

Palladium Catalyzed Oxidations of Secondary Alcohols

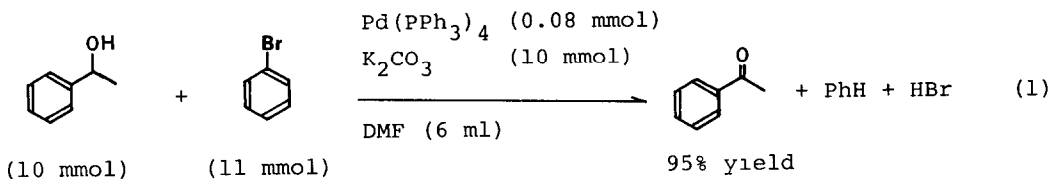
Yoshinao Tamaru, Youichi Yamamoto, Yoshimi Yamada, and Zen-ichi Yoshida*

Department of Synthetic Chemistry, Kyoto University,

Yoshida, Kyoto 606, JAPAN

Summary: Palladium catalyzed oxidations of secondary alcohols making use of bromobenzene as an oxidant have been described, where 6 kinds of alcohols have been oxidized to the corresponding ketones in excellent yields.

There have been reported a few papers on the oxidations of alcohols catalyzed by palladium.¹ However the reported methods seem to have some disadvantages from a practical point of view. This paper describes the very convenient and high yield oxidations of the secondary alcohols to the corresponding ketones catalyzed by palladium making use of bromobenzene as an oxidant,² as exemplified in eq 1.



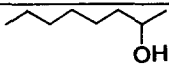
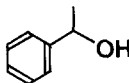
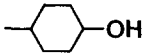

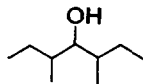
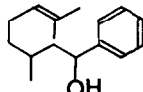
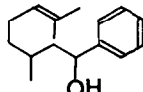
Results and reaction conditions are summarized in Table 1, which apparently reveals the versatility of the present oxidation. Generally the oxidations go essentially to completion with 1.3 mol% or less of palladium based on the starting alcohols, independently to the palladium species (Pd(0) or Pd(II)) firstly charged. The rates of reactions largely depend on the bases employed. For example, with triethylamine as a base the oxidation of isoborneol did not proceed to an appreciable extent at 100°C for 5 h, while with NaH it attained completion within 1.5 h at 70°C (entry 6). On the oxidation of 2-octyl alcohol in the presence of such a strong

base as NaH, the yield of 2-octanone fell down to 45% probably due to base catalyzed condensations. As a matter of fact, 2-(4'-methylcyclohexenyl)-4-methylcyclohexanone was isolated in 20% yield as a main condensation product together with 73% of 4-methylcyclohexanone (entry 4). These condensations are not serious for the reactions to give sterically hindered ketones (camphor and 2,6-dimethyl-5-heptenyl phenyl ketone). Although the oxidations using K_2CO_3 as a base become pretty slow compared to those using NaH and require higher temperatures and longer reaction times, K_2CO_3 is the best choice of the bases. With this base, condensations could be eliminated almost completely and the yields become as high as 90~100% even for the oxidations of 2-octyl alcohol and 1-phenylethyl alcohol (entries 2 and 3, respectively). The oxidation of 2,6-dimethyl-5-heptenylphenylcarbinol deserves some comments (entries 10 and 11): (1) Except for this case, yields and conversions were not affected by the kinds of phosphines employed. For this oxidation, triphenylphosphine was a superior cocatalyst than bis(diphenylphosphino)ethane on the bases of conversions and isolated yields. (2) The oxidation of the hydroxyl group proceeded selectively remaining the double bond intact.³

We are now examining the compatibility of the present oxidation with the functional groups susceptible to ordinary oxidizing agents and trying to modify the reaction to be applicable for the oxidations of primary alcohols.

A typical experiment is as follows (entry 3): Onto an argon purged mixture of tetrakis(triphenylphosphine)palladium (93 mg, 0.08 mmol) and K_2CO_3 (1.38 g, 10.0 mmol) was added a solution of 1-phenylethyl alcohol (1.222 g, 10.0 mmol) and bromobenzene (1.727 g, 11.0 mmol) in 6 ml of anhydrous DMF (dried over CaH_2) by means of a syringe through a rubber septum. The reaction mixture was stirred and heated at 110°C for 7.5 h. After allowed to cool to room temperature, the reaction mixture was diluted with 50 ml of ether and filtered through a cellulose column 2 cm long to remove palladium black and inorganics. The filtrate was washed three times with water (30 + 10 + 10 ml), dried over $MgSO_4$, and then condensed through a

Table 1. Palladium Catalyzed Oxidations of Secondary Alcohols

Entry	Alcohol	Catalyst (mol%) ^a	Base	Solv. ^b	Temp (°C)	Time (h)	Conv. (%) ^c	Yield (%) ^d
1		Tet (1.3)	NaH	NMP	70	3.6	73	45
2	"	Tet (1.0)	K ₂ CO ₃	DMF	110	4.5	84	100
3		Tet (0.8)	K ₂ CO ₃	DMF	110	7.5	95	95
4		Pal (0.67) Dip (1.34)	NaH	DMF	70	3.0	90	73 ^e
5	"	Tet (1.0)	K ₂ CO ₃	DMF	110	7.0	86	88
6		Pal (0.67) Dip (1.34)	NaH	NMP	70	1.5	100	93 ^f
7	"	Tet (1.3)	K ₂ CO ₃	DMF	110	3.0	100	100 ^f
8		Tet (1.3)	NaH	NMP	70	3.0	95	67
9	"	Tet (1.0)	K ₂ CO ₃	DMF	120	6.0	80	92
10		Pal (1.3) Tri (5.2)	NaH	NMP	70	5.0	95	91
11		Pal (1.3) Dip (2.6)	NaH	NMP	70	5.0	77	73

- a. The symbols Tet, Pal, Dip, and Tri are meant to refer to tetrakis(tri-phenylphosphine)palladium, palladium acetate, bis(diphenylphosphino)-ethane, and triphenylphosphine, respectively. The values in parentheses refer to mol% of catalysts based on starting alcohols.
- b. N-Methylpyrrolidone (NMP); N,N-dimethylformamide (DMF).
- c. Based on starting alcohols, as determined by VPC.
- d. Yields are the isolated ones (except for entries 6 and 7) for spectrally and gas chromatographically homogeneous ketones based on recovered alcohols.
- e. In addition to 73% of 4-methylcyclohexanone, 2-(4'-methylcyclohexenyl)-4-methylcyclohexanone was isolated in 20% yield [distillation (157°C/1 mmHg), followed by column purification (silica gel, hexane-benzene gradient)].
- f. Vpc yields.

Vigreux column. Distillation of the residue under reduced pressure (160°C/100 mmHg, Kugel rohr) gave 1.15 g of a mixture of acetophenone and 1-phenylethyl alcohol in a ratio of 95:5, as determined by vpc.

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