Stereoselective Synthesis of Spiro Tricyclic Polyoxygenated Compounds: Solvolytic Behavior of 1-(Tosyloxymethyl)spiro[2.4]hepta-4,6-diene

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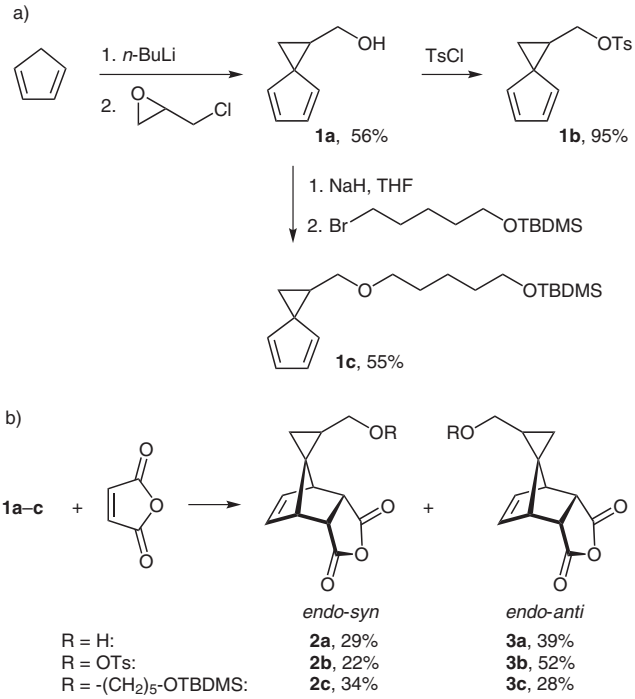
Abstract: The Diels–Alder reaction of spirobicyclic cyclopentadiene derivatives, prepared by reaction of cyclopentadienyllithium and epichlorohydrin, with maleic anhydride gave a simple access to spiro tricyclic polyoxygenated compounds of synthetic interest. The solvolytic behavior of 1-(tosyloxymethyl)spiro[2.4]hepta-4,6-diene, a 5-spirocyclopentadiene, shows that the ionization of the tosylate was unlikely.

Key words: tricyclic compounds, Diels–Alder reaction, spiro compounds, stereoselective synthesis

Diels–Alder reaction of cyclopentadienes with maleic anhydride allows the formation of building blocks useful for the preparation of polypodal diphenylphosphino ligands,[1] and particularly polypodal ligands with a side chain. We have previously reported the Diels–Alder reaction of fulvenes with maleic anhydride.[2]

Now, we report on the Diels–Alder reaction between the spirobicyclic cyclopentadienes **1a–c**, prepared from cyclopentadienyllithium and epichlorohydrin,[3] and maleic anhydride. The Diels–Alder adducts **2** and **3** could potentially be employed as building blocks for the preparation of supported ligands. Only the *endo*-adducts were obtained as a mixture 1.33:1 of *anti*- and *syn*-isomers **3a** and **2a**, respectively (Scheme 1). A previous addition of **1a** (or related compounds with a protected hydroxy group) to 2-chloroacrylonitrile afforded only the corresponding *anti*-isomer[3b] (the stereochemistry of the cycloaddition with alkyl acrylates,[3f,n] methyl vinyl ketone,[3f] acrylonitrile,[3n] dimethyl azodicarboxylate,[3c] or dialkyl fumarate,[3n] appears not to have been determined), while *N*-phenylmaleimide gave a 1:1 mixture of the two *endo*-adducts.[3k] The postulated stereochemistry *syn* or *anti* results from comparison of the NMR spectra, which led us to assign the higher field position of the methylene signal of the cyclopropane to the *syn*-isomer, which is attributable to shielding by the endocyclic double bond (Scheme 2); more subtle analysis of the NMR results confirmed this.[4]

The Diels–Alder reaction of the tosylate **1b**[3m,n] with maleic anhydride led mainly to the *endo-anti*-isomer **3b** (*anti*/*syn*-isomers: **3b/2b**, 2.35:1). The stereochemistry was confirmed by an X-ray crystal structure determination of **3b** (Figure 1).



Scheme 1 (a) Synthesis of spiro[2.4]hepta-4,6-diene-1-methanol (**1a**) and derivatives; (b) Diels–Alder reaction of **1a–c** with maleic anhydride

This stereoselectivity results mainly from kinetic parameters, and the *anti* π facial selectivity could be attributed to steric hindrance. Indeed, calculations at the B3LYP/6-31++G(d,p) level of the theory[5] (without zero-point energy correction) show that **3b** is the most stable isomer by 0.85 kcal/mol, which should lead to better selectivity (**2b**, $E = -1581.636\ 057$ hartree; **3b**, $E = -1581.637\ 417$ hartree).

We have increased the steric shielding of one face of the cyclopentadiene by the etherification of **1a** with 1-bromo-

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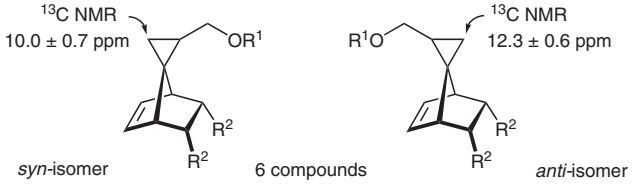
5-(*tert*-butyldimethylsiloxy)pentane[6] to give the ether **1c**. In this case, the Diels–Alder reaction with maleic anhydride gave the *syn*-isomer **2c** with a narrow majority (*syn*/*anti*-isomers: **2c/3c** 1.21:1).

The π facial selectivity in Diels–Alder reactions has been correlated with hyperconjugative stabilization involving the donation of electron density from the substituent.[7] In the case of **1a–c**, among the substituents, the best donor group, favoring the *syn*-isomer, is the ether of **1c** with a contrasteric addition to the most nucleophilic diene face.[7c]



Scheme 2 Stereochemistry of adducts according to the ^{13}C NMR spectra

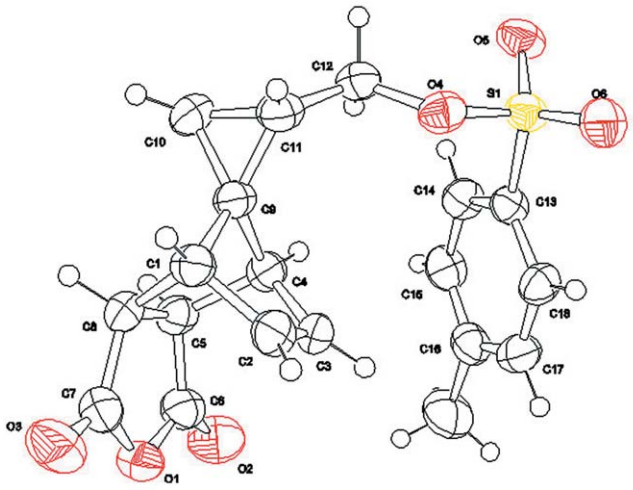
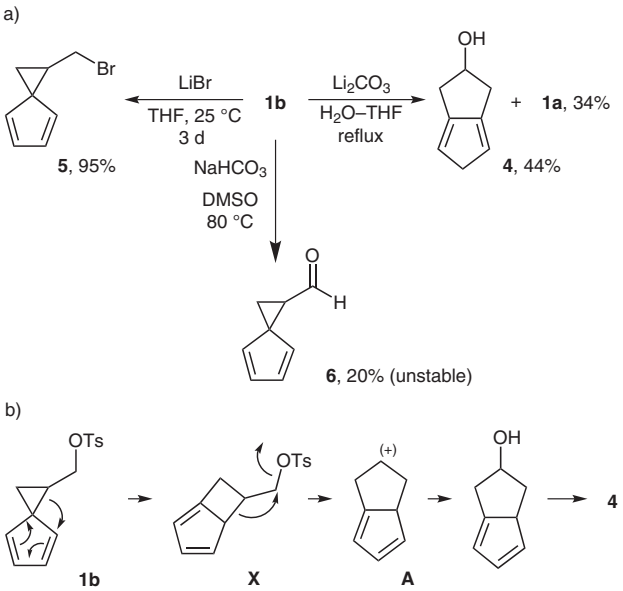


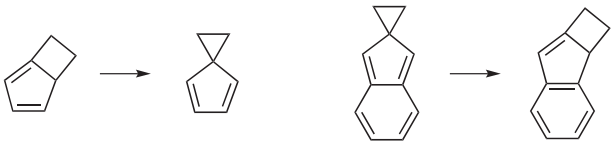
Figure 1 ORTEP diagram of tosylate **3b**

The reactivity of the tosylate **1b** has not been previously investigated although it is an interesting example of a cyclopropylcarbinyl system with the possibility of the formation of nonclassical ions with a resonance between the structures **B**, **C**, and **D** (Scheme 4).[8] Moreover, compounds **4–6** might be used for the preparation of supported ligands.[2] In fact, very clean substitution reactions occurred [Scheme 3 (a)]. Hydrolysis of **1b** afforded the precursor alcohol **1a** and bicyclo[3.3.0]octa-5,8-dien-3-ol (**4**). The reduced number of signals in the NMR spectra confirmed the symmetry of the alcohol **4**. A facile and reversible 1,5-alkyl shift converts the spiro-tosylate **1b** into the cyclobutyl tosylate **X** [Scheme 3 (b)]. Oda and Breslow have already reported that bicyclo[3.2.0]hepta-1,3-diene undergoes a fast isomerization to give spiro[2.4]hepta-4,6-diene.[9] On the other hand, cyclobutano[*a*]indene was spontaneously formed by the rearrangement of spiro[cyclopropane-1,2′-indene] (Scheme 4).[10] Calculations at the B3LYP/6-311++G(d,p) level of the theory[5] (without zero-point energy correction) show that **1b** is more stable than tosylate **X** by 10.6 kcal/mol (**1b**, $E = -1205.202\ 115$ hartree; **X**, $E = -1205.185\ 190$ hartree). From **X**, a Wagner–Meerwein transposition gave the bicyclo[3.3.0]octa-1,3-dien-7-yl carbocation **A**, precursor of **4**.

Treatment of **1b** with lithium bromide in tetrahydrofuran gave rise to the cyclopropylmethyl bromide **5**[3e] in good yields; treatment with sodium carbonate in dimethyl sulfoxide led to the unstable aldehyde **6**[3d,e,g,h] according to the Kornblum reaction.[11]



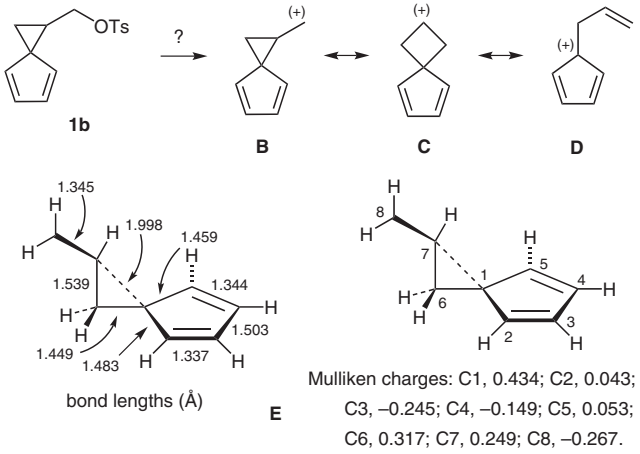
Scheme 3 Reactivity of the tosylate **1b**



Scheme 4 Spontaneous isomerizations of spirocyclopentadienes

The structure of the nonclassical ion **B** arising from the hypothetical release of the tosylate anion of **1b** has been calculated at the B3LYP/6-311++G(3df,2pd) level of the theory ($E = -310.004\ 752$ hartree, without zero-point energy correction) (Scheme 5). Among the three mesomeric structures **B**, **C**, and **D**, the most similar structure to **E**, which was obtained by calculation, corresponds to **D**, as demonstrated by the length 2.0 Å of the C1–C7 bond of the cyclopropane. But this structure fits to a cyclopentadienyl cation with an 'antiaromatic' character.[12] Indeed, the calculated structure shows that the conjugation in the cyclopentadiene moiety is reduced, as given by the length of the C3–C4 bond (1.503 Å instead of 1.474 Å in the calculated structure of cyclopentadiene at the same level of theory). The relative sizes of component atomic orbitals of the LUMO (29th MO), show that this MO was mainly localized on C1 and C8 (Figure 2). The spiro carbocation **C**

(E = –309.980 542 hartree) is less stable than **E** by 15.2 kcal/mol (at the same level of theory). The isomeric bicyclic cation **A** [Scheme 3 (b)] (E = –310.000 155 hartree) is more stable than **E** by 12.3 kcal/mol, confirming the instability of the former. In conclusion, this theoretical study shows that the ionization of the tosylate **1b** was improbable and explained that mainly direct substitution reactions occurred. In particular, all attempts to open the cyclopropane of alcohol **1a** by heating in the presence of trifluoroacetic acid failed.



Scheme 5 Structure of the cation **E** resulting from the hypothetical ionization of the tosylate **1b**

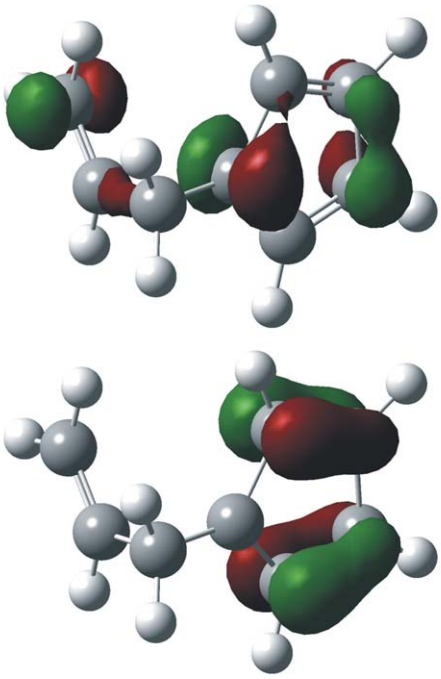
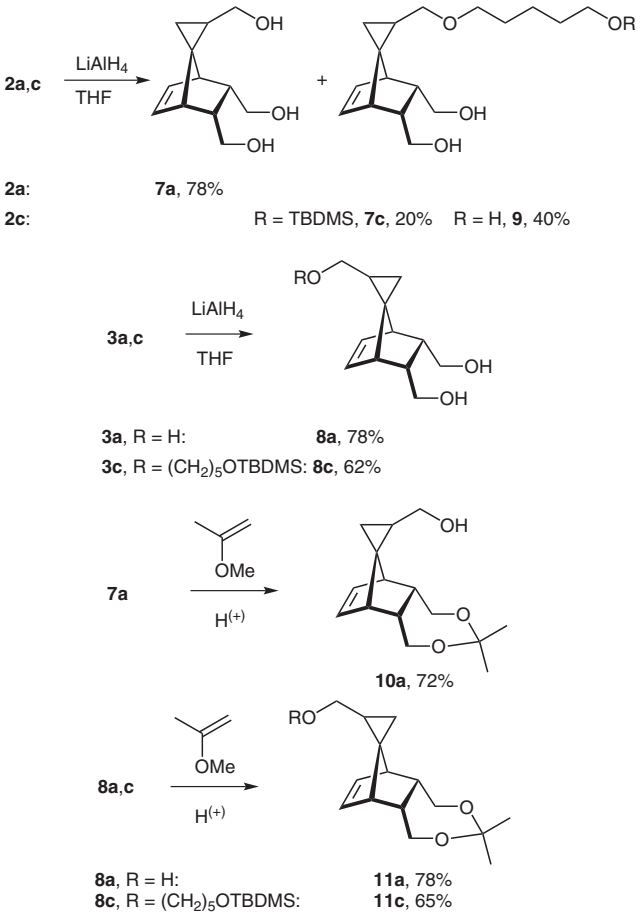


Figure 2 LUMO (29th MO)(up) and HOMO (28th MO)(down) of the cation **E** (B3LYP/6-311G++(3df,3pd) level of theory)

From the Diels–Alder adducts **2a**,**c**, some polyoxygenated tricyclic products of synthetic interest for the preparation of polypodal ligands can be easily obtained (Scheme 6).



Scheme 6 Synthesis of various polyoxygenated tricyclic products

The reduction of anhydride **2c**, with *syn* structure, mainly occurred with the loss of the TBDMS protective group to give triol **9**. It is well known that the presence of a reducible group near the TBDMS-protected alcohol promotes deprotection. Moreover, for the minor product **7c**, the TBDMS group was transferred to a hydroxymethyl group (following the formation of a cyclic pentavalent silicon anion intermediate).[13]

In summary, we have shown that the spirocyclopentadienyl alcohol **1a**, easily obtained from generally available reagents, gives access to various polyoxygenated tricyclic compounds with good control of the stereochemistry. The spirocyclopentadienyl tosylate **1b** presented special behavior in the course of solvolytic displacement reactions.

THF was freshly distilled from Na/benzophenone; CH_2Cl_2 and pyridine from CaH_2 under argon. Other reagents and solvents were obtained from commercial sources and used as received. All experiments were conducted under an atmosphere of argon. Flash column chromatography (FC): Merck 230–400 mesh silica gel; EtOAc, Et_2O, and petroleum ether (PE) as eluents. TLC: Macherey-Nagel silica gel UV_{254} analytical plate. NMR spectroscopy: Bruker AC 300 (^{1}H, 300 MHz; ^{13}C, 75 MHz); relative to $CDCl_3$ (signals for residual $CHCl_3$ in the $CDCl_3$: δ = 7.26 (^{1}H) and 77.00 (central, ^{13}C). Carbon–proton couplings were determined by DEPT sequence experiments. MS: Applied Biosystems SCIEX QStar Elite. Mp: uncorrected, Büchi capillary apparatus. Products **2**, **3**, **7**, **8**, **10**, and **11** all had the following relative configuration, (1*S**,2*R**,3*S**,4*R**).

Spiro[2.4]hepta-4,6-diene-1-methanol (1a)
Freshly distilled cyclopentadiene (1.12 g, 17.0 mmol) was added dropwise to a soln of 2.5 M BuLi in hexane (8.7 mL, 21.6 mmol) in anhyd THF (40 mL) stirred at –20 °C. The mixture was stirred for 0.5 h and then epichlorohydrin (0.45 mL, 5.40 mmol) was slowly added. The soln was stirred at 0 °C for 18 h and then cooled to –10 °C and H_2O (40 mL) and Et_2O (40 mL) were added successively. The organic phase was stirred with brine and then it was separated, dried ($MgSO_4$), filtered, and concentrated in vacuo. The crude product was flash chromatographed (silica gel, PE–EtOAc, 70:30) to give **1a** (371 mg, 3.04 mmol, 56%) as a yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.61 (dt, *J* = 5.3, 1.8 Hz, 1 H), 6.48 (dt, *J* = 5.2, 1.7 Hz, 1 H), 6.25 (dt, *J* = 5.2, 1.7 Hz, 1 H), 6.09 (dt, *J* = 5.0, 1.7 Hz, 1 H), 3.97 (dd, *J* = 11.7, 6.0 Hz, 1 H), 3.58 (dd, *J* = 11.7, 8.5 Hz, 1 H), 2.47–2.37 (m, 1 H), 1.85 (dd, *J* = 8.6, 4.3 Hz, 1 H), 1.67 (dd, *J* = 7.1, 4.3 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 139.4 (d), 133.9 (d), 131.7 (d), 128.6 (d), 64.9 (t), 41.9 (s), 30.0 (t), 17.6 (d).

1-(Tosyloxymethyl)spiro[2.4]hepta-4,6-diene (1b)
To a cooled soln (–20 °C) of alcohol **1a** (1.11 g, 9.12 mmol) in anhyd pyridine (20 mL) was added TsCl (3.47 g, 18.2 mmol); the soln was stirred for 5 h. The mixture was poured onto ice and extracted with Et_2O (3 × 60 mL). The combined organic phase was washed with 1 M HCl (60 mL) and aq 10% $CuSO_4$ (50 mL), dried ($MgSO_4$), and then concentrated in vacuo to give **1b** (2.39 g, 8.66 mmol, 95%) as an oil, which was used in the following steps without further purification.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.76 (d, *J* = 8.1 Hz, 2 H), 7.32 (d, *J* = 8.1 Hz, 2 H), 6.50 (m, 1 H), 6.44 (m, 1 H), 5.99 (m, 2 H), 4.21 (dd, *J* = 10.7, 8.0 Hz, 1 H), 4.12 (dd, *J* = 10.7, 7.0 Hz, 1 H), 2.44 (s, 3 H), 2.33 (quint, *J* = 7.6 Hz, 1 H), 1.79 (dd, *J* = 8.5, 4.7 Hz, 1 H), 1.58 (dd, *J* = 6.7, 4.7 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.9 (s), 138.4 (d), 133.5 (d), 131.6 (d), 129.8 (d, 2 C), 129.3 (d), 127.8 (d, 2 C), 72.0 (t), 41.5 (s), 24.7 (d), 21.6 (q), 17.0 (t).

1-{[5-(*tert*-Butyldimethylsiloxy)pentyloxy]methyl}spiro[2.4]hepta-4,6-diene (1c)
To a suspension of NaH (4.92 g, 123 mmol) in anhyd THF (100 mL) cooled to 0 °C was added dropwise **1a** (10.0 g, 82.0 mmol) in anhyd THF (75 mL) and TBAI (2.20 g). The mixture was stirred for 1 h, 1-(*tert*-butyldimethylsiloxy)-5-bromopentane (CAS 85514-43-8) (32.7 g, 123 mmol) was added dropwise, and the soln was refluxed for 24 h. After usual workup (CH_2Cl_2), the crude product was flash chromatographed (silica gel, PE–EtOAc, 90:10 to 70:30) to give **1c** (14.5 g, 45 mmol, 55%) as a yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.55 (dt, *J* = 5.2, 1.8 Hz, 1 H), 6.47 (dt, *J* = 5.0, 1.8 Hz, 1 H), 6.24 (dt, *J* = 5.2, 1.8 Hz, 1 H), 6.22 (dt, *J* = 5.2, 1.8 Hz, 1 H), 3.62–3.57 (m, 4 H), 3.56–3.38 (m, 2 H), 2.39–2.29 (m, 1 H), 1.77 (dd, *J* = 8.6, 4.2 Hz, 1 H), 1.67 (dd, *J* = 7.2, 4.2 Hz, 1 H), 1.64–1.46 (m, 4 H), 1.42–1.32 (m, 2 H), 0.87 (s, 9 H), 0.02 (s, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 139.3 (d), 134.9 (d), 130.6 (d), 128.6 (d), 72.0 (t), 70.6 (t), 63.1 (t), 41.7 (s), 32.6 (t), 29.4 (t), 26.9 (d), 26.0 (q, 3 C), 22.4 (t), 18.3 (s), 17.5 (t), –5.3 (q, 2 C).

Anal. Calcd for $C_{19}H_{34}O_2Si$ (322.56): C, 70.75; H, 10.62. Found: C, 70.65; H, 10.55.

(2′-*syn*)- (2a) and (2′-*anti*)-2′-(Hydroxymethyl)spiro[bicyclo[2.2.1]hept-5-ene-7,1′-cyclopropane]-2,3-dicarboxylic Anhydride (3a)
Hydroxymethyl spiro derivative **1a** (3.00 g, 24.6 mmol) was added to a stirred soln at 0 °C of maleic anhydride (3.40 g, 34.7 mmol) in CH_2Cl_2 (150 mL). The mixture was stirred at 20 °C for 1 d; the crude product was filtered, concentrated in vacuo and flash chromatographed (silica gel, Et_2O) to give the *syn*-isomer **2a** (1.56 g, 7.1 mmol, 29%) as a white powder and then the *anti*-isomer **3a** (2.09 g, 9.5 mmol, 39%) also as a white powder (CAS 52497-51-5).

***syn*-Isomer 2a**
Mp 142 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.39 (ddd, *J* = 5.8, 2.8, 1.0 Hz, 1 H), 6.35 (ddd, *J* = 5.8, 2.8, 1.0 Hz, 1 H), 4.01 (dd, *J* = 8.1, 4.8 Hz, 1 H), 3.92 (dd, *J* = 11.0, 5.3 Hz, 1 H), 3.73 (dd, *J* = 8.1, 4.8 Hz, 1 H), 3.20 (dd, *J* = 11.0, 9.5, Hz, 1 H), 3.16 (m, 1 H), 2.90–2.87 (m, 1 H), 1.24–1.13 (m, 1 H), 0.76 (dd, *J* = 9.0, 5.9 Hz, 1 H), 0.44 (t, *J* = 5.6 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.5 (s), 171.4 (s), 135.3 (d), 135.0 (d), 63.6 (t), 53.2 (s), 51.5 (d), 47.3 (d, 2 C), 47.2 (d), 22.6 (d), 10.1 (t).

***anti*-Isomer 3a**
Mp 128 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.35 (t, *J* = 3.9 Hz, 2 H), 3.67 (m, 2 H), 3.51 (dd, *J* = 11.4, 6.8, Hz, 1 H), 3.32 (dd, *J* = 11.4, 7.6, Hz, 1 H), 3.12 (br sext, *J* = 2.0 Hz, 1 H), 2.86 (br sext, *J* = 2.0 Hz, 1 H), 1.28 (br sext, *J* = 7.2 Hz, 1 H), 0.69 (dd, *J* = 8.8, 5.7 Hz, 1 H), 0.41 (t, *J* = 5.6 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.1 (s, 2 C), 135.8 (d), 135.4 (d), 63.3 (t), 52.8 (s), 51.1 (d), 47.1 (d), 46.9 (d), 46.6 (d), 21.5 (d), 12.0 (t).

Anal. Calcd for $C_{12}H_{12}O_4$ (220.22): C, 65.45; H, 5.49. Found: C, 65.41; H, 5.55.

(2′-*syn*)- (2b) and (2′-*anti*)-2′-(Tosyloxymethyl)spiro[bicyclo[2.2.1]hept-5-ene-7,1′-cyclopropane]-2,3-dicarboxylic Anhydride (3b); Typical Procedure
Tosylate **1b** (200 mg, 0.72 mmol) in anhyd CH_2Cl_2 (2 mL) was added to a soln of maleic anhydride (96.0 mg, 0.98 mmol) in anhyd CH_2Cl_2 (10 mL). The mixture was stirred at r.t. for 24 h, the solvent was eliminated in vacuo, and the crude product was flash chromatographed (silica gel, PE–EtOAc, 70:30) to give *syn*-isomer **2b** (59 mg, 0.16 mmol, 22%) and then *anti*-isomer **3b** (140 mg, 0.37 mmol, 52%).

***syn*-Isomer 2b**
Mp 121 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.79 (d, *J* = 8.1 Hz, 2 H), 7.38 (d, *J* = 8.1 Hz, 2 H), 6.36 (m, 2 H), 4.39 (dd, *J* = 11.0, 5.3 Hz, 1 H), 3.82 (dd, *J* = 8.2, 4.7 Hz, 1 H), 3.67 (dd, *J* = 8.2, 4.7 Hz, 1 H), 3.50 (t, *J* = 10.7 Hz, 1 H), 2.97 (m, 1 H), 2.88 (m, 1 H), 2.47 (s, 3 H), 1.42–1.29 (m, 1 H), 0.88 (dd, *J* = 9.1, 6.1 Hz, 1 H), 0.48 (t, *J* = 5.7 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.8 (s), 170.7 (s), 145.2 (s), 135.2 (d), 134.8 (d), 132.4 (s), 130.0 (d, 2 C), 127.6 (d, 2 C), 71.6 (t), 53.0 (s), 50.9 (d), 47.1 (d), 46.6 (d), 46.57 (d), 21.4 (d), 19.3 (q), 10.6 (t).

***anti*-Isomer 3b[14]**
Mp 99 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.76 (d, *J* = 8.2 Hz, 2 H), 7.35 (d, *J* = 8.2 Hz, 2 H), 6.33 (br quint, *J* = 4.75 Hz, 2 H), 4.02 (dd, *J* = 10.7, 7.3, 1 H), 3.79 (dd, *J* = 10.7, 8.07, 1 H), 3.66 (d, *J* = 2.3 Hz, 1 H), 3.65 (d, *J* = 2.3 Hz, 1 H), 2.98 (br s, 1 H), 2.88 (br s, 1 H), 2.46 (s, 3 H), 1.40 (qd, *J* = 8.0, 5.3 Hz, 1 H), 0.81 (dd, *J* = 8.8, 6.1 Hz, 1 H), 0.50 (t, *J* = 5.7 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.7 (s), 170.5 (s), 145.0 (s), 135.4 (d), 134.9 (d), 132.9 (s), 129.8 (d, 2 C), 127.7 (d, 2 C), 71.4

(t), 52.9 (s), 50.9 (d), 46.9 (d), 46.8 (d), 46.5 (d), 21.5 (d), 18.0 (q), 12.9 (t).

Anal. Calcd for $C_{19}H_{18}O_6S$ (374.41): C, 60.95; H, 4.85. Found: C, 61.01; H, 4.75.

(2′-*syn*)- (2c) and (2′-*anti*)-2′-{[5-(*tert*-Butyldimethylsiloxy)pentyloxy]methyl}spiro[bicyclo[2.2.1]hept-5-ene-7,1′-cyclopropane]-2,3-dicarboxylic Anhydride (3c)

Following the typical procedure for **2b/3b** using **1c** (232 mg, 0.72 mmol) gave, after flash chromatography on silica gel (PE–EtOAc, 80:20), *syn*-isomer **2c** (103 mg, 0.24 mmol, 34%) as an oil and then *anti*-isomer **3c** (85.0 mg, 0.20 mmol, 28%) also as an oil.

***syn*-Isomer 2c**

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.36 (m, 2 H), 3.68 (dd, 8.3, 4.7 Hz, 2 H), 3.60 (t, *J* = 6.4 Hz, 2 H), 3.44–3.32 (m, 2 H), 3.11 (br s, 1 H), 2.93 (t, *J* = 10.0 Hz, 1 H), 2.86 (br s, 1 H), 1.54 (sept, *J* = 7.0 Hz, 4 H), 1.41–1.33 (m, 2 H), 1.25–1.15 (m, 2 H), 0.88 (s, 9 H), 0.78 (dd, *J* = 9.0, 5.8 Hz, 1 H), 0.42 (t, *J* = 5.6 Hz, 1 H), 0.03 (s, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.4 (s), 171.3 (s), 135.3 (d), 135.0 (d), 71.7 (t), 71.1 (t), 63.0 (t), 53.0 (s), 51.5 (d), 47.4 (d), 47.2 (d), 47.1 (d), 32.5 (t), 29.5 (t), 25.9 (q, 3 C), 22.5 (t), 20.5 (d), 18.3 (s), 10.2 (t), –5.3 (q, 2 C).

***anti*-Isomer 3c**

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.37 (m, 2 H), 3.68 (dd, *J* = 3.0, 1.6 Hz, 2 H), 3.42–3.20 (m, 6 H), 3.11 (br s, 1 H), 2.89 (br s, 1 H), 1.59–1.47 (m, 2 H), 1.39–1.31 (m, 3 H), 1.70 (m, 2 H), 0.88 (s, 9 H), 0.72 (dd, *J* = 8.8, 5.6 Hz, 1 H), 0.45 (t, *J* = 5.6 Hz, 1 H), 0.03 (s, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.0 (s, 2 C), 135.7 (d), 134.8 (d), 71.2 (t), 70.7 (t), 63.0 (t), 52.6 (s), 51.4 (d), 47.3 (d), 47.2 (d), 46.8 (d), 32.6 (t), 29.4 (t), 25.9 (q, 3 C), 22.4 (t), 19.4 (d), 18.3 (s), 12.6 (t), –5.3 (q, 2 C).

Anal. Calcd for $C_{23}H_{36}O_5Si$ (420.61): C, 65.68; H, 8.63. Found: C, 65.61; H, 8.75.

Bicyclo[3.3.0]octa-1,4-dien-7-ol (4)

Li_2CO_3 (0.64 g, 8.6 mmol) and tosylate **1b** (1.0 g, 3.62 mmol) in THF (20 mL) and H_2O (20 mL) were refluxed for 6 h, cooled to 20 °C, and filtered. After usual workup (Et_2O), the crude product was flash chromatographed (silica gel, PE–EtOAc, 70:30) to give **4** (194 mg, 1.60 mmol, 44%) as a yellow oil and **1a** (152 mg, 1.24 mmol, 34%).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.93 (m, 2 H), 4.74 (quint, *J* = 5.0 Hz, 1 H), 2.82–2.72 (m, 2 H), 2.48–2.38 (m, 4 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 150.1 (s) (2 C), 121.3 (d, 2 C), 77.9 (d), 46.7 (t), 35.8 (t, 2 C).

Anal. Calcd for $C_8H_{10}O$ (120.16): C, 78.65; H, 8.25. Found: C, 78.61; H, 8.35.

1-(Bromomethyl)spiro[2.4]hepta-4,6-diene (5)

LiBr (434 mg, 5 mmol) and **1b** (244 mg, 1 mmol) in anhyd THF (5 mL) were stirred at 25 °C for 3 d. Then the mixture was concentrated in vacuo. To the residue, H_2O and CH_2Cl_2 were added; after decantation, the aqueous fraction was extracted with CH_2Cl_2. The organic layers were dried ($MgSO_4$), filtered, and concentrated in vacuo. The crude product was then subjected to flash chromatography on silica gel (pentane) to give **5** (184 mg, 0.95 mmol, 95%) as an oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.61 (dt, *J* = 5.2, 1.8 Hz, 1 H), 6.50 (dt, *J* = 5.1, 1.7 Hz, 1 H), 6.20 (dt, *J* = 5.2, 1.7 Hz, 1 H), 6.07 (dt, *J* = 5.1, 1.7 Hz, 1 H), 3.64–3.52 (m, 2 H), 2.61–2.51 (m, 1 H), 1.97 (dd, *J* = 8.5, 4.7 Hz, 1 H), 1.71 (dd, *J* = 7.0, 4.7 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 138.6 (d), 133.5 (d), 131.7 (d), 129.3 (d), 45.7 (s), 35.1 (t), 29.5 (d), 20.6 (t).

1-Formylspiro[2.4]hepta-4,6-diene (6)

$NaHCO_3$ (124 mg, 1.47 mmol) and **1b** (300 mg, 1.09 mmol) in anhyd DMSO (8 mL) were stirred and heated at 80 °C for 5 h. The residue was poured onto ice and after the usual workup (Et_2O), the crude product was flash chromatographed (silica gel, PE–EtOAc, 80:20) to give **6** (unstable) (26 mg, 0.218 mmol, 20%) as an oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.43 (s, 1 H), 6.55 (m, 2 H), 6.33 (m, 1 H), 6.02 (m, 1 H), 2.33 (m, 1 H), 1.60 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 197.5 (d), 136.6 (d), 132.6 (d), 132.0 (d), 131.1 (d), 45.6 (s), 35.1 (d), 16.6 (t).

(2′-*syn*)- (7a) and (2′-*anti*)-2,2′,3-Tris(hydroxymethyl)spiro[bicyclo[2.2.1]hept-5-ene-7,1′-cyclopropane] (8a); Typical Procedure

To a stirred suspension of $LiAlH_4$ (280 mg, 7.38 mmol) in anhyd THF (10 mL) at –20 °C was added dropwise a soln of **2a** or **3a** (440 mg, 2 mmol) in THF (5 mL); the mixture was refluxed for 3 h. After cooling to –20 °C, H_2O (0.28 mL), 1 M NaOH (0.28 mL), and H_2O (0.84 mL) were added successively. The suspension was stirred for 2 h and then filtered (salts were washed with Et_2O, 3 ×) concentrated in vacuo and flash chromatographed (silica gel, MeOH–CH_2Cl_2, 2:98) to give *syn*-isomer **7a** or *anti*-isomer **8a** (327 mg, 1.56 mmol, 78%) as a yellow oil.

***syn*-Isomer 7a**

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.13 (m, 2 H), 3.73–3.59 (m, 6 H), 3.42 (m, 4 H), 2.48 (s, 1 H), 2.17 (s, 1 H), 0.63 (m, 2 H), 0.26 (t, *J* = 5.1 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 134.4 (d), 134.3 (d), 63.7 (t), 62.9 (t), 62.8 (t), 52.2 (d), 49.9 (s), 47.9 (d), 45.9 (d), 45.8 (d), 22.7 (d), 9.5 (t).

***anti*-Isomer 8a**

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.14 (t, *J* = 2.9 Hz, 2 H), 3.54–3.32 (m, 7 H), 3.24 (dd, *J* = 11.1, 8.2 Hz, 2 H), 2.62 (m, 2 H), 2.39 (br s, 1 H), 2.18 (br s, 1 H), 0.62 (dd, *J* = 8.5, 5.5 Hz, 2 H), 0.30 (t, *J* = 5.2 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 136.6 (d), 134.4 (d), 64.6 (t), 62.9 (t), 62.8 (t), 52.1 (d), 49.6 (s), 47.1 (d), 45.7 (d), 45.2 (d), 20.8 (d), 12.0 (t).

Anal. Calcd for $C_{12}H_{18}O_3$ (210.27): C, 68.54; H, 8.63. Found: C, 68.51; H, 8.55.

(2′-*syn*)- (7c) and (2′-*anti*)-2′-{[5-(*tert*-Butyldimethylsiloxy)pentyloxy]methyl}-2,3-bis(hydroxymethyl)spiro[bicyclo[2.2.1]hept-5-ene-7,1′-cyclopropane] (8c) and 2,3-Bis(hydroxymethyl)-2′-[(5-hydroxypentyloxy)methyl]spiro[bicyclo[2.2.1]hept-5-ene-7,1′-cyclopropane] (9)

Following the typical procedure for **8a** using **3c** (841 mg, 2 mmol), but the soln was stirred at r.t. for 8 h to give, after flash chromatography on silica gel (MeOH–CH_2Cl_2, 5:95), **8c** (510 mg, 1.24 mmol, 62%) as an oil.

Following the typical procedure for **8a** using **2c** with the same conditions, gave **7c** (164 mg, 0.4 mmol, 20%) and triol **9** (237 mg, 0.8 mmol, 40%). **7c** appeared as a mixture because the *tert*-butyldimethylsiloxy group was distributed on various positions.

***anti*-Isomer 8c**

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.06 (m, 2 H), 3.55 (t, *J* = 6.4 Hz, 4 H), 3.44–3.14 (m, 4 H), 2.63 (br d, *J* = 5.9 Hz, 2 H), 2.33 (br s, 1 H), 2.14 (br s, 1 H), 1.56–1.44 (m, 5 H), 1.36–1.28 (m, 2 H), 1.16–

1.06 (m, 2 H), 0.85 (s, 9 H), 0.62 (dd, *J* = 8.4, 5.4 Hz, 1 H), 0.29 (t, *J* = 5.2 Hz, 1 H), 0.00 (s, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 134.8 (d), 134.2 (d), 72.2 (t), 70.3 (t), 63.1 (t), 62.73 (t), 62.67 (t), 52.0 (d), 49.0 (s), 47.3 (d), 45.6 (d), 45.0 (d), 32.5 (t), 29.3 (t), 25.9 (q, 3 C), 22.3 (t), 18.3 (s), 18.2 (d), 12.5 (t), –5.4 (q, 2 C).

Anal. Calcd for $C_{23}H_{42}O_4Si$ (410.66): C, 67.27; H, 10.31. Found: C, 67.22; H, 10.35.

syn-Hydroxy Derivative 9

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.10 (m, 2 H), 3.64–3.56 (m, 4 H), 3.53–3.30 (m, 6 H), 3.13 (dd, *J* = 10.0, 9.0 Hz, 1 H), 2.86 (m, 1 H), 2.73 (m, 1 H), 2.41 (br s, 1 H), 2.14 (br s, 1 H), 1.66–1.45 (m, 8 H), 1.12 (m, 1 H), 0.61 (dd, *J* = 8.8, 5.1 Hz, 1 H), 0.24 (t, *J* = 5.2 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 134.45 (d), 134.42 (d), 72.0 (t), 70.4 (t), 62.8 (t, 2 C), 62.5 (t), 53.4 (s), 52.3 (d), 49.6 (s), 47.9 (d), 45.76 (d), 45.3 (d), 32.3 (t), 29.4 (t), 23.1 (t), 19.9 (d), 9.4 (t).

Anal. Calcd for $C_{17}H_{28}O_4$ (296.40): C, 68.89; H, 9.52. Found: C, 68.95; H, 9.48.

(2′-_syn_)- (10a) and (2′-_anti_)-2′,2,3-Tris(hydroxymethyl)spiro[bicyclo[2.2.1]hept-5-ene-7,1′-cyclopropane] Acetonide (11a); Typical Procedure

To a soln of **7a** or **8a** (210 mg, 1 mmol) in anhyd CH_2Cl_2 (5 mL) was added 2-methoxypropene (0.2 mL, 2.03 mmol) and some crystals of 10-camphorsulfonic acid. The soln was stirred until completion of the reaction (TLC, PE–EtOAc, 50:50). Anhyd K_2CO_3 (ca. 50 mg) was added and the soln was stirred, filtered, and concentrated in vacuo. The crude product was flash chromatographed (silica gel, PE–EtOAc, 50:50) to give **10a** (180 mg, 0.72 mmol, 72%) or **11a** (195 mg, 0.78 mmol, 78%).

syn-Isomer 10a

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.16 (br s, 2 H), 3.73–3.60 (m, 4 H), 3.41 (t, *J* = 12.7 Hz, 2 H), 3.27 (dd, *J* = 11.0, 8.4 Hz, 1 H), 2.80–2.62 (m, 2 H), 2.32 (s, 1 H), 2.06 (s, 1 H), 1.30 (s, 3 H), 1.29 (s, 3 H), 0.59 (dd, *J* = 8.5, 5.2 Hz, 1 H), 0.29 (t, *J* = 5.1 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 134.5 (d), 134.4 (d), 101.2 (s), 64.4 (t, 2 C), 63.3 (t), 51.4 (d), 50.9 (s), 47.1 (d), 45.8 (d), 45.6 (d), 29.6 (q), 22.7 (d), 19.6 (q), 9.9 (t).

anti-Isomer 11a

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.29 (dd, *J* = 5.8, 2.8, Hz, 1 H), 6.25 (dd, *J* = 5.8, 2.7, Hz, 1 H), 3.73–3.64 (m, 4 H), 3.50–3.40 (m, 2 H), 3.14 (dd, *J* = 11.1, 9.0 Hz, 1 H), 2.82–2.76 (m, 2 H), 2.34 (br s, 1 H), 2.13 (br s, 1 H), 1.34 (s, 3 H), 1.33 (s, 3 H), 0.66 (dd, *J* = 8.6, 5.6 Hz, 1 H), 0.33 (t, *J* = 5.4 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 136.8 (d), 134.5 (d), 101.3 (s), 64.56 (t), 64.54 (t), 64.5 (t), 51.2 (d), 51.2 (s), 46.3 (d), 45.7 (d), 45.1 (d), 29.7 (q), 20.8 (d), 19.7 (q), 12.0 (t).

Anal. Calcd for $C_{15}H_{22}O_3$ (250.33): C, 71.97; H, 8.86. Found: C, 71.88; H, 8.85.

2′-{[5-(_tert_-Butyldimethylsiloxy)pentyloxy]methyl}-2,3-bis(hydroxymethyl)spiro[bicyclo[2.2.1]hept-5-ene-7,1′-cyclopropane] Acetonide (11c)

Following the typical procedure for **11a** using **8c** (411 mg, 1 mmol) gave, after chromatiography on silica gel (PE–Et_2O, 50:50), **11c** (293 mg, 0.65 mmol, 65%).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.17 (t, *J* = 1.8 Hz, 2 H), 3.72–3.64 (m, 2 H), 3.57 (t, *J* = 6.4 Hz, 2 H), 3.51–3.16 (m, 4 H), 2.77 (br d, *J* = 9.0 Hz, 2 H), 2.28 (br s, 1 H), 2.08 (br s, 1 H), 1.58–1.45 (m, 5 H), 1.35 (s, 3 H), 1.33 (s, 3 H), 1.27 (m, 2 H), 1.10 (m, 2 H), 0.87 (s, 9 H), 0.64 (dd, *J* = 8.3, 5.3 Hz, 1 H), 0.31 (t, *J* = 5.3 Hz, 1 H), 0.02 (s, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 135.0 (d), 134.4 (d), 101.2 (s), 72.2 (t), 70.4 (t), 64.7 (t), 64.6 (t), 63.1 (t), 51.2 (s), 50.7 (d), 46.6 (d), 45.7 (d), 45.2 (d), 32.6 (t), 29.4 (t), 25.9 (q, 3 C), 24.4 (q), 22.4 (t), 19.7 (q), 18.3 (s), 18.2 (d), 12.5 (t), –5.3 (q, 2 C).

Anal. Calcd for $C_{26}H_{46}O_4Si$ (450.73): C, 69.28; H, 10.29. Found: C, 69.48; H, 10.35.

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