

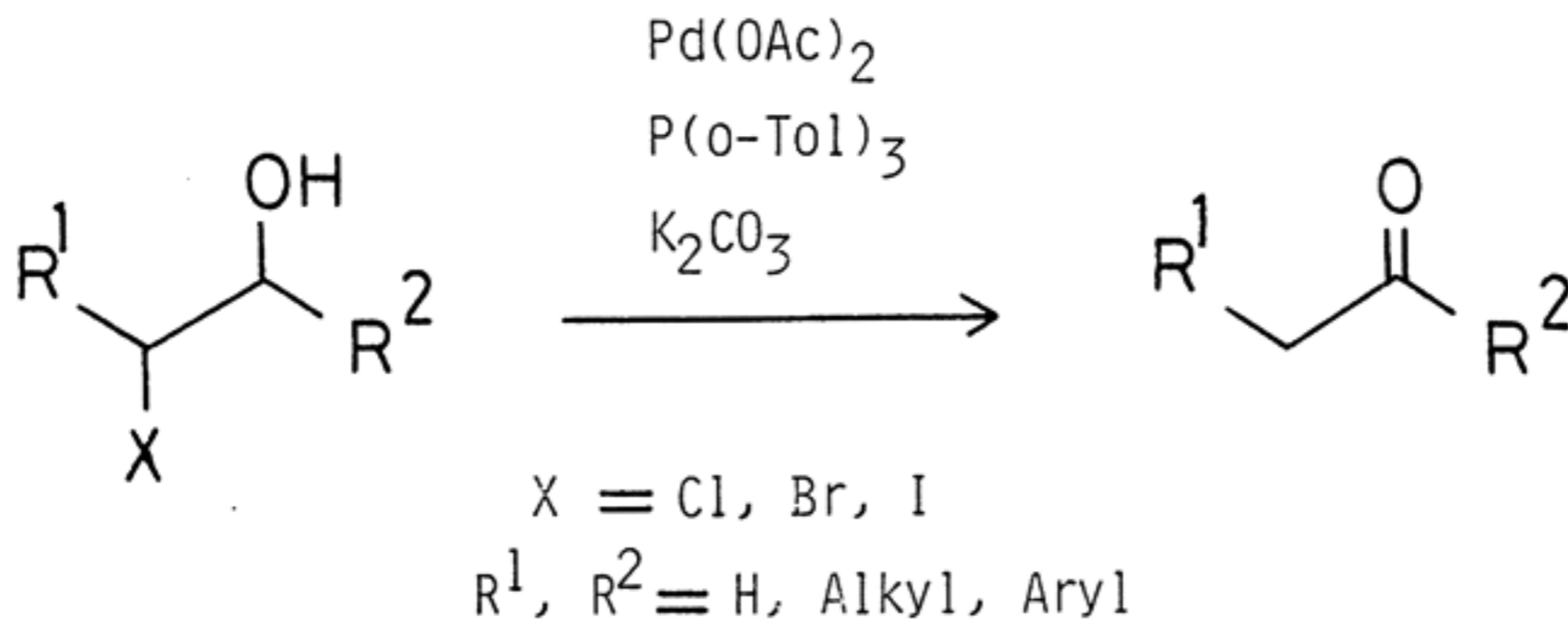
A PALLADIUM CATALYZED CONVERSION OF HALOHYDRINS TO KETONES

Jiro TSUJI*, Hideo NAGASHIMA, and Koji SATO

Summary: $\text{Pd}(\text{OAc})_2$ combined with $\text{P}(o\text{-Tol})_3$ catalyzes the conversion of halohydrins to ketones in the presence of K_2CO_3 . Various halohydrins, which are easily available from olefins, can be converted to ketones in high yields.

Conversion of halohydrins to ketones promoted by ethylmagnesium halide or silver nitrate has been reported by House.¹⁾ However, this method is not satisfactory due to poor yields of ketones. Halohydrins are easily available from olefins, and in some cases, regioselective preparation is possible.²⁾ Thus, the preparation of halohydrins from olefins and the subsequent conversion of halohydrins to ketones are expected to be a useful preparative method of ketones from olefins.

In our previous paper,³⁾ we have reported that palladium catalyzed reaction of CCl_4 and BrCCl_3 with allylic alcohols affords γ,γ,γ -trichloro ketones in high yields. In the course of mechanistic studies of this reaction, we found that usual addition reaction took place at first, and then the adduct having halohydrin structure was converted to the γ,γ,γ -trichloro ketone. In this paper, we wish to report the palladium catalyzed conversion of halohydrins to ketones. By this procedure, a useful preparative method of ketones from olefins is established.



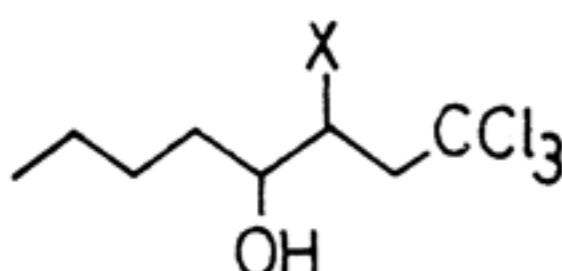
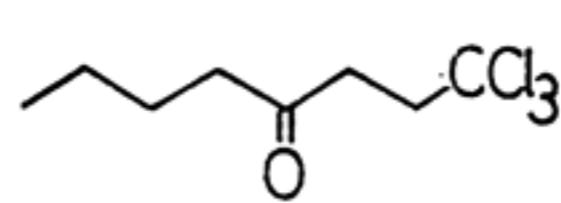
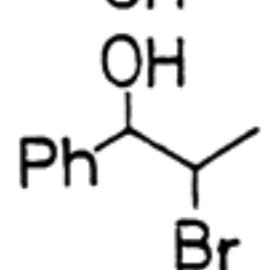
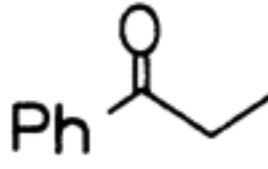
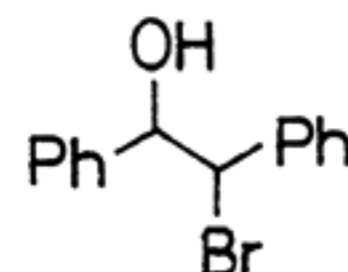
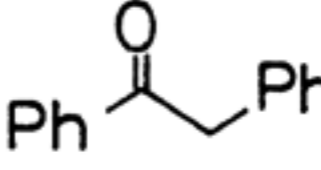
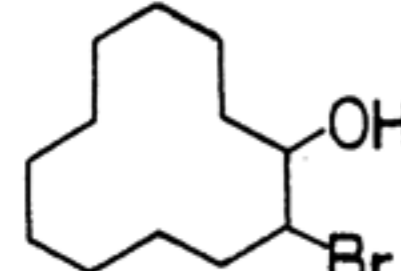
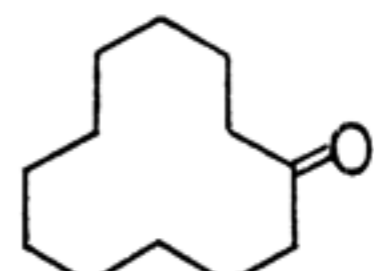
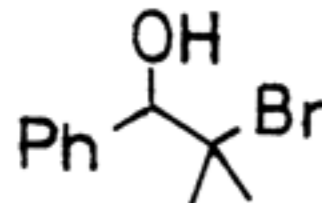
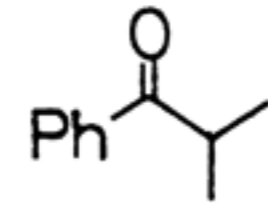
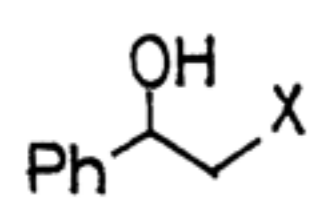
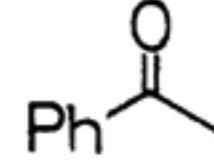
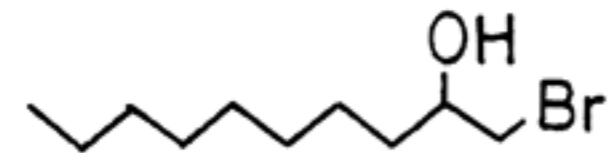
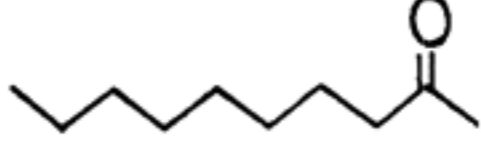
As described in our previous paper, reaction of 1-hepten-3-ol with BrCCl_3 or CCl_4 catalyzed by $\text{Pd}(\text{OAc})_2$ combined with tri-*o*-tolylphosphine [$\text{P}(\text{o-Tol})_3$] affords 1,1,1-trichloro-4-octanone (8) in the presence of K_2CO_3 at 110°C . When this reaction was carried out at 40°C otherwise under the same conditions, the halohydrins 1a and 1b were formed as the main product. This result suggests that 1a and 1b are intermediates to form 8. We found that treatment of 1a and 1b with a catalytic amount of $\text{Pd}(\text{OAc})_2$ combined with $\text{P}(\text{o-Tol})_3$ in the presence of K_2CO_3 at 110°C afforded 8 in 87 and 57% yields, respectively. In the absence of palladium, only a trace amount of the ketone was formed. In this reaction, choice of ligand and solvent is important. $\text{P}(\text{o-Tol})_3$ as the ligand gave higher yields of 8 than PPh_3 , tricyclohexylphosphine, and 1,2-bis(diphenylphosphino)ethane. Use of polar solvents such as *t*-butyl alcohol, acetonitrile, and THF decreased the yield of 8. In all cases, a small amount of 1-(2,2,2-trichloroethyl)-2-butyloxirane was detected. This epoxide formation is considered to take place with the aid of K_2CO_3 .

As shown in the Table, other halohydrins were also converted to the corresponding ketones by using $\text{Pd}(\text{OAc})_2/\text{P}(\text{o-Tol})_3$ catalyst in the presence of K_2CO_3 in benzene or toluene at $80 - 110^\circ\text{C}$. In the reaction of bromohydrins, 2, 3, and 4, which possess secondary bromide, and 5, which possesses tertiary bromide, the corresponding ketones were obtained in reasonable yields. Only trace amounts of the corresponding epoxides were detected. (entries 2-5) On the other hand, halohydrins having primary halide such as 6 and 7 were converted to the corresponding ketones in lower than 50% yields. (entries 6 and 7) In these cases, considerable amounts of the corresponding epoxides were also formed.

In a typical example, in a flask fitted with a reflux condenser were placed $\text{Pd}(\text{OAc})_2$ (2 mg, 0.01 mmol), $\text{P}(\text{o-Tol})_3$ (6 mg, 0.02 mmol), and K_2CO_3 (138 mg, 1 mmol) and the atmosphere was replaced by argon. The bromohydrin 2 (215 mg, 1 mmol) dissolved in benzene was added, and the suspension was refluxed for 5 h under argon atmosphere. The potassium salts were filtered off, and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (silica-gel, hexane-ether) to give propiophenone (9) in 87% yield.

As noted above, preparation of halohydrins from olefins and subsequent conversion of the halohydrins to ketones provide a preparative method of ketones from olefins. As a typical example, we carried out the reaction of isosafrole (15). Treatment of 15 with *N*-bromosuccinimide in aqueous DMSO afforded the bromohydrin 16 in quantitative yield as a sole product. No regioisomeric bromohydrin was detected. Then, 16 was treated with $\text{Pd}(\text{OAc})_2$ (5 mol%)/ $\text{P}(\text{o-Tol})_3$ (10 mol%) catalyst in the presence of K_2CO_3 (100 mol%) in benzene at 80°C for 3 h to give the ethyl ketone 17 in 75% yield. It is worthwhile to point out that by other preparative methods of ketones from olefins, such as palladium mediated oxidation of olefinic bond,⁴⁾ and epoxidation of olefins and subsequent Lewis acid catalyzed isomerization of the epoxides to ketones,⁵⁾ isosafrole (15) is

Table. Conversion of Various Halohydrins to Ketones^a

Entry	Substrates	Temp (°C)	Time (h)	Products	Yields ^b (%)	
1		<u>1a</u> X=Cl	110	3		57
		<u>1b</u> X=Br	110	3		<u>8</u>
2		<u>2</u>	80	5		<u>9</u> 87
3		<u>3</u>	80	3		<u>10</u> 63
4		<u>4</u>	110	6		<u>11</u> 68
5		<u>5</u>	80	3		<u>12</u> 79
6		<u>6a</u> X=Cl	100	3		28 (34) ^{c,d}
		<u>6b</u> X=Br	100	3		<u>13</u> 44 (22) ^{c,d}
		<u>6c</u> X=I	100	3		46 (20) ^{c,d}
7		<u>7</u>	100	3		<u>14</u> 41 (28) ^d

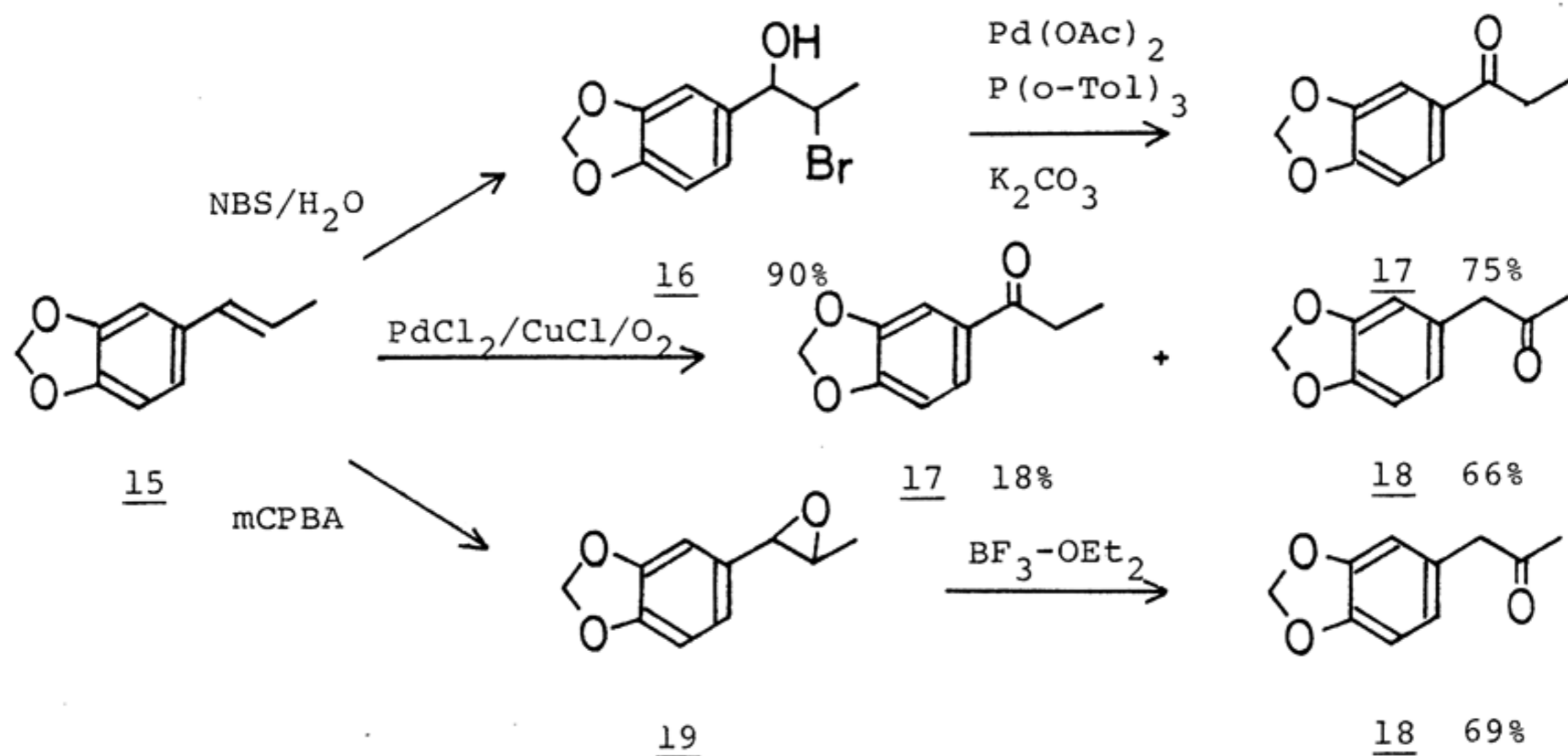
^a All reactions were carried out in the presence of Pd(OAc)₂ (1 mol%), P(*o*-Tol)₃ (2 mol%), and K₂CO₃ (100 mol%) in benzene or toluene under argon atmosphere.

^b Isolated yields.

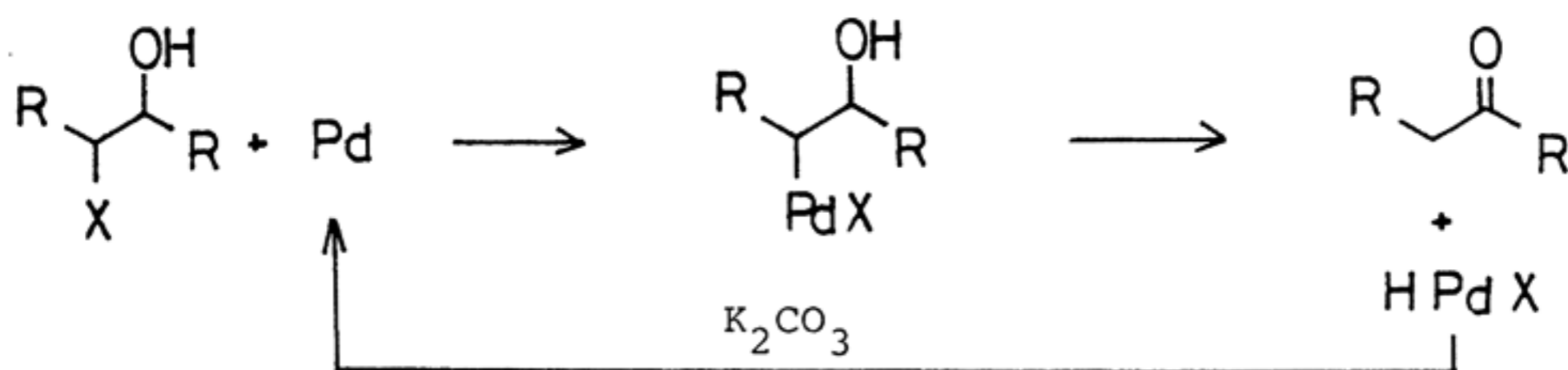
^c Determined by GLC.

^d Values in parentheses are yields of epoxides.

converted to the methyl ketone 18 with high selectivity. These results imply that the preparative method of ketones from olefins via bromohydrins is useful, especially when the bromohydrins are formed from olefins with high regioselectivity.



As a mechanism of this palladium catalyzed conversion of halohydrins to ketones, oxidative addition of the carbon-halogen bond of halohydrins to palladium and subsequent β -hydride elimination to form the ketones seem to be the most probable. Although the oxidative addition of vinyl, allyl, aryl, and benzyl halides to palladium is well-known, few studies on the oxidative addition of alkyl halides to palladium have been undertaken.⁶⁾ Thus, further studies should be awaited for elucidation of the mechanism.



References

- 1) H. O. House, *J. Am. Chem. Soc.*, 77, 5083 (1955).
- 2) D. R. Dalton, V. P. Dutta, and D. C. Jones, *J. Am. Chem. Soc.*, 90, 5948 (1968).
- 3) H. Nagashima, K. Sato, and J. Tsuji, *Chem. Lett.*, 1981, 1605.
- 4) J. Tsuji, I. Shimizu, and K. Yamamoto, *Tetrahedron Lett.*, 1976, 2975.
- 5) For example, D. R. Reif and H. O. House, *Org. Syn.*, Coll. Vol. 4, 375 (1963).
- 6) J. P. Collman and L. S. Hegedus, "Principles and Applications of Organotransition Metal Chemistry," University of Science Books, California (1980).