

0040-4039(95)01294-X

Palladium-Catalyzed Arylation of Allylic Diols: Highly Selective Synthesis of Phenyl-Substituted Allylic Diols

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Abstract: The coupling reaction of iodobenzene with allylic diols in the presence of $Pd(OAc)_2$ and nBu_3P as catalysts using K_2CO_3 as base afforded the phenyl-substituted allylic diols. However, under the same reaction conditions with Et₃N as base, phenyl-substituted α -hydroxy ketone was obtained.

Palladium-catalyzed reaction of organic halides with alkenes (Heck-type reaction) is known to be a very convenient method for forming carbon-carbon bonds at unsubstituted vinylic positions.¹ In the case of allylic alcohols, any account with a romatic halides leads to the formation of β -aromatic carbonyl compound which is the usual pathway of the Heck reaction.² Recently Jeffery³ reported that in the presence of a stoichiometric amount of silver acetate or silver carbonate, a highly selective formation of conjugated aromatic allylic alcohols can be achieved from aromatic halides and allylic alcohols. The selective formation of the substituted allylic alcohols was rationalized^{3c} by assuming a four-membered intermediate, where the hydrogen atom on the hydroxyl-bearing carbon is located unfavorably toward a syn palladium hydride elimination. Alternatively, Cacci⁴ reported that the use of vinyl triflates instead of vinyl iodides with allylic alcohols in the presence of Pd(0) catalyst provided $\alpha,\beta,\gamma,\delta$ -unsaturated alcohols by alternation of the reaction course. Recently, Tamaru⁵ utilized O-substituted allylic alcohols to direct the coupling without elimination of proton adjacent to oxygen-bearing carbon. As a part of our program to utilize chiral dihydroxy compounds which can be synthesized from ethyl L-tartrate as 'chiral pool' or olefins by asymmetric dihydroxylation,⁶ we have found that treatment of allylic diols with iodobenzene in the presence of Pd(OAc), nBu₂P, and K₂CO₃ as base resulted in the formation of phenyl-substituted diols. Alternatively, using the same catalyst system under the same conditions using Et₄N as base, phenyl-substituted hydroxy ketones were obtained, as shown in Scheme 1.



Scheme 1

The results of Pd-catalyzed arylation of allylic diols are summarized in Table 1. The allylic diol 1 was reacted with iodobenzene in the presence of a catalytic amount of $Pd(OAc)_2$, nBu_3P , and 1.3 equiv of Et_3N in DMF to afford phenyl-substituted α -hydroxy ketone 3⁷ as the only isolated product in 85% yield (entry 1). On the other hand, highly selective formation of aromatic conjugated diol 4⁷ as sole product was achieved in the presence of the same catalyst system using K₂CO₃ as base (entry 2).⁸ Also, Na₂CO₃, and Cs₂CO₃ as bases gave the diol 4 in 90% and 93% yields, respectively. For the above results, in the case of inorganic bases, it is presumed that there is an influence of the diol functionality, which can be explained by simultaneous coordination of palladium with two oxygens (intermediate A), or chelation of β -hydroxy group to palladium (intermediate B) which might be unfavorable for syn palladium hydride eliminatin of the hydrogen on the exocyclic phenyl-bearing methylene carbon would give 4 and elimination of the hydrogen on the encocyclic hydroxy-bearing carbon to give 3 will be unfavorable (Fig. 1).



Fig. 1 (H* is favorable for syn β -elimination)

Dramatic regioselection of β -elimination could be also explained by the comparison of the nature of bases in the process of regeration of Pd(0) species from Pd(II) complex. In refluxing DMF, K₂CO₃ might be stronger base than Et₃N, which makes HPdI liberated in catalytic cycle to convert into Pd(0) species faster to provide kinetically favored compound 4. Presumably, with Et₃N as weaker base, the regeneration of Pd(0) from HPdX will be slow, which makes HPdX add to the compound 4 to form σ -alkylpalladium intermediate D, which subsequently undergoes β -hydride elimination to give the enol **E**. Eventually, the enol **E** will tautomerize to the ketones 3 by shifting the equilibria (Scheme 2).



However, in the contrast to the reported method,³ the use of a stoichiometric amount of AgOAc, 1:1

mixture of the substituted diol 3 and the substituted α -hydroxy ketone 4 were obtained (entry 3). Finally, treatment of exomethylene diol 2 with iodobenzene in the presence of K₂CO₃ and Pd(OAc)₂, and nBu₃P catalysts afforded phenyl substituted allylic diol 5⁷ (entry 4).

Entry	Substrate	Base	Temp(^o C)	Time(h)	Product ^b	Yield(%) ^c
1		Et ₃ N	100	1.5		85
2	1	K ₂ CO ₃ d	120	1		93
3	1	AgOAc	100	3	3 + 4 (6:4)	89
4		K ₂ CO ₃	80	ì	Ph OH	91

Table 1. Palladium-Catalyzed Arylation of Allylic Diols.^a

^a All the reactions were run in the presence of Pd(OAc)₂(10 mol %), nBu₃P(20 mol %), Phl(1.3 equiv) in DMF. ^b $[\alpha]_{D}^{25}$ values in CHCl₃. 3: +13.3(c 0.7); 4: -10.5(c 0.1). ^c The yields are isolated yields. ^d The use of NaHCO₃, Na₂CO₃, and Cs₂CO₃ also gave the diol 4.

As supporting evidence for the requirment of diol functionality in controlling regioselections, the same conditions were applied to allylic alcohol 6. Treatment of allylic alcohol 6 and iodobenzene with a combination of Pd(OAc)₂, nBu_3P , and K_2CO_3 or Pd(OAc)₂, nBu_3P , and Et₃N afforded mixtures of the substituted ketone 7 and the allylic alcohol 8,⁹ which is shown in Scheme 3.



Scheme 3

The typical procedure is as follows. Preparation of 4: To a stirred solution of Pd(OAc)₂(19 mg, 10 mol %), nBu_3P (34 mg, 20 mol %), and K₂CO₃ (151 mg, 1.10 mmol) in dry DMF (1 mL) was added 1 (200 mg, 0.84 mmol) followed by iodobenzene (223 mg, 1.10 mmol). The reaction mixture was stirred at 100 °C for 1 h and then cooled and extracted with ether. The organic layer was dried over anhydrous MgSO₄ and evaporated *in vacuo*. The crude product was purified by SiO₂ column chromatography (EtOAc/hexanes 1 : 1, R_f = 0.45) to afford 4 (246 mg, 93%).

In summary, the outcome of arylation of allylic diols can be highly controlled by the appropriate choice

of base in the presence of catalyst system. We can now control at will the product, β -aromatic hydroxy carbonyl or β -aromatic α , β -unsaturated diols from aromatic halides and allylic diols by the choice of base under relatively mild conditions with high stereocontrol.

Acknowledgment. Generous financial support by KOSEF-OCRC and Ministry of Education (BSRI-94-3420) is greatefully acknowledged.

REFERENCES AND NOTES

- 1. (a) Heck, R. F. Org. React. 1982, 27, 345. (b) Heck, R. F. Acc. Chem. Res. 1972, 12, 146.
- (a) Melpolder, J. B.; Heck, R. F. J. Org. Chem. 1976, 41, 265. (b) Chalk, A. J.; Magennis, S. A. *ibid.* 1976, 41, 273. (c) Frank, W. C.; Kim, Y. C.; Heck, R. F. J. Org. Chem. 1978, 43, 2947. (d) Tamaru, Y.; Yamada, Y.; Yoshida, Z-i. J. Org. Chem. 1978, 43, 3396. (e) Tamaru, Y.; Yamada, Y.; Yoshida, Z. Tetrahedron 1979, 35, 329. and reference therein. (f) Jeffery, T. J. Chem. Soc. Chem. Commun. 1984, 1287.
- (a) Jeffery, T. Tetrahedron Lett. 1991, 32, 2121. (b) Jeffery, T. J. Chem. Soc., Chem. Commun. 1991, 324. (c) Jeffery, T. Tetrahedron Lett. 1993, 34, 1133.
- 4. Bernocchi, E.; Cacchi, S.; Crattini, P. G.; Morera, E.; Ortar, G. Tetrahedron Lett. 1992, 33, 3073.
- 5. Ono, K.; Fugami, K.; Tanaka, S.; Tamaru, Y. Tetrahedron Lett. 1994, 35, 4133.
- Johnson, R. A.; Sharpless, K. B. Catalytic Asymmetric Synthesis; Ojima, I., Ed., VCH: New York 1993; Chap. 4.
- 7. Satisfactory spectral and physical data were obtained for the new compounds in accord with the structure. Selected physical and spectral data are as follows. 3: TLC, SiO₂, EtOAc/hexanes 1 : 1, $R_r = 0.74$. ¹H-NMR (300 MHz, CDCl₃) & 2.70 (m, 2H), 2.83 (m, 2H), 3.50 (m, 2H), 3.75 (m, 1H), 3.80 (s, 3H), 4.10 (m, 1H), 4.35 (m, 2H), 6.75 (d, 2H, J = 8.6 Hz), 7.10 (m, 5H). IR (neat) 3470, 2930, 2865, 1716, 1611, 1248 cm⁻¹. MS (m/e) 314 (M⁺), 138, 137, 121, 105, 91, 77 (base peak). 4: TLC, SiO₂, EtOAc/hexanes 1 : 1, $R_r = 0.45$. ¹H-NMR (300 MHz, CDCl₃) & 2.80 (bs, 2H), 3.45 (m, 2H), 3.75 (m, 1H), 3.80 (s, 3H), 4.20 (m, 1H), 4.35 (m, 2H), 6.10 (dd, 1H, J = 15.9, 6.8 Hz), 6.50 (d, 1H, J = 15.9 Hz), 6.75 (d, 2H, J = 8.6 Hz), 7.18 (m, 7H),. IR (neat) 3375, 2932, 2869, 1611, 1246 cm⁻¹. MS (m/e) 314 (M⁺), 180, 179, 163, 137(base peak), 121. 5: TLC, SiO₂, EtOAc/hexanes 1 : 1, $R_r = 0.58$. ¹H-NMR (300 MHz, CDCl₃) & 3.05 (bs, 2H), 4.32 (s, 2H), 4.37 (s, 2H), 6.56 (s, 1H), 7.20 (m, 5H). IR (neat) 3412, 2923, 2853 cm⁻¹. MS (m/e) 164 (M⁺), 146, 133, 115 (base peak), 105, 77.
- 8. The diol 1 with *o*-iodotoluene under the same catalysts with Et_3N in DMF at 100 °C for 10 h provided *o*-tolyl substituted α -hydroxy ketone in 83% yield. Under the same conditions with K_2CO_3 , *o*-tolyl substituted allylic diol was obtained in 90% yield.
- 9. Treatment of homoallylic alcohol with Pd(OAc)₂, *n*Bu₃P in the presence of K₂CO₃ or Et₃N afforded the substituted homoallylic alcohol, which is the normal Heck-type product.



(Received in Japan 6 February 1995; revised 19 June 1995; accepted 8 July 1995)