

Solid Trichlorotitanium (IV) Trifluoromethanesulfonate TiCl_3 (OTf) Catalyzed Highly Efficient Protection of Aldehydes as their Acylals at Room Temperature under Solvent-Free Conditions

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$\text{TiCl}_3(\text{OTf})$ catalyzed efficiently the protection of aromatic aldehydes with acetic anhydride in the absence of solvent at room temperature with excellent yields. By this method, aliphatic aldehydes were also converted to their corresponding acylals, in the presence of a mixture of acetic anhydride and acetic acid at high yields.

INTRODUCTION

The protection of aldehyde groups is an essential problem in multi-step organic synthesis. One of the most popular methods is the protection of carbonyl groups as their corresponding acetals through the reaction between aldehydes and an alcohol. Most of the acetals obtained are liquid, which may contain impurities, and their purification may be a tedious and a time-consuming process; in addition, acetals are very labile towards acidic conditions. The transformation of aldehydes to their 1,1-diacetates (acylals) is a synthetically important reaction for the protection of aldehyde groups. The importance of 1,1-diacetates is due to their remarkable stability towards a variety of reaction conditions, such as aqueous acids, neutral and mild basic media [1].

Moreover, 1,1-diacetates of aromatic aldehydes are solid compounds, the purification of which is easily accomplished by crystallization. In addition, gem diacetates are synthetically important precursors for the preparation of 1-acetoxydienes [2]; valuable synthetic intermediates for Diels-Alder cycloaddition reactions. Homoallyl acetates [3,4] and 1,1-diacetate functional-

ity have found industrial applications as cross-linking agents for cellulose in cotton [5]. In general, 1,1-diacetates are obtained from the reaction between aldehydes and acetic anhydride, in the presence of strong proton acids as catalysts, such as H_2SO_4 [6] and $\text{CH}_3\text{SO}_3\text{H}$ [7], Lewis acids, such as FeCl_3 [1], $\text{Sc}(\text{OTf})_3$ [8], I_2 [9], InCl_3 [10], GaI_3 [11], InBr_3 [12] and LiOTf [13], or inorganic solid catalysts, such as Nafion H [14], Zeolites [15,16], heteropoly acids [17,18], LiClO_4 [19], silica sulfuric acid [20], KHSO_4 [21], $\text{P}_2\text{O}_5/\text{Al}_2\text{O}_3$ [22], $\text{HBF}_4\text{-SiO}_2$ [23], PEG-supported sulfonic acid [24], $\text{Zn}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$ [25] and CAN [26] and also, in reactions under neutral conditions, such as when using NBS [27]. However, these methods usually encounter difficulties and have several drawbacks. Strong protic acids are corrosive, NBS and CAN are strong oxidizing agents and perchlorates are potentially explosive compounds. Other problems are the use of toxic organic solvents, which have long reaction times, high reaction temperatures and use a high excess of equivalent amounts of acetic anhydride in order to proceed the reaction to completion.

Performing the reactions under solvent free conditions is economically advantageous and usually reaction rates and yields are increased and work up procedure is easier. Titanium tetrachloride has been widely used in the process industries. It is a highly aggressive material whose major hazardous potential comes from the clouds of HCl and titanium compounds created when this substance is exposed to moisture. However,

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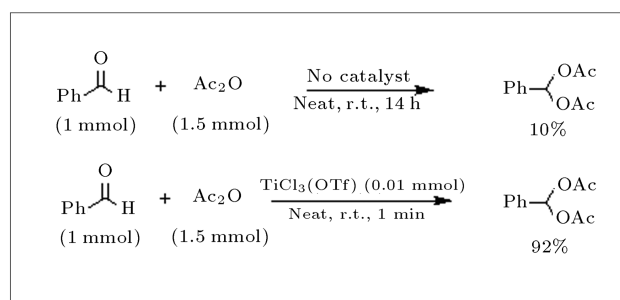
its handling needs serious precautions. Therefore, the design of new titanium based reagents that are convenient to use yet retain their high catalytic activity is of considerable importance to the synthetic community. Trichlorotitanium (IV) trifluoromethanesulfonate, $\text{TiCl}_3(\text{OTf})$ is a solid compound and its handling is much easier than TiCl_4 . Previously, Iranpoor and Zeynizadeh have reported application of $\text{TiCl}_3(\text{OTf})$ for the conversion of epoxides to 1,3-dioxolanes [28], aldol condensation of cycloalkanones with aromatic aldehydes [29] and the conversion of acetophenones to 1,3,5-triarylbenzenes [30]. Very recently, this compound has also been used as an efficient catalyst for esterification and transesterification reactions [31].

In this paper, another application of $\text{TiCl}_3(\text{OTf})$ is disclosed as an effective solid catalyst for the transformation of aldehydes to their 1,1-diacetates (acylals) under solvent-free conditions with short reaction times.

RESULTS AND DISCUSSION

Trichlorotitanium (IV) trifluoromethanesulfonate, $\text{TiCl}_3(\text{OTf})$ was prepared according to the literature [32]. At first, in order to show the merit of the catalyst, the reaction of benzaldehyde with acetic anhydride in the absence of $\text{TiCl}_3(\text{OTf})$ was examined. It was observed that no considerable amount (10%) of the corresponding 1,1-diacetate was formed, even after 14 h. On the other hand, a similar reaction in the presence of a catalytic amount of $\text{TiCl}_3(\text{OTf})$ (0.01 mmol), benzaldehyde was converted into its 1,1-diacetate (acylal) with an excellent yield under neat conditions (Scheme 1).

The merit of the catalyst is shown in Table 1 by comparison of the results obtained using the other catalysts for the reaction of benzaldehyde with Ac_2O .



Scheme 1. Reaction of benzaldehyde with acetic anhydride in the presence of $\text{TiCl}_3(\text{OTf})$ (0.01 mmol) as a catalyst and also in the absence of the catalyst.

Then various types of aldehydes were treated with acetic anhydride in the presence of $\text{TiCl}_3(\text{OTf})$ (1 mol%) under solvent-free conditions at room temperature (Table 2). Most of the aromatic aldehydes were converted into their corresponding acylals with excellent yields under solvent-free conditions (Table 2, entries 1-6 and 10-12). The reaction of solid aromatic aldehydes (3-nitro-, 4-nitro- and 4-N,N-dimethylamino- benzaldehyde) was conducted in CH_2Cl_2 . 3-Nitrobenzaldehyde produced the corresponding 1,1-diacetate with an excellent yield (Table 2, entry 7), whereas the reaction of 4-nitrobenzaldehyde and 4-N,N-dimethylamino-benzaldehyde with acetic anhydride was not satisfactory by this protocol (Table 2, entries 8 and 9). Moreover, this method could work equally well with trans-cinnamaldehyde as an α , β -unsaturated aldehyde (Table 2, entry 13).

Reports regarding the production of acylals from aliphatic aldehydes are rather limited in the literature. In this investigation, the reaction of heptanal has been studied as an aliphatic aldehyde in the presence of $\text{TiCl}_3(\text{OTf})$ (1 mol%) with acetic anhydride at room temperature. The reaction proceeded to completion,

Table 1. Comparison of acylal formation of benzaldehyde with Ac_2O catalyzed by $\text{TiCl}_3(\text{OTf})$ and some other catalysts at room temperature.

Entry	Lewis Acid (mol %) Benzaldehyde (mmol): Ac_2O (mmol)	Time (min)	Isolated Yield %	Ref.
1	LiClO_4 (200 mol%) (3 mmol): (5 mmol)	25	92	[19]
2	KHSO_4 (20 mol%) (1 mmol): (2 mmol)	1	99	[21]
3	$\text{P}_2\text{O}_5/\text{Al}_2\text{O}_3$ (15 mol%) (2 mmol): (5 mmol)	45	86	[22]
4	PEG-supported sulfonic acid (10 mol%) (1 mmol): (20 mL)	35	92	[24]
5	$\text{Zn}(\text{ClO}_4)_2$ (1 mol%) (1 mmol): (1.5 mmol)	2	93	[25]
6	$\text{TiCl}_3(\text{OTf})$ (1 mol%) (1 mmol): (1.5 mmol)	1	92	-

Table 2. TiCl₃(OTf) catalyzed acetylation of aldehydes with Ac₂O at room temperature under solvent-free conditions^{a,b}.

Entry	Substrate	Product	Time	Isolated Yield %
1	Benzaldehyde	1a	1 min	92
2	4-Me-Benzaldehyde	2a	1 min	90
3	4-Cl-Benzaldehyde	3a	5 min	91
4	2-Cl-Benzaldehyde	4a	4 min	90
5	2,6-Dichlorobenzaldehyde	5a	1 min	96
6	Anisaldehyde	6a	10 min	94
7	3-NO ₂ -Benzaldehyde ^c	7a	20 min	95
8	4-NO ₂ -Benzaldehyde ^c	8a	1 h	nr
9	4-N(Me) ₂ -Benzaldehyde ^c	9a	5 h	nr
10	Furfural	10a	5 min	85
11	1-Naphthaldehyde	11a	5 min	93
12	2-Naphthaldehyde	12a	5 min	94
13	Cinnamaldehyde	13a	3 min	87
14	Heptanal ^d	14a	10 min	54
		14b		17
15	Octanal ^d	15a	10 min	60
		15b		15
16	Acetophenone	16a	4 h	nr

a: All of the products were characterized with comparison of their spectral data with those of known samples;

b: The molar ratio of substrate/ Ac₂O/ TiCl₃(OTf) is 1: 1.5: 0.0 1;

c: The reaction was accomplished in CH₂Cl₂ (2 mL) as solvent;

d: The reaction was carried out at -20°C.

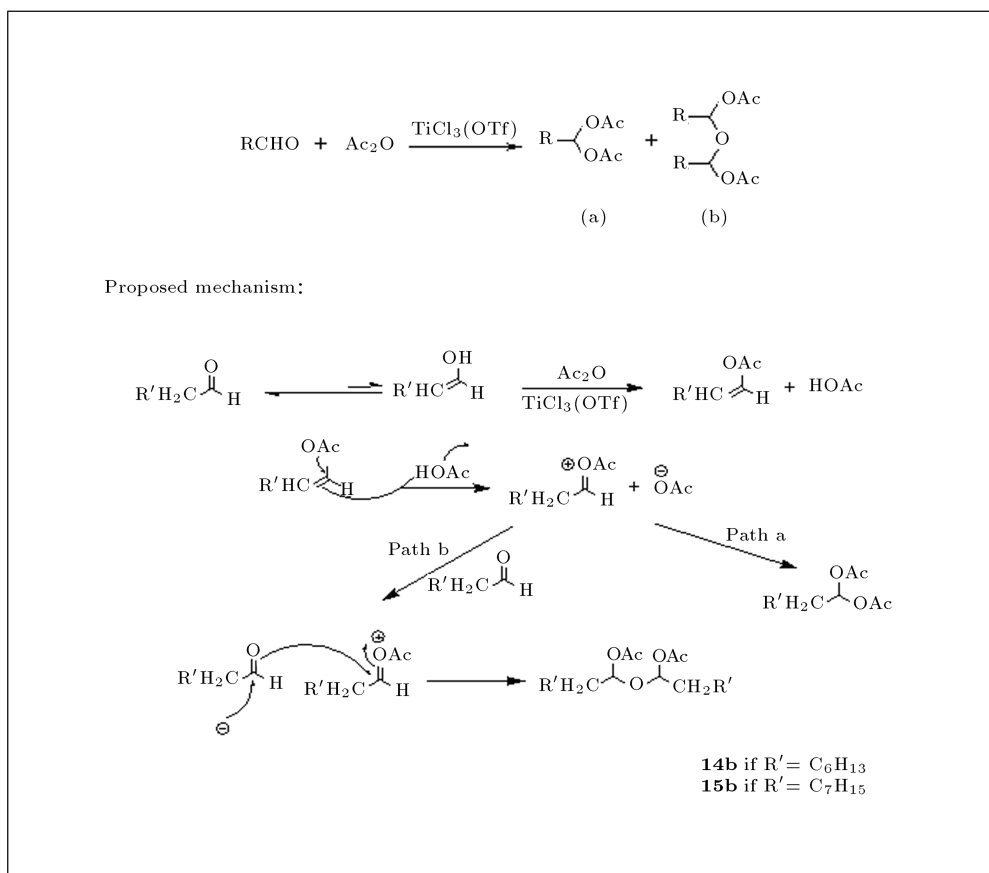
although a mixture of several unidentified products was obtained. Then, a similar reaction was conducted at lower temperatures. It was found that at -20°C the reaction proceeded well to completion, with the production of the corresponding acylal at 54% isolated yield plus a side product of **14b** at 17% isolated yield. The reaction of octanal proceeded similarly under similar reaction conditions to give the acylal in 60% isolated yield plus a side product at 15% yield. It was of interest to determine the structure of the side products, **14b** and **15b**, in order to know whether the yield of the acylals can be increased by eliminating the pathway leading to the side product formations. The structures of **14b** and **15b** were assigned by their spectral data (¹H NMR, ¹³C NMR and mass spectra), as indicated by Scheme 2. The authors have proposed a mechanism for the formation of the side products presented in Scheme 2. According to the proposed mechanism, if the concentration of the acetate ion increases in the reaction mixture, acylal formation

via **pathway a** will be more facilitated. For this purpose, NaOAc, NH₄OAc and HOAc were added to the reaction mixture. Surprisingly, in the presence of HOAc (2 mmol), the reaction of heptanal or octanal with acetic anhydride proceeded to completion and, after 5 min, the desired corresponding acylals were isolated at 80 and 85%, respectively (Scheme 3).

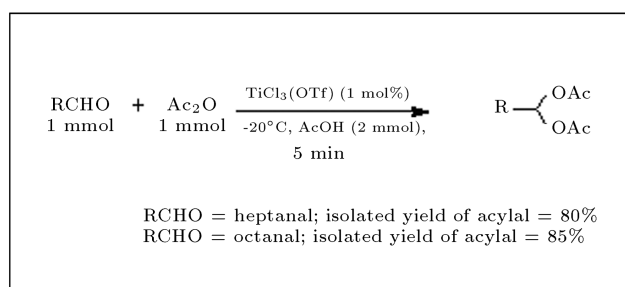
It is also worth mentioning that acetophenone did not produce the corresponding 1,1-diacetate under similar reaction conditions (Table 2, entry 16).

CONCLUSION

In conclusion, in this article, an easy handling solid analogue of TiCl₄ has been introduced, which is applied as an efficient catalyst for the preparation of 1,1-diacetates (acylals) from aldehydes. By this method, acylals were obtained, after a short reaction time, at room temperature, with high to excellent yields. TiCl₃(OTf) can be considered as a bench top catalyst,



Scheme 2. Proposed mechanism for the formation of the side product from the reaction of aliphatic aldehydes and acetic anhydride using $\text{TiCl}_3(\text{OTf})$ as a catalyst.



Scheme 3. Reaction of aliphatic aldehydes with acetic anhydride in the presence of acetic acid catalyzed by $\text{TiCl}_3(\text{OTf})$ (0.01 mmol).

which can be stored in a bottle for weeks without losing its catalytic activity. Other catalytic applications of this catalyst are, at present, being researched.

EXPERIMENTAL

General Procedure for the Preparation of 1,1-Diacetates from Aromatic Aldehydes

$\text{TiCl}_3(\text{OTf})$ (0.01 mmol) was added to a magnetically stirred mixture of aldehyde (1 mmol) and freshly

distilled acetic anhydride (1.5 mmol) at room temperature. The reaction mixture was stirred until complete disappearance of the starting material (as monitored by TLC); reaction was quenched with water (25 mL). The resulting mixture was extracted with Et_2O (2×15 mL). The organic layer was separated and washed with saturated NaHCO_3 (2×15 mL) and water (10 mL), from which, after drying over anhydrous Na_2SO_4 and evaporation of the solvent under reduced pressure, the almost pure 1,1-diacetate was obtained. For further purification, if necessary, column chromatography also gives the corresponding pure product at excellent yields (Table 2).

General Procedure for the Preparation of 1,1-Diacetates from Aliphatic Aldehydes

$\text{TiCl}_3(\text{OTf})$ (0.01 mmol) was added to a magnetically stirred mixture of aldehyde (1 mmol), freshly distilled acetic anhydride (1 mmol) and acetic acid (2 mmol) at -20°C . The reaction mixture was stirred for 5 min and then was quenched with water (25 mL). The reaction mixture was extracted with Et_2O (2×15 mL) and the organic layer was separated. Then it was washed with

saturated NaHCO₃ (2 × 15 mL) and water (10 mL) and was dried over anhydrous Na₂SO₄. After filtration and evaporation of the solvent under reduced pressure, the almost pure 1,1-diacetates were obtained. For further purification, if necessary, column chromatography with the appropriate solvents gave the corresponding pure products (Scheme 3).

Spectral Data of the Side Products of Aliphatic Aldehydes

14b: Oil, ¹H NMR δ (ppm): 0.90 (t, J = 5 Hz, 6H), 1.30-1.42 (m, 16H), 1.70-1.76 (m, 4H), 2.07 (s, 6H), 6.02 (t, J = 5.5 Hz, 2H); ¹³C NMR δ (ppm): 14.0, 21.2, 22.4, 23.6, 28.8, 31.6, 34.2, 96.4, 169.8; MS (70 eV), m/e: 272 (M), 271(M-1), 227 (M-CH₃CO), 210 (M-CH₃CO₂H), 157 (M-C₇H₁₄OAc), 113 (C₆H₁₃CO⁺), 97 (C₇H₁₃⁺).

15b: Oil, ¹H NMR δ (ppm): 0.89 (t, J = 5.1 Hz, 6H), 1.20-1.44 (m, 20H), 1.66-1.74 (m, 4H), 2.08 (s, 6H), 6.00 (t, J = 5.5 Hz, 2H); ¹³C NMR δ (ppm): 14.0, 21.2, 22.8, 23.6, 28.8, 29.1, 31.7, 34.3, 96.4, 170.4; MS (70 eV), m/e: 300 (M), 299 (M-1), 255 (M-CH₃CO), 238 (M-CH₃CO₂H), 171 (M-C₈H₁₆OAc), 127 (C₇H₁₅CO⁺), 111(C₈H₁₅⁺).

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