Asymmetric [2 + 1] Cycloaddition Reactions of 1-Seleno-2-silylethene

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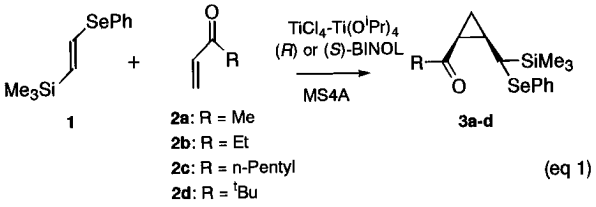
The reaction of (*E*)-1-(phenylseleno)-2-(trimethylsilyl)ethene (**1**) and vinyl ketones **2a**−**d** in the presence of a chiral Lewis acid prepared from $TiCl_4$, $Ti(O^iPr)_4$, (*R*)- or (*S*)-1,1′-binaphthol (BINOL), and MS4A gave enantiomerically enriched *cis* cyclopropane products **3a**−**d**. The enantiomeric excess and chemical yield varied depending on the ratio of $TiCl_4$ and $Ti(O^iPr)_4$ to **1**. Reproducible results (43−47% ee/33−41% yields) for *cis*-1-acetyl-2-[(phenylseleno)(trimethylsilyl)methyl]cyclopropane (**3a**) were obtained using 1.1 equiv of $TiCl_4$, 0.54−0.65 equiv of $Ti(O^iPr)_4$, and 1.65 equiv of BINOL. The observed enantioselectivity was explained by consideration of the structure of the postulated intermediates, alkoxy titanium−carbonyl complexes, *via ab initio* MO calculations.

The development of new synthetic methodology for preparation of optically active cyclopropane derivatives is an important objective. Recently, various methods for the synthesis of cyclopropanes have been developed, in part because the cyclopropyl group is found to be a basic structural unit in a wide range of biologically active natural and non-natural products.[1] We have recently reported a novel [2 + 1] cycloaddition synthesis of 1,2-*trans* cyclopropanes by the combination of (*E*)-1-(phenylseleno)-2-silylethenes and vinyl ketones in the presence of $SnCl_4$.[2] It is of synthetic and mechanistic interest to investigate the possibility of asymmetric synthesis in this novel [2 + 1] cycloaddition. Herein, we report that the reaction of (*E*)-1-(phenylseleno)-2-(trimethylsilyl)ethene (**1**) and vinyl ketones **2a**−**d** in the presence of a chiral Lewis acid gave enantiomerically enriched 1,2-*cis* cyclopropane products **3a**−**d** (eq 1). The Lewis acid was prepared from $TiCl_4$, $Ti(O^iPr)_4$, (*R*)- or (*S*)-1,1′-binaphthol (BINOL), and MS4A. In order to understand the observed enantioselectivity, the structure of a Lewis acid−carbonyl complex was determined by *ab initio* MO calculations, and a possible mechanism is discussed.



Asymmetric [2 + 1] Cycloaddition of 1. After extensive experimentation involving screening of various Lewis acids and chiral ligands, the best chiral Lewis acid was prepared as follows: into a flask containing activated powdered molecular sieves (MS4A)[3] was added a solution of $TiCl_4$ and $Ti(O^iPr)_4$ in CH_2Cl_2 followed by (*R*)-BINOL. The mixture was stirred for 1 h at room temperature and then cooled to −78 °C. To the mixture were then added successively a solution of **1** in CH_2Cl_2 and vinyl ketones **2a**−**d**. The mixture was then warmed to −30 °C and stirred for 4−5.5 h. Quenching with triethylamine gave enantiomerically enriched *cis* cyclopropane products **3a**−**d** as the major products. The chemical yield and enantiomeric excess for **3a** depended on the ratio of $TiCl_4$ and $Ti(O^iPr)_4$ to **1** and varied from 12% (57% ee) to 45% (26% ee) as shown in Table 1.[4,5] Reproducible results (43−47% ee/33−41% yields) for **3a** were obtained using 1.1 equiv of $TiCl_4$, 0.54−0.65 equiv of $Ti(O^iPr)_4$, and 1.65 equiv of BINOL (entries 5−7 in Table 1). The % ee of the produced cyclopropanes **3a**−**d** was determined by HPLC analysis by using a chiral column (CHIRALCEL OF).

The absolute configuration of **3a** was determined by conversion to two different known compounds **6** and **7** (*vide infra*) (eq 2). Thus, (+)-**3a** (29% ee) prepared using (*R*)-BINOL was oxidized with $NaIO_4$ in a THF−H_2O solution at room temperature to give the sila-Pummerer product (+)-**4**. The aldehyde (+)-**4** was further oxidized

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(1) For recent examples of asymmetric synthesis of cyclopropanes, see: (a) Doyle, M. P.; Austin, R. E.; Bailey, A. S.; Dwyer, M. P.; Dyatkin, A. B.; Kalinin, A. V.; Kwan, M. M. Y.; Liras, S.; Oalmann, C. J.; Pieters, R. J.; Protopopova, M. N.; Raab, C. E.; Roos, G. H.; Zhou, Q.-L.; Martin, S. F. *J. Am. Chem. Soc.* **1995**, *117*, 5763 and references cited therein. (b) Charette, A. B.; Prescott, S.; Brochu, C. *J. Org. Chem.* **1995**, *60*, 1081 and references cited therein. (c) Denmark, S. E.; Christenson, B. L.; Coe, D. M.; O'Connor, S. P. *Tetrahedron Lett.* **1995**, *36*, 2215. Denmark, S. E.; Christensen, B. L.; O'Connor, S. P. *Tetrahedron Lett.* **1995**, *36*, 2219. (d) Salaün, J.; Baird, M. S. *Curr. Med. Chem.* **1995**, *2*, 511. (e) White, J. D. *J. Am. Chem. Soc.* **1995**, *117*, 6224. (f) White, J. D.; Kim, T-S.; Mambu, M. *J. Am. Chem. Soc.* **1995**, *117*, 5612. (g) Critcher, D. I.; Connolly, S.; Wills, M. *Tetrahedron Lett.* **1995**, *36*, 3763. (h) Armstrong, R. W.; Maurer, K. W. *Tetrahedron Lett.* **1995**, *36*, 357. Barrett, A. G. M.; Doubleday, W. W.; Kasdorf, K.; Tustin, G. J.; White, A. J. P.; Williams, D. J. *J. Chem. Soc., Chem. Commun.* **1995**, 407. (i) Zhao, Y.; Yang, T.; Lee, M.; Lee, D.; Newton, M. G.; Chu, C. K. *J. Org. Chem.* **1995**, *60*, 5236. (j) Hanessian, S.; Andreotti, D.; Gomtsyan, A. *J. Am. Chem. Soc.* **1995**, *117*, 10393 and references cited therein.

(2) (a) Yamazaki, S.; Tanaka, M.; Yamaguchi, A.; Yamabe, S. *J. Am. Chem. Soc.* **1994**, *116*, 2356. (b) Yamazaki, S.; Katoh, S.; Yamabe, S. *J. Org. Chem.* **1992**, *57*, 4.

(3) Molecular sieves (MS4A) were dried overnight at 250 °C in vacuum or at 350 °C in air before use. The effect of molecular sieves on enantioselectivity in this reaction was not examined. For previous examples of the use of molecular sieves in reactions of chiral titanium alkoxides, see: (a) Hanson, R. M.; Sharpless, K. B. *J. Org. Chem.* **1986**, *51*, 1922. Gao, Y.; Hanson, R. M.; Klunder, J. M.; Ko, S. Y.; Masamune, H.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765. (b) Narasaka, K.; Iwasawa, N.; Inoue, M.; Yamada, T.; Nakashima, M.; Sugimori, J. *J. Am. Chem. Soc.* **1989**, *111*, 5340. Narasaka, K.; Hayashi, Y.; Shimadzu, H.; Niihata, S. *J. Am. Chem. Soc.* **1992**, *114*, 8869. (c) Mikami, K.; Terada, M.; Nakai, T. *J. Am. Chem. Soc.* **1989**, *111*, 1940. Mikami, K.; Terada, M.; Nakai, T. *J. Am. Chem. Soc.* **1990**, *112*, 3949. Mikami, K.; Motoyama, Y.; Terada, M. *J. Am. Chem. Soc.* **1994**, *116*, 2812. (d) Seebach, D.; Dahinden, R.; Marti, R. E.; Beck, A. K.; Plattner, D. A.; Kühnle, F. N. M. *J. Org. Chem.* **1995**, *60*, 1788.

(4) All reactions were carried out using 1.0 mmol of **1**. When $TiCl_4$ and $Ti(O^iPr)_4$ were measured by volume using syringe, the method gave **3a**−**d** with unreproducible % ee and chemical yield. Therefore, $TiCl_4$ and $Ti(O^iPr)_4$ were measured by weight each time. All results shown in Table 1 were obtained by the latter method.

(5) Using 0.68 equiv of $TiCl_4$ and 0.55 equiv of $Ti(O^iPr)_4$ gave **3a** in very low chemical yields (5%, 68% ee).

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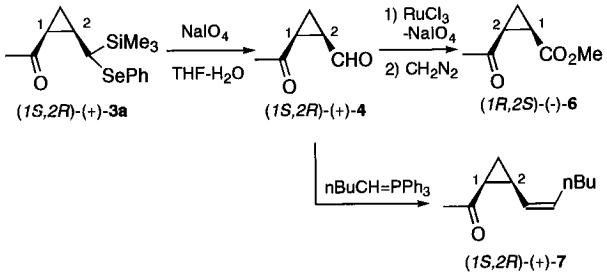
Table 1. Asymmetric [2 + 1] Cycloaddition of 1 and 2a−d (eq 1).

entry	vinyl ketone	$TiCl_4$ (equiv)	$Ti(O^iPr)_4$ (equiv)	BINOL (equiv)	% yield **3a−d**[a]	% ee **3a−d**	recovered **1** (%)
1	**2a**	1.57	0.69	1.10 (*R*)	45[b]	26	9
2	**2a**	1.11	0.60	1.10 (*R*)	35[c]	44	22
3	**2a**	1.09	0.73	1.10 (*R*)	12[c]	57	44
4	**2a**	1.58	1.06	1.10 (*R*)	36[d]	30	22
5	**2a**	1.11	0.56	1.65 (*R*)	39[c]	44	32
6	**2a**	1.11	0.65	1.65 (*R*)	33[c]	47	49
7	**2a**	1.11	0.54	1.65 (*S*)	41[c]	43	35
8	**2a**	1.24	0.50	1.10 (*R*)	46[e]	32	14
9	**2b**	1.10	0.59	1.65 (*R*)	42[c]	43	25
10	**2c**	1.10	0.55	1.65 (*R*)	27	33	26
11	**2d**	1.13	0.58	1.65 (*R*)	4[f]	40	45

[a] Isolated yield. [b] 9% of *trans* cyclopropane isomer (0% ee, by HPLC using a chiral column (CHIRALCEL OG)) was also isolated. [c] A trace amount of the *trans* cyclopropane isomer was produced but not isolated. [d] 6% of the *trans* cyclopropane isomer was also isolated. % ee was not determined. [e] 10% of the *trans* cyclopropane isomer was also isolated. % ee was not determined. [f] Purification by column chromatography was difficult. Less than 15% of **3d** was produced (^{1}H NMR of crude product).

to carboxylic acid **5** by $RuCl_3$-$NaIO_4$.[6] Treatment of **5** with diazomethane in ether gave the enantiomer of known methyl ester (+)-**6**. (−)-**6** was assigned as (1*R*,2*S*) by comparison with the sign of optical rotation of known (1*S*,2*R*)-(+)-**6** and by chiral GC comparison with authentic (1*S*,2*R*)-(+)-**6**.[7] By GC, the enantiopurity of (−)-**6** prepared from (+)-**3a** (29% ee) was determined to be 29% ee, indicating retention of configuration in the transformation of **3a** to **6**. Furthermore, Wittig reaction of (+)-**4** prepared from (+)-**3a** (44% ee) with salt-free triphenylpentylidenephosphorane[3,8] gave (+)-**7** in 45% yield (45% ee by GC). (1*R*,2*S*)-(−)-**7** has been described by Meyers and co-workers as an intermediate for a natural product, dictyopterene C′.[7] Both the measured optical rotations and chiral GC indicate retention of configuration. Thus, the absolute configuration of (+)-**3a** was assigned as (1*S*,2*R*).

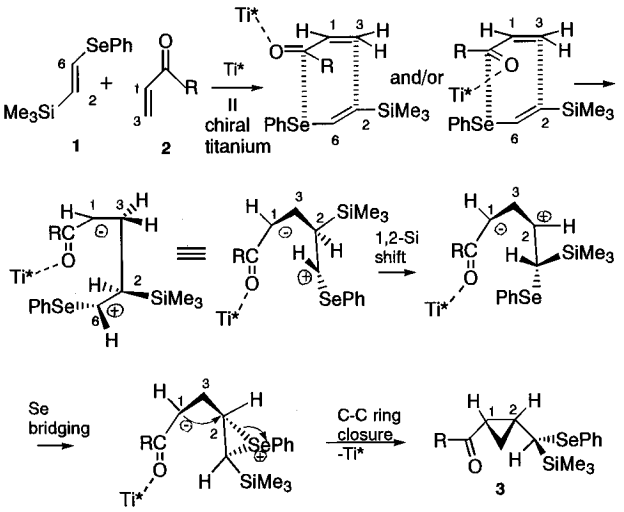


(eq 2)

When (*R*,*R*)-diphenylethanediol (1.65 equiv) was used as a chiral ligand with $TiCl_4$ (1.1 equiv) and $Ti(OiPr)_4$ (0.55 equiv) in eq 1 instead of (*R*)-BINOL, (1*R*,2*S*)-**3a** was obtained with lower % ee and chemical yield (13% ee/16% yield). Use of $TiBr_4$ instead of $TiCl_4$ using (*R*)-BINOL gave (1*R*,2*S*)-**3a** with only 7% ee (25% yield).

Origin of Enantioselectivity in [2 + 1] Cycloaddition of 1. In order to understand the observed enantioselectivity in this [2 + 1] cycloaddition reaction of **1**, the total reaction mechanism was depicted as previously discussed in systems with achiral ligands (Scheme 1).[2,9] In the first step, a chiral titanium−vinyl ketone complex will be attacked by selenosilyl nucleophile **1**. The titanium−vinyl ketone complex can adopt an *s-cis* or *s-trans* conformation (*vide post*). Synclinal stereoselective addition (due to a stabilizing secondary orbital interaction, Se- - -C=O) may affect the face-selectivity. Subsequent 1,2-silicon migration, generation of a selenium-bridged intermediate by minimum motion, and ring closure give the cyclopropane **3**. *Cis* selectivity was observed with this Lewis acid; thus single-bond rotation of C_1-C_3 as well as C_2-C_3 must be a slower process than ring closure.[2,10] Since the stereochemistry of the original synclinal addition step is retained throughout this proposed mechanism, the origin of the observed enantioselectivity in **3** should arise from the first addition step. The experimental results for **3a** indicate that the major approach of **1** should occur from the *re* face of C_1 (for the numbering, see Scheme 1).

Scheme 1



The composition of Lewis acids generated under our best conditions can be considered as follows. First, $TiCl_4$ and $Ti(O^iPr)_4$ equilibrate to give a Ti(IV) species represented by $(TiCl_x(O^iPr)_y)$,[12] which then leads to a mixture

(6) Carlsen, P. H. J.; Katsuki, T.; Martin, V. S.; Sharpless, K. B. *J. Org. Chem.* **1981**, *46*, 3936.

(7) Romo, D.; Romine, J. L.; Midura, W.; Meyers, A. I. *Tetrahedron* **1990**, *46*, 4951.

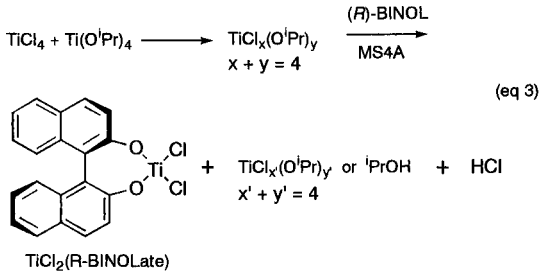
(8) Bestmann, H.; Stransky, W.; Vostrowsky, O. *Chem. Ber.* **1976**, *109*, 1694.

(9) Relative stereochemistry of C_2 and *C*H(SePh)($SiMe_3$) in **3a** (for numbering, see eq 2) is determined as (*R*,*R*) by 2D-NOESY. See ref 8 in the following paper: Yamazaki, S.; Tanaka, M.; Inoue, T.; Morimoto, N.; Kumagai, H.; Yamamoto, Y. *J. Org. Chem.* **1995**, *60*, 6546.

(10) Lewis acid dependence in the *cis*−*trans* selectivity in these [2 + 1] cycloadditions has been observed earlier, as follows, and still remains unclear, although mechanistic interpretation is underway. $AlCl_3$ (−78 °C),[2] $TiCl_4$ (1.1 equiv)/$Ti(O^iPr)_4$ (0.55 equiv)/(±)-BINOL (1.65 equiv) (−30 °C), or $TiCl_4$ (1.1equiv)/$Ti(O^iPr)_4$ (0.59 equiv) (−78 °C),[11] gave *cis* cyclopropane predominantly. $SnCl_4$ (−78 °C),[2] $TiCl_4$ (2.2 equiv)/$Ti(O^iPr)_4$ (1.1 equiv) (−78 °C),[11] or $TiCl_4-PPh_3$ (−78 °C)[11] gave *trans* cyclopropane predominantly.

(11) Yamazaki, S.; Tanaka, M. Unpublished results.

of $TiCl_2$((*R*)-BINOLate) and ($TiCl_x(O^iPr)_y$) with evolution of HCl and alcohol exchange by addition of (*R*)-BINOL in the presence of MS4A (eq 3).[3c] In our best, reproducible conditions ($TiCl_4$ (1.1 equiv), $Ti(O^iPr)_4$ (0.56−0.65 equiv), and (*R*)-BINOL (1.65 equiv)), $TiCl_2$((*R*)-BINOLate) is the major Lewis acid.[13,14]



Addition of a vinyl ketone to the Lewis acid system leads to a chiral titanium−vinyl ketone complex. The structure of this chiral complex is probably the origin of the observed enantioselectivity. Recently, the structure of a complex of chiral alkoxytitanium with a bidentate α,β-unsaturated carbonyl compound, which is postulated as the intermediate in an asymmetric Diels−Alder reaction, was elucidated by X-ray analysis and the reaction mechanism discussed.[15] However, the structure of a complex of alkoxytitanium with monodentate carbonyl compounds such as aldehydes and vinyl ketones (those described in this paper) is still unknown. There are several possibilities for the coordination structure of a complex of titanium with vinyl ketone **2**. These possibilities were examined by the use of model systems and *ab inito* calculations (see supporting information, part II).

For the model **H** (see Scheme 5 and Figures 6 and 7 of supporting information, part II), ethylene glycoxide was replaced by (*R*)-BINOLate.[16] The geometry of the postulated $TiCl_2$((*R*)-BINOLate)−methyl vinyl ketone (**2a**) complex, **A** (R = Me), was fully optimized. Restricted Hartree−Fock (RHF) calculations with the LANL1MB basis set were carried out for geometry optimizations. LANL1MB consists of the effective core (pseudo) potential of inner-shell electrons and valence minimal basis set.[17] The RHF/LANL1MB was found to verify the reaction mechanism of systems containing metal−chloride coordination bonds.[2a] All the molecular orbital calculations were performed, using Gaussian 92 and 94 program packages.[18] The obtained structure is shown in Figure 1. Cartesian coordinates and other computational details are given in the supporting information (part III). In Figure 2, the proposed synclinal approaches of **1** to **A** (R = Me) from the *si* face and *re* face of C_1 are outlined, where C_3- - -C_2 and O=*C*- - -Se distances are set to ca. 3.0 Å. The approach from the *si* face of C_1 shows steric repulsion of C_1 between the upper portion of the naphthalene ring and the $Si(CH_3)_3$ group. In contrast, approach from the *re* face of C_1 seems to be free of steric repulsion. This indicates that **A** (R = Me) should be attacked by the selenosilylethene nucleophile **1** from the *re* face of C_1 of methyl vinyl ketone (for numbering, see eq 4). The conclusion of this discussion is consistent with the experimental observation that the preferred isomer for **3a** is the (1*S*,2*R*) isomer when (*R*)-BINOL is used. However, the observed moderate enantioselectivity may partially result from competing cyclopropane formation

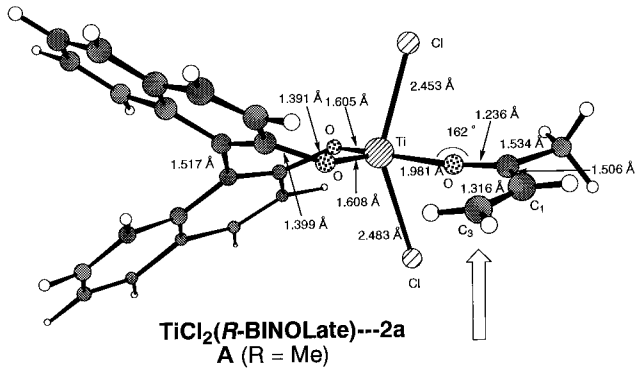
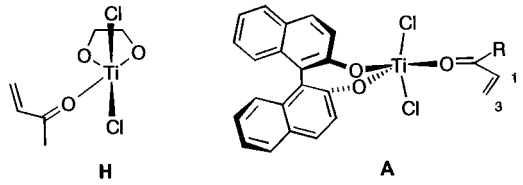
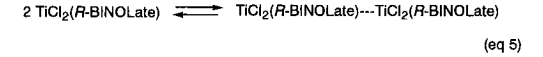


Figure 1. *Ab initio* RHF/LANL1MB-optimized[17,18] geometry of $TiCl_2$(*R*-BINOLate)−**2a**, **A** (R = Me). Positions of all atoms are fully optimized. The bold arrow indicates the approach from *re* face of C_1 of the methyl vinyl ketone ligand.



(12) Dijkgraaf, C.; Roussrau, J. P. G. *Spectrochim. Acta A* **1968**, *2*, 1213.

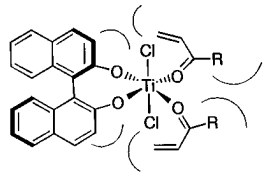
(13) In practice, $TiCl_2$(*R*-BINOLate) may exist in dimeric form, as shown in eq 5. The dimer may be weakly bound and readily dissociated to a monomer.[14]



(14) (a) Duthaler, R. O.; Hafner, A. *Chem. Rev.* **1992**, *92*, 807, and references cited therein. (b) Watenpaugh, K.; Caughlan, C. N. *Inorg. Chem.* **1966**, *5*, 1782. (c) Terada, M.; Mikami, K.; Nakai, T. *J. Chem. Soc., Chem. Commun.* **1990**, 1623.

(15) (a) Gothelf, K. V.; Hazell, R. G.; Jørgensen, K. A. *J. Am. Chem. Soc.* **1995**, *117*, 4435. (b) Gothelf, K. V.; Jørgensen, K. A. *J. Org. Chem.* **1995**, *60*, 6847. See also: (c) Haase, C.; Sarko, C. R.; DiMare, M. *J. Org. Chem.* **1995**, *60*, 1777. Reference 3d.

(16) Although we have considered a hexacoordinate (Lewis acid: carbonyl compound = 1:2) form by the use of model compounds (formaldehyde as a carbonyl compound, see Figure 4 in supporting information, part II), $TiCl_2$(*R*-BINOLate)−(**2**)$_2$ must be sterically crowded. Also, in view of the stoichiometry of $TiCl_2$(*R*-BINOLate) and **2**, $TiCl_2$(*R*-BINOLate)−(**2**)$_2$ will be in very low concentration, even if it is produced. Furthermore, in view of the reactivity of a carbonyl compound, dicoordinate vinyl ketones must be less reactive than monocoordinate vinyl ketones.



(17) (a) Hay, P. J.; Wadt, W. R. *J. Chem. Phys.* **1985**, *82*, 270. (b) Wadt, W. R.; Hay, P. J. *J. Chem. Phys.* **1985**, *82*, 284. (c) Hay, P. J.; Wadt, W. R. *J. Chem. Phys.* **1985**, *82*, 299.

(18) (a) Frisch, M. J.; Trucks, G. W.; Head-Gordon, M.; Gill, P. M. W.; Wong, M. W.; Foresman, J. B.; Johnson, B. G.; Schlegel, H. B.; Robb, M. A.; Repologle, E. S.; Gomperts, R.; Andreas, J. L.; Raghavachrni, K.; Binkley, J. S.; Gonzalez, C.; Martin, R. L.; Fox, D. J.; DeFrees, D. J.; Baker, J.; Stewart, J. J. P.; Pople, J. A. Gaussian 92, Revision C; Gaussian, Inc., Pittsburgh, PA, 1992. (b) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Robb, M. A.; Cheeseman, J. R.; Keith, T.; Petersson, G. A.; Montgomery, J. A.; Raghavachari, K.; Al-Laham, M. A.; Zakrzewski, V. G.; Ortiz, J. V.; Foresman, J. B.; Cioslowski, J.; Stefanov, B. B.; Nanayakkara, A.; Challacombe, M.; Peng, C. Y.; Ayala, P. Y.; Chen, W.; Wong, M. W.; Andres, J. L.; Replogle, E. S.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Binkley, J. S.; Defrees, D. J.; Baker, J.; Stewart, J. J. P.; Head-Gordon, M.; Gonzalez, C.; Pople, J. A. Gaussian 94, Revision B.1, Gaussian, Inc., Pittsburgh, PA, 1995. *Ab initio* calculations using Gaussian 92 and 94 were made on the Convex spp1200/XA at the Information Processing Center (Nara University of Education).

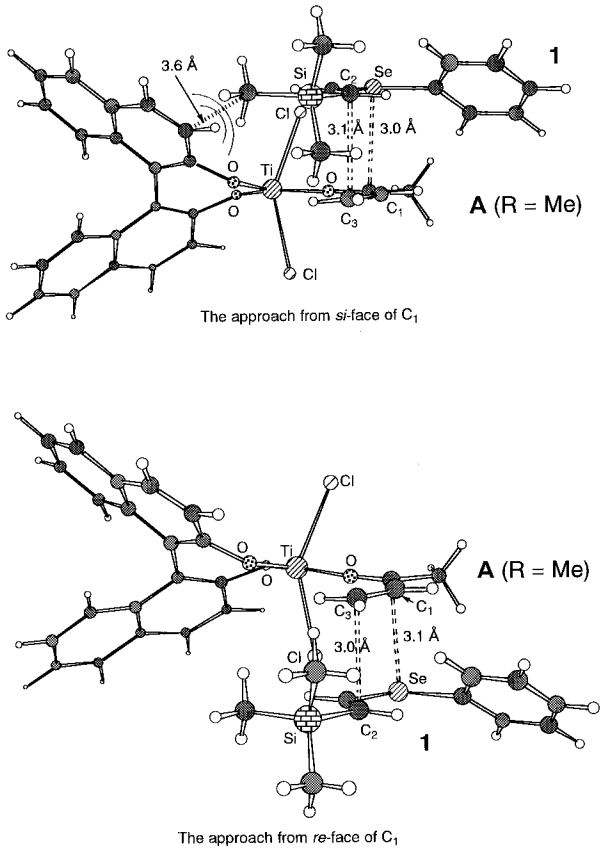
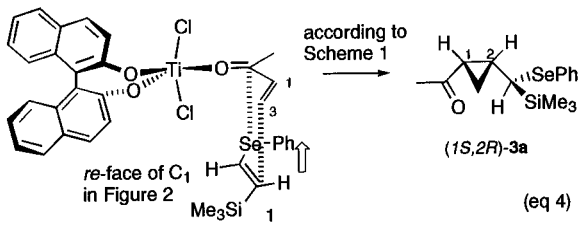


Figure 2. Proposed synclinal approaches of **1** to **A** (R = Me). For the structure of **1**, standard bond lengths and bond angles are used. C_3- - -C_2 and O=*C*- - -Se distances are set to 3.0−3.1 Å.

promoted by the achiral complexes also present in the reaction of general formula $TiCl_x(O^iPr)_y$ (see eq 3).



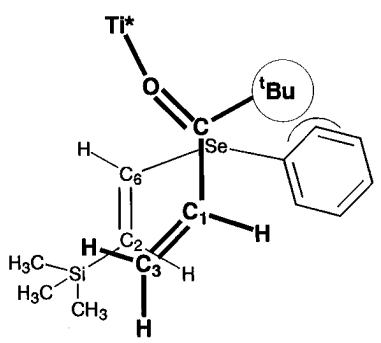
Poor results of [2 + 1] cycloadditions with vinyl ketone **2d** (R = ^{t}Bu) (entry 11 in Table 1) can be explained as follows. The synclinal approach of **1** to **A** (R = ^{t}Bu) from the *re* side of C_1 is retarded by steric hindrance between the ^{t}Bu group and phenyl ring (Scheme 2), indicating that size limitations exist in the choice of R.

We have shown clearly that *ab initio* RHF/LANL1MB calculations can be applied to complex asymmetric reactions involving large molecules such as binaphthol in this work. Further work is in progress on the design of reactions of **1** with more reactive electrophilic olefins in the presence of suitable chiral Lewis acids.

Experimental Section

General Methods. IR spectra were recorded in the FT-mode. NMR spectra were recorded in $CDCl_3$ at 200 MHz. Chemical shifts are reported in ppm relative to Me_4Si or residual nondeuterated solvent. Mass spectra were determined by electron impact. HPLC analysis was performed with a UV detector (detection, 254 nm light) and a flow rate of 0.5 mL/min using a CHIRALCEL OF (0.46 cm × 25 cm) column

Scheme 2



The view from *si*-side of C_1 of **A** (R = ^{t}Bu) which was attacked by *re*-side by **1**

for **3a**−**d**. GC analysis was performed using a Chiraldex B-PH (20 m × 0.25 mm i.d.) column with flame-ionization detectors and He as carrier gas. Optical rotations were measured with a 1 cm × 5 cm cell. All reactions were carried out under a nitrogen atmosphere.

Typical Experimental Procedure Using $TiCl_4$−Ti(O-^{i}Pr)$_4$−(*R*)-BINOL/MS4A in Table 1 (Entry 6). A typical experimental procedure is described for entry 6 in Table 1. To a flask containing MS4A (1.3 g) were added a solution of $TiCl_4$ (212 mg, 1.11 mmol) and $Ti(O^iPr)_4$ (184 mg, 0.65 mmol) in dichloromethane (1.7 mL), followed by (*R*)-BINOL (472 mg, 1.65 mmol), and the mixture was stirred at room temperature for 1 h. To the mixture cooled to −78 °C was added a solution of **1** (255 mg, 1.0 mmol) in dichloromethane (0.4 mL), followed by **2a** (0.11 mL, 1.3 mmol). The mixture was warmed to −30 °C and stirred for 4 h. The reaction was quenched by triethylamine (0.32 mL, 2.3 mmol), and then saturated aqueous $NaHCO_3$ was added to the mixture. The mixture was extracted with dichloromethane, and the organic phase was washed with water, dried (Na_2SO_4), and evaporated *in vacuo*. The residue was purified by column chromatography over silica gel eluting with hexane−ether (2:1) to give recovered **1** (125 mg, 49%) and the product **3a** (109 mg, 33%) (47% ee by HPLC analysis) (R_f = 0.4).

(1*S*,2*R*)-(+)-1-Acetyl-2-[(phenylseleno)(trimethylsilyl)-methyl]cyclopropane (3a): ^{1}H NMR of **3a** was identical with that reported previously;[2] HPLC (hexane−^{i}PrOH = 200:1) minor peak t_{R1} 14.3 min, major peak t_{R2} 23.0 min; optical rotation for **3a** was measured for a sample whose ee% was determined as 21%ee by HPLC analysis, $[\alpha]^{23}_D$ = +19° (*c* 0.84, $CHCl_3$).

(1*R*,2*S*)-(−)-3a. (entry 7 in Table 1): HPLC (hexane−^{i}PrOH = 200:1) major peak t_{R1} 14.5 min, minor peak t_{R2} 23.9 min, 43% ee; $[\alpha]^{24}_D$ = −36° (*c* 1.33, $CHCl_3$).

(+)-*cis*-1-Propionyl-2-[(phenylseleno)(trimethylsilyl)-methyl]cyclopropane (3b) (entry 9 in Table 1) (R_f = 0.6 (hexane:ether = 2:1)): pale yellow oil; HPLC (hexane−^{i}PrOH = 200:1) minor peak t_{R1} 10.4 min, major peak t_{R2} 12.5 min, 43% ee; $[\alpha]^{24}_D$ = +38° (*c* 1.40, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm) 0.063 (s, 9H), 0.928 (t, *J* = 7.2 Hz, 3H), 1.20−1.27 (m, 2H), 1.66 (dddd, *J* = 12.2, 8.1, 8.0, 8.0 Hz, 1H), 2.17 (ddd, *J* = 8.1, 7.0, 6.1 Hz, 1H), 2.46 (q, *J* = 7.2 Hz, 2H), 2.67 (d, *J* = 12.0 Hz), 7.21−7.26 (m, 3H), 7.49−7.54 (m, 2H); ^{13}C NMR (50.1 MHz, $CDCl_3$) δ (ppm) −1.705, 7.988, 18.35, 26.53, 28.49, 29.01, 38.18, 127.2, 128.8, 130.1, 134.5, 209.4; IR (neat) 3060, 2958, 2900, 1694, 1578, cm^{-1}; MS (70 eV) *m*/*z* 340 (M^+); exact mass M^+ 340.0776 (calcd for $C_{16}H_{24}OSeSi$ 340.0761).

(+)-*cis*-1-Hexanoyl-2-[(phenylseleno)(trimethylsilyl)-methyl]cyclopropane (3c) (entry 10 in Table 1) (R_f = 0.6 (hexane:ether = 2:1)): pale yellow oil; HPLC (hexane−^{i}PrOH = 400:1) minor peak t_{R1} 12.7 min, major peak t_{R2} 14.5 min, 33% ee; $[\alpha]^{24}_D$ = +24° (*c* 1.02, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm) 0.063 (s, 9H), 0.851 (t, 6.7 Hz, 3H), 1.19−1.75 (m, 9H), 2.15 (dd, *J* = 7.1, 7.1 Hz, 1H), 2.36−2.47 (m, 2H), 2.70 (d, *J* = 12.0 Hz, 1H), 7.20−7.24 (m, 3H), 7.49−7.53 (m, 2H); ^{13}C NMR (50.1 MHz, $CDCl_3$) δ (ppm) −1.734, 14.00, 18.50, 22.56, 23.52, 26.56, 28.28, 29.10, 31.40, 45.07, 127.1, 128.8, 130.1, 134.4, 209.1; IR (neat) 2958, 1692, 1578 cm^{-1}; MS (70

eV) *m*/*z* 382 (M^+); exact mass M^+ 382.1234 (calcd for $C_{19}H_{30}OSeSi$ 382.1231).

(+)-*cis*-1-Pivaloyl-2-[(phenylseleno)(trimethylsilyl)methyl]cyclopropane (3d) (entry 11 in Table 1) (R_f = 0.65 (hexane:ether = 2:1)): pale yellow oil; HPLC (hexane−^{i}PrOH = 400:1) minor peak t_{R1} 9.4 min, major peak t_{R2} 11.1 min, 40% ee; $[\alpha]^{24}_D$ = +31° (*c* 0.15, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm) 0.016 (s, 9H), 1.09−1.37 (m, 2H), 1.20 (s, 9H), 1.63 (dddd, *J* = 12.4, 7.9, 7.9, 7.8 Hz, 1H), 2.42 (ddd, *J* = 7.8, 5.7, 5.7 Hz, 1H), 2.80 (d, *J* = 12.4 Hz, 1H), 7.18−7.28 (m, 3H), 7.45−7.50 (m, 2H); ^{13}C NMR (50.1 MHz, $CDCl_3$) δ (ppm) −1.705, 20.05, 22.21, 26.82, 27.58, 28.86, 44.63, 126.7, 128.8, 130.8, 133.4, 214.0; IR (neat) 2968, 1684, 1580 cm^{-1}; MS (70 eV) *m*/*z* 368 (M^+); exact mass M^+ 368.1038 (calcd for $C_{18}H_{28}OSeSi$ 368.1074).

(1*S*,2*R*)-(+)-1-Acetyl-2-formylcyclopropane (4) in eq 2. To a solution of (+)-**3a** (33% ee, 100 mg, 0.307 mmol) in THF (5.3 mL) and H_2O (0.71 mL) was added $NaIO_4$ (154 mg, 0.718 mmol). The mixture was stirred vigorously for 2 h. The reaction mixture was poured into ether and saturated aqueous $NaHCO_3$ solution and extracted with ether (×3). The combined organic layer was dried ($MgSO_4$) and concentrated *in vacuo* (with ice-cooling). Distillation of the residue gave **4** (32 mg, ca. 93%, including a trace amount of impurity (PhSeSePh by ^{1}H NMR). **4**: colorless oil; bp 60−70 °C/20−21 mmHg; ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm) 1.52 (ddd, *J* = 4.6, 4.6, 8.0 Hz, 1H), 1.93−2.17 (m, 2H), 2.36 (s, 3H), 2.54 (ddd, *J* = 6.7, 6.7, 8.0 Hz, 1H), 9.28 (d, *J* = 6.4 Hz, 1H); ^{13}C NMR (50.1 MHz, $CDCl_3$) δ (ppm) 14.59, 30.44, 31.55, 32.34, 199.7, 204.9; IR (neat) 1705 cm^{-1}; MS (25 eV) *m*/*z* 112 (M^+); exact mass M^+ 112.0517 (calcd for $C_6H_8O_2$ 112.0524); optical rotation was measured for samples which were prepared from (+)-**3a** (20% ee), $[\alpha]^{23}_D$ = +21° (*c* 0.16, CH_2Cl_2), and (−)-**3a** (25% ee), $[\alpha]_D^{23}$ = −22° (*c* 0.26, CH_2Cl_2).

(1*R*,2*S*)-(+)-Methyl 2-Acetylcyclopropane-1-carboxylate (6) in eq 2. A flask was charged with CCl_4 (3 mL), MeCN (3 mL), water (3 mL), compound (+)-**4** (prepared from (+)-**3a** (29% ee) (59 mg, 0.526 mmol)), and $NaIO_4$ (783 mg, 3.66 mmol). To the mixture was added ruthenium trichloride hydrate (11 mg, ∼0.053 mmol), and the reaction mixture was stirred vigorously for 1 h at room temperature. Water was added, and the the mixture was extracted three times with CH_2Cl_2. The combined organic extracts were dried (Na_2SO_4) and concentrated to give crude (1*R*,2*S*)-2-acetylcyclopropane-1-carboxylic acid (**5**) (21 mg, ca. 31%). The low yield probably comes from the volatility of the starting material **4**. The reaction was not optimized. Immediate treatment of crude **5** (21 mg, 0.164 mmol) with diazomethane in ether and purification by column chromatography (silica gel, hexane−ether (1:4)) gave **6** (29% ee by GC analysis, 17 mg, 73% yield from crude **5**) (R_f = 0.4). **6**: colorless oil; $[\alpha]^{21}_D$ = −8°; GC (85 °C) minor peak t_{R1} = 16.4 min, major peak t_{R2} = 16.9 min, GC analysis of (1*S*,2*R*)-(+)-**6** prepared according to the literature[7] was identical with t_{R1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm) 1.24 (ddd, 4.9, 4.9, 8.2 Hz, 1H), 1.71 (ddd, 4.9, 4.9, 6.6 Hz, 1H), 2.06−2.32 (m, 2H), 2.28 (s, 3H), 3.69 (s, 3H); ^{13}C NMR (50.1 MHz, $CDCl_3$) δ (ppm) 12.60, 23.23, 28.78, 30.73, 52.19, 170.5, 204.0; IR (neat) 2958, 1736, 1441 cm^{-1}; MS (70 eV) *m*/*z* (relative intensity) 142 (19) M^+, 127 (100), 111 (32), 110 (80), 100 (9.5), 99 (9.0), 69 (13); exact mass M^+ 142.0632 (calcd for $C_7H_{10}O_3$ 142.0630).

(1*S*,2*R*)-(+)-(*Z*)-1-Acetyl-2-(1′-pentenyl)cyclopropane (7). (+)-**4** (prepared from (+)-**3** (44% ee)) (130.6 mg, 1.16 mmol) was dissolved in 4.6 mL of THF and cooled to −78 °C. To this solution was added 4.6 mL (1.27 mmol) of a 0.275 M THF solution of salt-free triphenylpentylidenephosphorane.[7,8] The resulting mixture was allowed to warm to room temperature and stirred overnight. Water was added to the mixture. The mixture was extracted with ether (3×). The ethereal extracts were washed with brine and then dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by column chromatography over silica gel eluting with hexane−ether (2:1) to give **7** (45% ee by GC analysis, 86.9 mg, 45%) (R_f = 0.4). **7**: colorless oil; $[\alpha]^{23}_D$ = +182° (*c* 0.87, $CHCl_3$) (reported optical rotation for (1*R*,2*S*)-(−)-**7**, $[\alpha]^{22}_D$ = −390° (*c* 1.54, $CHCl_3$)[7]); GC (90 °C) minor peak t_{R1} = 15.2 min, major peak t_{R2} = 16.2 min; ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm) 0.903 (t, *J* = 6.7 Hz, 3H), 1.13−1.23 (m, 1H), 1.32−1.39 (m, 4H), 2.11−2.30 (m, 4H), 2.23 (s, 3H), 5.19 (dd, *J* = 9.8, 10.3 Hz, 1H), 5.45 (td, *J* = 7.2, 10.3 Hz, 1H); ^{13}C NMR (50.1 MHz, $CDCl_3$) δ (ppm) 14.06, 15.26, 22.18, 22.38, 27.34, 29.10, 31.84, 125.8, 132.3, 206.0; IR (neat) 2962, 2930, 1700 cm^{-1}; MS (70 eV) *m*/*z* 166 (M^+); exact mass M^+ 166.1353 (calcd for $C_{11}H_{18}O$ 166.1357).

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra for compounds **3b**−**d**, **4**, **6** and **7,** results of theoretical analyses of model coordination compounds, and *Z*-matrix of $TiCl_2$(*R*-BINOLate)−**2a**, **A** (R = Me) (33 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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