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Dedicated to Full Member of the Russian Academy of Sciences G.A. Tolstikov on his 80th anniversary

Optical Resolution of Racemic 4-Hydroxy-3,5-diisobornylbenzaldehyde

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Abstract—Optical resolution of racemic 4-hydroxy-3,5-diisobornylbenzaldehyde was accomplished via transformation into diastereoisomeric esters by treatment with (1*S*)-camphanoyl chloride. The absolute configuration of the enantiomers was determined on the basis of the X-ray diffraction data for one diastereoisomeric camphanate.

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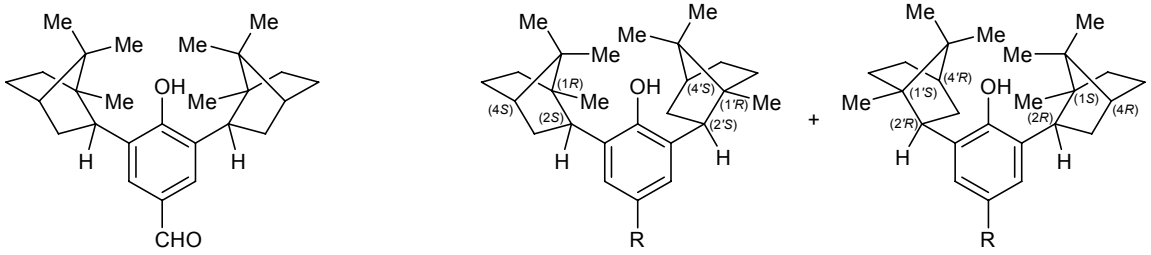
Substituted and unsubstituted *p*-hydroxybenzaldehydes are precursors of fused derivatives and phosphorus-containing compounds [1–5]; such aldehydes are especially important for the synthesis of symmetric and unsymmetric tetraarylporphyrins [6–10]. We previously described tetrapyrrole condensation of the *meso* diastereoisomer of 4-hydroxy-3,5-diisobornylbenzaldehyde (*meso*-**I**), which produced tetra(*meso*-aryl)porphyrin bearing isobornyl substituents as a mixture of atropisomers due to different configurations of isobornyl fragments in the initial aldehyde molecule [10]. Enantiopure (or enantiorich) formyl derivatives with diisobornylphenol fragments attract interest from the viewpoint of studying their antioxidant and pharmacological properties. To obtain them it was necessary to synthesize pure enantiomers of 4-hydroxy-3,5-diisobornylbenzaldehyde (**I**). The present article reports on the preparation of its enantiomerically enriched samples by optical resolution of racemic aldehyde *rac*-**I**.

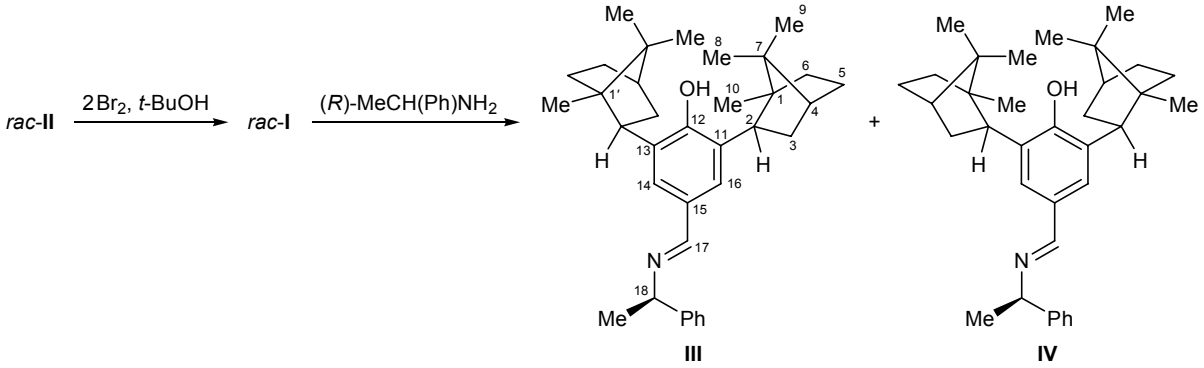
Aldehyde *rac*-**I** was synthesized by oxidation of racemic 2,6-diisobornyl-4-methylphenol (*rac*-**II**) at the 4-methyl group with bromine in *tert*-butyl alcohol according to the procedure for the synthesis of *meso*-**I** [11] (Scheme 1). Enantiomeric isobornyl-substituted salicylaldehydes and 4-hydroxy-3-isobornyl-5-methylbenzaldehydes were previously separated via transformation into the corresponding diastereoisomeric Schiff bases by treatment with (*R*)-1-phenylethanamine and subsequent fractional crystallization



meso-**I** *rac*-**I**, *rac*-**II**

I, R = CHO; **II**, R = Me.

Scheme 1.



[12, 13]. However, we failed to separate by crystallization diastereoisomeric Schiff bases **III** and **IV** obtained in a similar way from *rac*-**I** (Scheme 1).

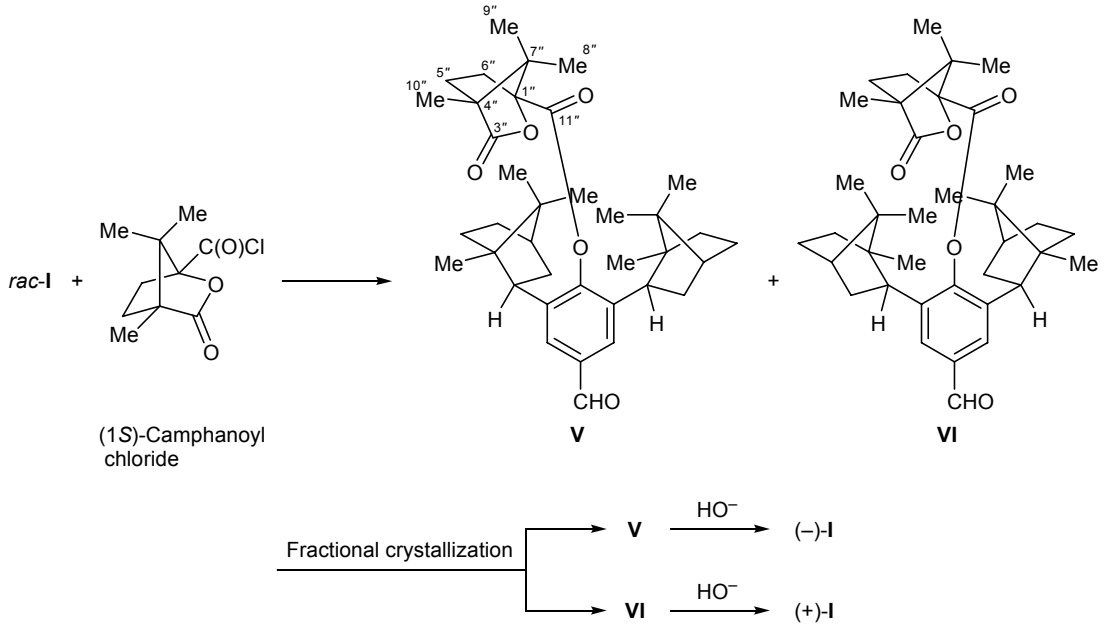
Schiff bases **III** and **IV** were characterized by *E* configuration with respect to the double C=N bond. The NOESY spectrum of mixture **III**/**IV** revealed coupling between 17-H and 18-H, indicating spatially close location of these protons.

Aldehyde *rac*-**I** was converted into diastereoisomeric esters **V** and **VI** by treatment with (1*S*)-camphanoyl chloride, and stereoisomers **V** and **VI** were separated by fractional crystallization from toluene. We thus isolated diastereoisomerically enriched camphanates **V** and **VI** whose alkaline hydrolysis gave enantiomerically enriched samples of (–)-**I** and (+)-**I** (Scheme 2; atom numbering in the camphane skeleton is shown for the sake of convenience in NMR signal assignment). The diastereoisomeric purity of **V** and **VI** in the course of their separation and the enantiomeric purity of the isolated aldehydes (+)-**I** and (–)-**I** were determined by analytical HPLC using Chiralcel OD-H and Chiralpak AD columns.

The structure of compounds **I** and **III**–**VI** was confirmed by spectral and analytical data. The absolute configuration of **V** was determined on the basis of anomalous X-ray scattering; it coincided with the relative configuration determined on the basis of the known configuration of the camphane fragment. The chiral centers in the isobornyl fragments of **V** and (–)-**I** have (1*S*,2*R*,4*R*) configuration, while configuration of the isobornyl substituents in **VI** and (+)-**I** is the opposite, (1*R*,2*S*,4*S*).

The symmetry-independent part of a unit cell of **V** includes one molecule (Fig. 1). The ester fragment is

Scheme 2.



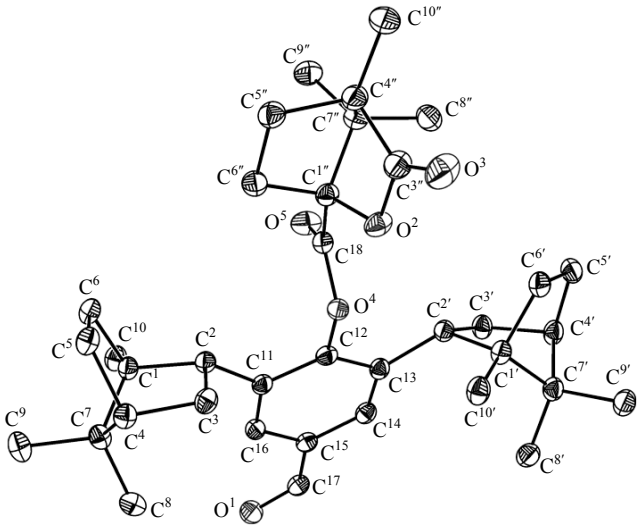


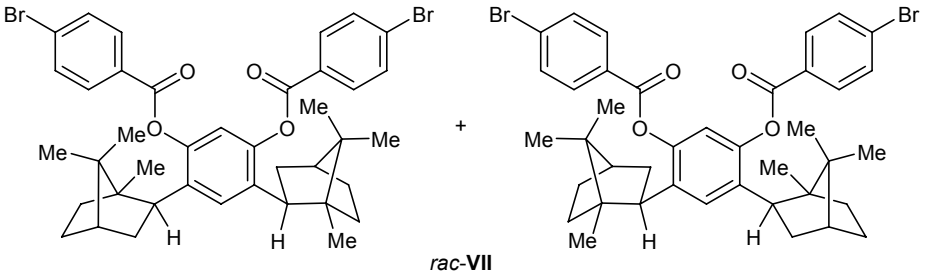
Fig. 1. Structure of the molecule of 4-formyl-2,6-bis-{(1*S*,2*R*,4*R*)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl}-phenyl (1*S*,4*R*)-4,7,7-trimethyl-3-oxo-2-oxabicyclo[2.2.1]-heptane-1-carboxylate (**V**) according to the X-ray diffraction data. Non-hydrogen atoms are shown as thermal vibration ellipsoids with a probability of 50%.

almost orthogonal to the benzene ring plane [torsion angle $C^{11}C^{12}O^4C^{18}$ −88.66(11)°]. Orientation of the isobornyl substituents in molecule **V** is characterized by the torsion angles $C^{16}C^{11}C^2C^3$ 99.27(12) and $C^{14}C^{13}C^{2'}C^{3'}$ 20.29(15)°. The corresponding torsion angle in most isobornylphenols studied previously approaches 20° [11, 12, 14−19]. Conformational analysis of model isobornylbenzene [18] showed that such mutual orientation corresponds to the global minimum on the potential energy surface and that a torsion angle of about 90° matches a local minimum with an energy higher by 1.7 kcal/mol. Thus, orientation of one isobornyl substituent in molecule **V** may be regarded as optimal, whereas the second one occupies a local energy minimum, presumably due to the lack of steric effects of other substituents.

Analogous pattern was observed previously for diacyl derivative of diisobornyl-substituted resorcinol *rac*-**VII** [18], but factors responsible for the observed orientations of the terpene fragments in **V** and *rac*-**VII** are different. The main factor determining the substituent orientation in *rac*-**VII** was intermolecular interactions, whereas the situation with camphanate **V** was different.

To get a deeper insight into the steric structure of **V**, conformational analysis was performed by varying the torsion angles $C^{16}C^{11}C^2C^3$ and $C^{14}C^{13}C^{2'}C^{3'}$, the relative position of the other substituents remaining unchanged (as in crystal). The calculations were performed at the B972/6-31G* level of theory (as in [18]) with the aid of GAUSSIAN software package [20]. The potential energy curves shown in Fig. 2 differ considerably from each other. The dependence of E_{rel} on the torsion angle $C^{14}C^{13}C^{2'}C^{3'}$ resembles that found for isobornylbenzene (weak effect of the ester group), whereas the dependence of E_{rel} on $C^{16}C^{11}C^2C^3$ is quite different: the torsion angle 100° corresponds to the global minimum. The reason is that the terpene fragments in molecule **V** have the same absolute configuration, and mutual orientations of each isobornyl fragment and the ester group are different. The ester fragment and isobornyl substituent on C^{13} appear at the opposite sides of the aromatic ring, so that there are no steric hindrances, and the orientation of the isobornyl fragment is almost the same as in unsubstituted isobornylbenzene. If the torsion angle $C^{16}C^{11}C^2C^3$ were equal to 20°, the isobornyl fragment on C^{11} and the ester group would be located at the same side of the benzene ring. This should lead to steric repulsion and cause the isobornyl fragment to turn away as observed in crystal. Thus the conformation of molecule **V** is determined mainly by intramolecular interactions.

According to the NMR data, introduction of a camphane fragment into molecule *rac*-**I** makes the terpene fragments magnetically nonequivalent, and some proton signals become distinguishable. The difference in the signal position may be rationalized by the same factors as those operating in crystal, which provides an additional support to the assumption that mutual orientation of substituents in **V** is determined by intramolecular interactions.



rac-**VII**

EXPERIMENTAL

The IR spectra were recorded in KBr on a Shimadzu IR Prestige 21 spectrometer. The ^{1}H and ^{13}C NMR spectra were measured on a Bruker Avance II 300 instrument at 300.17 and 75.48 MHz, respectively, from solutions in $CDCl_3$ relative to the residual proton and carbon signals of the solvent ($CHCl_3$, δ 7.26 ppm; $CDCl_3$, δ_C 77.00 ppm). Signals were assigned on the basis of the *J*-modulation ^{13}C NMR spectra and HSQC, COSY, and NOESY experiments. The melting points were determined on a Kofler hot stage and were not corrected. The optical rotations were measured on a P3002RS Kruss Optronic automatic digital polarimeter (λ 589 nm).

The progress of reactions was monitored by TLC on Sorbfil plates. Aldehyde **I** was detected on the chromatograms by treatment with a solution prepared from 15 g of $KMnO_4$, 300 ml of H_2O, and 0.5 ml of concd. H_2SO_4. Esters **V** and **VI** were detected by treatment with a solution of Bromocresol Purple, followed by heating to 100–120°C. HPLC analyses were performed on an Agilent 1100 chromatograph equipped with a UV detector (λ 219 nm, 20°C). The diastereoisomeric purity of compounds **V** and **VI** was estimated using a Chiralcel OD-H column (Daicel, 25 cm × 4.6 mm, grain size 5 μm; eluent hexane–*i*-PrOH, 99:1, flow rate 1.0 ml/min); the enantiomeric purity of (+)-**I** and (–)-**I** was estimated using a Chiralpak AD column (Daicel, 25 cm × 4.6 mm, grain size 10 μm; eluent hexane–*i*-PrOH, 97:3, flow rate 1.0 ml/min).

The products were purified by column chromatography (wet packing) on silica gel (70–230 μm, Alfa Aesar). Toluene was dried over anhydrous $CaCl_2$ and distilled over metallic sodium. 4-Å Molecular sieves were activated by calcination at 140°C over a period of 3 h. Commercial (*R*)-1-phenylethanamine (ChiPros®, enantiomeric purity >99%), (1*S*)-camphanoyl chloride (Alfa Aesar), 4-dimethylaminopyridine (Acros Organics), and triethylamine (Sigma–Aldrich) were used without additional purification. Racemic 2,6-diisobornyl-4-methylphenol (*rac*-**II**) was isolated from the alkylation products of *p*-cresol with camphene according to modified procedure [21].

Single crystals of **V** suitable for X-ray analysis were obtained by slow evaporation of its solution in benzene. Colorless crystals ($C_{37}H_{50}O_5$, *M* 574.77); rhombic crystal system, space group $P2_12_12_1$; unit cell parameters: a = 7.10570(10), b = 20.8831(3), c = 21.3122(3) Å; V = 3162.50(8) Å^3; Z = 4; d_{calc} = 1.207 g/cm^3. Total of 43373 reflection intensities were measured on a Bruker Smart Apex2 CCD diffractometer (λCuK_α = 1.54178 Å, θ_{max} = 67.35°) at 100 K from a 0.19 × 0.14 × 0.11-mm single crystal. The initial array of reflection intensities was processed with a correction for absorption using SAINT and SADABS programs built in APEX2 software package [22]. The structure was solved by the direct method and was refined against F^2_{hkl} by the full-matrix least-squares procedure in anisotropic approximation for non-hydrogen atoms. Hydrogen atoms were placed into positions calculated on the basis of geometry considerations and were refined according to the riding model [U_{iso}(H) = nU_{eq}(C, O); n = 1.5 for methyl carbon atoms, n = 1.2 for the other carbon atoms]. The final divergence factors were wR_2 = 0.0643 (for 5596 independent reflections, R_{int} = 0.0284) and R_1 = 0.0253 [for 5516 reflections with $I > 2\sigma(I)$]. All calculations were performed on an IBM PC using SHELXTL software [23]. The coordinates of atoms and their temperature factors were deposited to the Cambridge Crystallographic Data Centre (entry no. CCDC 910121).

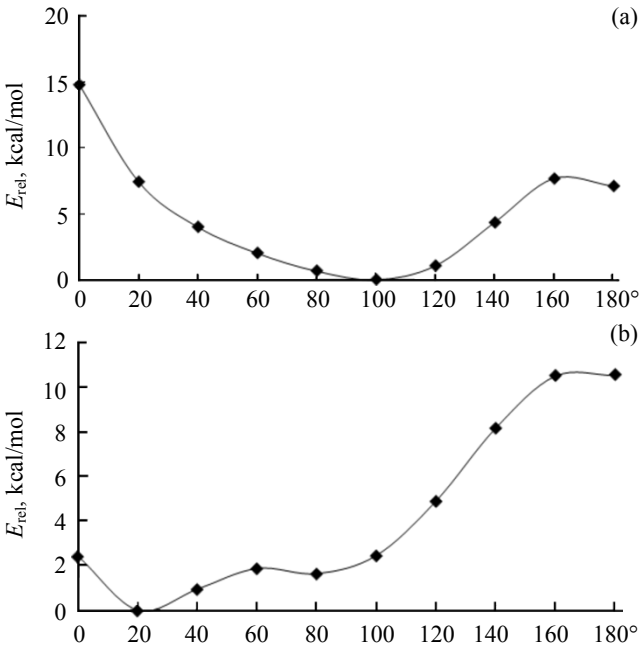


Fig. 2. Plots of the relative conformational energy of compound **V** versus torsion angles (a) $C^{16}C^{11}C^2C^3$ and (b) $C^{14}C^{13}C^{2'}C^{3'}$.

4-Hydroxy-3,5-bis(1,7,7-trimethylbicyclo[2.2.1]-heptan-2-*exo*-yl)benzaldehyde (*rac*-I). Compound *rac*-**II**, 8.4 g (22 mmol), was dissolved in 420 ml of *tert*-butyl alcohol on slight heating, the solution was cooled to ~40°C, and 2.27 ml (44 mmol) of bromine was added in small portions. The mixture was stirred for 3 h at room temperature and left overnight. The

solvent was distilled off, 80 ml of chloroform was added to the residue, the mixture was washed with a saturated solution of $Na_2S_2O_3$ (3×50 ml) and water (2×50 ml) and dried over anhydrous sodium sulfate, the solvent was distilled off, and the residue was recrystallized from petroleum ether. Yield 4.1 g (47%), colorless powder, mp 190–192°C (possibly with decomposition). IR spectrum, ν, cm^{-1}: 3591, 3296 (OH), 2951, 2878, 1448 (Me, CH_2), 1665 (C=O). ^{1}H NMR spectrum, δ, ppm: 0.75 s (6H, 10-H, 10′-H), 0.85 s (6H, 9-H, 9′-H), 0.90 s (6H, 8-H, 8′-H); 1.31–1.50 m, 1.59–1.79 m, and 1.82–2.02 m (4H each, 3-H, 3′-H, 4-H, 4′-H, 5-H, 5′-H, 6-H, 6′-H), 2.26–2.35 m (2H, 3-H, 3′-H), 3.06 t (2H, 2-H, 2′-H, J = 8.7 Hz), 5.40 s (1H, OH), 7.72 s (2H, 14-H, 16-H), 9.84 s (1H, CHO). ^{13}C NMR spectrum, δ_C, ppm: 12.49 (C^{10}, $C^{10'}$), 20.34 (C^9, $C^{9'}$), 21.33 (C^8, $C^{8'}$), 27.52 (C^5, $C^{5'}$), 34.46 (C^3, $C^{3'}$), 40.17 (C^6, $C^{6'}$), 45.43 (C^4, $C^{4'}$), 46.12 (C^2, $C^{2'}$), 48.36 (C^7, $C^{7'}$), 49.80 (C^1, $C^{1'}$), 128.06 (C^{14}, C^{16}), 128.45 and 129.53 (C^{11}, C^{13}, C^{15}), 159.57 (C^{12}), 191.65 (CHO). Found, %: C 81.98; H 9.91. $C_{27}H_{38}O_2$. Calculated, %: C 82.18; H 9.71.

4-Methyl-2,6-bis(1,7,7-trimethylbicyclo[2.2.1]heptan-2-*exo*-yl)phenol (*rac*-II). A mixture of 10.5 g (97 mmol) of *p*-cresol, 26.4 (194 mmol) of camphene, and 1.05 g (3 mmol) of $(4\text{-MePhO})_3Al$ as catalyst was heated at 180°C until complete conversion of *p*-cresol (TLC, eluent petroleum ether). The mixture was cooled, diluted with diethyl ether until it turned homogeneous, and washed with 18% aqueous HCl to decompose the catalyst. The ether extract was washed with 5% aqueous NaOH to remove unreacted *p*-cresol and with water to neutral reaction and dried over anhydrous sodium sulfate. The solvent was distilled off, and the residue was subjected to column chromatography using petroleum ether–diethyl ether as eluent to isolate 8.9 g (24%) of *rac*-**II** as colorless powder with mp 169–172°C. IR spectrum, ν, cm^{-1}: 3505, 3442 (OH), 2988, 2947, 2874, 1458 (Me, CH_2), 1178 (C–O). ^{1}H NMR spectrum, δ, ppm: 0.78 s (6H, 10-H, 10′-H), 0.88 s and 0.93 s (6H each, 9-H, 9′-H, 8-H, 8′-H); 1.40–1.50 m, 1.58–1.71 m, and 1.89–1.90 m (4H each, 3-H, 3′-H, 4-H, 4′-H, 5-H, 5′-H, 6-H, 6′-H), 2.22–2.31 m (2H, 3-H, 3′-H), 2.31 s (3H, 17-H), 3.08 t (2H, 2-H, 2′-H, J = 9.0 Hz), 4.64 s (1H, OH), 6.99 s (2H, 14-H, 16-H). ^{13}C NMR spectrum, δ_C, ppm: 12.44 (C^{10}, $C^{10'}$), 20.32 and 21.46 (C^8, $C^{8'}$, C^9, $C^{9'}$, C^{17}), 27.60 (C^5, $C^{5'}$), 34.40 (C^3, $C^{3'}$), 40.14 (C^6, $C^{6'}$), 45.43 and 46.12 (C^2, $C^{2'}$, C^4, $C^{4'}$), 48.17 and 49.61 (C^1, $C^{1'}$, C^7, $C^{7'}$), 125.95 (C^{14}, C^{16}), 127.39 and 128.23 (C^{11}, C^{13}, C^{15}), 151.60 (C^{12}). Found, %: C 85.38; H 10.33. $C_{27}H_{40}O$. Calculated, %: C 85.20; H 10.59.

Schiff bases III and IV. A mixture of 1.38 g (3.5 mmol) of *rac*-**I** dissolved in 25 ml of toluene, 0.45 ml (3.5 mmol) of (*R*)-(+)-1-phenylethanamine, and 6.5 g of 4-Å molecular sieves was heated for 3.5 h under reflux while stirring in a stream of argon. The solution was filtered through a glass filter, the molecular sieves were washed with chloroform, and the filtrate was evaporated. The residue was recrystallized in succession from pentane, hexane, cyclohexane, benzene, and toluene.

2,6-Bis{(1*R*,2*S*,4*S*)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl}-4-{(*E*)-[(*R*)-1-phenylethylimino]methyl}phenol (III) and 2,6-bis{(1*S*,2*R*,4*R*)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl}-4-{(*E*)-[(*R*)-1-phenylethylimino]methyl}phenol (IV) (mixture of diastereoisomers at a ratio of ~1:1**).** Yield 1.71 g (98%), red–orange caramel-like material. IR spectrum, ν, cm^{-1}: 3597, 3418 (OH); 2949, 2876, 1456 (Me, CH_2); 1641 (C=N); 1699 (C=O); 1290 (C–O). ^{1}H NMR spectrum, δ, ppm: 0.74/0.76* s (6H, 10-H, 10′-H), 0.85 s and 0.92 s (6H each, 8-H, 8′-H, 9-H, 9′-H), 1.30−1.47 m (4H, 5-H, 5′-H, 6-H, 6′-H), 1.54/1.56* d (3H, 19-H, J = 6.2/6.4 Hz), 1.61−1.74 m (4H, 3-H, 3′-H, 6-H, 6′-H), 1.81−1.98 m (4H, 4-H, 4′-H, 5-H, 5′-H), 2.24−2.47 m (2H, 3-H, 3′-H), 3.06 t (1H, 2-H, 2′-H, J = 8.6 Hz), 4.49 q (1H, 18-H, J = 6.6 Hz), 5.02 br.s (1H, OH), 7.16−7.45 (5H, C_6H_5), 7.63/7.64* s (14-H, 16-H), 8.27 br.s (1H, 17-H). ^{13}C NMR spectrum, δ_C, ppm: 12.42/12.47* (C^{10}, $C^{10'}$), 20.21/20.33,* and 21.43 (C^9, $C^{9'}$, C^8, $C^{8'}$), 25.12/25.43* (C^{19}), 27.59 (C^5, $C^{5'}$), 34.46/34.49* (C^3, $C^{3'}$), 40.15/40.19* (C^6, $C^{6'}$), 45.51 (C^4, $C^{4'}$), 46.17 (C^2, $C^{2'}$), 48.28 (C^7, $C^{7'}$), 49.70 (C^1, $C^{1'}$), 69.41 (C^{18}); 125.95, 126.48/126.64,* 128.22/128.28,* 129.02 (C^{14}, C^{16}, C^{21}, $C^{21'}$, C^{22}, $C^{22'}$, C^{23}); 127.68 and 128.71 (C^{11}, C^{13}, C^{15}), 146.21 (C^{20}), 156.21 (C^{12}), 159.49/159.62* (C^{17}). Found, %: C 84.09; H 9.94. $C_{35}H_{47}NO$. Calculated, %: C 84.45; H 9.52.

Esters V and VI. A mixture of 2.37 g (6.0 mmol) of *rac*-**I** dissolved in 25 ml of toluene, 1.56 g (7.2 mmol) of (1*S*)-camphanoyl chloride, 1.0 ml (7.2 mmol) of triethylamine, and 0.073 g (0.6 mmol) of 4-dimethylaminopyridine was heated for 4 h under reflux while stirring in a stream of argon. The solution was evaporated, and the residue was subjected to column chromatography using cyclohexane–chloroform as eluent to isolate 2.87 g (83%) of a mixture of diastereoisomers **V** and **VI**. The isomer mixture was dissolved in 25 ml of hot toluene, and the solution was left to stand for crystallization at –20°C over a period

* Signals from different diastereoisomers.

of 48 h. The colorless precipitate was separated and dried under reduced pressure. Yield of **V** 1.05 g (61%), diastereoisomeric purity >95%. The second diastereoisomer was isolated from the mother liquor after two additional crystallizations. Yield of **VI** 1.38 g (80%), diastereoisomeric purity >85%.

4-Formyl-2,6-bis{(1*S*,2*R*,4*R*)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl}phenyl (1*S*,4*R*)-4,7,7-trimethyl-3-oxo-2-oxabicyclo[2.2.1]heptane-1-carboxylate (V). Colorless finely crystalline powder, mp 250–252°C, $[\alpha]_D^{21}$ = –103.7° (*c* = 0.36, $CHCl_3$); retention time (HPLC) 9.53 min. IR spectrum, ν, cm^{-1}: 2959, 2878, 1458 (Me, CH_2), 1798, 1755 (C=O, ester), 1699 (C=O, aldehyde), 1258 (C–O). ^1H NMR spectrum, δ, ppm: 0.72 s (3H) and 1.17 s (6H) (10-H, 10′-H, 10″-H), 0.83 s and 0.96 s (3H each, 9-H, 9′-H), 0.87 s and 1.09 s (3H each, 8-H, 8′-H), 1.14 s (3H, 9″-H), 1.23 s (3H, 8″-H); 1.14–1.36 m (3H), 1.38–1.52 m (1H), 1.53–1.72 m (4H), 1.72–1.92 m (5H), 1.95–2.14 m (2H), 2.17–2.40 m (2H), and 2.44–2.57 m (1H) (3-H, 3′-H, 4-H, 4′-H, 5-H, 5′-H, 5″-H, 6-H, 6′-H, 6″-H); 2.63 t and 2.78 t (1H each, 2-H, 2′-H, *J* = 8.6, 8.7 Hz); 7.82 s and 7.86 s (1H each, 14-H, 16-H), 9.94 s (1H, 17-H). ^{13}C NMR spectrum, δ_C, ppm: 9.58 ($C^{10''}$), 12.32 and 14.73 (C^{10}, $C^{10'}$), 16.94 and 17.09 ($C^{8''}$, $C^{9''}$), 20.57 (C^9, $C^{9'}$), 21.54 and 23.22 (C^8, $C^{8'}$), 27.21 and 27.50 (C^5, $C^{5'}$), 28.97 ($C^{5''}$), 31.74 ($C^{6''}$), 34.26 and 43.50 (C^3, $C^{3'}$), 39.30 and 39.37 (C^6, $C^{6'}$), 45.49 (C^4, $C^{4'}$), 45.74 and 46.53 (C^2, $C^{2'}$), 48.49 (C^7, $C^{7'}$), 50.50 (C^1, $C^{1'}$), 54.09 ($C^{4''}$), 54.71 ($C^{7''}$), 90.07 ($C^{1''}$), 127.80 and 128.02 (C^{14}, C^{16}); 133.01, 136.78, 139.83 (C^{11}, C^{13}, C^{15}); 153.62 (C^{12}), 166.10 and 177.66 ($C^{3''}$, $C^{11''}$), 191.84 (C^{17}). Found, %: C 74.05; H 8.24. $C_{28}H_{36}O_5$. Calculated, %: C 74.31; H 8.02.

4-Formyl-2,6-bis{(1*R*,2*S*,4*S*)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl}phenyl (1*S*,4*R*)-4,7,7-trimethyl-3-oxo-2-oxabicyclo[2.2.1]heptane-1-carboxylate (VI). Light brown powder, mp 192–194°C, $[\alpha]_D^{21}$ = +58.5° (*c* = 0.33, $CHCl_3$); retention time (HPLC) 10.36 min. IR spectrum, ν, cm^{-1}: 2955, 2880, 1458 (Me, CH_2), 1798, 1753 (C=O, ester), 1699 (C=O, aldehyde), 1258 (C–O). ^1H NMR spectrum, δ, ppm: 0.74 s (3H), 1.18 s (6H), 1.20 s (6H) (8″-H, 9″-H, 10-H, 10′-H, 10″-H); 0.83 s and 0.95 s (3H each, 9-H, 9′-H); 0.87 s and 1.06 s (3H each, 8-H, 8′-H); 1.12–1.45 (3H), 1.49–1.93 (10H), 1.93–2.13 (2H), 2.13–2.43 (2H), and 2.45–2.61 (1H) (3-H, 3′-H, 4-H, 4′-H, 5-H, 5′-H, 5″-H, 6-H, 6′-H, 6″-H); 2.61–2.84 m (2H, 2-H, 2′-H); 7.85 s and 7.87 s (1H each, 14-H, 16-H), 9.94 s (1H, 17-H). ^{13}C NMR spectrum, δ_C, ppm: 9.65 ($C^{10''}$), 12.43 and 14.99 (C^{10}, $C^{10'}$), 16.83 ($C^{8''}$, $C^{9''}$), 20.48 and 20.56 (C^9, $C^{9'}$), 21.53 and 23.27 (C^8, $C^{8'}$), 27.28 (C^5, $C^{5'}$), 28.90 ($C^{5''}$), 32.17 ($C^{6''}$), 34.19 and 43.36 (C^3, $C^{3'}$), 39.02 and 40.09 (C^6, $C^{6'}$), 45.51 (C^4, $C^{4'}$), 45.81 and 46.83 (C^2, $C^{2'}$), 48.29 and 48.47 (C^7, $C^{7'}$), 50.51 (C^1, $C^{1'}$), 54.50 ($C^{4''}$), 54.85 ($C^{7''}$), 90.23 ($C^{1''}$), 127.83 and 128.08 (C^{14}, C^{16}); 132.93, 136.59, 140.37 (C^{11}, C^{13}, C^{15}); 153.80 (C^{12}), 166.05 and 177.74 ($C^{3''}$, $C^{11''}$), 191.81 (C^{17}). Found, %: C 74.05; H 8.24. $C_{28}H_{36}O_5$. Calculated, %: C 74.31; H 8.02.

Enantiomerically enriched aldehydes (+)-I and (–)-I (*general procedure*). Camphanate **V** or **VI**, 0.3 g (0.52 mmol), was dissolved in 6 ml of THF (compound **V** was dissolved on slight heating), 6 ml of 12 M aqueous KOH was added, and the mixture was heated for 12 h under reflux with vigorous stirring. The organic phase was separated, washed with several portions of a saturated solution of sodium chloride, and dried over anhydrous sodium sulfate, the solvent was distilled off, and the residue was subjected to column chromatography using benzene as eluent.

4-Hydroxy-3,5-bis{(1*S*,2*R*,4*R*)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl}benzaldehyde (–)-(I). Yield 0.161 g (78%), enantiomeric purity 98.7%, colorless or light brown powder, mp 227–229°C (possibly with decomposition), $[\alpha]_D^{23}$ = –41.9° (*c* = 0.32, $CHCl_3$); retention time (HPLC) 9.36 min.

4-Hydroxy-3,5-bis{(1*R*,2*S*,4*S*)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl}benzaldehyde (+)-(I). Yield 0.167 g (81%), enantiomeric purity 85%, colorless or light brown powder, mp 219–222°C (possibly with decomposition), $[\alpha]_D^{23}$ = +40.2° (*c* = 0.27, $CHCl_3$); retention time (HPLC) 11.45 min.

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