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Asymmetric Allylboration of Aldehydes with Pinacol Allylboronates Catalyzed by 1,1′-Spirobiindane-7,7′-diol (SPINOL) Based Phosphoric Acids

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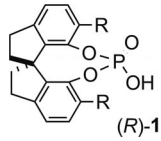
The asymmetric allylboration of aldehydes with pinacol allylboronates catalyzed by 1,1′-spirobiindane-7,7′-diol (SPINOL) based phosphoric acids is described. 6,6′-Bis(2,4,6-triisopropylphenyl)SPINOL-based phosphoric acid was found to be a general, highly enantioselective catalyst for such allylboration reactions and excellent enantioselectivities were obtained for different types of aldehydes including aromatic aldehydes, α,β-unsaturated aldehydes, propargylic aldehydes, and aliphatic aldehydes.

Introduction

Catalytic asymmetric allylation of aldehydes constitutes one of the most efficient ways to access optically active homoallylic alcohols,[1,2] which are useful compounds for organic synthesis.[1a] Different chiral catalysts such as chiral Lewis acids,[3] Lewis bases,[4] and Brønsted acids[5] have been reported as suitable catalysts for allylation reactions of allyltin reagents, allylsilanes, and allylboronates with aldehydes.[6] Among the catalytic asymmetric allylation reactions developed, the recently reported BINOL-based phosphoric acid catalyzed allylboration of aldehydes with pinacol allylboronates represented the most promising one.[5a] This BINOL-based phosphoric acid catalyzed allylboration used moisture-stable pinacol allylboronates as allylation reagents and an air/moisture-stable BINOL-based phosphoric acid as the catalyst. Although high enantioselectivities were obtained for aromatic aldehydes without an *ortho* substituent and α,β-unsaturated aldehydes, the enantioselectivities for *ortho*-substituted aromatic aldehydes and aliphatic aldehydes were less satisfactory, ranging from 73% to 93% *ee*. The search for general allylation catalysts that are highly enantioselective for all types of aldehydes continues.

In our laboratory, we are interested in developing optically active 1,1′-spirobiindane-7,7′-diol (SPINOL) based phosphoric acids (Figure 1) and derivatives as novel chiral catalysts, including Brønsted acids, for bond-forming reactions. Our interest in part originated from the consideration that the rigidity of the spirocyclic framework of C_2-symmetric SPINOLs may render optically active SPINOL-based phosphoric acids more enantioselective than reported axially chiral diol-based phosphoric acids.[7,8] In this context, we have recently reported optically active SPINOL-based phosphoric acid catalyzed enantioselective addition reactions of indoles with imines and β,γ-unsaturated α-keto esters.[9,10] Our study showed that SPINOL-based phosphoric acids indeed exhibited higher enantioselectivities than BINOL-based phosphoric acids for these reactions.[11,12] On the basis of these results and the recently reported BINOL-based phosphoric acid catalyzed allylboration reactions of aldehydes with allylboronates,[5a] we surmised that optically active SPINOL-based phosphoric acids might be highly enantioselective catalysts for such asymmetric allylboration reactions. Herein, we report our results on such SPINOL-based phosphoric acid catalyzed allylboration reactions, specifically, 6,6′-bis(2,4,6-triisopropylphenyl)SPINOL-based phosphoric acid as a general, highly enantioselective catalyst for the allylboration reaction of pinacol allylborates with different types of aldehydes including aromatic aldehydes, α,β-unsaturated aldehydes, propargylic aldehydes, and aliphatic aldehydes.



(*R*)-**1**

a: Ar = Ph
b: Ar = 1-naphthyl
c: Ar = 2-naphthyl
d: Ar = 3,5-$(CH_3)_2C_6H_3$
e: Ar = 3,5-$(CF_3)_2C_6H_3$
f: Ar = biphenyl
g: R = 9-phenanthyl
h: R = $SiPh_3$
i: Ar = 2,4,6-$(i\text{Pr})_3C_6H_2$

Figure 1. Optically active SPINOL-based phosphoric acids.

Results and Discussion

We began our study by examining the allylboration reaction of pinacol allylboronate with 2-methylbenzaldehyde. A series of SPINOL-based phosphoric acids (*R*)-**1a**–**i**, pre-

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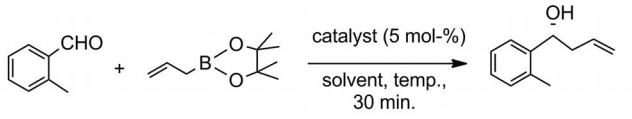
pared from optically active (*R*)-SPINOL (see the Supporting Information),[9] were examined (Table 1, Entries 1–8). Although low to moderate enantioselectivities were observed for SPINOL-based phosphoric acids (*R*)-**1a**–**h** (Table 1, Entries 1–8), SPINOL-based phosphoric acid (*R*)-**1i** exhibited promising enantioselectivity (Table 1, Entry 9). Further testing showed that toluene was a better solvent (Table 1, Entries 9–11). Lowering the reaction temperature improved the enantioselectivity (Table 1, Entries 9, 12, and 13). By carrying out the reaction at –70 °C, a 98% *ee* was obtained (Table 1, Entry 14). For comparison, we also carried out the reaction at –30 °C and a 95% *ee* was observed (Table 1, Entry 13). This enantioselectivity was higher than that obtained with the BINOL-based phosphoric acid as the catalyst, which was 93% *ee*, under the same reaction condition.[5a] Reducing the catalyst loading to 2 mol-% affected the reaction rate but not the enantioselectivity (Table 1, Entry 15).

Table 1. SPINOL-based phosphoric acid catalyzed reaction of pinacol allylboronate with 2-methylbenzaldehyde.[a]

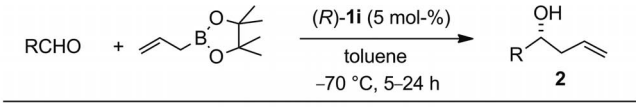


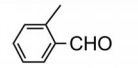
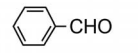
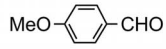
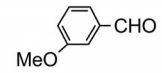
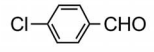
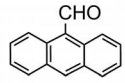
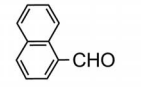
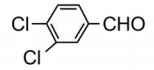
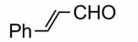
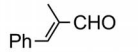
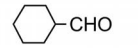
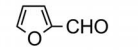
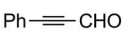
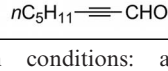
Entry	Catalyst	Solvent	*T* (°C)	Conv. (%)[b]	*ee* (%)[c]
1	(*R*)-**1a**	toluene	r. t.	45	1
2	(*R*)-**1b**	toluene	r. t.	82	44
3	(*R*)-**1c**	toluene	r. t.	81	27
4	(*R*)-**1d**	toluene	r. t.	75	27
5	(*R*)-**1e**	toluene	r. t.	65	13
6	(*R*)-**1f**	toluene	r. t.	56	24
7	(*R*)-**1g**	toluene	r. t.	54	2
8	(*R*)-**1h**	toluene	r. t.	99	49
9	(*R*)-**1i**	toluene	r. t.	99	82.5
10	(*R*)-**1i**	CH_2Cl_2	r. t.	80	56.5
11	(*R*)-**1i**	$ClCH_2CH_2Cl$	r. t.	75	56
12	(*R*)-**1i**	toluene	0	99	90
13	(*R*)-**1i**	toluene	–30	99	95
14	(*R*)-**1i**	toluene	–70	99	98[d]
15	(*R*)-**1i**	toluene	–70	99	98[e]

[a] Reaction conditions: aldehyde (1.0 equiv.), pinacol allylboronate (1.0 equiv.). [b] Based on ^{1}H NMR analysis. [c] Based on HPLC (Chiralcel OD column) analysis. [d] Reaction time: 5 h. [e] 2 mol-% catalyst loading, 7 h.

By using SPINOL-based phosphoric acid (*R*)-**1i** as the catalyst, we next examined different aldehydes for the asymmetric allylboration reaction, and our results are listed in Table 2. High yields and excellent enantioselectivities were obtained not only for aromatic aldehydes and α,β-unsaturated aldehydes, but also for aliphatic aldehydes (Table 2, Entries 1–15). The enantioselectivity was observed to be, in general, higher than that obtained with BINOL-based phosphoric acid as catalysts. In particular, a significant increase in enantioselectivity was observed for *ortho*-substituted aromatic aldehydes and aliphatic aldehydes, substrates for which lower enantioselectivities were observed with BINOL-based phosphoric acids as catalysts (Table 2, Entries 1, 7, 12–15). In addition, excellent enantioselectivities were also obtained for 2-furylaldehyde and propargylic al-

Table 2. SPINOL-based phosphoric acid (*R*)-**1i**-catalyzed reaction of aldehydes with pinacol allylboronate.[a]



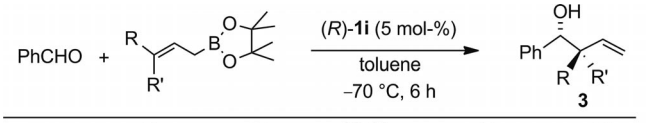
Entry	RCHO	Product	Yield (%)[b]	*ee* (%)[c,d]
1		**2a**	98	98 (93)[e]
2		**2b**	97	99 (98)[e]
3		**2c**	95	99 (98)
4		**2d**	94	99 (97)
5		**2e**	96	99 (96)
6		**2f**	89	99 (99)
7		**2f**	92	97 (91)
8		**2h**	93	99.5 (98)
9		**2i**	99	98
10		**2j**	99	98 (96)
11		**2k**	99	94 (93)
12	$PhCH_2CHO$	**2l**	86	98 (90)
13	$PhCH_2CH_2CHO$	**2m**	80	93.5 (87)
14	$PhCH_2OCH_2CHO$	**2n**	99	96 (79)[f]
15		**2o**	90	91 (73)[f]
16		**2p**	91	99
17		**2q**	87	99
18		**2r**	98	98[f]

[a] Reaction conditions: allylboronate (1.5 equiv.), aldehyde (1.0 equiv.), phosphoric acid (*R*)-**1i** (5 mol-%), toluene, –70 °C, 2 h. [b] Isolated yield. [c] Based on HPLC (Chiralcel OD column) analysis. [d] In parentheses: reported *ee* value with 5 mol-% of BINOL-based phosphoric acids at –30 °C, see ref.[5a] [e] 2 mol-% catalyst loading was used. [f] The *ee* value was determined from the benzoate ester of the alcohol product.

dehydes (Table 2, Entries 16–18). These results showed that SPINOL-based phosphoric acid (*R*)-**1i** is a general, highly enantioselective catalyst for the asymmetric allylboration reactions of pinacol allylboronate with different types of aldehydes.

The asymmetric allylboration reaction was also extended to pinacol crotylboronates.[5a] We found that high diastereoselectivity and excellent enantioselectivity were observed for both *trans*- and *cis*-crotylboronates (Table 3).

Table 3. SPINOL-based phosphoric acid (*R*)-**1i**-catalyzed addition reactions of benzaldehyde with pinacol crotylboronates.[a]



Entry	R	R'	Yield (%)[b]	*dr*[c]	*ee* (%)[d]
1	CH_3	H	98	99:1	99 (99)[e]
2	H	CH_3	99	1:99	99 (94)[f]

[a] Reaction conditions: allylboronate (1.5 equiv.), aldehyde (1.0 equiv.), phosphoric acid (*R*)-**1i** (5 mol-%), toluene, –70 °C, 6 h. [b] Isolated yield. [c] Based on ^{1}H NMR analysis. [d] Based on HPLC (Chiralcel OD column) analysis. [e] In parentheses: reported *ee* value with 5 mol-% of BINOL-based phosphoric acid at 0 °C, see ref.[5a] [f] In parentheses: reported *ee* value with 5 mol-% of BINOL-based phosphoric acid at –30 °C, see ref.[5a]

Conclusions

We demonstrated that SPINOL-based phosphoric acids catalyzed the asymmetric allylboration of aldehydes with pinacol allylboronates. 6,6′-Bis(2,4,6-triisopropylphenyl)-SPINOL-based phosphoric acid (*R*)-**1i** was found to be a general, highly enantioselective catalyst for such allylboration reactions and excellent enantioselectivities were obtained for different types of aldehydes including aromatic aldehydes, α,β-unsaturated aldehydes, propargylic aldehydes, and aliphatic aldehydes. The enantioselectivity was observed to be higher than that obtained with BINOL-based phosphoric acids as catalysts, particularly for substrates such as *ortho*-substituted aromatic aldehydes and aliphatic aldehydes. Our study provides a highly enantioselective phosphoric acid catalyst for the asymmetric allylboration of aldehydes and an efficient method to access a broad spectrum of optically active homoallylic alcohols. Our study also suggests that SPINOL-based phosphoric acids might also be enantioselective catalysts for allylation-related reactions such as propargylation and allenylation reactions.[13,14] Work towards this direction is actively underway.

Experimental Section

General Procedure for the SPINOL-Based Phosphoric Acid Catalyzed Allylboration of Aldehydes with Pinacol Allylboronate: In a vial, aldehyde (0.1 mmol, 1.0 equiv.) and SPINOL-based phosphoric acid (*R*)-**1i** (5 mol-%) were dissolved in toluene (0.5 mL) under an atmosphere of N_2. The mixture was stirred and cooled to –70 °C with a dry ice/2-propanol bath. Then, pinacol allylboronate (0.15 mmol, 1.5 equiv.) was added in one portion through a microsyringe. The reaction mixture was stirred at this temperature until all aldehyde was converted (monitored by ^{1}H NMR spectroscopy). Column chromatography on silica gel (hexanes/diethyl ether or pentane/diethyl ether) afforded the product.

Supporting Information (see footnote on the first page of this article): Reaction procedures and characterization of the products of the SPINOL-based phosphoric acid catalyzed allylboration reactions.

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