

Application of heterogeneous catalysts for an efficient synthesis of β -keto enol ethers[☆]

Biswanath Das^{*}, Keetha Laxminarayana, B. Ravikanth

Organic Chemistry Division I, Indian Institute of Chemical Technology, Hyderabad 500 007, India

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Abstract

The synthesis of β -keto enol ethers involving the treatment of cyclic β -diketones with alcohols in the presence of various heterogeneous catalysts has been investigated. $\text{HClO}_4 \cdot \text{SiO}_2$ was found to be the most effective catalyst for this reaction to form the β -keto enol ethers in high yields and in short reaction times at room temperature.

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β -Keto enol ethers are useful intermediates in several organic transformations [1]. Their conversions into 4-alkylated-2-cyclohexenones, 2-aryl and 2-alkenyl-3-alkoxycyclohexenones and bicyclo [2,2,2] octenones are of important synthetic utility [2]. Several β -keto enol ethers act as dienophiles in Diels–Alder reactions [2b], and are valuable in the preparation of enantiomerically pure bioactive compounds [1a]. The conversion of cyclic β -diketones into β -keto enol ethers was previously carried out by treatment with alcohols in the presence of a catalyst such as *p*-toluene sulfonic acid monohydrate under reflux, TiCl_3 , iodine, $\text{B}(\text{C}_6\text{F}_5)_3$, CAN and $\text{Yb}(\text{OTf})_3$ [3]. This conversion was also carried out using methoxide [1d] and diazomethane [1c]. However, the application of an improved heterogeneous catalyst in the preparation of β -keto enol ethers is felt to be highly useful and practical. Here, we report our recent result of the synthesis of these compounds employing various heterogeneous catalysts.

In recent years heterogeneous catalysts have gained significant importance in organic syntheses because of economic and environmental considerations. These catalysts are generally less expensive, eco-friendly, high reactive, easy to handle and recov-

erable. In continuation of our work [4] on the applications of different heterogeneous catalysts to carry out various useful transformations we have recently studied the reaction of cyclic β -diketones with alcohols using these catalysts and observed that silica-supported perchloric acid ($\text{HClO}_4 \cdot \text{SiO}_2$) is most efficient for this conversion (Scheme 1).

Initially 1,3-cyclohexadione was treated with methanol at room temperature in the presence of various heterogeneous catalysts (Table 1). Considering the reaction times and yields of the corresponding β -keto enol ether, $\text{HClO}_4 \cdot \text{SiO}_2$ [5] was found to be the most effective catalyst. However the activity of other catalysts, Amberlyst-15 and $\text{TaCl}_5 \cdot \text{SiO}_2$ was weak. Montmorillonite clay and sulfated Zirconia were completely unsuitable to carry out the conversion. Thus $\text{HClO}_4 \cdot \text{SiO}_2$ was utilized subsequently for the preparation of a series of β -keto enol ethers from various cyclic β -diketones and alcohols (Table 2).

The present conversion proceeded rapidly (within 5–15 min) to form the products in high yields (71–95%). Primary, secondary and allyl alcohols underwent this conversion smoothly. Previously, some of the methods did not apply secondary and allyl alcohols for the preparation of β -keto enol ethers [3b]. In the present conversion no other solvent was used. The catalyst could easily be separated from the reaction mixture by simple filtration keeping the reaction profile clear. The structures of the products were settled from their spectral (^1H NMR and MS) data.

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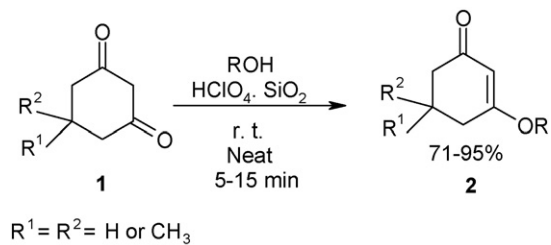
^{*} Corresponding author. Tel.: +91 40 27160512; fax: +91 40 27160512.

E-mail address: biswanathdas@yahoo.com (B. Das).

Table 1
Reaction of 1,3-cyclohexadione with methanol using various heterogeneous catalysts^a

Entry	Catalyst	Time (min)	Yield (%)
a	HClO ₄ ·SiO ₂	5	95
b	Amberlyst-15	20	75
c	TaCl ₅ ·SiO ₂	60	65
d	Montmorillonite clay	Over night	5
e	Sulfated zirconia	Over night	Trace amount

^a 1,3-Cyclohexadione (1 mmol) and MeOH (5 ml) were used in the presence of a heterogeneous catalyst (100 mg) at r.t.



Scheme 1.

Table 2
Synthesis of β-keto enol ethers using HClO₄·SiO₂^a

Entry	Substrate 1	Alcohol	Product	Time (min)	Isolated yield (%)
a		EtOH		5	91
b				9	87
c				10	92
d				12	89
e		Ph-CH ₂ -OH		15	71
f				14	81
g		MeOH		5	95
h				7	84
i				6	89
j				12	83

^a All the products were characterized from spectral (¹H NMR and MS) data.

In conclusion, we have efficiently applied an inexpensive heterogeneous catalyst, $\text{HClO}_4 \cdot \text{SiO}_2$ for rapid and high-yielding synthesis of β -keto enol ethers from cyclic β -diketones under very mild reaction conditions.

1. Experimental section

1.1. General procedure for the preparation of β -keto enol ethers:

To a solution of a β -diketone (1 mmol) in an alcohol (5 ml) $\text{HClO}_4 \cdot \text{SiO}_2$ (100 mg, prepared by reported method [5]) was added. The mixture was stirred at room temperature and reaction was monitored by TLC. After completion, the mixture was filtered and the filtrate was concentrated. The residue was purified by column chromatography over silica gel using hexane–EtOAc (4:1) to obtain pure β -keto enol ether.

The spectral (^1H NMR and MS) data of some representative compounds are given below.

- Compound **2b**: ^1H NMR (200 MHz, CDCl_3): δ 5.29 (1H, s), 4.44 (1H, m), 2.23 (2H, s), 2.18 (2H, s), 1.31 (6H, d, $J=7.0$ Hz), 1.06 (6H, s). FABMS: m/z 183 $[M+H]^+$.
- Compound **2e**: ^1H NMR (200 MHz, CDCl_3): δ 7.40–7.29 (5H, m), 5.42 (1H, s), 4.88 (2H, s), 2.32 (2H, s), 2.20 (2H, s), 1.09 (6H, s). FABMS: m/z 231 $[M+H]^+$.
- Compound **2j**: ^1H NMR (200 MHz, CDCl_3): δ 5.92 (1H, m), 5.41–5.22 (3H, m), 4.38 (2H, d, $J=7.0$ Hz), 2.49–2.41 (2H, m), 2.39–2.28 (2H, m), 2.09–1.91 (2H, m). FABMS: m/z 153 $[M+H]^+$.

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