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Asymmetric Diels-Alder Reaction of Cyclopentadiene and Methyl Acrylate Catalyzed by Chiral Organoaluminum Reagents

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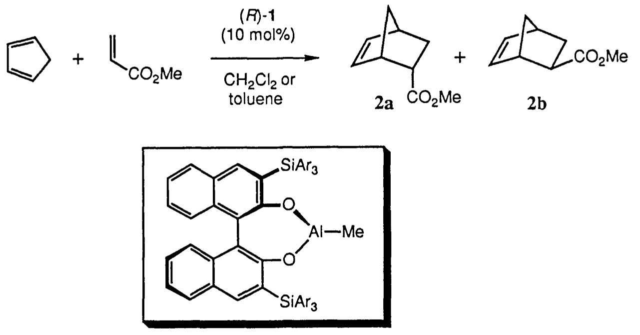
Synopsis. The asymmetric Diels-Alder reaction of cyclopentadiene and methyl acrylate has been effected with high enantioselectivity under the influence of catalytic amounts of chiral organoaluminum reagents.

The development of chiral Lewis acids in catalytic asymmetric Diels-Alder reaction is now the subject of intense research for the most effective means of creating an asymmetric carbon-carbon bond.[1] In spite of increasing efforts directed to the chiral Lewis acid-promoted Diels-Alder reaction using α,β-unsaturated aldehydes[2] and oxazolidinones[3] as reactive dienophiles, only a few examples are known for the asymmetric Diels-Alder reaction of α,β-unsaturated esters.[4] This is partly ascribable to the relatively low reactivity of α,β-unsaturated esters as dienophiles for these reactions. Here we wish to report our results on the asymmetric Diels-Alder reaction of cyclopentadiene and methyl acrylate under the influence of catalytic amounts of chiral organoaluminum reagents. (Scheme 1.)



(*R*)-**1**

Scheme 1.

The chiral organoaluminum reagent (*R*)-**1** (Ar=Ph) was prepared from trimethylaluminum and (*R*)-(+)-3,3′-bis(triphenylsilyl)-1,1′-bi-2-naphthol in CH_2Cl_2 as described previously.[5] Treatment of methyl acrylate (1 molar amount) and cyclopentadiene (2 molar amounts) with 10 mol% of chiral organoaluminium reagent (*R*)-**1** (Ar=Ph) in CH_2Cl_2 at 0 °C for 9 h produced Diels-Alder adducts **2a** and **2b** in 83% yield, and the *endo*/*exo* ratio of the cycloadducts **2a** and **2b** was 97 : 3 by GLC analysis. The optical yield was established to be 58% ee by GLC analysis using an optically active capillary column. The absolute configuration was determined to be *S* by comparison with the $[\alpha]_D$ value of an authentic sample.[2a]

The solvent, temperature, and ligand effect was examined for this asymmetric Diels-Alder reaction and selected results are given in Table 1.[6,7] The optical yield appeared to be increased by lowering the reaction

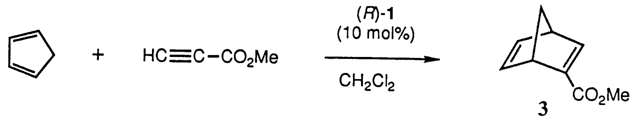
Table 1. Asymmetric Diels-Alder Reaction of Cyclopentadiene and Methyl Acrylate with Chiral Aluminum Catalysts[a]

Entry	Reagent (*R*)-**1**	Conditions solvent; °C, h	Yield[b] %	Ratio[c]	% ee[d] (confign)[e]
1	Ar=Ph	CH_2Cl_2; 0, 9	83	97 : 3	58 (*S*)
2		CH_2Cl_2; −20, 11	65	97 : 3	64 (*S*)
3		CH_2Cl_2; −78, 2; −20, 5; 0, 10	82	96 : 4	67 (*S*)
4		Toluene; 0, 9	81	95 : 5	64 (*S*)
5		Toluene; −20, 11	32	95 : 5	69 (*S*)
6		Toluene; −40, 4; −20, 4	20	97 : 3	77 (*S*)
7	Ar_3=Bu^tPh_2	CH_2Cl_2; 0, 11	68	97 : 3	64 (*S*)
8		CH_2Cl_2; −20, 11	61	97 : 3	72 (*S*)
9		Toluene; 0, 11	62	97 : 3	69 (*S*)
10		Toluene; −20, 11	34	95 : 5	73 (*S*)
11	Ar=3,5-Diethylphenyl	CH_2Cl_2; −78, 2; −20, 5; 0, 10	65	96 : 4	36 (*S*)
12	Ar=4-$Bu^tC_6H_4$	CH_2Cl_2; −78, 2; −20, 5; 0, 10	35	95 : 5	65 (*S*)

a) The asymmetric Diels-Alder reaction of cyclopentadiene and methyl acrylate was carried out under the influence of 10 mol% of chiral organoaluminum reagents (*R*)-**1** in CH_2Cl_2 or toluene solvent. b) Isolated yield. c) The *endo*/*exo* ratio was determined by GLC analysis. d) Determined by GLC analysis using an optically active capillary column. e) See Ref. 2a.

temperature, but was not as sensitive to the silyl groups of chiral ligands such as triphenylsilyl, *t*-butyldiphenylsilyl, and tris(4-*t*-butylphenyl)silyl groups. Other chiral ligands including tris(3,5-diethylphenyl)silyl group showed no good selectivity. Use of the nonpolar solvent, toluene produced higher enantiofacial selectivity than polar CH_2Cl_2. Further, the enantioselectivity gradually decreased when the methyl substituent of the acrylate was replaced by ethyl or *t*-butyl.

The present methodology is also applicable to the asymmetric Diels–Alder reaction of methyl propiolate and cyclopentadiene with catalytic (*R*)-**1**, giving the cycloadduct **3** in 55% ee.[8] It should be noted that the asymmetric Diels–Alder reaction of acetylenecarboxylate and cyclopentadiene in the presence of a chiral Lewis acid has never been documented in the literature.



Experimental

Infrared (IR) spectra were recorded on a Shimadzu FTIR-8100 spectrometer. ^1H NMR spectra were measured on Varian Gemini-200 and VXR 500 spectrometers. Analytical gas-liquid phase chromatography (GLC) was performed on Gasukuro Kogyo Model 370 and Shimadzu GC-8A instruments equipped with a frame ionization detector and a capillary column of PEG-HT (0.25×25,000 mm) and CP-CYCLODEX-B 236M (0.25×25,000 mm) using nitrogen as carrier gas. All experiments were carried out under an atmosphere of dry argon. For thin-layer chromatography (TLC) analysis throughout this work, Merck precoated TLC plates (silica gel 60 GF_{254}, 0.25 mm) were used. The products were purified by preparative column chromatography on silica gel E. Merck Art. 9385. Microanalyses were accomplished at the Faculty of Agriculture, Nagoya University.

In experiments requiring dry solvents, ether and tetrahydrofuran (THF), are freshly distilled from sodium metal using sodium diphenylketyl as indicator. Hexane and toluene are dried over sodium metal. Dichloromethane is stored over 4A molecular sieves. Cyclopentadiene is obtained by pyrolysis of dicyclopentadiene and stored over 4A molecular sieves in the freezer. Trimethylaluminum is obtained from Toso-Akzo Chem. Co., Ltd., Japan. Other chemicals are purchased and used as such.

Preparation of Optically Pure Bis(triarylsilyl)binaphthols. Optically pure (*R*)-(+)-3,3′-bis(triphenylsilyl)-1,1′-bi-2-naphthol, (*R*)-(+)-3,3′-bis[tris(3,5-diethylphenyl)silyl]-1,1′-bi-2-naphthol, and (*R*)-(+)-3,3′-bis[tris(4-*t*-butylphenyl)silyl]-1,1′-bi-2-naphthol were prepared according to the literature procedure.[6]

Preparation of Chiral Organoaluminum Reagent (*R*)-1. To a solution of optically pure (*R*)-(+)-3,3′-bis(triphenylsilyl)-1,1′-bi-2-naphthol (80 mg, 0.1 mmol) in degassed CH_2Cl_2 (5 mL) was added at room temperature a 0.5 mol cm^{-3} hexane solution of Me_3Al (0.2 mL, 0.1 mmol). The methane gas evolved immediately. The resulting pink to wine-red solution was stirred at room temperature for 100 min and used as a solution of the chiral organoaluminum reagent (*R*)-**1** (Ar=Ph) in CH_2Cl_2 or toluene without any purification.

Other chiral organoaluminum reagents (*R*)-**1** (Ar_3=Bu^tPh_2; Ar=3,5-diethylphenyl or 4-*t*-butylphenyl) were prepared in a similar manner as described above.

General Method for the Asymmetric Diels–Alder Reaction of Cyclopentadiene and Methyl Acrylate. To a solution of the chiral organoaluminum reagent (*R*)-**1** (Ar=Ph) (0.1 mmol) in CH_2Cl_2 (5 mL) was added a mixture of cyclopentadiene (165 μL, 2 mmol) and methyl acrylate (90 μL, 1 mmol) at −78 °C. The solution was stirred under the condition indicated in Table 1. The reaction mixture was then poured into 10% HCl and extracted with CH_2Cl_2. Evaporation of solvent and purification of the residue by column chromatography (ether/hexane=1 : 30 as eluant) gave the Diels–Alder adducts **2a** and **2b** in the yields as shown in Table 1. The *endo*/*exo* ratio of the cycloadducts **2a** and **2b** was determined by a capillary GLC analysis: t_R (*endo*-adduct **2a**)=24.2 min, t_R (*exo*-adduct **2b**)=19.9 min at the column temperature of 100 °C. The optical yield was established by GLC analysis using an optically active capillary column: t_R (*endo*-adduct **2a**)=24.3 min, t_R (enantiomer of **2a**)=24.8 min at the column temperature of 100 °C. The absolute configuration was determined to be *S* by comparison with the $[\alpha]_D$ value of an authentic sample.[2a] These results are indicated in Table 1.

The major *endo*-adduct **2a** (Entry 9): $[\alpha]^{26}_{D}$=−85.9° (*c* 1.0, EtOH); IR (neat) 2976, 2951, 2870, 1742, 1435, 1337, 1200, 1177, 1032, 901, 712 cm^{-1}; 200 MHz ^1H NMR ($CDCl_3$) δ=6.21 (1H, dd, *J*=3, 5.8 Hz, CH=), 5.94 (1H, dd, *J*=3, 5.8 Hz, CH=), 3.64 (3H, s, CH_3), 3.21 (1H, br s, CH–C=C), 2.98 (1H, dt, *J*=1.6, 4 Hz, CH–C=O), 2.93 (1H, br d, *J*=4 Hz, C=C–CH–C–C=O), 1.98 (1H, ddd, *J*=3.6, 9.4, and 12 Hz, CH), 1.25—1.49 (3H, m, CH and CH_2).

Since the optical rotation value of the authentic, optically pure **2a** is reported to be $[\alpha]_D$ −141° (95% EtOH),[2a] this Diels–Alder adduct possesses the *S* configuration.

Asymmetric Diels–Alder Reaction of Cyclopentadiene and Other Acrylates. The asymmetric Diels–Alder reaction of cyclopentadiene with ethyl and *t*-butyl acrylates (2 molar amounts) was carried out in the presence of 10 mol% (*R*)-**1** (Ar=Ph) under the conditions as described in Entry 3 (Table 1). The results are as follows: with ethyl acrylate, 56% yield, *endo*/*exo*=95 : 5, 55% ee; with *t*-butyl acrylate, 42% yield, *endo*/*exo*=99 : 1, 30% ee.

Asymmetric Diels–Alder Reaction of Cyclopentadiene and Methyl Propiolate. To a solution of the chiral organoaluminum reagent (*R*)-**1** (Ar=Ph) (0.1 mmol) in CH_2Cl_2 (5 mL) was added a mixture of cyclopentadiene (413 μL, 5 mmol) and methyl propiolate (89 μL, 1 mmol) at −78 °C. The solution was stirred at −40 °C for 3 h and at 0 °C for 11 h. The reaction mixture was then poured into 10% HCl and extracted with CH_2Cl_2. Evaporation of solvent and purification of the residue by column chromatography (ether/hexane=1 : 30 as eluant) gave the Diels–Alder adduct **3** in 22% yield: $[\alpha]^{25}_{D}$=+27.7° (*c* 0.99, $CHCl_3$); IR (neat) 2942, 2872, 1717, 1435, 1325, 1293, 1240, 1152, 1098, 1065, 760, 696 cm^{-1}; 200 MHz ^1H NMR ($CDCl_3$) δ=7.66 (1H, d, *J*=3.1 Hz, CH=C–C=O), 6.92 (1H, dd, *J*=3.1, 5.2 Hz, CH=), 6.74 (1H, dd, *J*=3.1, 5.2 Hz, CH=), 3.91 (1H, br s, CH–C=C), 3.72 (1H, br s, CH–C=C), 3.74 (3H, s, CH_3), 2.13 (2H, m, CH_2).

The optical yield was established to be 55% ee by GLC analysis using an optically active capillary column: t_R (*endo*-adduct **2a**)=26.5 min, t_R (enantiomer of **2a**)=27.4 min at the column temperature of 100 °C. Since the optical rotation value of the authentic, enantiomeric **3** is reported to be $[\alpha]_D$ −39.2° (*c* 0.2, $CHCl_3$),[8] this Diels–Alder adduct possesses the absolute configuration as indicated in the text.

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