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Convergent, asymmetric synthesis of vicinal amino alcohols *via* Rh-catalyzed addition of α-amido trifluoroborates to carbonyls†

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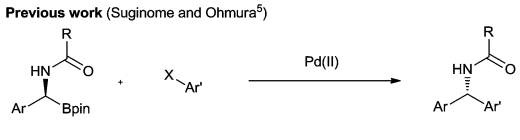
We describe the Rh-catalyzed addition of α-sulfinamido trifluoroborates to carbonyl compounds for the convergent, asymmetric synthesis of vicinal amino alcohols. This method represents the first application of α-amino boron reagents as reaction partners in rhodium-catalyzed couplings. Reactions with trifluoromethyl ketones proceed in reasonable yields and with good diastereoselectivity along with complete retention at the organoboron stereocenter. The potential of this method is further highlighted by the exploration of a variety of nitrogen substituents and addition to benzaldehyde and trityl-protected isatin.

Introduction

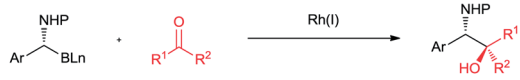
The importance of the α-amino boronic acid pharmacophore for protease inhibition, as best exemplified by the cancer drug bortezomib (Velcade), has inspired the development of a number of methods for the asymmetric synthesis of α-amino boronic acid derivatives.[1–3] Given the enormous utility of organoboron reagents for transition metal catalyzed C–C bond formation, these α-amino boronic acid derivatives might also prove to be exceptionally versatile functionalized organometallic reagents for the convergent, asymmetric synthesis of branched amine compounds.[4] In seminal work, Suginome and Ohmura have demonstrated the Pd-catalyzed cross-coupling of homochiral *N*-acyl α-amino boronate esters with aryl halides for the asymmetric synthesis of diarylmethanamines (eqn (1)).[5] Rh-catalyzed couplings of organoboron reagents are also tremendously versatile with additions of arylboron reagents to alkenes, alkynes, aldehydes, ketones, imines, and isocyanates all having been demonstrated.[6] However, to our knowledge there are no examples of Rh-catalyzed additions of α-heteroatom substituted boron reagents to any of these electrophiles. Herein, we report the first Rh-catalyzed couplings of α-amino boronic acid derivatives as demonstrated by additions to carbonyl compounds for the convergent, asymmetric synthesis of vicinal amino alcohols, which are common in drugs and natural products as well as ligands for asymmetric synthesis (eqn (2)).[7]

Previous work (Suginome and Ohmura[5])



(1)

This work



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Results and discussion

Previously, we reported the Cu-catalyzed asymmetric borylation of *N-tert*-butanesulfinyl imines to provide one of the most efficient methods to prepare homochiral α-amino boronic acid derivatives.[2a] Additionally, these α-sulfinamido boronic acid derivatives should be particularly useful for transition metal catalyzed couplings because the *N*-sulfinyl group can readily be cleaved from coupling products in high yields by simple treatment with acid.[8] We therefore selected these reagents to start our investigation of Rh-catalyzed couplings.

We chose to initially investigate additions to trifluoromethyl ketones because of the well documented value of introducing trifluoromethyl substituents in medicinal chemistry and agrochemical development to reduce metabolism and alter physicochemical properties.[9–12] Notably, alternative methods for the asymmetric synthesis of these types of trifluoromethyl substituted amino alcohols have not yet been developed.[13]

We observed modest conversion for the addition of α-sulfinamido boronate ester **1a** to 2,2,2-trifluoroacetophenone (eqn (3)). Vicinal amino alcohol **2a** was obtained in 15% yield employing the catalyst and solvent system used by Aggarwal for the addition of α-alkyl benzylboron reagents to aldehydes[14,15]

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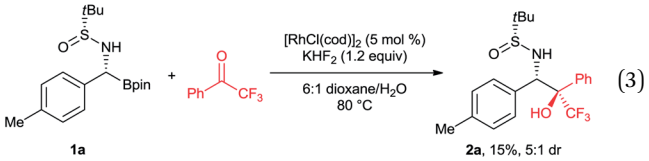
and employing the base KHF_2, which was recently reported by Yun.[14c]



(3)

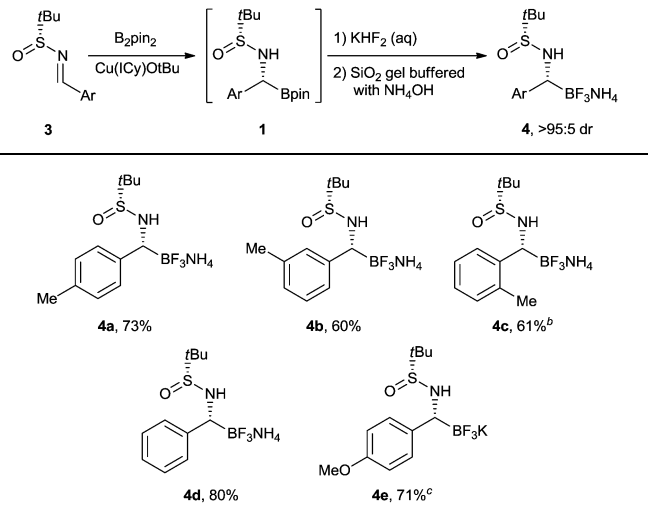
One of the major challenges in developing these Rh-catalyzed additions is the relatively poor stability of the benzylic α-amino boronate esters, which complicates their isolation, storage, and use under different reaction conditions. Given previously reported additions of benzyltrifluoroborates to aldehydes[14] and that KHF_2 was an effective base for our system (eqn (3)), we chose to develop a telescoped synthesis of α-sulfinamido trifluoroborates due to the reported enhanced stability of trifluoroborates over the corresponding boronate esters.[16,17]

Cu-catalyzed borylation of *N-tert*-butanesulfinyl imine **3** provided the intermediate boronate ester **1** as previously reported,[2a] and subjection of the crude boronate ester to aqueous KHF_2 afforded benzylic α-sulfinamido trifluoroborates **4** (Table 1). Isolation *via* silica gel chromatography under NH_4OH buffered conditions provided the pure trifluoroborates **4a–4d** as their ammonium salts in good overall yields (60–80% over two steps). Alternatively, the potassium trifluoroborate **4e** was isolated by precipitation. This telescoped strategy enabled the consistent preparation of gram-scale quantities of the α-sulfinamido trifluoroborates **4**, which were stable to storage for >2 months.

The reaction of trifluoroborate **4a** with 2,2,2-trifluoroacetophenone was evaluated with a variety of Rh catalysts and a range of reaction parameters (Table 2). Under conditions developed for the boronate esters (eqn (3)), the trifluoroborate showed diminished reactivity (entry 1). Although lowering the temperature improved the selectivity, no improvement in yield was observed (entry 2). However, dramatic improvement was achieved by evaluating different Rh catalysts. While $[RhOH(cod)]_2$ (entry 3) outperformed $[RhCl(cod)]_2$ (entry 2), the best results were observed when employing cationic Rh complexes (entries 4 and 5). Due to its stability, $[Rh(cod)(MeCN)_2]BF_4$ was used in further investigations. A range of solvent systems were evaluated with DCE proving to be an optimal co-solvent (entries 6–8). Similar yields were obtained with either H_2O or EtOH as the other co-solvent (entries 6 and 7). EtOH was chosen for further evaluation to avoid potential complications associated with the biphasic DCE–H_2O system. Investigation of reaction concentration demonstrated comparable yields from 0.19 M to 1.2 M, and therefore 0.74 M was selected to minimize the volume of solvent used while maintaining ease of manipulation (entry 8). The limiting factor in many Rh-catalyzed reactions of organoboron reagents is decomposition of the organoboron reagent; as a result, this reaction partner is often used in excess.[18] However, for this coupling reaction, reversing the stoichiometry such that the more expensive trifluoroborate was used in excess actually proved to be detrimental (entry 9).

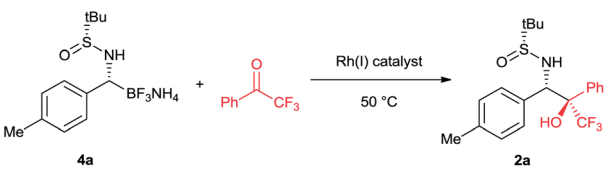
Having optimized the reaction parameters for α-sulfinamido trifluoroborates **4**, we also subjected the boronate ester **1a** to the optimized reaction conditions utilizing KHF_2 as a base (eqn (4)). This reaction provided a yield comparable to that of the trifluoroborate under the same conditions (Table 2, entry 7).

Table 1 Synthesis of α-sulfinamido trifluoroborates[a]



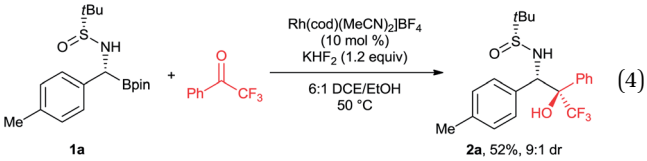
[a] See ESI for detailed reaction conditions. [b] Isolated product (96% w/w) contained a small amount of pinacol. [c] Isolated *via* precipitation.

Table 2 Optimization of reaction conditions[a]



Entry	Rh(I) catalyst	Solvent	Yield[b] (%)	dr[c]
1[d]	$[RhCl(cod)]_2$	6 : 1 dioxane–H_2O	5	2 : 1
2	$[RhCl(cod)]_2$	6 : 1 dioxane–H_2O	6	≥2 : 1
3	$[RhOH(cod)]_2$	6 : 1 dioxane–H_2O	13	6 : 1
4	$[Rh(cod)_2]BF_4$	6 : 1 dioxane–H_2O	39	10 : 1
5	$[Rh(cod)(MeCN)_2]BF_4$	6 : 1 dioxane–H_2O	37	10 : 1
6	$[Rh(cod)(MeCN)_2]BF_4$	6 : 1 DCE–H_2O	60	12 : 1
7	$[Rh(cod)(MeCN)_2]BF_4$	6 : 1 DCE–EtOH	55	11 : 1
8[e]	$[Rh(cod)(MeCN)_2]BF_4$	6 : 1 DCE–EtOH	62	12 : 1
9[f]	$[Rh(cod)(MeCN)_2]BF_4$	6 : 1 DCE–EtOH	21	n.d.[g]

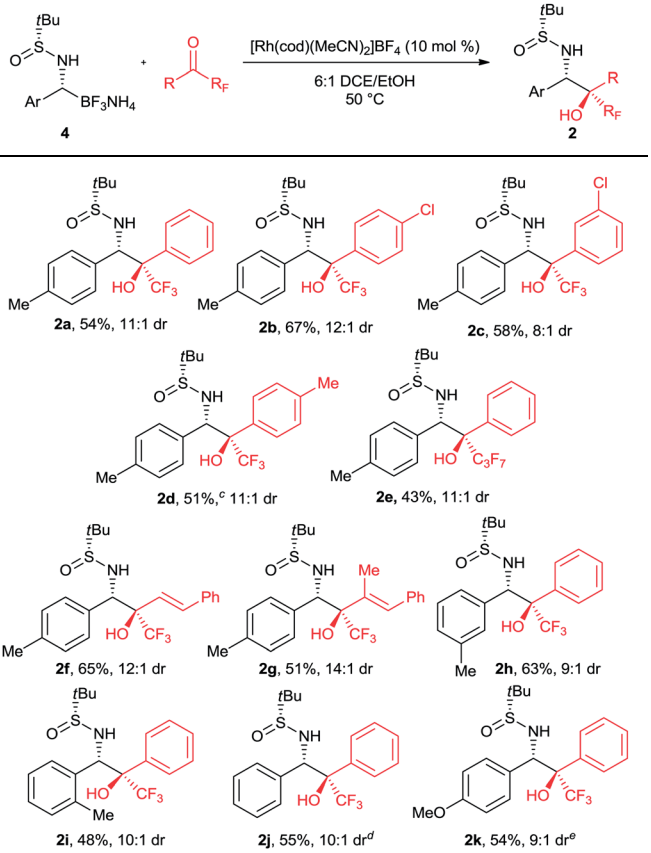
[a] *Conditions*: **4a** (1.0 equiv.), ketone (2.0 equiv.), Rh cat. (5 mol% dimer or 10 mol% monomer) in solvent (0.19 M). [b] Determined by ^1H NMR relative to 1,3,5-trimethoxybenzene as an external standard. [c] Determined by ^1H NMR. [d] Reaction conducted at 80 °C. [e] Reaction conducted at 0.74 M. [f] *Conditions*: **4a** (2.0 equiv.), ketone (1.0 equiv.), $[Rh(cod)(MeCN)_2]BF_4$ (10 mol%). [g] Not determined.



(4)

The scope of the reaction was next investigated (Table 3). A variety of electrophilic ketones were effective substrates for the method. Trifluoroacetophenones with no substitution (**2a**), electron-withdrawing groups (**2b** and **2c**), and electron-donating substituents (**2d**) all provided the amino alcohol products in reasonable yields and with good selectivity. An extended perfluoroalkyl group in place of the trifluoromethyl group also provided the product although with a slight reduction in yield (**2e**). Interestingly, α,β-unsaturated trifluoromethyl ketones also coupled efficiently with exclusive 1,2-addition selectivity and with good diastereoselectivity (**2f** and **2g**). While many examples of the Rh-catalyzed 1,4-addition of boron reagents to α,β-unsaturated carbonyl compounds have been reported,[6a,c,g,h] to our knowledge this represents the first example of high regioselectivity for 1,2-addition of boron reagents to α,β-unsaturated ketones.

Table 3 Substrate scope with fluorinated ketones[a,b]



[a] *Conditions*: **4** (1.0 equiv.), ketone (2.0 equiv.), $[Rh(cod)(MeCN)_2]BF_4$ (10 mol%) in 6 : 1 DCE–EtOH (0.74 M). [b] Isolated yields of a single diastereomer after silica gel chromatography. Diastereomeric ratio determined by ^1H NMR of the crude product. [c] Isolated as a 94 : 6 mixture of diastereomers. [d] Diastereomeric ratio determined by ^{19}F NMR. [e] Reaction conducted with potassium trifluoroborate. Yield when using the ammonium trifluoroborate was 27% as determined by ^1H NMR.

The reaction also accommodated different substitution patterns on the aromatic ring of the α-sulfinamido trifluoroborate. In addition to a methyl group at the para position (**2a–2g**), trifluoroborates with methyl substituents at the meta (**2h**) and even ortho (**2i**) position provided comparable yields and selectivities. An unsubstituted trifluoroborate also reacted readily (**2j**) as did a *para*-methoxy-substituted derivative (**2k**). However, in the latter case, the potassium salt gave an improved yield. Electron-withdrawing substituents on the aromatic ring (*e.g.* 4-Cl) and alkyl α-sulfinamido trifluoroborates were not effective coupling partners (not shown). The absolute stereochemistry of amino alcohol **2j** was confirmed by X-ray crystallography.[19] As observed for the Rh-catalyzed addition of α-alkyl benzylboron reagents to aldehydes,[14] retention of stereochemistry at the α-carbon is observed.

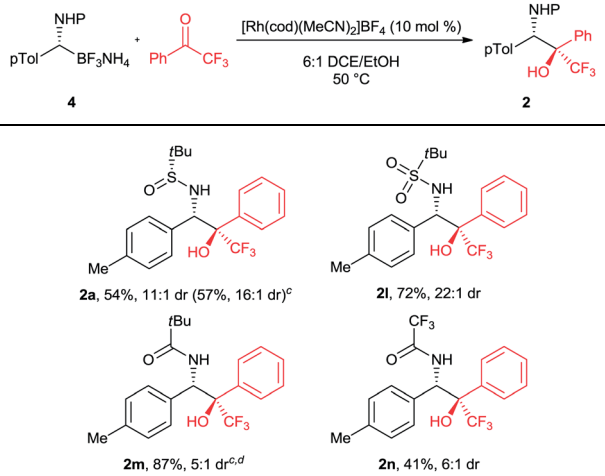
Removal of the *tert*-butanesulfinyl group could be achieved under standard conditions using dilute HCl in MeOH.[8] Deprotection of amino alcohol **2h** proceeded in high yield to afford the amine hydrochloride **5** without erosion of the diastereomeric ratio (eqn (5)).

(5)

In addition to the *tert*-butanesulfinyl group, other common nitrogen substituents were also evaluated to assess their effect on the yield and stereoselectivity for Rh-catalyzed additions to 2,2,2-trifluoroacetophenone (Table 4). The *tert*-butanesulfonyl (Bus) protecting group[20] provided both improved yield and diastereoselectivity (**2l**). This result also establishes that the benzylic stereocenter, and not the sulfinyl group, is the major controlling element for addition stereoselectivity.[21] Moreover, the enantiomeric purity of amino alcohol **2l** (97 : 3 er) was determined by chiral HPLC analysis and established negligible loss of stereochemical purity during Rh-catalyzed coupling.

Amide groups, which were used in Pd-catalyzed cross-coupling of α-amino boronate esters,[5] were also compatible with the Rh-catalyzed addition. The pivaloyl-protected α-amino trifluoroborate reacted with excellent yield but diminished diastereoselectivity (**2m**). In this case, the tetrabutylammonium salt was used because isolation of the corresponding ammonium and potassium salts proved difficult. As a control, the tetrabutylammonium salt of the α-sulfinamido trifluoroborate (**4a′**) was also evaluated and gave comparable yields and slightly improved selectivity when compared to the ammonium salt (Table 4, **2a**). The base-labile trifluoroacetyl protecting group was also evaluated, but a lower yield and selectivity was obtained (**2n**). The enantiomeric purities of the amide products

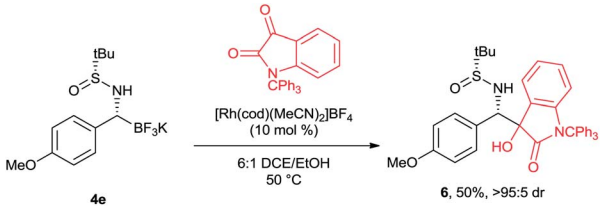
Table 4 Substrate scope of protected α-amino trifluoroborates[a,b]



[a] *Conditions*: **4** (1.0 equiv.), ketone (2.0 equiv.), $[Rh(cod)(MeCN)_2]BF_4$ (10 mol%) in 6 : 1 DCE–EtOH (0.74 M). [b] Isolated yields of a single diastereomer after silica gel chromatography. Diastereomeric ratio determined by ^1H NMR of the crude product. [c] Reaction conducted with the tetrabutylammonium trifluoroborate. [d] Isolated as a 90 : 10 mixture of diastereomers.

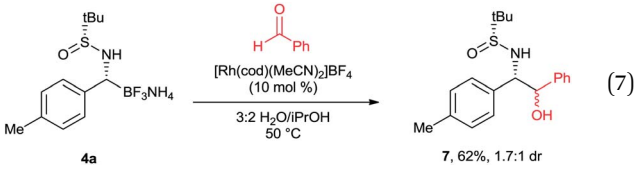
2m and **2n** were determined by chiral HPLC analysis. No loss of stereochemical purity occurred during the coupling to give *N*-pivaloyl amino alcohol **2m**.[22] In contrast, a small but appreciable loss of stereochemical purity was observed in the preparation of the *N*-trifluoroacetyl amino alcohol **2n** (88 : 12 er). Overall, it is clear that the nitrogen substituent can have an appreciable effect on both the reaction yield and stereoselectivity and therefore is an important variable to consider for Rh-catalyzed additions to other electrophiles.

The addition of α-sulfinamido trifluoroborates **4** to carbonyl compounds other than trifluoromethyl ketones was also explored. Trityl-protected isatin reacted readily with trifluoroborate **4e** to give amino alcohol **6** with exceptional diastereoselectivity (eqn (6)). In contrast, unactivated ketones such as acetone couple with very poor efficiency (data not shown). In a preliminary investigation the addition of α-sulfinamido trifluoroborate **4a** to benzaldehyde was also explored and provided the desired amino alcohol **7** in good yield, albeit with low selectivity (eqn (7)). Oxidation of the amino alcohol **7** provided the corresponding α–amino ketone in >95 : 5 dr, establishing that in the Rh-catalyzed addition, excellent stereochemical retention is observed for the carbinamine stereocenter and that



(6)

lack of control in the formation of the carbinol stereocenter results in the observed poor diatereoselectivity.[19]



(7)

Conclusions

The Rh-catalyzed addition of protected α-amino trifluoroborates to aryl and alkenyl trifluoromethyl ketones and trityl isatin proceed in reasonable yields, with good diastereoselectivity, and with complete retention at the α-amino stereocenter. Additionally, the Bus-, pivaloyl-, and trifluoroacetyl-nitrogen substituents were each evaluated and found to influence the yield and stereoselectivity. Finally, the work described here sets the stage for exploration of additions of α-amino trifluoroborates to other electrophiles known to be competent in Rh-catalyzed transformations.

Acknowledgements

This work was supported by the NSF. We gratefully acknowledge Louise Guard for solving the crystal structure of **2j**.

Notes and references

1 For a review of boron-containing protease inhibitors, see: R. Smoum, A. Rubinstein, V. M. Dembistky and M. Srebnick, *Chem. Rev.*, 2012, **112**, 4156.

2 For the asymmetric synthesis of α-amino boronic acid derivatives via the borylation of imines, see: (*a*) M. A. Beenen, C. An and J. A. Ellman, *J. Am. Chem. Soc.*, 2008, **130**, 6910; (*b*) C. Solé, H. Gulyás and E. Fernández, *Chem. Commun.*, 2012, **48**, 3769; (*c*) K. Wen, H. Wan, J. Chen, H. Zhang, X. Cui, C. Wei, E. Fan and Z. Sun, *J. Org. Chem.*, 2013, **78**, 3405; (*d*) K. Wen, J. Chen, F. Gao, P. S. Bhadury, E. Fan and Z. Sun, *Org. Biomol. Chem.*, 2013, **11**, 6350; (*e*) K. Hong and J. P. Morken, *J. Am. Chem. Soc.*, 2013, **135**, 9252; (*f*) S.-S. Zhang, Y.-S. Zhao, P. Tian and G.-Q. Lin, *Synlett*, 2013, **24**, 437.

3 For leading references on the strategies developed by Matteson and coworkers, see: D. S. Matteson, *J. Org. Chem.*, 2013, **78**, 10009.

4 For the synthesis of other α-sulfinamido organometallic reagents and their application in the synthesis of branched amines, see: (*a*) K. W. Kells and J. M. Chong, *Org. Lett.*, 2003, **5**, 4215; (*b*) K. W. Kells and J. M. Chong, *J. Am. Chem. Soc.*, 2004, **126**, 15666; (*c*) D. M. Ballweg, R. C. Miller, D. L. Gray and K. A. Scheidt, *Org. Lett.*, 2005, **7**, 1403.

5 (*a*) T. Ohmura, T. Awano and M. Suginome, *Chem. Lett.*, 2009, 664; (*b*) T. Ohmura, T. Awano and M. Suginome, *J. Am. Chem. Soc.*, 2010, **132**, 13191; (*c*) T. Awano,

T. Ohmura and M. Suginome, *J. Am. Chem. Soc.*, 2011, **133**, 20738.

6 (*a*) T. Hayashi and K. Yamasaki, *Chem. Rev.*, 2003, **103**, 2829; (*b*) K. Fagnou and M. Lautens, *Chem. Rev.*, 2003, **103**, 169; (*c*) T. Hayashi, *Bull. Chem. Soc. Jpn.*, 2004, **77**, 13; (*d*) T. Miura, Y. Takahashi and M. Murakami, *Chem. Commun.*, 2007, 3577; (*e*) N. Miyaura, *Bull. Chem. Soc. Jpn.*, 2008, **81**, 1535; (*f*) S. W. Youn, *Eur. J. Org. Chem.*, 2009, 2597; (*g*) H. J. Edwards, J. D. Hargrave, S. D. Penrose and C. G. Frost, *Chem. Soc. Rev.*, 2010, **39**, 2093; (*h*) D. Müller and A. Alexakis, *Chem. Commun.*, 2012, **48**, 12037; (*i*) P. Tian, H.-Q. Dong and G.-Q. Lin, *ACS Catal.*, 2012, **2**, 95.

7 (*a*) O. N. Burchak and S. Py, *Tetrahedron*, 2009, **65**, 7333; (*b*) T. J. Donohoe, C. K. A. Callens, A. Flores, A. R. Lacy and A. H. Rathi, *Chem. – Eur. J.*, 2011, **17**, 58.

8 M. T. Robak, M. A. Herbage and J. A. Ellman, *Chem. Rev.*, 2010, **110**, 3600.

9 For Rh-catalyzed additions of arylboron reagents to trifluoromethyl ketones, see: (*a*) S. L. X. Martina, R. B. C. Jagt, J. G. de Vries, B. L. Feringa and A. J. Minnaard, *Chem. Commun.*, 2006, 4093; (*b*) J. R. White, G. J. Price, P. K. Plucinski and C. G. Frost, *Tetrahedron Lett.*, 2009, **50**, 7365; (*c*) V. R. Jumde, S. Facchetti and A. Iuliano, *Tetrahedron: Asymmetry*, 2010, **21**, 2775; (*d*) R. Luo, K. Li, Y. Hu and W. Tang, *Adv. Synth. Catal.*, 2013, **355**, 1297.

10 For a review of trifluoromethyl ketones, see: C. B. Kelly, M. A. Mercadante and N. E. Leadbeater, *Chem. Commun.*, 2013, **49**, 11133.

11 For reviews of fluorine in biologically active molecules, see: (*a*) P. Jeschke, *ChemBioChem*, 2004, **5**, 570; (*b*) K. Müller, C. Faeh and F. Diederich, *Science*, 2007, **317**, 1881; (*c*) W. K. Hagmann, *J. Med. Chem.*, 2008, **51**, 4359; (*d*) S. Purser, P. R. Moore, S. Swallow and V. Gouverneur, *Chem. Soc. Rev.*, 2008, **37**, 320.

12 For selected, recent examples of trifluoromethyl-substituted chiral tertiary carbinols in drug development efforts, see: (*a*) S. G. Ouellet, D. Gauvreau, M. Cameron, S. Dolman, L.-C. Campeau, G. Hughes, P. D. O'Shea and I. W. Davies, *Org. Process Res. Dev.*, 2012, **16**, 214; (*b*) J. T. Reeves, D. R. Fandrick, Z. Tan, J. J. Song, S. Rodriguez, B. Qu, S. Kim, O. Niemeier, Z. Li, D. Byrne, S. Campbell, A. Chitroda, P. DeCross, T. Fachinger, V. Fuchs, N. C. Gonella, N. Grinberg, N. Haddad, B. Jäger, H. Lee, J. C. Lorenz, S. Ma, B. A. Narayanan, L. J. Nummy, A. Premasiri, F. Roschanger, M. Sarvestani, S. Shen, E. Spinelli, X. Sun, R. J. Varsolona, N. Yee, M. Brenner and C. H. Senanayake, *J. Org. Chem.*, 2013, **78**, 3616; (*c*) Z.-K. Wan, E. Chenail, H.-Q. Li, M. Ipek, J. Xiang, V. Suri, S. Hahm, J. Bard, K. Svenson, X. Xu, X. Tian, M. Wang, X. Li, C. E. Johnson, A. Qadri, D. Panza, M. Perreault, T. S. Mansour, J. F. Tobin and E. Saiah, *ACS Med. Chem. Lett.*, 2013, **4**, 118.

13 G. Mlostoń, E. Obijalska and H. Heimgartner, *J. Fluorine Chem.*, 2010, **131**, 829.

14 (*a*) A. Ros and V. K. Aggarwal, *Angew. Chem., Int. Ed.*, 2009, **48**, 6289; (*b*) X. Feng and J. Yun, *Chem. – Eur. J.*, 2010, **16**, 13609; (*c*) C. Zhang and J. Yun, *Org. Lett.*, 2013, **15**, 3416.

15 For leading references on other synthetic applications of chiral branched organoboron reagents, see: (*a*) H. K. Scott and V. K. Aggarwal, *Chem. – Eur. J.*, 2011, **17**, 13124; (*b*) B. M. Partridge, L. Chausset-Boissarie, M. Burns, A. P. Pulis and V. K. Aggarwal, *Angew. Chem., Int. Ed.*, 2012, **51**, 11795; (*c*) A. P. Pulis, D. J. Blair, E. Torres and V. K. Aggarwal, *J. Am.Chem. Soc.*, 2013, **135**, 16054; (*d*) J. L.-Y. Chen, H. K. Scott, M. J. Hesse, C. L. Willis and V. K. Aggarwal, *J. Am. Chem. Soc.*, 2013, **135**, 5316; (*e*) M. Mohiti, C. Rampalakos, K. Feeney, D. Leonori and V. K. Aggarwal, *Chem. Sci.*, 2014, **5**, 602.

16 (*a*) G. A. Molander and N. Ellis, *Acc. Chem. Res.*, 2007, **40**, 275; (*b*) S. Darses and J.-P. Genet, *Chem. Rev.*, 2008, **108**, 288; (*c*) G. A. Molander and B. Canturk, *Angew. Chem., Int. Ed.*, 2009, **48**, 9240.

17 For leading references on aminomethyl trifluoroborates and their applications in Pd-catalyzed cross-coupling, see: (*a*) G. A. Molander and M.-H. Hiebel, *Org. Lett.*, 2010, **12**, 4876; (*b*) G. A. Molander, N. Fleury-Bégeot and M.-H. Hiebel, *Org. Lett.*, 2011, **13**, 1694; (*c*) J. Raushel, D. L. Sandrock, K. V. Josyula, D. Pakyz and G. A. Molander, *J. Org. Chem.*, 2011, **76**, 2762; (*d*) G. A. Molander and I. Shin, *Org. Lett.*, 2013, **15**, 2534.

18 (*a*) See ref. 6*b*; (*b*) D. G. Hall, *Boronic Acids: Preparation and Applications in Organic Synthesis and Medicine*, ed. D. G. Hall, Wiley-VCH, Somerset, NJ, 2nd edn, 2012, vol. 1, ch. 1, pp. 1–133.

19 See ESI.†

20 P. Sun, S. M. Weinreb and M. Shang, *J. Org. Chem.*, 1997, **62**, 8604.

21 Oxidation of **2a** to give **2l** established the same relative and absolute stereochemistry. See ESI.†

22 Acid-mediated removal of the sulfinyl group from **2a** followed by pivaloylation to give **2m** confirmed the same relative and absolute stereochemistry. See ESI.†