ether in light petroleum as the eluent to give *8-ethylidene-6-(3-methylbut-1-yn-3-yl)-1,4-dioxaspiro[4.5]decane* (1.19 g, 81%) as a pale yellow oil containing both (*E*)- and (*Z*)-isomers in a ratio of 1:2. υ_{max} (film)/cm^{-1} 2110 (C≡C) and 1427 (C=C); ^{1}H NMR (400 MHz, CDCl$_3$): δ 1.33-1.41 (7H, 1 x m + 4 x s, (C*H*$_3$)$_2$CC*H*), 1.59 (3H, m, (=CHC*H*$_3$), 1.71 (1H, m), 1.84 (1H, m), 1.90-2.28 (3H, overlapping m), 2.45 (1H, m), 2.90 (1H, m), 3.95-4.06 (4H, overlapping m, OCH$_2$CH$_2$O) and 5.21 (1H, m, (=C*H*CH$_3$); ^{13}C NMR (100 MHz, CDCl$_3$): δ 13.0, 13.1, 24.7, 28.3, 28.4, 28.9, 30.2, 30.4, 33.4, 33.5, 34.1, 35.9, 36.9, 37.1, 51.4, 52.0, 63.5 (O*C*H$_2$CH$_2$O), 63.8 (O*C*H$_2$CH$_2$O), 63.9 (OCH$_2$*C*H$_2$O), 68.0 (≡CH), 68.1 (≡CH), 92.8 (C≡), 93.0 (C≡), 112.2 (OCO), 112.3 (OCO), 116.7 (=*C*HCH$_3$), 117.0 (=*C*HCH$_3$), 137.4 (*C*=CH) and 137.7 (*C*=CH); HRMS (EI) *m/z* Calc. for $C_{15}H_{22}O_2$ (M$^+$): 234.16198. Found: 234.16165. Also isolated from this reaction was the starting aldehyde **7a/7b** (0.14 g).



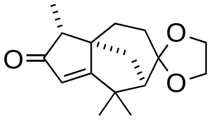
Hexacarbonyl((*E*)/(*Z*)-8-ethylidene-6-[μ-[(1,2-η:1,2-η)-3-methylbut-1-yn-3-yl]]-1,4-dioxaspiro[4.5]decane)dicobalt-(Co-Co) 8a/8b

A solution of (*E*)/(*Z*)-8-ethylidene-6-(3-methylbut-1-yn-3-yl)-1,4-dioxaspiro[4.5]decane (1.18 g, 5.04 mmol) in light petroleum (10 ml) was added to a stirred solution of octacarbonyldicobalt (1.78 g, 5.20 mmol) in light petroleum (40 ml) over a 5 min period at 25˚C. The mixture was stirred for 2 h before it was filtered through a pad of silica using 10% diethyl ether in light petroleum as the eluent. The filtrate was evaporated under reduced pressure to leave a crude residue, which was purified by column chromatography on silica using a 0-10% diethyl ether in light petroleum gradient as the eluent to give hexacarbonyl((*E*)/(*Z*)-8-ethylidene-6-[μ-[(1,2-η:1,2-η)-3-

methylbut-1-yn-3-yl]]-1,4-dioxaspiro[4.5]decane)dicobalt-(Co-Co) **8** (2.60 g, 99%) as a red oil containing both (*E*)- and (*Z*)-isomers in a ratio of 1:2. υ_{max} (film)/cm^{-1} 2089 (C=O), 2013 (C=O), 1465 (C=C) and 1442 (C=C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.88-1.44 (7H, m), 1.57-1.76 (4H, m), 1.85-1.99 (1H, m), 2.01-2.23 (2H, m), 2.39-2.53 (1H, m), 2.97 (1H, d, *J* 13.1), 4.02 (4H, m, OCH_2CH_2O), 5.20 (1H, m, =C*H*CH_3) and 6.17 + 6.22 (1H, 2 x s, ≡CH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.4, 13.7, 14.5, 22.8, 24.8, 28.3, 30.1, 30.2, 32.0, 32.2, 33.5, 34.6, 36.1, 37.0, 37.2, 42.1, 42.3, 52.2, 53.0, 63.3 (O*C*H_2CH_2O), 63.8 (OCH_2*C*H_2O), 75.5, 75.9, 113.2 (OCO), 113.4 (OCO), 116.8 (=*C*HCH_3), 117.4 (=*C*HCH_3), 137.4 (*C*=CH), 137.7 (*C*=CH) and 200.8 (CO); HRMS (EI) *m/z* Calc. for $C_{20}H_{22}O_7Co_2$ (M^+-CO): 492.00295. Found: 492.00162.

Cyclopentenones 9a and 9b

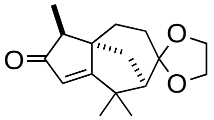
A solution of hexacarbonyl((*E*)/(*Z*)-8-ethylidene-6-[μ-[(1,2-η:1,2-η)-3-methylbut-1-yn-3-yl]]-1,4-dioxaspiro[4.5]decane)dicobalt-(Co-Co) **8a/8b** (188.0 mg, 0.36 mmol) and *n*-butyl methyl sulfide (0.16 g, 1.54 mmol) in 1,2-dichloroethane (5 ml) was heated under reflux for 30 min. The black mixture was then filtered through a pad of silica using diethyl ether as the eluent. The filtrate was evaporated under reduced pressure to leave a crude residue, which was purified by column chromatography on silica using a 0-50% diethyl ether in light petroleum gradient as the eluent to give *cyclopentenones* **9a** and **9b** (90.0 mg, 95% combined) as a 2:1 mixture (by proton-NMR). Compounds **9a** and **9b** were subsequently separated by column chromatography on silica using a 0-30% diethyl ether in light petroleum gradient as the eluent. This afforded **9a** (59.0 mg) as a colourless crystalline solid and **9b** (31.0 mg) also as a colourless crystalline solid.



Analytical data for **9a** are as follows: m.p. 90-91˚C; υ_{max} (film)/cm^{-1} 3042 (vinyl C-H), 2978, 2927, 2876, 1702 (C=O) and 1625 (C=C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.99 (3H, d, *J* 7.5, CHC*H*$_3$), 1.17 (3H, s, (C*H*$_3$)$_2$C), 1.28 (1H, m), 1.47 (3H, s, $(CH_3)_2C$), 1.70-2.03 (6H, overlapping m), 2.18 (1H, q, *J* 7.5, C*H*CH_3), 3.82 (1H, m, OCH_2CH_2O), 3.91 (2H, m, OCH_2CH_2O), 3.98 (1H, m, OCH_2CH_2O) and 5.70 (1H, s, C*H*=C); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.9 (CH*C*H$_3$), 22.8 ((*C*H$_3$)$_2$C), 31.8, 32.7, 32.9 ((*C*H$_3$)$_2$C), 39.3, 42.5 ((CH_3)$_2$*C*), 52.7 (*C*HCH_3), 55.8 (C*C*HCH_2), 57.2 (CH_2*C*CHCH_3), 63.7 (O*C*H_2CH_2O), 65.0 (OCH_2*C*H_2O), 110.2 (OCO), 119.8 (*C*H=C), 201.3 (CH=*C*) and 213.8 (C=O); HRMS (EI) *m/z* Calc. for $C_{16}H_{22}O_3$ (M^+): 262.15689. Found: 262.15650.

Single crystals of cyclopentenone **9a** were obtained from diethyl ether/light petroleum, mounted in an inert oil, and transferred to the cold gas stream of the diffractometer.

Crystal Data. $C_{16}H_{22}O_3$, *M* = 262.16, monoclinic, a = 6.0402(13), b = 31.423(4), c = 7.7111(13) Å, β = 107.469(15)˚, *U* = 1396.1(4) Å^3, *T* = 295 K, space group *P*2$_1$/n (no. 14), Z = 4, μ(Mo-Kα) = 0.085 mm^{-1}, 2977 reflections measured, 2721 unique (R_{int} = 0.0609) which were used in all calculations. Final $R1$ = 0.0481. The final $wR(F^2)$ was 0.1418 (all data). See full CIF files for this crystal data at the end of this Supporting Information.



Analytical data for **200** are as follows: m.p. 87-88˚C; υ_{max} (film)/cm^{-1} 3039 (vinyl C-H), 2966, 2940, 2883, 1702 (C=O), 1625 (C=C), 1453, 1370, 1108 and 1095); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.07 (3H, d, *J* 7.2, $CHCH_3$), 1.15 (1H, m), 1.19 (3H, s, $(CH_3)_2C$), 1.47 (3H, s, $(CH_3)_2C$), 1.71-1.86 (4H, overlapping m), 1.97 (1H, d, *J* 5.0, $CCHCH_2$), 2.22 (1H, d, *J* 11.8), 2.27 (1H, q, *J* 7.2, $CHCH_3$), 3.83 (1H, m, OCH_2CH_2O), 3.91 (2H, m, OCH_2CH_2O), 4.00 (1H, m, OCH_2CH_2O) and 5.80 (1H, s, CH=C); ^{13}C NMR (100 MHz, $CDCl_3$): δ 9.0 ($CHCH_3$), 22.8 ($(CH_3)_2C$), 31.2, 33.0 ($(CH_3)_2C$), 33.9 (CCH_2CH_2), 38.0, 42.5 ($(CH_3)_2C$), 55.2 ($CHCH_3$), 56.5 ($CCHCH_2$), 56.7 (CH_2CCHCH_3), 63.7 (OCH_2CH_2O), 65.0 (OCH_2CH_2O), 110.2 (OCO), 121.1 (CH=C), 200.5 (CH=C) and 211.6 (C=O); HRMS (EI) *m/z* Calc. for $C_{16}H_{22}O_3$ (M^+): 262.15689. Found: 262.15698.

Single crystals of cyclopentenone **9b** were obtained from diethyl ether/light petroleum, mounted in an inert oil, and transferred to the cold gas stream of the diffractometer.

Crystal Data. $C_{16}H_{22}O_3$, M = 262.16, monoclinic, a = 6.069(3), b = 16.253(5), c = 14.087(3) Å, β = 93.40(3)˚, U = 1387.1(7) Å^3, T = 123 K, space group $P2_1/n$ (no. 14), Z = 4, μ(Mo-Kα) = 0.085 mm^{-1}, 3105 reflections measured, 2835 unique (R_{int} = 0.032) which were used in all calculations. Final $R1$ = 0.067. The final $wR(F^2)$ was 0.084 (all data). See full CIF files for this crystal data at the end of this Supporting Information.

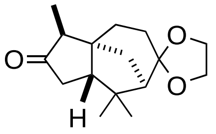
Cyclopentenones **9a** and **9b** were also prepared by the following methods:

Trimethylamine *N*-oxide dihydrate (0.18 g, 1.62 mmol) was added to a stirred solution of hexacarbonyl((*E*)/(*Z*)-8-ethylidene-6-[μ-[(1,2-η:1,2-η)-3-methylbut-1-yn-3-yl]]-1,4-dioxaspiro[4.5]decane)dicobalt-(Co-Co) **8a/8b** (95.0 mg, 0.18 mmol) in acetone (3 ml) at 25˚C. The mixture was stirred for 16 h before it was filtered through a pad of silica using diethyl ether as the eluent. The filtrate was evaporated under reduced pressure to leave a crude residue, which was purified by column chromatography on silica using a 0-50% diethyl ether in light petroleum gradient as the eluent to give *cyclopentenones* **9a** and **9b** (43.0 mg, 91% combined) as a 2:1 mixture (by proton-NMR). Analytical data were as given above.

N-Methylmorpholine *N*-oxide monohydrate (0.20 g, 1.48 mmol) was added to a stirred solution of hexacarbonyl((*E*)/(*Z*)-8-ethylidene-6-[μ-[(1,2-η:1,2-η)-3-methylbut-1-yn-3-yl]]-

1,4-dioxaspiro[4.5]decane)dicobalt-(Co-Co) **8a/8b** (99.0 mg, 0.19 mmol) in dichloromethane (3 ml) at 25˚C. The mixture was stirred for 16 h before it was filtered through a pad of silica using diethyl ether as the eluent. The filtrate was evaporated under reduced pressure to leave a crude residue, which was purified by column chromatography on silica using a 0-50% diethyl ether in light petroleum gradient as the eluent to give *cyclopentenones* **9a** and **9b** (42.0 mg, 84% combined) as a 2:1 mixture (by proton-NMR). Analytical data were as given above.

A mixture of hexacarbonyl((*E*)/(*Z*)-8-ethylidene-6-[μ-[(1,2-η:1,2-η)-3-methylbut-1-yn-3-yl]]-1,4-dioxaspiro[4.5]decane)dicobalt-(Co-Co) **8a/8b** (54.0 mg, 0.10 mmol) and polymer-supported sulfide (1 mmol g^{-1}, 0.36 g, 0.36 mmol) in 1,2-dichloroethane (3 ml) was heated under reflux for 30 min. The mixture was then filtered through a pad of silica using diethyl ether as the eluent. The filtrate was evaporated under reduced pressure to leave a crude residue, which was purified by column chromatography on silica using a 0-50% diethyl ether in light petroleum gradient as the eluent to give *cyclopentenones* **9a** and **9b** (21.0 mg, 80% combined) as a 2:1 mixture (by proton-NMR). Analytical data were as given above.



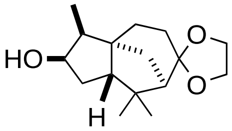
Ketone 11

10% Palladium on charcoal (30 mg) was added to a solution of cyclopentenone **9b** (365.0 mg, 1.39 mmol) in toluene (20 ml). The mixture was placed under 45 psi of hydrogen gas and agitated using a Cook apparatus for 3 h. The mixture then filtered through a pad of silica using diethyl ether as the eluent. The filtrate was evaporated under reduced pressure to give *ketone* **11** (365.0 mg, 99%) as a colourless crystalline solid, m.p. 44-45˚C. υ_{max} (film)/cm^{-1} 2959, 2921, 2876, 1704 (C=O), 1459 and 1363; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.95 (3H, d, *J* 7.6, $CHCH_3$), 0.96 (3H, s, $(CH_3)_2C$), 1.22 (3H, s, $(CH_3)_2C$), 1.52 (2H, overlapping m), 1.62-1.69 (2H, overlapping m), 1.75 (1H, m), 1.83-1.94 (2H, m), 2.03 (1H, dt, *J* 8.6 and 1.2), 2.14 (1H, q, *J* 7.6, $CHCH_3$), 2.24 (1H, ddd, *J* 18.2, 6.9 and 1.5, $O{=}CCH_2CH$), 2.34 (1H, dd, *J* 18.1 and 10.8, $O{=}CCH_2CH$), 3.76-3.89 (3H, overlapping m, OCH_2CH_2O) and 3.96 (1H, m, OCH_2CH_2O); ^{13}C NMR (100 MHz, $CDCl_3$): δ 11.8 ($CHCH_3$), 26.7 ($(CH_3)_2C$), 29.2 ($(CH_3)_2C$), 30.5, 31.3, 38.3 ($O{=}CCH_2CH$), 41.9 ($(CH_3)_2C$), 42.2 (CCH_2CH), 49.4 (CH_2CCHCH_3), 49.5 ($O{=}CCH_2CH$), 50.9 ($CHCH_3$), 56.2 ($CCHCH_2$), 63.4 (OCH_2CH_2O), 64.8 (OCH_2CH_2O), 111.0 (OCO) and 221.4 (C=O); HRMS (EI) *m/z* Calc. for $C_{16}H_{24}O_3$ (M^+): 264.17254. Found: 264.17280.

Single crystals of ketone **11** were obtained from diethyl ether/light petroleum, mounted in an inert oil, and transferred to the cold gas stream of the diffractometer.

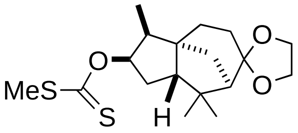
Crystal Data. $C_{16}H_{24}O_3$, *M* = 264.17, monoclinic, a = 8.3280(3), b = 8.3930(3), c = 10.2120(4) Å, β = 106.696(2)˚, *U* = 683.70(4) $Å^3$, *T* = 150 K, space group $P2_1/n$ (no. 14), Z

= 2, μ(Mo-Kα) = 0.087 mm^{-1}, 5455 reflections measured, 3107 unique (R_{int} = 0.0273) which were used in all calculations. Final $R1$ = 0.0340. The final $wR(F^2)$ was 0.0825 (all data). See full CIF files for this crystal data at the end of this Supporting Information.



Alcohol 12

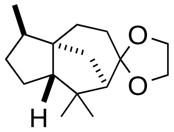
Lithium aluminium hydride (37.0 mg, 0.97 mmol) was added to a stirred solution of ketone **11** (260.0 mg, 0.985 mmol) in diethyl ether (20 ml) at 0˚C. The mixture was stirred for 2 h before it was allowed to warm to 25˚C and the reaction was quenched by the addition of water (0.04 ml) then 10% aqueous sodium hydroxide solution (0.04 ml) and, lastly, another portion of water (0.12 ml). This resulted in a white granular precipitate, which was removed by filtration through a pad of silica using diethyl ether as the eluent. The filtrate was evaporated under reduced pressure to give *alcohol* **12** (259 mg, 99%) as a colourless crystalline solid, m.p. 75-85˚C. υ_{max} (film)/cm^{-1} 3317 (O-H), 2959, 2889, 1459, 1376, 1114 and 1051; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.94 (3H, d, *J* 7.0, $CHCH_3$), 0.98 (3H, s, $(CH_3)_2C$), 1.18 (3H, s, $(CH_3)_2C$), 1.28-1.52 (4H, overlapping m), 1.63-1.93 (8H, overlapping m), 3.57 (1H, m, CHOH), 3.75-3.87 (3H, overlapping m, OCH_2CH_2O) and 3.95 (1H, m, OCH_2CH_2O); ^{13}C NMR (100 MHz, $CDCl_3$): δ 12.4 ($CHCH_3$), 26.5 ($(CH_3)_2C$), 28.7 ($(CH_3)_2C$), 30.6, 31.9, 35.6 ($HOCHCH_2CH$), 40.7 ($(CH_3)_2C$), 42.8, 50.2 (CH_2CCHCH_3), 50.4 ($CHCH_3$), 52.6 ($HOCHCH_2CH$), 57.9 ($CCHCH_2$), 63.3 (OCH_2CH_2O), 64.7 (OCH_2CH_2O), 81.5 (HOCH) and 111.8 (OCO); HRMS (EI) *m/z* Calc. for $C_{16}H_{26}O_3$ (M^+): 266.18819. Found: 266.18727.



Xanthate ester 13

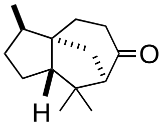
A solution of *n*-butyllithium in hexanes (2.5 M, 0.30 ml, 0.75 mmol) was added over a 5 min period to a stirred solution of alcohol **12** (187.0 mg, 0.703 mmol) in tetrahydrofuran (5 ml) at 0˚C. The mixture was stirred for 5 min before carbon disulfide (85.0 mg, 0.067 ml, 1.12 mmol) was added and the mixture was allowed to warm to 25˚C. The mixture was stirred for 80 min before the reaction was quenched by the addition of methyl iodide (0.12 g, 0.052 ml, 0.84 mmol) and then stirred for a further 30 min. The mixture was then partitioned between diethyl ether (30 ml) and water (30 ml), the organic phase separated, and the aqueous phase extracted with another portion of diethyl ether (30 ml). The combined organic phase was dried, filtered, and evaporated under reduced pressure to leave a crude residue, which was purified by column chromatography on silica using a 0-30% diethyl ether in light petroleum gradient as the eluent. This gave *xanthate ester* **13** (235.0 mg, 94%) as a pale yellow oil which was characterised by infrared and NMR spectroscopy and was then used immediately in the next synthetic step. υ_{max} (film)/cm^{-1} 2966, 1485, 1376, 1223 and 1057; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.94 (3H, d, *J* 7.2, $CHCH_3$), 1.01 (3H, s,

$(C\mathit{H}_3)_2C$), 1.20 (3H, s, $(C\mathit{H}_3)_2C$), 1.47-1.57 (3H, m), 1.68-1.92 (6H, overlapping m), 2.06 (1H, m), 2.23 (1H, m), 2.55 (3H, s, CH_3S), 3.79-3.90 (3H, overlapping m, OCH_2CH_2O), 3.97 (1H, m, OCH_2CH_2O) and 5.37 (1H, m, $C\mathit{H}OC{=}S$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 12.9, 19.0, 26.6, 28.7, 31.9, 32.0, 32.8, 41.3, 42.5, 46.9, 50.0, 52.8, 58.0, 63.8 ($O\mathit{C}H_2CH_2O$), 65.2 ($OCH_2\mathit{C}H_2O$), 92.1 ($\mathit{C}HOC{=}S$), 111.5 (OCO) and 216.2 (OC=S).



Acetal 14

A solution of xanthate ester **13** (45.0 mg, 0.126 mmol), tri-*n*-butyltin hydride (0.50 g, 1.71 mmol), and AIBN (13.0 mg, 0.08 mmol) in deoxygenated benzene (20 ml) was heated under reflux for 48 h. The solvent was evaporated under reduced pressure to leave a crude residue, which was purified by column chromatography on silica using a 0-20% diethyl ether in light petroleum gradient as the eluent to give *acetal* **14** (24.0 mg, 76%) as a colourless oil. υ_{max} (film)/cm^{-1} 2959, 2876, 1472, 1363 and 1102; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.84 (3H, d, *J* 7.1, $CHC\mathit{H}_3$), 0.97 (3H, s, $(C\mathit{H}_3)_2C$), 1.17 (3H, s, $(C\mathit{H}_3)_2C$), 1.24-1.90 (13H, overlapping m), 3.78-3.90 (3H, overlapping m, OCH_2CH_2O) and 3.97 (1H, m, OCH_2CH_2O); ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.7 ($CH\mathit{C}H_3$), 25.8, 26.9 ($(\mathit{C}H_3)_2C$), 28.2 ($(\mathit{C}H_3)_2C$), 31.4, 31.6, 37.3 ($\mathit{C}H_2CHCH_3$), 41.6 ($(CH_3)_2\mathit{C}$), 41.7, 41.8 ($\mathit{C}HCH_3$), 53.6 ($CH_2\mathit{C}CHCH_3$), 56.7 ($CH_2CH_2\mathit{C}HC$), 58.1 ($C\mathit{C}HCH_2$), 63.4 ($O\mathit{C}H_2CH_2O$), 64.8 ($OCH_2\mathit{C}H_2O$) and 112.2 (OCO); HRMS (EI) *m/z* Calc. for $C_{16}H_{26}O_2$ (M^+): 250.19328. Found: 250.19432.



Cedrone 10[1,2]

Triphenylphosphine (2.6 mg, 0.01 mmol) and carbon tetrabromide (3.3 mg, 0.01 mmol) were added to a stirred solution of acetal **14** (32.0 mg, 0.13 mmol) in acetone (5 ml) at 25˚C. The mixture was stirred for 1 h before the solvent was evaporated under reduced pressure to leave a crude residue, which was purified by column chromatography on silica using a 5-20% diethyl ether in light petroleum gradient as the eluent to give *cedrone* **10** (26.1 mg, 99%) as a colourless oil. υ_{max} (film)/cm^{-1} 2960, 2877, 1715 and 1460; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.89 (3H, d, *J* 7.1, $CHC\mathit{H}_3$), 1.00 (3H, s, $(C\mathit{H}_3)_2C$), 1.01 (3H, s, $(C\mathit{H}_3)_2C$), 1.42 (1H, m), 1.51 (1H, m), 1.56-1.76 (4H, overlapping m), 1.80-2.00 (4H, overlapping m), 2.27-2.36 (2H, overlapping m, $O{=}CC\mathit{H}CH_2$ + $CH_2C\mathit{H}_2C{=}O$) and 2.48 (1H, dd, *J* 18.3 and 7.8, $CH_2C\mathit{H}_2C{=}O$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.7 ($CH\mathit{C}H_3$), 25.7, 26.0 ($(\mathit{C}H_3)_2C$), 26.4 ($(\mathit{C}H_3)_2C$), 32.1, 36.8, 37.0, 41.5, 41.8, 43.0 ($(CH_3)_2\mathit{C}$), 54.6 ($CH_2\mathit{C}CHCH_3$), 57.1 ($CH_2CH_2\mathit{C}HC$), 67.3 ($O{=}C\mathit{C}HCH_2$) and 214.4 (C=O); HRMS (EI) *m/z* Calc. for $C_{14}H_{22}O$ (M^+): 206.16707. Found: 206.16753.

References.

1. Stork, G.; Clark, F. H., Jr. *J. Am. Chem. Soc.* **1955**, *77*, 1072.
2. Breitholle, E. G.; Fallis, A. G. *J. Org. Chem.* **1978**, *43*, 1964.