



## Efficient syntheses of enantiomerically pure 1,2-dicyclohexenyl- and 1,2-dicyclohexyl-1,2-ethanediol using *B*-2-cyclohexen-1-yl-diisopinocampheylborane<sup>†</sup>

Guang-Ming Chen and P. Veeraraghavan Ramachandran\*

H. C. Brown and R. B. Wetherill Laboratories of Chemistry, Purdue University, West Lafayette, Indiana 47907-1393, USA

**Abstract:** The reaction of (+)-*B*-2-cyclohexen-1-yl-diisopinocampheylborane with glyoxal at  $-78^{\circ}\text{C}$  yields 98% stereoisomerically pure (1*S*,2*S*,1'*R*,1''*R*)-(+)-1,2-bis(2-cyclohexenyl)-1,2-ethanediol in 81% yield. A simple crystallization of the above diol from hexane followed by hydrogenation over Raney Ni provides an essentially quantitative yield of enantiomerically pure (*S,S*)-1,2-dicyclohexyl-1,2-ethanediol. © 1997 Elsevier Science Ltd. All rights reserved.

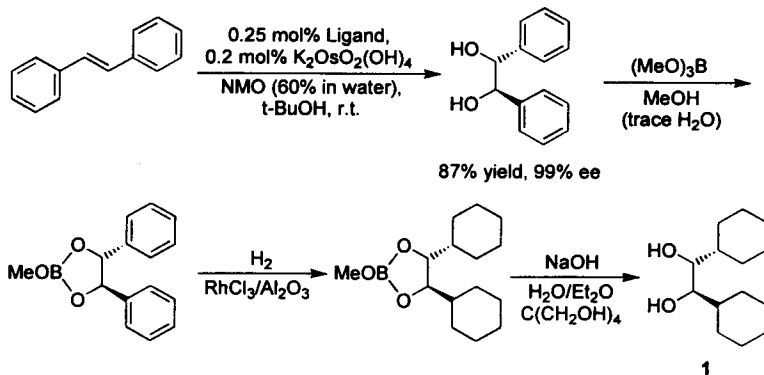
Enantiomerically pure 1,2-dicyclohexyl-1,2-ethanediol (**1**) is a versatile  $C_2$ -symmetric chiral auxiliary that has been successfully applied for various asymmetric syntheses. For example, Hoffmann and coworkers synthesized invictolide, a queen recognition pheromone of the red fire ant, and a fragment of erythronolide A, a macrolide antibiotic, using a boronate containing **1**.<sup>1</sup> Matteson's group developed asymmetric homologations using **1** as the chiral auxiliary and applied this methodology for the syntheses of natural products.<sup>2</sup> Meijere *et al.* carried out an intramolecular Pauson–Khand reaction to obtain spiro[cyclopropane-1,4'-bicyclo[3.3.0]oct-1-en-3-ones] in high diastereoselectivity.<sup>3</sup> Stürmer described a novel kinetic resolution procedure for the preparation of enantiomerically enriched (*Z*)-(1-methyl-2-butenyl)boronic esters with the aid of this chiral auxiliary.<sup>4</sup>

Hoffmann and coworkers synthesized **1** via the hydrogenation (over rhodium on alumina at  $60^{\circ}\text{C}$  and 7 atm) of enantiomerically pure hydrobenzoin.<sup>1,5</sup> Matteson and coworkers extensively studied the hydrogenation procedure and made several modifications.<sup>2a,d,e</sup> The most recent of these reported that better results can be achieved by the hydrogenation of hydrobenzoin borate, instead of hydrobenzoin itself, at 10–11 atm and  $50^{\circ}\text{C}$ , within several days. The diol was then obtained by the hydrolysis of the hydrogenation product (Scheme 1).<sup>6</sup>

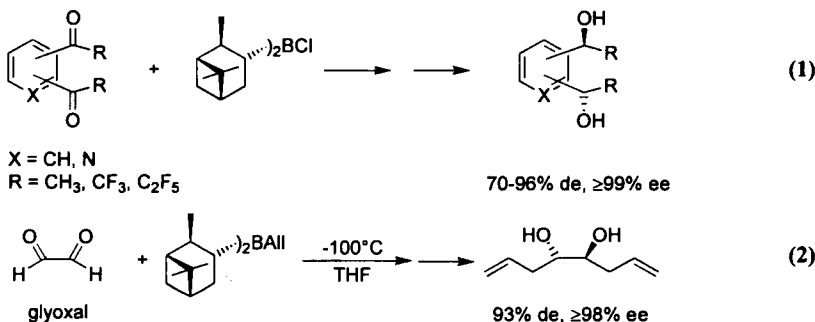
Recently, we reported the syntheses of a series of aromatic and aliphatic  $C_2$ -symmetric diols in very high de and ee via asymmetric reduction of appropriate diketones with *B*-chlorodiisopinocampheylborane (eqn 1)<sup>7</sup> and via allylboration of appropriate dialdehydes with *B*-allyldiisopinocampheylborane (eqn 2).<sup>8</sup> The success achieved using these procedures encouraged us to extend the asymmetric methodologies based on  $\alpha$ -pinene as chiral auxiliary for the synthesis of several other  $C_2$ -symmetric diols and diamines.

<sup>†</sup> Dedicated to Professor Herbert C. Brown on the occasion of his 85<sup>th</sup> birthday.

\* Corresponding author.



Scheme 1.



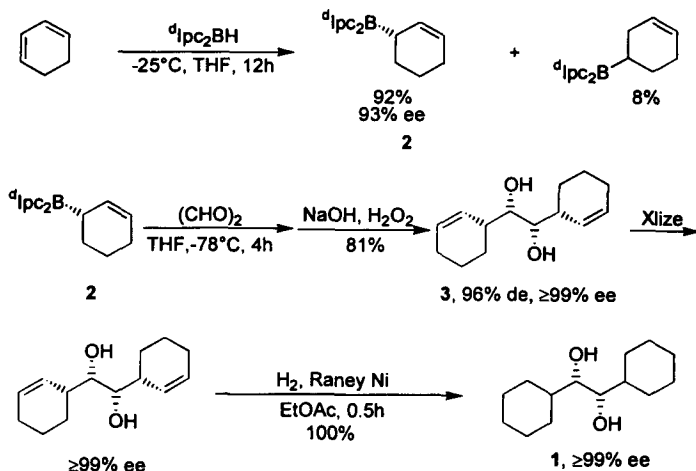
It was reported by Brown and coworkers that the hydroboration of 1,3-cyclohexadiene with (+)-diisopinocampheylborane provides predominantly (*S*)-*B*-2-cyclohexen-1-yl diisopinocampheylborane (**2**) (93% ee and 92% regioselectivity), which upon treatment with acetaldehyde at  $-78^\circ\text{C}$ , followed by oxidative work-up, yields the corresponding (1*R*,1'*R*)-(+)-1-(2-cyclohexenyl)-1-ethanol in  $\geq 99\%$  de and 94% ee.<sup>9</sup> We envisaged the synthesis of (1*S*,2*S*,1'*R*,1''*R*)-(+)-1,2-bis(2-cyclohexenyl)-1,2-ethanediol (**3**) by the treatment of **2** with glyoxal. Indeed, such a reaction in THF at  $-78^\circ\text{C}$  was complete within 4 h and the usual work-up provided **3** in 81% yield. Gas chromatographic (GC) analysis of the bis-trifluoroacetate of **3** on a  $\beta$ -DEX 120 capillary column (Supelco) revealed a 98:2 mixture of **3** and an unassigned stereoisomer. A simple crystallization from hexane provided enantiomerically pure **3**.

The hydrogenation of **3** over Raney Ni at 1 atm and rt proceeded to completion within 30 min yielding enantiomerically pure (*S,S*)-**1** quantitatively (Scheme 2).

Thus, we have achieved a simple synthesis of enantiomerically pure 1,2-dicyclohexenyl-1,2-ethanediol in high yield. The precursor to this diol, (1*S*,2*S*,1'*R*,1''*R*)-1,2-bis(2-cyclohexenyl)-1,2-ethanediol, may also possess chiral-directing properties. We are currently investigating this possibility. The ready availability of both enantiomers of the inexpensive chiral auxiliary,  $\alpha$ -pinene, makes this synthesis especially attractive.

### Experimental

All operations were carried out under an inert atmosphere.<sup>10</sup> Glyoxal monomer was freshly generated from glyoxal trimer dihydrate following the literature procedure.<sup>11</sup> While stirring, a solution of glyoxal (0.74 g, 12.8 mmol) in THF (8.0 mL) was added dropwise to a cooled ( $-78^\circ\text{C}$ ) solution of **2**, prepared from *d*-diisopinocampheylborane (9.10 g, 32 mmol) and 1,3-cyclohexadiene (2.56 g, 32 mmol) in THF (30 mL). The mixture was stirred at this temperature for 4 h when the reaction was complete (<sup>11</sup>B NMR shift from  $\delta$  80 to 52 ppm). Addition of methanol (1 mL) to the solution, followed by alkaline



Scheme 2.

$\text{H}_2\text{O}_2$  oxidation at room temperature, yielded a crude product which was chromatographed (ethyl acetate:hexane; 3:7 as eluent) to provide 2.30 g (81%) of **3**. GC analysis of the bis-trifluoroacetate on a  $\beta$ -DEX 120 capillary column revealed the diol to be 98% stereoisomerically pure. Crystallization from hexane provided enantiomerically pure **3**: mp 113–4°C;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  (ppm): 5.80–5.90 (m, 2H); 5.55–5.63 (m, 2H); 3.55–3.64 (m, 2H); 2.30–2.45 (m, 4H); 1.45–2.10 (m, 12H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  (ppm): 130.11; 128.20; 74.06; 38.37; 25.28; 23.47; 21.11.  $[\alpha]_{\text{D}}^{24} = +83.67$  ( $c$  4.3,  $\text{CHCl}_3$ ).

The commercial (Aldrich) Raney Ni (0.5 g, 50% in water) was washed with ethanol (2×10 mL), ethyl acetate (2×10 mL), and suspended in ethyl acetate (30 mL). Following the addition of **3** (0.14 g), the system was charged with hydrogen and stirred vigorously. The hydrogen uptake ceased within 0.5 h. Filtration and evaporation of the solvent provided an essentially quantitative yield of chemically and enantiomerically pure (*S,S*)-**1** (0.14 g):  $[\alpha]_{\text{D}}^{24} = +2.61$  ( $c$  0.71,  $\text{CHCl}_3$ ) [lit.<sup>1</sup>  $[\alpha]_{\text{D}}^{20} = +2.6$ , ( $c$  0.78,  $\text{CHCl}_3$ )].

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