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Efficient Tetrahydropyranylation of Alcohols and Detetrahydropyranylation Reactions in the Presence of Catalytic Amount of Trichloroisocyanuric Acid (TCCA) as a Safe, Cheap Industrial Chemical

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Efficient Tetrahydropyranylation of Alcohols and Detetrahydropyranylation Reactions in the Presence of Catalytic Amount of Trichloroisocyanuric Acid (TCCA) as a Safe, Cheap Industrial Chemical

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ABSTRACT

Preparation and cleavage of THP ethers of different hydroxy functional groups are easily and efficiently performed in the presence of trichloroisocyanuric acid (TCCA) in the absence of solvent with high yields.

Key Words: Trichloroisocyanuric acid; Tetrahydropyranylation; Detetrahydropyranylation; Solvent-free.

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INTRODUCTION

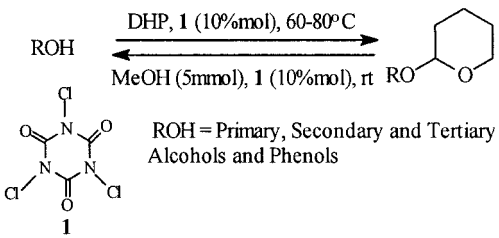
The worldwide production of trichloroisocyanuric acid, 1, 3, 5-2, 4, 6-(1H, 3H, 5H)trione (TCCA) and its monosodium salt (DCCA) is about 100,000 t/year and the demand is increasing by 8–10% per year for swimming pools and 3–5% for food processing. This safe chemical has never had a real breakthrough in organic laboratories and its uses in organic chemistry are mostly limited to chlorination and oxidation reactions.[1] Recently, dehydrogenation of indolines,[2] urazoles,[3a] and *N*-nitrosation of secondary amines[3b] have been achieved in the presence of TCCA.

The first catalytic application of trichloroisocyanuric acid was reported by our research group for efficient thioacetalization and transthioacetalization reactions.[4]

Tetrahydropyranylation of alcohols and phenols is a useful tool for masking hydroxy functional groups for further manipulation in organic synthesis. This transformation has found important synthetic applications because of the stability of the tetrahydropyranyl derivatives towards basic media, Grignard reagents, and reactions involving oxidation and reduction by inorganic hydride transfer agents.[5] In this article we have presented another catalytic application of TCCA in tetrahydropyranylation and detetrahydropyranylation reactions.

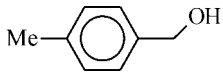
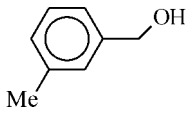
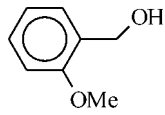
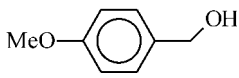
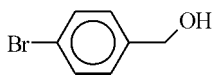
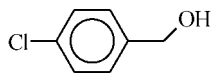
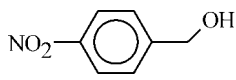
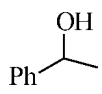
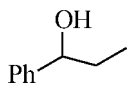
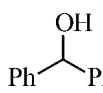
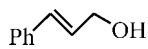
RESULTS AND DISCUSSION

In continuation of our interest in functional group transformation under mild reaction conditions, we now report that TCCA can be employed as an efficient catalyst for the protection of primary, secondary, and tertiary alcohols and phenols with 3,4-dihydro-2-H-pyran (DHP) at 60–80°C under solvent-free conditions. In this study, we have shown that primary and secondary benzylic alcohols substituted with electron-donating and electron-withdrawing groups can be effectively protected in the presence of 0.1 molar ratio of TCCA to their corresponding tetrahydropyranyl ethers in high yields (Sch. 1, Table 1, entries 1–11).



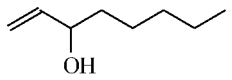
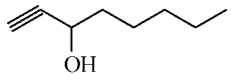
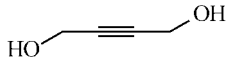
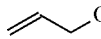
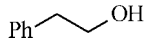
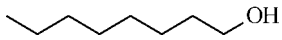
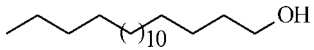
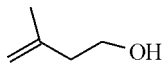
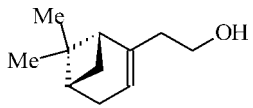
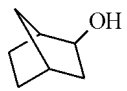
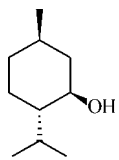
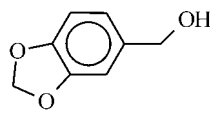
Scheme 1.

Table 1. Tetrahydropyranylation of alcohols and phenols catalyzed by TCCA under solvent-free conditions.

		Time (h)		Yield (%)[a,c,d]	
Entry	Subs.	Prot.	Deprot.	Prot.	Deprot.
1		5	3	92	95
2		5	4	92	96
3		5	3.5	93	95
4		5.5	3	94	95
5		5	4	94	94
6		5.5	4	91	95
7		5	4	92	94
8		8	6	87	92
9		6	4	92	94
10		6	4	90	92
11		7	4	90	90
12		5	3	92	95

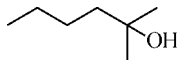
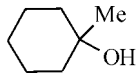
(*continued*)

Table 1. Continued.

Entry	Subs.	Time (h)		Yield (%)[a,c,d]	
		Prot.	Deprot.	Prot.	Deprot.
13		8	5	88	95
14		8	6	87	92
15		10	6	89	91
16		8	7	92[b]	95[b]
17		6	5	95	96
18		5.5	5	94	94
19		7	6	90	95
20		6	6	89	94
21		7	6	87[b]	92[b]
22		5	4	92	95
23		6	5	90	94
24		5	4	91	93
25		6	4	90	94
26		5	4	90	92

(*continued*)

Table 1. Continued.

Entry	Subs.	Time (h)		Yield (%)[a,c,d]	
		Prot.	Deprot.	Prot.	Deprot.
27		24	7	75[b]	91[b]
28		24	8	80[b]	90[b]
29	1-adamantanol	8	5	89	90
30	phenol	36	6	85	92
31	4-bromo phenol	38	7	87	90
32	cholesterol	5	4	88	90
33	4-hydroxybenzaldehyde	36	7	85	91

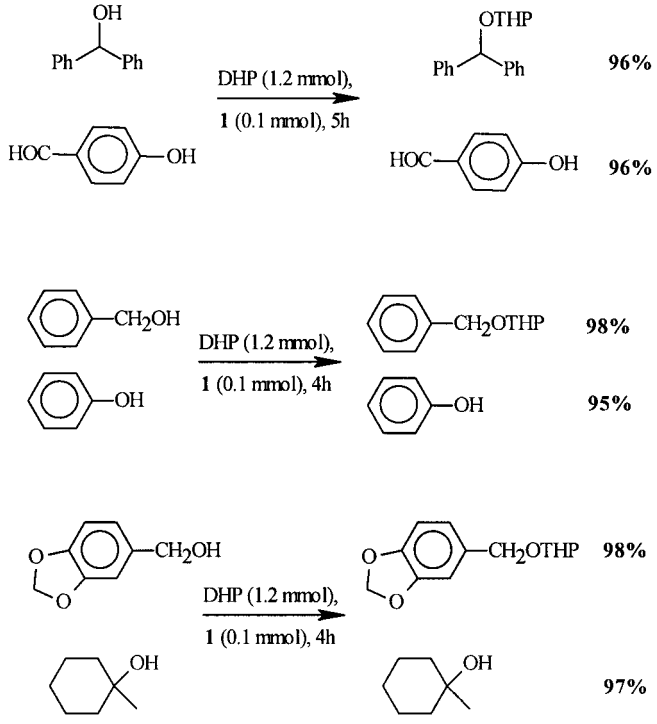
[a]Isolated yields.
[b]GC yields using internal standard.
[c]The amount of DHP was 1.2–1.6 mmol per 1 mmol of the substrate.
[d]Structures were confirmed by IR, ^{1}H-NMR, ^{13}C-NMR, mp/bp.

Cinnamyl, primary and secondary allylic and propargylic alcohols were also efficiently converted to their tetrahydropyranyl ethers in excellent yields without isomerization of the C-C double and triple bonds (Table1, entries 12–16). Primary and secondary acyclic and cyclic saturated alcohols were also effectively transformed to their tetrahydropyranyl ethers with high yields (Table 1, entries 17–25). Preparation of tertiary ethers is not an easy task and is usually accompanied by the formation of olefins and usually with low yields. Therefore, we applied this method for the preparation of tetrahydropyranyl ethers from tertiary benzylic alcohols such as 1-methylcyclohexanol, 2-methyl-2-hexanol, and 1-adamantol in good yields (Table 1, entries 27–29). Protection of phenolic hydroxy groups has been achieved in the presence of this catalyst. Phenol, 4-bromophenol and 4-hydroxy benzaldehyde were converted to their corresponding ethers in high yields (Table 1, entries 30, 31, and 33). The hydroxy functional group of cholesterol was also efficiently converted to its THP ether under solvent-free conditions in the presence of this catalyst in 88% yield (Table 1, entry 34). When the method is applied for the synthesis of multifunctional organic molecules, selectivity of the method shows its importance. We have observed that reactions conducted in the presence of this catalyst proceeded with high selectivity in excellent yields. As we have observed, steric hindrance and nucleophilicity of hydroxyl groups are important for differentiation between different hydroxyl groups.

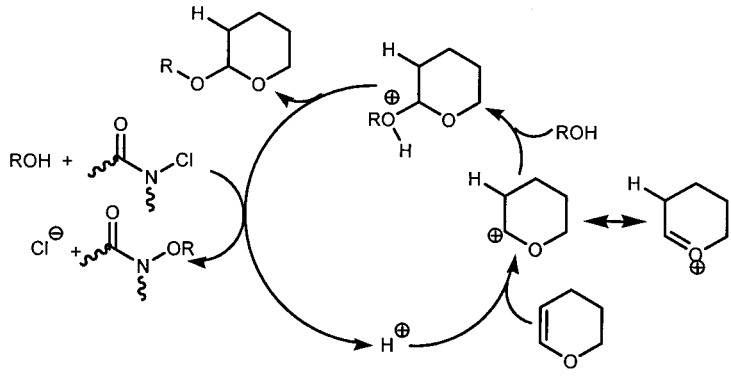
In order to show the selectivity of the method, we have performed several competitive reactions. The results are shown in Sch. 2, which presents the high selectivity of the catalyst under reaction conditions.

Deprotection of THP ethers is important in organic synthesis and there are many reported methods for this purpose.[5,6] TCCA can be employed very easily for the highly efficient catalytic detetrahydropyranylation reactions in the presence of CH_3OH (5 mmol) at room temperature in excellent yields (Sch. 1, Table 1). We have also proposed a mechanism in which the role of TCCA for the protection of hydroxyl functional groups by DHP ether by the in situ generation of catalytic amounts of HCl is clarified (Sch. 3).

In conclusion, we have introduced a new selective and efficient catalytic system for tetrahydropyranylation and detetrahydropyranylation reactions under mild and neat conditions. TCCA is a safe, commercially available, cheap industrial chemical.



Scheme 2.



Scheme 3.

EXPERIMENTAL

All the products are known and commercially available compounds. Therefore, their physical data are not given. The products were purified by column or plate chromatography on silica gel; when necessary, the purity determination of the products was accomplished by GC on a Shimadzu model GC-14A instrument or by TLC on silica gel polygram SIL G/UV 254 plates. The IR spectra were recorded on a Perkin Elmer 781 spectrophotometer. The NMR spectra were recorded on a Bruker advance DPX 250 MHz spectrometer.

General procedure for tetrahydropyranylation of alcohols and phenols catalyzed by TCCA:

To a mixture of an alcohol or a phenol (5 mmol), DHP (0.51–0.67 g, 6–8 mmol), TCCA (0.12 g, 0.5 mmol) was added. The mixture was stirred at 60–80°C for the appropriate reaction time (Table 1). After completion of the reaction (GC or TLC), the resulting mixture was applied on a silica gel pad (5-cm thick) and was washed with a mixture of petroleum ether (bp 60–80°C)/EtOAc (10 : 1, 100 mL). Evaporation of the solvent under reduced pressure gave the desired compound in high purity. Spectroscopic data (IR, NMR) of the isolated ethers were in agreement with those reported for the authentic samples.

General procedure for detetrahydropyranylation reactions catalyzed by TCCA:

To a mixture of tetrahydropyranyl ether (5 mmol) in CH_3OH (25 mmol), TCCA (0.12 g, 0.5 mmol) was added. The mixture was stirred at room temperature for the appropriate reaction time (Table 1). After completion of the

reaction (GC or TLC), CH_2Cl_2 (50 mL) was added to the reaction mixture. The resulting mixture was washed with aqueous solution of $Na_2S_2O_3$ (10%, 10 mL), decanted, and the organic phase was dried over anhydrous $MgSO_4$. Evaporation of the solvent under reduced pressure gave the hydroxy compound in high yields. Spectral data (IR, NMR) of the isolated products were identical with those reported for the authentic samples.

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