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Synthesis of Optically Active Dendritic Binaphthols and Their Metal Complexes for Asymmetric Catalysis

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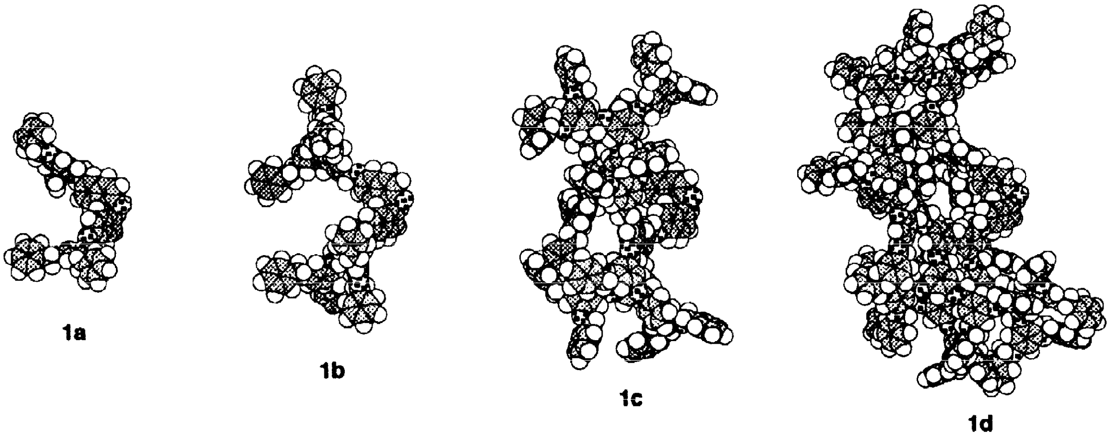
Abstract: Optically active binaphthols bearing dendritic substituents at the 6,6-positions were synthesized by the base promoted reaction of 6,6'-dihydroxyl-2,2'-binaphthol and the dendritic benzyl bromides. Despite the bulky dendritic substituents, the dendritic binaphthols were found to form metal complexes and catalyze asymmetric C-C bond forming reactions.

The synthesis of dendritic polymers are of considerable interest due to their unique physical and chemical properties.[1] The use of dendrimer-based catalysts have been an interesting topic[2, 3, 4] because these structurally well-defined macromolecules serve as a homogeneous catalyst in solution, but are also readily recoverable after the reaction mixture using physical methods, e.g., ultrafiltration.[5] We have been interested in metal-centered dendrimers[4, 6] because of their potential application to the selective reaction, which would mimic the high selectivity like enzymatic reactions. Recent examples of the shape selective encapsulation of guests into the cavity of dendrimers[7] as well as induced circular dichroism (CD) from achiral molecules encapsulated into a chiral dendritic box[8] would suggest that the interior of the dendrimers would be suitable for the selective reactions. It is also interesting to see that the bulky dendritic substituents near the metal center would alter the structure of the metal complexes, such as aggregation, and, thus, would influence the reactivities. Until now, several periphery modified[2] and core modified dendritic catalyses[3] have been reported, but only a few examples have been used as an asymmetric catalyst.[4] We now report the synthesis of a new class of optically active dendritic binaphthols **1** (n = 1 - 4), which would serve as potential candidates for the new design of metal ligands for asymmetric synthesis.



1a **1b** **1c** **1d**

[**Figure 1.** Computer generated structures of **1** (MacroModel Ver. 6).]

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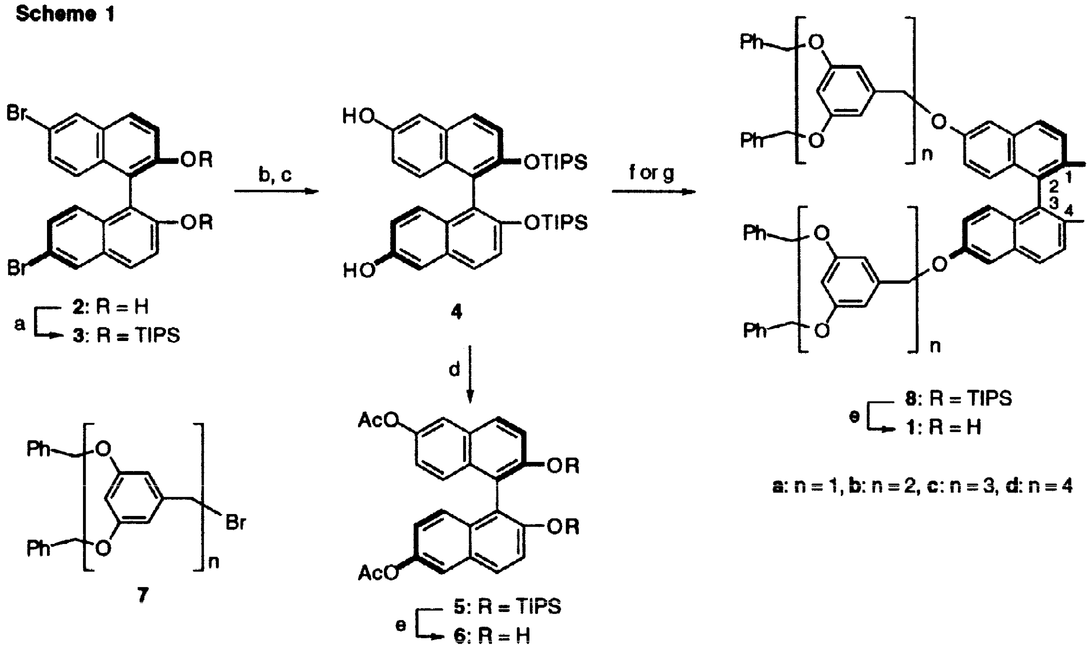
The synthesis of dendritic binaphthols was achieved in a straightforward manner from commercially available (*R*)-6,6'-dibromo-1,1'-binaphthol **2** (>99.7 %ee)[9] (Scheme I). The hydroxyl group of **2** was protected with the triisopropylsilyl (TIPS) group, and the resulting protected dibromide **3** was lithiated by *t*-BuLi. Transmetallation from lithium to boron by the addition of $B(OMe)_3$, hydrolysis of the boric ester to the boric acid by aqueous HCl, followed by oxidation of the C-B bonds by 30% H_2O_2 produced (*R*)-6,6'-dihydroxy-1,1'-binaphthol **4** in excellent yield.[10] The optical purity of **4** was determined by chiral HPLC analysis of the (*R*)-6,6'-diacetoxy-1,1'-binaphthol **6**, which was prepared by acetylation of the 6,6'-hydroxyl groups of **4** followed by deprotection of the TIPS group by TBAF, was >99.7% ee (SUMICHIRAL OA-4700, elution with hexane/1,2-dichloroethane/EtOH = 30/3/1), indicating that there was no racemization during these manipulations.

The coupling of dendritic benzyl bromide **7b** (n = 2) and **7c** (n = 3) with **4** was successfully carried out using Frechét's conditions (K_2CO_3/18–C–6, acetone, reflux)[11] to give **8b** (n = 2) and **8c** (n = 3) in 57% and 75% yields, respectively. However, the syntheses of **8a** (n = 1) and **8d** (n = 4) failed under the same conditions due to the competitive desilylation and/or migration of the silyl group from the 2,2'- to the 6,6'-hydroxyl group. Finally, the synthesis of **8a** and **8d** were achieved by NaH deprotonation of **4** in DMF followed by coupling with **7a** and **7d** to give 80% and 33% yields, respectively. Deprotection of the TIPS group by TBAF afforded **1** in quantitative yield. The products were purified by both silica gel and gel permeation chromatography.

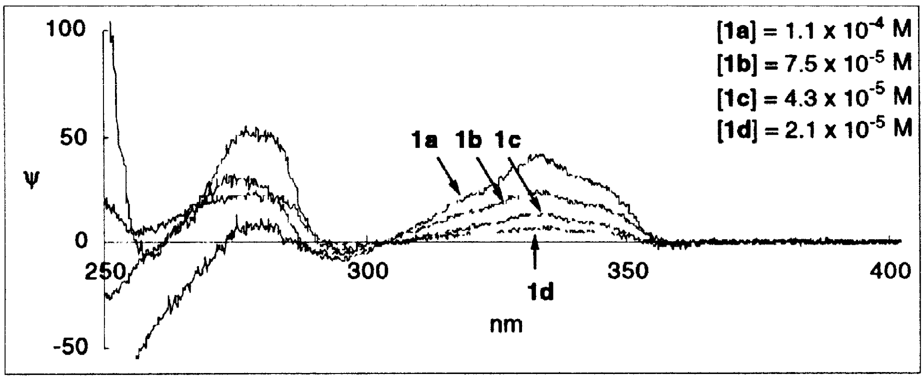
Scheme 1



(a) TBDMSCl (2.2 eq), Imidazole (2.2 eq), DMF, r.t., 149 h, quant.; (b) *t*-BuLi (4.0 eq), THF, -78 °C, 0.5 h; $B(OMe)_3$ (5.0 eq), -78 °C – r.t. (c) 10% HCl/THF, r.t., 0.5 h; 30% H_2O_2 (2.2 eq), 87%. (d) Ac_2O, pyridine, r.t. (e) TBAF, THF. (f) **7** (2.0 eq), K_2CO_3 (2.5 eq), 18-C-6 (0.2 eq), acetone, reflux. (g) NaH (2.5 eq), **7** (2.0 eq), DMF, 0 °C - r.t.

The structure of **1** was confirmed by ^1H and ^{13}C NMR as well as MS analyses. In the ^1H NMR spectra, peak intensities of the dendritic moiety increased twice as much as those of the binaphthol moiety as the generation of the dendrimers grew from n = 1 to 2, 3, and 4. The same tendency was also observed in the ^{13}C NMR spectra. The structure of **1** was further confirmed by MS analyses. The FAB MS spectra of **1a** showed the M^+ ion as 922. The MALDI TOF MS spectra of **1b**, **1c**, and **1d** showed the $(M + Na)^+$ ions as 1772, 3470, and 6866, respectively. These results clearly demonstrated the formation of monodispersed dendritic binaphthols.

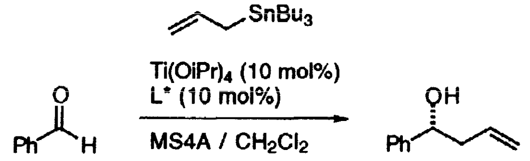
The chiroptical properties of **1** showed very unique features.[12] The sign of the specific rotation of **1** reverted from (+)-(*R*)-2,2'-binaphthol, and the $[\alpha]_D$ value in THF (c 1.0) decreased with the increase in the dendritic generation from n = 1 to 4 (**1a**: $[\alpha]_D^{20} = -30.1$; **1b**: $[\alpha]_D^{20} = -23.3$; **1c**: $[\alpha]_D^{20} = -9.7$; **1d**: $[\alpha]_D^{20} = -3.0$). However, the molecular optical rotation was almost identical regardless of the generation (**1a**: $[\phi]_D = -2.8 \times 10^2$; **1b**: $[\phi]_D = -4.1 \times 10^2$; **1c**: $[\phi]_D = -3.4 \times 10^2$; **1d**: $[\phi]_D = -2.1 \times 10^2$), which is in good agreement with the existence of a single chiral group. The CD spectra also showed that the decrease in the ellipticity (ψ) in the range of 300 - 360 nm in CH_2Cl_2 was in the proper proportion with the growth of the dendritic generation (Figure 2). These results are consistent with the fact that **1** exists as the same chiral environment regardless of the bulkiness of the dendritic substituents.



[**Figure 2.** CD spectra of **1** in THF at 20 °C.]

Figure 1 shows the computer generated folded structure of **1**,[13] which would mimic the structure of the metal complexes. While the dendritic substituents create considerable steric bulkiness, direct interaction of the substituents with the metal center seemed to be rather difficult in the monomeric species. However, the dihedral angle C^1-C^2-C^3-C^4 of **1** is slightly different for each of the others (**1a**: -88.5 °; **1b**: -84.1 °; **1c**: -85.6 °; **1d**: -81.8 °). This result suggests that the dendritic substituents would affect the bite angle of the corresponding metal complexes and, thus, the reactivities and selectivities.

Despite the bulky substituents, the dendritic binaphthols were found to form metal complexes and catalyzed C-C bond forming reactions. We selected the Ti-binaphthol catalyzed allylation reaction of the aldehyde and allyl stanane as the model reaction. [14] In this and analogous reactions, oligometallic Ti catalyst has been proposed,[15] and, therefore, it is interesting whether the bulky dendritic moiety would alter the reactivity as well as the selectivity. The reaction was carried out according to Keck's procedure with 10 mol% of $Ti(OiPr)_4$ and **1** (eq 1). The enantiomeric purity of the product was determined by chiral HPLC analysis (SUMICHIRAL OA-4700) of the corresponding 3,5-dinitorophenyl carbamate, which was prepared by the homoallyl alcohol and 3,5- dinitorophenylisocyanate. As shown in Table I, the selectivity using **1** was almost identical with that of the binaphthol.[16] The observed selectivity clearly demonstrated the formation of the metal complexes, regardless of the bulkiness of dentritic substituents. Further synthetic utilities of **1** are now under investigation.



(1)

Table I. Asymmetric Allylation Catalyzed by Ti–1 complex

L*	%yield	%ee
1a	18	92
1b	36	89
1c	36	88
(*R*)-binaphthol	31	87

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16. We could not reproduce the results described by Keck even after several attempts. We did not examine **1d** due to the insufficient supply of **1d** to carry out an accurate experiment.