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Selective Reduction of Aromatic Nitro Compounds with Sodium Borohydride-Stannous Chloride[1)]

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Aromatic nitro group was selectively reduced by treatment with sodium borohydride-stannous chloride in ethanol in the presence of other reducible functional groups such as keto, ester, cyano, oxime or olefinic bonds.

Keywords——reduction; sodium borohydride; stannous chloride; aromatic nitro group; selectivity

During the last decade, sodium borohydride-transition metal salt systems in hydroxylic solvents have proved to be very useful for the reduction of various kinds of functional groups.[2)]

Aromatic nitro compounds, which are not normally reduced by treatment with sodium borohydride, can be reduced to aniline derivatives by using a combination of sodium borohydride and a suitable heterogeneous catalyst such as platinum/carbon,[3)] palladium/carbon[4)] or transition metal boride.[2a)] It was also reported that sodium borohydride in the presence of rhodium chloride complexed with pyridine gives a homogeneous system which readily reduces aromatic nitro compounds to aniline derivatives.[5)]

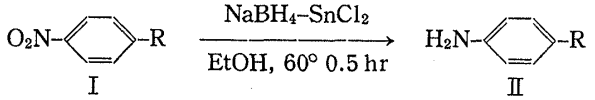
The sodium borohydride-stannous chloride system described here belongs to the homogeneous category and shows very high selectivity for aromatic nitro groups even in the presence of keto, or olefinic bonds, which are known to be reduced easily by treatment with sodium borohydride or sodium borohydride-transition metal salt systems.[2d)]

Reduction of Ethyl *p*-Nitrobenzoate(I) with $NaBH_4$-$SnCl_2 \cdot 2H_2O$ in Ethanol

An alcoholic solution containing **1** and $SnCl_2 \cdot 2H_2O$ (three to ten mol equivalents with respect to **1**) was heated at 60° and $NaBH_4$ (0.5 mol equivalent with respect to **1**) in ethanol was added dropwise. There was no evolution of hydrogen and no appearance of a black precipitate (as was seen with a $NaBH_4$–transition metal salt system); the reduction proceeded homogeneously in solution.

The yield of ethyl *p*-aminobenzoate (**2**) was highly dependent on the molar ratio of $SnCl_2 \cdot 2H_2O$ to **1**. When three, five and ten mol equivalents of $SnCl_2 \cdot 2H_2O$ were used, the yields

Table I. Yields of *p*-Substituted Anilines



I II

R[8)]	Yield of (II) (%)	Hammett constant (σ)[6)]
$-COOC_2H_5$	95	+0.45
$-Cl$	84	+0.25
$-H$	79	0
$-CH_3$	75	−0.17
$-OC_2H_5$	65	−0.24

of **2** were 56, 95 and 29%, respectively. Lower yields of **2** were obtained when larger amounts of $SnCl_2 \cdot 2H_2O$ were employed.

Reduction of *p*-Substituted Nitrobenzenes with $NaBH_4$-$SnCl_2 \cdot 2H_2O$ in Ethanol

Various *p*-substituted nitrobenzenes were converted into the corresponding primary amines under the optimal reaction conditions found for the reduction of **1** ($NaBH_4$: 0.5 mol equivalent, $SnCl_2 \cdot 2H_2O$: 5 mol equivalents).

The yields of *p*-substituted anilines from the corresponding nitrobenzenes seem to depend on their Hammett constants, *i.e.* the more electron-attracting the substituent, the higher the yield of aniline (Table I).

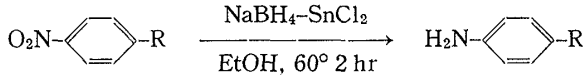
Similar results have been reported for the reduction of *p*-substituted nitrobenzenes with $SnCl_2$ in acidic solution[7] and with $NaBH_4$-$CoCl_2 \cdot 6H_2O$ in methanol.[2b]

Selectivity in the Reduction of Nitro Groups by $SnCl_2 \cdot NaBH_4$

Nitrobenzene derivatives having reducible functional groups were treated with $NaBH_4$–$SnCl_2 \cdot 2H_2O$ to examine the selectivity of the reducing system.

The results are shown in Table II.

TABLE II. Selective Reduction of *p*-Substituted Nitrobenzenes



R[8]	Yield of reduction product (%)
$-CN$	75
$-COCH_3$	98
$-HC{=}CHCOOC_2H_5$	71
$-C(=NOH)-CH_3$	84[a,b]
$-OCOCH_3$	96[c]

a) Anhydrous stannous chloride was used instead of the dihydrate.
b) The use of the hydrate afforded a considerable amount (15%) of *p*-aminoacetophenone.
c) Ethyl acetate–*tert*-butanol (9:1) was used as the solvent instead of ethanol to avoid solvolysis (see "Experimental")

Experimental

All melting points were determined on a micro hot stage apparatus and are uncorrected. IR absorption spectra were obtained with a Shimazu model IR-27G spectrometer. Gas chromatographic mass spectrometry was carried out on a Shimazu GC–MS 9000B instrument. Quantitative analysis was by gas chromatography (a Shimazu model GC-6AMPYTF apparatus equipped with a 2 m × 3 mm column containing 5% silicon OV-17 on Gaschrom Q), and the corresponding nitro compounds were used as internal standards.

A typical experimental procedure was as follows.

Ethyl *p*-nitrobenzoate (1.0 g, 5.1 mmol) and $SnCl_2 \cdot 2H_2O$ (5.75 g, 25.5 mmol) were dissolved in ethanol (100 ml) and heated to 60°. Sodium borohydride (97 mg, 2.55 mmol) in ethanol (30 ml) was added over a period of 30 min with stirring. After being stirred for further 30 min, the reaction mixture was cooled to 5—10° and 100 ml of chilled water was added, followed by neutralization with chilled 3.5 N NaOH to pH 7. The ethanol was evaporated off, and the aqueous solution was continuously extracted with ether. The ethereal solution was dried over Na_2SO_4 and concentrated to give a white solid, which was recrystallized from ethanol to yield 570 mg (63%) of ethyl *p*-aminobenzoate, mp 89—90°.

For quantitative analysis, the ethereal solution was analyzed directly by gas chromatography.

Reduction of *p*-Nitrophenyl Acetate (**3**)——A solution of **3** (3.0 g, 16.6 mmol) and $SnCl_2 \cdot 2H_2O$ (18.6 g, 82.5 mmol) in 100 ml of AcOEt–*tert*-BuOH (9:1) was heated at 60° for 1 hr. Sodium borohydride (0.31 g, 8.2 mmol) was then added portionwise with stirring at 60°. The solution was stirred for 2 hr at the same temperature, then evaporated to dryness. Cold water (300 ml) was added to the residue and the pH of the aqueous solution was adjusted to 7.6 with chilled 5% $NaHCO_3$ and the solution was extracted with AcOEt

(200 ml × 4). The combined AcOEt layers were washed with saturated aqueous NaCl solution and dried over Na_2SO_4. Removal of the solvent by evaporation yielded 2.40 g of *p*-aminophenyl acetate (96%). Recrystallization from petroleum ether gave white needles, mp 74—75° (lit.[9] 74°). MS *m/e*: 151 (M^+). IR ν_{max} cm^{-1}: 1748 (C=O). *Anal.* Calcd for $C_8H_9NO_2$: C, 63.57; H, 6.00; N, 9.27. Found: C, 63.59; H, 5.83; N, 9.18.

References and Notes

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The Constituents of *Paris verticillata* M.*v.* Bieb.

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Nine compounds (**1**—**9**) have been isolated from the whole plants of *Paris verticillata* M.*v.* Bieb. (Liliaceae) and their structures characterized. They can be divided into four groups; phytosteryl derivatives (**1**, phytosteryl (6′-palmitoyl)-β-D-glucopyranoside; **2**, the despalmitate of **1**), phytoecdysones (**3**, ecdysone; **4**, ajugasterone A; **5**, ecdysterone), pennogenin glycosides (**6**, pennogenin tetraglycoside (T-g); **7**, prototype glycoside of **6**), and kaempferol glycosides (**8**, kaempferol 3-O-α-L-rhamnopyranosyl-(1→2)-β-D-glucopyranoside; **9**, 7-O-β-D-glucopyranosyl kaempferol 3-O-α-L-rhamnopyranosyl-(1→2)-β-D-glucopyranoside).

Keywords——*Paris verticillata*; Liliaceae; phytosteryl (6′-palmitoyl)-glucoside; ecdysone; ajugasterone A; ecdysterone; pennogenin glycoside; furostanol glycoside; kaempferol glycoside

As a part of our studies on the constituents of *Paris* and *Trillium* plants (Liliaceae) with a view to obtaining the physiologically active components, we have surveyed whole plants of *Paris verticillata* M.*v.* Bieb. and have isolated nine compounds (**1**—**9**) including ecdysone.[1] It is noteworthy that the latter was obtained in a yield of 0.035% from this plant. This report deals with the isolation and the structure elucidation of the nine compounds by spectral and chemical means.