



Enantiomerically Pure Diels-Alder Adducts of Maleic Anhydride to Furfural Acetals Through Thermodynamic Control. Single Crystal and Molecular Structure of (1*S*,4*R*,4'*S*,5'*S*)-1-(4',5'-dimethyldioxolan-2'-yl)-5,6-dimethylidene-7-oxabicyclo[2.2.1]hept-2-ene.

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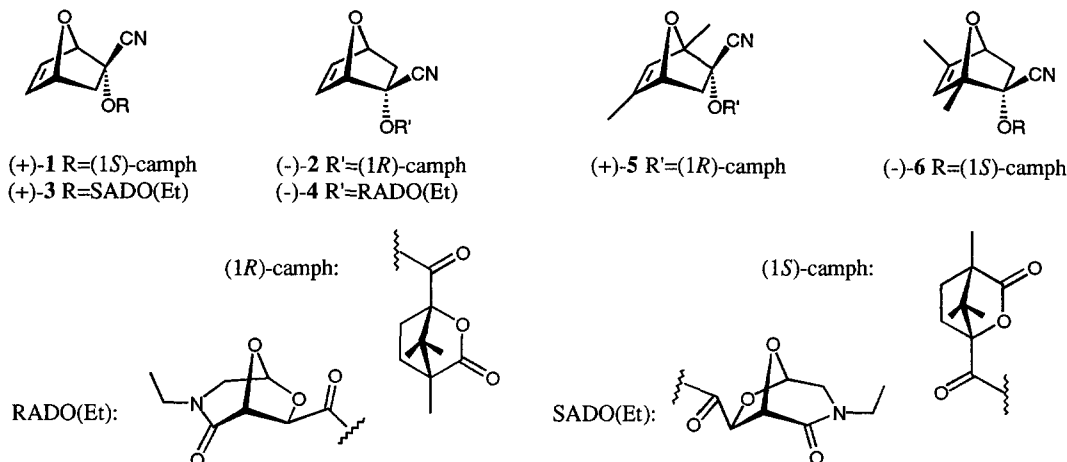
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Abstract: The acetal of (2*S*,3*S*)-butane-2,3-diol and furfural is equilibrated in molten maleic anhydride with one major crystalline product which is a 1:1 complex of maleic anhydride and (1*S*,2*R*,3*S*,4*R*,4'*S*,5'*S*)-1-(4',5'-dimethyldioxolan-2'-yl)-7-oxabicyclo[2.2.1]hept-5-ene-2-*exo*,3-*exo*-dicarboxylic anhydride. This compound was converted into (1*S*,4*R*,4'*S*,5'*S*)-1-(4',5'-dimethyldioxolan-2'-yl)-5,6-dimethylidene-7-oxabicyclo[2.2.1]hept-2-ene (+)-12, the circular dichroism spectrum of which suggests a slightly skew *s*-cis-butadiene chromophore as confirmed by X-ray diffraction. Copyright © 1996 Elsevier Science Ltd

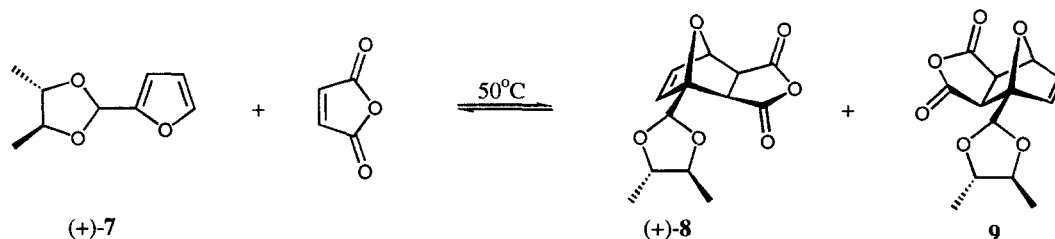
Derivatives of 7-oxabicyclo[2.2.1]heptene have proven to be useful starting materials in the synthesis of a large variety of natural products and of compounds of biological interest.¹ These bicyclic systems are available most simply through intermolecular Diels-Alder additions of furans to activated dienophiles. Furfural and furan are very inexpensive compounds obtained as waste products from agriculture.² Because of the aromaticity of furans, their intermolecular Diels-Alder additions to olefinic dienophiles are reversible at room temperature or at temperatures close to it.³ Asymmetric cycloadditions can be induced with homochiral Lewis acid catalysts only if the reactions can be carried out at low temperature. Corey and Loh have found such a catalyst for the cycloadditions of furan to 2-chloro and 2-bromoacrolein.^{4a} Alternatively, enantiomerically pure 7-oxabicyclo[2.2.1]heptenes have been obtained by chemical^{4b} or enzymatic⁵ resolution of racemic derivatives, by desymmetrisation of *meso* systems through homochiral reagents⁶ or enzymatic processes.⁷ For highly reactive (electron-rich) furans and (electron-poor) dienophiles, the use of either a homochiral furan⁸ or homochiral dienophile⁹ can lead to kinetically controlled diastereoselectivity when the cycloadditions are run below 20°C. For our part, we have exploited the reversibility of the furan¹⁰ and 2,4-dimethylfuran¹¹ additions to 1-cyanovinyl esters derived from enantiomerically pure carboxylic acids (chiral auxiliaries) to generate enantiomerically pure adducts such as (+)-1 - (-)-4 ("naked sugars of the first generation"^{1c}) and (+)-5 and (-)-6 ("naked sugars of the second generation"^{11,12}). In this report we show that the Diels-Alder adducts of the (2*S*,3*S*)- and the (2*R*,3*R*)-butanediol acetal of furfural to maleic anhydride can be obtained in enantiomerically pure form. This can be achieved by choosing equilibrating conditions under which one of the two *exo* adducts

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generates a 1:1 complex with maleic anhydride that gives crystals which are more stable than the other diastereomeric adducts. Diels-Alder adducts of achiral furfural acetal to maleic anhydride have been used as starting materials in the synthesis of natural products.¹³ Furthermore, some of their platinum derivatives are antineoplastic agents.¹⁴



Acid-catalyzed (camphorsulfonic acid) acetalization of furfural with (2*S*,3*S*)-butanediol (>98% e.e.) gave (+)-7 (92%). When a 1:1 mixture of (+)-7 and maleic anhydride was heated to 55°C (24 h), a 1:1 mixture of the two possible *exo* adducts (+)-8 and 9 was obtained (by ¹H-NMR of the crude). Recrystallization from hexane afforded a solid which comprised a 1:4 mixture of (+)-8 and 9 (75%). When a 1:2 mixture of (+)-7 and maleic anhydride was heated to 55°C (24 h) and allowed to crystallize, a solid composed of a 7:2 mixture of (+)-8 and 9 (80%) was isolated. These experiments suggested that the excess of maleic anhydride has an effect on the adduct diastereomeric ratio. We finally found that an enantiomerically pure 1:1 complex of (+)-8 and maleic anhydride could be obtained in good yield (78%) after heating (+)-7 with a 6-7 fold excess of maleic anhydride without solvent (50°C, 1 d; then 55°C, 7 d) and extraction with toluene. The 1:1 complex of (+)-8 and maleic anhydride was then treated with an excess of isoprene which reacted with maleic anhydride giving the corresponding Diels-Alder adduct that was extracted with hexane. The crude adduct (+)-8 was then recrystallized from EtOAc to give (+)-8 in 60% yield (based on (+)-7). The diastereomeric purity of (+)-8 was determined (by 400 MHz ¹H-NMR, using ¹³C satellite signals) to be better than 98%.



Reduction of (+)-8 or of the 1:1 complex of (+)-8 and maleic anhydride with LiAlH₄ (THF, 0-5°C, 3 h, then 65°C, 3 h) afforded the corresponding diol (-)-10 (75%) which was esterified by CH₃SO₂Cl and pyridine to give the dimesylate (-)-11 (80%). Double elimination of mesylic acid with *t*-BuOK in 5:1 DMF/HMPT

provided triene (+)-**12** (60%). Starting with (2*R*,3*R*)-butane-2,3-diol led to the corresponding enantiomers (-)-**8**, (+)-**10**, (+)-**11** and (-)-**12** with the same ease.

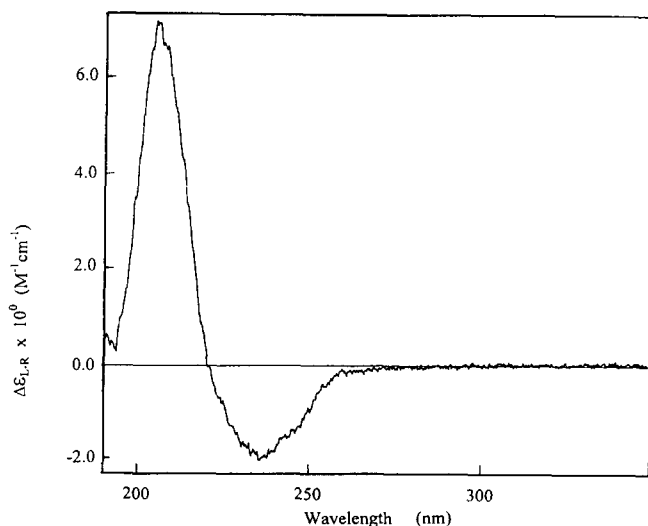
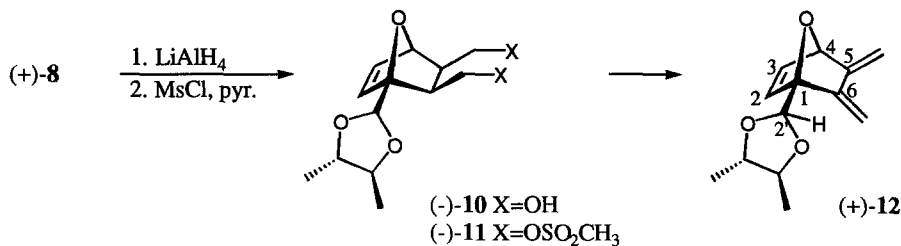


Figure 1. Circular dichroism spectrum of (+)-**12** (isooctane) (same spectrum was recorded in MeOH)

The circular dichroism spectrum of (+)-**12** (Figure 1) displays a negative Cotton Effect at $\lambda = 237$ nm corresponding to the λ_{max} : 230 nm of its UV absorption spectrum associated with the $V \leftarrow N$ transition of the *s-cis*-butadiene chromophore.¹⁵ For steric reasons, the dioxanyl substituent at the bridgehead centre C(1) induces the bending of the methyldene group at C(6) toward the *endo* face of the 7-oxabicyclo[2.2.1]heptene system. This forces the *s-cis*-butadiene to adopt a skew conformation with negative helicity.¹⁶ This hypothesis is confirmed by single crystal X-ray diffraction studies of (+)-**12** (see Figure 2, Table 1) which shows a dihedral angle for $\text{H}_2\text{C}=\text{C}(5)-\text{C}(6)=\text{CH}_2$ of $-2.3(0.5)^\circ$. This is a relatively small out of plane deviation which might be due to lattice effects in the crystal. Therefore, one cannot yet exclude the possibility that the dichroic properties of (+)-**12** arise from an allylic substituent effect¹⁷ of the dioxanyl group and/or from dipole/dipole coupling between the *s-cis*-butadiene and the C(2)-C(3) olefinic chromophores.

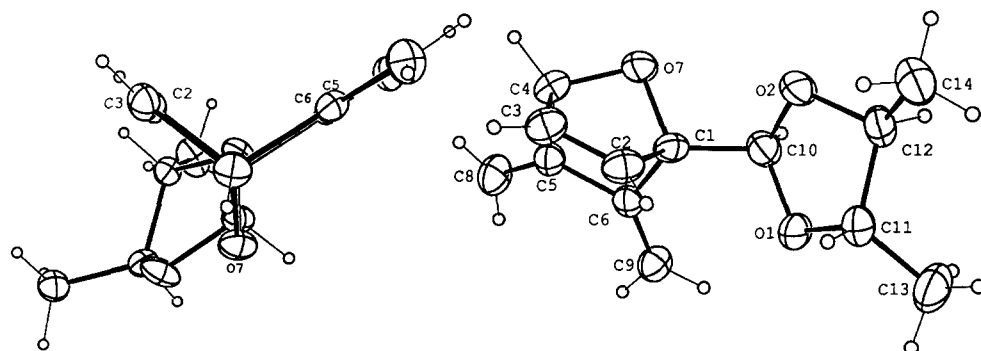


Figure 2. ORTEP¹⁸ representation of (+)-**12** (50% probability ellipsoids for non-H atoms)

The X-ray structure of (+)-**12** shows that the dioxanyl group adopts a conformation which minimizes the gauche interactions of this substituent with the methylene moiety at C(6).

Table 1. Selected bond lengths, bond angles and torsion angles for crystalline (+)-**12** (C₁₃H₁₅O₃, nonclitic, P2₁; atom numbering: see Figure 2)

<i>Distances (Å)</i>		<i>Angles (°)</i>	
C(1)–C(2)	1.525(4)	C(2)–C(1)–C(6)	104.9(2)
C(2)–C(3)	1.322(4)	C(1)–O(7)–C(4)	96.1(2)
C(3)–C(4)	1.515(4)	C(3)–C(4)–C(5)	105.8(2)
C(4)–C(5)	1.526(4)	C(1)–C(2)–C(3)	105.5(2)
C(5)–C(6)	1.487(4)	C(1)–C(6)–C(5)	102.3(2)
C(1)–C(6)	1.538(3)	C(4)–C(5)–C(6)	102.9(2)
C(1)–O(7)	1.445(3)	O(7)–C(1)–C(10)	111.2(2)
C(4)–O(7)	1.451(3)	O(1)–C(10)–O(2)	107.9(2)
C(5)–C(8)	1.316(4)		
C(6)–C(9)	1.319(4)	<i>Torsion angles (°)</i>	
C(1)–C(10)	1.502(4)	C(8)–C(5)–C(6)–C(9)	–2.3(5)
C(10)–O(1)	1.417(3)	C(4)–C(5)–C(6)–C(1)	–0.9(2)
C(10)–O(2)	1.403(3)	C(1)–C(2)–C(3)–C(4)	0.5(3)
		C(6)–C(1)–C(10)–O(1)	–65.3(3)
		C(6)–C(1)–C(10)–O(2)	175.8(2)

Simple conditions have been found to generate enantiomerically pure Diels–Alder adducts of maleic anhydride to the (2*S*, 3*S*)- and (2*R*, 3*R*)-butane-2,3-diol acetals of furfural. Triene (+)-**12** and (-)-**12** add to non-symmetrical dienophiles with high regio- and stereoselectivity,¹⁹ allowing one to prepare a variety of enantiomerically pure 1,2,3,4-tetrahydronaphthalene derivatives. This will be described in a forthcoming report.

Experimental Part

General remarks, see ref. 20. Circular dichroism spectra were recorded on JOBIN YVON MARK V Optical Rotation, on JASCO, DIP-370 digital polarimeter. Crystal of (+)-**12**: colourless needle, 0.35 x 0.12 x 0.06 mm, mounted on a glass fiber; monoclinic *P*2₁; *a* = 7.531(3), *b* = 7.785(2), *c* = 10.160(2) Å, β = 98.88(3)°; *V* = 589(1) Å³; *Z* = 2, *D*_x = 1.24 g/cm³; λ (Mo *K*α) = 0.71073 Å; μ = 0.8 cm⁻¹; *F*(000) = 236; *T* = 193 ± 1 K. X-ray diffractometer: Enraf-Nonius CAD4, graphite monochromator, ω - 2 θ scan technique, backgrounds obtained from analysis of the scan profile,²¹ unit cell constants from the setting angles of 25 reflections in the range 9 < θ < 16°, empirical absorption correction (from 0.902 to 0.997 on *I*), maximum 2 θ = 52.0°, 0 < *h* < 9; -9 < *k* < 9; -12 < *l* < 12; anisotropic decay (from 0.947 to 1.236 on *I*), reflection averaging *R*(int) = 4.2%, 2506 total reflections measured, 2328 unique, 1779 reflections with *F*_o² > 3.0σ(*F*_o²), solution by direct methods,²² refinement by full-matrix least-squares, function minimized was $\sum w(|F_o| - |F_c|)^2$, weight *w* is defined as 4*F*_o²/σ²(*F*_o²), hydrogen atoms located and refined isotropically, 209 refined parameters, *R* = 0.044, *wR* = 0.054, *S* = 1.18, largest shift = 0.02σ, high peak in final difference map 0.29(7) e/Å³, low peak -0.38(7) e/Å³. Scattering factors for neutral atoms and the values for Δ*f*' and Δ*f*'' were taken from International Tables for X-ray Crystallography;²³ computer programs MolEN.^{24,25}

(4'*S*, 5'*S*)-2-(4', 5'-Dimethyldioxolan-2'-yl)furan ((+)-**7**). A mixture of furfural (7.5 g, 78 mmol), (2*S*, 3*S*)-butane-2,3-diol (Fluka, ≥98% e.e., 4.98 g, 54.9 mmol), benzene (400 ml) and (+)-camphorsulfonic acid (200 mg, 0.86 mmol) was heated under reflux in a Dean-Stark apparatus. After 8 h (control by tlc on silica gel, EtOAc/light petroleum 1:15), the mixture was cooled to 20°C and was washed with sat. aqueous solution of NaHCO₃ (50 ml, 3 times) and then with water (50 ml, 3 times). After drying (MgSO₄), the solvent was evaporated and the residue purified by flash chromatography (silica gel, EtOAc/light petroleum 1:15), yielding 8.51 g (92%), colourless oil. $[\alpha]_{589}^{25} = +21$, $[\alpha]_{578}^{25} = +22$, $[\alpha]_{546}^{25} = +25$, $[\alpha]_{436}^{25} = +42$, $[\alpha]_{365}^{25} = +74$ (*c* = 1.0 *n*-hexane). UV (CH₃CN): $\lambda_{\max}$: 223 nm (ϵ = 2500). IR (film) ν : 3060, 3020, 2980, 2930, 2880, 1500, 1380, 1350, 1320, 1310, 1250, 1225, 1150, 1095 cm⁻¹. ¹H-NMR (250 MHz, CDCl₃) δ_{H} : 7.42 (dd, ³*J* = 2.0, ⁴*J* = 1.0, H-C(5)); 6.45 (dd, ³*J* = 3.5, ⁴*J* = 1.0, H-C(3)); 6.33 (dd, ³*J* = 3.5, 2.0, H-C(4)); 5.98 (s, H-C(2')); 3.89–3.67 (2xdq, ³*J* = 8.0, 6.0, H-C(4'), H-C(5')); 1.48 (d, ³*J* = 6.0, CH₃); 1.37 (d, ³*J* = 6.0, CH₃). ¹³C-NMR (100.61 MHz, CDCl₃) δ_{C} : 152.1 (s, C(2)); 142.8 (d, ¹*J*(C,H) = 202, C(5)); 110.0, 108.3 (2d, ¹*J*(C,H) = 175, 176, C(3), C(4)); 96.5 (d, ¹*J*(C,H) = 169, C(2')), 79.7, 78.0 (2d, ¹*J*(C,H) = 148, 148, C(4'), C(5')); 16.6, 16.3 (2q, ¹*J*(C,H) = 127, 127 CH₃). CI-MS (NH₃) *m/z*: 180 (79), 170 (15), 169 (10, [M+1]⁺), 162 (27), 132 (8), 114 (19), 100 (13), 95 (16), 85 (19), 78 (93), 77 (20), 84 (100), 72 (21). Anal. calc. for C₉H₁₂O₃ (168.19): C 64.27, H 7.19; found: C 64.20, H 7.20.

(1*S*, 2*R*, 3*S*, 4*R*, 4'*S*, 5'*S*)-1-(4', 5'-Dimethyldioxolan-2'-yl)-7-oxabicyclo[2.2.1]hept-5-ene-2-exo,3-exo-dicarboxylic anhydride ((+)-**8**). A mixture of freshly sublimed maleic anhydride (2.61 g, 26.6 mmol) and (+)-**7** (1.5 g,

8.9 mmol) was heated at 50°C for 1 day, in the dark under an Ar atmosphere. More maleic anhydride (2.75 g, 28.0 mmol) was added and the mixture was heated to 55°C, in the dark under an Ar atmosphere for one week. The hot mixture was poured into toluene (20 ml) with vigorous stirring. After stirring at 20°C for 2 h, the crystals were collected (4.1 g of a 1:1 complex of (+)-**8** and maleic anhydride, 78%). The crystals were dissolved at 20°C in isoprene (7 ml) and the mixture stirred at 20°C for 24 h. The excess of isoprene was recovered by distillation under vacuum and the residue was poured at once into boiling hexane (75 ml). After stirring for 1 min, the crystals were collected and washed again with boiling hexane (75 ml). Recrystallization from EtOAc/light petroleum (charcoal can be used to decolourize if necessary) yielded 1.4 g (60%), colourless crystals, m.p. 106–109°C. $[\alpha]_{589}^{25} = +0.5$, $[\alpha]_{578}^{25} = +1.2$, $[\alpha]_{546}^{25} = +0.3$, $[\alpha]_{436}^{25} = -5.9$, $[\alpha]_{365}^{25} = -23$ ($c = 1.0$, CHCl₃). UV (CH₃CN): final abs. $\epsilon_{220} = 690$. IR (KBr) ν : 2975, 2895, 1785, 1775, 1705, 1630, 1585, 1550, 1445, 1430, 1380, 1255, 1235, 1110, 1070, 985, 925, 865, 850 cm⁻¹. ¹H-NMR (400 MHz, CDCl₃) δ_{H} : 6.61 (dd, ³ $J = 5.8, 1.7$, H-C(5)); 6.53 (d, ³ $J = 5.8$, H-C(6)); 5.54 (s, H-C(2')); 5.49 (d, ³ $J = 1.7$, H-C(4)); 3.84–3.74 (m, H-C(4'), H-C(5')); 3.34, 3.27 (2d, AB, ³ $J = 6.8$, H-C(2), H-C(3)); 1.37 (d, ³ $J = 5.7$, CH₃); 1.34 (d, ³ $J = 5.7$, CH₃). ¹³C-NMR (100.61 MHz, CDCl₃) δ_{C} : 169.5 (s, COO); 167.4 (s, COO); 137.3, 136.9 (2d, ¹ J (C,H) = 179, 181, C(5), C(6)); 98.6 (d, ¹ J (C,H) = 171, C(2')); 92.9 (s, C(1)); 82.6 (d, ¹ J (C,H) = 172, C(4)); 80.8, 79.4 (2d, ¹ J (C,H) = 136, 144, C(4'), C(5')); 51.7, 48.8 (2d, ¹ J (C,H) = 149, 151, C(2), C(3)); 17.1, 16.5 (2q, ¹ J (C,H) = 129, 128, CH₃). CI-MS (NH₃) m/z : 395 (0.3), 284 (1), 267 (1, [M+1]⁺), 266 (0.2, M⁺), 265 (3), 194 (1), 177 (2), 169 (12), 167 (20), 124 (10), 101 (100), 97 (15), 95 (43), 80 (25), 73 (30), 72 (34). Anal. calc. for C₁₃H₁₄O₆ (266.25): C 58.63, H 5.30; found: C 58.57, H 5.34.

(1*S*,2*R*,3*S*,4*R*,4'*S*,5'*S*)-1-(4',5'-Dimethyldioxolan-2'-yl)-7-oxabicyclo[2.2.1]hept-5-ene-2-exo,3-exo-dimethanol ((-)-**10**). LiAlH₄ (425 mg, 11.2 mmol) in dry THF (8 ml) was cooled to 0°C under Ar atmosphere. A solution of (+)-**8** (1 g, 3.8 mmol) in dry THF (5 ml) was added dropwise to the vigorously stirred suspension maintained at 0°C. The ampoule of addition was rinsed with THF (1 ml). The mixture was stirred at 0°C for 3 h and then heated under reflux for 3 h (tlc control, silica gel, AcOEt). It was then cooled to 0°C, and the excess of hydride was destroyed by slow addition of triethanolamine (2 ml), so that the temperature was maintained below 5°C. Et₂O (4 ml) was added and the mixture was stirred at 20°C for 15 min. The solution was filtered through a Celite pad, then twice through Dowex 50Wx8 (17 g, rinsing with MeOH), and evaporated. The residue was purified by flash chromatography (AcOEt); yielding 692 mg (76%), colourless crystals, m.p. 95–98°C. $[\alpha]_{589}^{25} = -2.7$, $[\alpha]_{577}^{25} = -4.3$, $[\alpha]_{546}^{25} = -3.8$, $[\alpha]_{435}^{25} = -0.8$, $[\alpha]_{405}^{25} = +3.1$ ($c = 1.43$, MeOH). UV (CH₃CN): final abs. $\epsilon_{220} = 750$. IR (KBr) ν : 3440, 3320, 2965, 2925, 2895, 1465, 1445, 1380, 1330, 1295, 1185, 1135, 1095, 1040, 990, 950, 930, 895, 875, 815, 735, 705, 645 cm⁻¹. ¹H-NMR (400 MHz, CDCl₃) δ_{H} : 6.45 (dd, ³ $J = 5.8, 1.6$, H-C(5)); 6.33 (d, ³ $J = 5.8$, H-C(6)); 5.46 (s, H-C(2')); 4.88 (d, ³ $J = 1.6$, H-C(4)); 3.93–3.86 (br. m, 2 x CH₂OH); 3.77 (m, H-C(4'), H-C(5')); 2.06 (m, H-C(2), H-C(3)); 1.35 (d, ³ $J = 5.7$, CH₃); 1.26 (d, ³ $J = 5.7$, CH₃). ¹³C-NMR (100.61 MHz, CDCl₃) δ_{C} : 136.3, 135.8 (2d, ¹ J (C,H) = 176, 178, C(5), C(6)); 100.3 (d, ¹ J (C,H) = 166, C(2')); 90.3 (s, C(1)); 81.4 (d, ¹ J (C,H) = 163, C(4)); 80.6, 78.9 (2d, ¹ J (C,H) = 154, 145, C(4'), C(5')); 61.9, 59.5 (2t, ¹ J (C,H) = 144, 143, CH₂OH); 44.4, 43.6 (2d, ¹ J (C,H) = 136, C(2), C(3)); 17.1, 16.5 (2q, ¹ J (C,H) = 126, 128, CH₃). CI-MS (NH₃) m/z : 318 (1), 257 (8, [M+1]⁺), 227 (8), 209 (9), 169 (9), 168 (29), 167 (15), 140 (3), 133 (4), 114 (29), 101 (100), 95 (22), 80 (14), 80 (14), 73 (32). Anal. calc. for C₁₃H₂₀O₅ (256.30): C 60.92, H 7.87; found: C 60.94, H 7.19.

(1*S*,2*R*,3*S*,4*R*,4'*S*,5'*S*)-1-(4',5'-Dimethyldioxolan-2'-yl)-7-oxabicyclo[2.2.1]hept-5-ene-2-exo,3-exo-dimethyl dimethanesulfonate ((-)-**11**). (-)-**10** (50 mg, 0.206 mmol) was dissolved in dry pyridine (1 ml) and cooled to -15°C under Ar atmosphere. CH₃SO₂Cl (0.1 ml, 1.28 mmol) was added over 5 min. and the mixture was stirred at 0°C for 3 h (tlc control, silica gel AcOEt/light petroleum 10:1). It was then poured into cold water (100 ml), extracted with CH₂Cl₂ (50 ml, 3 times). The combined extracts were dried (MgSO₄) and the solvent was evaporated. Recrystallization from MeOH yielded 68 mg (80%), colourless crystals, m.p. 104–106°C. [α]₅₈₉²⁵ = -20, [α]₅₇₇²⁵ = -20, [α]₅₄₆²⁵ = -23, [α]₄₃₅²⁵ = -38 (*c* = 1.11, MeOH). UV (CH₃CN): final abs. ϵ_{220} = 150. IR (KBr) ν : 3020, 1385, 1345, 1165, 1090, 1065, 1030, 980, 960, 865, 820, 815 cm⁻¹. ¹H-NMR (400 MHz, CDCl₃) δ _H: 6.44 (dd, ³*J* = 5.8, 1.5, H-C(5)); 6.41 (d, ³*J* = 5.8, H-C(6)); 5.37 (s, H-C(2')); 5.00 (d, ³*J* = 1.5, H-C(4)); 4.66–4.61 (2xdd, ³*J* = 10.1, 5.2, H₂COMs); 4.27–4.20 (m, ³*J* = 10.0, H₂COMs); 3.78–3.70 (br. m, H-C(4'), H-C(5')); 3.07 (s, OMs); 2.35 (2xm, H-C(2), H-C(3)); 1.34 (d, ³*J* = 5.7, CH₃); 1.29 (d, ³*J* = 5.7, CH₃). ¹³C-NMR (100.61 MHz, CDCl₃) δ _C: 136.2, 135.5 (2d, ¹*J*(C,H) = 173, 177, C(5), C(6)); 99.5 (d, ¹*J*(C,H) = 167, C(2')); 90.6 (s, C(1)); 80.6, 80.5 (2d, ¹*J*(C,H) = 150, 150, C(4'), C(5')); 79.1 (d, ¹*J*(C,H) = 156, C(4)); 69.3 (t, ¹*J*(C,H) = 147, CH₂OMs); 66.7 (t, ¹*J*(C,H) = 150, CH₂OMs); 42.0, 41.8 (2d, ¹*J*(C,H) = 142, 140, C(2), C(3)); 37.7, 37.4 (2q, ¹*J*(C,H) = 139, 139, Ms); 17.1, 16.5 (2q, ¹*J*(C,H) = 129, 2 CH₃). CI-MS (NH₃) *m/z*: 430 (4), 414 (2, [M+1]⁺), 317 (6), 245 (9), 220 (3), 198 (2), 168 (6), 167 (12), 140 (5), 124 (5), 114 (21), 102 (10), 101 (100), 95 (14), 81 (14), 80 (20), 79 (26), 73 (23). Anal. calc. for C₁₅H₂₄O₉S₂ (412.09): C 43.68, H 5.86, S 15.55; found: C 43.59, H 5.99, S 15.44.

(1*S*,4*R*,4'*S*,5'*S*)-1-(4',5'-Dimethyldioxolan-2'-yl)-5,6-dimethylidene-7-oxabicyclo[2.2.1]hept-2-ene ((+)-**12**). A mixture of (-)-**11** (350 mg, 0.848 mmol), dry DMF (3.5 ml) and dry HMPT (0.7 ml) was cooled to -15°C under Ar atmosphere. *t*-BuOK (1.05 g, 9.36 mmol) was added over 10 min. and the mixture was stirred at -15°C for 8 h. It was then poured in water (25 ml) and extracted with light petroleum (25 ml, 11 times). The combined extracts were dried (MgSO₄) and the solvent was evaporated without heating. The residue was purified by flash chromatography on Florisil (light petroleum/AcOEt 10:1) and recrystallized from light petroleum yielding 110 mg (60%), colourless crystals, m.p. 73–74°C. [α]₅₈₉²⁵ = +50, [α]₅₇₇²⁵ = +51, [α]₅₄₆²⁵ = +57, [α]₄₃₅²⁵ = +97, [α]₄₀₅²⁵ = +117 (*c* = 1.24, CHCl₃). CD (MeOH): $\Delta\epsilon_{233}$ = -0.66; $\Delta\epsilon_{227}$ = 0; $\Delta\epsilon_{208}$ = 6.9 (*c* = 0.082 mg/ml). UV (MeOH): $\lambda_{\max}$: 230 (ϵ = 7110). IR (KBr) ν : 2970, 2890, 2870, 1670, 1645, 1635, 1445, 1380, 1320, 1260, 1180, 1090, 1030, 1020, 985, 890, 810, 675 cm⁻¹. ¹H-NMR (250 MHz, CDCl₃) δ _H: 6.50 (dd, ³*J* = 5.5, 1.6, ⁵*J* = 0.7, H-C(3)); 6.42 (d, ³*J* = 5.5, H-C(2)); 5.54 (s, H-C(2')); 5.38 (s, H-C=C(6)); 5.35 (s, H-C=C(6)); 5.27 (d, ⁵*J* = 0.7, H-C=C(5)); 5.21 (br. s, H-C(4)); 5.10 (s, H-C=C(5)); 3.76 (m, H-C(4'), H-C(5')); 1.36 (d, ³*J* = 5.9, CH₃); 1.32 (d, ³*J* = 5.9, CH₃). ¹³C-NMR (100.61 MHz, CDCl₃) δ _C: 144.3, 142.7 (2s, C(5), C(6)); 136.4, 134.4 (2d, ¹*J*(C,H) = 178, 179, C(2), C(3)); 103.3, 102.1 (2t, ¹*J*(C,H) = 159, 159, CH₂=C(5), CH₂=C(6)); 100.0 (d, ¹*J*(C,H) = 168, C(2')); 90.9 (s, C(1)); 82.7 (d, ¹*J*(C,H) = 167, C(4)); 80.0, 79.3 (2d, ¹*J*(C,H) = 145, 150, C(4'), C(5')); 17.0, 16.5 (2q, ¹*J*(C,H) = 127, 129, CH₃). CI-MS (NH₃) *m/z*: 238 (8), 221 (3), 220 (2, M⁺), 203 (5), 191 (2), 169 (3), 167 (2), 105 (7), 101 (100), 91 (17), 73 (12). Anal. calc. for C₁₃H₁₆O₃ (220.27): C 70.89, H 7.32; found: C 70.70, H 7.19.

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