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A NEW POWERFUL AND SELECTIVE REDUCING AGENT SODIUM BOROHYDRIDE-PALLADIUM CHLORIDE SYSTEM

Toshio SATOH*, Naoki MITSUO, Mayumi NISHIKI,
Kenryo NANBA†, and Shuichi SUZUKI†
School of Pharmacy, Tokushima University of Arts & Science, Tokushima 770
†Research Laboratory of Resources Utilization, Tokyo Institute of Technology,
Nagatsuda, Midori-ku, Yokohama 227

A new reducing agent, sodium borohydride-palladium chloride system reduces aryl ketones, aryl chlorides, and benzylic alcohols to corresponding hydrocarbons. It also reduces hindered steroidal ketones to alcohols in good yields.

Sodium borohydride is a mild reducing agent with high selectivity. In this decade it has been attempted by us and other groups to enhance the reducing ability of it with the addition of transition metal salt.[1-7] Recently we found that sodium borohydride-palladium chloride system reduces aryl ketones, benzylic alcohols, and aryl chlorides to corresponding hydrocarbons, and hindered ketones to corresponding alcohols. Now we wish to report here the new powerful and selective reducing agent. Many functional groups can be tolerated in the reduction, so it may be applicable to a wide range of natural product synthesis.

A typical experiment of the reduction as follows. In a methanol solution (150ml) of a reducible substance (25mmol), $PdCl_2$(50mmol) was suspended. $NaBH_4$ (250mmol) was added to it during 30 min at 20°. After further stirring for 1 h at 20°, precipitated elemental palladium was removed off with filteration, and was washed twice with methanol. The combined washings and filtrate were evaporated to dryness under reduced pressure. Addition of water to the residue and extraction with benzene followed by working-up in the usual way gave the reduced product.

Though $LiAlH_4$-$AlCl_3$ system[8] reduces aralkyl ketones to alkylarenes, protic solvent cannot be available in it. Differing from $NaBH_4$-$BF_3 \cdot Et_2O$[9] or $NaBH_4$-$AlCl_3$[9] system which reduces diaryl ketones to hydrocarbons, but aralkyl ketones to alcohols, $NaBH_4$-$PdCl_2$ system reduces both kinds of ketones to corresponding hydrocarbons in

Table I. Reduction of Aryl Ketones or Benzylic Alcohols to Hydrocarbons

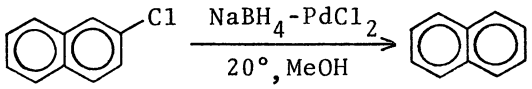
Ar	R	O-Function	yield
Ph	Ph	C=O	83
Fluorenyl		C=O	73[b]
Ph	Me	C=O	40[a]
p-MeOPh	Me	C=O	53
Ph	Ph	CHOH	91
Ph	Me	CHOH	25[a]
Fluorenyl		CHOH	69[b]

$$ArCOR \ (Ar\overset{OH}{C}HR) \xrightarrow[20°, MeOH]{NaBH_4\text{-}PdCl_2} ArCH_2R \qquad R=Aryl \text{ or } Alkyl$$

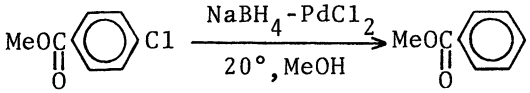
a) The reaction was carried out at 7° in water to extract directly without evaporation of the solvent.

b) Tetrahydrofuran-water (5:1) was used as the solvent.

good yields. This method is useful for the preparation of alkylbenzenes via aralkyl ketones readily obtainable. Its utility is that this reduction proceeds under mild conditions (room temperature, almost neutral pH) in a short time, and has high selectivity. The other method, for example, Clemmensen reduction uses strong acid, and the reaction time is very long. Wolff-Kishner reduction needs strong base and high reaction temperature. Though catalytic reduction over Pd/C proceeds under mild conditions, the selectivity is low. Benzylic alcohols, which are initially formed as intermediates in the reduction of aryl ketones, are similarly reduced to hydrocarbons in good yields. On the other hand, the system rarely reduces the hydroxyl group bonded to alkyl side chain at β or γ position to benzene ring.



y.66%

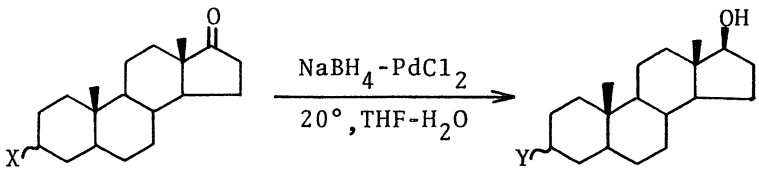


y.55%

It became apparent that this system removes chlorine atoms attached to aromatic rings reductively. Contrary to the Egli's method[10] using alkaline solution, the present reduction proceeds under almost neutral conditions. Consequently it is applicable to chloroarenes having alkali-sensitive functional groups. For instance, methyl p-chlorobenzoate was readily reduced to methyl benzoate, and the ester group was not affected.

Furthermore, this reduction system reduced the hindered steroidal 17-ketones, difficult to be reduced with $NaBH_4$ alone, to the corresponding β-alcohols. The configuration of 17-OH was determined according to the Zürcher's method.[11] Even if the steroids have the ester groups, the ketones were reduced selectively.

Table II. Reduction of Hindered Steroidal Ketones



X	Y	yield (%)
O=	HO▶	96
HO‴	HO‴	96
AcO‴	AcO‴	84
HO▶	HO▶	91
AcO▶	AcO▶	94

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