ChemComm

COMMUNICATION

View Article Online
View Journal | View Issue

Cite this: *Chem. Commun.*, 2014, **50**, 7538

Received 28th March 2014,
Accepted 22nd May 2014

DOI: 10.1039/c4cc02295e

www.rsc.org/chemcomm

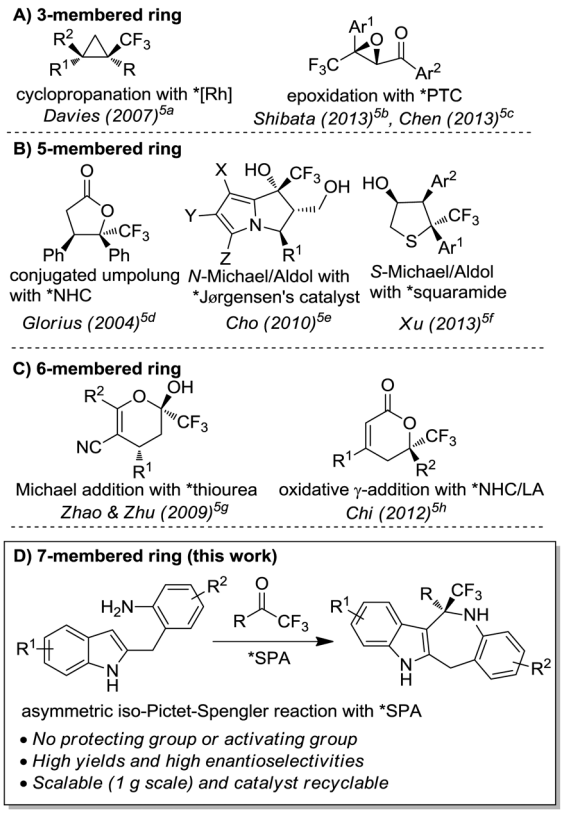
Enantioselective synthesis of benzazepinoindoles bearing trifluoromethylated quaternary stereocenters catalyzed by chiral spirocyclic phosphoric acids†

Xuejian Li, Di Chen, Haorui Gu and Xufeng Lin*

The first highly enantioselective iso-Pictet–Spengler reaction of C-2-linked *o*-aminobenzylindoles with trifluoromethyl ketones was developed using chiral spirocyclic phosphoric acids as organocatalysts, which afforded optically active benzazepinoindoles bearing trifluoromethylated quaternary stereocenters.

Chiral trifluoromethylated compounds have shown a great diversity of superior biological properties mainly due to improved chemical and metabolic stability, lipophilicity, and membrane permeability of the molecules.[1] In particular, some biologically active molecules with a CF_3-containing cyclic quaternary stereocenter are representative examples, including the HIV reverse transcriptase inhibitor (Efavirenz),[2a] the progesterone receptor antagonist,[2b] the NK-1 receptor antagonist (CJ-17493),[2c] and antimalarial agents (fluoroartemisinin).[2d]

Thus, great efforts have been devoted to the synthesis of functionalized molecules with a CF_3-containing stereocenter.[3] In particular, the catalytic enantioselective construction of trifluoromethylated quaternary stereocenters has recently generated a tremendous amount of interest.[4] In this context, a facile and flexible asymmetric catalytic cyclization reaction for the construction of cyclic quaternary stereocenters bearing a CF_3 moiety has not been well explored and remains a challenging project in organic synthesis. To date, only a few examples with a 3, 5 or 6-membered ring have been documented (Scheme 1).[5] These elegant asymmetric cyclization reactions were realized by transition metal catalysis[5a] or cooperative catalysis of chiral N-heterocyclic carbene (NHC) and Lewis acid,[5h] as well as organocatalysis with a chiral phase-transfer catalyst (PTC),[5b,c] NHC,[5d] Jørgensen's catalyst,[5e] squaramide[5f] and thiourea.[5g] In spite of these notable advances, to the best of our knowledge, no example has thus far been reported for the catalytic asymmetric cyclization reaction for the synthesis of CF_3-containing seven-membered heterocycles. Therefore, the development of a novel and elegant method to meet this challenge is highly desirable.



Scheme 1 Approaches to the construction of cyclic quaternary stereocenters bearing a CF_3 moiety through asymmetric catalytic cyclization reactions. * = chiral reagent.

Over the past few years, the catalytic asymmetric Pictet–Spengler reaction for construction of chiral N-heterocycle frameworks has attracted enormous attention and witnessed significant progress.[6] However, there is still no general solution to a catalytic, highly enantioselective Pictet–Spengler reaction

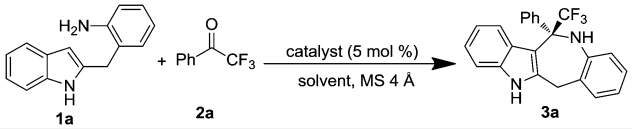
Laboratory of Asymmetric Catalysis and Synthesis, Department of Chemistry, Zhejiang University, Hangzhou 310027, P. R. China. E-mail: lxfok@zju.edu.cn

† Electronic supplementary information (ESI) available: Experimental procedures and characterization data for all new compounds. CCDC 953552 (**3aa**). For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c4cc02295e

with simple ketone substrates.[7] We recently developed a novel class of chiral spirocyclic phosphoric acids (SPAs), which proved to be highly efficient in asymmetric catalysis.[8,9] Employing such chiral SPAs we now report the first highly enantioselective catalytic iso-Pictet–Spengler reaction of C-2-linked *o*-aminobenzylindoles with commercial trifluoromethylated ketones to provide optically active benzazepinoindoles bearing trifluoromethylated quaternary stereocenters (Scheme 1D).[10]

In our initial study, we examined the model reaction between C-2-linked *o*-aminobenzylindole (**1a**) and phenyl trifluoromethyl ketone (**2a**) using chiral phosphoric acid catalysts in chloroform in the presence of powdered 4 Å molecular sieves. The reactions were run at 35 °C with a catalyst loading of 5 mol% and were stopped after 2 days. To our delight, the corresponding cyclization product **3aa** was obtained with 92% ee, albeit in a low yield, when (*S*)-**4a**, with bulky 6,6′-bis(9-anthracenyl) moieties, was used as the catalyst (Table 1, entry 1). We next screened chiral SPAs with various substituents in the 6,6′-positions, and found that (*S*)-**4b**, with 6,6′-bis(3,5-bis-trifluoromethylphenyl) moieties, gave the highest yield and excellent enantioselectivity (90% yield and 93% ee, Table 1, entry 2), whereas (*S*)-**4e**, with 6,6′-bis(4-nitrophenyl) moieties, exhibited no catalytic activity even under reflux (Table 1, entry 5). Furthermore, it should be noted that with a BINOL-based phosphoric acid (PA) catalyst system[11] ((*R*)-**5**, with 3,3′-bis(3,5-bis-trifluoromethylphenyl) moieties), only 20% yield was obtained and 84% ee was observed (Table 1, entry 6). The absolute configuration of the product was coincident with that of the product formed with the (*S*)-**4b** catalyst because (*S*)-PA and (*S*)-SPA are considered to be "pseudoenantiomers" owing to the difference in the nomenclature. Subsequent optimization suggested that the solvent remarkably affected the catalytic activity. The use of 1,2-dichloroethane as a solvent provided both excellent yield and enantioselectivity (95% yield and 93% ee, Table 1, entry 8), whereas the reaction hardly occurred in coordinating solvents, such as CH_3CN or THF even at reflux temperature (Table 1, entries 9 and 10).

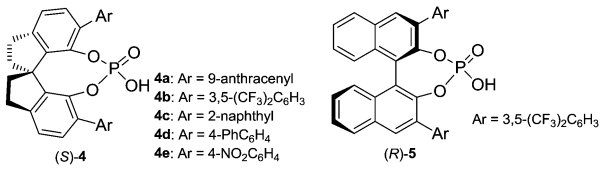
Table 1 Optimization of reaction parameters[a]



1a 2a 3a

Entry	Catalyst	Solvent	*t* [h]	Yield[b] (%)	ee[c] (%)
1	(*S*)-**4a**	$CHCl_3$	48	35	92
2	(*S*)-**4b**	$CHCl_3$	48	90	93
3[d]	(*S*)-**4c**	$CHCl_3$	48	10	86
4	(*S*)-**4d**	$CHCl_3$	48	50	93
5[d]	(*S*)-**4e**	$CHCl_3$	48	Trace	—
6	(*R*)-**5**	$CHCl_3$	48	20	84
7	(*S*)-**4b**	CH_2Cl_2	24	90	88
8	(*S*)-**4b**	CH_2ClCH_2Cl	24	95	93
9[d]	(*S*)-**4b**	CH_3CN	48	Trace	—
10[d]	(*S*)-**4b**	THF	48	Trace	—
11	(*S*)-**4b**	Toluene	24	85	89

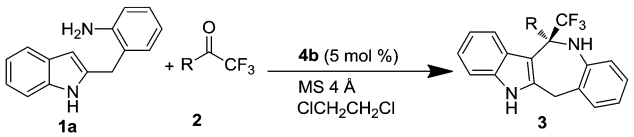
[a] Reaction conditions: catalyst (5 mol%, 0.005 mmol), **1a** (0.1 mmol), **2a** (0.12 mmol), molecular sieves (MS 4 Å, 0.1 g), solvent (0.6 mL), 35 °C. [b] Isolated yields. [c] Determined by chiral HPLC analysis. [d] Under reflux.



(*S*)-**4** (*R*)-**5**

We next turned our attention to assessing the substrate scope of the reaction. The optimized reaction conditions summarized in entry 8 in Table 1 were firstly used to study the scope of a series of commercially available trifluoromethyl ketones. All the reactions with aromatic trifluoromethyl ketones (**2a–2o**) provided the expected products **3aa–3ao** in good yields (80–95%) with high enantiomeric excess (87–>99.5%) (Table 2). Product **3aa** is a crystalline compound, and the ee could be easily increased to 99% by one simple recrystallization (Table 2, entry 1). For substrates **2b–2e** bearing a halogen X (X = F, Cl, Br or I) in the *para* position of the aromatic ring, the reactions occurred readily to give the desired products in high yields and excellent enantioselectivities (Table 2, entries 2–5), and the halogen-substituted products can participate in subsequent transformations such as cross-coupling reactions. We found that the best level of stereocontrol was obtained for 4-nitrophenyl trifluoromethyl ketone **2h** which possesses a strong electron-withdrawing group (>99.5% ee, Table 2, entry 8). *Meta*-substituents on the aryl ring of trifluoromethyl ketones (**2i–2k**) had a negligible impact on the yield and enantioselectivity (Table 2, entries 9–11). Notably, trifluoroacetophenones (**2l–2n**), with two additional substituents on the aromatic ring, could also serve as substrates in this reaction (Table 2, entries 12–14). Introduction of an electron-donating group resulted in a slightly lower ee (Table 2, entry 15). Switching to the trifluoromethyl alkyl ketone (**2p**) afforded significantly diminished enantioselectivity (Table 2, entry 16).

Table 2 Scope of the reaction with respect to the trifluoromethyl ketone[a]



1a 2 3

Entry	R	Product	Yield[b] (%)	ee[c] (%)
1	Ph (**2a**)	**3aa**	95	93 (99)[d]
2	4-FC_6H_4 (**2b**)	**3ab**	95	94
3	4-ClC_6H_4 (**2c**)	**3ac**	88	95
4	4-BrC_6H_4 (**2d**)	**3ad**	92	96
5[e]	4-IC_6H_4 (**2e**)	**3ae**	88	92
6	4-$CF_3C_6H_4$ (**2f**)	**3af**	92	93
7[e]	4-CNC_6H_4 (**2g**)	**3ag**	84	93
8[e]	4-$NO_2C_6H_4$ (**2h**)	**3ah**	86	>99.5
9	3-FC_6H_4 (**2i**)	**3ai**	95	96
10	3-BrC_6H_4 (**2j**)	**3aj**	87	95
11[e]	3-$CF_3C_6H_4$ (**2k**)	**3ak**	87	90
12[e]	3,5-$F_2C_6H_3$ (**2l**)	**3al**	82	94
13	3,5-$Cl_2C_6H_3$ (**2m**)	**3am**	80	96
14	3,4-$F_2C_6H_3$ (**2n**)	**3an**	90	96
15	4-MeC_6H_4 (**2o**)	**3ao**	93	87
16	Benzyl (**2p**)	**3ap**	93	55

[a] Reaction conditions: **4b** (5 mol%, 0.005 mmol), **1** (0.1 mmol), **2** (0.12 mmol), molecular sieves (MS 4 Å, 0.1 g), 1,2-dichloroethane (0.6 mL), 35 °C, for 24–48 h. [b] Isolated yields. [c] Determined by chiral HPLC analysis. [d] Data in parentheses were obtained after single recrystallization. [e] Under reflux.

Table 3 Scope of the reaction with respect to the *o*-aminobenzylindole substrate[a]

1 2 3

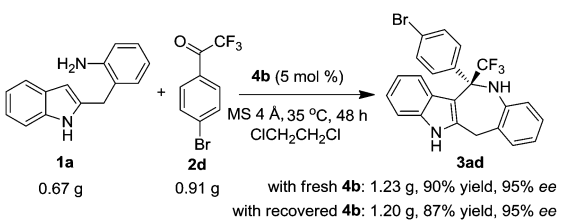
Entry	$R^1/R^2/R^3/R^4/R^5$	R	Product	Yield[b] (%)	ee[c] (%)
1	H/Br/H/H/Br (**1b**)	4-FC_6H_4 (**2b**)	**3bb**	80	88
2	H/Br/H/H/Br (**1b**)	4-ClC_6H_4 (**2c**)	**3bc**	88	90
3	H/Br/H/H/Br (**1b**)	4-BrC_6H_4 (**2d**)	**3bd**	90	96
4	Cl/H/H/Cl/H (**1c**)	4-BrC_6H_4 (**2d**)	**3cd**	95	90
5	Cl/H/H/Cl/H (**1c**)	3,5-$Cl_2C_6H_3$ (**2k**)	**3ck**	87	90
6[d]	H/Me/H/H/Me (**1d**)	Ph (**2a**)	**3da**	98	81
7	H/Me/H/H/Me (**1d**)	4-FC_6H_4 (**2b**)	**3db**	75	84
8[d]	H/Me/H/H/Me (**1d**)	4-ClC_6H_4 (**2c**)	**3dc**	86	93
9[d]	H/Me/H/H/Me (**1d**)	4-BrC_6H_4 (**2d**)	**3dd**	95	90
10	H/H/Bn/H/H (**1e**)	Ph (**2a**)	**3ea**	0	—

[a] Reaction conditions: **4b** (5 mol%, 0.005 mmol), **1** (0.1 mmol), **2** (0.12 mmol), molecular sieves (MS 4 Å, 0.1 g), 1,2-dichloroethane (0.6 mL), reflux for 24–96 h. [b] Isolated yields. [c] Determined by chiral HPLC analysis. [d] 50 °C.

The effects of *o*-aminobenzylindole substitution were then evaluated under the optimized conditions (Table 3). Good yields (75–98%) and high enantioselectivities (81–96% ee) were achieved with substrates **1** bearing either electron-withdrawing or electron-donating groups when the reactions were conducted at elevated temperatures and with a prolonged reaction time, although these substrates (**1b–1d**) showed slightly reduced reactivity (Table 3, entries 1–9). When *N*-benzylindole derivative (**1e**) was prepared and treated with phenyl trifluoromethyl ketone (**2a**), no desired product was observed even under reflux (Table 3, entry 10). We suspect that the hydrogen atom on the N atom of the indole is crucial for the activation of the substrate by SPA **4** in this iso-Pictet–Spengler reaction (*vide infra*).

We next carried out a scale-up experiment (3.0 mmol of **1a**) (Scheme 2). This reaction proceeded without compromising the yield or enantioselectivity, and a gram-scale preparation of **3ad** (1.23 g) was realized with 90% yield and 95% ee as well as 90% recovery of catalyst **4b**. The recovered catalyst was recycled with negligible loss in reactivity or stereoselectivity.

The absolute configuration (*S*) of the quaternary stereogenic center in product **3** was determined by X-ray crystallographic analysis of a single crystal of **3aa**.[12] Although the mechanism of this reaction has not been studied in depth, we believe that the bifunctional nature of the chiral phosphoric acid concurrently activates both the nucleophilic group and the electrophilic group



Scheme 2 Gram-scale preparation of **3ad**.

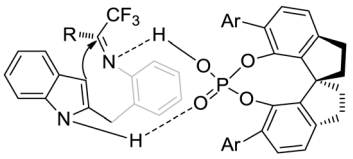


Fig. 1 Proposed reaction model.

of the ketoimine intermediate through hydrogen bonding. In this model, the indole π system attacks the ketoimine moiety from the *Si* face, leading to (*S*)-**3** (Fig. 1).[13]

In summary, we have presented a general, mild, and flexible method providing access to enantiomerically enriched benzazepinoindoles bearing trifluoromethylated quaternary stereocenters by utilizing the catalytic asymmetric iso-Pictet–Spengler reaction. The reaction employs the powerful and fully recyclable chiral spirocyclic phosphoric acid catalyst **4b**, and involves a simple scalable experimental procedure without a protecting group or an activating group. Further exploration of the potential of our chiral SPAs in asymmetric catalysis is currently ongoing.

This work was supported by the National Natural Foundation of China (21272202 and J1210042).

Notes and references

1 (*a*) M. A. McClinton and D. A. McClinton, *Tetrahedron*, 1992, **48**, 6555–6666; (*b*) G. K. S. Prakash and A. Yudin, *Chem. Rev.*, 1997, **97**, 757–786; (*c*) S. Purser, P. R. Moore, S. Swallow and V. Gouverneur, *Chem. Soc. Rev.*, 2008, **37**, 320–330; (*d*) K. Müüller, C. Faeh and F. Diederich, *Science*, 2007, **317**, 1881–1886; (*e*) J. Liu and J.-B. Hu, *Future Med. Chem.*, 2009, **1**, 875–888.

2 (*a*) J. W. Corbett, S. S. Ko, J. D. Rodgers, L. A. Gearhart, N. A. Magnus, L. T. Bacheler, S. Diamond, S. Jeffrey, R. M. Klabe, B. C. Cordova, S. Garber, K. Logue, G. L. Trainor, P. S. Anderson and S. K. Erickson-Viitanen, *J. Med. Chem.*, 2000, **43**, 2019–2030; (*b*) A. Cleve, U. Klar and W. Schwede, *J. Fluorine Chem.*, 2005, **126**, 217–220; (*c*) S. Caron, N. M. Do, J. E. Sieser, P. Arpin and E. Vazquez, *Org. Process Res. Dev.*, 2007, **11**, 1015–1024; (*d*) G. Magueur, B. Crousse, S. Charneau, P. Grellier, J.-P. Bégué and D. Bonnet-Delpon, *J. Med. Chem.*, 2004, **47**, 2694–2699.

3 (*a*) J.-A. Ma and D. Cahard, *Chem. Rev.*, 2004, **104**, 6119–6146; (*b*) K. Mikami, Y. Itoh and M. Yamanaka, *Chem. Rev.*, 2004, **104**, 1–16; (*c*) J.-P. Bégué, D. Bonnet-Delpon, B. Crousse and J. Legros, *Chem. Soc. Rev.*, 2005, **34**, 562–572; (*d*) J.-A. Ma and D. Cahard, *Chem. Rev.*, 2008, **108**, PR1–PR43; (*e*) Y. Zheng and J.-A. Ma, *Adv. Synth. Catal.*, 2010, **352**, 2745–2750; (*f*) J. Nie, H.-C. Guo, D. Cahard and J.-A. Ma, *Chem. Rev.*, 2011, **111**, 455–529; (*g*) N. Shibata, S. Mizuta and H. Kawai, *Tetrahedron: Asymmetry*, 2008, **19**, 2633–2644; (*h*) G. Valero, X. Companyó and R. Rios, *Chem. – Eur. J.*, 2011, **17**, 2018–2038; (*i*) F.-L. Qing and F. Zheng, *Synlett*, 2011, 1052–1072.

4 Selected recent examples: (*a*) H.-X. Xie, Y.-N. Zhang, S.-L. Zhang, X.-B. Chen and W. Wang, *Angew. Chem., Int. Ed.*, 2011, **50**, 11773–11776; (*b*) Q.-H. Deng, H. Wadepohl and L. Gade, *J. Am. Chem. Soc.*, 2012, **134**, 10769–10772; (*c*) H. Kawai, S. Okusu, E. Tokunaga, H. Sato, M. Shiro and N. Shibata, *Angew. Chem., Int. Ed.*, 2012, **51**, 4959–4962; (*d*) C. J. Douglas and L. E. Overman, *Proc. Natl. Acad. Sci. U. S. A.*, 2004, **101**, 5363–5367; (*e*) J. Nie, G.-W. Zhang, L. Wang, A. Fu, Y. Zheng and J.-A. Ma, *Chem. Commun.*, 2009, 2356–2358.

5 (*a*) J. R. Denton, D. Sukumaran and H. M. L. Davies, *Org. Lett.*, 2007, **9**, 2625–2628; (*b*) H. Kawai, S. Okusu, Z. Yuan, E. Tokunaga, A. Yamano, M. Shiro and N. Shibata, *Angew. Chem., Int. Ed.*, 2013, **52**, 2221–2225; (*c*) S. Wu, D. Pan, C. Cao, Q. Wang and F.-X. Chen, *Adv. Synth. Catal.*, 2013, **355**, 1917–1923; (*d*) C. Burstein and F. Glorius, *Angew. Chem., Int. Ed.*, 2004, **43**, 6205–6208; (*e*) J.-Y. Bae, H.-J. Lee, S.-H. Youn, S.-H. Kwon and C.-W. Cho, *Org. Lett.*, 2010, **12**, 4352–4355; (*f*) Y. Su, J. Ling, S. Zhang and P.-F. Xu, *J. Org. Chem.*, 2013, **78**, 11053–11058;

(*g*) P. Li, Z. Chai, S. Zhao, Y. Yang, H. Wang, C. Zheng, Y. Cai, G. Zhao and S.-Z. Zhu, *Chem. Commun.*, 2009, 7369–7371; (*h*) J. Mo, X. Chen and Y.-R. Chi, *J. Am. Chem. Soc.*, 2012, **134**, 8810–8813.

6 (*a*) A. Moyano and R. Rios, *Chem. Rev.*, 2011, **111**, 4703–4832; (*b*) J. Royer, M. Bonin and L. Micouin, *Chem. Rev.*, 2004, **104**, 2311–2352; (*c*) M. Chrzanowska and M. D. Rozwadowska, *Chem. Rev.*, 2004, **104**, 3341–3370; (*d*) A. P. Stöckigt, F. Antonchick, F. Wu and H. Waldmann, *Angew. Chem., Int. Ed.*, 2011, **50**, 8538–8564; (*e*) M. S. Taylor and E. N. Jacobsen, *J. Am. Chem. Soc.*, 2004, **126**, 10558–10559; (*f*) M. J. Wanner, R. N. S. van der Haas, K. R. de Cuba, J. H. van Maarseveen and H. Hiemstra, *Angew. Chem., Int. Ed.*, 2007, **46**, 7485–7487; (*g*) R. S. Klausen and E. N. Jacobsen, *Org. Lett.*, 2009, **11**, 887–890; (*h*) J. Seayad, A. M. Seayad and B. List, *J. Am. Chem. Soc.*, 2006, **128**, 1086–1087; (*i*) D. J. Cheng, H. B. Wu and S. K. Tian, *Org. Lett.*, 2011, **13**, 5636–5639; (*j*) Y. He, M. Lin, Z. Li, X. Liang, G. Li and J. C. Antilla, *Org. Lett.*, 2011, **13**, 4490–4493.

7 (*a*) F. R. Bou-Hamdan and J. L. Leighton, *Angew. Chem., Int. Ed.*, 2009, **48**, 2403–2406; (*b*) C. A. Holloway, M. E. Muratore, R. I. Storer and D. J. Dixon, *Org. Lett.*, 2010, **12**, 4720–4723; (*c*) S. Duce, F. Pesciaioli, L. Gramigna, L. Bernardi, A. Mazzanti, A. Ricci, G. Bartoli and G. Bencivenni, *Adv. Synth. Catal.*, 2011, **353**, 860–864; (*d*) Y. Lee, R. S. Klausen and E. N. Jacobsen, *Org. Lett.*, 2011, **13**, 5564–5567; (*e*) H. Schönherr and J. L. Leighton, *Org. Lett.*, 2012, **14**, 2610–2613; (*f*) M. E. Muratore, C. A. Holloway, A. W. Pilling, R. I. Storer, G. Trevitt and D. J. Dixon, *J. Am. Chem. Soc.*, 2009, **131**, 10796–10797.

8 (*a*) F. Xu, D. Huang, C. Han, W. Shen, X. F. Lin and Y. G. Wang, *J. Org. Chem.*, 2010, **75**, 8677–8680; (*b*) D. Huang, F. Xu, X. F. Lin and Y. G. Wang, *Chem. – Eur. J.*, 2012, **18**, 3148–3152; (*c*) F. Xu, D. Huang, X. F. Lin and Y. G. Wang, *Org. Biomol. Chem.*, 2012, **10**, 4467–4470; (*d*) X. Li, Y. Zhao, H. Qu, Z. Mao and X. F. Lin, *Chem. Commun.*, 2013, **49**, 1401–1403; (*e*) D. Huang, X. Li, F. Xu, L. Li and X. F. Lin, *ACS Catal.*, 2013, **3**, 2244–2247; (*f*) D. Huang, F. Xu, T. Chen, Y. G. Wang and X. F. Lin, *RSC Adv.*, 2013, **3**, 573–578; (*g*) Y. Zhao, X. Li, F. Mo, L. Li and X. F. Lin, *RSC Adv.*, 2013, **3**, 11895–11901.

9 For selected examples of SPAs reported by other groups, see: (*a*) I. Ćorić, S. Müller and B. List, *J. Am. Chem. Soc.*, 2010, **132**, 17370–17373; (*b*) C.-H. Xing, Y.-X. Liao, J. Ng and Q.-S. Hu, *J. Org. Chem.*, 2011, **76**, 4125–4131; (*c*) B. Xu, S.-F. Zhu, X.-L. Xie, J.-J. Shen and Q.-L. Zhou, *Angew. Chem., Int. Ed.*, 2011, **50**, 11483–11486; (*d*) S. Müller, M. Webber and B. List, *J. Am. Chem. Soc.*, 2011, **133**, 18534–18537; (*e*) C.-H. Xing, Y.-X. Liao, Y. Zhang, D. Sabarova, B. Assous and Q.-S. Hu, *Eur. J. Org. Chem.*, 2012, 1115–1118; (*f*) D. M. Rubush, M. A. Morges, B. J. Rose, D. H. Thamm and T. Rovis, *J. Am. Chem. Soc.*, 2012, **134**, 13554–13557; (*g*) Z.-L. Chen, B.-L. Wang, Z.-B. Wang, G.-Y. Zhu and J.-W. Sun, *Angew. Chem., Int. Ed.*, 2013, **52**, 2027–2031; (*h*) Q. Cai, X.-W. Liang, S.-G. Wang and S.-L. You, *Org. Biomol. Chem.*, 2013, **11**, 1602–1605; (*i*) J. Wu, Y. Wang, A. Drljevic, V. Rauniyar, R. Phipps and F. D. Toste, *Proc. Natl. Acad. Sci. U. S. A.*, 2013, **110**, 13729–13733; (*j*) J. Guin, G. Varseev and B. List, *J. Am. Chem. Soc.*, 2013, **135**, 2100–2103; (*k*) Z. Chen, B. Wang and J. Sun, *Chem. – Eur. J.*, 2013, **19**, 8426–8430; (*l*) B. Wang, Z. Chen and J. Sun, *Angew. Chem., Int. Ed.*, 2013, **52**, 6685–6688; (*m*) A. Martinez, M. J. Webber, S. Müller and B. List, *Angew. Chem., Int. Ed.*, 2013, **52**, 9486–9490; (*n*) C. Yang, X. S. Xue, J. L. Jin, X. Li and J. P. Cheng, *J. Org. Chem.*, 2013, **78**, 7076–7085; (*o*) Z. Chen and J. Sun, *Angew. Chem., Int. Ed.*, 2013, **52**, 13593–13596; (*p*) S. G. Wang and S.-L. You, *Angew. Chem., Int. Ed.*, 2014, **53**, 2194–2197; (*q*) B. Xu, S.-F. Zhu, Z.-C. Zhang, Z.-X. Yu, Y. Ma and Q.-L. Zhou, *Chem. Sci.*, 2014, **5**, 1442–1448; (*r*) V. Gobé and X. Guinchard, *Org. Lett.*, 2014, **16**, 1924–1927.

10 For a racemic version with benzaldehyde or acetophenone, see: S. K. Sharma, S. Sharma, P. K. Agarwal and B. Kundu, *Eur. J. Org. Chem.*, 2009, 1309–1312.

11 For recent reviews, see: (*a*) T. Akiyama, *Chem. Rev.*, 2007, **107**, 5744–5758; (*b*) M. Terada, *Chem. Commun.*, 2008, 4097–4112; (*c*) M. Rueping, A. Kuenkel and I. Atodiresei, *Chem. Soc. Rev.*, 2011, **40**, 4539–4549; (*d*) D. Kampen, C. M. Reisinger and B. List, in *Topics in Current Chemistry*, ed. B. List, Springer, Berlin, 2010, vol. 291, pp. 395–456; (*e*) J. Yu, F. Shi and L. Gong, *Acc. Chem. Res.*, 2011, **44**, 1156–1171.

12 See the ESI† for full details. CCDC 953552.

13 For the computational proof of a similar model, see: L. Simón and J. M. Goodman, *J. Org. Chem.*, 2010, **75**, 589–597.