Rapid cleavage of azo compounds to amine/s using Raney nickel and ammonium formate or formic acid

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Azo compounds, both symmetrical and unsymmetrical are cleaved to amines by using Raney nickel and ammonium formate or formic acid in methanol at room temperature. The reductive cleavage is very fast, clean, cost effective and high yielding as compared to earlier methods and many other functionalities such as -OH, -CH3, -OCH3, -COOH, -COCH3 and halogen remained unaffected.

Reductive cleavage of azo and azoxy compounds continues to be a useful tool in structure analysis of these compounds, particularly in dye industry. Numerous reagents have been developed for the reductive cleavage of azo compounds to amines including metals (notably zinc) and acids,12 Na2S2O4, and borane3. Though some of these are widely used, still they have limitations based on chemo-selectivity and economic considerations. Catalytic hydrogenation is also commonly used4, although the success of reaction is sensitive towards catalyst, solvent and substrate. Further, catalytic hydrogenation employs highly diffusable, low molecular weight, flammable hydrogen gas and requires pressure equipment.

Now a days, heterogeneous catalytic transfer hydrogenation method has proved to be a potent choice for reduction of organic compounds over traditional hydrogenation or other methods of reduction as it involves mild reaction condition, easy work-up and high degree of selectivity5-8. The application of catalytic transfer hydrogenation for reduction and reductive cleavage of organic compounds and in peptide synthesis is mainly centered on the use of expensive catalysts like Pd/C, Ru/Ca, Pd/CAO, and Ru/C. Earlier reports reveal that, catalytic transfer hydrogenation of azo compounds to amines have been achieved with systems like ammonium formate/10% Pd-C,8 cyclohexene/5% Pd on asbestos,9 cyclohexene/10% Pd-C10 or hydrazine/10% Pd-C11. But these systems require longer reaction duration as long as 16-48 hr at reflux and expensive catalysts like 10% Pd-C/20% HCOOH12 and 10% Pd-C/triethyl ammonium formate13 could reduce the nitrile group to a methyl group and remove the halogen from aromatic rings. Hence reductive cleavage of azo compounds with these systems serves chemoselectivity to a little extent.

In our earlier report we have used ammonium formate or formic acid with Raney nickel14, for the selective reduction of nitro compounds to their corresponding amines. In this communication, we wish to report a rapid, selective and simple cleavage of substituted azo compounds to the corresponding amine derivative/s by employing Raney nickel and ammonium formate or formic acid at room temperature in methanol, tetrahydrofuran or dioxane (Scheme 1). This new system cleaved with ease a wide variety of azo compounds to the corresponding amine/s. Many primary and secondary functional groups like halogens, -CH3, -OH, -COOH, -COCH3 and -OCH3 are tolerated.

The cleavage of azo compound in the presence of Raney nickel and ammonium formate or formic acid was complete within 5 to 20 min. The course of reaction was monitored by TLC and IR spectra. The work-up and isolation of the products were easy. Thus, all the compounds reduced (few examples are

\[
\begin{align*}
\text{Ni/HCO}_2\text{NH}_4 \text{ or HCO}_2\text{H} & \quad \text{MeOH, r.t.} \\
\text{Y or X} & = \text{-H, halogen, -OH, -OCH}_3, \text{-COOH, -CH}_3, \text{-SO}_3\text{Na, -NH}_2, \text{-N(CH}_3)_2 \text{ and -COCH}_3
\end{align*}
\]

Scheme 1
Table 1 — Rapid cleavage of azo compounds to amine/s using raney nickel and ammonium formate or formic acid.

<table>
<thead>
<tr>
<th>SL No</th>
<th>Substrate</th>
<th>Product</th>
<th>Time (min)</th>
<th>Yield (%)&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Found m.p. (°C)</th>
<th>Lit. m.p. (°C)</th>
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<tbody>
<tr>
<td>1</td>
<td>H</td>
<td>H</td>
<td>3</td>
<td>95</td>
<td>112&lt;sup&gt;a&lt;/sup&gt;</td>
<td>114&lt;sup&gt;a&lt;/sup&gt;</td>
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<tr>
<td>2</td>
<td>2-CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>2'-CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>6</td>
<td>94</td>
<td>142&lt;sup&gt;b&lt;/sup&gt;</td>
<td>144&lt;sup&gt;b&lt;/sup&gt;</td>
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<td>3</td>
<td>3-CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>3'-CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>5</td>
<td>95</td>
<td>126&lt;sup&gt;b&lt;/sup&gt;</td>
<td>125&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>4</td>
<td>2-Br</td>
<td>2'-Br</td>
<td>7</td>
<td>93</td>
<td>115&lt;sup&gt;b&lt;/sup&gt;</td>
<td>116&lt;sup&gt;b&lt;/sup&gt;</td>
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<tr>
<td>5</td>
<td>3-OC&lt;sub&gt;2&lt;/sub&gt;H&lt;sub&gt;5&lt;/sub&gt;</td>
<td>3'-OC&lt;sub&gt;2&lt;/sub&gt;H&lt;sub&gt;5&lt;/sub&gt;</td>
<td>7</td>
<td>94</td>
<td>82&lt;sup&gt;c&lt;/sup&gt;</td>
<td>80&lt;sup&gt;c&lt;/sup&gt;</td>
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<tr>
<td>6</td>
<td>H</td>
<td>4'-COOH</td>
<td>10</td>
<td>95,80</td>
<td>113&lt;sup&gt;c&lt;/sup&gt;,188</td>
<td>114&lt;sup&gt;c&lt;/sup&gt;,186&lt;sup&gt;c&lt;/sup&gt;</td>
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<tr>
<td>7</td>
<td>4-N(CH&lt;sub&gt;3&lt;/sub&gt;)&lt;sub&gt;2&lt;/sub&gt;</td>
<td>H</td>
<td>8</td>
<td>95,95</td>
<td>52,113&lt;sup&gt;c&lt;/sup&gt;</td>
<td>53&lt;sup&gt;c&lt;/sup&gt;,114&lt;sup&gt;c&lt;/sup&gt;</td>
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<tr>
<td>8</td>
<td>4-N(CH&lt;sub&gt;3&lt;/sub&gt;)&lt;sub&gt;2&lt;/sub&gt;</td>
<td>4'-SO&lt;sub&gt;3&lt;/sub&gt;Na</td>
<td>13</td>
<td>92,55</td>
<td>52,n.d.</td>
<td>53&lt;sup&gt;c&lt;/sup&gt;,114&lt;sup&gt;c&lt;/sup&gt;</td>
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<td>2' -COOH</td>
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<td>92,93</td>
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<td>3'-CO&lt;sub&gt;2&lt;/sub&gt;H&lt;sub&gt;5&lt;/sub&gt;</td>
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<td>101&lt;sup&gt;c&lt;/sup&gt;</td>
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<td>4'-Cl</td>
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<td>71</td>
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<td>93,95</td>
<td>140,113</td>
<td>141&lt;sup&gt;c&lt;/sup&gt;,114&lt;sup&gt;c&lt;/sup&gt;</td>
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<tr>
<td>14</td>
<td>2-OH</td>
<td>2'-OH</td>
<td>7</td>
<td>89</td>
<td>172</td>
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<td>15</td>
<td>1,1'-azonaphthylene</td>
<td>1-aminonaphthylene</td>
<td>16</td>
<td>85</td>
<td>188</td>
<td>190&lt;sup&gt;c&lt;/sup&gt;</td>
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<tr>
<td>16</td>
<td>4,4'-azo bipheryl</td>
<td>4-amino bipheryl</td>
<td>18</td>
<td>85</td>
<td>53</td>
<td>52&lt;sup&gt;c&lt;/sup&gt;</td>
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<tr>
<td>17</td>
<td>2,2'-azo fluorene</td>
<td>2-amino fluorene</td>
<td>20</td>
<td>80</td>
<td>162</td>
<td>160&lt;sup&gt;c&lt;/sup&gt;</td>
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</table>

<sup>a</sup>Isolated yields are based on single experiment and the yields were not optimised.
<sup>b</sup>Melting point of benzoyl derivative.
<sup>c</sup>Melting point of acetyl derivative.
<sup>d</sup>The low yield is due to its water soluble nature, TLC analysis indicates 95-98% cleavage.
<sup>n.d.</sup>Not determined
<sup>e</sup>Satisfactory elemental analysis is obtained for this compound.

(In the case of unsymmetrical azo compounds, the first mentioned data refers to the left hand side fragment azo compound and the next mentioned data refers to the right hand side fragment of the reductively cleaved azo compound).

listed in Table 1) by this system were obtained in good yields (80-95%). The products were characterized by comparison of their melting points, TLC and IR spectra with authentic samples. The disappearance of a strong absorption band between 1630-1575 cm<sup>-1</sup> due to the -N=N- stretching and the appearance of a strong absorption band between 3500-3300 cm<sup>-1</sup> due to the -NH<sub>2</sub> group clearly showed that the azo compounds had been cleaved into their constituent amine/s. Furthermore there was no absorption between 2290-2440 cm<sup>-1</sup>, which clearly indicated the absence of the -NH-NH- group. A control experiment was carried out using azo compounds with ammonium formate or formic acid, but without Raney nickel did not yield the desired product. The appearance of one spot in TLC in the case of symmetrical azo compounds and two spots, in the case of unsymmetrical azo compounds clearly indicated that no hydrazo compounds were formed during the reductive cleavage of the azo compounds.

Thus the cleavage of azo compounds can be accomplished at room temperature in a short time with Raney nickel instead of expensive platinum or palladium etc., without effecting the reduction of any of the reducible or hydrogenolyseable substituents. The yields are virtually quantitative and the products are analytically pure. This procedure will therefore be of general use, especially in cases where rapid, mild and selective reduction or cleavage is required.
**Experimental Section**

All the azo compounds, ammonium formate and formic acid were purchased from Aldrich Chemical Company (USA). Raney nickel was purchased from Merck (India). All the solvents used were of analytical grade or were purified according to standard procedures. TLC was carried out on silica gel plates obtained from Whatman Inc. The melting points were determined by using Thomas–Hoover melting point apparatus and are uncorrected. IR spectra were recorded on SHIMADZU FTIR-8300 spectrometer. For preparative TLC, the plates were prepared from Kieselgel 60 GF$_{254}$, Merck, Darmstadt and for column chromatography 60-120 mesh silica gel was used obtained from SISCO Research Laboratories, Bombay (India).

**Typical procedure for the reduction of azo compounds**

A suspension of the azo compound (2 g) and Raney nickel (1 g) in methanol or in any other suitable solvent (10 mL or the requisite amount) and ammonium formate (2 g) or formic acid (3 mL) was stirred under a nitrogen atmosphere at room temperature. After the completion of the reaction (monitored by TLC or by the disappearance starting material colour) the reaction mixture was filtered through a celite pad and washed with solvent. When ammonium formate was used, the combined filtrate and washings were concentrated in vacuo. The residue was taken into 15 mL chloroform or ether, washed twice with 15 mL saturated brine solution and finally with water. The organic layer was dried over anhydrous magnesium sulfate and the solvent was removed using a rotary evaporator. For further purification/separation of products, the residue was purified either by preparative TLC or by column chromatography. When formic acid was used, the filtrate and washings were neutralized with ammonia then evaporated in vacuo and worked up, as mentioned above. After chromatographic separation/purification, the IR spectra and melting points were compared with authentic samples.

Note: (i) Some substituted amines like p-aminobenzoic acid are soluble in water to a considerable extent. In such cases, successive extractions and careful washing optimized the yields. (ii) Both the donors are competitive in reductively cleaving the azo compounds. There is only slight variation in reaction duration and in yield. Therefore only one reaction duration and yield is coated for both the donors in the table.

**Acknowledgement**

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**References**