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A facile and convenient synthesis of substituted tetrazole derivatives from ketones or α,β-unsaturated ketones.

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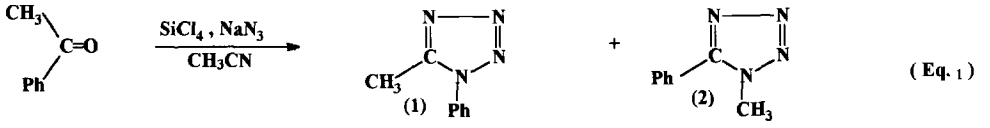
Abstract: *Triazidochlorosilane ($SiCl_4$ - NaN_3 in situ) is a new and efficient reagent for the direct conversion of ketones or α,β-unsaturated ketones to the corresponding tetrazole derivatives in nearly quantitative yield.*

Silyl azides behave as 1,3-dipole toward acetylenes[1-3], olefins[4] and nitriles[5] to give the corresponding cyclo - adducts. We have recently reported[6] the synthesis of triazidochlorosilane (TACS) from the reaction of one mole of tetrachlorosilane with three moles of sodium azide in acetonitrile at room temperature. The mixture (TACS in situ) proved to be equivalent to the isolated reagent. Triazidochlorosilane was a suitable and improved reagent for the direct conversion of aldehydes to the corresponding nitriles[6]. Also it was used for the efficient oxidation of aldehydes to the corresponding acyl azides in the presence of active manganese dioxide[7]. On the basis of our earlier work[6,7], triazidochlorosilane is a conveniently prepared in situ and provides an expedients source of azide, soluble in most organic solvents and should not form cumbersome insoluble salts after cleavage of the silicon - nitrogen bond. As part of an investigation into the reactivity and potential of TACS, its reaction with ketones and α,β-unsaturated ketones has been investigated. When a mixture of TACS (in situ) and ketones was stirred at room temperature in acetonitrile the corresponding tetrazole derivatives were yielded.

The reaction of acetophenone derivatives (entries 1, 2, 3) was found to give a mixture of two isomeric tetrazoles as shown in Table 1. In equation 1 the major product was compound (1) in 87% yield. The tetrazole (2) was determined by NMR analysis in less than 5% yield. IR spectra of the products showed absorption bands for C=N and N=N groups of tetrazole, and the absence of the absorption band of the azido group for imidoyl azide derivatives.



(Eq. 1)

Results of the reaction with acetophenone derivatives (entries 1, 2, 3) demonstrated that migration of the aryl group was greatly favored .

(3) (4)

(Eq. 2)

(5) (6) (Eq. 3)

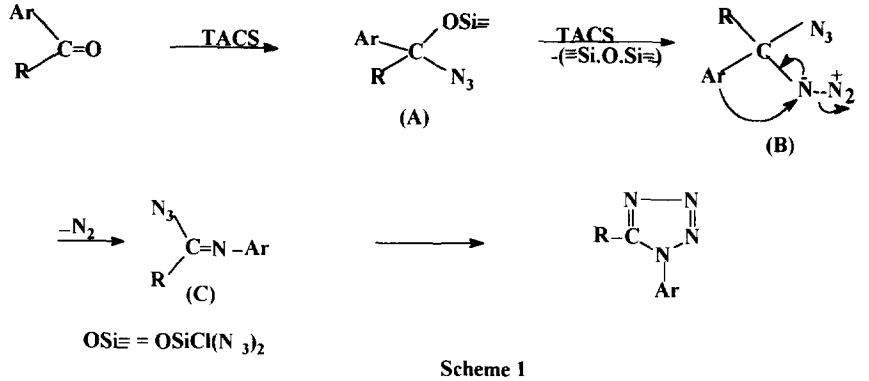
The results are summarized in Table 1. They show that the system provides a convenient procedure for acyclic (entry 5) and cyclic aliphatic substrates (entry 6), oxacyclic (entry 8, eq. 2); azacyclic (entry 9, eq. 3); or aromatic ketones (entries 1,2,3,4,7) and mostly affords nearly quantitative yields the corresponding tetrazole derivatives.

Table 1 Reaction of ketones with TACS (TCS / NaN_3 in situ)

Entry no.	Substrate	Time (hr)	Products[b]	yield (%)
1.	Acetophenone	12	5-Methyl-1-phenyltetrazole(1) +	87
			1-Methyl-5-phenyltetrazole (2)[a]	5
2.	4'-Chloroacetophenone	15	5-Methyl-1-(4-chlorophenyl)tetrazole +	87
			1-Methyl-5-(4-chlorophenyl)tetrazole[a]	5
3.	3'-Nitroacetophenone	24	5-Methyl-1-(3-nitrophenyl)tetrazole +	60
			1-Methyl-5-(3-nitrophenyl)tetrazole[a]	5
4.	Benzophenone	15	1,5-Diphenyltetrazole	97
5.	Acetone	12	1,5-Dimethyltetrazole	98
6.	Cyclohexanone	20	6,7,8,9-Tetrahydro-5H-tetrazolo [1,5-a] azepine	95
7.	1-Indanone	13	4,5-Dihydrotetrazolo [1,5-a] quinoline	93
8.	2,3-Dihydro naphtho [2,1-b] pyran-1-one (3)	12	Compound (4)	40
9.	5,6,8,9,10,11-Hexahydro-4H-pyrido [3,2,1-jk] carbazol-4-one (5)	6	Compound (6)	90

a) Products were determined by NMR analysis.
b) Other products were crystallized and fully characterized by NMR, mass spectra and elemental analysis.

The suggested reaction pathway is shown in Scheme 1. The reaction proceeds via the formation of siloxy azide (A), and subsequent formation of gem-diazidoalkane[8] (B). The latter intermediate undergoes a rearrangement similar to the Beckmann rearrangement with predominant migration of the aryl group, giving the imidoyl azide (C), followed by cyclization to the tetrazole derivatives.



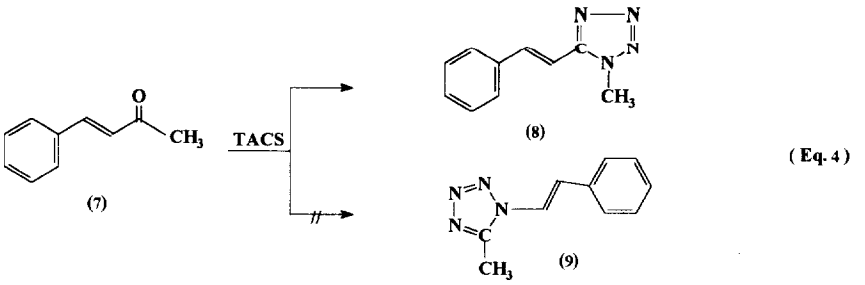
Scheme 1

Table 2. Reaction of α,β-unsaturated ketones with TACS (TCS /NaN_3 in situ) .

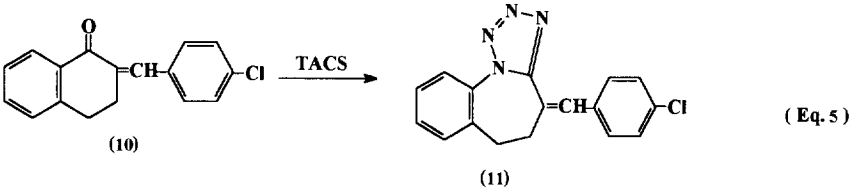
Entry no.	Substrate	Time (hr)	Product[a]	Yield[b] (%)
10.	Benzalacetone (7)	12	1-Methyl-5-styryltetrazole (8)	95
11.	Benzalacetophenone	12	1-Phenyl-5-styryltetrazole	94
12.	4-Methoxybenzalacetophenone	15	5-(4-Methoxystyryl)-1-phenyltetrazole	90
13.	4-Chlorobenzalacetophenone	10	5-(4-chlorostyryl)-1-phenyltetrazole	95
14.	2-(4-Chlorobenzal)-1-tetralone (10)	18	4-(4-Chlorobenzal)-5,6-dihydro-4H-tetrazolo[1,5-a]-1-benzazepine (11)	80
15.	2,6-Dibenzalcyclohexanone	14	5,9-Dibenzal-5,6,7,8-tetrahydro-9H-tetrazolo[1,5-a]azepine	90
16.	Isophorone	5	6,8,8-Trimethyl-7,8-dihydro-9H-tetrazolo[1,5-a]azepine	95

a)All the reactions were carried out as in the typical experimental procedure.
b) All products were crystallized and fully characterized by NMR, mass spectra and elemental analysis.

In continuation of our studies we now have found in TACS a highly efficient reagent system that allows formation of regiospecifically substituted tetrazole derivatives from α,β-unsaturated ketones. In contrast to other silyl azides[9] the reaction of TACS afforded rearranged tetrazole derivatives with preferential migration of the aryl or alkyl groups, rather than the alkenyl groups (eqs. 4 & 5), and without any catalysts[10-15] (Table 2) in very good yield. As an example, the reaction of benzalacetone (7) gave only 1-methyl-5-styryltetrazole[16] (8) and not 1-styryl-5-methyltetrazole (9) as shown in equation 4.



(Eq. 4)



(Eq. 5)

In a typical procedure for the reaction of TACS with ketones and α,β-unsaturated ketones; a mixture of tetrachlorosilane (5 mmol), sodium azide (15 mmol) in dry acetonitrile (10 ml) and benzalacetone (7) (5 mmol) was stirred at 25°C for 12 hr.(TLC monitoring) with exclusion of moisture. The reaction mixture was poured into ice-cold sodium carbonate solution and extracted with chloroform (3x20 ml). The chloroform was distilled off under reduced pressure to give 1-methyl-5-styryltetrazole (8), which was purified by crystallization from n-hexane : acetone (30:1), m.p =120°C.

Thus, the present procedure is a more broadly applicable, higher - yielding route to novel substituted tetrazoles with wide structural variations. At the same time, it is of high interest, not only for the compounds reported , but for the introduction of triazidochlorosilane (in situ) as a versatile synthetic reagent.

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16. IR (KBr plate) ν = 1640 (C=N), 1570 (N=N) cm^{-1}; ^{1}H-NMR, δ ($CDCl_3$) = 7.90 (d, 1H, J=16 Hz), 7.60 (m, 2H, ArH), 7.45 (m, 3H, ArH), 6.85 (d, 1H, J=16Hz), 4.15 (s, 3H, NCH_3).

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