Nickel-Mediated Photoreductive Cross Coupling of Carboxylic Acid Derivatives for Ketone Synthesis

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Experimental Procedures

General Information

Solvents and reagents
Unless stated otherwise, all solvents and reagents were obtained from commercial suppliers and used without prior purification. Hantzsch-ester was synthesized following a literature procedure.[1] Solvents used for photoreactions were degassed for 10 minutes by sparging with argon.

Chromatography
Preparative column chromatography was performed using an Isolera One automatic flash chromatography system (Biotage) using either cyclohexane and ethyl acetate (35–70 μm, Acros Organics normal phase) or water and acetonitrile (C18 modified silica, reverse phase). Thin-layer chromatography (TLC) was carried out on silica plates (TLC Silica 60 F254, Merck, Darmstadt). Visualization of the compounds was accomplished by illumination with UV-light of the developed plates and by staining with 2,4-dinitrophenylhydrazine.

NMR spectra
NMR spectra were recorded on a Bruker Avance-III HD (1H-NMR: 300 MHz, 13C-NMR: 75.5 MHz) or a Bruker Avance-II (1H-NMR: 400 MHz, 13C-NMR: 100.6 MHz) spectrometer. Chemical shifts are referenced to residual solvent signals (CDCl3: 7.26 ppm and 77.16 ppm, DMSO-d6: 2.50 ppm and 39.52 ppm for 1H-NMR and 13C-NMR, acetonitrile-d6: 1H-NMR δ/ppm = 1.94, 13C-NMR δ/ppm = 118.7 respectively) and reported in parts per million (ppm) relative to tetramethylsilane (TMS). Multiplicities of NMR signals are abbreviated as follows: br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet and combinations thereof, app = apparent.

UV-Vis spectra
UV-Vis spectra were recorded on an Evolution 201 UV-Visible Spectrophotometer by Thermo Scientific using either a quartz cuvette with either a layer thickness of 10 mm (for dilute solutions) or 1 mm (for concentrated solutions).

Fluorescence spectra
Fluorescence spectra were recorded on an FP-8300 spectrofluorometer by JASCO in a quartz cuvette with a septum-screw cap by Starna (Pfungstadt). The cuvette was flushed with argon before the sample was injected and then degassed with argon for a further minute.

Mass spectra
Electron spray ionization (ESI) mass spectra were recorded on a 1200-series HPLC- system (Agilent-Technologies) with binary pump and integrated diode array detector coupled to an LC/MSD-Trap-XTC-mass spectrometer (Agilent-Technologies) or on a Micromass-Q-TOF-Ultima-3-mass spectrometer (Waters). High resolution mass spectra were recorded on a Micromass-Q-TOF-Ultima-3-mass spectrometer (Waters) with LockSpray-interface and a suitable external calibrant.

Gas chromatography
GC-MS was performed using an Agilent 8890 GC gas chromatograph coupled to a 5977 GC/MS detector and an FID (flame ionization detector), both being connected via a Dean-Switch. As the stationary phase, an Agilent Technologies HP 5MS UI GC column
(30 m x 0.25 mm x 0.25 µm) and helium as a carrier gas were used. Yields were determined by using a calibration curve and the FID.

Photochemical Setup

Reactions were performed using Kessil LED lamps (San Francisco) of the PR160L series and cooling was employed using a fan. Two lamps were used at their full intensity. The set-up was as shown in Figure S1.

Figure S1: Reaction set-up for the photochemical synthesis of ketones.
Optimization of the reaction solvent

To study the influence on different solvents on our reaction we classified the solvents by their Kamlet-Taft parameters\textsuperscript{[2,3]} of polarity ($\pi^*$) and basicity ($\beta$). The parameters of the used solvent are taken from literature\textsuperscript{[4,5]}\textsuperscript{[4,5]}. We found that a high polarity as well as a basicity is needed for the reaction to take place. It is known, that the formation of EDA-complexes and exciplexes is highly dependent on the solvent polarity\textsuperscript{[6]} and that the solvent can also interact with the substrates in EDA-complex formation.\textsuperscript{[7]} The amide group in the solvent also plays a role in the reaction, as seen in figure 2.

![Figure S2: Yield of 6a in dependence of the Kamlet-Taft parameters of the solvent (without the addition of LiBr), black crosses are the projections onto the xy-plane. Very polar solvent (high $\pi^*$) and high basicity ($\beta$) seem to be beneficial.](image)

Compound Characterization

\(N\)-Benzoylsaccharin (1a) was prepared according to general procedure 1b in the main text. The compound was obtained as a colorless solid (700 mg, 2.4 mmol, 80%).

\[
\begin{align*}
&\text{MS (ESI): } m/z \text{ (\%)} = 597.1 \text{ (100) } [2\text{M+Na}]^+ \\
&\text{Mp.} = 151.1–152.3 \, ^\circ\text{C} \quad \text{Lit.}:[^8] 151–152 \, ^\circ\text{C}
\end{align*}
\]

\(1^H\text{-NMR} \text{ (300 MHz, CDCl}_3\text{): } \delta/\text{ppm} = 8.17–8.11 \text{ (m, 1H)}, \ 8.03–8.00 \text{ (m, 2H)}, \ 7.98–7.90 \text{ (m, 1H)}, \ 7.83–7.73 \text{ (m, 2H)}, \ 7.73–7.61 \text{ (m, 1H)}, \ 7.61–7.45 \text{ (m, 2H).}
\]

\(13^C\text{-NMR} \text{ (75 MHz, CDCl}_3\text{): } \delta/\text{ppm} = 166.5, \ 157.5, \ 138.4, \ 136.6, \ 135.0, \ 134.0, \ 132.4, \ 129.6, \ 128.5, \ 126.4, \ 125.5, \ 121.3.
\]

The spectroscopic data are in accordance with literature.[^8]

\(N\)-(4-Methylbenzoyl)saccharin (1b) was prepared according to general procedure 1b in the main text. The compound was obtained as a colorless solid (690 mg, 2.29 mmol, 76%).

\[
\begin{align*}
&\text{MS (ESI): } m/z \text{ (\%)} = 625.1 \text{ (100) } [2\text{M+Na}]^+, \ 324.0 \text{ (35\%)} \ [\text{M+Na}]^+ \\
&\text{Mp.} = 156.1–156.9 \, ^\circ\text{C} \quad \text{Lit.}:[^8] 157–158 \, ^\circ\text{C}
\end{align*}
\]

\(1^H\text{-NMR} \text{ (300 MHz, CDCl}_3\text{): } \delta/\text{ppm} = 8.14 \text{ (dt, } J = 7.5, \ 1.1 \text{ Hz, 1H)}, \ 8.05–7.99 \text{ (m, 2H)}, \ 7.99–7.89 \text{ (m, 1H)}, \ 7.75–7.66 \text{ (m, 2H)}, \ 7.32 \text{ (d, } J = 8.0 \text{ Hz, 2H)}, \ 2.47 \text{ (s, 3H).}
\]

\(13^C\text{-NMR} \text{ (75 MHz, CDCl}_3\text{): } \delta/\text{ppm} = 166.5, \ 157.7, \ 145.4, \ 138.4, \ 136.4, \ 134.9, \ 130.0, \ 129.5, \ 129.2, \ 126.4, \ 125.6, \ 121.3, \ 21.9.
\]

The spectroscopic data are in accordance with literature.[^8]

\(N\)-(4-Methoxybenzoyl)saccharin (1c) was prepared according to general procedure 1b in the main text. The compound was obtained as a colorless solid (670 mg, 2.11 mmol, 70%).

\[
\begin{align*}
&\text{MS (ESI): } m/z \text{ (\%)} = 651.1 \text{ (100) } [2\text{M+Na}]^+, \ 340.0 \text{ (47\%)} \ [\text{M+Na}]^+ \\
&\text{Mp.} = 138.9–140.1 \, ^\circ\text{C} \quad \text{Lit.}:[^8] 143–144 \, ^\circ\text{C}
\end{align*}
\]
The spectroscopic data are in accordance with literature.\cite{8}

**N-(4-Chlorobenzoyl)saccharin (1d)** was prepared according to general procedure 1b in the main text. The compound was obtained as a colorless solid (708 mg, 2.2 mmol, 79%).

\[
\begin{align*}
\text{MS (ESI):} & \quad m/z \text{ (%) = 366.1 (100) [M+Na]^+} \\
\text{Mp.} & \quad 201.2–202.5 \text{ °C Lit.}^{[8]} \quad 202–203 \text{ °C}
\end{align*}
\]

**\(^{1}H\)-NMR (400 MHz, CDCl\(_3\)):** \(\delta /\text{ppm} = 8.14 \text{ (dt, } J = 7.7, 1.0 \text{ Hz, } 1H), 8.04–7.99 \text{ (m, } 2H), 7.93 \text{ (dt, } J = 7.6, 4.3 \text{ Hz, } 1H), 7.77–7.66 \text{ (m, } 2H), 7.55–7.46 \text{ (m, } 2H).\)

**\(^{13}C\)-NMR (101 MHz, CDCl\(_3\)):** \(\delta /\text{ppm} = 165.4, 157.4, 140.6, 138.4, 136.6, 135.0, 131.9, 131.0, 130.7, 128.9, 126.5, 125.4, 121.3.\)

The spectroscopic data are in accordance with literature.\cite{9}

**N-(4-Bromobenzoyl)saccharin (1e)** was prepared according to general procedure 1b in the main text. The compound was obtained as a colorless solid (489 mg, 1.3 mmol, 45%).

\[
\begin{align*}
\text{MS (ESI):} & \quad m/z \text{ (%) = 389.3 (100) [M+Na]^+} \\
\text{Mp.} & \quad 191.2–193.1 \text{ °C Lit.}^{[10]} \quad 191–193 \text{ °C}
\end{align*}
\]

**\(^{1}H\)-NMR (300 MHz, DMSO):** \(\delta /\text{ppm} = 8.16 \text{ (dt, } J = 7.1, 1.2 \text{ Hz, } 1H), 8.06–7.90 \text{ (m, } 3H), 7.90–7.80 \text{ (m, } 2H), 7.77–7.67 \text{ (m, } 2H).\)

**\(^{13}C\)-NMR (75 MHz, DMSO):** \(\delta /\text{ppm} = 167.1, 161.5, 140.0, 135.9, 135.1, 132.2, 131.8, 130.4, 128.2, 127.4, 125.2, 121.6.\)

The spectroscopic data are in accordance with literature.\cite{10}

**N-(3,4-Dimethoxybenzoyl)saccharin (1f)** was prepared according to general procedure 1a in the main text. The compound was obtained as a colorless solid (498 mg, 1.43 mmol, 49%).
**MS (ESI):** m/z (%) = 717.1 (100) [2M+Na]^+

**Mp.** = 202.1–203.4 °C

**1H-NMR** (400 MHz, CDCl₃) δ/ppm = 8.15 (dt, J = 7.6, 1.0 Hz, 1H), 8.02 – 7.97 (m, 2H), 7.91 (ddd, J = 7.6, 5.5, 3.1 Hz, 1H), 7.51 (dd, J = 8.4, 2.1 Hz, 1H), 7.45 (d, J = 2.1 Hz, 1H), 6.93 (d, J = 8.5 Hz, 1H), 3.97 (s, 3H), 3.94 (s, 3H).

**13C-NMR** (101 MHz, CDCl₃) δ/ppm = 165.1, 158.3, 154.7, 149.1, 138.5, 136.3, 134.8, 126.3, 125.6, 124.5, 121.3, 112.5, 110.2, 56.2, 56.2.

The spectroscopic data are in accordance with literature.[11]

**N-(2-(4-(Benzyloxy)-3-methoxybenzoyl))saccharin** (1g) was prepared according to general procedure 1a in the main text. The compound was obtained as a colorless solid (931 mg, 2.20 mmol, 73 %).

**MS (ESI):** m/z (%) = 446.1 (100) [M+Na]^+

**HR-MS (ESI):** 446.0669 ([M+Na]^+ (calc. for C₂₂H₁₇NO₆SNa⁺:446.0669)

**Mp.** = 173.2–174.5 °C

**1H-NMR** (400 MHz, CDCl₃) δ/ppm = 8.16 – 8.09 (m, 1H), 8.01 – 7.94 (m, 2H), 7.90 (ddd, J = 7.6, 5.0, 3.5 Hz, 1H), 7.48 – 7.41 (m, 4H), 7.41 – 7.36 (m, 2H), 7.36 – 7.30 (m, 1H), 6.97 – 6.91 (m, 1H), 5.24 (s, 2H), 3.93 (s, 3H).

**13C-NMR** (101 MHz, CDCl₃) δ/ppm = 165.1, 158.2, 153.9, 149.4, 138.5, 136.28, 135.9, 134.9, 128.8, 128.3, 127.3, 126.3, 126.0, 125.4, 124.7, 121.3, 112.90, 112.03, 71.0, 56.2.

**N-(3-chlorobenzoyl)-saccharin** (1h) was prepared according to general procedure 1a in the main text. The compound was obtained as a colorless solid (642 mg, 1.99 mmol, 66 %).

**MS (ESI):** m/z (%) = 366.1 (100) [M+Na]^+

**HR-MS (ESI):** 343.9765 ([M+Na]^+ (calc. for C₁₄H₈ClNO₄SNa⁺: 343.9760)

**Mp.** = 153.9–154.2 °C
^{1}H\text{-NMR} \ (400 \text{ MHz, CDCl}_3) \ \delta /\text{ppm} = 8.14 \ (dt, \ J = 7.6, \ 1.0 \text{ Hz, 1H}), \ 8.05 - 8.00 \ (m, \ 2H), \ 7.98 - 7.90 \ (m, \ 1H), \ 7.71 \ (t, \ J = 1.9 \text{ Hz, 1H}), \ 7.65 - 7.57 \ (m, \ 2H), \ 7.44 \ (t, \ J = 7.9 \text{ Hz, 1H}).

^{13}C\text{-NMR} \ (101 \text{ MHz, CDCl}_3) \ \delta /\text{ppm} = 165.2, \ 157.3, \ 136.6, \ 135.1, \ 134.6, \ 134.0, \ 133.7, \ 129.8, \ 129.3, \ 127.5, \ 126.6, \ 121.3.

N-(Benzo[d][1,3]dioxole-5-carbonyl)saccharin (1i) was prepared according to general procedure 1b in the main text. The compound was obtained as a colorless solid (803 mg, 2.40 mmol, 80%).

\[
\begin{align*}
\text{MS (ESI): } m/z \ (%)) &= 685.0 \ (100) \ [2M+Na]^+ \\
\text{Mp.} &= 166.8-169.4 \ ^\circ\text{C}
\end{align*}
\]

^{1}H\text{-NMR} \ (400 \text{ MHz, CDCl}_3) \ \delta /\text{ppm} = 8.14 \ (dt, \ J = 7.6, \ 1.0 \text{ Hz, 1H}), \ 8.02 - 7.97 \ (m, \ 2H), \ 7.92 \ (dd, \ J = 7.6, \ 5.2, \ 3.4 \text{ Hz, 1H}), \ 7.46 \ (dd, \ J = 8.2, \ 1.8 \text{ Hz, 1H}), \ 7.27 \ (d, \ J = 1.8 \text{ Hz, 1H}), \ 6.90 \ (d, \ J = 8.2 \text{ Hz, 1H}).

^{13}C\text{-NMR} \ (101 \text{ MHz, CDCl}_3) \ \delta /\text{ppm} = 164.9, \ 157.9, \ 153.2, \ 148.0, \ 138.5, \ 136.3, \ 134.9, \ 127.2, \ 126.4, \ 126.1, \ 125.8, \ 121.3, \ 109.9, \ 108.2, \ 102.4.

The spectroscopic data are in accordance with literature.[^{12}]

N-(Phenylacetyl)saccharin (1j) was prepared according to general procedure 1a in the main text. The compound was obtained as a colorless solid (780 mg, 2.60 mmol, 87%).

\[
\begin{align*}
\text{MS (ESI): } m/z \ (%)) &= 625.0 \ (100) \ [2M+Na]^+ \\
\text{HR-MS (APCI): } m/z \ (%)) &= 324.0308 \ [M+Na]^+ \ (\text{calc. for } C_{15}H_{11}NO_4SNa^+: 324.0306) \\
\text{Mp.} &= 182.1-183.4 \ ^\circ\text{C}
\end{align*}
\]

^{1}H\text{-NMR} \ (400 \text{ MHz, CDCl}_3) \ \delta /\text{ppm} = 8.15 \ (dt, \ J = 7.6, \ 1.0 \text{ Hz, 1H}), \ 8.02 - 7.94 \ (m, \ 2H), \ 7.90 \ (dd, \ J = 7.6, \ 6.0, \ 2.6 \text{ Hz, 1H}), \ 7.35 \ (d, \ J = 4.4 \text{ Hz, 4H}), \ 7.33 - 7.28 \ (m, \ 1H), \ 4.38 \ (s, \ 2H).

^{13}C\text{-NMR} \ (101 \text{ MHz, CDCl}_3) \ \delta /\text{ppm} = 169.1, \ 157.5, \ 138.3, \ 136.5, \ 134.9, \ 131.6, \ 129.7, \ 128.8, \ 127.7, \ 126.4, \ 125.0, \ 121.3, \ 44.1.

N-(3,4,5-Trimethoxybenzoyl)saccharin (1k) was prepared according to general procedure 1b in the main text. The compound was obtained as a yellow solid (507 mg, 1.34 mmol, 40%).

\[
\begin{align*}
\text{MS (ESI): } m/z \ (%)) &= 507.0 \ (100) \ [2M+Na]^+ \\
\text{HR-MS (APCI): } m/z \ (%)) &= 324.0308 \ [M+Na]^+ \ (\text{calc. for } C_{15}H_{11}NO_4SNa^+: 324.0306) \\
\text{Mp.} &= 182.1-183.4 \ ^\circ\text{C}
\end{align*}
\]
**MS (ESI):** m/z (%) = 777.1 (100) [2M+Na]^+ 

**HR-MS (ESI):** 400.0462 ([M+Na]^+ (calc. for C_{17}H_{15}NO_{7}SNa^+: 400.0461) 

Mp. = 137.3-138.4 °C Lit.:\textsuperscript{[13]} 138–139 °C

\textsuperscript{1}H-NMR (400 MHz, CDCl\textsubscript{3}) δ/ppm = 8.09 (dt, J = 7.7, 1.0 Hz, 1H), 8.04 – 7.92 (m, 2H), 7.92 (s, 0H), 7.15 (s, 1H), 6.45 (s, 1H), 3.94 (s, 3H), 3.88 (s, 3H), 3.65 (s, 3H).

\textsuperscript{13}C-NMR (101 MHz, CDCl\textsubscript{3}) δ/ppm = 163.8, 157.2, 154.4, 153.7, 143.4, 138.5, 136.2, 134.8, 125.9, 125.9, 121.3, 113.2, 113.2, 96.4, 56.7, 56.4, 56.2.

\textsuperscript{N}-(3-Phenylpropanoyl)saccharin (1I) was prepared according to general procedure 1a in the main text. The compound was obtained as a colorless solid (790 mg, 2.50 mmol, 83 %).

\begin{center}
\includegraphics[width=0.5\textwidth]{saccharin.png}
\end{center}

**MS (ESI):** m/z (%) = 338.0 (100) [M+H]^+ 

Mp. = 147.2-149.6 °C

\textsuperscript{1}H-NMR (400 MHz, CDCl\textsubscript{3}) δ/ppm = 8.14 (dt, J = 7.7, 1.1 Hz, 1H), 8.03 – 7.95 (m, 2H), 7.91 (ddd, J = 7.6, 5.6, 2.9 Hz, 1H), 7.36 – 7.27 (m, 4H), 7.26 – 7.20 (m, 1H), 3.36 (dd, J = 8.4, 7.0 Hz, 2H), 3.09 (dd, J = 8.4, 7.0 Hz, 2H).

\textsuperscript{13}C-NMR (101 MHz, CDCl\textsubscript{3}) δ/ppm = 170.6, 157.6, 136.5, 135.0, 128.6, 126.8, 126.5, 126.3, 125.0, 121.3, 39.9, 29.5.

The spectroscopic data are in accordance with literature.\textsuperscript{[12]}

\textsuperscript{N}-(4-Diisopropylsulfamoylbenzoyl)saccharin (1m) was prepared according to general procedure 1b in the main text. The compound was obtained as a colorless solid (730 mg, 1.62 mmol, 55 %).

\begin{center}
\includegraphics[width=0.5\textwidth]{saccharin.png}
\end{center}

**MS (ESI):** m/z (%) = 451.1 (100) [M+H]^+ 

**HR-MS (ESI):** 451.1001 [M+H]^+, (calc. for C_{20}H_{22}N_{2}O_{6}S_{2}Na^+: 451.0998) 

Mp. = 172.3-174.5 °C

\textsuperscript{1}H-NMR (400 MHz, CDCl\textsubscript{3}) δ/ppm = 8.13 (dt, J = 7.7, 1.0 Hz, 1H), 8.08 – 7.99 (m, 2H), 7.99 – 7.93 (m, 1H), 7.93 – 7.89 (m, 2H), 7.87 – 7.78 (m, 2H), 3.16 – 3.08 (m, 4H), 1.64 – 1.49 (m, 4H), 0.87 (t, J = 7.4 Hz, 6H).

\textsuperscript{13}C-NMR (101 MHz, CDCl\textsubscript{3}) δ/ppm = 165.5, 157.1, 144.6, 138.3, 136.8, 135.6, 135.2, 129.8, 126.9, 126.6, 125.1, 121.4, 50.0, 22.0, 11.2.
\(N\)-(3,5-bis(Trifluoromethyl)benzoyl)saccharin (1n) was prepared according to general procedure 1b in the main text. The compound was obtained as a colorless solid (920 mg, 2.17 mmol, 72 \%).

\[
\text{MS (ESI): } m/z (\%) = 777.1 \ (100) \ [2\text{M+Na}]^+
\]

\[
\text{HR-MS (ESI): } 868.9879 \ [2\text{M+Na}]^+ \ (\text{calc. for } C_{32}H_{14}F_2N_2S_2Na: 868.9892)
\]

\[
\text{Mp. } = 163.7 - 165.5 \ ^\circ \text{C}
\]

\(1^H\)-NMR (400 MHz, CDCl\(_3\)) \(\delta/\text{ppm} = 8.17 \ (\text{dt, } J = 7.7, 1.0 \text{ Hz, 1H}), 8.13 \ (\text{d, } J = 3.5 \text{ Hz, 3H}), 8.08 - 8.03 \ (\text{m, 2H}), 7.97 \ (\text{ddd, } J = 7.6, 5.7, 2.9 \text{ Hz, 1H}).
\]

\(1^9F\)-NMR (376 MHz, CDCl\(_3\)) \(\delta/\text{ppm} = -64.10\).

\(1^3C\)-NMR (101 MHz, CDCl\(_3\)) \(\delta/\text{ppm} = 164.0, 157.1, 138.3, 137.0, 135.3, 134.4, 133.23 - 131.39 \ (\text{m}), 129.4, 126.9, 126.7, 126.7, 126.7, 124.8, 124.0, 121.5, 121.3.

\(N\)-(6-(Methoxycarbonyl)nicotinoyl)saccharin (1o) was prepared according to general procedure 1b in the main text. The compound was obtained as a colorless solid (360 mg, 1.04 mmol, 38 \%).

\[
\text{MS (ESI): } m/z (\%) = 347.0 \ (100) \ [\text{M+H}]^+
\]

\[
\text{HR-MS (ESI): } 369.0149 \ [\text{M+H}]^+ \ (\text{calc. for } C_{15}H_{10}N_2O_6SNa: 369.0157)
\]

\[
\text{Mp. } = 158.8 - 160.1 \ ^\circ \text{C}
\]

\(1^H\)-NMR (400 MHz, CDCl\(_3\)) \(\delta/\text{ppm} = 8.98 \ (\text{d, } J = 2.2 \text{ Hz, 1H}), 8.26 \ (\text{d, } J = 7.8 \text{ Hz, 1H}), 8.18 - 8.10 \ (\text{m, 2H}), 8.04 \ (\text{d, } J = 3.0 \text{ Hz, 2H}), 7.95 \ (\text{ddd, } J = 7.9, 5.0, 3.0 \text{ Hz, 1H}), 4.05 \ (\text{s, 3H}).
\]

\(1^3C\)-NMR (101 MHz, CDCl\(_3\)) \(\delta/\text{ppm} = 164.6, 164.2, 157.0, 150.8, 149.5, 138.3, 137.8, 137.0, 135.3, 131.3, 126.7, 124.8, 124.4, 121.5, 53.3.

\(N\)-(4-(Dimehtylamino)benzoyl)saccharin (1p) was prepared according to general procedure 1a in the main text. The compound was obtained as a bright yellow solid (697 mg, 2.12 mmol, 70 \%).
**MS (ESI):** m/z (%) = unstable, only the corresponding acid can be detected due to hydrolysis in the standard experimental configuration

**HR-MS (ESI):** 353.0561 [M+Na]$^+$ (calc. for C$_{16}$H$_{14}$N$_2$NaO$_4$S$^+$: 353.0566)

**Mp.** = 202.3 °C (decomposition)

**$^1$H-NMR** (600 MHz, CDCl$_3$) $\delta$/ppm = 8.13 (dt, $J = 7.8, 0.9$ Hz, 1H), 8.01 – 7.92 (m, 2H), 7.89 (td, $J = 7.4, 1.4$ Hz, 1H), 7.83 – 7.77 (m, 2H), 6.69 – 6.63 (m, 2H), 3.10 (s, 6H).

**$^{13}$C-NMR** (151 MHz, CDCl$_3$) $\delta$/ppm = 164.0, 158.6, 154.7, 138.7, 135.8, 134.6, 133.5, 126.5, 126.1, 121.2, 118.2, 110.7, 40.1.

**N-(4-Methyloxobutanoate)saccharin (1q)** was prepared according to general procedure 1a in the main text. The compound was obtained as a yellow solid (713 mg, 2.4 mmol, 80%).

![N-(4-Methyloxobutanoate)saccharin (1q)](image)

**MS (ESI):** m/z (%) = 320.0 (100) [M+Na]$^+$

**HR-MS (ESI):** 320.0187 [M+Na]$^+$ (calc. for C$_{12}$H$_{11}$NO$_6$SNa$^+$: 320.0199)

**Mp.** = 156.2 – 157.4 °C

**$^1$H-NMR** (400 MHz, CDCl$_3$) $\delta$/ppm = 8.17 (dt, $J = 7.6, 1.0$ Hz, 1H), 8.02 – 7.95 (m, 2H), 7.92 (ddd, $J = 7.6, 6.2, 2.4$ Hz, 1H), 3.72 (s, 3H), 3.38 (t, $J = 6.5$ Hz, 2H), 2.79 (t, $J = 6.5$ Hz, 2H).

**$^{13}$C-NMR** (101 MHz, CDCl$_3$) $\delta$/ppm = 172.1, 170.1, 157.7, 138.3, 136.5, 135.0, 126.4, 125.0, 121.3, 52.1, 33.3, 27.6.

**N-(3,3-Dimethylacryloyl)saccharin (1r)** was prepared according to general procedure 1a in the main text. The compound was obtained as a yellow solid (406 mg, 1.53 mmol, 51%).

![N-(3,3-Dimethylacryloyl)saccharin (1r)](image)

**MS (ESI):** [m/z] = 288.1 (100%) [M+Na]$^+$.

**HR-MS (ESI):** 266.0479. [M+H]$^+$ (calc. for C$_{12}$H$_{12}$NO$_4$S$^+$: 266.0482)

**Mp.** = 160.8–161.9 °C.

**$^1$H-NMR** (300 MHz, CDCl$_3$): $\delta$/ppm = 8.21–8.08 (m, 1H), 7.98–7.93 (m, 2H), 7.91–7.86 (m, 1H), 6.83 (s, 1H), 2.31 (s, 3H), 2.08 (s, 3H).

**$^{13}$C-NMR** (75 MHz, CDCl$_3$): $\delta$/ppm = 166.1, 162.6, 157.7, 138.3, 136.3, 134.9, 126.2, 125.4, 121.1, 115.9, 28.8, 22.3.
2-[(Cyclohexylcarbonyl)oxy]-1H-isoindole-1,3(2H)-dione (5a) was prepared according to general procedure 2a in the main text. The compound was obtained as a colorless solid (1.50 g, 5.49 mmol, 98%).

![Chemical Structure](image)

**MS (ESI):** m/z (%) = 296.1 (100) [M+Na]^+

**Mp.** = 69.1–70.4 °C  
Lit.:[14] 69.1–70.3 °C

**1H-NMR** (300 MHz, CDCl₃): δ/ppm = 7.92–7.86 (m, 2H), 7.82–7.76 (m, 2H), 2.75 (tt, J = 10.9, 3.7 Hz, 1H), 2.19–2.04 (m, 2H), 1.90–1.79 (m, 2H), 1.73–1.61 (m, 2H), 1.47–1.26 (m, 4H).

**13C-NMR** (75 MHz, CDCl₃): δ/ppm = 171.8, 162.1, 134.7, 129.0, 123.9, 40.5, 28.8, 25.5, 25.0. The spectroscopic data are in accordance with literature.[14]

2-[(2-Methylbutylcarbonyl)oxy]-1H-isoindole-1,3(2H)-dione (5b) was prepared according to general procedure 2a in the main text. The compound was obtained as a colorless solid (630 mg, 2.3 mmol, 82%).

![Chemical Structure](image)

**MS (ESI):** m/z (%) = 284.1(100) [M+Na]^+

**Mp.** = 29.6–31.3 °C  
Lit.:[14] 29.8–31.2 °C

**1H-NMR** (300 MHz, CDCl₃): δ/ppm = 7.87–7.81 (m, 2H), 7.77–7.70 (m, 2H), 2.89–2.71 (m, 1H, CH), 1.88–1.71 (m, 1H), 1.65–1.39 (m, 3H), 1.33 (d, J = 7.0 Hz, 3H), 0.95 (t, J = 7.2 Hz, 3H).

**13C NMR** (75 MHz, CDCl₃): δ/ppm = 172.9, 162.1, 134.7, 129.0, 123.9, 36.9, 35.8, 20.1, 17.0, 13.9. The spectroscopic data are in accordance with literature.[15]

2-[(Pentylcarbonyl)oxy]-1H-isoindole-1,3(2H)-dione (5c). was prepared according to general procedure 2a in the main text. The compound was obtained as a colorless solid (1.89 g, 7.23 mmol, 84%).

![Chemical Structure](image)

**MS (ESI):** m/z (%) = 262.1(100) [M+H]^+

**Mp.** = 40.9–42.8.3 °C  
Lit.:[14] 41.2–42.9 °C
**1H-NMR** (400 MHz, CDCl₃): δ/ppm 7.90–7.86 (m, 2H), 7.81–7.76 (m, 2H), 2.68 (t, J = 7.4 Hz, 2H), 1.82 (q, J = 7.6 Hz, 2H), 1.48–1.40 (m, 4H), 0.95 (t, J = 7.4 Hz, 3H).

**13C-NMR** (101 MHz, CDCl₃): δ/ppm 169.8, 162.1, 134.8, 129.1, 139.9, 31.0, 24.4, 22.2, 13.8.

The spectroscopic data are in accordance with literature.[14]

2-[(4-Methoxyphenylmethylcarbonyl)oxy]-1H-isooindole-1,3(2H)-dione (5d) was prepared according to general procedure 2a in the main text. The compound was obtained as a colorless solid (980 mg, 3.2 mmol, 57%).

![Chemical structure of 2-[(4-Methoxyphenylmethylcarbonyl)oxy]-1H-isooindole-1,3(2H)-dione](image)

**MS (ESI):** m/z (%) = 334.3 (100) [M+ Na]⁺

**Mp.** = 102.2–103.1°C  Lit.:[16] 102.0–103.9°C

**1H-NMR** (300 MHz, CDCl₃): δ/ppm = 7.90–7.80 (m, 2H), 7.77–7.70 (m, 2H), 7.35–7.24 (m, 2H), 6.95–6.82 (m, 2H), 3.94 (s, 2H), 3.78 (s, 3H).

**13C NMR** (75 MHz, CDCl₃): δ/ppm = 168.0, 161.9, 159.2, 134.9, 130.4, 128.8, 124.0, 123.6, 114.3, 56.3, 36.8.

The spectroscopic data are in accordance with literature.[16]

2-[(Phenoxyethylcarbonyl)oxy]-1H-isooindole-1,3(2H)-dione (5e) was prepared according to general procedure 2b in the main text. The compound was obtained as a colorless oil (587 mg, 1.97 mmol, 99%).

![Chemical structure of 2-[(Phenoxyethylcarbonyl)oxy]-1H-isooindole-1,3(2H)-dione](image)

**MS (ESI):** m/z (%) = 298.0 (100) [M+H]⁺

**1H-NMR** (400 MHz, CDCl₃): δ/ppm = 7.96 – 7.86 (m, 2H), 7.86 – 7.74 (m, 2H), 7.41 – 7.29 (m, 2H), 7.10 – 6.96 (m, 3H), 5.04 (s, 2H).

**13C-NMR** (101 MHz, CDCl₃) δ/ppm = 165.6, 161.5, 157.3, 135.0, 129.8, 128.8, 124.2, 122.5, 114.9, 63.4.

The spectroscopic data are in accordance with literature.[17]

2-[(Pentanoyl)oxy]-1H-isooindole-1,3(2H)-dione (5f) was prepared according to general procedure 2b in the main text. The compound was obtained as a colorless oil (487 mg, 1.97 mmol, 99 %)
**MS (ESI):** m/z (%) = 270.1 (100) [M+Na]^+

^1^H-NMR (400 MHz, CDCl\textsubscript{3}) δ/ppm = 7.92 – 7.84 (m, 2H), 7.83 – 7.75 (m, 2H), 2.67 (t, J = 7.5 Hz, 2H), 1.84 – 1.72 (m, 2H), 1.55 – 1.41 (m, 2H), 0.97 (t, J = 7.4 Hz, 3H).

^1^3^C-NMR (101 MHz, CDCl\textsubscript{3}) δ/ppm = 169.7, 162.0, 134.7, 129.0, 124.0, 30.7, 26.7, 22.0, 13.6.

The spectroscopic data are in accordance with literature.\textsuperscript{[18]}

2-[(Lauroyl)oxy]-1\textit{H}-isoindole-1,3(2\textit{H})-dione (5g) was prepared according to general procedure 2b in the main text. The compound was obtained as a colorless oil (487 mg, 1.99 mmol, 99 %)

**MS (ESI):** m/z (%) = 368.2 (100) [M+ Na]^+

**HR-MS:** 346.2013 [M+H]^+ (calc for C\textsubscript{20}H\textsubscript{28}NO\textsubscript{4}+: 346.2013)

Mp. = 54.6–56.7 °C

^1^H-NMR (400 MHz, CDCl\textsubscript{3}) δ/ppm = 7.88 (dd, J = 5.5, 3.1 Hz, 2H), 7.78 (dd, J = 5.5, 3.1 Hz, 2H), 2.65 (t, J = 7.5 Hz, 2H), 1.78 (p, J = 7.5 Hz, 2H), 1.49 – 1.38 (m, 2H), 1.38 – 1.14 (m, 1H), 0.92 – 0.83 (m, 3H).

^1^3^C-NMR (101 MHz, CDCl\textsubscript{3}) δ/ppm = 169.7, 162.0, 134.7, 129.0, 124.0, 31.9, 31.0, 29.6, 29.4, 29.3, 29.1, 28.8, 24.7, 22.7, 14.1.

2-[(3-Oxobutylcarbonyl)oxy]-1\textit{H}-isoindole-1,3(2\textit{H})-dione (5h) was prepared according to general procedure 2b in the main text. The compound was obtained as a colorless solid (513 mg, 1.96 mmol, 98 %).

**MS (ESI):** m/z (%) = 262.1 (100) [M+ H]^+

Mp. = 90.8–91.6 °C

^1^H-NMR (400 MHz, CDCl\textsubscript{3}) δ/ppm = 7.94 – 7.84 (m, 2H), 7.80 (dd, J = 5.5, 3.1 Hz, 2H), 3.02 – 2.95 (m, 2H), 2.95 – 2.89 (m, 2H), 2.24 (s, 3H).

^1^3^C-NMR (101 MHz, CDCl\textsubscript{3}) δ/ppm = 205.0, 169.2, 161.8, 134.8, 128.9, 124.0, 37.6, 29.7, 25.1.

The spectroscopic data are in accordance with literature.\textsuperscript{[19]}
2-[(1-\textit{tert}-Butoxycarbonyl)pyrrolidinylcarbonyloxy]-1\textit{H}-isoindole-1,3(2\textit{H})-dione (5i) was prepared according to general procedure 2a in the main text. The compound was obtained as a colorless solid (1.38 g, 3.8 mmol, 69%).

\textbf{MS (ESI):} m/z (\%) = 743.3 (100) [2M+Na]^+

\textbf{Mp.:} 70.1–70.9 °C

\textbf{\textsuperscript{1}H-NMR} (300 MHz, CDCl\textsubscript{3}): δ/ppm = 7.91–7.86 (m, 2H), 7.80 (m, 2H, m, 2H), 4.62 (dd, \(J = 8.6, 3.9\) Hz, 1H), 3.69–3.43 (m, 2H), 2.55–2.28 (m, 2H), 2.20–1.86 (m, 2H), 1.52 (s, 9H).

\textbf{\textsuperscript{13}C-NMR} (75 MHz, CDCl\textsubscript{3}): δ/ppm = 169.7, 161.7, 153.5, 134.8, 128.9, 124.0, 81.1, 57.2, 46.3, 31.4, 28.1, 23.6.

The spectroscopic data are in accordance with literature.\cite{20}

2-[(Tetrahydrofuran-2-ylcarbonyloxy]-1\textit{H}-isoindole-1,3(2\textit{H})-dione (5j) was prepared according to general procedure 2a in the main text. The compound was obtained as a colorless solid (700 mg, 2.7 mmol, 48%).

\textbf{MS (ESI):} m/z (\%) = 284.1(100) [M+Na]^+

\textbf{Mp.} = 56.6–57.8 °C

\textbf{\textsuperscript{1}H-NMR}, COSY (300 MHz, CDCl\textsubscript{3}): δ/ppm = 7.96–7.86 (m, 2H), 7.86–7.77 (m, 2H), 4.89 (dd, \(J = 8.3, 5.2\) Hz, 1H), 4.18–3.95 (m, 2H), 2.56–2.31 (m, 2H), 2.22–1.92 (m, 2H).

\textbf{\textsuperscript{13}C-NMR}, HSQC, HMBC (75 MHz, CDCl\textsubscript{3}): δ/ppm = 169.8, 161.7, 134.8, 128.9, 124.0, 75.0, 69.9, 30.9, 25.1.

The spectroscopic data are in accordance with literature.\cite{20}

2-[(1-(4-Chlorobenzoyl)-5-methoxy-methyl-1\textit{H}-indol-3-yl)carbonyloxy]-1\textit{H}-isoindole-1,3(2\textit{H})-dione (5k) was prepared according to general procedure 2b in the main text. The compound was obtained as a colorless solid (879 mg, 1.75 mmol, 87%).

\textbf{MS (ESI):} m/z (\%) = 503.1(100) [M+H]^+
Mp. = 170.1–171.8°C  Lit.:[21] 170–172°C

$^1$H-NMR (400 MHz, DMSO) δ/ppm = 8.03 – 7.96 (m, 2H), 7.94 (dt, J = 4.9, 3.8 Hz, 2H), 7.73 – 7.61 (m, 4H), 7.18 (d, J = 2.5 Hz, 1H), 6.96 (d, J = 9.0 Hz, 1H), 6.75 (dd, J = 9.0, 2.6 Hz, 1H), 4.34 (s, 2H), 3.81 (s, 3H), 2.30 (s, 3H).

$^{13}$C-NMR (101 MHz, DMSO) δ/ppm = 168.5, 168.4, 162.3, 156.2, 138.3, 136.6, 136.0, 134.4, 131.7, 130.7, 130.4, 129.6, 128.7, 124.5, 115.2, 112.4, 111.2, 101.8, 55.9, 26.7, 13.7.

The spectroscopic data are in accordance with literature.[22]

2-[(RS)-1-[4-(2-Methylpropyl)phenyl]ethyloxy]-1H-isindole-1,3(2H)-dione (5l) was prepared according to general procedure 2a in the main text. The compound was obtained as a colorless solid (937 mg, 2.5 mmol, 89%).

![Chemical structure](image)

**MS (ESI):** m/z (%) = 374.1 (100) [M+Na]+

Mp. = 59.6–60.7 °C

$^1$H-NMR (300 MHz, CDCl$_3$): δ/ppm = 7.90–7.86 (m, 2H), 7.82–7.78 (m, 2H), 7.36–7.30 (m, 2H), 7.23–7.14 (m, 2H), 4.12 (q, J = 7.2 Hz, 1H), 2.50 (d, J = 7.2 Hz, 2H), 1.89 (dp, J = 13.5, 6.7 Hz, 1H), 1.69 (d, J = 7.2 Hz, 3H), 0.93 (d, J = 6.6 Hz, 6H).

$^{13}$C NMR (75 MHz, CDCl$_3$): δ/ppm = 171.0, 161.9, 141.3, 135.6, 134.7, 129.6, 129.0, 127.3, 123.9, 45.0, 42.6, 30.2, 22.4, 19.0.

The spectroscopic data are in accordance with literature.[23]

1,3-Dioxoisoindolin-2-yl-3-(thiophen-2-yl)propanoate (5m) was prepared according to general procedure 2b in the main text. The compound was obtained as a colorless solid (490 mg, 1.6 mmol, 81%).

![Chemical structure](image)

**MS (ESI):** m/z (%) = 302.0 (100) [M+H]+

Mp. = 102.9–104.7 °C

$^1$H-NMR (400 MHz, CDCl$_3$) δ/ppm = 7.88 (dd, J = 5.5, 3.1 Hz, 2H), 7.83 – 7.74 (m, 2H), 7.17 (dd, J = 5.1, 1.2 Hz, 1H), 6.95 (dd, J = 5.1, 3.4 Hz, 1H), 6.91 (dt, J = 3.5, 1.0 Hz, 1H), 3.31 (ddd, J = 8.0, 6.7, 0.8 Hz, 2H), 3.09 – 3.00 (m, 2H).

$^{13}$C-NMR (101 MHz, CDCl$_3$) δ/ppm = 168.5, 161.9, 141.4, 134.8, 128.9, 127.1, 125.3, 124.0, 33.0, 24.8.

The spectroscopic data are in accordance with literature.[24]
[(1Z-Docos-13-enoyloxy)-1H-isoindole-1,3(2H)-dione (5n) was prepared according to general procedure 2b in the main text. The compound was obtained as a colorless oil (1.379 g, 2.85 mmol, 95%).

MS (ESI): \( m/z \) (\%) = 484.1 (100) \([M+H]^+\)

HRMS (ESI): 484.3425 \([M+H]^+\) (calculated for \( C_{30}H_{46}NO_4^+ \): 484.3421)

\(^1\)H-NMR (300 MHz, CDCl\(_3\)): \( \delta/\text{ppm} = 7.89\) (dd, \( J = 5.5, 3.1 \) Hz, 2H), 7.78 (dd, \( J = 5.5, 3.1 \) Hz, 2H), 5.34 (t, \( J = 4.9 \) Hz, 2H), 2.66 (t, \( J = 7.5 \) Hz, 2H), 2.01 (q, \( J = 6.2 \) Hz, 2H), 1.78 (p, \( J = 7.4 \) Hz, 4H), 1.49–1.18 (m, 28H), 0.94–0.76 (m, 3H).

\(^13\)C-NMR (75 MHz, CDCl\(_3\)): \( \delta/\text{ppm} = 169.8, 162.2, 134.9, 130.0, 129.1, 124.1, 32.0, 31.1, 29.9, 29.7, 29.7, 29.5, 29.5, 29.3, 29.0, 27.3, 24.8, 22.8, 14.3.

2-[(1H-Indol-3-ylpropyl)oxy]-1H-isoindole-1,3(2H)-dione (5o) was prepared according to general procedure 2b in the main text. The compound was obtained as a colorless oil (1983 mg, 2.94 mmol, 98%).

MS (ESI): \( m/z \) (\%) = 335.1 (100%) \([M+H]^+\).

\( \text{Mp.} = 155.2–157.0 \) °C    Lit.: 155–157 °C.[25]

\(^1\)H-NMR (300 MHz, CDCl\(_3\)): \( \delta/\text{ppm} = 8.05\) (s, 1H), 7.96–7.87 (m, 2H), 7.84–7.73 (m, 2H), 7.38 (dt, \( J = 8.1, 1.0 \) Hz, 1H), 7.23 (dd, \( J = 7.0, 1.3 \) Hz, 1H), 7.18 (dd, \( J = 5.6, 1.4 \) Hz, 1H), 7.15 (dd, \( J = 4.3, 1.5 \) Hz, 1H), 3.36–3.16 (m, 2H), 3.15–2.95 (m, 2H).

\(^13\)C-NMR, HSQC, HMBC (75 MHz, CDCl\(_3\)): \( \delta/\text{ppm} = 169.4, 162.1, 136.4, 134.9, 129.1, 127.1, 124.1, 122.3, 122.1, 119.7, 118.6, 113.8, 111.4, 32.0, 20.5.

The spectroscopic data are in accordance with literature.[25]

2-[(3-Phenylpropanoyl)oxy]-1H-isoindole-1,3(2H)-dione (5p) was prepared according to general procedure 2b in the main text. The compound was obtained as a colorless solid (877 mg, 2.97 mmol, 99%).

MS (ESI): \([m/z]\) = 296.1 (100%) \([M+H]^+\).

\( \text{Mp.} = 82.4–83.8 \) °C    Lit.: 84–85 °C.[26]
1H-NMR (300 MHz, CDCl3): δ/ppm = 7.90 (dd, J = 5.5, 3.1 Hz, 2H), 7.79 (dd, J = 5.5, 3.1 Hz, 2H), 7.39–7.29 (m, 2H), 7.28–7.24 (m, 3H), 3.11 (ddd, J = 8.8, 7.0, 1.8 Hz, 2H), 2.99 (ddd, J = 8.7, 7.0, 1.8 Hz, 2H).

13C-NMR (75 MHz, CDCl3): δ/ppm = 169.0, 162.0, 139.3, 134.9, 128.9, 128.4, 126.9, 124.1, 32.8, 30.7.

The spectroscopic data are in accordance with literature.[26]

1,3-dioxoisindolin-2-yl(1R)-4-((3R,5S,7R,8R,9S,10S,12S,13R,14S,17R)-3,7,12-trihydroxy-10,13-dimethylhexadecahydro-1H-cyclopenta[a]phenanthren-17-yl)pentanoate (5q) was prepared according to general procedure 2a in the main text. The compound was obtained as a colorless solid (1.402 mg, 2.56 mmol, 85%).

MS (ESI): [m/z] = 518.3 (100%) [M-H2O-OH]+, 576.3 (6%) [M+Na]+.

Mp. = 102.5–104.1 °C  Lit.: 99–105 °C.[27]

1H-NMR (400 MHz, CDCl3) δ/ppm = 7.88 (dd, J = 5.5, 3.1 Hz, 2H), 7.78 (dd, J = 5.5, 3.1 Hz, 2H), 3.98 (d, J = 3.1 Hz, 1H), 3.84 (q, J = 2.8 Hz, 1H), 3.45 (tt, J = 11.0, 4.3 Hz, 1H), 2.83–2.67 (m, 5H), 2.61 (dt, J = 15.7, 7.8 Hz, 1H), 2.31–2.14 (m, 2H), 2.04–1.27 (m, 20H), 1.18–0.90 (m, 4H), 0.88 (s, 3H), 0.70 (s, 3H).

13C-NMR (101 MHz, CDCl3) δ/ppm = 170.1, 162.0, 134.7, 129.0, 124.0, 73.0, 72.0, 68.5, 46.9, 46.5, 41.7, 41.5, 39.5, 35.3, 35.1, 34.8, 34.6, 30.6, 28.1, 27.5, 26.4, 23.2, 22.5, 17.3, 12.5.

The spectroscopic data are in accordance with literature.[27]

tert-Butyl (1,3-dioxoisindolin-2-yl) succinate (5r) was prepared according to general procedure 2b in the main text. The compound was obtained as a colorless solid (620 mg, 1.98 mmol, 99%).

MS (ESI): [m/z] = 342.1 (100%) [M+Na]+.

Mp. = 104.2–105.9 °C

1H-NMR (300 MHz, CDCl3) δ/ppm = 7.91–7.83 (m, 2H), 7.81–7.74 (m, 2H), 2.95 (t, J = 7.2 Hz, 2H), 2.71–2.65 (m, 2H), 1.45 (s, 9H).

13C-NMR (75 MHz, CDCl3) δ/ppm = 170.1, 168.8, 161.8, 134.8, 128.9, 124.0, 81.5, 30.0, 28.0, 26.5.
The spectroscopic data are in accordance with literature.[28]

1,3-dioxoisooindolin-2-yl pivalate (5s) was prepared according to general procedure 2b. The compound was obtained as a colorless solid (460 mg, 1.86 mmol, 93%).

MS (ESI): [m/z] = 248.0 (100%) [M+H]+.

Smb. = 78.0–79.1 °C  Lit.: 76.5–79.3 °C[14]

1H-NMR (400 MHz, CDCl3): δ/ppm = 7.87 (dd, J = 5.5, 3.1 Hz, 2H), 7.77 (dd, J = 5.5, 3.1 Hz, 2H), 1.43 (s, 9H).

13C-NMR (101 MHz, CDCl3): δ/ppm = 174.5, 162.2, 134.8, 129.1, 124.0, 38.5, 27.1.

The spectroscopic data are in accordance with literature.[14]
Cyclohexylphenylmethanone (6a) was prepared according to general procedure 3 in the main text. The product was obtained as a colorless oil (60 mg, 0.32 mmol, 88%).

**MS (ESI):** m/z (%) = 189.1 (100) [M+H]+

$^1$H-NMR (400 MHz, CDCl$_3$) δ/ppm = 7.98 – 7.88 (m, 2H), 7.57 – 7.49 (m, 1H), 7.49 – 7.39 (m, 2H), 3.25 (tt, $J = 11.4$, 3.3 Hz, 1H), 1.94 – 1.78 (m, 4H), 1.73 (dtt, $J = 12.7$, 3.3, 1.5 Hz, 1H), 1.59 – 1.19 (m, 5H).

$^{13}$C-NMR (101 MHz, CDCl$_3$) δ/ppm = 203.8, 136.4, 132.7, 128.6, 128.3, 45.6, 29.4, 26.0, 25.9.

The spectroscopic data are in accordance with literature.\[29\]

2-Methyl-1-phenylpentan-1-one (6b) was prepared according to general procedure 3 in the main text. The product was obtained as a colorless oil (41 mg, 0.23 mmol, 58%).

**MS (ESI):** m/z (%) = 177.1 (100) [M+H]+

$^1$H-NMR, COSY (400 MHz, CDCl$_3$): δ/ppm = 8.00–7.96 (m, 2H), 7.60–7.55 (m, 1H), 7.52–7.46 (m, 2H), 3.51 (h, $J = 6.8$ Hz, 1H), 1.81 (dtt, $J = 12.7$, 8.5, 6.3 Hz, 1H), 1.51–1.29 (m, 3H), 1.21 (d, $J = 6.8$ Hz, 3H), 0.93 (t, $J = 7.2$ Hz, 3H).

$^{13}$C-NMR, HSQC, HMBC (101 MHz, CDCl$_3$): δ/ppm = 204.6 (CO), 136.8 (C-1), 132.8 (C-4), 128.6 (2C, C-3, 5), 128.3 (2C, C-2, 6), 40.3 (COCH$_2$), 35.9 (C-3'), 20.6 (C-4'), 17.2 (C1-CH$_3$), 14.2 (C-5').

The spectroscopic data are in accordance with literature.\[30\]

Valerophenone (6c) was prepared was prepared according to general procedure 3 in the main text. The product was obtained as a colorless oil (49 mg, 0.30 mmol, 76%).

**MS (ESI):** m/z (%) = 163.1 (100) [M+H]+

$^1$H-NMR (400 MHz, CDCl$_3$) δ/ppm = 7.99 – 7.91 (m, 2H), 7.57 – 7.49 (m, 1H), 7.49 (tt, $J = 8.1$, 1.0 Hz, 2H), 2.95 (td, $J = 7.5$, 1.1 Hz, 2H), 1.71 (p, $J = 7.5$ Hz, 2H), 1.47 – 1.33 (m, 2H), 0.94 (t, $J = 7.3$ Hz, 3H).

$^{13}$C-NMR (101 MHz, CDCl$_3$) δ/ppm = 200.5, 137.1, 132.89 128.5, 128.1, 38.3, 26.5, 22.5, 14.0.

The spectroscopic data are in accordance with literature.\[31\]

Caprophenone (6d) was prepared according to general procedure 3 in the main text. The product was obtained as a colorless solid (47 mg, 0.27 mmol, 67%).
MS (ESI): m/z (%) = 177.1 (100) [M+H]^+

Mp. = 19.8–20.2 °C    Lit.:[32] 23–24 °C

^1H-NMR, COSY (300 MHz, CDCl₃): δ/ppm = 8.03–7.92 (m, 2H), 7.62–7.52 (m, 1H), 7.52–7.43 (m, 2H), 3.03–2.92 (m, 2H), 1.81–1.70 (m, 2H), 1.47–1.33 (m, 4H), 1.02–0.84 (m, 3H).

^13C-NMR, HSQC, HMBC (75 MHz, CDCl₃): δ/ppm = 200.6, 137.1, 132.9, 128.6, 128.1, 38.6, 31.6, 24.0, 22.6, 14.0.

The spectroscopic data are in accordance with literature.[33]

Dodecanophenone (6e) was prepared according to general procedure 3 in the main text. The product was obtained after reverse-phase-flash column chromatography as a colorless solid (65 mg, 0.25 mmol, 63%).

MS (ESI): m/z (%) = 261.2 (100) [M+H]^+

Mp. = 41.6–43.0 °C    Lit.:[34] 41–42 °C

^1H-NMR (400 MHz, CDCl₃) δ/ppm = 8.00 – 7.92 (m, 2H), 7.59 – 7.51 (m, 1H), 7.50 – 7.41 (m, 2H), 2.99 – 2.93 (m, 2H), 1.73 (p, J = 7.4 Hz, 2H), 1.42 – 1.20 (m, 16H), 0.92 – 0.83 (m, 3H).

^13C-NMR (101 MHz, CDCl₃) δ/ppm = 200.7, 137.1, 132.9, 128.6, 128.1, 38.7, 31.9, 29.6, 29.5, 29.4, 29.4, 24.4, 22.7, 14.2.

The spectroscopic data are in accordance with literature.[34]

1,3-Diphenylpropan-1-one (6f) was prepared according to general procedure 3 in the main text. The product was obtained as a colorless oil (61 mg, 0.29 mmol, 72%).

MS (ESI): [m/z] = 211.1 (100%) [M+H]^+.

^1H-NMR (300 MHz, CDCl₃): δ/ppm = 8.06–7.91 (m, 2H), 7.61–7.53 (m, 1H), 7.51–7.42 (m, 2H), 7.35–7.29 (m, 4H), 7.24–7.16 (m, 1H), 3.40–3.23 (m, 2H), 3.14–2.97 (m, 2H).

^13C-NMR (75 MHz, CDCl₃): δ/ppm = 199.3, 141.4, 136.9, 133.2, 128.7, 128.6, 128.5, 128.1, 126.2, 40.6, 30.2.

The spectroscopic data are in accordance with literature.[35]
1-Phenylpentane-1,4-dione (6g) was prepared according to general procedure 3 in the main text. The product was obtained after flash column chromatography as a colorless oil (38 mg, 0.22 mmol, 54%).

MS (ESI): m/z (%) = 177.1 (100) [M+H]^+

$^1$H-NMR (400 MHz, CDCl$_3$): $\delta$/ppm = 8.03 – 7.95 (m, 2H), 7.62 – 7.53 (m, 1H), 7.52 – 7.43 (m, 2H), 3.29 (t, $J$ = 6.8 Hz, 2H), 2.90 (t, $J$ = 6.3 Hz, 2H), 2.27 (s, 3H).

$^{13}$C-NMR (101 MHz, CDCl$_3$): $\delta$/ppm = 207.4, 198.6, 136.7, 133.3, 128.7, 128.2, 37.1, 32.5, 30.2.

The spectroscopic data are in accordance with literature.$^{[36]}$

3-(1H-indol-3-yl)-1-phenylpropan-1-one (6h) was prepared according to general procedure 3 in the main text. The product was obtained as a colorless oil (53 mg, 0.21 mmol, 53%).

MS (ESI): [m/z] = 250.0 (100%) [M+H]^+

$^1$H-NMR (300 MHz, CDCl$_3$): $\delta$/ppm = 8.02 (s, 1H), 8.01–7.92 (m, 2H), 7.70–7.61 (m, 1H), 7.60–7.51 (m, 1H), 7.51–7.42 (m, 2H), 7.41–7.34 (m, 1H), 7.28–7.10 (m, 2H), 7.08–7.01 (m, 1H), 3.52–3.34 (m, 2H), 3.3–3.06 (m, 2H).

$^{13}$C-NMR, HSQC, HMBC (75 MHz, CDCl$_3$): $\delta$/ppm = 200.1, 137.1, 136.4, 133.1, 128.7, 128.2, 127.4, 122.1, 121.7, 119.4, 118.8, 115.5, 111.3, 39.5, 19.8.

The spectroscopic data are in accordance with literature.$^{[37]}$

1-Phenyl-3-(thiophen-2-yl)-propan-1-one (6i) was prepared according to general procedure 3 in the main text. The product was obtained as a colorless solid (58 mg, 0.27 mmol, 67%).

MS (ESI): m/z (%) = 217.1 (100) [M+H]^+

Mp. = 54.3–56.1 °C  Lit.:$^{[38]}$ 54–56 °C

$^1$H-NMR (400 MHz, CDCl$_3$): $\delta$/ppm = 8.02 – 7.93 (m, 2H), 7.61 – 7.53 (m, 1H), 7.52 – 7.43 (m, 2H), 7.13 (dd, $J$ = 5.1, 1.2 Hz, 1H), 6.93 (dd, $J$ = 5.1, 3.4 Hz, 1H), 6.87 (dq, $J$ = 3.3, 1.0 Hz, 1H), 3.41 – 3.34 (m, 2H), 3.30 (ddt, $J$ = 7.7, 5.5, 1.2 Hz, 2H).

$^{13}$C-NMR (101 MHz, CDCl$_3$): $\delta$/ppm = 198.6, 143.9, 136.8, 133.2, 128.7, 128.1, 126.9, 124.7, 123.4, 40.6, 24.2.

The spectroscopic data are in accordance with literature.$^{[38]}$
(Z)-1-Phenyldocos-11-en-1-one (6j) was prepared according to general procedure 3 in the main text. The product was obtained as a colorless oil (61 mg, 0.12 mmol, 38%).

\[
\text{MS (ESI)}: \text{not detected.}
\]

HRMS (ESI): 399.3621 [M+H]^+ (calc. for C_{28}H_{47}O: 399.3621)

\(^1\)H-NMR \((300 \text{ MHz, CDCl}_3\): \(\delta/\text{ppm} = 7.96 \text{ (dd, } J = 7.1, 1.8 \text{ Hz, 2H}), 7.61-7.50 \text{ (m, 1H), } 7.46 \text{ (dd, } J = 8.2, 6.6 \text{ Hz, 2H}), 5.35 \text{ (t, } J = 4.9 \text{ Hz, 2H}), 2.96 \text{ (t, } J = 7.4 \text{ Hz, 2H}), 2.01 \text{ (q, } J = 6.2 \text{ Hz, 4H), } 1.73 \text{ (t, } J = 7.2 \text{ Hz, 2H}), 1.27 \text{ (t, } J = 5.0 \text{ Hz, 28H), 0.98-0.70 \text{ (m, 3H).}
\]

\(^{13}\)C-NMR \((75 \text{ MHz, CDCl}_3\): \(\delta/\text{ppm} = 200.7, 137.2, 133.0, 130.0, 128.7, 128.2, 38.8, 32.1, 29.9, 29.8, 29.7, 29.5, 29.5, 27.4, 24.5, 22.8, 14.3.
\]

2-(4-Methoxyphenyl)acetophenone (6k) was prepared according to general procedure 3 in the main text. The product was obtained as a colorless solid (41 mg, 0.18 mmol, 45%).

\[
\text{MS (ESI)}: \text{m/z (%)} = 227.1 \text{ (100) [M+H]^+}
\]

Mp. = 90.1–91.8 °C \(\quad\) Lit.:\([39]\) 52–57 °C

\(^1\)H-NMR, COSY \((300 \text{ MHz, CDCl}_3\): \(\delta/\text{ppm} = 8.09-7.99 \text{ (m, 2H), 7.64-7.53 \text{ (m, 1H, 1H), 7.48 \text{ (dd, } J = 8.2, 6.6, 1.3 \text{ Hz, 2H), 7.25-7.16 \text{ (m, 2H), 6.95-6.84 \text{ (m, 2H), 4.26 \text{ (s, 2H), 3.81 \text{ (s, 3H).}
\]

\(^{13}\)C-NMR, HSQC, HMBC \((75 \text{ MHz, CDCl}_3\): \(\delta/\text{ppm} = 198.0, 158.6, 136.6, 133.1, 130.5, 128.7, 128.6, 126.5, 114.2, 55.3, 44.7.
\]

The spectroscopic data are in accordance with literature.\([40]\)

2-Phenoxy-1-phenyl-ethanone (6l) was prepared according to general procedure 3 in the main text. The product was obtained after column chromatography as a colorless oil (23 mg, 0.11 mmol, 27%, contains traces of the corresponding HE-pyridine).

\[
\text{MS (ESI)}: \text{m/z (%)} = 213.1 \text{ (100) [M+H]^+}
\]

\(^1\)H-NMR \((400 \text{ MHz, CDCl}_3\): \(\delta/\text{ppm} = 8.06-7.99 \text{ (m, 2H), 7.67-7.58 \text{ (m, 1H), 7.55-7.47 \text{ (m, 2H), 7.34-7.26 \text{ (m, 2H), 7.03-6.90 \text{ (m, 3H), 5.28 \text{ (s, 2H).}
\]

\(^{13}\)C-NMR \((101 \text{ MHz, CDCl}_3\): \(\delta/\text{ppm} = 194.6, 158.0, 133.9, 129.6, 128.9, 128.2, 121.7, 114.8, 70.8.
\]

The spectroscopic data are in accordance with literature.\([36]\)
4-oxo-4-phenyl-butyric acid-tert-butylester (6m) and 4-oxo-4-phenyl-butyric acid (6ma) was prepared according to general procedure 3 in the main text. The product was obtained as the 'Bu-Ester after column chromatography with slide impurities. The product was obtained after reverse-phase column chromatography as a colorless solid (38 mg, 0.21 mmol, 54%) 

MS (ESI): m/z (%) = 179.1 (100) [M+H]^+

Mp. = 111.4–113.0 °C    Lit.:[41] 112–114 °C

^1H-NMR (300 MHz, CDCl₃, crude 'Bu-ester) δ/ppm = 8.03 – 7.93 (m, 2H), 7.62 – 7.51 (m, 1H), 7.51 – 7.40 (m, 2H), 3.25 (t, J = 6.7 Hz, 1H), 2.68 (t, J = 6.6 Hz, 2H), 1.44 (s, 9H).

^1H-NMR (300 MHz, CDCl₃) δ/ppm = 9.61 (s, 1H), 8.04 – 7.94 (m, 2H), 7.64 – 7.52 (m, 1H), 7.52 – 7.41 (m, 2H), 3.32 (t, J = 6.5 Hz, 2H), 2.82 (t, J = 6.6 Hz, 2H).

^13C-NMR (75 MHz, CDCl₃) δ/ppm = 197.9, 178.9, 136.4, 133.4, 128.7, 128.1, 33.2, 28.1.

The spectroscopic data are in accordance with literature. [41]

3α,7α,12α-Trihydroxy-24-phenyl-5β-cholanone-(24) (6n) was prepared according to general procedure 3 in the main text. The product was obtained as a colorless oil in a complex mixture and the yield determined via ^1H-NMR using 1,4-Bis(trimethylsilyl)benzene as an internal standard (56 mg, 0.12 mmol, 30%).

MS (ESI): [m/z] = 433.3 (100%) [M-H₂O-OH]^+, 491.3 (5%) [M+Na]^+

HRMS (ESI): 469.3301 [M+H]^+ (calculated for C₃₀H₄₅O₄^+: 469.3312)

^1H-NMR (300 MHz, CDCl₃, only characteristic signals) δ/ppm = 8.01 – 7.90 (m, 2H), 7.59 – 7.49 (m, 1H), 7.45 (dd, J = 8.2, 6.6 Hz, 2H, 3.97 (s, 1H), 3.83 (d, J = 3.0 Hz, 1H), 0.66 (s, 2H).

2-(1-(4-Chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl)-1-phenylethan-1-one (6o) was prepared according to general procedure 3 in the main text. The product was obtained after reverse-phase-flash column chromatography as a colorless solid (102 mg, 0.24 mmol, 61%).
**MS (ESI):** \( m/z \) (%) = 418.1 (100) \([\text{M+H}]^+\)

**HR-MS (ESI):** 418.1194 \([\text{M+H}]^+\), calc. for \( \text{C}_{25}\text{H}_{21}\text{ClNO}_3^+ \): 418.1204

**Mp.** = 169.8°C (decomposition)

**\(^1\)H-NMR** (400 MHz, CDCl\(_3\)) \( \delta/\text{ppm} = 8.11 – 8.04 \) (m, 2H, \( \text{H}_{\text{Ar}-2,5} \)), 7.69 – 7.64 (m, 2H, \( \text{H}^{\text{Cl}-2,6} \)), 7.64 – 7.58 (m, 1H, \( \text{H}^{\text{Ar}-4} \)), 7.54 – 7.48 (m, 2H, \( \text{H}^{\text{Cl}-3,5} \)), 7.48 – 7.44 (m, 2H, \( \text{H}^{\text{Ar}-3,5} \)), 6.88 (d, \( J = 9.0 \) Hz, 1H, \( \text{H}^{\text{Indol}-7} \)), 6.66 (dd, \( J = 9.0, 2.6 \) Hz, 1H), 4.32 (s, 2H), 3.79 (s, 3H), 2.36 (s, 3H).

**\(^{13}\)C-NMR** (101 MHz, CDCl\(_3\)) \( \delta/\text{ppm} = 196.5, 168.3, 156.0, 139.2, 136.7, 135.9, 134.0, 133.4, 131.2, 131.0, 129.1, 128.7, 128.4, 115.0, 113.0, 111.5, 101.4, 55.7, 34.7, 13.7.

**Ethane-1,2-diylbis(5-methoxy-2-methyl-1H-indole-3,1-diyl))bis((4-chlorophenyl)methanone** was isolated during the preparation of 6k according to general procedure 3 in the main text. The side product was obtained after reverse-phase-flash column chromatography as a yellow oil (110 mg, 0.18 mmol, 22%).

**MS (ESI):** \( m/z \) (%) = 625.2 (100) \([\text{M+H}]^+\)

**HR-MS (ESI):** 625.1623 \([\text{M+H}]^+\), calc. for \( \text{C}_{36}\text{H}_{31}\text{ClNO}_4^+ \): 625.1655

**\(^1\)H-NMR** (400 MHz, CDCl\(_3\)) \( \delta/\text{ppm} = 7.43 – 7.35 \) (m, 8H, 2x \( \text{p-Cl-Ar} \)), 6.92 (d, \( J = 8.9 \) Hz, 2H), 6.68 (d, \( J = 2.5 \) Hz, 2H), 6.64 (dd, \( J = 8.9, 2.6 \) Hz, 2H), 3.62 (s, 6H), 3.00 (s, 4H), 2.02 (s, 6H).

**\(^{13}\)C-NMR** (101 MHz, CDCl\(_3\)) \( \delta/\text{ppm} = 168.3, 155.9, 139.0, 134.3, 134.1, 131.4, 131.0, 130.8, 129.1, 118.8, 115.0, 111.4, 100.6, 55.4, 23.7, 13.0.

**2-(4-Isobutylphenyl)-1-phenylpropan-1-one (6p)** was prepared according to general procedure 3 in the main text. The product was obtained as a colorless oil (12 mg, 0.05 mmol, 11%).

**MS (ESI):** \( m/z \) (%) = 267.1 (100) \([\text{M+H}]^+\)

**HR-MS (ESI):** 267.1738 \([\text{M+H}]^+\), calc. for \( \text{C}_{19}\text{H}_{23}\text{O}^+ \): 267.1748

**\(^1\)H-NMR** (300 MHz, CDCl\(_3\)) \( \delta/\text{ppm} = 8.02–7.95 \) (m, 2H), 7.54–7.46 (m, 1H), 7.44–7.36 (m, 2H), 7.24–7.17 (m, 2H), 7.12–7.06 (m, 2H), 4.68 (q, \( J = 6.8 \) Hz, 1H), 2.42 (d, \( J = 7.2 \) Hz, 2H), 1.83 (dp, \( J = 13.3, 6.7 \) Hz, 1H), 1.54 (d, \( J = 6.8 \) Hz, 3H), 0.8 (d, \( J = 6.6 \) Hz, 6H).
\[ ^{13}\text{C-NMR} \ (75 \text{ MHz, CDCl}_3): \delta/\text{ppm} = 200.6, 140.3, 138.6, 136.6, 132.7, 129.7, 128.8, 128.5, 127.5, 47.5, 45.0, 30.2, 22.4, 19.5. \]

4,4'-\{Butane-2,3-dimethyl\}bis(isobutylbenzol) was isolated during the preparation of 6k according to general procedure 3 in the main text. The product was obtained as a colorless oil (59 mg, 0.17 mmol, 21%).

\[ \text{MS (ESI): } m/z \ (%) = 346.5 \ (100) \ [\text{M+H}]^+ \]

\[ ^1\text{H-NMR} \ (300 \text{ MHz, CDCl}_3) \delta/\text{ppm} = 7.20–7.06 \ (m, 4H), 7.01–6.89 \ (m, 4H), 3.00–2.84 \ (m, 1H), 2.79 \ (ddq, J = 6.3, 4.1, 2.5, 1.9 \text{ Hz}, 1H), 2.50 \ (dd, J = 7.2, 5.0 \text{ Hz}, 2H), 2.43 \ (d, J = 7.2 \text{ Hz}, 2H), 1.87 \ (ddp, J = 23.2, 13.6, 6.7 \text{ Hz}, 2H), 1.36–1.22 \ (m, 3H), 1.12–0.99 \ (m, 3H), 0.95 \ (dd, J = 6.6, 2.0 \text{ Hz}, 6H), 0.89 \ (dd, J = 6.6, 0.9 \text{ Hz}, 6H). \]

\[ ^{13}\text{C-NMR} \ (75 \text{ MHz, CDCl}_3) \delta/\text{ppm} = 143.8, 143.2, 139.3, 138.9, 128.4, 127.6, 127.5, 127.3, 47.0, 46.3, 45.1, 45.0, 30.0, 30.3, 22.5, 22.4, 21.1, 17.4. \]

The spectroscopic data are in accordance with literature. \[^{42}\]

\((\text{tert-Butyloxycarbonyl-1-(4-(benzyloxy)-3-methoxybenzoyl)pyrrolidin-2-yl})\text{methanone} \ (6q)\) was prepared according to general procedure 3 in the main text. The product was obtained flash column chromatography as a slightly reddish oil (98 mg, 0.24 mmol, 59%).

\[ \text{MS (ESI): } m/z \ (%) = 312.1 \ (100) \ [\text{M+H-Boc}]^+ \]

\[ \text{HR-MS (ESI): } 434.1928 \ [\text{M+Na}]^+ \ (\text{calc. for } \text{C}_{24}\text{H}_{29}\text{NO}_5\text{Na}^+: 434.1938) \]

\[ ^1\text{H-NMR} \ (400 \text{ MHz, CD}_3\text{CN}) \delta/\text{ppm}= 7.62 \ (ddd, J = 9.7, 8.4, 2.0 \text{ Hz}, 1H), 7.52 \ (t, J = 1.7 \text{ Hz}, 1H), 7.48 – 7.33 \ (m, 5H), 7.07 \ (dd, J = 8.5, 2.4 \text{ Hz}, 1H), 5.27–5.19 \ (m, 1H), 5.16 \ (s, 2H), 3.86 \ (s, 3H), 3.53 – 3.38 \ (m, 2H), 2.38 – 2.26 \ (m, 1H), 1.92 – 1.76 \ (m, 3H), 1.42 \ (s, 4H), 1.21 \ (s, 5H). \]

\[ ^{13}\text{C-NMR} \ (101 \text{ MHz, CD}_3\text{CN, 2 rotamers}) \delta/\text{ppm}= 198.7, 197.9, 155.0, 154.5, 153.6, 150.4, 150.4, 137.5, 129.5, 129.4, 129.2, 129.0, 128.9, 123.7, 123.5, 113.2, 113.1, 111.7, 111.7, 79.8, 79.7, 71.4, 61.9, 61.7, 56.5, 56.4, 47.7, 47.4, 31.8, 30.9, 28.6, 28.4, 25.0, 24.2. \]

\((3,4\text{-Dimethoxyphenyl})(\text{tetrahydrofuran-2-yl})\text{methanone} \ (6r)\) was prepared according to general procedure 3 in the main text. The product was obtained flash column chromatography as a colorless oil (35 mg, 0.15 mmol, 37%).
**MS (ESI):** m/z (%) = 237.1 (100) [M+H]^+

**HR-MS (ESI):** 259.0954 [M+Na]^+ (calc. for C_{13}H_{16}O_{4}Na^+: 259.0946)

**¹H-NMR (400 MHz, CDCl₃)** δ/ppm = 7.64 (dd, J = 8.4, 2.0 Hz, 1H), 7.57 (d, J = 2.0 Hz, 1H), 6.89 (d, J = 8.4 Hz), 5.23 (dd, J = 8.3, 5.8 Hz, 1H), 4.08 – 3.96 (m, 2H), 3.95 (s, 3H), 3.94 (s, 3H), 2.33 – 2.21 (m, 1H), 2.20 – 2.11 (m, 1H), 1.98 (p, J = 7.1 Hz, 2H).

**¹³C-NMR (101 MHz, CDCl₃)** δ/ppm = 197.4, 153.6, 149.2, 128.4, 123.6, 111.0, 110.2, 79.9, 69.5, 56.2, 29.6, 25.8.
Cyclohexyl(p-tolylmethanone (8a) was prepared according to general procedure 3 in the main text. The product was obtained as a colorless oil (63 mg, 0.31 mmol, 78%).

\[
\text{MS (ESI): } m/z \% = 203.1(100) \ [M+H]^+ 
\]

\[^1\text{H-NMR} \ (300 \text{ MHz, CDCl}_3): \delta/\text{ppm} = 7.98 - 7.91 \text{ (m, 2H), } 7.32 - 7.23 \text{ (m, 2H), } 3.26 \text{ (tt, } J = 11.3, 3.2 \text{ Hz, 1H), } 2.43 \text{ (s, 3H), } 1.97 - 1.67 \text{ (m, 5H), } 1.54 - 1.25 \text{ (m, 5H).}
\]

\[^{13}\text{C-NMR} \ (75 \text{ MHz, CDCl}_3): \delta/\text{ppm} = 203.6, 143.5, 133.8, 129.3, 128.4, 45.5, 29.5, 26.0, 25.9, 21.6.
\]

The spectroscopic data are in accordance with literature.[43]

Cyclohexyl-(4-methoxyphenyl)methanone (8b) was prepared according to general procedure 3 in the main text. The product was obtained as a colorless oil (59 mg, 0.27 mmol, 68%).

\[
\text{MS (ESI): } m/z \% = 219.1 \ (100) \ [M+H]^+ 
\]

\[^1\text{H-NMR} \ (300 \text{ MHz, CDCl}_3): \delta/\text{ppm} = 8.01 - 7.90 \text{ (m, 2H), } 7.01 - 6.90 \text{ (m, 2H), } 3.89 \text{ (s, 3H), } 3.24 \text{ (tt, } J = 11.4, 3.2 \text{ Hz, 1H), } 1.96 - 1.71 \text{ (m, 5H), } 1.61 - 1.23 \text{ (m, 5H).}
\]

\[^{13}\text{C-NMR} \ (75 \text{ MHz, CDCl}_3): \delta/\text{ppm} = 202.5, 163.2, 130.5, 129.3, 113.7, 55.5, 45.3, 29.6, 26.0,
\]

The spectroscopic data are in accordance with literature.[44]

(4-Chlorophenyl)-cyclohexylmethanone (8c) was prepared according to general procedure 3 in the main text. The product was obtained after flash column chromatography as a colorless oil (56 mg, 0.25 mmol, 63%).

\[
\text{GC-MS: } m/z \% = 222.09 \ [M]^+ 
\]

\[^1\text{H-NMR} \ (400 \text{ MHz, CDCl}_3): \delta/\text{ppm} = 7.91 - 7.85 \text{ (m, 2H), } 7.47 - 7.39 \text{ (m, 2H), } 3.20 \text{ (tt, } J = 11.3, 3.2 \text{ Hz, 1H), } 1.86 \text{ (dtt, } J = 9.4, 6.3, 3.2 \text{ Hz, 4H), } 1.74 \text{ (dddt, } J = 12.9, 4.9, 3.3, 1.6 \text{ Hz, 1H), } 1.55 - 1.18 \text{ (m, 5H).}
\]

\[^{13}\text{C-NMR} \ (101 \text{ MHz, CDCl}_3): \delta/\text{ppm} = 202.6, 139.1, 134.6, 129.7, 128.9, 45.7, 29.4, 25.9, 25.8.
\]

The reported spectroscopic data is in agreement to literature.[45]
(4-Bromoophenyl)-cyclohexylmethanone (8d) was prepared according to general procedure 3 in the main text. The product was obtained after reverse-phase-flash column chromatography as a colorless solid (32 mg, 0.14 mmol, 35%).

\[ \text{GC-MS: m/z (\%) = 226.06 [M]^+} \]

Mp. = 76.4–78.1 °C  
Lit.\textsuperscript{[43]} 77–78 °C

\( ^1 \text{H-NMR} \) (400 MHz, CDCl\textsubscript{3}) \( \delta / \text{ppm} = 7.84 – 7.76 (m, 2H), 7.63 – 7.56 (m, 2H), 3.19 (tt, \( J = 11.3, 3.2 \text{ Hz}, 1H \)), 1.86 (tq, \( J = 10.7, 9.3, 3.2, 2.6 \text{ Hz}, 4H \)), 1.74 (dddt, \( J = 11.1, 4.9, 3.2, 1.6 \text{ Hz}, 1H \)), 1.56 – 1.20 (m, 5H).

\( ^{13} \text{C-NMR} \) (101 MHz, CDCl\textsubscript{3}) \( \delta / \text{ppm} = 202.8, 135.0, 131.9, 129.8, 127.8, 45.6, 29.4, 25.9, 25.8. \)

The reported spectroscopic data is in agreement to literature.\textsuperscript{[45]}

(4-Cyclohexylphenyl)-cyclohexylmethanone (8e) was isolated during the preparation of 6p according to general procedure 3 in the main text. The side product was obtained after reverse-phase-flash column chromatography as a colorless oil (24 mg, 0.09 mmol, 23%).

\[ \text{MS (ESI): m/z (\%) = 271.1 (100) [M+H]^+} \]

\[ \text{HR-MS (ESI): 271.2057 [M+H]^+ (calc. for C}_{19}H_{27}O^+: 271.2061} \]

\( ^1 \text{H-NMR} \) (400 MHz, CD\textsubscript{3}CN) \( \delta / \text{ppm} = 7.84 – 7.75 (m, 2H), 7.31 – 7.21 (m, 2H), 3.26 (tt, \( J = 11.1, 3.3 \text{ Hz}, 1H \)), 2.50 (td, \( J = 10.8, 9.5, 5.3 \text{ Hz}, 1H \)), 1.81 – 1.56 (m, 10H), 1.44 – 1.25 (m, 8H), 1.25 – 1.06 (m, 2H).

\( ^{13} \text{C-NMR} \) (101 MHz, CD\textsubscript{3}CN) \( \delta / \text{ppm} = 202.0, 153.0, 128.2, 126.9, 44.8, 44.3, 33.8, 29.3, 26.4, 25.8, 25.7, 25.4. \)

(3-chlorophenyl)-cyclohexylmethanone(8f) was prepared according to general procedure 3 in the main text. The product was obtained after flash column chromatography as a colorless oil, yield determined using internal standard (15 mg, 0.07 mmol, 17%).

\[ \text{GC-MS: m/z (\%) = 222.09 [M]^+} \]

\( ^1 \text{H-NMR} \) (400 MHz, CDCl\textsubscript{3}) \( \delta / \text{ppm} = 7.89 (t, \( J = 1.9 \text{ Hz}, 1H \)), 7.80 (dt, \( J = 7.7, 1.4 \text{ Hz}, 1H \)), 7.57 – 7.48 (m, 1H), 7.45 – 7.36 (m, 1H), 3.19 (tt, \( J = 11.3, 3.2 \text{ Hz}, 1H \)), 1.86 (dddd, \( J = 13.7, 10.0, 4.6, 2.3 \text{ Hz}, 4H \)), 1.74 (dqd, \( J = 12.7, 3.1, 1.4 \text{ Hz}, 1H \)), 1.55 – 1.18 (m, 5H).
$^{13}$C-NMR (101 MHz, CDCl$_3$) $\delta$/ppm = 202.5, 138.0, 134.9, 132.6, 129.9, 128.4, 126.3, 45.8, 29.3, 25.9, 25.8.

The reported spectroscopic data is in agreement to literature.$^{[43]}$

Cyclohexyl(3,4-dimethoxyphenyl)methanone (8g) was prepared according to general procedure 3 in the main text. The product was obtained flash column chromatography as a colorless oil (74 mg, 0.30 mmol, 75%).

\[ \text{MS (ESI): m/z (%) = 249.1 (100) [M+H]$^+$} \]

$^1$H-NMR (400 MHz, CDCl$_3$) $\delta$/ppm = 7.58 (dd, $J$ = 8.4, 2.0 Hz, 1H), 7.53 (d, $J$ = 2.0 Hz, 1H), 6.88 (d, $J$ = 8.4 Hz, 1H), 3.94 (s, 3H), 3.93 (s, 3H), 3.24 (tt, $J$ = 11.5, 3.2 Hz, 1H), 1.92 – 1.80 (m, 3H), 1.79 – 1.69 (m, 1H), 1.63 – 1.22 (m, 6H).

$^{13}$C-NMR (101 MHz, CDCl$_3$) $\delta$/ppm = 202.6, 153.0, 149.1, 129.5, 122.6, 110.6, 109.9, 56.1, 56.0, 45.2, 29.7, 26.9, 25.9.

The reported spectroscopic data is in agreement to literature.$^{[43]}$

Cyclohexyl(3,4,5-trimethoxyphenyl)methanone (8h) was prepared according to general procedure 3 in the main text. The product was obtained flash column chromatography as a colorless solid (58 mg, 0.21 mmol, 56%).

\[ \text{MS (ESI): m/z (%) = 279.1 (100) [M+H]$^+$} \]

HR-MS (ESI): 279.1595 [M+H]$^+$ (calc. for C$_{16}$H$_{23}$O$_4$$: 279.1596)

\[ \text{M.p. = 82.1–84.2 °C Lit.:}$^{[46]}$ 82–84 °C

$^1$H-NMR (400 MHz, CDCl$_3$) $\delta$/ppm = 7.30 (s, 1H), 6.49 (s, 1H), 3.94 (s, 3H), 3.90 (s, 3H), 3.86 (s, 3H), 3.30 (tt, $J$ = 11.0, 3.2 Hz, 1H), 1.99 – 1.86 (m, 2H), 1.84 – 1.76 (m, 2H), 1.75 – 1.65 (m, 1H), 1.47 – 1.18 (m, 5H).

$^{13}$C-NMR (101 MHz, CDCl$_3$) $\delta$/ppm = 204.3, 154.3, 153.2, 143.1, 119.4, 113.1, 96.6, 56.4, 56.3, 56.1, 50.0, 29.2, 26.2, 26.2.

The reported spectroscopic data is in agreement to literature.$^{[46]}$

Benzo[d][1,3]dioxol-5-yl(cyclohexyl)methanone (8i) was prepared according to general procedure 3 in the main text. The product was obtained flash column chromatography as a colorless solid (65 mg, 0.25 mmol, 63%).
MS (ESI): m/z (%) = 233.0 (100) [M+H]^+

Mp. = 67.9–68.4 °C Lit.:^{[47]} 68–69 °C

^1^H-NMR (400 MHz, CDCl₃) δ/ppm = 7.55 (dd, J = 8.2, 1.7 Hz, 1H), 7.42 (d, J = 1.7 Hz, 1H), 6.84 (d, J = 8.2 Hz, 1H), 6.03 (s, 2H), 3.16 (tt, J = 11.4, 3.1 Hz, 1H), 1.90 – 1.79 (m, 4H), 1.78 – 1.70 (m, 1H), 1.52 – 1.21 (m, 5H).

^13^C-NMR (101 MHz, CDCl₃) δ/ppm = 202.0, 151.5, 148.2, 131.1, 124.3, 108.2, 107.9, 101.8, 45.5, 29.6, 26.0, 25.9.

The reported spectroscopic data is in agreement to literature.^{[48]}

Cyclohexyl(4-benzyloxy-3-methoxy-phenyl)methanone (8j) was prepared according to general procedure 3 in the main text. The product was obtained flash column chromatography as a colorless oil (103 mg, 0.32 mmol, 76%).

MS (ESI): m/z (%) = 325.1 (100) [M+H]^+

HR-MS (ESI): 325.1805 [M+H]^+ (calc. for C_{21}H_{25}O_{3}^+: 325.1804)

^1^H-NMR (400 MHz, CDCl₃) δ/ppm = 7.55 (d, J = 2.0 Hz, 1H), 7.53 – 7.47 (m, 1H), 7.49 – 7.31 (m, 5H), 6.88 (d, J = 8.3 Hz, 1H), 5.23 (s, 2H), 3.94 (s, 3H), 3.25 – 3.17 (m, 1H), 1.93 – 1.78 (m, 4H), 1.78 – 1.68 (m, 1H), 1.55 – 1.18 (m, 5H).

^13^C-NMR (101 MHz, CDCl₃) δ/ppm = 202.5, 152.2, 149.6, 136.4, 129.7, 128.7, 128.1, 127.2, 122.4, 112.1, 111.0, 70.8, 56.1, 45.2, 29.7, 26.0, 25.9.

(4-Dimethylamino)phenyl(cyclohexyl)methanone (8k) was prepared according to general procedure 3 in the main text. The product was obtained flash column chromatography as a colorless solid (68 mg, 0.29 mmol, 73%).

MS (ESI): m/z (%) = 232.1 (100) [M+H]^+

Mp. = 81.7–82.9 °C

^1^H-NMR (400 MHz, CDCl₃) δ/ppm = 7.93 – 7.84 (m, 2H), 6.71 – 6.63 (m, 2H), 3.20 (tt, J = 11.5, 3.1 Hz, 1H), 3.05 (s, 6H), 1.84 (dqd, J = 12.1, 4.0, 1.7 Hz, 4H), 1.72 (dddt, J = 14.0, 4.9, 3.4, 1.6 Hz, 1H), 1.58 – 1.18 (m, 5H).
$^{13}$C-NMR (101 MHz, CDCl$_3$) $\delta$/ppm = 202.1, 153.1, 130.4, 124.3, 110.9, 44.9, 40.1, 29.7, 26.1, 26.1.

The reported spectroscopic data is in agreement to literature.$^{[46]}$

5-Methyl-1-phenylhex-4-en-3-one (8l) was prepared according to general procedure 3 in the main text. The product was obtained as a colorless oil (crude 63 mg) which was contaminated with 1,5-Diphenylpentanone. The yield was calculated based on $^1$H-NMR (47 mg, 0.25 mmol, 63%).

MS (ESI): [m/z] = 189.1 (100%) [M+H]$^+$

$^1$H-NMR (300 MHz, CDCl$_3$, only characteristic signals): $\delta$/ppm = 6.08 (s, 1H), 2.17 (s, 3H), 1.89 (s, 3H).

$^{13}$C-NMR (75 MHz, CDCl$_3$): $\delta$/ppm = 199.9, 155.5, 141.5, 128.5, 128.4, 126.0, 123.7, 45.8, 30.2, 27.8, 20.9.

The spectroscopic data are in accordance with literature.$^{[49]}$

1-Cyclohexyl-2-phenylethanone (8m) was prepared according to general procedure 3 in the main text. The product was obtained as a colorless oil after column chromatography, the yield is corrected by NMR to account for the impurity of dicyclohexylketone (45 mg, 0.22 mmol, 56%).

$^1$H-NMR (400 MHz, CDCl$_3$) $\delta$/ppm = 7.36 – 7.24 (m, 5H), 7.17 (dd, $J = 13.8$, 7.4 Hz, 2H), 2.45 (td, $J = 11.4$, 5.8 Hz, 1H), 1.79 (dd, $J = 21.0$, 12.3 Hz, 4H), 1.64 (dd, $J = 11.4$, 6.1 Hz, 1H), 1.33 – 1.12 (m, 5H).

$^{13}$C-NMR (101 MHz, CDCl$_3$) 211.4, 134.6, 129.6, 128.7, 127.2, 127.0, 50.3, 48.0, 28.7, 26.0, 25.8.

The spectroscopic data are in accordance with literature.$^{[50]}$

1-Cyclohexyl-3-phenyl-1-propanone (8n) was prepared according to general procedure 3 in the main text. The product was obtained as a colorless oil in a mixture with dicyclohexylketone, the yield is corrected by NMR to account for the impurity (49 mg, 0.23 mmol, 57%).

$^1$H-NMR (400 MHz, CDCl$_3$) $\delta$/ppm = 7.33 – 7.25 (m, 2H), 7.20 (td, $J = 5.3$, 2.9 Hz, 3H), 2.90 (t, $J = 7.6$ Hz, 2H), 2.80 – 2.74 (m, 2H), 2.32 (tt, $J = 11.2$, 3.4 Hz, 1H), 1.89 – 1.71 (m, 12H (impurity)), 1.48 – 1.12 (m, 16H (impurity)).

$^{13}$C-NMR (101 MHz, CDCl$_3$) $\delta$/ppm = 213.1, 141.4, 128.4, 128.3, 126.0, 51.0, 42.2, 29.8, 28.6, 25.9, 25.7.
The spectroscopic data (without the impurity) are in accordance with literature.\footnote{51}

\textbf{6-(1H-indol-3-yl)-4-oxohexanoicacid-methylester (8o) was prepared according to general procedure 3 in the main text. The product was obtained reverse-flash column chromatography as a colorless oil (22 mg, 0.08 mmol, 21 \%).}

\begin{center}
\includegraphics[width=0.2\textwidth]{structure.png}
\end{center}

\textbf{MS (ESI):} [m/z] = 260.1 (100\%) [M+H]$^+$

\textbf{HRMS (ESI):} 260.1285. [M+H]$^+$ (calc. for C\textsubscript{15}H\textsubscript{18}NO\textsubscript{3}$^+$: 260.1281)

\textbf{\textsuperscript{1}H-NMR (300 MHz, CDCl\textsubscript{3}):} $\delta$/ppm = 7.99 (s, 1H), 7.59 (dd, J = 7.7, 1.1 Hz, 1H), 7.35 (dd, J = 8.0, 2.0 Hz, 1H), 7.22–7.09 (m, 2H), 7.04–6.94 (m, 1H), 3.67 (s, 3H), 3.15–3.01 (m, 2H), 2.95–2.81 (m, 2H), 2.76–2.67 (m, 2H), 2.58 (ddd, J = 7.1, 6.2, 1.1 Hz, 2H).

\textbf{\textsuperscript{13}C-NMR (75 MHz, CDCl\textsubscript{3}):} $\delta$/ppm = 208.8, 173.5, 136.4, 127.3, 122.2, 121.6, 119.4, 118.8, 115.3, 111.3, 51.9, 43.3, 37.4, 27.8, 19.4.
Results and Discussion

Spectroscopic Studies

Stern-Volmer-quenching

Under argon the following solutions were prepared:

a) Hantzsch-ester (0.507 mg, 0.002 mmol) in 10 mL dry and degassed DMAc, resulting in a 0.2 mM solution
b) Ni(phen)Br₂ (16.01 mg, 0.04 mmol) in 10 mL dry and degassed DMAc, resulting in a 4 mM solution
c) N-Benzoylsaccharin (11.89 mg, 0.04 mmol) in 10 mL dry and degassed DMAc, resulting in a 4 mM solution

The prepared solution was mixed in the cuvette according to table 1, degassed for 1 min with argon and measured.

Table S1: Preparation of the samples for Stern-Volmer quenching.

| V_QUENcher/mL | V_Hantzsch-ester/mL | V_DMAc/mL | C_QUENcher/mL |
|---------------|---------------------|-----------|---------------|
| 0.5           | 0.5                 | 2.5       | 0.57          |
| 1.0           | 0.5                 | 2.0       | 1.1           |
| 1.5           | 0.5                 | 1.5       | 1.7           |
| 2             | 0.5                 | 1         | 2.3           |

Figure S3: Stern-Volmer quenching plots for the nickel catalyst and the saccharin derivate.

The following Stern-Volmer plots show no quenching for the N-benzoyslaccharin (1a) and dynamic and static quenching for the nickel catalyst.

The linear regression yields the following equation:

\[
\left( \frac{I_0}{I} - 1 \right) \frac{1}{[Q]} = 0.06532 [Q] - 0.01437
\]

As a negative intercept and a positive slope indicate two negative quenching constants which is physically impossible, the calculation of the quenching constants was omitted. The negative intercept is probably due to measurement inaccuracies or a poor fit of the model.
UVvis and CV Studies

Figure S4: UVvis studies regarding the formation of EDA complexes. The absorption band of HE shows a weak bathochromic shift indicating the formation of EDA complexes.

Figure S5: Fluorescence spectra of HE for different concentrations of RAE. Absorption spectra of the solution used for the Stern-Volmer quenching, showing no bathochromic shift, indicating no EDA-formation according to literature.\textsuperscript{[52]}
Figure S6: UVvis spectra of all reaction components, showing relevant absorption at 390 nm only for Hantzsch-ester.

Figure S7: Cyclic voltammogram of 1a, showing two irreversible reduction peaks.
Computational studies

All calculations were performed using the GAUSSIAN 16 Rev A.03 program package.\textsuperscript{[53]}

Carbonyl Substitution Nitrogen Atom Replacement

Following the procedure of Greenberg et al.\textsuperscript{[54]} the COSNAR methodology was employed to determine the amide resonance and its influence on the reactivity of the different acyl surrogates. Following the literature procedure $E_{\text{COSNAR}}$ is the reaction energy $\Delta G_r$ of the following isodesmic reaction:

\[
\begin{array}{c}
\text{R}^1\text{R}^2\text{R}^3 + \text{N}^1\text{N}^2\text{R}^2 \rightarrow \text{R}^1\text{R}^2\text{R}^3 + \text{N}^1\text{N}^2\text{R}^2 \quad \Delta G_r = \Delta G_{\text{COSNAR}}
\end{array}
\]

Scheme S1: Isodesmic reaction to determine the amide resonance energy as proposed by Greenberg et al.\textsuperscript{[54]}

We used B3LYP/6-311G(d,p) and the SMD model to simulate the influence of DMAc on the different compounds.

Table S2: Calculated energies of the different reactions compounds for the determination of $E_{\text{COSNAR}}$.

| Compound 1a | Energy / H | Compound 4 | Energy / H |
|-------------|------------|------------|------------|
| I1          | -1292.966397 | I1         | -740.446005 |
| I2          | -1202.858939 | I2         | -650.344028 |
| I3          | -1276.8910267 | I3         | -724.376161 |
| I4          | -1218.9266693 | I4         | -666.401251 |
| $E_{\text{COSNAR}}$ | -4.79 kcal/mol | $E_{\text{COSNAR}}$ | -7.92 kcal/mol |

| Compound 3 | Energy / H | Compound 2 | Energy / H |
|------------|------------|------------|------------|
| I1         | -724.440910 | I1         | -705.239317 |
| I2         | -634.327602 | I2         | -615.118165 |
| I3         | -708.361491 | I3         | -689.153815 |
| I4         | -650.393344 | I4         | -631.209238 |
| $E_{\text{COSNAR}}$ | -8.58 kcal/mol | $E_{\text{COSNAR}}$ | 3.50 kcal/mol |
Figure S8: $E_{\text{COSNAR}}$ of the different acyl surrogates and the yield of the reaction procedure, showing no real correlation between the two.

As the correlation between yield and $E_{\text{COSNAR}}$ was not given, we expected that the BDE and the yield should show a correlation if the oxidative addition is the yield-determining factor. We employed the same level of theory (B3LYP/6-311G(d,p)) as before to compare the results directly with those from $E_{\text{COSNAR}}$. This time, we found the expected correlation indicating that BDE is a more reliable tool to estimate the reactivity of the acyl donors. During our analysis, we also found the energetic stabilization of the $\pi^*$-Orbital of the C(O)−N bond through hyperconjugation with the carbonyl- and sulfonyl-group to be very strong, as it lowered the energy of the corresponding MO even under the $\pi$-MOs of the benzoyl moiety.

Table S3: Calculated BDE for the acyl surrogates used in this study.

| Compound               | BDE / kcal/mol |
|------------------------|----------------|
| N-Benzoylsaccharin 1a  | 49.66          |
| N-Benzoylsuccinimde 2  | 79.64          |
| N-Benzoylbenzotriazole 3 | 65.39        |
| N-Benzoylimidazole 4   | 64.09          |

Figure S9: BDE of the different acyl surrogates and the yield of the reaction procedure, showing correlation between the two.
Figure S10: Molecular orbitals of 1a, showing a high stabilization of the antibonding orbital of the amide bond, and the HOMO as a reference.
Trapping experiments

Following general procedure 3 in the main text a sample was prepared using 1a (0.1 mmol, 29 mg) and 5a (0.2 mmol, 55 mg) and an additional 100 equiv. of styrene (10 mmol, 1.1 mL). After 24 h of irradiation a sample of the reaction mixture was measured using GC-MS in accordance to Hong et al.[36]

Scheme S2: Performed trapping experiment as well as observed products.

As shown in figure S11, the GC-MS still shows product formation (blue, 6.937 min), however a new peak A (green, 6.714 min) appears, which corresponds to the product of the reaction of styrene with the cyclohexyl radical. Also a smaller second new peak B (red, 7.103 min) appears. The mass and fragmentation indicate the formal acyl adduct to styrene which is in accordance to literature for a similar reaction using N-acylsuccinimide.[36] Comparing their area in the FID reveals a ratio from 4:1 (corrected to the relative ratio of N-acylsaccharin and RAE-Ester).
Figure S12: Mass spectrum of the peak at 6.71 min.

Figure S13: Mass spectrum of the peak at 7.10 min.
We also performed a similar trapping experiment employing TEMPO as a radical scavenger using LC-MS to analyze the reaction mixture. This experiment again showed the formation of smaller amounts of the acyl radical as well as larger amounts of the alkyl radical adduct. In this case, product formation was not observed. It should be noted that alcoholysis of the N-acylsaccharin by reduced TEMPO yields the same products as trapping of the acyl radical.

![Diagram](image)

Scheme S3: Performed trapping experiment as well as possible products.
Figure S15: LC-MS of the reaction mixture after 24 h.

Figure S16: Mass spectra of the peak at 5.99 min.
Figure S17: Mass spectra of the peak at 0.93 min
Spectra 1: $^1$H-NMR of 1a.

Spectra 2: $^{13}$C-NMR of 1a.
Spectra 3: $^1$H-NMR of 1b.

Spectra 4: $^{13}$C-NMR of 1b.
Spectra 5: \(^1\)H-NMR of 1c.

Spectra 6: \(^{13}\)C-NMR of 1c.
Spectra 7: $^1$H-NMR of 1d.

Spectra 8: $^{13}$C-NMR of 1d.
Spectra 9: $^1$H-NMR of $1h$.

Spectra 10: $^{13}$C-NMR of $1h$. 
Spectra 11: $^1$H-NMR of 1f.

Spectra 12: $^{13}$C-NMR of 1f.
Spectra 13: $^1$H-NMR of 1g.

Spectra 14: $^{13}$C-NMR of 1g.
Spectra 15: $^1$H-NMR of 1i.

Spectra 16: $^{13}$C-NMR of 1i.
Spectra 17: $^1$H-NMR of $1j$.

Spectra 18: $^{13}$C-NMR of $1j$. 
Spectra 19: $^1$H-NMR of 1k.

Spectra 20: $^{13}$C-NMR of 1k.
Spectra 1: $^1$H-NMR of 1.

Spectra 2: $^{13}$C-NMR of 1.
Spectra 23: $^1$H-NMR of 1q.

Spectra 24: $^{13}$C-NMR of 1q.
Spectra 25: $^1$H-NMR of 1p.

Spectra 26: $^{13}$C-NMR of 1p.
Spectra 27: $^1$H-NMR of 1r.

Spectra 28: $^{13}$C-NMR of 1r.
Spectra 29: $^1$H-NMR of 1o.

Spectra 30: $^{13}$C-NMR of 1o.
Spectra 31: $^1$H-NMR of 1m.

Spectra 32: $^{13}$C-NMR of 1m.
Spectra 33: $^1$H-NMR of 1n.

Spectra 34: $^{13}$C-NMR of 1n.
Spectra 35: $^{19}$F-NMR of 1n.
Spectra 36: $^1$H-NMR of 5a.

Spectra 37: $^{13}$C-NMR of 5a.
Spectra 38: $^1$H-NMR of 5b.

Spectra 39: $^{13}$C-NMR of 5b.
Spectra 40: $^1$H-NMR of 5c.

Spectra 41: $^{13}$C-NMR of 5c.
Spectra 42: $^1$H-NMR of 5d.

Spectra 43: $^{13}$C-NMR of 5d.
Spectra 44: $^1$H-NMR of 5e.

Spectra 45: $^{13}$C-NMR of 5e.
Spectra 46: $^1$H-NMR of 5f.

Spectra 47: $^{13}$C-NMR of 5f.
Spectra 48: $^1$H-NMR of 5g.

Spectra 49: $^{13}$C-NMR of 5g.
Spectra 50: $^1$H-NMR of 5h.

Spectra 51: $^{13}$C-NMR of 5h.
Spectra 52: $^1$H-NMR of 5i.

Spectra 53: $^{13}$C-NMR of 5i.
Spectra 54: $^1$H-NMR of 5j.

Spectra 55: $^{13}$C-NMR of 5j.
Spectra 56: $^1$H-NMR of 5k.

Spectra 57: $^{13}$C-NMR of 5k.
Spectra 58: \(^1\text{H-NMR of 5l.}\)

Spectra 59: \(^{13}\text{C-NMR of 5l.}\)
Spectra 60: $^1$H-NMR of 5m.

Spectra 61: $^{13}$C-NMR of 5m.
Spectra 62: $^1$H-NMR of 5q.

Spectra 63: $^{13}$C-NMR of 5q.
Spectra 64: $^1$H-NMR of 5r.

Spectra 65: $^{13}$C-NMR of 5r.
Spectra 66: $^1$H-NMR of 5n.

Spectra 67: $^{13}$C-NMR of 5n.
Spectra 68: $^1$H-NMR of 5o.

Spectra 69: $^{13}$C-NMR of 5o.
Spectra 70: $^1$H-NMR of 5p.

Spectra 71: $^{13}$C-NMR of 5p.
Spectra 74: $^1$H-NMR of 6a.

Spectra 75: $^{13}$C-NMR of 6a.
Spectra 76: $^1$H-NMR of 6b.

Spectra 77: $^{13}$C-NMR of 6b.
Spectra 78: $^1$H-NMR of 6c.

Spectra 79: $^{13}$C-NMR of 6c.
Spectra 80: $^1$H-NMR of 6d.

Spectra 81: $^{13}$C-NMR of 6d.
Spectra 82: $^1$H-NMR of 6e.

Spectra 83: $^{13}$C-NMR of 6e.
Spectra 84: $^1$H-NMR of 6f.

Spectra 85: $^{13}$C-NMR of 6f.
Spectra 86: $^1$H-NMR of 6g.

Spectra 87: $^{13}$C-NMR of 6g.
Spectra 88: $^1$H-NMR of 6h.

Spectra 89: $^{13}$C-NMR of 6h.
Spectra 90: $^1$H-NMR of 6i.

Spectra 91: $^{13}$C-NMR of 6i.
Spectra 92: $^1$H-NMR of 6j.

Spectra 93: $^{13}$C-NMR of 6j.
Spectra 94: $^1$H-NMR of 6k.

Spectra 95: $^{13}$C-NMR of 6k.
Spectra 96: $^1$H-NMR of 6l.

Spectra 97: $^{13}$C-NMR of 6l.
Spectra 98: $^1$H-NMR of 6m.

Spectra 99: $^1$H-NMR of 6ma.
Spectra 100: $^{13}$C-NMR of 6ma.

Spectra 101: $^1$H-NMR of the complex mixture of 6n.
Spectra 102: \(^1\)H-NMR of 6o.

Spectra 103: \(^{13}\)C-NMR of 6o.
Spectra 104: $^1$H-NMR of 6oa.

Spectra 105: $^{13}$C-NMR of 6oa.
Spectra 106: $^1$H-NMR of 6p.

Spectra 107: $^{13}$C-NMR of 6p.
Spectra 108: $^1$H-NMR of 6pa.

Spectra 109: $^{13}$C-NMR of 6pa.
Spectra 110: $^1$H-NMR of 6q.

Spectra 111: $^{13}$C-NMR of 6q.
Spectra 112: $^1$H-NMR of 6r.

Spectra 113: $^{13}$C-NMR of 6r.
Spectra 114: $^1$H-NMR of 8a.

Spectra 115: $^{13}$C-NMR of 8a.
Spectra 116: $^1$H-NMR of 8b.

Spectra 117: $^{13}$C-NMR of 8b.
Spectra 118: $^1$H-NMR of 8c.

Spectra 119: $^{13}$C-NMR of 8c.
Spectra 120: \textsuperscript{1}H-NMR of 8d.

Spectra 121: \textsuperscript{13}C-NMR of 8d.
Spectra 122: $^1$H-NMR of 8e.

Spectra 123: $^{13}$C-NMR of 8e.
Spectra 124: $^1$H-NMR of $8f$.

Spectra 125: $^{13}$C-NMR of $8f$. 
Spectra 126: $^1$H-NMR of 8g.

Spectra 127: $^{13}$C-NMR of 8g.
Spectra 128: $^1$H-NMR of 8h.

Spectra 129: $^{13}$C-NMR of 8h.
Spectra 130: $^1$H-NMR of 8i.

Spectra 131: $^{13}$C-NMR of 8i.
Spectra 132: $^1$H-NMR of 8j.

Spectra 133: $^{13}$C-NMR of 8j.
Spectra 134: $^1$H-NMR of 8k.

Spectra 135: $^{13}$C-NMR of 8k.
Spectra 136: $^1$H-NMR of 8l.

Spectra 137: $^{13}$C-NMR of 8l.
Spectra 138: $^1$H-NMR of 8m.

Spectra 139: $^{13}$C-NMR of 8m.
Spectra 140: $^1$H-NMR of 8n.

Spectra 141: $^{13}$C-NMR of 8n.
Spectra 142: $^1$H-NMR of 8o.

Spectra 143: $^{13}$C-NMR of 8o.
Cartesian Coordinates

![Chemical Structure]

Energy: -454623.3394920 H

N  -1.52855  -1.97279  -0.66334
C  -0.36768  -1.39651  -0.60116
N  -0.43303  -0.06326  -0.18932
C  -2.45561  -1.00040  -0.27748
C  -1.79692   0.21252   0.00526
C  -3.84190  -1.10148  -0.15344
C  -4.53909   0.03192   0.25459
C  -3.87043   1.23653   0.53404
C  -2.48637   1.35208   0.41426
H  -1.97605   2.28122   0.62157
H  -4.34914  -2.03497  -0.36838
H  -5.61730  -0.01224   0.35934
H  -4.44437   2.10138   0.84728
C   0.62311   0.87378  -0.12487
C   2.00632   0.33813   0.00267
O   0.37881   2.06341  -0.16261
C   3.02865   0.98698  -0.70235
C   4.34475   0.55704  -0.57039
C   2.31566  -0.72363   0.86255
C   3.63879  -1.13418   1.00844
C   4.65147  -0.50221   0.28680
H   1.53503  -1.20866   1.43611
H   2.78367   1.81534  -1.35644
H   5.13148   1.04858  -1.13128
H   3.87736  -1.94563   1.68639
H   5.67917  -0.83079   0.39497
H   0.57634  -1.85260  -0.85368

Energy: -398046.5769716 H

N  -1.54623   1.92443  -0.52735
C  -0.38903   1.37648  -0.63536
C  -0.36521  -0.12910  -0.43641
C  -2.46747   0.88083  -0.23856
C  -1.83152  -0.36923  -0.16941
C  -3.83589   1.01374  -0.03902
C  -4.56954  -0.14234   0.23801
C  -3.94407  -1.38970   0.31046
C  -2.56431  -1.51378   0.10599
H  -2.09140  -2.48888  0.16274
H  -4.30869  1.98675  -0.09889
H  -5.63939  -0.07218  0.39937
H  -4.53489  -2.27255  0.52702
C   0.59185  -0.61299  0.68656
C   2.05525  -0.36418  0.39004
H   0.42402  -1.68466  0.83065
C   2.75417  -1.19283  0.49627
C   4.09654  -0.96080  0.78679
C   2.74033   0.70166  0.98222
C   4.08440   0.93780  0.69503
C   4.76645   0.10806  -0.19222
H   2.21851   1.35072  1.67839
H   2.24505  -2.03368  -0.95806
H   4.62101  -1.61681  -1.47273
H   4.59793   1.76797  1.16723
H   5.81182   0.28879  -0.41526
H   0.49491   1.96624  -0.85763
H  -0.05626  -0.60255  -1.37858
H   0.30935  -0.12196  1.62166

Energy: -444503.5428396

H  0.49491  1.96624  -0.85763
H  0.30935  -0.12196  1.62166

N  1.74755   0.54830  1.99103
C  -0.88141   1.51884  -0.30495
H   0.93898   2.53104  -0.11034
C  -1.75370   0.32106  -0.09941
O  -1.31164   2.51503  -0.85475
C  -1.32618  -0.83976  0.55821
C  -3.06911   0.38403  -0.58626
C  -3.93506  -0.68833  -0.41858
C  -3.50046  -1.84021  0.24029
C  -2.19730  -1.91301  0.72779
H  -0.31772  -0.92022  0.93838
H  -3.38967   1.28640  -1.09163
H  -4.94861  -0.62944  -0.79856
|   | X         | Y         | Z         |
|---|-----------|-----------|-----------|
| H | -4.17627  | -2.67785  | 0.37234   |
| H | -1.85616  | -2.80561  | 1.23916   |
| H | 0.30450   | 1.97141   | 2.42590   |

![Chemical Structure](image)

Energy: -408127.9818976 H

|   | X         | Y         | Z         |
|---|-----------|-----------|-----------|
| C | -2.33838  | 2.17604   | -0.37301  |
| C | -1.27497  | 1.34464   | -0.70706  |
| C | -3.47696  | 1.68432   | 0.29403   |
| C | -3.58706  | 0.34555   | 0.64677   |
| C | -1.39389  | 0.00003   | -0.35284  |
| C | -2.52994  | -0.50917  | 0.31839   |
| H | -2.28776  | 3.22833   | -0.62837  |
| H | -4.28144  | 2.36925   | 0.53639   |
| H | -0.39635  | 1.73210   | -1.20862  |
| H | -4.46061  | -0.03839  | 1.15996   |
| N | -0.55933  | -1.09393  | -0.52894  |
| C | -1.22037  | -2.16726  | 0.02922   |
| N | -2.38352  | -1.87133  | 0.54210   |
| C | 0.73749   | -1.11806  | -1.18622  |
| C | 1.85268   | -0.41794  | -0.42541  |
| C | 1.88532   | -0.39682  | 0.97090   |
| C | 2.89703   | 0.17904   | -1.13648  |
| C | 3.96155   | 0.77903   | -0.46622  |
| C | 3.98861   | 0.79431   | 0.92690   |
| C | 2.94639   | 0.20703   | 1.64253   |
| H | 1.07426   | -0.84169  | 1.53629   |
| H | 2.87846   | 0.17806   | -2.22223  |
| H | 4.76356   | 1.23987   | -1.03185  |
| H | 4.81215   | 1.26558   | 1.45109   |
| H | 2.95656   | 0.22101   | 2.72657   |
| H | -0.77705  | -3.15396  | 0.01789   |
| H | 0.99530   | -2.17124  | -1.33531  |
| H | 0.63783   | -0.67665  | -2.18272  |

![Chemical Structure](image)

Energy: -238027.6445170 H

|   | X         | Y         | Z         |
|---|-----------|-----------|-----------|
| C | 0.25044   | 1.65873   | -0.00000  |
| C | 1.66287   | 1.45942   | -0.00000  |
| C | -0.55738  | 0.53443   | 0.00000   |
| C | 0.00000   | -0.77218  | 0.00000   |
| C | 1.37058   | -0.96737  | -0.00000  |
| C | 2.20438   | 0.19001   | -0.00000  |
| H | -0.16831  | 2.65866   | -0.00000  |
Energy: -464636.8791666 H

N   -1.48539    1.95649    0.48007
N   -0.33049    1.42319    0.41656
N   -0.46521    0.07612    0.09356
C   -2.44985    0.99701    0.21117
C   -1.81043   -0.22857   -0.02705
C   -3.84213    1.11635    0.15992
C   -4.56189   -0.02991   -0.13394
C   -3.91175   -1.26031   -0.36884
C   -2.53045   -1.39095   -0.31990
H   -2.03384   -2.33481   -0.48723
H   -4.32226    2.06917    0.34429
H   -5.64347    0.01240   -0.18397
H   -4.51194   -2.13523   -0.59111
C   0.62878    -0.83061    0.03435
C   2.01734   -0.29464   -0.01264
O   0.38092   -2.01747    0.02059
C   3.01995   -1.14432    0.47842
C   4.35377   -0.76059    0.42480
C   2.37393    0.93412    0.58396
C   3.71435    1.30263    0.65480
C   4.70366    0.46407   -0.14494
H   1.61519    1.59751   -0.97166
H   2.73522   -2.10092    0.89811
H   5.12027   -1.41654    0.82081
H   3.98444    2.24988   -1.10682
H   5.74504    0.76197   -0.19404

Energy: -408097.0358753 H

N    1.57583   -1.94472   -0.23168
N    0.40700   -1.51474   -0.37620
C    0.37370   -0.01770   -0.38342
C    2.49707   -0.85985   -0.11960
| Atom | X       | Y       | Z       |
|------|---------|---------|---------|
| C    | 1.81291 | 0.35270 | -0.19822|
| C    | 3.87362 | -0.93761| 0.05080 |
| C    | 4.57040 | 0.26665 | 0.14486 |
| C    | 3.89676 | 1.49201 | 0.06893 |
| C    | 2.50995 | 1.54954 | -0.10410|
| H    | 2.00656 | 2.50849 | -0.16293|
| H    | 4.37447 | -1.89651| 0.10742 |
| H    | 5.64588 | 0.25771 | 0.27912 |
| H    | 4.46272 | 2.41360 | 0.14567 |
| C    | -0.60529| 0.51448 | 0.69189 |
| C    | -2.06908| 0.30526 | 0.36709 |
| C    | -2.85560| 1.38207 | -0.05567|
| C    | -4.20519| 1.20911 | -0.36116|
| C    | -2.66705| -0.95578| 0.47854 |
| C    | -4.01506| -1.13104| 0.17541 |
| C    | -4.78918| -0.05003| -0.24574|
| H    | -2.06776| -1.80386| 0.78763 |
| H    | -2.41078| 2.36907 | -0.14063|
| H    | -4.79815| 2.05766 | -0.68419|
| H    | -4.46159| -2.11498| 0.26693 |
| H    | -5.83859| -0.18860| -0.48037|
| H    | 0.00202 | 0.26776 | -1.37523 |
| H    | -0.41206| 1.58430 | 0.80839 |
| H    | -0.35024| 0.04271 | 1.64565 |

Energy: -454552.9001636 H

```
N=N
      \       \     \\     \\
          \     \    \     
            \     \    \  
```

C  3.57217  1.29097 -0.80358
C  2.44562  1.42213 0.01391
C  4.02738  0.03519 -1.22768
C  3.36411 -1.13024 -0.84855
C  1.78728  0.26127 0.39372
C  2.24357 -0.98366 -0.03881
H  4.10672  2.18072 -1.11670
H  4.90524 -0.02694 -1.86028
H  2.09585  2.39500 0.33618
H  3.69638 -2.11087 -1.16668
C  0.58301 -0.04423 1.23657
N  0.47582 -1.52790 1.15973
N  1.40532 -2.01435 0.46869
C -0.64321  0.83730 0.86377
H  0.76306  0.17764 2.29575
C -1.88804  0.31314 0.23059
O  -0.50245  2.02321 1.08838
C -2.24974 -1.04097 0.20138
C -2.75075  1.26597 -0.34077
C -3.93736  0.87092 -0.94081
C  4.29004 -0.48076 -0.96712
C  -3.44895  -1.42997  -0.39262
H   -1.60528  -1.78229   0.65348
H  -2.46715   2.31017  -0.30369
H  -4.59033   1.61217  -1.38721
H  -5.21926  -0.78965  -1.43311
H  -3.72387  -2.47834  -0.40375

Energy:  -418173.0951164

C  -2.40909   2.17093  -0.16167
C  -1.32769   1.42262  -0.59615
C  -3.51592   1.58016   0.49301
C  -3.56962   0.21878   0.73197
C  -1.38856   0.04312  -0.35507
C  -2.48380  -0.55446   0.29694
H  -2.40803  3.24281  -0.32371
H  -4.33426   2.21440   0.81302
H  -0.47977   1.88557  -1.08486
H  -4.41083  -0.24411   1.23299
N  -0.55924  -1.00840  -0.62511
N  -1.11515  -2.16642  -0.16273
N  -2.25272  -1.91014   0.38515
C   0.73634  -1.03339  -1.28901
C   1.85276  -0.39293  -0.48482
C   2.03842  -0.71604   0.86312
C   2.73530   0.49874  -1.09725
C   3.79124  1.05920  -0.37834
C   3.96881   0.73483   0.96414
C   3.08874  -0.15368   1.58302
H  1.35800  -1.40736   1.34851
H  2.59971   0.75753  -2.14296
H  4.46891   1.75070  -0.86626
H  4.78599   1.17188   1.52662
H  3.22225  -0.41042   2.62784
H  0.94456  -2.09034  -1.46970
H  0.64177  -0.54328  -2.26193

Energy:  -248065.6440343

C   1.39899  -0.94457   0.00000
C   2.18704   0.21816   0.00000
C   0.00000  -0.77435   0.00000
C  -0.57947   0.51445  -0.00000
C   0.18858   1.65665   0.00000


Energy: -442544.3496204 H

C 1.60432 1.48151 0.00000
H 1.84589 -1.93156 0.00000
H 3.26622 0.12876 0.00000
H 2.23625 2.36143 0.00000
H -0.24838 2.64807 -0.00000
N -0.99687 -1.67867 -0.00000
N -2.17354 -0.95203 -0.00000
N -1.95771 0.32815 -0.00000

Energy: -385992.4730324 H

C 3.09771 1.15486 -0.63565
C 3.52040 -0.32646 -0.57482
C 2.30574 -1.09833 -0.05133
H 4.35965 -0.50729 0.10084
Energy: -432450.5442439 H

H 3.80621  -0.73640  -1.54737
C 1.08277  -0.17445  -0.05037
C 1.70883   1.21818   0.00319
H 3.01197   1.51816  -1.66502
H 3.77059   1.83487  -0.11168
O 2.31779  -2.24465   0.31744
O 1.21742   2.19720   0.50607
C -0.02706  -0.50509   0.95945
C -1.43040  -0.26330   0.44060
C -2.21446  -1.33534   0.00082
C -3.50082  -1.12545  -0.49535
C -4.02356   0.16449  -0.55684
C -1.96617   1.02897   0.37557
C -3.25177   1.24035  -0.11874
H -1.36706   1.86852   0.71034
H -1.81699  -2.34422   0.05302
H -4.09441  -1.96996  -0.82793
H -3.65251   2.24737  -0.15890
H -5.02464   0.33020   0.93892
H  0.69054  -0.26329  -1.07856
H  0.14175   0.08782   1.86296
H  0.08600  -1.55677   1.23400

\[
\begin{align*}
\text{Energy: } & -432450.5442439 \\
C & (-2.94166, 0.88726, -0.94076) \\
C & (-3.34826, -0.46283, -0.32354) \\
C & (-2.33159, -0.75298, 0.77621) \\
H & (-3.27726, -1.28093, -1.04564) \\
H & (-4.35503, -0.47700, 0.09723) \\
C & (-1.09831, 0.13840, 0.57007) \\
C & (-1.65002, 1.32062, -0.24698) \\
H & (-3.68550, 1.67583, -0.80749) \\
H & (-2.74039, 0.81752, -2.01362) \\
O & (-2.47689, -1.52001, 1.69042) \\
O & (-1.15393, 2.41588, -0.30323) \\
C & (-0.04629, -0.61571, -0.27383) \\
C & (1.39251, -0.28196, 0.07774) \\
C & (2.34610, -1.16404, 0.60952) \\
C & (3.70126, -0.89817, -0.46683) \\
C & (4.11998, 0.26043, 0.19101) \\
C & (1.81927, 0.87879, 0.58120) \\
C & (3.17934, 1.15013, 0.70618) \\
H & (1.09935, 1.59141, 0.96334) \\
H & (2.00222, -2.05202, -1.12515) \\
H & (4.43316, -1.58972, -0.86800) \\
H & (3.50311, 2.05656, 1.20417)
\end{align*}
\]
Energy: -396089.7738399 H

C  2.99117  0.76778  0.88335
C  2.99124  0.76741  0.88372
C  1.82815  1.16724  0.01444
H  3.90762  1.20486  0.48283
H  2.83182  1.20384  1.87174
N  1.21793  0.00020  0.47221
C  1.82813  1.16708  0.01508
H  2.83162  1.20464  1.87116
H  3.90756  1.20513  0.48237
O  1.47506  2.28625  0.30436
O  1.47502  2.28593  0.30564
C  0.04673  0.00043  1.35949
C  1.26888  0.00014  0.60659
C  1.88126  1.20627  0.25155
C  3.08784  1.20617  0.44591
C  3.69397  0.00038  0.79557
C  1.88216  1.20627  0.25222
C  3.08876  1.20567  0.44521
H  1.40844  2.14446  0.51967
H  1.40684  2.14425  0.51850
H  3.55517  2.14734  0.71341
H  3.55680  2.14664  0.71217
H  4.63431  0.00057  1.33547
H  0.13070  0.88913  1.98563
H  0.13079  0.88785  1.98622

Energy: -225967.1900313 H

C  0.75135  1.25452  0.00036
C  0.75135  1.25452  0.00036
C  1.09499  0.26131  0.00017
H  1.20134  1.69255  0.89195
H  1.20167  1.69279  0.89102
C  1.09498  0.26132  0.00022
H  1.20134  1.69258  0.89193
H  1.20167  1.69275  0.89105
N  0.00000  1.06826  0.00001
Energy: -811348.6575238

Energy: -754805.3741503

O  2.23521  0.70070  0.00019
O  -2.23522  0.70070 -0.00022

Energy: -811348.6575238 H
C  -2.70641  0.15915  0.41450
C  -4.05954 -0.01666  0.69078
C  -4.68815 -1.18813  0.28397
C  -3.97574 -2.17597 -0.40222
C  -2.62677 -1.99214 -0.66817
C  -1.97040 -0.82373 -0.25742
H  -4.59197  0.76238  1.22165
H  -5.74159 -1.32811  0.49776
H  -4.47342 -3.08296 -0.72281
H  -2.04598 -2.74513 -1.18590
S  -0.92546  2.04527 -0.12279
N   0.08653  0.53631 -0.18821
C  -0.50970 -0.70278 -0.51683
O  -0.22958  2.95661  0.77238
O  -2.10242  1.30553  0.88424
O   0.14724 -1.61196 -0.97882
C   1.42437  0.83256 -0.65706
O   1.57393  1.77513 -1.40235
C   2.53252  0.01024 -0.12520
C   3.75203  0.03006 -0.81482
C   4.83622 -0.68933 -0.32861
C   4.71542 -1.41713  0.85636
C   2.41460 -0.72140  1.06197
C   3.50741 -1.42697  1.55309
H   5.77576 -0.68199 -0.86877
H   5.56381 -1.97426  1.23774
H   3.83038  0.60920 -1.72643
H   1.47857 -0.72219  1.60543
H   3.41766 -1.98452  2.47800

Energy: -754805.3741503 H
C   2.45240  0.36738  0.13885
C   3.76288  0.76761  0.35841
C  -4.73321 -0.22931  0.44516
C  -4.39167 -1.58209  0.31436
C  -3.07292 -1.96353  0.09557
|   |   |   |   |
|---|---|---|---|
|C  | -2.09219 | -0.97165 | 0.01087 |
|H  | -4.02032 | 1.81484 | 0.45738 |
|H  | -5.76727 | 0.04732 | 0.61555 |
|H  | -5.16603 | -2.33677 | 0.38664 |
|H  | -2.79054 | -3.00452 | -0.00562 |
|S  | -1.02963 | 1.45317 | -0.04785 |
|C  | 0.19700 | 0.06079 | -0.03253 |
|C  | -0.64390 | -1.21291 | -0.21739 |
|O  | -1.05407 | 2.07913 | -1.37442 |
|O  | -0.88034 | 2.29414 | 1.14345 |
|O  | -0.16142 | -2.28241 | -0.51109 |
|C  | 1.35497 | 0.24358 | -1.03771 |
|C  | 2.71924 | -0.01031 | -0.42787 |
|C  | 3.16623 | -1.31538 | -0.18932 |
|C  | 4.41701 | -1.54216 | 0.38088 |
|C  | 5.23862 | -0.46830 | 0.72268 |
|C  | 3.55025 | 1.05965 | -0.08227 |
|C  | 4.80187 | 0.83385 | 0.48956 |
|H  | 4.75142 | -2.55876 | 0.55609 |
|H  | 6.21242 | -0.64580 | 1.16501 |
|H  | 2.52772 | -2.15230 | -0.45088 |
|H  | 3.21832 | 2.07688 | -0.26401 |
|H  | 5.43458 | 1.67527 | 0.74921 |
|H  | 0.56241 | 0.06163 | 0.99865 |
|H  | 1.18973 | -0.43515 | -1.87727 |
|H  | 1.31221 | 1.25628 | -1.44431 |

![Diagram of the molecule](image)

Energy: -801261.2101103 H
|         |          |          |          |
|---------|----------|----------|----------|
| C       | -3.43710 | 1.11156  | -0.95623 |
| C       | -4.77731 | 0.75288  | -0.92316 |
| C       | -5.20259 | -0.28412 | -0.08980 |
| C       | -2.93971 | -0.59498 | 0.68666  |
| C       | -4.28298 | -0.95944 | 0.70978  |
| H       | -5.49273 | 1.27667  | -1.54649 |
| H       | -6.24923 | -0.56610 | -0.06650 |
| H       | -3.08669 | 1.90743  | -1.60134 |
| H       | -2.24221 | -1.14332 | 1.30818  |
| H       | -4.60915 | -1.77082 | 1.34960  |
| H       | -0.51596 | 0.06003  | 1.73962  |
| O       | -0.68821 | 1.66766  | -1.06080 |

Energy: -764888.0270087 H

|         |          |          |          |
|---------|----------|----------|----------|
| C       | -2.33897 | 0.36556  | 0.59319  |
| C       | -3.53366 | 0.34712  | 1.30679  |
| C       | -4.38068 | -0.74888 | 1.18380  |
| C       | -4.04219 | -1.81866 | 0.35052  |
| C       | -2.84149 | -1.79672 | -0.34492 |
| C       | -1.96909 | -0.70708 | -0.23087 |
| H       | -3.77786 | 1.18843  | 1.94309  |
| H       | -5.31322 | -0.76483 | 1.73622  |
| H       | -4.70925 | -2.66675 | 0.25537  |
| H       | -2.53863 | -2.62511 | -0.97324 |
| S       | -0.71014 | 1.93034  | -0.68733 |
| N       | 0.11312  | 0.39629  | -0.90443 |
| C       | -0.63418 | -0.78008 | -0.89770 |
| O       | 0.32515  | 2.88649  | -0.29171 |
| O       | -1.50534 | 1.45716  | 0.76087  |
| O       | -0.19044 | -1.81246 | -1.36530 |
| C       | 1.49558  | 0.38803  | -1.43908 |
| C       | 2.51709  | -0.08135 | -0.42287 |
| C       | 3.06362  | -1.36353 | -0.51229 |
| C       | 4.01788  | -1.78984 | 0.41095  |
| C       | 4.42955  | -0.93813 | 1.43356  |
| C       | 2.93305  | 0.76910  | 0.60724  |
| C       | 3.88395  | 0.34234  | 1.53042  |
| H       | 4.43504  | -2.78761 | 0.33244  |
| H       | 5.17077  | -1.26927 | 2.15240  |
| H       | 2.73064  | -2.03188 | -1.29830 |
| H       | 2.50475  | 1.76285  | 0.68511  |
| H       | 4.20150  | 1.00964  | 2.32394  |
| H       | 1.50193  | -0.25775 | -2.31763 |
| H       | 1.72700  | 1.40612  | -1.75446 |
Energy: -594802.9444121 H
C -2.22595  -1.55612  -0.09792
C -3.32869  -0.81567  0.25036
C  -0.92787   -0.93243  -0.28293
C  -0.83874   0.51124  -0.04759
C  -3.21453   0.57586  0.42941
C  -1.97501  1.22486  0.26717
H  -2.28404  -2.62471  -0.26867
H  -4.29209  -1.29536  0.37769
H  -4.08735   1.16017  0.69511
H  -1.91193  2.29680  0.41239
S  2.54339  -0.34864  -0.15980
N  1.55810   0.65306  0.46109
C  0.44757  1.25422  -0.16404
O  0.05432  -1.60720  -0.66894
O  3.58123  -0.77538  0.79795
O  0.53367  2.36985  -0.63077

Energy: -216511.7169472 H
C  1.28180  1.33032  0.00000
C  2.17530  0.25388  -0.00000
C  -0.08747  1.09665  0.00000
H  1.65717  2.34747  0.00000
C  -0.56364  -0.22656  0.00000
C  1.70359  -1.05968  -0.00000
H  3.24317  0.44277  -0.00000
C  0.33288  -1.30289  0.00000
H  -0.78979  1.92226  0.00000
H  2.40152  -1.88890  -0.00000
H  -0.05118  -2.31674  0.00000
C  -2.00731  -0.50245  0.00000
O  -2.93397  0.24469  -0.00000
References

[1] L. M. Schneider, V. M. Schmiedel, T. Pecchioli, D. Lentz, C. Merten, M. Christmann, *Org. Lett.* **2017**, *19*, 2310–2313.
[2] M. J. Kamlet, J. L. Abboud, R. W. Taft, *J. Am. Chem. Soc.* **1977**, *99*, 6027–6038.
[3] M. J. Kamlet, R. W. Taft, *J. Am. Chem. Soc.* **1976**, *98*, 377–383.
[4] A. Mouret, L. Leclercq, A. Mühlbauer, V. Nardello-Rataj, *Green Chem.* **2014**, *16*, 269–278.
[5] P. G. Jessop, D. A. Jessop, D. Fu, L. Phan, *Green Chem.* **2012**, DOI 10.1039/c2gc16670d.
[6] C. N. Henderson, B. K. Selinger, A. R. Watkins, *J. Photochem.* **1981**, *16*, 215–222.
[7] A. Mouret, L. Leclercq, A. Mühlbauer, V. Nardello-Rataj, *Green Chem.* **2014**, *16*, 269–278.
[8] A. Fawcett, J. Pradeilles, Y. Wang, T. Mutsuga, E. L. Myers, V. K. Aggarwal, *Science* (80-. ). **2017**, eaan3679.
[9] Z. Luo, L. Xiong, T. Liu, Y. Zhang, S. Lu, Y. Chen, W. Guo, Y. Zhu, Z. Zeng, *J. Org. Chem.* **2019**, *84*, 10559–10568.
[10] C. Liu, G. Meng, M. Szostak, *J. Org. Chem.* **2016**, *81*, 12023–12030.
[11] S. Karthik, T. Gandhi, *Org. Lett.* **2017**, *19*, 5486–5489.
[12] Z. He, Z. Wang, J. Ru, Y. Wang, T. Liu, Z. Zeng, *Adv. Synth. Catal.* **2020**, *362*, 5794–5800.
[13] H. Wu, T. Liu, M. Cui, Y. Li, J. Jian, H. Wang, Z. Zeng, *Org. Biomol. Chem.* **2017**, *15*, 536–540.
[14] L. M. Kammer, A. Rahman, T. Opatz, *Molecules* **2018**, DOI 10.3390/molecules23040764.
[15] R. Mao, A. Frey, J. Balon, X. Hu, *Nat. Catal.* **2018**, *1*, 120–126.
[16] Y.-L. Zhang, L. Yang, J. Wu, C. Zhu, P. Wang, *Org. Lett.* **2020**, *22*, 7768–7772.
[17] M. Koy, F. Sandfort, A. Tlahuext-Aca, L. Quach, C. G. Daniliuc, F. Glorius, *Chem. – A Eur. J.* **2018**, *24*, 4552–4555.
[18] X. Xu, J. Sun, Y. Lin, J. Cheng, P. Li, X. Jiang, R. Bai, Y. Xie, *European J. Org. Chem.* **2017**, *2017*, 7160–7166.
[19] H. Li, C. P. Breen, H. Seo, T. F. Jamison, Y.-Q. Fang, M. M. Bio, *Org. Lett.* **2018**, *20*, 1338–1341.
[20] Z. Xiao, L. Wang, J. Wei, C. Ran, S. H. Liang, J. Shang, G.-Y. Chen, C. Zheng, *Chem. Commun.* **2020**, *56*, 4164–4167.
[21] T. Qin, L. R. Malins, J. T. Edwards, R. R. Merchant, A. J. E. Novak, J. Z. Zhong, R. B. Mills, M. Yan, C. Yuan, M. D. Eastgate, P. S. Baran, *Angew. Chemie Int. Ed.* **2017**, *56*, 260–265.
[22] T. Yang, Y. Jiang, Y. Luo, J. J. H. Lim, Y. Lan, M. J. Koh, *J. Am. Chem. Soc.* **2020**, *142*, 21410–21419.
[23] D. Wang, N. Zhu, P. Chen, Z. Lin, G. Liu, *J. Am. Chem. Soc.* **2017**, *139*, 15632–15635.
[24] L. Yu, M.-L. Tang, C.-M. Si, Z. Meng, Y. Liang, J. Han, X. Sun, *Org. Lett.* **2018**, *20*, 4579–4583.
[25] H. Song, R. Cheng, Q. Q. Min, X. Zhang, *Org. Lett.* **2020**, *22*, 7747–7751.
[26] M. C. Sheikh, S. Takagi, M. Sakai, H. Abe, H. Morita, *Org. Biomol. Chem.* **2008**, *6*, 4505–4508.
[27] K. M. M. Huihui, J. A. Caputo, Z. Melchor, A. M. Olivares, A. M. Spiewak, K. A. Johnson, T. A. DiBenedetto, S. Kim, L. K. G. Ackerman, D. J. Weix, *J. Am. Chem. Soc.* **2016**, *138*, 5016–5019.
[28] W.-T. Jiang, S. Yang, M.-Y. Xu, X.-Y. Xie, B. Xiao, *Chem. Sci.* **2020**, *11*, 488–493.
Author Contributions

Jan Brauer designed the experiment and optimization studies, performed the synthesis of the compounds and the computational investigations. Jan Brauer and Till Opatz wrote the original draft in equal parts, with Lisa Marie Kammer providing support. Elisabeth Quraishi performed the synthesis of the compounds in a supporting role. Till Opatz choose the topic, designed the general study, provided interpretation for the experimental results in a leading role, with Lisa Marie Kammer providing support in these points. Till Opatz acquired the funding for this project and provided the materials.