



Iodine as a versatile catalyst for the hydroalkylation of vinyl arenes with 1,3-diketones

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ABSTRACT

The vinyl arenes undergo smooth hydroalkylation with 1,3-diketones in the presence of 10 mol % of iodine to afford phenethyl diketones and ketoesters in good yields in short reaction times. The use of inexpensive and readily available molecular iodine makes this method quite simple, more convenient and practical.

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The hydroalkylation of alkenes by 1,3-dicarbonyl compounds is one of the most common methods for C–C bond formation.¹ Consequently, there have been some reports on intermolecular hydroalkylation of alkenes using AuCl₃/AgOTf, AgOTf, *cis*-[Ru(6,6'-Cl₂bipy)₂(H₂O)₂](ClO₄)₂, Bi(OTf)₃, FeCl₃, PWA, [bmim]OTf/Cu(OTf)₂ or SnBr₄.^{2–4} A few intramolecular hydroalkylation of olefins have also been reported using PdCl₂(CH₃CN)₂, Pd(acac)₂ and [PtCl₂(CH₂=CH₂)]₂/EuCl₃.⁵ Besides hydroalkylation of olefins, there have been some reports on hydroalkylation of alkynes employing (PPh₃)₃AuOTf⁶ and Ni(acac)₂.⁷ However, many of these reports involve the use of expensive noble metal catalysts and require tedious work-up procedures which limit their use in large-scale synthesis. Since β-diketones and their derivatives have become increasingly useful and important in the synthesis of biologically active heterocycles, the hydroalkylation of alkenes remains an important and challenging strategy.

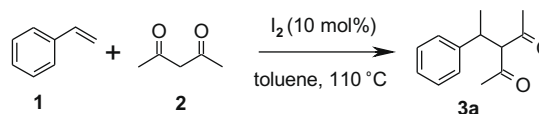
Recently, molecular iodine has received considerable attention in organic synthesis because of its low cost and ready availability. The mild Lewis acidity associated with iodine has enhanced its use in organic synthesis to perform several organic transformations using stoichiometric levels to catalytic amounts.⁸

Following our interest in the catalytic uses of molecular iodine,⁹ we herein report a mild and practical method for the hydroalkylation of vinyl arenes with 1,3-diketones using molecular iodine. Initially, we attempted the hydroalkylation of a readily available styrene (**1**) with acetylacetone (**2**) in the presence of 10 mol % of I₂. The reaction proceeded well in toluene at 110 °C and the prod-

uct 3-(1-phenylethyl)-2,4-pentanedione (**3a**) was isolated in 92% yield (Scheme 1).

This result provided the incentive for further study of reactions with different olefins and β-diketones. Interestingly, various vinyl arenes such as *p*-methyl-, *p*-*t*-butyl-, *p*-chloro-, *p*-methoxy-, *o*-bromo and β-naphthyl underwent smooth hydroalkylation with acetylacetone under identical conditions (Table 1, entries b–g). The reactions proceeded smoothly by 10 mol % iodine in refluxing toluene under neutral conditions to afford the corresponding products in excellent yields. In all cases, the products were formed by the selective addition of 1,3-diketones at benzylic position. Furthermore, the cyclic olefin, for example, indene (**4**) also participated well in this reaction to give the corresponding 3-(2,3-dihydro-1*H*-1-indenyl)-2,4-pentanedione (**3h**) in good yield (Table 1, entry h, Scheme 2).



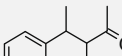
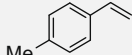

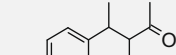
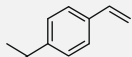

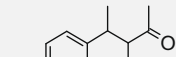
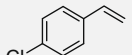

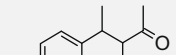
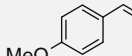

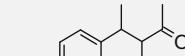


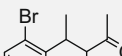
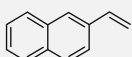

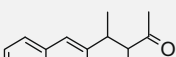


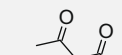
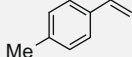

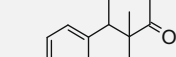

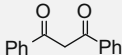
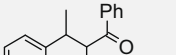
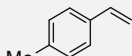
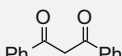
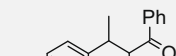
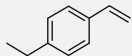
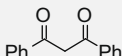
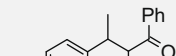
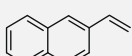
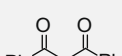
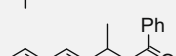

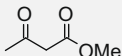
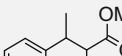


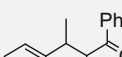
Subsequently, we studied the reaction of alkenes with different β-diketones such as 3-methylacetylacetone, dibenzoylmethane and 1-phenylbutane-1,3-dione (Table 1). Interestingly, 3-methylpentane-2,4-dione also underwent smooth addition onto styrenes under similar conditions (Table 1, entry i). Furthermore, β-ketoesters, for example, methyl acetoacetate also reacted smoothly with styrene to produce methyl 2-acetyl-3-phenylbutanoate (Table 1, entry n). The yields are generally high and the reaction times are



Scheme 1. Reaction between styrene and acetyl acetone.

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E-mail address: yadavpub@iict.res.in (J.S. Yadav).

Table 1
Iodine-catalyzed intermolecular addition of 1,3-diketones to vinyl arenes

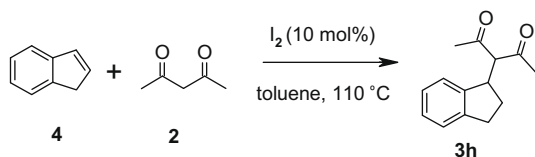
Entry	Alkene	1,2-Diketones	Product ^a	Time (h)	Yield ^b (%)
a				6.0	92
b				4.5	94
c				3.5	96
d				5.5	86
e				6.5	85
f				6.0	80
g				5.5	90
h				7.0	65
i				6.0	75
j				5.5	88
k				7.0	90
l				6.0	92
m				6.5	88
n				8.0	80 (48:52)
o				6.5	86 (45:55)

^a The products were characterized by ¹H NMR, IR and mass spectrometry.

^b Yield refers to pure products after chromatography.

quite reasonable. In general, the hydroalkylation was clean and no by-products such as iodo derivatives were detected under these conditions. As a solvent, toluene appeared to give the best results. In the absence of catalyst, the reaction did not proceed even after a

long reaction time (10–24 h). To realize the reaction mechanism, we have performed hydroalkylation of styrene with acetyl acetone using equimolar amounts of iodine and triethyl amine (10 mol % each). However, no reaction was observed in the presence of base.



Scheme 2. Reaction between indene and acetyl acetone.

But the reaction proceeds well in the presence of 10 mol % of HI. This clearly indicates that HI is responsible for the hydroalkylation, which may be generated in situ from iodine and 1,3-diketone. This method does not require the use of expensive or corrosive reagents and no precautions need to be taken to exclude moisture from the reaction medium. The scope and generality of this process are illustrated with respect to various olefins and 1,3-diketones and the results are presented in Table 1.¹⁰

In summary, we have described a simple and efficient protocol for the intermolecular hydroalkylation of vinyl arenes with 1,3-diketones using iodine as a catalyst under neutral conditions. The remarkable features of this procedure are atom efficiency, high conversions, operational simplicity and ready availability of reagents at low cost.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.03.024.

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- Experimental procedure, spectral data for new compounds and copies of ¹³C NMR spectra are provided in Supplementary data.