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THE OXYGENATION OF α-ISOPHORONE AND ITS SILYL ENOL ETHER WITH t-BuOOH IN THE PRESENCE OF METAL CATALYSTS

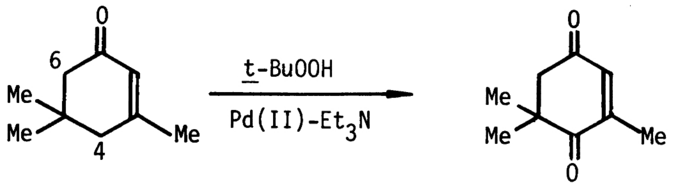
Takahiro HOSOKAWA,* Shiro INUI, and Shun-Ichi MURAHASHI*
Department of Chemistry, Faculty of Engineering Science, Osaka University,
Machikaneyama, Toyonaka, Osaka 560

Treatment of α-isophorone (1) with t-BuOOH in the presence of palladium(II) or copper(I) catalyst gives ketoisophorone (2) selectively. A similar treatment of silyl enol ether 7 derived from 1 affords 6-hydroxylisophorone 8.

The use of t-BuOOH in the presence of metal catalyst is one of the most efficient and mild method for achieving selective oxygenation of organic substrates with hydroperoxides,1) and its application in synthetic chemistry continues to increase. We report here a procedure for the selective oxygenation of α-isophorone (1) at either the C-4 or C-6 position with this reagent.

The oxygenation of 1 at the C-4 position can be performed with t-BuOOH in the presence of Pd(II) catalyst to give ketoisophorone (2). To our knowledge, this is the first direct transformation of α-isophorone into ketoisophorone2) which is known as one of the useful precursors for synthesizing natural carotenoides and flavoring materials such as in perfumes.3) The preparation of this compound so far reported is based on the metal-catalyzed oxygenation of β-isophorone by molecular oxygen.4)

The treatment of 1 with 80% t-BuOOH5) (2 equiv.) in the presence of catalytic amounts of Pd(OAc)$_2$ and Et$_3$N [1/Pd(OAc)$_2$/Et$_3$N=10/1/2, benzene, 50°C, 48 h] gives 2 in 49-55% GLC yield as the sole product.6) The reaction is in contrast to the recently reported oxygenation of 1 by molecular oxygen with FeCl$_3$ catalyst affording 3-formyl-5,5-dimethyl-2-cyclohexen-1-one predominantly.7) 5,5-Dimethyl-2-cyclohexen-1-one (3) is similarly oxygenated at the C-4 position to give the corresponding product in 32% yield. However, 3-methyl-2-cyclohexen-1-one (4) and 2-cyclohexen-1-one (5) produce m-cresol (27%) and phenol (~5%), respectively, showing that the aromatization of cyclohexene ring prevents the oxygenation.



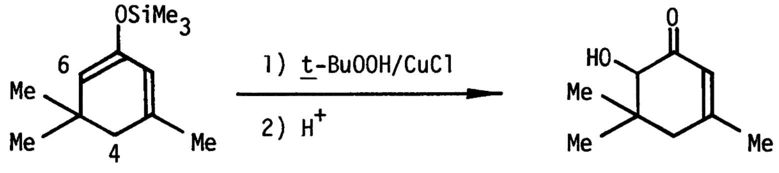
(1)

1 2

From a brief study of the reaction shown in eq. 1, the followings are to be noted. Firstly, the presence of a large excess of Et$_3$N [5 equiv. per Pd(II)] inhibits the reaction, and the absence of Et$_3$N reduces the product yield to 32%. Secondly, the use of other palladium(II) catalysts such as (PhCN)$_2$PdCl$_2$ and Pd(OCOCF$_3$)(OOt-Bu) affords similar results. Thirdly, treatment of 1 with Pd(OCOCF$_3$)(OOt-Bu) (1 equiv.) in benzene (24 h , 25°C) followed by addition of NaCl gives a π-allylpalladium(II) complex 6, di-μ-chloro-di(1-oxa-3,5,5-trimethyl-3-cyclohexenyl)dipalladium(II),8) in 19%

isolated yield. This suggests that the transformation of 1 ⟶ 2 could follow a pathway involving the complex 6. The use of CuCl in place of Pd(II) catalyst under the comparable conditions in the absence of Et_3N affords 2 in 52% yield. In this case, a radical process is likely involved since no reaction takes place in the presence of hydroquinone (5 mol%). By contrast, the Pd(II)-catalyzed reaction occurs even in the presence of hydroquinone.

The oxygenation of α-isophorone at the C-6 position was achieved by treatment of its silyl enol ether 7 with anhydrous t-BuOOH (2 equiv.) in the presence of CuCl catalyst (7/CuCl=10/1, benzene, 50°C, 19 h). The hydroxy enone 8 was isolated in 44% yield as the single product after acid hydrolysis of the reaction mixture (eq. 2) Other silyl enol ethers derived from 3-5 also gave the corresponding products in 38-60% yield. This method may be an alternative approach to the MCPBA oxidation of silyl enol ethers into α-hydroxy enones.[9)]



7 8 (2)

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2) This work was presented in part at 43rd Annual Meeting of the Chemical Society of Japan, Tokyo (April), Abstracts II, 843 (1981). As for related reactions: see, (a) S. Uemura, S. Fukuzawa, A. Toshimitsu, and M. Okano, Tetrahedron Lett., 23, 87 (1982); (b) S. Uemura and S. R. Patil, ibid., 23, 4353 (1982).

3) K. K. Light, B. M. Spencer, J. F. Vinals, J. Kiwala, M. H. Vock, and E. J. Shuster, U. S. Patent, 4 076 854 (1978); Chem. Abstr., 89, 23843d (1978).

4) M. Costantini, A. Dromard, M. Jouffret, B. Brossard, and J. Varagnat, J. Mol. Catal., 7, 89 (1980) and references cited therein.

5) 80% t-BuOOH was purchased from Maruwaka Chemical Ind. Ltd. (Osaka). The use of 70% t-BuOOH also gives similar results.

6) The yield was somewhat decreased by the isolation process performed by the usual workup followed by Kugelrohr distillation.

7) S. Ito and M. Matsumoto, 45th Annual Meeting of the Chemical Society of Japan, Tokyo (April), Abstracts II, 604 (1982).

8) 6: NMR(60 MHz, $CDCl_3$) δ1.10(s, 3H), 1.50 (s, 3H), 1.98 (d, J= 18Hz, 1H), 2.20 (s, 3H), 2.70 (d, J= 18Hz, 1H), 4.83 (s, 1H), and 4.95 (s, 1H); Anal. Calcd for $C_9H_{13}OPdCl$: C, 38.74; H, 4.69; Cl, 12.70. Found: C, 38.98; H, 4.76; Cl, 13.03.

9) G. M. Rubottom and J. M. Gruber, J. Org. Chem., 43, 1599 (1978).

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