CHEMISTRY LETTERS, pp. 405-408, 1983.

REACTIONS OF α-HETEROATOM-SUBSTITUTED ETHERS AND SULFIDES WITH SILYL ENOL ETHERS. CHEMOSELECTIVITY IN THE CLEAVAGE OF HETEROATOM-CARBON BONDS BY IODOTRIMETHYLSILANE AND TRIMETHYLSILYL TRIFLUOROMETHANESULFONATE[1)]

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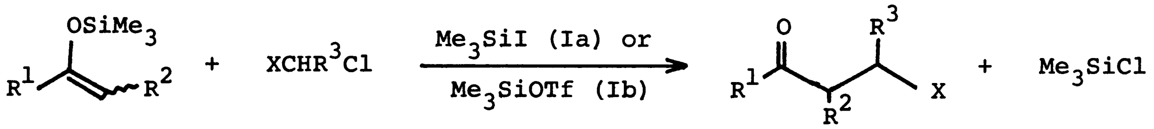
Reactions of α-heteroatom-substituted ethers and related compounds (R^1R^2CXY; X, Y = RO, RS and Cl) with silyl enol ethers and ketene silyl acetals took place in the presence of iodotrimethylsilane (Ia) and trimethylsilyl triflate (Ib) as a catalyst and factors influencing the activation of the heteroatom by I were examined.

Much attention has been focused to the synthesis of β-heteroatom-substituted ketones and esters which can be readily converted to α,β-enones including α-methyleneketones and α,β-unsaturated esters.[2)] For this purpose, introduction of an α-heteroatom-substituted alkyl group to the α site of ketones and esters is most widely used and a variety of synthetic methods along this line have been extensively investigated.[3)] We now report that a facile activation of the carbon-chlorine bond of α-chloro ethers and α-chloro sulfides among various α-heteroatom substituted alkanes (R^1R^2CXY; X, Y = RO, RS and Cl) occurs smoothly by iodotrimethylsilane (Ia) or trimethylsilyl trifluoromethanesulfonate (Ib) to react with silyl enol ethers and ketene silyl acetals giving β-heteroatom-substituted ketones and esters, respectively, and that not only the affinity of silicon to heteroatom but also the stabilizing effect of another heteroatom toward a carbocation control the selective activation.

Reactions of α-chloroethers (III) with silyl enol ethers (II) proceeded very rapidly in the presence of a catalytic amount of Ia or Ib to give the corresponding β-alkoxyketones (V) selectively, but no trace of β-chloroketones was observed. Ketene silyl acetals (II, R^1 = alkoxy) also reacted with III to afford β-alkoxyesters (V, R^1 = alkoxy) in good yield. (eq. 1) The results are summarized in Table 1.



(1)

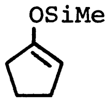
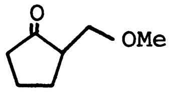
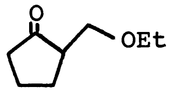
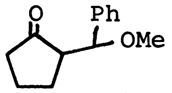
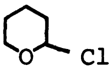
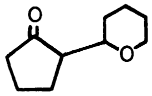
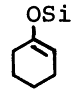
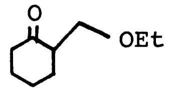
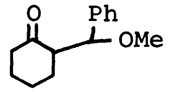
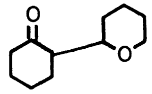
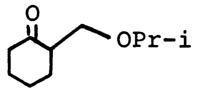
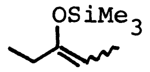
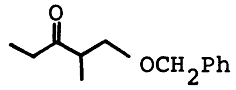
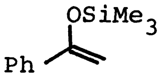
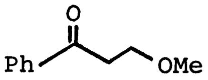
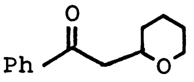
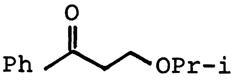
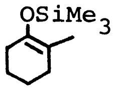
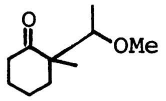
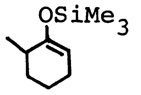
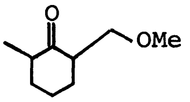
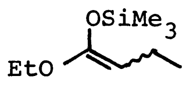
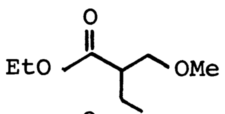
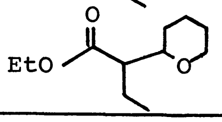
II

III, X=OR
IV, X=SR

V, X=OR
V, X=SR

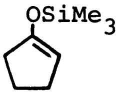
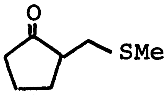
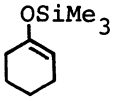
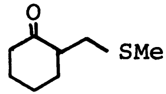
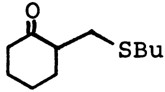
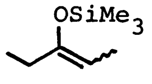
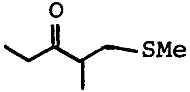
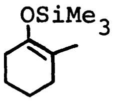
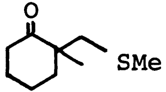
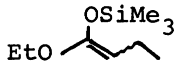
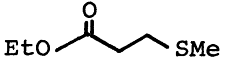
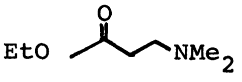
A variety of α-alkoxyalkyl groups can be readily introduced onto the α site of ketones and esters. Especially introduction of a cyclic ether which is of current

Table 1. Iodosilane (Ia)- and silyl triflate (Ib)-catalyzed reactions of α-chloroethers (III) with silyl enol ethers and ketene silyl acetals (II)

Entry	Silyl enol ether Ketene silyl acetal	α-Chloro ether	Conditions	Product	% Yield[a] (E/T)[b]
1	 (IIa)	$MeOCH_2Cl$ (IIIa)	Me_3SiI (Ia) CH_3CN, rt, 1.5 h		70
2	IIa	$EtOCH_2Cl$ (IIIb)	Ia, CH_3CN rt, 1 h		84
3	IIa	MeOCHPhCl(IIIc)	Ia, CH_2Cl_2 -78°, 5 min		85 (99/1)
4	IIa	 (IIId)	Ia, CH_2Cl_2 -78°, 5 min		80
5	 (IIb)	IIIb	Me_3SiCl-NaI CH_3CN, rt, 4 h		72
6	IIb	IIIc	Ia, CH_2Cl_2 -78°, 5 min		91 (99/1)
7	IIb	IIId	Ia, CH_2Cl_2 -78°, 5 min		75
8	IIb	i-$PrOCH_2Cl$(IIIe)	Me_3SiOTf (Ib) CH_3CN, -10°, 5 min		83
9	 (IIc)	$PhCH_2OCH_2Cl$ (IIIf)	Ia, CH_3CN rt, 1.5 h		84
10	 (IId)	IIIa	Ia, CH_3CN rt, 30 min		76
11	IId	IIId	Ia, CH_2Cl_2 -78°, 5 min		82
12	IId	IIIe	Ib, CH_2Cl_2 rt, 25 min		71
13	 (IIe)	MeOCHMeCl(IIIg)	Ia, CH_2Cl_2 -78°, 15 min		65
14	 (IIf)	IIIg	Ia, CH_2Cl_2 -78°, 20 min		67
15	 (IIg)	IIIa	Ib, CH_2Cl_2 0°, 30 min		56
16	IIg	IIId	Ia, CH_2Cl_2 -78°, 5 min		72

[a] Yield after isolation by TLC. [b] The ratio of erythro:threo was determined by NMR.

Table 2. Reactions of α-chlorosulfides (IV) with silyl enol ethers and ketene silyl acetals (II) catalyzed by iodosilane (Ia) or silyl triflate (Ib)

Entry	Silyl enol ether Ketene silyl acetal	α-Chloro sulfide	Conditions	Product (% Yield)
1	 (IIa)	$MeSCH_2Cl$ (IVa)	Me_3SiI(Ia), CH_2Cl_2 rt, 1h then reflux, 1h	 (58)
2	 (IIb)	IVa	la, CH_2Cl_2, rt, 1h then reflux, 1.5h	 (56)
3	IIb	n-$BuSCH_2Cl$(IVb)	Me_3SiOTf (Ib), CH_2Cl_2, rt, 4h	 (71)
4	 (IIc)	IVa	Ia, CH_2Cl_2 reflux, 8h	 (80)
5	 (IIe)	IVa	Ib, CH_2Cl_2 rt, 6h	 (78)
6	 (IIg)	IVa	Ib, CH_2Cl_2 rt, 3h	 (76)
7[b]	IIg	n-$BuOCH_2NMe_2$	Ib, CH_2Cl_2 rt, 3h	 (71)

[a] Yields after isolation by TLC. [b] See ref. 7.

interest [4)] is easily achieved. The stereoselectivity of the reaction is extremely high. (entry 3 and 6) Moreover a loss of the regiospecificity, recently reported in the case of kinetic silyl enol ether (IIf)[3f,g)] can be avoided by using the catalyst I.[5)] In addition to I, the reaction is also promoted by chlorotrimethylsilane-sodium iodide in acetonitrile.

Quite similarly α-chlorosulfides (IV) react with II in the presence of I to afford β-alkylthioketones (VI) selectively where the activation again takes place only at a C-Cl bond. The results are listed in Table 2. The reaction with IV is evidently slower than α-alkoxyalkylation with III.

Among other α-heteroatom-substituted alkanes, a hemithioacetal gave a sluggish result, presumably due to the ready dithioacetalization of products by the resulting thiosilane under the reaction conditions.[9d)] Although reactions of dithioacetals activated by I proceeded in some extent,[8)] the improvement of the yield could not be unfortunately attained. Dichloromethane and alkyl halides including allylic, benzylic and tertiary alkyl halides were intact for the activation by I.

In general, it has been known that Ia[9a,b)] and particularly Ib[9c,d,e)] tend to interact selectively with the oxygen atom of oxygen-containing substrates to form a silyloxomium ion. Indeed acetals can be readily activated by Ia[10a)] and Ib[3b,10b,c)] and furthermore aminomethyl ethers effectively undergo the activation at the oxygen atom rather than the nitrogen atom due to the high oxygenophilicity of I.[6)] Nevertheless, it is worth to note that the activation of III occurs exclusively at the chlorine atom, but not at the oxygen atom, since the Si-Cl bond has a large bond-dissociation evergy but is somewhat weak compared with the Si-O bond.11) Judging from results obtained in this work, the effective stabilization due to the heteroatom toward the incipiently formed carbocation12) may be responsible for the chemoselectivity in the cleavage of heteroatom-carbon bonds.

Acknowledgment: We thank Toshiba Silicone Co., Ltd., for a gift of chlorosilane. The work was supported by the Ministry of Education, Science, and Culture (Grant-in-Aid for Special Project Research No.57118002).

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(Received January 14, 1983)