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TETRAHEDRON

BMPD, a Novel C_2-Chiral 1,3-Diketone Ligand; Synthesis and Application to an Asymmetric Catalytic Reaction[1]

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Dedicated to Professor Satoru Masamune, Massachusetts Institute of Technology on the occasion of his 70's birthday

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Abstract: The synthesis of BMPD, 1,3-bis(2-methylferrocenyl)propane-1,3-dione, was achieved *via* the Claisen condensation of a homochiral ferrocenecarboxylate and an acetylferrocene derived from the same chiral formylferrocene. Several metal complexes were prepared to exemplify the complexation ability of BMPD. A BMPD-yttrium complex was found to act as a new catalyst for silylcyanation of aldehydes with remarkable efficiency. As little as 0.2 mol% of the complex catalyzed the reaction of benzaldehyde and cyanotrimethylsilane to afford the cyanohydrin in 95% yield with 87% ee.

INTRODUCTION

Efforts continue to develop an efficient and practical catalyst for asymmetric reactions.[3] 1,3-Diketones are well known as ligands of variety of metals, but little attention has been paid for the use of chiral 1,3-diketones as a ligand for catalysts of asymmetric reactions.[4] Most of the chiral 1,3-diketones are derived from natural product (*e.g.* camphor) and their application to catalytic asymmetric synthesis is very limited. So far the reported examples include $Eu(hfc)_3$ and related complexes catalyzed hetero Diels-Alder reaction,[5] Mukaiyama aldol reaction,[6] Diels-Alder reaction[7] and $Cu(hfc)_2$ catalyzed cyclopropanation.[8] Here we would like to describe a synthesis of 1,3-bis(2-methylferrocenyl)propane-1,3-dione (BMPD, **1**) as a new chiral 1,3-diketone type ligand and an application of a novel chiral 1,3-dicarbonyl compound to the asymmetric silylcyanation reaction in detail.[9]

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RESULTS AND DISCUSSION

Design and synthesis of BMPD

We have designed BMPD as a chiral 1,3-diketone ligand capable of forming metal complexes useful as a Lewis acid catalyst, based on the following considerations: 1) use of C_2-symmetric ligand to reduce the possible isomers of a metal complex or the Lewis acid-carbonyl complex. 2) use of ferrocenyl group as a bulky blocking group to effect selectivities. (Figure 1)

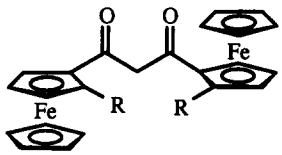
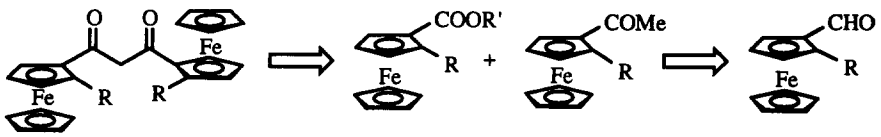


Fig. 1. Structure of 1,3-Bis(2-Methylferrocenyl)Propane-1,3-Dione (BMPD, **1**) (R=Me)

From a retrosynthetic analysis, chiral bisferrocenyl-1,3-diketones could be prepared by Claisen condensation of the corresponding homochiral ester and methyl ketone of the same sense, both of which would be derived from the same chiral 2-substituted-formylferrocene. (Eq. 1)

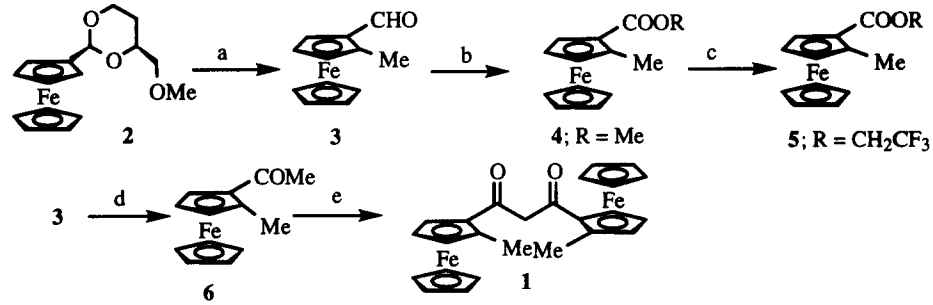


(Eq. 1)

The starting material for the lowest family of chiral 2-substituted-formylferrocenes, chiral 2-methylformylferrocene (**3**) was synthesized in quantity using the Kagan's protocol.[10] Directed ortho-lithiation of the chiral acetal (**2**) followed by the alkylation with methyl iodide afforded (*R*)-2-methylformylferrocene (**3**)[11] in 90% isolated yield after acid hydrolysis. **3** was transformed to the methyl ester (**4**)[12] as well as the acetyl derivative (**6**)[13] by MnO_2 oxidation (MnO_2, NaCN, AcOH, MeOH; 85%) or Grignard reaction followed by MnO_2 oxidation (75%, 2 steps), respectively. The optical purity of **4** was determined to be 94% ee by the HPLC analysis (Chiarcel® OD, i-PrOH:hexane=1:10), which also means the optical purity of **3** and **6** should be 94% ee assuming that the transformations did not cause epimerization. With the requisite chiral methyl ketone and ester in hand, the Claisen condensation was pursued. The condensation of the hindered components was problematic by either slow consumption of the starting materials or contamination with O-acylated product. After extensive survey of the various combination of esters (*e.g.*, methyl, phenyl, trifluoroethyl esters) and bases (*e.g.*, $NaNH_2$, LDA, KH), we found that the combination of KH and trifluoroethyl ester was optimum without formation of O-acylated product. Thus, the treatment of methyl ketone (**6**) and the trifluoroethyl ester (**5**), which was prepared from **4** by the two-step operation (i; NaOH, EtOH, ii; trifluoroethanol, DCC, DMAP, 90%) with 2 equivalents of

KH in THF at room temperature afforded 1,3-diketone in 80% yield. Under this conditions any O-acylated product could not be detected. Recrystallization of the raw product from hexane and methylenechloride to remove the meso isomer gave the pure (*R*, *R*)-BMPD **1** as dark red crystals (mp 150-151°C). (Scheme 1)

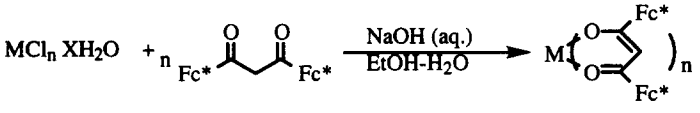
Scheme 1



Key: a; i) t-BuLi, MeI, ether, ii) HCl, aqMeOH, 90% from **2**. b; MnO_2, HCN, MeOH, 85%. c; i) NaOH, EtOH, 97%, ii) CF_3CH_2OH, DCC, DMAP, 90%. d; i) MeMgBr, THF, ii) MnO_2, benzene, 75% from **3**. e; KH, THF, **5**, then recrystallization, 80%.

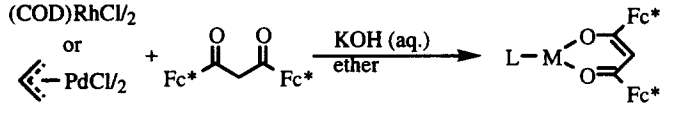
Preparation of metal complexes

In order to ascertain the complexation ability of BMPD, several types of metal complexes were prepared. Trivalent metal chloride (YCl_3 and $NdCl_3$) reacted with 3 equivalents of BMPD in aqueous ethanol in the presence of 3 equivalents of NaOH to afford the corresponding 3:1 complexes (**7a**, **7b**) in high yields. Although $Pd(BMPD)_2$ (**7c**) was synthesized under the similar reaction conditions, we could not isolate the corresponding Cu(II) and Zn complexes. (Eq. 2)[14] Rh(cod)(BMPD) (**8a**) and (allyl)Pd(BMPD) (**8b**) were synthesized quantitatively by the reaction of BMPD and the corresponding metal chloride in the presence of aqueous KOH in ether. (Eq. 3) Et_2B-BMPD (**9**) was prepared by the reaction of BMPD and Et_3B in toluene under reflux. (Eq. 4)



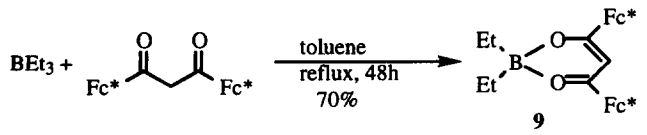
(Eq. 2)

7a M=Y, n=3, 85%; **7b** M=Nd, n=3, 80%; **7c** M=Pd, n=2, 55%



(Eq. 3)

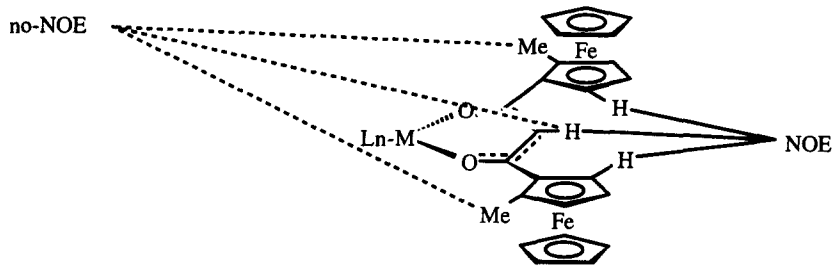
8a M=Rh, L=cod, 100%; **8b** M=Pd, L=allyl, 100%



9

(Eq. 4)

It should be noted that the single isomer of $Y(BMPD)_3$ (from possible two isomers; Δ, Λ) was observed in the ^1H and ^{13}C NMR, and NOE experiment of $Y(BMPD)_3$, $Pd(BMPD)_2$ and (allyl)Pd(BMPD) suggested that the conformation of the complexes would be as described in Figure 2.

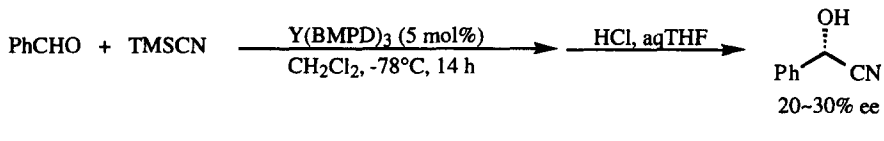


7a: M=Y, L=BMPD, n=2; **7c**: M=Pd, L=BMPD, n=1; **8b**: M=Pd, L=allyl, n=1

Fig. 2. NOE results of the BMPD complexes

Catalytic asymmetric silylcyanation

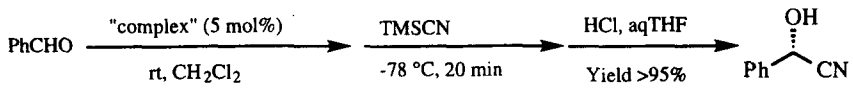
From the survey of several asymmetric catalytic reactions with BMPD complexes, we have found that the yttrium complex **7a** catalyzed the silylcyanation[15] of aldehyde. The reaction of benzaldehyde and TMSCN proceeded enantioselectively at -78 °C for 14 h with 5 mol % of $Y(BMPD)_3$ to afford the chiral cyanohydrin after hydrolysis. (Eq. 5) However, the enantioselectivities remained marginal under various reaction conditions (20~30% ee). The enantioselectivity of the cyanohydrin was determined by HPLC analysis of the corresponding (*R*)-MTPA ester.[16]



(Eq.5)

This unsatisfactory asymmetric induction by the isolated $Y(BMPD)_3$ complex[17] led us to use an anhydrous complex of yttrium and BMPD. An anhydrous $Y(BMPD)_3$ complex would be obtained *in situ* by the treatment of BMPD with a yttrium alkoxide base. Thus, the complexes were prepared from the commercial $Y(OiPr)_3$,[18] and BMPD with varying ratios at room temperature for 16 h in CH_2Cl_2 and tested for the silylcyanation reaction. (Table 1)

Table 1. Effect of the Molar Ratio



entry	BMPD: $Y(OiPr)_3$	% ee
1	0.8 : 1	61
2	1.0 : 1	87
3	1.2 : 1	69
4	1.5 : 1	59
5	2.0 : 1	74
6	3.0 : 1	48

The *in situ* prepared anhydrous complexes were far more reactive than the isolated $Y(BMPD)_3$ and the reaction of benzaldehyde and TMSCN was completed within 20 min at -78 °C in the presence of 5 mol% of the complexes. The ratio of the ligand (BMPD) and yttrium isopropoxide critically affected the enantioselectivity. Interestingly, the 3:1 complex was less selective than the 2:1 complex, and 1:1 ratio of BMPD and $Y(OiPr)_3$ provided optimal enantioselectivity of 87% ee. It should be noted that the manner of complexation affected the enantioselectivity and it was necessary to treat a mixture of the ligand and $Y(OiPr)_3$ for 16 h at room temperature to attain high selectivity. (Table 2) Also the manner of the addition of the reagents was very important. Thus, benzaldehyde must be added to an *in situ* prepared complex at *room temperature* for high enantioselectivity. When benzaldehyde was added at -78 °C followed by TMSCN, the enantioselectivity dropped significantly. (*vide infra*) Because of uncertain quality of commercial $Y(OiPr)_3$, which was found to be a mixture of several species by NMR analysis (Figure 3), we turned our attention to use $Y_5(O)(OiPr)_{13}$, pentameric yttrium isopropoxide. $Y_5(O)(OiPr)_{13}$ was prepared by recrystallization of commercial $Y(OiPr)_3$ from iPrOH or by the known procedures,[19] and irrespective to the method of preparation (Eq 6-7), highly reactive and selective catalyst was obtained by complexation of crystalline $Y_5(O)(OiPr)_{13}$ and BMPD in CH_2Cl_2 at room temperature for 1 h ("complex A"). Under the reaction conditions, enantioselectivity was increased to 90% ee. Either prolonged treatment (room temperature for 16 h) or azeotropic removal of iPrOH with toluene afforded less selective catalysts. (Table 2)

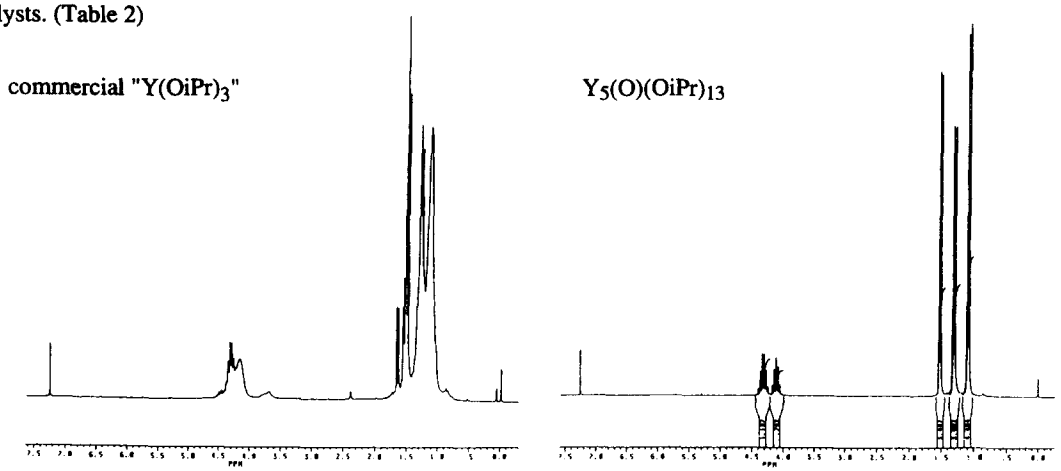
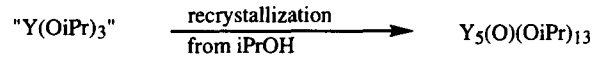
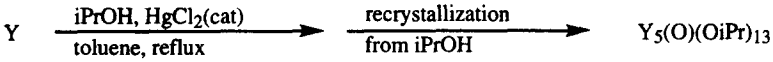


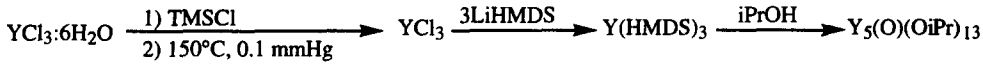
Fig. 3. ^1H NMR spectra of the commercial "$Y(OiPr)_3$" and $Y_5(O)(OiPr)_{13}$



(Eq. 6)

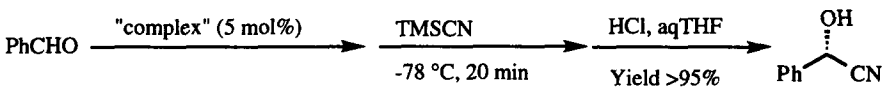


(Eq. 7)



(Eq. 8)

Table 2. Effect of the Source and Complexation Conditions



Entry	Source of yttrium	complexation conditions	% ee
1	$Y(OiPr)_3$	CH_2Cl_2, rt, 2 h	35
2	$Y(OiPr)_3$	CH_2Cl_2, rt, 4 h	55
3	$Y(OiPr)_3$	CH_2Cl_2, rt, 16 h	87
4	$Y_5(O)(OiPr)_{13}$	CH_2Cl_2, rt, 1 h	90
5	$Y_5(O)(OiPr)_{13}$	CH_2Cl_2, rt, 16 h	65
6	$Y_5(O)(OiPr)_{13}$	toluene, 60 °C, 3 h	70

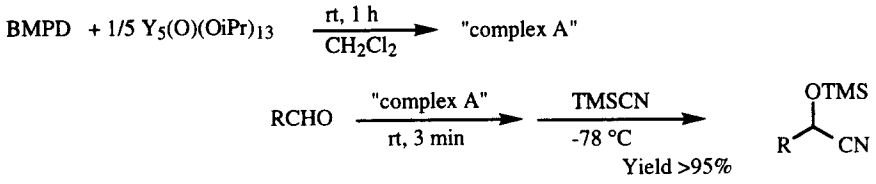
Then, the solvent for the reaction was screened. (Table 3) Higher enantioselectivity was observed in relatively nonpolar solvents and in polar solvents enantioselectivity was diminished dramatically. CH_2Cl_2 was the solvent of choice.

Table 3. Effect of the Solvent

Entry	solvent	yield (%)	% ee
1	CH_2Cl_2	>95	90
2	toluene	>95	75
3	diethyl ether	>95	70
4	THF	90	38
5	CH_3CN	30	0

The present catalyst system was proved to be remarkably efficient. Thus, the catalyst loading could be reduced to as little as 0.2 mol% without loss of both chemical and optical yields. With 1 mol% of the BMPD-yttrium complex, a variety of aldehydes were silylcyanated in nearly quantitative yields under the standard conditions. (Table 4) Aromatic aldehydes, except for those with electron withdrawing groups, showed good to excellent enantioselectivities, but for aliphatic aldehydes the selectivity was only moderate with reversed enantioface selection.[20] It should be noted that with lower catalyst loadings, the concentration of "polar" aldehyde severely affect the polarity of the reaction medium, and the slow addition technique had to be employed in order to maintein the low polarity of the reaction mixture.

Table 4. Asymmetric Silylcyanation of Aldehydes

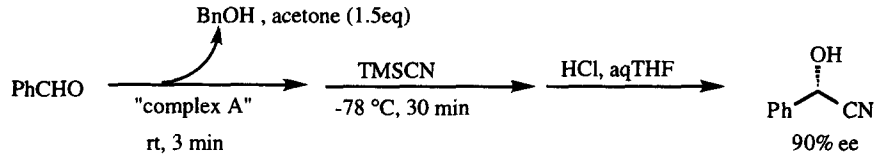


Entry	aldehyde	catalyst (mol %)	$[\alpha]_D$ (c, in $CHCl_3$)	confign	% ee
1	benzaldehyde	1	-39.1 (0.80)	*S*	90
2	benzaldehyde[a)]	0.2	-37.8 (0.90)	*S*	86
3	*p*-tolualdehyde	1	-47.2 (1.60)	*S*	91
4	*p*-phenylbenzaldehyde	1	-33.3 (0.72)	*S*[b)]	90
5	*p*-methoxybenzaldehyde	1	-38.3 (1.86)	*S*	84
6	*p*-t-butylbenzaldehyde	1	-28.5 (1.08)	*S*[b)]	72
7	*p*-fluorobenzaldehyde	1	-30.7 (1.50)	*S*[b)]	81
8	*p*-chlorobenzaldehyde	1	-23.5 (1.48)	*S*[b)]	60
9	*p*-cyanobenzaldehyde	1	-11.2 (1.00)	*S*	30
10	*p*-trifluoromethylbenzaldehyde	1	-2.4 (1.20)	*S*[b)]	10
11	*o*-methoxybenzaldehyde	1	-23.8 (3.05)	*S*[b)]	75
12	*m*-phenoxybenzaldehyde	1	-13.6 (1.80)[c)]	*S*	79
13	1-naphthaldehyde	1	-38.0 (1.02)	*S*[b)]	58
15	2-naphthaldehyde	1	-11.0 (1.50)	*S*	73
16	(E)-cinnamaldehyde	1	-17.6 (2.30)	*S*	68
17	pivalaldehyde	1	+5.9 (1.65)	*R*	49
18	cyclohexanecarboxyaldehyde	1	+6.8 (1.70)	*R*	49

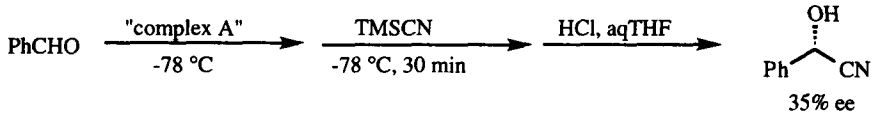
a) The aldehyde and TMSCN were added during 5 h.
b) Absolute stereochemistry was estimated by analogy.
c) $[\alpha]_D$ in benzene.

Although the structure of the catalyst and the exact mechanism of the reaction are still elusive, some considerations concerning the reaction pathway including complexation, generation of the catalytic species and catalytic cycle should be noted on the basis of the following observations:

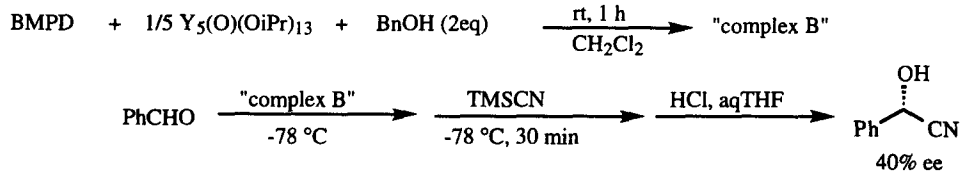
(1) NMR experiments did not give any information about the structure of the complex, but it was found that after the addition of benzaldehyde at *room temperature*, benzyl alcohol and acetone, each 1.5 equivalent to the complex, were produced by Meerwein-Ponndorf-Verley (MPV) reaction. The MPV reaction, probably accompanied with the structure change of the initial complex, was essential for the high selectivity.(Eq. 9) One quievalent (to the catalyst) of the TMSCN was consumed to silylate the alcohol, which was produced upon complexation of yttrium isopropoxide with BMPD. When benzaldehyde was added at -78 °C followed by TMSCN, the enantioselectivity dropped to 35% ee, and benzyl alcohol was not detected at all by HPLC analysis. (Eq. 10) The effect of benzyl alcohol for high enantioselectivity was ruled out by the control experiments.(Eq. 11~13) Thus, complexation in the presence of benzyl alcohol (Eq. 11) or addition of benzyl alcohol to the complex (Eq. 12) did not afford high enantioselectivity unless benzaldehyde was added at room temperature (Eq. 13). When TMSCN was added at higher temperature (0 °C), the complex reacted with TMSCN and TMSOiPr was produced, and the enantioselectivity was 25% ee. (Eq. 14)



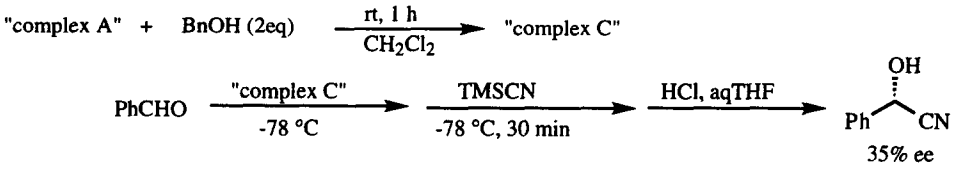
(Eq. 9)



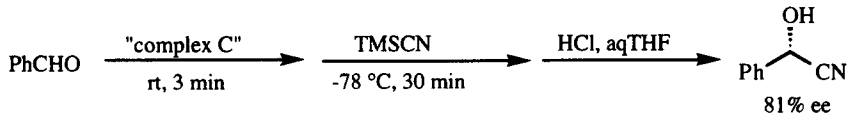
(Eq. 10)



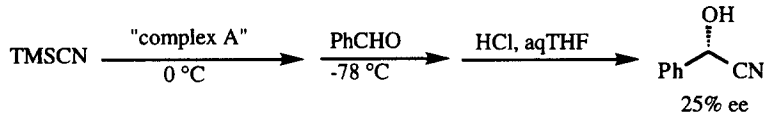
(Eq. 11)



(Eq. 12)

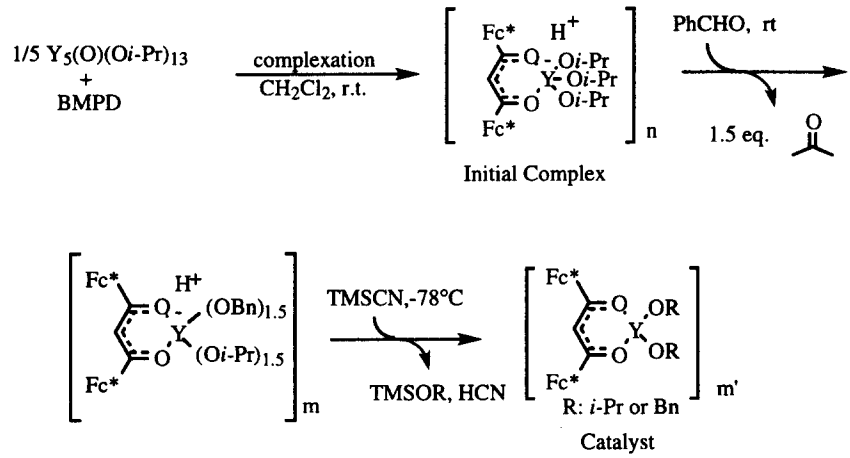


(Eq. 13)



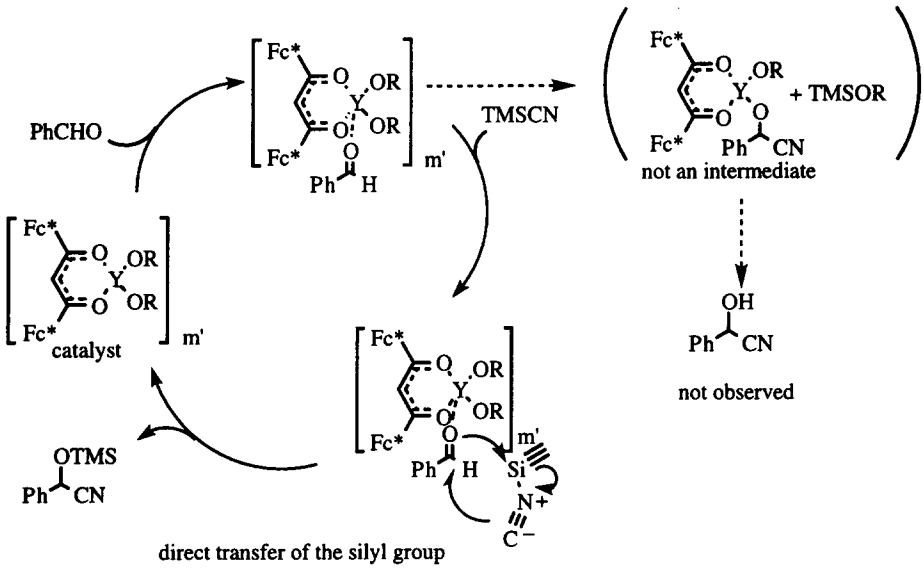
(Eq. 14)

(2) During the course of the reaction, all the product (cyanohydrin) were silylated at any conversions under any catalyst loadings, even in the presence of excess aldehyde. This excludes the possible mechanism of the stepwise silylation of the intermediate yttrium derivative of the cyanohydrin. Rather, the mechanism which includes the concomitant transfer of the silyl group of TMSCN to the oxygen atom of the carbonyl group with C-C bond formation,[21] would be plausible. Based on the results described above, the whole scheme for the catalyst generation and silylcyanation reaction is summarized in Scheme 2 and 3. The remarkably high catalytic activity of BMPD-yttrium complex would be attributed to the direct silyl group transfer mechanism.



*different order of aggregation was designated as n, m, m'

Scheme 2. Plausible scheme for catalyst generation



Scheme 3. Plausible scheme for catalytic cycle of the silylcyanation

CONCLUSION

In conclusion, we have synthesized novel chiral 1,3-diketone, BMPD, as a first designed chiral 1,3-dicarbonyl type ligand and demonstrated the potential of BMPD as a chiral ligand in asymmetric catalytic reactions. The remarkably efficient catalytic asymmetric silylcyanation reaction of BMPD-yttrium isopropoxide complex showed the possibility of a practical application of Lewis acid catalysts.

EXPERIMENTAL

Synthesis of (*R,R*)-BMPD **1**

(*2S,4S*)-2-Ferrocenyl-4-hydroxymethyl-1,3-dioxane[10b]

A solution of (dimethoxymethyl)ferrocene (26 g, 0.1 mol), (*S*)-1,2,4-butanetriol (11.6 g, 0.11 mol) and a catalytic amount of p-TsOH in CH_2Cl_2 (300 ml) was stirred at room temperature for 4 h. The reaction was treated with 1N NaOH solution and washed with brine. Usual workup including a chromatographic purification (Hex: EtOAc = 4 : 1) afforded the title compound, which was further purified by recrystallization from toluene to give the title compound in a diasteromerically pure form (25.7 g, 85%).

^{1}H NMR ($CDCl_3$) δ 5.39 (1H, s), 4.31 (2H, m), 4.16 (1H, m), 4.12 (5H, s), 4.11 (2H, m), 3.92 (2H, m), 3.66 (2H, m), 2.08 (1H, m), 1.85 (1H, m), 1.49 (1H, m).

(*2S,4S*)-2-Ferrocenyl-4-methoxymethyl-1,3-dioxane (**2**)[10b]

To a solution of (*2S,4S*)-2-ferrocenyl-4-hydroxymethyl-1,3-dioxane (15.1 g, 0.05 mol) in THF (200 ml) was added NaH (5 g, 60% in mineral oil). After stirred at room temperature for 30 min, MeI (10 ml, 0.16 mol) was added. The reaction was stirred at room temperature for 1 h, and quenched by the addition of water. The mixture was extracted with EtOAc and worked up as usual. Purification by a short column chromatography afforded **2** (15.8 g 100%) as a red oil.

^{1}H NMR ($CDCl_3$) δ 5.38 (1H, s), 4.35 (2H, m), 4.18 (5H, s), 4.10 (2H, m), 3.80~4.30 (3H, m), 3.47 (2H, m), 3.42 (3H, s), 1.79 (1H, m), 1.49 (1H, m).

(*R*)-2-Methylformylferrocene (**3**)[11]

To a solution of **2** (15.8 g, 0.05 mol) in diethyl ether (150 ml) was added a solution of tert-BuLi in hexane (1.7 M, 30 ml, 0.051 mol) at -78 °C. After being stirred at -78 °C for 15 min and at room temperature for 2 h, MeI (10 ml) was added at -30 °C. The reaction was let to warm to room temperature during 2 h and quenched with aqueous $NaHCO_3$ solution. Separated organic layer was concentrated and treated with 1N HCl (50 ml) and MeOH (100 ml) at room temperature for 1 h. The mixture was diluted with H_2O (200 ml) and extracted with EtOAc. Extracts were washed with brine and dried over $MgSO_4$. Usual workup afforded **3** (10.2 g, 90%) as a red oil.

$[\alpha]_D$ 212 (c 0.35, EtOH). ^{1}H NMR ($CDCl_3$) δ 10.12 (1H, s), 4.69 (1H, m), 4.46 (2H, m), 4.18 (5H, s), 2.25 (3H, s).

Methyl (*R*)-2-methylferrocenecarboxylate (**4**)[12]

To a solution of **3** (11.4 g, 0.05 mol) in MeOH (250 ml) was added NaCN (0.7 g) and AcOH (0.5 ml), followed by MnO_2 (50 g). The mixture was stirred at room temperature for 24 h and filtered through a pad of Celite. The filtrate was concentrated and purified by chromatography to afford **4** as a red oil (11.0 g, 85%).

$[\alpha]_D$ -10.0 (c 1.9, benzene). ^{1}H NMR ($CDCl_3$) δ 4.72 (1H, m), 4.31 (1H, m), 4.23 (1H, m), 4.13 (5H, s), 3.82 (3H, s), 2.30 (3H, s).

HPLC analysis on a chiral column showed 94% ee. (Chiralcel OD, iPrOH : Hex = 1 : 10, 1 ml/min; Rt = 9.9 min (*S*) and 11.7 min (*R*)).

(*R*)-2-Methylferrocenecarboxylic acid[22]

A solution of **4** (7.74 g, 0.03 mol) in EtOH (100 ml) and 4N NaOH (100 ml) was stirred at room temperature for 16 h. The reaction was washed with CH_2Cl_2 and the aqueous layer was made pH = 2 with 2N HCl. Extractive workup with EtOAc afforded the title acid as yellow crystals (7.1 g, 97%).

$[\alpha]_D$ 25.5 (c 0.80, EtOH). ^{1}H NMR ($CDCl_3$) δ 4.82 (1H, m), 4.40 (1H, m), 4.32 (1H, m), 4.20 (5H, s), 2.32 (3H, s).

2,2,2-Trifluoroethyl (*R*)-2-methylferrocenecarboxylate (**5**)

To a solution of (*R*)-2-Methylferrocenecarboxylic acid (7.32 g, 0.03 mol) and trifluoroethanol (4.4 ml, 0.06 mol) in CH_2Cl_2 (100 ml) was added DCC (8.5 g, 0.04 mol) and DMAP (0.5g, 4 mmol). The reaction was stirred at room temperature for 16 h and filtered. The filtrate was concentrated and purified by chromatography to afford **5** (8.8 g, 90%).

$[\alpha]_D$ -503.9 (c 1.49, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ 4.80 (1H, m), 4.40~4.80 (2H, m), 4.40 (1H, m), 4.34 (1H, m), 4.28 (5H, s), 2.29 (3H, s).

(*R*)-2-Methylacetylferrocene (**6**)[13]

To a solution of **3** (11.4 g, 0.05 mol) in diethyl ether (150 ml) was added an etheral solution of MeMgBr (3M, 20 ml, 0.06 mol) at 0 °C. The reaction was stirred at room temperature for 2 h and quenched by saturated aqueous NH_4Cl solution. Usual workup afforded crude alcohols as a mixture of diastereoisomers, which were used for the next reaction without purification. To a solution of the above mentioned alcohols in benzene (250 ml) was added MnO_2 (80 g). The mixture was stirred at room temperature for 24 h and filtered through a pad of Celite. The filtrate was concentrated and the residue was purified by chromatography to afford **6** as a red oil (9.1 g, 75%).

$[\alpha]_D$ -486 (c 0.71, benzene).^{1}H NMR ($CDCl_3$) δ 4.58 (1H, m), 4.42 (1H, m), 4,30 (1H, m), 4.09 (5H, s), 2.42 (3H, s), 2.33 (3H, s).

HPLC analysis on a chiral column showed 94% ee. (Chiralcel OD, iPrOH : Hex = 1 : 15, 1 ml/min; Rt = 8.7 min (*S*) and 10.6 min (*R*)).

(*R,R*)-1,3-Bis(2-methylferrocenyl)-1,3-propanedione **1**

To a suspension of KH (1.60 g, 40 mmol) in THF (40 ml) was added dropwise a solution of **6** (4.84 g, 20 mmol) in THF (10 ml) at room temperature. The reaction mixture was stirred for 20 min, when the evolution of hydrogen ceased, and a solution of **5** (6.85 g, 21 mmol) in THF (20 ml) was added dropwise at room temperature during 1 h. After stirred at room temperature for 4 h, the reaction was quenched with aqueous $NaHCO_3$ solution. The extractive workup with EtOAc followed by the purification by chromatography afforded **1** as red crystals. Recrystallization from CH_2Cl_2 and hexane to remove the meso isomer afforded the chiral **1** as dark red crystals, 7.5 g, 80%.

mp. 150~151 °C. $[\alpha]_D$ -75.8 (c 0.80, $CHCl_3$). FAB MS; m/z 468 (M^+). ^1H NMR (C_6D_6) (enol form) δ 10.49 (1H, br), 6.20 (1H, s), 4.57 (2H, m), 4.10 (2H, m), 4.04 (2H, m), 3.96 (10H, s), 2.36 (6H, s). ^{13}C NMR (C_6D_6) 190.5, 96.1, 86.1, 77.2, 71.1, 70.8, 69.2, 69.1, 15.6. Anal Calcd for $C_{25}H_{24}O_2Fe_2$; C:64.14, H:5.17. Found C:63.93, H:5.23.

Tris[(*R,R*)-bis(2-methylferrocenyl)propane-1,3-dionato]yttrium (**7a**)

To a suspension of $YCl_3 \cdot 6H_2O$ (30.3 mg, 0.1mmol) in 15 ml of EtOH-H_2O was added a solution of (*R,R*)-BMPD (140.4mg, 3 mmol) and 0.3 ml 1N NaOH(aqueous) in ethanol. After stirred at room temperature for 3 h, the reaction mixture was filtered and the precipitate was washed with H_2O and ethanol, and then dried under vaccum at 100 °C to give $Y(BMPD)_3$ (127 mg, 85%). mp 260 °C (dec.). $[\alpha]_D$ -61.1 (c 0.90, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 6.20 (3H, s), 4.59 (6H, m), 4.27 (6H, m), 4.19 (6H, m), 4.05 (30H, s), 2.43 (18H, s). ^{13}C NMR ($CDCl_3$) δ 189.3, 98.8, 86.7, 80.4, 73.4, 70.7, 68.9, 68.0, 15.7. FAB-MS: 1490(M^+). HR-MS Calcd for $C_{75}H_{69}O_6Fe_6Y$; 1490.0249. Found; 1490.0266.

Tris[(*R,R*)-bis(2-methylferrocenyl)propane-1,3-dionato]neodium (**7b**)

Prepared as described for $Y(BMPD)_3$ by using $NdCl_3.6H_2O$ instead of $YCl_3.6H_2O$. (yield, 80%)

mp 160 °C (dec.). $[\alpha]_D$ -60.6 (c 0.87, $CHCl_3$). FAB-MS: 1543(M^+). HR-MS Calcd for $C_{75}H_{69}O_6Fe_6Nd$; 1543.0268. Found; 1543.0310.

Bis[(*R,R*)-bis(2-methylferrocenyl)propane-1,3-dionato]plladium (**7c**)

To a suspension of $PdCl_2$ (26.6 mg, 0.15 mmol) in 15 ml of ethanol was added a solution of (*R,R*)-BMPD (140.4 mg, 0.3 mmol) and 0.3 ml 1N NaOH (aqueous) in ethanol. After stirred at room temperature for 24 h, the reaction mixture was filtered and the filtrate was concentrated, and then chromatographed on silica gel to afford $Pd(BMPD)_2$ as dark red crystal. (117 mg, 75%)

mp 259-260 °C. $[\alpha]_D$ -89.1 (c 0.66, $CHCl_3$). FAB-MS 1040 (M^+). ^1H NMR (C_6D_6) δ 6.09 (2H, s), 4.57 (4H, m), 4.32 (4H, m), 4.23 (4H, m), 4.16 (10H, s), 2.38 (6H, s). ^{13}C NMR (C_6D_6) δ 184.6, 97.8, 86.2, 78.8, 73.2, 70.8, 69.0, 68.1, 15.7. HR-MS Calcd for $C_{50}H_{46}O_4Fe_4Pd$; 1039.9828. Found; 1039.9855.

(1,5-Cyclooctadiene)[(*R,R*)-bis(2-methylferrocenyl)propane-1,3-dionato]rhodium(I) (**8a**)

To a suspension of (COD)RhCl/2 (74.0 mg, 0.15 mmol) and (*R,R*)-BMPD (140.4 mg, 0.3 mmol) in 5 ml of ether was added 0.6 ml of 1N KOH (aqueous) at -78 °C. The reaction mixture was allowed to warm to room temperature and stirred for 1 h. Saturated $NaHCO_3$ aqueous solution was introduced to quench the reaction. The organic layer was seperated, washed with brine and dried over $MgSO_4$. Concentrated and recrystallized from hexane-CH_2Cl_2 to give title compound as orange crystal. (204 mg, 100%) mp 237-238 °C. $[\alpha]_D$ -7.25 (c 0.91, $CHCl_3$). FAB-MS 678(M^+). ^1H NMR ($CDCl_3$) δ 6.04 (1H, s), 4.48 (2H, m), 4.23 (2H, m), 4.15 (2H, m), 4.08 (10H, s), 2.55 (4H, m), 2.17 (6H, s), 1.86 (4H, m). ^{13}C NMR δ 184.6, 95.7, 85.7, 81.0, 76.7, 75.4, 73.0, 70.5, 68.7, 67.5, 30.9, 30.0, 15.5. HR-MS Calcd for $C_{33}H_{35}O_2Fe_2Rh$; 678.0391. Found; 678.0392.

Allylpalladium (*R,R*)-bis(2-methylferrocenyl)propane-1,3-dionate (**8b**)

Prepared as described for (COD)Rh(BMPD) by using (Allyl)PdCl/2 instead of (COD)RhCl/2. (yield:100%) mp 76-77 °C. $[\alpha]_D$ -40.3 (c 0.92, $CHCl_3$). FAB-MS 614(M^+). ^1H NMR ($CDCl_3$) δ 6.19 (1H, s), 5.60 (1H, m), 4.58 (2H, m), 4.25 (2H, m), 4.18 (2H, m), 4.12 (5H, s), 4.08 (5H, s), 3.83 (2H, d, J = 6.7 Hz), 2.94 (1H, d, J = 3.0 Hz), 2.88 (1H, d, J = 3.0 Hz), 2.29 (3H, s), 2.28 (s, 3H). ^{13}C NMR ($CDCl_3$) δ 185.4, 112.0, 97.2, 85.4, 82.4, 72.8, 70.5, 69.1, 67.6, 54.6, 54.5, 15.5. HR-MS Calcd for $C_{28}H_{28}O_2Fe_2Pd$; 613.9823. Found; 613.9839.

Diethylboron (*R,R*)-bis(2-methylferrocenyl)propane-1,3-dionate (**9**)

To a solution of (*R,R*)-BMPD (140.4 mg, 0.3 mmol) in 15 ml of toluene was added 1 ml of BEt_3 (1M in hexane). After being refluxed for 48 h, the reaction mixture was concentrated and chromatographed to give Et_2B(BMPD) as dark red crystal. (121 mg, 70%).
mp 82-83°C. $[\alpha]_D$ -58.1 (c 0.97, $CHCl_3$). FAB-MS 536 (M^+). ^1H NMR ($CDCl_3$) δ 5.92 (1H, s), 4.65 (2H, m), 4.45 (2H, m), 4.38 (2H, m), 4.16 (10H, s), 2.31 (6H, s), 0.92 (6H, m), 0.59 (4H, m). ^{13}C NMR ($CDCl_3$) δ 186.9, 93.5, 87.3, 75.1, 74.8, 71.0, 69.9, 69.0, 15.5, 9.0. HR-MS Calcd for $C_{29}H_{33}O_2BFe_2$; 536.1272, Found; 536.1279.

General procedure for the silylcyanation reaction: Reaction with benzaldehyde.

A solution of $Y_5(O)(OiPr)_{13}$ (13.3 mg, 0.01 mmol) and (*R,R*)-BMPD (23.4 mg, 0.05 mmol) in 2 ml CH_2Cl_2 was stirred at room temperature for 1 h. Benzaldehyde (106 mg, 1 mmol) was added at room temperature and after 3 min. the reaction mixture was cooled to -78 °C. Benzaldehyde (426 mg, 4 mmol) and TMSCN (750 mg, 7.5 mmol) were added in three portion in every 30 min. The reaction mixture was stirred for another 30 min and poured into a mixture of 1N HCl (aqueous) and THF. The resulting two phase mixture was vigrously stirred for 1 h to hydrolyze the silyl ether. Usual work up followed by chromatographic purification afforded (*S*)-(-)-α-hydroxyphenylacetonitrile, 890 mg, 98%, $[\alpha]_D$=-39.1 (c=2.21, $CHCl_3$). The enantiomeric purity of the product was determined as 90% ee by HPLC analysis of its MTPA ester: [eluent, hexane-ethyl acetate (15:1) 1 ml/min; Rt = 9.2 min (*R*) and 10.5 min (*S*)]

Characterization of the cyanohydrins:

(*S*)-α-Hydroxyphenylacetonitrile[23]

$[\alpha]_D$ -39.1 (c = 0.80, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 7.40~7.60 (5H, m), 5.55 (1H, s), 2.90 (1H, bs). ^{13}C NMR ($CDCl_3$) δ 135.2, 129.8, 129.1, 126.6, 118.8, 63.5. Enantiomeric purity was 90 %ee by HPLC analysis of the (*R*)-MTPA ester. (μ-Porasil, Hexane : EtOAc = 15 : 1, 1 ml/min; Rt = 9.2 min (*R*) and 10.5 min (*S*)).

(*S*)-2-Hydroxy(4-methylphenyl)acetonitrile[16]

$[\alpha]_D$ -47.2 (c 1.60, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 7.41 (2H, d, J = 8.2 Hz), 7.24 (2H, d, J = 8.2 Hz), 5.48 (1H, s), 3.28 (1H, bs), 2.38 (3H, s). ^{13}C NMR ($CDCl_3$) δ 139.9, 132.3, 129.8, 126.6, 119.0, 63.3, 21.2. Enantiomeric purity was 91% ee by HPLC analysis of the (*R*)-MTPA ester. (μ-Porasil, Hexane : EtOAc = 15 : 1, 1 ml/min; Rt = 8.2 min (*R*) and 9.1 min (*S*)).

(*S*)-2-Hydroxy(4-phenylphenyl)acetonitrile

mp 105-106 °C. $[\alpha]_D$ -33.3 (c 0.72, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 7.30~7.70 (9H, m), 5.54 (1H, d, J = 6.9 Hz), 2.88 (1H, d, J = 6.9 Hz). ^{13}C NMR ($CDCl_3$) δ 142.9, 139.9, 134.1, 128.7, 127.9, 127.1, 118.4, 63.5. Enantiomeric purity was 90% ee by HPLC analysis of the (*R*)-MTPA ester. (μ-Porasil, Hexane : EtOAc = 15 : 1, 1 ml/min; Rt = 9.9 min (*R*) and 11.2 min (*S*)).

(*S*)-2-Hydroxy(4-methoxyphenyl)acetonitrile[16]
mp 72-73 °C. $[\alpha]_D$ -38.3 (c 1.86, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 7.44 (2H, m), 6.95 (2H, m), 5.47 (1H, d, J = 6.8 Hz), 3.83 (3H, s), 3.08 (1H, d, J = 6.8 Hz). ^{13}C NMR ($CDCl_3$) δ 160.6, 128.3, 127.5, 118.9, 114.5, 63.2, 55.4. Enantiomeric purity was 84% ee by HPLC analysis of the (*R*)-MTPA ester. (μ-Porasil, Hexane : EtOAc = 15 : 1, 2 ml/min; Rt = 9.8 min (*R*) and 11.3 min (*S*)).

(*S*)-2-Hydroxy(4-tert-butylphenyl)acetonitrile
$[\alpha]_D$ -28.5 (c 1.08, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.48 (4H, s), 5.49 (1H, s), 3.48 (1H, s), 1.32 (9H, s). Enantiomeric purity was 72% ee by HPLC analysis of the (*R*)-MTPA ester. (μ-Porasil, Hexane : EtOAc = 15 : 1, 1 ml/min; Rt = 6.7 min (*R*) and 7.3 min (*S*)).

(*S*)-2-Hydroxy(4-fluorophenyl)acetonitrile
$[\alpha]_D$ -30.7 (c 1.50, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 7.50 (2H, m), 7.16 (2H, m), 5.51 (1H, bs), 3.66 (1H, bs). ^{13}C NMR ($CDCl_3$) δ 163.3 (d, J = 249.5 Hz), 130.9, 128.6 (d, J = 8.5 Hz), 118.7, 116.2 (d, J = 22.1 Hz), 62.7. Enantiomeric purity was 81% ee by HPLC analysis of the (*R*)-MTPA ester. (μ-Porasil, Hexane : EtOAc = 15 : 1, 1 ml/min; Rt = 10.1 min (*R*) and 11.5 min (*S*)).

(*S*)-2-Hydroxy(4-chlorophenyl)acetonitrile
$[\alpha]_D$ -23.5 (c =1.48, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 7.41 (4H, m), 5.51 (1H, s), 3.50 (1H, s). Enantiomeric purity was 60% ee by HPLC analysis of the (*R*)-MTPA ester. (μ-Porasil, Hexane : EtOAc = 15 : 1, 1 ml/min; Rt = 9.1 min (*R*) and 10.2 min (*S*)).

(*S*)-α-Hydroxy(4-cyanophenyl)acetonitrile[16]
mp 63-64 °C. $[\alpha]_D$ -11.2 (c 1.00 , $CHCl_3$). ^1H NMR ($CDCl_3$) δ 7.73 (4H, m), 5.64 (1H, d, J = 6.5 Hz), 3.70 (1H, d, J = 6.5 Hz). ^{13}C NMR ($CDCl_3$) δ 140.1, 132.9, 127.2, 118.0, 117.9, 113.3, 62.5. Enantiomeric purity was 30% ee by NMR analysis of the (*R*)-MTPA ester.

(*S*)-2-Hydroxy(4-trifluoromethylphenyl)acetonitrile
$[\alpha]_D$ -2.4 (c =1.20, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 7.68 (4H, m), 5.53 (1H, bs), 3.58 (1H, bs). The ee of the product was determined as 10% ee by ^1H NMR analysis of its MTPA ester.

(*S*)-2-Hydroxy(2-methoxyphenyl)acetonitrile
$[\alpha]_D$ -23.8 (c = 3.05, $CHCl_3$).^1H NMR ($CDCl_3$) δ 7.40 (2H, m), 6.90 (2H, m), 5.59 (1H, d, J = 7.0Hz), 3.94 (3H, s), 3.73 (1H, d, J = 7.0 Hz). Enantiomeric purity was 75% ee by HPLC analysis of the (*R*)-MTPA ester. (μ-Porasil, Hexane : EtOAc = 15 : 1, 1 ml/min; Rt = 8.4 min (*R*) and 10.0 min (*S*)).

(*S*)-α-hydroxy(3-phenoxyphenyl)acetonitrile[24]
$[\alpha]_D$ -13.6 (c 1.80, benzene). ^1H NMR ($CDCl_3$) δ 6.85~7.55 (9H, m), 5.48 (1H, d, J = 3.6 Hz), 3.24 (1H, d, J = 3.6 Hz). ^{13}C NMR ($CDCl_3$) δ 158.1, 156.3, 137.0, 130.5, 129.9, 123.9, 120.9, 119.6, 119.3, 118.6, 116.6, 63.1. Enantiomeric purity was 79% ee by HPLC analysis of the (*R*)-MTPA ester. (μ-Porasil, Hexane : EtOAc = 15 : 1, 1 ml/min; Rt = 9.9 min (*R*) and 11.0 min (*S*)).

(*S*)-2-Hydroxy(1-naphthyl)acetonitrile
$[\alpha]_D$ -38.0 (c 1.02, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 8.20-7.40 (7H, m), 6.15 (1H, d, J = 6.9Hz), 3.41 (1H, d, J = 6.9 Hz). Enantiomeric purity was 58% ee by HPLC analysis of the (*R*)-MTPA ester. (μ-Porasil, Hexane : EtOAc = 15 : 1, 1 ml/min; Rt = 10.0 min (*R*) and 11.2 min (*S*)).

(*S*)-2-Hydroxy(2-naphthyl)acetonitrile[16]
$[\alpha]_D$ -11.0 (c 1.50, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 7.90 (4H, m), 7.50 (3H, m), 5.72 (1H, bs), 2.97 (1H, bs). Enantiomeric purity was 73% ee by HPLC analysis of the (*R*)-MTPA ester. (μ-Porasil, Hexane : EtOAc = 15 : 1, 1 ml/min; Rt = 9.6 min (*R*) and 10.7 min (*S*)).

(*S*)-(E)-2-Hydroxy-4-phenyl-3-butenenitrile[16]
$[\alpha]_D$ -17.6 (c 2.30, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 7.39 (5H, m), 6.91 (1H, dd, J = 15.8, 1.2 Hz), 6.25 (1H, dd, J = 15.8, 5.9 Hz), 5.18 (1H, m), 2.98 (1H, d, J = 7.3 Hz). Enantiomeric purity was 68% ee by HPLC analysis of the (*R*)-MTPA ester. (μ-Porasil, Hexane : EtOAc = 15 : 1, 1 ml/min; Rt = 9.7 min (*R*) and 11.0 min (*S*)).

(*R*)-2-hydroxy-3,3-dimethylbutyronitrile[16]
$[\alpha]_D$ 5.81 (c 1.65, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 4.08 (1H, bs), 2.70 (1H, bs), 1.01 (9H, s). ^{13}C NMR ($CDCl_3$) δ 119.1, 70.4, 35.3, 24.9. Enantiomeric purity was 49% ee by HPLC analysis of the (*R*)-MTPA ester. (μ-Porasil, Hexane : EtOAc = 15 : 1, 1 ml/min; Rt = 6.2 min (*R*) and 7.8 min (*S*)).

(*R*)-α-hydroxycyclohexaneacetonitrile[16]
$[\alpha]_D$ 6.8 (c 1.70, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 4.27 (1H, t, J = 6.3 Hz), 2.86 (1H, d, J = 6.4 Hz), 1.61~1.95 (6H, m), 1.03~1.45 (5H, m). ^{13}C NMR ($CDCl_3$) δ 119.3, 66.2, 42.1, 28.1, 27.8, 25.9, 25.4, 25.3.
Enantiomeric purity was 49% ee by HPLC analysis of the (*R*)-MTPA ester. (μ-Porasil, Hexane : EtOAc = 15 : 1, 1 ml/min; Rt = 6.1 min (*R*) and 7.4 min (*S*)).

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