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Highly Stereoselective Synthesis of Functionalized Pyrrolo[3,2-*c*]quinolines *via* *N*-Heterocyclic Carbene Catalyzed Cascade Sequence

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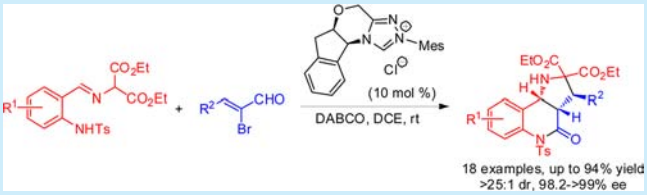
Supporting Information

ABSTRACT: An *N*-heterocyclic carbene-catalyzed stereoselective Michael–Mannich–lactamization cascade reaction of tosyl-protected *o*-amino aromatic aldimines and 2-bromoenals for the construction of functionalized pyrrolo[3,2-*c*]quinolines with three consecutive stereocenters was achieved in good yields with excellent diastereo- and enantioselectivities.



The pyrrolo[3,2-*c*]quinoline is an important structural unit that is found in several biological active natural products and pharmaceutics. For example, martinellic acid and martinelline (Figure 1), which were isolated from the roots of the tropical

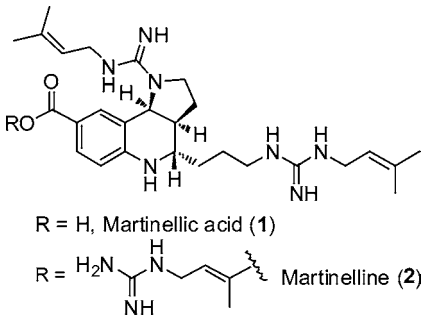
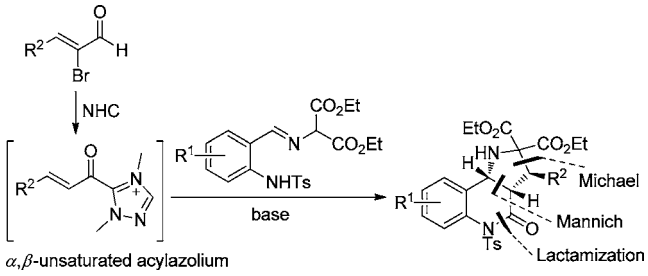


Figure 1. Structure of martinellic acid and martinelline.

plant *Martinella iquitosensis*,[1] are the first naturally occurring nonpeptide bradykinin B_1 and B_2 receptor antogonists.[2] Owing to the unusual tricyclic core of Martinella alkaloids and unique biological activity, the synthesis of the pyrroloquinoline core and total synthesis of martinellic acid or martinelline have garnered considerable attention from several research groups. Until now, numerous synthetic methods have been established.[3,4] However, little effort has been focused on enantioselective synthesis of the tricyclic core of Martinella alkaloids.

N-Heterocyclic carbenes (NHCs) have been widely employed as organocatalysts in synthetic transformations in recent decades. NHC-catalyzed reactions are well developed and offer a broad range of unconventional transformations.[5,6] Organocatalytic cascade reactions, which are important in synthetic chemistry and pharmaceutical science, are strongly dominated by secondary amines and Brønsted acids. NHC-catalyzed cascade reactions have received growing attention in recent years.[7−9,10c] *α,β*-Unsaturated acylazolium intermediates, which are efficient 1,3-biselectrophiles, can be used for many transformations.[10−13] However, few applications of the carbonyl, *α*- and *β*-carbon atoms of the 1,3-biselectrophile are used for cascade reactions.[8e,10c,11e,12b,c,13d] A novel methodology for the construction of pyrrolo[3,2-*c*]quinoline could efficiently promote the total synthesis of Martinella alkaloids. As our group is working on the development of a practical NHC-catalyzed stereoselecive cascade reaction based on *α,β*-unsaturated acylazolium intermediates,[10c] in this paper, we report an efficient NHC-catalyzed strategy for the synthesis of functionalized pyrrolo[3,2-*c*]quinolines via a stereoselective cascade reaction of tosyl-protected *o*-amino aromatic aldimines and 2-bromoenals (Scheme 1). Three new bonds and three consecutive stereogenic centers are established thus, in a single cascade sequence.

Scheme 1. NHC-Catalyzed Stereoselective Cascade Reaction



Initial studies screened *N*-heterocyclic carbene catalysts for their ability to promote the stereoselective cascade reaction of tosyl-protected *o*-amino aromatic aldimine **1a** and 2-bromoenal **2a** (Table 1). Treatment of **1a** and **2a** with catalyst **3a** (10 mol %) and 1,8-diazabicyclic[5.4.0]undec-7-ene (DBU) (1.1 equiv) in dichloromethane gave the desired product **4a** in 20% yield, 1:2

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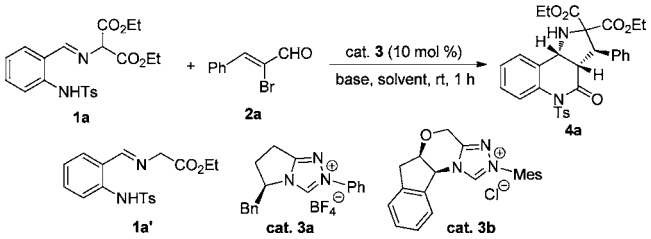
Table 1. Optimization of Reaction Conditions[a]



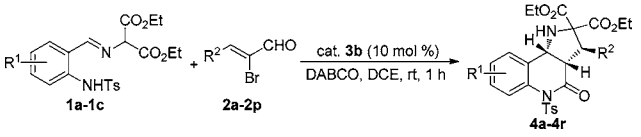
entry	cat.	base	solvent	yield (%)[b]	dr[c]	ee (%)[d]
1	cat. **3a**	DBU	DCM	20	1:2	>99
2	cat. **3b**	DBU	DCM	44	1:1	>99
3	cat. **3b**	NEt_3	DCM	55	1:1	>99
4	cat. **3b**	Cs_2CO_3	DCM	50	1:1.6	>99
5	cat. **3b**	DABCO	DCM	52	15:1	>99
6	cat. **3b**	DABCO	CH_3Ph	53	5:1	>99
7	cat. **3b**	DABCO	THF	52	6:1	>99
8	cat. **3b**	DABCO	MeCN	53	4:1	>99
9	cat. **3b**	DABCO	DCE	59	>25:1	>99
10[e]	cat. **3b**	DABCO	DCE	64	>25:1	>99
11[f]	cat. **3b**	DABCO	DCE	71	>25:1	>99
12[g]	cat. **3b**	DABCO	DCE	92	>25:1	>99

[a]Reaction conditions: **1a**/**2a**/base = 1:1:1.1 (molar ratio). [b]Isolated yield. [c]Determined by ^{1}H NMR (400 MHz) of the crude product. [d]Determined by chiral HPLC analysis. [e]**1a**/**2a** = 1.25:1 (molar ratio). [f]**1a**/**2a** = 1.5:1 (molar ratio). [g]**1a**/**2a** = 1.75:1 (molar ratio).

dr, and >99% ee (entry 1). For (*E*)-ethyl 2-((2-(4-methylphenylsulfonamido)benzylidene)amino)acetate (**1a′**), trace desired product was formed. The results show that the cyclization reaction is benefiting from the favorable pK_a and the Thorpe−Ingold effect of malonate.[14] When this reaction was performed in the presence of catalyst **3b** (10 mol %), which derived from (2*S*,1*R*)-amino indanol, a distinct improvement in the yield was observed (entry 2). For entries 3−5, the effect of the bases was examined. The results showed that the use of DABCO favored the stereoselective cascade reaction with high diastereoselectivity (15:1 dr) being afforded (entry 5). Further screening of the solvent revealed 1,2-dichloroethane (DCE) was the best choice and the desired product was obtained in 59% yield with excellent diastereo- and enantioselectivities (entry 9). To further improve the yield, the molar ratio of the substrates was optimized. The results demonstrated that 1.75 equiv of aldimine **1a** gave the product **4a** in 92% yield, >25:1 dr, and with >99% ee (entry 12). When the substrate with a Boc group was used for protecting the aromatic amine, and used for this asymmetric cascade reaction, the adduct was obtained in 43% yield, 2:1 dr, and 98% ee. Based on the above results, the optimal conditions that were found for the preparation of **4a** used catalyst **3b** (10 mol %) and DABCO (1.1 equiv) in DCE at rt.

Under the optimal conditions, the generality of the NHC-catalyst **3b**-promoted cascade reaction was investigated (Table 2). When the reactions of tosyl-protected *o*-amino aromatic aldimine **1a** and 2-bromoenals **2a**−**2o** were examined, the products **4a**−**4o** were obtained in excellent diastereo- and enantioselectivities (entries 1−15). The less sterically hindered substituted 2-bromoenals (except entry 10) gave good yields ranging from 81% to 94% (entries 1, 3−9, and 14). On the other hand, the 2-chlorophenyl and 1-naphthyl substituted 2-bromoenals resulted in a lower yield due to steric hindrance (entries 2 and 13). The cascade reaction for 2-bromo-enals **2j**−**2l** and **2o**, which contain electron-rich aromatic rings or strong

Table 2. Substrate Scope of the NHC-Catalyzed Cascade Reaction[a]



entry	R^1	R^2	prod	yield (%)[b]	dr[c]	ee (%)[d]
1	H (**1a**)	Ph (**2a**)	**4a**	92	>25:1	>99
2	H (**1a**)	2-ClC_6H_4 (**2b**)	**4b**	73	>25:1	>99
3	H (**1a**)	3-FC_6H_4 (**2c**)	**4c**	81	>25:1	>99
4	H (**1a**)	3-ClC_6H_4 (**2d**)	**4d**	87	>25:1	>99
5	H (**1a**)	3-BrC_6H_4 (**2e**)	**4e**	83	>25:1	>99
6	H (**1a**)	4-FC_6H_4 (**2f**)	**4f**	88	>25:1	>99
7	H (**1a**)	4-ClC_6H_4 (**2g**)	**4g**	92	>25:1	>99
8	H (**1a**)	4-BrC_6H_4 (**2h**)	**4h**	94	>25:1	98.8
9	H (**1a**)	4-MeC_6H_4 (**2i**)	**4i**	90	>25:1	>99
10	H (**1a**)	4-MeOC_6H_4 (**2j**)	**4j**[e]	78	>25:1	>99
11	H (**1a**)	4-$CF_3C_6H_4$ (**2k**)	**4k**	74	>25:1	>99
12	H (**1a**)	4-$NO_2C_6H_4$ (**2l**)	**4l**	63	>25:1	>99
13	H (**1a**)	1-naphthyl (**2m**)	**4m**	71	>25:1	>99
14	H (**1a**)	2-naphthyl (**2n**)	**4n**	83	>25:1	>99
15	H (**1a**)	2-thienyl (**2o**)	**4o**	68	>25:1	>99
16	H (**1a**)	Me (**2p**)	**4p**[e]	79[f]	3:1	98.2
17	5-Cl (**1b**)	Ph (**2a**)	**4q**	77	>25:1	>99
18	5-Br (**1c**)	Ph (**2a**)	**4r**	76	>25:1	>99

[a]Reaction conditions: **1**/**2**/catalyst **3b**/DABCO = 1.75:1:0.1:1.1 (molar ratio). [b]Isolated yield. [c]Determined by ^{1}H NMR (400 MHz) of the crude product. [d]Determined by chiral HPLC analysis. [e]Reaction time: 2 h. [f]Total yield of two diastereoisomers.

electron-withdrawing groups, gave the products in moderate yield (entries 10−12 and 15). For alkyl-substituted 2-bromoenal **2p**, product **4p** was afforded in 79% yield[15] with 3:1 dr and 98.2% ee (entry 16). In addition, substituted tosyl-protected *o*-amino aromatic aldimines **1b** and **1c** were also investigated. The desired products were accessed in moderate yield with excellent diastereo- and enantioselectivities (entries 17−18). To validate the influence of the stereochemistry of the 2-bromoenal, (*E*)-2-bromo-3-(4-fluorophenyl)acrylaldehyde (**2f′**) was used for this reaction and the product **4f** was obtained in 62% yield with 3:2 dr and >99% ee.

The absolute configuration of the products was determined to be (3*R*,3a*S*,9b*R*) by using X-ray crystal analysis of compound **4b** (Figure 2). Other product configurations were assigned tentatively by analogy. In addition, the effect of the ee value of

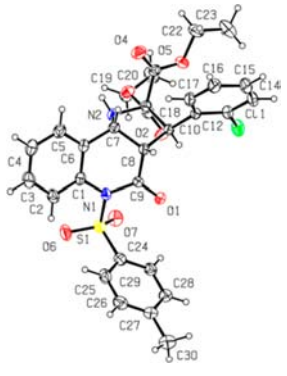


Figure 2. X-ray crystallography of compound **4b**.

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the catalyst on the products was investigated. The results revealed a positive nonlinear effect (Figure 3), which suggested

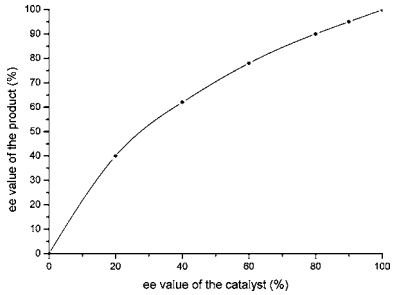
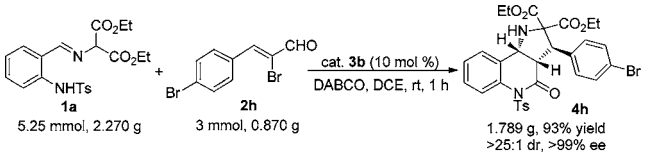


Figure 3. Nonlinear effect.

that the NHC catalyst of the opposite absolute configuration accelerates the rate of this stereoselective cascade reaction. The potential ultility of this stereoselective cascade reaction was demonstrated by a gram scale synthesis (Scheme 2); the reaction proceeded smoothly, affording the adduct **4h** in 93% yield, >25:1 dr, and >99% ee.

Scheme 2. Gram Scale Synthesis of the Adduct 4h



A plausible catalytic cycle for this cascade reaction is outlined in Figure 4. The catalytic cycle begins with the addition of the NHC catalyst to 2-bromoenals **2** to generate Breslow intermediate **I**, which is then transformed into **III** through tautomerization and debromination. The Michael addition of tosyl-protected *o*-amino aromatic aldimine **1** to intermediate **III** from the *re*-face provides enolate **IV**.[6h] It undergoes intramolecular Mannich reaction and lactamization to give the desired product **4**.

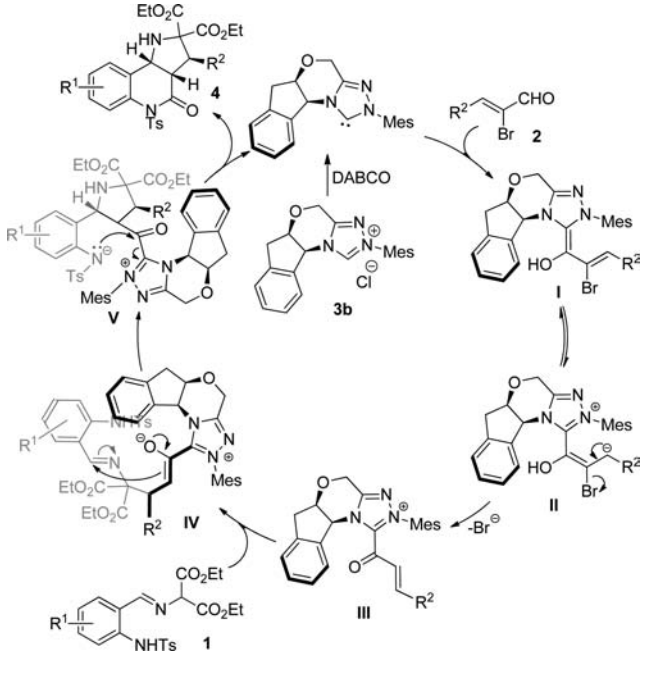


Figure 4. Proposed catalytic cycle.

In conclusion, we have developed an efficient NHC-catalyzed stereoselective Michael–Mannich–lactamization cascade reaction of tosyl-protected *o*-amino aromatic aldimines and 2-bromoenals for the synthesis of functionalized pyrrolo[3,2-*c*]quinolines. The products with three consecutive stereogenic centers were obtained in good yields with excellent diastereo- and enantioselectivities under mild reaction conditions. A gram scale synthesis of functionalized pyrrolo[3,2-*c*]quinoline and the nonlinear effect of the NHC catalyst have also been investigated. In addition, this approach is attractive due to the potential utilization value for efficient synthesis of Martinella alkaloids.

■ ASSOCIATED CONTENT

Supporting Information

Experimental procedure, characterization data for the products, and crystallographic data of compound **4b** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) Witherup, K. M.; Ransom, R. W.; Graham, A. C.; Bernard, A. M.; Salvatore, M. J.; Lumma, W. C.; Anderson, P. S.; Pitzenberger, S. M.; Varga, S. L. *J. Am. Chem. Soc.* **1995**, *117*, 6682.

(2) Lovely, J. C.; Mahmud, H. *Tetrahedron Lett.* **1999**, *40*, 2097.

(3) Selected examples of synthesis of the pyrroloquinoline core: (a) Gurjar, M. K.; Pal, S.; Rao, A. V. R. *Heterocycles* **1997**, *45*, 231. (b) Ho, T. C. T.; Jones, K. *Tetrahedron* **1997**, *53*, 8287. (c) Snider, B. B.; Ahn, Y.; Foxman, B. M. *Tetrahedron Lett.* **1999**, *40*, 3339. (d) Nieman, J. A.; Ennis, M. D. *Org. Lett.* **2000**, *2*, 1395. (e) Nyerges, M.; Fejes, I.; Tőke, L. *Tetrahdron Lett.* **2000**, *41*, 7951. (f) Hadden, M.; Nieuwenhuyzen, M.; Potts, D.; Stevenson, P. J.; Thompson, N. *Tetrahedron* **2001**, *57*, 5615. (g) Batey, R. A.; Powell, D. A. *Chem. Commun.* **2001**, 2362. (h) Hara, O.; Sugimoto, K.; Makino, K.; Hamada, Y. *Synlett* **2004**, 1625. (i) Yadav, J. S.; Subba, R. B. V.; Sunitha, V.; Srinivasa, R. K.; Ramakrishna, K. V. S. *Tetrahedron Lett.* **2004**, *45*, 7947. (j) Ng, P. Y.; Masse, C. E.; Shaw, J. T. *Org. Lett.* **2006**, *8*, 3999. (k) Testa, M. L.; Lamartina, L.; Mingoia, F. *Tetrahedron* **2004**, *60*, 5873. (l) Nyerges, M. *Heterocycles* **2004**, *63*, 1685. (m) Zhang, Z.; Zhang, Q.; Yan, Z.; Liu, Q. *J. Org. Chem.* **2007**, *72*, 9808. (n) Dagousset, G.; Retailleau, P.; Masson, G.; Zhu, J. *Chem.—Eur. J.* **2012**, *18*, 5869. (o) Zheng, H.-F.; Yu, Z.-H.; Yuan, W.; Tang, Z.-L.; Clough, J.; Gu, Y.-C.; Shi, D.-Q. *Chem.—Eur. J.* **2014**, *20*, 1711.

(4) Selected examples of total synthesis of martinellic acid and/or martinelline: (a) Ma, D.; Xia, C.; Jiang, J.; Zhang, J. *Org. Lett.* **2001**, *3*, 2189. (b) Snider, B. B.; Ahn, Y.; O'Hare, S. M. *Org. Lett.* **2001**, *3*, 4217. (c) Powell, D. A.; Batey, R. A. *Org. Lett.* **2002**, *4*, 2913. (d) Miyata, O.; Shirai, A.; Yoshino, S.; Takeda, Y.; Sugiura, M.; Naito, T. *Synlett* **2006**, 893. (e) Takeda, Y.; Nakabayashi, T.; Shirai, A.; Fukumoto, D.; Kiguchi, T.; Naito, T. *Tetrahedron Lett.* **2004**, *45*, 3481. (f) Hadden, M.; Nieuwenhuyzen, M.; Potts, D.; Stevenson, P. J.; Thompson, N.; Walker, A. D. *Tetrahedron* **2006**, *62*, 3977. (g) He, Y.; Mahmud, H.; Moningka, R.; Lovely, C. J.; Dias, H. V. R. *Tetrahedron* **2006**, *62*, 8755. (h) Ikeda, S.;

dx.doi.org/10.1021/ol5023917 | *Org. Lett.* 2014, 16, 5048–5051

Shibuya, M.; Iwabuchi, Y. *Chem. Commun.* **2007**, 504. (i) Shirai, A.; Miyata, O.; Tohnai, N.; Miyata, M.; Procter, D. J.; Sucunza, D.; Naito, T. *J. Org. Chem.* **2008**, *73*, 4464. (j) Ueda, M.; Kawai, S.; Hayashi, M.; Naito, T.; Miyata, O. *J. Org. Chem.* **2010**, *75*, 914. (k) Davies, S. G.; Fletcher, A. M.; Lee, J. A.; Lorkin, T. J. A.; Roberts, P. M.; Thomson, J. E. *Org. Lett.* **2013**, *15*, 2050. (l) Hu, J.; Hirao, H.; Li, Y.; Zhou, J. (Steve). *Angew. Chem., Int. Ed.* **2013**, *52*, 8676.

(5) For selected reviews on NHC catalysis, see: (a) Enders, D.; Niemeier, O.; Henseler, A. *Chem. Rev.* **2007**, *107*, 5606. (b) Marion, N.; Díez-González, S.; Nloan, S. P. *Angew. Chem., Int. Ed.* **2007**, *46*, 2988. (c) Moore, J. L.; Rovis, T. *Top. Curr. Chem.* **2010**, *291*, 118. (d) Grossmann, A.; Enders, D. *Angew. Chem., Int. Ed.* **2012**, *51*, 314. (e) Izquierdo, J.; Hutson, G. E.; Cohen, D. T.; Scheidt, K. A. *Angew. Chem., Int. Ed.* **2012**, *51*, 11686. (f) Bugaut, X.; Glorius, F. *Chem. Soc. Rev.* **2012**, *41*, 3511. (g) Douglas, J.; Churchill, G.; Smith, A. D. *Synthesis* **2012**, 2295. (h) Vora, H. U.; Wheeler, P.; Rovis, T. *Adv. Synth. Catal.* **2012**, *354*, 1617. (i) Ryan, S. J.; Candish, L.; Lupton, D. W. *Chem. Soc. Rev.* **2013**, *42*, 4906. (j) Studer, A.; De Sarkar, S.; Biswas, A.; Samanta, R. C. *Chem.—Eur. J.* **2013**, *19*, 4664.

(6) For selected recent examples on NHC-catalyzed reactions, see: (a) Mo, J.; Chen, X.; Chi, Y. R. *J. Am. Chem. Soc.* **2012**, *134*, 8810. (b) DiRocco, D. A.; Rovis, T. *J. Am. Chem. Soc.* **2012**, *134*, 8094. (c) DiRocco, D. A.; Rovis, T. *Angew. Chem., Int. Ed.* **2012**, *51*, 5904. (d) Lv, H.; Tiwari, B.; Mo, J.; Xing, C.; Chi, Y. R. *Org. Lett.* **2012**, *14*, 5412. (e) Bhunia, A.; Yetra, S. R.; Bhojgude, S. S.; Biju, A. T. *Org. Lett.* **2012**, *14*, 2830. (f) Jia, M.-Q.; Liu, C.; You, S.-L. *J. Org. Chem.* **2012**, *77*, 10996. (g) Jia, M.-Q.; You, S.-L. *Chem. Commun.* **2012**, *48*, 6363. (h) Izquierdo, J.; Orue, A.; Scheidt, K. A. *J. Am. Chem. Soc.* **2013**, *135*, 10634. (i) White, N. A.; DiRocco, D. A.; Rovis, T. *J. Am. Chem. Soc.* **2013**, *135*, 8504. (j) Jin, Z.; Xu, J.; Yang, S.; Song, B.-A.; Chi, Y. R. *Angew. Chem., Int. Ed.* **2013**, *52*, 12354. (k) McCusker, E. O.; Scheidt, K. A. *Angew. Chem., Int. Ed.* **2013**, *52*, 13616. (l) Sun, L.-H.; Liang, Z.-Q.; Jia, W.-Q.; Ye, S. *Angew. Chem., Int. Ed.* **2013**, *52*, 5803. (m) Mo, J.; Shen, L.; Chi, Y. R. *Angew. Chem., Int. Ed.* **2013**, *52*, 8588. (n) Cheng, J.; Huang, Z.; Chi, Y. R. *Angew. Chem., Int. Ed.* **2013**, *52*, 8592. (o) Chen, X.-Y.; Xia, F.; Cheng, J.-T.; Ye, S. *Angew. Chem., Int. Ed.* **2013**, *52*, 10644. (p) Fu, Z.; Xu, J.; Zhu, T.; Leong, W. W. Y.; Chi, Y. R. *Nat. Chem.* **2013**, *5*, 835. (q) Wheeler, P.; Vora, H. U.; Rovis, T. *Chem. Sci.* **2013**, *4*, 1674. (r) Wang, M.; Huang, Z.; Xu, J.; Chi, Y. R. *J. Am. Chem. Soc.* **2014**, *136*, 1214. (s) Kowalczyk, M.; Lupton, D. W. *Angew. Chem., Int. Ed.* **2014**, *53*, 5314. (t) Xu, J.; Mou, C.; Zhu, T.; Song, B.-A.; Chi, Y. R. *Org. Lett.* **2014**, *16*, 3272.

(7) For reviews on NHC-catalyzed cascade reactions, see: (a) Grossmann, A.; Enders, D. *Angew. Chem., Int. Ed.* **2012**, *51*, 314. (b) Chauhan, P.; Enders, D. *Angew. Chem., Int. Ed.* **2014**, *53*, 1485.

(8) For selected examples on NHC-catalyzed cascade reactions, see: (a) Sánchez-Larios, E.; Gravel, M. *J. Org. Chem.* **2009**, *74*, 7536. (b) Sun, F.-G.; Huang, X.-L.; Ye, S. *J. Org. Chem.* **2010**, *75*, 273. (c) Biju, A. T.; Wurz, N. E.; Glorius, F. *J. Am. Chem. Soc.* **2010**, *132*, 5970. (d) Sánchez-Larios, E.; Holmes, J. M.; Daschner, C. L.; Gravel, M. *Org. Lett.* **2010**, *12*, 5772. (e) Biswas, A.; De Sarkar, S.; Fröhlich, R.; Studer, A. *Org. Lett.* **2011**, *13*, 4966. (f) Wu, K.-J.; Li, G.-Q.; Li, Y.; Dai, L.-X.; You, S.-L. *Chem. Commun.* **2011**, *47*, 493. (g) Fang, X.; Jiang, K.; Xing, C.; Hao, L.; Chi, Y. R. *Angew. Chem., Int. Ed.* **2011**, *50*, 1910.

(9) For selected examples on dual catalytic cascade reactions with NHCs, see: (a) Lathrop, S. P.; Rovis, T. *J. Am. Chem. Soc.* **2009**, *131*, 13628. (b) Filloux, C. M.; Lathrop, S. P.; Rovis, T. *Proc. Natl. Acad. Sci. U.S.A.* **2010**, *107*, 20666. (c) Hong, B.-C.; Dange, N. S.; Hsu, C.-S.; Liao, J.-H. *Org. Lett.* **2010**, *12*, 4812.

(10) For selected examples formed from 2-bromoenals for asymmetric reactions, see: (a) Sun, F.-G.; Sun, L.-H.; Ye, S. *Adv. Synth. Catal.* **2011**, *353*, 3134. (b) Reddy, Y. S.; Kaicharla, T.; Kunte, S. S.; Gonnade, R. G.; Biju, A. T. *Org. Lett.* **2013**, *15*, 5202. (c) Zhang, H.-R.; Dong, Z.-W.; Yang, Y.-J.; Wang, P.-L.; Hui, X.-P. *Org. Lett.* **2013**, *15*, 4750. (d) Yetra, S. R.; Bhunia, A.; Patra, A.; Mane, M. V.; Vanka, K.; Biju, A. T. *Adv. Synth. Catal.* **2013**, *355*, 1089. (e) Xiao, Z.; Yu, C.; Li, T.; Wang, X.-S.; Yao, C. *Org. Lett.* **2014**, *16*, 3632. (f) Ni, Q.; Song, X.; Raabe, G.; Enders, D. *Chem.—Asian J.* **2014**, *9*, 1535. (g) Yetra, S. R.; Roy, T.; Bhunia, A.; Porwal, D.; Biju, A. T. *J. Org. Chem.* **2014**, *79*, 4245.

(11) For selected examples formed from ynals, see: (a) Zeitler, K. *Org. Lett.* **2006**, *8*, 637. (b) Kaeobamrung, J.; Mahatthananchai, J.; Zheng, P.; Bode, J. W. *J. Am. Chem. Soc.* **2010**, *132*, 8810. (c) Zhu, Z.-Q.; Xiao, J.-C. *Adv. Synth. Catal.* **2010**, *352*, 2455. (d) Romanov-Michailidis, F.; Besnard, C.; Alexakis, A. *Org. Lett.* **2012**, *14*, 4906. (e) Zhou, B.; Luo, Z.; Li, Y. *Chem.—Eur. J.* **2013**, *19*, 4428. (f) Du, D.; Hu, Z.; Jin, J.; Lu, Y.; Tang, W.; Wang, B.; Lu, T. *Org. Lett.* **2012**, *14*, 1274.

(12) For selected examples formed from acyl fluorides, see: (a) Ryan, S. J.; Candish, L.; Lupton, D. W. *J. Am. Chem. Soc.* **2009**, *131*, 14176. (b) Ryan, S. J.; Candish, L.; Lupton, D. W. *J. Am. Chem. Soc.* **2011**, *133*, 4694. (c) Candish, L.; Lupton, D. W. *J. Am. Chem. Soc.* **2013**, *135*, 58.

(13) For selected examples formed from enals with an oxidant, see: (a) De Sarkar, S.; Studer, A. *Angew. Chem., Int. Ed.* **2010**, *49*, 9266. (b) Zhu, Z.-Q.; Zheng, X.-L.; Jiang, N.-F.; Wan, X.; Xiao, J.-C. *Chem. Commun.* **2011**, *47*, 8670. (c) Rong, Z.-Q.; Jia, M.-Q.; You, S.-L. *Org. Lett.* **2011**, *13*, 4080. (d) Biswas, A.; De Sarkar, S.; Tebben, L.; Studer, A. *Chem. Commun.* **2012**, *48*, 5190. (e) Kravina, A. G.; Mahatthananchai, J.; Bode, J. W. *Angew. Chem., Int. Ed.* **2012**, *51*, 9433.

(14) Jung, M. E.; Piizzi, G. *Chem. Rev.* **2005**, *105*, 1735.

(15) The two diastereoisomers cannot be purified by flash column chromatography on silica gel.

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