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Trichloroisocyanuric Acid: a versatile and efficient chlorinating and oxidizing reagent

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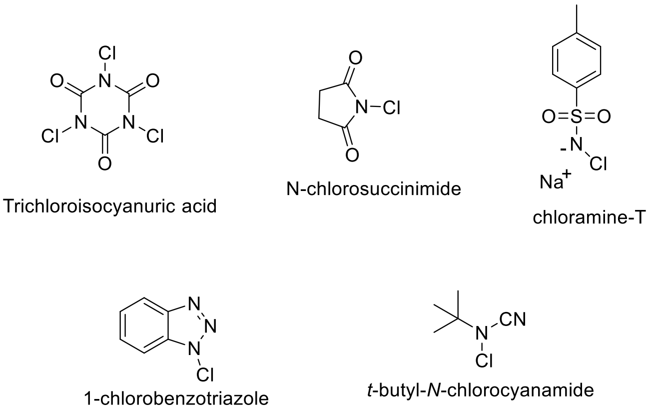
Abstract: Trichloroisocyanuric acid (TCCA) is a versatile and efficient reagent for chlorination and oxidation reactions. Depending on the reaction conditions employed, it can release either an electrophile chlorine atom (Cl$^+$) or a radical chlorine atom (Cl$^{\cdot}$) promoting selectively different path ways of reaction. It was effectively used to synthesize many classes of compounds such as: chlorinated arenes, *N*-chloramines and amides, α-halo-carbonyl compounds, benzyl chlorides, esters, carboxylic anhydrides and amides. The procedures, which make use of TCCA, have mild reaction conditions and optimal stoichiometric molar ratio of reactants and avoid the use of any metal-based catalysts. In any case very high yield and selectivity were observed. The easy and safe handling, the stability and the low cost of this reagent make it particularly attractive for large-scale use and industrial applications.

Introduction

Trichloroisocyanuric acid [1,3,5-trichloro-1,3,5-triazine-2,4,6-(1*H*, 3*H*, 5*H*)-trione], TCCA, is a part of ~~to~~ the large group of *N*-chloroimides and *N*-chloroamides. They are extensively used as bleaching agents, disinfectants, and bactericides due to their chlorinating and oxidizing properties.[1] Their reactivity is analogous to those of *N*-chloramines, which, however, are less stable. *N*-chloramides are commonly used in the protocol for purification of water and as sanitizing agents. *N*-chloramides are easy to handle and to store and due to these properties are widely used in organic synthesis.

The most commonly used *N*-chloramide is *N*-chlorosuccinimide (NCS), which differently to TCCA is thermally unstable and can explode at elevated temperature. Compared to other *N*-chlorinated analogues, such as *N*-chlorosuccinimide, chloramine-T, *t*-butyl-*N*-chlorocyanamide and 1-chlorobenzotriazole, TCCA owns three chlorine atoms per molecule (Scheme 1).



Scheme 1. *N*-chloramides

TCCA can transfer all of the 3 chlorines to the substrates, allowing reactions with high atom economy. For this reason, the stoichiometry of reactions involving TCCA is frequently 3:1 (substrate: TCCA). The cyanuric acid by-product obtained from TCCA can be recovered and re-transformed to TCCA through a green methodology using NaCl and oxone™.[2]

Last, but not least important, TCCA has a high solubility in many organic solvents and water and releases a high concentration of active chlorine per liter of solvent (Table1).[3]

Table 1. TCCA solubility in organic solvent.

Solvent	Solubility (g/L)	mol active chlorine/L
acetone	350	4.56
ethyl acetate	385	5.02
toluene	70	0.91
water	10	0.13

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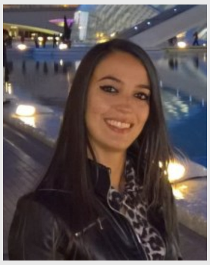
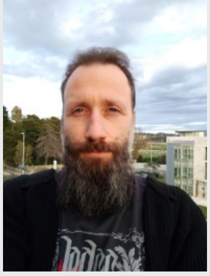


Silvia Gaspa received her BSc and her MSc in Chemical Sciences from Università degli Studi di Sassari under the guidance of Professor Lidia De Luca (July 2014). She obtained her PhD in Chemical Sciences and Technologies from Università degli Studi di Sassari in agreement with the Università degli Studi di Cagliari under the supervision of Professor Lidia De Luca (March 2018). She joined Prof. De Luca's group as a postdoctoral research in November, 2017. She has been focusing on cross oxidative coupling reactions, photochemistry and sustainable organic process.



Massimo Carraro graduated in Chemistry (2003 MSc and 2008 PhD) at the Università di Padova under the supervision of Prof. Sandro Campestrini. In 2008-2009 he spent a year as postdoctoral fellow at Florida State University in the group of Prof. Tyler D. McQuade. Since November 2012, he is assistant professor of Organic Chemistry at the Dipartimento di Chimica e Farmacia of the Università degli Studi di Sassari. His interests comprise catalysis in oxidation reactions and green alternative solvents.

Luisa Pisano after graduation in Chemistry in 1993 at the Università degli Studi di Sassari was awarded a 1-year fellowship by the Italian CNR. Later on, she started doctoral studies at the Università degli Studi di Sassari under the guidance of Professor G. Melloni and Professor J. Marquet (Autonoma University of Barcellona). In 1999 she was awarded a postdoctoral Marie Curie fellowship to join Prof. J.-M. Lluch's group at the Autonoma University of Barcellona. Since 2001 she is Researcher/Assistant Professor at the Università degli Studi di Sassari and her research interest involves organometallic chemistry, green processes and molecular structure elucidations by computational NMR.

Andrea Porcheddu received his B.Sc in Chemistry from Università degli Studi di Sassari in 1995. He then undertook doctoral research under the supervision of Prof. Maurizio Taddei at the Università degli Studi di Sassari and was awarded his Ph.D. in 1999. He completed post-doctoral studies (2000) in the group of Prof. Charles Mioskowowsky at the Louis Pasteur University (Strasbourg, France). In 2001, he moved back to Università degli Studi di Sassari where he was appointed Assistant Professor. In January 2015, he joined the Dipartimento di Chimica of the Università di Cagliari, where he currently has a permanent position as Associate Professor. Now, his main interest is directed toward the development of novel Borrowing Hydrogen, Transfer Hydrogenation strategies and no conventional green procedures via ball milling.

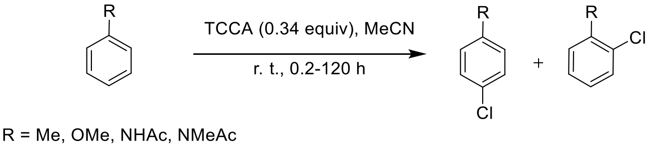
Lidia De Luca obtained her MSc degree in Chemistry (1999) and her PhD degree in Chemistry (2003) from Università degli Studi di Sassari under the supervision of Professor Giampaolo Giacomelli. In 2004 she has joined as Researcher of Organic Chemistry and in 2016 as Associate Professor of Organic Chemistry at Università degli Studi di Sassari. Her research interest hare focused on cross-oxidative coupling reactions, sustainable organic processes and photochemistry.

1. TCCA as chlorinating reagent

1.1. TCCA as chlorinating ~~a~~ reagent of aromatics

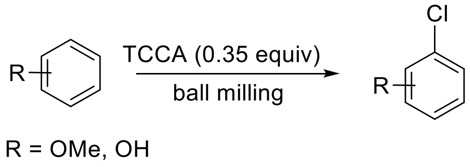
Trichloroisocyanuric acid was studied as the chlorinating reagent of arenes in aromatic electrophilic substitution reactions (S_EAr). One of the most important properties of *N*-chloramides is the electrophilic nature of the halogen resulting from the link with the electron-deficient amide nitrogen, which makes the N-Cl bond highly polar.

In fact, TCCA can furnish electrophilic chloronium ion (Cl^+). An application of this feature consists of the halogenation of aromatic rings. In 2007, de Mattos reported an interesting example where TCCA dissolved in acetonitrile showed to have a good reactivity with electron-rich aromatic rings leading to monochlorinated products in 60-95% yields. ~~Unlikely~~ Unfortunately TCCA did not have displayed a good regioselectivity and a mixture of regioisomeric chlorinated products was obtained in different ratios, with the para isomer being predominant (Scheme 2).[4]



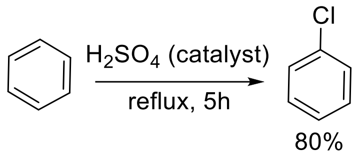
Scheme 2. Chlorination of electron-rich arenes

Another example of direct chlorination of electron-rich aromatic rings carried out by the use of TCCA was reported by Moorthy.[5] The reaction proceeds with solid aromatic compounds under solvent-free and ball-milling conditions, within a few hours affording high yields of mono-halogenated products (Scheme 3).



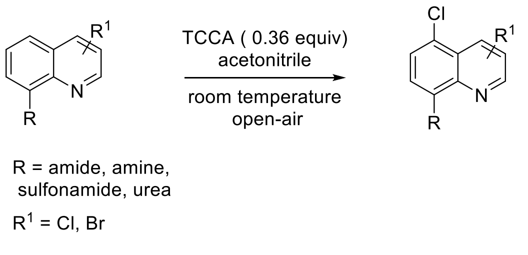
Scheme 3. Chlorination of electron-rich arenes under solvent-free and ball-milling conditions

Non activated arenes, like benzene and naphthalene, require acid catalysis ($FeCl_3$ or 50% H_2SO_4) to be chlorinated by TCCA (Scheme 4); while phenol and aniline stopped to react to the stage of monochlorination. These observations suggest the involvement of a charge transfer complex intermediate and differentiate TCCA from Cl_2 in terms of selectivity.[6] Afterwards the TCCA in H_2SO_4 was employed as an efficient super electrophilic reagent for chlorination of some benzene derivatives, but low regioselectivity was found.[7]



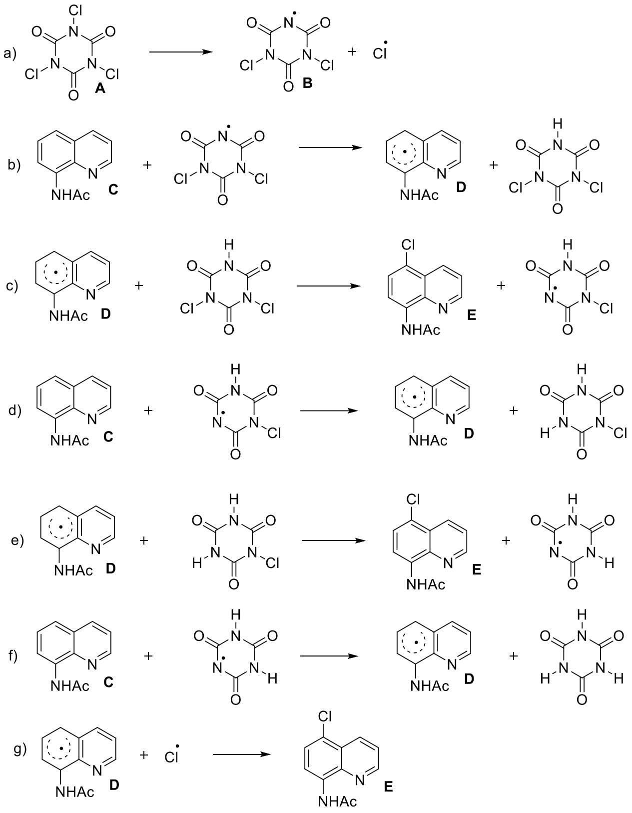
Scheme 4. Chlorination of benzene with TCCA and H_2SO_4 as a catalyst.

TCCA was effectively employed for remote C5-H halogenation of a broad range of 8-substituted quinoline derivatives. The reaction was carried out with 0.36 equiv. of TCCA, under air, at room temperature and in acetonitrile as a solvent (Scheme 5).[8] The methodology has shown to have complete regioselectivity.



Scheme 5. TCCA promoted C5-H halogenation of 8-substituted quinolines.

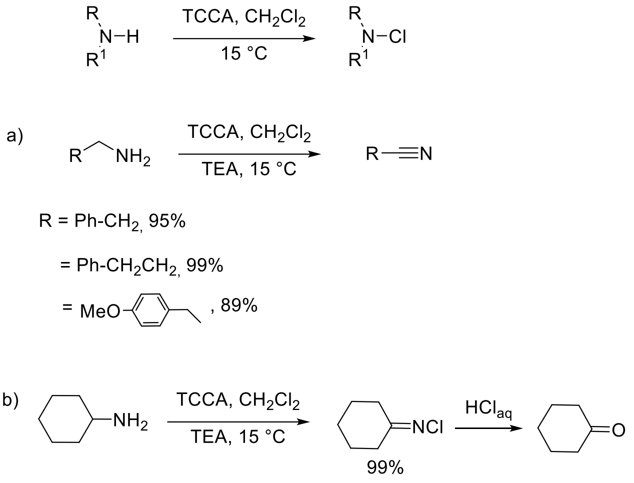
From experimental results and literature reports,[9] the authors proposed for this reaction a plausible mechanistic pathway (Scheme 6). The reaction initiates through homolytic cleavage of *N*-Cl bond of TCCA **A** to generate the nitrogen-centered radical radical **B** and a chlorine radical. The reaction propagates via abstraction of the C5 hydrogen of the quinoline **C** generating the intermediate **D**. The intermediate **D** was quenched by chloride transfer generating the C5-chlorinated product **E**.



Scheme 6. Mechanism of TCCA promoted C5-H halogenation of 8-substituted quinolines.

1.2. TCCA as chlorinating reagent of amines and amides

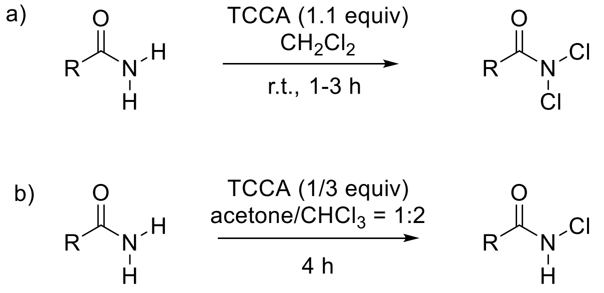
N-halo compounds are versatile intermediates in organic synthesis.[10] The chlorination of amines and amides constitutes a very useful functional group transformation in organic synthesis and there is a great deal of interest in finding out new methods, which proceed under mild conditions. In this context, we have employed TCCA to chlorinate primary, aliphatic and benzylic and secondary aliphatic amines.[11] The reaction proceeds in dichloromethane as a solvent at low temperature (<20 °C) and after one hour the amine was converted entirely into the corresponding *N*-chloramine. Introducing TEA (Triethylamine) directly in the reaction mixture was possible to transform, under a one-pot procedure, directly a primary amine into a nitrile (Scheme 7, path a). α-branched amines afforded the corresponding *N*-chlorimines, which can be converted into carbonyl compounds under acidic hydrolysis (Scheme 7, path b).



Scheme 7. Chlorination of amines.

In continuing our studies for developing new methods of transformation of functional groups under mild and sustainable conditions by the use of TCCA, we have developed a procedure to convert amides and carbamates into their *N*-chloro derivatives.

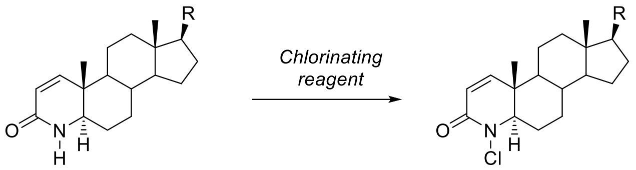
N-chloramides and *N*-chlorocarbamates are useful sources of amidyl and carbamoyl radicals[12] and precursors of α,β-dehydro amino acids (Scheme 8).[13] The procedure consists in the treatment of amide with TCCA in dichloromethane as a solvent at room temperature. Both primary and secondary amides can be employed.



Scheme 8. Chlorination of amides.

When primary amides are reacted with 1.1 equivalent of TCCA in dichloromethane as a solvent *N*,*N*-dichloroamides were obtained in high yields (Scheme 8, path a). Changing the molar ration of the reactants and the solvent, was possible to form the mono *N*-chloramides selectively. 0.33 equivalent of TCCA and acetone: chloroform 1:2 were employed to carry out this transformation (Scheme 8, path b).

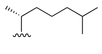
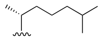
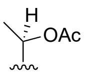
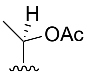
In 1991 Back and co-workers[14] reported an interesting example of *N*-chlorination of azasteroid lactams.



Scheme 9. *N*-chlorination of azasteroid lactams.

In the paper an effective comparison of TCCA and NCS is reported, and TCCA showed a better performance in terms of yields and reaction times (Table 2).

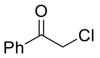
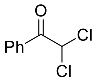
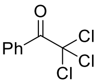
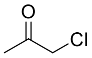
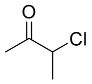
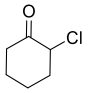
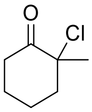
Table 2. Comparison between NCS and TCCA as chlorinating reagent in *N*-chlorination of azasteroid lactams.

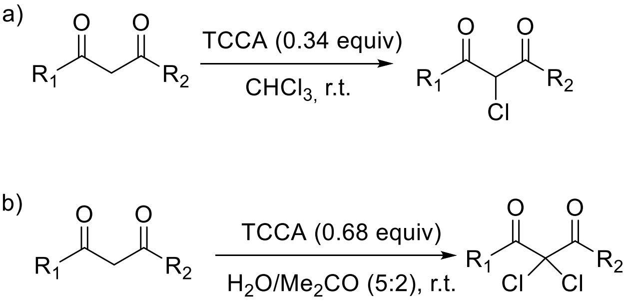
Entry	R	Reagent (molar equiv)	Time	Yield (%)
1		NCS (5.2)	12 h	85
2		TCCA (0.5)	2 h	99
3	OAc	NCS (5.5)	18 h	80
4	OAc	TCCA (0.74)	30 min	100
5		NCS (6.1)	16 h	78
6		TCCA (0.5)	45 min	97

1.3. TCCA as chlorinating reagent of carbonyl compounds

α-Halogenation of carbonyl compounds is a conventional method for the functionalization of aldehydes and ketones. α-halogenated carbonyl compounds are versatile building blocks widely used in natural product synthesis[15] and particularly useful in heterocycle synthesis.[16] The first example of α-chlorination of ketones was reported in 1985 by Hiegel and Peyton.[17] In this procedure a ketone, both aromatic and aliphatic, was reacted with TCCA, in the presence of boron trifluoride etherate. Depending on some parameters, as the molar ratio of reactants, time, temperature, it is possible to obtain selectively mono, bi and tri chlorinated products (Table 3, entries 1, 2 and 3). Unsymmetrical ketones gave chlorination preferentially at the more substituted position when a high ratio of boron trifluoride is used (Table 3, entries 5 and 7). Addition of azobisisobutyronitrile did not increase the reaction rate indicating that probably, in this case, an ionic pathway is involved.

Table 3. α-chlorination of ketones.

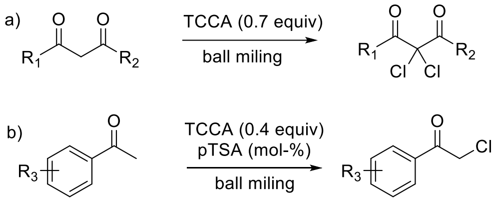
Entry	Mole Ratio Reactant TCCA : Ketone : BF₃	Time (hour)-Temperature	Product	Yield
1	0.33 : 1 : 0.315	0.25-80 °C		50
2	1 : 1 : 0.315	17-80 °C		81
3	2 : 1 : 0	5-reflux		81
4	1 : 20.4 : 0.023	60-reflux		88
5	1: 17.4 : 2.40	90-r.t.		58
6	1 : 2.40 : 0.0054	50-80 °C		77
7	1 : 1.98 : 2	90- r.t.		87



Scheme 10. Halogenation of β-dicarbonyl compounds.

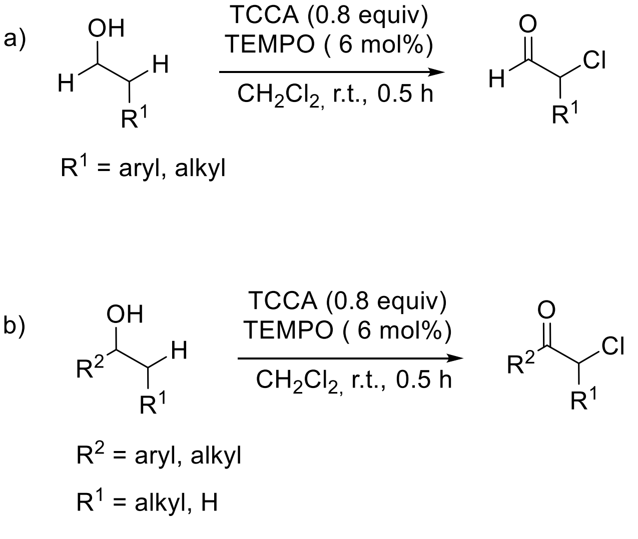
TCCA was also efficiently employed as an efficient reagent for regioselective mono- and di-halogenation of 1,3-dicarbonyl compounds. [18] The reaction of (β-ketoesters and β-diketones) was carried out with 0.34 mol equiv of trichloroisocyanuric acid in chloroform and produced regioselectively the corresponding α-monohalo β-dicarbonyl compound (Scheme 10, path a). Using 0.68 mol equiv of the trihaloisocyanuric acid in H$_2$O/Me$_2$CO (5:2) as a solvent, the α,α-dihalo β-dicarbonyl compound was obtained (Scheme 10, path b).

Recently a halogenation of carbonyl compounds in the solid state carried out by the use of TCCA, as a halogen source, in the solid state by ball milling was reported.[5] Crystalline 1,3-diketones are shown to undergo direct α,α-dichlorination with 0.7 equiv of TCCA with ball milling (Scheme 11, path a). Monoketones are also shown to be α-chlorinated in excellent yields in the presence of *p*-toluenesulfonic acid (*p*TSA) in 25 mol% (Scheme 11, path b).



Scheme ~~10~~11. Halogenation of carbonyl compounds in the solid state by ball milling.

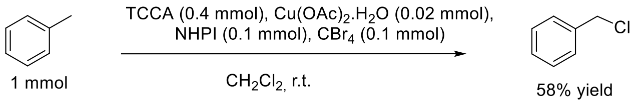
Studer and co-workers have reported a one-pot conversion of primary and secondary alcohols into the corresponding α-chloro aldehydes and α-chloro ketones making use of TCCA~~,~~. In this methodology trichloroisocyanuric acid was used as both stoichiometric oxidant and α-halogenating reagent. For the oxidation of primary alcohols, TEMPO was added as an oxidation catalyst (Scheme 12, path a). To oxidize secondary alcohols (TEMPO-free protocol), MeOH was added as an additive and was indispensable to promote chlorination of ketones (Scheme 12, path b).[19]



Scheme 12. Chlorination of amides.

1.4. TCCA as chlorinating reagent of alkyl aromatic hydrocarbons

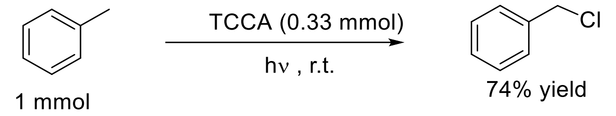
Benzyl chloride and substituted benzyl chloride are extensively used in the industrial productions of amphetamine class drugs, artificial resins, dyes, gum petrol inhibitor and photographic developer.[20] Recently Parra and Schreiner have reported a powerful methodology for the chlorination of benzylic position of alkyl aromatic hydrocarbons (Scheme 13).[21]



Scheme 13. α- chlorination of alkylaromatic hydrocarbons by TCCA.

The reaction proceeds with 1 mmol of toluene (or toluene derivatives), 0.4 mmol of TCCA as the chlorine source, *N*-hydroxyphthalimide (NHPI) as a radical initiator and catalytic amounts of CBr_4 and $Cu(OAc)_2$ as a catalyst. The corresponding benzyl chloride was obtained in 58 % of yield.

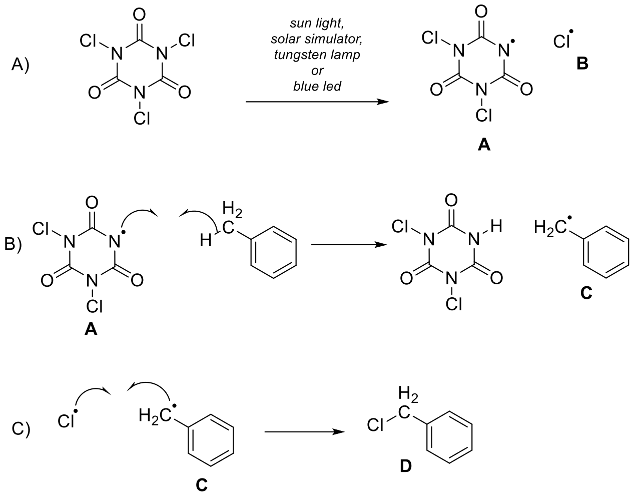
Concerning to our interest in the development and improvement of green and solvent-free procedures in the use of trichloroisocyanuric acid as an oxidizing and chlorinating reagent, we have carried out a selective and mild procedure for the α-H chlorination of toluene and alkyl aromatic hydrocarbons.[22]



Scheme 14. α-chlorination of alkyl aromatic hydrocarbons by visible light and TCCA.

The method makes use exclusively of toluene (or toluene derivatives) both as reagent and solvent and TCCA in 3:1 stoichiometric ratio, under visible light irradiation (sunlight, solar simulator or blue led) (Scheme 14). The desired products were obtained in very high yields and purities. Notably, the formation of by-products due to the aromatic ring chlorination was not observed. Furthermore the conversion of toluene was almost quantitative (94%).

A plausible mechanism for the α-chlorination of toluene (and his derivatives) with TCCA is shown in Scheme 15. The reaction is supposed to go by a radical mechanism.[23] Visible-light-initiates the homolytic cleavage of N-Cl bond in TCCA to form dichloroisocyanuric acid radical **A** and chlorine radical atom **B**.[24] The N-centered amidyl radical **A** then abstracts an hydrogen atom at the benzylic position of toluene forming the benzylic radical **C**. The benzylic radical **C** and chlorine radical **B** react together to produce the desired benzyl chloride **D**.



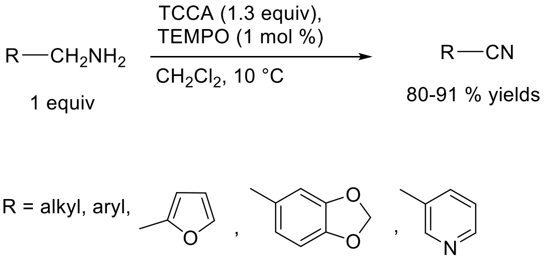
Scheme 15. Proposed mechanism for α-chlorination of alkyl aromatic hydrocarbons by TCCA and visible light.

2. TCCA as oxidizing reagent

2.1. TCCA as oxidizing reagent of amines

Nitriles are versatile intermediates in organic synthesis, and are readily converted into carboxylic acids, esters, and amides. A plethora of methodologies has been developed for their synthesis.[25] The preparation of nitriles starting from amines emerges to be the most direct and suitable.-Amines are suitable to be subjected a variety of oxidative processes that leads to an array of products. Due to this, the selective oxidation of primary amines to nitriles presents many complications.

In this context, TCCA was efficiently used to oxidize primary aliphatic and aromatic amines to nitriles (Scheme 16).[26]



Scheme 16. Oxidation of primary amines to nitriles with TCCA.

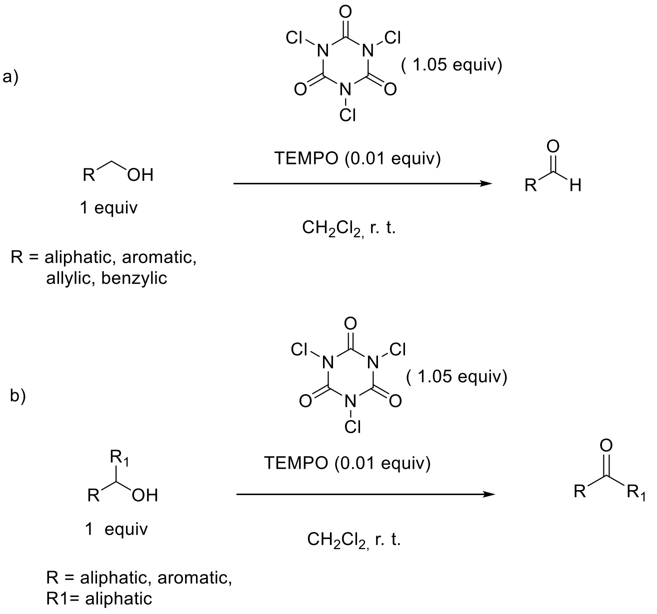
The reaction proceeds with 1 equiv of the substrate, 1.3 equiv of TCCA as an oxidant, in the presence of 1 mol% TEMPO as a catalyst in mild condition. The reaction scope is very broad: aliphatic, benzylic, allylic amines were converted effectively into the corresponding nitriles in excellent yields. Many functional groups such as benzyloxy, double bond, alcohols and phenols were unaffected under the reaction conditions.

2.2. TCCA as oxidizing reagent of alcohols

The chemo selective oxidation of primary alcohols to aldehydes without overoxidation to carboxylic acid is a fundamental task of organic chemists. Aldehydes are widely used in organic synthesis as intermediates, and the most powerful synthetic transformations involve carbonyl functional groups.

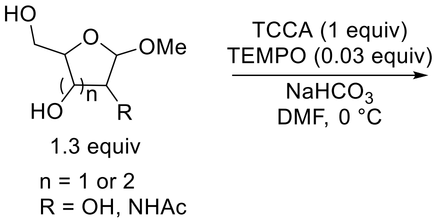
Usually these transformations are carried out using stoichiometric oxidizing agents such as $KMnO_4$, MnO_2, CrO_3, and Br_2. Oxidations by stoichiometric toxic oxidizing agents are costly methods and the main goal is to replace these with more environmentally friendly and mild methods.[27]

In 2001 De Luca and co-workers reported an efficient oxidation procedure of primary alcohols and β-amino alcohols to the corresponding aldehydes and α-amino aldehydes which makes use of TCCA.[28] The reaction proceeds at room temperature and in methylene chloride as solvent, using trichloroisocyanuric acid as an oxidant in the presence of catalytic TEMPO (Scheme 17). The methodology was applied to aliphatic, benzylic, and allylic alcohols, and β-amino alcohols, which were rapidly oxidized to the corresponding aldehydes without overoxidation to carboxylic acids. Secondary carbinols are slowly oxidized so that the methodology shows highly chemo selectivity. The methodology has shown to be convenient avoiding drastic reaction conditions and the use of toxic reagents.



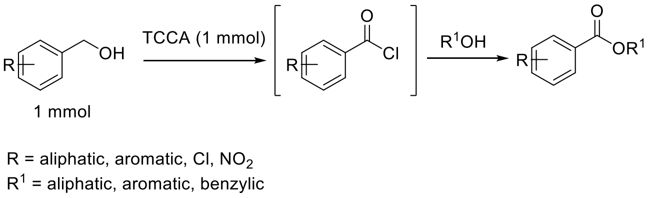
Scheme 17. Oxidation of alcohols to carbonyl compounds with TCCA.

Afterwards, Ramstrom and co-workers developed a remarkable application of this methodology.[29] They carried out selective oxidation of the primary hydroxy group of unprotected methyl glycosides to their corresponding oxo-derivatives (Scheme 18).



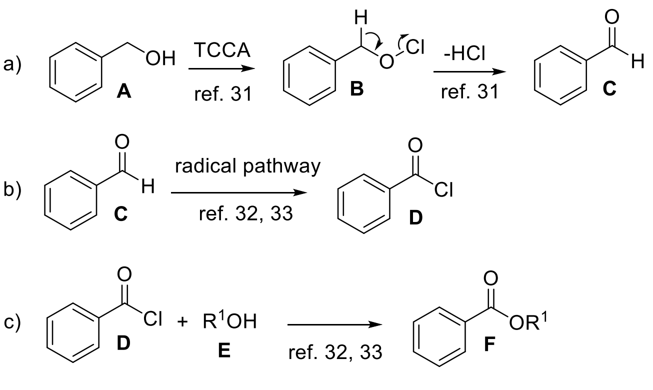
Scheme 18. Oxidation of primary hydroxyl group of glycosides with TCCA.

The selective construction of new bonds between carbon and another carbon atom or heteroatom is one of the main challenges of synthetic organic chemistry. Oxidative cross-coupling reactions based on transition-metal catalysts and oxidants have established as potent tools to build molecular complexity.[30] To fit oxidative cross-couplings with the "green chemistry" concept many scientists have studied the possibility to carry out these transformations in a metal-free fashion.In this context during 2016, De Luca and co-workers have proposed a metal-free cross oxidative esterification of alcohols to esters by the use of TCCA.[31] The alcohols (1 mmol) were converted *in situ* into the corresponding acyl chloride by the treatment with TCCA (1 mmol), which then were reacted with a wide range of alcohols (Scheme 19). The methodology has shown to have a very wide scope, an optimal stoichiometric molar ratio of reactants, and to make use of mild reaction conditions and cheap and readily available reagents.



Scheme 19. Metal-free oxidative cross esterification of alcohols.

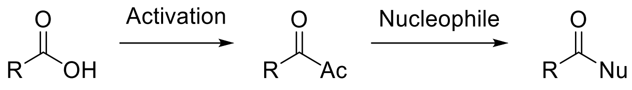
A reaction mechanism was proposed (Scheme 20). TCCA oxidizes alcohol **A** by a hypochlorite compound **B**, which loses hydrogen chloride to form the aldehyde **C**.[32] On the basis of previously reported studies, aldehyde **C** is converted into the acyl chloride **D**, through a radical pathway. [33, 34] Finally the acyl chloride **D** reacts with alcohol **E** to give the ester **F**.



Scheme 20. Proposed mechanism for metal-free oxidative cross esterification of alcohols.

2.3. TCCA as oxidizing reagent of aldehydes to carboxylic derivatives

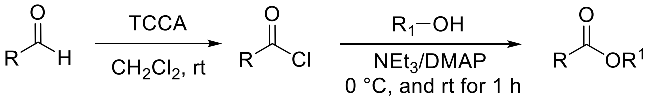
Classically the carboxylic acid derivatives as esters, carboxylic anhydrides and amides are prepared thought nucleophilic substitutions of activated carboxylic acids (Scheme 21).



Ac = Activating group
Nu = R-OH, RCOOH, $NR^1R^2R^3$

Scheme 21. Classical synthesis of carboxylic acid derivatives.

This approach suffers from many drawbacks, as an additional step necessary to obtain activated carboxylic acids, which leads to an increase of by-products and reduction of yields and involves the use of toxic reagents. To avoid these problems recently an alternative approach is rising which consists of the use of different starting materials such as aldehydes. Classically esters are synthesized by nucleophilic substitution of carboxylic acid derivatives (carboxylic halides, anhydrides, and activated esters) with alcohols.[35] The oxidative esterification of aldehydes is an elegant and powerful alternative strategy to classical ester synthesis.[36] In this context, De Luca and co-workers have proposed a metal-free direct oxidation of aldehydes to esters using TCCA.[33] The methodology consists in the reaction of both aliphatic and aromatic aldehydes with TCCA in CH_2Cl_2 at room temperature for 5 days. After that, the aldehydes were quantitatively transformed into the corresponding acyl chlorides, which were treated with an alcohol to obtain the desired esters (Scheme 22).

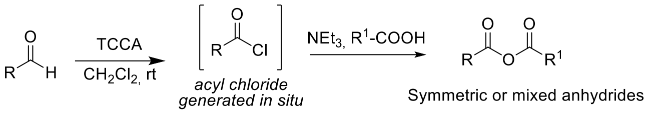


R = aliphatic, aromatic, benzylic
R^1 = primary, secondary, aliphatic, allylic,
allylic, propargylic, benzylic, phenols

Scheme 22. Metal-free direct oxidation of aldehydes to esters using TCCA.

By this procedure, esters were prepared directly from both aliphatic and aromatic aldehydes with an array of alcohols. A plethora of alcohols as primary and secondary aliphatic, benzylic, allylic, and propargylic alcohols and phenols were employed and well tolerated. The method has shown to be very general and selective, to have an optimal stoichiometric molar ratio of reactants, and to make use of green reagents and to proceed under mild reaction conditions.

Later on, De Luca and co-workers have extended this methodology to the synthesis of carboxylic anhydrides directly from aldehydes.[37]

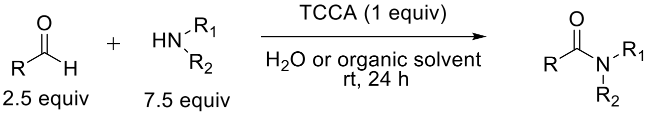


R, R^1 = aliphatic, aromatic

Scheme 23. Metal-free direct oxidation of aldehydes to carboxylic anhydrides using TCCA.

Also in this case, the aldehyde was transformed into the acyl chloride by TCCA (Scheme 23), which was then treated with a carboxylic acid in the presence of triethylamine and the corresponding carboxylic anhydrides were obtained in very good yields. The procedure appeared to have general applicability and was used to prepare both aromatic and aliphatic symmetrical and mixed anhydrides.

Further development of this methodology was carried out by Wang and co-workers to obtain amides from aldehydes and amines using TCCA as an oxidizing and chlorinating reagent (Scheme 24).[38]



R = alkyl, aryl
R^1 = alkyl, aryl
R^2 = alkyl, aryl, H

Scheme 24. Amidation aldehydes using TCCA.

This reaction appears to be a useful oxidative amidation of aldehydes and amines. It can proceed efficiently in either aqueous solutions or organic solvents, can be employed with a wide range of both aliphatic and aromatic aldehydes, and primary and secondary amines.

Summary and Outlook

Trichloroisocyanuric acid is a stable, cheap and commercially available reactant.

TCCA was extensively employed in many reactions as both chlorinating and oxidizing agent for a wide range of organic molecules.

Generally, the reactions proceed in mild conditions and do not require special precautions.

In relation to the reaction conditions employed, TCCA works either as a chlorinating or as an oxidizing agent. Moreover, depending on the solvent used, it can release either an electrophile chlorine atom (Cl^+) or a radical chlorine atom ($Cl^{\cdot}$) promoting selectively different path ways of reaction.

The difference in selectivity that are often observed between TCCA and other chlorinating agents (e.g. Cl_2 or NCS) make it not just a mere substitute to them but a reactive with peculiar and useful properties.

In comparison to other employed *N*-haloamides, TCCA is more atom economical while all three chlorine atoms are active. It is also highly soluble in organic solvents as well as very cheap and easily to handle and stable, thus making it the better choice for industrial large-scale use.

Usually chlorinating industrial processes involve the use of aqueous (corrosive) HCl, the use of gaseous (Cl_2) and/or toxic reagents ($SOCl_2$, CBr_4) which are hazardous and aggressive reagent and requires the design and construction of custom expensive reactors.

In this context TCCA would be a very effective green and sustainable alternative.

In order to valorize the polyhedral reactivity of TCCA, another potentially emerging field would be the design of reaction allowed by green energy sources such as sunlight, ball milling and microwave irradiation.

Actually, the procedure carried out by enabling green technologies are a central and characterizing tool for both academic and industrial research.

In this context the use of stable, safe and recyclable reagents, which is TCCA, appears very appropriate and appropriately developable.

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Keywords: trichloroisocyanuric acid • aromatic electrophilic substitution • oxidation • chlorination • radical reactions

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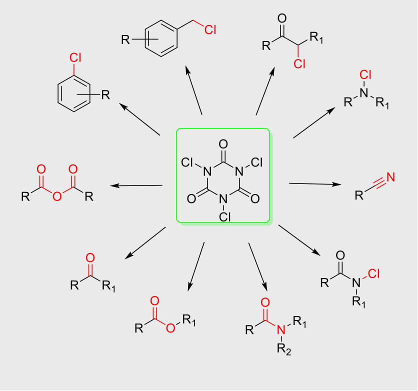
Entry for the Table of Contents (Please choose one layout)

Layout 1:

MINIREVIEW

Trichloroisocyanuric acid (TCCA) is a versatile and efficient reagent for chlorination and oxidation reactions. It was effectively used to synthesize many classes of compounds such as: chlorinated arenes, N-chloramines and amides, α-halo-carbonyl compounds, benzyl chlorides, esters, carboxylic anhydrides and amides.



Key Topic* chlorination and oxidation reactions

*Silvia Gaspa, Massimo Carraro, Luisa Pisano, Andrea Porcheddu, Lidia De Luca**

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Title
Trichloroisocyanuric Acid: a versatile and efficient chlorinating and oxidizing reagent