

# Iodine as an extremely powerful catalyst for the acetylation of alcohols under solvent-free conditions

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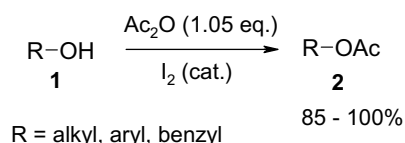
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**Abstract**—Iodine was found to promote quantitative acetylation of alcohols in a very short time with an equimolar amount of acetic anhydride under solvent-free conditions at room temperature.

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## 1. Introduction

Acylation of alcohols is an important and routinely utilised transformation in organic synthesis.<sup>1</sup> The most commonly used reagent combination for this reaction uses an acid anhydride in the presence of an acid or base catalyst.<sup>2</sup> This process is activated by addition of tertiary amines such as triethylamine, pyridine or DMAP.<sup>3</sup> Tributyl phosphine was subsequently introduced for acylation of base sensitive substances.<sup>4</sup> Various metal salts such as  $\text{CoCl}_2$ ,<sup>5</sup>  $\text{ZnCl}_2$ ,<sup>6</sup>  $\text{TiCl}_4\text{-AgClO}_4$ ,<sup>7</sup>  $\text{Me}_3\text{SiCl}$ ,<sup>8</sup>  $\text{LiClO}_4$ ,<sup>9</sup>  $\text{Mg}(\text{ClO}_4)_2$ <sup>10</sup> and some metal triflates such as  $\text{Sc}(\text{OTf})_3$ ,<sup>11</sup>  $\text{Me}_3\text{SiOTf}$ ,<sup>12</sup>  $\text{In}(\text{OTf})_3$ ,<sup>13</sup>  $\text{Cu}(\text{OTf})_2$ <sup>14</sup> and  $\text{Bi}(\text{OTf})_3$ ,<sup>15</sup> have been investigated to meet the demand for more efficient and selective methods. In most of the cases the catalyst is either less or not effective for secondary and tertiary alcohols or longer reaction times are necessary in order to achieve good yields. These drawbacks are eliminated by the use of Lewis acids but many of the Lewis acids employed are moisture sensitive and metal triflates are highly expensive. Recently perchlorates<sup>9,10</sup> have been reported to be effective activators for this transformation, however, perchlorates are potentially explosive.<sup>16</sup> Moreover,  $\text{Mg}(\text{ClO}_4)_2$  should be anhydrous in order to obtain good yields.<sup>10</sup> In recent years, iodine has been used as a Lewis acid catalyst for various organic transformations.<sup>17</sup> We recently reported on the effectiveness of iodine in catalysing Mukaiyama aldol reactions.<sup>18</sup> We describe herein an efficient and



**Scheme 1.**

convenient procedure for acetylation of alcohols under solvent-free conditions in the presence of a catalytic amount of iodine (Scheme 1).

Initially a systematic study was carried out for catalytic evaluation of iodine for acetylation of 1-octanol (Table 1). The reaction is very slow in the absence of catalyst. When the reaction was carried out in dichloromethane it was not complete in 12 h. Surprisingly, there was an abrupt change in the rate of acetylation when the reaction was carried out without additional solvent.

Several examples illustrating this novel and rapid procedure for acetylation of alcohols are presented in

**Table 1.** Acetylation of 1-octanol under different conditions<sup>a</sup>

Run	Solvent	I <sub>2</sub> (mol%)	Time	Yield (%)
1	—	Nil	72 h	42 <sup>b</sup>
2	CH <sub>2</sub> Cl <sub>2</sub> (2 mL)	10	12 h	72 <sup>b</sup>
3	—	10	1 min	>99
4	—	5	5 min	>99

<sup>a</sup> 1-Octanol: 1 mmol,  $T = 25^\circ\text{C}$ ;  $\text{Ac}_2\text{O}$ : 1.05 equiv.

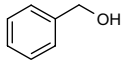
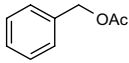
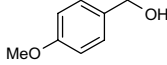
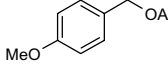
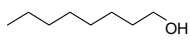
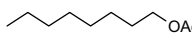
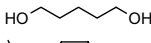
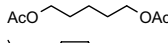
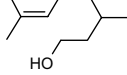
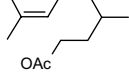
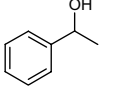
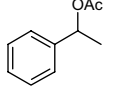
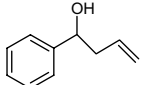
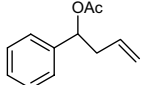
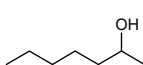
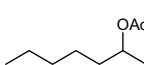
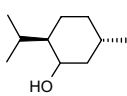
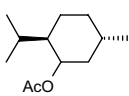


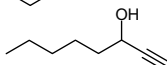
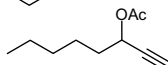
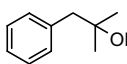
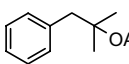
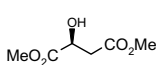
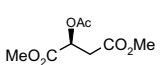


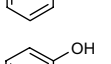
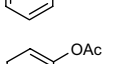
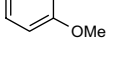
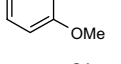
<sup>b</sup> Remainder is unreacted octanol.

Table 2. The general efficiency of this reaction is evident from the variety of hydroxy compounds including primary, secondary, tertiary, benzylic alcohols and phenols, which react in excellent yields within a very short time, primary alcohols being acetylated within a minute. In general, this method works well with a 1:1.05 M ratio of alcohol to  $\text{Ac}_2\text{O}$  in the presence of a catalytic amount of iodine (0.1 M equiv) without solvent. In the case of menthol (**1i**) 3.5 equiv of  $\text{Ac}_2\text{O}$  were used in order to solubilise the substrate. The tertiary alcohol **1i** was

acetylated in 10 min in very good yield and functional groups such as chloro, double bonds and triple bonds were not affected during the reaction. The rate of acetylation is comparable to reactions catalysed by  $\text{TMSOTf}^{12}$  but the major drawback of  $\text{TMSOTf}$  is that it is moisture sensitive.

In conclusion, iodine shows very strong catalytic activity for acetylation of alcohols when the reaction is carried out without added solvent. Near equimolar amounts of

**Table 2.** Acetylation of various alcohols catalysed by iodine<sup>a</sup>

Entry	Substrate <b>1</b>	<i>t</i> (min)	Product <sup>b</sup> <b>2</b>	Yield <sup>c</sup> (%)
a		1		>99
b		1		>99
c		1		>99
d		1		98 <sup>d</sup>
e		1		98
f		3		97
g		7		96
h		2		99
i		8		95 <sup>e</sup>
j		2		99
k		2		>99
l		10		85
m		12		97
n		1		>99
o		1		>99
p		1		>99

<sup>a</sup> Reaction conditions: substrate = 1 mmol,  $\text{Ac}_2\text{O}$  = 1.05 mmol, iodine = 0.1 mmol, 25 °C.

<sup>b</sup> Products were characterised by IR, NMR and MS spectroscopy and matched with literature data.

<sup>c</sup> Isolated yield.

<sup>d</sup>  $\text{Ac}_2\text{O}$  (2.1 equiv) were used.

<sup>e</sup>  $\text{Ac}_2\text{O}$  (3.5 equiv) were used.

alcohol and Ac<sub>2</sub>O are typically used avoiding waste and providing very simple experimental and workup procedures.

## 2. Experimental

### 2.1. General procedure for acylation

To a stirred mixture of the alcohol (1 mmol) and iodine (0.1 mmol), Ac<sub>2</sub>O (1.05 mmol) was added and stirring continued at room temperature for the appropriate time (TLC). After completion of the reaction, iodine was destroyed by adding saturated sodium thiosulfate solution (5 mL). Diethyl ether (10 mL) was added and the phases were separated. The organic phase was washed with saturated NaHCO<sub>3</sub> solution (2 × 5 mL), brine (2 × 5 mL), dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated to give the pure product.

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