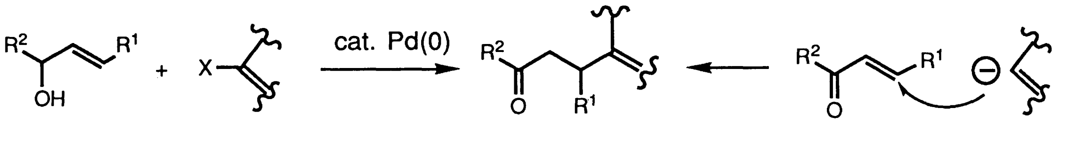
CHEMISTRY LETTERS, pp. 1971-1974, 1989.

Palladium Catalyzed Alkenylation of 1-Siloxycyclopent-2-ene Leading to Enol Silyl Ether of 3-Alkenylcyclopentanones

Sigeru TORII,* Hiroshi OKUMOTO, Takayuki KOTANI, and Fumihiko AKAHOSHI
Department of Applied Chemistry, Faculty of Engineering,
Okayama University, Tsushima Naka, Okayama 700

Palladium catalyzed coupling reaction of alkenyl halides and silylated cyclopentenol in the presence of potassium carbonate produced the corresponding enol silyl ether of 3-alkenylcyclopentanones regioselectively.

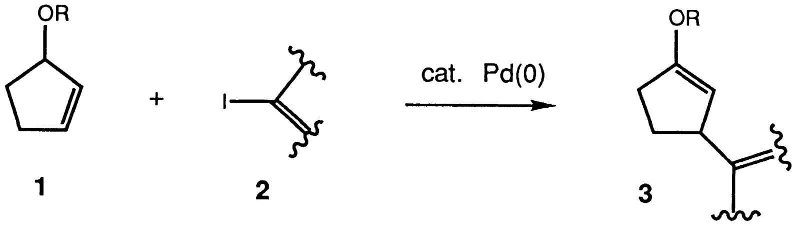
Palladium catalyzed alkenylation of olefins has been widely used in organic synthesis since the pioneering works of Mizoroki$^{1)}$ and Heck.$^{2a)}$ Acyclic allyl alcohols as olefins are well known to produce the corresponding carbonyl compounds,$^{2)}$ which are considered to be analogous to the usual 1,4-addition of a vinylic nucleophile to enones (Eq. 1). However, formation of enol ether from protected allyl alcohols has not been reported to our knowledges.



(1)

X = halogen, OTf

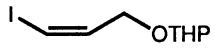
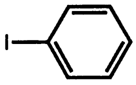
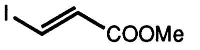
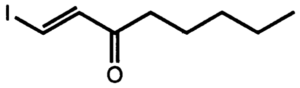
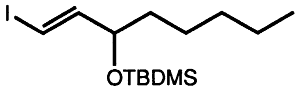
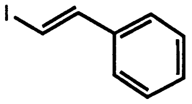
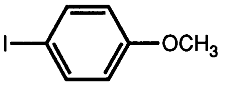
The mild condition of the above palladium catalyzed coupling reaction inspired us to examine the introduction of vinylic substituents onto a five-membered framework.$^{3)}$ Recently, the coupling of vinylic halides and cycloalkenes accompanying the migration of double bonds to produce 1,4-dienes has been reported, where the vinylation of cyclopentenes may open an approach to prostaglandins.$^{4)}$ These current communications enabled us to report our results on the alkenylation of cyclopentenol silyl ether **1** with alkenyl iodide **2** to produce the enol silyl ether **3** as shown in Eq. 2. In general, the regioselective enol ether formation has been achieved by 1,4-addition of organocopper reagents to cyclopentenone followed by trapping with silyl chloride.$^{5)}$ However, a catalytic reaction under mild conditions is more preferable.



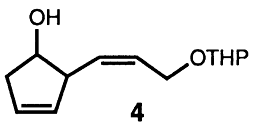
(2)

Although several reaction conditions were investigated, the following typical procedure gave the better results. A mixture of the silyl ether **1** and the alkenyl iodide **2** was refluxed in acetonitrile in the presence of palladium acetate (10 mol%) and potassium carbonate (1.5 equiv.) under argon atmosphere. After cooled to room temperature, the reaction mixture was filtered through a short alumina pad. Concentration of the filtrate and subsequent purification by flash chromatography afforded **3**. The results are summarized in Table 1.

Table 1. Palladium catalyzed alkenylation of cyclopentenol **1** [a]

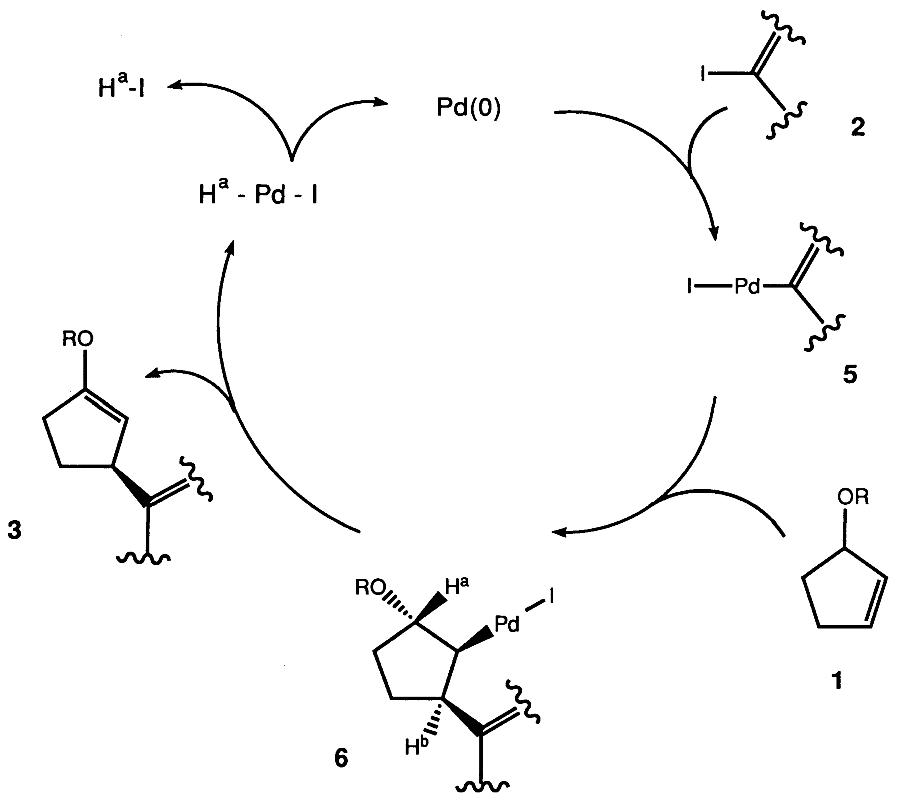
Entry	**1** (R)	**2**	Time / h	**3**, Yield / % [b]
1	TBDMS [c]		12	83
2	H	〃	27	53 [d]
3	〃		23	48
4	TBDMS [c]		23	64
5	〃		8	--
6	〃		5	--
7	〃		24	60
8	〃		26	74
9	〃		24	41

a) Carried out in the presence of $Pd(OAc)_2$ (10 mol%) and potassium carbonate (1.5 equiv.) in refluxing acetonitrile (3 ml) under argon atmosphere. b) Isolated yields. Satisfactory spectral data [IR, ^1H NMR (200 MHz), ^{13}C NMR (50 MHz)] were obtained for each product, which showed retention of the olefin geometry of **2**. c) *tert*-butyldimethylsilyl. d) Structural isomer **4** was obtained in 9%.



4

As shown in Entry 1, the reaction of the silylated **1** (R = tert-butyldimethylsilyl(TBDMS)) gave the expected enol silyl ether **3** (R = TBDMS) in 83% yield. On the other hand, the non-protected cyclopentenol (**1**, R = H) produced the 3-substituted cyclopentanone **3** (R = H) in 53% yield together with 9% of the structural isomer **4**, but the reaction was relatively sluggish. Interestingly, protection of alcohol with TBDMS group suppressed the formation of the isomer **4**$^{6)}$ and the yield of **3** is better. Several types of iodides were also subjected to the coupling reaction by using the silyl ether **1**.$^{7)}$ Both acyclic and aromatic iodides could afford the corresponding enol silyl ether **3** in moderate to good yields. However, among them, the vinyl iodides conjugated with carbonyl functions such as ester and ketone gave unidentified products in spite of smooth consumption of the starting materials (Entries 5 and 6). Fortunately, a common side-chain of prostaglandins was introduced in 60% yield (Entry 7).



Scheme 1. Reaction path.

The plausible reaction path is shown in Scheme 1. This olefin migrating alkenylation can be elucidated by taking account of the following two principles in palladium catalysis: (1) insertion of olefin to alkenylpalladium takes place in a cis fashion and (2) β-elimination of palladium hydride also proceeds by abstraction of the syn proton.$^{2)}$ Thus, the alkenylpalladium species **5** generated by the oxidative addition of the alkenyl iodide **2** to Pd(0) undergoes insertion from the less crowded face of the olefin of **1**. Therefore, the intermediate **6** should have the configuration as depicted. The alkylpalladium **6** collapses into **3** by picking up the syn proton, i.e. H^a, because the conformation of the 5-membered skeleton is fixed so rigidly that the H^b can not be syn to palladium. As a result of such a stereochemical relationship, the elimination of palladium hydride to close catalytic cycle gives rise to the anticipated enol silyl ether **3** regioselectively.

Although a similar reaction of allyl trimethylsilyl ether with aryl halides has been reported, the intermediary enol silyl ether undergoes further palladium catalyzed reaction to produce an enal.[6] In contrast, our case suppressed such a conjugated system. Thus obtained tert-butyldimethylsilyl enol ether **3** is a suitable intermediate for 2,3-disubstituted cyclopentanones such as prostaglandins by alkylation at 2-position.[8] Further investigation on asymmetric alkenylation directed toward prostaglandins are in progress and will be published shortly.

A partial financial support by a Grant-in-Aid for Scientific Research (No. 01649512) from the Ministry of Education, Science and Culture is appreciated and we are grateful to the SC-NMR Laboratory of Okayama University for obtaining high resolution NMR spectra.

References

1) T. Mizoroki, K. Mori, and A. Ozaki, Bull. Chem. Soc. Jpn., 44, 581 (1971).
2) a) R. F. Heck, J. P. Nolley, Jr., J. Org. Chem., 37, 2320 (1972); b) R. Benhaddou, S. Czernecki, G. Ville, and A. Zegar, Organometallics, 7, 2435 (1988); for reviews see: R. F. Heck, "Palladium Reagents in Organic Syntheses," Academic Press, London (1985); J. Tsuji, "Organic Synthesis with Palladium Compounds," Springer-Verlag, Berlin (1980).
3) S. Torii, H. Okumoto, and F. Akahoshi, Abstracts of The Fourth International Kyoto Conference on New Aspects of Organic Chemistry (IKCOC-4), 1988, p.81 (15-L-16).
4) R. C. Larock and W. H. Gong, J. Org. Chem., 54, 2047 (1989); R. C. Larock, W. H. Gong, and B. E. Baker, Tetrahedron Lett., 30, 2603 (1989).
5) For reviews see: G. H. Posner, "An Introduction to Synthesis Using Organocopper Reagents," John Wiley & Sons, New York (1980); W. P. Weber, "Silicon Reagents for Organic Synthesis," Springer-Verlag, Berlin (1983), p.261; E. W. Colvin, "Silicon in Organic Synthesis," Butterworths, London (1981), Chap. 17; Examples in prostaglandin synthesis: T. Tanaka, S. Kurozumi, T. Toru, M. Kobayashi, S. Miura, and S. Ishimoto, Tetrahedron Lett ., 1975, 1535; A. F. Kluge, K. G. Untch, and J. H. Fried, J. Am. Chem. Soc., 94, 7827 (1972); J. W. Patterson, Jr. and J. H. Fried, J. Org. Chem., 39, 2506 (1974); G. Stork, Pure and Applied Chem., 17, 383 (1968).
6) T. Hirao, J. Enda, Y. Ohshiro, and T. Agawa, Chem. Lett., 1981, 403.
7) The reaction of the corresponding silyl ether of cyclohexenol proceeded very slowly to produce the enol silyl ether in low yield.
8) Y. Kita, J. Segawa, J. Haruta, H. Yasuda, and Y. Tamura, J. Chem. Soc., Perkin 1, 1982, 1099.

(Received August 10, 1989)