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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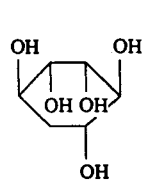
(31.V.88)

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 (DIBAH) 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 $NaBH_4$, AlH_3, and $LiAlH_4$ 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.

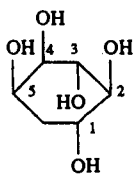
Introduction. – Whereas inositols (cyclohexanehexols) are ubiquitous in nature and have been widely studied [1] [2], only three of the sixteen possible cyclohexanepentols are natural products and have been found in plants. Among them, (+)-quercitol ((+)-**1**, acorn sugar [3]) is by far the most common 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 *Hérissey* 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 synthetized by *Posternak* from 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 $^{14}CO_2$ 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

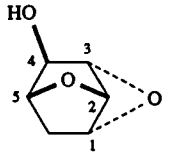
effect on the growth of seedlings of *Pisum sativum* [18]; however, it has an antivitamine action against *meso*-inositol in 'inositol-less' *Neurospora crassa* [19]. Recently, *Soloway et al.* [20] found that derivatives of 1,3:2,5-dianhydroviburnitol ((±)-**3**), the (±)-4,7-dioxatricyclo[3.2.1.$0^{3,6}$]oct-2-yl ethers (±)-**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.



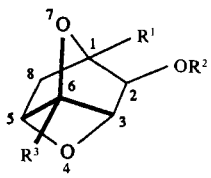
(+)-1



(-)-2

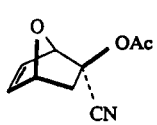


(+)-3

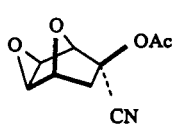


(±)-4

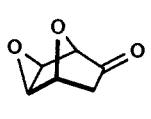
Results and Discussion. – Our starting material is the 'naked sugar' (−)-**5** ((−)-(1*R*,2*R*,4*R*)-*endo*-cyano-7-oxabicyclo[2.2.1]hept-5-en-2-*exo*-yl acetate, e.e. > 99%) [21] obtained by optical resolution of the corresponding cyanohydrines with brucine [22] [23]. On treatment with *m*-chloroperbenzoic 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°.



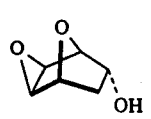
(-)-5



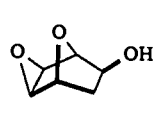
(-)-6



(+)-7



(+)-8



(-)-9

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*

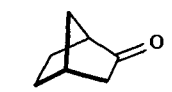
Hydride	No. of H^- equiv.	Solvent	Conditions	Isolated yields [%]			Ratio *endo/exo*-alcohols
				8	**9**	**7**	
$NaBH_4$	4	i-PrOH	0°, 90 min[a])	63	30	4	2.1:1
$NaBH_4$	2.7	MeOH	−78°, 3 h	53	31	14	1.7:1
$NaBH_4$	2.7	THF	sat. in LiCl, 65°, 24 h	36	22	–	1.6:1
$LiAlH_4$	8	Et_2O	36°, 15 h	41	28	6	1.45:1
AlH_3	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.



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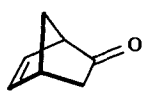

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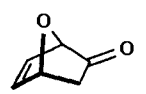

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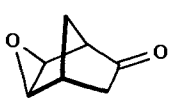

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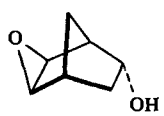

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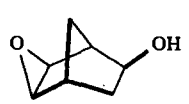
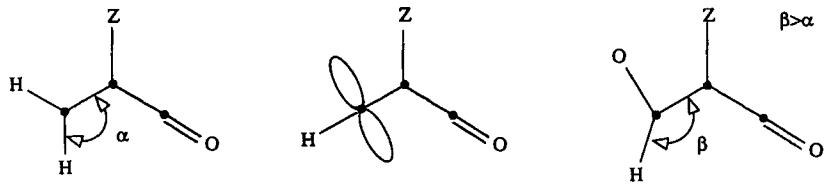


15

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 ^{1}H-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.

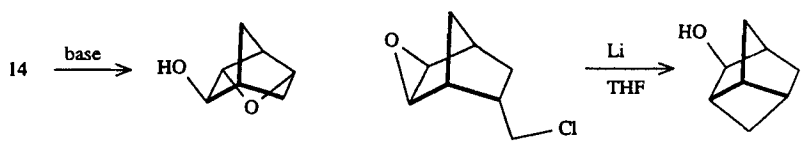


10 **11, 12** **7, 13**

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 ^{1}H-NMR spectra [24] and by double-irradiation experiments including nuclear *Overhauser* effect (NOE) measurements (see *Exper. Part*).

Scheme



16 **17** **18**

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].

(−)-(1R,2R,4R,5R,6R)-2-endo-Cyano-5,6-exo-epoxy-7-oxabicyclo[2.2.1]hept-2-exo-yl Acetate ((−)-**6**). Compound (−)-**5** (4 g, 22 mmol; $[\alpha]_{589}^{25} = +57.7$, 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°. $[\alpha]_{589}^{25} = -8.4$, $[\alpha]_{578}^{25} = -8.6$, $[\alpha]_{546}^{25} = -10$, $[\alpha]_{436}^{25} = -17.3$, $[\alpha]_{365}^{25} = -26.5$ ($CHCl_3$, $c = 2$). Spectral data: identical with those reported for (±)-**6** [24]. Anal. calc. for $C_9H_9NO_4$ (195.173): C 55.38, H 4.61; found: C 55.49, H 4.57.

(+)-(1R,4R,5R,6R)-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. H_2CO) and K_2CO_3 in MeOH, yielding 1.57 g (80%) of colourless crystals. M.p. 55–56°. $[\alpha]_{589}^{25} = +374$, $[\alpha]_{578}^{25} = +393$, $[\alpha]_{546}^{25} = +462$, $[\alpha]_{436}^{25} = +962$, $[\alpha]_{365}^{25} = +2245$ ($CDCl_3$, $c = 2$). UV (isooctane): 322 (16), 310 (27), 299 (26). UV (EtOH): 320 (sh, 11), 301 (23). CD (isooctane, $c = 8 \cdot 10^{-4}$ M): 321 (+2.8), 309 (+4.2), 298 (+3.9), 289 (sh, +2.6). CD (EtOH, $c = 8 \cdot 10^{-4}$ M): 315 (sh, +0.85), 305 (+1.33), 298 (+1.27). IR, ^{1}H- and ^{13}C-NMR, and MS: identical with those reported for (±)-**7** [24]. Anal. calc. for $C_6H_6O_3$ (126.110): C 57.15, H 4.80; found: C 57.23, H 4.75.

*(+)-(1S,2R,4R,5R,6S)-5,6-*exo*-Epoxy-7-oxabicyclo[2.2.1]heptan-2-*endo*-ol* ((+)-**8**) *and (−)-(1S,2S,4R,5R,6S)-5,6-*exo*-Epoxy-7-oxabicyclo[2.2.1]heptan-2-*exo*-ol* ((−)-**9**). $NaBH_4$ (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 $NaBH_4$ (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°). $[\alpha]_{589}^{25} = +39$, $[\alpha]_{578}^{25} = +41$, $[\alpha]_{546}^{25} = +47$, $[\alpha]_{436}^{25} = +81$, $[\alpha]_{365}^{25} = +130$ ($CHCl_3$, $c = 2$). IR (KBr): 3440, 3000, 2950, 1445, 1370, 1300, 1225, 1155, 1095, 1065, 1020, 985, 940, 920, 860, 805, 770. ^{1}H-NMR ($CDCl_3$, 360 MHz): 4.48 (*ddd*, $^3J = 8.8, 4.7, 2.8$, H–C(2)); 4.45 (*d*, $^3J = 5.3$, H–C(4)); 4.35 (*d*, $^3J = 4.7$, H–C(1)); 3.59 (*AB*, $^3J = 3.4$, $\nu_o\delta = 94.3$, H–C(5), H–C(6)); 2.4 (br. *s*, OH); 2.20 (*ddd*, $^2J = 12.8$, $^3J = 8.8, 5.3$, H_{exo}–C(3)); 1.25 (*dd*, $^2J = 12.8$, $^3J = 2.8$, H_{endo}–C(3)). ^{13}C-NMR ($CDCl_3$, 90.55 MHz): 75.0 (*dm*, ^1J(C,H) = 168), 74.6 (*dt*, ^1J(C,H) = 165, ^nJ(C,H) = 9, C(1), C(4)); 73.3 (*d*, ^1J(C,H) = 152, C(2)); 49.8 (*dm*, ^1J(C,H) = 193), 48.2 (*d*, ^1J(C,H) = 198, C(5), C(6)); 35.8 (*t*, ^1J(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 $C_6H_8O_3$ (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). $[\alpha]_{589}^{25} = -6.5$, $[\alpha]_{578}^{25} = -6.7$, $[\alpha]_{546}^{25} = -7.1$, $[\alpha]_{436}^{25} = -8.4$, $[\alpha]_{365}^{25} = -6.1$ ($CHCl_3$, $c = 2$). IR (KBr): 3430, 3060, 3000, 2940, 1445, 1320, 1250, 1205, 1105, 1060, 1030, 1010, 950, 920, 860, 695. ^{1}H-NMR ($CDCl_3$, 360 MHz): 4.44 (*d*, $^3J = 5$, H–C(4)); 4.27 (*s*, H–C(1)); 3.93 (*dd*, $^3J = 7, 2.3$, H–C(2)); 3.24 (br. *s*, OH); 3.19 (*AB*, $^3J = 3.5$, $\nu_o\delta = 13.3$, H–C(5), H–C(6)); 1.89 (*dd*, $^2J = 13.2$, $^3J = 7$, H_{endo}–C(3)); 1.54 (*ddd*, $^2J = 13.2$, $^3J = 5, 2.3$, H_{exo}–C(3)). ^{13}C-NMR ($CDCl_3$, 90.55 MHz): 80.1, 73.3 (2*dm*, ^1J(C,H) = 165, C(1), C(4)); 71.8 (*d*, ^1J(C,H) = 150, C(2)); 50.3 (*dm*, ^1J(C,H) = 195), 47.2 (*d*, ^1J(C,H) = 193, C(5), C(6)); 39.5 (*t*, ^1J(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 $C_6H_8O_3$ (128.1262): C 56.25, H 6.29; found: C 56.39, H 6.40.

(+)-(1R,2R,3S,5R,6S)-4,7-Dioxatricyclo[3.2.1.0^{3,6}]octan-2-ol (= (+)-1,3:2,5-Dianhydroviburnitol; (+)-**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°). H_2O (5 ml) and 2N 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), H_2O (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°). $[\alpha]_{589}^{25} = +1.4$, $[\alpha]_{578}^{25} = +1.75$, $[\alpha]_{546}^{25} = +2.1$, $[\alpha]_{436}^{25} = +5$, $[\alpha]_{365}^{25} = +13$ ($CHCl_3$, $c = 2$). IR (KBr): 3410, 2995, 1430, 1405, 1285, 1135, 1080, 1035, 995, 950, 885, 855, 790. ^{1}H-NMR ($CDCl_3$, 360 MHz): 5.41 (br. *t*, $^3J = 3.3$, H–C(6)); 4.88 (br. *d*, $^3J = 4.5$, ^4J(H–C(1), H–C(3)) = 1, H–C(1)); 4.80 (*m*, $^3J = 4.5, 3.3$, ^4J(H–C(3), H–C(5) = 3, H–C(5)); 4.53 (*m*, $^3J = 3.3$, $^4J = 3$, 1, H–C(3)); 4.00 (*s*, H–C(2)); 2.10 (br. *s*, OH); 2.00 (*d*, $^2J = 13.3$, H_{endo}–C(8)); 1.64 (br. *dt*, $^2J = 13.3$, $^3J = 4.5$, 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). ^{13}C-NMR ($CDCl_3$, 90.55 MHz): 87.8 (*d*, ^1J(C,H) = 169); 84.2 (*dd*, ^1J(C,H) = 169, ^nJ(C,H) = 4.5); 81.8 (br. *d*, ^1J(C,H) = 164); 76.9 (*dm*, ^1J(C,H) = 172); 73.9 (*dd*, ^1J(C,H) = 156, ^nJ(C,H) = 6, C(2)); 36.1 (*t*, ^1J(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 $C_6H_8O_3$ (128.1262): C 56.25, H 6.29; found: C 56.33, H 6.34.

*(1RS,2RS,4SR,5SR,6RS)-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. 153–154° (sealed capillary tube). IR (KBr): 3420, 2970, 1380, 1345, 1215, 1105, 1055, 1010, 990, 850. ^{1}H-NMR ($CDCl_3$, 360 MHz): 3.87 (br. *d*, ^3J = 6.9, H–C(2)); 3.02 (br. *AB*, ^3J = 3.6, $v_o\delta$ = 31.4, H–C(5), H–C(6)); 2.48 (*m*, H–C(1), H–C(4)); 1.79 (*ddd*, ^2J = 13.2, ^3J = 6.9, ^4J(H–C(3), H_{anti}–C(7)) = 2.6, H_{endo}–C(3)); 1.74 (br. *s*, OH); 1.35 (*ddd*, ^2J = 13.2, ^3J = 4, ^3J(H–C(2),H–C(3)) = 2.4, H_{exo}–C(3)); 1.29 (*dm*, ^2J = 10, H_{anti}–C(7)); 1.15 (br. *d*, ^2J = 10, H_{syn}–C(7)). ^{13}C-NMR ($CDCl_3$, 90.55 MHz): 71.1 (*dd*, ^1J(C,H) = 150, ^3J(C,H) = 5, C(2)); 51.95 (*dm*, ^1J(C,H) = 191), 48.85 (br. *d*, ^1J(C,H) = 190, C(5), C(6)); 45.3 (br. *d*, ^1J(C,H) = 148, C(1) or C(4)); 38.4 (*td*, ^1J(C,H) = 132, ^3J(C,H) = 9, C(3)); 36.6 (br. *d*, ^1J(C,H) = 148, C(1) or C(4)); 22.7 (br. *t*, ^3J(C,H) = 138, C(7)). MS (70 eV): 126 (1, $M^{+\cdot}$), 108 (16), 107 (8), 105 (6), 95 (7), 83 (12), 82 (99), 81 (100). Anal. calc. for $C_7H_{10}O_2$ (126.154): C 66.65, H 7.99; found: C 66.61, H 7.88.

*(1*RS,*2*SR,*4*SR,*5*SR,*6*RS*)-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 25–30° (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. 177–179° (sealed capillary tube; [29]: 185–187° (sealed capillary tube); [33b]: 160–162° (*Kofler* block)). IR (KBr): 3410, 2950, 2900, 1440, 1375, 1340, 1305, 1220, 1150, 1120, 1060, 1040, 990, 965, 840. ^{1}H-NMR ($CDCl_3$, 360 MHz): 4.39 (*ddd*, ^3J = 9, 4, 3, H–C(2)); 3.46 (br. *d*, ^3J = 3.5, H–C(6)); 3.28 (br. *d*, ^3J = 3.5, H–C(5)); 2.61 (*m*, H–C(1)); 2.47 (*m*, H–C(4)); 2.01 (*ddd*, ^2J = 13, ^3J = 9, 4.5, H_{exo}–C(3)); 1.7 (br. *s*, OH); 1.28 (*dddd*, ^2J = 10.5, ^4J(H_{endo}–C(3),H–C(7)) = 3.8, ^3J(H–C(1),H–C(7)) = 2, ^3J(H–C(4),H–C(7)) = 1.8, H_{anti}–C(7)); 1.01 (*ddd*, ^2J = 13, ^4J = 3.8, ^3J = 3, H_{endo}–C(3)); 0.75 (br. *d*, ^2J = 10.5, H_{syn}–C(7)). ^{13}C-NMR ($CDCl_3$, 90.55 MHz): 74.4 (*dm*, ^1J(C,H) = 150, C(2)); 51.25 (*dm*, ^1J(C,H) = 190), 48.65 (*dq*, ^1J(C,H) = 195, ^3J(C,H) = 6, C(5), C(6); 42.4 (*dm*, ^1J(C,H) = 147), 37.4 (*dm*, ^1J(C,H) = 148, C(1), C(4)); 35.3 (*tm*, ^1J(C,H) = 132, C(3)); 25.2 (*tm*, ^1J(C,H) = 138, C(7)). MS (70 eV): 126 (1, $M^{+\cdot}$), 124 (2), 122 (2), 108 (30), 107 (17), 106 (11), 105 (9), 96 (19), 83 (22), 82 (99), 81 (100). Anal. calc. for $C_7H_{10}O_2$ (126.154): C 66.65, H 7.99; found: C 66.52, H 8.08.

*(1*RS,*4*RS,*5*RS,*6*SR*)-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. 132–134° (sealed capillary tube; [29]: 138–139° (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}H-NMR) to be a 2:1 mixture of **14** and **15**.

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