Electronic Supplementary Material (ESI) for New Journal of Chemistry.

Supplementary Information

Silica gel-mediated chemical degradation of dimeric pyranonaphthoquinones into their monomeric units

Chiharu Ozakai, Kei Kitamura,* and Hiroto Kaku*

Faculty of Pharmaceutical Sciences, Tokushima Bunri University, Yamashiro-cho, Tokushima, 770-8514

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1. General

Infrared (IR) spectra were measured on a JASCO FT/IR-4200 spectrophotometer. 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-700 (EI/CI) or a JEOL JMS-S3000 Spiral TOF mass spectrometers (MALDI). For column chromatography, silica gel 60 N (Spherical, 63–210 μm, Kanto Chemical Co., Inc.) was used. For thin-layer chromatography (TLC) analysis, Merck precoated silica gel plates 60 F_{254} were used. Preparative TLC (PTLC) was performed with Merck precoated silica gel plates ($60F_{254}$). ^1H 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 ($CDCl_3$: δ_H 7.26; methanol-d_4: δ_H 3.31). ^{13}C NMR spectra were recorded with a Bruker AVANCE-III (125 MHz) spectrometer; chemical shifts were referenced to the residual solvent signal ($CDCl_3$: δ_C 77.0; methanol-d_4: δ_C 49.3).

2. Screening and optimization

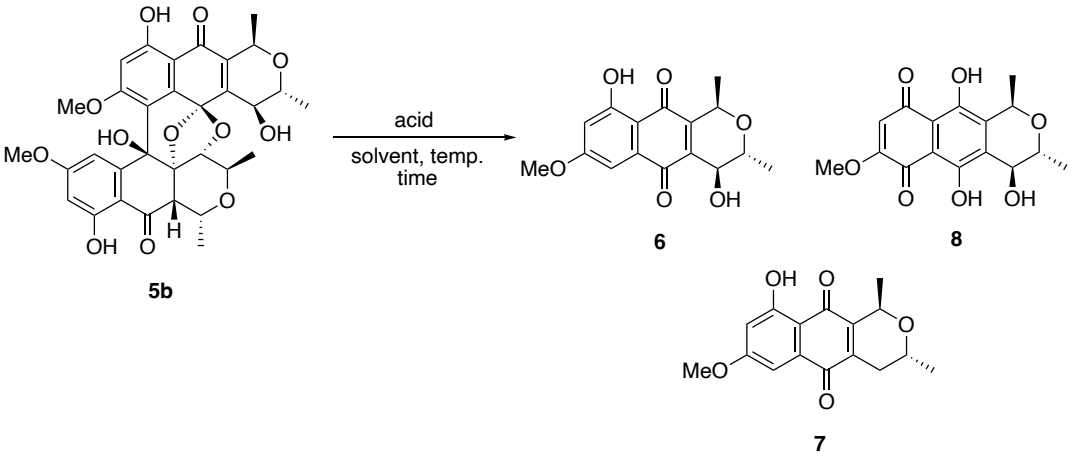


Table S1. Screening of acid.

entry	acid (equiv)	solvent	temp. (°C)	time (h)	result
1	alumina (pH 4.5)[a]	MeOH	50	6	decomposition
2	montmorillonite K10[a]	MeOH	50	6	decomposition
3	amberlite IR-120B[a]	MeOH	reflux	24	decomposition
4	AcOH[b]	—	reflux	24	decomposition
5	$TsOH \cdot H_2O$ (45)	MeOH	reflux	15	decomposition
6	H_2SO_4 (120)	MeOH	reflux	8	decomposition
7	$TsOH \cdot H_2O$ (45)	toluene	80	15	decomposition
8	H_2SO_4 (120)	toluene	80	8	decomposition

[a] 54 g/mmol of solid acid was used. [b] AcOH was used as a solvent (2.0 mM).

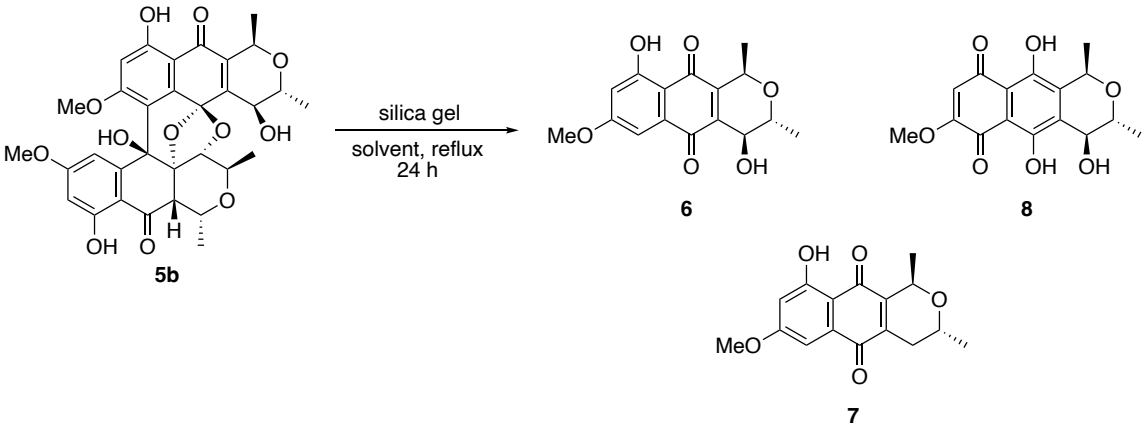


Table S2. Screening of solvent[a].

entry	silica gel	solvent	yield (%)			recovery (%) (**5a**:**5b**)
			6	**7**	**8**	
1	silica gel	MeOH	21	21	28	0
2	silica gel	—	0	0	0	56 (1.1:1)
3	—	MeOH	0	0	4	71 (1:2.0)
4	silica gel	toluene	0	0	0	83 (1:2.6)
5	silica gel	chlorobenzene	0	0	0	67 (1:1.5)
6	silica gel	EtOAc	0	0	0	88 (1:6.1)
7	silica gel	*n*-PrOH	9	11	6	35 (2.5:1)
8	silica gel	MeOH/H_2O = 1/1	9	6	46	0

[a] The reaction was performed using silica gel (54 g/mmol) in solvent (2.0 mM).

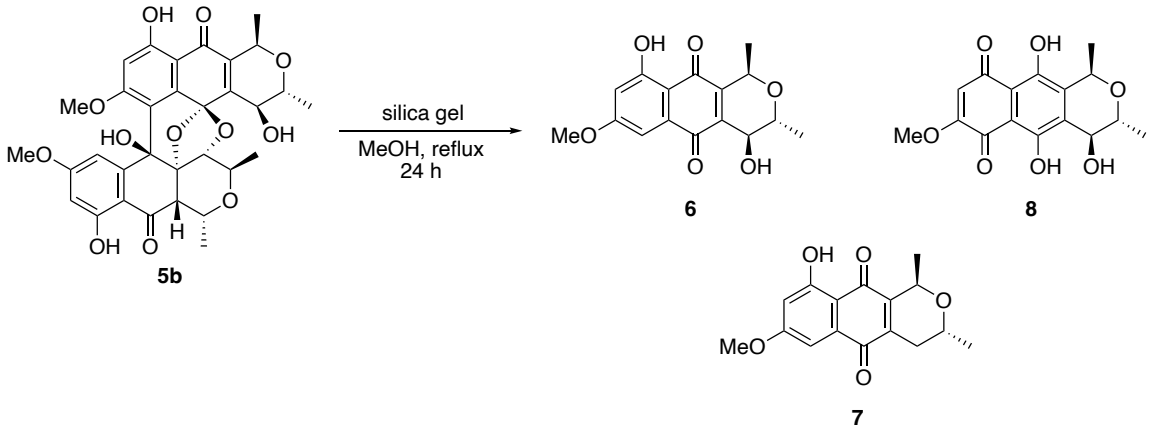


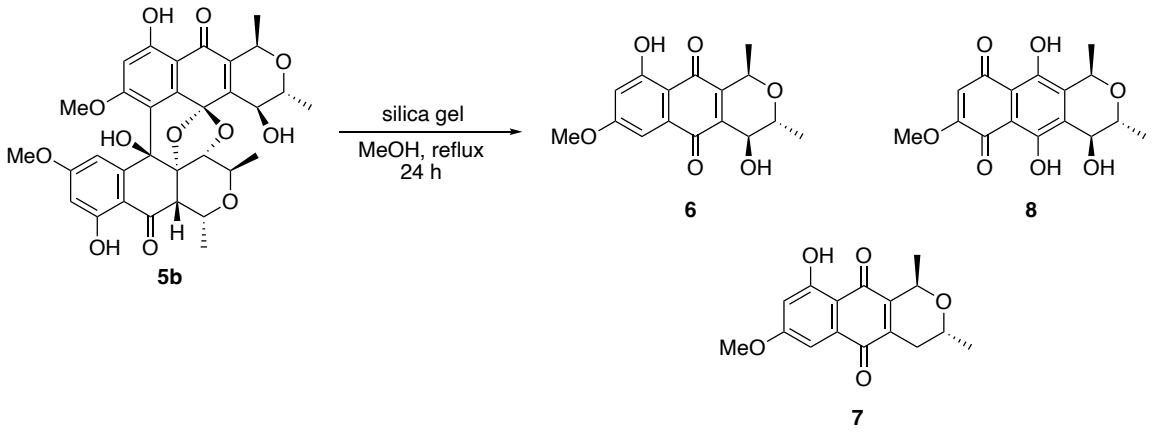
Table S3. Screening of silica gel[a].

entry	silica gel	manufacturer	yield (%)			recovery (%) (**5a**:**5b**)
			6	**7**	**8**	
1	silica gel (pH 7, 63–210 μm)	Kanto Chemical Co., Inc.	21	21	28	0
2	silica gel (pH 7, 40–50 μm)	Kanto Chemical Co., Inc.	12	14	29	0
3	silica gel (pH 7, 64–210 μm)	FUJIFILM Wako Pure Chemical Co., Inc.	22	15	24	0
4	silica gel (pH 6, 63–210 μm)	Kanto Chemical Co., Inc.	0	0	0	29 (1:1.5)
5	oxalated silica gel[1]	—	0	2	0	37 (1:1.6)

[a] The reaction was performed using silica gel (54 g/mmol) in methanol (2.0 mM).

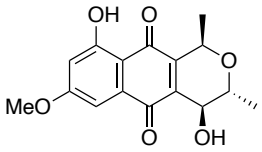
3. Experimental procedure

3-1. Silica gel-induced degradation of **5b**



5b **6** **8** **7**

To a solution of compound **5b** (43.2 mg, 71.0 μmol) in MeOH (36 mL) was added silica gel (3.84 g, dried with a heat gun under vacuum). After stirring for 24 h under reflux, the suspension was filtered through a Celite® pad, and washed with EtOAc. The filtrate was concentrated and purified by silica gel column chromatography (*n*-hexane/EtOAc = 5/1 → 3/1 → 1/1) to afford pyranonaphthoquinones **6** (9.1 mg, 21%) as yellow solids, **7** (8.5 mg, 21%) as yellow solids, and **8** (12.7 mg, 28%) as red solids.



6

R_f 0.61 (*n*-hexane/EtOAc = 1/1);

$[\alpha]_D^{21}$ –34.2 (*c* 0.50, $CHCl_3$);

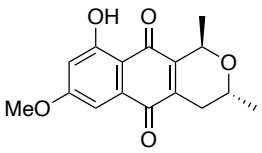
IR (ATR) 3511, 2981, 2920, 2855, 1635, 1610, 1568, 1302, 1263, 1206, 1145, 1107, 1081, 1062, 1044, 985, 847, 787, 752, 721, 620 cm^{-1};

^1H NMR ($CDCl_3$, 500 MHz) δ 1.41 (d, 3H, *J* = 6.2 Hz), 1.62 (d, 3H, *J* = 6.8 Hz), 3.82 (d, 1H, *J* = 2.2 Hz), 3.87 (dq, 1H, *J* = 8.0 Hz, 6.2 Hz), 3.91 (s, 3H), 4.44 (brd, 1H, *J* = 8.0 Hz), 4.92 (brq, 1H, *J* = 6.8 Hz), 6.65 (d, 1H, *J* = 2.5 Hz), 7.17 (d, 1H, *J* = 2.5 Hz), 12.16 (s, 1H);

^{13}C NMR ($CDCl_3$, 125 MHz) δ 18.6, 19.2, 56.1, 67.16, 67.17, 67.8, 106.4, 108.5, 109.4, 133.2, 141.2, 148.5, 164.6, 166.2, 185.4, 186.6;

HRMS (MALDI) calcd for $C_{16}H_{16}O_6$ $[M]^-$ *m/z* 304.0941; found *m/z* 304.0950;

Mp 128–129 °C.



7

R_f 0.81 (*n*-hexane/EtOAc = 1/1);

$[\alpha]_D^{20}$ +53.2 (*c* 0.50, $CHCl_3$);

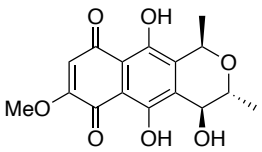
IR (ATR) 3074, 2975, 2930, 2896, 1645, 1608, 1383, 1326, 1293, 1266, 1252, 1203, 1147, 1140, 1100, 1054, 991, 842, 821, 789, 741, 614 cm^{-1};

^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.35 (d, 3H, *J* = 6.2 Hz), 1.56 (d, 3H, *J* = 6.9 Hz), 2.22 (ddd, 1H, *J* = 2.1 Hz, 10.2 Hz, 19.3 Hz), 2.72 (dd, 1H, *J* = 3.3 Hz, 19.3 Hz), 3.90 (s, 3H), 4.00 (ddq, 1H, *J* = 3.3 Hz, 10.2 Hz, 6.2 Hz), 5.00 (dq, 1H, *J* = 2.1 Hz, 6.9 Hz), 6.63 (d, 1H, *J* = 2.5 Hz), 7.18 (d, 1H, *J* = 2.5 Hz), 12.27 (s, 1H);

^{13}C NMR ($CDCl_3$, 125 MHz) δ 19.9, 21.5, 29.9, 56.0, 62.5, 67.0, 106.1, 107.8, 109.4, 133.3, 142.0, 146.8, 164.4, 165.9, 183.3, 186.8;

HRMS (MALDI) calcd for $C_{16}H_{16}O_5$ $[M]^-$ *m/z* 288.0992; found *m/z* 288.0993;

Mp 151–152 °C.



8

R_f 0.29 (*n*-hexane/EtOAc = 1/1);

$[\alpha]_D^{21}$ +14.3 (*c* 0.50, $CHCl_3$);

IR (ATR) 3592, 2981, 2919, 2849, 1600, 1568, 1464, 1427, 1371, 1352, 1281, 1249, 1208, 1107, 1070, 1053, 1030, 958, 854, 792, 742, 596 cm^{-1};

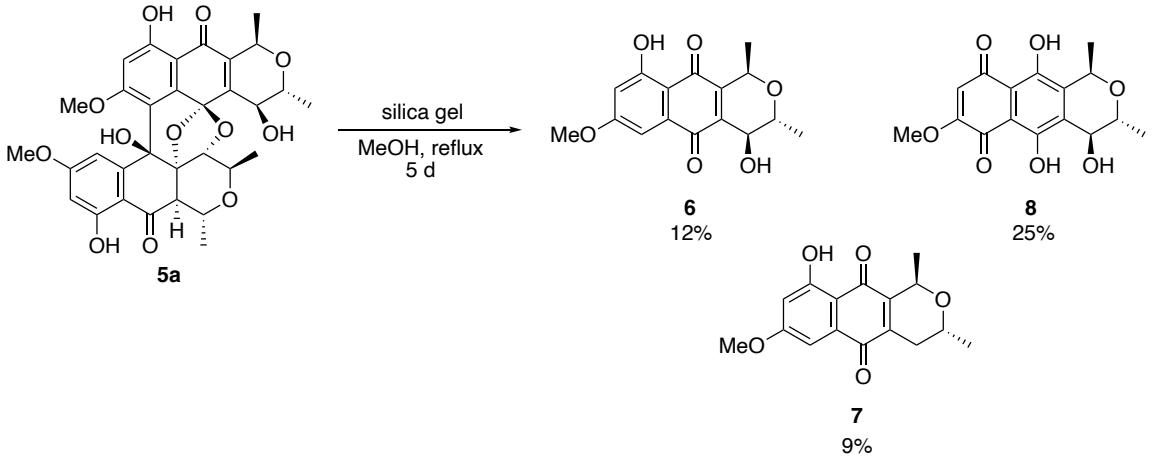
^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.46 (d, 3H, *J* = 6.8 Hz), 1.68 (d, 3H, *J* = 6.8 Hz), 3.80 (d, 1H, *J* = 2.6 Hz), 3.97 (s, 3H), 4.00 (dq, 1H, *J* = 7.9 Hz, 6.8 Hz), 4.61 (dd, 1H, *J* = 2.6 Hz, 7.9 Hz), 5.11 (q, 1H, *J* = 6.8 Hz), 6.22 (s, 1H), 12.99 (s, 1H), 13.05 (s, 1H);

^{13}C NMR ($CDCl_3$, 125 MHz) δ 18.3, 18.8, 56.9, 67.3, 67.7, 67.8, 108.8, 110.1, 110.3, 135.2, 144.0, 156.3, 159.9, 160.7, 179.8, 185.8;

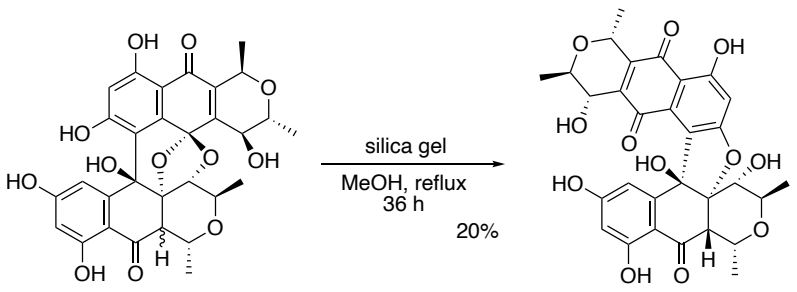
HRMS (EI) calcd for $C_{16}H_{16}O_7$ $[M]^+$ *m/z* 320.0896; found *m/z* 320.0893;

Mp 141–142 °C.

3-2. Silica gel-induced degradation of **5a**



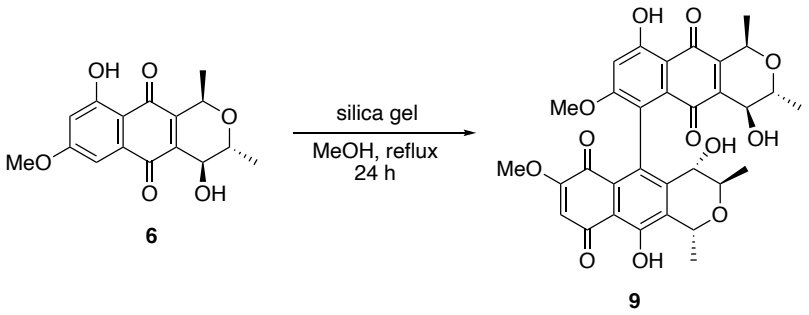
3-3. Silica gel-promoted isomerization of uroleuconaphin B_2 (**S1**) to uroleuconaphin B_1 (**S2**)



uroleuconaphin B_2 (**S1**) uroleuconaphin B_1 (**S2**)

Yellow pigment **S1** (15.3 mg, 26.4 μmol) was dissolved in EtOAc, which was charged with silica gel (418 mg). The mixture was concentrated under reduced pressure, and the residue was suspended in MeOH (15 mL). After stirring for 36 h under reflux, the suspension was filtered through a Celite® pad and was washed with EtOAc. The filtrate was concentrated and purified by silica gel chromatography ($CHCl_3$/MeOH = 40/1 → 10/1) to afford the red pigment **S2** (3.0 mg, 20%).

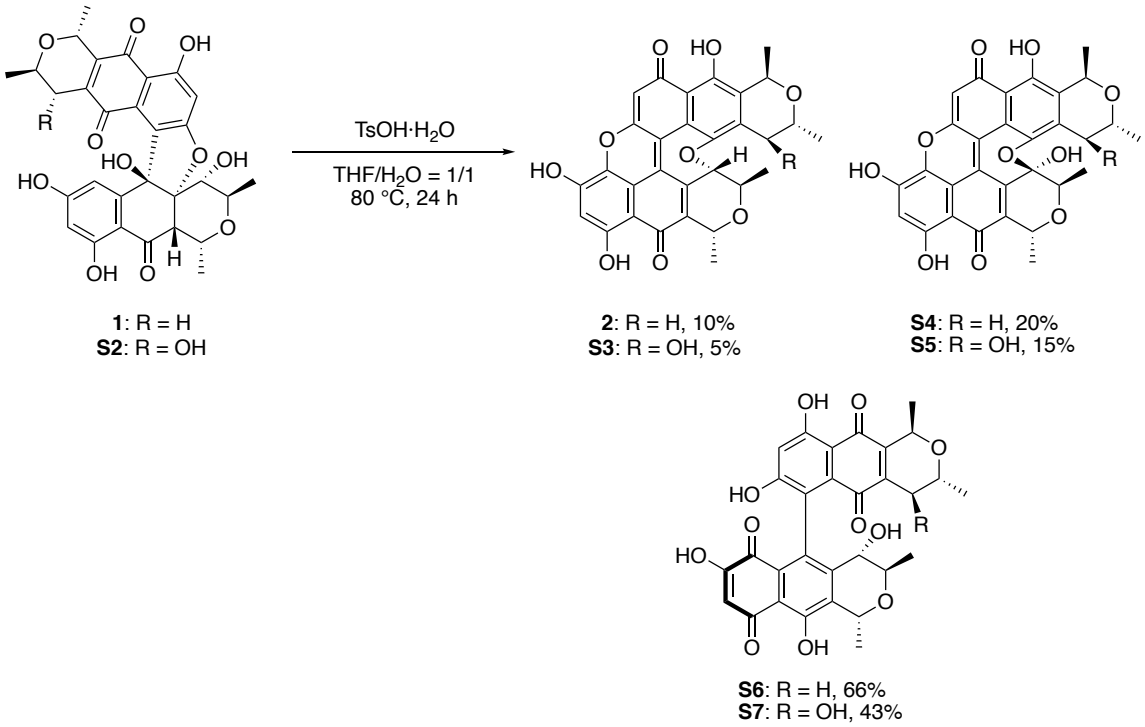
3-4. Silica gel-induced regiospecific dimerization of **6**



6 **9**

To a solution of compound **6** (6.3 mg, 0.021 mmol) in MeOH (5 mL) was added silica gel (1.1 g, dried with a heat gun under vacuum). After stirring for 24 h under reflux, the suspension was filtered through a Celite® pad and was washed with EtOAc. The filtrate was concentrated and purified by silica gel chromatography (*n*-hexane/EtOAc = 5/1 → 2/1 → 1/1) to afford bisquinone **9** (1.5 mg, 24%) as a 1:1 mixture of atropisomers, and starting material **6** (1.7 mg, 27%) was recovered. The atropisomers of **9** were separated by preparative TLC (*n*-hexane/EtOAc = 2/1×2).

The axial chirality of each diastereomer was determined as follows: We previously reported the strong acid-promoted conversion of uroleuconaphin A_1 (**1**)[2] to viridaphins **2** and **S4**, along with **S6** (Scheme S1). The absolute stereochemistry of the axis in **S6** was determined by X-ray analysis after bis-MOM protection.[3] Under these conditions, **S7** derived from **S2** was methylated by $TMSCHN_2$ to obtain **9a**. The spectroscopic data of **9a** was in good agreement with the less polar diastereomer of **9**. The more polar diastereomer of **9** was then assigned as **9b**.



1: R = H
S2: R = OH

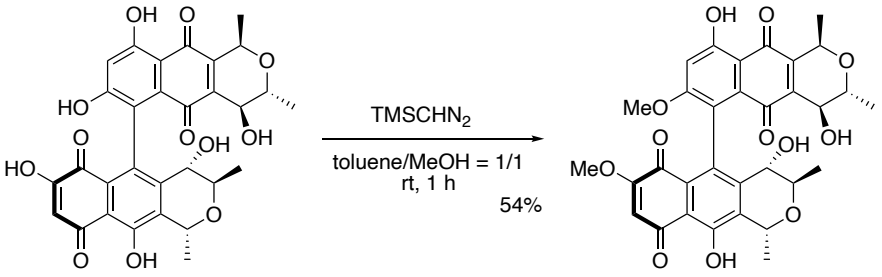
2: R = H, 10%
S3: R = OH, 5%

S4: R = H, 20%
S5: R = OH, 15%

S6: R = H, 66%
S7: R = OH, 43%

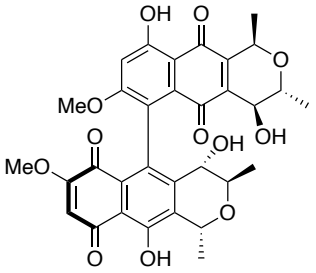
Scheme S1. Acid-promoted chemical conversion of pigments **1** and **S2**.

Methylation of biaryl compound **S7**



S7 **9a**

To a solution of biaryl compound **S7** (3.8 mg, 6.6 μmol) in toluene/MeOH (0.3 mL/0.3 mL) was added trimethylsilyldiazomethane (0.6 M in *n*-hexane, 385 μL, 231 μmol) at room temperature. After stirring for 15 h, the reaction was quenched by adding AcOH aqueous at this temperature. The products were extracted with EtOAc (×3), and the combined organic extracts were washed with brine, dried over $MgSO_4$. Concentration and purification by silica gel column chromatography (*n*-hexane/EtOAc = 2/1) afforded compound **9a** (2.2 mg, 54%) as an orange solid.



9a

R_f 0.23 (*n*-hexane/EtOAc = 1/1×2);

$[\alpha]_D^{21}$ +57.6 (*c* 0.09, $CHCl_3$);

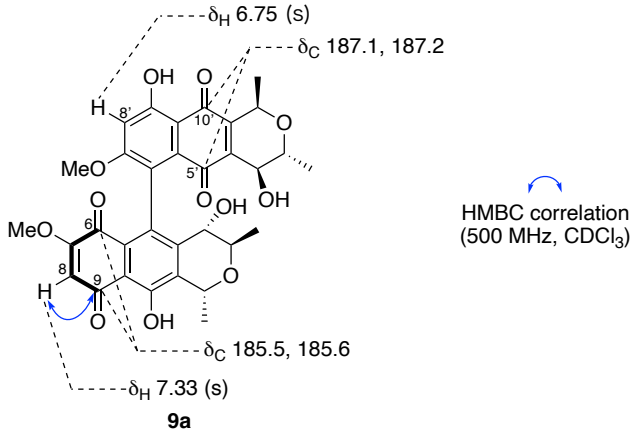
IR (ATR) 3522, 2963, 2928, 2853, 1640, 1609, 1381, 1261, 1232, 1206, 1114, 1084, 1029, 799, 780, 760, 473, 444, 412 cm^{-1};

^1H NMR ($CDCl_3$, 500 MHz) δ 1.34 (d, 3H, *J* = 6.2 Hz), 1.42 (d, 3H, *J* = 6.0 Hz), 1.61 (d, 3H, *J* = 6.8 Hz), 1.62 (d, 3H, *J* = 6.8 Hz), 3.46 (d, 1H, *J* = 2.4 Hz), 3.80 (s, 3H), 3.81–3.86 (m, 5H), 3.89–3.92 (m, 1H), 4.26 (brd, 1H, *J* = 8.0 Hz), 4.47 (brd, 1H, *J* = 8.0 Hz), 4.91 (q, 1H, *J* = 6.8 Hz), 4.93 (q, 1H, *J* = 6.8 Hz), 6.75 (s, 1H), 7.33 (s, 1H), 12.06 (s, 1H), 12.91 (s, 1H);

^{13}C NMR ($CDCl_3$, 125 MHz) δ 18.57, 18.58, 19.0, 19.2, 56.5, 56.6, 66.9, 67.1, 67.2, 67.3, 67.5, 67.8, 103.1, 104.5, 109.7, 110.2, 117.0, 119.4, 130.4, 132.2, 141.1, 141.9, 147.2, 148.1, 160.4, 163.4, 164.3, 165.4, 185.5, 185.6, 187.1, 187.2;

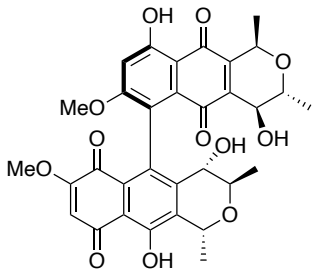
HRMS (MALDI) calcd for $C_{32}H_{30}O_{12}Na$ $[M+Na]^+$ *m/z* 629.1630; found *m/z* 629.1642;

Mp 66.8–67.0 °C.



9a

Figure S1. Key HMBC correlation of **9a**



9b

R_f 0.18 (*n*-hexane/EtOAc = 1/1×2);

$[\alpha]_D^{22}$ –282 (*c* 0.07, $CHCl_3$);

IR (ATR) 3522, 2930, 2855, 1642, 1609, 1381, 1361, 1311, 1291, 1269, 1231, 1114, 1081, 1036, 794, 755, 432 cm^{-1};

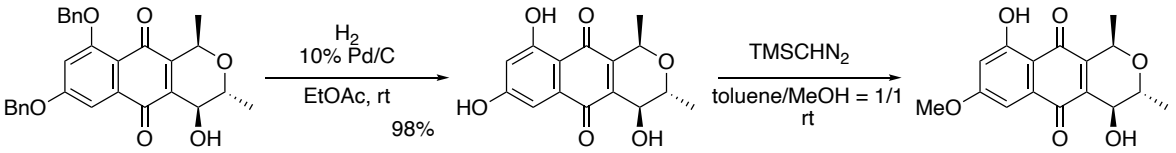
^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.34 (d, 3H, *J* = 6.0 Hz), 1.43 (d, 3H, *J* = 6.0 Hz), 1.62 (d, 3H, *J* = 6.5 Hz), 1.63 (d, 3H, *J* = 6.5 Hz), 3.42 (brs, 1H), 3.79 (s, 3H), 3.81–3.86 (m, 5H), 3.88–3.93 (m, 1H), 4.28 (brd, 1H, *J* = 8.0 Hz), 4.47 (brd, 1H, *J* = 8.0 Hz), 4.92 (q, 2H, *J* = 6.5 Hz), 6.75 (s, 1H), 7.31 (s, 1H), 12.07 (s, 1H), 12.91 (s, 1H);

^{13}C NMR ($CDCl_3$, 125 MHz) δ 18.5, 18.6, 19.1, 19.3, 56.5, 56.6, 66.8, 67.17, 67.20, 67.3, 67.5, 67.8, 103.3, 104.6, 109.7, 110.4, 117.0, 119.5, 130.3, 132.2, 141.2, 141.8, 147.3, 148.1, 161.1, 162.5, 164.3, 165.5, 185.6, 185.7, 187.1, 187.3;

HRMS (MALDI) calcd for $C_{32}H_{30}O_{12}Na$ $[M+Na]^+$ *m/z* 629.1630; found *m/z* 629.1616;

Mp 105–106 °C.

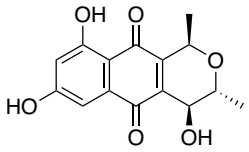
3-5. Preparation of **6**



S9 **S10** **6**

To a solution of pyranonaphthoquinone **S9**[4] (232 mg, 0.492 mmol) in EtOAc (25 mL) was added 10% Pd/C (28.0 mg, 26.3 μmol) at room temperature. After stirring for 11 h under hydrogen atmosphere, the reaction was filtered through a short pad of silica gel on Celite® and washed with CH_2Cl_2. The filtrate was concentrated in vacuo to afford the compound **S10** (140 mg, 98%) as red solids.

To a solution of compound **S10** (160 mg, 0.551 mmol) in toluene/MeOH (11 mL/11 mL) was added trimethylsilyldiazomethane (0.6 M in THF, 8.5 mL, 5.1 mmol) at room temperature. After stirring for 4 h, the reaction was quenched by adding AcOH (300 μL) at this temperature. Concentration and purification by silica gel column chromatography (*n*-hexane/Acetone = 9/1) afforded compound **6** (90.9 mg, 54%) as yellow solids.



S10

R_f 0.48 (*n*-hexane/acetone = 6/4);

$[\alpha]_D^{22}$ –27.0 (*c* 0.43, $CHCl_3$);

IR (ATR) 3235, 2979, 1608, 1269, 1178, 1067, 854, 763, 629 cm^{-1};

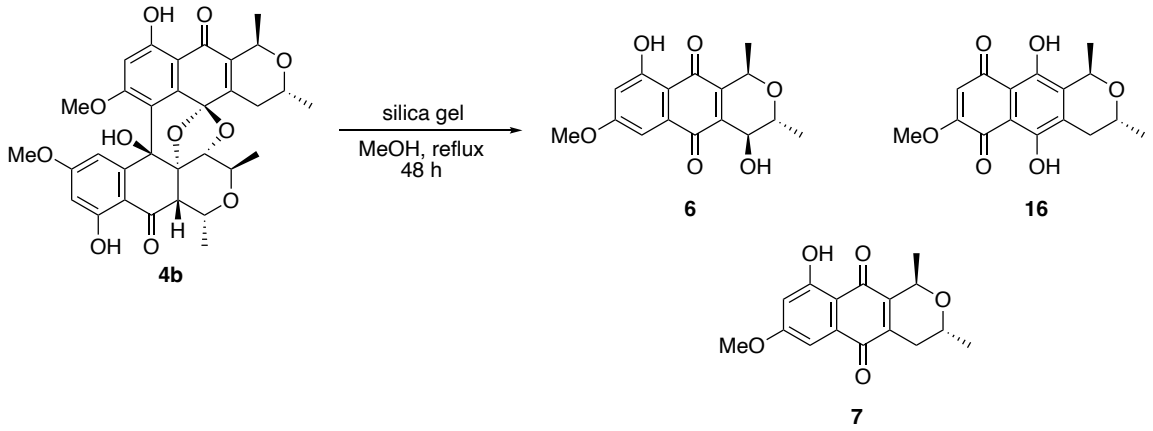
^1H NMR ($CDCl_3$, 500 MHz) δ 1.41 (d, 3H, *J* = 6.1 Hz), 1.62 (d, 3H, *J* = 6.9 Hz), 3.86 (brs, 1H), 3.89 (dq, 1H, *J* = 8.1, 6.1 Hz), 4.44 (d, 1H, *J* = 8.1 Hz), 4.92 (q, 1H, *J* = 6.9 Hz), 6.32 (brs, 1H), 6.61 (d, 1H, *J* = 2.4 Hz), 7.06 (d, 1H, *J* = 2.4 Hz), 12.06 (s, 1H);

^{13}C NMR ($CDCl_3$, 125 MHz) δ 18.6, 19.1, 67.11, 67.12, 67.8, 108.6, 108.8, 109.6, 133.5, 140.8, 148.5, 162.8, 164.5, 185.2, 186.5;

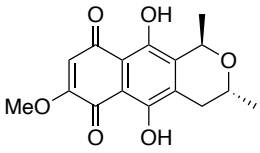
HRMS (CI) calcd for $C_{15}H_{15}O_6$ $[M+H]^+$ *m/z* 291.0863; found *m/z* 291.0870;

Mp 107–108 °C.

3-6. Silica gel-induced degradation of **4b**



To a solution of compound **4b** (44.5 mg, 75.1 mmol) in MeOH (38 mL) was added silica gel (4.06 g; dried with a heat gun under vacuum). After stirring for 48 h under reflux, the suspension was filtered through a Celite® pad, and washed with EtOAc. The filtrate was concentrated and purified by silica gel column chromatography (*n*-hexane/EtOAc = 5/1 → 2/1) to afford the compounds **6** (1.0 mg, 2%) as yellow solids, **7** (8.5 mg, 24%) as yellow solids, and **16** (8.0 mg, 22%) as red solids.



16

R_f 0.35 (*n*-nexane/EtOAc = 2/1);

$[\alpha]_D^{22}$ +90.4 (*c* 0.65, $CHCl_3$);

IR (ATR) 2973, 2936, 1596, 1439, 1387, 1298, 1238, 1202, 1106, 1055, 990, 966, 856, 811, 753, 708, 645, 600, 492, 445 cm^{-1};

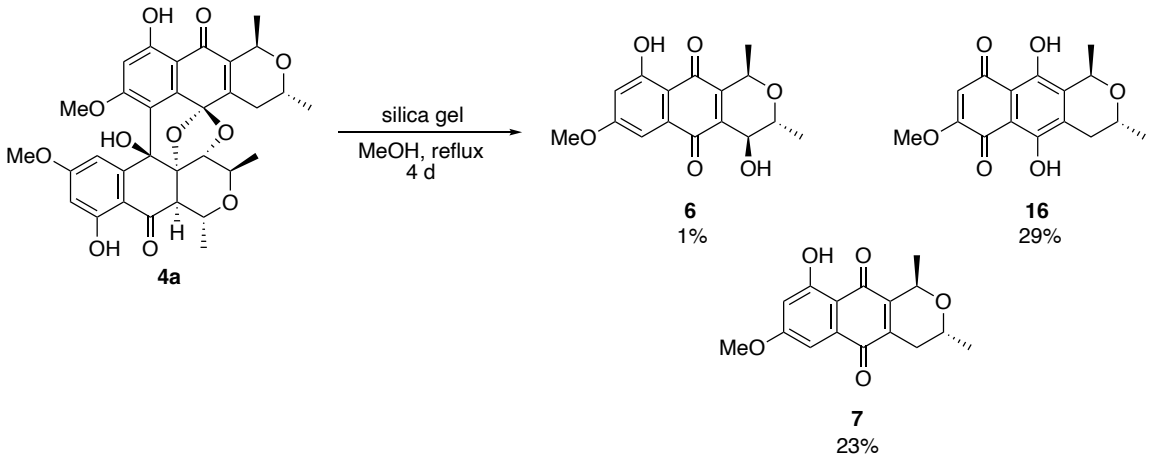
^1H NMR ($CDCl_3$, 500 MHz) δ 1.38 (d, 3H, *J* = 6.1 Hz), 1.59 (d, 3H, *J* = 6.7 Hz), 2.37 (dd, 1H, *J* = 10.5 Hz, 18.4 Hz), 2.87 (dd, 1H, *J* = 3.4 Hz, 18.4 Hz), 3.94 (s, 3H), 4.06 (ddq, 1H, *J* = 3.4 Hz, 10.5 Hz, 6.1 Hz), 5.15 (q, 1H, *J* = 6.7 Hz), 6.18 (s, 1H), 12.72 (s, 1H), 13.17 (s, 1H);

^{13}C NMR ($CDCl_3$, 125 MHz) δ 19.2, 21.7, 30.0, 56.7, 62.1, 68.1, 107.7, 109.6, 109.8, 135.0, 142.7, 157.7, 160.5, 160.6, 178.5, 184.9;

HRMS (CI) calcd for $C_{16}H_{16}O_6$ $[M]^+$ *m/z* 304.0947; found *m/z* 304.0947;

Mp 187–188 °C.

3-7. Silica gel-induced degradation of **4a**



4a

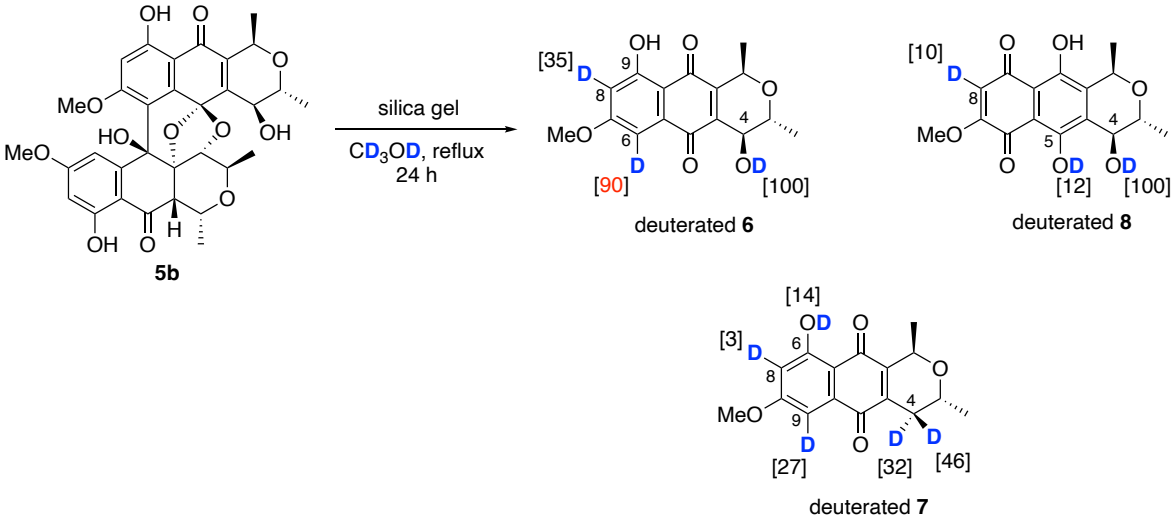
6
1%

16
29%

7
23%

4. Mechanistic study

4-1. Silica gel-induced degradation of **5b** in methanol-d_4.



To a solution of compound **5b** (14.4 mg, 23.7 μmol) in CD_3OD (12 mL) was added silica gel (1.28 g; dried with a heat gun under vacuum). After stirring for 24 h under reflux, the suspension was filtered through a Celite® pad, and washed with EtOAc. The filtrate was concentrated and purified by silica gel column chromatography (*n*-hexane/EtOAc = 5/1 → 3/1 → 2/1 → 1/1) to afford the deuterated compounds **6** (4.3 mg, 30%) as yellow solids, **7** (0.4 mg, 3%) as yellow solids, and **8** (3.2 mg, 21%) as red solids.

5. UV–Vis spectra

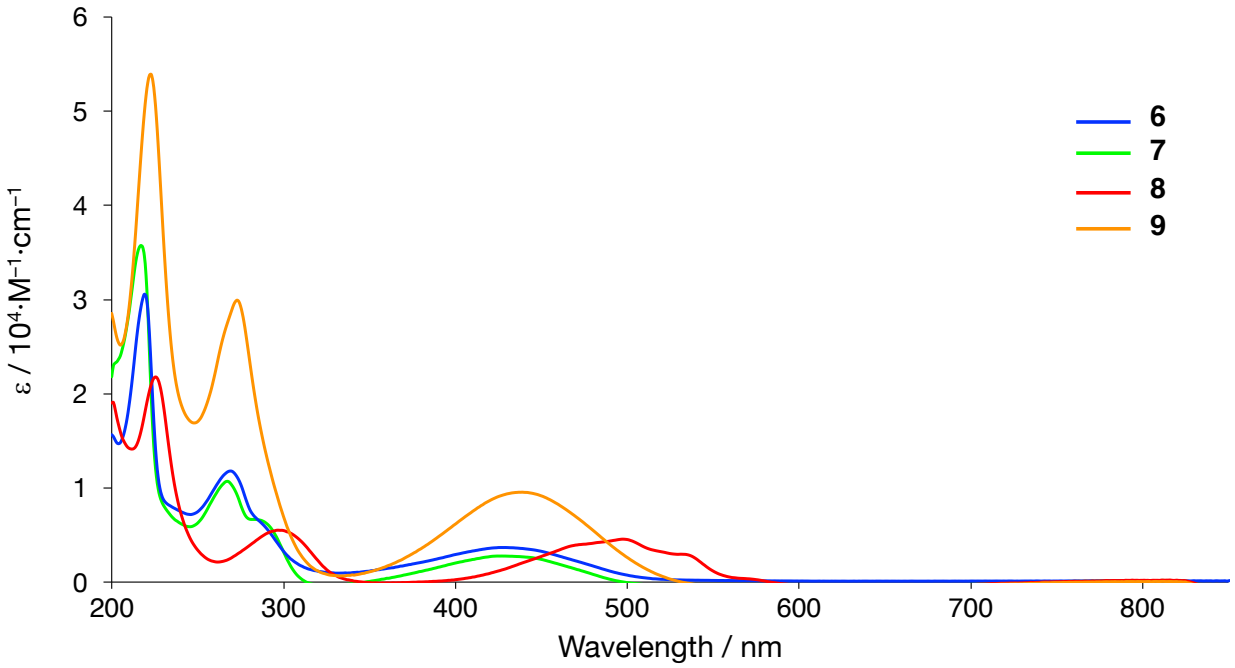
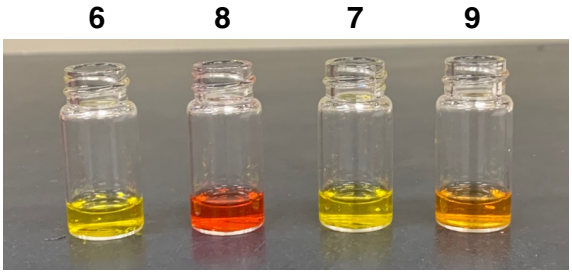


Figure S2. UV–Vis spectra (MeOH, 2.0×10^{-5} M).

	λ_{max} nm (log ε)
6	269 (4.07), 429 (3.57)
7	297 (3.74), 498 (3.66), 531 (3.47) 267 (4.03), 427 (3.45)
8	297 (3.74), 498 (3.66), 531 (3.47)
9	273 (4.48), 439 (3.98)



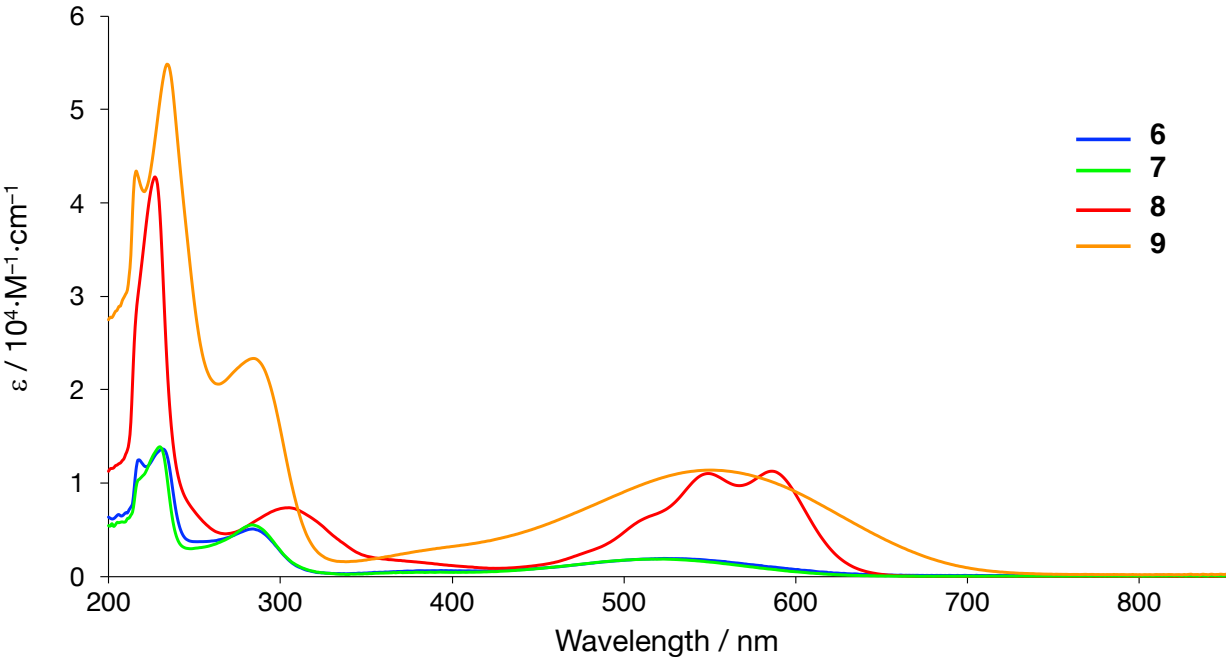
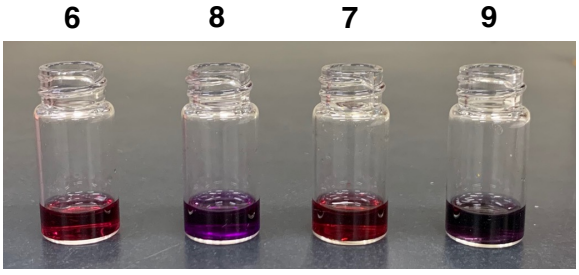


Figure S3. UV–Vis spectra (0.09 M NaOH/MeOH, 2.0×10^{-5} M).

	λ_{max} nm (log ε)
6	284 (3.71), 523 (3.29)
7	284 (3.74), 523 (3.27)
8	305 (3.87), 549 (4.04), 586 (4.05)
9	284 (4.37), 550 (4.06)



6. ^{1}H and ^{13}C NMR spectra

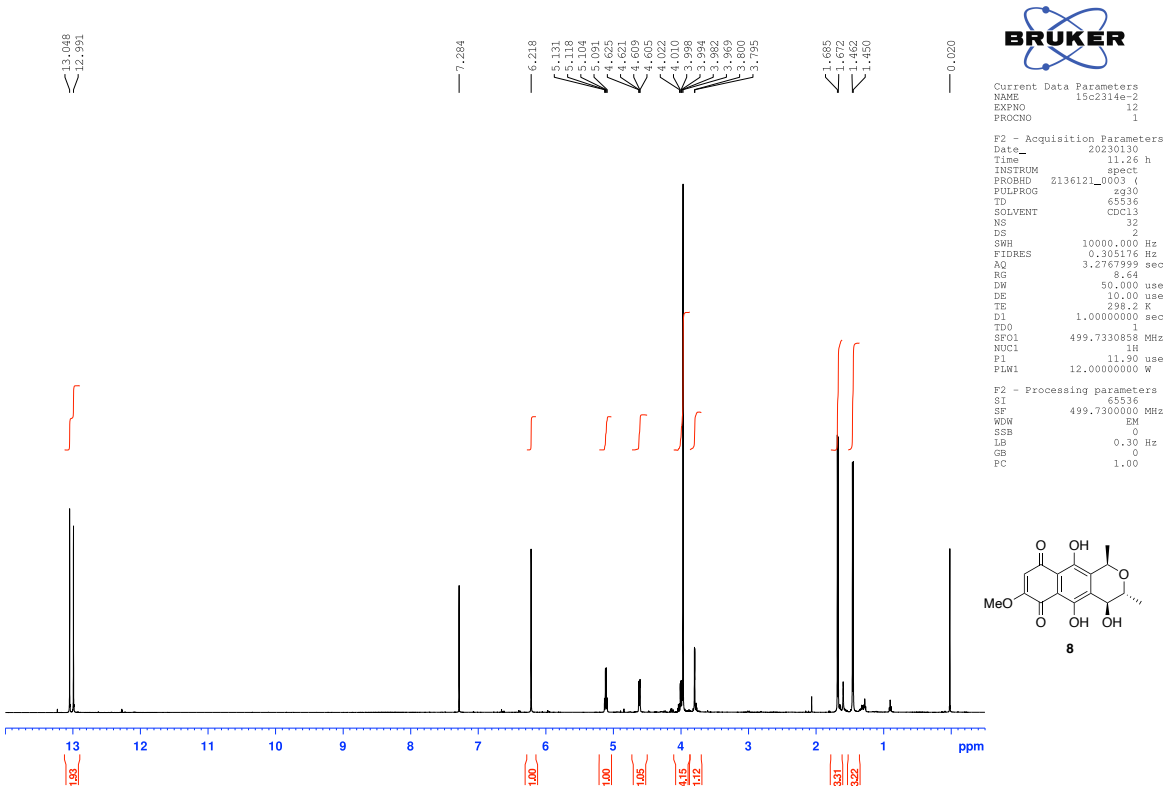


Figure S4. ^{1}H NMR spectrum of **8** (500 MHz, $CDCl_3$).

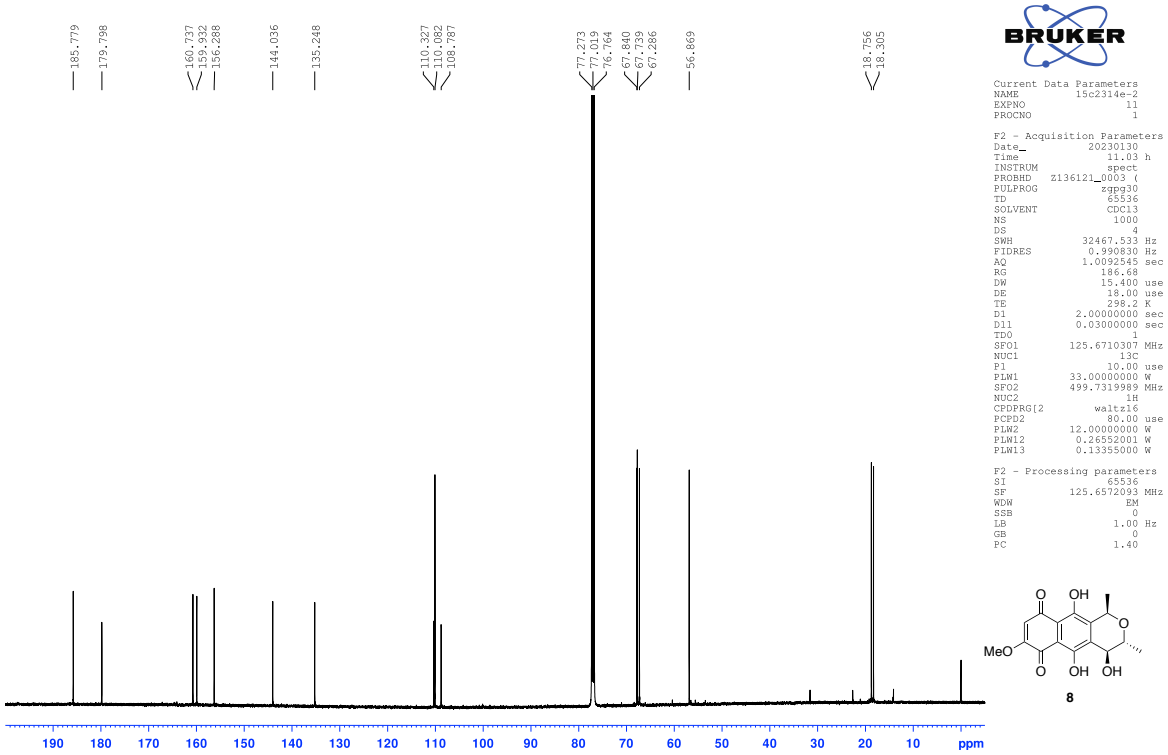


Figure S5. ^{13}C NMR spectrum of **8** (125 MHz, $CDCl_3$).

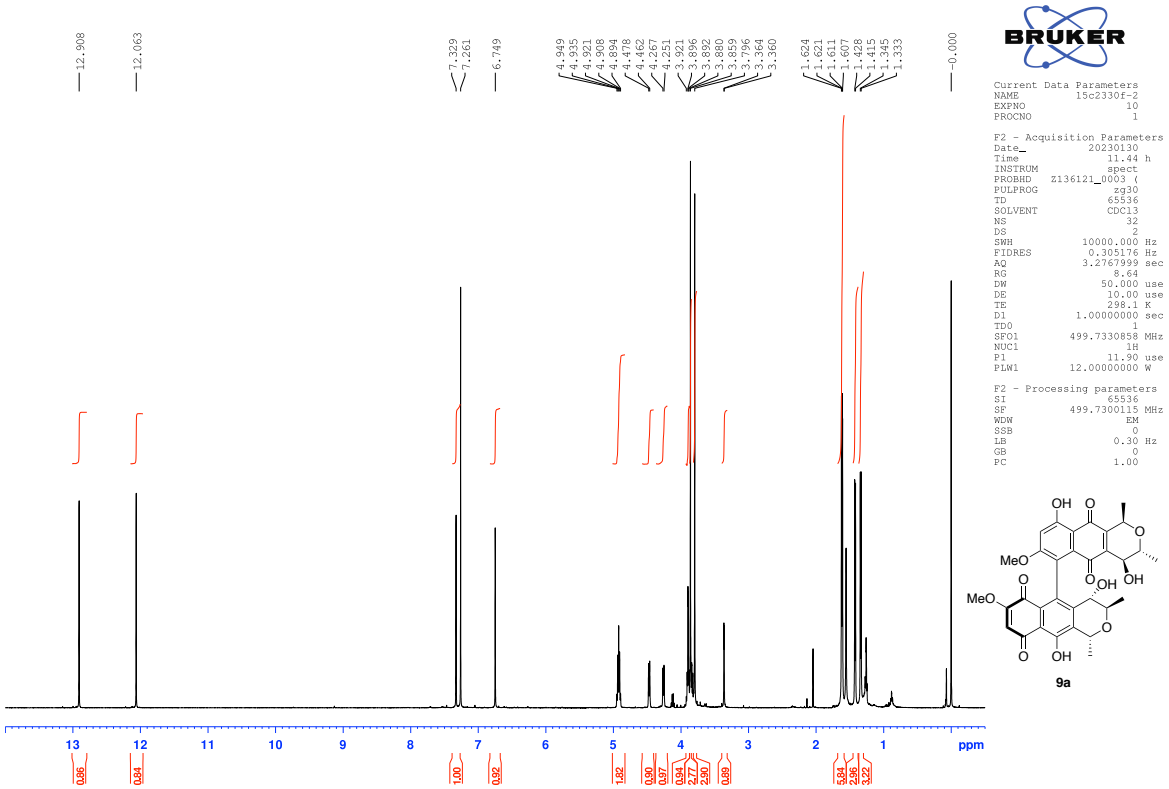


Figure S6. ^{1}H NMR spectrum of **9a** (500 MHz, $CDCl_3$).

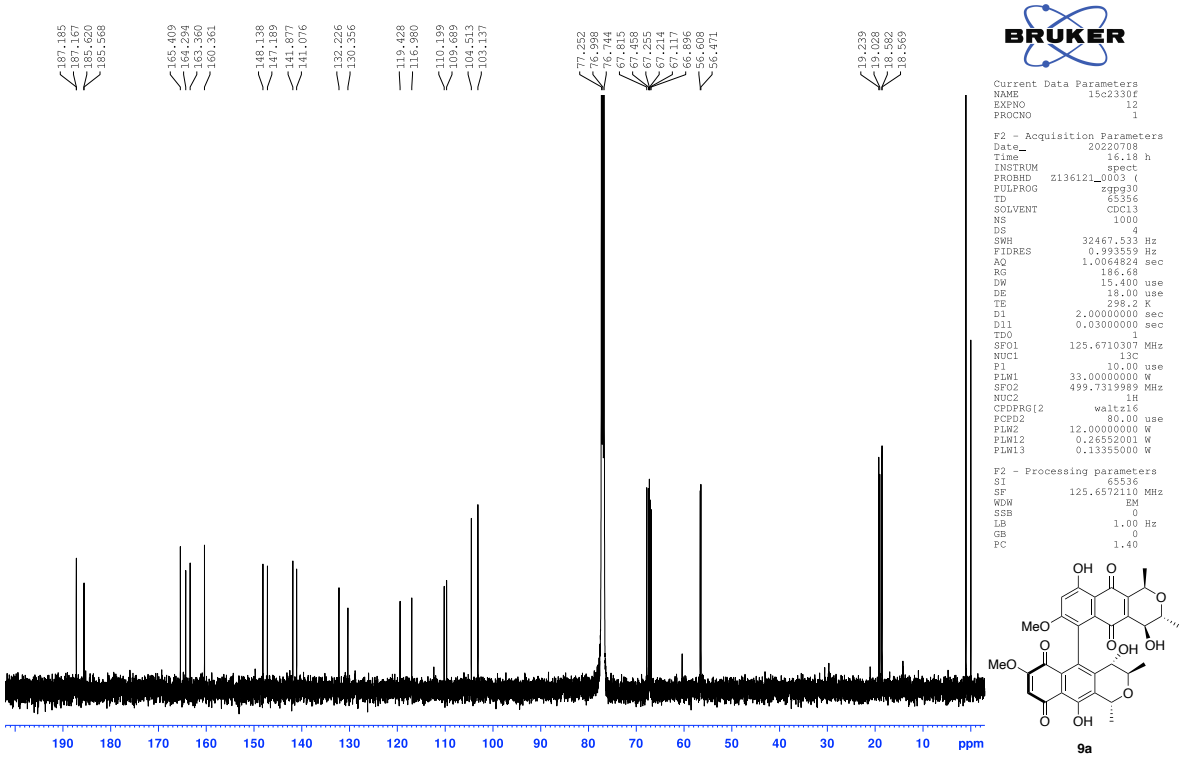


Figure S7. ^{13}C NMR spectrum of **9a** (125 MHz, $CDCl_3$).

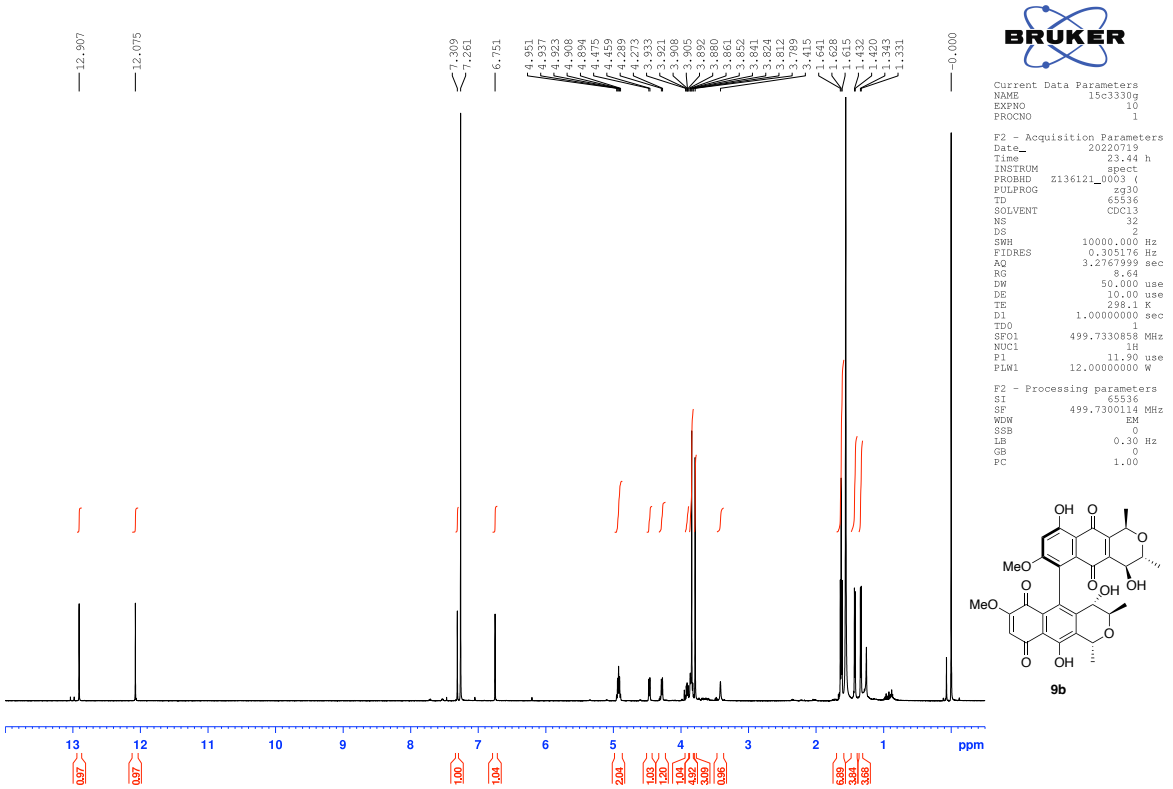


Figure S8. ^{1}H NMR spectrum of **9b** (500 MHz, $CDCl_3$).

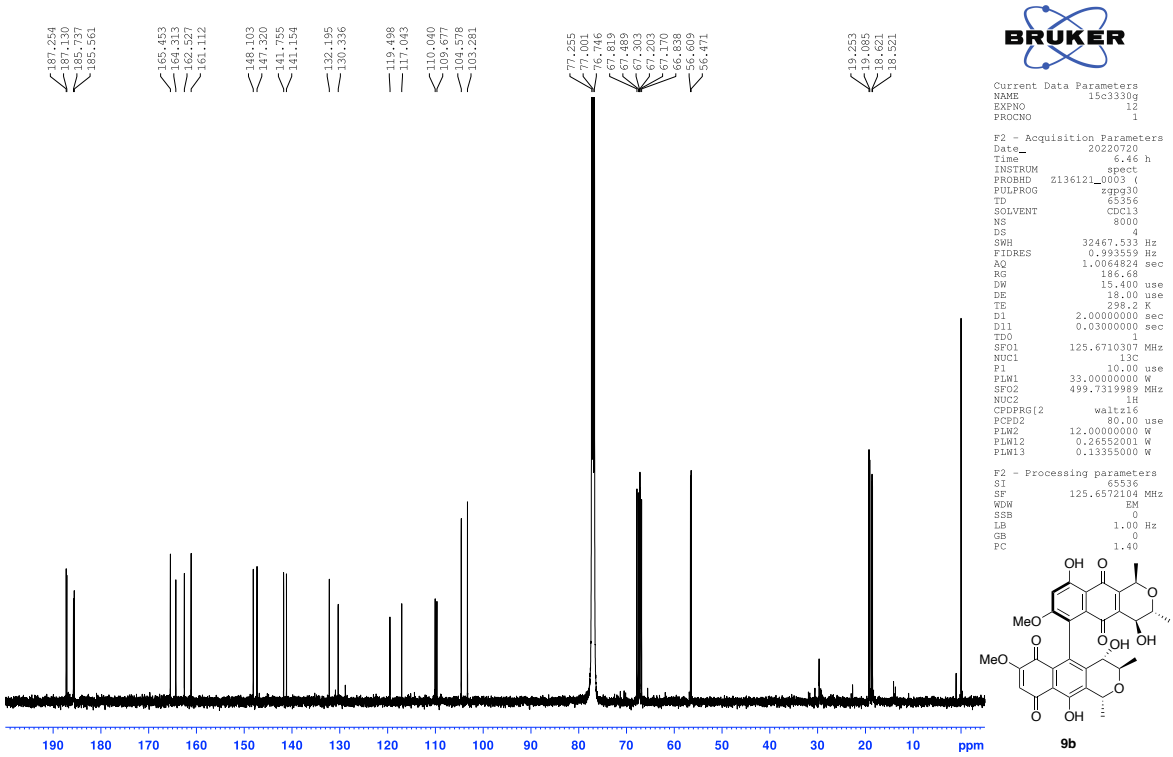


Figure S9. ^{13}C NMR spectrum of **9b** (125 MHz, $CDCl_3$).

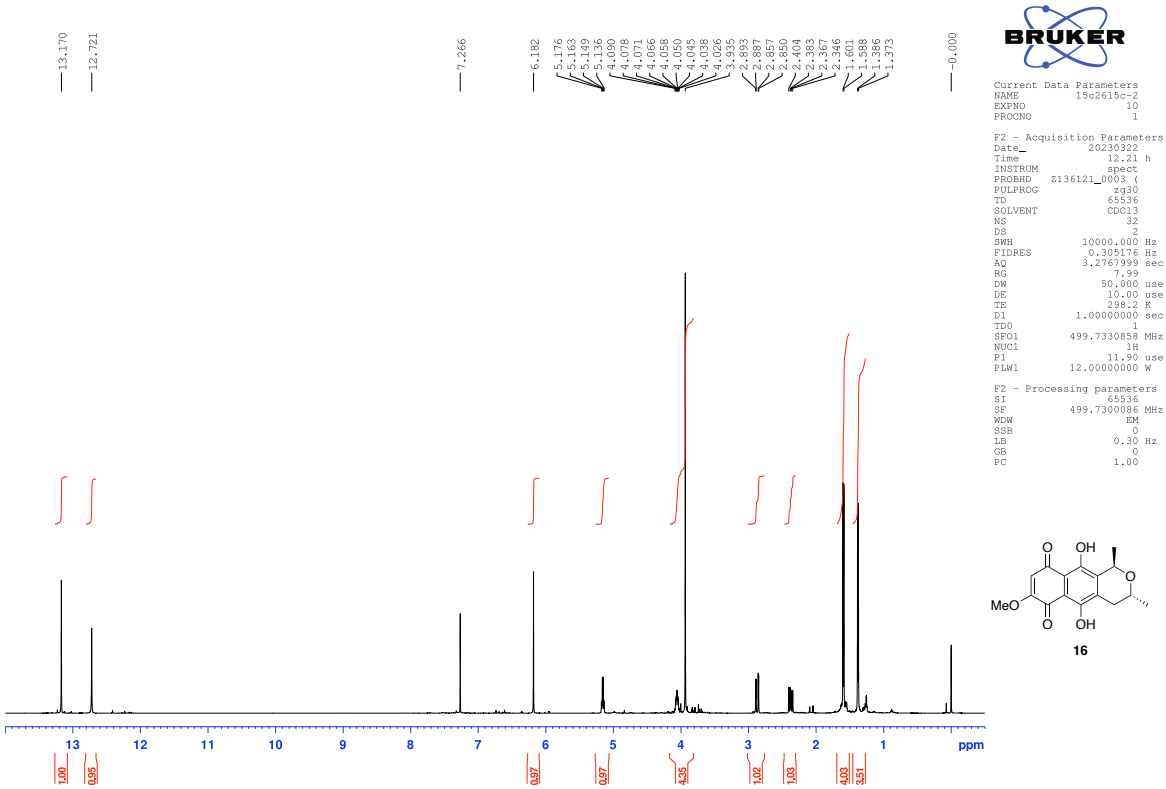


Figure S10. ^{1}H NMR spectrum of **16** (500 MHz, $CDCl_3$).

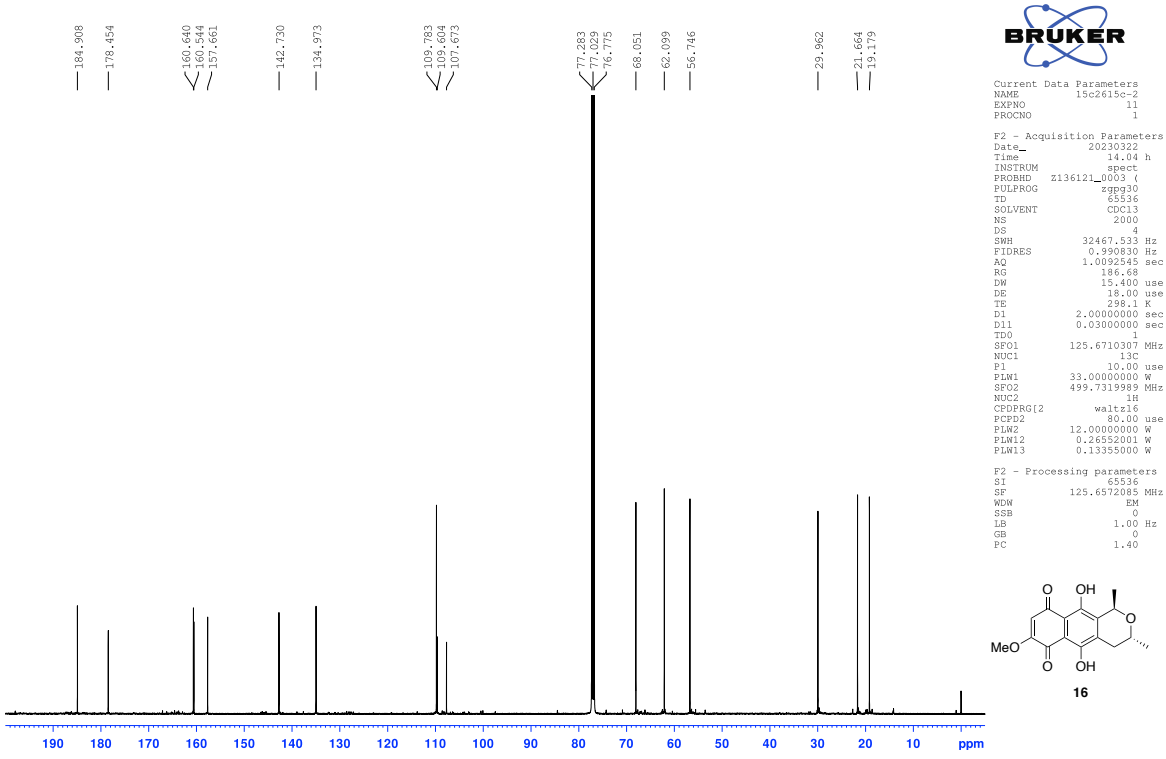


Figure S11. ^{13}C NMR spectrum of **16** (125 MHz, $CDCl_3$).

7. Reference

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