Pergamon

Tetrahedron 56 (2000) 7187–7191

TETRAHEDRON

Asymmetric Cyclopropanation of Styrene Catalyzed by Cu–(Chiral Schiff-Base) Complexes

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Received 1 March 2000; revised 21 June 2000; accepted 6 July 2000

Abstract—Asymmetric cyclopropanation of olefins was carried out with chiral copper–Schiff base complexes derived from copper acetate monohydrate, substituted salicylaldehydes and a chiral amino alcohol. Substituents on salicylaldehyde framework demonstrate a significant effect on the steroselectivities. Those with electron-withdrawing properties enhance the selectivities, whereas bulky sustituents in *ortho* position to the phenol hydroxy group decrease the selectivities. An ee of more than 98% was achieved for the reaction of styrene with diazoacetate.

Introduction

Chiral cyclopropyl esters are very important intermediates in the synthesis of optically pure molecules, in particular, biologically active compounds.[1,2] Catalytic asymmetric cyclopropanation of diazoacetate with alkene has been one of the most efficient synthetic methods for this kind of compound. Among the efficient catalysts which have been developed, copper–Schiff base complexes derived from chiral amino alcohols are of particular significance because they are effective for the intermolecular cyclopropanation of various substituted olefins including mono-, di-, and tri-substituted olefins, as well as for intramolecular cyclopropanation.[3–8] The successful industrial application of this kind of catalysts in the synthesis of chiral 2,2-dimethylcyclopropanecarboxylic acid makes it a significant achievement in asymmetric catalysis.[9] Even though it has received so much attention, to our knowledge, modification of this kind of catalyst to obtain higher enantioselectivity had only focused on the modification of chiral amino alcohols until 1999, Cai reported that copper–Schiff base complexes derived from 2-hydroxyl-5-methyl-1,3-benzenebisaldehyde were used as the catalyst.[10] However, other modifications of salicylaldehyde to achieve high ee has not been reported so far. Here we report our results of ee higher than 98% for the cyclopropanation of styrene with copper–Schiff base catalysts modified on the framework of the benzene ring of salicylaldehyde. This is the highest ee for the reaction of styrene with a copper–(Schiff base) complex as the catalyst. It is also the first catalyst without C_2 symmetry giving ee's comparable to those obtained with the most efficient catalysts with a C_2 symmetry developed in the last decade.[11–23]

Results and Discussion

According to the proposed mechanism of asymmetric cyclopropanation,[6] metal-carbenes (**A1** and **A2**) (Scheme 1) are involved as the intermediates. Approach of the alkene to the metal-carbene occurs from the less hindered side, giving rise to the enantioselectivity. The decision to study the electronic and steric effects of substituents on the salicylaldehyde framework was based on the hypothesis that substituents R^1 and R^2 may affect the stability of the metal-carbene and the metallacyclobutane (**B1**, **B2**, **B3** and **B4**), key intermediates of this reaction, thus altering the enantioselectivity. We therefore attempted to replace some hydrogen atoms on the salicylaldehyde framework with other substituents. The positions of substitution were *para* or *ortho*, *para* to the hydroxy group of salicylaldehyde, and the substituents include *t*-butyl, chloro, and nitro groups as a consequence of their ready synthesis and their different steric and electronic properties. Structures of these catalysts are shown in Scheme 2. They were synthesized according to the route in Scheme 3.

The results of asymmetric cyclopropanation of styrene are shown in Table 1. Firstly, it is noteworthy that this kind of catalyst is different from the previous chiral copper catalysts in that the ee's for the *cis* isomer are higher than those for the *trans* isomer for the cyclopropanation of styrene.[2] Similar phenomena were reported by Doyle[9] and Cai[10] with Rh(II)–carboxamide and Cu–Schiff base as the catalyst, respectively, even though Cai's catalysts afford the opposite result in most cases. Secondly, substituents on salicylaldehyde ring show a significant influence upon

Keywords: asymmetric cyclopropanation; styrene; Schiff base.
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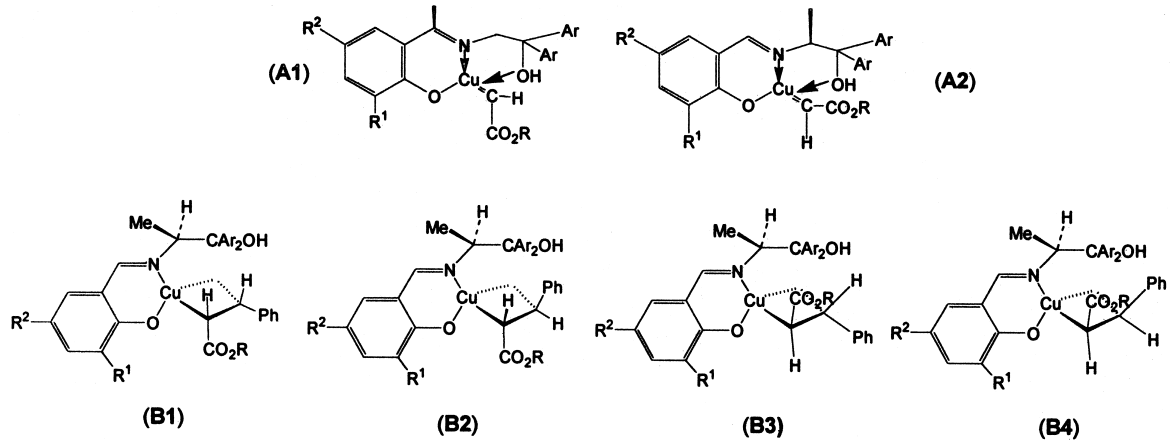
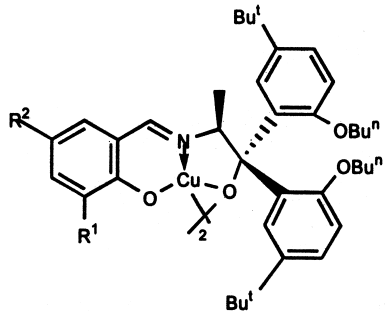
PII: S0040-4020(00)00623-2



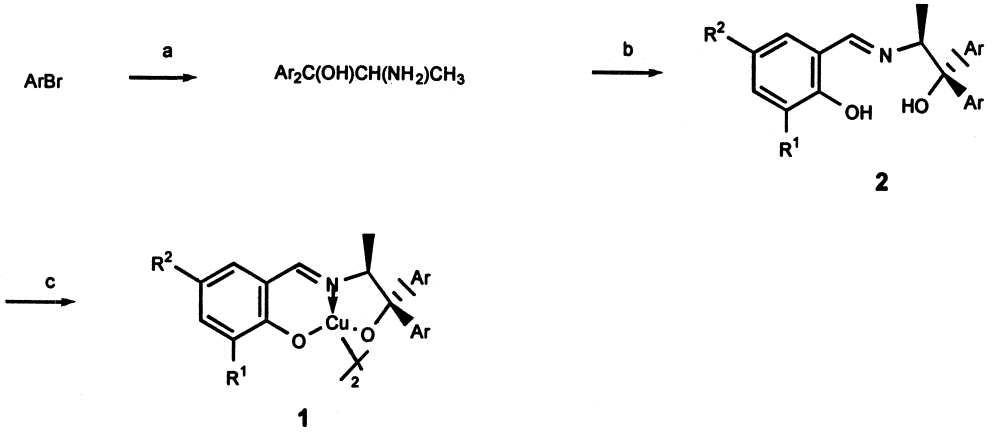
Scheme 1. Some intermediates in asymmetric cyclopropanation.



	R^1	R^2
1a	H	H
1b	H	^{t}Bu
1c	^{t}Bu	^{t}Bu
1d	H	Cl
1e	Cl	Cl
1f	H	NO_2
1g	NO_2	NO_2

Scheme 2. Structures of catalysts **1a**–**1g**.

the yields and enantioselectivities of the products. With catalyst **1a** derived from salicylaldehyde and a chiral amino alcohol, an ee around 80% was obtained for the reaction of styrene with ethyl diazoacetate. Only low to moderate ee were obtained with catalysts **1b** and **1c** bearing a *t*-butyl group, a sterically demanding and electron-donating group (entries 2–5). Substitution of the *para*-hydrogen atom in catalyst **1a** with electron-withdrawing substituents, such as a nitro group or a chlorine atom, resulted in an increase of the yield and ee of both *trans* and *cis* isomers (entries 6, 8 and 10). Catalyst **1e** with one more chlorine atom, gave rise to a higher ee of the cyclopropyl esters than catalyst **1d**. Thus, reducing the electron density on salicylaldehyde favors the enantioselectivity. The best results were obtained with catalyst **1f** when ethyl diazoacetate was used (entries 10 and 11). However, introduction of two nitro groups resulted in a decrease of the ee (entry 10 vs. entry 12), even though it decreased the electron density on the salicylaldehyde ring. The results reveal the complexity of the substituents on the salicylaldehyde ring upon the reaction. The negative effect of the second nitro group can be explained more reasonably as a steric effect because the introduction of a nitro group, which is larger than hydrogen and chlorine atoms, to the *ortho* position of



Scheme 3. Synthesis of catalysts **1a**–**1g**. Ar=2-*n*-butoxyl-5-butylphenyl: (a) i: Mg, 1,2-dimethoxyethane; ii: methyl alaninate hydrochloride; (b) substituted salicylaldehyde; (c) copper acetate monohydrate, NaOH.

Table 1. Asymmetric cyclopropanation of styrene

Entry	Cat.	R in RDA[a]	Yield (%)[b]	*cis*/*trans*[c]	ee % of *cis*[c,d]	ee% of *trans*[c,e]
1	**1a**	Et	53	33.5:55.5	79.3	71.6
2	**1b**	Et	52	37.7:62.3	75.6	59.5
3	**1b**	*i*-Bu	45	31.1:68.9	78.7	56.9
4	**1c**	Et	65	33.8:66.2	56.9	38.8
5	**1c**	*i*-Bu	36	28.6:71.4	38.8	18.6
6	**1d**	Et	47	38.1:61.9	80.1	67.7
7	**1d**	*i*-Bu	44	31.0:69.0	>98.0	68.9
8	**1e**	Et	85	41.4:58.6	89.6	77.0
9	**1e**	*i*-Bu	48	32.0:68.0	89.9	70.6
10	**1f**	Et	92	46.9:53.1	89.2	82.8
11	**1f**	*i*-Bu	50	33.6:66.4	>98.0	73.9
12	**1g**	Et	59	44.3:55.7	80.5	68.5
13	**1g**	*i*-Bu	53	34.4:65.6	78.6	60.7

Reaction conditions: 1 mmol of alkyl diazoacetate, 1.0 mL of styrene, 1 mol% of catalyst (based on diazoacetate), 3.0 mL of dichloroethane, 40°C.

[a] Alkyl diazoacetate.

[b] Based on alkyl diazoacetate and determined by GC analysis with diethyl adipate as the internal standard.

[c] Determined by GC analysis (β-cyclodextrin chiral capillary column, 30 m×0.25 mm ID, 0.25 mm film, column temp. 130°C); configurations of the products were determined by the comparison of GC elution order of the enantiomers with authentic samples prepared according to the literature.[10]

[d] 1*R*,2*S* as the major enantiomer.

[e] 1*R*,2*R* as the major enantiomer.

Table 2. Cyclopropanation of other olefins

Olefin	*trans*/*cis*	ee of *cis* isomers	ee of *trans* isomers
1,1-Diphenylethene		92.7	
5,5,5-Trichloro-2-methyl-2-pentene	34.9:65.1	55.1	26.1
2,5-Dimethyl-2,4-hexadiene	71.8:28.2	35.0	74.0

Reaction conditions: **1f** was used as the catalyst, 0.114 g of ethyl diazoacetate when 1,1-diphenylethene or 5,5,5-trichloro-2-methyl-2-pentene was used as olefin, and 0.224 g of *l*-menthyl diazoacetate was used for the reaction of 2,5-dimethyl-2,4-hexadiene, 1.0 mL of olefin, 4.0 mL of 1,2-dichloroethane, 40°C.

the hydroxylate in the phenol framework of the catalyst, leads to a steric repulsion. The enantioselectivity is very sensitive to the size of the subsituent in the *ortho* position of the phenol phenoxide of the catalyst since it is very close to and has a steric repulsion with the ester groups in **B1** and **B2**, which yield the major isomers of the products. A bulky substituent will therefore decrease the ee.

From Table 1, the conclusion can be drawn that an electron-withdrawing substituent on the salicylaldehyde group of the catalyst favors the ee of both *trans* and *cis* products, which is different to the case when Co–Salen catalyzes cyclopropanation.[17] A bulky substituent at the *ortho*-position to the phenol hydroxy group, however, decreases the ee.

The use of *i*-butyl diazoacetate instead of ethyl diazoacetate results in an increase in ee for the *cis* isomer and a decrease in ee for the *trans* isomer when there is a *para*-substituent instead of a hydrogen atom on the salicylaldehyde. Values of ee higher than 98% were obtained when *i*-butyl diazoacetate was used in the presence of catalyst **1d** or **1f**. These results are comparable to the results with the most efficient catalysts reported to date, including Cu–semicorrin, Cu–bisoxazoline, Cu–bipyridine, etc.[10–19] Furthermore, when one or two chlorine atoms or nitro groups are introduced, the ligands formed are easy to purify due to their high melting points. A recrystallization is sufficient to purify them. However, the ee of both *cis* and *trans* isomers decreases with the use of *i*-butyl diazoacetate instead of ethyl diazoacetate when there are substituents in both the *ortho* and *para* positions, even when the subtstituent is a chlorine atom. This rarely occurs when other kinds of catalyst were used in cyclopropanation. It is generally known that the ee will increase when a diazoacetate with a bulkier alkyl is used. The interaction between the alkyl group in RDA and the substituent at the *ortho* position to hydroxylate in the salicylaldehyde ring will inhibit the formation of **B1** and **B2** as shown in Scheme 1, which yield the predominant isomers of *cis* and *trans* isomers, respectively. The ee of the product will decrease by the steric repulsion between the alkyl in RDA and the group in the *ortho* position. A dramatic decrease in the ee was observed with the catalyst derived from *o*,*p*-di(*t*-butyl)salicylaldehyde when *i*-butyl diazoacetate was used instead of ethyl diazoacetate, whereas only a small (or no) decrease was found with the catalyst derived from *o*,*p*-dichloro and dinitro-salicylaldehyde.

This kind of catalyst is effective for the asymmetric cyclopropanation of various substituted olefins. Some results are summarized in Table 2. High stereoselectivities are obtained for disubstituted and trisubstituted olefins.

Experimental

Unless otherwise noted, all reactions were carried out under an argon atmosphere. Substituted salicylaldehydes were synthesized according to literature methods.[24–26] Optical rotations were measured on a SEPA-200 high sensitive polarimeter. NMR spectra were recorded on a Bruker DRX-400NMR spectrometer with tetramethyl silane as an

internal standard (δ value in $CDCl_3$). The yields and ee values of cyclopropyl derivatives were determined by GC analyses with a chiral capillary column (30 m×0.25 mm permethyl cyclopdextrin, ID, 0.25 μm film) at 130°C. The configurations of phenylcyclopropanecarboxylate were determined using GC by comparison of GC elution order of the enantiomers with authentic samples prepared according to the literature.

(*S*)-2-Amino-1,1-di(2-*n*-butoxy-5-*t*-butylphenyl)propanol. The hydrochloride salt of methyl L-alaninate (0.90 g, 7.14 mmol) was added to a cooled Grignard solution derived from 2-*n*-butoxy-5-*t*-butyl bromobenzene[10,27] (15.5 g, 54.0 mmol) and magnesium (1.44 g, 59.3 mmol) with vigorous stirring. The mixture was refluxed overnight, and then cooled to room temperature. Saturated aqueous solution of ammonium chloride (50 mL) was added to the cooled mixture, and the organic phase was separated. The aqueous phase was extracted with chloroform (3×50 mL). The combined organic solution was washed with aqueous sodium bicarbonate, saturated brine, dried and concentrated. The residue was purified with a silica gel column with petroleum ether–diethyl ether (8:1 to 1:1) as eluent and gave the product as a viscous oil (2.40 g, 70%); [Found: C, 77.0%; H, 9.9%; N, 2.8%. $C_{31}H_{49}NO_3$ requires: C, 76.97%; H, 10.21%; N, 2.90%]; $[\alpha]_D=-36.1$ (*c* 1.776, $CHCl_3$); ^{1}H NMR: 7.67 (s, 1H), 7.65 (s, 1H), 7.14 (d, *J*=8.3 Hz, 1H), 7.11 (d, *J*=6.9 Hz, 1H), 6.69 (d, *J*=8.5 Hz, 1H), 6.62 (d, *J*=8.5 Hz, 1H), 4.20 (br, 3H), 3.77–3.69 (m, 4H), 1.52–1.47 (m, 4H), 1.34 (s, 9H), 1.33 (s, 9H), 1.28 (m, 7H), 0.88 (m, 6H); ^{13}C NMR: 154.1, 153.3, 142.1, 141.8, 132.8, 132.0, 125.6, 125.1, 124.5, 124.1, 112.1, 111.5, 80.0, 68.1, 67.8, 49.7, 34.2 (2C), 31.5 (^{t}Bu), 31.4 (^{t}Bu), 31.1, 29.9, 19.3 (2C), 16.8, 13.9 (2C).

Schiff bases. *General procedure:* (*S*)-2-amino-1,1-di(2-*n*-butoxy-5-*t*-butylphenyl)propanol (0.102 g, 2.11 mmol) and 2-hydroxy-3,5-dinitrobenzaldehyde (0.0448 g, 2.11 mmol) were dissolved in ethanol (10 mL) and the mixture was stirred for 6 h. Most of ethanol was removed in vacuum and the residue was purified by column chromatography to afford pure Schiff base **2g** (0.094 g, 66%) as a yellow solid; mp 197–198°C; [Found: C, 67.5%; H, 7.4%; N, 6.3%. $C_{38}H_{51}N_3O_8$ requires C, 67.33%; H, 7.58%; N, 6.20%]; $[\alpha]_D=166.8$ (*c* 0.698, benzene); IR: 3480, 3070 (w), 2960, 2870, 1656, 1620, 1557, 1500, 1460, 1362, 1315, 1230, 1172, 1150, 1094, 1032, 980, 935, 904, 810 (m), 752 (w), 710 cm^{-1}; ^{1}H NMR: ($CDCl_3$) δ 14.20 (s, br, 1H, OH), 8.88 (d, *J*=2.9 Hz, H), 8.17 (s, 1H), 7.85 (s, 1H), 7.57 (s, 1H), 7.54 (s, 1H), 7.26 (d, *J*=7.1 Hz, 1H), 7.14 (d, *J*=8.5 Hz, 1H), 6.77 (d, *J*=8.5 Hz, 1H), 6.73 (d, *J*=8.5 Hz, 1H), 5.61 (s, 1H), 5.24 (m, 1H), 3.80 (m, 4H), 1.55–1.50 (d, 7H), 1.36 (s, 9H, ^{t}Bu), 1.28–1.29 (m, 4H), 1.15 (s, 9H, ^{t}Bu), 0.91 (t, *J*=7.3 Hz, 6H); ^{13}C NMR: 170.6, 164.6, 153.3, 152.7, 142.9, 142.2, 140.7, 135.9, 130.8, 129.6, 128.9, 128.2, 125.7, 125.5, 125.2, 124.6, 116.5, 112.5, 112.0, 78.9, 68.2, 68.1, 62.1, 34.2, 34.1, 31.5 (^{t}Bu), 31.3 (^{t}Bu), 30.9, 30.8, 19.1, 19.0, 16.3, 13.7 (2C).

2a. Yellow viscous oil; [Found: C, 77.4%; H, 9.0%; N, 2.5%. $C_{38}H_{53}NO_4$ requires C, 77.64%; H, 9.09%; N, 2.38%]; $[\alpha]_D=130.4$ (*c* 2.676, benzene); IR: 3510, 3040, 2960, 2863, 1632, 1620, 1580, 1500, 1460, 1390, 1365, 1283, 1268, 1243, 1140, 1075, 1030, 970, 910, 811, 758, 700 cm^{-1}; ^{1}H NMR: 13.51 (s, br, 1H, OH), 8.12 (s, 1H), 7.64 (s, 2H), 7.17–7.09 (m, 3H), 7.01–7.00 (m, 2H), 6.77–6.56 (m, 2H), 5.14 (s, 1H), 3.68 (m, 2H), 3.60 (t, *J*=7.1 Hz, 2H), 1.41–1.37 (m, 7H), 1.30 (s, 9H), 1.26–1.23 (m, 4H), 1.17 (s, 9H), 0.82 (t, *J*=7.1 Hz, 6H); ^{13}C NMR: 163.5, 162.4, 153.8, 153.2, 141.9 (2C), 132.7, 132.5, 131.5, 131.0, 125.7 (2C), 124.7, 124.4, 118.7, 117.4, 117.2, 111.9, 111.7, 80.0, 68.0, 67.2, 66.0, 34.2, 34.1, 31.6 (^{t}Bu), 31.4 (^{t}Bu), 31.0 (2C), 19.1 (2C), 17.2, 13.7 (2C).

2b. Yellow viscous oil; [Found: C, 78.7%; H, 9.4%; N, 1.97%. $C_{42}H_{61}NO_4$ requires C, 78.34%; H, 9.55 %; N, 2.18%]; $[\alpha]_D=70.6$ (*c* 0.666, benzene); IR: 3510, 3040 (w), 2960, 2910, 2870, 1640, 1590, 1490, 1465, 1390, 1268, 1242, 1184, 1145, 1075, 1030, 1013, 970, 830, 811, 747 cm^{-1}; ^{1}H NMR: 13.40 (s, br, 1H), 8.25 (s, 1H), 7.71 (s, 1H), 7.69 (s, 1H), 7.22 (d, *J*=8.7 Hz, 1H), 7.18 (d, *J*=8.5 Hz, 1H), 7.08–7.06 (m, 2H), 6.76 (d, *J*=8.7 Hz, 1H), 6.72 (d, *J*=8.6 Hz, 1H), 6.63 (d, *J*=8.5 Hz, 1H), 5.20 (s, 1H), 4.86 (m, 1H), 3.72 (t, *J*=7.3 Hz, 2H), 3.65 (m, 2H), 1.43–1.39 (m, 7H), 1.34 (s, 9H), 1.26 (s, 9H), 1.25 (s, 9H), 1.33–1.22 (m, 4H), 0.86 (t, *J*=7.3 Hz, 6H); ^{13}C NMR: 164.0, 159.9, 153.8, 153.3, 141.8 (2C), 139.9, 132.2, 129.0 (2C), 127.4, 125.7, 125.6, 124.3 (2C), 118.0, 116.6, 111.9, 111.7, 79.4, 68.0, 67.9, 65.7, 34.1, 34.0, 33.7, 31.6 (^{t}Bu), 31.4 (^{t}Bu), 31.2 (^{t}Bu), 31.0 (2C), 19.1 (2C), 17.1, 13.7 (2C).

2c. Yellow viscous oil; [Found: C, 78.7%; H, 10.2%; N, 2.2%. $C_{46}H_{69}NO_4$ requires C, 78.92%; H, 9.93%; N, 2.00%]; $[\alpha]_D=59.45$ (*c* 0.656, benzene); IR: 3520, 2960, 2870, 1630, 1610, 1500, 1475, 1390, 1362, 1268, 1250, 1150, 1075, 1030, 980, 882, 810 cm^{-1}; ^{1}H NMR: 13.96 (s, br, 1H), 8.24 (s, 1H), 7.79 (s, 1H), 7.71 (s, 1H), 7.27 (s, 1H), 7.18 (d, *J*=8.50 Hz, 1H), 7.08 (d, *J*=8.5 Hz, 1H), 6.92 (s, 1H), 6.71 (d, *J*=8.6 Hz, 1H), 6.63 (d, *J*=8.6 Hz, 1H), 5.20 (s, 1H), 4.83 (m, 1H), 3.70 (t, *J*=7.6 Hz, 2H), 3.62 (t, *J*=7.3 Hz, 2H), 1.43–1.41 (m, 7H), 1.39 (s, 9H), 1.34 (s, 9H), 1.32 (s, 9H), 1.29 (s, 9H), 1.28–1.22 (m, 4H), 0.86 (t, *J*=7.2 Hz, 6H); ^{13}C NMR: 165.1, 158.7, 153.9, 153.4, 142.0, 141.8, 138.9, 136.4, 132.4, 131.8, 126.2, 125.7 (3C), 124.3 (2C), 118.0, 112.9, 112.7, 79.6, 68.0, 67.8, 66.2, 34.9, 34.1 (2C), 33.9, 31.6 (^{t}Bu), 31.5 (^{t}Bu) 31.3 (^{t}Bu), 31.0 (^{t}Bu), 29.4, 29.2, 19.1 (2C), 17.5, 13.7 (2C).

2d. Yellow viscous oil; [Found: C, 73.5%; H, 8.6%; N, 2.2%. $C_{38}H_{52}ClNO_4$ requires C, 73.35%; H, 8.42%; N, 2.25%]; $[\alpha]_D=81.5$ (*c* 0.956, benzene); IR: 3520, 3040 (w), 2960, 2872, 1638, 1580, 1500, 1478, 1385, 1282, 1269, 1244, 1143, 1088, 1030, 1013, 970, 825 cm^{-1}; ^{1}H NMR 13.87 (s, br, 1H), 8.07 (s, 1H), 7.65 (s, 1H), 7.20–7.18 (m, 2H), 7.09–7.06 (m, 2H), 7.01 (m, 1H), 6.73 (m, 2H), 6.64–6.62 (m, 1H), 5.23 (s, 1H), 4.84 (m, 1H), 3.73 (t, *J*=7.9 Hz, 2H), 3.66 (t, *J*=6.9 Hz, 2H), 1.45–1.42 (m, 7H), 1.35 (s, 9H), 1.34–1.20 (m, 4H), 1.21 (s, 9H), 0.87 (t, *J*=7.3 Hz, 3H), 0.86 (t, *J*=7.3 Hz, 3H); ^{13}C NMR 162.7, 161.4, 153.8, 153.0, 141.9, 141.8, 131.9, 131.7, 130.0, 125.6, 125.4, 124.5 (2C), 121.6, 119.2, 119.0, 111.9, 111.7, 79.3, 68.0, 67.9, 65.6, 34.1, 34.0, 31.5 (^{t}Bu), 31.5 (^{t}Bu), 31.0 (2C), 19.1 (2C), 16.0, 13.7 (2C).

2e. Yellow solid, mp 110–112°C; [Found: C, 69.3; H, 7.9%;

N, 2.1%. $C_{38}H_{51}ClNO_4$ requires C, 69.50%; H, 7.83%; N, 2.13%]; $[\alpha]_D$=144.23 (*c* 0.936, benzene); IR: 3500, 2960, 2930, 2858, 1640, 1500, 1460, 1378, 1290, 1268, 1242, 1220, 1150, 1105, 990, 860, 814, 750 cm^{-1}; ^1H NMR: 14.82 (s, br, 1H), 7.77 (s, 1H), 7.62 (s, 1H), 7.57 (s, 1H), 7.30 (s, 1H), 7.22 (m, 1H), 7.08 (d, *J*=6.9 Hz, 1H), 6.81 (s, 1H), 6.73 (d, *J*=8.6 Hz, 1H), 6.65 (d, *J*=8.6 Hz, 1H), 5.34 (s, 1H), 4.95 (m, 1H), 3.76–3.69 (m, 4H), 1.47 (m, 7H), 1.35 (s, 9H), 1.32–1.26 (m, 4H), 1.17 (s, 9H), 0.89 (t, *J*=7.3 Hz, 3H), 0.88 (t, *J*=7.3 Hz, 3H); ^{13}C NMR: 164.2, 162.0, 153.6, 152.8, 142.4, 141.9, 133.1, 131.0, 130.7, 128.8, 125.8, 125.5, 125.2, 124.9 (2C), 118.1, 116.5, 112.0, 111.9, 79.0, 68.0 (2C), 63.2, 34.1, 34.0, 31.5 (^{t}Bu), 31.3 (^{t}Bu), 31.0, 30.9, 19.1 (2C), 16.9, 13.7 (2C).

2f. Yellow solid; [Found: C, 72.3%; H, 8.2%; N, 4.2%. $C_{38}H_{52}N_2O_6$ requires C, 72.12%; H, 8.28%; N, 4.43%]; $[\alpha]_D$=89.6 (*c* 1.208, benzene); IR: 3500, 2960, 2870, 1650, 1613, 1543, 1500, 1470, 1391, 1364, 1327, 1232, 1180, 1146, 1128, 1096, 815 cm^{-1}; ^1H NMR: 14.75 (s, br, 1H), 8.03 (s, 1H), 8.01 (s, 1H), 7.82 (s, 1H), 7.62 (s, 1H), 7.56 (m, 1H), 7.22 (m, 1H), 7.10 (m, 1H), 6.75 (d, *J*=8.6 Hz, 1H), 6.69 (d, *J*=8.6 Hz, 1H), 6.66 (d, *J*=9.4 Hz, 1H), 5.50 (s, 1H), 5.09 (s, 1H), 3.79 (t, *J*=7.4 Hz, 2H), 3.75 (t, *J*=7.1 Hz, 2H), 1.52–1.51 (m, 7H), 1.36 (s, 9H), 1.34–1.30 (m, 4H), 1.16 (s, 9H), 0.90 (t, *J*=7.3 Hz, 3H), 0.89 (t, *J*=7.3 Hz, 3H); ^{13}C NMR: 177.3, 163.6, 153.5, 152.8, 142.6, 142.1, 135.3, 131.0, 130.5, 130.1, 129.2, 125.4, 125.3 (2C), 125.2, 122.7, 113.5, 112.2, 112.0, 79.1, 68.1, 68.0, 62.1, 34.2, 34.1, 31.6 (^{t}Bu), 31.3 (^{t}Bu), 31.0 (2C), 19.2 (2C), 16.4, 13.8, 13.7.

Catalyst

General procedure: Schiff base **2d** (0.305 g, 0.491 mmol) was dissolved in ethanol (30 mL), and copper acetate monohydrate (0.100 g, 5.00 mmol) solution was added to the above solution. The mixture was stirred and aqueous sodium hydroxide solution (5%, 2.7 mL) was added to the mixture, and the stirring was continued for 1 h. Water (50 mL) was added to the mixture and the mixture was extracted with benzene (3×10 mL). After washing with water, drying and removal of benzene in vacuum, the catalyst **1d** was obtained as a violet powder (0.245 g, 73%); [Found: C, 67.1%; H, 7.6%; N, 2.0%. $CuC_{38}H_{50}ClNO_4$ requires C, 66.75%; H, 7.37%; N, 2.05%]; $[\alpha]_D$=−226.13 (*c* 0.398, benzene); IR: 3030, 2954, 2860, 1641, 1610, 1520, 1493, 1457, 1390, 1376, 1358, 1310, 1260, 1239, 1170, 1105, 1020, 1002, 900, 826, 807, 719 cm^{-1}.

Cyclopropanation

Under argon, a few drops of a solution of ethyl diazoacetate (0.114 g, 1.00 mmol) in 1,2-dichloethane (2.0 mL) was added to a mixture of the catalyst (6.0 mg, 0.01 mmol), styrene (1.0 mL) and 1,2-dichloethane (2.0 mL) at 80°C to initiate the reaction. After the mixture was cooled to 40°C, the rest of the diazoacetate solution was added to the mixture slowly and the mixture was stirred for another 4 h after all the diazoacetate was added. The solvent was removed in vacuum and the residue was passed through a short silica gel column to remove the catalyst, and was analyzed by GC (permethyl β-cyclopdextrin chiral capillary column, 30 m×0.25 mm ID, 0.25 μm film, column temp. 130°C) using an internal method with ethyl adipate as a standard. When ethyl diazoacetate and styrene were used as reactants, the retention time of the cyclopropyl derivatives is 30.09, 31.37, 35.14, 35.94 min for (1*S*,2*R*), (1*R*,2*S*), (1*R*,2*R*), (1*S*,2*S*) isomers, respectively.

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