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Trichloroisocyanuric acid: A cost effective commercial and mild system for the oxidation of primary alcohols to aldehydes

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ABSTRACT

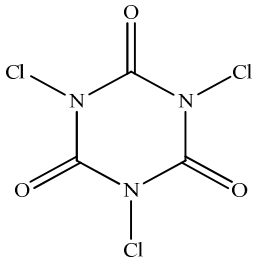
An improved and efficient synthetic process developed for an oxidation of primary alcohols to related aldehydes with commercially cheaper trichloroisocyanuric acid in presence of catalyst TEMPO (2, 2, 6, 6-tetra methyl-1-piperidinyloxy Free radical). This synthetic approach efficiently provides highly pure aldehydes without formation of the acid impurity. In the present process overall yields are around 90-95%.

Keywords: Acid, Primary alcohol, aldehyde
MSNRD Communication No.028

INTRODUCTION

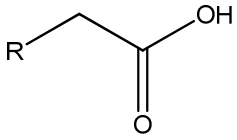
As synthetic chemists are concerned with increasingly sophisticated targets, it is a permanent demand to develop more and more selective synthetic methods able to discriminate efficiently various functional groups. Therefore, selective methods allowing for oxidation of primary alcohols to aldehydes without over oxidation to carboxylic acids and without competitive oxidation of secondary alcohols remain challenging. Relatively few methods allow this type of selectivity [1-8]. During the past few years, N-oxoammonium salts have become synthetic reagents of growing importance, mainly for the oxidation of alcohols to carbonyl compounds. They can be used stoichiometrically, either in an isolated form [9-11] or generated “in situ” via nitroxide dismutation [12-14]. Several catalytic procedures have also been developed, the active species being regenerated by stoichiometric amounts of various cooxidants, including m-chloroperbenzoic acid [14-17], high-valence metal salts, [18-20] sodium bromite,[21] sodium or calcium hypochlorite, [22-27] and electrooxidation. Interestingly, a proper choice of the nitroxide catalyst, of the cooxidant, and of the reaction conditions is able to tune very finely the selectivity of these oxidizing systems. For example, several chemo selective systems of preparative value for the oxidation of primary alcohols have recently been developed. In this paper we describe a new oxidation method where Trichloroisocyanuric acid is used as an oxidation reagent along with catalytic amounts of 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO). Under these conditions, primary alcohols are quantitatively oxidized to aldehydes, without any noticeable over oxidation to carboxylic acids. Moreover, the TEMPO inhibits a possible autoxidation of the aldehyde by molecular oxygen, making unnecessary the use of an inert atmosphere during the reaction.

Trichloroisocyanuric acid [1,3,5-trichloro-1,3,5-triazine-2,4,6-(1H,3H,5H)-trione] is a relatively stable and inexpensive reagent which has been used synthetically for the oxidation of various types of compounds.



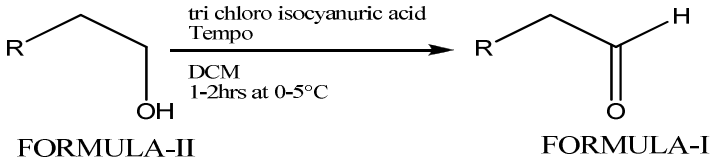
Trichloroisocyanuric acid

In the preparation of aldehydes from primary alcohols the formation of acid impurity is imperative and it leads to low yields of aldehyde using oxidative reagents like sodium hypo chloride. Use of trichloroisocyanuric acid in the presence of catalyst like TEMPO provides good yields of aldehyde is obtained from primary alcohols, without formation of acid impurity (Formula-III).



Formula-III
Acid Impurity

Scheme-1



Where R= aliphatic or aromatic substituents

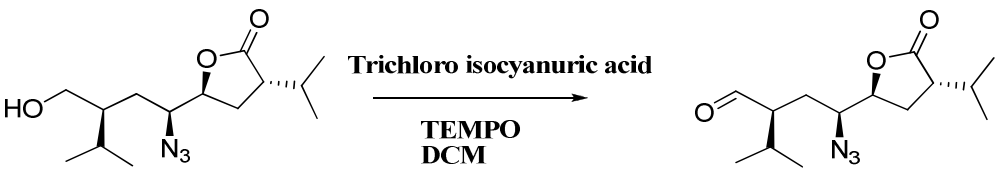
The reaction reported in Scheme 1 was applied to different important alcohol intermediates which are used in the synthesis of important active pharmaceutical ingredients.

MATERIALS AND METHODS

General procedure:

Take Tri chloro isocyanuric acid and DCM in to round bottom flask with thermal socket in cooling vessel. Dissolve alcohol compound and TEMPO in DCM and add slowly at 0-5°C. Maintain for 2 hrs and check the TLC for completion of reaction. Filter the byproduct. Wash the filtrate with aqueous sodium bi carbonate solution and concentrate the reaction mixture to give corresponding aldehydes (1-4).

Experiment-1:



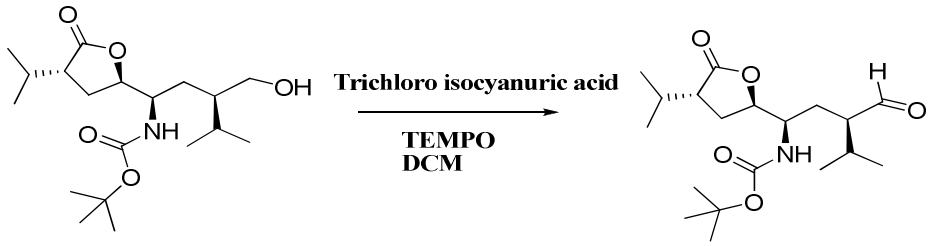
1a 1

Take neat and dry round bottom flask with thermal socket at cooling vessel. Charge DCM (20ml), Trichloroisocyanuric acid (8.9gm—1.10mole ratio). Stir 10-15mints at 25-30°C. Cool to 0-5°C. Prepare compound-1a (10gm—1.0mole ratio) and TEMPO (0.10gm—0.018 mole ratio) Solution with DCM (80ml). Slowly add above solution for 20-30 minutes at 0-5°C. Maintain reaction mass for 1-2 hrs at 0-5°C. Monitor the compound-1a by TLC. Filter the byproduct and wash the bed with DCM (20ml). Take filtrate and wash with 5% sodium bi carbonate solution (10ml). Wash the organic layer with water followed by with brine solution (10ml). Dry the organic layer

with Sodium Sulphate and concentrate with vacuum to gives compound-1 (9.0gm) with 91% of yield and 95% of quality as per TLC.

1H-NMR (400MHz, $CDCl_3$): δ 0.898-1.0491(2H), 1.504-1.921(2H), 2.130-2.243(4H), 2.531-2.577(1H), 2.635-2.690(1H), 3.253-3.299(1H), 4.391-4.438(1H), 9.716(1H).

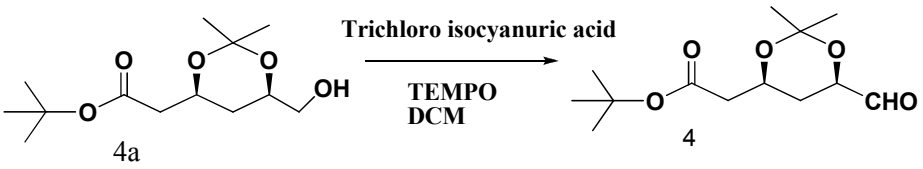
Experiment-2:



2a 2

Follow experimental procedure-1 process gives compound-2 (9.0gm) with 91% of yield and 92% of quality as per TLC. **Melting point:** 126-128°C.

Experiment-3:

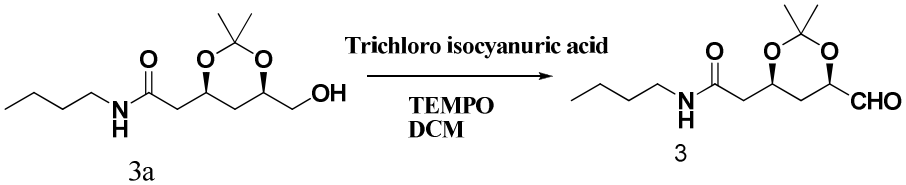


4a 4

Take neat and dry round bottom flask with thermal socket at cooling vessel. Charge DCM (20ml), Tri chloro isocyanuric acid (9.82gm—1.10mole ratio). Stir 10-15mints at 25-30°C. Cool to 0-5°C. Prepare compound-4a (10gm—1.0mole ratio) and TEMPO (0.10gm—0.018 mole ratio) Solution with DCM (80ml). Slowly add above solution for 20-30 minutes at0-5°C. Maintain reaction mass for 1-2 hrs at 0-5°C. Monitor the compound-3a by TLC. Filter the byproduct and wash the bed with DCM (20ml). Take filtrate wash with 5% sodium bi carbonate solution (10ml). Wash the organic layer with water followed by brine solution (10ml). Dry the organic layer with Sodium Sulphate and concentrate with vacuum to gives compound-4 (8.5gm) with 85% of yield and 95% of quality as per TLC.

1H-NMR (300MHz, $CDCl_3$): δ 1.40(9H, s), 1.50(6H, s), 4.28-5.30 (2H, d), 7.27 (2H, t), 9.58 (1H, s).

Experiment-4:



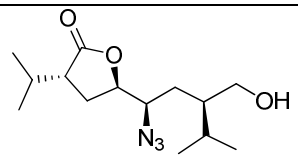
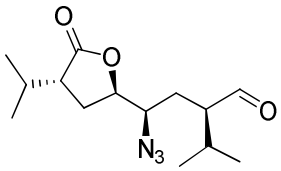
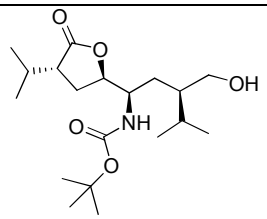
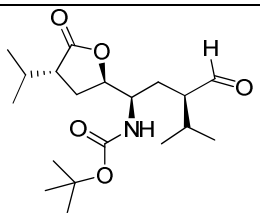
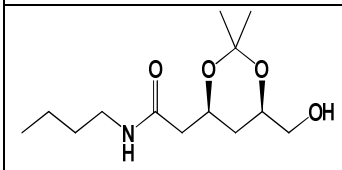
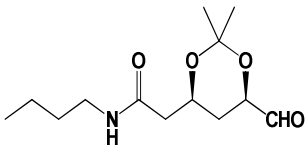
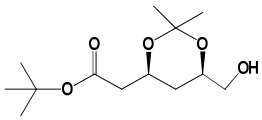
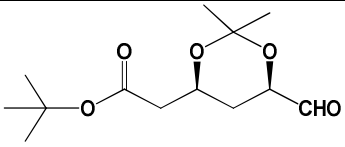
3a 3

Follow experimental procedure-3 process and gives compound-4 (8.5gm) with 85% of yield and 98% of quality as per TLC.

1H-NMR (300MHz, $CDCl_3$): δ 0.9-0.95(3H, t), 1.23-1.49(10H, m), 1.7-1.9(2H, m), 2.35-2.43 (2H, d), 3.16-3.34 (2H, m), 3.9-4.38 (2H, m), 9.6(1H, s).

RESULTS AND DISCUSSION

Using of trichloroisocyanuric acid in the presence of catalyst like TEMPO provides good yield of aldehyde is obtained from primary alcohols, The following table illustrates a few examples for oxidation of primary alcohol to aldehyde.

Alcohols	Product	Time for completion of reaction	Yield	Remarks
 1a	 1	1hr 30min	91%	It is key intermediate in the synthesis of Aliskiren
 2a	 2	1hr 30min	90%	It is key intermediate in the synthesis of Aliskiren
 3a	 3	1hr 30min	92%	It is key intermediate in the synthesis of Rosuvastatin
 4a	 4	1hr 30min	91%	It is key intermediate in the synthesis of Rosuvastatin

TEMPO: (2, 2, 6, 6-tetra methyl-1- piperidinyloxy Free radical)
DCM: Dichloromethane
TLC: Thin layer chromatography

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REFERENCES

[1]. Tomioka, H; Takai, K; Oshima, K; Nozaki, H *Tetrahedron Lett*. **1981**, 22, 1605-1608.
[2] Nakano, T; Terada, T; Ishii, Y; Ogawa, M *Synthesis* **1986**, 774-776.
[3] Singh, J; Kolsi, P S; Jawanda, G S; Chhabra, B R *Chem. Ind*. **1986**, 21, 751-752.
[4] Stevens, R V; Chapman, K T; Stubbs C A; Tam, W W; Albizati, K F *Tetrahedron Lett*. **1982**, 23, 4647-4650.
[5] Tomioka, H; Oshima, K; Nozaki, H *Tetrahedron Lett*. **1982**, 23, 539-542.
[6] Kaneda, K; Kawanishi, Y; Jitsukawa, K; *Tetrahedron Lett*. **1983**, 24, 5009-5010.
[7] Kanemoto S; Tomioka, H; Nozaki, H *Bull. Chem. Soc. Jpn*. **1986**, 59, 105-108.
[8] Rozen, S; Bareket, Y; Kol, M *Tetrahedron* **1993**, 49, 8169-8178.
[9] Miyazawa, T; Endo, T; Shiihashi, S; Okawara, M *J. Org. Chem.* **1985**, 50, 1332-1334.
[10] Miyazawa, T; Endo, T *J. Org. Chem.* **1985**, 50, 3930-3931.
[11] Bobbitt, J M; Flores, M C L *Heterocycles* **1988**, 27, 509-533
[12] Ma, Z; Bobbitt, J M *J. Org. Chem.* **1991**, 56, 6110-6114.
[13] Banwell, M G; Bridges, V S; Dupuche, J R; Richards, S L; Walter, J M *J. Org. Chem.* **1994**, 59, 6338- 6343.
[14] Ma, Z; Huang, Q; Bobbitt, J M *J. Org. Chem.* **1993**, 58, 4837-4843.
[15] Cella, J A; Kelley, J A; Kenhan, E F *J. Org. Chem.* **1975**, 40, 1860-1862.
[16] Ganem, B *J. Org. Chem.* **1975**, 40, 1998-2000.
[17] Cella, J A; Mc Grath, J P; Kelley, J A; El Soukkary, O; Hilpert, L *J. Org. Chem.* **1977**, 42, 2077-2080.
[18] Miyazawa, T; Endo, T *J. Mol. Catal.* **1985**, 31, 217-220.
[19] Miyazawa, T; Endo, T *J. Mol. Catal.* **1985**, 32, 357-360.

[20] Semmelhack, M F; Schmid, C R; Cortes, D A; Chou, C S *J. Am. Chem. Soc*. **1984**, 106, 3374-3376.
[21] Inokuchi, T; Matsumoto, S; Nishiyama, T; Torii, S *J. Org. Chem.* **1990**, 55, 462-466.
[22] Anelli, P L; Biffi, C; Montanari, F; Quici, S *J. Org. Chem.* **1987**, 52, 2559-2562.
[23] Anelli, P L; Banfi, S; Montanari, F; Quici, S *J. Org. Chem.* **1989**, 54, 2970-2972.
[24] Siedlecka, R; Skarzewski, J; Mlochowski, J *Tetrahedron Lett.* **1990**, 31, 2177- 2180.
[25] Leanna, M R; Sorvin, T J; Morton, H E *Tetrahedron Lett.* **1992**, 33, 5029-5032.
[26] Davies, N J; Flitsch, S L *Tetrahedron Lett*. **1993**, 34, 1181-1184.
[27] Rychnovsky, S D; Mc Lernon, T L; Rajapakse, H *J. Org.Chem.* **1996**, 61, 1194-1195.