924 © 1982 The Chemical Society of Japan Bull. Chem. Soc. Jpn., 55, 924—927 (1982) [Vol. 55, No. 3

The Configurations of Benzylmethyl(*o*- or *p*-tolyl)silylmethylamine and the Stereochemistry of the Reactions of Benzylmethylmethoxyphenylsilane with Some Organometallic Agents

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(Received September 9, 1981)

Optically active α-amino organosilanes such as benzylmethyl(*o*- or *p*-tolyl)silylmethylamine were converted into benzylmethylphenyl(*o*- or *p*-tolyl)silane, of which the configurations had been known. From these observations, it was found that (+)- and (−)-benzylmethyl(*o*- or *p*-tolyl)silylmethylamine has *S* and *R* configuration respectively. Furthermore, the stereochemistry of the reaction of benzylmethyl(methoxy)phenylsilane with some organometallic agents was investigated.

Previously, we reported on the successful optical resolutions of the α-amino organosilanes, *i.e.*, benzylmethylphenylsilylmethylamine(**1**), benzylmethyl(*o*-(**2**), *m*-(**3**), and *p*-tolyl(**4**))silylmethylamine, and on the determination of the configuration of **1**.[1] In this paper, we wish to report on the determination of the configurations of **2** and **4**, and on the stereochemistry of the nucleophilic substitutions of benzylmethylmethoxy(phenyl(**23**) and *p*-tolyl(**6**))silane by some organometallic agents.

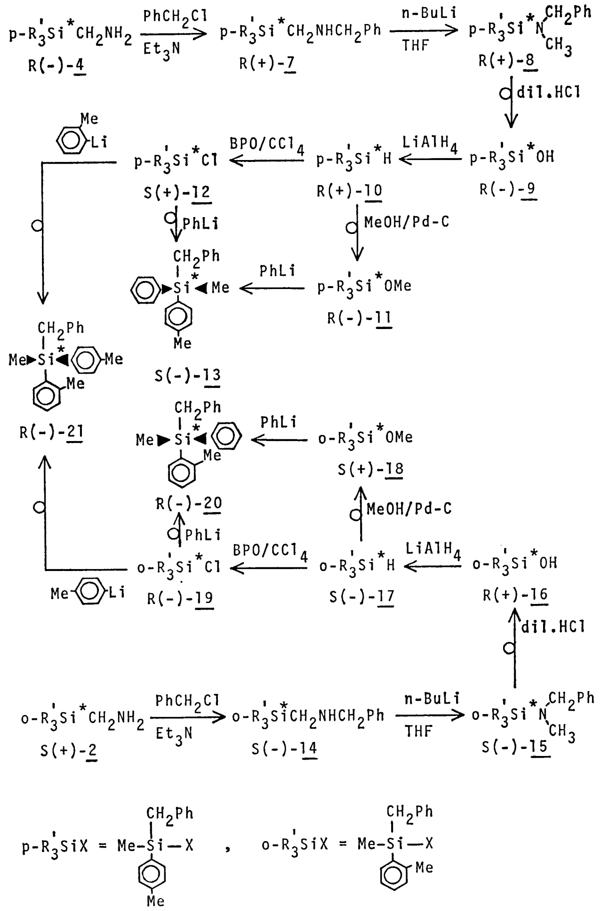
Results and Discussion

Chemical Conversions of 2 and 4. In order to determine the configuration of **4**, the chemical conversion of **4** into benzylmethylphenyl-*p*-tolylsilane, of which the absolute configuration was known, was undertaken, following the route described in our prior paper[1] (Scheme 1). Thus, (−)-**4**, which was obtained from the less soluble salt of **4** with (+)-tartaric acid by the fractional crystallization, was converted into (+)-benzylmethyl-*p*-tolylsilane(**10**). The treatment of **10** with methanol in the presence of Pd–C at 0 °C, and with a catalytic amount of BPO in CCl_4 at 80 °C gave (−)-benzylmethylmethoxy-*p*-tolylsilane (**11**) and (+)-benzyl(chloro)methyl-*p*-tolylsilane(**12**) respectively. Both reactions of (−)-**11** and (+)-**12** with phenyllithium in ether gave *S*(−)-benzylmethylphenyl-*p*-tolylsilane(**13**). In these chemical conversions, it is already known that the three of them, *i.e.*, the hydrolysis of **8**, the replacement of hydrogen by methoxyl radical, and the reaction of **12** with phenyllithium, proceed with inversion of the configurations, and the others proceed with retention of the configurations.[2]

On the other hand, *R*(−)-benzylmethylphenyl-*o*-tolylsilane(**20**) was obtained from (+)-**2** in the manner similar to that described above.

From these observations, it was noted that (−)-**4** and (+)-**2** had *R* and *S* configurations respectively. These configurations were furthermore confirmed by treating *S*(+)-**12** with *o*-tolyllithium, and *R*(−)-**19** with *p*-tolyllithium to give the product of the same sign of the optical rotation, *i.e.*, *R*(−)-benzylmethyl-*o*-tolyl-*p*-tolylsilane(**21**).

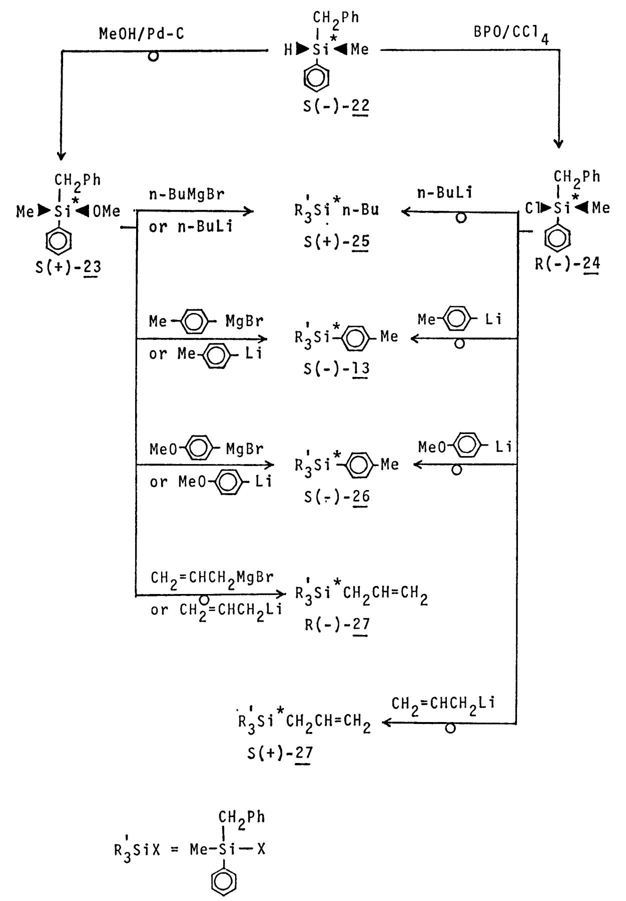
Reaction of the Methoxysilanes with Organometallic Agents. It is generally known that the stereochemistry of nucleophilic substitution at silicon is mainly controlled by the nature of leaving groups on silicon, and the electronic character of the nucleophiles.



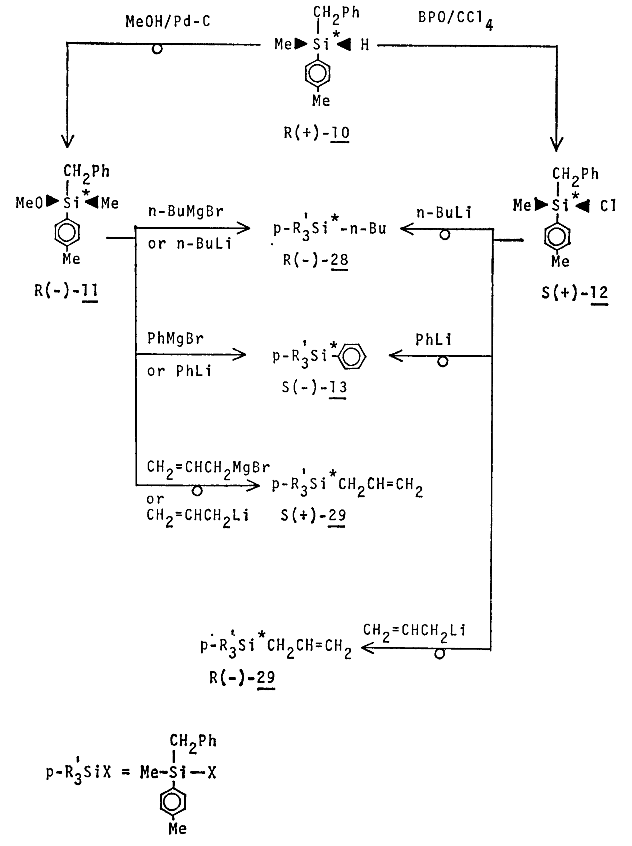
Scheme 1.

However, the stereochemistry of the reaction of methoxysilane with organometallic agents seems to be complex. There have been conflicting reports in the literature concerning the stereochemistry of the reaction of methoxysilanes: an inversion reaction of the configuration of benzylphenylmethylmethoxysilane with the aryl Grignard reagents such as mesityl-, and 1-naphthylmagnesium bromide,[3] and a retention reaction of the configuration of methylmethoxy(1-naphthyl)phenylsilane with allyllithium.[4]

On the other hand, we indicated previously that the stereochemical courses of the reaction of *S*(+)-**23** with the organolithium agents such as butyl-, *p*-methoxyphenyl-, and allyllithium, were in agreement with those for methylmethoxy(1-naphthyl)phenylsilane.[1]



Scheme 2.



Scheme 3.

Thus, the investigation of the reaction courses of $S(+)$-benzylphenylmethylmethoxysilane(**23**) with the Grignard reagents were carried out (Scheme 2).

The stereochemical courses of the reaction of $S(+)$-**23** with the Grignard reagents were also in accordance with those of organolithium agents, *i.e.*, the reaction of $S(+)$-**23** with the alkyl-, and arylmagnesium bromide proceed with a retention of the configuration, whereas that of $S(+)$-**23** with allylmagnesium bromide proceeds with an inversion of configuration.

Furthermore, the reactions of $R(-)$-**11** and S(+)-**12** with some organometallic agents were investigated (Scheme 3). It was noted that these results were in fair agreement with those of the benzylmethylphenylsilyl system.

Experimental

The boiling points are uncorrected. The IR spectra were determined with a JASCO IR-A2 spectrometer. The NMR spectra were determined at 60 MHz with a Varian A-60D spectrometer in CCl_4, using TMS as an internal standard. The optical rotations were measured with a JASCO DIP-181 polarimeter. All the reactions of the chlorosilanes and methoxysilanes with organometallic agents were carried out under a dry nitrogen atmosphere. Optically active (+)-**2**, (−)-**4**, and (−)-**22** were obtained in manners described in our report.[1]

*(+)-N-Benzylbenzylmethyl-p-tolylsilylmethylamine (**7**).* A solution of (−)-**4** (18.1 g, 0.071 mol) $[\alpha]_D$ −6.6° (c=3, Et_2O), benzyl chloride (9.0 g, 0.071 mol), and Et_3N (21.6 g, 0.213 mol) was stirred for 4 h at 110 °C. Water (30 ml) and hexane (100 ml) were added to the reaction mixture. The organic layer was separated, washed three times with 10% NaOH, and then dried (Na_2SO_4). Subsequent evaporation and distillation gave (+)-**7**. Bp 159—162 °C/0.1 Torr.** Yield 15.0 g (61%). $[\alpha]_D$ 0° (c=2, Et_2O). NMR δ 0.20 (s, 3, Si–CH_3), 1.0 (s, 1, NH), 2.22 (s, 2, $SiCH_2N$), 2.38 (s, 5, $SiCH_2Ph$, C–CH_3), 3.70 (s, 2, N–CH_2Ph), 6.8—7.5 (m, 14, aromatic protons). Found: N, 3.90%. Calcd for $C_{23}H_{27}NSi$: 4.05%.

*(+)-N-Benzyl-N-methylbenzylmethyl-p-tolylsilylamine (**8**).* To a solution of (+)-**7** (14.8 g, 0.043 mol) in THF (150 ml), was added n-BuLi (5 ml of 10% w/v hexane solution) by means of a syringe under nitrogen atmosphere. After stirring the solution for 10 h at room temperature, water was added to the solution at 0 °C. The organic layer was separated, washed with water, and then dried (K_2CO_3). Subsequent evaporation and distillation gave (+)-**8**. Bp 163—165 °C/0.16 Torr. Yield 14.4 g (97%). $[\alpha]_D$ +3.6° (c=2, Et_2O). NMR δ 0.29 (s, 3, Si–CH_2), 2.38 (s, 6, N–CH_3, C–CH_3), 2.47 (broad s, 2, Si–CH_2Ph), 3.85 (s, 2, N–CH_2Ph), 6.8—7.5 (m, 14, aromatic protons).

*(−)-Benzylmethyl-p-tolylsilanol (**9**).* A solution of (+)-**8** (14.3 g, 0.041 mol) $[\alpha]_D$ +3.6° (c=2, Et_2O), in ether (100 ml) was treated with 0.2 M HCl (150 ml)*** in a separating funnel at 0 °C. The organic layer was separated, washed two times with cold water, and then dried (K_2CO_3). Evaporation of the solvent gave (−)-**9**. It was used in the next reaction without further purification. $[\alpha]_D$ −9.7° (c=1, pentane). NMR δ 0.28 (s, 3, Si–CH_3), 2.1 (s, 1, OH), 2.30 (s, 2, $SiCH_2Ph$), 2.35 (s, 3, C–CH_3), 6.8—7.5 (m, 9, aromatic protons).

** 1 Torr ≈ 133.322 Pa.

*** 1 M = 1 mol dm^{-3}.

*(+)-Benzylmethyl-*p*-tolylsilane (**10**).* A solution of (−)-**9** (8.7 g) in dibutyl ether (100 ml) was added to a suspension of $\mathrm{LiAlH_4}$ (4.7 g, 0.125 mol) in ether (110 ml). The mixture had been kept at 90 °C for 30 min, and then the ether was removed. The mixture was stirred for additional 3 h at 140—145 °C. The usual workup of the mixture gave (+)-**10**. Bp 106—107 °C/1.0 Torr. Yield 6.0 g (74%). $[\alpha]_D$ +11.1° (c=2, pentane). NMR δ 0.25 (d, J=3.5 Hz, 3, Si-$\mathrm{CH_3}$), 2.33 (s, 5, Si$\mathrm{CH_2}$–, C$\mathrm{CH_3}$), 4.45 (q, J=3.5 Hz, 1, Si-H), 6.8—7.5 (m, 9, aromatic protons).

*(−)-Benzylmethylmethoxy-*p*-tolylsilane (**11**).* Methanol (1.6 g, 0.048 mol) was added slowly to the mixture of (+)-**10** (5.8 g, 0.025 mol) $[\alpha]_D$ +11.1° (c=2, pentane), and 5% Pd/C (0.47 g) in pentane at 0 °C. After evolution of hydrogen ceased, the catalyst was removed off by filtration. Subsequent evaporation and distillation gave (−)-**11**. Bp 123 °C/1.0 Torr. Yield 5.8 g (90%). $[\alpha]_D$ −2.6° (c=2, pentane). NMR δ 0.23 (s, 3, Si-$\mathrm{CH_3}$), 2.31 (s, 5, Si-$\mathrm{CH_2}$Ph, C-$\mathrm{CH_3}$), 6.8—7.5 (m, 9, aromatic protons).

*(+)-Benzyl(chloro)methyl-*p*-tolylsilane (**12**).* A solution of (+)-**10** (1.0 g, 4.4 mmol) and BPO (78 mg, 0.23 mmol) in $\mathrm{CCl_4}$ (4 ml) was sealed in a sample tube under nitrogen atmosphere. The tube was then maintained for 11 h at 80 °C. The subsequent evaporation gave (+)-**12**. The chlorosilane (+)-**12** was extreamly moisture-sensitive, and extensive racemization of (+)-**12** was observed in the presence of a trace of $\mathrm{H_2O}$. The product was used without further purification. $[\alpha]_D$ +5.2° (c=1.3, $\mathrm{CCl_4}$). NMR δ 0.55 (s, 3, Si-$\mathrm{CH_3}$), 2.36 (s, 3, C-$\mathrm{CH_3}$), 2.54 (s, 2, Si$\mathrm{CH_2}$Ph), 6.8—7.5 (m, 9, aromatic protons).

*Preparation of the Series of the Benzylmethyl-*o*-tolylsilyl Systems, (−)-**14**—(−)-**19**.* In manners similar to that described above, the series of benzylmethyl-*o*-tolylsilyl systems *i.e.*, (−)-**14**, (−)-**15**, (+)-**16**, (−)-**17**, (+)-**18**, and (−)-**19** were obtained from (+)-**2** (22.8 g, 0.089 mol) $[\alpha]_D$ +5.1° (c=2, $\mathrm{Et_2O}$).

*(−)-**14***: Yield 22.8 g (74%). Bp 175—180 °C/0.3 Torr. $[\alpha]_D$ −7.9° (c=2, $\mathrm{Et_2O}$). NMR δ 0.29 (s, 3, Si-$\mathrm{CH_3}$), 0.9 (s, 1, NH), 2.28 (s, 2, Si$\mathrm{CH_2}$N), 2.34 (s, 3, C-$\mathrm{CH_3}$), 2.38 (s, 2, Si$\mathrm{CH_2}$Ph), 3.68 (s, 2, N$\mathrm{CH_2}$Ph), 6.5—7.5 (m, 14, aromatic protons). Found: N, 4.10%. Calcd for $\mathrm{C_{23}H_{27}NSi}$: N, 4.05%.

*(−)-**15***: $[\alpha]_D$ −9.4° (c=2, $\mathrm{Et_2O}$). NMR δ 0.32 (s, 3, Si-$\mathrm{CH_3}$), 2.36 (s, 6, N-$\mathrm{CH_3}$, C-$\mathrm{CH_3}$), 3.90 (s, 2, Si$\mathrm{CH_2}$Ph), 6.7—7.5 (m, 14, aromatic protons).

*(+)-**16***: $[\alpha]_D$ +8.2° (c=1.2, pentane). NMR δ 0.33 (s, 3, Si-$\mathrm{CH_3}$), 1.7 (broad s, 1, OH), 2.38 (s, 2, Si$\mathrm{CH_2}$Ph), 2.43 (s, 3, C-$\mathrm{CH_3}$), 6.6—7.5 (m, 9, aromatic protons).

*(−)-**17***: Yield 8.5 g (57% from (−)-**14** employed). Bp 114 °C/1.5 Torr. $[\alpha]_D$ −16.8° (c=2.2, pentane). NMR δ 0.29 (d, J=3.5 Hz, 3, Si-$\mathrm{CH_3}$), 2.35 (s, 5, Si$\mathrm{CH_2}$–, C-$\mathrm{CH_3}$), 4.55 (q, J=3.5 Hz, 1, SiH), 6.8—7.5 (m, 9, aromatic protons).

*(+)-**18***: Bp 130 °C/1.5 Torr. $[\alpha]_D$ +5.3° (c=2, pen tane). NMR δ 0.30 (s, 3, Si-$\mathrm{CH_3}$), 2.39 (s, 5, Si$\mathrm{CH_2}$Ph, C-$\mathrm{CH_3}$), 3.40 (s, 3, O-$\mathrm{CH_3}$), 6.8—7.6 (m, 9, aromatic protons).

*(−)-**19***: $[\alpha]_D$ −14.5° (c=1.3, $\mathrm{CCl_4}$). NMR δ 0.65 (s, 3, Si-$\mathrm{CH_3}$), 2.25 (s, 3, C-$\mathrm{CH_3}$), 2.60 (s, 2, Si$\mathrm{CH_2}$Ph), 6.8—7.5 (m, 9, aromatic protons).

*(−)-Benzylmethylphenyl-*p*-tolylsilane (**13**).*[1] To a solution of PhLi (*ca.* 12 mmol) in ether (10 ml) was added a solution of (−)-**11** (1.0 g, 3.9 mmol) $[\alpha]_D$ −2.6° (c=2, pentane), in THF (10 ml) at 0 °C by means of a syringe. The mixture was refluxed for 2 h with stirring. The usual workup of the reaction mixture gave (−)-**13** in a 36% (0.43 g) yield. Bp 160 °C/0.2 Torr. $[\alpha]_D$ −1.9° (c=8.7, $\mathrm{CH_2Cl_2}$).

In a manner similar to that described above, the reaction of (−)-**11**, $[\alpha]_D$ −2.6° (c=2, pentane) with PhMgBr gave (−)-**13** in 20% yield. $[\alpha]_D$ −1.7° (c=4.6, $\mathrm{CH_2Cl_2}$). The reaction of (+)-**12**, $[\alpha]_D$ +5.2° (c=1.3, $\mathrm{CCl_4}$) with PhLi gave (−)-**13** in 80% (0.91 g) yield. $[\alpha]_D$ −2.6° (c=8.7, $\mathrm{CH_2Cl_2}$).

*(−)-Benzylmethylphenyl-*o*-tolylsilane (**20**).*[1] In manners similar to that described above, reaction of (+)-**18** with PhLi and PhMgBr, and of (−)-**19** with PhLi was carried out. The reaction of (+)-**18**, $[\alpha]_D$ +5.3° (c=2, pentane) with PhLi gave (−)-**20** in a 52% yield. $[\alpha]_D$ −7.0° (c=2, $\mathrm{CH_2Cl_2}$). The reaction of (+)-**18** $[\alpha]_D$ +5.3° (c=2, pentane) with PhMgBr gave (−)-**20** in a 30% yield. $[\alpha]_D$ −5.2° (c=2, $\mathrm{CH_2Cl_2}$). The reaction of (−)-**19**, prepared from (−)-**17** $[\alpha]_D$ −16.8° (c=2.2, pentane), with PhLi gave (−)-**20** in a 60% yield. $[\alpha]_D$ −12.1° (c=7, $\mathrm{CH_2Cl_2}$).

*(−)-Benzylmethyl-*o*-tolyl-*p*-tolylsilane (**21**).* To a solution of (−)-**19**, prepared from (−)-**17** (1 g, 4.4 mmol) $[\alpha]_D$ −16.8° (c=2, pentane) in $\mathrm{Et_2O}$ (10 ml), was added a solution of two fold excess of *p*-tolyllithium by means of a syringe at 0 °C. The mixture was stirred for 1 h at room temperature, and then refluxed for additional 1 h with stirring. The usual workup of the mixture gave (−)-**21** in a 60% (0.84 g) yield. $[\alpha]_D$ −14.5° (c=5.5, $\mathrm{CH_2Cl_2}$). NMR δ 0.41 (s, 3, Si-$\mathrm{CH_3}$), 2.19 (s, 3, *o*-$\mathrm{CH_3}$), 2.32 (s, 3, *p*-$\mathrm{CH_3}$), 2.63 (s, 2, Si$\mathrm{CH_2}$Ph), 6.6—7.5 (m, 13, aromatic protons).

In a manner silmilar to that described above, (−)-**21** was obtained from (+)-**10** $[\alpha]_D$ +11.1° (c=2, pentane) in a 51% yield. $[\alpha]_D$ −5.5° (c=3, $\mathrm{CH_2Cl_2}$).

*(+)-Benzylbutylmethylphenylsilane (**25**).*[1] (+)-**23** (1 g, 4.1 mmol) $[\alpha]_D$ +3.5° (c=2, pentane) in $\mathrm{Et_2O}$ (10 ml) was added to a large excess amount of n-BuMgBr in $\mathrm{Et_2O}$. The mixture was refluxed for 90 h with stirring. The usual workup of the mixture gave (+)-**25** in an 83% (0.92 g) yield. $[\alpha]_D$ +3.5° (c=10, $\mathrm{CH_2Cl_2}$).

*(−)-Benzyl(*p*-methoxyphenyl)methylphenylsilane (**26**).*[1] To a solution of (+)-**23** (1 g, 4.1 mmol) $[\alpha]_D$ +3.5° (c=2, pentane) in $\mathrm{Et_2O}$ (10 ml) was added a large excess amount of *p*-methoxyphenylmagnesium bromide in $\mathrm{Et_2O}$. The mixture was refluxed for 80 h with strring. The usual workup of the mixture gave (−)-**26** in a 31% (0.41 g) yield. $[\alpha]_D$ −6.6° (c=4, $\mathrm{CH_2Cl_2}$).

*(−)-Allylbenzylmethylphenylsilane (**27**).*[1] To a solution of (+)-**23** (1 g, 4.1 mmol) $[\alpha]_D$ +3.5° (c=2, pentane) in $\mathrm{Et_2O}$ (10 ml), was added a solution of allylmagnesium bromide (*ca.* 6.9 mmol) in $\mathrm{Et_2O}$. The mixture was refluxed for 50 h with stirring. The usual workup of the mixture gave (−)-**27** in a 71% (0.74 g) yield. $[\alpha]_D$ −0.42° (c=12.3, $\mathrm{CH_2Cl_2}$).

*(−)-Benzylbutylmethyl-*p*-tolylsilane (**28**).* To a solution of (−)-**11** (1 g, 3.9 mmol) $[\alpha]_D$ −2.6° (c=2, pentane) in $\mathrm{Et_2O}$ (20 ml) was added 4 ml of a 10% w/v solution of n-BuLi by means of a syringe at 0 °C. After stirring for 1 h at 0 °C, the mixture was hydrolyzed. The usual workup of the mixture gave (−)-**28**. Yield 59% (0.65 g). $[\alpha]_D$ −3.3° (c=11, $\mathrm{CH_2Cl_2}$). NMR δ 0.19 (s, 3, Si$\mathrm{CH_3}$), 0.5—1.5 (m, 9, n-Bu), 2.28 (s, 2, Si$\mathrm{CH_2}$Ph), 2.34 (s, 3, C$\mathrm{CH_3}$), 6.7—7.4 (m, 9, aromatic protons).

In a manner similar to that described above, the treatment of (−)-**11** with butylmagnesium bromide gave (−)-**28** $[\alpha]_D$ −0.96° (c=14, $\mathrm{CH_2Cl_2}$) in a 73% yield. The reaction of (+)-**12** $[\alpha]_D$ +3.2° (c=1.3, $\mathrm{CCl_4}$), prepared from (+)-**10** (1.0 g, 4.4 mmol) $[\alpha]_D$ +6.8° (c=2, pentane) with n-BuLi gave (−)-**28** $[\alpha]_D$ −0.72 (c=10, $\mathrm{CH_2Cl_2}$) in a 56% (0.69 g) yield.

*(+)-, and (−)-Allylbenzylmethyl-*p*-tolylsilane (**29**).* To a solution of allyllithium (*ca.* 8 mmol) in $\mathrm{Et_2O}$ (70 ml) was added (−)-**11** (1.0 g, 3.9 mmol) $[\alpha]_D$ −2.6° (c=2, pentane)

in ether (10 ml) with stirring at 0 °C. After the mixture had been stirred for 2 h at 0 °C, the usual workup of the mixture gave (+)-**29** $[\alpha]_D$ +1.6° (c=3, CH_2Cl_2) in a 24% (0.25 g) yield. Bp 140 °C/0.2 Torr. NMR δ 0.20 (s, 3, $Si-CH_3$), 1.72 (d, J=8 Hz, 2, $Si-CH_2-C$), 2.29 (s, 2, $SiCH_2Ph$), 2.34 (s, 3, CCH_3), 4.6—5.0 (m, 2, $=CH_2$), 5.3—6.1 (m, 1, CH=C), 6.7—7.4 (m, 9, aromatic protons).

In a manner similar to that described above, the reaction of (−)-**11** (1.0 g, 3.9 mmol) with Allylmagnesium bromide gave (+)-**29** $[\alpha]_D$ +1.6° (c=6, CH_2Cl_2) in a 76% (0.79 g) yield. The reaction of (+)-**12**, prepared from (+)-**10** (1.0 g, 4.4 mmol) $[\alpha]_D$ +6.8° (c=2, pentane) with allyllithium in Et_2O (70 ml), gave (−)-**29** $[\alpha]_D$ −0.63° (c=4.7, CH_2Cl_2) in a 39% (0.28 g) yield.

The authors wish to thank the Shin-etsu Chemical Industry Co. for the gift of dichlorodimethylsilane.

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