Synthesis of novel silyl enol ethers from chlorodimethyl(naphthylphenylmethyl)silanes having a chiral centre and a ketone and their chirality transfer effects in crossed-aldol reactions

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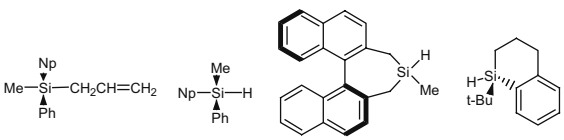
X-ray crystallography was used to determine the stereo structure of a novel chiral organosilicon compound, (2*R*)-(–)-(1-cyclohexenyloxy)dimethyl(1-naphthylphenylmethyl) silane, which has a chiral centre next to the silicon atom. The crossed-aldol reaction of the silyl enol ether with benzaldehyde gave the corresponding aldol products with high chirality transfer.

Keywords: chirality, asymmetric synthesis, stereoselective synthesis, aldol reactions, organometallic reagents

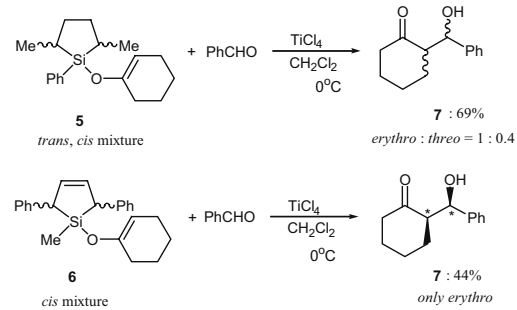
Previously, Hathaway and Paquette reported that the chirality transfer reaction of the chiral allyl silane, (1*S*)-(–)-allylmethyl(1-naphthyl)phenylsilane (**1**), with acetals showed rather low ee values. (3.9–5.5%).[1] Fry and co-workers[2] also demonstrated that the chirality transfer of alkyl aryl ketones using (1*S*)-(+)-methyl(1-naphthyl)phenylsilane (**2**) in hydride reduction resulted in 6.6–12.7%ee. In addition, Jung *et al*.[3] reported that the enantioselectivity of a crossed Mukaiyama-aldol reaction using (*S*)-binaphthylic cyclic silane **3** and 2-(hydroxyphenylmethyl)cyclohexanone showed relatively low ee values (*erythro*: 17%, *threo*: 35%).[4] Oestreich also reported enhanced chiral transfer with a silane compound **4** that had a chiral centre on the Si atom (71%ee).[5] Thus, reactions, that use chiral organosilicon compounds and result in greater asymmetric induction are highly desired.



1 **2** **3** **4**

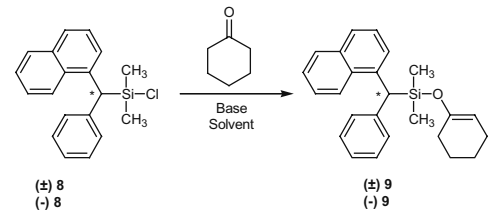
The significant result of these previous studies is that use of an organosilicon compound, the whole molecule of which is chiral, results in greater asymmetry than use of compounds with a chiral centre only at the Si atom. Hence, the purpose of the present study was to design a novel organosilicon compound with a chiral centre next to the Si atom and to investigate the asymmetric reaction using the novel organosilicon compound.

Previously, we developed two novel silyl enol ethers **5** and **6**, with a 2,5-dimethyl-1-phenyl-1-silacyclopentane[6] unit and a 2,5-diphenylsilacyclopent-3-ene[7-11] moiety, respectively, and examined the crossed-aldol reaction of the silyl enol ethers with benzaldehyde (Scheme 1).[12] When the reaction with silyl ether **5** was performed, the corresponding aldol product **7** was obtained as a mixture of *erythro* and *threo* adducts in good yield. In contrast, the reaction using silyl enol ether **6** produced only the *erythro* product **7** in moderate yield. The silane compound **6** which contained a 2,5-diphenylsilacyclopentene unit, showed good diastereomeric selectivity in the aldol reaction. Unfortunately, because the starting material—silyl enol ether **6**—was not optically active, the reaction did not show enantioselectivity. We now synthesise the novel organosilicon compound **8** with a chiral centre next to the silicon atom, chlorodimethyl(1-naphthylphenylmethyl)silane,



Scheme 1

as shown in Scheme 2. To our knowledge, chiral transfer with this type of a chiral organosilicon compound having high enantioselectivity, has not previously been reported. This paper details the results of this asymmetric synthesis.



(±) 8 **(±) 9**
(-) 8 **(-) 9**

Scheme 2

In this paper, we first describe both the preparation of the silane compounds and their molecular structure, as determined by X-ray crystallography. We also describe the crossed-aldol reactions of these chiral silyl enol ethers with benzaldehyde in the presence of a Lewis acid, such as $TiCl_4$, resulting in the stereoselective production of the corresponding aldol products. The crossed-aldol reaction using the chiral organosilicon compound showed one of the greatest known rates of chiral introduction into aldol products.

Results and discussion

According to the method reported in the literature,[13-15] we initially attempted to synthesise optically pure (2*R*)-(–)-chlorodimethyl(1-naphthylphenylmethyl)silane (**(–) 8**) using the reaction path shown in Scheme 3. The Grignard reagent generated from 1-bromonaphthalene (**10**) was coupled with benzyl chloride in the presence of $Pd(PPh_3)_4$ to produce 1-benzylnaphthalene (**11**) in 82% yield. The alkyllithium

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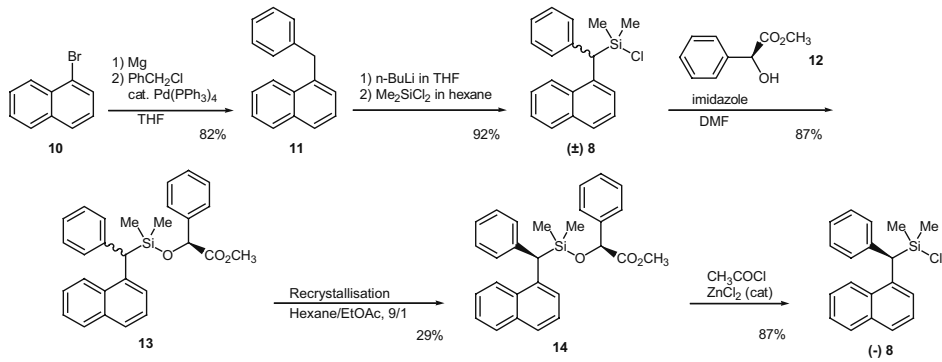


Scheme 1

compound generated from naphthalene **11** with *n*-BuLi was then treated with dichlorodimethylsilane to produce the corresponding racemic chlorodimethyl(1-naphthylphenylmethyl)silane (**(±) 8**) in 92% yield. When the racemic-**(±) 8** was reacted with (*S*)-(+)-methylmandelate (**12**) in the presence of imidazole in DMF at room temperature, the expected [(1'*S*)-(methoxycarbonyl)phenylmethoxy]dimethy(1-naphthylphenylmethyl)silane (**13**) was obtained in 87% yield without purification. To isolate the diastereomeric products, we recrystallised the diastereomeric mixture **13** twice using solvent mixtures comprised of hexane and EtOAc (first: 19/1 and second: 9/1) to afford crystalline (–)-(2*R*,1'*S*)-[(methoxycarbonyl)phenylmethoxy]dimethy(1-naphthylphenylmethyl)silane (**14**) in 29% yield. The absolute configuration of **14** was unambiguously determined to be the *R*-form of the diastereomer using X-ray structure analysis, as shown in Fig. 2. The refining factor of crystalline **14** was 4.6% and the value was well refined. Finally, when a previously reported method,[13-15] was used to treat the silyl ether **14** with acetyl chloride in the presence of $ZnCl_2$, the desired chiral (2*R*)-(–)-chlorodimethyl(1-naphthylphenylmethyl)silane (**(–) 8**) was produced in 87% yield.

When the reaction of chloro(naphthylphenylmethyl) silanes **(±) 8** and **(–) 8** with cyclohexanone was examined in the presence of a base, such as lithium diisopropylamide (LDA) or triethylamine (Et_3N), the corresponding starting materials, silyl enol ethers **(±) 9** and (2*R*)-(–)-dimethyl(1-cyclohexenyloxy)(1-naphthylphenylmethyl)silane (**(–) 9**), were obtained in the yields shown in Table 1. The structure of silyl enol ether **(±) 9** was characterised using spectral data, and subsequently confirmed using X-ray structure analysis. The refinement factor of crystalline **(±) 9** was 11.3%. The molecular structure proved to be a pair of enantiomers, as indicated in Fig. 3.

Next, the crossed-aldol reactions of the prepared enol ethers **(±) 9**, **(–) 9** and benzaldehyde were performed in the presence of a stoichiometric amount of $TiCl_4$ having no chirality effect. Pure chirality transfer effects of novel organosilicon compound having a chiral centre were checked by use of $TiCl_4$. All reactions proceeded cleanly to give the four

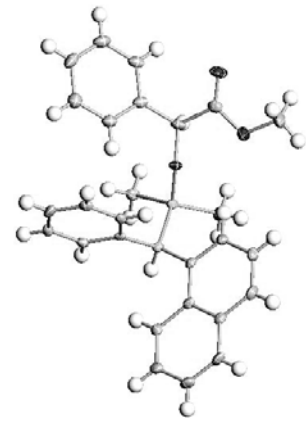


Fig. 2 Molecular structure of **14**.

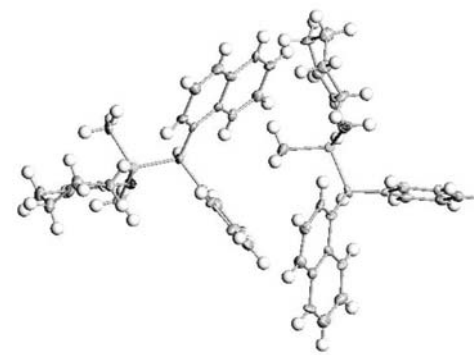


Fig. 3 Molecular structure of (±) **9**.

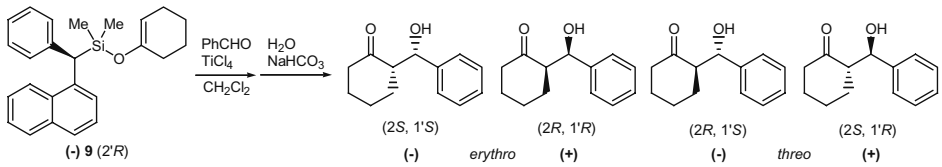
corresponding products in moderate yield with the formation of an unidentified compound having naphthyl, phenyl, methylene ring and silylmethyl groups. For example, when

Table 1 Synthesis of silyl enol ether **9** from the chlorosilane **8**[a,b]

Run	Chlorosilane	Base	Solv.	Temp./°C	Product	Yield/%
1[a]	**(±) 8**	Et_3N	DMF	Reflux	**(±) 9**	63[c]
2[b]	**(±) 8**	LDA	THF	–78	**(±) 9**	80[c]
3[b]	**(–) 8**	LDA	THF	–78	**(–) 9**	70[d]

[a]Molar ratio: Chlorosilane (**8**): Cyclohexanone: Et_3N = 1: 2: 2.
[b]Molar ratio: Chlorosilane (**8**): Cyclohexanone: LDA = 1: 1: 1.1.
[c]Isolated yields by crystallisation from EtOH after chromatographic purification (eluent: benzene).
[d]Isolated yields by chromatography (eluent: benzene).

Table 2 Crossed-aldol reaction of silyl enol ether (–) **9** with benzaldehyde[a]



Run	Silyl enol ether	Temp./°C	Time/h	Product	Yield[d]/%	dr[b] *erythro*: *threo* **15**: **16**	er[c] *erythro* **15** (–: +)	ee/%	er[c] *threo* **16** (–: +)	ee/%
1	**(–) 9**	–78	1	**15** and **16**	38	28: 72	94:6	88	20:80	60
2	**(–) 9**	0	1	**15** and **16**	38	31: 69	100:0	100	48:52	4

[a]Reaction of silyl enol ether with $TiCl_4$ at –78 or 0 °C for 1 h. Molar ratio: silyl enol ether: C_6H_5CHO: $TiCl_4$ = 1 : 1.1 : 1.5.
[b]Diastereomer ratios were determined by ^1H NMR analysis of the reaction mixtures before chromatographic separation.
[c]Enantiomer ratios were determined by HPLC using CSP column (eluent: hexane/*i*-PrOH = 19/1).
[d]Isolated yields by chromatography (eluent: hexane/EtOAc = 3/1).
The products were fully characterised by ^1H NMR, ^{13}C NMR and mass spectra.

the reaction was carried out with **(–) 9**, mixtures of the *erythro* **15** and *threo* **16** isomers were obtained in 38% yield in Table 2 (runs 1 and 2). Although the *threo* product was obtained prior to the *erythro* product, enantiomer excess was not observed for either the *threo* or *erythro* product. The enantiomeric selectivity was determined by HPLC using a CSP column after standard separation of the *erythro* and *threo* isomers. In contrast, the reaction using silyl enol ether **(–) 9** gave a mixture of **15** and **16** in 38% yield (run 1). Neither the yield nor the isomer ratio was improved when the similar reaction was conducted at 0 °C. The isomers were separated using silica gel (eluent: hexane/EtOAc = 3/1). For *threo* isomer **16**, the enantiomer ratio (–)/(+) is 48/52 in the reaction at 0 °C. The enantioselectivity, however, increased to 20/80 at –78 °C. The enantiomer excess of isolated **15** was 88%ee and that of **16** was 60%ee. Furthermore, when the reaction was conducted at 0 °C, the enantiomer excess of **15** was dramatically enhanced, such that only one diastereomer **(–) 15** with high chiral purity was obtained and that of **16** was 4%ee (run 2).

The reaction using silyl enol ether **(–) 9** gave a *threo*-rich isomer. As described above, the crossed-aldol reaction with silyl enol ether **(–) 9** showed the highest enantiomeric selectivity for asymmetric induction compared with selectivity values previously reported for organosilicon compounds with a chiral moiety. The most stable structure for **(–) 9** in the crystal, in which the cyclohexene and the naphthyl ring on the silylether are located in nearly the same plane, is shown in Fig. 3. Based on the ORTEP drawing, we found that the *2S* form of both the *threo* and *erythro* aldol products more readily formed than the *2R* form, because at –78 °C nucleophilic attack by the silyl enol ether occurred at the hydrogen atom side, which is less sterically hindered than the phenyl group side. To better illustrate the reason for the superior enantiomeric selectivity, plausible transition-states for the crossed-aldol reaction using **(–) 9** are shown in Fig. 4. The images in the left-side panel of Fig. 4 show the transition-states for the reaction of **9**, benzaldehyde and $TiCl_4$, and the right-side panel shows Newman drawings of the aldol products. The transition-state **I** gives the *erythro* (–) isomer **15** by the reaction with the *si*-face of benzaldehyde and the hydrogen atom side of the diasterotopic-face of the silyl enol ether **(–) 9**. On the other hand, the transition state II gives the *erythro* (+) isomer **15** by the reaction with the *re*-face of benzaldehyde and the phenyl group side of the diasterotopic-

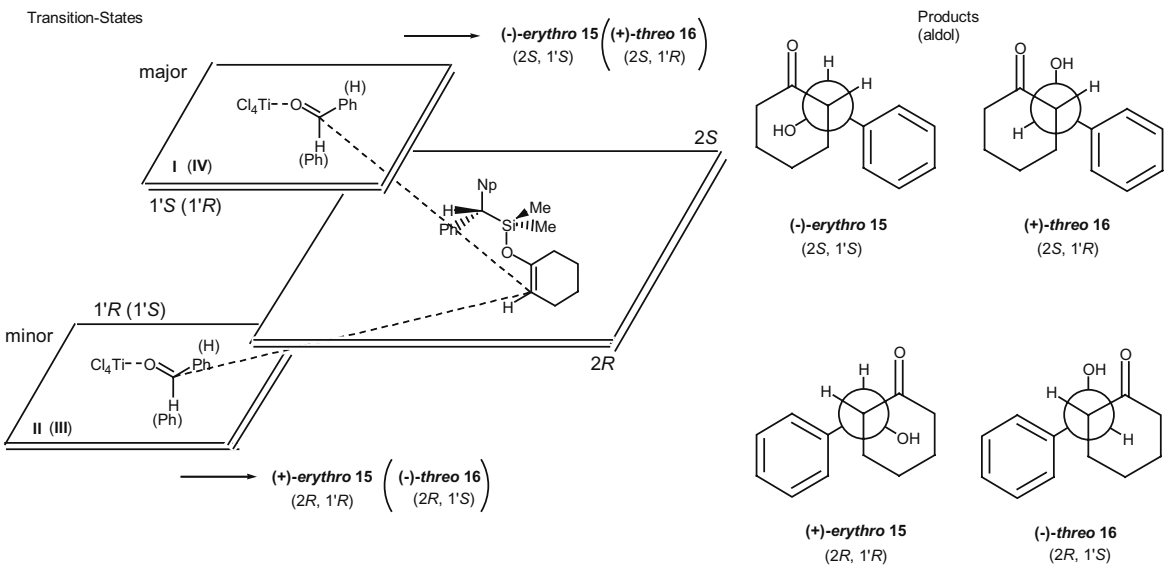


Fig. 4 Illustration of the transition-state of the crossed-aldol reaction of **(–) 9**.

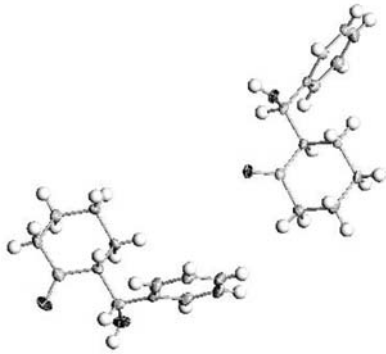


Fig. 5 Molecular structure of **(±) 15**.

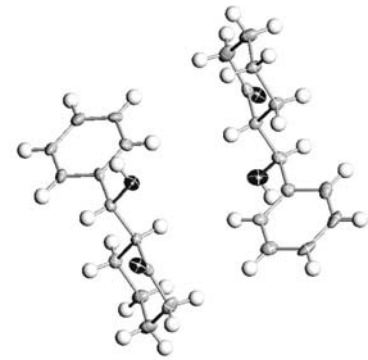


Fig. 6 Molecular structure of **(±) 16**.

face of **(–) 9**. Alternatively, **III** and **IV** give the desired *threo* (–) or (+) isomers **16**. The conformation of *threo* **(+) 16** was the most stable structure and this aldol was obtained as the major product. The *erythro* **15** and *threo* **16** isomers of the aldols obtained from **(–) 9** were liquid. However, crystals of the aldols were easily obtained from the reaction of **(±) 9** and benzaldehyde, because a pair of enantiomers of the aldols is solid. Each the structure of crystallised **15** and **16** was directly determined using X-ray structure analysis. The ORTEP drawings are shown in Figs 5 and 6. The refinement factors of crystalline **15** and **16** were 7.3% and 6.6%, respectively. These values were well refined. Kitamura and his coworker have reported crystal data of both *racemic-erythro* and *racemic-threo* aldols.[16] In the case of *erythro* **15**, their crystal data are almost same as ours. However, their crystal system of *threo* **16** is different from ours. Although they reported the crystal to be monoclinic, our crystal of *threo* **16** is seen to be orthorhombic (see Experimental).

Conclusion

We developed a method for the preparation of novel racemic silyl enol ethers, and the chiral silyl enol ether, (2*R*)-(–)-(1-cyclohexenyloxy)dimethyl(1-naphthylphenylmethyl) silane, starting from the precursor, chlorodimethyl(1-naphthylphenylmethyl)silane. The molecular structure of silyl enol ether **(±) 9** was unambiguously confirmed using X-ray structure analysis. Moreover, the crossed-aldol reaction of these silyl enol ethers with benzaldehyde produced the corresponding aldols, the stereoselectivity of which depended on the steric effect of both the phenyl group and hydrogen atom of benzaldehyde. The aldol reaction using **(–) 9** in the presence of $TiCl_4$, produced *threo* aldols as the major product. We found that the reaction using silyl enol ether **(–) 9** gives the greatest enantiomeric selectivity compared with selectivity values previously reported for silyl enol ethers in similar reactions.

Experimental

General

All reactions were carried out under a nitrogen atmosphere, unless otherwise noted. Column chromatography was performed using silica gel (Wakogel C-200), and components were visualised using UV light. ^{1}H NMR (500 MHz), ^{13}C NMR (125 MHz) and ^{29}Si NMR (99 MHz) spectra were recorded using a JOEL EPC-500 spectrometer in $CDCl_3$. The stereochemistry of the isomers was assigned on the basis of X-ray results, and the ratios of the diasteromer were determined by NMR spectra prior to purification. The enantioselectivity was determined by HPLC analysis using a CSP column (Chiralcel OD-H, Daicel Chemical Industries Ltd.). Commercially available $TiCl_4$ was distilled under a nitrogen atmosphere before use.

Chlorodimethyl(1-naphthylphenylmethyl)silanes **(±) 8** *and* **(–) 8:** We have developed the general procedure for the preparation of **(–) 8**, which was similar to a previously reported method,[13-15] and is shown in Scheme 3. The compound **(±) 8** was prepared using a method described in the literature[13-15] with minor modification.

Benzylnaphthalene (**11**):[13-15] To a THF solution (600 ml) containing granular Mg was added 1-bromonaphthalene (**10**) (87.3 g, 432 mmol), and the reaction was allowed to proceed for 30 min at room temperature. The resulting Grignard reagent was added for 30 min to a THF solution (200 ml) containing benzyl chloride (60.8 g, 480 mmol) and palladium tetrakis(triphenylphosphine) (2.32 g, 2.00 mmol) at room temperature, and the mixture was stirred for an additional 15 h. The reaction was quenched by addition of water (20 ml) and 1N HCl aq. (200 ml). The resulting organic layer was extracted with ether, washed with 1N HCl aq. (200 ml), water (200 ml × 2) and brine (200 ml), and dried over anhydrous Na_2SO_4. The filtrate was condensed and distilled under reduced pressure (b.p. 160–175 °C/0.2 mmHg) to give **11**. The distilled product was recrystallised from ethanol at room temperature to give pure **11** in 82% yield. White solid, m.p. 61.0–62.0 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.00–7.97 (m, 1 H, ArH), 7.86–7.83 (m, 1 H, ArH), 7.77–7.74 (m, 1 H, ArH), 7.46–7.39 (m, 3 H, ArH), 7.29–7.24 (m, 3 H, ArH), 7.20–7.16 (m, 2 H, ArH), 4.44 (s, 2 H, aliphatic CH_2). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 140.6, 136.6, 133.9, 132.1, 128.7, 128.7, 128.4, 127.3, 127.1, 126.0, 126.0, 125.5, 124.3, 39.0. MS (FAB): *m/z* (%) = 218 $[M]^+$ (10), 207 (4), 147 (5), 129 (14), 128 (100), 127 (11), 73 (19), 59 (4).

Racemic-(±)-chlorodimethyl(1-naphthylphenylmethyl)silane **((±) 8)**:[13-15] To a THF solution (80 ml) of **11** (16.4 g, 75.0 mmol), was added dropwise 1.6 M *n*-butyl lithium in hexane (51.6 ml, 82.5 mmol) for 30 min at –78 °C. After heating a solution of dichlorodimethylsilane (29.1 g, 225 mmol) in hexane (57 ml) to room temperature, the synthesised lithium compound was added dropwise for 30 min at –78 °C; the mixture was stirred for an additional 15 h at room temperature. The reaction mixture was evaporated and the residue was distilled under reduced pressure (b.p. 156–170 °C/0.2 mmHg) to give *racemic*-**(±) 8** in 92% yield. Pale white solid, m.p. 85.5–86.2 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.09–8.06 (m, 1 H, ArH), 7.83–7.81 (m, 1 H, ArH), 7.76–7.71 (m, 2 H, ArH), 7.50–7.42 (m, 3 H, ArH), 7.33–7.30 (m, 2 H, ArH), 7.25–7.21 (m, 2 H, ArH), 7.14–7.10 (m, 1 H, ArH), 4.55 (s, 1 H, SiCH aliphatic CH), 0.51 (s, 3H, $Si(CH_3)_2$), 0.48 (s, 3H, $Si(CH_3)_2$). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 140.3, 136.5, 134.5, 132.6, 128.9, 128.7, 128.4, 127.4, 127.3, 126.1, 125.7, 125.6, 125.1, 123.8, 41.7, 2.0, 1.9. ^{29}Si NMR (99 MHz, $CDCl_3$): δ = –22.43. MS (EI): *m/z* (%) = 310 $[M]^+$ (100), 311 (35), 312 $[M + 2]^+$ (55), 218 (98), 217 (64), 216 (83), 215 (93), 202 (100).

[(1'S)-(Methoxycarbonyl)dimethy(1-naphthylphenylmethyl) phenylmethoxy]silane **(13)**:[13-15] To a DMF solution (50 ml) of a mixture of (+)-(*S*)-methylmandelate (**12**) (5.82 g, 35.0 mmol) and imidazole (2.72 g, 40.0 mmol), was added to synthesised *racemic*-**(±) 8** (10.9 g, 32.0 mmol) at room temperature, followed by stirring for 15 h. The reaction mixture was neutralised by addition of saturated $NaHCO_3$ aq. (50 ml) at 0 °C. Hexane/EtOAc = 1/1 was added to the resulting organic layer. The extract was washed with saturated $NaHCO_3$ aq. (25 ml), water (25 ml × 2) and brine (25 ml × 2), and dried over anhydrous Na_2SO_4. The mixture was filtered and condensed under reduced pressure to give crude **13** in 87% yield. Pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.09–8.05 (m, 1 H, ArH), 7.86–7.68 (m, 3 H, ArH), 7.46–7.05 (m, 13 H, ArH), 4.99 (s, 1 H [50%], OCH), 4.96 (s, 1 H [50%], OCH), 4.38 (s, 1 H [50%],

SiCH), 4.34 (s, 1 H [50%], SiCH), 3.60 (s, 3 H [50%], CO_2CH_3), 3.57 (s, 3 H [50%], CO_2CH_3), 0.21 (s, 3 H [50%], $Si(CH_3)_2$), 0.18 (s, 3 H [50%], $Si(CH_3)_2$), 0.17 (s, 3 H [50%], $Si(CH_3)_2$), 0.15 (s, 3 H [50%], $Si(CH_3)_2$).

(–)-(2R,1'S)-[(Methoxycarbonyl)phenylmethoxy]dimethy(1-naphthylphenylmethyl)silane **(14)**:[13-15] The synthesised **13** was recrystallised in hexane/EtOAc = 95/5 to give crude **14**, which was then recrystallised in hexane/EtOAc = 90/10 to give pure **14** in 29% yield. White solid; m.p. 112.5–113.5 °C.^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.09–8.05 (m, 1 H, ArH), 7.84–7.78 (m, 2 H, ArH), 7.73–7.69 (m, 1 H, ArH), 7.47–7.38 (m, 3 H, ArH), 7.35–7.23 (m, 7 H, ArH), 7.18–7.13 (m, 2 H, ArH), 7.10–7.05 (m, 1 H, ArH), 4.99 (s, 1 H, OCH), 4.34 (s, 1 H, SiCH), 3.62 (s, 3 H, CO_2CH_3), 0.21 (s, 3 H, $Si(CH_3)_2$), 0.15 (s, 3 H, $Si(CH_3)_2$). Crystal data for **14**: $C_{28}H_{28}O_3Si$, M = 440.59, colourless crystal, 0.50 × 0.15 × 0.10 mm^3, monoclinic, space group P2(1), a = 10.8990(14) Å, b = 8.3205(11) Å, c = 12.8498(17) Å, α = 90°, β = 97.877(2)°, γ = 90°, V = 1154.3(3) Å^3, Z = 2, Dc = 1.268 Mg/m^3, F(000) = 468, Ac = 0.129 mm^{-1}. Intensity data were collected on a Smart-APEX diffractometer with graphite monochromated MoK_α radiation (λ = 0.71073 Å) using the ω scan mode with 1.60° < θ < 28.25°. 7123. Unique reflections were measured and reflections with $I > 2\ \sigma\ (I)$ were used in the Fourier techniques. The final refinement converged to R = 0.0462 and wR = 0.1100.

(2R)-(–)-Chlorodimethyl(1-naphthylphenylmethyl)silane **((–) 8)**[13-15]: Acetyl chloride (2.98 g, 38.0 mmol) was added to the synthesised **14** (3.17 g, 7.20 mmol) to create a suspension, which was then cooled to 0 °C, followed by addition of 0.5 M zinc chloride in THF (28 µl, 14.0 µmol). The mixture was heated to room temperature and stirred for 1 h, after which the reaction mixture became homogeneous and was stirred for an additional 15 h. The excess acetyl chloride was removed by distillation under reduced pressure. Hexane (1.7 ml) and acetone (0.17 ml) were added, and the mixture was stirred for 45 min. The solvent was removed by distillation under reduced pressure, followed by distillation of the reaction mixture under reduced pressure (b.p. 155–165 °C/0.8 mmHg) to give **(–) 8** in 87% yield. Pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.10–8.06 (m, 1 H, ArH), 7.84–7.81 (m, 1 H, ArH), 7.77–7.70 (m, 2 H, ArH), 7.50–7.41 (m, 3 H, ArH), 7.33–7.29 (m, 2 H, ArH), 7.26–7.22 (m, 2 H, ArH), 7.14–7.11 (m, 1 H, ArH), 4.55 (s, 1 H, SiCH), 0.51 (s, 3 H, $Si(CH_3)_2$), 0.48 (s, 3 H, $Si(CH_3)_2$). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 140.3, 136.5, 134.5, 132.6, 128.9, 128.7, 128.4, 127.4, 127.3, 126.1, 125.7, 125.6, 125.1, 123.8, 41.7, 2.0, 1.9. ^{29}Si NMR (99 MHz, $CDCl_3$): δ = –22.43. MS (EI): m/z (%) = 310 $[M]^+$ (100), 311 (35), 312 $[M + 2]^+$ (55), 218 (98), 215 (95), 216 (85), 217 (65), 202 (100).

Reaction of 1-chlorosilanes with cyclohexanone using triethylamine

(1-cyclohexenyloxy)dimethyl(1-naphthylphenylmethyl)silane **(9):** A DMF solution (2 ml) of **(±) 8** (4.13 g, 13.3 mmol) was added dropwise to a DMF solution (2 ml) of triethylamine (2.69 g, 26.6 mmol), and the reaction mixture was stirred. A DMF solution (2 ml) of cyclohexanone (2.61 g, 26.6 mmol) was added to the former solution, and the reaction mixture was stirred under reflux for 6 h. The mixture was cooled, and hexane was added to the solution. The precipitate was removed by filtration and purified by silica gel column chromatography (benzene) to afford the corresponding silyl enol ether **(±) 9** in 63.3% yield.

Reaction of chlorosilanes with cyclohexanone using lithium diisopropylamide

(1-Cyclohexenyloxy)dimethyl(1-naphthylphenylmethyl)silane **(9):** A THF solution (10 ml) of cyclohexanone (981 mg, 10.0 mmol) was added dropwise to a THF solution (10 ml) of 1.5 M LDA (7.33 ml, 11.0 mmol) at –78 °C, and the reaction mixture was stirred for 1 h at this temperature. To this mixture was added a THF solution (10 ml) of **(±) 8** (3.11 g, 10.0 mmol) and the resulting mixture was stirred at –78 °C. After 1–3 h, the resulting organic layer was extracted with ether; the extract was washed with brine and dried over anhydrous Na_2SO_4. The extract solution was condensed under reduced pressure, and the residue was purified using silica gel column chromatography (benzene) to afford the corresponding silyl enol ether **(±) 9** (yield 79.6%). A single crystal of **(±) 9** was obtained by recrystallisation of **(±) 9** from ethanol. White solid; m.p. 92.5–94.5 °C. IR (KBr): 1089 (Si-O) cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.12–8.09 (m, 1 H, ArH), 7.83–7.80 (m, 1 H, ArH), 7.76–7.71 (m, 2 H, ArH), 7.48–7.40 (m, 3 H, ArH), 7.33–7.29 (m, 2 H, ArH), 7.23–7.18 (m, 2 H, ArH), 7.10–7.06 (m, 1 H, ArH), 4.79–4.76 (br, 1 H, vinyl =CH), 4.42 (s, 1 H, aliphatic SiCH), 1.94–1.82 (m, 4 H, cyclohexane like CH_2), 1.58–1.38 (m, 4 H, cyclohexane like CH_2), 0.24 (s, 3 H, $Si(CH_3)_2$), 0.23 (s, 3 H, $Si(CH_3)_2$). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 150.3, 141.9, 137.7, 134.4, 132.8, 128.8, 128.7, 128.1, 127.8, 126.6, 125.8, 125.2, 125.0, 124.1, 104.5, 40.5, 29.7, 23.8, 23.0, 22.2, –0.9, –1.3. MS (FAB): m/z (%) = 373 $[M + H]^+$ (27), 372 $[M]^+$ (20), 275 (18), 217 (28), 215 (16), 197 (30), 155 (100), 75 (47). Anal. Calcd for $C_{25}H_{28}OSi$: C, 80.59; H, 7.57. Found: C, 80.50; H, 7.52. Crystal data for **(±) 9**: $C_{50}H_{56}O_2Si_2$, M = 745.13, colourless crystal, 0.16 × 0.08 × 0.08 mm^3, triclinic, space group P-1, a = 9.7708(16) Å, b = 13.425(2) Å, c = 15.498(3) Å, α = 84.840(3)°, β = 80.970(3)°, γ = 89.184(3)°, V = 1999.5(6) Å^3, Z = 4, Dc = 1.238 Mg/m^3, F(000) = 800, Ac = 0.130 mm^{-1}. Intensity data were collected on a Smart-APEX diffractometer with graphite monochromated MoK_α radiation (λ = 0.71073 Å) using the ω scan mode with 1.34° < θ < 28.15°. 10931. Unique reflections were measured and reflections with $I > 2\ \sigma\ (I)$ were used in the Fourier techniques. The final refinement was converged to R = 0.1126 and wR = 0.3015.

(2R)-(–)-(1-Cyclohexenyloxy)dimethyl(1-naphthylphenylmethyl) silane **((–)9):** Pale yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.12–8.09 (m, 1 H, ArH), 7.83–7.80 (m, 1 H, ArH), 7.76–7.71 (m, 2 H, ArH), 7.48–7.40 (m, 3 H, ArH), 7.33–7.29 (m, 2 H, ArH), 7.23–7.18 (m, 2 H, ArH), 7.10–7.06 (m, 1 H, ArH), 4.79–4.76 (br, 1 H, vinyl =CH), 4.42 (s, 1 H, aliphatic SiCH), 1.94–1.82 (m, 4 H, cyclohexane like CH_2), 1.58–1.38 (m, 4 H, cyclohexane like CH_2), 0.24 (s, 3 H, $Si(CH_3)_2$), 0.23 (s, 3H, $Si(CH_3)_2$). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 150.3, 141.9, 137.7, 134.4, 132.8, 128.8, 128.7, 128.1, 127.8, 126.6, 125.8, 125.2, 125.0, 124.1, 104.5, 40.5, 29.7, 23.8, 23.0, 22.2, –0.9, –1.2. MS (FAB): m/z (%) = 373 $[M + H]^+$ (32), 372 $[M]^+$ (26), 275 (30), 217 (43), 215 (31), 197 (68), 155 (100), 75 (78). Optical rotation: $[\alpha]^D_{25}$ = –18.8° (c = 2.0, $CHCl_3$).

Reaction of (1-cyclohexenyloxy)dimethyl(1-naphthylphenylmethyl) silane with benzaldehyde in the presence of titanium tetrachloride

2-(hydroxyphenylmethyl)cyclohexanone **(15, 16):** To a CH_2Cl_2 solution (15 ml) containing either dimethyl(1-cyclohexenyoxy) (1-naphthylphenylmethyl)silane **(±) 9** or **(–) 9** (745 mg, 2.00 mmol) was added benzaldehyde (265 mg, 2.50 mmol) in dry methylene chloride (5 ml) at 0 °C or –78 °C. $TiCl_4$ (569 mg, 3.00 mmol) in dry methylene chloride (5 ml) was added to the reaction mixture at the same temperature and the reaction mixture was stirred for 1 h. After hydrolysis and neutralisation by addition of aqueous $NaHCO_3$ at either 0 °C or –78 °C, the resulting organic layer was extracted with ether. The extract was then washed with water and dried over anhydrous Na_2SO_4. The mixture was condensed under reduced pressure, and the residue was purified using silica gel column chromatography (hexane/EtOAc = 3/1) to afford the *erythro* and *threo* aldol compounds, **15** and **16**, respectively. The *erythro* (2R^*,1'R^*): *threo* (2R^*,1'S^*) ratio was determined by ^{1}H NMR analysis. The enantio selectivities of the *erythro* and *threo* isomers were determined using HPLC equipped with a CSP column; eluent, hexane/*i*-PrOH = 19/1; flow rate = 1.0 ml/min; and UV detection λ = 265 nm. The retention times for the isomers were determined previously to be: $t_{(-)\text{-}erythro}$ = 10.67 min (2S,1'S), $t_{(+)\text{-}erythro}$ = 12.37 min (2R,1'R), $t_{(+)\text{-}threo}$ = 14.87 min (2S,1'R), $t_{(-)\text{-}threo}$ = 20.27 min (2R,1'S).[17-18]

erythro-2-(Hydroxyphenylmethyl)cyclohexanone **(15):** White solid; m.p. 102.5–103.5 °C. UV (hexane/*i*-PrOH = 19/1): λ_{max} = 265.5 nm. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.36–7.23 (m, 5 H, ArH), 5.41–5.39 (br, 1 H, methine O–CH), 3.01 (d, 1 H, OH), 2.63–2.58 (m, 1 H, cyclohexanone CH–C=O), 2.48-2.44 (m, 1 H, cyclohexanone CH_2), 2.42–2.34 (m, 1 H, cyclohexanone CH_2), 2.12–2.06 (m, 1 H, cyclohexanone CH_2), 1.88–1.82 (m, 1 H, cyclohexanone CH_2), 1.78–1.70 (m, 2 H, cyclohexanone CH_2), 1.70–1.63 (m, 1 H, cyclohexanone CH_2), 1.57–1.47 (m, 1 H, cyclohexanone CH_2). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 217.6, 141.6, 128.2, 127.0, 125.8, 70.6, 57.2, 42.69, 28.0, 26.0, 24.9.MS (FAB): m/z (%) = 205 $[M + H]^+$ (20), 203 (12), 187 (100), 169 (24), 143 (18), 117 (13), 105 (20), 91 (25). HRMS (Ion mode: FAB$^+$) m/z (%): Found/205.1208 (100), Calcd for $C_{13}H_{17}O_2$/205.1229. Crystal data for **(±)15**: $C_{26}H_{32}O_4$, M = 408.52, colourless crystal, 0.33 × 0.32 × 0.27 mm^3, monoclinic, space group P2(1)/c, a = 25.796(6) Å, b = 5.7048(14) Å, c = 15.456(4) Å, α = 90°, β = 106.433(4)°, γ = 90°, V = 2181.7(9) Å^3, Z = 4, Dc = 1.244 Mg m^{-3}, F(000) = 880, Ac = 0.082 mm^{-1}. Intensity data were collected on a Smart-APEX diffractometer with graphite monochromated MoK_α radiation (λ = 0.71073 Å) using the ω scan mode with 1.65° < θ < 28.40°. 12411. Unique reflections were measured and reflections with $I > 2\ \sigma\ (I)$ were used in the Fourier techniques. The final refinement was converged to R = 0.0730 and wR = 0.2133.

threo-2-(Hydroxyphenylmethyl)cyclohexanone **(16):** White solid; m.p. 70.5–71.5 °C UV (hexane/*i*-PrOH = 19/1): λ_{max} = 266.5 nm. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.37–7.27 (m, 5 H, ArH), 4.78 (dd, 1 H, methine O–CH), 3.96 (d, 1 H, OH), 2.65–2.59 (m, 1 H,

cyclohexanone CH–C=O), 2.51-2.46 (m, 1 H, cyclohexanone CH_2), 2.40–2.33 (m, 1 H, cyclohexanone CH_2), 2.12–2.05 (m, 1 H, cyclohexanone CH_2), 1.82–1.76 (m, 1 H, cyclohexanone CH_2), 1.72–1.62 (m, 1 H, cyclohexanone CH_2), 1.61–1.50 (m, 2 H, cyclohexanone CH_2), 1.35–1.25 (m, 1 H, cyclohexanone CH_2). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 215.6, 140.9, 128.4, 127.9, 127.0, 74.8, 57.4, 42.7, 30.9, 27.8, 24.7. MS (FAB): *m/z* (%) = 205 $[M + H]^+$ (20),203 (12), 187 (100), 169 (24), 143 (18), 117 (13), 105 (20), 91 (25). HRMS (Ion mode: FAB $^+$) *m/z* (%): Found/205.1225 (100), Calcd for $C_{13}H_{17}O_2$/205.1229. Crystal data for **(±)16**: $C_{26}H_{32}O_4$, M = 408.52, colourless crystal, 0.42 × 0.35 × 0.25 mm^3, orthorhombic, space group Pna2(1), a = 20.609(3) Å, b = 5.7569(8) Å, c = 18.451(3) Å, α = 90°, β = 90°, γ = 90°, V = 2189.1(5) $Å^3$, Z = 4, Dc = 1.240 Mg/m^3, F(000) = 880, Ac = 0.082 mm^{-1}. Intensity data were collected on a Smart-APEX diffractometer with graphite monochromated MoK_α radiation (λ = 0.71073 Å) using the ω scan mode with 1.98° < θ < 28.41°. 12619. Unique reflections were measured and reflections with $I > 2\ \sigma\ (I)$ were used in the Fourier techniques. The final refinement was converged to R = 0.0659 and wR = 0.1662.

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