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Zinc perchlorate hexahydrate [$Zn(ClO_4)_2{\cdot}6H_2O$] as acylation catalyst for poor nucleophilic phenols, alcohols and amines: Scope and limitations

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Abstract

Commercially available zinc perchlorate hexahydrate [$Zn(ClO_4)_2{\cdot}6H_2O$] was found to be a highly efficient catalyst for acylation of electron deficient phenols, sterically hindered alcohols and electron deficient and sterically hindered amines. The acetylated derivatives were obtained in excellent yields under solvent-free conditions and at room temperature. However, the reaction of highly electron deficient and sterically hindered phenol, e.g., 2,4-dinitrophenol required heating at 80 °C. In case of reactions with alkoxy or dialkoxy benzylic alcohols, a complex product mixtures were formed containing the corresponding dibenzylic ethers. The catalyst was found to be of general use with respect to other acylating agents such as propionic, *iso*-butyric, pivalic, benzoic and chloroacetic anhydrides. However, the rate of acylation was influenced by the steric and electronic factors of the anhydrides and followed the order $Ac_2O > (PhCO)_2O > (EtCO)_2O > (^iPrCO)_2O > (^tBuCO)_2O \gg (ClCH_2CO)_2O$. Benzoylation and pivalation of phenols (including electron deficient phenols), dihydric phenol and sterically hindered alcohol afforded excellent yields. The catalytic activity of various zinc compounds was found to be of the order $Zn(ClO_4)_2{\cdot}6H_2O > ZnI_2 \sim ZnBr_2 > ZnCl_2 \gg Zn(OAc)_2 > ZnCO_3$ and was parallel to the acidic strength of the corresponding protic acids.

Keywords: Acylation; Electron deficient phenols; Sterically hindered phenols; Sterically hindered alcohols; Electron deficient and sterically hindered amines; Electronic effect; Steric effect; $Zn(ClO_4)_2{\cdot}6H_2O$; Catalyst; Solvent-free

1. Introduction

The presence of the phenolic/alcoholic hydroxyl and amino groups in a wide spectrum of biologically active compounds necessitates the manipulation of the chemical reactivity of these functional groups during the synthesis of multifunctional synthetic targets possessing one or more of these groups. The protection of phenols, alcohols and amines as their acylated derivatives [1] is a straightforward approach due to the feasibility of regeneration of the parent compound by nucleophilic deprotection [2]. Acylation reactions are frequently used in the preparation of drug candidate molecules and comprise 12% of the total chemical reactions involved in the synthesis of drugs [3]. Acylation is normally achieved by treatment with anhydrides in the presence of suitable catalyst. Various organic (e.g., DMAP and Bu_3P) and inorganic (e.g., halides, triflate and tetrafluoroborate of transition, rare earth and alkali metals) catalysts have been employed for this purpose [1]. Recent efforts for the development of various catalysts such as NBS [4], solid acids [5], metal salts, e.g., perchlorates [6], halides [7], triflates [8], metal complex [9] and the use of ionic liquid [10] highlight the importance of heteroatom acylation.

The reported methodologies suffer from one or more of the following disadvantages: (i) potential health hazard (DMAP is highly toxic (e.g., intravenous LD_{50} in the rat: 56 mg/kg) [11] and Bu_3P is flammable (flash point: 37 °C) [12], need to use halogenated solvents), (ii) difficulty in handling (Bu_3P undergoes aerial oxidation and triflates are moisture sensitive), (iii) high cost of the catalysts (e.g., triflates), (iv) requirement of special efforts to prepare the catalysts [$Bi(OTf)_3$ [13], Nafion-H, yttria-zirconia, $AlPW_{12}O_{40}$, and Mn(haacac)Cl], (v) the lack of atom economy (use of excess of acetylating agents), (vi) stringent reaction conditions and the requirement of longer reaction times, (vii) in many cases the reported acylation methodologies are applicable to alcohols only and not suitable for acid-sensitive substrates and (viii) few catalysts are reported

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for acylation of challenging substrates such as electron deficient and sterically hindered phenols, sterically hindered alcohols and electron deficient as well as sterically hindered amines. Thus, there is a need for development of a suitable catalyst for acylation of challenging substrates.

In continuation of our efforts for development of newer and efficient acylation catalysts [14], we thought that a metal salt derived from a strong protic acid should be an ideal choice. On this account, metal triflates are very strong Lewis acids due to the large negative H_0 value of −14.1 of TfOH [15] and have found application as acylation catalysts [8]. However, the TfOH liberated *in situ* as a result ligand exchange reaction between the metal triflates and the substrates may be the actual catalytic agent [16] during the triflate catalyzed acylation reactions and might be responsible for the potential side reactions (e.g., dehydration, rearrangement, etc.) with acid-sensitive substrates. Thus, metal triflate-catalyzed acylation reactions are often require low temperatures (−8 to −60 °C) and excess of acylating agent. This brought the attention to $HNTf_2$ as it is a weaker Brønsted acid than TfOH [17] and ligand exchange has not been observed with triflimides [18]. This led us and others to develop metal triflimides as acylation catalysts [19]. However, triflimides are costly and some are not available commercially and involve a high cost for preparation and therefore are not good contender for industrial applications. Moreover, the strong acidic property of $Sc(NTf_2)_3$ necessitates the use of solvent, large excess of Ac_2O and low temperature (−20 °C) for substrates that are likely to experience side reaction (e.g., tertiary alcohol) [19b]. Thus, we diverted our attention to $HClO_4$ as it is the next strongest protic acid. Our earlier study demonstrated that $HClO_4$–SiO_2 is an excellent catalyst system for heteroatom acylation [14a] and recently we found this to be effective for dithiolane/dithiane [20] and carbamate [21] formation. However, special effort is needed for its preparation and it tends to loose catalytic efficiency on storing for long period due to absorption of moisture and requires reactivation by heating at ∼100 °C under vacuum prior to use. Thus, we thought of metal perchlorates as suitable alternatives. Although $LiClO_4$ was shown to have catalytic property for acetylation of alcohols [6a], subsequently $BiOClO_4{\cdot}H_2O$ [14b] and $Mg(ClO_4)_2$ [6b,14c] were found to be superior to $LiClO_4$. That $Mg(ClO_4)_2$ possesses a versatile 'electrophilic activation' property was demonstrated by its application as catalyst for imine formation [22]. However, the high cost of $BiOClO_4{\cdot}H_2O$ does not make it suitable for large scale application and the catalytic efficiency of $Mg(ClO_4)_2$ decreases on being exposed to air/moisture [6b,14c].

We felt that the comparable Z^2/r values of 5.56 and 5.33 $e^2\,m^{-10}$ of Mg^{2+} and Zn^{2+} ions [23], respectively, should make the corresponding perchlorates equally effective 'electrophilic activating' agents but the higher hydrolysis constant (pK_h) value of 11.42 of Mg^{2+} compared to that of 9.60 of Zn^{2+} [24] should make the zinc perchlorate less susceptible to moisture (non-anhydrous conditions). Thus, commercially available $Zn(ClO_4)_2{\cdot}6H_2O$ should be an efficient catalyst. After the completion of this study, $Zn(ClO_4)_2{\cdot}6H_2O$ was reported as acylation catalyst [6c]. However, this report deals with alcohols (good nucleophiles) and only two examples of phenols. As phenols have poor nucleophilic property compared to alcohols we shifted our focus towards more challenging substrates and planned to elaborate the scope and limitations of $Zn(ClO_4)_2{\cdot}6H_2O$ for acylation of sterically hindered and electron deficient phenols, sterically hindered alcohols and electron deficient and sterically hindered amines being inspired by our recent observations on the catalytic property of $Zn(ClO_4)_2{\cdot}6H_2O$ for acylal formation [25] and thia-Michael addition reaction [26].

2. Results and Discussion

To find out the efficiency of $Zn(ClO_4)_2{\cdot}6H_2O$ as a general acylation catalyst for electron deficient (poor nucleophilic) phenol, we choose 4-nitrophenol (**1**) as a representative electron deficient phenol and treated with various anhydrides such as acetic, propionic, *iso*-butyric, pivalic, benzoic and chloroacetic anhydrides under solvent-free conditions (Table 1). Our initial attempts for reaction with acetic anhydride showed that excellent conversion to 4-nitrophenylacetate took place after 30 min at room temperature but the reactions with higher anhydrides took longer times at room temperature. However, the reactions were completed in 2–5 min at 80 °C under solvent-free conditions affording the corresponding acylated derivatives in excellent yields (82–100%) except that the reaction with chloroacetic anhydride formed the 4-nitrophenyl chloroacetate in 60% yield after 3 h. The rate of acylation was influenced by the steric and electronic factors of the anhydrides and followed the order $Ac_2O > (PhCO)_2O > (EtCO)_2O > (^iPrCO)_2O > (^tBuCO)_2O \gg (ClCH_2CO)_2O$. The larger amount of the anhydride (1.5 equiv.) and longer time (5 min) required for the reactions with $(EtCO)_2O$, $(^iPrCO)_2O$ and $(^tBuCO)_2O$ compared to those required for the reaction with Ac_2O (1.2 equiv. and 2 min) were due to the steric effect of the alkyl groups of the former anhydrides (compare entry 2 with entries 3–5, Table 1). The requirement of 1.5 equiv. of $(PhCO)_2O$ as against 1.2 equiv. of Ac_2O (compare entries 2 and 6, Table 1) was due to the combined effect of the steric and electronic factors of the phenyl group in $(PhCO)_2O$. The phenyl group makes the carbonyl group in $(PhCO)_2O$ less electrophilic due to the resonance (electronic effect). The inferior yield and longer reaction time

Table 1
Acylation of **1** with various anhydrides catalysed by $Zn(ClO_4)_2{\cdot}6H_2O$[a]

Entry	Anhydride	Equiv.[b]	Time (min)	Yield (%)[c]
1	Ac_2O	1	30	100[d]
2	Ac_2O	1.2	2	100
3	$(EtCO)_2O$	1.5	5	93
4	$(^iPrCO)_2O$	1.5	5	88
5	$(^tBuCO)_2O$	1.5	5	82
6	$(PhCO)_2O$	1.5	2	100
7	$(ClCH_2CO)_2O$	1.5	180	60

[a] **1** (2.5 mmol) was treated with the anhydride at 80 °C (except for entry 1) in the presence of $Zn(ClO_4)_2{\cdot}6H_2O$ (1 mol%).
[b] Molar equivalent with respect to the phenolic substrate.
[c] Isolated yield of the corresponding acylated derivative.
[d] The reaction was carried out at room temperature.

Table 2
Reaction of **1** with Ac_2O catalysed by various zinc salts[a]

Entry	Catalyst	Yield (%)[b,c]
1	$Zn(ClO_4)_2·6H_2O$	100
2	ZnI_2	89
3	$ZnBr_2$	96
4	$ZnCl_2$	86
5	$ZnCO_3$	45
6	$ZnCO_3 + HClO_4$[d]	73
7	$Zn(OAc)_2$	65[e]

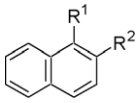
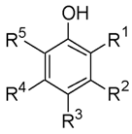
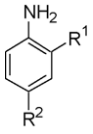
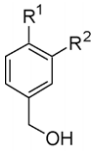
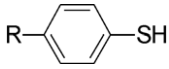
[a] **1** (2.5 mmol) was treated with Ac_2O (2.5 mmol) at room temperature for 30 min (except for entry 8) in the presence of catalyst (1 mol%) (except for entry 7) under solvent-free condition.
[b] Isolated yield of 4-nitrophenylacetate.
[c] The unreacted **1** was recovered wherever applicable.
[d] The reaction was carried out in the presence of 2 equiv. (with respect to $ZnCO_3$) of $HClO_4$ (48% aqueous solution).
[e] The reaction was carried out for 60 min.

observed during the reaction with $(ClCH_2CO)_2O$ were due to the poor electrophilicity of the carbonyl group in $(ClCH_2CO)_2O$ in addition to the steric effect of the chloromethyl group.

To find the role of the counter anion, zinc salts of various protic acids such as $Zn(ClO_4)_2·6H_2O$, ZnI_2, $ZnBr_2$, $ZnCl_2$, $ZnCO_3$ and $Zn(OAc)_2$ were used as catalyst during the reaction of **1** with acetic anhydride (Table 2). The best result was obtained with $Zn(ClO_4)_2·6H_2O$ (yield 100%). 4-Nitrophenylacetate was formed in 86–96% yields with ZnI_2, $ZnBr_2$ and $ZnCl_2$. The use of $Zn(OAc)_2$ and $ZnCO_3$ provided moderate yields (45–65%). The catalytic activity followed the order $Zn(ClO_4)_2·6H_2O > ZnI_2 \sim ZnBr_2 \sim ZnCl_2 \gg Zn(OAc)_2 > ZnCO_3$ and was in consonance with the relative acidic strength of the respective protic acids [27]. That the perchloric acid salt is a better catalyst was further demonstrated by the observation that when, in a separate experiment, 2 equiv. of $HClO_4$ (48% aqueous solution) was added to the reaction mixture of the $ZnCO_3$-catalysed reaction, 4-nitrophenylacetate was formed in 73% yield (entry 7, Table 2) as compared to a 45% yield obtained when the reaction was carried out using $ZnCO_3$ alone as the catalyst. Thus, the *in situ* formed $Zn(ClO_4)_2$, by reaction of $HClO_4$ with $ZnCO_3$, was the actual catalytic agent. However, the inferior yield obtained in this case as compared to the use of commercially available catalyst (compare entries 1 and 6, Table 2) was due to the fact that the excess amount of water (as a 48% aqueous $HClO_4$ was used) decreased the catalytic property of the *in situ* formed $Zn(ClO_4)_2$.

To establish the general applicability of $Zn(ClO_4)_2·6H_2O$ as an acetylation catalyst, various phenols, electron deficient amines, sterically hindered alcohol and aryl thiols were treated with acetic anhydride (Table 3). Excellent results were obtained in each case affording the corresponding *O*-, *N*- and *S*-acetylated derivatives in 75–100% yields after 5–60 min at room temperature under solvent-free conditions. The catalyst was compatible with various functional groups such as OMe, Br, COMe, CO_2R, CN and NO_2 that are expected to undergo competitive complex formation with the catalyst. The excellent 'electrophilic activation' property of $Zn(ClO_4)_2·6H_2O$ was demonstrated by the high yields obtained for phenols having electron withdrawing groups

Table 3
$Zn(ClO_4)_2·6H_2O$-catalysed reaction of different phenols, amines, alcohols and thiols with Ac_2O[a]

Entry	Substrate	Time (min)	Yield (%)[b,c]
			
1	R^1=H; R^2=OH	10	90
2	R^1=OH; R^2=H	15	90
			
3	R^1=R^2=R^4=R^5=H; R^3=COMe	30	85
4	R^1=COMe; R^2=R^3=R^4=R^5=H	30	75
5	R^1=R^2=R^4=R^5=H; R^3=CO_2Me	60	85
6	R^1=R^2=R^4=R^5=H; R^3=CO_2Et	60	91
7	R^1=R^2=R^4=R^5=H; R^3=CO_2Pr^i	60	96
8	R^1=R^2=R^4=R^5=H; R^3=CN	30	85
9	R^1=CN; R^2=R^3=R^4=R^5=H	60	77
10	R^1=R^2=R^4=R^5=H; R^3=NO_2	30	93
11	R^1=NO_2; R^2=R^3=R^4=R^5=H	60	82
12	R^1=R^3=R^4=R^5=H; R^2=NO_2	60	93
13	R^1=R^3=NO_2; R^2=R^4=R^5=H	5	100[d]
14	R^1=NO_2; R^2=R^3=R^5=H; R^4=Me	30	90[d]
15	R^1=R^2=R^4=R^5=H; R^3=Br	15	81
16	R^1=OMe; R^2=R^3=R^4=R^5=H	30	93
17	R^1=R^5=Bu^t; R^2=R^4=H; R^3=Me	60	73
			
18	R^1=NO_2; R^2=H	60	75
19	R^1=R^2=NO_2	15	85
20		30	95
			
21	R^1=OMe; R^2=H	30	–[e]
22	R^1=R^2=OMe	30	–[e]
			
23	R=H	60	90
24	R=Me	60	92

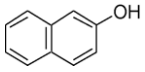
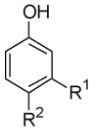
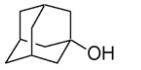
[a] The substrate (2.5 mmol) was treated with Ac_2O (2.5 mmol) in the presence of $Zn(ClO_4)_2·6H_2O$ (1 mol%) at room temperature (~25–30 °C) (except for entries 13 and 14) under solvent-free conditions.
[b] Isolated yield of the corresponding *O*-/*N*-/*S*-acetylated derivative.
[c] The products were characterized by IR, NMR, and MS.
[d] The reaction was carried out at 80 °C.
[e] A complex mixture containing the dibenzylic ether was obtained (GCMS).

(entries 3–14, Table 3) that decrease the nucleophilic property of the phenolic hydroxyl group. The requirement of heating for the reaction of 2,4-dinitrophenol (entry 13, Table 3) was due to the presence of two nitro groups, which drastically reduced the nucleophilicity of the hydroxyl group. Sterically hindered phenol e.g., 2,6-di-*tert*-butyl-4-methylphenol (entry 17, Table 3) provided the *O*-acetylated product in 73% yield. Excellent result was obtained in case of sterically hindered alcohol (entry 20, Table 3). However, substituted benzylic alcohols (entries 21 and 22, Table 3) led to the formation of a mixture of products containing the corresponding dibenzyl ether (GCMS). The presence of the nitro group(s) in 2-nitroaniline and 2,4-dinitroaniline make the amino group of these substrates poor nucleophilic. Further, the nitro group adjacent to the amino group exhibits steric hindrance for approach of the amino group towards the electrophile. Thus, although amines are, in general, very good nucleophiles and may not require any catalytic assistance for acetylation with acetic anhydride [9f], 2-nitroaniline and 2,4-dinitroaniline are difficult substrates for acetylation. Excellent yields of the corresponding acetamides were obtained at room temperature on treatment of 2-nitroaniline and 2,4-dinitroaniline with Ac_2O at room temperature under solvent-free conditions in the presence of $Zn(ClO_4)_2{\cdot}6H_2O$ (entries 18 and 19, Table 3). Surprisingly, the reaction of 2,4-dinitroaniline with Ac_2O was faster than that of 2-nitroaniline (compare entries 18 and 19, Table 3). Similar observation was made in previous reports [14b,e–g]. On the contrary, as expected, the reaction of 2-nitrophenol was much faster than that of 2,4-dinitrophenol (compare entries 11 and 13, Table 3). The faster rate of reaction of 2,4-dinitroaniline compared to that of 2-nitroaniline may be due to the reason that after the nucleophilic attack by the amino group on the carbonyl group of Ac_2O (complexed with the catalyst), the proton release from the ammonium ion intermediate becomes more facile in case of 2,4-dinitroaniline due to increased acidic property of the hydrogen atom of the NH_2 group. In case of 2-nitrophenol and 2,4-dinitrophenol, as the phenolic oxygen is inherently less nucleophilic compared to the nitrogen atom of aniline derivatives, the presence of two nitro groups in 2,4-dinitrophenol reduced the nucleophilicity of the hydroxyl group drastically and hence 2,4-dinitrophenol is less reactive compared to 2-nitrophenol.

We next planned to evaluate the catalytic efficiency of $Zn(ClO_4)_2{\cdot}6H_2O$ for benzoylation with benzoic anhydride as the steric and electronic effect of the phenyl group makes benzoic anhydride a poor electrophile. Thus, 2-naphthol, resorcinol (a representative dihydric phenol), 3-nitro, 4-nitro and 4-cyano phenols (representatives of electron deficient phenol) and adamantanol (representative sterically hindered alcohol) were treated with benzoic anhydride in the presence of $Zn(ClO_4)_2{\cdot}6H_2O$ (1 mol%) (Table 4). The *O*-benzoyl derivatives were obtained in 70–100% yields. In case of dihydric phenol (entry 2, Table 4) the *O*-di-benzoyl product was formed. The comparison of the results obtained with 3- and 4-nitrophenols (entries 3 and 4, Table 4) demonstrates the dramatic influence of the electron withdrawing substituent. It is to mention that 3- and 4-nitrophenols exhibited comparable reactivity during reaction with Ac_2O (entries 10 and 12, Table 3) as the good electrophilic property of Ac_2O was less discriminatory to the nucleophilicity of 3- and 4-nitrophenols. However, the poor electrophilicity of $(PhCO)_2O$ (due to the steric and resonance effects of the phenyl group) recognised the difference in the nucleophilic property of 3- and 4-nitrophenols. Thus, in case of 4-nitrophenol the reaction was carried out at 80 °C while in case of 3-nitrophenol benzoylation took place at room temperature as the former was less nucleophilic due to the resonance effect of the 4-nitro group. An interesting observation was made during the reaction of 3-nitrophenol. Immediately after the addition of $Zn(ClO_4)_2{\cdot}6H_2O$ to the mixture of 3-nitrophenol (solid) and benzoic anhydride (solid) a liquid melt was obtained which on further being stirred magnetically at room temperature formed a solid mass indicating the product formation (TLC, IR). This provides visual means of monitoring the reaction of solid reactants.

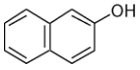
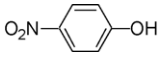
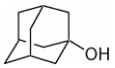
Since the presence of the *tert*-butyl group in pivalic anhydride reduces the rate of reaction of pivalic anhydride with nucleophiles, protection of hydroxyl group by pivalation is a rarely observed synthetic exercise. Hence, we planned to test the effectiveness of $Zn(ClO_4)_2{\cdot}6H_2O$ for pivalation and choose 2-naphthol, 4-nitrophenol and adamantanol as model substrates (Table 5). Excellent result was obtained with 2-naphthol and the 2-naphthyl pivalate was formed in 98% yield after 60 min at room temperature under solvent-free condition (entry 1, Table 5). The poor nucleophilicity of the hydroxyl group in 4-nitrophenol required the reaction to be carried out at 80 °C and the desired product was obtained in 82% yield after 5 min in the absence of solvent. However, the reaction of adamantanol was carried out in dichloromethane (DCM) at room temperature.

Table 4
$Zn(ClO_4)_2{\cdot}6H_2O$-catalysed reaction of phenols and sterically hindered alcohol with $(PhCO)_2O$[a]

Entry	Substrate	Time (min)	Yield (%)[b,c]
1		15	90[d]
2	 R^1=OH; R^2=H	60	60[e]
3	R^1=NO_2; R^2=H	5	70[f]
4	R^1=H; R^2=NO_2	2	100
5	R^1=H; R^2=CN	120	80[f]
6		60	89

[a] The substrate (2.5 mmol) was treated with $(PhCO)_2O$ (2.5 mmol per OH) in the presence of $Zn(ClO_4)_2{\cdot}6H_2O$ (1 mol%) at 80 °C (except for entries 3 and 5) under solvent-free conditions.
[b] Isolated yield of the corresponding *O*-benzoylated derivative.
[c] The products were characterized by IR, NMR and MS.
[d] The benzoate was formed in 90% yields in carrying out the reaction in DCM at room temperature.
[e] Yield of the dibenzoate.
[f] The reaction was carried out at room temperature.

Table 5
$Zn(ClO_4)_2{\cdot}6H_2O$-catalysed reaction of phenols and sterically hindered alcohol with $(^tBuCO)_2O$[a]

Entry	Substrate	Time (min)	Yield (%)[b,c]
1		60	98
2		5	82[d]
3		60	92[e]

[a] The substrate (2.5 mmol) was treated with $(^tBuCO)_2O$ (3.75 mmol) in the presence of $Zn(ClO_4)_2{\cdot}6H_2O$ (1 mol%) at room temperature (except for entry 2) under solvent-free conditions (except for entry 3).
[b] Isolated yield of the corresponding *O*-pivaloylated derivative.
[c] The products were characterized by IR, NMR and MS.
[d] The reaction was carried out at 80 °C.
[e] The reaction was carried out in the DCM.

3. Conclusion

In conclusion, the scope and limitations of commercially available $Zn(ClO_4)_2{\cdot}6H_2O$ was evaluated for acylation of electron deficient and sterically hindered phenols, sterically hindered alcohols and electron deficient and sterically hindered amines. The treatment of substituted benzylic alcohols with acetic anhydride in the presence of $Zn(ClO_4)_2{\cdot}6H_2O$ led to the formation of complex mixture containg the corresponding dibenzylic ether. The applicability of $Zn(ClO_4)_2{\cdot}6H_2O$ as a general acylation catalyst with respect to various anhydrides was demonstrated by the excellent yields obtained by reaction of 4-nitrophenol with acetic, propionic, *iso*-butyric, pivalic, benzoic and chloroacetic anhydrides. The rate of acylation of a common substrate with different anhydrides was influenced by the steric and electronic nature of the anhydride and was observed to follow the order $Ac_2O > (PhCO)_2O > (EtCO)_2O > (^iPrCO)_2O > (^tBuCO)_2O \gg (ClCH_2CO)_2O$. Although the acetylation was in general effective at room temperature, acylation with other anhydrides required heating. The reaction of 4-nitrophenol with chloroacetic anhydride was found to be very slow compared to that with other anhydrides. The catalytic efficiency for acylation was influenced by the counter anion associated with the zinc salt and followed the order $Zn(ClO_4)_2{\cdot}6H_2O > ZnI_2 \sim ZnBr_2 > ZnCl_2 \gg Zn(OAc)_2 > ZnCO_3$ that was parallel to the acidic strength of the corresponding protic acids. The overall advantages are: (i) use of cheap and easily available catalyst, (ii) requirement of small amount (1 mol%) of the catalyst, (iii) short reaction times, (iv) solvent-free operation and (v) high yields.

4. Experimental

The ^1H and ^{13}C NMR spectra were recorded on Bruker Avance DPX 300 (300 MHz) spectrometer in $CDCl_3$ using TMS as internal standard. The IR spectra were recorded on Nicolet Impact 400 spectrometer as KBr pellets for solid and neat for liquid samples. The reactions were monitored by TLC (silica gel-G) and Shimadzu QP 5000 GCMS. Evaporation of solvents was performed at reduced pressure, using a Büchi rotary evaporator.

4.1. Typical experimental prodecure for acetylation

A mixture of 4-nitrophenol (**1**) (345 mg, 2.5 mmol), Ac_2O (0.24 mL, 2.5 mmol) and $Zn(ClO_4)_2{\cdot}6H_2O$ (9.4 mg, 1 mol%) was stirred magnetically under neat conditions at 80 °C for 5 min. The reaction mixture was diluted with H_2O (10 mL) and extracted with Et_2O (3× 15 mL). The combined ethereal extracts were washed successively with 2% aqueous NaOH (15 mL) and saturated brine (15 mL), dried (Na_2SO_4) and concentrated under reduced pressure to afford the product (450 mg, 100%), which was in full agreement (m.p., IR, NMR, MS) with an authentic sample of 4-nitrophenylacetate [14]. All the remaining reactions were carried out following this standard procedure except that the reaction mixture was heated at room temperature, wherever applicable. In each occasion the product obtained after the routine workup was of sufficient purity (spectral data) and did not require further purification.

4.2. Typical procedure for benzoylation

A mixture of 4-nitrophenol (**1**) (345 mg, 2.5 mmol), benzoic anhydride (565 mg, 2.5 mmol) and $Zn(ClO_4)_2{\cdot}6H_2O$ (9.4 mg, 1 mol%) was stirred magnetically under neat conditions at 80 °C for 2 min. The reaction mixture was diluted with H_2O (10 mL) and extracted with Et_2O (3× 15 mL). The combined ethereal extracts were washed successively with 2% aqueous NaOH (15 mL) and saturated brine (15 mL), dried (Na_2SO_4) and concentrated under reduced pressure to afford the product (607 mg, 100%), which was in full agreement (m.p., IR, NMR, MS) with an authentic sample of 4-nitrophenylbenzoate [9].

4.3. Spectral data of representative compounds

4.3.1. 4-Nitrophenylacetate

IR (KBr): 1740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.36 (s, 3H), 7.29 (d, J = 9.0 Hz, 2H), 8.28 (d, J = 9.0 Hz, 2H); EIMS (m/z) 181 (M^+), 43 (100).

4.3.2. 4-Nitrophenylbenzoate

IR (KBr): 1740 cm^{-1}; m.p. 144 °C; ^1H NMR ($CDCl_3$) δ 7.43 (d, J = 8.8 Hz, 2H), 7.54 (t, J = 7.6 Hz, 2H), 7.70 (t, J = 7.5 Hz, 1H), 8.21 (d, J = 7.6 Hz, 2H), 8.34 (d, J = 9.0 Hz, 2H); EIMS (m/z) 243 (M^+), 105 (100).

The spectral data (IR, NMR and MS) of all known products were identical with those of authentic compounds.

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