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Iodine-catalyzed synthesis of β-keto enol ethers

Rajesh S. Bhosale,[a] Sidhanath V. Bhosale,[b] Sheshanath V. Bhosale,[b] Tianyu Wang[b] and P. K. Zubaidha[a,*]

[a] *School of Chemical Sciences, SRTM University, Nanded 431606, India*
[b] *Institute of Chemistry-Organic Chemistry, Freie Universität, Takustrassa-3, Berlin-14195, Germany*

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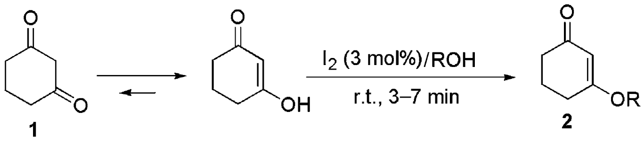
Abstract—The use of iodine, as a catalyst for the synthesis of β-keto enol ethers at room temperature is reported.

β-Keto enol ethers have been widely used as key intermediates in organic synthesis.[1–5] For example, they have been employed for the preparation of enantiomerically pure compounds.[5,6] A literature survey revealed that several methods have been reported to synthesize β-keto enol ethers from cyclic β-diketones. The treatment of cyclic β-diketones with diazomethane yields β-keto enol ethers.[1] Etherification of cyclic β-diketones has been reported using an alcohol with *p*-toluenesulfonic acid monohydrate under reflux,[2] and from 3-chlorocycloalk-2-enones with methoxide.[3,4] Recently Porta and co-workers reported conversion of cyclic β-diketones to β-keto enol ethers using $TiCl_4$ in methanol.[7] In recent years, iodine has been used as a versatile reagent for several reactions.[8–11] Iodine acts as a mild Lewis acid in the dehydration of tertiary alcohols to alkenes.[12] Iodine was also used in the synthesis of mixed benzyl–alkyl ethers[13] and was found to serve as an excellent catalyst in the *O*-isopropylidination of sugars and sugar alcohols.[14] Iodine-mediated synthesis of mixed ethers under hydrogen (80 bar) at 100 °C was reported.[15]

In this communication, we describe the etherification of cyclic β-diketones with different alcohols. At room temperature β-keto enol ethers were obtained cleanly and in very high yields with iodine as a catalyst (Table 1) whereas bis-acetals were not obtained (Scheme 1). In the absence of iodine, the reaction did not proceed even after 24 h.



Scheme 1.

Typical experimental procedure: To a stirred solution of the substrate **1** (0.5 g, 44.6 mmol) in methanol (10 mL), was added iodine (3 mol%). The reaction was monitored by TLC. After the reaction was complete, the solvent was removed under reduced pressure. The residue was extracted with a suitable solvent and washed with aq sodium thiosulfate solution, and subsequently with water and brine. The organic layer was dried over magnesium sulfate, filtered and the solvent was removed under reduced pressure. The product obtained was purified by column chromatography on SiO_2 (ethyl acetate/hexane, 1:10) and identified by comparison with an authentic sample by TLC and ^1H NMR.

In summary, the results shown above provide evidence that excellent yields of the expected products can be obtained in short reaction times. Further investigations into the scope of iodine-mediated reactions in connection with acetals are in progress and will be reported in due course.

Keywords: Etherification; Cyclic-β-diketones; β-Keto enol ethers; Iodine.

[*] Corresponding author. Tel.: +91 2462229242; fax: +91 2462229245; e-mail: rsbhosale03@yahoo.co.in

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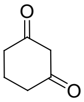
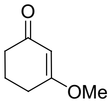
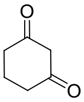
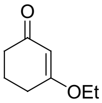
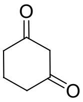
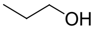
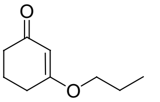
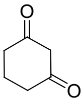
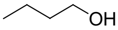
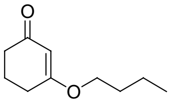
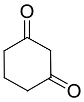
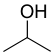
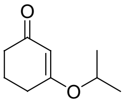
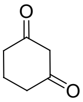
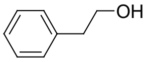
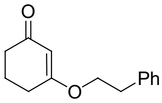
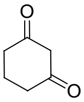
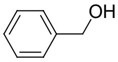
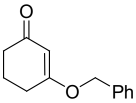
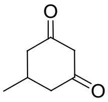
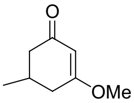
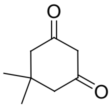
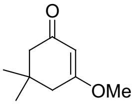
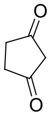
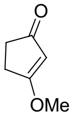
Table 1. Iodine-catalyzed etherification of cyclic β-diketones[a]

Entry	Substrate	Alcohol	Product	Time (min)	Yield (%)[b]
1		MeOH		3	94
2		EtOH		3	96
3				3	95
4				4	94
5				7	65
6				5	91
7				5	90
8		MeOH		3	95
9		MeOH		3	96
10		MeOH		4	93

[a] Alcohol used as solvent.

[b] Isolated yield.

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