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Enantioselective biomimetic cyclization of 2′-hydroxychalcones to flavanones

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ABSTRACT

A new family of organocatalysts based on aminoquinoline and pyrrolidine have been developed and shown to catalyze the direct and highly enantioselective cyclization of 2′-hydroxychalcones in imitation of the natural process of chalcone cyclization. The straightforward synthetic process occurs under mild reaction conditions, tolerates moisture and air, and gives an enantiomeric excess up to 99%. This approach provides a facile and efficient access to chiral flavanones.

Flavonoids make up a large family of versatile secondary metabolites that fulfill many functions in plants such as UV filtration, symbiotic nitrogen fixation, and floral pigmentation.[1] In addition to their biological roles, many flavonoids have been studied for potential human health benefits. A subgroup of flavonoids called flavanones contain 'privileged structures' that exhibit a broad range of biological activities including anticancer, antitumor, antibacterial, antimicrobial, antioxidant, estrogenic, and anti-estrogenic.[2] Flavanones are also precursors of numerous other plant metabolites such as flavanols, dihydroflavanols, deoxyantocyanidins, and various polyphenolics.[3] Given their range of interesting physiological roles in plants and health-promoting roles in humans, significant efforts have been devoted to isolation of flavanones from plants as well as synthesis in laboratories.

Since flavanones cannot be isolated efficiently from plants, they are quite attractive to synthetic chemists.[4] Despite numerous efforts, researchers have developed few ways to synthesize flavanones enantioselectively.[5,6] In early work, researchers obtained enantio-enriched flavanones by resolving racemic flavanone mixtures[7] or performing asymmetric reduction of flavones.[8] Recent work focused on the intramolecular Mitsunobu reaction of β-hydroxy ketone[9] and on intermolecular conjugate addition of a metal-based nucleophile to a 4-chromone.[10] More recently, intramolecular asymmetric conjugate addition has been achieved using chalcones activated by C-2 *tert*-butyl ester, yielding the corresponding flavanone-3-carboxylic esters. These esters were then decarboxylated under acidic conditions to afford flavanones (Scheme 1, a).[11] All these synthetic procedures involve more steps and are less efficient and enantioselective than in nature, where the enzyme chalcone isomerase (CHI) catalyzes the cyclization of 2′-hydroxychalcones to yield (2*S*)-flavanones (Scheme 1, b).[12] This enzyme-catalyzed intramolecular oxa-Michael addition occurs in a simple and elegant one-step reaction, generates no byproducts, and is completely enantioselective.

To approach the efficiency of the CHI-catalyzed reaction, many investigators have searched without success for a catalyst that facilitates the direct enantioselective cyclization of 2′-hydroxychalcones into the desired flavanones.[11a,13] These failures can be ascribed to the reversibility and poor reactivity of chalcones.[10j,11a,14] Hintermann et al. achieved a breakthrough when they used chiral quaternary ammonium salts (e.g., 9-anthracenylmethlycinchoninium chloride) and NaH as small-molecule co-catalysts to achieve the cyclization of 2′-hydroxychalcones (**1**) into flavanones (**2**) with 38–87% ee.[15] However, this method should be performed under argon to prolong the life of the strongly basic NaH co-catalyst.

As part of our efforts to develop a more practical catalytic system that mimics the direct asymmetric cyclization of 2′-hydroxychalcones to flavanones in nature, we present here a novel organocatalyst that facilitates the enantioselective synthesis of flavanones from a broad range of substrates with ee up to 99%.

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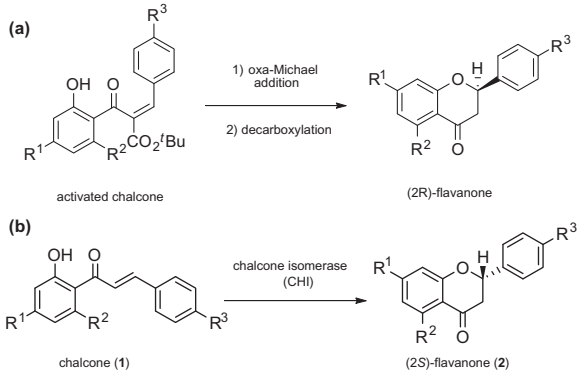
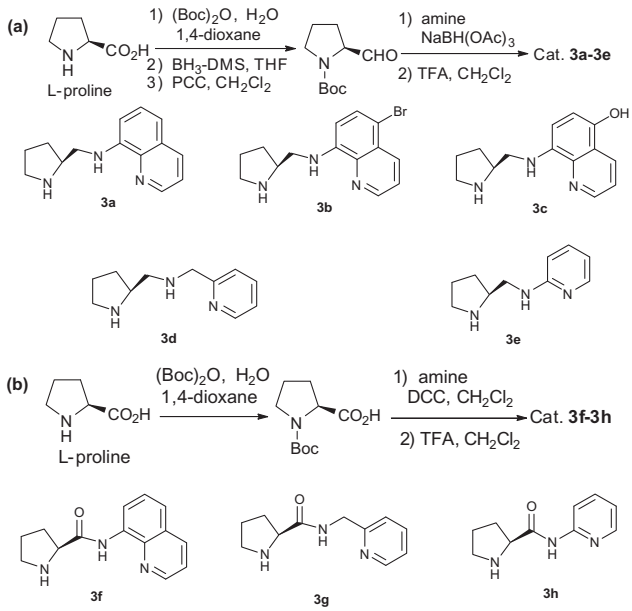


Scheme 1. (a) Strategy for synthesizing chiral flavanone using chalcones activated by C-2 *tert*-butyl ester as substrates. (b) Enzymatic cyclization of chalcones to flavanones.

The reaction is conducted at room temperature and it tolerates moisture and air, bringing it much closer to the simplicity of the CHI-catalyzed reaction.

Organocatalysis, one of the main branches of enantioselective synthesis,[16] can be quite effective for synthesizing complex structures because of its operational simplicity and both the ready availability and low toxicity of organocatalysts.[16g] These advantages make organocatalysis particularly useful in pharmaceutical synthesis.[16d] In the field of organocatalysis, the discovery and design of new efficient catalysts is an everlasting subject.[16d] In searching for structurally diverse organocatalysts, recently we developed a new class of H-bond catalysts readily prepared from L-proline in 87% overall yield in five simple steps (Scheme 2a): Boc-protection, reduction, oxidation, amination, and deprotection (**3a**–**3d**). We envisioned that this kind of organocatalyst might catalyze the intramolecular oxa-Michael addition of 2′-hydroxychalcone to flavanone via a transition state as shown in Figure 1. The bifunctional catalyst may activate both enone and phenol hydroxyl simultaneously through the formation of an iminium-ion intermediate and hydrogen bond, directing the oxygen nucleophile to stereoselectively attack at the *Si*-face of the double bond to form the product.



Scheme 2. Preparation of organocatalysts.

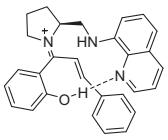
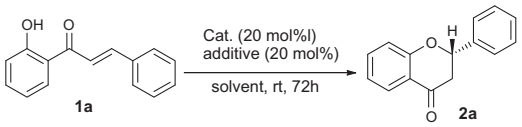


Figure 1. Possible transition state in the organocatalytic cyclization of 2′-hydroxychalcone to flavanone.

We tested the organocatalysts for their ability to catalyze the biomimetic cyclization of 2′-hydroxychalcones (**1**) to flavanones (**2**). The reaction was first performed in the presence of 20 mol % catalyst **3a** in toluene. To our delight, 2′-hydroxychalcone reacted smoothly to give the desired (2*S*)-flavanone in 35% yield with 49% ee (Table 1, entry 1). This result indicates that this kind of catalyst supports the enantioselective cyclization of 2′-hydroxychalcone to flavanone, acting analogously to CHI. Switching from catalyst **3a** to the analogous catalysts **3b** and **3c**, which contain, respectively, an additional electron-withdrawing group (Br) or electron-donating group (OH), led to lower yield and enantioselectivity (entries 2 and 3). The amide catalyst **3f** and pyridine-derived catalysts **3d** and **3g** gave only trace amounts of flavanone (**2a**) (entries 4–6). These results demonstrate that the chemical properties and structure of the catalyst are important for its ability to promote the enantioselective oxa-Michael reaction.

The optimal catalyst **3a** was then used to screen reaction conditions. We were pleased to find that lowering the reaction temperature to 15 °C increased the enantiomeric excess to 95% (Table 1, entry 7). This is, to our knowledge, the highest ee value ever reported for direct cyclization of 2′-hydroxychalcone to flavanone using a man-made catalyst. However, using this temperature slo-

Table 1
Optimization of reaction conditions[a,b]

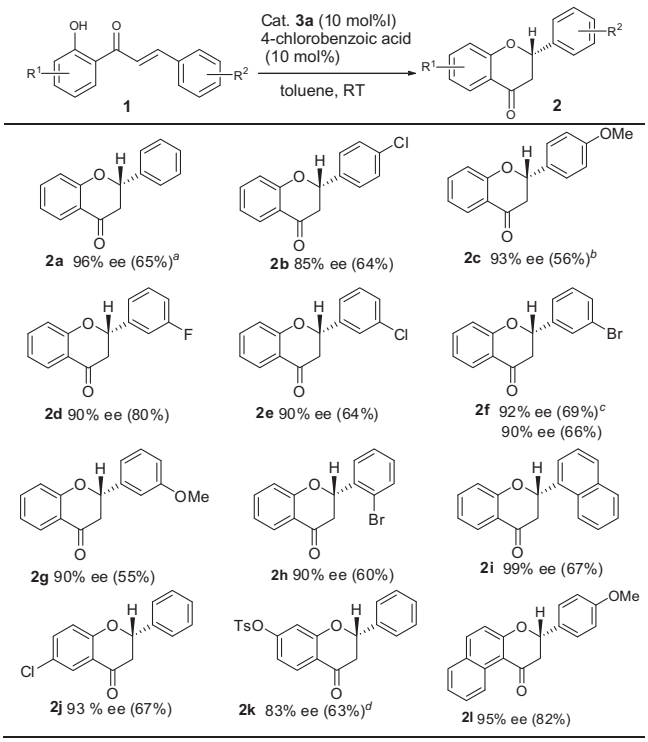


Entry	cat	Additive	Solvent	Temp (°C)	Yield[b] (%)	ee[c,d] (%)
1	**3a**	—	Toluene	25	35	49
2	**3b**	—	Toluene	25	27	42
3	**3c**	—	Toluene	25	13	37
4	**3f**	—	Toluene	25	<5	—
5	**3d**	—	Toluene	25	<5	—
6	**3g**	—	Toluene	25	<5	—
7	**3a**	—	Toluene	15	10	95
8	**3a**	—	Toluene	50	90	23
9	**3a**	—	Methanol	15	47	5
10	**3a**	—	DCM	15	13	38
11	**3a**	—	THF	15	48	8
12	**3a**	—	EA	15	25	41
13	**3a**	$C_6H_5CO_2H$	Toluene	25	71	37
14	**3a**	4-$ClC_6H_4CO_2H$	Toluene	25	68	96
15	**3a**	4-$FC_6H_4CO_2H$	Toluene	25	75	45
16	**3a**	2-$NO_2C_6H_4CO_2H$	Toluene	25	55	39
17	**3a**	2-$FC_6H_4CO_2H$	Toluene	25	64	47
18[e]	**3a**	4-$ClC_6H_4CO_2H$	Toluene	25	65	96
19	**3e**	4-$ClC_6H_4CO_2H$	Toluene	25	NR	—
20	**3h**	4-$ClC_6H_4CO_2H$	Toluene	25	NR	—

[a] Reaction conditions: **1a** (0.1 mmol), catalyst (20 mol %) and additive (20 mol %) in 0.3 mL solvent at RT (25 °C) for 72 h.
[b] Yield of isolated product.
[c] Determined by HPLC using a chiral stationary phase (See the Supporting information).
[d] Absolute configuration was determined as *S* by comparison of optical rotation to literature values (See the Supporting information).
[e] 10 mol % **3a** was used and the reaction time was 96 h. NR=no reaction.

wed the reaction such that conversion was only 12% after 72 h. Raising the reaction temperature increased the yield to 90% but the enantioselectivity decreased dramatically to 23% ee (entry 8). Varying the solvent could not enhance reactivity or enantioselectivity (entries 9–12). Given that adding organic acid could accelerate the formation of the iminium-ion intermediate,[17] we tested a series of organic acids in our cyclization system. As expected, the oxa-Michael reaction of 2′-hydroxychalcone was much faster in the presence of a catalytic amount of various benzoic acids (entries 13–17). The best result was obtained by adding 4-chlorobenzoic acid, which gave the desired flavanone in 68% yield with 96% ee (entry 14). Gratifyingly, the enantioselectivity was maintained and the yield remained mostly unchanged with decreased catalyst amount to 10 mol %, albeit a little longer time was needed (entry 18). We were intrigued to find that 2-aminopyridine derivatives could not substitute for **3a** to catalyze the oxa-Michael reaction of 2′-hydroxychalcone under the same reaction conditions (entries 19 and 20). We expected 2-aminopyridine derivatives to work because they are excellent H-bond catalysts reported previously.[18]

Under the optimized reaction conditions, a variety of representative 2′-hydroxychalcones were investigated (Scheme 3). Various substituted 2′-hydroxychalcones reacted smoothly in moderate to good yield with high enantioselectivity. Both electron-withdrawing and electron-donating groups were tolerated on the right aryl ring, yielding the desired products in 55–80% yield and 84–96% ee (Scheme 3, **2a–2h**). In particular, 2′-hydroxychalcone bearing naphthalene as the right aryl ring reacted smoothly to afford the corresponding flavanone in 67% yield with 99% ee (Scheme 3, **2i**). This high enantioselectivity is probably due to good arene π-stacking between substrate and catalyst.



Scheme 3. Substrate scope. General reaction conditions: **1** (0.1 mmol), catalyst **3a** (10 mol %) and 4-chlorobenzoic acid (10 mol %) in 0.3 mL toluene at rt. Values for ee were determined by HPLC using a chiral stationary phase (see the Supporting information). Yields of isolated products are shown in parentheses. The absolute configuration of **2a–2c** and **2i** were determined as *S* by comparison of optical rotation to literature values (see the Supporting information details). [a]1 mmol substrate was used. [b]2,4-Dichlorobenzoic acid was used as additive, 20 mol % **3a** was used. [c]Recovered catalyst **3a** was used. [d]The reaction was performed at 50 °C without additive.

We also examined the effect of electronic and structural variations on the left aryl ring. Previous study, in which chiral flavanones were generated from chalcones activated by C-2 *tert*-butyl ester (Scheme 1a), reported that electron-poor substituents on the phenol moiety dramatically decreased the enantioselectivity of the oxa-Michael reaction[11b]; for example, flavanone substituted with chloride (**2j**) was produced with only 40% ee.[11b] We were pleased to find that adding Cl to the phenol moiety created a suitable Michael donor for our cyclization reaction; the substrate generated the corresponding product **2j** in good yield with 93% ee (Scheme 3, **2j**). Placing an electron-withdrawing 4′-TsO group on the phenol moiety also afforded the desired flavanone in 63% yield with 83% ee (Scheme 3, **2k**).

2′-Hydroxy-naphthol chalcones were challenging substrates for the oxa-Michael reaction in the literature, for instance, flavanone (**2l**) was obtained with 46% ee.[15a] Pleasingly, this substrate could be converted into the desired flavanone in good yield with high enantioselectivity by our approach (e.g., **2l** 82% yield and 95% ee, Scheme 3). Our organocatalytic process was readily scaled up to 1 mmol without loss of reactivity or enantioselectivity (Scheme 3, **2a**). In addition, the catalyst was conveniently recovered using an acid–base conversion procedure. The recovered catalyst could promote the biomimetic cyclization of 2′-hydroxychalcone in good yield albeit with slightly decreased enantioselectivity (Scheme 3, **2f**). These reaction conditions tolerated certain functional substituents, including F, Cl, Br, and TsO, which can subsequently be transformed into other functionalities.

In summary, we have designed and synthesized a new family of organocatalysts based on aminoquinoline and pyrrolidine. The organocatalysts can promote enantioselective oxa-Michael reaction of 2′-hydroxychalcones to afford flavanones in good yield with high enantioselectivity. The simple and straightforward biomimetic cyclization is performed under mild conditions and it tolerates moisture and air. This approach provides a facile and efficient access to chiral flavanones. Studies of the mechanism and applications of this catalytic system are in progress.

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Supplementary data

Supplementary data (Experiment details, copies of HPLC, ^{1}H and ^{13}C NMR spectra for products. This material is available free of charge via the Internet at doi.) associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2014.04.032.

References and notes

1. (a)*The Flavonoids: Advances in Research Since 1980*; Harborne, J. B., Ed.; Chapman and Hall: New York, 1988; (b) Andersen, Ø. M.; Markham, K. R. *Flavonoids: Chemistry, Biochemistry and Applications*; CRC, Taylor & Francis: Boca Raton, FL, 2006; (c) Veitch, N. C.; Grayer, R. J. *Nat. Prod. Rep.* **2011**, *28*, 1626–1695.
2. (a) Prasad, S.; Phromnoi, K.; Yadav, V. R.; Chaturvedi, M. M.; Aggarwal, B. B. *Planta Med.* **2010**, *76*, 1044–1063; (b) Williams, R. J.; Spencer, J. P. E. *Free Radical Biol. Med.* **2012**, *52*, 35–45.
3. Keller, R. B. *Flavonoids: Biosynthesis, Biological Effects and Dietary Sources*; Nova Science: Hauppauge, NY, 2009.
4. Selected examples: (a) Tanaka, K.; Sugino, T. *Green Chem.* **2001**, *3*, 133–137; (b) Sarvanamurugan, S.; Palanichamy, M.; Arabindoo, B.; Murugesan, V. *J. Mol. Catal. A: Chem.* **2004**, *218*, 101–105.

5. For reviews: (a) Nibbs, A. E.; Scheidt, K. A. *Eur. J. Org. Chem.* **2012**, 449; (b) Marais, J. P. J.; Ferreira, D.; Slade, D. *Phytochemistry* **2005**, *66*, 2145.
6. (a) Zhao, D.; Beiring, B.; Glorius, F. *Angew. Chem., Int. Ed.* **2013**, *52*, 8454–8458; (b) Holder, J. C.; Marziale, A. N.; Gatti, M.; Mao, B.; Stoltz, B. M. *Chem. Eur. J.* **2013**, *19*, 74–77; (c) Zhou, S.; Zhou, Y.; Xing, Y.; Wang, N.; Cao, L. *Chirality* **2011**, *23*, 504–506; (d) Chen, J.; Liao, J. *Chin. J. Synth. Chem.* **2010**, *18*, 529–532; (e) Kawasaki, M.; Asano, Y.; Katayama, K.; Inoue, A.; Hiraoka, C.; Kakuda, H.; Tanaka, A.; Goto, M.; Toyooka, N.; Kometani, T. *J. Mol. Catal. B: Enzym.* **2008**, *54*, 93–102; (f) Fang, Y.-T.; Lin, C.-N.; Wu, H.-T.; Lee, Y.-J. *J. Chin. Chem. Soc.* **2007**, *54*, 817–822; (g) Ramadas, S.; Krupadanam, G. L. D. *Tetrahedron: Asymmetry* **2004**, *15*, 3381–3391; (h) Todoroki, T.; Saito, A.; Tanaka, A. *Biosci. Biotechnol. Biochem.* **2002**, *66*, 1772–1774; (i) Augustyn, J. A. N.; Bezuidenhoudt, B. C. B.; Ferreira, D. *Tetrahedron* **1990**, *46*, 2651–2660; (j) Takahashi, H.; Li, S.; Harigaya, Y.; Onda, M. *Chem. Pharm. Bull.* **1988**, *36*, 1877–1881; (k) Saengchantara, S. T.; Wallace, T. W. *J. Chem. Soc., Chem. Commun.* **1986**, 1592–1595; (l) Takahashi, H.; Kubota, Y.; Miyazaki, H.; Onda, M. *Chem. Pharm. Bull.* **1984**, *32*, 4852–4857.
7. (a) Corey, E. J.; Mitra, R. B. *J. Am. Chem. Soc.* **1962**, *84*, 2938–2941; (b) Rakosi, M.; Tokes, A. L.; Bognar, R. *Tetrahedron Lett.* **1970**, *11*, 2305–2308; (c) Takahashi, H.; Kubota, Y.; Miyazaki, H.; Onda, M. *Heterocycles* **1984**, *22*, 1147–1153; (d) Izumi, T.; Hino, T.; Kasahara, A. *J. Chem. Soc., Perkin Trans. 1* **1992**, 1265–1267; (e) Izumi, T.; Suenaga, K. *J. Heterocycl. Chem.* **1997**, *34*, 1535–1538; (f) Tanaka, T.; Kumamoto, T.; Ishikawa, T. *Tetrahedron Lett.* **2000**, *41*, 10229–10232; (g) Izumi, T.; Murakami, S. *J. Heterocycl. Chem.* **1995**, *32*, 1125–1127; (h) van Rensburg, H.; van Heerden, P. S.; Bezuidenhoudt, B. C. B.; Ferreira, D. *Tetrahedron* **1997**, *53*, 14141–14152; (i) Jew, S.; Kim, H.; Bae, S.; Kim, J.; Park, H. *Tetrahedron Lett.* **2000**, *41*, 7925–7928; (j) Kawasaki, M.; Kakuda, H.; Goto, M.; Kawabata, S.; Kometani, T. *Tetrahedron: Asymmetry* **2003**, *14*, 1529–1534; (k) Metz, P.; Schwab, P. WO 2008/003774 A1, Jan. 10, 2008.; (l) Lei, B.-L.; Ding, C.-H.; Yang, X.-F.; Wan, X.-L.; Hou, X.-L. *J. Am. Chem. Soc.* **2009**, *131*, 18250–18251.
8. (a) Bokel, H.; Mackert, R.; Muramann, C.; Schweickert, N. U.S. Patent 66646136 B1, Nov. 11, 2003.; (b) Gontcharov, A. V.; Nikitenko, A. A.; Raveendranath, P.; Shaw, C.; Wilk, B. K.; Zhou, D. WO 2007/123941 A2, Nov. 1, 2007.; (c) Pfaltz, A.; Valla, C.; Baeza, A.; Menges, F. *Synlett* **2008**, 3167–3171; (d) Fu, G. C.; Chung, Y. K. *Angew. Chem., Int. Ed.* **2009**, *48*, 2225–2227; (e) Sridharan, V.; Suryavanshi, P. A.; Menéndez, J. C. *Chem. Rev.* **2011**, *111*, 7157–7259.
9. (a) Hodgetts, K. J. *Tetrahedron Lett.* **2001**, *42*, 3763–3766; (b) Noda, Y.; Watanabe, M. *Helv. Chim. Acta* **2002**, *85*, 3473–3477; (c) Hodgetts, K. J. *Tetrahedron* **2005**, *61*, 6860–6870; (d) But, T. Y. S.; Toy, P. H. *Chem. Asian J.* **2007**, *2*, 1340–1355; (e) Swamy, K. C. K.; Kumar, N. N. B.; Balaraman, E.; Kumar, K. V. P. P. *Chem. Rev.* **2009**, *109*, 2551–2651.
10. (a) Saengchantara, S. T.; Wallace, T. W. *Tetrahedron* **1990**, *46*, 6553–6564; (b) Solladie, G.; Gehrold, N.; Maignan, J. *Tetrahedron: Asymmetry* **1999**, *10*, 2739–2747; (c) Ueda, M.; Miyaura, N. *J. Organomet. Chem.* **2000**, *595*, 31–35; (d) Ramnauth, J.; Poulin, O.; Bratovanov, S. S.; Rakhit, S.; Maddaford, S. P. *Org. Lett.* **2001**, *3*, 2571–2573; (e) Brown, M. K.; Degrado, S. J.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2005**, *44*, 5306–5310; (f) Shintani, R.; Yamagami, T.; Kimura, T.; Hayashi, T. *Org. Lett.* **2005**, *7*, 5317–5319; (g) Ueura, K.; Miyamura, S.; Satoh, T.; Miura, M. *J. Organomet. Chem.* **2006**, *691*, 2821–2826; (h) Shintani, R.; Tsutsumi, Y.; Nagaosa, M.; Nishimura, T.; Hayashi, T. *J. Am. Chem. Soc.* **2009**, *131*, 13588–13589; (i) Chen, J.; Chen, J. M.; Lang, F.; Zhang, X. Y.; Cun, L. F.; Zhu, J.; Deng, J. G.; Liao, J. *J. Am. Chem. Soc.* **2010**, *132*, 4552–4553; (j) Liao, J.; Han, F. Z.; Chen, G. H.; Zhang, X. Y. *Eur. J. Org. Chem.* **2011**, 2928–2931; (k) Korenaga, T.; Hayashi, K.; Akaki, Y.; Maenishi, R.; Sakai, T. *Org. Lett.* **2011**, *13*, 2022–2025.
11. (a) Biddle, M. M.; Lin, M.; Scheidt, K. A. *J. Am. Chem. Soc.* **2007**, *129*, 3830–3831; (b) Wang, L. J.; Liu, X. H.; Dong, Z. H.; Fu, X.; Feng, X. M. *Angew. Chem., Int. Ed.* **2008**, *47*, 8670–8673; (c) Farmer, R. L.; Biddle, M. M.; Nibbs, A. E.; Huang, X. K.; Bergan, R. C.; Scheidt, K. A. *ACS Med. Chem. Lett.* **2010**, *1*, 400–405; (d) Feng, Z.; Zeng, M.; Xu, Q.; You, S. *Chin. Sci. Bull.* **2010**, *55*, 1723–1725; (e) Liu, X. Q.; Lu, Y. X. *Org. Lett.* **2010**, *12*, 5592–5595; (f) Wang, H.-F.; Xiao, H.; Wang, X.-W.; Zhao, G. *Tetrahedron* **2011**, *67*, 5389–5394.
12. (a) Ngaki1, M. N.; Louie, G. V.; Philippe, R. N.; Manning, G.; Pojer, F.; Bowman, M. E.; Li, L.; Larsen, E.; Wurtele, E. S.; Noel, J. P. *Nature* **2012**, *485*, 530–533; (b) Jez, J. M.; Noel, J. P. *J. Biol. Chem.* **2002**, *277*, 1361–1369; (c) Jez, J. M.; Bowman, M. E.; Noel, J. P. *Biochemistry* **2002**, *41*, 5168–5176; (d) Jez, J. M.; Bowman, M. E.; Dixon, R. A.; Noel, J. P. *Nat. Struct. Biol.* **2000**, *7*, 786–791.
13. (a) Maruyama, K.; Tamanaka, K.; Nishinaga, A.; Inada, A.; Nakanishi, T. *Tetrahedron Lett.* **1989**, *30*, 4145–4148; (b) Tanaka, K.; Sugino, T. *Green Chem.* **2001**, *3*, 133–134; (c) Patonay, T.; Varma, R. S.; Vass, A.; Lévai, A.; Dudás, J. *Tetrahedron Lett.* **2001**, *42*, 1403–1406; (d) Chandrasekhar, S.; Vijeender, K.; Reddy, K. V. *Tetrahedron Lett.* **2005**, *46*, 6991–6993.
14. (a) Wang, H. F.; Cui, H. F.; Chai, Z.; Li, P.; Zheng, C. W.; Yang, Y. Q.; Zhao, G. *Chem. Eur. J.* **2009**, *15*, 13299–13303; (b) Cui, H. F.; Li, P.; Chai, Z.; Zheng, C. W.; Zhao, G.; Zhu, S. Z. *J. Org. Chem.* **2009**, *74*, 1400–1402.
15. (a) Hintermann, L.; Dittmer, C. *Eur. J. Org. Chem.* **2012**, 5573–5584; (b) Dittmer, C.; Raabe, G.; Hintermann, L. *Eur. J. Org. Chem.* **2007**, 5886–5898.
16. (a) Bertelsen, S.; Jøgensen, K. A. *Chem. Soc. Rev.* **2009**, *38*, 2178–2189; (b) Barbas, C. F., III *Angew. Chem., Int. Ed.* **2008**, *47*, 42–47; (c) Dondoni, A.; Massi, M. *Angew. Chem., Int. Ed.* **2008**, *47*, 4638–4660; (d) MacMillan, D. W. C. *Nature* **2008**, *455*, 304–308; (e) Melchiorre, P.; Marigo, M.; Carlone, A.; Bartoli, G. *Angew. Chem., Int. Ed.* **2008**, *47*, 6138–6171; (f) Mukherjee, S.; Yang, J. W.; Hoffmann, S.; List, B. *Chem. Rev.* **2007**, *107*, 5471–5569; (g) Gaunt, M. J.; Johansson, C. C. C.; McNally, A.; Vo, N. T. *Drug Discovery Today* **2007**, *12*, 8–27; (h)*Enantioselective Organocatalysis*; Dalko, P. I., Ed.; Wiley-VCH: Weinheim, Germany, 2007; (i) Figueiredo, R. M.; de Christmann, M. *Eur. J. Org. Chem.* **2007**, 2575–2600; (j) List, B. *Chem. Commun.* **2006**, 819–824; (k) Taylor, M. S.; Jacobsen, E. N. *Angew. Chem., Int. Ed.* **2006**, *45*, 1520–1543.
17. (a) Nising, C. F.; Bräse, S. *Chem. Soc. Rev.* **2012**, *41*, 988–999; (b) Reyes, E.; Talavera, G.; Vicario, J. L.; Badía, D.; Carrillo, L. *Angew. Chem., Int. Ed.* **2009**, *48*, 5701–5704; (c) Erkkilä, A.; Majander, I.; Pihko, P. M. *Chem. Rev.* **2007**, *107*, 5416–5470.
18. (a) Tang, Z.; Cun, L.-F.; Cui, X.; Mi, A. Q.; Jiang, Y. Z.; Gong, L.-Z. *Org. Lett.* **2006**, *8*, 1263–1266; (b) Xu, X.-Y.; Tang, Z.; Wang, Y.-Z.; Luo, S.-W.; Cun, L.-F.; Gong, L.-Z. *J. Org. Chem.* **2007**, *72*, 9905–9913; (c) Takenaka, N.; Chen, J.; Captain, B.; Sarangthem, R. S.; Chandrakumar, A. *J. Am. Chem. Soc.* **2010**, *132*, 4536–4537; (d) Yu, C.; Qiu, J.; Zheng, F.; Zhong, W. *Tetrahedron Lett.* **2011**, *52*, 3298–3302.