

An effective method for the selective synthesis of geminal diacetates (acylals) from aromatic aldehydes using alumina-supported InCl_3

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Abstract

Aliphatic and aromatic aldehydes can be converted to acylals in mild conditions by a treatment with acetic anhydride in the presence of $\text{InCl}_3/\text{Al}_2\text{O}_3$ (indium chloride loading = 1.2 mmol g^{-1}). For all reactions, $\text{InCl}_3/\text{Al}_2\text{O}_3$ is the best catalyst with reusable and highly activity. © 2005 Elsevier B.V. All rights reserved.

Keywords: Acylal; Acylation; Alumina-supported; Protecting groups

1. Introduction

Acylals have been used as protecting groups for carbonyl compounds because of their stability in neutral and basic media as well as aqueous acids [1,2]. The acylals are important starting materials for the synthesis of valuable intermediates in the Diels-Alder cycloaddition reactions [3]. Acylals have been applied as crosslinking reagents for cellulose in cotton [4]. Hence, there are considerable methods for synthesis of acylals. Some of the catalysts which have been developed for this purpose are including: sulfuric acid [5a], triflic acid [5b], PCl_3 [5c], TMSCl-NaI [5d], ZnCl_2 [5e], I_2 [5f], anhydrous ferrous sulfate [5g], FeCl_3 [5h], NBS [5i], zeolites [6a], sulfated zirconia [6b], montmorillonite clay [6c], expansive graphite [6d], aluminum dodecatungstophosphate [6e], zeolite HSZ-360 [6f], layered zirconium sulfophenyl phosphonate [6g], $\text{Cu}(\text{OTf})_2$ (2.5 mol%) [7a], $\text{Sc}(\text{OTf})_3$ (2 mol%) [7b], $\text{Bi}(\text{OTf})_3$ (0.1 mol%) [7c], $\text{Zn}(\text{BF}_4)_2$ [7d], ZrCl_4 [7e] and bismuth nitrate [7f] which are also efficient for this conversion.

Many of the reported methods, however, involve strongly acidic or oxidising conditions, corrosive reagents, high temperature, high catalyst loading, longer reaction time and cum-

bersome procedures. Moreover, some of these are not selective in terms of aldehydes and keto carbonyl functional groups. In view of these, the search for finding a cost effective, mild and simple selective protocol for synthesis of acylals from aldehydes is still relevant. In recent years, indium compound has been used as a potential Lewis acid for many organic transformations [8]. In continuation of our research programmed on In(III) mediated organic reactions [9], we herein report the results of $\text{InCl}_3/\text{Al}_2\text{O}_3$ catalysed expedient, simple and cost effective, selective conversion of aldehydes to acylals (Table 1).

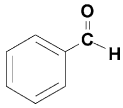
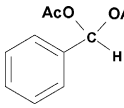
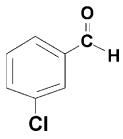
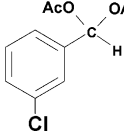
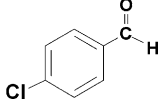
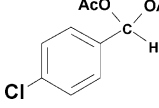
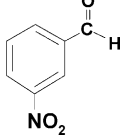
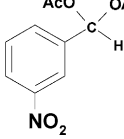
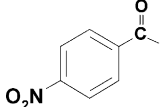
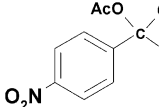
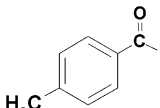
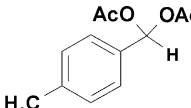
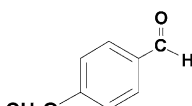
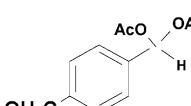
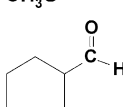
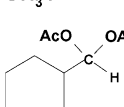
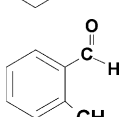
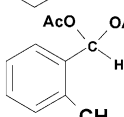
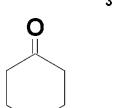
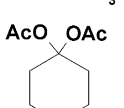
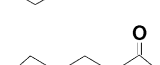
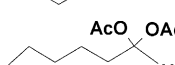
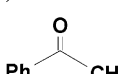
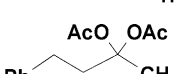
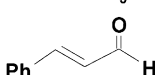
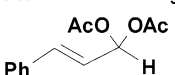
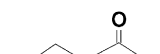
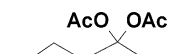
2. Experimental

2.1. Preparation of heterogeneous catalyst

Heterogeneous catalysts were prepared by impregnating acidic alumina (Merck: Art No. 1078, aluminium oxide 90 active acidic, 0.063–0.200 mm, it was activated at 500°C for 8 h before use) with anhydrous indium(III) chloride (purity 99.99% Aldrich) from their acetonitrile solution by incipient wetness technique [12e], and evaporating the solvent in vacuum oven at 120°C for 10 h (loading of metal chloride = 1.2 mmol g^{-1}). At the end of the reaction, the catalyst was separated by filtration, thoroughly washed with solvent

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Table 1
Alumina-supported indium chloride acylal formation and deprotection

Entry	Substrate	1,1-Diacetates ^a	Preparation		Deprotection	
			Yield (%) ^b	Time	Yield (%) ^b	Time (h)
1			86	10 min	87	3
2			88	10 min	88	3
3			91	10 min	90	3
4			89	10 min	89	3
5			94	10 min	91	3
6			99	10 min	93	3
7			97	10 min	92	3
8			82	50 min	36	6
9			80	30 min	79	3
10			9	24 h	^c	24
11			8	24 h	^c	24
12			7	24 h	^c	24
13			73	3 h	85	3
14			35	4 h	72	6

^a All the products were characterized by comparison (TLC and physical constant) with authentic samples prepared by the conventional method [2,7,11].

^b Isolated yields.

^c No reaction.

and reused under similar conditions. Although the analysis of the recovered catalysts by atomic absorption spectroscopy (AAS) showed no reduction in the amount of metal ions, they showed a slightly lower catalytic activity. These catalysts can also be reused for the reaction several times. However, there is an appreciable loss in the activity in the reuse of these catalysts. This is expected mostly because of the leaching of the active catalyst component during the reaction.

2.2. Typical procedure for the preparation of 1,1-diacetates

To a stirred suspension of aldehydes (1 mmol) and $\text{InCl}_3/\text{Al}_2\text{O}_3$ (20 mg) acetic anhydride (3 mmol) was added at room temperature with progress of reaction monitored by GC–MS. Stirring was continued for the appropriate time (see Table 1). The catalyst was then filtered and washed with hexane; the organic layer was washed twice with a 5% solution of sodium bicarbonate, dried over anhydrous sodium sulfate and evaporated under reduced pressure. The residue was purified by flash chromatography (eluent hexane/ethyl acetate 19:1) or crystallization to give the corresponding 1,1-diacetates. All compounds were characterized by ^1H NMR and GC–MS. The catalyst washed with dioxane and dried at 150°C , can be reused for several experiments. The reaction in entry 6 (Table 1) has been repeated three times with the following yields: 99, 97, and 95%. All the products were characterized by comparison (TLC and physical constant) with authentic samples prepared by the conventional method [2,7a,9], using sulfuric acid as the catalyst. All the yields were calculated from crystallized products, their purity was established by GLC, being better than 98%.

2.3. Typical procedure for the deprotection of 1,1-diacetates

To a stirred solution of 1,1-diacetate (1 mmol) in commercial dioxane (1 ml) was added $\text{InCl}_3/\text{Al}_2\text{O}_3$ (20 mg) at 50°C . Stirring was continued for the appropriate time (see Table 1) with progress of reaction monitored by GC–MS. The catalyst was then filtered and washed with hexane. The organic layer was washed twice with a 5% solution of sodium bicarbonate, dried over anhydrous sodium sulfate and evaporated under reduced pressure. The residue was purified by flash chromatography (eluent hexane/EtOAc 15:1) to give the corresponding aldehydes.

3. Results and discussion

The heterogenisation of homogenous catalysts is an interesting field for continuing investigations. Although some of homogeneous transition metal complexes exhibit remarkable catalytic properties (activities and selectivity), they are unsuitable to separate intact materials from the reaction medium making their reuse difficult and contaminating the reaction

products. Thus, the heterogenisation is always a toxicological and environmental challenge. Moreover, it has an economical significance unless the activities of the homogeneous catalysts are exceptionally high. We have done the heterogenisation by supporting the InCl_3 on alumina. Therefore, the development of new reagents with more efficiency, shorter reaction time, non-corrosive, environmentally benign, present fewer disposal problems, separation from liquid products, repeated use and better yield are which interest. Recently, we had reported the development of heterogeneous reactions, which are facilitated by supported reagents on various solid surfaces [10].

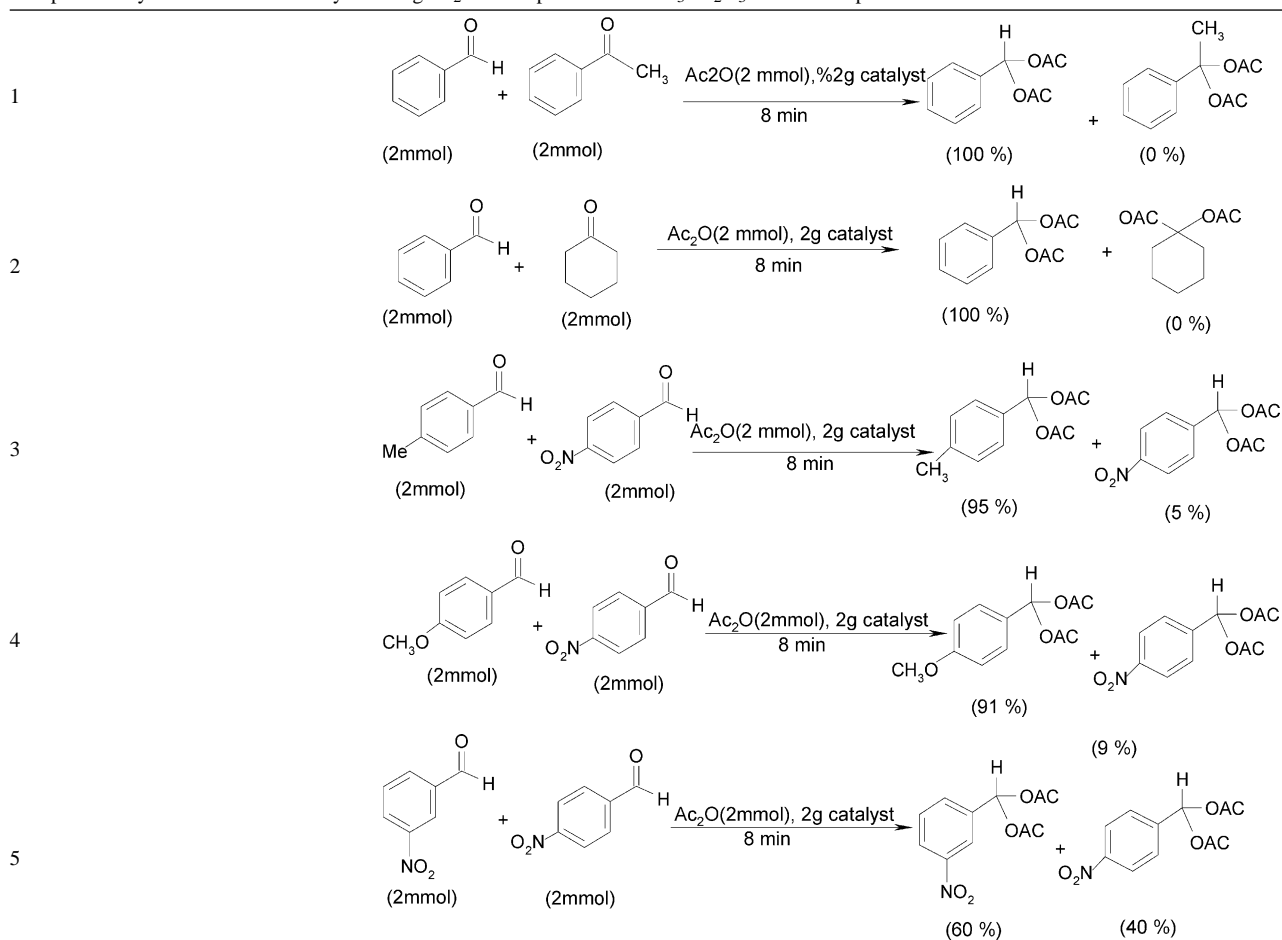
Herein, we report a new mild method for the preparation of acylals from aldehydes using $\text{InCl}_3/\text{Al}_2\text{O}_3$ as catalysts (Table 1). As summarized in Table 1, when the aldehydes reacts with acetic anhydride in the presence of $\text{InCl}_3/\text{Al}_2\text{O}_3$, to give the corresponding 1,1-diacetates in excellent yields at room temperature. The nature of the substituents on the aromatic ring seems to have no effect on the reaction system. Aliphatic as well as α,β -unsaturated aldehydes react under the same conditions yielding acylals in good yield. It is worth noting that ketones were acetylated under these conditions in very low yield (entry 10–12, Table 1), or did not react at the above method because represent a selective preparation of acylals from aldehydes in the presence of ketones (Table 3). We next investigated the use of $\text{InCl}_3/\text{Al}_2\text{O}_3$ as catalyst in deprotection of acylals to the corresponding aldehydes by treatment of acylals in dioxane at 50°C by this procedure only aromatic and α,β -unsaturated acylals have been transformed into the corresponding aldehydes in high yields (Table 1). When the reaction was carried out using aliphatic acylals, obtained low yields (35% for entry 14).

In order to show the merit of the present work in comparison with recently reported protocols, we compared the results of the *gem*-diacetate synthesis from 4-methylbenzaldehyde in the presence of $\text{AlPW}_{12}\text{O}_{40}$, $\text{Bi}(\text{OTf})_3$, $\text{Sc}(\text{OTf})_3$, $\text{Cu}(\text{OTf})_3$, LiBF_4 , NBS, InCl_3 , $\text{Zr}(\text{CH}_3\text{PO}_3)_{1.2}(\text{O}_3\text{PC}_6\text{H}_4\text{SO}_3\text{H})_{0.8}$ and Fe^{3+} -montmorillonite with respect to the amounts of the products (Table 2). The results show that $\text{InCl}_3/\text{Al}_2\text{O}_3$ promotes the reactions more effectively than InCl_3 , NBS, LiBF_4 , metal triflates and zirconium sulfophenyl phosphonate as far the amount of catalyst and reaction times are concerned. Re-

Table 2
Comparison of the effect of catalysts for *gem*-diacetate synthesis from 4-methylbenzaldehyde

Ref.	Yield	Time	Catalyst	Entry
[6e]	96	1 min	$\text{AlPW}_{12}\text{O}_{40}$	1
[7c]	85	30 min	$\text{Bi}(\text{OTf})_3$	2
[7b]	95	10 min	$\text{Sc}(\text{OTf})_3$	3
[7a]	98	2 h	$\text{Cu}(\text{OTf})_2$	4
[2]	92	24 h	LiBF_4	5
[12]	93	9 h	NBS	6
[13]	96	1 h	InCl_3	7
[6g]	75	0.2 h	$\text{Zr}(\text{CH}_3\text{PO}_3)_{1.2}(\text{O}_3\text{PC}_6\text{H}_4\text{SO}_3\text{H})_{0.8}$	8
This work	99	10 min	$\text{InCl}_3/\text{Al}_2\text{O}_3$	9

Table 3

Competitive acylal formation of aldehydes using Ac₂O in the presence of InCl₃/Al₂O₃ at room temperature

The percentage of the products in the reaction mixtures was determined by GC analysis and products were separated by prepared TLC in *n*-hexane:EtOAc (8:2).

action in the presence of LiBF₄ is required higher temperature with longer reaction time. Preparation of acylals with InCl₃, zirconium sulfophenyl phosphonate, Fe³⁺-montmorillonite, and metal triflates as catalyst were performed in solvent such as CH₃CN and at room temperature but the reaction times and also the yields of the products were lower than those obtained with InCl₃/Al₂O₃.

In order to show the high selectivity of the method, we studied competitive reaction for the acylation of aldehydes in the presence of ketones using InCl₃/Al₂O₃ as the catalyst at room temperature. Using this catalytic system, the highly selective conversion of aldehydes in the presence of ketones was observed. We also studied the acylation of 4-methylbenzaldehyde versus 4-nitrobenzaldehyde and 3-nitrobenzaldehyde in the presence of 4-nitrobenzaldehyde. These reactions also proceeded with high selectivity in the presence of this catalyst and showed the importance of electronic effects upon these reactions (Table 3). Some aliphatic and aromatic ketones were also checked for the reaction: acetone, butanone, acetophenone and ethyl *n*-butyl ketone, they have not reacted under the described experimental conditions.

4. Conclusion

In conclusion, we have introduced a new mild reaction condition, simple work up and recyclable nature of the catalyst for the preparation of acylals from aldehydes in the presence of acetic anhydride at room temperature in high yields. The method is highly selective for the sole preparation of acylals from aldehydes in the presence of ketones. In contrast to many other Lewis acids, storage of this catalyst does not need special precautions, e.g. it can be stored on a bench top for months without losing its catalytic activity. In addition, as a non-corrosive and water stable catalyst, the handling of InCl₃/Al₂O₃ is easy which makes this catalyst suitable for the large-scale operations.

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