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A NOVEL AND CONVENIENT REGIO-CONTROLLED SYNTHESIS OF α-HALOGEN-SUBSTITUTED ALLYLSILANES. STEREOSELECTIVE SYNTHESIS OF Z-ALKENYL HALIDES[1)]

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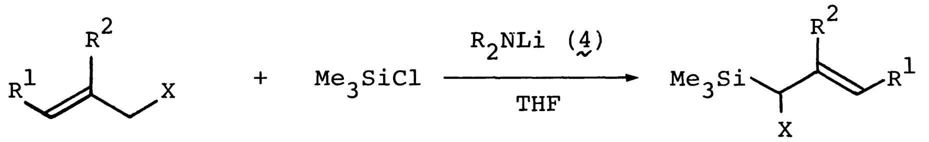
α-Halogen-substituted allylsilanes, prepared conveniently by the in situ reaction of lithiated allyl halides with chlorosilane in a regio-controlled manner, react with various electrophiles to give the corresponding alkenyl halides with high Z preference.

Allylsilanes have advantages over other allylation reagents in being versatile and regiospecific in the allyl transfer.[2)] Therefore many efforts have been directed to the regio-controlled preparations of allylsilanes bearing various functional groups.[3)] In particular, halogen-substituted allylsilanes are interesting and important as readily convertible reagents for further functional group transformations. However, except for the studies on β- and γ-halogen-substituted allylsilanes,[4)] no efficient synthesis nor the reaction of α-halogen-substituted allylsilanes is known to date.[5)] We now report that isomerically pure α-halogen-substituted allylsilanes of the type **1**, prepared conveniently from metalated allylic halides by a simple procedure, provide a stereoselective and facile entry to vinylic halides with high Z preference.[6)]

The requisite α-halogen-substituted allylsilanes (**1**) are prepared quite easily by the in situ reaction of metalated allyl halides, obtained from allyl halides (**2**, X = Cl and Br) and lithium dialkylamide (**4**),[7)] with chlorotrimethylsilane (**3**) in tetrahydrofuran at a temperature lower than -78 °C for 2-4 h.[8)] (Eq. 1) No regioisomers, γ-halogen-substituted allylsilanes, can be found in the reaction mixture by thorough spectroscopic and chromatographic analyses. It is worth noting that sterically more hindered lithium dicyclohexylamide (LDCA) brings more satisfactory results rather than lithium diisopropylamide (LDA) as a proton-abstracting base.



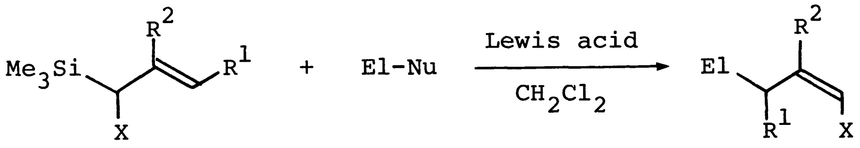
(1)

2, X = Cl, Br

3

1a; X = Cl, $R^1 = R^2 = H$
b; X = Br, $R^1 = R^2 = H$
c; X = Cl, $R^1 = H$, $R^2 = Me$
d; X = Cl, $R^1 = Me$, $R^2 = H$

Analogously to other substituted allylsilanes, **1** reacts with a variety of electrophiles activated by a Lewis acid very smoothly to afford the corresponding γ-haloallylation products regiospecifically in excellent yield,[9)] although **1** reveals rather low reactivity toward carbonyl compounds. (Eq. 2) The major



1 **5** **6** (2)

results of our findings are illustrated in Table 1.

One of the most notable features of the present allylation is the Z stereoselectivity in the formation of alkenyl halides (**6**), in addition to the well-known regiospecificity of the allyl transfer. For example 1-chloro-4-ethoxy-6-phenyl-1-hexene (**6b**) was obtained stereoselectively (Z/E = 90/10) in 92% yield by the reaction of (1-chloro-2-propenyl)trimethylsilane (**1a**) with 3-phenylpropanal diethylacetal (**5b**) promoted by titanium chloride. Similarly the corresponding α-bromine-substituted allylsilane (**1b**) gave the expected Z-alkenyl bromide (**6g**) predominantly in a highly stereoselective mode. (Z/E = 83/17, 83% yield) Thus this constitutes an unprecedented and expedient route to a variety of homoallyl alcohols, homoallyl ethers, β,γ-enones and δ,ε-enones containing Z-halide moiety, in contrast to E-selective allylations with α-alkyl- and aryl-substituted allylsilanes.10)

Although reactions of **1a** and **1b** with ketones and aldehydes are sluggish and result in an unsatisfactory yield of the corresponding homoallyl alcohols, **1c**, bearing a methyl group on the double bond, displays sufficiently high reactivity even toward these carbonyl compounds. It is apparent that diminished reactivities of **1a** and **1b** are due to the electron-withdrawing effect of chlorine and bromine atoms which lowers nucleophilicity of the double bond otherwise activated by effective σ(Si-C)-π conjugation in allyltrimethylsilane.11)

The origin of the interesting stereochemical outcomes in the allylation with **1** is still unclear and further studies are required before the mechanism of the reaction can be fully understood. However, from the mechanistic aspects, it is important to point out some trends: (1) the stereochemistry is almost independent upon the Lewis acid, (2) the Z selectivity is observed even for the conjugate allylation toward α,β-enones and (3) **1d** reveals the high diastereoselectivity12) together with overwhelming Z preference.

Irrespective of mechanistic possibilities, the results of the present study provide a synthetically useful method of introducing a halogen atom to a double bond in regio- and stereoselective modes. The synthetic utility of Z-vinyl halides, thus obtained, was demonstrated further by the stereospecific Grignard cross-coupling reaction13) and the transformation to terminal alkynes.

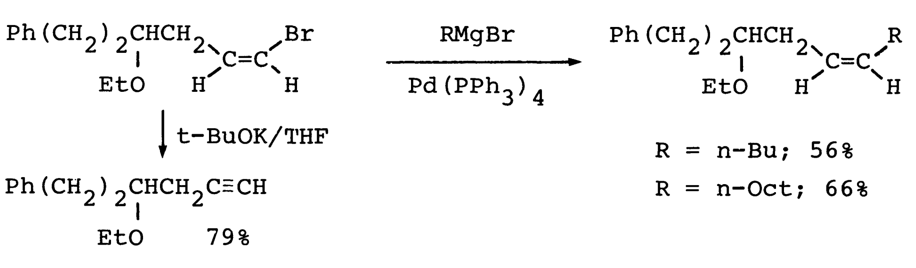


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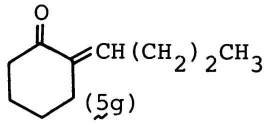
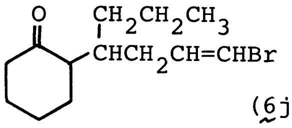
Table 1. Reactions of α-halogen-substituted allylsilanes with electrophiles[a]

Entry	Allylsilane (1)	Electrophile (5)	Conditions	Product[b]	% Yield (Z/E)[c]
1	$Me_3Si\underset{Cl}{C}HCH=CH_2$ (1a)	$PhCH(OMe)_2$ (5a)	$BF_3 \cdot OEt_2$ 0 °C-rt, 10 h	$Ph\underset{OMe}{C}HCH_2CH=CHCl$ (6a)	85 (85/15)
2	1a	$Ph(CH_2)_2CH(OEt)_2$ (5b)	$TiCl_4$ -78 °C, 2 h	$Ph(CH_2)_2\underset{OEt}{C}HCH_2CH=CHCl$ (6b)	92 (90/10)
3	1a	5b	$SnCl_4$ -78 °C, 2 h	6b	87 (88/12)
4	1a	5b	$AlCl_3$[d] -78 °C, 5 h	6b	88 (87/13)
5	1a	$Ph(CH_2)_3CH(OEt)_2$ (5c)	$TiCl_4$ -78 °C, 4 h	$Ph(CH_2)_3\underset{OEt}{C}HCH_2CH=CHCl$ (6c)	79 (91/ 9)
6	1a	$CH_3(CH_2)_4COCl$ (5d)	$TiCl_4$ -78 °C, 6 h	$CH_3(CH_2)_4COCH_2CH=CHCl$ (6d)	85 (74/26)
7	1a	$PhCH_2CH_2CHO$ (5e)	$TiCl_4$ -78--20 °C, 8 h	$PhCH_2CH_2\underset{OH}{C}HCH_2CH=CHCl$ (6e)	35 (77/23)
8	$Me_3Si\underset{Br}{C}HCH=CH_2$ (1b)	5a	$BF_3 \cdot OEt_2$ 0 °C-rt, 12 h	$Ph\underset{OMe}{C}HCH_2CH=CHBr$ (6f)	87 (79/21)
9	1b	5b	$TiCl_4$ -78 °C, 3 h	$Ph(CH_2)_2\underset{OEt}{C}HCH_2CH=CHBr$ (6g)	83 (83/17)
10	1b	5c	$TiCl_4$ -78 °C, 2 h	$Ph(CH_2)_3\underset{OEt}{C}HCH_2CH=CHBr$ (6h)	98 (71/29)
11	1b	$CH_3(CH_2)_3CH(OMe)_2$ (5f)	$TiCl_4$ -78 °C, 5 h	$CH_3(CH_2)_3\underset{OMe}{C}HCH_2CH=CHBr$ (6i)	77 (61/39)
12	1b	 (5g)	$TiCl_4$ -78 °C, 4 h	 (6j)	63[e]
13	$Me_3Si\underset{Cl}{C}H-\underset{CH_3}{C}=CH_2$ (1c)	5b	$TiCl_4$ -78 °C, 3 h	$Ph(CH_2)_2\underset{OEt}{C}HCH_2\underset{CH_3}{C}=CHCl$ (6k)	88[f]
14	1c	$CH_3(CH_2)_4CHO$ (5h)	$TiCl_4$ -78 °C, 3 h	$CH_3(CH_2)_4\underset{OH}{C}HCH_2\underset{CH_3}{C}=CHCl$ (6l)	69[f]
15	1c	$Ph(CH_2)_2CHO$ (5i)	$TiCl_4$ -78 °C, 3 h	$Ph(CH_2)_2\underset{OH}{C}HCH_2\underset{CH_3}{C}=CHCl$ (6m)	93[f]
16	$Me_3Si\underset{Cl}{C}HCH=CHCH_3$ (1d)	5a	$BF_3 \cdot OEt_2$ -78 °C, 3 h	$Ph\underset{MeO}{C}H\underset{CH_3}{C}HCH=CHCl$ (6n)	53[g]
17	1d	5b	$TiCl_4$ -78 °C, 3 h	$Ph(CH_2)_2\underset{EtO}{C}H\underset{CH_3}{C}HCH=CHCl$ (6o)	95[g]
18	1d	$CH_3(CH_2)_4CH(OMe)_2$ (5j)	$TiCl_4$ -78 °C, 2 h	$CH_3(CH_2)_4\underset{MeO}{C}H\underset{CH_3}{C}HCH=CHCl$ (6p)	92[g]

a) All reactions were conducted in CH_2Cl_2. b) Isolated by TLC. c) Determined by ^1H NMR. d) Two equivalents of $AlCl_3$ toward 1 were used. e) The Z selectivity was observed in 6j consisting of two diastereomers. f) Not determined. g) Almost one diastereomer with Z preference was confirmed by ^1H NMR.

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8) A representative procedure is as follows. A solution of LDCA, prepared from dicyclohexylamine (10.9 g, 0.06 mol) and n-BuLi in hexane (1.3 M, 40 ml, 0.052 mol) in THF (60 ml) at -78-0 °C, was slowly added to a mixture of allyl chloride (3.83 g, 0.05 mol) and Me$_3$SiCl (6.52 g, 0.06 mol) in THF (120 ml) at -78 °C. After stirring for 2 h, the mixture was hydrolysed with aqueous NH$_4$Cl. After usual work-up, **1a** (4.88 g, 0.033 mol) was isolated by distillation in 66% yield. Bp 67.5-68.0 °C (90 mmHg); ^{1}H NMR (CCl$_4$) δ 0.20 (s, 9H), 3.87 (d, J = 7.5 Hz, 1H), 5.00-5.37 (dd, J = 10.5, 14.0 Hz, 2H), 5.80-6.16 (ddd, J = 7.5, 10.5, 15.0 Hz, 1H); ^{13}C NMR (CDCl$_3$) δ -3.92 (q), 52.09 (d), 114.10 (t), 135.78 (d); MS (m/e) 148 (M$^+$, 1), 113 (0.3), 73 (100). **1b**: 55%; bp 74 °C (64 mmHg). **1c**: 40%; bp 77 °C (45 mmHg). **1d** (Z/E = 15/85) : 32%; bp 76 °C (58 mmHg). All new compounds obtained in this work gave satisfactory spectral data and elemental analysis.

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