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REACTIONS OF ENOL SILYL ETHERS WITH N-HALOSUCCINIMIDE - A STEPWISE PROCESS

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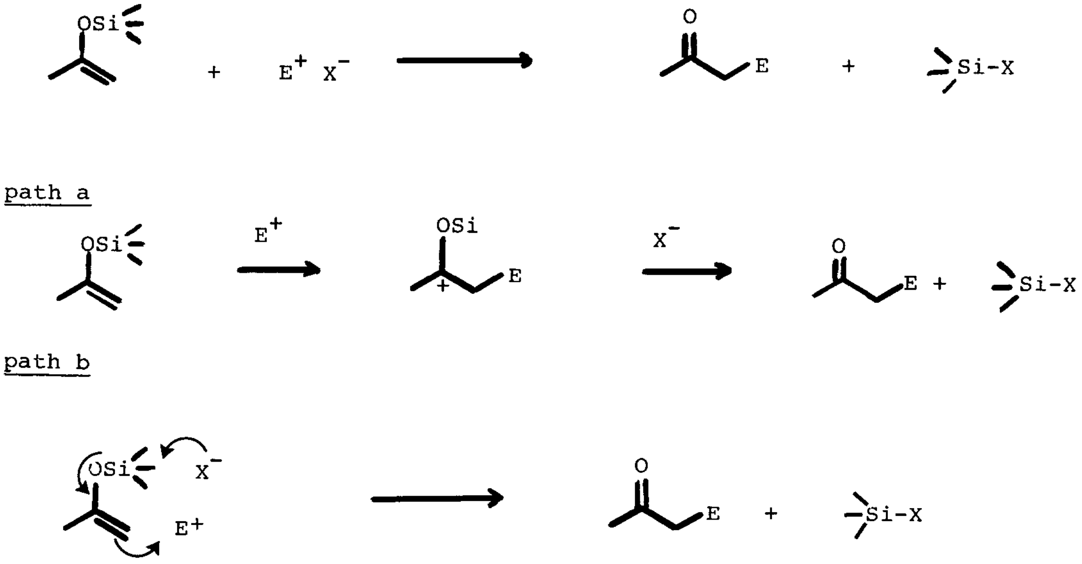
Summary: The N-chlorosuccinimide (NSC) reaction of a number of cyclic and acyclic trimethylsilyl enol ethers was investigated. Based on product analyses, the mechanism of the reaction is postulated to involve a step-wise process.

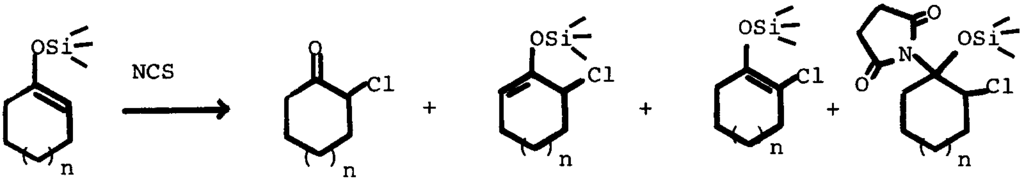
The chemistry of enol silyl ethers has undergone dramatic development since their first introduction into organic synthesis in the late sixties[1-5]. Most of the reactions of enol silyl ethers are with electrophiles. Thus, halogenation[6], acylation[7], Lewis-acid mediated reactions equivalent to Aldol[8], Michael[9], Stobbe[10] etc. can all be performed with enol silyl ethers according to the general scheme 1. In spite of the many reactions unravelled for enol silyl ethers and their growing popularity in organic synthesis, there is little mechanistic information on their reactions[11]. For example, it is not known whether the reaction of enol silyl ether with electrophile proceeds by a stepwise mechanism (path a) involving a silicon-containing intermediate or by

Scheme 1:



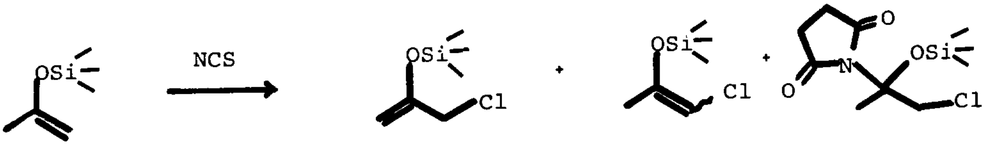
a synchronous process (path b or variation thereof) where cleavage of the silyl moiety occurs more or less concurrently with the electrophilic attack.

Reaction of enol silyl ethers with N-halo-succinimide has been reported to give the corresponding halo-ketones in good yields[6]. The reaction was examined mainly from the synthetic perspective. We found that when trimethylsiloxycyclohexene (2, n=1) and N-chlorosuccinimide (NCS) were allowed to react in CH_2Cl_2 a 0°, the chloroketone 3 was only a minor product; the major products were the two isomeric chlorides 4, 5 as well as the adduct 6. The products could be separated by flash chromatography (CH_2Cl_2-hexane as eluent)[12] and characterised by the usual methods[13]. On mild hydrolysis, they were all converted to 2-chlorocyclohexanone (3). The high yield of α-halo ketones normally associated with N-halo-succinimide reactions of enol silyl ethers is likely due to the hydrolytic work-up.



2 3 4 5 6

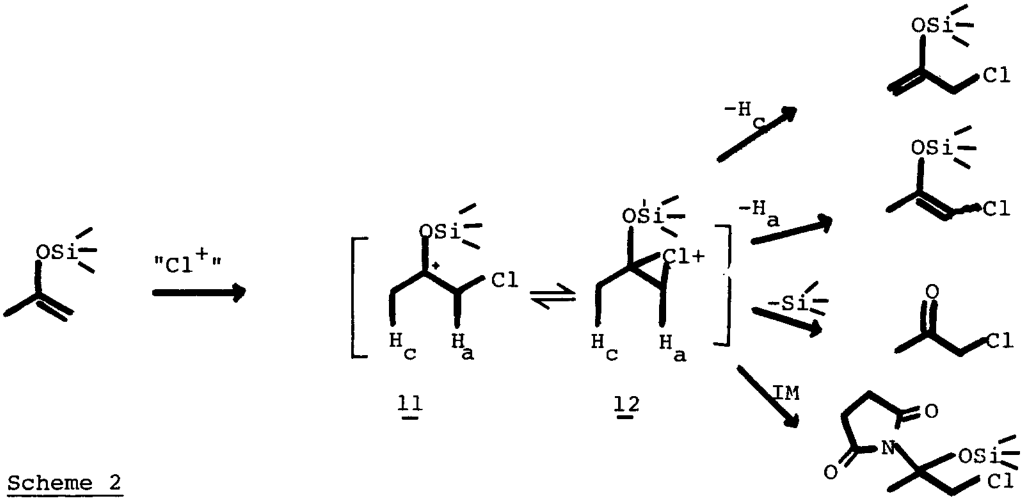
The results of the NCS reaction of trimethylsiloxycyclopentene (2, n=0) and trimethylsiloxycycloheptene (2, n=2) closely paralleled those of the 6-membered analog, as outlined in Table 1. Similar results were found in the reaction of NCS with acylic enol silyl ethers. Thus, 2-trimethylsiloxypropene (7) reacted with NCS to give the isomeric chlorides 8, 9 (E & Z) and the adduct 10.



7 8 9 10

3-Trimethylsiloxypent-2-ene and 4-methyl-2-trimethylsiloxypentene gave similar results on reaction with NCS (Table 1). Reaction of N-bromosuccinimide with 2 (n=1) also gave 3-bromo-2-trimethylsiloxycyclohexene, but the compound was less stable and isolation proved to be more difficult.

From these results, it seems that formation of a silicon-containing intermediate 11 or 12 (scheme 2) would be more consistent in accounting for the product distribution. Whether the ionic intermediate has the open structure 11 or the cyclic structure 12 cannot be established with certainty at this time.



Scheme 2

On the other hand, the addition of N-halosuccinimide to alkenes has been suggested to proceed by a radical pathway[15]. A radical intermediate involving the addition of Cl to enol silyl ether can be similarly invoked. We have no evidence to favour one possibility over the other, but irrespective of the finer details of mechanism, it is clear that enol silyl ethers react with N-halosuccinimide by a stepwise process.

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References and footnotes

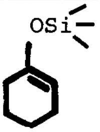
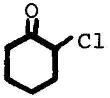
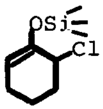
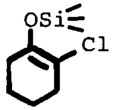
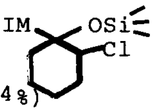
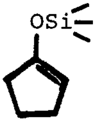
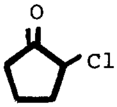
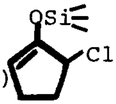
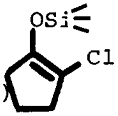
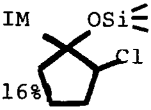
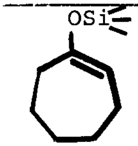
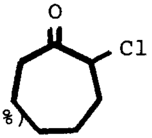
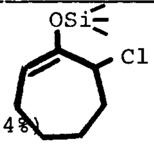
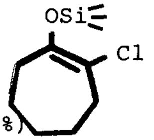
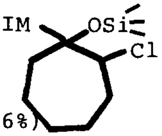
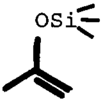
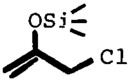
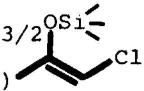
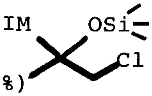
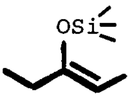
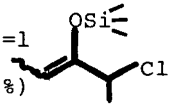
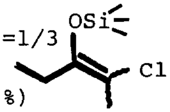
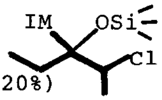
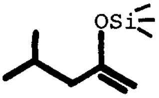
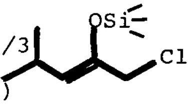
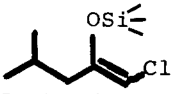
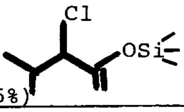
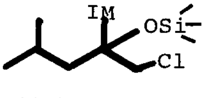
(1) G. Stork and P.F. Hudrlik, J. Amer. Chem. Soc., 90, 4462 (1968).
(2) H.O. House, L.J. Czuba, M. Gall and H.D. Olmstead, J. Org. Chem., 34, 2324 (1969).
(3) J.K. Rasmussen, Synthesis, 91 (1977).
(4) P. Brownbridge, Synthesis, 1 and 85 (1983).
(5) F. Brisse, D. Thoraval and T.H. Chan, Can. J. Chem., in press (1986).
(6) (a) R.H. Reuss and A. Hassner, J. Org. Chem., 39, 1785 (1974).
(b) L. Blanco, P. Amice and J.M. Conia, Synthesis, 194 (1976).
(7) S. Murai, Y. Kuroki, K. Hasigwa and S. Tsutsumi, J. Chem. Soc., Chem. Commun., 946 (1972).
(8) T. Mukaiyama, K. Banno and K. Narasaka, J. Amer. Chem. Soc., 96, 7503 (1974).
(9) M. Miyashita, J. Amer. Chem. Soc., 98, 4679 (1976).
(10) P. Brownbridge and T.H. Chan, Tetrahedron Letters, 21, 3427 (1980).
(11) T.H. Chan and M. Brook, Tetrahedron Letters 26, 2943 (1985) and references therein.
(12) W.C. Still, M. Kahn and A. Mitra, J. Org. Chem., 43, 2923 (1978).
(13) General experimental procedure: To a stirred, refluxing solution of 5.0 g of the enol silyl ether in 150 ml CH_2Cl_2, an equivalent amount of NCS in 250 ml CH_2Cl_2 was added. The progress of the reaction was monitored by GC. When the reaction was completed (usually within 15 min.), the solvent

was evaporated. To the mixture, 100 ml of pentane was added. The succinimide was filtered off and the filtrate was evaporated. The crude product was purified by either distillation or flash chromatography using either CH_2Cl_2 or CH_2Cl_2-hexane (80:20) as eluent. For trimethylsiloxycyclohexene, products 3, 4 and 5 were identified by comparison of their spectroscopic data with literature values[14]. The adduct 6 had: IR(CCl_4): 1718 cm^{-1}; ^1H nmr ($CDCl_3$): δ 5.1 (m, 1H) 1.1-2.5 (m, 12H), 0.2 (s, 9H); MS: m/z 305, 303; exact mass for $C_{13}H_{22}{}^{35}ClNO_3Si$ Calcd 303.105; Found: 303.096.

(14) H.O. House, W.F. Fisher, M. Gall, T.E. McLaughlin and N.P. Peet, J. Org. Chem., 36, 3429 (1971).

(15) J.M. Landesberg and M. Siegel, J. Org. Chem., 35, 1674 (1970). For a radical mechanism in the α-chlorination of enol silyl ethers, see Y. Itoh M. Nakatsuka and T. Seagusa, J. Org. Chem., 45, 2022 (1980).

Table 1: Reaction of enol silyl ethers with NCS

Reactant	Product (% yield)^{a,b}			
	(6%) 	(50%) 	(10%) 	(14%) 
	(9%) 	(58%) 	(7 %) 	(16%) 
	(10%) 	(44%) 	(11%) 	(16%) 
	(27%) 	E/Z=3/2 (35%) 	(26%) 	
	E/Z=1 (61%) 	E/Z=1/3 (8%) 	(20%) 	
	E/Z=1/3 (19%) 	(55%) E/Z=1 	(15%) 	(4%) 

(a) The ratio of products were determined by GC and NMR of the crude product mixture. The individual compounds were purified by flash chromatography and identified.

(b) IM=succinimidyl.

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