New unsymmetrical salen-type ligand from enantiomerically pure 2-hydroxypinan-3-one*

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The reaction of enantiomerically pure (—)-2-hydroxypinan-3-one with ethylenediamine was studied. Depending on the reagent ratio, the reaction can afford either mono- or bis-Schiff's bases. The enantiomerically pure unsymmetrical terpenoid salen-type ligand was prepared by the reaction of 3-[(2-aminoethyl)imino]pinan-2-ol with salicylaldehyde.

Key words: α-pinene, (—)-2-hydroxypinan-3-one, ethylenediamine, Schiff's bases, chiral ligand, X-ray diffraction analysis.

In the last decade, numerous of C_2-symmetrical transition metal complexes with salen-type ligands have been synthesized. These complexes are used as catalysts for various asymmetric reactions, such as epoxidation of nonfunctionalized olefins,[1,2] oxidation,[3,4] cyclopropanation,[5] and trimethylsilylcyanation of aldehydes,[6,7] Diels—Alder reactions,[8,9] asymmetric syntheses of α-amino acids,[10] *etc.* Most of the known salen ligands contain two identical salicylaldehyde fragments, *i.e.*, they are symmetrical. The synthesis of such ligands is generally highly efficient and rather simple, whereas unsymmetrical salen-type ligands are less readily accessible. In recent years, several studies were devoted to unsymmetrical chiral salen ligands, which were synthesized by stepwise condensation of 1,2-diamine with various salicylaldehyde derivatives through the intermediate formation of monoimines.[11,12] However, these syntheses are complicated by the fact that intermediate monoimines are contaminated with C_2-symmetrical bis-imine even after purification. Recently, a procedure was developed[13] for the synthesis of unsymmetrical salen-type ligands by condensation of 1,2-diamine successively with 1-(2-hydroxyphenyl) ketone and salicylaldehyde derivatives. Aromatic ketones react with 1,2-diamines much more difficultly than salicylaldehyde derivatives due to which monoketimines are formed selectively.

It seems evident that terpenoid derivatives, which are isolated in sufficient amounts from renewable plant materials, can be used in the above successive condensations. It is known that monoterpenoids, in particular, amino alcohols, are widely used for the construction of chiral ligands.[14,15] In the study,[16] a procedure was developed for the preparation of P-, N-, and O-chiral ligands for metal complex catalysts for reduction and oxidation from higher terpenoids.

In the present study, we describe a simple and efficient procedure for the synthesis of unsymmetrical salen-type dioxydiimine containing a chiral terpene fragment. We chose the product of oxidation of α-pinene **1** with an aqueous-acetone solution of $KMnO_4$—(—)-2-hydroxypinan-3-one (**2**) as the starting compound. This product is successfully used as a chiral inductor[17] in the asymmetric synthesis.

The scheme of the synthesis of the target ligand **5** involves the formation of chiral monoimine **3** followed by its condensation with salicylaldehyde.

Monoimine **3** was synthesized in 79% yield by heating a solution of ketone **2** and a 20-fold excess of ethylenediamine in benzene in the presence of $F_3B \cdot OEt_2$ and molecular sieves. Imine **3** thus prepared was contaminated only with a small amount of C_2-symmetrical bis-imine **4** as a by-product. The latter was identified in the reaction mixture by TLC based on comparison with a sample, which was prepared by the independent synthesis using the reaction of ketone **2** with a threefold excess of ethylenediamine. Recrystallization of monoimine **3** from hexane afforded a product free from an impurity of bis-imine **4** (^{1}H NMR spectroscopic data, 400 MHz). The reaction of monoimine **3** with salicylaldehyde in MeOH at room temperature gave unsymmetrical dihydroxydiimine **5** in 93% yield (after crystallization).

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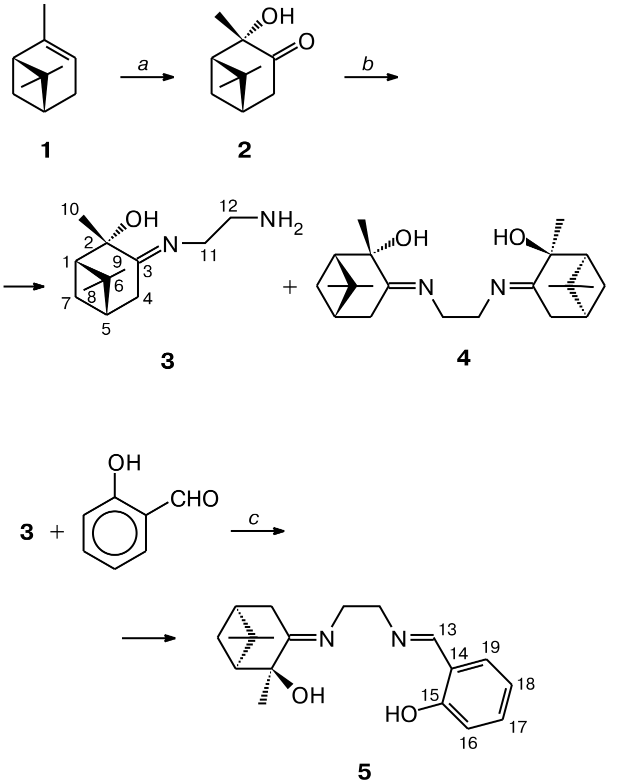

Reagents and conditions: *a*. $KMnO_4$, Me_2CO/H_2O, 0—5 °C; *b*. $H_2N(CH_2)_2NH_2$, PhH, 80 °C, $F_3B \cdot OEt_2$; *c*. MeOH, 20 °C.

Note. The atomic numbering scheme is given for convenience of consideration of NMR spectra.

The structures of compounds **3—5**, which were prepared for the first time, were confirmed by NMR spectroscopy and elemental analysis.

The three-dimensional structure of compound **5** was established by X-ray diffraction analysis (Fig. 1). The bond lengths and bond angles are given in Table 1. In the crystal, there are two crystallographically independent molecules, which have very similar geometric parameters (bond lengths and bond angles) but adopt somewhat different conformations (different angles of rotation about the $CH_2—CH_2$ single bonds). The analogous N(11)—C(11)—C(12)—N(12) and N(21)—C(31)—C(32)—N(22) torsion angles are 72.3 and 64.3°, respectively.

Mono- and diimines were synthesized in the enantiomerically pure form. The preparation of transition metal complexes with such compounds offers considerable possibilities of studying the latter as chiral ligands. Earlier, it has been demonstrated that catalytic cyclopropanation of styrene with methyl diazoacetate using the Cu^{II} complex with diimine **5** gave a chiral cyclopropane derivative.[18]

Experimental

The IR spectra were recorded on a Specord M-80 spectrometer in KBr pellets. The ^1H and ^{13}C NMR spectra were measured on a Bruker AM-400 spectrometer (operating at 400.13 and 100.61 MHz, respectively) in $CDCl_3$ with the use of the signals of chloroform as the internal standard (δ_H 7.24 and δ_C 77.00). The assignment of the signals was made based on ^{13}C NMR spectra recorded using J modulation (JMOD).

The melting points were determined on a Kofler stage. The specific rotation was measured on a CM-3 circular polarimeter; the specific rotation is given in (deg mL) (g dm)$^{-1}$ and the concentration of the solution is given in g (100 mL)$^{-1}$.

The course of the reactions was monitored by TLC on Silufol UV-254 and Sorbfil plates using 2 : 1 $Et_2O—C_6H_{14}$ and 100 : 10 : 1 $CHCl_3$—MeOH—concentrated NH_3 solvent systems; visualization was carried out by spraying with vanilline or ninhydrin solutions followed by heating to 100—120 °C.

Benzene was dried over $CaCl_2$ and distilled over Na metal. Anhydrous MeOH was prepared by refluxing over magnesium methoxide followed by distillation. Diethyl ether was dried over $CaCl_2$ and distilled over Na metal. Hexane was distilled imme-

Table 1. Selected geometric characteristics of compound **5***

Bond	*d*/Å	Bond	*d*/Å	Angle	ω/deg
Molecule **5A**		Molecule **5B**		Molecule **5A**	
O(11)—C(1)	1.436(2)	O(21)—C(21)	1.431(3)	C(2)—N(11)—C(11)	120.9(2)
O(11)—H(11)	0.85(3)	O(21)—H(21)	0.78(3)	C(13)—N(12)—C(12)	118.7(3)
O(12)—C(19)	1.344(3)	O(22)—C(39)	1.351(4)	N(11)—C(11)—C(12)	110.4(3)
O(12)—H(12)	0.88(3)	O(22)—H(22)	0.84(3)	N(12)—C(12)—C(11)	110.9(3)
N(11)—C(2)	1.271(2)	N(21)—C(22)	1.272(3)	N(12)—C(13)—C(14)	122.8(3)
N(11)—C(11)	1.467(3)	N(21)—C(31)	1.462(3)	Molecule **5B**	
N(11)—H(21)	2.17(3)	N(21)—H(11)	2.11(3)	C(22)—N(21)—C(31)	121.0(2)
N(12)—C(13)	1.275(4)	N(22)—C(33)	1.270(3)	C(33)—N(22)—C(32)	118.9(2)
N(12)—C(12)	1.464(4)	N(22)—C(32)	1.455(4)	N(21)—C(31)—C(32)	109.1(2)
N(12)—H(12)	1.87(3)	N(22)—H(22)	1.83(3)	N(22)—C(32)—C(31)	109.3(2)
C(11)—C(12)	1.507(4)	C(31)—C(32)	1.514(4)	N(22)—C(33)—C(34)	121.9(3)
C(13)—C(14)	1.441(4)	C(33)—C(34)	1.447(4)		

* Two independent molecules.

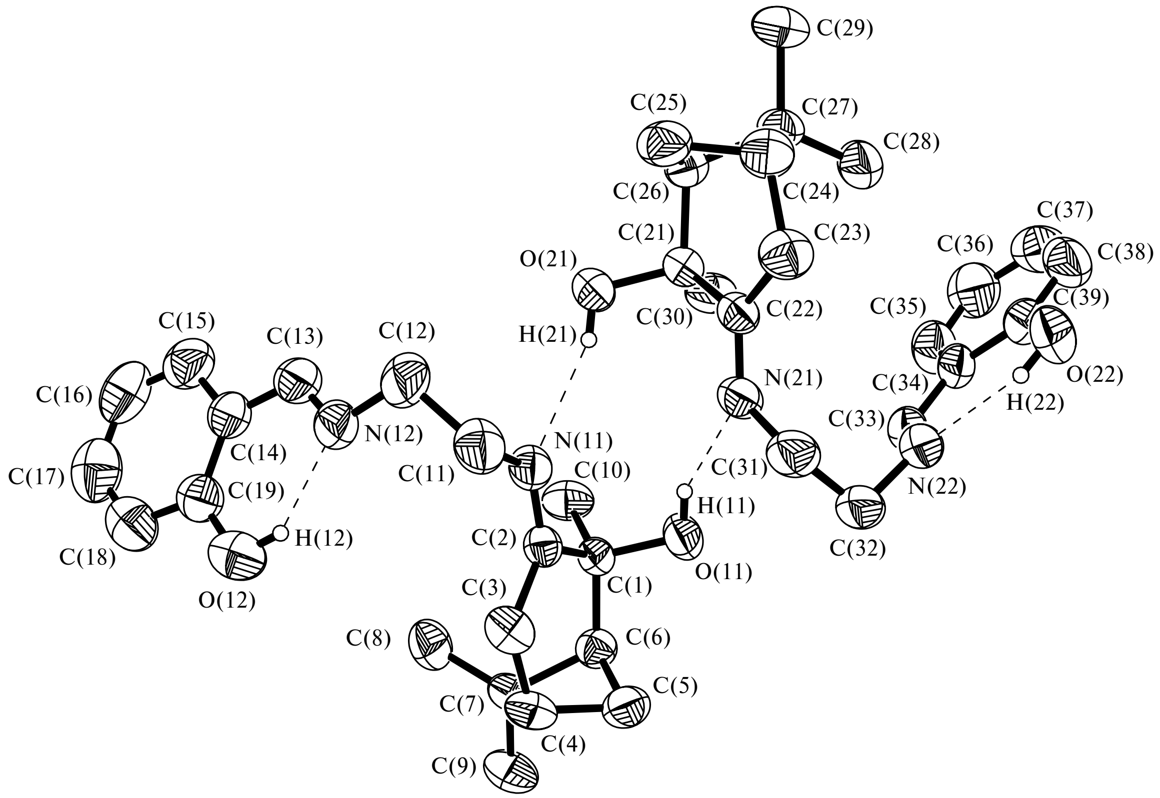

Fig. 1. Molecular structure of compound **5**. Two independent molecules are linked by two O—H...N hydrogen bonds.

diately before use. Boron trifluoride etherate was distilled at 46 °C (10 Torr) over CaH$_2$.

(−)-(1*S*,2*S*,5*S*)-2-Hydroxypinan-3-one (**2**) with $[\alpha]^{20}_{\mathrm{D}}$ −40.5 (*c* 1.8, CHCl$_3$), m.p. 39—40 °C (*cf.* lit. data[19]: m.p. 36—38 °C, $[\alpha]^{20}_{\mathrm{D}}$ −39.5), was prepared by oxidation of α-pinene ($[\alpha]^{20}_{\mathrm{D}}$ +20 (without a solvent); α-pinene was prepared by rectification of turpentine oil) with potassium permanganate according to a known procedure.[20] Ethylenediamine was refluxed and distilled over Na metal. Salicylaldehyde was purchased from Lancaster.

(1*S*,2*S*,5*S*)-3-[(2-Aminoethyl)imino]-2,6,6-trimethylbicyclo[3.1.1]heptan-2-ol (3). A solution of ketol **2** (3.0 g, 18.0 mmol) and ethylenediamine (21.6 g, 360.2 mmol) in anhydrous benzene (30 mL) was refluxed in the presence of F$_3$B • OEt$_2$ (1.5 g, 10.8 mmol) and calcined 4 Å molecular sieves (9 g) for 4 h. The reaction mixture was filtered and the molecular sieves were washed with Et$_2$O. The solvent and the major portion of unconsumed ethylenediamine were removed from the filtrate by distillation *in vacuo*. A saturated aqueous NaCl solution was added to the residue and the mixture was extracted with Et$_2$O (3×50 mL). The combined organic extracts were washed with a saturated aqueous NaCl solution (50 mL) and dried with anhydrous K$_2$CO$_3$. The solvent was removed *in vacuo* to prepare a yellowish oily liquid, which crystallized out upon storage. Recrystallization from hexane afforded white crystals of monoimine **3** (3.0 g, 79%): m.p. 62—64 °C, $[\alpha]^{20}_{\mathrm{D}}$ +6.6 (*c* 10.1, CHCl$_3$). Found (%): C, 68.43; H, 10.84; N, 13.20. C$_{12}$H$_{22}$N$_2$O. Calculated (%): C, 68.53; H, 10.54; N, 13.32. IR, ν/cm^{-1}: 3368 (OH); 3296 (NH$_2$); 1658 (C=N); 1596 (NH); 1388 and 1370 (C(CH$_3$)$_2$). ^{1}H NMR (CDCl$_3$), δ: 0.85 (s, 3 H, Me); 1.32 (s, 3 H, Me); 1.47 (s, 3 H, Me); 1.55 (d, 1 H, H$_\beta$(7), *J* = 10.6 Hz); 2.04 (m, 4 H, Hα(7) and H(1) and NH$_2$); 2.33 (m, 1 H, H(5)); 2.51 (m, 2 H, H$_2$C(4)); 2.99 (m, 2 H, H$_2$C(12)); 3.30 (m, 2 H, H$_2$C(11)). ^{13}C NMR (CDCl$_3$), δ: 22.80 (C(9)); 27.28 (C(8)); 28.09 (C(7)); 28.25 (C(10)); 33.67 (C(4)); 38.30 (C(5)); 38.40 (C(12)); 42.59 (C(6)); 50.37 (C(1)); 53.35 (C(11)); 76.21 (C(2)); 176.73 (C(3)).

3,3´-(Ethylenediimino)bis((1*S*,2*S*,5*S*)-2,6,6-trimethylbicyclo[3.1.1]heptan-2-ol) (4). A solution of ketone **2** (1.0 g, 5.94 mmol) and ethylenediamine (0.54 g, 8.91 mmol) in anhydrous toluene (50 mL) was refluxed in the presence of F$_3$B • OEt$_2$ (0.5 g, 3.57 mmol) and calcined 4 Å molecular sieves (6 g) for 18 h. The reaction mixture was filtered and the molecular sieves were washed with Et$_2$O. The solvent was removed from the filtrate by distillation *in vacuo*. A saturated aqueous NaCl solution was added to the residue and the mixture was extracted with Et$_2$O (3×50 mL). The combined organic extracts were washed with a saturated aqueous NaCl solution (50 mL) and dried with anhydrous K$_2$CO$_3$. The solvent was removed *in vacuo*. Crystallization from an Et$_2$O—hexane mixture afforded bisimine **4** (0.46 g, 43%) as a white powder, m.p. 163—164 °C (with decomp.), $[\alpha]^{20}_{\mathrm{D}}$ −17.6 (*c* 4.2, EtOH). Found (%): C, 73.01; H, 10.14; N, 7.78. C$_{22}$H$_{36}$N$_2$O$_2$. Calculated (%): C, 73.29; H, 10.06; N, 7.77. IR, ν/cm^{-1}: 3284 (OH); 1664 (C=N). ^{1}H NMR (CDCl$_3$), δ: 0.87 (s, 6 H, Me); 1.33 (s, 6 H, Me); 1.45 (s, 6 H, Me); 1.54 (d, 2 H, H$_\beta$(7), *J* = 10.6 Hz); 2.05 (m, 4 H, H$_\alpha$(7) and H(1)); 2.33 (m, 2 H, H(5)); 2.55 (br.s, 2 H, OH); 2.60 (m, 4 H, C(4)H$_2$); 3.63 (s, 4 H, C(11)H$_2$). ^{13}C NMR

($CDCl_3$), δ: 22.78 (C(9)); 27.18 (C(8)); 27.96 (C(7)); 28.24 (C(10)); 33.53 (C(4)); 38.18 (C(5)); 38.27 (C(6)); 50.40 (C(1)); 51.22 (C(11)); 76.13 (C(2)); 176.33 (C(3)).

(1*S*,2*S*,5*S*)-3-[{2-[(2-Hydroxybenzylidene)amino]ethyl}imino]-2,6,6-trimethylbicyclo[3.1.1]heptan-2-ol (5). A solution of monoimine **3** (2.0 g, 9.51 mmol) and salicylaldehyde (1.2 g, 9.51 mmol) in anhydrous MeOH (30 mL) was stirred at ~20 °C for 4 h. After removal of the solvent *in vacuo*, the residue was recrystallized from an Et_2O—hexane mixture. The yellow crystals that precipitated were filtered off and washed with hexane. Dioxydiimine **5** was obtained in a yield of 2.78 g (93%), m.p. 97—98 °C, $[\alpha]^{20}{}_D$ +78.5 (*c* 1.02, EtOH). Found (%): C, 72.52; H, 7.94; N, 8.83. $C_{19}H_{26}N_2O_2$. Calculated (%): C, 72.58; H, 8.34; N, 8.91. IR, ν/cm^{-1}: 3276 (OH); 1638, 1658 (C=N). ^{1}H NMR ($CDCl_3$), δ: 0.66 (s, 3 H, Me); 1.26 (s, 3 H, Me); 1.40 (s, 3 H, Me); 1.44 (d, 1 H, H_β(7), *J* = 10.6 Hz); 1.99 (m, 2 H, H_α(7) and H(1)); 2.27 (m, 1 H, H(5)); 2.49 (m, 2 H, H_2C(4)); 2.63 (br.s, 1 H, HOCMe); 3.59—3.67 (m, 2 H, C(12)H_2); 3.88—3.99 (m, 2 H, C(11)H_2); 6.83—6.93 and 7.21—7.30 (both m, 4 H, Ar); 8.33 (s, 1 H, H(13)); 13.48 (br.s, 1 H, HO—Ar). ^{13}C NMR ($CDCl_3$), δ: 22.57 (C(9)); 27.23 (C(8)); 28.01 (C(7)); 28.33 (C(10)); 33.71 (C(4)); 38.29 (C(5) and C(6)); 50.22 (C(1)); 50.53 (C(11)); 59.72 (C(12)); 76.41 (C(2)); 116.95 (C(16)); 118.42 (C(18)); 118.64 (C(14)); 131.17 (C(17)); 132.15 (C(19)); 166.03 (C(13)).

X-ray diffraction analysis of compound 5. X-ray data were collected on an automated Enraf-Nonius CAD 4 diffractometer at ~20 °C (Mo-*K*α radiation, λ = 0.71073 Å, graphite monochromator). Crystals of **5** ($C_{19}H_{26}N_2O_2$, M = 314.42) are orthorhombic, space group $P2_12_12_1$, a = 11.420(4), b = 14.097(5), c = 22.259(8) Å, V = 3583(2) Å^3, Z = 8, d_{calc} = 1.166 g cm^{-3}, μ(Mo-*K*α) = 0.076 mm^{-1}, F(000) = 1360. A total of 6676 reflections were measured (of which 5283 reflections are independent, R_{int} = 0.0171) using the ω-scanning technique in the range $2.00 < \theta < 24.98°$ ($-13 \le h \le 2$, $-16 \le k \le 3$, $-26 \le l \le 5$). The intensities of reflections were corrected for the Lorentz and polarization factors.[21] Absorption was ignored. The structure was solved by direct methods (SHELX-86[22]). All nonhydrogen atoms were refined anisotropically by the full-matrix least-squares method against F^2 (SHELXL-97[23]). All hydrogen atoms, except for H(11), H(12), H(21), and H(22), were placed in calculated positions; four hydroxy H atoms were revealed from difference electron density syntheses. All hydrogen atoms were refined isotropically. The final reliability factors were R_1 = 0.0291 and wR_2 = 0.0674 for 3143 reflections with $I > 2\sigma(I)$; 624 parameters were refined; GOOF = 0.977.

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