

152. Synthesis of (+)-1,3:2,5-Dianhydroviburnitol (+)-(1*R*,2*R*,3*S*,5*R*,6*S*)-4,7-Dioxatricyclo[3.2.1.0^{3,6}]octan-2-ol)

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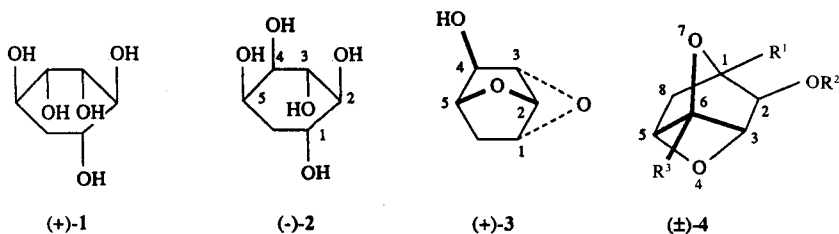
(31.V.88)

Epoxidation of (–)-(1*R*,2*R*,4*R*)-2-*endo*-cyano-7-oxabicyclo[2.2.1]hept-5-en-2-*exo*-yl acetate ((–)-5) followed by saponification afforded (+)-(1*R*,4*R*,5*R*,6*R*)-5,6-*exo*-epoxy-7-oxabicyclo[2.2.1]heptan-2-one ((+)-7). Reduction of (+)-7 with diisobutylaluminium hydride (DIBALH) gave (+)-1,3:2,5-dianhydroviburnitol (= (+)-(1*R*,2*R*,3*S*,4*R*,6*S*)-4,7-dioxatricyclo[3.2.1.0^{3,6}]octan-2-ol; (+)-3). Hydride reductions of (±)-7 were less *exo*-face selective than reductions of bicyclo[2.2.1]heptan-2-one and its derivatives with NaBH₄, AlH₃, and LiAlH₄ probably because of smaller steric hindrance to *endo*-face hydride attack when C(5) and C(6) of the bicyclo[2.2.1]heptan-2-one are part of an *exo* oxirane ring.

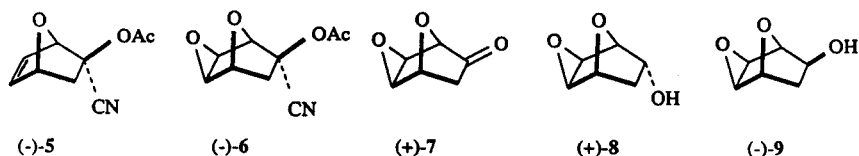
Introduction. – Whereas inositols (cyclohexanehexols) are ubiquitous in nature and have been widely studied [1] [2], only three of the sixteen possible cyclohexanepentols are natural products and have been found in plants. Among them, (+)-quercitol ((+)-1, acorn sugar [3]) is by far the most common and has been recognized since 1851 [4]. Its enantiomer, (–)-quercitol, has been found in the leaves of an eucalypt [5a] and in mistletoe [5b]. (–)-Viburnitol ((–)-2) was isolated first in 1904 from the leaves of *Gymnema sylvestre* by Power and Tutin [6], who named it '1-quercitol', and then, in 1935, by Hérissé and Poirot [7] from the fruit and leaves of *Viburnum Tinus*. In 1950, the two cyclitols were proved to be identical, and the structure was elucidated [8]. Since then, (–)-viburnitol has been found in many plant families [9–11]. (–)-Viburnitol is often a very minor constituent of the cyclitol fraction [11]; this suggests that its actual presence could have been overlooked in certain cases where the individual cyclitols were obtained only by crystallization from the extract [9].

The non-natural enantiomer, (+)-viburnitol, has been synthesized by Posternak from 1*D*-*chiro*-inositol [12], whereas racemic (±)-viburnitol was obtained either from an inosamine derived from D-glucose [13] or from *myo*-inositol in three steps [14]. Thus, (±)-viburnitol can be used as the starting material for the synthesis of deoxyinosamines [15]. It has also been noted that in acidic medium (–)-viburnitol and (+)-quercitol are readily interconverted [16]. As part of a detailed study of the biosynthesis of cyclitols, Kindl and Hoffmann-Ostenhof found that, among several possible precursors, only D-glucose was incorporated into (–)-viburnitol [11]. There was, for example, no interconversion between (–)-viburnitol and (+)-quercitol. The biosynthetic pathway is believed to be different from those of the various inositols [17]. It was shown by ¹⁴CO₂ incorporation studies in *Cynanchum vincetoxicum* that (–)-viburnitol was rather quickly build up and destroyed [11]. In non-leguminous nodulated plants, the presence of (–)-viburnitol is perhaps related to the symbiotic nitrogen fixation [10]. (–)-Viburnitol has no

effect on the growth of seedlings of *Pisum sativum* [18]; however, it has an antivitaminic action against *meso*-inositol in 'inositol-less' *Neurospora crassa* [19]. Recently, Soloway *et al.* [20] found that derivatives of 1,3:2,5-dianhydroviburnitol (($\pm$)-3), the ($\pm$)-4,7-dioxatricyclo[3.2.1.0^{3,6}]oct-2-yl ethers ($\pm$)-4, are efficient herbicides and plant-growth regulators. In connection with this work, we have developed an efficient total synthesis of optically pure (+)-1,3:2,5-dianhydroviburnitol ((+)-3) which is reported here.



Results and Discussion. – Our starting material is the 'naked sugar' (–)-5 ((–)-(1*R*,2*R*,4*R*)-*endo*-cyano-7-oxabicyclo[2.2.1]hept-5-en-2-*exo*-yl acetate, e.e. > 99%) [21] obtained by optical resolution of the corresponding cyanohydrins with brucine [22] [23]. On treatment with *m*-chloroperbenzoic acid in CHCl_3 , (–)-5 gave the corresponding epoxide (–)-6 in 92% yield. Saponification of (–)-6 with K_2CO_3 in aqueous MeOH in the presence of formaline afforded epoxyketone (+)-7 (85%) [24]. Reductions of (+)-7 with various metallic hydrides gave mixtures of *endo*- and *exo*-alcohols (+)-8 and (–)-9, respectively (see *Table*). In contrast with the high *exo*-face selectivity of the hydride reductions of bicyclo[2.2.1]heptan-2-one (10) [25–27] and of bicyclo[2.2.1]hept-5-en-2-one (11) [26], giving the corresponding *endo*-alcohols as major products, reductions of the epoxy-ketone 7 were less stereoselective (see *Table*). With AlH_3 in THF at 25°, the major product was the *exo*-alcohol 9 (ratio 8/9 0.74:1). The desired *endo*-isomer 8 was obtained with a reasonable selectivity by using diisobutylaluminium hydride (DIBAH) in THF at –78°.



Under the conditions described in the *Table*, the hydride reduction of 7-oxabicyclo[2.2.1]hept-5-en-2-one (12) gave mostly 7-oxabicyclo[2.2.1]hept-5-en-2-*endo*-ol (less than 5% of the *exo*-isomer). This suggested that the lack of *exo*-face selectivity of hydride attack on the carbonyl function in the epoxy ketone 7 cannot be attributed to coordination of the O(7) bridge to the hydride reagents, thus hindering the access to the *exo* face by the nucleophile (*cf.* [28]). Reduction of 5,6-*exo*-epoxybicyclo[2.2.1]heptan-2-one [29] (13); prepared from commercially available bicyclo[2.2.1]hept-5-en-2-*endo*- and -2-*exo*-ols, see *Exper. Part*) with NaBH_4 in *i*-PrOH at 0° gave a 2:1 mixture of the corresponding *endo*- and *exo*-alcohols 14 and 15, respectively, in 95% isolated yield. Under the same conditions, 10 and 11 gave 6:1 and 19:1 mixtures, respectively of the corresponding *endo*-

Table. Reductions of (+)-7

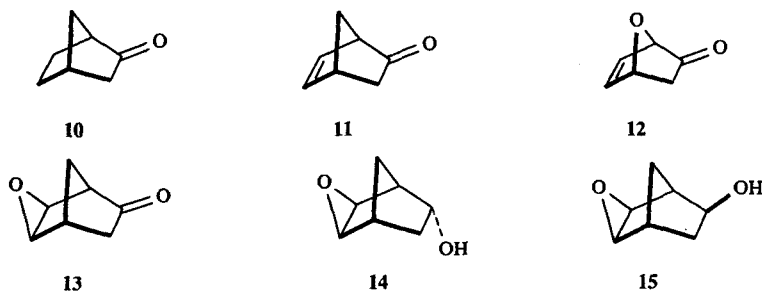
Hydride	No. of H ⁻ equiv.	Solvent	Conditions	Isolated yields [%]			Ratio <i>endo</i> / <i>exo</i> -alcohols
				8	9	7	
NaBH ₄	4	i-PrOH	0°, 90 min ^{a)}	63	30	4	2.1:1
NaBH ₄	2.7	MeOH	–78°, 3 h	53	31	14	1.7:1
NaBH ₄	2.7	THF	sat. in LiCl, 65°, 24 h	36	22	–	1.6:1
LiAlH ₄	8	Et ₂ O	36°, 15 h	41	28	6	1.45:1
AlH ₃	1.4	THF	25°, 70 min ^{b)}	31	49	– ^{c)}	1:1.35
AlH ₃	1.9	THF	–78°, 70 min	39	23	35	1.7:1
DIBAH	1.3	THF	–78°, 30 min	70	12	– ^{d)}	7.3:1

^{a)} When the reaction mixture was allowed to warm to 20° and stand at 20° for 10 h, 22% of **8**, 31% of **9** and 41% of **3** were isolated.

^{b)} When **8** was treated under these reaction conditions, 70% of **8** was recovered, and only **3** (15%) was obtained, the amount of **9** being less than 1%, *i.e.*, no significant equilibration between **8** and **9** occurred during the reduction [27c].

^{c)} 5% of **3** was also obtained.

^{d)} 18% of **3** was also obtained.



and *exo*-alcohols [26]. Therefore, our results indicate that the loss of *exo*-face preference for hydride attack in epoxy ketones **7** and **13** is associated mainly with the presence of the epoxy function. Indeed, *Dreiding* models of **7**, **10**, and **13** show that the *endo* face of the epoxy ketones **7** and **13** is sterically less hindered than that in **10** as shown in the *Figure* by comparison of angles β and α . The high *exo*-face preference for hydride attack on the carbonyl function in **12**, as in **11**, confirms the proposal of *Brown et al.* [26] that the etheno bridge in **11** (and **12**) has the same bulk as that of the ethano bridge in **10**.

Treatment of *endo*-alcohol (+)-**8** with 1.5 equiv. of KH in dimethoxyethane/hexamethylphosphoric triamide (HMPA) 10:1 (20°, 2 h) afforded (+)-**3** in 86% isolated yield (*e.e.* > 99%, by 360-MHz ¹H-NMR of the *Mosher* ester [30]). The (+)-1,3:2,5-dianhydroviburnitol (+)-**3** could also be obtained in a shorter way by allowing the reaction mixture of DIBAH reduction of epoxy ketone (+)-**7** in THF at –78° to warm up slowly to 20° within *ca.* 15 h (81% yield). Under these conditions, the aluminium alcoholate derived from the *endo*-alcohol (+)-**8** has time to open the *exo*-epoxide ring and to generate the oxetane ring. It is interesting that no products of direct hydride reduction of the epoxide moiety in **8** and **9** were observed.

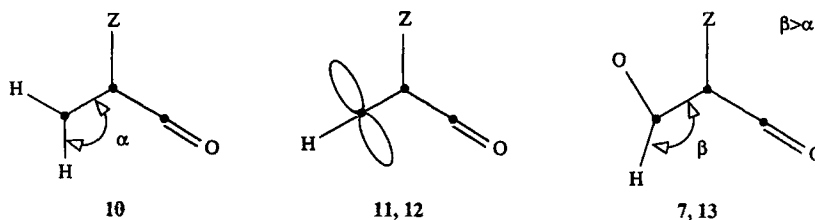
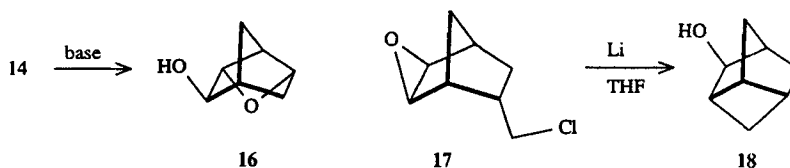


Figure. Representations of the geometries of bicyclo[2.2.1]heptan-2-ones

The structures of (+)-7, (+)-8, (–)-9, and (+)-3 follow from their mode of formation, elemental analysis, and spectral data. The relative configuration (*exo* vs. *endo*) of the alcohols was deduced from the H,H coupling constants [31] observed in the 360-MHz ¹H-NMR spectra [24] and by double-irradiation experiments including nuclear *Overhauser* effect (NOE) measurements (see *Exper. Part*).

Scheme



Our synthesis of (+)-3 applies a non-photochemical approach to oxetanes [32] which has already been exploited to prepare the carba-analog **16** of (+)-3 [33]. The synthesis of 2-*exo*-norbrendanol **18** has used a similar approach based on the Li reduction of the chloro epoxide **17** [34].

Conclusion. – A short synthesis of optically pure (e.e. > 99%) (+)-1,3:2,5-dianhydroviburnitol ((+)-3) has been realized in three steps from the naked sugar (–)-5 in 63% overall yield.

We are grateful to the Swiss National Science Foundation, to the Fonds Herbette, Lausanne, and to F. Hoffmann-La Roche & Co. AG, Basel, for financial support.

Experimental Part

General. See [24] [35].

(–)-(1*R*,2*R*,4*R*,5*R*,6*R*)-2-endo-Cyano-5,6-*exo*-epoxy-7-oxabicyclo[2.2.1]hept-2-*exo*-yl Acetate ((–)-6). Compound (–)-5 (4 g, 22 mmol; [α]_D²⁵ = +57.7, e.e. > 99%; prepared according to [23]) was treated with *m*-chloroperbenzoic acid, following the procedure used for (±)-5 [24], yielding 4.0 g (92%) of colourless crystals. M.p. 114–115°. [α]_D²⁵ = –8.4, [α]_D²⁵ = –8.6, [α]_D²⁵ = –10, [α]_D²⁵ = –17.3, [α]_D²⁵ = –26.5 (CHCl₃, *c* = 2). Spectral data: identical with those reported for (±)-6 [24]. Anal. calc. for C₉H₉NO₄ (195.173): C 55.38, H 4.61; found: C 55.49, H 4.57.

(+)-(1*R*,4*R*,5*R*,6*R*)-5,6-*exo*-Epoxy-7-oxabicyclo[2.2.1]heptan-2-one ((+)-7). According to the procedure used for (±)-7 [24], (–)-6 (3 g, 15 mmol) was treated with formaline (40% aq. H₂CO) and K₂CO₃ in MeOH, yielding 1.57 g (80%) of colourless crystals. M.p. 55–56°. [α]_D²⁵ = +374, [α]_D²⁵ = +393, [α]_D²⁵ = +462, [α]_D²⁵ = +962, [α]_D²⁵ = +2245 (CDCl₃, *c* = 2). UV (isooctane): 322 (16), 310 (27), 299 (26). UV (EtOH): 320 (sh, 11), 301 (23). CD (isooctane, *c* = 8·10^{–4} M): 321 (+2.8), 309 (+4.2), 298 (+3.9), 289 (sh, +2.6). CD (EtOH, *c* = 8·10^{–4} M): 315 (sh, +0.85), 305 (+1.33), 298 (+1.27). IR, ¹H- and ¹³C-NMR, and MS: identical with those reported for (±)-7 [24]. Anal. calc. for C₆H₆O₃ (126.110): C 57.15, H 4.80; found: C 57.23, H 4.75.

(+)-(1*S*,2*R*,4*R*,5*R*,6*S*)-5,6-exo-Epoxy-7-oxabicyclo[2.2.1]heptan-2-endo-ol ((+)-8) and (–)-(1*S*,2*S*,4*R*,5*R*,6*S*)-5,6-exo-Epoxy-7-oxabicyclo[2.2.1]heptan-2-exo-ol ((–)-9). NaBH₄ (90 mg, 2.4 mmol) was added to a soln. of (+)-7 (740 mg, 5.9 mmol) in dry MeOH (50 ml) at –78°. After 1 h at –78°, a further amount of NaBH₄ (60 mg, 1.6 mmol) was added and the mixture stirred for 2 h at –78°. Acetone (1 ml, 14 mmol) was added and the temp. allowed to rise to –20°. AcOH (1 ml, 18 mmol) was added and the mixture warmed up to 20°, evaporated to ca. 10 ml, and filtered through a 25-cm column of silica gel (AcOEt/MeOH 19:1). After evaporation, the eluate was purified by column chromatography on silica gel (*Lobar*, AcOEt), yielding first (+)-7 (105 mg, 14%), then (+)-8 (400 mg, 53%) as colourless crystals, m.p. 131–133°, and finally (–)-9 (233 mg, 31%) as colourless crystals, m.p. 93–95°. TLC (silica gel, AcOEt/MeOH 9:1): *R_f* 0.34 and 0.47 for (+)-8 and (–)-9, resp.

Data of (+)-8: Recrystallization from AcOEt/petroleum ether yielded 375 mg (50%) of colourless crystals. M.p. 133–134° ((±)-8 (obtained from (±)-7), m.p. 135–136°). [α]_D²⁵ = +39, [α]_D²⁵ = +41, [α]_D²⁵ = +47, [α]_D²⁵ = +81, [α]_D²⁵ = +130 (CHCl₃, *c* = 2). IR (KBr): 3440, 3000, 2950, 1445, 1370, 1300, 1225, 1155, 1095, 1065, 1020, 985, 940, 920, 860, 805, 770. ¹H-NMR (CDCl₃, 360 MHz): 4.48 (*ddd*, ³*J* = 8.8, 4.7, 2.8, H–C(2)); 4.45 (*d*, ³*J* = 5.3, H–C(4)); 4.35 (*d*, ³*J* = 4.7, H–C(1)); 3.59 (*AB*, ³*J* = 3.4, *v_o*δ = 94.3, H–C(5), H–C(6)); 2.4 (*br. s*, OH); 2.20 (*ddd*, ²*J* = 12.8, ³*J* = 8.8, 5.3, H_{endo}–C(3)); 1.25 (*dd*, ²*J* = 12.8, ³*J* = 2.8, H_{endo}–C(3)). ¹³C-NMR (CDCl₃, 90.55 MHz): 75.0 (*dm*, ¹*J*(C,H) = 168), 74.6 (*dt*, ¹*J*(C,H) = 165, ⁿ*J*(C,H) = 9, C(1), C(4)); 73.3 (*d*, ¹*J*(C,H) = 152, C(2)); 49.8 (*dm*, ¹*J*(C,H) = 193), 48.2 (*d*, ¹*J*(C,H) = 198, C(5), C(6)); 35.8 (*t*, ¹*J*(C,H) = 134, C(3)). MS (70 eV): 128 (1.2, *M*⁺), 110 (15), 99 (65), 97 (11), 96 (13), 95 (19), 84 (72), 82 (15), 81 (58), 71 (93), 70 (46), 69 (90), 68 (71), 55 (100). Anal. calc. for C₆H₈O₃ (128.1262): C 56.25, H 6.29; found: C 56.35, H 6.33.

Data of (–)-9: Recrystallization from AcOEt/petroleum ether gave 215 mg (29%) of colourless crystals. M.p. 95–96° ((±)-9 (obtained from (±)-7) remained an oil, despite all crystallization attempts). [α]_D²⁵ = –6.5, [α]_D²⁵ = –6.7, [α]_D²⁵ = –7.1, [α]_D²⁵ = –8.4, [α]_D²⁵ = –6.1 (CHCl₃, *c* = 2). IR (KBr): 3430, 3060, 3000, 2940, 1445, 1320, 1250, 1205, 1105, 1060, 1030, 1010, 950, 920, 860, 695. ¹H-NMR (CDCl₃, 360 MHz): 4.44 (*d*, ³*J* = 5, H–C(4)); 4.27 (*s*, H–C(1)); 3.93 (*dd*, ³*J* = 7, 2.3, H–C(2)); 3.24 (*br. s*, OH); 3.19 (*AB*, ³*J* = 3.5, *v_o*δ = 13.3, H–C(5), H–C(6)); 1.89 (*dd*, ²*J* = 13.2, ³*J* = 7, H_{endo}–C(3)); 1.54 (*ddd*, ²*J* = 13.2, ³*J* = 5, 2.3, H_{exo}–C(3)). ¹³C-NMR (CDCl₃, 90.55 MHz): 80.1, 73.3 (*2dm*, ¹*J*(C,H) = 165, C(1), C(4)); 71.8 (*d*, ¹*J*(C,H) = 150, C(2)); 50.3 (*dm*, ¹*J*(C,H) = 195), 47.2 (*d*, ¹*J*(C,H) = 193, C(5), C(6)); 39.5 (*t*, ¹*J*(C,H) = 134, C(3)). MS (70 eV): 110 (10, *M*⁺ – 18), 109 (2), 99 (35), 84 (45), 82 (15), 81 (57), 71 (92), 69 (48), 57 (60), 55 (100), 53 (93). Anal. calc. for C₆H₈O₃ (128.1262): C 56.25, H 6.29; found: C 56.39, H 6.40.

(+)-(1*R*,2*R*,3*S*,5*R*,6*S*)-4,7-Dioxatricyclo[3.2.1.0^{3,6}]octan-2-ol (= (+)-1,3:2,5-Dianhydroadipic acid; (+)-3). DIBAH (20% soln. in toluene, 6 ml, 7 mmol) was added to a soln. of (+)-7 (620 mg, 4.9 mmol) in dry THF (30 ml) at –78°. The mixture was stirred for 15 h in a dry-ice/acetone bath, allowing the temp. to rise slowly (final temperature 20°). H₂O (5 ml) and 2*N* HCl (3 ml) were added successively, and the mixture was filtered through a 25-cm column of silica gel (AcOEt). After evaporation, the eluate was separated by column chromatography on silica gel (*Lobar*, AcOEt), yielding first 442 mg (70%) of (+)-3 as colourless crystals, m.p. 99–101°, then a 2nd fraction (100 mg, 16%) of an oily 2:1 mixture (+)-3/(+)-8, and finally 82 mg (13%) of (–)-9 as colourless crystals, m.p. 93–95°. The 2nd fraction was transformed to pure (+)-3 by the following procedure. To a soln. of (+)-3/(+)-8 (100 mg, 0.78 mmol) in dimethoxyethane/HMPA 10:1 (6 ml), KH (50 mg, 1.2 mmol; prepared by 4 successive washings with pentane of a 20% suspension in oil) was added at 20°. After stirring for 2 h, EtOH (1 ml), H₂O (1 ml), and AcOH (0.2 ml) were added successively, and the mixture was filtered through a short column of silica gel (AcOEt). After evaporation, the eluate was purified by chromatography on silica gel (*Lobar*, AcOEt), giving 91 mg (14%) of (+)-3 as colourless crystals, m.p. 98–100°. Recrystallization of the combined crops of (+)-3 from AcOEt/petroleum ether gave 508 mg (81%) of colourless crystals. M.p. 103–105° ((±)-3 (obtained from (±)-7), m.p. 99–101°). [α]_D²⁵ = +1.4, [α]_D²⁵ = +1.75, [α]_D²⁵ = +2.1, [α]_D²⁵ = +5, [α]_D²⁵ = +13 (CHCl₃, *c* = 2). IR (KBr): 3410, 2995, 1430, 1405, 1285, 1135, 1080, 1035, 995, 950, 885, 855, 790. ¹H-NMR (CDCl₃, 360 MHz): 5.41 (*br. t*, ³*J* = 3.3, H–C(6)); 4.88 (*br. d*, ³*J* = 4.5, ⁴*J*(H–C(1), H–C(3)) = 1, H–C(1)); 4.80 (*m*, ³*J* = 4.5, 3.3, ⁴*J*(H–C(3), H–C(5)) = 3, H–C(5)); 4.53 (*m*, ³*J* = 3.3, ⁴*J* = 3, 1, H–C(3)); 4.00 (*s*, H–C(2)); 2.10 (*br. s*, OH); 2.00 (*d*, ²*J* = 13.3, H_{endo}–C(8)); 1.64 (*br. dt*, ²*J* = 13.3, ³*J* = 4.5, H_{exo}–C(8)); NOE's between H–C(1)/H–C(2) (0.6%), H–C(1)/H_{endo}–C(8) (0.4%), H–C(2)/H–C(3) (0.4%), H–C(2)/H_{endo}–C(8) (1%), H–C(5)/H_{endo}–C(8) (0.2%); no NOE for H–C(3)/H–C(5). ¹³C-NMR (CDCl₃, 90.55 MHz): 87.8 (*d*, ¹*J*(C,H) = 169); 84.2 (*dd*, ¹*J*(C,H) = 169, ⁿ*J*(C,H) = 4.5); 81.8 (*br. d*, ¹*J*(C,H) = 164); 76.9 (*dm*, ¹*J*(C,H) = 172); 73.9 (*dd*, ¹*J*(C,H) = 156, ⁿ*J*(C,H) = 6, C(2)); 36.1 (*t*, ¹*J*(C,H) = 134, C(8)). MS (70 eV): 110 (2.5, *M*⁺ – 18), 97 (3), 95 (3), 85 (4), 84 (58), 81 (15), 71 (25), 70 (10), 69 (100), 60 (81). Anal. calc. for C₆H₈O₃ (128.1262): C 56.25, H 6.29; found: C 56.33, H 6.34.

(1*R*,2*R*,3*S*,4*S*,5*R*,6*S*)-5,6-exo-Epoxybicyclo[2.2.1]heptan-2-exo-ol (15). The commercial mixture of epimers of bicyclo[2.2.1]hept-5-en-2-ols (*Aldrich*) was separated by column chromatography on silica gel (AcOEt/petroleum ether 4:1). *m*-Chloroperbenzoic acid (85%, *Fluka*; 2.2 g, 11 mmol) was added to a soln. of the minor,

less polar *exo*-alcohol (1.25 g, 11 mmol) in CHCl_3 (40 ml) at 20° for 2 h. After addition of AcOEt (140 ml), the mixture was washed successively with sat. aq. NaHCO_3 soln. (30 ml) and sat. aq. NaCl soln. (10 ml). After drying (MgSO_4) and solvent evaporation, the residue was purified by column chromatography on silica gel (AcOEt /petroleum ether 1:1), yielding 1.27 g of slowly crystallizing oil. Crystallization from Et_2O /petroleum ether gave 1.06 g (74%) of colourless crystals. M.p. $153\text{--}154^\circ$ (sealed capillary tube). IR (KBr): 3420, 2970, 1380, 1345, 1215, 1105, 1055, 1010, 990, 850. $^1\text{H-NMR}$ (CDCl_3 , 360 MHz): 3.87 (br. *d*, $^3J = 6.9$, $\text{H-C}(2)$); 3.02 (br. *AB*, $^3J = 3.6$, $\nu_o\delta = 31.4$, $\text{H-C}(5)$, $\text{H-C}(6)$); 2.48 (*m*, $\text{H-C}(1)$, $\text{H-C}(4)$); 1.79 (*ddd*, $^2J = 13.2$, $^3J = 6.9$, $^4J(\text{H-C}(3), \text{H}_{\text{anti}}\text{-C}(7)) = 2.6$, $\text{H}_{\text{endo}}\text{-C}(3)$); 1.74 (br. *s*, OH); 1.35 (*ddd*, $^2J = 13.2$, $^3J = 4$, $^3J(\text{H-C}(2), \text{H-C}(3)) = 2.4$, $\text{H}_{\text{exo}}\text{-C}(3)$); 1.29 (*dm*, $^2J = 10$, $\text{H}_{\text{anti}}\text{-C}(7)$); 1.15 (br. *d*, $^2J = 10$, $\text{H}_{\text{syn}}\text{-C}(7)$). $^{13}\text{C-NMR}$ (CDCl_3 , 90.55 MHz): 71.1 (*dd*, $^1J(\text{C}, \text{H}) = 150$, $^3J(\text{C}, \text{H}) = 5$, $\text{C}(2)$); 51.95 (*dm*, $^1J(\text{C}, \text{H}) = 191$), 48.85 (br. *d*, $^1J(\text{C}, \text{H}) = 190$, $\text{C}(5)$, $\text{C}(6)$); 45.3 (br. *d*, $^1J(\text{C}, \text{H}) = 148$, $\text{C}(1)$ or $\text{C}(4)$); 38.4 (*td*, $^1J(\text{C}, \text{H}) = 132$, $^3J(\text{C}, \text{H}) = 9$, $\text{C}(3)$); 36.6 (br. *d*, $^1J(\text{C}, \text{H}) = 148$, $\text{C}(1)$ or $\text{C}(4)$); 22.7 (br. *t*, $^3J(\text{C}, \text{H}) = 138$, $\text{C}(7)$). MS (70 eV): 126 (1, M^+), 108 (16), 107 (8), 105 (6), 95 (7), 83 (12), 82 (99), 81 (100). Anal. calc. for $\text{C}_7\text{H}_{10}\text{O}_2$ (126.154): C 66.65, H 7.99; found: C 66.61, H 7.88.

(1RS,2SR,4SR,5SR,6RS)-5,6-*exo*-Epoxybicyclo[2.2.1]heptan-2-endo-ol (14). *m*-Chloroperbenzoic acid (85%; 7 g, 34.5 mmol) was added to a soln. of bicyclo[2.2.1]hept-5-en-2-endo-ol (*vide supra*; 3.7 g, 33.6 mmol) in CHCl_3 (50 ml). After 2 h at $25\text{--}30^\circ$ (occasional cooling with a cold-water bath was necessary), the mixture was poured into AcOEt (250 ml) and washed successively with sat. aq. NaHCO_3 soln. (25 ml, twice) and sat. aq., NaCl soln. (25 ml). After drying (MgSO_4), solvent evaporation, and column chromatography on silica gel (AcOEt /petroleum ether 1:1), the white solid obtained (3.9 g) was recrystallized from AcOEt /petroleum ether, giving 3.5 g (83%) of white crystals. M.p. $177\text{--}179^\circ$ (sealed capillary tube; [29]: $185\text{--}187^\circ$ (sealed capillary tube); [33b]: $160\text{--}162^\circ$ (Kofler block)). IR (KBr): 3410, 2950, 2900, 1440, 1375, 1340, 1305, 1220, 1150, 1120, 1060, 1040, 990, 965, 840. $^1\text{H-NMR}$ (CDCl_3 , 360 MHz): 4.39 (*ddd*, $^3J = 9$, 4, 3, $\text{H-C}(2)$); 3.46 (br. *d*, $^3J = 3.5$, $\text{H-C}(6)$); 3.28 (br. *d*, $^3J = 3.5$, $\text{H-C}(5)$); 2.61 (*m*, $\text{H-C}(1)$); 2.47 (*m*, $\text{H-C}(4)$); 2.01 (*ddd*, $^2J = 13$, $^3J = 9$, 4.5, $\text{H}_{\text{exo}}\text{-C}(3)$); 1.7 (br. *s*, OH); 1.28 (*dddd*, $^2J = 10.5$, $^4J(\text{H}_{\text{endo}}\text{-C}(3), \text{H-C}(7)) = 3.8$, $^3J(\text{H-C}(1), \text{H-C}(7)) = 2$, $^3J(\text{H-C}(4), \text{H-C}(7)) = 1.8$, $\text{H}_{\text{anti}}\text{-C}(7)$); 1.01 (*ddd*, $^2J = 13$, $^4J = 3.8$, $^3J = 3$, $\text{H}_{\text{endo}}\text{-C}(3)$); 0.75 (br. *d*, $^2J = 10.5$, $\text{H}_{\text{syn}}\text{-C}(7)$). $^{13}\text{C-NMR}$ (CDCl_3 , 90.55 MHz): 74.4 (*dm*, $^1J(\text{C}, \text{H}) = 150$, $\text{C}(2)$); 51.25 (*dm*, $^1J(\text{C}, \text{H}) = 190$), 48.65 (*dq*, $^1J(\text{C}, \text{H}) = 195$, $^3J(\text{C}, \text{H}) = 6$, $\text{C}(5)$, $\text{C}(6)$); 42.4 (*dm*, $^1J(\text{C}, \text{H}) = 147$), 37.4 (*dm*, $^1J(\text{C}, \text{H}) = 148$, $\text{C}(1)$, $\text{C}(4)$); 35.3 (*tm*, $^1J(\text{C}, \text{H}) = 132$, $\text{C}(3)$); 25.2 (*tm*, $^1J(\text{C}, \text{H}) = 138$, $\text{C}(7)$). MS (70 eV): 126 (1, M^+), 124 (2), 122 (2), 108 (30), 107 (17), 106 (11), 105 (9), 96 (19), 83 (22), 82 (99), 81 (100). Anal. calc. for $\text{C}_7\text{H}_{10}\text{O}_2$ (126.154): C 66.65, H 7.99; found: C 66.52, H 8.08.

(1RS,4RS,5RS,6SR)-5,6-*exo*-Epoxybicyclo[2.2.1]heptan-2-one (13). A soln. of 14 (4.5 g, 36 mmol) in CH_2Cl_2 (20 ml) was added to a mechanically stirred mixture of pyridinium chlorochromate (12 g, 55.7 mmol) and AcONa (1.6 g, 19.5 mmol) in CH_2Cl_2 (170 ml). After stirring at 20° for 3 h, the supernatant soln. was filtered through a short column of *Celite*. The black gum was stirred with Et_2O (100 ml, 3 times) and the solvent filtered through the *Celite* column, which was finally eluted with AcOEt . After evaporation, the combined eluate was purified by column chromatography on silica gel (*Lobar*, size C, AcOEt /petroleum ether 1:2), yielding 2.22 g (50%) of 13 as a colourless solid and 0.8 g (18%) of 14. Recrystallization of 13 from Et_2O /petroleum ether gave 1.98 g (45%) of white crystals. M.p. $132\text{--}134^\circ$ (sealed capillary tube; [29]: $138\text{--}139^\circ$ (sealed capillary tube)).

*Reduction of Ketone 13 by NaBH_4 in *i*-PrOH.* NaBH_4 (45 mg, 1.2 mmol) was added to a soln. of 13 (110 mg, 0.89 mmol) in *i*-PrOH (15 ml) cooled to 0° . After stirring at 0° for 16 h, acetone (0.3 ml, 4 mmol) and AcOH (0.2 ml, 3.5 mmol) were successively added, and the mixture was filtered through a 25-cm column of silica gel (AcOEt). After evaporation, the eluate was purified by column chromatography on silica gel (*Lobar*, AcOEt /petroleum ether 1:1), yielding 106 mg (95%) of a slowly crystallizing colourless oil, which was shown ($^1\text{H-NMR}$) to be a 2:1 mixture of 14 and 15.

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