Rh-catalyzed Cascade C–H Activation/C–C Cleavage/Cyclization of Carboxylic Acids with Cyclopropanols

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**General Remark**

All chemicals were obtained from commercial suppliers and were used as received unless otherwise noted. $^1$H and $^{13}$C NMR spectra were recorded using CDCl$_3$ as a solvent on a Bruker 500 or 600 MHz NMR spectrometer. The chemical shift is given in dimensionless $\delta$ values and is referenced relative to TMS in $^1$H and $^{13}$C NMR spectroscopy. High resolution mass spectra were obtained on a Waters Xevo G2-XS QTOF or an Agilent 6230 LC-TOF MS spectrometer. The compounds were analyzed using a Waters C18 column (ACQUITY UPLC BEH C18, 1.7 m, 2.1 x 50 mm) and eluted with 70% methanol containing 0.1% formic acid. Mass spectra of small molecule were recorded in the mass range of 200-3000 or 600-2000 under high resolution mass-spec mode (HRMS, standard 3200 m/z, 4 GHz). Key source parameters: drying nitrogen gas flow of 11 L/min; nebulizer pressure of 40 psi; gas temperature of 35 °C; fragmenter voltage of 175 V; skimmer voltage of 65 V; and capillary voltage of 4000 V. Column chromatography was performed on silica gel (200-300 mesh) with freshly distilled ethyl acetate (EA) and petroleum ether (PE).
General procedure to the preparation of cyclopropanols

Cyclopropanols were synthesized according to literature procedure\(^1\). Under the protection of nitrogen, EtMgBr (2.8 equiv., 1 M in THF, 28 mL) was slowly added to a solution of the ester (10.0 mmol) and Ti(O\(_{\text{Pr}}\)\(_4\) (14.0 mmol, 4.3 mL) in 6 mL of anhydrous THF at 0°C over 30 min. The dark mixture was warmed to room temperature and allowed to stir overnight. Then 5 mL of water was slowly added to quench the reaction. After the precipitate was removed by filtration, the filtrate was extracted by Et\(_2\)O (20 mL × 3) and the combined organic phase was dried over anhydrous Na\(_2\)SO\(_4\). The crude products were purified by column chromatography (PE/EA = 1/1 to 20/1) to afford the pure cyclopropanols.

Synthesis of several starting materials

Preparation of 2p

Preparation of II: 1H-imidazole (2.5 g, 36 mmol) and t-butyldimethylsilyl chloride (TBDMSCI) (4.5 g, 30 mmol) were added to a solution of methyl hyodeoxycholate (1.2 g, 3 mmol) in 3mL of anhydrous DMF. The mixture was allowed to stir overnight at room temperature. Aqueous NaCl was added and the mixture was extracted with ethyl acetate (5 mL × 3). Combined organic phase was dried over anhydrous Na\(_2\)SO\(_4\).
crude products were purified by column chromatography (PE/EA = 80/1) to afford the pure product II (1.22 g, 63%).

Preparation of 2p: Under the protection of nitrogen, EtMgBr (9 mmol, 1M in THF, 9mL) was dropwise added to a solution of II (2 mmol, 1.2 g) and Ti(OiPr)₄ (3 mmol, 1.5 mL) in 40 mL of anhydrous THF at 0 °C over 30 min. The dark mixture was warmed to room temperature and allowed to stir overnight. Then 10 mL of water was slowly added to quench the reaction. After the precipitate was removed by filtration, the filtrate was extracted by Et₂O (20 mL × 3) and the combined organic phase was dried over anhydrous Na₂SO₄. The crude products were purified by column chromatography (PE/EA = 20/1) to afford the product 2p (0.816 g, 67%).

Preparation of 2q

Preparation of IV: MeI (1.2 equiv.) was added to a solution of S(+)-Ibuprofen (1.03 g, 5 mmol) and K₂CO₃ (3 equiv.) in DMF (10 mL) at room temperature. The mixture was allowed to stir overnight at room temperature. After pouring 10 mL of water, the mixture was extracted by EtOAc (10 mL × 3). The combined organic layer was washed by brine and dried over anhydrous Na₂SO₄. The residue was purified by silica gel chromatography using PE/EA (10/1) to obtain pure compound IV (95%, 1.05 g).

Preparation of 2q: According to the general procedure to the preparation of cyclopropanes, the pure 2q was obtained in 90% yield (933 mg).

Preparation of 1s
Preparation of **VI**: NaH (600 mg, 60% in mineral oil, 15 mmol) was added to a solution of mefenamic acid (1.21 g, 5 mmol) in DMF (10 mL) in an ice-water bath. The mixture was stirred for 30 minutes followed by the addition of MeI (933 μL, 15 mmol). Then the resulting mixture was stirred at room temperature overnight. After pouring 10 mL of water, the mixture was extracted by EtOAc (10 mL × 3). The combined organic layer was washed by brine and dried over anhydrous Na₂SO₄. The residue was purified by silica gel chromatography using PE/EA (10/1) to obtain pure compound **VI** (1.30 g, 96%).

Preparation of **1s**: The pure compound **VI** was hydrolyzed with sodium hydroxide (10 equiv.) in a solution of 1:1 ethanol/water heated to reflux for 24 h. Then the mixture was cooled down to room temperature and was acidified with 1 M HCl to pH = 1, followed by extracting with EtOAc. The combined organic layer was washed with brine and dried over anhydrous Na₂SO₄. The residue was purified by silica gel chromatography using PE/EA (from 10/1 to 1/1) to obtain pure compound (1.20 g, 98%).

**General procedure for C-H activation**

![Chemical Reaction Diagram]

Standard Condition 1

A teflon-capped vial was charged with the benzoic acids (0.1 mmol, 1.0 equiv.), cyclopropanols (0.25 mmol, 2.5 equiv.), Cs₂CO₃ (0.1 mmol, 1 equiv.), [Cp*RhCl₂]₂ (4 mol%), AgOAc (2 equiv.), 4Å Ms (10 mg) under an air atmosphere. The reaction...
mixture was stirred at 80 °C for 24 h. After that, the mixture was cooled down and was extracted with EtOAc. The organic layers were combined, filtered through a pad of Celite and concentrated \textit{in vacuo}. The residue was purified by silica gel chromatography using EA/PE to afford compounds.

**Standard Condition 2**

A teflon-capped vial was charged with the benzoic acids (0.1 mmol, 1.0 equiv.), cyclopropanols (0.25 mmol, 2.5 equiv.), K$_3$PO$_4$ (0.1 mmol, 1 equiv.), [Cp*RhCl$_2$]$_2$ (4 mol%), AgOAc (2 equiv.), 4Å Ms (10 mg) under an air atmosphere. The reaction mixture was stirred at 80 °C for 24 h. After that, the mixture was cooled down and was extracted with EtOAc. The organic layers were combined, filtered through a pad of Celite and concentrated \textit{in vacuo}. The residue was purified by silica gel chromatography using EA/PE to afford compounds.

**The potential utility of the reaction**

**Preparation of 3pa**

A teflon-capped vial was charged with the 1a (13.6 mg, 0.1 mmol, 1.0 equiv.), 2p (25μL, 0.25 mmol, 2.5 equiv.), Cs$_2$CO$_3$ (33mg, 0.1 mmol, 1 equiv.), [Cp*RhCl$_2$]$_2$ (2.5
mg, 4 mol%), AgOAc (34 mg, 2 equiv.), 4Å Ms (10 mg) under an air atmosphere. The reaction mixture was stirred at 80 °C for 48 h. After that, the mixture was cooled down and was extracted with EtOAc. The organic layers were combined, filtered through a pad of Celite and concentrated in vacuo. The residue was purified by silica gel chromatography using EA/PE to afford pure compound 3pa (30 mg) in 40% isolated yield and the value of dr is 1:1.

**Preparation of 3ar**

A teflon-capped vial was charged with the 1r (45.2 mg, 0.1 mmol, 1.0 equiv.), 2a (25 μL, 0.25 mmol, 2.5 equiv.), K3PO4 (21.2 mg, 0.1 mmol, 1 equiv.), [Cp*RhCl2]2 (2.5 mg, 4 mol%), AgOAc (34 mg, 2 equiv.), 4Å Ms (10 mg) under an air atmosphere. The reaction mixture was stirred at 80 °C for 24 h. After that, the mixture was cooled down and was extracted with EtOAc. The organic layers were combined, filtered through a pad of Celite and concentrated in vacuo. The residue was purified by silica gel chromatography using EA/PE to afford pure compound 3ar (23 mg) in 40% isolated yield and the value of dr is 1:1.

**Preparation of 4**
A teflon-capped vial was charged with the 1r (45.2 mg, 0.1 mmol, 1.0 equiv.), 2q (158 mg, 0.25 mmol, 2.5 equiv.), K₃PO₄ (21.2 mg, 0.1 mmol, 1 equiv.), [Cp*RhCl₂]₂ (2.5 mg, 4 mol%), AgOAc (34 mg, 2 equiv.), 4Å Ms (10 mg) under an air atmosphere. The reaction mixture was stirred at 80 °C for 24 h. After that, the mixture was cooled down and was extracted with EtOAc. The organic layers were combined, filtered through a pad of Celite and concentrated in vacuo. The residue was purified by silica gel chromatography using EA/PE to afford pure compound 4 (40 mg) in 37% isolated yield and the value of dr is 1:1.

Preparation of 5

A teflon-capped vial was charged with the 1r (45.2 mg, 0.1 mmol, 1.0 equiv.), 2q (54.6 mg, 0.25 mmol, 2.5 equiv.), K₃PO₄ (21.2 mg, 0.1 mmol, 1 equiv.), [Cp*RhCl₂]₂ (2.5 mg, 4 mol%), AgOAc (34 mg, 2 equiv.), 4Å Ms (10 mg) under an air atmosphere. The reaction mixture was stirred at 80 °C for 24 h. After that, the mixture was cooled down and was extracted with EtOAc. The organic layers were combined, filtered
through a pad of Celite and concentrated in vacuo. The residue was purified by silica gel chromatography using EA/PE to afford pure compound 5 (51 mg) in 77% isolated yield and 1:1 dr value.

**Preparation of 6**

A teflon-capped vial was charged with the 1s (25.5 mg, 0.1 mmol, 1.0 equiv.), 2q (54.6 mg, 0.25 mmol, 2.5 equiv.), K3PO4 (21.2 mg, 0.1 mmol, 1 equiv.), [Cp*RhCl2]2 (2.5 mg, 4 mol%), AgOAc (34 mg, 2 equiv.), 4Å Ms (10 mg) under an air atmosphere. The reaction mixture was stirred at 80 °C for 24 h. After that, the mixture was cooled down and was extracted with EtOAc. The organic layers were combined, filtered through a pad of Celite and concentrated in vacuo. The residue was purified by silica gel chromatography using EA/PE to afford pure compound 6 (42 mg) in 90% isolated yield and the value of dr is 1:1.

**Reaction in gram scale of 5**
To the solution of the 1r (2.26 g, 5 mmol, 1 equiv.), 2q (2.73 g, 12.5 mmol, 2.5 equiv.), [Cp*RhCl₂]₂ (125 mg, 4 mol %), AgOAc (1.7 g, 2 equiv.), K₃PO₄ (1.06 g, 1 equiv.) was added in MeCN (50 mL). The solution was stirred at 80 °C for 24 hours. After that, the mixture was cooled down and the mixture was extracted with EtOAc. The organic layers were combined, filtered through a pad of Celite and concentrated in vacuo. The residue was purified by silica gel chromatography using EA/PE to afford compound 5 (2.43 g) in 73% isolated yield and the value of dr is 1:1.

X-ray molecular structure and crystallographic data

![3aa](image)

Table 2. Crystal data for 3aa

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Table 3. Fractional Atomic Coordinates (×10⁴) and Equivalent Isotropic Displacement Parameters (Å²×10³). Ueq is defined as 1/3 of of the trace of the
### orthogonalised U\text{ij} tensor

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### Table 4. Anisotropic Displacement Parameters (Å²×10³). The Anisotropic displacement factor exponent takes the form: \(-2\pi²[h2a²U\text{11}+2hkaxb\text{12}+…].

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### Table 5. Bond Lengths

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### Table 6. Bond Angles

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Table 7. Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3)

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Mechanistic Studies

Independent KIE study

A teflon-capped vial was charged with the 2-methoxyl benzoic acid (1g) or mono-deuterated 2-methoxyl benzoic acid (1g-d) (0.1 mmol, 1.0 equiv.), 2a (0.25 mmol, 2.5 equiv.), K3PO4 (0.1 mmol, 1equiv.), [Cp*RhCl2]2 (4 mol%), AgOAc (2 mol, 2 equiv.) and 4Å Ms (10 mg) in MeCN (1 mL) under an air atmosphere. The reaction mixture was allowed to stir at 80 °C for 10 min. After that, the mixture was cooled down and was extracted with EtOAc. The organic layers were combined, filtered through a pad of Celite and concentrated in vacuo. The crude reaction mixture was diluted with CDCl3, CH2Br2 as internal standard was added and the mixture was analyzed via 1H NMR spectroscopy. The yields of 3ag were obtained in 13.6 % and 5.2 % respectively.
(determined as an average of 2 runs), resulting in an $k_H/k_D$ of 2.6.
A teflon-capped vial was charged with 2-methoxyl benzoic acid (1g) (0.1 mmol, 1 equiv.), D$_2$O (1.0 mmol, 10 equiv.), K$_3$PO$_4$ (0.1 mmol, 1 equiv.), [Cp*RhCl$_2$]$_2$ (4 mol%), AgOAc (0.2 mmol) at 1 mL of MeCN under an air atmosphere. The reaction mixture was allowed to stir at 80 °C for 2 h. The reaction mixture was cooled down to room temperature and acidified with 1M HCl to pH = 1. Then poured into water, the mixture was extracted by EtOAc, followed by dried with anhydrous Na$_2$SO$_4$. Then the solvent was removed under reduced pressure and the residue was purified by silica gel chromatography using EA/PE to afford compounds. The ratio was identified by $^1$HNMR (59% D).
A teflon-capped vial was charged with the benzoic acids (0.1 mmol, 1.0 equiv.), 1-phenylprop-2-enone 7 (0.25 mmol, 2.5 equiv.), Cs$_2$CO$_3$ (0.1 mmol, 1 equiv.), [Cp*RhCl$_2$]$_2$ (5 mol%), AgOAc (2 equiv.), 4Å Ms (10 mg) under an air atmosphere. The reaction mixture was stirred at 80 °C for 24 h. After that, the mixture was cooled down and the mixture was extracted with EtOAc. The organic layers were combined, filtered through a pad of Celite and concentrated in vacuo. The residue was purified by silica gel chromatography using EA/PE to afford pure compound 3aa in 44% isolated yield.
Characterization data of compounds

1- phenylcyclopropan-1-ol (2a)

\[\text{H NMR (600 MHz, CDCl}_3): \delta 7.37 - 7.17 \text{ (m, 5H), 1.30 - 1.23 (m, 2H), 1.07 - 1.03 (m, 2H).} \]

1-(2-methylphenyl)cyclopropan-1-ol (2b)

\[\text{H NMR (600 MHz, CDCl}_3): \delta 7.33 \text{ (d, } J = 7.1 \text{ Hz, 1H), 7.24 - 7.10 \text{ (m, 3H), 2.33 (s, 3H), 1.18 - 1.11 (m, 2H), 0.94 - 0.88 \text{ (m, 2H).} \]

1-(2-fluorophenyl)cyclopropan-1-ol (2c)

\[\text{H NMR (500 MHz, CDCl}_3): \delta 7.38 \text{ (td, } J = 7.6, 1.8 \text{ Hz, 1H), 7.29 - 7.25 \text{(m, 1H), 7.10 (td, } J = 7.6, 1.8 \text{ Hz, 1H), 7.05 (ddd, } J = 11.0, 7.6, 1.8\text{Hz, 1H), 1.43 - 1.37 \text{(m, 2H), 1.18-1.11(m, 2H).} \]

1-(3-chlorophenyl)cyclopropan-1-ol (2d)

\[\text{H NMR (600 MHz, CDCl}_3): \delta 7.29 \text{ (t, } J = 2 \text{ Hz, 1H), 7.26 - 7.21 \text{ (m, 1H), 7.18 (t, } J = 7.8 \text{ Hz, 1H), 7.12 (dt, } J = 7.8, 2 \text{ Hz, 1H), 1.30 - 1.25 \text{(m, 2H), 1.06 - 1.00 \text{ (m, 2H).} \]

1-(4-methoxyphenyl)cyclopropan-1-ol (2e)
$^1$H NMR (600 MHz, CDCl$_3$): δ 7.36 - 7.16 (m, 2H), 6.96 - 6.81 (m, 2H), 3.8 (s, 3H), 1.23 - 1.14 (m, 2H), 1.01 - 0.92 (m, 2H).

1-(2-furanyl)cyclopropan-1-ol (2f)

$^1$H NMR (600 MHz, CDCl$_3$): δ 7.32 - 7.29 (m, 1H), 6.32 (dd, $J$ = 3.2, 1.8, 1H), 6.21 (d, $J$ = 3.2, 1H), 1.18 - 1.13 (m, 2H), 1.09 - 1.05 (m, 2H).

1-benzylcyclopropan-1-ol (2g)

$^1$H NMR (500 MHz, CDCl$_3$): δ 7.36 - 7.29 (m, 4H), 7.26 (tt, $J$ = 7, 1.5 Hz, 1H), 2.88 (s, 2H), 0.85 - 0.78 (m, 2H), 0.67 - 0.61 (m, 2H).

1-(2-methoxybenzyl)cyclopropan-1-ol (2h)

$^1$H NMR (500 MHz, CDCl$_3$): δ 7.28 - 7.21 (m, 2H), 6.94 (td, $J$ = 7.5, 1 Hz, 1H), 6.91 (d, $J$ = 7.5 Hz, 1H), 3.85 (s, 3H), 2.96 (s, 2H), 0.79 - 0.74 (m, 2H), 0.64 - 0.59 (m, 2H).

1-(naphthalenylmethyl)cyclopropan-1-ol (2i)

$^1$H NMR (500 MHz, CDCl$_3$): δ 8.17 (d, $J$ = 8.5 1H), 7.90 (dd, $J$ = 8.0, 1 Hz, 1H), 7.81 (dt, $J$ = 8.0, 1 Hz, 1H), 7.59 - 7.43 (m, 4H), 3.47 (s, 2H), 0.91 - 0.84 (m, 2H), 0.75 - 0.67 (m, 2H).

1-(phenoxy)methyl)cyclopropan-1-ol (2j)
$^1\text{H NMR}$ (500MHz, CDCl$_3$): δ 7.33 - 7.27 (m, 2H), 6.98 (tt, $J = 7.3$, 1 Hz, 1H), 6.96 - 6.91 (m, 2H), 4.01 (s, 2H), 1.12 - 0.84 (m, 2H), 0.86 - 0.56 (m, 2H).

$[1,1^\prime$-bi(cyclopropan)]-1-ol (2k)

$^1\text{H NMR}$ (500 MHz, CDCl$_3$): δ 1.37 (tt, $J = 8$, 5 Hz, 1H), 0.74 - 0.67 (m, 2H), 0.54 - 0.48 (m, 2H), 0.45 - 0.41 (m, 2H), 0.23 - 0.18 (m, 2H).

1-cyclobutylcyclopropan-1-ol (2l)

$^1\text{H NMR}$ (600 MHz, CDCl$_3$): δ 2.5 (q, $J = 8.4$ Hz, 1H), 2.00 - 1.93 (m, 2H), 1.85 - 1.69 (m, 4H), 0.72 - 0.67 (m, 2H), 0.52 - 0.47 (m, 2H).

1-cyclopentylcyclopropan-1-ol (2m)

$^1\text{H NMR}$ (600 MHz, CDCl$_3$): δ 1.92 - 1.82 (m, 1H), 1.77 - 1.69 (m, 2H), 1.68 - 1.60 (m, 2H), 1.58 - 1.50 (m, 2H), 1.41 - 1.30 (m, 2H), 0.72 - 0.66 (m, 2H), 0.49 - 0.45 (m, 2H).

1-(tetrahydropyran-4-yl)cyclopropan-1-ol (2n)

$^1\text{H NMR}$ (600 MHz, CDCl$_3$): δ 4.03 (dt, $J = 10.8$, 3 Hz, 2H), 3.46 - 3.29 (m, 2H), 1.68 - 1.52 (m, 4H), 1.36 - 1.17 (m, 1H), 0.76 - 0.61 (m, 2H), 0.58 - 0.37 (m, 2H).
1-undecylcyclopropan-1-ol (2o)

\[
\begin{align*}
\text{H NMR} \ (600 \text{ MHz, CDCl}_3): & \quad \delta 1.59 - 1.54 \text{ (m, 2H)}, 1.54 - 1.49 \text{ (m, 2H)}, 1.38 - 1.22 \text{ (m, 16H)}, 0.9 \text{ (t, } J = 6.9 \text{ Hz, 3H)}, 0.77 - 0.71 \text{ (m, 2H)}, 0.48 - 0.42 \text{ (m, 2H)}. \\
\end{align*}
\]

(4R)-4-((3R,5R,6S,8S,10R,13R,14S)-3,6-bis((tert-butyldimethylsilyl)oxy)-5,10,13-trimethylhexadecahydro-1H-cyclopenta[a]phenanthren-17-yl)pentanoate (II)

\[
\begin{align*}
\text{H NMR} \ (500 \text{ MHz, CDCl}_3): & \quad \delta 4.00 \text{ (dt, } J = 11.7, 4.3 \text{ Hz, 1H)}, 3.69 \text{ (s, 3H)}, 3.59 - 3.51 \text{ (m, 1H)}, 2.38 \text{ (ddd, } J = 15.5, 10.0, 5.0 \text{ Hz, 1H)}, 2.24 \text{ (ddd, } J = 15.5, 9.5, 6.0 \text{ Hz, 1H)}, 2.00 - 1.72 \text{ (m, 5H)}, 1.65 - 1.54 \text{ (m, 2H)}, 1.52 - 1.26 \text{ (m, 11H)}, 1.25 - 0.97 \text{ (m, 8H)}, 0.95 - 0.85 \text{ (m, 24H)}, 0.66 \text{ (s, 3H)}, 0.09 - 0.04 \text{ (m, 12H)}. \\
\end{align*}
\]

1-((3R)-3-((3R,5R,6S,8S,10R,13R,14S)-3,6-bis((tert-butyldimethylsilyl)oxy)-5,10,13-trimethylhexadecahydro-1H-cyclopenta[a]phenanthren-17-yl)butyl)cyclopropan-1-ol (2p)

\[
\begin{align*}
\text{H NMR} \ (500 \text{ MHz, CDCl}_3): & \quad \delta 4.20 - 3.86 \text{ (m, 1H)}, 3.57 - 3.49 \text{ (m, 1H)}, 1.97 - 1.91 \text{ (m, 1H)}, 1.91 - 1.79 \text{ (m, 2H)}, 1.78 - 1.69 \text{ (m, 1H)}, 1.67 - 1.62 \text{ (m, 2H)}, 1.60 - 1.52 \text{ (m, 3H)}, 1.49 - 1.35 \text{ (m, 9H)}, 1.27 - 1.22 \text{ (m, 2H)}, 1.16 - 1.05 \text{ (m, 4H)}, 1.02 - 0.94 \text{ (m, 2H)}, 0.93 - 0.82 \text{ (m, 24H)}, 0.78 - 0.67 \text{ (m, 2H)}, 0.63 \text{ (s, 3H)}, 0.48 - 0.37 \text{ (m, 2H)}, 0.08 - 0.01 \text{ (m, 12H)}. \\
\end{align*}
\]

methyl (S)-2-(4-isobutylphenyl)propanoate (IV)
1H NMR (500 MHz, CDCl$_3$): δ 7.23 - 7.17 (m, 2H), 7.13 - 7.08 (m, 2H), 3.70 (d, $J = 7.5$ Hz, 1H), 3.66 (s, 3H), 2.45 (d, $J = 7.0$ Hz, 2H), 1.90 - 1.80 (m, 1H), 1.49 (d, $J = 7.5$ Hz, 3H), 0.90 (d, $J = 7.0$ Hz, 6H).

(S)-1-(1-(4-isobutylphenyl)ethyl)cyclopropan-1-ol (2q)

1H NMR (500 MHz, CDCl$_3$) δ 7.25 - 7.21 (m, 2H), 7.13 - 7.10 (m, 2H), 2.54 (q, $J = 7.2$ Hz, 1H), 2.46 (d, $J = 7.5$ Hz, 2H), 1.91 - 1.81 (m, 1H), 1.68 (s, 1H), 1.39 (d, $J = 7.2$ Hz, 3H), 0.92 (d, $J = 6.5$ Hz, 6H), 0.86 - 0.80 (m, 1H), 0.75 - 0.65 (m, 2H), 0.64 - 0.58 (m, 1H).

methyl 2-((2,3-dimethylphenyl)(methyl)amino)benzoate (VI)

1H NMR (600 MHz, CDCl$_3$): δ 7.43 (dd, $J = 7.8$, 1.8 Hz, 1H), 7.37 - 7.33 (m, 1H), 7.03 (t, $J = 7.5$ Hz, 1H), 6.97 (d, $J = 7.2$ Hz, 1H), 6.95 (d, $J = 8.4$ Hz, 1H), 6.87 (t, $J = 7.5$ Hz, 1H), 6.81 (d, $J = 7.8$ Hz, 1H), 3.41 (s, 3H), 3.16 (s, 3H), 2.29 (s, 3H), 2.18 (s, 3H).

2-((2,3-dimethylphenyl)(methyl)amino)benzoic acid (1s)

1H NMR (500 MHz, CDCl$_3$): δ 8.29 (dd, $J = 8.0$, 1.5 Hz, 1H), 7.48 - 7.40 (m, 2H), 7.31 (dd, $J = 7.5$, 1.0 Hz, 1H), 7.22 - 7.17 (m, 2H), 7.09 - 7.05 (m, 1H), 6.90 (dd, $J = 8.0$, 1.0 Hz, 1H), 3.18 (s, 3H), 2.24 (s, 3H), 1.89 (s, 3H).

7-methyl-3-(2-oxo-2-phenylethyl)isobenzofuran-1(3H)-one (3aa)
The product was synthesized by standard condition 1 in 75% yield.

\textbf{1H NMR} (500 MHz, CDCl$_3$): $\delta$ 7.98 - 7.93 (m, 2H), 7.62 - 7.56 (m, 1H), 7.53 - 7.44 (m, 3H), 7.34 (d, $J = 8.0$ Hz, 1H), 7.28 (d, $J = 7.5$ Hz, 1H), 6.11 (t, $J = 6.5$ Hz, 1H), 3.71 (dd, $J = 17.5$, 6.5 Hz, 1H), 3.38 (dd, $J = 17.5$, 6.5 Hz, 1H), 2.70 (s, 3H).

\textbf{13C NMR} (151 MHz, CDCl$_3$): $\delta$ 196.26, 170.47, 150.38, 139.98, 136.39, 134.12, 133.96, 131.17, 128.96, 128.32, 123.48, 120.06, 76.30, 44.01, 17.53.

\textbf{ESI-MS} calcd. for C$_{17}$H$_{14}$O$_3$Na [M+Na$^+$]: 289.0840, found: 289.0837.

7-methyl-3-(2-oxo-2-(o-tolyl)ethyl)isobenzofuran-1(3H)-one (3ba)

The product was synthesized by standard condition 1 in 75% yield.

\textbf{1H NMR} (500 MHz, CDCl$_3$): $\delta$ 7.65 (dd, $J = 7.5$, 1 Hz, 1H), 7.55 (t, $J = 7.6$ Hz, 1H), 7.43 (td, $J = 7.5$, 1 Hz, 1H), 7.36 (d, $J = 7.5$, 1H), 7.33 - 7.30 (m, 2H), 7.28 (dd, $J = 7.5$, 1 Hz, 1H), 6.11 (t, $J = 6.5$ Hz, 1H), 3.66 (dd, $J = 17$, 6.5 Hz, 1H), 3.37 (dd, $J = 17$, 6.5 Hz, 1H), 2.72 (s, 3H), 2.61 (s, 3H).

\textbf{13C NMR} (126 MHz, CDCl$_3$): $\delta$ 199.51, 170.43, 150.45, 140.01, 139.07, 136.72, 134.08, 132.42, 132.26, 131.13, 129.08, 126.01, 123.53, 119.83, 76.50, 46.50, 21.74, 17.50.

\textbf{ESI-MS} calcd. for C$_{18}$H$_{16}$O$_3$Na [M+Na$^+$]: 303.0996, found: 303.0998.

3-(2-(2-fluorophenyl)-2-oxoethyl)-7-methylisobenzofuran-1(3H)-one (3ca)

The product was synthesized by standard condition 1 in 61% yield.

\textbf{1H NMR} (500 MHz, CDCl$_3$): $\delta$ 7.96 (dt, $J = 7.5$, 2 Hz, 1H), 7.56 (ddd, $J = 8$, 7.5, 2 Hz, 1H), 7.52 (t, $J = 7.5$, 1H), 7.33 (d, $J = 7.5$, 1H), 7.30 - 7.23 (m, 2H), 7.14 (ddd, $J = 8$, 6, 1 Hz, 1H), 6.09 (t, $J = 6.5$, 1H), 3.64 (ddd, $J = 18$, 6.5, 3 Hz, 1H), 3.45 (ddd, $J = 18$, 6.5, 3 Hz, 1H), 2.69 (s, 3H).

\textbf{13C NMR} (126 MHz, CDCl$_3$): $\delta$ 194.16, 170.45, 163.31, 161.28, 150.25, 139.99, 135.57 (d, $J = 9.3$ Hz), 134.08, 131.13, 130.84 (d, $J = 1.5$ Hz), 124.88, 123.54, 119.85, 116.93 (d, $J = 23.8$ Hz), 75.92, 48.78 (d, $J = 8.2$ Hz), 17.50.

\textbf{ESI-MS} calcd. for C$_{19}$H$_{13}$FO$_3$Na [M+Na$^+$]: 307.0746, found: 307.0750.

\textbf{19F NMR} (500 MHz, CDCl$_3$): $\delta$ -108.87.
3-(2-(3-chlorophenyl)-2-oxoethyl)-7-methylisobenzofuran-1(3H)-one (3da)

![Chemical Structure](image1)

The product was synthesized by standard condition 1 in 63% yield.

$^1$H NMR (600 MHz, CDCl$_3$): δ 7.94 (t, $J$ = 1.8 Hz, 1H), 7.83 (d, $J$ = 7.8 Hz, 1H), 7.58 (ddd, $J$ = 7.8, 1.8, 1.2 Hz, 1H), 7.53 (t, $J$ = 7.8, 1H), 7.44 (t, $J$ = 7.8 Hz, 1H), 7.33 (d, $J$ = 7.8 Hz, 1H), 6.10 (t, $J$ = 6.3 Hz, 1H), 3.68 (dd, $J$ = 17.4, 6.3 Hz, 1H), 3.38 (dd, $J$ = 17.4, 6.3 Hz, 1H), 2.71 (s, 3H).

$^{13}$C NMR (151 MHz, CDCl$_3$): δ 195.00, 170.31, 150.09, 140.08, 137.87, 135.36, 134.17, 133.86, 131.26, 130.30, 128.40, 126.42, 123.46, 119.91, 75.99, 44.10, 17.50.

ESI-MS calcd. for C$_{17}$H$_{13}$ClO$_3$Na [M+Na$^+$]: 323.0450, found: 323.0447.

3-(2-(4-methoxyphenyl)-2-oxoethyl)-7-methylisobenzofuran-1(3H)-one (3ea)

![Chemical Structure](image2)

The product was synthesized by standard condition 1 in 44% yield.

$^1$H NMR (500 MHz, CDCl$_3$): δ 7.96 - 7.89 (m, 2H), 7.50 (t, $J$ = 7.6 Hz, 1H), 7.35 - 7.30 (m, 1H), 7.30 - 7.24 (m, 1H), 6.97-6.91 (m, 2H), 6.09 (t, $J$ = 6.5 Hz, 1H), 3.87 (s, 3H), 3.66 (dd, $J$ = 17.5, 6.5 Hz, 1H), 3.31 (dd, $J$ = 17.5, 6.5 Hz, 1H), 2.69 (s, 3H).

$^{13}$C NMR (126 MHz, CDCl$_3$): δ 194.68, 170.51, 164.18, 150.55, 139.91, 134.07, 131.09, 130.68, 129.59, 123.50, 120.13, 114.11, 76.56, 55.68, 43.65, 17.50.

ESI-MS calcd. for C$_{18}$H$_{16}$O$_4$Na [M+Na$^+$]: 319.0946, found: 319.0950.

3-(2-(furan-2-yl)-2-oxoethyl)-7-methylisobenzofuran-1(3H)-one (3fa)

![Chemical Structure](image3)

The product was synthesized by standard condition 1 in 51% yield.

$^1$H NMR (600 MHz, CDCl$_3$): δ 7.61 - 7.59 (m, 1H), 7.51 (t, $J$ = 7.5 Hz, 1H), 7.31 (d, $J$ = 7.5 Hz, 1H), 7.28 (d, $J$ = 7.5 Hz, 1H), 7.25 (d, $J$ = 3.6 Hz, 1H), 6.57 (dd, $J$ = 3.6, 1.8 Hz, 1H), 6.04 (t, $J$ = 6.6 Hz, 1H), 3.53 (dd, $J$ = 17.5, 6.6 Hz, 1H), 3.24 (dd, $J$ = 17.5, 6.6 Hz, 1H), 2.69 (s, 3H).

$^{13}$C NMR (126 MHz, CDCl$_3$): δ 184.91, 170.35, 152.40, 150.06, 147.22, 140.03, 134.12, 131.20,
The product was synthesized by standard condition 2 in 40% yield.

1H NMR (500 MHz, CDCl3): \( \delta \) 7.47 (t, \( J = 7.6 \) Hz, 1H), 7.36 - 7.31 (m, 2H), 7.30 - 7.27 (m, 1H), 7.26 - 7.24 (m, 1H), 7.22 - 7.19 (m, 2H), 7.20 - 7.15 (m, 1H), 5.84 (t, \( J = 6.5 \) Hz, 1H), 3.80 (d, \( J = 15.5 \) Hz, 1H), 3.76 (d, \( J = 15.5 \) Hz, 1H), 3.08 (dd, \( J = 17.5, 6.5 \) Hz, 1H), 2.86 (dd, \( J = 17.5, 6.5 \) Hz, 1H), 2.67 (s, 3H).

13C NMR (126 MHz, CDCl3): \( \delta \) 204.54, 170.29, 149.95, 140.00, 134.07, 133.30, 131.13, 129.08, 129.61, 127.54, 123.37, 119.61, 75.92, 50.92, 46.78, 17.47.

ESI-MS calcd. for C\(_{15}\)H\(_{12}\)O\(_{4}\)H [M+H\(^+\)]: 257.0814, found: 257.0819.

7-methyl-3-(2-oxo-3-phenylpropyl)isobenzofuran-1(3H)-one (3ga)

The product was synthesized by standard condition 2 in 64% yield.

1H NMR (500 MHz, CDCl3): \( \delta \) 7.47 (t, \( J = 7.6 \) Hz, 1H), 7.26 - 7.24 (m, 1H), 7.22 - 7.19 (m, 2H), 7.20 - 7.15 (m, 1H), 5.84 (t, \( J = 6.5 \) Hz, 1H), 3.80 (d, \( J = 15.5 \) Hz, 1H), 3.76 (d, \( J = 15.5 \) Hz, 1H), 3.08 (dd, \( J = 17.5, 6.5 \) Hz, 1H), 2.86 (dd, \( J = 17.5, 6.5 \) Hz, 1H), 2.67 (s, 3H).

13C NMR (126 MHz, CDCl3): \( \delta \) 205.23, 170.44, 157.34, 150.31, 139.84, 133.96, 131.38, 131.01, 129.05, 123.38, 122.78, 120.95, 119.84, 110.63, 76.04, 55.44, 46.67, 45.60, 17.46.

ESI-MS calcd. for C\(_{16}\)H\(_{16}\)O\(_{4}\)Na [M+Na\(^+\)]: 303.0996, found: 303.0991.

3-(3-(2-methoxyphenyl)-2-oxopropyl)-7-methylisobenzofuran-1(3H)-one (3ha)

The product was synthesized by standard condition 2 in 76% yield.

1H NMR (500 MHz, CDCl3): \( \delta \) 7.47 (t, \( J = 7.6 \) Hz, 1H), 7.26 - 7.24 (m, 1H), 7.24 - 7.21 (m, 2H), 7.14 (dd, \( J = 7.4, 1.6 \) Hz, 1H), 6.92 (td, \( J = 7.4, 1.0 \) Hz, 1H), 6.86 (dd, \( J = 8.5, 1.0 \) Hz, 1H), 5.87 (t, \( J = 6.5 \) Hz, 1H), 3.77 (s, 3H), 3.74 - 3.72 (m, 2H), 3.11 (dd, \( J = 17.5, 6.5 \) Hz, 1H), 2.84 (dd, \( J = 17.5, 6.5 \) Hz, 1H), 2.67 (s, 3H).

13C NMR (126 MHz, CDCl3): \( \delta \) 205.52, 170.44, 157.34, 150.31, 139.84, 133.96, 131.38, 131.01, 129.05, 123.38, 122.78, 120.95, 119.84, 110.63, 76.04, 55.44, 46.67, 45.60, 17.46.

ESI-MS calcd. for C\(_{16}\)H\(_{18}\)O\(_{4}\)H [M+H\(^+\)]: 311.1283, found: 311.1287.

7-methyl-3-(3-(naphthalen-1-yl)-2-oxopropyl)isobenzofuran-1(3H)-one (3ia)
The product was synthesized by standard condition 2 in 78% yield.

\(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 7.91 - 7.84 (m, 2H), 7.80 (d, \(J = 8.0\) Hz, 1H), 7.58 - 7.48 (m, 2H), 7.45 - 7.35 (m, 3H), 7.22 (d, \(J = 7.5\) Hz, 1H), 7.09 (d, \(J = 7.6\) Hz, 1H), 5.82 (t, \(J = 6.5\) Hz, 1H), 4.23 (d, \(J = 16.0\) Hz, 1H), 4.18 (d, \(J = 16.0\) Hz, 1H), 3.05 (dd, \(J = 17.5, 7.0\) Hz, 1H), 2.79 (dd, \(J = 17.5, 7.0\) Hz, 1H), 2.65 (s, 3H).

\(^13\)C NMR (126 MHz, CDCl\(_3\)): \(\delta\) 205.02, 170.23, 149.87, 139.91, 134.06, 133.98, 132.20, 131.06, 130.02, 129.02, 128.63, 128.55, 126.89, 126.19, 125.73, 123.74, 123.31, 119.57, 75.95, 49.15, 46.32, 17.42.

ESI-MS calcd. for \(\text{C}_{22}\text{H}_{18}\text{O}_3\)Na [M+Na\(^+\)]: 353.1153, found: 353.1158.

7-methyl-3-(2-oxo-3-phenoxypropyl)isobenzofuran-1(3H)-one (3ja)

The product was synthesized by standard condition 2 in 78% yield.

\(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 7.52 (t, \(J = 7.6\) Hz, 1H), 7.35 - 7.21 (m, 4H), 7.00 (dd, \(J = 7.5, 1.0\) Hz, 1H), 6.89 - 6.85 (m, 2H), 5.92 (t, \(J = 6.5\) Hz, 1H), 4.65 (d, \(J = 16.5\) Hz, 1H), 4.61 (d, \(J = 16.5\) Hz, 1H), 3.27 (dd, \(J = 18.0, 7.5\) Hz, 1H), 3.09 (dd, \(J = 18.0, 6.0\) Hz, 1H), 2.68 (s, 3H).

\(^13\)C NMR (126 MHz, CDCl\(_3\)): \(\delta\) 204.15, 170.07, 149.87, 139.48, 133.98, 132.20, 131.06, 130.02, 129.02, 128.63, 128.55, 126.89, 126.19, 125.73, 123.74, 123.31, 119.57, 75.25, 73.01, 44.41, 17.37.

ESI-MS calcd. for \(\text{C}_{18}\text{H}_{16}\text{O}_4\)Na [M+Na\(^+\)]: 319.0946, found: 319.0951.

3-(2-cyclopropyl-2-oxoethyl)-7-methylisobenzofuran-1(3H)-one (3ka)

The product was synthesized by standard condition 1 for 48h in 52% yield.

\(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 7.50 (t, \(J = 7.6\) Hz, 1H), 7.27 (d, \(J = 7.5\) Hz, 1H), 7.24 (d, \(J = 7.5\) Hz, 1H), 5.88 (t, \(J = 6.5\) Hz, 1H), 3.22 (dd, \(J = 17.0, 6.5\) Hz, 1H), 3.02 (dd, \(J = 17.0, 6.0\) Hz, 1H), 2.68 (s, 3H), 1.97 (dd, \(J = 8.0, 4.5\) Hz, 1H), 1.18 - 1.08 (m, 2H), 1.02 - 0.91 (m, 2H).

\(^13\)C NMR (126 MHz, CDCl\(_3\)): \(\delta\) 206.72, 170.07, 157.42, 149.65, 140.02, 134.06, 131.15, 129.81, 123.29, 122.05, 119.45, 114.50, 75.25, 73.01, 44.41, 17.37.

ESI-MS calcd. for \(\text{C}_{16}\text{H}_{16}\text{O}_3\)Na [M+Na\(^+\)]: 253.0946, found: 253.0951.

3-(2-cyclobutyl-2-oxoethyl)-7-methylisobenzofuran-1(3H)-one (3la)
The product was synthesized by standard condition 1 for 48h in 71% yield.

**H NMR** (500 MHz, CDCl₃): \( \delta 7.50 (t, J = 7.5 \text{ Hz}, 1\text{H}), 7.27 (d, J = 7.5 \text{ Hz}, 1\text{H}), 7.24 (d, J = 7.5 \text{ Hz}, 1\text{H}), 5.88 (t, J = 6.5 \text{ Hz}, 1\text{H}), 3.30 (p, J = 8.6 \text{ Hz}, 1\text{H}), 2.99 (dd, J = 17.5, 7.0 \text{ Hz}, 1\text{H}), 2.79 (dd, J = 17.5, 6.0 \text{ Hz}, 1\text{H}), 2.67 (s, 3\text{H}), 2.36 - 2.10 (m, 4\text{H}), 2.02 - 1.93 (m, 1\text{H}), 1.89 - 1.80 (m, 1\text{H}).

**C NMR** (126 MHz, CDCl₃): \( \delta 207.18, 169.78, 149.63, 139.38, 133.46, 130.49, 122.82, 118.99, 75.44, 45.35, 44.39, 23.59, 17.17, 16.87.


3-(2-cyclopentyl-2-oxoethyl)-7-methylisobenzofuran-1(3H)-one (3ma)

![3-(2-cyclopentyl-2-oxoethyl)-7-methylisobenzofuran-1(3H)-one (3ma)](image)

The product was synthesized by standard condition 1 for 48h in 72% yield.

**H NMR** (500 MHz, CDCl₃): \( \delta 7.50 (t, J = 7.5 \text{ Hz}, 1\text{H}), 7.26 (d, J = 7.5 \text{ Hz}, 1\text{H}), 7.23 (d, J = 7.5 \text{ Hz}, 1\text{H}), 5.90 (t, J = 6.5 \text{ Hz}, 1\text{H}), 3.10 (dd, J = 17.5, 7.0 \text{ Hz}, 1\text{H}), 2.95 - 2.82 (m, 2\text{H}), 2.68 (s, 3\text{H}), 1.87 - 1.54 (m, 8\text{H}).

**C NMR** (126 MHz, CDCl₃): \( \delta 209.15, 170.41, 150.32, 139.96, 134.05, 131.06, 123.45, 119.61, 76.18, 52.06, 46.68, 28.76, 28.59, 26.12, 26.08, 17.47.

**ESI-MS** calcd. for C₁₆H₁₈O₄Na [M+Na⁺]: 281.1153, found: 281.1149.

7-methyl-3-(2-oxo-2-(tetrahydro-2H-pyran-4-yl)ethyl)isobenzofuran-1(3H)-one (3na)

![7-methyl-3-(2-oxo-2-(tetrahydro-2H-pyran-4-yl)ethyl)isobenzofuran-1(3H)-one (3na)](image)

The product was synthesized by standard condition 1 for 48h in 77% yield.

**H NMR** (500 MHz, CDCl₃): \( \delta 7.70 (t, J = 7.5 \text{ Hz}, 1\text{H}), 7.27 - 7.21 (m, 2\text{H}), 7.22 (d, J = 7.5 \text{ Hz}, 1\text{H}), 5.88 (t, J = 6.5 \text{ Hz}, 1\text{H}), 4.03 - 3.95 (m, 2\text{H}), 3.44 - 3.38 (m, 2\text{H}), 3.09 (dd, J = 17.5, 7.0 \text{ Hz}, 1\text{H}), 2.87 (dd, J = 17.5, 6.0 \text{ Hz}, 1\text{H}), 2.67 (s, 3\text{H}), 2.60 (tt, J = 11.2, 4.2 \text{ Hz}, 1\text{H}), 1.83 - 1.63 (m, 4\text{H}).

**C NMR** (126 MHz, CDCl₃): \( \delta 208.02, 170.26, 150.06, 140.05, 134.12, 131.17, 123.39, 119.52, 76.01, 67.17, 48.16, 45.39, 27.98, 17.45.

**ESI-MS** calcd. for C₁₆H₁₆O₄H [M+H⁺]: 275.1283, found: 275.1290.

7-methyl-3-(2-oxotridecyl)isobenzofuran-1(3H)-one (3oa)
The product was synthesized by standard condition 1 for 48h in 63% yield.

\[ {\text{H NMR (500 MHz, CDCl}}_3 \]: \( \delta \) 7.50 (t, \( J = 7.5 \) Hz, 1H), 7.27 (d, \( J = 7.5 \) Hz, 2H), 7.23 (d, \( J = 7.5 \) Hz, 1H), 5.87 (t, \( J = 6.5 \) Hz, 1H), 3.04 (dd, \( J = 17.5, 7.0 \) Hz, 1H), 2.84 (dd, \( J = 17.5, 6.0 \) Hz, 1H), 2.68 (s, 3H), 2.56 - 2.39 (m, 2H), 1.63 - 1.57 (m, 2H), 1.31 - 1.22 (m, 16H), 0.87 (t, \( J = 6.9 \) Hz, 3H).

\[ {\text{C NMR (126 MHz, CDCl}}_3 \]: \( \delta \) 207.12, 170.23, 150.06, 139.88, 133.94, 130.98, 123.30, 119.49, 75.93, 47.46, 43.70, 31.90, 29.59, 29.44, 29.37, 29.33, 29.11, 23.52, 22.68, 17.34, 14.11.

\[ {\text{ESI-MS calcd. for C}}_{22}\text{H}_{32}\text{O}_3\text{Na [M+Na}^+\text{]: 367.2248, found: 367.2241.} \]

3-(2-oxo-2-phenylethyl)-7-phenylisobenzofuran-1(3H)-one (3ab)

The product was synthesized by standard condition 2 in 69% yield.

\[ {\text{H NMR (600 MHz, CDCl}}_3 \]: \( \delta \) 8.01 - 7.95 (m, 2H), 7.68 (t, \( J = 7.5 \) Hz, 1H), 7.64 - 7.58 (m, 1H), 7.57 - 7.52 (m, 3H), 7.52 - 7.40 (m, 6H), 6.17 (t, \( J = 6.6 \) Hz, 1H), 3.78 (dd, \( J = 17.4, 6.0 \) Hz, 1H), 3.45 (dd, \( J = 17.4, 6.6 \) Hz, 1H).

\[ {\text{C NMR (151 MHz, CDCl}}_3 \]: \( \delta \) 196.28, 169.03, 151.20, 142.94, 136.48, 136.34, 134.21, 133.99, 131.35, 129.66, 128.96, 128.52, 128.32, 128.12, 121.97, 121.55, 77.35, 44.06.

\[ {\text{ESI-MS calcd. for C}}_{22}\text{H}_{16}\text{O}_3\text{Na [M+Na}^+\text{]: 351.0996, found: 351.1001.} \]

3-(2-oxo-2-phenylethyl)-6-phenylisobenzofuran-1(3H)-one (3ac)

The product was synthesized by standard condition 2 in 40% yield.

\[ {\text{H NMR (500 MHz, CDCl}}_3 \]: \( \delta \) 8.12 (d, \( J = 1.6 \) Hz, 1H), 8.00 – 7.96 (m, 2H), 7.88 (dd, \( J = 8.0, 1.7 \) Hz, 1H), 7.66 – 7.59 (m, 4H), 7.54 – 7.45 (m, 4H), 7.44 – 7.38 (m, 1H), 6.27 – 6.19 (m, 1H), 3.84 (dd, \( J = 17.7, 5.6 \) Hz, 1H), 3.44 (dd, \( J = 17.6, 7.6 \) Hz, 1H).

\[ {\text{C NMR (126 MHz, CDCl}}_3 \]: \( \delta \) 196.26, 170.30, 148.64, 143.21, 139.49, 136.27, 134.08, 133.55, 129.25, 129.01, 128.33, 127.39, 126.79, 124.11, 123.44, 77.35, 43.91.

\[ {\text{ESI-MS calcd. for C}}_{22}\text{H}_{16}\text{O}_3\text{Na [M+Na}^+\text{]: 351.0996, found: 351.1001.} \]
7-fluoro-3-(2-oxo-2-phenylethyl)isobenzofuran-1(3H)-one (3ad)

![Chemical structure of 7-fluoro-3-(2-oxo-2-phenylethyl)isobenzofuran-1(3H)-one (3ad)](image)

The product was synthesized by standard condition 2 in 52% yield.

\(^1\)H NMR (600 MHz, CDCl\(_3\)): \(\delta 8.00 - 7.94\) (m, 2H), 7.72 - 7.59 (m, 2H), 7.53 - 7.49 (m, 2H), 7.38 (d, \(J = 7.8\) Hz, 1H), 7.19 (t, \(J = 8.5\) Hz, 1H), 6.18 (d, \(J = 7.2\) Hz, 1H), 3.81 (dd, \(J = 17.4, 6.0\) Hz, 1H), 3.43 (dd, \(J = 17.4, 7.0\) Hz, 1H).

\(^{13}\)C NMR (151 MHz, CDCl\(_3\)): \(\delta 195.92, 166.32, 159.77\) (d, \(J = 264.8\) Hz), 152.45, 137.01 (d, \(J = 7.8\) Hz), 136.13, 134.15, 129.03, 128.30, 118.95 (d, \(J = 4.4\) Hz), 116.59 (d, \(J = 18.7\) Hz), 113.91 (d, \(J = 14.4\) Hz), 76.98, 43.70.

ESI-MS calcd. for C\(_{16}\)H\(_{11}\)FO\(_3\)H [M+H\(^+\)]: 271.0770, found: 271.0764.

\(^{19}\)F NMR (500 MHz, CDCl\(_3\)): \(\delta -113.95\).

7-chloro-3-(2-oxo-2-phenylethyl)isobenzofuran-1(3H)-one (3ae)

![Chemical structure of 7-chloro-3-(2-oxo-2-phenylethyl)isobenzofuran-1(3H)-one (3ae)](image)

The product was synthesized by standard condition 2 in 77% yield.

\(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta 7.97 - 7.93\) (m, 2H), 7.64 - 7.54 (m, 2H), 7.52 - 7.45 (m, 4H), 6.14 - 6.10 (m, 1H), 3.78 (dd, \(J = 17.5, 5.5\) Hz, 1H), 3.39 (dd, \(J = 17.5, 7.0\) Hz, 1H).

\(^{13}\)C NMR (126 MHz, CDCl\(_3\)): \(\delta 195.98, 167.17, 152.25, 136.17, 135.37, 134.14, 133.55, 131.00, 129.03, 128.31, 122.76, 121.42, 75.94, 43.75.

ESI-MS calcd. for C\(_{16}\)H\(_{11}\)ClO\(_3\)Na [M+Na\(^+\)]: 309.0294, found: 309.0291.

3-(2-oxo-2-phenylethyl)-7-(trifluoromethyl)isobenzofuran-1(3H)-one (3af)

![Chemical structure of 3-(2-oxo-2-phenylethyl)-7-(trifluoromethyl)isobenzofuran-1(3H)-one (3af)](image)

The product was synthesized by method 2 in 68% yield.

\(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta 7.98 - 7.93\) (m, 2H), 7.86 - 7.81 (m, 2H), 7.80 - 7.75 (m, 1H), 7.64 - 7.60 (m, 1H), 7.52 - 7.46 (m, 2H), 6.19 (dd, \(J = 7.5, 5.0\) Hz, 1H), 3.84 (dd, \(J = 17.8, 5.5\) Hz, 1H), 3.42 (dd, \(J = 17.8, 7\) Hz, 1H).
The product was synthesized by standard condition 2 in 60% yield.

**1H NMR (500 MHz, CDCl₃):** δ 7.96 - 7.92 (m, 2H), 7.62 - 7.56 (m, 2H), 7.51 - 7.43 (m, 2H), 7.07 (d, J = 8.0 Hz, 1H), 6.94 (d, J = 8.0 Hz, 1H), 6.08 (t, J = 6.5 Hz, 1H), 3.99 (s, 3H), 3.71 (dd, J = 17.5, 6.0 Hz, 1H), 3.37 (dd, J = 17.5, 7.0 Hz, 1H).

**13C NMR (126 MHz, CDCl₃):** δ 196.16, 168.26, 158.79, 152.76, 136.29, 134.05, 128.31, 114.40, 113.46, 111.15, 76.65, 56.00, 43.98.

**ESI-MS calcd. for C₁₇H₁₄O₄[M+H⁺]:** 283.0970, found: 283.0966.
The product was synthesized by standard condition 2 in 31% yield.

\[ \text{H NMR (500 MHz, CDCl}_3\): } \delta 8.01 - 7.93 (m, 4H), 7.63 - 7.58 (m, 1H), 7.57 - 7.52 (m, 1H), 7.51 - 7.40 (m, 4H), 6.95 (d, J = 2.1 Hz, 1H), 6.86 - 6.81 (m, 1H), 6.09 - 6.02 (m, 1H), 3.85 (s, 3H), 3.75 (dd, J = 17.6, 5.9 Hz, 1H), 3.48 - 3.32 (m, 5H).

\[ \text{C NMR (126 MHz, CDCl}_3\): } \delta 199.19, 196.39, 169.91, 164.73, 153.67, 144.79, 136.84, 136.35, 134.00, 133.24, 128.98, 128.72, 128.33, 128.32, 118.00, 115.61, 105.12, 76.05, 55.96, 44.08, 39.39, 26.63.

ESI-MS calcd. for C26H22O5H [M+H\(^+\): 415.1545, found: 415.1551.

**6,7-dimethoxy-3-(2-oxo-2-phenylethyl)isobenzofuran-1(3\(H\))one (3ai)**

The product was synthesized by standard condition 2 in 55% yield.

\[ \text{H NMR (500 MHz, CDCl}_3\): } \delta 7.88 - 7.83 (m, 2H), 7.53 - 7.45 (m, 1H), 7.41 - 7.34 (m, 2H), 7.12 - 7.01 (m, 2H), 5.94 (d, J = 6.5 Hz, 1H), 4.00 (s, 3H), 3.80 (s, 3H), 3.62 (dd, J = 17.5, 5.5 Hz, 1H), 3.25 (dd, J = 17.5, 7.5 Hz, 1H).

\[ \text{C NMR (126 MHz, CDCl}_3\): } \delta 196.28, 167.62, 152.79, 148.37, 142.71, 136.28, 133.83, 128.17, 119.53, 118.14, 117.31, 75.90, 62.38, 56.88, 44.15.

ESI-MS calcd. for C18H16O5Na [M+Na\(^+\): 335.0895, found: 335.0890.

**6-fluoro-7-methoxy-3-(2-oxo-2-phenylethyl)isobenzofuran-1(3\(H\))one (3aj)**

The product was synthesized by standard condition 2 in 86% yield.

\[ \text{H NMR (500 MHz, CDCl}_3\): } \delta 8.00 - 7.94 (m, 2H), 7.63 (t, J = 7.4 Hz, 1H), 7.51 (t, J = 7.8 Hz, 2H), 7.38 (dd, J = 12.0, 8.5 Hz, 1H), 7.16 (dd, J = 8.5, 3.4 Hz, 1H), 6.08 (d, J = 6.5 Hz, 1H), 4.22 (d, J = 2.5 Hz, 3H), 3.77 (dd, J = 17.5, 5.5 Hz, 1H), 3.40 (dd, J = 17.5, 7.5 Hz, 1H).

\[ \text{C NMR (126 MHz, CDCl}_3\): } \delta 196.11, 167.02, 155.24, 153.27, 146.87, 136.20, 134.06, 128.98, 128.27, 123.89 (d, J = 21.9 Hz), 118.43 (d, J = 3.9 Hz), 116.77 (d, J = 7.7 Hz), 75.99, 62.47 (d, J = 5.4 Hz), 43.91.
ESI-MS calcd. for C_{17}H_{13}FO_4H [M+H^+]: 301.0876, found: 301.0880.

$^1$F NMR (500 MHz, CDCl$_3$): -131.14.

5,6-dimethoxy-3-(2-oxo-2-phenylethyl)isobenzofuran-1(3H)-one (3ak)

The product was synthesized by standard condition 2 in 50% yield.

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.99 – 7.95 (m, 2H), 7.64 – 7.59 (m, 1H), 7.50 (t, $J = 7.8$ Hz, 2H), 7.29 (s, 1H), 7.01 (s, 1H), 6.10 – 6.01 (m, 1H), 3.94 (s, 6H), 3.82 (dd, $J = 17.7, 5.2$ Hz, 1H), 3.35 (dd, $J = 17.7, 8.0$ Hz, 1H).

$^{13}$C NMR (126 MHz, CDCl$_3$): $\delta$ 196.77, 170.65, 154.96, 150.77, 144.57, 136.28, 134.08, 129.01, 128.29, 117.84, 106.12, 104.57, 76.83, 56.55, 56.44, 44.10.

ESI-MS calcd. for C_{18}H_{16}O_5Na [M+Na^+]: 335.0895, found: 335.0890.

3-(2-oxo-2-phenylethyl)-4,5,6,7-tetrahydroisobenzofuran-1(3H)-one (3al)

The product was synthesized by standard condition 2 in 66% yield.

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.95 – 7.90 (m, 2H), 7.62 – 7.57 (m, 1H), 7.51 - 7.44 (m, 2H), 5.53 - 5.48 (m, 1H), 3.41 (dd, $J = 17.1, 6.7$ Hz, 1H), 3.22 (dd, $J = 17.1, 6.0$ Hz, 1H), 2.38 - 2.30 (m, 1H), 2.27 - 2.18 (m, 3H), 1.79 - 1.62 (m, 4H).

$^{13}$C NMR (126 MHz, CDCl$_3$): $\delta$ 196.05, 173.19, 163.69, 136.50, 133.91, 128.95, 128.58, 127.19, 78.96, 41.40, 23.72, 21.74, 21.61, 20.12.

ESI-MS calcd. for C_{18}H_{16}O_3Na [M+Na^+]: 279.0996, found: 279.1001.

5-(2-oxo-2-phenylethyl)-3,4-dihydro-2H-furo[3,4-b]pyran-7(5H)-one (3am)

The product was synthesized by standard condition 2 in 66% yield.

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.97 - 7.92 (m, 2H), 7.64 - 7.58 (m, 1H), 7.51 - 7.46 (m, 2H), 5.56 - 5.52 (m, 1H), 4.27 - 4.20 (m, 1H), 4.16 - 4.09 (m, 1H), 3.54 (dd, $J = 17.2, 5.9$ Hz, 1H), 3.24 (dd,
$J = 17.2, 7.0 \text{ Hz}, 1H), 2.43 \text{ (dt, } J = 18.4, 5.5 \text{ Hz}, 1H), 2.23 \text{ (dt, } J = 18.4, 6.6 \text{ Hz}, 1H), 2.02 - 1.95 \text{ (m, 2H).}$

$^{13}C \text{ NMR (126 MHz, CDCl}_3): \delta 196.12, 166.72, 141.49, 136.36, 134.02, 133.86, 129.00, 128.33, 76.77, 67.88, 42.29, 21.38, 20.25.$

ESI-MS calcd. for C$_{15}$H$_{14}$O$_4$Na [M+Na$^+$]: 281.0789, found: 281.0795.

7-(2-oxo-2-phenylethyl)-2,3-dihydro-[1,4]dioxino[2,3-e]isobenzofuran-9(7H)-one (3an)

The product was synthesized by standard condition 2 in 32% yield.

$^1H \text{ NMR (500 MHz, CDCl}_3): \delta 7.99 - 7.89 \text{ (m, 2H), 7.63 - 7.56 \text{ (m, 1H), 7.52 - 7.46 \text{ (m, 2H), 7.13 \text{ (d, } J = 8.0 \text{ Hz}, 1H), 6.94 \text{ (dd, } J = 8.0, 0.9 \text{ Hz, 1H), 6.06 - 6.01 \text{ (m, 1H), 4.47 - 4.42 \text{ (m, 2H), 4.34 - 4.29 \text{ (m, 2H), 3.71 \text{ (dd, } J = 17.5, 5.5 \text{ Hz, 1H), 3.34 \text{ (dd, } J = 17.5, 7.0 \text{ Hz, 1H).}}}$

$^{13}C \text{ NMR (126 MHz, CDCl}_3): \delta 196.31, 168.00, 144.10, 143.98, 142.60, 136.43, 133.95, 128.96, 128.31, 124.32, 114.71, 114.06, 76.41, 65.19, 64.26, 44.14.$

ESI-MS calcd. for C$_{18}$H$_{14}$O$_5$Na [M+Na$^+$]: 333.0738, found: 333.0733.

3,4-dimethyl-5-(2-oxo-2-phenylethyl)furan-2(5H)-one (3ao)

The product was synthesized by standard condition 2 in 72% yield.

$^1H \text{ NMR (600 MHz, CDCl}_3): \delta 7.99 - 7.82 \text{ (m, 2H), 7.67 - 7.56 \text{ (m, 1H), 7.54 - 7.42 \text{ (m, 2H), 5.45 \text{ (t, } J = 6.1 \text{ Hz, 1H), 3.33 \text{ (dd, } J = 17.4, 7.2 \text{ Hz, 1H), 3.25 \text{ (dd, } J = 17.4, 5.2 \text{ Hz, 1H), 1.99 \text{ (s, 3H), 1.83 \text{ (s, 3H).}}}$

$^{13}C \text{ NMR (151 MHz, CDCl}_3): \delta 195.99, 174.15, 159.03, 136.47, 133.89, 128.92, 128.35, 124.19, 79.22, 41.10, 12.37, 8.69.$

ESI-MS calcd. for C$_{14}$H$_{14}$O$_3$Na [M+Na$^+$]: 253.0840, found: 253.0833.

3-methyl-5-(2-oxo-2-phenylethyl)furan-2(5H)-one (3ap)

The product was synthesized by standard condition 2 in 46% yield.
\[ ^1H \text{ NMR} \ (500 \text{ MHz}, \text{CDCl}_3): \delta \ 8.00 - 7.89 \ (m, \ 2\text{H}), 7.67 - 7.55 \ (m, \ 1\text{H}), 7.52 - 7.43 \ (m, \ 2\text{H}), 7.30 \ (p, \ J = 1.6 \text{ Hz}, \ 1\text{H}), 5.54 - 5.42 \ (m, \ 1\text{H}), 3.66 \ (dd, \ J = 17.5, 6.0 \text{ Hz}, \ 1\text{H}), 3.11 \ (dd, \ J = 17.5, 8.3 \text{ Hz}, \ 1\text{H}), 1.93 \ (t, \ J = 1.8 \text{ Hz}, \ 3\text{H}). \]

\[ ^{13}C \text{ NMR} \ (126 \text{ MHz, CDCl}_3): \delta 196.20, 173.90, 148.91, 136.22, 134.02, 130.42, 128.99, 128.23, 77.33, 42.28. \]

ESI-MS calcd. for C\(_{13}\)H\(_{12}\)O\(_3\)Na [M+Na\(^+\)]: 239.0683, found: 239.0670.

3-benzyl-5-(2-oxo-2-phenylethyl)furan-2(5\text{H})-one (3aq)

The product was synthesized by standard condition 2 in 27% yield.

\[ ^1H \text{ NMR} \ (500 \text{ MHz, CDCl}_3): \delta 7.93 - 7.87 \ (m, \ 2\text{H}), 7.65 - 7.56 \ (m, \ 1\text{H}), 7.51 - 7.44 \ (m, \ 2\text{H}), 7.35 - 7.30 \ (m, \ 2\text{H}), 7.28 - 7.25 \ (m, \ 1\text{H}), 7.25 - 7.21 \ (m, \ 2\text{H}), 7.10 \ (q, \ J = 1.5 \text{ Hz}, \ 1\text{H}), 5.54 - 5.45 \ (m, \ 1\text{H}), 3.69 - 3.57 \ (m, \ 3\text{H}), 3.09 \ (dd, \ J = 17.5, 8.5 \text{ Hz}, \ 1\text{H}). \]

\[ ^{13}C \text{ NMR} \ (126 \text{ MHz, CDCl}_3): \delta 196.01, 173.04, 149.30, 137.29, 136.10, 134.79, 134.05, 129.08, 128.98, 128.94, 128.23, 127.02, 77.62, 42.14, 31.96. \]

ESI-MS calcd. for C\(_{19}\)H\(_{16}\)O\(_3\)Na [M+Na\(^+\)]: 315.0996, found: 315.0992.

3-((5\text{R})-5-((3\text{R},5\text{R},6\text{S},8\text{S},10\text{R},13\text{R},14\text{S})-3,6-bis((tert-butyldimethylsilyl)oxy)-10,13-dimethylhexadecahydro-1H-cyclopenta[a]phenanthren-17-yl)-2-oxohexyl)-7-methylisobenzofuran-1(3\text{H})-one (3pa)

\[ ^1H \text{ NMR} \ (500 \text{ MHz, CDCl}_3): \delta 7.50 \ (t, \ J = 7.5 \text{ Hz}, \ 1\text{H}), 7.27 \ (d, \ J = 7.5 \text{ Hz}, \ 1\text{H}), 7.23 \ (d, \ J = 7.5 \text{ Hz}, \ 1\text{H}), 5.87 \ (t, \ J = 6.5 \text{ Hz}, \ 1\text{H}), 4.07 - 3.92 \ (m, \ 1\text{H}), 3.57 - 3.47 \ (m, \ 1\text{H}), 3.11 - 3.01 \ (m, \ 1\text{H}), 2.90 - 2.80 \ (m, \ 1\text{H}), 2.68 \ (s, \ 3\text{H}), 2.59 - 2.33 \ (m, \ 2\text{H}), 1.97 - 1.68 \ (m, \ 4\text{H}), 1.65 - 1.51 \ (m, \ 2\text{H}), 1.53 - 1.46 \ (m, \ 1\text{H}), 1.46-1.26 \ (m, \ 10\text{H}), 1.21 - 0.99 \ (m, \ 8\text{H}), 0.90 - 0.86 \ (m, \ 24\text{H}), 0.62 \ (s, \ 3\text{H}), 0.07 - 0.01 \ (m, \ 12\text{H}). \]

\[ ^{13}C \text{ NMR} \ (126 \text{ MHz, CDCl}_3): \delta 207.55, 170.35, 150.19, 140.00, 134.07, 131.11, 123.43, 119.64, 76.03, 73.08, 68.76, 56.26, 56.07, 49.70, 47.63, 47.59, 42.99, 40.70, 40.10, 39.73, 36.10, 36.06, 35.56, 35.36, 35.33, 35.02, 31.18, 29.95, 29.63, 29.57, 28.29, 26.14, 26.02, 24.33, 23.66, 20.91, 18.55, 18.25, 17.48, 12.19, -4.36, -4.49, -4.62, -4.64. \]

ESI-MS calcd. for C\(_{46}\)H\(_{77}\)O\(_5\)Si\(_2\) [M+H\(^+\)]: 765.5309, found: 765.5314.
2-(7-ethoxy-1-oxo-3-(2-oxo-2-phenylethyl)-1,3-dihydroisobenzofuran-5-yl)-N-((S)-3-methyl-1-(2-(piperidin-1-yl)phenyl)butyl)acetamide (3ar)

\[
\text{dr} \sim 1:1
\]

\(^1\)H NMR (500 MHz, CDCl\(_3\)): δ 7.96 - 7.90 (m, 2H), 7.64 - 7.56 (m, 1H), 7.52 - 7.43 (m, 2H), 7.23 - 7.10 (m, 3H), 7.09 - 7.02 (m, 1H), 6.94 - 6.80 (m, 2H), 6.00 (t, \(J = 6.5\) Hz, 1H), 5.36 - 5.26 (m, 1H), 4.22 - 4.04 (m, 2H), 3.70 - 3.63 (m, 1H), 3.62 - 3.52 (m, 2H), 3.35 - 3.26 (m, 1H), 2.92 (s, 2H), 2.65 (s, 2H), 1.78 - 1.69 (m, 2H), 1.65 - 1.58 (m, 4H), 1.57 - 1.48 (m, 2H), 1.48 - 1.38 (m, 4H), 0.98 - 0.86 (m, 6H).

\(^{13}\)C NMR (126 MHz, CDCl\(_3\)): δ 196.14, 168.50, 167.83, 158.12, 153.10, 145.00, 138.53, 136.33, 133.96, 128.23, 128.32, 125.53, 123.06, 114.81, 112.98, 112.45, 75.78, 64.74, 55.30, 50.28, 46.63, 44.56, 43.92, 29.84, 26.83, 25.48, 24.15, 22.88, 22.65, 14.56, 14.53.

ESI-MS calcd. for C\(_{36}\)H\(_{43}\)N\(_2\)O\(_5\) [M+H\(^+\)]: 583.3172, found: 583.3167.

2-(3-((5R)-5-((3R,5R,6S,10R,13R,14S)-3,6-bis((tert-butyldimethylsilyl)oxy)-10,13-dimethylhexadecahydro-1H-cyclopenta[a]phenanthren-17-yl)-2-oxohexyl)-7-ethoxy-1-oxo-1,3-dihydroisobenzofuran-5-yl)-N-((S)-3-methyl-1-(2-(piperidin-1-yl)phenyl)butyl)acetamide (4)

\[
\text{dr} \sim 1:1
\]

\(^1\)H NMR (500 MHz, CDCl\(_3\)): δ 7.26 - 7.19 (m, 2H), 7.16 - 7.05 (m, 2H), 7.05 - 6.97 (m, 1H), 6.89 - 6.76 (m, 2H), 5.81 - 5.74 (m, 1H), 5.42 - 5.33 (m, 1H), 4.20 - 4.04 (m, 2H), 3.99 (dt, \(J = 11.6, 4.2\) Hz, 1H), 3.63 - 3.49 (m, 3H), 3.03 - 2.91 (m, 3H), 2.85 - 2.72 (m, 1H), 2.72 - 2.59 (m, 2H), 2.55 - 2.32 (m, 2H), 1.97 - 1.81 (m, 3H), 1.81 - 1.52 (m, 15H), 1.51 - 0.95 (m, 29H), 0.96 - 0.81 (m, 38H), 0.66 - 0.62 (m, 3H), 0.08 - 0.03 (m, 12H).

\(^{13}\)C NMR (126 MHz, CDCl\(_3\)): δ 206.75, 167.63, 167.08, 157.48, 152.28, 151.97, 144.32, 138.04, 138.00, 127.57, 127.43, 124.76, 124.72, 122.57, 113.78, 113.74, 112.38, 112.26, 111.76, 74.92,
2-(7-ethoxy-3-((S)-3-(4-isobutylphenyl)-2-oxobutyl)-1-oxo-1,3-dihydroisobenzofuran-5-yl)-N-((S)-3-methyl-1-(2-(piperidin-1-yl)phenyl)butyl)acetamide (5)

\[ \text{ESI-MS calcd. for } 
\text{C}_{65} \text{H}_{104} \text{N}_{2} \text{O}_{7} \text{Si}_{2} \text{Na [M+Na}^{+} \text{]}: 1103.7279, \text{found:1103.7283.} \]

\[ \text{H NMR} (500 \text{ MHz, CDCl}_3): \delta \text{ 7.26 - 7.19 (m, 2H), 7.17 - 6.96 (m, 7H), 6.86 - 6.60 (m, 2H), 5.78 - 5.66 (m, 1H), 5.45 - 5.28 (m, 1H), 4.18 - 4.00 (m, 2H), 3.82 - 3.67 (m, 1H), 3.63 - 3.43 (m, 2H), 3.06 - 2.79 (m, 3H), 2.79 - 2.57 (m, 3H), 2.51 - 2.37 (m, 2H), 1.90 - 1.69 (m, 4H), 1.68 - 1.50 (m, 6H), 1.48 - 1.37 (m, 8H), 0.97 - 0.86 (m, 13H).} \]

\[ \text{C NMR} (126 \text{ MHz, CDCl}_3): \delta \text{ 206.98, 168.26, 157.99, 152.85, 144.87, 141.16, 138.70, 136.82, 129.97, 128.12, 127.66, 125.26, 123.07, 114.46, 114.18, 112.82, 112.21, 76.06, 75.41, 64.63, 55.33, 53.70, 53.11, 50.22, 46.82, 45.88, 45.42, 45.09, 44.45, 30.21, 26.89, 25.45, 24.21, 22.87, 22.49, 17.15, 14.49.} \]

\[ \text{ESI-MS calcd. for } 
\text{C}_{42} \text{H}_{54} \text{N}_{2} \text{O}_{5} \text{[M+Na}^{+} \text{]}: 689.3930, \text{found: 689.3923.} \]

7-((2,3-dimethylphenyl)(methyl)amino)-3-((S)-3-(4-isobutylphenyl)-2-oxobutyl)isobenzofuran-1(3H)-one (6)

\[ \text{H NMR} (500 \text{ MHz, CDCl}_3): \delta \text{ 7.25 - 7.16 (m, 1H), 7.14 - 7.07 (m, 5H), 7.07 - 7.03 (m, 1H), 6.70 - 6.55 (m, 1H), 6.49 - 6.34 (m, 1H), 5.82 - 5.67 (m, 1H), 3.85 - 3.71 (m, 1H), 3.51 - 3.40 (m, 3H), 3.07 - 2.87 (m, 1H), 2.85 - 2.64 (m, 1H), 2.51 - 2.39 (m, 2H), 2.29 (s, 3H), 2.04 (s, 3H), 1.91 - 1.79 (m, 1H), 1.46 - 1.37 (m, 3H), 0.91 - 0.86 (m, 6H).} \]

\[ \text{C NMR} (126 \text{ MHz, CDCl}_3): \delta \text{ 207.29, 168.25, 152.74, 150.79, 147.46, 141.11, 138.79, 136.96, 134.66, 134.13, 129.95, 127.88, 127.75, 126.55, 123.45, 118.29, 112.24, 111.62, 75.66, 75.13, 53.68, 53.23, 46.45, 45.94, 45.12, 43.76, 30.26, 22.50, 20.64, 17.22, 14.40.} \]
ESI-MS calcd. for C$_{31}$H$_{35}$NO$_3$Na [M+Na$^+$]: 492.2514, found: 492.2520.
3ma

3na
Reference