ISSN: 0974 - 7516 Volume 9 Issue 1

Trade Science Inc.

Organic CHEMISTRY

An Indian Journal

Full Paper

OCAIJ, 9(1), 2013 [28-33]

2, 4, 6-trichloro [1, 3, 5] triazine (TCT) as a fast, inexpensive and highly efficient catalyst for acetalization of aromatic aldehydes

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ABSTRACT

This paper describes a simple, efficient and inexpensive method for transformation of aromatic aldehydes to corresponding dimethyl and/or diethyl acetals using TCT as catalyst. Comparing other known methods, this method is fast and effective without obligation of using ortho-esters as acetalization reagent. Also this new method is chemoselective for aromatic aldehydes versus aromatic ketones.

KEYWORDS

Protection;
Aldehyds;
Acetalization;
2, 4, 6-trichloro [1, 3, 5] triazine (TCT).

INTRODUCTION

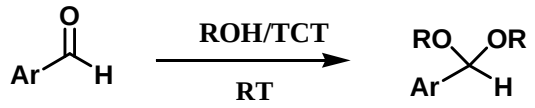
Acetalization is one of the most important and useful protecting methods for aldehydes and ketons[1-3]. Furthermore they can be easily converted to a vast variety of other useful compounds so serve as useful intermediates in organic synthesis. Acetalyzation is usually carried out by reaction between carbonyl group and alcohol and/or its corresponding ortho-ester in presence of an acid catalyst. Several methods have already been reported for formation of dimethyl acetals[4-6] and diethyl acetals[7-10]. Also there are different methods for the formation of 1, 3-dioxolanes by using ethylene glycol in presence of an acide catalyst[11,12]. Furthermore there are different mild methods for the acetalization of aldehydes under neutral conditions[13-17].

2, 4, 6-trichloro [1, 3, 5] triazine (cyanuric chloride or TCT) is an inexpensive, non-volatile, safe and adequate reagent. Its high solubility in organic solvents, which makes it an ideal catalyst for organic syntheses also its waste product (cyanuric acid) which is a non-hazardous substance and is readily removable by water made it as a good candidate in organic synthesis. For these reasons, it has already been used vastly for preparation of different compounds such as benzoxanthens[18], dihydroxypyridines[19], Thiiranes[20], bis indolyl methanes[19], isonitriles[21], alkyl chlorides[22], α, α'-bis (substituted-benzylidene) cycloalkanones[23], ddihydropyrimidinone[23] and Beckmann rearrangement product[24,25].

RESULT AND DISCUSSION

In continuation of our studies on developing inexpensive and environmentally benign methodologies for organic reactions[26-31], we reveal herein for the first time, TCT catalyzed the conversion of aldehydes to the corresponding acetals in good to excellent yields with a vast variety of aldehydes using both methanol and ethanol as the reaction medium at room temperature (Scheme 1). The versatility of TCT and its low cost, also its efficiency in the vast variety of organic transformations and its facile work-up encourage us to investigate present study. To the best of our knowledge, there

is no literature report on the acetalization of aldehydes under these conditions (Scheme 1).



Scheme 1 : Acetalization reaction from aromatic aldehydes using TCT

As we mentioned earlier TCT has not yet been used for these types of acetalization so we decided to use it as catalyst. For example DDQ have been used for this acetalization but it is however rather corrosive and toxic from TCT[32].

To establish the best conditions for acetalization of aromatic aldehydes, we started with benzaldehyde. To study the limitation of catalyst amounts we explored some reaction conditions which results are summarized in TABLE 1.

TABLE 1: The optimization of TCT concentration in dimethylacetalization of benzaldehyde at room temperature

Entry	TCT/mmol	MeOH/mL	Time/min	%Yield[a]
1	0.000	9	1440	No Reaction
2	0.005	9	5	85
3	0.016	9	5	92
4	0.027	9	5	88
5	0.038	9	5	86

[a] yields are detected by GC

As it is shown in TABLE 1, the best quantity of TCT is 0.016 mmol And more quantities of catalyst decreases the total yields (TABLE 1, *entries* 3, 4 and 5) so we used 0.016 mmol Of TCT in all our experiences.

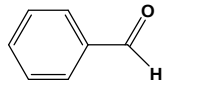
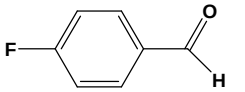
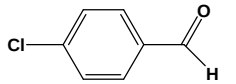
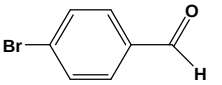
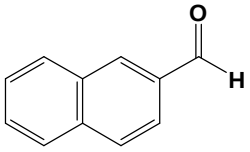
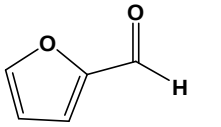
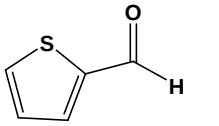
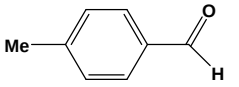
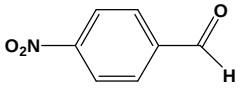
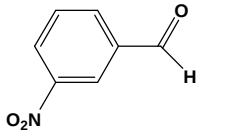
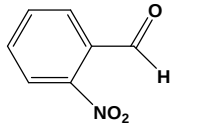
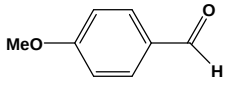
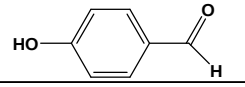
TABLE 2 : The optimization of methanol in acetalization reaction between benzaldehyde and methanol in presence of 0.016 mmol of TCT at room temperature

Entry	Time/min.	MeOH/mL	%Yield[a]
1	5	3	82
2	5	4	84
3	5	5	89
4	5	6	92
5	5	7	92
6	5	9	92

[a] yields are detected by GC

As in this reaction, alcohol is employed as one of the reactant as well as the solvent so in second goal we decided to optimize alcohol concentration in the acetalization reaction. To study the limitation of alcohol amounts, we investigated some reaction conditions.

TABLE 3 : Optimization of acetalization of different aldehydes with methanol at room temperature[a]

Entry	Aldehyde	Time/min.	Yield%[b]
1		5	92 (90)[c]
2		17	93
3		15	96
4		13	96
5		7	80
6		12	89
7		15	79
8		6	81
9		180 (90)[d]	97
10		180 (90)[d]	97
11		360 (180)[d]	83
12		30	70[c]
13		30	65[c]

[a] reaction condition: aldehyde (2 mmol), methanol (6 mL), TCT (0.016 mmol); [b] yields are detected by GC; [c]isolated yield; [d] reflux

The results of the acetalization reaction between benzaldehyde and methanol in presence of 0.016 mmol

of TCT as catalyst at room temperature are summarized in TABLE 2.

As it indicated in TABLE 2, the best yields were obtained by employing 6 mL. or more methanol as reactant and solvent (*entries* 4, 5 and 6) so we used it in all our experiences.

To study the scope of this procedure, the acetalization reactions of a series of various aldehydes with methanol at room temperature have been studied. The results are summarized in TABLE 3.

As indicated in TABLE 3, the reaction works easily for a vast variety of aromatic aldehydes with different groups to give corresponding dimethyl acetal in good to excellent yields.

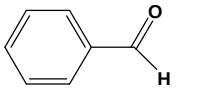
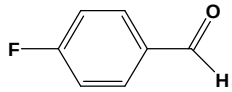
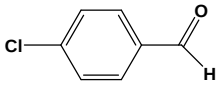
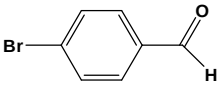
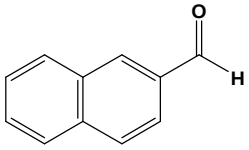
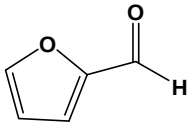
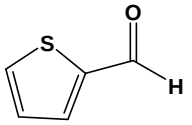
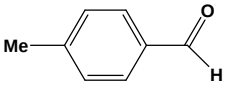
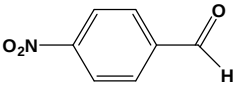
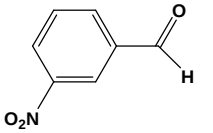
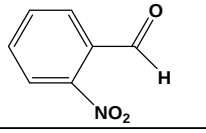
It is important to note that it seems that aldehydes with halogen groups on para position (TABLE 3, *entries* 2, 3, 4) provide higher yields. Also it is notable that this condition is reliable for other aromatic aldehydes like 2-naphtaldehyde, furan-2-carbaldehyde and thiophen-2-carbaldehyde (TABLE 3, *entries* 5, 6, 7).

On the other hand, it seems that in the case of aromatic aldehydes with a strong electron withdrawing group, the reaction complete slower but the yields are excellent (TABLE 3, *entries* 9, 10 and 11). It also seems that in the case where the nitro group is in *ortho* position, the reaction is slower. The reason however, seems to be the steric hindence. It would be interesting to test this hypothesis as well, but it felt outside the scope of the current investigation.

As there are more limitations in the synthesis of diethyl acetals[33], we decided to test our new condition for diethyl acetals too. To study this goal, the acetalization reactions of a series of various aldehydes with ethanol in the same conditions at room temperature also have been studied. The results are summarized in TABLE 4.

Fortunately as indicated in TABLE 4, the reaction works easily for the vast variety of aromatic aldehydes with different groups to give corresponding diethyl acetal in good to excellent yields too. However in a first glance it seems that the yields are lower comparing with dimethyl acetals, but comparing the other methods of diethyl acetalization, the yields are compatible and even in some cases they are bette[33]. However, the aldehydes with halogen groups on para position (TABLE 4, *entries* 2, 3, 4) provide higher yields as their corresponding dimethyl acetals. Also it works well for other aromatic aldehydes like 2-naphtaldehyde, furan-2-carbaldehyde and thiophen-2-carboxaldehyde (TABLE 4, *entries* 5, 6, 7).

TABLE 4 : Optimization of acetalization of different aldehydes with ethanol at room temperature[a]

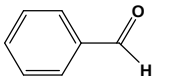
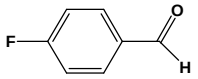
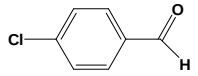
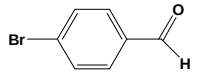
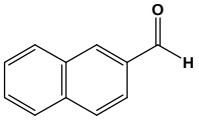
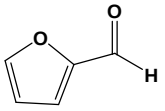
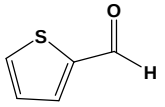
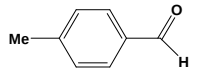
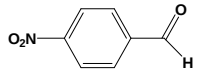
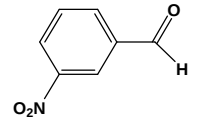
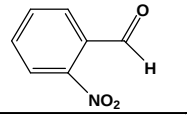
Entry	Aldehyde	Time/h	Yield%[b]
1		0.30	78
2		0.50	83
3		0.60	90
4		0.50	90
5		0.40	64 (95)[c]
6		0.25	81
7		0.30	62 (95)[c]
8		0.15	66 (97)[c]
9		5.00	81 (99)[c]
10		4.50	88 (99)[c]
11		8.00	65 (99)[c]

[a] reaction condition: aldehyde (2 mmol), ethanol (6 mL), TCT (0.016 mmol); [b] yields are detected by GC; [c] reflux

On the other hand, it seems that the same order exists for aromatic aldehydes with a strong electron withdrawing group, it means that the yields are lower and the reaction needs to more time to be complete but by refluxing the yields would be excellent (TABLE 4, *entries* 9, 10 and 11).

As indicated above, in the case of aromatic aldehydes with an electron withdrawing group (TABLES 3 and 4, *entries* 9-11) there is a notable difference between the yields at room temperature and reflux condition. It means that in the case of aromatic aldehydes with an electron withdrawing group, refluxing the reaction mixture decreases the reaction time and/or increases the yields. Although the reaction was sufficiently fast and efficient for other aromatic aldehydes, we have decided to investigate some experiences to study the temperature effect on acetalization reaction. The results are summarized in TABLE 5.

TABLE 5 : Optimization of acetalization of different aldehydes with methanol[a]

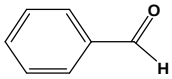
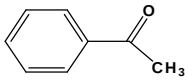
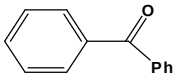
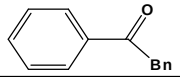
Entry	Aldehyde	Time/min.	Temperature	Yield%[b]
1		5	ambient	92
			reflux	92
2		17	ambient	93
			reflux	94
3		15	ambient	96
			reflux	96
4		13	ambient	96
			reflux	97
5		7	ambient	80
			reflux	90
6		12	ambient	89
			reflux	89
7		15	ambient	79
			reflux	79
8		6	ambient	81
			reflux	81
9		90	ambient	65
			reflux	97
10		90	ambient	65
			reflux	97
11		180	ambient	60
			reflux	83

[a] reaction condition: aldehyde (2 mmol), methanol (6 mL), TCT (0.016 mmol); [b] yields are detected by GC

As indicated in TABLE 5, for most of the aromatic aldehydes the reaction is sufficiently fast and efficient and refluxing does not change the obtained yield. But in the case of aromatic aldehydes with electron attracting groups, it seems that the reaction rate is slow and refluxing could ameliorate the rate and the yields (TABLE 6, *entries* 5, 9-11).

Finally to test the chemoselectivity of this method we investigated some experiences. We tested our optimum conditions for acetalization reaction of some aromatic ketones like actophenone, benzophenone and benzyl phenyl ketone. The results are summarized in TABLE 6.

TABLE 6 : Chemoselectivity on acetalization of aromatic carbonyl compounds with different alcohols in presence of TCC at room temperature[a]

Entry	Carbonyl	Alcohol	Time	Yield%[b]
1		MeOH	5 min.	92
		EtOH	20 min.	78
		PrOH	1 day	nr
2		MeOH	1 day	nr
		EtOH	1 day	nr
		n-PrOH	1 day	nr
3		MeOH	1 day	nr
		EtOH	1 day	nr
		n-PrOH	1 day	nr
4		MeOH	1 day	nr
		EtOH	1 day	nr
		n-PrOH	1 day	nr

[a] reaction condition: aldehyde (2 mmol), alcohol (6 mL), TCT (0.016 mmol); [b] yields are detected by GC

As indicated in TABLE 6, the reaction does not work for aromatic ketons even after 24 hours (TABLE 6, *entries* 2 and 3). So this method is totally chemoselective for aromatic aldehydes and aromatic ketons. As the reaction does not work for n-propanol (TABLE 6, *entry* 4) the steric hindence should be at the origin of these facts.

CONCLUSION

In conclusion to the best of our knowledge there is no report available in the literature for acetalization of aldehydes using TCT as catalyst furthermore our new method provides a simple, fast, efficient and inexpensive way to transformation of aromatic aldehydes to corresponding methyl and ethyl acetals in good to excellent yields. Furthermore this method is simple, fast and efficient without obligation of using orthoesters as acetalization

reagent and also does not involve halogenated solvents which are important from economic and environmental view point. Also this new method is chemoselective for aromatic aldehydes versus aromatic ketones.

EXPERIMENTAL SECTION

General

The chemicals were purchased from the Fluka, Merck, and Aldrich chemical companies. TLC on commercial aluminum-backed plates of silica gel 60 F254 was used to monitor the progress of reactions. Also in almost all cases the progress of reactions was followed by GC. These analyses were performed by a GC-17A Shimadzu instrument. The IR spectra were taken on a Perkin-Elmer, model 783 spectrophotometer. The NMR spectra have been recorded by a Bruker AMX-300 (300 MHz) spectrometer with 7-10 mM solutions in $CDCl_3$ in the presence of tetramethyl silan as internal standard. The chemical shifts are expressed in parts per million (ppm), and tetramethylsilane (TMS) was used as internal reference.

General procedure for the acatilization of aromatic aldehyde

In a typical general experimental procedure, a solution of benzaldehyde (2 mmol) in 6 mL of methanol in the presence of TCT (0.016 mmol) was stirred at room temperature and the reaction was followed by TLC until the starting materials were totally consumed. The resulting reaction mixture was quenched by saturated sodium bicarbonate (1 mL). Water (3 mL) then was added and the solution was added with diethyl ether (3x15 mL). The organic layer were collected, washed with water (2x3 mL), dried over $MgSO_4$ and finally evaporated under vacuum. The crude product was purified by column chromatography and/or vacuum micro distillation.

ACKNOWLEDGEMENTS

We thank the department of chemistry of Semnan University for supporting this work.

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