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Supplementary Information

Base-induced isomerization of red uroleuconaphins revisited: Characterization and absolute stereochemistry of the yellow aphid pigments uroleuconaphins A_2 and B_2

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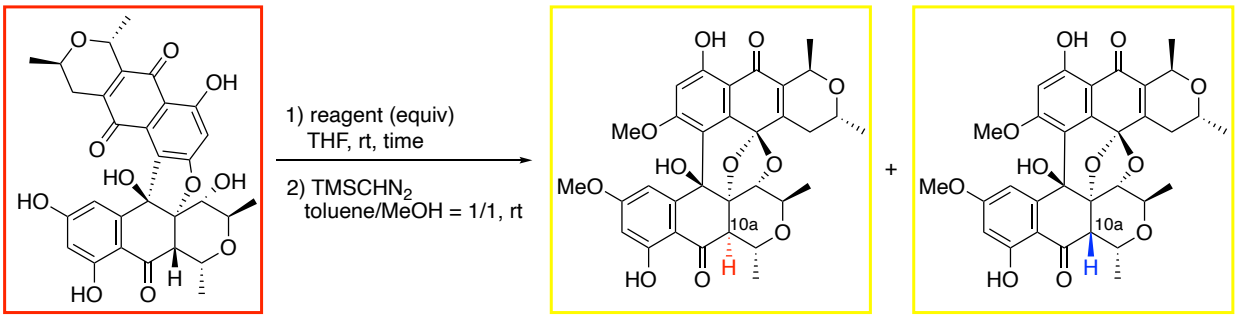
1. General

Infrared (IR) spectra were measured on a JASCO FT/IR-4200 spectrophotometer. Circular dichroism (CD) spectra were recorded on a JASCO J-725 spectropolarimeter. Ultraviolet–visible (UV–vis) spectra were measured on a JASCO V-650 spectrophotometer. Melting points (Mp) were determined on a Büchi B-545 apparatus, and were uncorrected. Optical rotations ($[\alpha]_D$) were measured with a JASCO P-2300 polarimeter. High-resolution mass spectra (HRMS) were recorded on a JEOL JMS-S3000 Spiral TOF. High-performance liquid chromatography (HPLC) was performed using a Cosmosil 5C18-MS-II (5 μm, 4.6 × 250 mm, Nacalai Tesque Inc.) for column, a JASCO PU-980 pump and a JASCO UV-2070 Plus UV detector (detection: 254 nm). For column chromatography, silica gel 60 N (Spherical, 63–210 μm, Kanto Chemical Co., Inc.) was used. Preparative HPLC was performed with a Cosmosil 5C18-MS-II (5 μm, 20 × 250 mm, Nacalai Tesque Inc.) for column, a JASCO PU-4180 pump and a JASCO MD-4010 photodiode array detector (detection: 254 nm). For thin-layer chromatography (TLC) analysis, Merck precoated silica gel plates 60 F_{254} were used. ^{1}H NMR spectra were recorded on a Bruker AVANCE-III (500 MHz) spectrometer; chemical shifts were referenced to tetramethylsilane as an internal standard and the residual solvent signal (acetone-d_6: δ_H 2.05; $CDCl_3$: δ_H 7.26). ^{13}C NMR spectra were recorded with a Bruker AVANCE-III (125 MHz) spectrometer; chemical shifts were referenced to the residual solvent signal (acetone-d_6: δ_C 29.8; $CDCl_3$: δ_C 77.0).

2. Optimization of conversion of uroleuconaphin A_1 (1) and B_1 (2)

2-1. Conversion of uroleuconaphin A_1 (**1**)

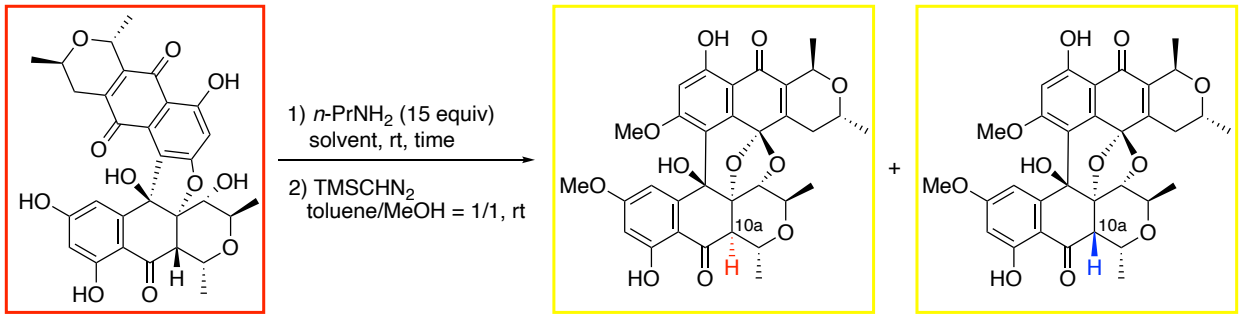


uroleucanaphin A_1 (**1**) **5a** **5b**

Table S1. Screening of base

entry	reagent (equiv)	pK_{aH} (THF)[1]	time (h)	yield (%) (**5a**:**5b**)
1[a]	pyridine (excess)	5.5	18	20 (4.2:1)
2	ethylenediamine (15)	13.6	0.2	95 (3.6:1)
3	*n*-$PrNH_2$ (15)	13.8	0.5	97 (3.9:1)
4	*t*-$BuNH_2$ (15)		4	67 (1:1.6)
5	Et_3N (15)	12.5	7	56 (1:6.3)
6	*n*-Bu_3N (15)	12.7	24	54 (1:2.7)
7	*t*-BuOK (2.0)		2	77 (1:6.7)

[a] Pyridine was used as a solvent (0.02 M) at 50 °C.

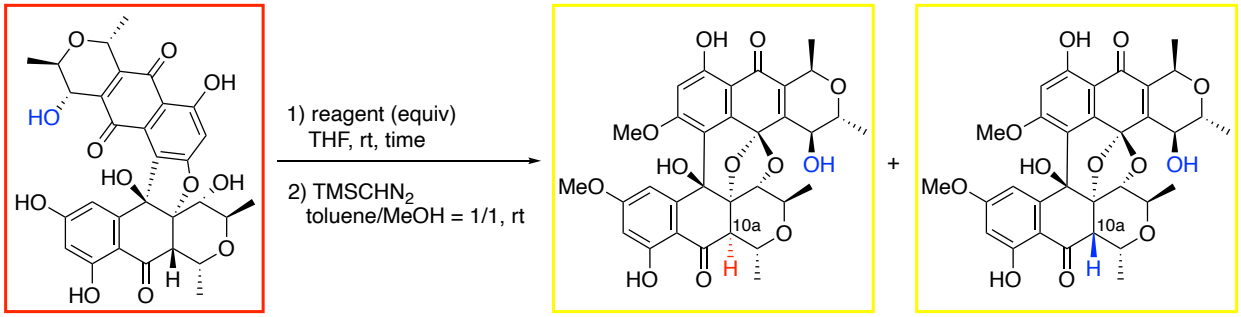


uroleucanaphin A_1 (**1**) **5a** **5b**

Table S2. Screening of solvent

entry	solvent	time (h)	yield (%) (**5a**:**5b**)
1	THF	0.5	97 (3.9:1)
2	THF/H_2O	0.5	70 (1:1.2)
3	CH_2Cl_2	1.5	74 (4.8:1)
4	toluene	0.5	90 (4.5:1)
5	MeOH	0.5	37 (3.6:1)
6	acetone	1.5	69 (1:1.4)

2-2. Conversion of uroleuconaphin B_1 (**2**)



uroleucanaphin B_1 (**2**)

6a

6b

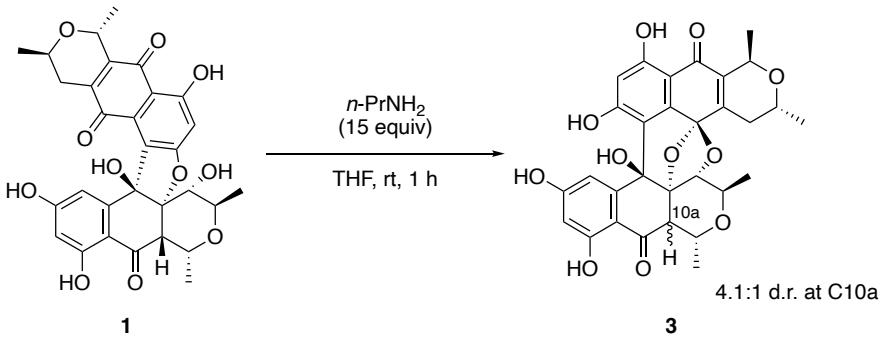
Table S3. Screening of base

entry	reagent (equiv)	pK_{aH} (THF)[1]	time (h)	yield (%) (**6a**:**6b**)
1[a]	pyridine (excess)	5.5	1.0	45 (2.1:1)
2	imidazole (15)	9.4	24	47 (1.9:1)
3	piperidine (15)	14.3	0.2	60 (2.3:1)
4	proton sponge (15)	11.1	24	68 (1.1:1)
5	ethylenediamine (15)	13.6	0.5	70 (2.3:1)
6	*n*-$PrNH_2$ (15)	13.8	1.0	71 (2.5:1)
7	*n*-$BuNH_2$ (15)	13.4	1.0	68 (1.8:1)
8	*t*-$BuNH_2$ (15)		1.0	76 (2.5:1)
9	*n*-Bu_2NH (15)	12.6	1.0	59 (1.6:1)
10	Et_3N (15)	12.5	1.5	40 (1:5.0)
11	*n*-Pr_3N (15)	13.0	1.0	28 (1:2.2)
12	*n*-Bu_3N (15)	12.7	17	56 (1:1.2)
13	DBU (15)	16.9	0.2	trace
14	NaOMe (25)		50	64 (1:1.4)
15	*t*-BuOK (2.0)		0.5	89 (1:1)
16	$LiOH·H_2O$ (105)		72	trace
17	NaH (35)		72	16 (1:1.1)

[a] Pyridine was used as a solvent (0.02 M) at 50 °C.

3. Conversion of uroleuconaphin A_1 (1) to uroleuconaphin A_2 (3)

To a solution of red pigment **1** (236 mg, 418 μmol) in THF (42 mL) was added *n*-$PrNH_2$ (0.52 mL, 6.3 mmol) at room temperature. After stirring for 1 h, the reaction was quenched by adding 1 M aqueous HCl at room temperature. The products were extracted with EtOAc (×3), and the combined organic extracts were washed with water, dried over Na_2SO_4. Concentration and purification by silica gel column chromatography ($CHCl_3$/MeOH = 50/1→30/1→10/1) afforded yellow pigment **3** (200 mg, 85%) as a yellow powder.



1 **3**

*Note: Yellow pigment **3** gradually converted to red pigment **1** by extraction and purification process.*

R_f 0.37 (hexane/EtOAc = 1/1);

IR (ATR) 3235, 2977, 2930, 1668, 1620, 1605, 1454, 1369, 1332, 1260, 1165, 1147, 1102, 1073, 1053, 1036, 982, 837, 817, 800, 789, 757, 716, 653, 596, 553, 515, 492, 472, 452, 425, 406 cm^{-1};

^1H NMR (acetone-d_6, 500 MHz) δ 1.20 (d, 6H, *J* = 6.0 Hz), *1.23 (d, 3H, *J* = 6.1 Hz), 1.49 (d, 3H, *J* = 6.7 Hz), 1.54 (d, 3H, *J* = 6.0 Hz), *1.58 (d, 3H, *J* = 6.8 Hz), 2.09–2.11 (m, 1H), *2.13–2.19 (m, 1H), 2.47 (dd, 1H, *J* = 19.5 Hz, 2.8 Hz), *2.55 (brd, 1H, *J* = 19.7 Hz), 3.10 (d, 1H, *J* = 10.7 Hz), 3.88 (dq, 1H, *J* = 9.9 Hz, 6.0 Hz), 3.93–3.98 (m, 1H), 4.22 (d, 1H, *J* = 9.9 Hz), *4.24 (d, 1H, *J* = 5.8 Hz), *4.28 (d, 1H, *J* = 6.2 Hz), 4.35 (dq, 1H, *J* = 10.7 Hz, 6.0 Hz), *4.62–4.68 (m, 2H), 4.66 (q, 1H, *J* = 6.7 Hz), *6.24 (brs, 1H), 6.28 (brs, 1H), *6.40 (brs, 1H), 6.46 (brs, 1H), *6.50 (s, 1H), 6.56 (s, 1H), *12.17 (s, 1H), 12.21 (s, 1H), *12.78 (s, 1H), 13.16 (s, 1H);

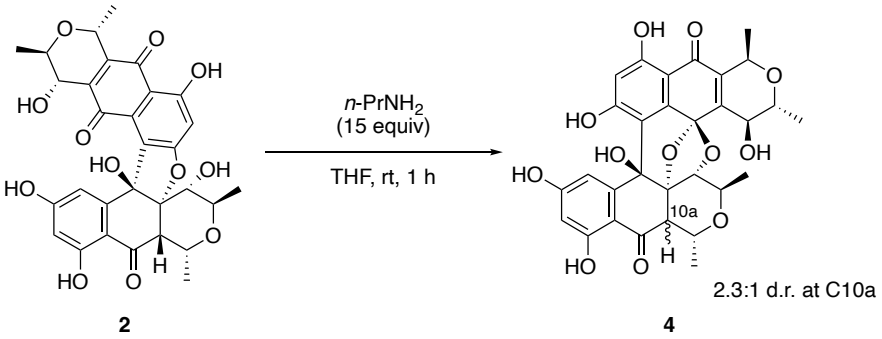
^{13}C NMR (acetone-d_6, 125 MHz) δ *16.0, 18.9, *19.8, 19.9, 21.8, 23.0, 30.4, *31.1, 54.2, 62.6, 66.8, 67.9, *69.2, 71.1, *75.2, 75.4, 77.7, 85.7, 98.3, *99.9, 103.3, *103.4, *104.7, 104.8, 106.7, *108.7, 108.8, 109.5, *109.8, 114.2, *139.3, 139.7, 139.8, *139.9, 146.3, 147.8, *164.5, 164.7, *164.8, 165.0, *166.2, 167.3, 167.7, *186.9, 187.0, *198.9, 199.0;

The signals marked with an asterisk (*) were assigned to the minor diastereomer.

HRMS (MALDI) calcd for $C_{30}H_{27}O_{11}$ $[M–H]^+$ *m/z* 563.1548; found *m/z* 563.1545.

4. Conversion of uroleuconaphin B_1 (2) to uroleuconaphin B_2 (4)

To a solution of red pigment **2** (212 mg, 365 μmol) in THF (36 mL) was added *n*-$PrNH_2$ (0.46 mL, 5.6 mmol) at room temperature. After stirring for 1 h, the reaction was quenched by adding 1 M aqueous HCl at room temperature. The products were extracted with EtOAc (×3), and the combined organic extracts were washed with water, dried over Na_2SO_4. Concentration and purification by silica gel column chromatography ($CHCl_3$/MeOH = 15/1) afforded yellow pigment **4** (189 mg, 89%) as a yellow powder.



*Note: Yellow pigment **4** gradually converted to red pigment **2** by extraction and purification process.*

R_f 0.31 (hexane/EtOAc = 1/1);

IR (ATR) 3361, 2981, 2942, 1706, 1623, 1606, 1455, 1369, 1262, 1171, 1099, 1079, 1033, 998, 981, 966, 889, 790, 758, 719, 656, 534, 463, 454, 443, 419 cm^{-1};

^1H NMR (acetone-d_6, 500 MHz) δ 1.19 (d, 3H, *J* = 6.0 Hz), 1.21 (d, 3H, *J* = 6.2 Hz), *1.24 (d, 3H, *J* = 6.1 Hz), *1.45 (d, 3H, *J* = 7.3 Hz), 1.54 (d, 3H, *J* = 6.0 Hz), 1.55 (d, 3H, *J* = 6.6 Hz), 3.32 (d, 1H, *J* = 10.6 Hz), 3.78–3.84 (m, 1H), 3.90 (qd, 1H, *J* = 6.0 Hz, 10.0 Hz), 4.11 (brd, 1H, *J* = 8.6 Hz), 4.14–4.19 (m, 1H), 4.19 (d, 1H, *J* = 10.0 Hz), 4.34 (qd, 1H, *J* = 6.0 Hz, 10.6 Hz), *4.40 (brs, 1H), *4.47 (brs, 1H), 4.57 (brq, 1H, *J* = 6.6 Hz), *4.70 (qd, 1H, *J* = 6.6 Hz, 7.4 Hz), *6.30 (d, 1H, *J* = 2.0 Hz), 6.31 (d, 1H, *J* = 2.0 Hz), 6.35 (d, 1H, *J* = 2.0 Hz), *6.38 (brs, 1H), *6.49 (s, 1H), 6.51 (s, 1H), *12.06 (s, 1H), 12.08 (s, 1H), *12.87 (s, 1H), 13.15 (s, 1H);

^{13}C NMR (acetone-d_6, 125 MHz) δ *16.6, 18.8, 18.9, *19.1, *19.2, 19.4, 23.0, *42.3, 53.8, 66.8, *67.5, *67.6, 67.7, 68.0, 68.7, 71.1, *72.4, *74.3, 75.0, *76.3, 77.8, 85.9, *87.9, 99.2, *99.8, 103.4, *104.4, 104.5, 108.9, 109.4, *109.5, 109.7, *112.7, 113.8, 139.8, *141.8, 142.0, 145.2, 147.9, 164.8, 164.9, *165.9, 166.1, *166.9, *167.2, 167.6, 187.7, *198.3, 199.3;

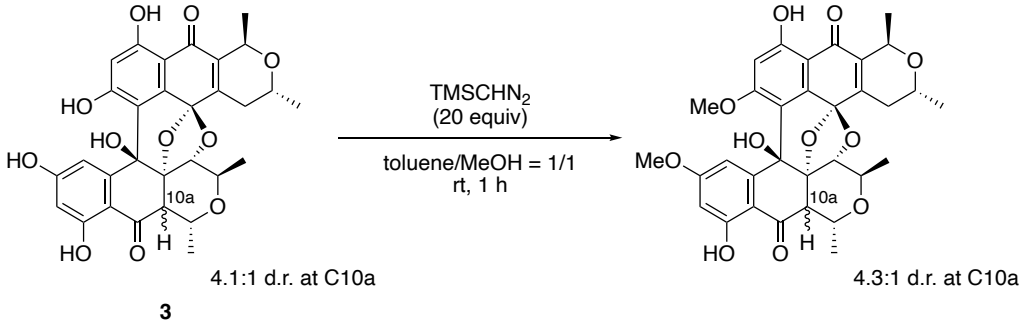
*The signals marked with an asterisk (*) were assigned to the minor diastereomer.

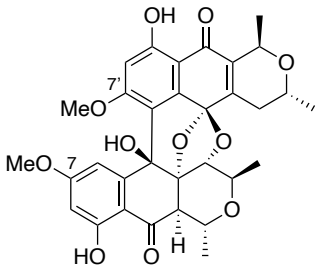
HRMS (MALDI) calcd for $C_{30}H_{27}O_{12}$ $[M–H]^+$ *m/z* 579.1497; found *m/z* 579.1511.

5. Dimethylation of uroleuconaphin A_2 (3) and B_2 (4)

5-1. Dimethylation of uroleuconaphin A_2 (**3**)

To a solution of yellow pigment **3** (19.6 mg, 34.8 μmol) in toluene/MeOH (1.8 mL/1.8 mL) was added trimethylsilyldiazomethane (0.6 M in hexane, 1.2 mL, 0.72 mmol) at room temperature. After stirring for 1 h, the reaction was quenched by adding AcOH at room temperature. The products were extracted with EtOAc (×3), and the combined organic extracts were dried over Na_2SO_4. Concentration and purification by silica gel column chromatography (hexane/acetone = 3/1) afforded dimethyl ethers **5a** and **5b** (20.3 mg, 98%) as a pale yellow powder. These diastereomers were separated by preparative HPLC (MeOH/H_2O/TFA = 80/20/0.1, flow rate 8.0 mL/min).





7-*O*, 7'-*O*-dimethyl uroleuconaphin A_{2a} (**5a**)

R_f 0.67 (hexane/EtOAc = 1/1);

$[\alpha]_D^{23}$ +36.8 (*c* 0.105, $CHCl_3$);

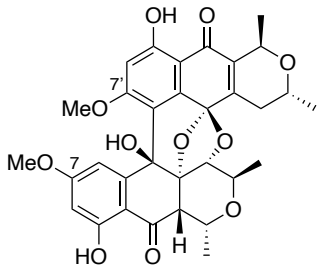
IR (ATR) 3522, 2977, 2930, 1604, 1443, 1370, 1260, 1201, 1146, 1107, 922, 958, 837, 756, 709, 554, 433, 408 cm^{-1};

^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.28 (d, 3H, *J* = 6.1 Hz), 1.30 (d, 3H, *J* = 6.0 Hz), 1.56 (d, 3H, *J* = 6.7 Hz), 1.63 (d, 3H, *J* = 6.1 Hz), 2.18 (ddd, 1H, *J* = 19.2 Hz, 10.1 Hz, 1.8 Hz), 2.31 (dd, 1H, *J* = 19.2 Hz, 3.5 Hz), 2.93 (d, 1H, *J* = 10.5 Hz), 3.71 (qd, 1H, *J* = 6.0 Hz, 9.9 Hz), 3.74 (s, 3H), 3.95–4.00 (m, 1H), 4.00 (s, 3H), 4.19 (d, 1H, *J* = 9.9 Hz), 4.37 (qd, 1H, *J* = 6.1 Hz, 10.5 Hz), 4.75 (brq, 1H, *J* = 6.7 Hz), 4.83 (s, 1H), 5.95 (d, 1H, *J* = 2.4 Hz), 6.36 (d, 1H, *J* = 2.4 Hz), 6.61 (s, 1H), 12.42 (s, 1H), 13.24 (s, 1H);

^{13}C NMR ($CDCl_3$, 125 MHz) δ 18.6, 19.7, 21.6, 22.7, 29.9, 53.5, 55.6, 56.4, 62.0, 66.1, 67.7, 70.9, 74.3, 77.1, 84.5, 97.5, 100.1, 100.5, 106.9, 108.2, 108.6, 113.8, 137.6, 139.0, 145.4, 146.2, 163.7, 164.6, 166.2, 167.1, 186.2, 197.9;

HRMS (MALDI) calcd for $C_{32}H_{32}O_{11}Na$ $[M+Na]^+$ *m/z* 615.1837; found *m/z* 615.1833;

Mp 188 °C (dec).



7-*O*, 7'-*O*-dimethyl uroleuconaphin A_{2b} (**5b**)

R_f 0.67 (hexane/EtOAc = 1/1);

$[\alpha]_D^{23}$ +32.3 (*c* 0.120, $CHCl_3$);

IR (ATR) 3523, 2975, 2933, 1666, 1605, 1442, 1367, 1280, 1258, 1202, 1139, 1107, 1055, 991, 957, 931, 909, 875, 837, 814, 736, 703, 656, 628, 563, 527, 451, 433, 412 cm^{-1};

^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.28 (d, 3H, *J* = 6.1 Hz), 1.36 (d, 3H, *J* = 6.5 Hz), 1.54 (d, 3H, *J* = 6.7 Hz), 1.59 (d, 3H, *J* = 6.7 Hz), 2.24 (ddd, 1H, *J* = 19.0 Hz, 10.1 Hz, 1.6 Hz), 2.44 (dd, 1H, *J* = 19.0 Hz, 3.5 Hz), 3.73 (s, 3H), 3.92 (qd, 1H, *J* = 6.5 Hz, 6.0 Hz), 3.96–4.03 (m, 1H), 4.05 (s, 3H), 4.27 (d, 1H, *J* = 6.0 Hz), 4.28 (d, 1H, *J* = 6.0 Hz), 4.71–4.76 (m, 2H), 5.07 (s, 1H), 6.05 (d, 1H, *J* = 2.3 Hz), 6.33 (d, 1H, *J* = 2.3 Hz), 6.59 (s, 1H), 12.40 (s, 1H), 12.98 (s, 1H);

^{13}C NMR ($CDCl_3$, 125 MHz) δ 15.8, 19.5, 19.6, 21.6, 30.4, 44.4, 55.5, 56.5, 62.0, 66.2, 67.6, 68.7, 73.8, 74.8, 87.9, 99.0, 99.9, 100.1, 106.2, 108.7, 108.9, 113.1, 138.5, 139.0, 145.5, 146.4, 163.5, 164.3, 165.9, 166.0, 186.0, 197.5;

HRMS (MALDI) calcd for $C_{32}H_{32}O_{11}Na$ $[M+Na]^+$ *m/z* 615.1837; found *m/z* 615.1848; Mp 180 °C (dec).

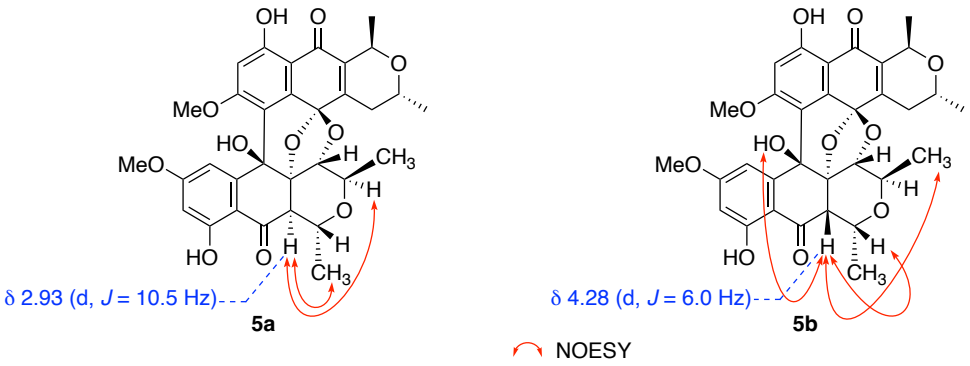
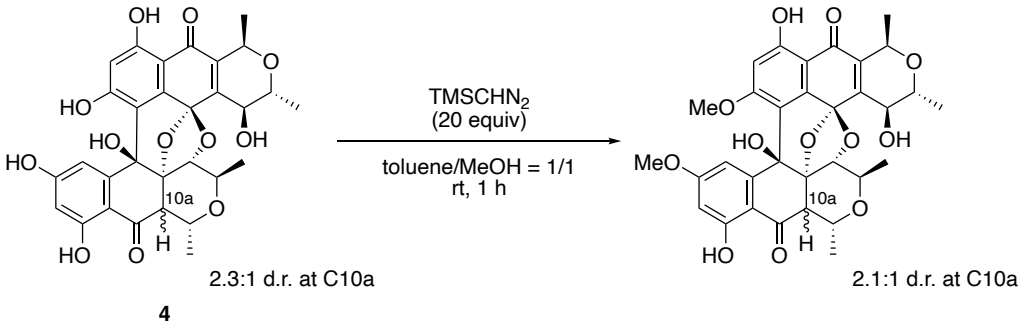
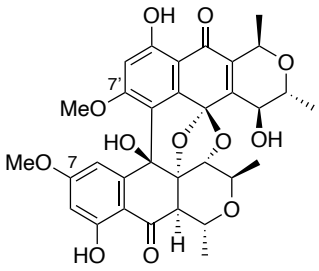


Figure S1. Key 2D NMR correlations of **5a** and **5b** in $CDCl_3$

5-2. Dimethylation of uroleuconaphin B_2 (**4**)

To a solution of yellow pigment **4** (20.1 mg, 34.6 μmol) in toluene/MeOH (1.8 mL/1.8 mL) was added trimethylsilyldiazomethane (0.6 M in hexane, 1.2 mL, 0.72 mmol) at room temperature. After stirring for 1 h, the reaction was quenched by adding AcOH at room temperature. The products were extracted with EtOAc (×3), and the combined organic extracts were dried over Na_2SO_4. Concentration and purification by column chromatography (silica gel, hexane/acetone = 3/1) afforded dimethyl ethers **6a** and **6b** (20.1 mg, 96%) as a pale yellow powder. These diastereomers were separated by preparative HPLC (MeCN/H_2O/TFA = 75/25/0.1, flow rate 8.0 mL/min).





7-*O*, 7'-*O*-dimethyl uroleuconaphin B_{2a} (**6a**)

R_f 0.60 (hexane/EtOAc = 1/1);

$[\alpha]_D^{23}$ +32.8 (*c* 0.110, $CHCl_3$);

IR (ATR) 3528, 2977, 2936, 1617, 1604, 1442, 1365, 1262, 1200, 1160, 959, 894, 788, 756, 554, 464, 437, 418 cm^{-1};

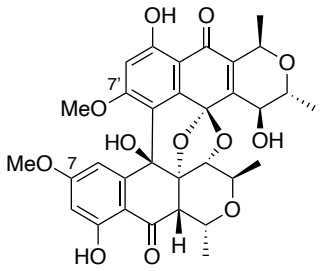
^1H NMR ($CDCl_3$, 500 MHz) δ 1.30 (d, 6H, *J* = 6.1 Hz), 1.62 (d, 3H, *J* = 6.1 Hz), 1.63 (d, 3H, *J* = 6.7 Hz), 2.98 (d, 1H, *J* = 10.5 Hz), 3.71–3.75 (m, 1H), 3.75 (s, 3H), 3.87 (qd, 1H, *J* = 6.1 Hz, 7.5

Hz), 4.02 (s, 3H), 4.22 (d, 1H, *J* = 10.0 Hz), 4.27 (d, 1H, *J* = 7.5 Hz), 4.35 (qd, 1H, *J* = 6.1 Hz, 10.5 Hz), 4.65 (q, 1H, *J* = 6.7 Hz), 4.82 (s, 1H), 5.95 (d, 1H, *J* = 2.4 Hz), 6.38 (d, 1H, *J* = 2.4 Hz), 6.64 (s, 1H), 12.26 (s, 1H), 13.22 (s, 1H);

^{13}C NMR ($CDCl_3$, 125 MHz) δ 18.3, 18.6, 19.2, 22.6, 53.5, 55.6, 56.5, 66.1, 67.3, 67.6, 68.4, 71.0, 74.0, 77.2, 84.9, 98.6, 100.1, 100.8, 106.7, 108.1, 108.6, 114.0, 136.7, 141.9, 142.2, 145.8, 164.1, 164.7, 166.2, 167.2, 186.5, 197.5;

HRMS (MALDI) calcd for $C_{32}H_{32}O_{12}Na$ $[M+Na]^+$ *m/z* 631.1786; found *m/z* 631.1782;

Mp 185 °C (dec).



7-*O*, 7'-*O*-dimethyl uroleuconaphin B_{2b} (**6b**)

R_f 0.60 (hexane/EtOAc = 1/1);

$[\alpha]_D^{23}$ +34.9 (*c* 0.111, $CHCl_3$);

IR (ATR) 3477, 2977, 2936, 1617, 1606, 1444, 1363, 1282, 1201, 1151, 963, 787, 756, 504, 444, 426, 412 cm^{-1};

^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.33 (d, 3H, *J* = 6.5 Hz), 1.46 (d, 3H, *J* = 7.5 Hz), 1.55 (d, 3H, *J* = 6.5 Hz), 1.62 (d, 3H, *J* = 7.0 Hz), 3.75 (s, 3H), 3.90 (qd, 1H, *J* = 6.5 Hz, 6.0 Hz), 4.02 (s, 3H), 4.06 (d, 1H, *J* = 8.0 Hz), 4.17–4.25 (m, 2H), 4.46 (s, 1H), 4.59 (d, 1H, *J* = 1.9 Hz), 4.64 (q, 1H, *J* = 7.0 Hz), 4.74 (qd, 1H, *J* = 6.5 Hz, 8.0 Hz), 4.87 (s, 1H), 5.93 (d, 1H, *J* = 2.5 Hz), 6.37 (d, 1H, *J* = 2.5 Hz), 6.60 (s, 1H), 12.25 (s, 1H), 12.99 (s, 1H);

^{13}C NMR ($CDCl_3$, 125 MHz) δ 15.9, 18.9, 19.0, 40.8, 55.6, 56.5, 65.1, 66.7, 67.4, 67.5, 72.5, 72.8, 76.0, 86.5, 98.8, 100.0, 100.2, 106.3, 109.0, 109.1, 112.2, 138.6, 141.0, 143.9, 146.0, 164.0, 164.4, 166.1, 166.6, 186.9, 197.4;

HRMS (MALDI) calcd for $C_{32}H_{32}O_{12}Na$ $[M+Na]^+$ *m/z* 631.1786; found *m/z* 631.1802;

Mp 188 °C (dec).

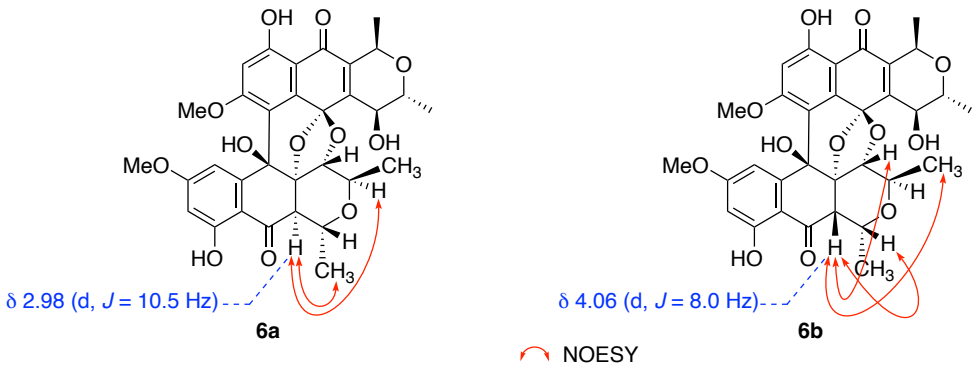
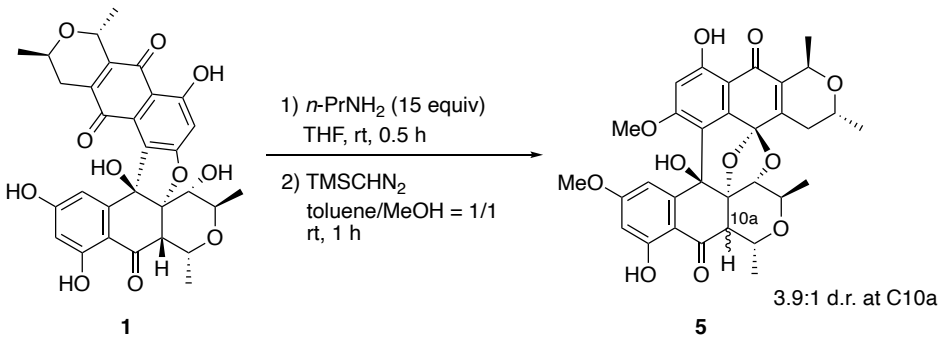


Figure S2. Key 2D NMR correlations of **6a** and **6b** in $CDCl_3$

6. Two-step procedure for conversion of uroleuconaphin A_1 (1) and B_1 (2)

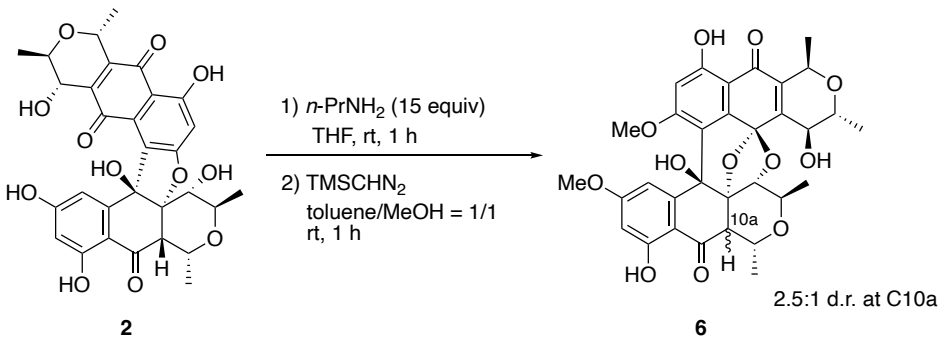
6-1. Conversion of uroleuconaphin A_1 (**1**) to 7-*O*, 7'-*O*-dimethyl uroleuconaphin A_2 (**5**)

To a solution of red pigment **1** (19.7 mg, 34.9 μmol) in THF (3.5 mL) was added *n*-$PrNH_2$ (43.0 μL, 525 μmol) at room temperature. After stirring for 0.5 h, the reaction was quenched by adding 1 M aqueous HCl at room temperature. The products were extracted with EtOAc (×3), and the combined organic extracts were washed with water, dried over Na_2SO_4, and concentrated in vacuo. To a solution of crude material in toluene/MeOH (1.1 mL/1.1 mL) was added trimethylsilyldiazomethane (0.6 M in hexane, 0.70 mL, 0.42 mmol) at room temperature. After stirring for 1 h, the reaction was quenched by adding AcOH at room temperature. The products were extracted with EtOAc (×3), and the combined organic extracts were dried over Na_2SO_4. Concentration and purification by silica gel column chromatography (hexane/acetone = 3/1) afforded dimethyl ethers **5a** and **5b** (20.1 mg, 97%) as a pale yellow powder. These diastereomers were separated by preparative HPLC (MeOH/H_2O/TFA = 80/20/0.1, flow rate 8.0 mL/min).



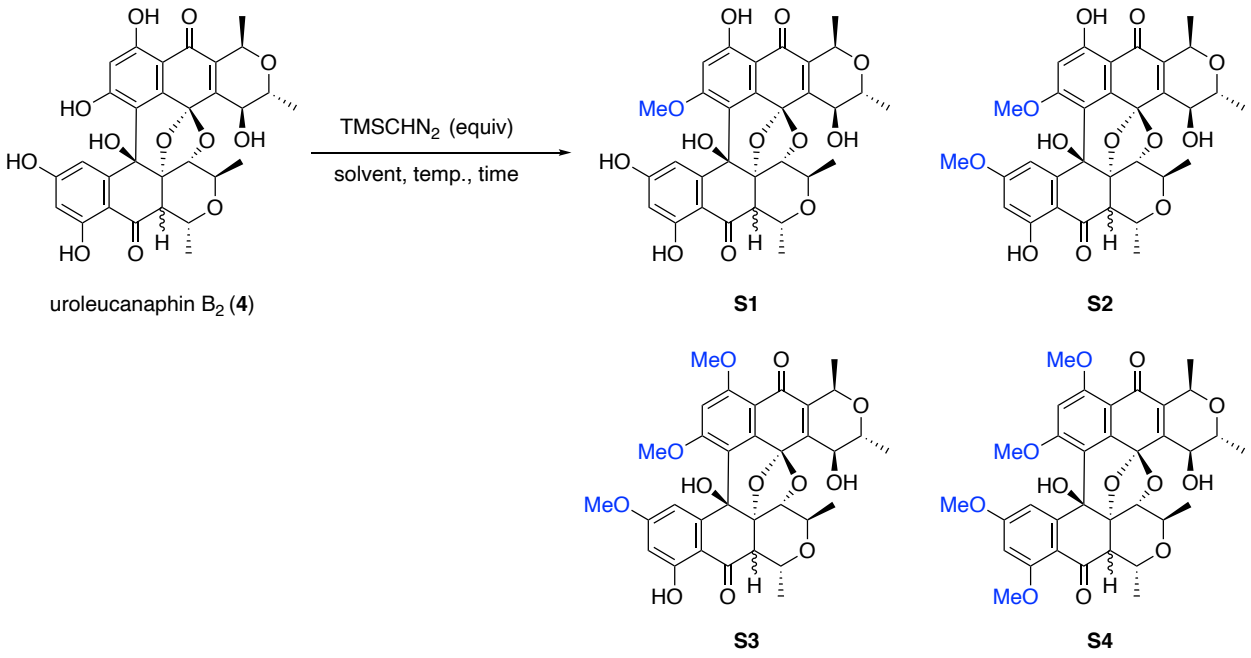
6-2. Conversion of uroleuconaphin B_1 (**2**) to 7-*O*, 7'-*O*-dimethyl uroleuconaphin B_2 (**6**)

To a solution of red pigment **2** (20.3 mg, 35.0 μmol) in THF (3.5 mL) was added *n*-$PrNH_2$ (43.0 μL, 525 μmol) at room temperature. After stirring for 1 h, the reaction was quenched by adding 1 M aqueous HCl at room temperature. The products were extracted with EtOAc (×3), and the combined organic extracts were washed with water, dried over Na_2SO_4, and concentrated in vacuo. To a solution of crude material in toluene/MeOH (0.9 mL/0.9 mL) was added trimethylsilyldiazomethane (0.6 M in hexane, 0.88 mL, 0.53 mmol) at room temperature. After stirring for 1 h, the reaction was quenched by adding AcOH at room temperature. The products were extracted with EtOAc (×3), and the combined organic extracts were dried over Na_2SO_4. Concentration and purification by column chromatography (silica gel, hexane/acetone = 3/1) afforded dimethyl ethers **6a** and **6b** (15.2 mg, 71%) as a pale yellow powder. These diastereomers were separated by preparative HPLC ($MeCN/H_2O$/TFA = 75/25/0.1, flow rate 8.0 mL/min).



2 **6**

7. Conditions for methylation of uroleuconaphin B_2 (4)



uroleucanaphin B_2 (**4**)

S1

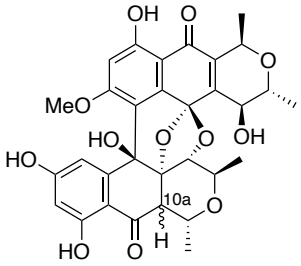
S2

S3

S4

Table S4. Conditions for methylation of uroleuconaphin B_2 (**4**)

entry	equiv	solvent	temp. (°C)	time (h)	yield (%)			
					S1	**S2**	**S3**	**S4**
1	100	MeOH	–15→rt	4	0	75	0	0
2	15	toluene/MeOH = 1/1	rt	1	90	trace	0	0
3	30	toluene/MeOH = 1/1	0→rt	1	0	94	0	0
4	60	toluene/MeOH = 1/1	rt	5	0	0	19	39



2.0:1 d.r. at C10a

S1

R_f 0.52 (hexane/EtOAc = 1/1);

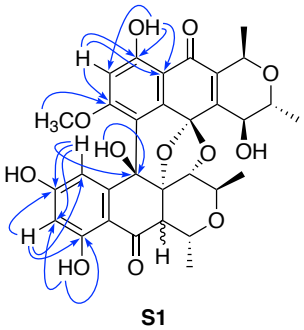
IR (ATR) 3522, 2981, 2936, 1620, 1445, 1370, 1265, 1167, 841, 431, 421 cm^{-1};

^1H NMR ($CDCl_3$, 500 MHz) δ 1.30 (d, 6H, *J* = 6.1 Hz), *1.33 (d, 3H, *J* = 6.1 Hz), *1.45 (d, 3H, *J* = 7.5 Hz), *1.55 (d, 3H, *J* = 6.6 Hz), 1.61 (d, 3H, *J* = 6.1 Hz), 1.63 (d, 3H, *J* = 6.0 Hz), 2.80 (d, 1H, *J* = 4.3 Hz), 2.98 (d, 1H, *J* = 10.4 Hz), 3.73 (qd, 1H, *J* = 6.1 Hz, 10.0 Hz), 3.85–3.93 (m, 1H), 4.02 (s, 3H), *4.03 (s, 3H), *4.06 (d, 1H, *J* = 8.0 Hz), 4.17–4.30 (m, 2H), 4.34 (qd, 1H, *J* = 6.1 Hz, 10.4 Hz), *4.45 (s, 1H), 4.61–4.67 (m, 1H), *4.74 (qd, 1H, *J* = 6.6 Hz, 8.0 Hz), 4.86 (s, 1H), *4.89 (s 1H), *5.87 (d, 1H, *J* = 2.1 Hz), 5.90 (d, 1H, *J* = 2.2 Hz), *6.30 (d, 1H, *J* = 2.1 Hz), 6.31 (d, 1H, *J* = 2.2 Hz), *6.60 (s, 1H), 6.63 (s, 1H), *12.23 (s, 1H), 12.25 (s, 1H), *12.87 (s, 1H), 13.08 (s, 1H);

^{13}C NMR ($CDCl_3$, 125 MHz) δ *15.9, 18.3, 18.5, *18.8, *18.9, *19.0, 19.2, 22.6, *40.8, 53.4, 56.6, *65.1, 66.1, *66.7, 67.3, *67.4, *67.5, 67.6, 68.4, 71.1, *72.5, *72.8, 73.9, *76.0, 77.0, 84.9, *86.5, 98.6, *98.8, *100.2, 100.8, *103.3, 103.4, *106.3, 106.7, 107.8, *108.3, 108.6, *109.4, *112.1, 113.8, 136.7, *138.6, *141.0, 141.8, 142.1, *143.7, 146.9, *147.1, *162.7, 162.8, 164.0, *164.4, 164.6, *166.1, 166.6, 186.5, *186.8, *197.4, 197.5;

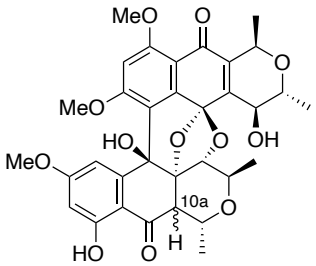
The signals marked with an asterisk (*) were assigned to the minor diastereomer.

HRMS (MALDI) calcd for $C_{31}H_{30}O_{12}Na$ $[M+Na]^+$ *m/z* 617.1629; found *m/z* 617.1633.



S1

Key HMBC correlations in $CDCl_3$



2.4:1 d.r. at C10a

S3

R_f 0.48 (hexane/acetone = 1/1);

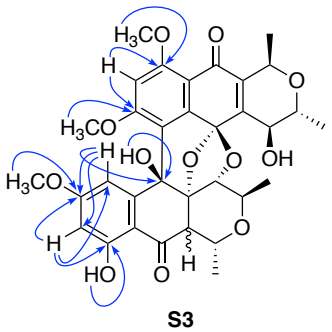
IR (ATR) 3511, 2974, 2936, 1620, 1596, 1462, 1333, 1266, 1205, 1162, 1045, 835, 473, 446, 432, 419 cm^{-1};

^1H NMR ($CDCl_3$, 500 MHz) δ 1.29 (d, 6H, *J* = 6.1 Hz), *1.32 (d, 3H, *J* = 6.5 Hz), *1.45 (d, 3H, *J* = 7.5 Hz), 1.63 (d, 3H, *J* = 6.1 Hz), 1.65 (d, 3H, *J* = 6.5 Hz), 3.00 (d, 1H, *J* = 10.4 Hz), 3.72–3.74 (m, 1H), *3.75 (s, 3H), 3.76 (s, 3H), 3.83–3.91 (m, 2H), *3.97–4.00 (m, 1H), 4.04 (s, 3H), 4.05 (s, 3H), 4.06 (s, 3H), *4.07 (s, 3H), 4.17 (d, 1H, *J* = 9.9 Hz), 4.20–4.28 (m, 1H), 4.36 (qd, 1H, *J* = 6.1 Hz, 10.4 Hz), *4.42 (s, 1H), 4.59–4.63 (m, 1H), *4.75 (qd, 1H, *J* = 6.5 Hz, 8.2 Hz), 4.95 (s, 1H), *5.01 (s 1H), *5.89 (d, 1H, *J* = 2.4 Hz), 5.93 (d, 1H, *J* = 2.4 Hz), *6.37 (d, 1H, *J* = 2.4 Hz), 6.39 (d, 1H, *J* = 2.4 Hz), *6.64 (s, 1H), 6.67 (s, 1H), *13.02 (s, 1H), 13.24 (s, 1H);

^{13}C NMR ($CDCl_3$, 125 MHz) δ *16.0, 18.5, 18.6, *18.8, *19.1, 19.4, 22.6, *40.8, 53.3, 55.6, 56.3, 56.4, *65.1, 66.1, *66.6, *67.4, 67.5, 68.1, *68.2, 68.3, 71.0, *72.6, *72.9, 74.0, *76.2, 77.3, 84.2, *85.7, *95.8, 96.4, 99.1, *99.4, *99.8, 100.0, 108.1, 108.7, *109.0, *109.2, *110.9, 111.4, *112.2, 113.8, 138.6, 138.8, *139.6, *140.8, *142.6, 143.4, 145.8, *146.0, 162.6, 162.7, *166.0, 166.1, *166.6, 167.2, 181.1, *181.4, *197.5, 197.7;

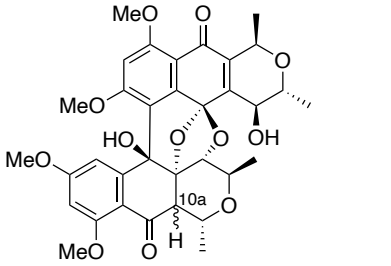
The signals marked with an asterisk (*) were assigned to the minor diastereomer.

HRMS (MALDI) calcd for $C_{33}H_{34}O_{12}Na$ $[M+Na]^+$ *m/z* 645.1942; found *m/z* 645.1937.



S3

Key HMBC correlations in $CDCl_3$



6.4:1 d.r. at C10a

S4

R_f 0.26 (hexane/acetone = 1/1);

IR (ATR) 3514, 2980, 2936, 1733, 1651, 1597, 1569, 1457, 1373, 1329, 1266, 1202, 1162, 1068, 1046, 831, 698, 634, 580, 537, 498, 484, 468, 451, 423, 410 cm^{-1};

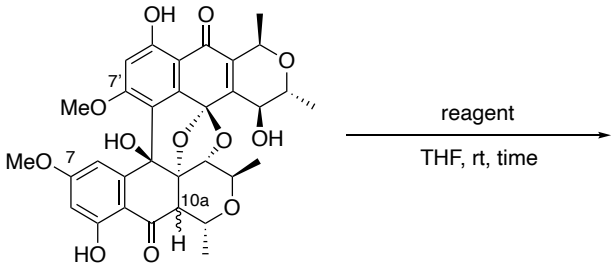
^1H NMR ($CDCl_3$, 500 MHz) δ 1.28 (d, 3H, *J* = 6.1 Hz), 1.30 (d, 3H, *J* = 6.1 Hz), *1.34 (d, 3H, *J* = 6.7 Hz), 1.62 (d, 3H, *J* = 6.2 Hz), 1.65 (d, 3H, *J* = 6.7 Hz), 2.76–2.80 (m, 2H), 3.66–3.70 (m, 1H), 3.71 (s, 3H), *3.75 (s, 1H), 3.84–3.89 (m, 1H), 3.92 (s, 3H), *3.94 (s, 1H), *3.95 (s, 3H), *3.99–4.00 (m, 1H), 4.01 (s, 3H), 4.05 (s, 3H), *4.09–4.13 (m, 2H), 4.15 (d, 1H, *J* = 8.6 Hz), 4.26 (ddd, 1H, *J* = 7.8 Hz, 3.4 Hz, 1.0 Hz), 4.35 (qd, 1H, *J* = 6.2 Hz, 8.3 Hz), 4.63 (brd, 1H, *J* = 6.7 Hz), 4.78 (s, 1H), *5.68 (d, 1H, *J* = 2.1 Hz), 5.77 (d, 1H, *J* = 2.1 Hz), *6.42 (d, 1H, *J* = 2.1 Hz), 6.46 (d, 1H, *J* = 2.1 Hz), *6.63 (s, 1H), 6.65 (s, 1H);

^{13}C NMR ($CDCl_3$, 125 MHz) δ *16.4, 18.4, 18.6, 19.3, 23.9, *24.1, 54.9, 55.2, *55.9, 56.2, 56.3, 56.4, *66.2, 67.1, 67.6, 68.0, 68.2, *69.4, 69.9, *90.9, *72.9, 74.4, *74.8, 77.0, 84.4, *84.8, *95.4, 95.9, *97.2, 97.5, 98.7, *102.3, 105.9, *106.3, 111.2, 113.7, 114.3, 138.4, 139.1, 143.1, 147.2, *159.6, 161.0, *161.2, 162.6, 162.7, 163.5, 181.2, 192.6, *192.9;

The signals marked with an asterisk (*) were assigned to the minor diastereomer.

HRMS (MALDI) calcd for $C_{34}H_{36}O_{12}Na$ $[M+Na]^+$ *m/z* 659.2099; found *m/z* 659.2101.

8. The ratio of isomers of 7-*O*, 7'-*O*-dimethyl uroleuconaphin B_2 (6) in equilibrium



mixture of **6a** and **6b**

(**6a**: 10a-Hα
6b: 10a-Hβ)

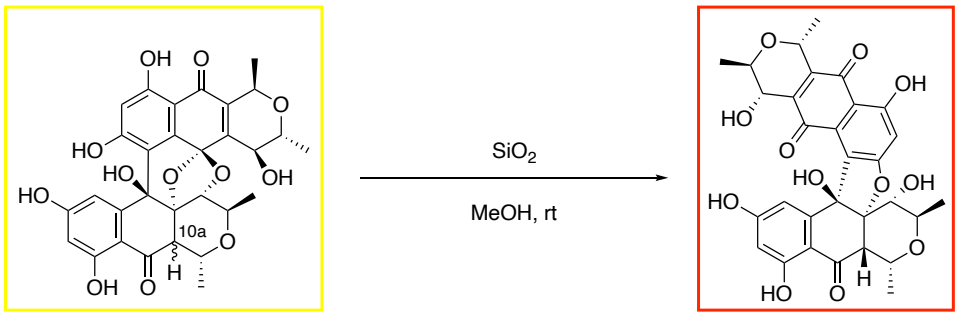
Table S5. Ratio of **6a** and **6b**[a]

time	**6a** / **6b**			
	n-$PrNH_2$	Et_3N	Et_3N	*t*-BuOK
0 h	2.5:1	23.5:1	1:23.5	1:1
1 h	3.7:1	15.7:1	1:8.1	2.1:1
6 h	3.4:1	4.6:1	1:1	2.2:1
12 h	3.5:1	3.5:1	3.2:1	2.5:1
24 h	3.5:1	3.5:1	3.2:1	2.5:1

[a] Determined by ^{1}H-NMR (acetone-d_6).

9. Reverse reaction of uroleuconaphin B_2 (4)

Yellow pigment **4** (4.0 mg, 6.9 μmol) adsorbed on silica gel (120 mg) was suspended in MeOH (4.3 mL). After stirring at room temperature for some time, the suspension was filtered by a glass filter, and concentrated. The residue was analyzed by ^{1}H-NMR without purification.



uroleucanaphin B_2 (**4**)
(**4a**: 10a-Hα
4b: 10a-Hβ)

uroleucanaphin B_1 (**2**)

Table S6. Reverse reaction of uroleuconaphin B_2 (**4**) promoted by silica gel[a]

time	**4** (**4a**:**4b**) / **2**			
	1	2	3	4
10 min	>99 (78:22) / 1	>99 (55:45) / 1	>99 (31:69) / 1	>99 (20:80) / 1
12 h	94 (77:23) / 6	>99 (55:45) / 1	81 (48:52) / 19	84 (29:71) / 16
24 h	94 (80:20) / 6	88 (52:48) / 12	78 (52:48) / 22	70 (43:57) / 30
48 h	91 (84:16) / 9	85 (58:42) / 15	74 (64:36) / 26	67 (43:57) / 33
72 h	91 (84:16) / 9	84 (63:37) / 16	73 (70:30) / 27	62 (50:50) / 38

[a] Determined by ^{1}H-NMR (acetone-d_6).

10. Isolation of uroleuconaphin A_2 (3) and B_2 (4)

Based on our previously reported procedure, [2, 3] the extraction and purification of yellow pigments **3** and **4** were performed as follows. The red aphid, *Uroleucon nigrotuberculatum* was obtained from *Solidago altissima L*. The aphids (total mass, 297 g) were crushed with diethyl ether using a pestle, and filtered using by a Buchner funnel. The aphid pigments were extracted with diethyl ether (total volume, 5.5 L) by further grinding the aphids. The combined ethereal extracts were concentrated to obtain crude extracts (26.8 g). The residue was purified by silica gel chromatography (hexane/EtOAc = 4/1→1/2) to afford the red pigments **1** (3.6 g) and **2** (1.3 g) and then further eluted by $CHCl_3$/MeOH (50/1→30/1) to afford the yellow pigments **3** (0.95 g, **3a**:**3b** = 2.8:1) and **4** (0.42 g, **4a**:**4b** = 3.6:1).

Fig. 1. Collecting aphids

Fig. 2. Crushing aphids in diethylether

Before

After

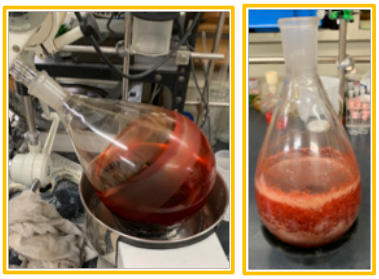
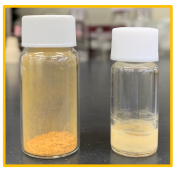


Fig. 3. Concentration the extract

Fig. 4. Purification by silica gel chromatography (hexane/EtOAc and $CHCl_3$/MeOH)

Right: Uroleuconaphin B_1 (**2**)
Left: Uroleuconaphin A_1 (**1**)

Fig. 6. TLC
Eluent: hexane/EtOAc = 1/1
Right: **2**
Center: cospot of **1** and **2**
Left: **1**



Right: Uroleuconaphin B_2 (**4**)
Left: Uroleuconaphin A_2 (**3**)

Fig. 6. TLC
Eluent: $CHCl_3$/MeOH = 10/1
Right: **4**
Center: cospot of **3** and **4**
Left: **3**

Figure S3. Isolation method

11. UV–Vis spectra

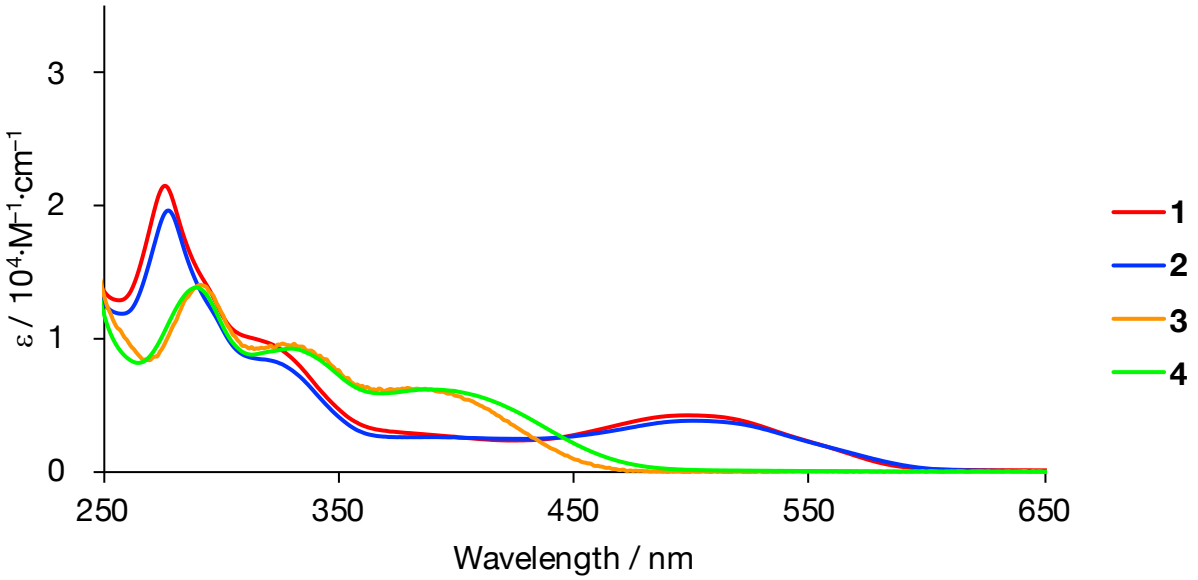


Figure S4. UV–Vis spectra (MeOH, 2.0×10^{-5} M)

	λ_{max} nm (log ε)
1	276 (4.33), 498 (3.42)
2	278 (4.29), 326 (3.91), 500 (3.59)
3	291 (4.15), 326 (3.98), 379 (3.80)
4	289 (4.14), 330 (3.97), 389 (3.79)

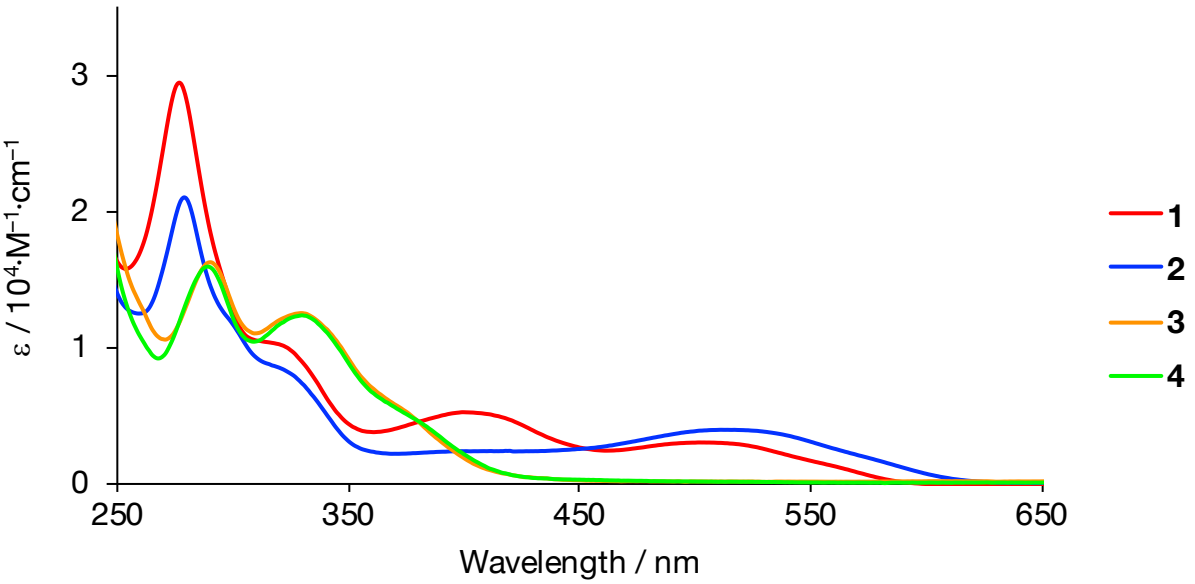


Figure S5. UV–Vis spectra ($CHCl_3$, 2.0×10^{-5} M)

	λ_{max} nm (log ε)
1	277 (4.47), 400 (3.73), 502 (3.49)
2	279 (4.10), 420 (2.82), 511 (2.19)
3	290 (4.17), 330 (3.87)
4	289 (4.20), 330 (4.09)

12. CD spectra

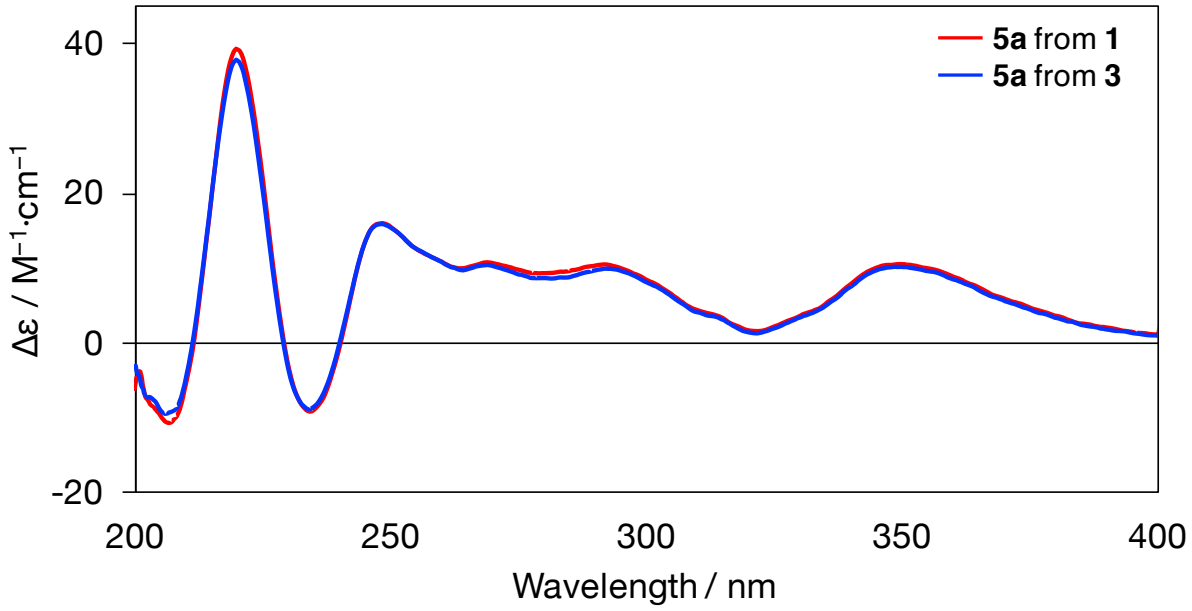


Figure S6. CD spectra of 7-*O*, 7'-*O*-dimethyl uroleuconaphin A_{2a} (**5a**) (2×10^{-5} M, MeOH)

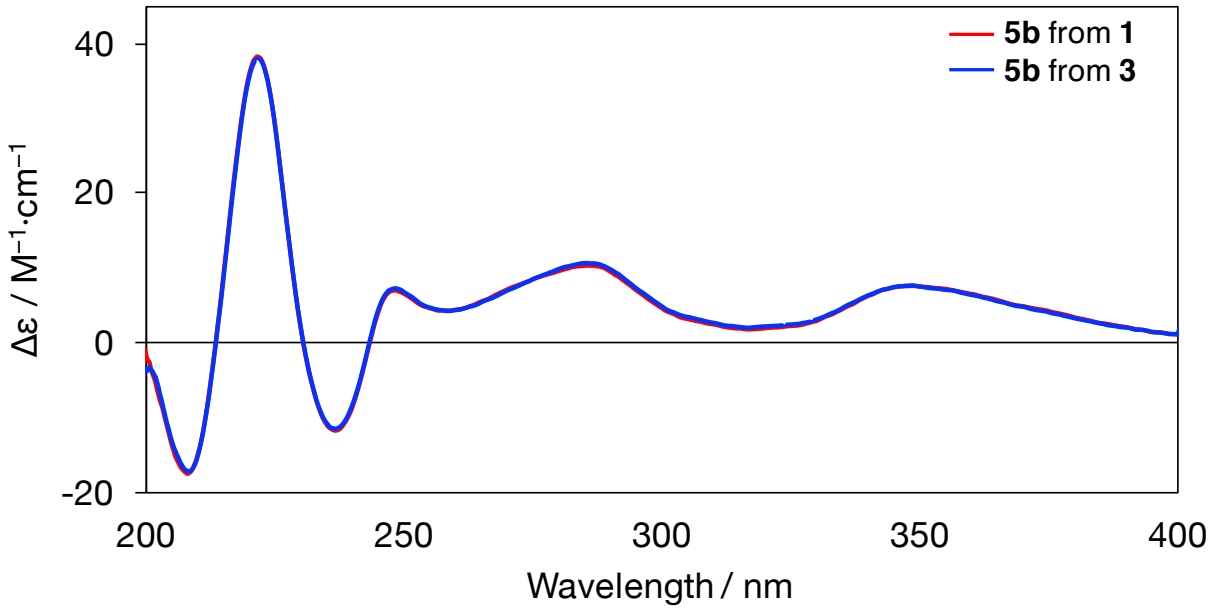


Figure S7. CD spectra of 7-*O*, 7'-*O*-dimethyl uroleuconaphin A_{2b} (**5b**) (2×10^{-5} M, MeOH)

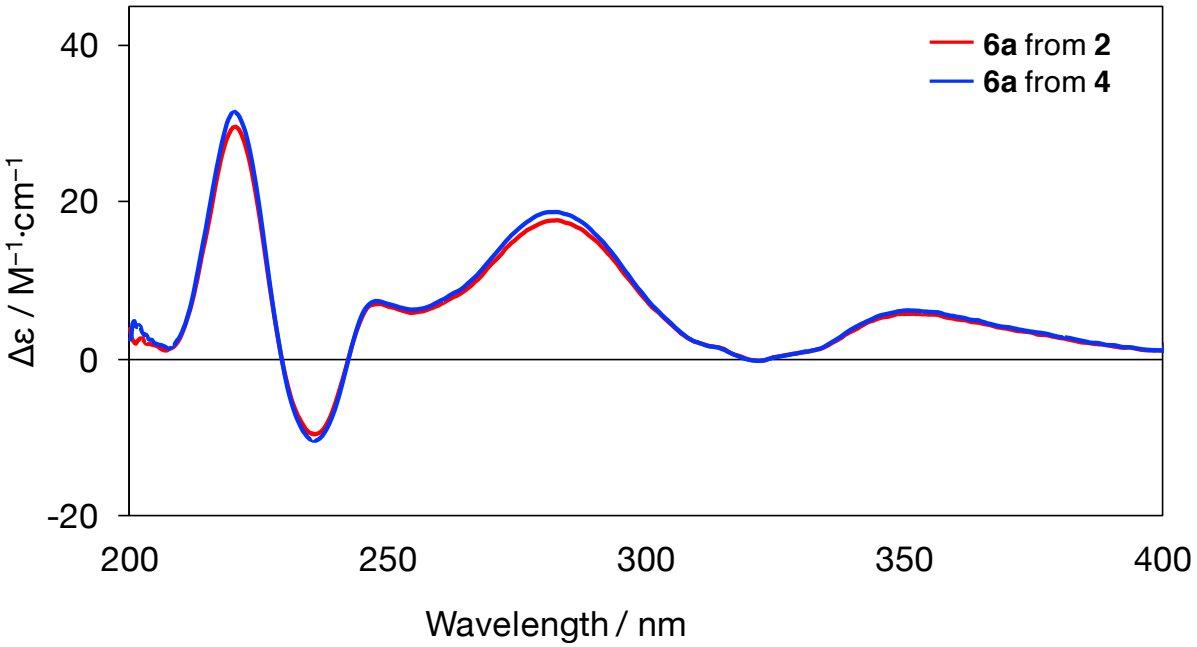


Figure S8. CD spectra of 7-*O*, 7'-*O*-dimethyl uroleuconaphin B_{2a} (**6a**) (2×10^{-5} M, MeOH)

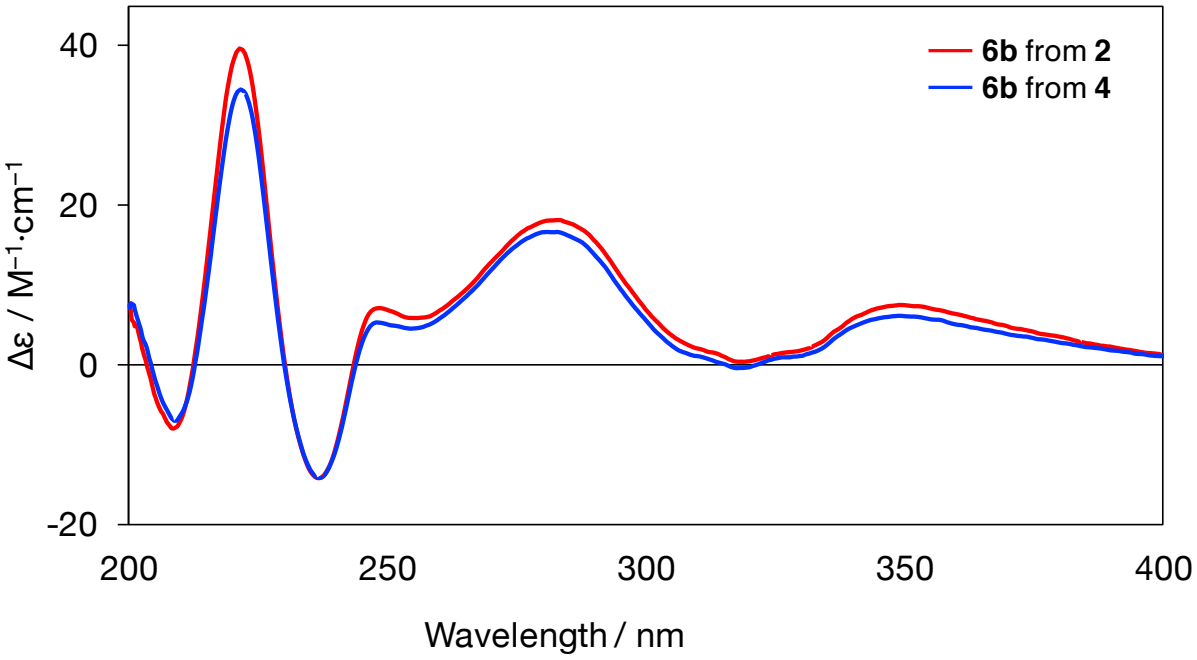


Figure S9. CD spectra of 7-*O*, 7'-*O*-dimethyl uroleuconaphin B_{2b} (**6b**) (2×10^{-5} M, MeOH)

13. Optical rotation

Table S7. Optical rotation of compound **5a**, **5b**, **6a** and **6b**[a]

compound	$[\alpha]_D$	temp. (°C)	*c* (g / dL)
5a from **1**	+36.9	23	0.105
from **3**	+36.8	23	0.105
5b from **1**	+32.3	23	0.120
from **3**	+32.2	23	0.153
6a from **2**	+32.8	23	0.110
from **4**	+32.1	23	0.100
6b from **2**	+34.9	23	0.111
from **4**	+34.7	24	0.123

[a] $CHCl_3$ was used for solvent.

14. IR spectra

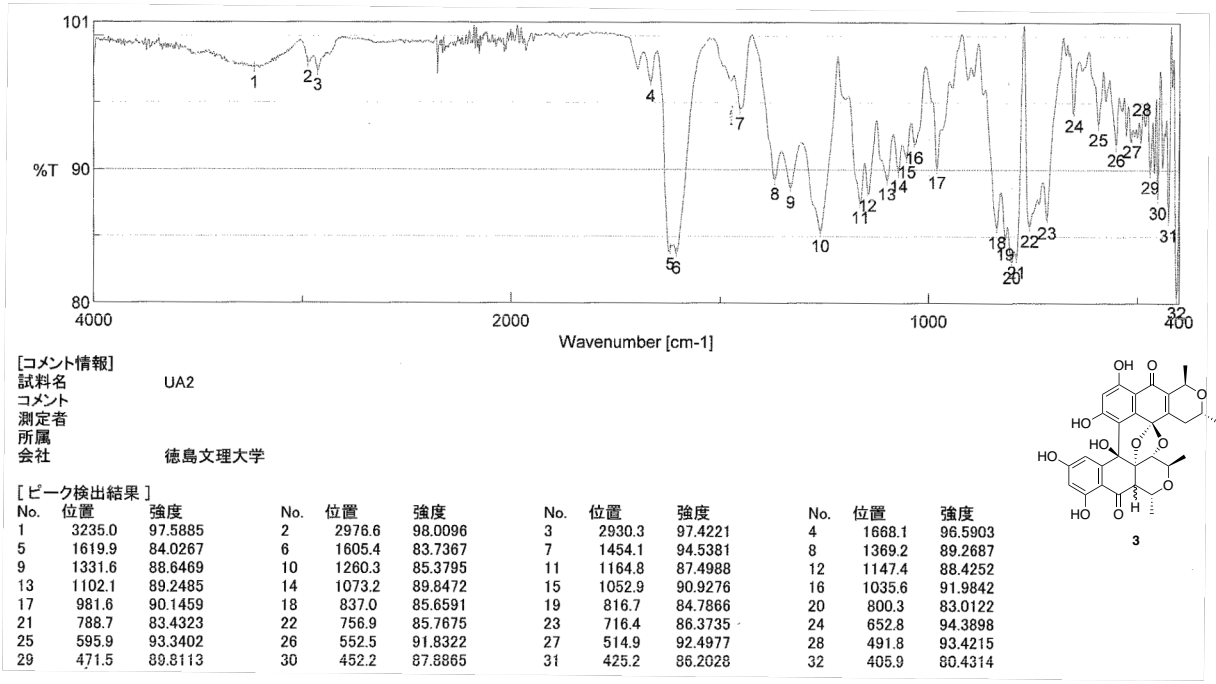


Figure S10. IR spectrum of uroleuconaphin A_2 (**3**)

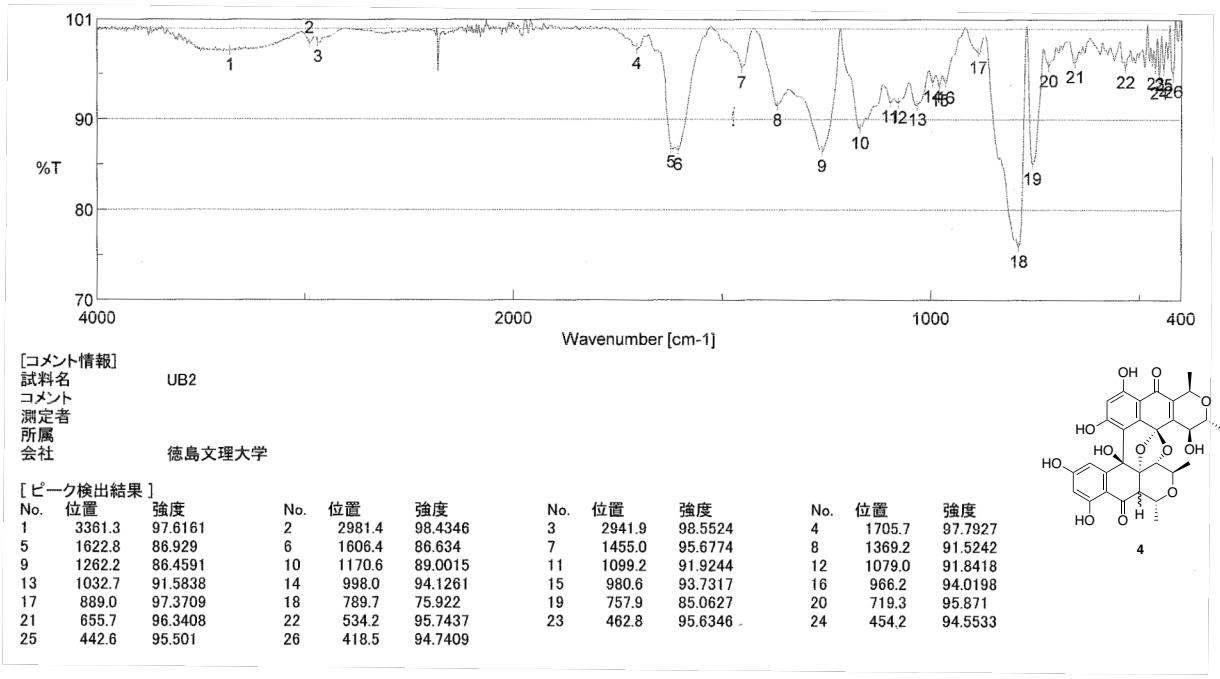
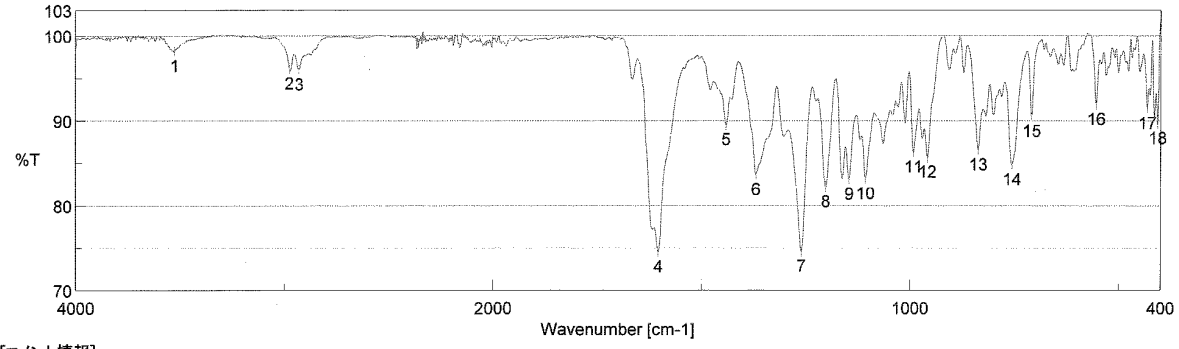


Figure S11. IR spectrum of uroleuconaphin B_2 (**4**)



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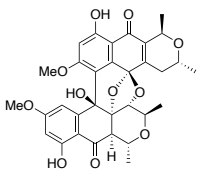
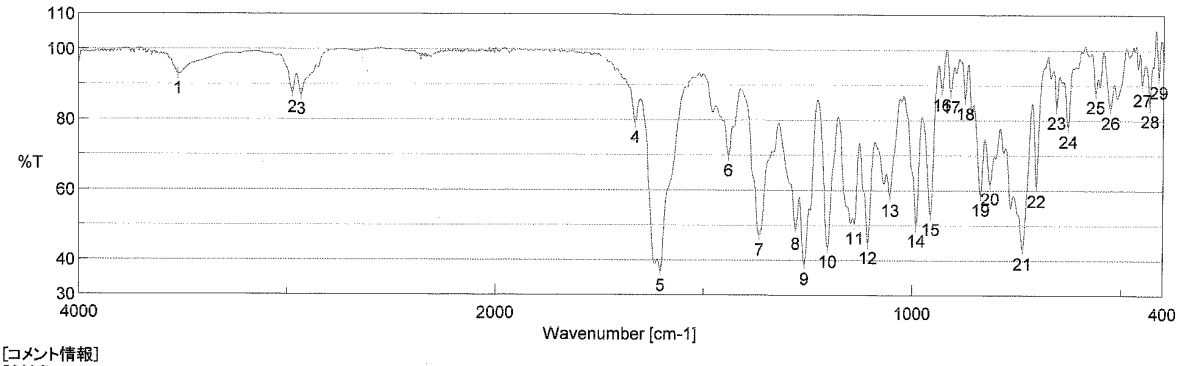


5a

[ピーク検出結果]

No.	位置	強度	No.	位置	強度	No.	位置	強度	No.	位置	強度
1	3522.3	98.1803	2	2976.6	96.1112	3	2930.3	95.9917	4	1603.5	74.5309
5	1442.5	89.5236	6	1370.2	83.6251	7	1260.3	74.5925	8	1201.4	82.2162
9	1145.5	83.1206	10	1106.9	83.1774	11	992.2	86.2931	12	958.4	85.7126
13	837.0	86.5491	14	756.0	84.8221	15	708.7	90.5134	16	554.4	91.9346
17	432.9	91.4388	18	407.9	89.6737						

Figure S12. IR spectrum of 7-*O*, 7'-*O*-dimethyl uroleuconaphin A_{2a} (**5a**)



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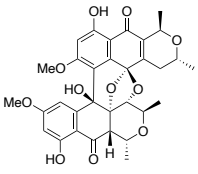
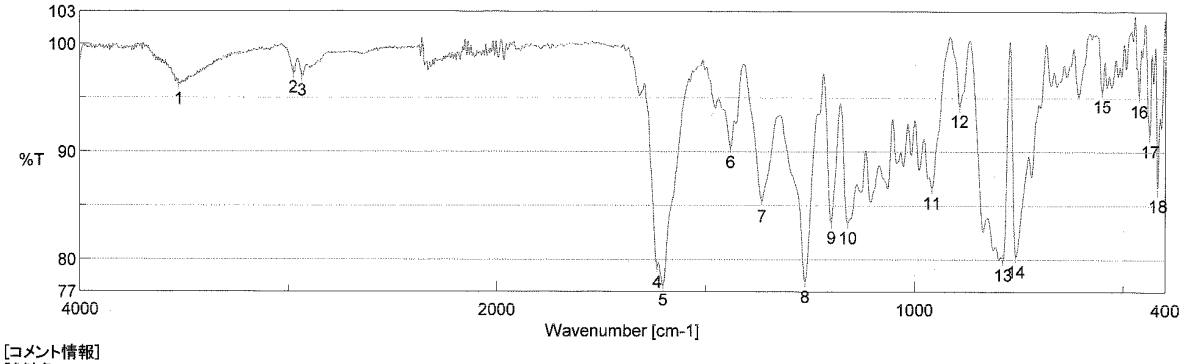


5b

[ピーク検出結果]

No.	位置	強度	No.	位置	強度	No.	位置	強度	No.	位置	強度
1	3523.3	92.892	2	2974.7	87.6551	3	2933.2	87.1345	4	1666.2	79.2265
5	1604.5	36.9359	6	1441.5	69.825	7	1367.3	47.1113	8	1279.5	48.9012
9	1258.3	38.8183	10	1202.4	43.7873	11	1138.8	50.474	12	1106.9	44.8967
13	1054.9	58.4375	14	991.2	49.739	15	956.5	53.0375	16	930.5	88.5701
17	909.3	87.9603	18	874.6	86.0451	19	837.0	58.6033	20	813.8	61.8119
21	735.7	43.1956	22	702.9	61.1576	23	655.7	83.5167	24	627.7	78.0913
25	563.1	87.9651	26	527.4	83.5343	27	451.3	90.0799	28	432.9	83.9893
29	411.7	92.2657									

Figure S13. IR spectrum of 7-*O*, 7'-*O*-dimethyl uroleuconaphin A_{2b} (**5b**)



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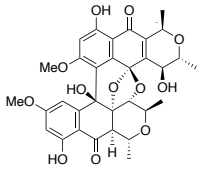
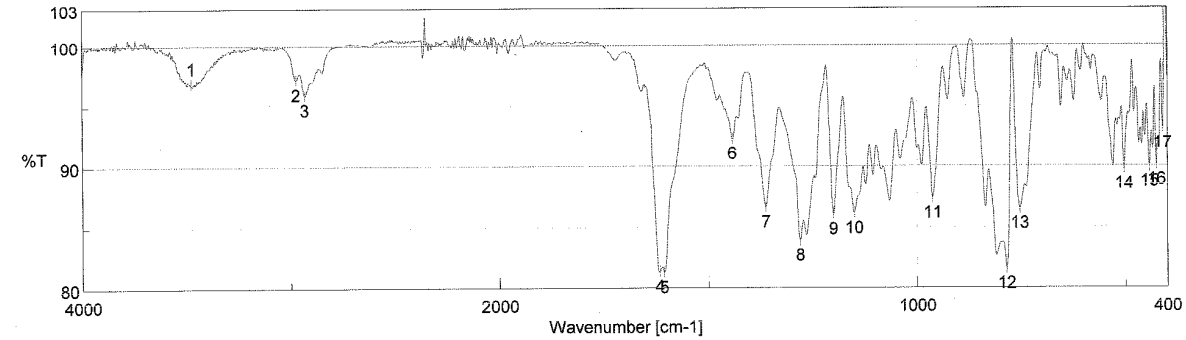


[ピーク検出結果]

No.	位置	強度	No.	位置	強度	No.	位置	強度	No.	位置	強度
1	3528.1	96.2088	2	2976.6	97.3127	3	2936.1	97.042	4	1617.0	79.2648
5	1603.5	77.6203	6	1441.5	90.3841	7	1365.4	85.3802	8	1262.2	77.9103
9	1199.5	83.3731	10	1160.0	83.3677	11	959.4	86.5939	12	893.8	94.1777
13	787.8	79.9317	14	756.0	80.2503	15	553.5	95.5932	16	463.8	95.1507
17	436.8	91.4285	18	417.5	86.3625						

Figure S14. IR spectrum of 7-*O*, 7'-*O*-dimethyl uroleuconaphin B_{2a} (**6a**)



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試料名 UB2b
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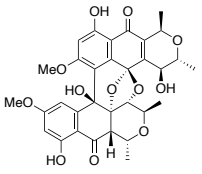


[ピーク検出結果]

No.	位置	強度	No.	位置	強度	No.	位置	強度	No.	位置	強度
1	3477.0	96.8962	2	2976.6	97.1569	3	2936.1	95.9194	4	1617.0	81.353
5	1606.4	81.2707	6	1443.5	92.2818	7	1363.4	86.644	8	1281.5	83.9015
9	1201.4	86.0824	10	1151.3	86.1694	11	963.3	87.3699	12	786.8	81.5759
13	756.0	86.5325	14	504.3	89.727	15	443.5	89.9078	16	426.2	90.0592
17	411.7	93.1434									

Figure S15. IR spectrum of 7-*O*, 7'-*O*-dimethyl uroleuconaphin B_{2b} (**6b**)

15. HRMS spectra

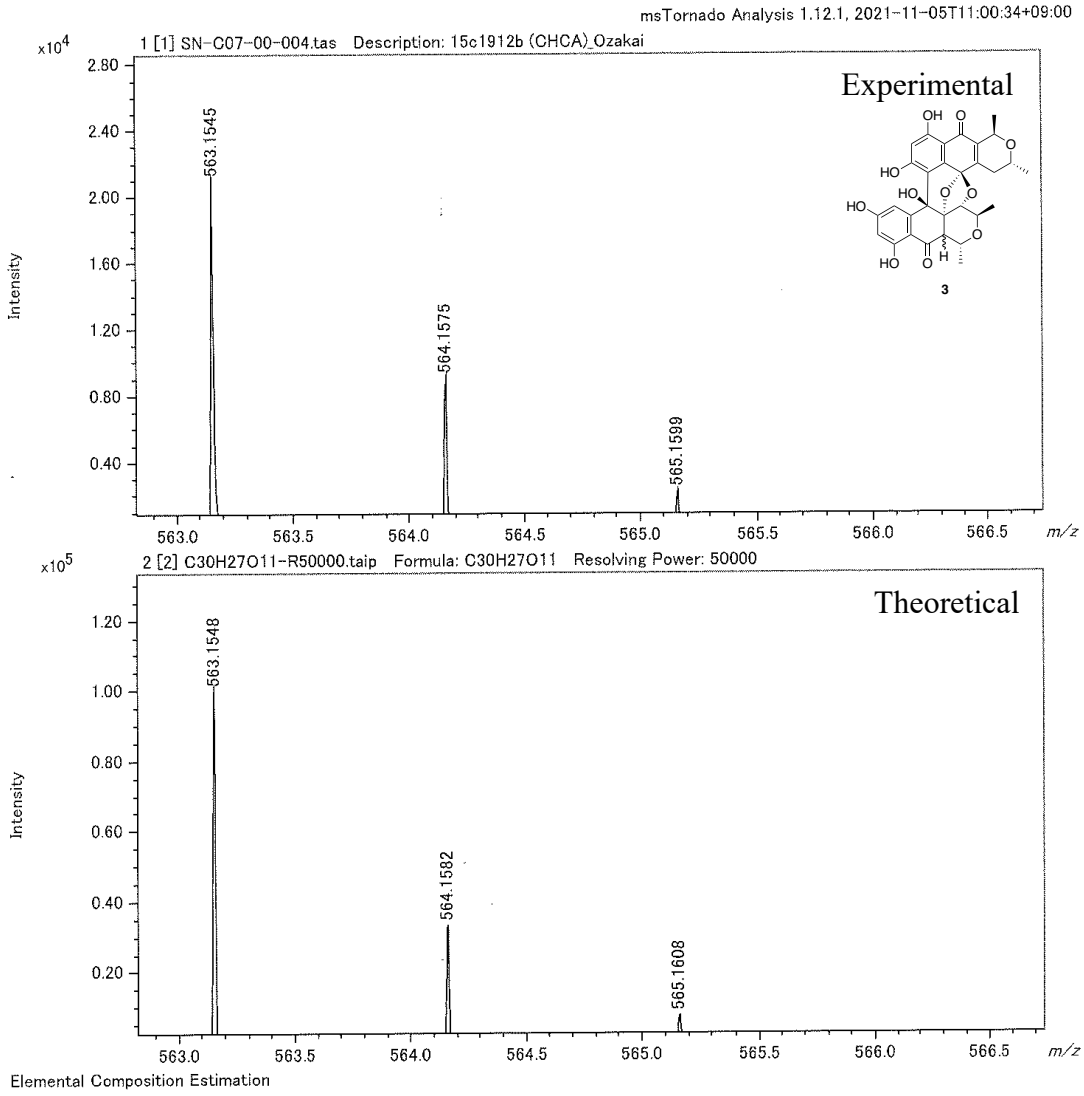


Figure S16. HRMS (MALDI) spectrum of uroleuconaphin A_2 (**3**)

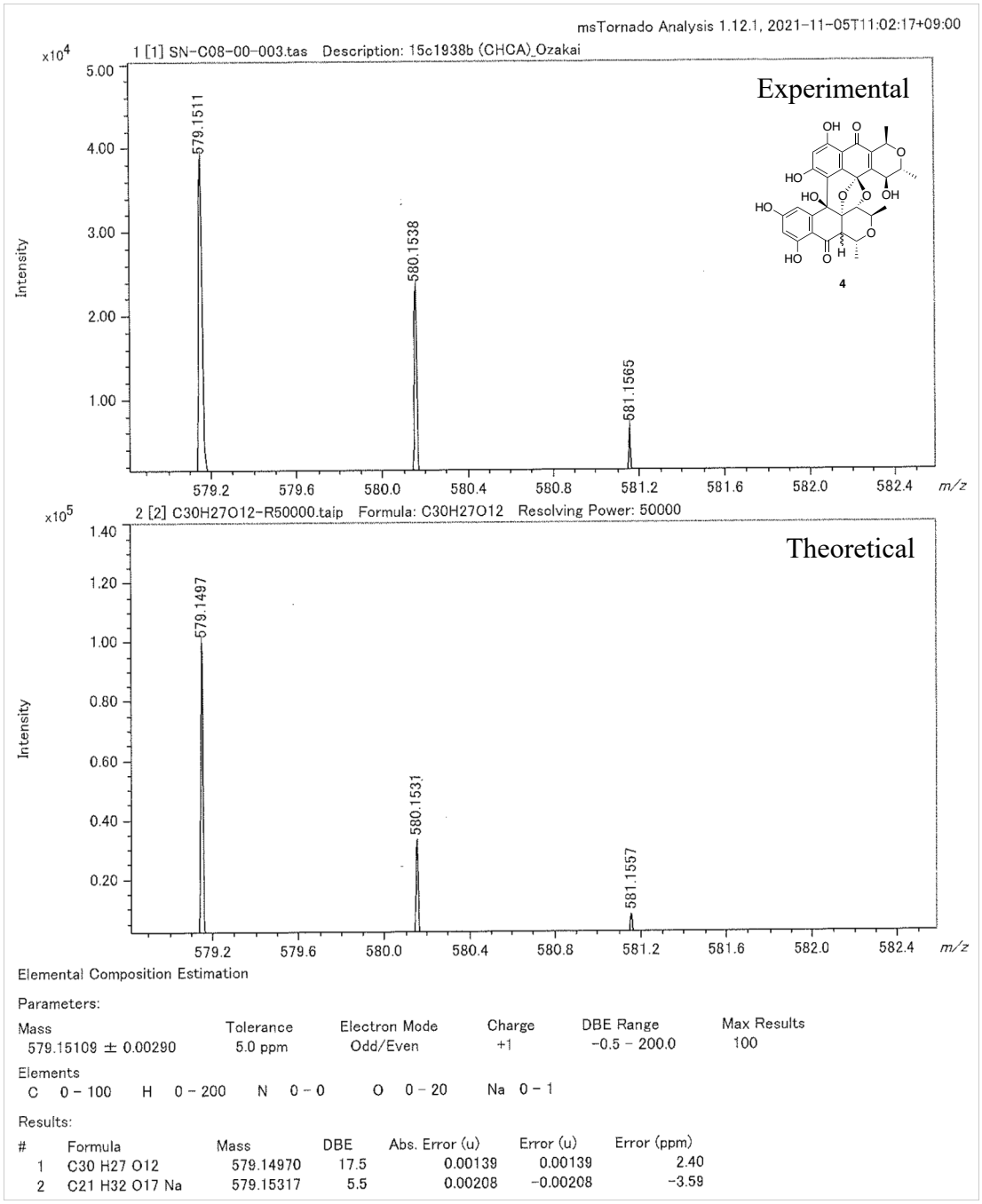
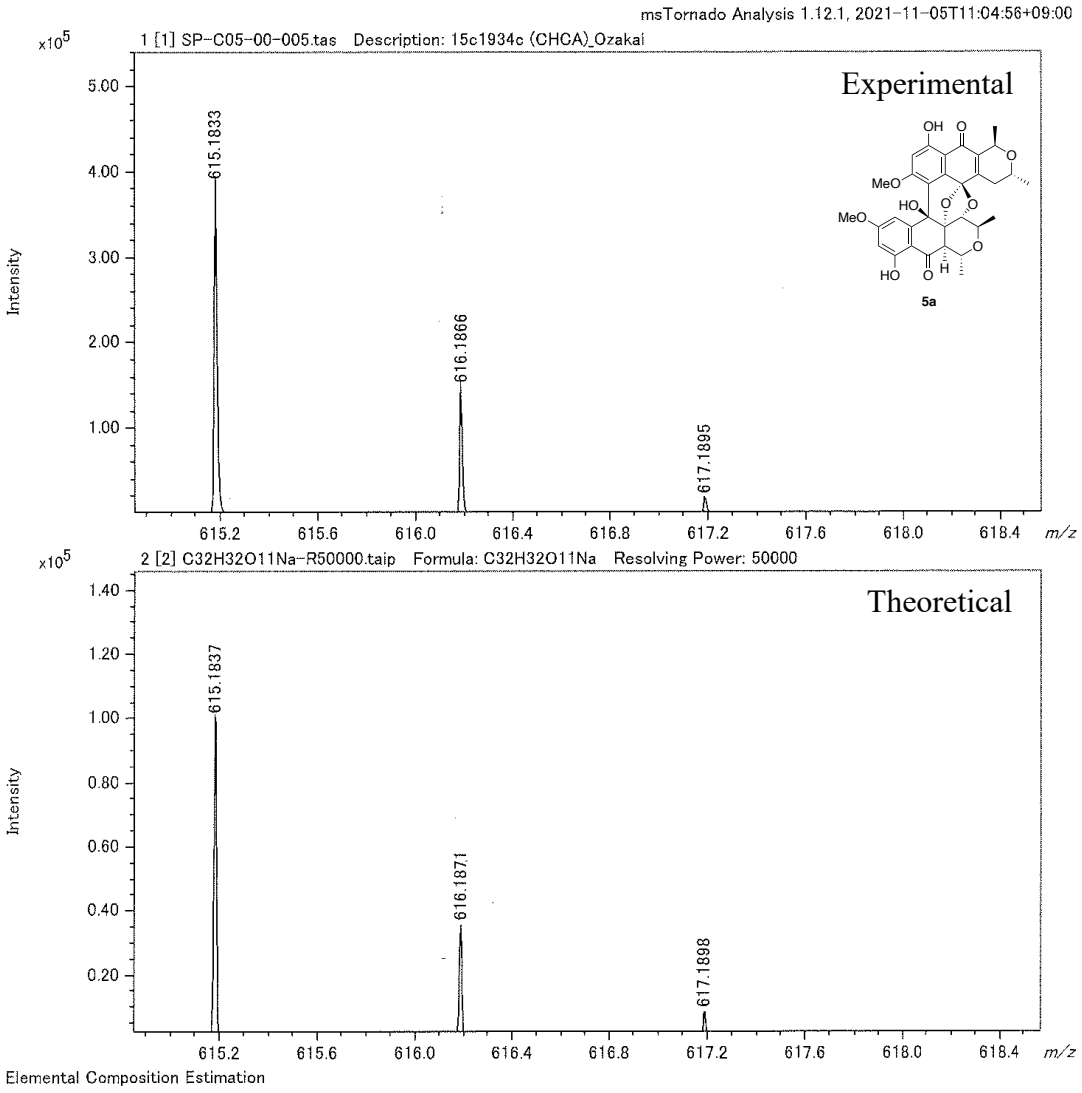


Figure S17. HRMS (MALDI) spectrum of uroleuconaphin B_2 (**4**)



Elemental Composition Estimation

Parameters:

Mass	Tolerance	Electron Mode	Charge	DBE Range	Max Results
615.18329 ± 0.00308	5.0 ppm	Odd/Even	+1	-0.5 – 200.0	100

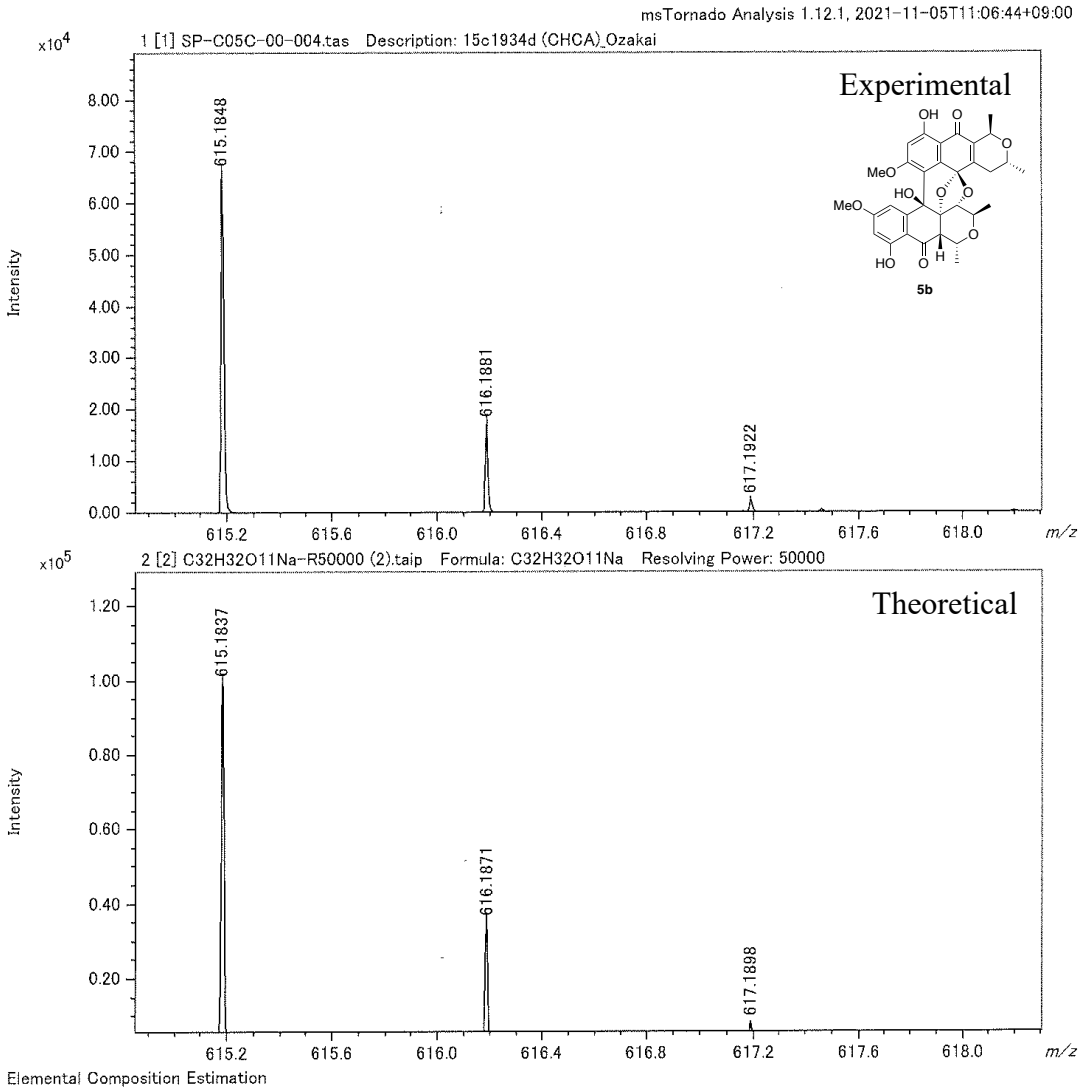
Elements

C 0 – 100 H 0 – 200 N 0 – 0 O 0 – 20 Na 0 – 1

Results:

#	Formula	Mass	DBE	Abs. Error (u)	Error (u)	Error (ppm)
1	C32 H32 O11 Na	615.18368	16.5	0.00040	-0.00040	-0.65
2	C34 H31 O11	615.18609	19.5	0.00280	-0.00280	-4.56
3	C41 H27 O6	615.18022	28.5	0.00307	0.00307	4.99

Figure S18. HRMS (MALDI) spectrum of 7-*O*, 7'-*O*-dimethyl uroleuconaphin A_{2a} (**5a**)



Elemental Composition Estimation

Parameters:

Mass	Tolerance	Electron Mode	Charge	DBE Range	Max Results
615.18478 ± 0.00308	5.0 ppm	Odd/Even	+1	-0.5 – 200.0	100

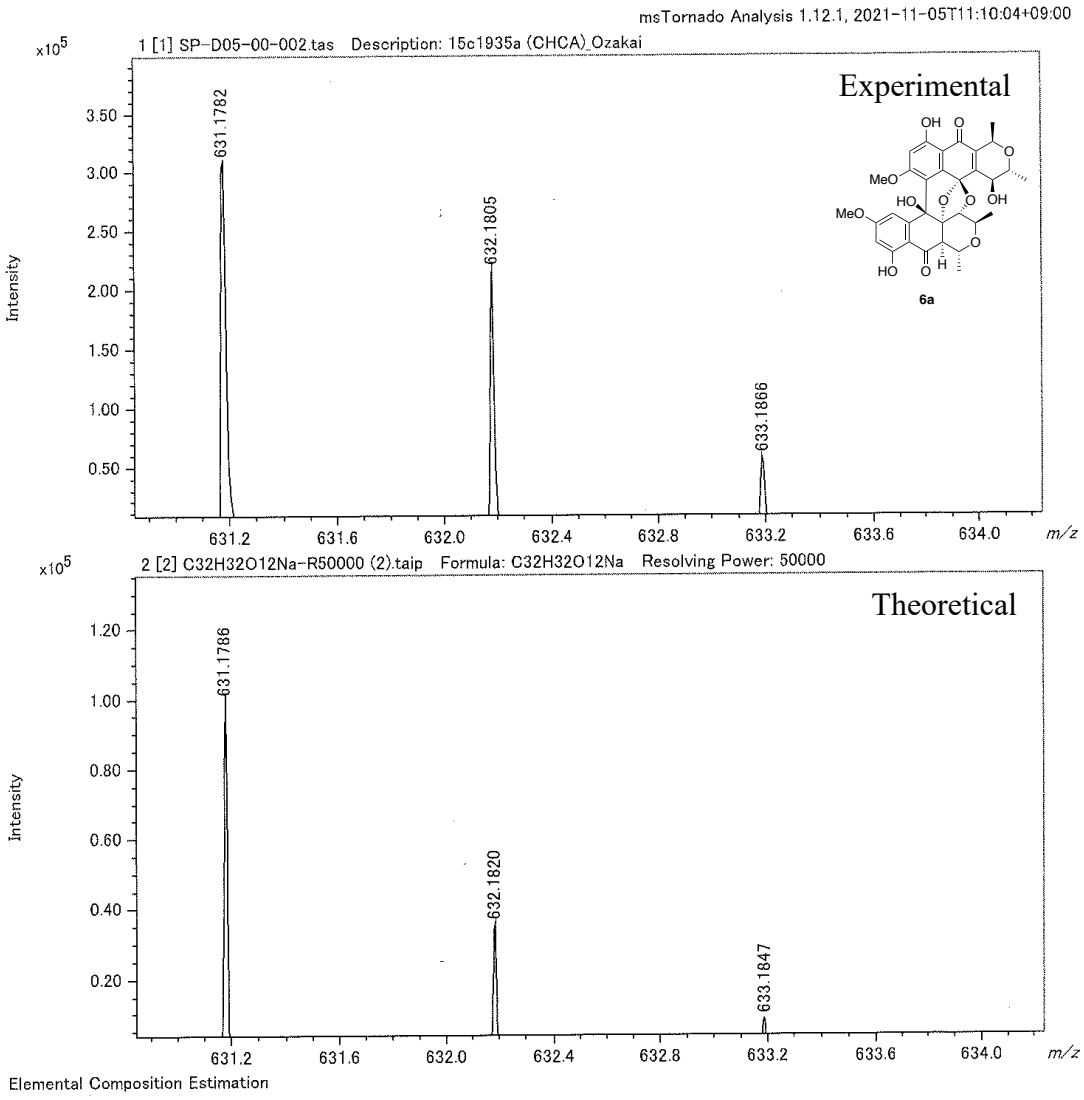
Elements

C 0 – 100 H 0 – 200 N 0 – 0 O 0 – 20 Na 0 – 1

Results:

#	Formula	Mass	DBE	Abs. Error (u)	Error (u)	Error (ppm)
1	C32 H32 O11 Na	615.18368	16.5	0.00109	0.00109	1.78
2	C34 H31 O11	615.18609	19.5	0.00131	-0.00131	-2.13

Figure S19. HRMS (MALDI) spectrum of 7-*O*, 7'-*O*-dimethyl uroleuconaphin A_{2b} (**5b**)



Elemental Composition Estimation

Parameters:

Mass	Tolerance	Electron Mode	Charge	DBE Range	Max Results
631.17819 ± 0.00316	5.0 ppm	Odd/Even	+1	−0.5 – 200.0	100

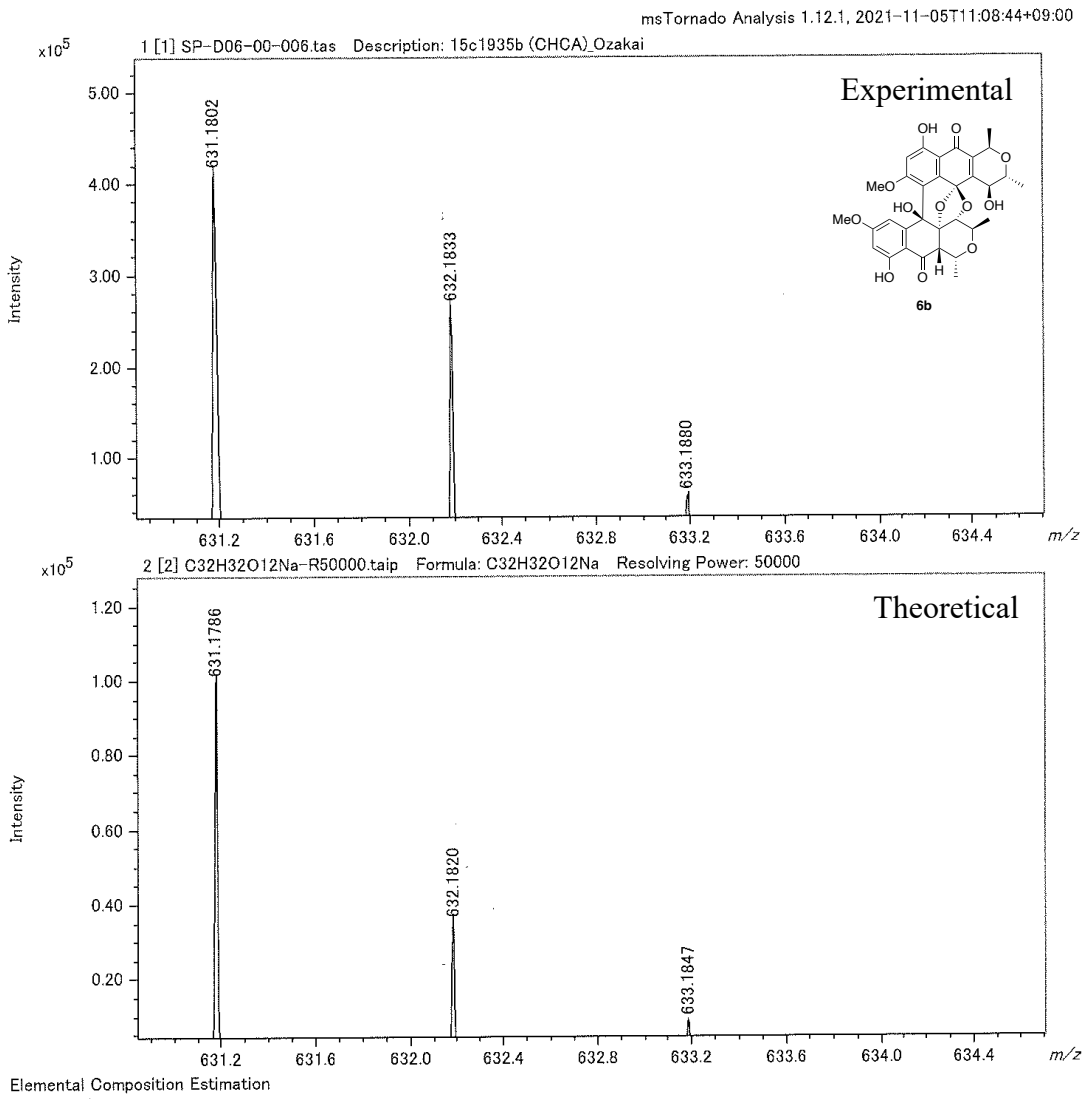
Elements

C 0 – 100 H 0 – 200 N 0 – 0 O 0 – 20 Na 0 – 1

Results:

#	Formula	Mass	DBE	Abs. Error (u)	Error (u)	Error (ppm)
1	C32 H32 O12 Na	631.17860	16.5	0.00041	−0.00041	−0.65
2	C34 H31 O12	631.18100	19.5	0.00281	−0.00281	−4.46
3	C41 H27 O7	631.17513	28.5	0.00306	0.00306	4.85

Figure S20. HRMS (MALDI) spectrum of 7-*O*, 7'-*O*-dimethyl uroleuconaphin B_{2a} (**6a**)



Elemental Composition Estimation

Parameters:

Mass	Tolerance	Electron Mode	Charge	DBE Range	Max Results
631.18021 ± 0.00316	5.0 ppm	Odd/Even	+1	-0.5 - 200.0	100

Elements

C 0 - 100 H 0 - 200 N 0 - 0 O 0 - 20 Na 0 - 1

Results:

#	Formula	Mass	DBE	Abs. Error (u)	Error (u)	Error (ppm)
1	C34 H31 O12	631.18100	19.5	0.00079	-0.00079	-1.25
2	C32 H32 O12 Na	631.17860	16.5	0.00161	0.00161	2.56

Figure S21. HRMS (MALDI) spectrum of 7-*O*, 7'-*O*-dimethyl uroleuconaphin B_{2b} (**6b**)

16. HPLC spectra

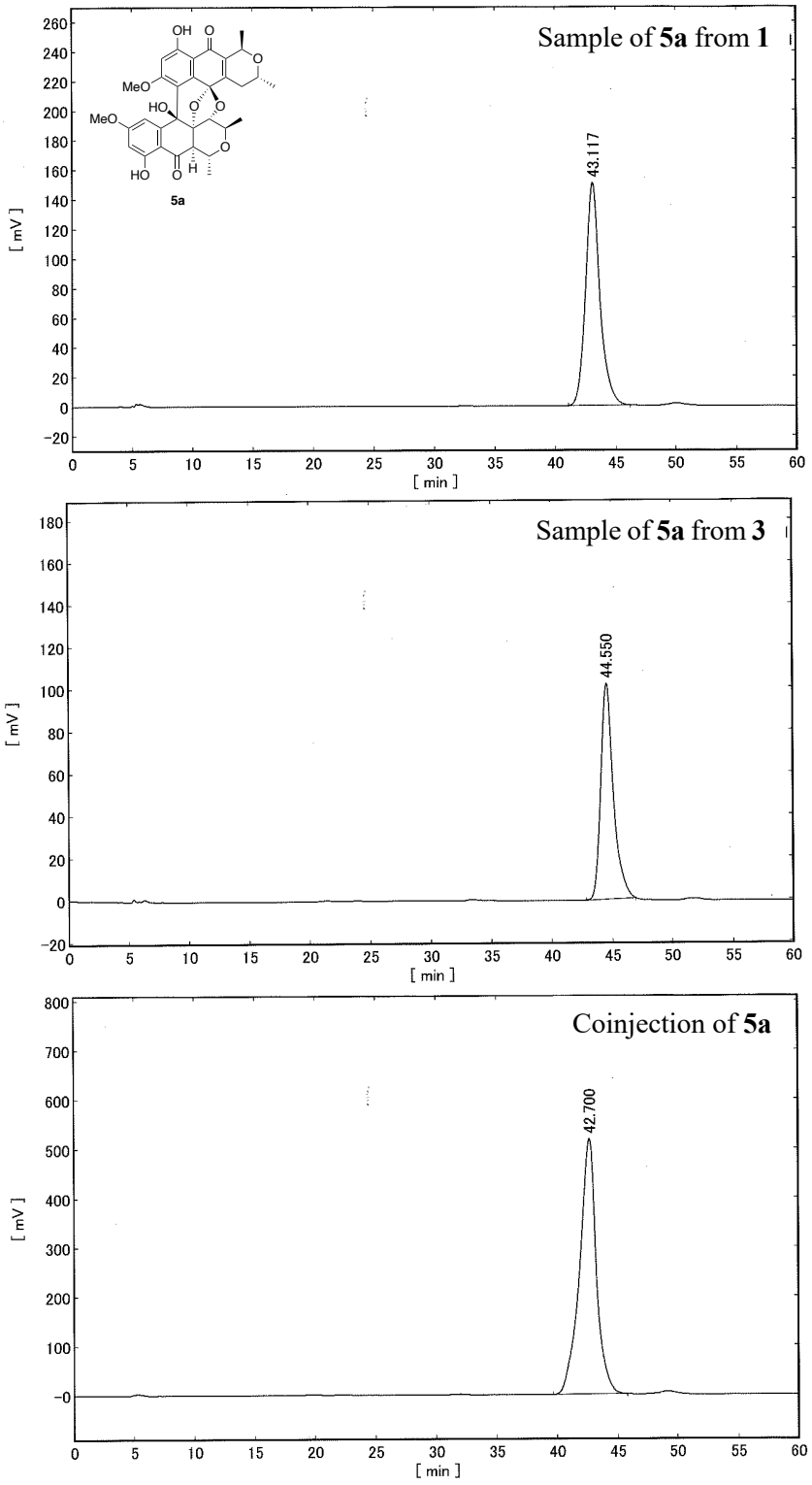


Figure S22. HPLC chromatogram of 7-*O*, 7'-*O*-dimethyl uroleuconaphin A_{2a} (**5a**) (ODS, MeOH/H_2O/TFA = 80/20/0.1, flow rate: 0.8 mL/min, detector UV: 254 nm)

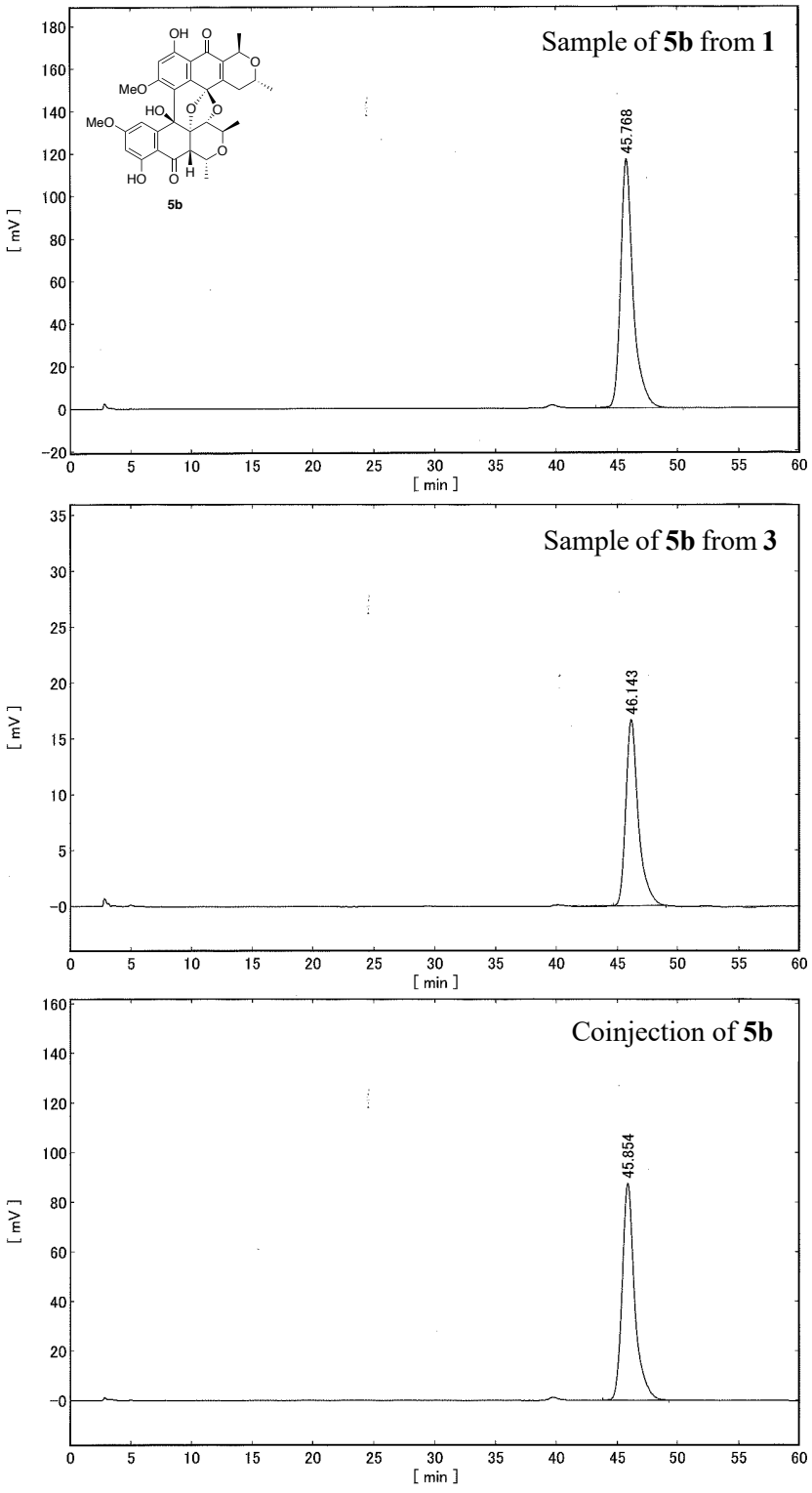


Figure S23. HPLC chromatogram of 7-*O*, 7'-*O*-dimethyl uroleuconaphin A_{2b} (**5b**) (ODS, MeOH/H_2O/TFA = 80/20/0.1, flow rate: 0.8 mL/min, detector UV: 254 nm)

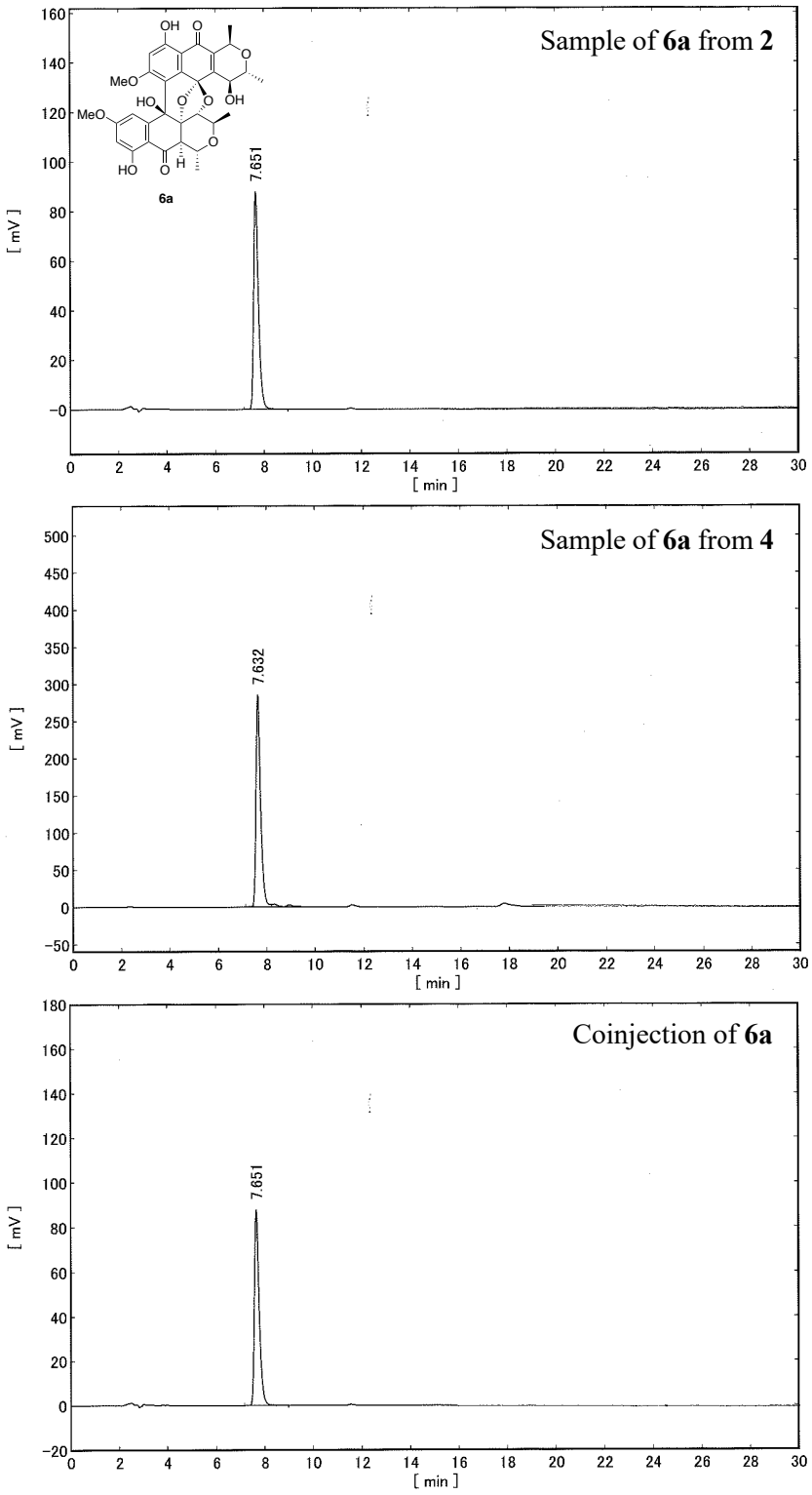


Figure S24. HPLC chromatogram of 7-*O*, 7'-*O*-dimethyl uroleuconaphin B_{2a} (**6a**) (ODS, MeCN/H_2O/TFA = 75/25/0.1, flow rate: 1.0 mL/min, detector UV: 254 nm)

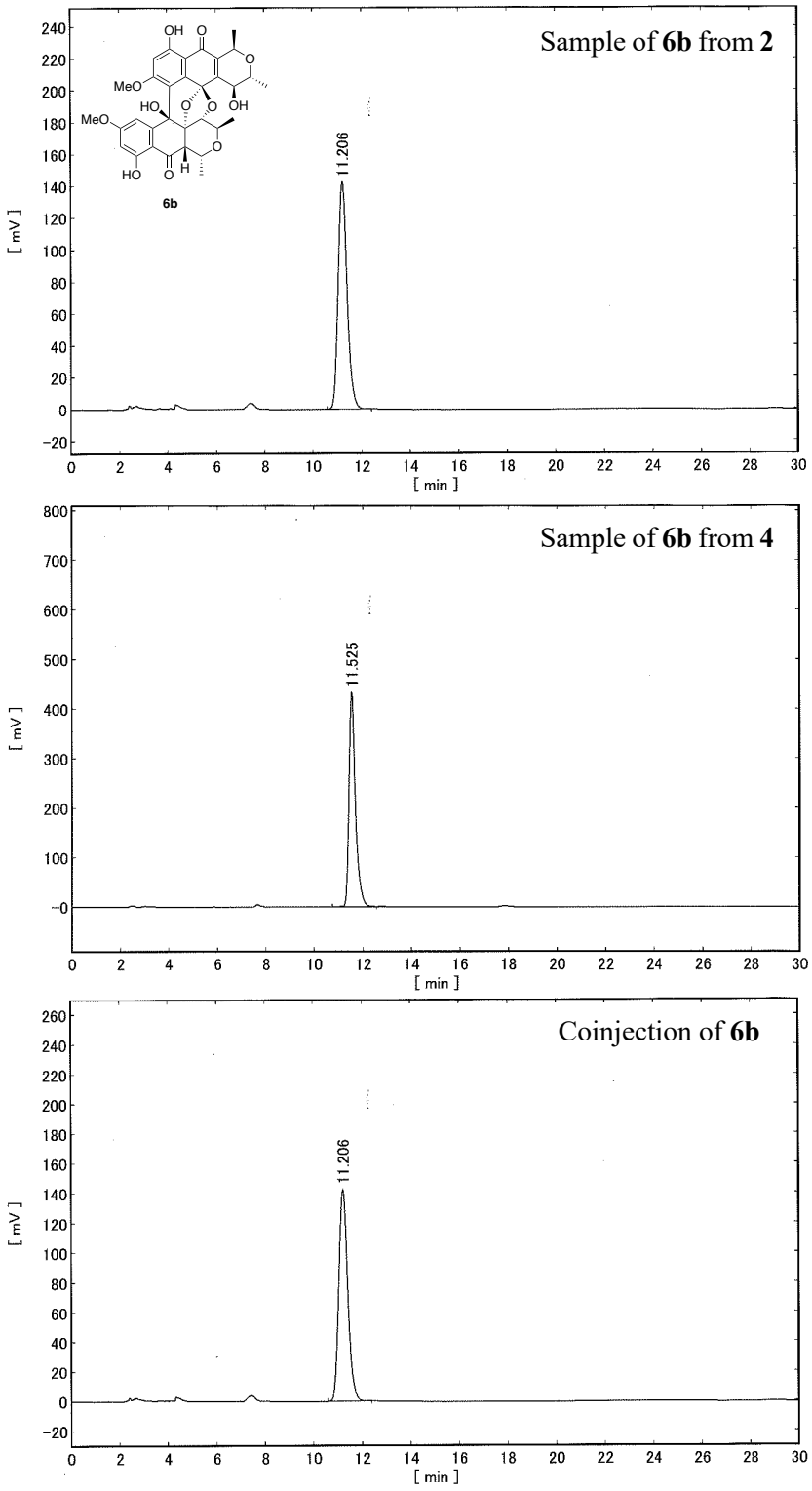
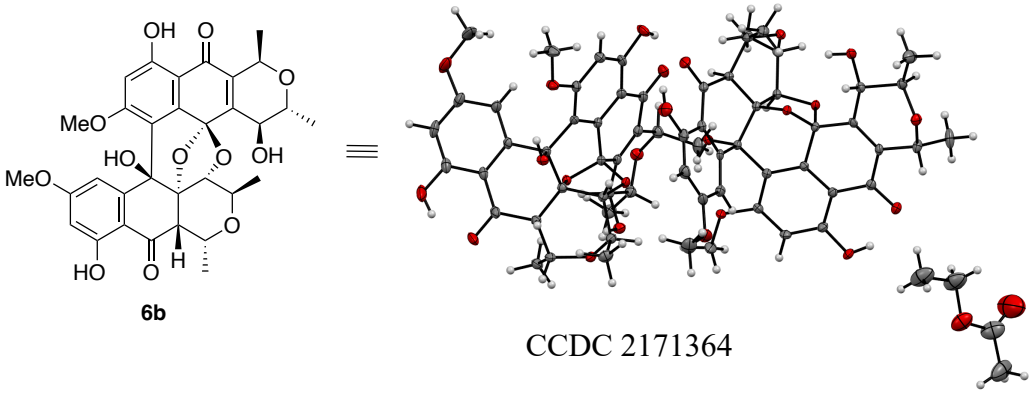


Figure S25. HPLC chromatogram of 7-*O*, 7'-*O*-dimethyl uroleuconaphin B_{2b} (**6b**) (ODS, MeCN/H_2O/TFA = 75/25/0.1, flow rate: 1.0 mL/min, detector UV: 254 nm)

17. Single crystal X-ray diffraction data



Identification code	CCDC 2171364
Moiety formula	2 ($C_{32}H_{32}O_{12}$), $C_4H_8O_2$
Formula weight	3057.83
Temperature	100 K
Wavelength	0.71073 Å
Crystal system	monoclinic
Space group	$P2_1$
Until cell dimensions	a = 11.4954 (7) Å α = 90°
	b = 20.8647 (13) Å β = 110.359 (1)°
	c = 13.5984 (9) Å γ = 90°
Volume	3057.8 (3) Å^3
Z	2
Density (calculated)	1.331 g/cm^3
Absorption coefficient	0.099 mm^{-1}
F (000)	1296.0
Crystal size	0.030 × 0.100 × 0.200 mm^3
Theta range for data collection	1.597 to 29.243°
Index ranges	–15<=h<=12, –26<=k<=27, –15<=l<=18
Reflections collected	18984
Independent reflections	11076 [R(int) = 0.0388]
Absorption correction	none

Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	12642 / 1 / 864
Goodness-of-fit on F^2	1.025
Final R indices [I>2σ (I)]	R_1= 0.0388, wR_2 = 0.0915
R indices (all data)	R_1 = 0.0475, wR_2 = 0.0961
Absolute structure parameter	0.3 (3)

18. NMR spectra

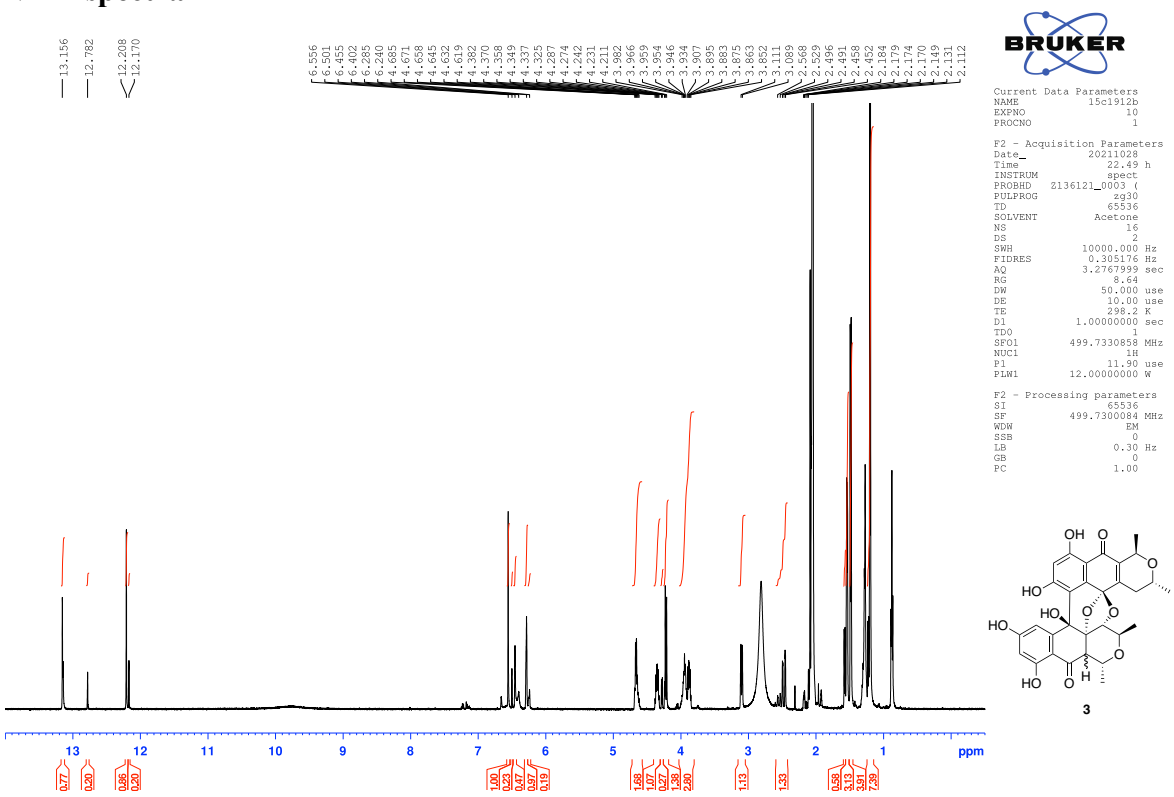


Figure S26. ^{1}H NMR spectrum of uroleuconaphin A_2 (**3**) (500 MHz, acetone-d_6)

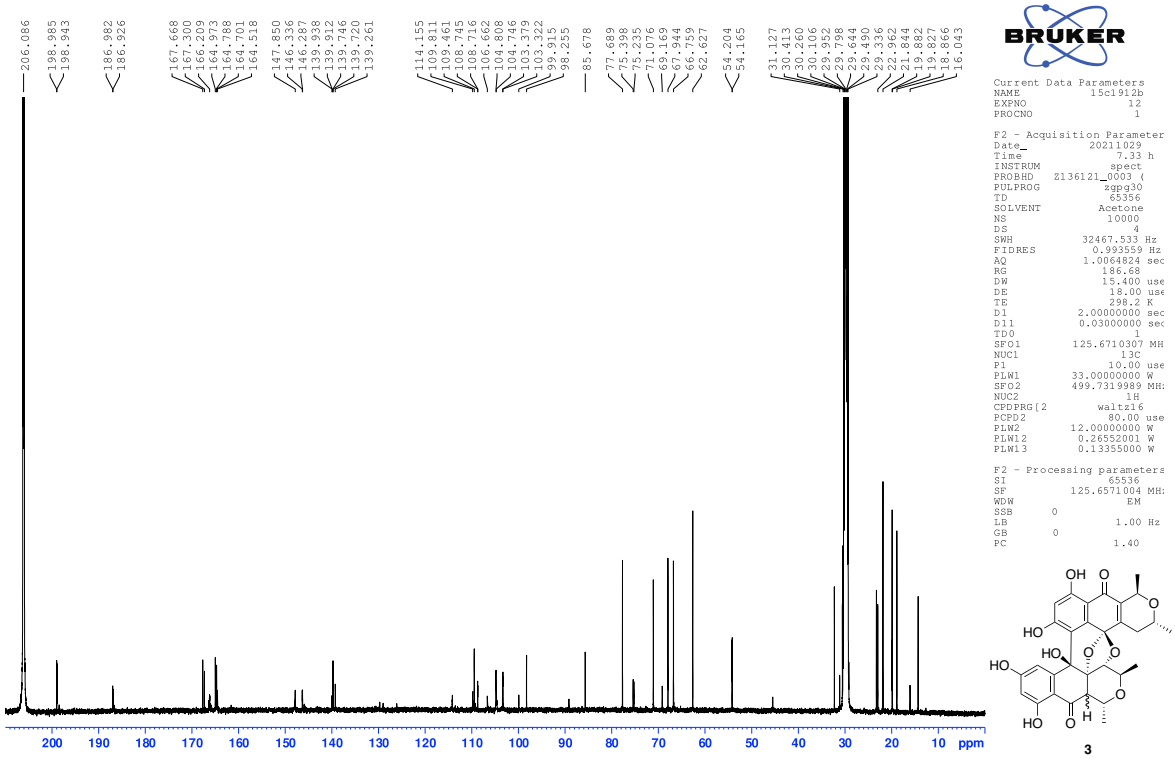


Figure S27. ^{13}C NMR spectrum of uroleuconaphin A_2 (**3**) (125 MHz, acetone-d_6)

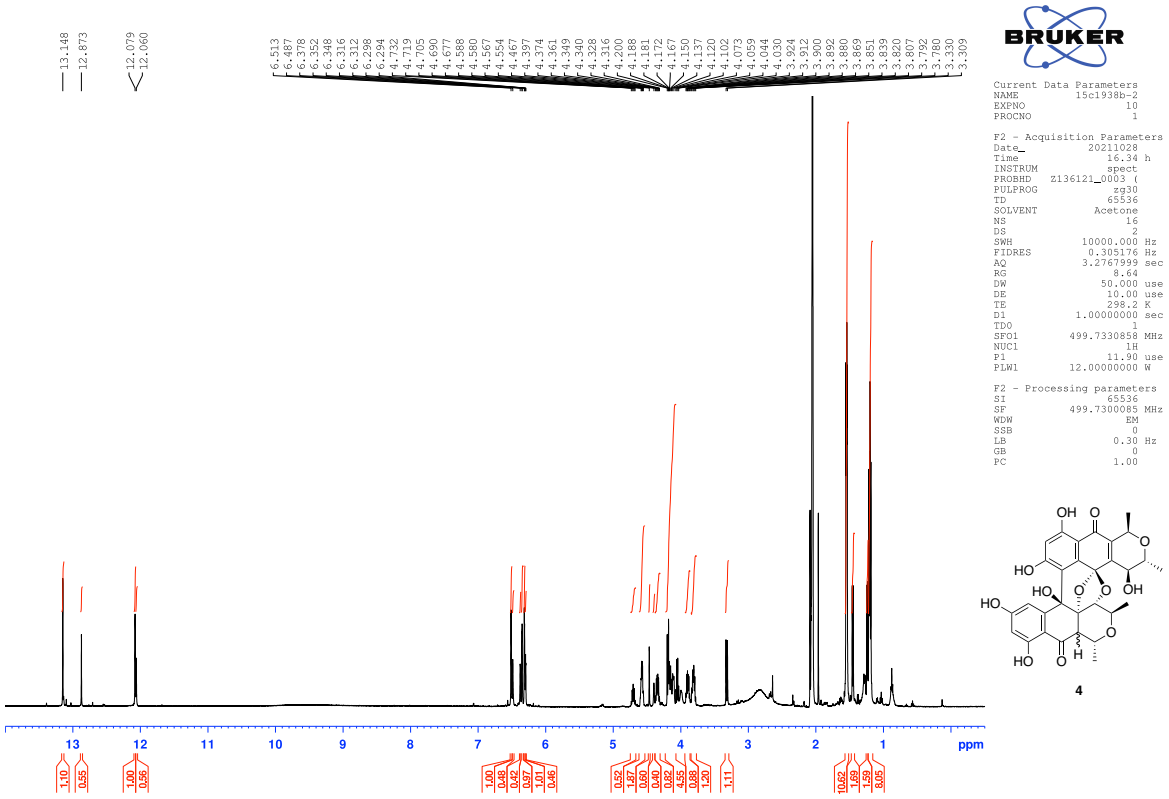


Figure S28. ^{1}H NMR spectrum of uroleuconaphin B_2 (**4**) (500 MHz, acetone-d_6)

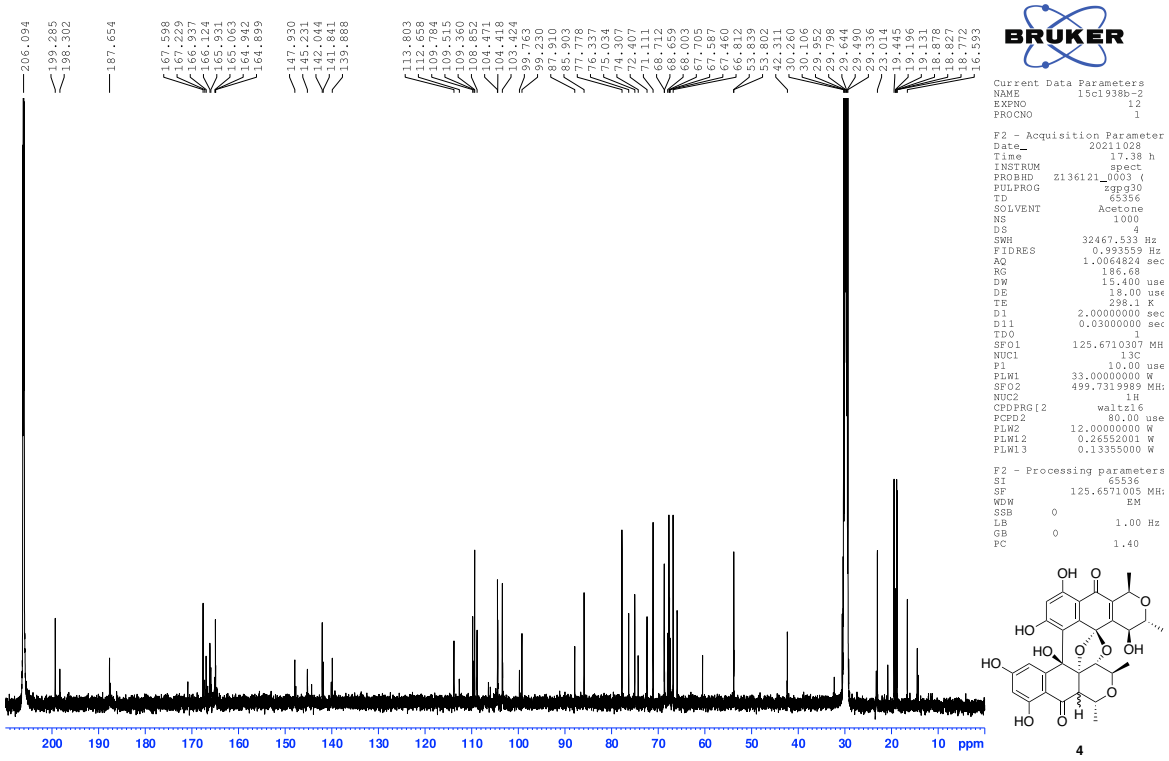


Figure S29. ^{13}C NMR spectrum of uroleuconaphin B_2 (**4**) (125 MHz, acetone-d_6)

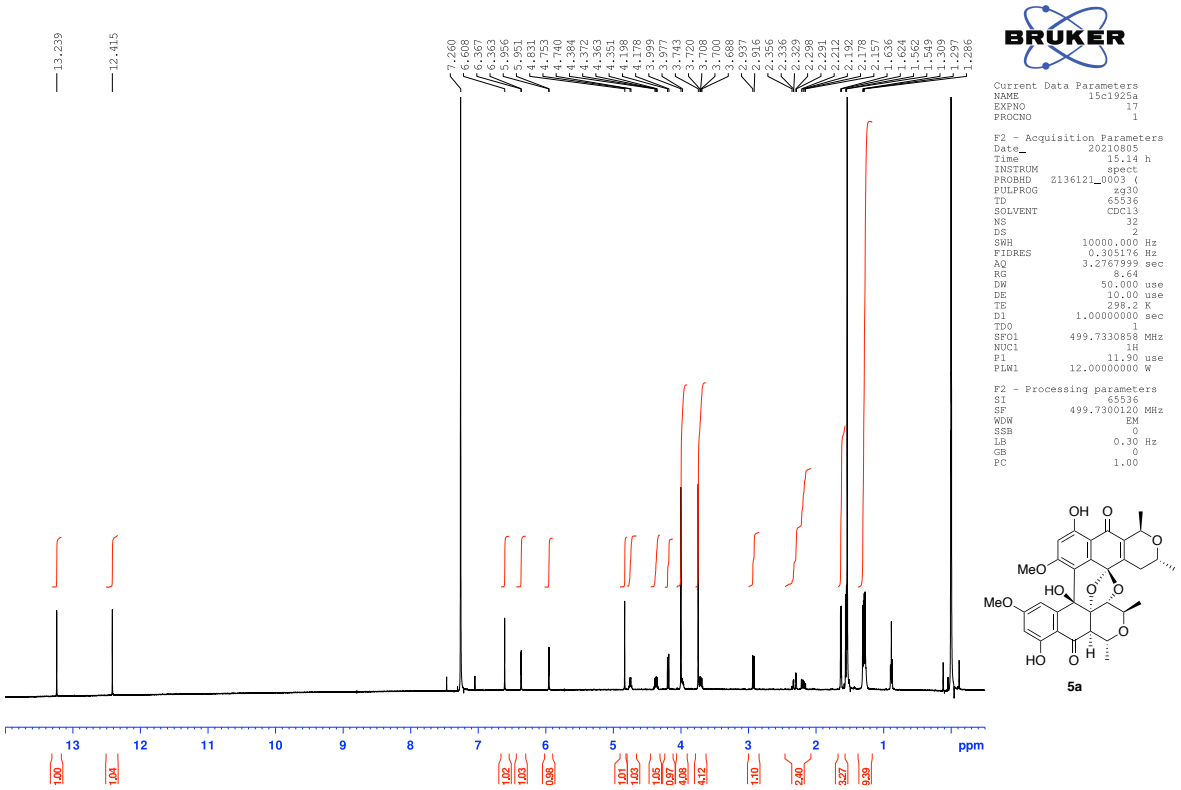


Figure S30. ^{1}H NMR spectrum of 7-*O*, 7'-*O*-dimethyl uroleuconaphin A_{2a} (**5a**) (500 MHz, $CDCl_3$)

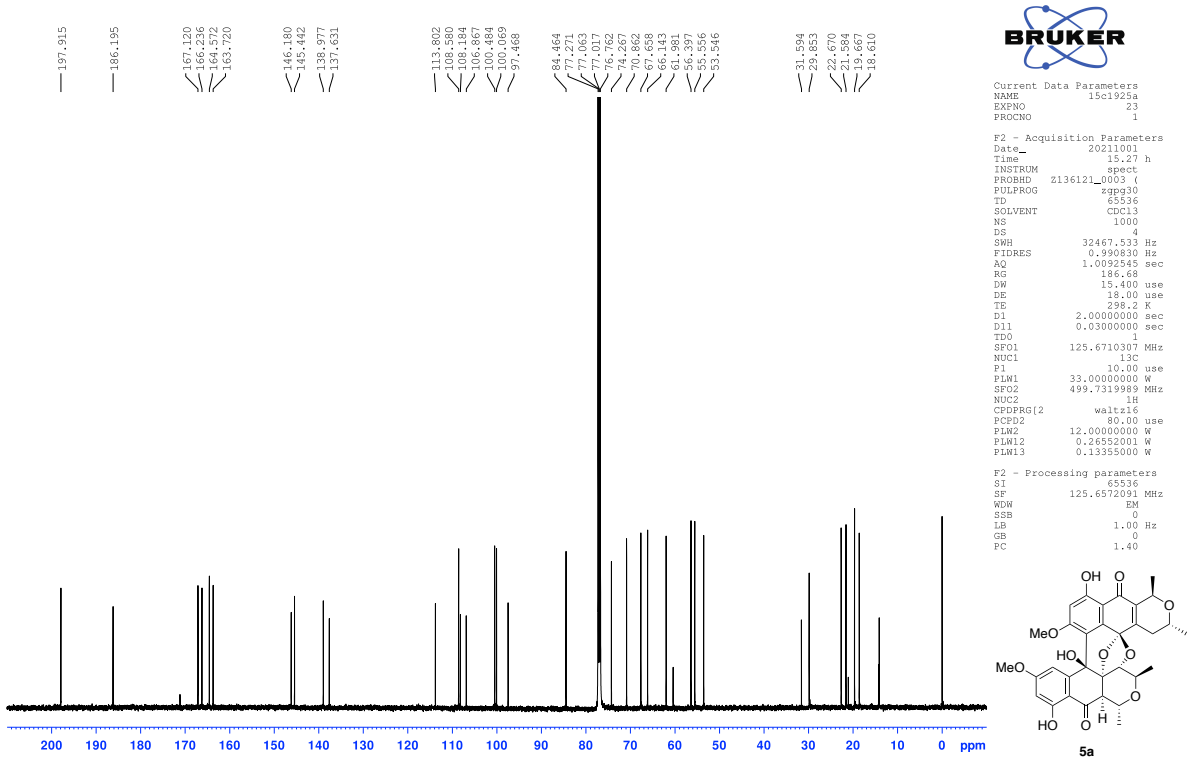


Figure S31. ^{13}C NMR spectrum of 7-*O*, 7'-*O*-dimethyl uroleuconaphin A_{2a} (**5a**) (125 MHz, $CDCl_3$)

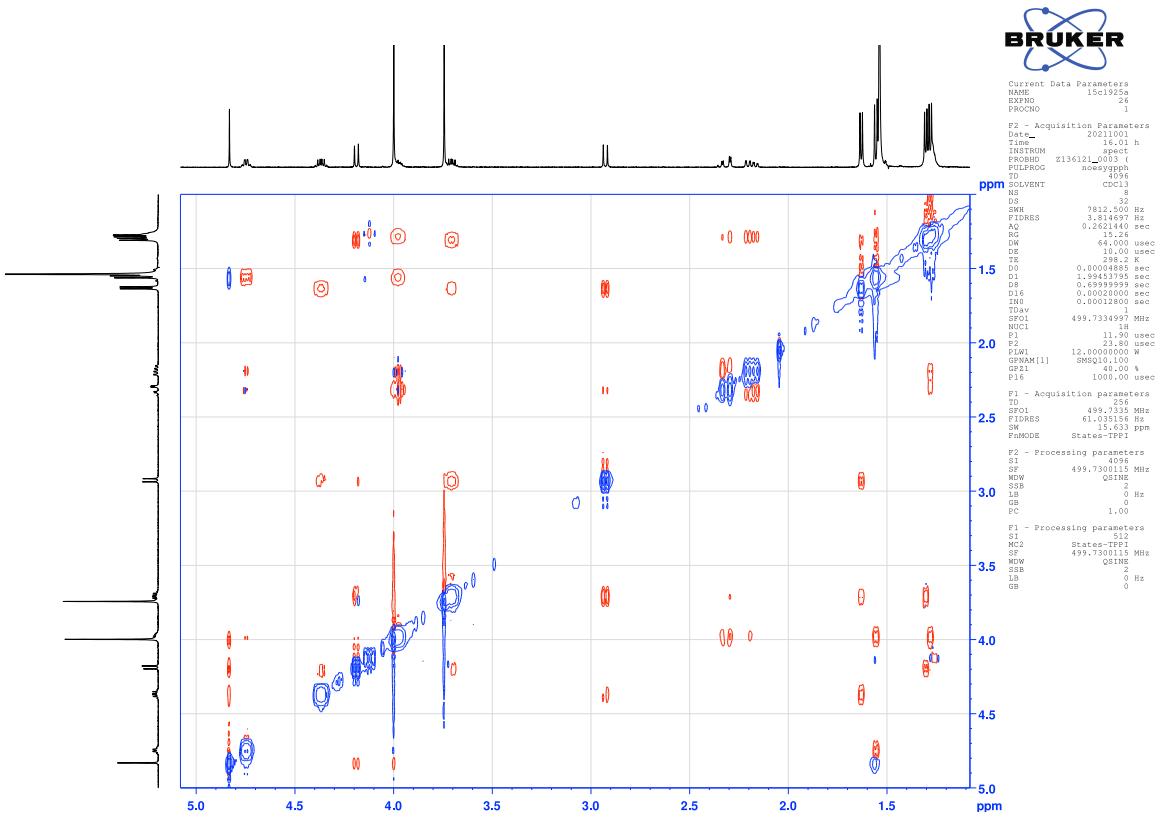


Figure S32. NOESY spectrum of 7-*O*, 7'-*O*-dimethyl uroleuconaphin A_{2a} (**5a**) ($CDCl_3$)

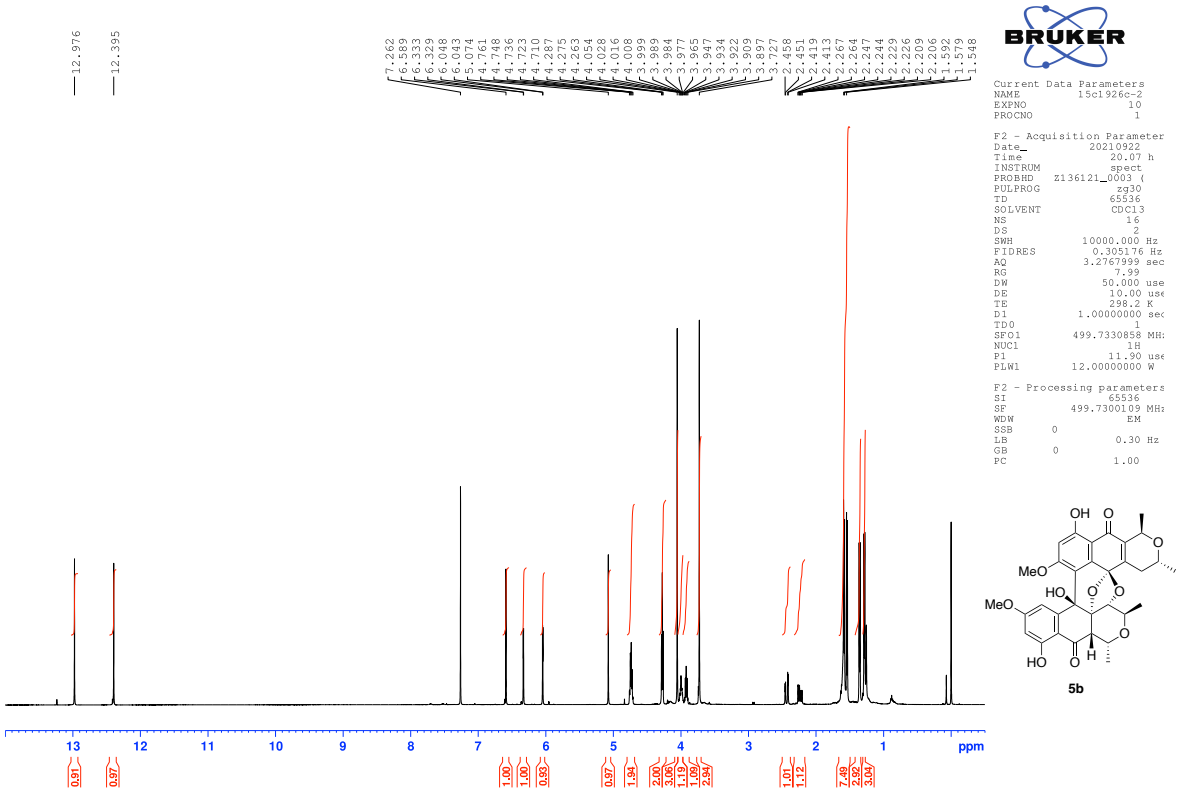


Figure S33. ^{1}H NMR spectrum of 7-*O*, 7'-*O*-dimethyl uroleuconaphin A_{2b} (**5b**) (500 MHz, $CDCl_3$)

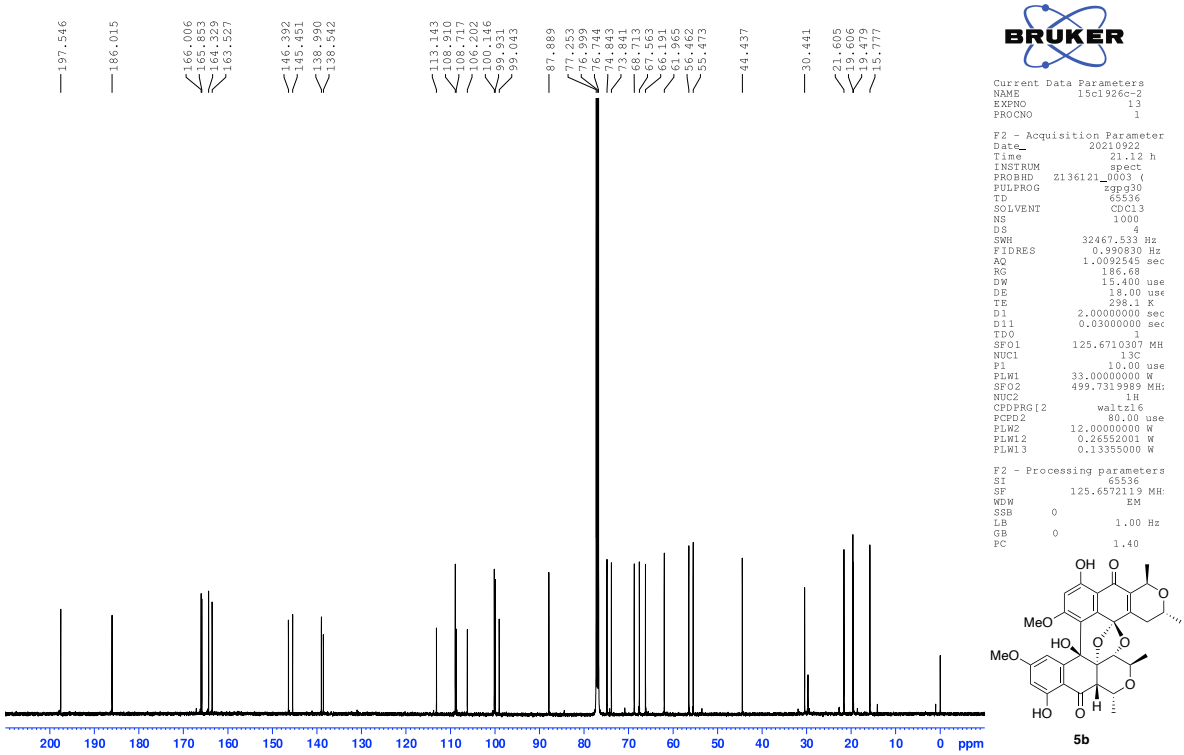


Figure S34. ^{13}C NMR spectrum of 7-*O*, 7'-*O*-dimethyl uroleuconaphin A_{2b} (**5b**) (125 MHz, $CDCl_3$)

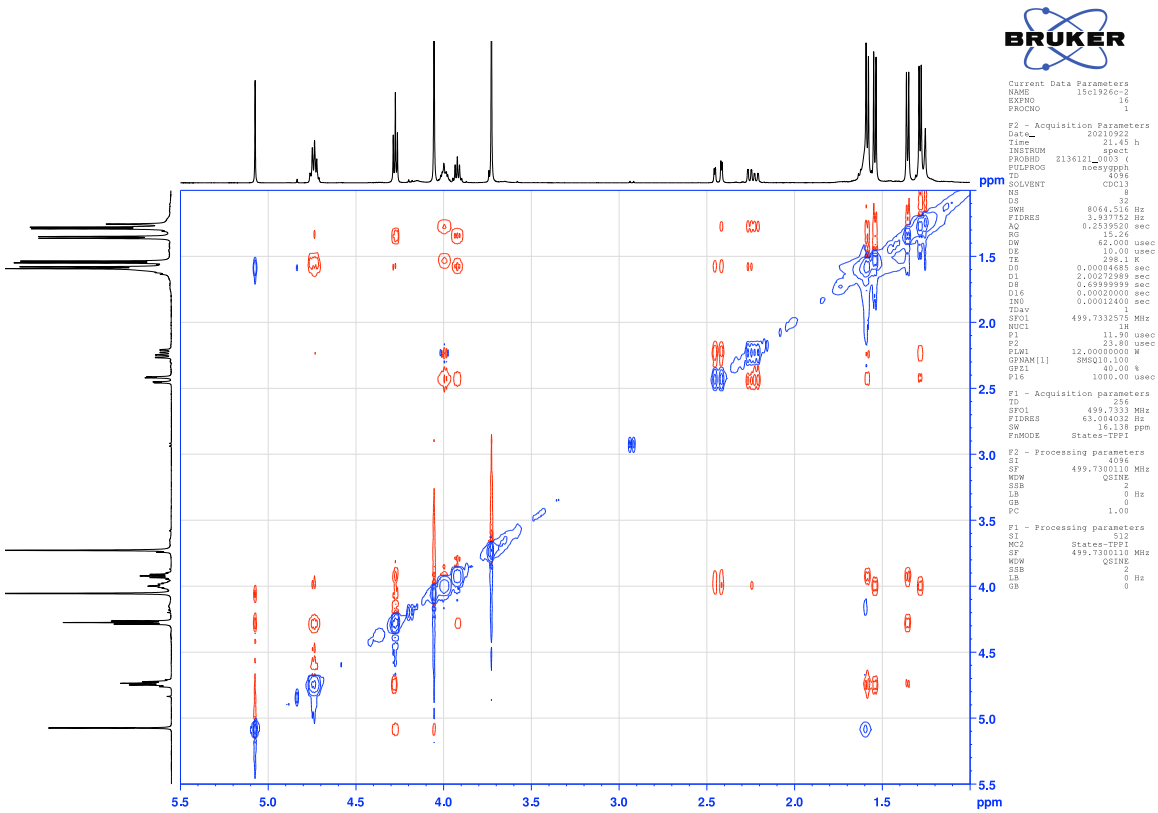


Figure S35. NOESY spectrum of 7-*O*, 7'-*O*-dimethyl uroleuconaphin A_{2b} (**5b**) ($CDCl_3$)

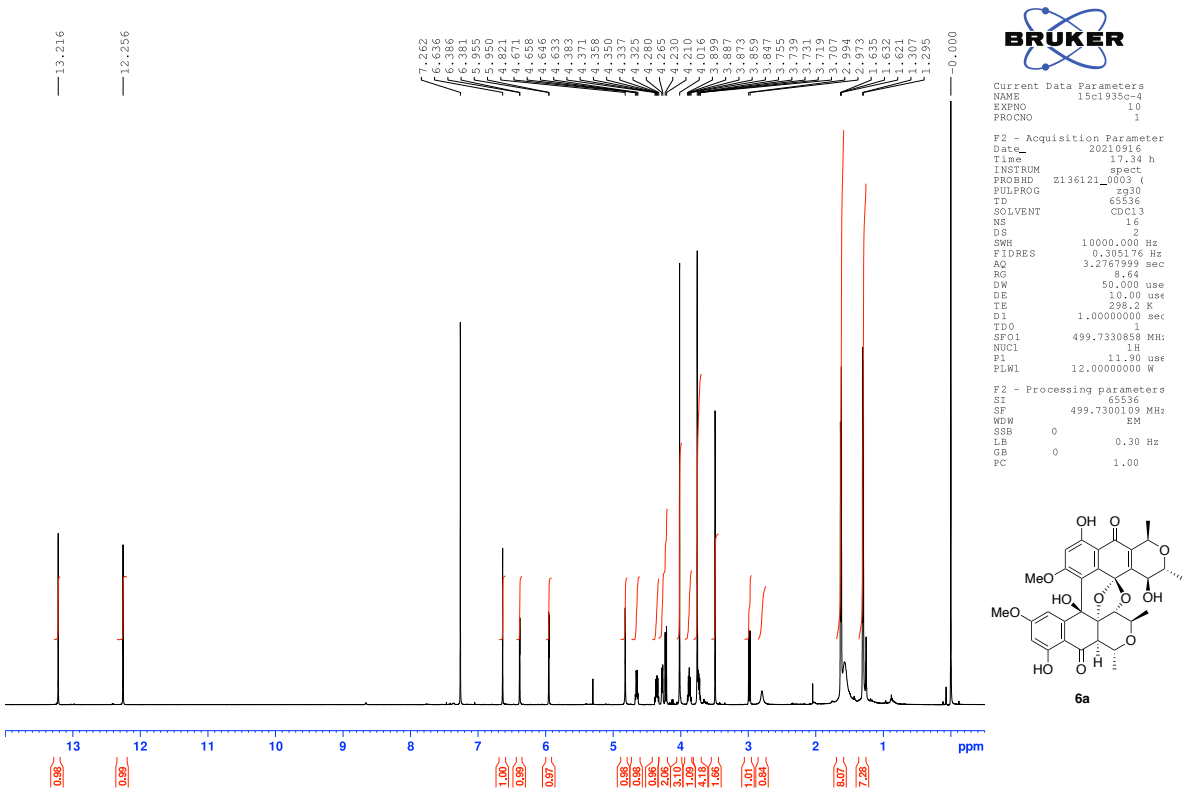


Figure S36. ^{1}H NMR spectrum of 7-*O*, 7'-*O*-dimethyl uroleuconaphin B_{2a} (**6a**) (500 MHz, $CDCl_3$)

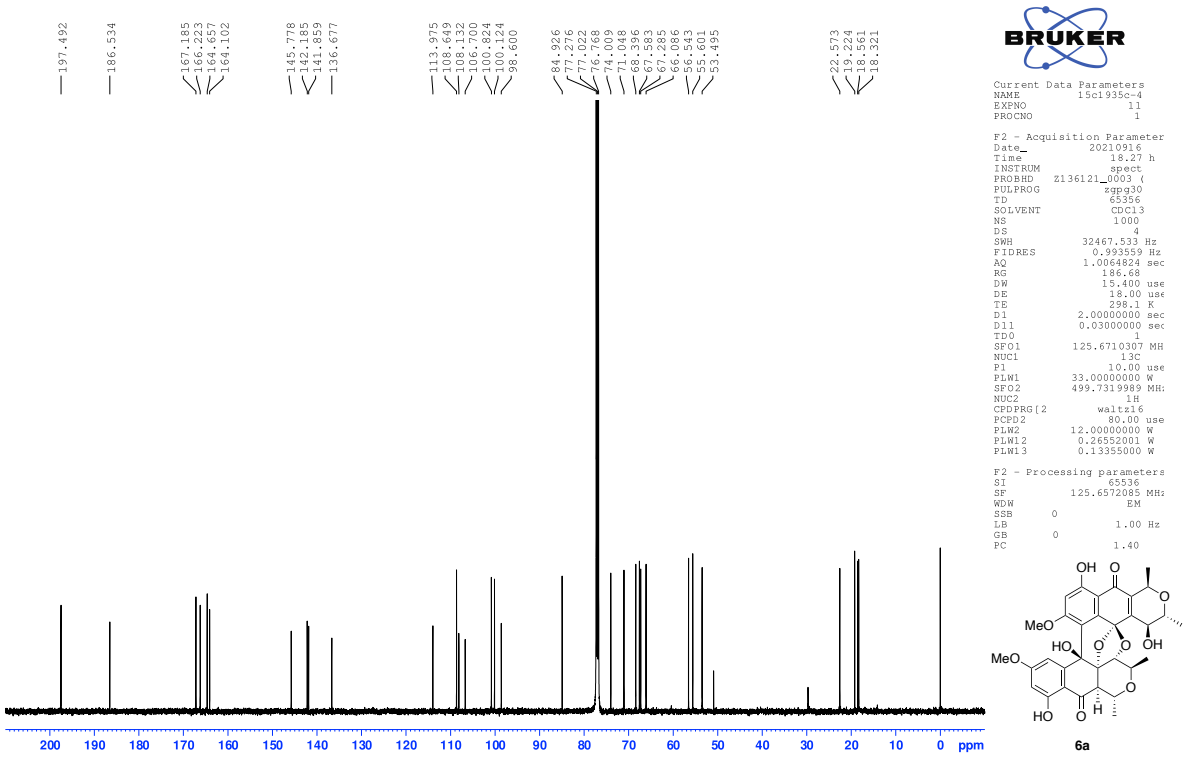


Figure S37. ^{13}C NMR spectrum of 7-*O*, 7'-*O*-dimethyl uroleuconaphin B_{2a} (**6a**) (125 MHz, $CDCl_3$)

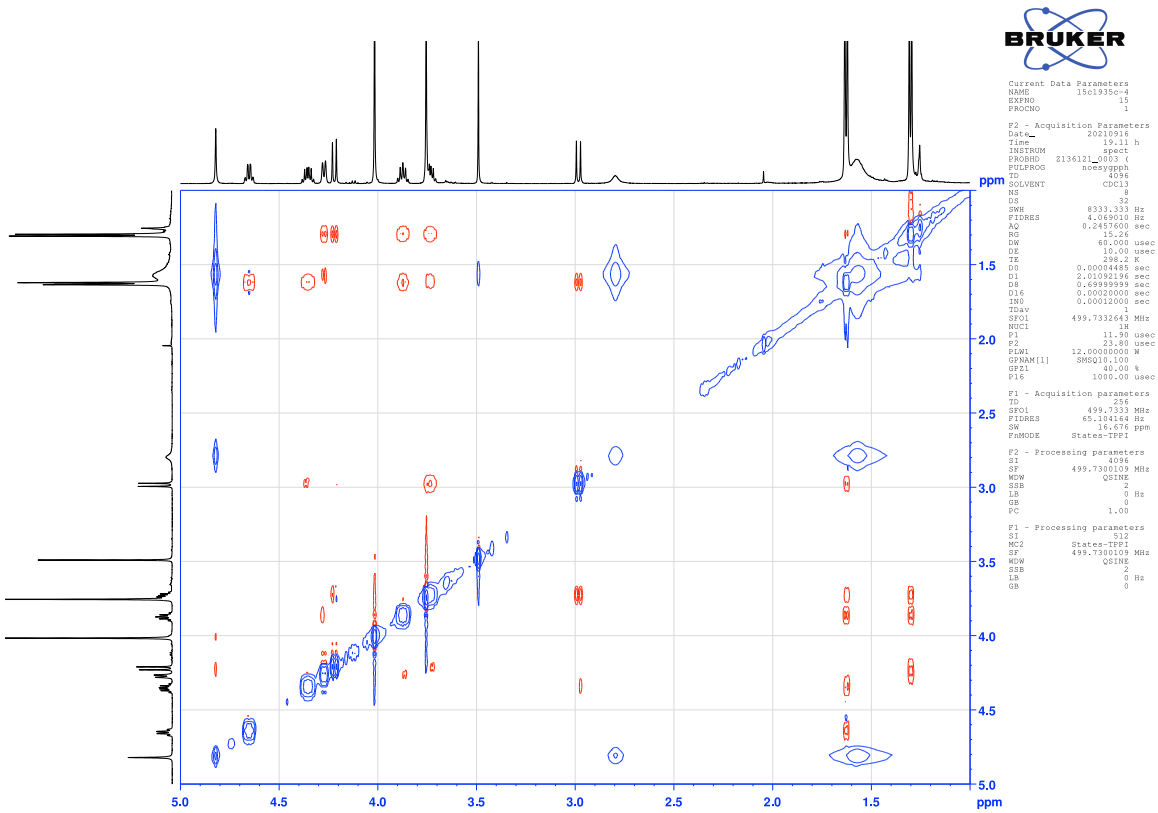


Figure S38. NOESY spectrum of 7-*O*, 7'-*O*-dimethyl uroleuconaphin B_{2a} (**6a**) ($CDCl_3$)

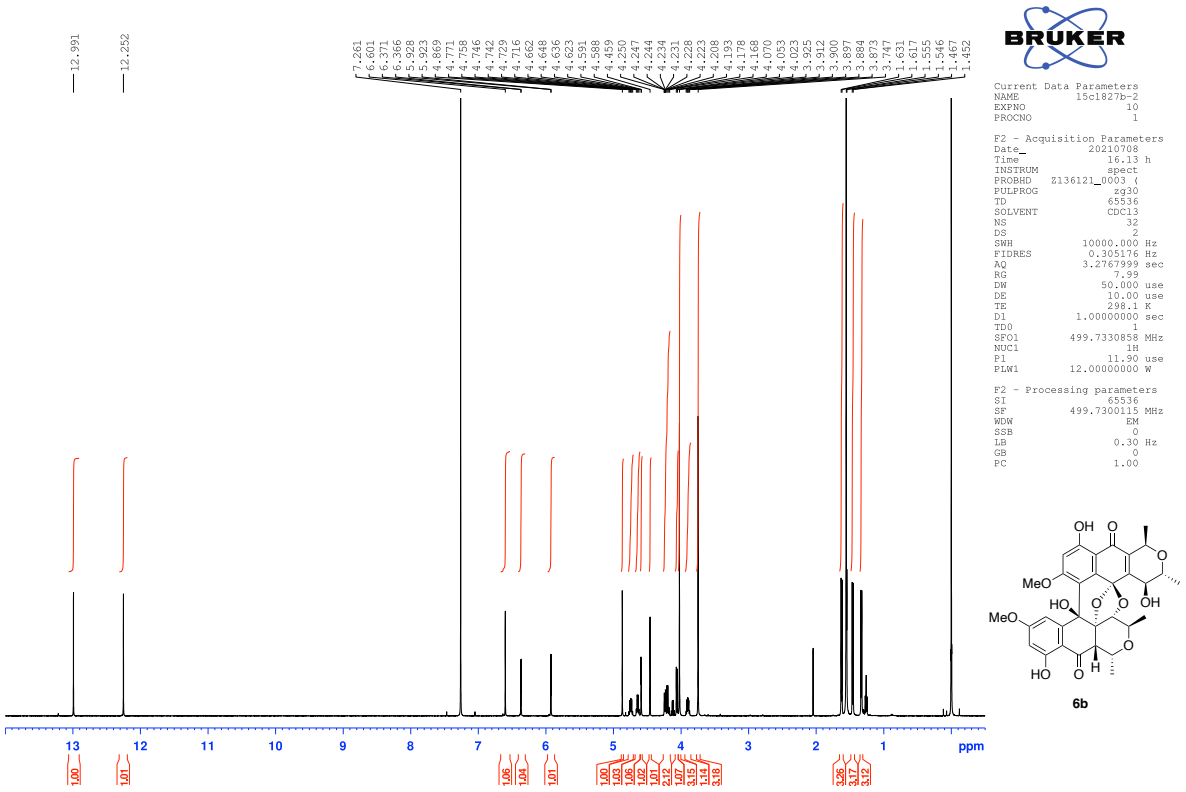


Figure S39. ^{1}H NMR spectrum of 7-*O*, 7'-*O*-dimethyl uroleuconaphin B_{2b} (**6b**) (500 MHz, $CDCl_3$)

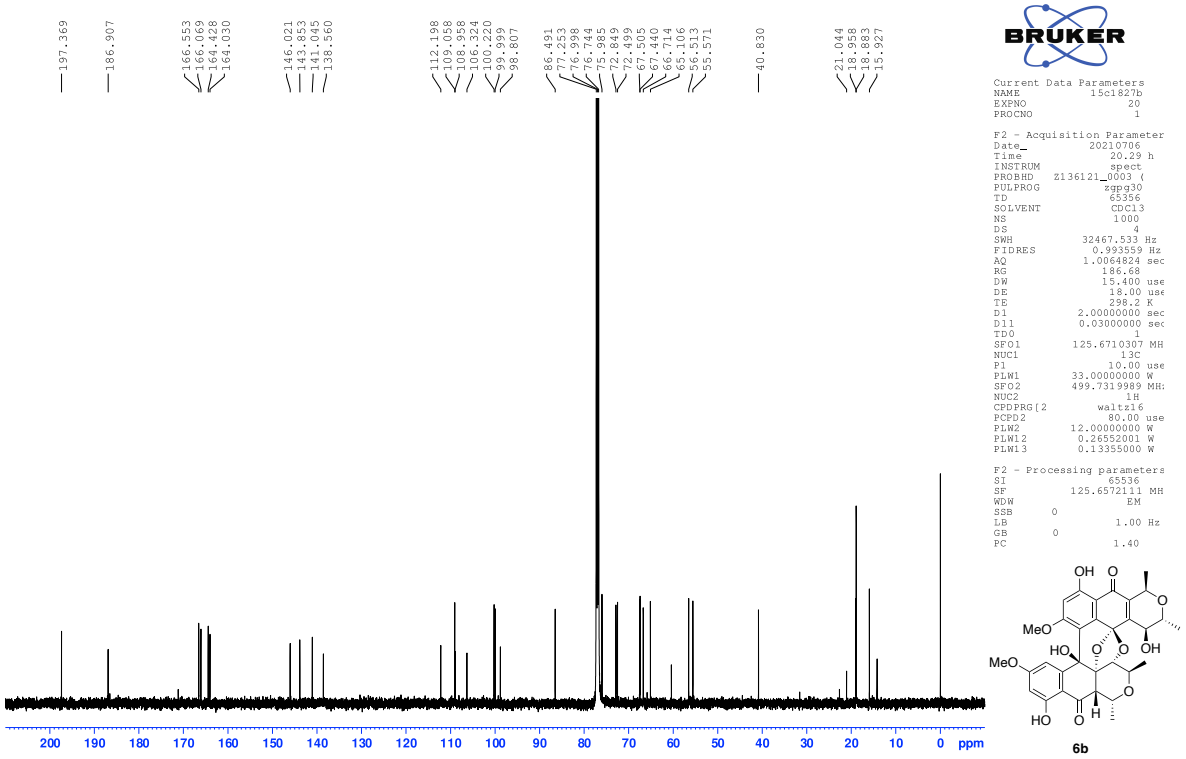


Figure S40. ^{13}C NMR spectrum of 7-*O*, 7'-*O*-dimethyl uroleuconaphin B_{2b} (**6b**) (125 MHz, $CDCl_3$)

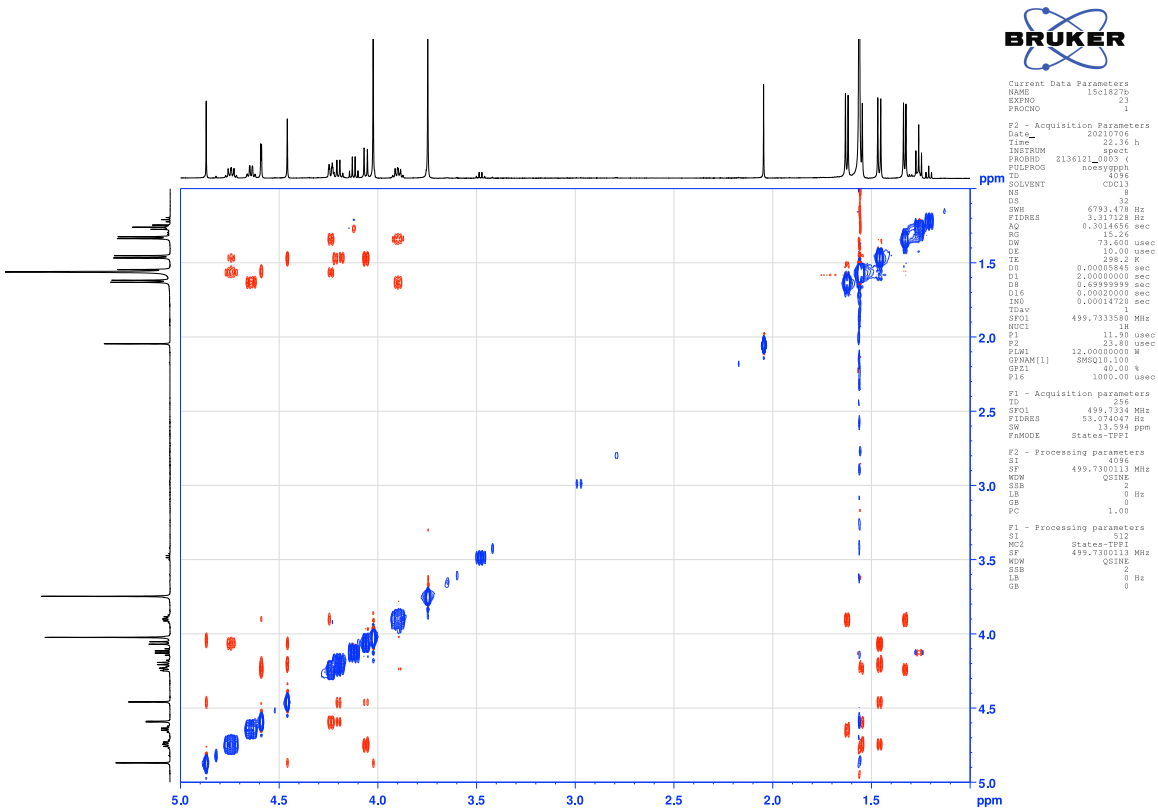


Figure S41. NOESY spectrum of 7-*O*, 7'-*O*-dimethyl uroleuconaphin B_{2b} (**6b**) ($CDCl_3$)

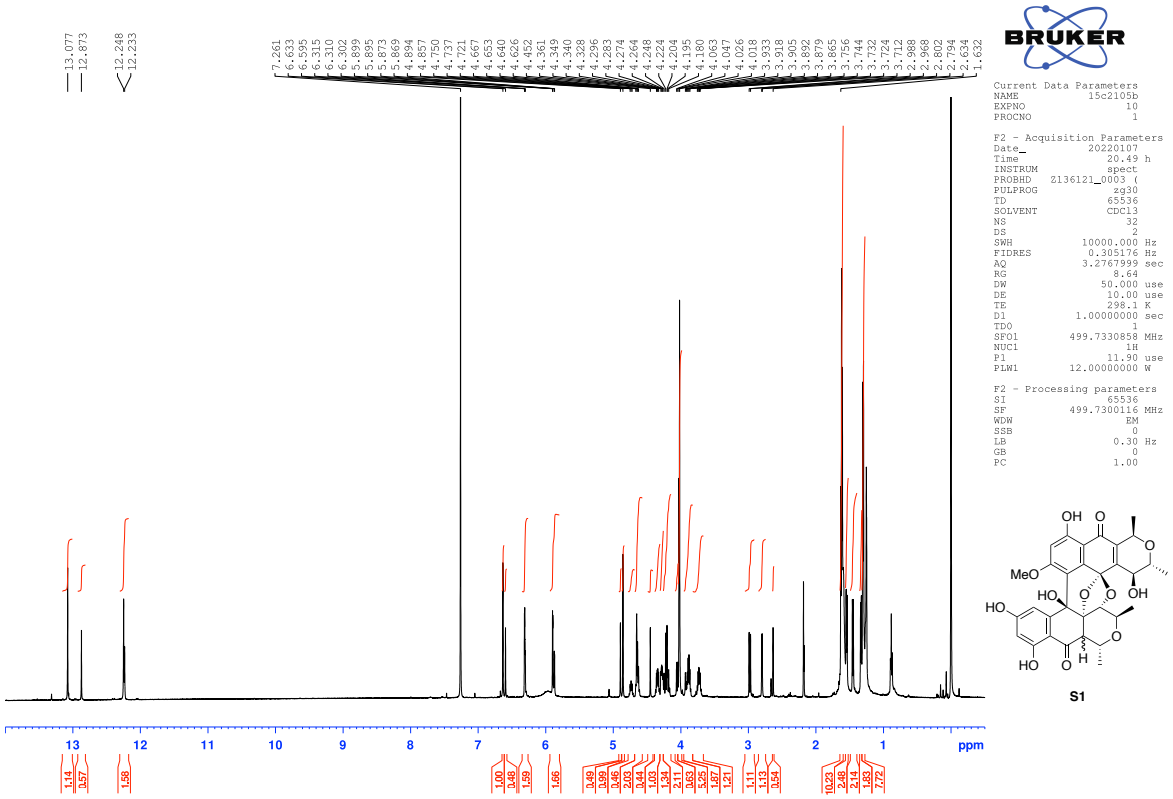


Figure S42. ^{1}H NMR spectrum of **S1** (500 MHz, $CDCl_3$)

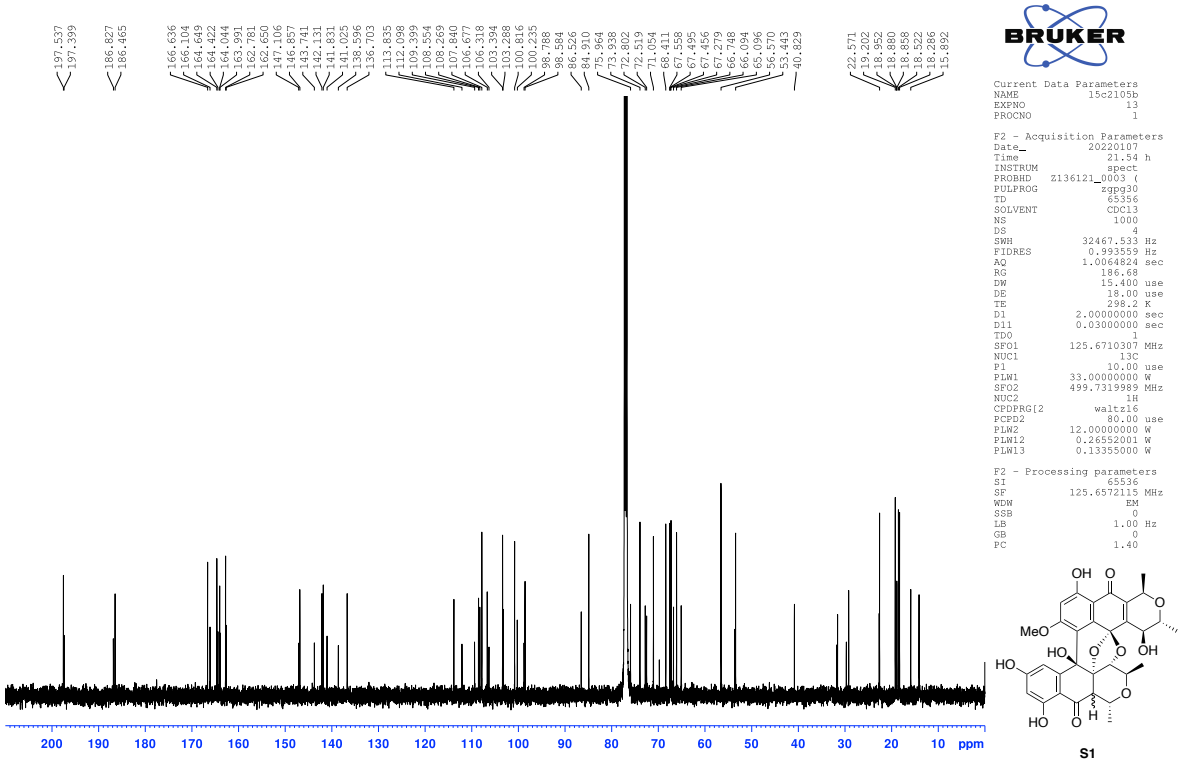


Figure S43. ^{13}C NMR spectrum of **S1** (125 MHz, $CDCl_3$)

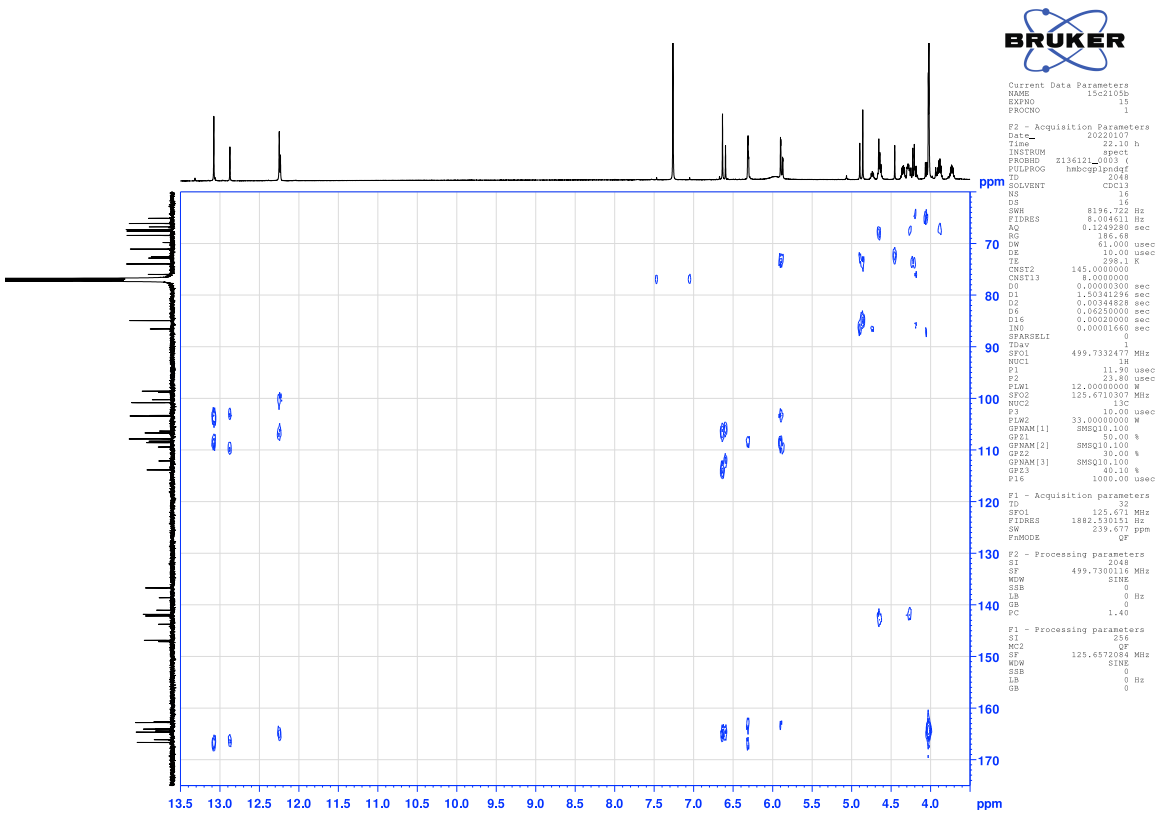


Figure S44. HMBC spectrum of **S1** ($CDCl_3$)

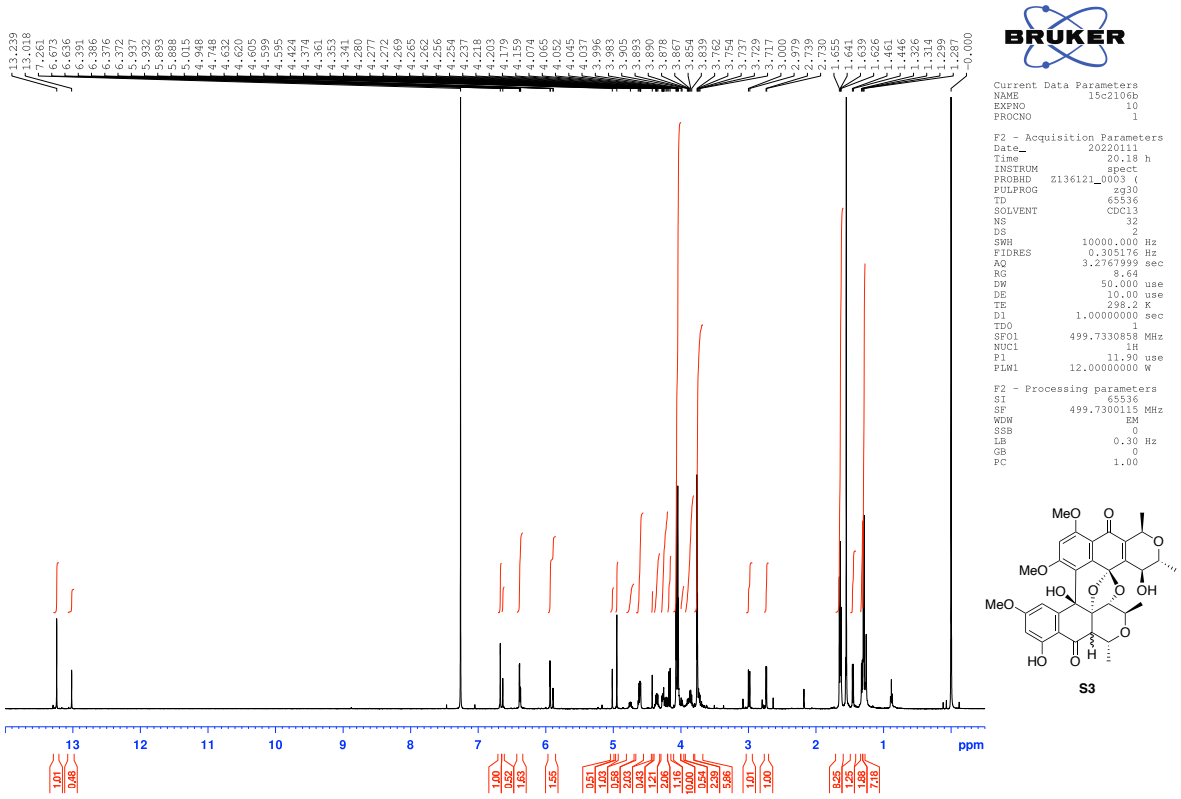


Figure S45. ^{1}H NMR spectrum of **S3** (500 MHz, $CDCl_3$)

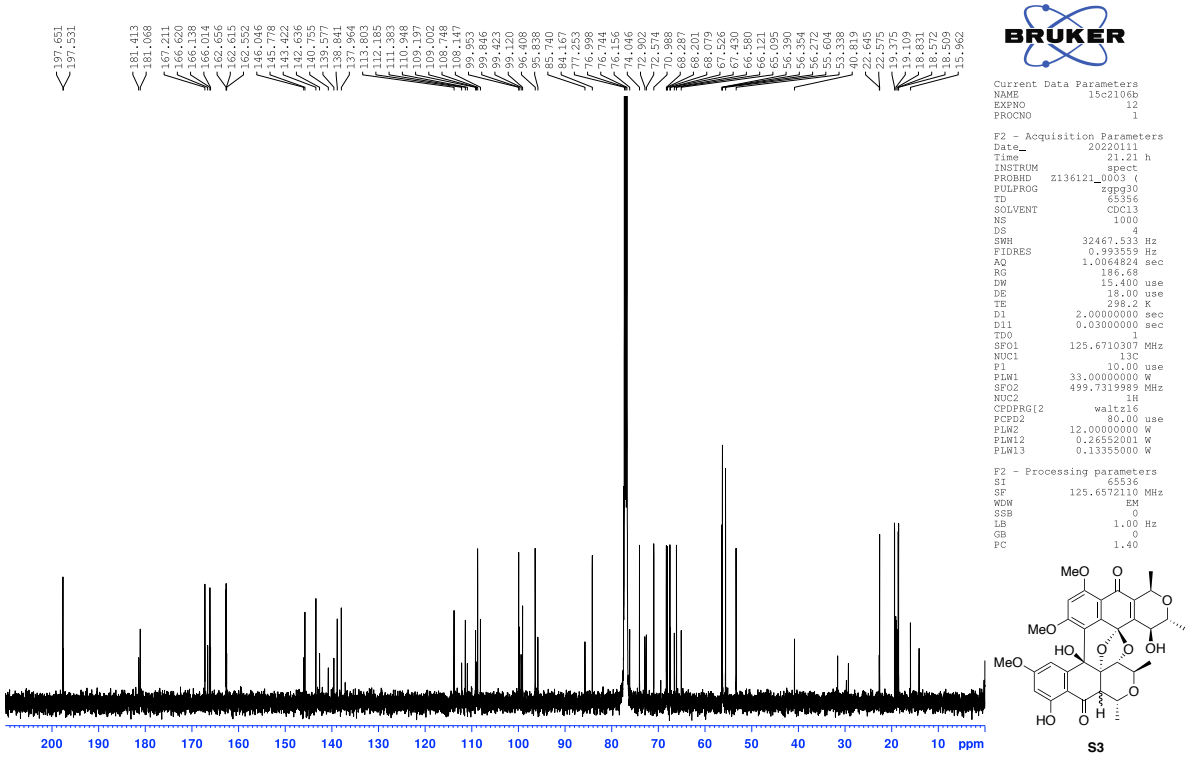


Figure S46. ^{13}C NMR spectrum of **S3** (125 MHz, $CDCl_3$)

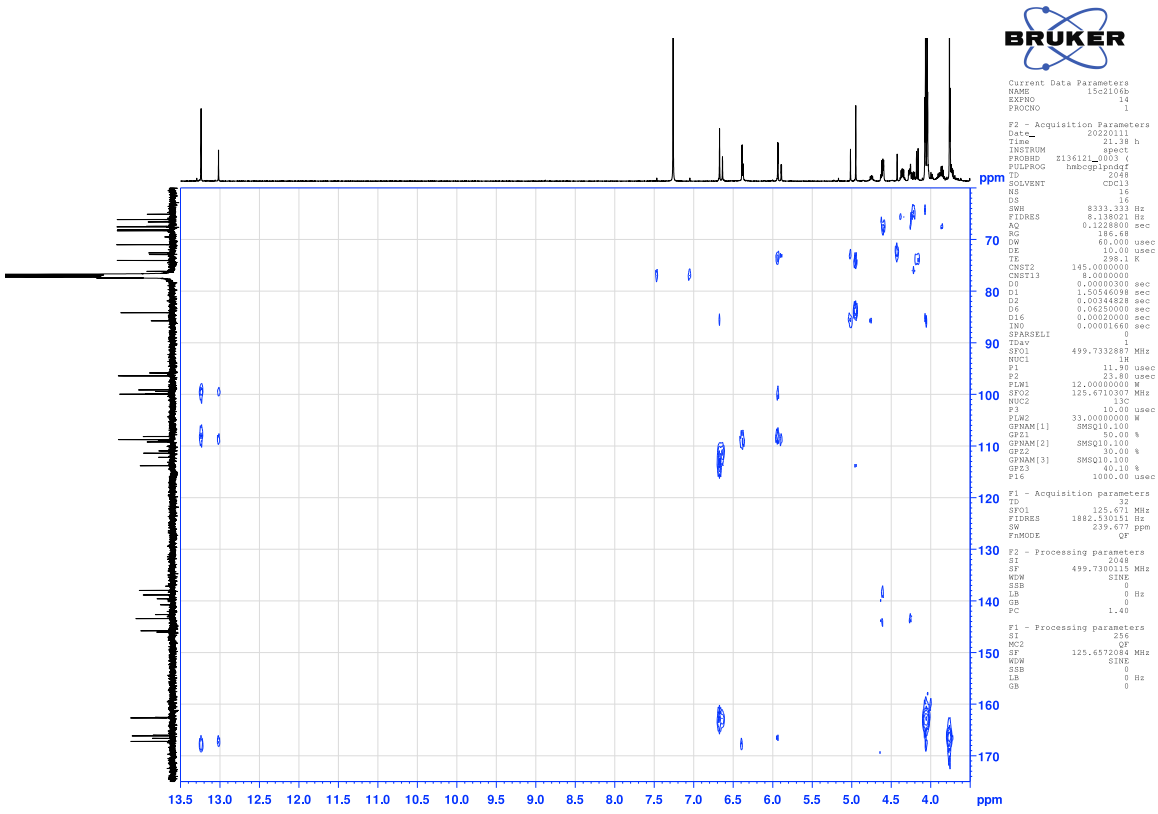


Figure S47. HMBC spectrum of **S3** ($CDCl_3$)

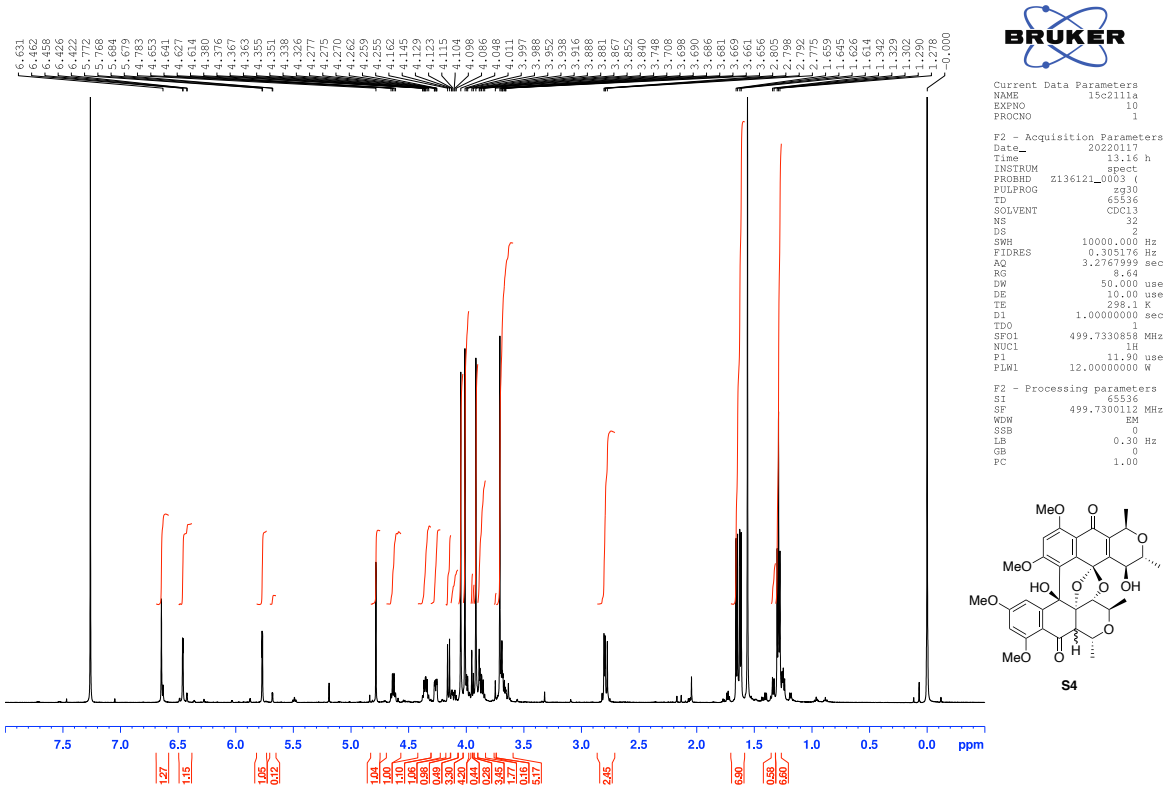


Figure S48. ^{1}H NMR spectrum of **S4** (500 MHz, $CDCl_3$)

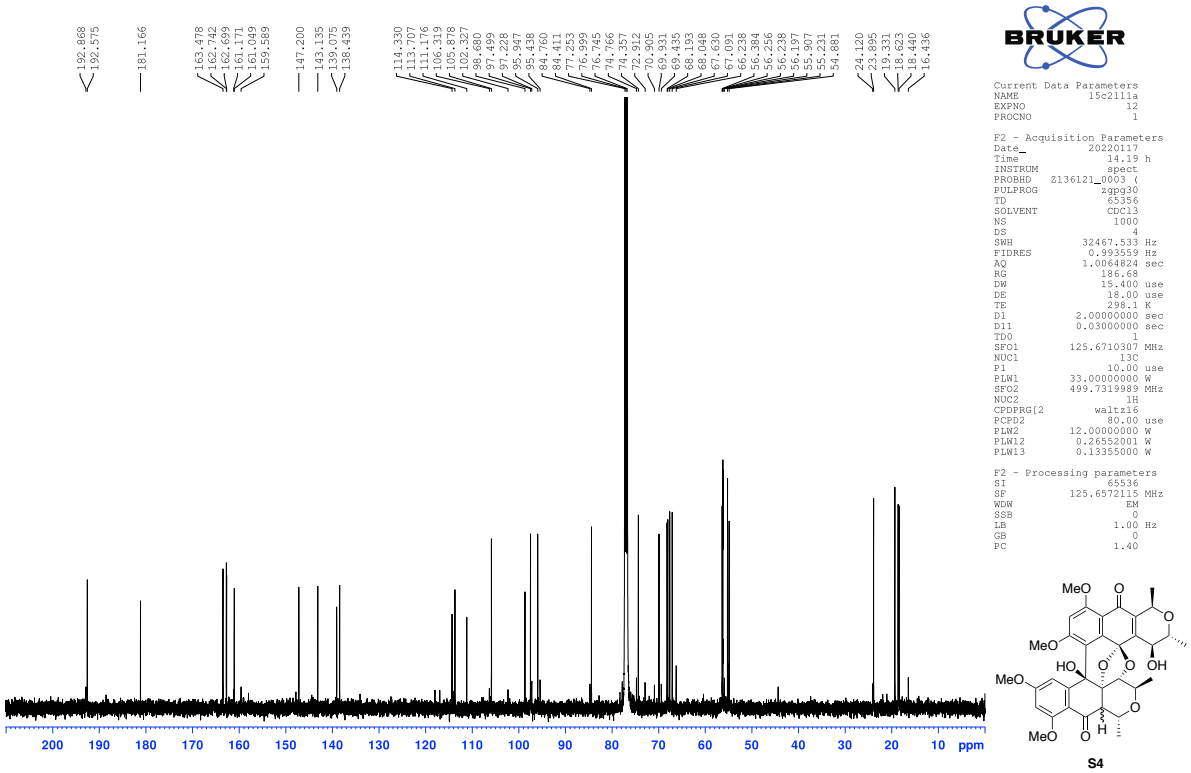


Figure S49. ^{13}C NMR spectrum of **S4** (125 MHz, $CDCl_3$)

19. Calculations

DFT calculations were performed with the Gaussian 16 program.[4] Geometry optimizations were carried out at the RB3LYP level of density functional theory with the 6-311G(d) basis set for compounds **4a** and **4b**.

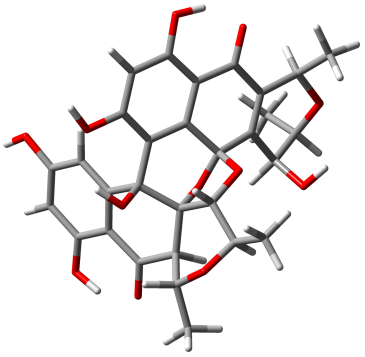


Table S8. Cartesian coordinates of the optimized structure for uroleuconaphin B_{2a} (**4a**)

Atom	X	Y	Z
C	4.0099203	2.1265355	2.3564977
C	4.0383345	0.7614064	2.0628434
C	3.1941062	0.2229061	1.046209
C	2.3437226	1.1061059	0.3267699
C	2.3196216	2.4490704	0.6423885
C	3.1512221	2.9558355	1.6550003
H	4.6630795	2.498914	3.1396164
H	1.6761468	3.1491822	0.1319707
C	1.5353493	0.5542062	-0.8604271
O	2.3902376	0.4204301	-1.9951189
H	2.6229005	1.3064429	-2.3025866
C	1.055622	-0.8828101	-0.5471132
C	0.2856404	1.3989912	-1.1691946
C	0.3296254	2.5961554	-1.914861
C	-0.9655726	0.9871833	-0.7268838
C	-0.8040234	3.3621691	-2.1460394
C	-2.1307046	1.7448172	-0.9170898
C	-2.0407116	2.9648341	-1.6330476
H	-0.7537088	4.2870904	-2.7125811

O	0.0953943	-0.7611315	0.5249594
C	3.1738516	-1.2173428	0.8429184
O	3.9414604	-1.9704314	1.4604961
C	2.1545273	-1.84792	-0.0943038
H	1.6459769	-2.5968079	0.5219389
C	2.8444232	-2.6110755	-1.2729266
H	3.571461	-1.9412012	-1.7372754
C	0.196835	-1.4593184	-1.7124822
H	0.3608029	-0.8800613	-2.6240129
O	1.9186781	-2.9356105	-2.3250409
O	-1.1561441	-1.3099091	-1.2625758
C	0.5334058	-2.9178056	-1.9940359
H	0.3237502	-3.5208101	-1.1003995
C	3.5250634	-3.9011578	-0.8254801
H	4.3060626	-3.7148983	-0.0898173
H	2.7960902	-4.5862798	-0.3816925
H	3.9611775	-4.3905963	-1.6990009
C	-3.3992247	1.3159293	-0.3285306
O	-4.4257615	2.0007399	-0.4577004
C	-3.4251099	0.0878841	0.5141902
C	-2.3130762	-0.6454176	0.7035157
C	-1.0935133	-0.41148	-0.1478499
C	-0.2322856	-3.4891325	-3.1725311
H	-1.3066758	-3.4405324	-2.9843043
H	-0.0063892	-2.9260355	-4.0818762
H	0.0502189	-4.5308584	-3.3371776
C	-4.7259974	-0.2502128	1.2237467
H	-5.0018805	0.6000871	1.8634064
O	-4.610374	-1.4297423	2.0241805
C	-2.2676761	-1.7766214	1.7118698
H	-1.2886625	-1.7821631	2.1927519
C	-3.3799462	-1.5831324	2.7449359

H	-3.5019762	-2.5353569	3.2665673
C	-5.8806928	-0.5336873	0.2616606
H	-6.7396699	-0.8762936	0.8419209
H	-6.1556617	0.3592948	-0.2946745
H	-5.6064081	-1.3252801	-0.4403051
C	-3.1269511	-0.4792662	3.7690874
H	-3.9982651	-0.3677633	4.4184009
H	-2.2704664	-0.7391174	4.3970713
H	-2.9169456	0.488756	3.3086965
O	-2.3750458	-3.0510528	1.0809542
H	-3.2608274	-3.0999998	0.6973092
O	-3.0948006	3.7566444	-1.847532
H	-3.8732733	3.3366622	-1.4145679
O	4.8723906	0.004818	2.7795394
H	4.7708111	-0.9261302	2.4642901
O	3.0653161	4.2891092	1.8942216
H	3.6659837	4.53527	2.6078502
O	1.5490585	2.9909189	-2.3955451
H	1.4683627	3.8143256	-2.8912441

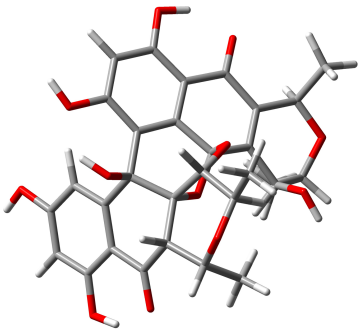


Table S9. Cartesian coordinates of the optimized structure for uroleuconaphin B_{2b} (**4b**)

Atom	X	Y	Z
C	4.252631	1.4196759	2.4036661
C	4.0567861	0.0994939	1.995017
C	3.2045681	-0.1964388	0.8931617
C	2.5400054	0.8687205	0.2248438

C	2.7387849	2.1663606	0.6555805
C	3.5971941	2.4389238	1.733062
H	4.9124049	1.6094146	3.2446432
H	2.2500586	3.0094508	0.1931106
O	4.7002736	-0.8528129	2.6778186
H	4.4636537	-1.7211998	2.2736836
O	3.735681	3.7456722	2.0758821
H	4.3328722	3.8269934	2.8290628
C	1.6389776	0.585791	-1.0079595
C	0.4777249	1.5865729	-1.0904946
C	0.5909696	2.8743704	-1.6540872
C	-0.769769	1.2307441	-0.5995101
C	-0.4698347	3.7688919	-1.6676062
C	-1.8621874	2.1089838	-0.5774646
C	-1.6999292	3.4116941	-1.112337
H	-0.3654072	4.7608293	-2.0966785
C	1.0513019	-0.8578478	-0.8957868
C	0.0822694	-1.2262417	-2.0549056
H	0.327502	-0.6401266	-2.943357
C	2.2038271	-1.8497497	-0.7475942
H	2.8669458	-1.5848945	-1.5823881
C	3.0317162	-1.5832794	0.4868881
O	3.5846332	-2.5233572	1.0741014
O	-2.6818592	4.3169306	-1.1200642
H	-3.4695324	3.9026486	-0.6981567
O	1.8047619	3.227892	-2.18362
H	1.7669284	4.1167265	-2.5560743
O	2.4247527	0.5754293	-2.1984003
H	2.6958234	1.4827541	-2.3904431
O	0.1628294	-0.8395706	0.2395442
O	-1.2152883	-0.8440719	-1.5586078
C	1.8434044	-3.3261192	-0.9962415

H	2.7845466	-3.8664952	-1.1101669
C	1.0276462	-4.0310389	0.0880146
H	0.0904439	-3.5237769	0.3145572
H	0.7993756	-5.0473397	-0.244442
H	1.6180734	-4.0933503	1.0024882
C	-0.0135517	-2.7353004	-2.3880761
H	-0.7176146	-3.1601019	-1.6666481
C	-0.5396994	-2.9629037	-3.7946886
H	0.1612484	-2.5666001	-4.5346146
H	-0.6659513	-4.0310799	-3.9821173
H	-1.5059588	-2.4698227	-3.9238168
O	1.243532	-3.3985381	-2.2941056
C	-3.1342892	1.69748	0.0134011
O	-4.0959394	2.4785773	0.0669625
C	-3.2372681	0.3458834	0.6329834
C	-2.2010233	-0.5080433	0.6006142
C	-1.005633	-0.2332074	-0.2765707
C	-4.5249749	0.0236	1.3678018
H	-4.7067683	0.8236675	2.0997015
C	-5.7270627	-0.0663745	0.4245744
H	-6.6006862	-0.3726413	1.0035777
H	-5.9305114	0.8922443	-0.0483495
H	-5.5405535	-0.824238	-0.3390914
C	-2.2055407	-1.7697318	1.4259534
H	-1.2037072	-1.8896759	1.8562105
C	-3.2308358	-1.647196	2.5627001
H	-3.4290452	-2.6555891	2.9424679
O	-4.4863536	-1.2351098	2.0392963
C	-2.7487776	-0.779157	3.7279564
H	-3.5410802	-0.6955345	4.4748034
H	-1.8748232	-1.2262436	4.2099931
H	-2.4724083	0.2293122	3.4115692

O	-2.4877565	-2.8667765	0.5532081
H	-2.3645447	-3.6867872	1.0469756

20. Reference

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3. M. Horikawa, M. Tanaka, H. Kaku, T. Nishii, T. Tsunoda, *Tetrahedron* 2008, **64**, 5515.
4. Gaussian 16, Revision C.01, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, G. A. Petersson, H. Nakatsuji, X. Li, M. Caricato, A. V. Marenich, J. Bloino, B. G. Janesko, R. Gomperts, B. Mennucci, H. P. Hratchian, J. V. Ortiz, A. F. Izmaylov, J. L. Sonnenberg, D. Williams-Young, F. Ding, F. Lipparini, F. Egidi, J. Goings, B. Peng, A. Petrone, T. Henderson, D. Ranasinghe, V. G. Zakrzewski, J. Gao, N. Rega, G. Zheng, W. Liang, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, K. Throssell, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. J. Bearpark, J. J. Heyd, E. N. Brothers, K. N. Kudin, V. N. Staroverov, T. A. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. P. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, J. M. Millam, M. Klene, C. Adamo, R. Cammi, J. W. Ochterski, R. L. Martin, K. Morokuma, O. Farkas, J. B. Foresman and D. J. Fox, Gaussian, Inc., Wallingford CT, 2016.