Solvent-Free Addition of Ethynylbenzene to Ketones

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The addition of ethynylbenzene to ketones proceeded efficiently in the absence of a solvent to give tertiary alkynols in good yields.

The alkoxide-catalyzed addition of terminal alkynes to ketones, which proceeds in DMSO, has been known.1 Recently, Tzalis et al. reported that CsOH·H2O allowed a catalytic C–H activation of various alkynes in solution that leads, in the presence of aliphatic aldehydes or ketones, to propargylic alcohols.2 We found that the solvent-free addition of ethynylbenzene to ketones using potassium t-butoxide or potassium hydroxide proceed efficiently at room temperature. We now report on an ecologically and economically valuable formation of new carbon–carbon bonds by the solvent-free addition of ethynylbenzene to ketones.

For example, after cyclohexanone 1k (1.0 g, 10.2 mmol), ethynylbenzene 2 (1.1 g, 10.2 mmol), and potassium t-butoxide (1.1 g, 10.2 mmol) were well-mixed with agate mortar and pestle, the mixture was kept at room temperature for 20 min. Then 1k, 2, and potassium t-butoxide were well-mixed in the air, the reaction occurred immediately. After 20 min, the mixture was kept in the crystalline state. Also, the reaction product was kept at room temperature for 20 min. Also, the reaction product was mixed with 10% aqueous sodium chloride to give 1-(phenylethynyl)cyclohexanol (3k) as colorless crystals (1.7 g, 83% yield). We found that these reactions proceed more efficiently in the absence of a solvent than in a DMSO solution (Table 1).

The addition of ethynylbenzene to ketones using potassium hydroxide in solution, which give tertiary alkynols, had been reported by Favorskii.3 This reaction is known as the Favorskii reaction.3 Tertiary alkynols 3 were also obtained using potassium hydroxide instead of potassium t-butoxide. For example, after cyclohexanone 1k (1.0 g, 10.2 mmol), ethynylbenzene 2 (1.1 g, 10.2 mmol), and potassium hydroxide (1.1 g, 10.2 mmol) were well-mixed with agate mortar and pestle, the mixture was kept at room temperature for 20 min. Also, the reaction product was mixed with 10% aqueous sodium chloride to give 1-(phenylethynyl)cyclohexanol (3k) as colorless crystals (1.34 g, 66% yield). The addition of ethynylbenzene to 2-butanone (1b) using potassium hydroxide in the absence of a solvent also gave the corresponding tertiary alkynols (3b) in 76% yield.

Table 1. Yield of Tertiary Alkynols (3) at Room Temperature in the Absence of a Solvent and Solution3

<table>
<thead>
<tr>
<th>Ketone</th>
<th>Product and yield/%</th>
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<tbody>
<tr>
<td>1</td>
<td>2</td>
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<tr>
<td>R1</td>
<td>R2</td>
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<tr>
<td>a</td>
<td>Me</td>
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<td>b</td>
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</tr>
<tr>
<td>5</td>
<td>Me</td>
</tr>
<tr>
<td>b</td>
<td>b</td>
</tr>
</tbody>
</table>

a) All reaction in solution were carried out in DMSO.
b) No reaction occurred.

Scheme 1.
yield.

The solvent-free addition of alkyne to carbonyl compounds with diastereotopic faces, such as 2-methylcyclohexanone (1n), gave a 1:1 mixture of diastereomeric propargyl alcohols (3n)² in 70% yield.

Various organic reactions have also been found to proceed efficiently in the solid state.⁴

In summary, we have found that the addition of ethynylbenzene to ketones is very useful and proceeds more efficiently in the absence of a solvent than in a DMSO solution at room temperature.

**Experimental**

**General Methods.** IR spectra were measured with a JASCO FT/IR-350 IR spectrometer, using Nujol mulls. ¹H NMR spectra were recorded in CDCl₃ on a JEOL JNM-LA300 (300 MHz) spectrometer.

**Typical Procedure in the Absence of a Solvent: Preparation of 2-Methyl-4-phenyl-1-butyne-2-ol (3a) in the Absence of a Solvent.** After acetonitrile 1a (1.0 g, 17.2 mmol), ethynylbenzene 2 (1.8 g, 17.2 mmol), and potassium tert-butoxide (1.9 g, 17.2 mmol) were well-mixed with agate mortar and pestle, the mixture was kept at room temperature for 20 min. The reaction product was mixed with 10% aqueous sodium chloride, filtered, washed with water, and dried to give 3a as colorless crystals (2.6 g, 94% yield).

**Preparation of 1-(Phenylethynyl)cyclohexanol (3k) in DMSO.** A mixture of cyclohexanone 1k (1.0 g, 10.2 mmol), ethynylbenzene 2 (1.0 g, 10.2 mmol), and potassium tert-butoxide (0.22 g, 2.0 mmol) was stirred in DMSO 10 mL at room temperature for 15 h. The reaction product was mixed with 10% aqueous sodium chloride, filtered, and washed with water, and dried to give 1-(phenylethynyl)cyclohexanol (3k) as colorless crystals (1.3 g, 66% yield).

**Preparation of 1-(Phenylethynyl)cyclohexanol (3k) in DMSO.** A mixture of cyclohexanone 1k (1.0 g, 10.2 mmol), ethynylbenzene 2 (1.0 g, 10.2 mmol), and potassium tert-butoxide (0.22 g, 2.0 mmol) was stirred in DMSO 10 mL at room temperature for 15 h. The reaction product was mixed with 10% aqueous sodium chloride, filtered, and washed with water, and dried to give 1-(phenylethynyl)cyclohexanol (3k) as colorless crystals (1.3 g, 66% yield).

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**References**