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Synthesis of norbornanepentols: analogues of inositols

Azzouz Ben Cheikh, Leslie E. Craine, Jiri Zemlicka,
Department of Chemistry, Michigan Cancer Foundation and Department of Internal Medicine, Wayne State University School of Medicine, Detroit, Michigan 48201 (U.S.A.)

Mary-Jane Heeg
Department of Chemistry, Wayne State University, Detroit, Michigan 48202 (U.S.A.)

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ABSTRACT

The syntheses of *endo*-5,6-*exo*-2,3-*syn*-7-norbornanepentol (**5**), *endo*-5-*exo*-2,3,6-*syn*-7-norbornanepentol (**14**), and 7-*exo*-2,3,5,6-norbornanepentol (**16**) are described. *cis*-Hydroxylation of 7-*tert*-butoxynorbornadiene (**1**) gave the *exo*-diol **2**, *endo*-diol **3**, and tetrol **4**. The latter was deprotected to give pentol **5**. Oxidation of alkene **6** afforded diacid **7** and two minor products: the *exo*-diol **8** and α-hydroxyketone **9**. *cis*-Hydroxylation of **6** gave the *endo*- and *exo*-diols **10** and **8**. Acetalation of **8** furnished the bis(dioxolane) **11**. Reduction of ketone **9** gave the *trans*-diol **12**. Deblocking of **8** and **12** led the tetrol **15** or pentols **16** and **14**. The structure of tetrol **4** was confirmed by X-ray diffraction. Compounds **4**, **5** and **16** were devoid of antitumor or antiviral activity.

INTRODUCTION

Inositols (cyclitols, cyclohexanehexols) form a large group of carbohydrate-related natural products[1]. They may be considered as "hydroxycarbocyclic" analogues of pyranosidic sugars where the ring oxygen atom is replaced with a CHOH function[2]. *myo*-Inositol (**A**), a *meso* isomer, is especially widespread in Nature, occurring in plants as the corresponding hexaphosphate (phytin) and as a component of phosphatides. More recently, *myo*-inositol 1,4,5-triphosphate and phosphatidylinositol 4,5-diphosphate have been recognized as important secondary cellular messengers[3,4] activating, among other processes, protein kinase C, implicated in the process of oncogenesis[5]. *exo*-2,3,5,6-Norbornanetetrol (**B**) reportedly[6] resembles *myo*-inositol (**A**) in its capability to induce chromosomal changes in mitotic human and plant cells. It was therefore of interest to study additional norbornanepolyols, including those carrying a hydroxy group at the bridge position. Such compounds could also be of importance as molecules with chemically distinct surfaces[7].

RESULTS AND DISCUSSION

Synthesis. — 7-*tert*-Butoxynorbornadiene (**1**) was chosen as a particularly advan-

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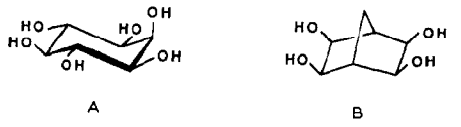
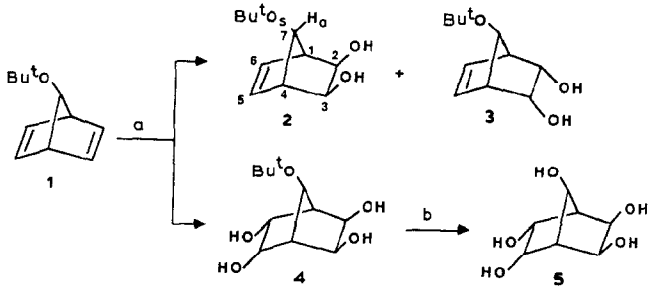
tageous starting material because it has oxygen at the bridge position (Scheme I). In fact, compound **1** was recently used for the synthesis of 6′*β*-hydroxyaristeromycin[2].

Reaction of **1** with OsO_4 and trimethylamine oxide gave, in addition to the major product[2] **2** (58%), two minor components, the *endo*-diol **3** (5%) and the *endo-exo* tetrol **4** (7%), a product of *cis*-hydroxylation of *exo*-diol **2**. The oxidation is usually conducted on a large scale and, therefore, sufficient amounts of **3** and **4** can be generated without difficulties.

Structural assignment of compound **3** as an *endo*-diol followed from a comparison of its ^{1}H-n.m.r. spectrum with those of the *exo*-diol[2] **2** and 2,3-*endo*-5-norbornenediol[8]. Thus, the pattern of the H-5,6 signal and H-7, along with spin-decoupling, indicated the *anti* relationship of H-7 and the alkenic bond[9,10]. The comparison of chemical shifts of the bicyclic framework of **3** with those of 2,3-*endo*-5-norbornenediol[8] was also straightforward. As expected[8], H-2 and H-3 of **3** resonate significantly downfield from these signals of the *exo*-diol **2**. Very striking is a strong shielding of H-7 (δ 3.60) in **3** relative to that in **2** (δ 4.40)[2] which has a juxtaposed *cis*-diol moiety. A similar shift of H-7 signals was previously observed in 5-norbornene-*exo*- and *endo*-2,3-diols[8,11]. An apparent $J_{1,2} = J_{3,4}$ value of 2 Hz was somewhat smaller than values reported in similar *endo*-diols ($\sim$ 4 Hz)[6,8,11]. Nevertheless, resonance of *exo* protons as a singlet was recently noted in somewhat related, bicyclic *endo*-diol[12].

The structure of tetrol **4** was established as follows. A pair of protons resonating at δ 4.02 was assigned in agreement with similar cases[6,8] as *exo*-H-5,6, with an *endo*-H-2,3 pair slightly upfield at δ 3.95. Double-resonance experiments have shown that the





Scheme I

a. OsO_4 (cat.), Me_3N-O, aqueous Me_2CO.
b. 6 M HCl, MeOH, Δ.

For numbering, see formula **2**.

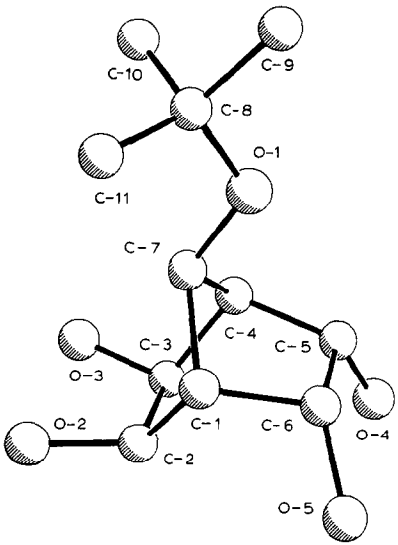
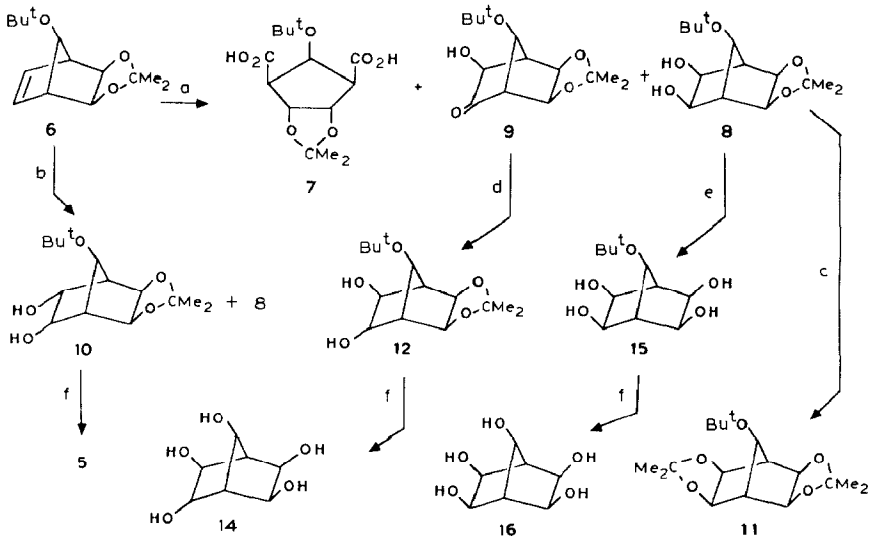


Fig. 1. Molecular drawing of *syn*-7-*tert*-butoxy-*endo*-5,6-*exo*-2,3-norbornanetetrol (**4**). The molecule is viewed down the crystallographic axis. The numbering of norbornane skeleton is the same as in formula **2** (Scheme I).

H-5,6 but not H-2,3 are coupled with H-1,4 ($J_{1,6} = J_{4,5} = 2$ Hz). Similarly, exchange with D_2O afforded for a sharp singlet H-2,3, but the profile of the H-5,6 signal changed to a triplet. As expected, no long-range ($^4J_{anti,endo}$ or "W-coupling") was found. Such an interaction was reported[6] for norbornane systems having H-7 situated *anti* to *endo* proton(s). Although these data allowed us to formulate **4** as an *endo-exo* tetrol, the final confirmation of its structure was provided by X-ray diffraction (Fig. 1). Deprotection of tetrol **4** with methanolic HCl gave the desired pentol **5** in 96% yield.

The protected *exo*-diol **6** (Scheme II) is also a convenient starting material for norbornanepolyols. Previous experiments showed[2] that oxidation of **6** with aqueous $KMnO_4$ gave the dicarboxylic acid **7** in 80% yield, together with a water-insoluble side-product. The latter was resolved by chromatography into diol **8** (2%) and α-hydroxyketone **9** (3%). Again, accumulation of both components does not present any problems despite the low yields because oxidation of **6** is usually conducted on a large scale. The structures of both products were elucidated by spectroscopic methods, particularly ^{1}H-n.m.r. The presence of a keto group in **9** was established by i.r., ^{13}C-n.m.r., and mass spectrometry. A complex ^{1}H-n.m.r. spectrum was expected because ketone **9** has no element of symmetry and it contains six asymmetric carbon atoms. Thus, the $J_{1(4),6}$ value is only 0.5 Hz, suggesting the presence of an *exo* hydroxy group. In addition, the H-6 signal (δ 4.21) was transformed to a poorly resolved triplet after deuterium exchange, which is in agreement with the ^{1}H-n.m.r. spectra of similar *exo*-hydroxyketones derived from camphor[13,14]. An *exo*-hydroxy structure was also confirmed by a long-range (W-coupling)[6] between the H-7 and H-6 ($J_{6,7} = 2.6$ Hz). By contrast, such a coupling was not observed with H-2 of H-3. There are significant large



Scheme II

a. Aqueous $KMnO_4$.
b. $KMnO_4$,Me_2CO, $-70°$.
c. Me_2CO, $CuSO_4$.
d. $NaBH_4$, MeOH, Δ.
e. 1.5 M HCl, MeOH.
f. 6 M HCl, MeOH, Δ.

Bu'O, *tert*-butoxy; a, anti; s, syn.

differences in $J_{1,2}$ and $J_{3,4}$ (4.8–5 Hz) of ketone **9** and the corresponding simpler models such as 2,3-*O*-dimethylmethylenedioxynorbornanes[6] or compound[2] **6**, wherein $J_{1,2} = J_{3,4} = 0$.

Diol **8** has a plane of symmetry and the ^{1}H-n.m.r. spectrum is simpler. Nevertheless, overlapping and fine structure of H-5,6 and H-2,3 (δ 4.35 and 4.31 respectively) complicated the spin-decoupling experiments. The latter signals appeared as an apparent triplet and quartet* ($J_{5(6),OH}$ 10 Hz). Irradiation at δ 2.50 led to a collapse of the quarted portion to a singlet, whereas the higher-field doublet of triplets belonging to H-5,6 became more exposed. The OH and H-7 signals were little influenced. Thus, the H-5,6 carrying *exo* hydroxy functions are, unlike H-2,3, not coupled with H-1,4. After irradiation at δ 4.35–4.31, the OH signal was transformed into a singlet and H-1,4 to a poorly resolved doublet, but only some loss of fine structure was apparent at H-7. Decoupling at δ 3.13 changed the pattern of H-5,6 and H-2,3 to a clearly separated singlet and quartet. The D_2O exchange led to a similar but less distinct profile. These

*In some spectra, the fine structure was lost and signals at δ 4.35 and 4.31 appeared as a simple singlet–quartet pattern which was transformed to two apparent singlets after decoupling at δ 2.50. The OH resonance was a broad singlet.

data allowed us to formulate compound **8** as an *exo*-diol, despite the fact that evidence for W-coupling was not firm.

It is of significant interest that both diol **8** and ketone **9** arose from an attack at the *exo* side of the double bond of **6** which is hindered by a bulky *tert*-butoxy group. The formation of both products is readily rationalized in terms of the accepted mechanism of $KMnO_4$ oxidation by invoking the respective manganese(V) cyclic ester[15,16] undergoing a simple (diol **8**) of oxidative hydrolysis (ketone **9**). Oxidation of **6** with $KMnO_4$ in acetone at $-70°$ in an effort to suppress over-oxidation to acid **7** did indeed afford *exo*-diol **8** (6%) in addition to the expected major product, the *endo*-diol **10** (22%). Compound **8** was identical with the product obtained by oxidation of **6** with aqueous $KMnO_4$. This result indicates that steric hindrance in **6** at the *exo* face of the 5,6-double bond caused by the *tert*-butoxy group is relieved and oxidative attack at this site is possible. By contrast, *cis*-hydroxylation of 7-*tert*-butoxynorbornadiene (**1**) gave only products of attack at the unhindered *exo* side (compound **2**) or *endo* position (diol **3** and tetrol **4**). It is likely that annelation of a third (dioxolane) ring system "opens" the norbornene structure with concomitant lessening of steric hindrance. The structure of **10** was readily confirmed by deprotection to pentol **5**.

Somewhat surprisingly, the ^{1}H-n.m.r. spectrum of diol **10** was simple and indicated a lack of any substantive coupling. In contrast to compounds **8** and **9**, H-2,3 (δ 4.53) appeared as a sharp singlet and H-5,6 (δ 4.42) as a poorly resolved doublet that collapsed to a broad singlet after exchange with D_2O. It is then apparent that $J_{1,6} = J_{4,5}$ must be of low magnitude. As expected, the *exo*-H-5,6 signals are located downfield from the corresponding *endo* protons in *exo*-diol **8** but, as in case of the *exo-endo*-tetrol **4**, the difference is small ($\Delta\delta \sim 0.1$ p.p.m.). The *cis*-diol **8** was smoothly transformed with acetone–$CuSO_4$ reagent[2] into the corresponding bis(dioxolane) **11** in 64% yield. It is of interest that both chemical shifts and coupling constants of H-1–6 in **11** are substantially different from the parent compound **8** (Bu^{t}O = H)[6]. This could reflect conformational changes of the norbornane system induced by the presence of the bulky *tert*-butoxy group.

Hydroxyketone **9** was readily reduced with $NaBH_4$ in methanol to the corresponding *trans*-diol **12**. This stereochemical course may be explained by hydride attacking **9** from the *exo* side, probably via complexation of reducing agent with the hydroxy group (intermediate **13**). As expected, compound **12** failed to react with acetone–$CuSO_4$ reagent or form a borate complex (Table I). The ^{1}H- and ^{13}C-n.m.r. spectra both indicated a complete loss of symmetry in *trans*-diol **12**. Thus, H-1,4,5,6 and the corresponding carbon resonances are all well separated.

Total deprotection of *trans*-diol **12** by refluxing in 6M methanolic HCl gave pentol **14** in almost quantitative yield. Deblocking of *cis*-diol **8** with 1.5M methanolic HCl at room temperature for 4 h removed selectively the isopropylidene group to give tetrol **15** in 75% yield. More-vigorous conditions, reflux in 6M methanolic HCl, then led to pentol **16** (91%). A comparison of ^{1}H-n.m.r. spectra of the *endo-exo*-pentol **5** and di-*exo*-pentol **16** is of interest because it clearly accentuates the difficulties with assignments in this series (see also ref. 12). Thus, in the deuterium-exchanged spectrum in CD_3SOCD_3 or

D_2O, the *endo* H-2,3 protons of **5** form a singlet whereas 5,6-*exo* protons appear downfield as a poorly resolved triplet. It is noteworthy that differences in chemical shifts of both *endo*-2,3 and -5,6 protons in the di-*exo* isomer **16** are much more pronounced than in the corresponding *endo*-*exo* pair of **5**.

Interestingly, all reaction products, with the exception of ketone **9**, diol **12**, and pentol **14**, are *meso* forms.

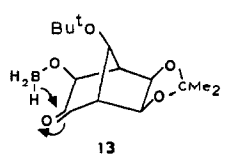
TABLE I

Paper electrophoresis of borate complexes of norbornenediols and norbornanepolyols

Compound	*Mobility*[a]
2	0.66
3	0.73
4	1.02
5	1.33
8	0.63
10	0.36
12	0.00
14	1.29
15	1.16
16	1.45

[a]Relative to uridine = 1.00. Whatman No. 1 paper, 0.02M $Na_2B_4O_7$ (pH 9.0), 40 V·cm^{-1}, 15°, 1 h. Spots were detected with $NaIO_4$–benzidine spray[17]. Benzidine in the reagent was replaced with a non-carcinogenic 3,5,3′,5′-tetramethylbenzidine[18].

Borate complexes. — The structure of norbornane derivatives containing vicinal glycol system(s) were further corroborated by formation of complexes with $Na_2B_4O_7$ at pH 9 that were identified by paper electrophoresis (Table I). It is noteworthy that there is little difference among derivatives containing a single *cis*-diol group (**2**, **3**, and **8**, including the *exo* and *endo* diols), but the substantially lower mobility of **10** is difficult to explain. Complexes of pentols **5**, **14**, and **16** containing two vicinal glycol moieties moved approximately twice as fast as mono-*cis*-diols. The *tert*-butoxytetrols **4** and **15**



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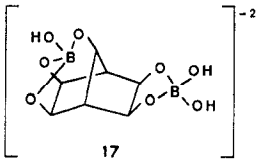

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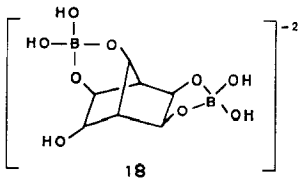

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were somewhat less mobile. It is recognized that pentol **16** can form a tridentate complex **17**. However, it is not possible to confirm this from electrophoresis data alone. By contrast, mobility of the borate complex with pentol **14** clearly corresponds to a species involving four hydroxy groups (formula **18**).

As expected, *trans*-diol **12** does not form a complex.

Crystallographic results. — Figure 1 illustrates the molecular geometry* of compound **4**. The norbornane ring is saturated and it carries substituent hydroxy groups at the 2, 3, 5, and 6 positions and a *tert*-butoxy group at the bridge (7) position. The hydroxy groups are attached *exo*, *exo*, *endo*, *endo* with respect to the boat and the *tert*-butoxy group is *syn* with respect to the *endo* end of the boat. An approximate noncrystallographic mirror-plane passes through the molecule; only the *tert*-butyl group seriously violates this symmetry. As is often the case, the methyl groups are disordered and exhibit large thermal parameters. The bond lengths and angles observed here in the norbornane fragment are typical for strained systems of this type. The C–C bonds at the base of the envelope average 1.569(5)Å and are somewhat longer than the C–C bonds comprising the envelope sides [1.527(5) Å average]. The endocyclic angles in the 6-membered boat-ring average 110.1(8)° at C-1 and C-4, and 103.2(2)° at C-2, C-3, C-5, and C-6. The dihedral angles between the envelope and flap are 58.2(3) and 56.5(3)°. The dihedral angle describing the bend in the boat is 65.3(3)°. The endocyclic angle at the bridge carbon atom C-7 is 94.8(4)°. Other averaged parameters include C–OH = 1.431(7), C–O(Bu^{t}O) = 1.428(7), O–C (Bu^{t}O) = 1.400 (9), and C–C(Me) = 1.45(3) Å. For other examples of closely related *tert*-butoxynorbornanes, see refs. 19–21. Two strong intermolecular hydrogen bonds link adjacent molecules. These distances are H(O-3)···O-4 = 1.720 Å and H(O-5)···O-2 = 1.78 Å. Other longer H···O contacts are also evident. No reasonable hydrogen bonds to O-1 are seen.

Biology. — Preliminary biological tests have shown that compounds **4**, **5** and **16** did not inhibit the growth of murine leukemia L 1210 cells in culture ($IC_{50} > 100$ $\mu g.mL^{-1}$). Tetrol **4** and pentol **5** were also inactive against mouse C38 tumor cells *in vitro* and they were devoid of antiviral activity.

EXPERIMENTAL

General procedures. — See ref 2. T.l.c. was performed in the following solvent systems: 9:1 CH_2Cl_2–MeOH (*A*), 4:1 CH_2Cl_2–MeOH (*B*); 7:3 C_6H_6–acetone (*C*); S_4, 19:1 CH_2Cl_2–MeOH (*D*); 7:1:2, 2-propanol–NH_4OH–H_2O (*E*); 4:1 C_6H_6–acetone (*F*); 9:1

*Nicolet R3 diffractometer, filtered CuKα radiation, ambient temperature, trigonal system, cell constants: $a = b = 27.6533$, (18) $c = 8.2304$ (6) Å, V = 5451.45 (.75) Å^3, Z = 18, space group R3, density (calc.) = 1.273 gcm^{-3}, $\Theta/2\Theta$ scans, $2\Theta_{max} = 110°$, 2–10°/min, $\mu = 7.94$ cm^{-1}, anisotropic refinement on all non-hydrogen atoms. A description of the crystallographic experiment and all pertinent resulting tables are deposited with, and can be obtained from, Elsevier Science Publishers, B.V., BBA Data Deposition, P.O. Box 1527, Amsterdam, The Netherlands. Reference should be made to No. BBA/DD/431/*Carbohydr. Res.*, 199 (1990) 19–30.

C_6H_6–acetone (*G*), and 3:2 CH_2Cl_2–MeOH (*H*). Acid solutions were quenched with triethylamine before application. Infrared spectra (KBr) were determined with a Perkin–Elmer 1330 spectrophotometer and maxima are expressed in cm^{-1}. The ^1H- and ^{13}C-n.m.r. spectra were obtained with a QE-300 instrument at 300 and 75.48 MHz, respectively, with Me_4Si as an internal reference. $CDCl_3$ was used as solvent for both ^1H-n.m.r. and ^{13}C-n.m.r. spectra unless stated ontherwise. Electron-impact and chemical ionization mass spectra were recorded with a Kratos MS80 RFA high-resolution spectrometer. They are reported as *m/z* (ion, relative intensity). Paper electrophoresis was performed with a flat-bed instrument (Savant, Hicksville, New York); for data see Table I.

endo-*2,3*-syn-*7*-tert-*Butoxy-5-norbornenediol (**3**) and* endo-*5,6*-exo-*2,3*-syn-*7*-tert-*butoxynorbornanetetrol (**4**).* — Oxidation of diene **1** with OsO_4 was effected as described previously[2] on a 100-g (0.61 mol) scale. The mixture of products was resolved by chromatography on a column (950 g, i.d. 7.5 cm) of silica gel which was washed consecutively with (CH_2Cl_2 (3L), 9:1 CH_2Cl_2–acetone (2L) 4:1 CH_2Cl_2–acetone (2.5L), 9:1 CH_2Cl_2–MeOH (0.5L) and 4:1 CH_2Cl_2–MeOH (1.5L). The major fraction gave diol **2** (69.95 g, 58%) followed by a more-polar component, tetrol **4**, 15 g (11%), homogeneous on t.l.c. (*B*). This product, containing some colored impurities, was refluxed in EtOH (300 mL) with Norit A (5 g). After cooling, the mixture was filtered through a Celite bed and the filtrate was evaporated. A slightly green solid was crystallized from 2:1 ethanol–cyclohexane (180 mL), yielding pure tetrol **4**, 9.67 g (7%), mp. 202–203.5° as a white solid, homogeneous on t.l.c. (*A*); ν_{max} 3600–3050 (OH); ^1H-n.m.r. (CD_3SOCD_3): δ 4.42 (dd, 2 H) and 4.21 (dd, 2 H, OH) (dd, 1 H) and 4.21 (dd, 2 H) (OH), 4.16 (t, 1 H, H-7), 4.02 (m, 2 H) and 3.95 (dd, 1 H) (H-2,3,5,6), 1.91 (q, 2 H, H-1,4), 1.09 (s, 9 H, CH_3); ^{13}C-n.m.r. δ 73.40 (C-7), 72.96 (CO, ButO), 66.46.64.88 (C-2,3,5,6), 52.94 (C-1,4), 28.01 (CH_3).

Anal. Calc. for $C_{11}H_{20}O_5$: C, 56.88; H, 8.68, Found: C, 57.00; H, 8.80.

Crystals suitable for X-ray diffraction were obtained by slow evaporation of a solution of **4** in ethanol.

In another experiment with diene **1** (20 g, 0.12 mol), diol **3** was isolated from an intermediary fraction obtained after elution of **2** but before tetrol **4**. Pure **3** (0.84 g) as well as a mixture of **3** and **4** (3.13 g) were obtained. The latter was rechromatographed on a column of silica gel (20 g) in 4:1 CH_2Cl_2–acetone to give diol **3** (0.69 g). Both pure fractions were combined and crystallized from 5:1 cyclohexane–benzene (10 mL) to give, 1.17 g (5%) of **3**, mp. 130–132°, homogeneous on t.l.c. (*A*), ν_{max} 3450 (OH); ^1H-n.m.r.: δ 6.19 (m, 2 H, H-5,6), 4.16 (br s, 2 H, H-2,3), 3.60 (s, 1 H, H-7), 3.06 (sextet, 2 H, H-1,4), 2.79 (br s, 2 H, OH), and 1.13 (s, 9 H, CH_3); ^{13}C-n.m.r. 131.19 (C-5,6), 81.86 (C-7), 68.98 (C-2,3), 54.46 (C-1,4), 73.73 (CO, Bu^{t}O), and 28.08 (CH_3); *m/z* (e.i.) 199 (M + H, 0.1), 143 (0.7), 124 (7.0), 106 (7.8), 95 (41.0), 82 (28.6), 67 (11.9), and 57 (100.3).

Anal. Calc. for $C_{11}H_{18}O_3$:C, 66.64; H, 9.15. Found: C, 66.81; H, 8.97.

5,6-endo-*2,3*-exo-*7*-syn-*Norbornanepentol (**5**).* — A solution of tetrol 4, (0.5 g, 2.2 mmol) in 6M HCl in methanol (5 mL) was refluxed for 90 min. T.l.c. (*E*) showed the absence of **4**. The mixture was evaporated and methanol (10-mL portions) was evap-

orated repeatedly from the oily residue until it solidified to give pentol **5**, homogeneous on t.l.c. (*B*), m.p. >260°; yield 364 mg (96%). A 100-mg sample was crystallized from ethanol (5 mL) to give 65 mg of colorless crystals, mp. 299–302°; ν_{max} 3700–3000 (OH); ^{1}H-n.m.r. (CD_3SOCD_3): δ 4.38 (dd, 2 H,) and 4.22 (dd, 2 H) (OH), 4.18 (q, 1 H, H-7), 4.07 (m, 2 H), 3.94 (dd, 2 H, H-2,3,5,6), 1.92 (s, 2, H-1,4); (D_2O) 4.47 (s, 1 H, H-7), 4.37 (poorly resolved t, 2 H, H-5,6), 4.23 (s, 2 H, H-2,3), and 2.33 (d, 2 H, H-1,4); ^{13}C-n.m.r. (CD_3SOCD_3); 72.32 (C-7), 66.37, 65.32 (C-2,3,5,6), and 52.89 (C-1,4).

Anal. Calc. for $C_7H_{12}O_5$: C, 47.72; H, 6.87. Found: C, 47.81; H, 6.68.

exo-*2,3*-O-*Dimethylmethylenedioxy*-exo-*5,6*-syn-*7*-tert-*butoxynorbornanediol* (**8**) *and* exo-*2,3*-O-*dimethylmethylenedioxy*-syn-*7*-tert-*butoxynorbornane*-exo-*6*-*ol*-*5*-*one* (**9**). – Oxidation of alkene **6** with aqueous $KMnO_4$ (2.61 g, 10.8 mmol) was performed as described previously[2]. After filtration of MnO_2, the pH of the filtrate was adjusted to 7 and the insoluble portion was filtered off (130 mg, m.p. 167–169°). This product consisted, according to t.l.c. (*C*), of two components. Column chromatography on silica gel in (7:2:1) CH_2Cl_2–benzene–THF gave ketone **9** as the first product, homogeneous on t.l.c. (*C*); yield 78 mg (3%); m.p. 188–190° ν_{max} 3520 (OH), 1760 (CO); ^{1}H-n.m.r.: δ 4.68 (q, 1 H), and 4.58 (d of q, 1 H) and (H-2,3), 4.21 (q, 1 H, H-7), 4.07 (dd, 1 H, H-6), 3.18 (d, 1 H, OH), 2.97 (d of t, 1 H) and 2.74 (m, 1 H) (H-1,4), 1.39, 1.27 (2s, 6 H, CH_3, CMe_2), and 1.21 (s, 9 H, CH_3,Bu^{t}O); ^{13}C-n.m.r.: 212.04 (C-5), 112.74 (OCO, CMe_2), 76.75 (C-7), 76.20 (CO, Bu^{t}O), 74.66, 73.81 (C-2,3), 71.78 (C-6), 60.62 (C-4), 50.04 (C-1), 27.86 (CH_3, Bu^{t}O), 25.04, and 24.06 (CH_3, CMe_2); *m/z* (e.i.) 271 (M + H, 0.3), 270 (M, 0.1), 255 (1.3), 215 (4.1), 213 (5.8), 157 (14.0), 139 (6.9), 111 (26.9), 82 (51.1), 576 (100.0). *m/z* (c.i.) 271 (7.9), 215 (32.5), and 157 (100.0).

Anal. Calc. for $C_{14}H_{22}O_5$: C, 62.21; H, 8.19. Found: C, 62.18; H, 8.20.

Diol **8** was eluted as the second fraction, homogeneous on t.l.c. (*C*), 40 mg (2%), m.p. 166–168°; ν_{max} 3520 (OH); ^{1}H-n.m.r.: δ 4.35 and 4.31 (apparent t + q, 4 H, H-2,3,5,6), 3.86 (t, 1 H, H-7), 3.13 (d of t, 2 H, OH), 2.50 (qt, 2 H, H-1,4), 1.45, 1.26 (2s, 6 H, CH_3, CMe_2), 1.24 (s, 9 H, CH_3,Bu^{t}O); ^{13}C-n.m.r.: 112.09 (OCO, CMe_2), 78.47 (C-7), 75.77 (CO, Bu^{t}O), 73.97 (C-2,3), 70.53 (C-5,6), 51.63 (C-1,4), 27.87 (CH_3, Bu^{t}O), 25.10, and 24.23 (CH_3,CMe_2); *m/z* (e.i.) 273 (M + H, 2.1), 217 (77.7), 183 (16.8), 139 (13.9), 123 (22.4), 111 (31.5), 95 (46.5), 86 (28.4), 73 (25.3), and 57 (100.0).

Anal. Calc. for $C_{14}H_{24}O_5$: C, 61.74; H, 8.88. Found: C, 61.63; H, 8.95.

exo-*2,3*-*Dimethylmethylenedioxy*-endo-*5,6*-syn-*7*-tert-*butoxynorbornanediol* (**10**) *and the corresponding* exo-*diol* **8**. — A solution of alkene **6** (1 g, 4.2 mmol) was cooled to −70° in acetone (60 mL) and solid $KMnO_4$ (0.71 g, 4.5 mmol) was added in small portions with vigorous stirring. The progress of the reaction was monitored by t.l.c. (*D*). After 2 h, a solution of Na_2SO_3 (6.32 g, 50 mmol) in water (50 mL) was added dropwise at −70° to −65°. The mixture was kept overnight at room temperature. The MnO_2 was filtered off, washed with acetone, and the filtrate evaporated. The aqueous solution was extracted with CH_2Cl_2 (3 × 50 mL) after addition of KCl (2.5 g). The organic phase was dried ($MgSO_4$) and evaporated. The crude product (clear oil, 560 mg) was chromatographed on a column of silica gel (20 g) using solvent *D* to give the following materials: starting alkene **6** (200 mg, 20%), *exo*-diol **8** [70 mg, 6%, identical

(t.l.c.-*A*) with the product obtained by oxidation of **6** with aqueous $KMnO_4$] and, finally, *endo*-diol **10** (250 mg, 22%), mp. 120–125°, homogeneous on t.l.c. (*D*); ν_{max} 3500 and 3315 (OH); ^{1}H-n.m.r. δ 4.53 (s, 2 H, H-2,3), 4.42 (br d, 2 H, H-5,6), 4.14 (t, 1 H, H-7), 2.89 (br s, 2 H, OH), 2.42 (d, 2 H, H-1,4), 1.54, 1.30 (2s, 6 H, CH_3, CMe_2), and 1.18 (2, 9 H, CH_3, Bu^{t}O); ^{13}C-n.m.r.: 108.09 (OCO, CMe_2), 73.95 (CO, Bu^{t}O), 73.86 (C-2,3), 73.36 (C-7), 66.95 (C-5,6), 49.22 (C-1,4), 28.08 (CH_3, Bu^{t}O), 25,56, and 23.64 (CH_3, CMe_2); *m/z* (e.i.) 273 (M + H, 1.0), 257 (M $-CH_3$, 22.3), 183 (42.7), 140 (16.2), 123 (30.4), 111 (19.1), 95 (38.8), 86 (34.0), 73 (21.3), and 57 (100.0).

Anal. Calc. for $C_{14}H_{24}O_5$: C, 61.74; H, 8.88. Found: C, 61.70; H, 9.00.

Diol **10** was hydrolyzed with 6M HCl in methanol at 60° to give pentol **5** identical (i.r., t.l.c.,-*E*) with an authentic sample obtained by deprotection of tetrol **4**.

exo-*2,3,5,6-Bis(dimethylmethylenedioxy)-7*-tert-*butoxynorbornane* (**11**). — A mixture of diol **8** (100 mg, 0.36 mmol), anhydrous $CuSO_4$ (350 mg, 2.2 mmol), and acetone (4 mL) was stirred for 6 h at room temperature. T.l.c. (*C*) showed the complete disappearance of **8**. The solids were filtered off, washed with acetone (2 × 2 mL), and the filtrate was evaporated to give crude **11** as a slightly yellow solid. The latter was chromatographed on a column of silica gel (20 g) in solvent *C*. The appropriate fractions were pooled and they were evaporated giving compound **11**, 70 mg (64%), m.p. 88–90°, uniform on t.l.c. (*C*); ν_{max} 2980 2960 (C-H), 1170 1050 (C-O); ^{1}H-n.m.r.: δ 4.65 (d, 2 H, H-2,3), 4.34 (q, 2 H, H-5,6), 3.56 (t, 1 H, H-7), 2.67 (qt, 2 H, H-1,4), 1.55, 1.43, 1.31, 1.25 (4s, 12 H, CH_3, CMe_2), 1.19 (s, 9 H, CH_3, Bu^{t}O); ^{13}C-n.m.r.: 111.66, 108.90 (OCO, CMe_2), 76.66 (C-7), 76.57, 73.72 (C-2,3,5,6), 74.37 (CO, Bu^{t}O), 48.63 (C-1,4), 27.96 (CH_3, Bu^{t}O), 25.23, 25.09, 23.92, and 23.75 (CH_3, CMe_2); *m/z* (e.i.) 297 (M $-CH_3$, 100.0), 257 (11.2), 241 (16.5), 183 (25.4), 123 (65.0), 95 (47.5), 81 (18.3), and 57 (95.7).

Anal. Calc. for $C_{17}H_{28}O_5$: C, 65.36; H, 9.02. Found: C, 65.55; H, 8.97.

exo-*2,3-Dimethylmethylenedioxy*-syn-*7*-tert-*butoxy-5*-endo-*6*-exo-*norbornanediol* (**12**). — Solid $NaBH_4$ (100 mg, 26 mmol) was added in small portions to a solution of ketone **9** (150 mg, 0.56 mmol) in methanol (10 mL) with stirring at room temperature. The reaction was monitored by t.l.c. (*C* and *E*). After 2 h there was only a little product present, and therefore, the mixture was heated for 30 min at 60°, whereupon the conversion into **12** was complete. After cooling, the solids were filtered off, washed with methanol (10 mL) and the filtrate was evaporated to a syrup. The latter was partitioned between water (20 mL) and CH_2Cl_2 (3 × 20 mL), the organic phase was dried ($MgSO_4$) and it was evaporated to give diol **12**, m.p. 174–176°, 145 mg (97%), homogeneous on t.l.c. (*B*, *F*, and *G*); ν_{max} 3540 (OH); ^{1}H-n.m.r. δ 4.45 (d + q, 3 H, H-2,3 and OH), 4.37 (poorly resolved d, 1 H, H-6), 4.00 (d of t, 1 H, H-5), 3.76 (q, 1 H, H-7), 2.75 (d, 1 H, OH), 2.59 (m, 1 H), and 2.34 (m, 1 H, H-1,4), 1.59, 1.22 (2s, 6 H, CMe_2), 1.13 (s, 9 H, CH_3, Bu^{t}O); ^{13}C-n.m.r.: 112.47 (OCO, CMe_2), 85.06, 77.45, 77.00, 76.61, 75.18 (C-2,3,5,6,7), 76.14 (CO, Bu^{t}O), 51.90, 48.83 (C-1,4), 27.87 CH_3, Bu^{t}O), 25.25, and 23.16 (CH_3, CMe_2); *m/z* (e.i.) 273 (M + H, 3.3), 257 (M $-CH_3$, 3.9), 215 (17.6), 183 (7.2), 139 (16.0), 123 (12.4), 111 (29.4), 95 (20.6), 86 (32.4), 73 (26.6), and 57 (100.0); *m/z* (c.i.) 273 (M + H, 100.0).

Anal. Calc. for $C_{14}H_{24}O_5$: C, 61.74; H, 8.88. Found: C, 61.53; H, 8.53.

7-tert-*Butoxy*-exo-*2,3,5,6-norbornanetetrol* (**15**). — A solution of diol **8** (40 mg, 0.15 mmol) in 1.5M HCl in MeOH (6 mL) was stirred for 4 h at room temperature. T.l.c. (*A*) showed complete removal of the 2,3-*O*-dimethylmethylene group. The mixture was evaporated to a syrup that crystallized during drying *in vacuo* to give tetrol **15**; yield 30 mg (75%), m.p. 186–188°, homogeneous on t.l.c. (*A*); ν_{max} 3300–3600 (OH); ^{1}H-n.m.r. (CD_3SOCD_3): δ 4.37 (s, 2 H), 3.74, 3.64 (apparent s + m, 5 H) (H-2,3,5,6,7 and OH), 4.09 (d, 2 H, OH), 2.08 (s, 2 H, H-1,4), and 1.12 (s, CH_3, Bu^{t}O); ^{13}C-n.m.r. 74.37, 73.85 (C-7 + CO, Bu^{t}O), 69.05, 64.68 (C-2,3,5,6), 53.88 (C-1,4), and 27.86 (CH_3); *m/z* (e.i.) 233 (M + H, 0.3), 177 (10.5), 157 (10.2), 111 (29.0), 86 (57.1), 73 (37.9), and 57 (100.0).

Anal. Calc. for $C_{11}H_{20}O_5$: C, 56.88; H, 8.68. Found: C, 56.65; H, 8.41.

endo-*5*-exo-*2,3,6*-syn-*7-Norbornanepentol* (**14**). —Diol **12** (79 mg, 0.29 mmol) was refluxed in 6M methanolic HCl (2 mL) for 2 h. The solution was evaporated and was evaporated several times methanol from the syrupy residue, whereupon it crystallized to give **14**; yield 50 mg (98%), m.p. > 170° (transition point), unchanged after crystallization from ethanol, homogeneous on t.l.c. (*B* and *E*); ^{1}H-n.m.r. (CD_3SOCD_3): δ 5.54 (d, 1 H), 5.16 (d, 1 H), 4.91 (d, 1 H), 4.33 (apparent t, 2 H, OH + H-6), 4.06 (d, 1 H, OH), 3.97 (d, 1 H, H-5), 3.85 (m, 2 H, H-2,3), 3.67 (s, 1 H, H-7), 2.24 (t, 1 H) and 2.08 (d, 1 H) (H-1,4); ^{13}C-n.m.r.: 83.97, 74.42, 72.76, 68.74, 65.84 (C-2,3,5,6), 53.85, and 49.00 (C-1,4); *m/z* (e.i.) 177 (M + H, 1.5), 111 (11.3), 99 (19.8), 86 (100.0), 73 (54.1), 66 (19.3), and 57 (40.1).

Anal. Calc. for $C_7H_{12}O_5$: C, 47.72; H, 6.87. Found: C, 47.58; H, 7.00.

7-exo-*2,3,5,6-Norbornanepentol* (**16**). —A solution of diol **8** (170 mg, 0.62 mmol) in 6M HCl in methanol (6 mL) was refluxed for 1 h. The progress of deprotection was monitored by t.l.c. (*C* and *G*). After cooling, the solution was evaporated to give a yellow oil which crystallized during drying *in vacuo*. The resulting solid was washed with solvent system *A* (2 mL) to give pentol **16**; yield 100 mg (91%), m.p. 238–240°, homogeneous on t.l.c. (*H*). For analysis the product was crystallized from ethanol; yield 80 mg (73%), m.p. 243–245°, ν_{max} 3500–3300 (OH). ^{1}H-n.m.r. (CD_3SOCD_3) δ 4.75 (d, 1 H, OH), 4.36 (d, 1 H), 3.67 (apparent t, 3 H) (H-2,3,5,6,7), 4.12 (d, 4 H, OH), 2.10 (apparent s, 2 H, H-1,4); (D_2O) 4.38 (s, 2 H), 4.00 (t, 2 H) (H-2,3,5,6), 3.96 (t, 1 H, H-7), 2.46 (qt, 2 H, H-1); ^{13}C-n.m.r. (CD_3SOCD_3); 74.10 (C-7), 68.99, 65.11 (C-2,3,5,6), and 53.88 (C-1,4); *m/z* (e.i.) 177 (M + H, 8.5), 123 (12.0), 111 (21.9), 99 (34.0), 86 (100.0). *m/z* (c.i.) 177 (M + H, 100.0), 141 (8.2), 123 (24.5), 112 (8.7), 99 (14.6), and 86 (33.9).

Anal. Calc. for $C_7H_{12}O_5$: C, 47.72; H, 6.87. Found: C, 47.91; H, 6.87.

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