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THE FIRST SYNTHESIS OF AN OPTICALLY ACTIVE MOLECULAR BEVEL GEAR WITH ONLY TWO COGS ON EACH WHEEL

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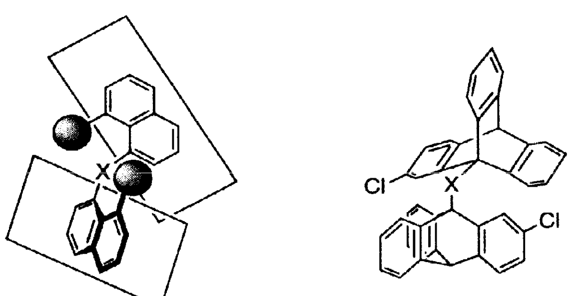
Abstract: Both enantiomers of the molecular bevel gear **1** having only two cogs on each wheel consisting of 8,8'-disubstituted 1,1'-binaphthyl ether were synthesized for the first time.

Bis(9-triptycyl) derivatives, including bis(9-triptycyl)methane and bis(9-triptycyl) ether, have been studied extensively from the viewpoint of physical chemistry.[1,2] These derivatives are molecular gears possessing three cogs on each wheel. Introduction of a substituent to one of the three benzene rings in each triptycyl unit affords three isomers including *d*-, *l*- and a *meso*-form. Interconversion of one isomer to another occurs through gear slippage. This type of isomerization is known as residual stereoisomerism[3] or phase isomerism.[2] On the other hand, such a stereoisomerism gives only *d*- or *l*-isomer in the simplest molecular bevel gear possessing only two cogs on each wheel, the gear slippage of which results in racemization.[4] Here, we report the first synthesis of an optically active molecular bevel gear with only two cogs consisting of two naphthalene rings.



1 **2** : X = CH_2, NH, O

Derivatives of 1,1'-binaphthyl, especially 2,2'-dihydroxy-1,1'-binaphthyl, have been extensively studied as a basic structure for catalytic asymmetric reactions,[5] a chiral auxiliary in stoichiometric asymmetric reactions,[6] and a chiral unit in asymmetric molecular recognition.[6] Advantages of compounds with axial chirality as a chiral source include that they provide an effective chiral environment produced by two planes consisting of π-electrons, and that the chiral environment is flexible enough to relieve or adjust the steric interaction by changing the dihedral angle between two aromatic planes. Since an optically active molecular bevel gear has two covalent bonds that can be rotated, it must therefore be more flexible than the normal atropisomers in terms of accommodating the steric interactions. Therefore, in addition to its interest for investigations of physicochemical properties, the optically active molecular bevel gear with only two cogs on each wheel deserves to be studied as a chiral source for asymmetric syntheses and molecular recognition. We chose compounds of type **1** with substituents at the 8- and 8'-positions as a basic structure for the bevel gear with two cogs, because the naphthyl ring has a large

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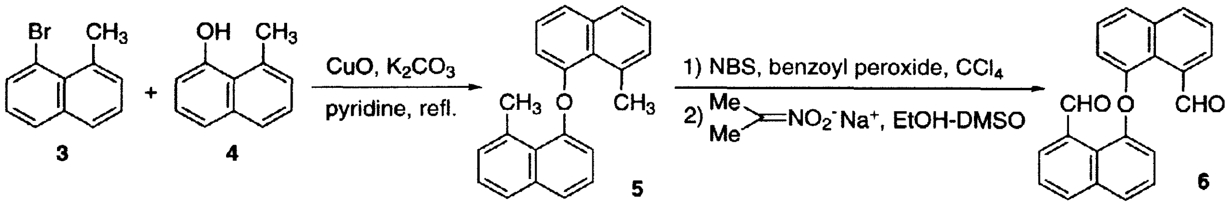
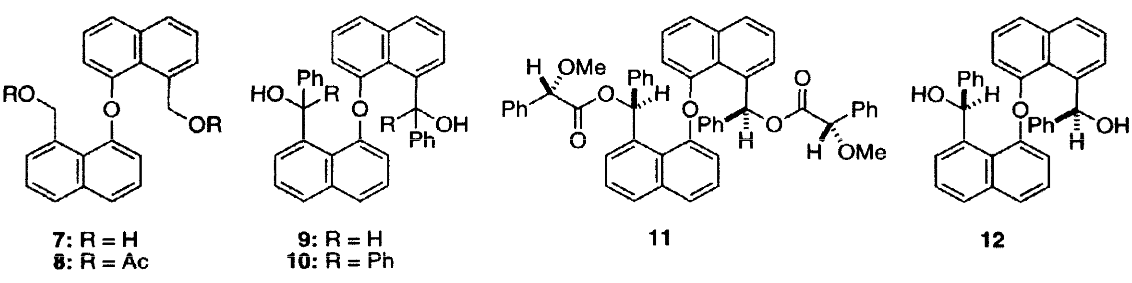
blade area and because a substituent demanding large steric interaction should be required to prevent the gear slippage. Iwamura *et al.*[8] reported that the gear slippage barrier of bis(9-triptycyl) derivative **2** was highest when two triptycyl groups were connected with the oxygen atom due to the orders of the relevant bond lengths and the stretching and bending force constants. Accordingly, we decided to connect two naphthyl rings with the oxygen atom to synthesize the compounds **1** (X=O), the enantiomers of which were expected to be isolated more easily than those of **1** ($X=CH_2$) and **1** (X=NH).

Scheme 1.



The synthesis of the 8,8'-diformyl-1,1'-binaphthyl ether **6** is shown in Scheme 1. The Ullmann ether synthesis[9] with 1-bromo-8-methylnaphthalene (**3**)[10] and 1-hydroxy-8-methylnaphthalene (**4**)[11] gave binaphthyl ether **5** in 31% yield. Bromination of **5** with NBS followed by oxidation with sodium salt of 2-nitropropane[12] afforded dialdehyde **6** in 61% yield. Reduction of **6** with lithium aluminum hydride gave the corresponding diol **7** in 98% yield, which was converted to diacetate **8** (92%). The diacetate **8** was shown to be a racemic mixture by HPLC analysis using a chiral column. The activation energy for the racemization (gear slippage) was found to be 93.3 kJ/mol at 20 °C ($t_{1/2}$ = 38 min) by measuring the time-dependent decrease in the enantiomeric excess of **8** by HPLC.[13]



Introduction of a bulky group at the 8- and 8'-positions was expected to increase the activation energy sufficiently to isolate each enantiomer of the bevel gear with two cogs. The reaction of **6** with phenyllithium gave *dl*-**9** (47%) and *meso*-**9** (12%) . The Jones oxidation of **9** followed by the reaction with phenyllithium gave diol **10** in 30% yield for two steps. Enantiomers of **10** were separated by preparative HPLC on a chiral column.[14] The diester (+)-(*S, S ,S ,S*)-**11** (mp. 200-202 °C, $[\alpha]_D^{20}$ +154 (*c*, 0.8, $CHCl_3$)) was isolated in 7% yield from a mixture obtained by the reaction of *dl*-**9** with (*S*)-(+)-α-methoxy-1-phenylacetic acid.[15] Figure 1A and B shows the crystal structure of **11** and the effective transition moment of the two naphthyl rings, suggesting their negative chirality.[16] An interesting finding of the X-ray analysis is that one of the naphthyl rings is almost planar, while another is slightly distorted (Fig. 2), though both naphthyl rings are expected to be completely identical, even with respect to the substituents at the peri-position. Hydrolysis of (*S, S, S, S*)-**11** gave (*S, S*)- **12** (mp. 130-133 °C, $[\alpha]_D^{20}$ -178 (*c*, 0.9, $CHCl_3$)). The CD spectra of **11** and **12** gave rise to exciton-split bands

Figure 1. X-ray crystal structure of **11**, (A) showing full atoms except hydrogens, (B) showing the basic skeleton of **11** to indicate the direction of the effective transition moment.

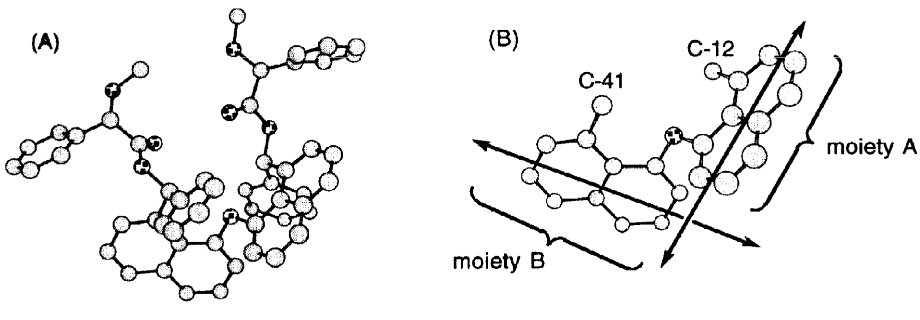


Figure 2. Two views of the X-ray structure of **11** emphasizing the difference between two naphthyl rings: (A) through the axis between C-41 and the ether oxygen; (B) through the axis between C-12 and the ether oxygen.

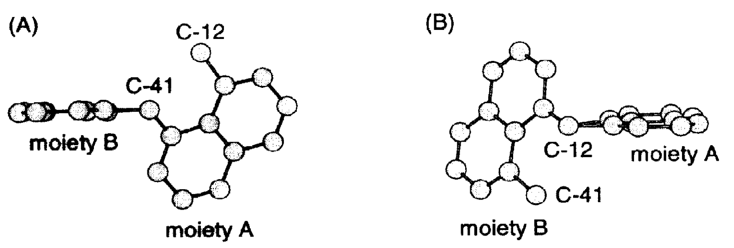
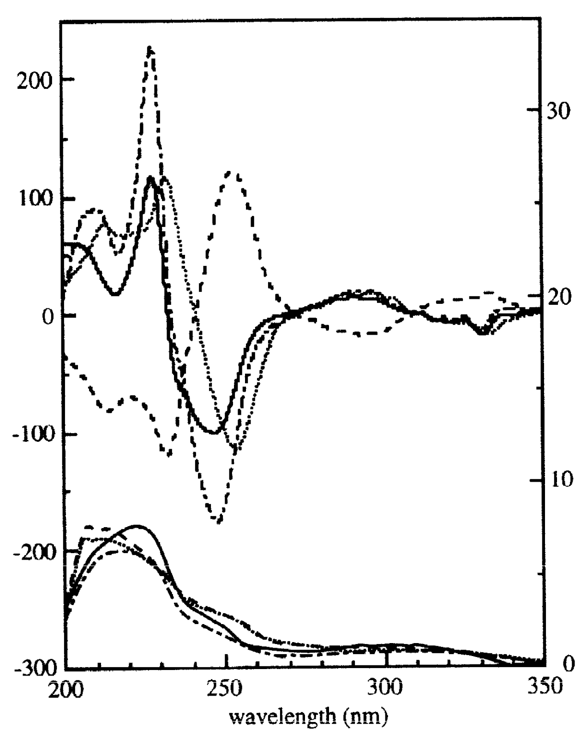


Figure 3. CD and UV data of (+)-**10** (..................), (-)-**10** (- - - - -), **11** (-.-.-.-.-), **12** (————) in methanol.



with negative Cotton effects at longer wavelength (Fig. 3).[17] Comparison of the CD spectra of (+)- and (-)-**10** with those of **11** and **12** led to the conclusion that the sense of chirality of (+)-**10** is the same as those of them, and vice versa for (-)-**10** (Fig. 3). The activation energy for gear-slippage (racemization) of optically active **10** was determined to be 126.4 kJ/mol at 111 °C in toluene ($t_{1/2}$ = 3.8 h at 111 °C, $t_{1/2}$ ~ 8 months at 20 °C).

Utilization of this novel chiral source for molecular recognition and asymmetric syntheses is currently underway in our laboratory.

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13. HPLC analysis was performed by Daicel Chiralpak AD (8% ^{i}PrOH-hexane). Isolation of enantiomerically enriched **8** (90% ee) was accomplished by preparative HPLC on the same conditions. Due to the readily-racemizing nature of **8**, enantiomerically enriched **8** was kept at -78 °C except when HPLC analysis was running.
14. Daicel Chiralpak OA, 0.5% ^{i}PrOH-hexane; t_R = 6 min for (+)-**10**, mp. 171-171.5 °C, $[\alpha]_D^{20}$ +127 (*c*, 1.0, $CHCl_3$); t_R = 11 min for (-)-**10**.
15. Condensation of *dl*-**9** with (*S*)-(+)-α-methoxy-1-phenylacetic acid gave (+)-(*S, S, S, S*)-**11** (7%), (-)-**11** (4%), and the corresponding mono esters (21%).
16. Crystal data: Orthorhombic, space group $P2_12_12_1$, a = 13.258(8), b = 32.559(9), c = 9.749(8) Å, V = 4208(4) Å^3, Z = 4, Dcalc = 1.229 g/cm^3. The structure was refined to R = 0.051, Rw = 0.041. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre.
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