ENANTIOSPECIFIC RING EXPANSION OF OXETANES: STEREOSELECTIVE SYNTHESIS OF TETRAHYDROFURANS

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Abstract-Enantiospecific ring expansion of oxetanes to tetrahydrofurans with diazoacetic acid ester was found to be catalyzed by the copper complex of (7*R*,7'*R*)-7,7'-di(1-*tert*-butyldimethylsiloxy-1-methylethyl)-6,6',7,7'-tetrahydro-5*H*,5'*H*-2,2'-bi-1,1'-pyrindine (**4**). For example, the reaction of (*R*)-2-phenyloxetane of 89% ee and *tert*-butyl diazoacetate with Cu-**4** complex as a catalyst provided (2*S*,3*R*)-*tert*-butyl 3-phenyltetrahydrofuran-2-carboxylate of 92% ee as a major product, while that of (*S*)-2-phenyloxetane of 85% ee provided (2*S*,3*S*)-*tert*-butyl 3-phenyltetrahydrofuran-2-carboxylate of 93% ee as a major one.

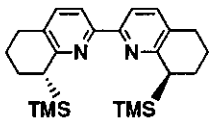
Asymmetric synthesis of tetrahydrofuran derivatives has received much attention due to their ubiquitous presence in many naturally occurring biologically active substances[1] and a considerable effort has been directed toward this subject.[2] Although there have been reported many syntheses of optically active tetrahydrofuran derivatives, the methodologies used in these syntheses are limited to a few reactions: e.g., intramolecular haloetherification and acid-catalyzed cyclization of unsaturated alcohols and epoxy alcohols.[3] Accordingly development of a new methodology for the efficient construction of tetrahydrofuran unit is still strongly required. In 1966, Nozaki *et al.* for the first time reported asymmetric

This paper is dedicated to the memory of the late Dr. Yoshio Ban.

cyclopropanation and C-O insertion reaction.[4] Since then, many effective methodologies for catalytic asymmetric cyclopropanation have been reported[5] but asymmetric C-O insertion reaction has been left without attracting chemist's notice, though it may provide a new entry to asymmetric synthesis of tetrahydrofuran derivatives. Recently, we found that the copper complex of chiral C_2-symmetric biquinoline (**1**) was an effective catalyst for asymmetric cyclopropanation.[6] This chiral copper complex was also expected to be a good catalyst for asymmetric C-O insertion reaction which proceeds *via* oxygen ylid formed by the reaction of copper-carbenoid complex with ether oxygen atom, since the enantioface of the carbenoid is strongly regulated by the chiral bipyridine ligand as shown in cyclopropanation reaction. Under this expectation, we examined the carbene insertion reaction to oxetanes catalyzed by optically active copper complex, giving tetrahydrofurans. In this paper, we describe a new methodology for asymmetric synthesis of tetrahydrofurans based on highly enantiospecific ring expansion of oxetanes using the new chiral copper-bipyrindine complex as a catalyst.[7]

Modification of Chiral Ligand

In our previous communications, we have reported that the copper complexes of chiral biquinolines



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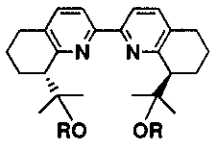
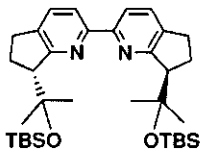


2: R=Me
3: R=TBS



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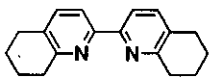

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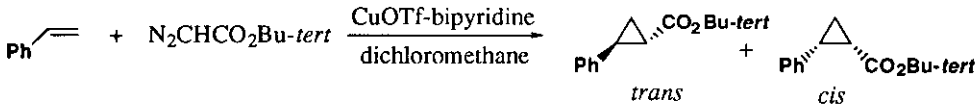


Table 1. Asymmetric cyclopropanation of styrene

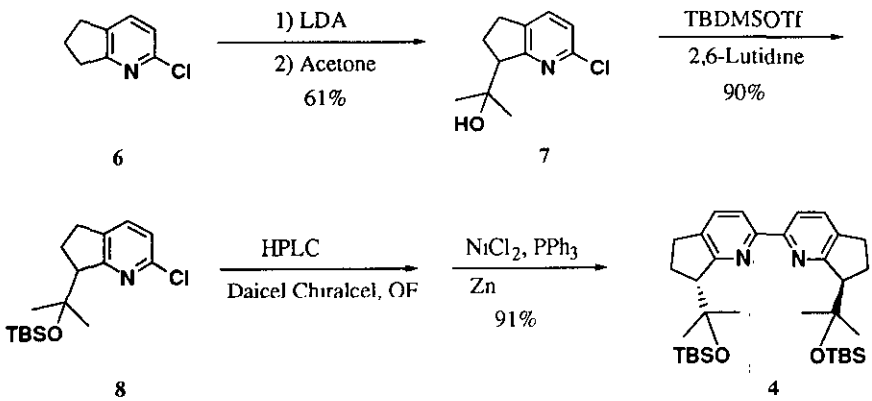
Entry	Bipyridine	Yield/%	*trans* : *cis* [a]	% ee (*trans*)[b]
1	**1**	75	86 : 14	92
2	**2**	53	66 : 34	83
3	**3**	85	81 : 19	92
4	**4**	76	81 : 19	94

a) Ratio of *trans*- and *cis*-isomers was determined by using capillary GC (NEUTRA BOND-1; 130 °C).
b) E.e. was determined by the reported procedure (Ref. 11).

bearing 8,8'-substituents such as **1** and **2** are good catalysts for the cyclopropanation of olefins and that Cu-**1** complex showed an excellent level of enantioselectivity.[6b,c] However, biquinoline ligand (**1**) is unstable and can not be stored for long time. Thus we seeked for a stable and high asymmetry-inducing chiral ligand in lieu of **1** and found that biquinoline (**3**) with bulkier *tert*-butyldimethylsiloxy group was a chiral ligand equally effective to **1** in the cyclopropanation of styrene (Table 1, Entries 1 and 3). Furthermore, the chiral ligand (**4**) bearing 6,6',7,7'-tetrahydro-5*H*,5'*H*-2,2'-bi-1,1'-pyrindine structure was found to show slightly higher asymmetric induction than the corresponding biquinoline ligand (**3**) bearing 5,5',6,6',7,7',8,8'-octahydro-2,2'-biquinoline structure (Entry 4). Fortunately ligands (**3**) and (**4**) were stable and could be stored for months in a refrigerator. Accordingly, we examined ring expansion of oxetanes with the copper complex of **4** as a catalyst.

Synthesis of New Bipyrindine Ligand (4)

Synthesis of new bipyrindine (**4**) started from 2-chloro-6,7-dihydro-5*H*-1-pyrindine (**6**) which was prepared according to the literature procedure[8] (Scheme 1). Compound (**6**) was successively treated with



6 7 8 4

Scheme 1

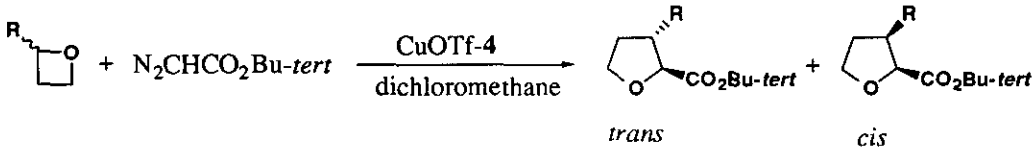
LDA and acetone at -78 °C to give alcohol (**7**), which was protected as a *tert*-butyldimethylsilyl ether (*dl*-**8**) by treatment with *tert*-butyldimethylsilyl triflate in the presence of 2,6-lutidine. Resolution of *dl*-**8** was smoothly performed with aid of hplc using optically active column (Daicel Chiralcel OF) and the less polar enantiomer (>99% ee), the configuration of which was presumed to be 7*R* (see the experimental section) was used for the next reaction. Optically active **8** was then subjected to nickel-mediated homocoupling reaction[9] to give the desired bipyrindine ligand (**4**).

Enantiospecific Ring Expansion of Oxetanes

With chiral bipyrindine (**4**) in hand, we first examined the reaction of *dl*-2-phenyloxetane with 0.5 equiv. of *tert*-butyl diazoacetate in the presence of the copper complex of **4**, expecting the kinetic resolution of *dl*-2-phenyloxetane (Table 2). Reaction proceeded smoothly at room temperature but, against our expectation, the optical purity of the unreacted oxetane was very poor (<5% ee), suggesting that the efficiency of kinetic resolution was very low (Entry 1). Both the enantiomers of *dl*-2-phenyloxetane were consumed at almost equal rate even in the presence of chiral copper catalyst and *trans*- and *cis*-tetrahydrofuran derivatives were produced in almost equimolar amounts. Interestingly, however, optical purity of *trans*- and *cis*-tetrahydrofurans was as high as 75 and 81% ee, respectively (Entry 1). On the other hand, the reaction using the copper complex of achiral ligand (**5**) as a catalyst showed modest *trans*-selectivity (Entry 2). These results strongly suggested that the chirality of Cu-**4** catalyst regulated the steric course of the reaction and that one enantiomer of the starting oxetane was converted stereospecifically into the one isomer of the product and another enantiomer into the other isomer of the product. To clarify the steric course of the reaction, we then prepared (*R*)- and (*S*)-2-phenyloxetanes and examined the ring expansion reaction (Entries 3 and 4). As expected, the reaction proceeded enantiospecifically: the reaction of (*R*)-2-phenyloxetane gave *trans*-isomer and that of (*S*)-2-phenyloxetane did *cis*-isomer as a major isomer, respectively. However, the formation of a small amount of diastereomeric product which suggested the partial participation of the cationic intermediate, was observed in each case (*vide infra*). Calculation based on the experimental data (*trans-cis* product ratio, % ees of *trans*- and *cis*-products) indicated that the face selectivities of the copper-carbenoid species were as high as 84 and 72% de for the reaction with (*R*)- and (*S*)-2-phenyloxetanes, respectively. However, epimerization *via* the cationic intermediate occurred at the rate of 3-41%, depending on the reaction pathway.[10] Interestingly the epimerization occurred to small extent (3-8%) in the reaction pathway giving the major products and to larger extent (17-41%) in the reaction pathway giving the minor products.[10] This strongly supported the idea that the reaction proceeded through the oxygen-ylid copper complex instead of free oxygen-ylid (Figure 1).

Next we examined the reaction of several other substrates. The reaction of *dl*-2-(*p*-chlorophenyl)oxetane showed the same level of enantioselectivity as *dl*-2-phenyloxetane (Entry 5). However, the reaction of *dl*-2-(*p*-methylphenyl)oxetane exhibited the diminished enantioselectivity to some extent (Entry 6), though the reason for the lowered enantioselectivity is unclear at present. The reaction of *dl*-2-(2-

phenylethynyl)oxetane also showed the almost same level of enantioselectivity as that of *dl*-2-



trans *cis*

Table 2. Ring expansion of several oxetanes with Cu-**4** complex as a catalyst

Entry	Oxetane	Yield/%, (% ee) (recovered oxetane)	Yield/% (*trans* : *cis* [a]) (tetrahydrofuran)	% ee (*trans*)	% ee (*cis*)
1	*dl*-2-phenyloxetane	30, (<5)[b]	36 (59 : 41)	75 (2*S*,3*R*)[c,d]	81 (2*S*,3*S*)[c,d]
2	*dl*-2-phenyloxetane[e]	-	31 (76 : 24)	-	-
3	(*R*)-2-phenyloxetane (89% ee)[f]	30, (87)[b]	35 (89 : 11)	92 (2*S*,3*R*)[c,d]	16 (2*S*,3*S*)[c,d]
4	(*S*)-2-phenyloxetane (85% ee)[f]	36, (87)[b]	30 (25 : 75)	11 (2*S*,3*R*)[c,d]	93 (2*S*,3*S*)[c,d]
5	*dl*-2-(*p*-chlorophenyl)oxetane	35, (1)[g]	40 (54 : 46)	75[h,i]	80[h,i]
6	*dl*-2-(*p*-methylphenyl)oxetane	-[j]	31 (50 : 50)	50[b,i]	76[i,k]
7	*dl*-2-(2-phenylethynyl)oxetane	43, (2)[k]	38 (59 : 41)[l]	75[i,m]	71[i,k]

a) Ratio of *trans*- and *cis*-isomers was determined by using capillary GC (FFAP Bonded; 200 °C), unless otherwise noted.
b) Determined by hplc using optically active column: (Daicel Chiralcel OJ; Hexane/*i*-PrOH 400:1).
c) Determined by hplc using optically active column: (Daicel Chiralcel OJ; Hexane/*i*-PrOH 15:1).
d) See the experimental section for the determination of absolute configuration of products.
e) Complex (**5**) was used instead of **4**.
f) Reaction was carried out with 0.5 equiv. of diazoacetate, since the starting oxetane was not optically pure.
g) Determined by hplc using optically active column: (Daicel Chiralpack AD; Hexane/*i*-PrOH 100:1).
h) Determined by hplc using optically active column: (Daicel Chiralcel OF; Hexane/*i*-PrOH 9:1).
i) Absolute configuration has not determined.
j) The unreacted oxetane was decomposed under the reaction conditions.
k) Determined by hplc using optically active column: (Daicel Chiralcel OJ; Hexane/*i*-PrOH 100:1).
l) Based on isolated product.
m) Determined by hplc using optically active column: (Daicel Chiralcel OD; Hexane/*i*-PrOH 100:1).

phenyloxetane (Entry 7). We next examined the ring expansion of styrene oxide. However, in agreement with the observation of Nozaki *et al.*,[4a,c] the reaction gave a complicated mixture. 2-Phenyltetrahydrofuran was inert to the reaction conditions and only the formation of di-*tert*-butyl fumarate and maleate was observed.

As described above, the ring expansion of oxetanes was considered to proceed through oxygen-ylid copper complex (**A**). If we could assume that the oxygen-ylid formation step is a crucial step for the face selection of the prochiral carbenoid carbon and that oxetanes approach from the same side as olefins do in

asymmetric cyclopropanation using Cu-**1** or Cu-**2** as a catalyst, the stereochemistry observed can be rationalized as follows (Figure 1). Oxetanes approach the carbenoid-carbon along the pathway **a**

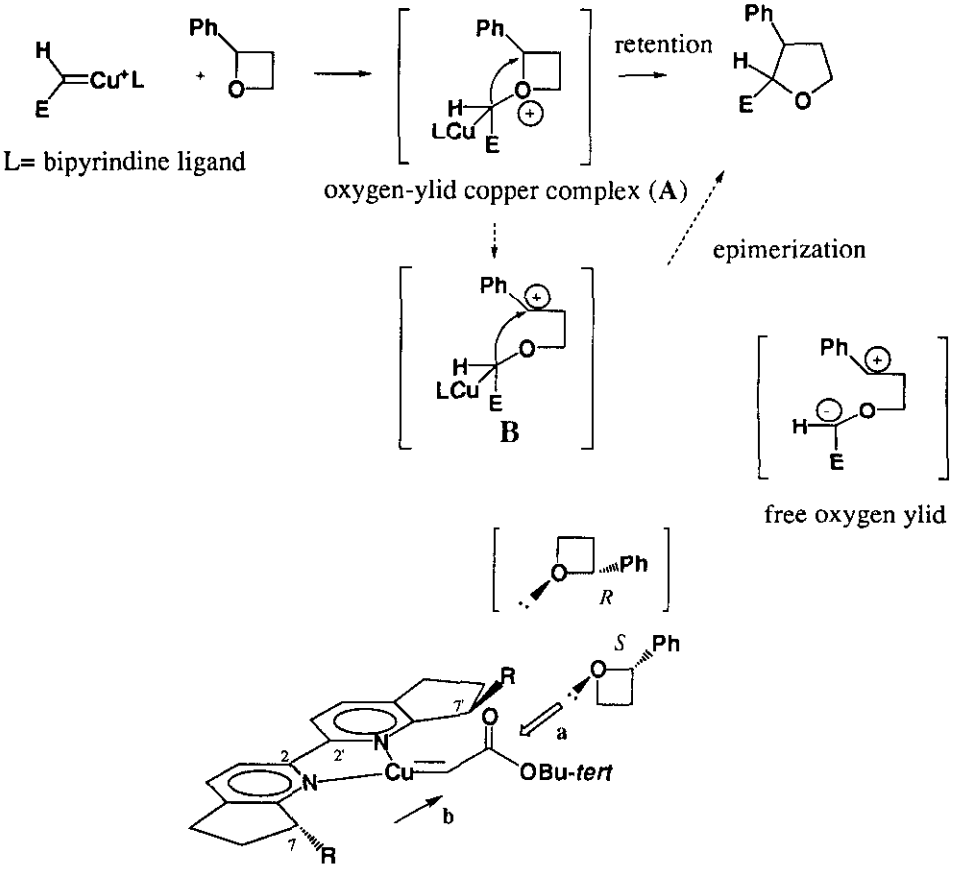


Figure 1.

preferentially, because the approach along the pathway **b** causes steric repulsion between the carbenoid ester group and C7'- substituent R on the bipyrindine ligand as the reaction proceeds.[11] Thus, the lone pair electrons *trans* to 2-phenyl group attack the *si* face of carbenoid carbon. The oxygen-ylid thus formed rearranges preferentially with retention of the configuration. Accordingly the reaction with (*R*)-2-phenyloxetane gives *trans*-isomer preferentially and that with (*S*)-2-phenyloxetane gives *cis*-isomer. However, the oxygen-ylid copper complex partially rearranges through a cationic species (**B**), causing partial epimerization. The presence of the latter pathway is supported from the absolute configuration of the minor isomer in which the configuration of C3-carbon is reversed (Entries 2 and 3).[10] Although the precise reaction mechanism is unclear at present, this proposal well explains our results.

In conclusion, we described a new approach to the optically active tetrahydrofuran derivatives, though there is still a room for improvement.

EXPERIMENTAL

Nmr spectra were recorded at 270 MHz on a JEOL EX-270 instrument. All signals were expressed as ppm down field from tetramethylsilane used as an internal standard (δ-value in $CDCL_3$). Ir spectra were obtained with a SHIMADZU FTIR-8600 instrument. Optical rotation was measured with a JASCO DIP-360 automatic digital polarimeter. High-resolution mass spectra were recorded on a JEOL JMS-SX/SX 102A instrument. Column chromatography was conducted on Silica Gel 60, 70-230 mesh ASTM, available from E. Merck. Preparative thin layer chromatography was performed on 0.5 mm x 20 cm x 20 cm E. Merck silica gel plate (60 F-254). Solvents were dried and distilled shortly before use. Reactions were carried out under an atmosphere of nitrogen or argon if necessary. $CuOTf{\cdot}0.5C_6H_6$[12] and oxetanes[13] were prepared according to the literature procedure.

(*d,l*)-2-Chloro-7-(1-hydroxy-1-methylethyl)-6,7-dihydro-5*H*-1-pyrindine (7)

Butyllithium (0.625ml, 1.6 mol dm^{-3} in hexane) was added to a solution of diisopropylamine (140 μl, 1 mmol) in THF (4 ml) at 0 °C. After being stirred for 30 min, the mixture was cooled to -78 °C. To this solution was added **6** (153 mg, 1 mmol) in THF (1 ml) dropwise and the mixture was gradually raised to -20 °C. After stirred 1 h at the temperature, the mixture was cooled to -78 °C. To this solution was added the pre-cooled (-78 °C) acetone (90 μl, 1.02 mmol) in THF (1 ml) *via* cannula. After stirred for 10 min, the mixture was quenched with saturated aqueous NH_4Cl, extracted with ether, and the extract was dried over $MgSO_4$, and concentrated. Silica gel chromatography of the residue (hexane-ethyl acetate = 9:1) gave alcohol (**7**) (128 mg, 61%) as an oil. ^1H Nmr (270 MHz): δ 7.47 (d, *J*= 7.9 Hz, 1H), 7.10 (d, *J*= 7.9 Hz, 1H), 4.91 (s, 1H), 3.32 (t, *J*= 9.2 Hz, 1H), 2.95-2.75 (m, 2H), 2.36-2.23 (m, 1H) 1.79 (dq, *J*= 9.2, and 13.2 Hz, 1H), 1.29 (s, 1H), 1.05 (s, 1H). Ir (KBr): 3450, 2972, 2937, 2876, 1638, 1585, 1570, 1423, 1402, 1379, 1171, 1123, 1092, 932, 880, 824, 673, 494 cm^{-1}. Anal. Calcd for $C_{11}H_{14}NOCl$: C, 62.41; H, 6.67; N, 6.62. Found: C, 62.43; H, 6.65; N, 6.64.

(*d,l*)-2-Chloro-7-(1-*tert*-butyldimethylsiloxy-1-methylethyl)-6,7-dihydro-5*H*-1-pyrindine (8)

To a stirred solution of alcohol (**7**) (68 mg, 0.32 mmol) and 2,6-lutidine (51 μl, 0.39 mmol) in CH_2Cl_2 (1.3 ml) was added *tert*-butyldimethylsilyl trifluoromethanesulfonate (89 μl, 0.39 mmol) at 0 °C. After

being stirred for 30 min, the mixture was quenched with saturated aqueous $NaHCO_3$, extracted with ether, and the extract was dried over $MgSO_4$, and concentrated. Silica gel chromatography of the residue (hexane-ethyl acetate = 19:1) gave silyl ether (**8**), (94 mg, 90%) as an oil. ^{1}H Nmr (270 MHz): δ 7.40 (d, *J*= 7.9 Hz, 1H), 7.05 (d, *J*= 7.9 Hz, 1H), 3.11 (dd, *J*= 5.3 and 9.2 Hz, 1H), 2.97-2.85 (m, 2H), 2.79-2.68 (m, 1H), 2.38-2.12 (m, 1H), 1.48 (s, 3H), 1.29 (s, 3H), 0.75 (s, 9H), 0.07 (s, 3H), -0.02 (s, 3H). Ir (KBr): 3454, 2957, 2930, 2895, 2856, 1638, 1587, 1566, 1472, 1421, 1383, 1366, 1254, 1167, 1042, 835, 773, 687. Anal. Calcd for $C_{17}H_{28}NOClSi$: C, 62.74; H, 8.68; N, 4.31. Found: C, 62.73; H, 8.66; N, 4.39.

Chromatographic resolution of (*d,l*)-8 by hplc using optically active column

(*d,l*)-Silyl ether (**8**), (200 mg) was dissolved in hexane (400 μl) and 10 μl of this solution was injected each time to hplc equipped with Daicel Chiralcel OF; (0.46 cm x 25 cm, hexane/*i*-PrOH 1000:1, flow rate: 0.35 ml/min). The eluent was separated into three fractions: A [(*R*)-**8**;>99% ee, 96.7 mg], B[(*R*)-**8** : (*S*)-**8** = 2.5 : 97.5, 40.1 mg], C [(*S*)-**8**; >99% ee, 59.8 mg]. Chromatographic data was as follows: $t_{(R)\text{-}8}$= 11.41 min; $t_{(S)\text{-}8}$= 16.58 min; $k_{(R)\text{-}8'}$= 0.42; $k_{(S)\text{-}8'}$= 1.06; α= 2.52; R_S= 0.49. Although the absolute configuration of each enantiomer of **8** was not determined yet, the configuration of sample A was presumed to be 7*R* from the following observations. i) Sample A showed the same behavior in HPLC analysis using chiral column as (7*R*)-2-chloro-7-methyl-6,7-dihydro-5*H*-1-pyrindine (**i**).[6a] That is, compound (7*R*)-**i** was less polar than (7*S*)-**i**. ii) Both samples A and (7*R*)-**i** showed negative optical rotation in chloroform. iii) Copper complex of **4** derived from sample A and that of (7*R*,7*R'*)-7,7'-dimethyl-6,6',7,7'-tetrahydro-5*H*,5'*H*-2,2'-bi-1,1'-pyrindine showed the same sense of asymmetric induction in cyclopropanation.

(7*R*,7*R'*)-7,7'-Di(1-*tert*-butyldimethylsiloxy-1-methylethyl)-6,6',7,7'-tetrahydro-5*H*,5'*H*-2,2'-bi-1,1'-pyrindine (4)

To a stirred solution of $NiCl_2$·$6H_20$ (54.3 mg, 0.23 mmol) and triphenylphosphine (239.5 mg, 0.92 mmol) in DMF (1.2 ml) was added zinc powder (15 mg, 0.23 mmol) at 50 °C. After the mixture was stirred for 1 h, a solution of silyl ether ((7*R*)-**8**), (75.0 mg, 0.23 mmol) in DMF (1.5 ml) was added at the same temperature. After another 2 h, the mixture was poured into a mixture of aqueous 10% NH_3 and $CHCl_3$, washed three times with water, the organic layer was dried over $MgSO_4$, and concentrated. Silica gel chromatography of the residue (hexane-dichrolomethane = 3:1) gave bipyrindine (**4**), (61 mg, 91 %) as colorless crystals. **4**; $[\alpha]_D^{26}$ -125.9° (*c* 0.18, $CHCl_3$). mp 134-135 °C. ^{1}H Nmr (270 MHz): δ 8.19 (d,

J= 7.9 Hz, 2H), 7.54 (d, *J*= 7.9 Hz, 2H), 3.24 (dd, *J*= 6.3 and 8.6 Hz, 2H), 2.96-2.81 (m, 4H), 2.38-2.21 (m, 4H), 1.63 (s, 6H), 1.33 (s, 6H), 0.77 (s, 18H), 0.89 (s, 6H), -0.02 (s, 6H). Ir (KBr): 3474, 2957, 2930, 2893, 2856, 1636, 1560, 1472, 1421, 1364, 1252, 1186, 1153, 1036, 831, 806, 772. HREIms m/z Calcd for $C_{34}H_{56}N_2O_2Si_2$: 580.3880. Found 580.3888 (M^+).

General procedure for asymmetric carbene C-O insertion using bipyrindine (4) as a chiral ligand

To a suspension of $CuOTf{\cdot}0.5C_6H_6$ (0.7 mg, 2.8 μmol) in CH_2Cl_2 (0.5 ml) was added a solution of **4** (1.8 mg, 3.1 μmol) in CH_2Cl_2 (0.15 ml). After 30 min, the mixture was filtered through a packed adsorbent cotton under argon and to the filtrate was added *dl*-2-phenyloxetane (33.5 mg, 0.25 mmol). To the solution was added dropwise a solution of *tert*-butyl diazoacetate (17.8 mg, 0.125 mmol) in CH_2Cl_2 (0.125 ml) over a period of 30 min at room temperature. The reaction mixture was directly subjected to preparative tlc (hexane/*i*-Pr_2O 5:1), giving the recovered starting material (30%), *trans*-isomer (21%), and *cis*-isomers (15%). Optical purities of these materials were determined by hplc as described in the footnote of Table 2. The stereochemistry of *cis*- and *trans*-isomers was ascertained by the NOE experiment. In the case of the *trans-isomer*, NOE was observed between the C2-hydrogen atom and the *ortho*-hydrogen atom of the C3-phenyl group. The absolute configurations were determined by chiroptical comparison with the published value [A. I. Meyers, R. K. Smith, and C. E. Whitten, *J. Org. Chem.*, 1979, **44**, 2250.] after their conversion to 4-phenyltetrahydro-2*H*-pyran-2-one by the sequence: i) reduction with SmI_2-THF-HMPA in methanol and ii) acid-catalyzed lactonization of the resulting hydroxy ester with TFA.

(2*S*,3*S*)-*tert*-Butyl 3-Phenyltetrahydrofuran-2-carboxylate (81% ee); $[\alpha]_D^{25}$ +73.9° (*c* 0.30, $CHCl_3$) . ^{1}H Nmr (270 MHz): δ 7.30-7.20 (m, 5H), 4.55 (d, *J*= 7.9 Hz, 1H), 4.38 (ddd, *J*= 5.6, 6.9 and 7.9 Hz, 1H), 4.00 (q, *J*= 7.9 Hz, 1H), 3.69 (q, *J*= 7.9 Hz, 1H), 2.41-2.31 (m, 2H), 1.04 (s, 9H). Ir (KBr): 3449, 2978, 2934, 2885, 1736, 1638, 1497, 1456, 1367, 1250, 1223, 1159, 1101, 845, 750, 700, 552. HREIms m/z Calcd for $C_{15}H_{20}O_3$: 248.1412. Found 248.1405 (M^+).

(2*S*,3*R*)-*tert*-Butyl 3-Phenyltetrahydrofuran-2-carboxylate (75% ee); $[\alpha]_D^{26}$ +61.4° (*c* 0.48, $CHCl_3$). ^{1}H Nmr (270 MHz): δ 7.38-7.20 (m, 5H), 4.32 (d, *J*= 6.3 Hz, 1H), 4.22-4.09 (m, 2H), 3.44 (dt, *J*= 6.3 and 7.9 Hz, 1H), 2.47-2.35 (m, 1H), 2.09 (dq, *J*= 7.9 and 12.5 Hz, 1H), 1.41 (s, 9H). Ir (KBr): 3462, 2978, 2934, 2885, 1744, 1495, 1456, 1367, 1298, 1252, 1159, 1099, 978, 930, 845, 758, 700, 521. HREIms m/z Calcd for $C_{15}H_{20}O_3$: 248.1412. Found 248.1416 (M^+).

***cis-tert*-Butyl 3-(*p*-Chrolophenyl)tetrahydrofuran-2-carboxylate** (80% ee); $[\alpha]_D^{27}$ +62.6° (*c* 0.28, $CHCl_3$). ^1H Nmr (270 MHz): δ 7.36-7.21 (m, 4H), 4.52 (d, *J*= 7.9 Hz, 1H), 4.37 (dt, *J*= 4.3 and 7.9 Hz, 1H), 3.99 (q, *J*= 7.9 Hz, 1H), 3.66 (q, *J*= 7.9 Hz, 1H), 2.43-2.24 (m, 2H), 1.09 (s, 9H). Ir (KBr): 3449, 2982, 2934, 2885, 1744, 1635, 1493, 1367, 1250, 1225, 1163, 1103, 1015, 845, 650, 534. HREIms m/z Calcd for $C_{15}H_{19}ClO_3$: 282.1023. Found 282.1016 (M^+).

***trans-tert*-Butyl 3-(*p*-Chrolophenyl)tetrahydrofuran-2-carboxylate** (75% ee); $[\alpha]_D^{26}$ +74.6° (*c* 0.46, $CHCl_3$). ^1H Nmr (270 MHz): δ 7.37-7.23 (m, 4H), 4.27 (d, *J*= 6.3 Hz, 1H), 4.21-4.09 (m, 2H), 3.48 (dt, *J*= 6.3 and 7.9 Hz, 1H), 2.47-2.35 (m, 1H), 1.89 (dq, *J*= 7.9 and 12.5 Hz, 1H), 1.43 (s, 9H). Ir (KBr): 3460, 2980, 2936, 2885, 1744, 1638, 1495, 1458, 1393, 1367, 1300, 1252, 1221, 1159, 1099, 1015, 843, 824, 770, 525. HREIms m/z Calcd for $C_{15}H_{19}ClO_3$: 282.1023. Found 282.1022 (M^+).

***cis-tert*-Butyl 3-(*p*-Methylphenyl)tetrahydrofuran-2-carboxylate** (76% ee); $[\alpha]_D^{27}$ +58.0° (*c* 0.19, $CHCl_3$). ^1H Nmr (270 MHz): δ 7.15-7.07 (m, 4H), 4.53 (d, *J*= 7.9 Hz, 1H), 4.37 (ddd, *J*= 5.6, 6.9 and 7.9 Hz, 1H), 3.99 (q, *J*= 7.9 Hz, 1H), 3.66 (q, *J*= 7.9 Hz, 1H), 2.37-2.29 (m, 2H), 2.31 (s, 3H), 1.06 (s, 9H). Ir (KBr): 3447, 2982, 2958, 2885, 1734, 1518, 1458, 1367, 1225, 1157, 1097, 1076, 989, 841, 820, 741, 723, 664, 552, 486. HREIms m/z Calcd for $C_{16}H_{22}O_3$: 262.1569. Found 262.1573 (M^+).

***trans-tert*-Butyl 3-(*p*-Methylphenyl)tetrahydrofuran-2-carboxylate** (50% ee); $[\alpha]_D^{27}$ +71.3° (*c* 0.17, $CHCl_3$). ^1H Nmr (270 MHz): δ 7.19-7.11 (m, 4H), 4.29 (d, *J*= 6.3 Hz, 1H), 4.22-4.08 (m, 2H), 3.42 (dt, *J*= 6.3 and 7.9 Hz, 1H), 2.46-2.32 (m, 1H), 2.33 (s, 3H), 2.06 (dq, *J*= 7.9 and 12.2 Hz, 1H), 1.43 (s, 9H). Ir (KBr): 3447, 2978, 2931, 2883, 1746, 1638, 1516, 1479, 1458, 1393, 1367, 1296, 1252, 1219, 1159, 1099, 930, 845, 814, 530. HREIms m/z Calcd for $C_{16}H_{22}O_3$: 262.1569. Found 262.1568 (M^+).

***cis-tert*-Butyl 3-(2-Phenylethynyl)tetrahydrofuran-2-carboxylate** (71% ee); $[\alpha]_D^{20}$ +3.0° (*c* 0.51, $CHCl_3$). ^1H Nmr (270 MHz): δ 7.39-7.27 (m, 5H), 4.47 (d, *J*= 7.6 Hz, 1H), 4.31 (dt, *J*= 6.0 and 7.9 Hz, 1H), 3.98 (dt, *J*= 6.9 and 7.9 Hz, 1H), 3.50 (q, *J*= 7.6 Hz, 1H), 2.38-2.24 (m, 2H), 1.46 (s, 9H). Ir (KBr): 3449, 2978, 2930, 2893, 2230, 1738, 1638, 1599, 1491, 1367, 1599, 1491, 1367, 1223, 1159, 1103, 986, 918, 843, 758, 692, 542. HREIms m/z Calcd for $C_{17}H_{20}O_3$: 272.1412. Found 272.1407 (M^+).

***trans-tert*-Butyl 3-(2-Phenylethynyl)tetrahydrofuran-2-carboxylate** (75% ee); $[\alpha]_D^{20}$ +111.5° (*c* 0.74, $CHCl_3$). ^1H Nmr (270 MHz): δ 7.44-7.27 (m, 5H), 4.37 (d, *J*= 6.6 Hz, 1H), 4.10 (m, *J*= 6.9 Hz, 2H), 3.31 (ddd, *J*= 6.6, 6.9 and 7.9 Hz, 1H), 2.35 (ddt, *J*= 6.9, 7.9 and 12.2 Hz, 1H), 2.13 (dq, *J*= 6.9 and 12.2 Hz, 1H), 1.50 (s, 9H). Ir (KBr): 3456, 2984, 2930, 2872, 2230, 1740, 1638, 1491, 1448, 1371, 1339, 1248, 1157, 1103, 935, 843, 793, 760, 696, 540. HREIms m/z Calcd for $C_{17}H_{20}O_3$: 272.1412. Found 272.1409 (M^+).

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10. In the following Scheme, y and z stand for the diastereoface selectivity of the carbenoid species and

a, b, c, and d stand for the epimerization ratio during ring expansion reaction. The relative amount [P] of each isomer of the products is correlated by the equations 1-4 with diastereoface selectivity and epimerization ratio. The values of *cis trans* ratio, ee(*cis*), and ee(*trans*) are derived from the experimentals. (*R*)- and (*S*)-oxetanes are presumed to react with copper carbenoid species at the same reaction rate.

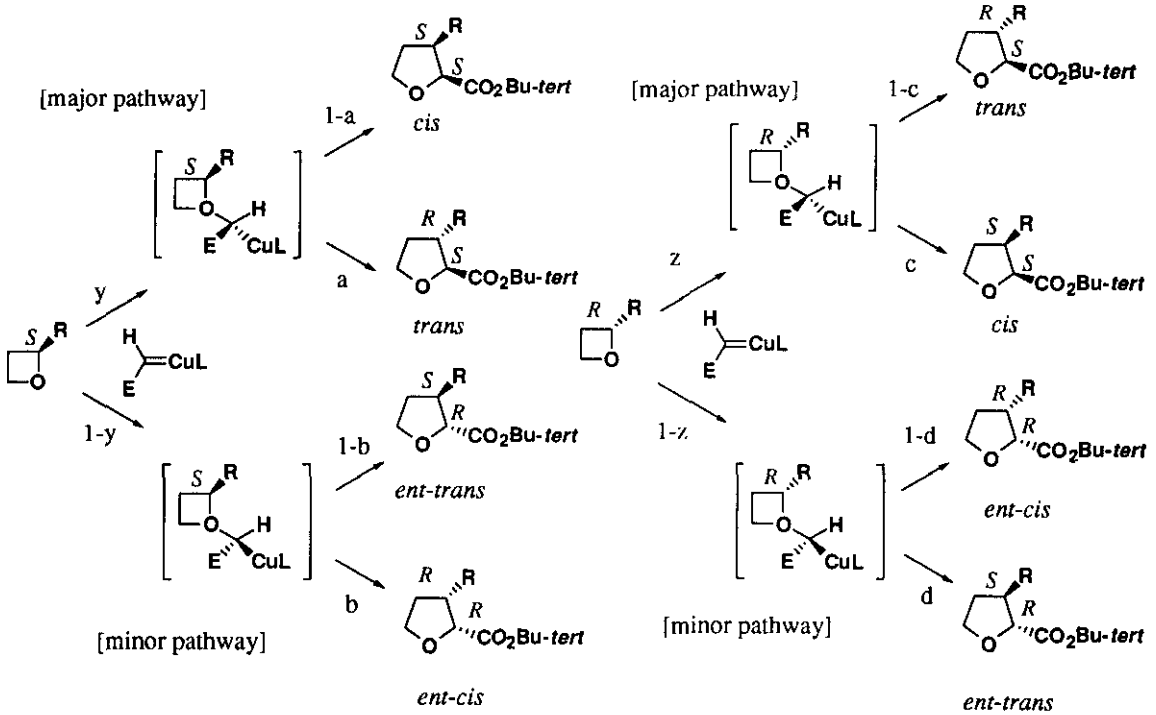
[P]*cis* = f_S x y x (1-a) + f_R x z x c (Eq. 1)

$f_S + f_R = 1$ Ee(oxetane)= $|f_S - f_R|$ f_S , f_R = fraction of *S* or *R* isomer of the starting oxetanes

[P]*trans*= f_S x y x a + f_R x z x (1-c) (Eq. 2)

[P]ent-*cis* = f_S x (1-y) x b + f_R x (1-z) x (1-d) (Eq. 3)

[P]ent-*trans* = f_S x (1-y) x (1-b) + f_R x (1-z) x d (Eq. 4)



L= bipyrindine ligand

cis : *trans*= {[P]*cis* + [P]ent-*cis* } : {[P]*trans*+ [P]ent-*trans*}

Ee(*cis*)= {[P]*cis* - [P]ent-*cis* }/{[P]*cis* + [P]ent-*cis* }

Ee(*trans*)= {[P]*trans* - [P]ent-*trans*}/{[P]*trans*+ [P]ent-*trans*}

From the calculation using the above equations based on the experimental data (Table 2, entries 3 and 4), we can find y= 0.86, z= 0.92, a= 0.08, b= 0.17, c= 0.03, and d= 0.41 on the average.

Thus face selectivity (% de) of carbenoids is:

With (*S*)-oxetane, % de= [y - (1-y)] x 100 = [2y - 1] x 100 = 72

With (*R*)-oxetane, % de= [z - (1-z)] x 100 = [2z - 1] x 100 = 84

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