Phenyl group acceleration of [1,4] carbon-to-oxygen silicon-mediated elimination–rearrangement in β-silyl sulfones. Synthesis of *O*-silylated cinnamyl alcohols †

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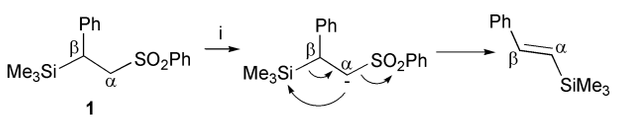
A very fast [1,4] carbon-to-oxygen silicon migration-rearrangement leading to *O*-silylated cinnamyl alcohols occurs when the carbanion generated from sulfone **1** is reacted with carbonyl compounds. The mandatory role of the adjacent phenyl ring in this process is demonstrated when compared to the behaviour of the corresponding unsubstituted sulfone **3**.

Introduction

Some years ago we discovered a new rearrangement involving [1,2] carbon-to-carbon silicon migration [1–3] which occurs when, *inter alia*, the β-silyl sulfone **1** is reacted with a strongly basic, poor silicophilic species, like lithium diisopropylamide (LDA) as described in Scheme 1.



Scheme 1 *Reagents and conditions*: *i*: LDA, THF, reflux.

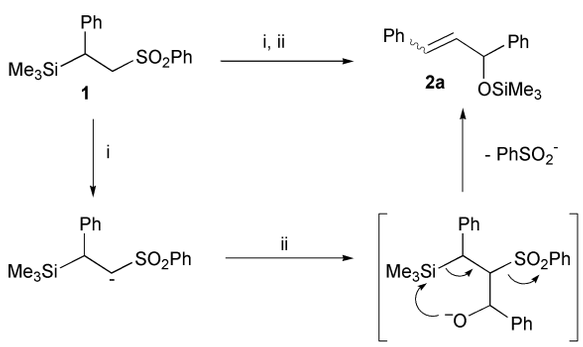
We proved that migration of silicon (not phenyl) and formation of an intermediate carbanion species are among the features of this process. Moreover, we verified that the phenyl group on Cβ is mandatory to encourage Si–C bond cleavage.[1–3]

Results and discussion

Looking for more insight into this process we decided to functionalise compound **1** at Cα by reacting the corresponding carbanion with electrophiles. Thus sulfone **1** was reacted with BuLi (or LDA) in dry THF at −78 °C followed by addition of benzaldehyde. After work-up we could isolate the *O*-silylated cinnamyl alcohol **2a**, as the only reaction product, in 85% yield as a 60 : 40 mixture of *E* and *Z* isomers (Scheme 2). The formation of **2a** can be rationalised considering that the reaction of the α-sulfonyl carbanion with benzaldehyde affords an unstable oxy anion which, in turn, undergoes a fast rearrangement with [1,4] carbon-to-oxygen silicon migration ([1,4] Brook rearrangement [4]) and phenylsulfonyl group elimination, as depicted in Scheme 2.

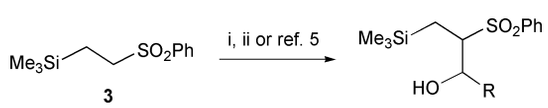
All the attempts to trap the intermediate oxy anion by quenching the reaction immediately after the addition of the aldehyde at −78 °C, using either water or Me_3SiCl as electrophiles, were unsuccessful, indicating a very fast oxygen attack on silicon followed by migration and rearrangement.

This confirms our previous observation on the mandatory role of the phenyl ring in weakening the Si–C bond of these silanes,[3,5] and is in sharp contrast with the behaviour of 1-phenylsulfonyl-2-trimethylsilylethane (**3**). In fact it is well documented that sulfone **3** can be easily functionalised at Cα using various electrophiles, giving rise to reasonably stable products.[6] From these functionalised silyl sulfones the formation of the double bond, by phenylsulfonyl group elimination, can be achieved only by fluoride ion attack on silicon.[6,7]



Scheme 2 *Reagents and conditions*: *i*: *n*-BuLi, THF, −78 °C, 20 min; *ii*: PhCHO, −78 °C then rt.

Indeed by reacting silylated sulfone **3** with BuLi followed by addition of benzaldehyde, the stable alcohol **4**,[6] as a 55 : 45 mixture of diastereoisomers, was isolated in 86% yield (Scheme 3). As a further demonstration of the role of the phenyl ring in weakening the carbon–silicon bond, no trace of the carbon-to-oxygen silicon migration-rearrangement was observed, even after 7 h at reflux in THF, of the lithium alkoxide of alcohol **4**, which was then easily completely recollected after acidification.



Scheme 3 *Reagents and conditions*: *i*: *n*-BuLi, THF, −78 °C, 20 min; *ii*: PhCHO, −78 °C then rt.

On the other hand the [1,4] Brook rearrangement of the phenyl substituted sulfone **1** proved to be general and occurred with aromatic, aliphatic and α,β-unsaturated aldehydes as well

† Dedicated to Professor Giuseppe Capozzi on the occasion of his 60th birthday.

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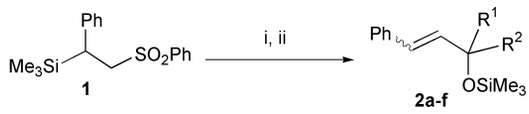
as with non-enolisable ketones,‡ affording in all cases good yields of the corresponding *O*-silylated cinnamyl alcohols **2a**–**f**, as mixtures of *E* and *Z* isomers (Scheme 4).



Entry	R^1	R^2	Product **2** (yield %)	*E*/*Z*
1	Ph	H	**2a** (85%)	60/40
2	Pr^i	H	**2b** (86%)	86/14
3	Bu^n	H	**2c** (67%)	53/47
4	Bu^t	H	**2d** (83%)	96/4
5	Ph	H	**2e** (73%)	44/56
6	Ph	Ph	**2f** (70%)	> 98/2

Scheme 4 *Reagents and conditions*: *i*: *n*-BuLi, THF, −78 °C, 20 min; *ii*: R^1COR^2, −78 °C then rt.

With respect to the stereoselectivity of the formation of the double bond, the paper of Tokoroyama and coworkers[8] regarding a similar [1,4] silicon migration-rearrangement, demonstrated that the silicon mediated β-elimination occurs exclusively with an *anti* geometry.[9] Consequently, in our case, we can consider that the rearrangement with 1,2-elimination occurs only from the intermediate oxy-anions **A** and **B** which afford (*E*)- and (*Z*)-cinnamyl alcohols, respectively, both through an *anti* elimination (Fig. 1).

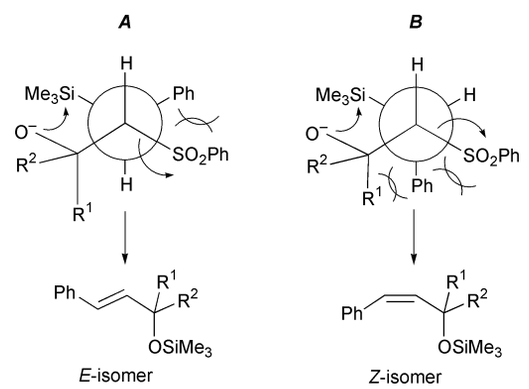


Fig. 1 A rational for the stereoselectivity observed in the silicon migration-rearrangement with phenylsulfonyl elimination.

While in **A** there is only some steric interaction between the phenyl on Cβ and the phenylsulfonyl on Cα in **B**, the phenyl ring on Cβ also interacts with the groups on the former carbonyl carbon, thus explaining the experimental observation that the greater the steric demand of the carbonyl compounds, the lower the amount of *Z* isomer formed (Scheme 4, Fig. 1).

In conclusion we have shown a further example of the ability of an adjacent phenyl ring to weaken a carbon–silicon bond and the possibility to obtain, in a single step, silylated cinnamyl alcohols *via* a silicon mediated elimination–rearrangement. Potential applications of this new process in organic synthesis are under investigation.

‡ Unreacted sulfone **1** was recovered using acetophenone or cyclohexanone as electrophile, probably in this case the sulfonyl anion deriving from **1** undergoes α-deprotonation, with formation of the corresponding enolates, instead of attack on the carbonyl-carbon. Similarly no reaction was detected using cyclohexene and styrene oxides as electrophiles.

Experimental

^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ at 200 and 50 MHz respectively, using residual $CHCl_3$ at δ_H 7.26 and the central line of $CDCl_3$ at δ_D 77.0 as references. GC-MS spectra were obtained on a Carlo Erba QM 1000 equipped with an OV-1 30 m capillary column. Melting points are uncorrected. THF was distilled from sodium benzophenone ketyl. Aldehydes were distilled before use, silyl sulfones **1** and **3** were prepared as reported elsewere.[3]

General procedure for the preparation of alcohols 2a–f

To a solution of the sulfone **1** (318 mg, 1.0 mmol) in dry THF (10 cm^3) kept at −78 °C, *n*BuLi 1.6 M in hexane (0.69 cm^3, 1.1 mmol) was added. After 20 min the carbonyl compound (1.1 mmol) in dry THF (5 cm^3) was added to the orange solution and the mixture allowed to reach room temperature. The mixture was then diluted with ether (50 cm^3), washed with saturated ammonium chloride and with brine, dried over anhydrous sodium sulfate and evaporated to give a crude product which was purified by silica gel flash chromatography using petroleum ether–ethyl acetate as the eluent.

Silyl alcohols **2a**–**c**, and **2e** were obtained as inseparable mixtures of *E* and *Z* isomers. *E* : *Z* Ratios were measured from the crude reaction mixture by ^{1}H NMR integral ratios (see Scheme 4). The following spectroscopic data refer to the mixtures obtained after column chromatography. Derivatives **2d** and **2f** were isolated as *E* isomers.

1-Phenyl-*O*-trimethylsilylcinnamyl alcohol 2a. Petroleum ether–ethyl acetate = 10 : 1, colourless oil (240 mg, 85%). Found: C, 76.32; H, 8.01. Calcd. for $C_{18}H_{22}OSi$: C, 76.54; H, 7.85%. *E* isomer: δ_H(200 MHz, $CDCl_3$) 0.22 (9 H, s), 5.42 (1 H, d, *J* 6.6 Hz), 6.37 (1 H, dd, *J* 15.8 and 6.6 Hz), 6.69 (1 H, d, *J* 15.8 Hz), 7.20–7.57 (5 H, m). δ_C(50 MHz, $CDCl_3$) 0.1 (q), 75.4 (d), 126.0 (d), 126.4 (d), 127.0 (d), 127.3 (d), 128.1 (d), 128.3 (d), 129.1 (d), 134.1 (d), 136.6 (s), 143.4 (s). *m*/*z* (%): 282 (M^+, 72), 205 (12), 193 (53), 115 (97), 73 (100). *Z* isomer: δ_H(200 MHz, $CDCl_3$) 0.09 (9 H, s), 5.73 (1 H, d, *J* 9.2 Hz), 5.98 (1 H, dd, *J* 11.4 and 9.2 Hz), 6.69 (1 H, d, *J* 15.8 Hz), 7.20–7.57 (5 H, m). δ_C(50 MHz, $CDCl_3$) 0.1 (q), 70.1 (d), 126.1 (d), 126.7 (d), 127.2 (d), 128.1 (d), 128.2 (d), 128.4 (d), 128.7 (d), 141.0 (d), 136.6 (s), 143.5 (s). *m*/*z* (%): 282 (M^+, 72), 205 (12), 193 (53), 115 (97), 73 (100).

1-Isopropyl-*O*-trimethylsilylcinnamyl alcohol 2b. Petroleum ether–ethyl acetate = 30 : 1, colourless oil (213 mg, 86%). Found: C, 72.46; H, 9.88. Calcd. for $C_{15}H_{24}OSi$: C, 72.52; H, 9.74%. *E* isomer: δ_H(200 MHz, $CDCl_3$) 0.15 (9 H, s), 0.92 (3 H, d, *J* 6.8 Hz), 0.96 (3 H, d, *J* 6.7 Hz), 1.65–1.85 (1 H, m), 3.97 (1 H, t, *J* 6.7 Hz), 6.20 (1 H, dd, *J* 15.9 and 6.7 Hz), 6.49 (1 H, d, *J* 15.9 Hz), 7.15–7.45 (5 H, m). δ_C(50 MHz, $CDCl_3$) 0.4 (q), 18.3 (q), 18.5 (q), 34.8 (d), 78.9 (d), 126.3 (d), 127.3 (d), 128.5 (d), 130.0 (d), 131.9 (d), 137.2 (s). *m*/*z* (%): 248 (M^+, 3), 205 (100), 115 (20), 73 (75). *Z* isomer: δ_H(200 MHz, $CDCl_3$) −0.02 (9 H, s), 0.96 (3 H, d, *J* 6.8 Hz), 0.99 (3 H, d, *J* 6.7 Hz), 1.65–1.85 (1 H, m), 4.37 (1 H, dd, *J* 9.6 and 6.0 Hz), 5.69 (1 H, dd, *J* 12.0 and 9.6 Hz), 6.52 (1 H, d, *J* 12.0 Hz), 7.15–7.45 (5 H, m). δ_C(50 MHz, $CDCl_3$) 0.2 (q), 17.9 (q), 18.9 (q), 29.7 (d), 72.9 (d), 126.8 (d), 128.1 (d), 128.6 (d), 129.3 (d), 135.0 (d), 137.2 (s). *m*/*z* (%): 248 (M^+, 3), 205 (100), 115 (20), 73 (75).

1-Butyl-*O*-trimethylsilylcinnamyl alcohol 2c. Petroleum ether–ethyl acetate = 20 : 1, colourless oil (166 mg, 67%). Found: C, 72.79; H, 9.91. Calcd. for $C_{15}H_{24}OSi$: C, 72.52; H, 9.74%. *E* isomer: δ_H(200 MHz, $CDCl_3$) 0.16 (9 H, s), 0.95 (3 H, d, *J* 7.3 Hz), 1.30–1.70 (4 H, m), 4.27 (1 H, q, *J* 6.5 Hz), 6.19 (1 H, dd, *J* 15.9 and 6.5 Hz), 6.50 (1 H, d, *J* 15.9 Hz), 7.20–7.42 (5 H, m). δ_C(50 MHz, $CDCl_3$) 0.3 (q), 14.0 (q), 18.8 (t), 40.5 (t), 73.4 (d),

126.3 (d), 128.1 (d), 128.5 (d), 128.6 (d), 133.3 (d), 137.1 (s). *m*/*z* (%): 248 (M^+, 10), 205 (100), 115 (12), 73 (25). *Z* isomer: δ_H(200 MHz, $CDCl_3$) −0.01 (9 H, s), 0.95 (3 H, d, *J* 7.3 Hz), 1.30–1.70 (4 H, m), 4.58–4.65 (1 H, m), 5.69 (1 H, dd, *J* 11.8 and 9.2 Hz), 6.46 (1 H, d, *J* 11.8 Hz), 7.20–7.42 (5 H, m). δ_C(50 MHz, $CDCl_3$) 0.2 (q), 14.0 (q), 18.7 (t), 40.1 (t), 68.2 (d), 126.9 (d), 127.3 (d), 128.2 (d), 128.9 (d), 136.4 (d), 137.1 (s). *m*/*z* (%): 248 (M^+, 10), 205 (100), 115 (12), 73 (25).

(*E*)-1-*tert*-Butyl-*O*-trimethylsilylcinnamyl alcohol 2d. Petroleum ether–ethyl acetate = 40 : 1, colourless oil (217 mg, 83%). Found: C, 73.12; H, 9.87. Calcd. for $C_{16}H_{26}OSi$: C, 73.22; H, 9.98%. δ_H(200 MHz, $CDCl_3$) 0.18 (9 H, s), 0.96 (9 H, s), 3.86 (1 H, d, *J* 6.9 Hz), 6.22 (1 H, dd, *J* 15.9 and 6.9 Hz), 6.47 (1 H, d, *J* 15.9 Hz), 7.15–7.49 (5 H, m). δ_C(50 MHz, $CDCl_3$) 0.4 (q), 26.0 (q), 35.8 (s), 81.6 (d), 126.3 (d), 126.3 (d), 127.2 (d), 128.5 (d), 130.7 (d), 130.8 (d), 137.3 (s). *m*/*z* (%): 262 (M^+, 0.2), 247 (6), 205 (100), 115 (30), 73 (70).

1-[(*E*)-β-Styryl]-*O*-trimethylsilylcinnamyl alcohol 2e. Petroleum ether–ethyl acetate = 30 : 1, colourless oil (225 mg, 73%). Found: C, 78.00; H, 7.77. Calcd. for $C_{20}H_{24}OSi$: C, 77.87; H, 7.84%. *E* isomer: δ_H(200 MHz, $CDCl_3$) 0.25 (9 H, s), 5.05 (1 H, t, *J* 7.0 Hz), 6.36 (2 H, dd, *J* 15.8 and 7.0 Hz), 6.65 (2 H, d, *J* 15.8 Hz), 7.15–7.50 (10 H, m). δ_C(50 MHz, $CDCl_3$) 0.4 (q), 74.2 (d), 126.5 (d), 127.5 (d), 128.2 (d), 129.5 (d), 131.3 (d), 136.8 (s). *m*/*z* (%): 308 (M^+, 20), 231 (10), 217 (75), 203 (30), 73 (100). *Z* isomer: δ_H(200 MHz, $CDCl_3$) 0.11 (9 H, s), 5.24–5.36 (1 H, m), 5.80 (1 H, dd, *J* 11.8 and 8.1 Hz), 6.30 (1 H, dd, *J* 15.8 and 7.0 Hz), 6.66 (1 H, d, *J* 15.8 Hz), 6.70 (1 H, d, *J* 11.8 Hz), 7.15–7.50 (10 H, m). δ_C(50 MHz, $CDCl_3$) 0.3 (q), 69.3 (d), 126.5 (d), 127.2 (d), 127.5 (d), 128.2 (d), 128.5 (d), 128.6 (d), 129.5 (d), 131.1 (d), 133.6 (d), 136.7 (s), 136.9 (s). *m*/*z* (%): 308 (M^+, 20), 231 (10), 217 (75), 203 (30), 73 (100).

(*E*)-1,1′-Diphenyl-*O*-trimethylsilylcinnamyl alcohol 2f. Petroleum ether–ethyl acetate = 20 : 1, white solid, mp 39–40 °C (250 mg, 70%). Found: C, 80.24; H, 7.18. Calcd. for $C_{24}H_{26}OSi$: C, 80.40; H, 7.31%. δ_H(200 MHz, $CDCl_3$) 0.01 (9 H, s), 6.45 (1 H, d, *J* 15.8 Hz), 6.82 (1 H, d, *J* 15.8 Hz), 7.15–7.43 (15 H, m). δ_C(50 MHz, $CDCl_3$) 2.1 (q), 81.8 (s), 126.6 (d), 126.9 (d), 127.5 (d), 127.6 (d), 127.8 (d), 128.6 (d), 130.1 (d), 135.7 (d), 136.8 (s), 146.5 (s).

1-(Trimethylsilylmethyl)-2-phenyl-1-(phenylsulfonyl)ethan-2-ol 4

To a solution of the sulfone **3** (242 mg, 1.0 mmol) in dry THF (10 cm^3) kept at −78 °C, *n*BuLi 1.6 M in hexane (0.69 cm^3, 1.1 mmol) was added. After 20 min benzaldehyde (117 mg, 1.1 mmol) in dry THF (5 cm^3) was added to the orange solution and the mixture allowed to reach room temperature. The mixture was then diluted with ether (50 cm^3), washed with saturated ammonium chloride and with brine, dried over anhydrous sodium sulfate and evaporated to give a crude product which was purified by silica gel flash chromatography using petroleum ether–ethyl acetate 5 : 1 as the eluent which allowed separation of the two diastereoisomers (299 mg, 86% overall yield).

Major **4**: Colourless oil. Found: C, 62.17; H, 7.09. Calcd. for $C_{18}H_{24}O_3SSi$: C, 62.03; H, 6.94%. δ_H(300 MHz, $CDCl_3$) −0.42 (9 H, s), 1.05–1.25 (2 H, AB part of an ABX system, J_{AB} 16.5 Hz), 3.22 (1 H, br t, *J* 5.8 Hz), 3.58 (1 H, d, *J* 1.8 Hz, OH), 5.28 (1 H, br s), 7.14–7.32 (5 H, m), 7.60–7.74 (3 H, m), 7.94–8.00 (2 H, m). δ_C(75 MHz, $CDCl_3$) −2.0 (q), 5.9 (t), 67.2 (d), 69.6 (d), 125.6 (d), 127.7 (d), 128.4 (d), 128.8 (d), 129.4 (d), 134.0 (d), 137.6 (s), 139.7 (s).

Minor **4**: Colourless oil. δ_H(300 MHz, $CDCl_3$) −0.26 (9 H, s), 0.79 (1 H, dd, *J* 15.9 and 7.2 Hz), 1.1 (1 H, dd, *J* 15.9 and 4.2 Hz), 3.46–3.54 (1 H, m), 4.43 (1 H, d, *J* 4.5 Hz, OH), 4.89 (1 H, dd, *J* 7.5 and 4.5 Hz), 7.20–7.64 (8 H, m), 7.75–7.80 (2 H, m). δ_C(75 MHz, $CDCl_3$) −1.5 (q), 12.5 (t), 67.2 (d), 74.4 (d), 127.0 (d), 128.2 (d), 128.4 (d), 128.7 (d), 128.9 (d), 133.5 (d), 138.3 (s), 140.0 (s).

Acknowledgements

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