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Reaction of 3-Chloroallyltrimethylsilane with Acid Chloride and Exploitation of a New Regioselective Synthesis of αβ-Unsaturated Epoxide

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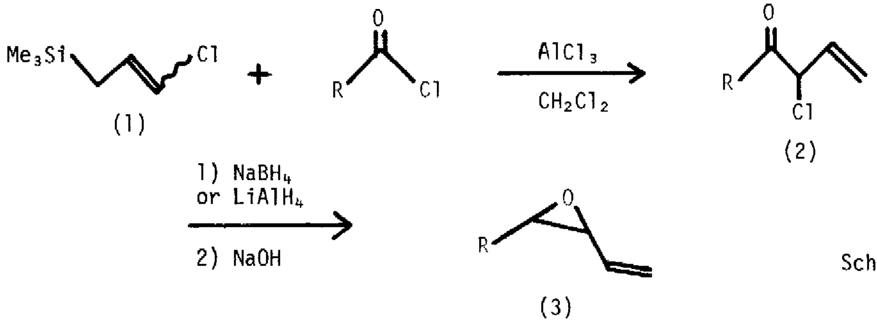
Summary : α-Chloro-βγ-unsaturated ketone (2) was synthesized from the reaction of 3-chloroallyltrimethylsilane (1) with acid chloride. The ketone was converted into αβ-unsaturated epoxide (3) regioselectively in good yield *via* reduction with $NaBH_4$ or $LiAlH_4$ followed by treatment with NaOH. Treatment with methyl lithium instead of reduction gave homologous epoxide (5).

Allylsilanes are the important synthetic reagents for the introduction of allyl group in the sense that they are allylically stable and react with various kinds of electrophiles in the presence of Lewis acid.[1] Their hetero-substituted derivatives, 1-trialkylsiloxy-,[2a] 1,1-dichloro-,[2b] 3-(1-pyrrolidinyl)-,[2c] and 1-benzenesulfenyl-allylsilane,[2d] have also been shown to be useful for organic synthesis. We have interested in the chemistry of 3-chloroallyltrimethylsilane (1) and tried its reaction with aldehyde.[3] We now wish to report the reaction of 3-chloroallyltrimethylsilane (1) with acid chloride in the presence of $AlCl_3$[4] and synthesis of αβ-unsaturated epoxide, which are summarized in Scheme 1.



Scheme 1

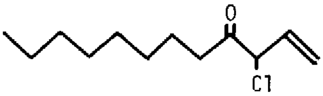
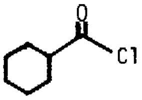
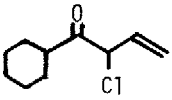
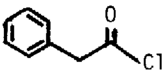
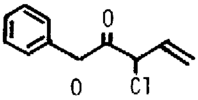
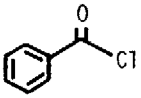
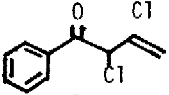
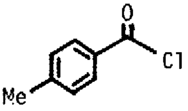
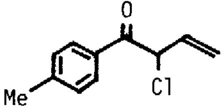
Generally, αβ-unsaturated epoxide is versatile compound, since it is easily convertible to E- and Z-allylic alcohols stereoselectively.[5] However there have been published only few reports about its general synthesis.[6]

It seemed more convenient for synthesis of αβ-unsaturated epoxide (3) to use ketone or aldehyde instead of acid chloride, because it would produce chlorohydrin directly. Actually the reaction of silane (1) with aldehyde, however, gave homoallylic alcohol methyl ether, while no reaction was observed with ketone.[3] The use of acid chloride has a further advantage for formation of di- and tri-substituted epoxides as described below.

The first step reaction of allylsilane (1) (a mixture of E- and Z- isomers) with acid chloride proceeded smoothly to give α-chloro-βγ-unsaturated ketone (2) in good yield. The results are summarized in Table 1.

A typical procedure is as follows. To the stirred suspension of $AlCl_3$ (400 mg, 3 mmol) in dichloromethane (8 ml) was added dropwise cyclohexanecarboxylic acid chloride (337 mg, 2.3 mmol) at -20°C in nitrogen. After stirring for an hour, a solution of allylsilane (1) (446 mg, 3 mmol) in dichloromethane (3 ml) was added dropwise to the solution and the reaction mixture was stirred at -20°C for 2 hr. Hydrolysis, extraction with ether, and the Kugelrohr distillation gave α-chloro ketone (2c) (319 mg, 74% yield, bp 75-80° at 0.7 mmHg).

Table I Reaction of (1) with Acid Chloride in the Presence of $AlCl_3$ in Dichloromethane[a]

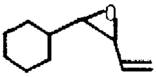
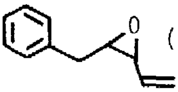
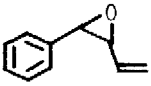
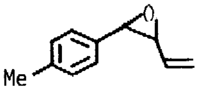
acid chloride	product		yield (%)[b]
		(2a)	80
		(2b)	77[c]
		(2c)	74
		(2d)	82
		(2e)	71
		(2f)	50

a) Reaction condition; -20°C for 2 hr. b) Isolated yield. c) Contaminated with a small amount of isomerized αβ-unsaturated ketone.

Reactions took place with both aliphatic and aromatic acid chlorides and the products (2) were distillable at reduced pressure without isomerization to the more stable α-chloro-αβ-unsaturated ketones except for the case of (2b). They were decomposed, however, when they were made in touch with silica gel for a long time.

Subsequent conversion of (2) to αβ-unsaturated epoxide (3) was straightforward. The ketone (2) on $NaBH_4$ reduction in methanol and subsequent treatment with aqueous methanolic NaOH afforded a mixture of cis and trans epoxides (3) in good yield (Table II). The step of hydride attack to α-chloro ketone (2) determines the stereochemistry of the epoxide. The predominant isomer obtained actually was proved to be that (cis-epoxide) expected from the dipolar model proposed by Cornforth.[7]

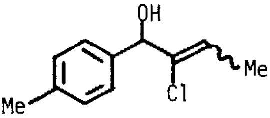
Table II Synthesis of αβ-Unsaturated Epoxide

α-chloro ketone	reaction condition[a]	epoxide	ratio (cis/trans)	yield (%)[d]
(2a)	A	 (3a)	$1^{b,c}$	94
(2c)	A	 (3c)	2^{b}	100
(2d)	A	 (3d)	1^{c}	88
(2d)	C	(3d)	1^{c}	83
(2e)	A	 (3e)	$4^{b,c}$	71
(2f)	B	 (3f)	$2^{b,c}$	75

a) A: 1) $NaBH_4/MeOH/0°C$, 2) NaOH
B: 1) $LiAlH_4/Et_2O/0°C$, 2) NaOH
C: 1) DIBAH/THF, 2) NaOH

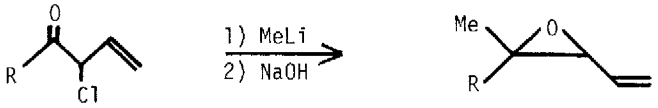
b) Determined by NMR.
c) Determined by GLC.
d) Isolated yield.

On reduction with $NaBH_4$ in methanol, the ketone (2f) gave an undesirable alcohol (4) accompanied by the isomerization to αβ-unsaturated ketone; the desirable chlorohydrin was obtained by reduction of (2f) with $LiAlH_4$ in ether.



(4)

Methylation of ketone (2) with methyl lithium followed by treatment with NaOH afforded tri-substituted epoxide (5) as shown.



(2) (5)

R = $C_6H_5CH_2$; 52 %
R = C_6H_5 ; 56 %

Reaction of allylsilane (1) with αβ-unsaturated acid chloride proceeds well; it will be the subject of a further publication.

References and Notes

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