

친환경 촉매 Iron (III) phosphate: 실온/무용매 반응조건에서 알코올과 페놀의 선택적인 아실화 반응

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Iron (III) Phosphate as a Green and Reusable Catalyst Promoted Chemo Selective Acetylation of Alcohols and Phenols with Acetic Anhydride Under Solvent Free Conditions at Room Temperature

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요약. 알코올과 페놀 계 화합물을 아실화시키는 반응에서, iron (III) phosphate 촉매를 사용했을 때에, 좋은 수율로 아실화 화합물을 얻었다. Iron (III) phosphate 촉매는 또한 친환경 반응에 재사용할 수 있는 친환경 촉매이다.

주제어: 아실화 반응, 알코올과 페놀, 무용매 (Solvent free), 촉매, Iron (III) phosphate

ABSTRACT. Iron (III) phosphate was employed as an efficient catalyst for the chemo selective acetylation of alcohols and phenols under solvent free condition at room temperature and with high yields. Iron (III) phosphate is also a potential green catalyst due to solid intrinsically, reusable and with high catalytic activity.

Keywords: Acetylation, Alcohols and Phenols, Solvent free, Catalyst, Iron (III) phosphate

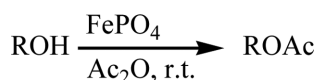
INTRODUCTION

Iron (III) phosphate, a cheap and safe catalyst, is prepared¹ and purchased as commercially. Iron (III) phosphate² is being petitioned for use as a pesticide (molluscicide) to prevent extensive damage to and/or destruction of vegetables, citrus and non-citrus fruit, berries, field crops, ornamentals, greenhouse and nursery plants, lawns, and gardens for seed production. It is known that iron (III) phosphate lacks toxicity for fish, birds, and non-target insects such as rove beetles, ground beetles and earthworms. It is a stable compound that does not persist or form undesirable products in the environment under normal conditions of use and storage. Using iron (III) phosphate as a molluscicide is very compatible with sustainable agriculture. Not only does ferric phosphate safe-environmental, but also allows organic growers to effectively control a devastating garden pest. Chemically, iron (III) phosphate is very stable and will not dissociate unless in

the presence of concentrated acid which is not present in natural surroundings.

So far, iron (III) phosphate has limitedly been employed in transformation of organic compounds such as the selective oxidation of CH₄ to CH₃OH,³ benzene to phenol,⁴ one-pot synthesis of dihydropyrimidinones and thiones⁵ and one-pot three component synthesis of 2,4,5-triaryl-ated imidazoles.⁶

On the other hand, acetylation of hydroxyl groups is a frequently used transformation method in organic synthesis. Among the various protecting groups used for the hydroxyl function, acetyl is the most convenient group in view of its easy introduction, being stable to the acidic reaction conditions, and also easily removable by mild alkaline hydrolysis.⁶ Commonly used reagent for this reaction uses acetic anhydride in the presence of an acid or base catalyst.⁷ Various metal salts such as CoCl₂,⁸ TiCl₄-AgClO₄,⁹ Me₃SiCl,¹⁰ LiClO₄,¹¹ Mg(ClO₄)₂,¹² and some metaltriflates such as Se(OTf)₃,¹³ MeSiOTf,¹⁴ In(OTf)₃,¹⁵



Scheme 1. Aliphatic and benzylic alcohols and phenols were acetylated by acetic anhydride using FePO₄.

Cu(OTf)₂,¹⁶ and Bi(OTf)₃,¹⁷ have been investigated to meet the demands for more efficient and selective methods. In spite of these waves of interest, due to the importance of acetylation, it is necessary to develop inexpensive, eco-friendly and reusable catalyst to promote acetylation process. Therefore, in continuing previously our research to introduce the efficient and green method for the acetylation of hydroxyl groups using eco-friendly catalyst,¹⁸ herein iron (III) phosphate is reported as a green, reusable, recyclable, safe-environmentally, inexpensive and commercially catalyst for the acetylation of alcohols and phenols under solvent-free conditions at room temperature (*Scheme 1*).

RESULTS AND DISCUSSION

In order to establish the optimized reaction condition, we have performed study using 1.0 mmol benzyl alcohol as a model substrate in the presence of 2.5 mmol acetic acid without catalyst. The reaction did not proceed for 48 h. Thus 5 mol% FePO₄ was added to the reaction mixture. Conversion was 15% after 48 h. Increasing 10 mol% of the catalyst and 10 mmol acetic acid didn't affect on conversion. Ongoing, 2.5 mmol acetic anhydride was subjected as acetylating agent. In this case, the reaction was completed for 10 h and so was chosen as a model reaction. To aim giving generality to reaction model, acetylation of a variety of alcohols and phenols with acetic anhydride was carried out in the presence of FePO₄ at room temperature. The results have been listed in *Table 1*. As can be seen, the yields of the acetylation hydroxyl group compounds with acetic anhydride were excellent.

Accordingly, various primary and secondary benzyl alcohols having electron donating and electron withdrawing substituent undergo acetylation in high yield in most cases (entries 10-15). This indicates that electronic effects of substituent groups don't have influence on the acetylation reaction. In addition to benzylic alcohols, this catalyst is effective for the variety of aliphatic alcohols (entries 1-9). Primary alcohols acetylated within less time than secondary and tertiary alcohols. The longer reaction time could be due to the steric effect exerted by bulky groups. It is very interesting to note that tertiary and secondary alcohols such as *t*-butanol can also be acetylated with satisfactory yield and there was no elimination product in the reaction mixture.

Also, isoamyl acetate is a kind of flavor reagent with fruit taste. It is traditionally prepared with H₂SO₄ as catalyst.⁷ The use of H₂SO₄ often causes the problems such as corrosion for equipments and pollution for environment. Until now, the tried replaces include FeCl₃, CuSO₄, ferric tri-dodecane sulfonate, FeCl₃/MnO₂, KH₂PO₄, sulfonated polystyrene, TiSiW₁₂O₄₀/TiO₂ and so on,⁸⁻¹⁴ but some shortcomings limit them being widely applied in industry such as higher wastage for materials, lower yield of product or higher cost in catalyst preparation. Based on these reasons, isoamyl alcohol was chosen as a starting material and isoamyl acetate was resulted in 95% yield (entry 5).

This method tolerates other functionalities on the substrate such as double and triple bonds. In fact, allyl, cinnamyl and propargyl alcohols were subjected as unsaturated alcohols. We would have expected to carry out hydration reaction on double and triple bond in acidic media beside acetylation reaction, so far hydrated products didn't observed at all (entries 16-18). Heterocyclic furfuryl alcohol gives corresponding acetate with excellent yield (entries 26). This may recommend that adjacent heterocyclic ring have no influence at all on the reaction.

Interestingly, phenols too underwent acetylation smoothly under the same reaction condition. Phenols with activating and deactivating groups altogether carried out acetylation rapidly with very high yield (entries 19-25). Strongly electron-withdrawing group such as nitro substituent produces 95% yield (entries 22).

In order to investigate further chemo selectivity of this protocol, 3- and 4-hydroxy benzaldehydes were utilized in acetylation reaction (entries 24, 25). It was observed that aldehydic carbonyl group didn't change at all. In these cases, IR spectra showed wave number; $\nu_{\text{max}}=1699.16$, 1703.84 cm^{-1} for aldehydic carbonyl group of 3- and 4-formylphenyl acetate while 1666.03 , and 1667.09 cm^{-1} were for aldehydic carbonyl group of 3- and 4-hydroxy benzaldehyde. It is depicted that intermolecular hydrogen bonding in substrate has been disappeared after acetylation of hydroxyl group and absorption band of the aldehydic carbonyl group has shifted to higher frequency.

Therefore, this method introduces chemo selective acetylation of hydroxyl group compounds using FePO₄ as a green, economically and reusable catalyst which can efficiently promote the acetylation with the advantages of wide scope of substrates such as aliphatic, benzylic, allylic, propargylic alcohols and phenols under solvent free conditions, excellent recyclability, insensitivity to air and water, and extremely convenient from a practical and facile separation work-up point of view.

Table 1. Acetylation of aliphatic, allylic, benzylic, propargylic alcohols and phenols was catalyzed by FePO₄

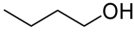
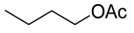
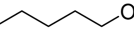
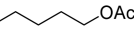
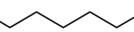
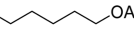


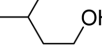



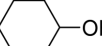
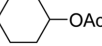
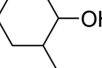
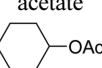


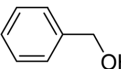
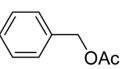
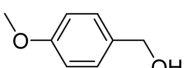
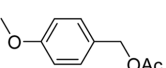
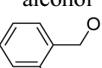
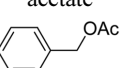
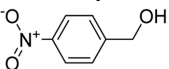
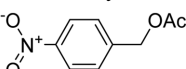
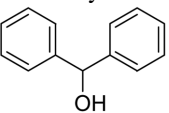
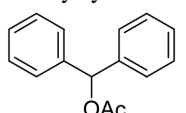
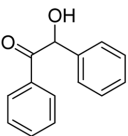
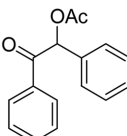


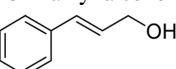
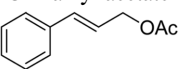


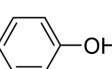
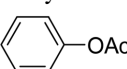
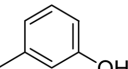
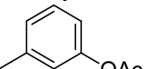
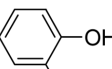
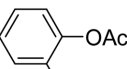
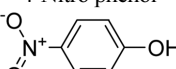
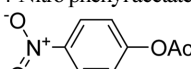
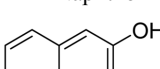
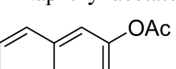
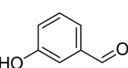
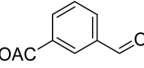
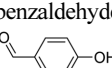
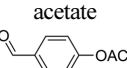


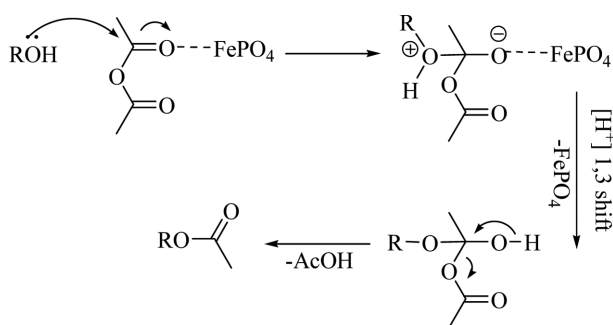
Entry	ROH	Time(h)	ROAc	Yield% ^a
1	1-Butanol 	10	1-Butyl acetate 	88
2	n-Amyl alcohol 	8	n-Amyl acetate 	88
3	1-Hexanol 	8	Methyl acetate 	98
4	2-Methyl-1-propanol 	10	2-Methyl-1-propyl acetate 	86
5	Isoamyl alcohol 	11	Isoamyl acetate 	95
6	2-Butanol 	13	2-Butyl acetate 	85
7	Cyclohexanol 	15	Cyclohexyl acetate 	92
8	2-Methyl cyclohexanol 	15	2-Methyl cyclohexyl acetate 	95
9	tert-Butyl alcohol 	15	tert-Butyl acetate 	91
10	Benzyl alcohol 	10	Benzyl acetate 	92
11	4-Methoxy benzyl alcohol 	10	4-Methoxy benzyl acetate 	93
12	2-Methyl benzyl alcohol 	10	2-Methyl benzyl acetate 	87
13	4-Nitro benzyl alcohol 	12	4-Nitro benzyl acetate 	86
14	Benzhydrol 	13	Benzhydryl acetate 	96

Table 1. (continued)

15	2-Hydroxy-1,2-diphenylethanone 	13	2-Oxo-1,2-diphenyl-ethyl acetate 	85
16	Allyl alcohol 	13	Allyl acetate 	89
17	Cinnamyl alcohol 	13	Cinnamyl acetate 	90
18	Propargyl alcohol 	14	Propargyl acetate 	90
19	Phenol 	12	Phenyl acetate 	94
20	m-Cresol 	11	m-Cresyl acetate 	96
21	o-Cresol 	11	o-Cresyl acetate 	92
22	4-Nitro phenol 	12	4-Nitro phenyl acetate 	95
23	2-Naphthol 	11	2-Naphthyl acetate 	95
24	3-Hydroxy benzaldehyde 	11	3-Formylphenyl acetate 	94
25	4-Hydroxy benzaldehyde 		4-Formylphenyl acetate 	87
26	Furfuryl alcohol 		Furfuryl alcohol 	96

^aYields refer to GC analysis.

The plausible duty of the FePO₄ may be due to the activation of carbonyl group of acetic anhydride by coordination, triggering the acetylation process with concomitant regeneration of FePO₄, followed by the loss of acetic acid (Scheme 2). This mechanism is in adapt to the catalytic



Scheme 2. Proposed mechanism for the acetylation of alcohols and phenols using FePO_4 .

nature of FePO_4 in this reaction.

EXPERIMENTAL

IR spectra were recorded on Perkin Elmer FT-IR spectrometer did scanning between $4000\text{--}400\text{ cm}^{-1}$. ^1H NMR spectra were obtained on Bucker DRX-400MHZ NMR instrument. All starting materials purchased from Merck Company and used of them without further purification.

Acetylation of benzyl alcohol with acetic anhydride by FePO_4 . Typical procedure

To mixture of 0.108 g benzyl alcohol (1.0 mmol), 0.50 g acetic anhydride (2.5 mmol) and 0.0075 g FePO_4 (0.05 mmol) was added. The mixture was stirred at ambient temperature for 10 h. The progress of reaction was monitored by TLC (eluent, n-hexane: ethyl acetate, 4:1). After completion of the reaction, 15 ml CH_2Cl_2 was added and the catalyst was filtrated off. Liquor moderate was neutralized by 15 ml sodium bicarbonate (10%) and extracted with CH_2Cl_2 . The organic phase was dried by Na_2SO_4 and evaporated under reduce pressure. Then, benzyl acetate was resulted in 92% yield (entry 10, Table 1). IR (KBr) 3034(m), 2952(w), 1739(s), 1497(m), 1454(m), 1382(m), 1364(m), 1233(s), 1027(s), 750(s) cm^{-1} . ^1H NMR (400 MHZ, CDCl_3): $\delta = 2.00$ (s, 3H), 5.01 (s, 2H), 7.32-7.37 (m, 5H).

Recycling of the catalyst

At the end of the reaction, the catalyst was removed, washed with dichloromethane and ethyl acetate, dried at 80 for 1 h, and reused in another reaction. The recycled catalyst was subjected to three reactions without appreciable loss in its activity.

CONCLUSION

In conclusion we have developed a catalytic and sol-

vent less system for acetylation of alcohols and phenols using available, inexpensive and extremely safe reagent such as iron(III) phosphate for the mild and high yielding acetylation of alcohols and phenols. The salient features of these reactions are, use of 2.5-1.0 equivalent of acetic anhydride to substrate and catalytic amounts of iron(III) phosphate which are concomitant with solvent less and catalytic nature of the reaction. Neither use of solvent nor elevation of reaction temperature makes operations more convenient. The catalyst can be recycled at least three times without significant lose of catalytic activity. We believe iron(III) phosphate is one of the greenest catalyst which has ever been used for acetylation of alcohols and phenols and this heterogeneous catalytic and solvent less acetylation will find many applications in organic synthesis and industry.

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