Stereospecific synthesis of bisdihydroxylated dicyclopentadiene

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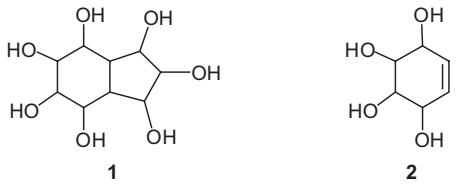
The first bisdihydroxylation of dicyclopentadiene (**3)** with OsO_4–NMO gave the *exo*-tetrol **4a** as a sole product in one step. The stereoselectivity in bisdihydroxylation of **3** has been determined by an X-ray diffraction analysis of the compound **4a** and tetraacetate **4b.**

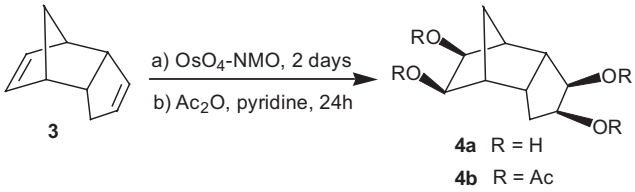
Keywords: cyclitols, crystal structure, bisdihydroxylation, dicyclopentadiene

Recently, polycyclitols have been used as fused (annulated) polycarbocyclic systems with a dense hydroxyl functionalisation.[1,2] A typical example is the hydrindane system **1,** which can be considered as an annulated conduritol **2** or carbasugar[1-3] (Scheme 1). Cyclitols have generated a great deal of synthetic interest as they usually possess a wide variety of interesting biological activities.

In a previous study, Dryuk *et al.*[4a] synthesised a trans tetrol from the diepoxide of dicyclopentadiene (**3**) in many steps and in a low total yield. Sanderson *et al.*[4b] also synthesised a mixture of a tetraacetate and diacetate by treatment of dicyclopentadiene (**3)** with an excess of acetic anhydride in the presence of nickel borate at 100°C in a yield[4b] of 76%. In this study, we describe an efficient and convenient procedure for the preparation of *cis*-tetrol **4a** (Scheme 2). The hydroxylation was performed at room temperature with a catalytic amount of OsO_4 and N-methylmorpholine N-oxide (NMO) as the co-oxidant. The tetrol was converted to the tetraacetate **4b** for further characterisation in 93% overall yield.



Scheme 1



Scheme 2

Results and discussion

Osmium tetroxide-catalysed dihydroxylation of olefins is one of the most reliable methods for the preparation of vicinal diols.[5-7] Four products might be formed by the *cis*-hydroxylation of dicyclopentadiene (**3**). Surprisingly, osmium tetroxide-catalysed bisdihydroxylation of dicyclopentadiene (**3**) resulted in the formation of a single tetrol derivative **4a** in 95% yield. The tetrol **4a** was converted to the acetate derivative **4b** for further characterisation (Scheme 2).

^{1}H and ^{13}C NMR spectra of **4a** and its acetate derivative **4b** show that four oxygen functionalities were incorporated to dicyclopentadiene **(3)**. The alkoxy C(H)–O protons of tetrol gave three signals at δ 3.88, 3.79(2H), 3.72. The *endo*-configuration of H-8 and H-9 were also elucidated by NMR analysis that these two protons at δ 3.88 and 3.72 aroused only as an AB system (J = 4.8 Hz) without further coupling with similar systems[8] confirmed the *endo*-position of these two protons. However, ^{1}H NMR coupling constants of H-3 and H-4 protons did not reveal the stereochemistry of the two –OH groups. These coupling constants vary from 4.0 Hz to 6.2 Hz. The *cis*- and *trans*-coupling constants of five-membered rings are too close to each other to decide the stereochemistry based on coupling constants. Therefore, we decided to perform an X-ray analysis of **4a** and its acetate derivate **4b** to elucidate the stereochemistry.

Catalytic bisdihydroxylation of dicyclopentadiene **(3)** proceeded with complete *exo*-face selectivity in case of tricyclic *endo*-allylic alcohol[2a] as well as norbornadiene[9] and norbornene derivatives.[2b,10]

The molecular structures of **4a** with the atom labeling are shown in Fig.1. Compound **4a** crystallises in monoclinic space group P21/n (no: 14) with eight molecules in the unit cell. The asymmetric unit contains two crystallographically

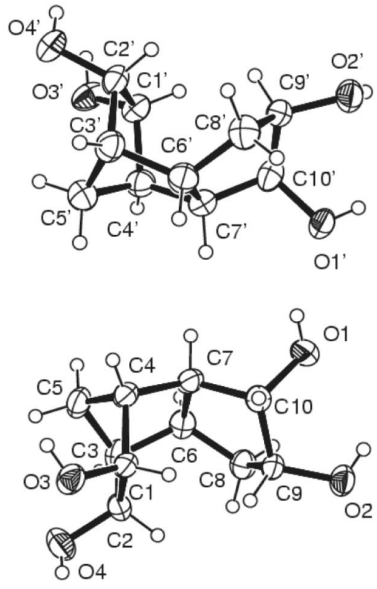


Fig. 1 ORTEP view of **4a** with displacement ellipsoids drawn at the 50% probability level.

independent molecules with nearly identical geometries.

Hydroxyl geometries are as expected, with corresponding exactly to typical single bond lengths [C2–O4, 1.425(3) Å; C2'–O4', 1.418(3) Å; C1–O3 1.417(3) Å; C1'–O3' 1.428(3) Å]. All the hydroxylic H atoms are in a hydrogen-bonding environment. The average O···O distance is 2.858 Å, the range is 2.732(4)–3.043(4) Å. These values agree with those given by Jeffrey and Saenger.[11] The crystal structure is stabilised by an extensive network of intermolecular hydrogen bonds.

In the bicyclo[2.2.1]heptane skeleton, the two five-membered rings have an envelope conformation. In the present case, only atom C5 is non-planar with the other atoms of the

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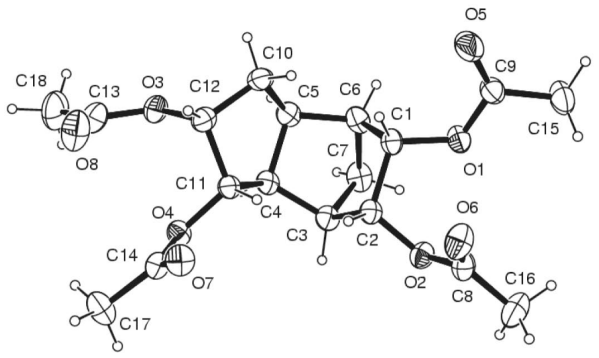

Fig. 2 ORTEP view of **4b** with displacement ellipsoid drawn at the 50% probability level.

ring. Maximum deviations from the mean planes delivered by the atoms C3/C2/C1/C4 and C3/C6/C7/C4 are 0.865 Å and 0.886 Å, respectively. The other five-membered ring which shares a common C–C bond [C6–C7 = 1.572(4) Å] also has the envelope conformation. The C9 atom deviates 0.880(Å) from the mean plane (C6/C7/C10/C8).

The molecular structure of **4b** with the atom labeling is shown in Fig. 2. Compound **4b** crystallises in monoclinic space group C2/c (no: 15) with $Z = 8$. It contains a central tricyclic dicyclopentadiene fragment like **4a**. The all-*cis* stereochemistry of the –OAc groups was determined unequivocally. It has three five-membered rings and all have the envelope conformation; C7 atom deviates 0.879(3) and 0.895(3) Å from the planes A(C1/C2/C3/C6) and B(C3/C4/C5/C6), respectively; C12 atom deviates 0.618(3) Å from the planes A(C4/C5/C10/C11). The angles between A, B, C planes are as follows; A/B = 64.6(2)°, A/C = 63.1(2)° and B/C = 52.4(2)°.

The O=C bond lengths agree with the values reported in the literature[9] (1.197(6) Å in (2RS, 3SR, 5RS, 6SR)-bicyclo[2.2.1]heptane-2,3,5,6-tetryl tetraacetate).

In summary, we have achieved the stereospecific synthesis of the *exo*-tetrol **4a** in one step starting from the readily available dicyclopentadiene **(3)** at room temperature and in high yield. The stereochemistry of the tetrol **4a** and the tetraacetate **4b** was elucidated by the single crystal X-ray diffraction analysis.

Experimental

General

IR spectra were recorded with a Mattson 1000 FT-IR spectrometer. The ^{1}H and ^{13}C NMR spectra were recorded on the Varian Gemini 400 (100) MHz spectrometer and are reported in δ units with $SiMe_4$ as an internal standard. All column chromatography was performed on silica gel (60 mesh, Fluka). The TLC was carried out on Merck 0.2 mm silica gel 60 F_{254} analytical aluminum plates.

Synthesis of(3R(S),4S(R),8R(S),9S(R))-3,4,8,9-tetraacetoxy-tricyclo [5.2.1.0^{2,6}]decane (**4b**): A 100 ml three-necked, round-bottomed flask, equipped with a magnetic stirrer and a nitrogen inlet, was charged with NMO 9.19 g (68.10 mmol), water 5 ml, and acetone 15 ml. To this solution were added *ca.* OsO_4 204 mg (0.816 mmol) and dicyclopentadiene **(3)** 3.0 g (22.70 mmol). The resulting mixture was stirred vigorously under nitrogen at room temperature. After 2 days, the reaction was complete. Sodium hydrosulfite (2.0 g) and 2.0 g of Florisil slurried in 5 ml of water were added, the slurry was stirred for 30 min. and the mixture was filtered through a pad of celite 0.5 g in a 50 ml sintered-glass funnel. The celite cake was washed with acetone (4 × 40 ml). The mixture was evaporated and the residue was purified by column chromatography on silica gel (150 g) elution with methanol/ethyl acetate (1/3) and afforded tetrol **4a** (4.3 g, 95%). Tetrol **4a** was converted to the corresponding acetate **4b**. To a magnetically stirred solution of tetrol **4a** (4.3 g, 21.5 mmol) in 15 ml of pyridine was added Ac_2O (15.35 g, 0.15 mol). The reaction mixture was stirred at room temperature for 24 h. The mixture was cooled to 0°C and 300 ml of 1 N HCl solution added, and the mixture was extracted with ether (5 × 60 ml). The combined organic extracts were washed with $NaHCO_3$ solution (30 ml) and water (30 ml) and then dried (Na_2SO_4). Removing of the solvent under reduced pressure and recrystallisation of the product from methylene chloride–hexane gave **4b** in nearly quantitative yield (7.76 g, 21.09 mmol), colourless crystals, m.p. 151–153°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.27 (br. q, J = 4.5 Hz, 1H, H-4), 5.04 (m, 3H, H-3, H-8, H-9), 2.72 (m, 1H, H-6), 2.52 (dt, J = 12.4, J = 5.5 Hz,1H, H-2), 2.38 (d, J = 4.0 Hz, 1H, H-1 or H-7), 2.19 (d, J = 4.0 Hz, 1H, H-1 or H-7), 2.14 (dt, J = 12.4, 10.2 Hz, one of H-10), 2.02 (s, 3H), 2.01 (s, 3H), 1.99 (s, 3H), 1.98 (s, 3H), 1.88 (m, 2H, two H-5), 1.49 (d, J = 10.2 Hz, 1H, one of H-10). ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.8, 20.9, 21.0, 21.1, 28.4, 38.8, 40.3, 43.8, 45.1, 47.0, 71.8, 73.0, 77.6, 169.9, 170.0, 170.2, 170.4. IR (KBr): 2960, 1738, 1637, 1373, 1259, 1048, 902, 602 cm^{-1}. Analysis calculated for $C_{18}H_{24}O_8$: C 58.7, H 6.6%; found: C 58.9, H 6.5%.

Synthesis of (3R(S),4S(R),8R(S),9S(R))-3,4,8,9-tetrahydroxy-tricyclo[5.2.1.0^{2,6}]decane (**4a**): (3R(S),4S(R),8R(S),9S(R))-3,4,8,9-Tetraacetoxy-tricyclo[5.2.1.0^{2,6}]decane (**4b**) (2.0 g, 5.43 mmol) was dissolved 200 ml of absolute methanol. While dry NH_3 was passed through solution, the mixture was stirred for 8 h at room temperature. Evaporation of methanol and formed acetamide gave (3R(S), 4S(R), 8R(S),9S(R))-3,4,8,9-tetrahydroxy-tricyclo[5.2.1.0^{2,6}]decane (**4a**) in nearly quantative yield (1.08 g, 5.40 mmol); m.p. 84–86°C from absolute ethanol/acetone. **4a:** ^{1}H NMR (400 MHz, D_2O) δ 3.88 (quasi t, 1H, H-4, J = 5.7 Hz), 3.79 (m, 2H, H-9 or H-8 and H-3, A part of AB system), 3.72 (d, 1H, H-9 or H-8, J = 4.8 Hz, B part of AB system), 2.45 (m, 1H, H-6), 2.21 (ddd, J = 11.7, 4.5, 4.5 Hz, 1H, H-2), 2.11 (d, J = 5.1 Hz, 1H, H-1), 1.94 (d, J = 5.1 Hz, one of H-7), 1.71 (d, 1H, one of H-10, J = 10.6 Hz), 1.65 (ddd, 1H, one of H-5, J = 14.3, 5.5, 5.5 Hz), 1.48 (ddd, 1H, one of H-5, J = 14.3, 9.5, 7.0 Hz), 1.24 (d, 1H, one of H-10, J = 10.6 Hz). ^{13}C NMR (100 MHz, D_2O) δ 30.0, 35.9, 39.6, 45.7, 47.1, 48.9, 70.0, 70.6, 72.7, 76.1. IR (KBr): 3411, 2956, 1662, 1395, 1053, 962,585 cm^{-1}. Analysis calculated for $C_{10}H_{16}O_4$: C 60.0, H 8.1%; found: C 59.8, H 8.2%.

X-Crystal structure determination: Diffraction experiment was carried out on a four-circle Rigaku R-AXIS RAPID-S diffractometer equipped with a two-dimensional area IP detector. The graphite-monochromatised Mo Kα radiation (λ = 0.71073 Å) and oscillation scans technique with $\Delta\omega = 5°$ for one image were used for data collection. Images for (**4a**) and (**4b**) was taken successfully by varying ω with three sets of different χ and φ values. For each compounds the 108 images for six different runs covering about 99.7% of the Ewald spheres were performed. The lattice parameters were determined by the least-squares methods on the basis of all reflections with $F^2 > 2\sigma(F^2)$. Integration of the intensities, correction for Lorentz and polarisation effects and cell refinement was performed using CrystalClear software[12]. The structures were solved by direct methods (SHELXS-97)[13] and non-H atoms were refined by full-matrix least-squares method with anisotropic temperature factors (SHELXL-97).[13]

Crystal data **4a:** $C_{10}H_{16}O_4$, monoclinic, P21/n; a = 7.6789(2), b = 12.1195(2), c = 20.0744(7)Å, β = 95.02(2)°; V = 1861 Å^3; Z = 8; calculated density: 1.43 mg/m^3; absorption coefficient: 0.110 mm^{-1}; F(000): 864; θ range for data collection 2.9–30.6°; completeness to θ: 30.6°, 99.7%; refinement method: full-matrix least-square on F^2; data/restraints/parameters: 3728/0/253; goodness-of-fit on F^2: 1.109; final R indices [$I > 2\sigma(I)$]: R_1 = 0.080, wR_2 = 0.112; largest diff. peak and hole: 0.807 and 0.335 eÅ^{-3}; CCDC-626645.

Crystal data **4b:** $C_{18}H_{24}O_8$ Monoclinic, *C2/c*, a = 15.910(3), b = 14.578(2), c = 16.578(4), β = 94.370(4), V = 3902 Å^3; Z = 8; calculated density: 1.25 mg/m^3; absorption coefficient: 0.099 mm^{-1}; F(000): 1568; θ range for data collection 2.4–30.6°; completeness to θ: 30.6°, 99.8%; refinement method: full-matrix least-square on F^2; data/restraints/parameters: 3178/0/240; goodness-of-fit on F^2: 1.166; final R indices [$I > 2\sigma(I)$]: R_1 = 0.089, wR_2 = 0.130; largest diff. peak and hole: 0.164 and 0.144 eÅ^{-3}; CCDC-626644.

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