Marine Furanocembranoids-Inspired Macrocycles Enabled by Pd-catalyzed Unactivated C(sp$^3$)-H Olefination Mediated by Donor/Donor Carbenes

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Supplementary Methods

General comments

NMR spectra were recorded at room temperature on the following spectrometers: Bruker Avance III 400 Spectrometer (400 MHz) and Bruker Avance III 500 (Cryo) Spectrometer (500 MHz). Chemical shifts are given in ppm and coupling constants in Hz. \(^1\)H spectra were calibrated in relation to the reference measurement of TMS (0.00 ppm). \(^13\)C spectra were calibrated in relation to deuterated solvents. The following abbreviations were used for \(^1\)H NMR spectra to indicate the signal multiplicity: s (singlet), d (doublet), t (triplet), q (quartet) and m (multiplet) as well as combinations of them. For HRMS data, the ESI-positive method was applied on the Agilent G6520 Q-TOF. Chemicals were purchased from commercial suppliers. Unless stated otherwise, all the substrates and solvents were purified and dried according to standard methods prior to use.

1. General Procedure for the Synthesis of the starting materials

1.1 Synthesis of 1-Bromo-2-tert-butylbenzenes

\[
\text{1a} \quad \text{1b} \quad \text{1c} \quad \text{1d} \quad \text{1e} \\
\text{1f} \quad \text{1g} \quad \text{1h} \quad \text{1i} \quad \text{i}j
\]

1a was prepared by following method A\(^1\). 1b, 1c, 1d, 1e, 1f, and 1i were prepared by following method B\(^2\). 1g and 1i have commercial sources. 1h were prepared by following method C\(^3\).
**Method A:**

2-tert-Butylaniline (2.50 g, 16.7 mmol) was added to 13 mL 48% w/w hydrobromic acid. The thus formed pale pink suspension was cooled to -56 ℃. Then, sodium nitrite (1.68 g, 24.4 mmol) was added portion-wise. After stirring for 1 hour, 20 mL Et₂O was added slowly. The temperature was adjusted to -8 ℃ over 2 hours and kept at -8 ℃ for an additional 2 hours. Next, the system was cooled to -40 ℃ again. 3.06 g Na₂CO₃ was added. The reaction was then warming up slowly to room temperature over 3 hours and stirred overnight. The reaction was diluted with water and extracted with EtOAc. The organic layer was washed with water, NaHCO₃ (aq.), brine, dried over Na₂SO₄, concentrated in vacuo, and purified by silica gel column chromatography with petroleum ether to afford 1-bromo-2-(tert-butyl)benzene as a colorless oil. (1.49 g, 42% yield)

**Method B:**

Under nitrogen atmosphere, TiCl₄ (1 M in CH₂Cl₂, 2.2 equiv.) was added to anhydrous CH₂Cl₂ (0.3 M) and cooled to -40 ℃. Then, a solution of Me₂Zn (1 M in hexane, 2.2 equiv.) was added dropwise. After stirring for 15 minutes, a solution of aryl ketone in anhydrous CH₂Cl₂ (1 M) was added dropwise. The reaction was warm to 0 ℃ slowly (over 3 hours), stirred at 0 ℃ overnight, and poured into ice water. The aqueous phase was extracted with CH₂Cl₂. The combined organic layers were washed with NaHCO₃ (aq.), brine, dried over Na₂SO₄, filtered and concentrated in vacuo. (If necessary, the crude product was dissolved in CH₂Cl₂, treated with 3-chloroperoxybenzoic acid (m-CPMA) and stirred at room temperature to remove the
aryl propene, a by-product of the reaction, which is not easy to be separated from the desired product by silica gel column chromatography). The crude product was purified by silica gel column chromatography with petroleum ether/ethyl acetate to afford the corresponding aryl bromide. (45-67% yield)

**Method C:**

![Chemical reaction diagram]

To a stirred solution of HMDS (4.25 mL, 20.0 mmol) in THF (36.8 mL) was added n-BuLi (1.60 M in hexane, 12.5 mL, 20.0 mmol) at 0 °C. After the mixture was stirred for 1.5 h, a solution of methyl 2-(2-bromophenyl)acetate (1.2 g, 5.0 mmol) in THF (25.0 mL) was added, and the mixture was stirred for 2 h at room temperature. Then CH₃I (1.20 mL, 20.0 mmol) was added at 0 °C, and the mixture was stirred for 12 h at room temperature. Then the reaction was quenched by addition of 1 M HCl at 0 °C. The crude mixture was extracted with EtOAc (x4) and the combined organic extracts were washed with brine, dried (Na₂SO₄) and concentrated in vacuo. The crude product was purified by silica gel column chromatography with petroleum ether/ethyl acetate to afford the corresponding product as a colorless oil. (1g, 78% yield)

**1.2 Synthesis of complex 1-Bromo-2-tert-butylbenzenes from drug molecules (1k ~ 1p)**

![Chemical reaction diagram]

3-bromo-4-(tert-butyl)aniline (70 mg, 0.3 mmol), and the corresponding complex acids (0.36 mmol), and HATU (171 mg, 0.45 mmol), DIPEA (156 mg, 1.2 mmol) were in 5 mL DMF. The mixture was stirred at rt for 12 h. The reaction was diluted with water and extracted with EtOAc. The organic layer was washed with brine, dried over
Na₂SO₄, concentrated in vacuo, and purified by silica gel column chromatography with PE and EA (PE = petroleumether, EA = ethyl acetate) to afford corresponding products.

**1.3 Synthesis of Ene-Yne-Ketones**

The ene-yne-ketones used in this study were prepared by two steps starting from terminal alkynes and 1,3-dicarbonyl compounds.

\[
\begin{align*}
\text{R}^1\equiv & \xrightarrow{\text{nBuLi, DMF}} \text{R}^1\equiv \text{CHO} \quad \text{AcOH, MgSO}_4 \\
& \xrightarrow{\text{THF, rt, 1 h}} \text{AcOH, MgSO}_4
\end{align*}
\]

The alkyne (10 mmol) was dissolved in dry THF (15 mL) and the solution was cooled to -40 °C under nitrogen, n-butyllithium (1.6 M in hexanes, 6.8 mL, 11 mmol) was added dropwise over 2 minutes while maintaining the temperature between -35 and -40 °C. After completion of the addition, anhydrous DMF (1.55 mL, 20 mmol) was added in one portion and the cold bath was removed. The reaction mixture was warm to room temperature and aged for 30 minutes. The THF solution was poured into a vigorously stirred biphasic solution prepared from aqueous solution of KH₂PO₄ (50 mL, 30 mmol) and Et₂O (30 mL) cooled over ice to about 5 °C. Layers were separated and the organic extract was washed with water (2 x 30 mL). Combined aqueous layers were back extracted with Et₂O (30 mL). Combined organic layers were dried over Na₂SO₄ and filtered. Then solvent was removed in vacuo carefully under 0 °C to leave a crude acetylenic aldehyde.

The crude product was then dissolved in THF (8 mL), and 1,3-dicarbonyl compounds (10 mmol) was added into the solution. Then AcOH (2 mmol) and MgSO₄ (2 mmol) was added to the reaction mixture. The mixture was stirred at room temperature for about one hour. When the reaction was completed as monitored by TLC, filtration through celite and removal of the solvent by rotary evaporation gave the crude product. The ene-yne-ketones was purified by chromatography on silica gel with the appropriate
mixture of PE and EA (PE = petroleum ether, EA = ethyl acetate) with about 50-70% yields (two steps). 4

1.4 Synthesis of Allenes (4a ~ 4h)

To an ice-cooled (0°C) solution of s1 (7.89 mmol) and triethylamine (1.1 ml, 7.89 mmol) in 23 ml of dry dichloromethane stirred under argon was added dropwise a solution of 2-phenylbutanoyl chloride (2.02 g, 7.89 mmol) in 8 ml of dry dichloromethane. The resulting bright yellow solution was stirred for 2 h. After removal of half of the solvent, the residue was diluted with diethyl ether to precipitate triphenylphosphine oxide. After filtration, silica gel was added to adsorb the reaction products and the solvent was evaporated in vacuo. Flash Silica column chromatography (1:10 EtOAc/hexanes) gave the corresponding products (21-50% yield).

2. Procedure for the Gram-Scale reaction for 3ba and the transformation

A screw-capped vial was charged with 2-bromo-1-(tert-butyl)-4-methylbenzene 1b (2.0 mmol, 454 mg, 1.0 equiv.), the respective 3-(4,4-dimethylpent-2-yn-1-ylidene)pentane-2,4-dione 2a (4.0 mmol, 770 mg, 2.0 equiv.), [Pd(Cl(allyl))]2 (5 mol%), tBuXphos (30 mol%), NaOAc (3.0 equiv.), DMF (5.0 mL). The reaction mixture was stirred at 100 °C under N2 for 4 h, and then quenched with saturated aqueous NaCl and
extracted with ethyl acetate. After drying over Na$_2$SO$_4$ for 30 min, the combined organic phase was concentrated, and the residue was purified by silica gel column chromatography with petroleum ether/ethyl acetate to afford the product 3ba as a yellow oil. (560 mg, 83% yield)

The product 3ba (0.1 mmol, 34 mg, 1.0 equiv.) was dissolved in DCM (2.0 mL), and m-CPBA (0.2 mmol, 35 mg, 2.0 equiv.) was added into the solution. The mixture was stirred at rt. When the reaction was completed as monitored by TLC, filtration through celite and removal of the solvent by rotary evaporation gave the crude product. The residue was purified by chromatography on silica gel with the appropriate mixture of PE and EA (PE = petroleumether, EA = ethyl acetate) to afford the product 3ba-1 as a colorless oil. (23.5 mg, 66% yield)

3. The preparation of the macrolactams

3.1 Synthesis of 6a

![Chemical structure](image)

Synthesis of 3qa:
Please refer to 3ba

From 3qa to S1:

To a solution of 3qa (50 mg, 0.14 mmol) in DCM (2 mL) were added EDCI (51.5 mg, 0.27 mmol), HOBt (36.6 mg, 0.27 mmol), Boc-Phe-OH (42.4 mg, 0.16 mmol). The stirring of the solution was continued at r.t. for 18 h. Then the solution was washed with water, and the organic phase was evaporated under reduced pressure and the residue was purified by FCC to get the desired product S1 (54.9 mg, yield: 66%).

From S1 to S2:

The S1 (54.9 mg, 0.09 mmol) was dissolved in DCM (2 mL) and TFA (0.2 mL) were added slowly. The stirring of the solution was continued at r.t. for 4 h. Then the solution was evaporating under reduced pressure. And the residue was used in the next step without further purification.

The residue was dissolved in DCM (5 mL). And EDCI (51.5 mg, 0.27 mmol), HOBt (36.6 mg, 0.27 mmol), Boc-NH-(CH₂)₁₁-COOH (56.7 mg, 0.18 mmol) were added. The stirring of the solution was continued at r.t. for 24 h. Then the solution was washed with water, and the organic phase was evaporated under reduced pressure and the residue was purified by FCC to get the desired product S2 (54.2 mg, 74% yield in two steps from S1).

From S2 to 6a:

The S2 (54.2 mg, 0.07 mmol) was dissolved in DCM (2 mL) and TFA (0.2 mL) were added slowly. The stirring of the solution was continued at r.t. for 4 h. Then the solution was evaporating under reduced pressure. And the residue was used in the next step without further purification.

The residue was dissolved in MeOH (2 mL) and the solution of NaOH (100 mg) in H₂O were added slowly. The stirring of the solution was continued at 50 °C for 4 h. Then the solution was acidified by HCl, followed by evaporating under reduced
pressure. And the residue was used in the next step without further purification.

The residue was dissolved in DCM (40 mL). And EDCI (76.4 mg, 0.4 mmol), HOBt (54.0 mg, 0.4 mmol) were added. The stirring of the solution was continued at r.t. for 24 h. Then the solution was washed with water, and the organic phase was evaporated under reduced pressure and the residue was purified by FCC to get the desired product 6a as a white solid (11.8 mg, 27.2% yield in three steps from S2).

3.2 Synthesis of 6b

This compound was prepared form 3qa and Boc-Ala-OH using the procedure described for 6b and was isolated as a white solid, 2.5 mg, 2.9% yield in six steps from 3qa.
3.3 Synthesis of 6c

This compound was prepared from 3qa and Boc-Val-OH using the procedure described for 6c and was isolated as a white solid, 4.6 mg, 5.5% yield in six steps from 3qa.

3.4 Synthesis of 6d
Synthesis of 6d:

This compound was prepared from 3qa and Boc-Pro-OH using the procedure described for 6d and was isolated as a white solid, 9.1 mg, 10.9% yield in six steps from 3qa.

3.5 Synthesis of 6e

Synthesis of 6e:

This compound was prepared from S1 and Boc-Val-OH using the procedure described for 6e and was isolated as a white solid, 4.1 mg, 6.1% yield in seven steps from S1.
3.6 Synthesis of 6f

Synthesis of 6f:

This compound was prepared from S1 and Boc-Met-OH using the procedure described for 6f and was isolated as a white solid, 2.8 mg, 3.6% yield in seven steps from S1.

3.7 Synthesis of 6g

From S1 to S13:

To a solution of S1 (100 mg, 0.27 mmol) in DCM (2 mL) were added EDCI (103 mg, 0.54 mmol), HOBt (73.2 mg, 0.54 mmol), Fmoc-NH-(CH2)11-COOH (141.6 mg, 0.32 mmol). The stirring of the solution was continued at r.t. for 18 h. Then the solution was washed with water, and the organic phase was evaporated under reduced pressure and the residue was purified by FCC to get the desired product S13 (131.2 mg, yield:
64\%).

From **S13** to **6g**:

The **S13** (100 mg) was dissolved in MeOH (2 mL) and the solution of NaOH (100 mg) in H\textsubscript{2}O were added slowly. The stirring of the solution was continued at 50 °C for 4 h. Then the solution was acidified by HCl, followed by evaporating under reduced pressure. And the residue was used in the next step without further purification.

The residue was dissolved in DCM (40 mL). And EDCI (95.5 mg, 0.5 mmol), HOBt (67.5 mg, 0.5 mmol) were added. The stirring of the solution was continued at r.t. for 24 h. Then the solution was washed with water, and the organic phase was evaporated under reduced pressure and the residue was purified by FCC to get the desired product **6g** (17.8 mg, yield: 27\%).

3.8 Synthesis of **6h**

From **S13** to **S14**:

To a solution of **S13** in DCM were added DBU (10 eq) slowly and stirring of the solution was continued at r.t. for 1 h. Then the solution was washed with water and extracted by EtOAc. Then the organic phase was evaporated under reduced pressure and the residue was purified by FCC (DCM/EtOH = 2:1).

The product purified was dissolved in DCM. And EDCI (3 eq), HOBt (3 eq) were added followed by \(((9\text{H-fluoren-9-yl})\text{methoxy})\text{carbonyl})\text{valine. The stirring of the solution was continued at r.t. for 18 h. Then the solution was washed with water, and
the organic phase was evaporated under reduced pressure and the residue was purified by FCC (DCM/MeOH = 1% - 5%) to get the desired product S14.

From S14 to 6h:

The S14 was dissolved in MeOH and the solution of 10% LiOH in H2O were added. The stirring of the solution was continued at 50 °C for 4 h. Then the pH of solution was adjusted to 7-8. Then the solvent was evaporated under reduced pressure. And the residue was used in the next step without further purification.

The residue was dissolved in DCM. And EDCI (3 eq), HOBt (3 eq) were added. The stirring of the solution was continued at r.t. for 24 h. Then the solution was washed with water and extracted by EtOAc. Then the organic phase was evaporated under reduced pressure and the residue was purified by FCC to get the desired product 6h.

4. The DFT calculated details

Density functional theory (DFT) calculations were carried out at the M06 level of theory. All the molecular geometries were fully optimized without constraints in DMF (n, n-dimethylformamide) solvent by employing the SMD model. Frequency calculations at the same level of theory have also been performed to identify all the stationary points as minima (zero imaginary frequencies) or transition states (one imaginary frequency) and to provide free energies at 298.15K, which include entropic contributions. Transition states were located using the Berny algorithm. Intrinsic reaction coordinates (IRC) analysis were calculated at the same level of theory as geometry optimization to confirm these transition states indeed connect two relevant minima. The Stuttgart-Dresden-Bonn basis set was used to describe Pd and P atoms, with polarization functions for Pd (ζf = 1.472), and P (ζd = 0.387) being added. The 6-31G**
basis set was used for the other atoms. All calculations were performed using Gaussian 09 package. \(^\text{17}\)

**Supplementary Figure 1.** Energy profiles calculated for the path A' which is similar with Path A starting from IM4B. The solvation-corrected relative free energies and electronic energies (in parentheses) are given in kcal/mol.

**Supplementary Figure 2.** Energy profile calculated for the \(\beta\)-Hydride elimination from a highly unstable isomeric agostic species (cf. IM8B in Figure 3(c) in the main text). The solvation-corrected relative free energies and electronic energies (in parentheses) are given in kcal/mol.
Supplementary Figure 3. Energy profiles calculated (using the experimentally employed ligand) for an alternative pathway considering an alkyne activation cyclization immediately after oxidative addition. The results here indicate that such an alkyne activation cyclization is reversible in view of the inaccessibly high lying TS_{5,6-b-r-1} and TS_{5,6-b-r-2}. The solvation-corrected relative free energies and electronic energies (in parentheses) are given in kcal/mol.

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* through 6-membered ring

* through 4-membered ring
Supplementary Figure 4. Energy profile calculated for alkyne activation cyclization using the experimentally employed ligand. The barrier is compatible with that obtained by using the model ligand (cf. Figure 3(b) in the main text), but is much smaller than the corresponding step shown in Figure 3 (from IM1-r to TS_{2,3-b-r}). The solvation-corrected relative free energies and electronic energies (in parentheses) are given in kcal/mol.
Supplementary Table 1 Cytotoxicity (CC$_{50}$, µM) and anti-inflammatory effects (IC$_{50}$, µM) of selected compounds.

| Compds | IC$_{50}$(µM) | CC$_{50}$(µM) |
|--------|---------------|---------------|
|        | TNF-$\alpha$ | IL-6 | IL-1$\beta$ |        |
| 6a     | >250          | 53.59 | 12.84 | 152.2 |
| 6b     | 2.15          | 7.28  | 3.40  | 39.67 |
| 6c     | 11.5          | 10.52 | 4.38  | 154   |
| 6d     | 107.1         | 195.7 | 17.55 | 27.67 |
| 6e     | >250          | 80.78 | 3.05  | >250  |
| 6f     | 10.03         | 29.46 | 8.61  | 214.5 |
| 6g     | 0.45          | 1.59  | 0.59  | >250  |
| 6h     | 56.43         | 0.95  | 0.0041| 56.43 |
| DEX    | 0.008         | 10.54 | 0.0004| 152.2 |


1-bromo-2-(tert-butyl)benzene (1a): Colorless oil.

\[ ^1\text{H NMR} \ (400 \text{ MHz, CDCl}_3) \delta 7.58 \ (d, J = 7.9 \text{ Hz, 1H}), 7.43 \ (d, J = 8.1 \text{ Hz, 1H}), 7.23 \ (t, J = 7.6 \text{ Hz, 1H}), 7.01 \ (t, J = 7.6 \text{ Hz, 1H}), 1.51 \ (s, 9H). \]

2-bromo-1-(tert-butyl)-4-methylbenzene (1b): Colorless oil.

\[ ^1\text{H NMR} \ (400 \text{ MHz, CDCl}_3) \delta 7.45 \ (s, 1H), 7.34 \ (d, J = 8.0 \text{ Hz, 1H}), 7.06 \ (d, J = 8.0 \text{ Hz, 1H}), 2.30 \ (s, 3H), 1.51 \ (s, 9H). \]

2-bromo-1-(tert-butyl)-4-methoxybenzene (1c): Colorless oil.

\[ ^1\text{H NMR} \ (400 \text{ MHz, CDCl}_3) \delta 7.35 \ (d, J = 8.8 \text{ Hz, 1H}), 7.17 \ (d, J = 2.7 \text{ Hz, 1H}), 6.79 \ (dd, J = 8.8, 2.7 \text{ Hz, 1H}), 3.78 \ (s, 3H), 1.49 \ (s, 9H). \]

1-bromo-2-(tert-butyl)-4-methoxybenzene (1d): Colorless oil.

\[ ^1\text{H NMR} \ (500 \text{ MHz, CDCl}_3) \delta 7.47 \ (d, J = 8.6 \text{ Hz, 1H}), 7.01 \ (d, J = 3.1 \text{ Hz, 1H}), 6.59 \ (dd, J = 8.7, 3.1 \text{ Hz, 1H}), 3.78 \ (s, 3H), 1.49 \ (s, 9H). \]
2-bromo-1-(tert-butyl)-4-fluorobenzene (1e): Colorless oil.

\[ ^1\text{H NMR} \ (400 \text{ MHz, CDCl}_3) \ \delta \ 7.40 \ (dd, J = 9.0, 6.3 \text{ Hz, 1H}), \ 7.34 \ (dd, J = 8.3, 2.7 \text{ Hz, 1H}), \ 6.96 \ (ddd, J = 9.0, 7.8, 2.7 \text{ Hz, 1H}), \ 1.50 \ (s, 9\text{H}). \]

2-bromo-3-(tert-butyl)naphthalene (1f): Colorless oil.

\[ ^1\text{H NMR} \ (400 \text{ MHz, CDCl}_3) \ \delta \ 8.55 \ (dt, J = 8.7, 0.9 \text{ Hz, 1H}), \ 7.79 \ (dd, J = 10.0, 8.2 \text{ Hz, 2H}), \ 7.67 \ (d, J = 8.8 \text{ Hz, 1H}), \ 7.59 \ (ddd, J = 8.5, 6.8, 1.4 \text{ Hz, 1H}), \ 7.50 \ (ddd, J = 7.9, 6.8, 1.2 \text{ Hz, 1H}), \ 1.69 \ (s, 9\text{H}). \]

2-(2-bromophenyl)-2-methylpropanenitrile (1g): Yellow oil.

\[ ^1\text{H NMR} \ (300 \text{ MHz, CDCl}_3) \ \delta \ 7.67 \ (dd, J_1 = 8.1 \text{ Hz, } J_2 = 1.5 \text{ Hz, 1H}), \ 7.48 \ (dd, J_1 = 7.8 \text{ Hz, } J_2 = 1.5 \text{ Hz, 1H}), \ 7.35 \ (td, J_1 = 7.5 \text{ Hz, } J_2 = 1.2 \text{ Hz, 1H}), \ 7.19 \ (td, J_1 = 7.8 \text{ Hz, } J_2 = 1.8 \text{ Hz, 1H}), \ 1.90 \ (s, 6\text{H}). \]

Methyl 2-(2-bromophenyl)-2-methylpropanoate (1h): Colorless oil.

\[ ^1\text{H NMR} \ (500 \text{ MHz, CDCl}_3) \ \delta \ 7.56 \ (dd, J = 7.9, 1.4 \text{ Hz, 1H}), \ 7.42 \ (dd, J = 7.8, 1.7 \text{ Hz, 1H}), \ 7.32 \ (td, J = 7.6, 1.4 \text{ Hz, 1H}), \ 7.12 \ (td, J = 7.6, 1.7 \text{ Hz, 1H}), \ 3.68 \ (s, 3\text{H}), \ 1.64 \ (s, 6\text{H}). \]

1-bromo-2-(2-phenylpropan-2-yl)benzene (1i): Colorless oil.
\[ ^1H \text{ NMR} (400 \text{ MHz, CDCl}_3) \delta 7.70 \text{ (dd, } J = 7.9, 1.6 \text{ Hz, 1H}), 7.54 \text{ (dd, } J = 7.9, 1.4 \text{ Hz, 1H}), 7.39 \text{ (td, } J = 7.6, 1.4 \text{ Hz, 1H}), 7.29 \text{ (td, } J = 7.1, 1.3 \text{ Hz, 2H}), 7.24 - 7.19 \text{ (m, 1H), 7.19 - 7.10 (m, 3H), 1.80 (s, 6H).} \]

3-bromo-4-(tert-butyl)aniline (ij): Colorless oil.

\[ ^1H \text{ NMR} (400 \text{ MHz, CDCl}_3) \delta 7.16 \text{ (d, } J = 8.6 \text{ Hz, 1H}), 6.97 \text{ (d, } J = 3.0 \text{ Hz, 1H), 6.59 \text{ (dd, } J = 8.4, 2.8 \text{ Hz, 1H), 1.43 (s, 9H).} \]

(S)-N-(3-bromo-4-(tert-butyl)phenyl)-2-ethoxy-4-(2-((3-methyl-1-(2-(piperidin-1-yl)phenyl)butyl)amino)-2-oxoethyl)benzamide (1k): White solid.

\[ ^1H \text{ NMR} (500 \text{ MHz, CDCl}_3) \delta 10.00 \text{ (s, 1H), 8.18 \text{ (d, } J = 8.0 \text{ Hz, 1H), 7.95 \text{ (d, } J = 2.4 \text{ Hz, 1H), 7.51 \text{ (dd, } J = 8.7, 2.4 \text{ Hz, 1H), 7.39 \text{ (d, } J = 8.7 \text{ Hz, 1H), 7.24 - 7.15 \text{ (m, 2H), 7.11 \text{ (dd, } J = 7.6, 1.5 \text{ Hz, 1H), 7.04 \text{ (dd, } J = 7.9, 6.4, 2.0 \text{ Hz, 1H), 7.00 - 6.88 \text{ (m, 3H), 5.38 \text{ (td, } J = 8.7, 6.4 \text{ Hz, 1H), 4.22 - 4.03 \text{ (m, 2H), 3.54 \text{ (s, 2H), 2.94 \text{ (t, } J = 9.0 \text{ Hz, 2H), 2.61 \text{ (t, } J = 9.1 \text{ Hz, 2H), 1.72 \text{ (q, } J = 6.9, 6.4 \text{ Hz, 2H), 1.64 - 1.52 \text{ (m, 9H), 1.50 (s, 9H), 1.44 dt, } J = 13.4, 6.7 \text{ Hz, 1H), 0.92 \text{ (dd, } J = 6.5, 2.1 \text{ Hz, 6H).}})\]

\[ ^13C \text{ NMR} (126 \text{ MHz, CDCl}_3) \delta 168.49, 162.73, 156.58, 152.29, 143.07, 141.14, 138.46, 137.02, 132.50, 127.90, 127.68, 127.55, 126.51, 124.85, 122.60, 122.34, 122.02, 119.77, 118.32, 112.85, 64.86, 49.65, 46.43, 43.76, 36.04, 35.50, 29.85, 29.59, 26.54, 25.11, 23.89, 22.55, 22.30, 14.59. \]

HRMS (ESI): C_{37}H_{49}BrN_{3}O_{3}^+, calcd. 662.2952, found 662.2961.

N-(3-bromo-4-(tert-butyl)phenyl)-2-(11-oxo-11-dihydrodibenzo[b,f]oxepin-2-yl)acetamide (1l): White solid.

\[ ^1H \text{ NMR} (500 \text{ MHz, CDCl}_3) \delta 8.16 \text{ (d, } J = 2.4 \text{ Hz, 1H), 7.87 \text{ (dd, } J = 7.8, 1.3 \text{ Hz, 1H), 7.65 \text{ (d, } J = 2.6 \text{ Hz, 2H), 7.56 \text{ (td, } J = 7.5, 1.4 \text{ Hz, 1H), 7.52 - 7.43 \text{ (m, 2H), 7.41 - 7.34 \text{ (m, 2H), 7.29 \text{ (d, } J = 8.6 \text{ Hz, 1H), 7.05 \text{ (d, } J = 8.4 \text{ Hz, 1H), 5.18 \text{ (s, 2H), 3.72 \text{ (s, 2H), 1.44 (s, 9H).}})\]
\( ^{13}C\text{ NMR} \) (126 MHz, CDCl\(_3\)) \( \delta \) 191.01, 169.09, 160.79, 143.78, 140.31, 136.43, 135.53, 132.97, 132.49, 129.50, 129.36, 128.23, 128.07, 127.92, 126.69, 125.30, 122.36, 121.71, 118.63, 73.65, 43.94, 36.26, 29.76.

**HRMS** (ESI): C\(_{26}\)H\(_{25}\)BrNO\(_3\), calcd. 478.1012, found 478.1016.

\[ \text{1m} \]

\( (E)-N-(3\text{-bromo-4-(tert-butyl)phenyl})\text{-6-(4-hydroxy-6-methoxy-7-methyl-3-oxo-1,3-dihydroisobenzofuran-5-yl)-4-methylhex-4-enamide (1m): White solid.} \)

\( ^{1}H\text{ NMR} \) (500 MHz, CDCl\(_3\)) \( \delta \) 7.67 (s, 1H), 7.63 (t, \( J = 1.3 \text{ Hz, 1H} \)), 7.38 (d, \( J = 11.0 \text{ Hz, 1H} \)), 7.30 (d, \( J = 1.3 \text{ Hz, 2H} \)), 5.40 – 5.25 (m, 1H), 5.17 (s, 2H), 3.74 (s, 3H), 3.41 (d, \( J = 6.9 \text{ Hz, 2H} \)), 2.51 – 2.32 (m, 4H), 2.11 (s, 3H), 1.88 – 1.73 (m, 3H), 1.47 (s, 9H).

\( ^{13}C\text{ NMR} \) (126 MHz, CDCl\(_3\)) \( \delta \) 172.94, 171.07, 163.65, 153.54, 144.13, 143.48, 136.55, 134.44, 128.00, 126.66, 123.42, 122.32, 121.91, 118.61, 116.85, 106.40, 70.09, 61.04, 35.84, 34.98, 29.81, 29.79, 22.67, 16.23, 11.57.

**HRMS** (ESI): C\(_{27}\)H\(_{33}\)BrNO\(_5\), calcd. 530.1537, found 530.1539.

\( \text{6-(3-((3r,5r,7r)-adamantan-1-yl)-4-methoxyphenyl)-N-(3-bromo-4-(tert-butyl)phenyl)-2-naphthamide (1n): White solid.} \)

\( ^{1}H\text{ NMR} \) (500 MHz, CDCl\(_3\)) \( \delta \) 8.39 – 8.30 (m, 2H), 7.98 (dd, \( J = 8.7, 2.0 \text{ Hz, 2H} \)), 7.92 – 7.85 (m, 3H), 7.78 (dd, \( J = 8.5, 1.8 \text{ Hz, 1H} \)), 7.69 (dd, \( J = 8.6, 2.4 \text{ Hz, 1H} \)), 7.63 (d, \( J = 2.4 \text{ Hz, 1H} \)), 7.53 (dd, \( J = 8.3, 2.3 \text{ Hz, 1H} \)), 7.43 (d, \( J = 8.7, 1H \)), 7.01 (d, \( J = 8.5 \text{ Hz, 1H} \)), 3.93 (s, 3H), 2.23 (d, \( J = 2.9 \text{ Hz, 6H} \)), 2.20 – 2.12 (m, 3H), 1.86 (d, \( J = 3.1 \text{ Hz, 6H} \)), 1.55 (s, 9H).

\( ^{13}C\text{ NMR} \) (126 MHz, CDCl\(_3\)) \( \delta \) 166.11, 158.93, 143.85, 141.05, 139.02, 136.86, 135.32, 132.49, 131.27, 131.23, 129.36, 128.74, 128.22, 127.53, 127.18, 126.67, 125.94, 125.74, 124.67, 123.90, 122.54, 119.10, 112.15, 55.20, 40.66, 37.24, 37.18, 36.36, 29.87, 29.16.

**HRMS** (ESI): C\(_{38}\)H\(_{41}\)BrNO\(_2\), calcd. 622.2315, found 622.2308.
(4R)-N-(3-bromo-4-(tert-butyl)phenyl)-4-((5S,9S,10S,13R,14S,17R)-10,13-dimethyl-3,7,12-trioxohexadecahydro-1H-cyclopenta[a]phenanthren-17-yl)pentanamide (1l): White solid.

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.43 (s, 1H), 7.75 (d, $J$ = 2.3 Hz, 1H), 7.47 (dd, $J$ = 8.6, 2.4 Hz, 1H), 7.32 (d, $J$ = 8.8 Hz, 1H), 3.01 – 2.79 (m, 3H), 2.44 (ddd, $J$ = 14.1, 10.1, 4.5 Hz, 2H), 2.38 – 2.23 (m, 4H), 2.24 – 2.16 (m, 3H), 2.10 (dd, $J$ = 12.4, 5.0 Hz, 1H), 2.06 – 1.88 (m, 5H), 1.82 (td, $J$ = 11.3, 7.1 Hz, 1H), 1.60 (td, $J$ = 14.6, 4.4 Hz, 1H), 1.46 (s, 9H), 1.39 (s, 3H), 1.37 – 1.21 (m, 4H), 1.05 (s, 3H), 0.83 (d, $J$ = 6.6 Hz, 3H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 212.28, 209.41, 209.17, 172.05, 143.21, 137.04, 128.07, 126.51, 122.34, 118.48, 56.92, 51.79, 48.99, 46.81, 45.43, 45.35, 45.02, 42.81, 38.69, 36.46, 36.22, 36.01, 35.28, 35.25, 34.02, 30.76, 29.82, 27.63, 25.16, 21.85, 18.76, 11.88.

HRMS (ESI): C$_{34}$H$_{47}$BrNO$_4^+$, calcd. 612.2683, found 612.2682.

N-(3-bromo-4-(tert-butyl)phenyl)-2-ethoxy-4-((3aR,7aS)-octahydro-2H-isindol-2-yl)-2-oxoethyl)benzamide (1p): Yellow solid.

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 10.04 (s, 1H), 8.21 (d, $J$ = 8.0 Hz, 1H), 7.94 (d, $J$ = 2.4 Hz, 1H), 7.54 (dd, $J$ = 8.6, 2.3 Hz, 1H), 7.40 (d, $J$ = 8.7 Hz, 1H), 7.05 (d, $J$ = 1.6 Hz, 1H), 6.98 (dd, $J$ = 8.0, 1.6 Hz, 1H), 4.29 (q, $J$ = 7.0 Hz, 2H), 3.67 (s, 2H), 3.31 (dd, $J$ = 9.9, 5.9 Hz, 1H), 2.30 – 2.11 (m, 2H), 1.61 (t, $J$ = 7.1 Hz, 2H), 1.51 (s, 9H), 1.42 – 1.33 (m, 4H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 169.29, 163.10, 156.85, 143.28, 140.96, 137.34, 132.61, 128.15, 126.79, 122.59, 122.42, 119.99, 118.60, 113.14, 65.22, 51.05, 49.84, 41.98, 37.68, 36.30, 35.92, 29.86, 25.72, 22.74, 22.53, 14.91.

HRMS (ESI): C$_{29}$H$_{38}$BrN$_2$O$_3^+$, calcd. 541.2060, found 541.2053
3-(4,4-dimethylpent-2-yn-1-ylidene)pentane-2,4-dione (2a): Yellow oil.  
$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 6.72 (s, 1H), 2.49 (s, 3H), 2.31 (s, 3H), 1.27 (s, 9H).  

![Structure 2b]

ethyl (E)-2-acetyl-6,6-dimethylhept-2-en-4-ynoate (2b): Colorless oil.  
$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 6.81 (s, 1H), 4.34 (q, $J$ = 7.1, 2H), 2.46 (s, 3H), 1.38 (t, $J$ = 7.1, 3H), 1.29 (s, 9H).

![Structure 2c]

2-(4,4-dimethylpent-2-yn-1-ylidene)-1,3-diphenylpropane-1,3-dione (2c): White solid.  
$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.05 – 7.97 (m, 2H), 7.84 – 7.77 (m, 2H), 7.67 – 7.40 (m, 6H), 6.76 (s, 1H), 0.97 (s, 9H).

![Structure 2d]

2-(4,4-dimethylpent-2-yn-1-ylidene)-1,3-di(thiophen-2-yl)propane-1,3-dione (2d): Yellow solid.  
$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.77 – 7.72 (m, 2H), 7.68 – 7.64 (m, 2H), 7.15 (dd, $J$ = 4.8, 4.0 Hz, 1H), 7.08 (dd, $J$ = 4.9, 3.9 Hz, 1H), 6.89 (s, 1H), 1.04 (s, 9H).

![Structure 2e]

3-(4-methyl-4-((trimethylsilyl)oxy)pent-2-yn-1-ylidene)pentane-2,4-dione (2e): Colorless oil.  
$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 6.73 (s, 1H), 2.49 (s, 3H), 2.34 (s, 3H), 1.54 (s, 6H), 0.19 (s, 9H).
1,4-diphenylhexa-2,3-dien-1-one (4a): Yellow oil.

\(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.91 – 7.82 (m, 2H), 7.54 – 7.45 (m, 1H), 7.44 – 7.32 (m, 6H), 7.31 – 7.26 (m, 1H), 6.71 (t, \(J = 3.3\) Hz, 1H), 2.64 – 2.52 (m, 2H), 1.15 (t, \(J = 7.4\) Hz, 3H).

1-(4-methoxyphenyl)-4-phenylhexa-2,3-dien-1-one (4b): Yellow oil.

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.96 – 7.92 (m, 2H), 7.47 – 7.29 (m, 6H), 6.91 – 6.86 (m, 2H), 6.73 (t, \(J = 3.4\) Hz, 1H), 3.86 (s, 3H), 2.65 – 2.56 (m, 2H), 1.20 (t, \(J = 7.3\) Hz, 3H).

4-phenyl-1-(p-tolyl)hexa-2,3-dien-1-one (4c): Yellow oil.

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.96 – 7.92 (m, 2H), 7.47 – 7.29 (m, 6H), 6.91 – 6.86 (m, 2H), 6.73 (t, \(J = 3.4\) Hz, 1H), 2.65 – 2.56 (m, 2H), 2.38 (s, 3H), 1.20 (t, \(J = 7.3\) Hz, 3H).

1-(4-chlorophenyl)-4-phenylhexa-2,3-dien-1-one (4d): Yellow oil.

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.88 – 7.74 (m, 2H), 7.42 – 7.38 (m, 3H), 7.37 (d, \(J = 2.1\) Hz, 1H), 7.35 – 7.29 (m, 3H), 6.68 (t, \(J = 3.4\) Hz, 1H), 2.65 – 2.56 (m, 2H), 1.17 (t, \(J = 7.3\) Hz, 3H).

1-(naphthalen-2-yl)-4-phenylhexa-2,3-dien-1-one (4e): Yellow oil.
$^1\text{H NMR}$ (400 MHz, CDCl$_3$) $\delta$ 8.39 (t, $J = 1.1$ Hz, 1H), 7.97 (dd, $J = 8.6$, 1.8 Hz, 1H), 7.86 (d, $J = 8.5$ Hz, 2H), 7.64 (d, $J = 8.1$ Hz, 1H), 7.58 (ddd, $J = 8.2$, 6.8, 1.3 Hz, 1H), 7.52 – 7.39 (m, 5H), 7.38 – 7.31 (m, 1H), 6.80 (t, $J = 3.3$ Hz, 1H), 2.65 – 2.56 (m, 2H), 1.18 (t, $J = 7.3$ Hz, 3H).

1-(furan-2-yl)-4-phenylhexa-2,3-dien-1-one (4f): Yellow oil.

$^1\text{H NMR}$ (400 MHz, CDCl$_3$) $\delta$ 7.61 (dd, $J = 1.7$, 0.8 Hz, 1H), 7.48 – 7.44 (m, 2H), 7.42 – 7.36 (m, 2H), 7.36 – 7.29 (m, 1H), 7.23 (dd, $J = 3.6$, 0.8 Hz, 1H), 6.69 (t, $J = 3.5$ Hz, 1H), 6.51 (dd, $J = 3.6$, 1.7 Hz, 1H), 2.65 – 2.56 (m, 2H), 1.23 (t, $J = 7.3$ Hz, 3H).

4-phenyl-1-(thiophen-2-yl)hexa-2,3-dien-1-one (4g): Yellow oil.

$^1\text{H NMR}$ (400 MHz, CDCl$_3$) $\delta$ 7.85 (dd, $J = 3.8$, 1.2 Hz, 1H), 7.60 (dd, $J = 5.0$, 1.2 Hz, 1H), 7.51 – 7.46 (m, 2H), 7.44 – 7.36 (m, 2H), 7.36 – 7.28 (m, 1H), 7.09 (dd, $J = 5.0$, 3.8 Hz, 1H), 6.65 (t, $J = 3.6$ Hz, 1H), 2.65 – 2.56 (m, 2H), 1.24 (t, $J = 7.3$ Hz, 3H).

4-(4-phenylhexa-2,3-dienoyl)benzonitrile (4h): Yellow oil.

$^1\text{H NMR}$ (400 MHz, CDCl$_3$) $\delta$ 7.92 – 7.86 (m, 2H), 7.69 – 7.64 (m, 2H), 7.47 – 7.30 (m, 5H), 6.66 (t, $J = 3.4$ Hz, 1H), 2.64 – 2.52 (m, 2H), 1.14 (t, $J = 7.3$ Hz, 3H).

(Z)-1-(2-methyl-5-(2,2,5-trimethyl-5-phenylhex-3-en-3-yl)furan-3-yl)ethan-1-one (3aa): Yellow oil, 24.6 mg.
\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.22 – 7.06 (m, 5H), 6.12 (s, 1H), 5.64 (s, 1H), 2.44 (s, 3H), 2.22 (s, 3H), 1.32 (s, 6H), 1.07 (s, 9H).

\(^13\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 194.34, 156.32, 150.13, 148.68, 141.68, 138.89, 127.58, 126.17, 125.03, 121.59, 109.99, 40.19, 36.38, 30.91, 29.62, 28.92, 14.29

HRMS (ESI): C\(_{22}\)H\(_{29}\)O\(_2\)\(^+\), calcd. 325.2162, found 325.2171.

(Z)-1-(2-methyl-5-(2,2,5-trimethyl-5-(p-tolyl)hex-3-en-3-yl)furan-3-yl)ethan-1-one (3ba) Yellow oil, 27.7 mg.

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.02 (q, \(J = 8.3\) Hz, 4H), 6.09 (s, 1H), 5.65 (s, 1H), 2.45 (s, 3H), 2.29 (s, 3H), 2.23 (s, 3H), 1.30 (s, 6H), 1.06 (s, 9H)

\(^13\)C NMR (126 MHz, CDCl\(_3\)) \(\delta\) 194.41, 156.42, 148.74, 147.18, 141.77, 138.61, 134.51, 128.30, 126.10, 121.57, 109.97, 39.90, 36.38, 30.85, 29.62, 28.86, 20.84, 14.29

HRMS (ESI): C\(_{23}\)H\(_{31}\)O\(_2\)\(^+\), calcd. 339.2319, found 339.2321.

(Z)-1-(5-(5-(4-methoxyphenyl)-2,2,5-trimethylhex-3-en-3-yl)-2-methylfuran-3-yl)ethan-1-one (3ca) Yellow solid, 32.9 mg.

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.05 (d, \(J = 8.8\) Hz, 2H), 6.72 (d, \(J = 8.8\) Hz, 2H), 6.07 (s, 1H), 5.68 (s, 1H), 3.76 (s, 3H), 2.46 (s, 3H), 2.24 (s, 3H), 1.30 (s, 6H), 1.06 (s, 9H)

\(^13\)C NMR (126 MHz, CDCl\(_3\)) \(\delta\) 194.40, 157.21, 156.37, 148.76, 142.15, 141.84, 138.57, 127.14, 121.68, 112.87, 109.82, 55.14, 39.62, 36.36, 30.95, 29.60, 28.88, 14.29

HRMS (ESI): C\(_{23}\)H\(_{31}\)O\(_3\)\(^+\), calcd. 355.2268, found 355.227.
(Z)-1-(5-(5-(3-methoxyphenyl)-2,2,5-trimethylhex-3-en-3-yl)-2-methylfuran-3-yl)ethan-1-one (3da) Yellow solid, 34.3 mg.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.10 (t, $J = 7.9$ Hz, 1H), 6.76 (ddd, $J = 7.8, 1.7, 0.9$ Hz, 1H), 6.69 (t, $J = 2.2$ Hz, 1H), 6.66 – 6.61 (m, 1H), 6.08 (s, 1H), 5.68 (s, 1H), 3.76 (s, 3H), 2.45 (s, 3H), 2.23 (s, 3H), 1.31 (s, 6H), 1.07 (s, 9H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 194.28, 159.00, 156.36, 151.70, 148.65, 141.46, 138.81, 128.44, 121.61, 118.89, 112.73, 110.05, 109.74, 55.00, 40.29, 36.37, 30.84, 29.62, 28.86, 14.27

HRMS (ESI): C$_{23}$H$_{31}$O$_3^+$, calcd. 355.2268, found 355.2274.

(Z)-1-(5-(5-(4-fluorophenyl)-2,2,5-trimethylhex-3-en-3-yl)-2-methylfuran-3-yl)ethan-1-one (3ea) Yellow solid, 30.4 mg.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.08 (dd, $J = 8.8, 5.4$ Hz, 2H), 6.85 (t, $J = 8.8$ Hz, 2H), 6.08 (s, 1H), 5.69 (s, 1H), 2.44 (s, 3H), 2.25 (s, 3H), 1.31 (s, 6H), 1.05 (s, 9H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 194.25, 160.74 ($J_{CF} = 256.4$ Hz), 156.42, 148.60, 145.68 ($J_{CF} = 2.8$ Hz), 141.50, 139.21, 127.65 ($J_{CF} = 8.1$ Hz), 121.66, 114.12 ($J_{CF} = 21.2$ Hz), 109.82, 39.78, 36.40, 31.09, 29.55, 28.88, 14.26

HRMS (ESI): C$_{22}$H$_{28}$FO$_2^+$, calcd. 343.2068, found 343.2074.
(Z)-1-(2-methyl-5-(2,2,5-trimethyl-5-(naphthalen-2-yl)hex-3-en-3-yl)furan-3-yl)ethan-1-one (3fa) Yellow solid, 19.8 mg.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.79 – 7.72 (m, 1H), 7.67 (dd, $J = 8.5, 5.3$ Hz, 2H), 7.45 – 7.32 (m, 4H), 6.16 (s, 1H), 5.50 (s, 1H), 2.17 (s, 3H), 1.79 (s, 3H), 1.47 (s, 6H), 1.06 (s, 9H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 193.95, 156.18, 148.31, 146.90, 141.55, 139.68, 133.13, 131.45, 127.50, 127.18, 126.90, 126.51, 125.78, 125.19, 123.33, 121.50, 109.81, 40.22, 36.35, 30.92, 29.53, 28.32, 13.98

HRMS (ESI): C$_{26}$H$_{31}$O$_2$+, calcd. 375.2319, found 375.2311.

![3ga](image)

(Z)-4-(4-acetyl-5-methylfuran-2-yl)-2,5,5-trimethyl-2-phenylhex-3-enenitrile (3ga) White oil, 17.42 mg.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.36 – 7.23 (m, 5H), 5.98 (d, $J = 6.7$ Hz, 2H), 2.45 (s, 3H), 2.25 (s, 3H), 1.81 (s, 3H), 1.14 (s, 9H)

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 194.10, 157.83, 146.43, 145.25, 142.63, 131.53, 128.65, 127.22, 125.56, 122.06, 121.53, 112.08, 41.62, 36.77, 31.97, 29.35, 28.99, 14.23

HRMS (ESI): C$_{22}$H$_{26}$NO$_2$+, calcd. 336.1958, found 336.195.

![3ga](image)

Methyl-(Z)-4-(4-acetyl-5-methylfuran-2-yl)-2,5,5-trimethyl-2-phenylhex-3-enoate (3ha) White solid, 19.2 mg.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.23 (d, $J = 2.7$ Hz, 5H), 6.56 (s, 1H), 5.84 (s, 1H), 3.53 (s, 3H), 2.48 (s, 3H), 2.27 (s, 3H), 1.59 (s, 3H), 1.11 (s, 9H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 194.17, 175.47, 156.82, 148.19, 143.99, 140.56,
HRMS (ESI): C\textsubscript{23}H\textsubscript{29}O\textsubscript{4}\textsuperscript{+}, calcd. 369.206, found 369.2062.

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\text{3ja}
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(Z)-1-(5-(5-(4-aminophenyl)-2,2,5-trimethylhex-3-en-3-yl)-2-methylfuran-3-yl)ethan-1-one (3ja) Yellow solid, 21.0 mg.

\(^1\)H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 6.93 (d, \(J = 8.5\) Hz, 2H), 6.53 (d, \(J = 8.5\) Hz, 2H), 6.05 (s, 1H), 5.73 (s, 1H), 2.49 (s, 3H), 2.29 (s, 3H), 1.25 (s, 6H), 1.05 (s, 9H).

\(^1\)H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 6.93 (d, \(J = 8.5\) Hz, 2H), 6.53 (d, \(J = 8.5\) Hz, 2H), 6.05 (s, 1H), 5.73 (s, 1H), 2.49 (s, 3H), 2.29 (s, 3H), 1.25 (s, 6H), 1.05 (s, 9H).

HRMS (ESI): C\textsubscript{22}H\textsubscript{30}NO\textsubscript{2}\textsuperscript{+}, calcd. 339.2198, found 339.2194.

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\text{3ab}
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Ethyl-(Z)-2-methyl-5-(2,2,5-trimethyl-5-phenylhex-3-en-3-yl)furan-3-carboxylate (3ab) Yellow solid, 27.3 mg.

\(^1\)H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 7.19 (d, \(J = 6.1\) Hz, 4H), 7.11 (ddd, \(J = 6.1, 5.1, 2.6\) Hz, 1H), 6.06 (s, 1H), 5.92 (s, 1H), 4.26 (q, \(J = 7.1\) Hz, 2H), 2.42 (s, 3H), 1.35 (t, \(J = 7.1\) Hz, 3H), 1.31 (s, 6H), 1.07 (s, 9H).

\(^1\)H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 7.19 (d, \(J = 6.1\) Hz, 4H), 7.11 (ddd, \(J = 6.1, 5.1, 2.6\) Hz, 1H), 6.06 (s, 1H), 5.92 (s, 1H), 4.26 (q, \(J = 7.1\) Hz, 2H), 2.42 (s, 3H), 1.35 (t, \(J = 7.1\) Hz, 3H), 1.31 (s, 6H), 1.07 (s, 9H).

HRMS (ESI): C\textsubscript{23}H\textsubscript{31}O\textsubscript{5}\textsuperscript{+}, calcd. 355.2268, found 355.2267.
(Z)-phenyl(2-phenyl-5-(2,2,5-trimethyl-5-phenylhex-3-en-3-yl)furan-3-yl)methanone (3ac) Yellow solid, 38.1 mg.

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.75 – 7.69 (m, 2H), 7.62 – 7.57 (m, 2H), 7.55 – 7.48 (m, 1H), 7.38 (t, J = 7.7 Hz, 2H), 7.31 – 7.26 (m, 5H), 7.21 (dd, J = 8.5, 6.9 Hz, 2H), 7.11 – 7.04 (m, 1H), 6.18 (s, 1H), 5.99 (s, 1H), 1.41 (s, 6H), 1.16 (s, 9H).

$^{13}$C NMR (101 MHz, CDCl$_3$) δ 191.67, 154.34, 150.10, 149.85, 141.48, 138.41, 138.27, 132.51, 130.00, 129.64, 128.56, 128.16, 128.12, 127.83, 127.41, 126.12, 125.37, 121.16, 113.34, 40.57, 36.71, 31.08, 29.75.

HRMS (ESI): C$_{32}$H$_{33}$O$_2$+, calcd. 449.2475, found 449.2474.

(Z)-thiophen-2-yl(2-(thiophen-2-yl)-5-(2,2,5-trimethyl-5-phenylhex-3-en-3-yl)furan-3-yl)methanone (3ad) Yellow solid, 41.8 mg.

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.83 (dd, J = 3.8, 1.2 Hz, 1H), 7.65 (dd, J = 4.9, 1.1 Hz, 1H), 7.39 (dd, J = 5.0, 1.2 Hz, 1H), 7.35 (dd, J = 3.8, 1.2 Hz, 1H), 7.30 – 7.25 (m, 2H), 7.21 (dd, J = 8.6, 6.9 Hz, 2H), 7.12 – 7.04 (m, 3H), 6.22 (s, 1H), 6.10 (s, 1H), 1.42 (s, 6H), 1.17 (s, 9H).

$^{13}$C NMR (126 MHz, CDCl$_3$) δ 181.49, 150.89, 149.93, 149.65, 144.94, 141.98, 138.37, 133.43, 133.34, 132.05, 127.95, 127.89, 127.78, 127.41, 127.37, 126.16, 125.45, 119.43, 112.52, 40.51, 36.65, 31.26, 29.73.

HRMS (ESI): C$_{28}$H$_{29}$O$_2$S$_2$+, calcd. 461.1603, found 461.1603.
(E)-1-(5-(2,5-dimethyl-5-phenyl-2-((trimethylsilyl)oxy)hex-3-en-3-yl)-2-methylfuran-3-yl)ethan-1-one (3ae) Yellow oil, 21.1 mg.

$^1$H NMR (500 MHz, CDCl$_3$) δ 7.17 – 7.12 (m, 4H), 7.07 (ddd, $J = 6.1, 5.1, 2.6$ Hz, 1H), 6.36 (s, 1H), 5.71 (s, 1H), 2.40 (s, 3H), 2.19 (s, 3H), 1.33 (s, 6H), 1.31 (s, 6H), 0.15 (s, 9H).

$^{13}$C NMR (126 MHz, CDCl$_3$) δ 194.33, 156.65, 149.75, 147.94, 142.06, 137.15, 127.59, 126.21, 125.12, 121.70, 110.49, 75.96, 40.05, 30.77, 30.40, 28.92, 14.29, 2.54.

HRMS (ESI): C$_{24}$H$_{35}$O$_3$Si$^+$, calcd. 399.235, found 399.2349.

(E)-2-ethyl-3-(2-methyl-2-phenylpropylidene)-2,5-diphenyl-2,3-dihydrofuran (5aa) Yellow oil, 18.24 mg.

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.58 – 7.53 (m, 2H), 7.49 (dd, $J = 7.7, 1.7$ Hz, 2H), 7.39 – 7.29 (m, 10H), 7.23 – 7.17 (m, 1H), 5.50 (s, 1H), 5.17 (d, $J = 1.0$ Hz, 1H), 2.30 (dq, $J = 14.3, 7.2$ Hz, 1H), 2.09 (dq, $J = 14.3, 7.2$ Hz, 1H), 1.53 (s, 3H), 1.48 (s, 3H), 0.97 (t, $J = 7.2$ Hz, 3H).

$^{13}$C NMR (126 MHz, CDCl$_3$) δ 160.09, 150.36, 145.73, 144.82, 130.59, 128.92, 128.32, 128.20, 128.11, 127.17, 126.53, 125.58, 125.48, 125.41, 125.02, 98.83, 92.84, 40.84, 33.58, 31.36, 31.15, 7.92.

HRMS (ESI): C$_{28}$H$_{29}$O$^+$, calcd. 381.2213, found 381.2226.
(E)-2-ethyl-5-(4-methoxyphenyl)-3-(2-methyl-2-phenylpropylidene)-2-phenyl-2,3-dihydrofuran (5ab) Yellow solid, 27.9 mg.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.54 – 7.47 (m, 3H), 7.38 (ddt, $J = 8.0, 6.0, 1.5$ Hz, 3H), 7.34 – 7.29 (m, 3H), 7.24 – 7.18 (m, 1H), 6.88 (d, $J = 8.8$ Hz, 2H), 5.40 (d, $J = 0.9$ Hz, 1H), 5.13 (d, $J = 1.0$ Hz, 1H), 3.84 (s, 3H), 2.30 (dq, $J = 14.4, 7.2$ Hz, 1H), 2.10 (dq, $J = 14.4, 7.2$ Hz, 1H), 1.54 (s, 3H), 1.49 (s, 3H), 0.98 (t, $J = 7.2$ Hz, 3H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 160.28, 160.07, 150.49, 145.94, 144.94, 128.16, 128.06, 127.10, 126.99, 126.53, 125.50, 125.02, 124.22, 123.40, 113.77, 97.18, 92.78, 55.34, 40.76, 33.52, 31.38, 31.15, 7.92.

HRMS (ESI): C$_{29}$H$_{31}$O$_2$ $^+$, calcd. 411.2319, found 411.233.

(E)-2-ethyl-3-(2-methyl-2-phenylpropylidene)-2-phenyl-5-(p-tolyl)-2,3-dihydrofuran (5ac) Yellow solid, 27.6 mg.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.50 (ddd, $J = 11.2, 7.7, 1.7$ Hz, 4H), 7.42 – 7.36 (m, 4H), 7.32 (ddt, $J = 9.0, 7.3, 2.4$ Hz, 3H), 7.25 – 7.15 (m, 3H), 5.49 (d, $J = 0.9$ Hz, 1H), 5.17 (d, $J = 1.0$ Hz, 1H), 2.39 (s, 3H), 2.31 (dq, $J = 14.3, 7.2$ Hz, 1H), 2.10 (dq, $J = 14.3, 7.2$ Hz, 1H), 1.55 (s, 3H), 1.50 (s, 3H), 0.99 (t, $J = 7.2$ Hz, 3H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 160.32, 150.44, 145.89, 144.93, 139.04, 129.03, 128.17, 128.09, 127.85, 127.12, 126.52, 125.54, 125.45, 125.01, 124.76, 98.10, 92.76, 40.81, 33.56, 31.38, 31.17, 21.44, 7.93.

HRMS (ESI): C$_{29}$H$_{31}$O$^+$, calcd. 395.2369, found 395.2381.
**(E)-5-(4-chlorophenyl)-2-ethyl-3-(2-methyl-2-phenylpropylidene)-2-phenyl-2,3-dihydrofuran** (5ad) Yellow oil, 10.4 mg.

**1H NMR** (400 MHz, CDCl$_3$) $\delta$ 7.48 – 7.43 (m, 4H), 7.40 – 7.29 (m, 9H), 7.23 – 7.18 (m, 1H), 5.45 (d, $J = 1.0$ Hz, 1H), 5.19 (d, $J = 1.1$ Hz, 1H), 2.28 (dp, $J = 13.1$, 6.9 Hz, 1H), 2.03 (dp, $J = 13.1$, 6.9 Hz, 1H), 1.53 (s, 3H), 1.48 (s, 3H), 0.95 (t, $J = 7.2$ Hz, 3H).

**13C NMR** (126 MHz, CDCl$_3$) $\delta$ 158.96, 150.21, 145.41, 144.59, 134.63, 129.06, 128.54, 128.24, 128.14, 127.27, 126.71, 126.52, 126.11, 125.64, 124.98, 99.23, 93.08, 40.88, 33.57, 31.31, 31.12, 7.90.

**HRMS** (ESI): C$_{28}$H$_{28}$ClO$^+$, calcd. 415.1823, found 415.1828.

**[(E)]-2-ethyl-3-(2-methyl-2-phenylpropylidene)-5-(naphthalen-2-yl)-2-phenyl-2,3-dihydrofuran** (5ae) Yellow solid, 24.5 mg.

**1H NMR** (400 MHz, CDCl$_3$) $\delta$ 8.16 (s, 1H), 7.91 – 7.84 (m, 1H), 7.84 – 7.80 (m, 1H), 7.77 (d, $J = 8.6$ Hz, 1H), 7.57 – 7.47 (m, 5H), 7.40 (dt, $J = 7.7$, 3.7 Hz, 4H), 7.34 (t, $J = 7.5$ Hz, 3H), 7.24 (t, $J = 7.2$ Hz, 1H), 5.66 (s, 1H), 5.23 (s, 1H), 2.37 (dq, $J = 14.2$, 6.8 Hz, 1H), 2.16 (dq, $J = 14.4$, 7.3 Hz, 1H), 1.58 (s, 3H), 1.52 (s, 3H), 1.03 (t, $J = 7.2$ Hz, 3H).

**13C NMR** (101 MHz, CDCl$_3$) $\delta$ 160.13, 150.35, 145.75, 144.85, 133.52, 133.19, 128.53, 128.25, 128.15, 127.86, 127.77, 127.66, 127.23, 126.55, 126.51, 126.43, 125.77, 125.63, 125.05, 124.46, 123.39, 99.69, 92.95, 40.93, 33.55, 31.38, 31.16, 7.96.

**HRMS** (ESI): C$_{32}$H$_{31}$O$^+$, calcd. 431.2369, found 431.2364.
(E)-5-ethyl-4-(2-methyl-2-phenylpropylidene)-5-phenyl-4,5-dihydro-2,2'-bifuran (5af) Yellow oil, 7.5 mg.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.49 – 7.43 (m, 2H), 7.43 – 7.26 (m, 8H), 7.22 – 7.16 (m, 1H), 6.63 (d, $J$ = 3.4 Hz, 1H), 6.43 (dd, $J$ = 3.4, 1.8 Hz, 1H), 5.51 (d, $J$ = 1.0 Hz, 1H), 5.15 (d, $J$ = 1.1 Hz, 1H), 2.27 (dq, $J$ = 14.4, 7.3 Hz, 1H), 2.07 (dq, $J$ = 14.4, 7.3 Hz, 1H), 1.52 (s, 3H), 1.47 (s, 3H), 0.96 (t, $J$ = 7.2 Hz, 3H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 152.15, 150.38, 146.50, 144.89, 144.56, 143.35, 128.21, 128.11, 127.29, 126.39, 125.80, 125.57, 125.07, 111.46, 109.04, 98.59, 93.34, 40.81, 33.31, 31.36, 30.98, 7.83.

HRMS (ESI): $\text{C}_{26}\text{H}_{27}\text{O}_2^+$, calcd. 371.2006, found 371.1996.

(E)-2-ethyl-3-(2-methyl-2-phenylpropylidene)-2-phenyl-5-(thiophen-2-yl)-2,3-dihydrofuran (5ag) Yellow oil, 12.0 mg.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.51 – 7.45 (m, 2H), 7.40 – 7.27 (m, 8H), 7.25 (dd, $J$ = 3.7, 1.2 Hz, 1H), 7.23 – 7.18 (m, 1H), 7.02 (dd, $J$ = 5.0, 3.7 Hz, 1H), 5.36 (d, $J$ = 1.0 Hz, 1H), 5.15 (d, $J$ = 1.1 Hz, 1H), 2.27 (dq, $J$ = 14.4, 7.3 Hz, 1H), 2.09 (dq, $J$ = 14.4, 7.3 Hz, 1H), 1.52 (s, 3H), 1.47 (s, 3H), 0.97 (t, $J$ = 7.2 Hz, 3H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 155.34, 150.23, 145.26, 144.59, 133.81, 128.17, 128.08, 127.54, 127.21, 126.46, 126.24, 125.57, 125.40, 125.35, 125.00, 98.50, 93.40, 40.82, 33.44, 31.26, 31.04, 7.86.

HRMS (ESI): $\text{C}_{26}\text{H}_{27}\text{OS}^+$, calcd. 386.1704, found 386.1710.
(E)-4-(5-ethyl-4-(2-methyl-2-phenylpropylidene)-5-phenyl-4,5-dihydrofuran-2-yl)benzonitrile (5ah) Yellow solid, 7.3 mg.

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.64 – 7.54 (m, 4H), 7.47 – 7.42 (m, 2H), 7.40 – 7.29 (m, 7H), 7.26 – 7.20 (m, 1H), 5.53 (d, $J = 1.1$ Hz, 1H), 5.29 (d, $J = 1.2$ Hz, 1H), 2.37 – 2.22 (m, 1H), 2.15 – 2.00 (m, 1H), 1.53 (s, 3H), 1.48 (s, 3H), 0.95 (t, $J = 7.2$ Hz, 3H).

$^{13}$C NMR (126 MHz, CDCl$_3$) δ 157.84, 149.86, 144.87, 144.19, 134.61, 132.08, 128.42, 128.30, 128.21, 127.44, 126.52, 125.78, 125.73, 124.93, 118.82, 111.69, 101.93, 93.38, 41.03, 33.60, 31.24, 31.08, 7.87.

HRMS (ESI): C$_{29}$H$_{28}$NO$^+$, calcd. 405.2093, found 405.2090.

(E)-2-ethyl-3-(2-(4-methoxyphenyl)-2-methylpropylidene)-2-phenyl-5-(p-tolyl)-2,3-dihydrofuran (5cc) Yellow solid, 21.6mg.

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.48 (dd, $J = 8.4$, 1.7 Hz, 4H), 7.43 – 7.30 (m, 3H), 7.28 – 7.24 (m, 2H), 7.16 (d, $J = 8.0$ Hz, 2H), 6.87 – 6.81 (m, 2H), 5.53 (d, $J = 1.1$ Hz, 1H), 5.13 (d, $J = 1.0$ Hz, 1H), 3.82 (s, 3H), 2.38 (s, 3H), 2.28 (dq, $J = 14.3$, 7.2 Hz, 1H), 2.09 (dq, $J = 14.4$, 7.2 Hz, 1H), 1.50 (s, 3H), 1.45 (s, 3H), 0.97 (t, $J = 7.2$ Hz, 3H).

$^{13}$C NMR (126 MHz, CDCl$_3$) δ 160.20, 157.34, 145.67, 144.94, 142.62, 139.00, 129.00, 128.14, 127.83, 127.43, 127.07, 125.43, 124.96, 124.93, 113.34, 98.13, 92.70, 55.21, 40.13, 33.51, 31.57, 31.26, 21.40, 7.89.

HRMS (ESI): C$_{30}$H$_{33}$O$_2^+$, calcd. 425.2475, found 425.2473.
(E)-2-ethyl-3-(2-(4-fluorophenyl)-2-methylpropylidene)-2-phenyl-5-(p-tolyl)-2,3-dihydrofuran (5ec) Yellow solid, 27.2 mg.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.51 – 7.45 (m, 4H), 7.40 – 7.34 (m, 2H), 7.33 – 7.26 (m, 3H), 7.17 (d, $J = 8.0$ Hz, 2H), 7.01 – 6.94 (m, 2H), 5.46 (d, $J = 1.0$ Hz, 1H), 5.12 (d, $J = 1.0$ Hz, 1H), 2.38 (s, 3H), 2.30 (dq, $J = 14.4$, 7.2 Hz, 1H), 2.10 (dq, $J = 14.4$, 7.2 Hz, 1H), 1.52 (s, 3H), 1.45 (s, 3H), 0.97 (t, $J = 7.2$ Hz, 3H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 160.92 ($J_{C}$-$F$ = 244.4 Hz), 160.65, 159.95, 146.23, 146.19, 144.83, 139.24, 129.09, 127.97 ($J_{C}$-$F$ = 8.1 Hz), 127.94, 127.71, 127.18, 125.49, 124.93, 124.30, 114.69 ($J_{C}$-$F$ = 20.5 Hz), 97.84, 92.77, 40.35, 33.48, 31.66, 31.28, 21.45, 7.91.

HRMS (ESI): C$_{29}$H$_{30}$F$_2$O$^+$, calcd. 413.2275, found 413.2262.

(E)-4-(1-(2-ethyl-2-phenyl-5-(p-tolyl)furan-3(2H)-ylidene)-2-methylpropan-2-yl)aniline (5jc) Yellow oil, 15.6 mg.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.47 (td, $J = 5.9$, 2.7 Hz, 4H), 7.38 – 7.31 (m, 2H), 7.30 – 7.24 (m, 1H), 7.19 – 7.12 (m, 4H), 6.69 (d, $J = 8.5$ Hz, 2H), 5.54 (d, $J = 1.0$ Hz, 1H), 5.10 (d, $J = 1.1$ Hz, 1H), 2.36 (s, 3H), 2.26 (dq, $J = 14.4$, 7.2 Hz, 1H), 2.05 (dq, $J = 14.4$, 7.2 Hz, 1H), 1.47 (s, 3H), 1.42 (s, 3H), 0.95 (t, $J = 7.2$ Hz, 3H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 160.19, 145.59, 144.97, 139.02, 129.06, 128.15, 127.86, 127.38, 127.08, 125.47, 125.06, 124.98, 116.15, 98.18, 92.71, 40.15, 33.56, 31.52, 31.20, 21.43, 7.91.

HRMS (ESI): C$_{29}$H$_{32}$NO$^+$, calcd. 410.2478, found 410.2484.
(S,Z)-N-(4-(4-(4-acetyl-5-methylfuran-2-yl)-2,5,5-trimethylhex-3-en-2-yl)phenyl)-2-ethoxy-4-((3-methyl-1-(2-(piperidin-1-yl)phenyl)butyl)amino)-2-oxoethyl)benzamide (3ka) Yellow solid, 71.2 mg.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 10.00 (s, 1H), 8.21 (d, $J = 7.9$ Hz, 1H), 7.50 – 7.45 (m, 2H), 7.25 – 7.17 (m, 2H), 7.13 (td, $J = 6.5$, 6.0, 3.3 Hz, 3H), 7.06 (ddd, $J = 7.9$, 6.3, 2.2 Hz, 1H), 6.96 (ddd, $J = 11.6$, 6.4, 3.0 Hz, 3H), 6.08 (s, 1H), 5.73 (s, 1H), 5.40 (td, $J = 8.7$, 6.4 Hz, 1H), 4.23 – 4.07 (m, 2H), 3.57 (s, 2H), 2.92 (d, $J = 28.4$ Hz, 2H), 2.61 (q, $J = 11.0$, 9.9 Hz, 2H), 2.45 (s, 3H), 2.21 (s, 3H), 1.99 (s, 2H), 1.78 – 1.68 (m, 2H), 1.67 – 1.58 (m, 4H), 1.57 – 1.41 (m, 4H), 1.31 (s, 6H), 1.05 (s, 9H), 0.93 (dd, $J = 6.5$, 2.0 Hz, 6H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 192.63, 167.00, 160.93, 154.95, 154.55, 150.65, 146.84, 143.98, 139.73, 139.24, 136.99, 136.90, 133.95, 130.86, 126.04, 125.84, 124.92, 123.17, 120.89, 120.33, 119.85, 118.48, 117.35, 111.17, 108.08, 63.18, 47.90, 44.81, 42.13, 38.04, 34.52, 28.97, 27.71, 27.07, 24.91, 23.49, 22.29, 20.96, 20.67, 12.99, 12.47.

HRMS (ESI): C$_{49}$H$_{64}$N$_3$O$_5$$^+$, calcd. 774.484, found 774.4839.

(Z)-N-(4-(4-(4-acetyl-5-methylfuran-2-yl)-2,5,5-trimethylhex-3-en-2-yl)phenyl)-2-(11-oxo-11,11-dihydrodibenzo[b,f]oxepin-2-yl)acetamide (3la) Yellow solid, 49 mg.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.17 (d, $J = 2.4$ Hz, 1H), 7.89 (dd, $J = 7.7$, 1.3 Hz, 1H), 7.74 (s, 1H), 7.60 – 7.45 (m, 3H), 7.38 (dd, $J = 7.5$, 1.2 Hz, 1H), 7.31 (d, $J = 2.0$ Hz, 1H), 7.10 – 7.00 (m, 3H), 6.03 (s, 1H), 5.68 (s, 1H), 5.20 (s, 2H), 3.71 (s, 2H), 2.42 (s, 3H), 2.20 (s, 3H), 2.10 (s, 1H), 1.27 (s, 6H), 1.03 (s, 9H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 194.70, 190.93, 168.86, 160.68, 156.48, 148.69, 146.06, 141.48, 140.34, 138.73, 136.40, 135.56, 135.15, 132.92, 132.40, 129.50,
(E)-N-((Z)-4-(4-acetyl-5-methylfuran-2-yl)-2,5,5-trimethylhex-3-en-2-yl)phenyl)-6-(4-hydroxy-6-methoxy-7-methyl-3-oxo-1,3-dihydroisobenzofuran-5-yl)-4-methylhex-4-enamide (3ma) Yellow solid, 33.3 mg.

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.72 (s, 1H), 7.38 (s, 1H), 7.24 (d, $J = 8.5$ Hz, 2H), 7.07 – 7.00 (m, 2H), 6.04 (s, 1H), 5.70 (s, 1H), 5.36 – 5.27 (m, 1H), 5.20 (s, 2H), 3.76 (s, 3H), 3.42 (d, $J = 6.9$ Hz, 2H), 2.47 – 2.38 (m, 7H), 2.22 (s, 3H), 2.14 (s, 3H), 1.85 (s, 3H), 1.28 (s, 6H), 1.04 (s, 9H).

$^{13}$C NMR (101 MHz, CDCl$_3$) δ 194.57, 172.89, 170.80, 163.64, 156.41, 153.57, 148.66, 145.70, 144.07, 141.44, 138.66, 135.24, 134.55, 126.58, 123.08, 122.04, 121.71, 119.02, 116.79, 109.91, 106.38, 70.05, 61.02, 39.91, 36.36, 36.07, 35.14, 30.78, 29.56, 28.95, 22.65, 16.24, 14.33, 11.57.

HRMS (ESI): C$_{39}$H$_{48}$NO$_7$+, calcd. 642.3425, found 642.3409.

N-(4-((Z)-4-(4-acetyl-5-methylfuran-2-yl)-2,5,5-trimethylhex-3-en-2-yl)phenyl)-6-(3-(3r,5r,7r)-adamantan-1-yl)-4-methoxyphenyl)-2-naphthamide (3na) Yellow solid, 50.6 mg.

$^1$H NMR (400 MHz, CDCl$_3$) δ 8.33 (d, $J = 39.0$ Hz, 2H), 8.04 – 8.01 (m, 1H), 7.99 – 7.92 (m, 3H), 7.81 (dd, $J = 8.6$, 1.8 Hz, 1H), 7.63 (d, $J = 2.3$ Hz, 1H), 7.58 – 7.52 (m, 3H), 7.16 (d, $J = 8.6$ Hz, 2H), 7.01 (d, $J = 8.5$ Hz, 1H), 6.10 (s, 1H), 5.76 (s, 1H), 3.92 (s, 3H), 2.49 (s, 3H), 2.26 (s, 3H), 2.22 (d, $J = 2.9$ Hz, 6H), 2.14 (t, $J = 3.4$ Hz, 3H), 1.84 (d, $J = 3.0$ Hz, 6H), 1.35 (s, 6H), 1.08 (s, 9H).
\[ ^{13}C\text{ NMR} \text{ (101 MHz, CDCl}_3\text{)} \delta 194.68, 165.77, 158.89, 156.47, 148.73, 146.10, 141.54, 140.95, 139.00, 138.80, 135.47, 135.25, 132.53, 131.75, 131.36, 129.34, 128.73, 127.32, 126.83, 126.68, 125.94, 125.71, 124.71, 123.93, 121.85, 119.48, 112.13, 109.98, 55.18, 40.63, 40.00, 37.23, 37.15, 36.40, 30.88, 29.59, 29.13, 29.02, 14.43. \]

HRMS (ESI): \( \text{C}_{50}\text{H}_{56}\text{N}_{4}\text{O}_{4}^+ \), calcd. 734.4204, found 734.4192.

(4R)-N-(4-((Z)-4-(4-acetyl-5-methylfuran-2-yl)-2,5,5-trimethylhex-3-en-2-yl)phenyl)-4-((10S,13R,17R)-10,13-dimethyl-3,7,12-trioxohexadecahydro-1H-cyclopenta[al]phenanthren-17-yl)pentanamide (3oa) Yellow solid, 65.8 mg.

\[ ^{1}H\text{ NMR} \text{ (400 MHz, Chloroform-}d\text{)} \delta 7.68 \text{ (s, 1H), 7.31 (d, } J = 8.6 \text{ Hz, 2H), 7.07 – 7.00 (m, 2H), 6.03 (s, 1H), 5.68 (s, 1H), 2.97 – 2.80 (m, 3H), 2.48 – 2.43 (m, 1H), 2.42 (s, 3H), 2.38 – 2.22 (m, 6H), 2.21 (s, 3H), 2.17 – 2.09 (m, 3H), 2.06 – 2.02 (m, 3H), 1.99 – 1.89 (m, 2H), 1.84 (td, } J = 11.4, 7.1 \text{ Hz, 1H), 1.61 (td, } J = 14.5, 4.4 \text{ Hz, 1H), 1.48 (dtd, } J = 14.2, 9.1, 5.3 \text{ Hz, 1H), 1.40 (s, 3H), 1.38 – 1.30 (m, 3H), 1.27 (s, 6H), 1.07 (s, 3H), 1.02 (s, 9H), 0.86 (d, } J = 6.6 \text{ Hz, 3H).} \]

\[ ^{13}C\text{ NMR} \text{ (126 MHz, CDCl}_3\text{)} \delta 210.34, 207.43, 207.08, 192.72, 169.68, 154.52, 146.79, 143.68, 139.63, 136.78, 133.58, 124.73, 119.78, 117.02, 107.98, 55.01, 49.88, 47.07, 44.91, 43.61, 43.51, 43.09, 40.88, 37.96, 36.76, 34.56, 34.44, 34.10, 33.48, 33.34, 32.39, 29.04, 28.95, 28.87, 27.64, 27.06, 25.73, 23.25, 19.96, 16.85, 12.43, 9.98. \]

HRMS (ESI): \( \text{C}_{46}\text{H}_{60}\text{N}_{6}^+ \), calcd. 722.4426, found 722.4422.

(3pa) Yellow solid, 49.6 mg.

\[ ^{1}H\text{ NMR} \text{ (400 MHz, CDCl}_3\text{)} \delta 10.02 (s, 1H), 8.22 (d, } J = 8.0 \text{ Hz, 1H), 7.47 (d, } J = 8.6 \text{ Hz, 2H), 7.14 – 7.08 (m, 2H), 7.04 (d, } J = 1.5 \text{ Hz, 1H), 6.98 (dd, } J = 8.0, 1.5 \text{ Hz, 1H), 6.07 (s, 1H), 5.71 (s, 1H), 4.29 (q, } J = 7.0 \text{ Hz, 2H), 3.68 (s, 2H), 3.51 – 3.37 (m,} \]
3H), 3.32 (dd, J = 9.9, 5.8 Hz, 1H), 2.44 (s, 3H), 2.26 (td, J = 14.0, 12.8, 6.7 Hz, 2H), 2.20 (s, 3H), 2.20 – 2.14 (m, 1H), 1.62 (t, J = 6.9 Hz, 3H), 1.58 – 1.34 (m, 8H), 1.31 (s, 6H), 1.04 (s, 9H).

$^{13}$C NMR (101 MHz, CDCl$_3$) δ 194.49, 169.39, 162.88, 156.81, 156.39, 148.68, 145.75, 141.60, 140.63, 138.84, 135.88, 132.52, 126.76, 122.26, 121.71, 120.27, 119.20, 113.04, 109.95, 65.13, 51.04, 49.83, 41.98, 39.89, 37.65, 35.89, 30.83, 29.57, 25.70, 22.72, 22.52, 14.89, 14.33.

HRMS (ESI): C$_{41}$H$_{51}$N$_2$O$_5$$^-$, calcd. 651.3803, found 651.3798.

2-ethoxy-N-(4-((E)-1-(2-ethyl-2-phenyl-5-(p-tolyl)furan-3(2H)-ylidene)-2-methylpropan-2-yl)phenyl)-4-2-((S)-3-methyl-1-(2-(piperidin-1-yl)phenyl)butyl)amino)-2-oxoethyl)benzamide (5kc) Yellow solid, 49.7 mg.

$^1$H NMR (400 MHz, CDCl$_3$) δ 10.06 (s, 1H), 8.26 (d, J = 8.0 Hz, 1H), 7.61 – 7.56 (m, 2H), 7.48 (d, J = 8.0 Hz, 4H), 7.40 – 7.30 (m, 5H), 7.23 (dd, J = 6.5, 1.9 Hz, 2H), 7.17 – 7.06 (m, 4H), 7.01 – 6.93 (m, 2H), 6.87 (d, J = 8.8 Hz, 1H), 5.58 (s, 1H), 5.44 – 5.35 (m, 1H), 5.14 (d, J = 1.0 Hz, 1H), 4.25 – 4.07 (m, 2H), 3.59 (s, 2H), 2.96 (d, J = 11.4 Hz, 2H), 2.64 (d, J = 9.9 Hz, 2H), 2.35 (s, 3H), 2.28 (dt, J = 14.0, 7.0 Hz, 1H), 2.10 (dt, J = 14.1, 7.1 Hz, 1H), 1.74 (s, 3H), 1.67 – 1.55 (m, 9H), 1.52 (s, 3H), 1.46 (s, 3H), 1.01 – 0.91 (m, 9H).

$^{13}$C NMR (126 MHz, CDCl$_3$) δ 168.85, 162.83, 160.45, 156.86, 152.57, 146.41, 146.08, 144.92, 140.91, 139.07, 138.65, 136.09, 132.87, 129.03, 128.19, 127.97, 127.88, 127.79, 127.12, 127.05, 125.51, 125.15, 124.98, 124.55, 122.97, 122.23, 120.56, 119.67, 113.04, 98.14, 92.74, 65.08, 50.08, 46.67, 44.11, 40.43, 33.55, 31.59, 31.17, 26.80, 25.37, 24.15, 22.80, 22.58, 21.42, 14.90, 7.93.

HRMS (ESI): C$_{56}$H$_{65}$ClN$_3$O$_4$$,^-$ calcd. 878.4669, found 878.4663.
(E)-N-(4-(1-(2-ethyl-2-phenyl-5-(p-tolyl)furan-3(2H)-ylidene)-2-methylpropan-2-yl)phenyl)-2-(11-oxo-11-dihydrodibeno[b,f]oxepin-2-yl)acetamide (5lc) Yellow solid, 48.8 mg.

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.19 (d, \(J = 2.4\) Hz, 1H), 7.92 (dd, \(J = 7.7, 1.4\) Hz, 1H), 7.60 (td, \(J = 7.4, 1.4\) Hz, 1H), 7.52 (ddd, \(J = 7.6, 6.1, 1.9\) Hz, 2H), 7.49 – 7.42 (m, 4H), 7.40 (d, \(J = 7.4\) Hz, 1H), 7.38 – 7.30 (m, 4H), 7.25 (t, \(J = 7.5\) Hz, 3H), 7.18 (s, 1H), 7.12 (dd, \(J = 15.6, 8.2\) Hz, 3H), 5.51 (s, 1H), 5.23 (s, 2H), 5.10 (s, 1H), 3.75 (s, 2H), 2.36 (s, 3H), 2.26 (dq, \(J = 14.3, 7.2\) Hz, 1H), 2.07 (dq, \(J = 14.2, 7.1\) Hz, 1H), 1.47 (s, 3H), 1.41 (s, 3H), 0.94 (t, \(J = 7.2\) Hz, 3H).

\(^13\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 190.83, 168.71, 160.74, 160.51, 147.04, 146.19, 144.84, 140.37, 139.09, 136.42, 135.47, 134.98, 132.92, 132.56, 129.52, 129.34, 129.01, 128.31, 128.16, 127.88, 127.10, 126.92, 125.49, 125.36, 124.90, 124.34, 121.75, 119.67, 98.01, 92.70, 73.66, 43.72, 40.34, 33.45, 31.54, 31.06, 21.41, 7.87.

HRMS (ESI): C\(_{45}\)H\(_{40}\)NO\(_4\)^+, calced. 658.2963, found 658.2949.

6a: White solid.

\(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.87 (s, 1H), 7.36 – 7.31 (m, 2H), 7.29 – 7.22 (m, 3H), 7.10 (dd, \(J = 23.0, 8.7\) Hz, 4H), 6.38 (d, \(J = 7.4\) Hz, 1H), 6.10 (s, 1H), 5.68 (t, \(J = 5.5\) Hz, 1H), 5.31 (s, 1H), 4.85 (dd, \(J = 13.9, 7.7\) Hz, 1H), 3.32 (dd, \(J = 13.5, 7.0\) Hz, 2H), 3.23 (dd, \(J = 13.6, 6.0\) Hz, 1H), 3.10 (dd, \(J = 13.7, 8.1\) Hz, 1H), 2.41 (s, 3H), 2.35 – 2.19 (m, 2H), 1.68 (dt, \(J = 15.2, 7.0\) Hz, 2H), 1.57 (m, 2H), 1.38 – 1.31 (m, 14H), 1.28 (d, \(J = 3.4\) Hz, 6H), 1.09 (s, 9H).
$^{13}$C NMR (126 MHz, CDCl$_3$) δ 173.40, 169.13, 167.04, 164.28, 154.10, 148.54, 147.40, 141.11, 136.57, 134.00, 129.36, 128.85, 127.22, 126.82, 120.16, 115.97, 108.12, 55.17, 39.69, 39.47, 38.75, 36.41, 36.22, 31.39, 30.96, 29.70, 29.48, 28.12, 28.00, 27.66, 27.61, 27.39, 27.25, 26.43, 24.68, 13.40.

MS (ESI): C$_{42}$H$_{58}$N$_{5}$O$_{4}$$^+$, calcd. 668.4422, found 668.4425.

6b: White solid.

$^1$H NMR (500 MHz, CDCl$_3$) δ 8.43 (s, 1H), 7.33 (d, $J$ = 7.9 Hz, 2H), 7.12 (d, $J$ = 8.1 Hz, 2H), 6.25 (d, $J$ = 6.9 Hz, 1H), 6.09 (s, 1H), 5.63 (t, $J$ = 5.9 Hz, 1H), 5.38 (s, 2H), 4.67 (dd, $J$ = 14.3, 7.4 Hz, 1H), 3.33 (dd, $J$ = 13.1, 6.6 Hz, 2H), 2.43 (s, 3H), 2.26 – 2.21 (m, 2H), 2.09 – 2.00 (m, 2H), 1.72 – 1.67 (m, 2H), 1.49 (d, $J$ = 6.8 Hz, 3H), 1.37 – 1.32 (m, 14H), 1.28 (s, 6H), 1.07 (s, 9H).

$^{13}$C NMR (126 MHz, CDCl$_3$) δ173.63, 170.35, 154.28, 148.63, 141.05, 139.54, 134.65, 129.74, 126.82, 119.84, 115.91, 108.03, 49.44, 39.82, 39.36, 36.42, 36.21, 31.39, 30.79, 29.70, 29.36, 28.17, 28.06, 27.77, 27.56, 27.48, 27.23, 26.32, 24.76, 22.69, 17.97, 14.11, 13.36.

MS (ESI): C$_{36}$H$_{54}$N$_{5}$O$_{4}$$^+$, calcd. 592.4109, found 592.4106.

6c: White solid.

$^1$H NMR (500 MHz, CDCl$_3$) δ 8.38 (s, 1H), 7.33 (d, $J$ = 8.6 Hz, 2H), 7.12 (d, $J$ = 8.6 Hz, 2H), 6.27 (d, $J$ = 8.7 Hz, 1H), 6.09 (s, 1H), 5.76 (t, $J$ = 6.0 Hz, 1H), 5.45 (s, 1H), 4.55-4.47 (m, 1H), 3.40-3.27 (m, 2H), 2.41 (s, 3H), 2.38-2.32 (m, 1H), 2.30-2.18
(m, 2H), 1.73-1.67 (m, 2H), 1.62-1.55 (m, 2H), 1.38-1.30 (m, 14H), 1.28 (s, 6H),
1.11-1.06 (m, 12H), 1.05 (d, J = 6.8 Hz, 3H).

$^{13}$C NMR (126 MHz, CDCl$_3$) δ 173.55, 169.91, 164.34, 154.02, 148.60, 147.07,
140.98, 139.72, 134.42, 126.78, 120.28, 116.09, 108.21, 58.96, 39.78, 39.43, 36.42,
34.68, 31.59, 29.72, 29.39, 28.10, 27.78, 26.93, 26.34, 25.29, 24.80, 22.66, 19.30, 18.47,
14.12, 13.36.

HRMS (ESI): C$_{38}$H$_{58}$N$_3$O$_4$+, calcd. 620.4422, found 620.4419.

$^{6d}$: White solid.

$^1$H NMR (500 MHz, CDCl$_3$) δ 9.65 (s, 1H), 7.39 (d, J = 8.7 Hz, 2H), 7.14 (d, J =
8.7 Hz, 2H), 6.06 (s, 1H), 5.53 (t, J = 5.6 Hz, 1H), 5.48 (s, 1H), 4.80 (t, J = 9.4 Hz, 1H),
3.75 (q, J = 7.0 Hz, 1H), 3.62-3.53 (m, 1H), 3.51-3.43 (m, 1H), 3.43-3.35 (m, 1H), 3.35-
3.24 (m, 1H), 2.63 (dd, J = 12.4, 6.5 Hz, 1H), 2.50 (s, 3H), 2.42-2.32 (m, 2H), 2.22-
2.03 (m, 2H), 1.92-1.81 (m, 1H), 1.78-1.68 (m, 2H), 1.63-1.55 (m, 2H), 1.41-1.33 (m,
14H), 1.30 (s, 6H), 1.07 (s, 9H).

$^{13}$C NMR (126 MHz, CDCl$_3$) δ 174.47, 169.12, 164.16, 154.78, 148.86, 146.41,
140.76, 138.88, 135.64, 126.50, 119.56, 115.67, 107.74, 60.44, 47.70, 40.03, 39.27,
36.49, 34.32, 30.85, 30.69, 29.72, 29.25, 28.31, 28.24, 28.06, 27.88, 27.58, 26.46, 26.28,
25.14, 23.87, 13.39.

MS (ESI): C$_{38}$H$_{56}$N$_3$O$_4$+, calcd. 618.4265, found 618.4270.

$^{6e}$: White solid.
**1H NMR** (500 MHz, CDCl₃) δ 8.33 (s, 1H), 7.44 – 7.32 (m, 5H), 7.27 (d, J = 7.2 Hz, 2H), 7.11 (d, J = 8.6 Hz, 2H), 6.49 – 6.08 (m, 1H), 6.08 (d, J = 7.0 Hz, 1H), 6.06 (s, 1H), 5.62 (s, 1H), 5.48 (s, 1H), 4.90 (dd, J = 15.3, 6.9 Hz, 1H), 3.88 (t, J = 7.6 Hz, 1H), 3.49 – 3.40 (m, 1H), 3.33 – 3.22 (m, 3H), 2.43 (s, 3H), 2.33 – 2.16 (m, 4H), 2.06 – 1.97 (m, 1H), 1.60 – 1.55 (m, 2H), 1.35 (s, 6H), 1.31 – 1.26 (m, 14H), 1.07 (s, 9H), 0.94 (d, J = 6.7 Hz, 3H), 0.78 (d, J = 6.7 Hz, 3H).

**13C NMR** (126 MHz, CDCl₃) δ 174.56, 171.68, 168.94, 164.28, 154.68, 148.75, 146.92, 141.00, 138.92, 136.66, 134.77, 129.33, 128.86, 127.17, 126.51, 120.38, 115.70, 107.83, 60.35, 54.79, 40.01, 39.13, 37.78, 36.44, 36.16, 31.17, 30.35, 29.93, 29.68, 29.08, 28.52, 28.42, 28.34, 28.10, 26.25, 25.24, 18.99, 18.69, 13.41.

**MS (ESI):** C₄₇H₇₁N₄O₅⁺, calcd. 767.5106, found 767.5106.

**6f:** White solid.

**1H NMR** (500 MHz, MeOD) δ 7.45 (d, J = 8.6 Hz, 2H), 7.33-7.29 (m, 3H), 7.28-7.21 (m, 2H), 7.14 (d, J = 8.7 Hz, 2H), 6.13 (s, 1H), 6.11 (d, J = 1.6 Hz, 1H), 4.85-4.82 (m, 1H), 4.28 (t, J = 7.2 Hz, 1H), 3.47-3.39 (m, 2H), 3.24-3.19 (m, 1H), 2.96-2.89 (m, 1H), 2.35 (s, 3H), 2.29-2.17 (m, 4H), 2.15-2.04 (m, 2H), 2.01 (s, 3H), 1.83-1.74 (m, 2H), 1.65-1.50 (m, 6H), 1.37 (s, 6H), 1.35-1.30 (m, J = 10.3, 5.2 Hz, 14H), 1.29 (s, 6H), 1.09 (s, 9H).

**13C NMR** (126 MHz, MeOD) δ 175.24, 172.89, 170.07, 165.14, 154.79, 148.57, 146.27, 141.02, 138.94, 137.31, 134.94, 128.90, 128.20, 126.50, 126.07, 120.37, 115.45, 108.41, 54.95, 53.38, 39.73, 38.65, 37.30, 35.90, 34.98, 30.42, 30.34, 30.08, 29.93, 29.38, 29.26, 28.77, 28.57, 28.52, 28.27, 26.13, 25.18, 13.71, 12.24.

**MS (ESI):** C₄₇H₇₁N₄O₅S⁺, calcd. 799.4827, found 799.4844.
6g: White solid.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.31 (s, 1H), 7.21 (d, $J=8.5$ Hz, 2H), 7.04 (d, $J=8.5$ Hz, 2H), 6.13 (s, 1H), 5.84 (m, 1H), 5.24 (s, 1H), 3.31 (dd, $J=14.3$, 6.4 Hz, 2H), 2.42 – 2.31 (m, 5H), 1.80 – 1.73 (m, 2H), 1.62 – 1.50 (m, 2H), 1.48 – 1.34 (m, 14H), 1.32 (s, 6H), 1.05 (s, $J=13.3$ Hz, 9H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 171.65, 164.49, 153.32, 148.41, 147.00, 141.74, 140.43, 134.42, 126.98, 120.38, 116.32, 108.47, 77.26, 39.57, 39.34, 36.87, 36.30, 31.51, 29.63, 29.21, 27.18, 27.12, 26.88, 26.65, 26.22, 25.87, 25.50, 24.28, 13.35.

HRMS (ESI): C$_{33}$H$_{49}$N$_2$O$_3$ $^+$, calcd. 520.2135, found 520.2128.

6h: White solid.

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 9.50 (s, 1H), 7.35 (d, $J=8.6$ Hz, 2H), 7.00 (d, $J=8.6$ Hz, 2H), 6.23 (s, 1H), 6.13 (dd, $J=7.9$, 3.9 Hz, 1H), 5.42 (d, $J=9.3$ Hz, 1H), 4.39 (s, 1H), 4.11 (t, $J=9.1$ Hz, 1H), 3.75 (dq, $J=15.9$, 7.9 Hz, 1H), 3.07 – 2.99 (m, 1H), 2.48 (s, 3H), 2.42 (ddd, $J=14.0$, 10.0, 6.7 Hz, 1H), 2.36 – 2.27 (m, 1H), 1.96 (td, $J=13.4$, 6.7 Hz, 1H), 1.88 – 1.73 (m, 2H), 1.61 – 1.55 (m, 2H), 1.46 – 1.24 (m, 20H), 1.01 (d, $J=6.7$ Hz, 3H), 0.99 (s, 9H), 0.94 (d, $J=6.7$ Hz, 3H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 172.29, 171.84, 164.10, 155.13, 148.56, 148.07, 143.10, 140.87, 135.57, 126.94, 120.22, 114.87, 107.33, 77.22, 59.07, 38.83, 38.55, 37.09, 36.28, 33.96, 31.19, 29.56, 28.63, 28.50, 28.34, 27.65, 27.37, 27.10, 26.83, 25.11, 24.82, 19.30, 19.04, 13.46.

HRMS (ESI): C$_{38}$H$_{58}$N$_3$O$_4$ $^+$, calcd. 620.2195, found 620.2191.
Supplementary Figure 5 \(^1\)H NMR (400 MHz, CDCl\(_3\)) spectrum of compound 1k

Supplementary Figure 6 \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) spectrum of compound 1k
Supplementary Figure 7 $^1$H NMR (400 MHz, CDCl$_3$) spectrum of compound 11

Supplementary Figure 8 $^{13}$C NMR (101 MHz, CDCl$_3$) spectrum of compound 11
Supplementary Figure 9 $^1$H NMR (400 MHz, CDCl$_3$) spectrum of compound 1m

Supplementary Figure 10 $^{13}$C NMR (101 MHz, CDCl$_3$) spectrum of compound 1m
Supplementary Figure 11 $^1$H NMR (400 MHz, CDCl$_3$) spectrum of compound 1n

Supplementary Figure 12 $^{13}$C NMR (101 MHz, CDCl$_3$) spectrum of compound 1n
Supplementary Figure 13 $^1$H NMR (400 MHz, CDCl$_3$) spectrum of compound 1o

Supplementary Figure 14 $^{13}$C NMR (101 MHz, CDCl$_3$) spectrum of compound 1o
Supplementary Figure 15 $^1$H NMR (400 MHz, CDCl$_3$) spectrum of compound 1p

Supplementary Figure 16 $^{13}$C NMR (101 MHz, CDCl$_3$) spectrum of compound 1p
**Supplementary Figure 17** $^1$H NMR (400 MHz, CDCl$_3$) spectrum of compound 3aa

**Supplementary Figure 18** $^{13}$C NMR (101 MHz, CDCl$_3$) spectrum of compound 3aa
Supplementary Figure 19 $^1$H NMR (400 MHz, CDCl$_3$) spectrum of compound 3ba

Supplementary Figure 20 $^{13}$C NMR (101 MHz, CDCl$_3$) spectrum of compound 3ba
Supplementary Figure 21 $^1$H NMR (400 MHz, CDCl$_3$) spectrum of compound 3ca

Supplementary Figure 22 $^{13}$C NMR (101 MHz, CDCl$_3$) spectrum of compound 3ca
Supplementary Figure 23 $^1$H NMR (400 MHz, CDCl$_3$) spectrum of compound 3da

Supplementary Figure 24 $^{13}$C NMR (101 MHz, CDCl$_3$) spectrum of compound 3da
Supplementary Figure 25 $^1$H NMR (400 MHz, CDCl$_3$) spectrum of compound 3ea

Supplementary Figure 26 $^{13}$C NMR (101 MHz, CDCl$_3$) spectrum of compound 3ea
Supplementary Figure 27 $^1$H NMR (400 MHz, CDCl$_3$) spectrum of compound 3fa

Supplementary Figure 28 $^{13}$C NMR (101 MHz, CDCl$_3$) spectrum of compound 3fa
Supplementary Figure 29 $^1$H NMR (400 MHz, CDCl$_3$) spectrum of compound 3ga

Supplementary Figure 30 $^{13}$C NMR (101 MHz, CDCl$_3$) spectrum of compound 3ga
Supplementary Figure 31 $^1$H NMR (400 MHz, CDCl$_3$) spectrum of compound 3ha

Supplementary Figure 32 $^{13}$C NMR (101 MHz, CDCl$_3$) spectrum of compound 3ha
**Supplementary Figure 33** $^1$H NMR (400 MHz, CDCl$_3$) spectrum of compound 3ja

**Supplementary Figure 34** $^{13}$C NMR (101 MHz, CDCl$_3$) spectrum of compound 3ja
Supplementary Figure 35 $^1$H NMR (400 MHz, CDCl$_3$) spectrum of compound 3ka

Supplementary Figure 36 $^{13}$C NMR (101 MHz, CDCl$_3$) spectrum of compound 3ka
Supplementary Figure 37 $^1$H NMR (400 MHz, CDCl$_3$) spectrum of compound 3la

Supplementary Figure 38 $^{13}$C NMR (101 MHz, CDCl$_3$) spectrum of compound 3la
Supplementary Figure 39 $^1$H NMR (400 MHz, CDCl$_3$) spectrum of compound 3ma

Supplementary Figure 40 $^{13}$C NMR (101 MHz, CDCl$_3$) spectrum of compound 3ma
Supplementary Figure 41 $^1$H NMR (400 MHz, CDCl$_3$) spectrum of compound 3na

Supplementary Figure 42 $^{13}$C NMR (101 MHz, CDCl$_3$) spectrum of compound 3na
Supplementary Figure 43 $^1$H NMR (400 MHz, CDCl$_3$) spectrum of compound 3oa

Supplementary Figure 44 $^{13}$C NMR (101 MHz, CDCl$_3$) spectrum of compound 3oa
Supplementary Figure 45 $^1$H NMR (400 MHz, CDCl$_3$) spectrum of compound $3pa$

Supplementary Figure 46 $^{13}$C NMR (101 MHz, CDCl$_3$) spectrum of compound $3pa$
Supplementary Figure 47 $^1$H NMR (400 MHz, CDCl$_3$) spectrum of compound 3ab

Supplementary Figure 48 $^{13}$C NMR (101 MHz, CDCl$_3$) spectrum of compound 3ab
Supplementary Figure 49 $^1$H NMR (400 MHz, CDCl$_3$) spectrum of compound 3ac

Supplementary Figure 50 $^{13}$C NMR (101 MHz, CDCl$_3$) spectrum of compound 3ac
Supplementary Figure 51 $^1$H NMR (400 MHz, CDCl$_3$) spectrum of compound 3ad

Supplementary Figure 52 $^{13}$C NMR (101 MHz, CDCl$_3$) spectrum of compound 3ad
Supplementary Figure 53 $^1$H NMR (400 MHz, CDCl$_3$) spectrum of compound 3ae

Supplementary Figure 54 $^{13}$C NMR (101 MHz, CDCl$_3$) spectrum of compound 3ae
Supplementary Figure 55 $^1$H NMR (400 MHz, CDCl$_3$) spectrum of compound 5aa

Supplementary Figure 56 $^{13}$C NMR (101 MHz, CDCl$_3$) spectrum of compound 5aa
Supplementary Figure 57 $^1$H NMR (400 MHz, CDCl$_3$) spectrum of compound 5ab

Supplementary Figure 58 $^{13}$C NMR (101 MHz, CDCl$_3$) spectrum of compound 5ab
**Supplementary Figure 59** $^1$H NMR (400 MHz, CDCl$_3$) spectrum of compound 5ac

**Supplementary Figure 60** $^{13}$C NMR (101 MHz, CDCl$_3$) spectrum of compound 5ac
Supplementary Figure 61 $^1$H NMR (400 MHz, CDCl$_3$) spectrum of compound 5ad

Supplementary Figure 62 $^{13}$C NMR (101 MHz, CDCl$_3$) spectrum of compound 5ad
Supplementary Figure 63 $^1$H NMR (400 MHz, CDCl$_3$) spectrum of compound 5ae

Supplementary Figure 64 $^{13}$C NMR (101 MHz, CDCl$_3$) spectrum of compound 5ae
Supplementary Figure 65 $^1$H NMR (400 MHz, CDCl$_3$) spectrum of compound 5af

Supplementary Figure 66 $^{13}$C NMR (101 MHz, CDCl$_3$) spectrum of compound 5af
Supplementary Figure 67 $^1$H NMR (400 MHz, CDCl$_3$) spectrum of compound 5ag

Supplementary Figure 68 $^{13}$C NMR (101 MHz, CDCl$_3$) spectrum of compound 5ag
Supplementary Figure 69 $^1$H NMR (400 MHz, CDCl$_3$) spectrum of compound 5ah

Supplementary Figure 70 $^{13}$C NMR (101 MHz, CDCl$_3$) spectrum of compound 5ah
Supplementary Figure 71 $^1$H NMR (400 MHz, CDCl$_3$) spectrum of compound 5cc

Supplementary Figure 72 $^{13}$C NMR (101 MHz, CDCl$_3$) spectrum of compound 5cc
Supplementary Figure 73 $^1$H NMR (400 MHz, CDCl$_3$) spectrum of compound 5ec

Supplementary Figure 74 $^{13}$C NMR (101 MHz, CDCl$_3$) spectrum of compound 5ec
Supplementary Figure 75 $^1$H NMR (400 MHz, CDCl$_3$) spectrum of compound 5jc

Supplementary Figure 76 $^{13}$C NMR (101 MHz, CDCl$_3$) spectrum of compound 5jc
Supplementary Figure 77 $^1$H NMR (400 MHz, CDCl$_3$) spectrum of compound 5kc

Supplementary Figure 78 $^{13}$C NMR (101 MHz, CDCl$_3$) spectrum of compound 5kc
Supplementary Figure 79 $^1$H NMR (400 MHz, CDCl$_3$) spectrum of compound 5lc

Supplementary Figure 80 $^{13}$C NMR (101 MHz, CDCl$_3$) spectrum of compound 5lc
Supplementary Figure 81 $^1$H NMR (400 MHz, CDCl$_3$) spectrum of compound 3ba-1

Supplementary Figure 82 $^{13}$C NMR (101 MHz, CDCl$_3$) spectrum of compound 3ba-1
Supplementary Figure 83 $^1$H NMR (400 MHz, CDCl$_3$) spectrum of compound 6a

Supplementary Figure 84 $^{13}$C NMR (101 MHz, CDCl$_3$) spectrum of compound 6a
Supplementary Figure 85 $^1$H NMR (400 MHz, CDCl$_3$) spectrum of compound 6b

Supplementary Figure 86 $^{13}$C NMR (101 MHz, CDCl$_3$) spectrum of compound 6b
Supplementary Figure 87 $^1$H NMR (400 MHz, CDCl$_3$) spectrum of compound 6c

Supplementary Figure 88 $^{13}$C NMR (101 MHz, CDCl$_3$) spectrum of compound 6c
Supplementary Figure 89 $^1$H NMR (400 MHz, CDCl$_3$) spectrum of compound 6d

Supplementary Figure 90 $^{13}$C NMR (101 MHz, CDCl$_3$) spectrum of compound 6d
Supplementary Figure 91 $^1$H NMR (400 MHz, CDCl$_3$) spectrum of compound 6e

Supplementary Figure 92 $^{13}$C NMR (101 MHz, CDCl$_3$) spectrum of compound 6e
Supplementary Figure 93 $^1$H NMR (400 MHz, CDCl$_3$) spectrum of compound 6f

Supplementary Figure 94 $^{13}$C NMR (101 MHz, CDCl$_3$) spectrum of compound 6f
Supplementary Figure 95 $^1$H NMR (400 MHz, CDCl$_3$) spectrum of compound 6g

Supplementary Figure 96 $^{13}$C NMR (101 MHz, CDCl$_3$) spectrum of compound 6g
**Supplementary Figure 97** $^1$H NMR (400 MHz, CDCl$_3$) spectrum of compound 6h

**Supplementary Figure 98** $^{13}$C NMR (101 MHz, CDCl$_3$) spectrum of compound 6h
Supplementary Figure 99. Uncropped and unprocessed scans of blots showed in Figure 6b.

Supplementary References

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