Asymmetric organocatalysis

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Highly Enantioselective Synthesis of α-Amino Acid Derivatives by an NHC-Catalyzed Intermolecular Stetter Reaction**

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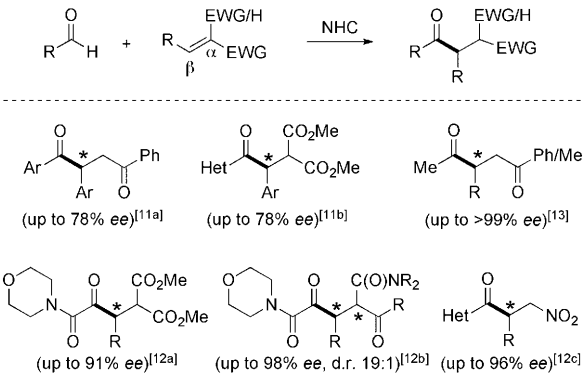
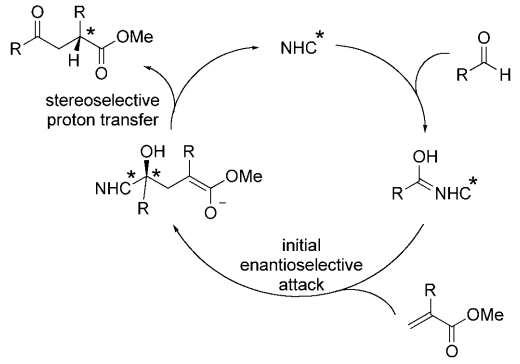
Dedicated to Professor Ronald Breslow on the occasion of his 80th birthday

α-Amino acids are one of the most important classes of compounds in nature and synthetic chemistry, and, consequently, many approaches have been developed for the synthesis of enantioenriched α-amino acids.[1] Among these synthetic routes, a particularly versatile and challenging method to set up the chirality at the α position of α-amino acids is the formation of a transient enolate through a Michael addition followed by a stereoselective protonation. Enantioselective protonation is important in many biosynthetic sequences, and the development of powerful catalytic processes remains an ongoing challenge.[2,3] Many different approaches for catalyzed enantioselective protonations have been realized; however, the combination of a conjugate addition with the asymmetric protonation of a transiently formed enolate stands out as being especially efficient and atom economic.[4–6] In the context of α-amino acid synthesis, this strategy was first explored by Pracejus et al. in 1977 for the synthesis of cysteine derivatives with moderate enantioselectivities (up to 54% *ee*) by using methyl 2-phthalimidoacrylate as the Michael acceptor and cinchona alkaloids as the chiral catalysts.[7] More recently, asymmetric approaches based on the use of organocatalysts[4c] or metal-based catalysts[6] have shown improved selectivities, but the scope has remained limited.

The cyanide or N-heterocyclic carbene (NHC) catalyzed[8] addition of an aldehyde to a Michael acceptor, the Stetter reaction,[8,9] is a versatile synthetic transformation. Whereas the intramolecular asymmetric Stetter reaction has been investigated extensively by the research groups of Enders, Rovis, and others,[8,10] the more versatile *intermolecular* asymmetric version has proven to be much more challenging. In the last two years, the first moderately to highly enantioselective intermolecular Stetter reactions were reported by the research groups of Enders[11] and Rovis,[12] and very recently an enzyme-catalyzed variant was reported by Müller and co-workers[13] (Scheme 1). However, selectivities are not yet optimal and the substrate scope seems to be very limited—a general system remains to be found. In addition, a stereocenter is formed in the β position in each of these cases. An asymmetric Stetter reaction that builds up only α stereocenters seems to be even more challenging. The key to success might be a highly stereoselective intramolecular proton transfer that relays the stereochemical information after the initial enantioselective attack of the Breslow intermediate on the Michael acceptor (Scheme 2). Herein we report a highly asymmetric intermolecular Stetter reac-



Scheme 1. Chiral NHC-[11,12] or enzyme-catalyzed[13] intermolecular asymmetric Stetter reactions. EWG = electron-withdrawing group, Ar = aromatic group, Het = heteroaromatic group, R = rest.



Scheme 2. Proposed reaction pathway for an intermolecular enantioselective Stetter reaction.

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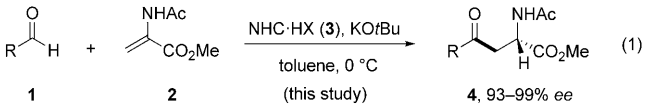
tion, starting from two rather simple starting materials (aldehydes and *N*-acylamido acrylate) and resulting in the formation of valuable highly enantioenriched α-amino acid derivatives [Eq. (1)].



1 **2** **4**, 93–99% *ee* (1)

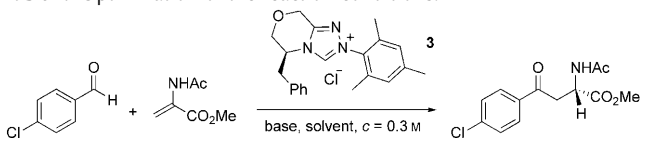
In the course of our research on NHC organocatalysis[14] we decided to explore an enantioselective Stetter reaction in which a stereoselective protonation was the key step by using aromatic or aliphatic aldehydes and a dehydroamino ester as the Michael acceptor. Our study commenced with the observation that the reaction between aldehyde **1a** and Michael acceptor **2** was catalyzed by chiral NHC **3** (Table 1).[15] The Stetter product **4a** was obtained with an excellent enantioselectivity of 97% but with a poor yield of only 10% (Table 1, entry 1). An extensive screening of the reaction conditions revealed several crucial parameters. We first showed that the use of TBD as the base and toluene as a solvent gave an improved yield compared to dioxane or THF (Table 1, entries 2–4); however, the enantioselectivity decreased to 84%. Similar results were obtained with DBU or K_2CO_3 as the base (Table 1, entries 5 and 6). Additionally, we observed that the use of two equivalents of the Michael acceptor had a positive effect on conversion (Table 1, entries 6 and 7). Switching to stronger bases such as KHMDS and KO*t*Bu restored the enantioselectivity to 95%, and the conversion increased substantially (67% and 65%; Table 1, entries 8 and 9, respectively).[16] We surmise that these bases are strong enough to be fully protonated by the triazolium salt, so that free base, which might racemize the product, is no longer present in the reaction mixture. Lowering the reaction temperature to 0°C led to full conversion and high levels of enantioinduction after only 4 h (Table 1, entry 10). Clearly, racemization is not a problem under these mild reaction conditions, even with a prolonged reaction time (Table 1, entry 11).

Two equivalents of **2** were essential for full conversion under these conditions (Table 1, entry 12). Nevertheless, the catalyst and base loadings could be further reduced without affecting the yield or enantioselectivity; this led to the optimized reaction conditions (Table 1, entry 13; highlighted in bold). The reaction has also been applied successfully on a gram scale (5 mmol) under these optimized conditions to yield enantiomerically enriched α-amino acid derivative **4a** in excellent yield and stereoinduction (Table 1, entry 13). However, lowering the amount of catalyst significantly below 10 mol% resulted in an incomplete reaction (not shown).

Furthermore, we tried other Michael acceptors in the reaction to evaluate their reactivity. Other amino protecting groups such as *tert*-butoxycarbonyl (Boc) or phthalimido failed to provide the desired product. In addition, the N-H group of the amide seems to be crucial for the reactivity, since the tertiary N-methylated variant of Michael acceptor **2** did not react.[17] Similarly, the β-substituted acrylate (*Z*)-methyl-acetamido cinnamate (MAC) also did not react under our standard conditions.

Thereafter, we studied the scope and the generality of this reaction. First, we screened aromatic aldehydes bearing an electron-withdrawing group (Scheme 3). Methyloxycarbonyl (**4b**), trifluoromethyl (**4c**), and cyano (**4d**) groups were compatible with the reaction conditions. In all cases, the reaction led to the desired products in good yields and with excellent *ee* values over 90%. It is noteworthy that halides such as bromide in position 4 or 3 (products **4e** and **4f**, respectively) or chloride (product **4g**) were also tolerated, and the corresponding products could undergo further functionalization by cross-coupling reactions for the construction of more elaborate molecules. Challenging aldehydes with a substituent in the *ortho* position were then evaluated. With 2-fluorobenzaldehyde, we obtained the desired product **4h** with an exceptional enantioselectivity (99% *ee*). More sterically hindered aldehydes such as 2-methylbenzaldehyde or 2-chlorobenzaldehyde failed to participate in the reaction (not shown). Notably, heteroaromatic aldehydes such as furfuraldehyde were also successful in yielding the expected product **4i** with high stereocontrol (98% *ee*). The highly reactive 2-naphthalenecarboxaldehyde can also participate in the reaction to give the desired product in excellent yield and selectivity. As often reported, electron-rich aromatic aldehydes are known to be less reactive in NHC-catalyzed processes. For example, attempts to carry out the reaction

Table 1: Optimization of the reaction conditions.[a]



1a **2** **4a**

Entry	Base	Solvent	*T* [°C]	*t* [h]	Yield [%][b]	*ee* [%]
1[c]	KHMDS	dioxane	25	24	(10)	97
2[d]	TBD	dioxane	25	24	22	n.d.
3[d]	TBD	THF	25	24	17	n.d.
4[d]	TBD	toluene	25	24	41	84
5[d]	DBU	toluene	25	24	49	85
6[d]	K_2CO_3	toluene	25	24	23	n.d.
7	K_2CO_3	toluene	25	24	31	90
8[e]	KHMDS	toluene	25	24	67	95
9[e]	KO*t*Bu	toluene	25	24	65	95
10[e]	KO*t*Bu	toluene	0	4	99 (98)	95
11[e]	KO*t*Bu	toluene	0	65	99	95
12[e,f]	KO*t*Bu	toluene	0	24	72	n.d.
13[g]	**KO*t*Bu**	**toluene**	**0**	**3**	**95 (93)**	**95**

[a] General reaction conditions: **1a** (0.2 mmol, 1.0 equiv), **2** (0.4 mmol, 2.0 equiv), NHC·HCl **3** (10 mol%), base (10 mol%), 0.67 mL solvent (0.3 M). [b] Yield determined by ^{1}H NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard. Yields of isolated products are given in parentheses. [c] **1a** (0.4 mmol, 2.0 equiv), **2** (0.2 mmol, 1.0 equiv). [d] **2** (0.22 mmol, 1.1 equiv). [e] NHC·HCl **3** (15 mol%). [f] **2** (0.3 mmol, 1.5 equiv). [g] Base (8 mol%). On a 5 mmol scale, 95% yield and 94% *ee* were obtained. n.d. = not determined. DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene, KHMDS = potassium hexamethyldisilazide, TBD = 1,5,7-Triazabicyclo[4.4.0]dec-5-ene.

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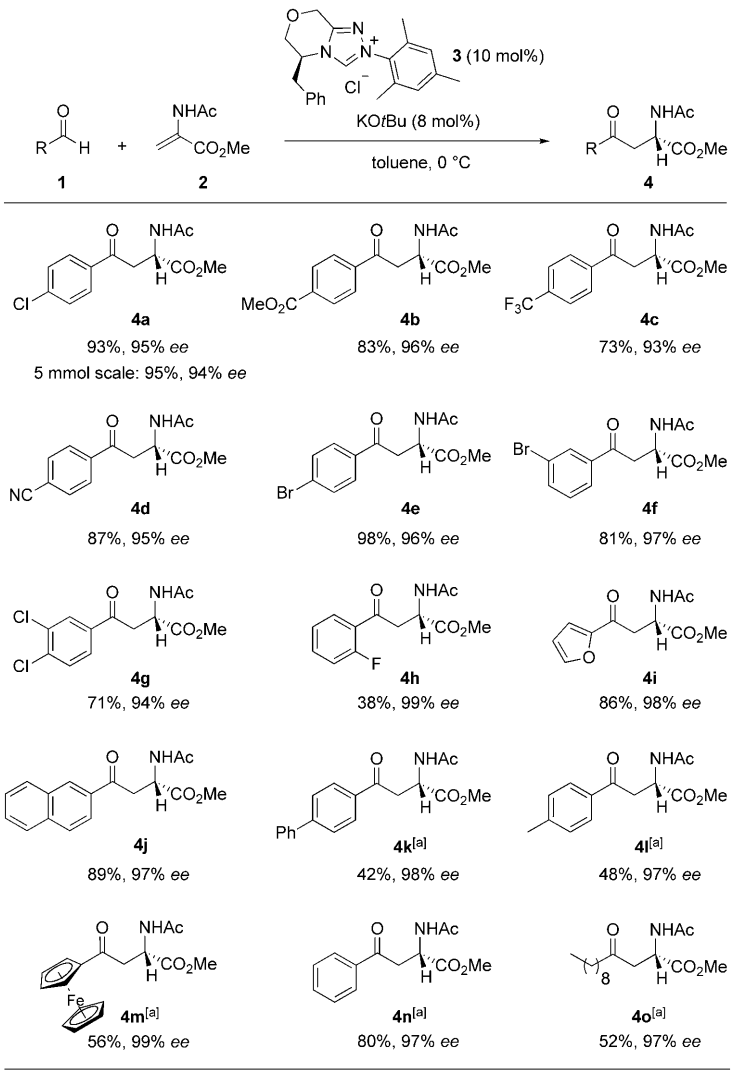
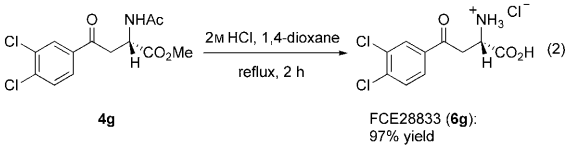


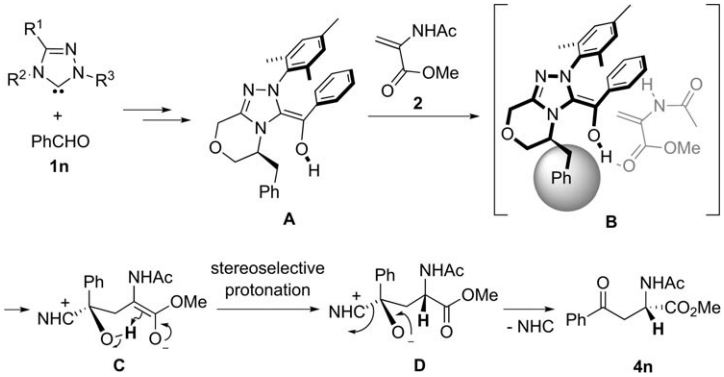
Scheme 3. Substrate scope of the enantioselective Stetter reaction. General reaction conditions: **1** (0.5 mmol), **2** (1.0 mmol), NHC·HCl **3** (10 mol%), KO*t*Bu (8 mol%) in toluene (1.8 mL) at 0 °C for 3–24 h. [a] Using NHC·HCl **3** (20 mol%) and KO*t*Bu (16 mol%).

starting from 4-methoxybenzaldehyde have only led to a low conversion (10% yield). Gratefully, however, the use of 20 mol% **3** in the reaction with 4-methylbenzaldehyde provided **4l** in moderate yield but excellent enantioselectivity. In addition, 4-phenylbenzaldehyde and ferrocenecarboxaldehyde also furnished the desired products **4k** and **4m** in moderate yield but in high enantioselectivity. Benzaldehyde was also suitable and led to the desired amino ester derivative **4n** in good conversion and high enantioselectivity. Moreover, an aliphatic aldehyde such as dodecanal is also a good substrate, thus demonstrating the value of this new synthetic method to make enantioenriched α-amino acid derivatives. In all cases, the absolute configuration of the major enantiomer can be assigned as *S* by comparison with optical rotations described previously.[17,18] To show the versatility of the products **4** we converted product **4g** into the selective kynurenine 3-hydroxylase inhibitor FCE28833 **6g**.[19] Simple deprotection under standard conditions gave the hydrochloride salt **6g** quantitatively and without apparent racemization [Eq. (2)].[17]



The mechanism and the asymmetric induction of this transformation can be rationalized as follows. First, the reaction between the free carbene derived from **3** and the aldehyde **1** leads to the formation of a nucleophilic enamine, the Breslow intermediate **A** (Scheme 4).[20] It can be assumed on the basis of computational calculations performed by Dudding and Houk[21] that the shown *E* isomer of **A** is more favorable than the *Z* isomer (not shown). The benzyl group in intermediate **A** successfully shields the top face of the Breslow intermediate. Thus, the Michael acceptor **2** approaches from the bottom face in an *anti* fashion, most likely supported by a hydrogen bond between the enol hydrogen atom and the carbonyl oxygen atom of the Michael acceptor (**B**). In this process, enolate **C** bearing a new but transient stereocenter is formed highly stereoselectively. The configuration is relayed to the α position by a stereoselective protonation of the transiently formed enolate. Finally, the NHC is released, thereby destroying the initially generated stereocenter and forming the final product **4**. However, **C** might not be a local energy minimum of this reaction and a concerted conjugate addition/protonation mechanism[22,23] cannot be ruled out.

In conclusion, we have developed an NHC-catalyzed enantioselective Stetter reaction with a highly stereoselective proton transfer as the key step



Scheme 4. Proposed stepwise mechanism for the enantioselective Stetter reaction.

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that leads to amino acid derivatives. This reaction is attractive for a number of reasons: rather simple and general starting materials are highly stereoselectively coupled under mild reaction conditions. Two valuable steps, C–C bond formation between the Breslow intermediate and the Michael acceptor and an asymmetric protonation, are efficiently combined. Further studies on the mechanism of this transformation and the development of related reactions should be worthwhile.

Experimental Section

General procedure: Dry KO*t*Bu (4.5 mg, 0.04 mmol) and the triazolium salt **3** (18.5 mg, 0.05 mmol) were added to a flame-dried screw-capped test tube equipped with a magnetic stir bar in a glove box. The mixture was dissolved in toluene (1.8 mL) under argon outside the glovebox. The resulting reaction mixture was stirred at 25 °C for 30 min and then cooled to 0 °C. After 10 min, 4-chlorobenzaldehyde (**1a**; 70.3 mg, 0.5 mmol) and the Michael acceptor **2** (143.2 mg, 1.0 mmol) were added successively. After 3 h (TLC monitoring showed completion of the reaction), the mixture was diluted with EtOAc (2 mL) and filtered through a pad of silica gel and eluted with EtOAc (10 mL). Evaporation of the solvent followed by purification by flash chromatography (40 % EtOAc in pentane then 60 %) afforded the corresponding amino ester **4a** as a white solid (131.6 mg, 93 % yield, 95 % *ee*).

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[1] For reviews on the stereoselective synthesis of α-amino acids, see a) C. Nájera, J. M. Sansano, *Chem. Rev.* **2007**, *107*, 4584; b) K. Maruoka, T. Ooi, *Chem. Rev.* **2003**, *103*, 3013.

[2] For an excellent review, see J. T. Mohr, A. Y. Hong, B. M. Stoltz, *Nat. Chem.* **2009**, *1*, 359.

[3] NHC-catalyzed asymmetric protonations: a) N. T. Reynolds, T. Rovis, *J. Am. Chem. Soc.* **2005**, *127*, 16406; b) B. E. Maki, A. Chan, K. A. Scheidt, *Synthesis* **2008**, 1306; for a very recent example of an NHC-catalyzed intramolecular, moderately diastereoselective protonation, see c) A. Kena Diba, C. Noll, M. Richter, M. T. Gieseler, M. Kalesse, *Angew. Chem.* **2010**, *122*, 8545; *Angew. Chem. Int. Ed.* **2010**, *49*, 8367.

[4] For organocatalyzed tandem conjugate addition and asymmetric protonations, see a) Y. Wang, X. Liu, L. Deng, *J. Am. Chem. Soc.* **2006**, *128*, 3928; b) B. Wang, F. Wu, Y. Wang, Y. Liu, L. Deng, *J. Am. Chem. Soc.* **2007**, *129*, 768; c) D. Leow, S. Lin, S. K. Chittimalla, X. Fu, C.-H. Tan, *Angew. Chem.* **2008**, *120*, 5723; *Angew. Chem. Int. Ed.* **2008**, *47*, 5641; d) M. Rueping, T. Theissmann, S. Raja, J. W. Bats, *Adv. Synth. Catal.* **2008**, *350*, 1001; e) M. Rueping, A. P. Antonchick, *Angew. Chem.* **2007**, *119*, 4646; *Angew. Chem. Int. Ed.* **2007**, *46*, 4562; f) M. Rueping, A. P. Antonchick, T. Theissmann, *Angew. Chem.* **2006**, *118*, 3765; *Angew. Chem. Int. Ed.* **2006**, *45*, 3683.

[5] For metal-catalyzed tandem conjugate addition and asymmetric protonations, see a) M. Morita, L. Drouin, R. Motoki, Y. Kimura, I. Fujimori, M. Kanai, M. Shibasaki, *J. Am. Chem. Soc.* **2009**, *131*, 3858; b) M. P. Sibi, J. Coulomb, L. M. Stanley, *Angew. Chem.* **2008**, *120*, 10061; *Angew. Chem. Int. Ed.* **2008**, *47*, 9913; c) M. P. Sibi, H. Tatamidani, K. Patil, *Org. Lett.* **2005**, *7*, 2571; d) A. D. Sadow, I. Haller, L. Fadini, A. Togni, *J. Am. Chem. Soc.* **2004**, *126*, 14704; e) R. J. Moss, K. J. Wadsworth, C. J. Chapman, C. G. Frost, *Chem. Commun.* **2004**, 1984; f) Y. Hamashima, H. Somei, Y. Shimura, T. Tamura, M. Sodeoka, *Org. Lett.* **2004**, *6*, 1861; for metal-catalyzed hydrogen atom transfer, see g) M. P. Sibi, J. B. Sausker, *J. Am. Chem. Soc.* **2002**, *124*, 984.

[6] For metal-catalyzed tandem conjugate addition and asymmetric protonations leading to the asymmetric synthesis of α-amino acid derivatives, see a) L. Navarre, R. Martinez, J.-P. Genet, S. Darses, *J. Am. Chem. Soc.* **2008**, *130*, 6159; b) L. Navarre, S. Darses, J.-P. Genet, *Angew. Chem.* **2004**, *116*, 737; *Angew. Chem. Int. Ed.* **2004**, *43*, 719; hydrogen atom transfer: c) M. P. Sibi, Y. Asano, J. B. Sausker, *Angew. Chem.* **2001**, *113*, 1333; *Angew. Chem. Int. Ed.* **2001**, *40*, 1293.

[7] H. Pracejus, F. W. Wilcke, K. Hanemann, *J. Prakt. Chem.* **1977**, *319*, 219.

[8] For reviews on NHC organocatalysis, see a) V. Nair, S. Vellalath, B. P. Babu, *Chem. Soc. Rev.* **2008**, *37*, 2691; b) D. Enders, O. Niemeier, A. Henseler, *Chem. Rev.* **2007**, *107*, 5606; c) N. Marion, S. Díez-González, S. P. Nolan, *Angew. Chem.* **2007**, *119*, 3046; *Angew. Chem. Int. Ed.* **2007**, *46*, 2988; d) E. M. Phillips, A. Chan, K. A. Scheidt, *Aldrichimica Acta* **2009**, *42*, 55; e) J. L. Moore, T. Rovis, *Top. Curr. Chem.* **2010**, *291*, 77; for a recent review on the physicochemical properties of NHCs, see f) T. Dröge, F. Glorius, *Angew. Chem.* **2010**, *122*, 7094; *Angew. Chem. Int. Ed.* **2010**, *49*, 6940.

[9] For seminal work, see a) H. Stetter, M. Schreckenberg, *Angew. Chem.* **1973**, *85*, 89; *Angew. Chem. Int. Ed. Engl.* **1973**, *12*, 81; b) H. Stetter, H. Kuhlmann, *Angew. Chem.* **1974**, *86*, 589; *Angew. Chem. Int. Ed. Engl.* **1974**, *13*, 539; for reviews, see c) H. Stetter, H. Kuhlmann, *Org. React.* **1991**, *40*, 407; d) D. Enders, T. Balensiefer, *Acc. Chem. Res.* **2004**, *37*, 534; e) T. Rovis, *Chem. Lett.* **2008**, *37*, 2.

[10] For pioneering studies, see a) D. Enders, K. Breuer, J. Runsink, J. H. Teles, *Helv. Chim. Acta* **1996**, *79*, 1899; b) M. S. Kerr, J. Read de Alaniz, T. Rovis, *J. Am. Chem. Soc.* **2002**, *124*, 10298; for further selected examples, see c) J. Pesch, K. Harms, T. Bach, *Eur. J. Org. Chem.* **2004**, 2025; d) S. M. Mennen, J. T. Blank, M. B. Tran-Dube, J. E. Imbriglio, S. J. Miller, *Chem. Commun.* **2005**, 195; e) J. Read de Alaniz, T. Rovis, *J. Am. Chem. Soc.* **2005**, *127*, 6284; f) Q. Liu, T. Rovis, *J. Am. Chem. Soc.* **2006**, *128*, 2552.

[11] a) D. Enders, J. Han, A. Henseler, *Chem. Commun.* **2008**, 3989; b) D. Enders, J. Han, *Synthesis* **2008**, 3864.

[12] a) Q. Liu, S. Perreault, T. Rovis, *J. Am. Chem. Soc.* **2008**, *130*, 14066; b) Q. Liu, T. Rovis, *Org. Lett.* **2009**, *11*, 2856; c) D. A. DiRocco, K. M. Oberg, D. M. Dalton, T. Rovis, *J. Am. Chem. Soc.* **2009**, *131*, 10872.

[13] For the highly selective, although low-yielding enzyme-catalyzed intermolecular Stetter reaction, see C. Dresen, M. Richter, M. Pohl, S. Lüdeke, M. Müller, *Angew. Chem.* **2010**, *122*, 6750; *Angew. Chem. Int. Ed.* **2010**, *49*, 6600.

[14] a) N. Kuhl, F. Glorius, *Chem. Commun.* **2011**, *47*, 573; b) M. Padmanaban, A. T. Biju, F. Glorius, *Org. Lett.* **2011**, DOI: 10.1021/ol102626p; c) R. Lebeuf, K. Hirano, F. Glorius, *Org. Lett.* **2008**, *10*, 4243; d) K. Hirano, I. Piel, F. Glorius, *Adv. Synth. Catal.* **2008**, *350*, 984.

[15] M. Wadamoto, E. M. Phillips, T. E. Reynolds, K. A. Scheidt, *J. Am. Chem. Soc.* **2007**, *129*, 10098.

[16] 10 mol % base and 15 mol % NHC·HCl **3** were used and stirred in toluene for 30 min before addition of the starting materials to ensure that there is no free base.

[17] See the Supporting Information for details.

[18] Methyl ester **4n** was converted into the corresponding ethyl ester **5n** without epimerization. The optical rotation data for this ethyl ester was compared with literature data for the same compound with known absolute configuration.[17]

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[19] A. Giordani, L. Corti, M. Cini, R. Bormetti, M. Marconi, O. Veneroni, C. Speciale, M. Varasi, *Adv. Exp. Med. Biol.* **1996**, *398*, 531.
[20] For a truly pioneering report, see R. Breslow, *J. Am. Chem. Soc.* **1958**, *80*, 3719.
[21] a) T. Dudding, K. N. Houk, *Proc. Natl. Acad. Sci. USA* **2004**, *101*, 5770; for additional insightful mechanistic studies of the Stetter reaction, see b) K. J. Hawkes, B. F. Yates, *Eur. J. Org. Chem.* **2008**, 5563; c) R. L. Knight, F. J. Leeper, *J. Chem. Soc. Perkin Trans. 1* **1998**, 1891.
[22] For NHC-catalyzed hydroacylation reactions of unactivated alkenes, alkynes, and arynes that might proceed by a related concerted transition state, see a) K. Hirano, A. T. Biju, I. Piel, F. Glorius, *J. Am. Chem. Soc.* **2009**, *131*, 14190; b) A. T. Biju, N. E. Wurz, F. Glorius, *J. Am. Chem. Soc.* **2010**, *132*, 5970; c) A. T. Biju, F. Glorius, *Angew. Chem.* **2010**, *122*, 9955; *Angew. Chem. Int. Ed.* **2010**, *49*, 9761; for a related work, see d) J. He, S. Tang, J. Liu, Y. Su, X. Pan, X. She, *Tetrahedron* **2008**, *64*, 8797.
[23] For analogous concerted transformations proceeding through five-membered transition states, see a) D. Niu, K. Zhao, *J. Am. Chem. Soc.* **1999**, *121*, 2456; b) J.-G. Roveda, C. Clavette, A. D. Hunt, S. I. Gorelsky, C. J. Whipp, A. M. Beauchemin, *J. Am. Chem. Soc.* **2009**, *131*, 8740; c) A. M. Beauchemin, J. Moran, M.-E. Lebrun, C. Séguin, E. Dimitrijevic, L. Zhang, S. I. Gorelsky, *Angew. Chem.* **2008**, *120*, 1432; *Angew. Chem. Int. Ed.* **2008**, *47*, 1410.

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