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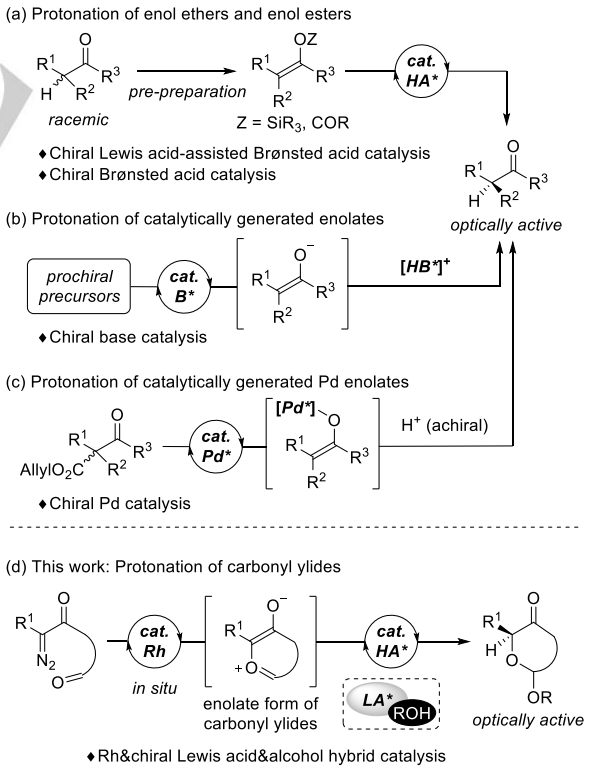
Enantioselective Protonation of Cyclic Carbonyl Ylides by Chiral Lewis Acid Assisted Alcohols

Yasunori Toda,[a] Takayuki Yoshida,[a] Kaoru Arisue,[a] Kazuaki Fukushima,[b] Hiroyoshi Esaki,[b] Ayaka Kikuchi,[a] and Hiroyuki Suga*[a]

Abstract: Chiral Lewis acid-catalyzed asymmetric alcohol addition reactions to cyclic carbonyl ylides generated from *N*-(α-diazocarbonyl)-2-oxazolidinones featuring a dual catalytic system are reported. Construction of a chiral quaternary heteroatom-substituted carbon center was accomplished in which the unique heterobicycles were obtained in good yields with high stereoselection. The alcohol adducts were successfully converted to optically active oxazolidine-2,4-diones by hydrolysis. Mechanistic studies by DFT calculations revealed that alcohols could be activated by Lewis acids, enabling enantioselective protonation of the carbonyl ylides.

Asymmetric protonation of enolates represents one of the most straightforward approaches for the construction of chiral tertiary carbon centers, which are found in a large number of optically active and biologically relevant organic compounds.[1] The development of catalytic asymmetric protonation has long been considered arduous owing to the nature of the proton. Its empty 1s orbital makes the construction of a highly-controlled asymmetric environment challenging. Additionally, the smallest element in the Periodic Table can cause fast proton exchanges, which lead to non-enantioselective processes. It is also necessary to prevent racemization of the stereocenter and to control the enolate *E*/*Z* geometry. To-date, several strategies have been employed for enantioselective protonation, including (a) protonation of enol ethers and enol esters by chiral proton donors, (b) protonation of enolates generated by chiral Brønsted base catalysts, and (c) protonation of Pd enolates by achiral Brønsted acids (Scheme 1).[1g,k,l] In the cases involving chiral proton catalysis, pre-preparation of the enolate equivalents is typically required for activation of the carbonyl compounds. In contrast to these strategies, we envisioned a novel enantioselective protonation of *in situ*-generated transient enolate equivalents. For this purpose, we focused on cyclic carbonyl ylides derived from diazo compounds. Until now, there have been no examples of enantioselective protonation of 1,3-dipole type ylide species by chiral Lewis acid catalysis.[2,3]

Rh(II)-catalyzed intramolecular carbenoid-carbonyl cyclization reactions of diazo carbonyl compounds are realized as one of the most efficient methods for the generation of cyclic carbonyl ylides.[4,5] We have demonstrated that a dual catalytic system including a chiral Lewis acid was effective in performing enantioselective 1,3-dipolar cycloadditions.[6] In order to expand this attractive 1,3-dipolar system, we sought to explore the enantioselective protonation of carbonyl ylides. This would be accomplished by electrophilic activation of an alcohol by a chiral Lewis acid catalyst as if the alcohol behaved like the dipolarophile in a 1,3-dipolar system. Although a few examples of alcohol addition reactions to cyclic carbonyl ylides have been reported,[7,8] there are a number of issues to be overcome for the chiral Lewis acid-catalyzed enantioselective reaction as follows: (1) efficient activation of alcohols by Lewis acids; (2) asymmetric induction by chiral Lewis acids; and (3) undesired β-elimination when α-alkyl diazo carbonyl substrates possessing a β-hydrogen are utilized as the cyclic carbonyl ylide precursors.[9] In this communication, we demonstrate the first example of an enantioselective protonation of cyclic carbonyl ylides generated



Scheme 1. Strategies for enantioselective protonation of enolate derivatives.

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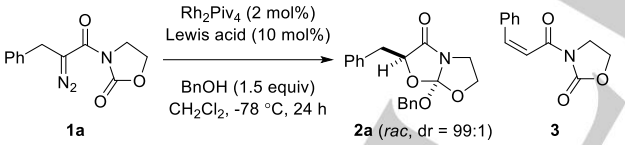
from α-alkyl diazo carbonyl compounds using a dual catalytic system that consists of a Rh(II) complex and chiral Lewis acids. Computational studies to gain insight into the addition mechanism are also described.

Initially, the reaction of 3-(3-phenyl-2-diazo-1-propanoyl)-2-oxazolidinone (**1a**) with benzyl alcohol (1.5 equiv) was carried out in the absence of a Lewis acid using a dirhodium complex (2 mol%) as the sole catalyst. We selected dirhodium tetrapivaloate (Rh_2Piv_4) to avoid undesired β-elimination from the corresponding carbenoid.[9] As a result, desired alcohol adduct **2a** was obtained in 27% NMR yield with high diastereoselectivity (dr = 99:1) (Table 1, entry 1). The β-elimination product, (*Z*)-3-cinnamoyl-2-oxazolidinone (**3**), was also detected in 8% NMR yield along with 61% NMR yield[10] of starting diazo substrate **1a**. In contrast, the addition of 10 mol% of Lewis acids was effective in accelerating the addition of the alcohol to give **2a** in 71–95% NMR yields (entries 2–9). By-product **3** was also reduced to less than 2% NMR yield[10] in most cases. Although product **2a** was partly decomposed by column chromatography due to its instability, it could be isolated in a relatively good yield (Table 1, entry 6). The reactions of diazo compound **1b**, bearing dimethyl groups at the 5-position, with ethanol, *p*-methoxybenzyl alcohol, and *p*-bromobenzyl alcohol using $Zn(BF_4)_2$•xH_2O afforded stable alcohol adducts **2b**–**2d**, respectively, in high to good yields with high diastereoselectivities, and the products could be isolated by column chromatography (Scheme 2). The unique structure and relative configuration of **2d** were unambiguously confirmed by X-ray structure analysis, revealing that *syn*-addition of the alcohol to the carbonyl ylides occurred.[11]

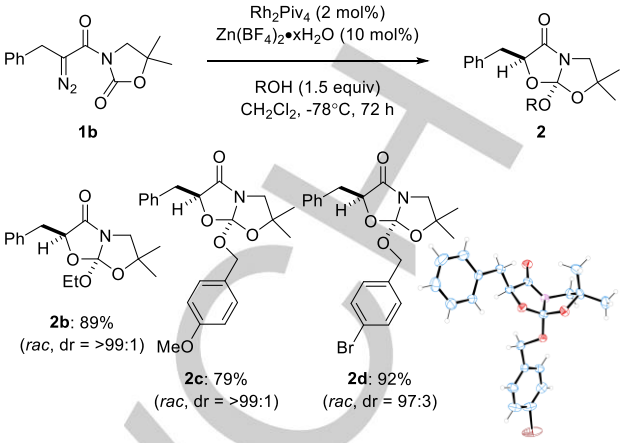
The role of the Lewis acid in the alcohol addition to cyclic carbonyl ylides was studied by density functional theory (DFT). To simplify the calculations, MeOH and the carbonyl ylide in Figure 1 were used as models. All calculations were performed

Table 1. Screening of achiral Lewis acids in the reaction of **1a** with BnOH[a]



Entry	Lewis acid	**2a** / Yield[b] (%)
1	None	27
2	$Fe(ClO_4)_2$•$6H_2O$	83
3	$Co(ClO_4)_2$•$6H_2O$	83
4	$Ni(ClO_4)_2$•$6H_2O$	71
5	$Cu(ClO_4)_2$•$6H_2O$	95
6	$Zn(ClO_4)_2$•$6H_2O$	86 (71)[c]
7	$AgClO_4$•$6H_2O$	85
8	$Zn(BF_4)_2$•xH_2O[d]	81
9	$Zn(OTf)_2$	75

[a] The Reaction was carried out using diazo compound **1a**, benzyl alcohol (1.5 equiv), Rh_2pPiv_4 (2 mol%), and a Lewis acid (10 mol%) in CH_2Cl_2 (0.05 M) at –78 °C for 24 h. [b] Determined by ^1H NMR analysis using $(CH_2Cl)_2$ as an internal standard. [c] Isolated yield. [d] Hexa- or heptahydrate.



Scheme 2. Alcohol addition reactions to a cyclic carbonyl ylide generated from diazo compound **1b**.

with Gaussian09 D.01 and Gaussian16 C.01.[12] Geometries were optimized using the M06-2X/6-311+G(d,p) (H,C,N,O,Cl) + SDD (Zn) level of theory in the gas phase. The intrinsic reaction coordinate (IRC) approach was used to search for reactants and products.[13] The energies were then refined by M06-2X/def2-TZVPP single-point energy calculations in solution (CH_2Cl_2) using the SMD solvation model.[14] The refined energies were converted to zero-point energy-corrected free energies at 298.15 K and 1 atm with use of the M06-2X/6-311+G(d,p) (H,C,N,O,Cl) + SDD (Zn) harmonic frequencies. Our goal in this study was to elucidate whether the activation of alcohols by Lewis acids was possible. We considered three types of coordination of $Zn(ClO_4)_2$ as shown in Figure 1: (1) to an unshared electron pair of MeOH (Model **I**); (2) to each one of the two unshared electron pairs on the carbonyl group of the carbonyl ylide (Models **II** and **III**).[15] Two transition states (**TS1a** and **TS1b**) are obtained in the case of Model **I**, suggesting a stepwise mechanism consisting of protonation of the carbonyl ylide followed by addition of MeOH. The first protonation step is rate-limiting since the energy of **TS1a** is higher than that of **TS1b** (Figure 2). In contrast, Model **II** affords a concerted-type mechanism, wherein C-H bond formation (protonation) and C-O bond formation (MeOH addition) occur simultaneously. On the other hand, Model **III** corresponds to another stepwise mechanism derived from the Lewis acid activation of the carbonyl ylide. In this mechanism, the carbonyl ylide undergoes MeOH addition before protonation. Although **R2** (ΔG = 0.0 kcal mol^{-1}) is energetically more stable than **R1** (ΔG = 1.9 kcal mol^{-1}), the stepwise protonation/addition mechanism would be the most favored pathway in terms of relative Gibbs energies of each transition state in the whole

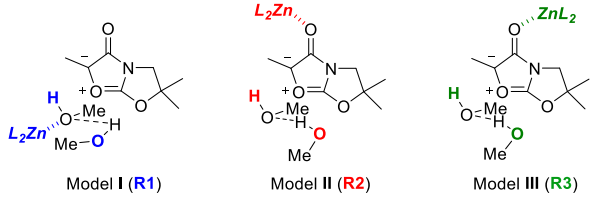


Figure 1. Possible types of coordination (L = ClO_4^-).

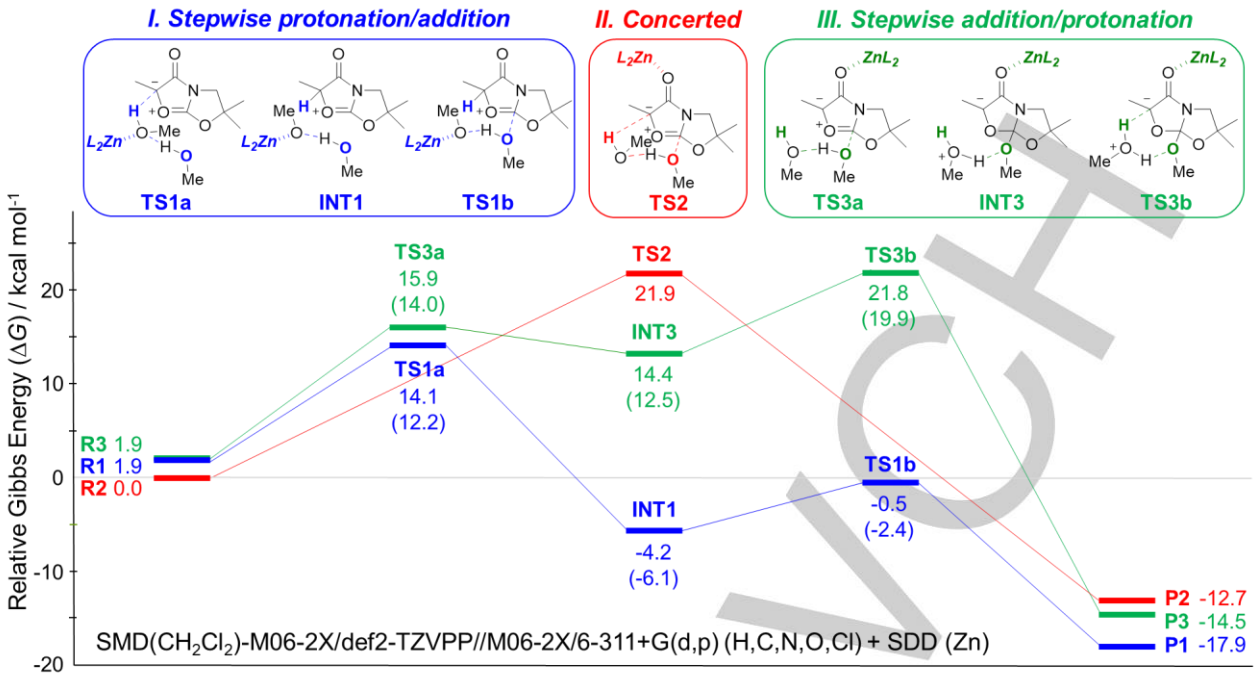
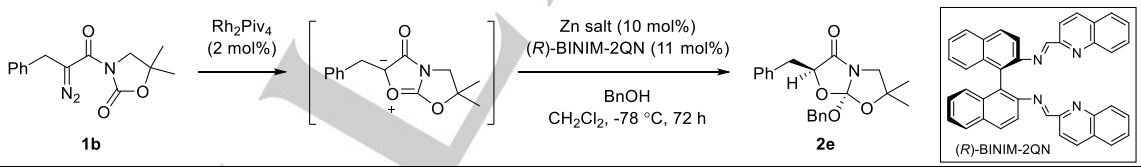


Figure 2. Energy profiles of the Lewis acid-catalyzed reaction between the carbonyl ylide and MeOH (L = ClO_4^-). The relative energies based on **R2** are shown. Energy deference from each reactant (**R1** or **R3**) is shown in parenthesis. All energies in kcal mol^{-1}.

energy profiles. It is hence concluded that this transformation can be extended to enantioselective protonation because the protonation step is not only a rate-determining step but also a stereo-determining step.

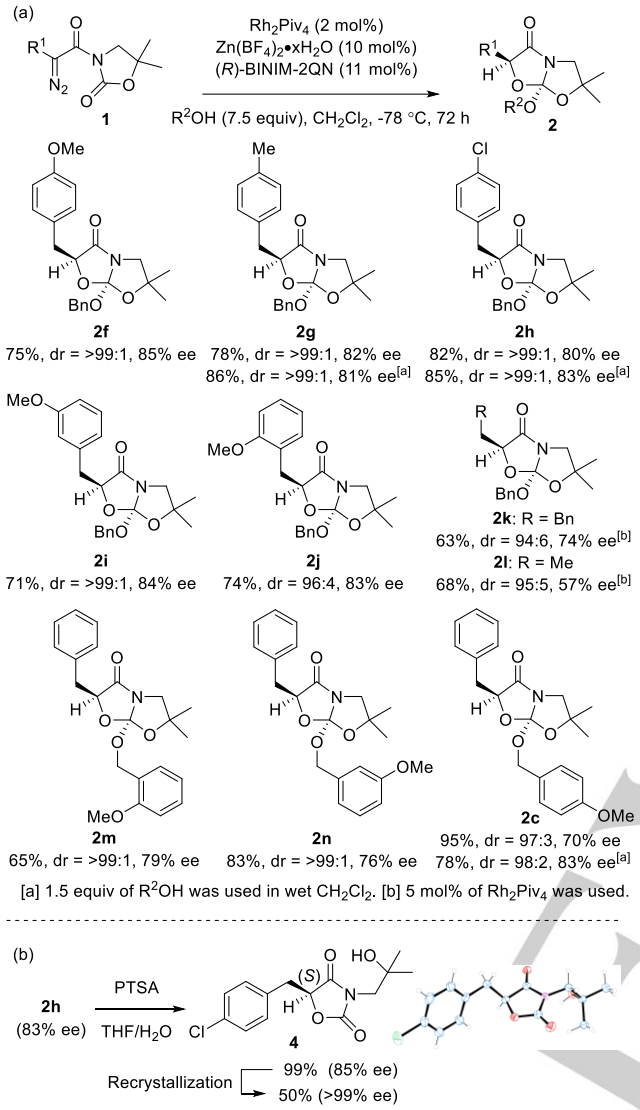
Encouraged by these computational studies, we attempted the enantioselective protonation of the cyclic carbonyl ylide by chiral Lewis acids (Table 2). The chiral Lewis acids were first prepared by mixing Zn salts with (*R*)-*N*,*N*'-(2-quinolylmethylene)-2,2'-binaphthyldiamine[16] ((*R*)-BINIM-2QN) in CH_2Cl_2 at room temperature for 6 h, and then the reaction was carried out at –78 °C for 72 h after successively adding Rh_2Piv_4 (2 mol%), benzyl alcohol (1.5 equiv), and diazo compound **1b**. An initial investigation using $Zn(BF_4)_2$•xH_2O in dry CH_2Cl_2 showed promising enantioselectivity (68% ee) with good yield of **2e** (entry 1). It is interesting to note that improved enantioselectivity (83% ee) was observed when the reaction was performed in wet CH_2Cl_2 (entry 2).[17] By the investigation of counter anions for zinc salts, BF_4^- was revealed to exhibit slightly better enantioselectivity than ClO_4^- and OTf^- (entries 2–4). To further explore the effect of wet CH_2Cl_2, we tested the reaction in dry

Table 2. Chiral Lewis acid-catalyzed enantioselective protonation of a cyclic carbonyl ylide[a]



Entry	Zn salt	BnOH (equiv)	Solvent	Yield[b] (%)	Dr (*trans*:*cis*)	ee[c] (%)
1	$Zn(BF_4)_2$•xH_2O	1.5	dry CH_2Cl_2	86	> 99:1	68
2	$Zn(BF_4)_2$•xH_2O	1.5	wet CH_2Cl_2	86	> 99:1	83
3	$Zn(ClO_4)_2$•$6H_2O$	1.5	wet CH_2Cl_2	87	> 99:1	82
4	$Zn(OTf)_2$	1.5	wet CH_2Cl_2	59	> 99:1	81
5	$Zn(BF_4)_2$•xH_2O	1.5	dry CH_2Cl_2 + H_2O[d]	85	> 99:1	81
6	$Zn(BF_4)_2$•xH_2O	3.5	dry CH_2Cl_2	88	> 99:1	72
7	$Zn(BF_4)_2$•xH_2O	5.5	dry CH_2Cl_2	89	> 99:1	84
8	$Zn(BF_4)_2$•xH_2O	7.5	dry CH_2Cl_2	87	> 99:1	85
9	$Zn(BF_4)_2$•xH_2O	9.5	dry CH_2Cl_2	87	> 99:1	85

[a] The reactions were carried out using **1b**, benzyl alcohol, Rh_2Piv_4 (2 mol%), Zn salt (10 mol%), and (*R*)-BINIM-2QN (11 mol%) in CH_2Cl_2 (0.05 M) at –78 °C for 72 h. [b] Isolated yield. [c] Determined by HPLC analysis. [d] 2.0 equiv based on **1b**.



Scheme 3. Substrate scope and derivatization.

CH_2Cl_2 in the presence of 2.0 equiv of H_2O (entry 5). Notably, the addition of H_2O was effective in achieving good enantioselection (entry 5, 81% ee), as high as that obtained in wet CH_2Cl_2 (entry 2, 83% ee). Thus, we examined the influence of the amount of benzyl alcohol on enantioselectivity (entries 6–9). To our delight, increasing the amount of benzyl alcohol improved the enantioselectivity up to 85% ee (entries 8 and 9).

With the optimal conditions in hand, we investigated the scope of substrates (Scheme 3a). Diazo substrates bearing an electron-withdrawing or electron-donating substituent on a benzene ring afforded **2f**–**2j** with good enantioselectivities (80–85% ee), although *o*-substitution slightly affected the diastereoselectivity of **2j**. A one carbon chain-extended alkyl chain was tolerated to show relatively good enantioselectivity (**2k**: 74% ee). *o*-, *m*- and *p*-Methoxy benzyl alcohols were also applicable to give the corresponding products with moderate to good selectivities (**2m**: 79% ee, **2n**: 76% ee, **2c**: 83% ee). Alcohol adduct **2h** was easily hydrolyzed by treatment with *p*-toluenesulfonic acid in a THF/H_2O mixed solvent, providing oxazolidine-2,4-dione **4** in quantitative yield without loss of enantiopurity (Scheme 3b). Enantiomerically pure (*S*)-**4** (>99% ee) was obtained by recrystallization from CH_2Cl_2/hexane, which was then used for X-ray crystallographic analysis to determine the absolute configuration.[11]

In summary, we have demonstrated an enantioselective protonation of cyclic carbonyl ylides generated from α-alkyl diazo carbonyl compounds. The reactions were effectively catalyzed by a chiral Lewis acid in the presence of alcohols. The unique heterobicyclic products having a quaternary heteroatom-substituted carbon center were obtained with high diastereo- and enantioselectivities. DFT calculations indicated that coordination of the Lewis acid to alcohols in a stepwise manner was favored. Current investigations are directed towards the development of other types of enantioselective transformations of cyclic carbonyl ylides.

Acknowledgements

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Keywords: asymmetric protonation • enantioselective reaction • chiral Lewis acid • carbonyl ylide • diazo compound

[1] Selected reviews: a) C. Fehr, *Angew. Chem. Int. Ed.* **1996**, *35*, 2566-2587; *Angew Chem.* **1996**, *108*, 2726-2748; b) J. Eames, N. Weerasooriya, *Tetrahedron: Asymmetry* **2001**, *12*, 1-24; c) L. Duhamel, P. Duhamel, J.-C. Plaquevent, *Tetrahedron: Asymmetry* **2004**, *15*, 3653-3691; d) J. Blanchet,. J. Baudoux,. M. Amere, M.-C. Lasne, J. Rouden, *Eur. J. Org. Chem.* **2008**, 5493-5506; e) J. T. Mohr, A. Y. Hong, B. M. Stoltz, *Nat. Chem.* **2009**, *1*, 359-369; f) A. Claraz, S. Oudeyer, V. Levacher, *Curr. Org. Chem.* **2012**, *16*, 2192-2205; g) C. Wang, C. M. T. Goh, S. Xiao, W. Ye, C.-H. Tan, *J. Synth. Org. Chem. Jpn.* **2013**, *71*, 1145-1151; h) D. Leow, J. Shen, Y. Su, G.-R. Peh, *Mini-Reviews in Org. Chem.* **2014**, *11*, 410-423; i) S. Oudeyer, J.-F. Brière, V. Levacher, *Eur. J. Org. Chem.* **2014**, 6103-6119; j) J. P. Phelan, J. A. Ellman, *Beilstein J. Org. Chem.* **2016**, *12*, 1203-1228; k) C. Kingston, J. James, P. J. Guiry, *J. Org. Chem*. **2019**, *84*, 473-485; l) J. Muzart, *Adv. Synth. Catal.* **2019**, *361*, 1464-1478.

[2] An asymmetric N-H insertion reaction was proposed to procced by asymmetric protonation of ammonium ylides: B. Xu, S.-F. Zhu, X.-L. Xie, J.-J. Shen, Q.-L. Zhou, *Angew. Chem. Int. Ed.* **2011**, *50*, 11483-11486; *Angew. Chem.* **2011**, *123*, 11685-1168.

[3] Enantioselective reduction of a carbonyl ylide using a rhodium complex/chiral Brønsted acid binary system has been reported: M. Terada, Y. Toda, *Angew. Chem. Int. Ed.* **2012**, *51*, 2093-2097; *Angew. Chem.* **2012**, *124*, 2135-2139.

[4] Selected reviews and books, see: a) A. Padwa, S. F. Hornbuckle, *Chem. Rev.* **1991**, *91*, 263-309; b) A. Padwa, *Acc. Chem. Res.* **1991**, *24*, 22-28; c) A. Padwa, K. E. Krumpe, *Tetrahedron* **1992**, *48*, 5385-5453; d) A. Padwa, M. D. Weingarten, *Chem. Rev.* **1996**, *96*, 223-269; e) G. Mehta, S. Muthusamy, *Tetrahedron* **2002**, *58*, 9477-9504; f) M. C. MacMills, D. Wright, Carbonyl Ylides, in *Synthetic Applications of 1,3-Dipolar Cycloaddition Chemistry Toward Heterocycles and Natural Products* (Eds. A. Padwa, W. H. Pearson) Wiley, Hoboken, NJ, **2003**, ch. 4, pp. 253-314; g) A. Padwa, *Pure Appl. Chem.* **2004**, *76*, 1933-

1952; h) A. Padwa, *Helv. Chim. Acta* **2005**, *88*, 1357-1374; i) A. Padwa, *J. of Organometallic Chem.* **2005**, *690*, 5533-5540; j) S. France, L. H. Phun, *Curr. Org. Synth.* **2010**, *7*, 332-347; k) A. Padwa, *Tetrahedron* **2011**, *67*, 8057-8072; l) D. M. Hodgson, A. H. Labande, S. Muthusamy, Cycloadditions of Carbonyl Ylides Derived from Diazocarbonyl Compounds, in *Org. React.* (ed. S. D. Denmark) Wiley, Hoboken, NJ, **2013**, vol. 80, pp. 133-496; m) T. Hashimoto, K. Maruoka, *Chem. Rev.* **2015**, *115*, 5366-5412; n) A. Ford, H. Miel, A. Ring, C. N. Slattery, A. R. Maguire, M. A. McKervey, *Chem. Rev.* **2015**, *115*, 9981-10080; o) A. Padwa, *Russ. Chem. Bull. Int. Ed.* **2016**, *65*, 2183-2194.

[5] For seminal works, see: a) D. M. Hodgson, P. A. Stupple, C. Johnstone, *Chem. Commun.* **1999**, 2185-2186; b) S. Kitagaki, M. Anada, O. Kataoka, K. Matsuno, C. Umeda, N. Watanabe, S. Hashimoto, *J. Am. Chem. Soc.* **1999**, *121*, 1417-1418.

[6] a) H. Suga, K. Inoue, S. Inoue, A. Kakehi, *J. Am. Chem. Soc.* **2002**, *124*, 14836-14837; b) H. Suga, D. Ishimoto, S. Higuchi, M. Ohtsuka, T. Arikawa, T. Tsuchida, A. Kakehi, T. Baba, *Org. Lett.* **2007**, *9*, 4359-4362; c) H. Suga, Y. Hashimoto, S. Yasumura, R. Takezawa, K. Itoh, A. Kakehi, *J. Org. Chem.* **2013**, *78*, 10840-10852; d) H. Suga, Y. Sekikawa, S. Misawa, D. Kinugawa, R. Oda, K. Itoh, Y. Toda, R. Kiyono, *J. Org. Chem.* **2015**, *80*, 6687-6696.

[7] a) S. Muthusamy, C. Gunanathan, *Chem. Commun.* **2003**, 440-441; b) S. Muthusamy, B. Gnanaprakasam, E. Suresh, *Org. Lett.* **2005**, *7*, 4577-4580; c) H. Shen, J. Fu, J. Gong, Z. Yang, *Org. Lett.* **2014**, *16*, 5588-5591.

[8] Asymmetric alkynylbenzaldehyde cyclizations through an alcohol addition to a cyclic carbonyl ylide Au^{I}/carbene species have been reported: S. Handa and L. M. Slaughter, *Angew. Chem. Int. Ed.* **2012**, *51*, 2912-2915; *Angew. Chem.* **2012**, *124*, 2966-2969.

[9] a) D. F. Taber, R. J. Herr, S. K. Pack, J. M. Geremia, *J. Org. Chem.* **1996**, *61*, 2908-2910; b) P. Panne, J. M. Fox, *J. Am. Chem. Soc.* **2007**, *129*, 22-23; c) A. DeAngelis, P. Panne, G. P. A. Yap, J. M. Fox, *J. Org. Chem.* **2008**, *73*, 1435-1439; d) A. DeAngelis, M. T. Taylor, J. M. Fox, *J. Am. Chem. Soc.* **2009**, *131*, 1101-1105.

[10] The NMR yields were determined by ^{1}H NMR analysis using $(CH_2Cl)_2$ as an internal standard.

[11] Deposition numbers 2052387 (for **2d**) and 2052388 (for **4**) contain the supplementary crystallographic data for this paper. These data are provided free of charge by the joint Cambridge Crystallographic Data Centre and Fachinformationszentrum Karlsruhe Access Structures service.

[12] a) Y. Zhao, D. Truhlar, *Theor. Chem. Acc.* **2008**, *120*, 215-241; b) Y. Zhao, D. Truhlar, *Acc. Chem. Res.* **2008**, *41*, 157-167; c) F. Weigend, R. Ahlrichs, *Phys. Chem. Chem. Phys*. **2005**, *7*, 3297-3305; d) M. Dolg, U. Wedig, H. Stoll, H. Preuss, *J. Chem. Phys*. **1987**, *86*, 866-872; e) M. J. Frisch et al., Gaussian09; Gaussian, Inc.: Wallingford, CT, 2013 (see Supporting Information for full list of authors). f) M. J. Frisch et al., Gaussian16; Gaussian, Inc.: Wallingford, CT, 2016 (see Supporting Information for full list of authors).

[13] K. Fukui, *Acc. Chem. Res.* **1981**, *14,* 363-368.

[14] A. V. Marenich, C. J. Cramer, D. G Truhlar, *J. Phys. Chem. B* **2009**, *113*, 6378-6396.

[15] Initially, we calculated TSs of the methanol addition in the absence of a Lewis acid. As a result, the TS involving two molecules of methanol was found to be favored. See Supporting Information for details.

[16] For selected examples of the reactions using chiral binaphthyldiimine-metal complexes: a) H. Suga, A. Kakehi, M. Mitsuda, *Bull. Chem. Soc. Jpn.* **2004**, *77*, 561-568; b) H. Suga, T. Kitamura, A. Kakehi, T. Baba, *Chem. Commun.* **2004**, 1414-1415; c) H. Suga, T. Nakajima, K. Itoh, A. Kakehi, *Org. Lett.* **2005**, *7*, 1431-1434; d) H. Suga, A. Funyu, A. Kakehi, *Org. Lett.* **2007**, *9*, 97-100; e) H. Suga, Y. Adachi, K. Fujimoto, Y. Furihata, T. Tsuchida, A. Kakehi, T. Baba, *J. Org. Chem.* **2009**, *74*, 1099-1113.

[17] After vigorously stirring dry CH_2Cl_2 with water for overnight, the organic layer was simply used as wet CH_2Cl_2.

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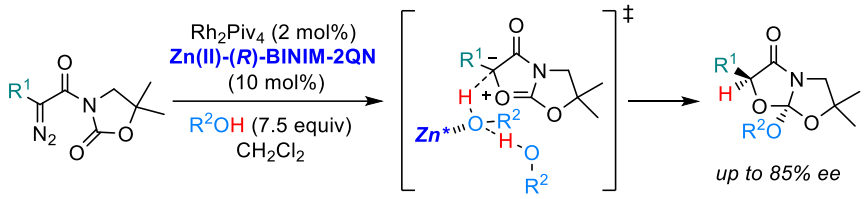
Entry for the Table of Contents



Enantioselective protonation of cyclic carbonyl ylides by chiral Lewis acid-assisted alcohol addition reactions featuring a dual catalytic system is reported. The unique heterobicyclic products bearing a quaternary heteroatom-substituted carbon center were obtained with high diastereo- and enantioselectivities. The alcohol adducts were successfully converted to optically active oxazolidine-2,4-diones by hydrolysis. Computational mechanistic studies indicated that a stepwise *syn*-addition of alcohols under the influence of a Lewis acid was favored.