Low-valent dialkoxytitanium(II): a useful tool for the synthesis of functionalized seven-membered ring compounds

Florent Bodinier*a, Youssouf Sanogoa, Janick Ardissona, Marie-Isabelle Lannoua, Geoffroy Sorin*a

Abstract: Herein, we describe an unprecedented access to all-carbon or heterocyclic seven-membered ring frameworks from 1,8-ene-yynes promoted by inexpensive low-valent titanium(II) species, readily available from Ti(OiPr)4 and Grignard reagent. A broad range of cycloheptane, azepane or oxepane derivatives has been obtained (19 examples) with moderate to good yields and an excellent selectivity (up to 95/5 d.r.).

*a Unité CNRS UMR 8038 Université Paris de Paris, Faculté de Pharmacie, Sorbonne Paris Cité, 4 avenue de l’Observatoire, 75270 PARIS cedex 06, (France)

E-mail: geoffroy.sorin@parisdescartes.fr*a
# Contents

1/ General information ............................................................................................................................3

2/ Reaction optimization ........................................................................................................................4

3/ Assumed mechanism ..........................................................................................................................5

4/ Preparation of the cyclization precursors ..........................................................................................6


   b. Protected alcohol .........................................................................................................................18

   c. Spiro-ketal type precursors .......................................................................................................19

   d. Azepane type precursors ..........................................................................................................24

   e. Oxepane type precursors .........................................................................................................28

5/ Cyclization reactions ........................................................................................................................32

   a. Tetrahydro-benzo[7]annulene type .........................................................................................33

   b. Protected alcohol .....................................................................................................................37

   c. Spiro-ketal type precursors .....................................................................................................37

   d. Azepane type ............................................................................................................................39

   e. Oxepane type ............................................................................................................................41

6/ References .......................................................................................................................................43

7/ RMN spectra ....................................................................................................................................43
1/ General information
All reactions sensitive to moisture and/or air were carried out under argon atmosphere in dry, freshly distilled solvents under anhydrous conditions using oven-dried glassware, unless otherwise noted. THF and toluene were distilled over sodium/benzophenone system, DCM, DMSO and DMF were distilled over calcium hydride. Reactions were monitored by TLC (silica gel 60 F254plates) and visualization was accomplished with UV light (254 nm & 366 nm) and subsequent use of phosphomolybdic acid solution in EtOH (5%), KMnO₄ solution or vanillin/sulphuric acid solution in EtOH, followed by heating at 100-110 °C. Flash chromatography was performed with silica gel 60 (particle size 0.040-0.063 μm).

Yield refers to chromatographically and spectroscopically pure compounds, unless otherwise noted. ¹H NMR spectra were recorded at 300 and 400 MHz. Chemical shifts are expressed in ppm, relative to the residual ¹H solvent signal (CDCl₃: δ = 7.26 ppm) as the internal reference. Coupling constants (J) are reported in hertz (Hz). The following abbreviations are used to designate the multiplicities: s = singlet; d = doublet; t = triplet; q = quartet; quint. = quintet; sext. = sextet; sept. = septet; m = multiplet; br = broad. ¹H NMR assignments were confirmed by 2D COSY spectra. The given multiplicities reflect apparent signal patterns. Diastereomer ratio (dr) was estimated by ¹H NMR spectroscopic analysis (300 and 400 MHz), unless otherwise noted. ¹³C NMR spectra were recorded at 75 MHz and 100 MHz. Chemical shifts are given in ppm relative to the residual ¹³C solvent signal (CDCl₃: δ = 77.16 ppm). ¹³C NMR assignments were confirmed by 2D HSQC and HMBC spectra. Coupling constants (J) are given in Hz for all NMR spectroscopic data. IR spectra were recorded with a FT-IR spectrometer. High-resolution mass spectra (HRMS) were measured on a mass spectrometer equipped with a TOF system and an electrospray ionization (ESI) ion source. Deuterated solvents were used as supplied.
## 2/ Reaction optimization

<table>
<thead>
<tr>
<th>Entry</th>
<th>Base</th>
<th>Time</th>
<th>T (°C)</th>
<th>Titanium</th>
<th>equiv</th>
<th>T (°C)</th>
<th>Time with Ti IV</th>
<th>RMX</th>
<th>equiv</th>
<th>T (°C)</th>
<th>Solvent</th>
<th>Concentration</th>
<th>T (°C)</th>
<th>Time</th>
<th>Conversion</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>iPrMgCl</td>
<td>15 min</td>
<td>0</td>
<td>Ti(OiPr)₄</td>
<td>2</td>
<td>0</td>
<td>10 min</td>
<td>iPrMgCl</td>
<td>4</td>
<td>-40</td>
<td>toluene</td>
<td>0,1M</td>
<td>-40</td>
<td>5h30</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>iPrMgCl</td>
<td>15 min</td>
<td>0</td>
<td>Ti(OiPr)₄</td>
<td>2</td>
<td>0</td>
<td>10 min</td>
<td>iPrMgCl</td>
<td>4</td>
<td>-40</td>
<td>toluene</td>
<td>0,1M</td>
<td>-20</td>
<td>5h30</td>
<td>20%</td>
</tr>
<tr>
<td>3</td>
<td>iPrMgCl</td>
<td>15 min</td>
<td>0</td>
<td>Ti(OiPr)₄</td>
<td>2</td>
<td>0</td>
<td>10 min</td>
<td>iPrMgCl</td>
<td>4</td>
<td>-40</td>
<td>toluene</td>
<td>0,1M</td>
<td>0</td>
<td>2h</td>
<td>43%</td>
</tr>
<tr>
<td>4</td>
<td>iPrMgCl</td>
<td>15 min</td>
<td>0</td>
<td>Ti(OiPr)₄</td>
<td>2</td>
<td>0</td>
<td>10 min</td>
<td>iPrMgCl</td>
<td>4</td>
<td>-40</td>
<td>toluene</td>
<td>0,1M</td>
<td>RT</td>
<td>30 min</td>
<td>59%</td>
</tr>
<tr>
<td>5</td>
<td>iPrMgCl</td>
<td>15 min</td>
<td>0</td>
<td>Ti(OiPr)₄</td>
<td>2</td>
<td>0</td>
<td>10 min</td>
<td>iPrMgCl</td>
<td>4</td>
<td>-40</td>
<td>toluene</td>
<td>0,1M</td>
<td>RT</td>
<td>1h</td>
<td>33%</td>
</tr>
<tr>
<td>6</td>
<td>iPrMgCl</td>
<td>15 min</td>
<td>0</td>
<td>Ti(OiPr)₄</td>
<td>2</td>
<td>0</td>
<td>10 min</td>
<td>c phenylMgBr₄BuLi</td>
<td>4</td>
<td>-40</td>
<td>toluene</td>
<td>0,1M</td>
<td>RT</td>
<td>1h</td>
<td>-</td>
</tr>
<tr>
<td>7</td>
<td>nBuLi</td>
<td>15 min</td>
<td>0</td>
<td>Ti(OiPr)₄</td>
<td>2</td>
<td>0</td>
<td>10 min</td>
<td>nBuLi</td>
<td>4</td>
<td>-40</td>
<td>toluene</td>
<td>0,1M</td>
<td>RT</td>
<td>1h</td>
<td>-</td>
</tr>
<tr>
<td>8</td>
<td>iPrMgCl</td>
<td>15 min</td>
<td>0</td>
<td>Ti(OiPr)₄</td>
<td>2</td>
<td>0</td>
<td>10 min</td>
<td>iPrMgCl</td>
<td>4</td>
<td>-40</td>
<td>toluene</td>
<td>0,1M</td>
<td>RT</td>
<td>1h</td>
<td>-</td>
</tr>
<tr>
<td>9</td>
<td>iPrMgCl</td>
<td>15 min</td>
<td>0</td>
<td>Ti(OiPr)₄</td>
<td>2</td>
<td>0</td>
<td>10 min</td>
<td>iPrMgCl</td>
<td>4</td>
<td>-40</td>
<td>toluene</td>
<td>0,1M</td>
<td>RT</td>
<td>1h</td>
<td>29%</td>
</tr>
<tr>
<td>10</td>
<td>iPrMgCl</td>
<td>15 min</td>
<td>0</td>
<td>Ti(OiPr)₄</td>
<td>2</td>
<td>0</td>
<td>10 min</td>
<td>iPrMgCl</td>
<td>4</td>
<td>-40</td>
<td>Dioxane</td>
<td>0,1M</td>
<td>RT</td>
<td>1h</td>
<td>-</td>
</tr>
<tr>
<td>11</td>
<td>iPrMgCl</td>
<td>15 min</td>
<td>0</td>
<td>Ti(OiPr)₄</td>
<td>1</td>
<td>0</td>
<td>10 min</td>
<td>iPrMgCl</td>
<td>2</td>
<td>-40</td>
<td>toluene</td>
<td>0,1M</td>
<td>RT</td>
<td>45 min</td>
<td>-</td>
</tr>
<tr>
<td>12</td>
<td>iPrMgCl</td>
<td>15 min</td>
<td>0</td>
<td>Ti(OiPr)₄</td>
<td>4</td>
<td>0</td>
<td>10 min</td>
<td>iPrMgCl</td>
<td>8</td>
<td>-40</td>
<td>toluene</td>
<td>0,1M</td>
<td>RT</td>
<td>30 min</td>
<td>50%</td>
</tr>
<tr>
<td>13</td>
<td>NaH</td>
<td>15 min</td>
<td>0</td>
<td>Ti(OiPr)₄</td>
<td>2</td>
<td>0</td>
<td>10 min</td>
<td>iPrMgCl</td>
<td>4</td>
<td>-40</td>
<td>toluene</td>
<td>0,1M</td>
<td>RT</td>
<td>30 min</td>
<td>22%</td>
</tr>
<tr>
<td>14</td>
<td>nBuLi</td>
<td>-</td>
<td>-57</td>
<td>Ti(OiPr)₄</td>
<td>2</td>
<td>0</td>
<td>10 min</td>
<td>iPrMgCl</td>
<td>4</td>
<td>-40</td>
<td>toluene</td>
<td>0,1M</td>
<td>RT</td>
<td>30 min</td>
<td>-</td>
</tr>
<tr>
<td>15</td>
<td>nBuLi</td>
<td>15 min</td>
<td>-78</td>
<td>Ti(OiPr)₄</td>
<td>2</td>
<td>-78</td>
<td>10 min</td>
<td>iPrMgCl</td>
<td>4</td>
<td>-78</td>
<td>toluene</td>
<td>0,1M</td>
<td>RT</td>
<td>30 min</td>
<td>20%</td>
</tr>
<tr>
<td>16</td>
<td>nBuLi</td>
<td>15 min</td>
<td>-78</td>
<td>Ti(OiPr)₄</td>
<td>2</td>
<td>-78</td>
<td>10 min</td>
<td>iPrMgCl</td>
<td>4</td>
<td>-78</td>
<td>toluene</td>
<td>0,1M</td>
<td>RT</td>
<td>30 min</td>
<td>44%</td>
</tr>
<tr>
<td>17</td>
<td>iPrMgCl</td>
<td>15 min</td>
<td>0</td>
<td>Ti(OiPr)₄</td>
<td>2</td>
<td>0</td>
<td>10 min</td>
<td>iPrMgCl</td>
<td>4</td>
<td>-40</td>
<td>toluene</td>
<td>0,2 M</td>
<td>RT</td>
<td>30 min</td>
<td>42%</td>
</tr>
<tr>
<td>18</td>
<td>iPrMgCl</td>
<td>15 min</td>
<td>0</td>
<td>Ti(OiPr)₄</td>
<td>2</td>
<td>0</td>
<td>10 min</td>
<td>iPrMgCl</td>
<td>4</td>
<td>-40</td>
<td>toluene</td>
<td>0,05 M</td>
<td>RT</td>
<td>30 min</td>
<td>50%</td>
</tr>
<tr>
<td>19</td>
<td>iPrMgCl</td>
<td>15 min</td>
<td>0</td>
<td>TiCl₂CP₂</td>
<td>1</td>
<td>0</td>
<td>10 min</td>
<td>iPrMgCl</td>
<td>2</td>
<td>-40</td>
<td>toluene</td>
<td>0,1M</td>
<td>RT</td>
<td>30 min</td>
<td>-</td>
</tr>
<tr>
<td>20</td>
<td>iPrMgCl</td>
<td>15 min</td>
<td>0</td>
<td>TiCl₂CP₂</td>
<td>2</td>
<td>0</td>
<td>10 min</td>
<td>iPrMgCl</td>
<td>4</td>
<td>-40</td>
<td>toluene</td>
<td>0,1M</td>
<td>RT</td>
<td>30 min</td>
<td>-</td>
</tr>
<tr>
<td>21</td>
<td>iPrMgCl</td>
<td>30 min</td>
<td>0</td>
<td>Ti(OiPr)₄</td>
<td>2</td>
<td>0</td>
<td>10 min</td>
<td>iPrMgCl</td>
<td>4</td>
<td>-40</td>
<td>toluene</td>
<td>0,1M</td>
<td>RT</td>
<td>30 min</td>
<td>44%</td>
</tr>
<tr>
<td>22</td>
<td>iPrMgCl</td>
<td>15 min</td>
<td>0</td>
<td>Ti(OiPr)₄</td>
<td>2</td>
<td>0</td>
<td>20 min</td>
<td>iPrMgCl</td>
<td>4</td>
<td>-40</td>
<td>toluene</td>
<td>0,1M</td>
<td>RT</td>
<td>30 min</td>
<td>27%</td>
</tr>
<tr>
<td>23</td>
<td>iPrMgCl</td>
<td>3 min</td>
<td>0</td>
<td>Ti(OiPr)₄</td>
<td>2</td>
<td>0</td>
<td>10 min</td>
<td>iPrMgCl</td>
<td>4</td>
<td>-40</td>
<td>toluene</td>
<td>0,1M</td>
<td>RT</td>
<td>30 min</td>
<td>58%</td>
</tr>
<tr>
<td>24</td>
<td>iPrMgCl</td>
<td>15 min</td>
<td>0</td>
<td>Ti(OiPr)₄</td>
<td>2</td>
<td>0</td>
<td>2 min</td>
<td>iPrMgCl</td>
<td>4</td>
<td>-40</td>
<td>toluene</td>
<td>0,1M</td>
<td>RT</td>
<td>30 min</td>
<td>61%</td>
</tr>
<tr>
<td>25</td>
<td>iPrMgCl</td>
<td>3 min</td>
<td>0</td>
<td>Ti(OiPr)₄</td>
<td>2</td>
<td>0</td>
<td>2 min</td>
<td>iPrMgCl</td>
<td>4</td>
<td>-40</td>
<td>toluene</td>
<td>0,1M</td>
<td>RT</td>
<td>10 min</td>
<td>64%</td>
</tr>
<tr>
<td>26</td>
<td>iPrMgCl</td>
<td>3 min</td>
<td>0</td>
<td>Ti(OiPr)₄</td>
<td>1</td>
<td>0</td>
<td>2 min</td>
<td>iPrMgCl</td>
<td>2</td>
<td>-40</td>
<td>toluene</td>
<td>0,1M</td>
<td>RT</td>
<td>30 min</td>
<td>-</td>
</tr>
<tr>
<td>27</td>
<td>iPrMgCl</td>
<td>6 min</td>
<td>0</td>
<td>Ti(OiPr)₄</td>
<td>2</td>
<td>0</td>
<td>4 min</td>
<td>iPrMgCl</td>
<td>4</td>
<td>-40</td>
<td>toluene</td>
<td>0,1M</td>
<td>RT</td>
<td>10 min</td>
<td>64%*</td>
</tr>
<tr>
<td>28</td>
<td>iPrMgCl</td>
<td>6 min</td>
<td>0</td>
<td>Ti(OiPr)₄</td>
<td>2</td>
<td>0</td>
<td>4 min</td>
<td>iPrMgCl</td>
<td>4</td>
<td>-40</td>
<td>toluene</td>
<td>0,1M</td>
<td>45 directly</td>
<td>10 min</td>
<td>57%</td>
</tr>
<tr>
<td>29</td>
<td>iPrMgCl</td>
<td>6 min</td>
<td>0</td>
<td>Ti(OiPr)₄</td>
<td>2</td>
<td>0</td>
<td>-40</td>
<td>iPrMgCl</td>
<td>4</td>
<td>-40</td>
<td>toluene</td>
<td>0,1M</td>
<td>RT</td>
<td>10 min</td>
<td>33%**</td>
</tr>
</tbody>
</table>

*6 min deprotonation and 4 min with Ti(IV) afforded a cleaner crude than 3 min deprotonation and 2 min with Ti(IV). The isolated yield is 60% with d.r. > 95:5. **iPrMgCl was added immediately after Ti(OiPr)₄. Many degradation products were observed as well as a complete loss of diastereoselectivity.
3/ Assumed mechanism

a/ Cyclization

b/ Trapping of the titanacyclopentene intermediate by acetone
c/ Assumed elimination pathway for the oxepane derivative
4/ Preparation of the cyclization precursors


1,2-phenylenedimethanol 1a

To a stirred solution of lithium aluminium hydride (9.5 g, 250 mmol, 2 equiv) in dry THF (100 mL, 2.5 M) was added dropwise, at 0 °C, a solution of phthalic anhydride (20.16 g, 136 mmol, 1 equiv) in dry THF (100 mL, 1.36 M). The green-grey solution was then stirred for 40 min at 0°C and overnight at room temperature. Reaction was quenched by a slow addition at 0 °C of water (10 mL), NaOH 15% (10 mL) and water (24 mL). The white precipitate was filtered through a Celite® pad and washed with ethyl acetate (100 mL). Concentration under reduced pressure afforded 1a (15.17 g, 110 mmol, 81 %) as a colourless oil which solidify after a few minutes as a colourless cristal. Clean 1a was used without further purification

Spectroscopic data were in accordance with those reported in literature¹.

¹H NMR (300 MHz, CDCl₃): δ 7.36 - 7.29 (m, 4H), 4.71 (s, 4H), 3.22 (s, 2H)
¹³C NMR (75 MHz, CDCl₃): δ 139.6, 129.9, 128.8, 64.5

(2-(bromomethyl)phenyl)methanol 1b

A solution of 1a (5 g, 36 mmol, 1 equiv) in toluene (70 mL, 0.5 M) was heated at 70°C. At this temperature was slowly added a solution of HBr 48 % (4.6 mL, 41 mmol, 1.14 equiv) and the solution was stirred for 4 hours at 70 °C. After total completion, monitored by TLC, the heterogeneous mixture was cooled at 0°C, quenched by addition of a saturated NaHCO₃ solution (10 mL) and extracted by diethyl ether (3 × 40 mL). The combined organic layers were washed with water (60 mL), dried over

MgSO₄ and concentrated under reduced pressure, affording clean desired 1b (5.823 g, 29 mmol, 80 %) as a brown solid which was used without further purification.

Spectroscopic data were in accordance with those reported in literature³.

\(^{1}H\) NMR (300 MHz, CDCl₃): δ 7.44 - 7.28 (m, 4H), 4.84 (d, J = 5.5 Hz, 2H), 4.64 (s, 2H), 1.92 (t, J = 5.5 Hz, 1H)

\(^{13}C\) NMR (75 MHz, CDCl₃): δ 139.3, 135.9, 130.8, 129.4, 129.1, 128.6, 62.9, 31.1

((2-(bromomethyl)benzyl)oxy)(tert-butyl)dimethylsilane 1c

To a solution of 1b (1.650 g, 8.21 mmol, 1 equiv) under argon atmosphere in dry dichloromethane (35 mL, 0.23M), was added at room temperature 2.6-lutidine (1.91 mL, 16.42 mmol, 2 equiv) and the mixture was stirred for 10 min. Tert-butyldimethylsilyl trifluoromethanesulfonate (2.64 mL, 12.31 mmol, 1.5 equiv) was then added dropwise and the solution was stirred at room temperature for 3 hours. After total completion, monitored by TLC, water (20 mL) was added and the aqueous layer was extracted by ethyl acetate (2 × 40 mL). The combined organic layers were dried over MgSO₄ and concentrated under reduced pressure. Purification of the crude by flash chromatography over silica gel (cyclohexane/ethyl acetate 1/0 to 80/20) afforded quantitatively pure 1c (2.587 g, 8.21 mmol) as a light brown oil.

Spectroscopic data were in accordance with those reported in literature³.

\(^{1}H\) NMR (300 MHz, CDCl₃): δ 7.46 - 7.44 (m, 1H), 7.35 - 7.22 (m, 3H), 4.87 (s, 2H), 4.59 (s, 2H), 0.95 (s, 9H), 0.12 (s, 6H)

\(^{13}C\) NMR (75 MHz, CDCl₃): δ 140.0, 135.0, 130.5, 129.1, 127.9, 127.8, 62.7, 31.2, 27.1, 26.2, -5.0

tert-butyldimethyl((2-(4-(trimethylsilyl)but-3-yn-1-yl)benzyl)oxy)silane 1d

To a solution of 1-(trimethylsilyl)propyne (1.82 mL, 8.21 mmol, 1.5 equiv) under argon atmosphere in dry THF (10 mL, 0.8 M) was added dropwise at -78 °C a solution of n-butyllithium (13.14 mmol, 1.6 equiv). The bright yellow solution was stirred for 30 min at -78 °C and 30 min further at 0 °C before a dropwise addition of a solution of 1c (2.587 g, 8.21 mmol, 1 equiv) in dry THF (10 mL, 0.8 M). The black solution was stirred for 4 hours at room temperature. After total completion, monitored by TLC, water (15 mL) was added and the aqueous layer was extracted by diethyl ether (3 × 20 mL). The combined organic layers were washed with brine, dried over MgSO₄, and concentrated under reduced pressure afforded crude 1d which was directly used without further purification.

General procedure to remove the tert-butyldimethylsilyl group (GP1):
To a solution of the corresponding tert-butyldimethylsilylether (6.27 mmol, 1 equiv) in THF (100 mL, 0.06 M), was added p-TsOH.H₂O (2.386 g, 12.54 mmol, 2 equiv) and the mixture was stirred for 1h30

at room temperature. After total completion, monitored by TLC, a saturated NaHCO₃ solution (50 mL) was added before extraction by ethyl acetate (2 × 50 mL). The combined organic layers were washed with brine (30 mL), dried over MgSO₄ and concentrated under reduced pressure. Purification of the crude by flash chromatography over silica gel afforded pure alcohol.

(2-(4-(trimethylsilyl)but-3-yn-1-yl)phenyl)methanol 1e

![Diagram of 1e](image)

Compound 1e was obtained from 1d following GP1 on 6.27 mmol scale (2.175 g). Purification by flash chromatography over silica gel (cyclohexane/ethyl acetate 1/0 to 80/20) afforded pure 1e as a colourless liquid (1.123 g, 4.83 mmol, 77%).

Spectroscopic data were in accordance with literature⁴.

¹H NMR (300 MHz, CDCl₃): δ 7.38 - 7.35 (m, 1H), 7.27 - 7.21 (m, 3H), 4.74 (s, 2H), 2.93 (t, J = 7.2 Hz, 2H), 2.55 (t, J = 7.2 Hz, 2H), 0.13 (s, 9H)

¹³C NMR (75 MHz, CDCl₃): δ 139.0, 138.6, 129.9, 128.8, 128.2, 126.9, 106.8, 85.6, 63.4, 31.3, 22.1, 0.2

General procedure for the Dess-Martin oxidation (GP2):
To a solution of corresponding alcohol (6.88 mmol, 1 equiv) in dichloromethane (43 mL, 0.16 M), was added Dess-Martin reagent (3.210 g, 7.57 mmol, 1.1 equiv) and the mixture was stirred for 2h at room temperature. After total completion, monitored by TLC, a saturated NaHCO₃ solution (50 mL) was added before extraction by dichloromethane (2 × 40 mL). The combined organic layers were washed with water (40 mL), dried over MgSO₄ and concentrated under reduced pressure. Pentane and diethyl ether (80/20) were added and the white insoluble solid was filtered. The resulting filtrate was concentrated under reduced pressure, affording the desired clean aldehyde which was directly used without further purification.

2-(4-(trimethylsilyl)but-3-yn-1-yl)benzaldehyde 1f

![Diagram of 1f](image)

Clean compound 1f was obtained from the corresponding alcohol 1e following GP2 on 6.88 mmol scale (1.600 g) as a yellow liquid.

Spectroscopic data were in accordance with literature⁵.

¹H NMR (300 MHz, CDCl₃): δ 10.26 (s, 1H), 7.86 - 7.83 (m, 1H), 7.56 - 7.51 (m, 1H), 7.44 - 7.39 (m, 1H), 7.35 - 7.32 (m, 1H), 3.24 (t, J = 7.2 Hz, 2H), 2.56 (t, J = 7.2 Hz, 2H), 0.10 (s, 9H)

General procedure for the addition of Grignard reagent on aldehydes (GP3):
To a solution of the corresponding aldehyde (6.88 mmol, 1 equiv) under argon atmosphere in dry THF (10 mL, 0.65 M), was added dropwise a solution of the corresponding Grignard reagent (8.26 mmol, 1.2

---

equiv) at 0 °C. The orange-brown mixture was stirred at room temperature for 2 hours. After total completion, monitored by TLC, the reaction was quenched by slow addition of a saturated NH₄Cl solution (20 mL) and extracted by ethyl acetate (3 × 20 mL). The combined organic layers were washed with brine, dried over MgSO₄ and concentrated under reduced pressure. Purification of the crude by flash chromatography over silica gel afforded pure desired allylic alcohol.

1-(2-(4-(trimethylsilyl)but-3-yn-1-yl)phenyl)prop-2-en-1-ol 1

Compound 1 was obtained by addition of vinylmagnesium bromide on the aldehyde 1f following GP3 on 6.88 mmol scale (1.584 g). Purification by flash chromatography over silica gel (cyclohexane/ethyl acetate 1/0 to 90/10) afforded pure 1 as an orange-yellow oil (1.634 g, 6.32 mmol, 92 % over 2 steps).

1H NMR (400 MHz, CDCl₃): δ 7.46 - 7.42 (m, 1H), 7.28 - 7.20 (m, 3H), 6.09 (dd, J = 17.2, 10.4, 5.2 Hz, 1H), 5.50 (d, J = 5.2 Hz, 1H), 5.36 (dd, J = 17.2, 1.2 Hz, 1H), 5.24 (dd, J = 10.4, 1.2 Hz, 1H), 2.95 (t, J = 7.6 Hz, 2H), 2.53 (t, J = 7.6 Hz, 2H), 1.94 (s, 1H), 0.14 (s, 9H)

13C NMR (100 MHz, CDCl₃): δ 140.4, 140.1, 138.2, 130.0, 128.0, 127.1, 126.9, 115.2, 106.7, 85.7, 71.5, 31.4, 22.2, 0.2

HRMS (ESI): m/z calculated for [M+H]+ 259.1513 g.mol⁻¹, found 259.1521 g.mol⁻¹, calculated for [M+Na]+ 281.1332 g.mol⁻¹, found 281.1340 g.mol⁻¹

FTIR (film cm⁻¹): ν 3345, 2958, 2173, 1641, 1488, 1450, 1335, 1248, 1114, 1038, 988, 925, 837, 755, 697

(16A and 16B) Compounds 16A and 16B were obtained by the addition of prop-1-en-1-ylmagnesium bromide on the aldehyde 1f following GP3 on 1.27 mmol scale (293 mg). Purification by flash chromatography over silica gel (cyclohexane/ethyl acetate 1/0 to 95/5) afforded a clean inseparable mixture of 16A and 16B as a yellow oil (293 mg, 1.08 mmol, 85 % over 2 steps).

16A

1H NMR (400 MHz, CDCl₃): δ 7.58 – 7.52 (m, 1H), 7.29 – 7.17 (m, 3H), 5.79 (d, J = 6.8 Hz, 1H), 5.70 – 5.61 (m, 2H), 2.99 – 2.83 (m, 2H), 2.58 – 2.42 (m, 2H), 1.98 (s, 1H), 1.86 – 1.78 (m, 3H), 0.15 (s, 9H)

13C NMR (100 MHz, CDCl₃): δ 141.6, 137.7, 132.8, 129.8, 127.6, 127.0, 126.9, 126.2, 106.9, 85.5, 66.4, 31.6, 21.9, 13.6, 0.2

HRMS (ESI): m/z calculated for [M+H]+ 273.1669 g.mol⁻¹, found 273.1678 g.mol⁻¹, calculated for [M+Na]+ 295.1489 g.mol⁻¹, found 295.1496 g.mol⁻¹

FTIR (film cm⁻¹): ν 3337, 3020, 2958, 2173, 1487, 1450, 1249, 1037, 971, 886, 838, 757, 698

16B
\[ ^1H \text{NMR (400 MHz, CDCl}_3\text{): } \delta 7.50 - 7.46 (m, 1H), 7.29 - 7.17 (m, 3H), 5.76 - 5.70 (m, 2H), 5.43 (d, J = 4.2 Hz, 1H), 2.99 - 2.83 (m, 2H), 2.58 - 2.42 (m, 2H), 2.01 (s, 1H), 1.74 - 1.71 (m, 3H), 0.15 (s, 9H) \]

\[ ^{13}C \text{NMR (100 MHz, CDCl}_3\text{): } \delta 141.1, 137.8, 133.4, 129.9, 127.7, 127.5, 127.0, 126.5, 106.8, 85.5, 71.4, 31.5, 22.0, 17.9, 0.21 \]

HRMS (ESI): m/z calculated for [M+H]^+ 273.1669 g.mol\(^{-1}\), found 273.1678 g.mol\(^{-1}\), calculated for [M+Na]^+ 295.1489 g.mol\(^{-1}\), found 295.1496 g.mol\(^{-1}\)

FTIR (film cm\(^{-1}\)): 3337, 3020, 2958, 2173, 1487, 1450, 1249, 1037, 971, 886, 838, 757, 698

2-methyl-1-(2-(4-(trimethylsilyl)but-3-yn-1-yl)phenyl)prop-2-en-1-ol 15

[Diagram of compound 15]

Compound 15 was obtained by the addition of prop-1-en-2-ylmagnesium bromide on the aldehyde 1f following GP3 on 1.74 mmol scale (400 mg). Purification by flash chromatography over silica gel (cyclohexane/ethyl acetate 1/0 to 90/10) afforded pure 15 as a yellow oil (371 mg, 1.36 mmol, 78 % over 2 steps).

\[ ^1H \text{NMR (400 MHz, CDCl}_3\text{): } \delta 7.45 - 7.36 (m, 1H), 7.29 - 7.18 (m, 3H), 5.36 (s, 1H), 5.20 (dq, J = 1.6, 0.8 Hz, 1H), 5.04 - 5.03 (m, 1H), 3.05 - 2.86 (m, 2H), 2.53 (t, J = 7.5 Hz, 2H), 2.08 (s, 1H), 1.64 (dt, J = 1.6, 0.7 Hz, 3H), 0.15 (s, 9H) \]

\[ ^{13}C \text{NMR (100 MHz, CDCl}_3\text{): } \delta 146.4, 139.5, 138.7, 130.0, 127.9, 127.0, 126.9, 111.6, 106.8, 85.5, 73.8, 31.4, 22.1, 19.5, 0.2 \]

HRMS (ESI): m/z calculated for [M+Na]^+ 295.1489 g.mol\(^{-1}\), found 295.1495 g.mol\(^{-1}\)

FTIR (film cm\(^{-1}\)): 3353, 2958, 2174, 1488, 1450, 1275, 1249, 1040, 993, 902, 838, 757, 699

General procedure for the methanolyis of silylated alkynes (GP4):

To a solution of the corresponding silylated alkyne (2.31 mmol, 1 equiv) in methanol (15 mL, 0.15 M) was added potassium carbonate (5.76 mmol, 2.5 equiv) and the heterogeneous mixture was vigorously stirred overnight at room temperature. After total completion, monitored by TLC, the mixture was concentrated under reduced pressure, diluted into water (30 mL) and extracted by ethyl acetate (2 × 50 mL). The combined organic layers were washed with brine (50 mL), dried over MgSO\(_4\) and concentrated under reduced pressure. Purification of the crude over silica gel afforded pure corresponding desired terminal alkyne.

1-(2-(4-(trimethylsilyl)but-3-yn-1-yl)phenyl)prop-2-en-1-ol 1g
Compound 1g was obtained from 1 following GP4 on 2.31 mmol scale (600 mg). Purification by flash chromatography over silica gel (cyclohexane/ethyl acetate 50/50) afforded pure 1g as a colourless oil (411 mg, 2.19 mmol, 95%).

**1H NMR** (300 MHz, CDCl₃): δ 7.48-7.44 (m, 1H), 7.29-7.21 (m, 3H), 6.09 (ddd, J = 17.1, 10.5, 5.4 Hz, 1H), 5.50 (d, J = 5.4 Hz, 1H), 5.36 (dd, J = 17.1, 1.5 Hz, 1H), 5.24 (dd, J = 10.5, 1.5 Hz, 1H), 2.96 (t, J = 7.5 Hz, 2H), 2.50 (dt, J = 7.5, 2.7 Hz, 2H), 2.00 (t, J = 2.7 Hz, 1H), 1.92 (s, 1H)

**13C NMR** (75 MHz, CDCl₃): δ 140.4, 140.1, 138.1, 129.9, 128.1, 127.2, 127.0, 115.4, 84.0, 71.6, 69.3, 31.3, 20.7

**HRMS** (ESI): calculated for [M+Na]⁺ 209.0937 g.mol⁻¹, found 209.0941 g.mol⁻¹

**FTIR** (film cm⁻¹): ν 3530, 3384, 3298, 3062, 2912, 2117, 1641, 1488, 1450, 1429, 1265, 1178, 1114, 1019, 988, 925, 756, 737, 702

**General procedure for the Sonogashira coupling (GP5):**

To a stirred solution of the corresponding iodophenyl derivative (1.2 mmol, 1.2 equiv) under argon atmosphere in distilled triethylamine (3 mL, 0.33 M) was added dropwise a solution of the corresponding alkyne (1 mmol, 1 equiv) in triethylamine (1 mL). PdCl₂(PPh₃)₂ (15 mg, 0.02 mmol, 2 mol%), CuI (9 mg, 0.04 mmol, 4 mol%) and PPh₃ (11 mg, 0.04 mmol, 4 mol%) were successively added and the heterogeneous yellow mixture was stirred with argon bubbling for 20 minutes. Further vigorous stirring overnight at room temperature gave a thick paste which was concentrated under reduced pressure. Purification of the crude over silica gel afforded pure desired coupling product.

1-(2-(4-phenylbut-3-yn-1-yl)phenyl)prop-2-en-1-ol 7

Compound 7 was obtained by coupling reaction between 1g and iodobenzene following GP5 on 1 mmol scale (186 mg). Purification by flash chromatography over silica gel (cyclohexane/ethyl acetate 1/0 to 85/15) afforded pure 7 as a yellow liquid (226 mg, 0.86 mmol, 86%).

**1H NMR** (400 MHz, CDCl₃): δ 7.48 – 7.46 (m, 1H), 7.40 – 7.36 (m, 2H), 7.31 – 7.25 (m, 6H), 6.11 (ddd, J = 17.1, 10.4, 5.3 Hz, 1H), 5.57 (d, J = 5.3 Hz, 1H), 5.37 (dt, J = 17.1, 1.5 Hz, 1H), 5.24 (dt, J = 10.4, 1.5 Hz, 1H), 3.04 (t, J = 7.7 Hz, 2H), 2.73 (t, J = 7.7 Hz, 2H), 1.95 (s, 1H)

**13C NMR** (100 MHz, CDCl₃): δ 140.4, 140.1, 138.3, 131.7, 130.0, 128.4, 128.1, 127.8, 127.1, 126.9, 123.8, 115.3, 89.5, 81.6, 71.6, 31.6, 21.7

**HRMS** (ESI): calculated for [M+H]⁺ 263.1430 g.mol⁻¹, found 263.1437 g.mol⁻¹, calculated for [M+Na]⁺ 285.1250 g.mol⁻¹, found 285.1256 g.mol⁻¹

**FTIR** (film cm⁻¹): ν 3351, 3036, 2906, 1640, 1597, 1571, 1489, 1441, 1338, 1265, 1018, 987, 924, 837, 752, 690

1-(2-(4-(4-methoxyphenyl)but-3-yn-1-yl)phenyl)prop-2-en-1-ol 9
Compound 9 was obtained by coupling reaction between 1g and 1-iodo-4-methoxybenzene following GP5 on 0.46 mmol scale (86 mg). Purification by flash chromatography over silica gel (cyclohexane/ethyl acetate 1/0 to 60/40) afforded pure 9 as a yellow oil (101 mg, 0.34 mmol, 75 %).

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta 7.50 – 7.44 (m, 1H), 7.34 – 7.30 (m, 2H), 7.27 – 7.26 (m, 3H), 6.84 – 6.79 (m, 2H), 6.10 (ddd, \(J = 17.2, 10.4, 5.2\) Hz, 1H), 5.60 – 5.54 (m, 1H), 5.36 (dt, \(J = 17.2, 1.5\) Hz, 1H), 5.23 (dt, \(J = 10.4, 1.5\) Hz, 1H), 3.79 (s, 3H), 3.03 (t, \(J = 7.8\) Hz, 2H), 2.70 (t, \(J = 7.8\) Hz, 2H), 2.03 (s, 1H)

\(^1\)C NMR (100 MHz, CDCl\(_3\)): \(\delta 159.3, 140.4, 140.1, 138.3, 133.0, 129.9, 128.0, 127.0, 126.9, 115.9, 115.2, 114.0, 87.9, 81.4, 71.6, 55.4, 31.6, 21.7\)

HRMS (ESI): calculated for [M+H]\(^+\) 293.1536 g.mol\(^{-1}\), found 293.1543 g.mol\(^{-1}\)

FTIR (film cm\(^{-1}\)): \(\nu 3394, 2918, 2837, 1605, 1508, 1462, 1441, 1288, 1243, 1172, 1106, 1030, 988, 927, 831, 756\)

Compound 1i was obtained from 1d following GP4 on 15.8 mmol scale (5.50 g). Purification by flash chromatography over silica gel (cyclohexane/ethyl acetate 1/0 to 90/10) afforded pure 1i as a brown liquid (4.35 g, 15.8 mmol, quant.).

\(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta 7.46-7.41 (m, 1H), 7.27-7.21 (m, 3H), 4.78 (s, 2H), 2.90 (t, \(J = 7.6\) Hz, 2H), 2.51 (dt, \(J = 7.6, 2.4\) Hz, 2H), 2.01 (t, \(J = 2.4\) Hz, 1H), 0.96 (s, 9H), 0.13 (s, 6H)

\(^1\)C NMR (75 MHz, CDCl\(_3\)): \(\delta 138.9, 138.0, 129.2, 127.7, 127.5, 126.7, 84.2, 69.0, 63.5, 31.3, 26.1, 20.2, -5.0\)

HRMS (ESI): calculated for [M+Na]\(^+\) 297.1645 g.mol\(^{-1}\), found 297.1246 g.mol\(^{-1}\)

FTIR (film cm\(^{-1}\)): \(\nu 3313, 2918, 2954, 2927, 2855, 1739, 1463, 1379, 1361, 1253, 1186, 1118, 1075, 1006, 835, 775, 753\)

\(\text{tert-butyldimethyl(2-(4-(tert-butyldimethylsilyl)but-3-yn-1-yl)benzyl)oxy)dimethylsilane 3a}\)
To a solution of **1i** (1.0 g, 3.64 mmol, 1 equiv) under argon atmosphere in dry THF (8 mL, 0.45 M) was added dropwise at -78 °C a solution of *n*-butyllithium (4.0 mmol, 1.1 equiv). The dark solution was stirred for 30 min at -78 °C before a dropwise addition of *tert*-butyldimethylsilyl triflate (1.82 mL, 4.0 mmol, 1.1 equiv). The solution was stirred for 1 hour at -78°C. After total completion, monitored by TLC, water (30 mL) was added and the aqueous layer was extracted by ethyl acetate (2 × 30 mL). The combined organic layers were washed with brine, dried over MgSO₄, and concentrated under reduced pressure affording crude **3a** which was directly used without further purification.

**tert**-butyldimethyl((2-(pent-3-yn-1-yl)benzyl)oxy)silane **5a**

To solution of **1i** (1 g, 3.64 mmol, 1 equiv) under argon atmosphere in dry THF (36 mL, 0.1 M) was added dropwise at -78 °C a solution of *n*-butyllithium (5.46 mmol, 1.5 equiv). The dark solution was stirred for 30 min at -78 °C before dropwise addition of iodomethane (0.32 mL, 5.10 mmol, 1.4 equiv). The black mixture was slowly warmed to room temperature and then stirred for 3 hours. After total completion, monitored by TLC, the reaction was quenched by slow addition of a saturated ammonium chloride solution (20 mL) and the aqueous layer was extracted by ethyl acetate (3 × 20 mL). The combined organic layers were washed with brine, dried over MgSO₄, and concentrated under reduced pressure affording crude **5a** which was directly used without further purification.

**diethyl (4-(2-(((tert-butyldimethylsilyl)oxy)methyl)phenyl)but-1-yn-1-yl)phosphonate** **11a**

To a solution of **1i** (972 mg, 3.54 mmol, 1 equiv) under argon atmosphere in dry THF (10 mL, 0.35 M) was added dropwise at -78 °C a solution of *n*-butyllithium (3.89 mmol, 1.1 equiv). The dark solution was stirred for 1 hour at -78 °C before a dropwise addition of a solution of diethylchlorophosphate (0.56 mL, 3.89 mmol, 1.1 equiv) in 4 mL of dry THF. The solution was stirred for 1 hour at -78°C and 4 hour at room temperature. After total completion, monitored by TLC, a saturated NH₄Cl solution (20 mL) was added and the aqueous layer was extracted by ethyl acetate (3 × 20 mL). The combined organic layers were washed with brine, dried over MgSO₄, and concentrated under reduced pressure affording crude **11a** which was directly used without further purification.

**(2-(4-((tert-butyldimethylsilyl)but-3-yn-1-yl)phenyl)methanol** **3b**
Compound 3b was obtained from 3a following GP1 on 3.64 mmol scale (1.415 g). Purification by flash chromatography over silica gel (cyclohexane/ethyl acetate 1/0 to 90/10) afforded pure 3b as a yellow liquid (703 mg, 2.55 mmol, 70% over 2 steps).

\[ ^1H \text{NMR } (300 \text{ MHz, CDCl}_3): \delta 7.37-7.34 (m, 1H), 7.27-7.21 (m, 3H), 4.74 (s, 2H), 2.94 (t, J = 7.5 \text{ Hz,} 2H), 2.56 (t, J = 7.5 \text{ Hz,} 2H), 1.59 (bs, 1H), 0.88 (s, 9H), 0.06 (s, 6H) \]

\[ ^{13}C \text{NMR } (75 \text{ MHz, CDCl}_3): \delta 139.0, 138.5, 129.9, 128.8, 128.3, 126.8, 107.2, 83.8, 63.5, 31.3, 29.9, 26.2, 22.0, -4.3 \]

HRMS (ESI): calculated for [M+H]\(^+\) 275.1826 g.mol\(^{-1}\), found 275.1823 g.mol\(^{-1}\)

FTIR (film cm\(^{-1}\)): \( \nu 3309, 2953, 2927, 2855, 2172, 1471, 1462, 1361, 1275, 1249, 1039, 1007, 836, 824, 809, 773, 751, 680 \)

(2-(pent-3-yn-1-yl)phenyl)methanol 5b

Compound 5b was obtained from 5a following GP1 on 3.64 mmol scale (1.050 g). Purification by flash chromatography over silica gel (cyclohexane/ethyl acetate 1/0 to 80/20) afforded pure 5b as a yellow liquid (371 mg, 2.11 mmol, 58% over 2 steps).

\[ ^1H \text{NMR } (300 \text{ MHz, CDCl}_3): \delta 7.38-7.35 (m, 1H), 7.31-7.20 (m, 3H), 4.71 (s, 2H), 2.89 (t, J = 7.5 \text{ Hz,} 2H), 2.45 (tq, J = 7.5, 2.7 \text{ Hz}), 1.96 (s, 1H), 1.76 (t, J = 2.7 \text{ Hz,} 3H) \]

\[ ^{13}C \text{NMR } (75 \text{ MHz, CDCl}_3): \delta 139.3, 138.7, 129.7, 128.8, 128.3, 126.8, 78.9, 76.7, 63.3, 31.8, 20.9, 3.6 \]

HRMS (ESI): calculated for [M+H]\(^+\) 175.1117 g.mol\(^{-1}\), found 175.1117 g.mol\(^{-1}\)

FTIR (film cm\(^{-1}\)): \( \nu 3341, 3020, 2919, 1491, 1453, 1210, 1183, 1005, 836, 824, 753 \)

diethyl (4-(2-(hydroxymethyl)phenyl)but-1-yn-1-yl)phosphonate 11b

Compound 11b was obtained from 11a following GP1 on 3.54 mmol scale (1.453 g). Purification by flash chromatography over silica gel (cyclohexane/ethyl acetate 50/50 to 20/80) afforded pure 11b as a yellow liquid (673 mg, 2.27 mmol, 64% over 2 steps).

\[ ^1H \text{NMR } (300 \text{ MHz, CDCl}_3): \delta 7.44-7.41 (m, 1H), 7.27-7.18 (m, 3H), 4.74 (s, 2H), 4.10-3.98 (m, 4H), 2.97 (t, J = 7.2 \text{ Hz,} 2H), 2.67 (dt, J = 7.2, 4.5 \text{ Hz,} 2H), 2.23 (s, 1H), 1.30 (t, J = 7.2 \text{ Hz,} 6H) \]

\[ ^{31}P \text{NMR } (300 \text{ MHz, CDCl}_3): \delta -6.21 \]

\[ ^{13}C \text{NMR } (75 \text{ MHz, CDCl}_3): \delta 139.2, 137.6, 129.5, 128.6, 128.1, 127.1, 102.6 (d, J = 52.7 \text{ Hz}), 71.5 (d, J = 301.6 \text{ Hz}), 63.2, 63.1, 29.8 (d, J = 2.3 \text{ Hz}), 21.4 (d, J = 4.5 \text{ Hz}), 16.2, 16.1 \]

HRMS (ESI): calculated for [M+H]\(^+\) 297.1250 g.mol\(^{-1}\), found 297.1247 g.mol\(^{-1}\)

FTIR (film cm\(^{-1}\)): \( \nu 3394, 2984, 2930, 2203, 1455, 1393, 1245, 1163, 1015, 974, 889, 797, 756 \)

2-(4-((tert-butyldimethylsilyl)but-3-yn-1-yl)benzaldehyde 3c
Crude compound 3c was obtained from the corresponding alcohol 3b following GP2 on 1.80 mmol scale (490 mg) and was directly used without purification.

2-(pent-3-yn-1-yl)benzaldehyde 5c

Crude compound 5c was obtained from the corresponding alcohol 5b following GP2 on 1.91 mmol scale (329 mg) and was directly used without purification.

diethyl (4-(2-formylphenyl)but-1-yn-1-yl)phosphonate 11c

Crude compound 11c was obtained from the corresponding alcohol 11b following GP2 on 2.27 mmol scale (673 mg) and was directly used without purification.

1-(2-(4-((tert-butyldimethylsilyl)but-3-yn-1-yl)phenyl)prop-2-en-1-ol 3

Compound 3 was obtained by the addition of vinylmagnesium bromide on the aldehyde 3c following GP3 on 1.80 mmol scale (490 mg). Purification by flash chromatography over silica gel (cyclohexane/ethyl acetate 80/20) afforded pure 3 as a yellow oil (351 mg, 1.17 mmol, 65 % over 2 steps).

\textbf{1H NMR} (400 MHz, CDCl$_3$): $\delta$ 7.45 - 7.42 (m, 1H), 7.27 - 7.23 (m, 3H), 6.07 (ddd, $J = 17.2, 10.4, 5.2$ Hz, 1H), 5.44 (dt, $J = 5.2, 1.6$ Hz, 1H), 5.35-5.30 (m, 1H), 5.24-5.21 (m, 1H), 2.94 (t, $J = 7.6$ Hz, 2H), 2.53 (t, $J = 7.6$ Hz, 2H), 2.45 (s, 1H), 0.94 (s, 9H), 0.14 (s, 6H)

\textbf{13C NMR} (100 MHz, CDCl$_3$): $\delta$ 140.2, 140.0, 138.1, 130.0, 127.8, 126.9, 126.8, 115.1, 107.2, 83.6, 71.4, 31.5, 26.2, 21.9, 16.6, -4.4

\textbf{HRMS} (ESI): calculated for [M+H]$^+$ 301.1982 g.mol$^{-1}$, found 301.1985 g.mol$^{-1}$, calculated for [M+Na]$^+$ 323.1802 g.mol$^{-1}$, found 323.1803 g.mol$^{-1}$

\textbf{FTIR} (film cm$^{-1}$): $\nu$ 3342, 2953, 2928, 2856, 2172, 1489, 1471, 1462, 1408, 1361, 1249, 1115, 1037, 1007, 989, 926, 884, 836, 824, 809, 773, 754, 679
1-(2-(pent-3-yn-1-yl)phenyl)prop-2-en-1-ol 5

Compound 5 was obtained by the addition of vinylmagnesium bromide on the aldehyde 5c following GP3 on 1.91 mmol scale (329 mg). Purification by flash chromatography over silica gel (cyclohexane/ethyl acetate 80/20) afforded pure 5 as a colourless oil (206 mg, 1.03 mmol, 54 % over 2 steps).

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.46 – 7.42 (m, 1H), 7.28 – 7.19 (m, 3H), 6.09 (ddd, $J = 17.1$, 10.4, 5.3 Hz, 1H), 5.52 (d, $J = 5.3$ Hz, 1H), 5.36 (dt, $J = 17.2$, 1.5 Hz, 1H), 5.23 (dt, $J = 10.4$, 1.5 Hz, 1H), 2.91 (t, $J = 7.6$ Hz, 2H), 2.47 – 2.41 (m, 2H), 1.99 (s, 1H), 1.77 (t, $J = 2.5$ Hz, 3H)

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 140.4, 140.1, 138.6, 129.8, 128.0, 127.0, 126.9, 115.2, 78.7, 76.7, 71.5, 31.9, 21.1, 3.6

HRMS (ESI): calculated for [M+H]$^+$ 201.1274 g.mol$^{-1}$, found 201.1279 g.mol$^{-1}$, calculated for [M+Na]$^+$ 223.1093 g.mol$^{-1}$, found 223.1097 g.mol$^{-1}$

FTIR (film cm$^{-1}$): $\nu$ 3354, 2918, 2852, 1640, 1603, 1488, 1450, 1338, 1247, 1178, 1112, 1019, 987, 924, 829, 753, 674

diethyl (4-(2-(1-hydroxyallyl)phenyl)but-1-yn-1-yl)phosphonate 11

Compound 11 was obtained by the addition of vinylmagnesium bromide on the aldehyde 11c following GP3 on 2.27 mmol scale (673 mg). Purification by flash chromatography over silica gel (cyclohexane/ethyl acetate 50/50 to 20/80) afforded pure 11 as a viscous brown oil (460 mg, 1.43 mmol, 63 % over 2 steps).

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.45-7.42 (m, 1H), 7.19-7.08 (m, 3H), 5.98 (ddd, $J = 17.2$, 10.4, 5.2 Hz, 1H), 5.40 (d, $J = 5.2$ Hz, 1H), 5.18-5.13 (m, 1H), 5.09-5.06 (m, 1H), 4.02-3.95 (m, 2H), 3.95-3.84 (m, 2H), 2.97-2.83 (m, 2H), 2.66-2.51 (m, 2H), 1.25 (t, $J = 7.2$ Hz, 3H), 1.19 (t, $J = 7.2$ Hz)

$^{31}$P NMR (400 MHz, CDCl$_3$): $\delta$ -5.93(s)

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 141.4, 140.4, 136.4, 129.3, 127.4, 126.96, 126.94, 114.6, 102.7 (d, $J = 210$ Hz), 71.2 (d, $J = 1199$ Hz), 71.1, 63.0 (d, $J = 22$ Hz), 29.6, 21.2 (d, $J = 17$ Hz), 15.9 (t, $J = 29$ Hz)

HRMS (ESI): calculated for [M+Na]$^+$ 345.1226 g.mol$^{-1}$, found 345.1224 g.mol$^{-1}$

FTIR (film cm$^{-1}$): $\nu$ 3390, 2982, 2923, 2846, 2204, 1639, 1449, 1393, 1247, 1164, 1099, 1021, 979, 799, 760

1-(2-(4-(trimethylsilyl)but-3-yn-1-yl)phenyl)ethanol 13a
Crude compound 13a was obtained by the addition of methylmagnesium bromide on the aldehyde 1f following GP3 on 2.17 mmol scale (500 mg) and was directly used without purification.

1-(2-(4-(trimethylsilyl)but-3-yn-1-yl)phenyl)ethanone 13b

Crude compound 13b was obtained from 13a following GP2 and was directly used without purification.

2-(2-(4-(trimethylsilyl)but-3-yn-1-yl)phenyl)but-3-en-2-ol 13

Compound 13 was obtained by the addition of vinylmagnesium bromide on the ketone 13b following GP3 on 2.17 mmol scale (530 mg). Purification by flash chromatography over silica gel (cyclohexane/ethyl acetate 1/0 to 98/2) afforded pure 13 as a colourless oil (244 mg, 0.89 mmol, 41 % over 3 steps).

\[ ^1 H \text{NMR (400 MHz, CDCl}_3\): } \delta 7.48 – 7.40 (m, 1H), 7.31 – 7.14 (m, 3H), 6.22 (ddd, \ J = 17.4, 10.6, 1.0 Hz, 1H), 5.15 (dt, \ J = 17.4, 1.0 Hz, 1H), 5.13 (dt, \ J = 10.6, 1.0 Hz, 1H), 3.21 – 2.97 (m, 2H), 2.58 – 2.49 (m, 2H), 1.72 (s, 3H), 0.13 (s, 9H) \]

\[ ^13 C \text{NMR (100 MHz, CDCl}_3\): } \delta 145.6, 143.5, 139.6, 131.7, 127.6, 126.3, 126.1, 112.7, 107.7, 85.4, 75.9, 32.5, 30.4, 22.6, 0.3 \]

\[ \text{HRMS (ESI): calculated for [M+H]^+ 273.1669 g.mol}^{-1}, \text{found 273.1672 g.mol}^{-1}, \text{calculated for [M+Na]^+ 295.1489 g.mol}^{-1}, \text{found 295.1488 g.mol}^{-1} \]

\[ \text{FTIR (film cm}^{-1})\text{: } \nu 3453, 2959, 2172, 1673, 1487, 1445, 1407, 1368, 1335, 1248, 1216, 1098, 1044, 994, 922, 838, 757, 698 \]

b. Protected alcohol

tert-butyldimethyl(1-(2-(4-(trimethylsilyl)but-3-yn-1-yl)phenyl)allyl)oxy)silane 19
To a solution of 1 (250 mg, 0.97 mmol, 1 equiv) under argon atmosphere in dry dichloromethane (5 mL, 0.23M), was added at room temperature 2.6-lutidine (0.22 mL, 1.94 mmol, 2 equiv) and the mixture was stirred for 10 min. tert-butyldimethylsilyl trifluoromethanesulfonate (0.31 mL, 1.45 mmol, 1.5 equiv) was then added dropwise and the solution was stirred at room temperature for 2 hours. After total completion, monitored by TLC, water (10 mL) was added and the aqueous layer was extracted by ethyl acetate (2 × 20 mL). The combined organic layers were dried over MgSO\(_4\) and concentrated under reduced pressure. Purification of the crude by flash chromatography over silica gel (cyclohexane/ethyl acetate 1/0 to 90/10) afforded pure 19 (315 mg, 0.84 mmol, 87 %) as a brown liquid.

\( ^1H\) NMR (400 MHz, CDCl\(_3\)): \( \delta \) 7.48 – 7.42 (m, 1H), 7.25 – 7.14 (m, 3H), 5.95 (ddd, \( J = 17.0, 10.3, 5.2 \) Hz, 1H), 5.36 (ddd, \( J = 5.2, 1.6, 1.6 \) Hz, 1H), 5.23 (ddd, \( J = 17.0, 1.6, 1.6 \) Hz, 1H), 5.07 (ddd, \( J = 10.3, 1.6, 1.6 \) Hz, 1H), 2.94 – 2.89 (m, 2H), 2.53 – 2.42 (m, 2H), 0.91 (s, 9H), 0.16 (s, 9H), 0.08 (s, 3H), -0.04 (s, 3H)

\( ^{13}C\) NMR (100 MHz, CDCl\(_3\)): \( \delta \) 141.4, 141.2, 137.1, 129.5, 127.2, 126.7, 113.7, 106.9, 85.2, 77.4, 73.1, 31.5, 26.0, 21.6, 18.4, 0.3, -4.5, -4.6

HRMS (ESI): m/z, calculated for [M+H]\(^+\) 373.2383 g.mol\(^{-1}\), found 373.2375 g.mol\(^{-1}\), calculated for [M+Na]\(^+\) 395.2202 g.mol\(^{-1}\), found 395.2196 g.mol\(^{-1}\)

FTIR (film cm\(^{-1}\)): \( \nu \) 2956, 2929, 2897, 2857, 2175, 1471, 1462, 1407, 1249, 1128, 1101, 1064, 1034, 988, 921, 833, 774, 753, 697, 676

(4-(2-(1-methoxyallyl)phenyl)but-1-yn-1-yl)trimethylsilane 21

To a suspension of NaH (60 mg, 1.5 mmol, 1.5 equiv) under argon atmosphere in dry THF (3 mL, 0.5M), was added at 0 °C a solution of 1 (258 mg, 1 mmol, 1 equiv) in dry THF (1 mL). Stirring was kept 30 minutes at 0 °C before dropwise addition of iodomethane (0.1 mL, 1.5 mmol, 1.5 equiv) and the mixture was stirred overnight at room temperature. After total completion, monitored by TLC, a saturated NH\(_4\)Cl solution (25 mL) was added and the aqueous layer was extracted by ethyl acetate (2 × 25 mL). The combined organic layers were washed with brine (25 mL), dried over MgSO\(_4\) and concentrated under reduced pressure. Purification of the crude by flash chromatography over silica gel (cyclohexane/ethyl acetate 1/0 to 80/20) afforded pure 21 (227 mg, 0.83 mmol, 83 %) as a yellow liquid.

\( ^1H\) NMR (400 MHz, CDCl\(_3\)): \( \delta \) 7.42 – 7.37 (m, 1H), 7.28 – 7.20 (m, 3H), 5.97 (ddd, \( J = 16.9, 10.6, 6.3 \) Hz, 1H), 5.25 (dt, \( J = 7.8, 1.4 \) Hz, 1H), 5.21 (d, \( J = 1.3 \) Hz, 1H), 4.88 (dt, \( J = 6.2, 1.3 \) Hz, 1H), 3.32 (s, 3H), 2.94 – 2.87 (m, 2H), 2.52 – 2.45 (m, 2H), 0.15 (s, 9H)

\( ^{13}C\) NMR (100 MHz, CDCl\(_3\)): \( \delta \) 138.5, 138.4, 129.9, 127.8, 127.2, 127.0, 116.7, 106.7, 85.3, 81.2, 77.4, 56.6, 31.7, 21.8, 0.2

HRMS (ESI): m/z calculated for [M+H]\(^+\) 273.1669 g.mol\(^{-1}\), found 273.1672 g.mol\(^{-1}\)

FTIR (film cm\(^{-1}\)): \( \nu \) 3073, 3020, 2958, 2931, 2898, 2820, 2174, 1488, 1450, 1337, 1249, 1082, 1041, 991, 926, 885, 839, 756, 699

c. Spiro-ketal type precursors
General procedure for the silylation of a terminal alkyne with an alcohol (GP6):
To a stirred solution of the corresponding terminal alkyne (35.7 mmol, 1 equiv) in dry THF (75 mL, 0.5 M) under argon atmosphere was added dropwise a n-butyllithium solution (75 mmol, 2 equiv) at -78°C. Stirring was kept at this temperature for 30 minutes before the dropwise addition of freshly distilled trimethylsilyl chloride (9.1 mL, 71.4 mmol, 2.1 equiv). Stirring was kept further 30 minutes at -78°C before slow addition of a concentrated HCl solution (25 mL). The aqueous layer was extracted by ethyl acetate (2 × 30 mL). The combined organic layers were washed with a saturated NaHCO₃ solution (50 mL), dried over MgSO₄, and concentrated under reduced pressure.

3-(trimethylsilyl)prop-2-yn-1-ol 24a

Compound 24a was obtained from commercially available propargylic alcohol following GP6 on 35.7 mmol scale (2.07 mL). Pure 24a was quantitatively obtained after concentration under reduced pressure (4.578 g, 35.7 mmol) as a clear yellow liquid.

Spectroscopic data were in accordance with those reported in literature⁶.

¹H NMR (300 MHz, CDCl₃): δ 4.27 (s, 2H), 0.18 (s, 9H)
¹³C NMR (75 MHz, CDCl₃): δ 103.9, 90.8, 51.8, -0.1

(3-bromoprop-1-yn-1-yl)trimethylsilane 24b

To a stirred solution of 24a (4.578 g, 35.7 mmol, 1 equiv) in dry Et₂O (35 mL, 1 M) under argon atmosphere was added dropwise at room temperature phosphorus tribromide (12.5 mL, 12.5 mmol, 1 M in CH₂Cl₂, 0.35 equiv). After stirring overnight at room temperature, a saturated NaHCO₃ solution (80

---

mL) was slowly added. The aqueous layer was extracted by Et₂O (2 × 45 mL). The combined organic layers were dried over MgSO₄, and cautiously concentrated under reduced pressure (700 mbar at 30°C) affording quantitatively pure 24b (6.824 g, 35.7 mmol) as a yellow liquid and was used without further purification.

Spectroscopic data were in accordance with those reported in literature⁷.

¹H NMR (300 MHz, CDCl₃): δ 3.91 (s, 2H), 0.18 (s, 9H)

diethyl 2-(3-(trimethylsilyl)prop-2-yn-1-yl)malonate 24c

Commercially available diethylmalonate (16.3 mL, 107.1 mmol, 3 equiv) was added dropwise at 0°C to a solution of sodium hydride (1.43 g, 35.7 mmol, 60% in mineral oil, 1 equiv) in dry THF (85 mL, 0.4 M) under argon atmosphere. After stirring 30 minutes at room temperature, 24b (6.824 g, 35.7 mmol, 1 equiv) was added dropwise at 0°C. The dark-brown solution was then vigorously stirred overnight at room temperature. After total completion, monitored by TLC, the reaction was quenched by slow addition of water (50 mL). The aqueous layer was extracted by ethyl acetate (3 × 50 mL). The combined organic layers were dried over MgSO₄ and concentrated. Distillation under reduced pressure (15 mbar, 65°C) of the crude mixture afforded pure 24c (4.647 g, 17.14 mmol, 48 %) as a colourless liquid.

Spectroscopic data were in accordance with those reported in literature⁸.

¹H NMR (300 MHz, CDCl₃): δ 4.22 (q, J = 7.2 Hz, 4H), 3.55 (t, J = 7.8 Hz, 1H), 2.80 (d, J = 7.8 Hz, 2H), 1.28 (t, J = 7.2 Hz, 6H), 0.12 (s, 9H)
¹³C NMR (75 MHz, CDCl₃): δ 168.1, 102.4, 76.6, 61.8, 51.5, 20.0, 14.2, 0.1

diethyl 2-(but-3-en-1-yl)-2-(3-(trimethylsilyl)prop-2-yn-1-yl)malonate 24d

24c (4.624 g, 17.1 mmol, 1 equiv) was added dropwise at 0°C to a solution of sodium hydride (750 mg, 18.8 mmol, 60% in mineral oil, 1.1 equiv) in dry DMF (15 mL, 1.25 M) under argon atmosphere. After stirring 30 minutes, allyl bromide (1.91 mL, 18.8 mmol, 1.1 equiv) was added dropwise. The dark solution was then vigorously stirred overnight at room temperature. After total completion, monitored by TLC, the reaction was quenched by slow addition of a saturated NH₄Cl solution (50 mL). The aqueous layer was extracted by diethyl ether (2 × 45 mL). The combined organic layers were washed by brine (50 mL), dried over MgSO₄ and concentrated under reduced pressure affording crude 24d which was directly used without further purification.

2-(but-3-en-1-yl)-2-(3-(trimethylsilyl)prop-2-yn-1-yl)propane-1,3-diol 24e

---

To a stirred solution of LiAlH$_4$ (1.3 g, 34.2 mmol, 2 equiv) in dry THF (35 mL, 1 M) under argon atmosphere was dropwise added a solution of 24d (5.548 g, 17.1 mmol, 1 equiv) in dry THF (15 mL, 1.25 M) via cannula at 0°C. The green-grey solution was then stirred 4 h at room temperature. After total completion, monitored by TLC, water (4 mL) was added dropwise at 0°C, followed by NaOH 15% (4 mL) and water (12 mL). The white precipitate was filtered through a Celite® pad and washed with ethyl acetate (60 mL). The organic layer was washed by water (40 mL), brine (40 mL), dried over MgSO$_4$ and concentrated under pressure affording crude 24e which was directly used without further purification.

(3-(5-(but-3-en-1-yl)-2,2-dimethyl-1,3-dioxan-5-y1)prop-1-yn-1-yl)trimethylsilane 24f

To a solution of 24d (4.111 g, 17.1 mmol, 1 equiv) in 85 mL of dichloromethane, were successively added 2,2-dimethoxypropane (10.4 mL, 85 mmol, 5 equiv) and pyridinium p-toluenesulfonate (430 mg, 1.71 mmol, 0.2 equiv). The solution was then stirred overnight at room temperature. After total completion, monitored by TLC, a saturated NaHCO$_3$ solution (60 mL) was added and the aqueous layer was extracted by dichloromethane (3 × 50 mL). The combined organic layers were washed with brine (50 mL), dried over MgSO$_4$ and concentrated under reduced pressure. Purification of the crude by flash chromatography over silica gel (cyclohexane/ethyl acetate 1/0 to 90/10) afforded pure 24f (3.933 g, 14.0 mmol, 83% over 3 steps) as a colourless liquid.

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 5.80 (ddt, $J = 17.1, 10.2, 6.6$ Hz, 1H), 5.04 (ddt, $J = 17.1, 1.8, 1.5$ Hz, 1H), 4.99-4.93 (m, 1H), 3.71-3.61 (m, 4H), 2.45 (s, 2H), 2.06-1.98 (m, 2H), 1.48-1.40 (m, 8H), 0.14 (s, 9H)

$^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 138.7, 114.9, 114.8, 103.6, 98.2, 87.4, 67.2, 32.2, 27.2, 26.3, 23.7, 21.5, 0.2

HRMS (ESI): calculated for [M+H]$^+$ 281.1931 g.mol$^{-1}$, found 281.1930 g.mol$^{-1}$

FTIR (film cm$^{-1}$): $\nu$ 2992, 2957, 2860, 2174, 1642, 1453, 1370, 1249, 1196, 1155, 1120, 1072, 1038, 838, 759, 732, 698

General procedure for the ozonolysis reactions (GP7):
A stirred solution of the corresponding alkene (6.96 mmol, 1 equiv) in dichloromethane (14 mL, 0.5M) was bubbled with ozone at -78°C. After total completion, monitored by TLC, triphenylphosphine (2.74 g, 10.4 mmol, 1.5 equiv) was slowly added at -78°C. The orange mixture was allowed to warm to room temperature and stirred for 2 hours. Concentration under reduced pressure afforded the crude desired aldehyde with triphenylphosphine and triphenylphosphine oxide which was directly further used without purification.

3-(2,2-dimethyl-5-(3-(trimethylsilyl)prop-2-yn-1-yl)-1,3-dioxan-5-yl)propanal 24g
Crude aldehyde 24g was obtained from 24f following GP7 on 6.96 mmol scale (1.952 g).

5-(2,2-dimethyl-5-(3-(trimethylsilyl)prop-2-yn-1-yl)-1,3-dioxan-5-yl)pent-1-en-3-ol 24

Compound 24 was obtained by addition of vinylmagnesium bromide on the aldehyde 24g following GP3 on 6.96 mmol scale (1.95 g). Purification by flash chromatography over silica gel (cyclohexane/ethyl acetate 1/0 to 70/30) afforded pure 24 a colourless liquid (1.982 g, 6.38 mmol, 92 % over 2 steps).

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 5.84 (ddd, $J = 16.8$, 10.4, 6.0 Hz, 1H), 5.23 (dd, $J = 16.8$, 1.2 Hz, 1H), 5.12 (dd, $J = 10.4$, 1.2 Hz, 1H), 4.05 (br s, 1H), 3.67-3.58 (m, 4H), 2.45 (d, $J = 16.8$ Hz, 1H), 2.38 (d, $J = 16.8$ Hz, 1H), 1.76 (br s, 1H), 1.52-1.45 (m, 7H), 0.12 (s, 9H)

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 140.9, 115.3, 103.6, 98.3, 87.4, 73.6, 67.3, 67.2, 35.1, 28.3, 26.2, 23.6, 21.5, 0.2

HRMS (ESI): calculated for [M+H]$^+$ 311.2037 g.mol$^{-1}$, found 311.2044 g.mol$^{-1}$

FTIR (film cm$^{-1}$): $\nu$ 3447, 2992, 2921, 2861, 2173, 1644, 1453, 1426, 1371, 1249, 1195, 1155, 1121, 1078, 1036, 990, 922, 839, 759, 731, 698

5-(2,2-dimethyl-5-(prop-2-yn-1-yl)-1,3-dioxan-5-yl)pent-1-en-3-ol 24h

Compound 24h was obtained from 24 following GP4 on 1.61 mmol scale (500 mg). Purification by flash chromatography over silica gel (cyclohexane/ethyl acetate 70/30) afforded quantitatively pure 24h as a colourless oil (383 mg, 1.61 mmol).
Compound 26 was obtained by coupling reaction between 24h and iodobenzene following GP5 on 0.5 mmol scale (120 mg). Purification by flash chromatography over silica gel (cyclohexane/ethyl acetate 1/0 to 70/30) afforded pure 26 as a yellow oil (137 mg, 0.44 mmol, 88 % over 2 steps).

Compound 28 was obtained by coupling reaction between 24h and 1-iodo-4-methoxybenzene following GP5 on 0.5 mmol scale (120 mg). Purification by flash chromatography over silica gel (cyclohexane/ethyl acetate 1/0 to 60/40) afforded pure 28 as a yellow oil (144 mg, 0.42 mmol, 84 % over 2 steps).
**13C NMR** (100 MHz, CDCl₃): δ 159.2, 140.9, 133.0, 116.0, 115.3, 113.9, 98.3, 84.8, 82.9, 73.6, 67.4, 67.3, 55.4, 35.5, 30.1, 28.5, 26.5, 23.2, 21.3

**HRMS** (ESI): calculated for [M+H]+ 345.1988 g.mol⁻¹, found 345.2059 g.mol⁻¹, calculated for [M+Na]+ 367.1880 g.mol⁻¹, found 367.1878 g.mol⁻¹

**FTIR** (film cm⁻¹): ν 3452, 2991, 2937, 2862, 1606, 1508, 1453, 1372, 1287, 1244, 1195, 1172, 1076, 1030, 991, 924, 828, 750, 687, 666

### d. Azepane type precursors

![Diagram of azepane type precursors](image)

**4-methyl-N-(prop-2-yn-1-yl)benzenesulfonylamide 30a**

To a stirred solution of commercially available propargylamine (3.84 mL, 60 mmol, 1.2 equiv) in dry dichloromethane (50 mL, 1.2 M) under argon atmosphere was added triethylamine (9.5 mL, 70 mmol, 1.4 equiv), followed by tosyl chloride (9.53 g, 50 mmol, 1 equiv) portionwise at 0°C. After stirring overnight at room temperature, water (50 mL) was added. The aqueous layer was extracted by dichloromethane (2 × 50 mL). The combined organic layers were dried over MgSO₄ and concentrated under reduced pressure affording quantitatively pure **30a** (10.463 g, 50 mmol) as a white solid which was used without further purification.

Spectroscopic data were in accordance with those reported in literature⁹.

**¹H NMR** (300 MHz, CDCl₃): δ 7.77 (d, J = 8.1 Hz, 2H), 7.31 (d, J = 8.1 Hz, 2H), 4.41 (s, 1H), 3.82 (d, J = 2.7 Hz, 2H), 2.43 (s, 3H), 2.10 (t, J = 2.7 Hz, 1H)

**¹³C NMR** (75 MHz, CDCl₃): δ 143.9, 136.5, 129.8, 127.5, 78.1, 73.1, 32.9, 21.7

**N-(but-3-en-1-yl)-4-methyl-N-(prop-2-yn-1-yl)benzenesulfonylamide 30b**

To a stirred solution of sodium hydride (1.05 g, 26.3 mmol, 60% in mineral oil, 1.1 equiv) in dry DMF (26 mL, 1 M) under argon atmosphere was added dropwise a solution of **30a** (5 g, 23.9 mmol, 1 equiv) in dry DMF (5 mL) via cannula at 0°C. After stirring 30 minutes at 0°C, homo-allyl bromide (2.55 mL, 25.1 mmol, 1.05 equiv) was added dropwise. The orange-brown solution was then stirred overnight at

room temperature. After total completion, monitored by TLC, a saturated NH₄Cl solution (50 mL) was slowly added. The aqueous layer was extracted by diethyl ether (2 × 45 mL). The combined organic layers were washed with brine, dried over MgSO₄ and concentrated under reduced pressure. Purification by flash chromatography over silica gel (cyclohexane/ethyl acetate 1/0 to 75/25) afforded pure 30b (4.530 g, 17.2 mmol, 72 %) as a colourless liquid.

Spectroscopic data were in accordance with those reported in literature¹⁰.

¹H NMR (300 MHz, CDCl₃): δ 7.80 – 7.63 (m, 2H), 7.33 – 7.26 (m, 2H), 5.77 (ddt, J = 17.0, 10.2, 6.7 Hz, 1H), 5.19 – 4.95 (m, 2H), 4.14 (d, J = 2.5 Hz, 2H), 3.35 – 3.12 (m, 2H), 2.42 (s, 3H), 2.40 – 2.25 (m, 2H), 2.03 (t, J = 2.5 Hz, 1H)

¹³C NMR (75 MHz, CDCl₃): δ 143.6, 136.0, 134.6, 129.6, 127.8, 117.4, 76.7, 73.9, 45.8, 36.5, 32.3, 21.7

General procedure for the silylation of a terminal alkyne (GP8):
To a stirred solution of the corresponding terminal alkyne (17 mmol, 1 equiv) in dry THF (35 mL, 0.5 M) under argon atmosphere was added dropwise a nbutyllithium solution (18.7 mmol, 1.1 equiv) at -78°C. Stirring was kept at this temperature for 30 minutes before the dropwise addition of freshly distilled trimethylsilyl chloride (2.4 mL, 18.7 mmol, 1.1 equiv). Stirring was kept further 30 minutes at -78°C before slow addition of a saturated NH₄Cl solution (30 mL). The aqueous layer was extracted by ethyl acetate (2 × 20 mL). The combined organic layers were washed with a saturated NaHCO₃ solution (30 mL), dried over MgSO₄, and concentrated under reduced pressure.

N-(but-3-en-1-yl)-4-methyl-N-(3-(trimethylsilyl)prop-2-yn-1-yl)benzenesulfonamide 30c

Crude compound 30c was obtained from 30b following GP8 on 17 mmol scale (4.477 g) and was directly used without purification.

4-methyl-N-(3-oxopropyl)-N-(3-(trimethylsilyl)prop-2-yn-1-yl)benzenesulfonamide 30d

Crude aldehyde 30d was obtained from 30c following GP7 on 8.94 mmol scale (3 g).

N-(3-hydroxypent-4-en-1-yl)-4-methyl-N-(3-(trimethylsilyl)prop-2-yn-1-yl)benzenesulfonamide 30

Compound 30 was obtained by addition of vinylmagnesium bromide on the crude aldehyde 30d following GP3 on 8.94 mmol scale (1.95 g). Purification by flash chromatography over silica gel (cyclohexane/ethyl acetate 1/0 to 80/20) afforded pure 30 as a white solid (1.765 g, 4.83 mmol, 54 % over 2 steps).

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.76 – 7.71 (m, 2H), 7.32 – 7.27 (m, 2H), 5.90 (ddd, $J = 17.2$, 10.5, 5.7 Hz, 1H), 5.29 (dt, $J = 17.3$, 1.5 Hz, 1H), 5.13 (dt, $J = 10.5$, 1.4 Hz, 1H), 4.34 – 4.28 (m, 1H), 4.25 (d, $J = 18.7$ Hz, 1H), 4.05 (d, $J = 18.7$ Hz, 1H), 3.46 (dddd, $J = 13.9$, 8.9, 6.1, 1.0 Hz, 1H), 3.21 (d, $J = 4.9$ Hz, 1H), 2.45 (d, $J = 4.6$ Hz, 1H), 2.41 (s, 3H), 1.84 (ddddd, $J = 14.1$, 8.9, 6.6, 3.9 Hz, 1H), 1.72 – 1.61 (m, 1H), 0.00 (s, 9H)

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 143.6, 140.3, 135.7, 129.7, 127.9, 114.9, 98.0, 91.2, 69.4, 43.0, 37.7, 34.7, 21.7, -0.3

HRMS (ESI): calculated for [M+H]$^+$ 366.1554 g.mol$^{-1}$, found 366.1550 g.mol$^{-1}$, calculated for [M+Na]$^+$ 388.1373 g.mol$^{-1}$, found 388.1380 g.mol$^{-1}$, calculated for [M+K]$^+$ 404.1112 g.mol$^{-1}$, found 404.1110 g.mol$^{-1}$

FTIR (film cm$^{-1}$): $\nu$ 3532, 2958, 2924, 2177, 1598, 1495, 1426, 1345, 1249, 1158, 1119, 1090, 990, 918, 840, 813, 759, 735, 662

MP 55°C

N-(3-hydroxypent-4-en-1-yl)-4-methyl-N-(prop-2-yn-1-yl)benzenesulfonamide 30e

Compound 30e was obtained from 30 following GP4 on 4.1 mmol scale (1.5 g). Purification by flash chromatography over silica gel (cyclohexane/ethyl acetate 60/40) afforded pure 30e as a very viscous orange oil (1.109 mg, 3.77 mmol, 92 %).

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.76 – 7.72 (m, 2H), 7.32 – 7.28 (m, 2H), 5.90 (ddd, $J = 17.1$, 10.5, 5.7 Hz, 1H), 5.32 – 5.25 (m, 1H), 5.15 – 5.12 (m, 1H), 4.34 – 4.28 (m, 1H), 4.24 (dd, $J = 18.4$, 2.6 Hz, 1H), 4.06 (dd, $J = 18.4$, 2.6 Hz, 1H), 3.52 – 3.42 (m, 1H), 3.22 (ddd, $J = 14.1$, 6.8, 4.5 Hz, 1H), 2.42 (s, 3H), 2.35 (br s, 1H), 2.05 (t, $J = 2.6$ Hz, 1H), 1.90 – 1.79 (m, 1H), 1.67 (ddd, $J = 13.9$, 9.1, 6.4, 4.5 Hz, 1H)

$^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 143.8, 140.3, 135.7, 129.7, 127.8, 115.0, 76.8, 74.0, 69.5, 43.2, 36.8, 34.8, 21.7

HRMS (ESI): calculated for [M+H]$^+$ 294.1158 g.mol$^{-1}$, found 294.1162 g.mol$^{-1}$, calculated for [M+Na]$^+$ 316.0978 g.mol$^{-1}$, found 316.0981 g.mol$^{-1}$, calculated for [M+K]$^+$ 332.0717 g.mol$^{-1}$, found 332.0711 g.mol$^{-1}$

FTIR (film cm$^{-1}$): $\nu$ 3525, 2958, 2926, 1734, 1598, 1495, 1429, 1329, 1306, 1289, 1245, 1185, 1155, 1120, 1090, 1018, 992, 924, 883, 814, 742, 704, 657

N-(3-hydroxypent-4-en-1-yl)-4-methyl-N-(3-phenylprop-2-yn-1-yl)benzenesulfonamide 32
Compound 32 was obtained by coupling reaction between 30e and iodobenzene following GP5 on 1.87 mmol scale (550 mg). Purification by flash chromatography over silica gel (cyclohexane/ethyl acetate 1/0 to 70/30) afforded pure 32 as a bright yellow and very viscous oil (465 mg, 1.25 mmol, 67%).

$^1$H NMR (400 MHz, CDCl$_3$): δ 7.81 – 7.76 (m, 2H), 7.29 – 7.21 (m, 5H), 7.11 – 7.04 (m, 2H), 5.92 (ddd, $J = 17.2, 10.5, 5.7$ Hz, 1H), 5.30 (dt, $J = 17.2, 1.5$ Hz, 1H), 5.14 (dt, $J = 10.5, 1.4$ Hz, 1H), 4.47 (d, $J = 18.6$ Hz, 1H), 4.39 – 4.32 (m, 1H), 4.26 (d, $J = 18.6$ Hz, 1H), 3.54 (ddd, $J = 14.0, 8.9, 6.2, 1.0$ Hz, 1H), 3.29 (ddd, $J = 13.9, 6.6, 4.6$ Hz, 1H), 2.45 (d, $J = 4.5$ Hz, 1H), 2.34 (s, 3H), 1.93 – 1.84 (m, 1H), 1.72 (ddddd, $J = 14.0, 9.1, 6.2, 4.6$ Hz, 1H)

$^{13}$C NMR (100 MHz, CDCl$_3$): δ 143.7, 140.3, 135.8, 131.6, 129.7, 128.6, 128.3, 127.9, 122.2, 115.0, 85.9, 81.9, 69.5, 43.3, 37.6, 34.8, 21.7

HRMS (ESI): calculated for [M+H]$^+$ 370.1471 g.mol$^{-1}$, found 370.1465 g.mol$^{-1}$, calculated for [M+Na]$^+$ 392.1291 g.mol$^{-1}$, found 392.1295 g.mol$^{-1}$, calculated for [M+K]$^+$ 408.1030 g.mol$^{-1}$, found 408.1026 g.mol$^{-1}$

FTIR (film cm$^{-1}$): ν 3525, 2924, 1598, 1490, 1442, 1343, 1329, 1257, 1155, 1118, 1089, 1069, 1028, 1018, 991, 813, 756, 713, 690, 656

$N$-(3-hydroxypent-4-en-1-yl)-$N$-(3-(4-methoxyphenyl)prop-2-yn-1-yl)-4-methylbenzenesulfonamide 34

Compound 34 was obtained by coupling reaction between 30e and 1-iodo-4-methoxybenzene following GP5 on 1.87 mmol scale (550 mg). Purification by flash chromatography over silica gel (cyclohexane/ethyl acetate 1/0 to 70/30) afforded pure 34 as a yellow oil (229 mg, 0.58 mmol, 31%).

$^1$H NMR (400 MHz, CDCl$_3$): δ 7.82 – 7.69 (m, 2H), 7.26 – 7.24 (m, 2H), 7.07 – 6.92 (m, 2H), 6.79 – 6.68 (m, 2H), 5.91 (ddd, $J = 17.3, 10.5, 5.7$ Hz, 1H), 5.29 (dt, $J = 17.3, 1.5$ Hz, 1H), 5.12 (dt, $J = 10.5, 1.4$ Hz, 1H), 4.44 (d, $J = 18.6$ Hz, 1H), 4.38 – 4.31 (m, 1H), 4.24 (d, $J = 18.6$ Hz, 1H), 3.78 (s, 3H), 3.57 – 3.47 (m, 1H), 3.28 (ddd, $J = 14.0, 6.6, 4.6$ Hz, 1H), 2.55 (d, $J = 4.5$ Hz, 1H), 2.35 (s, 3H), 1.88 (ddddd, $J = 14.2, 8.8, 6.6, 3.9$ Hz, 1H), 1.71 (ddddd, $J = 13.9, 9.1, 6.2, 4.7$ Hz, 1H)

$^{13}$C NMR (100 MHz, CDCl$_3$): δ 159.7, 143.6, 140.3, 135.7, 133.0, 129.6, 127.8, 114.8, 114.2, 113.8, 85.7, 80.3, 69.4, 55.3, 43.1, 37.6, 34.8, 21.5

HRMS (ESI): calculated for [M+H]$^+$ 400.1577 g.mol$^{-1}$, found 400.1568 g.mol$^{-1}$, calculated for [M+Na]$^+$ 422.1396 g.mol$^{-1}$, found 422.1390 g.mol$^{-1}$, calculated for [M+K]$^+$ 438.1136 g.mol$^{-1}$, found 438.1124 g.mol$^{-1}$

FTIR (film cm$^{-1}$): ν 3526, 2926, 2238, 1606, 1508, 1456, 1442, 1342, 1330, 1290, 1246, 1156, 1118, 1107, 1028, 991, 916, 882, 832, 813, 799, 771, 670

e. Oxepane type precursors
1-allylcyclopentanol 37a

To a vigorously stirred solution of commercially available cyclopentanone (2.66 mL, 30 mmol, 1 equiv) in THF (120 mL, 0.25 M) were successively added at 0°C zinc dust (2.95 g, 45 mmol, 1.5 equiv), ammonium acetate (3.70 g, 45 mmol, 1.5 equiv) and allyl bromide (3.9 mL, 45 mmol, 1.5 equiv). The dark-grey heterogeneous mixture was stirred 1 hour at 0°C before slow addition of a saturated NaHCO$_3$ solution (100 mL) and stirred further 20 minutes. The white precipitate was filtered through a Celite® pad and washed with ethyl acetate (30 mL). The aqueous layer was extracted by ethyl acetate (3 × 40 mL). The combined organic layers were washed with brine (40 mL), dried over MgSO$_4$ and concentrated under pressure affording quantitatively pure 37a as a colourless liquid which was used without further purification.

Spectroscopic data were in accordance with those reported in literature$^{11}$.

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 5.95 (ddt, $J = 18.0, 9.3, 7.5$ Hz, 1H), 5.23-5.21 (m, 1H), 5.19-5.16 (m, 1H), 2.39 (d, $J = 7.5$ Hz, 2H), 1.90-1.81 (m, 2H), 1.74-1.61 (m, 6H)

$^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 134.7, 118.7, 81.4, 46.0, 39.5, 24.0

1-allyl-1-(prop-2-yn-1-yloxy)cyclopentane 37b

To a stirred solution of sodium hydride (0.96 g, 24 mmol, 60% in mineral oil, 1.6 equiv) in dry THF (50 mL, 0.5 M) under argon atmosphere was added dropwise a solution of 37a (1.89 g, 15 mmol, 1 equiv) in 5 mL of THF at 0°C via cannula. After stirring 30 minutes at room temperature, propargyl bromide (2 mL, 18 mmol, 80% in toluene, 1.2 equiv) was added dropwise and the mixture was stirred overnight at room temperature. After total completion, monitored by TLC, water (20 mL) was slowly added. The aqueous layer was extracted by ethyl acetate (3 × 50 mL). The combined organic layers were washed with brine (50 mL), dried over MgSO$_4$ and concentrated under pressure. Purification by flash chromatography over silica gel (cyclohexane/ethyl acetate 1/0 to 8/2) afforded pure 37b (877 mg, 5.4 mmol, 36 %) as a bright yellow oil.

---

\[ \text{H NMR} \ (300 \text{ MHz, CDCl}_3): \ \delta \ 5.93 \ (\text{ddt, } J = 17.7, 9.7, 7.0 \text{ Hz, 1H}), \ 5.17-5.15 \ (\text{m, 1H}), \ 5.11 \ (\text{br s, 1H}), \ 4.11 \ (\text{d, } J = 2.6 \text{ Hz, 2H}), \ 2.43 \ (\text{m, 3H}), \ 1.92-1.78 \ (\text{m, 4H}), \ 1.66-1.53 \ (\text{m, 4H}) \]

\[ \text{C NMR} \ (75 \text{ MHz, CDCl}_3): \ \delta \ 134.6, \ 117.4, \ 88.0, \ 81.4, \ 73.2, \ 50.8, \ 40.9, \ 36.1, \ 23.9 \]

\[ \text{HRMS} \ (\text{ESI}): \text{ compound not detected} \]

\[ \text{FTIR} \ (\text{film cm}^{-1}): \nu \ 3293, \ 2924, \ 2854, \ 2115, \ 1959, \ 1737, \ 1456, \ 1258, \ 1160, \ 1070, \ 751 \]

(3-((1-allylcyclopentyl)oxy)prop-1-yn-1-yl)trimethylsilane \[ 37c \]

Compound \[ 37c \] was obtained from \[ 37b \] following \[ \text{GP8} \] on 5.23 mmol scale (860 mg). Pure \[ 37c \] was quantitatively obtained after concentration under reduced pressure (1.236 g, 5.23 mmol) as an orange-red oil.

\[ \text{H NMR} \ (300 \text{ MHz, CDCl}_3): \ \delta \ 5.88 \ (\text{ddt, } J = 17.7, 9.7, 7.0 \text{ Hz, 1H}), \ 5.09-5.04 \ (\text{m, 2H}), \ 4.07 \ (\text{s, 2H}), \ 2.36 \ (\text{d, } J = 7.0 \text{ Hz, 2H}), \ 1.87-1.72 \ (\text{m, 4H}), \ 1.62-1.46 \ (\text{m, 4H}), \ 0.16 \ (\text{s, 9H}) \]

\[ \text{C NMR} \ (75 \text{ MHz, CDCl}_3): \ \delta \ 134.8, \ 117.3, \ 103.5, \ 89.7, \ 88.0, \ 51.6, \ 40.9, \ 36.1, \ 23.9, \ 0.0 \]

\[ \text{FTIR} \ (\text{film cm}^{-1}): \nu \ 2958, \ 2175, \ 1640, \ 1438, \ 1356, \ 1334, \ 1250, \ 1064, \ 996, \ 913, \ 841, \ 760, \ 699 \]

2-(1-((3-(trimethylsilyl)prop-2-yn-1-yl)oxy)cyclopentyl)acetaldehyde \[ 37d \]

Crude aldehyde \[ 37d \] was obtained from \[ 37c \] following \[ \text{GP7} \] on 2.61 mmol scale (618 mg).

1-(1-((3-(trimethylsilyl)prop-2-yn-1-yl)oxy)cyclopentyl)but-3-en-2-ol \[ 37 \]

Compound \[ 37 \] was obtained by addition of vinylmagnesium bromide on the crude aldehyde \[ 37d \] following \[ \text{GP3} \] on 2.61 mmol scale (622 mg). Purification by flash chromatography over silica gel (cyclohexane/ethyl acetate 1/0 to 90/10) afforded pure \[ 37 \] as a colourless liquid (317 mg, 1.20 mmol, 46 % over 3 steps).

\[ \text{H NMR} \ (400 \text{ MHz, CDCl}_3): \ \delta \ 5.86 \ (\text{ddd, } J = 17.2, 10.6, 5.7 \text{ Hz, 1H}), \ 5.27 \ (\text{dd, } J = 17.2, 1.3 \text{ Hz, 1H}), \ 5.07 \ (\text{dd, } J = 10.6, 1.3 \text{ Hz, 1H}), \ 4.46-4.42 \ (\text{m, 1H}), \ 4.11 \ (\text{d, } J = 15.7 \text{ Hz, 1H}), \ 4.04 \ (\text{d, } J = 15.7 \text{ Hz, 1H}), \ 3.39 \ (\text{br s, 1H}), \ 2.05-1.95 \ (\text{m, 3H}), \ 1.85-1.71 \ (\text{m, 2H}), \ 1.67-1.56 \ (\text{m, 4H}), \ 1.46-1.39 \ (\text{m, 1H}), \ 0.16 \ (\text{s, 9H}) \]

\[ \text{C NMR} \ (100 \text{ MHz, CDCl}_3): \ \delta \ 141.1, \ 113.9, \ 102.4, \ 90.6, \ 89.2, \ 70.7, \ 51.5, \ 42.8, \ 36.2, \ 36.2, \ 23.7, \ 23.5, \ 0.2 \]

\[ \text{HRMS} \ (\text{ESI}): \text{ calculated for } [\text{M+Na}]^+ \ 289.1594 \text{ g.mol}^{-1}, \text{ found } 2891598 \text{ g.mol}^{-1} \]
FTIR (film cm\(^{-1}\)): \(\nu\) 3450, 2959, 2176, 1645, 1449, 1365, 1250, 1057, 992, 920, 840, 760, 699

(3-((1-allylcyclopentyl)oxy)prop-1-yn-1-yl)benzene 39a

Compound 39a was obtained by coupling reaction between 37b and iodobenzene following GP5 on 2.14 mmol scale (352 mg). Purification by flash chromatography over silica gel (cyclohexane/ethyl acetate 1/0 to 95/5) afforded pure 39a as a red oil (434 mg, 1.80 mmol, 84%).

\(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 7.45-7.42 (m, 2H), 7.31-7.27 (m, 3H), 5.93 (ddt, \(J = 16.5, 11.0, 7.0\) Hz, 1H), 5.15-5.11 (m, 1H), 5.09-5.07 (m, 2H), 4.30 (s, 2H), 2.45-2.42 (m, 2H), 1.93-1.78 (m, 2H), 1.63-1.52 (m, 5H)

\(^1\)C NMR (75 MHz, CDCl\(_3\)): \(\delta\) 134.8, 131.8, 128.3, 123.1, 117.4, 88.0, 86.9, 84.9, 51.6, 41.0, 36.2, 27.1, 23.9

2-(1-((3-phenylprop-2-yn-1-yl)oxy)cyclopentyl)acetaldehyde 39b

Crude aldehyde 39b was obtained from 39a following GP7 on 1.80 mmol scale (434 mg).

1-(1-((3-phenylprop-2-yn-1-yl)oxy)cyclopentyl)but-3-en-2-ol 39

Compound 39 was obtained by addition of vinylmagnesium bromide on the crude aldehyde 39b following GP3 on 1.80 mmol scale (436 mg). Purification by flash chromatography over silica gel (cyclohexane/ethyl acetate 1/0 to 90/10) afforded pure 39 as a yellow oil (165 mg, 0.61 mmol, 34 % over 2 steps).

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.44-7.41 (m, 2H), 7.35-7.27 (m, 3H), 5.89 (ddt, \(J = 17.2, 10.4, 5.7\) Hz, 1H), 5.28 (dd, \(J = 17.2, 1.6\) Hz, 1H), 5.08 (dd, \(J = 10.4, 1.6\) Hz, 1H), 4.51-4.47 (m, 1H), 4.35 (d, \(J = 
15.4 Hz, 1H), 4.27 (d, $J$ = 15.4 Hz, 1H), 3.47 (br s, 1H), 2.12-2.02 (m, 3H), 1.86-1.76 (m, 2H), 1.71-1.57 (m, 4H), 1.52-1.44 (m, 1H)

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 141.1, 131.9, 128.5, 128.3, 128.3, 122.8, 114.1, 89.3, 86.0, 85.7, 70.9, 51.6, 42.9, 36.4, 36.4, 23.8, 23.7

HRMS (ESI): calculated for [M+H]$^+$ 271.1693 g.mol$^{-1}$, found 271.1690 g.mol$^{-1}$, calculated for [M+Na]$^+$ 293.1512 g.mol$^{-1}$, found 293.1509 g.mol$^{-1}$

FTIR (film cm$^{-1}$): $\nu$ 3455, 2956, 2871, 1645, 1598, 1490, 1442, 1370, 1335, 1259, 1214, 1176, 1046, 993, 947, 844, 755, 690

5/ Cyclization reactions

General procedure A (GP-A):

To a solution of the corresponding cyclization precursor (0.4 mmol, 1 equiv) under argon atmosphere in dry toluene (4 mL, 0.1 M), was added dropwise a solution of isopropylmagnesium chloride in diethyl ether (0.4 mmol, 1 equiv) at 0 °C. After stirring for 6 min, titanium isopropoxide (0.24 mL, 0.8 mmol, 2 equiv) was added dropwise and the light yellow mixture was stirred for 4 min at 0 °C. Isopropylmagnesium chloride in diethyl ether (1.6 mmol, 4 equiv) was added dropwise at -40 °C and the cooling bath was immediately removed before stirring the dark solution for 10 min at room temperature. After total completion, monitored by TLC, water (2 mL) and HCl (10 mL, 0.1 M) were successively added and the heterogeneous mixture was vigorously stirred until solubilisation of the grey salts. The aqueous layer was extracted by diethyl ether (3 × 15 mL), the combined organic layers were successively washed with a saturated NaHCO$_3$ solution (20 mL), brine (20 mL), dried over MgSO$_4$ and concentrated under reduced pressure. Purification of the crude by flash chromatography over silica gel afforded pure desired cyclized product.

General procedure B (GP-B):

To a solution of the corresponding cyclization precursor (0.4 mmol, 1 equiv) under argon atmosphere in dry toluene (4 mL, 0.1 M), was added dropwise a solution of isopropylmagnesium chloride in diethyl ether (0.4 mmol, 1 equiv) at 0 °C. After stirring for 3 min, titanium isopropoxide (0.24 mL, 0.8 mmol, 2 equiv) was added dropwise and the light yellow mixture was stirred for 2 min at 0 °C. Isopropylmagnesium chloride in diethyl ether (1.6 mmol, 4 equiv) was added dropwise at -40 °C and the cooling bath was immediately removed before stirring the dark solution for 10 min at room temperature. After total completion, monitored by TLC, water (2 mL) and HCl (10 mL, 0.1 M) were successively added and the heterogeneous mixture was vigorously stirred until solubilisation of the grey salts. The aqueous layer was extracted by diethyl ether (3 × 15 mL), the combined organic layers were successively washed with a saturated NaHCO$_3$ solution (20 mL), brine (20 mL), dried over MgSO$_4$ and concentrated under reduced pressure. Purification of the crude by flash chromatography over silica gel afforded pure desired cyclized product.

General procedure C (GP-C):

To a solution of the corresponding cyclization precursor (0.4 mmol, 1 equiv) under argon atmosphere in dry toluene (4 mL, 0.1 M), was added dropwise a solution of isopropylmagnesium chloride in diethyl ether (0.4 mmol, 1 equiv) at 0 °C. After stirring for 6 min, titanium isopropoxide (0.24 mL, 0.8 mmol, 2 equiv) was added dropwise and the light yellow mixture was stirred for 4 min at 0 °C. Isopropylmagnesium chloride in diethyl ether (1.6 mmol, 4 equiv) was added dropwise at -40 °C and the cooling bath was immediately removed before stirring the dark solution for 10 min at room temperature. After total completion, monitored by TLC, acetone (0.6 mL, 8 mmol, 20 equiv) was added dropwise at 0 °C. Stirring was kept for 10 minutes at 0 °C. After total completion, monitored by TLC, water (2 mL) and HCl (10 mL, 0.1 M) were successively added and the heterogeneous mixture was vigorously stirred until solubilisation of the grey salts. The aqueous layer was extracted by diethyl ether (3 × 15 mL), the combined organic layers were successively washed with a saturated NaHCO$_3$ solution (20 mL), brine (20 mL), dried over MgSO$_4$ and concentrated under reduced pressure. Purification of the crude by flash chromatography over silica gel afforded pure desired cyclized product.


Cyclization was performed following GP-A starting from 1 (104 mg, 0.4 mmol). Purification by flash chromatography over silica gel (cyclohexane/ethyl acetate 1/0 to 95/5) afforded 2 as a colourless oil (63 mg, 0.24 mmol, 60%).

Cyclization was also performed following GP-A starting from 1 (388 mg, 1.5 mmol). Purification by flash chromatography over silica gel (cyclohexane/ethyl acetate 1/0 to 95/5) afforded 2 as a colourless oil (157 mg, 0.60 mmol, 40%).

\[^1\text{H}\text{ NMR}\] (400 MHz, CDCl\(_3\)): \(\delta\) 7.46 - 7.44 (m, 1H), 7.26 - 7.22 (m, 1H), 7.21 - 7.17 (m, 1H), 7.12 - 7.10 (m, 1H), 5.42 (s, 1H), 4.87 (s, 1H), 2.87 (dd, \(J = 14.2, 8.2, 1.9\) Hz, 1H), 2.79 (dq, \(J = 6.9, 1.8\) Hz, 1H), 2.69 - 2.61 (m, 1H), 2.46 (dd, \(J = 13.5, 8.5, 1.8\) Hz, 1H), 2.29 (dd, \(J = 13.3, 10.9, 1.9\) Hz, 1H), 1.99 (s, 1H), 0.86 (d, \(J = 6.9\) Hz, 3H), 0.17 (s, 9H)

\[^{13}\text{C}\text{ NMR}\] (100 MHz, CDCl\(_3\)): \(\delta\) 161.5, 141.3, 139.5, 129.3, 127.2, 126.4, 126.4, 125.9, 75.8, 52.0, 35.5, 33.0, 14.7, 0.6

HRMS (ESI): calculated for [M-H] \(^{-}\) 259.1524 g.mol\(^{-1}\), found 259.1521 g.mol\(^{-1}\), calculated for [M+H]\(^{+}\) 261.1669 g.mol\(^{-1}\), found 261.1677 g.mol\(^{-1}\), calculated for [M+Na]\(^{+}\) 283.1489 g.mol\(^{-1}\), found 283.1498 g.mol\(^{-1}\)

FTIR (film cm\(^{-1}\)): \(\nu\) 3392, 2953, 2926, 2853, 1608, 1486, 1454, 1355, 1259, 75.8, 52.0, 35.5, 33.0, 14.7, 0.6


Cyclization was performed following GP-C starting from 1 (104 mg, 0.4 mmol). Purification by flash chromatography over silica gel (pentane/diethyl ether 1/0 to 60/40) afforded 18 as a yellow oil (34 mg, 0.11 mmol, 27%).

\[^1\text{H}\text{ NMR}\] (400 MHz, CDCl\(_3\)): \(\delta\) 7.54 (dt, \(J = 7.7, 1.2\) Hz, 1H), 7.26 (td, \(J = 7.5, 1.5\) Hz, 1H), 7.17 (td, \(J = 7.3, 1.2\) Hz, 1H), 7.09 (dd, \(J = 7.4, 1.5\) Hz, 1H), 5.46 (s, 1H), 4.90 (d, \(J = 2.0\) Hz, 1H), 3.05 (td, \(J = 6.3, 5.8\) Hz, 1H), 2.84 (dd, \(J = 14.1, 6.7, 1.6\) Hz, 1H), 2.67 - 2.58 (m, 1H), 2.54 (d, \(J = 13.3\) Hz, 1H), 1.97 (dd, \(J = 13.7, 12.5, 1.6\) Hz, 1H), 1.45 – 1.36 (m, 1H), 1.19 (s, 3H), 1.15 (s, 3H), 1.03 (dd, \(J = 14.7, 5.6\) Hz, 1H), 0.15 (s, 9H)

\[^{13}\text{C}\text{ NMR}\] (100 MHz, CDCl\(_3\)): \(\delta\) 162.8, 141.6, 138.8, 128.9, 126.7, 126.3, 126.3, 125.9, 74.5, 71.2, 54.9, 41.7, 35.6, 31.7, 31.3, 28.5, 0.5

HRMS (ESI): calculated for [M+H]\(^{+}\) 319.2088 g.mol\(^{-1}\), found 319.2083 g.mol\(^{-1}\), calculated for [M+Na]\(^{+}\) 341.1907 g.mol\(^{-1}\), found 341.1908 g.mol\(^{-1}\)

FTIR (film cm\(^{-1}\)): \(\nu\) 3312, 2953, 1604, 1454, 1364, 1275, 1247, 1153, 1125, 1040, 926, 836, 752, 706, 689, 663
(+/-)-(5S,6R,E)-6-ethyl-7-((trimethylsilyl)methylene)-6,7,8,9-tetrahydro-5H-benzo[7]annulen-5-ol 17

\[
\begin{align*}
\text{Cyclization was performed following GP-A starting from 16 (109 mg, 0.4 mmol). Purification by flash chromatography over silica gel (pentane/diethyl ether 1/0 to 90/10) afforded 17 as a colourless oil (22 mg, 0.08 mmol, 20 %).}
\end{align*}
\]

\[^1H\] NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.52 - 7.55 (m, 1H), 7.28 - 7.24 (m, 1H), 7.20 - 7.16 (m, 1H), 7.12 - 7.10 (m, 1H), 5.40 (s, 1H), 4.98 (s, 1H), 2.84 (ddd, \(J = 14.4, 7.2, 2.0\) Hz, 1H), 2.65-2.59 (m, 1H), 2.58 - 2.49 (m, 2H), 2.07-2.00 (m, 2H), 1.45-1.34 (m, 1H), 0.78-0.71 (m, 4H), 0.86, 0.17 (s, 9H)

\[^{13}C\] NMR (100 MHz, CDCl\(_3\)): \(\delta\) 159.5, 141.5, 139.0, 129.0, 127.8, 126.9, 126.3, 125.3, 74.5, 60.9, 35.3, 31.9, 20.2, 12.1, 0.6

HRMS (ESI): m/z calculated for [M+H]\(^+\) 275.1826 g.mol\(^{-1}\), found 275.1833 g.mol\(^{-1}\), calculated for [M+Na]\(^+\) 297.1645 g.mol\(^{-1}\), found 297.1654 g.mol\(^{-1}\)

\(^\text{FTIR}\) (film cm\(^{-1}\)): \(\nu\) 3375, 2955, 2871, 1603, 1485, 1454, 1356, 1246, 1101, 1030, 904, 847, 834, 779, 752, 689, 669

(+/-)-(5S,6R,E)-7-((tert-butyldimethylsilyl)methylene)-6-methyl-6,7,8,9-tetrahydro-5H-benzo[7]annulen-5-ol 4

\[
\begin{align*}
\text{Cyclization was performed following GP-A starting from 3 (120 mg, 0.4 mmol). Purification by flash chromatography over silica gel (pentane/diethyl ether 1/0 to 90/10) afforded 4 as a colourless oil (67 mg, 0.22 mmol, 55 %).}
\end{align*}
\]

\[^1H\] NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.48-7.46 (m, 1H), 7.27-7.23 (m, 1H), 7.21-7.17 (m, 1H), 7.12-7.10 (m, 1H), 5.42 (s, 1H), 4.90 (s, 1H), 2.87-2.81 (m, 2H), 2.67-2.60 (m, 1H), 2.50 (ddd, \(J = 13.6, 8.0, 1.6\) Hz, 1H), 2.27-2.21 (m, 1H), 2.03 (s, 1H), 0.93 (s, 9H), 0.83 (d, \(J = 7.2\) Hz, 3H), 0.15 (s, 3H), 0.14 (s, 3H)

\[^{13}C\] NMR (100 MHz, CDCl\(_3\)): \(\delta\) 162.2, 141.3, 139.4, 129.2, 127.1, 126.3, 126.1, 123.0, 75.5, 52.7, 35.3, 32.7, 26.7, 17.1, 14.6, -3.6, -3.6

HRMS (ESI): calculated for [M+H]\(^+\) 303.2139 g.mol\(^{-1}\), found 303.2141 g.mol\(^{-1}\), calculated for [M+Na]\(^+\) 325.1958 g.mol\(^{-1}\), found 325.1959 g.mol\(^{-1}\)

\(^\text{FTIR}\) (film cm\(^{-1}\)): \(\nu\) 3369, 2952, 2926, 2854, 1605, 1470, 1462, 1360, 1248, 1038, 1024, 1007, 995, 835, 824, 809, 779, 771, 753, 707, 670

(+/-)-(5S,6R,E)-7-ethylidene-6-methyl-6,7,8,9-tetrahydro-5H-benzo[7]annulen-5-ol 6
Cyclization was performed following **GP-A** starting from **5** (80 mg, 0.4 mmol). Purification by flash chromatography over silica gel (pentane/diethyl ether 1/0 to 90/10) afforded **6** as a colourless oil (38 mg, 0.19 mmol, 47 %).

**1H NMR** (400 MHz, CDCl₃): δ 7.46 (d, J = 7.5 Hz, 1H), 7.27 – 7.22 (m, 1H), 7.18 (td, 1H), 7.12 (dd, J = 7.3 Hz, 1H), 5.46 (q, J = 6.6 Hz, 1H), 4.88 (d, J = 1.9 Hz, 1H), 2.82 (ddd, J = 14.2, 7.9, 1.8 Hz, 1H), 2.73 (qd, J = 7.1, 1.9 Hz, 1H), 2.62 (ddd, J = 13.9, 11.3, 1.7 Hz, 1H), 2.53 (ddd, J = 13.9, 7.9, 1.7 Hz, 1H), 2.11 – 2.01 (m, 2H), 1.69 (d, J = 6.6 Hz, 3H), 0.81 (d, J = 7.1 Hz, 3H)

**13C NMR** (100 MHz, CDCl₃): δ 143.0, 141.5, 139.8, 129.3, 127.0, 126.2, 126.2, 120.0, 76.1, 49.3, 35.1, 26.3, 14.3, 12.9

**HRMS** (ESI): calculated for [M+Na]⁺ 225.1250 g.mol⁻¹, found 225.1255 g.mol⁻¹

**FTIR** (film cm⁻¹): ν 3374, 1962, 2928, 2857, 1485, 1453, 1372, 1024, 994, 829, 775, 753, 661

(+/-)-diethyl ((E)-((5S,6R)-5-hydroxy-6-methyl-8,9-dihydro-5H-benzo[7]annulen-7(6H)-ylidene)methyl)phosphonate **12**

Cyclization was performed following **GP-A** starting from **11** (129 mg, 0.4 mmol). Purification by flash chromatography over silica gel (pentane/diethyl ether 50/50 to 5/95) afforded **12** as a colourless oil (40 mg, 0.12 mmol, 30 %).

**1H NMR** (400 MHz, CDCl₃): δ 7.50 (dt, J = 7.5, 1.1 Hz, 1H), 7.23 (td, J = 7.5, 1.5 Hz, 1H), 7.16 (td, J = 7.4, 1.5 Hz, 1H), 7.09 (dd, J = 7.4, 1.5 Hz, 1H), 5.53 (d, J = 19.1 Hz, 1H), 4.92 (s, 1H), 4.20 – 3.87 (m, 4H), 3.23 (s, 1H), 3.16 (dd, J = 13.7, 7.7 Hz, 1H), 2.97 – 2.79 (m, 2H), 2.65 (ddd, J = 14.2, 11.6, 1.7 Hz, 1H), 2.30 (ddt, J = 14.0, 11.6, 2.4 Hz, 1H), 1.39 – 1.19 (m, 6H), 0.81 (d, J = 7.0 Hz, 3H)

**31P NMR** (400 MHz, CDCl₃): δ 17.90 (s)

**13C NMR** (100 MHz, CDCl₃): δ 168.6 (d, J = 6.6 Hz, 140.7, 138.8, 129.1, 127.2, 126.4, 126.2, 112.8 (d, J = 186.7 Hz), 74.0, 61.6 (d, J = 5.9 Hz), 61.5 (d, J = 5.6 Hz), 51.0 (d, J = 22.3 Hz), 33.6 (d, J = 2.4 Hz), 29.7 (d, J = 7.6 Hz), 16.5 (d, J = 3.0 Hz), 16.4 (d, J = 2.9 Hz), 14.1

**HRMS** (ESI): calculated for [M+H]⁺ 325.1563 g.mol⁻¹, found 325.1567 g.mol⁻¹, calculated for [M+Na]⁺ 347.1383 g.mol⁻¹, found 347.1390 g.mol⁻¹, calculated for [M+K]⁺ 363.1122 g.mol⁻¹, found 363.1132 g.mol⁻¹

**FTIR** (film cm⁻¹): ν 3369, 2978, 2930, 1616, 1455, 1392, 1368, 1217, 1163, 1097, 1048, 1020, 955, 834, 810, 793, 779, 755, 736, 672

(+/-)-(5(5S,6R,E)-7-benzylidene-6-methyl-6,7,8,9-tetrahydro-5H-benzo[7]annulen-5-ol **8**

---

35
Cyclization was performed following GP-A starting from 7 (105 mg, 0.4 mmol). Purification by flash chromatography over silica gel (pentane/diethyl ether 1/0 to 80/20) afforded 8 as a colourless oil (64 mg, 0.24 mmol, 60 %).

1H NMR (400 MHz, CDCl3): δ 7.54 (d, J = 7.6 Hz, 1H), 7.37 (t, J = 7.6 Hz, 2H), 7.29 – 7.21 (m, 5H), 7.13 (d, J = 7.3 Hz, 1H), 6.54 (s, 1H), 5.08 (s, 1H), 2.94 – 2.84 (m, 2H), 2.85 – 2.77 (m, 1H), 2.73 (t, J = 12.6 Hz, 1H), 2.17 – 2.10 (m, 2H), 0.91 (d, J = 7.0 Hz, 3H)

13C NMR (100 MHz, CDCl3): δ 145.8, 141.2, 139.4, 138.0, 129.3, 129.2, 128.2, 127.1, 126.4, 126.3, 126.2, 125.9, 75.5, 49.7, 35.1, 26.8, 14.1

HRMS (ESI): calculated for [M+Na]+ 287.1406 g.mol−1, found 287.1414 g.mol−1

FTIR (film cm−1): ν 3390, 3057, 3021, 2965, 2930, 1488, 1453, 1275, 1262, 1180, 1102, 1038, 1024, 997, 917, 892, 855, 753, 740, 699, 666

(+/-)-(5S,6R,E)-7-(4-methoxybenzylidene)-6-methyl-6,7,8,9-tetrahydro-5H-benzo[7]annulen-5-ol 10

Cyclization was performed following GP-A starting from 9 (100 mg, 0.34 mmol). Purification by flash chromatography over silica gel (pentane/diethyl ether 1/0 to 80/20) afforded 10 as a yellow oil (39 mg, 0.16 mmol, 39 %).

1H NMR (400 MHz, CDCl3): δ 7.53 (d, J = 7.6 Hz, 1H), 7.30 – 7.25 (m, 1H), 7.23 - 7.16 (m, 3H), 7.16 – 7.12 (m, 1H), 6.92 – 6.89 (m, 2H), 6.47 (s, 1H), 5.06 (s, 1H), 3.84 (s, 3H), 2.93 – 2.84 (m, 2H), 2.83 – 2.76 (m, 1H), 2.72 (t, J = 12.7 Hz, 1H), 2.17 – 2.10 (m, 2H), 0.90 (d, J = 7.0 Hz, 3H)

13C NMR (100 MHz, CDCl3): δ 158.2, 144.7, 141.2, 139.4, 130.4, 130.4, 129.2, 127.1, 126.3, 125.9, 125.7, 113.7, 75.6, 55.4, 49.7, 35.2, 26.8, 14.1

HRMS (ESI): calculated for [M+H]+ 295.1693 g.mol−1, found 295.1702 g.mol−1

FTIR (film cm−1): ν 3395, 2918, 2836, 1606, 1508, 1462, 1441, 1288, 1243, 1172, 1106, 1030, 989, 927, 831, 756

(+/-)-(5S,6R,E)-5,6-dimethyl-7-((trimethylsilyl)methylene)-6,7,8,9-tetrahydro-5H-benzo[7]annulen-5-ol 14
Cyclization was performed following GP-A starting from 13 (109 mg, 0.4 mmol). Purification by flash chromatography over silica gel (pentane/diethyl ether 1/0 to 80/20) afforded 14 as a colourless oil (47 mg, 0.17 mmol, 43%).

\[ \text{1H NMR (400 MHz, CDCl}_3\text{): } \delta 7.73-7.71 \text{ (m, 1H), 7.27-7.23 \text{ (m, 1H), 7.17-7.14 \text{ (m, 1H), 7.09-7.07 \text{ (m, 1H), 5.39 (s, 1H), 2.98-2.90 \text{ (m, 1H), 2.79 (d, } J = 14.4, 5.2, 2.8 \text{ Hz, 1H), 2.71 (q, } J = 6.8 \text{ Hz, 1H), 2.59 (dd, } J = 13.2, 4.8 \text{ Hz, 2.4 Hz, 1H), 2.30 (dt, } J = 13.2, 2.8 \text{ Hz, 1H), 1.86 (s, 1H), 1.53 (s, 3H), 0.87 (d, } J = 6.8 \text{ Hz, 3H), 0.14 (s, 9H)} \]

\[ \text{13C NMR (100 MHz, CDCl}_3\text{): } \delta 161.0, 144.9, 137.6, 130.7, 126.7, 126.7, 126.4, 77.06, 57.7, 36.4, 31.2, 28.6, 14.8, 0.6 \]

HRMS (ESI): calculated for [M-H] \(-273.1673 \text{ g.mol}^{-1}\), found 273.1680 g.mol\(^{-1}\), calculated for [M+H]\(^+\) 275.1826 g.mol\(^{-1}\), found 275.1828 g.mol\(^{-1}\), calculated for [M+Na]\(^+\) 297.1645 g.mol\(^{-1}\), found 297.1646 g.mol\(^{-1}\)

FTIR (film cm\(^{-1}\)): \( \nu \) 3480, 2952, 1608, 1484, 1451, 1370, 1278, 1245, 1121, 1063, 1016, 995, 883, 844, 835, 759, 749, 715, 688

b. Protected alcohol

\((E)-((Z)-5,6\text{-dihydrobenzo}[8]annulen-7(8H)-ylidene)methyl)trimethylsilane 22\]

Cyclization was performed following GP-A starting from 21 (82 mg, 0.3 mmol). Purification by flash chromatography over silica gel (pentane/diethyl ether 1/0 to 97/3) afforded 22 as a white solid (27 mg, 0.11 mmol, 37%).

\[ \text{1H NMR (400 MHz, CDCl}_3\text{): } \delta 7.57 – 7.48 \text{ (m, 1H), 7.23 – 7.07 \text{ (m, 3H), 6.77 (d, } J = 15.3 \text{ Hz, 1H), 6.11 (dt, } J = 15.3, 7.4 \text{ Hz, 1H), 5.45 (s, 1H), 3.06 (d, } J = 7.4 \text{ Hz, 2H), 2.88 – 2.77 \text{ (m, 2H), 2.38 – 2.25 \text{ (m, 2H), 0.19 (s, 9H)} \]

\[ \text{13C NMR (100 MHz, CDCl}_3\text{): } \delta 156.9, 139.1, 135.3, 131.1, 130.2, 127.7, 127.5, 127.1, 126.6, 125.4, 45.9, 36.6, 34.2, 0.6 \]

HRMS (ESI): compound not detected

FTIR (film cm\(^{-1}\)): \( \nu \) 3019, 2952, 2925, 1608, 1484, 1451, 1370, 1278, 1245, 1121, 1063, 1016, 995, 883, 844, 835, 759, 749, 715, 688

Mp 62-64°C

c. Spiro-ketal type precursors

\((+/-)-(9R,10R,E)-3,3,10\text{-trimethyl-11-}((\text{trimethylsilyl})\text{methylene})-2,4\text{-dioxaspiro[5.6]dodecan-9-ol 25}\]

Cyclization was performed following GP-B starting from 24 (124 mg, 0.4 mmol). Purification by flash chromatography over silica gel (pentane/diethyl ether 1/0 to 80/20) afforded 25 as a yellow oil (66 mg, 0.21 mmol, 53%).
Cyclization was also performed following GP-B starting from 24 (310 mg, 1 mmol). Purification by flash chromatography over silica gel (pentane/diethyl ether 1/0 to 60/40) afforded 25 as a yellow oil (150 mg, 0.48 mmol, 48%).

**H NMR** (400 MHz, CDCl₃): δ 5.36 (s, 1H), 3.72 (ddd, J = 6.1, 4.0, 3.0 Hz, 1H), 3.65 (dd, J = 11.6, 1.1 Hz, 1H), 3.59 (dd, J = 11.6, 1.1 Hz, 1H), 3.58 (dd, J = 11.5, 1.1 Hz, 1H), 3.46 (dd, J = 11.5, 1.1 Hz, 1H), 2.48 (d, J = 14.4 Hz, 1H), 2.42 (qd, J = 7.2, 3.0 Hz, 1H), 2.04 (d, J = 14.4 Hz, 1H), 1.78 – 1.65 (m, 2H), 1.68 – 1.56 (m, 1H), 1.54 – 1.39 (m, 2H), 1.41 (s, 3H), 1.39 (s, 3H), 1.11 (d, J = 7.2 Hz, 3H), 0.13 (s, 9H)

**C NMR** (100 MHz, CDCl₃): δ 156.0, 128.3, 98.2, 71.7, 69.9, 69.7, 47.5, 41.6, 34.8, 29.9, 25.9, 24.1, 23.8, 17.4, 0.7

**HRMS** (ESI): calculated for [M+H]+ 313.2193 g.mol⁻¹, found 313.2193 g.mol⁻¹, calculated for [M+Na]+ 335.2013 g.mol⁻¹, found 335.2015 g.mol⁻¹

**FTIR** (film cm⁻¹): ν 3447, 2927, 2859, 1602, 1453, 1370, 1246, 1196, 1157, 1121, 1083, 832, 753, 732, 689

(+/-)-(9R,10R,E)-11-benzylidene-3,3,10-trimethyl-2,4-dioxaspiro[5.6]dodecan-9-ol 27

Cyclization was performed following GP-B starting from 26 (94 mg, 0.3 mmol). Purification by flash chromatography over silica gel (pentane/diethyl ether 1/0 to 90/10) afforded 27 as a colourless oil (39 mg, 0.12 mmol, 41%).

**H NMR** (400 MHz, CDCl₃): δ 7.32-7.29 (m, 2H), 7.22-7.20 (m, 3H), 6.48 (s, 1H), 3.86 (dt, J = 6.8, 3.2 Hz, 1H), 3.40 (d, J = 11.6 Hz, 1H), 3.33 (d, J = 11.6 Hz, 1H), 3.29 (d, J = 11.6 Hz, 1H), 3.25 (d, J = 11.6 Hz, 1H), 2.60-2.55 (m, 2H), 1.99 (d, J = 14.4, 1H), 1.79-1.58 (m, 4H), 1.51 (m, 1H), 1.30 (s, 3H), 1.24 (s, 3H), 1.23 (d, J = 7.3 Hz, 3H)

**C NMR** (100 MHz, CDCl₃): δ 139.8, 138.4, 129.1, 128.8, 128.4, 126.5, 97.9, 72.8, 69.6, 69.3, 47.4, 36.0, 34.4, 29.0, 25.8, 25.2, 22.3, 16.0

**HRMS** (ESI): calculated for [M+H]+ 317.2111 g.mol⁻¹, found 317.2112 g.mol⁻¹, calculated for [M+Na]+ 339.1931 g.mol⁻¹, found 339.1932 g.mol⁻¹

**FTIR** (film cm⁻¹): ν 3453, 2989, 2927, 2860, 1493, 1452, 1370, 1347, 1259, 1195, 1114, 1083, 1036, 905, 990, 968, 933, 919, 878, 830, 732, 699

(+/-)-(9R,10R,E)-11-(4-methoxybenzylidene)-3,3,10-trimethyl-2,4-dioxaspiro[5.6]dodecan-9-ol 29
Cyclization was performed following **GP-B** starting from **28** (90 mg, 0.26 mmol). Purification by flash chromatography over silica gel (pentane/diethyl ether 1/0 to 80/20) afforded **29** as a colourless oil (49 mg, 0.14 mmol, 54 %). 

*Only *\( ^1 \)H NMR are available due to the high unstability of the product and its rapid decomposition occurring even during neat at -20°C.*

\[ \text{**1H NMR** (400 MHz, CDCl}_3\text{): } \delta 7.20 – 7.11 \text{ (m, 2H), 6.89 – 6.80 (m, 2H), 6.40 (s, 1H), 3.85 (dt, } J = 7.2, 3.6 \text{ Hz, 1H), 3.80 (s, 3H), 3.42 (d, } J = 11.6 \text{ Hz, 1H), 3.36 (d, } J = 11.6 \text{ Hz, 1H), 3.31 – 3.25 (m, 2H), 2.58 (d, } J = 14.3 \text{ Hz, 1H), 2.56 – 2.49 (m, 1H), 1.97 (d, } J = 14.3 \text{ Hz, 1H), 1.80 – 1.55 (m, 5H), 1.49 (ddd, } J = 14.7, 8.3, 1.9 \text{ Hz, 1H), 1.32 (s, 3H), 1.28 (s, 3H), 1.21 (d, } J = 7.1 \text{ Hz, 3H)} \]

HRMS (ESI): calculated for [M+H]+ 347.2217 g.mol\(^{-1}\), found 347.2214 g.mol\(^{-1}\)

FTIR (film cm\(^{-1}\)): \( \nu 3453, 2989, 2925, 2857, 1606, 1508, 1454, 1370, 1245, 1196, 1177, 1156, 1120, 1033, 991, 969, 933, 881, 832, 751, 732 \)

**d. Azepane type**

(+/-)-(4\(R\),5\(R\),Z)-5-methyl-1-tosyl-6-((trimethylsilyl)methylene)azepan-4-ol **31**

Cyclization was performed following **GP-A** starting from **30** (146 mg, 0.4 mmol). Purification by flash chromatography over silica gel (pentane/diethyl ether 1/0 to 40/60) afforded **31** as a white solid (75 mg, 0.2 mmol, 51 %).

\[ \text{**1H NMR** (400 MHz, CDCl}_3\text{): } \delta 7.70 – 7.64 \text{ (m, 2H), 7.35 – 7.30 (m, 2H), 5.55 (s, 1H), 4.11 (d, } J = 13.7 \text{ Hz, 1H), 3.76 – 3.70 (m, 1H), 3.63 (d, } J = 13.7 \text{ Hz, 1H), 3.42 – 3.35 (m, 1H), 2.91 (q, } J = 7.1 \text{ Hz, 1H), 2.67 (ddd, } J = 14.6, 10.8, 1.9 \text{ Hz, 1H), 2.43 (s, 3H), 1.92 (ddt, } J = 14.4, 10.8, 3.4 \text{ Hz, 1H), 1.86 – 1.77 (m, 1H), 1.64 (bs, 1H), 1.18 (d, } J = 7.1 \text{ Hz, 3H), -0.02 (s, 9H)} \]

\[ \text{**13C NMR** (100 MHz, CDCl}_3\text{): } \delta 153.1, 143.6, 135.5, 130.4, 129.9, 127.1, 71.0, 53.9, 43.9, 41.9, 38.0, 21.6, 16.7, 0.1 \]

HRMS (ESI): calculated for [M+H]+ 368.1710 g.mol\(^{-1}\), found 368.1707 g.mol\(^{-1}\), calculated for [M+Na]+ 390.1530 g.mol\(^{-1}\), found 390.1526 g.mol\(^{-1}\)

FTIR (film cm\(^{-1}\)): \( \nu 3526, 2951, 2923, 1599, 1451, 1335, 1248, 1158, 1107, 1089, 1030, 935, 835, 814, 757, 733, 713, 656 \)

Mp 87°C

(+/-)-(4\(R\),5\(R\),Z)-5-(2-hydroxy-2-methylpropyl)-1-tosyl-6-((trimethylsilyl)methylene)azepan-4-ol **36**

Cyclization was performed following **GP-C** starting from **30** (73 mg, 0.2 mmol). Purification by flash chromatography over silica gel (pentane/diethyl ether 50/50 to 0/1) afforded **36** as a colourless liquid (23 mg, 0.05 mmol, 27 %).
\( ^1H \text{NMR (400 MHz, CDCl}_3 \): } \delta 7.70 - 7.62 (m, 2H), 7.36 - 7.29 (m, 2H), 5.62 (s, 1H), 4.07 (d, J = 13.7 Hz, 1H), 3.77 - 3.72 (m, 1H), 3.69 (d, J = 13.7 Hz, 1H), 3.28 (dt, J = 14.0, 4.6 Hz, 1H), 2.97 (td, J = 5.9, 3.2 Hz, 1H), 2.76 (dt, J = 20.2, 6.4 Hz, 1H), 2.43 (s, 3H), 2.00 (dd, J = 14.9, 5.9 Hz, 1H), 1.88 (td, J = 7.2, 3.8 Hz, 2H), 1.80 (dd, J = 14.9, 5.9 Hz, 1H), 1.68 (bs, 1H), 1.28 (s, 3H), 1.21 (s, 3H), -0.05 (s, 9H)

\( ^{13}C \text{NMR (100 MHz, CDCl}_3 \): } \delta 153.3, 143.6, 135.2, 132.2, 129.9, 127.2, 73.9, 71.4, 52.7, 50.2, 42.7, 40.8, 36.5, 31.8, 28.4, 21.6, -0.1

HRMS (ESI): calculated for [M+H]+ 426.2129 g.mol\(^{-1}\), found 426.2116 g.mol\(^{-1}\), calculated for [M+Na]+ 448.1948 g.mol\(^{-1}\), found 448.1941 g.mol\(^{-1}\), calculated for [M+K]+ 464.1688 g.mol\(^{-1}\), found 464.1675 g.mol\(^{-1}\)

FTIR (film cm\(^{-1}\)): \( \nu \) 3359, 2952, 1599, 1444, 1335, 1248, 1158, 1091, 1035, 914, 851, 835, 752, 736, 716, 660

(+/-)-(4\( R \),5\( R \),Z)-6-benzylidene-5-methyl-1-tosylazepan-4-ol 33A and (+/-)-(4\( R \),5\( S \),Z)-6-benzylidene-5-methyl-1-tosylazepan-4-ol 33B

Cyclization was performed following GP-A starting from 32 (148 mg, 0.4 mmol). Purification by flash chromatography over silica gel (pentane/diethyl ether 50/50 to 20/80) afforded a clean mixture of 33A and 33B (syn/anti 40/60) as a colourless oil (63 mg, 0.17 mmol, 42%).

33\( A \)
\( ^1H \text{NMR (400 MHz, CDCl}_3 \): } \delta 7.67 - 7.59 (m, 2H), 7.33 - 7.17 (m, 5H), 7.10 - 7.03 (m, 2H), 6.56 (s, 1H), 4.25 - 4.21 (m, 1H), 4.00 (dd, J = 10.9, 1.4 Hz, 1H), 3.85 (s, 1H), 3.24 (ddd, J = 3.3, 3.3, 2.8 Hz, 1H), 3.04 - 2.93 (m, 1H) 2.86 (ddd, J = 14.5, 10.1, 2.0 Hz, 1H), 2.39 (s, 3H), 1.95 (ddd, J = 14.5, 10.1, 4.1, 2.8 Hz, 1H), 1.89 - 1.79 (m, 2H), 1.32 (d, J = 7.1 Hz, 3H)
\( ^{13}C \text{NMR (100 MHz, CDCl}_3 \): } \delta 143.4, 137.1, 136.3, 135.8, 131.0, 130.0, 128.9, 128.3, 127.1, 127.0, 72.1, 49.8, 43.1, 42.4, 37.1, 21.6, 16.0

HRMS (ESI): calculated for [M+H]+ 372.1628 g.mol\(^{-1}\), found 372.1629 g.mol\(^{-1}\), calculated for [M+Na]+ 394.1447 g.mol\(^{-1}\), found 394.1451 g.mol\(^{-1}\)

FTIR (film cm\(^{-1}\)): \( \nu \) 3526, 2923, 1598, 1493, 1445, 1329, 1305, 1289, 1184, 1154, 1091, 1035, 914, 851, 835, 752, 736, 716, 660

33\( B \)
\( ^1H \text{NMR (400 MHz, CDCl}_3 \): } \delta 7.67 - 7.59 (m, 2H), 7.33 - 7.17 (m, 5H), 7.10 - 7.03 (m, 2H), 6.56 (s, 1H), 4.25 - 4.21 (m, 1H), 3.96 (dd, J = 10.6, 1.4 Hz, 1H), 3.76 - 3.67 (m, 1H), 3.27 (ddd, J = 6.4, 3.3, 3.3 Hz, 1H), 3.06 - 3.02 (m, 1H), 2.73 (m, 1H), 2.40 (s, 3H), 2.06 (ddd, J = 14.8, 10.0, 3.6, 2.7 Hz, 1H), 1.84 – 1.73 (m, 2H), 1.34 (d, J = 7.0 Hz, 3H)
\( ^{13}C \text{NMR (100 MHz, CDCl}_3 \): } \delta 143.4, 136.9, 136.3, 135.5, 131.6, 129.8, 128.9, 128.3, 127.1, 127.0, 73.3, 48.4, 47.8, 42.1, 35.4, 21.6, 16.3

HRMS (ESI): calculated for [M+H]+ 372.1628 g.mol\(^{-1}\), found 372.1629 g.mol\(^{-1}\), calculated for [M+Na]+ 394.1447 g.mol\(^{-1}\), found 394.1451 g.mol\(^{-1}\)

FTIR (film cm\(^{-1}\)): \( \nu \) 3526, 2923, 1598, 1493, 1445, 1329, 1305, 1289, 1184, 1154, 1091, 1035, 1018, 963, 923, 907, 885, 699, 657
Cyclization was performed following GP-A starting from 34 (160 mg, 0.4 mmol). Purification by flash chromatography over silica gel (pentane/diethyl ether 1/0 to 50/50) afforded a clean mixture of 35A and 35B (syn/anti 31/69) as a yellow oil (23 mg, 0.06 mmol, 14 %).

35A

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta 7.69 – 7.61\) (m, 2H), 7.31 – 7.23 (m, 2H), 7.06 – 6.97 (m, 2H), 6.86 – 6.77 (m, 2H), 6.50 (s, 1H), 4.24 (d, \(J = 14.3\) Hz, 1H), 3.98 (dd, \(J = 14.3, 1.4\) Hz, 1H), 3.86 – 3.83 (m, 1H), 3.81 (s, 3H), 3.30 – 3.26 (m, 1H), 3.02 – 2.95 (m, 1H), 2.84 (dd, \(J = 10.3, 2.0\) Hz, 1H), 2.41 (s, 3H), 2.00 – 1.87 (m, 1H), 1.87 – 1.80 (m, 1H), 1.68 (s, 1H), 1.31 (d, \(J = 7.2\) Hz, 3H)

\(^13\)C NMR (100 MHz, CDCl\(_3\)): \(\delta 158.7, 143.4, 136.0, 135.5, 130.4, 130.2, 130.0, 128.8, 127.1, 113.8, 72.0, 55.4, 50.0, 43.0, 42.4, 37.2, 21.6, 16.7\)

HRMS (ESI): calculated for [M+H]\(^+\) 402.1733 g.mol\(^{-1}\), found 402.1731 g.mol\(^{-1}\), calculated for [M+Na]\(^+\) 424.1553 g.mol\(^{-1}\), found 424.1548 g.mol\(^{-1}\), calculated for [M+K]\(^+\) 440.1292 g.mol\(^{-1}\), found 440.1290 g.mol\(^{-1}\)

FTIR (film cm\(^{-1}\)): \(\nu 3525, 2926, 1606, 1574, 1508, 1456, 1331, 1304, 1290, 1247, 1156, 1106, 1089, 1030, 964, 908, 887, 833, 813, 733, 703, 666, 657\)

35B

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta 7.69 – 7.61\) (m, 2H), 7.31 – 7.23 (m, 2H), 7.06 – 6.97 (m, 2H), 6.86 – 6.77 (m, 2H), 6.50 (s, 1H), 4.25 (d, \(J = 13.6\) Hz, 1H), 3.94 (dd, \(J = 13.6, 1.1\) Hz, 1H), 3.81 (s, 3H), 3.72 – 3.68 (m, 1H), 3.33 – 3.30 (m, 1H), 2.80 (dd, \(J = 10.3, 2.0\) Hz, 1H), 2.76 – 2.64 (m, 1H), 2.42 (s, 3H), 2.09 – 2.00 (m, 1H), 1.80 – 1.72 (m, 1H), 1.68 (s, 1H), 1.33 (d, \(J = 7.2\) Hz, 3H)

\(^13\)C NMR (100 MHz, CDCl\(_3\)): \(\delta 158.8, 143.4, 135.7, 135.1, 131.5, 130.2, 130.0, 128.8, 127.2, 113.8, 73.2, 55.4, 48.4, 48.1, 42.0, 35.3, 21.6, 15.9\)

HRMS (ESI): calculated for [M+H]\(^+\) 402.1733 g.mol\(^{-1}\), found 402.1731 g.mol\(^{-1}\), calculated for [M+Na]\(^+\) 424.1553 g.mol\(^{-1}\), found 424.1548 g.mol\(^{-1}\), calculated for [M+K]\(^+\) 440.1292 g.mol\(^{-1}\), found 440.1290 g.mol\(^{-1}\)

FTIR (film cm\(^{-1}\)): \(\nu 3525, 2926, 1606, 1574, 1508, 1456, 1331, 1304, 1290, 1247, 1156, 1106, 1089, 1030, 964, 908, 887, 833, 813, 733, 703, 666, 657\)

e. Oxepane type

Cyclization was performed following GP-A starting from 37 (106 mg, 0.4 mmol). Purification by flash chromatography over silica gel (pentane/diethyl ether 1/0 to 80/20) afforded 38 as a yellow oil (46 mg, 0.17 mmol, 43 %).

\[ \text{1H NMR (400 MHz, CDCl}_3\text{):} \delta 5.34 (d, J = 1.5 Hz 1H), 4.26 (dd, J = 15.7, 1.5 Hz, 1H), 4.16 (dd, J = 15.7, 1.5 Hz, 1H), 3.84 (br s, 1H), 2.92 (dq, J = 6.9, 3.2 Hz, 1H), 1.91-1.80 (m, 4H), 1.75-1.66 (m, 2H), 1.65-1.56 (m, 2H), 1.53 (br s, 1H), 1.49-1.37 (m, 2H), 1.14 (d, J = 6.9 Hz, 3H), 0.11 (s, 9H) \]

\[ \text{13C NMR (100 MHz, CDCl}_3\text{):} \delta 159.1, 123.4, 85.7, 71.6, 66.8, 44.7, 44.6, 38.2, 38.2, 23.6, 23.5, 14.1, 0.0 \]

HRMS (ESI): calculated for [M+Na]^+ 291.1751 g.mol\(^{-1}\), found 291.1754 g.mol\(^{-1}\)

\[ \text{FTIR (film cm}^{-1}\text{):} \nu 3392, 2953, 2873, 1604, 1440, 1363, 1247, 1211, 1101, 1088, 1036, 987, 833, 765, 747, 730, 689 \]

1-(2-hydroxybut-3-en-1-yl)cyclopentanol 42

\[ \text{1H NMR (300 MHz, CDCl}_3\text{):} \delta 5.88 (ddd, J = 17.2, 10.6, 5.9 Hz, 1H), 5.25 (dd, J = 17.2, 1.0, 1H), 5.08 (dd, J = 10.6, 1.0 Hz, 1H), 4.48 (dt, J = 7.9, 1.8 Hz, 1H), 3.34-3.19 (br m, 1H), 2.99-2.86 (br m, 1H), 1.95-1.77 (m, 4H), 1.73-1.53 (m, 6H) \]

\[ \text{13C NMR (75 MHz, CDCl}_3\text{):} \delta 141.2, 114.3, 83.0, 72.2, 46.3, 41.9, 38.5, 23.8, 23.5 \]

HRMS (ESI): calculated for [M+H]^+ 157.1223 g.mol\(^{-1}\), found 157.1224 g.mol\(^{-1}\), calculated for [M+Na]^+ 179.1048 g.mol\(^{-1}\), found 179.1043 g.mol\(^{-1}\)

\[ \text{FTIR (film cm}^{-1}\text{):} \nu 3359, 2957, 2873, 1709, 1435, 1319, 1039, 993, 909, 854, 731 \]


Cyclization was performed following GP-A starting from 39 (108 mg, 0.4 mmol). Purification by flash chromatography over silica gel (pentane/diethyl ether 1/0 to 60/40) afforded 40 as a yellow oil (30 mg, 0.11 mmol, 28 %).

\[ \text{1H NMR (400 MHz, CDCl}_3\text{):} \delta 7.37 – 7.32 (m, 2H), 7.28 – 7.15 (m, 3H), 6.35 (s, 1H), 4.41 (d, J = 15.6 Hz, 1H), 4.34 (d, J = 15.7 Hz, 1H), 3.98 (dt, J = 8.6, 3.9 Hz, 1H), 3.02 (qd, J = 7.2, 3.5 Hz, 1H), 1.98 (dd, J = 14.3, 9.3 Hz, 1H), 1.84 (dd, J = 14.3, 4.1 Hz, 1H), 1.81 – 1.73 (m, 1H), 1.68 – 1.63 (m, 2H), 1.59 – 1.52 (m, 3H), 1.51 – 1.37 (m, 2H), 1.29 (d, J = 7.2 Hz, 3H) \]

\[ \text{13C NMR (100 MHz, CDCl}_3\text{):} \delta 143.0, 137.2, 129.0, 128.3, 126.7, 125.7, 85.6, 72.0, 63.5, 44.2, 43.4, 39.0, 37.6, 23.8, 23.6, 13.8 \]

HRMS (ESI): calculated for [M+Na]^+ 295.1668 g.mol\(^{-1}\), found 295.1673 g.mol\(^{-1}\)

\[ \text{FTIR (film cm}^{-1}\text{):} \nu 3412, 3023, 2958, 2871, 1598, 1493, 1444, 1332, 1211, 1094, 1079, 1030, 989, 917, 867, 753, 699 \]
6/ References


7/ NMR spectra
<table>
<thead>
<tr>
<th>f1 (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.42</td>
</tr>
<tr>
<td>7.43</td>
</tr>
<tr>
<td>7.44</td>
</tr>
<tr>
<td>7.45</td>
</tr>
<tr>
<td>7.46</td>
</tr>
<tr>
<td>7.47</td>
</tr>
<tr>
<td>7.48</td>
</tr>
<tr>
<td>7.49</td>
</tr>
<tr>
<td>7.50</td>
</tr>
<tr>
<td>7.51</td>
</tr>
<tr>
<td>7.52</td>
</tr>
<tr>
<td>7.53</td>
</tr>
<tr>
<td>7.54</td>
</tr>
<tr>
<td>7.55</td>
</tr>
<tr>
<td>7.56</td>
</tr>
<tr>
<td>7.57</td>
</tr>
<tr>
<td>7.58</td>
</tr>
<tr>
<td>7.59</td>
</tr>
<tr>
<td>7.60</td>
</tr>
<tr>
<td>7.61</td>
</tr>
<tr>
<td>7.62</td>
</tr>
<tr>
<td>7.63</td>
</tr>
<tr>
<td>7.64</td>
</tr>
<tr>
<td>7.65</td>
</tr>
<tr>
<td>7.66</td>
</tr>
<tr>
<td>7.67</td>
</tr>
<tr>
<td>7.68</td>
</tr>
<tr>
<td>7.69</td>
</tr>
<tr>
<td>7.70</td>
</tr>
<tr>
<td>7.71</td>
</tr>
<tr>
<td>7.72</td>
</tr>
<tr>
<td>7.73</td>
</tr>
<tr>
<td>7.74</td>
</tr>
<tr>
<td>7.75</td>
</tr>
<tr>
<td>7.76</td>
</tr>
<tr>
<td>7.77</td>
</tr>
<tr>
<td>7.78</td>
</tr>
<tr>
<td>7.79</td>
</tr>
<tr>
<td>7.80</td>
</tr>
<tr>
<td>7.81</td>
</tr>
<tr>
<td>7.82</td>
</tr>
<tr>
<td>7.83</td>
</tr>
<tr>
<td>7.84</td>
</tr>
<tr>
<td>7.85</td>
</tr>
<tr>
<td>7.86</td>
</tr>
<tr>
<td>7.87</td>
</tr>
<tr>
<td>7.88</td>
</tr>
<tr>
<td>7.89</td>
</tr>
<tr>
<td>7.90</td>
</tr>
<tr>
<td>7.91</td>
</tr>
<tr>
<td>7.92</td>
</tr>
<tr>
<td>7.93</td>
</tr>
<tr>
<td>7.94</td>
</tr>
<tr>
<td>7.95</td>
</tr>
<tr>
<td>7.96</td>
</tr>
<tr>
<td>7.97</td>
</tr>
<tr>
<td>7.98</td>
</tr>
<tr>
<td>7.99</td>
</tr>
<tr>
<td>8.00</td>
</tr>
<tr>
<td>8.01</td>
</tr>
<tr>
<td>8.02</td>
</tr>
<tr>
<td>8.03</td>
</tr>
<tr>
<td>8.04</td>
</tr>
<tr>
<td>8.05</td>
</tr>
<tr>
<td>8.06</td>
</tr>
<tr>
<td>8.07</td>
</tr>
<tr>
<td>8.08</td>
</tr>
<tr>
<td>8.09</td>
</tr>
<tr>
<td>8.10</td>
</tr>
<tr>
<td>8.11</td>
</tr>
<tr>
<td>8.12</td>
</tr>
<tr>
<td>8.13</td>
</tr>
<tr>
<td>8.14</td>
</tr>
<tr>
<td>8.15</td>
</tr>
<tr>
<td>8.16</td>
</tr>
<tr>
<td>8.17</td>
</tr>
<tr>
<td>8.18</td>
</tr>
<tr>
<td>8.19</td>
</tr>
<tr>
<td>8.20</td>
</tr>
<tr>
<td>8.21</td>
</tr>
<tr>
<td>8.22</td>
</tr>
<tr>
<td>8.23</td>
</tr>
<tr>
<td>8.24</td>
</tr>
<tr>
<td>8.25</td>
</tr>
<tr>
<td>8.26</td>
</tr>
<tr>
<td>8.27</td>
</tr>
<tr>
<td>8.28</td>
</tr>
<tr>
<td>8.29</td>
</tr>
<tr>
<td>8.30</td>
</tr>
<tr>
<td>8.31</td>
</tr>
<tr>
<td>8.32</td>
</tr>
<tr>
<td>8.33</td>
</tr>
<tr>
<td>8.34</td>
</tr>
<tr>
<td>8.35</td>
</tr>
<tr>
<td>8.36</td>
</tr>
<tr>
<td>8.37</td>
</tr>
<tr>
<td>8.38</td>
</tr>
<tr>
<td>8.39</td>
</tr>
<tr>
<td>8.40</td>
</tr>
<tr>
<td>8.41</td>
</tr>
<tr>
<td>8.42</td>
</tr>
<tr>
<td>8.43</td>
</tr>
<tr>
<td>8.44</td>
</tr>
<tr>
<td>8.45</td>
</tr>
<tr>
<td>8.46</td>
</tr>
<tr>
<td>8.47</td>
</tr>
<tr>
<td>8.48</td>
</tr>
</tbody>
</table>

**Diagram:**

![Chemical Structure](image)
<table>
<thead>
<tr>
<th>f1 (ppm)</th>
<th>6.00</th>
<th>9.00</th>
<th>0.91</th>
<th>2.00</th>
<th>2.00</th>
<th>1.00</th>
<th>1.00</th>
<th>1.00</th>
<th>1.00</th>
<th>1.00</th>
<th>3.12</th>
<th>1.00</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>H</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>O</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Si</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>H</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>H</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>H</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>H</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>H</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>H</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>H</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>H</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>H</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
[Chemical structure diagram]

[1H NMR spectrum]

[99]
\begin{align*}
\text{O} & \quad \text{H} \\
\text{C} & \quad \text{H}_3 \\
\text{O} & \quad \text{C} \\
\text{H}_3 & \quad \text{O} \\
\end{align*}

\begin{align*}
\text{HO} & \quad \text{CH}_3 \\
\end{align*}