Reduction of carbonyl compounds with sodium borohydride in the presence of clays in aprotic solvents

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The selective reduction of carbonyl group of various aromatic and aliphatic compounds bearing different functional groups with sodium borohydride in the presence of clay in aprotic solvents give 72-93% yield of corresponding alcohols.

Keywords: Reduction, carbonyl compounds, sodium borohydride, alcohols, clay

IPC: Int.C17 C 07 C

Heterogeneous reactions that are facilitated by clays have received great attention in recent years1-3. Montmorillonite clays have been used in a number of oxidation4, reduction5 and other organic reactions6 as catalyst and also as solid support for the reagents7,8. We have previously developed efficient and convenient methods for the synthesis of porphyrins9 and deprotection of 1,3-oxathiolanes10 catalyzed by montmorillonite K10 clay. The successful use of supported reagents in organic chemistry is an important development, both in the context of supported reagent chemistry and in the development of new cleaner chemical methods and processes11,12. The salient features of the reactions catalyzed by clay supported reagents are the enhanced reaction rate, ease of work-up and formation of pure products in high yields.

The reduction of carbonyl compounds to corresponding alcohols is an important reaction in the organic transformations. Sodium borohydride has been extensively used as a reducing reagent in protic solvents for the reduction of carbonyl compounds. However, very few reports are available in literature for this reaction in the presence of phase transfer catalyst in aprotic solvents13-16 or in solid state17,18. The major disadvantages associated with these solid state reduction reactions are longer reaction times, low yields, excess of hydride reagent and tedious work-up procedure. We report, herein, a convenient method for the reduction of carbonyl compounds with sodium borohydride in the presence of clay in aprotic solvents (Scheme I).

![Scheme I](image-url)

**Results and Discussion**

The reduction of carbonyl compounds was carried out by stirring carbonyl compound with clay and sodium borohydride at ambient temperature in hexane or benzene for 1-3 hr giving alcohols in excellent yields in the range 72-93% (Table I). The products were characterized by IR, 1H NMR spectroscopy and by comparison of their m.ps or b.ps with literature values (Table I). The reaction was clean and did not suffer from the formation of any by-products. The pure alcohols were obtained by filtration of clay, washing it with diethyl ether, followed by evaporation of the solvent under reduced pressure and column chromatography over silica gel. It is emphasized that from economical and environmental point of view, use of hexane as solvent is favourable. The reduction reaction of carbonyl compounds with sodium borohydride supported on clays is fast and simple. The system is selective for carbonyl compounds and other reducible functionalities like nitro, olefin and ester remain unaffected under these conditions (Table I).
Table I - Reduction of carbonyl compounds with NaBH₄ on clay in aprotic solvents

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Carbonyl Compd</th>
<th>Product⁺</th>
<th>Time (min)</th>
<th>m.p./b.p. (°C) (Lit.)²¹</th>
<th>Yield⁴ (%)</th>
<th>K10</th>
<th>KSF</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cyclohexanone</td>
<td>Cyclohexanol</td>
<td>60</td>
<td>160 (161)</td>
<td>92</td>
<td>86</td>
<td>86</td>
</tr>
<tr>
<td>2</td>
<td>Benzaldehyde</td>
<td>Benzylalcohol</td>
<td>60</td>
<td>92 at 10 mmHg</td>
<td>93</td>
<td>88</td>
<td>77</td>
</tr>
<tr>
<td>3</td>
<td>4-Chlorobenzaldehyde</td>
<td>4-Chlorobenzylalcohol</td>
<td>45</td>
<td>70-72 (71)</td>
<td>88</td>
<td>86</td>
<td>86</td>
</tr>
<tr>
<td>4</td>
<td>4-Nitrobenzaldehyde</td>
<td>4-Nitrobenzylalcohol</td>
<td>60</td>
<td>92-95 (92-94)</td>
<td>93</td>
<td>86</td>
<td>77</td>
</tr>
<tr>
<td>5</td>
<td>4-Methoxybenzaldehyde</td>
<td>4-Methoxybenzylalcohol</td>
<td>75</td>
<td>257-260 (259)</td>
<td>86</td>
<td>75</td>
<td>75</td>
</tr>
<tr>
<td>6</td>
<td>Acetophenone</td>
<td>1-Phenylethanol</td>
<td>75</td>
<td>95 at 15 mmHg</td>
<td>92</td>
<td>83</td>
<td>83</td>
</tr>
<tr>
<td>7</td>
<td>4-Chloroacetophenone</td>
<td>1-(4’-chlorophenyl)ethanol</td>
<td>90</td>
<td>65-68 (66)</td>
<td>85</td>
<td>75</td>
<td>75</td>
</tr>
<tr>
<td>8</td>
<td>2-Butanone</td>
<td>2-Butanol</td>
<td>60</td>
<td>(99.5)</td>
<td>92</td>
<td>84</td>
<td>84</td>
</tr>
<tr>
<td>9</td>
<td>Cinnamaldehyde</td>
<td>Cinnamyl alcohol</td>
<td>40</td>
<td>33 (258)</td>
<td>93</td>
<td>85</td>
<td>85</td>
</tr>
<tr>
<td>10</td>
<td>Vaniline</td>
<td>Vanillyl alcohol</td>
<td>75</td>
<td>113-115</td>
<td>84</td>
<td>72</td>
<td>72</td>
</tr>
<tr>
<td>11</td>
<td>Vetaldehyde</td>
<td>Vetalyl alcohol</td>
<td>75</td>
<td>87 at 10 mmHg</td>
<td>83</td>
<td>74</td>
<td>74</td>
</tr>
<tr>
<td>12</td>
<td>Ethylacetocetate</td>
<td>Ethyl-3-hydroxybutyrate</td>
<td>60</td>
<td>92 at 25 mmHg</td>
<td>91</td>
<td>79</td>
<td>79</td>
</tr>
<tr>
<td>13</td>
<td>Butyrophenone</td>
<td>1-Phenyl-1-butanol</td>
<td>60</td>
<td>46-48 (48)</td>
<td>90</td>
<td>80</td>
<td>80</td>
</tr>
</tbody>
</table>

⁺All products showed satisfactory spectral and elemental data. ⁴Isolated yields.

The reduction of unsaturated carbonyl compounds to corresponding hydroxy compounds with sodium borohydride in alcohol leads in general to substantial amounts of fully saturated alcohols along with β-alkoxy alcohols as side products¹⁹. The reduction of β-unsaturated carbonyl compounds to unsaturated hydroxy compounds in high yields might extend the utility of the present method. The role of clay is apparent from the fact that no conversion of cyclohexnone was observed in absence of clay, under similar conditions. We presume that the clay behaves as an acid and provides water molecules from its interlayer that is responsible for the enhancement of the reducing ability of sodium borohydride in aprotic solvents²⁰. The reaction was studied using different clays like montmorillonite K10 and KSF and montmorillonite K10 was found to be better catalyst under similar reaction conditions. The clay catalyst was recovered after the reaction by simple filtration. The recovered clay catalyst was washed thoroughly with diethyl ether and dried at 140°C for 1hr under vacuum. The recovered clay was successfully reused in the reduction of cyclohexanone with sodium borohydride and it was found that montmorillonite K10 showed consistent activity for five cycles and then activity begins to decrease. The sodium borohydride in presence of clay is a facile and practical method for the reduction of carbonyl compounds in aprotic solvents under mild conditions.

Experimental Section

The ¹H NMR spectra were recorded on a Brucker Heaven (300 MHz) spectrophotometer and the chemical shifts were expressed in ppm. The mass spectra were recorded on a JEOL-SX mass spectrometer. The elemental analyses were performed on a Perkin-Elmer CHNS/O analyzer series II PE 2400. The IR spectra were recorded on a Perkin-Elmer Spectrum 2000 infrared in KBr and νmax were expressed in cm⁻¹. The melting points were recorded on a Thomas HOOVER capillary melting point apparatus and all the melting points and boiling points were uncorrected. The carbonyl compounds were purchased from SRL India Ltd. Montmorillonite K10 and KSF were purchased from Fluka and treated directly for the reaction.

Representative procedure for the reduction of carbonyl compounds. The reduction of carbonyl compound (cyclohexanone, 5 mmol, 54 mL) was performed by stirring with clay (100 mg) and sodium borohydride (10.0 mmoles) in hexane (5.0 mL) for 2 hr at ambient temperature. The progress of the reaction was monitored by TLC and after completion of the reaction the clay catalyst was filtered off, washed with diethyl ether (2 × 20 mL). The filtrate was concentrated under reduced pressure, which on purification by column chromatography over silica gel (60-120 mesh) gave the products in 72-93% yields (Table I). The ¹H NMR spectral data and
m. ps or b. ps of the products compared well with the
authentic data available in the literature.

4-Nitrobenzyl alcohol: $^1$H NMR (300 MHz,
CDCl$_3$): $\delta$ 4.54 (s, 2H), 7.45 (d, $J = 7.5$ Hz, 2H), 8.32
(d, $J = 7.6$ Hz, 2H).

Cinnamyl alcohol: $^1$H NMR (300 MHz,
CDCl$_3$): 2.17 (brs, 1H), 4.11 (d, 2H), 6.25 (m, 1H), 6.87 (d, 1H),
7.13-7.28 (m, 3H), 7.42 (dd, 2H).

Ethyl-3-hydroxybutyrate: $^1$H NMR (300 MHz,
CDCl$_3$): $\delta$ 1.18 (d, 3H), 1.35 (t, 3H), 2.21 (brs, 1H),
2.14 (dd, 1H), 2.58 (dd, 1H), 3.96 (m, 1H), 4.15 (q, 2H).

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