

Influence of Phosphoramidites in Copper-Catalyzed Conjugate Borylation Reaction

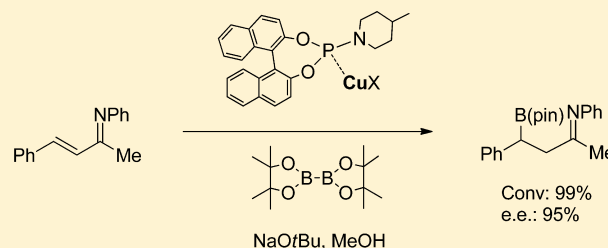
Cristina Sole,[†] Amadeu Bonet,[†] André H. M. de Vries,[‡] Johannes G. de Vries,[‡] Laurent Lefort,^{*,‡} Henrik Gulyás,^{*,†} and Elena Fernández^{*,†}

[†]Departamento de Química Física i Inorgànica, University Rovira i Virgili, C/Marcel·lí Domingo s/n, 43007 Tarragona, Spain

[‡]DSM Innovative Synthesis B.V., P.O. Box 18, 6160 MD Geleen, The Netherlands

Supporting Information

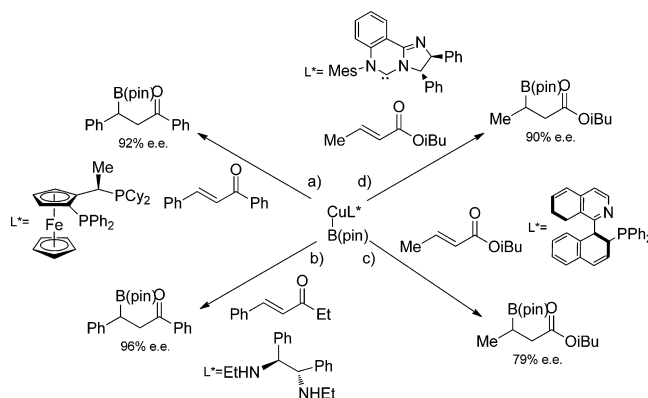
ABSTRACT: Copper(I) has become the preferred metal to catalyze the β -boration of α,β -unsaturated carbonyl compounds, and now we demonstrate that easily accessible monodentate chiral ligands, such as phosphoramidites and phosphites, can be convenient alternative ligands to induce asymmetry in the enantioselective version of this reaction, particularly in the β -boration of α,β -unsaturated imines.



INTRODUCTION

The progress in the direct enantioselective construction of α -chiral boranes through the asymmetric conjugate borylation reaction is motivated by the increased interest in difunctionalized organoboron compounds in medicine and organic synthesis.¹ Several transition metals catalyze the β -boration of α,β -unsaturated carbonyl compounds, (Pt,² Rh,³ and Ni⁴), but copper has emerged as the most convenient and efficient metal to mediate the chemoselective formation of β -borylated esters, ketones, nitriles, and amides,^{5a,b} from previous work by Miyaura and Hosomi.^{5c-e} Importantly, the first attempt to induce asymmetry in the β -boration of α,β -unsaturated carbonyl compounds was made by Yun and co-workers using a copper(I) salt modified with chiral diphosphines.⁶ The results suggested that ligands with combined planar and central chirality such as Josiphos or Mandyphos performed better than axially chiral ligands based on biaryl backbones (Scheme 1a). The enantiofacial differentiation in the conjugate borylation of cyclic β,β -disubstituted unsaturated ketones was achieved by Shibasaki and co-workers using copper(I) complexes modified with diphosphines with stereogenic phosphorus.⁷ The same authors found that chiral diamine ligands could also efficiently transfer the chiral information in the asymmetric conjugate borylation of acyclic α,β -unsaturated acceptors (Scheme 1b).⁸ Our research group has successfully applied copper complexes of hemilabile P–N ligands (Scheme 1c)⁹ and copper complexes of chiral N-heterocyclic carbene (NHC) ligands¹⁰ in the enantioselective β -boration of α,β -unsaturated esters. Further examples of chiral NHC ligands also delivered excellent results in the copper(I)-mediated boron addition reactions of a variety of α,β -unsaturated carbonyl compounds (Scheme 1d).¹¹ Despite the fact that other metals modified with chiral diphosphines have been postulated to be efficient catalytic systems for the enantioselective β -boration reaction (Pd, Ni,¹²

Scheme 1. Representative Examples of Copper-Mediated Enantioselective β -Boration of α,β -Unsaturated Esters and Ketones in the Presence of Chiral Ligands^a



^aB(pin) = pinacolboryl unit.

and Rh¹³), the copper(I) complexes are still the most attractive and economic enantioselective metal catalysts.

Our group has also identified several chiral phosphorus ligands, such as Taniaphos and Josiphos, which induced exceptional enantioselectivities in the β -boration of α,β -unsaturated imines, establishing a simple one-pot three-step synthetic route toward chiral γ -amino alcohols (Scheme 2).¹⁴

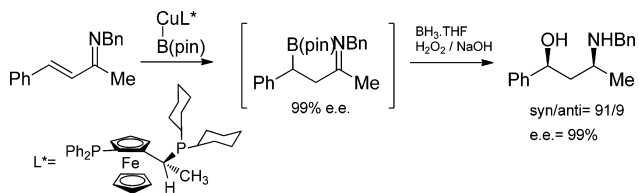
In our quest to develop both efficient and cost-effective catalytic systems for the asymmetric conjugate borylation reaction, we decided to investigate the possible application of very cheap phosphoramidite ligands in this copper-mediated

Special Issue: Copper Organometallic Chemistry

Received: March 9, 2012

Published: April 26, 2012

Scheme 2. One-Pot Synthesis of γ -Amino Alcohols by Copper-Mediated Enantioselective β -Boration of α,β -Unsaturated Imines Followed by Diastereoselective C=N Reduction and C–B Oxidation^a



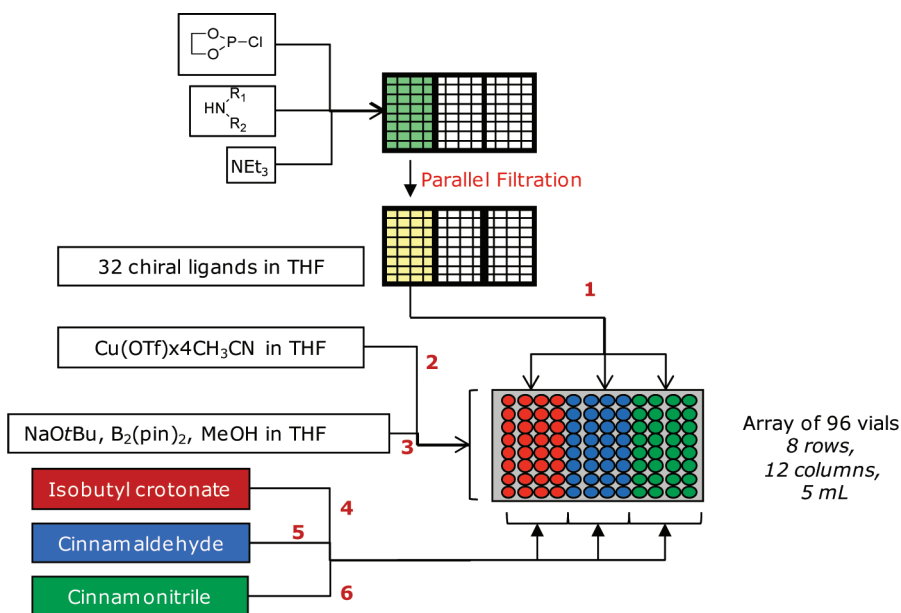
^aB(pin) = pinacolboronyl unit.

reaction. Although the price of the chiral ligand is obviously an important factor in the cost of the catalyst, we are not aware of

any systematic study carried out from this point of view in the area of catalytic boron conjugate addition reaction. Since the beginning of the century, there has been a revival of the applications of chiral monodentate phosphorus ligands in homogeneous catalysis.¹⁵ Among all classes of chiral monophosphorus ligands, phosphoramidites stand out as very cheap, easy-to-synthesize, structurally highly diverse, and chemically resistant compounds. Yun and co-workers briefly mentioned that in the β -boration of α,β -unsaturated esters and nitriles they had obtained incomplete conversions and very low enantiomeric excesses (<7%) with copper(I) complexes modified with binaphthol-derived phosphoramidites.⁶ Nevertheless, we reasoned that using a high-throughput experimentation, combined with the large set of diverse chiral phosphoramidites and phosphites accessible by DSM,¹⁶ a wider ligand screening could

Chart 1. Small Library of Chiral Phosphoramidite and Phosphite Ligands for the Copper-Mediated Enantioselective β -Boration of α,β -Unsaturated Esters, Aldehydes, and Nitriles

	A	B	C	D
1				
2				
3				
4				
5				
6				
7				
8				

Scheme 3. Parallel Ligand Synthesis and Their High Throughput Screening in the Copper-Mediated β -Boration Reaction Using a Zinsser Lissy RobotTable 1. Thirty-Two Parallel Copper(I)-Mediated β -Borations of Isobutyl Crotonate

	Conversion (%)				Enantioselectivity (%)			
	A	B	C	D	A	B	C	D
1	96	96	60	66	<5	8	-8	<5
2	97	86	97	96	8	<5	<5	-23
3	95	79	57	90	-15	7	41	-16
4	98	98	95	77	-19	<5	9	-14
5	94	86	94	74	<5	-7	<5	50
6	94	46	94	95	6	11	<5	51
7	72	73	67	89	<5	15	<5	6
8	81	96	76	83	<5	30	14	<5

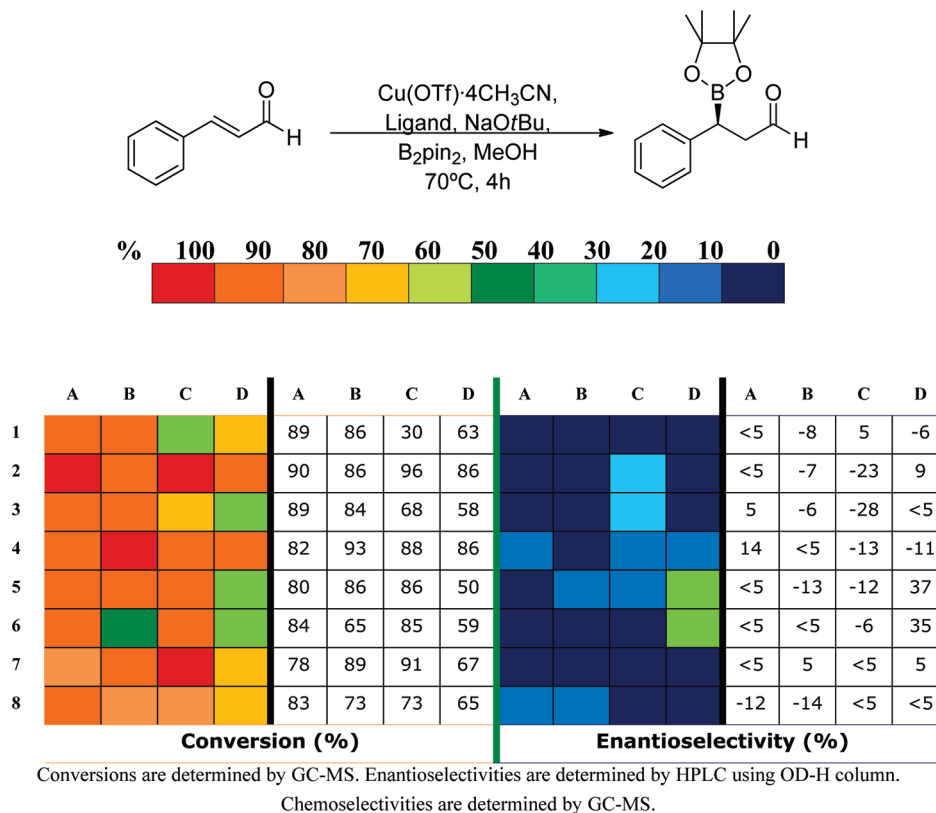
Conversions are determined by GC-MS. Enantioselectivities are determined by HPLC-MS

be carried out, hopefully leading to a more enantioselective copper catalytic system. Additionally, this effort could provide useful information on ligand structure–catalytic performance relationships.

RESULTS AND DISCUSSION

The initial screening was carried out at DSM Innovative Synthesis B.V. (Geleen, The Netherlands), and all chiral ligands included in this study were prepared according to the novel concept developed by DSM for parallel synthesis of ligand libraries.¹⁶ This concept involves the synthesis of chiral phosphoramidites¹⁷ and phosphites in one step from chlorophosphites and the corresponding amine or alcohol,

respectively. The reacting amine or triethylamine is used as acid scavenger, and, as the only purification step, the formed hydrochloride is removed by filtration. Up to 32 chiral ligands were tested in parallel in the asymmetric copper-catalyzed β -boration of three different substrates: isobutyl crotonate, cinnamaldehyde, and cinnamitrile as representative substrates for α,β -unsaturated ester, aldehyde, and nitrile, respectively. Through this set of 96 experiments, we expected to identify the structural features of the ligands that are the most relevant to achieve high enantioselectivities in the β -boration of the different activated olefins. The phosphoramidites and phosphites included in this study can be divided in several groups according to their structure (Chart 1).

Table 2. Thirty-Two Parallel Copper(I)-Mediated β -Borations of Cinnamaldehyde

The ligands prepared were mainly phosphoramidites having a binaphthyl or a partially hydrogenated H8-binaphthyl chiral core (C2–C6). Most were prepared from secondary amines, but primary amine derivatives (C3, C7, C8, D1) were also included in the study. Two of these phosphoramidites, C1 and C7, were prepared from aminophosphines and, thus, contain diphenylphosphanyl functionalities. They were considered to be chelating ligands. The remainder, despite the presence of hard donor atoms in some cases, were regarded as monodentate ligands. Some of the amines were chiral; thus, the corresponding phosphoramidites have both axial and central chirality (C8, D1–D4). Since taddol-derived monodentate phosphorus ligands had been successfully used in asymmetric Rh-hydroboration of styrene derivatives¹⁸ and Pd, Pt enantioselective diboration of allenes and alkenes,¹⁹ we also included the TADDOL-derived phosphoramidites D5 and D6 in the study. Although, in general, phosphites are more sensitive to protic solvents than phosphoramidites, we decided to test two binaphthol-derived phosphites (D7 and D8) in order to compare P–N versus P–O linkages in the monodentate ligands.

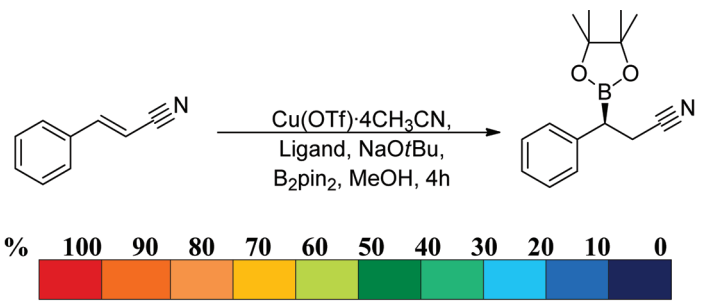
The first 96 reactions were performed in parallel. CuOTf·4CH₃CN was used as a copper(I) source instead of CuCl due to its complete solubility in THF (Scheme 3). Stock solutions of all reagents were prepared in THF, and an aliquot of a stock solution of CuOTf·4CH₃CN was dispensed into 96 (5 mL) vials with a liquid handling robot. Two equivalents of ligands relative to Cu were used in the case of monodentate phosphoramidites and phosphites, while one equivalent was used in the case of the two bidentate phosphoramidite-phosphine ligands C1 and C7. After 20 min of stirring, a freshly prepared stock solution of a mixture of 3 mol % NaOtBu relative to substrate, 1.1 equiv of bis(pinacolato)diboron

(B₂pin₂), and 2 equiv of methanol was dispensed into all 96 vials, followed by the stock solutions of the three substrates (isobutyl crotonate, cinnamaldehyde, and cinnamionitrile) with a substrate/catalyst ratio of 50. The β -boration reaction of isobutyl crotonate and cinnamionitrile was carried out at room temperature, and the reaction of the aldehyde was carried out at 70 °C, to favor the β -boration versus the 1,2-diboron addition.^{10,20}

Despite the relatively short reaction times (4 h), most of the copper(I) catalytic systems modified with the phosphoramidites provided good conversions in the β -boration of isobutyl crotonate (Table 1). Copper(I) modified with phosphoramidite ligands derived from primary amines (C3, C7, C8, and D1) provided only moderate conversions. Surprisingly, copper(I) modified with bidentate ligands, phosphoramidites-phosphines (C1, C7), gave similar but lower conversions (60–67%). The substituents on the binol backbone of the phosphoramidites exerted a subtle influence on the activity of the copper-mediated β -boration of the α,β -unsaturated ester. Among the 3,3'-substituted ligands (B4, B5, and B8) the methyl- and methoxycarbonyl-substituted derivatives allowed obtaining higher conversions (98% and 96%) than the bromo-substituted analogue (86%). Interestingly, 4,4'-bromo-substitution in ligand B6 resulted in an even more dramatic decrease of the activity (46%).

The enantioselectivity provided by the set of ligands was low in general. Nevertheless, three results should be highlighted, as they are well above the rest. Moderate enantioselectivities (around 50% ee) were achieved when the copper(I) precursor was modified with phosphoramidites with a taddol backbone (5D, 6D). Ligand C3, based on 3,3'-dimethyl binol and aminopyridine, also provided a higher than average enantioselectivity

Table 3. Thirty-Two Parallel Copper(I)-Mediated β -Borations of Cinnamitrile



	A	B	C	D	A	B	C	D	A	B	C	D	A	B	C	D
1	90	66	41	47	90	66	41	47	8	9	<5	-28	8	9	<5	-28
2	90	62	93	90	90	62	93	90	-12	-19	-28	9	-12	-19	-28	9
3	94	63	44	40	94	63	44	40	5	-20	-54	-11	5	-20	-54	-11
4	63	97	78	40	63	97	78	40	10	-17	-41	9	10	-17	-41	9
5	90	68	86	55	90	68	86	55	<5	-10	-45	-5	<5	-10	-45	-5
6	84	14	68	51	84	14	68	51	-17	8	-28	-10	-17	8	-28	-10
7	55	49	39	62	55	49	39	62	-32	-10	-5	44	-32	-10	-5	44
8	60	76	64	70	60	76	64	70	-24	18	-31	13	-24	18	-31	13
	Conversion (%)								Enantioselectivity (%)							

Conversions are determined by GC-MS. Enantioselectivities are determined by HPLC-MS

(41%). Enantiomeric excesses observed for the rest of the ligands did not exceed 30%.

In the case of the β -boration of α,β -unsaturated aldehydes the issue of chemoselectivity must be taken into consideration, since 1,2-addition of B_2pin_2 to the carbonyl group could take place under the reaction conditions.^{20,21} Nonetheless, more than half of the copper(I)-mediated β -borations of cinnamaldehyde (20/36) gave conversions higher than 80% (Table 2). We were pleased to see that two of the catalysts containing ligands **A2** and **B4** provided around 90–93% of conversion. Since the reactions were carried out at 70 °C, all the experiments showed total chemoselectivities toward the 1,4-addition. Enantioselectivities were poor in most cases, but interestingly, the best enantiomeric excesses were obtained again with copper(I) complexes modified with taddol-derived phosphoramidites (35% and 37% ee), as observed in the asymmetric β -boration of isobutyl crotonate (Table 2). These values are similar to the only example described so far in the literature for the β -boration of cinnamaldehyde, whereby 40% ee was obtained using copper(I) complexes modified with chiral N-heterocyclic carbene ligands.¹⁰

The copper(I)-catalyzed asymmetric β -boration of α,β -unsaturated nitriles was also studied using cinnamitrile as the model substrate (Table 3). In general, the average conversion into the corresponding β -borated product was lower than in the case of isobutyl crotonate and cinnamaldehyde. Nevertheless, copper(I) complexes modified with phosphoramidites **A1**, **A2**, **A3**, **A5**, **B4**, **C2**, and **D2** provided >90% conversions. The asymmetric induction in the β -boration of cinnamitrile was also moderate. The best performing ligands were phosphoramidites with an H8-binaphthyl chiral core (**C3**: 54% ee, **C4**: 41% ee, and **C5**: 45% ee) and the monophosphite prepared from binaphthol and phenol (**D7**: 44% ee).

Reproducibility of these reactions was checked at slightly higher scale with Schlenck-type techniques, obtaining comparable results in conversions and enantioselectivities. We also explored the influence of the ligand to metal ratio, and we observed that upon changing the ligand:copper ratio from 2:1 to 1:1, the enantioselectivities decreased in most cases. For example, in the β -boration of isobutyl crotonate with copper(I)-**D6** the enantiomeric excess decreased from 51% (when L:Cu = 2:1) to 40% (when L:Cu = 1:1). Also we became interested in knowing more about the influence of solvent on the reaction outcome, and we observed that upon replacing THF with toluene, the enantiomeric excesses in the β -boration of cinnamitrile could be slightly improved (from 28% to 43% with Cu(I)-**C8** and from 31% to 44% with Cu(I)-**D1**).

We next focused on the β -boration of α,β -unsaturated imines with $Cu(OTf)·4CH_3CN$ modified with some of the best performing phosphoramidite ligands in the presence of B_2pin_2 , encouraged by the results of earlier studies carried out in our group (Scheme 4).^{14a} Table 4 shows that copper(I) complexes

Scheme 4. Copper(I)-Mediated β -Boration of α,β -Unsaturated Imines and Further Functionalization

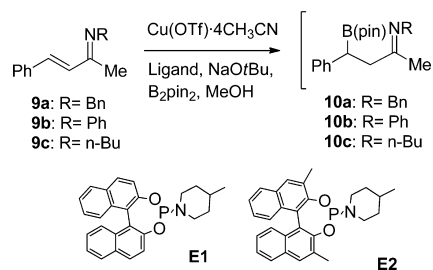


Table 4. Asymmetric Copper(I)–L* (L* = D5, D6, B3, E1, and E2)-Mediated β -Boration of α,β -Unsaturated Imines with B_2pin_2

Entry	Substrate	Catalytic system	Conv 10 (%) [Isolated Yield (%)]	e.e. 10 (%)
1 ^{a,b}		Cu(I)-D6	99 [86]	75
2 ^{a,b}	“	Cu(I)-E1	99	75
3 ^{a,b}		Cu(I)-D6	66	66
4 ^{a,b}	“	Cu(I)-E1	99 [83]	95
5 ^{a,b}		Cu(I)-D6	89 ^c	53
6 ^{a,b}	“	Cu(I)-E1	90 ^c	89
7 ^d		Cu(I)-D5	99	55
8 ^d	“	Cu(I)-D6	99	57
9 ^d	“	Cu(I)-B3	99	71
10 ^d	“	Cu(I)-E1	99	75
11 ^d	“	Cu(I)-E2	99	48
12 ^d		Cu(I)-D5	31	94
13 ^d	“	Cu(I)-D6	35	89
14 ^d	“	Cu(I)-B3	42	90
15 ^d	“	Cu(I)-E1	33	92
16 ^d	“	Cu(I)-E2	47	53
17 ^d		Cu(I)-D5	99 [85]	75
18 ^d	“	Cu(I)-D6	99	77
19 ^d	“	Cu(I)-B3	99 [82]	90
20 ^d	“	Cu(I)-E1	99	87
21 ^d	“	Cu(I)-E2	99	19

^a β -Boration conditions: 0.2 mmol of substrate, 2 mol % CuOTf \cdot 4CH₃CN, 4 mol % ligand, B₂pin₂ (1.1 equiv), NaOtBu (9 mol %), MeOH (2 equiv), THF (1 mL), 25 °C, 6 h. ^bReference 14a.

^cConversion and ee given on the γ -amino alcohol, reduction/oxidation: 3.0 equiv of reducing agent DIBAL-H, followed by the addition of NaOH/H₂O₂ (aqueous) in excess, *syn/anti* ratio = 99:1.

^d β -Boration conditions: 0.25 mmol of substrate, 2 mol % CuOTf \cdot 4CH₃CN, 4 mol % ligand, B₂pin₂ (1.1 equiv), NaOtBu (3 mol %), MeOH (2 equiv), THF (1 mL), 25 °C, 4 h.

modified with ligands D6 and E1 were able to efficiently β -borate the imines (*E*)-1-phenyl-*N*-(4-phenylbut-3-en-2-ylidene)methanimine (**9a**) (Table 4, entries 1, 2) and (*E*)-*N*-(4-phenylbut-3-en-2-ylidene)aniline (**9b**) (Table 4, entries 3, 4), with good to excellent enantioselectivities, within 6 h at room temperature. The conversion and the enantioselectivity of the α,β -unsaturated imine (*E*)-*N*-(4-phenylbut-3-en-2-ylidene)butan-1-amine (**9c**) were determined by the analysis of the corresponding γ -amino alcohol^{14a} (Table 4, entries 5, 6). It is worth mentioning that, in general, quantitative conversions and high enantioselectivities were observed. A particularly interesting example is the β -boration of imine **9b** with copper(I) modified with the phosphoramidite E1 (Table 4, entry 4), generating the β -borated product in quantitative conversion and up to 95% ee.

When we changed slightly the conditions in the present work (0.25 mmol of substrate, 3 mol % NaOtBu, 4 h reaction time),

to be able to compare them directly with those obtained in the high-throughput experimentation previously described, we found that in most of the experiments the catalytic activity was maintained, although in the case of the β -boration of **9b** the conversions decreased significantly (Table 4, entries 12–16). However, the enantiomeric excesses remained similar to what was found for the β -boration of **9b** with Cu(I)-E1 (92% ee, Table 4, entry 15). It is interesting to note that while the copper(I)-E1 catalytic system provided high enantiomeric excesses, the analogous copper(I)-E2 catalytic system induced much lower enantioselectivity (Table 4, entries 11, 16, 21). However, the catalytic system based on copper(I)-B3 was both very active and also very enantioselective, with ee values up to 90% in the β -boration of **9b** and **9c** (Table 4, entries 14, 19).

CONCLUSIONS

A library of monodentate phosphoramidite ligands has been screened in copper(I)-catalyzed β -boration of isobutyl crotonate, cinnamaldehyde, and cinnamitrile. Many of the ligands form highly active catalysts. The enantioselectivities significantly exceed the results previously reported in the literature for phosphoramidites, but do not reach values needed for industrial applications. However, the screening of this large library of ligands allowed us to identify certain structural elements consistently present in the best performing ligands, such as the taddol backbone in the case of the ester and the aldehyde. The best performance of the phosphoramidites has been observed in the copper(I)-catalyzed β -boration of α,β -unsaturated imines. In addition to very high conversions into the desired β -borated products, the enantioselectivities also exceeded 90% when phosphoramidites D5, B3, and E1 were used to modify the copper catalyst. The β -boration of α,β -unsaturated imines is the key step in a new methodology for the synthesis of enantio- and diastereopure γ -amino alcohols. The development of efficient and cost-effective copper catalysts might be a great step toward the application of this method on an industrial scale.

ASSOCIATED CONTENT

Supporting Information

This material is available free of charge via the Internet at <http://pubs.acs.org>.

AUTHOR INFORMATION

Corresponding Author

*E-mail: mariaelena.fernandez@urv.cat.

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

We thank MEC for funding (CTQ2010-16226). C.S. acknowledges the FPU grant; A. Bonet, an FPI grant. We thank AllyChem for the gift of bis(pinacolato)diboron.

REFERENCES

- (a) Schiffrer, J. A.; Mütter, K.; Oestreich, M. *Angew. Chem., Int. Ed.* **2010**, *49*, 1194. (b) Hartmann, E.; Vyas, D. J.; Oestreich, M. *Chem. Commun.* **2011**, 7917.
- (a) Lawson, Y. G.; Lesley, M. J. G.; Marder, T. B.; Norman, N. C.; Rice, C. R. *Chem. Commun.* **1997**, 2051. (b) Ali, H. A.; Goldberg, I.; Srebnik, M. *Organometallics* **2001**, *20*, 3962. (c) Bell, N. J.; Cox, A. J.; Cameron, N. R.; Evans, J. S. O.; Marder, T. B.; Duin, M. A.;

Elservier, C. J.; Baucherel, X.; Tilloch, A. A. D.; Tooze, R. P. *Chem. Commun.* **2004**, 1854.

(3) Kabalka, G. W.; Das, B. C.; Das, S. *Tetrahedron Lett.* **2002**, 43, 2323.

(4) Hirano, K.; Yorimitsu, H.; Oshima, K. *Org. Lett.* **2007**, 9, 5031.

(5) (a) Lillo, V.; Bonet, A.; Fernández, E. *Dalton Trans.* **2009**, 2899.

(b) Dang, L.; Lin, Z.; Marder, T. B. *Chem. Commun.* **2009**, 3987.

(c) Takahashi, K.; Isiyama, T.; Miyaura, N. *Chem. Lett.* **2000**, 982.

(d) Takahashi, K.; Isiyama, T.; Miyaura, N. *J. Organomet. Chem.* **2001**, 625, 47. (e) Ito, H.; Yamanaka, H.; Tateiwa, J.; Hosomi, A. *Tetrahedron Lett.* **2000**, 41, 682.

(6) (a) Mun, S.; Lee, J.-E.; Yun, J. *Org. Lett.* **2006**, 8, 4887. (b) Lee, J.-E.; Yun, J. *Angew. Chem., Int. Ed.* **2008**, 47, 145. (c) Sim, H.-S.; Feng, X.; Yun, J. *Chem.—Eur. J.* **2009**, 15, 1939. (d) Chea, H.; Sim, H.-S.; Yun, J. *Adv. Synth. Catal.* **2009**, 351, 855.

(7) Chen, I.-H.; Yin, L.; Itano, W.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2009**, 131, 11664.

(8) Chen, I.-H.; Kanai, M.; Shibasaki, M. *Org. Lett.* **2010**, 12, 4098.

(9) Fleming, W. J.; Müller-Bunz, H.; Lillo, V.; Fernández, E.; Guiry, P. J. *Org. Biomol. Chem.* **2009**, 7, 2520.

(10) Lillo, V.; Prieto, A.; Bonet, A.; Díaz-Requejo, M. M.; Ramírez, J.; Pérez, P. J.; Fernández, E. *Organometallics* **2009**, 28, 659.

(11) (a) Park, J. K.; Lackey, H. H.; Rexford, M. D.; Kovnir, K.; Shatruk, M.; McQuade, D. T. *Org. Lett.* **2010**, 12, 5008. (b) O'Brien, J. M.; Lee, K.-S.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2010**, 132, 10630. (c) Hirsch-Weil, D.; Abboud, K. A.; Hong, S. *Chem. Commun.* **2010**, 46, 7525.

(12) Lillo, V.; Geier, M. J.; Westcott, S. A.; Fernández, E. *Org. Biomol. Chem.* **2009**, 7, 4674.

(13) Shiomi, T.; Adachi, T.; Toribatake, K.; Zhou, L.; Nishiyama, H. *Chem. Commun.* **2009**, 5987.

(14) (a) Solé, C.; Whiting, A.; Gulyás, H.; Fernández, E. *Adv. Synth. Catal.* **2011**, 353, 376. (b) Solé, C.; Tatla, A.; Mata, J. A.; Whiting, A.; Gulyás, H.; Fernández, E. *Chem.—Eur. J.* **2011**, 17, 14248.

(15) For recent reviews on the synthesis and applications of monodentate phosphorus ligands in asymmetric catalysis see: (a) Bruneau, C.; Renaud, J.-L. In *Phosphorus Ligands in Asymmetric Catalysis*, 1st ed., Vol. 1; Börner, A., Ed.; Wiley-VCH: Weinheim, 2008; pp 5–35. (b) Bruneau, C.; Renaud, J.-L. In *Phosphorus Ligands in Asymmetric Catalysis*, 1st ed., Vol. 1; Börner, A., Ed.; Wiley-VCH: Weinheim, 2008; pp 36–64. (c) Lefort, L.; de Vries, J. G. In *Phosphorus Ligands in Asymmetric Catalysis*, 1st ed., Vol. 3; Börner, A., Ed.; Wiley-VCH: Weinheim, 2008; pp 1348–1376.

(16) Lefort, L.; Boogers, J. A. F.; de Vries, A. H. M.; de Vries, J. G. *Org. Lett.* **2004**, 6, 1733.

(17) de Vries, A. H. M.; Pineschi, M.; Arnold, L. A.; Imbos, R.; Feringa, B. L. *Angew. Chem., Int. Ed. Engl.* **1997**, 36, 2620.

(18) (a) Moteki, S. A.; Wu, D.; Chandra, K. L.; Reddy, D. S.; Takacs, J. M. *Org. Lett.* **2006**, 8, 3097. (b) Smith, S. M.; Thacker, N. C.; Takacs, J. M. *J. Am. Chem. Soc.* **2008**, 130, 3734.

(19) (a) Kliman, L. T.; Mlynarski, S. N.; Ferris, G. E.; Morken, J. P. *Angew. Chem., Int. Ed.* **2012**, 51, 521. (b) Pelz, N. F.; Woodward, A. R.; Burks, H. E.; Sieber, J. D.; Morken, J. P. *J. Am. Chem. Soc.* **2004**, 126, 16328. (c) Woodward, A. R.; Burks, H. E.; Chan, L. M.; Morken, J. P. *Org. Lett.* **2005**, 7, 5505.

(20) Bonet, A.; Lillo, V.; Ramírez, J.; Díaz-Requejo, M. M.; Fernández, E. *Org. Biomol. Chem.* **2009**, 7, 1533.

(21) (a) Laitar, D. S.; Müller, P.; Sadighi, J. P. *J. Am. Chem. Soc.* **2005**, 127, 17196. (b) Laitar, D. S.; Tsui, E. Y.; Sadighi, J. P. *J. Am. Chem. Soc.* **2006**, 128, 11036.