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Zinc dust: An extremely active and reusable catalyst in acylation of phenols, thiophenol, amines and alcohols in a solvent-free system

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ABSTRACT

A trace amount of zinc dust is able to promote instantaneous quantitative acylation of a large variety of functionalized phenols, thiophenol, amines and alcohols with acyl chlorides under solvent-free condition at 25 °C. The catalyst can be recovered and recycled making the procedure potentially useful for industrial applications.

1. Introduction

The acylation of phenols, thiophenols, amines and alcohols are important transformation in organic synthesis. Acylation of such functional groups is often necessary during the course of various transformations in a synthetic sequence, especially in the construction of polyfunctional molecules such as peptides, nucleosides, oligonucleotides, carbohydrates, steroids and other natural products [1-3]. Various catalysts developed for acylation with acyl halides include use of bases like pyridine and Et_3N [4-5], DMAP [6], and Bu_3P [7]. Acylation with acids [8, 9], acyl imidazoles [10], and acyl urea [11], are also known. Acid catalyzed acylation mainly requires polymeric acids [12,13]; and metal chlorides [14-16], metal triflates such as $Sc(OTf)_3/Bi(OTf)_3/Li(OTf)_3$ [17-19], metal perchlorates ($LiClO_4$ /$BiOClO_4$) [20,21] have also been utilized as Lewis acid catalysts for acylation of alcohols. Other reagents such as I_2 [22,23], [bmIm][dca] ionic liquid [24], solid supported reagents like $HClO_4$-SiO_2 [25], Py/basic alumina [26], neutral Al_2O_3 [27], Clay [28,29], $ZrOCl_2{\cdot}8H_2O$ [30] polyphosphate ester [31] and very recently ZnO [32], Sm [33] and $Mg(NTf_2)_2$ [34] have been employed for the same purpose. In this paper, we are describing our work on the successful use of non-toxic, environmentally benign and inexpensive zinc dust as a catalyst for the acylation of phenols, thiophenol, amines and alcohols with acid chlorides.

2. Experimental

2.1. Material and instrumentation

Phenols, thiophenol, amines, alcohols, acid chlorides, zinc dust and solvents were commercial, and all the solvents were distilled before use. Reactions were monitored on TLC by comparison with the authentic samples. Boiling/melting points were taken in open capillaries using paraffin bath and corrections are applied wherever necessary [35]. The IR spectra of the products were recorded on NICOLET 400D FT-IR spectrophotometer. ^{1}H NMR spectra were recorded on a 400 MHz Bruker spectrometer, LC-MS and GC-MS analysis was done using Agilent Technologies 1200 series and Shimadzu QP 5050 A instruments, respectively.

2.2. General procedure

Phenol (1.88 g, 20 mmol) and benzoyl chloride (3.36 g, 24 mmol) were taken in a 25 mL round bottom flask. To this zinc dust (0.130 g,) was added and stirred at 25 °C for a few seconds. The progress of the reaction was monitored by quenching the reaction with water at regular intervals on TLC, and by IR spectral analysis. After completion of the reaction, 25 mL ether was added and the organic layer was washed successively with saturated $NaHCO_3$ (10 mL), water (10 mL × 2) and dried over anhydrous Na_2SO_4, concentrated under vacuum and purified by silica gel column chromatography (ethyl acetate:light petrol; 0.5:9.5) to afford pure phenyl benzoate.

3. Results and Discussion

Earlier report from our laboratory described a convenient esterification by acid chlorides; as the reactions took a long time to go to completion, the reactions were studied under sonication to get the esters in high yield [36,37]. In continuation of work on the development of simple methods for the synthesis of useful products, we are reporting a novel method of acylation of phenol and alcohol with acid chloride using catalytic amount of zinc dust under solvent-free condition at 25 °C (Figure 1).

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Table 1. Reaction of *p*-cresol and benzoyl chloride in the presence of different amount of zinc under solvent-free condition at 25 °C.

Entry	Amount of Zinc (mmol)	Time (sec)	*p*-cresyl benzoate (%)*
1	10.0	25	80
2	7.5	30	84
3	5.0	38	86
4	1.0	40	90
5	0.1	45	94
6	—	24h	ND

* Isolated yield, ND: Not detected.

Table 2. Zn dust catalysed benzoylation of phenols, alcohols and thiophenol by benzoyl chloride under solvent- free condition at 25 °C.

Entry	Substrate	Product	Time (sec.)	Yield (%)[a]	C=O stretching (cm^{-1})	M.p./ B.p. (°C)	
						Found	Reported
1	Phenol[b]	Phenyl benzoate	55	92	1734	70	69–72[d]
2	*p*-Cresol[b]	*p*-Methylphenyl benzoate	45	94	1724	71	70–72[d]
3	*β*-Naphthol[c]	*β* -Naphthyl benzoate	50	88	1734	109	108–110[e]
4	*p*-Cl-Phenol[b]	*p*-Chlorophenyl benzoate	30	92	1726	86	86–88[e]
5	*m*-Cresol[b]	*m*-Methyl phenyl benzoate	50	92	1730	54	55 [24]
6	*o*-NO_2-Phenol[b]	*o*-Nitrophenyl benzoate	35	90	1735	49	50[24]
7	*p*-NO_2-Phenol[b]	*p*-Nitrophenyl benzoate	45	88	1724	143	142–144[e]
8	*α*-Naphthol[c]	*α* -Naphthyl benzoate	45	82	1725	55	56 [24]
9	Benzyl alcohol[b]	Benzyl benzoate	120	95	1719	20	18–20[e]
10	Thiophenol[b]	Thiophenyl benzoate	30	89	1670	54	55-56 [31]

[a] Isolated yield.

[b] Molar ratio of phenol/thiophenol/alcohol, acid chloride and Zn is 1:1.2:0.1.

[c] Molar ratio of phenol/thiophenol/alcohol, acid chloride and Zn is 1:2:0.1.

[d] Aldrich Handbook of Fine Chemicals, 2000-2001.

[e] Lancaster Research Chemicals, 2002-2003.

Table 3. Zn dust catalysed acetylation of phenols, alcohols and thiophenol by acetyl chloride under solvent free condition at 25°C.

Entry	Substrate	Product	Time (sec.)	Yield (%)[a]	C=O stretching (cm^{-1})	M.p./ B.p. (°C)	
						Found	Reported
1	Phenol[b]	Phenyl acetate	20	90	1766	195	195–196[e]
2	*p*-Cresol[b]	*p*-Methylphenyl acetate	25	92	1766	210	210–211[d]
3	*β*-Naphthol[c]	*β*-Naphthyl acetate	35	86	1760	69	68–70[e]
4	*p*-Cl-Phenol[b]	*p*-Chlorophenyl acetate	10	92	1734	41	40–42[d]
5	*o*-Cl-phenol[b]	*o*-Chlorophenyl acetate	15	90	1740	120	120–122[f]
6	*m*-Cresol[b]	*m*-Methylphenyl acetate	25	90	1766	209	212[f]
7	*o*-NO_2-Phenol[c]	*o*-Nitrophenyl acetate	25	86	1760	40	39–41[d]
8	*p*-NO_2-Phenol[c]	*p*-Nitrophenyl acetate	20	91	1766	78	77–79[e]
9	*α*-Naphthol[c]	*α*-Naphthyl acetate	30	88	1776	43	43–46[d]
10	*n*-Heptanol[b]	Methyl caprylate	30	92	1750	192	193–79[e]
11	*n*-Octanol[b]	Heptyl acetate	25	90	1745	209	211[d]
12	*n*-Decanol[b]	1-Decyl acetate	25	90	1745	246	244[d]
13	Allyl alcohol[b]	Allyl acetate	35	89	1740	103	103–104[d]
14	Benzyl alcohol[b]	Benzyl acetate	25	94	1734	96	95–97[e]
15	Cyclohexanol[b]	Cyclohexyl acetate	30	95	1745	174	172–173[d]
16	Thiophenol[b]	Thiophenyl acetate	30	89	1715	50	52-54 [31]

[a] Isolated yield.

[b] Molar ratio of phenol/thiophenol/alcohol, acid chloride and Zn is 1:1.2:0.1.

[c] Molar ratio of phenol/thiophenol/alcohol, acid chloride and Zn is 1:2:0.1.

[d] Aldrich Handbook of Fine Chemicals, 2000-2001.

[e] Lancaster Research Chemicals, 2002-2003.

[f] The Merck Index, 13th edition.

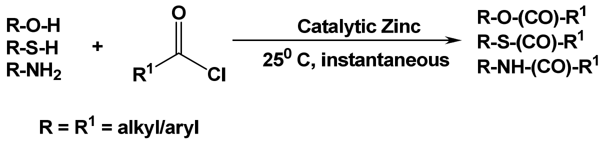

Figure 1. Acylation of phenols, thiophenol, amines and alcohols in a solvent-free system.

In order to standardize the reaction, different amounts of zinc dust was used to get *p*-cresyl benzoate from *p*-cresol and benzoyl chloride under solvent-free condition at 25 °C, and the results are summarized in Table 1. From Table 1, it is clear that, the reaction can be carried out in the presence of catalytic amount of zinc dust and the yields are excellent, it was found that the reaction is not possible without catalyst.

After these preliminary experiments, catalytic amount of zinc dust and solvent-free condition at 25 °C was used to convert a variety of functionalized phenols, thiophenol and alcohols with benzoyl chloride and acetyl chloride into respective esters, and the results are presented in Table 2 and 3. From the Table 2 and 3, it is clear that, compounds containing both electron withdrawing and electron donating groups react equally efficiently and instantaneously under the standard reaction conditions to give the acylated products in excellent yields.

The novel aspect of the present methodology was applied to amines also. All the substrates were found to react easily, giving good yields of the acylation products. The reactions took place readily with acetyl chloride and benzoyl chloride to afford simultaneous precipitation of the solid product. This has been tested with a number of aromatic amines baring electron withdrawing as well as electron donating groups and the results are summarized in Table 4 and 5. Finally the methodology was tested for sulfur containing compound such as thiophenol with acetyl chloride (Table 2, entry 10) and benzoyl chloride (Table 3, entry 16). In this case also the reaction vigoursly occurred to give respective acylated products in high yields. All the synthesized compounds are known and characterized by IR or GC-Mass spectral analysis and physical properties were found to agree with the reported values.

Furthermore, we have examined the recovery and reuse of the catalyst on the acylation of cyclohexanol with acetyl chloride to get cyclohexyl acetate under solvent-free condition at 25 °C, and found that, the yields of the product in the second and third use of the catalyst were almost same as that in the first use. In every case >90% of Zn was recovered by filtration, washed with water and dried at 120 °C (Table 6) before reuse.

Table 4. Zn dust catalyzed acetylation of amines by acetyl chloride under solvent free condition at 25 °C.

Entry	Substrate	Product	Time (min.)	Yield (%)[a]	C=O stretching (cm^{-1})	M.p./ B.p. (°C)	
						Found	Reported
1	Aniline	Acetanilide	10	92	1652	113	113–114[b]
2	*o*-Nitroaniline	*o*-Nitroacetanilide	15	90	1621	92	92–93[b]
3	*m*-Nitroaniline	*m*-Nitroacetanilide	20	89	1630	151	151–153[b]
4	*p*-Nitroaniline	*p*-Nitroacetanilide	15	90	1635	217	215–217[c]
5	*o*-Anisidine	*o*-Methoxyacetanilide	20	93	1635	152	154 [24]
6	*m*-Toluidine	*m*-Methylacetanilide	15	92	1640	66	65–67[c]
7	*p*-Toluidine	*p*-Methylacetanilide	15	93	1642	150	149–151[c]
8	Benzylamine	*N*-Acetylbenzylamine	10	90	1650	60	60 [25]
9	*p*-Chloroaniline	*p*-Chloroacetanilide	10	92	1647	178	178–180[b]

[a] Isolated yield.
[b] Lancaster Research Chemicals, 2002-2003.
[c] Aldrich Handbook of Fine Chemicals, 2000-2001.

Table 5. Zn dust catalyzed benzoylation of amines by benzoyl chloride under solvent free condition at 25 °C.

Entry	Substrate	Product	Time (min.)	Yield (%)[a]	C=O stretching (cm^{-1})	M.p./ B.p. (°C)	
						Found	Reported
1	Aniline	Benzanilide	40	90	1658	164	164–166[b]
2	*o*-Nitroaniline	*o*-Nitrobenzanilide	35	88	1630	98	98 [24]
3	*m*-Nitroaniline	*m*-Nitrobenzanilide	40	85	1645	157	157 [24]
4	*p*-Nitroaniline	*p*-Nitrobenzanilide	30	90	1655	200	199 [24]
5	*o*-Anisidine	*o*-Methoxybenzanilide	45	89	1652	58	60 [24]
6	*m*-Toluidine	*m*-Methylbenzanilide	40	90	1650	124	125 [24]
7	*p*-Toluidine	*p*-Methylbenzanilide	45	85	1652	159	158 [24]
8	Benzylamine	*N*-Benzoylbenzlyamine	35	90	1652	104	105–106 [24]
9	Cyclohexylamine	*N*-Benzoylcyclohexylamine	40	92	1636	147	147 [24]

[a] Isolated yield.
[b] Aldrich Handbook of Fine Chemicals, 2000-2001.

Table 6. Repeated use of Zn dust for acylation of cyclohexanol with acetyl chloride.

Number of uses	Time (sec)	Yield (%)[a]	Recovery of Zn (%)
1	30	95	95
2	35	90	93
3	40	88	90

[a] Isolated yield of cyclohexyl acaetate.

4. Conclusion

In conclusion, we have presented a novel, highly rapid, efficient and solvent-free protocol for the acylation of phenols, thiophenols, amines and alcohols using non-toxic, efficient and inexpensive Zn dust. The advantages of this environmentally benign and safe protocol include a simple reaction set up not requiring specialized equipment, all the reactions work at 25 °C, give excellent yields of products, require short-time, eliminate solvents and the catalyst can be recovered and recycled making the procedure potentially useful for industrial applications.

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