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New chiral allylaminosilanes and their use in asymmetric Sakurai reactions

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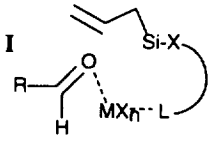
Abstract

The new allylaminosilanes **2a–c**, derived from chiral amines, react with benzaldehyde and pivalaldehyde in the presence of $SnCl_4$ to give homoallylic alcohols **4a–b** with enantiomeric excesses of up to 30%. © 1998 Elsevier Science Ltd. All rights reserved.

The addition of allylsilanes to carbonyl compounds under Lewis acid conditions, first described by Sakurai and Hosomi,[1] has been widely applied to the synthesis of homoallylic alcohols which are important building blocks in organic synthesis, and the possibility of using this reaction for asymmetric synthesis has attracted considerable attention. However, despite the substantial efforts devoted to stereochemical control, the level of stereoselectivity obtained to date is modest.[2] This fact has to be attributed to the generally accepted mechanism for these reactions, which usually proceed through open transition states with extended antiperiplanar character.[3] Attempts to improve the stereoselectivity have been reported by introducing ligands on the silyl moiety which are able to coordinate with the Lewis acid. Under these conditions, that favour[4] synclinal transition states **I**, enantiomeric excesses up to 50–56% have been obtained.[3,5]



Silafunctional compounds and in particular allylsilanes bearing a silicon–nitrogen bond have been so far subjected to a limited number of investigations[6] and their chiral counterparts are almost unprecedented.[7] We report herein the synthesis of a series of new chiral allylaminosilanes and our preliminary results using these compounds in the asymmetric version of the Sakurai reaction.

Allylaminosilanes were prepared by reaction of chiral amines[8] **1a–c** with allylchlorodimethylsilane as depicted in Scheme 1. The new chiral allylaminosilanes **2a–c** were isolated after distillation and proved to be indefinitely stable if kept under an inert atmosphere.[9]

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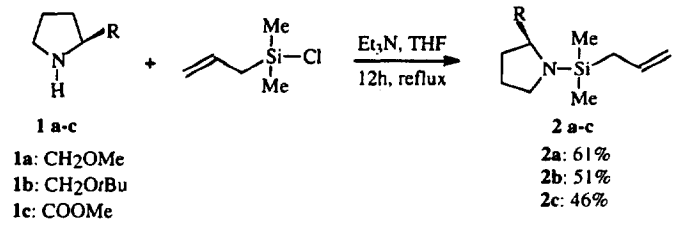
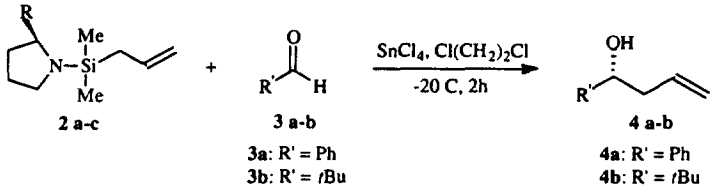


Scheme 1.

The allylsilanes modified by a homochiral pyrrolidine framework react with benzaldehyde **3a** and with pivalaldehyde **3b** in the presence of stoichiometric amounts of $SnCl_4$,[10] affording the expected homoallyl alcohols in satisfactory yields (Scheme 2, Table 1).



Scheme 2.

All the reactions were usually completed after 2–3 h at −20°C. By using allylaminosilane **2a**, homoallylic alcohols 1-phenyl-3-buten-1-ol **4a** and 2,2-dimethyl-5-hexen-3-ol **4b** were obtained (entries 1 and 2) with enantiomeric excesses up to 18% and 30%, respectively. They were found to possess the *R* configuration by means of polarimetric measurements.[11] From **2b**, **4a** and **4b** were formed in satisfactory yields but the presence of a *t*-butyl group in the side chain of the chiral moiety did not lead to efficient enantioselectivities (entries 3 and 4). As a possible explanation, the steric bulk of the *t*-butyl group on the chiral framework can prevent the coordination of the ethereal oxygen atom with the Lewis acid, thus favouring the antiperiplanar transition state versus the synclinal one. The introduction of better coordinating ligands onto the pyrrolidinylmethyl moiety (i.e. **2c**) did not increase the e.e. significantly (entries 5 and 6). Comparing these preliminary results, it is clear that the presence of a methoxy group enhances to some extent the stereoselectivity of the reaction.

An important feature of the reaction depicted in Scheme 1 is the easy removal and the recovery of the chiral auxiliary at the end of the reaction without racemization. Treatment of the water layer obtained in the reactions carried out with **2a**, after Kugelrohr distillation led to the starting chiral amine **1a** in 85% yield and with e.e.>98%.

In conclusion, we have prepared by a simple procedure new chiral allylaminosilanes. These silafunctional compounds react with aldehydes under Lewis acid conditions and show in the preliminary

Table 1
Reactions of allylaminosilanes **2a–c** with aldehydes **3a–b** in the presence of $SnCl_4$

Entry	Aminosilane	Aldehyde	Alcohol	Yield %[a)]	e.e.%
1	**2a**	**3a**	**4a**	65	18
2	**2a**	**3b**	**4b**	64	30
3	**2b**	**3a**	**4a**	56	1
4	**2b**	**3b**	**4b**	59	1
5	**2c**	**3a**	**4a**	55	11
6	**2c**	**3b**	**4b**	51	15

a) Isolated yields.

experiments enantiomeric excesses of up to 30%. Although the enantiomeric excess is not satisfactory at the present time, the results described herein suggest that these chiral silafunctional reagents based on a nitrogen–silicon bond might open a new field in asymmetric synthesis. Modifications of the chiral auxiliary in order to improve the enantiomeric excesses and further applications of these reagents are currently underway in our laboratory.

Acknowledgements

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8. Selected data for (*S*)-(+)-2-*t*-butoxymethyl pyrrolidine **1b**: b.p. 87–89°C/15 mmHg. $[\alpha]_D$=+5.5 (c=2.17, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$) δ=1.15 (s, 9H), 1.30–1.85 (m, 4H), 2.15 (s, 1H), 2.75–3.35 (m, 5H) ppm. MS (m/e): 157 (M^+), 100, 84, 70, 57. The (*S*)-(−)-2-(hydroxymethyl)-1-pyrrolidine carboxyaldehyde *t*-butyl ether, used for the synthesis of **1b**, has been obtained by adapting the procedure reported by Armstrong, A.; Brackenridge, I.; Jackson, R. F. W.; Kirk, J. M. *Tetrahedron Lett.* **1988**, *29*, 2483–2486. L-Proline methyl ester **1c** was purchased from Aldrich as chloridrate, and for this reason two equivalents of Et_3N (Scheme 1) were used. (*S*)-(+)-2-Methoxymethyl pyrrolidine **1a** has been prepared starting from L-proline according to Seebach, D.; Kalinowski, H. O. *Helv. Chim. Acta* **1977**, *60*, 300–325.
9. General procedure for the preparation of **2a**: To a solution of allylchlorodimethylsilane (7.15 mL, 49.2 mmol) in 12 mL of anhydrous THF was added triethylamine (7.53 mL, 54.12 mmol). After the addition of a solution of **1a** (5.66 g, 49.2 mmol) in 8 mL of THF, the mixture was refluxed for 12 h. After cooling to room temperature, the salts were filtered under an argon atmosphere and the solvent was removed by distillation at atmospheric pressure. Distillation under vacuum gave 6.42 g (61% yield) of 1-(allyldimethylsilanyl)-(*S*)-(+)-2-methoxymethyl pyrrolidine **2a** as a colourless oil. Selected spectroscopic data: 1-(allyldimethylsilanyl)-(*S*)-(+)-2-methoxymethyl pyrrolidine **2a**: b.p. 117–120°C/30 mmHg. $[\alpha]_D$=+2.4 (c=1, C_6H_6). ^1H NMR (200 MHz, C_6D_6/CCl_4) δ=0.05 (s, 6H), 1.45–1.70 (m, 6H), 2.85–3.50 (m, 5H), 3.15 (s, 3H), 4.75–4.90 (m, 2H), 5.65–5.90 (m, 1H) ppm. ^{13}C NMR (50.3 MHz, C_6D_6/CCl_4) δ=−1.85, 25.39, 26.06, 30.10, 47.25, 58.04, 58.98, 77.69, 113.35, 135.59 ppm. MS (m/e): 214 (M^+), 172, 168, 115, 99, 70, 59, 45. 1-(Allyldimethylsilanyl)-(*S*)-(+)-2-*t*-buthoxymethyl pyrrolidine **2b**: b.p. 93–96°C/15 mmHg. $[\alpha]_D$=+0.64 (c=3.1, C_6H_6). ^1H NMR (200 MHz, C_6D_6/CCl_4) δ=0.00 (s, 6H), 1.05 (s, 9H), 1.45–1.70 (m, 6H), 2.55–3.20 (m, 5H), 4.75–4.90 (m, 2H), 5.55–5.80 (m, 1H) ppm. ^{13}C NMR (50.3 MHz, C_6D_6/CCl_4) δ=0.94, 25.61, 27.36, 28.33, 28.54, 46.75, 59.43, 64.34, 73.00, 114.83, 134.94 ppm. 1-(Allyldimethylsilanyl)-pyrrolidine-(*S*)-(−)-2-carboxylic acid methyl ester (**2c**): b.p. 109–111°C/20 mmHg. $[\alpha]_D$=−56.3 (c=3.4, C_6H_6). ^1H NMR (200 MHz, C_6D_6/CCl_4) δ=0.20 (d, 6H), 1.65–2.10 (m, 6H), 3.10–3.30 (m, 2H), 3.65 (s, 3H), 3.95–4.05 (m, 1H), 4.90–5.05 (m, 2H), 5.75–6.00 (m, 1H) ppm. ^{13}C NMR (50.3 MHz, C_6D_6/CCl_4) δ=−2.72, −2.54, 24.76, 26.08, 31.69, 47.43, 51.19, 60.73, 113.31, 135.29, 175.81 ppm. MS (m/e): 227 (M^+), 212, 186, 168, 128, 99, 70, 59.
10. General procedure for the synthesis of **4a** and **4b**: To a solution of **3b** (258 mg, 3.0 mmol) in 5 mL of 1,2-dichloroethane at −30°C was added $SnCl_4$ (0.38 mL, 3.23 mmol) and after 15 min **2a** (639 mg, 3.0 mmol). When the aldehyde had been consumed (2 h) the mixture was poured into saturated $NaHCO_3$ and then extracted three times with diethyl ether. The organic layer was dried over anhydrous Na_2SO_4. The resulting crude material was purified by column chromatography using petroleum ether:diethyl ether (4:1) as eluent giving 245 mg (64%) of **4b** ($[\alpha]_D$=+2.8, c=10, C_6H_6).
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