Magnesium-induced pinacol coupling of aromatic aldehydes and ketones in water under ultrasound

Ji-Tai Li*, Yan-Jiang Bian, Shu-Ming Liu & Tong-Shuang Li

College of Chemistry & Environmental Science, Hebei University, Baoding 071002, P.R. China
Tel: +86-312-5079628; Fax: +86-312-5079628
Email: orgsyn@mail.hbu.edu.cn.

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The pinacol coupling of aromatic aldehydes and ketones has been carried out in 80-123% and 10-11% yields, respectively with Mg and Mg-MgCl₂ in water under ultrasound irradiation at room temperature for 3-4 hr.

1,2-Diols are very useful synthons for a variety of organic synthesis. They can be used as intermediates for the preparation of ketones and alkenes. More importantly the pinacol coupling has been applied to the synthesis of biologically active natural compounds. During the last several years, various metals such as Li⁺, Ln⁺, Al⁺, Mg⁺ have been developed to mediate the pinacol coupling reaction. However, some of the used reductants are expensive or the reduction conditions are critical.

Ultrasound has increasingly been used to promote or accelerate organic reactions. Many metal-involved organic reactions have been accelerated under ultrasound. Earlier data clearly show that ultrasound irradiation can activate the surface of metal powder, reduce the particle size, and bring about an effective surface modification. Recently, other metals such as Zn-Cu, indium and Zn have also been found to promote the pinacol coupling of aromatic aldehydes and ketones under ultrasonic irradiation. In this note, we report an efficient and convenient procedure for the synthesis of pinacols from some aromatic aldehydes using Mg or Mg-MgCl₂ respectively in water under ultrasound.

The coupling of aromatic aldehydes 1 gives pinacols 2 in high yields in the presence of Mg-MgCl₂ in water under ultrasonication (Scheme I, Table I). The data show that our procedure is a highly chemoselective method. For example, 1,2-diphenyl-1,2-ethanediol 2a, 1,2-di(p-methylphenyl)-1,2-ethanediol 2g and 1,2-di(p-methoxyphenyl)-1,2-ethanediol 2e were previously prepared in 80%, 65% and 89% yields, respectively using Mg-NH₄Cl at r.t for 12-24 hr. Whereas in our procedure, 2a, 2g, and 2e are obtained in 85%, 90% and 91% yields, respectively at r.t for 3 hr under ultrasound. The reactions in water have been interested due to environmental concerns. We tried to carry out the coupling reaction in the absence of MgCl₂. The results show that the pinacols are the main product. But, the yields of some pinacols are lower. MgCl₂ is a good Lewis acid in water, it can activate not only carbonyl group, but also resolve the Mg(OH)₂ producing thereby Mg and H₂O. So, MgCl₂ aqueous is in favour of the pinacol coupling reaction. It is well-known that pinacol coupling proceeds via a single electron-transfer mechanism. Accordingly, the sonication is in favour of the reaction via single electron transfer mechanism. Compared with reports using Mg-NH₄Cl under ultrasound (the ratios of dl/meso were about 1:1 with the Mg-NH₄Cl system in the literature), the reaction system improved the diastereoselectivity of pinacols (2a, 2c, 2e, 2g, 2l). The effect of the substituents of the aromatic ring on the dl/meso ratio is not clear.

When 4-chloroacetophenone, acetophenone, 4-methoxyacetophenone, is used as a substrate, pinacols are obtained in poor yields. Aliphatic aldehydes and ketones, such as, n-butyraldehyde and 4-methyl-2-pentanone are used as a substrate, no pinacol product is obtained. It indicates that the method has some limitations with respect to aromatic ketones, aliphatic aldehydes and ketones, and the reaction condition is impracticable for the pinacol coupling of aromatic ketones, aliphatic aldehydes and ketones.

In summary, we have found an efficient and convenient procedure for the synthesis of pinacols from some aromatic aldehydes using Mg-MgCl₂ in water under ultrasonic irradiation.

Experimental Section

Liquid substrates were purified by distillation prior to use. IR spectra in KBr were recorded on a Bio-Rad
### Table I—Pinacolization mediated by Mg-MgCl$_2$ or Mg in water under ultrasound*

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Reagent</th>
<th>Reaction time (hr)</th>
<th>Isolated yield, (%) (lit. $^2$)</th>
<th>d/l</th>
<th>meso</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>$\text{CHO}$</td>
<td>A</td>
<td>3</td>
<td>85(80)</td>
<td>4</td>
<td>31:69</td>
</tr>
<tr>
<td>b</td>
<td>$\text{CHO}$</td>
<td>B</td>
<td>3</td>
<td>62</td>
<td>7</td>
<td>—</td>
</tr>
<tr>
<td>c</td>
<td>$\text{CHO}$</td>
<td>A</td>
<td>4</td>
<td>20</td>
<td>0</td>
<td>meso</td>
</tr>
<tr>
<td>d</td>
<td>$\text{CHO}$</td>
<td>B</td>
<td>4</td>
<td>65(42)</td>
<td>0</td>
<td>55:45</td>
</tr>
<tr>
<td>e</td>
<td>$\text{CHO}$</td>
<td>A</td>
<td>3</td>
<td>91(89)</td>
<td>5</td>
<td>7:93</td>
</tr>
<tr>
<td>f</td>
<td>$\text{CHO}$</td>
<td>B</td>
<td>3</td>
<td>40</td>
<td>9</td>
<td>—</td>
</tr>
<tr>
<td>g</td>
<td>$\text{CHO}$</td>
<td>A</td>
<td>3</td>
<td>90(65)</td>
<td>5</td>
<td>92:8</td>
</tr>
<tr>
<td>h</td>
<td>$\text{CHO}$</td>
<td>B</td>
<td>4</td>
<td>62</td>
<td>20</td>
<td>—</td>
</tr>
<tr>
<td>i</td>
<td>$\text{CHO}$</td>
<td>A</td>
<td>3</td>
<td>44</td>
<td>4</td>
<td>—</td>
</tr>
<tr>
<td>j</td>
<td>$\text{CHO}$</td>
<td>B</td>
<td>4</td>
<td>60</td>
<td>5</td>
<td>—</td>
</tr>
<tr>
<td>k</td>
<td>$\text{CHO}$</td>
<td>A</td>
<td>3</td>
<td>45</td>
<td>0</td>
<td>58:42</td>
</tr>
<tr>
<td>l</td>
<td>$\text{CHO}$</td>
<td>B</td>
<td>4</td>
<td>20</td>
<td>45</td>
<td>—</td>
</tr>
</tbody>
</table>

*Isolated yield based on the substrate. Ratio of d/l|meso was calculated by $^1$H NMR. Reagent A: Mg-MgCl$_2$-H$_2$O; Reagent B: Mg-H$_2$O.

FTS-40 spectrometer; $^1$H NMR spectra on a VXR-300S spectrometer (300 MHz) using CDCl$_3$ as solvent and TMS as internal standard; and mass spectra on an AEI MS-50 SD90 spectrometer (EI, 70 eV). Sonication was performed in a Shanghai Branson-CQX ultrasonic cleaner with a frequency of 25 kHz and a nominal power 500 W. The reaction flask was located at the maximum energy area in the cleaner and the temperature of water-bath was controlled by addition or removal of water.

**General procedure.** A 100 mL Pyrex flask was charged with the desired aldehyde or ketone (1.1 mmole), Mg powder (0.5g), H$_2$O (10mL), or Mg powder (0.5g), MgCl$_2$ (0.3g) and H$_2$O (10mL). The mixture was irradiated in the water-bath of an ultrasonic cleaner at room temperature for a period as indicated in the Table I (sonication was monitored by TLC). The reaction was quenched with 3$M$ aqueous HCl (10mL) and extracted with ethyl acetate (3×15mL). The combined organic layers were washed with saturated aqueous NaHCO$_3$ solution and brine, dried over magnesium sulfate and filtered. The filtrate was concentrated in vacuo to give a crude material, which was separated by column chromatography on silica (200-300 mesh), eluted with petroleum ether (b.p. 60-90°C) or a mixture of petroleum ether and diethyl ether. The authenticity of the products was established by their spectra.

2a. $^1$H NMR: $\delta$ 2.28 (s, 2H, OH), 4.70 (s, d/l) and 4.83 (s, meso) (2H, PhCH$_3$), 7.11-7.30 (m, 10H).
Ar-H); MS: m/z (%), 214 (1), 180 (7.6), 167 (12.5), 149 (6.0), 107 (93.8), 79 (100), 77 (73.8); IR (KBr): 3400-3480 cm\(^{-1}\).

2b: \(^1\)H NMR: \(\delta\) 2.98 (s, 2H, OH), 5.49 (s, meso) (2H, PhCH\(-\)), 7.00-7.26 (m, 6H, Ar-H); MS: m/z (%), 352 (1), 305 (1.4), 233 (10), 175 (100), 145 (10), 111 (25), 77 (10); IR (KBr): 3320-3400 cm\(^{-1}\).

2c: \(^1\)H NMR: \(\delta\) 2.93 (s, 2H, 5-fur-H), 2.20 (s, 2H, OH), 7.08-7.26 (m, 8H, Ar-H); MS: m/z (%), 276 (14), 249 (32), 155 (100), 111 (8); IR (KBr): 3330-3550 cm\(^{-1}\).

2d: \(^1\)H NMR: \(\delta\) 2.37 (s, 2H, OH), 4.67 (s, dlf) and 4.90 (s, meso) (2H, PhCH\(-\)), 7.06-7.22 (m, 8H, Ar-H); MS: m/z (%), 263 (1.2), 251 (1.6), 178 (4.6), 165 (4.6), 141 (100), 113 (23.8), 77 (71.0); IR (KBr): 3260-3318 cm\(^{-1}\).

2e: \(^1\)H NMR: \(\delta\) 2.95 (s, 2H, OH), 3.75 (s, dlf) and 3.79 (s, meso) (s, OH, 2 x OCH\(^3\)), 4.64 (s, dlf) and 4.72 (s, meso) (2H, PhCH\(-\)), 6.84-7.25 (m, 8H, Ar-H); MS: m/z (%), 274(1), 256 (2), 227 (30), 137 (100), 109 (9), 77 (8); IR (KBr): 3300-3380 cm\(^{-1}\).

2f: \(^1\)H NMR: \(\delta\) 2.04 (s, 2H, -OH), 5.00 (s, dlf) and 5.02 (s, meso) (2H, fur-CH\(-\)), 6.27 (m, 4H, 3, 4-fur-H), 7.26 (m, 2H, 5-fur-H); MS: m/z (%), 196 (10), 178 (25), 152 (73), 137 (33), 98 (100), 84 (22), 49 (30); IR (KBr): 3240-3300 cm\(^{-1}\).

2g: \(^1\)H NMR: \(\delta\) 2.31 (s, 6H, CH\(_3\)), 2.60 (s, 2H, OH), 4.69 (s, dlf) and 4.75 (s, meso) (2H, PhCH\(-\)), 7.05-7.27 (m, 8H, Ar-H); MS: m/z (%), 242 (1), 195 (6), 121 (100), 107 (12), 93 (19), 77 (13); IR (KBr): 3280-3450 cm\(^{-1}\).

2j: \(^1\)H NMR: \(\delta\) 1.25 (s, dlf) and 1.48 (s, meso) (6H, -CCH\(_3\)), 2.20 (s, 2H, OH), 7.08-7.26 (m, 8H, Ar-H); MS: m/z (%), 276 (14), 249 (32), 155 (100), 111 (8); IR (KBr): 3330-3550 cm\(^{-1}\).

2k: \(^1\)H NMR: \(\delta\) 1.55 (s, dlf) and 1.62 (s, meso) (6H, -CCH\(_3\)), 2.12 (s, 2H, OH), 7.23-7.30 (m, 10H, Ar-H); MS: m/z (%), 225 (4), 206 (4), 181 (32), 165 (9), 121 (100), 105 (12), 77 (11), 43 (80); IR (KBr): 3364-3494 cm\(^{-1}\).

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References


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References