

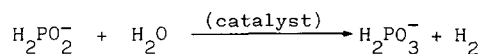
REDUCTION OF CARBON-CARBON DOUBLE BONDS AND HYDROGENOLYSIS BY SODIUM HYPOPHOSPHITE

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Summary : Sodium hypophosphite plus palladium-charcoal is a mild, economical, selective system for the reduction of carbon-carbon double bonds and hydrogenolysis of benzyl ethers and benzyl carbonates.

The reduction of C-C multiple bonds using hydrogen and a metal catalyst is familiar to all organic chemists. In many cases this reduction can also be carried out by means of a hydrogen donor and this process is named "catalytic transfer hydrogenation" (1). Most donors used are organic molecules (cyclohexene, formic acid, tetralin, limonene, α -phellandrene, alcohols and amines) though it is well documented that inorganic compounds such as hypophosphorous acid and its alkaline salts may generate hydrogen according to the following equation (2)



In spite of this, sodium hypophosphite has hitherto found little application in organic synthesis. It has been used for the reduction of aromatic nitriles into the corresponding aldehydes (3), of aromatic nitro groups into amines (4) or hydroxylamines (5), of alkynes into alkenes (6), of nitroolefins into enamines (7) and of the biliary pigment bilirubin into mesobilirubin (8).

We report here how sodium hypophosphite associated with palladium-charcoal can serve as a system in general use for the reduction of alkenes into alkanes (Table I) and for the hydrogenolysis of benzyl ethers and benzyl carbonates (Table II). Our results show that this reduction process offers an alternative to catalytic low-pressure hydrogenation. Advantageous features are that no special apparatus or particular precautions are required, the selectivity is good (carbonyl groups, carboxylic acids and derivatives, alkyl nitriles and halogen substituents on aromatic nuclei are not affected by this reducing system) and the yields are generally very high.

Table I

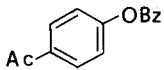
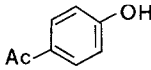
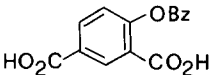
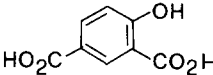
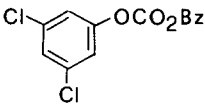
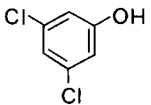
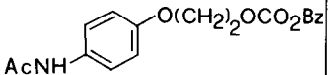
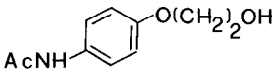
| Starting Compounds ^{a)} | Products ^{b)} | Reaction Conditions | Yields % ^{c)} |
|----------------------------------|------------------------|---|------------------------|
| | | EtOH/H ₂ O 20°C/45 min or H ₂ O/NaOH 50°C/1.5 h | 92 88 |
| | | EtOH/H ₂ O/NaOH 50°C/1.5 h or DMF/H ₂ O/NaOH 100°C/1 h | 90 84 |
| | | EtOH/H ₂ O reflux/3 h | 84 |
| | | EtOH/H ₂ O 50°C/1.5 h | 95 |
| | | EtOH/H ₂ O 20°C/0.5 h | 90 ^{d)} |

a) Ac = CH₃CO; b) Elemental analyses and ¹H-NMR data were in agreement with the structure of the products; c) Yields are reported as isolated products; d) 1:1 ratio of cis and trans configuration.

General Experimental Procedure

Ten mmol of starting compound were dissolved in 15–20 ml of alcohol (or tetrahydrofuran, dimethylformamide, acetic acid) or in 10 ml of 1N sodium hydroxide when the molecule carries an acidic function. To the resulting solution, Pd-C 10% (5–10% w/w starting compound) and a solution of 12–20 mmol of sodium hypophosphite in 5–10 ml of water were added. The mixture was stirred at temperatures between 20° and 100°C until the starting compound disappeared in TLC (0.5–5 h), then the catalyst was filtered off and the product isolated and purified by conventional methods.

Table II

| Starting Compounds ^{a)} | Products ^{b)} | Reaction Conditions | Yields % ^{c)} |
|---|---|---------------------------------------|------------------------|
|  |  | AcOH/H ₂ O reflux/5 h | 86 |
|  |  | EtOH/H ₂ O reflux/2.5 h | 95 |
|  |  | EtOH/H ₂ O 20°C/2.5 h | 93 |
|  |  | THF/H ₂ O 50°C/6 h | 98 |

a) Bz = C₆H₅CH₂; Ac = CH₃CO; b) Elemental analyses and ¹H-NMR data were in agreement with the structure of the products; c) Yields are reported as isolated products.

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