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Syntheses of Chiral Solid Catalysts Using Menthol and Application to the Asymmetric Diels–Alder Reaction

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A chiral solid catalyst as a heterogeneous Lewis acid prepared from trimethylaluminum, menthol and tetrachlorobisphenol A has been found to promote the asymmetric Diels–Alder reaction of 2-methyl-2-propenal with cyclopentadiene and is a reuseable catalyst.

The development of chiral Lewis acids is one of the most important objectives in carbon-carbon bond forming reactions.[1] Since achievement of the catalytic asymmetric Diels–Alder reaction using dichloromenthoxyaluminum designed by Koga[2] in 1979, many chiral Lewis acids have been developed.[3] However, these Lewis acids have several problems, which include separation of the reagent and reaction products, and the acids can not be reused. In the carbon–carbon bond forming reaction, the use of a solid catalyst as a heterogeneous Lewis acid which would resolve such problems is also a topic of growing interest. Recently, solid catalysts as heterogeneous Lewis acids have been developed by Aoyama,[4] Yamamoto[5] and their co-workers, and was applied to the catalytic Diels–Alder reaction. However, these solid catalysts were achiral. Itsuno[6] reported the usefulness of polymer-supported chiral catalysts in promoting asymmetric Diels–Alder reactions. These results prompted us to investigate new types of chiral solid catalysts. We report the synthesis of a chiral solid type of Lewis acid catalysts which contains aluminum as building blocks of polymer chain and we explain applications to the asymmetric Diels–Alder reaction (Chart 1).

Chiral solid catalysts **4a**, **4b**, and **5** are easily prepared, as shown in Scheme 1. The reaction of (−)-menthol with trimethylaluminum gave a clear solution of (−)-menthoxydimethylaluminum **2a**. The obtained solution was added to tetrachlorobisphenol A **3a** or tetrabromobisphenol A **3b**, and this mixture was stirred for 1 h. Insoluble colorless precipitates appeared, and then the reaction mixture was stirred for 19 h. The solid was collected by filtration and **4a**, **4b**, and **5** were obtained in 95, 95, and 93% yields, respectively. The obtained solid was quenched with 1 M HCl (1 M = 1 mol dm^{-3}); the ratio of (−)-menthol and tetrachlorobisphenol A **3a** in the residue was 1 : 1 based on 1H NMR spectrometry. And the direct measurement of aluminum cation in aqueous solution by means of atomic absorption analysis showed the existence of one equivalent of aluminum in the solid catalyst **4a**. This result indicated that the ratio of (−)-menthol, tetrachlorobisphenol A, and aluminum in the solid catalyst **4a** was also 1 : 1 : 1. The solid catalysts were used for the Diels–Alder reaction of cyclopentadiene with several dienophiles as shown in Table 1.[7] The kinds of dienophiles had an influence on the yield and enantiomeric excess of the cycloadducts (entries 1–3). No solvent effect was observed (entries 3 and 5). However, the enantiomeric excess was improved by increasing the amount of the solid catalyst **4a** (entries 6–9). When a stoichiometric amount of the chiral solid catalyst **4a** was used, the cycloadduct was produced in 93% yield and in 70 %ee (entry 9). The reason why such an amount of catalyst was necessary to perform this reaction is as follows: the percentage of useful reaction sites of this polymer catalyst may be low. On the other hand, the same reaction using **4b** led to the (S)-cycloadduct with the same degree of enantioselectivity as expected (entry 11). The reaction rate of this Diels–Alder reaction by using heterogeneous catalyst **4a** was slower (entry 13) than that by using homogeneous catalyst dichloromenthoxyaluminum (entry 14).[2a] The recovered chiral solid catalyst **4a** could be reused without reducing the yield and enantioselectivity (entries 16 and 17). We also propose a model to explain our results (Fig. 1). The benzene ring of tetrachlorobisphenol A moiety existing at the rear side of transition model would shield the front face of the coordi-

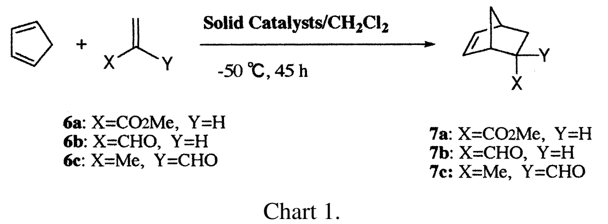
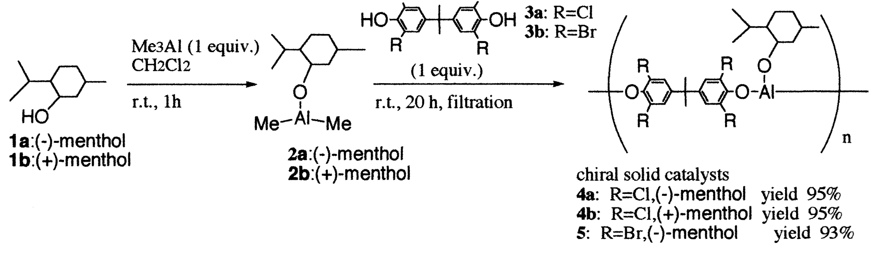


Chart 1.



Scheme 1. Synthesis of the chiral solid catalysts **4a**, **4b**, and **5**.

Table 1. Asymmetric Diels–Alder Reaction Using Chiral Solid Catalysts

Entry	Dienophile	Solid catalyst	Reaction temp/°C	Amount of solid catalyst/mol%	Product	Yield/%[a] [endo/exo][b]	ee/%[c] (cofig.)
1	**6a**	**4a**	−50	20	**7a**	18 [97/3]	3(R)
2	**6b**	**4a**	−50	20	**7b**	98 [86/14]	3(R)
3	**6c**	**4a**	−50	20	**7c**	86 [4/96]	22(R)
4[d]	**6c**	**4a**	−50	2	**7c**	78 [10/90]	6(R)
5[d]	**6c**	**4a**	−50	20	**7c**	84 [7/93]	22(R)
6	**6c**	**5**	−50	20	**7c**	83 [7/93]	5(R)
7	**6c**	**4a**	−50	40	**7c**	91 [5/95]	31(R)
8	**6c**	**4a**	−50	60	**7c**	93 [6/94]	57(R)
9	**6c**	**4a**	−50	100	**7c**	93 [6/94] (76)[f]	70(R)
10	**6c**	**4a**[g]	−20	100	**7c**	92 [6/94]	69(R)
11	**6c**	**4b**[h]	−50	100	**7c**	92 [7/93]	67(S)
12	**6c**	**4a**	−80	100	**7c**	90 [7/93]	70(R)
13[e]	**6c**	**4a**	−80	16	**7c**	7 [6/94]	19(R)
14[e]	**6c**	**X**[i]	−80	16	**7c**	100 [2/98]	72(S)
15[d]	**6c**	**4a**	−50	100	**7c**	86 [6/94]	68(R)
16[d]	**6c**	**4a**[g]	−50	100	**7c**	88 [6/94]	66(R)
17[d]	**6c**	**4a**[j]	−50	100	**7c**	86 [6/94]	67(R)

a) Isolated yield of the mixture of *endo-* and *exo-*cycloadducts. b) Determined by 1H NMR analysis. c) Absolute configuration in parentheses was determined by comparison of optical rotation to reported values (see Ref. 2a). d) Hexane was used as solvent. e) Reaction was carried out for 3 h. f) Isolated yield of *exo-*cycloadduct. g) Once used solid catalyst was used. h) (+)-Menthol was used as the chiral source. i) Dichloromethoxyaluminum (**X**) was used as catalyst. See Ref. 2a. j) Twice used catalyst was used.

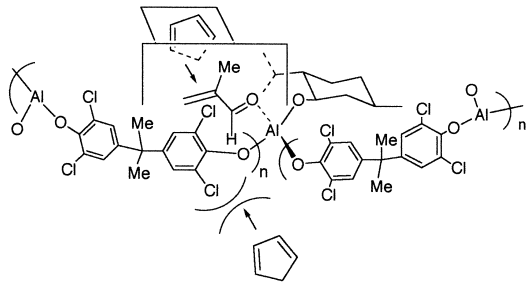


Fig. 1. A proposed transition state model.

nated 2-methyl-2-propenal; as a result, cyclopentadiene would approach from the back face to produce the (R)-cycloadduct.

In summary, we have designed and synthesized solid catalysts using menthol as the chiral source. The asymmetric Diels–Alder reaction of 2-methyl-2-propenal with cyclopentadiene in the presence of a stoichiometric amount of chiral solid catalyst **4a** gave the cycloadduct in 93% yield and in 70% ee. Although the catalytic asymmetric Diels–Alder reaction could not be achieved, the synthesis of this solid catalyst has superb simplicity and a variety of carbon–carbon bond forming reactions would be possible by selecting a suitable chiral source.

Experimental

A typical procedure (entry 9) is as follows: to a solution of (−)-menthol (468 mg, 3.0 mmol) in CH$_2$Cl$_2$ (6 mL) was added a 1 M hexane solution of Me$_3$Al (3.0 mL, 3.0 mmol) at room temperature for 1 h. The reaction solution was added to tetrachlorobisphenol A (1098 mg, 3.0 mmol) in CH$_2$Cl$_2$ (15 mL) at the same temperature, and stirred for 1 h. Insoluble colorless precipitates appeared, and then the reaction solution was stirred for 19 h. The solid catalyst **4a** was collected by filtration under argon atmosphere.[6] In a round-bottom flask was placed **4a** (1.49 g, 2.73 mmol) under an argon atmosphere. To this was added CH$_2$Cl$_2$ (10 mL) and the suspended solution was cooled to −50 °C, 2-methyl-2-propenal (191 mg, 2.73 mmol) was added, followed by cyclopentadiene (361 mg, 5.46 mmol). Stirring was continued at −50 °C for 45 h (Chart 1). The suspended solution was separated into the solid catalyst **4a** and the reaction solution by filtration under an argon atmosphere. Evaporation of the filtrate gave a 6:94 mixture of the *endo-* and *exo-*cycloadduct in 93% (352 mg) yield. Purification column chromatography (ether/pentane = 1/30) gave the (*R*)-*exo*-cycloadduct, $[\alpha]_D^{20}$ −16.3° (c = 3.0, EtOH) in 76% (294 mg) yield and in 70%ee.

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7 There was no cycloadduct when cycloaddition reaction of cyclopentadine with **6c** was tried under the presence of filtrate obtained from **4a**.