

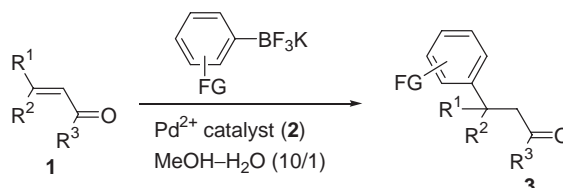
## Asymmetric 1,4-Addition of Potassium Aryltrifluoroborates [ArBF<sub>3</sub>]K to Enones Catalyzed by Dicationic Palladium(II) Complexes

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(Received March 10, 2005; CL-050326)

Asymmetric 1,4-addition of [ArBF<sub>3</sub>]K to cyclic and acyclic enones was carried out in aqueous methanol in the presence of a chiral phosphine-dicationic palladium(II) catalyst. A palladium complex of (*S,S*)-dipamp gave optically active  $\beta$ -arylketones of up to 96 % ee for 2-cyclohexenone and 2-cycloheptenone. A palladium-(*S,S*)-chiraphos complex resulted in 82–97 % ee for 2-cyclopentenone and acyclic enones.



Since metal-catalyzed 1,4-addition of organometallic reagents to  $\alpha,\beta$ -unsaturated carbonyl compounds yields a stereogenic center at the  $\beta$ -carbon, considerable efforts have been devoted to the development to asymmetric syntheses. Among these studies for asymmetric C–C bond formation, the reactions catalyzed by copper,<sup>1</sup> rhodium,<sup>2</sup> and palladium<sup>3</sup> complexes are of great value because of the availability of chiral ligands for these transition metals. We have reported a rhodium(I)–binap catalyst for achieving over 90 % ee in 1,4-addition reactions of aryl- and 1-alkenylboronic acids to cyclic and acyclic enones, esters and amides.<sup>2a,4</sup> Other catalysts that are effective for arylboronic acids are rhodium(I) complexes of chiral bisphosphine ligands such as chiraphos<sup>5</sup> and diphosphonites,<sup>6</sup> P–N ligands of amidomonophosphines,<sup>7</sup> and bis(alkene) ligands based on a norbornadiene skeleton.<sup>8</sup> Although the corresponding reactions of palladium catalysts are rare, we recently reported that dicationic palladium(II) complexes such as [Pd(dppe)(S)<sub>2</sub>]<sup>2+</sup> catalyze 1,4-addition of ArB(OH)<sub>2</sub>,<sup>9</sup> ArSi(OMe)<sub>3</sub>,<sup>10</sup> and Ar<sub>3</sub>Bi<sup>3</sup> to enones via a transmetalation–insertion–hydrolysis sequence<sup>11</sup> analogous to the catalytic cycle of rhodium(I)-catalyzed reactions. Recently, 1,4-addition of Ar<sub>3</sub>Bi was extended to an asymmetric version<sup>3</sup> because this reaction smoothly took place at lower temperatures (–5–0 °C) than that used ArB(OH)<sub>2</sub> and ArSi(OMe)<sub>3</sub> (20–75 °C). In this paper, we report 1,4-addition reaction of potassium aryltrifluoroborates (Scheme 1). Air- and water-stable [ArBF<sub>3</sub>]K, obtained by treatment of ArB(OH)<sub>2</sub> with KHF<sub>2</sub>,<sup>12</sup> is advantageous over ArB(OH)<sub>2</sub> in preparation and handling of pure and stable crystalline materials. Although these K<sup>+</sup> salts are highly insoluble in common organic solvents, the reaction worked well at temperatures lower than 0 °C when using fine powder suspended in aqueous MeOH.<sup>13</sup>

Asymmetric additions of [ArBF<sub>3</sub>]K to representative enones in aqueous MeOH are summarized in Table 1. The reaction was carried out by the following general procedure. To a flask charged with [ArBF<sub>3</sub>]K (1.5 mmol) was successively added MeOH (6 mL), water (0.6 mL), enone (1 mmol), and a Pd(2+) catalyst (**2**, 0.03 mmol, 3 mol %) under argon. After stirring for 21 h at the temperature shown in Table 1, the product was isolated by chromatography over silica gel. Enantiomer excess was determined by a chiral stationary column in comparison with a racemic authentic sample. The reaction was efficiently catalyzed by

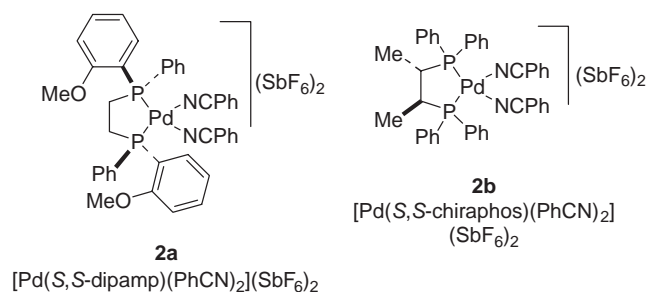


Figure 1.

benzonitrile complexes of **2** at –15–0 °C, very different from the corresponding reaction of Ar<sub>3</sub>Bi conducted in the presence of Cu(BF<sub>4</sub>)<sub>2</sub> for Pd(2+)–benzonitrile catalysts.<sup>3</sup> The copper salt was used for *in situ* generation of a highly electrophilic nitrile-free catalyst active for transmetalation *via* ligand exchange of benzonitrile between the palladium complex and copper(2+) salts.<sup>11</sup> In contrast, [ArBF<sub>3</sub>]K could be smoothly added to representative enones in the absence of such an activator because the reaction yields BF<sub>3</sub>, which is also effective for *in situ* generation of a nitrile-free catalyst such as [Pd(P–P)(solvent)<sub>2</sub>]<sup>2+</sup>. High catalyst efficiency specific for bisphosphines bridged by two carbon atoms was the same as in other 1,4-addition reactions catalyzed by dicationic palladium(II) complexes.<sup>11</sup> Thus, palladium(2+) complexes of dipamp and chiraphos were catalysts that meet this requirement. The dipamp complex (**2a**) gave the best enantioselectivities for 2-cyclohexenone (Entries 2–10) and 2-cycloheptenone (Entry 11), and the chiraphos complex (**2b**) afforded much higher selectivities than **2a** for 2-cyclopentenone (Entry 1) and acyclic enones (Entries 12–20). These effect of catalyst for enones were analogous to that of previous asymmetric reaction of Ar<sub>3</sub>Bi.<sup>3</sup> Acyclic enones catalyzed by **2b** resulted in relatively low enantioselectivities of around 82–83 % ee (Entries 12 and 16). The selectivities increased to 89 % ee by increasing the bulkiness of substituents of the ketone carbonyl group (R<sup>3</sup>) which would sterically interact with one of four P-bound phenyl groups of chiraphos ligand in coordination of an enone to the metal center (Entries 12–15). On the other hand, the bulkiness of aliphatic  $\beta$ -substituent (R<sup>1</sup>) of acyclic enones did not effect to increase the enantioselectivities (Entries 12, 16, and 17), but

**Table 1.** Asymmetric 1,4-addition of [ArBF<sub>3</sub>]K to enones (Scheme 1)<sup>a</sup>

Entry	[ArBF <sub>3</sub> ]K	Enone	Catalyst	Temp./°C	Yield%	%ee <sup>b</sup>
1	Ph	2-cyclopentenone	<b>2b</b>	-5	60	95 (S)
2	Ph	2-cyclohexenone	<b>2a</b>	-15	95	93 (R)
3	4-MeOC <sub>6</sub> H <sub>4</sub>	2-cyclohexenone	<b>2a</b>	-5	89	85 (R)
4	3-MeOC <sub>6</sub> H <sub>4</sub>	2-cyclohexenone	<b>2a</b>	-15	97	95
5	4-MeC <sub>6</sub> H <sub>4</sub>	2-cyclohexenone	<b>2a</b>	-5	70	90
6	3-MeC <sub>6</sub> H <sub>4</sub>	2-cyclohexenone	<b>2a</b>	-5	96	93
7	4-FC <sub>6</sub> H <sub>4</sub>	2-cyclohexenone	<b>2a</b>	-5	99	92
8	3-FC <sub>6</sub> H <sub>4</sub>	2-cyclohexenone	<b>2a</b>	-15	81	96
9	4-CF <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	2-cyclohexenone	<b>2a</b>	-5	33	87
10 <sup>c</sup>	4-CF <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	2-cyclohexenone	<b>2a</b>	-5	66	92
11	Ph	2-cycloheptenone	<b>2a</b>	-15	91	89 (R)
12	Ph	( <i>E</i> )- <i>n</i> -C <sub>5</sub> H <sub>11</sub> CH=CHCOCH <sub>3</sub>	<b>2b</b>	-15	93	82
13	Ph	( <i>E</i> )- <i>n</i> -C <sub>5</sub> H <sub>11</sub> CH=CHCOCH(CH <sub>3</sub> ) <sub>2</sub>	<b>2b</b>	-15	93	87
14	Ph	( <i>E</i> )- <i>n</i> -C <sub>5</sub> H <sub>11</sub> CH=CHCOc-C <sub>6</sub> H <sub>11</sub>	<b>2b</b>	-15	98	88
15	Ph	( <i>E</i> )- <i>n</i> -C <sub>5</sub> H <sub>11</sub> CH=CHCOPh	<b>2b</b>	-15	99	89
16	Ph	( <i>E</i> )-(CH <sub>3</sub> ) <sub>2</sub> CHCH=CHCOCH <sub>3</sub>	<b>2b</b>	-5	65	83 (S)
17	Ph	( <i>E</i> )-(c-C <sub>6</sub> H <sub>11</sub> )CH=CHCOCH <sub>3</sub>	<b>2b</b>	-5	22	78
18	3-MeOC <sub>6</sub> H <sub>4</sub>	( <i>E</i> )-PhCH=CHCOCH <sub>3</sub>	<b>2b</b>	0	90	95
19	3-MeOC <sub>6</sub> H <sub>4</sub>	( <i>E</i> )-PhCH=CHCOPh	<b>2b</b>	-5	94	97
20	3-MeOC <sub>6</sub> H <sub>4</sub>	( <i>E</i> )-1-naphthylCH=CHCOCH <sub>3</sub>	<b>2b</b>	0	73	96

<sup>a</sup>All reactions were carried out for 21 h using enone (1 mmol), [ArBF<sub>3</sub>]K (1.5 mmol), and Pd<sup>2+</sup> catalyst (0.03 mmol, 3 mol %) in MeOH–H<sub>2</sub>O (10/1), unless otherwise noted. <sup>b</sup>Enantiomer excess was determined by a chiral stationary column. <sup>c</sup>Reaction was conducted in MeOH without using water.

enones possessing an aromatic β-substituent such as phenyl and 1-naphthyl group exceptionally resulted in high selectivities exceeding 95 % ee (Entries 18–20).

Works aimed at characterization of chiral phosphine–palladium(2+) catalysts are in progress to elucidate enantioselective insertion of enones.

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