

Enantioselective *N*-Heterocyclic Carbene-Catalyzed Michael Addition to α,β -Unsaturated Aldehydes by Redox Oxidation

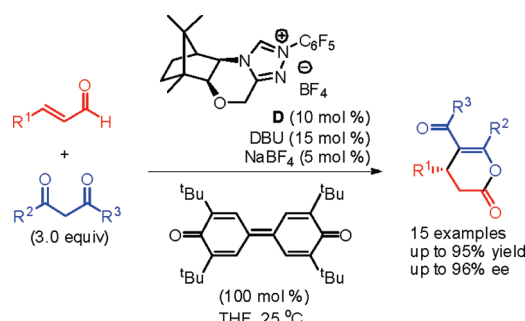
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ABSTRACT



Enantioselective *N*-heterocyclic carbene-catalyzed Michael addition reactions to α,β -unsaturated aldehydes by redox oxidation were realized. With 10 mol % of camphor-derived triazolium salt **D**, 15 mol % of DBU, 5 mol % of NaBF₄, and 100 mol % of quinone oxidant, the reactions of various dicarbonyl compounds with α,β -unsaturated aldehydes led to 3,4-dihydro- α -pyrones in good yields and excellent ee's.

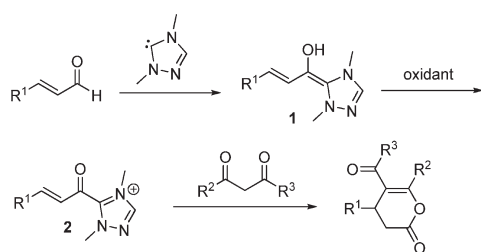
N-Heterocyclic carbenes (NHCs) have received enormous attention and experienced very rapid development in the past two decades.¹ The inversion of the normal reactivity (umpolung) of aldehydes catalyzed by NHCs has become an intense area recently, providing an unconventional access to designed target molecules.² The asymmetric reactions catalyzed by chiral NHCs have also witnessed significant progress over the past decade.^{1,3} In addition to umpolung reactions of aryl aldehydes such as the benzoin reaction⁴ and Stetter reaction,⁵ NHCs were also found to catalyze various redox type transformations of functionalized aldehydes containing reducible

functionalities.⁶ More recently, the elegant work by Studer and co-workers showed that the Breslow intermediate can be readily oxidized with an external organic oxidant to acylazolium ions,^{7,8} which can undergo *O*-acylation (amidation) with various oxygen (nitrogen) nucleophiles to afford esters (amides) or the Michael addition reaction

(1) For reviews: (a) Enders, D.; Balensiefer, T. *Acc. Chem. Res.* **2004**, *37*, 534. (b) Johnson, J. S. *Angew. Chem., Int. Ed.* **2004**, *43*, 1326. (c) Christmann, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 2632. (d) Zeitler, K. *Angew. Chem., Int. Ed.* **2005**, *44*, 7506. (e) Marion, N.; Díez-González, S.; Nolan, S. P. *Angew. Chem., Int. Ed.* **2007**, *46*, 2988. (f) Enders, D.; Niemeier, O.; Henseler, A. *Chem. Rev.* **2007**, *107*, 5606. (g) Nair, V.; Vellalath, S.; Babu, B. P. *Chem. Soc. Rev.* **2008**, *37*, 2691. (h) Jones, W. D. *J. Am. Chem. Soc.* **2009**, *131*, 15075. (i) Read de Alaniz, J.; Rovis, T. *Synlett* **2009**, 1189. (j) Phillips, E. M.; Chan, A.; Scheidt, K. A. *Aldrichimica Acta* **2009**, *42*, 55.

(2) For recent examples: (a) Ye, W.; Cai, G.; Zhuang, Z.; Jia, X.; Zhai, H. *Org. Lett.* **2005**, *7*, 3769. (b) Liu, Y.-K.; Li, R.; Yue, L.; Li, B.-J.; Chen, Y.-C.; Wu, Y.; Ding, L.-S. *Org. Lett.* **2006**, *8*, 1521. (c) He, J.; Zheng, J.; Liu, J.; She, X.; Pan, X. *Org. Lett.* **2006**, *8*, 4637. (d) Li, G.-Q.; Dai, L.-X.; You, S.-L. *Chem. Commun.* **2007**, 852. (e) Wong, F. T.; Patra, P. K.; Seayad, J.; Zhang, Y.; Ying, J. Y. *Org. Lett.* **2008**, *10*, 2333. (f) Phillips, E. M.; Wadamoto, M.; Roth, H. S.; Ott, A. W.; Scheidt, K. A. *Org. Lett.* **2009**, *11*, 105. (g) Li, Y.; Shi, F.-Q.; He, Q.-L.; You, S.-L. *Org. Lett.* **2009**, *11*, 3182. (h) Yadav, L. D. S.; Rai, V. K.; Singh, S.; Singh, P. *Tetrahedron Lett.* **2010**, *51*, 1657. (i) Lin, L.; Li, Y.; Du, W.; Deng, W.-P. *Tetrahedron Lett.* **2010**, *51*, 3571. (j) Nair, V.; Varghese, V.; Paul, R. R.; Jose, A.; Sinu, C. R.; Menon, R. S. *Org. Lett.* **2010**, *12*, 2653. (k) Gu, L.; Zhang, Y. *J. Am. Chem. Soc.* **2010**, *132*, 914. (l) Biju, A. T.; Glorius, F. *Angew. Chem., Int. Ed.* **2010**, *49*, 9761. (m) Padmanaban, M.; Biju, A. T.; Glorius, F. *Org. Lett.* **2011**, *13*, 98. (n) Wu, K.-J.; Li, G.-Q.; Li, Y.; Dai, L.-X.; You, S.-L. *Chem. Commun.* **2011**, 493. (o) Vedachalam, S.; Wong, Q.-L.; Maji, B.; Zeng, J.; Ma, J.; Liu, X.-W. *Adv. Synth. Catal.* **2011**, 353, 259.

Scheme 1. Oxidative NHC Catalysis to 3,4-Dihydro- α -pyrones by Studer et al.



with soft carbon nucleophiles (Scheme 1). Starting with the dicarbonyl compounds, the substituted dihydropyranones were obtained smoothly. Given the fact that 3,4-dihydro- α -pyrones are useful intermediates for the synthesis of γ -lactones, substituted benzenoids, pyridones, etc.,⁹ and their enantioselective synthesis is still limited,¹⁰ we decided to contribute a catalytically asymmetric synthesis of 3,4-dihydro- α -pyrones by a chiral NHC-catalyzed redox-type Michael addition reaction to α,β -unsaturated aldehydes.^{11,12} To our knowledge, there is no catalytic asymmetric report on this mechanistically interesting reaction. Herein, we report our preliminary results from the study of this subject.

Our studies began with an initial examination of several readily available chiral NHCs (Figure 1) developed in our laboratory, for the redox-type Michael addition reactions reported by Sarkar and Studer.^{7a} Cinnamaldehyde (**4a**) and 1,3-diphenylpropane-1,3-dione (**5a**) were used as model substrates. To our great delight, with 1 equiv of quinone

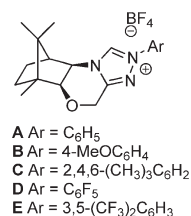


Figure 1. Several readily available chiral NHC precursors.

(**3**) as the oxidant, 10 mol % of triazolium salt (**A–E**), and 15 mol % of DBU in THF, the desired oxidative annulation reaction generally proceeded to afford dihydropyranone **6a**. The results are summarized in Table 1. The D-camphor-derived NHCs¹³ all led to the formation of **6a**

(3) Selected examples as nucleophilic catalysts: (a) Thomson, J. E.; Campbell, C. D.; Concellon, C.; Duguet, N.; Rix, K.; Slawin, A. M. Z.; Smith, A. D. *J. Org. Chem.* **2008**, *73*, 2784. (b) Huang, X.-L.; He, L.; Shao, P.-L.; Ye, S. *Angew. Chem., Int. Ed.* **2009**, *48*, 192. (c) Concellón, C.; Duguet, N.; Smith, A. D. *Adv. Synth. Catal.* **2009**, *351*, 3001. (d) Wang, X.-N.; Zhang, Y.-Y.; Ye, S. *Adv. Synth. Catal.* **2010**, *352*, 1892. (e) Shao, P.-L.; Chen, X.-Y.; Ye, S. *Angew. Chem., Int. Ed.* **2010**, *49*, 8412. (f) Jian, T.-Y.; Shao, P.-L.; Ye, S. *Chem. Commun.* **2011**, 2381.

(4) Selected recent examples: (a) Enders, D.; Kallfass, U. *Angew. Chem., Int. Ed.* **2002**, *41*, 1743. (b) Hachisu, Y.; Bode, J. W.; Suzuki, K. *J. Am. Chem. Soc.* **2003**, *125*, 8432. (c) Enders, D.; Niemeier, O.; Balensiefer, T. *Angew. Chem., Int. Ed.* **2006**, *45*, 1463. (d) Takikawa, H.; Hachisu, Y.; Bode, J. W.; Suzuki, K. *Angew. Chem., Int. Ed.* **2006**, *45*, 3492. (f) Ma, Y.-J.; Wei, S.-P.; Wu, J.; Yang, F.; Liu, B.; Lan, J.-B.; Yang, S.-Y.; You, J.-S. *Adv. Synth. Catal.* **2008**, *350*, 2645. (g) Zhao, H.; Foss, F. W., Jr.; Breslow, R. *J. Am. Chem. Soc.* **2008**, *130*, 12590. (h) Phillips, E. M.; Roberts, J. M.; Scheidt, K. A. *Org. Lett.* **2010**, *12*, 2830. (i) Enders, D.; Grossmann, A.; Fronert, J.; Raabe, G. *Chem. Commun.* **2010**, 6282. (k) O'Toole, S. E.; Rose, C. A.; Gundala, S.; Zeitler, K.; Connon, S. J. *J. Org. Chem.* **2011**, *76*, 347.

(5) Selected examples: (a) Kerr, M. S.; Read de Alaniz, J.; Rovis, T. *J. Am. Chem. Soc.* **2002**, *124*, 10298. (b) Kerr, M. S.; Rovis, T. *J. Am. Chem. Soc.* **2004**, *126*, 8876. (c) Read de Alaniz, J.; Rovis, T. *J. Am. Chem. Soc.* **2005**, *127*, 6284. (d) Liu, Q.; Rovis, T. *J. Am. Chem. Soc.* **2006**, *128*, 2552. (e) Enders, D.; Han, J.; Henseler, A. *Chem. Commun.* **2008**, 3989. (f) Liu, Q.; Perreault, S.; Rovis, T. *J. Am. Chem. Soc.* **2008**, *130*, 14066. (g) Alaniz, J. R.; Kerr, M. S.; Moore, J. L.; Rovis, T. *J. Org. Chem.* **2008**, *73*, 2033. (h) Cullen, S. C.; Rovis, T. *Org. Lett.* **2008**, *10*, 3141. (i) Orellana, A.; Rovis, T. *Chem. Commun.* **2008**, 730. (j) Enders, D.; Han, J. *Synthesis* **2008**, *23*, 3864. (k) DiRocco, D. A.; Oberg, K. M.; Dalton, D. M.; Rovis, T. *J. Am. Chem. Soc.* **2009**, *131*, 10872. (l) Filloux, C. M.; Lathrop, S. P.; Rovis, T. *Proc. Natl. Acad. Sci. U.S.A.* **2010**, *107*, 20666. (m) Hirano, K.; Biju, A. T.; Piel, I.; Glorius, F. *J. Am. Chem. Soc.* **2009**, *131*, 14190. (n) Biju, A. T.; Wurz, N. E.; Glorius, F. *J. Am. Chem. Soc.* **2010**, *132*, 5970. (o) Sun, F.-G.; Huang, X.-L.; Ye, S. *J. Org. Chem.* **2010**, *75*, 273. (p) Jousseume, T.; Wurz, N. E.; Glorius, F. *Angew. Chem., Int. Ed.* **2011**, *50*, 1410.

(6) Selected examples: (a) Chow, K. Y.-K.; Bode, J. W. *J. Am. Chem. Soc.* **2004**, *126*, 8126. (b) Reynolds, N. T.; Read de Alaniz, J.; Rovis, T. *J. Am. Chem. Soc.* **2004**, *126*, 9518. (c) Sohn, S. S.; Rosen, E. J.; Bode, J. W. *J. Am. Chem. Soc.* **2004**, *126*, 14370. (c) Burstien, C.; Glorius, F. *Angew. Chem., Int. Ed.* **2004**, *43*, 6205. (d) Reynolds, N. T.; Rovis, T. *J. Am. Chem. Soc.* **2005**, *127*, 16406. (e) Sohn, S. S.; Bode, J. W. *Org. Lett.* **2005**, *7*, 3873. (f) Chan, A.; Scheidt, K. A. *Org. Lett.* **2005**, *7*, 905. (g) Nair, V.; Vellalath, S.; Poonoth, M.; Mohan, R.; Suresh, E. *Org. Lett.* **2006**, *8*, 507. (h) Zeitler, K. *Org. Lett.* **2006**, *8*, 637. (i) He, M.; Ue, G. J.; Bode, J. W. *J. Am. Chem. Soc.* **2006**, *128*, 15088. (j) Sohn, S. S.; Bode, J. W. *Angew. Chem., Int. Ed.* **2006**, *45*, 6021. (k) Li, G.-Q.; Li, Y.; Dai, L.-X.; You, S.-L. *Org. Lett.* **2007**, *9*, 3519. (l) Phillips, E. M.; Wadamoto, M.; Chan, A.; Scheidt, K. A. *Angew. Chem., Int. Ed.* **2007**, *46*, 3107. (k) Chiang, P.-C.; Kaeobamrung, J.; Bode, J. W. *J. Am. Chem. Soc.* **2007**, *129*, 3520. (l) Bode, J. W.; Sohn, S. S. *J. Am. Chem. Soc.* **2007**, *129*, 13798. (m) He, M.; Bode, J. W. *J. Am. Chem. Soc.* **2008**, *130*, 418. (n) Phillips, E. M.; Reynolds, T. E.; Scheidt, K. A. *J. Am. Chem. Soc.* **2008**, *130*, 2416. (o) Chan, A.; Scheidt, K. A. *J. Am. Chem. Soc.* **2008**, *130*, 2740. (p) Rommel, M.; Fukuzumi, T.; Bode, J. W. *J. Am. Chem. Soc.* **2008**, *130*, 17266. (q) Seayad, J.; Patra, P. K.; Zhang, Y.; Ying, J. Y. *Org. Lett.* **2008**, *10*, 953. (r) Li, G.-Q.; Li, Y.; Dai, L.-X.; You, S.-L. *Adv. Synth. Catal.* **2008**, *350*, 1258. (s) Li, G.-Q.; Li, Y.; Dai, L.-X.; You, S.-L. *Adv. Synth. Catal.* **2008**, *350*, 1258. (t) Kaeobamrung, J.; Bode, J. W. *Org. Lett.* **2009**, *11*, 677. (u) Li, G.-Q.; Dai, L.-X.; You, S.-L. *Org. Lett.* **2009**, *11*, 1623. (v) Cardinal-David, B.; Raup, D. E. A.; Scheidt, K. A. *J. Am. Chem. Soc.* **2010**, *132*, 5345. (w) Thai, K.; Wang, L.; Dudding, T.; Bilodeau, F.; Gravel, M. *Org. Lett.* **2010**, *12*, 5708. (x) Vora, H. U.; Rovis, T. *J. Am. Chem. Soc.* **2010**, *132*, 2860. (y) Raup, D. E. A.; Cardinal-David, B.; Holte, D.; Scheidt, K. A. *Nat. Chem.* **2010**, *2*, 766. (z) Ling, K. B.; Smith, A. D. *Chem. Commun.* **2011**, 373. (aa) Fang, X.; Jiang, K.; Xing, C.; Hao, L.; Chi, Y. R. *Angew. Chem., Int. Ed.* **2011**, *50*, 1910.

(7) (a) De Sarkar, S.; Studer, A. *Angew. Chem., Int. Ed.* **2010**, *49*, 9266. (b) De Sarkar, S.; Grimme, S.; Studer, A. *J. Am. Chem. Soc.* **2010**, *132*, 1190. (c) De Sarkar, S.; Studer, A. *Org. Lett.* **2010**, *12*, 1992.

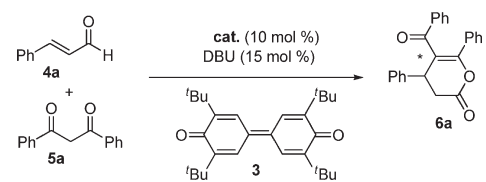
(8) For oxidation with MnO₂: Maki, B. E.; Scheidt, K. A. *Org. Lett.* **2008**, *10*, 4331.

(9) (a) Rosenthal, D.; Grabowich, P.; Sabo, E. F.; Fried, J. *J. Am. Chem. Soc.* **1963**, *85*, 3971. (b) Mandal, A. K.; Jawalker, D. G. *Tetrahedron Lett.* **1986**, *27*, 99. (c) Kume, T.; Iwasaki, H.; Yamamoto, Y.; Akiba, K. *Tetrahedron Lett.* **1988**, *29*, 3825. (d) Mandal, A. K.; Jawalker, D. J. *J. Org. Chem.* **1989**, *54*, 2364. (e) Robl, J. A. *Tetrahedron Lett.* **1990**, *31*, 3421. (f) Thang, S. H.; Rigg, D. J. *Synth. Commun.* **1993**, *23*, 2355. (g) Harrowen, D. C.; Hannam, J. C. *Tetrahedron* **1999**, *55*, 9333. (h) Zhang, F.-Y.; Corey, E. J. *Org. Lett.* **2000**, *2*, 1097.

(10) Selected examples: (a) Itoh, K.; Hasegawa, M.; Tanaka, J.; Kanemasa, S. *Org. Lett.* **2005**, *7*, 979. (b) Tozawa, T.; Nagao, H.; Yamane, Y.; Mukaiyama, T. *Chem.—Asian J.* **2007**, *2*, 123. (c) Zhu, M.-K.; Wei, Q.; Gong, L.-Z. *Adv. Synth. Catal.* **2008**, *350*, 1281. (d) Wang, J.; Yu, F.; Zhang, X.-J.; Ma, D.-W. *Org. Lett.* **2008**, *10*, 2561.

(11) For reactions with alkynyl aldehydes: (a) Zhu, Z.-Q.; Xiao, J.-C. *Adv. Synth. Catal.* **2010**, *352*, 2455. (b) Kaeobamrung, J.; Mahatthananchai, J.; Zheng, P.; Bode, J. W. *J. Am. Chem. Soc.* **2010**, *132*, 8810. (c) Mahatthananchai, J.; Zheng, P.; Bode, J. W. *Angew. Chem., Int. Ed.* **2011**, *50*, 1673.

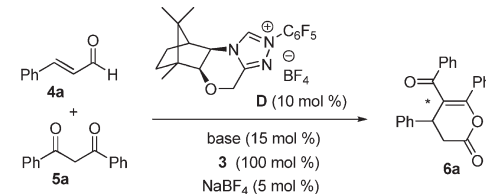
(12) Rearrangement of α,β -unsaturated enol esters: (a) Ryan, S. J.; Candish, L.; Lupton, D. W. *J. Am. Chem. Soc.* **2009**, *131*, 14176. (b) Candish, L.; Lupton, D. W. *Org. Lett.* **2010**, *12*, 4836.

Table 1. Screening of the Chiral NHC Catalysts and the Additives^a


entry	cat.	additive (mol %)	time (h)	yield (%) ^b	ee (%) ^c
1	A	—	24	59	45
2	B	—	12	80	62
3	C	—	2.5	85	52
4	D	—	24	61	16
5	E	—	27	<5	62
6	A	NaBF ₄ (5)	24	77	37
7	B	NaBF ₄ (5)	12	73	55
8	C	NaBF ₄ (5)	2.5	86	6
9	D	NaBF ₄ (5)	27	80	94
10	E	NaBF ₄ (5)	27	38	60
11	D	LiBF ₄ (5)	27	64	85
12	D	KBF ₄ (5)	27	63	15
13	D	NaBF ₄ (10)	27	72	90
14	D	NaBF ₄ (20)	27	62	90
15	D	NaBF ₄ (50)	27	37	89

^a Reaction conditions: **4a** (0.1 mmol), **5a** (0.3 mmol), **3** (0.1 mmol), 10 mol % of **cat.**, and 15 mol % of DBU in THF (1.0 mL) at 25 °C.
^b Isolated yield. ^c Determined by HPLC.

in moderate to good yields except catalyst **E**, which gave only a trace amount of the product. To our great surprise, a serendipitous testing of NaBF₄ as the additive provided very exciting results. With 5 mol % of NaBF₄, the catalyst generated from triazolium salt **D**, bearing a C₆F₅ group, gave dihydropyranone **6a** in a significantly improved enantioselectivity (94% ee) (entry 9, Table 1). By variation of the counter cations, we found that addition of the initially used NaBF₄ led to the best results and the use of LiBF₄ also enhanced the enantioselectivity significantly (entries 9, 11, and 12, Table 1). The loading of NaBF₄ was then examined, and the yields of **6a** decreased along with the increased amount of NaBF₄ while excellent enantioselectivity was maintained in all cases (entries 13–15, Table 1). The effects of the additives in this reaction have not been fully understood.¹⁴ In our opinion, it is likely that the

Table 2. Optimization of the Reaction Conditions^a


entry	base	solvent	time (h)	yield (%)	ee (%)
1	DBU	THF	27	80	94
2	DBU	toluene	40	66	92
3	DBU	xylene	40	70	91
4	DBU	CH ₂ Cl ₂	40	93	86
5	DBU	CHCl ₃	40	81	91
6	DBU	Et ₂ O	40	81	95
7	DIEA	THF	27	44	91
8	Et ₃ N	THF	27	44	92
9	KHMDS	THF	27	11	90
10	dabco	THF	27	20	88
11	no base	THF	27	NR	NR
12 ^b	DBU	THF	15	85	90
13 ^c	DBU	THF	24	73	93
14 ^d	DBU	THF	24	67	93
15 ^e	DBU	THF	24	83	92

^a Reaction conditions: **4a** (0.1 mmol), **5a** (0.3 mmol), **3** (0.1 mmol), 10 mol % of **D**, 5 mol % of NaBF₄, and 15 mol % of DBU in solvent (1.0 mL) at 25 °C, unless noted otherwise. ^b At 40 °C. ^c **4a/5a**: 1/2. ^d **4a/5a**: 1/1.2. ^e **4a/5a**: 2/1.

interaction between NaBF₄ and the C₆F₅ group of triazolium salt **D** impacted the transition state of the reaction and led to the high enantioselectivity.

In the presence of 10 mol % of triazolium salt **D** and 5 mol % of NaBF₄, different reaction parameters were further examined. The results are summarized in Table 2. All the tested solvents including toluene, xylene, CH₂Cl₂, CHCl₃, and ether were well tolerated (entries 2–6, Table 2). A slightly higher ee (95%) was obtained in ether, but the reaction was relatively slower. Several other organic bases (DIEA, Et₃N, and dabco) and KHMDS afforded the desired product **6a** in reduced yield but with excellent ee's (entries 7–10, Table 2). The reaction did not occur in the absence of the base (entry 11, Table 2). The reaction at 40 °C did not show any beneficial effect on either the reaction rate or the enantioselectivity of the reaction (entry 12, Table 2). Varying the ratios between the two substrates led to excellent enantioselectivities, but the yields were slightly decreased when 2 or 1.2 equiv of **5a** were used (entries 13–14, Table 2). When 2 equiv of **4a** and 1 equiv of **5a** were used, the yield of **6a** was not affected but the enantioselectivity was slightly decreased (entry 15, Table 2).

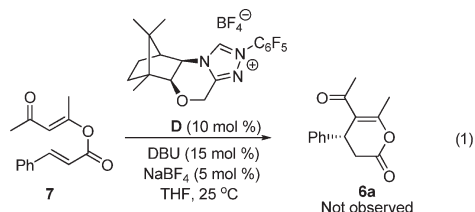
In the presence of 10 mol % of **D**, 15 mol % of DBU, 5 mol % of NaBF₄, and 100 mol % of quinone **3** in THF at 25 °C, the reactions of various dicarbonyl compounds with α,β-unsaturated aldehydes were tested to investigate the generality of the reaction. The results are summarized in

(13) (a) Li, Y.; Feng, Z.; You, S.-L. *Chem. Commun.* **2008**, 2263. (b) Li, Y.; Wang, X.-Q.; Zheng, C.; You, S.-L. *Chem. Commun.* **2009**, 5823. (c) Rong, Z.-Q.; Li, Y.; Yang, G.-Q.; You, S.-L. *Synlett* **2011**, 1033.

(14) For book and review: (a) Tchoubar, B.; Loupy, A. *Salt Effects in Organic and Organometallic Chemistry*; VCH: New York, 1992; pp 1–322. (b) Vogl, E. M.; Gröger, H.; Shibasaki, M. *Angew. Chem., Int. Ed.* **1999**, 38, 1570. For selected examples of salt effects: (c) Krasovskiy, A.; Knochel, P. *Angew. Chem., Int. Ed.* **2004**, 43, 3333. (d) Krasovskiy, A.; Malakhov, V.; Gavryushin, A.; Knochel, P. *Angew. Chem., Int. Ed.* **2006**, 45, 6040. (e) Ren, H.; Dunet, G.; Mayer, P.; Knochel, P. *J. Am. Chem. Soc.* **2007**, 129, 5376. (f) Ochiai, H.; Jang, M.; Hirano, K.; Yorimitsu, H.; Oshima, K. *Org. Lett.* **2008**, 10, 2681. (g) Hatano, M.; Ito, O.; Suzuki, S.; Ishihara, K. *Chem. Commun.* **2010**, 46, 2674. (h) Hatano, M.; Ito, O.; Suzuki, S.; Ishihara, K. *J. Org. Chem.* **2010**, 75, 5008. (i) Hevia, E.; Mulvey, R. E. *Angew. Chem., Int. Ed.* **2011**, 50, DOI: 10.1002/anie.201102054.

Table 3. When pentane-2,4-dione was used, the corresponding product **6b** was obtained in 78% yield and 93% ee (entry 2, Table 3). However, symmetrical 1,3-diketones with strong electron-withdrawing or bulky groups led to low reactivity (entries 3–4, Table 3). Moreover, β -keto esters were also demonstrated as suitable nucleophiles for NHC-catalyzed oxidative 1,4-additions, providing the desired 3,4-dihydro- α -pyrones in moderate yields with excellent ee's (entries 5–7, Table 3). The use of ethyl 3-oxo-3-phenylpropanoate provided high enantioselectivity albeit low yield (entry 8, Table 3). Various α,β -unsaturated aldehydes were then evaluated as suitable electrophiles with 1,3-diphenylpropane-1,3-dione (**5a**) (entries 9–17, Table 3). Both electron-donating and -withdrawing substituents were accommodated on the aromatic ring, with moderate to good yields and excellent levels of enantioselectivity obtained (entries 9–16, Table 3). Unfortunately, the use of crotonaldehyde under the optimal reaction conditions gave the desired product **6o** in 61% ee and 10% yield (entry 17, Table 3). To determine the absolute configuration of the product, the crystal structure of enantiopure **6g** was obtained, and a single crystal X-ray analysis determined its configuration as *S*.¹⁵

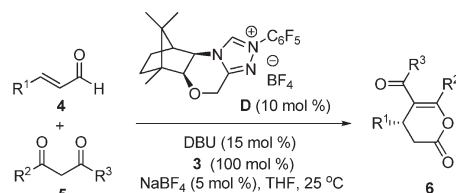
To shed light on the reaction mechanism, compound **7** was synthesized and subjected to the reaction conditions (eq 1). The fact that no desired product was observed in the reaction likely excludes enol ester (**7**) as the competent intermediate. However, either Michael addition of enolate to NHC-mediated α,β -unsaturated acceptor^{7a} or the Claisen rearrangement^{11b} pathway cannot be excluded for this asymmetric process.



In summary, we have developed an enantioselective *N*-heterocyclic carbene-catalyzed Michael addition reaction to α,β -unsaturated aldehydes using redox oxidation. The camphor-derived triazolium salt together with a catalytic amount of NaBF₄ was found to be highly efficient for this reaction providing enantioenriched substituted 3,4-dihydro- α -pyrones in good

(15) CCDC 827900 contains the supplementary crystallographic data for (*S*)-**6g**. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Table 3. NHC-Catalyzed Redox-Type Michael Addition of Dicarboxyl Compounds to α,β -Unsaturated Aldehydes^a



entry	R ¹	R ²	R ³	product	time (h)	yield (%) ^b	ee (%) ^c
1	Ph	Ph	Ph	6a	27	80	94
2	Ph	Me	Me	6b	30	78	93
3	Ph	CF ₃	CF ₃	—	NR	NR	NR
4	Ph	<i>t</i> -Bu	<i>t</i> -Bu	—	trace	trace	trace
5	Ph	Me	OMe	6c	42	58	89
6	Ph	Me	OEt	6d	28	70	91
7	Ph	Me	OCH ₂ CH=CH ₂	6e	30	50	91
8	Ph	Ph	OEt	6f	20	17	94
9	2-BrC ₆ H ₄	Ph	Ph	6g	1	95	96
10	4-BrC ₆ H ₄	Ph	Ph	6h	43	70	94
11	2-ClC ₆ H ₄	Ph	Ph	6i	1	90	96
12	3-ClC ₆ H ₄	Ph	Ph	6j	27	77	93
13	4-ClC ₆ H ₄	Ph	Ph	6k	43	69	94
14	4-CO ₂ MeC ₆ H ₄	Ph	Ph	6l	24	89	93
15	2-CH ₃ C ₆ H ₄	Ph	Ph	6m	19	79	92
16	4-OMeC ₆ H ₄	Ph	Ph	6n	60	45	89
17	Me	Ph	Ph	6o	70	10	61

^a Reaction conditions: **4** (0.2 mmol), **5** (0.6 mmol), **3** (0.2 mmol), 10 mol % of **D**, 5 mol % of NaBF₄, and 15 mol % of DBU in THF (2.0 mL) at rt, unless noted otherwise. ^b Isolated yield. ^c Determined by HPLC.

yields with excellent ee's. The mild reaction conditions and ready accessibility of both the starting materials and catalysts make the current methodology particularly attractive in organic synthesis.

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Supporting Information Available. Experimental procedures and characterization of the products. This material is available free of charge via the Internet at <http://pubs.acs.org>.