Microwave-enhanced Knoevenagel reaction catalyzed by calcium oxide

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Calcium oxide is employed both as heterogeneous catalyst and dehydrating agent in microwave-induced Knoevenagel reaction and gives the corresponding aryldiene compounds in good yields.

Knoevenagel reaction is an important name reaction by which the aralkynes are obtained from carbonyl compounds and active methylene compounds in the presence of a basic catalyst or Lewis acid catalyst.

Recently, the use of inorganic solids as catalysts is rapidly increasing, because of these reactions often involve milder reaction conditions, easier work-up and higher selectivity than similar homogeneous reactions. Consequently, the environmentally friendly solid bases such as AlPO₄·Al₂O₃³, alkylamine-functionalized silica gel⁴, ZnO or MgO⁵, xonolite⁶, KF/Al₂O₃⁷, aluminophosphate oxynitride⁸, amino-propyl-functionalized MCMs⁹, MCM-41 supported binary cesium-lanthanum oxide¹⁰, zirconophosphate oxynitride¹¹, modified Mg-Al hydroaluminate¹², zeolite CsX¹³, alkaline and alkaline earth carbonates¹⁴, diamino-functionalized MCM-41¹⁵, calcined Mg-Al hydroaluminate¹⁶, barium dimethyl aminoethyl phosphonate¹⁷ and zirconium dimethylaminoethylphosphonate-phosphate¹⁸ etc. have been employed in Knoevenagel condensation.

During the past decades, considerable attention has been focused on the application of microwave in organic synthesis, and a handful of papers in this field were reported¹⁹-²². Knoevenagel reaction was also be enhanced by microwave irradiation²³-³⁰.

We describe here a rapid and simple procedure for microwave-assisted Knoevenagel condensation. Various aromatic aldehydes react with active methylene compounds (malononitrile and ethyl cyanoacetate) catalyzed by calcium oxide under microwave irradiation (Scheme I). The reactions proceeded smoothly under reaction conditions, and gave desired products in good yields.

Note

The generality of this approach has been demonstrated by the condensation of a wide variety of aromatic aldehydes with active methylene compounds (Table I).

Our results show that solid base CaO is an efficient, inexpensive, nontoxic, stable and easily available catalyst for Knoevenagel reaction and that microwave irradiation greatly enhances the reaction. In Knoevenagel reactions, it is favourable to remove the water formed in the condensation. Kim et al²⁷,²⁸ have reported the use of dehydrant such as phosphorus pentoxide in Knoevenagel condensation. In our protocol, finely ground calcium oxide (≤200 mesh) acts both as heterogeneous catalyst and dehydrating agent and Ca(OH)₂, the hydrate of CaO, is also a solid base can catalyze this reaction. On completion the reaction, the solid could be separated by a simple filtration.

In comparing the rate enhancement effect of microwave irradiation on the investigated reaction. The condensation between benzoaldehyde and ethyl cyanoacetate was chosen as a model reaction. In similar experimental conditions with the same amount of starting materials and CuO, conventional heating needed ca 2 hr to gave the expected product in similar yield (86%). The reaction rate is enhanced about 24 times by using microwave irradiation. It can manifest the advantage and potentiality of microwave as a source of energy in Knoevenagel reactions.

The ratio of calcium oxide to aldehydes was 0.8. Further testing of two other inorganic solids – basic alumina and silica gel – revealed that CaO was most effective in promoting the reaction. Basic alumina, though less effective than CaO, was also effective, while silica gel was entirely ineffective.

In the scrutiny of the solvent effect on the condensation between benzoaldehyde and ethyl cyanoacetate, it was found that ethanol was the best solvent, acetonitrile was good too, while 1,4-dioxane and 1,2-dichloroethane were unsuitable for this reaction, respectively.
ethanol is used as solvent in the present study. Large presence of solvent. 

Evenagel reaction in terms of satisfactory yields, amount of tarry by-products were obtained in the absence of solvent. 

Experimental Section

Reactions were conducted in a MW-800 II multimode cavity refluxing system made by Microwave Research Center of East China Normal University. All products were known compounds and identified by comparison of their melting point and IR spectra. 

In conclusion, our results confirm that the CaO is an efficient catalyst for the microwave assisted Knoevenagel condensation in terms of satisfactory yields, facile work-up, and economically viable reagents. 

Table 1—CaO catalyzed Knoevenagel condensation under microwave irradiation

<table>
<thead>
<tr>
<th>Entry</th>
<th>Aldehydes</th>
<th>X</th>
<th>Time (min)</th>
<th>Yield (%)</th>
<th>m.p. (°C)</th>
<th>Obs.</th>
<th>Lit.</th>
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<tbody>
<tr>
<td>1</td>
<td>Benzaldehyde</td>
<td>CN</td>
<td>2</td>
<td>84</td>
<td>83</td>
<td>82</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Benzaldehyde</td>
<td>COOEt</td>
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<td>88</td>
<td>48</td>
<td>49</td>
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<tr>
<td>3</td>
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<td>159</td>
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<tr>
<td>4</td>
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<td>COOEt</td>
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<td>89</td>
<td>166</td>
<td>168</td>
<td></td>
</tr>
<tr>
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<td>4-Cl-C6H4CHO</td>
<td>CN</td>
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<td>84</td>
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<td>161</td>
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<tr>
<td>6</td>
<td>4-Cl-C6H4CHO</td>
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<td>89</td>
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<tr>
<td>7</td>
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<tr>
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<td>COOEt</td>
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<tr>
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<td>COOEt</td>
<td>5</td>
<td>82</td>
<td>99</td>
<td>100</td>
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<td>CN</td>
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<td>3</td>
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<td>94</td>
<td>93</td>
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</table>

All yields refer to isolated pure products.

In view of its polarity, low toxicity, and economy, ethanol is used as solvent in the present study. Large amount of tarry by-products were obtained in the absence of solvent.

References