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COMMUNICATION

BINOL derivatives-catalysed enantioselective allylboration of isatins: application to the synthesis of (*R*)-chimonamidine

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The asymmetric synthesis of the 3-allyl-3-hydroxyoxindole skeleton was accomplished in yields up to 99% *via* a metal-free and enantioselective allylation of isatins (90-96 % ee) using BINOL derivatives as catalysts and an optimized allylboronate. This methodology was applied at a gram-scale to the synthesis of the natural product (*R*)-chimonamidine.

The catalytic formation of carbon quaternary stereogenic centers from privileged structure such as isatins[1] continues to be a very challenging task for the organic chemistry community since the 3-substituted-3-hydroxyoxindole scaffold is widely found in natural products[2] and pharmacologically active molecules.[3] More specifically, 3-allyl-3-hydroxyoxindole structures can be versatile intermediates to access various alkaloids such as convolutamydine derivatives (**1**),[4] donaxaridine (**2**),[4-5] CPC-1 (**3**),[6] leucolusine (**4**)[7] and (*R*)-chimonamidine (**5**)[8] resulting from an oxindole rearrangement[9] (Fig. 1).

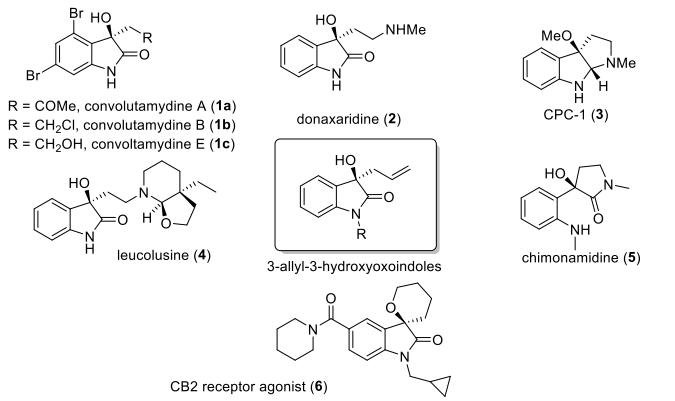


Fig. 1 Synthetic utility of 3-allyl-3-hydroxyoxindoles.

Moreover, due to the presence of the double bond which can be engaged in several intramolecular cyclization reactions, this class of compounds can serve as a platform for the synthesis of fused spirooxindole scaffolds of great interest in the medicinal chemistry area[10] such as spiroether **6**.[11] In addition to the asymmetric hydroxylation of 3-allyl-2-oxindoles[12] or allylation of 3-hydroxy-2-oxindoles,[13] efficient enantioselective preparations of 3-allyl-3-hydroxyoxindoles have been mainly realized by allylation of isatins with allylstannanes, catalysed by chiral metal complexes (Sc,[14] In[14-15] and Pd[16]) or organocatalysts.[6a, 17] The reactivity of the less toxic allylsilanes with isatins in the presence of Hg,[18] Sc[19] or Ag[20] chiral complexes was also explored with success. Other allyl donors such as allylic alcohols in the presence of chiral phosphoramidite-palladium complexes as catalyst led to moderate enantioselectivities,[21] while better results were obtained from allyl acetates and chiral iridium catalysts.[22] As 3-allyl-3-hydroxyoxindoles have a great potential for the synthesis of bioactive compounds, there is a need to avoid metals in their preparation.[23] Allylboron derivatives are key reagents in the development of metal-free procedures for the catalytic enantioselective allylation of carbonyl compounds.[24] While numerous organocatalysts have been reported for the efficient enantioselective allylboration of aldehydes,[24a-e] very few are valuable for non-activated ketones[25] or activated ketones.[26] In the case of *N*-substituted isatins, to the best of our knowledge, only one report describes the use of catalysts derived from aminophenol coupled to valine, to produce the expected 3-allyl-3-hydroxyoxindoles in good yields and with excellent enantiomeric excess (ee).[27] In view of our research programs targeted to the development of organoboron methodology leading to biologically active molecules,[28] and in line with our efforts directed towards the development of enantioselective transformations catalysed by BINOL-derived organocatalysts,[29] we speculated that chiral biphenols, prepared from commercially available BINOL enantiomers in both enantiomeric forms,[30] could efficiently catalyse an asymmetric allylation of isatins. In this paper, we describe our experimental findings related to this reaction. A convenient and efficient method was implemented with a wide range of isatin derivatives, including *N*-unprotected substrates. As this

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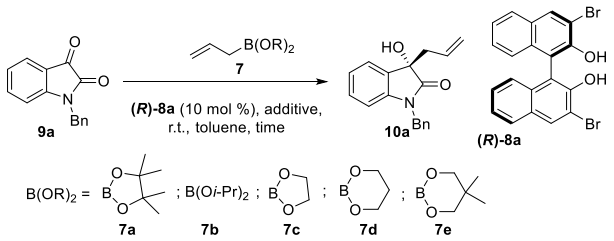
† Electronic Supplementary Information (ESI) available: Experimental procedures and ^{1}H and ^{13}C NMR spectra of all compounds as well as their corresponding HPLC chromatograms. See DOI: 10.1039/x0xx00000x

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catalytic process can be performed on a gram-scale, a synthesis of (*R*)-chimonamidine is also depicted.

As a starting point to find optimized reaction conditions, several allyl boronic esters **7** were screened for the allylation of *N*-benzylindoline-2,3-dione **9a** in toluene at room temperature and in the presence of (*R*)-3,3'-Br_2-BINOL **8a** as chiral catalyst because of its known efficiency when reacted with ketones (Table 1).[25a, 25b] The use of allylpinacol boronate **7a** under these conditions led to the product **10a** in good yield (75%) after 48 h. However, no enantioselectivity was detected (entry 1). The reaction with allyldiisopropoxyborane **7b**, a more reactive boronate, allowed to obtain a greater yield after only 16 h but with a low enantiomeric excess (entry 2). The *S* absolute configuration at the C3-position has been assigned by comparing the specific rotation and HPLC chromatographic analysis of **10a** described in the literature.[22] Based on Schaus's work concerning the enantioselective allylboration of ketones using **7b**,[25b, 25c] we added isopropyl alcohol in the catalytic process in order to improve the enantioselectivity. A better enantiomeric excess (77%) was obtained using 5 equivalents of *i*-PrOH (entry 3). Nevertheless, this result was disappointing when compared with those obtained with ketones.[25b, 25c] Moreover, the replacement of *i*-PrOH by *t*-BuOH caused a significant drop of the enantioselectivity justifying the development of a new catalytic system for this kind of substrates (entry 4). In the light of this facts, other cyclic boronates **7c-e** having an intermediary reactivity with carbonyl compounds have been attempted.[31] Reactions were completed after 16 h except for **7d-e** (entries 8 and 9). In terms of enantioselectivity, satisfactory results were obtained with **7c** and **7e** using an alcohol additive such as *t*-BuOH.

Table 1 Asymmetric allylboration of isatin **9a**

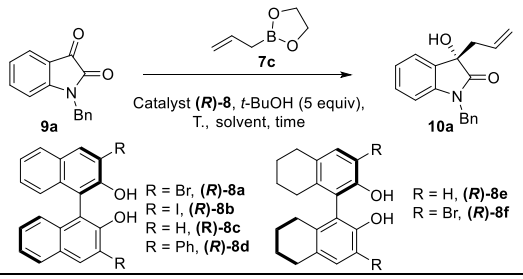


entry[a]	boronate	additive (5 equiv)	time (h)	yield (%)[b]	ee[c]
1	**7a**	-	48	75	0
2	**7b**	-	16	98	32
3	**7b**	*i*-PrOH	16	98	77
4	**7b**	*t*-BuOH	16	97	18
5	**7c**	-	16	98	53
6	**7c**	*i*-PrOH	16	97	2
7	**7c**	*t*-BuOH	16	98	88
8	**7d**	*t*-BuOH	22	98	74
9	**7e**	*t*-BuOH	22	98	84

[a] All reactions were performed with isatin **9a** (0.2 mmol), boronate **7** (0.3 mmol) and 3,3'-Br_2-BINOL (***R***)-**8a** (0.1 equiv) under Ar at room temperature. [b] Isolated yield after chromatography purification on silica. [c] Determined by chiral HPLC.

Taking the reactivity difference into account, the five-membered allylboronate **7c** was selected for the further studies in which different chiral BINOL-derived catalysts **8a-f** were evaluated as well as other parameters such as temperature and solvents (Table 2). The replacement of 3,3'-Br_2-BINOL **8a** by other organocatalysts was briefly screened. The importance of a halogen substituent at the 3,3'-positions of BINOL for the enantioselectivity was clearly demonstrated by the evaluation of parent BINOL **8c** and the phenyl-BINOL derivative **8d** for which a drop in the enantioselectivity was observed (entries 3-4). The result with iodo-BINOL **8b** was almost similar to the one obtained with the bromo analogue **8a** (entries 1-2). The use of H_8-BINOL catalysts **8e-f** led to a strong drop of selectivity (entries 5-6). The enantiomeric excess using 3,3'-Br_2-BINOL **8a** can be slightly increased by adding molecular sieves in the catalytic procedure (91% ee instead of 88% ee, entry 7). Using this catalyst, we focused on improving enantioselectivity by modifying solvent and temperature. Lower ee was obtained using CH_2Cl_2 and cyclohexane (entries 8-9). In the latter case, the allylboration reaction was slower (24h) due to the weak solubility of **9a** in cyclohexane. Higher ee was reached when decreasing the temperature up to -10° C (entries 10-11).[32] Under these conditions, the complete consumption of starting material **9a** required a longer reaction time (24 h instead of 16 h). At this stage, it is interesting to note that the catalyst loading is not an issue for this reaction since **8a** can easily be recovered during the chromatographic purification of homoallylic alcohol **10a**.

Table 2 Optimization of the reaction conditions



entry[a]	Cat. (mol%)	Solv.	T (°C)	time (h)	yield (%)[b]	ee[c]
1	**8a** (10)	toluene	r.t.	16	98	88
2	**8b** (10)	toluene	r.t.	16	98	84
3	**8c** (10)	toluene	r.t.	24	97	46
4	**8d** (10)	toluene	r.t.	24	95	30
5	**8e** (10)	toluene	r.t.	24	98	10
6	**8f** (10)	toluene	r.t.	24	98	40
7[d]	**8a** (10)	toluene	r.t.	16	98	90
8[d]	**8a** (10)	CH_2Cl_2	r.t.	16	98	78
9[d]	**8a** (10)	C_6H_{12}[e]	r.t.	24	97	86
10[d]	**8a** (10)	toluene	0	24	98	92
11[d]	**8a** (10)	toluene	-10	24	98	94
12[d]	**8a** (5)	toluene	-10	24	98	94

[a] All reactions were performed with isatin **9a** (0.2 mmol), boronate **7c** (0.3 mmol) under Ar at the temperature indicated. [b] Isolated yield after chromatography purification on silica. [c] Determined by chiral HPLC. [d] In the presence of molecular sieves (5Å). [e] Cyclohexane.

Despite this, we showed that the yield and enantioselectivity were maintained using only 5 mol% of 3,3'-Br_2 BINOL (*R*)-**8a** (98%, 94% ee, entry 12).

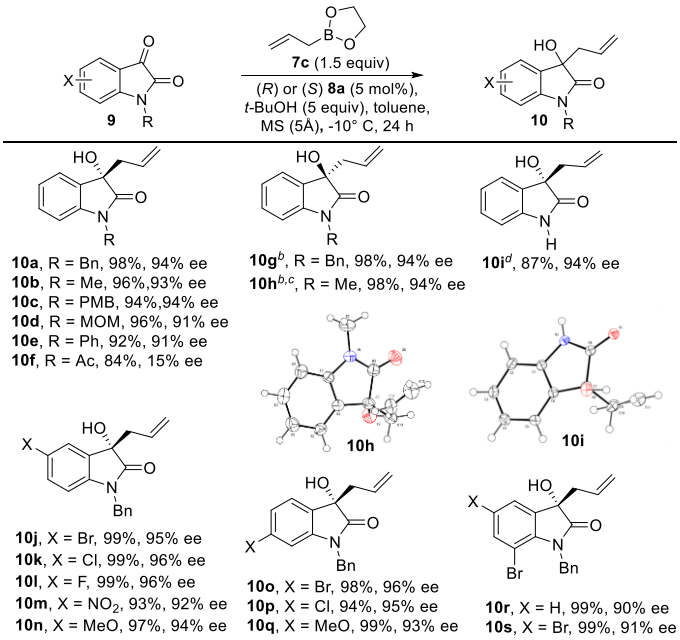
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These latter conditions were selected to explore the synthetic scope of this enantioselective allylboration process using an assortment of diversely substituted isatins (Table 3). The protecting group on the nitrogen did not show a crucial influence on the reactivity of isatins **9a-f** except with the *N*-acetyl derivative **9f**. In this case, the slower reaction rate as well as the dramatic drop of enantioselectivity could be mainly explained by two factors: the weaker solubility of **9f** under the reaction conditions and the presence of an additional carbonyl group in the molecule which could any way affect the mechanism of the reaction. As expected the use of the (*S*)-**8a** catalyst delivered the (*R*)-hydroxyoxindoles **10g-h** in the same range of yield and enantiomeric excess. More interestingly, we also showed that the asymmetric allylboration process is effective with *N*-unprotected isatin **9i**. In spite of a longer reaction time for an almost complete conversion (6 days instead of 24 h), the excellent enantiomeric excess (94%) was preserved. The single crystal X-Ray analysis of **10i** and **10h** confirmed the absolute configuration above-mentioned.[33] Whatever the electronic nature of substituents (e.g **10j-n** and **10p-s**) as well as their positions in the aromatic ring (**10j-k** compared with **10p-r**), high yields and no significant erosion of enantiopurity were obtained demonstrating the good level of reliability of this catalytic process.

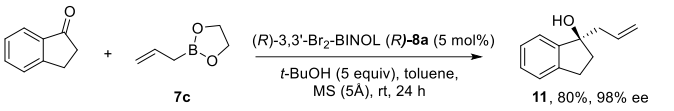
Table 3 Asymmetric allylboration of various isatins and ORTEP diagram of compound **10h** and **10i**[a)]



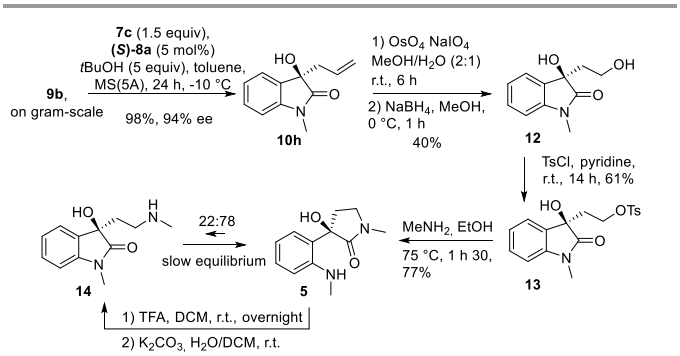
[a)] Unless otherwise stated, all reactions were performed with **9** (0.2 mmol), boronate **7c** (0.3 mmol), catalyst (*R*)-**8a** (5 mol%) in toluene (1 mL) under Ar. Isolated yields are shown. Enantiomeric excess was determined by chiral HPLC. [b)] Catalyst (*S*)-**8a** was used. [c)] The reaction was run starting from 6.5 mmol of **9h**. [d)] 6 days instead of 24 h.

At this stage of our study, the mechanism of the reaction with this type of substrates does not seem to be conventional,[34] in light of the result obtained with a non-activated ketone such as indan-1-one (Scheme 1). Indeed, under similar conditions with the chiral catalyst (*R*)-**8a**, the allylboronate **7c** adds to the face of the carbonyl group opposite to the one attacked with isatins. This experimental observation suggests a different mechanistic pathway for the formation of 3-allyl-3-hydroxyindoles **10** which will be the subject of a further work.

In order to highlight the synthetic interest of our methodology, we planned the gram-scale synthesis of the key intermediate **10h** for the preparation of (*R*)-chimonamidine **5** since the catalytic asymmetric allylboration approach was never employed to access this natural product.[35] We were pleased to observe that starting from 6.5 mmol of *N*-methyl isatin **9b** and using (*S*)-**8a** as catalyst, the homoallyl alcohol **10h** was obtained in 98% yield and with an excellent enantiomeric excess (94%) (Scheme 2). The oxidative cleavage of the double bond by OsO_4-$NaIO_4$ followed by $NaBH_4$ reduction gave the alcohol **12** in 40% yield. After treatment of **12** with tosyl chloride, tosylate **13** underwent a nucleophilic substitution reaction by methylamine followed by a spontaneous transamidation reaction that afforded the expected natural product **5**. (*R*)-Chimonamidine **5** was obtained with an enantiomeric excess of 94% in 19% overall yield from **10h**. After several hours in $CDCl_3$ we observed the apparition of a new compound coming from the transformation of **5**, whose structure was firstly attributed to **14**. As the acidic salts of 3-(β-aminoethyl)oxindoles are stable,[3c, 9] lactam **5** was reacted with TFA to generate the oxindole isomer **14** after extraction from a basic water phase. The two isomers **5** and **14** slowly equilibrated at room temperature in $CDCl_3$ solution (c = 45 mM), to reach a **5**/**14** ratio of 78:22 determined by ^1H NMR. In summary, we reported a new catalytic procedure for the enantioselective allylboration of isatins employing the easy-to-handle cyclic allyl boronate reagent **7c**. In addition, the enantiopure catalyst, 3,3'-Br_2 BINOL **8a** can be easily prepared and is also commercially available.



Scheme1 Face differentiation by the catalytic system in the case of indan-1-one



Scheme 2 Application to the synthesis of (*R*)-chimonamidine **5** and its isomer **14**.

The reaction is suitable for a large range of isatins including *N*-unprotected compounds which means a significant

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improvement compared with the only method using a boron-based reagent described to date for these substrates.[27] In order to demonstrate the synthetic utility of this asymmetric allylboration, a synthesis of (*R*)-chimonamidine and its isomer **14** was carried out. Further investigations concerning the application of this catalytic process to other cyclic activated ketones as well as mechanistic studies are ongoing and will be report in due course.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

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Notes and references

1. (a) G. S. Singh and Z. Y. Desta, *Chem. Rev.*, 2012, **112**, 6104-6155; (b) S. Mohammadi, R. Heiran, R. P. Herrera and E. Marques-Lopez, *ChemCatChem*, 2013, **5**, 2131-2148; (c) R. Moradi, G. M. Ziarani and N. Lashgari, *Arkivoc*, 2017, 148-201.
2. (a) Z.-Y. Cao, F. Zhou and J. Zhou, *Acc. Chem. Res.*, 2018, **51**, 1443-1454; (b) C.-L. Xie, J.-M. Xia, R.-Q. Su, J. Li, Y. Liu, X.-W. Yang and Q. Yang, *Nat. Prod. Res.*, 2018, **32**, 2553-2557; (c) H. Wen, X. Liu, Q. Zhang, Y. Deng, Y. Zang, J. Wang, J. Liu, Q. Zhou, L. Hu, H. Zhu, C. Chen and Y. Zhang, *Chem. Biodiversity*, 2018, **15**, e1700550.
3. (a) S. Peddibhotla, *Curr. Bioact. Compd.*, 2009, **5**, 20-38; (b) P. Brandão and A. J. Burke, *Tetrahedron*, 2018, **74**, 4927-4957; (c) N. Richy, D. Sarraf, X. Marechal, N. Janmamode, R. Le Guevel, E. Genin, M. Reboud-Ravaux and J. Vidal, *Eur. J. Med. Chem.*, 2018, **145**, 570-587.
4. T. Kawasaki, M. Nagaoka, T. Satoh, A. Okamoto, R. Ukon and A. Ogawa, *Tetrahedron*, 2004, **60**, 3493-3503.
5. H. B. Rasmussen and J. K. MacLeod, *J. Nat. Prod.*, 1997, **60**, 1152-1154.
6. (a) M. Kitajima, I. Mori, K. Arai, N. Kogure and H. Takayama, *Tetrahedron Lett.*, 2006, **47**, 3199-3202; (b) T. Itoh, H. Ishikawa and Y. Hayashi, *Org. Lett.*, 2009, **11**, 3854-3857.
7. G. Pandey and J. Khamrai, *Asian J. Org. Chem.*, 2016, **5**, 621-624.
8. H. Takayama, Y. Matsuda, K. Masubuchi, A. Ishida, M. Kitajima and N. Aimi, *Tetrahedron*, 2004, **60**, 893-900.
9. D. Sarraf, N. Richy and J. Vidal, *J. Org. Chem.*, 2014, **79**, 10945-10955.
10. P.-W. Xu, J.-S. Yu, C. Chen, Z.-Y. Cao, F. Zhou and J. Zhou, *ACS Catal.*, 2019, **9**, 1820-1882.
11. (a) P. J. D. Dollings, A. F. Donnell, A. M. Gilbert, M. Zhang, H. B. L., C. J. Stanton, S. V. O'Neil, L. M. Havran, D. C. Chong, *WO2010077839*, 2010; (b) B. Zhu, W. Zhang, R. Lee, Z. Han, W. Yang, D. Tan, K.-W. Huang and Z. Jiang, *Angew. Chem. Int. Ed.*, 2013, **52**, 6666-6670.
12. (a) T. Ishimaru, N. Shibata, J. Nagai, S. Nakamura, T. Toru and S. Kanemasa, *J. Am. Chem. Soc.*, 2006, **128**, 16488-16489; (b) D. Sano, K. Nagata and T. Itoh, *Org. Lett.*, 2008, **10**, 1593-1595.
13. R. He, S. Wu, H. Tang, X. Huo, Z. Sun and W. Zhang, *Org. Lett.*, 2018, **20**, 6183-6187.
14. N. V. Hanhan, A. H. Sahin, T. W. Chang, J. C. Fettinger and A. K. Franz, *Angew. Chem. Int. Ed.*, 2010, **49**, 744-747.
15. M. Takahashi, Y. Murata, F. Yagishita, M. Sakamoto, T. Sengoku and H. Yoda, *Chem. Eur. J.*, 2014, **20**, 11091-11100.
16. T. Wang, X.-Q. Hao, J.-J. Huang, K. Wang, J.-F. Gong and M.-P. Song, *Organometallics*, 2014, **33**, 194-205.
17. D. Ghosh, N. Gupta, S. H. R. Abdi, S. Nandi, N.-u. H. Khan, R. I. Kureshy and H. C. Bajaj, *Eur. J. Org. Chem.*, 2015, **2015**, 2801-2806.
18. Z.-Y. Cao, J.-S. Jiang and J. Zhou, *Org. Biomol. Chem.*, 2016, **14**, 5500-5504.
19. (a) N. V. Hanhan, N. R. Ball-Jones, N. T. Tran and A. K. Franz, *Angew. Chem. Int. Ed.*, 2012, **51**, 989-992; (b) N. V. Hanhan, Y. C. Tang, N. T. Tran and A. K. Franz, *Org. Lett.*, 2012, **14**, 2218-2221.
20. A. Yanagisawa, N. Yang and K. Bamba, *Eur. J. Org. Chem.*, 2017, **2017**, 6614-6618.
21. X.-C. Qiao, S.-F. Zhu and Q.-L. Zhou, *Tetrahedron Asymmetry*, 2009, **20**, 1254-1261.
22. J. Itoh, S. B. Han and M. J. Krische, *Angew. Chem. Int. Ed.*, 2009, **48**, 6313-6316.
23. K. S. Egorova, V. P. Ananikov, *Organometallics*, 2017, **36**, 4071-4090.
24. For reviews see (a) D. G. Hall, *Synlett*, 2007, 1644-1655; (b) H.-X. Huo, J. R. Duvall, M.-Y. Huang and R. Hong, *Org. Chem. Front.*, 2014, **1**, 303-320; (c) C. Diner and K. J. Szabó, *J. Am. Chem. Soc.*, 2017, **139**, 2-14; (d) D. M. Sedgwick, M. N. Grayson, S. Fustero and P. Barrio, *Synthesis*, 2018, **50**, 1935-1957; e) S. J. Kalita, F. Cheng and Y.-Y. Huang, Adv. Synth. Catal., 2020, doi 10.1002/adsc.202000413; In some cases, the enantioselective allylation of carbonyl compounds with allylboronates was performed in the presence of metal salts as co-catalyst, see (f) T. Sengoku, A. Sugiyama, Y. Kamiya, R. Maegawa, M. Takahashi and H. Yoda, *Eur. J. Org. Chem*., 2017, **2017**, 1285-1288; (g) J. Wang, Q. Zhang, Y. Li, X. Liu, X. Li and J.-P. Cheng, *Chem. Commun*., 2020, **56**, 261-264; (h) M. Yus, J. C. Gonzalez-Gomez, F. Foubelo, *Chem. Rev.*, 2011, **111**, 7774-7854; (i) X. Yang, S. J. Kalita, S. Maheshuni, Y.-Y. Huang, *Coord. Chem. Rev.*, 2019, **392**, 35-48.
25. (a) R. Alam, T. Vollgraff, L. Eriksson and K. J. Szabó, *J. Am. Chem. Soc.*, 2015, **137**, 11262-11265; (b) S. Lou, P. N. Moquist and S. E. Schaus, *J. Am. Chem. Soc.*, 2006, **128**, 12660-12661; (c) D. S. Barnett, P. N. Moquist and S. E. Schaus, *Angew. Chem. Int. Ed.*, 2009, **48**, 8679-8682; (d) Y. Zhang, N. Li, B. Qu, S. Ma, H. Lee, N. C. Gonnella, J. Gao, W. Li, Z. Tan, J. T. Reeves, J. Wang, J. C. Lorenz, G. Li, D. C. Reeves, A. Premasiri, N. Grinberg, N. Haddad, B. Z. Lu, J. J. Song and C. H. Senanayake, *Org. Lett.*, 2013, **15**, 1710-1713; (e) G.-L. Chai, B. Zhu and J. Chang, *J. Org. Chem.*, 2019, **84**, 120-127.
26. (a) D. W. Robbins, K. Lee, D. L. Silverio, A. Volkov, S. Torker and A. H. Hoveyda, *Angew. Chem. Int. Ed.*, 2016, **55**, 9610-9614; (b) K. Lee, D. L. Silverio, S. Torker, D. W. Robbins, F. Haeffner, F. W. van der Mei and A. H. Hoveyda, *Nat. Chem.*, 2016, **8**, 768-777; (c) F. W. van der Mei, C. Qin, R. J. Morrison and A. H. Hoveyda, *J. Am. Chem. Soc.*, 2017, **139**, 9053-9065.
27. D. L. Silverio, S. Torker, T. Pilyugina, E. M. Vieira, M. L. Snapper, F. Haeffner and A. H. Hoveyda, *Nature*, 2013, **494**, 216-221.
28. (a) R. Hemelaere, F. Carreaux and B. Carboni, *Eur. J. Org. Chem.*, 2015, **2015**, 2470-2481; (b) A. Mace, S. Touchet, P. Andres, F. Cossio, V. Dorcet, F. Carreaux and B. Carboni, *Angew. Chem. Int. Ed.*, 2016, **55**, 1025-1029; (c) S. Henrion, A. Mace, M. M. Vallejos, T. Roisnel, B. Carboni, J. M.

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Villalgordo and F. Carreaux, *Org. Biomol. Chem.*, 2018, **16**, 1672-1678.
29. (a) A. N. Ndimba, T. Roisnel, G. Argouarch and C. Lalli, *Synthesis*, 2019, **51**, 865-873; (b) C. Lalli and P. van de Weghe, *Chem. Commun.*, 2014, **50**, 7495-7498.
30. Y. Chen, S. Yekta and A. K. Yudin, *Chem. Rev.*, 2003, **103**, 3155-3212.
31. (a) H. C. Brown, U. S. Racherla and P. J. Pellechia, *J. Org. Chem.*, 1990, **55**, 1868-1874; (b) S. Kobayashi, T. Endo, T. Yoshino, U. Schneider and M. Ueno, *Chem. Asian J.*, 2013, **8**, 2033-2045.
32. Below this temperature, solubility of **9a** in toluene declines, the reaction time is considerably increased and the enantioselectivity is not improved.
33. CCDC 1984556 and CCDC 1956971 contains the supplementary crystallographic data for respectively compounds **10h** and **10i**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.
34. (a) R. S. Paton, J. M. Goodman and S. C. Pellegrinet, *Org. Lett.*, 2009, **11**, 37-40; (b) S. O. Simonetti and S. C. Pellegrinet, *Eur. J. Org. Chem.*, 2019, **2019**, 2956-2970.
35. (a) W.-B. Chen, X.-L. Du, L.-F. Cun, X.-M. Zhang and W.-C. Yuan, *Tetrahedron*, 2010, **66**, 1441-1446; (b) B. Zhu, W. Zhang, R. Lee, Z. Han, W. Yang, D. Tan, K.-W. Huang and Z. Jiang, *Angew. Chem., Int. Ed.*, 2013, **52**, 6666-6670; (c) U. V. Subba Reddy, M. Chennapuram, K. Seki, C. Seki, B. Anusha, E. Kwon, Y. Okuyama, K. Uwai, M. Tokiwa, M. Takeshita and H. Nakano, *Eur. J. Org. Chem.*, 2017, **2017**, 3874-3885; (d) M. Moskowitz and C. Wolf, *Angew. Chem., Int. Ed.*, 2019, **58**, 3402-3406.

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