A Chiral Scandium Catalyst for Enantioselective Diels–Alder Reactions

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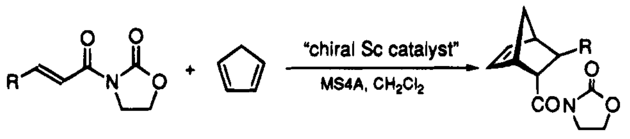
Summary: A chiral scandium catalyst, prepared from scandium trifluoromethanesulfonate ($Sc(OTf)_3$), (*R*)-(+)-1,1′-bi-2-naphthol, and a tertiary amine in dichloromethane, was quite effective in the enantioselective Diels–Alder reactions of acyl-1,3-oxazolidin-2-ones with dienes, and the corresponding Diels–Alder adducts were obtained in high yields with high diastereo- and enantioselectivities.

Although unique characteristics might be expected, scandium compounds are uncommon probably due to the lack of rich sources and to difficulties in separation, and their use in organic synthesis has been rather limited.[1] Recently, we found that scandium trifluoromethanesulfonate (scandium triflate, $Sc(OTf)_3$) was an excellent catalyst for Diels–Alder,[2] aldol,[3] and allylation reactions.[4] The catalyst is stable in water, and several advantages over conventional Lewis acids were revealed in these reactions. These novel properties encouraged us to design a chiral catalyst based on $Sc(OTf)_3$. In this paper, we wish to report the first chiral scandium catalyst, which is quite effective in enantioselective Diels–Alder reactions.

The chiral scandium catalyst was prepared from $Sc(OTf)_3$, (*R*)-(+)-1,1′-bi-2-naphthol ((*R*)-BINOL), and a tertiary amine in dichloromethane.[5] The catalyst was found to be effective in the Diels–Alder reactions of acyl-1,3-oxazolidin-2-ones with dienes.[6] Several examples of the present Diels–Alder reactions are shown in Table 1. The highest enantioselectivities were observed when *cis*-1,2,6-trimethylpiperidine[7] was employed as an amine. 3-(2-Butenoyl)-, 3-cinnamoyl-, and 3-(2-hexenoyl)-1,3-oxazolidin-2-ones reacted with cyclopentadiene smoothly in the presence of the chiral scandium catalyst to afford the corresponding Diels–Alder adducts in high yields and high selectivities. It should be noted that even 3 mol % of the catalyst was enough to complete the reaction and the endo adduct was obtained in a 92% ee.

Table 1. Enantioselective Diels–Alder Reactions Using a Chiral Scandium Catalyst



entry	R	catalyst (mol %)	yield (%)	endo/exo	ee (%) (endo)
1	Me	20	94	89/11	92
2		10	84	86/14	96
3		5	84	87/13	93
4		3	83	87/13	92
5	Ph	20	99	89/11	93
6		10	96	90/10	97
7	n-Pr	20	95	78/22	74
8		10	86	78/22	75

Although yields and selectivities have not yet been optimized, the catalyst was also found to be effective for the Diels–Alder reactions of an acrylic acid derivative.[8] 3-Acryloyl-1,3-oxazolidin-2-one reacted with 2,3-dimethylbutadiene to afford the corresponding Diels–Alder adduct in an 78% yield and a 73% ee under the conditions in entry 1 in Table 1,[9] whereas the reaction of 3-acryloyl-1,3-oxazolidin-2-one with cyclohexadiene under the conditions in entry 2 in Table 1[10] gave a 72% ee for the endo adduct (88% yield, endo/exo = 100/0).

A typical experimental procedure is described for the reaction of 3-cinnamoyl-1,3-oxazolidin-2-one with cyclopentadiene: To $Sc(OTf)_3$[11] (0.10 mmol), (*R*)-BINOL (0.12 mmol), and MS4A (125 mg) was added 1,2,6-trimethylpiperidine (0.24 mmol) in dichloromethane (1 mL) at −78 °C. The mixture was stirred for 30 min at this temperature, and then 3-cinnamoyl-1,3-oxazolidin-2-one (1.0 mmol) and cyclopentadiene (3.0 mmol, freshly distilled before use) in dichloromethane (0.5 mL) were successively added. The mixture was slowly warmed to 0 °C over 10 h. Water was then added to quench the reaction, and insoluble materials were filtered off. After a usual workup, the crude product was purified by silica gel column chromatography on silica gel to afford the desired Diels–Alder adduct (96% yield, endo/exo = 90/10). The diastereomer ratio was determined by ^1H NMR analysis, and the enantiomeric excess of the endo adduct was determined to be 97% ee by HPLC analysis (Daicel

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(1) Cotton, F. A.; Wilkinson, G. *Advanced Inorganic Chemistry*, 5th Ed.; John Wiley & Sons: New York, 1988; p 973.

(2) Kobayashi, S.; Hachiya, I.; Araki, M.; Ishitani, H. *Tetrahedron Lett.* **1993**, *34*, 3755.

(3) Kobayashi, S.; Hachiya, I.; Ishitani, H.; Araki, M. *Synlett* **1993**, 472.

(4) Hachiya, I.; Kobayashi, S. *J. Org. Chem.* **1993**, *58*, 6958.

(5) ^{13}C NMR (CD_2Cl_2) δ: 17.8, 18.5, 22.8, 25.1, 32.3, 37.5, 60.9, 63.7, 118.2, 124.1, 124.6, 127.4, 128.7, 129.7, 131.2, 134.0, 153.1 (amine: *cis*-1,2,6-trimethylpiperidine). Quite recently, we developed a chiral ytterbium triflate from ytterbium triflate ($Yb(OTf)_3$), (*R*)-BINOL, and a tertiary amine. Kobayashi, S.; Hachiya, I.; Ishitani, H.; Araki, M. *Tetrahedron Lett.* **1993**, *34*, 4535. Kobayashi, S; Ishitani, H. *J. Am. Chem. Soc.* **1994**, *116*, 4083. Although its structure has not yet been clear, this paper may provide a hint to clarify the Yb catalyst.

(6) Narasaka et al. reported an excellent chiral titanium catalyst for the Diels–Alder reactions. (a) Narasaka, K.; Iwasawa, N.; Inoue, M.; Yamada, T.; Nakashima, M.; Sugimori, J. *J. Am. Chem. Soc.* **1989**, *111*, 5340 and references cited therein. See also: (b) Chaouis, C.; Jurczak, J. *Helv. Chim. Acta* **1987**, *70*, 436. (c) Corey, E. J.; Imwinkelried, R.; Pikul, S.; Xiang, Y. B. *J. Am. Chem. Soc.* **1989**, *111*, 5493. (d) Evans, D. A.; Miller, S. J.; Lectka, T. *J. Am. Chem. Soc.* **1993**, *115*, 6460.

(7) Deno, N.; Fruit, R. E., Jr. *J. Am. Chem. Soc.* **1968**, *90*, 3502.

(8) Narasaka, K.; Tanaka, H.; Kanai, F. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 387.

(9) Twenty mol % of 3-benzoyl-1,3-oxazolidin-2-one was added to the scandium catalyst.

(10) Ten mol % of 3-benzoyl-1,3-oxazolidin-2-one was added to the scandium catalyst.

(11) $Sc(OTf)_3$ is prepared from the corresponding oxide (Sc_2O_3) and trifluoromethanesulfonic acid (TfOH): 1.5 equiv of Sc_2O_3 was added to an aqueous solution of TfOH (ca. 50% v/v), and the mixture was heated at 100 °C for 1 h. After filtration to remove the unreacted oxide, the water was evaporated under reduced pressure. The resulting white powder was dried by heating *in vacuo* at 200 °C. $Sc(OTf)_3$ thus prepared was used without further purification. See: Thom, K. F., US Patent 3615169 (1971); *Chem. Abstr.* **1972**, *76*, 5436a.

0022-3263/94/1959-3758$04.50/0

Chart 1. Chiral Scandium Catalyst

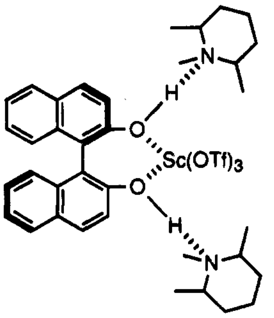


Table 2. Comparison of ^{13}C NMR Chemical Shifts of the Carbons of the *N*-Methyl Groups of *cis*-1,2,6-Trimethylpiperidine (TMP) and IR Wavenumbers (CH_2Cl_2) in the Region 930–1000 cm^{-1}

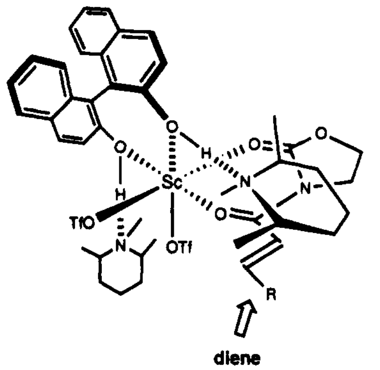
compd	δ (ppm)	wavenumber (cm^{-1})
TMP	38.2	947
TMP + (*R*)-BINOL	35.1	989, 947
TMP + TfOH	34.1	958
TMP + $Sc(OTf)_3$	37.8	947
TMP + $Sc(OTf)_3$ + (*R*)-BINOL	37.5	997, 956

Chiralpak AD). The absolute configuration was assigned to be 2*R*,3*R* tentatively by comparison of the optical rotation with that reported in the literature.[6a]

As for the chiral scandium catalyst, a unique structure was indicated from the following experiments (see Chart 1). (1) The amines employed in the preparation of the catalyst influenced the enantioselectivities strongly. For example, in the Diels–Alder reaction of 3-(2-butenoyl)-1,3-oxazolidin-2-one with cyclopentadiene (CH_2Cl_2, 0 °C), the enantiomeric excesses of the endo adduct depended crucially on the amines employed: aniline, 14% ee; lutidine, 46% ee; triethylamine, 51% ee; 2,2,6,6-tetramethylpiperidine, 51% ee; diisopropylethylamine, 69% ee; 2,6-dimethylpiperidine, 69% ee; 1,2,2,6,6-pentamethylpiperidine, 72% ee; and *cis*-1,2,6-trimethylpiperidine, 84% ee. (2) When *n*-BuLi was used instead of the tertiary amine as the base, only a 6% ee of the endo adduct was observed. (In this case, [(*R*)-1,1′-bi-2-naphthalenediolato-(2-)-*O,O′*]scandium triflate would be produced, and *this was not the catalyst.*) (3) The reaction proceeded sluggishly in the presence of only $Sc(OTf)_3$ and 1,2,6-trimethylpiperidine (without (*R*)-BINOL). (In the chiral scandium catalyst, the amine would not coordinate to Sc(III)). (4) As shown in Table 2, ^{13}C NMR spectroscopy of the catalyst indicated the existence of a weak interaction between the nitrogen of *cis*-1,2,6-trimethylpiperidine and the phenolic hydrogen of (*R*)-BINOL. IR data also supported this interaction.[12]

The coordination form of the $Sc(OTf)_3$–(*R*)-BINOL complex may be similar to that of lanthanide(III)–water or alcohol complexes[13] and this is quite different from those of usual Lewis acids. The sense of asymmetric induction in the present reactions can be rationalized by assuming an intermediate octahedral Sc(III)–dienophile complex (Chart 2). The axial chirality of (*R*)-BINOL is transferred to the amine, the *re* face of the acyl-1,3-oxazolidin-2-one is effectively shielded by the amine part, and a diene approaches the dienophile from the *si* face to afford the adduct in a high enantioselectivity.

Chart 2. Assumed Transition State



In summary, the first chiral scandium catalyst was synthesized, and it was shown to be quite effective for enantioselective Diels–Alder reactions. The catalyst can be easily prepared by simply mixing $Sc(OTf)_3$, (*R*)-BINOL, and an amine, and a unique coordination form, which has never been observed in other Lewis acid catalysts, was indicated. In the chiral catalyst, the axial chirality of (*R*)-BINOL is postulated to be transferred to the amine part, which would work as a "wall" in the transition state to shield one side of the dienophile. Since the amine part can be freely chosen, the design of the catalyst was easier than other catalysts based on (*R*)-BINOL.[14]

Further investigations to develop other asymmetric reactions using the chiral scandium catalyst are now in progress.

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Supplementary Material Available: IR, ^{1}H NMR, and HPLC spectra (9 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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[12] Fritsch, J.; Zundel, G. *J. Phys. Chem.* **1981**, *85*, 556.

[13] As we have already shown, $Sc(OTf)_3$ is a stable Lewis acid in water.[2-4] The same coordination form was also observed in $Ln(OTf)_3$. For example: Harrowfield, J. M.; Kepert, D. L.; Patrick, J. M.; White, A. H. *Aust. J. Chem.* **1983**, *36*, 483. Review: Hart, F. A. In *Comprehensive Coordination Chemistry;* Wilkinson, G., Ed.; Pergamon Press: New York, 1987; Vol. 3, p 1059.

[14] Some "modified" binaphthols were reported. Although they are effective as chiral sources, their preparations often require long steps. (a) Maruoka, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1989**, *111*, 789. (b) Bao, J.; Wulff, W. D.; Rheingold, A. L. *Ibid.* **1993**, *115*, 3814.