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Efficient Catalytic Effects of Lewis Acids in the 1,3-Dipolar Cycloaddition Reactions of Carbonyl Ylides with Imines

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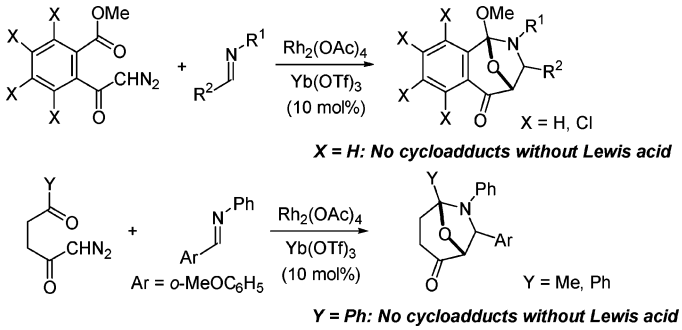

1,3-Dipolar cycloaddition reactions between imines and carbonyl ylides generated by tandem intramolecular carbenoid-carbonyl cyclizations were found to be effectively catalyzed by Lewis acids (10 mol %). The $Rh_2(OAc)_4$-catalyzed reactions of *o*-(methoxycarbonyl)-α-diazoacetophenone with imines such as *N*-[2-(benzyloxy)benzylidene]aniline in the absence of Lewis acid gave no 1,3-dipolar cycloaddition products, but rather the dimeric product of the corresponding carbonyl ylide. In contrast, in the presence of Lewis acids such as $Yb(OTf)_3$, the 1,3-dipolar cycloaddition reactions of the corresponding 1-methoxy-2-benzopyrylium-4-olate proceeded smoothly with several imines, giving in most cases *exo*-selectivity and no formation of the dimeric product. When $Yb(OTf)_3$ was used as a Lewis acid catalyst, a fundamental catalytic effect was also observed in the cycloaddition reactions of imines with carbonyl ylides generated from 1-diazo-5-phenyl-2,5-pentanedione, 1-diazo-2,5-hexanedione and diazomethyl 2,3,4,5-tetrachloro-6-methoxycarbonylphenly ketone. This efficient catalytic effect can be satisfactorily explained in terms of energetics of the cycloaddition in the absence and the presence of Lewis acid by calculations using the ONIOM (B3LYP/6-31G(d):PM3) method.

Introduction

Medium-sized polycyclic ethers containing epoxy-bridged moieties are well-known structural units in naturally occurring biologically active compounds such as brevicomin,[1] frontalin[1b,2] and zaragozic acids[3] (Figure 1). Biologically important epoxy-bridged bicyclic compounds containing a nitrogen atom, such as augastamine,[4] ribasine[5] and ribasine analogues,[6] are also present in nature (Figure 1). To construct the framework of these important epoxy-bridged bicyclic compounds, tandem intramolecular carbenoid-carbonyl cyclization-1,3-dipolar cycloaddition methodologies involving carbonyl ylides have proven to be an important tool.[7] Padwa has reported model studies directed toward the total synthesis of ribasine in which tandem intramolecular carbenoid-carbonyl cyclization-1,3-dipolar cycloadditions are applied.[5c] Surprisingly, however, only a few examples of cycload-

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(1) (a) Silverstein, R. M.; Brownlee, R. G.; Bellas, T. E.; Wood, D. L.; Browne, L. E. *Science* **1968**, *159*, 889. (b) Wood, D. L.; Browne, L. E.; Ewing, B.; Lindahl, K.; Bedard, W. D.; Tilden, P. E.; Mori, K.; Pittman, G. B.; Hughes, P. R. *Science* **1976**, *192*, 896. For a synthesis using carbonyl ylide cycloadditions, see: (c) Padwa, A.; Fryxell, G. E.; Zhi, L. *J. Am. Chem. Soc.* **1990**, *112*, 3100. (d) Padwa, A.; Chinn, R. L.; Zhi, L. *Tetrahedron Lett.* **1989**, *30*, 1491.

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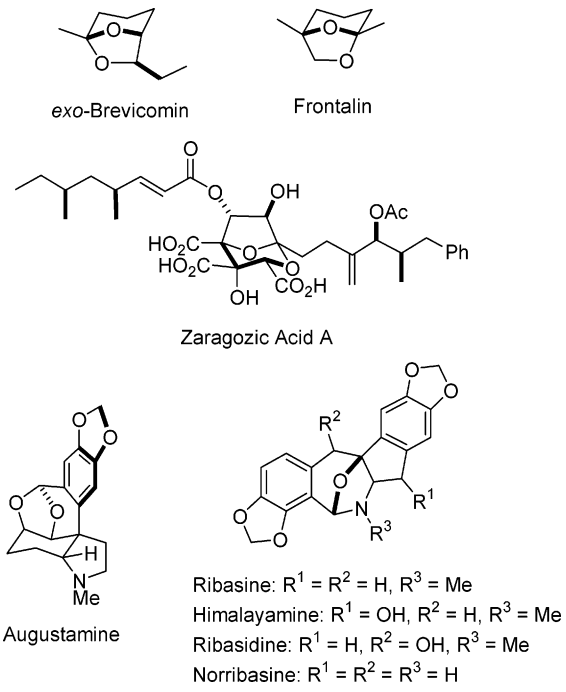

FIGURE 1. Naturally occurring biologically important compounds containing epoxy-bridged moieties.

dition reactions involving carbonyl ylides generated by tandem carbenoid-carbonyl cyclizations with imines have been reported.[5c,8] This is probably due to the low reactivity of imines as dipolarophiles; the stable *N*-benzylideneaniline derivatives provide an example of this. We have recently reported that Lewis acid catalysts, including rare earth metal triflates, were effective in controlling not only diastereoselevtivity but also enantioselectivity of the 1,3-dipolar cycloaddition reactions of 2-benzopyrylium-4-olate with carbonyl and olefinic dipolarophiles.[9] In this paper, we report that Lewis acids such as $Yb(OTf)_3$ are effective in promoting the 1,3-dipolar cycloaddition reactions of the carbonyl ylides generated from *o*-methoxycarbonyl-α-diazoacetophenone (**1**) and 1-diazo-5-phenyl-2,5-pentanedione (**5**) with imines, whereas in the absence of Lewis acid, no cycloaddition reactions with imines occur. Reactions of diazomethyl 2,3,4,5-tetrachloro-6-methoxycarbonylphenyl ketone (**10**) and 1-diazo-2,5-hexanedione (**8**), as carbonyl ylide precursors, with *N*-[(2-methoxy)-benzylidene]aniline (**2c**) are also revealed to be accelerated by the addition of $Yb(OTf)_3$ (10 mol %).

Results and Discussion

Reactions Using *o*-Methoxycarbonyl-α-diazoacetophenone as a Carbonyl Ylide Precursor. Initially, the reaction of *o*-methoxycarbonyl-α-diazoacetophenone (**1**) with *N*-[2-(benzyloxy)benzylidene]aniline (**2a**) was investigated in the absence of Lewis acid by using $Rh_2(OAc)_4$ (2 mol %) as a catalyst for the generation of the corresponding carbonyl ylide (Scheme 1). Surprisingly, no 1,3-dipolar cycloadducts were obtained either at room temperature in CH_2Cl_2 or under reflux in toluene, and only the corresponding dimeric product **4**[14d,16] was afforded in 50% yield after reflux in toluene (Table 1, entries 1 and 2). Although yields of the cycloadducts were low to modest when using Et_2AlCl or $Mg(OTf)_2$ as Lewis acids, other Lewis acids (10 mol %) investigated effectively catalyzed the cycloaddtion reaction of 2-benzopyrylium-4-olate **A** with imine **2a**, to give a mixture of *exo*- and *endo*-cycloadducts,[10] without formation of the dimeric product **4** (Scheme 1, Table 1, entries 3−9). Among Lewis acids used, lanthanoid triflates $Yb(OTf)_3$ and $La(OTf)_3$ showed a much higher yield than other Lewis acids and also a high *exo*-selectivity (entries 8 and 9). The *exo*-selectivity observed is probably due to the steric stability of the *exo*-cycloadduct. A number of

(2) (a) Kinzer, G. W.; Fentiman, A. F.; Page, T. F.; Foltz, R. L.; Vite, J. P.; Pitman, G. B. *Nature (London)* **1969**, *221*, 477. (b) Mori, K. *Tetrahedron* **1975**, *31*, 1381. For syntheses and studies, see: (c) Whitesell, J. K.; Buchanan, C. M. *J. Org. Chem.* **1986**, *51*, 5443. (d) Jarose, S.; Hicks, D. R.; Fraser-Reid, B. *J. Org. Chem.* **1982**, *47*, 935. (e) Lee, A. W. M. *J. Chem. Soc., Chem. Commun.* **1984**, 578. (f) Sato, T.; Kaneko, H.; Yamaguchi, S. *J. Org. Chem.* **1980**, *45*, 3778. (f) Lipkowitz, K. B.; Carter, J. *J. Org. Chem.* **1981**, *46*, 4005.

(3) For reviews, see: (a) Nicolaou, K. C.; Nadin, A. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1622. (b) Koert, U. *Angew. Chem., Int. Ed. Engl.* **1995**, 34, 773. (c) Procopiou, P. A.; Watson, N. S. *Prog. Med. Chem.* **1996**, *33*, 331. (d) Bergstrom, J. D.; Dufresne, C.; Bills, G. F.; Nallin-Omsteas, M.; Byrne, K. *Annu. Rev. Microbiol.* **1995**, *49*, 607. For the skeleton syntheses using carbonyl ylide cycloadditions, see: (e) Hodgson, D. M.; Bailley, J. M.; Villalonga-Barber, C.; Drew, M. G. B.; Harrison, T. *J. Chem. Soc., Perkin Trans. 1* **1989**, 721. (f) Hodgson, D. M.; Bailey, J. M.; Villalonga-Barber, C.; Drew, M. G. B.; Harrison, T. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3432. (g) Villalonga-Barber, C.; Hodgson, D. M. *Abstr. Pap. Am. Chem. Soc.* **2000**, *219*, 778. (h) Hodgson, D. M.; Villalonga-Barber, C. *Tetrahedron Lett.* **2000**, *41*, 5597. (i) Kataoka, O.; Kitagaki, S.; Watanabe, N.; Kobayashi, J.; Nakamura, S.; Shiro, M.; Hashimoto, S. *Tetrahedron Lett.* **1998**, *39*, 2371. (j) Koyoma, H.; Ball, R. G.; Berger, G. D. *Tetrahedron Lett.* **1994**, *35*, 9185. For total synthesis of zaragozic acid C using cycloadditions, see: (k) Nakamura, S.; Hirata, Y.; Kurosaki, T.; Anada, M.; Kataoka, O.; Kitagaki, S.; Hashimoto, S. *Angew. Chem., Int. Ed.* **2003**, *42*, 5351.

(4) (a) Ali, A. A.; Kating, H.; Frahm, A. W.; El-Moghazi, A. M.; Ramadan, M. A. *Phytochemistry* **1981**, *20*, 1121. (b) Ali, A. A.; Hambloch, H.; Frahm, A. W. *Phytochemistry* **1983**, *22*, 283. (c) Abd EI Hafiz, M. A.; Ramadan, M. A.; Jung, M. L.; Beck. J. P.; Anton, R. *Planta Med.* **1991**, *57*, 437. For a synthesis, see: (d) Pearson, W. H.; Lovering, F. E. *J. Am. Chem. Soc.* **1995**, *117*, 12336. (e) Pearson, W. H.; Lovering, F. E. *J. Org. Chem.* **1998**, *63*, 3607.

(5) (a) Boente, J. M.; Castedo, L.; Cuadros, R.; Saá, J. M.; Suau, R.; Perales, A.; Martínez-Ripoll, M.; Fayos, J. *Tetrahedron Lett.* **1983**, *24*, 2029. For a synthesis, see: (b) Ollero, L.; Castero, L.; Dominguez, D. *Tetrahedon Lett.* **1998**, *39*. 1413. For a synthetic study using carbonyl ylide cycloadditions, see: (c) Padwa, A.; Precedo, L.; Semones, M. A. *J. Org. Chem.* **1999**, *64*, 4079.

(6) (a) Allais, D. P.; Guineaudeau, H.; Freyer, A. J.; Shamma, M.; Ganguli, N. C.; Talapatra, B.; Talapatra, S. K. *Tetrahedron Lett.* **1983**, *24*, 2445. (b)Boente, J. M.; Campello, M. J.; Castedo, L.; Dominguez, D.; Saá, J. M.; Suau, R.; Vidal, M. *Tetrahedron Lett.* **1983**, *24*, 4481. (c) Allais, D. P.; Guineaudeau, H. *J. Nat. Prod.* **1990**, *53*, 1280.

(7) For reviews, see: (a) MacMills, M. C.; Wright, D. In *Synthetic Applications of 1,3-Dipolar Cycloaddition Chemistry Toward Heterocycles and Natural Products*; Padwa, A., Pearson, W. H., Eds.; John Wiley & Sons: Hoboken, 2003; Chapter 4, p 253. (b) Padwa, A.; Weingarten, M. D. *Chem. Rev.* **1996**, *96*, 223. (c) Padwa, A.; Hornbuckle, S. F. *Chem. Rev.* **1991**, *91*, 263.

(8) (a) Recently, the reaction with imines by intermolecular carbenoid-carbonyl cyclization for the generation of carbonyl ylides was reported, see: Torssell, S.; Kienle, M.; Somfai, P. *Angew. Chem., Int. Ed. Engl.* **2005**, *44*, 3096. (b) The reaction of a nonstabilized carbonyl ylide with *N*-tosyl imine was reported, see: Hojo, M.; Aihara, H.; Suginohara, Y.; Sakata, K.; Nakamura, S.; Murakami, C.; Hosomi, A. *J. Org. Chem.* **1997**, *62*, 8610.

(9) (a) Suga, H.; Ishida, H.; Ibata, T. *Tetrahedron Lett.* **1998**, *39*, 3165. (b) Suga, H.; Kakehi, A.; Ito, S.; Inoue, K.; Ishida, H.; Ibata, T. *Bull. Chem. Soc. Jpn.* **2001**, *74*, 1115. (c) Suga, H.; Kakehi, A.; Ito, S.; Inoue, K.; Ishida, H.; Ibata, T. *Org. Lett.* **2000**, *2*, 3145. (d) Inoue, K.; Suga, H.; Inoue, S.; Sato, H.; Kakehi, A. *Synthesis* **2003**, 1413. (e) Suga, H.; Inoue, K.; Inoue, S.; Kakehi, A. *J. Am. Chem. Soc.* **2002**, *124*, 14836. (f) Suga, H.; Inoue, K.; Inoue, S.; Kakehi, Shiro, M. *J. Org. Chem.* **2005**, *70*, 47.

(10) The *endo*-adduct is defined as the product in which the more important substituent is on the opposite side of the epoxy bridge, whereas the *exo*-adduct indicates the product in which the more important substituent is on the same side as the epoxy bridge, as defined for bridged bicyclic compounds.

SCHEME 1. Cycloaddition Reactions of 2-Benzopyrylium-4-olate with Imines

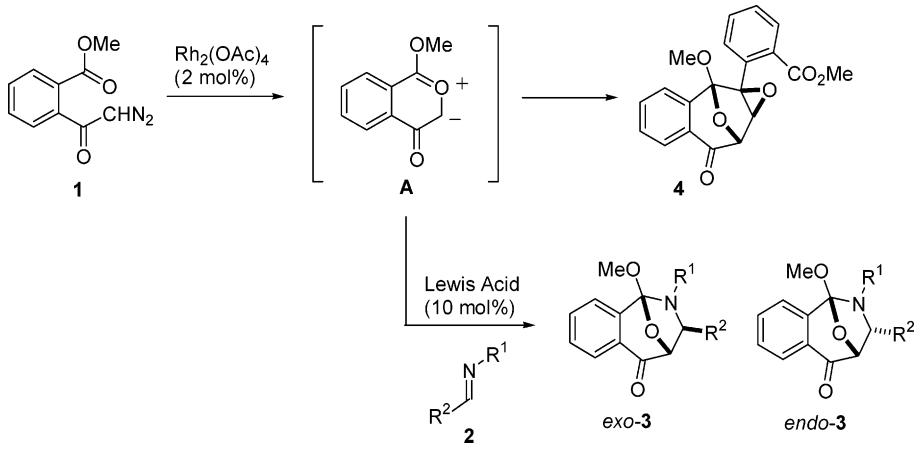

TABLE 1. $Rh_2(OAc)_4$-Catalyzed Reactions of *o*-Methoxycarbonyl-α-diazoacetophenone (1) with Imines 2 with and without Lewis Acids[a]

entry	imine	R^1	R^2	Lewis acid	solvent	temp (°C)	time (h)	products	yield (%)	*exo*:*endo*
1	**2a**	Ph	*o*-$BnOC_6H_4$	none	CH_2Cl_2	rt	18		complex mixture	
2	**2a**	Ph	*o*-$BnOC_6H_4$	none	toluene	reflux	1	**4**	50	
3	**2a**	Ph	*o*-$BnOC_6H_4$	Et_2AlCl	CH_2Cl_2	rt	1	**3a**	4	73:27
4	**2a**	Ph	*o*-$BnOC_6H_4$	$SnCl_4$	CH_2Cl_2	rt	1	**3a**	72	88:12
5	**2a**	Ph	*o*-$BnOC_6H_4$	$ZnCl_2$	CH_2Cl_2	rt	1	**3a**	74	94:6
6	**2a**	Ph	*o*-$BnOC_6H_4$	$Mg(OTf)_2$	CH_2Cl_2	rt	1	**3a**	36	94:6
7	**2a**	Ph	*o*-$BnOC_6H_4$	$Sc(OTf)_3$	CH_2Cl_2	rt	1	**3a**	76	90:10
8	**2a**	Ph	*o*-$BnOC_6H_4$	$Yb(OTf)_3$	CH_2Cl_2	rt	1	**3a**	92	92:8
9	**2a**	Ph	*o*-$BnOC_6H_4$	$La(OTf)_3$	CH_2Cl_2	rt	1	**3a**	89	94:6
10	**2b**	Ph	Ph	$Yb(OTf)_3$	CH_2Cl_2	rt	1	**3b**	84	62:38[b]
11	**2c**	Ph	*o*-$MeOC_6H_4$	$Yb(OTf)_3$	CH_2Cl_2	rt	1	**3c**	94	85:15[b]
12	**2d**	Ph	*p*-$MeOC_6H_4$	$Yb(OTf)_3$	CH_2Cl_2	rt	1	**3d**	75	77:23[b]
13	**2e**	Ph	*p*-ClC_6H_4	$Yb(OTf)_3$	CH_2Cl_2	rt	1	**3e**	62	73:27[b]
14	**2f**	*o*-$MeOC_6H_4$	Ph	none	toluene	reflux	1	**4**	22	
15	**2f**	*o*-$MeOC_6H_4$	Ph	$Yb(OTf)_3$	CH_2Cl_2	rt	1	**3f**	72	84:16[b]
16	**2f**	*o*-$MeOC_6H_4$	Ph	$Tm(OTf)_3$	CH_2Cl_2	rt	1	**3f**	85	88:12[b]
17	**2f**	*o*-$MeOC_6H_4$	Ph	$Ho(OTf)_3$	CH_2Cl_2	rt	1	**3f**	72	87:13[b]
18	**2f**	*o*-$MeOC_6H_4$	Ph	$Eu(OTf)_3$	CH_2Cl_2	rt	1	**3f**	56	88:12[b]
19	**2f**	*o*-$MeOC_6H_4$	Ph	$Sm(OTf)_3$	CH_2Cl_2	rt	1	**3f**	44	89:11[b]
20	**2f**	*o*-$MeOC_6H_4$	Ph	$La(OTf)_3$	CH_2Cl_2	rt	1	**3f**	52	89:11[b]
21	**2f**	*o*-$MeOC_6H_4$	Ph	$Sc(OTf)_3$	CH_2Cl_2	rt	1	**3f**	42	90:10[b]
22	**2g**	*p*-$MeOC_6H_4$	Ph	$Yb(OTf)_3$	CH_2Cl_2	rt	1	**3g**	76	88:12[b]
23	**2h**	*p*-ClC_6H_4	Ph	$Yb(OTf)_3$	CH_2Cl_2	rt	1	**3h**	42	76:44[b]
24	**2i**	*c*-C_6H_{11}	Ph	$Yb(OTf)_3$	CH_2Cl_2	rt	1	**3i**	21	81:19[b]
25	**2j**	Ph	*c*-C_6H_{11}	$Yb(OTf)_3$	CH_2Cl_2	rt	1 + 13[c]	**3j**	47	84:16[b]
26	**2k**	*c*-C_6H_{11}	*c*-C_6H_{11}	$Yb(OTf)_3$	CH_2Cl_2	rt	1 + 5	**3k**	31	12:88[b]
27	**2l**	$CHPh_2$	CO_2Et	$Yb(OTf)_3$	CH_2Cl_2	rt	1	**3l**	45	58:42[b]

[a] The reaction was carried out by adding a solution of diazo compound **1** in CH_2Cl_2 over a period of 1 h to a suspension of Lewis acid (10 mol %), MS 4Å, $Rh_2(OAc)_4$ (2 mol %) and imine **2** (2 equiv) in CH_2Cl_2. [b] Determined by ^1H NMR (400 MHz). [c] After adding diazo compound **1**, the mixture was stirred for an additional 13 h at room temperature. [d] After adding diazo compound **1**, the mixture was stirred for an additional 5 h at room temperature.

benzylideneaniline derivatives, **2b**−**2e**, bearing several substituted and unsubstituted phenyls on the iminocarbon also underwent reactions with carbonyl ylide **A** in the presence of $Yb(OTf)_3$, giving the cycloadducts in moderate to high yields (entries 10−13).

The cycloaddition reaction of carbonyl ylide **A** with *N*-benzylidene-*o*-anisidine (**2f**) gave the desired cycloadducts in the presence of 10 mol % $Yb(OTf)_3$ in CH_2Cl_2 at room temperature (entry 15), whereas no cycloaddition reaction proceeded in the absence of Lewis acid, and the dimeric product **4** was formed under toluene reflux (entry

(11) *Gaussian 03*, Revision C.02; Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A., Jr.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A.; Gaussian, Inc.: Wallingford CT, 2004.

(12) (a) Sustmann, R. *Tetrahedron Lett.* **1971**, 2717. (b) Sustmann, R.; Trill, H. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 838. (c) Huisgen, R. *J. Org. Chem.* **1976**, *41*, 403.

(13) (a) Svensson, M.; Humbel, S.; Froese, R. D. J.; Matsubara, T.; Sieber, S.; Morokuma, K. *J. Phys. Chem.* **1996**, *100*, 19357. (b) Humbel, S.; Sieber, S.; Morokuma, K. *J. Chem. Phys.* **1996**, *105*, 1959.

(14) (a) Ueda, K.; Ibata, T.; Takebayashi, M. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 2779. (b) Ibata, T.; Toyoda, J.; Sawada, M.; Takai, Y.; Tanaka, T. *Tetrahedron Lett.* **1988**, *29*, 317.

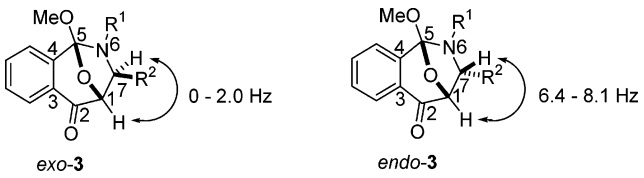

FIGURE 2. Coupling constants between H-1 and H-7 of the cycloadducts.

14). The rare earth metal triflates $Tm(OTf)_3$, $Ho(OTf)_3$, $Eu(OTf)_3$, $Sm(OTf)_3$, $La(OTf)_3$ and $Sc(OTf)_3$ all enabled the cycloaddition with imine **2f** (entries 16−21). Although the yield varied somewhat with the ionic radius of the metal, a good *exo*-selectivity was observed in all cases. Imines bearing electron-donating and electron-withdrawing groups as *para*-substitutents on the phenyl group at the imino-nitrogen reacted with the carbonyl ylide in the presence of $Yb(OTf)_3$ to give the cycloadducts (entries 22 and 23). *C*-Cyclohexylimine **2i**, *N*-cyclohexylimine **2j**, *C*,*N*-dicyclohexylimine **2k** and functionalized imine **2l** also reacted under similar $Yb(OTf)_3$-catalyzed conditions to give the cycloadducts in moderate yields (entries 24−27).

Stereochemistry of Cycloadducts 3. The coupling constant between H-1 and H-7 in the ^1H NMR spectrum was used to determine whether the cycloadduct adopted *exo*- or *endo*-configuration.[10] The protons at C-1 and C-7 of the major diastereomer obtained from the cycloaddition reaction of 2-benzopyrylium-4-olate with *N*-benzylidene-*p*-anisidine (**2g**) both appeared as singlets. Therefore, the *J* value between H-1 and H-7 is 0 Hz, indicating that the dihedral angle between these protons is approximately 90°, whereas the *J* value of the minor diastereomer was observed to be 6.4 Hz (Figure 2). From these observations, the structures of the diastereomers could be determined, with the major product having an *exo*-configuration and the minor product possessing an *endo*-configuration. The structures of the major isomer, *exo*-**3g**, and the minor isomer, *endo*-**3g**, were confirmed by X-ray structure analysis (see Supporting Information). The results were in agreement with the ^1H NMR structure determination, which showed that the dihedral angle between H-1 and H-7 of *exo*-**3g** is 98° and that of *endo*-**3g** is 41°. The structures of the other cycloadducts, **3a**−**f** and **3h**−**l**, were similarly determined using the ^1H NMR coupling constants (Figure 2).

Reaction Using 1-Diazo-5-phenyl-2,5-pentanedione as a Carbonyl Ylide Precursor. Cycloaddition reactions of the carbonyl ylide generated from 1-diazo-5-phenyl-2,5-pentanedione (**5**) were also investigated with and without Lewis acid (Scheme 2). Although yields of the cycloadducts were not satisfactory, the reaction with *N*-[(2-methoxy)benzylidene]aniline (**2c**) did give the cycloadducts in the presence of Lewis acids (10 mol %) such as $Sc(OTf)_3$, $Tm(OTf)_3$ and $Yb(OTf)_3$ (Table 2, entries 1, 3 and 5), whereas in the absence of Lewis acids, even under reflux in toluene, a complex mixture was formed. A survey of reaction solvents and temperatures (entries 6−9) reveals that Et_2O in the presence of $Yb(OTf)_3$ provides a slightly increased yield and an extremely high *exo*-selectivity (entry 8).

SCHEME 2. Reaction of 1-Diazo-5-phenyl-2,5-pentanedione (5) in the Presence of Lewis Acids

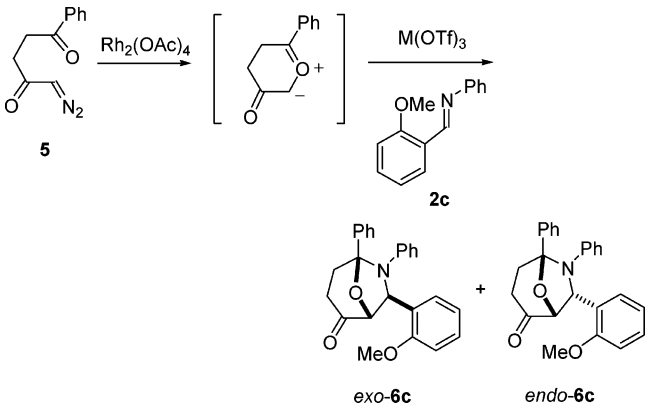

TABLE 2. Reaction of 1-Diazo-5-phenyl-2,5-pentanedione (5) with Imine 2c in the Presence of Lewis Acids[a]

entry	Lewis acid	solvent	temp (°C)	yield (%)	*exo*:*endo*[b]
1	$Sc(OTf)_3$	CH_2Cl_2	rt	34	89:11
2	$Sc(OTf)_3$	Et_2O	rt	21[c]	97:3
3	$Tm(OTf)_3$	CH_2Cl_2	rt	28	81:19
4	$Tm(OTf)_3$	Et_2O	rt	19[d]	93:7
5	$Yb(OTf)_3$	CH_2Cl_2	rt	28	88:12
6	$Yb(OTf)_3$	CH_2Cl_2	reflux	29	90:10
7	$Yb(OTf)_3$	toluene	80	trace	85:15
8	$Yb(OTf)_3$	Et_2O	rt	39[e]	99:1
9	$Yb(OTf)_3$	*t*-BuOMe	rt	trace	81:19

[a] The reaction was carried out by adding a solution of diazo compound **5** in CH_2Cl_2 over a period of 1 h to a suspension of Lewis acid (10 mol %), MS 4Å, $Rh_2(OAc)_4$ (2 mol %) and imine **2c** (2 equiv). [b] Determined by ^1H NMR (400 MHz). [c] 5-Ethoxy-1-phenyl-1,4-pentandione (**7**)[16] was obtained in 8% yield. [d] Compound **7** was obtained in 7% yield. [e] Compound **7** was obtained in 12% yield.

Reaction Using 1-Diazo-2,5-hexanedione and Diazomethyl 2,3,4,5-Tetrachloro-6-(methoxycarbonyl)phenyl Ketone as Carbonyl Ylide Precursors. In the case of the carbonyl ylides generated from 1-diazo-2,5-hexanedione (**8**) and diazomethyl 2,3,4,5-tetrachloro-6-methoxycarbonylphenyl ketone (**10**), cycloaddition reactions with imine **2c** proceeded without Lewis acid in CH_2Cl_2 at room temperature in low and moderate yields, respectively (Scheme 3, Table 3, entries 1 and 3). The addition of $Yb(OTf)_3$ (10 mol %) under similar reaction conditions led to the acceleration of the reactions of both diazo substrates **8** and **10**, with the cycloadducts being obtained in good to high yields (Table 3, entries 2 and 4). Interestingly, in the reaction of diazo compound **8**, the presence or absence of $Yb(OTf)_3$ switched which diastereomer was preferentially obtained. The *endo*-selectivity of the reaction of **8** in the presence of $Yb(OTf)_3$ also contrasted with the high *exo*-selectivity of the reaction of 1-diazo-5-phenyl-2,5-pentanedione (**5**).

Theoretical Studies of the Effect of Lewis Acid Using MO Calculations. Frontier molecular orbital theory was used to examine the effect of the Lewis acids

(15) In these calculations, we assume that rhodium catalyst is not involved in the cycloaddition step because, in a previous study,[9b] diastereoselectivity in the reaction of carbonyl ylide **A** with *N*-methylmaleimide was effectively changed by $Yb(OTf)_3$ (10 mol %, *endo*:*exo* = 98:2) without $Rh_2(OAc)_4$ conditions under benzene reflux, similarly to the $Rh_2(OAc)_4$ (2 mol %)-$Yb(OTf)_3$ (10 mol) catalytic system (*endo*:*exo* = 95:5) compared with the selectivity of the $Rh_2(OAc)_4$-catalyzed reaction in the absence of $Yb(OTf)_3$ (*endo*:*exo* = 11:89).

(16) Proposed mechanisms for formation of the compounds are shown in Supporting Information.

SCHEME 3. Reactions of Diazo Compounds 8 and 10 with Imine 2c

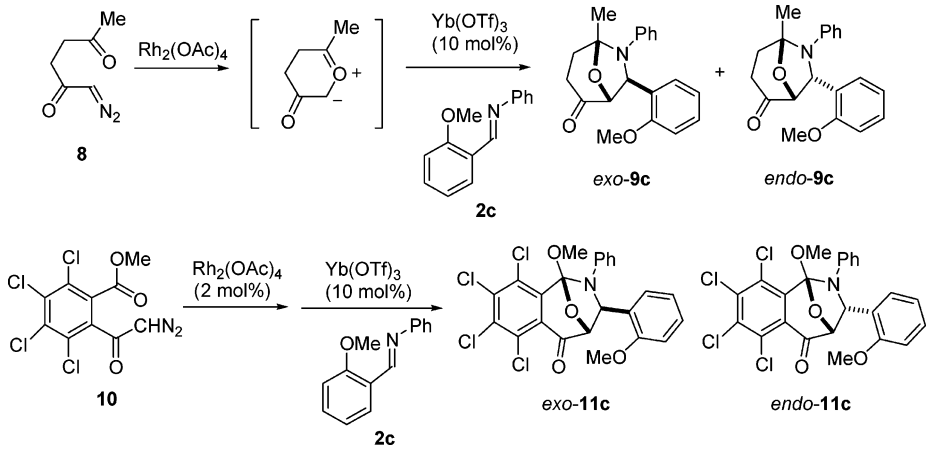

TABLE 3. Reactions of Diazo Compounds 8 and 10 with Imine 2c[a]

entry	diazo substrate	Lewis acid	yield (%)	*exo*:*endo*[b]
1	**8**	none	20	54:46
2	**8**	$Yb(OTf)_3$ (10 mol %)	74	28:72
3[c]	**10**	none	40[d]	85:15
4	**10**	$Yb(OTf)_3$ (10 mol %)	82	87:13

[a] The reaction was carried out by adding a solution of diazo compound **8** or **10** in CH_2Cl_2 over a period of 1 h to a suspension of MS 4Å, $Rh_2(OAc)_4$ (2 mol %) and imine **2c** (2 equiv). [b] Determined by ^1H NMR (400 MHz). [c] After adding diazo compound **10**, the mixture was stirred for an additional 95 h at room temperature. [d] Recovered **10**: 26%.

observed in the above reactions.[15] The structural optimization and calculations of HOMO and LUMO energy levels were carried out for carbonyl ylide **A** and imines **2c**−**e** using the ab initio RHF/3-21G method with the Gaussian 2003 program.[11] To simplify the calculations for the effect of the Lewis acid, the HOMO and the LUMO energy levels of the $ZnCl_2$-coordinated carbonyl ylide **A** and the appropriate imine were calculated. Coordination of imines to the $ZnCl_2$ considerably lowered the LUMO energy levels, and the corresponding energy gaps (HOMO-dipole LUMO-dipolarophile interaction, Sustmann type I[12]) were significantly decreased in comparison to the gaps in the absence of Lewis acid (see Supporting Information). The regiochemical outcomes, which could be estimated from the coefficients of the HOMO-dipole LUMO-dipolarophile interactions in terms of perturbation theory, were also in agreement with the regiochemistry observed in the experimental results (see Supporting Information).

The effect of Lewis acid catalyst could be confirmed with energetics of the cycloaddition of carbonyl ylide **A** with imine **2c** in the absence and the presence of $ZnCl_2$ by the calculations using the ONIOM (B3LYP/6-31G(d):PM3) method (Figures 3 and 4).[13] Energy profiles show that reactants form stable complexes at the early stage in these reactions. The process, in the presence of $ZnCl_2$, which consists of coordination of **2c** to $ZnCl_2$[17] and formation of a weakly associated complex of **A** and **2c**−$ZnCl_2$ was more exothermic, and ΔG was negative (−7.43 kcal/mol) despite the large negative entropy change (ΔS = −82.05 cal/mol·K) caused by the complex formations. The 1,3-dipolar cycloaddition steps from the weakly associated complexes to *exo*-**3c** and *exo*-**3c**−$ZnCl_2$ were also exothermic processes. The activation energy in the catalytic reaction (9.53 kcal/mol) was slightly lower than that in the absence of $ZnCl_2$ (9.80 kcal/mol). The $\Delta\Delta G$ in the $ZnCl_2$-catalyzed reaction is substantially lower (12.34 kcal/mol) than that in the reaction without $ZnCl_2$ (15.42 kcal/mol), which indicates the $ZnCl_2$ catalyst effectively accelerate the 1,3-dipolar cycloaddition step. The $\Delta\Delta S$ in the catalytic reaction was less negative (−10.48 cal/mol·K) than that in the absence of the catalyst (−19.33 cal/mol·K), which is responsible for the differences in the $\Delta\Delta G$ values. From the calculations of the transition state which produce *endo*-**3c**, the values of ΔE, ΔH, ΔS, and ΔG were shown to be 2.35 kcal/mol, 2.14 kcal/mol, 0.68 cal/mol·K, and 1.94 kcal/mol larger than those of the transition state for the corresponding *exo*-**3c**, respectively. These results also reasonably explain the *exo*-selectivity of this reaction.

Optimized structures of the transition states are shown in Figures 5 and 6. Geometrical features of the transition state in the reaction without Lewis acid were those in typical concerted 1,3-dipolar cycloadditions. A carbonyl ylide moiety in **A** and an imine group in **2c** were arranged in almost parallel fashion. The bond formations of C−C and C−N occurred simultaneously. The two bond-forming interactions restricted the motion of **A** and **2c**, which caused large negative $\Delta\Delta S$ in the step. On the other hand, at the transition state of **A** with **2c**−$ZnCl_2$, the formation of new σ-bonds was asynchronous. A $ZnCl_2$, which was chelated by **2c**, prevented the parallel approach of the carbonyl ylide moiety in **A** and the imine group in **2c**. In this stage, the C−C bond formation proceeded (C−C = 2.121 Å), while the C−N bond-forming interaction was weak (C−N = 3.292 Å). Thus binding of **A** at the transition state in the catalytic reaction was relatively loose compared with the case of noncatalytic reaction, which may be responsible for the less negative $\Delta\Delta S$ in the step.

(17) Although there is no absolute requirement of the chelated coordination for efficiency of the Lewis acid catalyzed processes, in this case, the bidentate chelated complex of **2c** was calculated because the LUMO energy level of the bidentate complex was lower than that of the corresponding monodentate one by ab initio RHF/3-21G calculations.

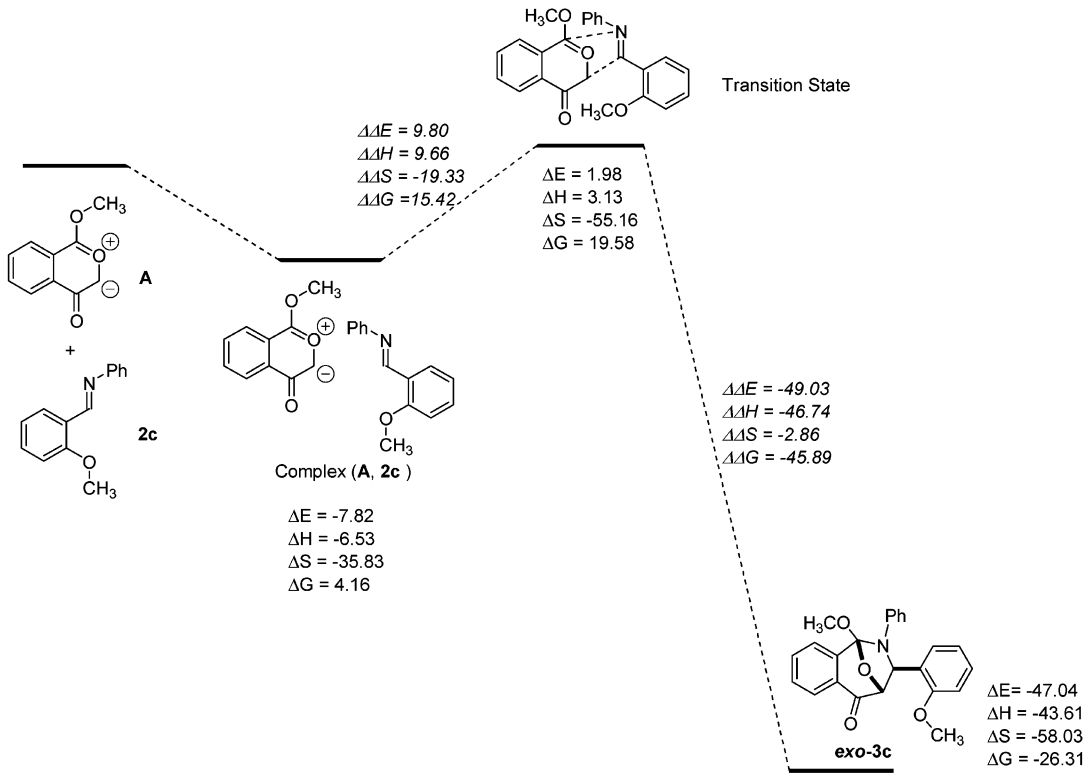

FIGURE 3. Energy profile of 1,3-dipolar cycloadition of carbonyl ylide **A** with imine **2c** calculated by the ONIOM(B3LYP/6-31G(d):PM3) method. Energies (kcal/mol), enthalpies (kcal/mol), entropies (cal/mol·K), and Gibbs energies (kcal/mol) are relative to those of reactants.

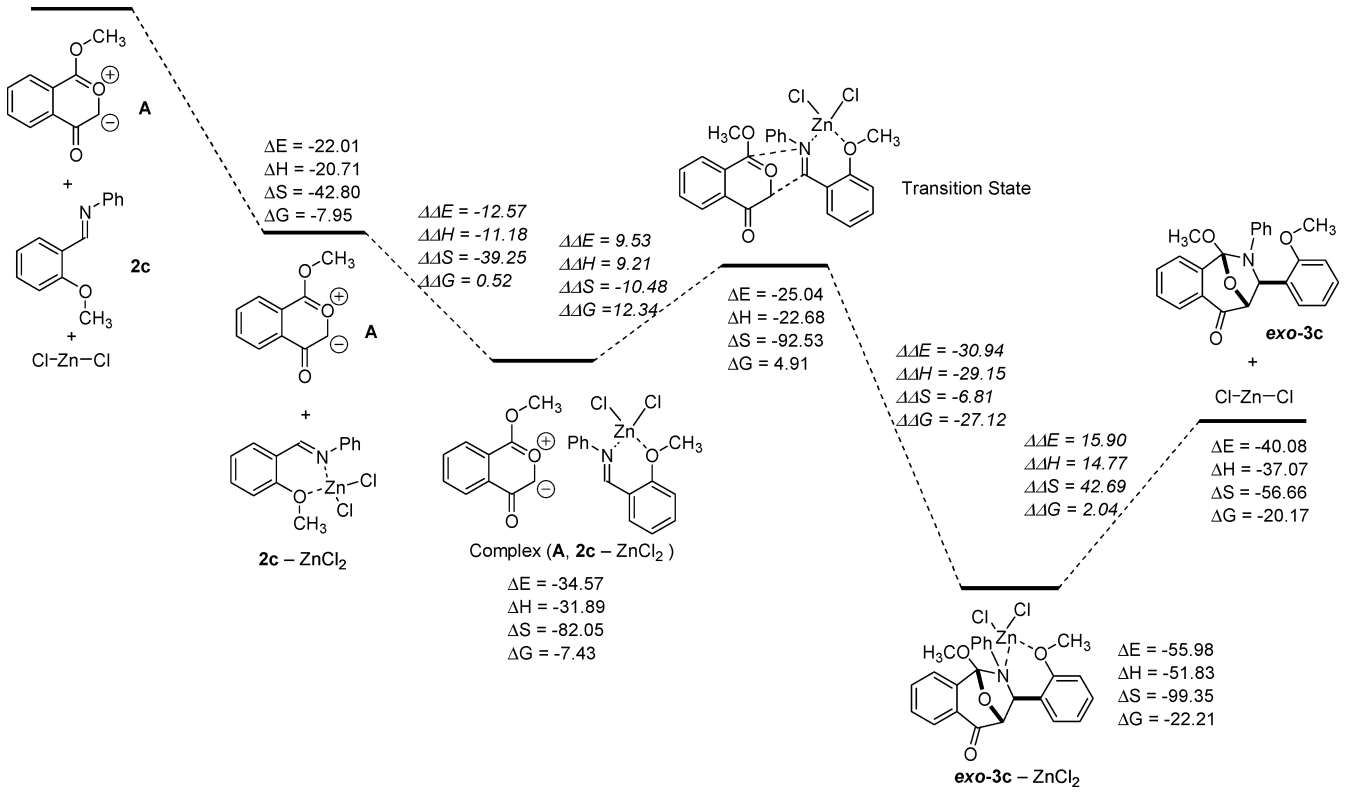

FIGURE 4. Energy profile of 1,3-dipolar cycloadition of carbonyl ylide **A** with imine **2c** catalyzed with $ZnCl_2$ calculated by the ONIOM(B3LYP/6-31G(d):PM3) method. Energies (kcal/mol), enthalpies (kcal/mol), entropies (cal/mol·K), and Gibbs energies (kcal/mol) are relative to those of reactants.

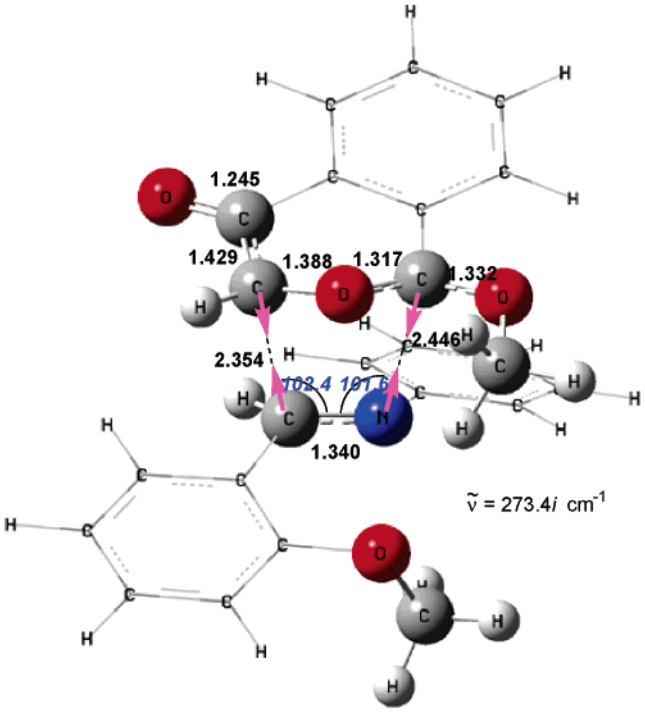

FIGURE 5. Bond lengths (Å), bond angles (deg, blue), and the lowest frequency of transition state for 1,3-dipolar cycloaddition of carbonyl ylide **A** with imine **2c** optimized by the ONIOM(B3LYP/6-31G(d):PM3) method. (Upper layer: ball and stick. Lower layer: wireframe)

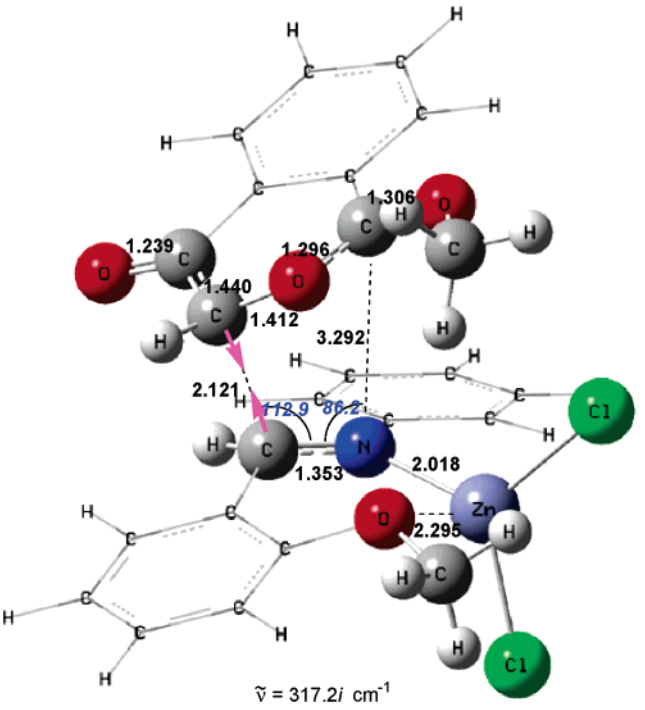

FIGURE 6. Bond lengths (Å), bond angles (deg, blue), and the lowest frequency of transition state for 1,3-dipolar cycloaddition of carbonyl ylide **A** with imine **2c** catalyzed with $ZnCl_2$ optimized by the ONIOM(B3LYP/6-31G(d):PM3) method. (Upper layer: ball and stick. Lower layer: wireframe)

Conclusion

In conclusion, Lewis acids, especially rare earth metal triflates, were found to be extremely effective in promoting and accelerating the cycloaddition reactions of carbonyl ylides generated by intramolecular carbenoid-carbonyl cyclization with imine dipolarophiles. It is noteworthy that this methodology offers an efficient procedure for the construction of the 6-aza-8-oxabenzo-[*c*]bicyclo[3.2.1]octane skeleton by means of cycloaddition reactions with imines. In particular, this method enables less reactive carbonyl ylides, such as those generated from diazo substrates such as *o*-methoxycarbonyl-α-diazoacetophenone (**1**) and 1-diazo-5-phenyl-2,5-pentanedione (**5**), to be reacted with imine dipolarophiles. This efficient catalytic effect can be satisfactorily explained in terms of frontier molecular orbital theory using ab initio RHF/3-21G calculations and energetics of the cycloaddition in the absence and the presence of $ZnCl_2$ by the calculations using the ONIOM (B3LYP/6-31G(d):PM3) method.

Experimental Section

For General Methods, Materials, and Computational Methods, see Supporting Information.

General Procedure for Reactions of α-Diazoacetophenone 1 with Imines Exemplified by the Reaction of 1 with 2a. To a suspension of *N*-[2-(benzyloxy)benzylidene]-aniline (**2a**) (287.4 mg, 1.0 mmol), $Rh_2(OAc)_4$ (4.4 mg, 0.01 mmol), $Yb(OTf)_3$ (31.1 mg, 0.05 mmol), and powdered 4 Å molecular sieves (MS 4Å, 0.50 g) in CH_2Cl_2 (5 mL) was added a solution of diazoacetophenone **1**[14] (102.1 mg, 0.5 mmol) in CH_2Cl_2 (5 mL) over a period of 1 h. After removal of MS 4Å through Celite, the reaction mixture was filtered through a plug of silica gel (3 cm) with AcOEt/hexane (1:1, 80 mL) as an eluent. The solvent was removed in vacuo. The resulting mixture was purified by medium-pressure liquid chromatography (MPLC) (silica gel, 1:99 AcOEt/hexane) to give *exo*-**3a** (199.2 mg, 85%) and *endo*-**3a** (16.1 mg, 7%).

7-*exo*-(*o*-Benzyloxyphenyl)-5-methoxy-6-phenyl-6-aza-8-oxabenzo[*c*]bicyclo[3.2.1]octan-2-one (*exo*-3a). Colorless prisms (ether−hexane); mp 173.5−174.5 °C; IR (KBr) 3024, 2947, 2878, 2361, 2339, 1712, 1599, 1496, 1483, 1454, 1431, 1371, 1321, 1290, 1263, 1248, 1215, 1153, 1130, 1099, 1057, 1033, 962, 914, 883 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.87 (3H, s), 4.88 (1H, d, J = 1.2 Hz), 4.89 (1H, bs), 5.28 (1H, d, J = 12.7 Hz), 5.34 (1H, d, J = 12.7 Hz), 6.72−6.75 (1H, m), 6.86−6.94 (3H, m), 7.04−7.11 (3H, m), 7.25−7.43 (5H, m), 7.52−7.63 (4H, m), 7.80−7.83 (1H, m), 7.99−8.01 (1H, m); ^{13}C NMR ($CDCl_3$) δ 192.4, 155.2, 142.3, 141.8, 136.5, 133.1, 128.79, 128.76, 128.4, 127.9, 127.8, 127.6, 127.5, 127.1, 126.8, 124.7, 120.7, 119.4, 114.8, 112.1, 110.5, 84.0, 70.3, 56.9, 50.3; MS (EI) *m/z* 464 (M^+ + 1), 372, 300, 286, 176, 163, 133, 105, 91, 77, 65, 47, 39, 28. Anal. Found: C, 77.79; H, 5.42; N, 2.99. Calcd for $C_{30}H_{25}NO_4$: C, 77.74; H, 5.44; N, 3.02.

7-*endo*-(*o*-Benzyloxyphenyl)-5-methoxy-6-phenyl-6-aza-8-oxabenzo[*c*]bicyclo[3.2.1]octan-2-one (*endo*-3a). Colorless prisms (ether−hexane); mp 168.0−168.5 °C; IR (KBr) 2947, 2361, 2339, 1705, 1599, 1500, 1454, 1350, 1283, 1262, 1155, 1095, 1013, 878, 803, 749, 696 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.37 (3H, s), 5.19 (1H, d, J = 11.2 Hz), 5.25 (1H, d, J = 11.2 Hz), 5.33 (1H, d, J = 6.4 Hz), 5.87 (1H, d, J = 6.4 Hz), 6.07−6.09 (1H, m), 6.41−6.45 (1H, m,), 6.71−6.78 (3H, m), 6.95−6.97 (1H, m), 7.07. − 7.14 (3H, m), 7.37−7.49 (4H, m), 7.57−7.59 (2H, m), 7.65−7.69 (1H, m), 7.75−7.77 (1H, m), 7.89−7.91 (1H, m); ^{13}C NMR ($CDCl_3$) δ 192.5, 156.3, 144.8, 140.7, 136.5, 133.5, 128.5, 128.4, 128.0, 127.9, 127.5, 126.8, 126.4, 121.7, 121.3, 120.2, 118.2, 114.2, 111.4, 109.2, 109.1, 80.9, 70.3, 55.3, 50.1; MS (EI) *m/z* 464 (M^+ + 1), 372, 300, 286, 176, 163, 133, 105, 91, 77, 65, 47, 39, 28. Anal. Found: C, 77.81; H, 5.43; N, 2.76. Calcd for $C_{30}H_{25}NO_4$: C, 77.74; H, 5.44; N, 3.02.

5-Methoxy-6,7-*exo*-diphenyl-6-aza-8-oxabenzo[*c*]bicyclo-[3.2.1]octan-2-one (*exo*-3b). Colorless prisms (ether−hex-

ane); mp 175.0−175.5 °C; IR (KBr) 3065, 3030, 3001, 2943, 2361, 1707, 1601, 1493, 1448, 1350, 1325, 1292, 1265, 1248, 1151, 1126, 1093, 1059, 1018, 983, 960, 893, 877, 781 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.87 (3H, s), 4.53 (1H, bs), 4.83 (1H, d, J = 0.73 Hz), 6.73−6.77 (1H, m), 6.91−6.94 (2H, m), 7.09−7.13 (2H, m), 7.32−7.43 (4H, m), 7.54−7.60 (3H, m), 7.82−7.84 (1H, m), 7.99−8.01 (1H, m); ^{13}C NMR ($CDCl_3$) δ 193.2, 142.3, 142.0, 139.7, 133.5, 128.9, 127.9, 127.6, 126.9, 126.4, 124.9, 119.6, 114.7, 110.7, 85.3, 61.8, 50.4; MS (EI) *m/z* 357 (M^+), 280, 267, 222, 194, 176, 163, 133, 105, 91, 84, 77, 51, 17. Anal. Found: C, 77.59; H, 5.34; N, 3.62. Calcd for $C_{23}H_{19}NO_3$: C, 77.29; H, 5.36; N, 3.92.

5-Methoxy-6,7-*endo*-diphenyl-6-aza-8-oxabenzo[*c*]bicyclo[3.2.1]octan-2-one (*endo*-3b). Colorless prisms (ether−hexane); mp 144.0−145.0 °C; IR (KBr) 2949, 2339, 1705, 1599, 1547, 1500, 1452, 1367, 1282, 1230, 1207, 1091, 1014, 970, 885, 850, 756 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.40 (3H, s), 5.13 (1H, J = 6.4 Hz), 5.53 (1H, d, J = 6.4 Hz), 6.70−6.78 (5H, m), 7.07−7.17 (5H, m), 7.42 (1H, t, J = 7.6 Hz), 7.69 (1H, t, J = 7.6 Hz), 7.82 (1H, d, J = 7.6 Hz), 7.93 (1H, d, J = 7.6 Hz); ^{13}C NMR ($CDCl_3$) δ 192.4, 145.2, 140.6, 133.7, 133.6, 129.5, 128.6, 128.5, 128.4, 128.0, 126.7, 126.6, 121.8, 118.6, 114.4, 109.6, 83.2, 61.6, 50.2; MS (EI) *m/z* 357 (M^+), 280, 267, 222, 194, 176, 163, 133, 104, 91, 84, 76, 63, 50, 39, 29, 14. Anal. Found: C, 77.41; H, 5.46; N, 3.70. Calcd for $C_{23}H_{19}NO_3$: C, 77.29; H, 5.36; N, 3.92.

5-Methoxy-7-*exo*-(*o*-methoxyphenyl)-6-phenyl-6-aza-8-oxabenzo[*c*]bicyclo[3.2.1]octan-2-one (*exo*-3c). Yellow prisms (ether−hexane); mp 200.5−201.5 °C; IR (KBr) 3003, 2361, 2341, 1703, 1599, 1491, 1437, 1325, 1263, 1207, 1128, 1045, 983, 794, 744, 692 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.86 (3H, s), 4.01 (3H, s), 4.77 (1H, bs), 4.82 (1H, d, J = 1.2 Hz), 6.75 (1H, t, J = 7.1 Hz), 6.88−6.86 (3H, m), 7.01 (1H, m), 7.09−7.14 (2H, m), 7.34 (1H, dt, J = 1.7, 7.8 Hz), 7.40 (1H, dt, J = 1.2, 7.6 Hz), 7.54−7.58 (2H, m), 7.82 (1H, dd, J = 0.73, 7.8 Hz), 8.01 (1H, dd, J = 1.2, 7.6 Hz); ^{13}C NMR ($CDCl_3$) δ 192.6, 156.2, 142.4, 141.8, 133.2, 128.8, 128.78, 128.74, 127.8, 127.1, 126.9, 126.8, 124.8, 120.4, 119.4, 115.0, 110.6, 110.3, 84.1, 57.1, 55.5, 50.3; MS (EI) *m/z* 387 (M^+), 295, 224, 210, 176, 163, 133, 119, 105, 93, 77, 57, 41, 26. Anal. Found: C, 74.67; H, 5.43; N, 3.38. Calcd for $C_{24}H_{21}NO_4$: C, 74.40; H, 5.46; N, 3.62.

5-Methoxy-7-*endo*-(*o*-methoxyphenyl)-6-phenyl-6-aza-8-oxabenzo[*c*]bicyclo[3.2.1]octan-2-one (*endo*-3c). Yellow powder (ether−hexane); mp 157.0−159.0 °C; IR (KBr) 2962, 2361, 2341, 1703, 1599, 1506, 1437, 1340, 1259, 1091, 1033, 879, 802, 758 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.39 (3H, s), 3.98 (3H, s), 5.34 (1H, d, J = 6.4 Hz), 5.87 (1H, d, J = 6.4 Hz), 6.07 (1H, d, J = 7.3 Hz), 6.43 (1H, t, J = 7.3 Hz), 6.73 (1H, t, J = 7.3 Hz), 6.78 (2H, d, J = 7.8 Hz), 6.89 (1H, d, J = 8.1 Hz), 7.10−7.14 (3H, m), 7.39 (1H, dt, J = 0.98, 7.6 Hz), 7.67 (1H, dt, J = 1.2, 7.6 Hz), 7.76 (1H, dd, J = 1.2, 7.6 Hz), 7.91 (1H, d, J = 7.6 Hz); ^{13}C NMR ($CDCl_3$) δ 192.7, 157.2, 145.2, 140.9, 133.6, 129.4, 128.7, 128.6, 128.2, 126.8, 126.6, 121.5, 121.4, 120.1, 118.4, 114.4, 110.2, 109.4, 81.2, 55.6, 55.4, 50.2; MS (EI) *m/z* 387 (M^+), 355, 295, 281, 224, 176, 163, 133, 105, 86, 73, 57, 43, 32. HRMS (EI) Calcd for $C_{24}H_{21}NO_4$ (M^+ + H): 387.1471. Found: 387.1496.

5-Methoxy-7-*exo*-(*p*-methoxyphenyl)-6-phenyl-6-aza-8-oxabenzo[*c*]bicyclo[3.2.1]octan-2-one (*exo*-3d). Colorless prisms (ether−hexane); mp 176.0−177.0 °C; IR (KBr) 3065, 2961, 2852, 2361, 1714, 1699, 1599, 1512, 1493, 1458, 1435, 1390, 1319, 1282, 1255, 1224, 1207, 1176, 1145, 1089, 1055, 1032, 966, 887, 833, 798, 742 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.81 (3H, s), 3.85 (3H, s), 4.49 (1H, bs), 4.79 (1H, d, J = 0.98 Hz), 6.73−6.76 (1H, m), 6.92−6.96 (4H, m), 7.09−7.13 (2H, m), 7.37−7.41 (1H, m), 7.49−7.57 (3H, m), 7.81−7.83 (1H, m), 7.97−8.00 (1H, m); ^{13}C NMR ($CDCl_3$) δ 193.3, 159.1, 142.3, 142.0, 133.4, 131.6, 128.8, 127.7, 127.5, 126.8, 124.8, 119.5, 114.7, 114.3, 110.7, 85.4, 61.4, 55.4, 50.3; MS (EI) *m/z* 387 (M^+), 355, 269, 176, 163, 138, 105, 77, 57, 36, 25, 12. Anal. Found: C, 74.55; H, 5.51; N, 3.41. Calcd for $C_{24}H_{21}NO_4$: C, 74.44; H, 5.46; N, 3.62.

5-Methoxy-7-*endo*-(*p*-methoxyphenyl)-6-phenyl-6-aza-8-oxabenzo[*c*]bicyclo[3.2.1]octan-2-one (*endo*-3d). Yellow prisms (ether−hexane); mp 109.0−110.0 °C; IR (KBr) 2949, 2361, 2341, 1707, 1599, 1502, 1458, 1350, 1261, 1157, 1080, 970, 881, 815, 748 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.39 (3H, s), 3.68 (3H, s), 5.10 (1H, d, J = 6.4 Hz), 5.48 (1H, d, J = 6.4 Hz), 6.63−6.78 (7H, m), 7.07−7.11 (2H, m), 7.42−7.46 (1H, m), 7.67−7.71 (1H, m), 7.84−7.86 (1H, m), 7.92−7.94 (1H, m); ^{13}C NMR ($CDCl_3$) δ 192.7, 159.0, 145.3, 140.6, 133.7, 129.6, 128.5, 128.3, 127.8, 126.7, 125.4, 121.8, 118.5, 114.5, 114.0, 109.5, 83.3, 61.1, 55.1, 50.1; MS (EI) *m/z* 387 (M^+), 295, 224, 210, 176, 163, 149, 133, 121, 105, 74, 57, 41, 25. HRMS (EI) Calcd for $C_{24}H_{21}NO_4$ (M^+ + H): 387.1471. Found: 387.1471

7-*exo*-(*p*-Chlorophenyl)-5-methoxy-6-phenyl-6-aza-8-oxabenzo[*c*]bicyclo[3.2.1]octan-2-one (*exo*-3e). Colorless prisms (ether−hexane); mp 203.0−204.0 °C; IR (KBr) 3007, 2361, 2341, 1695, 1599, 1493, 1458, 1437, 1412, 1315, 1294, 1251, 1228, 1153, 1124, 1099, 1035, 983, 968, 887, 783, 738 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.84 (3H, s), 4.49 (1H, bs), 4.78 (1H, d, J = 0.98 Hz), 6.75−6.79 (1H, m), 6.88−6.90 (2H, m), 7.10−7.14 (2H, m), 7.37−7.42 (3H, m), 7.52−7.58 (3H, m), 7.80−7.82 (1H, m), 7.98−7.99 (1H, m); ^{13}C NMR ($CDCl_3$) δ 192.9, 142.0, 141.9, 138.2, 133.7, 133.6, 129.1, 128.99, 128.96, 127.8, 127.5, 126.9, 124.9, 119.9, 114.7, 110.8, 85.1, 61.3, 50.3; MS (EI) *m/z* 391 (M^+), 256, 228, 214, 176, 163, 133, 77, 57, 36, 25, 12. Anal. Found: C, 70.65; H, 4.69; N, 3.35. Calcd for $C_{23}H_{18}ClNO_3$: C, 70.50; H, 4.63; N, 3.57.

7-*endo*-(*p*-Chlorophenyl)-5-methoxy-6-phenyl-6-aza-8-oxabenzo[*c*]bicyclo[3.2.1]octan-2-one (*endo*-3e). Colorless prisms (ether−hexane); mp 184.0−185.0 °C; IR (KBr) 3038, 2951, 2361, 1709, 1599, 1500, 1444, 1408, 1282, 1159, 1051, 1012, 968, 877, 808, 750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.38 (3H, s), 5.13 (1H, d, J = 6.4 Hz), 5.51 (1H, d, J = 6.4 Hz), 6.72−6.76 (5H, m), 7.08−7.12 (4H, m), 7.45 (1H, dt, J = 0.98, 7.6 Hz), 7.71 (1H, dt, J = 1.2, 7.6 Hz), 7.84 (1H, dd, J = 1.2, 7.6 Hz), 7.93 (1H, d, J = 7.6 Hz); ^{13}C NMR ($CDCl_3$) δ 192.3, 145.3, 140.3, 133.9, 133.7, 132.4, 129.4, 128.8, 128.7, 128.5, 128.0, 126.7, 121.8, 118.9, 114.5, 109.6, 83.0, 61.0, 50.2; MS (EI) *m/z* 391 (M^+), 299, 281, 269, 214, 193, 176, 163, 149, 119, 105, 91, 77, 57, 36, 12. HRMS (EI) Calcd for $C_{23}H_{18}ClNO_3$ (M^+ + H): 391.0975. Found: 391.1011.

5-Methoxy-6-(*o*-methoxyphenyl)-7-*exo*-phenyl-6-aza-8-oxabenzo[*c*]bicyclo[3.2.1]octan-2-one (*exo*-3f). Colorless prisms (ether−hexane); mp 112.5−114.0 °C; IR (KBr) 3070, 2991, 2955, 2837, 1703, 1603, 1495, 1456, 1340, 1282, 1263, 1238, 1145, 1122, 1107, 1091, 1055, 1022, 898, 879, 783 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.10 (3H, s), 3.90 (3H, s), 4.94 (1H, d, J = 0.73 Hz), 5.20 (1H, bs), 6.51−6.53 (1H, m), 6.79−6.83 (1H, m), 7.02−7.06 (2H, m), 7.12−7.14 (1H, m), 7.23−7.38 (5H, m), 7.59−7.61 (2H, m), 8.05−8.07 (1H, m); ^{13}C NMR ($CDCl_3$) δ 194.2, 156.4, 144.0, 142.3, 132.6, 131.5, 129.9, 129.2, 128.3, 127.9, 127.3, 127.1, 126.7, 125.4, 123.3, 120.5, 112.2, 111.4, 86.6, 61.6, 54.4, 50.1; MS (EI) *m/z* 387 (M^+), 310, 265, 224, 210, 176, 163, 133, 84, 77, 51, 32, 17. Anal. Found: C, 74.66; H, 5.52; N, 3.32. Calcd for $C_{24}H_{21}NO_4$: C, 74.40; H, 5.46; N, 3.62.

5-Methoxy-6-(*o*-methoxyphenyl)-7-*endo*-phenyl-6-aza-8-oxabenzo[*c*]bicyclo[3.2.1]octan-2-one (*endo*-3f). Yellow prisms (ether−hexane); mp 170−171.5 °C; IR (KBr) 2924, 2361, 1705, 1597, 1502, 1458, 1340, 1234, 1093, 1026, 887, 736 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.40 (3H, s), 3.53 (3H, s), 5.09 (1H, d, J = 6.4 Hz), 6.01 (1H, bs), 6.66 (1H, m), 6.74−6.86 (4H, m), 7.05−7.09 (4H, m), 7.46 (1H, m), 7.70 (1H, m), 7.85−7.93 (2H, m); MS (EI) *m/z* 387 (M^+), 310, 265, 224, 196, 176, 163, 133, 102, 87, 74, 57, 41, 26, 12. Satisfactory elemental analysis was not obtained because only a small amount of the *endo*-adduct was obtained.

5-Methoxy-6-(*p*-methoxyphenyl)-7-*exo*-phenyl-6-aza-8-oxabenzo[*c*]bicyclo[3.2.1]octan-2-one (*exo*-3g). Colorless prisms (ether−hexane); mp 135.5−136.5 °C; IR (KBr) 2994, 1707, 1510, 1454, 1439, 1319, 1292, 1269, 1203, 1151, 1097, 1055, 1020, 982, 885, 820, 787 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.64

(3H, s), 3.87 (3H, s), 4.46 (1H, s), 4.80 (1H, s), 6.66−6.70 (2H, m), 6.83−6.87 (2H, m), 7.30−7.42 (4H, m), 7.51−7.59 (3H, m), 7.72−7.74 (1H, m), 7.99−8.01 (1H, m); ^{13}C NMR ($CDCl_3$) δ 193.2, 153.3, 142.1, 139.1, 136.1, 133.5, 128.83, 128.79, 127.8, 127.6, 126.8, 126.4, 124.8, 116.4, 114.3, 111.0, 85.2, 62.0, 55.4, 50.2; MS (EI) *m/z* 387 (M^+), 310, 265, 224, 210, 196, 176, 163, 133, 105, 92, 77, 64, 41, 25, 12. Anal. Found: C, 74.62; H, 5.41; N, 3.45. Calcd for $C_{24}H_{21}NO_4$: C, 74.40; H, 5.41; N, 3.25.

5-Methoxy-6-(*p*-methoxyphenyl)-7-*endo*-phenyl-6-aza-8-oxabenzo[*c*]bicyclo[3.2.1]octan-2-one (*endo*-3g). Yellow prisms (ether−hexane); mp 205.0−206.5 °C; IR (KBr) 2949, 2835, 1699, 1601, 1514, 1456, 1294, 1238, 1161, 1037, 883, 814, 754 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.37 (3H, s), 3.68 (3H, s), 5.13 (1H, d, J = 6.4 Hz), 5.51 (1H, d, J = 6.4 Hz), 6.67−6.73 (4H, m), 6.79−6.81 (2H, m), 7.10−7.18 (3H, m), 7.43 (1H, dt, J = 0.98, 7.6 Hz), 7.69 (1H, dt, J = 1.2, 7.6 Hz), 7.84 (1H, dt, J = 1.2, 7.6 Hz), 7.90 (1H, m); MS (EI) *m/z* 387 (M^+), 269, 256, 224, 207, 182, 163, 123, 105, 92, 77, 60, 41, 25, 12. Anal. Found: C, 74.70; H, 5.44; N, 3.34. Calcd for $C_{24}H_{21}NO_4$: C, 74.40; H, 5.46; N, 3.62.

6-(*p*-Chlorophenyl)-5-methoxy-7-*exo*-phenyl-6-aza-8-oxabenzo[*c*]bicyclo[3.2.1]octan-2-one (*exo*-3h). Brown powder; mp 129.0−131.0 °C; IR (KBr) 3449, 2947, 2361, 1709, 1599, 1450, 1319, 1251, 1153, 1057, 881, 819, 731, 698 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.85 (3H, s), 4.46 (1H, bs), 4.83 (1H, d, J = 0.73 Hz), 6.83−6.87 (2H, m), 7.05−7.08 (2H, m), 7.33−7.47 (4H, m), 7.52−7.61 (3H, m), 7.79 (1H, m), 8.02 (1H, m); ^{13}C NMR ($CDCl_3$) δ 192.9, 141.6, 140.9, 139.2, 133.6, 129.1, 129.0, 128.8, 128.1, 127.6, 127.0, 126.3, 124.8, 124.7, 116.0, 110.7, 85.2, 61.9, 50.4; MS (EI) *m/z* 391 (M^+), 355, 281, 221, 214, 176, 149, 105, 91, 73, 57, 29, 16. HRMS (EI) Calcd for $C_{23}H_{18}ClNO_3$ (M^+ + H): 391.0975. Found: 391.0915.

6-(*p*-Chlorophenyl)-5-methoxy-7-*endo*-phenyl-6-aza-8-oxabenzo[*c*]bicyclo[3.2.1]octan-2-one (*endo*-3h). ^{1}H NMR ($CDCl_3$) δ 3.39 (3H, s), 5.14 (1H, d, J = 6.4 Hz), 5.49 (1H, d, J = 6.4 Hz), 6.67−6.71 (2H, m), 7.03−7.05 (2H, m), 7.11−7.18 (3H, m), 7.43−7.58 (3H, m), 7.70 (1H, m), 7.83−7.91 (2H, m). Although the minor *endo*-adduct was not isolated purely by chromatography, this product could be characterized by ^{1}H NMR.

6-*c*-Hexyl-5-methoxy-7-*exo*-phenyl-6-aza-8-oxabenzo[*c*]-bicyclo[3.2.1]octan-2-one (*exo*-3i). Yellow oil; IR (KBr) 3425, 2930, 2361, 1703, 1601, 1454, 1255, 1091, 1035, 941, 891, 738 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.58 (1H, m), 0.83−1.09 (5H, m), 1.42−1.44 (2H, m), 1.58 (1H, m), 1.91 (1H, m), 2.37 (1H, m), 3.81 (3H, s), 3.95 (1H, bs), 4.52 (1H, d, J = 0.98 Hz), 7.27−7.38 (3H, m), 7.48 (1H, m), 7.56−7.65 (4H, m), 8.06 (1H, d, J = 7.6 Hz); ^{13}C NMR ($CDCl_3$) δ 193.8, 144.1, 143.9, 133.9, 128.54, 128.49, 128.36, 127.4, 126.80, 126.77, 123.8, 111.7, 86.1, 60.1, 56.1, 49.5, 33.6, 30.2, 26.0, 25.6; MS (EI) *m/z* 363 (M^+), 320, 282, 222, 177, 163, 133, 105, 91, 77, 55, 35, 24. HRMS (EI) Calcd for $C_{23}H_{25}NO_3$ (M^+ + H): 363.1834. Found: 363.1860.

6-*c*-Hexyl-5-methoxy-7-*endo*-phenyl-6-aza-8-oxabenzo-[*c*]bicyclo[3.2.1]octan-2-one (*endo*-3i). ^{1}H NMR ($CDCl_3$) δ 0.88−1.96 (10H, m), 3.33 (1H, m), 3.58 (3H, s), 4.92 (1H, d, J = 7.8 Hz), 5.03 (1H, d, J = 7.8 Hz), 6.86−6.88 (2H, m), 7.04 − 7.09 (3H, m), 7.31 (1H, m), 7.43 (1H, m), 7.58−7.62 (2H, m). Although the minor *endo*-adduct was not isolated purely by chromatography, this product could be characterized by ^{1}H NMR.

7-*exo*-*c*-Hexyl-5-methoxy-6-phenyl-6-aza-8-oxabenzo[*c*]-bicyclo[3.2.1]octan-2-one (*exo*-3j). Yellow prisms (ether−hexane); mp 197.0−199.0 °C; IR (KBr) 2926, 2851, 2361, 1698, 1599, 1501, 1453, 1304, 1258, 1223, 1209, 1126, 1096, 1036, 1015, 980, 764, 727, 692, 580 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.28−2.09 (11H, m), 3.36 (1H, d, J = 6.1 Hz), 3.74 (3H, s), 4.79 (1H, s), 6.78 (1H, m), 6.91−6.93 (2H, m), 7.12−7.16 (2H, m), 7.31 (1H, m), 7.42 (1H, m), 7.56 (1H, m), 7.91 (1H, m); ^{13}C NMR ($CDCl_3$) δ 194.1, 143.3, 142.6, 133.1, 128.7, 128.5, 127.8, 126.5, 124.4, 120.1, 116.2, 110.9, 80.0, 61.9, 49.8, 40.9, 30.6, 28.9, 26.6, 26.5, 26.2; MS (EI) *m/z* 363 (M^+), 280, 176, 163, 149, 133, 95, 81, 60, 41, 26, 13. Anal. Found: C, 76.24; H, 6.95; N, 3.56. Calcd for $C_{23}H_{25}NO_3$: C, 76.01; H, 6.93; N, 3.85.

7-*endo*-*c*-Hexyl-5-methoxy-6-phenyl-6-aza-8-oxabenzo-[*c*]bicyclo[3.2.1]octan-2-one (*endo*-3j). ^{1}H NMR ($CDCl_3$) δ 0.84−2.04 (11H, m), 3.16 (1H, br), 3.37 (3H, s), 5.02 (1H, d, J = 7.8 Hz), 6.49−7.50 (8H, m), 7.98 (1H, m). Although the minor *endo*-adduct was not isolated purely by chromatography, this product could be characterized by ^{1}H NMR.

6,7-*endo*-Di(*c*-hexyl)-5-methoxy-6-aza-8-oxabenzo[*c*]-bicyclo[3.2.1]octan-2-one (*endo*-3k). Colorless crystals (ether−hexane); mp 117.0−118.5 °C; IR (KBr) 3063, 2363, 1709, 1601, 1451, 1373, 1262, 1246, 1175, 1154, 1086, 1066, 878, 847, 802, 764 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.72−1.94 (21H, m), 2.35 (1H, m), 3.33 (3H, s), 3.61 (1H, d, J = 8.1 Hz), 4.81 (1H, d, J = 8.1 Hz), 7.28 (1H, m), 7.44 (1H, m), 7.54 (1H, m), 7.97 (1H, m); ^{13}C NMR ($CDCl_3$) δ 194.3, 142.0, 132.5, 132.0, 128.5, 126.1, 125.9, 109.3, 84.0, 60.9, 55.9, 52.8, 49.6, 34.6, 33.3, 32.8, 28.9, 26.3, 25.5, 25.1, 25.0, 23.4, 22.8; MS (EI) *m/z* 369 (M^+), 206, 193, 177, 150, 133, 105, 83, 69, 55, 37, 26. Anal. Found: C, 74.89; H, 8.60; N, 3.45. Calcd for $C_{23}H_{31}NO_3$: C, 74.76; H, 8.46; N, 3.79.

6,7-*exo*-Di(*c*-hexyl)-5-methoxy-6-aza-8-oxabenzo[*c*]-bicyclo[3.2.1]octan-2-one (*exo*-3k). Colorless oil; IR (neat) 2926, 2852, 2361, 1707, 1601, 1450, 1288, 1261, 1111, 1030, 800, 717, 667 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.86−1.93 (21H, m), 2.55 (1H, m), 2.84 (1H, d, J = 2.0 Hz), 3.35 (3H, s), 4.37 (1H, d, J = 2.0 Hz), 7.39 (1H, d, J = 7.6 Hz), 7.47 (1H, dt, J = 0.98, 7.6 Hz), 7.60 (1H, dt, J = 1.2, 7.6 Hz), 8.01 (1H, dd, J = 1.2, 7.6 Hz); MS (EI) *m/z* 369 (M^+), 355, 327, 281, 221, 206, 177, 149, 104, 73, 55, 37, 24. HRMS (EI) Calcd for $C_{23}H_{31}NO_3$ (M^+ + H): 369.2304. Found: 369.2324. Although the *exo*-adduct was not isolated purely by chromatography, this product could be characterized by ^{1}H NMR.

7-*exo*-(Ethoxycarbonyl)-5-methoxy-6-(diphenylmethyl)-6-aza-8-oxabenzo[*c*]bicyclo[3.2.1]octan-2-one (*exo*-3l). Yellow oil: IR (neat) 3445, 2947, 2361, 2339, 1732, 1714, 1645, 1601, 1556, 1494, 1454, 1373, 1230, 1095, 1041, 669 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.21 (3H, t, J = 7.1 Hz), 3.23 (1H, d, J = 0.97 Hz), 3.73 (3H, s), 4.12−4.21 (2H, m), 4.33 (1H, s), 4.76 (1H, d, J = 0.97 Hz), 6.83−6.85 (2H, m), 7.07−7.09 (3H, m), 7.18−7.37 (6H, m), 7.53−7.62 (2H, m), 8.06 (1H, m); MS (EI) *m/z* 443 (M^+), 428, 411, 384, 370, 300, 238, 222, 182, 152, 133, 105, 91, 77, 50, 26. HRMS (EI) Calcd for $C_{27}H_{25}NO_5$ (M^+ + H): 443.1733. Found: 443.1752.

7-*endo*-(Ethoxycarbonyl)-5-methoxy-6-(diphenylmethyl)-6-aza-8-oxabenzo[*c*]bicycle[3.2.1]-octan-2-one (*endo*-3l). ^{1}H NMR ($CDCl_3$) δ 0.86 (3H, t, J = 7.1 Hz), 3.47 (3H, s), 3.52 (1H, dq, J = 7.1, 10.7 Hz), 3.67 (1H, dq, J = 7.1, 10.7 Hz), 4.51 (2H, d, J = 6.8 Hz), 4.90 (1H, d, J = 6.8 Hz), 5.15 (1H, s), 6.96 (1H, m), 7.10−7.34 (10H, m), 7.45−7.54 (2H, m), 7.99 (1H, m). Although the *endo*-adduct was not isolated purely by chromatography, this product could be characterized by ^{1}H NMR.

Satisfactory ^{13}C NMR data of *endo*-**3f**, **3g**, **3h**, **3i**, **3j**, **3l** and *exo*-**3l** were not obtained because only a small amount of the adducts could be separated from the corresponding mixtures of diastereomers by chromatography.

5,6-Diphenyl-7-*exo*-(2-methoxy)phenyl-6-aza-8-oxabicycle[3.2.1]octan-2-one (*exo*-6c). Colorless needles (ether−hexane); mp 158−160 °C; IR (KBr) 2961, 2361, 1736, 1601, 1500, 1462, 1448, 1413, 1356, 1278, 1207, 1151, 1107, 1028, 966, 883, 810, 752 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.39−2.54 (2H, m), 2.99 (1H, ddd, J = 6.8, 11.0, 13.7 Hz), 3.36 (1H, ddd, J = 1.7, 7.6, 13.7 Hz), 3.92 (3H, s), 4.49 (1H, s), 5.17 (1H, s), 6.55−6.57 (2H, m), 6.71 (1H, m), 6.92−6.96 (2H, m), 7.03−7.08 (2H, m), 7.30 (1H, m), 7.34−7.47 (3H, m), 7.61 (1H, m), 7.82−7.84 (2H, m); ^{13}C NMR ($CDCl_3$) δ 31.0, 32.7, 55.4, 62.0, 86.1, 95.9, 110.2, 114.5, 118.8, 120.5, 127.3, 128.5, 128.7, 128.8, 129.0, 139.2, 143.7, 156.0, 203.4; MS (EI) *m/z* 385 (M^+ + 1), 328, 212, 197, 180, 161, 149, 117, 105, 91, 77, 57, 41, 26, 16. Anal. Calcd for $C_{25}H_{23}NO_3$: C, 77.90; H, 6.01; N, 3.63. Found: C, 78.07; H, 6.14; N, 3.32.

5,6-Diphenyl-7-*endo*-(2-methoxy)phenyl-6-aza-8-oxabicycle[3.2.1]octan-2-one (*endo*-6c): ^{1}H NMR ($CDCl_3$) δ 2.54−2.69 (2H, m), 2.91−3.03 (1H, m), 3.10−3.15 (1H, m), 3.95 (3H, s), 5.16 (1H, d, J = 5.9 Hz), 5.75 (1H, d, J = 5.9 Hz), 6.36−6.38 (2H, m), 6.54−6.58 (1H, m), 6.71−6.76 (1H, m), 6.85−6.92 (3H, m), 7.05−7.09 (1H, m), 7.18−7.27 (4H, m), 7.40−7.48 (2H, m); ^{13}C NMR ($CDCl_3$) δ 34.7, 35.1, 55.6, 60.6, 83.4, 96.4, 110.4, 117.9, 118.8, 120.3, 121.7, 127.4, 127.7, 127.8, 128.2, 128.8, 138.6, 143.8, 157.2, 203.5. ^{1}H and ^{13}C NMR were assigned from a mixture of *exo*- and *endo*-adducts.

5-Ethoxy-1-phenyl-1,4-pentandione (7). Brown oil; IR (KBr) 3063, 2976, 2910, 1724, 1685, 1597, 1493, 1448, 1358, 1238, 1213, 1153, 1107, 1010, 758, 692 cm^{-1}; ^{1}H NMR($CDCl_3$) δ 1.27 (3H, t, J = 7.1 Hz), 2.88−2.91 (2H, m), 3.33−3.36 (2H, m), 3.59−3.64 (2H, q, J = 7.08 Hz), 4.20 (2H, s), 7.45−7.49 (2H, m), 7.57 (1H, m), 7.97−7.99 (2H, m); ^{13}C NMR ($CDCl_3$) δ 15.2, 32.3, 32.7, 67.3, 75.9, 127.9, 128.4, 133.0, 136.4, 198.1, 207.8; MS (EI) *m/z* 220 (M^+), 175, 161, 133, 105, 91, 77, 59, 41, 28. HRMS (EI) Calcd for $C_{13}H_{16}O_3$ (M^+): 220.1099. Found: 220.1089.

6-Diphenyl-7-*exo*-(2-methoxy)phenyl-5-methyl-6-aza-8-oxabicycle[3.2.1]octan-2-one (*exo*-9c). Colorless needles (ether−hexane); mp 162.0−163.5 °C; IR (KBr) 2957, 2363, 1732, 1601, 1502, 1489, 1415, 1354, 1309, 1238, 1099, 1020, 893, 806, 754 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.02 (3H, s), 2.24−2.47 (3H, m), 2.99−3.06 (1H, m), 3.91 (3H, s), 4.23 (1H, s), 5.00 (1H, s), 6.62−6.64 (2H, m), 6.74 (1H, m), 6.89−6.94 (2H, m), 7.15−7.19 (2H, m), 7.27−7.33 (2H, m); ^{13}C NMR ($CDCl_3$) δ 24.7, 33.0, 33.1, 55.5, 62.3, 85.3, 94.0, 110.1, 113.3, 117.3, 120.5, 127.1, 127.2, 128.7, 129.1, 143.0, 156.0, 204.6; MS (EI) *m/z* 323 (M^+), 266, 212, 161, 118, 91, 77, 65, 49, 24, 12. Satisfactory elemental analysis was not obtained because only a small amount of the *exo*-adduct was obtained.

6-Diphenyl-7-*endo*-(2-methoxy)phenyl-5-methyl-6-aza-8-oxabicycle[3.2.1]octan-2-one (*endo*-9c). Colorless needles (ether−hexane); mp 132−133 °C, IR (neat) 3038, 2939, 2361, 1728, 1599, 1439, 1383, 1305, 1244, 1116, 1053, 995, 910, 833, 787, 733 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.60 (3H, s), 2.28−2.55 (4H, m), 3.88 (3H, s), 4.93 (1H, d, J = 5.9 Hz), 5.52 (1H, d, J = 5.9 Hz), 6.71 (1H, m), 6.79−6.88 (4H, m), 7.08 (1H, m), 7.13−7.20 (3H, m); ^{13}C NMR ($CDCl_3$) δ 24.1, 34.6, 38.9, 55.5, 60.1, 82.4, 95.5, 110.2, 119.3, 120.2, 120.3, 122.2, 126.9, 128.46, 128.49, 144.3, 157.2, 204.1; MS (EI) *m/z* 323 (M^+), 266, 225, 212, 197, 160, 118, 91, 77, 65, 49, 28, 12. Anal. Calcd for $C_{20}H_{21}NO_3$: C, 74.28; H, 6.55; N, 4.33. Found: C, 74.31; H, 6.52; N, 4.33.

5-Methoxy-7-*exo*-(*o*-methoxyphenyl)-6-phenyl-6-aza-8-oxa(tetrachlorobenzo)[*c*]bicyclo-[3.2.1]octan-2-one (*exo*-11c). Yellow needles (chloroform-hexane); mp 259−260 °C; IR (KBr) 3344, 2941, 2361, 2208, 1716, 1601, 1502, 1489, 1437, 1251, 1190, 1109, 1028, 906, 794 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.83 (3H, s), 3.99 (3H, s), 4.94−4.95 (2H, m), 6.86−6.98 (3H, m), 7.07−7.10 (2H, m), 7.14−7.18 (2H, m), 7.32 (1H, m), 7.52 (1H, m); ^{13}C NMR ($CDCl_3$) δ 50.7, 55.5, 57.9, 83.3, 110.4, 112.0, 117.6, 120.3, 121.5, 126.0, 126.7, 127.1, 129.00, 129.04, 130.1, 133.7, 136.1, 140.3, 141.1, 141.3, 156.5, 189.9; MS (EI) *m/z* 525 (M^+ + 2), 433, 390, 301, 271, 224, 210, 167, 119, 93, 77, 49, 32. Anal. Calcd for $C_{24}H_{17}Cl_4NO_4$: C, 54.88; H, 3.26; N, 2.67. Found: C, 55.09; H, 3.24; N, 2.48.

5-Methoxy-7-*endo*-(*o*-methoxyphenyl)-6-phenyl-6-aza-8-oxa(tetrachlorobenzo)[*c*]bicyclo-[3.2.1]octan-2-one (*endo*-11c). Yellow oil; IR (neat) 3427, 2955, 2361, 1722, 1599, 1500, 1437, 1248, 1159, 1113, 1047, 979, 841, 802, 754 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.30 (3H, s), 3.97 (3H, s), 5.34 (1H, d, J = 5.9 Hz), 5.68 (1H, d, J = 5.9 Hz), 6.41 (1H, m), 6.57 (1H, m), 6.86−6.98 (4H, m), 7.15−7.21 (3H, m); ^{13}C NMR ($CDCl_3$) δ 50.5, 55.3, 57.4, 80.7, 110.0, 111.3, 117.7, 120.2, 120.5, 121.0, 126.5, 126.6, 127.7, 128.4, 128.8, 133.3, 135.3, 139.6, 140.8, 143.1, 156.8, 188.5; MS (EI) *m/z* 525 (M^+ + 2), 429, 355, 281, 224, 210, 167, 125, 106, 73, 57, 24. HRMS (EI) Calcd for $C_{24}H_{17}Cl_4NO_4$ (M^+): 522.9912. Found: 522.9926.

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra of the reaction products and X-ray structures of *exo*-**3g** and *endo*-**3g** in CIF format, with details of the calculations included. This material is available free of charge via the Internet at http://pubs.acs.org.

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