**Phosphinates as New Electrophilic Partners for Cross-Coupling Reactions**


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**Part A: Experimental Procedure for Suzuki Array Screening**

The protocol used to carry out arrays of 24 Suzuki reactions using a Radley’s Technologies Greenhouse Parallel Synthesiser is described in this Appendix. This procedure was adapted from one developed by Mr Ian B. Campbell of GlaxoSmithkline, Stevenage, UK and acknowledgement is made to him for the original protocol.

The conditions cover a range of catalysts, ligands, bases and solvents which have been employed regularly in Suzuki cross-coupling reactions. Arrays were carried out in a 24 array Greenhouse and followed by GC and GCMS. The reactions were carried out on 0.1 mmol scale using 3 mol% catalyst precursor, 6 mol% ligand and 3 equivalents base together with 1 equivalent of dodecane as an internal standard exploring a total of 4 catalysts, 7 ligands, 10 bases, 8 solvents as described in the table below.

**Table A1 Array Reaction Conditions**

<table>
<thead>
<tr>
<th>Greenhouse Tube</th>
<th>Catalyst</th>
<th>Ligand</th>
<th>Base</th>
<th>Solvent</th>
<th>% Yield by GC</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1</td>
<td>Pd(PPh₃)₄</td>
<td></td>
<td>Cs₂CO₃</td>
<td>DMF</td>
<td>N/A</td>
</tr>
<tr>
<td>A2</td>
<td>Pd(PPh₃)₄</td>
<td></td>
<td>K₃PO₄</td>
<td>DMF</td>
<td>23%</td>
</tr>
<tr>
<td>A3</td>
<td>Pd(PPh₃)₄</td>
<td></td>
<td>Na₂CO₃</td>
<td>DME / H₂O</td>
<td>no product</td>
</tr>
<tr>
<td>A4</td>
<td>Pd(PPh₃)₄</td>
<td></td>
<td>NaHCO₃</td>
<td>DME / H₂O</td>
<td>98%</td>
</tr>
<tr>
<td>A5</td>
<td>Pd(PPh₃)₄</td>
<td></td>
<td>Ba(OH)₂</td>
<td>DME / H₂O</td>
<td>72%</td>
</tr>
<tr>
<td>A6</td>
<td>Pd(PPh₃)₄</td>
<td></td>
<td>NaOH</td>
<td>DME / H₂O</td>
<td>&lt;10%</td>
</tr>
<tr>
<td></td>
<td>Pd(II) Compound</td>
<td>Base</td>
<td>Solvent</td>
<td>Yield (%)</td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>----------------</td>
<td>------</td>
<td>-------------</td>
<td>-----------</td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>Pd(OAc)$_2$</td>
<td></td>
<td>DME / H$_2$O</td>
<td>17%</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>Pd(OAc)$_2$</td>
<td>IMES</td>
<td>Toluene</td>
<td>&lt;10%</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>Pd(OAc)$_2$</td>
<td>IMES</td>
<td>DMF</td>
<td>&lt;10%</td>
<td></td>
</tr>
<tr>
<td>D</td>
<td>Pd$_2$(dba)$_3$</td>
<td>IMES</td>
<td>MeCN</td>
<td>&lt;10%</td>
<td></td>
</tr>
<tr>
<td>E</td>
<td>Pd$_2$(dba)$_3$</td>
<td>IMES</td>
<td>Dioxane / H$_2$O</td>
<td>11%</td>
<td></td>
</tr>
<tr>
<td>F</td>
<td>Pd(OAc)$_2$</td>
<td>IMES</td>
<td>DME / H$_2$O</td>
<td>No product</td>
<td></td>
</tr>
<tr>
<td>G</td>
<td>Pd(OAc)$_2$</td>
<td>(2-furan)$_3$P</td>
<td>Et$_3$N</td>
<td>No product</td>
<td></td>
</tr>
<tr>
<td>H</td>
<td>Pd(OAc)$_2$</td>
<td>Dppe</td>
<td>Et$_3$N</td>
<td>&lt;10%</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>Pd(OAc)$_2$</td>
<td>Dppb</td>
<td>Et$_3$N</td>
<td>&lt;10%</td>
<td></td>
</tr>
<tr>
<td>J</td>
<td>Pd(OAc)$_2$</td>
<td>Dppf</td>
<td>Et$_3$N</td>
<td>No product</td>
<td></td>
</tr>
<tr>
<td>K</td>
<td>Pd(OAc)$_2$</td>
<td>tBu$_2$P(BiPh)</td>
<td>K$_3$PO$_4$</td>
<td>EtOH / H$_2$O</td>
<td>44%</td>
</tr>
<tr>
<td>L</td>
<td>Pd(OAc)$_2$</td>
<td>tBu$_2$P(BiPh)</td>
<td>K$_3$PO$_4$</td>
<td>Toluene</td>
<td>&lt;10%</td>
</tr>
<tr>
<td>M</td>
<td>Pd$_2$(dba)$_3$</td>
<td>KOAc</td>
<td>Toluene/EtOH</td>
<td>31%</td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>Pd$_2$(dba)$_3$</td>
<td>IMES</td>
<td>Cs$_2$CO$_3$</td>
<td>Dioxane</td>
<td>&lt;10%</td>
</tr>
<tr>
<td>O</td>
<td>Pd$_2$(dba)$_3$</td>
<td>Dppf</td>
<td>Cs$_2$CO$_3$</td>
<td>No product</td>
<td></td>
</tr>
<tr>
<td>P</td>
<td>PdCl$_2$(Binap)</td>
<td>NaHCO$_3$</td>
<td>DME / H$_2$O</td>
<td>46%</td>
<td></td>
</tr>
<tr>
<td>Q</td>
<td>PdCl$_2$(Binap)</td>
<td>K$_3$PO$_4$</td>
<td>DMF</td>
<td>14%</td>
<td></td>
</tr>
<tr>
<td>R</td>
<td>PdCl$_2$(Binap)</td>
<td>CsF</td>
<td>THF / H$_2$O</td>
<td>63%</td>
<td></td>
</tr>
</tbody>
</table>

$tBu_2P(BiPh) = \begin{array}{c}
\text{Ph} \\
\text{Ph} \\
\text{Ph} \\
\text{Ph}
\end{array}$
Table A2- Dispense List – The following stock solutions were prepared

| A1  | Enol Phosphinate 3a | 0.2 M in THF |
| A1.5 | Dodecane | 0. |
| A2  | Boronic Acid 4a | 0.2 M in THF |
| A3  | Pd(PPh₃)₄ | 0.01 M in THF | 11.55 mg/ml |
| A4  | Pd(OAc)₂ | 0.01 M in THF | 2.24 mg/ml |
| A5  | Pd₂(dba)₃ | 0.01 M in THF | 9.14 mg/ml |
| A6  | Pd(Binap)Cl₂ | 0.01 M in THF | 8.0 mg/ml |
| B1  | IMES | 0.01 M in THF | 2.02 mg/ml |
| B2  | dpmm | 0.01 M in THF | 3.85 mg/ml |
| B3  | (2-furan)₃P | 0.01 M in THF | 2.32 mg/ml |
| B4  | dppe | 0.01 M in THF | 3.98 mg/ml |
| B5  | dppb | 0.01 M in THF | 4.26 mg/ml |
| B6  | dpf | 0.01 M in THF | 5.54 mg/ml |
| B7  | tBu₂P(BiPh) | 0.01 M in THF | 2.98 mg/ml |
| C1  | Na₂CO₃ | 1.0 M in H₂O | 106 mg/ml |
| C2  | NaHCO₃ | 1.0 M in H₂O | 84 mg/ml |
| C3  | NaOH | 1.0 M in H₂O | 40 mg/ml |
| C4  | Et₃N | |
| C5  | K₂CO₃ | 1.0 M in H₂O | 138 mg/ml |
| C6  | K₃PO₄ | 1.0 M in H₂O | 203 mg/ml |
| C7  | CsF | 1.0 M in H₂O | 151 mg/ml |
| D1  | DMF | |
| D2  | DME | |
| D3  | PhMe | |
| D4  | MeCN | |
| D5  | Dioxane | |
| D6  | H₂O | |
| D7  | EtOH | |
| D8  | THF | |

Table A3- Solid Samples were preweighed

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Cs₂CO₃</td>
<td>3 x 97.5 mg</td>
</tr>
<tr>
<td>K₃PO₄</td>
<td>3 x 60.9 mg</td>
</tr>
<tr>
<td>Ba(OH)₂</td>
<td>1 x 51.3 mg</td>
</tr>
<tr>
<td>KOAc</td>
<td>1 x 29.4 mg</td>
</tr>
</tbody>
</table>

Table A4- Protocol-

1. 500 µl A1 to vessels A1 – D6 (24 dispenses)
2. 500 µl A2 to vessels A1 – D6 (24 dispenses)
3. 500 µl A3 to vessels A1 – A6 (3 dispenses)
4. 500 µl A4 to vessels B1 – C6 (Not B4 and B5) (10 dispenses)
5. 500 µl A5 to vessels D1 – D3, B4 and B5 (5 dispenses)
6. 500 µl A6 to vessels D4 – D6 (3 dispenses)
7. 500 µl B1 to vessels B2 – B5 and D2 (5 dispenses)
8. 500 µl B2 to vessel B6 (1 dispenser)
9. 500 µl B3 to vessel C1 (1 dispense)
10. 500 µl B4 to vessel C2 (1 dispense)
11. 500 µl B5 to vessel C3
   (1 dispense)
12. 500 µl B6 to vessels C4 and D3
    (2 dispenses)
13. 500 µl B7 to vessels C5 and C6
    (2 dispenses)
14. All the samples were then evacuated using a Genevac vacuum centrifuge
    operating at full power for 12 minutes
15. 300 µl C1 to vessel A3
    (1 dispense)
16. 300 µl C2 to vessels A4, D4, and B6
    (3 dispenses)
17. 300 µl C3 to vessel A1
    (1 dispense)
18. 50 µl C4 to vessels B2 – C4 NOT B6
    (8 dispenses)
19. 300 µl C5 to vessel B1
    (1 dispense)
20. 300 µl C6 to vessel C5
    (1 dispense)
21. 300 µl C7 to vessel D6
    (1 dispense)
22. 1000 µl D1 to vessels A1, A2, B3, B7 – C4, D3, D5
    (9 dispenses)
23. 700 µl D1 to vessel B1
    (1 dispense)
24. 700 µl D2 to vessels A3 – A6, B6 and D4
    (6 dispenses)
25. 1000 µl D3 to vessels B2 and C6
    (2 dispenses)
26. 500 µl D3 to vessel D1
    (1 dispense)
27. 1000 µl D4 to vessel B4
    (1 dispense)
28. 500 µl D5 to vessel B5
    (1 dispense)
29. 1000 µl D5 to vessel D2
    (1 dispense)
30. 300 µl D6 to vessels A3 – A6, B1, B5, B6, C5, D4 and D6
    (10 dispenses)
31. 700 µl D7 to vessel C5
    (1 dispense)
32. 700 µl D8 to vessel D6
    (1 dispense)
33. Add Cs2CO3 97.5 mg to vessels A1, D2 and D3
34. Add K3PO4 60.9 mg to vessels A2, C6 and D5
35. Add Ba(OH)2 51.3 mg to vessel A5
36. Add KOAc 29.4 mg to vessel D1
37. Reaction array was then placed in the greenhouse reactor and heated at 80°C for
   18 h and then analysed by GC and GCMS

Part B: Experimental Procedures and Spectroscopic Data for Starting Lactams and all
Products

N-(Phenylloxycarbonyl)-2-oxo-azepane

To a cold (-78 °C) solution of caprolactam (1.06 g, 9.37 mmol) in dry THF (50 ml) was
added n-BuLi (1.0 M, 11.24 ml, 11.24 mmol) dropwise via a syringe and the reaction
mixture allowed to stir at -78 °C. After 2 h a cold (-78 °C) solution of phenyl
chloroformate (2.93 g, 18.73 mmol) in dry THF (30 ml) was added via cannula and the
resulting reaction mixture allowed to stir for an additional 3 h before warming to room
temperature. The reaction was quenched with NH4Cl(aq), concentrated and extracted with
EtOAc (150 ml). The organic phase was washed with brine (3 x 50 ml), NaHCO3 (aq)
(3 x 50 ml), dried over MgSO₄ and concentrated affording the crude material as a yellow oil. Flash chromatography ([50:1], [19:1] DCM/EtOAc) followed by recrystallisation (pet. ether) afforded the title compound as clear crystals (1.17 g, 4.99 mmol, 53%). mp. 70-71 °C. Found; C, 66.90; H, 6.45; N, 5.90%; Calc. for C₁₃H₁₅NO₃: C, 66.94; H, 6.48; N, 6.00%. νₘₐₓ (KBr) 2938, 2861, 1778 (CH₂C=O), 1731 and 1715 (O=C-O), 1265, 1182 cm⁻¹. δH (500 MHz) 1.85 (6H, m, 4-H₂, 5-H₂, 6-H₂), 2.78 (2H, m, 3-H₂), 3.98 (2H, m, 7-H₂), 7.18-7.22 (2H, m, 3'-H, 5'-H), 7.23-7.29 (1H, m, 4'-H), 7.37-7.42 (2H, m, 2'-H, 6'-H). δC (125MHz) 23.8 (C-4), 28.9 (C-6), 29.4 (C-5), 39.7 (C-3), 46.9 (C-7), 121.8 (C-3'), 126.4 (C-4'), 129.6 (C-2'), 151.1 (C-1'), 153.4 (OC=O), 157.9 (C-2). m/z (ES⁺) 234.1 (MH⁺).

N-(Benzyloxy carbonyl)-2-oxo-azepane

To a cold (-78 °C) solution of caprolactam (0.44 M, 2.00 g, 17.66 mmol) in dry THF (40 ml) was added n-BuLi (2.5 M, 9.2 ml, 22.97 mmol) dropwise via a syringe and the reaction mixture allowed to stir at -78 °C. After 30 min benzyl chloroformate was added slowly (6.03 g, 5.04 ml, 18.73 mmol) and the resulting reaction mixture allowed to stir for 1 h before warming to room temperature. The reaction was quenched with NH₄Cl (aq), concentrated and extracted with EtOAc (150 ml). The organic phase was washed with brine (3 x 50 ml), NaHCO₃(aq) (3 x 50 ml), dried over MgSO₄ and concentrated. Purification by flash chromatography ([4:1] DCM/EtOAc) afforded the title compound as a clear oil (2.25 g, 9.11 mmol, 52%). νₘₐₓ (ATR) 2932, 1767 (CH₂C=O), 1707 (O=C-O), 1378, 1264, 1163, 1014, 959, 736, 696 cm⁻¹. δH (500 MHz) 1.70-1.81 (6H, m, 4-H₂, 5-H₂, 6-H₂), 2.69 (2H, m, 3-H₂), 3.85 (2H, m, 7-H₂), 5.28 (2H, s, CO₂C₆H₅), 7.28-7.39 (3H, m, 3'-H, 4'-H), 7.43 (2H, m, 2'-H), 7.37-7.42. δC (125 MHz) 23.7, 28.9 and 29.4 (C-4, C-5, C-6), 39.7 (C-3), 46.6 (C-7), 68.8 (CO₂C₆H₅), 128.1, 128.4 and 128.8 (3 x ArC-H), 135.8 (C-1'), 154.5 (OC=O), 175.9 (C-2). m/z (ES⁺) 270.2 (MNa⁺), 517.0 (2MNa⁺). HRMS (ES⁺) found MNa⁺ 270.1101, C₁₄H₁₄NO₃Na requires M⁺ 270.1101.

N-([4'-Methylphenyl]sulfonyl)-2-oxo-azepane

Supplementary Material (ESI) for Organic & Biomolecular Chemistry
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Purification by flash chromatography ([85:15], [4:1], [65:35] pet. ether/EtOAc) afforded the title compound as a white solid (1.10 g, 4.12 mmol, 46%). mp 117-120 °C. Found; C, 58.11; H, 6.28; N, 4.92%; Calc. for C_{13}H_{17}NO_{3}S; C, 58.40; H, 6.41; N, 5.24%. \( \nu \text{max (KBr)} \) 2941, 2861, 1697 (NC=O), 1598, 1353 (SO\(_2\)), 253 (2H, t, J = 6 Hz, 3'-H), 3.79 (2H, t, J = 7 Hz, 2'-H), 2.92 (2H, d, J = 9 Hz, 3'-H, 5'-H), 7.87 (2H, d, J = 9 Hz, 2'-H, 6'-H). \( \delta \text{C} \) (125 MHz) 21.9 (4'-CH\(_3\)), 23.2 (C-4), 29.4 (C5), 29.6 (C-6), 39.0 (C-3), 46.7 (C-7), 128.8 (C-2'), 129.5 (C-3'), 136.8 (C-4'), 144.7 (C-1'), 175.1 (C-2). m/z (ES\(^+\)) 268.0 (MH\(^+\)).

\[
\text{N-[(4'-methylphenyl)sulfonyl]pyrroloidin-2-one}
\]

Obtained, following flash chromatography ([7:3] pet. ether/EtOAc), as a white solid (2.33 g, 9.74 mmol, 65%). mp 139-141 °C. \( \nu \text{max (ATR)} \) 3028, 1737 (C=O), 1598, 1359 (NSO\(_2\)), 1238, 1217, 1169 (NSO\(_2\)), 1121, 957, 662, 596, 558 cm\(^{-1}\). \( \delta \text{H} \) (500 MHz) 2.06 (2H, t, J = 8 Hz, 4'-H\(_2\)), 2.39-2.47 (5H, m, 4'-CH\(_3\), 3'-H\(_2\)), 3.88 (2H, t, J = 7 Hz, 5'-H\(_2\)), 7.33 (2H, d, J = 8 Hz, 3'-H), 7.91 (2H, d, J = 8 Hz, 2'-H). \( \delta \text{C} \) (125 MHz) 18.4 (C-4), 21.2 (CH\(_3\)), 32.5 (C-3), 47.5 (C-5), 128.3 (C-2'), 129.9 (C-3'), 135.3 (C-1'), 145.5 (C-4'), 173.7 (C=O). m/z (ES\(^+\)) 240 (MH\(^+\)). HRMS (ES\(^+\)) found MH\(^+\) 240.0691, C\(_{11}\)H\(_{14}\)NO\(_3\)SNa requires M\(^+\) 240.0689, found MNa\(^+\) 262.0509, C\(_{11}\)H\(_{14}\)NO\(_3\)SNa requires M\(^+\) 262.0508.

\[
\text{N-(Phenylxocarbonyl)pyrroloidin-2-one}
\]

To a cold solution (-78 °C) of pyrroloidinone (0.56 g, 6.58 mmol, 1 eq) in dry THF (10 ml, 0.66 M) was added n-BuLi (1.6 M, 4.9 ml, 7.90 mmol, 1.2 eq) dropwise via a syringe. The reaction mixture was allowed to stir at -78 °C for 1 h then Ph\(_2\)P(O)Cl (2.06 g, 13.16 mmol, 2 eq) was added as a cold solution in dry THF (4 ml). The reaction mixture was stirred for 1.5 h at -78 °C, warmed to room temperature and stirred for an additional 0.5 h then quenched with H\(_2\)O. The THF was removed under reduced pressure and the aqueous extracted into EtOAc (x 3), the combined organics were washed with H\(_2\)O, dried over MgSO\(_4\) and concentrated to a pink solid. Purification by flash chromatography afforded the title compound as a white solid (1.01 g, 4.94 mmol, 75%). mp 119-120 °C. Found; C, 64.33; H, 5.39; N, 6.81%; Calc. for C\(_{11}\)H\(_{16}\)NO\(_3\); C, 64.38; H, 5.40; N, 6.83%. \( \nu \text{max (ATR)} \) 2977, 1779 (OC=O), 1697 (NC=O), 1490, 1458, 1379, 1288, 1188, 1163, 1020, 988, 751, 693 cm\(^{-1}\). \( \delta \text{H} \) (700 MHz) 2.10 (2H, quint, J = 8 Hz, 4'-H\(_2\)), 2.60 (2H, t,
J = 8 Hz, CH₂), 3.93 (2H, t, J = 8 Hz, CH₂), 7.16 (2H, d, J = 8 Hz, 2'-H), 7.23 (1H, t, J = 8 Hz, 4'-H), 7.37 (2H, t, J = 8 Hz, 3'-H). δC (125 MHz) 17.8 (C-4), 33.1 (CH₂), 46.9 (CH₂), 121.7 (C-2'), 126.4 (C-4'), 129.6 (C-3'), 150.3 (C-1'), 150.5 (OC=O), 174.1 (C-2).
m/z (ES⁺) 206.1 (MH⁺), 223.1 (MH₂O⁺), 433.2 (2MNa⁺).

N-[(4'-methylphenyl)sulfonyl]piperidin-2-one

Obtained, following flash chromatography ((7:3] pet. ether/EtOAc), as a white solid (2.02 g, 7.9 mmol, 33%). mp. 136-138 °C. Found; C, 56.87; H, 5.97; N, 5.37%; Calc. for C₁₂H₁₅NO₃S; C, 56.90; H, 5.97; N, 5.53%. νmax (KBr) 2958, 1691 (C=O), 1457, 1354 (NSO₂), 1283, 1171 (NSO₂), 1089, 969, 830, 577, 549 cm⁻¹. δH (400 MHz) 1.74 (2H, quint, J = 6 Hz, 4-H₂), 1.87 (2H, quint, J = 6 Hz, 5-H₂), 2.28-2.48 (5H, m, 3-H₂, 4'-CH₃), 3.88 (2H, t, J = 6 Hz, 6-H₂), 7.28 (2H, d, J = 8 Hz, 3'-H, 5'-H), 7.87 (2H, d, J = 8 Hz, 2'-H, 6'-H). δC (100 MHz) 20.6 (C-4), 21.9 (C₄'-CH₃), 23.5 (C-5), 34.3 (C-3), 47.2 (C-6), 128.9 (C-2'), 129.5 (C-3'), 136.3 (C-1'), 145.0 (C-4'), 170.5 (C=O). m/z (ES⁺) 254.1 (MH⁺), 276.1 (MNa⁺), 308.1 (MNaMeOH⁺), 529 (2MNa⁺). HRMS (ES⁺) found MH⁺ 254.0847, C₁₂H₁₅NO₃S requires M⁺ 254.0845, found MNa⁺ 276.0666, C₁₂H₁₅NO₃SNa requires M⁺ 276.0665.

N-(tert-Butyloxycarbonyl)piperidin-2-one

To a solution of δ-valerolactam (4.96 g, 50 mmol, 1.0 eq) in THF (100 ml) was added 4-dimethylaminopyridine (7.33 g, 60 mmol, 1.2 eq) and di-tert-butylidicarbonate (13.10 g, 60 mmol, 1.2 eq). The resulting mixture was stirred at room temperature for 18 h. The mixture was concentrated and the aqueous extracted with EtOAc (x 3). The combined organic phases were washed with 5% HCl(aq), brine then dried over MgSO₄ and concentrated affording the title compound as a colourless oil (8.55 g, 86%). Rf (EtOAc): 0.7. Found; C, 59.33; H, 8.40; N, 6.89%; Calc. for C₁₀H₁₇NO₃; C, 60.28; H, 8.60; N, 7.03%. νmax (NaCl) 2977, 2947, 2879, 1773, 1732, 1480, 1459, 1392, 1243, 1134, 1057, 981, 853, 776, 660, 617 and 556 cm⁻¹. δH (400 MHz) 1.51 (9H, s, (CH₃)₂C), 1.81 (4H, m, 4-H₂, 5-H₂), 2.50 (2H, t, J = 6 Hz, 3-H₂), 3.64 (2H, t, J = 6 Hz, 6-H₂). δC (100 MHz) 20.6 (C-4), 22.9 (C-5), 28.1 (CH₃C), 35.0 (C-3), 46.4 (C-6), 83.0 ((CH₃)₂C), 152.9 (OC=O), 171.5 (C-2). m/z (ES⁺) 222.1 (MNa⁺).
\[ \text{N-(Phenyloxycarbonyl)piperidin-2-one} \]

Obtained, following flash chromatography ([19:1] DCM/EtOAc) followed by recrystallisation ([10:1] pet. ether/EtOAc), as a white solid (2.94 g, 13.42 mmol, 56%). mp. 114-116 °C. Found; C, 65.49; H, 5.99; N, 6.18%; Calc. for C\(_{12}\)H\(_{13}\)NO\(_3\); C, 65.74; H, 5.98; N, 6.39%. \(\nu\)\(_{\text{max}}\) (KBr) 3007, 2961, 1780 (C=O), 1714 (C=O), 1417, 1356, 1226, 1149, 824 cm\(^{-1}\). \(\delta\)\(_H\) (500 MHz) 1.93 (4H, m, 4-\text{-H}_2, 5-\text{-H}_2), 2.63 (2H, t, J = 6 Hz, 3-\text{-H}_2), 3.87 (2H, t, J = 8 Hz, 2'-\text{-H}_2), 7.20 (2H, d, J = 8 Hz, 2'-\text{-H}_2), 7.26 (1H, t, J = 8 Hz, 4'-\text{-H}_2), 7.40 (2H, t, J = 8 Hz, 3'-\text{-H}_2). \(\delta\)\(_C\) (125 MHz) 20.8 (C-4), 22.9 (C-5), 35.3 (C-3), 47.2 (C-6), 121.7 (C-2'), 126.3 (C-4'), 129.7 (C-3'), 151.0 (C-1'), 153.3 (OC=O), 171.5 (C-2). m/z (ES\(^+\)) 220.1 (MH\(^+\)), 461.1 (2MNa\(^+\)).

\[ \text{N-([4'-methylphenyl)sulfonyl]-2-oxoazocine} \]

Obtained, following flash chromatography ([7:3] pet. ether/EtOAc), as a white solid (3.46 g, 12.30 mmol, 80%). mp 116-118 °C. Found; C, 59.64; H, 6.82; N, 4.79%; Calc. for C\(_{14}\)H\(_{19}\)NO\(_3\)S; C, 59.76; H, 6.81; N, 4.98%. \(\nu\)\(_{\text{max}}\) (KBr) 2938, 1687 (C=O), 1448, 1358 (NSO\(_2\)), 1211, 1167 (NSO\(_2\)), 1119, 1083, 814, 683, 634, 542 cm\(^{-1}\). \(\delta\)\(_H\) (500 MHz) 1.46 (2H, qt, J = 6 Hz, 6-\text{-H}_2), 1.54 (2H, qt, J = 6 Hz, 5-\text{-H}_2), 1.75 (2H, qt, J = 6 Hz, 4-\text{-H}_2), 1.87 (2H, qt, J = 6 Hz, 7-\text{-H}_2), 2.41 (3H, s, 4'-CH\(_3\)), 2.48 (2H, m, 3-\text{-H}_2), 4.06 (2H, t, J = 6 Hz, 8-\text{-H}_2), 7.28 (2H, d, J = 9 Hz, 3'-\text{-H}, 5'-\text{-H}), 7.90 (2H, d, J = 9 Hz, 2'-\text{-H}, 6'-\text{-H}). \(\delta\)\(_C\) (125 MHz) 21.9 (4'-CH\(_3\)), 23.9 (C-6), 26.3 (C-5), 28.7 (C-4), 31.3 (C-7), 36.6 (C-3), 46.3 (C-8), 129.2, 129.4 (C-2', C-3'), 136.6 (C-1'), 144.8 (C-4'), 175.1 (CO). m/z (ES\(^+\)) 282.1 (MH\(^+\)).

\[ \text{N-(Phenyloxycarbonyl)-4,5,6,7-tetrahydro-1H-azepin-2-yl diphenylphosphinate 3b} \]

**NaHMDS Protocol:** Purification by flash chromatography afforded the title compound as a white crystalline solid (1.74 g, 4.02 mmol, 79%). mp. 84-85 °C. Found; C, 69.29; H, 5.57; N, 3.12%; Calc. for C\(_{25}\)H\(_{26}\)NO\(_4\)P; C, 69.28; H, 5.58; N, 3.23%. \(\nu\)\(_{\text{max}}\) (KBr) 3071,
2925, 1724 (C=O), 1685 (enol ether), 1441, 1375, 1351, 1322, 1197, 1126, 1093, 1057, 993, 871 cm$^{-1}$. $\delta_H$ (700 MHz) 1.35-1.6 (2H, broad, 5-H$_2$), 1.63-1.80 (2H, broad, 6-H$_2$), 2.08 (2H, m, 4-H$_2$), 3.10-3.60 (2H, broad, 7-H), 5.39-5.59 (1H, m, 3-H), 7.05 (2H, d, J = 8 Hz, 2″-H), 7.19 (1H, t, J = 8 Hz, 4″-H), 7.33 (2H, m, 3″-H), 7.42 (4H, m, 3′-H), 7.51 (2H, t, J = 7 Hz, 4′-H), 7.79-7.99 (4H, m, 2″-H), $\delta_C$ (175 MHz) 24.2 (C-5), 24.8 (C-4), 29.3 (C-6), 47.3 (C-7), 110.8 (C-3), 121.7 (C-2′″), 125.7 (C-4″″), 128.7, 128.8 (C-3′), 129.5 (C-3″), 131.0 (C-1′), and 131.9, 132.0 (C-2′), 132.7 (C-4′), 144.5 (C-2), 151.4 (C-1″), 152.6 (C=O). $\delta_p$ (283 MHz) 29.4. m/z (ES$^+$) 433.5 (MH$^+$). HRMS (ES$^+$) found MH$^+$ 434.1515, C$_{25}$H$_{25}$NO$_4$P requires M$^+$ 434.1515, found MNa$^+$ 456.1332, C$_{25}$H$_{24}$NNaO$_4$P requires M$^+$ 456.1335.

**N-(Benzyloxy carbonyl)-4,5,6,7-tetrahydro-1H-azepin-2-yl diphenylphosphinate 3c**

**NaHMDS Protocol for phosphinate formation:** Purification by flash chromatography ([4:1] DCM/EtOAc) and recrystallisation ([9:1] pet. ether/EtOAc) afforded the title compound as a crystalline solid (1.13 g, 2.53 mmol, 58%). mp. 83-85 °C. Found; C, 69.55; H, 5.81; N, 3.18%; Calc. for C$_{26}$H$_{26}$NO$_4$P; C, 69.79; H, 5.86; N, 3.13%. $\nu_{\text{max}}$(ATR) 2936, 1701 (C=O), 1672 (enol ether), 1441, 1395, 1345, 1327, 1285, 1241, 1168, 1121, 1057, 1016, 886, 763, 728, 694 cm$^{-1}$. $\delta_H$ (700 MHz) 1.29-1.55 (2H, broad, 5-H$_2$), 1.61 (2H, m, 6-H$_2$), 1.98 (2H, m, 4-H$_2$), 3.00-3.20 (2H, broad, 7-H$_2$), 5.00-5.20 (2H, m, OCH$_2$), 5.39-5.51 (1H, m, 3-H), 7.25-7.45 (9H, m, 9 x Ar-H), 7.49 (2H, t, J = 7 Hz, 4″-H), 7.63-7.97 (4H, m, 4 x Ar-H), $\delta_C$ (175 MHz) 24.2 (C-5), 24.7 (C-4), 29.4 (C-6), 47.1 (C-7), 67.6 (OCH$_2$), 110.9 (C-3), 128.2, 128.3, 128.6, 128.7 and 132.0 (ArC), 132.5 (C-4′), 136.5 (C-1′), 144.2 (C-2), 151.3 (C-1″), 154.1 (C=O). $\delta_p$ (283 MHz) 29.0. m/z (ES$^+$) 448.3 (MH$^+$), 917.3 (2MNa$^+$).

**N-[(4″-Methylphenyl)-sulfonyl]-4,5,6,7-tetrahydro-1H-azepin-2-yl diphenylphosphinate 3d**

**NaHMDS Protocol:** The crude material was collected as a yellow solid. Purification on a Horizon$^\text{®}$ column chromatography system ([19:1], [9:1] pet. ether/EtOAc) afforded the title compound as a white solid (0.80 g, 1.71 mmol, 73%). $\nu_{\text{max}}$(KBr) 3056, 2947, 2914, 2848, 1672, 1595, 1440, 1343, 1230, 1160, 1031, 993, 953, 869 cm$^{-1}$. $\delta_H$ (400 MHz)
1.34 (2H, quint, J = 6 Hz, 5-H2), 1.65 (2H, quint, J = 6 Hz, 6-H2), 1.85 (2H, q, J = 6 Hz, 4-H2), 2.35 (3H, s, 4''-CH3), 3.19 (2H, m, 7-H2), 5.52 (1H, dt, Jp = 2 Hz, JH = 8 Hz, 3-H), 7.07 (2H, d, J = 8 Hz, 3''-H, 5''-H), 7.41-7.47 (4H, m, Ar-H), 7.52-7.57 (2H, m, 4''-H), 7.67 (2H, d, J = 8 Hz, 2''-H, 6''-H), 7.78-7.86 (4H, m, Ar-H). δC (100 MHz) 21.9 (4''-CH3), 24.1 (C-5), 24.4 (C-4), 30.1 (C-6), 49.6 (C-7), 113.6 (C-3), 127.7 (C-2''), 128.8 (Ar-C-H) 129.9 (C-3''), 130.3 (Ar-C), 131.6 (Ar-C), 132.4 (ArCH), 132.8 (C-4'), 138.4 (Ar-C), 143.9 (C-2). δP (162MHz, ) 33.0. m/z (ES+) 468.2 (M+H), 490.3 (MNa+), 956.8 (2MNa+). HRMS (ES) found MH+ 468.1398, C25H27N1O4S1P1 requires M+ 468.1393, found MNa+ 490.1214, C25H26N1O4S1P1Na1 requires M+ 490.1212.

1-(tert-Butyloxycarbonyl)-4,5,6-trihydro-piperidin-2-diphenylphosphinate 3e

To a cold (-78 °C) solution of N-(tert-Butyloxycarbonyl)piperidin-2-one (2.23 g, 11.2 mmol, 1.0 eq) and TMEDA (1.86 ml, 12.32 mmol, 1.1 eq) in dry THF (50 ml) was added a solution of LDA (2.0 M, 6.16 ml, 12.32 mmol, 1.1 eq). The reaction mixture was stirred at -78 °C for 1 h, and diphenylphosphinic chloride (2.35 ml, 12.32 mmol, 1.1 eq) was added dropwise. The mixture was stirred at -78 °C for 1 h, and room temperature for a further 18 h. The solution was concentrated and extracted with EtOAc / brine, the organic phase was combined, dried over MgSO4, filtered and concentrated. Flash chromatography ([1:1] pet. ether/EtOAc) afforded the title compound as white solid (3.987 g, 89%). Rf (EtOAc): 0.70. mp. 122 °C. νmax (KBr) 3050, 2947, 1769, 1704, 1675, 1591, 1439, 1367, 1247, 1130, 953, 730, 700, 537, 524 and 436 cm⁻¹. This compound rapidly decomposed in CDCl3, CD3OD and d6-DMSO.

1-(Phenylxoycarbonyl)-4,5,6-trihydro-piperidin-2-diphenylphosphinate 3f

Obtained, following flash chromatography, ([9:1] DCM/EtOAc) as a clear oil which solidified on standing (1.27 g, 3.03 mmol, 61%). mp. 97-100 °C. Found; C, 68.61; H, 5.50; N, 3.31%; Calc. for C24H22NO4P; C, 68.73; H, 5.29; N, 3.34%. νmax (KBr) 3063, 2955, 1731 (C=O), 1677 (enol ether), 1439, 1364, 1345, 1207, 1175, 1131, 837, 545, 531 cm⁻¹. δH (400 MHz) 1.75 (2H, quint, J = 6 Hz, 5-H2), 2.12 (2H, m, 4-H2), 3.49 (2H, t, J = 6 Hz, 6-H2), 5.23 (1H, dt, 4JHP = 2 Hz, J = 6 Hz, 3-H), 7.09 (2H, dd, 4J = 1 Hz,
J = 8 Hz, 3''-H, 5''-H), 7.22 (1H, t, 4J = 1 Hz, J = 8 Hz, 4''-H), 7.31-7.43 (6H, m, 6 x Ar-H), 7.50 (2H, tq, J = 8 Hz, 4''-H), 7.86-7.93 (4H, m, 3'-H, 5'-H). δc (100 MHz) 21.8 (C-5), 23.0 (C-4), 46.0 (C-6), 101.1 (C-3), 121.8 (C-3''), 125.9 (C-4''), 128.6 (ArC), 128.8 (ArC), 129.6 (C-2''), 130.2 (C-2), 132.1, 132.2 (C-3' and C-5'), 132.65, 132.68 (2 x C-4'), 139.7, 139.8 (2 x C-1'), 151.2 (C-1''), 152.5 (C=O). δp (162 MHz) 31.1. m/z (ES+) 420.1 (MH+), 442.1 (MNa+), 861.3 (2MNa+).

1-Tosyl-4,5,6,7,8-quintahydro-1H-azepin-2-yl diphenylphosphinate 3g

Obtained, following column chromatography, ([95:5], [9:1] CHCl3/EtOAc) as a gummy oil which slowly solidified on standing (874 mg, 1.82 mmol, 51%). mp. 199-200 °C. HPLC, Rf = 6.02 min, 98.13%. νmax (KBr) 2928, 2851, 1671, 1593, 1440, 1348, 1235, 1156, 1126, 1076, 1006, 961, 874, 829, 730 cm⁻¹. δh (400 MHz) 1.43-1.60 (6H, m, 5-H2, 6-H2, 7-H2), 2.13 (2H, m, 4-H2), 2.36 (3H, s, 4''-CH3), 3.31 (2H, m, 8-H), 5.54 (1H, dt, 4JHP = 2 Hz, J = 8 Hz, 3-H), 7.09 (2H, d, J = 8 Hz, 3''-H, 5''-H), 7.38-7.45 (4H, m, Ar-H), 7.51-7.57 (2H, m, 4''-H), 7.63-7.70 (4H, m, Ar-H), 7.73 (2H, d, J = 8 Hz, 2''-H, 6''-H). δc (100 MHz) 21.9 (4''-CH3), 26.2 (C-4), 26.9 (C-6), 27.2 (C-7), 28.8 (C-5), 50.3 (C-8), 119.3 (C-3), 128.1 (C-2''), 128.8 (ArC-H), 129.8 (C-3''), 130.5 (ArC), 132.1 (ArC-H), 132.8 (C-4'), 137.7 (ArC), 138.4 (ArC), 143.6 (C-2). δp (162 MHz) 32.4. m/z (ES+) 482.1 (MH+), 980.4 (2MH2O+). HRMS (ES+) found MH+ 482.1554, C26H29N1O4SiP requires M+ 482.1550, found MNa+ 504.1367, C26H29N1O4SiP2Na+ requires M+ 504.1369.

N-(tert-Butyloxycarbonyl-2-(3',5'-Dimethylphenyl)-4,5,6,7-tetrahydro-azepane 5a-i

Suzuki protocol A: Flash chromatography ([19:1] pet. ether/EtOAc) afforded the title compound as a white solid (83%). mp. 113-115 °C. G.C. analysis: 1 peak, Rf 22.35 min. νmax (KBr) 2933, 1687 (C=O), 1391, 1357, 1161 cm⁻¹. δh (500 MHz) 1.10 (9H, s, C(CH3)3), 1.47 (2H, m, 7-H2), 1.79-1.89 (2H, m, 6-H2), 2.21-2.33 (10H, m, 3'-CH3, 5'-CH3, 4-H2, 5-H2), 5.85 (1H, t, J = 7 Hz, 3-H), 6.88 (1H, s, Ar-H), 6.92 (2H, s, Ar-H). δc (125 MHz) 21.5 (C-5), 24.4 (C-3', C-5'), 27.7 (C-4), 28.2 ((C(CH3)3), 28.7 (C-6), 48.2 (C-
Suzuki protocol A: Purification by flash chromatography ([19:1] pet. ether/EtOAc) afforded the title compound as a white solid (0.07 g, 0.24 mmol, 81%). mp. 95-97 °C. Found; C, 75.15; H, 8.88; N, 4.87%; Calc. for C_{18}H_{22}NO_2; C, 75.22; H, 8.77; N, 4.87%.

ν_{max} (KBr) 2979, 2933, 2856 (C-H), 1687 (C=O), 1392, 1357, 1160, 813 cm⁻¹. δ_\text{H} (400 MHz) 1.10 (9H, s, C(CH_3)_3), 1.46 (4H, s, 5-H_2, 7-H_2), 1.83 (2H, m, 6-H_2), 2.27 (2H, m, 4-H_2), 2.33 (3H, s, 4'-CH_3), 5.83 (1H, t, J = 7 Hz, 3'-H), 7.09 (2H, d, J = 9 Hz, 3'-H), 7.19 (2H, d, J = 9 Hz, 2'-H). δ_\text{C} (100 MHz) 21.4 (4'-CH_3), 24.5 (C-5), 27.7 (C-4), 28.2 ((C(CH_3)_3), 30.0 (C-6), 48.1 (C-7), 79.9 (C(CH_3)_3), 121.9 (C-3), 125.0 (C-2'), 128.9 (C-3'), 137.0 (C-1'), 137.2 (C-4'), 144.6 (C-2'), 154.6 (C=O). m/z (ES⁺) 311 (MH⁺), 351 (MNaMeCN⁻), 597 (2MNa⁺). HRMS (ES⁺) found MNa⁺ 310.1776, C_{18}H_{22}NO_2Na requires M⁺ 310.1777.

N-tert-Butyloxy carbonyl-2-(4'-methylphenyl)-4,5,6,7-tetrahydro-azepane 5a-ii

Suzuki protocol B: Purification on a Horizon® column chromatography system ([9:1] pet. ether/EtOAc) afforded the title compound as a white solid (0.06 g, 0.19 mmol, 99%).

Suzuki protocol A: Title compound isolated as a white solid (90%). mp. 72-74 °C. Found; C, 71.22; H, 8.35; N, 4.64%; Calc. for C_{18}H_{23}NO_3; C, 71.26; H, 8.31; N, 4.62%. ν_{max} (KBr) 2935 (C-H), 1687 (C=O), 1509, 1392, 1357, 1248, 1160 cm⁻¹. δ_\text{H} (500 MHz) 1.11 (9H, s, C(CH_3)_3), 1.46 (4H, m, 5-H_2, 7-H_2), 1.81 (2H, m, 6-H_2), 2.28 (2H, m, 4-H_2), 3.80 (3H, s, O-CH_3), 5.76 (1H, t, J = 6 Hz, 3'-H), 6.82 (2H, d, J = 9 Hz, 2'-H, 6'-H), 7.25 (2H, d, J = 9 Hz, 3'-H, 5'-H). δ_\text{C} (125 MHz) 24.5 (C-5), 27.6 (C-4), 28.2 ((C(CH_3)_3), 30.0 (C-6),
48.1 (C-7), 55.6 (O-CH₃), 79.8 (C(CH₃)₃), 113.6 (C-2’), 121.1 (C-3), 126.3 (C-3’), 132.6 (C-2), 144.3 (C-1’), 154.4 (C=O), 159.2 (C-4’). m/z (ES⁺) 629 (2MNa⁺).

*N-tert-Butyloxycarbonyl-2-(4’-fluorophenyl)-4,5,6,7-tetrahydro-azepane 5a-iv*

![Chemical Structure](image)

**Suzuki protocol B:** White solid (89%). Rᵣ (19:1 pet. ether/EtOAc): 0.30. mp. 68 °C. Found; C, 70.31; H, 7.68; N, 4.84%. Calc. for C₁₇H₂₂FNO₂: C, 70.08; H, 7.61; N, 4.81%. νmax (KBr) 3041, 3016, 2983, 2934, 2846, 1714, 1694, 1644, 1504, 1434, 1352, 1296, 1117, 1015, 922, 893, 820 and 589 cm⁻¹. δH (400 MHz) 1.03 (9H, s, (CH₃)₃C), 1.39 (2H, br, 5-H₂), 1.77 (2H, m, 6-H₂), 2.20 (2H, m, 4-H₂), 2.80-4.40 (2H, br, 7-H₂), 5.72 (1H, t, J = 6.5 Hz, 3-H), 6.90 (2H, m, 3’-H, 5’-H). δC (100 MHz) 24.2 (C-4), 27.6 (C-5), 28.1 ((CH₃)₃C), 29.7 (C-6), 48.1 (C-7), 80.0 ((CH₃)₃C), 114.9 and 115.1 (C-3’ and C-5’), 122.4 (C-3), 126.6 & 126.7 (C-2’ and C-6’), 136.1 (C-1’), 143.7 (C-2), 154.1 (O-C=O), 161.1 (C-4’). m/z (ES⁺) 314.0 (MNa⁺).

*N-tert-Butyloxycarbonyl-2-(3’,4’-dimethoxyphenyl)-4,5,6,7-tetrahydro-azepane 5a-v*

![Chemical Structure](image)

**Suzuki protocol A:** Flash chromatography ([4:1] pet. ether/EtOAc) afforded the title compound as a white solid (0.08 g, 0.24 mmol, 81%). mp. 95-97 °C. Found; C, 68.42; H, 8.26; N, 3.95%. Calc. for C₁₉H₂₂N₂O₄: C, 68.44; H, 8.16; N, 4.20%. νmax (KBr) 2936, 1688 (C=O), 1515, 1266, 1249, 1160 (C-O-C), 1140, 1027 cm⁻¹. δH (400 MHz) 1.12 (9H, s, C(CH₃)₃), 1.46 (4H, s, 5-H₂, 7-H₂), 1.83 (2H, m, 6-H₂), 2.27 (2H, m, 4-H₂), 3.87 (6H, m, 3’-OCH₃, 4’-OCH₃), 5.78 (1H, t, J = 7 Hz, 3-H), 6.78-6.95 (3H, m, 3 x Ar-H). δC (100 MHz) 24.4 (CH₂), 27.5 (C-4), 28.2 (C(CH₃)₃), 29.9 (CH₂), 48.2 (C-7), 56.1 and 56.2 (3’-OCH₃, 4’-OCH₃), 79.9 (C(CH₃)₃), 108.5, 110.9 and 117.6 (3 x Ar-C-H), 121.3 (C-3), 133.1 (C-2), 144.4 (C-1’), 148.8 and 148.9 (C-OMe), 154.4 (C=O). m/z (ES⁺) 688 (2MNa⁺), 397 (MNaMeCN⁺), 334 (MH⁺), 278 (MH – ‘Bu⁺).
**N-tert-Butyloxy carbonyl-2-(2',4',6'-trimethylphenyl)-4,5,6,7-tetrahydro-azepane 5a-vi**

**Suzuki protocol A:** Purification on a Horizon® column chromatography system ([19:1] pet. ether/EtOAc) afforded the title compound as a white solid (0.12 mmol, 36%) and recovered starting material (0.02 g, isolated yield = 63%). mp. 56-58 °C. Found; C, 76.07; H, 9.39; N, 4.53%; Calc. for C_{20}H_{29}NO_{2}; C, 76.15; H, 9.27; N, 4.44%. ν\(_{\text{max}}\) (KBr) 2933 (C-H), 1681 (C=O), 1392, 1367, 1161, 853 cm\(^{-1}\). δ\(_{\text{H}}\) (400 MHz) 1.07 (9H, s, C(CH\(_3\))\(_3\)), 1.72-1.80 (2H, m, 5-H\(_2\)). 1.81-1.90 (2H, m, 6-H\(_2\)). 2.22 (6H, s, 2'-CH\(_3\), 5'-CH\(_3\)). 2.25 (3H, s, 4'-CH\(_3\)). 2.29-2.39 (2H, m, 4-H\(_2\)). 3.81 (2H, t, J = 6 Hz, 7-H\(_2\)). 5.04 (1H, t, J = 5 Hz, 3-H). 6.79 (2H, s, 3'-H, 5'-H). δ\(_{\text{C}}\) (100 MHz) 21.1 (4'-CH\(_3\)), 21.5 (2'-CH\(_3\)), 24.1 (C-5), 27.8 (C-4), 27.9 (C-6), 28.1 (C(CH\(_3\))\(_3\)), 49.8 (C-7), 80.2 (C(CH\(_3\))\(_3\)), 122.7 (C-3), 128.7 (C-3'), 136.2 (C-4'), 136.7 (C-2'), 137.5 (C-1'), 140.9 (C-2), 154.4 (C=O). m/z (ES\(^+\)) 260 (MH - 'Bu'), 338 (MNa\(^+\)).

**N-tert-Butyloxy carbonyl-2-(3',5'-bis[trifluoromethyl]phenyl)-4,5,6,7-tetrahydro-azepane 5a-vii**

**Suzuki protocol A:** Purification on a Horizon® column chromatography system ([9:1] pet. ether/EtOAc) afforded the title compound as a white solid (0.09 g, 0.21 mmol, 87%). mp. 52-54 °C. Found; C, 55.79; H, 5.30; N, 3.29%; Calc. for C\(_{19}\)H\(_{21}\)NO\(_2\)F\(_6\); C, 55.75; H, 5.17; N, 3.42%. ν\(_{\text{max}}\) (KBr) 3019, 2936 (C-H), 1697 (C=O), 1357, 1222, 1209, 1182, 1170, 1020, 986, 901, 846, 794, 669 cm\(^{-1}\). δ\(_{\text{H}}\) (500 MHz) 1.07 (9H, s, C(CH\(_3\))\(_3\)), 1.46 (2H, m, 7-H\(_2\)). 1.60 (2H, broad, 5-H\(_2\)). 1.88 (2H, m, 6-H\(_2\)). 2.35 (2H, m, 4-H\(_2\)). 5.98 (0.79H, t, J = 7 Hz, 3-H). 6.17 (0.21H, t, J = 7 Hz, 3-H). 7.72 (2H, s, 2'-H). 7.75 (1H, s, 4'-H). δ\(_{\text{C}}\) (125MHz) 23.9 (C-5), 27.95 (C-4), 27.99 (C(CH\(_3\))\(_3\)), 29.4 (C-6), 48.5 (C-7), 80.7 (C(CH\(_3\))\(_3\)), 120.8 (C-4'), 122.5 (C-3'), 125.4 (C-2'), 125.9 (C-3), 131.4-132.2 (2 x CF\(_3\), q, J = 33 Hz), 142.3 (C-2), 142.7 (C-1'), 153.58 (C=O). HRMS (ES\(^+\)) found MNa\(^+\) 432.1369, C\(_{19}\)H\(_{21}\)NO\(_2\)F\(_6\)Na requires 432.1368.

**N-tert-Butyloxy carbonyl-2-(4'-Methoxycarbonylphenyl)-4,5,6,7-tetrahydro-azepane 5a-viii**
Suzuki protocol A: Purification on a Horizon® column chromatography system ([85:15] DCM/EtOAc) afforded the title compound as a white solid (0.06 g, 0.17 mmol, 72%). mp. 102-104 °C. ν_max (KBr) 3019, 2936, 1715 (C=O), 1694 (C=O), 1608, 1437, 1280, 1223, 1209, 795, 669 cm⁻¹. δ_H (500 MHz) 1.06 (9H, s, C(CH₃)₃), 1.44 (2H, s, 7-H₂), 1.59 (2H, broad, 5-H₂), 1.84 (2H, m, 6-H₂), 2.30 (2H, m, 4-H₂), 3.89 (3H, s, O-CH₃), 5.96 (1H, t, J = 7 Hz, 3'-H), 7.35 (2H, d, J = 9 Hz, 2'-H), 7.95 (2H, d, J = 9 Hz, 3'-H). δ_C (125MHz) 24.2 (C-5), 27.9 (C-4), 28.2 (C(CH₃)₃), 29.8 (C-6), 48.1 (C-7), 52.3 (O-CH₃), 80.3 (C(CH₃)₃), 125.0 (C-3), 125.1 (C-2'), 129.0 (C-1'), 129.8 (C-3'), 143.9 (C-2), 144.6 (C-4'), 154.0 (NC=O), 167.2 (ArC=O). HRMS (ES⁺) found MNa⁺ 354.1677, C₁₉H₂₅NNaO₄ requires M⁺ 354.1676.

N-tert-Butyloxycarbonyl-2-(2'-Methoxycarbonylphenyl)-4,5,6,7-tetrahydro-azepane 5a-ix

Suzuki protocol A: Stirred for 18 h at 85 °C. Purification by flash chromatography ([95:5], [6:4], [100:0] pet.ether/EtOAc) afforded the title compound as a white solid (0.60 mmol, 32%) and recovered starting material (0.19 mmol, 10%). The desired product contained a small amount of impurity due to homo coupled boronic acid which could not be removed, approx 8% by ¹H NMR analysis. δ_H (700 MHz) 1.02 (9H, s, C(CH₃)₃), 1.66 (2H, m, 5-H₂), 1.83 (2H, quint, J = 8 Hz, 6-H₂), 2.33 (2H, q, J = 8 Hz, 4-H₂), 3.64 (2H, broad, 7-H₂), 3.85 (3H, s, O-CH₃), 5.57 (1H, t, J = 8 Hz, 3-H), 7.27 (1H, m, 4'-H), 7.32-7.40 (2H, m, 5'-H, 6'-H), 7.42 (1H, m, 3'-H). δ_C (176MHz) 23.9 (C-5), 27.9 (C-6), 28.0 (C(CH₃)₃), 28.3 (C-4), 49.8 (C-7), 52.4 (O-CH₃), 80.2 ((C(CH₃)₃), 123.0 (C-3), 127.1 (C-4'), 128.1 (C-3'), 129.8 (ArC-H), 130.5 (ArC-H), 130.7 (C-2'), 140.7 (C-1'), 143.5 (C-2), 153.8 (NC=O), 170.1 (ArC=O). m/z (ES⁺) 232.1 (M – Boc⁺), 332.1 (MH⁺), 354.1 (MNa⁺), 685.3 (2MNa⁺). HRMS (ES⁺) found MH⁺ 332.1859, C₁₉H₂₅NO₄ requires M⁺ 322.1856, found MNa⁺ 354.1674, C₁₉H₂₅NO₄Na requires M⁺ 354.1676.
N-tert-Butyloxycarbonyl-2-Thiophen-2-yl-4,5,6,7-tetrahydro-azepane 5a-x

Suzuki protocol A: Purification by flash chromatography ([19:1] pet.ether/EtOAc, [4:1] DCM/EtOAc) afforded the title compound as a white solid (0.19 mmol, 38%) and recovered starting material (0.22 mmol, 44%). mp. 88-90 °C. \(\nu_{\text{max}}\) (KBr) 2979, 2936, 1691 (C=O), 1388, 1367, 1255, 1163 cm\(^{-1}\). \(\delta_H\) (500 MHz) 1.40 (13H, m, 2 x CH\(_2\), (CH\(_3\))\(_3\)), 1.54 (2H, m, CH\(_2\)), 2.08 (2H, m, 4-H\(_2\)), 5.87 (1H, t, J = 7 Hz, 3-H), 6.81 (1H, m, 4'-H), 6.87 (1H, m, Ar-H), 6.97 (1H, m, Ar-H). \(\delta_C\) (125 MHz) 24.3 (C-5), 27.4 (C-4), 28.0 (C(CH\(_3\))\(_3\)), 29.8 (C-6), 47.5 (C-7), 79.4 (C(CH\(_3\))\(_3\)), 122.0 (C-3), 122.7, 123.6 (C-2', C-3'), 127.1 (C-4'), 139.6 (C-2), 144.7 (C-1'), 153.6 (C=O). \(m/z\) (ES\(^+\)) 279.8 (MH\(^+\)), 302.2 (2MNa\(^+\)). HRMS (ES\(^+\)) found MNa\(^+\) 302.1185, C\(_{15}\)H\(_{21}\)NNaO\(_3\)S requires M\(^+\) 302.1185.

N-tert-Butyloxycarbonyl-2-furyl-2-yl-4,5,6,7-tetrahydro-azepane 5a-xi

Suzuki protocol B: (90%). Stille thermal protocol: (89%). Stille microwave protocol: (91%). Pale yellow solid. R\(_t\) ([19:1] pet. ether/EtOAc): 0.3. mp. 89 °C (Lit. 87 °C). Found: C, 68.60; H, 8.11; N, 5.28%. Calc. for C\(_{15}\)H\(_{21}\)NO\(_3\): C, 68.42; H, 8.04; N, 5.32%. \(\nu_{\text{max}}\) (KBr) 2974, 2931, 2854, 1698, 1651, 1492, 1443, 1385, 1353, 1252, 1163, 1012, 966 and 730 cm\(^{-1}\). \(\delta_H\) (400 MHz) 1.26 (9H, s, (CH\(_3\))\(_3\)C), 1.49 (2H, broad, 5-H\(_2\)), 1.80 (2H, m, 6-H\(_2\)), 2.25 (2H, m, 4-H\(_2\)), 2.70-4.30 (2H, broad, 7-H\(_2\)), 6.03 (1H, t, J = 7 Hz, 3-H), 6.17 (1H, d, J = 4 Hz, 2'-H), 6.34 (1H, m, 3'-H), 7.31 (1H, m, 4'-H). \(\delta_C\) (100 MHz) 24.4 (C-4), 27.1 (C-5), 28.2 ((CH\(_3\))\(_3\)C), 29.9 (C-6), 47.4 (C-7), 79.9 ((CH\(_3\))\(_3\)C), 105.1 (C-3), 111.2 (C-2'), 121.5 (C-3'), 135.9 (C-2), 141.4 (C-4'), 153.0 (OC=O), 154.1 (C-1'). \(m/z\) (ES\(^+\)) 286.2 (MNa\(^+\)).

N-tert-Butyloxycarbonyl-2-vinyl-4,5,6,7-tetrahydro-azepane 5a-xii
**Stille thermal protocol:** 82%. **Stille microwave protocol:** 85%. Colourless oil. Rf ([19:1] pet. ether/EtOAc): 0.30. Found; C, 69.11; H, 9.31; N, 6.09%. Calc. for C\textsubscript{13}H\textsubscript{21}NO\textsubscript{2}; C, 69.92; H, 9.48; N, 6.27%. \( \nu_{max} \) (NaCl) 3092, 2926, 2933, 2853, 1703, 1698, 1645, 1445, 1391, 1253, 1166, 985, 896 and 779 cm\(^{-1}\). \( \delta \)\(_H\) (400 MHz) 1.37 (9H, s, (CH\textsubscript{3})\textsubscript{3}C), 1.47 (2H, br, 5-\( H_2 \)), 1.78 (2H, quint, J = 6 Hz, 6-\( H_2 \)), 2.15 (2H, m, 4-\( H_2 \)), 2.90-3.70 (2H, br, 7-\( H_2 \)), 4.95 (1H, d, J = 10 Hz), 5.07 (1H, d, J = 17 Hz), 5.67 (t, 1H, J = 7 Hz, 3-\( H \)), 6.18 (1H, dd, J = 17 Hz, J = 10 Hz). \( \delta \)\(_C\) (100 MHz) 24.5 (C-5), 27.1 (C-4), 28.5 (C-3), 29.3 (C-6), 32.0 (C-7), 39.0 (C-8), 47.8 (C-10), 49.3 (C-11), 52.1 (C-12), 63.8 (C-13), 75.4 (C-14), 75.8 (C-16), 80.8 (C-17), 114.8 (C-18), 124.9 (C-19), 127.8 (C-20), 144.3 (C-21), 154.1 (O-C=O). mlz (ES\(^+\)) 246.0 (MNa\(^+\)).

**N-tert-Butyloxycarbonyl-2-phenylethynyl-4,5,6,7-tetrahydro-azepane 5a-xiii**

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\text{Stille thermal protocol:} 49%. \text{ Stille microwave protocol:} 54%. \text{ Yellow solid. Rf ([19:1] pet. ether/EtOAc): 0.35. mp. 94 °C. Found; C, 76.23; H, 7.70; N, 4.65%. Calc. for C\textsubscript{19}H\textsubscript{23}NO\textsubscript{2}; C, 76.73; H, 7.80; N, 4.71%. \( \nu_{max} \) (KBr) 3061, 2976, 2937, 2922, 2860, 2843, 1694, 1627, 1593, 1487, 1385, 1279, 1170, 1015, 901, 860, 759, 694 and 527 cm\(^{-1}\). \( \delta \)\(_H\) (400 MHz) 1.48 (9H, s, (CH\textsubscript{3})\textsubscript{3}C), 1.53 (2H, quint, J = 6 Hz, 5-\( H_2 \)), 1.78 (2H, quint, J = 6 Hz, 6-\( H_2 \)), 2.24 (2H, m, 4-\( H_2 \)), 3.52 (2H, broad, 7-\( H_2 \)), 6.02 (1H, t, J = 7 Hz, 3-\( H \)), 7.29 (3H, m, Ar-\( H \)), 7.41 (2H, m, Ar-\( H \)). \( \delta \)\(_C\) (100 MHz) 23.9 (C-4), 27.9 (C-5), 28.5 ((CH\textsubscript{3})\textsubscript{3}C), 29.7 (C-6), 47.4 (C-7), 80.5 ((CH\textsubscript{3})\textsubscript{3}C), 86.5 (N-C=O). mlz (ES\(^+\)) 320.1 (MNa\(^+\)).

**N-tert-Butyloxycarbonyl-2-phenyl-4,5,6,7-tetrahydro-azepane 5a-xiv**

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\text{Stille thermal protocol:} 45%. \text{ Stille microwave protocol:} 45%. \text{ Stille thermal protocol:} (PhSnMe\textsubscript{3}, 29%). \text{ White solid. Rf ([19:1] pet. ether/EtOAc): 0.35. mp. 85 °C (Lit. 83 °C). Found; C, 74.16; H, 8.47; N, 5.01%. Calc. for C\textsubscript{17}H\textsubscript{23}NO\textsubscript{2}; C, 74.69; H, 8.48; N, 5.12%. \( \nu_{max} \) (KBr) 3045, 2975, 2933, 2849, 1694, 1635, 1492, 1447, 1381, 1253, 1153, 1017, 892, 854, 763, 698 and 642 cm\(^{-1}\). \( \delta \)\(_H\) (400 MHz) 1.02 (9H, s, (CH\textsubscript{3})\textsubscript{3}C), 1.47 (2H, broad, 5-\( H_2 \)), 1.78 (2H, quint, J = 6 Hz, 6-\( H_2 \)), 2.22 (2H, m, 4-\( H_2 \)), 2.80-4.20 (2H, broad, 7-\( H_2 \)), 3.70 (C-3), 4.20 (C-4), 5.67 (t, 1H, J = 7 Hz, 3-\( H \)).
5.79 (1H, t, J = 7 Hz, 3-H), 7.15-7.25 (5H, m, Ar-H). δC (100 MHz) 24.3 (C-4), 27.6 (C-5), 28.0 ((CH₃)₃C), 29.8 (C-6), 40.1 (C-7), 79.8 ((CH₃)₃C), 122.6 (C-3), 125.1 (2CH), 127.3 (CH), 128.2 (2CH), 139.9 (C), 144.6 (C-2), 154.2 (O-C=O). mlz (ES+) 296.0 (MNa⁺).

*N*-tert-Butyloxy carbonyl-2-iso-propyl-4,5,6,7-tetrahydro-azepane 5a-xv

A suspension of 3a (0.413 g, 1.0 mmol) and 1,2-bis(diphenylphosphino)ethane nickel(II) chloride (26.4 mg, 0.05 mmol) in 1:1 Et₂O/THF (18 ml) was degassed by purging Ar for 10 minutes before iso-propylmagnesium bromide (2.0 M solution in Et₂O, 0.75 ml, 1.5 mmol) was added. The mixture was stirred for 18h at rt. Water (0.5 ml) was added to quench the reaction, and the resulting solution was extracted by EtOAc/brine. The organic phase was combined, dried (MgSO₄), filtered and evaporated. Rapid flash chromatography on silica (19:1 to 9:1 pet. Ether/EtOAc) gave the product as colourless oil (94 mg, 37%). Rf (19:1 pet. Ether/EtOAc): 0.50. Found; C, 70.76; H, 10.41; N, 5.64%: Calc. for C₁₅H₂₇NO₂; C, 71.10; H, 10.74; N, 5.53%. All signals in the NMR spectra were highly broadened and could not be resolved. νmax (LF) 2931, 2807, 1703, 1654, 1388, 1162, 1012 and 770 cm⁻¹.

*N*-Phenyloxy carbonyl-2-(3',5'-dimethylphenyl)-4,5,6,7-tetrahydro-azepane 5b-i

Suzuki protocol A: Purification by flash chromatography ([9:1], [1:1] pet.ether/EtOAc) afforded the title compound as a clear oil (69 mg, 0.21 mmol, 82%). νmax (ATR) 2932, 1717 (C=O), 1382, 1352, 1196, 1170, 748, 688 cm⁻¹. δH (500 MHz) 1.97 (2H, m, C₂H₂), 2.34 (6H, m, Ar-CH₃), 2.42 (2H, q, J = 7 Hz, 4-H₂), 2.69 (1H, broad, 7-HH), 4.32-4.74 (1H, broad, 7-HH), 6.16 (1H, t, J = 7 Hz, 3-H), 6.75 (2H, d, J = 8 Hz, 2'H₂), 6.96 (1H, s, 4'-H), 7.08 (2H, s, 2'-H₂), 7.11 (1H, t, J = 8 Hz, 4''-H), 7.24 (2H, t, J = 8 Hz, 3''-H). δC (125 MHz) 21.6 (Ar-CH₃), 24.4 (C-5 or 6), 27.6 (C-4), 30.0 (C-5 or 6), 48.9 (C-7), 121.9 (C-2'), 122.7 (C-2'), 124.1 (C-3), 125.4 (C-4'), 129.2 (C-3'), 129.7 (C-4'), 138.2 (C-1'), 144.0 (C-2), 151.5 (C-1''), 153.7 (C=O). mlz (ES+) 322.3 (MH⁺), 339.3 (MH₂O⁺) 665.6 (2MNa⁺). HRMS (ES+) found MNa⁺ 344.1621, C₂₁H₂₃NO₂Na requires M⁺ 344.1621.
N-Phenyloxycarbonyl-2-(4'-methoxyphenyl)-4,5,6,7-tetrahydro-azepane 5b-ii

Suzuki protocol A: Purification by flash chromatography ([9:1] pet. ether/EtOAc) afforded the title compound as a crystalline solid (0.06 g, 0.19 mmol, 81%). mp 92-94 °C. Found; C, 73.78; H, 6.50; N, 4.13%. Calc. for C_{20}H_{21}NO_{5}: C, 74.28; H, 6.55; N, 4.33%. \( \nu_{\text{max}} \) (ATR) 2931, 1710 (C=O), 1641, 1608, 1512, 1384, 1353, 1252, 1197, 1175, 1034, 812, 731 cm\(^{-1}\). \( \delta \_H \) (500 MHz) 1.69 (2H, m, 7-H\(_2\)), 1.91-2.07 (4H, m, 5-H\(_2\), 6-H\(_2\)), 2.40 (2H, m, 4-H\(_2\)), 3.85 (3H, s, O-CH\(_3\)), 6.08 (1H, t, J = 6 Hz, 3-H), 6.78 (2H, m, 2 x Ar-H), 6.91 (2H, d, J = 9 Hz, 3''-H, 5''-H), 7.10 (1H, t, J = 4''-H), 7.22 (2H, m, 2 x Ar-H), 7.38 (2H, d, J = 9 Hz, 2''-H, 6''-H). \( \delta \_C \) (125MHz) 24.8 (C-5), 27.9 (C-4), 30.1 (C-6), 49.0 (C-7), 55.9 (O-CH\(_3\)), 114.1 (C-3''), 122.0 (ArC), 123.0 (C-3), 125.2 (C-4''), 126.1 (C-2'), 129.7 (ArC), 131.2 (C-1'), 143.7 (C-2), 151.8 (C-1'/C-1''), 153.9 (C-O), 159.5 (C-4'). m/z (ES\(^{+}\)) 323.5 (MH\(^{+}\)). HRMS (ES\(^{+}\)) found MH\(^{+}\) 324.1592, C\(_{20}\)H\(_{22}\)NO\(_3\) requires M\(^{+}\) 324.1594.

N-Phenyloxycarbonyl-2-(3',5'-bis[trifluoromethyl]phenyl)-4,5,6,7-tetrahydro-azepane 5b-vi

Suzuki protocol A: Purification by flash chromatography ([1:1] CHCl\(_3\)/pet. ether) afforded the title compound as a white solid (83 mg, 0.19 mmol, 69%). mp 111-113 °C. Found; C, 58.18; H, 3.99; N, 3.08%. Calc. for C\(_{22}\)H\(_{17}\)NO\(_2\)F\(_6\): C, 58.74; H, 3.99; N, 3.26%. \( \nu_{\text{max}} \) (ATR) 2948, 1712 (C=O), 1354, 1279, 1203, 1179, 1165, 1121, 1110, 978, 898, 754, 731, 683 cm\(^{-1}\). \( \delta \_H \) (500 MHz) 1.59-1.90 (3H, broad, 5-H\(_2\), 7-HH), 2.01 (2H, m, 6-H\(_2\)), 2.48 (2H, m, 4-H\(_2\)), 3.91 (1H, broad, 7-HH), 6.35 (1H, t, J = 7 Hz, 3-H), 6.74 (2H, d, J = 8 Hz, 2''-H, 6''-H), 7.13 (1H, t, J = 8 Hz, 4''-H), 7.25 (2H, t, J = 8 Hz, 3''-H, 5''-H), 7.08 (1H, s, 4'-H), 7.88 (2H, s, 2''-H, 6''-H). \( \delta \_C \) (125MHz) 23.9 (C-5), 27.9 (C-4), 29.4 (C-6), 49.2 (C-7), 121.0 (C-2''), 121.7 (C-4''), 124.8 (C-2',) 125.8 (C-4''), 128.2 (C-3), 129.9 (C-3''), 139.7 (C-1'), 141.5 (C-2), 151.0 (C-1'/C-1''), 153.1 (C-O). m/z (ES\(^{+}\)) 430.3 (MH\(^{+}\)) 447.3 (MH\(^{2+}\)) 493.3 (MNaMeCN\(^{+}\)), 881.5 (2MNa\(^{+}\)). HRMS (ES\(^{+}\)) found MH\(^{+}\) 430.1237, C\(_{22}\)H\(_{18}\)NO\(_2\)F\(_6\) requires 430.1236.

N-Phenyloxycarbonyl-2-(4'-carbomethoxyphenyl)-4,5,6,7-tetrahydro-azepane 5b-viii

19
Suzuki protocol A: Purification by flash chromatography ([9:1] pet. ether/EtOAc) afforded the title compound as a clear oil (35 mg, 0.01 mmol, 37%). ν<sub>max</sub> (ATR) 2954, 1725 (C=O), 1710 (C=O), 1381, 1263, 1200, 1086, 767, 732, 688 cm<sup>-1</sup>. δ<sub>H</sub> (500 MHz) 1.75 (2H, quint, J = 6 Hz, 5-<H<sub>2</sub>), 1.92 (2H, quint, J = 6 Hz, 6-<H<sub>2</sub>), 2.42 (2H, q, J = 6 Hz, 4-<H<sub>2</sub>), 3.76-3.94 (5H, m, 7-<H<sub>2</sub>, CH<sub>3</sub>), 5.79 (1H, t, J = 6 Hz, 3-<H<sub>2</sub>), 6.64 (2H, d, J = 8 Hz, 2''-<H, 6''-<H), 7.07 (1H, m, 4''-<H), 7.19 (2H, t, J = 8 Hz, 3''-<H, 5''-<H). 7.30 (1H, t, J = 8 Hz, 4'-<H), 7.39 (1H, t, J = 8Hz, 5'-<H), 7.45 (1H, d, J = 8 Hz, 6'-<H). 7.52 (1H, d, J = 8 Hz, 3'-<H). δ<sub>C</sub> (125 MHz) 23.9 (C-5), 28.2 (C-4), 28.3 (C-6), 50.7 (C-7), 52.6 (CH<sub>3</sub>), 121.5 (C-2’’), 125.0 (C-3), 125.4 (C-4’’), 127.6 (C-4’’), 128.4 (C-3’’), 129.2 (C-3’’), 129.8 (C-6’’), 130.6 (C-2’’), 130.9 (C-5’’), 139.6 (C-1’’), 142.5 (C-2’’), 151.2 (C-1’’), 153.2 (NC=O), 170.0 (CO<sub>2</sub>Me). m/z (ES<sup>+</sup>) 352.3 (MH<sup>+</sup>), 374.3 (MNa<sup>+</sup>), 415.3 (MNaMeCN<sup>+</sup>), 725.5 (2MNa<sup>+</sup>). HRMS (ES<sup>+</sup>) found MNa<sup>+</sup> 374.1362, C<sub>21</sub>H<sub>21</sub>NO<sub>4</sub>Na requires 374.1363.

N-Benzylxocarbonyl-2-(2'-methylbenzoate)-4,5,6,7-tetrahydro-azepane 5c-viii

Suzuki protocol A (trifluoroborate salt): Reaction mixture stirred at 85 °C for 3 h. Purification by flash chromatography ([8:2], [6:4] pet. ether/EtOAc) afforded the title compound as a colourless oil (71 mg 0.20 mmol, 58%). ν<sub>max</sub> (ATR) 2930, 1726 (C=O), 1698 (C=O), 1398, 1254, 1162, 1112, 1085, 1022, 757, 696 cm<sup>-1</sup>. δ<sub>H</sub> (700 MHz) 1.64 (2H, m, 5-<H<sub>2</sub>), 1.85 (2H, t, J = 6 Hz, 6-<H<sub>2</sub>), 2.30 (2H, q, J = 6 Hz, 4-<H<sub>2</sub>), 3.70 (2H, broad, 7-<H<sub>2</sub>), 3.79 (3H, s, CH<sub>3</sub>), 4.82 (2H, s, OCH<sub>2</sub>), 5.66 (1H, t, J = 6 Hz, 3-H), 6.68 (2H, d, J = 8 Hz, 2''-<H, 6''-<H), 7.11 (2H, t, J = 8 Hz, 3''-<H, 5''-<H), 7.16 (1H, t, J = 8 Hz, 4'-<H), 7.22-7.36 (3H, m, 3 x Ar-<H), 7.38 (1H, d, J = 8 Hz, 6'-<H). δ<sub>C</sub> (176 MHz) 23.8 (C-5), 28.2 (C-4), 28.3 (C-6), 50.6 (C-7), 52.5 (CH<sub>3</sub>), 67.6 (OCH<sub>2</sub>), 124.8 (C-3), 127.3 (ArC-H), 127.7 (C-4’’), 127.9 (C-2’’), 128.2 (C-3’’), 128.3 (C-6’’), 129.4 (ArC-H), 130.60 (ArC-H), 130.64 (C-2’’), 136.1 (C-1’’), 139.5 (C-1’), 142.5 (C-2’), 154.8 (NC=O), 170.0 (CO<sub>2</sub>Me). m/z (ES<sup>+</sup>) 366.3 (MH<sup>+</sup>), 753.6 (2MNa<sup>+</sup>). HRMS (ES<sup>+</sup>) found MNa<sup>+</sup> 388.1518, C<sub>22</sub>H<sub>23</sub>NO<sub>4</sub>Na requires 388.1519.
N-[(4′-Methylphenyl)sulfonyl]-2-(4′-methylphenyl)-4,5,6,7-tetrahydro-azepane 5d-ii

Suzuki protocol A: Degassed by passing a stream of nitrogen through mixture prior to adding catalyst. Purification on a Horizon® column chromatography system ([19:1] DCM/EtOAc) afforded recovered starting material (114 mg, 0.32 mmol, 33%) and the title compound as a white solid (110 mg, 0.24 mmol, 43%). \( \nu_{\text{max}} \) (ATR) 2938, 2918, 1440, 1334, 1150, 1087, 1058, 950, 814, 763, 704 cm\(^{-1}\). \( \delta_H \) (400 MHz) 1.43 (2H, m, 5-H\(_2\)), 1.83 (2H, quint, J = 6 Hz, 6-H\(_2\)), 2.06 (2H, q, J = 6 Hz, 4-H\(_2\)), 2.34 (3H, s, CH\(_3\)), 2.41 (3H, s, CH\(_3\)), 6.04 (1H, t, J = 6 Hz, 3-H), 7.04 (2H, d, J = 8 Hz, 2 x Ar-H), 7.18 (4H, d, J = 8 Hz, 2 x Ar-H), 7.55 (2H, d, J = 8 Hz, 2 x Ar-H). \( \delta_C \) (100 MHz) 19.8 (CH\(_3\)), 20.2 (CH\(_3\)), 22.3 (C-5), 25.3 (C-4), 28.6 (C-6), 49.3 (C-7), 124.7 (Ar-C-H), 126.1 (Ar-C-H) 126.9 (C-3), 127.4 (Ar-C-H) 127.9 (Ar-C-H), 134.4 (Ar-C), 136.2 (C-2), 137.4 (Ar-C), 141.6 (Ar-C), 141.7 (Ar-C). m/z (ES\(^+\)) 342.3 (MH\(^+\)), 359.4 (MH\(_2\)O\(^+\)), 700.6 (2MH\(_2\)O\(^+\)). HRMS (ES\(^+\)) found MH\(^+\) 342.1523, C\(_{20}\)H\(_{23}\)NO\(_2\)S requires 342.1522, found M\(\text{Na}^+\) 364.1342, C\(_{20}\)H\(_{23}\)NO\(_2\)SN\(\text{Na}\) requires 364.1342.

N-(tert-Butyloxycarbonyl)-2-(4′-methoxyphenyl)-4,5,6-trihydro-piperidine 5e-iii

Obtained, following flash chromatography, as a white solid (41%). \( R_f \) ([19:1] pet. ether/EtOAc): 0.25. mp. 99 °C. \( \nu_{\text{max}} \) (KBr) 3042, 3004, 2931, 2838, 11693, 1644, 1609, 1509, 1365, 1246, 1153, 1033, 993, 831, 778 and 593 cm\(^{-1}\). \( \delta_H \) (400 MHz) 1.09 (9H, s, (CH\(_3\))\(_3\)C), 1.80 (2H, m, 5-H\(_2\)), 2.24 (2H, td, J = 7 Hz, 4 Hz, 4-H\(_2\)), 3.64 (2H, m, 6-H\(_2\)), 3.77 (3H, s, OCH\(_3\)), 5.27 (1H, t, J = 4 Hz, 3-H), 6.85 (2H, d, J = 9 Hz, 3′-H, 5′-H), 7.19 (2H, d, J = 9 Hz, 2′-H, 6′-H). \( \delta_C \) (100 MHz) 24.2 (C-4), 24.4 (C-5), 28.0 ((CH\(_3\))\(_3\)C), 45.4 (C-6), 55.9 (CH\(_3\)O), 80.6 ((CH\(_3\))\(_3\)C), 114.2 (C-3′ and C-5′), 114.6 (C-3), 127.3 (C-2′ and C-6′), 134.5 (C-1′), 140.9 (C-2), 154.7 (OC=O), 159.8 (C-4′). m/z (ES\(^+\)) 312.3 (M\(\text{Na}^+\)).

N-(tert-Butyloxycarbonyl)-2-furan-2′-yl-4,5,6-trihydro-piperidine 5e-x

Obtained, following flash chromatography, as a pale yellow solid (29%). \( R_f \) ([19:1] pet. ether/EtOAc): 0.4. mp. 54 °C. \( \nu_{\text{max}} \) (KBr) 3151, 2979, 2928, 2890, 2837, 1694, 1681,
1644, 1455, 1361, 1253, 1154, 1003, 919, 879, 755, 689 and 599 cm$^{-1}$. $\delta_H$ (400 MHz) 1.23 (9H, s, (CH$_3$)$_3$C), 1.80 (2H, m, 5-H$_2$), 2.24 (2H, td, J = 7 Hz, 4 Hz, 4-H$_2$), 3.58 (2H, m, 6-H$_2$), 5.53 (1H, t, J = 4 Hz, 3-H$^-$), 6.25 (1H, dd, J = 3, 1 Hz, 5$'$-H$^-$), 6.39 (1H, dd, J = 3 Hz, 2 Hz, 4$'$-H$^-$), 7.40 (1H, dd, J = 2 Hz, 1 Hz, 3$'$-H$^-$). $\delta_C$ (100 MHz) 23.7 and 24.2 (C-4 and C-5), 28.0 ((CH$_3$)$_3$C), 44.9 (C-6), 80.9 ((CH$_3$)$_3$C), 105.7 (C-3), 111.9 (C-2$'$), 115.2 (C-3$'$), 132.5 (C-2), 141.6 (C-4$'$), 153.9 (O-C=O), 154.6 (C-1$'$). m/z (ES$^+$) 272.3 (MNa$^+$).

**N-[(4$''$-Methylphenyl)sulfonyl]-2-(4$''$-methylphenyl)-4,5,6,7,8-quintahydro-1H-azocine 5g-ii**

Purification on a Horizon® column chromatography system ([100:0], [95:5], [7:3] EtOAc/CHCl$_3$ afforded recovered starting material 3g (164 mg, 0.34 mmol, 33%) and the title compound as a white solid (214 mg, 0.60 mmol, 58%). $v_{max}$ (KBr) 2924, 2855, 1691, 1447, 1340, 1155, 1118, 1086, 1010, 874, 815, 708 cm$^{-1}$. $\delta_H$ (400 MHz) 1.60 (4H, m, 5-H$_2$), 6-H$_2$), 1.72 (2H, m, 7-H$_2$), 2.31 (3H, s, CH$_3$), 2.36 (2H, m, 4-H$_2$), 2.40 (3H, s, CH$_3$), 3.63 (2H, m, 8-H$_2$), 6.39 (1H, t, J = 8 Hz, 3-H), 6.97 (2H, d, J = 8 Hz, Ar-H), 7.07 (2H, d, J = 8 Hz, Ar-H), 7.16 (2H, d, J = 8 Hz, Ar-H), 7.52 (2H, d, J = 8 Hz, Ar-H). $\delta_C$ (100 MHz) 21.0 (CH$_3$), 21.4 (CH$_3$), 26.5 (C-4), 27.0 (C-5 or 6), 27.4 (C-7), 28.3 (C-5 or 6), 52.6 (C-8), 125.7 (ArC-H), 127.4 (ArC-H), 128.8 (ArC-H), 129.1 (ArC-H), 132.4 (C-3), 134.1, 137.3, 138.0, 138.2 and 142.7 (tertiary-C). m/z (ES$^+$) 356.3 (MH$^+$), 373.2 (MH$_2$O$^+$), 728.4 (2MH$_2$O$^+$). HRMS (ES$^+$) found MH$^+$ 356.1680, C$_{21}$H$_{25}$NO$_2$SNa requires 356.1679, found MNa$^+$ 378.1498, C$_{21}$H$_{25}$NO$_2$SNa requires 378.1498.

5-(N-tert-butoxycarbonylamino)-1-(4$''$-methoxyphenyl)pentan-1-one

Compound 5e-iii (0.1 mmol) was dissolved in CDCl$_3$ (0.5 ml) and monitored by NMR and TLC. The sample completely converted into the title compound after 3 days. R$_f$ ([1:1] pet. ether/EtOAc): 0.85. $\delta_C$ (100 MHz) 1.42 (9H, s, (CH$_3$)$_3$C), 1.56 (2H, quint, J = 8 Hz, 2-H$_2$), 1.75 (2H, quint, J = 8 Hz, 3-H$_2$), 2.94 (2H, t, J = 7 Hz, 4-H$_2$), 3.15 (2H, 1-H$_2$), 3.86 (3H, s, OCH$_3$), 4.64 (1H, broad, NH), 6.92 (2H, d, J = 9 Hz, 8-H), 7.93 (2H, d, J = 9 Hz, 7-H). $\delta_C$ (100 MHz) 21.6 (C-3), 28.5 ((CH$_3$)$_3$C), 29.8 (C-2), 37.7 (C-4), 40.4 (C-1), 55.6 (CH$_3$O),
79.2 ((CH$_3$)$_3$C), 113.8 (C-3’ and C-5’), 130.1 (C-1’), 130.4 (C-2’ and C-6’), 156.2 (O-C=O), 163.5 (C-4’), 198.8 (Ar-C=O).

5-(N-tert-butoxycarbonylamino)-1-(2’-furyl)pentan-1-one

Compound 5e-xi (0.1 mmol) was dissolved in CDCl$_3$ (0.5 ml) and monitored by NMR and TLC. After 4 days 75% of the sample completely converted into the title compound. R$_f$ ([1:1] pet. ether/EtOAc): 0.80. δ$_c$ (100 MHz) 1.42 (9H, s, (CH$_3$)$_3$C), 1.54 (2H, quint, J = 8 Hz, 2-H$_2$), 1.73 (2H, quint, J = 8 Hz, 3-H$_2$), 2.83 (2H, t, J = 7 Hz, 4-H$_2$), 3.14 (2H, m, 1-H$_2$), 4.62 (1H, broad, NH), 6.51 (1H, dd, J = 4 Hz, J = 2 Hz, 3’-H), 7.18 (1H, d, J = 4 Hz, 2’-H), 7.56 (1H, d, J = 2 Hz, 4-H). δ$_c$ (100 MHz) 21.3 (C-3), 28.6 ((CH$_3$)$_3$C), 29.7 (C-2), 38.0 (C-4), 40.3 (C-1), 79.3 ((CH$_3$)$_3$C), 112.3 (C-2’), 117.1 (C-3’), 146.4 (C-4’), 152.9 (C-1’), 156.2 (O-C=O), 189.4 (Ar-C=O).
Part C 500 MHz $^1$H NMR spectra for 5a-i in CDCl$_3$ at rt and 60 °C to illustrate presence of rotomers

Spectra acquired at 60 °C

Spectra acquired at rt

ppm

7 6 5 4 3 2