Supporting Information

Chemoselective $\alpha,\beta$-Dehydrogenation of Saturated Amides
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# Table of Contents

1. **General Information** ........................................................................................................... 2
2. **Optimization** ................................................................................................................... 3
3. **Amides** ........................................................................................................................... 6
   3.1. Synthesis of Amides ......................................................................................................... 6
   3.2. Characterization ............................................................................................................... 7
4. **Products of desaturation** ................................................................................................. 17
   4.1. General Procedure C ...................................................................................................... 17
   4.2. Characterization ............................................................................................................. 18
   4.3. Application of our methodology ..................................................................................... 32
      4.3.1. Dihydroxylation ...................................................................................................... 32
      4.3.2. Enantioselective Michael addition ........................................................................... 32
      4.3.3. Synthesis of piperine ............................................................................................... 35
5. **Labelling experiments** ...................................................................................................... 37
6. **References** ...................................................................................................................... 38
7. **Spectra** ............................................................................................................................ 39
1. General Information

Unless otherwise stated, all glassware was flame-dried before use and all reactions were performed under an atmosphere of argon. All solvents were distilled from appropriate drying agents prior to use. Triflic anhydride was distilled over P₄O₁₀ prior to use. All other reagents were used as received from commercial suppliers unless otherwise stated. Reaction progress was monitored by thin layer chromatography (TLC) performed on aluminium plates coated with silica gel F₂₅₄ with 0.2 mm thickness. Chromatograms were visualized by fluorescence quenching with UV light at 254 nm or by staining using potassium permanganate or phosphomolybdic acid. Flash column chromatography was performed using silica gel 60 (230-400 mesh, Merck and co.). Neat infra-red spectra were recorded using a Perkin-Elmer Spectrum 100 FT-IR spectrometer. Wavenumbers (ν_max) are reported in cm⁻¹. Mass spectra were obtained using a Finnigan MAT 8200 or (70 eV) or an Agilent 5973 (70 eV) spectrometer, using electrospray ionization (ESI). All ¹H NMR, ¹³C NMR and ⁷⁷Se NMR spectra were recorded using a Bruker AV-400 or AV-600 spectrometer at 300K. Chemical shifts were given in parts per million (ppm, δ), referenced to the solvent peak of CDCl₃, defined at δ = 7.26 ppm (¹H NMR) and δ = 77.16 (¹³C NMR). Coupling constants are quoted in Hz (J). ¹H NMR splitting patterns were designated as singlet (s), doublet (d), triplet (t), quartet (q), pentet (p). Splitting patterns that could not be interpreted or easily visualized were designated as multiplet (m) or broad (br). Selected ¹³C NMR spectra were recorded using the attached proton test (APT) to facilitate the confirmation and assignment of the structure.
### 2. Optimization

\[
\begin{array}{cccccccc}
\text{Entry} & \text{Solvent 1} & [\text{Se}] & \text{Base} & \text{Oxidant/Add.} & \text{Solvent 2} & T \degree\text{C} & 1a^* & 4a^* \\
1 & DCE (2 mL) & \text{PhSeO}_2\text{H} & \text{Ag}_2\text{CO}_3 & - & \text{DCE (1 mL)} & \text{r.t.} & 15 & 40 & 15 & ND \\
2 & DCE (2 mL) & \text{PhSeO}_2\text{H} & \text{Ag}_2\text{CO}_3 & - & \text{DCE (1 mL)} & \text{r.t.} & 15 & 48 & 20 & ND \\
3 & DCE (2 mL) & \text{PhSeO}_2\text{H} & \text{Co}_2(\text{O})_2 & - & \text{DCE (1 mL)} & \text{r.t.} & 30 & 20 & 0 & 62 \\
4 & DCE (2 mL) & \text{PhSeO}_2\text{H} & \text{CaCO}_3 & - & \text{DCE (1 mL)} & \text{r.t.} & 38 & 0 & 29 & 0 \\
5 & DCE (2 mL) & \text{PhSeO}_2\text{H} & \text{AgClO}_3 & - & \text{DCE (1 mL)} & \text{r.t.} & 30 & 44 & 0 & 27 \\
6 & DCE (2 mL) & \text{PhSeO}_2\text{H} & \text{AgF} & - & \text{DCE (1 mL)} & \text{r.t.} & 25 & 27 & 26 & 19 \\
7 & DCE (2 mL) & \text{PhSeO}_2\text{H} & \text{Proton sponge} & - & \text{DCE (1 mL)} & \text{r.t.} & 16 & \text{traces} & 0 & 28 \\
8 & DCE (2 mL) & \text{PhSeO}_2\text{H} & \text{DBU} & - & \text{DCE (1 mL)} & \text{r.t.} & 15 & 0 & 27 & 50 \\
9 & DCE (2 mL) & \text{PhSeO}_2\text{H} & \text{NHEt} & - & \text{DCE (1 mL)} & \text{r.t.} & 14 & 0 & 24 & 50 \\
10 & DCE (2 mL) & \text{PhSeO}_2\text{H} & \text{DIPA} & - & \text{DCE (1 mL)} & \text{r.t.} & 14 & 0 & 25 & 50 \\
11 & DCE (2 mL) & \text{PhSeO}_2\text{H} & \text{NHEt} & - & \text{DCE (1 mL)} & \text{r.t.} & 12 & 10 & 10 & ND \\
12 & DCE (2 mL) & \text{PhSeO}_2\text{H} & \text{NHEt} & - & \text{DCE (1 mL)} & \text{r.t.} & 17 & 10 & 15 & ND \\
13 & DCE (2 mL) & \text{PhSeO}_2\text{H} & \text{NHEt} & - & \text{DCE (1 mL)} & \text{r.t.} & 25 & 22 & 12 & ND \\
14 & DCE (2 mL) & \text{PhSeO}_2\text{H} & \text{NHEt} & - & \text{DCE (1 mL)} & \text{r.t.} & 100 & 0 & 0 & 0 \\
15 & DCE (2 mL) & \text{PhSeO}_2\text{H} & \text{NHEt} & - & \text{DCE (1 mL)} & \text{r.t.} & 25 & 0 & 40 & ND \\
16 & DCM (2 mL) & \text{PhSeO}_2\text{H} & \text{NHEt} & - & \text{DCE (1 mL)} & \text{r.t.} & 60 & 0 & 18 & ND \\
17 & DCM (2 mL) & \text{PhSeO}_2\text{H} & \text{NHEt} & - & \text{DCE (1 mL)} & \text{r.t.} & 12 & 59 & 0 & 0 \\
18 & DCM (2 mL) & \text{PhSeO}_2\text{H} & \text{NHEt} & - & \text{DCE (1 mL)} & \text{r.t.} & 11 & 0 & 54 & ND \\
19 & DCM (2 mL) & \text{PhSeO}_2\text{H} & \text{NHEt} & - & \text{DCE (1 mL)} & \text{r.t.} & 11 & 42 & 0 & 0 \\
20 & DCM (2 mL) & \text{PhSeO}_2\text{H} & \text{NHEt} & - & \text{DCE (1 mL)} & \text{r.t.} & 10 & 61 & 2 & ND \\
21 & DCM (2 mL) & \text{PhSeO}_2\text{H} & \text{NHEt} & - & \text{DCE (1 mL)} & \text{r.t.} & 10 & 27 & 0 & ND \\
\end{array}
\]
| Entry | Solvent (mL) | Reagent | MeSoSeH (eq.) | DMP (eq.) | DCM (mL) | Temp | Yield | MeSoSeSePh (eq.) | MeCN (mL) | Temp | Yield |
|-------|-------------|---------|---------------|---------|----------|-------|-------|------------------|-----------|-------|-------|
| 22    | DCM (2 mL)  | PhSeO₂H (1 eq.) | NEt₃ (1.1 eq.) | DMP (1.1 eq.) | DCM (1 mL) | r.t. | 7    | 39               | 12        | ND    |
| 23    | DCM (2 mL)  | PhSeO₂H (1 eq.) | NEt₃ (2.2 eq.) | DMP (1.1 eq.) | DCM (1 mL) | r.t. | 10   | 55               | 5         | ND    |
| 24    | DCM (2 mL)  | PhSeO₂H (1 eq.) | NEt₃ (2.2 eq.) | DMP (2.2 eq.) | DCM (1 mL) | r.t. | 50   | 8                | 2         | ND    |
| 25    | DCM (2 mL)  | PhSeSePh (0.5 eq.) | NEt₃ (4.0 eq.) | DMP (4 eq.) | MeCN (1 mL) | r.t. | 15   | 0                | 0         | ND    |
| 26    | DCM (2 mL)  | PhSeO₂H (3 eq.) | -              | -         | -        | r.t. | 25   | 0                | 38        | 0     |
| 27    | DCM (2 mL)  | PhSeO₂H (1.1 eq.) | NEt₃ (1.1 eq.) | TEMPO (1.1 eq.) | DCM (1 mL) | r.t. | messy |
| 28    | DCM (2 mL)  | PhSeO₂H (1.1 eq.) | NEt₃ (1.1 eq.) | PIFA (1 eq.) | DCM (1 mL) | r.t. | 18   | 30               | n.d.     |
| 29    | DCM (2 mL)  | PhSeO₂H (1.1 eq.) | NEt₃ (1.1 eq.) | TBAIO₂ (1.1 eq.) | DCM (1 mL) | r.t. | 9    | 28               | 27        |
| 30    | DCM (2 mL)  | PhSeO₂H (1 eq.) | NEt₃ (2.2 eq.) | DMP (2.2 eq.) | DCM (1 mL) | r.t. | 16   | 62               | 10 <19%   |
| 31    | DCM (2 mL)  | PhSeO₂H (1 eq.) | NEt₃ (2.2 eq.) | DMP (2.2 eq.) | DCM (1 mL) | r.t. | 15   | 63               | 8         |
| 32    | DCM (2 mL)  | PhSeO₂H (1 eq.) | NEt₃ (2.2 eq.) | IBX (2.2 eq.) | DCM (1 mL) | r.t. | 21   | 29               | 45        |
| 33    | DCM (2 mL)  | PhSeO₂H (1 eq.) | NEt₃ (2.2 eq.) | DMP (2.2 eq.) | DCM (1 mL) | r.t. | 15   | 50               | 13        |
| 34    | DCM (4 mL)  | PhSeO₂H (1 eq.) | NEt₃ (2.2 eq.) | DMP (2.2 eq.) | DCM (2 mL) | r.t. | 17   | 66               | 11        |
| 35    | DCM (2 mL)  | PhSeO₂H (1 eq.) | NEt₃ (2.2 eq.) | DMP (3 eq.) | DCM (1 mL) | r.t. | 17   | 69               | -         |
| 36b   | DCE (2 mL)  | PhSeO₂H (1 eq.) | NEt₃ (2.2 eq.) | DMP (2.2 eq.) | DCM (1 mL) | r.t. | 45   | 21               | -         |
| 37c   | DCM (2 mL)  | PhSeO₂H (1 eq.) | NEt₃ (2.2 eq.) | DMP (2.2 eq.) | DCM (1 mL) | r.t. | 28   | 22               | -         |
| 38    | DCM (2 mL)  | MeSeO₂H (1 eq.) | NEt₃ (2.2 eq.) | DMP (2.2 eq.) | DCM (1 mL) | r.t. | 20   | 21               | -         |
| 39    | DCM (4 mL)  | PhSeO₂H (1 eq.) | 2.6-lutidine (2.2 eq.) | DMP (3 eq.) | DCM (2 mL) | r.t. | 22   | 59               | 4         |
| 40    | DCM (4 mL)  | PhSeO₂H (1 eq.) | NEt₃ (2.2 eq.) | DMP (3 eq.) | DCM (2 mL) | r.t. | 23   | 65               | -         |
| 41    | CH₃CN (4 mL) | PhSeO₂H (1 eq.) | NEt₃ (2.2 eq.) | DMP (3 eq.) | CH₃CN (2 mL) | r.t. | 45   | 37               | -         |
| 42    | DCM (2 mL)  | PhSeO₂H (1 eq.) | NEt₃ (2.2 eq.) | TFAA (1 eq.) | DCM (1 mL) | r.t. | 31   | 14               | 0         | 29    |
| 43    | DCM (2 mL)  | PhSeO₂H (1 eq.) | NEt₃ (2.2 eq.) | PTS Anhydride (1 eq.) | DCM (1 mL) | r.t. | 28   | 5                | 22        | 21    |
| 44    | DCM (2 mL)  | PhSeO₂H (1 eq.) | NEt₃ (2.2 eq.) | Yamaguchi’s reagent (1 eq.) | DCM (1 mL) | r.t. | 39   | 4                | 0         | 30    |
| 45    | DCM (2 mL)  | PhSeO₂H (1 eq.) | NEt₃ (2.2 eq.) | Pivalic anhydride (1 eq.) | DCM (1 mL) | r.t. | 24   | 9                | 0         | 41    |
| 46    | DCM (2 mL)  | PhSeO₂H (1 eq.) | NEt₃ (2.2 eq.) | TeO₂ (1 eq.) | DCM (1 mL) | r.t. | 30   | 16               | 0         | 20    |
|   |   |   |   |   |
|---|---|---|---|---|
| 47 | DCM (2 mL) | Benzene seleninic anhydride (1 eq.) | Tf₂O (1 eq.) | - | r.t. | 25 | 6 | 4 | 5 |
| 48 | DCM (2 mL) | Benzene seleninic anhydride (1 eq.) | NEt₃ (2.2 eq.) | Tf₂O (1 eq.) | DCM (1 mL) | r.t. | 15 | - | 0 | 20 |
| 49 | DCM (2 mL) | Benzene seleninic anhydride (1 eq.) | NEt₃ (2.2 eq.) + DMP (2eq.) | Tf₂O (1 eq.) | DCM (1 mL) | r.t. | 5 | 45 | - | 13 |
| 50 | DCM (2 mL) | Benzene seleninic anhydride (1 eq.) | AcOH (1 eq.) + NEt₃ (2.2 eq.) | Tf₂O (1 eq.) | DCM (1 mL) | r.t. | 23 | 5 | 30 | 30 |

aNMR yield (in %) determined with the use of bromoform as an internal reference. ²2-F-Py used instead of 2-I-Py. ²2-Cl-Py used instead of 2-I-Py. TFAA: trifluoroacetic anhydride; PTS Anhydride: para-toluene sulfonic anhydride; Yamaguchi’s reagent: 2,4,6-trichlorobenzoyl chloride; Tf₂O: trifluoromethane sulfonic anhydride.
3. Amides

3.1. Synthesis of Amides

**General Procedure A:**
To a solution of the amine (1.00 eq.) and triethylamine (2.00 eq.) in dichloromethane (0.1 M) at 0°C, the corresponding acyl chloride (1.20 eq.) was added dropwise and the resulting reaction mixture was allowed to warm to room temperature while stirring overnight (14 h). After this time, a saturated aqueous solution of sodium bicarbonate was added and the biphasic system was separated. The aqueous phase was extracted with dichloromethane (1×) and the organic phases were combined and dried over anhydrous sodium sulfate. The dried solution was filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography on silica gel to afford the desired compound.

**General Procedure B:**
To a solution of the amine (1.00 eq.), triethylamine (1.00 eq.), hydroxybenzotriazole (HOBt, 1.00 eq.) and 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride (EDCI·HCl, 1.00 eq.) in DCM (0.1 M), the corresponding carboxylic acid was added and the resulting solution was stirred at room temperature overnight (14 h). After this time, the organic solution was washed sequentially with 0.5 M aqueous hydrochloric acid, saturated aqueous sodium bicarbonate and saturated aqueous sodium chloride. The washed solution was dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography on silica gel (heptane/ethyl acetate) to afford the desired compound.

**Given the difficulty of separating the dehydrogenated products from the starting materials, we have reported Rf values in a solvent system which we found best provided some separation between the starting materials and products.**
3.2. Characterization

4-Phenyl-1-(pyrrolidin-1-yl)butan-1-one (1a)

General Procedure B was carried out on 12 mmol scale; purification by silica gel flash chromatography (EtOAc/heptanes 1:9 to 3:7) yielded the product as a colourless oil (2.16 g, 83 %) with R_f = 0.4 (acetone/heptanes 2:3). All analytical data were in good accordance with data reported in the literature.[1]

3-Cyclopentyl-1-(pyrrolidin-1-yl)propan-1-one (1b)

General Procedure A was carried out on 3 mmol scale (relative to the amine); purification by silica gel flash chromatography (EtOAc/heptanes 1:9 to 3:7) yielded the product as a colourless oil (580 mg, quant. yield) with R_f = 0.27 (acetone/heptanes 2:3). All analytical data were in good accordance with data reported in the literature.[1]

3-(4-Bromophenyl)-N,N-dimethylpropanamide (1c)

General Procedure B was carried out on 3 mmol scale (relative to the amine); purification by silica gel flash chromatography (EtOAc/heptanes 1:19 to 2:8) yielded the product as a white crystalline solid (730 mg, 95%) with R_f = 0.36 (acetone/heptanes 2:3). All analytical data were in good accordance with data reported in the literature.[2]

N,N-Dimethyl-3-phenylpropanamide (1d)

General Procedure A was carried out on 3.3 mmol scale (relative to the amine); purification by silica gel flash chromatography (EtOAc/heptanes 1:19 to 3:7) yielded the product as a pale yellow oil (586 mg, quant. yield) with R_f = 0.25 (acetone/heptanes 2:3). All analytical data were in good accordance with data reported in the literature.[2]
**N,N-Diethyl-3-phenylpropanamide (1e)**

General Procedure A was carried out on 5 mmol scale (relative to the amine); purification by silica gel flash chromatography (EtOAc/heptanes 1:19 to 2:8) yielded the product as a yellow oil (980 mg, 96%) with R<sub>f</sub> = 0.34 (acetone/heptanes 2:3). All analytical data were in good accordance with data reported in the literature.[2]

**(2,3-Dihydro-1H-inden-2-yl)(pyrrolidin-1-yl)methanone (1f)**

General Procedure B was carried out on 1.6 mmol scale; purification by silica gel flash chromatography (EtOAc/heptanes 1:19 to 1:9) yielded the product as a white crystalline solid (230 mg, 66%) with R<sub>f</sub> = 0.38 (acetone/heptanes 2:3). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>): δ 7.21 – 7.18 (m, 2H), 7.16 – 7.12 (m, 2H), 3.53 (dt, J = 13.7, 6.9 Hz, 4H), 3.47 – 3.38 (m, 1H), 3.35 – 3.29 (m, 2H), 3.16 – 3.09 (m, 2H), 1.99 (p, J = 6.8 Hz, 2H), 1.89 (p, J = 6.8 Hz, 2H); <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>): δ 173.2, 142.1 (2C), 126.5 (2C), 124.3 (2C), 46.7, 46.1, 43.7, 36.4 (2C), 26.3, 24.4; IR (neat) ν<sub>max</sub>: 3071, 3043, 2973, 2861, 1621, 1477, 1435, 1335, 1312, 1226, 1191, 1011, 910, 740; HRMS (ESI+): exact mass calculated for [M+Na]<sup>+</sup> (C<sub>14</sub>H<sub>17</sub>NNaO) requires m/z 238.1202, found m/z 238.1205.

**Cyclobutyl(pyrrolidin-1-yl)methanone (1g)**

General Procedure B was carried out on 2.0 mmol scale; purification by silica gel flash chromatography (EtOAc/heptanes 1:19 to 2:8) yielded the product as a colourless oil (220 mg, 74%) with R<sub>f</sub> = 0.36 (acetone/heptanes 2:3). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>): δ 3.40 (t, J = 6.9 Hz, 2H), 3.28 (t, J = 6.8 Hz, 2H), 3.15 (p, J = 8.6 Hz, 1H), 2.33 – 2.25 (m, 2H), 2.12 – 2.05 (m, 2H), 1.95 – 1.75 (m, 6H); <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>): δ 173.3, 45.9, 45.7, 38.5, 26.2, 24.7 (2C), 24.3, 18.1; IR (neat) ν<sub>max</sub>: 2972, 2946, 2871, 1632, 1433, 1341, 1312, 1257, 1226, 1191, 1171, 751; HRMS (ESI+): exact mass calculated for [M+Na]<sup>+</sup> (C<sub>9</sub>H<sub>15</sub>NNaO) requires m/z 176.1046, found m/z 176.1049.

All analytical data were in good accordance with data reported in the literature.[3]
1-(Piperidin-1-yl)pent-4-en-1-one (1h)

General Procedure B was carried out on 5.0 mmol scale; purification by silica gel flash chromatography (EtOAc/heptanes 1:49 to 1:9) yielded the product as a yellow oil (753 mg, 90%) with Rf = 0.46 (acetone/heptanes 2:3). All analytical data were in good accordance with data reported in the literature.[4]

1-(Pyrrolidin-1-yl)undec-10-yn-1-one (1i)

General Procedure B was carried out on 5.0 mmol scale; purification by silica gel flash chromatography (EtOAc/heptanes 1:19 to 2:8) yielded the product as a yellow oil (941 mg, 80%) with Rf = 0.44 (acetone/heptanes 1:2). 1H NMR (400 MHz, CDCl3): δ 3.44 (t, J = 6.9 Hz, 2H), 3.39 (t, J = 6.8 Hz, 2H), 2.27 – 2.20 (m, 2H), 2.16 (td, J = 7.1, 2.6 Hz, 2H), 1.97 – 1.89 (m, 3H), 1.87 – 1.79 (m, 2H), 1.68 – 1.59 (m, 2H), 1.55 – 1.46 (m, 2H), 1.41 – 1.26 (m, 8H); 13C NMR (101 MHz, CDCl3): δ 171.9, 84.9, 68.2, 46.7, 45.7, 34.9, 29.6, 29.4, 29.1, 28.8, 28.6, 26.3, 25.0, 24.5, 18.5; IR (neat) νmax: 3288, 3227, 2927, 2855, 1634, 1427, 1341, 1252, 1226, 1193, 1170, 914, 857, 725; HRMS (ESI+): exact mass calculated for [M+Na]+ (C15H25NNaO) requires m/z 258.1828, found m/z 258.1829.

4,4,4-Trifluoro-1-(pyrrolidin-1-yl)butan-1-one (1j)

General Procedure B was carried out on 1.6 mmol scale; purification by silica gel flash chromatography (EtOAc/heptanes 1:4 to 1:1) yielded the product as a yellow oil (310 mg, 79%) with Rf = 0.6 (acetone/heptanes 1:2). 1H NMR (400 MHz, CDCl3): δ 3.47 (t, J = 6.9 Hz, 2H), 3.41 (t, J = 6.8 Hz, 2H), 2.55 – 2.48 (m, 4H), 2.02 – 1.93 (m, 2H), 1.87 (qd, J = 6.8, 0.9 Hz, 2H); 13C NMR (151 MHz, CDCl3): δ 168.3, 127.3 (q, J = 275 Hz), 46.7, 46.0, 29.4 (q, J = 29.4 Hz), 27.4 (q, J = 2.8 Hz), 26.5, 24.5; 19F NMR (659 MHz, CDCl3): δ -66.7; IR (neat) νmax: 2960, 2878, 1639, 1443, 1380, 1344; HRMS (ESI+): exact mass calculated for [M+H]+ (C8H13NOF3) requires m/z 196.0944 found m/z 196.0945.
**N,N-Dibenzylpentanamide (1k)**

General Procedure A was carried out on 5 mmol scale (relative to the amine); purification by silica gel flash chromatography (EtOAc/heptanes 1:19 to 2:8) yielded the product as a yellow oil (1.40 g, quant. yield) with $R_f = 0.50$ (acetone/heptanes 2:3). All analytical data were in good accordance with data reported in the literature.[5]

**1-Morpholinobutan-1-one (1l)**

General Procedure A was carried out on 3.0 mmol scale; purification by silica gel flash chromatography (EtOAc/heptanes 1:5 to 1:1) yielded the product as a yellow oil (480 mg, 80%) with $R_f = 0.50$ (acetone/heptanes 1:2). All analytical data were in good accordance with data reported in the literature.[6]

**1-(Piperidin-1-yl)butan-1-one (1m)**

General Procedure A was carried out on 2 mmol scale; purification by silica gel flash chromatography (EtOAc/heptanes 1:19 to 1:4) yielded the product as a colourless oil (310 mg, 99%) with $R_f = 0.44$ (acetone/heptanes 2:3). All analytical data were in good accordance with data reported in the literature.[7]

**1-(Azepan-1-yl)butan-1-one (1n)**

General Procedure A was carried out on 2.0 mmol scale; purification by silica gel flash chromatography (EtOAc/heptanes 1:5 to 2:3) yielded the product as a yellow oil (330 mg, quant. yield) with $R_f = 0.65$ (acetone/heptanes 1:2). All analytical data were in good accordance with data reported in the literature.[7]
**N-Methyl-N-phenylpentanamide (1o)**

![Chemical Structure](image)

General Procedure A was carried out on 4.0 mmol scale; purification by silica gel flash chromatography (EtOAc/heptanes 1:9 to 1:4) yielded the product as an orange oil (650 mg, 85%) with Rf = 0.48 (acetone/heptanes 2:3). All analytical data were in good accordance with data reported in the literature.[8]

**N-(4-Methoxyphenyl)-N-methylbutyramide (1p)**

![Chemical Structure](image)

NaH (60% in paraffin oil, 248 mg, 6.2 mmol, 2.0 eq.) was added to a solution of N-(4-methoxyphenyl)butyramide (600 mg, 3.1 mmol, 1.0 eq., prepared in 57% yield according to general procedure A) in tetrahydrofuran (15 mL) at 0 °C and stirred for 4 hours. Subsequently methyl iodide (0.39 ml, 6.2 mmol, 1.0 eq.) was slowly added to the mixture and stirred for 12 hours. The mixture was poured into 50 mL of water, the aqueous layer extracted with dichloromethane (3 x 25 mL) and the organic phases were combined and dried over anhydrous sodium sulfate. The dried solution was filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography on silica gel (EtOAc/heptanes 1:9 to 3:7) to yield the product as a yellow oil (462 mg, 72%) with Rf = 0.40 (acetone/heptanes 2:3); 

\[
\begin{align*}
\text{H NMR (600 MHz, CDCl}_3\text{): } & \delta 7.08 \text{–} 7.05 (m, 2H), 6.92 \text{–} 6.88 (m, 2H), 3.81 (s, 3H), 3.20 (s, 3H), 2.03 \text{–} 1.99 (m, 2H), 1.60 \text{–} 1.52 (m, 2H), 0.80 (t, J = 7.4 Hz, 3H); \\
\text{C NMR (151 MHz, CDCl}_3\text{): } & \delta 173.6, 158.9, 137.2, 128.5 (2C), 114.9 (2C), 55.6, 37.5, 36.0, 19.0, 14.0; \\
\text{IR (neat)} \nu_{\text{max}}: & 2961, 2934, 2874, 1651, 1510, 1462, 1420, 1385, 1292, 1246, 1171, 1129, 1105, 1036, 839; \\
\text{HRMS (ESI+)}: & \text{exact mass calculated for [M+Na}^+\text{(C}_{13}\text{H}_{17}\text{NNaO}_2) \text{requires } m/z 230.1151, \text{found } m/z 230.1153.
\end{align*}
\]

**N-Allyl-N-benzylbutyramide (1q)**

![Chemical Structure](image)

General Procedure A was carried out on 6.1 mmol scale; purification by silica gel flash chromatography (EtOAc/heptanes 3:10 to 1:2) gave the product as a yellow oil (1.43 g, 82%) with an
$R_f = 0.6$ (acetone/heptanes 1:2). All analytical data were in good accordance with data reported in the literature.[5]

**Methyl 9-(azepan-1-yl)-9-oxononanoate (1r)**

![Methyl 9-(azepan-1-yl)-9-oxononanoate](image)

General Procedure B was carried out on a 0.82 mmol scale; purification by silica gel flash chromatography (EtOAc/heptanes 1:9 to 3:7) yielded the product as a colourless oil (237 mg, 72%) with $R_f = 0.35$ (acetone/heptanes 1:2); $^1$H NMR (600 MHz, CDCl₃): $\delta$ 3.66 (s, 3H), 3.53 – 3.49 (m, 2H), 3.43 – 3.40 (m, 2H), 2.30 – 2.28 (m, 4H), 1.74 – 1.68 (m, 4H), 1.62 (dt, $J = 13.7$, 6.8 Hz, 4H), 1.59 – 1.52 (m, 4H), 1.33 – 1.32 (m, 6H); $^{13}$C NMR (151 MHz, CDCl₃): $\delta$ 174.4, 172.8, 51.6, 48.0, 46.1, 34.2, 33.4, 29.5, 29.4, 29.2, 29.1, 27.8, 27.2, 27.0, 25.5, 25.0; IR (neat) $\nu_{\text{max}}$: 2925, 2854, 1736, 1637, 1426, 1357; HRMS (ESI+): exact mass calculated for [M+H]$^+$ (C$_{16}$H$_{30}$NO$_3$) requires $m/z$ 284.2220 found $m/z$ 284.2218.

**Methyl 9-(diethylamino)-9-oxononanoate (1s)**

![Methyl 9-(diethylamino)-9-oxononanoate](image)

General Procedure B was carried out on 1.0 mmol scale; purification by silica gel flash chromatography (EtOAc/heptanes 1:9 to 1:2) yielded the product as a colourless oil (178 mg, 69%) with $R_f = 0.66$ (acetone/heptanes 1:1). $^1$H NMR (400 MHz, CDCl₃): $\delta$ 3.65 (s, 3H), 3.36 (q, $J = 7.2$ Hz, 2H), 3.28 (q, $J = 7.2$ Hz, 2H), 2.27 (app q, $J = 7.6$ Hz, 4H), 1.67–1.56 (m, 4H), 1.36–1.28 (m, 6H), 1.16 (t, $J = 7.2$ Hz, 3H), 1.09 (t, $J = 7.2$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl₃): $\delta$ 174.4, 172.3, 51.5, 42.1, 40.1, 34.2, 33.2, 29.4, 29.2, 29.1, 25.5, 25.0, 14.5, 13.2; IR (neat) $\nu_{\text{max}}$: 2932, 2856, 1738, 1640, 1460, 1432, 1378, 1362, 1262, 1222, 1199, 1171; HRMS (ESI+): exact mass calculated for [M+Na]$^+$ (C$_{14}$H$_{27}$NO$_3$Na) requires $m/z$ 280.1883, found $m/z$ 280.1883.

**Methyl 9-(diisobutylamino)-9-oxononanoate (1t)**

![Methyl 9-(diisobutylamino)-9-oxononanoate](image)

General Procedure B was carried out on 1.0 mmol scale; purification by silica gel flash chromatography (EtOAc/heptanes 1:9 to 1:1) yielded the product as a colourless oil (313 mg, 94%) with $R_f = 0.44$ (acetone/heptanes 1:2); $^1$H NMR (400 MHz, CDCl₃): $\delta$ 3.68 – 3.60 (m, 3H), 3.21 – 3.13 (m, 2H), 3.09 – 3.02 (m, 2H), 2.33 – 2.23 (m, 4H), 2.05 – 1.82 (m, 2H), 1.67 – 1.52
(m, 4H), 1.36 – 1.25 (m, 6H), 0.90 (dd, J = 9.4, 4.6 Hz, 6H), 0.85 (dd, J = 9.5, 4.8 Hz, 6H); $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 174.4, 173.5, 55.7, 53.2, 34.2, 33.5, 29.4, 29.2, 28.1, 26.7, 25.7, 25.0, 20.3 (2C), 20.2 (2C); IR (neat) $\nu_{\text{max}}$: 2955, 2931, 2870, 1739, 1642, 1465, 1422, 1387, 1366, 1242, 1199, 1171, 1099; HRMS (ESI+): exact mass calculated for [M+Na]$^+$ (C$_{18}$H$_{35}$NO$_3$Na) requires m/z 336.2509, found m/z 336.2509.

Methyl 9-(indolin-1-yl)-9-oxononanoate (1u)

General Procedure B was carried out on 1.0 mmol scale; purification by silica gel flash chromatography (EtOAc/heptanes 1:9 to 1:1) yielded the product as an off-white solid (230 mg, 76%) with R$_f$ = 0.40 (acetone/heptanes 1:1); $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 8.23 (d, J = 8.0 Hz, 1H), 7.20 – 7.13 (m, 2H), 7.02 – 6.97 (m, 1H), 4.04 (t, J = 8.5 Hz, 2H), 3.66 (s, 3H), 3.18 (t, J = 8.4 Hz, 2H), 2.40 (t, J = 7.5 Hz, 2H), 2.30 (t, J = 7.5 Hz, 2H), 1.76 – 1.69 (m, 2H), 1.65 – 1.59 (m, 2H), 1.41 – 1.32 (m, 6H);

$^{13}$C NMR (151 MHz, CDCl$_3$): $\delta$ 174.4, 171.5, 143.2, 131.1, 127.7, 124.6, 123.6, 117.1, 51.6, 48.1, 36.0, 34.2, 29.3, 29.2, 29.1, 28.2, 25.0, 24.6; IR (neat) $\nu_{\text{max}}$: 2932, 2856, 1736, 1660, 1599, 1599, 1482, 1461, 1409, 1338, 1263, 1198, 1169, 1116, 1096, 756; HRMS (ESI+): exact mass calculated for [M+Na]$^+$ (C$_{18}$H$_{25}$NNaO$_3$) requires m/z 326.1727, found m/z 326.1726.

$N$-Benzyl-$N$-methyl-10-oxoundecanamide (1v)

Prepared from $N$-benzyl-$N$-methylundec-10-enamide according to the following procedure: To a solution of amide (949 mg, 3.3 mmol, 1.0 eq.) and Pd(OAc)$_2$ (74.1 mg, 0.33 mmol, 0.1 eq.) in 10 mL DMSO/water (0.33M, 9/1, v/v) in a Schlenk tube under oxygen atmosphere was added TFA (0.25 ml, 0.33 mmol, 0.1 eq.) and the reaction was heated to 70 °C for 15 hours. The reaction mixture was quenched with water and extracted with ethyl acetate. The organic phases were combined and washed with brine then dried over anhydrous sodium sulfate. The dried solution was filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography on silica gel (DMA mixture [90% DCM, 10% methanol, 1% NH$_2$OH]/DCM: 0 to 20%) to afford the desired compound as a yellow oil (230 mg, 23%, 97% BRSM) with R$_f$ = 0.60 (acetone/heptanes 1:1).

$^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 7.39 – 7.33 (m, 1H), 7.32 – 7.20 (m, 3H), 7.15 (d, J = 7.5 Hz, 1H), 4.58 (s, 1H), 4.53 (s, 1H), 2.93 (s, 1H), 2.90 (s, 2H), 2.44 – 2.30 (m, 4H), 2.12 (s, 2H), 2.11 (s, 1H), 1.70 – 1.60 (m, 2H), 1.41 – 1.32 (m, 6H), 1.33 – 1.25 (m, 6H), 0.90 (dd, J = 9.4, 4.6 Hz, 6H), 0.85 (dd, J = 9.5, 4.8 Hz, 6H)}
1.58 – 1.51 (m, 2H), 1.38 – 1.23 (m, 8H); \(^{13}\)C NMR (151 MHz, CDCl\(_3\)): \(\delta\) 209.5, 173.8, 173.4, 137.7, 136.9, 129.0, 128.7, 128.1, 127.7, 127.4, 126.4, 53.5, 50.9, 43.9, 35.0, 34.0, 33.6, 33.2, 30.0, 29.5, 29.5, 29.4, 29.3, 29.2, 25.5, 25.2, 23.9; IR (neat) \(\nu_{\text{max}}\): 2927, 2855, 1713, 1644, 1493, 1453, 1404, 1358, 1262, 1168, 1121, 1079, 735, 700; HRMS (ESI\(^{+}\)): exact mass calculated for [M+Na]\(^{+}\) (C\(_{19}\)H\(_{29}\)NNaO\(_2\)) requires \(m/z\) 326.2091, found \(m/z\) 326.2092.

7-Oxo-7-(pyrrolidin-1-yl)heptanenitrile (1w)

General Procedure B was carried out on 1.0 mmol scale; purification by silica gel flash chromatography (EtOAc/heptanes 1:9 to 1:1) yielded the product as a white crystalline solid (155 mg, 88%) with \(R_f = 0.44\) (acetone/heptanes 1:2); All analytical data were in good accordance with data reported in the literature. [7]

(Z)-1-(Pyrrolidin-1-yl)docos-13-en-1-one (1x)

General Procedure B was carried out on a 4.0 mmol scale; purification by silica gel flash chromatography (EtOAc/heptanes 1:9 to 1:1) yielded the product as a yellow oil (1.62 g, 82%) with \(R_f = 0.35\) (acetone/heptanes 1:2); \(^1\)H NMR (700 MHz, CDCl\(_3\)): \(\delta\) 5.34 (t, \(J = 4.5\) Hz, 2H), 3.46 (t, \(J = 6.9\) Hz, 2H), 3.40 (t, \(J = 6.8\) Hz, 2H), 2.27 – 2.22 (m, 2H), 2.01 (dd, \(J = 12.2, 6.5\) Hz, 4H), 1.97 – 1.91 (m, 2H), 1.84 (dd, \(J = 10.7, 4.2\) Hz, 2H), 1.67 – 1.61 (m, 2H), 1.38-1.20 (m, 28H), 0.88 (t, \(J = 6.9\) Hz, 3H); \(^{13}\)C NMR (151 MHz, CDCl\(_3\)): \(\delta\) 172.0, 130.0, 46.7, 45.7, 35.0, 32.0, 29.9, 29.7, 29.7, 29.6, 29.4, 27.3, 26.3, 25.1, 24.5, 22.8, 14.2; IR (neat) \(\nu_{\text{max}}\): 2921, 2851, 1646, 1425, 1343; HRMS (ESI\(^{+}\)): exact mass calculated for [M+H]\(^{+}\) (C\(_{26}\)H\(_{50}\)NO) requires \(m/z\) 392.3887, found \(m/z\) 392.3890.
(9S,10S,13R,14S,17R)-10,13-Dimethyl-17-((R)-5-oxo-5-(pyrrolidin-1-yl)pentan-2-yl)dodecahydro-3H-cyclopenta[a]phenanthrene-3,7,12(2H,4H)-trione (1y)

General Procedure B was carried out on 1.0 mmol scale; purification by silica gel flash chromatography (EtOAc/MeOH 1:0 to 95:5) yielded the product as a white solid (269 mg, 59%) with Rf = 0.15 (EtOAc); $^1$H NMR (400 MHz, CDCl$_3$): δ 3.43 (dt, $J = 15.3$, 7.0 Hz, 4H), 2.95–2.80 (m, 3H), 2.38–1.79 (m, 20H), 1.66–1.55 (m, 1H), 1.45–1.32 (m, 6H), 1.31–1.21 (m, 1H), 1.07 (s, 3H), 0.86 (d, $J = 6.3$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 212.2, 209.1, 208.8, 172.0, 57.1, 51.9, 49.1, 47.0, 46.7, 45.8, 45.7, 45.1, 42.9, 38.8, 36.6, 36.1, 35.6, 35.4, 31.7, 30.4, 27.6, 26.3, 25.3, 24.5, 22.0, 19.0, 12.1; IR (neat) $\nu_{\text{max}}$: 2968, 2928, 2866, 1700, 1633, 1422, 1383, 1338, 1283; HRMS (ESI+): exact mass calculated for [M+Na]$^+$ (C$_{28}$H$_{41}$NO$_4$Na) requires m/z 478.2928, found m/z 478.2924.

3-(5-Cyano-1-(4-fluorophenyl)-1,3-dihydroisobenzofuran-1-yl)-N,N-dimethylpropanamide (1z)

To a solution of 1-(4-fluorophenyl)-1,3-dihydroisobenzofuran-5-carbonitrile (1.2 g, 5 mmol, 1.0 eq.) in DMF (3 mL) was added sodium hydride (60% in paraffin oil, 40 mg, 0.1 mmol, 0.2 eq.) and the resulting mixture was stirred at room temperature (23 °C) for 30 min. Then, a solution of N,N-dimethylacrylamide (515 µL, 5 mmol, 1.0 eq.) in DMF (2 mL) was added in one portion. After 16 h, the reaction was quenched by addition of water. The biphasic mixture was extracted with ethyl acetate (3×) and the combined organic extracts were concentrated under reduced pressure. Flash column chromatography of the crude residue over silica gel (EtOAc/heptanes 1:1 to 8:2) afforded the product as an off-white foamy liquid (1.45 g, 86%) with Rf = 0.42 (acetone/heptanes 1:1).

$^1$H NMR (600 MHz, CDCl$_3$): δ 7.58 (br d, $J = 7.9$ Hz, 1H), 7.49 (br s, 1H), 7.45–7.39 (m, 3H), 7.03–6.98 (m, 2H), 5.19 (d, $J = 12.9$ Hz, 1H), 5.15 (d, $J = 12.9$ Hz, 1H), 2.86 (s, 3H), 2.85 (s, 3H), 2.61–2.54 (m, 1H), 2.47–2.41 (m, 1H), 2.25 (t, $J = 8.0$ Hz, 2H); $^{13}$C NMR (150 MHz, CDCl$_3$): δ 172.2, 162.2 (d, $J = 246$ Hz), 149.3, 140.0,
138.9 (d, $J = 3.1$ Hz), 132.1, 126.8 (d, $J = 8.1$ Hz, 2C), 125.3, 122.9, 118.7, 115.6 (d, $J = 21.4$ Hz, 2C), 111.9, 90.7, 71.3, 36.2, 35.5, 28.0; $^{19}$F NMR (659 MHz, CDCl$_3$): $\delta$ –115.1; IR (neat) $\nu_{\text{max}}$: 2927, 2230, 1640, 1506, 1400, 1225, 1159, 1145, 1046, 1030, 1014, 838, 600; HRMS (ESI+): exact mass calculated for [M+Na]$^+$ (C$_{20}$H$_{19}$FN$_2$O$_2$Na) requires $m/z$ 361.1323, found $m/z$ 361.1321.

1-Methylazacyclotridecan-2-one (1aa)

Sodium hydride (60% in paraffin oil, 88 mg, 2.2 mmol, 1.1 eq.) was added to a solution of lactam (395 mg, 2.0 mmol, 1.0 eq.) in DMF (10 mL) at 0 °C and stirred for 1 hours. Subsequently methyl iodide (377 µL, 6.0 mmol, 3.0 eq.) was slowly added to the mixture and stirred for 12 hours. The mixture was poured into 50 mL of water, the aqueous layer extracted with dichloromethane (3x25 mL) and the organic phases were combined and dried over anhydrous sodium sulfate. The dried solution was filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography on silica gel to afford the desired compound as an off-white solid (232 mg, 55%) with $R_f$ = 0.30 (acetone/heptanes 2:3); All analytical data were in good accordance with data reported in the literature.[9]

$N$-Cyclohexyl-9-oxo-9-(pyrrolidin-1-yl)nonanamide (1ab)

General Procedure B was carried out on a 5.0 mmol scale to give methyl 9-oxo-9-(pyrrolidin-1-yl)nonanoate as an yellow oil (1.21 g, 95% yield) with $R_f$ = 0.35 (acetone/heptanes 2:3) after column chromatography on silica gel (EtOAc/heptanes 1:3 to 1:1). All analytical data were in good accordance with data reported in the literature.[5] Subsequent hydrolysis of the methyl ester (1.21 g, 4.8 mmol, 1.0 eq.) with lithium hydroxide (0.22 g, 5 mmol, 1.1 equiv) in a tetrahydrofuran/water mixture (1/1 – 10 mL, v/v) gave the corresponding carboxylic acid. The crude material then used directly in general procedure B to give the amide, 1ab, after silica gel flash chromatography (EtOAc/heptanes 1:2 to 2:1) as a white solid (1.15 g, 73%) with $R_f$ = 0.45 (acetone/heptanes 2:3); $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 5.30 (m, 1H), 3.80 – 3.73 (m, 1H), 3.45 (t, $J = 6.9$ Hz, 2H), 3.40 (t, $J = 6.8$ Hz, 2H), 2.26 – 2.22 (m, 2H), 2.13 – 2.10 (m, 2H), 1.96 – 1.93 (m, 2H), 1.92 – 1.88 (m,
1H, 1.84 (p, J = 6.8 Hz, 2H), 1.71 – 1.67 (m, 2H), 1.64 – 1.60 (m, 6H), 1.35 – 1.32 (m, 6H), 1.18 – 1.06 (m, 4H). $^{13}$C NMR (151 MHz, CDCl$_3$): δ 172.2, 171.9, 48.2, 46.7, 45.7, 37.2, 34.9, 33.4, 29.4, 29.2, 29.2, 26.3, 25.9, 25.7, 25.0, 25.0, 24.6; IR (neat) $\nu_{\text{max}}$: 3285, 2926, 2853, 1622, 1542; HRMS (ESI+): exact mass calculated for [M+H]$^+$ (C$_{19}$H$_{35}$N$_2$O$_2$) requires m/z 323.2693 found m/z 323.2689.

4. Products of desaturation

4.1. General Procedure C

All reactions were run on a 0.2 mmol scale unless otherwise indicated.

To a solution of amide 1 (1.0 eq.) and 2-iodopyridine (2.2 eq.) in dichloromethane (2 mL, 0.1 M) at 0 °C was added trifluoromethanesulfonic anhydride (1.1 eq.) and the resulting mixture was stirred at 0 °C and colouration of the solution was observed. After 15 min, a previously prepared solution of A (1 mL, 0.2 M of PhSeO$_2$H) was added and the reaction mixture was stirred at 0 °C for 5 min. The resulting mixture was allowed to warm to ambient temperature (25 °C) over the course of 5 minutes to 1 h, after which time a saturated aqueous solution of sodium carbonate (5 mL) was added. The biphasic mixture was separated and the aqueous phase was extracted with dichloromethane (2 x 5 mL). The combined organic phases were dried over anhydrous sodium sulfate, the dried solution was filtered and the filtrate was concentrated under reduced pressure. The crude residue was purified by flash column chromatography (SiO$_2$, heptanes/ethyl acetate) to afford the compounds 4. In most cases, the dehydrogenated amide 4 was isolated with remnants of the corresponding starting material (typically 5 – 10%). A further purification was necessary in most cases and was carried out on preparative TLC, typically using an acetone/heptanes system – to both determine the yield and for full characterization of the product – see individual compounds for details.

Preparation of solution A: To a suspension of the seleninic acid (1 eq.) in dichloromethane (1 mL for 0.2 mmol of the seleninic acid) was added the triethylamine (3 eq.). Solubilisation of the suspension was observed and then Dess-Martin periodinane (2.2 eq.) was added at room temperature and stirred 2 hours.
4.2. Characterization

*(E)-4-Phenyl-1-(pyrrolidin-1-yl)but-2-en-1-one (4a)*

The product was prepared according to General Procedure C on 0.2 mmol scale. Following purification by silica gel flash chromatography (EtOAc/heptanes 1:9 to 4:6) and a further purification on preparative TLC (acetone/heptanes 1:1), the product was isolated as an off-white solid (26.7 mg, 62%) with R<sub>f</sub> = 0.40 (acetone/heptanes 3:7);<sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>): δ 7.31 – 7.26 (m, 2H), 7.23 – 7.15 (m, 3H), 7.09 – 7.02 (m, 1H), 6.08 (dd, <i>J</i> = 15.1, 1.4 Hz, 1H), 3.54 – 3.48 (m, 4H), 3.45 (t, <i>J</i> = 6.8 Hz, 2H), 1.96 – 1.88 (m, 2H), 1.87 – 1.79 (m, 2H);<sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>): δ 164.6, 143.7, 138.5, 128.8 (2C), 128.6 (2C), 126.5, 122.9, 46.5, 45.9, 38.6, 26.2, 24.4; IR (neat) ν<sub>max</sub>: 3026, 2970, 2950, 2871, 1659, 1608, 1494, 1425, 1338, 1306, 1252, 1227, 1192, 1169, 1037, 981, 915, 866, 847, 816, 795, 750, 701; HRMS (ESI+): exact mass calculated for [M+H]<sup>+</sup> (C<sub>14</sub>H<sub>18</sub>NO) requires <i>m/z</i> 216.1383, found <i>m/z</i> 216.1383.

2-Hydroxy-4-phenyl-1-(pyrrolidin-1-yl)butan-1-one (5)

To a solution of amide 1a (43.5 mg, 0.2 mmol, 1.0 eq.) and 2-iodopyridine (46.8 µL, 0.44 mmol, 2.2 eq.) in dichloromethane (2 mL, 0.1M) at 0 °C was added trifluoromethanesulfonic anhydride (37 µL, 0.22 mmol, 1.1 eq.) and the resulting mixture was stirred at 0 °C and colouration of the solution was observed. After 15 min, 2,6-lutidine N-oxide (22.4 µL, 0.2 mmol, 1.0 eq.) was added in one portion and the reaction mixture was stirred at 0 °C for 5 min. After this time, and the observation of colour-change, tetrabutyl ammonium hydroxide (480 mg, 0.6 mmol, 3 eq.). The resulting mixture was allowed to warm to ambient temperature (25 °C) over the course of 1 h, after which time a saturated aqueous solution of ammonium chloride (5 mL) was added. The biphasic mixture was separated and the aqueous phase was extracted with dichloromethane (2 × 5 mL). The combined organic phases were dried over anhydrous sodium sulfate, the dried solution was filtered and the filtrate was concentrated under reduced pressure. The crude residue was purified by silica gel flash chromatography (EtOAc/heptanes 1:9 to 2:3) to afford the compound 5 (28.0 mg, 60%) as a yellow oil with <i>R</i><sub>f</sub> = 0.35 (acetone/heptanes 3:7);<sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>): δ 7.31 – 7.24 (m, 2H), 7.23 – 7.17 (m, 3H), 4.15 (td, <i>J</i> = 8.8, 2.7 Hz, 1H), 3.73 (d, <i>J</i> = 7.3 Hz, 1H), 3.57 – 3.50 (m, 1H), 3.43 – 3.38 (m, 1H), 3.31 – 3.25 (m, 1H), 3.18 – 3.12 (m, 1H), 2.88 – 2.82 (m, 1H), 2.81 – 2.75 (m, 1H), 1.96 – 1.78 (m, 6H);<sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>): δ 172.8, 141.6, 128.7 (2C), 128.5 (2C), 126.1,
68.5, 46.4, 45.9, 36.2, 31.3, 26.2, 24.0; HRMS (ESI+): exact mass calculated for [M+Na]+ (C_{14}H_{19}NNaO_2) requires m/z 256.1308, found m/z 256.1304.

All analytical data were in good accordance with data reported in the literature.[10]

4-Phenyl-2-(phenylselanyl)-1-(pyrrolidin-1-yl)butan-1-one (6)

![Chemical structure of 4-Phenyl-2-(phenylselanyl)-1-(pyrrolidin-1-yl)butan-1-one (6)](image)

To a solution of amide 1a (43.5 mg, 0.2 mmol, 1.0 eq.) and 2-iodopyridine (46.8 µL, 0.44 mmol, 2.2 eq.) in dichloromethane (2 mL, 0.1 M) at 0 ºC was added trifluoromethanesulfonic anhydride (37 µL, 0.22 mmol, 1.1 eq.) and the resulting mixture was stirred at 0 ºC and colouration of the solution was observed. After 15 min, a previously prepared solution B (see below) was added and the reaction mixture was stirred at 0 ºC for 5 min. The resulting mixture was allowed to warm to ambient temperature (25 ºC) over the course of 1 h, after which time a saturated aqueous solution of ammonium chloride (5 mL) was added. The biphasic mixture was separated and the aqueous phase was extracted with dichloromethane (2 × 5 mL). The combined organic phases were dried over anhydrous sodium sulfate, the dried solution was filtered and the filtrate was concentrated under reduced pressure. The crude residue was purified by silica gel flash chromatography (EtOAc/heptanes 1:9 to 2:3) to afford compound 6 (23 mg, 64%) as a yellow oil with Rf 0.50 (acetone/heptanes 3:7).

Preparation of solution B: To a solution of the diselenide (187 mg, 0.6 mmol, 3 eq.) in dichloromethane (1 mL) was added the hydrogen peroxide solution (30% solution, 61.3 µL, 0.6 mmol 3 equiv.) at room temperature. The mixture was stirred 20 minutes until a yellow solid has appeared. Anhydrous magnesium sulfate (120 mg) was added. The mixture was stirred 10 more minutes before addition; ^1H NMR (600 MHz, CDCl₃): δ 7.55 (dd, J = 8.0, 1.1 Hz, 2H), 7.33 – 7.29 (m, 1H), 7.27 – 7.23 (m, 4H), 7.17 (t, J = 7.4 Hz, 1H), 7.11 (d, J = 7.1 Hz, 2H), 3.67 (dd, J = 9.3, 5.5 Hz, 1H), 3.48 – 3.43 (m, 1H), 3.40 – 3.34 (m, 1H), 3.12 – 3.07 (m, 1H), 3.00 – 2.95 (m, 1H), 2.79 – 2.73 (m, 1H), 2.65 – 2.58 (m, 1H), 2.51 – 2.44 (m, 1H), 2.13 – 2.05 (m, 1H), 1.81 – 1.66 (m, 4H); ^13C NMR (151 MHz, CDCl₃): δ 169.6, 141.1, 136.0 (2C), 129.1 (2C), 128.6 (2C), 128.6, 128.5 (2C), 127.7, 126.1, 46.4, 46.1, 42.1, 34.2, 33.8, 26.0, 24.3; ^77Se NMR (115 MHz, CDCl₃): δ 413.1; IR (neat) νₘₐₓ: 3057; 3025; 2968, 2948, 2926, 2870, 1633, 1578, 1495, 1476, 1427, 1341, 1254, 1227, 1190, 1168, 1022, 741, 696; HRMS (ESI+): exact mass calculated for [M+Na]+ (C_{20}H_{23}NOSeNa) requires m/z 396.0837, found m/z 396.0837.
(E)-3-Cyclopentyl-1-(pyrrolidin-1-yl)prop-2-en-1-one (4b)

The product was prepared according to General Procedure C on 0.2 mmol scale. Following purification by silica gel flash chromatography (EtOAc/heptanes 1:9 to 2:3), the product was isolated as a colourless oil (25.9 mg, 67% yield) with Rf = 0.22 (acetone/heptanes 2:3); \(^1\)H NMR (600 MHz, CDCl\(_3\)): \(\delta\) 6.89 (dd, \(J = 14.1, 8.2\) Hz, 1H), 6.06 (d, \(J = 14.5\) Hz, 1H), 3.51 (d, \(J = 6.2\) Hz, 4H), 2.63 – 2.52 (m, 1H), 1.99 – 1.91 (m, 2H), 1.89 – 1.77 (m, 4H), 1.73 – 1.66 (m, 2H), 1.63 – 1.55 (m, 2H), 1.46 – 1.37 (m, 2H); \(^{13}\)C NMR (151 MHz, CDCl\(_3\)): \(\delta\) 165.2, 150.2, 119.8, 46.6, 45.9, 43.2, 32.8 (2C), 26.3, 25.4 (2C), 24.5; IR (neat) \(\nu_{\text{max}}\): 2949, 2868, 1735, 1659, 1614, 1424, 1337, 1226, 1193, 981; HRMS (ESI+): exact mass calculated for [M+Na]\(^+\) (C\(_{12}\)H\(_{19}\)NNaO) requires \(m/z\) 216.1364, found \(m/z\) 216.1354.

(E)-3-(4-Bromophenyl)-N,N-dimethylacrylamide (4c)

The product was prepared according to General Procedure C on 0.2 mmol scale. Following purification by silica gel flash chromatography (acetone/heptanes 1:9 to 1:5), the product was isolated as a white solid (43 mg, 85%) with Rf = 0.32 (acetone/heptanes 2:3); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.60 (d, \(J = 15.5\) Hz, 1H), 7.52 – 7.47 (m, 2H), 7.41 – 7.36 (m, 2H), 6.87 (d, \(J = 15.4\) Hz, 1H), 3.17 (s, 3H), 3.07 (s, 3H); \(^{13}\)C NMR (151 MHz, CDCl\(_3\)): \(\delta\) 166.5, 141.2, 134.4, 132.1 (2C), 129.4 (2C), 123.8, 118.2, 37.6, 36.1; IR (neat) \(\nu_{\text{max}}\): 2920, 2851, 1647, 1610, 1584, 1561, 1485, 1388, 1134, 1066, 983, 810, 799; HRMS (ESI+): exact mass calculated for [M+Na]\(^+\) (C\(_{11}\)H\(_{12}\)BrN\(_2\)O) requires \(m/z\) 275.9994, found \(m/z\) 275.9990.

\(N,N\)-Dimethylcinnamamidate (4d)

The product was prepared according to General Procedure C on 0.2 mmol scale. Following purification by silica gel flash chromatography (EtOAc/heptanes 1:4 to 1:1) and a further purification on preparative TLC (acetone/heptanes 2:3), the product was isolated as an off-white solid (24.0 mg, 69%) with Rf = 0.16 (acetone/heptanes 2:3); \(^1\)H NMR (600 MHz, CDCl\(_3\)): \(\delta\) 7.67 (d, \(J = 15.4\) Hz, 1H), 7.53 (dd, \(J = 8.0, 1.2\) Hz, 2H), 7.40 – 7.32 (m, 3H), 6.89 (d, \(J = 15.4\) Hz, 1H), 3.18 (s, 3H), 3.07 (s, 3H);
\textbf{N,N-Diethylcinnamamide (4e)}

The product was prepared according to General Procedure C on 0.2 mmol scale. Following purification by silica gel flash chromatography (EtOAc/heptanes 1:5 to 4:6) and a further purification on preparative TLC (acetone/heptanes 1:1), the product was isolated as yellow oil (31.0 mg, 76\%) with \( R_f = 0.29 \) (acetone/heptanes 2:3); \textbf{\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3})}: \( \delta \) 7.71 (d, \( J = 15.4 \) Hz, 1H), 7.56 – 7.49 (m, 2H), 7.41 – 7.33 (m, 3H), 6.83 (d, \( J = 15.4 \) Hz, 1H), 3.56 – 3.39 (m, 4H), 1.26 (t, \( J = 6.9 \) Hz, 3H), 1.19 (t, \( J = 7.0 \) Hz, 3H); \textbf{\textsuperscript{13}C NMR (101 MHz, CDCl\textsubscript{3})}: \( \delta \) 165.9, 142.5, 135.7, 129.6, 128.9 (2C), 127.9 (2C), 118.0, 42.5, 41.2, 15.2, 13.4; \textbf{IR (neat) \( \nu_{\text{max}} \)}: 3079, 3059, 3027, 2973, 2931, 2874, 1740, 1648, 1607, 1453, 1429, 1245, 1139, 763; \textbf{HRMS (ESI\textsuperscript{+})}: exact mass calculated for [M+H]\textsuperscript{+} (C\textsubscript{13}H\textsubscript{18}NO) requires \( m/z \) 302.1751, found \( m/z \) 302.1750.

\textbf{(1H-Inden-2-yl)(pyrrolidin-1-yl)methanone (4f)}

The product was prepared according to General Procedure C on 0.2 mmol scale. Following purification by silica gel flash chromatography (acetone/heptanes 1:5 to 2:3) and a further purification on preparative TLC (acetone/heptanes 1:1), the product was isolated as an off-white solid (21.0 mg, 63\%) with \( R_f = 0.29 \) (acetone/heptanes 2:3); \textbf{\textsuperscript{1}H NMR (600 MHz, CDCl\textsubscript{3})}: \( \delta \) 7.50 (d, \( J = 7.1 \) Hz, 1H), 7.46 (d, \( J = 6.8 \) Hz, 1H), 7.34 – 7.26 (m, 2H), 7.22 (s, 1H), 3.80 (d, \( J = 1.1 \) Hz, 2H), 3.72 (t, \( J = 6.3 \) Hz, 2H), 3.64 (t, \( J = 6.5 \) Hz, 2H), 2.01 – 1.91 (m, 4H); \textbf{\textsuperscript{13}C NMR (151 MHz, CDCl\textsubscript{3})}: \( \delta \) 165.6, 143.6, 143.6, 142.2, 134.9, 126.8, 126.6, 124.1, 122.6, 49.0, 46.9, 40.7, 26.8 24.3; \textbf{IR (neat) \( \nu_{\text{max}} \)}: 3051, 2957, 2876, 1716, 1594, 1551, 1457, 1421, 1384, 1218, 1121, 1016, 920, 750, 710; \textbf{HRMS (ESI\textsuperscript{+})}: exact mass calculated for [M+Na]\textsuperscript{+} (C\textsubscript{14}H\textsubscript{15}NNaO) requires \( m/z \) 236.1046, found \( m/z \) 236.1043.
Cyclobut-1-en-1-yl(pyrrolidin-1-yl)methanone (4g)

The product was prepared according to General Procedure C on 1.0 mmol scale. Following purification by silica gel flash chromatography (acetone/heptanes 1:5 to 2:3) and a further purification on preparative TLC (acetone/heptanes 1:1), the product was isolated as a colourless oil (95.0 mg, 63%) with Rf = 0.32 (acetone/heptanes 2:3); \(^1\)H NMR (600 MHz, CDCl\(_3\)): δ 6.44 (s, 1H), 3.55 (t, J = 6.9 Hz, 2H), 3.50 (t, J = 6.9 Hz, 2H), 2.82 – 2.75 (m, 2H), 2.44 – 2.40 (m, 2H), 1.97 – 1.91 (m, 2H), 1.87 – 1.77 (m, 2H); \(^{13}\)C NMR (151 MHz, CDCl\(_3\)): δ 161.9, 142.4, 141.2, 47.0, 46.4, 30.9, 27.0, 26.5, 24.0; IR (neat) ν\(_{\text{max}}\): 2964, 2926, 2871, 1721, 1617, 1571, 1418, 1340, 1227, 1190, 914, 865, 729, 865; HRMS (ESI+): exact mass calculated for [M+Na]+ (C\(_9\)H\(_{13}\)NNaO) requires m/z 174.0889, found m/z 174.0887.

(E)-1-(Piperidin-1-yl)penta-2,4-dien-1-one (4h)

The product was prepared according to General Procedure C on 0.2 mmol scale. Following purification by silica gel flash chromatography (EtOAc/heptanes 1:10 to 2:3) and a further purification on preparative TLC (acetone/heptanes 1:1), the product was isolated as a colourless oil (13.2 mg, 40%) with Rf = 0.34 (acetone/heptanes 2:3); \(^1\)H NMR (400 MHz, CDCl\(_3\)): δ 7.25 – 7.16 (m, 1H), 6.53 – 6.35 (m, 2H), 5.59 – 5.49 (m, 1H), 5.43 – 5.36 (m, 1H), 3.68 – 3.46 (m, J = 32.2, 25.4 Hz, 4H), 1.69 – 1.62 (m, 2H), 1.62 – 1.54 (m, 4H); \(^{13}\)C NMR (151 MHz, CDCl\(_3\)): δ 165.4, 142.5, 135.5, 123.7, 121.8, 47.1, 43.4, 26.9, 25.7, 24.8; IR (neat) ν\(_{\text{max}}\): 3086, 3056, 3001, 2933, 2854, 1781, 1754, 1648, 1611, 1437, 1410, 1265, 1137, 1121, 1019, 852; HRMS (ESI+): exact mass calculated for [M+H]+ (C\(_{10}\)H\(_{16}\)NO) requires m/z 166.1226, found m/z 166.1232.

(E)-1-(Pyrrolidin-1-yl)undec-2-en-10-yn-1-one (4i)

The product was prepared according to General Procedure C on 0.2 mmol scale. Following purification by silica gel flash chromatography (EtOAc/heptanes 1:10 to 3:7) and a further purification on preparative TLC (acetone/heptanes 1:1), the product was isolated as a yellow oil (21.0 mg, 46%) with Rf = 0.35 (acetone/heptanes 1:2); \(^1\)H NMR (600 MHz, CDCl\(_3\)): δ 6.94 – 6.84 (m, 1H),
6.08 (dt, J = 15.1, 1.4 Hz, 1H), 3.53 – 3.48 (m, 4H), 2.22 – 2.14 (m, 4H), 1.98 – 1.90 (m, 3H), 1.88 – 1.81 (m, 2H), 1.54 – 1.48 (m, 2H), 1.48 – 1.42 (m, 2H), 1.42 – 1.37 (m, 2H), 1.35 – 1.30 (m, 2H); \(^{13}\text{C NMR (151 MHz, CDCl}_3\): δ 165.0, 145.7, 121.8, 84.7, 68.3, 46.6, 45.9, 32.4, 28.7, 28.6, 28.5, 28.4, 26.2, 24.4, 18.5; IR (neat) \(\nu_{\text{max}}\): 3297, 3221, 3040, 2969, 2929, 2112, 1659, 1610, 1424, 1420, 1337, 1226, 1191, 980, 691, 626; HRMS (ESI\(^+\)): exact mass calculated for [M+Na\(^+\)] (C\(_{15}\)H\(_{23}\)NNaO) requires m/z 256.1672, found m/z 256.1668.

\((E)-4,4,4\text{-Trifluoro-1-(pyrrolidin-1-yl)but-2-en-1-one (4j)}\)

\[
\text{N, N-Dibenzylcyclobut-1-ene-1-carboxamide (4k)}
\]

The product was prepared according to General Procedure C on 0.2 mmol scale. Following purification by silica gel flash chromatography (acetone/heptanes 1:5 to 1:1) and a further purification on preparative TLC (DCM/methanol 200:3), the product was isolated as a yellow oil (23.0 mg, 60\%) with R\(_f\) = 0.6 (acetone/heptanes 1:2); \(^1\text{H NMR (600 MHz, CDCl}_3\): δ 6.86 – 6.74 (m, 2H), 3.59 – 3.56 (m, 4H), 2.04 – 1.99 (m, 2H), 1.94 – 1.90 (m, 2H); \(^{13}\text{C NMR (151 MHz, CDCl}_3\): δ 168.3, 129.0 (q, J = 5.5 Hz), 129.0 (q, J = 35 Hz), 122.8 (q, J = 270 Hz), 46.9, 46.4, 26.2, 24.4; \(^{19}\text{F NMR (565 MHz, CDCl}_3\): δ -64.9 (d, J = 5.0 Hz); IR (neat) \(\nu_{\text{max}}\): 2929, 2881, 1723, 1684, 1626, 1447, 1344; HRMS (ESI\(^+\)): exact mass calculated for [M+H\(^+\)] (C\(_8\)H\(_{11}\)NOF\(_3\)) requires m/z 194.0787, found m/z 194.0788.

The product was prepared according to General Procedure C on 0.2 mmol scale. Following purification by silica gel flash chromatography (EtOAc/heptanes 1:5 to 1:1) and a further purification on preparative TLC (acetone/heptanes 1:1), the product was isolated as a yellow oil (32.3 mg, 58\%) with R\(_f\) = 0.38 (acetone/heptanes 2:3); \(^1\text{H NMR (400 MHz, CDCl}_3\): δ 7.42 – 7.15 (m, 10H), 7.11 (dt, J = 15.0, 6.5 Hz, 1H), 6.27 (dt, J = 15.0, 1.6 Hz, 1H), 4.65 (s, 2H), 4.51 (s, 2H), 2.27 – 2.18 (m, 2H), 1.04 (t, J = 7.4 Hz, 3H); \(^{13}\text{C NMR (101 MHz, CDCl}_3\): δ 167.6, 149.4, 137.6, 137.0, 129.0 (2C), 128.7 (2C), 128.5 (2C), 127.7, 127.5, 126.7 (2C), 119.4, 50.0, 48.6, 25.8, 12.8; IR (neat) \(\nu_{\text{max}}\): 3085, 3062, 3028, 2964, 2930, 2874, 1654, 1618, 1495, 1419, 1359, 1278, 1294, 1079, 972, 952, 747, 732, 695, 613, 531, 457; HRMS (ESI\(^+\)): exact mass calculated for [M+H\(^+\)] (C\(_{19}\)H\(_{22}\)NO) requires m/z 280.1701, found m/z 280.1699.
(E)-1-Morpholinobut-2-en-1-one (4l)

The product was prepared according to General Procedure C on 0.2 mmol scale. Following purification by silica gel flash chromatography (acetone/heptanes 1:4 to 1:1) and a further purification on preparative TLC (acetone/heptanes 2:3), the product was isolated as an orange solid (15.1 mg, 49%) with Rf = 0.4 (acetone/heptanes 1:2); 1H NMR (600 MHz, CDCl3): δ 6.94 – 6.87 (m, 1H), 6.23 (dq, J = 15.0, 1.6 Hz, 1H), 3.62 (d, J = 75.2 Hz, 8H), 1.89 (dd, J = 6.9, 1.7 Hz, 3H); 13C NMR (151 MHz, CDCl3): δ 165.8, 142.3, 121.1, 66.9, 46.2, 42.3, 18.4; IR (neat) νmax: 2961, 2851, 1646, 1549, 1530; HRMS (ESI+): exact mass calculated for [M+H]+ (C8H14NO2) requires m/z 156.1019, found m/z 156.1019.

(E)-1-(Piperidin-1-yl)but-2-en-1-one (4m)

The product was prepared according to General Procedure C on 0.2 mmol scale. Following purification by silica gel flash chromatography (EtOAc/heptanes 1:9 to 2:3) and a further purification on preparative TLC (acetone/heptanes 1:1), the product was isolated as a yellow oil (14.7 mg, 48%) with Rf = 0.38 (acetone/heptanes 2:3); 1H NMR (600 MHz, CDCl3): δ 6.83 (dq, J = 14.9, 6.8 Hz, 1H), 6.27 (dq, J = 14.9, 1.7 Hz, 1H), 3.59 (s, 2H), 3.48 (s, 2H), 1.87 (dd, J = 6.8, 1.7 Hz, 3H), 1.68 – 1.63 (m, 2H), 1.58 – 1.54 (m, 4H); 13C NMR (151 MHz, CDCl3): δ 165.7, 140.9, 122.1, 47.0, 43.2, 26.8, 25.7, 24.8, 18.4; IR (neat) νmax: 3051, 3000, 2931, 2853, 1735, 1660, 1611, 1432, 1283, 1249, 1218, 1140, 1101, 1024, 964, 972, 852; HRMS (ESI+): exact mass calculated for [M+H]+ (C9H16NO) requires m/z 154.1229, found m/z 154.1229.

(E)-1-(Azepan-1-yl)but-2-en-1-one (4n)

The product was prepared according to General Procedure C on 0.2 mmol scale. Following purification by silica gel flash chromatography (acetone/heptanes 1:5 to 1:1), the product was isolated as a yellow oil (16.8 mg, 51%) with Rf = 0.6 (acetone/heptanes 1:2); 1H NMR (600 MHz, CDCl3): δ 6.90 (dq, J = 20.7, 6.9 Hz, 1H), 6.32 – 6.17 (m, 1H), 3.59 – 3.54 (m, 2H), 3.50 – 3.46 (m, 2H), 1.87 (dd, J =
(E)-N-Methyl-N-phenylpent-2-enamide (4o)

The product was prepared according to General Procedure C on 0.2 mmol scale. Following purification by silica gel flash chromatography (EtOAc/heptanes 1:9 to 3:7), the product was isolated as a pale yellow oil (25.2 mg, 67%) with Rf = 0.38 (acetone/heptanes 2:3); \(^1\)H NMR (600 MHz, CDCl\(_3\)): \(\delta\) 7.40 (t, \(J = 7.7\) Hz, 2H), 7.32 (t, \(J = 7.4\) Hz, 1H), 7.17 (d, \(J = 7.3\) Hz, 2H), 6.93 (dt, \(J = 15.1, 6.6\) Hz, 1H), 5.72 (d, \(J = 15.1\) Hz, 1H), 3.33 (s, 3H), 2.13 – 2.01 (m, 2H), 0.92 (t, \(J = 7.4\) Hz, 3H); \(^{13}\)C NMR (151 MHz, CDCl\(_3\)): \(\delta\) 166.4, 147.5, 143.9, 129.6 (2C), 127.5 (3C), 120.6, 37.5, 25.5, 12.7; IR (neat) \(\nu_{\text{max}}\): 3061, 3037, 3011, 2964, 2931, 2875, 2856, 1726, 1661, 1629, 1595, 1495, 1419, 1369, 1291, 1119, 1025, 975, 851, 772, 700, 664, 567; HRMS (ESI\(^+\)): exact mass calculated for [M+H]\(^+\) (C\(_{12}\)H\(_{16}\)NO) requires \(m/z\) 190.1226, found \(m/z\) 190.1224.

(E)-N-(4-Methoxyphenyl)-N-methylbut-2-enamide (4p)

The product was prepared according to General Procedure C on 0.2 mmol scale. Following purification by silica gel flash chromatography (EtOAc/heptanes 1:9 to 3:7), the product was isolated as a yellow oil (27.1 mg, 66%) with Rf = 0.26 (acetone/heptanes 2:3); \(^1\)H NMR (700 MHz, CDCl\(_3\)): \(\delta\) 7.09 – 7.06 (m, 2H), 6.93 – 6.86 (m, 3H), 5.73 (d, \(J = 15.0\) Hz, 1H), 3.83 (s, 3H), 3.28 (s, 3H), 1.72 (d, \(J = 6.3\) Hz, 3H); \(^{13}\)C NMR (176 MHz, CDCl\(_3\)): \(\delta\) 166.5, 158.8, 141.0, 136.7, 128.6, 128.5, 122.8, 114.8 (2C), 55.6, 37.6, 18.1; IR (neat) \(\nu_{\text{max}}\): 3048, 3018, 3001, 2958, 2925, 2875, 2851, 2841, 1730, 1664, 1629, 1509, 1444, 1369, 1288, 1243, 1170, 1129, 1104, 1029, 965, 837, 766, 732, 680, 608, 567; HRMS (ESI\(^+\)): exact mass calculated for [M+H]\(^+\) (C\(_{12}\)H\(_{16}\)NO\(_2\)) requires \(m/z\) 206.1176, found \(m/z\) 206.1177.
(E)-N- Allyl-N-benzylbut-2-enamide (4q)

The product was prepared according to General Procedure C on 0.2 mmol scale. Following purification by silica gel flash chromatography (acetone/heptanes 1:5 to 1:2), and a further purification on preparative TLC (acetone/heptanes 1:2), the product was isolated as a yellow oil (17.1 mg, 40%) with R\(_f\) = 0.60 (acetone/heptanes 1:2); \(^1\)H NMR (700 MHz, CDCl\(_3\)) (rotameric effects present) δ 7.36 (t, J = 7.2 Hz, 1H), 7.32 – 7.28 (m, 1H), 7.25 (m, 1H), 7.19 (d, J = 7.3 Hz, 1H), 7.01 (dq, J = 13.6, 6.7 Hz, 1H), 6.23 (d, J = 14.9 Hz, 1H), 5.84 – 5.71 (m, 1H), 5.23 – 5.10 (m, 2H), 4.64 – 4.54 (m, 2H), 4.04 (d, J = 5.5 Hz, 1H), 3.88 (d, J = 3.3 Hz, 1H), 1.87 (dd, J = 34.7, 6.7 Hz, 3H); \(^{13}\)C NMR (151 MHz, CDCl\(_3\)): δ 167.2, 167.1, 142.8, 142.5, 137.8, 137.2, 133.2, 133.0, 129.0, 128.7, 128.4, 127.7, 127.4, 126.6, 121.8, 121.8, 117.6, 117.0, 50.1, 49.1, 48.8, 48.3, 18.4; IR (neat) \(\nu_{\text{max}}\): 2969, 2929, 1661, 1619, 1447, 1416; HRMS (ESI+): exact mass calculated for [M+H]+ (C\(_{14}\)H\(_{18}\)NO) requires m/z 216.1383, found m/z 216.1380.

Methyl (E)-9-(azepan-1-y1)-9-oxonon-7-enoate (4r)

The product was prepared according to General Procedure C at -20°C (NaCl and ice bath ratio of 1:3) on 0.2 mmol scale. Following purification by silica gel flash chromatography (acetone/heptanes 1:5 to 1:1), the product was isolated as a yellow oil (45.5 mg, 81%) with R\(_f\) = 0.35 (acetone/heptanes 1:2); \(^1\)H NMR (700 MHz, CDCl\(_3\)) δ 6.90 – 6.83 (m, 1H), 6.21 (dt, J = 15.0, 1.4 Hz, 1H), 3.65 (s, 3H), 3.58 – 3.55 (m, 2H), 3.50 – 3.46 (m, 2H), 2.29 (t, J = 7.5 Hz, 2H), 2.23 – 2.17 (m, 2H), 1.72 (dq, J = 24.0, 6.1 Hz, 4H), 1.63 (dd, J = 15.3, 7.6 Hz, 2H), 1.58 – 1.53 (m, 4H), 1.47 (dt, J = 15.1, 7.5 Hz, 2H), 1.37 – 1.33 (m, 2H); \(^{13}\)C NMR (151 MHz, CDCl\(_3\)) δ 174.3, 166.6, 145.9, 120.8, 51.6, 51.58, 48.0, 46.4, 34.1, 32.4, 29.4, 28.8, 28.2, 27.8, 27.1, 26.7, 24.8; IR (neat) \(\nu_{\text{max}}\): 2929, 2856, 1736, 1657, 1613, 1430; HRMS (ESI+): exact mass calculated for [M+H]+ (C\(_{16}\)H\(_{28}\)NO\(_3\)) requires m/z 282.2064 found m/z 282.2046.

Methyl (E)-9-(diethylamino)-9-oxonon-7-enoate (4s)
The product was prepared according to General Procedure C at -10 °C (acetone/ice bath) on 0.155 mmol scale. Following purification by silica gel flash chromatography (EtOAc/heptanes 1:5 to 1:2) and a further purification on preparative TLC (acetone/heptanes 1:1), the product was isolated as a colourless oil (23.3 mg, 59%) with Rf = 0.60 (acetone/heptanes 1:2); $^1$H NMR (700 MHz, CDCl$_3$): δ 6.90 – 6.86 (m, 1H), 6.18 (d, J = 15.0, 1H), 3.66 (s, 3H), 3.42 (q, J = 7.0 Hz, 2H), 3.36 (q, J = 7.0 Hz, 2H), 2.30 (t, J = 7.5 Hz, 2H), 2.21 (td, J = 8.0, 1.0 Hz, 2H), 1.66 – 1.61 (m, 2H), 1.50 – 1.44 (m, 2H), 1.38 – 1.33 (m, 2H), 1.19 (t, J = 7.0 Hz, 3H), 1.14 (t, J = 7.0 Hz, 3H); $^{13}$C NMR (176 MHz, CDCl$_3$): δ 174.3, 166.0, 145.9, 120.8, 51.6, 42.3, 40.9, 34.1, 32.4, 28.8, 28.2, 24.9, 15.0, 13.3; IR (neat) ν$_{max}$: 2971, 2930, 2857, 1735, 1659, 1617, 1430, 1361, 1253, 1219, 1172, 1136, 1097, 978; HRMS (ESI+): exact mass calculated for [M+H]$^+$ (C$_{14}$H$_{26}$NO$_3$) requires m/z 256.1907, found m/z 256.1907.

**Ethyl (E)-9-(diisobutylamino)-9-oxonon-7-enoate (4t)**

The product was prepared according to General Procedure C on 0.2 mmol scale. Following purification by silica gel flash chromatography (acetone/heptanes 1:5 to 1:2) and a further purification on preparative TLC (acetone/heptanes 1:1), the product was isolated as a yellow oil (32.0 mg, 55%) with Rf = 0.45 (acetone/heptanes 1:2); $^1$H NMR (600 MHz, CDCl$_3$): δ 6.91 – 6.76 (m, 1H), 6.19 (d, J = 15.0 Hz, 1H), 3.64 (s, 3H), 3.21 (d, J = 7.5 Hz, 2H), 3.12 (d, J = 7.5 Hz, 2H), 2.28 (t, J = 7.5 Hz, 2H), 2.21 – 2.16 (m, 2H), 2.04 – 1.96 (m, 1H), 1.92 – 1.86 (m, 1H), 1.65 – 1.58 (m, 2H), 1.48 – 1.42 (m, 2H), 1.36 – 1.29 (m, 2H), 0.88 (d, J = 6.7 Hz, 6H), 0.86 (d, J = 6.7 Hz, 6H); $^{13}$C NMR (151 MHz, CDCl$_3$): δ 174.2, 167.0, 145.6, 121.0, 56.0, 54.5, 51.6, 34.0, 32.4, 28.9, 28.8, 28.1, 27.0, 24.8, 20.4 (2C), 20.2 (2C); IR (neat) ν$_{max}$: 2955, 2869, 1735, 1653, 1618, 1465, 1437, 1420, 1386, 1231, 1170, 1139, 1100, 977, 819; HRMS (ESI+): exact mass calculated for [M+Na]$^+$ (C$_{18}$H$_{33}$NNaO$_3$) requires m/z 334.2353, found m/z 334.2351.

**Methyl (E)-9-(indolin-1-yl)-9-oxonon-7-enoate (4u)**
The product was prepared according to General Procedure C on 0.2 mmol scale. Following purification by silica gel flash chromatography (EtOAc/heptanes 1:9 to 2:3) and a further purification on preparative TLC (acetone/heptanes 1:1), the product was isolated as a yellow oil (31.6 mg, 52%) with $R_f$ = 0.34 (acetone/heptanes 2:3); $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 8.36 – 8.00 (m, 1H), 7.22 – 7.16 (m, 2H), 7.07 – 6.99 (m, 2H), 6.22 (d, $J$ = 14.1 Hz, 1H), 4.15 (t, $J$ = 8.5 Hz, 2H), 3.69 – 3.66 (m, 3H), 3.25 – 3.15 (m, 2H), 2.33 – 2.25 (m, 4H), 1.65 (dt, $J$ = 15.2, 7.5 Hz, 2H), 1.55 – 1.49 (m, 2H), 1.38 (dt, $J$ = 9.5, 7.6 Hz, 2H); $^{13}$C NMR (151 MHz, CDCl$_3$): $\delta$ 174.2, 147.5, 143.3, 131.5, 127.7, 124.6, 123.8, 122.3, 117.6, 51.6, 48.2, 34.1, 34.1, 32.4, 28.8, 28.1, 24.8; IR (neat) $\nu_{\text{max}}$: 3061, 3028, 2998, 2926, 2853, 1735, 1661, 1624, 1595, 1479, 1461, 1400, 1338, 1291, 1260, 1199, 1167, 1119, 975, 754, 605, 580; HRMS (ESI+): exact mass calculated for [M+H]$^+$ (C$_{18}$H$_{24}$NO$_3$) requires $m/z$ 302.1751, found $m/z$ 302.1750.

(E)-N-Benzyl-N-methyl-10-oxoundec-2-enamide (4v)

The product was prepared according to General Procedure C on 0.2 mmol scale. Following purification by silica gel flash chromatography (EtOAc/heptanes 1:9 to 2:3) and a further purification on preparative TLC (acetone/heptanes 1:1), the product was isolated as a yellow oil (37.7 mg, 63%) with $R_f$ = 0.55 (acetone/heptanes 2:3); $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 7.38 – 7.26 (m, 3H), 7.26 – 7.15 (m, 2H), 7.00 – 6.90 (m, 1H), 6.25 (dd, $J$ = 33.2, 15.0 Hz, 1H), 4.66 (d, $J$ = 16.6 Hz, 1H), 4.57 (d, $J$ = 19.6 Hz, 1H), 2.98 (s, 3H), 2.46 – 2.35 (m, 2H), 2.22 (dd, $J$ = 14.2, 7.2 Hz, 1H), 2.19 – 2.06 (m, 4H), 1.60 – 1.50 (m, 2H), 1.46 (dd, $J$ = 14.7, 7.3 Hz, 1H), 1.41 (dd, $J$ = 14.4, 7.3 Hz, 1H), 1.36 – 1.28 (m, 4H); $^{13}$C NMR (151 MHz, CDCl$_3$): $\delta$ 209.3, 167.5, 167.0, 147.1, 147.0, 137.6, 137.0, 129.0, 128.7, 128.2, 127.7, 127.4, 126.6, 120.4, 120.3, 53.5, 51.2, 43.8, 35.0, 34.2, 32.6, 32.5, 30.0, 29.1, 29.1, 29.0, 28.3, 28.3, 23.8; IR (neat) $\nu_{\text{max}}$: 3061, 3028, 2998, 2926, 2853, 1712, 1657, 1618, 1495, 1452, 1400, 1357, 1122, 1029, 975, 735, 700; HRMS (ESI+): exact mass calculated for [M+H]$^+$ (C$_{19}$H$_{28}$NO$_2$) requires $m/z$ 302.2115, found $m/z$ 302.2109.

(E)-7-Oxo-7-(pyrrolidin-1-yl)hept-5-enenitrile (4w)
The product was prepared according to General Procedure C on 0.2 mmol scale. Following purification by silica gel flash chromatography (EtOAc/heptanes 1:9 to 2:3) and a further purification on preparative TLC (acetone/heptanes 1:1), the product was isolated as a white crystalline solid (29.0 mg, 73%) with $R_f = 0.22$ (acetone/heptanes 1:2); $^1H$ NMR (600 MHz, CDCl$_3$): $\delta$ 6.79 (dt, $J =$ 14.7, 7.2 Hz, 1H), 6.19 (dt, $J =$ 15.1, 1.4 Hz, 1H), 3.51 (t, $J =$ 6.9 Hz, 4H), 2.41 – 2.34 (m, 4H), 1.99 – 1.92 (m, 2H), 1.90 – 1.79 (m, 4H); $^{13}$C NMR (151 MHz, CDCl$_3$): $\delta$ 164.3, 142.2, 123.9, 119.3, 46.6, 46.0, 30.9, 26.2, 24.4, 24.1, 16.6; IR (neat) $\nu_{\text{max}}$: 2970, 2951, 2940, 2876, 2244, 1717, 1660, 1599, 1430, 1338, 1227, 1191, 975; HRMS (ESI+) exact mass calculated for [M+Na]$^+$ (C$_{11}$H$_{16}$N$_2$NaO) requires $m/z$ 215.1155, found $m/z$ 215.1150.

(2E,13Z)-1-(Pyrrolidin-1-yl)docosa-2,13-dien-1-one (4x)

The product was prepared according to General Procedure C on 0.2 mmol scale. Following purification by silica gel flash chromatography (acetone/heptanes 1:5 to 2:1), the product was isolated as a yellow oil (56.8 mg, 72%) with $R_f = 0.45$ (acetone/heptanes 1:2); $^1H$ NMR (600 MHz, CDCl$_3$): 6.93 – 6.89 (m, 1H), 6.08 (d, $J =$ 15.2 Hz, 1H), 5.62 (m, 1H), 5.44 (dd, $J =$ 15.4, 7.2 Hz, 1H), 4.03 (m, 1H), 3.52 (m, 3H), 2.20 (dt, $J =$ 15.2, 7.7 Hz, 2H), 2.02 (m, 2H), 1.96 (dt, $J =$ 13.8, 7.0 Hz, 2H), 1.86 (m, 2H), 1.47 – 1.42 (m, 2H), 1.26 (m, 26H), 0.88 (t, $J =$ 6.4Hz, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$: 165.1, 145.9, 130.0, 130.0, 121.7, 46.6, 45.8, 32.5, 32.0, 29.9, 29.6, 29.5, 29.4, 29.3, 28.5, 27.3, 26.2, 24.4, 22.8, 14.2; IR (neat) $\nu_{\text{max}}$: 2924, 2853, 1660, 1606, 1439. HRMS (ESI+) exact mass calculated for [M+Na]$^+$ (C$_{26}$H$_{47}$N$_2$NaO) requires $m/z$ 412.3550, found $m/z$ 412.3549.

(8R,9S,10S,13R,14S,17R)-10,13-Dimethyl-17-((R,E)-5-oxo-5-(pyrrolidin-1-yl)pent-3-en-2-yl)dodecahydro-3H-cyclopenta[a]phenanthrene-3,7,12(2H,4H)-trione (4y)
The product was prepared according to General Procedure C on 0.2 mmol scale. Following purification by silica gel flash chromatography (EtOAc/MeOH 1:0 to 95:5), the product, as an inseparable mixture with starting material (15%), was isolated (74.0 mg, 67%) with $R_f = 0.15$ (EtOAc); $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 6.88 (dd, $J = 15.1, 8.7$ Hz, 1H), 6.06 (d, $J = 15.1$ Hz, 1H), 3.54 – 3.49 (m, 4H), 2.95 – 2.78 (m, 3H), 2.39 – 1.82 (m, 18H), 1.62 (td, $J = 14.2, 4.8$ Hz, 1H), 1.43 – 1.27 (m, 5H), 1.08 (s, 3H), 1.05 (d, $J = 6.8$ Hz, 3H); $^{13}$C NMR (151 MHz, CDCl$_3$): $\delta$ 211.8, 209.1, 208.8, 165.0, 150.0, 120.4, 56.9, 51.2, 49.0, 47.0, 46.7, 45.3, 45.1, 42.9, 39.6, 38.7, 36.7, 36.1, 35.4, 26.7, 26.3, 25.1, 24.5, 22.1, 20.5, 12.6; IR (neat) $\nu_{\text{max}}$: 2962, 2931, 2873, 1705, 1657, 1611, 1430, 1387; HRMS (ESI+): exact mass calculated for [M+Na]$^+$ (C$_{28}$H$_{39}$NNaO$_4$) requires $m/z$ 476.2777, found $m/z$ 476.2790.

$(E)$-3-(5-Cyano-1-(4-fluorophenyl)-1,3-dihydroisobenzofuran-1-yl)-N,N-dimethylacrylamide (4z)

The product was prepared according to General Procedure C on both 0.2 mmol and 4.18 mmol scale. Following purification by silica gel flash chromatography (acetone/heptanes 1:5 to 1:1), the product was isolated as an off-white foamy solid (46.7 mg, 69% or 884 mg, 63%) with $R_f = 0.39$ (acetone/heptanes 1:1); $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.64 – 7.60 (m, 1H), 7.57 (s, 1H), 7.34 – 7.28 (m, 3H), 7.23 (d, $J = 14.8$ Hz, 1H), 7.05 – 7.00 (m, 2H), 6.67 (d, $J = 14.8$ Hz, 1H), 5.26 (d, $J = 12.9$ Hz, 1H), 5.18 (d, $J = 12.9$ Hz, 1H), 3.08 (s, 3H), 3.01 (s, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 165.8, 162.7 (d, $J = 248$ Hz), 147.6, 144.2, 140.0, 137.4 (d, $J = 3.2$ Hz, 2C), 132.3, 128.6 (d, $J = 8.3$ Hz), 125.5, 124.0, 119.8, 118.6, 115.7 (d, $J = 21.6$ Hz, 2C), 112.5, 90.6, 71.5, 37.6, 36.0; $^{19}$F NMR (565 MHz, CDCl$_3$): $\delta$ -113.4; IR (neat) $\nu_{\text{max}}$: 3051, 2929, 2860, 2230, 1781, 1657, 1615, 1506, 1410, 1396, 1265, 1225, 1160, 1141, 1085, 1029, 1013, 978, 910, 832, 729, 700, 613, 597, 589, 559, 518; HRMS (ESI+): exact mass calculated for [M+H]$^+$ (C$_{20}$H$_{18}$FN$_2$O$_2$) requires $m/z$ 337.1343, found $m/z$ 337.1347.

$(E)$-1-Methylazacyclotridec-3-en-2-one (4aa)
The product was prepared according to General Procedure C on 0.2 mmol scale. Following purification by silica gel flash chromatography (EtOAc/heptanes 1:5 to 1:1) and a further purification on preparative TLC (acetone/heptanes 1:1), the product was isolated as a yellow oil (17.1 mg, 40%) with $R_f = 0.26$ (acetone/heptanes 2:3); $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 6.71 – 6.58 (m, 1H), 6.28 (dt, $J = 15.3$, 1.2 Hz, 1H), 3.38 (t, $J = 6.6$ Hz, 2H), 2.94 (s, 3H), 2.28 – 2.20 (m, 2H), 1.64 – 1.56 (m, 2H), 1.55 – 1.46 (m, 2H), 1.39 – 1.21 (m, 10H); $^1$C NMR (101 MHz, CDCl$_3$): $\delta$ 168.4, 144.1, 123.0, 48.4, 33.3, 33.0, 26.9 – 26.5 (m), 26.2, 25.4, 25.4, 23.4; IR (neat) $\nu_{\text{max}}$: 2924, 2856, 1735, 1654, 1614, 1438, 1395, 1198, 1168, 1106, 976, 820, 742, 701; HRMS (ESI+): exact mass calculated for [M+Na]$^+$ (C$_{13}$H$_{23}$NNaO) requires $m/z$ 232.1672, found $m/z$ 232.1670.

(E)-N-Cyclohexyl-9-oxo-9-(pyrrolidin-1-yl)non-7-enamide (4ab)

The product was prepared according to General Procedure C at -20°C (NaCl and ice bath ratio of 1/3) on 0.1 mmol scale. Following purification by silica gel flash chromatography (acetone/heptanes 1:2 to 4:1), the product was isolated as a yellow oil (16.3 mg, 51%) with $R_f = 0.40$ (acetone/heptanes 3:2); $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 6.90 – 6.71 (m, 1H), 6.02 (dt, $J = 15.1$, 1.5 Hz, 1H), 5.23 – 5.21 (m, $J = 6.0$ Hz, 1H), 3.69 (dt, $J = 10.6$, 9.3 Hz, 1H), 3.45 (dd, $J = 11.8$, 6.7 Hz, 3H), 2.16 – 2.10 (m, 2H), 2.07 – 2.03 (m, 2H), 1.92 – 1.85 (m, 2H), 1.82 – 1.78 (m, 2H), 1.65 – 1.60 (m, 2H), 1.58 – 1.52 (m, 2H), 1.43 – 1.33 (m, 2H), 1.32 – 1.22 (m, 6H), 1.11 – 1.02 (m, 2H), 0.81 – 0.78 (m, 2H); $^1$C NMR (151 MHz, CDCl$_3$): $\delta$ 172.1, 165.1, 145.7, 121.9, 48.2, 46.7, 46.0, 37.1, 33.4, 32.3, 29.9, 28.8, 28.2, 26.3, 25.7, 25.0, 24.5; IR (neat) $\nu_{\text{max}}$: 2925, 2854, 1736, 1637, 1426, 1357; HRMS (ESI+): exact mass calculated for [M+H]$^+$ (C$_{19}$H$_{33}$N$_2$O$_2$) requires $m/z$ 321.2537 found $m/z$ 321.2531.
4.3. Application of our methodology

4.3.1. Dihydroxylation

**Procedure:** Diol 7 was prepared following the procedure reported by Sharpless et al. starting from 0.3 mmol of the desaturated amide 4q.[11]

\[
\text{1-(Azepan-1-yl)-2,3-dihydroxybutan-1-one (7)}
\]

Following purification by silica gel flash chromatography (acetone/heptanes 1:4 to 2:1), the product was isolated as a yellow oil (40.0 mg, 69%) with \( R_f = 0.35 \) (acetone/heptanes 1:2); \(^1\)H NMR (700 MHz, MeOD): \( \delta 4.24 (d, J = 4.6 \text{ Hz}, 1\text{H}), 3.94 (qd, J = 6.4, 4.7 \text{ Hz}, 1\text{H}), 3.69 - 3.62 (m, 2\text{H}), 3.55 (ddd, J = 14.5, 7.0, 5.3 \text{ Hz}, 1\text{H}), 3.42 (ddd, J = 13.7, 8.0, 4.4 \text{ Hz}, 1\text{H}), 2.91 (d, J = 15.7 \text{ Hz}, 1\text{H}), 2.80 (d, J = 15.7 \text{ Hz}, 1\text{H}), 1.80 - 1.70 (m, 4\text{H}), 1.60 (tdd, J = 16.6, 12.0, 4.2 \text{ Hz}, 4\text{H}), 1.18 (d, J = 6.4 \text{ Hz}, 3\text{H}); \(^{13}\)C NMR (176 MHz, MeOD): \( \delta 173.4, 73.7, 69.8, 47.7, 43.8, 30.3, 28.4, 28.1, 27.3, 19.2 \); IR (neat) \( \nu_{\text{max}} \): 3411, 3301, 3260, 2929, 2857, 1723, 1608, 1442, 1440, 1373, 1200; HRMS (ESI\(^+\)): exact mass calculated for \([\text{M+H}]^+\) \( (C_{10}H_{20}NO_3) \) requires m/z 202.1438 found m/z 202.1438.

4.3.2. Enantioselective Michael addition

**Procedure:** Amide 8 was prepared following the procedure reported by Harutyunyan et al. starting from 0.2 mmol of the desaturated amide 4n.[12]

\[
\text{(S)-1-(Azepan-1-yl)-3-methylpentan-1-one (8)}
\]

Following purification by silica gel flash chromatography (acetone/heptanes 1:5 to 1:1), the compound was isolated as a yellow oil (36.0 mg, 91%) with \( R_f = 0.6 \) (acetone/heptanes 1:2); \(^1\)H NMR (600 MHz, CDCl\(_3\)): \( \delta 3.56 - 3.50 \) (m, 2H), 3.47 - 3.41 (m, 2H), 2.29 (dd, J = 14.7, 5.9 Hz, 1H), 2.12 (dd, J = 14.7, 8.0 Hz, 1H), 1.98 (dd, J = 13.4, 6.8 Hz, 1H), 1.70 (dd, J = 11.3, 5.7 Hz, 4H), 1.58 - 1.57 (m, 3H), 1.43 - 1.37 (m, 1H), 1.30 - 1.14 (m, 2H), 0.95 - 0.88 (m, 6H); \(^{13}\)C NMR (151 MHz, CDCl\(_3\)): \( \delta 172.4, 48.1, 46.1, 40.3, 32.0, 29.8, 29.4, 27.8, 27.1, 26.9, 19.6, 11.6 \); IR (neat) \( \nu_{\text{max}} \): 2958, 2927, 2855, 1638, 1453, 1424; HRMS (ESI\(^+\)): exact mass calculated for \([\text{M+H}]^+\) \( (C_{12}H_{24}NO) \) requires m/z 198.1852, found m/z 198.1850.
Report

Sample Information

Sample Name: Carlos_CP813F1_1mx-1
Sample ID: 1
Unit: 1
Injection Volume: 5 µL
Data File: Carlos_CP813F1_1mx-1_18072018_1_002.iov
Method File: Run_18072018_F1_50mL
Batch File: 18072018_F1_50mL
Report Format File: Run_18072018_F1_50mL
Date Acquired: 18.07.2018 11:39:01
Date Processed: 18.07.2018 12:26:43

Method Description:
Column: LiChrosorb (Chromatol OD-H) 250x4.6mm
Solvent System: n-Hexane:IPA, 98:2
Flow: 1 mL/min

Chromatogram

| Ret Time | Area   | Area% |
|----------|--------|-------|
| 10.097   | 100.000| 100.000|

Detector A Channel 1 210nm

Detector A Channel 2 254nm

| Ret Time | Area | Area% |
|----------|------|-------|
| 10.090   | 231  | 1.147 |
| Total    | 573   | 100.000|

S33
**Report**

**Sample Information**
- **Sample Name**: Carloz_C810F1_Rac_Lux-1
- **Sample ID**: 1
- **Injection Volume**: 10 µL
- **Data File**: Carloz_C810F1_Rac_Lux-1_18.07.2018_1_003.lcd
- **Method File**: Run_19021D_F1_PoS4.lcm
- **Batch File**: 18.07.2018_F.005
- **Report Format File**: Line_Calibration_01/08/19_2IPA_F1.lir
- **Date Acquired**: 18.07.2018 12:09:16
- **Date Processed**: 18.07.2018 12:29:00

**Method Description**:
- **Column**: Chiralcel OJ-H 250 x 4.6 mm
- **Solvent System**: n-Hexane:0.1%IPA/IPA 98:2
- **Flow**: 1 ml/min

**Chromatogram**

#### Detector A Channel 1 210nm

![Chromatogram 210nm](image)

#### Detector A Channel 2 254nm

![Chromatogram 254nm](image)

**Peak Table**

**Detector A Channel 1 210nm**

| Peak | Ret Time | Area   | Area%  |
|------|----------|--------|--------|
| 1    | 10.016   | 12019868 | 50.05% |
| 2    | 12.041   | 11993984 | 49.95% |
| Total|          | 24013857 | 100.00%|

**Detector A Channel 2 254nm**

| Peak ID | Ret Time | Area | Area%  |
|---------|----------|------|--------|
|         |          |      |        |
|         |          |      |        |
|         |          |      |        |
| Total   |          |      |        |

S34
4.3.3. Synthesis of piperine

Procedure: Allyl alcohol 10 was prepared following the procedure reported by Quayle et al.[13]

\[1\text{-}(\text{Benzo[d][1,3]dioxol-5-yl})\text{prop-2-en-1-ol} \ (10)\]

\[
\begin{array}{c}
\text{O} \\
\text{O} \\
\text{OH}
\end{array}
\]

Following purification by silica gel flash chromatography (acetone/heptanes 1:5 to 1:1), the product was isolated as a yellow oil (1.78 g, 96%) with \( R_f = 0.55 \) (acetone/heptanes 1:2); \( ^1\text{H NMR} \ (600 \text{ MHz, CDCl}_3)\): \( \delta \ 6.87 \ (d, J = 1.5 \text{ Hz, 1H}), 6.83 \ (dd, J = 8.0, 1.3 \text{ Hz, 1H}), 6.78 \ (d, J = 7.9 \text{ Hz, 1H}), 6.02 \ (ddd, J = 17.1, 10.3, 5.8 \text{ Hz, 1H}), 5.95 \ (s, 2H), 5.34 \ (dt, J = 17.1, 1.4 \text{ Hz, 1H}), 5.19 \ (dt, J = 10.3, 1.3 \text{ Hz, 1H}), 5.12 \ (d, J = 5.2 \text{ Hz, 1H}). \]

All analytical data were in good accordance with data reported in the literature.[13]

Procedure: Amide 12 was prepared following the procedure reported by Trauner et al.[14]

\[(\varepsilon)\text{-5-(benzo[d][1,3]dioxol-5-yl)-1-(piperidin-1-yl)pent-4-en-1-one} \ (12)\]

\[
\begin{array}{c}
\text{O} \\
\text{O} \\
\text{N}
\end{array}
\]

Following purification by silica gel flash chromatography (acetone/heptanes 1:5 to 1:1), the compound was isolated as a yellow oil (1.05 g, 73%) with \( R_f = 0.35 \) (acetone/heptanes 1:2); \( ^1\text{H NMR} \ (600 \text{ MHz, CDCl}_3)\): \( \delta \ 6.89 \ (d, J = 1.5 \text{ Hz, 1H}), 6.76 \ (dd, J = 8.0, 1.5 \text{ Hz, 1H}), 6.73 \ (d, J = 8.0 \text{ Hz, 1H}), 6.34 \ (d, J = 15.8 \text{ Hz, 1H}), 6.09 \ (dt, J = 15.7, 6.9 \text{ Hz, 1H}), 5.93 \ (s, 2H), 3.58 - 3.55 \ (m, 2H), 3.42 - 3.39 \ (m, 2H), 2.52 \ (ddd, J = 8.2, 7.1, 1.5 \text{ Hz, 2H}), 2.48 - 2.45 \ (m, 2H), 1.66 - 1.62 \ (m, 2H), 1.54 \ (dd, J = 13.5, 7.6 \text{ Hz, 4H}). \]

All analytical data were in good accordance with data reported in the literature.[15]

\[(2E,4E)\text{-5-(benzo[d][1,3]dioxol-5-yl)-1-(piperidin-1-yl)penta-2,4-dien-1-one} \ (13)\]

\[
\begin{array}{c}
\text{O} \\
\text{O} \\
\text{N}
\end{array}
\]

The product was prepared according to General Procedure C on 0.2 mmol scale. The yield of the reaction was determined to be 48% by NMR using mesitylene as an internal standard (24.0 mg, 2.0 eq.). Due to contamination with 2-iodobenzoic acid, a small sample was purified by preparative TLC (run twice in solvent system 3:1:1 heptane/ethyl acetate/dichloromethane) for analytical purposes; \( ^1\text{H NMR} \ (700 \text{ MHz, CDCl}_3)\): \( \delta \ 7.40 \ (dd, J = 14.6, 9.6 \text{ Hz, 1H}), 6.98 \ (d, J = 1.3 \text{ Hz, 1H}), ...)
6.89 (dd, \( J = 8.0, 1.4 \text{ Hz, } 1\text{H} \)), 6.79 – 6.73 (m, 3H), 6.44 (d, \( J = 14.7 \text{ Hz, } 1\text{H} \)), 5.98 (s, 2H), 3.64 (s, 2H), 3.53 (s, 2H), 1.66 (dd, \( J = 11.1, 5.8 \text{ Hz, } 2\text{H} \)), 1.61 – 1.57 (m, 4H); \( ^{13}\text{C} \text{ NMR (176 MHz, CDCl}_3 \)): \( \delta \) 165.6, 148.4, 148.3, 142.6, 138.4, 131.2, 125.5, 122.7, 120.2, 108.7, 105.8, 101.4, 47.1, 43.4, 26.9, 25.8, 24.8; \( \text{HRMS (ESI+)} \): exact mass calculated for \([\text{M+H}]^+ (\text{C}_{17}\text{H}_{20}\text{NO}_3) \) requires \( m/z \) 286.1438 found \( m/z \) 286.1437.

All analytical data were in good accordance with data reported in the literature.[16]
5. Labelling experiments

\[
\text{Ph} - \underset{2\text{-l-pyr (2.2 eq.)}}{\overset{\text{PhSeO}_2\text{H} (1.1 \text{ eq.})}{\longrightarrow}} \text{Ph}^{18}\overset{\text{NE}_3 (2.2 \text{ eq.}),}{\underset{\text{DMP (2.2 eq.),}{\overset{\text{H}_2^{18}\text{O} (2.2 \text{ eq.})}{\longrightarrow}} \text{Ph}}
\]

49% yield
26% \(^{18}\text{O}\) incorporation

---

**Mass Spectrum List Report**

| Analysis Info | Acquisition Date | Operator | Instrument/Seq# |
|---------------|------------------|----------|-----------------|
| Analysis Name | 6/14/2018 3:33:25 PM | msc | maxxIs 10 |
| Method | tune_low_MS_service_05.16.m | | |
| Sample Name | PAAC035 | | |
| Comment | AdlerMaude | | |

**Acquisition Parameters**

| Source Type | ESI | Ion Polarity | Positive | Set Neutralizer | D. Bar |
|-------------|-----|--------------|----------|-----------------|------|
| Focus | Full | Sat Capillary | 4500 V | Set Dry Heater | 180 °C |
| Scan Range | 50 m/z | Set Ind Plate Offset | -700 V | Set Dry Gas | 4.0 l/min |
| Scan End | 1000 m/z | Set Collision Cell RF | 800.0 Vpp | Set Divert Valve | Source |

---

**Mass Spectra**

| m/z | Intensity | 1201 1476 | 405 2512 | 210 1202 |
|-----|-----------|-----------|----------|----------|

| # | m/z | Intensity | 1201 1476 | 405 2512 | 210 1202 |
|---|-----|-----------|-----------|----------|----------|
| 1 | 218.1427 | 50173 |         |          |          |
| 2 | 238.1302 | 365971 |         |          |          |
| 3 | 238.1224 | 65890 |         |          |          |
| 4 | 240.1251 | 125910 |         |          |          |
| 5 | 256.1307 | 100527 |         |          |          |
| 6 | 256.1350 | 165374 |         |          |          |
| 7 | 260.1362 | 73952 |         |          |          |
| 8 | 260.1410 | 37500 |         |          |          |
| 9 | 300.1465 | 34013 |         |          |          |
| 10 | 453.2512 | 43450 |         |          |          |
| 11 | 454.2543 | 153030 |         |          |          |
| 12 | 455.2556 | 281390 |         |          |          |
| 13 | 456.2561 | 85524 |         |          |          |
| 14 | 457.2566 | 57000 |         |          |          |
| 15 | 473.2598 | 29993 |         |          |          |
| 16 | 599.2550 | 36219 |         |          |          |
| 17 | 601.2566 | 38728 |         |          |          |
| 18 | 668.2175 | 85200 |         |          |          |
| 19 | 618.2210 | 40835 |         |          |          |
| 20 | 611.2234 | 104529 |         |          |          |
| 21 | 612.2202 | 37791 |         |          |          |
| 22 | 631.2196 | 149433 |         |          |          |
| 23 | 641.2221 | 51858 |         |          |          |
| 24 | 615.2177 | 52208 |         |          |          |
| 25 | 1199.4470 | 38740 |         |          |          |
| 26 | 1200.4488 | 39098 |         |          |          |
| 27 | 1201.4476 | 45182 |         |          |          |
| 28 | 1202.4504 | 30353 |         |          |          |
| 29 | 1203.4498 | 54004 |         |          |          |
| # m/z | | 218.1363 2000 | 217.1416 314 | 218.1450 27 |
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7. Spectra

- **$^1$H**
  - CDCl$_3$
  - 600MHz

- **$^{13}$C (APT)**
  - CDCl$_3$
  - 151MHz
**$^1$H**

CDCl$_3$

600MHz

![$^1$H NMR spectrum of 1u](image)

**$^{13}$C (APT)**

CDCl$_3$

151MHz

![$^{13}$C NMR spectrum of 1u](image)
$^{19}\text{F}$

CDCl$_3$

659 MHz
$^1$H
CDCl$_3$
600MHz

$^{13}$C (APT)
CDCl$_3$
151MHz
$^{19}\text{F}$

CDCl$_3$

565MHz
$^1$H
CDCl$_3$
400MHz

$^{13}$C (APT)
CDCl$_3$
151MHz
(±)-7

$^{13}$C (APT)
CD$_3$OD
151MHz
$^{1}H$  
CDCl$_3$  
600MHz

$^{13}C$ (APT)  
CDCl$_3$  
151MHz
