Pergamon

Tetrahedron: *Asymmetry* 10 (1999) 1033–1039

TETRAHEDRON: *ASYMMETRY*

Synthesis and stereochemistry of some new derivatives of *cis*-dihydropinol

Stanisław Lochyński,[a,*] Bożena Frąckowiak,[a] Alicja Siemieniuk,[a] Krzysztof Piątkowski,[a] Zbigniew Ciunik [b] and Czesław Wawrzeńczyk [c]

[a] *Institute of Organic Chemistry, Biochemistry and Biotechnology, Wrocław University of Technology, Wybrzeże Wyspiańskiego 27, 50-370 Wrocław, Poland*

[b] *Faculty of Chemistry, University of Wrocław, Poland*

[c] *Department of Chemistry, Agricultural University, Wrocław, Poland*

Received 29 December 1998; accepted 16 February 1999

Abstract

The synthesis of four new derivatives of *cis*-hydroxy-*cis*-dihydropinol with allyl-, epoxyalkyl-, hydroxyalkyl- and ketoalkyl-groups substituted on the cyclohexane ring is presented. The *cis*-orientation of hydroxyl group at C-2 and the configuration of all stereogenic centers is confirmed by X-ray crystallography.

1. Introduction

Many terpenes are known as chiral reagents which are useful for the resolution of racemic mixtures and for the determination of enantiomeric purity: the best known are camphorsulfonic acid, menthoxyacetic acid and menthone.[1–4] Our interest in the synthesis of dihydropinol derivatives is also connected with their possible application as new chiral reagents for enantiomer separation or in asymmetric synthesis.

In a previous paper[5] we reported the synthesis of some dihydropinol derivatives with a cyano-, carboxyl- or hydroxymethyl group substituted on the cyclohexane ring. We now present the synthesis of some *cis*-hydroxy-*cis*-dihydropinol derivatives with three-carbon-unit side chains at C-2[†] with a terminal double bond, oxirane ring, and a hydroxyl or carbonyl group β to the cycloalkane ring. The compounds synthesized possess four or five stereogenic centers and at least two reactive functional groups. They

* Corresponding author. E-mail: lochynski@kchf.ch.pwr.wroc.pl

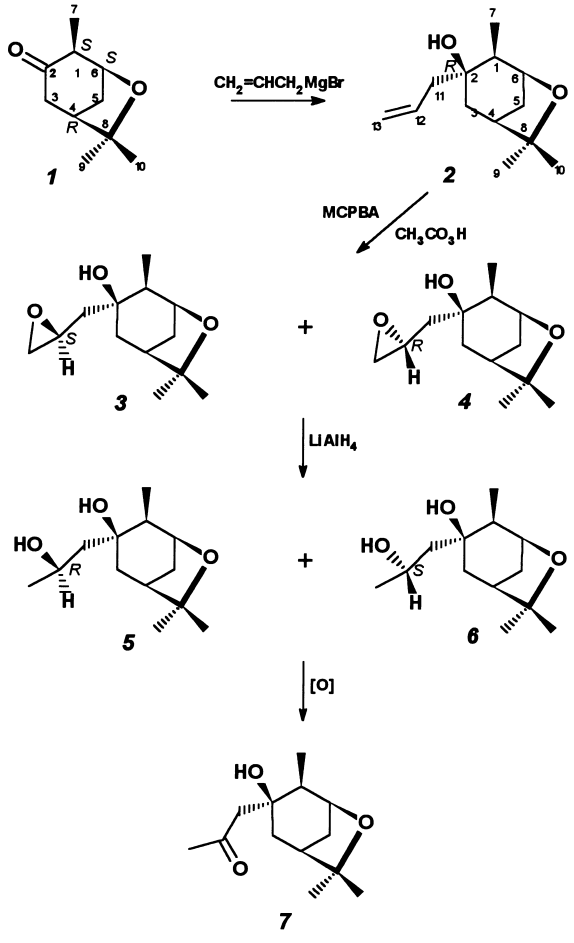
† The carbon atoms are numbered according to the customary terpene nomenclature[5,6] (accepted by IUPAC). In the Experimental, the names of the compounds synthesized are given according to both customary and principal IUPAC nomenclature rules.

0957-4166/99/$ - see front matter
PII: S0957-4166(99)00056-7

could be used for the derivatization of ketones, aldehydes or esters. The presence of the epoxide function allows for the possibility of derivatization of compounds by nucleophilic or electrophilic oxirane ring opening.

2. Results and discussion

The starting material for the synthesis, optically active (+)-2-keto-*cis*-dihydropinol **1**, was obtained by oxidation of (+)-*trans*-2-hydroxy-*cis*-dihydropinol according to the procedure described earlier.[6] The first derivative, with the allyl group at C-2, was obtained in good yield (84%) by the Grignard reaction of ketone **1** with allylmagnesium bromide. *cis*-2-Hydroxy-*trans*-2-allyl-*cis*-dihydropinol **2** was identified as the only product of this reaction (Scheme 1). The distinct difference in chemical shifts of geminal methyl groups (0.35 ppm) indicates the expected axial orientation of the hydroxyl group (*cis* to the methyl at C-1 and oxa ring). Similar effects were observed in the cases of *cis*-2-azido-, *cis*-2-amino-*cis*-dihydropinols[5] and *cis*-2-hydroxy-*cis*-dihydropinol.[7] The *cis*-position of the sterically shielded hydroxyl group was additionally suggested by the lack of formation of *p*-nitrobenzoic ester and phenylurethane. Finally, this axial orientation was confirmed by the crystal structures of diols **5** and **6**.



Scheme 1.

cis-Hydroxy-*trans*-allyl-*cis*-dihydropinol **2** was subjected to epoxidation with peracetic (50%) or *m*-chloroperbenzoic acids. In both experiments a mixture (ratio 1:1) of diastereomeric epoxy alcohols **3** and **4** was obtained. Column chromatography allowed us to separate **3** and **4** as pure diastereomers. Configurations of the stereogenic centers (C-12) were determined from the X-ray structures of diols **5** and **6**. These glycols, as crystals, were determined by reduction of epoxy alcohols with lithium aluminum hydride.

The structures of diols **5** and **6** (Fig. 1) were established by X-ray crystallographic analysis. It can be seen that the newly formed stereogenic center (C-12) has the *R*-configuration in **5** and *S* in **6**.

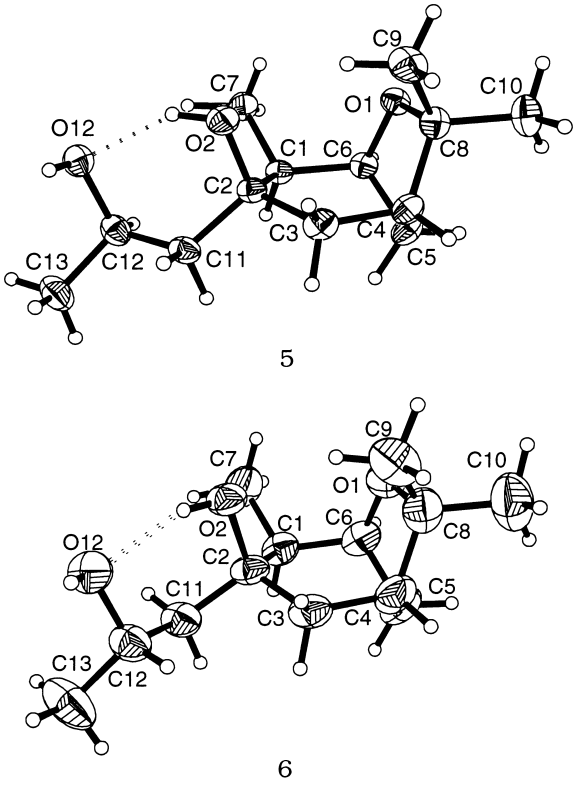


Figure 1. View of the molecules **5** and **6** with crystallographic numbering scheme. The dotted lines represent the intramolecular H-bond. The ellipsoids correspond to 30% probability contours of atomic displacement. The crystal data together with refinement details are given in the Experimental

A hydrogen bond between the oxygen atom of the -OH group at C-12 and the hydrogen atom of the -OH group at C-2 in these structures is observed. The comparison of the structures of **5** and **6** indicates that the cyclohexane ring in **5** is flattened. The torsion angle C(6)–C(1)–C(2)–C(3) in **5** is −17.9° whereas in **6** it has the value −26.5°. This difference in ring conformation is also visible in the torsion angle between C(7)–C(1) and C(2)–O(2) bonds. The angles −24.7° in structure of **5** and −33.0° in structure of **6** were found. The change of the cyclohexane ring conformation is probably caused by the different sterical requirements during the six-membered ring-formation process by hydrogen bonds (Table 1).

The last derivative of the *cis*-dihydropinol, hydroxy ketone **7**, was obtained by oxidation of diol **5**, as well as **6**, with the Brown–Garg method.[8] In addition, the result of this oxidation confirmed that the configuration at C-12 is the only difference in the structures of diols **5** and **6**.

Table 1
Geometry of the hydrogen bonds. H-bond lengths and angles

	D-H...A	D...A (Å)	H...A (Å)	< D-H...A (°)	Bond size
5	O(2) - H(2)...O(12)	2.803(3)	1.98(4)	149(3)	intramolecular
	O(12) - H(12)...O(1)*	2.770(5)	1.95(4)	169(3)	intermolecular
6	O(2) - H(2)...O(12)	2.701(4)	1.90(4)	158(4)	intramolecular
	O(12) - H(12)...O(1)**	2.705(4)	1.95(4)	164(4)	intermolecular

Symmetry equivalent atoms: (none) x, y, z; (*) 2-x, -1/2+y, 2-z. (**) 1-x, 1-x+y, 1/3-z.

3. Experimental

The course of all reactions, composition of products, and their purities were checked by means of thin-layer chromatography (TLC) and gas chromatography (GC). TLC was carried out on silica gel G (Merck). Chromatograms were developed with a mixture of petroleum ether, ethyl ether and acetone applied in various ratios and detected with 20% ethanolic H_2SO_4 with an admixture of 0.1% of anisaldehyde. Preparative column chromatography was carried out on silica gel (60–120 mesh, Merck) with a mixture of petroleum ether or hexane, ethyl ether and acetone (various ratios) as an eluent. Analytical GC was performed on a GCHF-18/3 (Giede) apparatus using the following packing: 25% Carbowax M-20 on Chromosorb G or 10% XE-60 on Chromosorb G. Column length: 2 or 3 m, temperature: 140–180°C. Melting points (uncorrected) were determined on a Boetius apparatus. IR spectra were taken for liquid films or in KBr on a Perkin–Elmer 621 spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded for $CDCl_3$ solutions on a Bruker Avance DRX 300 apparatus, with TMS as the internal standard. All crystal measurements were performed on a Kuma KM4CCD κ-axis diffractometer with graphite-monochromated MoKα radiation. The crystal was positioned at 65 mm from the KM4CCD camera. 612 Frames were measured at 0.75° intervals with a counting time of 30 s. The data were corrected for Lorentz and polarization effects. No absorption correction was applied. Data reduction and analysis were carried out with the Kuma Diffraction (Wrocław) programs. The structure was solved by direct methods (program SHELXS97[9]) and refined by the full-matrix least-squares method on all F^2 data using the SHELXL97[10] programs. Non-hydrogen atoms were refined with anisotropic thermal parameters; hydrogen atoms were included from the $\Delta\rho$ maps and refined with isotropic thermal parameters. Crystallographic data for structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre.

*3.1. (+)-2-Keto-*cis*-dihydropinol {(1*S*,2*S*,5*R*)-(+)-2,6,6-trimethyl-7-oxabicyclo[3.2.1]octan-3-one} **1**

(+)-*trans*-2-Hydroxy-*cis*-dihydropinol (34.10 g, 0.200 mol) in 400 ml of anhydrous acetone was oxidized by the standard Jones method.[6] After distillation in vacuo, 28.43 g (0.169 mol, 84.5%) of ketone **1** was obtained: b.p. 78–79°C/2 mmHg; n_D^{20}=1.4723; α_D^{20}=+84.84. ^{1}H NMR and IR spectra were in full agreement with the literature.[6] ^{13}C NMR (δ): 12.44 (q, C-7), 25.10 (q, C-9), 29.54 (q, C-10), 37.20 (t, C-5), 42.66 (d, C-4), 45.32 (t, C-3), 52.4 (d, C-1), 79.44 (d, C-6), 83.05 (s, C-8), 212.14 (s, C-2).

3.2. (+)-cis-*2-Hydroxy*-trans-*2-allyl*-cis-*dihydropinol {(1*S,*2*S,*3*R,*5*R*)-(+)-2,6,6-trimethyl-3-hydroxy-3-(2-propen-1-yl)-7-oxabicyclo[3.2.1]octane} **2**

Ketone **1** (4.21 g, 0.025 mol) in 25 ml anhyd. Et_2O was added to a mixture of allylmagnesium bromide formed from allyl bromide (6.68 g, 0.046 mol) and magnesium (1.22 g, 0.050 mol) in 75 ml anhyd. diethyl ether. The mixture was stirred for 12 h and then saturated NH_4Cl solution was added and the product was extracted with diethyl ether. The ethereal solution was washed with saturated NaCl solution and dried over $MgSO_4$. GC analysis of the crude product (5.10 g) showed 98% of compound **2** and 2% of unreacted ketone **1**. After distillation in vacuo, 4.50 g (0.021 mol, 84.0%) of homogenous alcohol **2** was obtained: b.p. 99.5°C/1 mmHg; $[\alpha]_D^{20}$=+56.9 (c=5.2, $CHCl_3$); n_D^{20}=1.4850; ^{1}H NMR (δ): 1.00 (d, J=7.1 Hz, 3H, -CH(C**H**$_3$)-), 1.19 and 1.51 (two s, 6H, -C(C**H**$_3$)$_2$-), 1.38 (d, J=11.6 Hz, 1H, **H-5$_{ax}$**), 1.58 (q, J=7.1 Hz, 1H, -C**H**(CH_3)-), 1.72 (dd, J=15.0 and 3.80 Hz, 1H, **H-3$_{ax}$**), 1.98–2.07 (two m, 2H, **H-4** and one of -C**H**$_2$CH=CH_2), 2.11 (dt, J=15.0 and 2.5 Hz, 1H, **H-3$_{eq}$**), 2.25 (dd, J=13.7 and 6.8 Hz, 1H, one of -C**H**$_2$CH=CH_2), 2.47 (m, 1H, **H-5$_{eq}$**), 2.47 (m, 1H, **H-5$_{eq}$**), 3.23 (s, 1H, -O**H**), 4.02 (d, J=7.0 Hz, 1H, **H-6**), 5.00–5.07 (m, 2H, -CH_2CH=C**H**$_2$), 5.87 (m, 1H, -CH_2C**H**=CH_2); ^{13}C NMR (δ): 12.95 (q, C-7), 24.39 (q, C-9), 29.66 (q, C-10), 37.78 (t, C-5), 39.47 (t, C-3), 42.99 (d, C-4), 44.87 (d, C-1), 45.91 (t, C-11), 73.75 (s, C-2), 80.66 (d, C-6), 83.29 (s, C-8), 117.72 (t, C-13), 134.12 (d, C-12); IR (cm^{-1}): 3540 (s b), 3084 (w), 998 (m), 912 (m), 1642 (m), 1385 (s), 1368 (s), 1130 (s). Elemental analysis: calculated for $C_{13}H_{22}O_2$ (210.32): 74.24% C, 10.54% H. Found: 74.14% C, 10.63% H.

3.3. (+)-cis-*2-Hydroxy*-trans-*2-epoxypropyl*-cis-*dihydropinol {(1*S,*2*S,*3*R,*5*R,*2′*S)-(+)-2,6,6-trimethyl-3-hydroxy-3-(2,3-epoxyprop-1-yl)-7-oxabicyclo[3.2.1]octane} **3** and {(1*S,*2*S,*3*R,*5*R,*2′*R)-(+)-2,6,6-trimethyl-3-hydroxy-3-(2,3-epoxyprop-1-yl)-7-oxabicyclo[3.2.1]octane} **4***

To alcohol **2** (4.20 g, 0.020 mol) in 25 ml anhydrous diethyl ether, a 50% mixture of peracetic acid (6.00 g, 0.040 mol, AcOOH) in 25 ml anhydrous diethyl ether was added dropwise. The mixture was refluxed for 12 h and the progress of the reaction was monitored by TLC. After cooling, the reaction mixture was shaken with a saturated solution of $NaHCO_3$, the layers were separated, and the aqueous layer was extracted with diethyl ether. The combined extracts were washed with water and saturated NaCl, and dried over $MgSO_4$. After evaporation of the solvent, the crude product (4.30 g) was distilled in vacuo (b.p. 133–139°C/2 mmHg) to give 3.44 g (0.0152 mol, 76.0%) diastereomeric mixture of epoxy alcohols **3** and **4** in the ratio 1:1. The mixture was separated by column chromatography (hexane:acetone, gradient from 9:1 to 5:1).

The spectroscopic and physical data of epoxy alcohols **3** and **4** are as follows:

3: $[\alpha]_D^{28.9}$=+44.8 (c=4.12, $CHCl_3$); n_D^{20}=1.4832; ^{1}H NMR (δ): 0.99 (d, J=7.1 Hz, 3H, -CH(C**H**$_3$)-), 1.14 (dd, J=14.2 and 5.5 Hz, 1H, -C**H**$_2$CH–CH_2O), 1.19 and 1.53 (two s, 6H, -C(C**H**$_3$)$_2$-), 1.44 (d, J=11.6 Hz, 1H, **H-5$_{ax}$**), 1.60 (q, J=7.1 Hz, 1H, -C**H**(CH_3)-), 1.85 (dd, J=15.0 and 3.7 Hz, 1H, **H-3$_{ax}$**), 1.96 (dd, J=14.2 and 3.2 Hz, 1H, -C**H**$_2$CH–CH_2O), 2.05 (m, 1H, **H-4**), 2.37 (dt, J=15.0 and 2.6 Hz, 1H, **H-3$_{eq}$**), 2.40 (dd, J=5.0 and 2.7 Hz, 1H, -CH–C**H**$_2$O), 2.51 (m, 1H, **H-5$_{eq}$**), 2.73 (dd, J=5.0 and 4.3 Hz, 1H, -CH–C**H**$_2$O), 3.13 (m, 1H, -C**H**–CH_2O), 3.34 (s, 1H, -O**H**), 4.03 (d, J=7.0 Hz, 1H, **H-6**); ^{13}C NMR (δ): 13.21 (q, C-7), 24.43 (q, C-9), 29.59 (q, C-7), 38.01 (t, C-5), 40.06 (t, C-3), 43.03 (d, C-4), 45.23 (t, C-11), 46.11 (d, C-1), 46.29 (t, C-13), 48.69 (d, C-12), 73.83 (s, C-2), 80.78 (d, C-6), 83.57 (s, C-8); IR (cm^{-1}): 3528 (s), 3045 (w), 2968 (vs), 2926 (vs), 1455 (s), 1383 (s), 1134 (s). Elemental analysis: calculated for $C_{13}H_{22}O_3$ (226.32): 68.99% C, 9.80% H. Found: 68.73% C, 10.08% H.

4: $[\alpha]_D^{28.9}$=+86.6 (c=2.94, $CHCl_3$), n_D^{20}=1.4841; ^{1}H NMR (δ, $CDCl_3$): 1.03 (d, J=7.1 Hz, 3H, -CH(C**H**$_3$)-), 1.18 and 1.51 (two s, 6H, -C(C**H**$_3$)$_2$-), 1.64 (q, J=7.1 Hz, 1H, -C**H**(CH_3)-), 1.43 (d, J=11.6 Hz, 1H, **H-5$_{ax}$**), 1.44 (dd, J=14.2 and 5.1 Hz, 1H, -C**H**$_2$CH–CH_2O), 1.74 (dd, J=14.2 and 6.2 Hz, 1H, -C**H**$_2$CH–CH_2O), 1.81 (dd, J=15.0 and 3.8 Hz, 1H, **H-3$_{ax}$**), 2.01 (m, 1H, **H-4**), 2.27 (dt, J=15.0 and 2.6 Hz, 1H, **H-3$_{eq}$**), 2.43 (dd, J=7.3 and 4.4 Hz, 1H, -CH_2CH–C**H**$_2$O), 3.04 (m, 1H, -C**H**–CH_2O), 3.30 (S, 11H, -O**H**), 4.02 (d, J=7.0 Hz, 1H, **H-6**); IR (cm^{-1}): 3524 (s), 2969 (s), 2929 (s), 1455 (m), 1884 (s), 1134 (s); ^{13}C NMR ($CDCl_3$): 13.18 (q, C-7), 24.36 (q, C-9), 29.65 (q, C-10), 37.89 (t, C-5), 40.63 (t, C-3), 42.95 (d, C-4), 44.79 (t, C-11), 45.60 (d, C-1), 47.03 (t, C-13), 48.60 (d, C-12), 73.63 (s, C-2), 80.61 (d, C-6), 83.39 (s, C-8). Elemental analysis: calculated for $C_{13}H_{22}O_3$ (226.32): 68.99% C, 9.80% H. Found: 68.73% C, 10.02% H.

3.4. (+)-cis-*2-Hydroxy*-trans-*2-(2-hydroxyprop-1-yl)*-cis-*dihydropinol {(1*S,*2*S,*3*R,*5*R,*2′*R)-(+)-2,6,6-trimethyl-3-hydroxy-3-(2-hydroxyprop-1-yl)-7-oxabicyclo[3.2.1]octane} **5** and {(1*S,*2*R,*3*R,*5*R,*2′S)-(+)-2,6,6-trimethyl-3-hydroxy-3-(2-hydroxyprop-1-yl)-7-oxabicyclo[3.2.1]octane} **6***

The epoxy alcohol **3** (0.85 g, 0.0037 mol in 10 ml anhyd. Et_2O) was reduced with $LiAlH_4$ (0.20 g, 0.005 mol in 10 ml anhyd. Et_2O). 10% H_2SO_4 was used for hydrolysis. After normal work up, 0.71 g (0.0031 mol, 83.8%) of a crude crystalline product of glycol **5** was obtained. Physical and spectral data of crystalline glycol **5** are as follows:

5: m.p. 102°C (recrystallization from hexane); $[\alpha]_D^{20}$=+61.4 (c=5.6, EtOH); ^{1}H NMR (δ): 1.13 (d, J=6.0 Hz, 3H, -CH(OH)C**H**$_3$), 1.14 (d, J=7.1 Hz, 3H, -CH(C**H**$_3$)-), 1.19 and 1.50 (two s, 6H, -C(C**H**$_3$)$_2$-), 1.42 (d, J=11.6 Hz, 1H, **H-5$_{ax}$**), 1.58–1.69 (two m, 3H, -C**H**(CH_3) and -C**H**$_2$- at C-11), 1.99 (m, 1H, **H-4**), 2.30 (dt, J=15.2 and 2.7 Hz, 1H, **H-3$_{eq}$**), 2.48 (m, 1H, **H-5$_{eq}$**), 3.21 (s, 2H, -O**H** and -O**H**), 3.99 (d, J=7.0 Hz, 1H, **H-6**), 4.16 (m, 1H, -C**H**(OH)-); ^{13}C NMR (δ): 14.86 (q, C-7), 24.54 (q, C-9 and C-13), 29.57 (q, C-10), 37.54 (t, C-5), 42.92 (t, C-3), 43.23 (d, C-4), 46.51 (d, C-1), 52.05 (t, C-11), 65.31 (d, C-12), 75.24 (s, C-2), 81.19 (d, C-6), 83.25 (s, C-8); IR (KBr, cm^{-1}): 3485 (s), 3300 (s b), 1370 (s), 1365 (s), 1135 (s). Elemental analysis: calculated for $C_{13}H_{24}O_3$ (228.34): 68.38% C, 10.59% H. Found: 68.71% C, 10.67% H. Crystal data: $C_{13}H_{24}O_3$, M_W=228.34, T=293 K, monoclinic, space group $P2_1$, *a*=7.281(2) Å, *b*=12.458(2) Å, *c*=7.419(2) Å, β=103.88(2) Å, *V*=653.3(3) Å^3, *Z*=2, D_c=1.161 Mg/m^3, μ=0.642 mm^{-1}, *F*(000)=252, crystal size 0.50×0.40×0.40 mm, diffractometer Kuma KM4CCD, 6≤θ≤80°, 1327 collected and independent refl. with $I>2\sigma(I)$, 242 parameters.

In the same manner the epoxy alcohol **4** (0.75 g, 0.0033 mol) was reduced with $LiAlH_4$ (0.17 g, 0.045 mol) giving 0.64 g (0.028 mol, yield 84.2%) of crude crystalline product of glycol **6**: m.p. 93–93°C, (recrystallization from hexane); $[\alpha]_D^{20}$=+94.1 (c=5.1, EtOH); ^{1}H NMR (δ): 1.05 (d, J=7.1 Hz, 3H, -CH(C**H**$_3$)-), 1.12 (d, J=6.1 Hz, 3H, -CH(OH)C**H**$_3$), 1.23 and 1.53 (two s, 6H, -C(C**H**$_3$)$_2$-), 1.46 (d, J=12.4 Hz, 1H, **H-5$_{ax}$**), 1.50 (m, 1H, one of -C**H**$_2$- at C-11), 1.58 (m, 1H, -C**H**(CH_3)-), 1.68 (dd, J=15.0 and 3.7 Hz, 1H, **H-3$_{ax}$**), 1.86 (dd, J=14.2 and 10.5 Hz, 1H, one of -C**H**$_2$- at C-11), 2.09 (m, 1H, **H-4**), 2.55–2.60 (m, 2H, **H-3$_{eq}$** and **H-5$_{ax}$**), 3.62 (s, 1H, -O**H** at C-2), 4.06 (d, J=7.1 Hz, 1H, **H-6**), 4.27 (m, 1H, -C**H**(OH)), 4.34 (s b, 1H, -O**H** at C-13); ^{13}C NMR (δ): 13.09 (q, C-7), 23.79 (q, C-13), 24.38 (q, C-9), 29.68 (q, C-10), 37.91 (t, C-5), 39.86 (t, C-3), 42.98 (d, C-4), 47.14 (d, C-1), 49.60 (t, C-11), 64.10 (d, C-12), 74.37 (s, C-2), 80.55 (d, C-6), 83.57 (s, C-8); IR (KBr, cm^{-1}): 3410 (s), 3280 (s b), 1370 (s), 1365 (s), 1140 (s). Elemental analysis: calculated for $C_{13}H_{24}O_3$ (228.34): 68.38% C, 10.59% H. Found: 68.64% C, 10.60% H. Crystal data: $C_{13}H_{24}O_3$, M_W=228.34, T=293 K, trigonal, space group $P3_12$, *a*=12.340(2) Å, *b*=12.340(2) Å, *c*=16.010(3) Å, *V*=2111.3(6) Å^3, *Z*=6, D_c=1.077 Mg/m^3, μ=0.074

mm^{-1}, *F*(000)=756, crystal size 0.25×0.20×0.20 mm, diffractometer Kuma KM4CCD 3.18≤θ≤28.97, 15 503 collected refl., 3562 independent refl. with $I>2\sigma(I)$, 242 parameters.

3.5. (+)-cis-2-Hydroxy-trans-2-acetonyl-cis-dihydropinol {(1S,2S,3R,5R)-(+)-2,6,6-trimethyl-3-hydroxy-3-(2-propanon-1-yl)-7-oxobicyclo[3.2.1]octane} **7**

Brown and Garg oxidation reagent (2.2 ml, formed from 5.0 g $Na_2Cr_2O_7 \cdot 2H_2O$+3.8 ml concentr. H_2SO_4+H_2O in 25 ml volume) was added dropwise to the glycol **5** (0.42 g, 0.0018 mol) in 15 ml anhyd. diethyl ether and was stirred for 3 h until the glycol was reacted completely. The mixture was then poured into water and the product was extracted with diethyl ether. After washing with $NaHCO_3$ solution and water, the extract was dried over $MgSO_4$ and the solvent was evaporated. The crude product 0.38 g (0.0016 mol, 88.9%) was purified by column chromatography (hexane:acetone; gradient from 9.5:0.5 to 8:2) giving ketol **7**: $[\alpha]_D^{28.2}$=+37.8 (c=2.4, $CDCl_3$), n_D^{20}=1.4851; ^{1}H NMR (δ): 1.03 (d, J=7.2 Hz, 3H, -CH(C**H**$_3$)-), 1.23 and 1.54 (two s, 6H, -C(C**H**$_3$)$_2$-), 1.61 (d, J=11.7 Hz, 1H, **H-5$_{ax}$**), 1.81 (m, 1H, -C**H**(CH$_3$)-), 1.98 (dd, J=14.7 and 3.8 Hz, 1H, **H-3$_{ax}$**), 2.05 (m, 1H, **H-4**), 2.22 (two s, 3H, -C(O)C**H**$_3$), 2.39 and 2.73 (two d, J=15.0 Hz, 2H, -C**H**$_2$- at C-12), 2.52 (m, 1H, **H-5$_{eq}$**), 4.06 (d, J=7.0 Hz, 1H, **H-6**); ^{13}C NMR (δ): 13.26 (q, C-7), 24.50 (q, C-9), 29.79 (q, C-10), 32.26 (q, C-13), 37.49 (t, C-5), 39.93 (t, C-3), 43.16 (d, C-4), 45.38 (d, C-1), 54.05 (t, C-11), 73.42 (s, C-2), 80.63 (d, C-6), 83.57 (s, C-8), 208.97 (s, C-12); IR (cm^{-1}): 3530 (s b), 1710 (s), 1380 (s), 1368 (s), 1130 (s), 1045 (s). Elemental analysis: calculated for $C_{13}H_{22}O_3$ (226.32): 68.99% C, 9.80% H. Found: 68.60% C, 10.02% H. Ketol **7** was also obtained by oxidation with the same method of glycol **6** and the mixture of diastereomers **5**+**6**.

Acknowledgements

We wish to express our thanks to the Polish State Committee for Scientific Research for supporting this work.

References

1. Wilen S. H.; Collet A.; Jacques J. *Tetrahedron* **1977**, *33*, 2725–2736.
2. Crosby J. *Tetrahedron* **1991**, *47*, 4789–4846.
3. Harada T.; Oku A. *Synlett* **1994**, *95*, 95–104.
4. Gerlach H. *Helv. Chim. Acta* **1968**, *51*, 1587–1593.
5. Szałkowska-Pągowska H.; Piątkowski K. *Pol. J. Chem*. **1985**, *59*, 1121–1134.
6. Siemieniuk A.; Mrozinska D.; Piątkowski K. *Pol. J. Chem*. **1978**, *52*, 727–736.
7. Wolinsky J.; Thorstenson J. H.; Vogel M. K. *J. Org. Chem*. **1977**, *42*, 253–257.
8. Brown H. C.; Garg C. P.; Liu K. T. *J. Org. Chem*. **1971**, *36*, 387–390.
9. Sheldrick G. M. SHELXS-97, program for solution of crystal structures, University of Göttingen, 1997.
10. Sheldrick G. M. SHELXL-97, program for crystal structure refinement, University of Göttingen, 1997.