Asymmetric Catalysis

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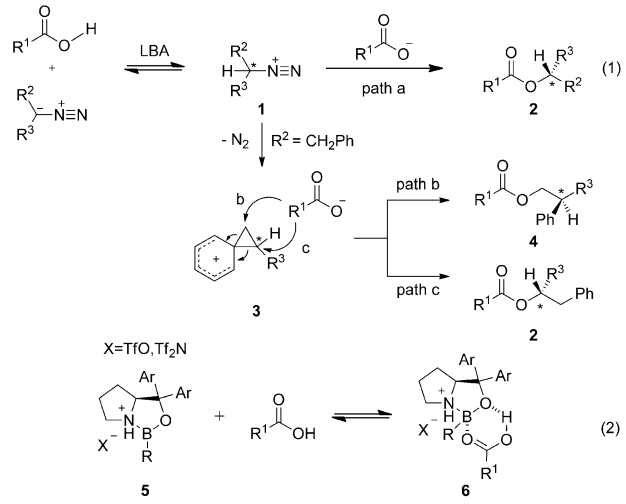
Catalytic Enantioselective Protonation/Nucleophilic Addition of Diazoesters with Chiral Oxazaborolidinium Ion Activated Carboxylic Acids

Ki-Tae Kang, Seung Tae Kim, Geum-Sook Hwang, and Do Hyun Ryu**

Abstract: *A new chiral Brønsted acid derived from carboxylic acid and a chiral oxazaborolidinium ion (COBI), as an activator, is introduced. This acid was successfully applied as a catalyst for the highly enantioselective protonation/nucleophilic addition of diazoesters with carboxylic acids.*

Enantioselective protonation has become a fascinating method for the construction of tertiary chiral carbon centers, which are frequently found in valuable biologically active natural products.[1] Various catalytic methods[1,2] have been developed for efficient enantioselective protonation since the first report by Pracejus.[3] Among these, catalytic tandem reactions incorporating an enantioselective protonation step have emerged recently, thus providing a powerful tool in the construction of structurally complex chiral molecules.[1c,e,2] Thus, the development of new types of catalytic tandem reactions involving enantioselective protonation should continue to serve as important tools for synthetic organic chemistry.

The formation of carboxylate esters by the reaction of carboxylic acids with diazo compounds, most commonly diazomethane (R^2, $R^3 = H$), is one of the most well-known reactions of diazo compounds.[4] The reaction proceeds by initial protonation of the diazo carbon atom to form a diazonium cation[4a,5] (**1**), which can react directly with a nucleophile or carboxylate [Scheme 1, Eq. (1), pathway a], or can lose nitrogen to give a more stable phenonium ion[6] **3** if the diazo compound has a neighboring phenyl group, for example, $R^2 = CH_2Ph$. Nucleophilic addition to the phenonium ion **3** occurs by two competing pathways to yield the acyloxy-substituted products **4** [Scheme 1, Eq. (1), pathway b] or **2** [Scheme 1, Eq. (1), pathway c]. In connection with our work on rearrangement reactions of chiral diazonium intermediates,[7] we speculated that enantioselective protonation in the initial step might give either **1** or **3**, and subsequent nucleophilic addition could provide chiral α- or β-acyloxy-substituted esters (**2** or **4**, $R^3 = COOR^4$), which are valuable building blocks for the construction of natural products and biologically active molecules.[8]



Scheme 1. Catalytic enantioselective protonation/nucleophilic addition of diazoesters using LBA.

Coordination of a Brønsted acid to a Lewis acid increases its acidity and reactivity. Yamamoto, Ishihara, and co-workers have developed Lewis acid assisted Brønsted acids (LBAs) as chiral proton reagents and have successfully applied these LBAs to various enantioselective reactions.[9] We envisioned that coordination of a carboxylic acid[10] to the chiral oxazaborolidinium ion (COBI)[11] **5** would generate the new chiral proton reagent **6** as an LBA [Scheme 1, Eq. (2)].[12] We decided to investigate whether **6** could facilitate an enantioselective protonation of a diazoester with subsequent nucleophilic addition to afford enantioenriched α- or β-acyloxy esters. Herein, we describe the first example of a catalytic enantioselective protonation/nucleophilic addition of diazoesters to afford highly optically active α-aryl-β-acyloxy esters.

To test this hypothesis, our exploration was initially carried out with achiral LBAs which were generated in situ from benzoic acid and various Lewis acids. While the reaction of α-benzyl diazoester and benzoic acid did not proceed without a Lewis acid activator, all achiral LBAs increased the acidity of benzoic acid and provided a mixture of α- and β-acyloxy ester compounds (Table 1, entries 1–5). Among the Lewis acids, only $BF_3{\cdot}OEt_2$-activated benzoic acid showed catalytic activity, thus giving the best yield and selectivity (entry 5). When the reaction was carried out at −78 °C in dichloromethane, the β-acyloxy ester **4** was obtained as the major product in 81 % yield by addition to the sterically less

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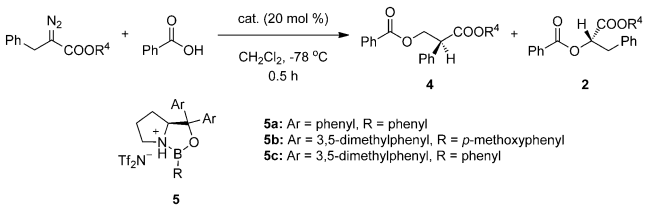
Table 1: Optimization of the enantioselective protonation/nucleophilic addition.[a]



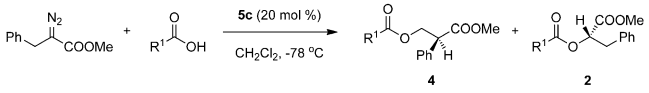
Entry	4	Cat.	R^4	**4**/**2**[b]	Yield [%][c]	*ee* [%][d]
1	–	none	Me	–	–	–
2	**4a**	$TiCl_4$	Me	67:33	13	–
3	**4a**	$Sc(OTf)_3$	Me	75:25	32	–
4	**4a**	$SnCl_4$	Me	67:33	21	–
5	**4a**	$BF_3{\cdot}OEt_2$	Me	88:12	81	–
6	**4a**	**5a**	Me	83:17	77	83
7	**4a**	**5b**	Me	86:14	81	98
8	**4a**	**5c**	Me	90:10	86	98
9[e]	**4a**	**5c**	Me	50:50	41	93
10	**4b**	**5c**	Et	86:14	82	98
11	**4c**	**5c**	*t*Bu	75:25	72	63

[a] The reaction of diazoester (0.22 mmol) with benzoic acid (0.2 mmol) was performed in the presence of catalyst (20 mol%) in 1.4 mL of dichloromethane at −78 °C for 0.5 h. [b] Determined by ^{1}H NMR analysis of the crude reaction mixture. [c] Yield of isolated **4**. [d] The *ee* value of **4** was determined by chiral-phase HPLC. [e] The reaction was performed in toluene. Tf = trifluoromethanesulfonyl.

hindered site of **3** (Scheme 1, pathway b). A minor product, the α-acyloxy ester **2**, was also isolated in 17% yield (Scheme 1, pathway a or c). Next, the enantioselective protonation/nucleophilic addition reaction was examined in the presence of 20 mol% COBI **5a** (Table 1, entry 6). When the reaction was carried out at −78 °C in dichloromethane, the β-acyloxy ester **4** was obtained as the major product in 77% yield and 83% *ee*. We then screened the catalyst structure and found that the catalyst system with Ar = 3,5-dimethylphenyl and R = phenyl gave the best result. The yield and *ee* value of **4** improved to 86 and 98%, respectively, with a **4**/**2** ratio of 90:10 (entry 8). Use of the nonpolar solvent toluene led to a decreased ratio of **4** (entries 8 and 9). Replacement of the methyl group of the diazoester to a more sterically hindered ethyl or *tert*-butyl group diminished the ratio of **4**/**2** as well as the enantioselectivities (entries 8, 10, and 11). For the successful implementation of the diazoester, methyl diazoester was selected for the enantioselective protonation/nucleophilic addition (entries 6–8).

Using the optimized reaction conditions for the new catalytic enantioselective protonation/nucleophilic addition, we evaluated this methodology with a range of substituted benzoic acids (Table 2).[13] As summarized in Table 2, regardless of the electronic properties of the R^1 group, the reactions proceeded with good regioselectivities, and the corresponding β-acyloxy esters **4** were obtained in good yields with high enantioselectivities (entries 1–9). Electron-withdrawing substituents such as either *p*-CF_3 or *p*-NO_2 significantly retarded the reaction in comparison with electron-donating substituents such as *p*-methyl or *p*-methoxy (entries 2, 3 and 6, 7). The sterically more hindered 2,4,6-trimethyl substituent reduced

Table 2: Substrate scope with respect to the carboxylic acid.[a]



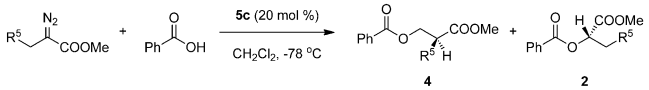
Entry	4	R^1	*t* [h]	**4**/**2**[b]	Yield [%][c]	*ee* [%][d]
1	**4a**	Ph	0.5	90:10	86	98
2	**4d**	4-MeC_6H_4	0.5	80:20	75	93
3	**4e**	4-$MeOC_6H_4$	0.5	83:17	81	92
4	**4f**	4-BrC_6H_4	1	75:25	70	92
5	**4g**	2,5-$F_2C_6H_3$	1	80:20	75	99
6[e]	**4h**	4-$CF_3C_6H_4$	4	83:17	83	86
7[e]	**4i**	4-$NO_2C_6H_4$	4	80:20	73	85
8[e]	**4j**	2,4,6-$Me_3C_6H_2$	3	67:33	66	85
9	**4k**	2-Np	1	80:20	77	90

[a] The reaction of diazoester (0.22 mmol) with carboxylic acid (0.2 mmol) was performed in the presence of **5c** (20 mol%) in 1.4 mL of dichloromethane at −78 °C. [b] Determined by ^{1}H NMR analysis of the crude reaction mixture. [c] Yield of isolated **4**. [d] The *ee* value of **4** was determined by chiral-phase HPLC. [e] The reaction was performed at 0 °C. Np = naphthyl.

the reaction rate to afford the desired product in lower yield and enantioselectivity (entry 8), presumably because the bulky 2,4,6-trimethyl benzoic acid significantly reduces the degree of complexation with **5** in the formation of **6** [Scheme 1, Eq. (2)]. 2-Naphthoic acid was a suitable substrate for the reaction, thus affording the corresponding product **4k** in 77% yield and 90% *ee* (entry 9).

To further investigate the substrate scope of the present catalytic system, we performed the catalytic enantioselective protonation/nucleophilic addition with a range of diazoesters. As summarized in Table 3, the electronic properties of the aryl group (R^5) in the diazoester obviously affected the yield and enantioselectivity of the product (entries 1–13). In cases

Table 3: Substrate scope with respect to the α-diazoester.[a]

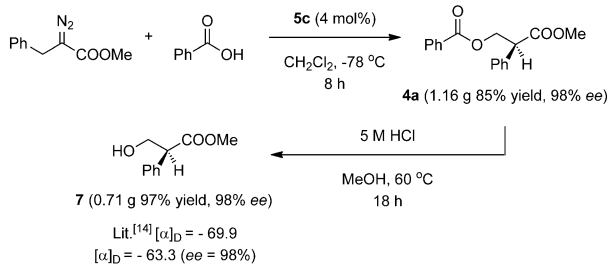


Entry	Product	R^5	*t* [h]	**4**/**2**[b]	Yield [%][c]	*ee* [%][d]
1	**4a**	Ph	0.5	90:10	86	98
2	**4l**	2-MeC_6H_4	2	94:6	91	90
3	**4m**	3-MeC_6H_4	2	75:25	73	85
4	**4n**	4-MeC_6H_4	0.5	94:6	93	95
5	**4o**	2-$MeOC_6H_4$	2	98:2	97	91
6	**4p**	3-$MeOC_6H_4$	2	67:33	60	99
7	**4q**	4-$MeOC_6H_4$	0.5	98:2	96	96
8	**4r**	1,3-benzodioxole	2	91:9	90	92
9	**4s**	2-Np	0.5	86:14	81	95
10	**4t**	4-BrC_6H_4	0.5	67:33	55	98
11	**4u**	4-FC_6H_4	0.5	67:33	57	96
12	**2v**	4-$CF_3C_6H_4$	0.5	6:94	92	98
13	**2w**	4-$NO_2C_6H_4$	0.2	3:97	95	64
14	**2x**	Me	0.5	< 5:95	47	76

[a] The reaction of diazoester (0.22 mmol) with benzoic acid (0.2 mmol) was performed in the presence of **5c** (20 mol%), in 1.4 mL of dichloromethane at −78 °C. [b] Determined by ^{1}H NMR analysis of the crude reaction mixture. [c] Yield of isolated major product. [d] The *ee* value of the major product was determined by chiral-phase HPLC.

of electron-rich substituted benzyl diazoester substrates, the β-acyloxy esters **4** were obtained as the major products with consistently high enantioselectivities (entries 2–8). Methyl- or methoxy-substituted benzyl diazoesters at the *meta* position significantly reduced the regioselectivity in comparison with *ortho*- or *para*-substituted diazoesters (entries 2, 4, 5, 7 and 3, 6). It is notable that the large 2-naphthyl-substituted α-methyl diazoester effectively reacted with benzoic acid to give good results (entry 9). While a weak electron-withdrawing group, such as *p*-halogen-substituted benzyl diazoesters, provided the corresponding β-acyloxy esters **4** in good yields and high enantioselectivities (entries 10 and 11), a strong electron-withdrawing group, for example, *p*-CF_3- or *p*-NO_2-substituted substrates, provided the α-acyloxy ester[8c] **2** as the major product instead of **4** (entries 12 and 13). We expect that this result reflects a more favorable pathway a [Scheme 1, Eq. (1)] because of the instability of **3**.[6e] As expected, reactions of α-diazobutanoate ester provided only the α-acyloxy ester **2** by pathway a in 47% yield with moderate enantioselectivity (Table 3, entry 14).

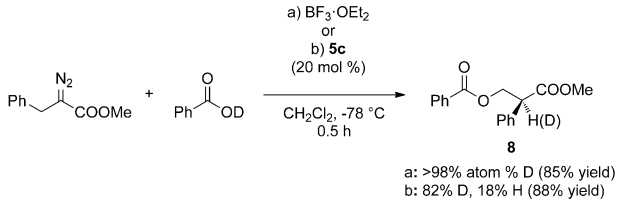
The feasibility of reducing the catalyst loading and increasing the reaction scale to gram scale was examined (Scheme 2). The loading of **5c** could be reduced to 4 mol%



Scheme 2. Gram-scale experiment and enantioselective synthesis of (*S*)-tropic acid methyl ester.

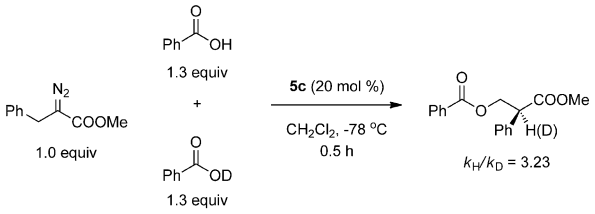
while maintaining excellent yields and enantioselectivities. The synthetic utility of the present reaction was further demonstrated by synthesis of (*S*)-tropic acid methyl ester (**7**). (*S*)-Tropic acid is an important building block for biologically active tropane alkaloids, such as atropine and scopolamine.[14] Comparison of the optical rotation data of **7** confirmed the absolute (*S*) stereochemistry of **4**.[15]

Our attention next turned to elucidating the mechanism of this novel transformation. On treatment of methyl α-benzyl diazoester with [D]benzoic acid (> 95% D) under $BF_3{\cdot}OEt_2$ catalysis, the protonation/nucleophilic addition proceeded to give the corresponding deuterated product **8** (Scheme 3, conditions a). The NMR spectrum revealed greater than 98% deuterium incorporation at the α-position of the diazoester. In addition, we performed a deuterium-labeling experiment with the COBI catalyst, and it yielded **8** with 82% deuterium incorporation at the chiral center (Scheme 3, conditions b). Considering about a 20% exchange of deuterium with the ammonium proton of COBI **5c**, this result indicates that the hydrogen atom on the chiral center was derived exclusively from the [D]benzoic acid. For further mechanistic insight, a kinetic isotope effect (KIE) experiment was conducted with



Scheme 3. Evidence of the enantioselective protonation/nucleophilic addition pathway.

a mixture of deuterated and nondeuterated benzoic acid, and the k_H/k_D was found to be 3.23 (Scheme 4), which suggests that protonation of the diazoester is under the influence of a primary kinetic isotope effect (PKIE),[5a] and that enantioselective protonation rather than nucleophilic addition is the rate-determining step.



Scheme 4. Kinetic isotope effect experiment.

The observed stereochemistry for the enantioselective protonation/nucleophilic addition using **6**, derived from (*S*)-COBI catalyst **5c**, can be rationalized using the transition state model shown in Figure 1. In the pre-transition state

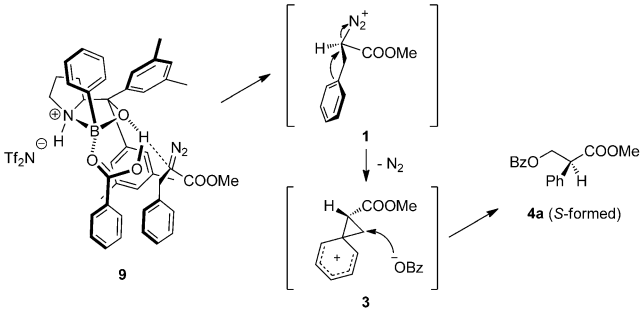


Figure 1. Transition-state model for the enantioselective protonation/nucleophilic addition of an α-benzyl diazoester with benzoic acid, catalyzed by **5c**.

assembly **9**, the carboxylic acid group is situated above the 3,5-dimethylphenyl group, which effectively shields the back face from attack by the diazoester. Because of the dipole–dipole interaction between the two carbonyl groups, the diazoester approaches the carboxylic acid for protonation with the ester group situated away from the carboxylic acid group. Meanwhile, an apparent π–π interaction between the aryl ring of the benzoic acid and the diazoester aryl group holds the two aryl rings together.[16] Thus, protonation of the

diazoester from the *si* face (back) of the diazoester is facilitated, thus leading to the chiral diazonium **1**. According to the KIE experiment, chiral proton transfer from the carboxylic acid group to the diazoester is the rate-determining step. After formation of **1**, subsequent loss of N_2 leads to stereospecific formation of **3**. Regioselective nucleophilic addition of benzoate leads to the product (*S*)-**4a** as the major enantiomer.

In summary, we report the first catalytic enantioselective protonation/nucleophilic addition of diazoesters using the new chiral LBA catalyst **6**, prepared from COBI as a Lewis acid, and a carboxylic acid as a Brønsted acid. In the presence of **6**, various α-aryl-β-acyloxy propanoates were obtained in good yields and high to excellent enantioselectivities. The resulting product can easily be converted into optically active (*S*)-tropic acid methyl ester without loss of optical purity. The absolute configuration of the product was the same as predicted by the transition state model in Figure 1. We believe that there are many potential uses for **6** in catalytic enantioselective syntheses beyond those outlined here. Other applications of **6** and further mechanistic studies are underway.

Acknowledgments

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Conflict of interest

The authors declare no conflict of interest.

Keywords: asymmetric catalysis · boron · Brønsted acid · diazo compounds · reaction mechanisms

[1] a) A. Yanagisawa, H. Yamamoto in *Comprehensive Asymmetric Catalysis*, *Vol. 3* (Eds.: E. N. Jacobsen, A. Pfaltz, H. Yamamoto), Springer, Heidelberg, **1999**, pp. 1295 – 1306; b) L. Duhamel, P. Duhamel, J.-C. Plaquevent, *Tetrahedron: Asymmetry* **2004**, *15*, 3653 – 3691; c) J. T. Mohr, A. Y. Hong, B. M. Stoltz, *Nat. Chem.* **2009**, *1*, 359 – 369; d) S. Oudeyer, J.-F. Brière, V. Levacher, *Eur. J. Org. Chem.* **2014**, 6103 – 6119; e) J. P. Phelan, J. A. Ellman, *Beilstein J. Org. Chem.* **2016**, *12*, 1203 – 1228.

[2] a) L. M. Repka, J. Ni, S. E. Reisman, *J. Am. Chem. Soc.* **2010**, *132*, 14418 – 14420; b) M. H. Wang, D. T. Cohen, C. B. Schwamb, R. K. Mishra, K. A. Scheidt, *J. Am. Chem. Soc.* **2015**, *137*, 5891 – 5894; c) B. E. Daniels, J. Ni, S. E. Reisman, *Angew. Chem. Int. Ed.* **2016**, *55*, 3398 – 3402; *Angew. Chem.* **2016**, *128*, 3459 – 3463; d) A. Roy, B. A. Bhat, S. D. Lepore, *Org. Lett.* **2016**, *18*, 1230 – 1233; e) A. Das, S. Ayad, K. Hanson, *Org. Lett.* **2016**, *18*, 5416 – 5419.

[3] H. Pracejus, *Justus Liebigs Ann. Chem.* **1960**, *634*, 9 – 22.

[4] a) M. Regitz, G. Maas, *Diazo Compounds: Properties and Synthesis*, Academic Press, Orlando, **1986**, chap. 3. For reviews on reactions of diazo compounds, see: b) D. J. Miller, C. J. Moody, *Tetrahedron* **1995**, *51*, 10811 – 10843; c) J. N. Johnston, H. Muchalski, T. L. Troyer, *Angew. Chem. Int. Ed.* **2010**, *49*, 2290 – 2298; *Angew. Chem.* **2010**, *122*, 2340 – 2349.

[5] a) J. Jones, Jr., A. J. Kresge, *J. Org. Chem.* **1993**, *58*, 2658 – 2662; b) E. Kühnel, D. D. P. Laffan, G. C. Lloyd-Jones, T. Martínez del Campo, I. R. Shepperson, J. L. Slaughter, *Angew. Chem. Int. Ed.* **2007**, *46*, 7075 – 7078; *Angew. Chem.* **2007**, *119*, 7205 – 7208; c) L. Dumitrescu, K. Azzouzi-Zriba, D. Bonnet-Delpon, B. Crousse, *Org. Lett.* **2011**, *13*, 692 – 695; d) V. L. Rendina, J. S. Kingsbury, *J. Org. Chem.* **2012**, *77*, 1181 – 1185.

[6] a) J. Clayden, N. Greeves, S. Warren, *Organic Chemistry*, 2nd ed., Oxford University Press, Oxford, **2001**, pp. 935 – 936; b) J. D. Roberts, C. M. Regan, *J. Am. Chem. Soc.* **1953**, *75*, 2069 – 2072; c) G. A. Olah, M. Alemayehu, A.-H. Wu, O. Farooq, G. K. S. Prakash, *J. Am. Chem. Soc.* **1992**, *114*, 8042 – 8045; d) N. Jiang, Z. Qu, J. Wang, *Org. Lett.* **2001**, *3*, 2989 – 2992; e) M. S. Than, S. Itoh, M. Mishima, *ARKIVOC* **2008**, *10*, 135 – 150; f) S. M. Banik, J. W. Medley, E. N. Jacobsen, *Science* **2016**, *353*, 51 – 54.

[7] a) L. Gao, B. C. Kang, G.-S. Hwang, D. H. Ryu, *Angew. Chem. Int. Ed.* **2012**, *51*, 8322 – 8325; *Angew. Chem.* **2012**, *124*, 8447 – 8450; b) S. I. Lee, G.-S. Hwang, D. H. Ryu, *J. Am. Chem. Soc.* **2013**, *135*, 7126 – 7129; c) L. Gao, B. C. Kang, D. H. Ryu, *J. Am. Chem. Soc.* **2013**, *135*, 14556 – 14559; d) S. H. Shin, E. H. Baek, G.-S. Hwang, D. H. Ryu, *Org. Lett.* **2015**, *17*, 4746 – 4749; e) B. C. Kang, D. G. Nam, G.-S. Hwang, D. H. Ryu, *Org. Lett.* **2015**, *17*, 4810 – 4813; f) S. Y. Shim, J. Y. Kim, M. Nam, G.-S. Hwang, D. H. Ryu, *Org. Lett.* **2016**, *18*, 160 – 163.

[8] For synthesis of α-acyloxy esters, see: a) E. D. Couch, T. J. Auvil, A. E. Mattson, *Chem. Eur. J.* **2014**, *20*, 8283 – 8287; b) A. C. Hunter, K. Chinthapally, I. Sharma, *Eur. J. Org. Chem.* **2016**, 2260 – 2263; c) F. Tan, X. Liu, X. Hao, Y. Tang, L. Lin, X. Feng, *ACS Catal.* **2016**, *6*, 6930 – 6934; For synthesis of β-acyloxy esters, see: d) M. R. Atuu, S. J. Mahmood, F. Laib, M. M. Hossain, *Tetrahedron: Asymmetry* **2004**, *15*, 3091 – 3101; e) M. R. Atuu, M. M. Hossain, *Tetrahedron Lett.* **2007**, *48*, 3875 – 3878. For catalytic asymmetric synthesis of α-hydroxy esters, see: f) S. F. Zhu, Q. L. Zhou, *Acc. Chem. Res.* **2012**, *45*, 1365 – 1377; g) T. C. Maier, G. C. Fu, *J. Am. Chem. Soc.* **2006**, *128*, 4594 – 4595; h) S. F. Zhu, Y. Cai, H. X. Mao, J. H. Xie, Q. L. Zhou, *Nat. Chem.* **2010**, *2*, 546 – 551.

[9] a) K. Ishihara, H. Yamamoto, *Acid Catalysis in Modern Organic Synthesis*, *Vol. 1*, Wiley-VCH, Weinheim, **2008**; b) H. Ishibashi, K. Ishihara, H. Yamamoto, *Chem. Rec.* **2002**, *2*, 177 – 188; c) C. H. Cheon, H. Yamamoto, *J. Am. Chem. Soc.* **2008**, *130*, 9246 – 9247.

[10] For activation of carboxylic acids with chiral phosphoric acid catalysts, see: a) M. R. Monaco, B. Poladura, M. Diaz de Los Bernardos, M. Leutzsch, R. Goddard, B. List, *Angew. Chem. Int. Ed.* **2014**, *53*, 7063 – 7067; *Angew. Chem.* **2014**, *126*, 7183 – 7187. For activation with boron catalysts, see: b) R. M. Al-Zoubi, O. Marion, D. G. Hall, *Angew. Chem. Int. Ed.* **2008**, *47*, 2876 – 2879; *Angew. Chem.* **2008**, *120*, 2918 – 2921; c) Y. Morita, T. Yamamoto, H. Nagai, Y. Shimizu, M. Kanai, *J. Am. Chem. Soc.* **2015**, *137*, 7075 – 7078; d) K. Ishihara, S. Ohara, H. Yamamoto, *J. Org. Chem.* **1996**, *61*, 4196 – 4197.

[11] a) Y.-Y. Yeung, S. Hong, E. J. Corey, *J. Am. Chem. Soc.* **2006**, *128*, 6310 – 6311; b) E. J. Corey, *Angew. Chem. Int. Ed.* **2009**, *48*, 2100 – 2117; *Angew. Chem.* **2009**, *121*, 2134 – 2151; c) B. K. Senapati, G.-S. Hwang, S. Lee, D. H. Ryu, *Angew. Chem. Int. Ed.* **2009**, *48*, 4398 – 4401; *Angew. Chem.* **2009**, *121*, 4462 – 4465; d) B. K. Senapati, L. Gao, S. I. Lee, G.-S. Hwang, D. H. Ryu, *Org. Lett.* **2010**, *12*, 5088 – 5091; e) B. Thirupathi, S. Breitler,

K. M. Reddy, E. J. Corey, *J. Am. Chem. Soc.* **2016**, *138*, 10842 – 10845.
[12] For NMR analysis of LBA **6**, see the Supporting Information.
[13] Enantioselective protonation-nucleophilic addition between acetic acid and methyl α-benzyl diazoester provided the α-acyloxy ester as a major product in about 40% yield and 40% *ee* with a **4/2** ratio of 1:3.
[14] a) E. Leete, *J. Am. Chem. Soc.* **1960**, *82*, 612 – 614; b) N. Kowanko, R. A. Newmark, E. Leete, *J. Am. Chem. Soc.* **1975**, *97*, 6826 – 6830; c) D. Klomp, J. A. Peters, U. Hanefeld, *Tetrahedron: Asymmetry* **2005**, *16*, 3892 – 3896; d) K. Kodama, N. Kurozumi, H. Shitara, T. Hirose, *Tetrahedron* **2014**, *70*, 7923 – 7928; e) C. Chen, F. Wu, J. Tang, J. Liu, *Bioorg. Med. Chem. Lett.* **2016**, *26*, 1715 – 1719.
[15] a) G. W. Youngson, M. B. Watson, *J. Chem. Soc. Perkin Trans. 1* **1972**, 1597 – 1598; b) T. M. Baker, G. J. Bodwell, S. G. Davies, A. J. Edwards, M. R. Metzler, *Tetrahedron* **1993**, *49*, 5635 – 5647.
[16] For selected reviews on π–π interactions, see: a) M. L. Waters, *Curr. Opin. Chem. Biol.* **2002**, *6*, 736 – 741; b) C. A. Hunter, K. R. Lawson, J. Perkins, C. J. Urch, *J. Chem. Soc. Perkin Trans. 2* **2001**, 651 – 669; c) L. M. Salonen, M. Ellermann, F. Diederich, *Angew. Chem. Int. Ed.* **2011**, *50*, 4808 – 4842; *Angew. Chem.* **2011**, *123*, 4908 – 4944. For a selected paper on π-π interaction, see: d) C. A. Hunter, J. K. M. Sanders, *J. Am. Chem. Soc.* **1990**, *112*, 5525 – 5534.

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Communications

Asymmetric Catalysis

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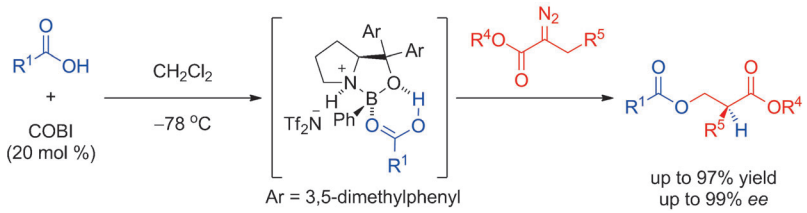
Catalytic Enantioselective Protonation/Nucleophilic Addition of Diazoesters with Chiral Oxazaborolidinium Ion Activated Carboxylic Acids



COBI-Wan: A new chiral Brønsted acid derived from a carboxylic acid and a chiral oxazaborolidinium ion (COBI), as an activator, is introduced. This acid was successfully applied as a catalyst for the highly enantioselective protonation/nucleophilic addition of diazoesters and carboxylic acids. Tf = trifluoromethanesulfonyl.

