Formal β-C–H Arylation of Aldehydes and Ketones by Cooperative Nickel and Photoredox Catalysis

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Supporting Information

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1. General information

All reactions involving air- or moisture-sensitive reagents or intermediates were carried out in flame-dried glassware under an argon atmosphere using standard Schlenk techniques. Acetonitrile, (CH\textsubscript{3}CN 99.9%, Extra Dry over Molecular Sieves) were purchased from Acros Organics. Otherwise noted, other commercially available reagents were purchased from TCI, Sigma-Aldrich, Alfa Aesar, Acros, ABCR or BLD pharm in the highest purity grade and used directly without further purification. Thin layer chromatography (TLC) was performed on Merck silica gel 60 F-254 plates and visualized by fluorescence quenching under UV light (254/366 nm). Column chromatography was performed on Merck or Fluka silica gel 60 (40-63 μm) using a forced flow of 0.5 bar. \textsuperscript{1}H NMR (300 MHz and 400 MHz), \textsuperscript{13}C NMR (76 MHz and 100 MHz) and \textsuperscript{19}F NMR (282 MHz) spectra were measured on a Bruker DPX 300 and Bruker AV 400 spectrometer at 300 K. The multiplicity of all signals was described as s (singlet), d (doublet), t (triplet), q (quartet) and m (multiplet). Chemical shifts (δ in ppm) were referenced on the residual peak of CDCl\textsubscript{3} (\textsuperscript{1}H NMR: δ = 7.26; \textsuperscript{13}C NMR: δ = 77.0). HRMS ESI (m/z) measurements were performed on a Bruker MicroTof and HRMS EI (m/z) on a Waters-Micromass QuattroMicro GC-MS. Reactions were performed with a 45 W (456 nm) Kessil blue LED. IR spectra were recorded on a Digilab 3100 FT-IR Excalibur Series spectrometer and the position of the absorption bands is given in wave numbers ν (cm\textsuperscript{-1}).
2. Substrate structures

Silyl enol ethers and enol ethers:

![Chemical structures](image1)

(hetero)aryl bromides:

![Chemical structures](image2)

1a-e\(^{[1]}\), 1f-l\(^{[2]}\), 1m-p\(^{[3]}\), 2d-h\(^{[4]}\), 2y-z\(^{[4]}\), 2x\(^{[5]}\), 2a-b\(^{[6]}\), 2ac\(^{[7]}\) and [Ni(dtbbpy)(H₂O)]Cl₂\(^{[8]}\) were prepared following the literature procedures. 2a-c, 2i-w, 2aa and 2ad-af were purchased from Sigma Aldrich, TCI, ABCR or Alfa Aesar and used directly without further purification.
3. General procedures

3.1 General procedure A to obtain β-arylated aldehydes and ketones.

To an oven-dried 10 mL Schlenk tube, 4-CzIPN (2.0 mg, 2.5 µmol, 2.5 mol%), [Ni(dtbbpy)(H₂O)₄]Cl₂ (4.7 mg, 0.010 mmol, 10 mol%) and aryl bromide (0.10 mmol, 1.0 eq.) were added. The reaction tube was evacuated and backfilled with argon four times. Next, MeCN (1.0 mL) was added, which was followed by the addition of a silyl enol ether (0.20 mmol, 2.0 eq.) and 2,4,6-collidine (18.2 mg, 0.15 mmol, 1.5 eq.). The resulting mixture was stirred for three minutes before irradiating with a 45 W blue LED at room temperature for 24 hours. After removal of the solvent under reduced pressure, THF (2.0 mL) was added to the residue, followed by the addition of TBAF (1.0 M in THF, 0.25 mL, 0.25 mmol) and HOAc (24.8 mg, 0.40 mmol, 4.0 eq.) at 0 °C. The resulting mixture was slowly allowed to warm to room temperature and stirred for 2 h. After addition of aqueous NH₄Cl solution and extraction with DCM, the organic extracts were dried over Na₂SO₄, filtered, and concentrated in vacuo. The crude product was purified by silica gel chromatography using a mixture of pentane and diethyl ether as eluent to get the desired product 3.

3.2 General procedure B for the β-arylation of enol ethers.

To an oven-dried 10 mL Schlenk tube, [Ir(dF(CF₃)ppy)₂(5,5'-d(CF₃)bpy)]PF₆ (3.4 mg, 3.0 µmol, 3.0 mol%), [Ni(dtbbpy)(H₂O)₄]Cl₂ (4.7 mg, 0.010 mmol, 10 mol%) and aryl bromide (0.10 mmol, 1.0 eq.) were added. The reaction tube was evacuated and backfilled with argon four times. Next, MeCN (1.0 mL) was added, which was followed by the addition of an enol ether (0.20 mmol, 2.0 eq.) and 2,4,6-collidine (18.2 mg, 0.15 mmol, 1.5 eq.). The resulting mixture was stirred for three minutes before irradiating with a 45 W blue LED at room temperature for 24 hours. After removal of the solvent under reduced pressure, the residue was purified by silica gel chromatography using a mixture of pentane and diethyl ether as eluent to get the desired product 3.

3.3 Procedure for the larger scale one-pot synthesis of β-arylated silyl enol ether 4a
2,4,6-Collidine (727.1 mg, 6.0 mmol, 3.0 equiv.) was added dropwise to a cooled (0 °C) solution of 2-methyl-propanal (144.2 mg, 2.0 mmol, 1.0 equiv.) in CH$_2$Cl$_2$ (4.0 mL). Triisopropylsilyl trifluoromethanesulfonate (918.0 mg, 3.0 mmol, 1.5 equiv.) was added dropwise at 0 °C. The reaction mixture was allowed to warm to room temperature, and was then stirred overnight at room temperature. After removal of the solvent under reduced pressure, the reaction tube was bubbled with argon. Next, MeCN (10.0 mL) was added, which was followed by the addition of 4-CzIPN (19.7 mg, 25 μmol, 2.5 mol%), [Ni(dtbbpy)(H$_2$O)$_4$]Cl$_2$ (47.0 mg, 0.10 mmol, 10 mol%) and methyl 4-bromobenzoate (214.0 mg, 1.0 mmol, 1.0 eq.). The resulting mixture was stirred for five minutes before irradiating with a 45 W blue LED at room temperature for 48 hours. After removal of the solvent under reduced pressure, the residue was purified by silica gel chromatography using a mixture of pentane and diethyl ether as eluent to get the desired product 4a as a colorless liquid (202.7 mg, 56%, E/Z = 12:1).

**FT IR** (neat) $\nu$ (cm$^{-1}$) = 2943, 2862, 2333, 2324, 1725, 1281, 1183.

**$^1$H NMR** (400 MHz, CDCl$_3$) (E- and Z-isomers) $\delta$ (ppm) = 8.00 – 7.90 (m, 2H), 7.31 – 7.20 (m, 2H), [6.32 (q, $J = 1.3$ Hz, E-isomer) + 6.28 (q, $J = 1.3$ Hz, Z-isomer), 1H], [3.90 (s, E-isomer) + 3.89 (s, Z-isomer), 3H], [3.48 (s, Z-isomer) + 3.21 (s, E-isomer), 2H], [1.51 (d, $J = 1.4$ Hz, E-isomer) + 1.44 (d, $J = 1.4$ Hz, Z-isomer), 3H], 1.23 – 1.04 (m, 21H).

**$^{13}$C NMR** (76 MHz, CDCl$_3$) (E-isomer) $\delta$ (ppm) = 167.18, 146.42, 136.45, 129.54, 128.67, 127.91, 115.01, 51.92, 40.26, 17.75, 12.51, 11.97.

**HRMS (ESI)** Calcd. for C$_{21}$H$_{34}$NaO$_3$Si$^+$ [M+Na]$^+$: 385.2169, found: 385.2168.

**4. Product derivatization**

**4.1 The cyclopropanation of silyl enol ether 4a**

An oven-dried 10 mL Schlenk tube was evacuated and backfilled with argon. Next, silyl enol ether 4a (0.2 mmol) and hexane (2.0 mL) were added, which was followed by the addition of Et$_2$Zn (0.44 mmol, 440 μL, 1 M in hexane). The mixture was cooled to 0 °C and diiodomethane (117.9 mg, 0.44 mmol, 2.2 eq.) was added dropwise. The resulting solution was allowed to warm to room temperature.
temperature and stirring was continued overnight. After the addition of aqueous NH₄Cl solution and extraction with DCM, the organic extracts were dried over Na₂SO₄, filtered, and concentrated in vacuo. The crude product was purified by silica gel chromatography using a mixture of pentane and diethyl ether as eluent to get the desired product 5a (73%, 54.9 mg, d.r. = 7:1). FT IR (neat) ν (cm⁻¹) = 2848, 2859, 2389, 2342, 1725, 1283, 1277, 776. ¹H NMR (400 MHz, CDCl₃) (mixture of diastereoisomers) δ (ppm) = 7.98 – 7.92 (m, 2H), [7.41 – 7.38 (m, minor diastereoisomer) + 7.28 – 7.22 (m, major diastereoisomer), 2H], 3.90 (s, 3H), [3.35 (dd, J = 6.6, 3.2 Hz, major diastereoisomer) + 3.28 (dd, J = 5.6, 3.8 Hz, minor diastereoisomer), 1H], [2.87 (d, J = 14.4 Hz, minor diastereoisomer) + 2.60 (d, J = 14.4 Hz, major diastereoisomer), 1H], [2.81 (d, J = 14.4 Hz, minor diastereoisomer) + 2.47 (d, J = 14.4 Hz, major diastereoisomer), 1H], 1.15 – 1.02 (m, 21H). ¹³C NMR (101 MHz, CDCl₃) (mixture of diastereoisomers) δ (ppm) = 167.20, 147.09, 145.53, 129.43, 129.34, 129.16, 127.94, 127.62, 58.03, 57.11, 51.96, 51.90, 44.26, 38.28, 21.90, 21.61, 21.59, 20.35, 17.99, 17.96, 17.91, 16.03, 12.04, 12.02. HRMS (ESI) Calcd. for C₂₂H₃₆NaO₃Si⁺ [M+Na]⁺: 399.2326, found: 399.2325.

4.2 Difunctionalization of the double bond of silyl enol ether 4a

An oven-dried 10 mL Schlenk tube was evacuated and backfilled with argon. Next, silyl enol ether 4a (0.2 mmol) and DCM (2.0 mL) were added, which was followed by the addition of allyl alcohol (11.6 mg, 0.20 mmol, 1.0 eq.) and N-iodosuccinimide (45.0 mg, 0.20 mmol, 1.0 eq.) at 0 °C. The mixture was further stirred at 0 °C for 2 h. After the addition of aqueous Na₂SO₃ solution and extraction with DCM, the organic extracts were dried over Na₂SO₄, filtered, and concentrated in vacuo. The crude product was purified by silica gel chromatography using a mixture of pentane and diethyl ether as eluent to get the desired product 5b (92.8 mg, 85%, d.r. = 1.3:1). FT IR (neat) ν (cm⁻¹) = 2954, 2861, 2359, 1728, 1340, 1263, 1111, 1050, 783. ¹H NMR (300 MHz, CDCl₃) (mixture of diastereoisomers) δ (ppm) = 8.04 – 7.91 (m, 2H), 7.46 – 7.36 (m, 2H), 6.08 – 5.83 (m, 1H), 5.42 – 5.26 (m, 1H), 5.25 – 5.15 (m, 1H), [4.87 (s, minor diastereoisomer) + 4.84 (s, major diastereoisomer), 1H], 4.47 – 4.13 (m, 2H), 3.91 (s, 3H), 3.54 – 3.36 (m, 1H), 3.12 – 2.97 (m, 1H), [1.86 (s, minor diastereoisomer) + 1.84 (s, major diastereoisomer), 3H], 1.28 – 1.05 (m, 21H). ¹³C NMR (101 MHz, CDCl₃) (mixture of diastereoisomers) δ (ppm) = 166.15, 142.17, 132.83, 132.82, 130.36, 130.32, 127.92, 127.59, 127.57, 115.77, 115.75, 102.76, 102.48, 70.89, 70.65, 58.53, 58.31, 51.01, 45.31, 44.39, 28.59, 27.66, 17.35, 17.33, 17.25, 17.24, 12.15, 12.12. HRMS (ESI) Calcd. for C₂₄H₃₆NaO₃Si⁺ [M+Na]⁺: 569.1555, found: 569.1552.
4.3 The fluorination of 4b to produce α-fluoro-β-arylated ketone 5c

To a solution of 4b (38.8 mg, 0.1 mmol) in MeCN (1.0 mL), Selectfluor (38.9 mg, 0.11 mmol) was added at 0 °C, and the resulting reaction mixture was allowed to warm to room temperature. After stirring for 3 h, the solvent was removed under reduced pressure. The crude residue was purified by column chromatography on silica gel (PE/EtOAc = 1:1 as eluent) to afford 5c as colorless oil (20.3 mg, 81%, anti:syn > 19:1). FT IR (neat) ν (cm⁻¹) = 2997, 2362, 2331, 1723, 1272, 1255, 774, 746. 

¹H NMR (300 MHz, CDCl₃) δ (ppm) = 8.08 – 7.98 (m, 2H), 7.42 – 7.32 (m, 2H), 5.02 (ddd, J = 48.7, 11.6, 1.1 Hz, 1H), 3.91 (s, 3H), 3.26 – 3.08 (m, 1H), 2.71 – 2.58 (m, 1H), 2.57 – 2.41 (m, 1H), 2.27 – 1.95 (m, 3H), 1.88 – 1.70 (m, 1H). 

¹³C NMR (76 MHz, CDCl₃) δ (ppm) = 203.69 (d, J = 14.4 Hz), 166.72, 144.96, 130.11, 129.44, 127.34, 94.96 (d, J = 197.6 Hz), 52.12, 51.40 (d, J = 18.2 Hz), 40.28, 31.62 (d, J = 7.6 Hz), 25.43. 

¹⁹F NMR (282 MHz, CDCl₃) δ (ppm) = -192.65. 

HRMS (ESI) Calcd. for C₁₄H₁₅FNaO₃⁺ [M+Na]⁺: 273.0897, found: 273.0898.

4.4 Reduction of 3o to afford γ-arylated propanol

To a solution of 3o (18.8 mg, 0.1 mmol) in MeOH (2.0 mL), NaBH₄ (5.7 mg, 0.15 mmol, 1.5 eq.) was added at 0 °C. The resulting mixture was further stirred at 0 °C for 6 h. After the addition of water and extraction with DCM, the organic extracts were dried over Na₂SO₄, filtered, and concentrated in vacuo. The crude product was purified by flash column chromatography (PE/EtOAc = 7/1 as eluent) to get the desired product 5d (17.5 mg, 92%). FT IR (neat) ν (cm⁻¹) = 2959, 2922, 2361, 2338, 1475, 1267, 1258, 1024, 765, 741. 

¹H NMR (300 MHz, CDCl₃) δ (ppm) = 7.59 (d, J = 2.1 Hz, 1H), 7.41 (d, J = 8.7 Hz, 1H), 7.39 (s, 1H), 7.11 (dd, J = 8.7, 1.8 Hz, 1H), 6.73 – 6.69 (m, 1H), 3.66 – 3.40 (m, 2H), 2.85 (dd, J = 13.8, 6.6 Hz, 1H), 2.53 (dd, J = 13.8, 7.9 Hz, 1H), 2.08 – 1.89 (m, 1H), 0.94 (d, J = 6.6 Hz, 3H). 

¹³C NMR (76 MHz, CDCl₃) δ (ppm) = 153.62, 145.07, 134.98, 125.51, 121.21, 121.12, 110.94, 106.35, 67.63, 39.55, 38.17, 16.46. HRMS (ESI) Calcd. for C₁₂H₁₄NaO₂⁺ [M+Na]⁺: 213.0886, found: 213.0886.

5. Mechanistic studies

5.1 Radical capture experiment
To an oven-dried 10 mL Schlenk tube, 4-CzIPN (2.0 mg, 2.5 μmol, 2.5 mol%), [Ni(dtbbpy)(H₂O)₄]Cl₂ (4.7 mg, 0.010 mmol, 10 mol%), methyl 4-bromobenzoate (21.4 mg, 0.10 mmol, 1.0 eq.) and TEMPO (31.2 mg, 0.20 mmol, 2.0 eq.) were added. The reaction tube was evacuated and backfilled with argon four times. Next, MeCN (1.0 mL) was added, which was followed by the addition of silyl enol ether 1a (45.6 mg, 0.20 mmol, 2.0 eq.) and 2,4,6-collidine (18.2 mg, 0.15 mmol, 1.5 eq.). The resulting mixture was stirred for three minutes before irradiating with a 45 W blue LED at room temperature for 24 hours. The yield of 4a was determined by GC-MS and GC with biphenyl as an internal standard. The reaction was fully suppressed upon addition of TEMPO, and the TEMPO-adduct could be detected by HRMS. HRMS (ESI): m/z [M+H]+ calcd for C₂₂H₄₆NO₂Si+: 384.3292, found: 384.3295; m/z [M+Na]+ calcd for C₂₂H₄₅NNaO₂Si+: 406.3112, found: 406.3113.
To an oven-dried 10 mL Schlenk tube, 4-CzIPN (2.0 mg, 2.5 µmol, 2.5 mol%), [Ni(dtbbpy)(H₂O)]₂Cl₂ (4.7 mg, 0.010 mmol, 10 mol%), methyl 4-bromobenzoate (21.4 mg, 0.10 mmol, 1.0 eq.) and 2-benzylidenemalononitrile (15.4 mg, 0.10 mmol, 1.0 eq.) were added. The reaction tube was evacuated and backfilled with argon four times. Next, MeCN (1.0 mL) was added, which was followed by the addition of silyl enol ether 1a (45.6 mg, 0.20 mmol, 2.0 eq.) and 2,4,6-collidine (18.2 mg, 0.15 mmol, 1.5 eq.). The resulting mixture was stirred for three minutes before irradiating with a 45 W blue LED at room temperature for 24 hours. After removal of the solvent under reduced pressure, the crude product was purified by silica gel chromatography using a mixture of pentane and diethyl ether as eluent to get the desired product 4a (13.0 mg, 36%) and 7 (30.2 mg, 79%, E/Z = 1.5:1).

**FT IR** (neat) υ (cm⁻¹) = 2947, 2868, 2361, 1669, 1461, 1272, 1195, 744, 692. **¹H NMR (300 MHz, CDCl₃)** (E- and Z-isomers) δ (ppm) = 7.45 – 7.32 (m, 5H), [6.30 (s, E-isomer) + 6.26 (s, Z-isomer), 1H], [4.02 (d, J = 4.8 Hz, Z-isomer) + 3.97 (d, J = 4.8 Hz, E-isomer), 1H], [3.51 – 3.40 (m, Z-isomer) + 3.40 – 3.28 (m, E-isomer), 1H], [2.99 – 2.88 (m, Z-isomer) + 2.54 – 2.41 (m, E-isomer), 1H], 2.68 – 2.54 (m, 1H), [1.63 (d, J = 1.5 Hz, E-isomer) + 1.48 (d, J = 1.5 Hz, Z-isomer), 3H], 1.19 – 0.95 (m, 21H). **¹³C NMR (76 MHz, CDCl₃)** (E- and Z-isomers) δ (ppm) = 138.66, 137.78, 136.96, 136.79, 129.07, 128.87, 128.80, 128.69, 128.10, 127.99, 112.53, 112.24, 111.73, 111.48, 110.40, 110.39, 44.55, 44.11, 36.86, 31.76, 29.06, 28.59, 17.76, 17.74, 17.65, 17.63, 17.36, 12.13, 11.88, 11.83. **HRMS (ESI)** Calcd. for C₂₃H₃₄N₂NaOSi⁺ [M+Na]⁺: 405.2333, found: 405.2332.

**5.2 Luminescence quenching experiments**

Emission intensities were recorded using a Jasco FP-8300 spectrofluorometer. All 4-CzIPN solutions were excited at 435 nm and the emission intensity was recorded at 548 nm. In a typical experiment, to a certain amount of a solution of 4-CzIPN in MeCN (5 mL), the appropriate amount of quencher (silyl enol ether 1a or methyl 4-bromobenzoate 2a) was added in a screw-top quartz cuvette. After degassing the solution by bubbling argon for 8 minutes, the emission of the sample was recorded. Stern-Volmer fluorescence quenching experiments revealed that only silyl enol ether 1a could quench the excited state of 4-CzIPN*, while no significant quenching was observed with methyl 4-bromobenzoate 2a. These results support the proposed reductive quenching pathway.
5.3 UV-visible spectroscopy

UV-visible absorption spectra were recorded on a Jasco V-650 spectrophotometer, equipped with a temperature control unit at 25 °C. The samples were measured in Starna Fluorometer Microquartz cuvettes (volume: 3.0 ml, path length: 10 mm) equipped with a PTFE-stopper. The spectra were acquired from 400 to 700 nm using 0.5 nm steps. All measurements were performed in dry MeCN at one quarter of concentrations used for the standard reaction. Note: Due to substantial insolubility of the Ni(II) complex, in some instances the baseline appears deviating from the zero value, owing to scattering effects.
UV–vis analysis of the individual reaction components and the reaction system showed the 4-CzIPN to be the only absorbing species in the visible range, indicating that only the organic photocatalyst should be activated by the light.

5.4 Procedures for quantum yield determination

Determination for the light intensity of Kessil 45 W-456 nm LED

Standard ferrioxalate actinometry\(^9,10\) was used to determine the photon flux of Kessil 45 W-456 nm LED. A solution of ferrioxalate (0.15 M) was prepared by dissolving potassium ferrioxalate trihydrate (737 mg, 1.50 mmol) in 10.0 mL of 0.20 M aqueous H\(_2\)SO\(_4\). A buffered solution of 1,10-phenanthroline (0.15 M) was prepared by dissolving NaOAc (1.23 g, 15.0 mmol) and 1,10-phenanthroline (541 mg, 3.00 mmol) in 20 mL of 0.20 M aqueous H\(_2\)SO\(_4\).

An oven-dried 10 mL Schlenk tube was evacuated and backfilled with argon four times. Then, the ferrioxalate solution (1.0 mL) was added. The tube was sealed and placed 2 cm away from Kessil 45 W-456 nm LED. After being irradiated for 20 seconds, the aqueous sulfuric acid (3.0 mL) and buffered solution (4.0 mL) was added immediately under argon atmosphere. The resulting mixture was then placed in the dark for 1 hour to allow the formed ferrous ions to react completely with 1,10-phenanthroline. An aliquot (25 µL) of the resulting solution was diluted with 3.0 mL of 0.20 M aqueous sulfuric acid, and the absorbance in a cuvette (l = 1.0 cm) at 510 nm was measured by UV-Vis spectrometer. The above procedure was repeated three more times, and the average absorption was used for the calculation of photon flux. A nonirradiated sample was also prepared and the absorbance at 510 nm was measured.

The photon flux was calculated as follows:

\[
\text{mol Fe}^{2+} = \frac{V \times \Delta A (510 \text{ nm})}{l \times \varepsilon} \tag{1}
\]

where V is the total volume (0.96 L) of the solution that was analyzed, \(\Delta A (0.208)\) is the difference between the average absorption of irradiated and non-irradiated solutions at 510 nm, l is the path length (1.00 cm), and \(\varepsilon\) is the molar absorptivity of the ferrioxalate actinometer at 510 nm (11,100 L·mol\(^{-1}\)·cm\(^{-1}\)).

The photon flux was calculated as follows:

\[
\text{photon flux} = \frac{\text{mol Fe}^{2+}}{\Phi \times t \times f} \tag{2}
\]

where \(\Phi\) is the quantum yield for the ferrioxalate actinometer (approximated as 0.845, which was reported at \(\lambda = 457.9 \text{ nm}\)\(^\text{11}\), t is the irradiation time (20 s), and f is the fraction of light absorbed at \(\lambda = 456 \text{ nm}\) by the ferrioxalate actinometer. This value is calculated using the following equation where \(A(456 \text{ nm})\) is the absorption of the ferrioxalate solution at 456 nm. An absorption spectrum gave an \(A(456 \text{ nm})\) value of > 3, indicating that the fraction of absorbed light (f) is > 0.999.

\[
f = 1 - 10^{-A(456 \text{ nm})} \tag{3}
\]

The average photon flux was thus calculated to be 1.06 \times 10^{-6} einsteins·s\(^{-1}\).
Determination of quantum yield

To an oven-dried 10 mL Schlenk tube, 4-CzIPN (2.0 mg, 2.5 μmol, 2.5 mol%), [Ni(dtbbpy)(H₂O)₄]Cl₂ (4.7 mg, 0.010 mmol, 10 mol%) and methyl 4-bromobenzoate (21.4 mg, 0.10 mmol, 1.0 eq.) were added. The reaction tube was evacuated and backfilled with argon four times. Next, MeCN (1.0 mL) was added, which was followed by the addition of silyl enol ether 1a (45.6 mg, 0.20 mmol, 2.0 eq.) and 2,4,6-collidine (18.2 mg, 0.15 mmol, 1.5 eq.). The resulting mixture was stirred for three minutes before irradiating with a 45 W blue LED at room temperature for 2 hours. 11% yield (1.1 × 10⁻⁵ mol) of 4a was determined by GC with biphenyl as an internal standard.

The quantum yield was calculated as follows:

\[
\Phi = \frac{\text{mol product}}{\text{flux} \times t \times f}
\]  

where flux is the photon flux determined by ferrioxalate actinometry (1.06 × 10⁻⁶ Einstein/s), t is the time (7200 s), and f is the fraction of light absorbed by the reaction mixture at 456 nm. This value is calculated using eq. 3 where A (456 nm) is the orption of the ferrioxalate solution at 456 nm. An absorption spectrum gave an A(456 nm) value of > 3, indicating that the fraction of absorbed light (f) is > 0.999.

\[
\Phi = \frac{1.1 \times 10^{-5}}{1.06 \times 10^{-6} \text{ Einstein/s} \times 7200 \text{ s} \times 1}
\]

Thus, the reaction quantum yield (Φ) was determined to be Φ = 0.0014.

5.5 Light on-off experiments
Four parallel reactions were performed between triisopropyl silyl enol ether 1a (45.6 mg, 0.20 mmol, 2.0 eq.) and methyl 4-bromobenzoate 2a (21.4 mg, 0.10 mmol, 1.0 eq.) according to the General Procedure. The yield of 4a was determined by GC with biphenyl as the internal standard at the given times. The white area indicates the light irradiation, while the grey area indicates time in the dark.

5.6 Synthesis of the Ni(II) complex

\[
\text{Ar}^+\text{Ni}^{II}\text{Br} \quad \xrightarrow{\text{Ni(COD)}_2, \text{THF, r.t., 12 h}} \quad \text{Ni}^{II}\text{Br} + \text{Cl}, \text{Br} \quad \xrightarrow{\text{THF, r.t., 4 h}} \quad \text{Ni}^{II}\text{Br}
\]

Ar−NiII−Br complex was synthesized according to a reported procedure. In an argon filled glove box, a 50 mL round bottom flash containing a stirring bar was charged with Ni(COD)₂ (138 mg, 0.500 mmol, 1.0 eq.), 4,4’-di-tert-butyl-2,2’-bipyridine (134 mg, 0.500 mmol, 1.0 eq.) and dry THF (5 mL). The dark purple mixture was stirred overnight at room temperature. Then, 4-bromo-1,2-dichlorobenzene (1.12 g, 5.00 mmol, 10 eq.) was added and the mixture was stirred for additional 2 h. Dry pentane (10 mL) was added to the orange mixture and filtered. The resulting precipitate was washed with dry pentane (3 × 10 mL) and dried under vacuum to obtain the Ni(II) complex as a brown solid, which was used without further purification.

5.7 Stoichiometric amount reactions of Ni(II) complex

To an oven-dried 10 mL Schlenk tube, 4-CzIPN (2.0 mg, 2.5 μmol, 2.5 mol%) and Ni(II) complex (55.0 mg, 0.10 mmol, 1.0 eq.) were added. The reaction tube was evacuated and backfilled with argon four times. Next, MeCN (1.0 mL) was added, which was followed by the addition of 2,4,6-collidine (18.2 mg, 0.15 mmol, 1.5 eq.). The resulting mixture was stirred for three minutes before irradiating with a 45 W blue LED at room temperature for 24 hours. After removal of the solvent under reduced pressure, THF (2.0 mL) was added to the residue, followed by the addition of TBAF (1.0 M in THF, 0.25 mL, 0.25 mmol) and HOAc (24.8 mg, 0.40 mmol, 4.0 eq.) at 0 °C. The resulting mixture was slowly allowed to warm to room temperature and stirred for 2 h. After addition of aqueous NH₄Cl solution and extraction with DCM, the organic extracts were dried over Na₂SO₄, filtered, and concentrated in vacuo. Only trace amount of product was obtained by silica gel
chromatography using a mixture of pentane and diethyl ether as eluent.

5.8 Catalytic reactions of Ni(II) complex

\[
\begin{array}{c}
\text{Cl} \quad \text{Cl} \\
2k \\
\text{Cl} \quad \text{Br} \\
\text{Ni(II) complex (10 mol%)} \\
4\text{-CzIPN, 2,4,6-collidine} \\
\text{MeCN, 45 W blue LED then TBAF, HOAc} \\
\end{array}
\]

To an oven-dried 10 mL Schlenk tube, 4-CzIPN (2.0 mg, 2.5 \( \mu \)mol, 2.5 mol%) and 4-bromo-1,2-dichlorobenzene (22.4 mg, 0.10 mmol, 1.0 eq.) were added. The reaction tube was evacuated and backfilled with argon four times. Next, MeCN (1.0 mL) was added, which was followed by the addition of 2,4,6-collidine (18.2 mg, 0.15 mmol, 1.5 eq.). The resulting mixture was stirred for three minutes before irradiating with a 45 W blue LED at room temperature for 24 hours. After removal of the solvent under reduced pressure, THF (2.0 mL) was added to the residue, followed by the addition of TBAF (1.0 M in THF, 0.25 mL, 0.25 mmol) and HOAc (24.8 mg, 0.40 mmol, 4.0 eq.) at 0 °C. The resulting mixture was slowly allowed to warm to room temperature and stirred for 2 h. After addition of aqueous NH\(_4\)Cl solution and extraction with DCM, the organic extracts were dried over Na\(_2\)SO\(_4\), filtered, and concentrated in vacuo. 56% yield of targeted product was obtained by silica gel chromatography using a mixture of pentane and diethyl ether as eluent.

6. Product characterization

**Methyl 4-(2-methyl-3-oxopropyl)benzoate (3a)**

\[
\begin{array}{c}
\text{H} \\
\text{Me} \\
\text{CO}_2\text{Me} \\
\end{array}
\]

The reaction was performed according to the general procedure A with 1a (0.2 mmol, 45.6 mg) and 2a (0.1 mmol, 21.4 mg). After purification by flash chromatography (PE/Et\(_2\)O = 10/1), the desired compound 3a was obtained as a colorless oil (17.7 mg, 86% yield).

**FT IR (neat) \( \nu \) (cm\(^{-1}\)) = 3324, 2969, 2880, 1414, 1379, 1019, 875, 767.

**\(^1\)H NMR (300 MHz, CDCl\(_3\)) \( \delta \) (ppm) = 9.71 (d, \( J = 1.2 \) Hz, 1H), 8.01 – 7.93 (m, 2H), 7.26 – 7.21 (m, 2H), 3.90 (s, 3H), 3.25 – 3.06 (m, 1H), 2.77 – 2.58 (m, 2H), 1.09 (d, \( J = 6.9 \) Hz, 3H).

**\(^13\)C NMR (76 MHz, CDCl\(_3\)) \( \delta \) (ppm) = 203.6, 166.9, 144.4, 129.8, 129.0, 128.5, 52.0, 47.7, 36.5, 13.2.

**HRMS (ESI)** Calcd. for C\(_{12}\)H\(_{14}\)NaO\(_3\)\(^+\) [M+Na\(^+\)]\(^+\): 229.0835, found: 229.0835.

**3-(4-Acetylphenyl)-2-methylpropanal (3b)**
The reaction was performed according to the general procedure A with 1a (0.2 mmol, 45.6 mg) and 2b (0.1 mmol, 21.4 mg). After purification by flash chromatography (PE/Et₂O = 5/1), the desired compound 3b was obtained as a colorless oil (16.2 mg, 85% yield).

**FT IR** (neat) ν (cm⁻¹) = 2972, 2920, 2359, 1723, 1679, 1273, 760.

**¹H NMR (300 MHz, CDCl₃)** δ (ppm) = 9.72 (d, J = 1.2 Hz, 1H), 7.94 – 7.85 (m, 2H), 7.32 – 7.22 (m, 2H), 3.21 – 3.06 (m, 1H), 2.83 – 2.61 (m, 2H), 2.58 (s, 3H), 1.11 (d, J = 6.9 Hz, 3H).

**¹³C NMR (76 MHz, CDCl₃)** δ (ppm) = 203.5, 197.7, 144.7, 135.6, 129.2, 128.6, 47.7, 36.5, 26.5, 13.3.

**HRMS (ESI)** Calcd. for C₁₂H₁₄NaO₂⁺ [M+Na]⁺: 213.0886, found: 213.0885.

4-(2-Methyl-3-oxopropyl)benzaldehyde (3c)

The reaction was performed according to the general procedure A with 1a (0.2 mmol, 45.6 mg) and 2c (0.1 mmol, 21.4 mg). After purification by flash chromatography (PE/Et₂O = 10/1), the desired compound 3c was obtained as a colorless oil (14.4 mg, 82% yield).

**FT IR** (neat) ν (cm⁻¹) = 3004, 2983, 2366, 2221, 1737, 1606, 1276, 758.

**¹H NMR (300 MHz, CDCl₃)** δ (ppm) = 9.98 (s, 1H), 9.72 (d, J = 1.1 Hz, 1H), 7.89 – 7.77 (m, 2H), 7.40 – 7.30 (m, 2H), 3.28 – 3.10 (m, 1H), 2.82 – 2.61 (m, 2H), 1.12 (d, J = 6.9 Hz, 3H).

**¹³C NMR (76 MHz, CDCl₃)** δ (ppm) = 203.3, 191.8, 146.3, 135.0, 130.0, 129.7, 47.7, 36.6, 13.3.

**HRMS (ESI)** Calcd. for C₁₁H₁₂NaO₂⁺ [M+Na]⁺: 199.0730, found: 199.0730.

2-Chloroethyl 4-(2-methyl-3-oxopropyl)benzoate (3d)

The reaction was performed according to the general procedure A with 1a (0.2 mmol, 45.6 mg) and 2d (0.1 mmol, 21.4 mg). After purification by flash chromatography (PE/Et₂O = 10/1), the desired compound 3d was obtained as a colorless oil (21.1 mg, 83% yield).

**FT IR** (neat) ν (cm⁻¹) = 2962, 2927, 2361, 1711, 1611, 1307, 1274, 1176, 1110, 753.
$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ (ppm) = 9.71 (d, $J = 1.2$ Hz, 1H), 8.05 – 7.95 (m, 2H), 7.29 – 7.21 (m, 2H), 4.63 – 4.49 (m, 2H), 3.89 – 3.76 (m, 2H), 3.30 – 3.03 (m, 1H), 2.85 – 2.56 (m, 2H), 1.10 (d, $J = 6.9$ Hz, 3H).

$^{13}$C NMR (76 MHz, CDCl$_3$) $\delta$ (ppm) = 203.52, 166.98, 144.84, 130.01, 129.13, 127.90, 64.38, 47.71, 41.67, 36.48, 13.21.

HRMS (ESI) Calcd. for C$_{13}$H$_{15}$ClNaO$_3$ $^+\ [M+Na]^+$: 277.0602, found: 277.0603.

But-3-en-1-yl 4-(2-methyl-3-oxopropyl)benzoate (3e)

![But-3-en-1-yl 4-(2-methyl-3-oxopropyl)benzoate](image)

The reaction was performed according to the general procedure A with 1a (0.2 mmol, 45.6 mg) and 2e (0.1 mmol, 21.4 mg). After purification by flash chromatography (PE/Et$_2$O = 10/1), the desired compound 3e was obtained as a colorless oil (19.4 mg, 79% yield).

FT IR (neat) $\nu$ (cm$^{-1}$) = 2979, 2932, 2354, 1716, 1279, 1176, 1110, 769.

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ (ppm) = 9.70 (d, $J = 1.2$ Hz, 1H), 8.03 – 7.91 (m, 2H), 7.44 (dd, $J = 1.8, 0.9$ Hz, 1H), 7.27 – 7.18 (m, 2H), 6.53 – 6.44 (m, 1H), 6.38 (dd, $J = 3.3, 1.9$ Hz, 1H), 5.30 (s, 2H), 3.23 – 3.06 (m, 1H), 2.78 – 2.56 (m, 2H), 1.08 (d, $J = 6.8$ Hz, 3H).

HRMS (ESI) Calcd. for C$_{16}$H$_{18}$NaO$_4$ $^+\ [M+Na]^+$: 295.0941, found: 295.0942.

Furan-2-ylmethyl 4-(2-methyl-3-oxopropyl)benzoate (3f)

![Furan-2-ylmethyl 4-(2-methyl-3-oxopropyl)benzoate](image)

The reaction was performed according to the general procedure A with 1a (0.2 mmol, 45.6 mg) and 2f (0.1 mmol, 21.4 mg). After purification by flash chromatography (PE/Et$_2$O = 10/1), the desired compound 3f was obtained as a colorless oil (22.3 mg, 82% yield).

FT IR (neat) $\nu$ (cm$^{-1}$) = 2976, 2924, 2852, 2359, 1723, 1272, 1178, 1110, 977, 765.

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ (ppm) = 9.70 (d, $J = 1.2$ Hz, 1H), 8.03 – 7.91 (m, 2H), 7.44 (dd, $J = 1.8, 0.9$ Hz, 1H), 7.27 – 7.18 (m, 2H), 6.53 – 6.44 (m, 1H), 6.38 (dd, $J = 3.3, 1.9$ Hz, 1H), 5.30 (s, 2H), 3.23 – 3.06 (m, 1H), 2.78 – 2.56 (m, 2H), 1.08 (d, $J = 6.8$ Hz, 3H).

HRMS (ESI) Calcd. for C$_{16}$H$_{18}$NaO$_4$ $^+\ [M+Na]^+$: 295.0941, found: 295.0942.
2-(Thiophen-2-yl)ethyl 4-(2-methyl-3-oxopropyl)benzoate (3g)

The reaction was performed according to the general procedure A with 1a (0.2 mmol, 45.6 mg) and 2g (0.1 mmol, 21.4 mg). After purification by flash chromatography (PE/Et₂O = 10/1), the desired compound 3g was obtained as a colorless oil (24.5 mg, 81% yield).

**FT IR (neat)** \(\nu\) (cm\(^{-1}\)) = 2962, 2931, 2714, 2366, 1714, 1613, 1272, 1129, 1110, 793.

**\(^1\)H NMR (300 MHz, CDCl\(_3\))** \(\delta\) (ppm) = 9.72 (d, \(J = 1.2\) Hz, 1H), 8.09 – 7.88 (m, 2H), 7.31 – 7.21 (m, 2H), 5.41 (d, \(J = 8.4\) Hz, 1H), 4.85 – 4.53 (m, 3H), 3.82 (s, 3H), 3.25 – 3.11 (m, 2H), 2.81 – 2.64 (m, 2H), 1.47 (s, 9H), 1.13 (d, \(J = 6.8\) Hz, 3H).

**\(^13\)C NMR (76 MHz, CDCl\(_3\))** \(\delta\) (ppm) = 203.48, 170.33, 165.80, 155.11, 144.93, 129.99, 129.15, 127.69, 80.38, 64.88, 53.00, 52.78, 47.70, 36.48, 28.24, 13.21.

**HRMS (ESI)** Calcd. for C\(_{17}\)H\(_{18}\)NaO\(_3\)S\(^+\): 325.0869, found: 325.0870.

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2-((Tert-butoxycarbonyl)amino)-3-methoxy-3-oxopropyl 4-(2-methyl-3-oxopropyl)benzoate (3h)

The reaction was performed according to the general procedure A with 1a (0.2 mmol, 45.6 mg) and 2h (0.1 mmol, 21.4 mg). After purification by flash chromatography (PE/Et₂O = 5/1), the desired compound 3h was obtained as a colorless oil (33.0 mg, 84% yield, d.r. = 1:1).

**FT IR (neat)** \(\nu\) (cm\(^{-1}\)) = 3361, 2999, 2978, 2356, 2333, 1788, 1274, 748.

**\(^1\)H NMR (300 MHz, CDCl\(_3\))** (mixture of diastereoisomers) \(\delta\) (ppm) = 9.74 (d, \(J = 1.2\) Hz, 1H), 8.02 – 7.89 (m, 2H), 7.36 – 7.22 (m, 2H), 5.41 (d, \(J = 8.4\) Hz, 1H), 4.85 – 4.53 (m, 3H), 3.82 (s, 3H), 3.25 – 3.11 (m, 2H), 2.81 – 2.64 (m, 2H), 1.47 (s, 9H), 1.13 (d, \(J = 6.8\) Hz, 3H).

**\(^13\)C NMR (76 MHz, CDCl\(_3\))** \(\delta\) (ppm) = 203.48, 170.33, 165.80, 155.11, 144.93, 129.99, 129.15, 127.69, 80.38, 64.88, 53.00, 52.78, 47.70, 36.48, 28.24, 13.21.

**HRMS (ESI)** Calcd. for C\(_{20}\)H\(_{27}\)NNaO\(_7\)S\(^+\): 416.1680, found: 416.1685.

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2-Methyl-3-(4-oxochroman-7-yl)propanal (3i)
The reaction was performed according to the general procedure A with 1a (0.2 mmol, 45.6 mg) and 2i (0.1 mmol, 21.4 mg). After purification by flash chromatography (PE/Et₂O = 5/1), the desired compound 3i was obtained as a colorless oil (16.6 mg, 76% yield).

**FT IR** (neat) ν (cm⁻¹) = 2983, 2931, 2359, 1683, 1613, 1428, 1256, 1153, 1036, 865.

**¹H NMR** (300 MHz, CDCl₃) δ (ppm) = 9.70 (d, J = 1.3 Hz, 1H), 7.82 (d, J = 8.0 Hz, 1H), 6.83 – 6.74 (m, 1H), 4.57 – 4.47 (m, 2H), 3.08 (dd, J = 13.5, 5.8 Hz, 1H), 2.88 – 2.74 (m, 2H), 2.73 – 2.62 (m, 1H), 2.57 (dd, J = 13.5, 8.2 Hz, 1H), 1.11 (d, J = 7.0 Hz, 3H).

**¹³C NMR** (76 MHz, CDCl₃) δ (ppm) = 203.38, 191.36, 161.90, 148.21, 127.37, 122.36, 119.83, 118.01, 67.05, 47.43, 37.67, 36.62, 13.28.

**HRMS (ESI)** Calcd. for C₁₃H₁₄NaO₃⁺ [M+Na⁺]: 241.0835, found: 241.0835.

3-(4-(Tert-butyl)phenyl)-2-methylpropanal (3j)

The reaction was performed according to the general procedure A with 1a (0.2 mmol, 45.6 mg) and 2j (0.1 mmol, 21.4 mg). After purification by flash chromatography (PE/Et₂O = 30/1), the desired compound 3j was obtained as a colorless oil (13.1 mg, 64% yield).

**FT IR** (neat) ν (cm⁻¹) = 2986, 2943, 1722, 1461, 1389, 1160, 1128, 1038, 822.

**¹H NMR** (400 MHz, CDCl₃) δ (ppm) = 9.75 (d, J = 1.6 Hz, 1H), 7.41 – 7.31 (m, 2H), 7.18 – 7.09 (m, 2H), 3.09 (dd, J = 13.5, 5.8 Hz, 1H), 2.75 – 2.65 (m, 1H), 2.61 (dd, J = 13.5, 8.1 Hz, 1H), 1.35 (s, 9H), 1.12 (d, J = 6.8 Hz, 3H).

**¹³C NMR** (101 MHz, CDCl₃) δ (ppm) = 204.41, 149.12, 135.62, 128.59, 125.31, 47.92, 36.07, 34.30, 31.30, 13.21.

**HRMS (ESI)** Calcd. for C₁₄H₂₀NaO⁺ [M+Na⁺]: 227.1406, found: 227.1406.

3-(3,4-Dichlorophenyl)-2-methylpropanal (3k)

The reaction was performed according to the general procedure A with 1a (0.2 mmol, 45.6 mg) and 2k (0.1 mmol, 21.4 mg). After purification by flash chromatography (PE/Et₂O = 20/1), the desired compound 3k was obtained as a colorless oil (12.5 mg, 58% yield).
FT IR (neat) ν (cm⁻¹) = 2980, 2928, 1704, 1394, 1164, 1128, 1031, 813.

¹H NMR (300 MHz, CDCl₃) δ (ppm) = 9.71 (d, J = 1.3 Hz, 1H), 7.37 (d, J = 8.2 Hz, 1H), 7.32 – 7.26 (m, 1H), 7.07 – 6.95 (m, 1H), 3.07 (dd, J = 13.5, 5.7 Hz, 1H), 2.82 – 2.48 (m, 2H), 1.13 (d, J = 7.0 Hz, 3H).

¹³C NMR (76 MHz, CDCl₃) δ (ppm) = 203.30, 139.22, 132.41, 130.90, 130.47, 130.39, 128.45, 47.67, 35.49, 13.22.

HRMS (ESI) Calcd. for C₁₀H₁₀Cl₂NaO⁺ [M+Na⁺]: 239.0001, found: 239.0001.

2-Methyl-3-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)propanal (3l)

The reaction was performed according to the general procedure A with 1a (0.2 mmol, 45.6 mg) and 2l (0.1 mmol, 21.4 mg). After purification by flash chromatography (PE/Et₂O = 15/1), the desired compound 3l was obtained as a colorless oil (15.1 mg, 55% yield).

FT IR (neat) ν (cm⁻¹) = 2978, 2917, 2356, 1723, 1608, 1386, 1265, 1146.

¹H NMR (300 MHz, CDCl₃) δ (ppm) = 9.71 (d, J = 1.4 Hz, 1H), 7.79 – 7.72 (m, 2H), 7.22 – 7.14 (m, 2H), 3.17 – 3.04 (m, 1H), 2.76 – 2.53 (m, 2H), 1.34 (s, 12H), 1.08 (d, J = 6.8 Hz, 3H).

¹³C NMR (76 MHz, CDCl₃) δ (ppm) = 204.16, 142.18, 135.03, 128.44, 83.74, 47.91, 36.80, 24.85, 13.15.

HRMS (ESI) Calcd. for C₁₆H₂₃BNaO₃⁺ [M+Na⁺]: 297.1632, found: 297.1634.

3-(6-Methoxynaphthalen-2-yl)-2-methylpropanal (3m)

The reaction was performed according to the general procedure A with 1a (0.2 mmol, 45.6 mg) and 2m (0.1 mmol, 21.4 mg). After purification by flash chromatography (PE/Et₂O = 20/1), the desired compound 3m was obtained as a colorless oil (9.8 mg, 43% yield).

FT IR (neat) ν (cm⁻¹) = 3006, 2987, 2359, 1725, 1273, 760.

¹H NMR (300 MHz, CDCl₃) δ (ppm) = 9.76 (d, J = 1.3 Hz, 1H), 7.72 – 7.64 (m, 2H), 7.54 (s, 1H), 7.30 – 7.22 (m, 1H), 7.18 – 7.09 (m, 2H), 3.92 (s, 3H), 3.30 – 3.13 (m, 1H), 2.84 – 2.66 (m, 2H), 1.12 (d, J = 6.7 Hz, 3H).

¹³C NMR (76 MHz, CDCl₃) δ (ppm) = 204.44, 157.42, 133.91, 133.23, 128.97, 128.94, 127.81, 127.29, 127.03, 118.92, 105.63, 55.29, 48.04, 36.64, 13.25.

HRMS (ESI) Calcd. for C₁₅H₁₆NaO₃⁺ [M+Na⁺]: 251.1043, found: 251.1043.
1,3-Bis(3-(2-methyl-3-oxopropyl)phenyl)((Tert-butoxycarbonyl)amino)urea (3n)

The reaction was performed according to the general procedure A with 1a (0.2 mmol, 45.6 mg) and 2n (0.1 mmol, 21.4 mg). After purification by flash chromatography (PE/Et₂O = 1/1), the desired compound 3n was obtained as a colorless oil (15.1 mg, 67% yield, d.r. = 1:1).

**FT IR** (neat) ν (cm⁻¹) = 2969, 2924, 2700, 2356, 1725, 1541, 1340, 1270, 1274, 1258, 1153, 755, 694.

**¹H NMR (300 MHz, CDCl₃)** (mixture of diastereoisomers) δ (ppm) = 10.94 (s, 1H), 9.74 (s, 1H), 9.72 (s, 1H), 7.52 (s, 1H), 7.41 – 7.31 (m, 2H), 7.30 – 7.15 (m, 2H), 7.12 – 7.05 (m, 1H), 7.02 (s, 1H), 6.91 (d, J = 7.0 Hz, 1H), 3.22 – 3.01 (m, 2H), 2.81 – 2.50 (m, 4H), 1.40 (s, 9H), 1.21 – 1.02 (m, 6H).

**¹³C NMR (76 MHz, CDCl₃)** δ (ppm) = 204.22, 203.89, 154.90, 151.93, 139.86, 139.63, 138.10, 138.00, 129.26, 128.98, 128.96, 128.56, 126.70, 124.51, 117.98, 84.09, 48.01, 47.90, 36.65, 36.25, 27.86, 13.17, 13.09.

**HRMS (ESI)** Calcd. for C₂₆H₃₂N₂NaO₅⁺ [M+Na]⁺: 475.2203, found: 475.2210.

3-(Benzofuran-5-yl)-2-methylpropanal (3o)

The reaction was performed according to the general procedure A with 1a (0.2 mmol, 45.6 mg) and 2o (0.1 mmol, 21.4 mg). After purification by flash chromatography (PE/Et₂O = 15/1), the desired compound 3o was obtained as a colorless oil (14.7 mg, 78% yield).

**FT IR** (neat) ν (cm⁻¹) = 2962, 2920, 2847, 2363, 1716, 1486, 1276, 1125, 870.

**¹H NMR (300 MHz, CDCl₃)** δ (ppm) = 9.74 (d, J = 1.4 Hz, 1H), 7.61 (d, J = 2.4 Hz, 1H), 7.43 (d, J = 8.4 Hz, 1H), 7.39 (d, J = 1.8 Hz, 1H), 7.10 (dd, J = 8.4, 1.8 Hz, 1H), 6.72 (dd, J = 2.2, 1.0 Hz, 1H), 3.29 – 3.09 (m, 1H), 2.82 – 2.63 (m, 2H), 1.10 (d, J = 6.6 Hz, 3H).

**¹³C NMR (76 MHz, CDCl₃)** δ (ppm) = 204.49, 153.81, 145.31, 133.20, 127.66, 125.28, 121.26, 111.25, 106.35, 48.49, 36.58, 13.22.

**HRMS (ESI)** Calcd. for C₁₂H₁₂N₂NaO₅⁺ [M+Na]⁺: 211.0730, found: 211.0729.

2-Methyl-3-(1-tosyl-1H-indol-5-yl)propanal (3p)
The reaction was performed according to the general procedure A with 1a (0.2 mmol, 45.6 mg) and 2p (0.1 mmol, 21.4 mg). After purification by flash chromatography (PE/Et₂O = 15/1), the desired compound 3p was obtained as a colorless oil (23.9 mg, 70% yield).

FT IR (neat) ν (cm⁻¹) = 2971, 2827, 2712, 1721, 1457, 1370, 1169, 1134, 1092, 679, 578.

¹H NMR (300 MHz, CDCl₃) δ (ppm) = 9.70 (d, J = 1.3 Hz, 1H), 7.94 – 7.83 (m, 1H), 7.80 – 7.71 (m, 2H), 7.57 – 7.50 (m, 1H), 7.31 (s, 1H), 7.25 – 7.16 (m, 2H), 7.15 – 7.06 (m, 1H), 6.61 – 6.54 (m, 1H), 3.21 – 3.05 (m, 1H), 2.76 – 2.60 (m, 2H), 2.33 (s, 3H), 1.07 (d, J = 6.6 Hz, 3H).

¹³C NMR (76 MHz, CDCl₃) δ (ppm) = 204.34, 144.88, 135.28, 133.84, 133.52, 130.99, 129.84, 126.75, 126.60, 125.65, 121.45, 113.42, 108.72, 48.22, 36.44, 21.49, 13.24.

HRMS (ESI) Calcd. for C₁₉H₁₉NNaO₃S⁺ [M+Na]⁺: 364.0978, found: 364.0978.

2-Methyl-3-(quinolin-6-yl)propanal (3q)

The reaction was performed according to the general procedure A with 1a (0.2 mmol, 45.6 mg) and 2q (0.1 mmol, 21.4 mg). After purification by flash chromatography (PE/Et₂O = 5/1), the desired compound 3q was obtained as a colorless oil (10.4 mg, 52% yield).

FT IR (neat) ν (cm⁻¹) = 2973, 2929, 2714, 1716, 1498, 1363, 1072, 898, 865.

¹H NMR (300 MHz, CDCl₃) δ (ppm) = 9.77 (d, J = 1.2 Hz, 1H), 8.85 – 8.77 (m, 2H), 8.05 (d, J = 8.6 Hz, 1H), 7.90 (d, J = 2.0 Hz, 1H), 7.62 (dd, J = 8.6, 2.0 Hz, 1H), 3.43 – 3.26 (m, 1H), 2.91 – 2.73 (m, 2H), 1.16 (d, J = 6.8 Hz, 3H).

¹³C NMR (76 MHz, CDCl₃) δ (ppm) = 203.40, 145.14, 144.88, 133.84, 133.52, 130.99, 129.84, 126.59, 126.45, 121.45, 113.05, 108.72, 48.22, 36.44, 21.49, 13.31.

HRMS (ESI) Calcd. for C₁₂H₁₂N₂NaO⁺ [M+Na]⁺: 223.0842, found: 223.0842.

3-(Benzo[d]thiazol-6-yl)-2-methylpropanal (3r)

The reaction was performed according to the general procedure A with 1a (0.2 mmol, 45.6 mg) and 2r (0.1 mmol, 21.4 mg). After purification by flash chromatography (PE/Et₂O = 5/1), the desired compound 3r was obtained as a colorless oil (17.0 mg, 83% yield).

FT IR (neat) ν (cm⁻¹) = 2992, 2931, 2361, 1723, 1468, 1405, 1269, 881, 748.
\[ ^1H \text{NMR (300 MHz, CDCl}_3 \] \( \delta \text{ (ppm)} = 9.74 \text{ (d,} J = 1.2 \text{ Hz, 1H),} 8.94 \text{ (s, 1H),} 8.05 \text{ (d,} J = 8.4 \text{ Hz, 1H),} 7.76 \text{ (d,} J = 1.8 \text{ Hz, 1H),} 7.32 \text{ (dd,} J = 8.4, 1.8 \text{ Hz, 1H),} 3.33 - 3.16 \text{ (m, 1H),} 2.84 - 2.65 \text{ (m, 2H),} 1.12 \text{ (d,} J = 6.6 \text{ Hz, 3H).} \]

\[ ^{13}C \text{NMR (76 MHz, CDCl}_3 \] \( \delta \text{ (ppm)} = 203.82, 153.51, 152.02, 136.71, 134.08, 127.49, 123.45, 121.86, 48.16, 36.47, 13.29. \]

HRMS (ESI) Calcd. for C\textsubscript{10}H\textsubscript{11}NNaOS\textsuperscript{+} [M+Na]\textsuperscript{+}: 228.0454, found: 228.0454.

2-Methyl-3-(quinolin-7-yl)propanal (3s)

The reaction was performed according to the general procedure A with 1a (0.2 mmol, 45.6 mg) and 2s (0.1 mmol, 21.4 mg). After purification by flash chromatography (PE/Et\textsubscript{2}O = 5/1), the desired compound 3s was obtained as a colorless oil (14.3 mg, 72% yield).

FT IR (neat) \( \nu \text{ (cm}^{-1}) = 2973, 2924, 2712, 2356, 1716, 1625, 1498, 1450, 849, 781. \]

\[ ^1H \text{NMR (300 MHz, CDCl}_3 \] \( \delta \text{ (ppm)} = 9.77 \text{ (d,} J = 1.2 \text{ Hz, 1H),} 8.89 \text{ (dd,} J = 4.2, 1.8 \text{ Hz, 1H),} 8.17 - 8.08 \text{ (m, 1H),} 7.90 \text{ (s, 1H),} 7.76 \text{ (d,} J = 8.4 \text{ Hz, 1H),} 7.42 - 7.33 \text{ (m, 2H),} 3.41 - 3.23 \text{ (m, 1H),} 2.89 - 2.72 \text{ (m, 2H),} 1.14 \text{ (d,} J = 6.3 \text{ Hz, 3H).} \]

\[ ^{13}C \text{NMR (76 MHz, CDCl}_3 \] \( \delta \text{ (ppm)} = 203.82, 150.63, 148.35, 140.59, 135.75, 128.94, 128.09, 127.95, 126.90, 120.77, 47.75, 36.71, 13.25. \]

HRMS (ESI) Calcd. for C\textsubscript{10}H\textsubscript{11}NNaO\textsuperscript{3+} [M+Na]\textsuperscript{+}: 222.0889, found: 222.0889.

Methyl 5-(2-methyl-3-oxopropyl)nicotinate (3t)

The reaction was performed according to the general procedure A with 1a (0.2 mmol, 45.6 mg) and 2t (0.1 mmol, 21.4 mg). After purification by flash chromatography (PE/Et\textsubscript{2}O = 5/1), the desired compound 3t was obtained as a colorless oil (14.9 mg, 72% yield).

FT IR (neat) \( \nu \text{ (cm}^{-1}) = 2988, 2924, 2354, 1770, 1274, 1227, 1110, 790. \]

\[ ^1H \text{NMR (300 MHz, CDCl}_3 \] \( \delta \text{ (ppm)} = 9.72 \text{ (d,} J = 0.9 \text{ Hz, 1H),} 9.07 \text{ (d,} J = 2.1 \text{ Hz, 1H),} 8.61 \text{ (d,} J = 2.4 \text{ Hz, 1H),} 8.15 - 8.07 \text{ (m, 1H),} 3.94 \text{ (s, 3H),} 3.23 - 3.07 \text{ (m, 1H),} 2.81 - 2.59 \text{ (m, 2H),} 1.14 \text{ (d,} J = 6.9 \text{ Hz, 3H).} \]

\[ ^{13}C \text{NMR (76 MHz, CDCl}_3 \] \( \delta \text{ (ppm)} = 202.76, 165.71, 154.04, 149.01, 137.31, 134.44, 125.81, 52.42, 47.46, 33.11, 13.23. \]

HRMS (ESI) Calcd. for C\textsubscript{11}H\textsubscript{13}NNaO\textsuperscript{3+} [M+Na]\textsuperscript{+}: 230.0788, found: 230.0787.

2-Methyl-3-(quinolin-3-yl)propanal (3u)
The reaction was performed according to the general procedure A with 1a (0.2 mmol, 45.6 mg) and 2u (0.1 mmol, 21.4 mg). After purification by flash chromatography (PE/Et₂O = 5/1), the desired compound 3u was obtained as a colorless oil (10.9 mg, 55% yield).

**FT IR** (neat) \(\nu\) (cm\(^{-1}\)) = 2969, 2927, 2712, 2354, 1704, 1494, 912, 783, 758.

**\(^1\)H NMR** (300 MHz, CDCl\(_3\)) \(\delta\) (ppm) = 9.76 (d, \(J = 1.2\) Hz, 1H), 8.77 (d, \(J = 2.4\) Hz, 1H), 8.11 – 8.05 (m, 1H), 7.93 (d, \(J = 2.4\) Hz, 1H), 7.77 (dd, \(J = 8.1, 1.5\) Hz, 1H), 7.73 – 7.64 (m, 1H), 7.59 – 7.48 (m, 1H), 3.37 – 3.21 (q, \(J = 9.3\) Hz, 1H), 2.90 – 2.68 (m, 2H), 1.17 (d, \(J = 6.6\) Hz, 3H).

**\(^13\)C NMR** (76 MHz, CDCl\(_3\)) \(\delta\) (ppm) = 203.29, 151.86, 147.04, 135.32, 131.66, 129.19, 129.02, 127.92, 127.36, 126.81, 47.70, 33.66, 13.29.

**HRMS (ESI)** Calcd. for C\(_{13}\)H\(_{13}\)NNaO\(_2\) \([M+Na]^+\): 222.0889, found: 222.0889.

**Methyl 4-(2-methyl-3-oxopropyl)thiophene-2-carboxylate (3v)**

The reaction was performed according to the general procedure A with 1a (0.2 mmol, 45.6 mg) and 2v (0.1 mmol, 21.4 mg). After purification by flash chromatography (PE/Et₂O = 15/1), the desired compound 3v was obtained as a colorless oil (14.2 mg, 67% yield).

**FT IR** (neat) \(\nu\) (cm\(^{-1}\)) = 2957, 2719, 2359, 2359, 1704, 1442, 1281, 1253, 1078, 776.

**\(^1\)H NMR** (300 MHz, CDCl\(_3\)) \(\delta\) (ppm) = 9.69 (d, \(J = 1.2\) Hz, 1H), 7.61 (d, \(J = 1.8\) Hz, 1H), 7.20 (d, \(J = 1.8\) Hz, 1H), 3.87 (s, 3H), 3.14 – 2.97 (m, 1H), 2.77 – 2.57 (m, 2H), 1.12 (d, \(J = 6.6\) Hz, 3H).

**\(^13\)C NMR** (76 MHz, CDCl\(_3\)) \(\delta\) (ppm) = 203.58, 162.53, 139.94, 134.35, 133.72, 129.02, 127.92, 127.36, 126.81, 47.15, 30.80, 13.35.

**HRMS (ESI)** Calcd. for C\(_{10}\)H\(_{12}\)NaO\(_3\)S \([M+Na]^+\): 235.0399, found: 235.0399.

**3-(2-Methyl-3-oxopropyl)thiophene-2-carbaldehyde (3w)**

The reaction was performed according to the general procedure A with 1a (0.2 mmol, 45.6 mg) and 2w (0.1 mmol, 21.4 mg). After purification by flash chromatography (PE/Et₂O = 10/1), the desired compound 3w was obtained as a colorless oil (12.4 mg, 68% yield).

**FT IR** (neat) \(\nu\) (cm\(^{-1}\)) = 2969, 2929, 2723, 2359, 1718, 1660, 1414, 1230, 758, 669.
1H NMR (300 MHz, CDCl3) δ (ppm) = 10.01 (s, 1H), 9.70 (d, J = 1.2 Hz, 1H), 7.67 (d, J = 5.0 Hz, 1H), 7.01 (d, J = 5.0 Hz, 2H), 3.41 (dd, J = 14.2, 6.5 Hz, 1H), 3.01 (dd, J = 14.2, 7.2 Hz, 1H), 2.84 – 2.66 (m, 1H), 1.15 (d, J = 7.2 Hz, 3H).

13C NMR (76 MHz, CDCl3) δ (ppm) = 203.00, 182.08, 147.96, 138.44, 134.56, 131.19, 47.46, 28.96, 13.48.

HRMS (ESI) Calcd. for C9H10NaO2S⁺ [M+Na⁺]: 205.0294, found: 205.0294.

3-(1-Acetyl-1H-indazol-3-yl)-2-methylpropanal (3x)

The reaction was performed according to the general procedure A with 1a (0.2 mmol, 45.6 mg) and 2x (0.1 mmol, 21.4 mg). After purification by flash chromatography (PE/Et2O = 10/1), the desired compound 3x was obtained as a colorless oil (17.3 mg, 75% yield).

FT IR (neat) ν (cm⁻¹) = 2978, 2932, 2810, 2352, 1709, 1435, 1382, 1333, 1211, 936, 748.

1H NMR (300 MHz, CDCl3) δ (ppm) = 9.85 (d, J = 0.9 Hz, 1H), 8.46 – 8.35 (m, 1H), 7.70 – 7.62 (m, 1H), 7.60 – 7.50 (m, 1H), 7.40 – 7.30 (m, 1H), 3.39 (dd, J = 15.0, 6.0 Hz, 1H), 3.18 – 2.93 (m, 2H), 2.72 (s, 3H), 1.27 (d, J = 7.2 Hz, 3H).

13C NMR (76 MHz, CDCl3) δ (ppm) = 203.40, 170.79, 149.46, 139.75, 129.51, 125.86, 124.26, 119.80, 115.77, 44.68, 27.58, 22.99, 13.91.

HRMS (ESI) Calcd. for C13H14N2NaO2⁺ [M+Na⁺]: 253.0947, found: 253.098.

(R)-2,8-dimethyl-2-((4S,8S)-4,8,12-trimethyltridecyl)chroman-6-yl 4-(2-methyl-3-oxopropyl)benzoate (3y)

The reaction was performed according to the general procedure A with 1a (0.2 mmol, 45.6 mg) and 2y (0.1 mmol, 21.4 mg). After purification by flash chromatography (PE/Et2O = 10/1), the desired compound 3y was obtained as a colorless oil (44.9 mg, 78% yield, d.r. = 1:1).

FT IR (neat) ν (cm⁻¹) = 2948, 2924, 2861, 2354, 1779, 1501, 1265, 1216, 1113, 795.

1H NMR (300 MHz, CDCl3) (mixture of diastereoisomers) δ (ppm) = 9.74 (d, J = 1.1 Hz, 1H), 8.15 – 8.06 (m, 2H), 7.34 – 7.27 (m, 2H), 6.80 (d, J = 2.8 Hz, 1H), 6.74 (d, J = 2.8 Hz, 1H), 3.27 – 3.12 (m, 1H), 2.86 – 2.62 (m, 4H), 2.18 (s, 3H), 1.91 – 1.69 (m, 2H), 1.65 – 0.97 (m, 27H), 0.91 – 0.82 (m, 12H).
**13C NMR (76 MHz, CDCl3) δ (ppm) =** 203.50, 165.59, 149.81, 144.88, 142.65, 130.34, 129.15, 128.22, 127.36, 121.19, 121.01, 119.12, 76.14, 40.11, 39.35, 37.43, 37.41, 37.27, 36.52, 32.78, 32.67, 31.01, 27.95, 24.78, 24.43, 24.22, 22.70, 22.60, 22.47, 20.95, 19.73, 19.64, 16.12, 13.22.

**HRMS (ESI) Calcd. for C_{38}H_{56}NaO_{4}^+ [M+Na]^+:** 599.4071, found: 599.4071.

4-(Benz[d]thiazol-2-yl)-2-methoxyphenyl 4-(2-methyl-3-oxopropyl)benzoate (3z)

The reaction was performed according to the general procedure A with 1a (0.2 mmol, 45.6 mg) and 2z (0.1 mmol, 21.4 mg). After purification by flash chromatography (PE/Et_{2}O = 10/1), the desired compound 3z was obtained as a colorless oil (28.0 mg, 65% yield).

**FT IR (neat) ν (cm⁻¹) =** 2973, 2929, 2357, 1728, 1480, 1405, 1267, 1165, 1061, 1061, 751.

**1H NMR (300 MHz, CDCl3) δ (ppm) =** 9.74 (d, J = 1.2 Hz, 1H), 8.21 – 8.14 (m, 2H), 8.08 (dt, J = 8.1, 1.0 Hz, 1H), 7.94 – 7.88 (m, 1H), 7.85 (d, J = 1.8 Hz, 1H), 7.65 (dd, J = 8.2, 2.0 Hz, 1H), 7.54 – 7.46 (m, 1H), 7.44 – 7.36 (m, 1H), 7.36 – 7.30 (m, 2H), 7.29 – 7.25 (m, 1H), 3.96 (s, 3H), 3.31 – 3.10 (m, 1H), 2.81 – 2.60 (m, 2H), 1.14 (d, J = 6.9 Hz, 3H).

**13C NMR (76 MHz, CDCl3) δ (ppm) =** 203.48, 167.20, 164.24, 154.05, 151.85, 145.32, 142.29, 135.15, 132.49, 130.63, 129.27, 127.36, 126.36, 125.26, 123.47, 123.20, 121.61, 120.53, 111.06, 56.20, 47.72, 36.54, 13.25.

**HRMS (ESI) Calcd. for C_{25}H_{21}NNaO_{4}S^+ [M+Na]^+:** 454.1083, found: 454.1082.

2-Methyl-5-phenylpent-4-enal (3aa)

The reaction was performed according to the general procedure A with 1a (0.2 mmol, 45.6 mg) and 2aa (0.1 mmol, 21.4 mg). After purification by flash chromatography (PE/Et_{2}O = 30/1), the desired compound 3aa was obtained as a colorless oil (6.3 mg, 36% yield, E/Z = 3:1).

**FT IR (neat) ν (cm⁻¹) =** 2966, 2931, 2361, 2333, 1730, 1274, 758, 746.

**1H NMR (300 MHz, CDCl3) (E- and Z-isomers) δ (ppm) =** 9.72 (d, J = 1.5 Hz, E-isomer) + 9.64 (d, J = 1.5 Hz, Z-isomer), 1H], 7.38 – 7.17 (m, 5H), 6.55 (d, J = 11.5 Hz, Z-isomer) + 6.46 (d, J = 15.9 Hz, E-isomer), 1H], 6.22 – 6.08 (m, E-isomer) + 5.70 – 5.57 (m, Z-isomer), 1H], 2.82 – 2.23 (m, 3H), 1.17 (d, J = 6.9 Hz, E-isomer) + 1.13 (d, J = 6.9 Hz, Z-isomer), 3H].
13C NMR (76 MHz, CDCl3) (E- and Z-isomers) δ (ppm) = 204.43, 204.38, 137.14, 137.09, 132.48, 131.17, 128.70, 128.52, 127.54, 127.27, 126.83, 126.56, 126.07, 46.67, 46.29, 33.97, 29.25, 18.05, 13.16.

HRMS (ESI) Calcd. for C12H14NaO+ [M+Na]+: 197.0937, found: 197.0937.

Methyl (E)-5-methyl-6-oxohex-2-enoate (3ab)

The reaction was performed according to the general procedure A with 1a (0.2 mmol, 45.6 mg) and 2ab (0.1 mmol, 21.4 mg). After purification by flash chromatography (PE/Et2O = 10/1), the desired compound 3ab was obtained as a colorless oil (8.4 mg, 54% yield).

FT IR (neat) υ (cm⁻¹) = 2935, 2927, 2850, 2361, 1714, 1435, 1267, 1162, 748.

1H NMR (300 MHz, CDCl3) δ (ppm) = 9.67 (d, J = 1.0 Hz, 1H), 6.99 – 6.83 (m, 1H), 5.89 (dt, J = 15.6, 1.5 Hz, 1H), 3.73 (s, 3H), 2.76 – 2.46 (m, 2H), 2.35 – 2.19 (m, 1H), 1.16 (d, J = 7.2 Hz, 3H).

13C NMR (76 MHz, CDCl3) δ (ppm) = 203.05, 166.52, 145.37, 123.32, 51.52, 45.19, 32.78, 13.23.

HRMS (ESI) Calcd. for C8H12NaO3+ [M+Na]+: 179.0679, found: 179.0678.

Ethyl 2-(2-methyl-3-oxopropyl)cyclohex-1-ene-1-carboxylate (3ac)

The reaction was performed according to the general procedure A with 1a (0.2 mmol, 45.6 mg) and 2ac (0.1 mmol, 21.4 mg). After purification by flash chromatography (PE/Et2O = 10/1), the desired compound 3ac was obtained as a colorless oil (14.8 mg, 66% yield).

FT IR (neat) υ (cm⁻¹) = 2929, 2859, 2709, 1707, 1449, 1228, 1078, 1041, 762.

1H NMR (300 MHz, CDCl3) δ (ppm) = 9.62 (d, J = 2.1 Hz, 1H), 4.16 (q, J = 7.2 Hz, 2H), 2.86 – 2.73 (m, 1H), 2.66 – 2.50 (m, 1H), 2.47 – 2.37 (m, 1H), 2.34 – 2.23 (m, 2H), 2.15 – 2.06 (m, 2H), 1.66 – 1.53 (m, 4H), 1.27 (t, J = 7.2 Hz, 3H), 1.09 (d, J = 6.9 Hz, 3H).

13C NMR (76 MHz, CDCl3) δ (ppm) = 204.76, 168.70, 145.23, 127.10, 60.07, 45.54, 36.05, 31.72, 26.63, 22.16, 22.12, 14.24, 13.54.

HRMS (ESI) Calcd. for C13H20NaO3+ [M+Na]+: 247.1305, found: 247.1304.

2-Methyl-5-((triisopropylsilyl)pent-4-ynal (3ad)
The reaction was performed according to the general procedure A with 1a (0.2 mmol, 45.6 mg) and 2ad (0.1 mmol, 21.4 mg). After purification by flash chromatography (PE/Et₂O = 30/1), the desired compound 3ad was obtained as a colorless oil (9.6 mg, 38% yield).

FT IR (neat) ν (cm⁻¹) = 2938, 2859, 2354, 2178, 1735, 1454, 1267, 1064, 984, 888, 751, 650.

¹H NMR (300 MHz, CDCl₃) δ (ppm) = 9.73 (s, 1H), 2.71 – 2.40 (m, 3H), 1.24 (d, J = 6.6 Hz, 3H), 1.11 – 0.96 (m, 21H).

¹³C NMR (76 MHz, CDCl₃) δ (ppm) = 203.33, 104.83, 83.00, 45.32, 21.37, 18.57, 13.04, 11.21.

HRMS (ESI) Calcd. for C₁₅H₂₈NaOSi⁺ [M+Na]⁺: 275.1802, found: 275.1802.

2-Methyl-4-oxo-4-phenylbutanal (3ae)

The reaction was performed according to the general procedure A with 1a (0.2 mmol, 45.6 mg) and 2ae (0.1 mmol, 21.4 mg). After purification by flash chromatography (PE/Et₂O = 10/1), the desired compound 3ae was obtained as a colorless oil (11.1 mg, 63% yield).

FT IR (neat) ν (cm⁻¹) = 2966, 2930, 2783, 1725, 1701, 1688, 1443, 1255, 1209, 1007, 751, 687.

¹H NMR (300 MHz, CDCl₃) δ (ppm) = 9.79 (d, J = 0.7 Hz, 1H), 8.02 – 7.93 (m, 2H), 7.62 – 7.53 (m, 1H), 7.52 – 7.43 (m, 2H), 3.49 (dd, J = 17.6, 6.3 Hz, 1H), 3.20 – 3.06 (m, 1H), 3.01 (dd, J = 17.6, 6.3 Hz, 1H), 1.24 (d, J = 7.2 Hz, 3H).

¹³C NMR (76 MHz, CDCl₃) δ (ppm) = 203.37, 197.73, 136.57, 133.31, 128.64, 128.06, 41.63, 39.37, 13.74.

HRMS (ESI) Calcd. for C₁₁H₁₂NaO₂⁺ [M+Na]⁺: 199.0730, found: 199.0730.

(E)-2-methyl-4-o xohept-5-enal (3af)

The reaction was performed according to the general procedure A with 1a (0.2 mmol, 45.6 mg) and 2af (0.1 mmol, 21.4 mg). After purification by flash chromatography (PE/Et₂O = 10/1), the desired compound 3af was obtained as a colorless oil (7.6 mg, 54% yield).

FT IR (neat) ν (cm⁻¹) = 2 964, 2927, 2361, 2338, 1725, 1276, 1258, 755.

¹H NMR (400 MHz, CDCl₃) δ (ppm) = 9.71 (d, J = 0.6 Hz, 1H), 6.89 (dq, J = 15.9, 6.8 Hz, 1H), 6.14 (dq, J = 15.9, 1.7 Hz, 1H), 3.08 – 2.90 (m, 2H), 2.63 – 2.52 (m, 1H), 1.91 (dd, J = 6.8, 1.7 Hz, 3H), 1.15 (d, J = 7.2 Hz, 1H).

¹³C NMR (101 MHz, CDCl₃) δ (ppm) = 203.43, 197.63, 143.38, 131.70, 41.55, 40.42, 18.27, 13.58.

HRMS (ESI) Calcd. for C₈H₁₂NaO₂⁺ [M+Na]⁺: 163.0730, found: 163.0729.
Methyl 4-(3-oxopropyl)benzoate (3ba)

\[
\text{O} \quad \text{H} \quad \text{CO}_2\text{Me} \\
\text{C}_\text{6} \quad \text{H}_\text{3} \quad \text{O} \quad \text{H} \quad \text{CO}_2\text{Me}
\]

The reaction was performed according to the general procedure B with 1b (0.2 mmol, 45.6 mg) and 2a (0.1 mmol, 21.4 mg). After purification by flash chromatography (PE/Et\textsubscript{2}O = 10/1), the desired compound 3ba was obtained as a colorless oil (16.1 mg, 84\% yield).

**FT IR** (neat) \(\nu\) (cm\(^{-1}\)) = 2955, 2920, 2850, 2730, 2361, 1709, 1274, 1108, 753.

**\(^1\)H NMR** (300 MHz, CDCl\(_3\)) \(\delta\) (ppm) = 9.82 (t, \(J = 1.3\) Hz, 1H), 8.01 – 7.89 (m, 2H), 7.30 – 7.21 (m, 2H), 3.90 (s, 3H), 3.01 (t, \(J = 7.5\) Hz, 2H), 2.90 – 2.74 (m, 2H).

**\(^{13}\)C NMR** (76 MHz, CDCl\(_3\)) \(\delta\) (ppm) = 200.76, 166.92, 145.78, 129.91, 128.33, 52.01, 44.77, 28.00.

**HRMS (ESI)** Calcd. for C\(_{11}\)H\(_{12}\)NaO\(_3\)+ [M+Na]+: 215.0679, found: 215.0678.

Methyl 4-(1-oxohexan-3-yl)benzoate (3ca)

\[
\text{O} \quad \text{H} \quad \text{CO}_2\text{Me} \\
\text{C}_\text{6} \quad \text{H}_\text{3} \quad \text{O} \quad \text{H} \quad \text{CO}_2\text{Me}
\]

The reaction was performed according to the general procedure B with 1c (0.2 mmol, 45.6 mg) and 2a (0.1 mmol, 21.4 mg). After purification by flash chromatography (PE/Et\textsubscript{2}O = 10/1), the desired compound 3ca was obtained as a colorless oil (11.2 mg, 48\% yield).

**FT IR** (neat) \(\nu\) (cm\(^{-1}\)) = 2955, 2929, 2873, 2363, 1714, 1433, 1286, 1106, 765.

**\(^1\)H NMR** (300 MHz, CDCl\(_3\)) \(\delta\) (ppm) = 9.67 (t, \(J = 1.9\) Hz, 1H), 8.01 – 7.94 (m, 2H), 7.35 – 7.18 (m, 2H), 3.90 (s, 3H), 3.26 (p, \(J = 7.3\) Hz, 1H), 2.74 (dd, \(J = 7.2, 1.8\) Hz, 2H), 1.73 – 1.58 (m, 2H), 1.31 – 1.08 (m, 2H), 0.86 (t, \(J = 7.2\) Hz, 3H).

**\(^{13}\)C NMR** (76 MHz, CDCl\(_3\)) \(\delta\) (ppm) = 201.16, 166.91, 149.45, 129.96, 128.57, 127.53, 52.02, 50.32, 39.69, 38.52, 20.37, 13.84.

**HRMS (ESI)** Calcd. for C\(_{14}\)H\(_{18}\)NaO\(_3\)+ [M+Na]+: 257.1148, found: 257.1148.

Methyl 4-(4-methyl-1-oxopentan-3-yl)benzoate (3da)

\[
\text{O} \quad \text{H} \quad \text{CO}_2\text{Me} \\
\text{C}_\text{6} \quad \text{H}_\text{3} \quad \text{O} \quad \text{H} \quad \text{CO}_2\text{Me}
\]

The reaction was performed according to the general procedure B with 1d (0.2 mmol, 45.6 mg) and 2a (0.1 mmol, 21.4 mg). After purification by flash chromatography (PE/Et\textsubscript{2}O = 10/1), the desired compound 3da was obtained as a colorless oil (9.6 mg, 41\% yield).

**FT IR** (neat) \(\nu\) (cm\(^{-1}\)) = 2945, 2924, 2864, 2719, 2354, 1730, 1484, 1281, 1153, 678.
$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ (ppm) = 9.62 (t, $J = 2.0$ Hz, 1H), 8.01 – 7.92 (m, 2H), 7.29 – 7.19 (m, 2H), 3.90 (s, 3H), 3.10 – 2.95 (m, 1H), 2.91 – 2.70 (m, 2H), 1.97 – 1.79 (m, 1H), 0.95 (d, $J = 6.6$ Hz, 3H), 0.76 (d, $J = 6.6$ Hz, 3H).

$^{13}$C NMR (76 MHz, CDCl$_3$) $\delta$ (ppm) = 201.53, 166.93, 148.25, 129.71, 128.56, 128.28, 52.02, 47.09, 46.76, 33.28, 20.53, 20.24.

HRMS (ESI) Calcd. for C$_{14}$H$_{18}$NaO$_3$ $^[M+Na]^+$: 257.1148, found: 257.1148.

Methyl 4-(3-formylpentan-2-yl)benzoate (3ea)

![Chemical Structure](image)

The reaction was performed according to the general procedure A with 1e (0.2 mmol, 45.6 mg) and 2a (0.1 mmol, 21.4 mg). After purification by flash chromatography (PE/Et$_2$O = 10/1), the desired compound 3ea was obtained as a colorless oil (16.8 mg, 72% yield, d.r. = 1.3:1).

FT IR (neat) $\nu$ (cm$^{-1}$) = 2964, 2927, 2712, 1714, 1611, 1435, 1276, 1181, 1115, 779.

$^1$H NMR (300 MHz, CDCl$_3$) (mixture of diastereoisomers) $\delta$ (ppm) = [9.62 (d, $J = 3.9$ Hz, minor diastereoisomer) + 9.49 (d, $J = 3.0$ Hz, major diastereoisomer), 1H], 8.09 – 7.88 (m, 2H), 7.30 – 7.18 (m, 2H), 3.94 – 3.84 (m, 3H), 3.31 – 2.98 (m, 1H), 2.55 – 2.27 (m, 1H), 1.78 – 1.38 (m, 2H), [1.32 (d, $J = 7.2$ Hz, major diastereoisomer) + 1.26 (d, $J = 7.2$ Hz, minor diastereoisomer), 3H], [0.89 (t, $J = 7.4$ Hz, major diastereoisomer) + 0.78 (t, $J = 7.4$ Hz, minor diastereoisomer), 3H].

$^{13}$C NMR (76 MHz, CDCl$_3$) (mixture of diastereoisomers) $\delta$ (ppm) = 204.61, 204.37, 166.86, 166.85, 149.50, 149.47, 129.96, 129.90, 128.66, 128.59, 127.59, 127.57, 59.77, 59.28, 52.04, 52.01, 39.75, 39.54, 20.94, 20.12, 19.58, 18.29, 11.62, 11.40.

HRMS (ESI) Calcd. for C$_{14}$H$_{18}$NaO$_3$ $^[M+Na]^+$: 257.1148, found: 257.1148.

Methyl 4-(2-formylpenty)benzoate and Methyl 4-(2-methyl-1-oxopentan-3-yl)benzoate (mixture) (3fa)

![Chemical Structure](image)

The reaction was performed according to the general procedure A with 1f (0.2 mmol, 45.6 mg) and 2a (0.1 mmol, 21.4 mg). After purification by flash chromatography (PE/Et$_2$O = 10/1), the desired compound 3fa was obtained as a colorless oil (17.6 mg, 75% yield, r.r. = 1:1).

FT IR (neat) $\nu$ (cm$^{-1}$) = 2956, 2875, 2363, 1714, 1438, 1279, 1183, 1108, 762.

$^1$H NMR (300 MHz, CDCl$_3$) (mixture of diastereoisomers and regioisomers) $\delta$ (ppm) = 9.74 – 9.49 (m, 1H), 8.07 – 7.94 (m, 2H), 7.37 – 7.21 (m, 2H), 3.98 – 3.91 (m, 3H), 3.14 – 2.64 (m, 2H), 1.92 – 1.58 (m, 2H), 1.57 – 1.27 (m, 2H), 1.18 – 1.11 (m, 1H), 1.03 – 0.73 (m, 3H).
**Methyl 4-(2,4-dimethyl-3-oxopentyl)benzoate (3ga)**

The reaction was performed according to the general procedure A with 1g (0.2 mmol, 45.6 mg) and 2a (0.1 mmol, 21.4 mg). After purification by flash chromatography (PE/Et₂O = 10/1), the desired compound 3ga was obtained as a colorless oil (18.4 mg, 74% yield).

**FT IR** (neat) υ (cm⁻¹) = 2969, 2927, 2866, 2354, 1711, 1279, 1113, 1015, 767, 701.

**¹H NMR (300 MHz, CDCl₃) δ (ppm) = 7.98 – 7.88 (m, 2H), 7.23 – 7.15 (m, 2H), 3.89 (s, 3H), 3.08 – 2.93 (m, 2H), 2.69 – 2.56 (m, 1H), 2.55 – 2.41 (m, 1H), 1.09 (d, J = 6.5 Hz, 3H), 1.00 (d, J = 6.9 Hz, 3H), 0.85 (d, J = 6.9 Hz, 3H).

**¹³C NMR (76 MHz, CDCl₃) δ (ppm) = 217.18, 167.02, 145.57, 129.66, 129.06, 128.19, 51.98, 46.24, 40.27, 39.31, 17.89, 17.77, 17.32.

**HRMS (ESI)** Calcd. for C₁₄H₁₈NaO₃⁺ [M+Na]⁺: 257.1148, found: 257.1148.

**Methyl 4-(4-oxoheptan-2-yl)benzoate (3ha)**

The reaction was performed according to the general procedure B with 1h (0.2 mmol, 45.6 mg) and 2a (0.1 mmol, 21.4 mg). After purification by flash chromatography (PE/Et₂O = 10/1), the desired compound 3ha was obtained as a colorless oil (10.7 mg, 43% yield).

**FT IR** (neat) υ (cm⁻¹) = 2957, 2929, 2864, 2361, 1711, 1279, 1113, 755.

**¹H NMR (300 MHz, CDCl₃) δ (ppm) = 7.92 – 7.86 (m, 2H), 7.24 – 7.15 (m, 2H), 3.89 (s, 3H), 3.08 – 2.93 (m, 2H), 2.69 – 2.56 (m, 1H), 2.55 – 2.41 (m, 1H), 1.54 – 1.41 (m, 2H), 1.20 (d, J = 6.9 Hz, 3H), 0.77 (t, J = 7.4 Hz, 3H).

**¹³C NMR (76 MHz, CDCl₃) δ (ppm) = 209.38, 167.00, 151.77, 129.88, 128.24, 126.87, 51.98, 50.64, 45.42, 35.29, 21.72, 17.06, 13.64.

**HRMS (ESI)** Calcd. for C₁₅H₂₀NaO₃⁺ [M+Na]⁺: 271.1305, found: 271.1304.

**Methyl 4-(3-(4-chlorophenyl)-3-oxopropyl)benzoate (3ia)**
The reaction was performed according to the general procedure B with 1i (0.2 mmol, 45.6 mg) and 2a (0.1 mmol, 21.4 mg). After purification by flash chromatography (PE/Et₂O = 10/1), the desired compound 3ia was obtained as a colorless oil (16.9 mg, 56% yield).

**FT IR** (neat) v (cm⁻¹) = 2948, 2922, 2362, 1711, 1685, 1580, 1433, 1272, 1178, 1110, 977, 765.

**¹H NMR (300 MHz, CDCl₃)** δ (ppm) = 8.00 – 7.94 (m, 2H), 7.92 – 7.85 (m, 2H), 7.46 – 7.39 (m, 2H), 7.35 – 7.28 (m, 2H), 3.90 (s, 3H), 3.28 (t, J = 7.4 Hz, 2H), 3.12 (t, J = 7.4 Hz, 2H).

**¹³C NMR (76 MHz, CDCl₃)** δ (ppm) = 197.39, 166.96, 146.51, 139.65, 135.00, 129.88, 129.40, 128.95, 128.45, 128.23, 52.00, 39.76, 29.91.

**HRMS (ESI)** Calcd. for C₁₇H₁₅ClNaO₃⁺ [M+Na]⁺: 325.0602, found: 325.0603.

**Methyl 4-(2-methyl-3-oxo-3-phenylpropyl)benzoate (3ja)**

The reaction was performed according to the general procedure A with 1j (0.2 mmol, 45.6 mg) and 2a (0.1 mmol, 21.4 mg). After purification by flash chromatography (PE/Et₂O = 10/1), the desired compound 3ja was obtained as a colorless oil (19.5 mg, 69% yield).

**FT IR** (neat) v (cm⁻¹) = 2955, 2927, 2361, 1721, 1676, 1438, 1281, 1110, 975, 755, 704.

**¹H NMR (300 MHz, CDCl₃)** δ (ppm) = 7.97 – 7.87 (m, 4H), 7.59 – 7.51 (m, 1H), 7.50 – 7.40 (m, 2H), 7.33 – 7.22 (m, 2H), 3.89 (s, 3H), 3.81 – 3.71 (m, 1H), 3.23 (dd, J = 13.7, 6.9 Hz, 1H), 2.76 (dd, J = 13.7, 6.9 Hz, 1H), 1.21 (d, J = 6.9 Hz, 3H).

**¹³C NMR (76 MHz, CDCl₃)** δ (ppm) = 203.17, 167.00, 145.48, 136.26, 133.05, 129.70, 129.10, 128.68, 128.23, 128.20, 51.97, 42.45, 39.23, 17.66.

**HRMS (ESI)** Calcd. for C₁₈H₁₈NaO₃⁺ [M+Na]⁺: 305.1148, found: 305.1149.

**Methyl 4-(3,3-dimethyl-4-oxocyclopentyl)benzoate (3ka)**

The reaction was performed according to the general procedure B with 1k (0.2 mmol, 45.6 mg) and 2a (0.1 mmol, 21.4 mg). After purification by flash chromatography (PE/Et₂O = 10/1), the desired compound 3ka was obtained as a colorless oil (21.4 mg, 87% yield).
FT IR (neat) $\nu$ (cm$^{-1}$) = 2952, 2927, 2861, 2354, 1718, 1613, 1435, 1272, 1183, 1101, 1017, 762, 711.

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ (ppm) = 8.03 – 7.95 (m, 2H), 7.37 – 7.28 (m, 2H), 3.90 (s, 3H), 3.57 – 3.40 (m, 1H), 2.79 (dd, $J$ = 18.4, 7.7, 2.4 Hz, 1H), 2.39 (dd, $J$ = 18.4, 12.3 Hz, 1H), 2.26 (dd, $J$ = 12.3, 6.3, 2.4 Hz, 1H), 1.87 (t, $J$ = 12.3 Hz, 1H), 1.16 (s, 3H), 1.13 (s, 3H).

$^{13}$C NMR (76 MHz, CDCl$_3$) $\delta$ (ppm) = 221.00, 166.79, 148.58, 129.92, 128.59, 126.79, 46.49, 46.40, 44.53, 38.06, 24.24, 24.13.

HRMS (ESI) Calcd. for C$_{15}$H$_{18}$NaO$_3^+$ [M+Na]$^+$: 269.1148, found: 269.1148.

Methyl 4-(3-oxocyclohexyl)benzoate (3la)

The reaction was performed according to the general procedure B with 1l (0.2 mmol, 45.6 mg) and 2a (0.1 mmol, 21.4 mg). After purification by flash chromatography (PE/Et$_2$O = 10/1), the desired compound 3la was obtained as a colorless oil (15.1 mg, 65% yield).

FT IR (neat) $\nu$ (cm$^{-1}$) = 3006, 2987, 2362, 2340, 1714, 1274, 1262, 1108, 760.

$^1$H NMR (400 MHz, CDCl$_3$) (E- and Z-isomers) $\delta$ (ppm) = [8.01 – 7.97 (m, E-isomer) + 7.97 – 7.94 (m, Z-isomer), 2H], 7.36 – 7.30 (m, 2H), 7.28 – 7.23 (m, 1H), 6.86 – 6.76 (m, 2H), [6.35 – 6.32 (m, E-isomer) + 6.32 – 6.30 (m, Z-isomer), 1H], [3.91 (s, E-isomer) + 3.90 (s, Z-isomer), 3H], [3.59...
(s, Z-isomer) + 3.38 (s, E-isomer), 2H], [2.33 (s, Z-isomer) + 2.32 (s, E-isomer), 3H], [1.68 (d, J = 1.4 Hz, E-isomer) + 1.62 (d, J = 1.4 Hz, Z-isomer), 3H].

\(^{13}\)C NMR (101 MHz, CDCl\(_3\)) (E- and Z-isomers) \(\delta\) (ppm) = 167.04, 152.75, 145.39, 144.82, 137.95, 137.12, 136.00, 130.02, 129.73, 129.70, 128.94, 128.83, 128.35, 123.73, 123.68, 120.85, 120.02, 116.68, 116.64, 52.01, 51.94, 40.17, 35.67, 21.18, 21.16, 16.97, 13.23.

HRMS (ESI) Calcd. for C\(_{19}\)H\(_{19}\)ClNaO\(_3\)\([\text{M+Na}]^+\): 353.0915, found: 353.0916.

**Methyl 4-(3-(4-(2-((tert-butoxycarbonyl)amino)-3-methoxy-3-oxopropyl)phenoxy)-2-methylallyl)benzoate (3na)**

The reaction was performed according to the general procedure B with 1n (0.2 mmol, 45.6 mg) and 2a (0.1 mmol, 21.4 mg). After purification by flash chromatography (PE/Et\(_2\)O = 10/1), the desired compound 3na was obtained as a colorless oil (40.1 mg, 83% yield, E/Z = 9:1).

**FT IR** (neat) o (cm\(^{-1}\)) = 3011, 2978, 2370, 2345, 2112, 1721, 1285, 1264, 1115, 762.

\(^{1}\)H NMR (300 MHz, CDCl\(_3\)) (E- and Z-isomers) \(\delta\) (ppm) = 8.03 – 7.90 (m, 2H), 7.34 – 7.25 (m, 2H), 7.10 – 7.03 (m, 2H), 6.97 – 6.87 (m, 2H), 6.38 – 6.31 (m, 1H), [4.98 (d, J = 8.1 Hz, E-isomer) + 4.72 (d, J = 8.1 Hz, Z-isomer), 1H], [4.63 – 4.43 (m, E-isomer) + 4.42 – 4.25 (m, Z-isomer), 1H], [3.90 (s, E-isomer) + 3.89 (s, Z-isomer), 3H], 3.71 (s, 3H), [3.55 (s, Z-isomer) + 3.35 (s, E-isomer), 2H], 3.15 – 2.93 (m, 2H), [1.63 (d, J = 1.4 Hz, E-isomer) + 1.58 (d, J = 1.4 Hz, Z-isomer), 3H], 1.41 (s, 9H).

\(^{13}\)C NMR (76 MHz, CDCl\(_3\)) (E- and Z-isomers) \(\delta\) (ppm) = 172.27, 167.01, 156.58, 155.04, 145.01, 137.40, 136.41, 130.40, 129.71, 129.66, 128.77, 128.75, 128.29, 119.56, 116.05, 115.98, 79.97, 79.87, 54.46, 52.16, 51.95, 40.24, 37.52, 29.65, 28.25, 16.95, 13.14.

HRMS (ESI) Calcd. for C\(_{27}\)H\(_{33}\)NNaO\(_7\)\([\text{M+Na}]^+\): 506.2149, found: 506.2146.

**Methyl 4-(3-(2-allylphenoxy)-2-methylallyl)benzoate (3oa)**

The reaction was performed according to the general procedure B with 1o (0.2 mmol, 45.6 mg) and 2a (0.1 mmol, 21.4 mg). After purification by flash chromatography (PE/Et\(_2\)O = 50/1), the desired compound 3oa was obtained as a colorless oil (27.9 mg, 87% yield, E/Z = 9:1).
FT IR (neat) $\nu$ (cm$^{-1}$) = 2987, 2971, 2378, 2325, 1718, 1270, 1280, 1116, 760, 745.

$^1$H NMR (300 MHz, CDCl$_3$) ($E$- and $Z$-isomers) $\delta$ (ppm) = 8.05 – 7.95 (m, 2H), 7.37 – 7.29 (m, 2H), 7.23 – 7.16 (m, 2H), 7.07 – 6.89 (m, 2H), 6.41 – 6.33 (m, 1H), 6.11 – 5.92 (m, 1H), 5.15 – 5.00 (m, 2H), [3.92 (s, $E$-isomer) + 3.91 (s, $Z$-isomer), 3H], [3.59 (s, $Z$-isomer) + 3.38 (s, $E$-isomer), 2H], 3.46 (dt, $J = 6.6, 1.5$ Hz, 2H), [1.67 (d, $J = 1.5$ Hz, $E$-isomer) + 1.62 (d, $J = 1.5$ Hz, $Z$-isomer), 3H].

$^{13}$C NMR (76 MHz, CDCl$_3$) ($E$- and $Z$-isomers) $\delta$ (ppm) = 167.03, 155.24, 145.16, 137.78, 136.68, 130.24, 130.16, 129.71, 129.68, 129.24, 128.78, 128.27, 127.42, 127.36, 122.37, 122.31, 119.00, 118.62, 115.58, 115.55, 114.30, 51.96, 40.26, 35.63, 34.32, 17.00, 13.17.

HRMS (ESI) Calcd. for C$_{21}$H$_{22}$NaO$_3$ [M+Na]$^+$: 345.1461, found: 345.1463.

Methyl 4-(3-(benzyloxy)-2-methylallyl)benzoate (3pa)

The reaction was performed according to the general procedure B with 1p (0.2 mmol, 45.6 mg) and 2a (0.1 mmol, 21.4 mg). After purification by flash chromatography (PE/Et$_2$O = 50/1), the desired compound 3pa was obtained as a colorless oil (22.8 mg, 77% yield, $E/Z = 3.2:1$).

FT IR (neat) $\nu$ (cm$^{-1}$) = 2995, 2987, 2376, 2363, 1710, 1274, 1269, 1108, 1096, 761.

$^1$H NMR (400 MHz, CDCl$_3$) ($E$- and $Z$-isomers) $\delta$ (ppm) = 7.96 – 7.88 (m, 2H), 7.42 – 7.28 (m, 5H), 7.24 – 7.17 (m, 2H), 6.07 – 6.01 (m, 1H), 4.81 (s, 2H), [3.90 (s, $E$-isomer) + 3.90 (s, $Z$-isomer), 3H], [3.48 (s, $Z$-isomer) + 3.20 (s, $E$-isomer), 2H], [1.54 (d, $J = 1.2$ Hz, $E$-isomer) + 1.44 (d, $J = 1.2$ Hz, $Z$-isomer), 3H].

$^{13}$C NMR (101 MHz, CDCl$_3$) ($E$- and $Z$-isomers) $\delta$ (ppm) = 167.15, 146.26, 145.88, 141.97, 141.05, 137.75, 129.55, 128.71, 128.68, 128.48, 128.45, 128.00, 127.88, 127.82, 127.49, 127.38, 113.63, 113.23, 73.61, 73.56, 51.96, 51.92, 40.34, 35.49, 17.02, 13.01.

HRMS (ESI) Calcd. for C$_{19}$H$_{20}$NaO$_3$ [M+Na]$^+$: 319.1305, found: 319.1306.

Methyl 5'-(triisopropylsilyl)oxy)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-4-carboxylate (4b)

The reaction was performed according to the general procedure B with 1l (0.2 mmol, 50.8 mg) and 2a (0.1 mmol, 21.4 mg). After purification by flash chromatography (PE/Et$_2$O = 60/1), the desired compound 4b was obtained as a colorless oil (25.9 mg, 67% yield).

FT IR (neat) $\nu$ (cm$^{-1}$) = 2966, 2871, 2340, 2324, 1852, 1725, 1281, 1185, 1112.
$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ (ppm) = 8.00 – 7.91 (m, 2H), 7.33 – 7.25 (m, 2H), 4.93 – 4.86 (m, 1H), 3.90 (s, 3H), 3.60 – 3.46 (m, 1H), 2.28 – 2.04 (m, 2H), 2.01 – 1.87 (m, 1H), 1.86 – 1.59 (m, 2H), 1.48 – 1.33 (m, 1H), 1.28 – 1.00 (m, 21H).

$^{13}$C NMR (76 MHz, CDCl$_3$) $\delta$ (ppm) = 167.18, 152.99, 152.60, 129.63, 127.90, 127.67, 105.96, 51.93, 41.67, 32.36, 29.73, 21.60, 18.01, 12.65.

HRMS (ESI) Calcd. for C$_{23}$H$_{36}$NaO$_3$Si$^+$ [M+Na]$^+$: 411.2326, found: 411.2326.
7. References

[1] J. Li, S. Qu, W. Zhao, Angew. Chem. Int. Ed. **2020**, *59*, 2360-2364.
[2] H. Ito, H. Ohmiya, M. Sawamura, Org. Lett. **2010**, *12*, 4380-4383.
[3] K. Zhao, R. R. Knowles, J. Am. Chem. Soc. **2022**, *144*, 137-144.
[4] K. Liu, A. Studer, J. Am. Chem. Soc. **2021**, *143*, 4903-4909.
[5] V. Bacauanu, S. Cardinal, M. Yamauchi, M. Kondo, D. F. Fernández, R. Remy, D. W. C. MacMillan, Angew. Chem. Int. Ed. **2018**, *57*, 12543-12548.
[6] G. Casotti, G. Fusini, M. Ferreri, L. F. Pardini, C. Evangelisti, G. Angelici, A. Carpita, Synthesis **2020**, *52*, 1795-1803.
[7] Y. Li, Q. Shao, H. He, C. Zhu, X.-S. Xue, J. Xie, Nat. Commun. **2022**, *13*, 10.
[8] Á. Gutiérrez-Bonet, J. C. Tellis, J. K. Matsui, B. A. Vara, G. A. Molander, ACS Catal. **2016**, *6*, 8004-8008.
[9] H. J. Kuhn, S. E. Braslavsky, R. Schmidt, Pure Appl. Chem. **2004**, *76*, 2105–2146.
[10] M. A. Cismesia, T. P. Yoon, Chem. Sci. **2015**, *6*, 5426–5434.
[11] C. G. Hatchard, C. A. Parker, Proc. Roy. Soc. (London) **1956**, *A235*, 518–536.
[12] S.-Z. Sun, R. Martin, Angew. Chem. Int. Ed. **2018**, *57*, 3622–3625.
8. Copies of product NMR spectra

$^1$H NMR

$^1$C NMR
$^1$H NMR

$^1$C NMR

$^{13}$C NMR
$^1$H NMR

$^{13}$C NMR
$^1$H NMR

$^{13}$C NMR
$^{1}$H NMR

$^{13}$C NMR
$^1$H NMR

$^{13}$C NMR
$^1$H NMR

$^{13}$C NMR

3i
$^1$H NMR

![NMR spectrum]

$^{13}$C NMR

![NMR spectrum]
\( ^1\text{H NMR} \)

\[
\begin{align*}
\text{H} & \quad 9.73 \\
\text{Me} & \quad 3.39 \\
\text{O}\text{Me} & 
\end{align*}
\]

\( ^{13}\text{C NMR} \)

\[
\begin{align*}
\text{H} & \quad 204.43 \\
\text{Me} & \quad 157.47 \\
\text{O}\text{Me} & 
\end{align*}
\]
$^1$H NMR

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

\text{d.r. = 1:1}

$^{13}$C NMR

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

\text{d.r. = 1:1}
$^1$H NMR

$^{13}$C NMR
$^1$H NMR

![NMR spectrum graph]

$^{13}$C NMR

![NMR spectrum graph]
$^1$H NMR

![H NMR spectrum](image)

$^{13}$C NMR

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

$^{13}$C NMR
$^{1}H$ NMR

$^{13}C$ NMR
$^1$H NMR

$^{13}$C NMR
$^1$H NMR

$^{13}$C NMR
$^1$H NMR

$$d.r. = 1:1$$

$^{13}$C NMR

$$d.r. = 1:1$$
**$^1$H NMR**

![H NMR spectrum](image)

$E/Z = 3:1$

**$^{13}$C NMR**

![C NMR spectrum](image)

$E/Z = 3:1$
$^1$H NMR

H \quad \text{Me} \quad \text{CO}_2\text{Me}

$^{13}$C NMR

H \quad \text{Me} \quad \text{CO}_2\text{Me}
\[ ^1H\text{ NMR} \]

![H NMR spectrum](image)

\[ ^{13}C\text{ NMR} \]

![C NMR spectrum](image)
$^{1}$H NMR

$^{13}$C NMR
$^1$H NMR

$^{13}$C NMR
$^1$H NMR

3fa, 38%

3fa', 38% ($d.r. = 1:1$)

$^{13}$C NMR

3fa, 38%

3fa', 38% ($d.r. = 1:1$)
$^1$H NMR

$^{13}$C NMR
$^{1}H$ NMR

$^{13}C$ NMR
3ja

**$^1$H NMR**

![H NMR spectrum](image)

**$^{13}$C NMR**

![C NMR spectrum](image)
$^{1}H$ NMR

$^{13}C$ NMR
$^1$H NMR

![NMR Spectrum](image)

$^{13}$C NMR

![NMR Spectrum](image)
$^1$H NMR

$^{13}$C NMR
$^1$H NMR

$^{13}$C NMR
$^1$H NMR

$^{13}$C NMR
$^1$H NMR

$^{13}$C NMR
$^1$H NMR

$^{13}$C NMR
$^{19}\text{F NMR}$
$^1$H NMR

\[ \text{Chemical Shift (ppm)} \]

\[ \text{OH} \]

\[ \text{Me} \]

\[ \text{Constituent Peaks} \]

$^{13}$C NMR

\[ \text{Chemical Shift (ppm)} \]

\[ \text{OH} \]

\[ \text{Me} \]

\[ \text{Constituent Peaks} \]
$^1$H NMR

TIPSO\(\text{CN}\)

$^{13}$C NMR

TIPSO\(\text{CN}\)