Interesting Nickel-Catalyzed 1,2-Addition to *α,β*-Unsaturated Aldehydes with Arylborates

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Ni-Et-Duphos-catalyzed 1,2-addition of potassium aryltrifluoroborates to *α,β*-unsaturated aldehydes is described.

Key words nickel; arylation; 1,2-addition; borate; *α,β*-unsaturated aldehyde; Duphos

Arylboron reagents, in particular potassium aryltrifluoroborates ($ArBF_3K$), are useful reagents for safe and sustainable C–C bond formations, because their reagents are less toxic, air-stable, and easy to handle.[1] Many examples for Rh catalyzed 1,4-addition to *α,β*-unsaturated aldehydes with arylboron reagents have been reported.[2] On the other hand, in relation to 1,2-addition, only one example of Rh(I)-*t*-Bu_3P catalyzed addition to cinnamaldehyde with phenylboronic acid has been reported by Ueda and Miyaura.[3] Later, less attention has been focuced on metal catalyzed 1,2-addition of arylboron reagents to *α,β*-unsaturated aldehydes, although the control of 1,2-addition *vs.* 1,4-addition in this reaction is an important concern.[4] Recently, the corresponding authors of this paper have reported the use of a cheaper metal than Rh, Ni catalyst, for 1,2-addition of aromatic aldehydes with arylboron reagents[5,6]: from the viewpoint of cost and practical convenience, the use of a much more cheaper and naturally abundant Ni is considered to be desirable. In order to expand our above arylation, we decided to challenge the Ni-Et-Duphos-catalyzed 1,2-addition of $ArBF_3K$ to *α,β*-unsaturated aldehydes,[7] although it has been known that the combination of a Ni-catalyst and organometallic reagents promotes 1,4-addition to *α,β*-unsaturated carbonyl compounds.[8]

We examined the addition of $ArBF_3K$ to *α,β*-unsaturated aldehydes, and the reaction in only the 1,2-mode was found to proceed at 80—100 °C as shown in Table 1. As shown in entries 1—7, the reaction of cinnamaldehyde (**1**) with various $ArBF_3K$ proceeded with moderate to good yields, except for entry 6. The poor results of entry 6 was due to the decomposition of the product in purifying the crude product by silica gel column chromatography, although the reaction was proceeded. The *α*-substituted *α,β*-unsaturated aldehydes **2**, and the *β,β*-disubstituted **3** and **5** were also arylated in the 1,2-mode (entries 8, 9, 11). Unfortunately, the yield of *β*-aliphatic substituted *α,β*-unsaturated aldehydes **4** was quite low as shown in entry **10**: this low yield might be due to the decomposition of the starting aldehyde **4** under this reaction conditions.

In summary, Ni-Et-Duphos catalyst was found to promote 1,2-addtion of $ArBF_3K$[9] to *α,β*-unsaturated aldehyde. Development of synthetically useful enantioselective version is in progress.

Experimental

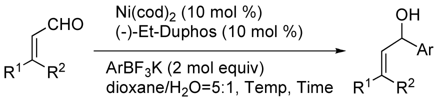
IR spectra were measured on a SHIMADZU FTIR-8100 diffraction grating IR spectrophotometer. ^1H- and ^{13}C-NMR spectra were measured on a JEOL JNM-EX-270 NMR spectrometer, operating at 270 MHz for ^1H-NMR and at 68 MHz for ^{13}C-NMR. ^1H- and ^{13}C-NMR spectra were reported in δ units, parts per million (ppm) downfield from tetramethylsilane ($\delta=0$). EI- and FAB-MS spectra were measured on a JEOL JMS-SX-102A instrument. The ee was determined by HPLC analysis (Daicel chiralcel OD-H, eluent: hexane/*i*-PrOH).

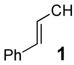
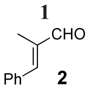
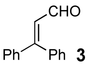
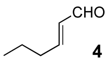
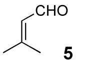
All aldehydes, reagents, and solvents were available from commercial sources and used without further purification. In general, all reactions were performed under an argon atmosphere. Silica gel column chromatography was performed on Fuji Silysia BW200.

Representative Procedure for the Synthesis of (*E*)-1,3-Diphenyl-2-propen-1-ol (Entry 1) To a stirred solution of (*R,R*)-Et-Duphos (8.6 mg, 0.0238 mmol) in dioxane/H_2O (5 : 1, 0.60 ml) were added $Ni(cod)_2$ (6.6 mg, 0.0238 mmol), $PhBF_3K$ (87.6 mg, 0.476 mmol) and cinnamaldehyde (**1**) (30 *μ*l, 31.5 mg, 0.238 mmol). The reaction mixture was stirred for 6 h at 80 °C, allowed to cool, diluted with water, and extracted with EtOAc. The organic extracts were successively washed with 10% HCl, water, saturated aq. $NaHCO_3$, water and brine, dried (Na_2SO_4) and concentrated. Purification by silica gel column (hexane : EtOAc = 10 : 1) afforded (*E*)-1,3-diphenyl-2-propen-1-ol (40.2 mg, 82%, 39% ee) as a colorless oil. The physical data were comparable to those reported.[10]

(*E*)-1-(4-Fluorophenyl)-3-phenyl-2-propen-1-ol (Entries 2, 3) IR (neat): 3306 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 2.05 (s, 1H), 5.37 (d, $J=6.4$ Hz, 1H), 6.34 (dd, $J=6.4$, 15.8 Hz, 1H), 6.67 (d, $J=15.8$ Hz, 1H), 6.95—7.09

Table 1. Ni-Catalyzed 1,2-Addition of $ArBF_3K$ to *α,β*-Unsaturated Aldehydes[a)]



Entry	*α,β*-Unsaturated aldehyde	$ArBF_3K$ (Ar=)	Temp. (°C)	Time (h)	Yield (%)
1	 **1**	Ph	80	6	82[b)]
2	**1**	4-F-C_6H_4	80	5	61[c)]
3	**1**	4-F-C_6H_4	100	5	66[c)]
4	**1**	4-Cl-C_6H_4	100	3	85[b)]
5	**1**	4-Me-C_6H_4	100	6	68[c)]
6	**1**	4-MeO-C_6H_4	100	12	<40
7	**1**	2-Me-C_6H_4	100	12	80
8	 **2**	Ph	100	12	60[c)]
9	 **3**	4-*t*-Bu-C_6H_4	100	4	100
10	 **4**	4-*t*-Bu-C_6H_4	100	12	27
11	 **5**	Ph	100	3	67

a) Other ligands such as dppe, dppp, dppb, dppf, BINAP, Segphos, and DIOP resulted in no reaction. *b*) The ees were as follows: entry 1 (39% ee), enrty 4 (36% ee). *c*) Major remainder, which was observed by TLC, was the starting aldehyde.

∗ To whom correspondence should be addressed. e-mail: kazu@gakushikai.jp; aoyama@phar.nagoya-cu.ac.jp (m, 2H), 7.21—7.42 (m, 7H). ^{13}C-NMR (CDCl$_3$) δ: 74.48, 115.19, 115.50, 126.51, 127.82, 127.89, 128.00, 128.51, 128.57, 130.69, 131.20, 136.23, 138.35, 138.40, 160.37, 163.98. EI-MS *m*/*z*: 228 (M$^+$), 123 (base peak). HR-MS (EI) Calcd for $C_{15}H_{13}OF$ [M$^+$]: 228.0951. Found: 228.0946.

(*E*)-1-(4-Chlorophenyl)-3-phenyl-2-propen-1-ol (Entry 4) IR (neat): 3470 cm^{-1}. ^{1}H-NMR (CDCl$_3$) δ: 2.00 (br d, J=3.4 Hz, 1H), 5.37 (br dd, J=3.4, 6.6 Hz, 1H), 6.33 (dd, J=6.6, 15.8 Hz, 1H), 6.68 (d, J=15.8 Hz, 1H), 7.22—7.40 (m, 9H). ^{13}C-NMR (CDCl$_3$) δ: 74.43, 126.51, 127.58, 127.85, 128.50, 128.58, 130.90, 130.93, 133.33, 136.12, 141.02. MS(EI) *m*/*z*: 246 (M$^+$), 244 (M$^+$), 139 (base peak). HR-MS (EI) Calcd for $C_{15}H_{13}{}^{35}ClO$ [M$^+$]: 244.0655. Found: 244.0654, $C_{15}H_{13}{}^{37}ClO$ [M$^+$]: 246.0626. Found: 246.0624.

(*E*)-1-(4-Methylphenyl)-3-phenyl-2-propen-1-ol (Entry 5) The physical data were comparable to those reported.[11)]

(*E*)-1-(2-Methylphenyl)-3-phenyl-2-propen-1-ol (Entry 7) The physical data were comparable to those reported.[12)]

(*E*)-1,3-Diphenyl-2-methyl-2-propen-1-ol (Entry 8) The physical data were comparable to those reported.[13)]

(*E*)-3,3-Diphenyl-1-(4-*t*-butylphenyl)-2-propen-1-ol (Entry 9) A white solid. IR (nujol): 3371 cm^{-1}. ^{1}H-NMR (CDCl$_3$) δ: 1.32 (s, 3H×3), 1.85 (br d, J=3.7 Hz, 1H), 5.24 (br dd, J=3.7, 9.6 Hz, 1H), 6.32 (d, J=9.6 Hz, 1H), 7.23—7.40 (m, 14H). ^{13}C-NMR (CDCl$_3$) δ: 31.40, 34.57, 71.39, 125.39, 125.82, 127.44, 127.48, 127.52, 128.02, 128.17, 129.76, 130.13, 139.04, 140.33, 141.50, 143.11, 150.39. MS(EI) *m*/*z*: 342 (M$^+$), 324 (base peak). HR-MS (EI) Calcd for $C_{25}H_{26}O$ [M$^+$]: 342.1984. Found: 342.1996.

(*E*)-1-(4-*t*-butylphenyl)-2-hexen-1-ol (Entry 10) A white solid. IR (neat): 3371 cm^{-1}. ^{1}H-NMR (CDCl$_3$) δ: 0.95 (br t, J=6.9 Hz, 3H), 1.26—1.47 (m, 2H), 1.31 (s, 9H), 1.55—1.67 (m, 3H), 4.27 (br d, J=6.4 Hz, 1H), 6.18 (br dd, J=6.9 Hz, J=15.8 Hz, 1H), 6.54 (br d, J=15.7 Hz, 1H), 7.25—7.33 (m, 4H). ^{13}C-NMR (CDCl$_3$) δ: 14.10, 18.76, 31.35, 34.63, 39.56, 72.96, 125.39, 126.07, 129.93, 131.73, 139.30, 150.62. MS(EI) *m*/*z*: 232 (M$^+$), 217 (base peak). HR-MS (EI) Calcd for $C_{16}H_{24}O$, [M$^+$]: 232.1827. Found: 232.1834.

(*E*)-3-Methyl-1-phenyl-2-buten-1-ol (Entry 11) The physical data were comparable to those reported.[14)]

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