

C–F Bond Activation



Kinetic Resolution of Allyl Fluorides by Enantioselective Allylic Trifluoromethylation Based on Silicon-Assisted C–F Bond Cleavage**

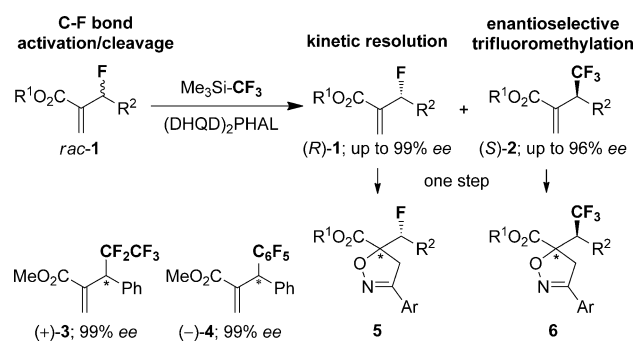
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Enantioenriched fluorinated molecules play an important role as pharmaceutically active compounds with impressive biological activities.^[1] The anti-HIV drug Efavirenz, for example, contains a chiral C*–CF₃ unit, and the broad-spectrum antibiotic Levofloxacin has a chiral C*–F moiety. Fluorinated molecules also offer opportunities for creating functional molecules with potential applications, such as liquid crystals.^[2] Metal- and/or organocatalyzed asymmetric transformations for the synthesis of organofluorine compounds that make use of fluorinated building blocks and direct enantioselective fluorination or trifluoromethylation are among the most powerful means to access chiral fluorinated synthons.^[3] However, these methods are not always applicable to the synthesis of a desired compound, and thus, the development of new approaches for the synthesis of chiral organofluorine compounds remains an area of great importance in modern organic chemistry.

Kinetic resolution is an alternative and complementary strategy for the preparation of a wide range of enantioenriched organic compounds.^[4] A possible drawback of this approach is that with the exception of dynamic kinetic resolution, a mixture of the product and unreacted starting material is often obtained. We envisaged that if both these compounds were potentially important fluorinated materials and produced in high enantiomeric excess, kinetic resolution would become a more attractive strategy, as it would allow the synthesis of two chiral fluorinated targets by a single transformation at the same time; we coined this process a “kill two birds by one stone” strategy (TBOS strategy).

The activation or cleavage of C–F bonds has recently also gained much attention.^[5,6] As C–F bonds are the strongest bonds that carbon can form, the cleavage of C–F bonds requires rather forced conditions, and therefore, the development of mild and effective methods for the activation of C–F bonds has become a crucial topic in general organic chemistry. Gouverneur and co-workers investigated the activation of

allylic C–F bonds and developed a palladium- or platinum-catalyzed substitution reaction of allyl fluorides with carbon, nitrogen, and oxygen nucleophiles.^[7] Paquin et al. also described the activation of allylic C–F bonds by palladium catalysis and hydrogen bonding.^[8] Recently, we reported the synthesis of a series of 2-fluoromethyl-oxazolidin-2-ones by desymmetrization of non-activated aliphatic difluorides by silicon-induced catalytic C–F bond cleavage.^[9] Our group also investigated the cinchona-alkaloid-catalyzed asymmetric allylic trifluoromethylation of Morita–Baylis–Hillman (MBH) carbonates with the Ruppert–Prakash reagent (Me₃SiCF₃) to deliver allylic trifluoromethylated compounds.^[10] As an application of the TBOS strategy and as an extension of our research on C–F bond activation^[9] and the enantioselective construction of chiral C*–CF₃^[11] and C*–F units,^[12] we herein disclose the first kinetic resolution of allyl fluorides by catalytic asymmetric allylic trifluoromethylation of MBH-type allyl fluorides **1**. Racemic allyl fluorides **1** can be converted into enantioenriched **1** and trifluoromethylated allyl compounds **2** with an excellent degree of enantiopurity by a single transformation; both compounds are potential chiral synthons for biologically important molecules. Racemate **1** was also kinetically resolved by asymmetric allylic pentafluoroethylation and pentafluorophenylation to furnish enantioenriched allyl fluorides **1**, along with pentafluoroethylated **3** and pentafluorophenylated **4** with 99% *ee* each. The key to these highly asymmetric transformations is the silicon-induced cleavage of an allylic C–F bond, which is assisted by S_N2' substitution with a bis(cinchona alkaloid), namely (DHQD)₂PHAL (Scheme 1). Enantioenriched allyl fluorides **1** are produced by kinetic resolution, while the enantioenriched trifluoromethylated allyl compounds **2** are simultaneously formed by enantioselective trifluoromethylation. The products can be transformed into the fluorine-



Scheme 1. Kinetic resolution of MBH-type allyl fluorides **1** by enantioselective fluoroalkylation through C–F bond activation/cleavage.

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containing isoxazolines **5** and **6**, which are interesting structures from an agrochemical point of view, in a single step.

Asymmetric reactions of MBH adducts have hitherto been studied by many groups,^[13] including by ourselves.^[10,14] Rios and co-workers described an organocatalyzed kinetic resolution of MBH carbonates,^[15] as did several other groups.^[16] The basic framework of MBH adducts contains an OR group (acetate or carbonate) at the allylic position, which can act as a leaving group. Therefore, we surmised that MBH-type fluorides **1**^[17] could also behave as conventional MBH starting materials for asymmetric allylic substitution; C–F bond activation should be rendered possible by a silicon-induced pathway. For a successful kinetic resolution, the C–F bond of **1** must nevertheless be sufficiently stable under the selected reaction conditions.

The kinetic resolution of racemic **1** with Me₃SiCF₃ was successfully carried out in the presence of a catalytic amount of (DHQD)₂PHAL and molecular sieves (4 Å), in 1,4-dioxane/THF (5:1; 0.5 M) at 0 °C, thus providing the enantioenriched allyl fluoride **1** and trifluoromethylated **2** (Table 1).^[18] The allyl fluorides **1** were slowly consumed by trifluoromethylation, and the reactions were stopped at about 50% conversion of **1**. A series of allyl fluorides **1a–i** with a variety of substituents on the aromatic ring, including methyl, methoxy, chloro, and bromo moieties, were converted into the trifluoromethylated products (*S*)-**2a–i** with excellent

enantioselectivities of 87–96% *ee*. The allyl fluorides (*R*)-**1a–i** were then recovered with excellent enantioselectivities of up to 99% *ee*, which corresponds to *s* factors of 24–64 (entries 1–9). The kinetic resolution of nitro-activated allyl fluoride **1j** was performed with a lower amount of Me₃SiCF₃ (0.7 equiv) because of the high reactivity of **1j**, and the reaction showed good selectivity; (*S*)-**2j** was obtained in 89% *ee* and 52% yield, while (*R*)-**1j** was recovered in 90% *ee* and 44% yield (*s* = 20; entry 10). The reaction of **1k** with a sterically demanding naphthyl moiety also gave the corresponding product in good chemical yield and selectivity (*s* = 22; entry 11). We next attempted the reaction of an alkyl-substituted compound; cyclohexyl-substituted allyl fluoride **1l** was converted into the desired (*S*)-**2l**, but the reaction was very slow.^[10] Increasing the amount of (DHQD)₂PHAL (30 mol %) slightly improved the reactivity to afford (*S*)-**2l** in 82% *ee* and 22% yield after 120 h (*s* = 18; entry 12). A series of bulky *tert*-butyl esters **1m–p** were converted into the corresponding products (*S*)-**2m–p** with good selectivity (87–96% *ee*, *s* = 14–105; entries 13–16), even though the reactivity was lower than for the methyl esters **1a–l**. The reaction of phenyl-substituted allyl fluoride **1m** proceeded particularly well; (*S*)-**2m** was obtained in 94% *ee* and 48% yield, and **1m** was recovered in 93% *ee* and 42% yield. The highest *s* factor that was observed during this study was thus measured for **1m** (*s* = 105; entry 13). We also succeeded in obtaining the

Table 1: Kinetic resolution of MBH-type allyl fluorides **1** by enantioselective trifluoromethylation.^[a]

Entry	1	R ¹	R ²	<i>t</i> [h]	Conv. ^[b] [%]	2 <i>ee</i> ^[c] (yield ^[d]) [%]	recovered 1 <i>ee</i> ^[c] (yield ^[d]) [%]	<i>s</i> ^[e]
1	1a	Me	Ph	36	54	95 (51)	97 (41)	44
2	1b	Me	4-MeC ₆ H ₄	60	53	95 (48)	96 (40)	50
3	1c	Me	3-MeC ₆ H ₄	50	53	96 (50)	97 (41)	64
4	1d	Me	3-MeOC ₆ H ₄	48	55	94 (50)	97 (40)	36
5	1e	Me	4-ClC ₆ H ₄	18	54	89 (51)	98 (43)	45
6	1f	Me	3-ClC ₆ H ₄	16	54	91 (50)	97 (41)	42
7	1g	Me	4-BrC ₆ H ₄	20	56	89 (52)	96 (42)	26
8	1h	Me	3-BrC ₆ H ₄	19	55	90 (52)	99 (41)	50
9	1i	Me	2-BrC ₆ H ₄	108	52	87 (36)	85 (31)	24
10 ^[f]	1j	Me	4-NO ₂ C ₆ H ₄	3	55	89 (52)	90 (44)	20
11	1k	Me	2-naphthyl	36	53	91 (48)	88 (42)	22
12 ^[g]	1l	Me	Cy	120	23	82 (22)	26 (54)	18
13	1m	<i>t</i> Bu	Ph	120	50	94 (48)	93 (42)	105
14	1n	<i>t</i> Bu	3-MeC ₆ H ₄	120	44	96 (37)	70 (47)	33
15	1o	<i>t</i> Bu	4-BrC ₆ H ₄	66	54	87 (51)	84 (42)	15
16	1p	<i>t</i> Bu	4-NO ₂ C ₆ H ₄	5	55	90 (48)	84 (43)	14
17 ^[h]	1a	Me	Ph	120	53	–62 (44)	–77 (42)	12

[a] Reactions were carried out using *rac*-**1** (0.1 mmol), Me₃SiCF₃ (1.0 equiv), (DHQD)₂PHAL (10 mol %), and molecular sieves (4 Å) in 1,4-dioxane/THF (5:1; 0.2 mL, 0.5 M) unless otherwise noted. [b] The conversion of **1** was determined by ¹⁹F NMR spectroscopy with an internal standard.

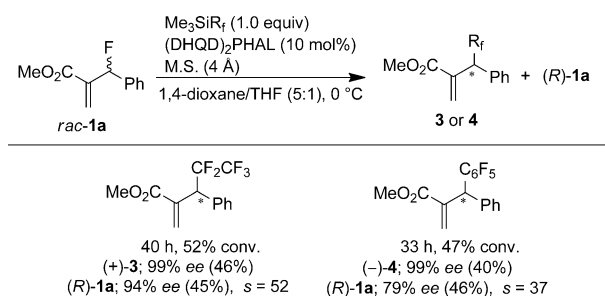
[c] Determined by HPLC analysis. [d] Yield of isolated product. [e] The selectivity factor (*s*) based on recovered **1** was determined by the equation $s = k_{\text{rel}}(\text{fast/slow}) = \ln[(1-C)(1-ee)] / \ln[(1-C)(1+ee)]$ (*C* = conversion; *ee* = enantiomeric excess of recovered **1**). [f] Me₃SiCF₃ (0.7 equiv).

[g] (DHQD)₂PHAL (30 mol %). [h] (DHQ)₂PYR used instead of (DHQD)₂PHAL. Cy = cyclohexyl, (DHQ)₂PYR = hydroquinine 2,5-diphenyl-4,6-pyrimidinediyl diether.

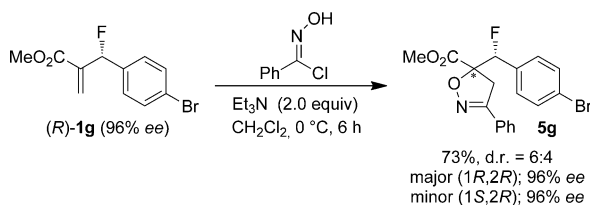
opposite set of enantiomers, namely (*R*)-**2a** in 62% *ee* and (*S*)-**1a** in 77% *ee*, in the presence of (DHQD)₂PYR, rather than (DHQD)₂PHAL, as the catalyst (*s* = 12; entry 17). The absolute configurations of the trifluoromethylated compounds **2** were determined by a comparison with previously reported HPLC retention times.^[10] The absolute configuration of recovered **1g** was unambiguously assigned to be *R* by X-ray crystallographic analysis^[19] of the isoxazoline derivative (1*R*,2*R*)-**5g** (see below and Scheme 3); the absolute stereochemistry of the other allyl fluorides was tentatively assumed to be *R* by analogy.

Interestingly, a kinetic resolution of **1a** was also achieved by enantioselective allylic pentafluoroethylation and pentafluorophenylation. Both of the reactions proceeded smoothly to provide the desired products, pentafluoroethylated **3** and pentafluorophenylated **4**, with excellent enantioselectivities of 99% *ee* and *s* factors of 52 and 37, respectively (Scheme 2).

Furthermore, the chiral allyl fluoride **1g** was smoothly converted into the biologically interesting heterocycle **5g** by a 1,3-dipolar cycloaddition (Scheme 3). The analogous transformation of chiral trifluoromethylated allyl compounds **2** into the corresponding isoxazolines **6** by the same procedure was previously reported by our group.^[10]



Scheme 2. Kinetic resolution of **1a** by enantioselective pentafluoroethylation or pentafluorophenylation.



Scheme 3. Conversion of allyl fluoride (*R*)-**1g** into isoxazoline **5g**.

To understand the high efficiency of the kinetic resolution of **1** by trifluoromethylation, the postulated mechanism must be considered. Kinetic resolution/trifluoromethylation begins with C–F bond activation of **1** by coordination to the silicon atom of Me₃SiCF₃,^[3a] this is followed by the addition of (DHQD)₂PHAL to the alkene moiety through the quinuclidine nitrogen atom in an S_N2' process that involves the loss of the fluoride as Me₃SiF to provide the ammonium salt **I**. This step is believed to be rate-determining. The catalyst (DHQD)₂PHAL preferentially attacks (*S*)-**1**, while (*R*)-**1** remains intact; kinetic resolution of **1** has therefore

occurred. The product **2** is formed by a second S_N2' substitution reaction of *E*-configured **I**, which was generated from (*S*)-**1**, with CF₃[−] as the nucleophile (Figure 1).^[10,14,20] A thorough investigation of the *ee* values of **1a** and **2a** at different conversions revealed that the enantiopurity of **2a** is not related to the conversion (Figure 2). Excellent enantioselectivities were persistently observed and found to be independent of the conversion and the *ee* of **1a**. Therefore, **2a** was produced by enantioselective trifluoromethylation. On

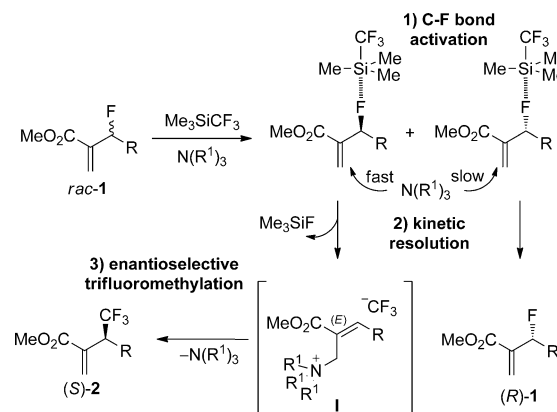


Figure 1. Proposed mechanism consisting of three steps: 1) C–F bond activation, 2) kinetic resolution, and 3) enantioselective trifluoromethylation. N(R')₃ = (DHQD)₂PHAL.

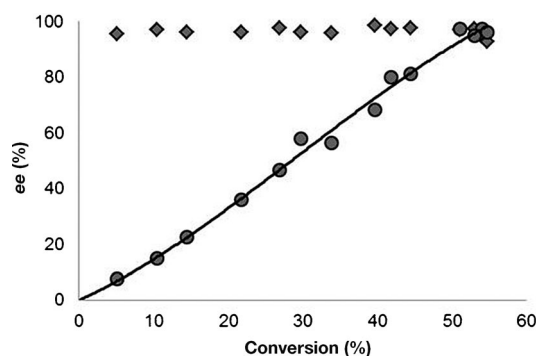


Figure 2. Kinetic resolution of **1a** (●) and enantioselective formation of **2a** (◆; see Table S2).

the other hand, the enantiopurity of **1a** constantly increased from 0 to 97% *ee* with increasing conversion. These data strongly support the idea that the enantioenriched allyl fluoride **1a** is generated by kinetic resolution through enantioselective trifluoromethylation.

In conclusion, the first kinetic resolution of allyl fluorides was realized by an enantioselective allylic trifluoromethylation of MBH-type allyl fluorides **1** under organocatalysis. The key for success was the cleavage of the strong C–F bond of (*S*)-**1** by a cooperative system that includes the bis(cinchona alkaloid) and the silicon atom of the trifluoromethylating reagent, while (*R*)-**1** remains intact. The features of the overall transformation include: 1) asymmetric synthesis of allyl fluorides,^[21] 2) enantioselective trifluoromethylation,

3) C–F bond activation by a cooperative system, 4) kinetic resolution, and 5) allylic trifluoromethylation.^[10,21c,22] Two chiral fluorinated compounds with C*–F and C*–CF₃ units, respectively can be accessed at the same time by the TBOS strategy. Further developments of this transformation to include different nucleophiles are currently under investigation.

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- [1] a) K. L. Kirk, *J. Fluorine Chem.* **2006**, *127*, 1013–1029; b) K. L. Kirk, *Org. Process Res. Dev.* **2008**, *12*, 305–321; c) I. Ojima, *Fluorine in Medicinal Chemistry and Chemical Biology*, Wiley-Blackwell, Oxford, **2009**.
- [2] a) M. Hird, *Chem. Soc. Rev.* **2007**, *36*, 2070–2095; b) Z. Hong, S. G. Weber, *Teflon AF Materials in Topics in Current Chemistry*, Vol. 308 (Ed.: I. T. Horváth), Springer, Berlin, **2012**, pp. 307–377.
- [3] a) K. Uneyama, *Organofluorine Chemistry*, Blackwell, Oxford, **2006**; b) J.-A. Ma, D. Cahard, *Chem. Rev.* **2008**, *108*, PR1–PR43; c) N. Shibata, S. Mizuta, H. Kawai, *Tetrahedron: Asymmetry* **2008**, *19*, 2633–2644; d) J. Nie, H.-C. Guo, D. Cahard, J.-A. Ma, *Chem. Rev.* **2011**, *111*, 455–529; e) C. Hollingworth, V. Gouverneur, *Chem. Commun.* **2012**, *48*, 2929–2942; f) T. Liang, C. N. Neumann, T. Ritter, *Angew. Chem.* **2013**, *125*, 8372–8423; *Angew. Chem. Int. Ed.* **2013**, *52*, 8214–8264.
- [4] a) E. Vedejs, M. Jure, *Angew. Chem.* **2005**, *117*, 4040–4069; *Angew. Chem. Int. Ed.* **2005**, *44*, 3974–4001; b) H. Pellissier, *Adv. Synth. Catal.* **2011**, *353*, 1613–1666.
- [5] a) H. Amii, K. Uneyama, *Chem. Rev.* **2009**, *109*, 2119–2183; b) T. Stahl, H. F. T. Klare, M. Oestreich, *ACS Catal.* **2013**, *3*, 1578–1587.
- [6] For examples of the activation of allylic C–F bonds, see: a) K. Hirano, H. Yorimitsu, K. Oshima, *Org. Lett.* **2004**, *6*, 4873–4875; b) K. Hirano, K. Fujita, H. Yorimitsu, H. Shinokubo, K. Oshima, *Tetrahedron Lett.* **2004**, *45*, 2555–2557; c) L. Hintermann, F. Läng, P. Maire, A. Togni, *Eur. J. Inorg. Chem.* **2006**, 1397–1412; d) M. Bergeron, T. Johnson, J.-F. Paquin, *Angew. Chem.* **2011**, *123*, 11308–11312; *Angew. Chem. Int. Ed.* **2011**, *50*, 11112–11116; e) D. Watanabe, M. Koura, A. Saito, H. Yanai, Y. Nakamura, M. Okada, A. Sato, T. Taguchi, *J. Fluorine Chem.* **2011**, *132*, 327–338; f) M. Bergeron, D. Guyader, J.-F. Paquin, *Org. Lett.* **2012**, *14*, 5888–5891.
- [7] a) A. Hazari, V. Gouverneur, J. M. Brown, *Angew. Chem.* **2009**, *121*, 1322–1325; *Angew. Chem. Int. Ed.* **2009**, *48*, 1296–1299; b) E. Benedetto, M. Keita, M. Tredwell, C. Hollingworth, J. M. Brown, V. Gouverneur, *Organometallics* **2012**, *31*, 1408–1416.
- [8] a) X. Pigeon, M. Bergeron, F. Barabé, P. Dubé, H. N. Frost, J.-F. Paquin, *Angew. Chem.* **2010**, *122*, 1141–1145; *Angew. Chem. Int. Ed.* **2010**, *49*, 1123–1127; b) J.-F. Paquin, *Synlett* **2011**, 289–293.
- [9] G. Haufe, S. Suzuki, H. Yasui, C. Terada, T. Kitayama, M. Shiro, N. Shibata, *Angew. Chem.* **2012**, *124*, 12441–12445; *Angew. Chem. Int. Ed.* **2012**, *51*, 12275–12279.
- [10] Alkyl-substituted compounds with less bulky groups, such as methyl substituents, are poor substrates for this transformation; see: T. Furukawa, T. Nishimine, E. Tokunaga, K. Hasegawa, M. Shiro, N. Shibata, *Org. Lett.* **2011**, *13*, 3972–3975; see also Ref. [14].
- [11] For the construction of chiral C*–CF₃ centers, see: a) S. Mizuta, N. Shibata, S. Akiti, H. Fujimoto, S. Nakamura, T. Toru, *Org. Lett.* **2007**, *9*, 3707–3710; b) S. Noritake, N. Shibata, Y. Nomura, Y. Huang, A. Matsnev, S. Nakamura, T. Torua, D. Cahard, *Org. Biomol. Chem.* **2009**, *7*, 3599–3604; c) H. Kawai, A. Kusuda, S. Nakamura, M. Shiro, N. Shibata, *Angew. Chem.* **2009**, *121*, 6442–6445; *Angew. Chem. Int. Ed.* **2009**, *48*, 6324–6327; d) H. Kawai, K. Tachi, E. Tokunaga, M. Shiro, N. Shibata, *Org. Lett.* **2010**, *12*, 5104–5107; see also Ref. [3].
- [12] For the construction of chiral C*–F centers, see: a) N. Shibata, E. Suzuki, Y. Takeuchi, *J. Am. Chem. Soc.* **2000**, *122*, 10728–10729; b) N. Shibata, E. Suzuki, T. Asahi, M. Shiro, *J. Am. Chem. Soc.* **2001**, *123*, 7001–7009; c) N. Shibata, J. Kohno, K. Takai, T. Ishimaru, S. Nakamura, T. Toru, S. Kanemasa, *Angew. Chem.* **2005**, *117*, 4276–4279; *Angew. Chem. Int. Ed.* **2005**, *44*, 4204–4207; d) D. S. Reddy, N. Shibata, J. Nagai, S. Nakamura, T. Toru, S. Kanemasa, *Angew. Chem.* **2008**, *120*, 170–174; *Angew. Chem. Int. Ed.* **2008**, *47*, 164–168.
- [13] a) D. Basavaiah, B. S. Reddy, S. S. Badsara, *Chem. Rev.* **2010**, *110*, 5447–5674; b) T.-Y. Liu, M. Xie, Y.-C. Chen, *Chem. Soc. Rev.* **2012**, *41*, 4101–4112; c) R. Rios, *Catal. Sci. Technol.* **2012**, *2*, 267–278.
- [14] T. Furukawa, J. Kawazoe, W. Zhang, T. Nishimine, E. Tokunaga, T. Matsumoto, M. Shiro, N. Shibata, *Angew. Chem.* **2011**, *123*, 9858–9862; *Angew. Chem. Int. Ed.* **2011**, *50*, 9684–9688.
- [15] X. Companyó, G. Valero, V. Ceban, T. Calvet, M. Font-Bardía, A. Moyano, R. Rios, *Org. Biomol. Chem.* **2011**, *9*, 7986–7989.
- [16] a) J. N. Kim, H. J. Lee, J. H. Gong, *Tetrahedron Lett.* **2002**, *43*, 9141–9146; b) M. G. Nascimento, S. P. Zanotto, S. P. Melegari, L. Fernandes, M. M. Sá, *Tetrahedron: Asymmetry* **2003**, *14*, 3111–3115; c) C.-W. Cho, J.-R. Kong, M. J. Krische, *Org. Lett.* **2004**, *6*, 1337–1339; d) C. E. Aroyan, M. M. Vasbinder, S. J. Miller, *Org. Lett.* **2005**, *7*, 3849–3851; e) C. Ó. Dálaigh, S. J. Connon, *J. Org. Chem.* **2007**, *72*, 7066–7069; f) F. Wang, S. Li, M. Qu, M.-X. Zhao, L.-J. Liu, M. Shi, *Chem. Commun.* **2011**, *47*, 12813–12815; g) Y. Wang, X. Feng, H. Du, *Org. Lett.* **2011**, *13*, 4954–4957; h) B. Hu, M. Meng, S. Jiang, W. Deng, *Chin. J. Chem.* **2012**, *30*, 1289–1294.
- [17] a) E. Farrington, M. Comes-Franchini, J. M. Brown, *Chem. Commun.* **1998**, 277–278; b) L. Bernardi, B. F. Bonini, M. Comes-Franchini, M. Fochi, M. Folegatti, S. Grilli, A. Mazzanti, A. Ricci, *Tetrahedron: Asymmetry* **2004**, *15*, 245–250.
- [18] For the optimization of the reaction conditions, see the Supporting Information, Table S1 and Scheme S1.
- [19] CCDC 959849 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
- [20] M. Baidya, G. Y. Remennikov, P. Mayer, H. Mayr, *Chem. Eur. J.* **2010**, *16*, 1365–1371. See also the Supporting Information, Figure S1.
- [21] a) T. Ishimaru, N. Shibata, T. Horikawa, N. Yasuda, S. Nakamura, T. Toru, M. Shiro, *Angew. Chem.* **2008**, *120*, 4225–4229; *Angew. Chem. Int. Ed.* **2008**, *47*, 4157–4161; b) M. H. Katcher, A. Sha, A. G. Doyle, *J. Am. Chem. Soc.* **2011**, *133*, 15902–15905; c) E. Benedetto, M. Tredwell, C. Hollingworth, T. Khotavivatana, J. M. Brown, V. Gouverneur, *Chem. Sci.* **2013**, *4*, 89–96, and references therein.
- [22] a) A. T. Parsons, S. L. Buchwald, *Angew. Chem.* **2011**, *123*, 9286–9289; *Angew. Chem. Int. Ed.* **2011**, *50*, 9120–9123; b) X. Wang, Y. Ye, S. Zhang, J. Feng, Y. Xu, Y. Zhang, J. Wang, *J. Am. Chem. Soc.* **2011**, *133*, 16410–16413; c) Y. Li, F. Liang, Q. Li, Y.-C. Xu, Q.-R. Wang, L. Jiang, *Org. Lett.* **2011**, *13*, 6082–6085; d) L. Chu, F.-L. Qing, *Org. Lett.* **2012**, *14*, 2106–2109; e) R. Shimizu, H. Egami, Y. Hamashima, M. Sodeoka, *Angew. Chem.* **2012**, *124*, 4655–4658; *Angew. Chem. Int. Ed.* **2012**, *51*, 4577–4580; f) S. Mizuta, O. Galicia-López, K. M. Engle, S. Verhoog, K. Wheelhouse, G. Rassias, V. Gouverneur, *Chem. Eur. J.* **2012**, *18*, 8583–8587, and references therein.