12th International Electronic Conference on Synthetic Organic Chemistry (ECSOC-12) 1-30 November 2008
http://www.usc.es/congresos/ecsoc/12/ECSOC12.htm & http://www.mdpi.org/ecsoc-12

[A002]

Tetrachlorosilane-A Versatile Reagent in Organic Synthesis

Tarek A. Salama*[a,b] , **Saad S. Elmorsy[a]** and **Mohamed A. Ismail[a]**
[a]*Chemistry Department, Faculty of Science, Mansoura University, 35516-Mansoura, Egypt.*
[b]*Chemistry Department, Faculty of Education, Amran University, Amran, Yemen*
Corresponding author; *E-mail: tasalama@yahoo.com*

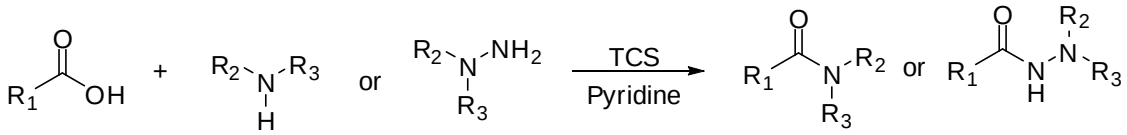
ABSTRACT- A recent increased attention is witnessed to the use of tetrachlorosilane (TCS), a cheap industrial intermediate, as a versatile reagent in organic synthesis. For example, TCS was used as an effective dehydrating agent, trans-silylating reagent and as a starting substrate for in situ preparation of other useful stoichiometric reagents in synthetic organic chemistry. Of these reagents TCS-NaI (Iodotrichlorosilane, ITCS), TCS-NaN_3 (azidochlorosilanes) and TCS in combination with $ZnCl_2$, Zn, KCN, Na_2S and others. Some selected synthetic applications of TCS as dehydrating agent as well as one of its based "*in situ*" reagents (TCS-NaN_3) are briefly highlighted herein.

1. Tetrachlorosilane (TCS) as a dehydrating agent:

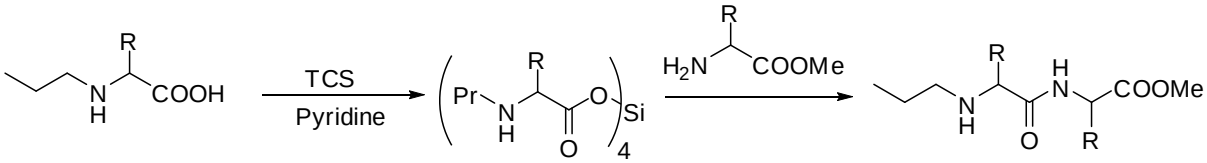
TCS is known as a dehydrating agent either in pyridine, dichloromethane in presence or absence of triethylamine or in absolute ethanol.

1.1. TCS mediated amide bond formation

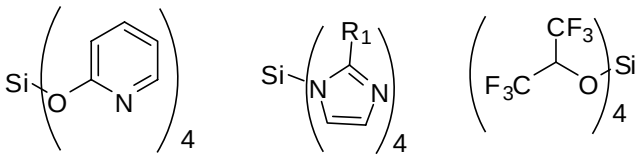
TCS acts as a simple and efficient dehydrating reagent for the formation of the amides[1-3] and hydrazides[4] from carboxylic acids by using pyridine as solvent.



This methodology was also extended to peptide synthesis through the reaction of *N*-protected amino acid with amino ester to afford dipeptides.[5]



Recently, three novel dehydrating reagents based on TCS were prepared by Mukaiyama group; Tetrakis(pyridin-2-yloxy)silane $[Si(OPy)_4]$[6], Tetrakis(imidazol-1- yl)silane[7] which prepared by trans-silylation between TCS and trimethyl(pyridin-2-yloxy)silane or 1-(trimethylsilyl)imidazoles respectively and tetrakis(1,1,1,3,3,3-hexafluoro- 2-propoxy)silane, $Si[OCH(CF_3)_2]_4$[8], prepared easily from TCS and sodium 1,1,1,3,3,3-hexafluoro-2-propoxide were effectively employed as mild dehydrating reagents in forming various carboxamides from the corresponding carboxylic acids and amines that involve secondary or tertiary alkyl substituted ones in good to high yields.

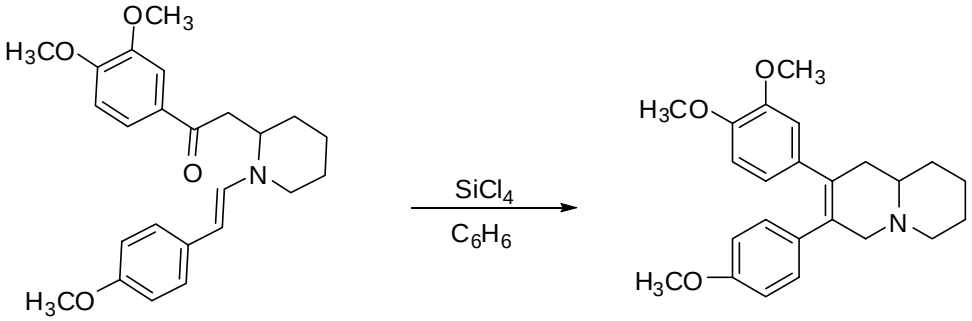


[Si(OPy)$_4$]

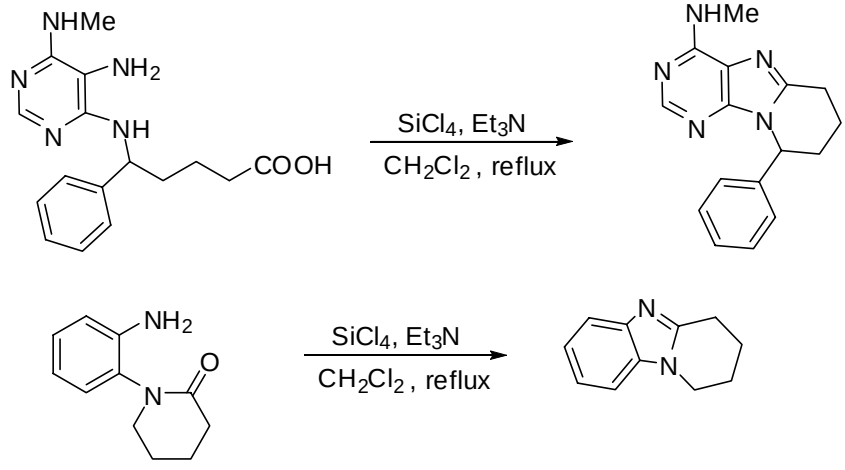
1.2. TCS-catalyzed cyclodehydration reactions:

1.2.1. General

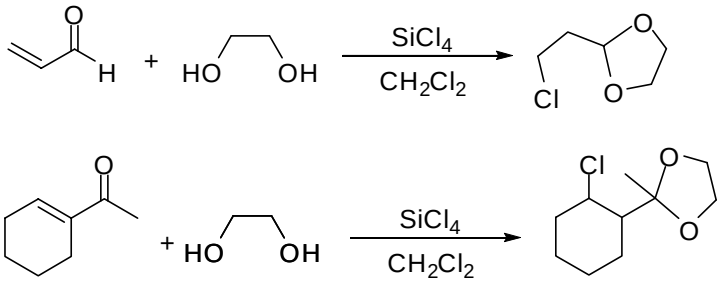
Among a range of Lewis acids, TCS was successeful as an alternative to $TiCl_4$ as a Lewis acid catalyst in cyclisation of enamine-ketone and in the subsequent dehydration leading to the alkaloid julandine.[9] This success suggested that TCS may find application in other reactions as an alternative to $TiCl_4$.



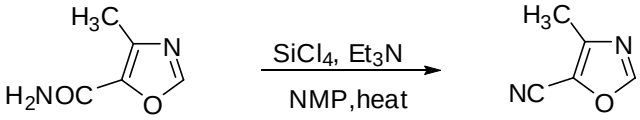
TCS, in the presence of triethylamine was used for the activation of tertiary amides, this concept was applied for the dehydration of N-alkyl N-acyl alanines leading to mesoionic oxazolones[10] and extended for the synthesis of imidazoheterocycles such as the cycloadenine derivatives and benzimidazoles through cyclodehydration reactions.[11]



TCS was used as chlorinating and dehydrating reagent in the preparation of ß-chloroacetals or ketals from the corresponding α, ß-unsaturated aldehydes or ketones with ethylene glycol.[12]

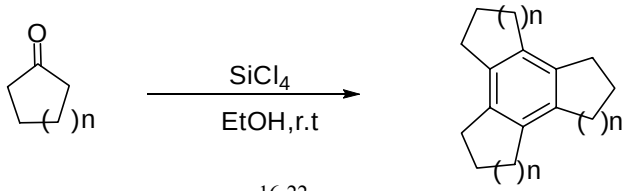


A Japanese patent reported the dehydration of primary amides to the corresponding nitriles by TCS in the presence of amines.[13] For examole, 5-cyano-4-methyl oxazole was prepared in high yield through the reaction of 5-cabamoyl-4-methyloxazole with TCS and triethylamine in *N*-methylpyrolidine as solvent.

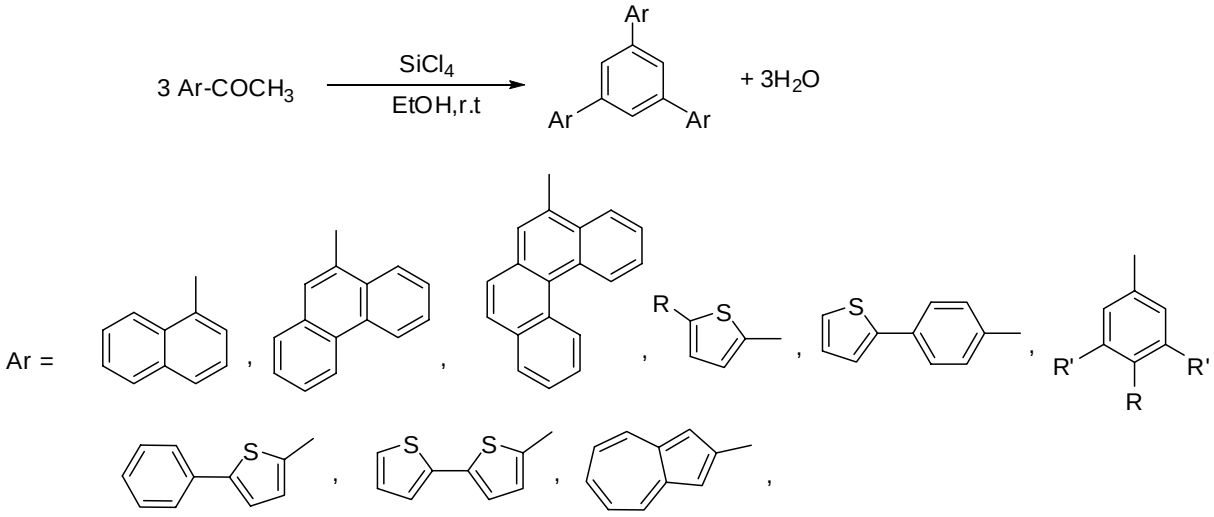


1.2.2. TCS/Ethanol

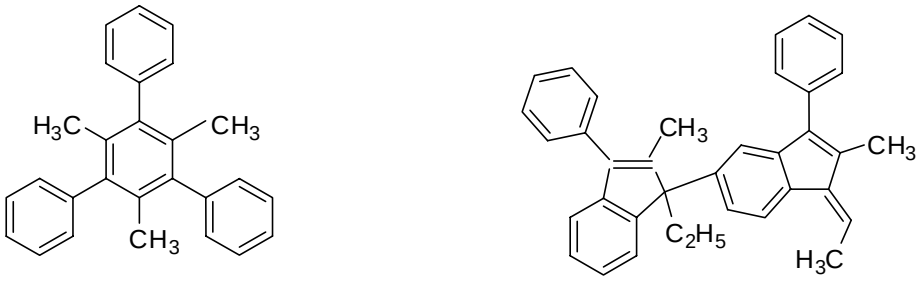
TCS reacts with dry ethanol with exclusion of moisture to produce a regent combination with the general formula $Si(OEt)_nCl_{4-n}.nHCl$.[14] This system was found to be an efficient reagent for achieving many cyclotrimerization reactions of active methylene ketones. TCS-ethanol induced self condensation of ketones to yield tri-or hexasubstituted benzene has been reported,[15] thus, treatment of cycloalkanones with TCS in ethanol gave the triannulated benzene.



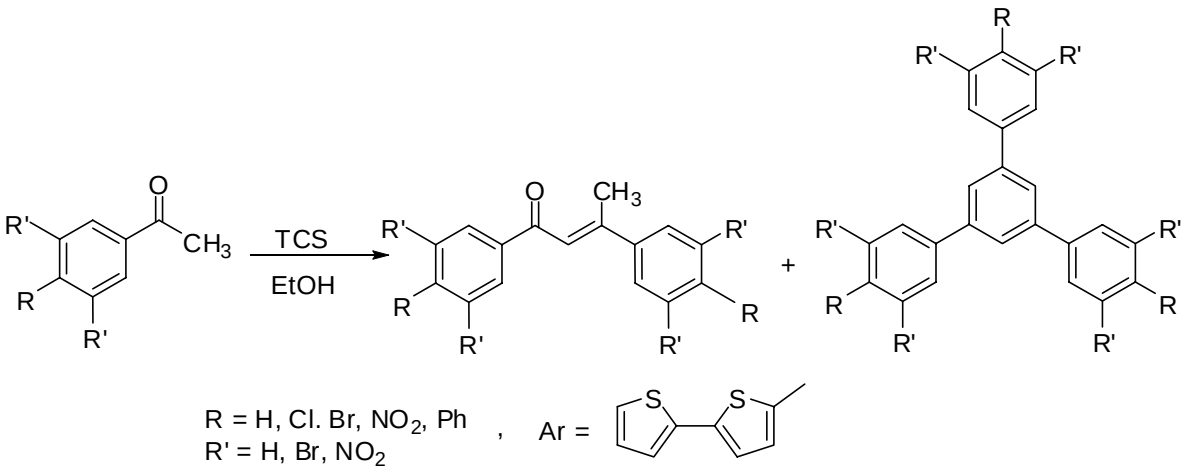
Similarly, a variety of aryl methyl ketones,[16-22] under the same conditions, gave good yields of 1,3,5-triaryl benzenes. This methodology was extended for a direct synthesis of conjugated star polyaromatics and organometallics as well, such as symmetrically substituted arenes[23] 1,3,5-$C_6H_3R_3$ where R = $(C_5H_4)Mn(CO)_3$ and $(C_5H_4)Fe(C_5H_5)$.



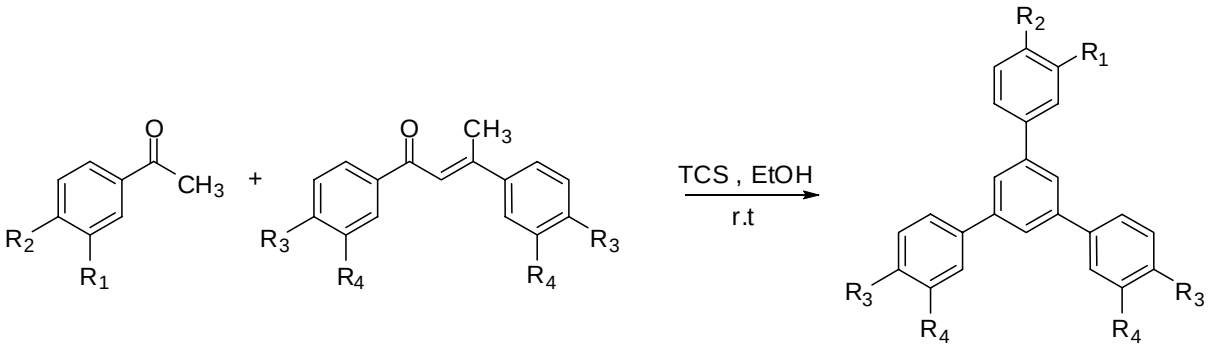
Instead of the expected hexasubstituted benzene 2,4,6-trimethyl-1,3,5-triphenylbenzene, reaction of proiophenone with TCS-EtOH gave a novel compound , which proposed as a result of three aldol type condensations of four molecules of propiophenone.[24]



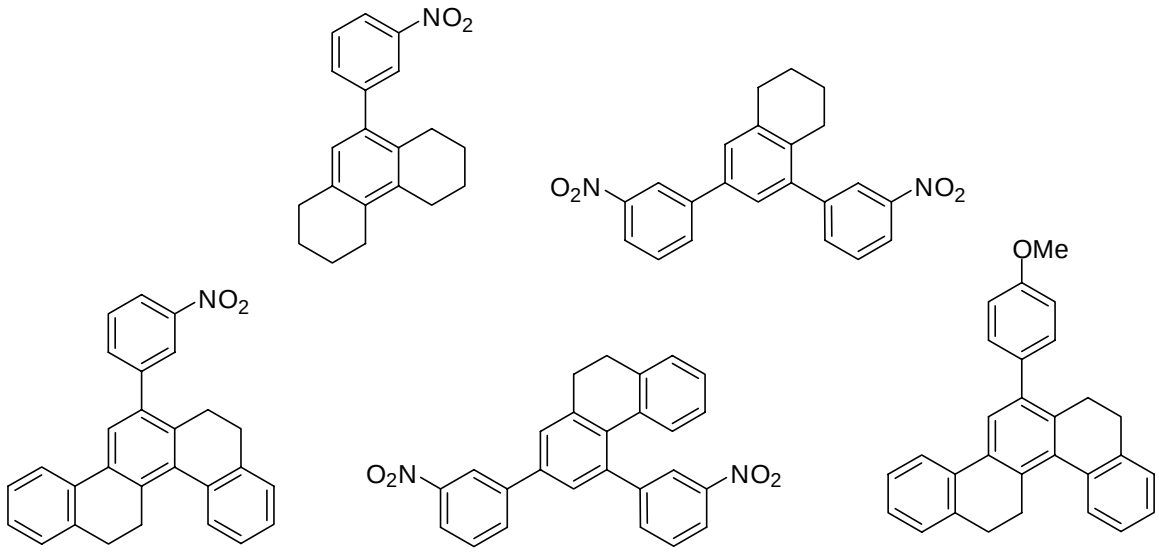
Dimmers of aryl methyl ketones, ß-methyl chalcones were isolated in some cases in lower amount.[25,26] By optimizing the reaction conditions, ß-methyl chalcones were isolated as major products. we have reported a new approach to the stereoselective synthesis of ß-methyl chalcones through the reaction of aryl methyl ketones with TCS in absolute ethanol under milder conditions.[27] ß-methyl chalcones were isolated as major products along with minor amounts of symmetrical 1,3,5-triaryl benzenes. Substituted acetophenones having strongly electron-withdrawing groups such as nitro group gave the ß-methyl chalcones only. Thus, 3 or 4- nitroacetophenones gave exclusively the corresponding ß-methyl chalcones in good yields.[27]



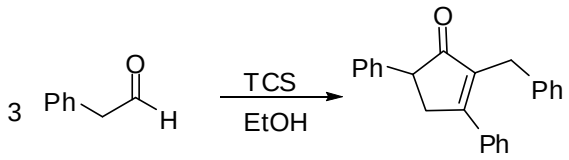
The above mentioned convenient synthesis of ß-methyl chalcones was efficiently used for a selective synthesis of unsymmetrical branched triarylbenzenes through the reaction of ß-methyl chalcones with variety of aryl methyl ketones in the presence of TCS-ethanol mixture.[28,29]



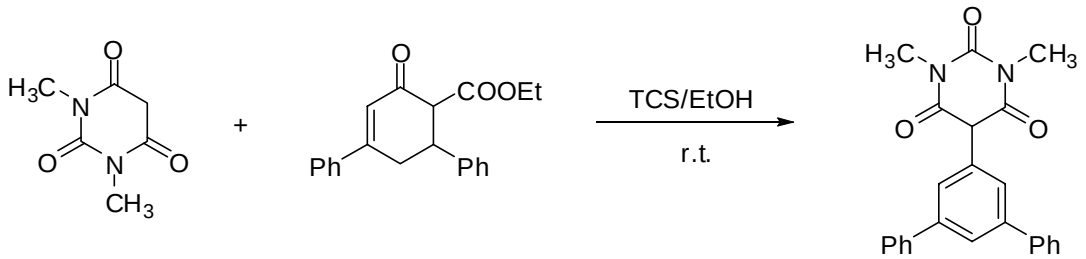
Compared with other synthetic routes to unsymmetrical triarylbenzenes, this method considered as an extremely efficient. An attractive and convenient route to branched fictionalized benzenoid compound has been reported by us through successive reactions of some cyclic ketones with aryl methyl ketones mediated by TCS-ethanol reagent. The reactions of cyclic ketones e.g. cyclohexanone, α-tetralone with nitro- or methoxyacetophenone have been examined. Some examples of the products from these condensations are listed below.



Self-condensation of aldyhydes having active methylene the presence of TCS-EtOH led to the formation alicyclic α,β-unsaturated ketones. Reaction of phenylacetaldehyde with TCS - EtOH resulted in 3,5-diphenyl-2-benzyl-2-cyclopenten-1-one via a double aldol reaction.[30]

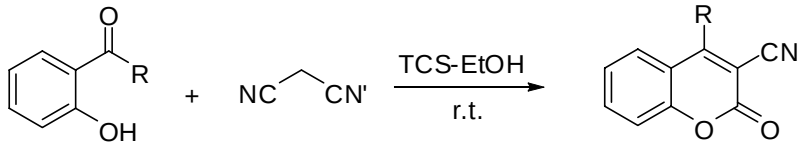


A unique condensation reaction of 1,3-dimethylbarbituric acid with the cyclic β-keto ester, 3,5-diphenyl-6-carboethoxy-2-cyclohexen-1-one to give 5-(3,5-diphenylphenyl)-1,3-dimethyl barbituric acid by the aid of TCS in absolute ethanol has been reported.[31]



TCS–ethanol mixture was used successfully as a hydrolyzing reagent, a facile conversion of nitriles into amides or esters was achieved on treatment with TCS in dry ethanol.[32]

TCS-EtOH induced knovenagell synthesis of coumarin-3-carbonitriles via condensation of o-hydroxy acetophenone or salicylaldehyde with malononitrile. Hydrolysis of a cyano group was proposed during this cyclisation.[33]



2. Tetrachlorosilane –Sodium Azide (TCS-NaN_3):

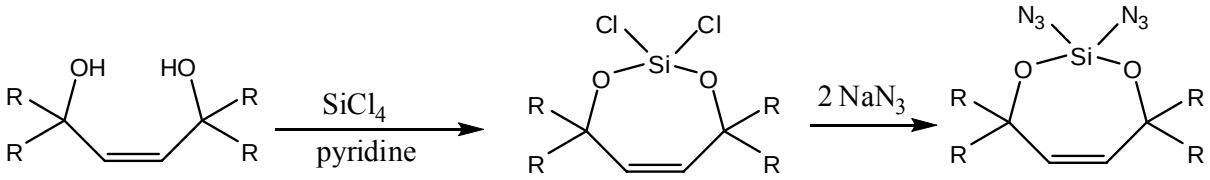
Hergs and Stark[34] have reported that silicon tetrachlorosilane reacts with sodium azide in acetonitrile at room temperature to form an equilibrated mixture chloroazidosilanes according to the molar ratio of added sodium azide.

$$\mathbf{SiCl_4 + \mathit{x}\ NaN_3 = SiCl_4 + N_3SiCl_3 + (N_3)_2SiCl_2 + (N_3)_3SiCl + Si(N_3)_4}$$

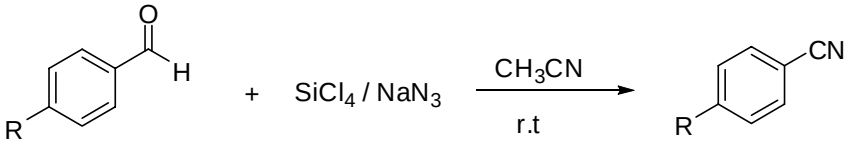
The ratios (%) of chloroazidosilanes in that reaction were determined by ^{29}Si-NMR spectroscopy. Increasing proportions of sodium azide shift the equilibrium towards the higher azides as shown in the following table:

$SiCl_4$	**2 NaN_3**	**2.5 NaN_3**	**3 NaN_3**
$SiCl_4$	6		
$Si(N_3)Cl_3$	30	12	3
$Si(N_3)_2Cl_2$	46	44	30
$Si(N_3)_3Cl$	18	44	49
$Si(N_3)_4$			18

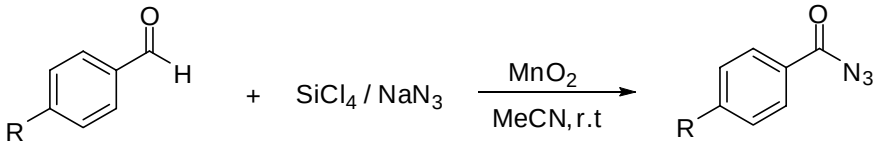
A separation and further characterization of the silanes $Si(N_3)_nCl_{4-n}$; (n = 1-4) was not attempted because of the explosive nature of these compounds. The above reaction was applied for the synthesis of 4,4`,7,7`-tetramethyl-2,2-diazido-1,2,3-dioxasila-5-cycloheptene which used for the chemical vapor deposition of quartz.



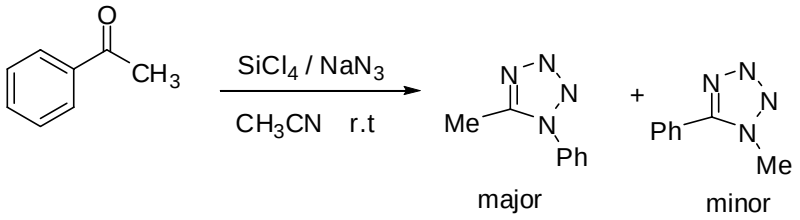
A novel conversion of aldehydes to nitriles in one-pot reaction was reported on treatment the aldehyde with $SiCl_4/NaN_3$ at room temperature.[35]



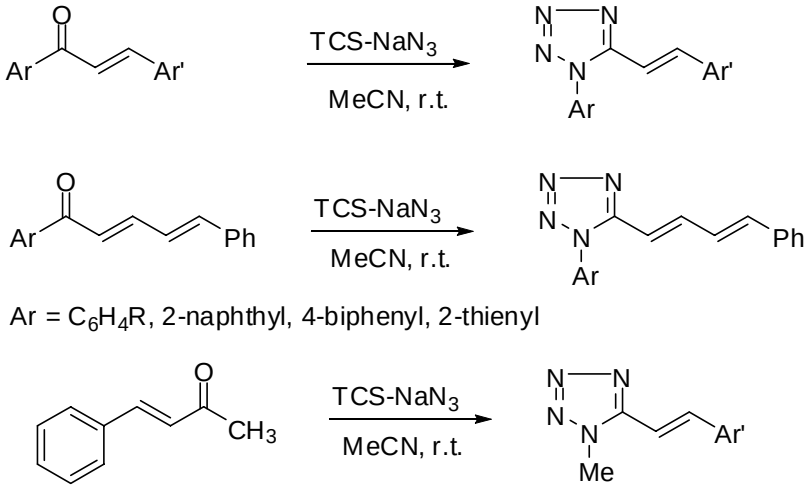
Under similar conditions, aldehydes were converted into acid azides in the presence of active manganese dioxide.[36]



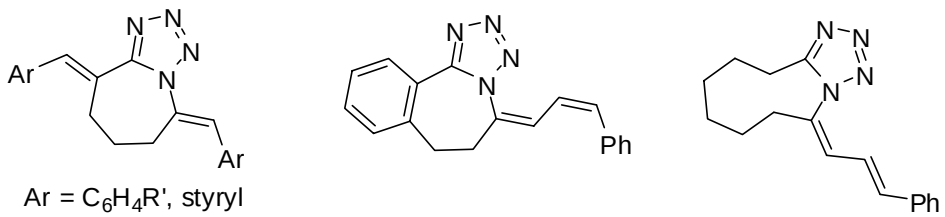
Ketones are converted to the corresponding tetrazole derivatives in nearly quantitative yield by their reaction with TCS/NaN_3 system (major triazidochlorosilane). The reaction was widely applicable for different ketonic compounds. It has succeeded with acyclic, cyclic, oxacyclic, azacyclic and aromatic ketones.[37] The reaction of acetophenone derivatives was found to give a mixture of two isomeric tetrazoles that indicates the preferential migration of aryl group.

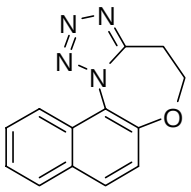
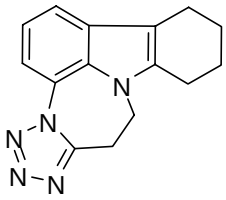


The reaction was further applied to the α,β-unsaturated ketones[37] as well as dienones[38] giving regiospecifically substituted tetrazole derivatives with preferential migration of the aryl or alkyl rather than alkenyl groups in arylidines of acetophenones. However, in case of arylidines of alicyclic ketones such that of cycloocatnone and benzosuberone, as proved by 2D NMR studies, alkenyl migration was favourable.[38]

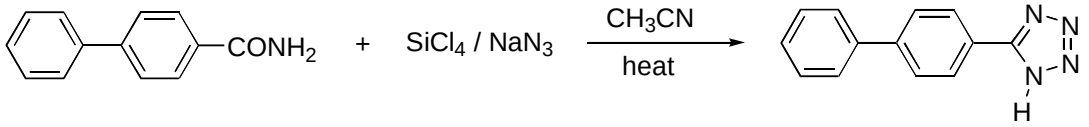


TCS-NaN_3 was proved as a powerful reagent in the preparation a great variety of tetrazole derivatives including tetrazoloheterocycles such as tetrazolo[1,5-a]-azepine, diazepine, oxazepine, azocine and azonine derivatives.

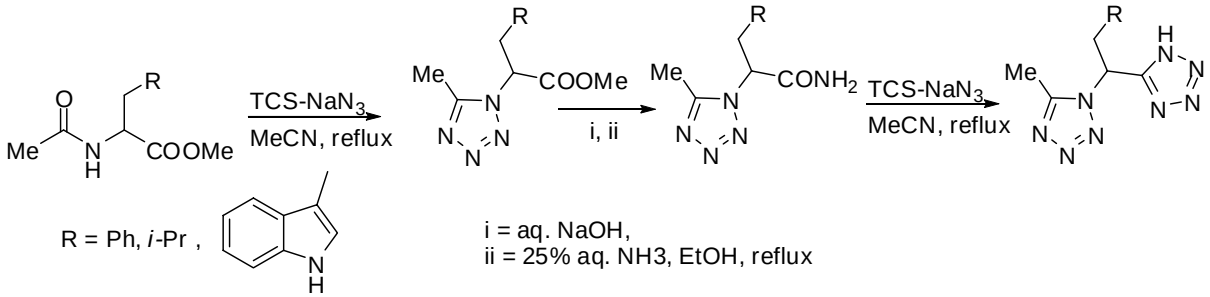


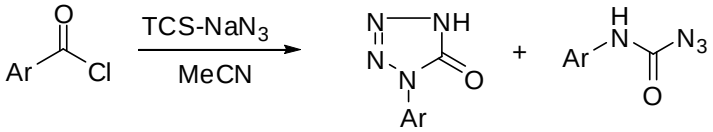
A new mild one-step method for the conversion of the primary acid amides to 5-substituted tetrazoles in nearly quantitative yields employing TCS-NaN_3 reagent has been reported.[65] Thus, acid amides on treatment with TCS/NaN_3 in situ in acetonitrile under reflux, yielded 5-aryltetrazole derivatives in high yields. [39,40]



Tetrazole-containing amino acid derivatives were also prepared through the reaction of TCS-NaN_3 reagent with N-acetyl-amino acid esters.[41,42]



Carboxylic acid chlorides react with the TCS-NaN_3 reagent to give tetrazolinones and/or carbamoyl azides in good yields presumably through the intermediacy of isocyante derivatives.[43]



Finally, TCS still finds an update interest in the scientific community[44-50] which will be followed in a forthcoming review.

In conclusion, we have presented herein an overview on the role of the inexpensive and readily available tetrachlorosilane as an efficient and versatile reagent in synthetic organic chemistry. It is expected that its use, together with a number of convenient "*in situ*"preparations, will continue to expand and find many additional applications.

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