Copper-catalysed hydroamidation for the formation of pyrrolinone derivatives

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Electronic Supplementary Information

Table of Contents

I General Information S2
II Optimisation Tables S3
III Synthesis of α-Keto Amides S5
IV Copper-catalysed Synthesis of Pyrrolinone Derivatives S20
V Gram-scale Synthesis of Pyrrolinone 3b S44
VI References S45
VII NMR Spectra S46
I. General Information

Reactions were performed under inert nitrogen atmosphere with anhydrous solvent unless otherwise stated. All glassware was oven dried at >100 °C, and allowed to cool to room temperature under a positive nitrogen pressure. Reactions were monitored by TLC until deemed complete using aluminum backed silica plates. Plates were visualized under ultraviolet light (254 nm) and/or by staining with KMnO₄. Cooling of reaction mixtures to 0 °C was achieved using an ice water bath.

Reagents were purchased from Sigma-Aldrich Chemical Co. Ltd., Alfa Aesar, Acros Organics Ltd., Fluorochem Ltd. or Strem Chemicals Inc. and were used as supplied. All alkynes were distilled and degassed with N₂ before use. Anhydrous solvents were obtained by passing through anhydrous alumina columns using an Innovative Technology Inc. PS-400-7 solvent purification system, and were degassed with nitrogen flow before use. Column chromatography was carried out using matrix 60 silica. Petrol refers to the fraction of light petroleum ether boiling in the range of 40 – 60 °C.

¹H NMR spectra were obtained on a Bruker AVIII400 (400 MHz) or AVIII500 (500 MHz) spectrometer using the residual solvent as an internal standard. ¹³C NMR spectra were obtained on a Bruker AVIII400 (101 MHz) spectrometer using the residual solvent as an internal standard. Chemical shifts (δ) were reported in parts per million (ppm) with the multiplicities of the spectra reported as following: bs, broad singlet; s, singlet; d, doublet; t, triplet; q, quartet; p, quintet; h, sextet; m, multiplet; app., apparent. Coupling constants (J) were given in Hertz (Hz) and rounded to the nearest 0.5 Hz.

Low resolution ESI mass spectra were recorded on a Waters LCT Premier spectrometer. High resolution mass spectrometry measurements were recorded on a Brucker Daltronics MicroTOF (ESI) spectrometer or on a Micromass LCT (FI) spectrometer by the internal service at Chemistry Research Laboratory, University of Oxford.

Infrared spectra were recorded as thin films on a Bruker Tensor 27 FT-IR spectrometer. Melting points were determined using a Stuart Scientific Melting Point Apparatus SMP1.
II. Optimisation Tables

Table S1. Copper catalyst screening for the reaction between 1a and 2a

![Chemical structure](image)

<table>
<thead>
<tr>
<th>entry</th>
<th>Copper (I) sources</th>
<th>yield&lt;sup&gt;b&lt;/sup&gt;</th>
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<tbody>
<tr>
<td>1</td>
<td>CuBr</td>
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</tr>
<tr>
<td>2</td>
<td>CuOAc</td>
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<tr>
<td>3</td>
<td>CuMeSal</td>
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<td>4</td>
<td>CuBr(PPh&lt;sub&gt;3&lt;/sub&gt;)&lt;sub&gt;3&lt;/sub&gt;</td>
<td>0%</td>
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<td>5</td>
<td>(CF&lt;sub&gt;3&lt;/sub&gt;SO&lt;sub&gt;3&lt;/sub&gt;Cu)&lt;sub&gt;2&lt;/sub&gt;:C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;6&lt;/sub&gt;</td>
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<td>6</td>
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<td>(CuMeCN)&lt;sub&gt;4&lt;/sub&gt;BPF&lt;sub&gt;4&lt;/sub&gt;</td>
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</tbody>
</table>

<sup>a</sup>Reaction condition: 130 °C, 20 h, under N<sub>2</sub>. <sup>b</sup>Yields determined by <sup>1</sup>H NMR spectra of the crude reaction mixtures using nitromethane as an internal standard. <sup>c</sup>KPF<sub>6</sub> (0.03 mmol) added.
Table S2. Solvent, base and ligand screening for the reaction between 1a and 2a

<table>
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<tr>
<th>entry</th>
<th>Solvent</th>
<th>Base</th>
<th>Ligand</th>
<th>yield$^b$</th>
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<td>Acetonitrile</td>
<td>-</td>
<td>-</td>
<td>0%</td>
</tr>
<tr>
<td>2</td>
<td>$o$-Xylene</td>
<td>-</td>
<td>-</td>
<td>15%</td>
</tr>
<tr>
<td>3</td>
<td>$p$-Xylene</td>
<td>-</td>
<td>-</td>
<td>16%</td>
</tr>
<tr>
<td>4</td>
<td>1,1,2-Trichloroethane</td>
<td>-</td>
<td>-</td>
<td>2%</td>
</tr>
<tr>
<td>5</td>
<td>1,2-Dichlorobenzene</td>
<td>-</td>
<td>-</td>
<td>52%</td>
</tr>
<tr>
<td>6</td>
<td>$a,a,a$-Trifluorotoluene</td>
<td>-</td>
<td>-</td>
<td>39%</td>
</tr>
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<td>7</td>
<td>Toluene</td>
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<td>0%</td>
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<td>Toluene</td>
<td>KH$_2$PO$_4$</td>
<td>-</td>
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<td>Toluene</td>
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<td>-</td>
<td>0%</td>
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<td>-</td>
<td>dppe</td>
<td>0%</td>
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<td>15</td>
<td>Toluene</td>
<td>-</td>
<td>1,10-phenanthroline</td>
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<tr>
<td>16</td>
<td>Toluene</td>
<td>-</td>
<td>bipyridine</td>
<td>0%</td>
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</table>

$^a$Reaction condition: 130 °C, 20 h, under N$_2$. $^b$Yields determined by $^1$H NMR spectra of the crude reaction mixtures using nitromethane as an internal standard.
III. Synthesis of α-keto amides

α-Keto acids were either commercially purchased or prepared by oxidation of the corresponding methyl ketones using SeO₂. The crude mixture was filtered through a plug of celite, dried under vacuum and used without further purification.

\[ N \text{-Benzy1-2-oxo-2-phenylacetamide (1a)} \]

\[
\begin{align*}
\text{General procedure } A. & \text{ To a solution of benzoylformic acid (675 mg, 4.5 mmol) and Et₃N (1.25 mL, 9.0 mmol) in 1,2-dichloroethane (12 mL) at 0 °C under N₂ atmosphere was added thionyl chloride (653 µL, 9.0 mmol) dropwise. The mixture was stirred at rt for 20 min before a solution of benzylamine (492 µL, 4.5 mmol) in 1,2-dichloroethane (6 mL) was added slowly at 0 °C. The solution was heated to 60 °C and left to stir for 16 h. The stirring solution was cooled to rt before the slow addition of aqueous solution of NaHCO₃ (sat., 20 mL). The organic layer was washed with water (3 × 10 mL), dried over MgSO₄, filtered and concentrated under vacuum. The residue was purified by column chromatography (Petrol/EtOAc = 9:1) and recrystallised (Petrol/CH₂Cl₂) to give 1a as a crystalline white solid (578 mg, 2.4 mmol, 54%).}
\end{align*}
\]

\[ ^1H \text{ NMR (400 MHz, CDCl₃)} \delta 8.36 (2H, d, } J = 7.5 \text{ Hz, Ar-}H), 7.63 (1H, t, } J = 7.5 \text{ Hz, Ar-}H), 7.49 (2H, t, } J = 7.5 \text{ Hz, Ar-}H), 7.45 (1H, bs, N-H), 7.39 – 7.29 (m, 5H, Ar-H), 4.58 (2H, d, } J = 6.0 \text{ Hz, CH₂)}; \text{ } ^{13}C \text{ NMR (101 MHz, CDCl₃)} \delta 187.7, 161.7, 137.2, 134.6, 133.4, 131.4, 129.0, 128.6, 128.0, 127.9, 43.6; \text{ LRMS (ESI) m/z: 262.1 [C}_{15}H_{13}NO_2Na, (M+Na)^+]. This data is consistent with literature.}^3
\]

\[ N \text{-Tosyl-2-oxo-2-phenylacetamide (1b)} \]

\[
\begin{align*}
\text{General procedure } B. & \text{ To a solution of benzoyleformic acid (1.50 g, 10 mmol) and 1 drop of DMF in CH₂Cl₂ (20 mL) was added oxalyl chloride (1.0 mL, 12 mmol) dropwise, and the yellow mixture was left to stir}
\end{align*}
\]
at rt for 3 h. The solvent was removed under vacuum and the residue was dissolved in toluene (10 mL). The resulting solution was then added dropwise to a solution of 4-methylbenzenesulfonamide (1.71 g, 10 mmol), DMAP (6.1 mg, 0.05 mmol) and Et₃N (2.8 mL, 20 mmol) in EtOAc (20 mL) at 0 °C. The mixture was left to stir at rt for 18 h. An aqueous solution of HCl (1 M) was added to the mixture until a clear organic layer was obtained. The aqueous layer was extracted with EtOAc (2 × 40 mL) and the combined organic layer was washed with brine, dried over MgSO₄, filtered and concentrated under vacuum. The residue was purified by column chromatography (CH₂Cl₂/EtOAc/AcOH = 90:10:2) to give 1b as a light yellow solid (1.91 g, 6.28 mmol, 63%).

1H NMR (400 MHz, CDCl₃) δ 9.64 (1H, bs, N-H), 8.25 (2H, d, J = 7.5 Hz, Ar-H), 8.03 (2H, d, J = 8.0 Hz, Ar-H), 7.64 (1H, t, J = 7.5 Hz, Ar-H), 7.45 (2H, t, J = 7.5 Hz, Ar-H), 7.36 (2H, d, J = 8.0 Hz, Ar-H), 2.43 (3H, s, CH₃); 13C NMR (101 MHz, CDCl₃) δ 184.1, 158.2, 145.8, 135.5, 135.0, 131.9, 131.5, 129.9, 128.9, 128.7, 21.8; LRMS (ESI) m/z: 326.0 [C₁₅H₁₃NO₄SNa, (M+Na)]⁺. This data is consistent with literature.

N-((4-Methoxyphenyl)sulfonyl)-2-oxo-2-phenylacetamide (1c)

Compound 1c was prepared according to general procedure B, using benzoylformic acid (300 mg, 2 mmol), oxalyl chloride (200 µL, 2.4 mmol), 1 drop of DMF in CH₂Cl₂ (4 mL), toluene (2 mL), 4-methoxybenzenesulfonamide (190 mg, 2 mmol), DMAP (1.2 mg, 0.01 mmol), Et₃N (558 µL, 4 mmol) and EtOAc (4 mL). The residue was purified by column chromatography (100% Et₂O) to give a white solid (250 mg, 0.79 mmol, 40%).

1H NMR (400 MHz, CDCl₃) δ 9.55 (1H, bs, N-H), 8.26 (2H, d, J = 7.0 Hz, Ar-H), 8.08 (2H, d, J = 9.0 Hz, Ar-H), 7.65 (1H, t, J = 7.5 Hz, Ar-H), 7.46 (2H, dd, J = 7.5, 7.0 Hz, Ar-H), 7.02 (2H, d, J = 9.0 Hz, Ar-H), 3.88 (3H, s, CH₃); 13C NMR (101 MHz, CDCl₃) δ 184.2, 164.5, 158.1, 135.5, 131.9, 131.6, 131.2, 129.2, 128.9, 114.4, 55.9; mp (Et₂O): 112 – 116 °C; IR (cm⁻¹) 1) ν = 3649, 3247, 2980, 2844, 2361, 2342, 1718, 1678, 1595, 1578, 1498, 1419, 1354, 1317, 1265, 1191, 1166, 1089, 1023, 1002, 977, 872, 835, 805, 771, 744, 687, 676, 665, 627; LRMS
**N-((4-Cyanophenyl)sulfonyl)-2-oxo-2-phenylacetamide (1d)**

Compound **1d** was prepared according to general procedure B, using benzoylformic acid (600 mg, 4 mmol), oxalyl chloride (406 µL, 4.8 mmol), 1 drop of DMF in CH₂Cl₂ (8 mL), toluene (4 mL), 4-cyanobenzesulfonamide (730 mg, 4 mmol), DMAP (2.4 mg, 0.02 mmol), Et₃N (1.1 mL, 8 mmol) and EtOAc (8 mL). The residue was purified by recrystallisation (Petrol/EtOAc) to give a white solid (823 mg, 2.6 mmol, 66%).

**¹H NMR (400 MHz, acetone-d₆)** δ 11.68 (1H, bs, N-H), 8.32 (2H, d, J = 8.5 Hz, Ar-H), 8.13 (2H, d, J = 8.5 Hz, Ar-H), 8.00 (2H, d, J = 8.0 Hz, Ar-H), 7.74 (1H, t, J = 7.5 Hz, Ar-H), 7.60 – 7.51 (2H, dd, J = 8.0, 7.5 Hz, Ar-H); **¹³C NMR (101 MHz, acetone-d₆)** δ 186.4, 162.6, 143.7, 135.9, 134.1, 133.0, 129.9, 129.8, 118.4, 118.0; **mp (Petrol/EtOAc):** 181 – 183 °C; **IR (cm⁻¹)** ν = 3657, 3265, 3098, 2981, 2888, 2361, 2341, 2233, 1738, 1673, 1594, 1473, 1462, 1447, 1430, 1383, 1359, 1270, 1172, 1117, 1085, 1003, 967, 955, 879, 846, 831, 803, 746, 686, 671, 643; **LRMS (ESI) m/z:** 313.0 [C₁₅H₁₅N₂O₄S, (M-H)]; **HRMS (ESI):** calcd for [C₁₅H₁₅N₂O₄S, (M-H)]: 313.02885; found 313.02881.

**N-((4-(Trifluoromethyl)phenyl)sulfonyl)-2-oxo-2-phenylacetamide (1e)**

Compound **1e** was prepared according to general procedure B, using benzoylformic acid (300 mg, 2 mmol), oxalyl chloride (200 µL, 2.4 mmol), 1 drop of DMF in CH₂Cl₂ (4 mL), toluene (2 mL), 4-(trifluoromethyl)benzenesulfonamide (450 mg, 2 mmol), DMAP (1.2 mg, 0.01 mmol), Et₃N (558 µL, 4 mmol) and EtOAc (4 mL). The residue was purified by column chromatography (CH₂Cl₂/EtOAc/AcOH = 90:10:2) to give a white solid (573 mg, 1.6 mmol, 80%).
1H NMR (400 MHz, CDCl₃) δ 9.71 (1H, bs, N-H), 8.34 – 8.23 (4H, m, Ar-H), 7.85 (2H, d, J = 8.0 Hz, Ar-H), 7.67 (1H, t, J = 7.5 Hz, Ar-H), 7.48 (2H, dd, J = 8.0, 7.5 Hz, Ar-H); 13C NMR (101 MHz, CDCl₃) δ 183.6, 158.1, 141.3, 136.1 (q, 2J_C-F = 33.0 Hz), 135.8, 131.7, 131.6, 129.4, 129.0, 126.5 (q, 3J_C-F = 4.0 Hz), 123.1 (q, 1J_C-F = 277.0 Hz); 19F NMR (377 MHz, CDCl₃) δ -63.3; mp (CH₂Cl₂/EtOAc/AcOH): 124 – 127 °C; IR (cm⁻¹) ν = 3657, 2981, 2972, 2930, 2890, 2859, 2360, 2342, 1742, 1684, 1597, 1461, 1449, 1375, 1323, 1242, 1172, 1139, 1110, 1092, 1063, 1019, 967, 956, 877, 845, 845, 796, 771, 744, 713, 688; LRMS (ESI) m/z: [C₁₅H₁₀F₃NNaO₄S, (M+Na)⁺]; HRMS (ESI): calcd for [C₁₅H₁₀F₃NNaO₄S, (M+Na)⁺]: 380.01748; found 380.01746.

**N-((4-Nitrophenyl)sulfonyl)-2-oxo-2-phenylacetamide (1f)**

![Structural formula](image.png)

Compound 1f was prepared according to general procedure B, using benzoylformic acid (750 mg, 5 mmol), oxalyl chloride (510 µL, 6 mmol), 1 drop of DMF in CH₂Cl₂ (10 mL), toluene (5 mL), 4-nitrobenzenesulfonamide (1.01 g, 5 mmol), DMAP (3 mg, 0.025 mmol), Et₃N (1.4 mL, 10 mmol) and EtOAc (10 mL). The residue was purified by recrystallisation (Petrol/CH₂Cl₂) to give a white solid (1.27 g, 3.8 mmol, 76%)

1H NMR (400 MHz, CDCl₃) δ 9.68 (1H, bs, N-H), 8.39 – 8.33 (4H, m, Ar-H), 8.28 (2H, d, J = 8.0 Hz, Ar-H), 7.72 – 7.63 (1H, m, Ar-H), 7.49 (2H, dd, J = 8.0, 8.0 Hz, Ar-H); 13C NMR (101 MHz, CDCl₃) δ 183.4, 158.0, 151.2, 143.3, 135.9, 131.64, 131.61, 130.3, 129.1, 124.5; mp (Petrol/CH₂Cl₂): 143 – 145 °C; IR (cm⁻¹) ν = 3657, 3240, 2981, 2888, 2360, 2341, 2163, 1736, 1674, 1594, 1527, 1473, 1462, 1449, 1384, 1355, 1313, 1270, 1252, 1171, 1086, 1002, 967, 956, 913, 890, 854, 823, 798, 737, 684, 672, 623; LRMS (ESI) m/z: 357.0 [C₁₄H₁₀N₂NaO₆S, (M+Na)⁺]; HRMS (ESI): calcd for [C₁₄H₁₀N₂NaO₆S, (M+Na)⁺]: 357.01518; found 357.01547.
**N-(Methylsulfonyl)-2-oxo-2-phenylacetamide (1g)**

[Chemical structure image]

Compound 1g was prepared according to general procedure B, using benzoyleformic acid (300 mg, 2 mmol), oxalyl chloride (200 µL, 2.4 mmol), 1 drop of DMF in CH₂Cl₂ (4 mL), toluene (10 mL), methanesulfonamide (190 mg, 2 mmol), DMAP (1.2 mg, 0.01 mmol), Et₃N (558 µL, 4 mmol) and EtOAc (4 mL). The residue was purified by column chromatography (CH₂Cl₂/EtOAc/AcOH = 80:20:2) to give a white solid (95 mg, 0.42 mmol, 21%).

**1H NMR (400 MHz, CDCl₃)**: δ 9.44 (1H, bs, N-H), 8.33 (2H, d, J = 8.0 Hz, Ar-H), 7.70 (1H, t, J = 8.0 Hz, Ar-H), 7.52 (2H, t, J = 8.0 Hz, Ar-H), 3.39 (3H, s, CH₃);

**13C NMR (101 MHz, CDCl₃)**: δ 183.5, 159.1, 135.5, 131.5, 131.3, 128.7, 41.4;

**mp (CH₂Cl₂/EtOAc/AcOH):** 128 – 131 °C;

**IR (cm⁻¹)**: 3238, 3045, 2981, 2360, 1714, 1687, 1598, 1432, 1400, 1332, 1320, 1279, 1135, 989, 970, 886, 684, 669, 607;

**LRMS (ESI) m/z:** 226.0 [C₉H₈NO₄S, (M-H)];

**HRMS (ESI):** calcd for [C₉H₉NO₄SNa⁺]: 250.01445; found 250.01466. This data is consistent with literature.

**N-Hexyl-2-oxo-2-phenylacetamide (1h)**

[Chemical structure image]

Compound 1h was prepared according to general procedure A, using benzoyleformic acid (750 mg, 5.0 mmol), Et₃N (1.4 mL, 10.0 mmol), thionyl chloride (725 µL, 10.0 mmol), hexylamine (660 µL, 5.0 mmol) and 1,2-dichloroethane (20 mL). The residue was purified by column chromatography (Petrol/Et₂O = 9:1) to give a yellow oil (1.0 g, 4.3 mmol, 86%).

**1H NMR (400 MHz, CDCl₃)**: δ 8.29 (2H, d, J = 7.5 Hz, Ar-H), 7.58 (1H, t, J = 7.5 Hz, Ar-H), 7.43 (2H, dd, J = 7.5, 7.5 Hz, Ar-H), 7.30 (1H, bs, N-H), 3.35 (2H, dt, J = 6.5, 6.5 Hz, NHCH₂), 1.62 – 1.49 (2H, m, NHCH₂CH₂), 1.40 – 1.21 (6H, m, 3 × CH₂), 0.87 (3H, t, J = 6.0 Hz, CH₃);

**13C NMR (101 MHz, CDCl₃)**: δ 188.1, 162.0, 134.3, 133.4, 131.1, 128.4, 39.5, 31.4, 29.2, 26.5, 22.5, 14.0;

**IR (cm⁻¹)**: 3657, 3308, 2981, 2931, 2889, 1659, 1597, 1523, 1449, 1381, 1260, 1177, 1155, 1073, 954, 816, 745, 687, 672;

**LRMS (ESI) m/z:** 234.2 [C₁₄H₂₀NO₂,
HRMS (ESI): calcd for \([C_{14}H_{20}NO_{2}, (M+H)^+]: 234.14886;\) found 234.14905. This data is consistent with literature.\(^5\)

\(N\text{-Cyclopropyl-2-oxo-2-phenylacetamide (1i)}\)

\[
\begin{align*}
\text{Compound 1i was prepared according to general procedure A, using benzoylformic acid (600 mg, 4.0 mmol), Et}_3\text{N (1.12 mL, 8.0 mmol), thionyl chloride (580 µL, 8.0 mmol), cyclopropylamine (280 µL, 4.0 mmol) and 1,2-dichloroethane (16 mL). The residue was purified by column chromatography (Petrol/Et}_2\text{O = 9:1) and recrystallisation (Petrol/Et}_2\text{O) to give a white solid (374 mg, 2.0 mmol, 49%).} \\
^{1}H\text{ NMR (400 MHz, CDCl}_3) \delta 8.33 (2H, d, J = 8.0 Hz, Ar-H), 7.61 (1H, t, J = 7.5 Hz, Ar-H), 7.46 (2H, dd, J = 8.0, 7.5 Hz, Ar-H), 7.17 (1H, bs, N-H), 2.89 – 2.83 (1H, m, NHCH), 0.92 – 0.85 (2H, m, CH\_2), 0.67 – 0.62 (2H, m, CH\_2); \text{IR (cm}^{-1}) \nu = 3275, 3068, 2981, 2360, 2341, 1653, 1596, 1519, 1449, 1362, 1284, 1234, 1202, 1180, 1051, 931, 850, 747, 688, 670; \text{LRMS (ESI) m/z: 188.1 [C}_{11}H_{10}NO\_2, (M-H)\}; \text{HRMS (ESI): calcd for [C}_{11}H_{12}NO\_2, (M+H)^+: 190.08626; found 190.08626} \\
\end{align*}
\]

\(N\text{-Cyclohexyl-2-oxo-2-phenylacetamide (1j)}\)

\[
\begin{align*}
\text{Compound 1j was prepared according to general procedure A, using benzoylformic acid (450 mg, 3.0 mmol), Et}_3\text{N (836 µL, 6.0 mmol), thionyl chloride (435 µL, 6.0 mmol), cyclohexanamine (343 µL, 3.0 mmol) and 1,2-dichloroethane (12 mL). The residue was purified by column chromatography (Petrol/Et}_2\text{O = 9:1) and recrystallisation (Petrol/Et}_2\text{O) to give a white solid (295 mg, 1.3 mmol, 43%).} \\
^{1}H\text{ NMR (400 MHz, CDCl}_3) \delta 8.33 (2H, d, J = 8.0 Hz, Ar-H), 7.61 (1H, t, J = 7.0 Hz, Ar-H), 7.47 (2H, dd, J = 8.0, 7.0 Hz, Ar-H), 6.99 (1H, bs, N-H), 3.85 (1H, tdt, J = 11.0, 8.0, 4.0 Hz, NHCH), 2.02 – 1.93 (2H, m, CH\_2), 1.79 – 1.73 (2H, m, CH\_2), 1.67 – 1.62 (1H, m, CH\_A), \\
\end{align*}
\]
1.47 – 1.33 (2H, m, CH₂), 1.31 – 1.19 (3H, m, CH₂, CH₃H₆); ¹³C NMR (101 MHz, CDCl₃) δ 188.2, 161.0, 134.4, 133.6, 131.3, 128.6, 48.6, 32.8, 25.5, 24.8; mp (Petrol/Et₂O): 114 – 116 °C; IR (cm⁻¹) ν = 3274, 3085, 2935, 2855, 2360, 1680, 1664, 1640, 1596, 1551, 1449, 1246, 1217, 1179, 1153, 1088, 961, 838, 752, 693, 672; HRMS (F1): calcd for [C₁₄H₁₈NO₂, (M+H)⁺]: 232.13321; found 232.13335. This data is consistent with literature.

**N-(Cyclopropylmethyl)-2-oxo-2-phenylacetamide (1k)**

![Image of N-(Cyclopropylmethyl)-2-oxo-2-phenylacetamide (1k)]

Compound 1k was prepared according to general procedure A, using benzoylformic acid (600 mg, 4.0 mmol), Et₃N (1.12 mL, 8.0 mmol), thionyl chloride (580 µL, 8.0 mmol), cyclopropylmethanamine (350 µL, 4.0 mmol) and 1,2-dichloroethane (16 mL). The residue was purified by column chromatography (Petrol/Et₂O = 95:5) and recrystallisation (Petrol/Et₂O) to give a white solid (381 mg, 1.9 mmol, 47%).

¹H NMR (400 MHz, CDCl₃) δ 8.33 (2H, d, J = 8.0 Hz, Ar-H), 7.61 (1H, t, J = 7.5 Hz, Ar-H), 7.47 (2H, dd, J = 7.5, 8.0 Hz, Ar-H), 7.21 (1H, bs, N-H), 3.25 (2H, dd, J = 6.5, 6.5 Hz, NHCH₂), 1.11 – 0.96 (1H, m, CH), 0.61 – 0.50 (2H, m, CH(CH₂)), 0.30 – 0.24 (2H, m, CH(CH₂)); ¹³C NMR (101 MHz, CDCl₃) δ 188.1, 161.7, 134.5, 133.5, 131.3, 128.6, 44.4, 10.6, 3.7; mp (Petrol/Et₂O): 38 – 40 °C; IR (cm⁻¹) ν = 3305, 3080, 2981, 2361, 2341, 1657, 1596, 1523, 1449, 1268 1217, 1023, 833, 746, 688, 672; LRMS (ESI) m/z: 226.0 [C₁₂H₁₃NNaO₂, (M+Na)⁺]; HRMS (ESI): calcd for [C₁₂H₁₃NNaO₂, (M+Na)⁺]: 226.08385; found 226.08417.

**N-(Cyclohexylmethyl)-2-oxo-2-phenylacetamide (1l)**

![Image of N-(Cyclohexylmethyl)-2-oxo-2-phenylacetamide (1l)]

Compound 1l was prepared according to general procedure A, using benzoylformic acid (600 mg, 4.0 mmol), Et₃N (1.12 mL, 8.0 mmol), thionyl chloride (580 µL, 8.0 mmol), cyclohexylmethanamine (510 µL, 4.0 mmol) and 1,2-dichloroethane (16 mL). The residue was purified by column chromatography (Petrol/Et₂O = 95:5) and recrystallisation (Petrol/Et₂O) to give a white solid (720 mg, 2.9 mmol, 73%).
**1H NMR (400 MHz, CDCl₃) δ 8.34 (2H, d, J = 8.0 Hz, Ar-H), 7.62 (1H, t, J = 7.5 Hz, Ar-H), 7.47 (2H, dd, J = 8.0, 7.5 Hz, Ar-H), 7.15 (1H, bs, N-H), 3.24 (2H, dd, J = 6.5, 6.5 Hz, NHC₂), 1.81–1.72 (4H, m, Cy₂CH₂), 1.71–1.63 (1H, m, Cy-CH₂H₆B), 1.51–1.64 (1H, m, NHCH₂), 1.33–1.08 (3H, m, Cy₂CH₂, Cy-CH₂H₆A), 1.04–0.94 (2H, m, Cy-CH₂); 13C NMR (101 MHz, CDCl₃) δ 188.1, 161.9, 134.5, 133.5, 131.4, 128.6, 45.7, 38.0, 30.9, 26.4, 25.9; mp (Petrol/Et₂O): 94–96 °C; IR (cm⁻¹) ν = 3273, 2981, 2926, 2854, 2361, 2341, 1664, 1597, 1524, 1449, 1225, 1178, 905, 726, 688, 672, 648; LRMS (ESI) m/z: 244.1 [C₁₅H₁₈NO₂, (M-H)]; HRMS (ESI): calcd for [C₁₅H₂₀NO₂, (M+H)⁺]: 246.14886; found 246.14874.

**N-(Thiophen-2-ylmethyl)-2-oxo-2-phenylacetamide (1m)**

Compound 1m was prepared according to general procedure A, using benzoic formic acid (750 mg, 5.0 mmol), Et₃N (1.4 mL, 10.0 mmol), thionyl chloride (725 µL, 10.0 mmol), 2-(aminomethyl)thiophene (513 µL, 5.0 mmol) and 1,2-dichloroethane (20 mL). The residue was purified by column chromatography (Petrol/Et₂O = 4:1) and recrystallisation (Petrol/Et₂O) to give a white solid (655 mg, 2.7 mmol, 53%).

**1H NMR (400 MHz, CDCl₃) δ 8.30 (2H, d, J = 7.0 Hz, Ar-H), 7.58 (1H, t, J = 7.5 Hz, Ar-H), 7.44 (2H, app. t, J = 7.5, 7.0 Hz, Ar-H), 7.41 (1H, bs, N-H), 7.21 (1H, d, J = 5.0 Hz, Ar-H), 6.99 (1H, d, J = 3.5 Hz, Ar-H), 6.92 (1H, dd, J = 5.0, 3.5 Hz, Ar-H), 4.69 (2H, d, J = 6.0 Hz, CH₂); 13C NMR (101 MHz, CDCl₃) δ 187.4, 161.4, 139.5, 134.6, 133.4, 131.4, 128.6, 127.1, 126.7, 125.8, 38.2; mp (Petrol/Et₂O): 95–97 °C; IR (cm⁻¹) ν = 3661, 3255, 3085, 2981, 2888, 2361, 2341, 1681, 1639, 1595, 1563, 1533, 1451, 1431, 1371, 1347, 1329, 1229, 1179, 1053, 1041, 1022, 1001, 940, 928, 853, 800, 749, 688, 672, 648; LRMS (ESI) m/z: 244.0 [C₁₃H₁₀NO₂S, (M-H)]; HRMS (ESI) m/z: calcd for [C₁₃H₁₀NO₂S, (M+H)⁺]: 246.04377; found 244.04355.

**N-Allyl-2-oxo-2-phenylacetamide (1n)**

Compound 1n was prepared according to general procedure A, using benzoic formic acid (450 mg, 3.0 mmol), Et₃N (836 µL, 6.0 mmol), thionyl chloride (435 µL, 6.0 mmol),
allylamine (343 µL, 3.0 mmol) and 1,2-dichloroethane (12 mL). The residue was purified by column chromatography (Petrol/Et₂O = 9:1) and recrystallisation (Petrol/Et₂O) to give a white solid (229 mg, 1.2 mmol, 40%).

\[ \text{H NMR (400 MHz, CDCl}_3\text{)} \delta 8.35 (2H, d, J = 8.0 Hz, Ar-H), 7.63 (1H, t, J = 7.0 Hz, Ar-H), 7.48 (2H, dd, J = 8.0, 7.0 Hz, Ar-H), 7.18 (1H, bs, N-H), 5.90 (ddt, J = 17.0, 10.0, 5.5 Hz, CH₂CH₂CH₂), 5.28 (1H, dd, J = 17.0, 1.0 Hz, CH₂CH₂), 5.22 (dd, J = 10.0, 1.0 Hz, CHCH₂), 4.02 (2H, dd, J = 5.5, 1.5 Hz, \text{CH}_2\text{CHCH}_2\text{A}); \text{C NMR (101 MHz, CDCl}_3\text{)} \delta 187.7, 161.7, 134.6, 133.4, 133.1, 131.4, 128.7, 117.4, 41.8; \text{mp (Petrol/Et}_2\text{O): 58 – 60 °C; IR (cm}^{-1}\text{)} \nu = 3259, 3098, 2918, 2360, 1681, 1653, 1635, 1595, 1571, 1451, 1430, 1265, 1227, 1179, 1018, 993, 943, 928, 892, 690; \text{HRMS (FI): calcd for [C}_{11}\text{H}_{12}\text{NO}_2, (M+H)}^+: 190.08625; found 190.08626. This data is consistent with literature.\

\text{N-Phenyl-2-oxo-2-phenylacetamide (1o)}

Compound 1o was prepared according to general procedure A, using benzoyleformic acid (600 mg, 4.0 mmol), Et₃N (1.12 mL, 8.0 mmol), thionyl chloride (580 µL, 8.0 mmol), aniline (364 µL, 4.0 mmol) and 1,2-dichloroethane (16 mL). The residue was purified by column chromatography (Petrol/Et₂O = 9:1) to give a yellow solid (788 mg, 3.5 mmol, 87%).

\[ \text{H NMR (400 MHz, CDCl}_3\text{)} \delta 9.04 (1H, bs, N-H), 8.40 (2H, d, J = 8.0 Hz, Ar-H), 7.71 (2H, d, J = 8.5 Hz, Ar-H), 7.64 (2H, dd, J = 8.0, 7.0 Hz, Ar-H), 7.49 (1H, t, J = 7.0 Hz, Ar-H), 7.39 (2H, dd, J = 8.5, 7.5 Hz, Ar-H), 7.20 (1H, t, J = 7.5 Hz, Ar-H); \text{C NMR (101 MHz, CDCl}_3\text{)} \delta 187.5, 159.1, 136.7, 134.7, 133.1, 131.5, 129.3, 128.6, 125.3, 120.0; \text{mp (Petrol/Et}_2\text{O): 59 – 61 °C; IR (cm}^{-1}\text{)} \nu = 3346, 3062, 1667, 1595, 1530, 1495, 1445, 1278, 1241, 1171, 1080, 1030, 1004, 989, 907, 879, 789, 744, 688; \text{HRMS (FI): calcd for [C}_{14}\text{H}_{12}\text{NO}_2, (M+H)}^+: 226.08626; found 226.08629. This data is consistent with literature.\]
**N-Benzyl-2-oxo-2-(p-tolyl)acetamide (1p)**

Compound 1p was prepared according to general procedure A, using crude 2-oxo-2-(p-tolyl)acetic acid (985 mg, 6.0 mmol), Et₃N (1.67 mL, 12.0 mmol), thionyl chloride (871 µL, 12.0 mmol), benzylamine (655 µL, 6.0 mmol) and 1,2-dichloroethane (24 mL). The residue was purified by column chromatography (100% CH₂Cl₂) and recrystallised in Petrol/Et₂O to give white crystals (341 mg, 1.3 mmol, 22%).

**¹H NMR (400 MHz, CDCl₃)** δ 8.29 (2H, d, J = 8.5 Hz, Ar-H), 7.45 (1H, s, N-H), 7.39 – 7.26 (7H, m, Ar-H), 4.57 (2H, d, J = 6.0 Hz, CH₂), 2.43 (3H, s, CH₃); **¹³C NMR (101 MHz, CDCl₃)** δ 187.1, 161.9, 145.8, 137.3, 131.5, 130.9, 129.4, 128.9, 128.0, 127.9, 43.6, 22.0; **mp (Petrol/Et₂O):** 82 – 84 °C; **IR (cm⁻¹)** ν = 3267, 3092, 2925, 1675, 1642, 1605, 1567, 1497, 1454, 1431, 1409, 1382, 1364, 1308, 1226, 1210, 1176, 1118, 1083, 1060, 1031, 1017, 939, 904, 839, 790, 767, 730, 697, 680, 618; **LRMS (ESI) m/z:** 276.0 [C₁₆H₁₅NNaO₂, (M+Na)⁺]; **HRMS (ESI) m/z:** calcd for [C₁₆H₁₅NNaO₂, (M+Na)⁺]: 276.09950; found 276.09949. This data is consistent with literature.

**N-Benzyl-2-oxo-2-(3-methoxyphenyl)acetamide (1q)**

Compound 1q was prepared according to general procedure A, using crude 2-(3-methoxyphenyl)-2-oxoacetic acid (1.26 g, 7.0 mmol), Et₃N (1.95 mL, 14.0 mmol), thionyl chloride (1.02 mL, 14.0 mmol), benzylamine (765 µL, 7.0 mmol) and 1,2-dichloroethane (28 mL). The residue was purified by column chromatography (100% CH₂Cl₂) to give an orange oil (893 mg, 3.3 mmol, 47%).

**¹H NMR (400 MHz, CDCl₃)** δ 8.01 (1H, d, J = 8.0 Hz, Ar-H), 7.86 (1H, s, Ar-H), 7.43 (1H, bs, N-H), 7.42 – 7.28 (6H, m, Ar-H), 7.18 (1H, d, J = 8.0 Hz, Ar-H), 4.57 (2H, d, J = 6.0 Hz, CH₂), 3.86 (3H, s, CH₃); **¹³C NMR (101 MHz, CDCl₃)** δ 187.4, 161.7, 159.6, 137.2, 134.5,
129.7, 129.0, 128.0, 127.95, 124.3, 121.7, 114.8, 55.6, 43.6; IR (cm\(^{-1}\)) \(\tilde{\nu} = 3307, 3066, 3031, 2980, 2836, 2361, 1658, 1596, 1580, 1521, 1485, 1454, 1429, 1360, 1324, 1288, 1252, 1195, 1174, 1082, 1042, 994, 952, 876, 823, 782, 765, 730, 699, 683; LRMS (ESI) m/z: 292.0 [C\(_{16}\)H\(_{18}\)NO\(_3\), (M+H)]\(^+\); HRMS (ESI) m/z: calcd for [C\(_{16}\)H\(_{18}\)NO\(_3\), (M+H)]\(^+\): 292.09441; found 292.09424.

\(N\)-Benzyl-2-oxo-2-(4-(trifluoromethyl)phenyl)acetamide (1r)

![Chemical structure of 1r](image)

Compound 1r was prepared according to general procedure A, using crude 2-oxo-2-(4-(trifluoromethyl)phenyl)acetic acid (1.31 g, 6.0 mmol), Et\(_3\)N (1.67 mL, 12.0 mmol), thionyl chloride (871 \(\mu\)L, 12.0 mmol), benzylamine (655 \(\mu\)L, 6.0 mmol) and 1,2-dichloroethane (24 mL). The residue was purified by column chromatography (Petrol/Et\(_2\)O 95:5) and recrystallised in Petrol/Et\(_2\)O to give light orange crystals (454 mg, 1.5 mmol, 25%).

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta 8.47 (2\text{H}, d, J = 8.0 \text{ Hz, Ar-H}), 7.74 (2\text{H}, d, J = 8.0 \text{ Hz, Ar-H}), 7.51 (1\text{H}, bs, N-H), 7.41 - 7.27 (5\text{H, m, Ar-H}), 4.58 (2\text{H, d, J = 6.0 Hz, CH}_2); ^{13}\text{C NMR (101 MHz, CDCl}_3) \delta 186.7, 160.9, 137.0, 136.1, 135.4 (q, J = 33.0 Hz), 131.7, 129.0, 128.1, 128.0, 125.6 (q, J = 4.0 Hz), 123.6 (q, J = 273.0 Hz), 43.7; ^{19}\text{F NMR (377 MHz, CDCl}_3) -63.3; mp (Petrol/Et}_2\text{O): 104 - 106 °C; IR (cm}\(^{-1}\)) \(\tilde{\nu} = 3377, 2981, 2889, 2361, 1665, 1532, 1506, 1455, 1409, 1323, 1248, 1213, 1167, 1124, 1110, 1068, 1029, 1016, 937, 901, 863, 830, 802, 765, 731, 698, 640; LRMS (ESI) m/z: 330.2 [C\(_{16}\)H\(_{12}\)F\(_3\)NNaO\(_2\), (M+Na)]\(^+\); HRMS (ESI) m/z: calcd for [C\(_{16}\)H\(_{12}\)F\(_3\)NO\(_2\), (M+H)]\(^+\): 308.08929; found 308.08939. This data is consistent with literature.\(^8\)

\(N\)-Benzyl-2-oxo-2-(3-nitrophenyl)acetamide (1s)

![Chemical structure of 1s](image)

S15
Compound 1s was prepared according to general procedure A, using crude 2-(3-nitropheryl)-2-oxoacetic acid (1.4 g, 5.0 mmol), Et$_3$N (1.39 mL, 10.0 mmol), thionyl chloride (725 µL, 10.0 mmol), benzylamine (546 µL, 5.0 mmol) and 1,2-dichloroethane (20 mL). The residue was purified by column chromatography (Petrol/CH$_2$Cl$_2$ 1:1) and recrystallised in Petrol/Et$_2$O to give light yellow crystals (380 mg, 1.3 mmol, 30%).

$^1$H NMR (400 MHz, CDCl$_3$) δ 9.21 (1H, s, Ar-H), 8.75 (1H, d, $J = 8.0$ Hz, Ar-H), 8.47 (1H, d, $J = 8.0$ Hz, Ar-H), 7.70 (1H, t, $J = 8.0$ Hz, Ar-H), 7.52 (1H, bs, N-H), 7.41 – 7.28 (5H, m, Ar-H), 4.59 (2H, d, $J = 6.0$ Hz, CH$_2$); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 185.3, 160.4, 148.3, 137.0, 136.8, 134.6, 129.9, 129.1, 128.6, 128.2, 128.1, 126.3, 43.8; mp (Petrol/Et$_2$O): 106 – 108 °C; IR (cm$^{-1}$) $\tilde{\nu} = 3385, 2980, 2888, 2361, 1669, 1613, 1530, 1497, 1474, 1455, 1437, 1382, 1349, 1251, 1214, 1153, 1081, 1030, 953, 732, 700, 670; LRMS (ESI) m/z: 307.0 [C$_{15}$H$_{12}$N$_2$NaO$_4$, (M+Na)$^+$]; HRMS (ESI) m/z: calcd for [C$_{15}$H$_{12}$N$_2$NaO$_4$, (M+Na)$^+$]: 307.06893; found 307.06903.

$N$-Benzyl-2-oxo-2-(3-bromophenyl)acetamide (1t)

Compound 1t was prepared according to general procedure A, using crude 2-(3-bromophenethyl)-2-oxoacetic acid (1.6 g, 7.0 mmol), Et$_3$N (1.95 mL, 14.0 mmol), thionyl chloride (1.02 mL, 14.0 mmol), benzylamine (765 µL, 7.0 mmol) and 1,2-dichloroethane (28 mL). The residue was purified by column chromatography (Petrol/Et$_2$O 95:5) and recrystallised in Petrol/Et$_2$O to give white crystals (839 mg, 2.6 mmol, 38%).

$^1$H NMR (400 MHz, CDCl$_3$) δ 8.53 (1H, bs, Ar-H), 8.35 (1H, d, $J = 8.0$ Hz, Ar-H), 7.77 (1H, d, $J = 8.0$ Hz, Ar-H), 7.49 (1H, s, N-H), 7.40 – 7.32 (6H, m, Ar-H), 4.58 (2H, d, $J = 6.0$ Hz, CH$_2$); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 186.2, 161.0, 137.4, 137.0, 135.1, 134.1(2 × C), 130.2, 130.0, 129.0, 128.0, 122.8, 43.7; mp (Petrol/Et$_2$O): 70 – 71 °C; IR (cm$^{-1}$) $\tilde{\nu} = 3308, 3065, 2981, 2889, 2360, 1680, 1663, 1587, 1561, 1521, 1497, 1455, 1414, 1383, 1361, 1289, 1242, 1211, 1166, 1070, 1029, 999, 950, 900, 776, 720, 698, 677; LRMS (ESI) m/z [relative intensity]: 340.0 [100, C$_{13}$H$_{13}$BrNO$_2$, (M+Br)$^+$], 342.0 [100, C$_{13}$H$_{13}$BrNO$_2$, (M+Br)+H]$^+$].
Compound 1u was prepared according to general procedure A, using 2-(3-cyanophenyl)-2-oxoacetic acid (1.05 g, 6.0 mmol), Et₃N (1.67 mL, 12.0 mmol), thionyl chloride (871 µL, 12.0 mmol), benzylamine (655 µL, 6.0 mmol) and 1,2-dichloroethane (24 mL). The residue was purified by column chromatography (Petrol/Et₂O 4:1) and recrystallised in Petrol/Et₂O to give white crystals (390 mg, 1.5 mmol, 25%).

1H NMR (400 MHz, CDCl₃) δ 8.73 (1H, s, Ar-H), 8.61 (1H, d, J = 8.0 Hz, Ar-H), 7.89 (1H, d, J = 8.0 Hz, Ar-H), 7.62 (1H, dd, J = 8.0, 8.0 Hz, Ar-H), 7.49 (1H, s, N-H), 7.41 – 7.30 (5H, m, Ar-H), 4.57 (2H, d, J = 6.0 Hz, CH₂); 13C NMR (101 MHz, CDCl₃) δ 185.4, 160.5, 137.2, 136.8, 135.3, 135.1, 134.2, 129.6, 129.1, 128.2, 128.1, 117.9, 113.2, 43.8; mp (Petrol/Et₂O): 70 – 71 °C; IR (cm⁻¹) ν = 3350, 3068, 2981, 2233, 1668, 1599, 1523, 1498, 1476, 1455, 1426, 1361, 1292, 1238, 1159, 1070, 1029, 953, 828, 788, 762, 730, 700, 680; LRMS (ESI) m/z: 287.0 [C₁₅H₁₂N₂NaO₂, (M+Na)⁺]; HRMS (ESI) m/z: calcd for [C₁₅H₁₃N₂O₂, (M+H)⁺]: 265.09715; found 265.09729.

Compound 1v was synthesised by modifying a literature procedure. A solution of 4-methyl-2-oxovaleric acid (370 µL, 3.0 mmol), Et₃N (418 µL, 3.0 mmol), DMAP (37 mg, 0.3 mmol), N,N’-dicyclohexylcarbodiimide (469 µL, 3.0 mmol) in 1,2-dichloroethane (10 mL) was stirred at rt until efferevescence was no longer observed. Benzylamine (328 µL, 3.0 mmol) was then added dropwise and the reaction mixture was left to stir at rt overnight before heating at 60 °C
for 4 hours. The crude mixture was then filtered through a plug of celite, purified by column chromatography (Petrol/Et₂O 95:5) and recrystallisation (Petrol/Et₂O) to give a white solid (125 mg, 0.6 mmol, 19%).

\(^1\)H NMR (400 MHz, CDCl₃) δ 7.39 – 7.24 (5H, m, Ar-\(H\)), 4.46 (2H, d, \(J = 6.0\) Hz, NCH₂), 2.83 (2H, d, \(J = 7.0\) Hz, CH₂), 2.24 – 2.12 (1H, m, CH), 0.95 (6H, dd, \(J = 7.0\) Hz, \(2 \times CH₃\));

\(^1^3\)C NMR (101 MHz, CDCl₃) δ 198.9, 160.2, 137.2, 129.0, 128.03, 127.99, 45.5, 43.6, 24.5, 22.7; mp (Petrol/Et₂O): 68 – 70 °C; IR (cm\(^{-1}\)) \(\tilde{\nu} = 3281, 2981, 2889, 2361, 1721, 1671, 1530, 1457, 1433, 1383, 1252, 1149, 1078, 954, 816, 750, 699, 679\); LRMS (ESI) m/z: 220.2 [C\(_{13}\)H\(_{18}\)NO\(_2\), (M+H)\(^+\)]; HRMS (ESI) m/z: calcd for [C\(_{13}\)H\(_{18}\)NO\(_2\), (M+H)\(^+\)]: 220.13321; found 220.13344.

\(N\)-Benzyl-2-cyclopentyl-2-oxoacetamide (1w)

\[
\text{\begin{tikzpicture}
\draw[thick] (0,0) circle (0.5cm);
\draw[thick] (0,0) -- (0.5cm,0.5cm);
\draw[thick] (0,0) -- (0.5cm,-0.5cm);
\draw[thick] (0,0) -- (-0.5cm,0.5cm);
\draw[thick] (0,0) -- (-0.5cm,-0.5cm);
\draw[thick] (0,0) -- (0.5cm,0.5cm) -- (1cm,0) -- (0.5cm,-0.5cm);
\draw[thick] (0,0) -- (-0.5cm,0.5cm) -- (-1cm,0) -- (-0.5cm,-0.5cm);
\end{tikzpicture}}
\]

Compound 1w was synthesised by modifying a literature procedure\(^9\). A solution of 4-methyl-2-oxovaleric acid (370 µL, 3.0 mmol), Et₃N (418 µL, 3.0 mmol), DMAP (37 mg, 0.3 mmol), \(N,N'\)-dicyclohexylcarbodiimide (469 µL, 3.0 mmol) in 1,2-dichloroethane (10 mL) was stirred at rt until efferevescence was no longer observed. Benzylamine (328 µL, 3.0 mmol) was then added dropwise and the reaction mixture was left to stir at rt overnight before heating at 60 °C for 4 hours. The crude mixture was then filtered through a plug of celite, purified by column chromatography (Petrol/Et₂O 95:5) and recrystallisation (Petrol/Et₂O) to give white crystals (94 mg, 0.4 mmol, 7%).

\(^1\)H NMR (400 MHz, CDCl₃) δ 7.39 – 7.25 (5H, m, Ar-\(H\)), 4.48 (2H, d, \(J = 6.0\) Hz, NCH₂), 3.81 (1H, tt, \(J = 9.0, 7.0\) Hz, CH), 2.00 – 1.87 (2H, m, CH₂), 1.81 – 1.70 (2H, m, CH₂), 1.69 – 1.57 (4H, m, \(2 \times CH₂\)); \(^{13}\)C NMR (101 MHz, CDCl₃) δ 200.9, 160.3, 137.2, 129.0, 128.0, 127.95, 44.8, 43.6, 29.1, 26.4; mp (Petrol/Et₂O): 47 – 49 °C; IR (cm\(^{-1}\)) \(\tilde{\nu} = 3328, 2980, 2889, 2360, 1717, 1680, 1666, 1534, 1496, 1473, 1453, 1428, 1382, 1252, 1153, 1126, 1070, 1028, 954, 881, 817, 781, 724, 695\); LRMS (ESI) m/z: 254.2 [C\(_{14}\)H\(_{17}\)NNaO\(_2\), (M+Na)\(^+\)]; HRMS (ESI) m/z: calcd for [C\(_{14}\)H\(_{18}\)NO\(_2\), (M+H)\(^+\)]: 232.13321; found 232.13306.
**N-Tosyl-2-(3-nitrophenyl)-2-oxo-acetamide (1x)**

![Chemical Structure](image)

Compound 1x was prepared according to general procedure B, using crude 2-(3-nitrophenyl)-2-oxoacetic acid (1.95 g, 10.0 mmol), oxaly chloride (1.01 mL, 12 mmol), 1 drop of DMF in CH$_2$Cl$_2$ (20 mL), toluene (10 mL), 4-methylbenzenesulfonamide (1.71 g, 10 mmol), DMAP (6 mg, 0.05 mmol), Et$_3$N (2.8 mL, 20 mmol) and EtOAc (20 mL). The residue was purified by recrystallisation (Petrol/Acetone) to give a light yellow solid (1.21 g, 3.5 mmol, 35%).

$^1$H NMR (400 MHz, d$_6$-DMSO) δ 8.53 (1H, d, $J = 8.0$ Hz, Ar-H), 8.49 (1H, s, Ar-H), 8.23 (1H, d, $J = 8.0$ Hz, Ar-H), 7.92 – 7.82 (4H, m, Ar-H), 7.49 (2H, d, $J = 8.0$ Hz, Ar-H), 2.43 (3H, s, CH$_3$); $^{13}$C NMR (101 MHz, d$_6$-DMSO) δ 185.3, 163.3, 148.3, 145.3, 136.6, 136.0, 133.7, 131.4, 130.3, 129.4, 128.1, 124.6, 21.6; mp (Petrol/Acetone): 189 – 190 °C; IR (cm$^{-1}$) $\tilde{\nu} =$ 3292, 3111, 3068, 2981, 2361, 2341, 1726, 1686, 1611, 1575, 1530, 1428, 1348, 1287, 1258, 1190, 1172, 1136, 1086, 1010, 948, 890, 861, 831, 816, 798, 786, 733, 695, 676; LRMS (ESI) m/z: 371.0[C$_{15}$H$_{12}$N$_2$NaO$_6$S, (M+Na)$^+$]; HRMS (ESI): calcd for [C$_{14}$H$_{10}$N$_2$NaO$_6$S, (M+Na)$^+$]: 371.03083; found 371.03088.
IV. Copper-catalysed Synthesis of Pyrrolinone Derivatives

*General procedure C:*

\[ \text{O} \quad \text{H} \quad \text{R}^2 \quad + \quad \text{H} \quad \text{C=C} \quad \text{R}_3 \quad 10 \text{ mol}\% \quad \text{[Cu(MeCN)}_4\text{]}\text{BF}_4 \quad \text{toluene, 130 °C, 20 h} \]

To an oven-dried, round-bottomed 10 mL microwave reaction vial equipped with a stirrer was added [Cu(MeCN)_4]BF_4 (9.4 mg, 0.03 mmol) and α-keto amide 1 (0.36 mmol, 1.2 equiv.). The vial was sealed with a microwave vial cap, and then evacuated under vacuum (<1 mbar) and back-filled with N_2 gas for 3 times. Degassed dry toluene (0.5 mL) and degassed alkyne (0.30 mmol, 1.0 equiv.) were then added respectively. The solution was stirred and heated at 130 °C for 20 h. The reaction mixture was diluted with CH_2Cl_2, filtered through a plug of celite and concentrated under reduced pressure. The residue was purified by column chromatography to give the resulting product.

\((E)-1\text{-Benzy1-5-hexylidene-3-phenyl-1,5-dihydro-2H-pyrrol-2-one (3a)}\)

Compound 3a was synthesised according to general procedure C using 1aa (86 mg, 0.36 mmol), 1-octyne (44 µL, 0.30 mmol), purified by column chromatography (Petrol/EtOAc = 95:5) and obtained as a yellow oil (60 mg, 0.14 mmol, 60%).

\(^1\text{H NMR (400 MHz, CDCl}_3\text{)} \delta 8.06 – 7.99 (2H, m, Ar-H), 7.44 – 7.38 (3H, m, 2 × Ar-H and C=CH), 7.37 – 7.28 (3H, m, Ar-H), 7.26 – 7.20 (3H, m, Ar-H), 5.39 (1H, t, J = 8.0 Hz, C=CHCH_2), 4.92 (2H, s, NCH_2), 2.32 (2H, app. q, J = 8.0 Hz, C=CHCH_2), 1.44 – 1.39 (2H, m, C=CHCH_2CH_2), 1.35 – 1.13 (4H, m, CH_2CH_2CH_2CH_3), 0.86 (3H, t, J = 7.0 Hz, CH_3); \(^{13}\text{C NMR (101 MHz, CDCl}_3\text{)} \delta 168.8, 137.9, 137.6, 133.4, 131.7, 128.8, 128.7, 128.6, 127.4, 127.2, 127.0, 125.2, 116.4, 42.9, 31.3, 30.0, 27.7, 22.5, 14.1; IR (cm\(^{-1}\)) \tilde{\nu} = 2927, 2858, 2360, 1683, 1494, 1402, 1346, 1177, 1075, 1029, 848, 751, 694, 668; LRMS (ESI) m/z: 354.2
[C_{23}H_{25}NONa, (M+Na)^+]; **HRMS (ESI):** calcd for [C_{23}H_{26}NO, (M+H)^+]: 332.20089; found 332.20068.

**(E)-isomer configuration was confirmed by NOESY experiments.**

Irradiation of H_A found that H_A and H_C are spatially closer together compared to H_A and H_B, indicating that **11a** has an **(E)-configuration.**
(E)-5-Hexylidene-3-phenyl-1-tosyl-1,5-dihydro-2H-pyrrol-2-one (3b)

Compound 3b was synthesised according to general procedure C using α-keto amide 1ab (109 mg, 0.36 mmol), 1-octyne (44 µL, 0.30 mmol), purified by column chromatography (Petrol/EtOAc = 9:1) and obtained as a yellow oil (98 mg, 0.25 mmol, 83%).

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.94 (2H, d, $J = 8.5$ Hz, Ar-H), 7.83 – 7.78 (2H, m, Ar-H), 7.58 (1H, s, C=CH), 7.39 – 7.29 (5H, m, Ar-H), 6.88 (1H, t, $J = 8.5$ Hz, C=CHCH$_2$), 2.43 (2H, q, $J = 8.5$ Hz, C=CHCH$_2$), 2.40 (3H, s, Ar-C$_3$H$_2$), 1.61 – 1.52 (2H, m, C=CHCH$_2$CH$_2$), 1.39 – 1.32 (4H, m, CH$_2$CH$_2$CH$_2$), 0.94 – 0.90 (3H, m, CH$_3$); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 166.9, 145.2, 135.9, 134.5, 131.4, 130.04, 130.01, 129.8, 129.4, 128.7, 128.1, 127.3, 122.9, 31.5, 29.7, 28.5, 22.6, 21.8, 14.1; IR (cm$^{-1}$) $\tilde{\nu}$ = 2970, 2927, 2360, 1698, 1635, 1597, 1493, 1447, 1306, 1220, 1171, 1145, 1124, 1092, 1006, 991, 814, 773; LRMS (ESI) m/z: 396.2 [C$_{23}$H$_{26}$NO$_3$S, (M+H)$^+$]; HRMS (ESI): calcd for [C$_{23}$H$_{26}$NO$_3$S, (M+H)$^+$]: 396.16279; found 396.16229.

(3c)

Compound 3c was synthesised according to general procedure C using α-keto amide 1ac (115 mg, 0.36 mmol), 1-octyne (44 µL, 0.30 mmol), purified by column chromatography (Petrol/EtOAc = 4:1) and obtained as a yellow solid (92 mg, 0.22 mmol, 75%).
\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.00 (2H, d, \(J = 9.0\) Hz, Ar-H), 7.80 (2H, d, \(J = 8.5\) Hz, Ar-H), 7.57 (1H, s, C=CH), 7.41 – 7.23 (3H, m, Ar-H), 6.96 (2H, d, \(J = 8.5\) Hz, Ar-H), 6.88 (1H, t, \(J = 8.0\) Hz, C=CHCH\(_2\)), 3.83 (3H, s, OCH\(_3\)), 2.43 (2H, q, \(J = 8.5\) Hz, C=CHCH\(_2\)).

\(^13\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 167.0, 164.0, 134.6, 131.4, 130.4, 130.3, 130.1, 129.9, 129.3, 128.7, 127.3, 122.9, 114.3, 55.8, 31.5, 29.7, 28.5, 22.6, 14.1; mp (Petrol/Et\(_2\)O): 96 – 98°C; IR (cm\(^{-1}\)) \(\bar{\nu}\) = 3084, 2955, 2927, 2857, 2362, 2342, 1718, 1635, 1595, 1578, 1498, 1461, 1449, 1417, 1388, 1364, 1305, 1246, 1190, 1168, 1143, 1122, 1092, 1025, 1007, 994, 920, 866, 834, 804, 785, 750, 718, 692, 666, 647, 627, 615; LRMS (ESI) \(m/z\): 412.2 [C\(_{25}\)H\(_{26}\)NO\(_4\)S, (M+H)+]; HRMS (ESI): calcd for [C\(_{25}\)H\(_{26}\)NO\(_4\)S, (M+H)+]: 412.15771; found 412.15759.

(E)-5-Hexylidene-1-((4-cyano)sulfonyl)-3-phenyl-1,5-dihydro-2H-pyrrol-2-one (3d)

![Chemical Structure](image)

Compound 3d was synthesised according to general procedure C, using \(\alpha\)-keto amide 1ad (113 mg, 0.36 mmol), 1-octyne (44 \(\mu\)L, 0.30 mmol), purified by column chromatography (Petrol/Et\(_2\)O = 9:1) and obtained as a white solid (79 mg, 0.19 mmol, 65%).

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.18 (2H, d, \(J = 8.5\) Hz, Ar-H), 7.82 (2H, d, \(J = 8.5\) Hz, Ar-H), 7.77 (2H, dd, \(J = 8.0, 2.0\) Hz, Ar-H), 7.62 (1H, s, C=CH), 7.42 – 7.30 (3H, m, Ar-H), 6.88 (1H, t, \(J = 8.5\) Hz, C=CHCH\(_2\)), 2.50 – 2.39 (2H, m, C=CHCH\(_2\)), 1.66 – 1.53 (2H, m, C=CHCH\(_2\CH\(_2\)), 1.41 – 1.31 (4H, m, CH\(_2\)CH\(_2\)CH\(_3\)), 0.93 (3H, t, \(J = 7.0\) Hz, CH\(_3\)); \(^13\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 166.8, 142.5, 134.2, 132.9, 131.3, 130.6, 129.7, 129.6, 128.83, 128.82, 127.3, 123.4, 117.7, 117.2, 31.5, 29.6, 28.6, 22.6, 14.1; mp (Petrol/Et\(_2\)O): 112 – 114°C; IR (cm\(^{-1}\)) \(\bar{\nu}\) = 3095, 2956, 2928, 2858, 2349, 2234, 1722, 1635, 1490, 1449, 1394, 1369, 1305 1285, 1244, 1189, 1174, 1120, 1090, 1007, 995, 867, 838, 785, 750, 720, 692, 631; LRMS (ESI) \(m/z\): 407.2 [C\(_{23}\)H\(_{23}\)N\(_2\)O\(_3\)S, (M+H)+]; HRMS (ESI): calcd for [C\(_{23}\)H\(_{23}\)N\(_2\)O\(_3\)S, (M+H)+]: 407.14239; found 407.14175.
(E)-5-Hexylidene-3-phenyl-1-((4-(trifluoromethyl)phenyl)sulfonyl)-1,5-dihydro-2H-pyrrol-2-one (3e)

![Chemical structure of 3e]

Compound 3e was synthesised according to general procedure C, using α-keto amide 1ae (129 mg, 0.36 mmol), 1-octyne (44 µL, 0.30 mmol), purified by column chromatography (Petrol/Et₂O = 9:1) and obtained as a yellow solid (94 mg, 0.21 mmol, 70%).

**¹H NMR** (400 MHz, CDCl₃) δ 8.21 (2H, d, J = 8.0 Hz, Ar-H), 7.80–7.77 (4H, m, Ar-H), 7.62 (1H, s, C=CH), 7.41–7.31 (3H, m, Ar-H), 6.90 (1H, t, J = 8.0 Hz, C=CHCH₂), 2.51–2.40 (2H, m, C=CHCH₂), 1.63–1.52 (2H, m, C=CHCH₂CH₂), 1.42–1.31 (4H, m, CH₂CH₂CH₃), 0.94 (3H, t, J = 7.0 Hz, CH₃); **¹³C NMR** (101 MHz, CDCl₃) δ 166.8, 142.1, 135.5 (q, J = 34.0 Hz), 134.3, 131.4, 130.5, 129.7, 129.6, 128.8, 128.7, 127.3, 126.3 (q, J = 3.0 Hz), 123.3, 123.1 (q, J = 273.0 Hz), 31.5, 29.6, 28.5, 22.6, 14.1; **¹⁹F NMR** (377 MHz, CDCl₃) δ -63.3; **mp** (Petrol/Et₂O): 85–87 °C; **IR (cm⁻¹)** ν = 2960, 2930, 2361, 2255, 1720, 1492, 1450, 1406, 1371, 1322, 1243, 1176, 1140, 1109, 1094, 1063, 1007, 995, 905, 843, 785, 726, 692, 649, 607; **LRMS (ESI) m/z**: 450.2 [C₂₃H₂₂F₃NO₃S, (M+H)⁺]; **HRMS (ESI)**: calcd for [C₂₃H₂₂F₃NO₃S, (M+H)⁺]: 450.13453; found 450.13440.

S24
(E)-5-Hexylidene-1-((4-nitrophenyl)sulfonyl)-3-phenyl-1,5-dihydro-2H-pyrrol-2-one (3f)

Compound 3f was synthesised according to general procedure C, using α-keto amide 1af (120 mg, 0.36 mmol), 1-octyne (44 µL, 0.30 mmol), purified by column chromatography (Petrol/EtO = 4:1) and obtained as a yellow solid (55 mg, 0.13 mmol, 43%).

1H NMR (400 MHz, CDCl3); δ 8.36 (2H, d, J = 9.0 Hz, Ar-H), 8.27 (2H, d, J = 9.0 Hz, Ar-H), 7.80 – 7.73 (2H, m, Ar-H), 7.62 (1H, s, C=CH), 7.41 – 7.32 (3H, m, Ar-H), 6.90 (1H, t, J = 8.0 Hz, C=CHCH2), 2.46 (2H, dd, J = 15.0, 8.0 Hz, C=CHCH2), 1.65 – 1.53 (2H, m, C=CHCH2CH2), 1.44 – 1.33 (4H, m, CH2CH2CH2), 0.93 (3H, t, J = 7.0 Hz, CH3); 13C NMR (101 MHz, CDCl3) δ 166.8, 150.9, 144.0, 134.2, 131.5, 130.6, 129.8, 129.7, 129.6, 128.9, 127.3, 124.4, 123.5, 31.6, 29.7, 28.6, 22.6, 14.2; mp (Petrol/EtO): 90 – 92 °C; IR (cm⁻¹) ̃ν = 3658, 2981, 2889, 2360, 2341, 1721, 1636, 1607, 1532, 1473, 1462, 1382, 1251, 1151, 1089, 1073, 1007, 955, 855, 816, 785, 741, 683, 669, 648, 609; LRMS (ESI) m/z: 427.2 [C22H23N2O5S, (M+H)+]; HRMS (ESI): calcd for [C22H23N2O5S, (M+H)+]: 427.13222; found 427.13232.

(E)-5-Hexylidene-1-(methylsulfonyl)-3-phenyl-1,5-dihydro-2H-pyrrol-2-one (3g)

Compound 3g was synthesised according to general procedure C, using α-keto amide 1ag (82 mg, 0.36 mmol), 1-octyne (44 µL, 0.30 mmol), purified by column chromatography (Petrol/EtOAc = 9:1) and obtained as a yellow oil (41 mg, 0.13 mmol, 43%).
1H NMR (400 MHz, CDCl3) δ 7.89 – 7.85 (2H, m, Ar-H), 7.64 (1H, s, C=CH), 7.47 – 7.33 (3H, m, Ar-H), 6.74 (1H, t, J = 8.0 Hz, C=CHCH2), 3.41 (3H, s, SO2CH3), 2.47 – 2.36 (2H, m, C=CHCH2), 1.56 – 1.50 (2H, m, C=CHCH2CH2), 1.37 – 1.32 (4H, m, CH2CH2CH3), 0.92 (3H, t, J = 7.0 Hz, CH3); 13C NMR (101 MHz, CDCl3) δ 167.7, 134.3, 131.2, 130.0, 129.9, 129.5, 128.8, 127.3, 123.4, 41.9, 31.5, 29.5, 28.5, 22.5, 14.0; IR (cm⁻¹) ν = 2929, 2960, 2361, 1714, 1492, 1449, 1355, 1325, 1220, 1165, 1124, 995, 963, 772, 691; LRMS (ESI) m/z: 342.0 [C17H21NO3SNa, (M+Na)⁺]; HRMS (ESI): calcd for [C17H22NO3S, (M+H)⁺]: 320.13149; found 320.13137.

(3H, m, Ar-H), δ 7.89 – 7.85 (2H, m, Ar-H), 7.64 (1H, s, C=CH), 7.47 – 7.33 (3H, m, Ar-H), 6.74 (1H, t, J = 8.0 Hz, C=CHCH2), 3.41 (3H, s, SO2CH3), 2.47 – 2.36 (2H, m, C=CHCH2), 1.56 – 1.50 (2H, m, C=CHCH2CH2), 1.37 – 1.32 (4H, m, CH2CH2CH3), 0.92 (3H, t, J = 7.0 Hz, CH3); 13C NMR (101 MHz, CDCl3) δ 167.7, 134.3, 131.2, 130.0, 129.9, 129.5, 128.8, 127.3, 123.4, 41.9, 31.5, 29.5, 28.5, 22.5, 14.0; IR (cm⁻¹) ν = 2929, 2960, 2361, 1714, 1492, 1449, 1355, 1325, 1220, 1165, 1124, 995, 963, 772, 691; LRMS (ESI) m/z: 342.0 [C17H21NO3SNa, (M+Na)⁺]; HRMS (ESI): calcd for [C17H22NO3S, (M+H)⁺]: 320.13149; found 320.13137.

Compounds 3h was synthesised according to general procedure C, using α-keto amide 1ah (84 mg, 0.36 mmol), 1-octyne (44 µL, 0.30 mmol), purified by column chromatography (Petrol/Et2O = 95:5) and obtained as a yellow oil (51 mg, 0.16 mmol, 52%).

1H NMR (400 MHz, CDCl3) δ 7.98 (2H, d, J = 7.5 Hz, Ar-H), 7.44 – 7.30 (4H, m, 3 × Ar-H, C=CH), 5.45 (1H, t, J = 8.0 Hz, C=CHCH2), 3.66 (2H, t, J = 7.5 Hz, NCH2), 2.46 – 2.35 (2H, m, C=CHCH2), 1.65 – 1.58 (2H, m, NCH2CH2), 1.57 – 1.46 (2H, m, C=CHCH2CH2), 1.41 – 1.22 (10H, m, N(CH2)2CH2CH2CH2, CH2CH2CH3), 0.96 – 0.84 (5H, m, N(CH2)4CH2, CH3); 13C NMR (101 MHz, CDCl3) δ 168.7, 138.3, 133.5, 131.9, 128.7, 128.6, 127.4, 124.7, 114.9, 39.3, 31.7, 31.5, 30.2, 29.0, 27.9, 26.7, 22.7, 22.6, 14.2; IR (cm⁻¹) ν = 3657, 2981, 2931, 2889, 2349, 1684, 1647, 1461, 1382, 1251, 1153, 1073, 956, 818, 787, 748, 693, 649; LRMS (ESI) m/z: 326.2 [C22H32NO, (M+H)⁺]; HRMS (ESI): calcd for [C22H32NO, (M+H)⁺]: 326.24784; found 326.24736.
(E)-1-Cyclopropyl-5-hexylidene-3-phenyl-1,5-dihydro-2H-pyrrol-2-one (3i)

![Structure of compound 3i]

Compound 3i was synthesised according to general procedure C, using α-keto amide 1ai (68 mg, 0.36 mmol), 1-octyne (44 µL, 0.30 mmol), purified by column chromatography (Petrol/Et₂O = 95:5) and obtained as a yellow oil (56 mg, 0.20 mmol, 69%).

$^1$H NMR (400 MHz, CDCl₃) δ 7.93 (2H, d, $J = 7.5$ Hz, Ar-H), 7.38 (2H, dd, $J = 7.5$, 7.5 Hz, Ar-H), 7.35 – 7.29 (2H, m, Ar-H, C=C₆H), 5.83 (1H, t, $J = 8.0$ Hz, C=C₆H₂(CH₃), 2.54 (1H, tt, $J = 7.0$, 4.0 Hz, NCH₃), 2.44 – 2.34 (2H, m, C=CHC₆H₂), 1.58 – 1.48 (2H, m, C=CHCH₂C₆H₃), 1.40 – 1.29 (4H, m, CH₂C₆H₂CH₃), 1.06 – 0.98 (2H, m, NCH₂), 0.94 – 0.88 (5H, m, CH₃, NCH₂); $^{13}$C NMR (101 MHz, CDCl₃) δ 169.4, 139.2, 133.0, 131.9, 128.6, 128.6, 127.4, 124.7, 116.1, 31.5, 30.2, 27.9, 22.6, 21.4, 14.2, 6.4; IR (cm⁻¹) $\tilde{\nu} = 3661, 2981, 2889, 2361, 2341, 1681, 1462, 1421, 1382, 1241, 1152, 1073, 904, 788, 724, 649$; LRMS (ESI) m/z: 282.2 [C₁₉H₂₄NO, (M+H)+]; HRMS (ESI): calcd for [C₁₉H₂₄NO, (M+H)+]: 282.18524; found 282.18494.

(E)-1-Cyclohexyl-5-hexylidene-3-phenyl-1,5-dihydro-2H-pyrrol-2-one (3j)

![Structure of compound 3j]

Compound 3j was synthesised according to general procedure C, using α-keto amide 1aj (83 mg, 0.36 mmol), 1-octyne (44 µL, 0.30 mmol), purified by column chromatography (Petrol/Et₂O = 95:5) and obtained as a yellow oil (41 mg, 0.12 mmol, 42%).

$^1$H NMR (400 MHz, CDCl₃) δ 7.95 (2H, d, $J = 7.0$ Hz, Ar-H), 7.43 – 7.27 (4H, m, 3 × Ar-H, C=C₆H), 5.61 (1H, t, $J = 8.0$ Hz, C=C₆H₂(CH₃), 3.96 (1H, p, $J = 12.0$ Hz, C₆H₂(CH₃), 2.43 – 2.37 (2H, m, C=CHC₆H₂), 2.26 – 2.11 (2H, m, C₆H₂(CH₃), 1.92 – 1.82 (2H, m, C₆H₂(CH₃), 1.77 – 1.68 (4H, m, 2 × C₆H₂(CH₃), 1.58 – 1.48 (2H, m, C=CHCH₂CH₂), 1.42 – 1.31 (4H, m, CH₂CH₂CH₂CH₃), 1.31 – 1.15
(2H, m, C\textsubscript{3}H\textsubscript{2}), 0.92 (3H, t, J = 6.5 Hz, CH\textsubscript{3}); \textsuperscript{13}C NMR (101 MHz, CDCl\textsubscript{3}) \( \delta \) 168.9, 138.0, 133.3, 131.9, 128.6, 128.5, 127.5, 125.1, 115.5, 52.2, 31.6, 30.4, 30.3, 28.2, 26.6, 25.6, 22.6, 14.2, 1.2; IR (cm\textsuperscript{-1}) \( \tilde{\nu} \) = 3661, 2981, 2933, 2361, 2341, 1676, 1640, 1450, 1308, 1347, 1259, 1205, 1152, 1073, 905, 788, 726, 693, 648; LRMS (ESI) m/z: 346.2 [C\textsubscript{22}H\textsubscript{29}NNaO\textsubscript{2}, (M+Na)\textsuperscript{+}]; HRMS (ESI): calcd for [C\textsubscript{22}H\textsubscript{30}NO\textsubscript{2}, (M+H)\textsuperscript{+}]: 324.23219; found 324.23199.

\((E)-1-(\text{Cyclopropylmethyl})-5\text{-hexylidene-3-phenyl-1,5-dihydro-2H-pyrrol-2-one (3k)}\)

\[
\begin{align*}
\text{N} & \quad \text{C=CHCH}_2\text{C=CHCH}_2\text{CH}_3 \quad \text{Me} \\
\text{O-} & \\
\triangle & \\
\text{C}_6\text{H}_5 & \\
\text{CH}_2\text{C=CH}_2 & \\
\end{align*}
\]

Compound 3k was synthesised according to general procedure C, using \( \alpha \)-keto amide 1ak (73 mg, 0.36 mmol), 1-octyne (44 \( \mu \)L, 0.30 mmol), purified by column chromatography (Petrol/Et\textsubscript{2}O = 95:5) and obtained as a yellow oil (44 mg, 0.15 mmol, 50%).

\(^1\text{H} NMR (400 MHz, CDCl}_3) \( \delta \) 7.97 (2H, d, \( J = 7.5 \) Hz, Ar-H), 7.42 – 7.37 (3H, m, 2 \times Ar-H, C=CH), 7.33 (1H, t, \( J = 7.5 \) Hz, Ar-H), 5.54 (1H, t, \( J = 8.0 \) Hz, C=CHCH\textsubscript{2}), 3.58 (2H, d, \( J = 7.0 \) Hz, NCH\textsubscript{2}), 2.48 – 2.37 (2H, m, C=CHCH\textsubscript{2}), 1.60 – 1.46 (2H, m, C=CHCH\textsubscript{2}CH\textsubscript{2}), 1.40 – 1.30 (4H, m, CH\textsubscript{2}CH\textsubscript{2}CH\textsubscript{3}), 1.15 – 1.01 (1H, m, CH(CH\textsubscript{2})\textsubscript{2}), 0.96 – 0.87 (3H, m, CH\textsubscript{3}), 0.54 – 0.44 (2H, m, 1 \times CH(CH\textsubscript{2})\textsubscript{2}), 0.43 – 0.34 (2H, m, 1 \times CH(CH\textsubscript{2})\textsubscript{2}); \textsuperscript{13}C NMR (101 MHz, CDCl\textsubscript{3}) \( \delta \) 168.8, 138.6, 133.6, 131.9, 128.7, 128.6, 127.4, 124.8, 115.1, 43.3, 31.5, 30.2, 27.9, 22.6, 14.2, 10.9, 3.9; IR (cm\textsuperscript{-1}) \( \tilde{\nu} \) = 3657, 2981, 2889, 2349, 1687, 1491, 1461, 1383, 1252, 1153, 1073, 1021, 955, 789, 749, 694, 650; LRMS (ESI) m/z: 296.2 [C\textsubscript{20}H\textsubscript{26}NO\textsubscript{2}, (M+H)\textsuperscript{+}]; HRMS (ESI): calcd for [C\textsubscript{20}H\textsubscript{26}NO\textsubscript{2}, (M+H)\textsuperscript{+}]: 296.20089; found 296.20062.

\((E)-1-(\text{Cyclohexylmethyl})-5\text{-hexylidene-3-phenyl-1,5-dihydro-2H-pyrrol-2-one (3l)}\)

\[
\begin{align*}
\text{N} & \quad \text{C=CHCH}_2\text{C=CHCH}_2\text{CH}_3 \quad \text{Me} \\
\text{O-} & \\
\text{C}_6\text{H}_5 & \\
\text{CH}_2\text{C=CH}_2 & \\
\end{align*}
\]
Compound 3l was synthesised according to general procedure C, using α-keto amide 1al (88 mg, 0.36 mmol), 1-octyne (44 µL, 0.30 mmol), purified by column chromatography (Petrol/Et₂O = 95:5) and obtained as a yellow oil (46 mg, 0.14 mmol, 45%).

^1^H NMR (400 MHz, CDCl₃) δ 7.98 (2H, d, J = 7.5 Hz, Ar-H), 7.43 – 7.35 (3H, m, 2 × Ar-H, C=CH), 7.32 (1H, t, J = 7.0 Hz, Ar-H), 5.45 (1H, t, J = 8.0 Hz, C=CH₂CH₂), 3.51 (2H, d, J = 7.0 Hz, NC₃H₂), 2.48 – 2.35 (2H, m, C=CH₂CH₂), 1.78 – 1.69 (3H, m, C₇H, C₅H₂), 1.68 – 1.61 (2H, m, C₅H₂), 1.56 – 1.47 (2H, m, C=CH₂CH₂), 1.40 – 1.30 (4H, m, CH₂CH₂CH₃), 1.22 – 1.14 (2H, m, C₅H₂), 1.08 – 0.95 (2H, m, C₅H₂), 0.95 – 0.88 (3H, m, C₃H₃); ^1^C NMR (101 MHz, CDCl₃) δ 169.1, 138.8, 133.3, 131.9, 128.7, 128.6, 126.7, 124.6, 115.3, 45.5, 37.7, 31.5, 31.1, 30.2, 27.9, 26.5, 26.0, 25.9, 22.6, 14.2; IR (cm⁻¹) ν = 3657, 2981, 2928, 2349, 1678, 1646, 1448, 1381, 1345, 1251, 1153, 1073, 956, 906, 838, 787, 727, 693, 649; LRMS (ESI) m/z: 338.2 [C₂₃H₃₂NO, (M+H)+]; HRMS (ESI) calcd for [C₂₃H₃₂NO, (M+H)+]: 338.24784; found 338.24756.

(E)-5-Hexylidene-3-phenyl-1-(thiophen-2-ylmethyl)-1,5-dihydro-2H-pyrrol-2-one (3m)

Compound 3m was synthesised according to general procedure C, using α-keto amide 1am (88 mg, 0.36 mmol), 1-octyne (44 µL, 0.30 mmol), purified by column chromatography (Petrol/Et₂O = 95:5) and obtained as a yellow oil (54 mg, 0.16 mmol, 53%).

^1^H NMR (400 MHz, CDCl₃) δ 7.94 (2H, d, J = 7.0 Hz, Ar-H), 7.39 – 7.31 (3H, m, Ar-H), 7.29 (1H, d, J = 7.0 Hz, Ar-H), 7.12 (1H, d, J = 5.0 Hz, Ar-H), 6.93 (1H, s, C=CH), 6.87 (1H, dd, J = 5.0, 3.5 Hz, Ar-H), 5.51 (1H, t, J = 8.0 Hz, C=CH₂CH₂), 4.99 (2H, s, NCH₂), 2.32 (2H, q, J = 8.0 Hz, C=CH₂CH₂), 1.48 – 1.36 (2H, m, CH₂CH₂CH₂CH₃), 1.32 – 1.17 (4H, m, CH₂CH₂CH₂CH₃), 0.84 (3H, t, J = 7.0 Hz, CH₃); ^1^C NMR (101 MHz, CDCl₃) δ 168.3, 140.2, 137.5, 133.3, 131.6, 128.8, 128.6, 127.4, 126.8, 125.9, 125.3, 125.0, 116.0, 37.8, 31.3, 30.0, 27.8, 22.6, 14.1; IR (cm⁻¹) ν = 3369, 3069, 2955, 2927, 2857, 2360, 1685, 1491, 1431, 1410, 1340, 1238, 1180,
MS (ESI) m/z: 338.2 [C_{21}H_{24}NOS, (M+H)^+]; HRMS (ESI) m/z: calcd for [C_{21}H_{24}NOS, (M+H)^+]: 338.15731; found 338.15689.

(E)-1- Allyl-5-hexylidene-3-phenyl-1,5-dihydro-2H-pyrrol-2-one (3n)

\[ \text{Compound 3n was synthesised according to general procedure C, using } \alpha \text{-keto amide 1an (68 mg, 0.36 mmol), 1-octyne (44 µL, 0.30 mmol), purified by column chromatography (Petrol/Et}_2\text{O = 95:5) and obtained as a yellow oil (43 mg, 0.15 mmol, 51%).} \]

\(^1\text{H NMR (400 MHz, CDCl}_3\) \(\delta 7.98 (2\text{H, d, } J = 7.0 \text{ Hz, Ar-H}), 7.43 – 7.30 (4\text{H, m, } 3 \times \text{Ar-H, C=CH}), 5.90 – 5.78 (1\text{H, m, NCH}_2\text{CH=CH}_2), 5.46 (1\text{H, t, } J = 8.0 \text{ Hz, C=CHCH}_2), 5.19 – 5.08 (2\text{H, m, NCH}_2\text{CH=CH}_2), 4.35 – 4.27 (2\text{H, m, NCH}_2\text{H}), 2.44 – 2.34 (2\text{H, m, C=CHCH}_2), 1.55 – 1.45 (2\text{H, m, C=CHCH}_2\text{CH}_2), 1.41 – 1.28 (4\text{H, m, CH}_2\text{CH}_2\text{CH}_3), 0.91 (3\text{H, t, } J = 6.5 \text{ Hz, CH}_3); \)

\(^13\text{C NMR (101 MHz, CDCl}_3\) \(\delta 168.5, 138.0, 133.3, 131.8, 128.8, 128.6, 127.4, 125.1, 116.4, 116.0, 100.1, 41.6, 31.5, 30.1, 27.9, 22.6, 14.2; \text{IR (cm}^{-1}\) \(\tilde{\nu} = 3661, 2981, 2889, 2361, 2341, 1681, 1647, 1382, 1251, 1153, 1073, 942, 905, 727, 693, 648; \text{LRMS (ESI) m/z: 304.2 [C}_{19}\text{H}_{23}\text{NNaO, (M+Na)^+]; HRMS (ESI): calcd for [C}_{19}\text{H}_{23}\text{NNaO, (M+Na)^+]: 304.16719; found 304.16727.} \)
(E)-5-Hexylidene-1,3-diphenyl-1,5-dihydro-2H-pyrrol-2-one and (Z)-5-Hexylidene-1,3-diphenyl-1,5-dihydro-2H-pyrrol-2-one (3o)

Compound 3o was synthesised according to general procedure C, using α-keto amide 1ao (81 mg, 0.36 mmol), 1-octyne (44 µL, 0.30 mmol), purified by column chromatography (Petrol/Et2O = 95:5) and obtained as a yellow oil containing an inseparable mixture of (E) and (Z) isomers (56 mg, 0.18 mmol, 59%), E/Z ratio 3:1.

Major (E)-isomer: ¹H NMR (400 MHz, CDCl₃) δ 8.12 (2H, d, J = 7.0 Hz, Ar-H), 7.65 (1H, s, C=CH), 7.59 – 7.36 (8H, m, Ar-H), 5.50 (1H, t, J = 8.5 Hz, C=CHCH₂), 2.53 – 2.42 (2H, m, C=CHCH₂), 1.59 – 1.48 (2H, m, C=CHCH₂CH₂), 1.46 – 1.36 (4H, m, CH₂CH₂CH₃), 1.05 – 0.94 (3H, m, CH₃); ¹³C NMR (101 MHz, CDCl₃) 168.3, 139.4, 134.8, 132.97, 131.7, 129.3, 128.9, 128.64, 128.4, 127.8, 127.51, 125.3, 117.0, 31.5, 29.9, 27.9, 22.6, 14.1; Minor (Z)-isomer: ¹H NMR (400 MHz, CDCl₃) δ 8.08 – 7.98 (2H, m, Ar-H), 7.76 – 7.67 (1H, m, Ar-H), 7.65 – 7.34 (7H, m, Ar-H), 7.25 (1H, s, C=CH), 5.38 (1H, t, J = 8.0 Hz, C=CHCH₂), 1.83 – 1.72 (2H, m, C=CHCH₂), 1.46 – 1.26 (4H, m, C=CH₂CH₂CH₂CH₂), 1.28 – 1.10 (2H, m, CH₂CH₃), 0.94 – 0.86 (3H, m, 3H, CH₃); ¹³C NMR (101 MHz, CDCl₃) 170.2, 138.1, 137.1, 133.04, 131.6, 129.2, 128.7, 128.60, 128.56, 128.2, 127.50, 127.2, 119.7, 31.4, 29.3, 27.4, 22.4, 14.0; IR (cm⁻¹) ν = 3065, 2955, 2927, 2856, 1693, 1597, 1500, 1449, 1404, 1352, 1224, 1159, 1120, 1073, 1027, 964, 909, 851, 785, 749, 730, 693, 651; LRMS (ESI) m/z: 318.2 [C₂₂H₂₄NO, (M+H)⁺]; HRMS (ESI): calcd for [C₂₂H₂₄NO, (M+H)⁺]: 318.18524; found 318.18493.
(E)-1-Benzyl-5-hexylidene-3-(p-tolyl)-1,5-dihydro-2H-pyrrol-2-one (4a)

Compound 4a was synthesised according to general procedure C, using α-keto amide 1ba (91 mg, 0.36 mmol), 1-octyne (44 µL, 0.30 mmol), purified by column chromatography (Petrol/Et₂O = 95:5) and obtained as a yellow oil (42 mg, 0.12 mmol, 41%).

\(^1\)H NMR (400 MHz, CDCl₃) δ 8.05 (2H, d, \(J = 8.0 \text{ Hz}, \text{Ar-H}\)), 7.50 (1H, s, C=CH), 7.45 – 7.40 (2H, m, Ar-H), 7.38 – 7.31 (5H, m, Ar-H), 5.48 (1H, t, \(J = 8.0 \text{ Hz}, \text{C=CHCH}_2\)), 5.03 (2H, s, NCH$_2$), 2.50 (3H, s, Ar-CH$_3$), 2.47 – 2.40 (2H, m, C=CHCH$_2$), 1.55 – 1.48 (2H, m, CH$_2$CH$_2$CH$_2$CH$_3$), 1.42 – 1.32 (4H, m, CH$_2$CH$_2$CH$_2$CH$_3$), 0.98 (3H, t, \(J = 7.0 \text{ Hz}, \text{CH}_3\)); \(^{13}\)C NMR (101 MHz, CDCl₃) δ 169.0, 138.8, 138.0, 137.7, 133.3, 129.4, 128.9, 128.7, 127.8, 127.2, 127.0, 124.3, 115.9, 42.9, 31.3, 30.0, 27.7, 22.5, 21.5, 14.1; IR (cm$^{-1}$) \(\tilde{\nu} = 2981, 2930, 2889, 2349, 1699, 1512, 1495, 1458, 1393, 1252, 1153, 1077, 954, 823, 748, 701, 648\); LRMS (ESI) m/z: 346.2 [C$_{24}$H$_{28}$NO, (M+H)$^+$]; HRMS (ESI): calcd for [C$_{24}$H$_{28}$NO, (M+H)$^+$]: 346.21654; found 346.21634.

(1E)-1-Benzyl-5-hexylidene-3-(3-methoxyphenyl)-1,5-dihydro-2H-pyrrol-2-one (4b)

Compound 4b was synthesised according to general procedure C, using α-keto amide 1bb (97 mg, 0.36 mmol), 1-octyne (44 µL, 0.30 mmol), purified by column chromatography (Petrol/Et₂O = 95:5) and obtained as a yellow oil (64 mg, 0.18 mmol, 59%).
$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.67 (1H, s, Ar-H), 7.55 (1H, d, $J = 7.5$ Hz, Ar-H), 7.41 (1H, s, C=CH), 7.34 – 7.25 (3H, m, Ar-H), 7.25 – 7.17 (3H, m, Ar-H), 6.90 (1H, d, $J = 8.0$ Hz, Ar-H), 5.38 (1H, t, $J = 8.0$ Hz, C=CHCH$_2$), 4.90 (2H, s, NCH$_2$), 3.84 (3H, s, OCH$_3$), 2.30 (2H, q, $J = 8.0$ Hz, CH$_2$CH$_2$CH$_2$CH$_3$), 1.32 – 1.13 (4H, m, CH$_2$CH$_2$CH$_3$), 0.84 (3H, t, $J = 7.0$ Hz, CH$_3$); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 168.8, 159.8, 137.9, 137.6, 133.1, 133.0, 129.6, 128.7, 127.3, 127.0, 125.5, 119.8, 116.6, 115.1, 112.3, 55.4, 42.9, 31.3, 29.9, 27.8, 22.5, 14.1; IR (cm$^{-1}$) $\tilde{\nu}$ = 2928, 2857, 2361, 2012, 1722, 1683, 1575, 1534, 1488, 1455, 1434, 1412, 1371, 1336, 1287, 1252, 1207, 1180, 1153, 1112, 1044, 1012, 963, 842, 790, 729, 695, 649; LRMS (ESI) m/z: 362.2 [C$_{24}$H$_{28}$NO$_2$, (M+H)$^+$]; HRMS (ESI) m/z: calcd for [C$_{24}$H$_{28}$NO$_2$, (M+H)$^+$]: 362.21146; found 362.21149.

(E)-1-Benzyl-5-hexylidene-3-(4-((trifluoromethyl)phenyl)-1,5-dihydro-2H-pyrrol-2-one (4c)

Compound 4c was synthesised according to general procedure C, using $\alpha$-keto amide 1bc (111 mg, 0.36 mmol), 1-octyne (44 µL, 0.30 mmol), purified by column chromatography (Petrol/Et$_2$O = 95:5) and obtained as a brown oil (85 mg, 0.21 mmol, 71%).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.07 (2H, d, $J = 8.0$ Hz, Ar-H), 7.59 (2H, d, $J = 8.0$ Hz, Ar-H), 7.45 (1H, s, C=CH), 7.28 – 7.20 (2H, m, Ar-H), 7.21 – 7.12 (3H, m, Ar-H), 5.40 (1H, t, $J = 8.0$ Hz, C=CHCH$_2$), 4.85 (2H, s, NCH$_2$), 2.28 (2H, q, $J = 8.0$ Hz, C=CHCH$_2$), 1.40 – 1.29 (2H, m, CH$_2$CH$_2$CH$_2$CH$_3$), 1.28 – 1.08 (4H, m, CH$_2$CH$_2$CH$_3$), 0.79 (3H, t, $J = 7.0$ Hz, CH$_3$); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 168.4, 137.7, 137.4, 135.2, 132.0, 130.4 (q, $J = 32.0$ Hz), 128.8, 127.6, 127.4, 127.0, 126.9, 125.5 (q, $J = 4.0$ Hz), 124.2 (q, $J = 273.0$ Hz), 118.1, 43.0, 31.3, 29.9, 27.9, 22.6, 14.1; $^{19}$F NMR (377 MHz, CDCl$_3$) -62.7; IR (cm$^{-1}$) $\tilde{\nu}$ = 2980, 2889, 1684, 1616, 1461, 1382, 1324, 1251, 1164, 1126, 1070, 1018, 954, 842, 757, 729, 698, 612; LRMS (ESI) m/z:
400.2 \[C_{24}H_{25}F_3NO, (M+H)^+\]; HRMS (ESI) \textit{m/z}: calcd for \[C_{24}H_{25}F_3NO, (M+H)^+\]: 400.18828; found 400.18787.

\((E)-1\)-Benzy1-5-hexylidene-3-(3-nitrophenyl)-1,5-dihydro-2\textit{H}-pyrrol-2-one (4\textit{d})

\[
\begin{align*}
\text{O} & \quad \text{N} \\
\text{Me} & \quad \text{Me}
\end{align*}
\]

Compound 4\textit{d} was synthesised according to general procedure C, using \(\alpha\)-keto amide 1\textit{bd} (102 mg, 0.36 mmol), 1-octyne (44 \(\mu\)L, 0.30 mmol), purified by column chromatography (Petrol/EtOAc = 9:1) and obtained as a light yellow solid (86 mg, 0.23 mmol, 76%).

\(^1\text{H NMR (400 MHz, CDCl}_3\) \(\delta\) 8.80 (1H, s, Ar-\(H\)), 8.49 (1H, d, \(J = 8.0\) Hz, Ar-\(H\)), 8.19 (1H, d, \(J = 8.0\) Hz, Ar-\(H\)), 7.65 – 7.57 (2H, m, Ar-\(H\), C=CH), 7.36 – 7.20 (5H, m, Ar-\(H\)), 5.52 (1H, t, \(J = 8.0\) Hz, C=CH\(CH_2\)), 4.93 (2H, s, NCH\(_2\)), 2.37 (2H, q, \(J = 8.0\) Hz, C=CH\(CH_2\)), 1.48 – 1.38 (2H, m, CH\(_2\)CH\(_2\)CH\(_3\)), 1.34 – 1.18 (4H, m, CH\(_2\)CH\(_2\)CH\(_3\)), 0.86 (3H, t, \(J = 7.0\) Hz, CH\(_3\)); \(^{13}\text{C NMR (101 MHz, CDCl}_3\) \(\delta\) 168.1, 148.5, 137.6, 137.2, 133.4, 133.3, 131.0, 129.7, 128.8, 127.5, 127.1, 127.0, 123.2, 122.0, 118.8, 43.0, 31.3, 29.9, 28.0, 22.5, 14.1; mp (Petrol/Et\(_2\)O): 80 – 82 \(^\circ\)C; IR (\textit{cm}^{-1}) \(\tilde{\nu}\) = 2980, 2889, 2360, 2341, 1724, 1686, 1529, 1473, 1462, 1382, 1350, 1252, 1152, 1073, 955, 810, 732, 701; LRMS (ESI) \textit{m/z}: 377.2 \([C_{23}H_{25}N_2O_3, (M+H)^+]\); HRMS (ESI) \textit{m/z}: calcd for \([C_{23}H_{25}N_2O_3, (M+H)^+]\): 377.18597; found 377.18582.
(E)-1-Benzyl-3-(3-bromophenyl)-5-hexylidene-1,5-dihydro-2H-pyrrol-2-one (4e)

![Chemical Structure](image)

Compound 4e was synthesised according to general procedure C, using α-keto amide 1be (115 mg, 0.36 mmol), 1-octyne (44 µL, 0.30 mmol), purified by column chromatography (Petrol/Et₂O = 95:5) and obtained as a brown oil (80 mg, 0.20 mmol, 65%).

**1H NMR (400 MHz, CDCl₃)** δ 8.08 (1H, s, Ar-H), 7.90 (1H, d, J = 8.0 Hz, Ar-H), 7.41 – 7.33 (2H, m, Ar-H), 7.25 – 7.09 (6H, m, Ar-H), 5.34 (1H, t, J = 8.0 Hz, C=CHCH₂), 4.81 (2H, s, NCH₂), 2.29 – 2.16 (2H, m, C=CHCH₂), 1.37 – 1.25 (2H, m, CH₂CH₂CH₂CH₃), 1.25 – 1.05 (4H, m, CH₂CH₂CH₃), 0.77 (3H, t, J = 7.0 Hz, CH₃); **13C NMR (101 MHz, CDCl₃)** δ 168.3, 137.7, 137.4, 133.7, 131.8, 131.6, 130.14, 130.13, 128.7, 127.3, 127.0, 126.1, 126.0, 122.8, 117.5, 42.9, 31.3, 29.9, 27.8, 22.5, 14.1; **mp (Petrol/Et₂O):** 65 – 67 °C; **IR (cm⁻¹)** ν = 2980, 2889, 1724, 1683, 1556, 1473, 1462, 1382, 1252, 1152, 1074, 954, 790, 729, 696; **LRMS (ESI) m/z:** 410.0 [C₂₃H₂₅⁷⁹BrNO, (M+H)⁺]; **HRMS (ESI) m/z:** calcd for [C₂₃H₂₅⁷⁹BrNO, (M+H)⁺]: 410.11140; found 410.11127.

(E)-3-(1-Benzyl-5-hexylidene-2-oxo-2,5-dihydro-1H-pyrrol-3-yl)benzonitrile (4f)

![Chemical Structure](image)

Compound 4f was synthesised according to general procedure C, using α-keto amide 1bf (95 mg, 0.36 mmol), 1-octyne (44 µL, 0.30 mmol), purified by column chromatography (Petrol/Et₂O = 9:1) and obtained as a yellow solid (79 mg, 0.22 mmol, 74%).
\( ^1 \)H NMR (400 MHz, CDCl\(_3\) \( \delta 8.34 \) (1H, s, Ar-H), \( 8.25 \) (1H, d, \( J = 8.0 \) Hz, Ar-H), \( 7.59 \) (1H, d, \( J = 8.0 \) Hz, Ar-H), \( 7.54 \) – \( 7.45 \) (2H, m, Ar-H, C=CH), \( 7.36 \) – \( 7.16 \) (5H, m, Ar-H), \( 5.49 \) (1H, t, \( J = 8.0 \) Hz, C=CHCH\(_2\)), \( 4.90 \) (2H, s, NCH\(_2\)), \( 2.34 \) (2H, q, \( J = 8.0 \) Hz, C=CHCH\(_2\)), \( 1.48 \) – \( 1.34 \) (2H, m, CH\(_2\)CH\(_2\)CH\(_2\)), \( 1.29 \) – \( 1.17 \) (4H, m, CH\(_2\)CH\(_2\)CH\(_2\))); \( ^{13} \)C NMR (101 MHz, CDCl\(_3\)) \( \delta 168.1, 137.5, 137.2, 132.9, 131.8, 131.5, 131.0, 130.8, 129.4, 128.7, 127.4, 127.0, 126.7, 118.7, 118.5, 112.8, 42.9, 31.2, 29.8, 27.9, 22.5, 14.0; \( \text{mp (Petrol/Et}_2\text{O):} 72 \) – \( 74 \) °C; \( \text{IR (cm}^{-1}\text{)} \theta = 2981, 2889, 2361, 2341, 2230, 1683, 1649, 1473, 1461, 1382, 1252, 1154, 1073, 955, 803, 729, 687, 655; \( \text{LRMS (ESI)} \text{ m/z:} 357.2 \) [C\(_{24}\)H\(_{25}\)N\(_2\)O, (M+H\(^+\))] ; \( \text{HRMS (ESI)} \text{ m/z:} \text{calcd for} \ [\text{C}_{24}\text{H}_{25}\text{N}_2\text{O}, (M+H\(^+\))] : 357.19614; \text{found} 357.19608.  

(E)-1-Benzyl-5-hexylidene-3-isobutyl-1,5-dihydro-2H-pyrrol-2-one (4g) 

\[
\begin{align*}
\text{Compounds} \quad 4g \text{ were synthesised according to general procedure C, using } \alpha-\text{keto amide} \quad 1bg \\
(79 \text{ mg, } 0.36 \text{ mmol), 1-octyne (44 } \mu\text{L, } 0.30 \text{ mmol), purified by column chromatography (Petrol/Et}_2\text{O = 95:5) and obtained as a brown oil (18 mg, 0.06 mmol, 19%).}
\end{align*}
\]

\( ^1 \)H NMR (400 MHz, CDCl\(_3\)) \( \delta 7.26 \) – \( 7.11 \) (3H, m, Ar-H), \( 7.11 \) – \( 7.06 \) (2H, m, Ar-H), \( 6.82 \) (1H, s, C=CH), \( 5.13 \) (1H, t, \( J = 8.0 \) Hz, C=CHCH\(_2\)), \( 4.75 \) (2H, s, NCH\(_2\)), \( 2.23 \) (2H, d, \( J = 7.0 \) Hz, CHCH\(_2\)), \( 2.15 \) (2H, q, \( J = 8.0 \) Hz, C=CHCH\(_2\)), \( 2.00 \) – \( 1.85 \) (1H, m, CHCH\(_2\)), \( 1.34 \) – \( 1.05 \) (6H, m, CH\(_2\)CH\(_2\)CH\(_2\)), \( 0.89 \) (6H, d, \( J = 6.5 \) Hz, \( 2 \times \) CH\(_3\)), \( 0.77 \) (3H, t, \( J = 7.0 \) Hz, CH\(_3\)); \( ^{13} \)C NMR (101 MHz, CDCl\(_3\)) \( \delta 170.6, 138.3, 137.9, 136.8, 128.6, 127.2, 127.0, 126.9, 114.1, 42.9, 34.9, 31.3, 30.0, 27.50, 27.48, 22.7, 22.5, 14.1; \( \text{IR (cm}^{-1}\text{)} \theta = 2980, 2889, 2361, 2341, 1690, 1473, 1462, 1383, 1252, 1153, 1074, 954, 819, 728, 697; \( \text{LRMS (ESI)} \text{ m/z:} 312.2 \) [C\(_{21}\)H\(_{30}\)NO, (M+H\(^+\))] ; \( \text{HRMS (ESI)} \text{ m/z:} \text{calcd for} \ [\text{C}_{21}\text{H}_{30}\text{NO}, (M+H\(^+\))] : 312.23219; \text{found} 312.23163.  

S36
(E)-1-Benzyl-3-cyclopentyl-5-hexylidene-1,5-dihydro-2H-pyrrol-2-one (4h)

![Chemical Structure of 4h]

Compound 4h was synthesised according to general procedure C, using $\alpha$-keto amide 1bh (83 mg, 0.36 mmol), 1-octyne (44 µL, 0.30 mmol), purified by column chromatography (Petrol/EtOAc = 95:5) and obtained as a yellow oil (39 mg, 0.12 mmol, 40%).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.27 – 7.07 (5H, m, Ar-H), 6.78 (1H, s, C=C-H), 5.12 (1H, t, $J$ = 8.0 Hz, C=CHCH$_2$), 4.75 (2H s, NC$_2$H$_2$), 2.93 – 2.80 (1H, m, C$_{cyclopentane}$H), 2.22 – 2.08 (2H, m, C=CHC$_2$H$_2$), 2.06 – 1.91 (2H, m, C$_{cyclopentane}$H$_2$), 1.75 – 1.43 (6H, m, 2 × C$_{cyclopentane}$H$_2$, CH$_2$CH$_2$CH$_2$CH$_3$), 1.34 – 1.07 (6H, m, C$_{cyclopentane}$H$_2$, CH$_2$CH$_2$CH$_3$), 0.78 (3H, t, $J$ = 7.0 Hz, CH$_3$); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 170.2, 142.1, 138.3, 137.9, 128.6, 127.2, 127.0, 124.1, 114.0, 42.8, 37.0, 32.2, 31.3, 30.0, 27.5, 25.4, 22.6, 14.1; IR (cm$^{-1}$) $\tilde{\nu}$ = 2981, 2889, 2361, 2341, 1704, 1679, 1456, 1393, 1252, 1152, 1072, 955, 817, 700; LRMS (ESI) m/z: 324.2 [C$_{22}$H$_{30}$NO, (M+H)$^+$]; HRMS (ESI) m/z: calcd for [C$_{22}$H$_{30}$NO, (M+H)$^+$]: 324.23219; found 324.23224.

(E)-1-Benzyl-5-(cyclohexylmethylene)-3-phenyl-1,5-dihydro-2H-pyrrol-2-one (5a)

![Chemical Structure of 5a]

Compound 5a was synthesised according to general procedure C using $\alpha$-keto amide 1aa (86 mg, 0.36 mmol) and 3-cyclohexyl-1-propyne (43 µL, 0.30 mmol), purified by column chromatography (Petrol/Et$_2$O = 9:1) and obtained as a yellow oil (52 mg, 0.15 mmol, 50%).
\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta \) 8.06 – 7.98 (2H, m, Ar-H), 7.45 – 7.39 (3H, m, 2 × Ar-H, C=CH), 7.38 – 7.27 (3H, m, Ar-H), 7.25 – 7.20 (3H, m, Ar-H), 5.27 (1H, d, \(J = 10.0 \) Hz, C=CHCH), 4.90 (2H, s, NCH\(_2\)), 2.57 – 2.43 (1H, m, C=CHCH), 1.78 – 1.61 (5H, m, 2 × CH\(_2\), CH\(_3\)H\(_3\)), 1.40 – 1.24 (2H, m, CH\(_2\)), 1.24 – 1.05 (3H, m, CH\(_2\), CH\(_3\)H\(_3\)); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta \) 168.9, 137.6, 136.7, 133.5, 128.8, 128.70, 128.65, 127.4, 127.3, 127.1, 125.5, 122.0, 42.9, 37.3, 34.1, 25.8, 25.7; IR (cm\(^{-1}\)) \(\tilde{\nu} = \) 2981, 2889, 1685, 1473, 1462, 1383, 1252, 1153, 1073, 954, 816, 695; LRMS (ESI) m/z: 344.2 [C\(_{24}\)H\(_{26}\)NO, (M+H\(^+\)]\); HRMS (ESI) m/z: calcd for [C\(_{22}\)H\(_{24}\)NO, (M+H\(^+\)]: 344.20089; found 344.20094.

1-Benzyl-5-cyclohexylidene-3-phenyl-1,5-dihydro-2H-pyrrol-2-one (5b)

**Compound 5b** was synthesised according to general procedure C using \(\alpha\)-keto amide 1aa (86 mg, 0.36 mmol) and cyclohexylacetylene (39 \(\mu\)L, 0.30 mmol), purified by column chromatography (Petrol/EtOAc = 95:5) and obtained as a yellow solid (45 mg, 0.14 mmol, 46%).

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta \) 8.06 – 8.00 (2H, m, Ar-H), 7.63 (1H, s, C=CH), 7.46 – 7.38 (2H, m, Ar-H), 7.37 – 7.28 (3H, m, Ar-H), 7.27 – 7.18 (1H, m, Ar-H), 7.12 (2H, d, \(J = 7.5 \) Hz, Ar-H), 5.18 (2H, s, CH\(_2\)), 2.53 – 2.45 (2H, m, CH\(_2\)), 2.44 – 2.34 (2H, m, CH\(_2\)), 1.70 – 1.60 (2H, m, CH\(_2\)), 1.59 – 1.48 (2H, m, CH\(_2\)), 1.31 – 1.19 (2H, m, CH\(_2\)); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta \) 170.9, 138.4, 132.6, 132.1, 131.8, 130.3, 128.7, 128.6, 128.3, 128.2, 127.2, 126.9, 126.0, 45.9, 33.0, 31.0, 28.1, 28.0, 26.5; mp (Petrol/Et\(_2\)O): 117 – 119 °C; IR (cm\(^{-1}\)) \(\tilde{\nu} = \) 2981, 2930, 2889, 2854, 2361, 2341, 1673, 1492, 1449, 1381, 1352, 1327, 1251, 1224, 1168, 1074, 1028, 997, 947, 892, 854, 787, 749, 725, 694, 652; LRMS (ESI) m/z: 330.2 [C\(_{23}\)H\(_{26}\)NO, (M+H\(^+\)]\); HRMS (ESI) m/z: calcd for [C\(_{22}\)H\(_{24}\)NO, (M+H\(^+\)]: 330.18524; found 330.18503.
1-Benzyl-5-cyclopentylidene-3-phenyl-1,5-dihydro-2H-pyrrol-2-one (5c)

![Chemical structure of 5c](image)

Compound 5c was synthesised according to general procedure C using α-keto amide 1aa (86 mg, 0.36 mmol) and cyclopentylacetylene (35 µL, 0.30 mmol), purified by column chromatography (Petrol/Acetone = 95:5) and obtained as a white solid (46 mg, 0.15 mmol, 48%).

$^1$H NMR (400 MHz, CDCl$_3$) δ 8.03 (2H, d, $J = 7.0$ Hz, Ar-H), 7.46 – 7.18 (7H, m, Ar-H), 7.13 (2H, d, $J = 7.0$ Hz, Ar-H), 5.13 (2H, s, NCH$_2$), 2.72 (2H, tp, $J = 5.0$, 2.0 Hz, CH$_2$), 2.51 (2H, tp, $J = 5.0$, 2.0 Hz, CH$_2$), 1.75 – 1.61 (4H, m, 2 × CH$_2$); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 169.9, 138.8, 133.9, 132.2, 131.7, 130.5, 128.8, 128.7, 128.6, 128.4, 127.2, 127.0, 125.9, 44.4, 33.0, 30.9, 27.2, 25.8; mp (Petrol/Et$_2$O): 143 – 146 °C; IR (cm$^{-1}$) $\tilde{\nu}$ = 2981, 2888, 2361, 2341, 1674, 1490, 1473, 1462, 1383, 1252, 1152, 1073, 954, 816, 787, 748, 725, 694, 669, 652; LRMS (ESI) m/z: 316.2 [C$_{22}$H$_{22}$NO, (M+H)$^+$]; HRMS (ESI) m/z: calcd for [C$_{22}$H$_{22}$NO, (M+H)$^+$]: 316.16959; found 316.16968.

(E)-1-Benzyl-5-(3-methylbutylidene)-3-phenyl-1,5-dihydro-2H-pyrrol-2-one (5d)

![Chemical structure of 5d](image)

Compound 5d was synthesised according to general procedure C using α-keto amide 1aa (86 mg, 0.36 mmol) and 5-methyl-1-hexyne (40 µL, 0.30 mmol), purified by column chromatography (Petrol/Et$_2$O = 95:5) and obtained as a yellow solid (52 mg, 0.16 mmol, 55%).
$^1$H NMR (400 MHz, CDCl$_3$) δ 8.02 (2H, d, $J = 7.0$ Hz, Ar-$H$), 7.45 – 7.40 (3H, m, Ar-$H$), 7.37 – 7.28 (3H, m, 2 × Ar-$H$, C=CH), 7.26 – 7.20 (3H, m, 2 × Ar-$H$, C=C=CH$_2$), 5.39 (1H, t, $J = 8.5$ Hz, C=C=CH$_2$), 4.93 (2H, s, NC$_2$H$_2$), 2.22 (2H, dd, $J = 8.5$, 7.0 Hz, C=CHCH$_2$), 1.73 – 1.59 (1H, m, CH(CH$_3$)$_2$), 0.84 (6H, d, $J = 7.0$ Hz, 2 × CH$_3$); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 168.9, 138.5, 137.6, 133.5, 131.8, 128.8, 128.71, 128.67, 127.5, 127.3, 127.0, 125.4, 115.2, 43.0, 36.7, 29.4, 22.3; mp (Petrol/Et$_2$O): 81 – 82 °C; IR (cm$^{-1}$) $\tilde{\nu}$ = 2981, 2889, 2361, 2341, 1683, 1648, 1490, 1462, 1383, 1296, 1153, 1073, 953, 854, 786, 749, 730, 694, 649; LRMS (ESI) m/z: 318.2 [C$_{22}$H$_{24}$NO, (M+H)$^+$]; HRMS (ESI) m/z: calcd for [C$_{22}$H$_{24}$NO, (M+H)$^+$]: 318.18524; found 318.18530.

(E)-1-Benzyl-3-phenyl-5-(2-phenylethylidene)-1,5-dihydro-2H-pyrrol-2-one (5e)

Compound 5e was synthesised according to general procedure C using $\alpha$-keto amide 1aa (86 mg, 0.36 mmol) and 4-phenyl-1-butyne (42 µL, 0.30 mmol), purified by column chromatography (Petrol/EtOAc = 95:5) and obtained as an off-white solid (48 mg, 0.14 mmol, 46%).

$^1$H NMR (400 MHz, CDCl$_3$) δ 8.01 (2H, d, $J = 7.0$ Hz, Ar-$H$), 7.50 (1H, s, Ar-$H$), 7.42 (2H, t, $J = 7.0$ Hz, Ar-$H$), 7.38 – 7.33 (1H, m, Ar-$H$), 7.31 – 7.18 (8H, m, Ar-$H$), 7.06 (2H, d, $J = 7.0$ Hz, Ar-$H$), 5.52 (1H, t, $J = 8.5$ Hz, CHCH$_2$), 4.92 (2H, s, CH$_2$), 3.67 (2H, d, $J = 8.5$ Hz, CHCH$_2$); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 169.0, 139.4, 138.7, 137.5, 134.3, 131.6, 129.1, 128.8, 128.7, 128.4, 127.5, 127.4, 127.1, 126.7, 125.1, 113.4, 43.0, 33.6; mp (Petrol/EtOAc): 116 – 118 °C; IR (cm$^{-1}$) $\tilde{\nu}$ = 3085, 3062, 3029, 2918, 2850, 2359, 2324, 2166, 2038, 1979, 1683, 1648, 1603, 1585, 1524, 1494, 1453, 1435, 1412, 1384, 1345, 1298, 1279, 1239, 1172, 1128, 1098, 1075, 1029, 1001, 974, 947, 906, 856, 786, 729, 695, 649, 609; LRMS (ESI) m/z: 352.2 [C$_{25}$H$_{22}$NO, (M+H)$^+$]; HRMS (ESI) m/z: calcd for [C$_{25}$H$_{22}$NO, (M+H)$^+$]: 352.16959; found 352.16971.
**Compound 5f** was synthesised according to general procedure C using α-keto amide 1ab (109 mg, 0.36 mmol) and hex-5-yenenitrile (32 µL, 0.30 mmol), purified by column chromatography (Petrol/EtOAc = 7:3) and obtained as a yellow solid (31 mg, 0.08 mmol, 27%).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.95 (2H, d, $J = 8.5$ Hz, Ar-H), 7.84 – 7.74 (2H, m, Ar-H), 7.54 (1H, s, C=CH), 7.39 – 7.34 (3H, m, Ar-H), 7.34 – 7.30 (2H, m, Ar-H), 6.80 (1H, t, $J = 8.5$ Hz, C=CHCH$_2$), 2.85 – 2.74 (2H, m, C=CHCH$_2$), 2.63 (2H, t, $J = 7.0$ Hz, CH$_2$CN), 2.40 (3H, s, CH$_3$); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 166.7, 145.6, 136.8, 135.5, 132.9, 129.94, 129.90, 129.5, 129.0, 128.8, 128.1, 127.6, 118.6, 115.7, 24.5, 21.8, 18.1; mp (Petrol/EtOAc): 120 – 122 °C; IR (cm$^{-1}$) $\tilde{\nu}$ = 3090, 2981, 2929, 2889, 2361, 2341, 2246, 1725, 1540, 1492, 1389, 1364, 1307, 1190, 1176, 1135, 1092, 1006, 994, 814, 785, 692, 660; LRMS (ESI) m/z: 379.1 [C$_{21}$H$_{19}$N$_2$O$_3$S, (M+H)$^+$]; HRMS (ESI) m/z: calcd for [C$_{21}$H$_{19}$N$_2$O$_3$S, (M+H)$^+$]: 379.11109; found 379.11096.

**(E)-5-(4-chlorobutylidene)-3-phenyl-1-tosyl-1,5-dihydro-2H-pyrrol-2-one (5g)**

S41
Compound 5g was synthesised according to general procedure C using α-keto amide 1ab (109 mg, 0.36 mmol) and 6-chlorohex-1-yne (36 µL, 0.30 mmol), purified by column chromatography (Petrol/Et₂O = 4:1) and obtained as a light yellow oil (30 mg, 0.07 mmol, 25%).

$^{1}$H NMR (400 MHz, CDCl₃) δ 7.94 (2H, d, J = 8.5 Hz, Ar-H), 7.86 – 7.76 (2H, m, Ar-H), 7.63 (1H, s, C=C), 7.42 – 7.26 (5H, m, Ar-H), 6.80 (1H, t, J = 8.5 Hz, C=CH₂), 3.60 (2H, t, J = 6.0 Hz, C₂H₂Cl), 2.64 (2H, dt, J = 8.5, 7.0 Hz, C=CH₂), 2.41 (3H, s, CH₃), 2.10 – 1.97 (2H, m, CH₂CH₂Cl); $^{13}$C NMR (101 MHz, CDCl₃) δ 166.8, 145.3, 135.8, 135.6, 131.9, 129.8, 129.75, 129.73, 129.5, 128.7, 128.0, 127.3, 119.6, 44.0, 32.0, 25.2, 21.70 (d); IR (cm⁻¹) ν = 2981, 2889, 2361, 2341, 1723, 1492, 1473, 1387, 1366, 1306, 1250, 1188, 1175, 1135, 1092, 1006, 994, 870, 785, 750, 711, 692, 660; LRMS (ESI) m/z: 402.1 [C₂₁H₂₁ClNO₅S, (M+H)⁺]; HRMS (ESI) m/z: calcd for [C₂₁H₂₁ClNO₅S, (M+H)⁺]: 402.09252; found 402.09244.

(E)-2-(4-(4-(3-nitrophenyl)-5-oxo-1-tosyl-1,5-dihydro-2H-pyrrol-2-ylidene)butyl)isoindoline-1,3-dione (5h)

Compound 5h was synthesised according to general procedure C using α-keto amide 1bg (125 mg, 0.36 mmol) and N-(5-hexynyl)phthalimide (68 mg, 0.30 mmol), purified by column chromatography (Petrol/Et₂OAc = 1:1) and obtained as a white solid (135 mg, 0.24 mmol, 81%).

$^{1}$H NMR (400 MHz, CDCl₃) δ 8.67 (1H, t, J = 2.0 Hz, Ar-H), 8.27 – 8.23 (1H, m, Ar-H), 8.20 – 8.16 (1H, m, Ar-H), 7.99 – 7.91 (2H, m, Ar-H), 7.86 – 7.84 (2H, m, Ar-H), 7.80 (1H, s, Ar-
$H$, 7.74 – 7.22 (2H, m, Ar-\(H\)), 7.56 (1H, t, \(J = 8.0\) Hz, Ar-\(H\)), 7.33 (1H, d, \(J = 8.0\) Hz, Ar-\(H\)), 6.95 (1H, t, \(J = 8.2\) Hz, C=CHCH\(_2\)), 3.79 (2H, t, \(J = 7.0\) Hz, CH\(_2\)N), 2.60 – 2.48 (2H, m, C=CHCH\(_2\)), 2.41 (3H, s, CH\(_3\)), 2.02 (2H, p, \(J = 7.0\) Hz, C=CHCH\(_2\)CH\(_2\)); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 168.6, 166.2, 148.5, 145.6, 135.6, 134.9, 134.3, 133.3, 132.1, 131.9, 131.7, 130.0, 129.9, 129.4, 128.2, 123.9, 123.5, 123.1, 122.3, 37.3, 28.7, 26.2, 21.9; IR (cm\(^{-1}\)) \(\tilde{\nu}\) = 3660, 2981, 2888, 2361, 2341, 1770, 1709, 1529, 1395, 1351, 1251, 1152, 1090, 1023, 955, 893, 774, 720, 699; LRM (ESI) m/z: 580.2 [C\(_{29}\)H\(_{23}\)NaN\(_3\)O\(_7\)S, (M+H)]\(^{+}\); HRMS (ESI) m/z: calcd for [C\(_{29}\)H\(_{23}\)NaN\(_3\)O\(_7\)S, (M+H)]\(^{+}\): 580.11489; found 580.11481.
V. Gram-scale Synthesis of Pyrrolinone 3b

Commercially purchased 1-octyne was purified prior to use by distillation. α-Keto amide 1ab was synthesised and purified as before. An oven-dried round bottom flask (100 mL) was charged with N-tosyl-2-oxo-2-phenylacetamide 1ab (1.31 g, 4.32 mmol, 1.2 equiv.) and [Cu(MeCN)₄]BF₄ (113 mg, 0.36 mmol, 0.10 equiv.). The flask was then evacuated under vacuum and back-filled with nitrogen three times. Degassed dry toluene (6 mL) and degassed 1-octyne (531 µL, 3.6 mmol, 1.0 equiv.) were added subsequently under nitrogen atmosphere, and the mixture was refluxed at 130 °C for 20 h under nitrogen. It was then cooled to room temperature, filtered through silica (washed down with CH₂Cl₂), concentrated in vacuo, and purified by column chromatography (5% Et₂O/Petrol to 10% Et₂O/Petrol) to give pyrrolinone 3b (1.18 g, 83%) as a yellow oil. The data is consistent as obtained for the small-scale reaction.
VI. References


N-Benzyl-2-oxo-2-phenylacetamide (1a)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
N-Tosyl-2-oxo-2-phenylacetamide (1b)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
$N$-((4-Methoxyphenyl)sulfonyl)-2-oxo-2-phenylacetamide (1c)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
$N$-((4-Cyanophenyl)sulfonyl)-2-oxo-2-phenylacetamide (1d)

$^1$H NMR (400 MHz, $d_6$-acetone)

$^{13}$C NMR (101 MHz, $d_6$-acetone)
$N$-((4-(Trifluoromethyl)phenyl)sulfonyl)-2-oxo-2-phenylacetamide (1e)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
N-((4-Nitrophenyl)sulfonyl)-2-oxo-2-phenylacetamide (1f)

\[ \text{H NMR (400 MHz, CDCl}_3) \]

\[ \text{C NMR (101 MHz, CDCl}_3) \]
$N$-(Methylsulfonyl)-2-oxo-2-phenylacetamide (1g)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
N-Hexyl-2-oxo-2-phenylacetamide (1h)

$\text{\textsuperscript{1}H NMR (400 MHz, CDCl}_3\text{)}$

$\text{\textsuperscript{13}C NMR (101 MHz, CDCl}_3\text{)}$
$N$-Cyclopropyl-2-oxo-2-phenylacetamide (1i)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
N-Cyclohexyl-2-oxo-2-phenylacetamide (1j)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
$N$-(Cyclopropylmethyl)-2-oxo-2-phenylacetamide (1k)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)

S56
$N$-(Cyclohexylmethyl)-2-oxo-2-phenylacetamide (11)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
\[ \text{N-(Thiophen-2-ylmethyl)-2-oxo-2-phenylacetamide (1m)} \]

\[ ^1H\text{ NMR (400 MHz, CDCl}_3) \]

\[ ^13C\text{ NMR (101 MHz, CDCl}_3) \]
$N$-Allyl-2-oxo-2-phenylacetamide (1n)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)

S59
$N$-Phenyl-2-oxo-2-phenylacetamide (1o)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)

S60
$N$-Benzy1-2-oxo-2-($p$-tolyl)acetamide (1p)

$^1$H NMR (400 MHz, CDCl$_3$)

$^1$C NMR (101 MHz, CDCl$_3$)
$N$-Benzyl-2-oxo-2-(3-methoxyphenyl)acetamide (1q)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)

S62
$N$-Benzyl-2-oxo-2-(4-(trifluoromethyl)phenyl)acetamide (1r)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
N-Benzyl-2-oxo-2-(3-nitrophenyl)acetamide (1s)

^1H NMR (400 MHz, CDCl₃)

^13C NMR (101 MHz, CDCl₃)
$N$-Benzyl-2-oxo-2-(3-bromophenyl)acetamide (1t)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
$N$-Benzyl-2-oxo-2-(3-cyanophenyl)acetamide (1u)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
N-Benzyl-4-methyl-2-oxopentanamide (1v)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
$N$-Benzyl-2-cyclopentyl-2-oxoacetamide (1w)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
N-Tosyl-2-(3-nitrophenyl)-2-oxo-acetamide (1x)

$^1$H NMR (400 MHz, $d_6$-DMSO)

$^{13}$C NMR (101 MHz, $d_6$-DMSO)
(E)-1-Benzyl-5-hexylidene-3-phenyl-1,5-dihydro-2H-pyrrol-2-one (3a)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
(E)-5-Hexylidene-3-phenyl-1-tosyl-1,5-dihydro-2H-pyrrol-2-one (3b)

\[ \text{Me} \]
\[ \text{O=S=O} \]
\[ \text{O} \]
\[ \text{N} \]
\[ \text{Me} \]

\[^1H\text{ NMR (400 MHz, CDCl}_3\text{)}\]

\[^{13}\text{C NMR (101 MHz, CDCl}_3\text{)}\]
(E)-5-Hexylidene-1-((4-methoxyphenyl)sulfonyl)-3-phenyl-1,5-dihydro-2H-pyrrol-2-one (3c)

\[\text{\textsuperscript{1}H NMR (400 MHz, CDCl}_3\text{)}\]

\[\text{\textsuperscript{13}C NMR (101 MHz, CDCl}_3\text{)}\]
(E)-5-Hexylidene-1-((4-cyano)sulfonyl)-3-phenyl-1,5-dihydro-2H-pyrrol-2-one (3d)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)

S73
(E)-5-Hexylidene-3-phenyl-1-(((4-(trifluoromethyl)phenyl)sulfonyl)-1,5-dihydro-2H-pyrrol-2-one (3e)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
\[(E)-5\text{-Hexylidene-1-((4-nitrophenyl)sulfonyl)-3-phenyl-1,5-dihydro-2H-pyrrol-2-one (3f)}\]

\[
\begin{align*}
\text{\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3})} \\
\text{\textsuperscript{13}C NMR (101 MHz, CDCl\textsubscript{3})}
\end{align*}
\]
*(E)-5-Hexylidene-1-(methylsulfonyl)-3-phenyl-1,5-dihydro-2H-pyrrol-2-one (3g)*

\[
\begin{align*}
\text{Me} & \quad \text{O=S=O} \\
\text{O} &= \text{N} \\
\text{Me} & \quad \text{O=S=O}
\end{align*}
\]

\[\text{\(\text{H NMR (400 MHz, CDCl}_3\)}\]

\[\text{\(\text{13C NMR (101 MHz, CDCl}_3\)}\]
(E)-1-Hexyl-5-hexylidene-3-phenyl-1,5-dihydro-2H-pyrrol-2-one (3h)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
(E)-1-Cyclopropyl-5-hexylidene-3-phenyl-1,5-dihydro-2H-pyrrol-2-one (3i)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
(E)-1-Cyclohexyl-5-hexylidene-3-phenyl-1,5-dihydro-2H-pyrrol-2-one (3j)

$^{1}$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
(E)-1-(Cyclopropylmethyl)-5-hexylidene-3-phenyl-1,5-dihydro-2H-pyrrol-2-one (3k)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
(E)-1-(Cyclohexylmethyl)-5-hexylidene-3-phenyl-1,5-dihydro-2H-pyrrolo-2-one (3l)

$^{1}H$ NMR (400 MHz, CDCl₃)

$^{13}C$ NMR (101 MHz, CDCl₃)
(E)-5-Hexylidene-3-phenyl-1-(thiophen-2-ylmethyl)-1,5-dihydro-2H-pyrrol-2-one (3m)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
(E)-1-Allyl-5-hexylidene-3-phenyl-1,5-dihydro-2H-pyrrol-2-one (3n)

1H NMR (400 MHz, CDCl3)

13C NMR (101 MHz, CDCl3)
(E)-5-Hexylidene-1,3-diphenyl-1,5-dihydro-2H-pyrrol-2-one and (Z)-5-Hexylidene-1,3-diphenyl-1,5-dihydro-2H-pyrrol-2-one (3o)

$\text{H NMR (400 MHz, CDCl}_3$)

$\text{C NMR (101 MHz, CDCl}_3$)
(E)-1-Benzyl-5-hexylidene-3-(p-tolyl)-1,5-dihydro-2H-pyrrol-2-one (4a)

\[
\text{O=NN=C} \begin{array}{l}
\text{Me} \\
\text{O} \\
\text{Me}
\end{array}
\]

\(^1\text{H NMR (400 MHz, CDCl}_3\))

\(^{13}\text{C NMR (101 MHz, CDCl}_3\))
(E)-1-Benzyl-5-hexylidene-3-(3-methoxyphenyl)-1,5-dihydro-2H-pyrrol-2-one (4b)

1H NMR (400 MHz, CDCl₃)

13C NMR (101 MHz, CDCl₃)
(E)-1-Benzyl-5-hexylidene-3-(4-(trifluoromethyl)phenyl)-1,5-dihydro-2H-pyrrol-2-one (4c)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
(E)-1-Benzyl-5-hexylidene-3-(3-nitrophenyl)-1,5-dihydro-2H-pyrrol-2-one (4d)

\[\text{\textbf{1H NMR (400 MHz, CDCl3)}}\]

\[\text{\textbf{13C NMR (101 MHz, CDCl3)}}\]
(E)-1-Benzyl-3-(3-bromophenyl)-5-hexylidene-1,5-dihydro-2H-pyrrol-2-one (4e)

\[ \text{Chemical Structure Image} \]

\[ ^1H \text{ NMR (400 MHz, CDCl}_3) \]

\[ ^13C \text{ NMR (101 MHz, CDCl}_3) \]
(E)-3-(1-Benzyl-5-hexylidene-2-oxo-2,5-dihydro-1H-pyrrol-3-yl)benzonitrile (4f)

$\text{H NMR (400 MHz, CDCl}_3$)

$\text{C NMR (101 MHz, CDCl}_3$)
(E)-1-Benzyl-5-hexylidene-3-isobutyl-1,5-dihydro-2H-pyrrol-2-one (4g)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
(E)-1-Benzyl-3-cyclopentyl-5-hexylidene-1,5-dihydro-2H-pyrrol-2-one (4h)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
(E)-1-Benzyl-5-(cyclohexylmethylene)-3-phenyl-1,5-dihydro-2H-pyrrol-2-one (5a)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
1-Benzyl-5-cyclohexylidene-3-phenyl-1,5-dihydro-2H-pyrrol-2-one (5b)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
1-Benzyl-5-cyclopentylidene-3-phenyl-1,5-dihydro-2H-pyrrol-2-one (5c)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
(E)-1-Benzyl-5-(3-methylbutyldiene)-3-phenyl-1,5-dihydro-2H-pyrrol-2-one (5d)

$^{1}$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
(E)-1-Benzyl-3-phenyl-5-(2-phenylethylidene)-1,5-dihydro-2H-pyrrol-2-one (5e)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
(E)-4-(5-oxo-4-phenyl-1-tosyl-1,5-dihydro-2H-pyrrol-2-ylidene)butanenitrile (5f)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
(E)-5-(4-chlorobutylidene)-3-phenyl-1-tosyl-1,5-dihydro-2H-pyrrol-2-one (5g)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
(E)-2-(4-(4-(3-nitrophenyl)-5-oxo-1-tosyl-1,5-dihydro-2H-pyrrol-2-ylidene)butyl)isoindoline-1,3-dione (5h)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)