Tetrahedron Letters, Vol. 34, No. 28, pp. 4535-4538, 1993
Printed in Great Britain

0040-4039/93 $6.00 + .00
Pergamon Press Ltd

Asymmetric Diels-Alder Reaction Catalyzed by a Chiral Ytterbium Trifluoromethanesulfonate

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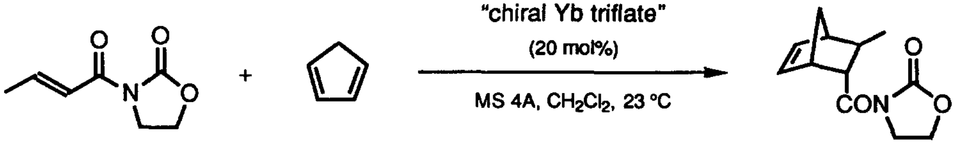
Abstract: *In the presence of a catalytic amount of chiral ytterbium trifluoromethanesulfonate (triflate), acyl-1,3-oxazolidin-2-ones or methacrolein reacted with cyclopentadiene to afford the corresponding Diels-Alder adduct in high yields and with moderate to excellent enantiomeric excesses.*

In the previous paper, we reported that lanthanide trifluoromethanesulfonate (lanthanide triflate, $Ln(OTf)_3$), especially ytterbium triflate ($Yb(OTf)_3$), was a good catalyst in the Diels-Alder reaction of some dienophiles with cyclopentadiene.1) The reactions proceeded smoothly in the presence of a catalytic amount of $Yb(OTf)_3$ to give the corresponding adducts in high yields. Moreover, the catalyst was stable in water and was easily recovered from aqueous layer after the reaction was completed, and could be reused. These unique properties were considered to be dependent on the specific coordination numbers and stereochemistry of lanthanide(III),2) and this prompted us to design a chiral lanthanide triflate which can work as an efficient catalyst in the asymmetric Diels-Alder reaction.

Recently, some asymmetric Diels-Alder reactions catalyzed by chiral Lewis acids were reported.3) The Lewis acids employed in these reactions are generally traditional ones such as titanium, boron, or aluminum reagents, and they are well modified to realize high enantioselectivities. Although lanthanide compounds have been expected as Lewis acid reagents, only a few asymmetric reactions catalyzed by chiral lanthanide Lewis acids were reported. Danishefsky's pioneer work demonstrated that $Eu(hfc)_3$ (a NMR shift reagent) catalyzed the hetero-Diels-Alder reaction of aldehydes with siloxydienes, however, enantiomeric excesses were moderate.4) In this paper, we report a chiral ytterbium triflate catalyzed Diels-Alder reaction of some dienophiles with cyclopentadiene, which affords the corresponding cyclic compounds in moderate to high enantiomeric excesses.



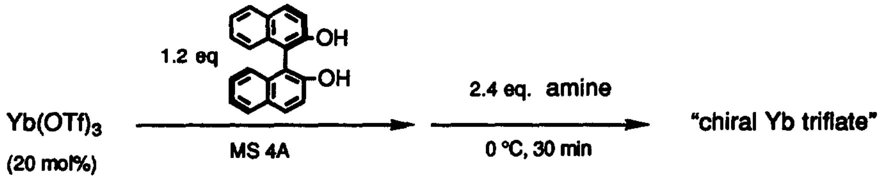
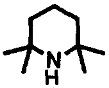
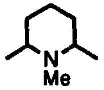
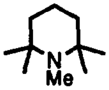
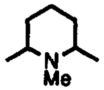
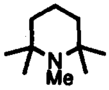


Table 1. Effect of Amine in the Asymmetric Diels-Alder Reaction [a)]

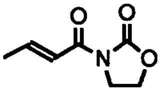
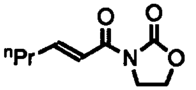
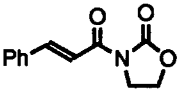
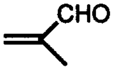
Entry	Amine	MS [b)]	Yield / % [c)]	endo / exo [d)]	ee / % [e)]
1	Et_3N	—	87	76 / 24	33
2	$^nBu_3N$	—	quant.	83 / 17	68
3	$^iPr_2NEt$	—	82	85 / 15	70
4		—	93	80 / 20	51
5	 (*cis*)	—	96	85 / 15	71
6		—	96	85 / 15	69
7	$^iPr_2NEt$	MS 3A	84	87 / 13	80
		MS 4A	88	87 / 13	83
		MS 5A	82	86 / 14	76
8	 (*cis*)	MS 4A	91	86 / 14	90
			77	89 / 11	95 [f)]
9		MS 4A	92	86 / 14	76

a) The reactions were carried out at room temperature unless otherwise noted (see the text). b) Molecular sieves. c) Isolated yield. d) Determined by ^1H NMR analysis. e) Ee's of endo forms, determined by HPLC analysis using DAICEL CHIRALPAK AD. f) The reaction was carried out at 0 °C.

The chiral ytterbium triflate was in situ prepared from Yb(OTf)$_3$, tertially amine, and (R)-(+)-binaphtol. First, crotonoyl-1,3-oxazolidin-2-one was chosen as a model and the reaction with cyclopentadiene was examined. Thus, in the presence of a chiral ytterbium triflate, prepared from Yb(OTf)$_3$, triethylamine, and (R)-(+)-binaphtol in dichloromethane at 0 °C, crotonoyl-1,3-oxazolidin-2-one reacted with cyclopentadiene at 23 °C to afford the corresponding Diels-Alder adduct in 87% yield (endo/exo=76/24) and the enantiomeric excess of the endo adduct was proved to be 33%ee. After screening several reaction conditions, the amine employed at the stage of the preparation of the chiral ytterbium triflate strongly influenced on the diastereo- and enantioselectivities (Table 1). In general, bulky amines gave better results and 70% and 71% ee's were observed by using diisopropylethylamine and *cis*-1,2,6-trimethylpiperidine,[5] respectively (entries 3 and 5). In addition, the better result was obtained when the amine was combined with molecular sieves 4A (*cis*-1,2,6-trimethylpiperidine, 91% yield, endo/exo=86/14, endo=90%ee), and the enantiomeric excess was further improved to be 95% when the reaction was carried out at 0 °C (entry 8).

Several examples of the present Diels-Alder reaction are listed in Table 2. Some acyl-1,3-oxazolidin-2-ones or methacrolein smoothly reacts with cyclopentadiene to afford the corresponding Diels-Alder adduct in high yields and with moderate to excellent enantiomeric excesses.

Table 2. Asymmetric Diels-Alder Reaction of Some Dienophiles with Cyclopentadiene Catalyzed by the chiral Yb triflate[a)]

Entry	Dienophile	Temp / °C	Yield / %[b)]	endo / exo[c)]	ee / %[d)]
1		0	77	89 / 11	95
		23	91	86 / 14	90
2		23	81	80 / 20	83
3		23	40	81 / 19	83
4		0	54	4 / 96	44

a) The chiral Yb triflate was prepared from Yb(OTf)$_3$, (R)-(+)-binaphtol, *cis*-1,2,6-trimethylpiperidine, and MS 4A in dichloromethane at 0 °C except for entry 4. 2,2,6,6,-Tetramethylpiperidine was used without MS 4A in entry 4. b) Isolated yield. c) Determined by ^{1}H NMR analysis. d) Determined by HPLC analysis using DAICEL CHIRALPAK AD (entries 1-3). For entry 4, see ref 6.

A typical experimental procedure is described for the reaction of crotonoyl-1,3-oxazolidin-2-one with cyclopentadiene; to a mixture of Yb(OTf)$_3$ (0.10 mmol), (R)-(+)-binaphtol (0.12 mmol), and MS 4A (125 mg) was added *cis*-1,2,6-trimethylpiperidine(0.24 mmol) in dichloromethane (1 ml) at 0 °C, and the mixture was stirred for 30 min at the same temperature. Crotonoyl-1,3-oxazolidin-2-one (0.50 mmol) in dichloromethane (0.25 ml) and cyclopentadiene (1.5 mmol, freshly distilled before use) in dichloromethane (0.25 ml) were successively added at 0 °C, and the mixture was stirred for 20 h at 23 °C. Water was then added to quench the reaction and insoluble materials were filtered. After usual work up, the crude product was purified by silica gel column chromatography on silica gel to afford the desired Diels-Alder adduct (91% yield, endo/exo=86/14). The diastereomer ratio was determined by ^{1}H NMR analysis and the enantiomeric excess of the endo adduct was determined to be 90%ee by HPLC analysis (DAICEL CHIRALPAK AD). The absolute configuration was assigned to be 2*S*, 3*R* by comparison of the optical rotation with that of the literature.3b) When the reaction was carried out at 0 °C, the diastereo- and enantioselectivities were rather improved (77% yield, endo/exo=89/11, endo=95%ee).

At present, the precise structure of the chiral ytterbium triflate is unclear. From ^{1}H, ^{13}C NMR, and IR analysis of the mixture of the chiral catalyst and crotonoyl-1,3-oxazolidin-2-one, coordination of two carbonyl oxygens of crotonoyl-1,3-oxazolidin-2-one to ytterbium(III) and absence of an ammonium salt (for example, a salt generated from an amine and TfOH) were confirmed. Broad peaks of crotonoyl-1,3-oxazolidin-2-one observed in ^{1}H and ^{13}C NMR spectra indicated chemical exchange under equilibrium. Since the reaction proceeded more slowly in the presence of $Yb(OTf)_3$ and an amine (without (R)-(+)-binaphtol), the amine in the chiral Yb triflate would interact with the phenolic hydrogen rather than with ytterbium(III).

Further investigations to clarify the precise structure of the chiral ytterbium catalyst and the mechanism of the present Diels-Alder reaction as well as to develop asymmetric reactions using the chiral ytterbium triflate are now in progress.

References and Notes

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(Received in Japan 26 March 1993)