

# Rapid reduction of chalcones to tetrahydrochalcones using nickel boride

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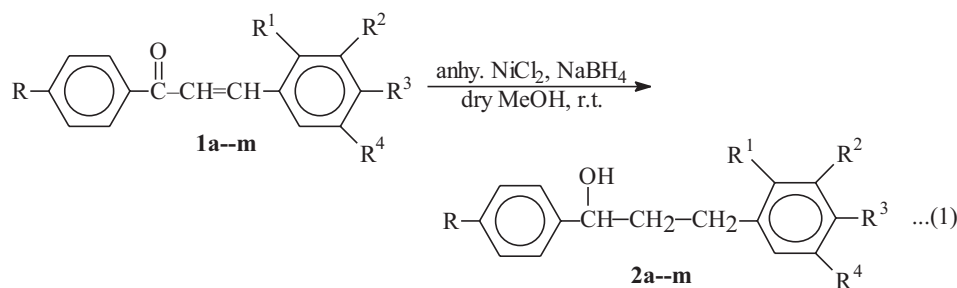
A variety of chalcones is rapidly reduced to the corresponding tetrahydrochalcones in high yields with nickel boride, generated *in situ*, in dry methanol at ambient temperature. The halo, methoxy and methyl groups remain unaffected under these conditions.

**Keywords:** chalcones, alcohols, nickel boride, reduction

Tetrahydrochalcones are important because they can be readily dehydrated to give 1,3-diarylpropenes which are useful synthons for a variety of compounds besides other applications. Therefore synthesis of tetrahydrochalcones by simple and convenient methods is desirable. Reduction of chalcones to tetrahydrochalcones is a useful transformation in organic synthesis. Various reducing agents are reported in the literature, each having its advantages and disadvantages.<sup>1-5</sup> Nickel boride has been reported as a catalyst for hydrogenation reactions earlier but now it is known as a reducing agent by itself because of adsorbed hydrogen.<sup>6</sup> Nickel boride offers several advantages over other reagents and is easy to prepare. We have reported deoxygenation, desulfurisation and reduction reactions<sup>7</sup> with nickel boride. In view of the importance of the said transformation, we have investigated

whether the nickel boride can be employed for the complete reduction of chalcones to tetrahydrochalcones.

A simple and convenient procedure is now reported for the rapid reduction of chalcones to the corresponding tetrahydrochalcones in high yields with nickel boride in dry methanol at ambient temperature. The nickel boride was generated *in situ* from anhyd. nickel(II) chloride and sodium borohydride. The reductions were rapid and were complete in ~5 min at ambient temperature (using a 1:2:6 molar ratio of substrate to nickel(II) chloride to sodium borohydride (eqn (1)) as monitored by thin layer chromatography. The halo substituted chalcones required slightly higher molar ratios of reagent (runs 5–8) probably due to their lower solubility in methanol. These results are summarised in Table 1.



**a:** R = R<sup>1</sup> = R<sup>2</sup> = R<sup>3</sup> = R<sup>4</sup> = H  
**b:** R = R<sup>1</sup> = R<sup>2</sup> = R<sup>4</sup> = H; R<sup>3</sup> = CH<sub>3</sub>  
**c:** R = R<sup>1</sup> = R<sup>2</sup> = R<sup>4</sup> = H; R<sup>3</sup> = OCH<sub>3</sub>  
**d:** R<sup>1</sup> = R<sup>2</sup> = R<sup>3</sup> = R<sup>4</sup> = H; R = OCH<sub>3</sub>  
**e:** R = R<sup>1</sup> = R<sup>2</sup> = R<sup>4</sup> = H; R<sup>3</sup> = Cl  
**f:** R<sup>1</sup> = R<sup>2</sup> = R<sup>3</sup> = R<sup>4</sup> = H; R = Cl  
**g:** R = R<sup>1</sup> = R<sup>2</sup> = R<sup>4</sup> = H; R<sup>3</sup> = Br

**h:** R<sup>1</sup> = R<sup>2</sup> = R<sup>3</sup> = R<sup>4</sup> = H; R = Br  
**i:** R<sup>1</sup> = R<sup>2</sup> = R<sup>4</sup> = H; R = R<sup>3</sup> = CH<sub>3</sub>  
**j:** R = R<sup>2</sup> = R<sup>3</sup> = R<sup>4</sup> = H; R<sup>1</sup> = OCH<sub>3</sub>  
**k:** R = R<sup>2</sup> = R<sup>4</sup> = H; R<sup>1</sup> = R<sup>3</sup> = Cl  
**l:** R = R<sup>2</sup> = R<sup>4</sup> = H; R<sup>1</sup> = R<sup>3</sup> = OCH<sub>3</sub>  
**m:** R = R<sup>1</sup> = H; R<sup>2</sup> = R<sup>3</sup> = R<sup>4</sup> = OCH<sub>3</sub>  
**n:** R = R<sup>1</sup> = R<sup>2</sup> = R<sup>4</sup> = H; R<sup>3</sup> = OH

**Table 1** Reduction of chalcones using nickel boride at ambient temperature in dry methanol<sup>a</sup>

Runs	Substrate(s)	Molar ratio S: NiCl <sub>2</sub> : NaBH <sub>4</sub>	Product	Time/min	Isolated yield/%
1	<b>1a</b>	1:2:6	<b>2a</b>	5	88
2	<b>1b</b>	1:2:6	<b>2b</b>	5	80
3	<b>1c</b>	1:2:6	<b>2c</b>	5	85
4	<b>1d</b>	1:2:6	<b>2d</b>	5	91
5	<b>1e</b>	1:4:12	<b>2e</b>	5	82
6	<b>1f</b>	1:4:12	<b>2f</b>	5	84
7	<b>1g</b>	1:4:12	<b>2g</b>	5	79
8	<b>1h</b>	1:4:12	<b>2h</b>	5	84
9	<b>1i</b>	1:2:6	<b>2i</b>	5	80
10	<b>1j</b>	1:2:6	<b>2j</b>	5	85
11	<b>1k</b>	1:2:6	<b>2k</b>	5	84
12	<b>1l</b>	1:2:6	<b>2l</b>	5	83
13	<b>1m</b>	1:2:6	<b>2m</b>	5	90
14	<b>1n</b>	1:2:6	<b>2n</b>	10	– <sup>b</sup>

<sup>a</sup>Reactions were performed with 25 ml of MeOH per g of substrate.

<sup>b</sup>A mixture of products obtained.

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Chalcone (**1a**) was chosen as a model substrate to investigate the appropriate conditions for the reduction of variously substituted chalcones. The molar ratio of substrate to anhydrous nickel(II) chloride to sodium borohydride was varied and reactions were attempted in different solvents like THF, acetonitrile, DMF and methanol. Reactions of chalcone (**1a**) in THF and acetonitrile were sluggish and were incomplete even after 24 h. Reaction in DMF was complete but the isolation of products was cumbersome. Reaction of **1a** with nickel boride in 1:2:6 molar ratio in dry methanol (run 1) was very rapid and yielded tetrahydrochalcones (**1a**) in 88 % yield. Therefore all subsequent reductions were carried out in dry methanol. The rapid reductions of chalcones were undoubtedly due to the involvement of nickel boride as the reducing species since chalcone (**1a**) was recovered unchanged when treated with anhydrous nickel(II) chloride alone under identical conditions and with NaBH<sub>4</sub> alone, the formation of the corresponding allyl alcohol was predominant and reactions required longer duration.<sup>5c,8</sup>

Small amounts of 1,3-diarylpropenes were also formed in some cases. The formation of small amounts of 1,3-diarylpropenes could not be eliminated completely. Our attempts to achieve higher conversion of tetrahydrochalcones into 1,3-diarylpropenes in reasonable yields with nickel boride, nickel(II) chloride or sodium borohydride were not successful. Nickel boride loses its activity with time since chalcone (**1a**) and *p*-methylchalcone (**1b**) were recovered unchanged when treated with a preformed solution of nickel boride after 72 h. The reductions are chemoselective as halo, methoxy and methyl groups remain unaffected under our reaction conditions. We conclude that chalcones can be reduced rapidly (~ 5 min) to the corresponding tetrahydro-chalcones with nickel boride generated *in situ* in dry methanol at ambient temperature.

## Experimental

To a solution of the substrate (*n* mmol) in dry methanol (25 ml/g) placed in a 100 ml round-bottomed flask fitted with a long double walled water condenser and a CaCl<sub>2</sub> guard tube, anhydrous nickel(II) chloride (2*n* mmol) and sodium borohydride (6*n* mmol) were added cautiously while stirring the solution vigorously. The reaction was exothermic and effervescent. The reaction was complete after 5 minutes as monitored by TLC using petroleum ether: ethyl acetate (95:5, v/v) as eluent. The reaction mixture was diluted with ~10 ml of methanol after 15 min. The reaction mixture was filtered through a celite pad (~1 inch) and the residual nickel boride was washed with methanol (2 × 10 ml). The combined filtrate was diluted with water (~100 ml) and extracted with dichloromethane (3 × 10 ml). The combined dichloromethane extracts were dried over anhydrous sodium sulfate, filtered and the solvent removed on a rotary evaporator. The product was dried under vacuum and purified by column chromatography on neutral alumina using petroleum ether: ethyl acetate (99:1, v/v) as eluent. The products were identified by m.p. (wherever applicable), IR and NMR (CDCl<sub>3</sub>) spectra.

**1,3-Diphenylpropan-1-ol: (2a)**<sup>5c</sup> Colourless oil; IR: 3390 cm<sup>-1</sup>, 2928 cm<sup>-1</sup>, 2856 cm<sup>-1</sup>; <sup>1</sup>H NMR (60 MHz): δ 7.1–7.4 (m, 10H), δ 4.7 (t, *J* = 5.5 Hz, 1H), δ 2.7–2.8 (m, 2H), δ 2.0–2.2 (m, 2H).

**3-(4'-methylphenyl)-1-phenylpropan-1-ol: (2b)**<sup>5b</sup> White solid m.p. 54–56 °C; IR: (KBr) 3270 cm<sup>-1</sup>, 2924 cm<sup>-1</sup>, 2855 cm<sup>-1</sup>; <sup>1</sup>H NMR (60 MHz): δ 7.2–7.5 (m, 10H), δ 4.7 (t, *J* = 5.4 Hz, 1H), δ 2.5–2.7 (t, *J* = 7.8 Hz, 2H), δ 2.3–2.4 (s, 3H), δ 2.0–2.2 (m, 2H).

**3-(4'-methoxyphenyl)-1-phenylpropan-1-ol: (2c)**<sup>2,9a</sup> White solid m.p. 65 °C, (lit. 52–53 °C); IR (KBr): 3359 cm<sup>-1</sup>, 2926 cm<sup>-1</sup>, 2857 cm<sup>-1</sup>; <sup>1</sup>H NMR (60 MHz): δ 7.2–7.5 (m, 9H), δ 4.7 (t, *J* = 5.5 Hz, 1H), δ 3.8 (s, 3H), δ 2.7–2.8 (m, 2H), δ 2.0–2.2 (m, 2H).

**1-(4'-methoxyphenyl)-3-phenylpropan-1-ol: (2d)**<sup>2,9b</sup> White solid m.p. 50 °C, (lit. 52–53 °C); IR (KBr): 3318 cm<sup>-1</sup>, 2930 cm<sup>-1</sup>, 2855 cm<sup>-1</sup>; <sup>1</sup>H NMR (60 MHz): δ 7.2–7.5 (m, 9H), δ 4.7 (t, *J* = 5.5 Hz, 1H), δ 3.8 (s, 3H), δ 2.6–2.8 (m, 2H), δ 2.0–2.3 (m, 2H).

**3-(4'-chlorophenyl)-1-phenylpropan-1-ol: (2e)**<sup>2,5c</sup> Solid m.p. 71–72 °C, (lit. 72 °C); IR (KBr): 3342 cm<sup>-1</sup>, 2937 cm<sup>-1</sup>, 2858 cm<sup>-1</sup>;

<sup>1</sup>H NMR (60 MHz): δ 7.1–7.3 (m, 9H), δ 4.6 (t, *J* = 5.7 Hz, 1H), δ 2.5–2.7 (m, 2H), δ 1.8–2.0 (m, 2H).

**1-(4'-chlorophenyl)-3-phenylpropan-1-ol: (2f)**<sup>2</sup> Solid m.p. 42 °C, \*lit. 44–45 °C; IR (KBr): 3359 cm<sup>-1</sup>, 2943 cm<sup>-1</sup>, 2853 cm<sup>-1</sup>; <sup>1</sup>H NMR (60 MHz): δ 7.1–7.3 (m, 9H), δ 4.6 (t, *J* = 5.7 Hz, 1H), δ 2.5–2.7 (m, 2H), δ 1.8–2.0 (m, 2H).

**3-(4'-Bromophenyl)-1-phenylpropan-1-ol: (2g)** Colourless oil; IR: 3374 cm<sup>-1</sup>, 2943 cm<sup>-1</sup>, 2865 cm<sup>-1</sup>; <sup>1</sup>H NMR (60 MHz): δ 7.2–7.5 (m, 9H), δ 4.6 (t, *J* = 5.5 Hz, 1H), δ 2.6–2.8 (m, 2H), δ 1.9–2.2 (m, 2H). Anal. Calcd. for C<sub>15</sub>H<sub>15</sub>BrO: C, 61.9; H, 5.2. Found: C 61.8; H, 5.2%.

**1-(4'-Bromophenyl)-3-phenylpropan-1-ol: (2h)** Colourless oil; IR: 3369 cm<sup>-1</sup>, 2941 cm<sup>-1</sup>, 2861 cm<sup>-1</sup>; <sup>1</sup>H NMR (60 MHz): δ 7.1–7.5 (m, 9H), δ 4.6 (t, *J* = 5.6 Hz, 1H), δ 2.5–2.8 (m, 2H), δ 2.0–2.2 (m, 2H). Anal. Calcd. for C<sub>15</sub>H<sub>15</sub>BrO: C, 61.9; H, 5.2. Found: C, 61.8; H, 5.2%.

**1,3-Bis-(4'-methylphenyl)propan-1-ol: (2i)** White solid m.p. 70 °C; IR (KBr): 3560 cm<sup>-1</sup>, 2925 cm<sup>-1</sup>, 2857 cm<sup>-1</sup>; <sup>1</sup>H NMR (60 MHz): δ 7.1–7.4 (m, 8H), δ 4.7 (t, *J* = 5.6 Hz, 1H), δ 2.5–2.8 (m, 2H), δ 2.3–2.5 (s, 6H), δ 1.9–2.2 (m, 2H). Anal. Calcd. for C<sub>17</sub>H<sub>20</sub>O: C, 85.0; H, 8.4. Found: C, 84.9; H, 8.4%.

**3-(2'-methoxyphenyl)-1-phenylpropan-1-ol: (2j)** Colourless oil; IR: 3401 cm<sup>-1</sup>, 2936 cm<sup>-1</sup>, 2853 cm<sup>-1</sup>; <sup>1</sup>H NMR (60 MHz): δ 7.0–7.4 (m, 9H), δ 4.7 (t, *J* = 5.4 Hz, 1H), δ 3.8 (s, 3H), δ 2.6–2.8 (m, 2H), δ 2.0–2.3 (m, 2H). Anal. Calcd. for C<sub>16</sub>H<sub>18</sub>O<sub>2</sub>: C, 79.3; H, 7.5. Found C, 79.3; H, 7.4%.

**3-(2',4'-Dichlorophenyl)propan-1-ol: (2k)** Colourless oil; IR: 3350 cm<sup>-1</sup>, 2939 cm<sup>-1</sup>, 2852 cm<sup>-1</sup>; <sup>1</sup>H NMR (60 MHz) δ 7.1–7.4 (m, 9H), δ 4.7 (t, *J* = 5.4 Hz, 1H), δ 2.5–2.8 (m, 2H), δ 1.9–2.2 (m, 2H). Anal. Calcd. for C<sub>15</sub>H<sub>14</sub>Cl<sub>2</sub>O: C, 64.1; H, 5.0. Found: C, 64.1; H, 5.0%.

**3-(2',4'-Dimethoxyphenyl)propan-1-ol: (2l)** Colourless oil; IR: 3418 cm<sup>-1</sup>, 2936 cm<sup>-1</sup>, 2859 cm<sup>-1</sup>; <sup>1</sup>H NMR (60 MHz): δ 6.9–7.4 (m, 9H), δ 4.6 (t, *J* = 5.7 Hz, 1H), δ 3.8–3.9 (s, 6H), δ 2.5–2.8 (m, 2H), δ 2.0–2.2 (m, 2H). Anal. Calcd. for C<sub>17</sub>H<sub>20</sub>O<sub>3</sub>: C, 75.0; H, 7.4. Found: C, 75.0; H, 7.4%.

**3-(3',4',5'-Trimethoxyphenyl)propan-1-ol: (2m)** Solid m.p. 84 °C; IR (KBr): 3435 cm<sup>-1</sup>, 2934 cm<sup>-1</sup>, 2854 cm<sup>-1</sup>; <sup>1</sup>H NMR (60 MHz): δ 7.2–7.5 (m, 9H), δ 4.7 (t, *J* = 5.7 Hz, 1H), δ 3.8 (s, 9H), δ 2.6–2.8 (m, 2H), δ 1.9–2.1 (m, 2H). Anal. Calcd. for C<sub>18</sub>H<sub>22</sub>O<sub>4</sub>: C, 71.5; H, 7.3. Found: C, 71.5; H, 7.3%.

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