

Supporting Information

**Taichunamides: Prenylated Indole Alkaloids from *Aspergillus taichungensis* (IBT 19404)**

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## Table of contents

Page	S3	<b>General experimental procedures.</b>
	S3	<b>Fungal strain and culture condition.</b>
	S3	<b>Extraction and isolation.</b>
	S5	<b>Structure determination of 4, 5, and 7.</b>
	S6	<b>Figure S1.</b> Key NOE correlations of 1-7.
	S6	<b>Conformational analyses of 4, 5, and 7 and ECD calculations for 3 and 6.</b>
	S7	<b>Measurement of Proteasome Inhibitory Activity.</b>
	S8	<b>Figure S2.</b> $^1\text{H}$ NMR spectrum of <b>1</b> in DMSO- $d_6$ .
	S8	<b>Figure S3.</b> $^{13}\text{C}$ NMR spectrum of <b>1</b> in DMSO- $d_6$ .
	S9	<b>Figure S4.</b> COSY spectrum of <b>1</b> in DMSO- $d_6$ .
	S9	<b>Figure S5.</b> HMQC spectrum of <b>1</b> in DMSO- $d_6$ .
	S10	<b>Figure S6.</b> HMBC spectrum of <b>1</b> in DMSO- $d_6$ .
	S10	<b>Figure S7.</b> NOESY spectrum of <b>1</b> in DMSO- $d_6$ .
	S11	<b>Figure S8.</b> ECD spectrum of <b>1</b> in MeOH.
	S11	<b>Figure S9.</b> $^1\text{H}$ NMR spectrum of <b>2</b> in DMSO- $d_6$ .
	S12	<b>Figure S10.</b> COSY spectrum of <b>2</b> in DMSO- $d_6$ .
	S12	<b>Figure S11.</b> HSQC spectrum of <b>2</b> in DMSO- $d_6$ .
	S13	<b>Figure S12.</b> HMBC spectrum of <b>2</b> in DMSO- $d_6$ .
	S13	<b>Figure S13.</b> NOESY spectrum of <b>2</b> in DMSO- $d_6$ .
	S14	<b>Figure S14.</b> ECD spectrum of <b>2</b> in MeOH.
	S14	<b>Figure S15.</b> $^1\text{H}$ NMR spectrum of <b>3</b> in DMSO- $d_6$ .
	S15	<b>Figure S16.</b> $^{13}\text{C}$ NMR spectrum of <b>3</b> in DMSO- $d_6$ for 600 MHz.
	S15	<b>Figure S17.</b> COSY spectrum of <b>3</b> in DMSO- $d_6$ .
	S16	<b>Figure S18.</b> HSQC spectrum of <b>3</b> in DMSO- $d_6$ .
	S16	<b>Figure S19.</b> HMBC spectrum of <b>3</b> in DMSO- $d_6$ .
	S17	<b>Figure S20.</b> NOESY spectrum of <b>3</b> in DMSO- $d_6$ .
	S17	<b>Figure S21.</b> ECD spectrum of <b>3</b> in MeOH.
	S18	<b>Figure S22.</b> $^1\text{H}$ NMR spectrum of <b>4</b> in DMSO- $d_6$ .
	S18	<b>Figure S23.</b> $^{13}\text{C}$ NMR spectrum of <b>4</b> in DMSO- $d_6$ .
	S19	<b>Figure S24.</b> COSY spectrum of <b>4</b> in DMSO- $d_6$ .
	S19	<b>Figure S25.</b> HSQC spectrum of <b>4</b> in DMSO- $d_6$ .
	S20	<b>Figure S26.</b> HMBC spectrum of <b>4</b> in DMSO- $d_6$ .

- S20 **Figure S27.** NOESY spectrum of **4** in DMSO-*d*<sub>6</sub>.
- S21 **Figure S28.** ECD spectrum of **4** in MeOH.
- S21 **Figure S29.** <sup>1</sup>H NMR spectrum of **5** in DMSO-*d*<sub>6</sub>.
- S22 **Figure S30.** COSY spectrum of **5** in DMSO-*d*<sub>6</sub>.
- S22 **Figure S31.** HSQC spectrum of **5** in DMSO-*d*<sub>6</sub>.
- S23 **Figure S32.** HMBC spectrum of **5** in DMSO-*d*<sub>6</sub>.
- S23 **Figure S33.** NOESY spectrum of **5** in DMSO-*d*<sub>6</sub>.
- S24 **Figure S34.** ECD spectrum of **5** in MeOH.
- S24 **Figure S35.** <sup>1</sup>H NMR spectrum of **6** in DMSO-*d*<sub>6</sub>.
- S25 **Figure S36.** COSY spectrum of **6** in DMSO-*d*<sub>6</sub>.
- S25 **Figure S37.** HSQC spectrum of **6** in DMSO-*d*<sub>6</sub>.
- S26 **Figure S38.** HMBC spectrum of **6** in DMSO-*d*<sub>6</sub>.
- S26 **Figure S39.** NOESY spectrum of **6** in DMSO-*d*<sub>6</sub>.
- S27 **Figure S40.** ECD spectrum of **6** in MeOH.
- S27 **Figure S41.** <sup>1</sup>H NMR spectrum of **7** in DMSO-*d*<sub>6</sub>.
- S28 **Figure S42.** COSY spectrum of **7** in DMSO-*d*<sub>6</sub>.
- S28 **Figure S43.** HSQC spectrum of **7** in DMSO-*d*<sub>6</sub>.
- S29 **Figure S44.** HMBC spectrum of **7** in DMSO-*d*<sub>6</sub>.
- S29 **Figure S45.** NOESY spectrum of **7** in DMSO-*d*<sub>6</sub>.
- S30 **Figure S46.** ECD spectrum of **7** in MeOH.
- S31 **Table S1.** <sup>1</sup>H and <sup>13</sup>C NMR data of **1** in DMSO-*d*<sub>6</sub>.
- S32 **Table S2.** <sup>1</sup>H and <sup>13</sup>C NMR data of **2** in DMSO-*d*<sub>6</sub>.
- S33 **Table S3.** <sup>1</sup>H and <sup>13</sup>C NMR data of **2** in acetone-*d*<sub>6</sub> and in CD<sub>3</sub>OD
- S34 **Table S4.** <sup>1</sup>H and <sup>13</sup>C NMR data of **3** in DMSO-*d*<sub>6</sub>.
- S35 **Table S5.** <sup>1</sup>H and <sup>13</sup>C NMR data of **4** in DMSO-*d*<sub>6</sub>.
- S36 **Table S6.** <sup>1</sup>H and <sup>13</sup>C NMR data of **5** in DMSO-*d*<sub>6</sub>.
- S37 **Table S7.** <sup>1</sup>H and <sup>13</sup>C NMR data of **6** in DMSO-*d*<sub>6</sub>.
- S38 **Table S8.** <sup>1</sup>H and <sup>13</sup>C NMR data of **7** in DMSO-*d*<sub>6</sub>.
- S39 **Table S9.** Calculated distances between designated hydrogens in **3a** and **3b**.
- S40 **Table S10.** Calculated distances between designated hydrogens in **6**.

## Experimental section

**General experimental procedures.** Optical rotations were determined with a HITACHI F-4500. ECD spectra were measured on a JASCO J-820 spectropolarimeter in MeOH. UV spectra were measured on a JASCO V-550. IR spectra were measured on a Perkin Elmer Frontier FT-IR spectrophotometer. NMR spectra were recorded on a JEOL JNM-ECX400, Bruker AVANCE III 600, or Bruker AVANCE III 500 spectrometer. Chemical shifts were referenced to residual solvent peaks ( $\delta_{\text{H}}$  2.49 and  $\delta_{\text{C}}$  39.5 for DMSO- $d_6$ ,  $\delta_{\text{H}}$  2.04 and  $\delta_{\text{C}}$  29.8 for acetone- $d_6$ , and  $\delta_{\text{H}}$  3.30 and  $\delta_{\text{C}}$  49.0 for CD<sub>3</sub>OD. ESI mass spectra were measured on a Bruker BioTOF-Q mass spectrometer.

**Fungal strain and culture condition.** The fungus *Aspergillus taichungensis* (IBT 19404) was isolated from soil in Taiwan. The fungus was cultured on rice medium (5 kg, dried weight) at 25 °C for 30 days.

**Extraction and isolation.** The cultured was extracted with *n*-BuOH and the extract partitioned with H<sub>2</sub>O. The *n*-BuOH layer was concentrated and then partitioned between *n*-hexane and 90% MeOH-H<sub>2</sub>O. The aqueous MeOH fraction (50 g) was subjected to ODS chromatography with 40, 75 (Fr. A), and 95% (Fr. B) MeOH-H<sub>2</sub>O. Fr. A was subjected to SiO<sub>2</sub> column chromatography with 50% *n*-hexane-EtOAc, EtOAc (Fr. A1), 50% CH<sub>2</sub>Cl<sub>2</sub>-MeOH (Fr. A2), and CH<sub>2</sub>Cl<sub>2</sub>-MeOH-H<sub>2</sub>O (6:4:1) (Fr. A3). Fr. A1 was purified by phenyl-hexyl HPLC with 65% MeOH-H<sub>2</sub>O to afford taichunamide B (**2**, 1.6 mg), taichunamide C (**3**, 0.35 mg), taichunamide E (**5**, 0.51 mg), taichunamide F (**6**, 0.47 mg), notoamide V (**9**, 5.3 mg), (+)-6-*epi*-notoamide F (**10**, 31 mg), (+)-6-*epi*-notoamide R (**11**, 4.8 mg), (+)-6-*epi*-stephacidin A (**13**, 160 mg), (+)-notoamide B (**15**, 5.3 mg), (-)-stephacidin A (**16**, 0.82 mg), notoamide C (**17**, 1.9 mg), notoamide Q (**18**, 0.30 mg), and (+)-6-*epi*-avrainvillamide (**21**, 63 mg). Fr. A2 was purified by phenyl-hexyl HPLC with 65% MeOH-H<sub>2</sub>O to afford notoamide D (**19**, 10 mg). Fr. A3 was subjected to SiO<sub>2</sub> chromatography with 50% *n*-hexane-EtOAc, EtOAc (Fr. A3-1), and 20% CH<sub>2</sub>Cl<sub>2</sub>-MeOH (Fr. A3-2). Fr. A3-1 was purified by NH<sub>2</sub> chromatography with 50% CH<sub>3</sub>CN-H<sub>2</sub>O followed by phenyl-hexyl HPLC with 65% MeOH-H<sub>2</sub>O and then Asahipak GS-310 HPLC with MeOH to afford taichunamide A (**1**, 14 mg), taichunamide G (**7**, 3.3 mg), (+)-versicolamide B (**14**, 19 mg), and deoxybrevianamide E (**20**, 16 mg). Fr. A3-2 was purified by NH<sub>2</sub> chromatography to afford (+)-notoamide U (**8**, 140 mg) in an eluent with 97% CH<sub>3</sub>CN-H<sub>2</sub>O and (+)-versiclamide C (**12**, 240 mg) in an eluent with 50% CH<sub>3</sub>CN-H<sub>2</sub>O. Fr. B was subjected to NH<sub>2</sub> chromatography with 50% CH<sub>3</sub>CN-H<sub>2</sub>O to afford taichunamide D (**4**, 0.50 mg).

**Taichunamide A (1):**  $[\alpha]_{\text{D}}^{20} +89$  (*c* 2.4, MeOH); UV (MeOH)  $\lambda_{\text{max}}$  (log  $\epsilon$ ) 204 nm (4.2), 250 nm (sh, 4.1),

256 nm (4.1), 264 nm (4.1); ECD (100  $\mu$ M, MeOH)  $\lambda_{\max}$  ( $\Delta\epsilon$ ) 222 (6.6), 248 (-11), and 272 (13) nm; NMR data (DMSO- $d_6$ ), see Table S1; IR (film)  $\nu_{\max}$  3357, 2924, 2854, 1678, 1576, 1458, 1398, 1340, 1264, 1208, 1166, 1111, 1083, 1044, 1026, 897, 818, 798, 742, 689, 580, 504, 410, 387 $\text{cm}^{-1}$ ; NOESY cross peaks, H-21/H-10 $\beta$  ( $\delta$  1.71); H-19/H-10 $\alpha$  ( $\delta$  2.63) and H<sub>3</sub>-23; H-1/H<sub>3</sub>-23 and H-10 $\alpha$ ; HRESIMS [M + H]<sup>+</sup>  $m/z$  448.2217 (calcd for C<sub>26</sub>H<sub>30</sub>N<sub>3</sub>O<sub>4</sub>, 448.2236).

**Taichunamide B (2):** [ $\alpha$ ]<sub>D</sub><sup>20</sup> +99 ( $c$  1.3, MeOH); UV (MeOH)  $\lambda_{\max}$  ( $\log \epsilon$ ) 206 nm (4.1), 236 nm (sh, 4.3), 244 nm (4.4), 254 nm (sh, 4.2), 266 nm (4.1), 276 nm (3.9), 326 nm (3.7), 338 nm (3.6); ECD (200  $\mu$ M, MeOH)  $\lambda_{\max}$  ( $\Delta\epsilon$ ) 214 (sh, 2.1), 222 (4.0), 237 (0.15), 255 (5.3), 284 (-1.5), 290 (sh, -1.3), 321 (1.6), 329 (1.5) nm; NMR data (DMSO- $d_6$ ), see Table S2; NMR data (acetone- $d_6$  and CD<sub>3</sub>OD), see Table S3; IR (film)  $\nu_{\max}$  3420, 3253, 3216, 3178, 3132, 2973, 2926, 2876, 2857, 1678, 1615, 1560, 1570, 1536, 1451, 1376, 1200, 1122, 1074, 764  $\text{cm}^{-1}$ ; NOESY cross peaks, H-21/H<sub>3</sub>-24; H-19/H<sub>3</sub>-23; HRESIMS [M + H]<sup>+</sup>  $m/z$  446.2064 (calcd for C<sub>26</sub>H<sub>28</sub>N<sub>3</sub>O<sub>4</sub>, 446.2080).

**Taichunamide C (3):** [ $\alpha$ ]<sub>D</sub><sup>20</sup> +120 ( $c$  0.83, MeOH); UV (MeOH)  $\lambda_{\max}$  ( $\log \epsilon$ ) 202 nm (4.2), 230nm (4.0); ECD (50  $\mu$ M, MeOH)  $\lambda_{\max}$  ( $\Delta\epsilon$ ) 203 (-21), 208 (sh, -18), 228 (23), 254 (2.2), 271 (4.0) nm; NMR data (DMSO- $d_6$ ), see Table S4; IR (film)  $\nu_{\max}$  3358, 2923, 2852, 1680, 1401  $\text{cm}^{-1}$ ; NOESY cross peaks, H-4/H-10 $\beta$  ( $\delta$  2.16); H-19/H<sub>3</sub>-23; H-21/H<sub>3</sub>-24; H-25/H-30 ( $\delta$  4.65); HRESIMS [M + H]<sup>+</sup>  $m/z$  494.2256 (calcd for C<sub>27</sub>H<sub>32</sub>N<sub>3</sub>O<sub>6</sub>, 494.2291).

**Taichunamide D (4):** [ $\alpha$ ]<sub>D</sub><sup>20</sup> +33 ( $c$  0.42, MeOH); UV (MeOH)  $\lambda_{\max}$  ( $\log \epsilon$ ) 204 nm (4.9), 250 nm (4.8), 288nm (4.4), 296 nm (4.4); ECD (200  $\mu$ M, MeOH)  $\lambda_{\max}$  ( $\Delta\epsilon$ ) 203 (-1.8), 207 (-1.9), 222 (3.9), 236 (0.05), 254 (5.3), 273 (1.6), 291 (2.4) nm; NMR data (DMSO- $d_6$ ), see Table S5; IR (film)  $\nu_{\max}$  3261, 2924, 2854, 1683, 1460, 1411, 1361, 1274, 1176, 1135, 1054, 958, 801, 722, 593  $\text{cm}^{-1}$ ; NOESY cross peaks, H-19/H<sub>3</sub>-23; H-21/H<sub>3</sub>-24; H-4/H-10 $\alpha$  and H10 $\beta$ ; H-26/H<sub>3</sub>-28; H-26/H<sub>3</sub>-29; HRESIMS [M + Na]<sup>+</sup>  $m/z$  532.1876 (calcd for C<sub>27</sub>H<sub>31</sub>N<sub>3</sub>NaO<sub>5</sub>S, 532.1882).

**Taichunamide E (5):** [ $\alpha$ ]<sub>D</sub><sup>20</sup> -29 ( $c$  0.36, MeOH); UV (MeOH)  $\lambda_{\max}$  ( $\log \epsilon$ ) 204 nm (5.0), 246 nm (5.0), 280nm (4.6), 292 nm (4.4); ECD (200  $\mu$ M, MeOH)  $\lambda_{\max}$  ( $\Delta\epsilon$ ) 208 (-4.4), 221 (0.13), 234 (-5.0), 250 (5.6), 265 (-2.7) nm; NMR data (DMSO- $d_6$ ), see Table S6; IR (film)  $\nu_{\max}$  3217, 2923, 2853, 1711, 1458, 1376, 1285, 1158, 1119  $\text{cm}^{-1}$ ; NOESY cross peaks, H-4/H-10 $\beta$ , H<sub>3</sub>-24; H-19/H-10 $\alpha$ , H<sub>3</sub>-23; H-21/H<sub>3</sub>-24; HRESIMS [M + Na]<sup>+</sup>  $m/z$  470.2035 (calcd for C<sub>26</sub>H<sub>29</sub>N<sub>3</sub>NaO<sub>4</sub>, 470.2056).

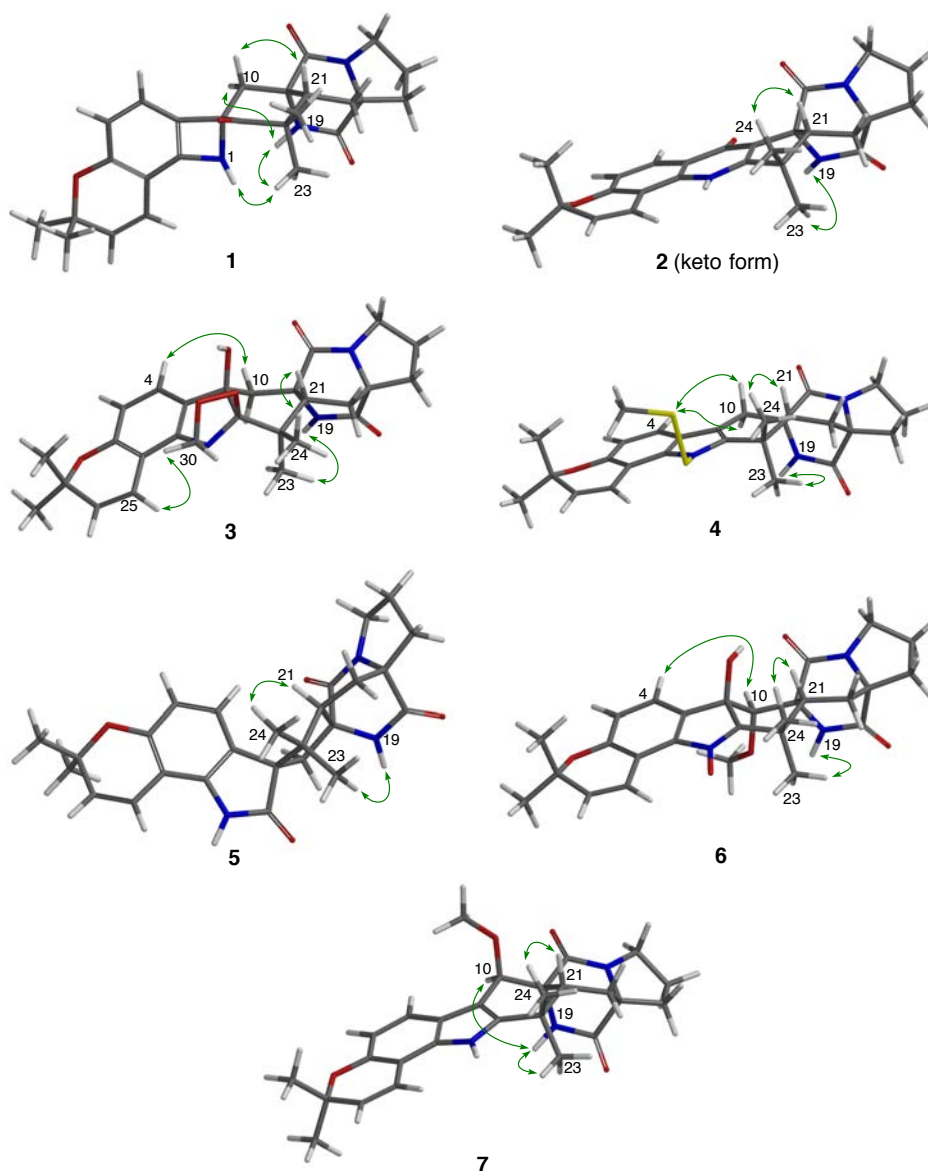
**Taichunamide F (6):**  $[\alpha]_D^{20}$  -3.4 (*c* 0.041, MeOH); UV (MeOH)  $\lambda_{\max}$  (log  $\epsilon$ ) 202 nm (4.2), 244 nm (sh, 3.8), 260 nm (3.8), 302 nm (3.5); ECD (200  $\mu$ M, MeOH)  $\lambda_{\max}$  ( $\Delta\epsilon$ ) 206 (-4.7), 222 (4.4), 241 (-3.4) nm; NMR data (DMSO-*d*<sub>6</sub>), see Table S7; IR (film)  $\nu_{\max}$  3363, 2920, 2851, 1680, 1557, 1457, 1391, 1272, 1166, 1114, 1083, 1025, 905, 825, 720, 515  $\text{cm}^{-1}$ ; NOESY cross peaks, H-4/H-10; H-19/ H<sub>3</sub>-23; H-21/H<sub>3</sub>-24; HRESIMS  $[\text{M} + \text{H}]^+$  *m/z* 494.2295 (calcd for C<sub>27</sub>H<sub>32</sub>N<sub>3</sub>O<sub>6</sub>, 494.2291).

**Taichunamide G (7):**  $[\alpha]_D^{20}$  +26 (*c* 0.84, MeOH); UV (MeOH)  $\lambda_{\max}$  (log  $\epsilon$ ) 202 nm (4.3), 238 nm (4.2), 278nm (3.7), 286 nm (3.7), 328 nm (3.5), 342 nm (3.5); ECD (94.3  $\mu$ M, MeOH)  $\lambda_{\max}$  ( $\Delta\epsilon$ ) 208 (-9.3), 228 (3.6), 246 (-4.5) nm; NMR data (DMSO-*d*<sub>6</sub>), see Table S8; IR (film)  $\nu_{\max}$  3273, 2922, 2854, 1688, 1673, 1654, 1456, 1411, 1261, 1185, 1117, 1058, 942, 898, 807, 739  $\text{cm}^{-1}$ ; NOESY cross peaks, H-19/H-10 and H<sub>3</sub>-23; H-21/H<sub>3</sub>-24; HRESIMS  $[\text{M} + \text{Na}]^+$  *m/z* 484.2240 (calcd for C<sub>27</sub>H<sub>31</sub>N<sub>3</sub>O<sub>4</sub>Na, 484.2212).

#### Structure determination of 5 and 7.

The planer structure of taichunamide E (**5**) was identical to those of (+)-versicolamide B (**14**) and (+)-notoamide B (**15**), which was established by HRESIMS and NMR experiments (Table S6). ECD spectrum showed 3*R*,11*S*,17*S*-configuration, and NOE correlations, H-19/H<sub>3</sub>-23 and H-21/H<sub>3</sub>-24 (Figure S1), showed *anti*-configuration for H-19/H-21, i.e. 21*R*-configuration. Therefore, **5** was determined to be 3-epimer of versicolamide B, which was corresponded to 21-epimer of notoamide B.

The molecular formula C<sub>27</sub>H<sub>31</sub>N<sub>3</sub>O<sub>4</sub> of **7** was established by HRESIMS, a CH<sub>2</sub> unit more than notoamide V (**9**). <sup>1</sup>H and <sup>13</sup>C NMR spectra of taichunamide G (**7**) (Table S8) were similar to those of **9** except for the presence of a methoxyl group ( $\delta_{\text{H}}$  3.42,  $\delta_{\text{C}}$  57.9). HMBC correlation from the methoxyl hydrogens to C-10 ( $\delta_{\text{C}}$  76.4) indicated that a hydroxy group in **11** was replaced with a methoxyl group in **7**. NOE correlations, H-19/H-10, H-21/H<sub>3</sub>-24 ( $\delta$  1.28) and H-19/H<sub>3</sub>-23 ( $\delta$  1.20) (Figure S1), and the positive cotton effect at 225nm showed 10*R*,11*R*,17*S*,21*R*-configuration.



**Figure S1.** Key NOE correlations of 1-7.

**Conformational analyses of 3, 4, 5, and 7 and ECD calculations for 3 and 6.**

Conformational searches were performed with Spartan'14 (Ver. 1.1.8 by Wavefunction Inc., Irvine, CA) using a commercially available PC (operating system: Windows 7 Professional SP1 64-bit, CPU: QuadCore Core i7-3770 processor 3.40 GHz, RAM 8 GB) and DFT calculations were conducted with Gaussian09 (Revision D.01 by Gaussian, Wallingford, CT)<sup>[1]</sup> with a PC (Operating System: CentOS a Linux, CPU: Intel Xeon E5-2603 v3 processors 1.60 GHz, RAM 32 GB). The input structures were constructed on a graphical user interface considering the absolute configurations of interest, and were subjected to conformational searches with Spartan'14 using MMFF<sup>[2]</sup> as the force field, in which the number of initial conformers was set to 10,000. The obtained most stable 100 conformers were further

optimized by the Hartree-Fock (HF) method with 3-21G. The resultant conformers of >1% were finally optimized by the density functional theory (DFT) method with B3LYP/6-31G\*, giving stable conformers for further simulations.

For the purpose of ECD calculations for **3** and **6**, the dominant conformers obtained were chosen to cover >99% of the population from the Boltzmann's law. Time-dependent density functional theory (TDDFT) calculations at the B3LYP/6-31G\* level were performed for these conformers, leading to rotational strengths for 29 excited states. These rotational strengths were converted into Gaussian curves (bandwidth  $\sigma = 3300 \text{ cm}^{-1}$ ) for the ECD spectrum of each conformer, in which no wavelength correction was employed because the corresponding electronic transitions led to the reproduction of the UV absorbance peak at 202 nm and the diagnostic positive ECD peak at 225 nm was also reasonably reproduced. These spectra were then correctively summed to give the resultant theoretical ECD spectrum of **3** and **6** (Figures 3b and 4b). As an accuracy evaluation, TDDFT calculations were also performed with the other hybrid functionals CAM-B3LYP and BHandHLYP in the same manner as described above, and resulted in the same conclusion in the configuration assignment.

#### Measurement of Proteasome Inhibitory Activity.

The chymotrypsin-like activity of the proteasome was measured with the human 20S proteasome from erythrocytes (Boston Biochem, Inc., E-360) and the fluorogenic substrate Suc-Leu-Leu-Val-Tyr-MCA (Peptide Institute, Inc).<sup>[3]</sup>

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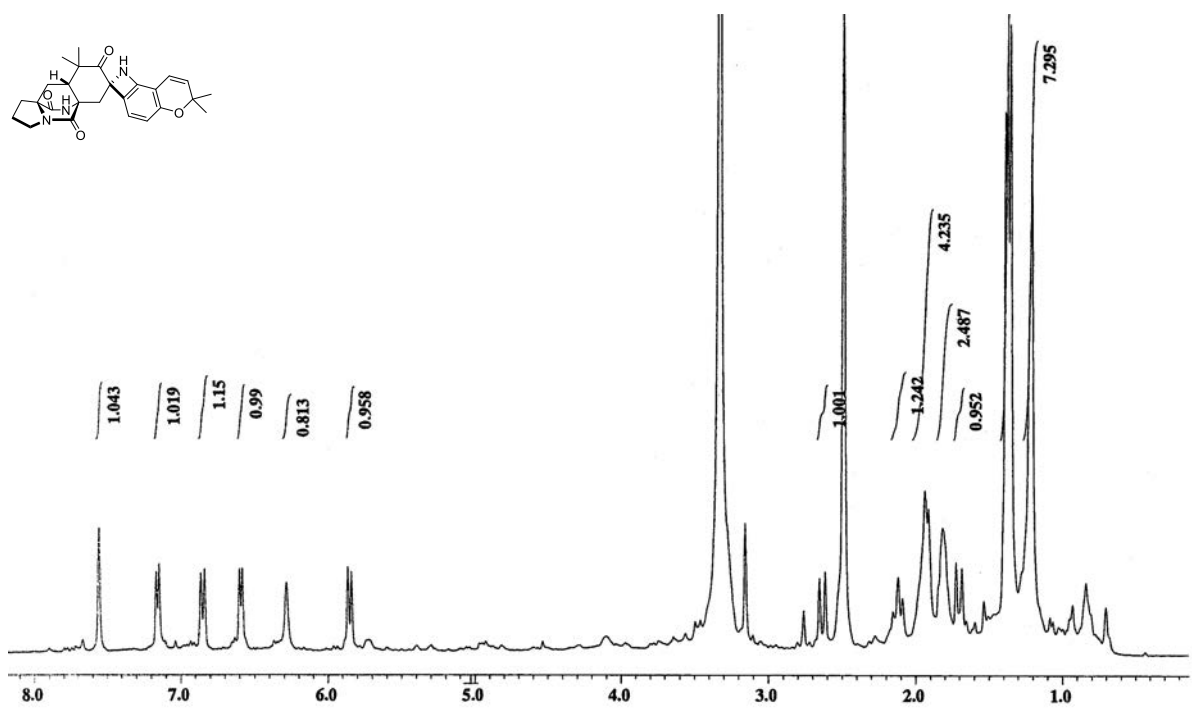


Figure S2. <sup>1</sup>H NMR spectrum of 1 in DMSO-*d*<sub>6</sub>.

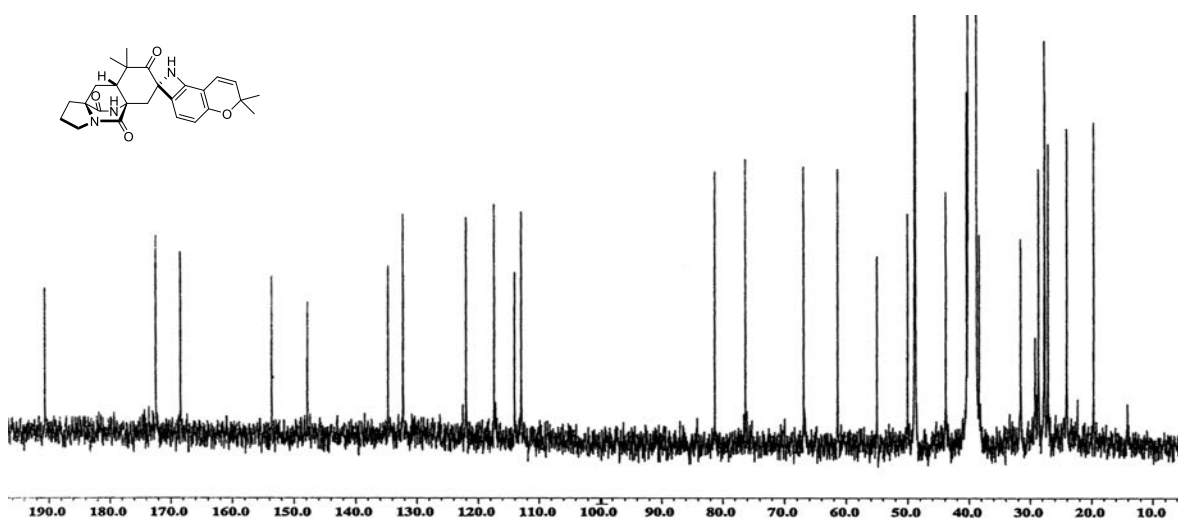


Figure S3. <sup>13</sup>C NMR spectrum of 1 in DMSO-*d*<sub>6</sub>.

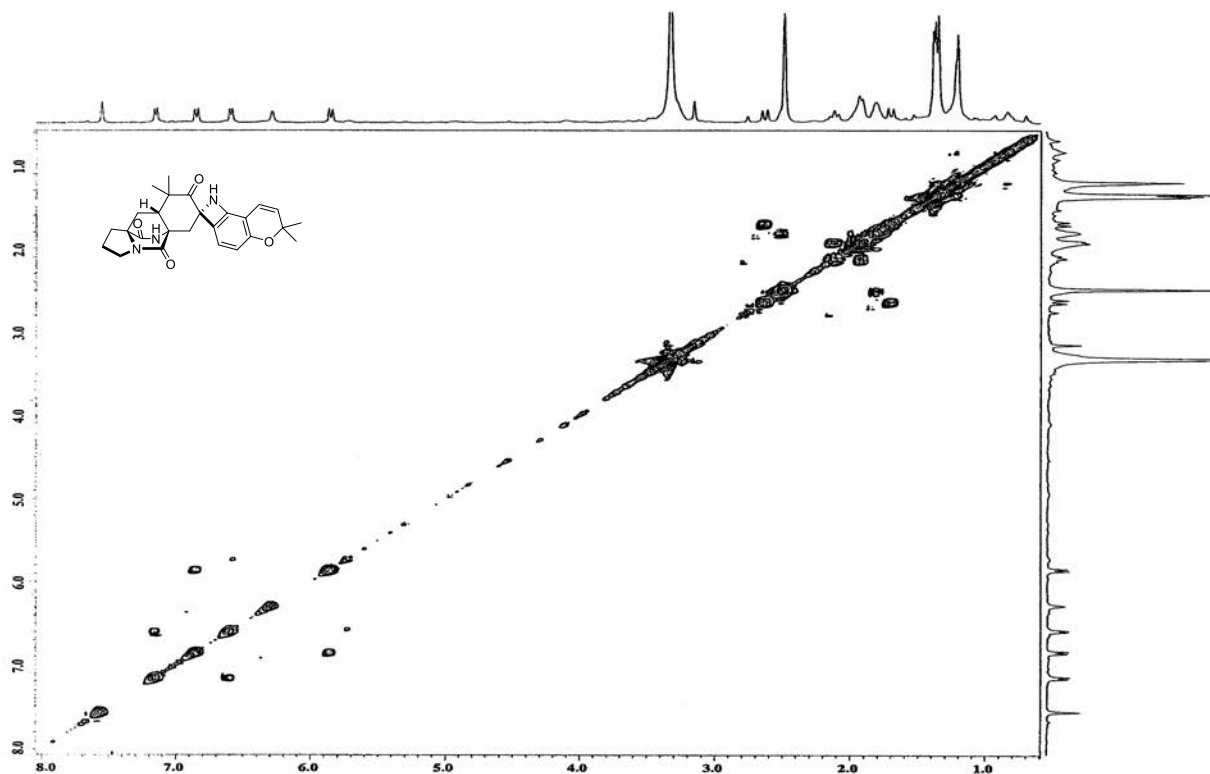


Figure S4. COSY spectrum of **1** in DMSO-*d*<sub>6</sub>.

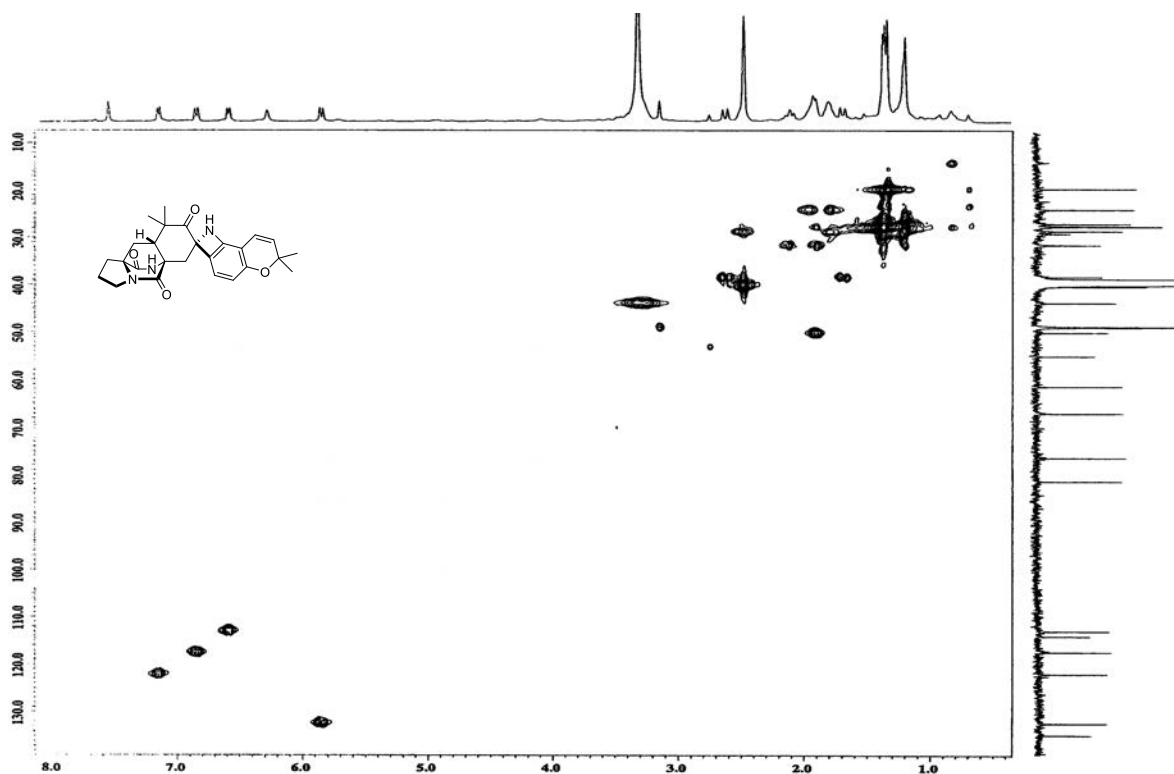


Figure S5. HMQC spectrum of **1** in DMSO-*d*<sub>6</sub>.

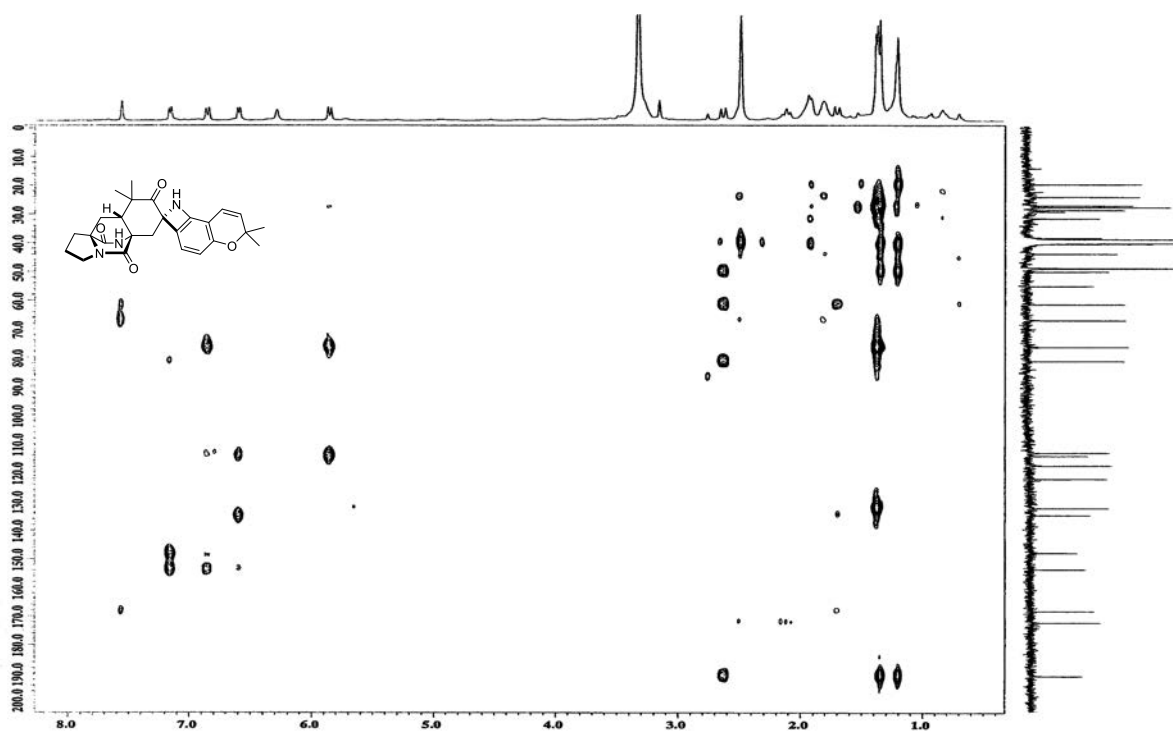


Figure S6. HMBC spectrum of **1** in DMSO- $d_6$ .

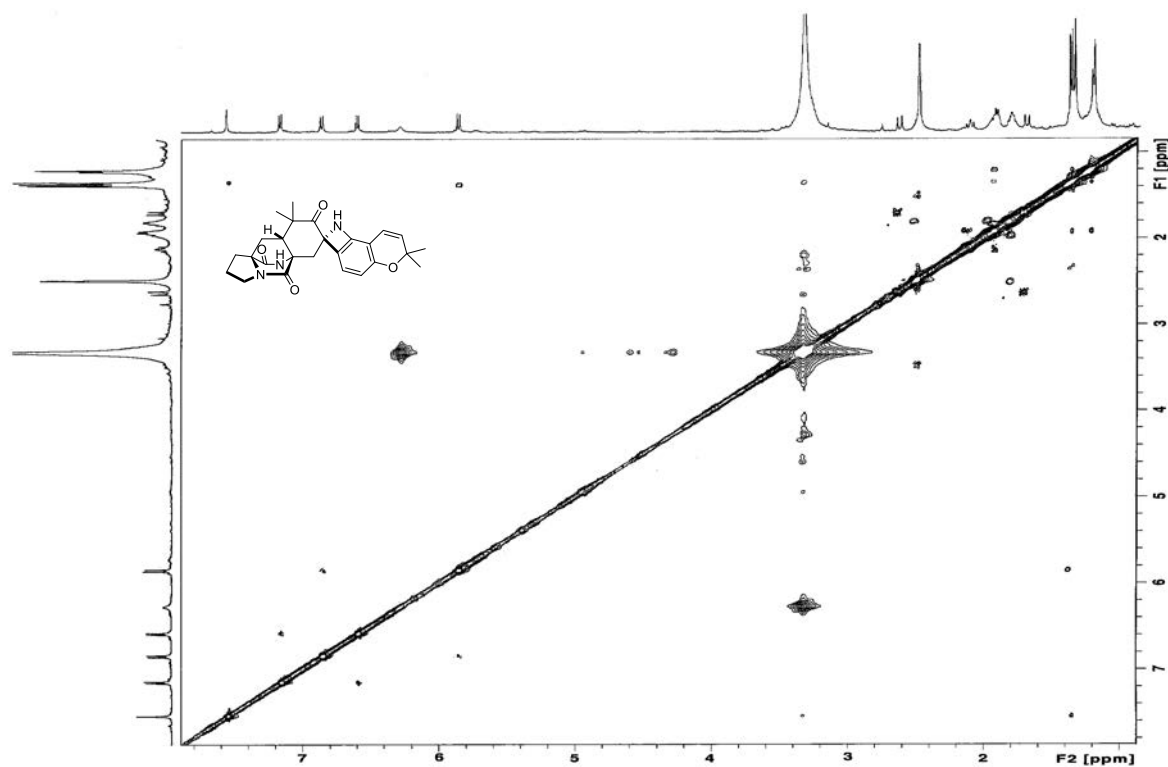


Figure S7. NOESY spectrum of **1** in DMSO- $d_6$ .

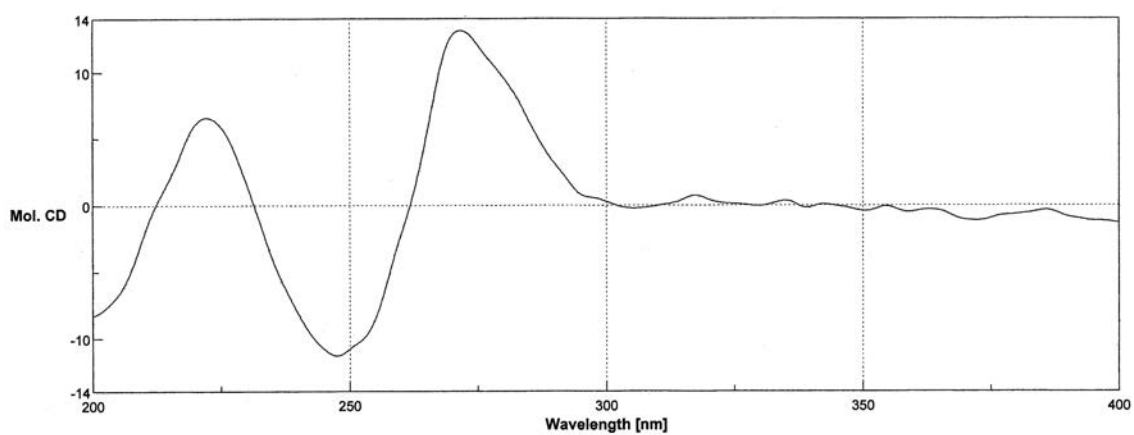


Figure S8. ECD spectrum of **1** in MeOH.

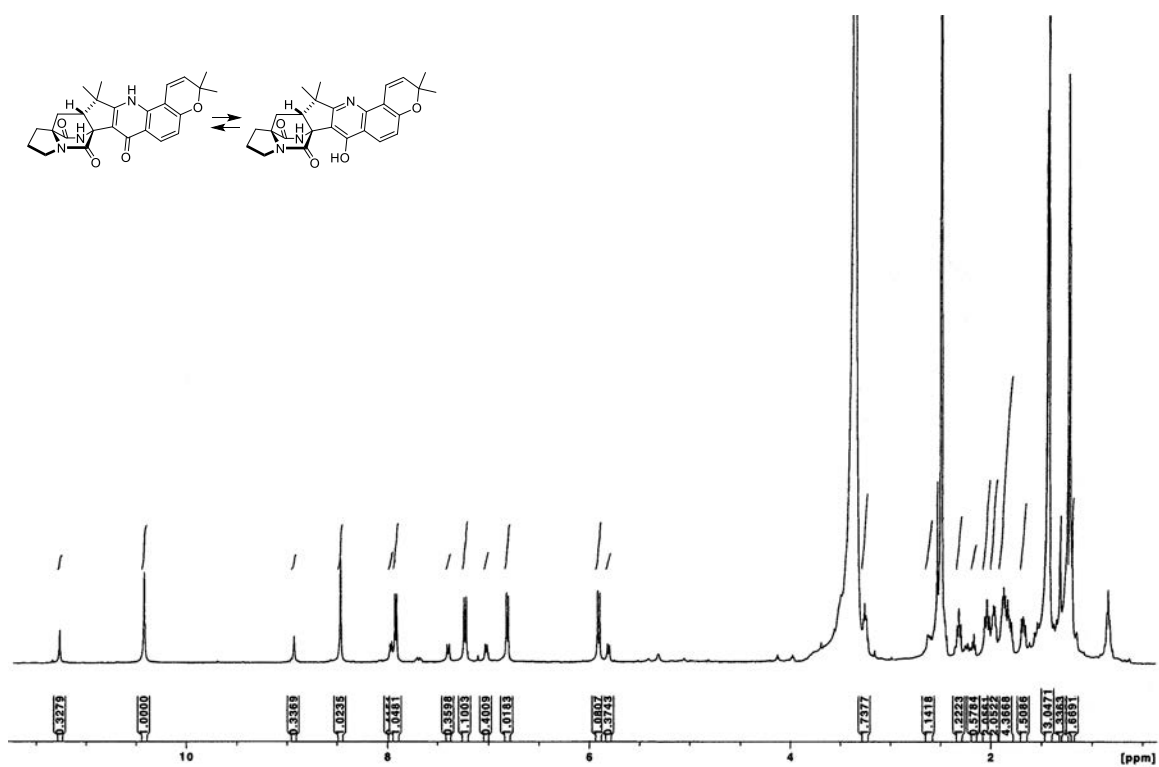


Figure S9.  $^1\text{H}$  NMR spectrum of **2** in  $\text{DMSO-}d_6$ .

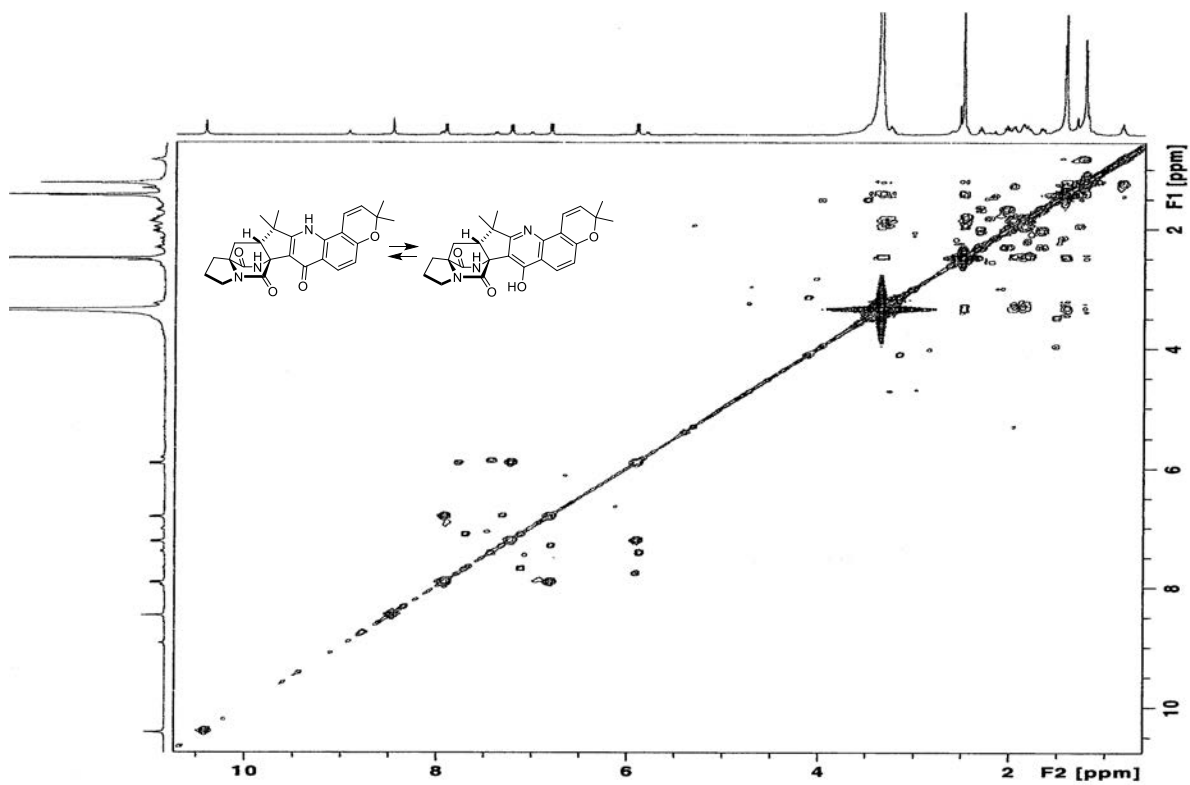


Figure S10. COSY spectrum of 2 in DMSO- $d_6$ .

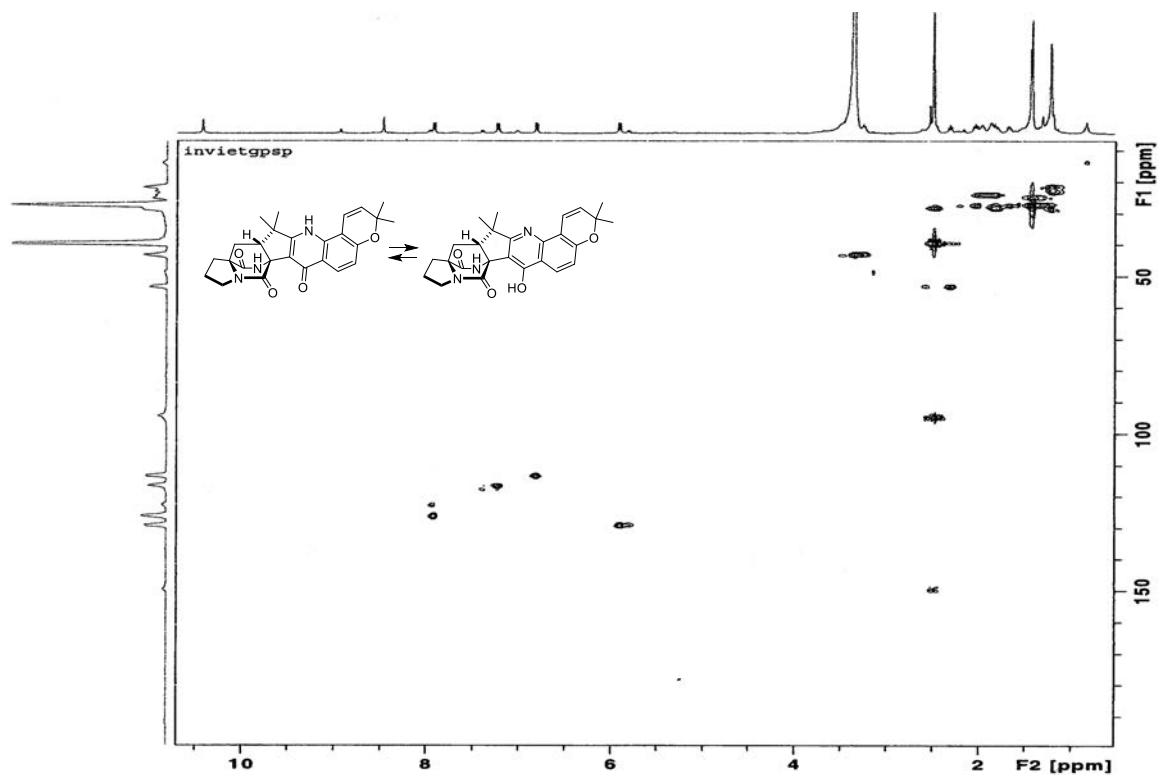


Figure S11. HSQC spectrum of 2 in DMSO- $d_6$ .

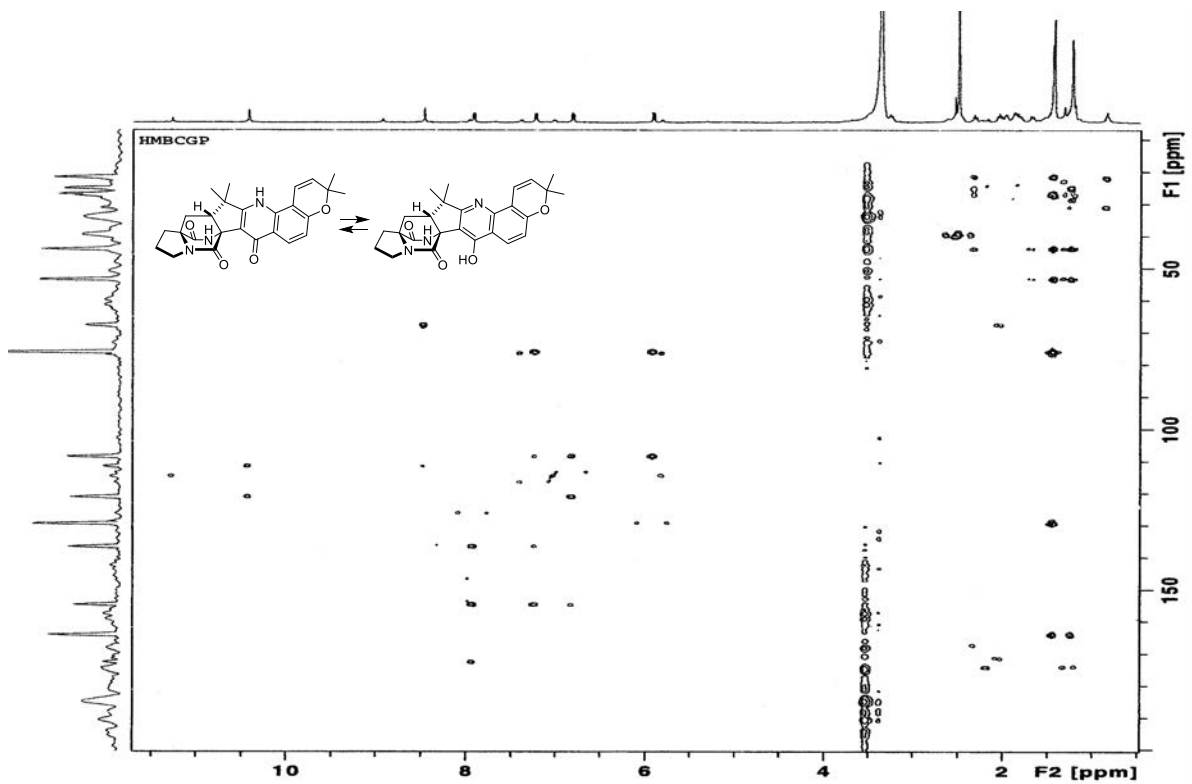


Figure S12. HMBC spectrum of 2 in DMSO- $d_6$ .

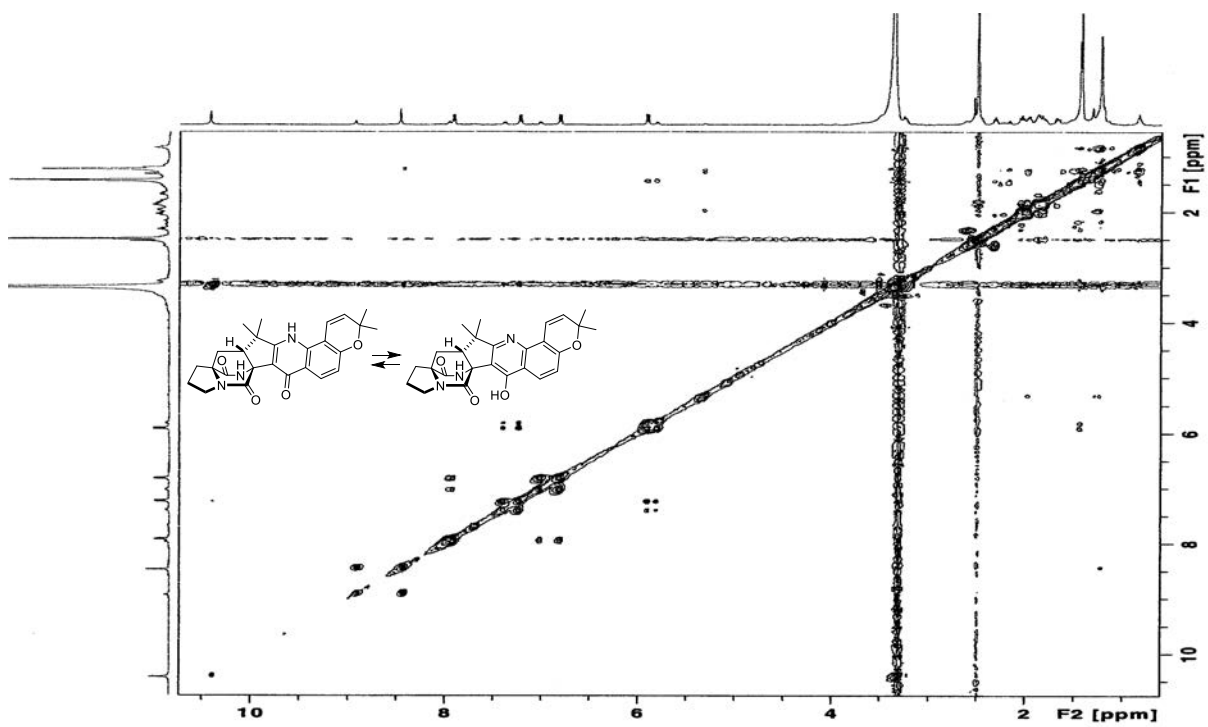


Figure S13. NOESY spectrum of 2 in DMSO- $d_6$ .

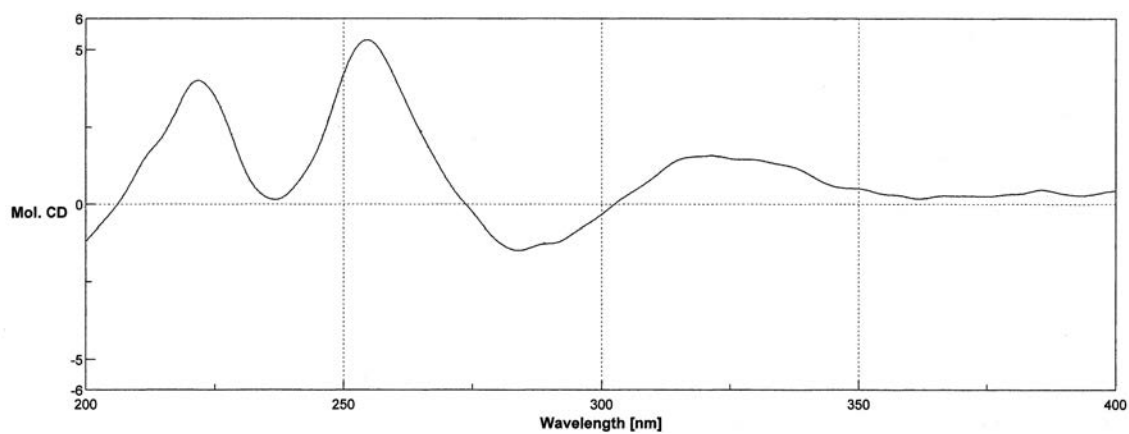


Figure S14. ECD spectrum of **2** in MeOH.

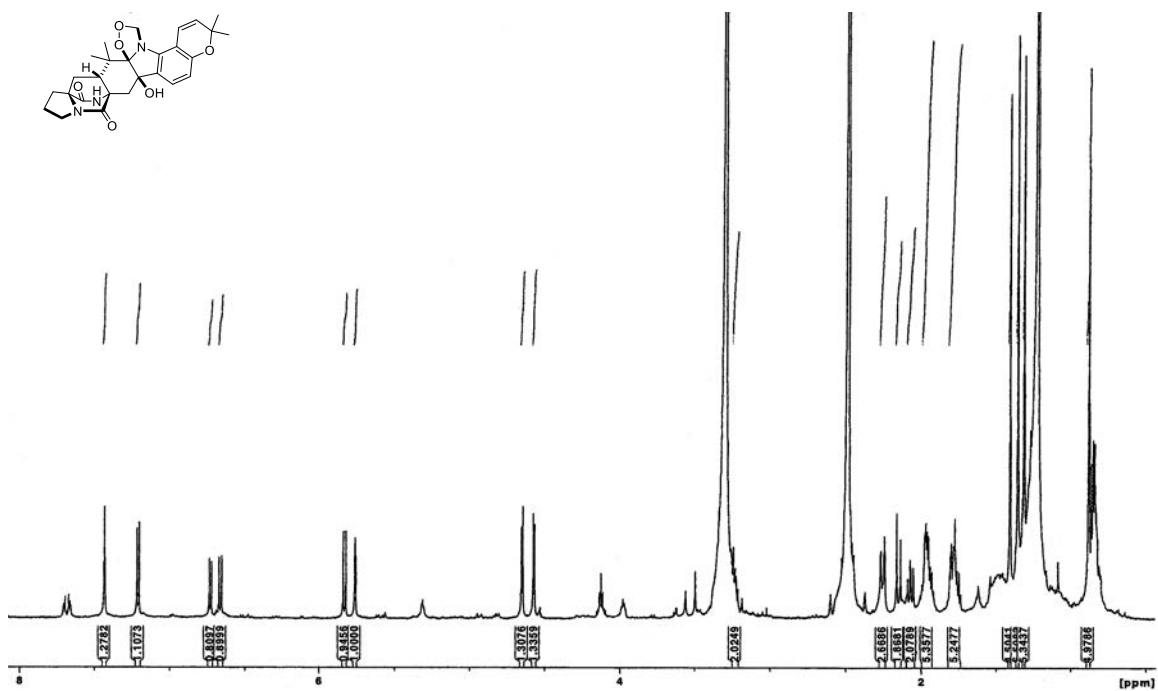


Figure S15. <sup>1</sup>H NMR spectrum of **3** in DMSO-*d*<sub>6</sub>.

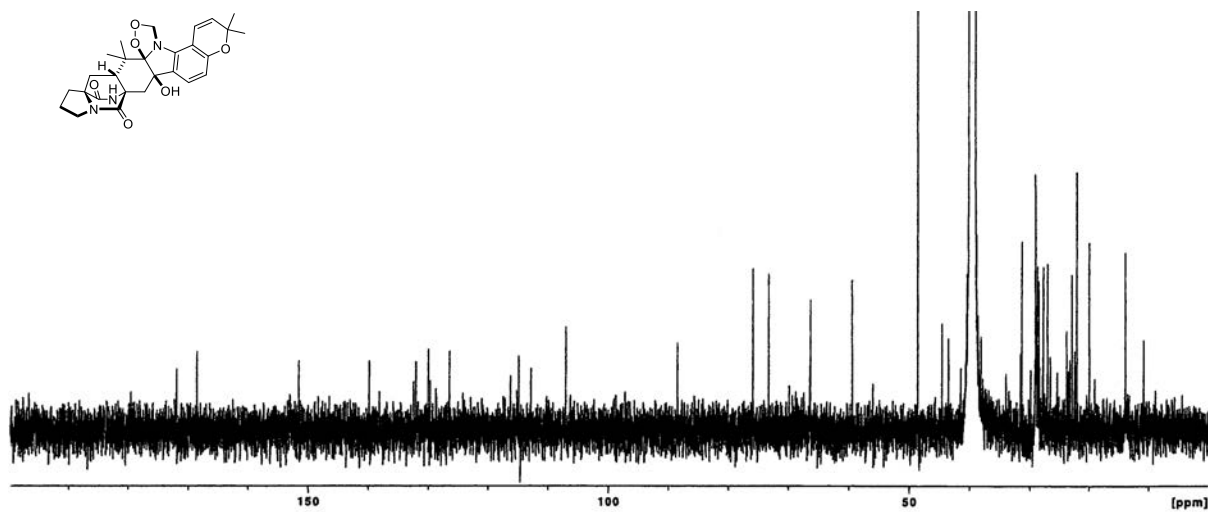


Figure S16.  $^{13}\text{C}$  NMR spectrum of 3 in  $\text{DMSO-}d_6$  for 600 MHz.

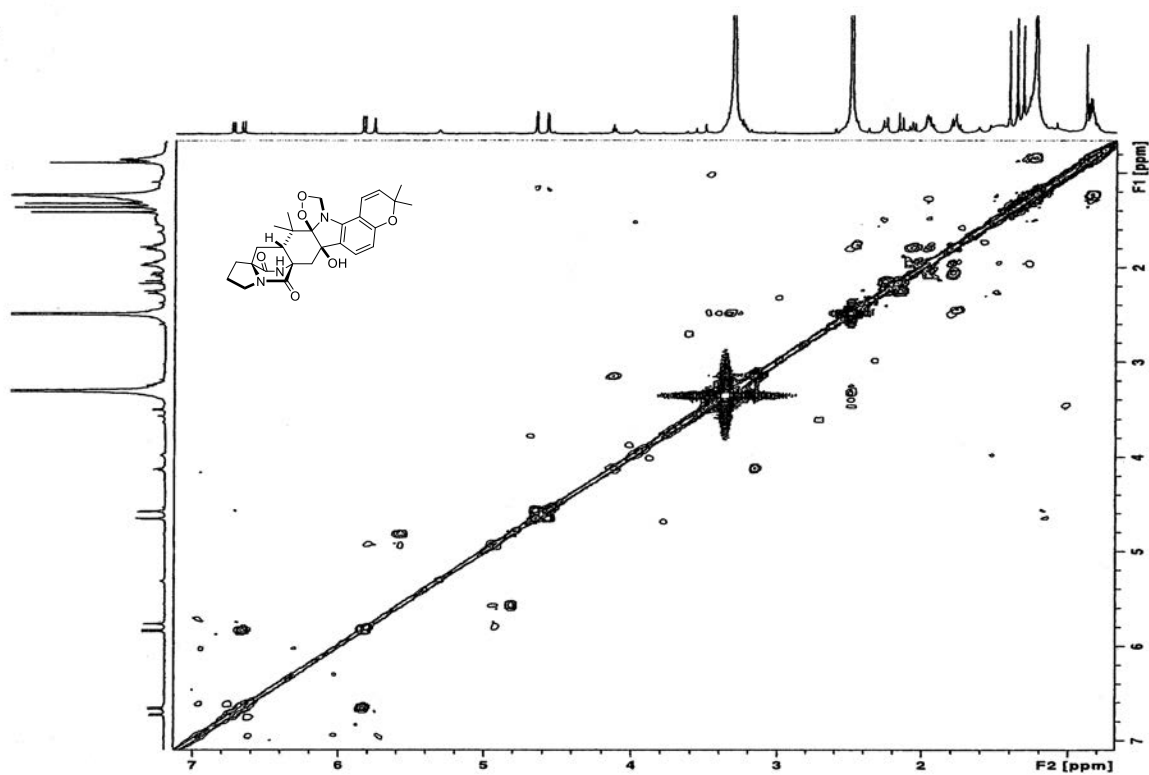


Figure S17. COSY spectrum of 3 in  $\text{DMSO-}d_6$ .



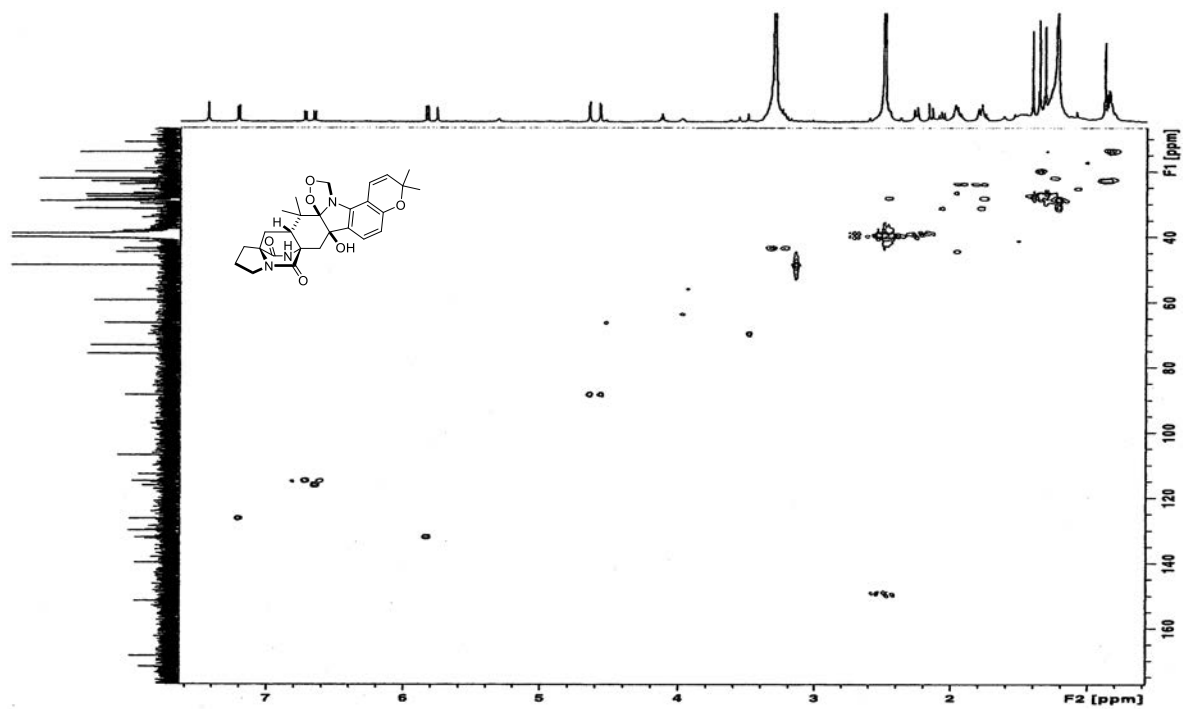


Figure S18. HSQC spectrum of 3 in DMSO- $d_6$ .

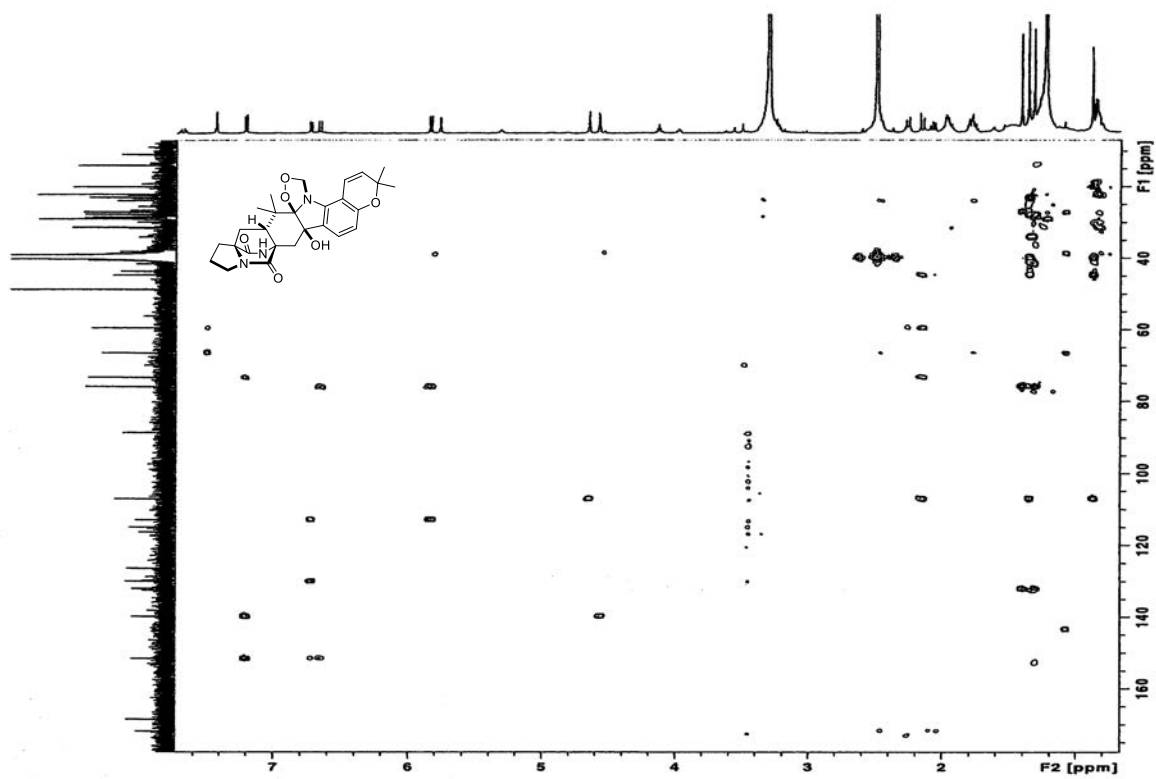


Figure S19. HMBC spectrum of 3 in DMSO- $d_6$ .

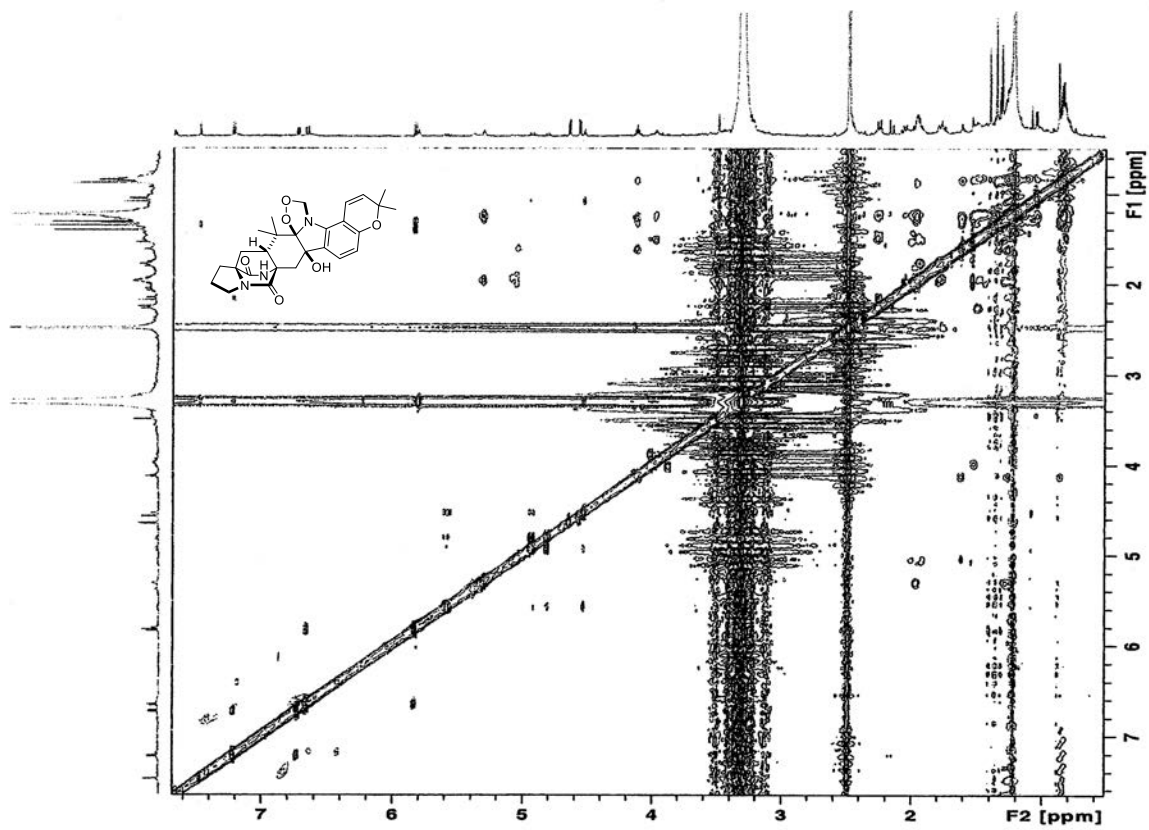


Figure S20. NOESY spectrum of 3 in DMSO-*d*<sub>6</sub>.

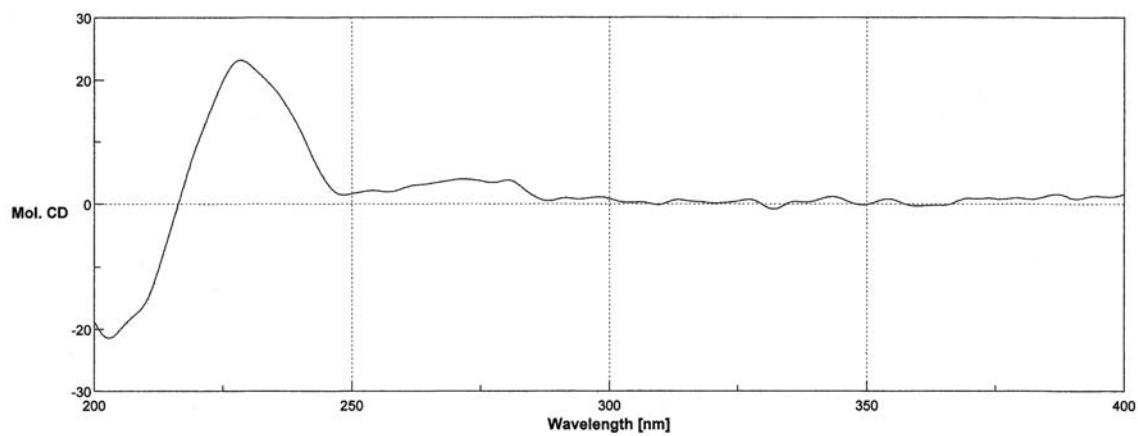


Figure S21. ECD spectrum of 3 in MeOH.

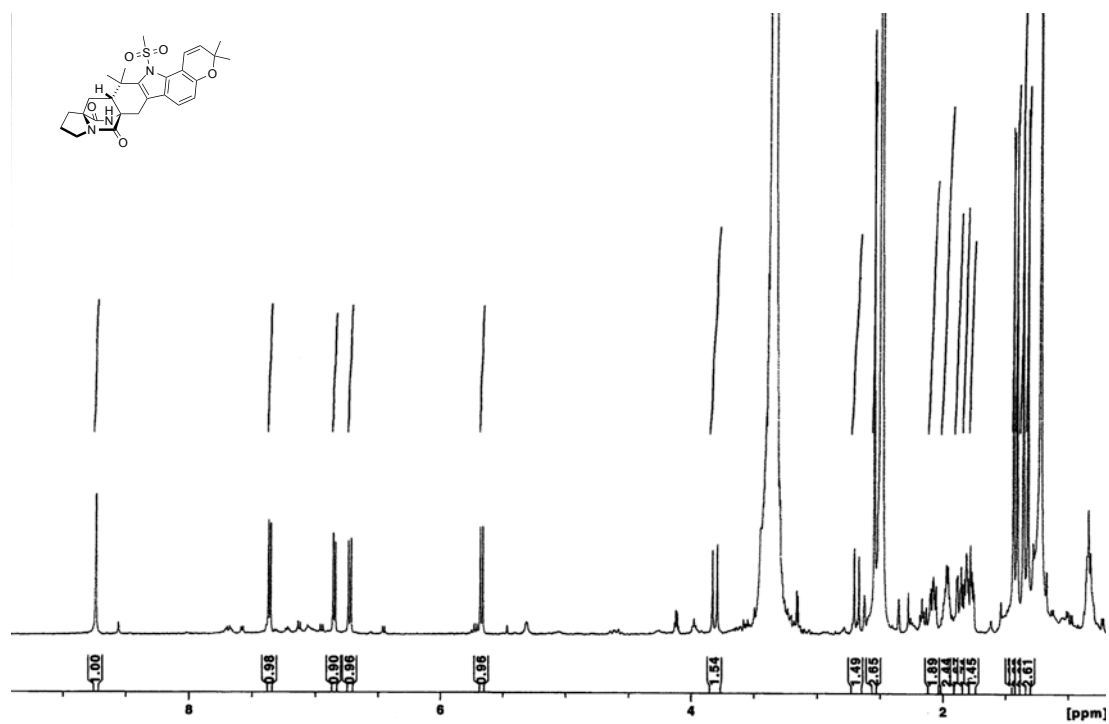


Figure S22. <sup>1</sup>H NMR spectrum of 4 in DMSO-*d*<sub>6</sub>.

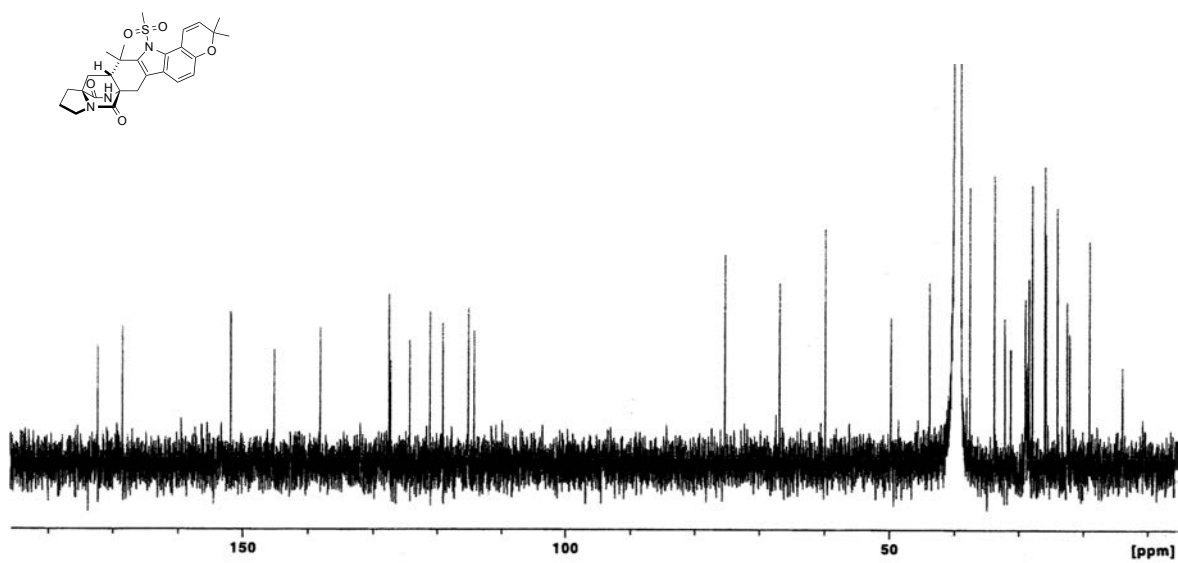


Figure S23. <sup>13</sup>C NMR spectrum of 4 in DMSO-*d*<sub>6</sub>.

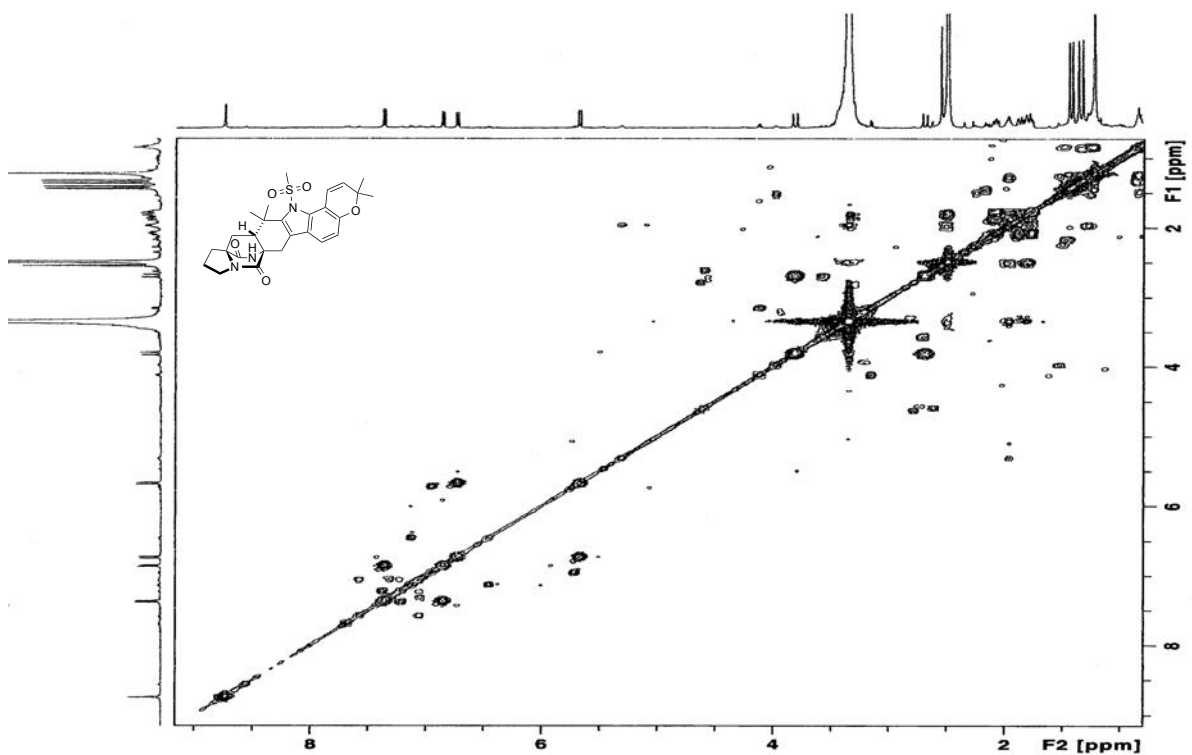


Figure S24. COSY spectrum of 4 in DMSO-*d*<sub>6</sub>.

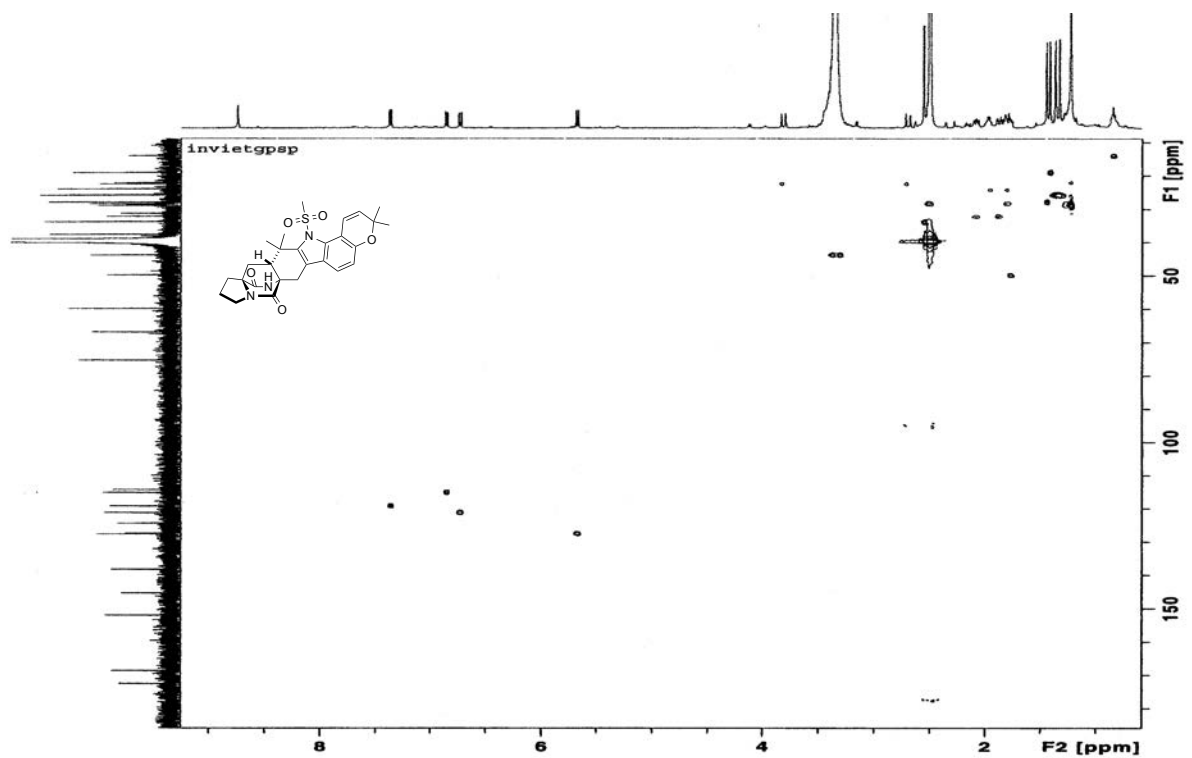


Figure S25. HSQC spectrum of 4 in DMSO-*d*<sub>6</sub>.

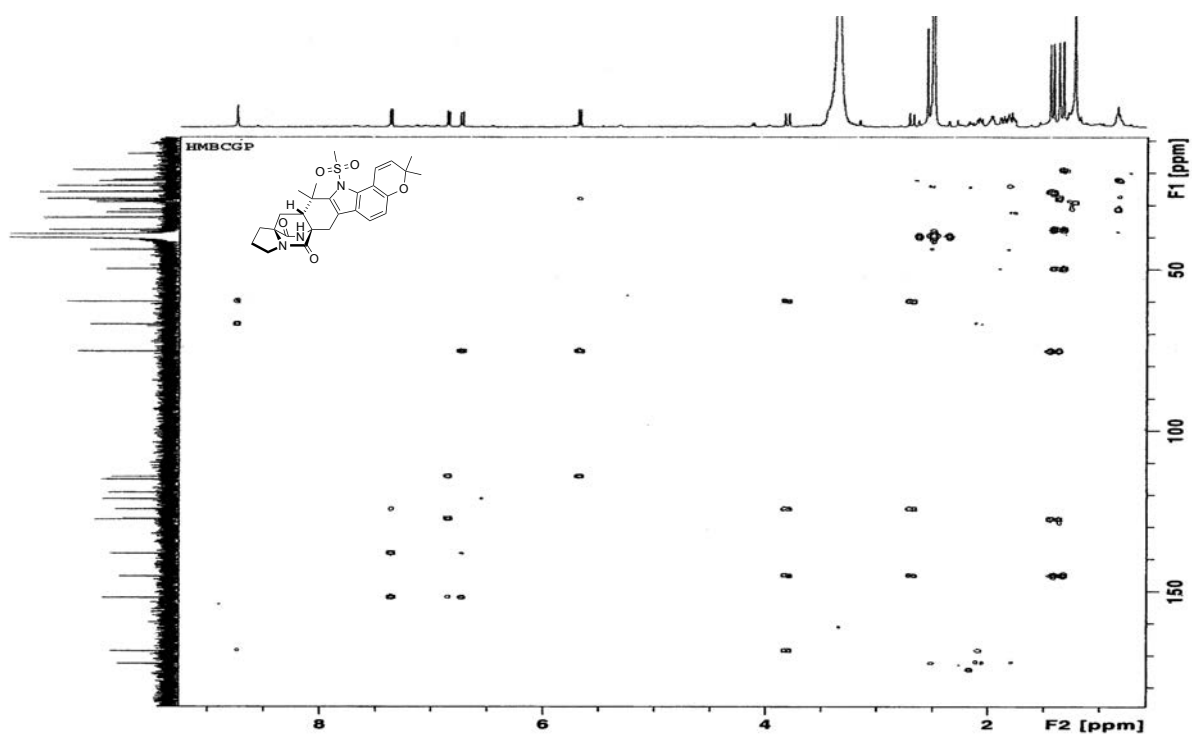


Figure S26. HMBC spectrum of 4 in DMSO-*d*<sub>6</sub>.

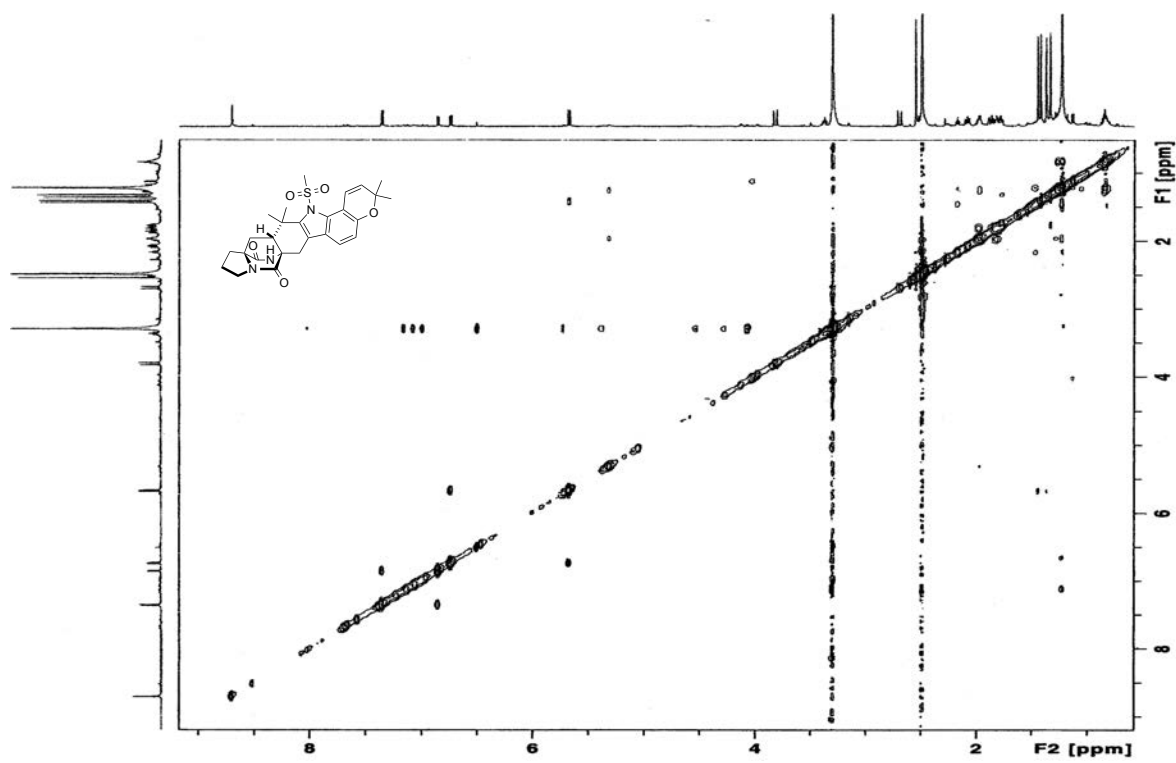


Figure S27. NOESY spectrum of 4 in DMSO-*d*<sub>6</sub>.

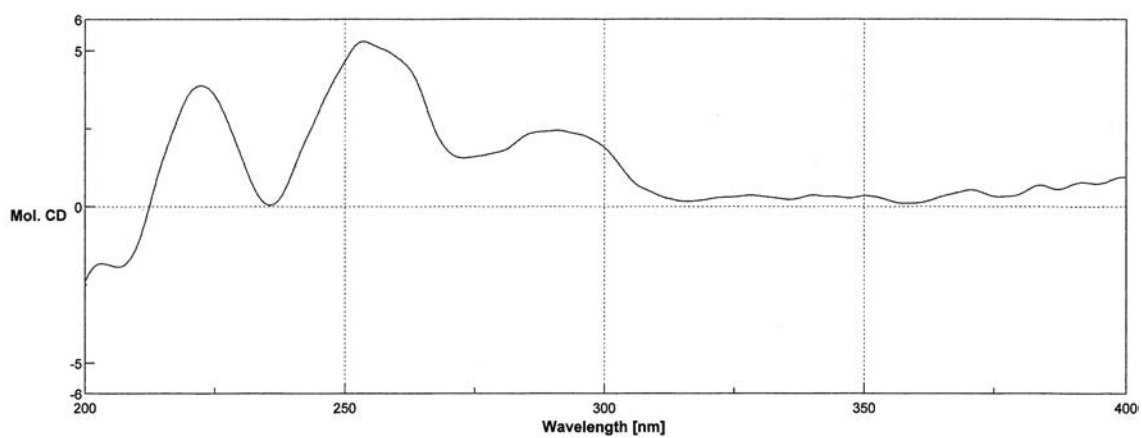


Figure S28. ECD spectrum of 4 in MeOH.

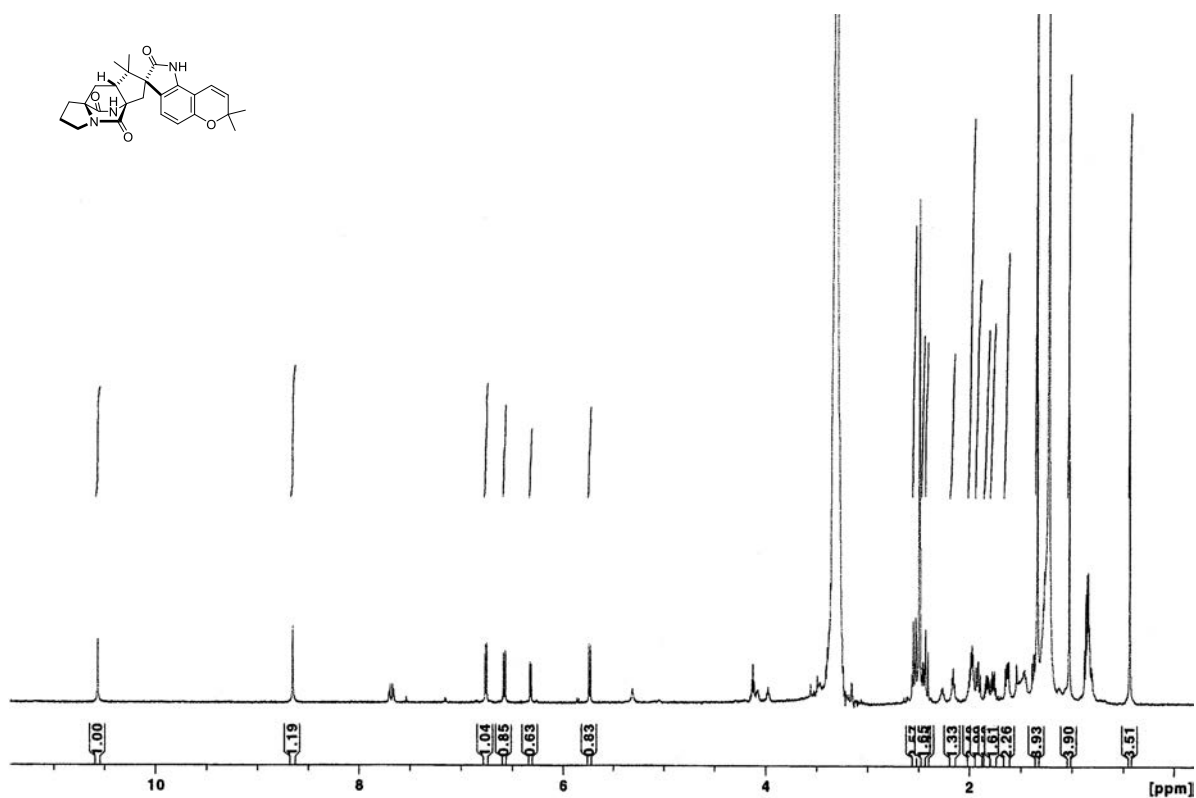


Figure S29.  $^1\text{H}$  NMR spectrum of 5 in  $\text{DMSO-}d_6$ .

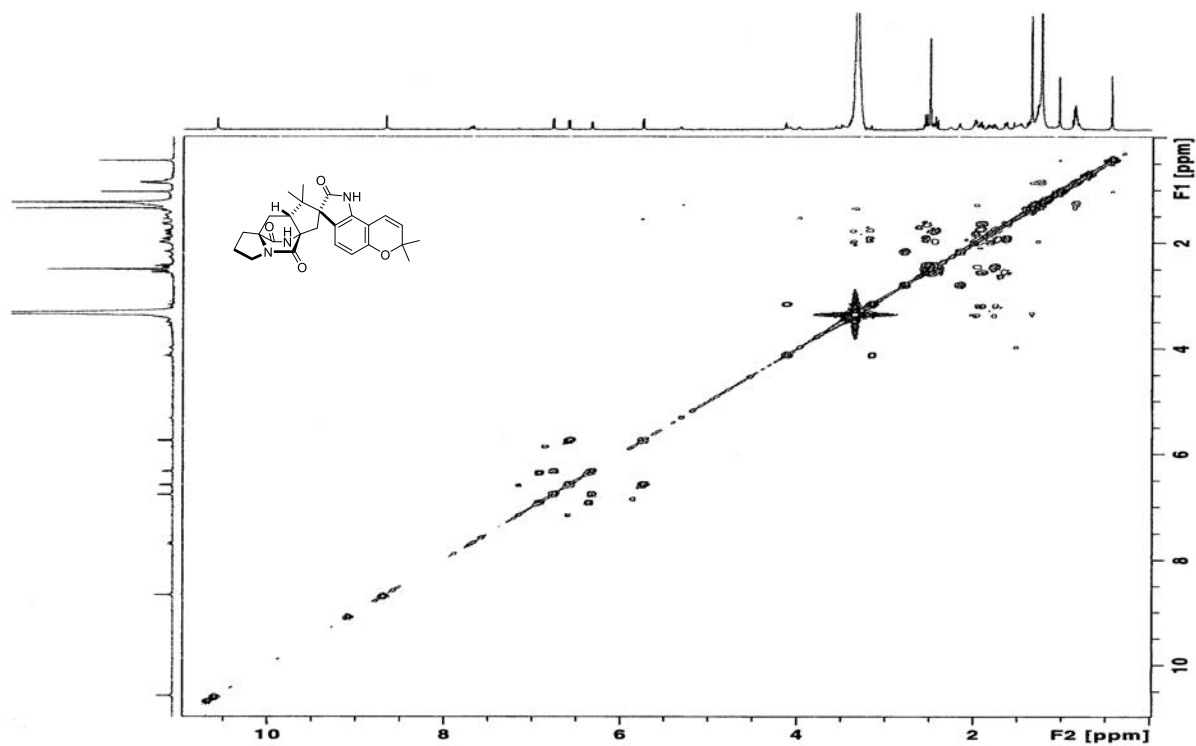


Figure S30. COSY spectrum of **5** in DMSO- $d_6$

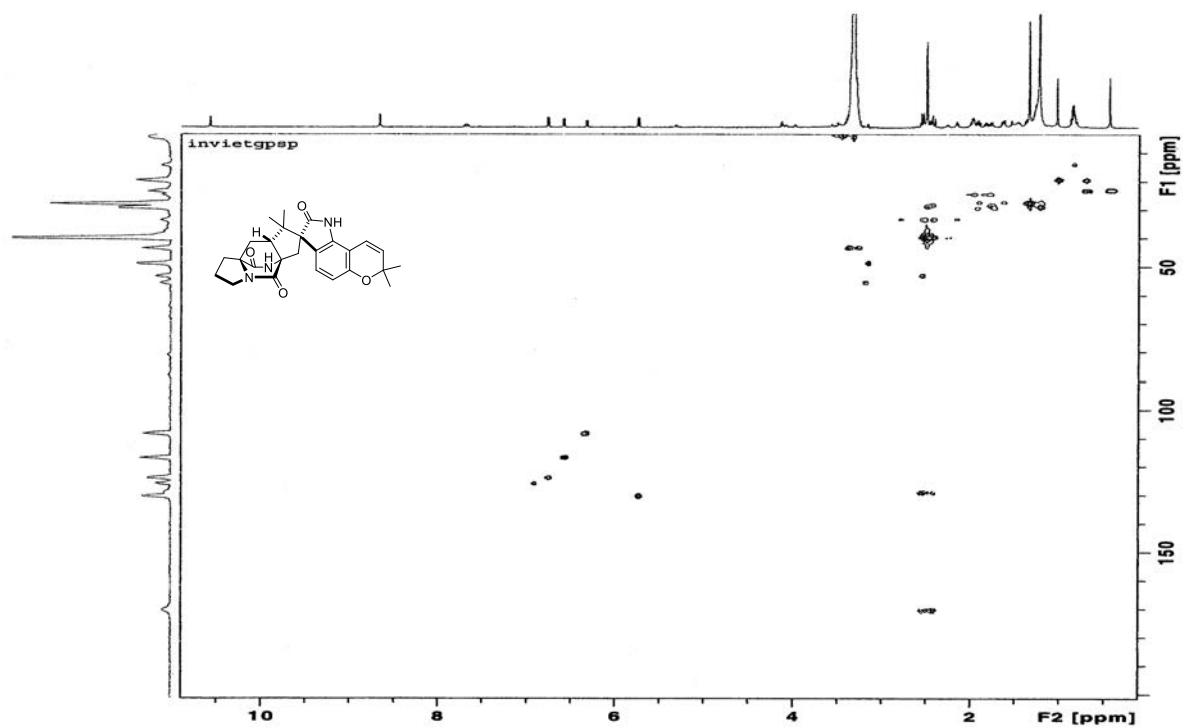


Figure S31. HSQC spectrum of **5** in DMSO- $d_6$ .

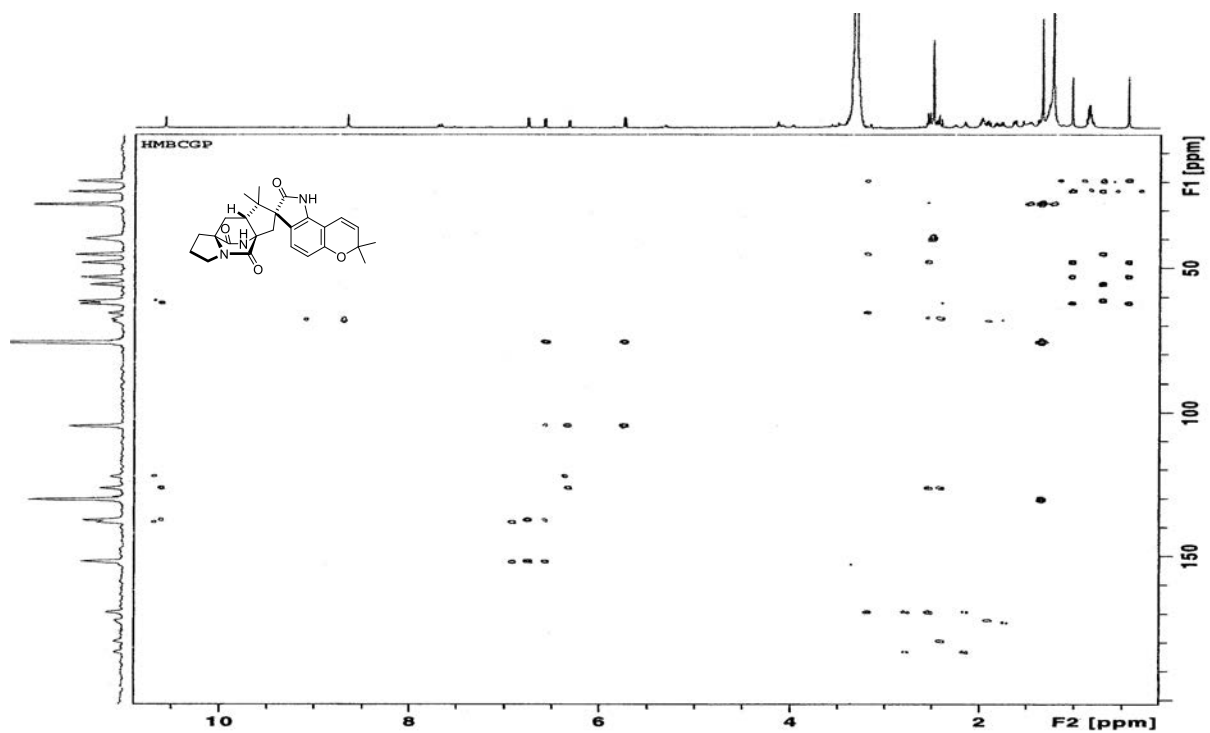


Figure S32. HMBC spectrum of 5 in DMSO- $d_6$ .

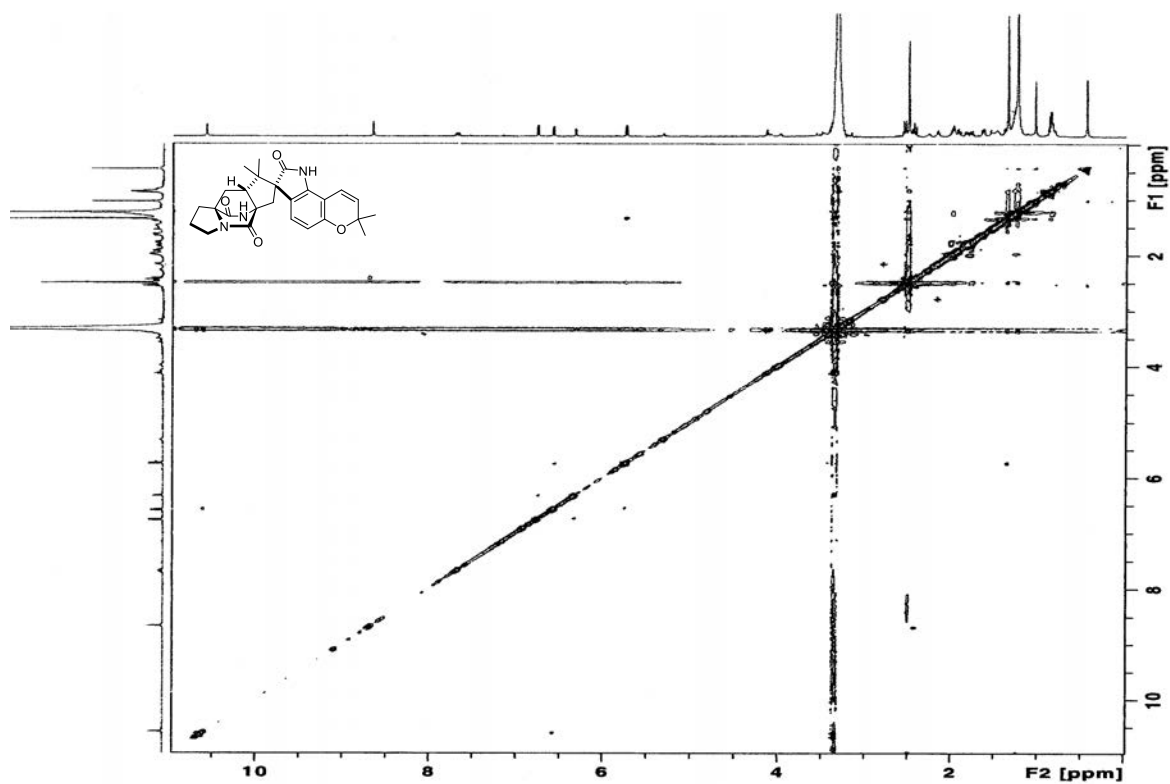


Figure S33. NOESY spectrum of 5 in DMSO- $d_6$ .



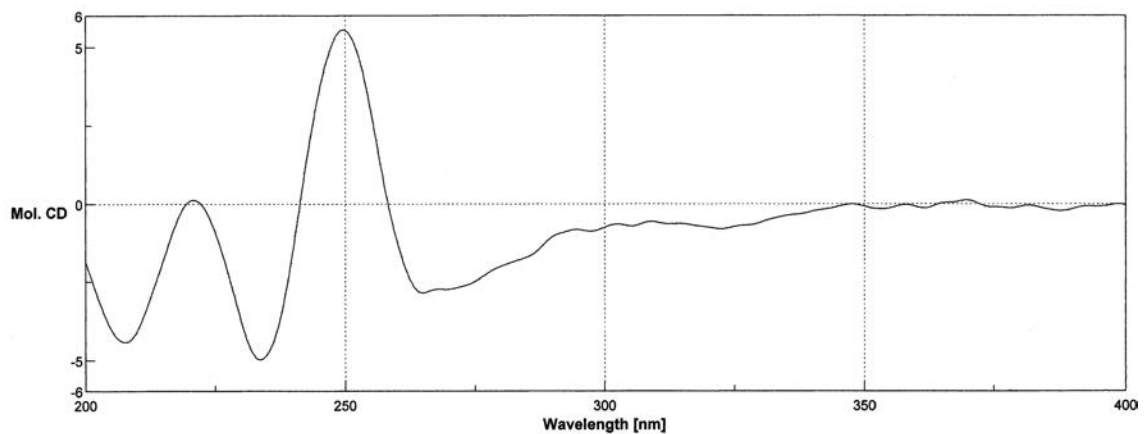


Figure S34. ECD spectrum of **5** in MeOH.

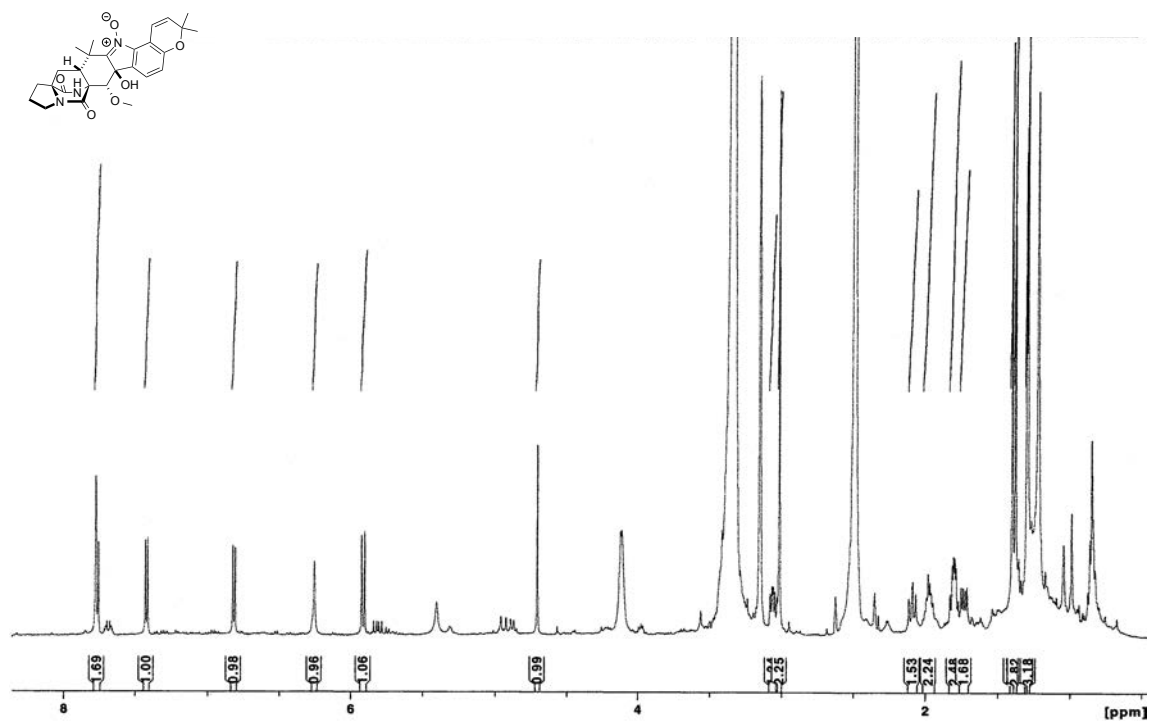


Figure S35.  $^1\text{H}$  NMR spectrum of **6** in  $\text{DMSO-}d_6$ .

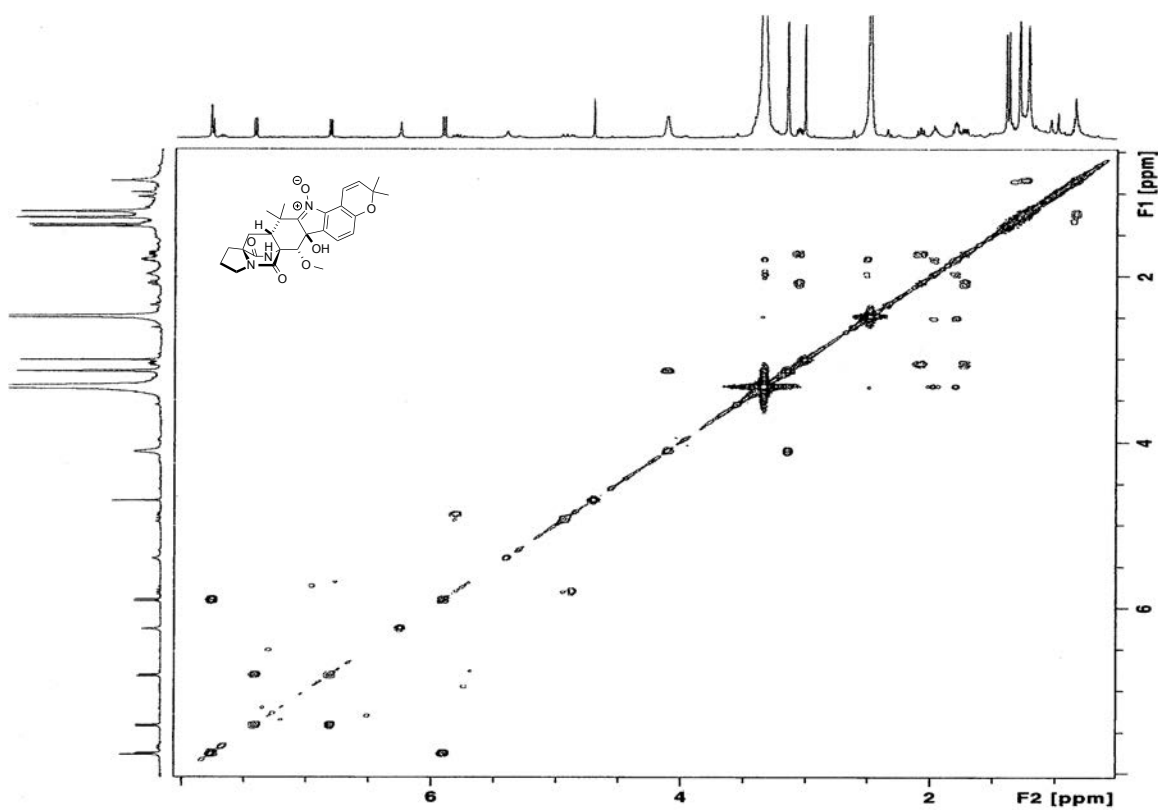


Figure S36. COSY spectrum of 6 in DMSO- $d_6$ .

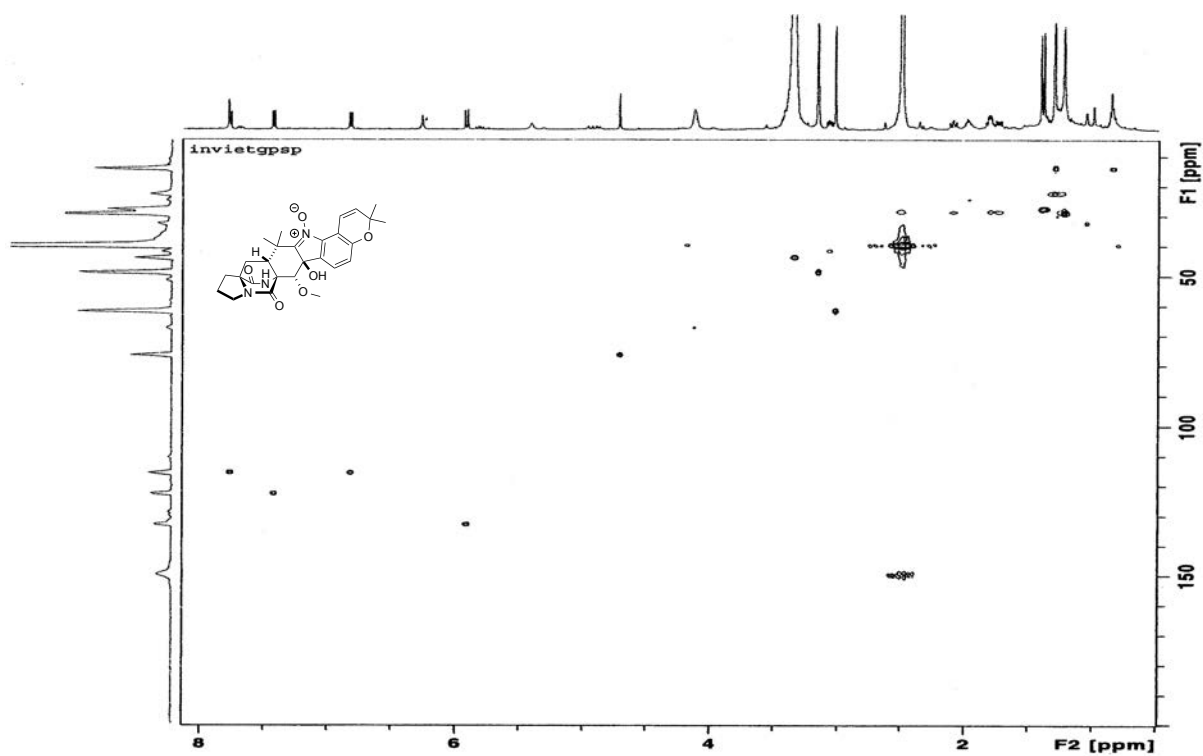


Figure S37. HSQC spectrum of 6 in DMSO- $d_6$ .

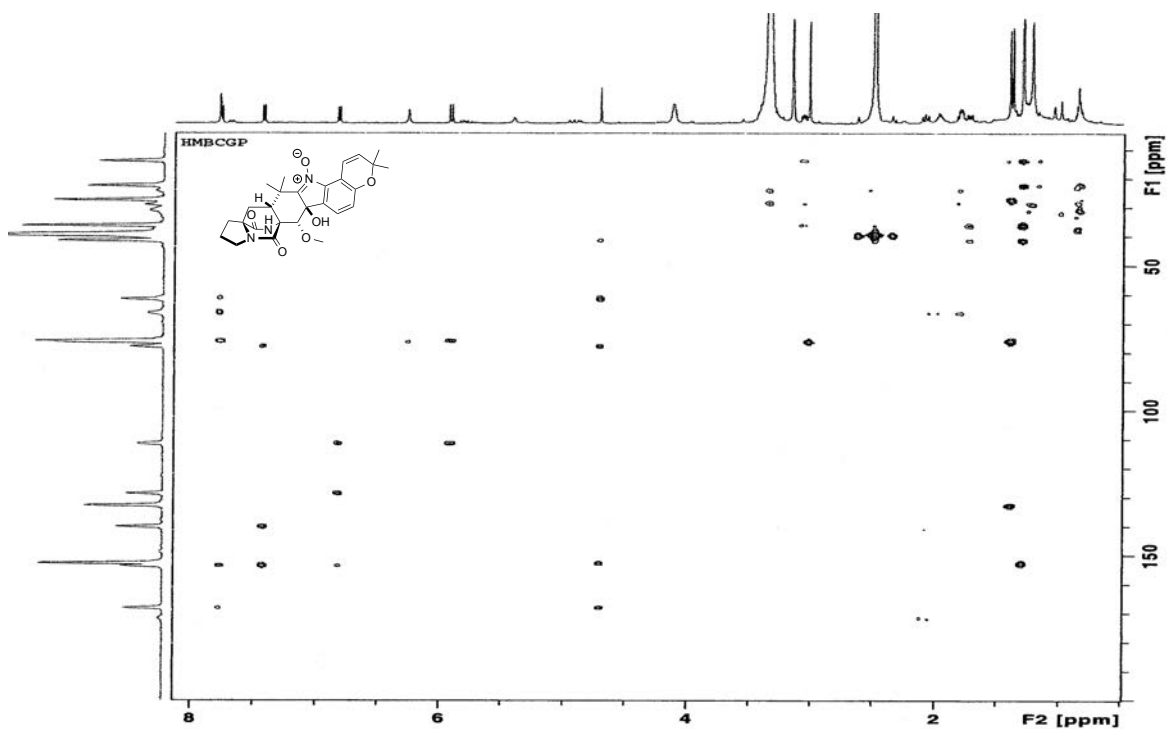


Figure S38. HMBC spectrum of **6** in DMSO- $d_6$ .

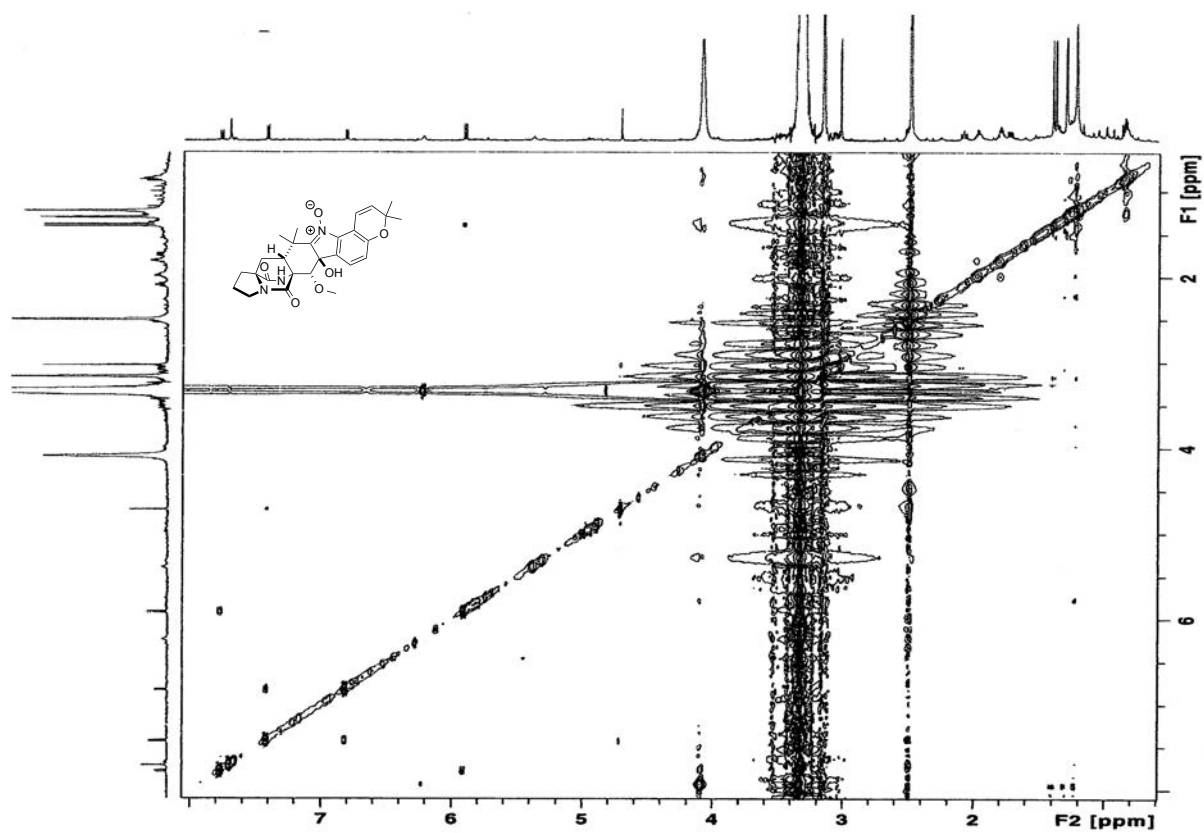


Figure S39. NOESY spectrum of **6** in DMSO- $d_6$ .

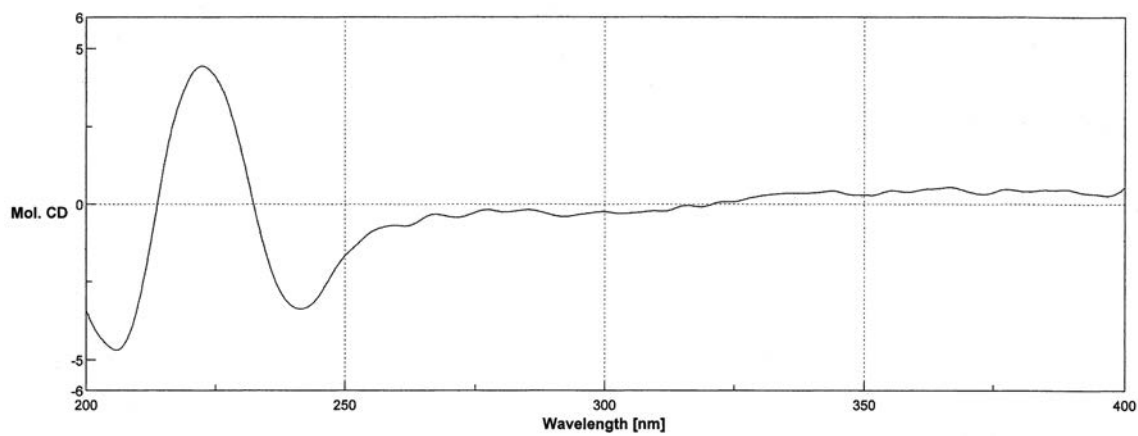


Figure S40. ECD spectrum of **6** in MeOH.

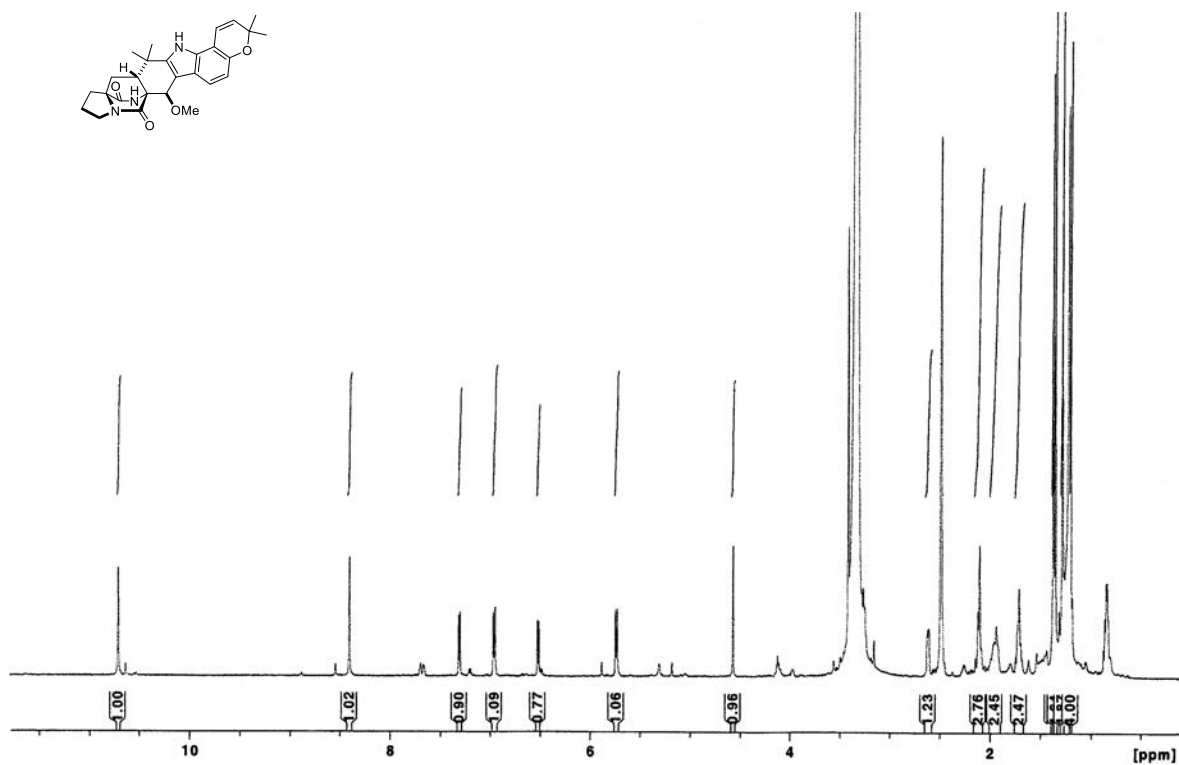


Figure S41.  $^1\text{H}$  NMR spectrum of **7** in  $\text{DMSO-}d_6$ .

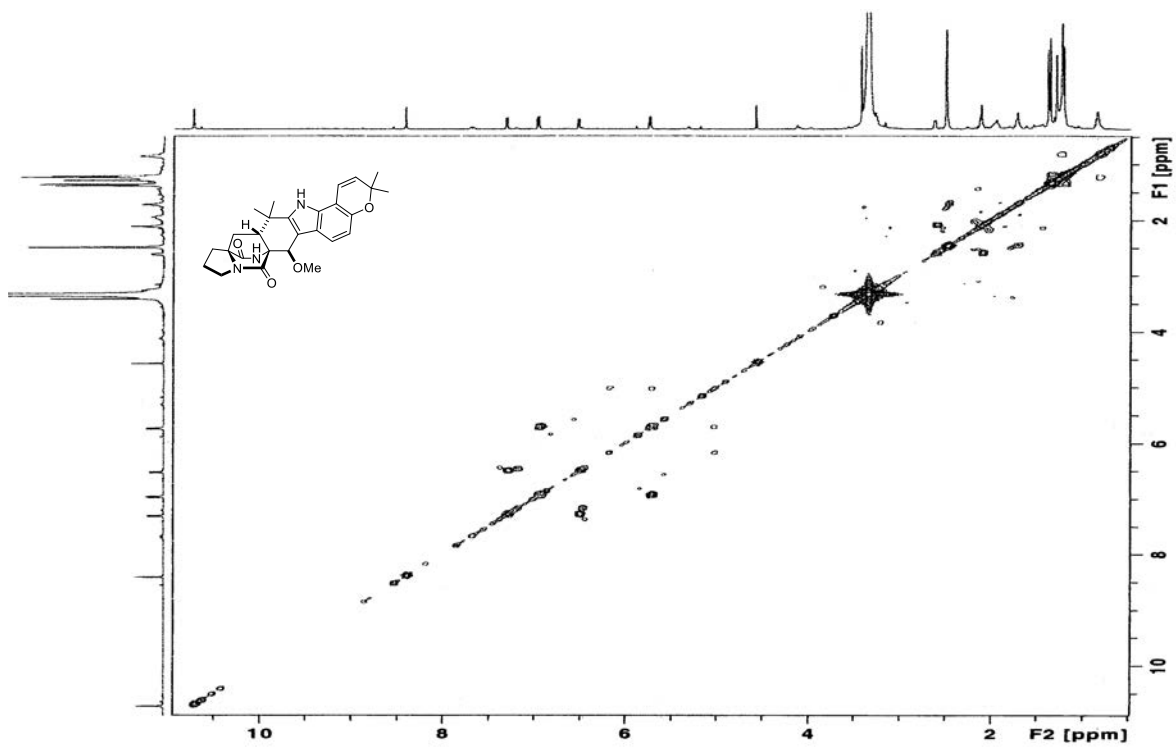


Figure S42. COSY spectrum of 7 in DMSO-*d*<sub>6</sub>.

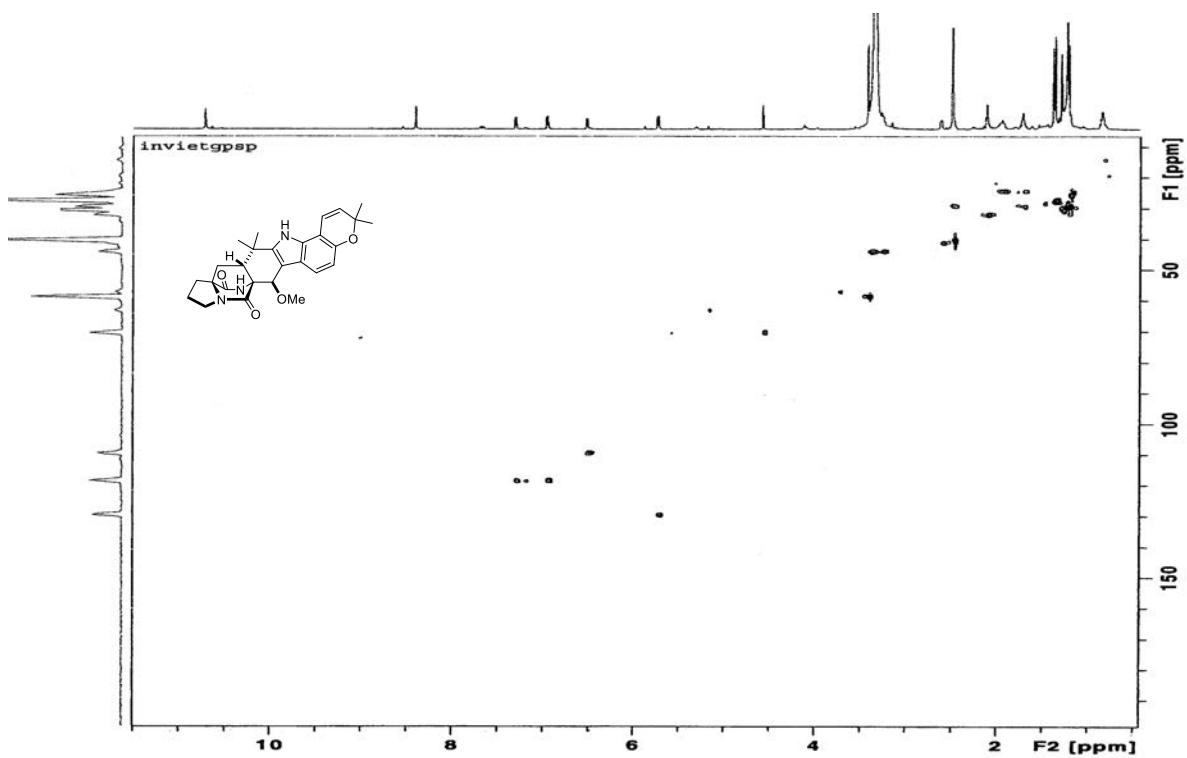


Figure S43. HSQC spectrum of 7 in DMSO-*d*<sub>6</sub>.

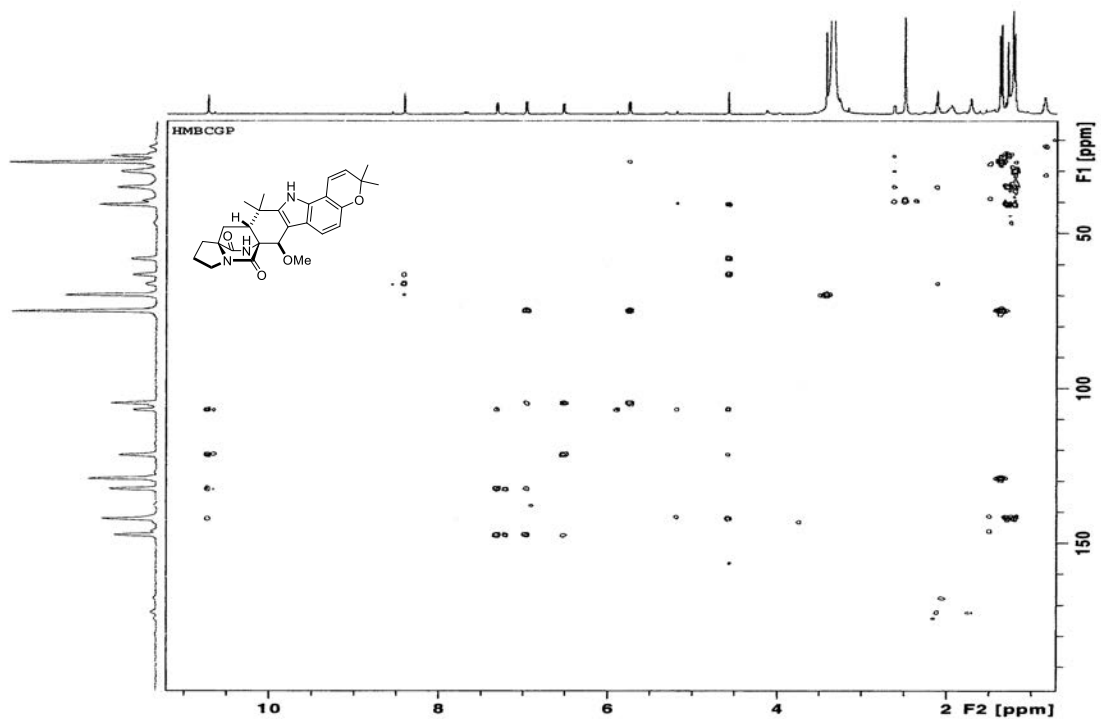


Figure S44. HMBC spectrum of 7 in DMSO- $d_6$ .

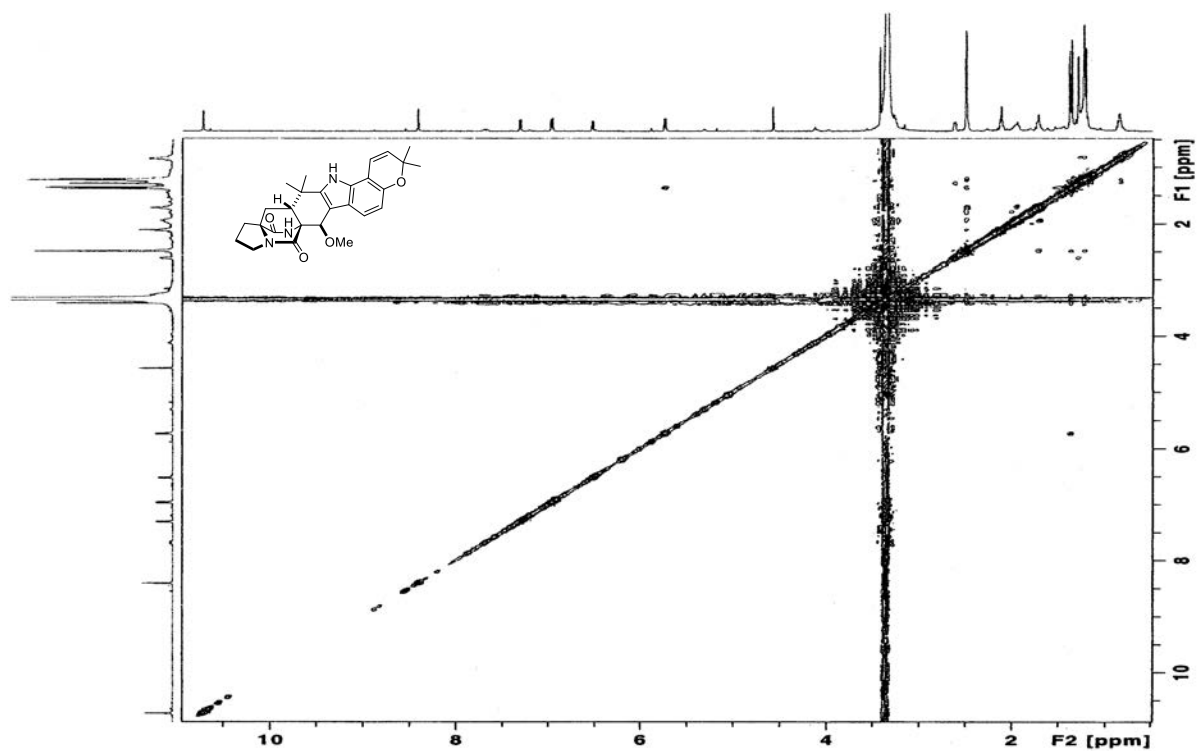
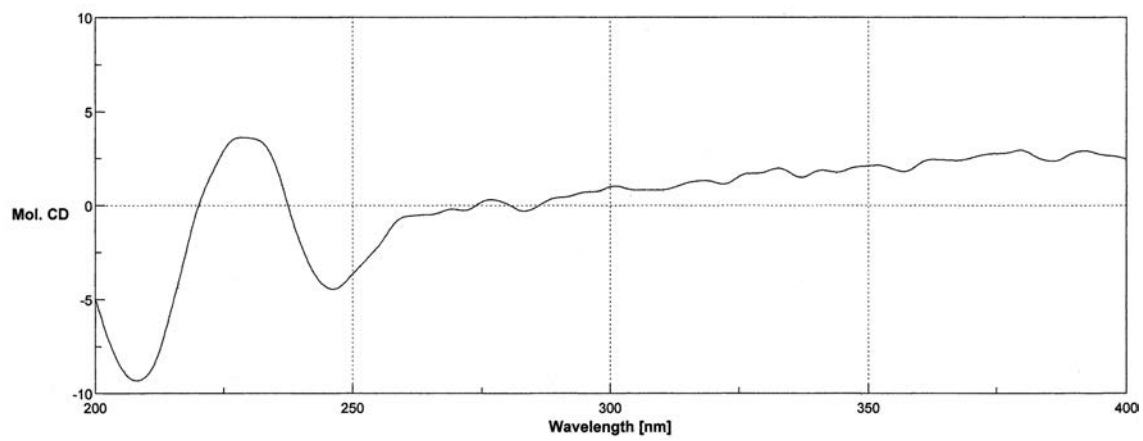


Figure S45. NOESY spectrum of 7 in DMSO- $d_6$ .



**Figure S46.** ECD spectrum of **7** in MeOH.

**Table S1.**  $^1\text{H}$  and  $^{13}\text{C}$  NMR data of **1** in  $\text{DMSO-}d_6$ .

no.	$\delta_{\text{C}}$ , mult.	$\delta_{\text{H}}$ , mult., ( $J$ in Hz)	COSY	HMBC
1		6.29, s		
2	190.7, C			
3	81.3, C			
4	122.0, CH	7.16, d (7.9)	5	3, 6, 8
5	113.0, CH	6.59, d (7.9)	4	6, 7, 9
6	153.6, C			
7	114.1, C			
8	147.9, C			
9	134.7, C			
10	25.1, $\text{CH}_2$	$\alpha$ 1.71, d (15.5) $\beta$ 2.63, d (15.5)	10 $\beta$ 10 $\alpha$	3, 9, 12 2, 3, 11, 12, 21
11	64.1, C			
12	168.4, C			
14	43.9, $\text{CH}_2$	$\alpha$ 3.27, m $\beta$ 3.32, m	14 $\beta$ , 15 $\alpha$ , 15 $\beta$ 14 $\alpha$ , 15 $\alpha$ , 15 $\beta$	15, 16, 17 15, 16, 17
15	24.1, $\text{CH}_2$	$\alpha$ 1.82, m $\beta$ 1.96, m	14 $\alpha$ , 14 $\beta$ , 15 $\beta$ , 16 $\beta$ 14 $\alpha$ , 14 $\beta$ , 15 $\alpha$ , 16 $\alpha$ , 16 $\beta$	14, 16, 17 14
16	28.7, $\text{CH}_2$	$\alpha$ 1.82, m $\beta$ 2.50, m	15 $\beta$ , 16 $\beta$ 15 $\alpha$ , 15 $\beta$ , 16 $\alpha$	15, 18 14, 15, 17, 18, 20
17	67.0, C			
18	172.4, C			
19		7.54, s		11, 12, 17
20	28.7, $\text{CH}_2$	$\alpha$ 1.92, m $\beta$ 2.12, t (13.3)	20 $\beta$ , 21 20 $\alpha$ , 21	11, 17, 23, 24 11, 17, 23, 24
21	50.1, CH	1.93, m	20 $\alpha$ , 20 $\beta$	22
22	40.5, C			
23	19.7, $\text{CH}_3$	1.35, s		2, 21, 22, 24
24	27.2, $\text{CH}_3$	1.21, s		2, 21, 22, 23
25	117.4, CH	6.85, d (9.9)	26	6, 7, 8, 26, 27
26	132.3, CH	5.85, d (9.9)	25	7, 27, 29
27	76.4, C			
28	27.66, $\text{CH}_3$	1.37, s		26, 27, 29
29	27.74, $\text{CH}_3$	1.39, s		26, 27, 28



**Table S2.**  $^1\text{H}$  and  $^{13}\text{C}$  NMR data of **2** in  $\text{DMSO}-d_6$ .

no.	Keto-form <sup>a</sup>				Enol-form <sup>a</sup>			
	$\delta_{\text{C}}$ , mult.	$\delta_{\text{H}}$ , mult., ( $J$ in Hz)	COSY	HMBC	$\delta_{\text{C}}$ , mult.	$\delta_{\text{H}}$ , mult., ( $J$ in Hz)	COSY	HMBC
1		10.42, s		7, 8, 9, 10				
2	164.1, C				172.4, C			
3	172.8, C				157.3, C			
4	126.6, CH	7.92, d (8.7)	5	3, 5, 6, 7, 8	122.9, CH	7.96, d (8.9)	5	3, 6, 8
5	113.7, CH	6.81, d (8.7)	4	6, 7, 9	116.5, CH	7.01, d (8.8)	4	7, 9
6	154.7, C				153.5, C			
7	108.7, C				114.4, C			
8	135.7, C				146.6, C			
9	121.1, C				114.4, C			
10	111.9, C				107.4, C			
11	68.1, C				69.3, C			
12	167.5, C				172.6, C			
14	43.2, CH <sub>2</sub>	$\alpha$ 3.33, m $\beta$ 3.23, m	14 $\beta$ , 15 $\alpha$ , 15 $\beta$ 14 $\alpha$ , 15 $\alpha$ , 15 $\beta$	16, 17	43.1, CH <sub>2</sub>	$\alpha$ 3.36, m $\beta$ 3.48, m	14 $\beta$ , 15 $\alpha$ , 15 $\beta$ 14 $\alpha$ , 15 $\alpha$ , 15 $\beta$	15, 16, 17
15	24.3, CH <sub>2</sub>	$\alpha$ 1.82, m  $\beta$ 1.92, m	14 $\alpha$ , 14 $\beta$ , 15 $\beta$ , 16 $\beta$ 14 $\alpha$ , 14 $\beta$ , 15 $\alpha$ , 16 $\alpha$ , 16 $\beta$	16 16, 17	24.0, CH <sub>2</sub>	$\alpha$ 1.87, m  $\beta$ 2.32, m	14 $\alpha$ , 14 $\beta$ , 15 $\beta$ , 16 $\beta$ 14 $\alpha$ , 14 $\beta$ , 15 $\alpha$ , 16 $\alpha$ , 16 $\beta$	
16	28.3, CH <sub>2</sub>	$\alpha$ 1.80, m $\beta$ 2.45, m	15 $\beta$ , 16 $\beta$ 15 $\alpha$ , 15 $\beta$ , 16 $\alpha$	15, 17 17, 18, 20	27.8, CH <sub>2</sub>	$\alpha$ 1.88, m $\beta$ 2.60, m	15 $\beta$ , 16 $\beta$ 15 $\alpha$ , 15 $\beta$ , 16 $\alpha$	
17	67.2, C				67.3, C			
18	171.6, C				174.6, C			
19		8.47, s		10, 11, 12, 17		8.93, s		10, 11, 12, 17
20	27.6, CH <sub>2</sub>	$\alpha$ 1.66, dd (7.7, 12.7) $\beta$ 2.02, dd (10.6, 12.3)	20 $\beta$ , 21 20 $\alpha$ , 21	16, 17, 18, 21, 22 11, 16, 17, 18, 21	33.6, CH <sub>2</sub>	$\alpha$ 2.15, m $\beta$ 2.22, m	20 $\beta$ 20 $\alpha$ , 21	18
21	53.5, CH	2.30, br, t (8.76)	20 $\alpha$ , 20 $\beta$	11, 12, 20, 23, 24	52.8, CH	2.15, m	20 $\beta$	2
22	43.7, C				43.8, C			
23	21.2, CH <sub>3</sub>	1.21, s		2, 21, 22, 24	22.7, CH <sub>3</sub>	1.18, s		2, 22
24	24.8, CH <sub>3</sub>	1.41, s		2, 21, 22, 23	26.7, CH <sub>3</sub>	1.30, s		2, 22
25	116.9, CH	7.23, d (10.0)	26	6, 7, 8, 26, 27	118.2, CH	7.39, d (9.9)	26	6, 27
26	129.6, CH	5.90, d (10.0)	25	6, 7, 27, 28, 29	129.2, CH	5.81, d (9.9)	25	7, 27, 29
27	75.9, C				76.4, C			
28	27.4, CH <sub>3</sub>	1.41, s		27, 29	27.3, CH <sub>3</sub>	1.42, s		
29	27.4, CH <sub>3</sub>	1.41, s		27, 28	27.3, CH <sub>3</sub>	1.42, s		
3-OH						11.27, s		3, 9, 10

<sup>a</sup> Keto- and enol-forms were observed in the ratio of 3:1.

**Table S3.**  $^1\text{H}$  and  $^{13}\text{C}$  NMR data of **2** in acetone- $d_6$  and in  $\text{CD}_3\text{OD}$ 

no.	acetone- $d_6$		$\text{CD}_3\text{OD}$	
	$\delta_{\text{C}}$ , mult.	$\delta_{\text{H}}$ , mult., ( $J$ in Hz)	$\delta_{\text{C}}$ , mult.	$\delta_{\text{H}}$ , mult., ( $J$ in Hz)
1				
2	175.1, C		167.4, C	
3	158.9, C		176.5, C	
4	123.8, CH	8.01, d (8.9)	127.8, CH	8.07, d (8.5)
5	117.3, CH	7.00, d (8.9)	116.1, CH	6.84, d (8.5)
6	155.4, C		157.7, C	
7	116.1, C		110.1, C	
8	148.6, C		138.7, C	
9	116.1, C		122.1, C	
10	108.3, C			
11	69.1, C			
12	173.6, C			
14	44.8, $\text{CH}_2$	3.45, m 3.67, m	44.8, $\text{CH}_2$	3.48 (2H), m
15	25.6, $\text{CH}_2$	1.99, m 2.14, m	25.4, $\text{CH}_2$	2.00, m 2.08, m
16	29.7, $\text{CH}_2$	2.05, m 2.71, m	30.0, $\text{CH}_2$	1.96, m 2.67, m
17	71.3, C		70.2, C	
18	172.1, C		174.7, C	
19		7.82, br, s		
20	29.0, $\text{CH}_2$	2.36, dd (6.7, 10.7) 2.06, m	28.7, $\text{CH}_2$	1.88, m 2.19, m
21	54.5, CH	2.74, m	55.4, CH	2.56, m
22	45.2, C		45.7, C	
23	23.7, $\text{CH}_3$	1.35, s	22.4, $\text{CH}_3$	1.35, s
24	28.4, $\text{CH}_3$	1.39, s	25.7, $\text{CH}_3$	1.52, s
25	119.3, CH	7.51, d (9.9)	117.0, CH	7.12, d (8.6)
26	129.5, CH	5.77, d (9.9)	131.3, CH	5.85, d (8.6)
27	77.5, C		77.7, C	
28	28.3, $\text{CH}_3$	1.48, s	28.0, $\text{CH}_3$	1.50, s
29	28.1, $\text{CH}_3$	1.46, s	27.6, $\text{CH}_3$	1.46, s

**Table S4.**  $^1\text{H}$  and  $^{13}\text{C}$  NMR data of **3** in  $\text{DMSO-}d_6$ .

no.	$\delta_{\text{C}}$ , mult.	$\delta_{\text{H}}$ , mult., ( $J$ in Hz)	COSY	HMBC
2	107.2, C			
3	73.2, C			
4	126.7, CH	7.21, d (8.4)	5	3, 6, 8
5	114.9, CH	6.73, d (8.4)	4	6, 7, 9
6	151.6, C			
7	113.0, C			
8	139.8, C			
9	130.1, C			
10	39.1, C	$\alpha$ 2.16, d (15.5) $\beta$ 2.26, d (15.5)	10 $\beta$ 10 $\alpha$	2, 3, 11, 21 11, 12
11	59.4, C			
12	168.8, C			
14	43.4, CH <sub>2</sub>	$\alpha$ 3.22, m $\beta$ 3.32, m	14 $\beta$ , 15 $\alpha$ , 15 $\beta$ 14 $\alpha$ , 15 $\alpha$ , 15 $\beta$	15, 16, 17 15, 16
15	24.0, CH <sub>2</sub>	$\alpha$ 1.79, m $\beta$ 1.93, m	14 $\alpha$ , 14 $\beta$ , 15 $\beta$ , 16 $\alpha$ , 16 $\beta$ 14 $\alpha$ , 14 $\beta$ , 15 $\alpha$ , 16 $\alpha$ , 16 $\beta$	17 17
16	28.1 CH <sub>2</sub>	$\alpha$ 1.46, m $\beta$ 2.45, m	15 $\alpha$ , 15 $\beta$ , 16 $\beta$ 15 $\alpha$ , 15 $\beta$ , 16 $\alpha$	15, 17, 18
17	66.3, C			
18	172.1, C			
19		7.50, s		11, 12, 17
20	31.2, CH <sub>2</sub>	$\alpha$ 1.77, m $\beta$ 2.07, m	20 $\beta$ , 21 20 $\alpha$ , 21	17, 18, 21 17, 21
21	52.8, CH	1.95, m	20 $\alpha$ , 20 $\beta$	22
22	39.7, C			
23	26.7, CH <sub>3</sub>	1.35, s		2, 21, 22, 24
24	22.7, CH <sub>3</sub>	0.87, s		2, 21, 22, 23
25	115.9, CH	6.66, d (10.0)	26	6, 8, 27
26	132.1, CH	5.84, d (10.0)	25	7, 27, 29
27	75.9, C			
28	27.2, CH <sub>3</sub>	1.31, s		26, 27, 29
29	27.2, CH <sub>3</sub>	1.40, s		26, 27, 28
30	88.4, CH <sub>2</sub>	$\alpha$ 4.57, d (5.4) $\beta$ 4.65, d (5.4)	30 $\beta$ 30 $\alpha$	8 2, 8
3-OH		5.75, br, s		9

**Table S5.**  $^1\text{H}$  and  $^{13}\text{C}$  NMR data of **4** in  $\text{DMSO-}d_6$ .

no.	$\delta_{\text{C}}$ , mult.	$\delta_{\text{H}}$ , mult., ( $J$ in Hz)	COSY	HMBC
2	145.0, C			
3	124.0, C			
4	119.2, CH	7.36, d (8.2)	5	3, 6, 7, 8
5	115.0, CH	6.85, d (8.2)	4	6, 7, 9
6	151.8, C			
7	114.0, C			
8	138.0, C			
9	127.3, C			
10	22.0, C	$\alpha$ 2.69, d (18.9) $\beta$ 3.81, d (18.9)	10 $\beta$ 10 $\alpha$	2, 3, 11, 21 2, 3, 11, 12
11	59.5, C			
12	168.3, C			
14	43.5, $\text{CH}_2$	$\alpha$ 3.20, m $\beta$ 3.37, m	14 $\beta$ , 15 $\alpha$ , 15 $\beta$ 14 $\alpha$ , 15 $\alpha$ , 15 $\beta$	
15	24.0, $\text{CH}_2$	$\alpha$ 1.81, m $\beta$ 1.97, m	14 $\alpha$ , 14 $\beta$ , 15 $\beta$ , 16 $\beta$ 14 $\alpha$ , 14 $\beta$ , 15 $\alpha$ , 16 $\alpha$ , 16 $\beta$	14, 17
16	28.1 $\text{CH}_2$	$\alpha$ 1.81, m $\beta$ 2.50, m	15 $\beta$ , 16 $\beta$ 15 $\alpha$ , 15 $\beta$ , 16 $\alpha$	14, 15, 17, 18 14, 15, 17, 18
17	66.8, C			
18	172.3, C			
19		8.74, s		10, 11, 12, 17
20	31.9, $\text{CH}_2$	$\alpha$ 1.87, m $\beta$ 2.08, m	20 $\beta$ , 21 20 $\alpha$ , 21	17, 18, 22
21	49.6, CH	1.77, m	20 $\alpha$ , 20 $\beta$	20
22	39.7, C			
23	18.7, $\text{CH}_3$	1.41, s		2, 21, 22, 24
24	25.6, $\text{CH}_3$	1.30, s		2, 21, 22, 23
25	121.2, CH	6.73, d (9.9)	26	6, 7, 8, 27
26	127.5, CH	5.67, d (9.9)	25	7, 27, 29
27	75.9, C			
28	25.6, $\text{CH}_3$	1.36, s		26, 27, 29
29	27.8, $\text{CH}_3$	1.44, s		26, 27
30	33.8, $\text{CH}_2$	2.55, s		

**Table S6.**  $^1\text{H}$  and  $^{13}\text{C}$  NMR data of **5** in  $\text{DMSO-}d_6$ .

no.	$\delta_{\text{C}}$ , mult.	$\delta_{\text{H}}$ , mult., ( $J$ in Hz)	COSY	HMBC
1		10.61, br s		3, 8, 9
2	179.7, C			
3	62.2, C			
4	124.0, CH	6.75, d (8.1)	5	6, 8
5	108.2, CH	6.32, d (8.1)	4	6, 7
6	152.1, C			
7	104.7, C			
8	137.6, C			
9	126.6, C			
10	33.3, CH	$\alpha$ 2.41, d (14.9) $\beta$ 2.53, d (14.9)	10 $\beta$ 10 $\alpha$	2, 3, 9, 11, 12 3, 9, 11, 12
11	67.6, C			
12	169.8, C			
14	43.2, $\text{CH}_2$	$\alpha$ 3.25, m $\beta$ 3.37, m	14 $\beta$ , 15 $\alpha$ , 15 $\beta$ 14 $\alpha$ , 15 $\alpha$ , 15 $\beta$	16
15	24.4, $\text{CH}_2$	$\alpha$ 1.78, m $\beta$ 1.98, m	14 $\alpha$ , 14 $\beta$ , 15 $\beta$ , 16 $\beta$ 14 $\alpha$ , 14 $\beta$ , 15 $\alpha$ , 16 $\alpha$ , 16 $\beta$	
16	28.7, $\text{CH}_2$	$\alpha$ 1.77, m $\beta$ 2.48, m	15 $\beta$ , 16 $\beta$ 15 $\alpha$ , 15 $\beta$ , 16 $\alpha$	14, 15 14
17	68.2, C			
18	172.4, C			
19		8.69, br s		10, 11
20	27.2, $\text{CH}_2$	$\alpha$ 1.91, dd (10.2, 12.9) $\beta$ 1.63, dd (7.3, 12.9)	20 $\beta$ , 21 20 $\alpha$ , 21	17, 18 21, 22
21	53.1, CH	2.54, m	20 $\alpha$ , 20 $\beta$	20, 22, 23, 24
22	48.0, C			
23	19.4, $\text{CH}_3$	1.02, s		3, 21, 22, 24
24	23.1, $\text{CH}_3$	0.43, s		2, 3, 22, 23
25	116.8, CH	6.58, d (9.9)	26	6, 7, 8, 27
26	130.5, CH	5.74, d (9.9)	25	7, 27, 28, 29
27	75.8, C			
28	27.4, $\text{CH}_3$	1.34, s		26, 27, 29
29	27.4, $\text{CH}_3$	1.34, s		26, 27, 28

**Table S7.**  $^1\text{H}$  and  $^{13}\text{C}$  NMR data of **6** in  $\text{DMSO-}d_6$ .

no.	$\delta_{\text{C}}$ , mult.	$\delta_{\text{H}}$ , mult., ( $J$ in Hz)	COSY	HMBC
2	152.8, C			
3	77.8, C			
4	122.7, CH	7.42, d (8.0)	5	3, 6, 8
5	115.6, CH	6.82, d (8.0)	4	6, 7, 9
6	153.7, C			
7	111.5, C			
8	140.2, C			
9	128.8, C			
10	76.4, CH	4.71, s		2, 3, 9, 11, 12, 21
11	61.4, C			
12	168.2, C			
14	43.7, $\text{CH}_2$	3.33 (2H), m	15 $\alpha$ , 15 $\beta$	12, 15, 16, 17
15	23.9, $\text{CH}_2$	$\alpha$ 1.78, m $\beta$ 1.95, m	14, 15 $\beta$ , 16 $\beta$ 14, 15 $\alpha$ , 16 $\alpha$ , 16 $\beta$	16, 17
16	28.2, $\text{CH}_2$	$\alpha$ 1.79, m $\beta$ 2.50, m	15 $\beta$ , 16 $\beta$ 15 $\alpha$ , 15 $\beta$ , 16 $\alpha$	14, 15, 17, 18, 20 15, 17, 18, 20
17	66.6, C			
18	171.8, C			
19		7.77, br s		10, 11, 12, 17
20	31.2, $\text{CH}_2$	$\alpha$ 1.73, dd (6.5, 13.1) $\beta$ 2.09, dd (10.3, 13.1)	20 $\beta$ , 21 20 $\alpha$ , 21	17, 18, 21, 22 11, 17, 18
21	41.4, CH	3.06, dd (6.5, 10.3)	20 $\alpha$ , 20 $\beta$	11, 12, 20, 22, 23, 24
22	36.1, C			
23	13.6, $\text{CH}_3$	1.29, s		2, 21, 22, 24
24	22.0, $\text{CH}_3$	1.30, s		2, 21, 22, 23
25	115.6, CH	7.77, d (9.8)	26	6, 8, 27
26	132.8, CH	5.91, d (9.8)	25	7, 27, 28
27	75.8, C			
28	27.4, $\text{CH}_3$	1.38, s		26, 27, 29
29	27.4, $\text{CH}_3$	1.40, s		26, 27, 28
3-OH		6.25, br s		3, 10
10-OMe	61.6, $\text{CH}_3$	3.02, s		10

**Table S8.**  $^1\text{H}$  and  $^{13}\text{C}$  NMR data of **7** in  $\text{DMSO-}d_6$ .

no.	$\delta_{\text{C}}$ , mult.	$\delta_{\text{H}}$ , mult., ( $J$ in Hz)	COSY	HMBC
1		10.73, br s		
2	141.8, C			
3	106.6, C			
4	117.8, CH	7.31, d (8.4)	5	6, 8
5	108.8, CH	6.52, d (8.4)	4	6, 7
6	147.1, C			
7	104.3, C			
8	132.3, C			
9	121.2, C			
10	69.4, CH	4.57, s		2, 3, 9, 11, 12, 21, 10-OMe
11	62.7, C			
12	168.2, C			
14	43.3, $\text{CH}_2$	$\alpha$ 3.27, m $\beta$ 3.40, m	14 $\beta$ , 15 $\alpha$ , 15 $\beta$ 14 $\alpha$ , 15 $\alpha$ , 15 $\beta$	15
15	23.6, $\text{CH}_2$	$\alpha$ 1.71, m $\beta$ 1.94, m	14 $\alpha$ , 14 $\beta$ , 15 $\beta$ , 16 $\beta$ 14 $\alpha$ , 14 $\beta$ , 15 $\alpha$ , 16 $\alpha$ , 16 $\beta$	16
16	28.6, $\text{CH}_2$	$\alpha$ 1.72, m $\beta$ 2.50, m	15 $\beta$ , 16 $\beta$ 15 $\alpha$ , 15 $\beta$ , 16 $\alpha$	15, 20
17	65.9, C			
18	172.1, C			
19		8.42, br s		10, 11, 17
20	31.1, $\text{CH}_2$	2.11 (2H), br m	21	17, 18, 22
21	40.5, CH	2.62, dd (4.3, 8.2)	20	22, 23, 24
22	34.7, C			
23	24.8, $\text{CH}_3$	1.20, s		2, 21, 22, 24
24	29.7, $\text{CH}_3$	1.28, s		2, 21, 22, 23
25	117.8, CH	6.96, d (9.8)	25	6, 7, 8, 27
26	128.8, CH	5.74, d (9.8)	26	7, 27
27	74.5, C			
28	26.7, $\text{CH}_3$	1.36, s		26, 27, 29
29	26.7, $\text{CH}_3$	1.38, s		27, 28
10-OMe	57.9, $\text{CH}_3$	3.42, s		10

**Table S9.** Calculated distances between designated hydrogens in **3a** and **3b**.<sup>a</sup>

	Boltzmann distributions	Distances (Å)			
		H-25/H30	H-4/H-10	H-19/H <sub>3</sub> -23	H-21/H <sub>3</sub> -24
<b>2R,3R-3a</b>	0.767	2.517	2.737	2.648	2.570
	0.391	2.511	2.732	2.653	2.571
	0.079	2.515	2.739	2.627	2.573
	0.079	2.509	2.732	2.631	2.572
	0.058	2.681	2.778	2.699	2.524
<b>2R,3S-3a</b>	0.731	2.360	2.776	2.464	2.397
	0.269	2.354	2.769	2.470	2.393
<b>2S,3R-3a</b>	0.765	2.335	2.886	2.570	2.233
	0.235	2.328	2.879	2.537	2.332
<b>2S,3S-3a</b>	0.757	2.750	2.414	2.665	2.530
	0.241	2.753	2.411	2.654	2.533
<b>2R,3R-3b</b>	0.409	3.611	2.636	2.666	2.563
	0.281	3.461	2.655	2.682	2.598
	0.239	3.672	2.622	2.757	2.539
	0.071	3.467	2.653	2.677	2.597
<b>2R,3S-3b</b>	0.734	3.291	2.751	2.478	2.342
	0.266	3.291	2.747	2.479	2.344
<b>2S,3R-3b</b>	0.763	3.309	2.907	2.863	2.239
	0.237	3.322	2.911	2.813	2.236
<b>2S,3S-3b</b>	0.777	3.288	2.972	2.341	2.465
	0.223	3.299	2.996	2.356	2.458

<sup>a</sup> Calculated by Spartan'14 using MMFF for searching low energy conformer, and Hartree-Fock 3-21G and B3LYP/6-31G\* for structural optimization.



**Table S10.** Calculated distances between designated hydrogens in **6**.<sup>a</sup>

	Boltzmann distributions	Distance (Å)		
		H-4/H-10	H-19/H-23	H-21/H-24
3 <i>R</i> ,10 <i>R</i>	0.655	2.989	2.543	2.364
	0.345	2.988	2.532	2.364
3 <i>R</i> ,10 <i>S</i>	0.547	3.795	2.691	2.368
	0.453	3.785	2.678	2.368
3 <i>S</i> ,10 <i>R</i>	0.634	3.483	2.746	2.360
	0.290	3.485	2.702	2.363
	0.076	3.686	2.721	2.356
3 <i>S</i> ,10 <i>S</i>	0.425	2.902	2.401	2.361
	0.407	2.893	2.412	2.360
	0.090	2.908	2.411	2.360
	0.078	2.898	2.415	2.359

<sup>a</sup> Calculated by Spartan'14 using MMFF for searching low energy conformers, and Hartree-Fock 3-21G and B3LYP/6-31G\* for structural optimization