Pergamon

Tetrahedron Letters, Vol. 35, No. 24, pp. 4133-4136, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $7.00+0.00

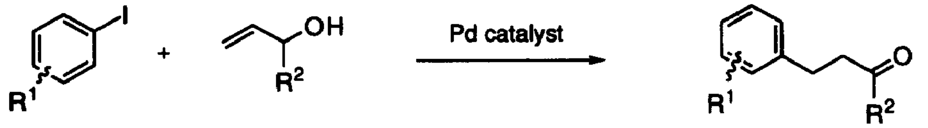
0040-4039(94)E0728-G

Palladium Catalyzed Arylation of *N*-Alkyl *O*-Allyl Carbamates: Synthesis of Cinnamyl Alcohols via Heck Arylation

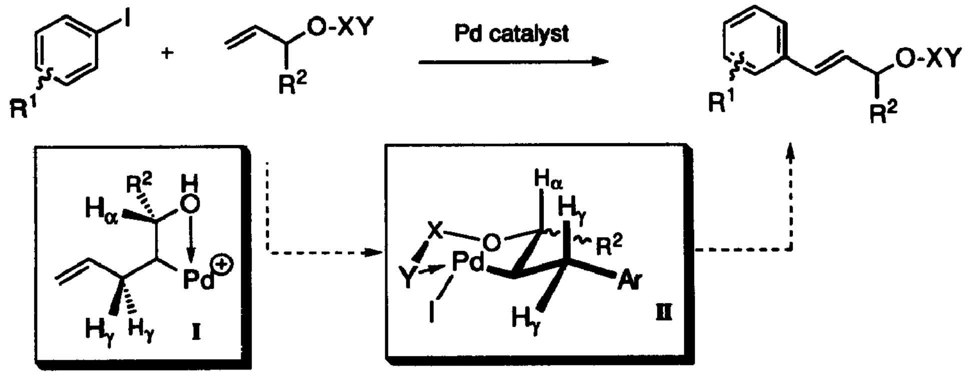
Keiji Ono, Keigo Fugami, Shuji Tanaka, and Yoshinao Tamaru*
Department of Applied Chemistry, Faculty of Engineering, Nagasaki University,
1-14 Bunkyo, Nagasaki 852, Japan

Abstract: *N*-Alkyl *O*-cinnamyl carbamates (3) were prepared in good yields by palladium catalyzed arylation of *N*-alkyl *O*-allyl carbamates (2) with aryl iodides.

Heck type arylation of allylic alcohols with aromatic[1] and heteroaromatic halides[2] is an efficient entry to the preparation of aromatic-substituted alkyl aldehydes and ketones (eq 1). Jeffery[3] recently reported that the similar reaction, in the presence of a stoichiometric amount of silver acetates, altered the course of the reaction, providing cinnamyl alcohols in synthetically useful yields (eq 2, XY = H). Based on the selective formation of $\alpha,\beta,\gamma,\delta$-unsaturated alcohols by the reaction of allyl alcohols with either vinyl triflates[4] or vinyl iodide in the presence of a stoichiometric amount of silver salt,[5] the alteration of the reaction course was rationalized by assuming a four-membered intermediate I (eq 2),[5,6] where the hydrogen atom (H_α) on the hydroxyl-bearing carbon is located unfavorably toward a syn palladium-hydride elimination and only the H_γ protons can participate in this dehydropalladation. Here the poor coordinating ability of a triflate anion or the sequestration of halide ion by silver cation, both of which may serve to generate an electron-deficient Pd(II) center, seems to promote the formation of a rather strained intermediate I.

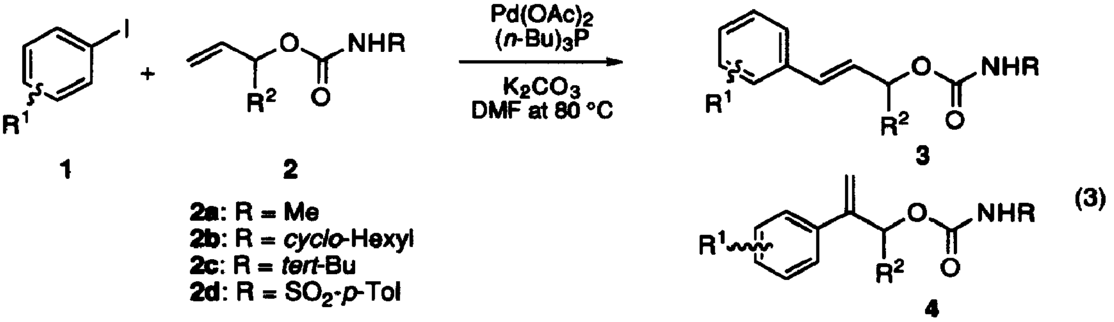


(1)



(2)

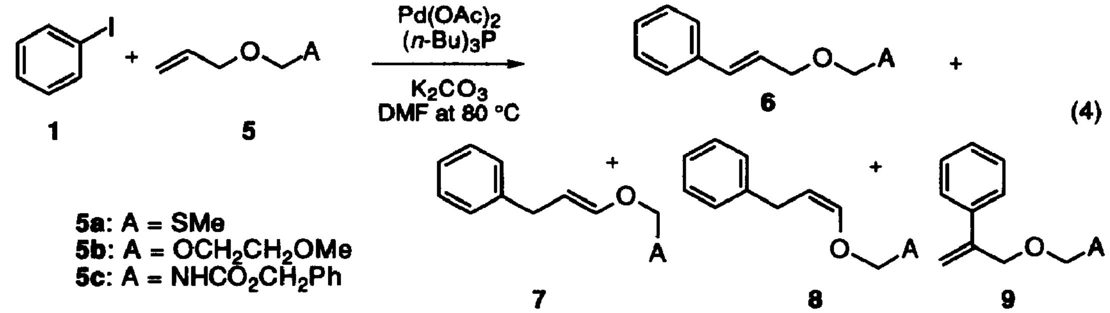
Since silver salts are rather expensive and it has been demonstrated that aryl triflate cannot be utilized for the arylation of allylic alcohols,[4] we examined another route for the cinnamyl alcohol synthesis based on the arylation of allyl alcohols with aryl iodides. Our idea to achieve this is to use such an auxiliary (XY, eq 2) as being able to coordinate Pd(II) to form a six-membered intermediate **II** and hence render the $H_\alpha Pd$ elimination unfavorable and also being able to be installed and removed[7] easily before and after the arylation reaction.



2a: R = Me
2b: R = *cyclo*-Hexyl
2c: R = *tert*-Bu
2d: R = SO_2-*p*-Tol

(3)

By a careful, systematic examination of the influence of a variety of auxiliaries [XY = C(=O)NHR, C(=O)SEt,[8] C(=S)SMe,[9] CH_2SCH_3, $CH_2OCH_2CH_2OCH_3$, $CH_2NHCO_2CH_2Ph$], catalysts [$Pd(PPh_3)_4$, $Pd_2(dba)_3$-$CHCl_3$, a wide range of ratios of $Pd(OAc)_2$ to ligands (n-Bu_3P, (o-Tol)$_3$P, $Ph_2PCH_2CH_2PPh_2$, or $Ph_2PCH_2CH_2CH_2PPh_2$)], solvents (DMF, dioxane, acetonitrile, benzene), bases (K_2CO_3, $NaHCO_3$, Cs_2CO_3, Et_3N), and temperature (50 - 110°C), we have been able to arrive at optimal conditions for the formation of the desired cinnamyl alcohol derivatives **3** (eq 3): 10 equiv of aryl iodide, 1 equiv of *N*-alkyl *O*-allyl carbamate **2a-c**, 0.1 equiv[10] of $Pd(OAc)_2$, 0.2 equiv of n-Bu_3P, and 1.3 equiv of K_2CO_3 at 80 °C in DMF (5 mL/mmol of **2**). Results for the arylation of *O*-allyl carbamates **2a-c** (eq 3) and allyl ethers **5a-c** (eq 4) are summarized in Tables 1 and 2, respectively.



5a: A = SMe
5b: A = OCH_2CH_2OMe
5c: A = $NHCO_2CH_2Ph$

(4)

The reaction accommodates important organic functionalities (Table 1) and the presence or absence of electron-donating or withdrawing groups on aryl iodide shows only a little effect on the yield and selectivity (**3** vs. **4**), except for *o*- and *p*-nitrophenyl iodides. These iodides provided mixtures of **3** and **4** only in less than 10% combined yields. Use of 10 equiv of aryl iodide (condition A, Table 1) is important to attain satisfactory yield. With 1.3 equiv of aryl iodide (condition B, Table 1), the reaction goes to completion, but the combined isolated yield of **3** and **4** is reduced generally to less than two third the corresponding one obtained under the condition A.

The yield and product selectivity (**3** vs. **4**) could be remarkably improved by a slight modification of the *N*-substituent of **2**[11] (**2b** vs. **2a**; runs 1 and 2 and 6 and 7, Table 1). The R^2 alkyl derivatives of **2a** provided **3** exclusively (runs 15 - 21, Table 1).

The complete absence of products due to $H_\alpha Pd$ elimination (e.g., vinyl carbamates, dihydrocinnamaldehydes) may indicate that the carbamate auxiliary has worked nicely to promote the selective $H_\gamma Pd$

Table 1. Palladium Catalyzed Arylation of *N*-Alkyl *O*-Allyl Carbamates 2

run	1	2	condition A[a]			condition B[b]		
	(R^1)	(R^2)	reaction time (h)	% conversion	% isolated yield 3/4[c]	reaction time (h)	% conversion	% isolated yield 3/4[c]
1	H	**2a** (H)	3	100	78/6	2	100	55/3
2	H	**2b** (H)	7	100	88/0			
3	H	**2c** (H)	3	100	81/9			
4	*o*-OMe	**2a** (H)	7	100	70/0	26	96	21/5
5	*m*-OMe	**2a** (H)	27	100	65/4	24	90	33/5
6	*p*-OMe	**2a** (H)	24	100	67/12	8	100	44/6
7	*p*-OMe	**2b** (H)	24	100	80/10			
8	*o*-Me	**2a** (H)	51	100	56/4	27	100	56/0
9	*m*-Me	**2a** (H)	19	100	64/5	24	95	41/4
10	*p*-Me	**2a** (H)	8	100	70/7	21	100	57/4
11	*m*-Cl	**2a** (H)	10	100	66/3			
12	*m*-CO$_2$Me	**2a** (H)	7	100	64/6	4	100	68/3
13	*p*-CO$_2$Me	**2a** (H)	7	100	80/6	4	94	46/8
14	*m*-NO$_2$	**2a** (H)	27	100	65/6	24	100	48/6
15	H	**2a** (Me)	3	100	84/0			
16	*m*-OMe	**2a** (Me)	9	100	86/0			
17	*o*-Me	**2a** (Me)	7	100	84/0			
18	*p*-CO$_2$Me	**2a** (Me)	27	100	61/0			
19	H	**2a** (Et)	8	100	72/0			
20	H	**2a** (*i*-Pr)	8	100	76/0			
21	H	**2a** (*i*-Bu)	8	100	88/0			

a) **Condition A**: aryl iodide (10 mmol), carbamate **2** (1 mmol), Pd(OAc)$_2$ (0.1 mmol), *n*-Bu$_3$P (0.2 mmol), K$_2$CO$_3$ (1.3 mmol) in DMF (5 mL) under N$_2$ at 80 °C.

b) **Condition B**: aryl iodide (1.3 mmol), carbamate **2** (1 mmol), Pd(OAc)$_2$ (0.1 mmol), *n*-Bu$_3$P (0.2 mmol), K$_2$CO$_3$ (1.3 mmol) in DMF (5 mL) under N$_2$ at 80 °C.

c) As a mixture of **3** and **4** after column chromatography over silica gel. The ratio determined by ^{1}H NMR elimination from **II** (eq 2). In this respect, ethereal auxiliaries (**5a-c**), on the other hand, turned out ineffective and provided vinyl ether derivatives **7** and **8** in substantial quantities (runs 1 - 4, Table 2).[12]

Table 2. Palladium Catalyzed Reaction of Allyl Ethers 5 with Phenyl Iodide[a]

run	allyl ether 5 (**A**)	phosphine (mmol)	temp. (°C)	time (h)	% conversion	% isolated yield **6**	**7**	**8**	**9**
1	**5a**: SCH_3	$(n\text{-Bu})_3P$ (0.2)	80	2	100	43	7	12	0
2	**5a**: SCH_3	$(o\text{-tol})_3P$ (0.3)	50	3	100	57	9	9	0
3	**5b**: $OCH_2CH_2OCH_3$	$(n\text{-Bu})_3P$ (0.2)	50	9	100	44[b]	19	9	11
4	**5b**: $OCH_2CH_2OCH_3$	$(o\text{-tol})_3P$ (0.3)	80	24	81	22[b]	15	21	7
5	**5c**: $NHCO_2CH_2Ph$	$(n\text{-Bu})_3P$ (0.2)	80	2	100	32	0	0	8

a) Phenyl iodide (1.3 mmol), **5** (1 mmol), $Pd(OAc)_2$ (0.1 mmol), phosphine (0.2-0.3 mmol), K_2CO_3 (1.3 mmol) in DMF (5 mL).

b) As mixtures of **6** and **9** and **7** and **8** after column chromatography over silica gel. The ratio was determined by ^1H NMR.

REFERENCES AND NOTES

(1) a) Melpolder, J. B.; Heck, R. F. *J. Org. Chem.* **1976**, *41*, 265. b) Chalk, A. J.; Magennis, S. A. *J. Org. Chem.* **1976**, *41*, 273 and 1206. c) Frank, W. C.; Kim, Y. C.; Heck, R. F. *J. Org. Chem.* **1978**, *43*, 2947. d) Heck, R. F. *Organic Reactions* **1982**, *27*, 345. See also, e) Larock, R. C.; Leung, W.-Y.; Stolz-Dunn, S. *Tetrahedron Lett.* **1989**, *30*, 6629. f) Larock, R. C.; Ding, S.; Tu, C. *Synlett* **1993**, 45 .

(2) a) Tamaru, Y.; Yamada, Y.; Yoshida, Z. *Tetrahedron Lett.* **1977**, 3365. b) Tamaru, Y.; Yamada, Y.; Arimoto, T.; Yoshida, Z. *Chem. Lett.* **1978**, 975. c) Tamaru, Y.; Yamada, Y.; Yoshida, Z. *J. Org. Chem.* **1978**, *43*, 3396. d) Tamaru, Y.; Yamada, Y.; Yoshida, Z. *Tetrahedron Lett.* **1978**, 919. e) Tamaru, Y.; Yamada, Y.; Yoshida, Z. *Tetrahedron* **1979**, *35*, 329.

(3) Jeffery, T. *Tetrahedron Lett.* **1991**, *32*, 2121.

(4) Bernocchi, E.; Cacchi, S.; Ciattini, P. G.; Morera, E.; Ortar, G. *Tetrahedron Lett.* **1992**, *33*, 3073.

(5) a) Jeffery, T. *Tetrahedron Lett.* **1990**, *31*, 6641. b) Jeffery, T. *J. Chem. Soc. Chem. Commun.* **1991**, 324. c) Jeffery, T. *Tetrahedron Lett.* **1993**, *34*, 1133.

(6) Filippini, L.; Gusmeroli, M.; Riva, R. *Tetrahedron Lett.* **1993**, *34*, 1643.

(7) Allylic carbamates **2** and **3** were formed (R-NCO (1 equiv)/Et_3N (0.5 equiv) or BF_3-OEt_2 (1 equiv), r.t., in ether) and hydrolyzed (KOH (6 equiv), 2 N in MeOH, reflux), respectively, in 75 - 90% yields.

(8) Allyl thiocarbonate was unreactive and recovered under the condition of run 1, Table 2.

(9) Allyl dithiocarbonate decomposed under the condition of run 1, Table 2.

(10) The amount of $Pd(OAc)_2$ may be reduced to 0.05 equiv at a slight expense in yield, e.g., a mixture of **3** and **4** (91:9) in 77% isolated yield for 3 h at 80°C (cf. run 1, Table 1).

(11) **2d** (R^2 = H), under the condition of run 1, Table 1, provided a mixture of **3** and **4** (91:9) in 60% yield together with *N*-*p*-toluenesulfonylcinnamylamine (8%).

(12) Support by the Ministry of Education, Science and Culture, Japanese Government, is gratefully acknowledged.

(*Received in Japan* 16 *February* 1994)