

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

Fumie SAKURAI, Kazuhiro KONDO,* and Toyohiko AOYAMA*

Graduate School of Pharmaceutical Sciences, Nagoya City University; 3-1 Tanabe-dori, Mizuho-ku, Nagoya 467-8603, Japan. Received November 25, 2008; accepted February 6, 2009; published online February 9, 2009

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*-Bu₃P catalyzed addition to cinnamaldehyde with phenylboronic acid has been reported by Ueda and Miyaura.³⁾ Later, less attention has been focused 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-addition 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 ¹³C-NMR spectra were measured on a JEOL JNM-EX-270 NMR spectrometer, operating at 270 MHz for ¹H-NMR and at 68 MHz for ¹³C-NMR. ¹H- and ¹³C-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/H₂O (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 μl , 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. NaHCO₃, water and brine, dried (Na₂SO₄) 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 (CDCl₃) 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)}

$\begin{array}{c} \text{CHO} \\ \\ \text{R}^1\text{C}=\text{C}-\text{R}^2 \end{array} \xrightarrow[\text{dioxane/H}_2\text{O}=5:1, \text{Temp, Time}]{\begin{array}{c} \text{Ni(cod)}_2 \text{ (10 mol \%)} \\ \text{(-)-Et-Duphos (10 mol \%)} \\ \text{ArBF}_3\text{K (2 mol equiv)} \end{array}} \begin{array}{c} \text{OH} \\ \\ \text{R}^1\text{C}=\text{C}-\text{Ar} \end{array}$					
Entry	α,β -Unsaturated aldehyde	ArBF_3K (Ar=)	Temp. (°C)	Time (h)	Yield (%)
1		Ph	80	6	82 ^{b)}
2	1	4-F-C ₆ H ₄	80	5	61 ^{c)}
3	1	4-F-C ₆ H ₄	100	5	66 ^{c)}
4	1	4-Cl-C ₆ H ₄	100	3	85 ^{b)}
5	1	4-Me-C ₆ H ₄	100	6	68 ^{c)}
6	1	4-MeO-C ₆ H ₄	100	12	<40
7	1	2-Me-C ₆ H ₄	100	12	80
8		Ph	100	12	60 ^{c)}
9		4- <i>t</i> -Bu-C ₆ H ₄	100	4	100
10		4- <i>t</i> -Bu-C ₆ H ₄	100	12	27
11		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), entry 4 (36% ee). c) Major remainder, which was observed by TLC, was the starting aldehyde.

(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 $\text{C}_{15}\text{H}_{13}\text{OF}$ [M^+]: 228.0951. Found: 228.0946.

(E)-1-(4-Chlorophenyl)-3-phenyl-2-propen-1-ol (Entry 4) IR (neat): 3470 cm^{-1} . ^1H -NMR (CDCl_3) δ : 2.00 (br d, $J=3.4\text{ Hz}$, 1H), 5.37 (br dd, $J=3.4, 6.6\text{ Hz}$, 1H), 6.33 (dd, $J=6.6, 15.8\text{ Hz}$, 1H), 6.68 (d, $J=15.8\text{ Hz}$, 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 $\text{C}_{15}\text{H}_{13}^{35}\text{ClO}$ [M^+]: 244.0655. Found: 244.0654, $\text{C}_{15}\text{H}_{13}^{37}\text{ClO}$ [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} . ^1H -NMR (CDCl_3) δ : 1.32 (s, $3\text{H} \times 3$), 1.85 (br d, $J=3.7\text{ Hz}$, 1H), 5.24 (br dd, $J=3.7, 9.6\text{ Hz}$, 1H), 6.32 (d, $J=9.6\text{ Hz}$, 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 $\text{C}_{25}\text{H}_{26}\text{O}$ [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} . ^1H -NMR (CDCl_3) δ : 0.95 (br t, $J=6.9\text{ Hz}$, 3H), 1.26—1.47 (m, 2H), 1.31 (s, 9H), 1.55—1.67 (m, 3H), 4.27 (br d, $J=6.4\text{ Hz}$, 1H), 6.18 (br dd, $J=6.9\text{ Hz}$, $J=15.8\text{ Hz}$, 1H), 6.54 (br d, $J=15.7\text{ Hz}$, 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 $\text{C}_{16}\text{H}_{24}\text{O}$ [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⁾

Acknowledgements We thank Mr. Hiroaki Matsuoka (Nagoya City University) and Mr. Hiroki Ozasa (Nagoya City University) for experimental assistant.

References and Notes

- 1) Miyaura N., Suzuki A., *Chem. Rev.*, **95**, 2457—2483 (1995).
- 2) Hayashi T., Yamasaki K., *Chem. Rev.*, **103**, 2457—2483 (2003).
- 3) Ueda M., Miyaura N., *J. Org. Chem.*, **65**, 4450—4452 (2000).
- 4) For a leading reference for 1,2-addition with organometallic reagents: Imamoto T., "Comprehensive Organic Synthesis," Vol. 1, ed. by Trost B. M., Fleming I., Ley S. V., Pergamon Press, Oxford, 1991, pp. 231—250.
- 5) Arao T., Kondo K., Aoyama, T., *Tetrahedron Lett.*, **48**, 4115—4117 (2007).
- 6) Yamamoto K., Tsurumi K., Sakurai F., Kondo K., Aoyama, T., *Synthesis*, **2008**, 3585—3590 (2008).
- 7) Cu-catalyzed asymmetric 1,2-addition of boron reagents to α,β -unsaturated aldehydes: Tomita D., Kanai M., Shibasaki M., *Chem. Asian J.*, **1**—2, 161—166 (2006).
- 8) Schwartz J., Loots M. J., Kosugi H., *J. Am. Chem. Soc.*, **102**, 1333—1340 (1980).
- 9) For a recent review of ArBF_3K , see: Darses S., Genet, J. P., *Chem. Rev.*, **108**, 288—325 (2008).
- 10) Moriuchi-Kawakami T., Matsuda H., Shibata I., Miyatake M., Suwa T., Baba A., *Bull. Chem. Soc. Jpn.*, **72**, 465—470 (1999).
- 11) von Matt P., Lloyd-Jones G. C., Minidis A. B. E., Pfaltz A., Macko L., Neuburger M., Zehnder M., Rüegg H., Pregosin P. S., *Helv. Chim. Acta*, **78**, 265—284 (1995).
- 12) Nonosita K., Maruoka K., Yamamoto H., *Bull. Chem. Soc. Jpn.*, **61**, 2241—2243 (1988).
- 13) Takai K., Kimura K., Kuroda T., Hiyama T., Nozaki H., *Tetrahedron Lett.*, **47**, 5281—5284 (1983).
- 14) Gau A.-H., Lin G.-L., Uang B.-J., Liao F.-L., Wang S.-L., *J. Org. Chem.*, **64**, 2194—2201 (1999).