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Pure Appl. Chem., Vol. 84, No. 11, pp. 2417–2430, 2012.
http://dx.doi.org/10.1351/PAC-CON-12-05-01

Boron-based pronucleophiles in catalytic (asymmetric) C(sp^3)–allyl cross-couplings*

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Abstract: Allylic and allenyl boronates or boranes were uncovered as suitable pronucleophiles in catalytic C–C bond formations with C(sp^3) electrophiles such as *O*,*O*-acetals and *N*,*O*-aminals or ethers and carbohydrates. These transformations were most efficiently catalyzed by In(I) triflate. Importantly, chiral counteranion-directed, catalytic asymmetric allylation and allenylation of *N*,*O*-aminals was developed by employing a catalyst system composed of In(I) chloride and a chiral silver 2,2'-dihydroxy-1,1'-binaphthalene (BINOL)-phosphate.

Keywords: allylation; asymmetric catalysis; boron; C–C bond formation; chiral counteranion; indium.

INTRODUCTION

Development of innovative metal catalysis using nontoxic reagents for selective bond formation is an important task in organic chemistry [1]. Group 13 occupies a distinguished position in the periodic table, being adjacent to group 14 with carbon as the element of central importance in organic chemistry. In general, the oxidation state +III is the most stable among group 13 elements; however, going down the group the oxidation state +I becomes increasingly relevant [2]. The group 13 metal indium is interesting for catalysis because In-based molecules have low toxicity, are selective, and are tolerant toward various functional groups [3]. Indeed, In(III) compounds with its vacant p-orbital are well-established (chiral) Lewis acid catalysts in (asymmetric) synthesis (Fig. 1, left) [4]. In contrast, the chemistry of indium in its low-oxidation state +I is underexplored; only sporadic examples of its use as a stoichiometric reagent have been reported [5]. Nevertheless, it has been shown that In(I) may act as an acid and as a base due to the presence of both vacant p-orbitals and an electron lone pair (Fig. 1, right) [6]. Thus, compared with In(III), In(I) is more electron-rich and therefore a weaker Lewis acid. However, the intriguing acid–base character of In(I), which is called ambiphilicity, may offer unique reactivity and unusual selectivity in synthesis, and may have significant implications for the development of dual catalytic processes.

Pure Appl. Chem.* **84, 2183–2498 (2012). A collection of invited papers based on presentations at the 14th International Meeting on Boron Chemistry (IMEBORON-XIV), Niagara Falls, Canada, 11–15 September 2011.
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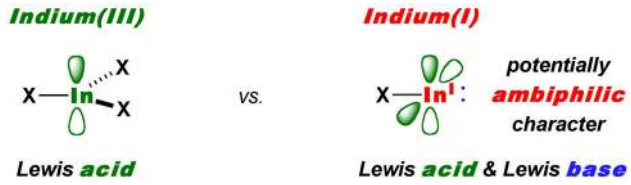


Fig. 1 In(III) vs. In(I).

Recently, Power has demonstrated that an electron-rich In(I) species can act as a metallic σ-donor to form a stoichiometric donor–acceptor complex with a boron electron-pair acceptor [7]. Based on this seminal report, we envisioned the development of innovative catalytic processes, provided (i) a boron-based compound with a transferable organic moiety is used, and (ii) the In–B interaction is relatively weak. We anticipated that nontoxic allylic boron-based reagents could be suitable targets. Conceptually, In(I) may be employed as a metallic Lewis base catalyst to activate Lewis acidic allylic boron pronucleophiles for bond formation with electrophiles such as ketones (Fig. 2, left). Alternatively, because it should still display Lewis acidity, In(I) may be envisaged as an ambiphilic catalyst that may activate both reagents (Fig. 2, right). This scenario would correspond to dual catalytic activation of two substrates at a single metal center. Importantly, asymmetric catalysis may be accessible if a chiral ligand is attached to In(I).

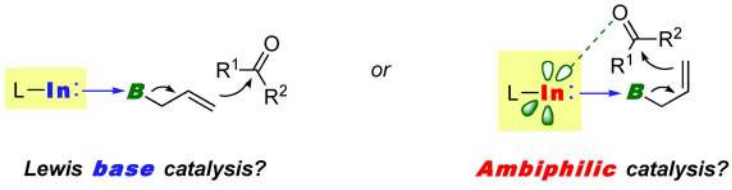
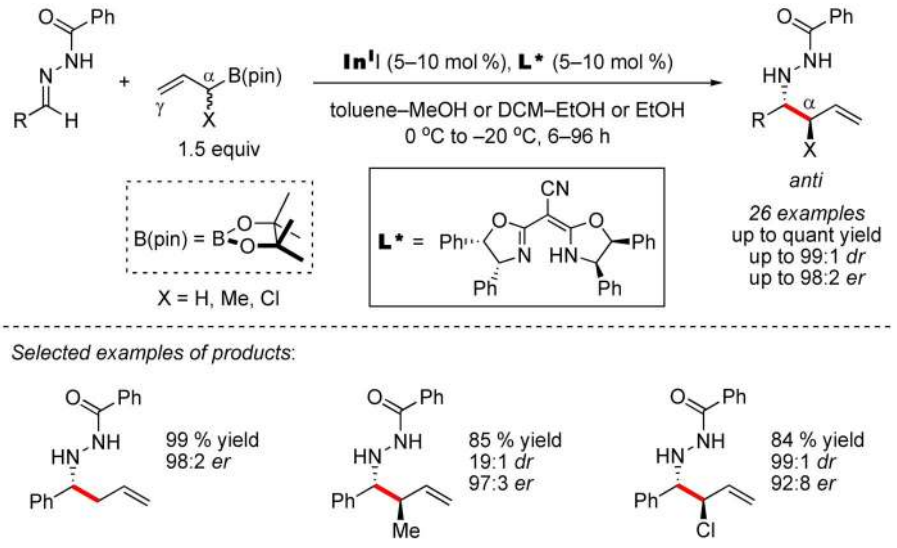


Fig. 2 Unprecedented In(I) catalysis?

Based on this innovative concept, we successfully developed the first catalytic applications of In(I) in organic synthesis. Indeed, catalytic activation of allylic boronates with In(I) iodide was achieved for allylation and *syn*-selective crotylation of C(sp^2) electrophiles such as ketones [8] and *N*-benzoylhydrazones being bench-stable imine surrogates [9,10]. These racemic bond formations proceeded with rare α-selectivity [11] and displayed excellent functional group tolerance. NMR-spectroscopic analyses suggested the in situ generation of reactive allylic In(I) species via transmetalation [10]. Based on literature reports on the crucial importance of In(I) ligation for both structural and physical properties [7,12] and chemical reactivity [13], we aimed to develop asymmetric catalysis because a chiral In(I) complex and its use for asymmetric C–C bond formation were unknown. After careful consideration of all reaction parameters, we successfully developed In(I)-catalyzed C–C bond formations between hydrazones and various allylic boronates, which proceeded with high regio-, diastereo-, and enantioselectivities (Scheme 1) [14]. Key to the success was the identification of an appropriate chiral semicorrin ligand that (i) stabilizes the intrinsically labile In(I) center against redox-disproportionation [2] or oxidative addition [13], and (ii) creates an excellent asymmetric environment. Matrix-assisted laser desorption/ionization with time-of-flight (MALDI–TOF) analyses revealed the in situ generation of a metal–ligand complex in a molar ratio of 1:1. We propose the in situ formation of chiral allylic In-ate complexes (chirally modified nucleophiles), which may undergo C–C bond formation with hydrazones (electrophiles) via a cyclic transition state. This chemistry [14] represents the first example of asymmetric In(I) catalysis, which is of fundamental importance. At the same time, we wondered whether this

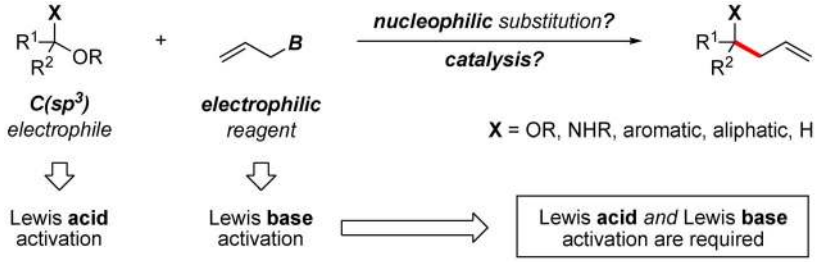


Scheme 1 In(I)-catalyzed asymmetric C–C bond formations between hydrazones and allylic boronates [14].

innovative methodology could be of use regarding challenging transformations between allylic boron-based pronucleophiles and C(sp^3) electrophiles such as acetals, aminals, ethers, and carbohydrates.

CATALYTIC C–C BOND FORMATION BETWEEN ALLYLIC OR ALLENYL BORONATES AND *O,O*-ACETALS OR *N,O*-AMINALS

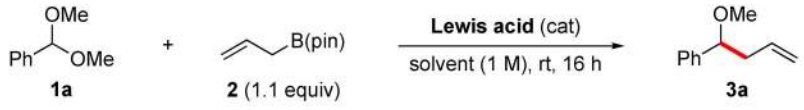
Allylic boronates have been employed for uncatalyzed additions to C(sp^2) electrophiles, such as aldehydes, to form homoallylic alcohols [15]. This unique reactivity is ascribed to internal Lewis base activation (C=O → B) in a cyclic transition state. After a seminal report on metal-catalyzed addition of allylic boronates to aldehydes [16], catalytic additions to ketones and imines have been developed [8,10,14,17]. Acetals, aminals, ethers, and carbohydrates are abundant in nature and play a key role in synthesis. Allylation of these C(sp^3) electrophiles provides the corresponding unsaturated products. Typically, this challenging C–C coupling proceeds via Lewis acid activation to form a stabilized carbenium ion that can react with a nucleophilic allylic silane in an acyclic transition state (Hosomi–Sakurai reaction) [18]. Electrophilic allylic boronates have not been employed in this context, although they may offer significant advantages, such as unique reactivity and selectivity. In the quest for new electrophiles compatible with our In(I) catalysis [8,10,14], we envisioned C(sp^3) electrophiles in nucleophilic substitutions with boronates, and sought a dual catalyst capable of activating both reagents (Scheme 2).



Scheme 2 Catalytic nucleophilic substitution with an electrophilic allylic boron reagent?

Initial experiments employing acetal **1a** and boronate **2** with or without In(I) halides in toluene proved to be disappointing (Table 1, entries 1–3) [19]. These poor results, likely due to the low solubility of In(I) halides, prompted us to examine the more soluble In(I) triflate [20]; to our delight the reaction proceeded smoothly to provide **3a** in excellent yield (entry 4). Next, we examined other metal triflates, and to our surprise these stronger Lewis acids were found to be ineffective (entries 5–9); note that In(I) proved to be substantially better than In(III) (entry 4 vs. entry 5). These results indicated that, in contrast to classic allylic silanes, a strong Lewis acid, for the activation of **1a**, is not sufficient to promote C–C bond formation with **2**. Rather, the ability to activate both reagents seems to be crucial. A solvent screening revealed toluene and hexane to be the best of those examined (entries 10–13). The catalyst loading could be reduced to 1 mol % (entry 14).

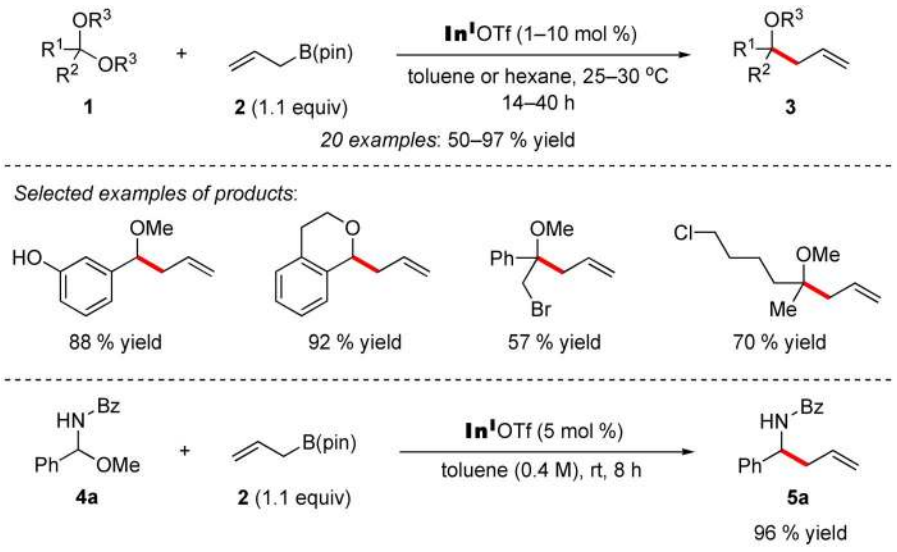
Table 1 Screening of Lewis acids for acetal allylation.



entry	**Lewis acid** (mol %)	solvent	conversion[a] (%)
1	–	toluene	NR
2	**In^{I}**I (20)	toluene	trace
3	**In^{I}**Br (20) or **In^{I}**Cl (20)	toluene	NR
4	**In^{I}**OTf (20)	toluene	>99 (95)[b]
5	**In^{III}**(OTf)$_3$ (20)	toluene	ND (12)[b]
6	**Ga^{III}**(OTf)$_3$ or **Al^{III}**(OTf)$_3$ or **Cu^{I}**OTf (20)	toluene	trace
7	**Sc^{III}**(OTf)$_3$ (20)	toluene	2
8	**Cu^{II}**(OTf)$_2$ (20)	toluene	5
9	**Ag^{I}**OTf or **Zn^{II}**(OTf)$_2$ (20)	toluene	NR
10	**In^{I}**OTf (5)	toluene	>99
11	**In^{I}**OTf (5)	hexane	>99
12	**In^{I}**OTf (5)	DCM	>95
13	**In^{I}**OTf (5)	THF	20
14	**In^{I}**OTf (1)	toluene	>99 (91)[b]

[a] Conversion of **1a** to **3a** determined by ^{1}H NMR spectroscopic analysis of aliquots of the reaction mixtures. [b] Isolated yield of homoallyl ether **3a** after purification on silicagel (PTLC); NR = no reaction; ND = not determined (due to the formation of by-products).

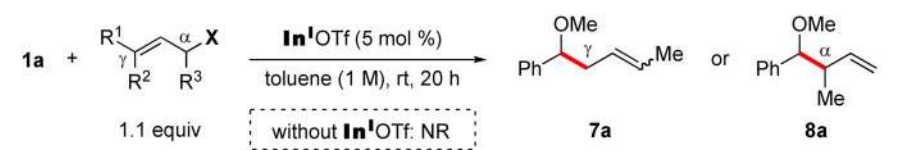
Next, we investigated the scope of this reaction (Scheme 3) [19]. The transformation proceeded smoothly with acyclic or cyclic aromatic, heteroaromatic, and aliphatic acetals **1**, and displays remarkable compatibility with free hydroxy, ether, aromatic bromo, ester, trifluoromethyl, and carbamoyl groups, as well as aliphatic bromo and chloro functionalities. Moreover, this protocol proved to be applicable to the allylation of aminal **4a** to furnish homoallylic amide **5a** (Scheme 3) [21].

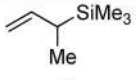
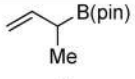
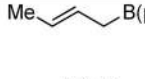
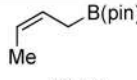


Scheme 3 Scope for acetal allylation; application to aminals.

Next, we turned our attention to the reaction mechanism by employing various substituted allylic reagents, to see whether γ- or α-adducts are observed (Table 2) [19]. As expected, the use of silane **6** provided the conventional γ-adduct **7a**; no α-adduct **8a** was detected. In sharp contrast, the use of boronate **9** resulted in the exclusive formation of the rare α-adduct **8a**. Both crotyl boronates **10** gave almost an identical result with respect to regio- and diastereoselectivity compared with **9**, suggesting the same reactive intermediate for all three boron reagents. The α-selectivity with **9** may indicate transmetalation, while the lower reactivity of **10** may be explained by slower transmetalation because of the steric demand at the γ-position.

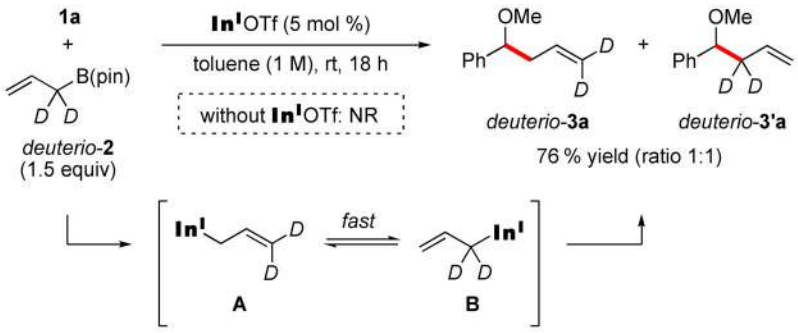
Table 2 Mechanistic control experiments.



allylic reagent	 **6**	 **9**	 (*E*)-**10**	 (*Z*)-**10**
product	**7a** (γ)	**8a** (α)	**8a** (α)	**8a** (α)
yield[a] (%)	87	83	11 (61)[b]	43 (77)[c]
ratio	*E*:*Z* = 1.2:1	*anti*:*syn* = 1.2:1	*anti*:*syn* = 1.2:1	*anti*:*syn* = 1.2:1

[a] Isolated yield of homoallylic ethers **7a** or **8a** after purification on silica gel (PTLC). [b] Conditions: (*E*)-**10** (1.5 equiv), 40 °C, 50 h. [c] Conditions: (*Z*)-**10** (1.5 equiv), rt, 50 h. **X** = *B* or *Si*; R¹, R², R³ = H or Me.

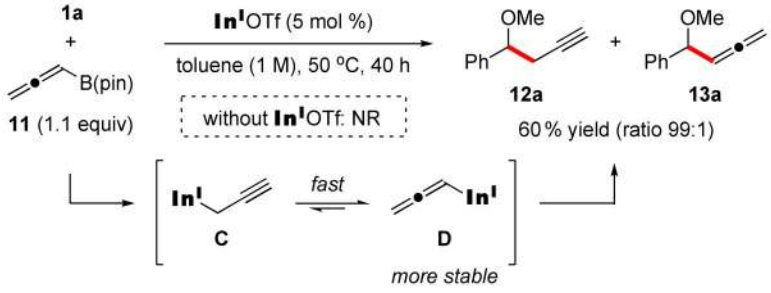
To test the transmetalation hypothesis, boronate deuterio-**2** was used (Scheme 4) [19]. We observed the formation of an equimolar mixture of regioisomers deuterio-**3a** and deuterio-**3'a**. This result may be ascribed to the transmetalative generation of the allylic In(I) species **A** and **B** (fast equilibrium), thereby scrambling the deuterium label. **A** and **B** display similar stability and equal reactivity.



Scheme 4 Deuterium labeling experiments.

Based on the observed reactivity and selectivity profile, we propose a transmetalative S_N1 mechanism, in which In(I) acts as a dual catalyst (vide infra). Importantly, this methodology proved to be also applicable to propargylation (Scheme 5) [19]. Indeed, **1a** was converted regiospecifically with **11** into homopropargyl ether **12a**; homoallenyl ether **13a** was only detected in trace amounts. This C–C coupling may also be explained with transmetalation to generate propargyl and allenyl In(I) species **C** and **D** (fast equilibrium). The more stable allenyl intermediate **D** may act as the real nucleophile.

This study represents the first main group metal-catalyzed activation of allylic boronates for C–C bond formation with C(sp^3) electrophiles.



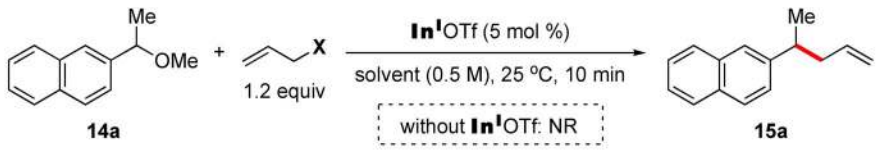
Scheme 5 Regiospecific acetal propargylation.

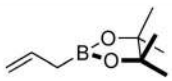
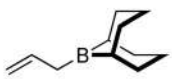
CATALYTIC C–C BOND FORMATION BETWEEN AN ALLYL BORANE AND ETHERS OR CARBOHYDRATES

Aliphatic ethers are important substrates in catalytic cross-couplings because they are readily available compounds. However, catalytic activation of ethers under mild conditions is challenging because of the relatively strong C–OR bond and the poor leaving ability of $^-$OR. Based on our earlier studies with acetals [19], we aimed to examine aliphatic ethers. In initial experiments, under our earlier In(I) conditions [19], we employed ether **14a** and boronate **2** (Table 3, entry 1) [22]. However, the desired product **15a** was hardly observed, which may be ascribed to the stable C–OMe bond of **14a**. Therefore, we used stronger Lewis acid cocatalysts in addition to In(I) triflate; however, all attempts failed. Thus, we anticipated that a more Lewis acidic boron compound may result in a facilitated C–B bond activation. To our delight, when 9-BBN-derived borane **16** was employed in apolar solvents, the desired reaction with **14a** proceeded smoothly to provide **15a** in full conversion (entries 2–6). A reaction did not occur in Lewis basic or polar solvents such as tetrahydrofuran (THF) or MeCN (entries 7 and 8). Strikingly, the use of other allyl reagents did not provide any desired product, or afforded very low yields after

extended reaction times. These results highlight the remarkable reactivity of borane **16**. Metal triflates other than In(I) were found to be significantly less efficient, or did not afford **15a**.

Table 3 Cross-coupling with an ether: screening of allyl reagents.

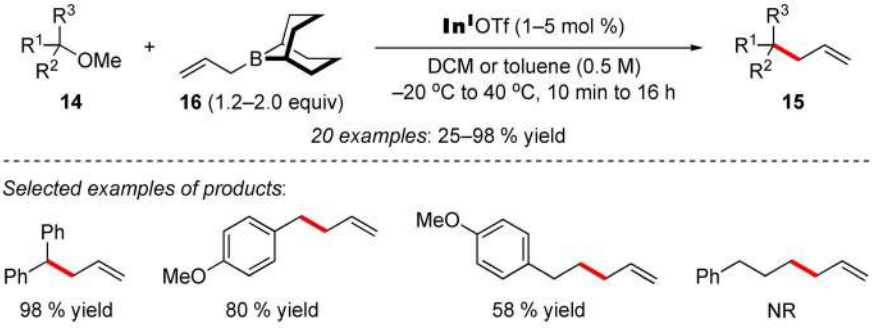


entry	allyl reagent	solvent	conversion[a] (%)
1	 **2**	DCM	trace[b]
2	 **16**	DCM	>99
3		$CDCl_3$	>99
4		toluene	>99
5		benzene	>99
6		hexane	>95
7		THF	NR
8		MeCN	NR
9		DCM	>99[c] (86)[d]

X = BF_3^- K^+, MgBr,[f] $Si(OMe)_3$, $SiMe_3$,[g] $SiCl_3$, $SnBu_3$

[a] Conversion of **14a** to **15a** was determined by ^1H NMR spectroscopic analysis of aliquots of the reaction mixtures. [b] Conversion: 14% after 24 h. [c] Conditions: In^IOTf (1 mol%), DCM (0.5 M), rt, 90 min. [d] Isolated yield of **15a** after purification on silicagel (PTLC). [e] NR = no reaction; no trace of **15a** even after 14 h. [f] A solution of the Grignard reagent (1 M in ether) was employed. [g] Conversion: less than 5% after 18 h.

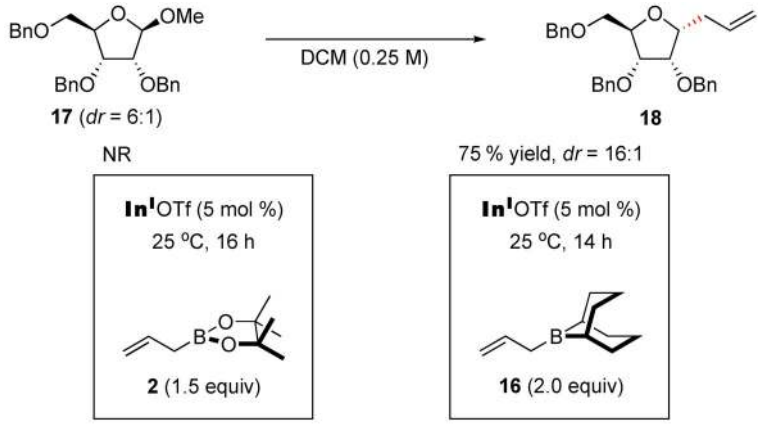
Next, we investigated the scope of this new method (Scheme 6) [22]. The cross-coupling proceeded smoothly with various primary, secondary, and tertiary benzylic, allylic, and propargylic ethers **14**. Importantly, a heteroaromatic moiety and functionalities such as aromatic bromo or methoxy and aliphatic chloro groups were tolerated.



Scheme 6 Scope for cross-coupling with ethers.

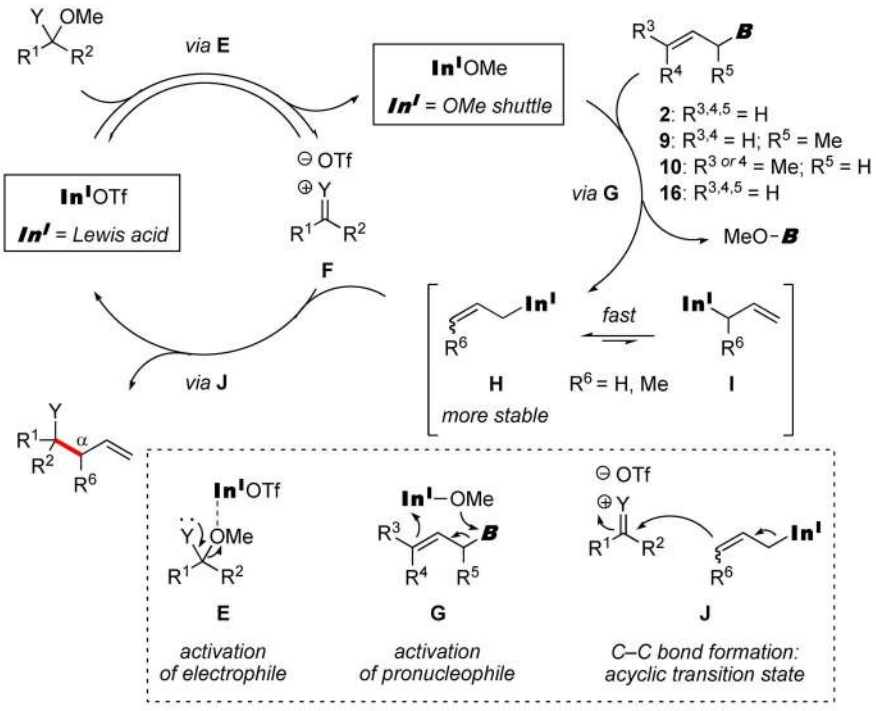
Although we cannot definitely exclude the possibility that the Lewis acidic boron atom of **16** may act as a stoichiometric Lewis acid to activate the C–OMe bond of ethers **14**, we propose again a transmetalative S_N1 mechanism, in which In(I) plays a dual role (vide infra). This transformation represents a rare example of (i) a main group metal-catalyzed cross-coupling, and (ii) the use of an allyl borane for C–C bond formation with C(sp^3) electrophiles.

Importantly, our concept employing borane **16**, rather than boronate **2** [22], proved to be applicable to carbohydrate chemistry, as demonstrated by the conversion **17** → **18** (Scheme 7) [23].



Scheme 7 C–C bond formation with carbohydrates: selected example.

Overall, regarding the reaction mechanism involving C(sp^3) electrophiles such as acetals, aminals, ethers, and carbohydrates, we propose the scenario as outlined in Scheme 8. In(I) triflate may activate the corresponding electrophile to form—via **E**—a stabilized carbenium ion **F** and In(I) methoxide. This In(I)-based Lewis base may activate the corresponding electrophilic boron-based reagent (**2**, **9**, **10**, or **16**) to generate—via **G**—the nucleophilic allyl In(I) species **H** or **I** (fast equilibrium). The more stable crotyl reagent **H** (if R^6 = Me) may react with the real electrophile, carbenium ion **F**, to provide—via acyclic transition state **J**—the α-adducts (C–C bond formation) with regeneration of In(I) triflate. Overall, we consider In(I) as a unique dual catalyst: (i) As a Lewis acid, it activates the formal electrophile (via **E**), and (ii) as a methoxide shuttle, it delivers the required Lewis base to the formal nucleophile (allylic boron-based reagent; via **G**). The proposed S_N1 mechanism, including transmetalation (cf. Scheme 4) and C–C bond formation via an acyclic transition state, is consistent with both the exclusive α-selectivity of **9** and the moderate diastereoselectivity (cf. Table 2). The almost identical result with both crotyl boronates **10** (cf. Table 2) may be explained with the more stable crotyl In(I) intermediate **H** (R^6 = Me) being the real nucleophile in all three cases (fast equilibrium). The proposed mechanism is fully consistent with the fact that the weaker Lewis acid In(I) is substantially more active than In(III) (cf. Table 1). Indeed, although In(I) is significantly larger than In(III), its Lewis acidity is sufficient to activate the corresponding electrophile (cf. **E**). On the other hand, In(I) may be more apt than In(III) for the following reasons: (i) The formed In^I–O bond within In(I) methoxide is longer than in case of In(III); thus, the O-Lewis basicity is stronger, which accounts for an easier activation of the Lewis acidic boron atom (hard–hard interaction; cf. **G**), (ii) the larger In(I) is more suitable for transmetalation at the C=C double bond than In(III) (soft–soft interaction; cf. **G**), and (iii) the generated In^I–C bond within the allyl In(I) reagent is longer than in case of In(III); this nucleophile is therefore more reactive toward the real electrophile **F** (cf. **J**).

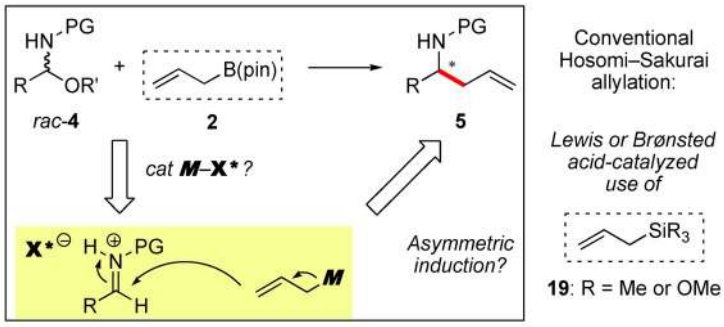


Scheme 8 Proposed catalytic cycle for In(I)-catalyzed allylation of C(sp^3) electrophiles with boron-based pronucleophiles.

The nature of the substituents on the boron atom of a trigonal boron compound determines its Lewis acidity, and thus its electrophilicity. The relative strength of the Lewis acidity of boron-based reagents can be estimated by the chemical shift δ in ^{11}B NMR spectroscopy. In the present In(I) catalysis, we observed a substantial improvement in reactivity by switching from allyl boronate **2** to allyl borane **16** (cf. Table 3 and Scheme 7). Judging from our ^{11}B NMR data, the Lewis acidity of the boron atom of borane **16** (δ = 85 ppm) is significantly higher than that of boronate **2** (δ = 32 ppm). Therefore, **16** would have a substantially increased affinity toward the in situ formed Lewis base, In(I) methoxide, resulting in a faster transmetalation (cf. **G**). This notable change might drain the equilibrium in the first step (cf. **E**) of the proposed mechanism to the right side, thus leading to a rate acceleration. Overall, contrary to boronate **2**, borane **16** can undergo smooth C–C bond formation with less reactive C(sp^3) electrophiles such as ethers and carbohydrates.

CATALYTIC ASYMMETRIC C–C BOND FORMATION BETWEEN ALLYL OR ALLENYL BORONATES AND *N,O*-AMINALS

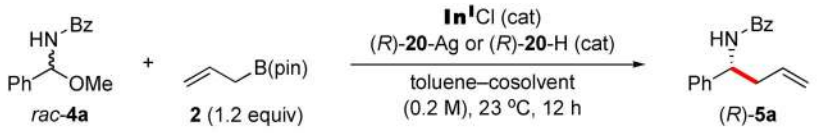
Based on our insight into the reaction mechanism and following our earlier racemic study with *N*,*O*-aminals (cf. Scheme 3) [21], we aimed to develop an asymmetric version. Initial metal screening for the reaction of *N*,*O*-aminal rac-**4a** with boronate **2** identified In(I) as the best catalyst (R = Ph, PG = Bz, R' = Me; Scheme 9) [21]. On the other hand, the corresponding Hosomi–Sakurai allylation [23] with silicon-based reagents **19** hardly proceeded. The substantially higher reactivity of **2** over **19** under mild conditions constitutes a prerequisite for asymmetric catalysis. Postulating dual catalytic activation of rac-**4a** and **2** to generate iminium ion and allyl In(I) intermediates (Scheme 9), we screened potential In(I) catalysts bearing chiral counteranions rather than chiral ligands. In these experiments, the combi-



Scheme 9 Asymmetric borono variant of the Hosomi–Sakurai reaction?

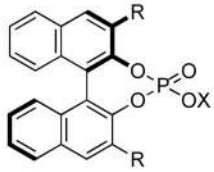
nation of In(I) chloride and chiral silver 2,2'-dihydroxy-1,1'-binaphthalene (BINOL)-phosphate (R)-**20a**–Ag [24] was found to be the most promising chiral catalyst system for the formation of product (R)-**5a** (Table 4). Here again, silanes **19** proved to be dramatically less effective than boronate **2** in terms of both reactivity and selectivity.

Table 4 Optimization and control experiments for asymmetric catalysis.



entry	InICl (mol %)	(*R*)-**20** (mol %)	cosolvent	yield[a] (%)	*er*[b]
1[c]	10	(*R*)-**20a**-Ag (10)	–	81	88:12
2[c]	10	(*R*)-**20b**-Ag (10)	–	96	94.5:5.5
3[c]	10	(*R*)-**20c**-Ag (10)	–	90	44.5:55.5
4[c]	10	(*R*)-**20d**-Ag (10)	–	91	49.5:50.5
5[c]	10	(*R*)-**20e**-Ag (10)	–	94	49.5:50.5
6[c]	10	(*R*)-**20b**-Ag (10)	CPME	96	95.5:4.5
7[c]	10	(*R*)-**20b**-Ag (13)	CPME	98	98.5:1.5
8[c,d]	5	(*R*)-**20b**-Ag (6.5)	CPME	96	97.5:2.5
9[d]	5	–	CPME	1	–
10[d]	–	(*R*)-**20b**-Ag (6.5)	CPME	5	57:43
11[d]	–	(*R*)-**20b**-H (6.5)	CPME	NR[e]	–
12[c,d]	5	(*R*)-**20b**-H (6.5)	CPME	88	62.5:37.5

[a] Isolated yield of **5a** after purification on silicagel (PTLC). [b] Enantiomeric ratio was determined by chiral HPLC. [c] The chiral catalyst was preformed in toluene at rt. [d] Reaction time: 18 h. [e] NR = a reaction was not detected (^{1}H NMR spectroscopy).

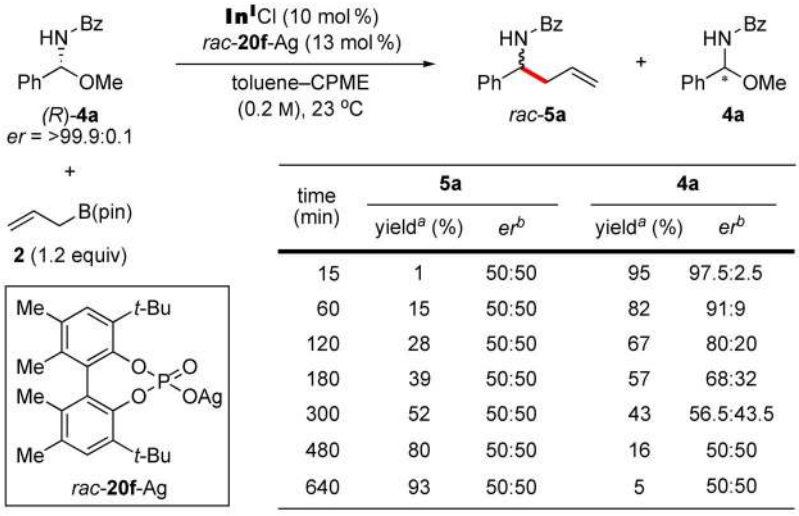


(*R*)-**20a**-Ag: R = 3,5-(^{t}Bu)$_2$-C$_6$H$_3$, X = Ag
(*R*)-**20b**-Ag: R = 3,5-(^{t}Bu)$_2$-4-MeO-C$_6$H$_2$, X = Ag
(*R*)-**20b**-H: R = 3,5-(^{t}Bu)$_2$-4-MeO-C$_6$H$_2$, X = H
(*R*)-**20c**-Ag: R = 3,5-(Me)$_2$-C$_6$H$_3$, X = Ag
(*R*)-**20d**-Ag: R = 2,4,6-(^{i}Pr)$_3$-C$_6$H$_2$, X = Ag
(*R*)-**20e**-Ag: R = SiPh$_3$, X = Ag

Next, we optimized the reaction conditions [21]. Screening of silver BINOL-phosphates identified (R)-**20b**–Ag as the best chiral source (Table 4, entries 1–5). Use of an apolar cosolvent and a slight excess of the chiral silver salt improved the asymmetric induction (entries 6–8). In the absence of In(I) chloride, (R)-**20b**–Ag displayed both low reactivity and enantioselectivity (entry 10). The use of chiral Brønsted acid (R)-**20b**–H that may be generated in situ under the present conditions, without or with In(I) chloride, did not lead to any reaction (entry 11) or provided low asymmetric induction (entry 12). Importantly, we confirmed that redox-disproportionation of In(I) [2] did not occur in the present catalysis. Thus, the combination of In(I) and (R)-**20b**–Ag was shown to be crucial for the highly enantioselective formation of (R)-**5a**. The results of our control experiments (entries 9–12) suggest the in situ generation of a chiral low-oxidation state In species as the active catalyst.

Next, we carried out a mechanistic control experiment (Table 5) [21]. We employed the optically enriched aminal (R)-**4a** (er ≥ 99.9:0.1) and **2** under standard conditions using In(I) chloride combined with racemic silver phosphate rac-**20f**–Ag as the catalyst system. This experiment was carefully analyzed over time by determining yields and enantiomeric ratios for both the generated product **5a** and the recovered substrate **4a**. The isolated product **5a** proved to be racemic at all stages, while the racemization of (R)-**4a** proceeded relatively slowly. These results strongly indicate an iminium ion intermediate for this reaction (S_N1 pathway). In turn, these data provide proof that the catalytic asymmetric version (cf. Table 4) proceeds via the postulated S_N1 mechanism with an iminium ion species as a key intermediate, thus confirming the critical role of the chiral counteranion (cf. Scheme 10). Overall, the present C–C bond-forming method relies on the generation of a chirally modified electrophile (acyclic transition state), and represents therefore an orthogonal approach compared with our related earlier study [14], in which we proposed a chirally modified nucleophile as a key intermediate (cyclic transition state).

Table 5 Mechanistic control experiment.

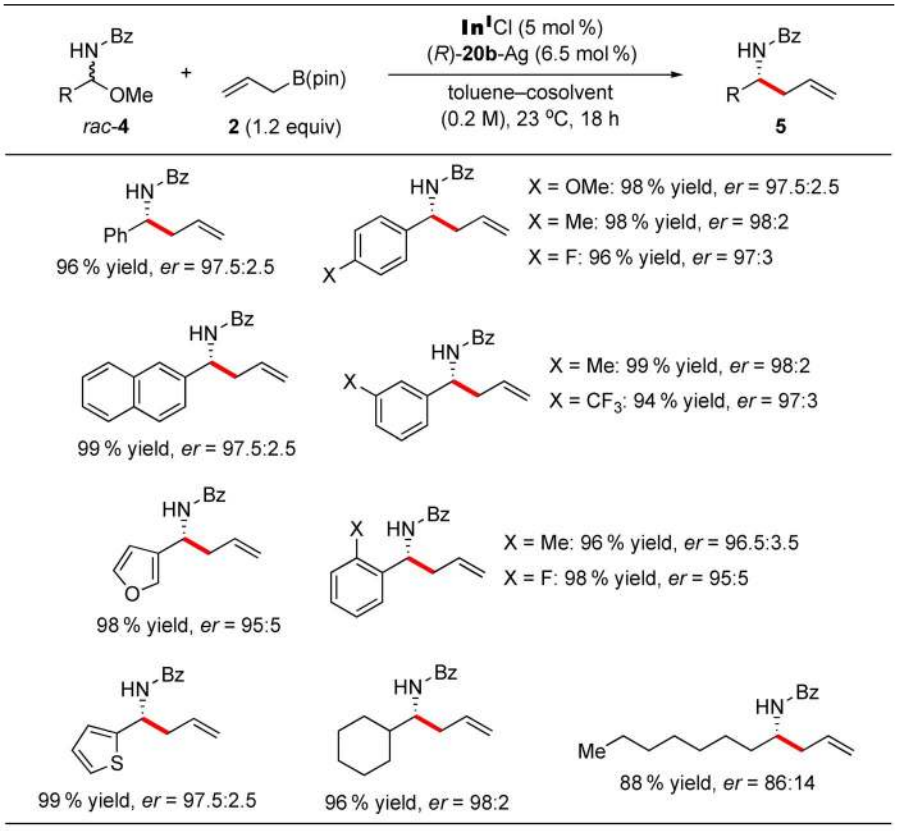


time (min)	5a		4a	
	yield[a] (%)	er[b]	yield[a] (%)	er[b]
15	1	50:50	95	97.5:2.5
60	15	50:50	82	91:9
120	28	50:50	67	80:20
180	39	50:50	57	68:32
300	52	50:50	43	56.5:43.5
480	80	50:50	16	50:50
640	93	50:50	5	50:50

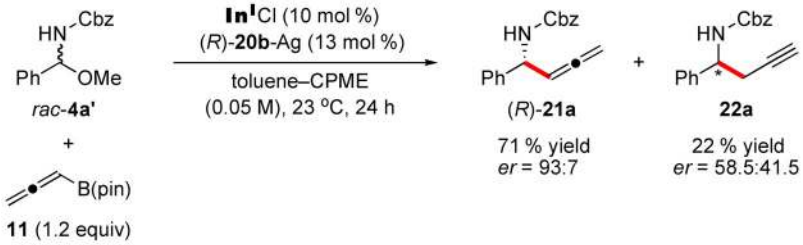
[a] Isolated yield of *rac*-**5a** and **4a** after purification on silicagel (PTLC). [b] Enantiomeric ratio was determined by chiral HPLC.

We then examined the scope for this catalytic asymmetric transformation (Table 6) [21]. Under optimized conditions the reactions between substituted aromatic, heteroaromatic, and aliphatic aminals rac-**4** and **2** proceeded smoothly to provide the desired products **5** with excellent asymmetric induction. Overall, we consider these results remarkable as the levels of asymmetric induction exceed or equal even those of the corresponding allylations of unactivated aldimines [C(sp^2) centers] with **2** [25] or **19** [26].

Table 6 Scope for enantioselective aminal allylation.



In addition, we were pleased to find that this chiral catalyst system was applicable to asymmetric allenylation (Scheme 10) [21]. The reaction of aminal rac-**4a'** with **11** afforded mainly homoallenyl carbamate (R)-**21a** with high asymmetric induction. The minor regioisomer **22a** was separated by chromatography. This regioselectivity is unprecedented for the use of **11** in asymmetric catalysis [27].



Scheme 10 Enantioselective aminal allenylation.

This chemistry features several notable characteristics. (i) Under mild conditions, boronates proved to be dramatically more reactive and selective than classic silicon-based reagents. (ii) The described transformations represent the first highly enantioselective Hosomi–Sakurai reactions with C(sp^3) centers [18b,26,28]. (iii) This study also constitutes the first main group metal-catalyzed activation of allyl boronates for asymmetric C–C bond formation with C(sp^3) centers. (iv) Chiral Brønsted acid catalysis with or without achiral metal salts proved to be inefficient. (v) In the context of asymmetric intermolecular carbon–carbon bond formation, the chemistry presented herein is a rare example not only of chiral counteranion-directed metal catalysis [24], but also of dynamic kinetic resolution [29].

CONCLUSION

Our initial studies dealt with In(I) iodide-catalyzed α-selective allylations of C(sp^2) electrophiles such as ketones and hydrazones, including a catalytic asymmetric version of these reactions using a chiral semicorrin ligand. Herein, we have described how the careful choice of both catalysts and boron-based pronucleophiles may lead to the successful development of unprecedented carbon–carbon bond formations with C(sp^3) electrophiles. Indeed, allylic and allenyl boronates were uncovered as suitable reagents in In(I) triflate-catalyzed transformations with *O*,*O*-acetals and *N*,*O*-aminals. On the other hand, a more Lewis acidic allyl borane was required for reactions with less reactive ethers and carbohydrates. Importantly, chiral counteranion-directed, catalytic asymmetric allylation and allenylation of *N*,*O*-aminals was developed by employing a catalyst system composed of In(I) chloride and a chiral silver BINOL-phosphate.

ACKNOWLEDGMENTS

This work was partially supported by CREST, SORST, ERATO (JST), a Grant-in-Aid for Scientific Research from the Japan Society for the Promotion of Science (JSPS), the Global COE Program, the University of Tokyo, and MEXT (Japan).

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