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CHEMOSELECTIVE SYNTHESIS OF 1,1-DIACETATES FROM ALDEHYDES USING ANHYDROUS COBALT(II) BROMIDE UNDER SOLVENT-FREE CONDITIONS

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A mild and efficient method has been developed for the chemoselective preparation of 1,1-diacetates (acylals) from aldehydes catalyzed in the presence of a catalytic amount (0.1 mmol) of anhydrous cobalt(II) bromide under solvent-free conditions. The remarkable selectivity under mild and neutral conditions, excellent yields, short reaction time, and easily available and inexpensive catalyst are important features of this method.

Keywords: Chemoselective; cobalt dibromide; 1,1-diacetates; solvent-free

INTRODUCTION

Simple, efficient, environmentally benign, and economically viable chemical processes or methodologies for widely used organic compounds are in great demand. Diacetylation reactions of aldehydes to develop various useful organic compounds have received considerable attention in organic synthesis. Selective protection and deprotection of carbonyl groups are essential steps in modern organic chemistry.^[1] Protective group acylals are fairly stable under neutral and basic conditions^[1b] as well as under critically controlled acidic conditions. Apart from mere protective groups, acylals are important synthons and useful precursors. The 1,1-diacetates derived from α,β -unsaturated aldehydes are important starting materials in the Diels–Alder reaction.^[2] These 1,1-diacetates have several synthetic and industrial applications and are used as cross-linking reagents^[3] in cellulose and the cotton industry and are also used as stain-bleaching agents. As synthons, their usefulness has been exploited in well-known reactions of organic chemistry, such as the Grignard,^[4] Barbier,^[4b] and Prins^[5] reactions, and condensation reactions, such as the Knoevenagel^[6] and Benzoin^[7] reactions. Because of their unique properties as protective groups as well as important synthons, an efficient, mild, and facile preparation of acylals is of current interest. Generally, acylals are prepared from aldehyde and acetic anhydride using strong protonic acids such as sulfuric, phosphoric, methanesulfonic, or perchloric acids.^[8] Use of strong Lewis acids^[9] such

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Scheme 1. R: Alkyl, phenyl.

as BF₃, PCl₃, ZnCl₂, LiBF₄, ZrCl₄, FeCl₃, FeCl₃/SiO₂, Zn(ClO₄)₂ \cdot 6H₂O, RuCl₃ \cdot xH₂O, and SbCl₃ have also been reported. Apart from these catalysts, expensive^[10] graphite, zeolite, tungstosilicic acid, and zirconium sulfophenyl phosphonate have also been employed in this protection process. Some of these methods still suffer from drawbacks such as prolonged reaction time (viz., up to 120 h in the case of 2-furyl aldehyde with PCl₃), poor yields [in the case of 4-nitrobenzaldehyde (4%) and cinnamaldehyde (30%) when PCl₃ is used], and in some cases the requirement of elevated temperature. Several of these catalysts are not very safe to handle, such as metal perchlorates and BF₃. Consequently, it seems desirable and necessary to develop a simple, safe, efficient, and facile method for the preparation of these gemdiacetates. In this communication, we report that anhydrous cobalt(II) bromide is an efficient and very mild catalyst under solvent-free conditions (Scheme 1).

RESULTS AND DISCUSSION

To find the most effective 1,1-diacetylation, benzaldehyde was chosen as a model substrate. It was treated with 2 equiv. of acetic anhydride in the presence of 1.0 mmol of $CoBr_2$ in different dry solvents at room temperature (Table 1).

 Table 1. 1,1-Diacetylation of benzaldehyde with acetic anhydride in the presence of cobalt(II) bromide at room temperature with different solvents



Entry	CoBr ₂ (mmol)	Solvent	Time (min)	Yield ^a (%)
1	1.0	THF	40	67
2	1.0	CH_2Cl_2	40	86
3	1.0	CHCl	40	76
4	1.0	Et ₂ O	40	80
5	1.0	EtOAc	40	78
6	1.0	DMF	40	82
7	1.0	CH ₃ CN	30	88
3	1.0		20	98^b
)	0.1	—	20	98^{b}

^aIsolated yield.

^bThe solvent-free reaction is more effective.

The reaction in tetrahydrofuran (THF), CH_2Cl_2 , $CHCI_3$, Et_2O , EtOAc, dimethylformamide (DMF), and CH_3CN (Table 1, entries 1–7) were less effective. Therefore, we carried out the reaction under solvent-free conditions with excellent yield (98%, entries 8 and 9).

The catalytic activity of $CoBr_2$ for the 1,1-diacetylation of benzaldehyde (2 mmol) with acetic anhydride (2 mmol) under room temperature was studied, and it was found that the application of less than 0.1 mmol of cobalt(II) bromide (22 mg) gave a moderate yield of the corresponding 1,1-diacetylation (Table 2, entries 1 and 2), whereas the use of more than 0.1 mmol gave excellent yield (Table 2, entries 3–5).

A variety of aromatic, aliphatic, and heterocyclic aldehydes were converted to corresponding 1,1-diacetates using acetic anhydride in the presence of anhydrous cobalt(II) bromide in excellent yields at room temperature and in short reaction times. The results are summarized in Table 3. All aromatic aldehydes carrying electron-donating or electron-withdrawing substituents reacted well and gave excellent yields (Table 3, entries 1–14). Aliphatics and α , β -unsaturated aldehydes produced acylals in good yields (Table 3, entries 16–19). Furfural was converted to its 1,1-diacetate in moderate yield (Table 3, entry 15). 4-(N,N-Dimethylamineo) benzaldehyde gave less yield under the same condition, which may be due to electron donation by the dimethylamino group (Table 3, entry 25). We also studied the aldehydes that have phenolic OH and carbonyl aldehyde groups under the same condition. We observed that both carbonyl and phenolic OH groups were acylated with similar yields (Table 3, entry 24).

To evaluate the selectivity of this method, we investigated competitive reactions for aldehydes in the presence of ketones using anhydrous cobalt(II) bromide as catalyst under solvent-free conditions. While employing this catalytic system, the highly selective conversion of aldehydes in the presence of ketones was observed (Table 4, entries 1 and 2). We also compared the acetylation of 4-nitro benzaldehyde with that of benzaldehyde and 4-methoxy benzaldehyde. These reactions proceeded with high selectivity in the presence of this catalyst, showing the importance of electronic effects upon these reactions in the presence of this catalyst (Table 3, entries 3 and 4). We also studied the acylation of 4-nitrobenzaldehyde in the presence of 3-phenyl propionaldehyde under the same conditions. As shown in

Entry	CoBr ₂ [mmol (mg)]	Time (min)	Yield (%) ^a
1	0.01 (2)	20	60
2	0.05 (11)	20	70
3	0.10 (22)	20	93
4	0.15 (33)	20	93
5	0.20 (44)	20	93

Table 2. Catalytic effect of $CoBr_2$ for the 1,1-diacetylation in the presence of cobalt(II) bromide at room temperature without solvent

^aIsolated yield of the corresponding sulfonylated product.

1,1-DIACETATES FROM ALDEHYDES

Table 3. CoBr₂-catalyzed 1,1-diacetylation of benzaldehyde



(Continued)

Substrates (a) Products (b)		Products (b)	Time (min)	Yield ^a (%)
11	МеО	MeO CH(OAc) ₂	25	90
12	МеО-СНО	MeO-CH(OAc) ₂	25	82
13	MeO MeO MeO	MeO MeO MeO	30	80
14	МеО МеО-СНО	MeO MeO CH(OAc) ₂	30	80
15	СНО	CH(OAC) ₂	30	70
16	н₃с∕∕сно	H ₃ C CH(OCH ₃)	25	92
17	Н₃С∕∕∕СНО	H ₃ C ^{CH(OAc)} ₂	25	90
18	Н₃С∕∕СНО	H ₃ C CH(OCH ₃)	25	90
19	СНО	CH(OAc) ₂	25	96
20	но-Сно	AcO CH(OAc) ₂	25	93
21	но Сно	AcO CH(OAc) ₂	30	87
22	мео он	MeO CH(OAc) ₂ OAc	30	90
23	сно	CH(OAc) ₂ OAc	25	92

Table 3. Continued

(Continued)



Table 3. Continued

"Yields refer to pure products, and all products were characterized by comparison of their infrared (IR) and ¹H NMR spectra.

Table 4. Chemoselective synthesis of acylals from aldehydes using acetic anhydride in the presence of anhydrous $CoBr_2$ at room temperature



Table 4 (entry 5), the rate of acylal formation of 3-phenyl propionaldehyde is less than 4-nitrobenzaldehyde, which may be due to enol formation of 3-phenyl propionaldehyde in the presence of this catalyst.

CONCLUSIONS

In conclusion, this article describes a method in which anhydrous cobalt(II) bromide (CoBr₂) is used as a highly efficient catalyst for the diacetylation of aldehydes. The advantages include the low cost, ease of catalyst handling, requirement of very small amount of catalyst (0.1 mol%, 22 mg) and Ac₂O, mild reaction conditions (room temperature), excellent yield, short reaction time, and no undesirable side products. The solvent-free conditions employed in the present method should make it environmentally friendly and useful for industrial applications.

EXPERIMENTAL

Typical Procedure

A mixture of aliphatic, aromatic, and heterocyclic aldehydes (2 mmol), 5 mmol acetic anhydride (Ac₂O), and 0.1 mol% (22 mg) anhydrous cobalt(II) bromide (CoBr₂) was stirred magnetically at room temperature, and the progress of the reaction was monitored by thin-layer chromatography (TLC). The reaction mixture was diluted with water (30 ml) and extracted with chloroform (3×30 ml). The combined chloroform extracts were washed successively with 10% sodium bicarbonate and water, dried with Na₂SO₄, and concentrated under reduced pressure. In all the cases, the product obtained after the usual workup gave satisfactory spectral data.

Characterization Data for Products

1,1-Diacetoxy-1-phenyl methane (1b). IR (KBr): 3040, 1760, 1588, 1517, 1456, 1372, 1239, 1203, 1061, 1010, 922, 846, 763, 699 cm⁻¹. ¹H NMR (300 MHz, CDCl3): $\delta = 7.7$ (s, 1H), 7.34–7.51 (m, 5H), 2.1 (s, 6H).

1,1-Diacetoxy-1-(4-nitrophenyl) methane (4b). IR (KBr): 3087, 1763, 1610, 1529, 1350, 1231, 1203, 1062, 1013, 976, 856 cm^{-1} . ¹H NMR (300 MHz, CDCl3): $\delta = 8.25$ (d, J = 8.2 Hz, 2H), 7.7 (d, J = 8.2 Hz, 2H), 7.25 (s, 1H), 2.15 (s, 6H).

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