

Dipyridine cobalt chloride as an efficient and chemoselective catalyst for the synthesis of 1,1-diacetates under solvent-free conditions

Sobhan Rezayati^{a,*}, Zahra Erfani^a, Saman Rezayati^a, Rahimeh Hajinasiri^b, Marzieh Rekavandi^b

^aDepartment of Chemistry, Payame Noor University, P.O. BOX 19395-4697, Tehran, Iran

^bChemistry Department, Qaemshahr Branch, Islamic Azad University, Qaemshahr, Iran

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Abstract

1,1-Diacetates (acylals) were prepared by direct condensation of various aldehydes with acetic anhydride using dipyridine cobalt chloride (CoPy_2Cl_2) as an efficient and green catalyst under solvent-free conditions at room temperature. The important features of this catalyst method are that the catalyst is solid, stable at high temperatures, soluble in water, stable in air, immiscible in common organic solvents, low toxic and, above all, it is reusable. CoPy_2Cl_2 can be recycled after a simple work-up and reused at least five runs without appreciable loss of its catalytic activity. High chemo-selectivity toward aldehyde in the presence of ketones is another advantage of the present method which provides selective protection of aldehydes in their mixtures with ketones.

Keywords: CoPy_2Cl_2 , acylation, protection, solvent-free conditions, carbonyl protection.

Introduction

Selective protection of carbonyl group plays an important role in the multistep organic synthesis of complex natural products [1]. Geminal-diacetates are one of the useful carbonyl protecting groups due to their stability under neutral and basic media as well as aqueous acids [2,3]. Moreover, the diacetates of α,β -unsaturated aldehydes serve

*Corresponding author: Sobhan Rezayati
Fax number: +98 (841) 2221053; Tel: +98 (841) 2228316
E-mail: sobhan.rezayati@yahoo.com

as an important precursor for Diels–Alder reactions [4] and some industrial uses of these compounds have also been reported [5,6]. Hence, methods for the synthesis and cleavage of acylals have received considerable attention. Usually, they are prepared from aldehydes and acetic anhydride using strong protic acids or Lewis acids. Some examples of the reagents and catalysts that have been developed for this purpose include LiOTf [7], InCl₃ [8], H₂SO₄ [9], NBS [10], ceric ammonium nitrate [11], TMSCl–NaI [12], I₂ [13], and PCl₃ [14]. Although some of these methods have convenient protocols with good to high yields, the majority of these methods suffer from at least one of the following disadvantages: reaction under oxidizing conditions, prolonged reaction time, high temperatures, use of sensitive moisture and expensive catalysts, use of solvents, stringent conditions, difficulty in scaling up, etc. Therefore, development of catalysts which are not associated with the above drawbacks is desirable. Recently, the use of solid catalysts and solvent-free conditions was developed because such reagents not only simplify the purification processes but also help to prevent the releasing of toxic reaction residues into the environment [15-18]. Dipyrindine cobalt chloride (CoPy₂Cl₂) as a solid acid catalyst was reported by Rajitha *et*

al. who attempted to use it for the 14-aryl-14H-dibenzo[a,j]xanthenes under solvent-free conditions [19].

Experimental

General

All reagents were purchased from Aldrich or Merck Fine Chemicals and used without further purification. Products were separated and purified by different chromatographic techniques and were identified by the comparison of their IR and NMR with those reported for the authentic samples. IR spectra of the compounds were obtained on a Perkin Elmer spectrometer version 10.03.06 using a KBr disk. The nuclear magnetic resonance (¹H NMR) spectra were recorded on a BRUKER DRX-400 AVANCE instrument at 400 MHz (in CDCl₃ solution) using TMS as internal standard. The purity of the substrate and reaction monitors was accompanied by TLC on Silica gel Polygram SILG/UV 254 plates. Melting points were determined using an electrothermal apparatus

General procedure for the synthesis of acylals

To a mixture of acetic anhydride (2 mmol) and CoPy₂Cl₂ (0.05 mmol) in a 10 mL round-bottomed flask, aldehyde (1 mmol) was added and the resulting mixture was stirred at room temperature. The yields and time required for

each reaction are summarized in Table 2. The reaction was followed by TLC (*n*-hexane:EtOAc, 9:1). After completion of the reaction, CH₂Cl₂ (10 mL) was added to the mixture and, then, filtered. The precipitate was washed with CH₂Cl₂ (2×5 mL) to give the recycled catalyst. The solvent of the filtrate was evaporated under reduced pressure to provide crude product. Products were purified by column chromatography to afford pure product in good to excellent yields.

1,1-Diacetoxy-1-phenyl methane

IR (KBr, cm⁻¹): 3564, 3367, 3068, 2934, 1762, 1669, 1572 1495, 1435; ¹H NMR (400 MHz, CDCl₃,)δ:2.14 (s, 6H, 2×CH₃), 7.412 7.448 (m, 3H, Ar-H), 7.52-7.55 (m, 2H, Ar-H), 7.70 (s, 1H, CH); ¹³CNMR (100 MHz, CDCl₃, δ/ ppm): δ20.8, 89.7, 126.6, 128.6, 129.7, 135.4, 168.8; Anal. Calcd. For C₁₁H₁₂O₄; C, 63.4; H, 5.8; Found: C, 63.7; H 5.7.

1,1-Diacetoxy-1-(3-chlorophenyl)methane

¹H NMR (400 MHz, CDCl₃,)δ:2.14 (s, 6H, 2×CH₃), 7.33-7.40 (m, 3H, Ar-H), 7.52 (m, 1H, Ar-H), 7.64 (s, 1H, CH); ¹³CNMR (100 MHz, CDCl₃, δ/ ppm): δ 20.8, 88.7, 125.0, 126.8, 129.9, 134.5, 137.2, 168.7; Anal. Calcd.

for C₁₁H₁₁ClO₄; C, 54.4; H, 4.57; Cl, 14.6; Found: C, 54.4; H, 4.63; Cl 14.50.

1,1-Diacetoxy-1-(furyl) methane

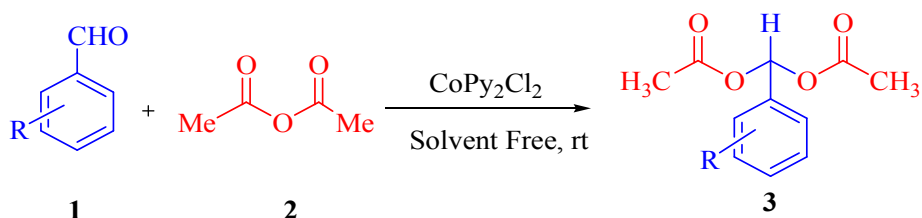
IR (KBr, cm⁻¹): 3473, 3161, 3129, 3018, 2942, 1758, 1608, 1505; ¹H NMR (400 MHz, CDCl₃,)δ:2.16 (s, 6H, 2×CH₃), 6.41-6.418 (dd, 1H, *J* = 1.6, *J* = 1.6, Ar-H), 6.55 (d, 1H, *J* = 3.2, Ar-H), 7.47-7.48 (dd, 1H, *J* = 0.8, *J* = 0.8, Ar-H), 7.73 (s, 1H, CH); ¹³CNMR (100 MHz, CDCl₃, δ/ ppm): 20.7, 83.4, 109.7, 110.4, 143.6, 147.8, 168.4.

1,1-Diacetoxy-1-(4-nitrophenyl) methane

IR (KBr, cm⁻¹): 3486, 3123, 3017, 2940, 2868, 1764, 1610; ¹H NMR (400 MHz, CDCl₃,)δ:2.17 (s, 6H, 2×CH₃), 7.70 (s, 1H, CH), 7.73-7.74 (d, 2H, *J* = 4 Hz, Ar-H), 8.28 (2H, d, Ar-H); ¹³CNMR (100 MHz, CDCl₃, δ/ ppm): δ 20.0, 88.3, 123.8, 127.8, 141.8, 148.5, 168.6.

Results and Discussion

Herein, we wish to report an extremely convenient, mild, and highly chemoselective procedure for the conversion of aldehydes to the corresponding acylals in the presence of acetic anhydride and catalytic amount of CoPy₂Cl₂ under solvent-free conditions at room temperature (Scheme 1).



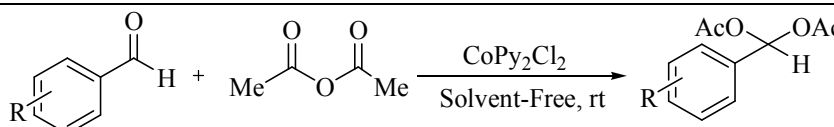
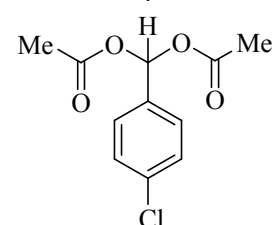
Scheme 1.

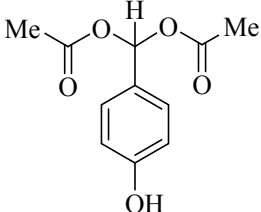
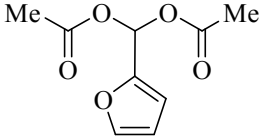
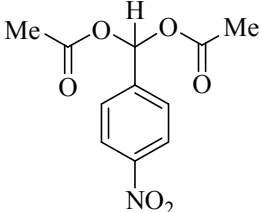
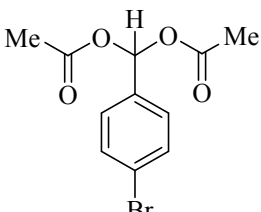
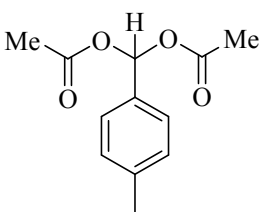
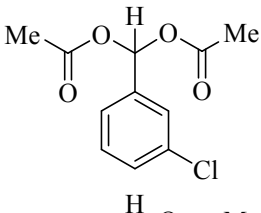
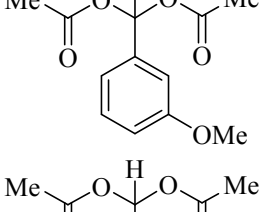
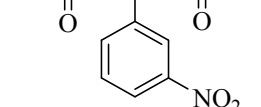
In order to optimize the reaction conditions, the reaction of benzaldehyde and acetic anhydride was selected as a model to investigate the effects of the catalyst amount on the yield. The best results were obtained by carrying out the reaction with 1:2 molar ratio of benzaldehyde:acetic anhydride and 0.05 mol% of dipyridine cobalt chloride at room temperature under solvent-free conditions. Under these conditions, the product was obtained in 99% yield after 5 min (Table 1, Entry 4). To determine the role of dipyridine cobalt chloride, the model reaction was carried out in the absence of catalyst at room temperature under solvent-free conditions in which the desired product was not obtained in trace yield after 120 min (Table 1, Entry 1). These results indicate that dipyridine cobalt chloride exhibits a high catalytic activity in this transformation.

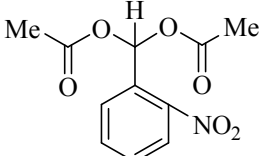
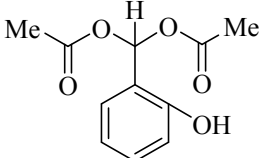
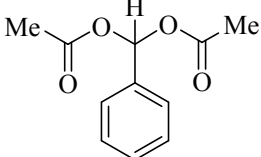
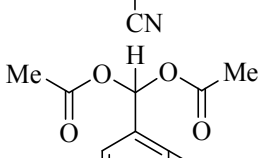
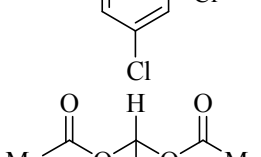
Table 1. Optimization of the amount of the CoPy_2Cl_2

Entry	Catalyst (mol%)	Time (min)	Yield (%) ^a
1	-	120	5
2	0.01	30	82
3	0.03	15	86
4	0.05	5	99
5	0.07	20	80
6	0.1	50	76

^aYield of isolated products.**Table 2.** Conversion of aldehydes to acylals using CoPy_2Cl_2 under solvent-free conditions at room temperature

Entry	Product	Time (min)	Yield (%) ^a	Melting Point (°C)	
				Found	Reported
1		5	99	43-44	44-45 [20]
2		4	98	80-82	82-83 [21]

3		12	95	91-92	90-92 [21]
4		5	99	52-54	52-53 [21]
5		3	98	126-127	125 [22]
6		5	97	84-85	84 [22]
7		10	91	81-83	81-82 [23]
8		8	93	63-65	65-66 [24]
9		15	87		Oil Oil [25]
10		7	92	65-68	64-66 [26]

11		10	91	88-87	85-86 [26]
12		7	94	101-102	101-103 [27]
13		7	99	99-101	98-102 [28]
14		10	87	87-89	88.5 [29]
15		7	96	98-100	101 [30]

^aYield of isolated products.

The method is environment -friendly and the work-up is simple, it can be completed in 3-15 min with excellent yields (87–99%). Both activated and deactivated aromatic aldehydes were converted to 1,1-diacetates. The tolerances of various functional groups have been examined (*e.g.*chloro, methyl, methoxy, cyano and nitro groups), and the reaction conditions are compatible with these functional groups. The results in Table 2 show that CoPy_2Cl_2 catalysis generally results in excellent yields with aromatic aldehydes

such as 4-chlorobenzaldehyde, 4-nitrobenzaldehyde, 4-chlorobenzaldehyde, 4-bromobenzaldehyde. This protocol was, then, applied to protect naphthaldehyde. The yield of the corresponding 1,1-diacetate of naphthaldehyde (Table 2, Entry 15) was good, although the time required for the completion of the reaction was longer compared to the other aldehydes. Furfural (Table 2, Entry 4) also led to the formation of acylals in 99% yield without the formation of any side products, it was normally observed under

strongly acidic conditions. The powerful electron-releasing substituent -OMe slightly decreased the yield and increased the reaction time (Table 2, Entry 9). These results showed that CoPy_2Cl_2 as a catalyst for this condensation is appropriate and it encouraged us to extend this catalyst for synthesizing other compounds. The reaction of benzaldehyde with

acetic anhydride has been studied with several catalysts in literature (Table 3). The present methodology offers several advantages, such as excellent yields, a simple procedure, short reaction times, easy synthesis, simple work-up and greener conditions, in contrast with other existing methods.

Table 3: Comparison of the present method with some other procedures for acylals synthesis

Entry	Catalyst	Time	Catalyst loading	Yield ^d (%)	Reference
4	NBS	8 h	10 mol%	98	[10]
1	I ₂	2 h	10 mol%	99	[13]
2	H ₂ SO ₄ -Silica	2 min	3 mg	98	[30]
3	Mg(CH ₃ SO ₃) ₂ -HOAc	12 h	1.5 mol%	55	[31]
5	H ₃ PW ₁₂ O ₄₀ /MCM-41 ^a	2 h	20 mg	61	[32]
6	SPD TSA ^b	4 min	10 mg	94	[33]
7	Amberlyst-15 ^c	1 h	500 mg	95	[34]
8	LiHSO ₄ /SiO ₂	10 min	20 mol%	97	[35]
9	[Hmim]HSO ₄	40 min	3.8 mol%	89	[36]
10	This Work	5 min	0.05 mol%	99	-

^aReaction conditions: at 60 °C temperature

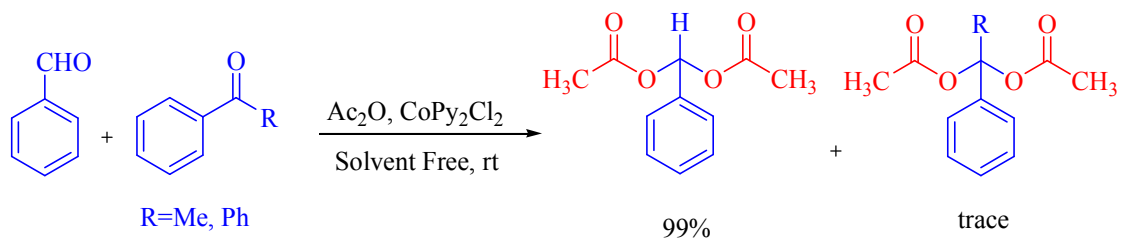
^bSilica-bonded propyl-diethylene-triamine-*N*-sulfamic acid

^cIn solvent CH₂Cl₂

^dIsolated yield

In order to show the high selectivity of the method, we studied competitive reactions for the acylation of aldehydes in the presence of ketones using CoPy_2Cl_2 as catalyst. Unfortunately, when propiophenone and acetophenone were used in this reaction, no corresponding product was isolated. In the case of substrates bearing aldehyde and ketone functionalities, the keto group remains unaffected and aldehyde is converted into 1,1-diacetate. This result indicates that the chemoselective protection of an aldehyde in

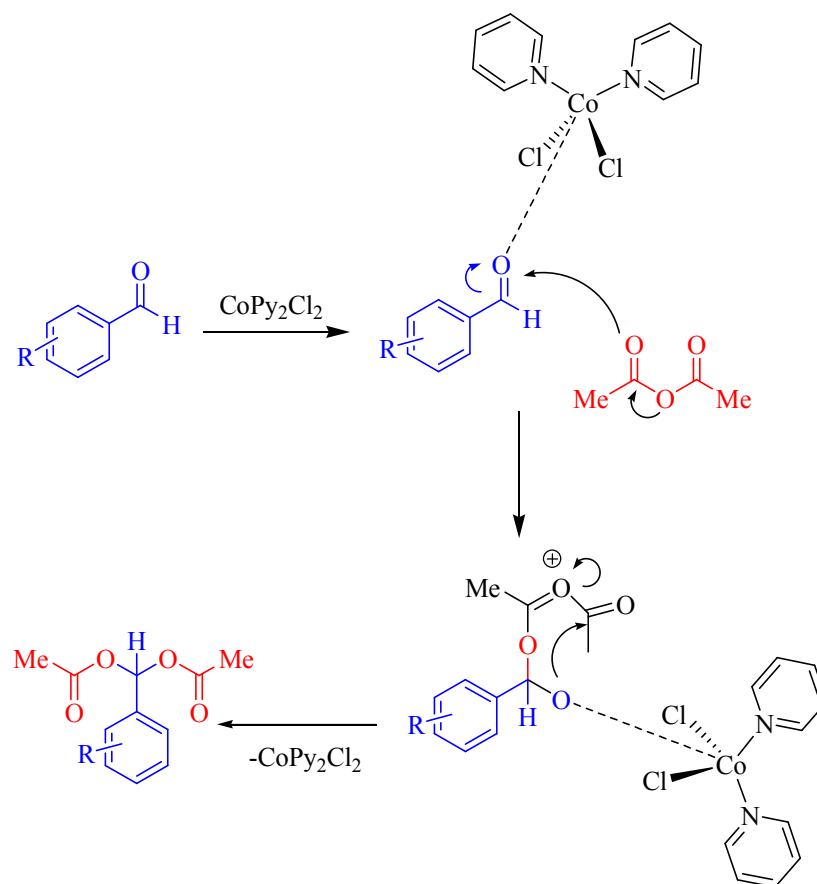
the presence of ketone could be achieved by this procedure (Scheme 2). Ease of recycling of the catalyst is one of the most advantages of our method. For the reaction of benzaldehyde with acetic anhydride, no significant loss of the product yield was observed when CoPy_2Cl_2 was reused even after five times recycling (Table 4). The proposed mechanism for dipyridine cobalt chloride catalyzed synthesis of 1,1-diacetates may be visualized to occur via a sequence of reactions as depicted in Scheme 3.



Scheme 2.

Table 4. The catalytic activity of CoPy_2Cl_2 in five cycles

Run	1	2	3	4	5
Yield (%)	99	98	96	95	93



Scheme 3. Proposed mechanism for CoPy_2Cl_2 -catalyzed 1,1-diacetates synthesis

Conclusion

In conclusion, we report an efficient and selective method for the preparation of 1,1-diacetates from aldehydes in solvent free conditions, and a selective regeneration of aromatic aldehydes from the corresponding acylals using CoPy_2Cl_2 as catalyst. The important features of this method are: mild reaction condition, easy work up, recyclable nature of the catalyst, it does not require particular skill for its preparation and finally we can witness the elimination of corrosive liquid acids. In addition, this reagent acts as a heterogeneous catalyst that could be removed from the reaction mixture by simple filtration and compliance with the green chemistry protocols.

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