# **FULL PAPER**

# The efficiency of the acid-catalyzed *vs* the mercury-cyclization in the synthesis of tetrahydrofurans from allylsilyl alcohols

((Abstract Text----Continued))

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The scope of the acid-catalyzed *vs* the mercury-cyclization of allylsilyl alcohols is described. This methodology has shown to be an efficient approach to the synthesis of highly substituted tetrahydrofurans. The stereoselectivity of the cyclization is dependent both on the substitution of the starting alcohol and on the catalyst. A plausible mechanism has been drawn, which is consistent with the results.

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# Introduction

Substituted tetrahydrofurans are structural motifs commonly present in a great number of natural products, such as macrodiolides,<sup>[1]</sup> lignans,<sup>[2]</sup> amphidinolides,<sup>[3]</sup> or antibiotic polyethers,<sup>[4]</sup> among others. Due to the important biological activities of these molecules, much effort has been made towards de development of new stereoselective routes to these oxacycles.<sup>[5]</sup> An efficient and widely used methodology for the synthesis of tetrahydrofurans is the electrophilic cyclization of  $\gamma$ , $\delta$ -unsaturated alcohols.<sup>[6]</sup>

Within others,<sup>[7]</sup> a commonly employed approach is the mercurycyclization. It has been reported that the stereoselectivity of the mercury-cyclizations depends on several factors such as the nature of mercury salt,<sup>[8]</sup> the structure of the unsaturated alcohol<sup>[9]</sup> and the presence or not of additives, such as water, <sup>[10]</sup> in the reaction media (Scheme 1).



Scheme 1. Mercury-cyclization of unsaturated alcohols.

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An alternative strategy to the synthesis of tetrahydrofurans is the acid-catalyzed cyclization of unsaturated alcohols, although this route has shown major limitations. However, Hosomi<sup>[11]</sup> has reported that the cyclization of vinylsilyl alcohols in the presence of a Lewis acid proceeds with high *trans*-selectivity. The plausible mechanism for this reaction involves electrophilic addition to the vinylsilane to give a  $\beta$ -silyl carbocation, which is then trapped by the internal hydroxy group to give the tetrahydrofuran derivative (Scheme 2).



Scheme 2. Acid-catalyzed cyclization of vinylsilyl alcohols.

Moreover, allylsilanes have been widely recognized as valuable synthons in controlling, in a very effective way, the regio- and stereochemical outcome of many chemical transformations,<sup>[12]</sup> especially in the area of stereoselective allylation processes.<sup>[10]</sup> Thus, these organosilicon compounds are nucleophilic units which, being stable towards most reagents and reaction conditions, are able to react with a wide range of electrophiles.

For many years our research group has been involved in the study of the synthetic applications of allylsilanes containing an electrophilic moiety within the same molecule.<sup>[13]</sup> The so-called allylsilane-terminated cyclization of these substrates has allowed the synthesis of different sized carbocycles such us methylenecyclopentanols,<sup>[14]</sup> methylenecyclohexanols,<sup>[15]</sup> methylenecycloheptanols<sup>[16]</sup> or spirocyclopropylcyclopentanols<sup>[17]</sup> (Scheme 3).



Scheme 3. Synthesis of medium-sized carbocycles from allylsilyl ketones.

# **Results and Discussion**

In this paper we describe an interesting approach towards the synthesis of tetrahydrofurans from allylsilyl alcohols, studying the ability of the mercury-cyclization *vs* the acid-catalyzed one.

Thus, following our methodology of silylcupration of allene and capture of the intermediate cuprate with  $\alpha$ , $\beta$ -unsaturated carbonylic compounds we were able to prepare allylsilyl aldehydes and ketones **1a-i**, in high yields. The corresponding allylsilyl alcohols needed for this study were readily obtained by reduction with LiAlH<sub>4</sub>, in a quantitative manner (Table 1).

Table 1. Synthesis of allylsilyl alcohols 2 and 3.



[a] All the alcohols are obtained as racemic mixtures.

First of all we studied the scope of this methodology in the synthesis of substituted tetrahydrofurans, comparing the efficiency of the acid-catalyzed vs the mercury-cyclization of allylsilyl alcohol **2e**.

The results are shown in Table 2.

Table 2. Cyclization of allylsilyl alcohol 2e.



Entry	Reagent	<mark>Mol</mark>	Temp	Time	Ratio <sup>[a]</sup>	Yield
		equiv	[°C]	[h]	4e:5e	[%]
1	$Hg(OCOCF_3)_2$	1	<b>-</b> 40→0	2	50:50	79
2	Hg(OAc) <sub>2</sub>	1	<b>-</b> 40→0	4	50:50	70 <sup>[b]</sup>
3	$Hg(OAc)_2$	1	<b>-</b> 60→0	16	50:50	65 <sup>[c]</sup>
4	HgCl <sub>2</sub>	1	t.a.	4		
5	TsOH	<mark>0.2</mark>	0	1	50:50	75
6	AlCl <sub>3</sub>	1	-78	2	55:45	62

[a] The ratio of isomers **4e** and **5e** were determined by <sup>1</sup>H-NMR analysis. [b] A 1:1 mixture of the corresponding 1-hydroxymethyl THF derivatives were also obtained in a 9% yield. [c] A 1:1 mixture of the corresponding 1hydroxymethyl THF derivatives were also obtained in a 7% yield.

As shown in Table 2 mercury-cyclization of 2e with Hg(OCOCF<sub>3</sub>)<sub>2</sub> afforded a 1:1 mixture of tetrahydrofurans 4e and 5e in good yield. The results using Hg(OAc)<sub>2</sub> are similar although yields are slightly decreased due to the formation of minor amounts of the 1-hydroxymethyl THF derivatives.<sup>[18]</sup> However, using HgCl<sub>2</sub> no cyclization products were obtained. In contrast to results showed by Landais et al., the stereoselectivity of this kinetically controlled mercuri-cyclization is not affected by the nature of the mercury salt, nor by the temperature of the reaction.<sup>8</sup>

Moreover, the acid catalyzed cyclization also yielded an equimolar mixture of diastereoisomers **4e** and **5e**. The use of a Lewis acid (AlCl<sub>3</sub>) provided similar results to the Brönsted acid (p-TsOH) regarding stereoselectivities, although yield is lower.

With these results in hand we decide to study the influence of the substituents of the allylsilyl alcohol in the stereoselectivity of the cyclization. The results are shown in Table 3.

#### Table 3. Scope of the cyclization of allylsilyl alcohols 2a-f.

As shown in Table 3, cyclization of allylsilanes 2b-2g with mercuric salts provided substituted tetrahydrofurans 4b-g and 5b-gin good yields, almost as an equimolar mixture of diastereoisomers (Table 3, Entries 2, 4, 5, 8, 10 and 12). On the other hand, the stereoselectivity of the acid-catalyzed cyclization of allylsilyl alcohols depends on their substitution patern. Thus, allylsilanes 2b, 2d with a  $\gamma$  substituent to the hydroxy group give 2,2,3trisubstituted tetrahydrofurans in high yields and with moderate selectivity towards the stereoisomers 4b and 4d with *trans*arrangement between the R<sup>2</sup> and the silylmethyl substituent (up to 3:1 dr) (Table 3, Entries 3 and 6), while substrates having an  $\alpha$  substituent to the hydroxy group 2e-2g provide substituted tetrahydrofurans almost as an equimolar mixture of diastereoisomers 4 and 5 (Table 3, Entries 9, 11 and 13).

We next decided to study the influence of substituents in the allylsilane both in  $\alpha$  and  $\gamma$  to the hydroxy group.

Table 4. Scope of the cyclization of allylsilyl alcohols 2h-i.

Table 5. Scope of the cyclization of allylsilyl alcohols 3h-i.

Allylsilanes **2h-2i** and **3h-3i** undergo cyclization in high yields to provide a mixture of two diasteroisomers, the major isomer (**4** or **6**) being the one with 2,3-*trans*-relationship between the R<sup>2</sup> and the silylmethyl group. As shown in Tables 4 and 5, in general the acidcatalyzed cyclization provides higher stereoselectivities than the corresponding mercury-cyclization.<sup>19</sup> It should be noted that a solution of these allylsilyl alcohols in refluxing chloroform also undergoes cyclization. In this case, HCl generated in situ would be the actual catalyst.  $^{\rm 20}$ 

On the other hand, the acid-mediated cyclizations show the best stereoselectivities and yields when p-TsOH is used as catalyst (Table 4, Entries 2 an 5; Table 5, Entry 2). Moreover, cyclization of stereoisomers 2h and 2i proceeds with better stereoselectivity (up to 5:1 *dr*) (Table 4, Entries 2 and 5) than the corresponding cyclization of 3h and 3i (up to 3.5:1 dr) (Table 5, Entries 2 and 5). A plausible mechanism for this acid-catalyzed cyclization involves the electrophilic addition of the proton to the allylsilane moiety to give a stabilized carbocation  $\beta$  to silicon which, in turn, is trapped by the internal hydroxy group. In the reactive conformation the C-Si bond is oriented parallel to the p empty orbital of the intermediate carbocation, in order to allow the corresponding  $\sigma$ -p hyperconjugative stabilization and, therefore, the attack of the internal nucleophile will occur *anti* to the hindered silyl group.

Hosomi et al. have described<sup>[11b]</sup> that the protonation step in the acid-catalyzed cyclization of vinylsilyl alcohols occurs through attachment of a proton or AlCl<sub>3</sub> to the hydroxy group, to form an oxonium ion, which will then deliver the proton to the double bond.<sup>21</sup> Moreover, they have reported that the addition of the hydroxy group and the proton proceeds stereospecifically to the same side of the  $\pi$  bond. Based on these observations, we will assume the same *syn* addition for our allylsilanes (Scheme 4).



Scheme 4. Mechanism of the acid-catalyzed cyclization.

Regarding the stereochemical outcome of the cyclization, two different reactive conformations can be drawn, such as I and II (Scheme 5).





Scheme 5. Stereochemical outcome of the cyclization.

In conformer II an unfavorable steric interaction between the 1,3diaxial substituents (Ph and H) would account for the major product proceeding from conformer I. This hypothesis is consistent with the fact that cyclization of allylsilyl alcohols 2h and 2iproceed with higher stereoselectivity than the corresponding cyclization of 3h and 3i, since now the diaxial steric strain between Ph and  $R^1$  is greater.

# Conclusions

In summary, we have shown that allylsilyl alcohols undergo both mercury- and acid-catalyzed cyclizations to give substituted tetrahydrofurans in high yields. The stereoselectivity of the annulation process depends both on the nature of the catalyst and on the substitution of the allylsilane. A mechanistic proposal has been outlined which is consistent with the stereochemical outcome of the cyclization.

# **Experimental Section**

#### **General Experimental**

All the reactions were carried out under an atmosphere of argon or nitrogen in dried glassware unless otherwise indicated. Materials were obtained from commercial suppliers and used without further purification except when otherwise noted. Solvents were dried and distilled according to the standard protocols. Flash column chromatography was performed on silica gel using the indicated solvent. The synthesis and spectroscopic data of allylsilyl aldehydes and ketones **1a-i** have been previously described.<sup>[12a,13]</sup>

Synthesis of allylsilyl alcohols 2 and 3. A solution of the allylsilyl aldehydes or ketones 1a-i (2 mmol) in dry ether (2 ml) was added to a suspension of 1.7 mmol of LiAlH<sub>4</sub> in dry ether (8 ml) at 0 °C. The mixturer was stirred for 1 hour at 0 °C and then quenched with 4 ml of NaHCO<sub>3</sub> (10%) and 4 ml of NaOH (20%). The organic layer was dried, the solvent evaporated and the mixture was purified by flash chromatography (EtOAc/hexane) to give alcohols 2 and 3.

[2*SR*,4*SR*]-5-Dimethylphenylsilylmethyl-4-phenyl-5-hexen-2-ol (2h). Chromatography gave complete separation of diastereoisomeric alcohols. Colorless oil (45%); IR  $v_{max}$ (film)/cm<sup>-1</sup> 3385, 1633, 1599, 1249, 1113; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.75-7.71 (m, 2H), 7.55-7.51 (m, 3H), 7.46-7.41 (m, 2H), 7.37-7.29 (m, 3H), 5.08 (s, 1H), 4.93 (s, 1H), 3.61-3.48 (m, 1H), 3.35 (dd, *J* = 10.1 y 4.4 Hz, 1H), 1.99-1.74 (m, 3H), 1.92 (d, *J* = 14.0 Hz, 1H), 1.76 (d, *J* = 14.0 Hz, 1H), 1.21 (d, *J* = 6.6 Hz, 3H), 0.52 (s, 3H, CH<sub>3</sub>-Si), 0.47 (s, 3H, CH<sub>3</sub>-Si); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  = 149.8 (C), 143.4 (C), 139.3 (C), 133.9 (CH), 129.2 (CH), 128.5 (CH), 128.0 (CH), 126.5 (CH), 107.8 (CH<sub>2</sub>), 65.4 (CH), 48.9 (CH), 44.0 (CH<sub>2</sub>), 26.0 (CH<sub>2</sub>), 24.5 (CH<sub>3</sub>), -2.5 (CH<sub>3</sub>), -2.9 (CH<sub>3</sub>); MS (EI): m/z 324 (M<sup>+</sup>), 309 (M<sup>+</sup>-Me), 247 (M<sup>+</sup>-Ph), 135 (SiMe<sub>2</sub>Ph); Anal. Calcd for  $C_{21}H_{28}OSi:$  C, 77.72; H, 8.70; Found: C, 78.04; H, 8.98.

[2*RS*,4*SR*]-5-Dimethylphenylsilylmethyl-4-phenyl-5-hexen-2-ol (3h). White solid (45%), mp 91-92 °C; IR  $v_{max}$ (film)/cm<sup>-1</sup> 3460, 1629, 1548, 1249, 1113; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.61-7.57 (m, 2H), 7.46-7.43 (m, 3H), 7.34-7.24 (m, 3H), 7.15-7.12 (m, 2H), 4.91 (s, 1H), 4.81 (s, 1H), 3.61-3.51 (m, 1H), 2.99 (t, *J* = 7.5 Hz, 1H), 1.86-1.81 (m, 2H), 1.76 (d, *J* = 14.1 Hz, 1H), 1.58 (d, *J* = 14.1 Hz, 1H), 1.32 (s, 1H), 1.07 (d, *J* = 6.1 Hz, 3H), 0.38 (s, 3H, CH<sub>3</sub>-Si), 0.33 (s, 3H, CH<sub>3</sub>-Si); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  = 148.6 (C), 143.5 (C), 139.1 (C), 133.7 (CH), 129.2 (CH), 128.4 (CH), 128.1 (CH), 127.9 (CH), 126.5 (CH), 107.7 (CH<sub>2</sub>), 66.2 (CH), 49.2 (CH), 43.9 (CH<sub>2</sub>), 25.6 (CH<sub>2</sub>), 23.2 (CH<sub>3</sub>), -2.6 (CH<sub>3</sub>), -3.3 (CH<sub>3</sub>); MS (EI): m/z 324 (M<sup>+</sup>), 309 (M<sup>+</sup>-Me), 247 (M<sup>+</sup>-Ph), 135 (SiMe<sub>2</sub>Ph); Anal. Calcd for C<sub>21</sub>H<sub>28</sub>OSi: C, 77.72; H, 8.70; Found: C, 78.06; H, 9.02.

[1*RS*,3*SR*]-4-Dimethylphenylsilylmethyl-1,3-diphenyl-4-penten-1-ol (2i). Chromatography gave complete separation of diastereoisomeric alcohols. Colorless oil (44%); IR  $v_{max}$ (film)/cm<sup>-1</sup> 3375, 1633,1249, 1112; <sup>1</sup>H NMR (300 MHz, acetone- $d_6$ )  $\delta$  = 7.55-7.49 (m, 2H), 7.36-7.14 (m, 13H), 4.83 (s, 1H), 4.68 (s, 1H), 4.29-4.23 (m, 1H), 4.13 (d, *J* = 4.7 Hz, 1H, OH), 3.62 (dd, *J* = 11.0 and 3.8 Hz, 1H), 2.15 (ddd, *J* = 13.9, 10.2 and 3.8 Hz, 1H), 2.04-1.96 (m, 1H), 1.77 (d, *J* = 13.9 Hz, 1H), 1.62 (d, *J* = 13.9 Hz, 1H), 0.33 (s, 3H, CH<sub>3</sub>-Si), 0.30 (s, 3H, CH<sub>3</sub>-Si); <sup>13</sup>C NMR (75 MHz, , acetone- $d_6$ )  $\delta$  = 150.9 (C), 147.5 (C), 144.0 (C), 139.7 (C), 134.3 (CH), 129.6 (CH), 129.3 (CH), 129.0 (CH), 128.8 (CH), 128.5 (CH), 127.4 (CH), 127.0 (CH), 126.3 (CH), 108.0 (CH<sub>2</sub>), 71.4 (CH), 49.6 (CH), 45.5 (CH<sub>2</sub>), 26.1 (CH<sub>2</sub>), -2.4 (CH<sub>3</sub>), -2.5 (CH<sub>3</sub>); MS (EI): m/z 368 (M<sup>+</sup>-H<sub>2</sub>O), 309 (M<sup>+</sup>-Ph), 135(SiMe<sub>2</sub>Ph); Anal. Calcd for C<sub>26</sub>H<sub>30</sub>OSi: C, 80.78; H, 7.82; Found: C, 81.12; H, 8.12.

**[1***SR*,3*SR***]**-4-Dimethylphenylsilylmethyl-1,3-diphenyl-4-penten-1-ol (3i). Colorless oil (44%); IR  $v_{max}$ (film)/cm<sup>-1</sup> 3395, 1633,1245, 1109; <sup>1</sup>H NMR (300 MHz, , acetone- $d_6$ ) δ = 7.43-7.09 (m, 15H), 4.92 (s, 1H), 4.72 (s, 1H), 4.49 (td, J = 6.9 y 4.2 Hz, 1H), 4.16 (d, J = 4.2 Hz, 1H, OH), 3.18 (t, J = 7.4 Hz, 1H), 2.27-2.10 (m, 2H), 1.69 (d, J = 13.9 Hz, 1H), 1.52 (d, J = 13.9 Hz, 1H), 0.18 (s, 3H, CH<sub>3</sub>-Si), 0.15 (s, 3H, CH<sub>3</sub>-Si); <sup>13</sup>C NMR (75 MHz, , acetone- $d_6$ ) δ = 149.7 (C), 146.5 (C), 144.5 (C), 139.6 (C), 134.2 (CH), 129.6 (CH), 129.0 (CH), 128.9 (CH), 128.4 (CH), 128.4 (CH), 127.8 (CH), 127.0 (CH), 126.9 (CH), 108.2 (CH<sub>2</sub>), 72.4 (CH), 49.4 (CH), 44.9 (CH<sub>2</sub>), 25.9 (CH<sub>2</sub>), -2.6 (CH<sub>3</sub>), -2.6 (CH<sub>3</sub>); MS (EI): m/z 368 (M<sup>+</sup>-H<sub>2</sub>O), 309 (M<sup>+</sup>-Ph), 135(SiMe<sub>2</sub>Ph).

Synthesis of tetrahydrofurans 4-7 using mercury salts. To a suspension of the mercury salt (1.09 mmol) and CaCO<sub>3</sub> (2.17 mmol) in 9 ml of dry THF at -40 °C was added a solution of the corresponding alcohol (1 mmol) in dry THF (1 ml). The stirred mixutre was allowed to warm to 0 °C and then NaBH<sub>4</sub> (0.72 mmol) in a 2.5 M solution of NaOH (4 ml) was added dropwise at 0 °C. The reaction mixture was vigorously stirred at 0°C for 1 hour and then saturated NaCl solution was added (4 ml). The aqueous layer was extracted with ether and the combined extracts were washed with brine, dried over MgSO<sub>4</sub> and evaporated in *vacuo* to give an oil which was purified by chromatography (EtOAc/hexane).

Synthesis of tetrahydrofurans 4-7 using acid catalysis. To a solution of the alcohol (1 mmol) in  $CH_2Cl_2$  (5 ml) was added the acid catalyst in  $CH_2Cl_2$  (0.5 ml). The mixture is stirred in the shown conditions (tables 2-5) and quenched with saturated solution of NaHCO<sub>3</sub> (5 ml). The organic layer was washed 3 times with NaHCO<sub>3</sub>, dried over MgSO<sub>4</sub>, evaporated in *vacuo* and purified by flash chromatography (EtOAc/hexane). The relative stereochemistry of all tetrahydrofurans was assigned on the basis of NOE experiments.

**2-Methyl-2-dimethylphenylsilylmethyltetrahydrofuran** (4a). Colorless oil (70%); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.59-7.52 (m, 2H), 7.41-7.33 (m, 3H), 3.81-3.76 (m, 2H), 1.98-1.85 (m, 2H), 1.71-1.62 (m, 2H), 1.39 (d, *J* = 14.7 Hz, 1H), 1.28 (d, *J* = 14.7 Hz, 1H), 1.21 (s, 3H), 0.39 (s, 6H, (CH<sub>3</sub>)<sub>2</sub>-Si); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  = 140.1 (C), 133.6 (CH), 128.7 (CH), 127.7 (CH), 82.9 (C), 66.3 (CH<sub>2</sub>), 39.4 (CH<sub>2</sub>), 30.5 (CH<sub>2</sub>), 28.5 (CH<sub>3</sub>), 26.0 (CH<sub>2</sub>), -1.2 (CH<sub>3</sub>), -1.3 (CH<sub>3</sub>); MS (EI): m/z 233 (M<sup>+</sup>-1), 219 (M<sup>+</sup>-Me), 157 (M<sup>+</sup>-Ph), 135 (SiMe<sub>2</sub>Ph); Anal. Calcd for C<sub>14</sub>H<sub>22</sub>OSi: C, 71.73; H, 9.46; Found: C, 72.04; H, 9.75.

[2RS,3RS]-2,3-Dimethyl-2-dimethylphenylsilylmethyl-tetrahydrofuran (4b). Chromatography gave complete separation of diastereoisometic tetrahydrofurans. Colorless oil (52%); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.57-7.51 (m, 2H), 7.37-7.31 (m, 3H), 3.80-3.73 (m, 1H), 3.71-3.63 (m, 1H), 2.02-1.94 (m, 1H), 1.92-1.85 (m, 1H), 1.63-1.50 (m, 1H), 1.37 (d, *J* = 14.9 Hz, 1H), 1.20 (d, *J* = 14.9 Hz, 1H), 1.00 (s, 3H), 0.89 (d, *J* = 6.6 Hz, 3H), 0.37 (s, 6H, (CH<sub>3</sub>)<sub>2</sub>-Si); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  = 140.9 (C), 133.7 (CH), 128.7 (CH), 127.7 (CH), 84.6 (C), 64.7 (CH<sub>2</sub>), 44.0 (CH), 33.7 (CH<sub>2</sub>), 29.7 (CH<sub>2</sub>), 23.6 (CH<sub>3</sub>), 14.8 (CH<sub>3</sub>), -0.8 (CH<sub>3</sub>), -1.0 (CH<sub>3</sub>); MS (EI): m/z 247 (M<sup>+</sup>-1), 233 (M<sup>+</sup>-Me), 171 (M<sup>+</sup>-Ph), 135 (SiMe<sub>2</sub>Ph); Anal. Calcd for C<sub>15</sub>H<sub>24</sub>OSi: C, 72.52; H, 9.74; Found: C, 72.84; H, 10.05.

#### $\label{eq:stars} [2SR, 3RS] \mbox{-} 2, \mbox{-} 3 \mbox{-} Dimethyl \mbox{-} 2 \mbox{-} dimethyl \mbox{-} phenyl \mbox{silylmethyl-tetrahydrofuran}$

(**5b**). Colorless oil (26%); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.58-7.51 (m, 2H), 7.39-7.31 (m, 3H), 3.71-3.62 (m, 1H), 3.59-3.49 (m, 1H), 2.00-1.93 (m, 1H), 1.86-1.78 (m, 1H), 1.61-1.51 (m, 1H), 1.21 (s, 3H), 1.09 (d, *J* = 14.9 Hz, 1H), 0.94 (d, *J* = 6.6 Hz, 3H), 0.78 (d, *J* = 14.9 Hz, 1H), 0.39 (s, 3H, CH<sub>3</sub>-Si), 0.38 (s, 3H, CH<sub>3</sub>-Si); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  = 141.1 (C), 133.7 (CH), 128.7 (CH), 127.7 (CH), 84.5 (C), 64.7 (CH<sub>2</sub>), 45.3 (CH), 33.3 (CH<sub>2</sub>), 27.6 (CH<sub>3</sub>), 23.1 (CH<sub>2</sub>), 14.5 (CH<sub>3</sub>), -0.8 (CH<sub>3</sub>), -1.1 (CH<sub>3</sub>); MS (EI): m/z 247 (M<sup>+</sup>-1), 233 (M<sup>+</sup>-Me), 171 (M<sup>+</sup>-Ph), 135 (SiMe<sub>2</sub>Ph).

#### 2-Methyl-2-dimethylphenylsilylmethyl-3-propyltetra-hydrofuran

([2RS,3SR] 4c and 5c [2SR,3SR]). Chromatography gave tetrahydrofurans 4c and 5c as a mixture. Colorless oil (85%); 4c: <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.61-7.53 (m, 2H), 7.39-7.32 (m, 3H), 3.84-3.73 (m, 1H), 3.72-3.66 (m, 1H), 2.02-1.96 (m, 1H), 1.78-1.69 (m, 1H), 1.61-1.49 (m, 1H), 1.39-1.25 (m, 4H), 1.32 (d, J = 14.9 Hz, 1H), 1.25 (d, J = 14.9 Hz, 1H), 1.01 (s, 3H), 0.88 (t, J = 6.6Hz, 3H), 0.40 (s, 6H, (CH<sub>3</sub>)<sub>2</sub>-Si); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ = 140.8 (C), 133.5 (CH), 128.5 (CH), 127.6 (CH), 84.2 (C), 64.7 (CH<sub>2</sub>), 49.4 (CH), 32.4 (CH<sub>2</sub>), 31.6 (CH<sub>2</sub>), 29.7 (CH<sub>2</sub>), 23.9 (CH<sub>3</sub>), 22.1 (CH<sub>2</sub>), 14.4 (CH<sub>3</sub>), -0.9 (CH<sub>3</sub>), -1.2 (CH<sub>3</sub>); MS (EI): m/z 275 (M<sup>+</sup>), 261 (M<sup>+</sup>-Me), 199 (M<sup>+</sup>-Ph), 135 (SiMe<sub>2</sub>Ph); 5c: (recognisable signals)  $^{1}$ H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  = 3.72-3.66 (m, 1H), 3.62-3.54 (m, 1H), 2.02-1.96 (m, 1H), 1.78-1.69 (m, 1H), 1.61-1.49 (m, 1H), 1.39-1.25 (m, 4H), 0.95 (t, J = 6.8Hz, 3H), 0.79 (d, J = 14.5 Hz, 1H), 0.42 (s, 3H, CH<sub>3</sub>-Si), 0.41 (s, 3H, CH<sub>3</sub>-Si); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  = 141.0 (C), 133.5 (CH), 128.5 (CH), 127.6 (CH), 84.1 (C), 64.7 (CH<sub>2</sub>), 51.3 (CH), 32.4 (CH<sub>2</sub>), 31.2 (CH<sub>2</sub>), 27.8 (CH<sub>3</sub>), 23.4 (CH<sub>2</sub>), 22.1 (CH<sub>2</sub>), 14.5 (CH<sub>3</sub>), -0.9 (CH<sub>3</sub>), -1.2 (CH<sub>3</sub>).

# $[2RS,\!3SR]\mbox{-}2\mbox{-}Methyl\mbox{-}2\mbox{-}dimethyl\mbox{phenylsilylmethyl\mbox{-}3\mbox{-}phenyl\mbox{-}}$

**tetrahydrofuran (4d).** Chromatography gave complete separation of diastereoisomeric tetrahydrofurans. Colorless oil (58%); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.66-7.59 (m, 2H), 7.42-7.39 (m, 3H), 7.36-7.26 (m, 3H), 7.25-7.18 (m, 2H), 4.10-4.03 (m, 1H), 3.92-3.87 (m, 1H), 3.08 (t, *J* = 8.5 Hz, 1H), 2.35-2.27 (m, 2H), 1.42 (d, *J* = 14.9 Hz, 1H), 1.32 (d, *J* = 14.9 Hz, 1H), 0.91 (s, 3H), 0.48 (s, 3H, CH<sub>3</sub>-Si), 0.45 (s, 3H, CH<sub>3</sub>-Si); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  = 141.0 (C), 140.5 (C), 133.7 (CH), 128.7 (CH), 128.3 (CH), 128.1 (CH), 127.7 (CH), 126.5 (CH), 85.2 (C), 64.9 (CH<sub>2</sub>), 55.7 (CH), 31.7 (CH<sub>2</sub>), 29.9 (CH<sub>2</sub>), 24.8 (CH<sub>3</sub>), -0.94 (CH<sub>3</sub>); MS (EI): m/z 310 (M<sup>+</sup>), 295 (M<sup>+</sup>-Me), 233 (M<sup>+</sup>-Ph), 135 (SiMe<sub>2</sub>Ph); Anal. Calcd for C<sub>20</sub>H<sub>26</sub>OSi: C, 77.36; H, 8.44; Found: C, 77.68; H, 8.75.

#### [2SR,3SR]-2-Methyl-2-dimethylphenylsilylmethyl-3-phenyl-

tetrahydrofuran (5d). Colorless oil (21%); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ = 7.53-7.47 (m, 2H), 7.39-7.31 (m, 5H), 7.29-7.21 (m, 3H), 3.91-3.76 (m, 2H), 3.06 (dd, *J* = 11.2 y 7.2 Hz, 1H), 2.46-2.31 (m, 1H), 2.28-2.15 (m, 1H), 1.34 (s, 3H), 1.15 (d, *J* = 14.9 Hz, 1H), 0.42 (d, *J* = 14.9 Hz, 1H), 0.36 (s, 3H, CH<sub>3</sub>-Si), 0.33 (s, 3H, CH<sub>3</sub>-Si); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ = 140.7 (C), 139.8 (C), 133.5 (CH), 128.4 (CH), 128.1 (CH), 127.5 (CH), 126.6 (CH), 84.8 (C), 64.6 (CH<sub>2</sub>), 56.7 (CH), 30.5 (CH<sub>2</sub>), 28.1 (CH<sub>3</sub>), 24.2 (CH<sub>2</sub>), -0.9 (CH<sub>3</sub>), -1.2 (CH<sub>3</sub>); MS (EI): m/z 310 (M<sup>+</sup>), 295 (M<sup>+</sup>-Me), 233 (M<sup>+</sup>-Ph), 135 (SiMe<sub>2</sub>Ph).

**2,5-Dimethyl-2-dimethylphenylsilylmethyltetrahydrofuran** ([*2RS,5SR*] **4e and 5e** [*2SR,5SR*]). Chromatography gave tetrahydrofurans **4e** and **5e** as a mixture. Colorless oil (79%); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.62-7.52 (m, 2H), 7.43-7.35 (m, 3H), 4.12-3.97 (m, 1H), 2.08-1.94 (m, 1H), 1.82-1.62 (m, 2H), 1.60-1.43 (m, 1H), 1.45 (d, *J* = 14.5 Hz, 1H), 1.33 (d, *J* = 14.5 Hz, 1H), 1.27 (s, 3H, CH<sub>3</sub>), 1.24 (d, *J* = 6.2 Hz, 3H), 0.42 (s, 6H, (CH<sub>3</sub>)<sub>2</sub>-Si); Isomer A: <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  = 140.2 (C), 133.6 (CH), 128.7 (CH), 127.7 (CH), 83.0 (C), 73.5 (CH), 39.6 (CH<sub>2</sub>), 33.6 (CH<sub>2</sub>), 32.0 (CH<sub>2</sub>), 28.8 (CH<sub>3</sub>), 21.8 (CH<sub>3</sub>), -1.1 (CH<sub>3</sub>); Isomer B: <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  = 140.1 (C), 133.6 (CH), 128.7 (CH), 127.7 (CH), 83.0 (C), 73.9 (CH), 40.3 (CH<sub>2</sub>), 34.0 (CH<sub>2</sub>), 31.0 (CH<sub>2</sub>), 30.4 (CH<sub>3</sub>), 22.0 (CH<sub>3</sub>), -1.2 (CH<sub>3</sub>); MS (EI): m/z 248 (M<sup>+</sup>), 233 (M<sup>+</sup>-Me), 171 (M<sup>+</sup>-Ph), 135 (SiMe<sub>2</sub>Ph).

#### $\label{eq:2-2-2-2} 5- Ethyl-2-methyl-2-dimethylphenylsilylmethyltetrahydro-furantial constraints of the second s$

([2*RS*,5*SR*] 4f and 5f [2*SR*,5*SR*]). Chromatography gave tetrahydrofurans 4f and 5f as a mixture. Colorless oil (72%); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.61-7.53 (m, 2H), 7.42-7.31 (m, 3H), 3.83-3.75 (m, 1H), 2.05-1.95 (m, 1H), 1.73-1.43 (m, 5H), 1.39-1.22 (m, 2H), 1.19 (s, 3H, isomer A), 1.17 (s, 3H, isomer B), 0.99-0.91 (m, 3H), 0.36 (s, 6H, (CH<sub>3</sub>)<sub>2</sub>-Si); Isomer A: <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  = 140.2 (C), 133.6 (CH), 128.7 (CH), 127.6 (CH), 82.8 (C), 79.1 (CH), 39.4 (CH<sub>2</sub>), 31.8 (CH<sub>2</sub>), 31.3 (CH<sub>2</sub>), 29.3 (CH<sub>2</sub>), 28.5 (CH<sub>3</sub>), 10.5 (CH<sub>3</sub>), -1.0 (CH<sub>3</sub>), -1.1 (CH<sub>3</sub>); Isomer B: <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  = 140.1 (C), 133.6 (CH), 128.7 (CH), 127.6 (CH), 82.7 (C), 79.5 (CH), 40.1 (CH<sub>2</sub>), 31.5 (CH<sub>2</sub>), 30.9 (CH<sub>2</sub>), 30.2 (CH<sub>2</sub>), 29.4 (CH<sub>3</sub>), 10.3 (CH<sub>3</sub>), -1.2 (CH<sub>3</sub>); ISO (EI): m/z 261 (M<sup>+</sup>-1), 247 (M<sup>+</sup>-Me), 185 (M<sup>+</sup>-Ph), 135 (SiMe<sub>2</sub>Ph).

#### 2, 3, 3, 5-Tetramethyl-2-dimethylphenylsilylmethyl-tetrahydrofuran

([2*RS*,5*SR*] 4g and 5g [2*SR*,5*SR*]). Chromatography gave tetrahydrofurans 4g and 5g as a mixture. Colorless oil (87%); 4g: <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.69-7.59 (m, 2H), 7.43-7.35 (m, 3H), 4.21-4.09 (m, 1H), 1.89 (dd, *J* = 12.1 y 7.2 Hz, 1H), 1.58 (dd, *J* = 12.1 y 7.8 Hz, 1H), 1.26 (d, *J* = 13.5 Hz, 1H), 1.24 (d, *J* = 6.3 Hz, 3H), 1.14 (s, 3H), 1.02 (s, 3H), 1.01 (d, *J* = 13.5 Hz, 1H), 1.00 (s, 3H), 0.47 (s, 3H, CH<sub>3</sub>-Si), 0.42 (s, 3H, CH<sub>3</sub>-Si); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  = 141.4 (C), 133.7 (CH), 128.6 (CH), 127.7 (CH), 86.5 (C), 71.1 (CH), 47.8 (CH<sub>2</sub>), 45.0 (C), 26.2 (CH<sub>2</sub>), 25.3 (CH<sub>3</sub>), 24.6 (CH<sub>3</sub>), 23.1 (CH<sub>3</sub>), -0.3 (CH<sub>3</sub>), -0.4 (CH<sub>3</sub>); MS (EI): m/z 275 (M<sup>+</sup>-1), 261 (M<sup>+</sup>-Me), 199 (M<sup>+</sup>-Ph), 135 (SiMe<sub>2</sub>Ph); **5g**: (recognisable signals) <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  = 4.01-3.89 (m, 1H), 1.99 (dd, *J* = 12.6 y 8.4 Hz, 1H), 1.44 (dd, *J* = 12.6 y 6.2 Hz, 1H), 1.29 (d, *J* = 14.0 Hz, 1H), 1.23 (d, *J* = 6.2 Hz, 3H), 1.16 (s, 3H), 1.01 (s, 3H), 0.99 (s, 3H), 0.82 (d, *J* = 14.0 Hz, 1H), 0.48 (s, 3H, CH<sub>3</sub>-Si); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  = 141.2 (C), 86.4 (C), 70.3 (CH), 47.4 (CH<sub>2</sub>), 45.2 (C), 25.6 (CH<sub>3</sub>), 24.4 (CH<sub>3</sub>).

#### [2RS,3SR,5SR]-2,5-Dimethyl-2-dimethylphenylsilylmethyl-3-phenyl-

tetrahydrofuran (4h). Chromatography gave complete separation of diastereoisomeric tetrahydrofurans. Colorless oil (72%); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.63-7.60 (m, 2H), 7.40-7.38 (m, 3H), 7.33-7.24 (m, 3H), 7.20-7.17 (m, 2H), 4.17-4.06 (m, 1H), 3.24 (dd, *J* = 11.2 y 6.8 Hz, 1H), 2.31-2.21 (m, 1H), 2.03-1.92 (m, 1H), 1.46 (d, *J* = 14.9 Hz, 1H), 1.35 (d, *J* = 6.1 Hz, 3H), 1.33 (d, *J* = 14.9 Hz, 1H), 0.88 (s, 3H), 0.48 (s, 3H, CH<sub>3</sub>-Si),

0.43 (s, 3H, CH<sub>3</sub>-Si); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  = 140.7 (C), 140.6 (C), 133.7 (CH), 128.6 (CH), 128.0 (CH), 127.7 (CH), 126.4 (CH), 85.0 (C), 72.4 (CH), 57.0 (CH), 39.6 (CH<sub>2</sub>), 30.9 (CH<sub>2</sub>), 27.4 (CH<sub>3</sub>), 22.1 (CH<sub>3</sub>), -0.9 (CH<sub>3</sub>), -1.0 (CH<sub>3</sub>); MS (EI): m/z 323 (M<sup>+</sup>-1), 309 (M<sup>+</sup>-Me), 247 (M<sup>+</sup>-Ph); Anal. Calcd for C<sub>21</sub>H<sub>28</sub>OSi: C, 77.72; H, 8.70; Found: C, 78.04; H, 9.03.

#### [2SR,3SR,5SR]-2,5-Dimethyl-2-dimethylphenylsilylmethyl-3-phenyl-

tetrahydrofuran (5h). Colorless oil (15%); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.47-7.44 (m, 2H), 7.32-7.27 (m, 5H), 7.25-7.22 (m, 3H), 4.22-4.11 (m, 1H), 3.23 (dd, *J* = 12.3 y 6.1 Hz, 1H), 2.22-2.14 (m, 1H), 2.09-1.98 (m, 1H), 1.35 (s, 3H), 1.26 (d, *J* = 5.7 Hz, 3H), 1.04 (d, *J* = 14.5 Hz, 1H), 0.36 (d, *J* = 14.5 Hz, 1H), 0.34 (s, 6H, (CH<sub>3</sub>)<sub>2</sub>-Si); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  = 141.0 (C), 139.9 (C), 133.6 (CH), 128.4 (CH), 128.3 (CH), 127.5 (CH), 126.5 (CH), 84.9 (C), 73.0 (CH), 57.9 (CH), 38.7 (CH<sub>2</sub>), 29.1 (CH<sub>3</sub>), 26.8 (CH<sub>2</sub>), 21.7 (CH<sub>3</sub>), -0.5 (CH<sub>3</sub>); MS (EI): m/z 323 (M<sup>+</sup>-1), 309 (M<sup>+</sup>-Me), 247 (M<sup>+</sup>-Ph).

#### [2RS,3SR,5RS]-2-Methyl-2-dimethylphenylsilylmethyl-3,5-diphenyl-

tetrahydrofuran (4i). Chromatography gave complete separation of diastereoisomeric tetrahydrofurans. Colorless oil (67%); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.62-7.53 (m, 2H), 7.40-7.30 (m, 7H), 7.27-7.15 (m, 6H), 5.01 (dd, *J* = 10.3 and 5.8 Hz, 1H), 3.35 (dd, *J* = 12.4 and 6.2 Hz, 1H), 2.47 (ddd, *J* = 12.4, 6.2 and 5.8 Hz, 1H), 2.29 (td, *J* = 12.4 and 10.3 Hz, 1H), 1.51 (d, *J* = 14.6 Hz, 1H), 1.37 (d, *J* = 14.6 Hz, 1H), 0.92 (s, 3H), 0.44 (s, 3H), 0.40 (s, 3H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  = 144.3 (C), 140.8 (C), 139.4 (C), 133.9 (CH), 128.8 (CH), 128.4 (CH), 128.4 (CH), 128.2 (CH), 127.8 (CH), 127.1 (CH), 126.8 (CH), 125.6 (CH), 85.7 (C), 78.2 (CH), 57.7 (CH), 40.2 (CH<sub>2</sub>), 31.2 (CH<sub>2</sub>), 27.1 (CH<sub>3</sub>), -0.6 (CH<sub>3</sub>), -0.7 (CH<sub>3</sub>); Anal. Calcd for C<sub>26</sub>H<sub>30</sub>OSi: C, 80.78; H, 7.82; Found: C, 81.17; H, 8.16.

#### [2SR,3SR,5RS]-2-Methyl-2-dimethylphenylsilylmethyl-3,5-diphenyl-

tetrahydrofuran (5i). Colorless oil (15%); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.40 -7.17 (m, 15H), 5.04 (dd, *J* = 10.4 and 5.2 Hz, 1H), 3.37 (dd, *J* = 12.1 and 6.2 Hz, 1H), 2.45 (ddd, *J* = 12.1, 6.2 and 5.2 Hz, 1H), 2.31 (td, *J* = 12.1 and 10.4 Hz, 1H), 1.44 (s, 3H), 1.10 (d, *J* = 14.7 Hz, 1H), 0.46 (d, *J* = 14.7 Hz, 1H), 0.28 (s, 3H), 0.27 (s, 3H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  = 142.6 (C), 141.0 (C), 140.2 (C), 133.7 (CH), 128.7 (CH), 128.7 (CH), 128.4 (CH), 128.3 (CH), 127.8 (CH), 127.3 (CH), 126.8 (CH), 126.3 (CH), 85.7 (C), 78.8 (CH), 58.3 (CH), 40.2 (CH<sub>2</sub>), 29.4 (CH<sub>3</sub>), 26.9 (CH<sub>2</sub>), -0.3 (CH<sub>3</sub>), -0.4 (CH<sub>3</sub>).

#### [2RS,3SR,5RS]-2,5-Dimethyl-2-dimethylphenylsilylmethyl-3-phenyl-

tetrahydrofuran (6h). Chromatography gave complete separation of diastereoisomeric tetrahydrofurans. Colorless oil (67%); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.62-7.59 (m, 2H), 7.42-7.36 (m, 3H), 7.33-7.20 (m, 5H), 4.39-4.29 (m, 1H), 3.17 (dd, *J* = 10.1 y 8.8 Hz, 1H), 2.51 (ddd, *J* = 12.7, 10.1 y 8.3 Hz, 1H), 1.86 (ddd, *J* = 12.7, 8.8 y 4.6 Hz, 1H), 1.39 (d, *J* = 14.9 Hz, 1H), 1.29 (d, *J* = 6.1 Hz, 3H), 1.23 (d, *J* = 14.9 Hz, 1H), 0.91 (s, 3H), 0.47 (s, 3H, CH<sub>3</sub>-Si), 0.42 (s, 3H, CH<sub>3</sub>-Si); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  = 140.8 (C), 140.0 (C), 133.7 (CH), 128.6 (CH), 128.4 (CH), 128.0 (CH), 127.6 (CH), 126.5 (CH), 85.7 (C), 71.5 (CH), 55.3 (CH), 38.0 (CH<sub>2</sub>), 30.3 (CH<sub>2</sub>), 23.9 (CH<sub>3</sub>), 23.1 (CH<sub>3</sub>), -0.7 (CH<sub>3</sub>); MS (EI): m/z 323 (M<sup>+</sup>-1), 309 (M<sup>+</sup>-Me), 247 (M<sup>+</sup>-Ph); Anal. Calcd for C<sub>21</sub>H<sub>28</sub>OSi: C, 77.72; H, 8.70; Found: C, 78.01; H, 8.98.

# $\label{eq:second} [2SR, 3SR, 5RS] \mbox{-} 2, 5 \mbox{-} Dimethyl \mbox{-} 2 \mbox{-} dimethyl \mbox{-} phenyl \mbox{-} light \mbox{-} ligh$

tetrahydrofuran (7h). Colorless oil (19%); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.52-7.45 (m, 2H), 7.39-7.19 (m, 8H), 4.10-4.00 (m, 1H), 3.15 (dd, *J* = 11.0 y 8.3 Hz, 1H), 2.61-2.50 (m, 1H), 1.83 (ddd, *J* = 12.8, 8.3 y 3.9 Hz, 1H), 1.35 (s, 3H), 1.25 (d, *J* = 14.9 Hz, 1H), 1.23 (d, J = 6.1 Hz, 3H), 0.41 (d, *J* = 14.9 Hz, 1H), 0.38 (s, 3H, CH<sub>3</sub>-Si), 0.35 (s, 3H, CH<sub>3</sub>-Si); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  = 140.7 (C), 139.4 (C), 133.5 (CH), 128.5 (CH), 128.0 (CH), 127.5 (CH), 126.5 (CH), 85.5 (C), 70.9 (CH), 56.3 (CH), 37.0 (CH<sub>2</sub>),

28.5 (CH<sub>3</sub>), 23.1 (CH<sub>3</sub>), 22.9 (CH<sub>2</sub>), -0.9 (CH<sub>3</sub>), -1.1 (CH<sub>3</sub>); MS (EI): m/z 323 (M<sup>+</sup>-1), 309 (M<sup>+</sup>-Me), 247 (M<sup>+</sup>-Ph).

# $\label{eq:2-Methyl-2-dimethylphenylsilylmethyl-3,5-diphenyl-tetrahydrofuran$

(**6i** + 7**i**). Chromatography gave tetrahydrofurans **6i** and 7**i** as a mixture. Colorless oil (79%); **6i**: <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.52-7.45 (m, 2H), 7.28-7.13 (m, 13H), 5. 18 (dd, *J* = 8.9 and 4.2 Hz, 1H), 3.15 (dd, *J* = 10.9 and 8.4 Hz, 1H), 2.88-2.80 (m, 1H), 2.20-2.13 (m, 1H), 1.42 (d, *J* = 14.6 Hz, 1H), 1.29 (d, *J* = 14.6 Hz, 1H), 0.96 (s, 3H), 0.38 (s, 3H, CH<sub>3</sub>-Si), 0.37 (s, 3H, CH<sub>3</sub>-Si); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  = 145.1 (C), 140.8 (C), 139.4 (C), 133.8 (CH), 128.8 (CH), 128.7 (CH), 128.5 (CH), 128.3 (CH), 127.8 (CH), 126.9 (CH), 126.8 (CH), 125.8 (CH), 86.6 (C), 76.8 (CH), 56.5 (CH), 39.3 (CH<sub>2</sub>), 30.4 (CH<sub>2</sub>), 23.0 (CH<sub>3</sub>), -0.4 (CH<sub>3</sub>), -0.5 (CH<sub>3</sub>); 7**i**: (recognisable signals) <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  = 14.51 (dd, *J* = 9.0 and 3.3 Hz, 1H), 3.13-3.08 (m, 1H), 2.88-2.80 (m, 1H), 2.20-2.13 (m, 1H), 0.27 (s, 3H, CH<sub>3</sub>-Si); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  = 145.3 (C), 140.9 (C), 139.2 (C), 133.8 (CH), 128.7 (CH), 128.6 (CH), 128.4 (CH), 127.8 (CH), 126.9 (CH), 125.8 (CH), 86.3 (C), 76.8 (CH), 55.9 (CH), 38.6 (CH<sub>2</sub>), 28.5 (CH<sub>2</sub>), 23.9 (CH<sub>3</sub>), -0.7 (CH<sub>3</sub>), -0.9 (CH<sub>3</sub>).

# Acknowledgments

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- [18] Small amounts of the oxidation products (2-hydroxymethyl-5methyl-2-dimethylphenylsilylmethyltetrahydrofurans) were also obtained.
- [19] The mercuri-cyclization would proceed through a mechanism involving a bridged mercurium ion, which will undergo attack of the alcohol to give a protonated tetrahydrofuran. The irreversible deprotonation step, under basic conditions, would lead to the corresponding mercuri-tetrahydrofuran intermediate.
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- [21] Hosomi has proposed that the acid-catalyzed cyclization is not reversible, since the recovered deuterium labeled vinylsilane maintains both the configuration and the deuterium.

Table 3. Scope of the cyclization of allylsilyl alcohols **2a-f**.



Entry	Compound			1	Reagent	Mol	Temp	Time	Ratio <sup>[a]</sup>	Yield
	$\mathbb{R}^1$	$\mathbb{R}^2$	<sup>2</sup> R <sup>3</sup>			equiv	[°C]	[h]	4:5	[%]
1	Н	Н	Η	2a	Hg(OAc) <sub>2</sub>	1	-40→0	2		70
2	Н	Me	Η	2b	$Hg(OAc)_2$	1	-40→0	4	50:50	68
3	Н	Me	Η	2b	p-TsOH	0.3	0	1.5	66:34	78
4	Н	Pr	Η	2c	Hg(OAc) <sub>2</sub>	1	-40→0	2	66:34	85
5	Η	Ph	Η	2d	Hg(OAc) <sub>2</sub>	1	<b>-</b> 40→0	4	50:50	68
6	Н	Ph	Η	2d	p-TsOH	0.3	0	1.5	73:27	79
7	Н	Ph	Η	2d	AlCl <sub>3</sub>	0.5	-78	2	72:28	67 <sup>[b]</sup>
8	Me	Н	Η	2e	$Hg(OCOCF_3)_2$	1	<b>-</b> 40→0	2	50:50	79
9	Me	Н	Η	2e	p-TsOH	0.2	0	1	50:50	75
10	Et	Н	Η	2f	Hg(OAc) <sub>2</sub>	1	-40→0	2.5	50:50	70
11	Et	Η	Η	2f	p-TsOH	0.2	0	1.5	50:50	72
12	Me	Me	Me	<mark>2g</mark>	Hg(OAc) <sub>2</sub>	1	<mark>-40→0</mark>	2	<mark>66:34</mark>	<mark>74</mark>
13	Me	Me	Me	2g	p-TsOH	0.2	0	1	<mark>60:40</mark>	<mark>87</mark>

[a] The ratio of isomers 4 and 5 were determined by <sup>1</sup>H-NMR analysis. [b] Yield calculated over recovered starting material.

Table 4. Scope of the cyclization of allylsilyl alcohols 2g-i.

Entry		Compound			Reagent	Mol	Temp	Time	Ratio <sup>[b]</sup>	Yield
-	$\mathbb{R}^1$	$\mathbb{R}^2$	<sup>-</sup> R <sup>3</sup>		-	equiv	[°C]	[h]	4:5	[%]
1	Me	Ph	Η	2h	Hg(OCOCF <sub>3</sub> ) <sub>2</sub>	1	-40→0	6	60:40	75
2	Me	Ph	Η	2h	p-TsOH	0.2	0	1	83:17	87
3	Me	Ph	Η	2h	AlCl <sub>3</sub>	1	-78	2	71:29	65 <sup>[c]</sup>
4	Me	Ph	Η	2h	CHCl <sub>3</sub> <sup>[a]</sup>		62	1	72:28	35
5	Ph	Ph	Η	2i	p-TsOH	0.2	0	1	81:19	82
6	Ph	Ph	Η	2i	AlCl <sub>3</sub>	1	-78	2	70:30	69 <sup>[c]</sup>
7	Ph	Ph	Н	2i	CHCl <sub>3</sub> <sup>[a]</sup>		62	1	60:40	34

[a]  $CHCl_3$  was used as solvent. [b] The ratio of isomers 4 and 5 were determined by <sup>1</sup>H-NMR analysis.

[c] Yield calculated over recovered starting material.

Table 5. Scope of the cyclization of allylsilyl alcohols **3h-i**.



Entr	у	Compound			Reagent	<mark>Mol</mark>	Temp	Time	Ratio <sup>[b]</sup>	Yield
	$\mathbf{R}^1$	$\mathbb{R}^2$	R <sup>3</sup>		-	equiv	[°C]	[h]	6:7	[%]
1	Me	Ph	Η	3h	$Hg(OCOCF_3)_2$	1	<mark>-40→0</mark>	5	63:37	80
2	Me	Ph	Н	3h	p-TsOH	<mark>0.2</mark>	0	1	78:22	86
3	Me	Ph	Н	3h	AlCl <sub>3</sub>	1	<mark>-78</mark>	2	74:26	65 <sup>[c]</sup>
4	Me	Ph	Η	3h	CHCl <sub>3</sub> <sup>[a]</sup>		<mark>62</mark>	2	76:24	33
5	Ph	Ph	Η	3i	p-TsOH	<mark>0.2</mark>	0	1	77:23	79
6	Ph	Ph	Η	3i	AlCl <sub>3</sub>	1	<mark>-78</mark>	2	78:22	69 <sup>[c]</sup>
7	Ph	Ph	Η	3i	CHCl <sub>3</sub> <sup>[a]</sup>	<mark></mark>	<mark>62</mark>	2	78:22	37

[a] CHCl<sub>3</sub> was used as solvent. [b] The ratio of isomers 6 and 7 were determined by <sup>1</sup>H-NMR analysis.

[c] Yield calculated over recovered starting material.

# Entry for the Table of Contents ((Please choose one layout.))

Layout 2:



tetrahydrofurans from allylsilylalcohols is described, comparing the efficiency of the mercury- vs the acid-catalyzed cyclization. ((Key Topic))

Francisco J. Pulido,\* Asunción Barbero,\* Patricia Val, Alberto Diez and Alfonso González-Ortega ...... Page No. – Page No.

The efficiency of the acid-catalyzed *vs* the mercury-cyclization in the synthesis of tetrahydrofurans from allylsilyl alcohols

Keywords: Allylsilanes / Stereoselective / Tetrahydrofurane / Cyclization / Allene