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TRIMETHYLSILYL TRICHLOROACETATE: A NEW REAGENT FOR SALT-FREE SILYLATIONS

James M. Renga*
Agricultural Products Research & Development
The Dow Chemical Company
2800 Mitchell Drive
Walnut Creek, California 94598

Pen-Chung Wang
Central Research, Organic Specialties Laboratory
The Dow Chemical Company, M. E. Pruitt Building
Midland, Michigan 48640

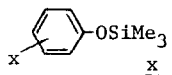
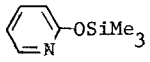
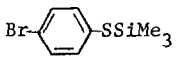
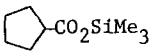
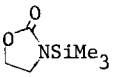
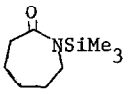
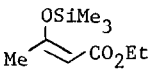
Abstract: Trimethylsilyl trichloroacetate (1) is a convenient reagent for the silylation of phenols, carboxylic acids, mercaptans, amides, acetylenes, and β-keto esters, while the reaction of 1 with aldehydes and ketones affords silylated trichloromethyl carbinols (5).

Among the various silylation reagents available,[1] those that can abstract protons as well as transfer silyl groups are particularly attractive from a synthetic standpoint. Because the co-products from these reagents are volatile hydrogen,[2] ammonia,[3] ammonia/CO_2,[4] dimethyl amine/CO_2,[5] propylene,[6] ethyl acetate,[7] and water,[8] product isolations are greatly simplified. Our recent success with using methyl trichloroacetate for the salt-free methylation of phenols[9] and carboxylic acids[10] prompted us to explore the silylation potential of trimethylsilyl trichloroacetate (1).[8a,11] We now wish to report that 1[12] readily silylates a variety of substrates (2), including phenols, mercaptans, carboxylic acids, amides, acetylenes, cyclic carbamates, and β-keto esters in the presence of a catalytic amount of K_2CO_3/18-crown-6, producing chloroform and carbon dioxide as the co-products (Table 1).

$$\underset{1}{CCl_3\overset{O}{\overset{\|}{C}}OSiMe_3} + \underset{2}{R\text{-}H} \xrightarrow[18\text{-crown-6}]{K_2CO_3} \underset{3}{R\text{-}SiMe_3} + CHCl_3 + CO_2$$

A typical silylation involves heating a rapidly stirred mixture of 1 (15 mmol), 2 (12.5 mmol), potassium carbonate (0.25 mmol), and 18-crown-6 (0.25 mmol) to around 100°C, where the evolution of chloroform and carbon dioxide commences. Depending upon the rate of gas evolution, the reaction temperature is maintained at 100°C or gradually raised to 150°C over a 1-2 hour period. A slight excess of 1 is used, due to the competing decarboxylation of 1 to trichloromethyltrimethylsilane.[11b]

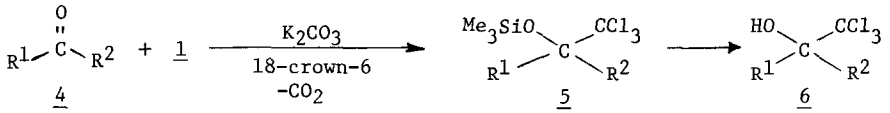
Table 1. Silylations Using Trimethylsilyl Trichloroacetate (1)

3[a]	Reaction[b] Temp., °C	% Isolated Yield
		
x = H	150	88
3-Me	"	90
4-t-Bu	"	90
2-Cl	"	85
4-Br	"	84
4-CN	"	88
4-NO_2	"	80
4-OMe	"	82
2-Ph	"	77
	100	94[c]
	100	91
$PhCO_2SiMe_3$	150	88
	100	90
	100	90
	110	75
$Ph-\equiv-SiMe_3$	130	88
	130	80

[a]These structures were assigned by ^{1}H-NMR.
[b]The reaction time is less than one hour.
[c]This compound is very sensitive to moisture.

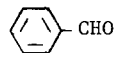
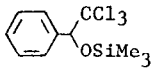
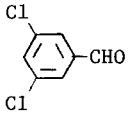
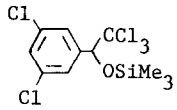
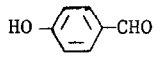
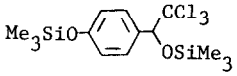
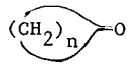
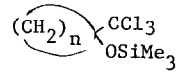
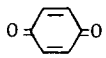
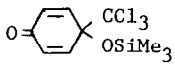
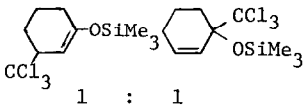
Quaternary ammonium and phosphonium salts, as well as 4-dimethylaminopyridine (DMAP), also catalyze the reaction. In a comparative study using p-methoxyphenol at 150°C with 2 mole % catalyst present, complete silylation was observed in less than 15 min. with K_2CO_3/18-crown-6, while with n-Bu_4NBr, n-Bu_4PBr, and DMAP the formation of 3 in 15 min. was 38%, 37%, and 32% respectively. Although complete silylation resulted within 45 min. for all three catalysts, considerable decomposition of the quaternary salts resulted.[13]

The reaction of 1 with aldehydes and ketones cleanly gives trimethylsilyl trichloromethyl carbinols (5) rather than silyl enol ethers (Table 2).



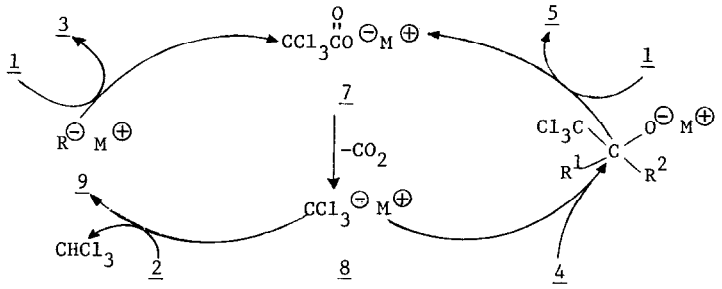
A 1,2-addition product is obtained with p-benzoquinone, while with 2-cyclohexen-1-one a 1:1 mixture of 1,2- and 1,4-addition products is isolated. Acid-catalyzed hydrolysis of 5 affords the corresponding trichloromethyl carbinols 6, thus offering a convenient alternative to the traditional formation of 6[14] from chloroform and base,[15] from the decomposition of sodium trichloroacetate,[16] or from the decomposition of trichloroacetic acid.[17]

Table 2. Formation of Trimethylsilyl Trichloromethyl Carbinols (5)

Carbonyl Compound	5[a,b]	% Isolated Yield
		93
		82
		75
		
	n = 3 n = 4 n = 5	96 90 88
		72
		80
	1 : 1	

[a]Satisfactory elemental analyses and spectral data were obtained for all compounds.
[b]The reaction temperature is 100°C and the reaction time is less than one hour.

The above results suggest a mechanism which involves a desilylation of 1 to give 7, followed by decarboxylation of 7 to give 8. However, a pathway involving intermediates derived from acyl attack of 9 on 1 cannot be eliminated at this point,[9] as the reaction of 1 with alcohols gives predominately a mixture of alkyl trichloroacetates and hexamethyldisiloxane.



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12. On a preparative scale, 1 can be prepared via the acid-catalyzed silylation of trichloroacetic acid with hexamethyldisiloxane.[8b] Trimethylsilyl trichloroacetate (1) is also commercially available from Petrarch Systems, Inc., Bristol, PA and Fluka Chemical Corp., Hauppauge, NY.

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