Selenium-catalysed Reduction of Aromatic Nitro Compounds to *N*-Arylhydroxylamines

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Metallic selenium catalyses the reduction of aromatic nitro compounds to the corresponding *N*-arylhydroxylamines with sodium borohydride under mild conditions.

Much attention has recently been given to the role of selenium as a microessential element in biological systems. For example, glutathione peroxidase is widely known to play important physiological roles as a redox catalysts.[1] In organic synthesis, reactions using selenium compounds as redox catalysts have been mainly oxidation,[2] and little attention has been paid to reduction. There is one example in which aromatic nitro compounds were converted into aromatic amines by selenium under a high pressure of carbon monoxide at an elevated temperature.[3] This prompted us to study the selenium-catalysed reduction of organic compounds under mild conditions from the viewpoint of synthetic and biological interests.

In this paper we report that the aromatic nitro compounds (**1**; X = NO_2, CN, CO_2Et, H, and Me) are reduced in good yields to the corresponding *N*-arylhydroxylamines (**2**) with sodium borohydride in the presence of a catalytic amount of metallic selenium. This new reaction proceeds smoothly in ethanol at room temperature.

$$\underset{(\mathbf{1})}{p\text{-X-C}_6\text{H}_4\text{-NO}_2} \xrightarrow{\text{Se/NaBH}_4} \underset{(\mathbf{2})}{p\text{-X-C}_6\text{H}_4\text{-NHOH}}$$

In a typical experiment, nitrobenzene (4.0 mmol) was added to a solution of sodium borohydride (9.6 mmol) and powdered metallic selenium (0.4 mmol) in ethanol (25 ml), and the reaction mixture was stirred at room temperature under argon. *N*-Phenylhydroxylamine was isolated by silica gel column chromatography (short column) after neutralization and extraction. The same product can also be obtained less effectively under similar reaction conditions using water instead of ethanol as a solvent. Table 1 shows the results obtained from several aromatic nitro compounds. In the absence of selenium, no appreciable reduction occurred except in the case (3%) of *p*-dinitrobenzene. The reactions were accelerated by electron-withdrawing groups and hindered by electron-donating groups. The nitro compounds bearing strongly electron-donating groups were entirely inert toward the reducing system. The yields of the hydroxylamines are good for nitro compounds bearing electron-withdrawing groups. Both the observed reactivity and the yield seem to reflect primarily the electronic effects of the substituent. On the other hand, when the aliphatic nitro compounds (1-nitropentane and nitrocyclohexane) were treated in ethanol for 27 h in the same manner as the aromatic nitro ones, the

Table 1. Selenium-catalysed reduction of aromatic nitro compounds.[a]

Nitro compound (**1**)	Solvent	Time/h	% Yield[b] of (**2**) [recovered (**1**)]
X = NO_2	EtOH	0.25	81[c]
X = CN	EtOH	1.5	86
X = CO_2Et	EtOH	0.5	88
X = H	EtOH	2.5	79
X = H	H_2O	30.0	37 (33)
X = Me	EtOH	6.5	54 (6)
X = OMe	EtOH	18.0	0[d] (21)
X = NH_2	EtOH	18.0	0 (99)
X = NMe_2	EtOH	18.0	0 (99)

[a] Conditions: $ArNO_2$ (4.0 mmol), Se (0.4 mmol), $NaBH_4$ (9.6 mmol in EtOH or 20 mmol in H_2O), solvent (25 ml), temperature (23—26 °C), under argon. [b] Isolated yield. [c] Monoamine (16%). [d] Complex mixture with the amine (6%).

corresponding oximes (8% and 33% yields respectively) could be isolated as the selenium-catalysed reduction products.

It is known that selenium is reduced by 1.1 equiv. of sodium borohydride in ethanol to give sodium hydrogen selenide *in situ*.[4] Since sodium hydrogen selenide (8.0 mmol) prepared in this way reduced nitrobenzene (4.0 mmol) to *N*-phenylhydroxylamine (89% yield) under the present reaction conditions, we presume that the active species of the selenium-catalysed reduction is the hydrogen selenide anion.

In conclusion, the present reaction performed under mild conditions provides an entry to the synthesis[5] of *N*-arylhydroxylamines bearing electron-withdrawing groups, and opens a new way to the use of selenium as a redox catalyst in organic synthesis. There is also interest from the biological point of view, since as yet there is no information on the role of selenium in the chemical transformation of nitro compounds in biological systems. Since hydrogen selenide anion is produced in the body,[6] a new role for selenium *in vivo* may be expected, if the present reaction is thought of as a model simulating biological changes of nitro compounds.

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