

Reduction of Nitro-compounds

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Nitro-compounds were reduced to amines in high yields by using palladium, platinum, or rhodium metal catalyst with formic, phosphinic, or phosphorous acid. With formic acid, nitro-compounds containing fluorine were reduced but not those containing chlorine, bromine, or iodine. With the other acids, nitro-compounds containing any of the halogens were reduced with retention of the halogen.

THE synthetically and industrially important reduction of nitro-compounds to amines has been effected in many ways.¹ Recently, we reported that catalytic transfer-hydrogenation with cyclohexene and palladium catalyst constituted a rapid and selective reduction of nitro-groups, and was particularly useful for the half-reduction of dinitro-compounds;³ in this process, halogen is usually eliminated reductively. In a search for more active hydrogen donors for transfer hydrogenation we have found that formic, phosphinic, and phosphorous acids or their salts in the presence of a catalyst reduce nitro-compounds to amines in high yield. For example, when palladium-charcoal catalyst (10%; 100 mg) was added to *m*-dinitrobenzene (500 mg) in formic acid (98%; 5 ml) evolution of carbon dioxide was observed and the temperature of the mixture rose from 25 to 100 °C within 2–3 min; the reaction was complete in *ca.* 10 min. After removal of catalyst, concentrated hydrochloric acid was added and the solution evaporated to dryness to yield *m*-phenylenediamine dihydrochloride (90%). Other aromatic and heterocyclic nitro-compounds behaved similarly, but the reaction sometimes needed heating to speed up or complete it. The catalyst recovered was washed with water and ethanol and could be re-used without apparent loss of activity. In some instances, the acidic solution of product containing the amine was simply filtered from the catalyst, cooled to 0 °C, and treated with aqueous sodium nitrite. The resulting diazo-compound was coupled with alkaline 2-naphthol to give the corresponding azo dye.

Under the above conditions, *p*-fluoronitrobenzene was reduced to *p*-fluoroaniline, but no reaction was observed with nitro-compounds containing halogen other than fluorine, such as 1-chloro-2,4-dinitrobenzene, *o*-bromonitrobenzene, and *p*-iodonitrobenzene. If, during the reduction of *m*-dinitrobenzene, either hydrogen chloride or chlorobenzene was added to the vigorously reacting mixture, the reaction ceased immediately; this suggests that halide is released during the reduction of chloro-, bromo-, and iodo-nitro-compounds and poisons the catalyst.

Removal of halogen from aromatic nuclei during catalytic reduction is frequently observed and yet not desirable, and special catalysts are available to circum-

vent this difficulty.² With either phosphinic or phosphorous acid and palladium-charcoal catalyst, we have found that reduction of nitro-groups occurs without removal of halogen. As examples, under conditions similar to those described with formic acid, reduction of 1-chloro-2,4-dinitrobenzene or 1,3,5-trichloro-2-nitrobenzene with phosphinic acid and palladium-charcoal afforded, respectively, 4-chloro-1,3-phenylenediamine and 2,4,6-trichloroaniline, in high yield.

As shown in the Experimental section, apart from halogen, the following functional groups did not interfere with the reduction: -NR₂, -CF₃, -SO₂Me, -CH₂OH, -OH, -CO₂H, -OMe, -CN, and -SO₃H; aromatic systems other than simple benzenoid ones were also reduced successfully. One substituent atom which did affect the reduction was divalent sulphur, but not in all cases. Thus, 3-methyl-5-nitrobenzo[*b*]thiophen was reduced, but not 5-nitrobenzisothiazole nor 5-nitro-1,2,3-benzothiadiazole.

This method of transfer hydrogenation does not reduce ethenes, ethynes, or nitriles, unlike normal catalytic hydrogenation, and therefore is not simply an alternative to the latter. Other catalysts such as platinum or rhodium have been found useful but not so effective as palladium. Sodium salts of formic, phosphinic, and phosphorous acids were also effective hydrogen donors. Although there is a slight evolution of hydrogen on addition of palladium catalyst to phosphinate, the reduction appears to take place through transfer of hydrogen on the catalyst surface, because reduction is much faster than evolution of hydrogen and other catalysts show little or no evolution of hydrogen. Also, phosphites reduce nitro-compounds with catalyst at 40 °C but no evolution of hydrogen is observed from phosphites and palladium catalysts alone until 90 °C.

Most of the nitro-compounds reduced have been aromatic or heteroaromatic but 2-nitropropane and β-nitrostyrene were also reduced under these conditions, the latter yielding phenylacetaldehyde oxime.

EXPERIMENTAL

All nitro- and amino-compounds are known and were obtained commercially or by known methods. Identification of starting materials and products rested on two or more of the following: m.p., t.l.c., i.r., n.m.r., and mass

² P. N. Rylander, 'Catalytic Hydrogenation over Platinum Metals,' Academic Press, New York, 1967, pp. 22 and 181–186.

³ I. D. Entwistle, R. A. W. Johnstone, and T. J. Povall, *J.C.S. Perkin I*, 1975, 1300.

¹ 'Methoden der Organischen Chemie' (Houben-Weyl), Band XI/I, 1957, Thieme, Stuttgart, pp. 360–1688; see also ref. 2, pp. 170–172 and M. S. Gibson in 'The Chemistry of the Amino Group,' ed. S. Patai, Interscience, New York, 1968, pp. 66–77.

spectra. Amines were frequently identified as hydrochlorides. Typical reductions are described.

Reductions with Formic acid and Formates.—2,5-Dimethoxy-1-nitrobenzene (0.3 g) in formic acid (98%; 5 ml) was stirred with palladium-charcoal (10%; 0.89 g) and heated to ca. 100 °C on a water-bath until effervescence had ceased (15 min). Concentrated hydrochloric acid (3 ml) was added, the catalyst was filtered off and washed with water, and the combined filtrates were evaporated to yield 2,5-dimethoxyaniline hydrochloride in 95% yield (from ethanol). Similarly, *m*-dinitrobenzene rapidly gave *m*-phenylenediamine dihydrochloride. When this reaction was attempted with either 5% rhodium- or 10% platinum-charcoal catalyst, reduction was observed but was much slower and required more prolonged heating.

Other nitro-compounds reduced to amines with formic acid and palladium-charcoal catalyst included: *p*-nitrobenzyl alcohol, *p*-nitrophenol, *m*-nitroaniline, *o*-nitroanisole, 1-nitronaphthalene, *p*-fluoronitrobenzene, *m*-nitrobenzoic acid, 1,4-dimethoxy-2,6-dinitrobenzene, 2,6-dinitroaniline, *o*-nitrobenzoic acid, *m*- and *p*-nitrobenzotrile, 4-fluoro-3-nitrobenzylidene fluoride, 1-fluoro-2-nitro-4-methylsulphonylbenzene, 2-methyl-4-nitroimidazole, and 5-nitro-2-trifluoromethylbenzimidazole.

Reduction in tetrahydrofuran or ethanol of *m*-dinitrobenzene to *m*-phenylenediamine proceeded smoothly with aqueous sodium formate and palladium-charcoal catalyst.

Reduction with Phosphinic Acid and Phosphinates.—Nitrobenzene (1 ml) in warm methanol (15 ml) was added to phosphinic acid (30%; 6 ml) and palladium-charcoal catalyst (10%; 0.5 g) was added to the stirred mixture. After initial effervescence had ceased, the mixture was heated under reflux for ca. 20 min and filtered. The filtrate was neutralized with aqueous sodium hydroxide and extracted with chloroform and the combined extracts were dried and evaporated to give aniline (70% yield). The reduction was repeated with sodium phosphinate.

Reduction of Halogen-containing Nitro-compounds.—1,2-Dichloro-4-nitrobenzene (2.0 g) in tetrahydrofuran (20 ml) was stirred with palladium-charcoal (10%; 0.2 g) and to this suspension was gradually added aqueous sodium

phosphinate (30%); effervescence was allowed to subside between additions. Addition of phosphinate was continued until t.l.c. revealed that no nitro-compound remained. The mixture was filtered and the filtrate poured into water (25 ml) and extracted with dichloromethane. The combined extracts were dried and evaporated to yield 3,4-dichloroaniline (90% yield).

Similarly, the following were reduced to amines in 75–90% yields by using palladium-charcoal catalyst and phosphinic acid, sodium phosphinate, phosphorous acid, or sodium phosphite: 1-chloro-4-nitrobenzene, 4-nitrophenol, 1-iodo-4-nitrobenzene, 1-chloro-2,6-dinitrobenzene, *m*-dinitrobenzene, *p*-nitrotoluene, 2-chloro-1-fluoro-4-nitrobenzene, *p*-nitrosodiphenylamine, 1-nitronaphthalene, 2-nitropyridine, 4-chloro-3-nitrobenzylidene fluoride.

Attempted Reduction of Compounds containing Divalent Sulphur.—Generally, with any of the above reagents, divalent sulphur compounds reacted less vigorously or not at all. Thus, after 60 min at 100 °C with formic acid and 50% by weight of palladium-charcoal (10%), none of the following was reduced: 2-nitrothiophen, 5-nitrobenzothiazole, 5-nitro-2,1,3-benzothiadiazole, 4-chloro-7-nitrobenzothiazole, 5-nitro-1,2,3-benzothiadiazole. Under the same conditions, 3-methyl-5-nitrobenzo[*b*]thiophen was reduced.

Reduction and Diazotization.—For example, sodium 2-methyl-5-nitrobenzenesulphonate was reduced with formic acid and palladium-charcoal catalyst as above. The solution of amine was filtered from catalyst, cooled to 0 °C, and treated with aqueous sodium nitrite dropwise, until there was a slight excess of nitrous acid. The resulting solution was added to an excess of alkaline 2-naphthol to give the corresponding azo dye, identified by m.p., t.l.c., and mass spectrometry. Similarly, the halogen-containing compounds, *p*-chloronitrobenzene, *o*-chloronitrobenzene, and 2,5-dichloro-1-nitrobenzene were reduced with phosphinic acid and palladium-charcoal to the corresponding amine, which was immediately diazotised and coupled with 2-naphthol, without isolation.

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