

## A Facile and Efficient Method for Catalytic Acetylation of Alcohols with Acetic Acid

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Protection of alcohol as corresponding acetate ester is one of the most fundamental and widely used strategies in contemporary organic chemistry.<sup>1</sup> Usually acetyl chloride and acetic anhydride are employed as the acylating agents in the presence of a convenient acidic or basic catalyst.<sup>2</sup> However, both the reagents are corrosive and lachrymator and involve the use of tertiary amines such triethylamine, pyridine and DMAP and therefore are not always ideal. Several catalytic systems involving Lewis acids<sup>3-7</sup> and metal triflates<sup>8-13</sup> have been explored for the esterification of alcohols using acetic anhydride. Recently acetic acid, which is the precursor of acetic anhydride, was used as acylating agent in presence of ferric perchlorate,<sup>14</sup> however perchlorates are potentially explosive. Therefore, development of simple and environmentally friendly method for acetylation of alcohols utilizing inexpensive and readily available reagent is still desirable. Among the various transition metals, iron is one of the most abundant metals on the earth, and one of the most inexpensive and environmentally friendly ones. Therefore recently iron based catalyst and reagents are frequently used to address economic and ecological challenges in various organic transformations.<sup>15</sup> Among the various reagents used in organic transformations, phase transfer reagents attract attention due to its unique features and potentiality in organic synthesis. These reagents have amphiphilic cations (mostly quaternary ammonium ions) as carriers of the catalyst unit to solubilize it in the reaction medium. Moreover, these types of phase-transfer reagents are also able to catalyze organic transformations,<sup>16</sup> but to the best of our knowledge the utilization of these types of reagents as catalyst are rarely exploited in single phase reaction. In this communication we wish to report the use of easily accessible and inexpensive cetyltrimethylammonium ferricyanide (CTAFeCN)<sup>17</sup> as a useful catalyst in acetylation various hydroxyl groups.

Initially to establish the catalytic activity of CTAFeCN in esterification reaction, we carried out a series of reactions using 1-octanol as model substrate. In a typical procedure, to a solution of the alcohol (1 mmol) and CTAFeCN (0.05 mmol), acetic acid (3 mL) was added and the reaction mixture was stirred at room temperature for 24 h. It was found that at room temperature the reaction did not proceed and substantial amount of 1-octanol was recovered from the reaction mixture (Table 1, entry 1). However, increase of the reaction temperature to 60 °C led to completion of reaction within 5 h (vide TLC) with 85% isolated yield (entry 2). Interestingly, increase of the reaction temperature up to 80 °C, resulted in the complete reaction within

**Table 1.** Acetylation of 1-octanol under different conditions

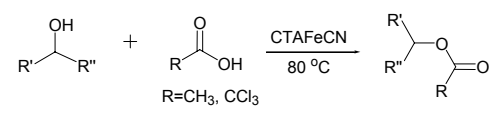
Entry	CTAFeCN (mmol)	Temperature (°C)	Time (h)	Yield (%)
1	0.05	rt	24	-
2	0.05	60	5	85
3	0.05	80	1	95
4	Nil	80	2	-
5	0.025	80	2	60

Yield refers to isolated pure acetate

1 h with 95% yield (entry 3). But the acetylation reaction did not proceed at all in absence of CTAFeCN (entry 4) and use of 0.025 mmol of catalyst led to dramatic decrease in isolated yields (entry 5). Fe (III) reagents are usually known for its strong oxidizing property.<sup>18</sup> But due to low oxidation potential of some ferric complexes, they were unable to oxidize alcohol<sup>19</sup> to the corresponding carbonyl compounds. In this acetylation reaction, the exact role of CTAFeCN has not been understood at this point, it may activate the acyl moiety by coordination, prompting the acetylation process.

To evaluate the scope and limitations of the current procedure, reactions of a wide array of electronically and structurally diverse alcohols were exposed to the above reaction conditions. The results were depicted in the Table 2. The effectiveness of the current method is evident from the fact that the variety hydroxy compounds including allylic, secondary, cyclic, aromatic, and benzylic were acetylated in high yield under the reaction conditions (entry 2-12). Dihydroxy compounds, such ethylene glycol could also be acetylated in high yield under the aforesaid reaction conditions (entry 9). Current method is also feasible for the acetylation of steroidal hydroxy group in high yield (entry 12). However this methodology is not compatible with tertiary alcohol. Use of substituted acetic acid e.g. trichloroacetic acid also led to the formation of corresponding acetate in good yields (entry 13-16). The sensitive functional groups such as bromo, double bonds, and triple bonds remained unaffected under the current reaction conditions.

In conclusion, we have developed a simple iron based catalyst for acetylation of alcohols and phenols using inexpensive and readily available acetic acid as acetyating agent in base free

**Table 2.** Acetylation of alcohols with acetic acid catalyzed by CTAFeCN


Entry	Substrate	R	Time (h)	Product	Yield (%)
1		CH <sub>3</sub>	1		95
2		CH <sub>3</sub>	1		90
3		CH <sub>3</sub>	1.5		94
4		CH <sub>3</sub>	3		78
5		CH <sub>3</sub>	1		92
6		CH <sub>3</sub>	2		88
7		CH <sub>3</sub>	1		92
8		CH <sub>3</sub>	1		90
9		CH <sub>3</sub>	4		85
10		CH <sub>3</sub>	1		97
11		CH <sub>3</sub>	2		85
12		CH <sub>3</sub>	3		85
13		CCl <sub>3</sub>	2		80
14		CCl <sub>3</sub>	1		90
15		CCl <sub>3</sub>	3		80
16		CCl <sub>3</sub>	1		85

All the products were characterized by <sup>1</sup>H NMR, IR, and Mass spectra. Yield refers to pure isolated yield.

conditions. The reaction is unique in using a phase transfer reagent as a catalyst in a single phase reaction.

### Experimental

**General procedure for acetylation.** To a stirred solution of 1-octanol (1 mmol) in acetic acid (3 mL), CTAFeCN (0.05 mmol) was added and heated at 80 °C for appropriate time

(TLC). After completion, the reaction mixture was allowed to cool to room temperature and diluted with ether (30 mL). The reaction mixture was filtered through celite pad and the filtrate washed with brine (3 × 20 mL). The organic phase was dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated under reduced pressure. The residue was chromatographed (silica gel, ethyl acetate:*n*-hexane = 1:10) to give the pure acetate (95% yield). IR (KBr) cm<sup>-1</sup> 1238.9, 1743.5. <sup>1</sup>H-NMR (400 MHz in CDCl<sub>3</sub>) δ 0.87 (t, *J* = 6.8 Hz, 3H), 1.23-1.32 (m, 10H), 1.57-1.69 (m, 2H), 2.08 (s, 3H), 4.08 (t, *J* = 6.8 Hz, 2H).

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- To a stirred solution of cetyltrimethylammonium chloride (3 mmol) in water (50 mL) was slowly added aqueous solution of K<sub>3</sub>[Fe(CN)<sub>6</sub>] (1 mmol, 10 mL) at room temperature. The mixture was stirred continuously until yellow solids were formed. The resulting reaction mixture was filtered off and washed with water and dried under vacuum to afford cetyltrimethylammonium ferricyanide (71% yield based on K<sub>3</sub>[Fe(CN)<sub>6</sub>]). IR (KBr) cm<sup>-1</sup> 2920.4, 2114.4, 1465.1. <sup>1</sup>H-NMR (400 MHz in CDCl<sub>3</sub>) δ 0.80 (t, *J* = 4.2 Hz, 9H), 1.13-1.25 (m, 78H), 2.50 (t, *J* = 6.2 Hz, 6H), 3.20-3.34 (m, 33H). Elemental analysis: Calculated: C, 71.30%; H, 11.80%; N, 11.80%. Found: C, 70.80%; H, 12.00%; N, 11.50%.
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