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Stereocontrol in a Ytterbium Triflate-Catalyzed 1,3-Dipolar Cycloaddition Reaction of Carbonyl Ylide with *N*-Substituted Maleimides and Dimethyl Fumarate

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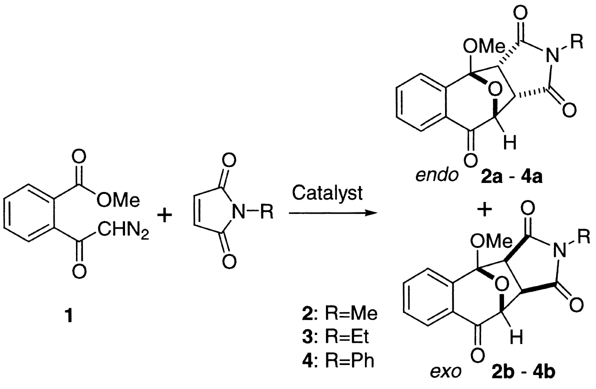
The addition of Yb(OTf)$_3$ (10 mol%) in a Rh$_2$(OAc)$_4$-catalyzed reaction of *o*-(methoxycarbonyl)-α-diazoacetophenone with *N*-methylmaleimide in CH$_2$Cl$_2$ or in diethyl ether gave cycloadducts with high *endo*-selectivity (*endo*:*exo* = 95:5–96:4). The CuOTf (20 mol%)- or CuCl-Yb(OTf)$_3$ (5 mol%)-catalyzed reaction also gave 1,3-dipolar cycloadducts in an *endo*-selective manner (*endo*:*exo* = 94:6). On the other hand, a reaction using only Rh$_2$(OAc)$_4$ (5 mol%) as the catalyst in benzene under reflux gave cycloadducts with *exo*-selectivity (*endo*:*exo* = 11:89). The reaction of *N*-ethyl- and *N*-phenylmaleimides under the same conditions showed a similar tendency in terms of the stereoselectivity.

Stereocontrol of 1,3-dipolar cycloadditions is extremely important for constructing heterocyclic compounds from the viewpoints of the synthesis of biologically active compounds. Although many examples of regio- and/or stereoselective 1,3-dipolar cycloadditions had been developed, their stereoselectivity mainly depended on the nature of the dipoles and dipolarophiles used.[1] As is well known, a Lewis acid is one of the most effective catalysts in achieving high *endo*-selectivity as well as enantioselectivity (in the case of a chiral Lewis acid) in a Diels–Alder reaction governed by an interaction between the HOMO of the diene and the LUMO of the dienophile. It has recently been demonstrated that a Lewis acid is also very effective to control the stereoselectivity in some 1,3-dipolar cycloaddition, although the deactivation or decomposition of 1,3-dipole may be considered by adding a Lewis acid. For example, chiral Lewis acid-catalyzed highly enantioselective 1,3-dipolar cycloadditions of nitrones with 3-crotonyloxazolidinone have been developed.[2] In those reactions, the *exo*:*endo* selectivity was also controlled by the property of the Lewis acid. However, those Lewis acid-catalyzed 1,3-dipolar cycloaddition reactions still have a limitation in terms of generality for the 1,3-dipole because of its basicity and instability.[1f]

Since we demonstrated the utility of a method by studying the metal-catalyzed decomposition of *o*-(alkoxycarbonyl)-α-diazoacetophenone,[3] the intramolecular carbenoid-carbonyl reaction has become one of the most effective methods for generating carbonyl ylides.[4] Our present goal is to control the stereoselectivity by metallic catalysts in the cycloaddition of carbonyl ylide. After our discovery was reported in a preliminary communication,[5] Hashimoto[6] and Hodgson[7] separately reported highly enantioselective carbonyl ylide cycloadditions catalyzed by a chiral rhodium-catalyst. However, there have been no reports concerning the successful stereocontrol by using a Lewis acid in the cycloaddition of carbonyl ylide.[8,9] In this paper, we report on full accounts of our investigations in dramatic changes of stereoselectivity caused by ytterbium triflate (Yb(OTf)$_3$) in the 1,3-dipolar cycloaddition of carbonyl ylide with *N*-substituted maleimides.[5] The stereoselectivity in the reaction of dimethyl fumarate in the presence of Yb(OTf)$_3$ is also reported.

Results and Discussion

Reaction with *N*-Methylmaleimide. To clarify the dependency of the stereoselectivity by kinds of metallic catalysts, we first examined the decomposition of *o*-(methoxycarbonyl)-α-diazoacetophenone (**1**) in the presence of *N*-methylmaleimide by using several metal-catalysts (5 mol%) which are typical for the decomposition of diazo compounds (Table 1, entries 1, 3, 4, 7, 8, 10, 11, 21, and 22; Scheme 1). Surprisingly, when metal-catalysts having Lewis acidity, such as CuOTf (*endo*:*exo* = 87:13) and Cu(OTf)$_2$ (*endo*:*exo* = 82:18), were



Scheme 1.

Table 1. Cycloaddition of Carbonyl Ylide with *N*-Methylmaleimide[a]

Entry	Catalyst/mol%	Solvent	Temp/°C	Yield/%	*endo*:*exo*[c]
1	CuOTf (5)	benzene	reflux	49	87:13
2	CuOTf (20)	benzene	reflux	34	94:6
3	[Cu(MeCN)$_4$]PF$_6$ (5)	benzene	reflux	49	65:35
4	CuCl (5)	benzene	reflux	81	26:74
5	CuCl (5), ZnBr$_2$ (5)	benzene	reflux	27	82:18
6	CuCl (5), Yb(OTf)$_3$ (5)	benzene	reflux	52	94:6
7	Cu(OTf)$_2$ (5)	benzene	reflux	24	82:18
8	[Cu(acac)$_2$] (5)	benzene	reflux	66	24:76
9	[Cu(acac)$_2$] (5), Yb(OTf)$_3$ (5)	benzene	reflux	46	83:17
10	[Cu(hfacac)$_2$] [e](5)	benzene	reflux	40	32:68
11	Rh$_2$(OAc)$_4$ (5)	benzene	reflux	70	11:89
12	Rh$_2$(OAc)$_4$ (5), Yb(OTf)$_3$ (5)	benzene	reflux	64[b]	61:39
13	Rh$_2$(OAc)$_4$ (5), Yb(OTf)$_3$ (5)	benzene	rt	89[b]	90:10
14	Rh$_2$(OAc)$_4$ (1), Yb(OTf)$_3$ (5)	benzene	rt	69[b]	88:12
15	Rh$_2$(OAc)$_4$ (2), Yb(OTf)$_3$ (10)	benzene	rt	98[b]	93:3
16	Rh$_2$(OAc)$_4$ (2), Yb(OTf)$_3$ (10)	CH$_2$Cl$_2$	rt	quant.[b]	95:5
17	Rh$_2$(OAc)$_4$ (2), Yb(OTf)$_3$ (10)	CH$_2$Cl$_2$	0	95[b]	95:5
18	Rh$_2$(OAc)$_4$ (2), Yb(OTf)$_3$ (10)	THF	rt	35[b]	99:1
19	Rh$_2$(OAc)$_4$ (2), Yb(OTf)$_3$ (10)	Et$_2$O	rt	67[b]	99:1
20	Rh$_2$(OAc)$_4$ (2), Yb(OTf)$_3$ (10)[d]	Et$_2$O	rt	89[b]	96:4
21	[Rh$_2$(tfa)$_4$][f] (5)	benzene	reflux	40[b]	22:78
22	[Rh$_2$(acm)$_4$][g] (5)	benzene	reflux	84[b]	35:65
23	Yb(OTf)$_3$ (10)[d]	benzene	reflux (5 h)	36	98:2
24	Sc(OTf)$_3$ (10)[d]	benzene	reflux (3 h)	60	77:23

a) A solution of diazo compound **1** was added to a solution of *N*-methylmaleimide (2 equiv) in the presence of the catalyst at the temperature cited in Table 1 over a period of 1 h. b) Determined by HPLC analysis (Nova-Pak C18, Waters). c) The ratio was determined by ^{1}H NMR and/or HPLC analysis (Nova-Pak C18, Waters). d) In the presence of MS 4A powder. e) Hexafluoroacetylacetonatocopper(II). f) Tetrakis(trifluoroacetato)dirhodium(II). g) Tetrakis(acetamido)dirhodium(II).

used, high *endo*-selectivity was observed, which is not usually found in this carbonyl ylide cycloaddition (entries 1 and 7).[10] The use of 20 mol% of CuOTf increased the *endo*-selectivity to *endo*:*exo* = 94:6 (entry 2) compared with the result of entry 1. In the case of other copper catalysts, such as CuCl, [Cu(acac)$_2$], and [Cu(hfacac)$_2$], moderate *exo*-selectivity was observed (entries 4, 8, and 10). The reaction using Rh(II) catalysts generally showed *exo*-selectivity (entries 11, 21, and 22). We also found that *endo*-selectivity was observed by adding 5 mol% of Lewis acid to 5 mol% of CuCl as a catalyst (entries 5 and 6). Although the yield was moderate, Yb(OTf)$_3$ was effective for *endo*-selectivity to give the ratio of *endo*:*exo* = 94:6 (entry 6). The moderate yields under Lewis acid-catalyzed conditions may be attributed to the decomposition of the products by a trace amount of water in the reaction mixture.

The ratio of *endo*- and *exo*-products in good yields must be discussed for a detailed consideration of the stereoselectivity in the cycloaddition of this carbonyl ylide, because the decomposition rate of the *endo*- and *exo*-products may be different under Lewis acid-catalyzed conditions. To find the optimum conditions for the highest yield and *endo*-selectivity, the kinds of metal-catalysts and reaction temperature were investigated (entries 9, 12, and 13). The combination of Rh$_2$(OAc)$_4$ and Yb(OTf)$_3$ at room temperature showed a better result (89% yield, *endo*:*exo* = 90:10, entry 13). After investigating the amounts of the catalysts and solvent (entries 14–20), we found that the conditions using 2 mol% of Rh$_2$(OAc)$_4$ and 10 mol% of Yb(OTf)$_3$ at room temperature in CH$_2$Cl$_2$ showed the best yield (quant.) and high *endo*-selectivity (*endo*:*exo* = 95:5). The reaction proceeded at 0 °C for the same reaction time under similar conditions to give *endo*-product **2a** also in high yield with high *endo*-selectivity (entry 17). An acceleration of the reaction by adding Yb(OTf)$_3$ was not clearly observed, probably due to the rate-determining step containing the ylide formation. Diethyl ether in the presence of MS 4A powder was also a good condition for high yield and high *endo*-selectivity (entry 20). In this case, MS 4A presumably plays the role to avoid hydrolysis of the products. Although the yield was low, it is interesting that the reaction using only Yb(OTf)$_3$ or Sc(OTf)$_3$ in benzene under reflux gives cycloadducts with *endo*-selectivity (entries 23 and 24).

Reaction with *N*-Ethyl- and *N*-Phenylmaleimides. The CuOTf- and CuCl-Yb(OTf)$_3$-catalyzed reactions of diazoacetophenone **1** with *N*-ethylmaleimide also showed *endo*-selectivity (Table 2, entries 1 and 4). The reaction using Rh$_2$(OAc)$_4$ showed moderate *exo*-selectivity (entry 5). The Rh$_2$(OAc)$_4$–Yb(OTf)$_3$-catalyzed reaction also achieved high *endo*-selectivity (*endo*:*exo* = 95:5 entry 6, *endo*:*exo* = 90:10 entry 7). The reactions with *N*-phenylmaleimide showed lower selectivity than that of the reactions with *N*-methyl- and *N*-ethylmaleimides. However, the tendency of the selectivity is almost the same. Thus, the CuOTf- and CuCl-Yb(OTf)$_3$-catalyzed reac-

Table 2. Cycloaddition of Carbonyl Ylide with *N*-Ethyl- and *N*-Phenylmaleimides[a]

Entry	R	Catalyst/mol%	Solvent	Temp/°C	Yield/%	*endo*:*exo*[b]
1	Et	CuOTf (5)	benzene	rt	44	82:18
2	Et	CuOTf (5)	benzene	reflux	55	70:30
3	Et	$[Cu(MeCN)_4]PF_6$ (5)	benzene	reflux	47	69:31
4	Et	CuCl (5), $Yb(OTf)_3$ (5)	benzene	reflux	40	88:12
5	Et	$Rh_2(OAc)_4$ (5)	benzene	reflux	85	22:78
6	Et	$Rh_2(OAc)_4$ (2), $Yb(OTf)_3$ (10)	CH_2Cl_2	rt	76	95:5
7	Et	$Rh_2(OAc)_4$ (2), $Yb(OTf)_3$ (10)[c]	CH_2Cl_2	rt	80	90:10
8	Ph	CuOTf (5)	benzene	rt	60	63:37
9	Ph	CuOTf (20)	benzene	rt	25	75:25
10	Ph	$[Cu(acac)_2]$ (5)	benzene	rt	51	21:79
11	Ph	CuI (20)	benzene	rt	31	20:80
12	Ph	CuCl (5), $Yb(OTf)_3$ (5)	benzene	reflux	43	77:23
13	Ph	CuCl (5), $Yb(OTf)_3$ (5)	MeCN	reflux	21	90:10
14	Ph	$Rh_2(OAc)_4$ (5)	benzene	reflux	88	40:60
15	Ph	$Rh_2(OAc)_4$ (2), $Yb(OTf)_3$ (10)	CH_2Cl_2	rt	57	54:46
16	Ph	$Rh_2(OAc)_4$ (2), $Yb(OTf)_3$ (10)	Et_2O	rt	10	92:8
17	Ph	$Rh_2(OAc)_4$ (2), $Yb(OTf)_3$ (10)[c]	Et_2O	rt	89	78:22
18	Ph	$Rh_2(OAc)_4$ (2), $Sc(OTf)_3$ (10)	CH_2Cl_2	rt	50	84:16
19	Ph	$Rh_2(OAc)_4$ (2), $Sc(OTf)_3$ (10)[c]	CH_2Cl_2	rt	82	49:51

a) A solution of diazo compound **1** was added to a solution of *N*-methylmaleimide (2 equiv) in the presence of the catalyst at the temperature cited in Table 2 over a period of 1 h. b) The ratio was determined by ^{1}H NMR and/or HPLC analysis (Nova-Pak C18, Waters). c) In the presence of MS 4A powder.

Table 3. Cycloaddition of Carbonyl Ylide with *N*-Substituted Maleimides in the Presence of Chiral Catalyst[a]

Entry	R	Catalyst/mol%	Solvent	Temp	Yield/%	*endo*:*exo*[b] %ee	*endo*/*exo*[c]
1	Me	CuOTf (5)	benzene	reflux	49	87:13	–/–
2	Me	**Ln**–CuOTf (5)	benzene	reflux	81	29:71	1/0
3	Me	**Ln**–CuOTf (5)	benzene	rt	69	50:50	3/0
4	Me	$Cu(OTf)_2$ (5)	benzene	reflux	24	82:18	–/–
5	Me	**Ln**–$Cu(OTf)_2$ (5)	benzene	reflux	79	49:51	1/0
6	Me	**Ln**–$Cu(OTf)_2$ (5)	benzene	rt	60	46:54	7/0
7	Me	$[Cu(MeCN)_4]PF_6$ (5)	benzene	reflux	49	65:35	–/–
8	Me	**Ln**–$[Cu(MeCN)_4]PF_6$ (5)	benzene	reflux	38	47:53	6/0
9	Me	$[Rh_2$(5*S*-MEPY$)_4]$ (5)	benzene	rt	75	23:77	0/2
10	Et	CuOTf (5)	benzene	rt	44	82:18	–/–
11	Et	**Ln**–CuOTf (5)	benzene	rt	51	33:67	7/0
12	Ph	CuOTf (5)	benzene	rt	60	63:37	–/–
13	Ph	CuOTf (20)	benzene	rt	25	75:25	–/–
14	Ph	**Ln**–CuOTf (5)	benzene	rt	83	43:57	6/0
15	Ph	**Ln**–CuOTf (10)	benzene	rt	61	47:53	4/0
16	Ph	**Ln**–CuOTf (20)[d]	benzene	rt	43	61:39	15/0
17	Ph	**Ln**–CuOTf (20)	benzene	rt	53	37:63	15/0
18	Ph	**Ln**–CuOTf (20)[e]	benzene	rt	53	42:58	5/0
19	Ph	**Ln**–CuOTf (20)[f]	benzene	rt	72	41:59	3/0
20	Ph	**Ln**–CuOTf (20)	benzene–hexane (1:1)[g]	rt	30	45:55	18/0
21	Ph	**Ln**–CuOTf (100)	benzene	rt	37	50:50	17/0
22	Ph	$[Rh_2$(5*S*-MEPY$)_4]$ (20)	benzene	rt	45	11:89	20/5
23	Ph	$Rh_2(OAc)_4$ (2), Yb[(*S*)-BNP$]_3$ (10)	CH_2Cl_2	rt	97	44:56	2/1

a) A solution of diazo compound **1** was added to a solution of *N*-substituted maleimide (2 equiv) in the presence of the catalyst at the temperature cited in Table 3 over a period of 1 h. b) The ratio was determined by ^{1}H NMR and/or HPLC analysis (Nova-Pak C18, Waters). c) Determined by HPLC analysis (Daicel Chiralpak AS). d) 1 Equiv of *N*-phenylmaleimide was used. e) 3 Equiv of *N*-phenylmaleimide was used. f) 5 Equiv of *N*-phenylmaleimide was used. g) Fifty mL of solvent was used.

tions in benzene showed moderate *endo*-selectivity (entries 8, 9, 12, and 13).

The $Rh_2(OAc)_4$–$Yb(OTf)_3$-catalyzed reaction in ether afforded the highest *endo*-selectivity in the reaction with *N*-phenylmaleimide (entries 16 and 17). The moderate-to-low yield of those adducts using a Lewis acid as an additive is probably

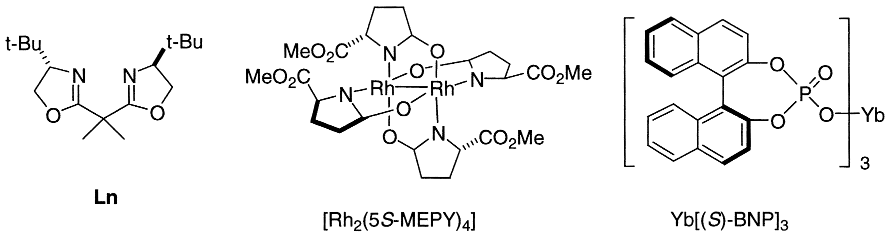


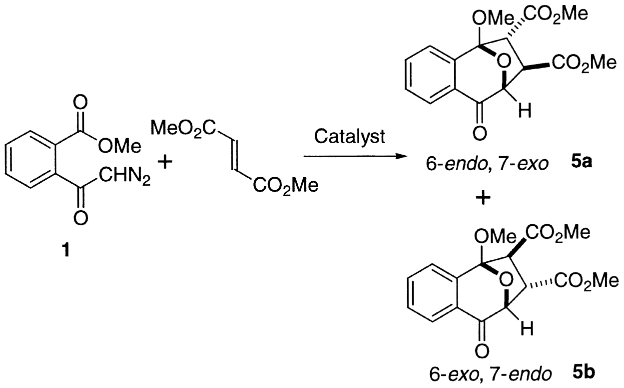
Chart 1.

due to interference of the formation of carbonyl ylides or the decomposition of adducts by the Lewis acid. The use of other copper catalysts, such as CuI and [Cu(acac)$_2$], and Rh(II) catalysts, as a sole catalyst resulted in *exo*-selectivity (entries 10, 11, and 14).

Reaction in the Presence of Chiral Catalysts. Chiral catalysts which were prepared from Cu(I) and Cu(II) salts were investigated in the reaction of **1** with *N*-substituted maleimides (Chart 1, Table 3). It is interesting that the *endo*-selectivity changed to *exo* excess in the CuOTf- or Cu(OTf)$_2$-catalyzed reaction when 2,2′-isopropylidenebis[(4*S*)-4-*t*-butyl-2-oxazoline] (**Ln**) was used as the ligand (1 vs 2, 4 vs 5, 7 vs 8, 12 vs 14). However, in a reaction with *N*-methyl- or *N*-ethylmaleimides in the presence of 5 mol% of chiral catalysts, almost no enantioselection was obtained. In the case of *N*-phenylmaleimide in the presence of more than 20 mol% of the catalyst, a small degree of asymmetric induction was observed (*endo*: 15–17% ee, entries 16, 17, 18 and 21). The amounts of *N*-phenylmaleimide influenced both the *endo*/*exo*-selectivity and the enantioselectivity. In the presence of an equimolar amount of *N*-phenylmaleimide, *endo*-product was predominantly obtained (entry 16). When more than 2 molar amounts of *N*-phenylmaleimide were used, the preference changed to *exo* excess (entries 17–19). Under those conditions, the enantioselectivity decreased as the amount of *N*-phenylmaleimide increased (entries 16–19). These results might suggest that the chiral catalysts affect not only the generation of carbenoid, but also the activation of a dipolarophile as a Lewis acid. Although the use of another solvent, such as toluene, diethyl ether, THF, MeCN, or CH$_2$Cl$_2$, gave no satisfactory result in terms of the enantioselectivity, the reaction in benzene-hexane (1:1) showed a slightly increased enantioselectivity (entry 20).

In reactions with *N*-phenylmaleimide, dirhodium(II) tetrakis[methyl 2-pyrrolidone-5(*S*)-carboxylate] ([Rh$_2$(5*S*-MEPY)$_4$]) was the best catalyst to obtain the *exo*-adduct selectively. It is also interesting to point out that a similar degree of asymmetric induction in a **Ln**–CuOTf catalyzed reaction was observed by using 20 mol% of [Rh$_2$(5*S*-MEPY)$_4$] (*endo*: 20% ee, *exo*: 5% ee, entry 22). In the Rh$_2$(OAc)$_4$-catalyzed reaction, the addition of ytterbium tris(*S*)-1,1′-binaphthyl-2,2′-diyl phosphonate (Yb[(*S*)-BNP]$_3$) (10 mol%), which showed moderate enantioselectivity in the reaction of diazoacetophenone **1** with benzyloxyacetaldehyde,[9] was investigated. However, no satisfactory result was obtained in terms of the enantioselectivity.

Reaction with Dimethyl Fumarate. The cycloaddition of 2-benzopyrylium-4-olate with dimethyl fumarate in the presence of Yb(OTf)$_3$ was also investigated (Scheme 2, Table 4). The Rh$_2$(OAc)$_4$-catalyzed reaction, itself, either under reflux in benzene or at rt in CH$_2$Cl$_2$, produced the 6-*endo*,7-*exo* product selectively (entries 1 and 2). The addition of Yb(OTf)$_3$ under these conditions caused only a decreasing yield, but no effect in the stereoselectivity (entries 3 and 4). However, the combination of Rh$_2$(OAc)$_4$, Yb(OTf)$_3$, and MS 4A was effective in increasing the yield and in achieving high 6-*endo*,7-*exo*



Scheme 2.

Table 4. Cycloadditions of Carbonyl Ylide with Dimethyl Fumarate[a)]

Entry	Catalyst/mol%	Solvent	Temp	Yield/%	**5a**:**5b**[b)]
1	Rh$_2$(OAc)$_4$ (5)	benzene	reflux	89	81:19
2	Rh$_2$(OAc)$_4$ (2)	CH$_2$Cl$_2$	rt	78	88:12
3	Rh$_2$(OAc)$_4$ (5), Yb(OTf)$_3$ (5)	benzene	reflux	38	82:18
4	Rh$_2$(OAc)$_4$ (2), Yb(OTf)$_3$ (10)	CH$_2$Cl$_2$	rt	34	89:11
5	Rh$_2$(OAc)$_4$ (2), Yb(OTf)$_3$ (10)[c)]	CH$_2$Cl$_2$	rt	72	96:4

a) A solution of diazo compound **1** was added to a solution of dimethyl fumarate (2 equiv) in the presence of the catalyst at the temperature cited in Table 4 over a period of 1 h. b) The ratio was determined by HPLC analysis (Nova-Pak C18, Waters). c) In the presence of MS 4A.

selectivity (6-*endo*,7-*exo* : 6-*exo*,7-*endo* = 96 : 4, entry 5).

We have already reported that the reactions of diazoacetophenone **1** with maleic anhydride and dimethyl maleate in the absence of a Lewis acid gave only *exo*-cycloadducts in moderate yields.[3f] The $Rh_2(OAc)_4$-catalyzed reaction of **1** with maleic anhydride and dimethyl maleate in the presence of $Yb(OTf)_3$ was investigated. However, the reaction in the presence of $Yb(OTf)_3$ did not give cycloadducts, presumably due to an instability of the adducts under the reaction conditions.

Mechanistic Considerations. The reason for the high *endo*-selectivity in the presence of $Yb(OTf)_3$ in the reaction of *N*-substituted maleimides is not clear at this point. However, the Lewis acid may control the *endo*-selectivity in the cycloadditon of carbonyl ylide due to an enhancement of secondary orbital interactions by coordination to *N*-substituted maleimides, as is well known in a Lewis acid-catalyzed Diels–Alder reaction. Thus, the reaction of this carbonyl ylide with *N*-substituted maleimides is governed by a strong interaction between the 1,3-dipole HOMO and the dipolarophile LUMO based on frontier orbital theory. The coordination of the Lewis acid to the carbonyl oxygen of *N*-substituted maleimides lowers the energy level of LUMO and also enlarges the orbital coefficient of the carbonyl carbon. As a result, the enhancement of the secondary orbital interaction between the carbonyl carbon of the carbonyl ylide and the carbonyl carbon of *N*-substituted maleimide could lead to a high *endo*-selectivity, as shown in Fig. 1.

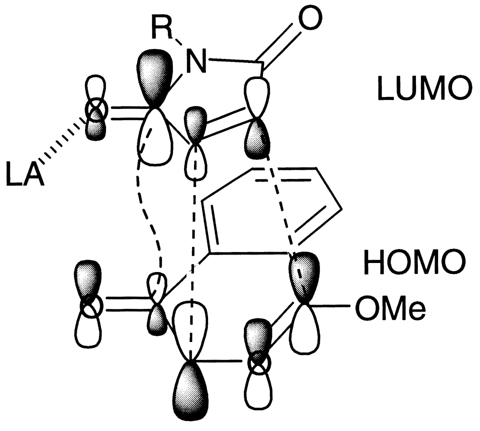


Fig. 1.

Another possibility is that the transition state leading to *endo*-products is preferred by coordination of the Lewis acid to both the carbonyl oxygen of *N*-substituted maleimides and the carbonyl oxygen or methoxy oxygen of carbonyl ylide.

The high 6-*endo*,7-*exo* selectivity of the reaction with dimethyl fumarate in the presence of $Yb(OTf)_3$ and MS 4A could not be explained by the secondary orbital interactions. Coordination of the Lewis acid to both the carbonyl oxygen of dimethyl fumarate and the methoxy oxygen of carbonyl ylide may be the only explanation.

Conclusions

We have demonstrated that the 1,3-dipolar cycloaddition reaction of carbonyl ylide, which was generated by the $Rh_2(OAc)_4$-catalyzed decomposition of *o*-(methoxycarbonyl)-α-diazoacetophenone (**1**), with *N*-substituted maleimides in the presence of 10 mol% of $Yb(OTf)_3$ showed high *endo*-selectivity, which is not usually found in this carbonyl ylide cycloaddition reaction. CuOTf and $Cu(OTf)_2$, having an ability for the decomposition of diazo compounds and Lewis acid character, were also effective catalyst to obtain *endo*-selectivity. On the other hand, in the $Rh_2(OAc)_4$-catalyzed decomposition of diazoacetophenone **1** in the presence of dimethyl fumarate, the addition of $Yb(OTf)_3$ did not change the stereoselectivity, but combination of $Yb(OTf)_3$-MS 4A increased the 6-*endo*,7-*exo* selectivity. We are continuing an investigation to find the general potential of Lewis acid effects on stereoselectivity in carbonyl ylide cycloadditions.

Experimental

General. For preparative column chromatography, Wakogel C-300 and silica gel 60 (Merck) were employed. Medium-pressure liquid chromatography was carried out using a column packed with silica gel 60 (Merck, size 0.040–0.063 mm). All reactions were carried out under an argon atmosphere in dried glassware.

Materials. *o*-(Methoxycarbonyl)-α-diazoacetophenone (**1**) was prepared by a procedure mentioned in a previous paper.[3a] Benzene, toluene, diethyl ether, and THF were freshly distilled from a sodium benzophenone ketyl under argon. CH_2Cl_2 was purified by distillation first from $CaCl_2$, and then CaH_2 under argon. MeCN was purified by distillation first from P_2O_5, and then CaH_2 under argon.

General Procedure is Given for the Reaction of α-Diazoacetophenone 1 with *N*-Methylmaleimide in the presence of $Yb(OTf)_3$. To a solution of *N*-methylmaleimide (111 mg, 1.0 mmol), $Rh_2(OAc)_4$ (4.4 mg, 0.01 mmol), and $Yb(OTf)_3$ (31.1 mg, 0.05 mmol) in CH_2Cl_2 (5.0 mL) was added diazoacetophenone **1** (102 mg, 0.5 mmol) in CH_2Cl_2 (5.0 mL) over a period of 1 h at room temperature. The reaction mixture was filtered through a plug of silica gel with AcOEt/hexane (1 : 1) as an eluent. The crude mixture was analyzed by HPLC (WATERS Nova-Pak C18 column, 6 : 4 $MeOH/H_2O$, flow rate = 0.5 mL min^{-1}, *endo*-isomer : t_R = 8.5 min, *exo*-isomer t_R = 9.3 min) using naphthalene as the internal standard.

The reaction in the presence of MS 4A was as follows. To a solution of *N*-methylmaleimide (111 mg, 1.0 mmol), $Rh_2(OAc)_4$ (4.4 mg, 0.01 mmol), $Yb(OTf)_3$ (31.1 mg, 0.05 mmol), and MS 4A (0.5 g) in diethyl ether (5.0 mL) was added diazoacetophenone **1** (102 mg, 0.5 mmol) in diethyl ether (5.0 mL) over a period of 1 h at room temperature. After removal of MS 4A through celite, the reaction mixture was filtered through a plug of silica gel with AcOEt/hexane (1 : 1) as an eluent. The crude mixture was analyzed by HPLC. The products could be separated by careful medium-pressure liquid chromatography.

General Procedure for the Reaction of 1 with *N*-substituted maleimide in the Presence of Chiral Catalyst. To a suspension of benzene–copper(I) trifluoromethanesulfonate(1/2) ($CuOTf{\bullet}0.5C_6H_6$, 25.2 mg, 0.10 mmol) in benzene (1.0 mL) was added 2,2′-isopropylidenebis[(4*S*)-4-*t*-butyl-2-oxazoline] (32.4 mg, 0.11 mmol) in benzene (4.0 mL) at room temperature. After stirring for 1 h, the mixture was filtered and washed with benzene (1.0 mL) under an argon atmosphere. After the addition of *N*-substituted maleimide (1.0 mmol), to this mixture was added diazoacetophenone **1** (102 mg, 0.5 mmol) over a period of 1 h. The mixture was stirred for 30 min and then concentrated in vacuo. The residue was chromatographed over silica gel (4:6 AcOEt/hexane) to give a mixture of *exo*- and *endo*-products. The *endo*:*exo* ratio and %ee were determined by HPLC analysis (Daicel Chiralpak AS).

Spectroscopic data of cycloadducts **2a**–**4a** and **2b**–**4b** were previously reported.[3f]

5,8-Epoxy-5-methoxy-*N*-methyl-9-oxo-6,7,8,9-tetrahydro-5*H*-benzocycloheptene-6,7-*endo*-dicarboximide (2a): ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.40 (3H, s, NMe), 3.55 (3H, s, OMe), 3.82 (1H, d, J = 9.6 Hz, CH), 4.14 (1H, dd, J = 9.2, 9.6 Hz, CH), 5.12 (1H, d, J = 9.2 Hz), 7.5–8.0 (4H, m, Ar-H). t_R = 29.3 min (minor), t_R = 53.4 min (major), 1:1 hexane/*i*-PrOH, flow rate = 0.5 mL min^{-1}.

5,8-Epoxy-5-methoxy-*N*-methyl-9-oxo-6,7,8,9-tetrahydro-5*H*-benzocycloheptene-6,7-*exo*-dicarboximide (2b): ^{1}H NMR (270 MHz, $CDCl_3$) δ 3.09 (3H, s, NMe), 3.28 (1H, d, J = 7.6 Hz, CH), 3.37 (1H, d, J = 7.6 Hz, CH), 3.51 (3H, s, OMe), 5.12 (1H, s, CH), 7.5–8.1 (4H, m, Ar-H). t_R = 24.7 min (minor), t_R = 37.6 min (major), 1:1 hexane/*i*-PrOH, flow rate = 0.5 mL min^{-1}.

5,8-Epoxy-5-methoxy-*N*-ethyl-9-oxo-6,7,8,9-tetrahydro-5*H*-benzocycloheptene-6,7-*endo*-dicarboximide (3a): ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.22 (3H, t, J = 7.3 Hz, Me), 3.01 (2H, q, J = 7.3 Hz, CH_2), 3.48 (3H, s, OMe), 3.73 (1H, d, J = 9.6 Hz, CH), 4.06 (1H, dd, J = 9.2, 9.6 Hz, CH), 5.06 (1H, d, J = 9.2 Hz), 7.4–8.0 (4H, m, Ar-H). t_R = 18.6 min (minor), t_R = 32.2 min (major), 5:1 hexane/*i*-PrOH, flow rate = 0.5 mL min^{-1}.

5,8-Epoxy-5-methoxy-*N*-ethyl-9-oxo-6,7,8,9-tetrahydro-5*H*-benzocycloheptene-6,7-*exo*-dicarboximide (3b): ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.23 (3H, t, J = 7.3 Hz, Me), 3.26 (1H, d, J = 7.6 Hz, CH), 3.34 (1H, d, J = 7.6 Hz, CH), 3.51 (3H, s, OMe), 3.64 (2H, q, J = 7.3 Hz, CH_2), 5.10 (1H, s, CH), 7.5–8.1 (4H, m, Ar-H). t_R = 34.0 min (minor), t_R = 47.0 min (major), 5:1 hexane/*i*-PrOH, flow rate = 0.5 mL min^{-1}.

5,8-Epoxy-5-methoxy-*N*-phenyl-9-oxo-6,7,8,9-tetrahydro-5*H*-benzocycloheptene-6,7-*endo*-dicarboximide (4a): ^{1}H NMR (270 MHz, $CDCl_3$) δ 3.59 (3H, s, OMe), 3.96 (1H, d, J = 9.6 Hz, CH), 4.31 (1H, dd, J = 9.2, 9.6 Hz, CH), 5.22 (1H, d, J = 9.2 Hz, CH), 6.3–6.5 (2H, m, Ar-H), 7.1–7.4 (2H, m, Ar-H), 7.5–7.8 (4H, m, Ar-H), 7.9–8.2 (1H, m, Ar-H). t_R = 32.4 min (minor), t_R = 110.2 min (major), 1:1 hexane/*i*-PrOH, flow rate = 0.5 mL min^{-1}.

5,8-Epoxy-5-methoxy-*N*-phenyl-9-oxo-6,7,8,9-tetrahydro-5*H*-benzocycloheptene-6,7-*exo*-dicarboximide (4b): ^{1}H NMR (270 MHz, $CDCl_3$) δ 3.44 (1H, d, J = 7.6 Hz, CH), 3.50 (1H, d, J = 7.6 Hz, CH), 3.56 (3H, s, OMe), 5.25 (1H, s, CH), 7.3–8.1 (9H, m, Ar-H). t_R = 27.4 min (minor), t_R = 37.8 min (major), 1:1 hexane/*i*-PrOH, flow rate = 0.5 mL min^{-1}.

General Procedure for the Reaction of 1 with Dimethyl Fumarate. To a solution of dimethyl fumarate (144.1 mg, 1.0 mmol), $Rh_2(OAc)_4$ (4.4 mg, 0.01 mmol), $Yb(OTf)_3$ (31.1 mg, 0.05 mmol), and MS 4A (0.5 g) in CH_2Cl_2 (5.0 mL) was added **1** (102.1 mg, 0.5 mmol) in CH_2Cl_2 (5.0 mL) over a period of 1 h at room temperature. After removal of MS 4A through celite, the solvent was removed under reduced pressure. The products were obtained as a mixture of 6-*exo*,7-*endo* isomer and 6-*endo*,7-*exo* isomer by medium-pressure liquid chromatography using AcOEt/hexane (1:4) as an eluent. The ratio was determined by either ^{1}H NMR and HPLC analysis (WATERS Nova-Pak C18 column, 6:4 $MeOH/H_2O$, flow rate = 0.5 mL min^{-1}, 6-*exo*,7-*endo* isomer t_R = 8.3 min, 6-*endo*,7-*exo* isomer t_R = 9.4 min).

Spectroscopic data of cycloadducts **5a** and **5b** were previously reported.[3f]

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