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Asymmetric Hetero Diels-Alder Reaction Catalyzed by Stable and Easily Prepared CAB Catalysts†

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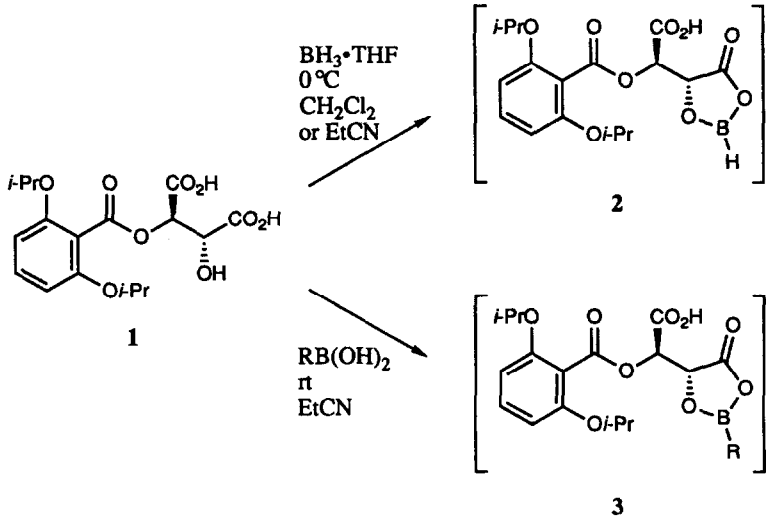
Abstract: A stable chiral (acyloxy)borane (CAB) complex is prepared *in situ* by mixing a tartaric acid derivative and arylboronic acids at room temperature. A solution of the catalyst is effective in catalyzing hetero Diels-Alder reactions to produce dihydropyrone derivatives of high optical purities.

We recently described a new method for catalytic enantioselective Diels-Alder reactions based on a chiral (acyloxy)borane (CAB) catalyst using tartaric acid[1] or an amino acid as a chiral controller unit.[2] Recent applications from this laboratory, which include aldol synthesis[3] and Sakurai-Hosomi reaction,[4] broaden the versatility of this catalyst. Excellent enantioselectivities and the wide applicability thus contribute to the outstanding utility of the CAB system. This paper reports several new developments in this area and further uses.[5]



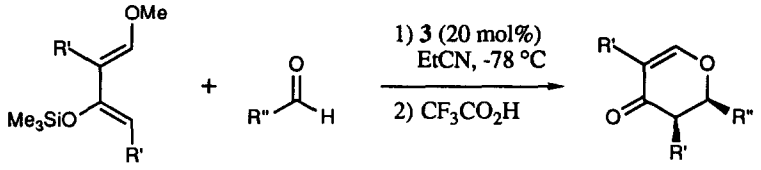
Scheme 1. Preparation of CAB Catalyst

†Dedicated with respect to Professors Ryoji Noyori and K. Barry Sharpless on the occasion of the Tetrahedron Prize for 1993.

In contrast to **2** which is both air and moisture sensitive, the B-alkylated catalyst **3**, R = Ph or alkyl, is stable and can be stored in closed containers at room temperature. This catalyst is easily prepared from phenyl- or alkylboronic acid and **1** in propionitrile at room temperature. Its molecular weight, found cryoscopically in benzene, corresponds closely with the value calculated for a monomeric species **3**, R = Ph. The product showed a new carbonyl absorption at 1821 cm^{-1}, characteristic of the five-membered ring carbonyl compound and different from that of the six-membered ring structure.[6]

A solution of the catalyst **3**, R = Ph, is sufficiently reactive to catalyze the Diels-Alder, Aldol, and Sakurai-Hosomi reactions. Although the asymmetric inductions achieved by this and related complexes are slightly less efficient than that of the corresponding hydride type catalyst,[7] the complexes were shown to be excellent catalysts for hetero Diels-Alder reactions[8,9] which is the subject of the present paper.

The new chiral (acyloxy)borane complexes **3** were easily prepared *in situ* by mixing a 1:1 molar ratio of tartaric acid derivative **1** and a phenylboronic acid in dry propionitrile at room temperature for 0.5 h. The hetero Diels-Alder reaction of aldehydes with Danishefsky diene **4** was promoted by 20 mol % of this catalyst solution at -78 °C for several hours. After usual workup, the crude adduct was treated with trifluoroacetic acid in CH_2Cl_2 to afford dihydropyrone **5**. Product diastereomer and enantiomer ratios were determined by analytical HPLC and absolute configurations were determined by comparison of the specific rotation values with those of the literature.[8] Some of the results are summarized in Table 1.

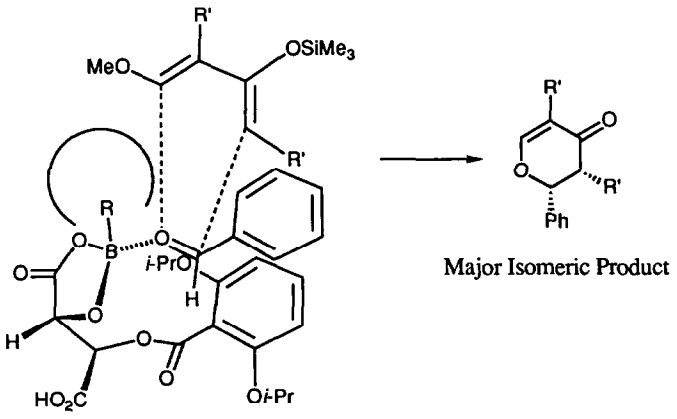


4a: R'=H
4b: R'=Me

5

The new CAB catalyst disclosed herein exhibited the following characteristic features: (1) An extent of asymmetric induction largely dependent on the structure of boronic acid. In general, bulky phenylboronic acid resulted in excellent asymmetric induction although bulky substituents exceptionally led to the eminent loss of reactivity (entry 11), while the alkoxy substituents increased the reactivity of the catalyst without significant loss of selectivity. The catalyst derived from 2,4,6-trialkylphenylboronic acid or *ortho*-alkoxyphenylboronic acid thus revealed high reactivity and asymmetric induction with diene **4a** (entries 4 and 5) and **4b** (entries 12,13, and 16), respectively. (2) Choice of alkoxyphenylboronic acid is crucial for obtaining the high *diastereoselectivities* with diene **4b** (entries 12,16,17) which is in accord with our previous observation.[8] (3) Judging from the product configuration, CAB catalyst (from natural tartaric acid) should effectively cover the *si* face of carbonyl when coordinated, and the selective approach of nucleophiles from the *re* face should agree well with the results of previously reported CAB catalyzed Diels-Alder,[1] aldol,[3] and Sakurai-Hosomi reactions.[4] In a separate study, difference NOE measurements establish that the effective shielding of *si*-face of the CAB-coordinated α,β-enal arises from π-stacking of 2,6-diisopropoxybenzene ring and the coordinated aldehyde.[1e] Also, X-ray diffraction analysis of 2-*O*-(2,6-dimethoxybenzoyl)tartaric acid revealed the folded structure rather than the extended structure, and this conformer is similar to the expected transition state assembly **A**.[1e] (4) Since unnatural tartaric

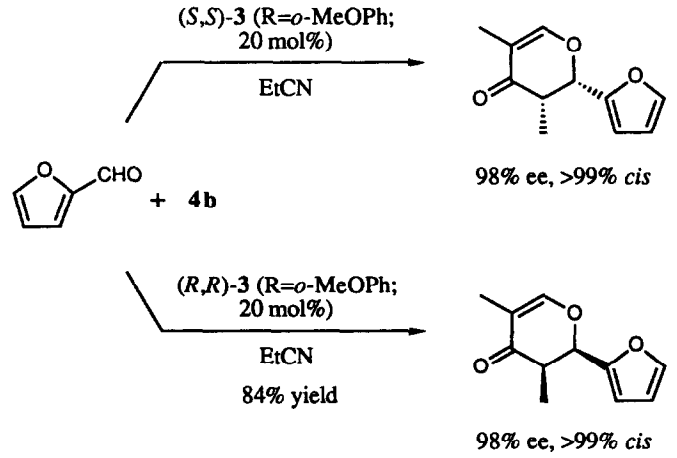
acid derivatives are equally accessible in optically pure form, the present method allows the synthesis of *both antipodal* products by choosing the handedness of the chiral auxiliary **1**.



Transition State Assembly (**A**)

Figure 1. Mechanism of Asymmetric Hetero Diels-Alder Reaction

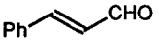
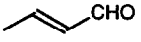
The power of the CAB catalytic reaction for the enantioselective route to carbon-branched pyranose derivatives is seen from the following example:[10]



Scheme 2. Enantioselective Hetero Diels-Alder Reaction

We believe that the experimental results outlined above will stimulate further exciting advances for designer Lewis acids and offer essential information on the direction of future design of CAB catalysts.

Table 1. CAB-Mediated Asymmetric Hetero Diels-Alder Reaction[a]

				product	
entry	aldehyde	diene	R of **3**	yield,[b] %	% ee (confign)[c]
1	PhCHO	**4a**	H[d]	11	52 (*R*)
2			Bu	67	73 (*R*)
3			Ph	63	75 (*R*)
4			2,4,6-$Me_3C_6H_2$	47	95 (*R*)
5			2,4,6-*i*-$Pr_3C_6H_2$	55	95 (*R*)
6			*o*-$MeOC_6H_4$	80	79 (*R*)
7			*o*-*i*-$PrOC_6H_4$	63[e]	84 (*R*)
8			*o*-$PhOC_6H_4$	58	81 (*R*)
9		**4b**	Bu	56 (12)	93 (2*R*,3*R*)
10			Ph	65 (29)	87 (2*R*,3*R*)
11			2,4,6-$Me_3C_6H_2$	<5	
12			*o*-$MeOC_6H_4$	95 (5)	97 (2*R*,3*R*)
13	4-MeC_6H_4CHO	**4b**	*o*-$MeOC_6H_4$	>99	97
14		**4a**	*o*-$MeOC_6H_4$	40	79 (*R*)
15			*o*-*i*-$PrOC_6H_4$	63[e]	86 (*R*)
16		**4b**	*o*-$MeOC_6H_4$	86 (6)	97 (2*S*,3*R*)
17		**4b**	*o*-$MeOC_6H_4$	79 (<1)[e]	92

[a] Unless otherwise noted, the reaction was carried out in freshly distilled propionitrile using 20 mol% of catalyst **3** and 1.2 equiv of the diene per aldehyde at -78 °C for 4-9 h. [b] Isolated yield by column chromatography; for the cis/trans mixture, the yield of the major cis isomer is designated; parentheses indicate yield of the trans isomer. [c] The ee values were determined by HPLC using a chiral column (Chiralcel OD or AD). The absolute configuration was determined by comparison of the sign of optical rotation; see reference 8. [d] In this case a solution of BH_3 in tetrahydrofuran (1.05 *M*) was used and the catalyst complex was prepared at 0 °C for 15 min. [e] The reaction was caried out at -78 °C for 20 h.

EXPERIMENTAL SECTION

General

Infrared (IR) spectra were recorded on a Shimadzu FTIR-8100 spectrometer. ^{1}H NMR spectra were measured on a Varian Gemini-200 spectrometer. High performance liquid chromatography (HPLC) was done with Shimadzu 6A, 10A and JASCO UVIDEC-100-II instruments using 4.6 mm x 25 cm Daicel chiralcel OD or AD. Optical rotations were measured on a JASCO DIP-140 digital polarimeter. 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 School of Agriculture, Nagoya University.

In experiments requiring dry solvents, propionitrile was freshly distilled from calcium hydride. Ether and tetrahydrofuran (THF) were purchased from Aldrich Chemical Company, Inc. and used as such. Benzene and toluene were dried over sodium metal. Dichrolomethane and dimethylformamide (DMF) were stored over 4A molecular sieves. BH_3•THF was obtained from Toso-Akzo Chem. Co. Ltd., Japan. Other simple chemicals were purchased and used as such.

Preparation of (2R,3R)-2-O-(2,6-diisopropoxybenzoyl)tartaric Acid (1)

Methyl 2,6-Dihydroxybenzoate. The reaction mixture of 2,6-dihydroxybenzoic acid (9.9 g, 64 mmol) and potassium carbonate (9.8 g, 71 mmol), iodomethane (8.8 mL, 142 mmol) and DMF (150 mL) was stirred at room temperature for 1 day. The solution was poured into 1 *N* aqueous HCl and extracted with ether twice. The combined organic layers were washed with a saturated brine solution and dried over Na_2SO_4, and concentrated *in vacuo*. The crude oil was used for the next step without further purification. IR (film) 3420, 1672, 1634, 1576, 1475, 1325, 1199, 1109, 812, 700, 594 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.09 (s, 3H, CH_3), 6.49 (d, *J*=8.2 Hz, 2H, *m*-ArH), 7.31 (t, *J*=8.2 Hz, 1H, *p*-ArH), 9.55-9.75 (br, 2H, 2OH); Anal. Calcd for $C_8H_8O_4$: C, 57.14, H, 4.80. Found: C, 56.87; H, 4.99.

Methyl 2,6-Diisopropoxybenzoate. The reaction mixture of methyl 2,6-dihydroxybenzoate (10 g of crude oil, <64 mmol), potassium carbonate (22.3 g, 160 mmol), 2-iodopropane (15.7 mL, 180 mmol), and DMF (150 mL) was stirred at room temperature for 2 days. The solution was poured into 1 *N* aqueous HCl and extracted with ether twice. The combined organic layers were washed with a saturated brine solution and dried over Na_2SO_4, and concentrated *in vacuo*. The crude residue was purified by column chromatography on silica gel eluant with 4 : 1 hexane/ethyl acetate to give methyl 2,6-diisopropoxybenzoate (8.3 g) as a white solid in 51% yield from 2,6-dihydroxybenzoic acid. mp 63.5~64.0 °C; IR (film) 2982, 1730, 1593, 1468, 1259, 1113, 1071, 783, 740, 665 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.30 (d, *J*=6.2 Hz, 12H, $2CH(CH_3)_2$), 3.87 (s, 3H, CO_2CH_3), 4.51 (septet, *J*=6.2 Hz, 2H, $2CHMe_2$), 6.52 (d, *J*=8.4 Hz, 2H, *m*-ArH), 7.20 (t, *J*=8.4 Hz, 1H, *p*-ArH); Anal. Calcd for $C_{14}H_{20}O_4$: C, 66.65; H, 7.99. Found: C, 66.42; H, 8.28.

2,6-Diisopropoxybenzoic Acid. Potassium hydroxide (20 g) was dissolved in a 9 : 1 mixed solvent of methanol (90 mL) and water (10 mL). To a 20 wt% KOH solution was added methyl 2,6-diisoporoxybenzoate (8.3 g), and the mixture was heated to 80 °C (oil bath temperature). After stirring for 13 h at 80 °C, the mixture

was cooled to room temperature, poured into 1 *N* aqueous HCl, and extracted with ether twice. The organic layers were concentrated *in vacuo*, and the crude solid was washed with hexane and dried to give 2,6-diisopropoxybenzoic acid (7.7 g) as a white solid in 98% yield. mp 106.0~106.3 °C; IR (KBr) 3000, 1700, 1600, 1468, 1304, 1259, 1115, 1072, 927, 740, 656 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.36 (d, *J*=6.2 Hz, 12H, $CH(CH_3)_2$), 4.59 (septet, *J*=6.2 Hz, 2H, $2CHMe_2$), 6.58 (d, *J*=8.6 Hz, 2H, *m*-ArH), 7.27 (t, *J*=8.6 Hz, 1H, *p*-ArH), other resonance (CO_2H) could not be discerned; Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.38; H, 7.97.

(2R,3R)-2-O-(2,6-Diisopropoxybenzoyl)tartaric Acid (1). To a slightly suspended solution of 2,6-diisopropoxybenzoic acid (4.77 g, 20 mmol) and dibenzyl tartrate (6.61 g, 20 mmol) in dry benzene (100 mL) was added trifluoroacetic anhydride (3.1 mL, 22 mmol) dropwise over a period of 20 min at room temperature. After being stirred for 30 min, the pale yellow solution was poured into saturated $NaHCO_3$ and extracted with ether repeatedly. The combined organic layer was dried over Na_2SO_4, concentrated and the residue was purified by column chromatography on silica gel using a mixture (3 : 1 : 5) of hexane, ether and dichloromethane as eluent to give 6.73 g (65%) of dibenzyl mono-(2,6-diisopropoxybenzoyl)tartrate as a colorless half solid. This tartrate was dissolved in ethyl acetate (50 mL) and to the solution was added 0.67 g of 10 % Pd/C powder under argon atmosphere. The argon was then replaced by hydrogen and the reaction mixture was stirred at atmospheric pressure and room temperature for 15 h. The mixture was filtered through a celite pad and the filtrate was concentrated in vacuo to afford 4.66 g (100%) of **1** as a colorless solid. mp 81 °C; $[\alpha]_D$ -28.5° (*c* 1.1, EtOH); IR (KBr) 2982, 1744, 1466, 1255, 1113, 1070 cm^{-1}; ^1H NMR ($CDCl_3$-DMSO-d_6) δ 1.245 (d, 6H, *J*=6 Hz, 2Me), 1.255 (d, 6H, *J*=6 Hz, 2Me), 4.49 (septet, 2H, *J*=6 Hz, $2CH(CH_3)_2$), 4.73 (d, 1H, *J*=1.4 Hz, $HOCHCO_2$), 5.70 (d, 1H, *J*=1.4 Hz, CO_2CHCO_2), 6.46 (d, 2H, *J*=8 Hz, *m*-C_6H_3), 7.17 (t, 1H, *J*=8 Hz, *p*-C_6H_3); Anal. Calcd for $C_{17}H_{22}O_4$: C, 55.13; H, 5.94. Found: C, 54.95; H, 6.24.

Preparation of Boronic Acids

o-Phenoxyphenylboronic Acid. To a mixed solution of diphenyl ether (1.7 g, 10 mmol) and *N,N,N',N'*-tetramethylethylenediamine (4.5 mL, 30 mmol) in 40 mL of THF was added BuLi (1.66 *M* solution in hexanes, 6.0 mL, 10 mmol) at 0 °C, and the reaction mixture was stirred for 20 min. To this yellow solution was added a solution of $B(OMe)_3$ (1.4 mL, 12 mmol) in 6 mL of THF at the same temperature, and the colorless suspended solution was stirred at room temperature for 1 h. Then the mixture was poured into diluted HCl (20 ml of 1 *N* HCl and 80 ml of water) and extracted with ether repeatedly. The combined ether layer was dried over Na_2SO_4, evaporated and the residue was purified by column chromatography on silica gel using EtOAc-hexane=1/3 as eluant. Recrystallizatiom from ether/hexane afforded the correponding boric acid as a white solid (0.91 g, 42% yield). mp 138~139 °C; IR ($CHCl_3$) 3550, 1447, 1348, 1323, 1225, cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.7-5.8 (2H, br, 2OH), 6.71 (1H, d, *J*=8 Hz, CHCO), 7.04-7.43 (7H, m), 7.91 (1H, dd, *J*=2, 7 Hz, CHCB); Anal. Calcd for $C_{12}H_{11}O_3B$: C, 67.35; H, 5.14. Found: C, 67.40; H, 5.10.

Preparation of the other boric acids was carried out in a similar manner. The physical properties and analytical data for the boronic acids are listed below.

Butylboronic Acid. Obtained from Tokyo Chemical Industry Co., Ltd., Japan.

Phenylboronic Acid. Obtained from Aldrich Chemical Company, Inc., USA.

2,4,6-Trimethylbenzeneboronic Acid: IR (KBr) 3300, 1612, 1441, 1350, 1103, 1014, 846, 656 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 2.25 (s, 3H, CH_3), 2.33 (s, 6H, $2CH_3$), 4.58 (br, 2H, $B(OH)_2$), 6.82 (s, 2H, ArH); Anal. Calcd for $C_9H_{13}O_2B$: C, 65.91; H, 7.99. Found: C, 65.91; H, 7.99.

2,4,6-Triisopropylbenzeneboronic Acid: IR (KBr) 3300, 1605, 1460, 1327, 1057, 875 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.15-1.30 (m, 18H, 6Me), 2.75-2.95 (m, 3H, $3CHMe_2$), 4.50 (br, 2H, $B(OH)_2$), 7.00 (s, 2H, ArH); Anal. Calcd for $C_{15}H_{25}O_2B$: C, 72.60; H, 10.15. Found: C, 72.63; H, 9.93.

o-Methoxyphenylboronic Acid: IR (KBr) 3350, 1601, 1228, 755, 650, 526 cm^{-1}; ^1H NMR (CDCl3, 200 MHz) δ 3.94 (s, 3H, Me), 5.65-6.10 (br, 2H, $B(OH)_2$), 6.93 (d, *J*=8.4 Hz, 1H, C(3)H of Ar), 7.05 (dt, *J*=0.8, 7.4 Hz, 1H, C(5)H of Ar), 7.42-7.51 (ddd, *J*=1.8, 7.4, 8.4 Hz, 1H, C(4)H of Ar), 7.86 (dd, *J*=1.8, 7.4 Hz, 1H, C(6)H of Ar); Anal. Calcd for $C_7H_9O_3B$: C, 55.33; H, 5.97. Found: C, 55.36; H, 5.95.

o-Isopropoxyphenylboronic Acid: IR (film) 3412, 1601, 1450, 1344, 1223, 1136, 951, 760 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.41 (d, *J*=6.2 Hz, 6H, 2Me), 4.71 (septet, *J*=6.2 Hz, 1H, $CHMe_2$), 6.04-6.22 (br, 2H, $B(OH)_2$), 6.91 (d, *J*=8.2 Hz, 1H, C(3)H of Ar), 7.00 (dd, *J*=7.2, 7.4 Hz, 1H, C(5)H of Ar), 7.42 (ddd, *J*=2.0, 7.2, 8.2 Hz, 1H, C(4)H of Ar), 7.84 (dd, *J*=2.0, 7.4 Hz, 1H, C(6)H of Ar); Anal. Calcd for $C_9H_{13}O_3B$: C, 60.05; H, 7.28. Found: C, 60.30; H, 7.44.

Preparation of Chiral (Acyloxy)borane Catalyst (2 or 3)

Method A: To a solution of mono-(2,6-diisopropoxybenzoyl)tartrate (74 mg, 0.2 mmol) in dry propionitrile (1 mL) was added BH_3•THF (0.189 mL of 1.06 *M* solution in THF, 0.2 mmol) at 0 °C under argon. The reaction mixture was stirred for 15~30 min at 0 °C and cooled to -78 °C.

Method B: To a mixure of mono-(2,6-diisopropoxybenzoyl)tartrate **1** (74 mg, 0.2 mmol) and the corresponding boronic acid (0.2 mmol) was added dry propionitrile (1 mL) at room temperature under argon. The reaction mixture was stirred for 30 min at room temperature and cooled to -78 °C.

Preparation of Dienes

trans-1-Methoxy-3-(trimethylsiloxy)-1,3-butadiene: Obtained from Aldrich Chemical Company, Inc., USA.

2,4-Dimethyl-1-methoxy-3-(trimethylsiloxy)-1,3-butadiene:[10,11] IR (film) 2790, 1650, 1317, 1252, 1226, 1140, 1068, 881, 845 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.17 (s, 9H, Me_3Si), 1.60 (d, *J*=6.5 Hz, 3H, CH_3CH), 1.64 (s, 3H, CH_3C=C), 3.62 (s, 3H, OMe), 4.70 (q, *J*=6.5 Hz, 1H, MeCH), 6.3 (s, 1H, CHOMe).

General Procedure for Asymmetric Hetero Diels-Alder Reaction

Ligand **1** (148 mg, 0.4 mmol) and alkylboronic acid (0.40 mmol) were dissolved in dry propionitrile (2 ml), the resulting solution was stirred at 25 °C for 30 min, and the reaction system was cooled to -78 °C.

Aldehyde (2.0 mmol) and then diene (2.4 mmol) were added successively and the reaction stirred a further 8 h at the same low temperature before pouring into 4 *N* HCl. The product was extracted with ether repeatedly and the combined ether layers were dried and concentrated. The residue was dissolved in CH_2Cl_2 (20 ml), treated with trifluoroacetic acid (0.184 ml, 2.4 mmol), and stirred at 0 °C for 1 h. Usual workup, yielding crude adduct, was followed by column chromatography to give the pure pyrone. Diastereomeric (*E*/*Z*) products could be separated by column chromatography.

The absolute configurations were determined by the comparison of optical rotation values with literature data, or, if necessary, the products were converted to the known compound. Stereochemistries (*E* or *Z*) of the diastereomeric products were determined by the comparison of analytical HPLC and ^1H NMR of the authentic samples, which were prepared by the corresponding hetero Diels-Alder reactions with trimethylaluminum. Diastereo- and enantiomeric ratios were determined by analytical HPLC and ^1H-NMR spectroscopy of the products.

The physical properties and analytical data of hetero Diels-Alder adducts obtained are listed below.

(R)-2-Phenyl-2,3-dihydro-4H-pyran-4-one: [2i,13,14] TLC (hexane/ethyl acetate=3 : 2) R_f=0.28; ^1H NMR ($CDCl_3$) δ 2.66 (dd, *J*=3.8, 16.8 Hz, 1H, C*H*HCHPh), 2.92 (dd, *J*=14.3, 16.8 Hz, 1H, CH*H*CHPh), 5.43 (dd, *J*=3.8, 14.3 Hz, 1H, C*H*Ph), 5.53 (d, *J*=6.0 Hz, 1H, OCH=C*H*), 7.41 (brs, 5H, C_6H_5), 7.49 (d, *J*=6.0 Hz, 1H, OC*H*=CH); HPLC (Daicel OD, hexane/*i*-PrOH=50 : 1, flow rate=1.0 mL/min) t_R=32.2 min (t_R=25.0 min for (*S*)-enantiomer).

(2R,3R)-3,5-Dimethyl-2-phenyl-2,3-dihydro-4H-pyran-4-one:[14] TLC (hexane/ether=3 : 1) R_f=0.26; IR (film) 1760, 1622, 1454, 1385, 1306, 1170, 928, 735, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.90 (d, *J*=7.0 Hz, 3H, C*H*$_3$CH), 1.73 (s, 3H, C*H*$_3$CH=CH), 2.60 (dq, *J*=3.3, 7.0 Hz, 1H, MeC*H*), 5.47 (d, *J*=3.3 Hz, 1H, PhC*H*), 7.27-7.45 (m, 6H, C=C*H*O and C_6H_5); HPLC (Daicel OD, hexane/*i*-PrOH=50 : 1, flow rate=0.6 mL/min) t_R=0.26 min (t_R=0.33 min for (2*S*,3*S*) isomer).

(2RS,3SR)-Diastereomer: TLC (hexane/ether=3 : 1) R_f=0.33; ^1H NMR ($CDCl_3$) δ 0.92 (d, *J*=7.0 Hz, 3H, C*H*$_3$CH), 1.75 (s, 3H, C*H*$_3$C=CH), 2.79 (dq, *J*=14.0, 7.0 Hz, 1H, MeC*H*), 4.92 (d, *J*=14.0 Hz, 1H, PhC*H*), 7.32 (s, 1H, C=CHO), 7.35-7.44 (m, 5H, C_6H_5).

(2RS,3RS)-3,5-Dimethyl-2-(p-tolyl)-2,3-dihydro-4H-pyran-4-one: TLC (hexane/ether=3 : 1) R_f=0.30; IR (film) 2928, 1670, 1622, 1383, 1172, 819 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.88 (d, *J*=7.6 Hz, 3H, CHC*H*$_3$), 1.71 (s, 3H, C*H*$_3$C=CH), 2.34 (s, 3H, C*H*$_3$Ar), 2.55 (dq, *J*=3.2, 7.6 Hz, 1H, CH$_3$C*H*), 5.42 (d, *J*=3.2 Hz, 1H, CH$_3$CHC*H*O), 7.19 (s, 4H, ArH), 7.35 (s, 1H, C=CHO); HPLC (Daicel OD, hexane/*i*-PrOH=50 : 1, flow rate=1.0 mL/min) t_R=19.8 min for major enantiomer (t_R=22.7 min for minor enantiomer); Anal. Calcd for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.65; H, 7.67.

(2RS,3SR)-Diastereomer: TLC (hexane/ether=3 : 1) R_f=0.37; ^1H NMR ($CDCl_3$, 200 MHz) δ 0.92 (d, *J*=7.0 Hz, 3H, CHC*H*$_3$), 1.72 (s, 3H, C*H*$_3$C=CH), 2.38 (s, 3H, C*H*$_3$Ar), 2.79 (dq, *J*=13.4, 6.8 Hz, 1H, CH$_3$C*H*), 4.88 (d, *J*=13.4 Hz, 1H, CH$_3$CHC*H*O), 7.19-7.32 (m, 5H, ArH and C=CHO).

(R)-2-((1E)-2-Phenylethenyl)-2,3-dihydro-4H-pyran-4-one:[15] TLC (hexane/ether=3 : 1) R_f=0.37; IR (film) 1669, 1615, 1498, 1390, 760, 695 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.59 (dd, *J*=4.4, 16.6 Hz, 1H, C*H*HC=O),

2.73 (dd, J=12.2, 16.6 Hz, 1H, CH*H*C=O), 4.95-5.13 (m, 1H, C*H*CH=CHPh), 5.45 (d, J=5.8 Hz, 1H, C*H*=CHO), 6.28 (dd, J=6.4, 15.8 Hz, 1H, PhCH=C*H*), 6.71 (d, J=15.8 Hz, 1H, PhC*H*=CH, 1H), 7.24-7.45 (m, 6H, CH=C*H*O and C_6H_5); HPLC (Daicel AD, hexane/*i*-PrOH=20 : 1, flow rate=1.0 mL/min) t_R=15.0 min (t_R=17.5 min for (*S*)-enantiomer).

(2R,3R)-3,5-Dimethyl-2-((1E)-2-phenylethenyl)-2,3-dihydro-4H-pyran-4-one:[14] TLC (hexane/ether=3 : 1) R_f=0.27; IR (film) 1670, 1620, 1385, 1302, 1170, 748, 694 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.12 (d, J=7.4 Hz, 3H, C*H*$_3$CH), 1.70 (s, 3H, C*H*$_3$C=CH), 2.58 (dq, J=3.6, 7.4 Hz, 1H, CH$_3$C*H*), 4.98-5.05 (m, 1H, CH=CHC*H*O), 6.25 (dd, J=6.4, 16.0 Hz, 1H, PhCH=C*H*), 6.74 (d, J=16.0 Hz, 1H, PhC*H*), 7.26-7.50 (m, 6H, C_6H_5 and MeC=C*H*O); HPLC (Daicel OD, hexane/*i*-PrOH=50 : 1, flow rate=1.0 mL/min) t_R=37.2 min (t_R=13.8 min for (2*S*,3*S*)-enantiomer)

(2RS,3SR)-Diastereomer: TLC (hexane/ether=3 : 1) R_f=0.36; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.13 (d, J=7.0 Hz, 3H, C*H*$_3$CH), 1.70 (s, 3H, C*H*$_3$C=CH), 2.58 (dq, J=12.4, 7.0 Hz, 1H, CH$_3$C*H*), 1.70 (s, 3H, C*H*$_3$C=CH), 2.58 (dq, J=12.4, 7.0 Hz, 1H, CH$_3$C*H*), 4.58 (dd, J=7.6, 12.4 Hz, 1H, CH=CHC*H*O), 6.27 (dd, J=7.6, 16.0 Hz, 1H, PhCH=C*H*), 6.72 (d, J=16.0 Hz, 1H, PhC*H*), 7.26-7.48 (m, 6H, C_6H_5 and MeC=C*H*O).

(2RS,3RS)-3,5-Dimethyl-2-((1E)-1-propenyl)-2,3-dihydro-4H-pyran-4-one:[15] TLC (hexane/ether=3 : 1) R_f=0.28; IR (film) 1670, 1620, 1458, 1385, 1300, 1172, 966, 912 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.06 (d, J=7.2 Hz, 3H, C*H*$_3$CHC=O), 1.66 (s, 3H, C*H*$_3$C=CH), 1.76 (dd, J=1.5, 7.2 Hz, 3H, C*H*$_3$CH=CH), 2.45 (dq, J=7.2, 3.8 Hz, 1H, MeC*H*C=O), 4.76 (dd, J=3.8, 7.1 Hz, 1H, C*H*CH=CHMe), 5.58 (ddd, J=1.5, 7.1, 15.4 Hz, 1H, MeCH=C*H*), 5.84 (dq, J=15.4, 7.2 Hz, 1H, MeC*H*=CH), 7.18 (s, 1H, MeC=C*H*O); HPLC (Daicel OD, hexane/*i*-PrOH=50 : 1, flow rate=0.3 mL/min) t_R=28.8 min (t_R=25.7 min for minor enantiomer).

(2RS,3SR)-Diastereomer: TLC (hexane/ether=3 : 1) R_f=0.48; ^1H NMR ($CDCl_3$) δ 1.05 (d, J=7.2 Hz, 3H, C*H*$_3$CHC=O), 1.65 (s, 3H, C*H*$_3$C=CH), 1.77 (d, J=6.2 Hz, 3H, C*H*$_3$CH=CH), 2.42 (dq, J=7.2, 12.2 Hz, 1H, CH$_3$C*H*C=O), 4.35 (dd, J=7.8, 12.2 Hz, 1H, C*H*CH=CHMe), 5.58 (ddd, J=1.4, 7.8, 15.4 Hz, 1H, CH$_3$CH=C*H*), 5.86 (dq, J=15.4, 6.2 Hz, 1H, CH$_3$C*H*=CH), 7.20 (s, 1H, CH$_3$C=C*H*O).

(2RS,3RS)-3,5-Dimethyl-(2-furyl)-2,3-dihydro-4H-pyran-4-one:[14] TLC (hexane/ethyl acetate=3 : 1) R_f=0.35; IR (film) 1670, 1624, 1387, 1165, 744 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.09 (d, J=7.2 Hz, 3H, CHC*H*$_3$), 1.70 (s, 3H, CH=CC*H*$_3$), 2.88 (dq, J=4.4, 7.2 Hz, 1H, C*H*CH$_3$), 5.44 (d, J=4.4 Hz, 1H, MeCHC*H*O), 6.34-6.39 (m, 2H, C=C*H*-C*H*=CH), 7.19 (s, 1H, C=CHO), 7.41 (d, J=1.8 Hz, 1H, OC*H*=CH-CH=C); HPLC (Daicel OD, hexane/*i*-PrOH=200 : 1, flow rate=0.6 mL/min) t_R=31.9 min (t_R=41.9 min for minor enantiomer).

(2RS,3SR)-Diastereomer: TLC (hexane/ethyl acetate=3 : 1) R_f=0.35; ^1H NMR ($CDCl_3$) δ 1.02 (d, J=7.0 Hz, 3H, CHC*H*$_3$), 1.70 (s, 3H, CH=CHC*H*$_3$), 3.02 (dq, J=12.6, 7.0 Hz, 1H, C*H*CH$_3$), 5.00 (d, J=12.6 Hz, 1H, CH$_3$CHC*H*O), 6.39-6.47 (m, 2H, C=C*H*-C*H*=CH), 7.24 (s, 1H, C=CHO), 7.47 (d, J=1.8 Hz, 1H, OC*H*=CH-CH=C).

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6. Five-membered ring carbonyl compound derived from lactic acid and phenylboronic acid: 1811 cm^{-1}; Six-membered ring structure derived from β-hydroxybutyric acid and phenylboronic acid: 1773 cm^{-1}. Carbonyl peak of 1817 cm^{-1} was observed for the cyclic product derived from the cyclohexanol C-1-mono-ester of **1** and phenylboronic acid.

7. With the catalyst generated from **1** and phenylboronic acid, the following preliminary results have been obtained: Diels-Alder with methacrolein and cyclopentadiene at -78 °C for 5 h; >95% yield and 79% ee: Aldol synthesis with benzaldehyde and silyl enol ether of acetophenone at -78 °C for 5 h; 94% yield and 78% ee: Sakurai-Hosomi reaction with benzaldehyde and 2-methyl-1-trimethylsilyl-2-propene at -40 °C for 5 h; 94% yield and 75% ee. Full details of these results will be reported in due course.

8. Our recent asymmetric hetero Diels-Alder reaction, see Maruoka, K.; Itoh, T.; Shirasaka, T.; Yamamoto, H. *J. Am. Chem. Soc.* **1988**, *110*, 310; Maruoka, K.; Nonoshita, K.; Yamamoto, H. *Synthetic Commun.* **1988**, *18*, 1453.

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