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CHIRAL ORGANOSILICON COMPOUNDS IN ORGANIC SYNTHESIS II.

ENANTIOSELECTIVE SYNTHESIS OF HOMOALLYLIC ALCOHOLS[1]

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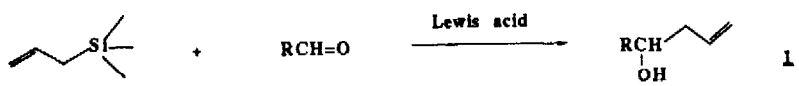
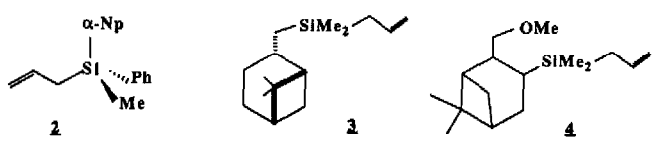
Summary: Condensations of 7a–c with aldehydes under Lewis acid conditions give optically active homoallylic alcohols with enantiomeric excess of up to 50%. The results are discussed in terms of competition between antiperiplanar and synclinal transition states.

In view of the usefulness of organosilicon compounds in organic synthesis, it is not surprising that considerable attention has recently been focussed on the use of chiral organosilicon compounds for asymmetric induction[1-9]. However, the stereoselectivity obtained thus far has been modest at best.

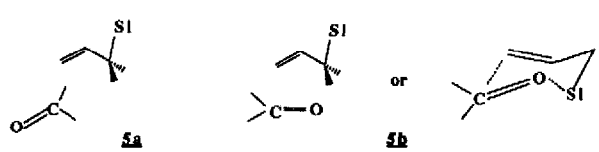


1

The synthetic utility of reaction of allylsilanes with aldehydes to give homoallylic alcohols 1, first reported by Hosomi and Sakmai[10], would be much enhanced if the reaction can be induced to give chiral alcohols with high enantioselectivity. In 1983, Hathaway and Paquette[4] examined the reaction of optically active α–naphthylphenylmethylallylsilane (2) with aldehydes and acetals and failed to observe significant chirality transfer (~ 5% ee). Recently, we used chiral allylsilane 3 derived from (–)–β–pinene and found modest enantioselectivity in the homoallylic alcohols formed (up to 15% ee)[11]. Somewhat better stereoselectivity (up to 46% ee) was found by Taddei et al using the chiral allylsilane 4, however the chemical yield of the homoallylic alcohols was low[7]. The modest stereoselectivity obtained in these reactions is not totally unexpected if one



2 3 4



5a 5b

considers the mechanism generally accepted for the reactions of allylsilanes with carbonyl compounds. From the work of Kumada[12] and Fleming[13], it has been concluded that the reaction proceeds through an antiperiplanar transition state 5a. That being the case, it would not be surprising that any chiral auxiliary, either at silicon or attached to silicon, would have little influence on the stereochemical outcome of the reaction. On the other hand, the work of Denmark[14] suggests that the synclinal transition state 5b may also be operative under certain conditions. It is possible that in 5b, the silyl group may have a greater effect on the stereochemical outcome of the reaction. An approach to favour the synclinal transition state 5b is to have on the silyl moiety ligands which can coordinate with the Lewis acid. We therefore examine the reactions of a number of chiral aminomethylsilanes 7.

A series of pyrrolidinylmethylallylsilanes 7 were prepared from allyldimethylbromomethylsilane (6)[15] and various (S)–pyrrolidines (8) by heating at 80°C between 5 – 20 hrs according to Scheme 1. In the reaction of 6 with (S)–2–hydroxymethylpyrrolidine (8e), alkylation occurred selectively at nitrogen. The product 7e was further transformed to the carbamate 7b by reaction with phenylisocyanate. The reactions of 7a–c with aldehydes were then examined and the results are summarized in Table 1.[16] The following observations can be made. The first is that the ee of the homoallylic alcohols 1 obtained is much improved (up to 50% ee) relative to those from 2 and 3. The chemical yield of the reaction is quite acceptable in giving cleanly the homoallylic alcohol products. The second observation is that the oxygen ligand in 7 (7a to 7c) is critical to the reaction since under identical reactions conditions, 7d failed to give significant amount of homoallylic alcohol (compare entries 3, 15 and 19 with 20). The third observation is that as the ratio of Lewis acid (e.g. $TiCl_4$) to aldehyde is increased from 1 to 10, the chemical yield of the product, within a fixed period of time, is increased, but the optical yield is decreased (see entries 1–4, 5–7). A ratio of $TiCl_4$ to aldehyde of 3:1 appears to give a reasonable balance between chemical and optical yields. These observations are consistent with the possibility that at lower Lewis acid concentrations, the Lewis acid coordinates with both the oxygen ligands in 7 and with the aldehyde, leading more to the synclinal transition state 5b as suggested by Denmark[14]. At higher Lewis acid concentrations, the antiperiplanar transition state 5a predominates with different molecules of Lewis acid coordinating separately to the aldehyde and to the oxygen ligand in 7. If this is the case, further structural modification on the silyl moiety to enhance the 5b pathway can be envisaged. We are continuing to explore such modifications.

Scheme 1

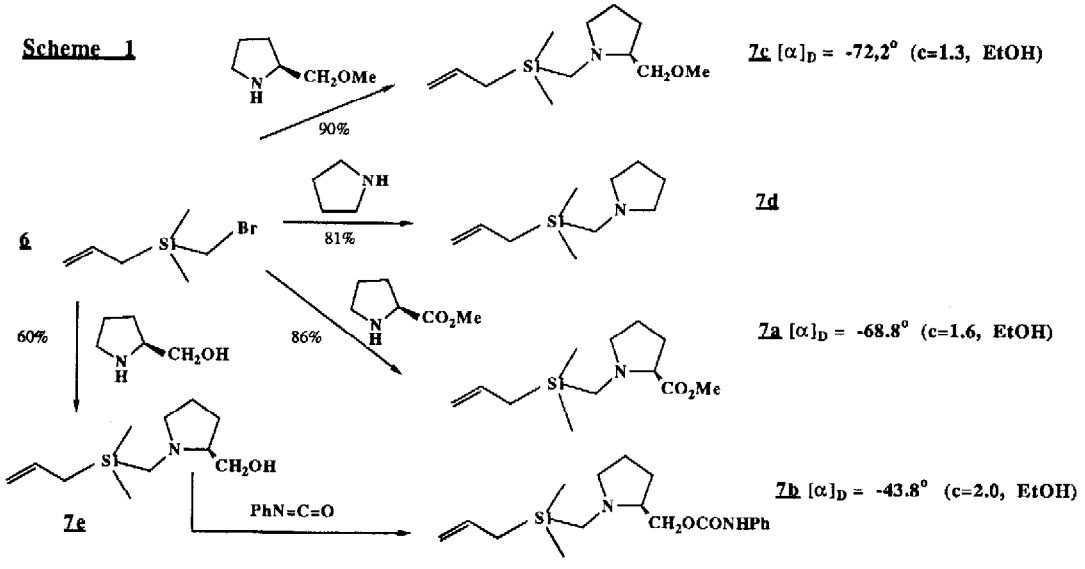
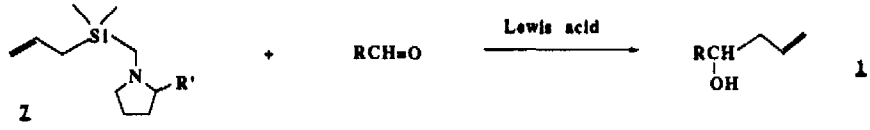


Table 1 Reaction of 7 with aldehydes under Lewis acid conditions



7 1

Entry	7	RCHO	Lewis Acid	Ratio L.A./RCHO	Reaction Conditions	Chemical Yield 1 (%)	Optical Yield of 1, % ee (Abs. Conf.)
1	R′=CO_2Me	n–$C_8H_{17}CHO$	$TiCl_4$	1:1	–50°C/20h	< 5	——
2	7a	"	$TiCl_4$	2:1	"	60	43 (S)
3	"	"	$TiCl_4$	3:1	"	61	43 (S)
4	"	"	$TiCl_4$	10:1	"	79	28 (S)
5	"	"	$TiCl_4$	3:1	–70°/30h	63	36 (S)
6	"	"	$TiCl_4$	5:1	–70°/30h	76	31 (S)
7	"	"	$TiCl_4$	10:1	–70°/30h	81	23 (S)
8	"	"	BF_3Et_2O	4:1	–50°/24h	58	30 (S)
9	"	"	BF_3Et_2O	10:1	–50°/3h	51	30 (S)
10	"	"	$SnCl_4$	3:1	–50°/20h	73	41 (S)
11	"	n–C_3H_7CHO	$TiCl_4$	2:1	–50°/20h	65	47 (S)
12	"	"	$SnCl_4$	2:1	–50°/20h	85	48 (S)
13	"	"	$SnCl_4$	3:1	–50°/20h	89	50 (S)
14	"	PhCHO	$TiCl_4$	2:1	–50°/22h	48	29 (S)
15	R′=CH_2–OCNHPh (O)	n–$C_8H_{17}CHO$	$TiCl_4$	3:1	–50°/25h	48	29 (S)
16	7b	"	$SnCl_4$	3:1	–50°/40h	< 5	——
17	"	n–C_3H_7CHO	$TiCl_4$	3:1	–50°/24h	36	48 (S)
18	"	"	$SnCl_4$	3:1	–50°/30h	< 5	——
19	R′=CH_2OMe 7c	n–$C_8H_{17}CHO$	$TiCl_4$	3:1	–50°/18h	70	37 (S)
20	R′=H 7d	n–$C_8H_{17}CHO$	$TiCl_4$	3:1	–50°/20h	< 5	——

References and Footnotes

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16. Typical procedure: To a solution of aldehyde (1.7 mmol) in CH_2Cl_2 (12 ml) at the temperature indicated was added dropwise a solution of Lewis acid in CH_2Cl_2 (5.5 ml) followed by stirring for 8 mins. A solution of 7 ~ (2.1 mmol) was added dropwise. The mixture was stirred for the indicated length of time and hydrolysed with saturated bicarbonate solution and warmed to room temperature. The mixture was extracted with ether and the organic layer was washed by brine, dried and evaporated. The residue was purified by flash chromatography to give the homoallylic alcohol 1. The enantiomeric excess of 1 was determined by optical rotation.

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