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Homologation Reaction of γ-Silicon Substituted Allylic Alcohols Using Organoaluminium Reagents and Diiodomethane

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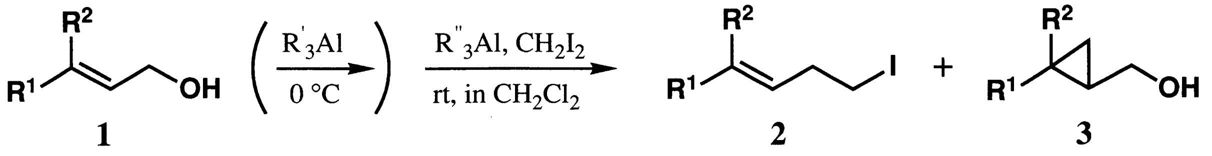
One carbon homologation reaction of γ-silicon substituted allylic alcohols was found to proceed by the treatment with triethylaluminium followed by diethylaluminium chloride and diiodomethane to afford homoallylic iodides instead of the corresponding cyclopropanes. Silicon function introduced to γ-position was crucial for the homologation reaction.

Iodomethyl metallic reagents have been used in organic chemistry primarily as cyclopropanating reagents. For example, the reagents prepared from zinc or diethylzinc,1) trialkylaluminium,2) and samarium or samarium diiodide3) have been widely known as convenient reagents for the transformation of olefins into cyclopropanes. Especially, cyclopropanation using iodomethyl zinc and samarium reagents was much prompted in the reaction with allylic alcohols.1a,3a) To the contrary, iodomethyl aluminium reagent was less reactive to allylic alcohols.2) In this paper, we report the homologation reaction of γ-silicon substituted allylic alcohols with iodomethyl aluminium reagent, derived from diiodomethane and organoaluminium reagent, to give the corresponding homoallylic iodides selectively instead of cyclopropanes.4,5)

The reaction of (*E*)-3-(dimethylphenylsilyl)-2-propen-1-ol (**1a**) with 3 equiv. of trimethylaluminium and 3 equiv. of diiodomethane in CH_2Cl_2 at room temperature was found to give not only the corresponding cyclopropane **3a** but also one carbon homologated homoallylic iodide **2a** in 50% and 24% yields, respectively.6−8) At the first stage of this reaction, dimethylaluminium alkoxide of **1a** was presumed to be generated from trimethylaluminium and the allylic alcohol **1a**. Then, iodomethyl aluminium reagent derived from trimethylaluminium and diiodomethane, might attack a carbon adjacent to oxygen in the alkoxide, instead of acting as carbenoid to olefin moiety, to afford the homoallylic iodide **2a**. In order to obtain the homoallylic iodide selectively, the reactions using various organoaluminium reagents were examined and the



a: R^1 = $PhMe_2Si$ R^2 = H
b: R^1 = $^tBuPh_2Si$ R^2 = H
c: R^1 = Ph_3Si R^2 = H
d: R^1 = $^tBuPh_2Si$ R^2 = Me
e: R^1 = H R^2 = $^tBuPh_2Si$
f: R^1 = Me R^2 = $^tBuPh_2Si$

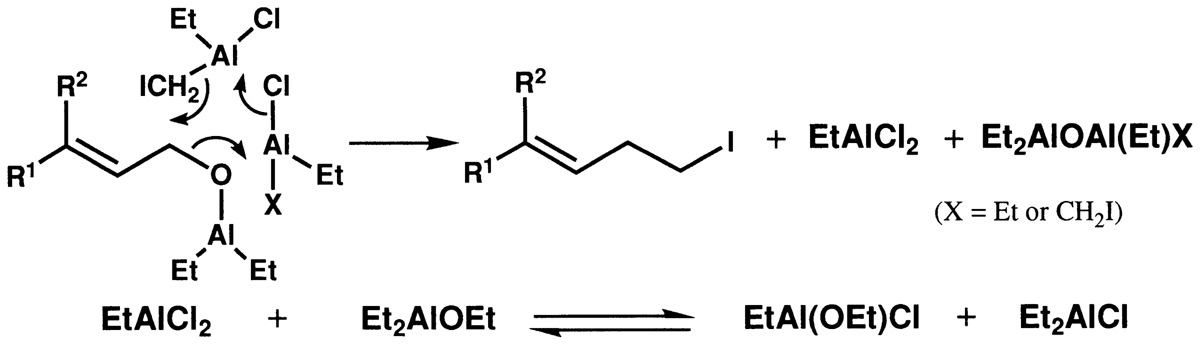
Table 1. Reaction of γ-Silicon Substituted Allylic Alcohols **1** with Organoaluminium Reagents and Diiodomethane

Entry	R^1	R^2	**1**	R'_3Al	R''_3Al	Additive[a)]	Time	Yield of **2**/%	Yield of **3**/%	Recovery of **1**/%
1[b)]	$PhMe_2Si$	H	**a**	---	Me_3Al	---	15 h	24	50	0
2[b)]				---	Et_3Al	---	12 h	35	31	10
3[b)]				---	Me_2AlCl	---	17 h	<1	0	78
4[b)]				---	Et_2AlCl	---	16 h	32	0	22
5[b)]				---	$EtAlCl_2$	---	1 h	0	0	0
6[c)]				Et_3Al	Et_2AlCl	---	16 h	43	5	9
7[c)]				Et_3Al	Et_2AlCl	Et_2AlOEt	2 d	63	8	8
8[c)]	$^tBuPh_2Si$	H	**b**	Et_3Al	Et_2AlCl	Et_2AlOEt	6 d	71	8	6
9[c)]	Ph_3Si	H	**c**	Et_3Al	Et_2AlCl	---	29 h	37	8	10
10[c)]	$^tBuPh_2Si$	Me	**d**	Et_3Al	Et_2AlCl	Et_2AlOEt	5 d	74	2	7
11[c)]	H	$^tBuPh_2Si$	**e**	Et_3Al	Et_2AlCl	Et_2AlOEt	37 h	6[d)]	<1	<1
12[c)]	Me	$^tBuPh_2Si$	**f**	Et_3Al	Et_2AlCl	Et_2AlOEt	4 d	58[e)]	13	6

a) 1 equiv. of additive was used. b) The ratio of **1** : R''_3Al : CH_2I_2 was 1 : 3 : 3. c) The ratio of **1** : R'_3Al : R''_3Al : CH_2I_2 was 1 : 1 : 2 : 3. d) The product was (*E*)-homoallylic iodide **2b**. e) The ratio of *Z* : *E* was 95 : 5.

results were summarized in Table 1. The reaction with triethylaluminium also gave considerable amount of cyclopropane (Entry 2). Although dimethylaluminium chloride was not effective for the homologation reaction (Entry 3), diethylaluminium chloride was found to be a reagent of choice to furnish homoallylic iodide quite selectively (Entry 4). By the use of ethylaluminium dichloride, allylic alcohol **1a** was immediately decomposed (Entry 5). When the reaction utilizing diethylaluminium chloride was continued for prolonged time to complete the homologation reaction, however, it was disappointing that the starting allylic alcohol **1a** and the produced homoallylic iodide **2a** were decomposed and the reaction only gave complicated mixture. In order to suppress the decomposition process, several reaction conditions were examined. It was revealed that diethylaluminium alkoxide prepared *in situ* from allylic alcohol and triethylaluminium prior to the homologation reaction could retard decomposition process though small amount of cyclopropane was yielded (Entry 6). Furthermore in the presence of other additional aluminium ethoxide, homoallylic iodide was obtained in enhanced yield in spite of prolonged reaction time (Entry 7). In this homologation reaction, the reason for the decomposition was at present not ascertained. One possible cause was that the some acidic species generated during the homologation reaction such as ethylaluminium dichloride decomposed the substrates. The acceptable role of aluminium ethoxide was that as a base for such acidic species decomposing the substrates (Scheme 1).

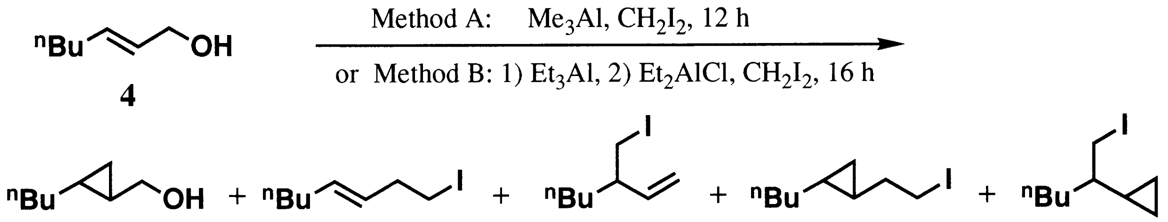
The influence of the silyl groups was subsequently investigated. Homologation reaction was much affected by the kind of silyl groups, *i.e.*, when the number of phenyl groups in silicon function was increased, the reaction rate was slower. (*E*)-3-(Triphenylsilyl)-2-propen-1-ol (**1c**) reacted very slowly even without



Scheme 1.

addition of aluminium ethoxide (Entry 9). Utilizing (*E*)-(*t*-butyldiphenylsilyl)-2-propen-1-ol (**1b**) as a substrate, the higher yield of homoallylic iodide **2b** was achieved (Entry 8). Homologation reaction of several other γ-silicon functionalized allylic alcohols was next examined. The reaction of (*E*)-3-(*t*-butyldiphenylsilyl)-2-buten-1-ol (**1d**) also proceeded to afford homoallylic iodide **2d** in good yield with little amount of cyclopropane (Entry 10). To the contrary, the reaction of (*Z*)-3-(*t*-butyldiphenylsilyl)-2-propen-1-ol (**1e**) gave isomerized (*E*)-homoallylic iodide **2b** in only 6% yield (Entry 11). Further (*Z*)-γ-silicon substituted butenol derivative **1f** still gave (*Z*)-homoallylic iodide **2f** containing small amount of (*E*)-isomer **2d** (Entry 12).

Instead of silicon functionalized allylic alcohols, (*E*)-2-hepten-1-ol (**4**) was submitted to the homologation reaction. The reaction with trimethylaluminium and diiodomethane (Method A) gave only a trace amount of homoallylic iodide, and cyclopropane **5** was mainly obtained and 21 % of unreacted **4** was recovered. On the other hand, the revised conditions *via* prior formation of aluminum alkoxide by triethylaluminium (Method B), made it possible to obtain homoallylic iodide **6** as a main product accompanied by regioisomer **7**[9)] and further cyclopropanated products **8**, **9**.



	5	**6**	**7**	**8**	**9**
Method A:	22%	<1%	0%	0%	0%
Method B:	19%	43%	4%	5%	1%

From these experiments described above, the role of silicon function introduced to γ-position of allylic alcohols was suggested to be 1) suppression of the over cyclopropanation of the produced homoallylic iodides,[10)] and 2) promotion of the substitution at the α-position of allylic alcohols. The latter was considered to be attributed to γ-silicon effect,[11)] which is known to accelerate the substitution reaction by γ-silyl group and to be much effective through "*W*" conformation for the Si-C-C-C-X (X; leaving group) backbone. The difference of the reactivity between (*E*)-silicon substituted allylic alcohols, which could shape "*W*" conformation, and (*Z*)-isomers might be also elucidated by γ-silicon effect.

The representative procedure for the homologation reaction of **1b**: To a CH_2Cl_2 (5 ml) solution of (*E*)-3-(*t*-butyldiphenylsilyl)-2-propen-1-ol (155 mg, 0.52 mmol) was added triethylaluminium (0.52 ml in hexane, 0.52 mmol) at 0 °C under nitrogen atmosphere. After 10 min, diethylaluminium ethoxide (0.57 ml in hexane, 0.52 mmol) was added and the solution was stirred for 5 min. Then, diethylaluminium chloride (1.07 ml in hexane, 1.05 mmol) was added, followed by the addition of a CH_2Cl_2 (2 ml) solution of diiodomethane (433 mg, 1.62 mmol) after 10 min. The reaction mixture was stirred for 6 days at room temperature and quenched by the addition of sat. aq $NaHCO_3$ (0.45 ml). The resulting precipitate was filtered off and the filtrate was condensed under the reduced pressure. The residue was separated by TLC on silica gel to give (*E*)-1-(*t*-butyldiphenylsilyl)-4-iodo-1-butene (157 mg, 71%) and *trans*-1-(*t*-butyldiphenylsilyl)-2-(hydroxylmethyl)-cyclopropane and unreacted allylic alcohol **1b** (8% and 6%, respectively).

In summary, unprecedented selective iodomethyl homologation reaction of allylic alcohols was achieved utilizing organoaluminium reagents and diiodomethane. The study of the scope of this unique reaction is currently underway in our laboratories.

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