Supporting Information

Total Synthesis of Ophiorrhine A, G and Ophiorrhiside E Featuring a Bioinspired Intramolecular Diels–Alder Cycloaddition

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Featuring a Bioinspired Intramolecular Diels-Alder Cycloaddition

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1. General information

All reactions were carried out in anhydrous solvents under an inert argon atmosphere unless otherwise stated. Tetrahydrofuran (THF) and diethyl ether (Et\(_2\)O) were distilled from sodium-benzophenone before use. Dichloromethane (CH\(_2\)Cl\(_2\)) and toluene (PhMe) were distilled from calcium hydride before use. Methanol (MeOH) and acetone were distilled from calcium hydride and stored under argon atmosphere. All others commercial reagent-grade chemicals and solvents were used directly without further treatment unless noted. Reactions were monitored with analytical thin-layer chromatography (TLC) on silica gel 60 F254 plates and visualized under UV (254 nm) and/or by staining with phosphomolybdic acid hydrate solution in EtOH followed by heating or with KMnO\(_4\) in a K\(_2\)CO\(_3\) and NaOH aqueous solution. Flash chromatography were performed on silica gel 60 [63-200 μm]) as stationary phase. Preparative thin-layer chromatography (prep. TLC) were performed on silica gel 60 F254 plates. NMR spectra were recorded on Bruker AVANCE I 250 (250 MHz for \(^1\)H), Bruker AVANCE I 300 (300 MHz for \(^1\)H and 75 MHz for \(^13\)C), Bruker AVANCE I 360 (360 MHz for \(^1\)H and 90 MHz for \(^13\)C) and Bruker AVANCE I 400 (400 MHz for \(^1\)H and 100 MHz for \(^13\)C) instruments, at 295 K. Chemical shifts were reported in part per million relative to residual peak (CDCl\(_3\): \(^1\)H δ 7.26 ppm, \(^1^3\)C δ 77.16 ppm; CD\(_3\)OD: \(^1\)H δ 3.31 ppm, \(^1^3\)C δ 49.0 ppm). The mentioned abbreviations were as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad). High-Resolution mass spectra (HRMS) were measured on a Bruker Daltonics MicrOTOF-Q instrument by means of Electrospray Ionization (ESI) technic, with accurate masses reported for molecular ion [M+H]\(^+\) or [M+Na]\(^+\). \([\alpha]\)\(_D\) were recorded on an Anton Paar MCP150 polarimeter.
2. Optimizations of reaction conditions

1.1 Attempts towards the oxidation of N-methyl pyridinium 29 into pyridone 30

![Chemical structure of 29 and 30]

**Table S1. Attempts with K₃Fe(CN)₆**

| Entry | Substrate | Oxidative Conditions | Yield of 30a |
|-------|-----------|----------------------|--------------|
| 1     | 29a       | 2 eq. K₃Fe(CN)₆, 3 equiv. NaOH, THF/H₂O (2/1), r.t., 12h | N.D.         |
| 2     | 29a       | 4 eq. K₃Fe(CN)₆, 6 equiv. NaOH, THF/H₂O (2/1), 40 °C, overnight | N.D.         |
| 3     | 29a       | 3 eq. K₃Fe(CN)₆, 0.5 mL H₂SO₄ (60%), r.t., 4h | N.D.         |
| 4     | 29b       | 11 eq. K₃Fe(CN)₆, 11 equiv. NaOH, THF/H₂O (2/1), r.t., 12h | Complex mixture |

Reaction conditions: 0.025 mmol of 29 and 1.0 mL solvent were used.

a: isolated yield.

N.D. = No detected.

**Table S2. Attempts with a base in air.**

| Entry | Substrate | Oxidative Conditions | Yield of 30a |
|-------|-----------|----------------------|--------------|
| 1     | 29a       | 2 eq. t-BuOK, DMSO, r.t., air, 24 h | N.D.         |
| 2     | 29a       | 2 eq. t-BuOK, DMSO, 60 °C, air, 72 h | N.D.         |
| 3     | 29a       | 4 eq. Et₃N, DMSO, 150 °C, air, 3 h | N.R.         |
| 4b    | 29a       | 4 eq. NaH, DMSO, 150 °C, air, 7 h | N.D (74% of 31) |

Reaction conditions: 0.01 mmol of 29 and 0.5 mL solvent were used.

a: isolated yield.

N.D. = No detected.

N.R. = No reaction.

**Table S3. Attempts with a photocatalyst.**

| Entry | Substrate | Oxidative Conditions | Yield of 30a |
|-------|-----------|----------------------|--------------|
| 1     | 29a       | 0.1 eq. 2-hydroxybenzaldehyde, 1.5 eq. K₃PO₄, DMSO, air, r.t., LED light, 72h | N.R.         |
| 2     | 29a       | 0.02 eq. EosinY, 1.5 eq. Cs₂CO₃, DMSO, air, r.t., LED light, 24h | N.D. (10% of 31) |
| 3     | 29a       | 0.02 eq. EosinY, 1.5 eq. Cs₂CO₃, THF, air, r.t., LED light, 24h | N.D. (10% of 31) |
| 4b    | 29b       | 0.02 eq. EosinY, 1.5 eq Cs₂CO₃, THF, air, r.t., LED light, 24h | Complex mixture |

Reaction conditions: 0.05 mmol of 29 and 1.0 mL solvent were used.

a: isolated yield.

N.D. = No detected.

N.R. = No reaction.

**Table S4. Attempts in electrochemical conditions.**

| Entry | Substrate | Oxidative Conditions | Yield of 30a |
|-------|-----------|----------------------|--------------|
| 1     | 29a       | Graphite (anode) and Pt (cathode), 20 mA O₂, 1.5 eq Cs₂CO₃, 5 eq. Bu₄NBF₄, MeCN/H₂O (4/1) | N.R.         |
| 2     | 29a       | Graphite (anode) and Pt (cathode), 20 mA O₂, 5 eq. KI, 1.5 eq Cs₂CO₃, MeCN/H₂O (4/1) | N.R.         |

Reaction conditions: 0.15 mmol of 29a and 3.0 mL solvent were used.

a: isolated yield.

N.R. = No reaction.
1.2 Conversion of pyridine 28 into triflyloxypyridine 37 via pyridine N-oxide 33

![Conversion of Pyridine 28 into Triflyloxypyridine 37](image)

**Table S5. Optimization of the oxidation of pyridine 28a into pyridine N-oxide 33a.**

| Entry | Solvent          | Temp. | Eq. m-CPBA | Yield of 33a<sup>a</sup> |
|-------|------------------|-------|------------|--------------------------|
| 1     | CHCl<sub>3</sub> | rt    | 3.0        | 62%                      |
| 2     | CH<sub>2</sub>Cl<sub>2</sub> | rt    | 3.0        | 46%                      |
| 3     | CHCl<sub>3</sub>:EtOH (1:1) | reflux | 3.0        | 75%                      |
| 4<sup>b</sup> | CHCl<sub>3</sub>:EtOH (1:1) | reflux | 5.0        | 83%                      |

Reaction Conditions: 28a (0.1 mmol) in solvent (c = 0.1M), overnight.

a. Isolated yields.

b. 1.0 mmol of 28a was used.

**Table S6. Optimization of synthesis of triflyloxypyridine 37a from pyridine N-oxide 33a with Tf<sub>2</sub>O.**

| Entry | Eq. Tf<sub>2</sub>O | Eq. Et<sub>3</sub>N | Temp. | Yield of 37a<sup>a</sup> |
|-------|---------------------|---------------------|-------|--------------------------|
| 1     | 1.1                 | 2.2                 | -78 °C | 23%                      |
| 2     | 5                   | 10                  | -78 °C | 25%                      |
| 3     | 5                   | 10                  | 0 °C   | 38%                      |
| 4     | 5                   | 10                  | r.t.   | 74%                      |
| 5     | 1.1                 | 2.2                 | r.t.   | 27%                      |
| 6     | 3                   | 6                   | r.t.   | 59%                      |
| 7     | 7                   | 14                  | r.t.   | 26%                      |

Reaction Conditions: 33a (0.1 mmol) and 1 mL of CH<sub>2</sub>Cl<sub>2</sub> were used.

a. Isolated yields.

1.3 Synthesis of hydroxypyridine 43a via A Pd-catalyzed coupling of indolyacetic acid with a nitrile
Table S8. Optimization of Pd-catalyzed synthesis of 43a from 15b/c and 42.

| Entry | 15b or 15c, eq. | Solvent                  | Yield of 43a<sup>c</sup> |
|-------|----------------|--------------------------|--------------------------|
| 1     | 15b, 0.67      | THF/HOAc (3:1)           | 17%                      |
| 2     | 15c, 0.67      | THF/HOAc (3:1)           | 22%                      |
| 3     | 15c, 5.00      | THF/HOAc (3:1)           | 45%                      |
| 4     | 15c, 5.00      | THF                      | 5%                       |
| 5     | 15c, 5.00      | NMF                      | trace                    |
| 6<sup>a</sup> | 15c, 5.00 | THF                      | trace                    |
| 6<sup>a</sup> | 15c, 5.00 | NMF                      | trace                    |
| 7     | 15c, 5.00      | THF/HOAc (3:1)           | N.D.                     |

Reaction conditions: 0.6 mmol of 42, 0.06 mmol of Pd(OAc)<sub>2</sub>, 0.072 mmol of bpy and 1.6 mL solvent were used.

a: 10 % TFA was used.
b: (E)-N,3,7-trimethyloct-6-en-1-imine was used instead of nitrile 42.
c: isolated yield.
N.D. = No detected.

1.4 Acylation of indolylacetic acid derivatives with a carboxylic acid

Table S9. Optimization of the acylation of indolylacetic acid methyl ester 15b with 5-hexenoic acid 44.

| Entry | X      | Lewis acid | Solvent  | Temp.   | Time   | Yield of 46b<sup>a</sup> |
|-------|--------|------------|----------|---------|--------|--------------------------|
| 1     | C(O)CF<sub>3</sub> | 3 eq. ZnCl<sub>2</sub> | CH<sub>2</sub>Cl<sub>2</sub> | r.t.    | 24 h   | 11%                      |
| 2     | C(O)CF<sub>3</sub> | 3 eq. BF<sub>3</sub>::OTef | CH<sub>2</sub>Cl<sub>2</sub> | r.t.    | 24 h   | 12%                      |
| 3     | Cl     | 0.1 eq. Bi(OTf)<sub>3</sub> | MeNO<sub>2</sub> | 0 °C    | 40 min | decomposed               |
| 4     | Cl     | 5.0 eq. TiCl<sub>4</sub> | Et<sub>2</sub>O | 0 °C to r.t. | overnight | Trace                   |
| 5     | Cl     | 2.0 eq. TiCl<sub>4</sub> | Et<sub>2</sub>O | 0 °C to r.t. | overnight | 17%                      |
| 6     | Cl     | 1.0 eq. TiCl<sub>4</sub> | Et<sub>2</sub>O | 0 °C to r.t. | overnight | 35%                      |
| 7     | Cl     | 0.5 eq. TiCl<sub>4</sub> | Et<sub>2</sub>O | 0 °C to r.t. | overnight | 35%                      |
| 8     | Cl     | 0.3 eq. TiCl<sub>4</sub> | Et<sub>2</sub>O | 0 °C to r.t. | overnight | 56%                      |
| 9     | Cl     | 0.1 eq. TiCl<sub>4</sub> | Et<sub>2</sub>O | 0 °C to r.t. | overnight | 59%                      |
| 10    | Cl     | 0.05 eq. TiCl<sub>4</sub> | Et<sub>2</sub>O | 0 °C to r.t. | overnight | 56%                      |
| 11    | Cl     | 0.1 eq. TiCl<sub>4</sub> | Et<sub>2</sub>O | 0 °C to r.t. | overnight | 63%                      |
| 12    | Cl     | 0.03 eq. SnCl<sub>4</sub> | Et<sub>2</sub>O | 0 °C to r.t. | overnight | 42%                      |
| 13    | Cl     | 0.05 eq. SnCl<sub>4</sub> | Et<sub>2</sub>O | 0 °C to r.t. | overnight | 49%                      |
| 14    | Cl     | 0.07 eq. SnCl<sub>4</sub> | Et<sub>2</sub>O | 0 °C to r.t. | overnight | 56%                      |
| 15    | Cl     | 0.09 eq. SnCl<sub>4</sub> | Et<sub>2</sub>O | 0 °C to r.t. | overnight | 56%                      |
| 16    | Cl     | 0.1 eq. SnCl<sub>4</sub> | Et<sub>2</sub>O | 0 °C to r.t. | overnight | 80%                      |
| 17    | Cl     | 0.3 eq. SnCl<sub>4</sub> | Et<sub>2</sub>O | 0 °C to r.t. | overnight | 73%                      |
| 18    | Cl     | 0.5 eq. SnCl<sub>4</sub> | Et<sub>2</sub>O | 0 °C to r.t. | overnight | 63%                      |
| 19    | Cl     | 1.0 eq. SnCl<sub>4</sub> | Et<sub>2</sub>O | 0 °C to r.t. | overnight | 56%                      |

Reaction conditions (entries 1-2): 0.6 mmol of 15b, 0.5 mmol of carboxylic acid, 0.65 mmol of trifluoroacetic anhydride and 1 mL solvent were used.
Reaction conditions (entries 3-19): 0.1 mmol of 15b, 0.12 mmol of carboxylic acid, 0.156 mmol of oxalyl chloride and 1 mL solvent were used.
a: Isolated yield.

Table S10. Optimization of the acylation of indolylacetamide 15a with 5-hexenoic acid 44.

| Entry | X  | Lewis acid | Solvent | Temp. | Time | Yield of 46a<sup>a</sup> |
|-------|----|------------|---------|-------|------|----------------------|
| 1     | C(O)CF<sub>3</sub> | 3 eq. ZnCl<sub>2</sub> | CH<sub>2</sub>Cl<sub>2</sub> | r.t.  | 24 h | trace                |
| 2     | C(O)CF<sub>3</sub> | 3 eq. BF<sub>3</sub>·OEt<sub>2</sub> | CH<sub>2</sub>Cl<sub>2</sub> | r.t.  | 24 h | trace                |
| 3     | Cl  | 0.1 eq. Bi(OTf)<sub>3</sub> | MeNO<sub>2</sub> | 0 °C | overnight | N.D.          |
| 4     | Cl  | 3.0 eq. SnCl<sub>4</sub> | Et<sub>2</sub>O | 0 °C to r.t. | | decomposed |
| 5     | Cl  | 2.5 eq. SnCl<sub>4</sub> | Et<sub>2</sub>O : CH<sub>2</sub>Cl<sub>2</sub> (3:1) | 0 °C to r.t. | 4 h | 24%          |
| 6     | Cl  | 2.0 eq. SnCl<sub>4</sub> | Et<sub>2</sub>O : CH<sub>2</sub>Cl<sub>2</sub> (3:1) | 0 °C to r.t. | 4 h | 10%          |
| 7     | Cl  | 1.5 eq. SnCl<sub>4</sub> | Et<sub>2</sub>O : CH<sub>2</sub>Cl<sub>2</sub> (3:1) | 0 °C to r.t. | 4 h | 14%          |
| 8     | Cl  | 1.0 eq. SnCl<sub>4</sub> | Et<sub>2</sub>O : CH<sub>2</sub>Cl<sub>2</sub> (3:1) | 0 °C to r.t. | 4 h | 45%          |
| 9     | Cl  | 0.5 eq. SnCl<sub>4</sub> | Et<sub>2</sub>O : CH<sub>2</sub>Cl<sub>2</sub> (3:1) | 0 °C to r.t. | 4 h | 38%          |
| 10    | Cl  | 1.0 eq. SnCl<sub>4</sub> | Et<sub>2</sub>O | 0 °C to r.t. | 4 h | 10%          |
| 11    | Cl  | 1.0 eq. SnCl<sub>4</sub> | CH<sub>2</sub>Cl<sub>2</sub> | 0 °C to r.t. | 4 h | 7%           |
| 12    | Cl  | 1.0 eq. SnCl<sub>4</sub> | Et<sub>2</sub>O : CH<sub>2</sub>Cl<sub>2</sub> (2:1) | 0 °C to r.t. | 4 h | 52%          |
| 13    | Cl  | 1.0 eq. SnCl<sub>4</sub> | Et<sub>2</sub>O : CH<sub>2</sub>Cl<sub>2</sub> (1:1) | 0 °C to r.t. | 4 h | 52%          |
| 14    | Cl  | 1.0 eq. SnCl<sub>4</sub> | Et<sub>2</sub>O : CH<sub>2</sub>Cl<sub>2</sub> (1:2) | 0 °C to r.t. | 4 h | 14%          |
| 15    | Cl  | 1.0 eq. SnCl<sub>4</sub> | Et<sub>2</sub>O : CH<sub>2</sub>Cl<sub>2</sub> (1:3) | 0 °C to r.t. | 4 h | 7%           |
| 16    | Cl  | 1.0 eq. SnCl<sub>4</sub> | Et<sub>2</sub>O : CH<sub>2</sub>Cl<sub>2</sub> (3:1) | 0 °C to r.t. | overnight | 45%          |
| 17    | Cl  | 2.5 eq. SnCl<sub>4</sub> | Et<sub>2</sub>O : CH<sub>2</sub>Cl<sub>2</sub> (3:1) | 0 °C to r.t. | 4 h | 24%          |
| 18    | Cl  | 2.0 eq. SnCl<sub>4</sub> | Et<sub>2</sub>O : CH<sub>2</sub>Cl<sub>2</sub> (3:1) | 0 °C to r.t. | 4 h | 10%          |
| 19    | Cl  | 1.5 eq. SnCl<sub>4</sub> | Et<sub>2</sub>O : CH<sub>2</sub>Cl<sub>2</sub> (3:1) | 0 °C to r.t. | 4 h | 14%          |
| 20    | Cl  | 1.0 eq. SnCl<sub>4</sub> | Et<sub>2</sub>O : CH<sub>2</sub>Cl<sub>2</sub> (3:1) | 0 °C to r.t. | 4 h | 45%          |
| 21    | Cl  | 0.5 eq. SnCl<sub>4</sub> | Et<sub>2</sub>O : CH<sub>2</sub>Cl<sub>2</sub> (3:1) | 0 °C to r.t. | 4 h | 38%          |

Reaction conditions (entries 1-2): 0.6 mmol of 15a, 0.5 mmol of carboxylic acid, 0.65 mmol of trifluoroacetic anhydride and 1 mL solvent were used.

Reaction conditions (entries 3-21): 0.12 mmol of 15a, 0.10 mmol of carboxylic acid, 0.13 mmol of oxalyl chloride and 1 mL solvent were used.
a: Isolated yield.
N.D. = No Detected.

Table S11. Optimization of acylation of indolylacetic acid methyl ester 15b with 24.

| Entry | Conditions                      | Yield of 50b<sup>a</sup> | Recovered 24<sup>a</sup> |
|-------|--------------------------------|------------------------|-----------------------|
| 1     | TiCl<sub>4</sub> (0.1 eq.), Et<sub>2</sub>O, 0 °C to r.t., overnight | 16%                    | 70%                   |
| 2     | SnCl<sub>4</sub> (0.1 eq.), Et<sub>2</sub>O, 0 °C to r.t., overnight | 27%                    | 56%                   |
| 3     | SnCl<sub>4</sub> (0.05 eq.), Et<sub>2</sub>O, 0 °C to r.t., overnight | 27%                    | 38%                   |
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Reaction conditions: 0.12 mmol of 15b, 0.1 mmol of carboxylic acid, 0.156 mmol of oxalyl chloride and 1 mL solvent were used.

a: isolated yield.
b: 0.2 mmol of oxalyl chloride was used.

| Entry  | Conditions | Yield of 50a o |
|--------|------------|---------------|
| 1      | 1.0 eq. SnCl4, Et2O : CH2Cl2 (1:1), 0 °C to r.t., 4 h | 9% |
| 2      | 1.0 eq. SnCl4, Et2O : CH2Cl2 (1:1), 0 °C to r.t., 24 h | 33% |
| 3      | 1.2 eq. SnCl4, Et2O : CH2Cl2 (1:1), 0 °C to r.t., 4 h | 6% |
| 4      | 8.0 eq. SnCl4, Et2O : CH2Cl2 (1:1), 0 °C, 10 min | 33% |
| 5      | 1.0 eq. SnCl4, Et2O : CH2Cl2 (3:1), 0 °C to r.t., 24 h | 40% |
| 6      | 2.0 eq. SnCl4, Et2O : CH2Cl2 (3:1), -20 °C (5 h) to 0 °C (19 h) | 44% |
| 7      | 1.0 eq. SnCl4, Et2O : CH2Cl2 (4:1), 0 °C to r.t., 24h | 44% |
| 8      | 1.0 eq. SnCl4, Et2O, 0 °C to r.t., 24 h | 33% |
| 9      | 2.0 eq. SnCl4, Et2O : CH2Cl2 (4:1), 0 °C, 24 h | 40% |
| 10     | 2.0 eq. SnCl4, Et2O : CH2Cl2 (4:1), -20 °C, 24 h | 30% |

Reaction conditions: Entries 1 and 3-10: 0.08 mmol of 15a, 0.04 mmol of carboxylic acid, 0.08 mmol of oxalyl chloride and 0.5 mL solvent were used. Entry 2: 0.16 mmol of 15a, 0.08 mmol of carboxylic acid, 0.16 mmol of oxalyl chloride and 1.0 mL solvent were used.
a: Isolated yield.

1.5 Cyclodehydration of protected ophiorrhine G and tandem Diels-Alder cycloaddition into protected ophiorrhine A.

| Entry  | Cyclodehydration Conditions | Recovered 50a | Yield of 54 | Yield of 55 |
|--------|-----------------------------|---------------|-------------|-------------|
| 1      | 5 eq. Et3N, AcOH, 80 °C, 3h | 77% | 0% | N.D. |
| 2      | 5 eq. Et3N AcOH, r.t. to 115 °C, 2 h | 40% | 20% | trace |
| 3      | 45 eq. Et3N (added in 3 times), AcOH - 115 °C, 3 h | 30% | 40% | trace |
| 4      | 45 eq. Et3N (added in 3 times), AcOH, 80 °C, 18 h | 41% | 8% | N.D. |
| 5      | 45 eq. Et3N, AcOH, 125 °C, 6 h | trace | 58% | 29% |
| 6      | 200 eq. Et3N, 200 eq. AcOH, 80 °C, 18h | 50% | 25% | N.D. |
| 7      | 5 eq. Et3N, AcOH, 80 °C, 43h | 22% | 45% | N.D. |

a: Isolated yield.
3. Experimental procedures and data of all compounds.

**Compound 28a: 1-isobutyl-9H-pyrido[3,4-b]indole**

Inspired from a known procedure.\(^1\)

To a solution of the L-tryptophan 12 (1.02 g, 5.00 mmol) in CH\(_2\)Cl\(_2\) (25 mL) at room temperature was added 3-methylbutanal 27 (1.07 mL, 10 mmol), and then TFA (1.48 mL, 20 mmol) dropwise at 0 °C. The temperature was then allowed to warm up to room temperature and the reaction mixture was stirred at this temperature overnight. Then, the reaction mixture was concentrated under reduced pressure to remove TFA and CH\(_2\)Cl\(_2\). The mixture was dissolved in 50 mL of DMF, followed by addition of NCS (1.4 g, 10.5 mmol) and Et\(_3\)N (1.75 mL, 12.5 mmol) dropwise at 0 °C. The mixture was stirred at room temperature for 3 h and then quenched with water. The mixture was diluted with EtOAc and washed 3 times with a saturated aqueous solution of NaCl after which the organic layer was dried over Na\(_2\)SO\(_4\), filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (CH\(_2\)Cl\(_2\)/MeOH 25:1 to 20:1) to give 627 mg of 28a as a colorless solid (56% yield).

\(R_f = 0.41\) (Petroleum ether/ Ethyl acetate 1:1)

\(^1\)H NMR (360 MHz, MeOD) \(\delta\) 8.16 (d, \(J = 5.4\) Hz, 1H), 8.08 (dt, \(J = 8.1, 1.1\) Hz, 1H), 7.86 (d, \(J = 5.4\) Hz, 1H), 7.56 (dt, \(J = 8.1, 1.1\) Hz, 1H), 7.50 (ddd, \(J = 8.1, 6.9, 1.1\) Hz, 1H), 7.20 (ddd, \(J = 8.1, 6.9, 1.1\) Hz, 1H), 2.98 (d, \(J = 7.5\) Hz, 2H), 2.31 – 2.18 (m, 1H), 0.97 (d, \(J = 6.6\) Hz, 6H).

\(^{13}\)C NMR (90 MHz, MeOD) \(\delta\) 146.5, 142.5, 137.8, 136.3, 130.0, 129.4, 122.6, 120.6, 114.0, 112.8, 43.5, 30.2, 22.9 (2C).

HRMS (m/z): [M + H]\(^+\) calcd. for C\(_{15}\)H\(_{17}\)N\(_2\) 225.1386, found 225.1380.

**Compound 29a: 1-isobutyl-2-methyl-9H-pyrido[3,4-b]indol-2-ium iodide**

Inspired from a known procedure.\(^2\)

To a solution of pyridine 28a (224 mg, 1.00 mmol) in CH\(_3\)CN (2 mL) was added CH\(_3\)I (3.1 mL, 50 mmol) under argon. The mixture was heated at 80 °C for 21 h and then cooled to room temperature. Removal of the solvent under reduced pressure afforded the crude product, which was purified by recrystallization in an CH\(_3\)CN/EtOAc cosolvent system to give 340 mg of 29a as a red solid (93% yield).

\(R_f = 0.30\) (CH\(_2\)Cl\(_2\)/MeOH 10:1)

\(^1\)H NMR (360 MHz, MeOD) \(\delta\) 8.54 – 8.46 (m, 2H), 8.38 (dt, \(J = 8.0, 1.0\) Hz, 1H), 7.84 – 7.75 (m, 2H), 7.46 (ddd, \(J = 8.0, 6.5, 1.0\) Hz, 1H), 4.48 (s, 3H), 3.43 (d, \(J = 7.7\) Hz, 2H), 2.42 – 2.32 (m, 1H), 1.10 (d, \(J = 6.6\) Hz, 6H).

\(^{13}\)C NMR (90 MHz, MeOD) \(\delta\) 145.6, 144.3, 137.0, 136.1, 133.7, 133.2, 124.2, 123.1, 121.4, 116.9, 113.8, 45.5, 38.2, 29.7, 22.6 (2C).
HRMS (m/z): [M]$^+$ calcd. for C$_{16}$H$_{19}$N$_2$ 239.1543, found 239.1537.

**Compound 31**: 2-(2-(hex-5-enoyl)-1H-indol-3-yl)-N-methylacetamide

Inspired from a known procedure.\(^3\)

To a solution of pyridinium 29a (18.3 mg, 0.0500 mmol) in DMSO (1 mL) at room temperature was added EosinY (1 mg) and Cs$_2$CO$_3$ (24.0 mg, 0.075 mmol). The reaction mixture was stirred at this temperature under CFL irradiation for about 1 day. The reaction mixture was washed with a saturated aqueous solution of NaCl after which the organic layer was dried over Na$_2$SO$_4$, filtered and concentrated under reduced pressure. The residue was purified by preparative TLC (CH$_2$Cl$_2$/MeOH:10/1) to afforded 31 (3 mg) as colorless solid in 10% yield.

To a solution of pyridinium 29a (5.0 mg, 0.0137 mmol) in DMSO (0.5 mL) was added NaH (1 mg, 4.0 eq) at room temperature. The reaction mixture was heated to 150 °C and stirred at this temperature overnight. The reaction mixture was cooled down to room temperature and diluted with 2 mL of CH$_2$Cl$_2$ and was washed with a saturated aqueous solution of NaCl. The organic layer was dried over Na$_2$SO$_4$, filtered and concentrated under reduced pressure. The residue was purified by preparative TLC (CH$_2$Cl$_2$/MeOH:10/1) to afford 31 (2 mg) as colorless solid in 74% yield.

R$_f$ = 0.50 (CH$_2$Cl$_2$/MeOH 10:1)

$^1$H NMR (360 MHz, MeOD) δ 7.99 (dt, $J = 8.1, 1.0$ Hz, 1H), 7.57 (dt, $J = 8.1, 1.0$ Hz, 1H), 7.47 (ddd, $J = 8.1, 6.8, 1.0$ Hz, 1H), 7.33 (d, $J = 6.9$ Hz, 1H), 7.22 (ddd, $J = 8.1, 6.8, 1.0$ Hz, 1H), 7.11 (d, $J = 6.9$ Hz, 1H), 3.73 (s, 3H).

$^{13}$C NMR (90 MHz, MeOD) δ 157.6, 141.3, 130.2, 128.1, 126.8, 123.5, 122.2, 121.1, 113.4, 102.8, 37.2.

HRMS (m/z): [M + H]$^+$ calcd. for C$_{12}$H$_{11}$N$_2$O 199.0866, found 199.0863

[M + Na]$^+$ calcd. for C$_{12}$H$_{11}$N$_3$NaO$^+$ 221.0685, found 221.0683.

**Compound (±)-28**: methyl -4-((9H-pyrido[3,4-b]indol-1-yl)methyl)-2-ethoxy-3-vinyl-3,4-dihydro-2H-pyran-5-carboxylate

Inspired from a known procedure.\(^1\)
To a solution of \(L\)-tryptophan 12 (46 mg, 0.228 mmol) in CH\(_2\)Cl\(_2\) (3 mL) at room temperature was added (±)-16 (29 mg, 0.114 mmol), which was prepared according our previous adaptation of Tietze procedures.\(^4\) TFA (65 mg, 0.571 mmol) was then added dropwise at 0 °C under argon. Then, the temperature was allowed to warm up to room temperature and the reaction mixture stirred at this temperature overnight. The reaction mixture was concentrated under reduced pressure to remove TFA and CH\(_2\)Cl\(_2\). The mixture was dissolved in 2 mL of DMF, followed by addition of NCS (64 mg, 0.479 mmol) and Et\(_3\)N (58 mg, 0.571 mmol) dropwise at 0 °C. Then the mixture was stirred at room temperature for 3 h and quenched with water. The mixture was diluted with EtOAc and washed 3 times with a saturated aqueous solution of NaCl. The organic phase was dried over Na\(_2\)SO\(_4\), filtered and concentrated under reduced pressure. The residue was purified by preparative TLC on silica gel (CH\(_2\)Cl\(_2\)/MeOH 18:1) to give 13 mg of (±)-28b as a pale yellow solid (29% yield).

\(R_f = 0.50\) (CH\(_2\)Cl\(_2\)/MeOH 10:1)

\(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 11.04 (s, 1H), 8.27 (d, \(J = 5.4\) Hz, 1H), 8.12 (dt, \(J = 8.0, 1.0\) Hz, 1H), 7.86 (d, \(J = 5.4\) Hz, 1H), 7.66 (dt, \(J = 8.0, 1.0\) Hz, 1H), 7.63 (s, 1H), 7.57 (ddd, \(J = 8.0, 7.0, 1.0\) Hz, 1H), 7.30 (ddd, \(J = 8.0, 7.0, 1.0\) Hz, 1H), 6.02 (dt, \(J = 17.0, 10.3\) Hz, 1H), 5.31 (d, \(J = 8.2\) Hz, 1H), 4.85 (dd, \(J = 17.0, 1.0\) Hz, 1H), 4.78 (dd, \(J = 10.3, 1.5\) Hz, 1H), 3.97 (dd, \(J = 9.7, 7.1\) Hz, 1H), 3.89 (s, 3H), 3.71 (dd, \(J = 9.7, 7.1\) Hz, 1H), 3.54 – 3.45 (m, 1H), 3.40 – 3.31 (m, 2H), 2.61 – 2.52 (m, 1H), 1.24 (t, \(J = 7.1\) Hz, 3H).

\(^13\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 169.5, 154.4, 144.3, 140.9, 136.3, 134.8, 129.0, 128.5, 121.8, 121.5, 119.9, 118.4, 113.7, 112.3, 109.3, 100.7, 66.0, 52.1, 46.3, 38.0, 35.0, 15.2.

HRMS (m/z): [M + H]\(^+\) calcd. for C\(_{27}\)H\(_{25}\)N\(_2\)O\(_4\) \(\delta\) 407.1965, found 407.1965.

**Compound (±)-29b:** 2-ethoxy-5-(methoxycarbonyl)-3-vinyl-3,4-dihydro-2\(H\)-pyran-4-yl)methyl)-2-methyl-9\(H\)-pyrido[3,4-b]indol-2-ium iodide \(^2\)

![Chemical Structure](image)

*Inspired from a known procedure.*

To a solution of (±)-28b (12.6 mg, 0.0321 mmol) in CH\(_3\)CN (1.5 mL) was added CH\(_3\)I (229 mg, 1.607 mmol) under argon. The mixture was heated at 80 °C (heated by oil bath) for 21 h and then cooled to room temperature. Removal of the solvent under reduced pressure afforded the crude product, which was purified by preparative TLC (CH\(_2\)Cl\(_2\)/MeOH:10:1) to give 11 mg of (±)-29b as a red solid (64% yield).

\(R_f = 0.31\) (CH\(_2\)Cl\(_2\)/MeOH 10:1)

\(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 12.24 (s, 1H), 8.24 – 8.20 (m, 2H), 8.13 – 8.06 (m, 2H), 7.71 (t, \(J = 7.8\) Hz, 1H), 7.43 (s, 1H), 7.40 (t, \(J = 7.8\) Hz, 1H), 6.33 (d, \(J = 9.3\) Hz, 1H), 5.90 (ddd, \(J = 17.0, 10.5, 7.8\) Hz, 1H), 5.35 (d, \(J = 10.5\) Hz, 1H), 5.32 (d, \(J = 17.0\) Hz, 1H), 4.25 – 4.05 (m, 5H), 3.93 (t, \(J = 13.0\) Hz, 1H), 3.12 – 2.99 (m, 2H), 2.78 (s, 3H), 2.66 – 2.55 (m, 1H), 1.32 (t, \(J = 7.1\) Hz, 3H).

\(^13\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 167.5, 156.2, 143.9, 141.4, 135.6, 134.4, 134.1, 131.9, 131.1, 123.0, 122.2, 119.7, 119.2, 116.1, 114.2, 105.0, 99.7, 66.4, 50.9, 44.6, 44.3, 35.0, 32.2, 15.6.

HRMS (m/z): [M]\(^+\) calcd. for C\(_{34}\)H\(_{27}\)N\(_2\)O\(_4\) \(\delta\) 407.1965, found 407.1965.
Compound 33a: 1-isobutyl-9H-pyrido[3,4-b]indole 2-oxide

Inspired from known procedures.\(^5\)

A solution of pyridine 28a (224 mg, 1.00 mmol) in 10 mL of CHCl\(_3\)\_EtOH (1:1) was treated with \(m\)-CPBA (865 mg, 5.0 mmol) at room temperature after which the reaction mixture was heated to 80 °C overnight. Then, the reaction mixture was cooled down and a saturated aqueous solution of NaHCO\(_3\) was added and stirred at 0 °C for about 10 min. The aqueous layer was extracted 3 times with CH\(_2\)Cl\(_2\). The combined organic layers were dried with Na\(_2\)SO\(_4\), filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (Petroleum ether/ EtOAc 1:1 to CH\(_2\)Cl\(_2\)/MeOH 30:1) to give 166 mg of 33a as a colorless solid (83% yield).

\(R_f = 0.66\) (CH\(_2\)Cl\(_2\)/Methanol 10:1)

\(^1\)H NMR (360 MHz, MeOD) \(\delta\) 8.11 (d, \(J = 6.7\) Hz, 1H), 8.04 (d, \(J = 7.9\) Hz, 1H), 7.94 (d, \(J = 6.7\) Hz, 1H), 7.50 – 7.47 (m, 2H), 7.24 (t, \(J = 7.9\) Hz, 1H), 3.15 (d, \(J = 6.9\) Hz, 2H), 2.51 – 2.43 (m, 1H), 0.99 (d, \(J = 6.9\) Hz, 6H).

\(^{13}\)C NMR (100 MHz, MeOD) \(\delta\) 143.7, 138.8, 137.5, 132.0, 129.4, 124.0, 122.3, 121.8, 115.6, 112.9, 36.3, 27.7, 22.8.

HRMS (m/z): [M + H]\(^+\) calcd. for C\(_{15}\)H\(_{17}\)N\(_2\)O\(^+\) 241.1334, found 241.1330.

Compound (±)-34a: 2-methyl-1-(9H-pyrido[3,4-b]indol-1-yl)propyl acetate

Inspired from known procedures.\(^5\)

A solution of pyridine N-oxide 33a (15 mg, 0.0625 mmol) in acetic anhydride (3.5 mL) was refluxed at 165 °C for 3 h. Then, the reaction mixture was cooled down and a saturated aqueous solution of NaHCO\(_3\) was added and the mixture was stirred at 0 °C for about 10 min. The resulting mixture was extracted 3 times with CH\(_2\)Cl\(_2\). The combined organic layers were dried over Na\(_2\)SO\(_4\), filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (CH\(_2\)Cl\(_2\)/MeOH 50:1 to 30:1) to give 11 mg of (±)-34a as a colorless solid (62% yield).

\(R_f = 0.66\) (CH\(_2\)Cl\(_2\)/Methanol 10:1)

\(^1\)H NMR (250 MHz, MeOD) \(\delta\) 8.24 (d, \(J = 5.3\) Hz, 1H), 8.15 (dt, \(J = 8.0, 1.0\) Hz, 1H), 8.01 (d, \(J = 5.3\) Hz, 1H), 7.62 (dt, \(J = 8.0, 1.0\) Hz, 1H), 7.55 (dd, \(J = 8.0, 7.0, 1.0\) Hz, 1H), 7.25 (dd, \(J = 8.0, 7.0, 1.0\) Hz, 1H), 5.90 (d, \(J = 8.6\) Hz, 1H), 2.63 – 2.36 (m, 1H), 2.12 (s, 3H), 1.16 (d, \(J = 6.6\) Hz, 3H), 0.81 (d, \(J = 6.6\) Hz, 3H).

\(^{13}\)C NMR (62.5 MHz, MeOD) \(\delta\) 172.3, 143.8, 142.8, 137.9, 135.1, 131.2, 129.8, 122.5, 122.1, 120.9, 115.4, 112.9, 80.7, 33.5, 20.7, 19.3, 18.8.

HRMS (m/z): [M + H]\(^+\) calcd. for C\(_{17}\)H\(_{18}\)N\(_2\)O\(_2\)\(^+\) 283.1441, found 283.1434.

Compound (±)-35a: 1-(1-acetoxy-2-methylpropyl)-9H-pyrido[3,4-b]indol-3-yl acetate
Inspired from known procedures. A solution of pyridine acetate (±)-34a (150 mg, 0.531 mmol) in CHCl₃/EtOH (1:1) 15 mL was treated with m-CPBA (450 mg, 2.65 mmol) at room temperature after which the reaction mixture was heated to 80 °C for about 18 h. Then, the reaction mixture was cooled down and a saturated aqueous solution of NaHCO₃ was added and the mixture was stirred at 0 °C for about 10 min. The resulting mixture was extracted 3 times with CH₂Cl₂. The combined organic layers were dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (CH₂Cl₂/MeOH 50:1 to 30:1) to give 124 mg of 1-acetoxy-2-methylpropyl-9H-pyrido[3,4-b]indole 2-oxide as a colorless solid (78% yield).

A solution of this pyridine N-oxide (120 mg, 0.402 mmol) in acetic anhydride (18 mL) was reflux at 165 °C for 3 h. Then the reaction mixture was cooled down and NaHCO₃ (aq.) was added and stirred at 0 °C for about 10 min. The resulting mixture was extracted 3 times with CH₂Cl₂. The combined organic layers were dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (CH₂Cl₂/MeOH 50:1 to 30:1) to give 32 mg of (±)-35a as a colorless solid (23% yield).

**Rf** = 0.38 (CH₂Cl₂/MeOH 30:1)

**¹H NMR** (360 MHz, MeOD) δ 8.15 (dt, J = 8.0, 1.0 Hz, 1H), 7.73 (s, 1H), 7.65 – 7.54 (m, 2H), 7.25 (ddd, J = 8.0, 6.7, 1.0 Hz, 1H), 5.84 (d, J = 8.7 Hz, 1H), 2.54 – 2.44 (m, 1H), 2.36 (s, 3H), 2.13 (s, 3H), 1.15 (d, J = 6.8 Hz, 3H), 0.83 (d, J = 6.8 Hz, 3H).

**¹³C NMR** (100 MHz, MeOD) δ 172.3, 171.7, 150.4, 144.0, 141.4, 134.6, 134.1, 130.3, 122.8, 122.1, 120.9, 113.1, 107.1, 80.3, 33.5, 21.0, 20.7, 19.3, 18.8.

**HRMS** (m/z): [M + H]⁺ calcd. for C₁₉H₂₁N₂O₂⁺ 341.1496, found 341.1483.

[**M + Na⁺**] calcd. for C₁₉H₂₀N₂NaO₂⁺ 363.1315, found 363.1304.

**Compound (±)-36a:** 1-(1-hydroxy-2-methylpropyl)-2-methyl-2,9-dihydro-3H-pyrido[3,4-b]indol-3-one

Inspired from a known procedure. To a solution of acetoxypyridine (±)-35a (13 mg, 0.0382 mmol) in MeOH (3 mL) was added K₂CO₃ (131.3 mg, 0.95 mmol) at room temperature. Then the mixture was stirred at 70 °C for 2 h. Then, Mel (5 ml) and acetone (24 mL) were added into the mixture which was stirred at 70 °C overnight. The reaction mixture was then concentrated directly under reduced pressure, and was then purified by preparative TLC on silica gel (CH₂Cl₂) to give 3 mg of (±)-36a as a yellow solid (29% yield).

**Rf** = 0.12 (CH₂Cl₂)
$^1$H NMR (360 MHz, MeOD) δ 8.08 (dt, $J = 8.0, 1.5$ Hz, 1H), 7.53 – 7.44 (m, 2H), 7.32 (s, 1H), 7.15 (ddd, $J = 8.0, 6.5, 1.5$ Hz, 1H), 4.78 (d, $J = 6.1$ Hz, 1H), 3.98 (s, 3H), 2.41 – 2.24 (m, 1H), 1.01 (d, $J = 6.8$ Hz, 3H), 0.94 (d, $J = 6.8$ Hz, 3H).

$^{13}$C NMR (100 MHz, MeOD) δ 158.4, 144.1, 143.9, 135.2, 131.4, 129.6, 122.6, 122.2, 119.8, 112.7, 96.9, 79.1, 54.8, 35.5, 19.6, 18.0.

HRMS (m/z): [M + H]$^+$ calcd. for C$^{16}$H$^{19}$N$^2$O$^2$ 271.1441, found 271.1428.

**Compound 37a:** 1-isobutyl-9H-pyrido[3,4-b]indol-3-yl trifluoromethanesulfonate

![Diagram of compound 37a]

To a solution of pyridine N-oxide 33a (24 mg, 0.100 mmol) in CH$_2$Cl$_2$ (1 mL), was added Tf$_2$O (28.2 mg, 0.5 mmol) and Et$_3$N (102 mg, 1 mmol) at room temperature. The reaction mixture was stirred at room temperature for about 30 min and was then quenched with water after which it was extracted 3 times with CH$_2$Cl$_2$. The combined organic layers were dried over Na$_2$SO$_4$, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (CH$_2$Cl$_2$) to give 28 mg of 37a as a colorless oil (74% yield).

$R_f = 0.66$ (CH$_2$Cl$_2$)

$^1$H NMR (400 MHz, CDCl$_3$) δ 8.22 (br, 1H), 8.09 (dt, $J = 8.0, 1.0$ Hz, 1H), 7.63 (s, 1H), 7.60 (ddd, $J = 8.0, 6.5, 1.0$ Hz, 1H), 7.54 (dt, $J = 8.0, 1.0$ Hz, 1H), 7.32 (ddd, $J = 8.0, 6.5, 1.0$ Hz, 1H), 2.90 (d, $J = 7.3$ Hz, 2H), 2.42 – 2.31 (m, 1H), 1.01 (d, $J = 6.6$ Hz, 6H).

$^{13}$C NMR (100 MHz, CDCl$_3$) δ 148.1, 143.6, 141.4, 134.6, 132.3, 129.6, 122.1, 121.6, 120.8, 119.0 (q, $J = 320.0$ Hz, CF$_3$), 112.0, 103.6, 42.5, 28.2, 22.7 (2C).

$^{19}$F NMR (235 MHz, CDCl$_3$) δ -72.79.

HRMS (m/z): [M + H]$^+$ calcd. for C$_{16}$H$_{15}$F$_3$N$_2$O$_3$ 373.0828, found 373.0821.

[M + Na]$^+$ calcd. for C$_{16}$H$_{15}$F$_3$N$_2$NaO$_3$ 395.0648, found 395.0641.

**Compound 38a:** 1-isobutyl-2-methyl-3-(((trifluoromethyl)sulfonyl)oxy)-9H-pyrido[3,4-b]indol-2-ium iodide

![Diagram of compound 38a]

To a solution of triflyloxypyridine 37a (15 mg, 0.0403 mmol) in acetone (5 mL) was added MeI (25 mL) and K$_2$CO$_3$ (12 mg, 0.088 mmol) at room temperature. Then, the mixture was stirred at 60 °C for 48 h. The reaction mixture was then directly concentrated under reduced pressure, and was purified by preparative TLC on silica gel (CH$_2$Cl$_2$/petroleum ether 1:1) to give 6 mg of 38a as a solid (30% yield).

$R_f = 0.85$ (CH$_2$Cl$_2$)

$^1$H NMR (300 MHz, CDCl$_3$) δ 8.10 (dt, $J = 8.0, 0.9$ Hz, 1H), 7.65 (s, 1H), 7.64 (ddd, $J = 8.0, 7.1, 0.9$ Hz, 1H), 7.47 (dt, $J = 8.0, 0.9$ Hz, 1H), 7.31 (ddd, $J = 8.0, 7.1, 0.9$ Hz, 1H), 4.11 (s, 3H), 3.18 (d, $J = 6.8$ Hz, 2H), 2.36-2.22 (m, 1H), 1.03 (d, $J = 6.8$ Hz, 6H).
$^{13}$C NMR (62.5 MHz, CDCl$_3$) $\delta$ 147.2, 143.8 (2C), 135.7, 133.4, 129.5, 121.9, 121.0, 120.4, 119.1 (q, $J$ = 318.8 Hz, CF$_3$), 110.0, 103.4, 43.9, 32.6, 29.3, 22.5 (2C).

$^{19}$F NMR (235 MHz, CDCl$_3$) $\delta$ -72.84.

HRMS (m/z): [M + H]$^+$ calcd. for C$_{17}$H$_{18}$F$_{3}$N$_2$O$_3$S$^+$ 387.0985, found 387.0969.

**Compound 39a:** 1-isobutyl-2-methyl-2,9-dihydro-3H-pyrido[3,4-b]indol-3-one

![Diagram](image)

Inspired from a known procedure.$^6$

A 1 M aqueous solution of LiOH (0.022 mL, 0.022 mmol) was added to a solution of triflyloxytripyrinium 38a (5 mg, 0.00973 mmol) in THF (0.5 mL). The mixture was stirred at 30 °C for about 20 h and the mixture was cooled to room temperature, followed by addition of water and careful acidification with a 1 M aqueous solution of HCl to pH 1–2. The resulting mixture was extracted 5 times with CH$_2$Cl$_2$ and the combined organic extracts were dried over MgSO$_4$. Removal of solvent under reduced pressure and purification by preparative TLC on silica gel (CH$_2$Cl$_2$/MeOH 20:1) gave 1.5 mg of 39a as a fluorescent yellow solid (60% yield).

$R_f = 0.14$ (CH$_2$Cl$_2$/MeOH 20:1)

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.93 (dt, $J = 8.2$, 1.2 Hz, 1H), 7.53 (ddd, $J = 8.2$, 7.3, 1.2 Hz, 1H), 7.20 (dt, $J = 8.2$, 1.2 Hz, 1H), 7.12 (ddd, $J = 8.2$, 7.3, 1.2 Hz, 1H), 7.01 (s, 1H), 3.80 (s, 3H), 3.04 (d, $J = 7.4$ Hz, 2H), 2.21 – 2.09 (m, 1H), 1.04 (d, $J = 6.6$ Hz, 6H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 162.3, 147.1, 140.8, 131.6, 130.5, 126.7, 120.9, 119.1, 108.9, 103.0, 39.1, 32.4, 30.5, 22.3 (2C).

HRMS (m/z): [M + H]$^+$ calcd. for C$_{16}$H$_{19}$N$_2$O$^+$ 255.1492, found 255.1486.

[M + Na]$^+$ calcd. for C$_{16}$H$_{18}$N$_2$NaO$^+$ 277.1311, found 277.1307.

**Compound (±)-33b:** 2-ethoxy-5-(methoxycarbonyl)-3-vinyl-3,4-dihydro-2$H$-pyran-4-yl)methyl)-9$H$-pyrido[3,4-b]indole 2-oxide

Inspired from known procedures.$^5$

To solution of pyridine (±)-28b (12 mg, 0.0306 mmol) in CHCl$_3$ (2 mL) was added m-CPBA (25.8 mg, 0.15 mmol) at room temperature and the reaction was stirred at this temperature for 1 h. Then the reaction mixture was quenched with a saturated aqueous solution of NaHCO$_3$ and the mixture was stirred at 0 °C for about 10 min. The resulting mixture was extracted 3 times with CH$_2$Cl$_2$. The combined organic layers were dried with Na$_2$SO$_4$, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (CH$_2$Cl$_2$ to EtOAc to CH$_2$Cl$_2$/MeOH 10:1) to give 5 mg of (±)-33b as a colorless solid (40% yield).

$R_f = 0.40$ (CH$_2$Cl$_2$/MeOH 10:1)
Chemical structures and NMR data for compound (±)-37b:

**1H NMR** (300 MHz, CDCl₃) δ 11.31 (s, 1H), 8.26 (d, J = 6.6 Hz, 1H), 8.01 (d, J = 7.8 Hz, 1H), 7.76 (d, J = 6.6 Hz, 1H), 7.66 (s, 1H), 7.65 (d, J = 7.8 Hz, 1H), 7.53 (t, J = 7.8 Hz, 1H), 7.30 (t, J = 7.8 Hz, 1H), 6.28 (dt, J = 17.0, 10.0 Hz, 1H), 5.55 (d, J = 8.8 Hz, 1H), 4.83 (d, J = 17.0 Hz 1H), 4.78 (d, J = 10.0 Hz, 1H), 4.16 (dd, J = 14.9, 10.2 Hz, 1H), 4.05 – 3.94 (m, 1H), 3.89 – 3.71 (m, 1H), 3.26 (dd, J = 10.1, 5.6 Hz, 1H), 3.02 (d, J = 14.9 Hz, 1H), 2.60 – 2.46 (m, 1H), 1.25 (t, J = 7.1 Hz, 3H).

**13C NMR** (90 MHz, CDCl₃) δ 169.6, 155.0, 141.6, 136.3, 136.0, 133.3, 131.4, 127.6, 121.5, 120.9, 120.6, 120.5, 118.5, 114.3, 112.2, 108.6, 100.8, 66.1, 52.2, 45.8, 35.5, 27.7, 15.2.

**HRMS** (m/z): [M + H]^+ calcd. for C_{23}H_{35}N_{2}O_{5}^+ 409.1758, found 409.1749.

**Compound (±)-37b**: methyl 2-ethoxy-4-((3-((trifluoromethyl)sulfonyl)oxy)-9H-pyrido[3,4-b]indol-1-yl)methyl)-3-vinyl-3,4-dihydro-2H-pyran-5-carboxylate

To a solution of pyridine N-oxide (±)-33b (10 mg, 0.0245 mmol) in CH₂Cl₂ (1 mL) was added Tf₂O (35 mg, 0.125 mmol) and Et₃N (25 mg, 0.25 mmol) at 0°C. Then the reaction mixture was stirred at 0°C for about 5 min and was quenched with water. The aqueous layer was extracted with CH₂Cl₂ for 3 times. The combined organic layers were dried with Na₂SO₄, filtered, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (Petroleum ether/EtOAc 10:1) to give 1 mg of (±)-37b as a colorless oil (7% yield).

**Rf** = 0.16 (Petroleum ether/EtOAc 10:1)

**1H NMR** (300 MHz, CDCl₃) δ 11.14 (s, 1H), 8.09 (dt, J = 7.9, 1.0 Hz, 1H), 7.70 – 7.55 (m, 3H), 7.59 (ddd, J = 7.9, 7.0, 1.0 Hz, 1H), 7.30 (ddd, J = 7.9, 7.0, 1.0 Hz, 1H), 5.90 (dt, J = 16.9, 9.6 Hz, 1H), 5.17 (d, J = 7.4 Hz, 1H), 4.97 (d, J = 16.9 Hz, 1H), 4.95 (dd, J = 9.6, 1.0 Hz, 1H), 4.00 – 3.91 (m, 1H), 3.90 (s, 3H), 3.76 – 3.65 (m, 1H), 3.50 (d, J = 14.2 Hz, 1H), 3.26 (dd, J = 10.2, 5.4 Hz, 1H), 3.12 (dd, J = 14.2, 10.2 Hz, 1H), 2.64 – 2.54 (m, 1H), 1.24 (d, J = 7.1 Hz, 3H).

**13C NMR** (100 MHz, CDCl₃) δ 169.6, 154.5, 147.2, 143.0, 136.0, 136.0, 133.3, 131.4, 127.6, 121.5, 120.9, 120.6, 120.5, 118.5, 114.3, 112.2, 108.6, 100.8, 66.1, 52.2, 45.8, 37.3, 34.4, 15.1.

**19F NMR** (235 MHz, CDCl₃) δ -73.26.

**HRMS** (m/z): [M + H]^+ calcd. for C_{24}H_{24}F_{3}N_{2}O_{7}S^+ 541.1251, found 541.1235.

**Compound 15b**: methyl 2-(1H-indol-3-yl)acetate

Prepared according to a known procedure.²
To a solution of indole-3-acetic acid 15c (2.10 g, 12.0 mmol) in methanol (24 mL) under argon at 0 °C was slowly added SOCl₂ (4.28 g, 36 mmol). The resulting mixture was heated to 68 °C over 12 h. The reaction was poured into a saturated aqueous solution of NaHCO₃ (40 mL). The resulting mixture was extracted three times with EtOAc (3 × 50 mL) and the combined organic layers were dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (Petroleum ether/ EtOAc 3:2) to give 2.064 g of 15b as a colorless solid (91% yield).

\[ R_f = 0.59 \text{(Petroleum ether/ EtOAc 3:2)} \]

\[ ^{1}H \text{ NMR (360 MHz, CDCl}_3 \] \( \delta \) 8.12 (br, 1H), 7.63 (dt, \( J = 8.1, 1.0 \text{ Hz} \), 1H), 7.35 (dt, \( J = 8.1, 1.0 \text{ Hz} \), 1H), 7.21 (ddd, \( J = 8.1, 7.0, 1.0 \text{ Hz} \), 1H), 7.15 (ddd, \( J = 8.1, 7.0, 1.0 \text{ Hz} \), 1H), 7.13-7.11 (m, 1H), 3.80 (d, \( J = 0.9 \text{ Hz} \), 2H), 3.72 (s, 3H).

\[ ^{13}C \text{ NMR (90 MHz, CDCl}_3 \] \( \delta \) 172.7, 136.2, 127.3, 123.2, 122.3, 119.8, 119.0, 111.3, 108.5, 52.1, 31.3.

\[ \text{HRMS (m/z): [M + H]}^{+}\text{ calcd. for C}_{11}\text{H}_{12}\text{NO}_{2}^{+} 190.0863, \text{ found 190.0861.} \]

\[ \text{[M + Na]}^{+}\text{ calcd. for C}_{11}\text{H}_{11}\text{NNaO}_{2}^{+} 212.0682, \text{ found 212.0680.} \]

Compound 15a: 2-(1H-indol-3-yl)-N-methylacetamide

Prepared according to a known procedure.⁸

To a solution of indole-3-acetic acid 15c (2.16 g, 12.33 mmol) in EtOH (24 mL) was added dropwise SOCl₂ (4.28 g, 36 mmol). The reaction was stirred to reflux for overnight. Upon completion of the reaction (monitoring by TLC), the mixture was concentrated to dryness and the crude material was directly treated for next step without isolation. The crude reaction mixture was dissolved in a solution of MeNH₂ (25 mL of 33% in EtOH). The mixture was stirred at 25 ºC for 24 h until ethyl 3-indoleacetate was fully consumed and was concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (Petroleum ether/EtOAc 1:3) to give 2.264 g of 15a as a colorless solid (98% yield).

\[ R_f = 0.13 \text{(Petroleum ether/EtOAc 1:3)} \]

\[ ^{1}H \text{ NMR (360 MHz, CDCl}_3 \] \( \delta \) 9.15 (br, 1H), 7.54 (dt, \( J = 8.0, 1.1 \text{ Hz} \), 1H), 7.41 (dt, \( J = 8.0, 1.1 \text{ Hz} \), 1H), 7.23 (ddd, \( J = 8.0, 7.0, 1.1 \text{ Hz} \), 1H), 7.14 (ddd, \( J = 8.0, 7.0, 1.1 \text{ Hz} \), 1H), 7.10 (d, \( J = 2.4 \text{ Hz} \), 1H), 5.89 (br, 1H), 3.74 (s, 2H), 2.71 (d, \( J = 4.8 \text{ Hz} \), 3H).

\[ ^{13}C \text{ NMR (90 MHz, CDCl}_3 \] \( \delta \) 172.8, 136.2, 127.1, 124.3, 122.5, 119.9, 118.6, 111.7, 108.5, 33.3, 26.5.

\[ \text{HRMS (m/z): [M + H]}^{+}\text{ calcd. for C}_{11}\text{H}_{13}\text{N}_{2}O^{+} 189.1022, \text{ found 189.1019.} \]

\[ \text{[M + Na]}^{+}\text{ calcd. for C}_{11}\text{H}_{12}\text{NNaO}_{2}^{+} 211.0842, \text{ found 211.0840.} \]

Compound (±)-40: 2,2'-(((3-methylbutane-1,1-diyl)bis(1H-indole-2,3-diyl))bis(N-methylacetamide)
Inspired from a known procedure.  

2-(1H-indol-3-yl)-N-methylacetamide 15a (18.8 mg, 0.100 mmol) and 3-methylbutanal 42 (9 mg, 0.1 mmol) were dissolved in TFA (1 mL) and the reaction was stirred for 40 min at room temperature. The solution was diluted with EtOAc and washed with a saturated aqueous solution of NaHCO₃. The organic layer was dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by preparative TCL on silica gel (CH₂Cl₂/MeOH 20:1) to give 6 mg of (±)-40 as a colorless solid (27% yield).

\[ R_f = 0.22 \text{ (CH}_2\text{Cl}_2/\text{MeOH 20:1)} \]

\[ ^1\text{H NMR} (300 \text{ MHz, CDCl}_3) \delta 10.22 (s, 2H), 7.45 (d, J = 8.0 \text{ Hz, 2H}), 7.32 (d, J = 8.0 \text{ Hz, 2H}), 7.17 - 7.02 (m, 4H), 5.91 (q, J = 4.8 \text{ Hz, 2H}), 4.73 (t, J = 7.5 \text{ Hz, 2H}), 3.84 (d, J = 16.0 \text{ Hz, 2H}), 3.76 (d, J = 16.0 \text{ Hz, 2H}), 2.66 (d, J = 4.8 \text{ Hz, 6H}), 2.23 (t, J = 7.5 \text{ Hz, 2H}), 1.60 - 1.47 (m, 1H), 0.96 (d, J = 6.6 \text{ Hz, 6H}). \]

\[ ^13\text{C NMR} (100 \text{ MHz, CDCl}_3) \delta 173.3 (2\text{C}), 138.2 (2\text{C}), 135.8 (2\text{C}), 128.3 (2\text{C}), 121.9 (2\text{C}), 119.6 (2\text{C}), 117.5 (2\text{C}), 111.5 (2\text{C}), 103.9 (2\text{C}), 41.7, 34.9, 32.6 (2\text{C}), 26.7 (2\text{C}), 26.2, 22.8 (2\text{C}). \]

\[ \text{HRMS (m/z): [M + H]}^+ \text{ calcd. for C}_{27}\text{H}_{33}\text{N}_4\text{O}_2^+ 445.2598, \text{ found 445.2581}. \]

\[ \text{[M + Na]}^+ \text{ calcd. for C}_{27}\text{H}_{32}\text{N}_4\text{NaO}_2^+ 467.2417, \text{ found 467.2402}. \]

**Compound 43a**: 1-propyl-2,9-dihydro-3H-pyrido[3,4-b]indol-3-one

Inspired from a known procedure.  

2-(1H-indol-3-yl)acetic acid 15c (525 mg, 3.00 mmol), butyronitrile (52 µL, 0.6 mmol), Pd(OAc)₂ (13.4 mg, 0.06 mmol), 2,2’-bipyridine (11.2 mg, 0.072 mmol) and HOAc/THF (v/v = 1/3, 1.6 mL) were placed in a sealed tube under argon atmosphere. The mixture was stirred at 120 °C overweekend. Then the mixture was cooled to room temperature, and a saturated aqueous solution of NaHCO₃ was added until no bubbles were generated. The resulting mixture was extracted five times with CH₂Cl₂. The combined organic layers were then dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by preparative TLC on silica gel (CH₂Cl₂/Methanol 10:1) to give 61 mg of 43a as a colorless solid (45% yield).

\[ R_f = 0.38 \text{ (CH}_2\text{Cl}_2/\text{Methanol 10:1)} \]

\[ ^1\text{H NMR} (300 \text{ MHz, MeOD}) \delta 7.97 (d, J = 8.0, 1.0 \text{ Hz, 1H}), 7.50 (ddd, J = 8.0, 7.1, 1.0 \text{ Hz, 1H}), 7.35 (dt, J = 8.0, 1.0 \text{ Hz, 1H}), 7.10 (ddd, J = 8.0, 7.1, 1.0 \text{ Hz, 1H}), 6.93 (s, 1H), 2.93 (dd, J = 8.6, 6.7 \text{ Hz, 2H}), 1.92 - 1.74 (m, 2H), 1.03 (t, J = 7.3 \text{ Hz, 3H}). \]

\[ ^13\text{C NMR} (100 \text{ MHz, MeOD}) \delta 162.9, 147.1, 141.6, 133.0, 131.7, 127.3, 123.8, 121.7, 120.2, 112.4, 102.2, 32.3, 23.4, 13.9. \]

\[ \text{HRMS (m/z): [M + H]}^+ \text{ calcd. for C}_{14}\text{H}_{15}\text{N}_2\text{O}_2^+ 227.1179, \text{ found 227.1184}. \]

**Compound 26**: O-(4-(trifluoromethyl)benzoyl)hydroxylamine

Inspired from a known procedure.  

2-(1H-indol-3-yl)acetic acid 15c (525 mg, 3.00 mmol), butyronitrile (52 µL, 0.6 mmol), Pd(OAc)₂ (13.4 mg, 0.06 mmol), 2,2’-bipyridine (11.2 mg, 0.072 mmol) and HOAc/THF (v/v = 1/3, 1.6 mL) were placed in a sealed tube under argon atmosphere. The mixture was stirred at 120 °C overweekend. Then the mixture was cooled to room temperature, and a saturated aqueous solution of NaHCO₃ was added until no bubbles were generated. The resulting mixture was extracted five times with CH₂Cl₂. The combined organic layers were then dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by preparative TLC on silica gel (CH₂Cl₂/Methanol 10:1) to give 61 mg of 43a as a colorless solid (45% yield).

\[ R_f = 0.38 \text{ (CH}_2\text{Cl}_2/\text{Methanol 10:1)} \]

\[ ^1\text{H NMR} (300 \text{ MHz, MeOD}) \delta 7.97 (dt, J = 8.0, 1.0 \text{ Hz, 1H}), 7.50 (ddd, J = 8.0, 7.1, 1.0 \text{ Hz, 1H}), 7.35 (dt, J = 8.0, 1.0 \text{ Hz, 1H}), 7.10 (ddd, J = 8.0, 7.1, 1.0 \text{ Hz, 1H}), 6.93 (s, 1H), 2.93 (dd, J = 8.6, 6.7 \text{ Hz, 2H}), 1.92 - 1.74 (m, 2H), 1.03 (t, J = 7.3 \text{ Hz, 3H}). \]

\[ ^13\text{C NMR} (100 \text{ MHz, MeOD}) \delta 162.9, 147.1, 141.6, 133.0, 131.7, 127.3, 123.8, 121.7, 120.2, 112.4, 102.2, 32.3, 23.4, 13.9. \]

\[ \text{HRMS (m/z): [M + H]}^+ \text{ calcd. for C}_{14}\text{H}_{15}\text{N}_2\text{O}_2^+ 227.1179, \text{ found 227.1184}. \]
To a solution of tert-butyl N-hydroxycarbamate (402 mg, 3.02 mmol), Et₃N (420 μL, 3.02 mmol) in CH₂Cl₂ (5 mL) was added 4-trifluoromethylbenzoyl chloride (314 mg, 1.51 mmol) dropwise at 0 °C for 30 min and stirred at 0 °C for another 10 min. Then, the mixture was poured into a saturated aqueous solution of NaHCO₃. The resulting mixture was extracted twice with CH₂Cl₂. The combined organic phases were then dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was then dissolved in dry CH₂Cl₂ (1 mL). Trifluoroacetic acid (2 ml) was then added dropwise at room temperature and the reaction mixture was stirred at 0 °C for another 30 min. Then, the mixture was poured into a saturated aqueous solution of NaHCO₃ and the resulting mixture was extracted twice with 25 mL of CH₂Cl₂. The combined organic layers were then dried over Na₂SO₄ and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (Petroleum ether/EtOAc 5:1) to give 132 mg of 26 as a white solid (42% yield).

Rf = 0.31 (Petroleum ether/Ethyl acetate 3:1)

¹H NMR (300 MHz, CDCl₃) δ 8.13 (d, J = 8.1 Hz, 2H), 7.72 (d, J = 8.1 Hz, 2H), 6.38 (s, 2H).

¹³C NMR (90 MHz, CDCl₃) δ 166.4, 135.10 (q, J = 32.4 Hz), 131.3, 130.0, 125.8 (q, J = 3.6 Hz), 123.6 (q, J = 270.9 Hz)

¹⁹F NMR (235 MHz, CDCl₃) δ -63.25.

Compound (±)-25: methyl -4-(cyanomethyl)-2-ethoxy-3-vinyl-3,4-dihydro-2H-pyran-5-carboxylate

Inspired from a known procedure.¹²

A 3 mL vial was equipped with a magnetic stir bar and was charged with (±)-16 (40 mg, 0.157 mmol), O-(4-(trifluoromethyl)benzoyl)hydroxylamine 26 (40 mg, 0.20 mmol, 1.2 equiv), and CSA (4 mg, 0.016 mmol, 0.1 equiv) in MeOH (2.0 mL). The mixture was then stirred at room temperature overnight, and was then concentrated under reduced pressure to remove MeOH. The residue was purified by preparative TCL on silica gel (Petroleum ether/EtOAc 5:1) to give 20 mg of (±)-25 as a white oil (50% yield).

Rf = 0.43 (Petroleum ether/EtOAc 2:1)

¹H NMR (300 MHz, CDCl₃) δ 7.54 (d, J = 1.6 Hz, 1H), 5.61 (ddd, J = 17.0, 10.5, 8.5 Hz, 1H), 5.41 (dd, J = 17.0, 1.0 Hz, 1H), 5.34 (d, J = 10.5, 1.7 Hz, 1H), 5.13 (d, J = 4.5 Hz, 1H), 3.89 – 3.82 (m, 1H), 3.71 (s, 3H), 3.69 – 3.60 (m, 1H), 3.17 (dd, J = 16.6, 3.9 Hz, 1H), 3.12 – 3.04 (m, 1H), 2.82 – 2.75 (m, 1H), 2.42 (dd, J = 16.6, 9.4 Hz, 1H), 1.22 (t, J = 7.1 Hz, 3H).

¹³C NMR (100 MHz, CDCl₃) δ 167.0, 154.1, 132.0, 121.6, 119.0, 106.0, 100.2, 65.2, 51.5, 44.5, 29.0, 18.0, 15.1.

HRMS (m/z): [M + H]⁺ calcd. for C₁₃H₁₈NO₄⁺ 252.1230, found 252.1226.
[M + Na]⁺ calcd. for C₁₃H₁₆NNaO₄⁺ 274.1050, found 274.1042.

Compound 46b: methyl-2-(2-(hex-5-enoyl)-1H-indol-3-yl)acetate
To a solution of hex-5-enoic acid 44 (13.7 mg, 0.120 mmol) in CH₂Cl₂ (0.5 mL) at 0 °C, was slowly added oxaly chloride (19.8 mg, 0.156 mol). The resulting mixture was allowed to warm up to room temperature, while stirring overnight. The reaction was concentrated under reduced pressure and used for next step without any purification. Then the reaction mixture was dissolved in 1 mL of Et₂O and methyl 2-(1H-indol-3-yl)acetate 15b (18.9 mg, 0.1 mmol) was added and then cooled to 0 °C. A solution of tin chloride (0.012 mL of 1 M in heptane) was added dropwise at 0 °C. The resulting mixture was allowed to warm up to room temperature and stirred at room temperature for overnight. The reaction mixture was quenched with a saturated aqueous KF solution and the resulting mixture was extracted 5 times with CH₂Cl₂. The combined organic layers were dried with Na₂SO₄ and concentrated under reduced pressure. The crude product was purified by preparative TLC on silica gel (Petroleum ether/EtOAc 7:3) to give 23 mg of 46b as a white solid (80% yield).

Rf = 0.60 (Petroleum ether/Ethyl acetate 7:3)

¹H NMR (360 MHz, CDCl₃) δ 9.29 (br, 1H), 7.67 (dt, J = 8.0, 1.0 Hz, 1H), 7.34 – 7.31 (m, 2H), 4.15 (s, 2H), 3.74 (s, 3H), 2.80 (t, J = 7.0 Hz, 2H), 2.13 (q, J = 7.0 Hz, 2H), 1.78 (pent, J = 7.0 Hz, 2H).

¹³C NMR (90 MHz, CDCl₃) δ 193.0, 171.8, 138.1, 135.9, 132.6, 128.3, 126.4, 120.9, 120.8, 115.4, 113.9, 112.5, 52.4, 39.4, 33.2, 31.3, 22.8.

HRMS (m/z): [M + H]⁺ calcd. for C₁₇H₂₀NO₃⁺ 286.1438, found 286.1428.

[M + Na]⁺ calcd. for C₁₇H₁₉NNaO₃⁺ 308.1257, found 308.1246.

**Compound 46a**: 2-(2-(hex-5-enoyl)-1H-indol-3-yl)-N-methylacetamide

Inspired from known procedures.¹³

To a solution of hex-5-enoic acid 44 (11.4 mg, 0.100 mmol) in CH₂Cl₂ (0.5 mL) at 0 °C, oxaly chloride (16.5 mg, 0.13 mmol) was added slowly and the resulting mixture was allowed to warm up to room temperature, while stirring overnight. The reaction mixture was concentrated under reduced pressure and used for next step without any purification. To the residue dissolved in 0.5 mL of Et₂O and 0.5 mL of CH₂Cl₂, 15a (23 mg, 0.12 mmol) was added and the mixture was cooled to 0 °C. A solution of tin chloride (0.1 mL of 1 M in CH₂Cl₂) was added dropwise at 0 °C. The resulting mixture was allowed to warm up to room temperature and stirred at room temperature for 4 h. The reaction mixture was
quenched with a saturated aqueous solution of KF and the resulting mixture was extracted 5 times with CH₂Cl₂. The combined organic layers were dried over Na₂SO₄, filtered and concentrated under reduced pressure. The crude products were purified by preparative TLC on silica gel (CH₂Cl₂/Methanol 15:1) to give 15 mg of 46a as a white solid (52% yield).

\[ R_f = 0.53 \ (\text{CH}_2\text{Cl}_2/\text{Methanol} \ 10:1) \]

\[ ^1\text{H NMR} \ (360 \text{ MHz, MeOD}) \delta 7.67 \ (d, J = 7.7 \text{ Hz, 1H}), 7.44 \ (d, J = 7.7 \text{ Hz, 1H}), 7.30 \ (t, J = 7.7 \text{ Hz, 1H}), 7.10 \ (t, J = 7.7 \text{ Hz, 1H}), 5.93 – 5.78 \ (m, 1H), 5.04 \ (d, J = 17.0 \text{ Hz, 1H}), 4.98 \ (d, J = 10.0 \text{ Hz, 1H}), 4.03 \ (s, 2H), 2.98 \ (t, J = 7.2 \text{ Hz, 2H}), 2.68 \ (s, 3H), 2.21 – 2.10 \ (m, 2H), 1.88 – 1.75 \ (m, 2H). \]

\[ ^{13}\text{C NMR} \ (90 \text{ MHz, MeOD}) \delta 195.9, 174.4, 139.3, 138.1, 133.6, 129.2, 127.0, 121.6, 121.5, 116.7, 115.6, 113.5, 40.3, 34.3, 33.6, 26.5, 24.4. \]

HRMS (m/z): [M + H]⁺ calcd. for C₁₇H₂₁N₂O₂ + 285.1598, found 285.1589.

[M + Na]⁺ calcd. for C₁₇H₂₀N₂NaO₂ + 307.1417, found 307.1408.

**Compound 47**: 2-methyl-1-(pent-4-en-1-yl)-2,9-dihydro-3H-pyrido[3,4-b]indol-3-one

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**Inspired from known procedures.**

A solution of MeNH₂ (0.4 mL of 33% in EtOH, 3.36 mmol) was added to a solution of 46b (16 mg, 0.0561 mmol) and NH₄OAc (13 mg, 0.168 mmol) in 1 mL of anhydrous toluene at room temperature. The reaction mixture was then heated to 95 °C and stirred overnight. After concentration under reduced pressure, the crude mixture was purified by preparative TLC on silica gel (CH₂Cl₂/Methanol 15:1) to give 10 mg of 47 as a fluorescent yellow solid (66% yield).

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**Inspired from known procedures.**

Et₃N (27 µL, 0.19 mmol) was added to a solution of 46a (11 mg, 0.0387 mmol) in 1 mL of acetic acid and the reaction mixture was stirred at reflux for 1.5 h. The mixture was then cooled-down and then poured into water, and a solution of ammonium hydroxide was added until it reached pH ≥ 7. Then the resulting mixture was extracted with 5 times CH₂Cl₂. The combined organic layers were dried over Na₂SO₄, filtered and concentrated under reduced pressure. The crude products were purified by preparative TLC on silica gel (CH₂Cl₂/Methanol 15:1) to give 9 mg of 47 as a fluorescent yellow solid (87% yield).

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A solution of 46a (14 mg, 0.0492 mmol) in 1 mL of acetic acid was stirred at reflux for 1.5 h. The mixture was then cooled-down and then poured into water, and a solution of ammonium hydroxide was added until it reached pH ≥ 7. Then the resulting mixture was extracted with 5 times CH₂Cl₂. The
combined organic layers were dried over Na$_2$SO$_4$, filtered and concentrated under reduced pressure. The crude products were purified by preparative TLC on silica gel (CH$_2$Cl$_2$/Methanol 15:1) to give 11 mg of 47 as a fluorescent yellow solid (85% yield).

$R_f$ = 0.41 (CH$_2$Cl$_2$/Methanol 10:1)

$^1$H NMR (360 MHz, MeOD) $\delta$ 7.92 (d, $J = 7.7$ Hz, 1H), 7.47 (t, $J = 7.7$ Hz, 1H), 7.32 (d, $J = 7.7$ Hz, 1H), 7.07 (t, $J = 7.7$ Hz, 1H), 6.98 (s, 1H), 5.91 (ddt, $J = 17.0$, 10.5, 7.5 Hz, 1H), 5.07 (d, $J = 17.0$ Hz, 1H), 5.00 (d, $J = 10.5$ Hz, 1H), 3.73 (s, 3H), 3.06 (t, $J = 7.5$ Hz, 2H), 2.25 (q, $J = 7.5$ Hz, 2H), 1.78 (pent, $J = 7.5$ Hz, 2H).

$^{13}$C NMR (90 MHz, MeOD) $\delta$ 162.9, 146.8, 139.5, 138.8, 134.0, 131.7, 128.1, 123.8, 121.5, 120.2, 116.0, 112.3, 102.6, 34.6, 33.0, 29.8, 28.3.

HRMS (m/z): [M + H]$^+$ calcd. for C$_{17}$H$_{19}$N$_2$O$^+$ 267.1492, found 267.1486.

**Inspired from a known procedure.**

A solution of pyridone 47 (50 mg, 0.188 mmol) in bromobenzene (5 mL) was heated to 156 ºC for about 14 h, then it was allowed to cool down to room temperature and concentrated under reduced pressure. The crude product was purified by preparative TLC (Petroleum ether /EtOAc 1:1) to give 20 mg of (±)-48 as a white solid (40% yield).

$R_f$ = 0.37 (CH$_2$Cl$_2$/MeOH 20:1) and 0.25 (Petroleum ether /EtOAc 1:1)

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 8.49 (s, 1H), 7.55 – 7.51 (m, 1H), 7.37 – 7.33 (m, 1H), 7.15 – 7.10 (m, 2H), 4.19 (s, 1H), 2.85 (s, 3H), 2.53 – 2.40 (m, 1H), 2.36 – 2.21 (m, 1H), 2.15 – 1.70 (m, 6H), 1.45 – 1.34 (m, 1H).

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 177.4, 143.2, 136.1, 124.8, 121.4, 120.4, 118.3, 113.3, 111.9, 69.5, 51.2, 42.8, 29.3, 28.6, 28.2, 25.5, 24.1.

HRMS (m/z): [M + H]$^+$ calcd. for C$_{17}$H$_{19}$N$_2$O$^+$ 267.1492, found 267.1482.

**Inspired from a known procedure.**

To a solution of aldehyde (±)-16 (55 mg, 0.216 mmol), which was prepared according to our modification of the Tietze procedure, in acetone (4 mL), a solution of the Jones reagent (0.12 mL of 2.67 M in water) was added dropwise at 0 ºC and the reaction mixture was stirred at 0 ºC for about 30 min. Upon completion of the reaction (monitoring by TLC), the reaction mixture was quenched with
isopropanol at 0 °C. The resulting mixture was filtered over celite and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (CH₂Cl₂/MeOH 10:1) to give 48 mg of (±)-23 as a white solid (83% yield).

R_f = 0.37 (CH₂Cl₂/MeOH 10:1)

¹H NMR (300 MHz, CDCl₃) δ 7.47 (d, J = 1.7 Hz, 1H), 5.59 (dt, J = 17.4, 9.7 Hz, 1H), 5.29 – 5.20 (m, 2H), 4.94 (d, J = 4.1 Hz, 1H), 3.85 (dq, J = 9.6, 7.1 Hz, 1H), 3.70 (s, 3H), 3.62 (dq, J = 9.6, 7.1 Hz, 1H), 3.36 – 3.24 (m, 1H), 2.94 (dd, J = 16.6, 5.2 Hz, 1H), 2.77 – 2.71 (m, 1H), 2.33 (dd, J = 16.6, 8.0 Hz, 1H), 1.22 (t, J = 7.1 Hz, 3H).

¹³C NMR (100 MHz, CDCl₃) δ 178.0, 167.6, 153.0, 135.2, 130.3, 120.3, 108.2, 100.5, 64.8, 51.4, 44.7, 34.7, 27.8, 15.2.

HRMS (m/z): [M + Na]^+ calcd. for C₁₅H₁₈NaO₆^+ 293.0996, found 293.0993.

Compound (±)-51: methyl 2-ethoxy-4-((2-methyl-3-oxo-3,9-dihydro-2H-pyrido[3,4-b]indol-1-yl)methyl)-3-vinyl-3,4-dihydro-2H-pyran-5-carboxylate

Inspired from known procedure.¹³⁻¹⁵

To a solution of (±)-23 (170 mg, 0.629 mmol) in CH₂Cl₂ (3 mL) at 0 °C was added dropwise oxalyl chloride (97 mg, 0.767 mmol) and then the reaction mixture was allowed to stir at room temperature overnight. It was then concentrated to dryness and the crude material was directly treated for next step without isolation. To the crude reaction mixture dissolved in Et₂O (6 mL) was added 15b (133.8 mg, 0.708 mmol) followed by a dropwise addition of a solution of SnCl₄ (0.06 mL of 1 M in heptane, 0.06 mmol) at 0 °C. The reaction mixture was then allowed to stir at room temperature for 2 h. The reaction mixture was quenched with a saturated aqueous solution of KF and the resulting mixture was extracted 5 times with CH₂Cl₂. The combined organic layers were dried over Na₂SO₄, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (CH₂Cl₂/Petroleum ether 10:1 to 5:1) to give 120 mg of acylation product in mixture with an unknown compound as a colorless oil.

To a solution of 13 mg of this mixture containing the acylation product in toluene (1 mL) were added H₂NMe (0.2 mL of 33% in EtOH) and NH₄OAc (7 mg, 0.09 mmol) at room temperature and the reaction mixture was stirred at 95 °C for about 6 h. Upon completion of the reaction (monitoring by TLC), the reaction mixture was allowed to cool down to room temperature and was then concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (CH₂Cl₂/MeOH 20:1 to 10:1) to give 4 mg of (±)-50 as a yellow solid (14% yield over 2 steps).

R_f = 0.41 (CH₂Cl₂/MeOH 10:1)

¹H NMR (360 MHz, CDCl₃) δ 9.08 (br, 1H), 7.89 (dt, J = 8.0, 1.2 Hz, 1H), 7.59 (s, 1H), 7.46 (ddd, J = 8.0, 7.1, 1.2 Hz, 1H), 7.30 (dt, J = 10.2, 1.2 Hz 1H), 7.09 (ddd, J = 8.0, 7.1, 1.2 Hz, 1H), 7.04 (s, 1H), 5.55 (ddd, J = 17.5, 10.3, 7.0 Hz, 1H), 5.25 (d, J = 2.7, 1H), 5.01 (d, J = 17.5 Hz, 1H), 4.92 (d, J = 10.3
Hz, 1H), 4.14 – 4.04 (m, 1H), 3.84 (s, 3H), 3.79 – 3.74 (m, 1H), 3.73 (s, 3H), 3.69 – 3.60 (m, 1H), 3.38 – 3.32 (m, 1H), 3.32 – 3.24 (m, 1H), 2.69 – 2.62 (m, 1H), 1.42 (t, J = 7.1 Hz, 3H).

\textbf{13C NMR} (100 MHz, CDCl$_3$) $\delta$ 168.4, 161.9, 153.0, 144.8, 137.8, 132.6, 130.4, 130.3, 126.6, 123.2, 121.2, 119.3, 118.9, 111.1, 109.5, 103.5, 100.2, 66.1, 52.0, 43.2, 32.9, 32.4, 30.6, 15.4.

\textbf{HRMS} (m/z): [M + H]$^+$ calcd. for C$_{24}$H$_{27}$N$_2$O$_5$ $^+$ 423.1914, found 423.1899.

Assignment of $^1$H ($\delta^1$H) and $^{13}$C ($\delta^{13}$C) NMR chemical shifts of compound (±)-51.

| Position | $\delta^1$H (ppm) 360 MHz, CDCl$_3$ | $\delta^{13}$C (ppm) 100 MHz, CDCl$_3$ |
|----------|-----------------------------------|-------------------------------------|
| 2        | -                                 | 126.6, C                             |
| 3        | -                                 | 130.4, C                             |
| 5        | -                                 | 161.9, C                             |
| 6        | 7.04, s                            | 103.5, CH                            |
| 7        | -                                 | 137.8, C                             |
| 8        | -                                 | 121.2, C                             |
| 9        | 7.89, dt (8.0, 1.2)                | 123.2, CH                            |
| 10       | 7.09, dddd (8.0, 7.1, 1.2)         | 119.3, CH                            |
| 11       | 7.46, ddd (8.0, 7.1, 1.2)          | 130.3, CH                            |
| 12       | 7.30, dt (8.0, 1.2)                | 111.1, CH                            |
| 13       | -                                 | 144.8, C                             |
| 14a      | 3.69 – 3.60, m                     | 30.6, CH$_2$                         |
| 14b      | 3.32 – 3.24, m                     |                                    |
| 15       | 3.38 – 3.32, m                     | 32.4, CH                             |
| 16       | -                                 | 109.5, C                             |
| 17       | 7.59, s                            | 153.0, CH                            |
| 18a      | 5.01, d (17.5)                     | 118.9, CH$_2$                        |
| 18b      | 4.92, d (10.3)                     | 118.9, CH                            |
| 19       | 5.55, dddd (17.7, 10.3, 7.0)       | 132.6, CH                            |
| 20       | 2.69 – 2.62, m                     | 43.2, CH                             |
| 21       | 5.25, d, (2.7)                     | 100.2, CH                            |
| 22       | -                                 | 168.4, C                             |
| 23a      | 4.14 – 4.04, m                     | 66.1, CH$_2$                         |
| 23b      | 3.79 – 3.74, m                     |                                    |
| 24       | 1.42, t (7.1)                      | 15.4, CH$_3$                         |
| N-Me     | 3.84, s                            | 32.9, CH$_3$                         |
| COOMe    | 3.73, s                            | 52.0, CH$_3$                         |
| NH       | 9.08, br                           | -                                   |
**Compound** (±)-53: methyl-4-ethoxy-13-methyl-14-oxo-4,4a,4b,5,6,11,12,12a-octahydro-11b,6-(epiminomethano)pyrano[3',4':3,4]cyclopenta[1,2-a]carbazole-1-carboxylate

![Chemical structure of (±)-53](image)

*Inspired from a known procedure.* A solution of (±)-51 (5 mg, 0.0118 mmol) in bromobenzene (1 mL) was stirred at 156 °C for about 5 h. Upon completion of the reaction (monitoring by TLC), the reaction mixture was allowed to cool down to room temperature and was then concentrated under reduced pressure. The crude product was purified by preparative TLC (CH₂Cl₂/MeOH 10:1) to give 3 mg of (±)-53 as a white solid (60% yield).

**Rf = 0.40 (CH₂Cl₂/MeOH 10:1)**

**¹H NMR** (360 MHz, CDCl₃) δ 8.08 (br, 1H), 7.55 – 7.50 (m, 1H), 7.41 (s, 1H), 7.36 – 7.30 (m, 1H), 7.15 – 7.10 (m, 2H), 4.97 (d, J = 2.9 Hz, 1H), 4.18 (t, J = 2.6 Hz, 1H), 3.95 – 3.87 (m, 1H), 3.78 (s, 3H), 3.58 – 3.43 (m, 1H), 3.43 – 3.33 (m, 1H), 3.21 (dd, J = 14.9, 8.4 Hz, 1H), 2.94 (s, 3H), 2.45 – 2.35 (m, 1H), 2.17 – 2.05 (m, 2H), 2.03 – 1.97 (m, 1H), 1.96 – 1.88 (m, 1H), 1.18 (t, J = 7.0 Hz, 3H).

**¹³C NMR** (100 MHz, CDCl₃) δ 177.3, 167.7, 152.3, 142.1, 136.1, 124.8, 121.7, 120.5, 118.5, 113.5, 112.9, 111.9, 102.1, 68.6, 65.9, 51.6, 49.1, 46.1, 42.7, 36.0, 34.9, 28.7, 28.6, 15.2.

**HRMS** (m/z): [M + H]⁺ calcd. for C₂₄H₂₇N₂O₅⁺ 423.1914, found 423.1900.
[M + Na]⁺ calcd. for C₂₄H₂₆N₂NaO₅⁺ 445.1734, found 445.1712.

**Assignment of **¹H (δH) and ¹³C (δC) NMR chemical shifts of compound (±)-53.**

| Position | δH (ppm) | δC (ppm) |
|----------|----------|----------|
|          | 360 MHz, CDCl₃ | 100 MHz, CDCl₃ |
| 2        | -        | 142.1, C  |
| 3        | -        | 68.6, C   |
| 5        | -        | 177.3, C  |
| 6        | 4.18, t (2.6) | 42.7, CH   |
| 7        | -        | 113.5, C  |
| 8        | -        | 124.8, C  |
| 9        | 7.55 – 7.50, m | 118.5, CH  |
| 10       | 7.15 – 7.10, m (overlap) | 120.5, CH   |
| 11       | 7.15 – 7.10, m (overlap) | 121.7, CH   |
| 12       | 7.36 – 7.30, m | 111.9, CH  |
| 13       | -        | 136.1, C  |
| 14a      | 3.21, dd (14.9, 8.4) | 34.9, CH₂   |
| 14b      | 2.03 – 1.97, m |          |

S25


|   | 3.43 – 3.33, m | 36.0, CH |
|---|----------------|---------|
| 15 | 7.41, s        | 152.3, C |
| 16 | 1.96 – 1.88, m | 49.1, CH |
| 17 | 2.17 – 2.05, m (overlap) | 28.7, CH₂ |
| 18a | 2.17 – 2.05, m (overlap) | 46.1, CH |
| 18b | 4.28 (dd, J = 12.4, 8.1 Hz, 1H), 5.10 (d, J = 9.5 Hz, 1H) | 102.1, CH |
| 19 | 2.45 – 2.35, m | - |
| 20 | 4.97, d (2.9) | 167.7, C |
| 21 | 3.95 – 3.87, m | 65.9, CH₂ |
| 22 | 3.58 – 3.44, m | 28.6, CH₃ |
| 23a | 2.35, m (overlap) | 51.6, CH₃ |
| 23b | 1.88, m (overlap) | - |
| 24 | 1.18, t (7.0) | - |
| N-Me | 2.94, s | - |
| COOMe | 3.78, s | - |
| NH | 8.08, br | - |

**Compound (−)-24**: 2-((2S,3R,4S)-5-(methoxycarbonyl)-2-((2S,3R,4S,5R,6R)-3,4,5-triacetoxy-6-(acetoxyethyl)tetrahydro-2H-pyran-2-yl)oxy)-3-vinyl-3,4-dihydro-2H-pyran-4-yl)acetic acid

![Chemical structure](image)

Prepared according to a known procedure. To secologanin tetraacetate (−)-17 (60 mg, 0.108 mmol), prepared according to our modifications of Ishikawa’s procedures in acetone (2 mL) at 0 ºC was added dropwise a solution of Jones Reagent (0.06 mL of 2.67 M in water) and the reaction mixture was stirred at 0 ºC for about 30 min. Upon completion of the reaction (monitoring by TLC), the mixture was quenched with isopropanol at 0 ºC and was filtered over celite and concentrated under reduced pressure. The crude product was purified by preparative TLC on silica gel (CH₂Cl₂/MeOH 10:1) to give 58 mg of (−)-24 as a white solid (93% yield).

**R₇**: 0.44 (CH₂Cl₂/MeOH 10:1)

**¹H NMR** (360 MHz, CDCl₃) δ 7.40 (d, J = 2.0 Hz, 1H), 5.53 (dt, J = 17.3, 9.9 Hz, 1H), 5.31 – 5.23 (m, 3H), 5.20 (d, J = 9.5 Hz, 1H), 5.10 (t, J = 9.5 Hz, 1H), 5.01 (dd, J = 9.5, 8.1 Hz, 1H), 4.88 (d, J = 8.1 Hz, 1H), 4.28 (dd, J = 12.4, 4.4 Hz, 1H), 4.14 (dd, J = 12.4, 2.1 Hz, 1H), 3.74 – 3.71 (m, 1H), 3.69 (s, 3H), 3.20 – 3.12 (m, 1H), 3.05 (dd, J = 17.2, 4.7 Hz, 1H), 2.92 – 2.86 (m, 1H), 2.30 (dd, J = 17.2, 9.1 Hz, 1H), 2.10 (s, 3H), 2.02 (s, 3H), 2.00 (s, 3H), 1.90 (s, 3H).

**¹³C NMR** (90 MHz, CDCl₃) δ 177.1, 170.9, 170.4, 169.5, 169.1, 166.9, 151.2, 132.0, 121.3, 109.6, 96.0, 95.7, 72.6, 72.4, 70.7, 68.2, 61.8, 51.5, 43.4, 33.6, 26.2, 20.9, 20.7, 20.7, 20.2.

HRMS (m/z): [M + Na]⁺ calcd. for C₂₂H₁₂NaO₁₅⁺ 595.1628, found 595.1618.

[α]₂²⁰ = −78.2 (c 0.55, CHCl₃)

**Compound (−)-50b**: (2R,3R,4S,5R,6S)-2-(acetoxyethyl)-6-(((2S,3R,4S)-4-((2-(3-(2-methoxy-2-o xoethyl)-1H-indol-2-yl)-2-oxoethyl)-5-(methoxycarbonyl)-3-vinyl-3,4-dihydro-2H-pyran-2-yl)oxy)tetrahydro-2H-pyran-3,4,5-triyl triacetate
Inspired from known procedures.\textsuperscript{13} To a solution of (−)-24 (47 mg, 0.0821 mmol) in CH$_2$Cl$_2$ (0.5 mL) at 0 °C was added dropwise oxalyl chloride (20 mg, 0.16 mmol) and then, the reaction mixture was allowed to stir at room temperature overnight. The reaction mixture was concentrated to dryness under reduced pressure and the crude material was directly treated for next step without isolation. To the crude reaction mixture dissolved in Et$_2$O (1 mL) at 0 °C were successively added 15b (30 mg, 0.16 mmol) and dropwise a solution of SnCl$_4$ (0.008 mL of 1 M in CH$_2$Cl$_2$, 0.008 mmol). The reaction mixture was allowed to stir at room temperature for 2 h. The reaction mixture was quenched with a saturated aqueous solution of KF. The resulting mixture was extracted 5 times with CH$_2$Cl$_2$. The combined organic layers were dried over Na$_2$SO$_4$, filtered and concentrated under reduced pressure. The crude product was purified by preparative TLC on silica gel (Dichloromethane/Ethyl acetate 5:1) to give 28 mg of (−)-50b as a colorless oil (46% yield).

$R_f = 0.42$ (Dichloromethane/Ethyl acetate 5:1)

$^1$H NMR (360 MHz, CDCl$_3$) δ 9.68 (br, 1H), 7.67 (dt, $J = 8.2, 1.0$ Hz, 1H), 7.46 (d, $J = 1.9$ Hz, 1H), 7.41 (dt, $J = 8.2, 1.0$ Hz, 1H), 7.34 (ddd, $J = 8.2, 6.5, 1.0$ Hz, 1H), 7.15 (ddd, $J = 8.2, 6.5, 1.0$ Hz, 1H), 5.57 (dt, $J = 17.0, 10.0$ Hz, 1H), 5.32 (d, $J = 3.4$ Hz, 1H), 5.26 – 5.18 (m, 2H), 5.17 – 5.14 (m, 1H), 5.13 – 5.06 (m, 1H), 4.99 (dd, $J = 9.5, 8.1$ Hz, 1H), 4.90 (d, $J = 8.1$ Hz, 1H), 4.28 (dd, $J = 12.4, 4.4$ Hz, 1H), 4.19 – 4.10 (m, 3H), 3.80 – 3.74 (m, 1H), 3.73 (s, 3H), 3.67 (s, 3H), 3.67 – 3.61 (m, 1H), 3.49 – 3.39 (m, 1H), 2.96 (ddd, $J = 10.0, 5.9, 3.4$ Hz, 1H), 2.81 (dd, $J = 16.3, 10.0$ Hz, 1H), 2.10 (s, 3H), 2.02 (s, 3H), 1.99 (s, 3H), 1.91 (s, 3H).

$^{13}$C NMR (90 MHz, CDCl$_3$) δ 191.3, 171.3, 170.8, 170.3, 169.3, 168.8, 167.5, 151.6, 135.8, 132.3, 132.0, 128.2, 126.2, 121.2, 120.9, 120.7, 114.5, 112.2, 109.9, 96.0, 95.9, 72.5, 72.2, 70.7, 68.1, 61.6, 52.1, 51.6, 43.2, 39.8, 31.1, 27.0, 20.8, 20.6, 20.2.

HRMS (m/z): [M + H]$^+$ calcd. for C$_{36}$H$_{42}$NO$_{16}$ + 744.2498, found 744.2463.

[M + Na]$^+$ calcd. for C$_{36}$H$_{41}$NNaO$_{16}$ + 766.2318, found 766.2283.

$[\alpha]^{25}_D = -90.0$ (c 0.35, CHCl$_3$)

Compound (−)-50a: (2R,3R,4S,5R,6S)-2-(acetoxymethyl)-6-(((2S,3R,4S)-5-(methoxycarbonyl)-4-(2-(3-(2-(methylamino)-2-oxoethyl)-1H-indol-2-yl)-2-oxoethyl)-3-vinyl-3,4-dihydro-2H-pyran-2-yl)oxy)tetrahydro-2H-pyran-3,4,5-triyl triacetate
Inspired from a known procedure. To a solution of \((-\)-24 (23 mg, 0.04017 mmol) in \(\text{CH}_2\text{Cl}_2\) (0.5 mL) at 0 °C, was added dropwise oxalyl chloride (7 \(\mu\)L, 0.08 mmol) and then the reaction mixture was allowed to stir at room temperature overnight. The reaction mixture was concentrated to dryness under reduced pressure and the crude material was directly treated for next step without purification. To the crude reaction mixture dissolved in \(\text{Et}_2\text{O}\) (0.4 mL) and \(\text{CH}_2\text{Cl}_2\) (0.1 mL) at 0 °C, was added 15a (15 mg,0.08 mmol) followed by the dropwise addition of a solution of tin chloride (0.04 mL, 1 M in \(\text{CH}_2\text{Cl}_2\), 0.04 mmol). The reaction mixture was allowed to stir at room temperature overnight. The reaction mixture was quenched with a saturated aqueous solution of KF and the resulting mixture was extracted 5 times with \(\text{CH}_2\text{Cl}_2\). The combined organic layers were dried over Na₂SO₄ and concentrated under reduced pressure. The crude product was purified by preparative TLC on silica gel (EtOAc) to give 13 mg of \((-\)-50a as a colorless oil (44% yield).

\(R_f = 0.46\) (Ethyl acetate)

\(^1\text{H NMR}\) (360 MHz, CDCl₃) \(\delta\) 9.94 (br, 1H), 7.80 (dt, \(J = 8.2, 0.9\) Hz, 1H), 7.46 (d, \(J = 1.9\) Hz, 1H), 7.43 (dt, \(J = 8.2, 0.9\) Hz, 1H), 7.37 (ddd, \(J = 8.2, 6.7, 0.9\) Hz, 1H), 7.18 (ddd, \(J = 8.2, 6.7, 0.9\) Hz., 1H), 6.23 (br, 1H), 5.58 (dt, \(J = 17.4, 9.6\) Hz, 1H), 5.34 (d, \(J = 3.4\) Hz, 1H), 5.26 – 5.16 (m, 3H), 5.09 (t, \(J = 9.5\) Hz, 1H), 4.96 (dd, \(J = 9.5, 8.1\) Hz, 1H), 4.88 (d, \(J = 8.1\) Hz, 1H), 4.28 (dd, \(J = 12.4, 4.4\) Hz, 1H), 4.19 – 4.10 (m, 1H), 4.02 (d, \(J = 2.7\) Hz, 2H), 3.73 (s, 3H), 3.73 – 3.70 (m, 1H), 3.62 (dd, \(J = 15.2, 2.3\) Hz, 1H), 3.44 – 3.37 (m, 1H), 2.89 (ddd, \(J = 9.6, 5.9, 3.4\) Hz, 1H), 2.75 – 2.67 (m, 1H), 2.70 (d, \(J = 4.5\) Hz, 3H), 2.10 (s, 3H), 2.02 (s, 3H), 1.98 (s, 3H), 1.88 (s, 3H).

\(^{13}\text{C NMR}\) (90 MHz, CDCl₃) \(\delta\) 192.3, 171.3, 170.9, 170.4, 169.5, 168.9, 167.8, 152.1, 136.4, 132.4, 131.7, 128.1, 126.9, 121.5, 121.5, 121.2, 117.1, 112.4, 109.6, 95.9 (2C), 72.5, 72.4, 70.7, 68.2, 61.7, 51.9, 43.5, 40.1, 33.7, 27.6, 26.5, 20.9, 20.7 (2C), 20.3.

\(\text{HRMS} (m/z): [M + H]^+\) calc'd. for \(\text{C}_{36}\text{H}_{43}\text{N}_{3}\text{O}_{15}\)^{+} 743.2658, found 744.2651.

\(\text{[M + Na]^+}\) calc'd. for \(\text{C}_{36}\text{H}_{43}\text{Na}_{3}\text{O}_{15}\)^{+} 765.2477, found 765.2469.

\(\beta\)D = \(-\)77.0 (c 1.00, CHCl₃)

**Compound \((-\)-7a: ophiorrhine G**

To a solution of \((-\)-50a (13 mg, 0.0175 mmol) of methanol (1 mL) at 0 °C, was added K₂CO₃ (7 mg, 0.05 mmol). The reaction mixture was stirred at 0 °C for 20 min and was then directly purified by silica gel preparative TLC (CH₂Cl₂[saturated with ammonium hydroxide]/MeOH 5:1) to give 10 mg of ophiorrhine G \((-\)-7a as a white solid (quant.).

\(R_f = 0.26\) (CH₂Cl₂ [saturated with ammonium hydroxide]/MeOH 5:1)

\(^1\text{H NMR}\) (400 MHz, MeOD) \(\delta\) 7.68 (dt, \(J = 8.3, 1.1\) Hz, 1H), 7.53 (d, \(J = 1.9\) Hz, 1H), 7.44 (dt, \(J = 8.3, 1.1\) Hz, 1H), 7.31 (ddd, \(J = 8.3, 6.8, 1.1\) Hz, 1H), 7.11 (ddd, \(J = 8.3, 6.8, 1.1\) Hz, 1H), 5.67 (dt, \(J = 17.0, 10.0\) Hz, 1H), 5.54 (d, \(J = 3.8\) Hz, 1H), 5.16 (dd, \(J = 17.0, 1.8\) Hz, 1H), 5.14 (dd, \(J = 10.0, 1.8\) Hz, 1H), 4.69 (d, \(J = 7.8\) Hz, 1H), 4.08 (d, \(J = 15.5\) Hz, 1H), 4.00 (d, \(J = 15.5\) Hz, 1H), 3.91 (dd, \(J = 12.0, 2.0\) Hz, 1H), 3.68 (dd, \(J = 12.0, 5.8\) Hz, 1H), 3.68 – 3.64 (m, 1H), 3.61 (s, 3H), 3.55 (dd, \(J = 17.1, 5.2\) Hz, 1H),
3.42 – 3.35 (m, 1H), 3.34 – 3.28 (m, 2H), 3.25 (dd, J = 9.2, 7.8 Hz, 1H), 2.97 (dd, J = 17.1, 8.0 Hz, 1H), 2.91 – 2.86 (m, 1H), 2.68 (s, 3H).

$^1$H NMR (100 MHz, MeOD) δ 194.5, 174.5, 169.1, 153.8, 138.1, 134.8, 133.6, 129.2, 127.0, 121.5 (2C), 120.5, 116.9, 113.5, 110.4, 100.0, 97.6, 78.4, 78.0, 74.6, 71.6, 62.8, 51.7, 45.4, 41.0, 33.7, 27.8, 26.6.

HRMS (m/z): [M + H]$^+$ calcd. for C$_{28}$H$_{35}$N$_2$O$_{11}$ 575.2235, found 575.2219.

[M + Na]$^+$ calcd. for C$_{28}$H$_{34}$N$_2$NaO$_{11}$ 597.2055, found 597.2039.

$\Box$$_{27}$$D$ = −105.0 (c 0.4, MeOH)

**Compound (−)-6a: ophiorrhiside E**

Inspired from known procedures.$^{14,15}$ To (−)-50a (18 mg, 0.024 mmol) in AcOH (1.0 mL) at room temperature was added Et$_3$N (50 µL, 0.364 mmol) and then the reaction mixture was stirred at 80 ºC for 1 h, after which an addition of Et$_3$N (50 µL, 0.364 mmol) was effected followed by a third addition of Et$_3$N (50 µL, 0.364 mmol) after an additional 1 h and the reaction mixture was stirred for an additional 14 h. Then the mixture was cooled to room temperature, diluted with CH$_2$Cl$_2$, and then quenched with a solution of ammonium hydroxide until it reached pH ≥ 7. The resulting mixture was extracted 5 times with CH$_2$Cl$_2$. The combined organic layers were dried over Na$_2$SO$_4$, filtered and concentrated under reduced pressure. The crude product was used directly in the next step without purification. It was dissolved in MeOH (1.0 mL) onto which K$_2$CO$_3$ (10 mg, 0.073 mmol) was added at 0 ºC. The reaction mixture was stirred for 30 min and was then directly purified by silica gel preparative TLC (CH$_2$Cl$_2$[saturated with ammonium hydroxide]/EtOAc[saturated with ammonium hydroxide] /MeOH 3:2:1) to give 8 mg of ophiorrhine G (−)-7a as a white solid (57%) and 4 mg of ophiorrhiside E (−)-6a as a yellow oil (30%).

To ophiorrhine G (−)-7a (6 mg, 0.0104 mmol) in AcOH (0.5 mL) at room temperature, was added Et$_3$N (22 µL, 0.15 mmol) and then the reaction mixture was stirred at 80 ºC for 1 h, after which an addition of Et$_3$N (22 µL, 0.15 mmol) was effected followed by a third addition of Et$_3$N (22 µL, 0.15 mmol) after an additional 1 h and the reaction mixture was stirred for an additional 14 h. Then the mixture was cooled to room temperature, diluted with CH$_2$Cl$_2$, and then quenched with a solution of ammonium hydroxide until it reached pH ≥ 7. The resulting mixture was extracted 5 times with CH$_2$Cl$_2$. The combined organic layers were dried over Na$_2$SO$_4$, filtered and concentrated under reduced pressure. The crude product was purified by silica gel preparative TLC (CH$_2$Cl$_2$[saturated with ammonium hydroxide] /MeOH 3:2:1) to give 7 mg of ophiorrhine G (−)-7a as a white solid (57%) and 3 mg of ophiorrhiside E (−)-6a as a yellow oil (30%).
hydroxide]/EtOAc[saturated with ammonium hydroxide]/MeOH 3:2:1) to give 1 mg of ophiorrhiside E (−)-6a as a yellow oil (20%).

\[ R_f = 0.12 \quad (\text{CH}_2\text{Cl}_2)[\text{saturated with ammonium hydroxide}]/\text{MeOH} 5:1 \]

\[ ^1\text{H NMR} \quad (400 \text{ MHz, MeOD}) \quad \delta \quad 7.95 \quad (d, \quad J = 8.0 \text{ Hz}, \quad 1H), \quad 7.49 \quad (t, \quad J = 8.0 \text{ Hz}, \quad 1H), \quad 7.45 \quad (s, \quad 1H), \quad 7.33 \quad (d, \quad J = 8.0 \text{ Hz}, \quad 1H), \quad 7.09 \quad (t, \quad J = 8.0 \text{ Hz}, \quad 1H), \quad 7.05 \quad (s, \quad 1H), \quad 6.02 \quad (d, \quad J = 9.2 \text{ Hz}, \quad 1H), \quad 6.00 \quad (\text{ddd}, \quad J = 17.5, \quad 10.7, \quad 7.7 \text{ Hz} \quad 1H), \quad 5.39 \quad (d, \quad J = 17.5 \text{ Hz}, \quad 1H), \quad 5.31 \quad (d, \quad J = 10.7 \text{ Hz}, \quad 1H), \quad 4.85 \quad (d, \quad J = 8.0 \text{ Hz}, \quad 1H), \quad 4.00 \quad (\text{ddd}, \quad J = 11.7, \quad 2.0 \text{ Hz}, \quad 1H), \quad 3.82 \quad (s, \quad 3H), \quad 3.71 \quad (\text{dd}, \quad J = 11.7, \quad 6.5 \text{ Hz}, \quad 1H), \quad 3.46 – 3.20 \quad (m, \quad 7H), \quad 3.07 \quad (s, \quad 3H), \quad 2.79 – 2.72 \quad (m, \quad 1H). \]

\[ ^{13}\text{C NMR} \quad (100 \text{ MHz, MeOD}) \quad \delta \quad 168.4, \quad 162.8, \quad 154.7, \quad 146.7, \quad 139.1, \quad 135.8, \quad 131.8, \quad 131.7, \quad 129.4, \quad 123.7, \quad 121.3, \quad 120.2, \quad 119.5, \quad 112.3, \quad 109.8, \quad 102.9, \quad 100.5, \quad 97.0, \quad 78.8, \quad 78.1, \quad 74.7, \quad 71.7, \quad 63.1, \quad 51.5, \quad 45.2, \quad 35.7, \quad 33.6, \quad 32.4. \]

\[ \text{HRMS (m/z):} \quad [\text{M} + \text{H}]^+ \quad \text{calcd. for C}_{28}\text{H}_{33}\text{N}_2\text{O}_{10}^+ \quad 557.2130, \quad \text{found} \quad 557.2104. \]

\[ [\text{M} + \text{Na}]^+ \quad \text{calcd. for C}_{28}\text{H}_{33}\text{N}_2\text{NaO}_{10}^+ \quad 579.1949, \quad \text{found} \quad 579.1923. \]

\[ [\alpha]^{25}_D = -265.0 \quad (c \quad 0.6, \quad \text{MeOH}) \]

**Compound (−)-54:** \( (2R,3R,4S,5R,6S)-2-(\text{acetoxymethyl})-6-\text{((4S,4aS,4bS,6R,11bS,12aS)-1-(methoxycarbonyl)-13-methyl-14-oxo-4,4a,4b,5,6,11,12a-octahydro-11b,6-(epiminomethano)pyran}[3',4';3,4]cyclopenta[1,2-a]carbazol-4-yi)oxy)\text{tetrahydro-2H-pyran-3,4,5-triyl triacetate}^2 \)

![](image)

To (−)-50a (7 mg, 0.00943 mmol) in AcOH (0.5 mL at room temperature) was added Et₃N (59 μL, 0.425 mmol) and the reaction mixture was stirred at 125 °C for about 6 h. Then the mixture was cooled down to room temperature, diluted with CH₂Cl₂, and then quenched with a solution of ammonium hydroxide until pH ≥ 7. The resulting mixture was extracted 5 times with CH₂Cl₂. The combined organic layers were dried over Na₂SO₄ and concentrated under reduced pressure. The crude product was purified by silica gel preparative TLC (EtOAc) to give 2.0 mg of (+)-55 (29%) as a white solid and 4.0 mg of (−)-54 as a white solid (58%).

\[ R_f = 0.56 \quad (\text{Ethyl acetate}) \]

\[ ^1\text{H NMR} \quad (400 \text{ MHz, CDCl}_3) \quad \delta \quad 8.13 \quad (\text{br}, \quad 1H), \quad 7.57 – 7.53 \quad (\text{m}, \quad 1H), \quad 7.38 – 7.34 \quad (\text{m}, \quad 1H), \quad 7.30 \quad (s, \quad 1H), \quad 7.19 – 7.13 \quad (\text{m}, \quad 2H), \quad 5.35 \quad (d, \quad J = 1.5 \text{ Hz}, \quad 1H), \quad 5.23 \quad (t, \quad J = 9.6 \text{ Hz}, \quad 1H), \quad 5.13 \quad (t, \quad J = 9.6 \text{ Hz}, \quad 1H), \quad 4.99 \quad (\text{dd}, \quad J = 9.6, \quad 8.1 \text{ Hz}, \quad 1H), \quad 4.84 \quad (d, \quad J = 8.1 \text{ Hz}, \quad 1H), \quad 4.31 \quad (\text{dd}, \quad J = 12.4, \quad 4.3 \text{ Hz}, \quad 1H), \quad 4.24 – 4.22 \quad (\text{m}, \quad 1H), \quad 4.16 \quad (\text{dd}, \quad J = 12.4, \quad 2.4 \text{ Hz}, \quad 1H), \quad 3.78 \quad (s, \quad 3H), \quad 3.73 \quad (\text{ddd}, \quad J = 9.6, \quad 4.3, \quad 2.4 \text{ Hz}, \quad 1H), \quad 3.32 – 3.20 \quad (\text{m}, \quad 2H), \quad 2.96 \quad (s, \quad 3H), \quad 2.33 \quad (\text{dd}, \quad J = 11.2, \quad 9.0 \text{ Hz}, \quad 1H), \quad 2.13 \quad (s, \quad 3H), \quad 2.18 – 2.09 \quad (\text{m}, \quad 1H), \quad 2.05 \quad (s, \quad 3H), \quad 2.03 \quad (s, \quad 3H), \quad 1.95 \quad (s, \quad 3H), \quad 1.94 – 1.87 \quad (\text{m}, \quad 3H). \]

\[ ^{13}\text{C NMR} \quad (100 \text{ MHz, CDCl}_3) \quad \delta \quad 176.2, \quad 170.8, \quad 170.4, \quad 169.5, \quad 169.1, \quad 167.1, \quad 148.9, \quad 141.9, \quad 136.0, \quad 124.7, \quad 121.9, \quad 120.7, \quad 118.5, \quad 114.1, \quad 113.5, \quad 111.9, \quad 96.1, \quad 94.3, \quad 72.6, \quad 72.3, \quad 70.8, \quad 68.2, \quad 67.8, \quad 61.7, \quad 51.7, \quad 50.8, \quad 45.1, \quad 42.3, \quad 33.5, \quad 31.2, \quad 28.7, \quad 26.6, \quad 20.9, \quad 20.7, \quad 20.7, \quad 20.3. \]

\[ \text{HRMS (m/z):} \quad [\text{M} + \text{H}]^+ \quad \text{calcd. for C}_{36}\text{H}_{40}\text{N}_2\text{O}_{14}^+ \quad 725.2552, \quad \text{found} \quad 725.2534. \]

\[ [\text{M} + \text{Na}]^+ \quad \text{calcd. for C}_{36}\text{H}_{40}\text{NaO}_{14}^+ \quad 747.2371, \quad \text{found} \quad 747.2355. \]

S30
To (−)-54 (5 mg, 0.00691 mmol) in AcOH (0.4 mL at room temperature) was added Et₃N (43 µL, 0.31 mmol) and the reaction mixture was stirred at 125 ºC for about 38 h. Then the mixture was cooled down to room temperature, diluted with CH₂Cl₂, and then quenched with a solution of ammonium hydroxide until pH ≥ 7. The resulting mixture was extracted 5 times with CH₂Cl₂. The combined organic layers were dried over Na₂SO₄ and concentrated under reduced pressure. The crude product was purified by silica gel preparative TLC (EtOAc/petroleum ether 7:3) to give 3.0 mg of (+)-55 as a pale solid (60%) and trace of (−)-54 as a white solid.

\(
R_f = 0.43 \text{ (EtOAc/ petroleum ether 7:3)}
\)

\(^1\)H NMR (360 MHz, CDCl₃) \(\delta 8.37 \text{ (d, } J = 8.1 \text{ Hz, 1H)}, 8.13 \text{ (s, 1H)}, 7.42 \text{ (s, 1H)}, 7.42 – 7.38 \text{ (m, 2H), 7.31 (s, 1H)}, 7.21 \text{ (dt, } J = 8.1, 4.1 \text{ Hz, 1H)}, 6.39 \text{ (q, } J = 4.8 \text{ Hz, 1H)}, 5.41 \text{ (d, } J = 4.3 \text{ Hz, 1H)}, 5.25 \text{ (t, } J = 9.4 \text{ Hz, 1H)}, 5.13 – 5.05 \text{ (m, 2H)}, 4.92 \text{ (d, } J = 7.9 \text{ Hz, 1H)}, 4.25 \text{ (dd, } J = 12.4, 4.8 \text{ Hz, 1H)}, 4.05 \text{ (dd, } J = 12.4, 2.4 \text{ Hz, 1H)}, 3.76 \text{ (s, 3H)}, 3.71 \text{ (ddd, } J = 10.0, 5.0, 2.4 \text{ Hz, 1H)}, 3.63 – 3.51 \text{ (m, 3H)}, 3.16 \text{ (d, } J = 4.8 \text{ Hz, 3H)}, 3.10 – 2.98 \text{ (m, 1H)}, 2.03 \text{ (s, 6H)}, 2.02 \text{ (s, 3H)}.

\(^{13}\)C NMR (90 MHz, CDCl₃) \(\delta 170.8, 170.40, 170.36, 169.6, 169.5, 167.4, 151.8, 140.1, 137.4, 136.8, 130.1, 126.5, 126.4, 123.9, 122.4, 120.2, 120.1, 115.9, 111.6, 110.8, 96.6, 95.5, 72.5, 72.4, 70.9, 68.4, 61.7, 51.6, 46.9, 36.0, 35.1, 31.7, 30.8, 20.8, 20.7, 20.6.

HRMS (m/z): [M + H]⁺ calcd. for C₃₆H₃₉N₂O₁₄⁺ 723.2396, found 723.2377.

[\(\alpha\)]²⁵_D = +6.7 (c 0.75, CHCl₃)

**Compound (+)-56:** methyl (4S,12aS)-6-(methylcarbamoyl)-4-(((2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2H-pyran-2-yl)oxy)-4a,11,12,12a-tetrahydro-4H-pyran[3′,4′:3,4]cyclopenta[1,2-a]carbazole-1-carboxylate

To a solution of (+)-55 (2 mg, 0.00277 mmol) in MeOH (0.5 mL) at 0 °C was added K₂CO₃ (1 mg, 0.07 mmol). The reaction mixture was stirred at 0 °C for 30 min and was then directly purified by silica gel preparative TLC (CH₂Cl₂ [saturated with ammonium hydroxide]/MeOH 5:1) to give 1.5 mg of (+)-56 as a white solid (98%).
$R_f = 0.21 \text{ (CH}_2\text{Cl}_2 \text{ [saturated with ammonium hydroxide]/MeOH 5:1)}$

$^1$H NMR (400 MHz, MeOD) $\delta$ 8.14 (d, $J = 8.0$ Hz, 1H), 7.55 (s, 1H), 7.47 (d, $J = 8.0$ Hz, 1H), 7.38 (t, $J = 8.0$ Hz, 1H), 7.35 (s, 1H), 7.12 (t, $J = 8.0$ Hz, 1H), 5.52 (d, $J = 6.2$ Hz, 1H), 4.74 (d, $J = 7.6$ Hz, 1H), 3.77 (s, 3H), 3.73 – 3.69 (m, 1H), 3.66 – 3.63 (m, 1H), 3.62 – 3.58 (m, 1H), 3.58 – 3.55 (m, 1H), 3.55 – 3.52 (m, 1H), 3.40 – 3.35 (m, 1H), 3.34 – 3.28 (m, 1H), 3.27 – 3.23 (m, 1H), 3.23 – 3.16 (m, 1H), 3.05 (s, 3H), 3.03 – 2.96 (m, 1H).

$^{13}$C NMR (100 MHz, MeOD) $\delta$ 174.1, 169.5, 153.8, 142.2, 139.0, 138.3, 130.4, 127.9, 126.8, 123.7, 123.1, 120.5, 119.9, 116.8, 112.2, 112.0, 100.5, 97.5, 78.4, 78.1, 74.8, 71.4, 62.4, 51.8, 48.1, 37.5, 36.8, 26.9.

HRMS (m/z): [M + Na]$^+$ calcld. for C$_{28}$H$_{30}$N$_2$NaO$_{10}$ $\delta$ 577.1793, found 577.1774.

$[\alpha]^{27}_D = +55.00 \text{ (c 0.4, MeOH)}$

Assignment of $^1$H ($\delta_H$) and $^{13}$C ($\delta_C$) NMR chemical shifts of compound (+)-56.

| Position | $\delta_H$ (ppm) | $\delta_C$ (ppm) |
|----------|-----------------|------------------|
|          | 400 MHz, CD$_2$OD | 100 MHz, CD$_2$OD |
| 2        | -               | 138.3, C          |
| 3        | -               | 127.9, C          |
| 5        | -               | 174.1, C          |
| 6        | -               | 130.4, C          |
| 7        | -               | 120.5, C          |
| 8        | -               | 123.1, C          |
| 9        | 8.14, d (8.0)   | 123.7, CH         |
| 10       | 7.12, t (8.0)   | 119.9, CH         |
| 11       | 7.38, t (8.0)   | 126.8, CH         |
| 12       | 7.47, d, (8.0)  | 112.0, CH         |
| 13       | -               | 142.2, C          |
| 14a      | 3.62 – 3.58, m  | 37.5, CH$_2$      |
| 14b      | 3.03 – 2.96, m  |                  |
| 15       | 3.66 – 3.63, m  | 36.8, CH          |
| 16       | -               | 112.2, C          |
| 17       | 7.55, s         | 153.8, CH         |
| 18       | 7.35, s         | 116.8, CH         |
| 19       | -               | 139.0, C          |
| 20       | 3.58 – 3.55, m  | 48.1, CH          |
| 21       | 5.52, d, (6.2)  | 97.5, CH          |
| 22       | -               | 169.5, C          |
| 1'       | 4.74, d (7.6)   | 100.5, CH         |
| 2'       | 3.34 – 3.28, m (overlap) | 74.8, CH |
| 3'       | 3.40 – 3.35, m  | 78.1, CH          |
| Compound | δ (ppm) | J (Hz)   | Assignments          |
|----------|---------|----------|-----------------------|
| 4'       | 3.27 – 3.23 | m        | 71.4, CH              |
| 5'       | 3.23 – 3.16 | m        | 78.4, CH              |
| 6'a      | 3.73 – 3.69 | m        | 62.4, CH₂              |
| 6'b      | 3.55 – 3.52 | m        |                        |
| N-Me     | 3.05, s   |          | 26.9, CH₃              |
| COOMe    | 3.77, s   |          | 51.8, CH₃              |

**Compound (−)-1a: opiorrhine A**

To (−)-54 (11 mg, 0.0148 mmol) dissolved in 1 mL methanol at 0 °C was added K₂CO₃ (6 mg, 0.0445 mmol). The reaction mixture was stirred at 0 °C for 20 min and was then directly purified by silica gel preparative TLC (CH₂Cl₂[saturated with ammonium hydroxide]/MeOH 5:1) to give 8.0 mg of opiorrhine A (−)-1a as a white solid (quant.).

R<sub>f</sub> = 0.29 (CH₂Cl₂[saturated with ammonium hydroxide]/MeOH 5:1)

**¹H NMR (400 MHz, MeOD)** δ 7.47 (d, J = 7.3, 1H), 7.37 (s, 1H), 7.33 (d, J = 7.3 Hz, 1H), 7.07 – 6.99 (m, 2H), 5.52 (d, J = 1.5 Hz, 1H), 4.59 (d, J = 7.9 Hz, 1H), 4.14 (t, J = 2.3 Hz, 1H), 3.87 (dd, J = 11.9, 1.7 Hz, 1H), 3.77 (s, 3H), 3.64 (dd, J = 11.9, 5.3 Hz, 1H), 3.39 – 3.23 (m, 5H), 3.17 (dd, J = 9.1, 7.9 Hz, 1H), 2.96 (s, 3H), 2.30 – 2.17 (m, 2H), 1.97 – 1.89 (m, 1H), 1.88 – 1.83 (m, 2H).

**¹³C NMR (100 MHz, MeOD)** δ 179.7, 169.1, 151.0, 144.1, 137.9, 125.5, 122.0, 120.7, 118.5, 114.7, 113.1, 112.5, 100.0, 95.7, 78.3, 77.9, 74.6, 71.5, 69.8, 62.6, 52.3, 51.9, 46.9, 43.4, 34.5, 32.5, 28.7, 28.0.

**HRMS (m/z):** [M + H]<sup>+</sup> calcd. for C₂₈H₃₃N₂O₁₀ <sup>557.2130</sup>, found 557.2111.

[M + Na]<sup>+</sup> calcd. for C₂₈H₃₂N₂NaO₁₀ <sup>579.1949</sup>, found 579.1931.

[α]<sub>27</sub><sup>D</sup> = − 68.6 (c 0.35, MeOH)
4. Comparison of $^1$H, $^{13}$C NMR data and optical rotations for natural and synthetic products

![Chemical structure of (-)-7a, ophiorrhine G](image)

**Comparison of the $^1$H NMR chemical shifts ($\delta$) of natural and synthetic ophiorrhine G**

| Position | Natural product Reported $\delta$$_H$ (ppm)$^{10}$ (Methanol-d$_4$, 600 MHz) | Natural product Recalibrated $\delta$$_H$ (ppm)$^a$ vs Methanol-d$_4$ at 3.31 ppm (Methanol-d$_4$, 600 MHz) | Our Synthetic product $\delta$$_H$ (ppm) vs Methanol-d$_4$ at 3.31 ppm (Methanol-d$_4$, 400 MHz) |
|----------|-------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------|
| 6a       | 3.88, d (15.5)                                                          | 3.98, d (15.5)                                                                                 | 4.00, d (15.5)                                                                       |
| 6b       | 3.98, d (15.5)                                                          | 4.08, d (15.5)                                                                                 | 4.08, d (15.5)                                                                       |
| 9        | 7.58, d (8.2)                                                           | 7.68, d (8.2)                                                                                 | 7.68 dt (8.3, 1.1)                                                                  |
| 10       | 7.02, t (8.2)                                                           | 7.12, t (8.2)                                                                                 | 7.11, ddd (8.3, 6.8, 1.1)                                                           |
| 11       | 7.22, t (8.2)                                                           | 7.32, t (8.2)                                                                                 | 7.31, ddd (8.3, 6.8, 1.1)                                                           |
| 12       | 7.34, d (8.2)                                                           | 7.44, d (8.2)                                                                                 | 7.44, dt (8.3, 1.1)                                                                 |
| 14a      | 3.44, dd (17.1, 5.2)                                                    | 3.54, dd (17.1, 5.2)                                                                          | 3.55, dd (17.1, 5.2)                                                                |
| 14b      | 2.86, dd (17.1, 8.0)                                                    | 2.96, dd (17.1, 8.0)                                                                          | 2.97, dd (17.1, 8.0)                                                                |
| 15       | 3.54, m                                                                 | 3.64, m                                                                                       | 3.68 – 3.64, m                                                                      |
| 17       | 7.45, d (1.8)                                                           | 7.55, d (1.8)                                                                                 | 7.53, d (1.9)                                                                       |
| 18a      | 5.04, m                                                                 | 5.14, m                                                                                       | 5.16, dd (17.0, 1.8)                                                                |
| 18b      | 5.56, m                                                                 | 5.66, m                                                                                       | 5.67, ddd (17.0, 10.1, 9.7)                                                         |
| 20       | 2.76, m                                                                 | 2.86, m                                                                                       | 2.91 – 2.86, m                                                                     |
| 21       | 5.43, d (3.7)                                                           | 5.53, d (3.7)                                                                                 | 5.54, d (3.8)                                                                       |
| 1'       | 4.58, d (7.9)                                                           | 4.68, d (7.9)                                                                                 | 4.69, d (7.8)                                                                       |
| 2'       | 3.15, dd (9.1, 7.9)                                                    | 3.25, dd (9.1, 7.9)                                                                            | 3.25, m (9.2, 7.8)                                                                  |
| 3'       | 3.27, m                                                                 | 3.37, m                                                                                       | 3.42 – 3.35, m                                                                     |
| 4'       | 3.19, m                                                                 | 3.29, m                                                                                       | 3.34 – 3.28, m (overlap)                                                            |
| 5'       | 3.22 m                                                                  | 3.32 m                                                                                       | 3.34 – 3.30, m (overlap)                                                            |
| 6a'      | 3.58, dd (12.0, 6.0)                                                    | 3.68, dd (12.0, 6.0)                                                                           | 3.68, dd (12.0, 5.8)                                                                |
| 6b'      | 3.81, dd (12.0, 2.0)                                                    | 3.91, dd (12.0, 2.0)                                                                           | 3.91, dd (12.0, 2.0)                                                                |
| N-Me     | 2.58, s                                                                 | 2.68, s                                                                                       | 2.68, s                                                                            |
| COOMe    | 3.51, s                                                                 | 3.61, s                                                                                       | 3.61, s                                                                            |

*a) the methanol-d$_4$ peak was at 3.21 ppm on the provided $^1$H NMR of natural ophiorrhine G$^{19}$
**Comparison of the $^{13}$C NMR chemical shifts (δ$_{13}$C) of natural and synthetic ophiorrhine G**

| Position | Natural product | Recalibrated δ$_{13}$C (ppm)$^a$ vs Methanol-d$_4$ at 49.0 ppm (Methanol-d$_4$, 150 MHz) | Our Synthetic product δ$_{13}$C (ppm) vs Methanol-d$_4$ at 49.0 ppm (Methanol-d$_4$, 100 MHz) |
|----------|-----------------|--------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------|
| 2        | 132.2, C        | 133.8, C                                                                                         | 133.6, C                                                                                            |
| 3        | 193.1, C        | 194.7, C                                                                                         | 194.5, C                                                                                            |
| 5        | 173.1, C        | 174.7, C                                                                                         | 174.5, C                                                                                            |
| 6        | 32.3, CH$_2$    | 33.9, CH$_2$                                                                                        | 33.7, CH$_2$                                                                                       |
| 7        | 115.5, C        | 117.1, C                                                                                         | 116.9, C                                                                                            |
| 8        | 127.5, C        | 129.1, C                                                                                         | 129.2, C                                                                                            |
| 9        | 120.2, CH       | 121.8, CH                                                                                         | 121.5, CH                                                                                            |
| 10       | 120.1, CH       | 121.7, CH                                                                                         | 121.5, CH                                                                                            |
| 11       | 125.8, CH       | 127.4, CH                                                                                         | 127.0, CH                                                                                            |
| 12       | 112.1, CH       | 113.7, CH                                                                                         | 113.5, CH                                                                                            |
| 13       | 136.7, C        | 138.3, C                                                                                         | 138.1, C                                                                                            |
| 14       | 39.5, CH$_2$    | 41.1, CH$_2$                                                                                        | 41.0, CH$_2$                                                                                       |
| 15       | 26.4, CH        | 28.0, CH                                                                                         | 27.8, CH                                                                                            |
| 16       | 109.0, C        | 110.6, C                                                                                         | 110.4, C                                                                                            |
| 17       | 152.5, CH       | 154.1, CH                                                                                         | 153.8, CH                                                                                            |
| 18       | 119.2, CH$_2$   | 120.8, CH$_2$                                                                                     | 120.5, CH$_2$                                                                                      |
| 19       | 133.4, CH       | 135.0, CH                                                                                         | 134.8, CH                                                                                            |
| 20       | 44.0, CH        | 45.6, CH                                                                                         | 45.4, CH                                                                                            |
| 21       | 96.2, CH        | 97.8, CH                                                                                         | 97.6, CH                                                                                            |
| 22       | 167.8, C        | 169.4, C                                                                                         | 169.1, C                                                                                            |
| 1’       | 98.6, CH        | 100.0, CH                                                                                         | 100.0, CH                                                                                            |
| 2’       | 73.2, CH        | 74.8, CH                                                                                         | 74.6, CH                                                                                            |
| 3’       | 76.5, CH        | 78.1, CH                                                                                         | 78.0, CH                                                                                            |
| 4’       | 70.1, CH        | 71.7, CH                                                                                         | 71.6, CH                                                                                            |
| 5’       | 77.0, CH        | 78.6, CH                                                                                         | 78.4, CH                                                                                            |
| 6’       | 61.3, CH$_2$    | 62.9, CH$_2$                                                                                        | 62.8, CH$_2$                                                                                       |
| N-Me     | 25.2, CH$_3$    | 26.8, CH$_3$                                                                                        | 26.6, CH$_3$                                                                                       |
| COOMe    | 50.4, CH$_3$    | 52.0, CH$_3$                                                                                        | 51.7, CH$_3$                                                                                       |

$^a$ the methanol-d$_4$ peak was at 47.4 ppm on the provided $^{13}$C NMR of natural ophiorrhine G$^{19}$

**Comparison of the optical rotation of natural and synthetic ophiorrhine G**

| Natural product Reported$^{19}$ [α]$^2$$_D$ | Our Synthetic product Measured [α]$^2$$_D$ |
|--------------------------------------------|-------------------------------------------|
| −260.0 (c 0.05, MeOH)                     | −105.0 (c 0.4, MeOH)                      |
Comparison of the $^1$H NMR chemical shifts ($\delta$$_H$) of natural and synthetic Ophiorrhiside E

| Position | Natural product | Our Synthetic product |
|----------|-----------------|-----------------------|
|          | Reported $\delta$$_H$ (ppm)$^{20,a}$ | $\delta$$_H$ (ppm) vs Methanol-d$_4$ at 3.31 ppm (Methanol-d$_4$, 400 MHz) |
| 6        | 7.01, s         | 7.05, s               |
| 9        | 7.93, br d (7.8) | 7.95, d (8.0)         |
| 10       | 7.07, dd (7.8, 7.8) | 7.09, t (8.0)         |
| 11       | 7.47, ddd (7.8, 7.8, 1.2) | 7.49, t (8.0, 8.0) |
| 12       | 7.31, d (7.8)   | 7.33, d (8.0)         |
| 14a      | 3.40 – 3.35, m (overlap) | 3.45 – 3.28, m (overlap) |
| 14a      | 3.30 – 3.15, m (overlap) | 3.45 – 3.28, m (overlap) |
| 15       | 3.40 – 3.35, m (overlap) | 3.42 – 3.33, m (overlap) |
| 17       | 7.44, s         | 7.45, s               |
| 18a      | 5.38, d (17.5)  | 5.39, d (17.5)        |
| 18b      | 5.30, d (10.7)  | 5.31, d (10.4)        |
| 19       | 5.99, ddd (17.5, 10.7, 8.5) | 6.00, ddd (17.5, 10.7, 7.7) |
| 20       | 2.74, m         | 2.79 – 2.72, m        |
| 21       | 6.02, d (9.5)   | 6.02, d (9.2)         |
| 1'       |                 | 4.85, d (8.0)         |
| 2'       | 3.30 – 3.15, m (overlap) | 3.29 – 3.20, m (overlap) |
| 3'       | 3.40 – 3.35, m (overlap) | 3.35 – 3.30, m (overlap) |
| 4'       | 3.30 – 3.15, m (overlap) | 3.31 – 3.26, m (overlap) |
| 5'       | 3.40 – 3.35, m (overlap) | 3.46 – 3.39, m (overlap) |
| 6'a      | 4.01, dd (11.8, 2.1) | 4.00, dd (11.7, 2.0) |
| 6'b      | 3.70, dd (11.8, 6.9) | 3.71, dd (11.7, 6.5) |
| N-Me     | 3.79, s         | 3.82, s               |
| COOMe    | 3.07, s         | 3.08, s               |

a) No reference for the chemical shifts ($\delta$$_H$) or copy of the $^1$H NMR spectra were provided.$^{20}$
Comparison of the $^{13}$C NMR chemical shifts ($\delta^{13}C$) of natural and synthetic ophiorrhiside E

| Position | Natural product Reported $\delta^{13}C$(ppm)$^{20,a}$ (Methanol-d4, 125 MHz) | Our Synthetic product $\delta^{13}C$(ppm) vs Methanol-d4 at 49.0 ppm (Methanol-d4, 100 MHz) |
|----------|--------------------------------------------------------------------------------|--------------------------------------------------------------------------------|
| 2        | 129.2, C                                                                        | 129.4, C                                                                        |
| 3        | 131.5, C                                                                        | 131.7, C                                                                        |
| 5        | 163.2, C                                                                        | 162.8, C                                                                        |
| 6        | 103.1, CH                                                                        | 102.9, CH                                                                        |
| 7        | 139.2, C                                                                        | 139.1, C                                                                        |
| 8        | 121.3, C                                                                        | 121.3, C                                                                        |
| 9        | 123.7, CH                                                                        | 123.7, CH                                                                        |
| 10       | 120.1, CH                                                                        | 120.2, CH                                                                        |
| 11       | 131.7, CH                                                                        | 131.8, CH                                                                        |
| 12       | 112.2, CH                                                                        | 112.3, CH                                                                        |
| 13       | 146.7, C                                                                        | 146.7, C                                                                        |
| 14       | 32.4, CH$_2$                                                                     | 32.4, CH$_2$                                                                     |
| 15       | 35.7, CH                                                                        | 35.7, CH                                                                        |
| 16       | 109.8, C                                                                        | 109.8, C                                                                        |
| 17       | 154.7, CH                                                                        | 154.7, CH                                                                        |
| 18       | 119.5, CH$_2$                                                                    | 119.5, CH$_2$                                                                    |
| 19       | 135.8, CH                                                                        | 135.8, CH                                                                        |
| 20       | 45.2, CH                                                                         | 45.2, CH                                                                         |
| 21       | 97.0, CH                                                                         | 97.0, CH                                                                         |
| 22       | 168.4, C                                                                         | 168.4, C                                                                         |
| 1’       | 100.5, CH                                                                         | 100.5, CH                                                                         |
| 2’       | 74.7, CH                                                                         | 74.7, CH                                                                         |
| 3’       | 78.0, CH                                                                         | 78.1, CH                                                                         |
| 4’       | 71.7, CH                                                                         | 71.7, CH                                                                         |
| 5’       | 78.8, CH                                                                         | 78.8, CH                                                                         |
| 6’       | 63.0, CH$_2$                                                                     | 63.1, CH$_2$                                                                     |
| N-Me     | 33.4, CH$_3$                                                                     | 33.6, CH$_3$                                                                     |
| COOMe    | 51.6, CH$_3$                                                                     | 51.5, CH$_3$                                                                     |

a) No reference for the chemical shifts ($\delta^{13}C$) or copy of the $^1$H NMR spectra were provided.$^{20}$

Comparison of the optical rotation of natural and synthetic ophiorrhiside E

| Natural product Reported$^{20}$ [$\alpha]^D$ | Our Synthetic product Measured [$\alpha]^D$ |
|---------------------------------------------|------------------------------------------|
| $-223.3$ (c 0.09, MeOH)                      | $-265.0$ (c 0.6, MeOH)                   |
Comparison of the \(^1\)H NMR chemical shifts (\(\delta_{\text{H}}\)) of natural and synthetic ophiorrhine A

| Position | Natural product Reported\(^{21}\) \(\delta_{\text{H}}\) (ppm) (Methanol-d4, 600 MHz) | Natural product Recalibrated\(^a\) \(\delta_{\text{H}}\) (ppm) vs Methanol-d4 at 3.31 ppm (Methanol-d4, 600 MHz) | Our Synthetic product \(\delta_{\text{H}}\) (ppm) vs Methanol-d4 at 3.31 ppm (Methanol-d4, 400 MHz) |
|----------|-------------------------------------------------|-------------------------------------------------|---------------------------------|
| 6        | 4.15, t (2.6)                                   | 4.15, t (2.6)                                   | 4.15, t (2.3)                   |
| 9        | 7.47, d (7.8)                                   | 7.47, d (7.8)                                   | 7.47, d (7.3)                   |
| 10       | 7.01, t (7.8)                                   | 7.01, t (7.8)                                   | 7.01, d (7.3)                   |
| 11       | 7.04, t (7.8)                                   | 7.04, t (7.8)                                   | 7.05, d (7.3)                   |
| 12       | 7.32, d (7.8)                                   | 7.32, d (7.8)                                   | 7.33, d (7.3)                   |
| 14a      | 3.25, m                                         | 3.25, m                                         | 3.25 – 3.32, m                  |
| 14b      | 2.22, m                                         | 2.22, m                                         | 2.28 – 2.22, m                  |
| 15       | 3.33, m                                         | 3.33, m                                         | 3.34 – 3.32, m                  |
| 17       | 7.37, s                                         | 7.37, s                                         | 7.37, s                         |
| 18a,b    | 1.85, ddd (6.8, 2.5, 2.1)                       | 1.85, ddd (6.8, 2.5, 2.1)                       | 1.88 – 1.84, m                  |
| 19       | 1.91, m                                         | 1.91, m                                         | 1.96 – 1.88, m                  |
| 20       | 2.20, m                                         | 2.20, m                                         | 2.25 – 2.19, m                  |
| 21       | 5.52, d (1.7)                                   | 5.52, d (1.7)                                   | 5.52, d (1.5)                   |
| 1\(^1\)  | 4.59, d (8.0)                                   | 4.59, d (8.0)                                   | 4.59, d (7.9)                   |
| 2\(^2\)  | 3.16, dd (9.2, 8.0)                             | 3.16, dd (9.2, 8.0)                             | 3.17, dd (9.1, 7.9)             |
| 3\(^3\)  | 3.35, m                                         | 3.35, m                                         | 3.37 – 3.31, m                  |
| 4\(^4\)  | 3.25, m                                         | 3.25, m                                         | 3.30 – 3.24, m                  |
| 5\(^5\)  | 3.28, m                                         | 3.28, m                                         | 3.28 – 3.30, m                  |
| 6a\(^6\) | 3.88, dd (11.8, 1.8)                            | 3.88, dd (11.8, 1.8)                            | 3.88, dd (11.7, 1.7)            |
| 6b\(^7\) | 3.65, dd (11.8, 5.7)                            | 3.65, dd (11.8, 5.7)                            | 3.65, dd (11.7, 5.3)            |
| N-Me     | 2.95, s                                         | 2.95, s                                         | 2.96, s                         |
| COOMe    | 3.76, s                                         | 3.76, s                                         | 3.77, s                         |

\(^a\) the methanol-d4 peak was at 3.31 ppm on the provided \(^1\)H NMR of natural ophiorrhine A\(^{21}\)
Comparison of the $^{13}$C NMR chemical shifts ($\delta_{^13}C$) of natural and synthetic ophiorrhine A

| Position | Natural product | | | Our Synthetic product |
|----------|----------------|----------------|----------------------|
|          | Reported $\delta_{^13}C$ (ppm)\(^{21}\) (Methanol-d$_4$, 150 MHz) | Natural product Recalibrated $\delta_{^13}C$ (ppm)\(^{a}\) vs Methanol-d$_4$ at 49.0 ppm (Methanol-d$_4$, 150 MHz) | | Our Synthetic product $\delta_{^13}C$ (ppm) vs Methanol-d$_4$ at 49.0 ppm (Methanol-d$_4$, 100 MHz) |
| 2 | 142.7, C | 144.1, C | 144.1, C |
| 3 | 68.3, C | 69.7, C | 69.8, C |
| 5 | 178.3, C | 179.7, C | 179.7, C |
| 6 | 41.9, CH | 43.3, CH | 43.4, CH |
| 7 | 111.1, C | 112.5, C | 112.5, C |
| 8 | 124.1, C | 125.5, C | 125.5, C |
| 9 | 117.1, CH | 118.5, CH | 118.5, CH |
| 10 | 119.3, CH | 120.7, CH | 120.7, CH |
| 11 | 120.6, CH | 122.0, CH | 122.0, CH |
| 12 | 111.7, CH | 113.1, CH | 113.1, CH |
| 13 | 136.5, C | 137.9, C | 137.9, C |
| 14 | 33.1, CH$_2$ | 34.5, CH$_2$ | 34.5, CH$_2$ |
| 15 | 31.1, CH | 32.5, CH | 32.5, CH |
| 16 | 113.3, C | 114.7, C | 114.7, C |
| 17 | 149.6, CH | 151.0, CH | 151.0, CH |
| 18 | 26.6, CH$_2$ | 28.0, CH$_2$ | 28.0, CH$_2$ |
| 19 | 50.8, CH | 52.2, CH | 52.3, CH |
| 20 | 45.5, CH | 46.9, CH | 46.9, CH |
| 21 | 94.2, CH | 95.6, CH C | 95.7, CH |
| 22 | 167.7, C | 169.1, C | 169.1, C |
| 1' | 98.5, CH | 99.9, CH | 100.0, CH |
| 2' | 73.2, CH | 74.6, CH | 74.6, CH |
| 3' | 76.5, CH | 77.9, CH CH | 77.9, CH |
| 4' | 70.1, CH | 71.5, CH | 71.5, CH |
| 5' | 76.9, CH | 78.3, CH | 78.3, CH |
| 6' | 61.2, CH$_2$ | 62.6, CH$_2$ | 62.6, CH$_2$ |
| N-Me | 27.4, CH$_3$ | 28.6, CH$_3$ | 28.7, CH$_3$ |
| COOME | 50.5, CH$_3$ | 51.9, CH$_3$ | 51.9, CH$_3$ |

\(^{a}\) the methanol-d$_4$ peak was at 47.6 ppm on the provided $^{13}$C NMR of natural ophiorrhine A\(^{21}\)

Comparison of the optical rotation of natural and synthetic ophiorrhine A

| Natural product | | | Our Synthetic product |
|----------------|----------------|----------------|----------------------|
| Reported\(^{21}\) $[\alpha]_D^{20}$ | | | Measured $[\alpha]_D^{20}$ |
| $-55.6$ (c 0.14, MeOH) | | | $-68.6$ (c 0.35, MeOH) |
5. NMR spectra of all compounds

$^1$H NMR (360 MHz, CD$_3$OD), 28a

$^{13}$C NMR (90 MHz, CD$_3$OD), 28a
$^1$H NMR (360 MHz, CD$_3$OD), 29a

$^1$C NMR (90 MHz, CD$_3$OD), 29a
$^1$H NMR (360 MHz, CD$_3$OD), 31

$^{13}$C NMR (90 MHz, CD$_3$OD), 31
\(^1\)H NMR (300 MHz, CDCl\(_3\)), (±)-28b

\(^1\)C NMR (75 MHz, CDCl\(_3\)), (±)-28b
$^1$H NMR (300 MHz, CDCl$_3$), (±)-29b

$^{13}$C NMR (75 MHz, CDCl$_3$), (±)-29b
$^1$H NMR (360 MHz, CD$_3$OD), 33a

$^{13}$C NMR (100 MHz, CD$_3$OD), 33a
\(^1\)H NMR (250 MHz, CD\(_3\)OD), (±)-34a

\[^{13}\text{C}\] NMR (62.5 MHz, CD\(_3\)OD), (±)-34a
$^1$H NMR (360 MHz, CD$_3$OD), (±)-35a

$^{13}$C NMR (100 MHz, CD$_3$OD), (±)-35a
$^1$H NMR (360 MHz, CD$_3$OD), (±)-36a

$^{13}$C NMR (100 MHz, CD$_3$OD), (±)-36a
$^1$H NMR (400 MHz, CDCl$_3$), 37a

$^{13}$C NMR (100 MHz, CDCl$_3$), 37a
$^{19}$F NMR (235 MHz, CDCl$_3$), 37a
$^1$H NMR (300 MHz, CDCl$_3$), 38a

$^{13}$C NMR (62.5 MHz, CDCl$_3$), 38a
$^{19}$F NMR (235 MHz, CDCl$_3$), 38a
$^{1}H$ NMR (400 MHz, CDCl$_3$), 39a

$^{13}C$ NMR (100 MHz, CDCl$_3$), 39a
$^1$H NMR (300 MHz, CDCl$_3$), (±)-33b

$^1$C NMR (90 MHz, CDCl$_3$), (±)-33b
$^1$H NMR (300 MHz, CDCl$_3$), (±)-37b

$^{13}$C NMR (100 MHz, CDCl$_3$), (±)-37b
COSY NMR (300 MHz, CDCl₃), (±)-37b

$^{19}$F NMR (235 MHz, CDCl₃), (±)-37b
$^1$H NMR (360 MHz, CDCl$_3$), 15b

$^{13}$C NMR (90 MHz, CDCl$_3$), 15b
$^1$H NMR (360 MHz, CDCl$_3$), 15a

$^{13}$C NMR (90 MHz, CDCl$_3$), 15a
$^1$H NMR (300 MHz, CDCl$_3$), ($\pm$)-40

$^{13}$C NMR (100 MHz, CDCl$_3$), ($\pm$)-40
$^1$H NMR (300 MHz, CD$_3$OD), 43a

$^{13}$C NMR (100 MHz, CD$_3$OD), 43a
$^1$H NMR (300 MHz, CDCl$_3$), 26

$^13$C NMR (90 MHz, CDCl$_3$), 26
$^{19}$F NMR (235 MHz, CDCl$_3$), 26
$^1$H NMR (300 MHz, CDCl$_3$), (±)-25

$^{13}$C NMR (100 MHz, CDCl$_3$), (±)-25
$^1$H NMR (360 MHz, CDCl$_3$), 46b

$^{13}$C NMR (90 MHz, CDCl$_3$), 46b
$^1$H NMR (360 MHz, CD$_3$OD), 46a

$^{13}$C NMR (90 MHz, CD$_3$OD), 46a
$^1$H NMR (360 MHz, CD$_3$OD), 47

$^{13}$C NMR (90 MHz, CD$_3$OD), 47
$^1$H NMR (300 MHz, CDCl$_3$), (±)-48

$^{13}$C NMR (75 MHz, CDCl$_3$), (±)-48
$^1$H NMR (300 MHz, CDCl$_3$), (±)-23

$^{13}$C NMR (100 MHz, CDCl$_3$), (±)-23

$^1$H NMR (360 MHz, CDCl$_3$), (±)-51
$^{13}$C NMR (100 MHz, CDCl$_3$), (±)-51

- 168.4
- 153.0
- 144.8
- 137.4
- 130.4
- 128.6
- 125.3
- 121.2
- 119.3
- 119.1
- 110.9
- 109.5
- 108.5
- 100.2
- 77.3
- 66.1
- 52.0
- 43.2
- 32.9
- 32.4
- 30.6
- 15.4
COSY (360 MHz, CDCl$_3$), (±)-51

HSQC (400 MHz, CDCl$_3$), (±)-51

HMBC (400 MHz, CDCl$_3$), (±)-51
DEPT (400 MHz, CDCl₃), (±)-51

NOESY (400 MHz, CDCl₃), (±)-51
$^1$H NMR (360 MHz, CDCl$_3$), (±)-53

$^{13}$C NMR (100 MHz, CDCl$_3$), (±)-53
COSY (360 MHz, CDCl₃), (±)-53

HSQC (360 MHz, CDCl₃), (±)-53
DEPT (360 MHz, CDCl₃), (±)-53

HMBC (400 MHz, CDCl₃), (±)-53
ROESY (600 MHz, CDCl$_3$), (±)-53
$^1$H NMR (360 MHz, CDCl$_3$), (−)-24

$^{13}$C NMR (90 MHz, CDCl$_3$), (−)-24

$^1$H NMR (360 MHz, CDCl$_3$), (−)-50b
$^{13}$C NMR (90 MHz, CDCl$_3$), (−)-$^{50b}$

$^1$H NMR (360 MHz, CDCl$_3$), (−)-$^{50a}$
$^{13}$C NMR (90 MHz, CDCl$_3$), (-)-50a

$^1$H NMR (400 MHz, CD$_3$OD), (-)-7a
$^1$C NMR (100 MHz, CD$_3$OD), (−)-7a

DEPT (400 MHz, CD$_3$OD), (−)-7a
COSY (400 MHz, CD$_3$OD), (-)-7a

HSQC (400 MHz, CD$_3$OD), (-)-7a
HMBC (400 MHz, CD$_3$OD), (−)-7a

NOESY (400 MHz, CD$_3$OD), (−)-7a
$^1$H NMR (400 MHz, CD$_3$OD), (−)-6a

$^{13}$C NMR (100 MHz, CD$_3$OD), (−)-6a
DEPT (400 MHz, CD$_3$OD), (−)-6a

COSY (400 MHz, CD$_3$OD), (−)-6a
HSQC (360 MHz, CD$_3$OD), (−)-6a

HMBC (400 MHz, CD$_3$OD), (−)-6a
$^1$H NMR (400 MHz, CDCl$_3$), (−)-54

$^{13}$C NMR (100 MHz, CDCl$_3$), (−)-54
$^1$H NMR (360 MHz, CDCl$_3$), (+)-55

$^{13}$C NMR (360 MHz, CDCl$_3$), (+)-55
$^1$H NMR (400 MHz, CD$_3$OD), (+)-56

$^{13}$C NMR (100 MHz, CD$_3$OD), (+)-56
DEPT (400 MHz, CD$_3$OD), (+)-56

COSY (360 MHz, CD$_3$OD), (+)-56
HSQC (360 MHz, CD$_3$OD), (+)-56

NOESY (360 MHz, CD$_3$OD), (+)-56
HMBC (360 MHz, CD$_3$OD), (+)-56

Key HMBC correlations

H14a,b (3.65 and 3.00 ppm) – C3 (127.9 ppm)
H18 (7.35 ppm) – C3 (127.9 ppm)
H18 (7.35 ppm) – C5 (174.1 ppm)
H18 (7.35 ppm) – C7 (120.5 ppm), H9 (8.14 ppm) – C7 (120.5 ppm)
H18 (7.35 ppm) – C20 (48.1 ppm)
H20 (3.56 ppm) – C19 (139.2 ppm)
$^1$H NMR (400 MHz, CD$_3$OD), (−)-1a

[Chemical structure image]

$^{13}$C NMR (100 MHz, CD$_3$OD), (−)-1a

[Chemical structure image]
DEPT (400 MHz, CD$_3$OD), (−)-1a

COSY (400 MHz, CD$_3$OD), (−)-1a
HSQC (400 MHz, CD$_3$OD), (−)-1a

HMBC (400 MHz, CD$_3$OD), (−)-1a
NOESY (400 MHz, CD$_3$OD), (−)-1a
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