Asymmetric 1,4-Addition of Potassium Aryltrifluoroborates [$ArBF_3$]K to Enones Catalyzed by Dicationic Palladium(II) Complexes

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Asymmetric 1,4-addition of [$ArBF_3$]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 β-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 α,β-unsaturated carbonyl compounds yields a stereogenic center at the β-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,[1] rhodium,[2] and palladium[3] 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.[2a,4] Other catalysts that are effective for arylboronic acids are rhodium(I) complexes of chiral bisphosphine ligands such as chiraphos[5] and diphosphonites,[6] P–N ligands of amidomonophosphines,[7] and bis(alkene) ligands based on a norbornadiene skeleton.[8] Although the corresponding reactions of palladium catalysts are rare, we recently reported that dicationic palladium(II) complexes such as $[Pd(dppe)(S)_2]^{2+}$ catalyze 1,4-addition of $ArB(OH)_2$,[9] $ArSi(OMe)_3$,[10] and Ar_3Bi[3] to enones via a transmetalation–insertion-hydrolysis sequence[11] analogous to the catalytic cycle of rhodium(I)-catalyzed reactions. Recently, 1,4-addition of Ar_3Bi was extended to an asymmetric version[3] because this reaction smoothly took place at lower temperatures (−5–0 °C) than that used $ArB(OH)_2$ and $ArSi(OMe)_3$ (20–75 °C). In this paper, we report 1,4-addition reaction of potassium aryltrifluoroborates (Scheme 1). Air- and water-stable [$ArBF_3$]K, obtained by treatment of $ArB(OH)_2$ with KHF_2,[12] is advantageous over $ArB(OH)_2$ in preparation and handling of pure and stable crystalline materials. Although these K^+ 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.[13]

Asymmetric additions of [$ArBF_3$]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 [$ArBF_3$]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

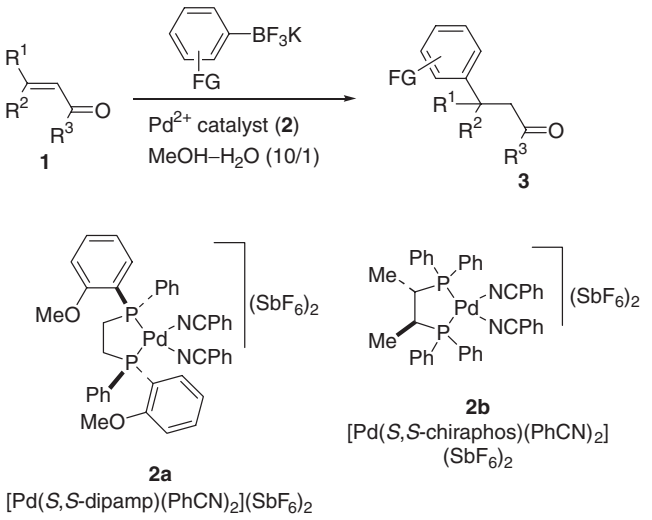

Figure 1.

benzonitrile complexes of **2** at −15–0 °C, very different from the corresponding reaction of Ar_3Bi conducted in the presence of $Cu(BF_4)_2$ for Pd(2+)–benzonitrile catalysts.[3] 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.[11] In contrast, [$ArBF_3$]K could be smoothly added to representative enones in the absence of such an activator because the reaction yields BF_3, which is also effective for in situ generation of a nitrile-free catalyst such as $[Pd(P–P)(solvent)_2]^{2+}$. 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.[11] 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_3Bi.[3] 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^3) 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 β-substituent (R^1) of acyclic enones did not effect to increase the enantioselectivities (Entries 12, 16, and 17), but

Table 1. Asymmetric 1,4-addition of $[ArBF_3]K$ to enones (Scheme 1)[a]

Entry	$[ArBF_3]K$	Enone	Catalyst	Temp./°C	Yield%	%ee[b]
1	Ph	2-cyclopentenone	**2b**	−5	60	95 (*S*)
2	Ph	2-cyclohexenone	**2a**	−15	95	93 (*R*)
3	4-$MeOC_6H_4$	2-cyclohexenone	**2a**	−5	89	85 (*R*)
4	3-$MeOC_6H_4$	2-cyclohexenone	**2a**	−15	97	95
5	4-MeC_6H_4	2-cyclohexenone	**2a**	−5	70	90
6	3-MeC_6H_4	2-cyclohexenone	**2a**	−5	96	93
7	4-FC_6H_4	2-cyclohexenone	**2a**	−5	99	92
8	3-FC_6H_4	2-cyclohexenone	**2a**	−15	81	96
9	4-$CF_3C_6H_4$	2-cyclohexenone	**2a**	−5	33	87
10[c]	4-$CF_3C_6H_4$	2-cyclohexenone	**2a**	−5	66	92
11	Ph	2-cycloheptenone	**2a**	−15	91	89 (*R*)
12	Ph	(*E*)-*n*-$C_5H_{11}CH{=}CHCOCH_3$	**2b**	−15	93	82
13	Ph	(*E*)-*n*-$C_5H_{11}CH{=}CHCOCH(CH_3)_2$	**2b**	−15	93	87
14	Ph	(*E*)-*n*-$C_5H_{11}CH{=}CHCO$*c*-C_6H_{11}	**2b**	−15	98	88
15	Ph	(*E*)-*n*-$C_5H_{11}CH{=}CHCOPh$	**2b**	−15	99	89
16	Ph	(*E*)-$(CH_3)_2CHCH{=}CHCOCH_3$	**2b**	−5	65	83 (*S*)
17	Ph	(*E*)-(*c*-C_6H_{11})$CH{=}CHCOCH_3$	**2b**	−5	22	78
18	3-$MeOC_6H_4$	(*E*)-$PhCH{=}CHCOCH_3$	**2b**	0	90	95
19	3-$MeOC_6H_4$	(*E*)-$PhCH{=}CHCOPh$	**2b**	−5	94	97
20	3-$MeOC_6H_4$	(*E*)-1-naphthyl$CH{=}CHCOCH_3$	**2b**	0	73	96

[a]All reactions were carried out for 21 h using enone (1 mmol), $[ArBF_3]K$ (1.5 mmol), and Pd^{2+} catalyst (0.03 mmol, 3 mol %) in MeOH–H_2O (10/1), unless otherwise noted. [b]Enantiomer excess was determined by a chiral stationary column. [c]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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