

# Novel Chemoselective Reduction of Aryldiazonium Fluoroborates with Zn-NiCl<sub>2</sub>·6H<sub>2</sub>O-THF<sup>†</sup>

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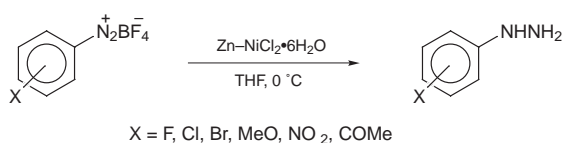
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Substituted aryldiazonium fluoroborates are selectively reduced to the corresponding phenylhydrazines by using Zn-NiCl<sub>2</sub>·6H<sub>2</sub>O in THF as a reducing agent.

Substituted phenylhydrazines are important for the synthesis of diphenylcarbazones which are used as analytical reagents<sup>1</sup> and antibacterial agents against mycobacterium tuberculosis.<sup>2</sup> Recently diphenylcarbazones have been used for *in vitro* study of human cell lines derived from nine types of cancer: leukemia, lung cancer, colon cancer, CNS cancer, melanoma, ovarian cancer, renal cancer, prostate cancer and breast cancer.<sup>3</sup> The Fischer indolization between substituted phenylhydrazines and appropriate carbonyl compounds<sup>4</sup> has been used for the synthesis of 1,8-diethyl-1,3,4,9-tetrahydropyrano[3,4-*b*]indole-1-acetic acid (Etodolac) and similar derivatives which are important non-steroidal analgesic and anti-inflammatory drugs.<sup>5</sup> Phenylhydrazines have commonly been prepared by reduction of diazonium salts with an excess of SnCl<sub>2</sub> in the presence of hydrochloric acid. However, this is not a selective method because other labile substituents also undergo simultaneous reduction. Recently reduction of substituted aryldiazonium fluoroborates to the corresponding phenylhydrazines has been carried out using borohydride exchange resin (BER) in methanol.<sup>6</sup> However, the long reaction time (6 h) required to prepare BER using an excess of the expensive NaBH<sub>4</sub> is a significant drawback of this methodology.

Herein, we report a novel and inexpensive reduction system consisting of zinc-nickel chloride hexahydrate in tetrahydrofuran for the chemoselective reduction of various substituted aryldiazonium fluoroborates to the corresponding phenylhydrazines (Scheme 1). The reductions generally proceeded with high yields under mild conditions (0 °C) and showed selectivity over other labile substituents.



**Scheme 1**

The high yields of the reduction products demonstrates the efficiency of this new method. Table 1 summarizes our results on reduction of substituted aryldiazonium fluoroborates. In all the reductions, aryldiazonium fluoroborates are reduced to the corresponding arylhydrazines and not to the hydrocarbons. At the same time, aryldiazonium fluoroborates are selectively reduced in the presence of an aromatic methoxy group (entry 8). For nitro-substituted aryldiazonium fluoroborates, the corresponding nitrophenylhydrazines were selectively obtained without any further reduction of the nitro group (entries

9 and 10). Furthermore, haloaryldiazonium fluoroborates showed remarkable selectivity to give the halophenylhydrazines without any dehalogenation (entries 2–7). In addition, it was worth commenting that 4-acetylphenyldiazonium fluoroborate was converted to the 4-acetylphenylhydrazine and the sensitive carbonyl group remains intact (entry 11).

**Table 1** Chemoselective reduction of aryldiazonium fluoroborates by using Zn-NiCl<sub>2</sub>·6H<sub>2</sub>O-THF

| Entry | Diazonium fluoroborate | Product <sup>a</sup> | Yield <sup>b</sup> (%) | Mp/Bp (Torr) [lit.] <sup>7</sup> / °C |
|-------|------------------------|----------------------|------------------------|---------------------------------------|
| 1     |                        |                      | 80                     | 242 (760) [243 (760)]                 |
| 2     |                        |                      | 75                     | 201 <sup>c</sup> [200–203]            |
| 3     |                        |                      | 78                     | 236 <sup>c</sup> [236]                |
| 4     |                        |                      | 82                     | 236 <sup>c</sup> [200–205]            |
| 5     |                        |                      | 72                     | 265 <sup>c</sup> [268]                |
| 6     |                        |                      | 71                     | 206 <sup>c</sup> [209]                |
| 7     |                        |                      | 70                     | 146 [146]                             |
| 8     |                        |                      | 85                     | 161 <sup>c</sup> [160–162]            |
| 9     |                        |                      | 75                     | 195 <sup>c</sup> [195–197]            |
| 10    |                        |                      | 90                     | 156 [156]                             |
| 11    |                        |                      | 70                     | 184 (760) [—]                         |

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<sup>†</sup> This is a **Short Paper** as defined in the Instructions for Authors, Section 5.0 [see *J. Chem. Research (S)*, 1999, Issue 1]; there is therefore no corresponding material in *J. Chem. Research (M)*.

<sup>a</sup> Products were characterised by their physical constants, spectral characteristics (IR, <sup>1</sup>H NMR) and comparison with authentic samples. <sup>b</sup> Yields are of pure isolated products. <sup>c</sup> As hydrochloride salt.

In conclusion, the present results demonstrate the novelty of zinc–nickel chloride hexahydrate–THF combination system which shows unique selectivity and constitutes a useful alternative to the commonly accepted procedure for the synthesis of various arylhydrazines. Moreover, this simple and easily reducible technique affords products in excellent yields without involvement of expensive materials and without formation of any undesirable side-products of the classical methods.

### Experimental

All chemicals were of analytical grade. The solvents were freshly distilled before use. Commercially available zinc powder and nickel chloride hexahydrate were used as received. All aryldiazonium fluoroborates were prepared by using standard synthetic methods.<sup>8</sup>

*General Procedure for Chemoselective Reduction of Substituted Aryldiazonium Fluoroborates.*—A mixture of zinc powder (2 mmol) and nickel chloride hexahydrate (3 mmol) and aryldiazonium fluoroborate (2 mmol) in tetrahydrofuran (10 ml) at 0 °C was stirred. A vigorous exothermic reaction takes place immediately which is controlled by keeping the reaction mixture in an ice-bath. After completion of the reaction, THF was removed under vacuum and the product was extracted with diethyl ether (3 × 10 ml). The ether layer was dried with anhydrous sodium sulfate and removal of the solvent under reduced pressure affords the arylhydrazine in almost pure form; further purification, if required, can be performed by chromatography.

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