Supporting Information

Quintaquinone, a merosesquiterpene from the yellow sponge *Verongula* cf. *rigida* Esper

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Experimental section

Sponge Identification.

Phylogenic analysis. Phylogenic analysis was performed according to the sequencing results from 28S rDNA C-region.[1] The specimen was cut into small pieces and incubated overnight in 200 µL of VLB solution (5 mL of 100 mM NaCl, 50 mM Tris HCl pH 8.0, 10 mM EDTA pH 8.0, 0.5% SDS, and 0.5 mL of 20 mg/mL protein kinase K) at 56 °C. The DNA was extracted with innuPREP bacteria DNA kit (analytikjena®), and filtered through a 0.025 µM MCE membrane (MF-Millipore™, Merck Millipore Ltd.). The PCR amplification was performed as followed; pre-denaturation at 95°C, 5 min; a 34-cycle of 95°C, 45 s; 48°C, 45 s; and 72°C, 30 s; and final extension at 72°C, 5 min (forward primer: C2; 5′-GAAAAGAACTTTGRARAGAGAGT-3′ and reverse primer: D2; 5′-TCCGTGTTTCAAGACGGG-3′). The PCR product was isolated using 1% agarose gel in 1x TAE buffer, 100 V, 35 min, and extracted with Zymoclean™ Large Fragment DNA recovery kit (Zymo research). DNA was inserted to pGEM®-T vector (Promega®), and transferred to *E. coli* XL1 blue chemically competent cells by heat shock transformation. The bacteria were cultured on an LB agar plate (doped with 40 µg/mL carbenicillin, 40 µg/mL X-Gal, and 0.1 mM IPTG) at 37°C overnight. White colonies were picked and analyzed by test PCR. The PCR conditions were as followed; pre-denaturation at 95°C, 5 min; a 34-cycle of 95°C, 45 s; 55°C, 45 s; and 72°C, 30 s; and final extension at 72°C, 5 min (primer SP6; ATTTAGGTGACACTATAG and T7; TAATACGACTCACTATAGGG). The PCR product was isolated, extracted, and sent for Sanger sequencing. Based on the sequencing results, one positive clone was selected and re-cultivated for plasmid isolation. The plasmid was sequenced for verification and the sequencing results were analyzed using BLAST® (National Center for Biotechnology Information). The

sponge was identified to *Verongula rigida* Esper (1794).[2] The partial sequence of the 28S rRNA gene after removal of vector sequences is as followed:

TCCGTGTTTCAAGACGGGTCGGATGGGACCGGCTAGGCGCCAGCGACCTCAGCGCA
CATCGTGACTGCACCGCGACGCCTCCGTCTCACTCARCRGGCACTGCACGCAGTCCC
CACCGGTCCGATGCAGTCGTCGCAGCCGTCCGGCCATTCGGCTTGCGCTGCTCGGGC
GAGGGCCGCCACTCTCTCAGTCTCTGCCGCGTCGCGCCCCAGGGGCCAACACCGAG
ACCCGAAGGACTCGGCCAACTGCCCCGCGGGACGCACGGCGCGGCGGAAACTGCCG
CTGACTGGTCCACGCGGGAGTGCGGTCGAGAGCGACGAGCGGTCCCACCGGCGACG
GGTCCCAGGGGGATCCCTCCGCCAGAGGGCGCTCATCGATCTGCCTGTTCCCACAGA
GGACCGAGCCGGCCTCATTCGCTTCCCTCCCAACGGTTTCACGCACTATTTGACTCTC
TCTCCAAAGTTCTTTTC

This sequence show 97.45% identity to *Verongula rigida* voucher P46 28S ribosomal RNA gene partial sequence (query coverage 100%).

References

(1) Chombard, C.; Boury-Esnault, N.; Tillier, S. *Syst. Biol*. **1998**, *47*, 351–366.

(2) Van Soest, R.W.; Boury-Esnault, N.; Hooper, J.N.; Rutzler, K.; de Voogd, N.J.; de Glasby, B.A.; Hajdu, E.; Pisera, A.B.; Manconi, R.; Schoenberg, C.; Janussen, D.; Tabachnick, K.R.; Klautau, M.; Picton, B.;; Kelly, M.; Vacelet, J. (ed). "*Verongula rigida*" World Porifera database. World Register of Marine Species. http://www.marinespecies.org/aphia.php?p=taxdetails&id=169675, retrieved September 11, 2019.

Morphological description

Verongula cf. *rigida* Esper (1974)

Material examined.

AP14-001-01 Authors' collections – Ko Ha Islets, Mu Ko Lanta National Park, Krabi, Thailand.

AP10-017-02 Authors' collections – Ko Ha Islets, Mu Ko Lanta National Park, Krabi, Thailand.

Description. Sponge with thickly spreading base from which elevated oscula arise. Oscules large conspicuous, scatter throughout sponge tissues. The surface is characterized by a honeycomb-like sculpturing and fine conulose at surface (Figure S-1).

Color in life. Outer color yellow, with greenish patches, produced by localized oxidation of the yellow pigment, which extends throughout the sponge. Upon surfacing, the specimen turns dark purple to black. Specimen color is brown in spirit, and is extracted dark purple solution.

Texture: Spongy, firm, dry sponge is tough compressible. The skeletal architecture is anastomosing with polygonal mesh. The conulose fiber is fasciculate fiber. Fibers 25-70 micron in diameter, thickest near the surface, pith invisible (Figure S-2).

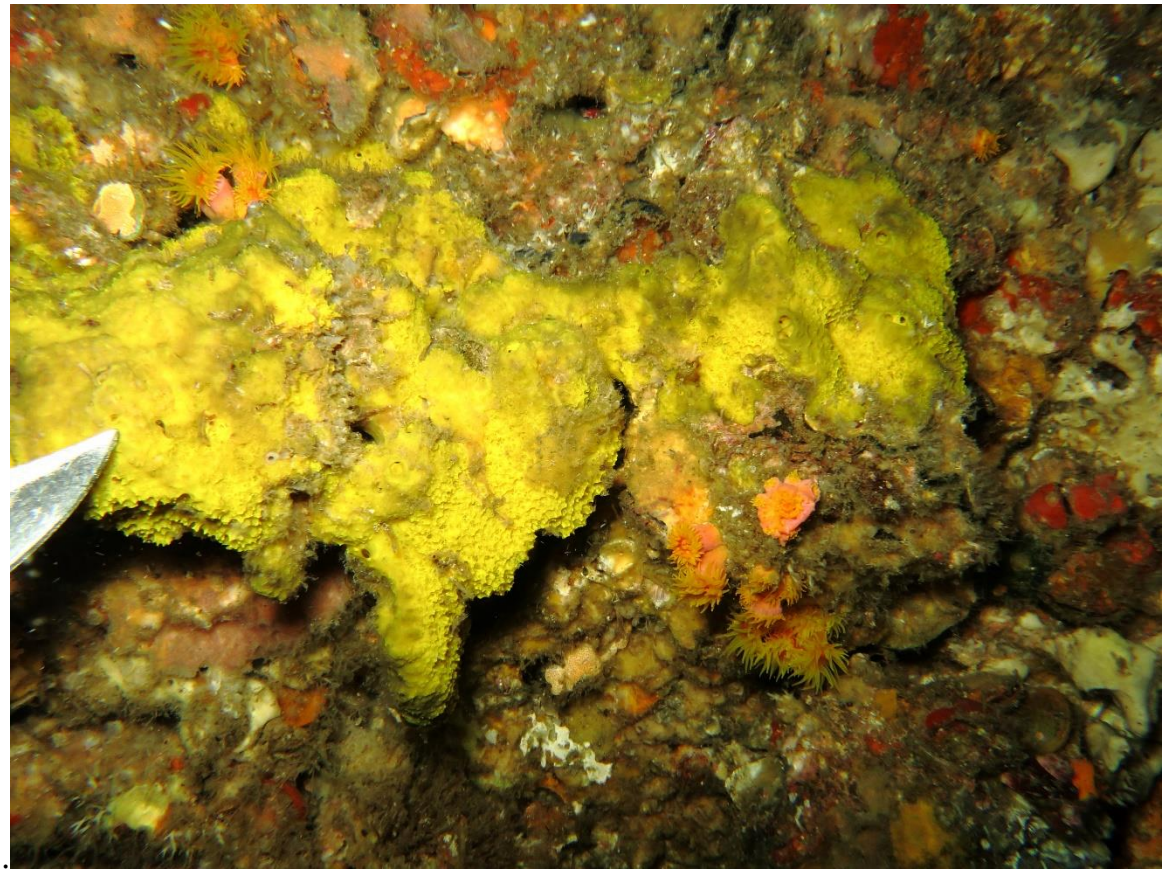


Figure S1 *Verongula* cf. *rigida* Esper (1974); AP10-017-02 in situ, Ko Ha Islet, Krabi, Thailand.

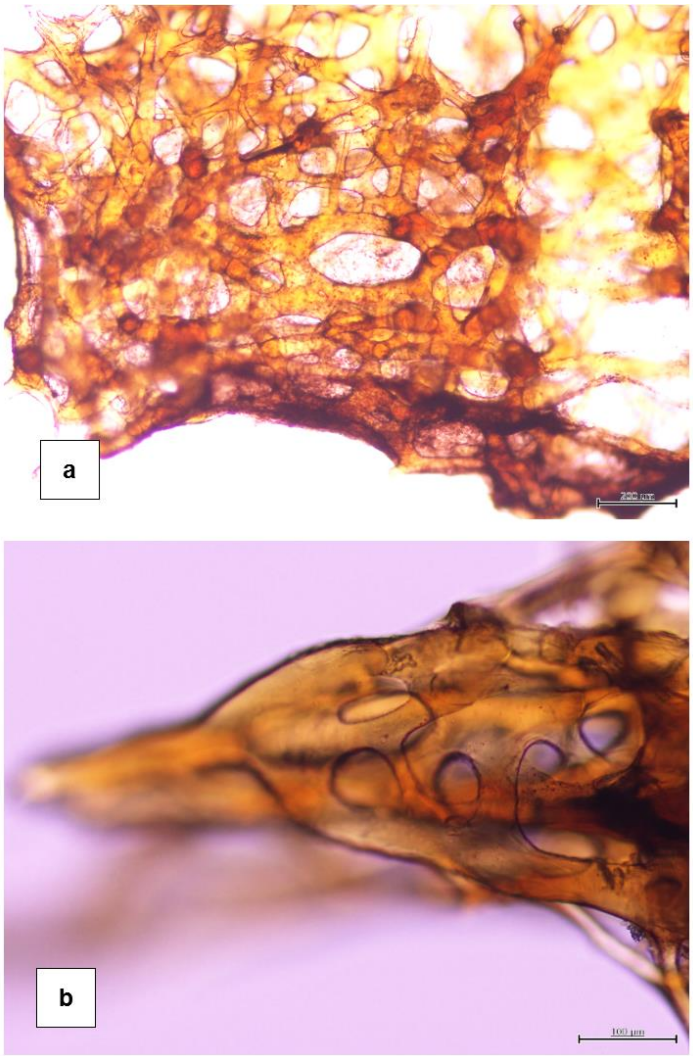


Figure S2 (a) skeletal architecture fiber of specimen AP10-017-02; (b) conulose fiber of specimen AP14-001-01.

Extraction and isolation. The sponge specimen from the 2010 expedition (1.8 kg, wet weight) was extracted with 1:1 MeOH/EtOAc (2.5 L) and EtOAc (3 × 2.5 L). The dried extracted (23 g) was partitioned to yield the hexane-, CH_2Cl_2-, and *n*-BuOH-extracts. An aliquot of the hexane-extract (2.6 g) was fractionated over the Sephadex LH20 (MeOH) and HPLC (C-18, Phenomenex®, 250×10 mm, 10 μm; 9:1 MeCN/water, 2.0 mL/min) columns, and dactylospontriol (6 mg) was obtained. Another aliquot of the hexane-extract (11.7 g) was subjected to the Sephadex LH20 (EtOAc), SiO_2 (98:2 CH_2Cl_2/MeOH), normal-phase HPLC (VertiSep GES Silica, 250×10 mm, 10 μM; 85:15 hexane/EtOAc, 2.0 mL/min), and reverse-phase HPLC (C18, Mightsill RP-18 GPII, 250 × 4.6 mm, 5 μm; 8:2 MeCN/water; 1.0 mL/min) columns to yield compound **3** (3 mg, t_R 13 min).

The sponge specimen from the 2014 expedition (325 g, dry weight) was extraction with hexane (5 × 3 L), CH_2Cl_2 (4 × 3 L), and MeOH (4 × 3 L). The hexane-extract (3 g) was chromatographed over SiO_2 (gradient 100:0 to 0:100 hexane/EtOAc) to yield six fractions. The major fraction 3 (872 mg) was chromatographed over the Sephadex LH20 (4:1 MeOH/EtOAc), SiO_2 (85:15 hexane/$CHCl_3$), and reverse-phase HPLC (C18 MightSill RP-18 GPII, 250 × 4.6 mm, 5 μM; 85:15 CH_3CN/water, 1 mL/min) columns to yield quintaquinone (**1**, 2 mg, t_R 16 min), smenospongidine (0.8 mg, t_R 21 min), smenospongorine (1.5 mg, t_R 22 min), a mixture of nakijiquinone L and smenospongiarine (8 mg, t_R 27 min), and a mixture of 5-*epi*-nakijiquinone L (**2**) and 5-*epi*-smenospongiarine (2 mg, t_R 29 min). Another major fraction 4 (797 mg) was chromatographed over Sephadex LH20 (4:1 MeOH/EtOAc) to yield three main fractions. The first one was separated using $AgNO_3$-impregnated SiO_2 column (4:1 hexane/EtOAc) to yield ilimaquinone (300 mg) and 5-*epi*-ilimaquionone (81 mg). The second fraction was separated with a reverse-phase HPLC column (C18, 7:3 CH_3CN/water, 1 mL/min) to yield

cyclospongiaquinone-1 (4.4 mg, t_R 18 min). The last main fraction was separated with a reverse-phase HPLC (C18, 7:3 CH_3CN/water, 1 mL/min) to yield smenodiol (9 mg, t_R 24 min).

Ilimaquinone (1). Yellow needles; $[\alpha]^{26}_D$ -42.7 (*c* 0.024, MeOH); UV (MeOH) λ_{max} (log ε) 288 (4.29) nm; ECD (*c* 0.34, MeOH) λ_{max} ($\Delta\varepsilon$) 285 (-1.40), 234 (-1.18), 207 (4.39); IR (neat) ν_{max} 3338, 3083, 2928, 2863, 1608, 1451, 1381, 1349, 1318, 1231, 1202 cm^{-1}; ^1H NMR (C_6D_6, 500 MHz) δ 7.37 (1H, s, 17-OH), 5.08 (1H, s, H-19), 4.58 (1H, dd, *J* = 1.6, 1.6 Hz, H-11a), 4.55 (1H, dd, *J* = 1.6, 1.6 Hz, H-11b), 2.68 (1H, d, *J* = 13.7 Hz, H-15a), 2.64 (3H, s, 20-OCH_3), 2.55 (1H, d, *J* = 13.7 Hz, H-15b), 2.35 (1H, dddd, *J* = 13.5, 11.5, 5.5, 1.6 Hz, H-3ax), 2.32 (1H, brdd, *J* = 11.5, 2.2 Hz, H-1eq), 2.13 (1H, dddd, *J* = 13.5, 4.5, 2.2, 2.2 Hz, H-3eq), 1.93 (1H, brddd, *J* = 11.7, 5.5, 2.2 Hz, H-2eq), 1.53 (1H, ddd, *J* = 11.8, 3.1, 3.1 Hz, H-6eq), 1.44 (1H, dddd, *J* = 11.5, 11.5, 11.3, 2.2 Hz, H-1ax), 1.43 (1H, dddd, *J* = 11.7, 11.5, 2.2, 2.2 Hz, H-2ax), 1.40 (1H, ddd, *J* = 11.8, 2.4, 2.4 Hz, H-6ax), 1.38 (1H, brdd, *J* = 5.8, 1.7 Hz, H-8), 1.36 (2H, H2-7), 1.16 (3H, d, *J* = 5.8 Hz, H3-13), 1.03 (3H, s, H3-12), 0.98 (1H, dd, *J* = 11.3, 2.2 Hz, H-10), 0.86 (3H, s, H3-14); ^{13}C NMR (C_6D_6, 125 MHz) δ 182.5 (C, C-18), 181.9 (C, C-21), 162.1 (C, C-20), 160.4 (C, C-4), 153.6 (C, C-17), 117.5 (C, C-16), 103.7 (CH_2, C-11), 102.1 (CH, C-19), 55.9 (CH_3, 20-OCH_3), 51.0 (CH, C-10), 43.8 (C, C-9), 41.1 (C, C-5), 38.8 (CH, C-8), 37.5 (CH_2, C-6), 33.7 (CH_2, C-3), 33.0 (CH_2, C-15), 29.5 (CH_2, C-2), 28.7 (CH_2, C-7), 23.9 (CH_2, C-1), 21.0 (CH_3, C-12), 18.6 (CH_3, C-13), 17.9 (CH_3, C-14); HRESIMS m/z 381.2025 $[M+Na]^+$ (calcd for $C_{22}H_{30}O_4Na$, 381.2034).

5-*Epi*-ilimaquinone. Yellow solid; $[\alpha]^{26}_D$ +10.9 (*c* 0.095, MeOH); UV (MeOH) λ_{max} (log ε) 286 (4.33) nm; ECD (*c* 12, MeOH) λ_{max} ($\Delta\varepsilon$) 298 (-1.47), 272 (1.05), 205 (-15.74); IR (neat) ν_{max} 3338, 3083, 2930, 2863, 1703, 1608, 1458, 1382, 1349, 1318, 1232, 1207 cm^{-1}; ^1H NMR (C_6D_6, 500 MHz) δ 7.36 (1H, s, 17-OH), 5.19 (1H, s, H-19), 4.81 (1H, dd, *J* = 1.7, 1.7 Hz, H-

11a), 4.78 (1H, dd, J = 1.7, 1.7 Hz, H-11b), 2.72 (1H, d, J = 13.6 Hz, H-15a), 2.70 (3H, s, 20-OCH_3), 2.60 (1H, d, J = 13.6 Hz, H-15b), 2.43 (1H, dddd, J = 13.9, 13.5, 6.4, 1.7 Hz, H-3ax), 2.34 (1H, brdd, J = 15.4, 4.3 Hz, H-1eq), 2.12 (1H, dd, J = 13.9, 5.5 Hz, H-3eq), 2.05 (1H, ddd, J = 13.9, 3.2, 3.2 Hz, H-6eq), 1.96 (1H, dddd, J = 15.4, 14.6, 6.4, 6.4 Hz, H-1ax), 1.83 (1H, dddd, J = 13.5, 13.5, 5.5, 5.5 Hz, H-2eq), 1.64 (1H, dddd, J = 13.5, 13.5, 11.7, 2.3 Hz, H-2ax), 1.61 (1H, ddd, J = 13.4, 6.4, 3.2 Hz, H-7eq), 1.37 (1H, ddd, J = 6.4, 6.4, 3.5 Hz, H-8), 1.36 (1H, dd, J = 6.4, 4.3 Hz, H-10), 1.22 (1H, dddd, J = 13.4, 7.7, 3.5, 3.2 Hz, H-7ax), 1.12 (3H, d, J = 6.4 Hz, H3-13), 1.10 (1H, ddd, J = 13.9, 7.7, 3.5 Hz, H-6ax), 1.10 (3H, s, H3-12), 1.00 (3H, s, H3-14); ^{13}C NMR (C_6D_6, 125 MHz) δ 182.7 (C, C-21), 181.9 (C, C-18), 162.2 (C, C-20), 153.7 (C, C-4), 153.6 (C, C-17), 117.9 (C, C-16), 106.6 (CH_2, C-11), 102.2 (CH, C-19), 55.9 (CH_3, 20-OCH_3), 49.4 (CH, C-10), 45.5 (C, C-9), 40.4 (CH, C-8), 40.2 (C, C-5), 38.7 (CH_2, C-6), 33.8 (CH_3, C-12), 32.7 (CH_2, C-3), 31.9 (CH_2, C-15), 28.7 (CH_2, C-7), 25.7 (CH_2, C-2), 23.3 (CH_2, C-1), 19.4 (CH_3, C-14), 19.1 (CH_3, C-13); HRESIMS m/z 381.2047 $[M+Na]^+$ (calcd for $C_{22}H_{30}O_4Na$, 381.2034).

Smenospongidine. Red solid; UV (MeOH) λ_{max} (log ε) 321(3.73) nm; IR (neat) ν_{max} 3267, 2922, 1588, 1381 cm^{-1}; ^{1}H NMR (C_6D_6, 500 MHz) δ 7.08 (2H, brd, J = 7.9 Hz, H-25, H-29), 7.05 (1H, brd, J = 7.5 Hz, H-27), 6.74 (2H, brd, J = 7.3 Hz, H-26, H-28), 5.91 (1H, brs, -NH), 5.12 (1H, s, H-19), 4.61 (1H, dd, J = 1.6, 1.6 Hz, H-11a), 4.57 (1H, brs, H-11b), 2.64 (1H, d, J = 13.8 Hz, H-15a), 2.53 (1H, d, J = 13.8 Hz, H-15b), 2.40 (2H, H2-22), 2.36 (1H, ddd, J =13.7, 13.7, 7.1 Hz, H-3ax), 2.33 (1H, brd, J = 12.6 Hz, H-1eq), 2.19 (1H, brd, J = 13.7 Hz, H-3eq), 2.04 (2H, H2-23), 1.94 (1H, ddd, J = 12.7, 5.9, 2.4 Hz, H-2eq), 1.55 (1H, dd, J = 13.5, 2.9 Hz, H-6eq), 1.46 (1H, overlapped, H-1ax), 1.42 (3H, overlapped, H-2ax, H2-7), 1.41 (1H, dd, J = 5.7, 3.1 Hz, H-8), 1.40 (1H, overlapped, H-6ax), 1.17 (3H, d, J = 5.4 Hz, H3-13), 1.06 (3H, s,

H3-12), 1.03 (1H, dd, J = 11.7, 2.2 Hz, H-10), 0.88 (3H, s, H3-14); ^{13}C NMR (C_6D_6, 125 MHz) δ 183.5 (C, C-21), 178.5 (C, C-18), 160.4 (C, C-4), 157.7 (C, C-17), 150.0 (C, C-20), 138.3 (C, C-24), 129.3 (CH, C-25, C-29), 129.1 (CH, C-26, C-28), 127.4 (CH, C-27), 113.8 (C, C-16), 103.8 (CH_2, C-11), 92.6 (CH, C-19), 50.9 (CH, C-10), 43.9 (CH_2, C-22), 43.5 (C, C-9), 41.2 (C, C-5), 38.7 (CH, C-8), 37.5 (CH_2, C-6), 34.2 (CH_2, C-23), 33.9 (CH_2, C-3), 33.3 (CH_2, C-15), 29.7 (CH_2, C-2), 28.8 (CH_2, C-7), 24.0 (CH_2, C-1), 21.1 (CH_3, C-12), 18.8 (CH_3, C-13), 18.0 (CH_3, C-14); HRESIMS m/z 448.2846 $[M+H]^+$ (calcd for $C_{29}H_{38}NO_3$, 448.2842).

Smenospongorine. Red solid; UV (MeOH) λ_{max} (log ε) 211(3.75), 322 (3.62) nm; IR (neat) ν_{max} 3271, 2956, 2925, 1587, 1382 cm^{-1}; ^{1}H NMR (C_6D_6, 500 MHz) δ 6.02 (1H, brs, -NH), 5.17 (1H, s, H-19), 4.60 (1H, dd, J = 1.6, 1.6 Hz, H-11a), 4.56 (1H, dd, J = 1.6, 1.6 Hz, H-11b), 2.66 (1H, d, J = 13.8 Hz, H-15a), 2.57 (1H, d, J = 13.8 Hz, H-15b), 2.38 (1H, ddd, J = 12.4, 5.3, 2.2 Hz, H-1eq), 2.35 (1H, ddd, J = 13.7, 13.7, 5.3 Hz, H-3ax), 2.17 (1H, ddd, J = 13.7, 2.4, 2.4 Hz, H-3eq), 2.03 (2H, H2-22), 1.97 (1H, ddd, J = 11.5, 5.3, 2.4 Hz, H-2eq), 1.55 (1H, ddd, J = 12.4, 8.9 ,2.9 Hz, H-6eq), 1.45 (1H, ddd, J = 12.4, 9.7, 2.4 Hz, H-1ax), 1.44 (1H, ddd, J = 11.5, 5.3, 2.4 Hz, H-2ax), 1.43 (1H, ddq, J = 12.4, 10.0, 5.8 Hz, H-8), 1.40 (3H, overlapped, H-6ax, H2-7), 1.20 (3H, d, J = 5.8 Hz, H3-13), 1.12 (1H, ddd, J = 13.5, 6.8, 6.8 Hz, H-23), 1.06 (3H, s, H3-12), 1.04 (1H, dd, J = 9.7, 2.2 Hz, H-10), 0.89 (3H, s, H3-14), 0.45 (6H, d, J = 6.0 Hz, H3-24, H3-25); ^{13}C NMR (C_6D_6, 125 MHz) δ 183.7 (C, C-21), 178.4 (C, C-18), 160.4 (C, C-4), 157.8 (C, C-17), 150.5 (C, C-20), 113.9 (C, C-16), 103.7 (CH_2, C-11), 92.5 (CH, C-19), 50.9 (CH, C-10), 50.0 (CH_2, C-22), 43.5 (C, C-9), 41.2 (C, C-5), 38.8 (CH, C-8), 37.5 (CH_2, C-6), 33.9 (CH_2, C-3), 33.3 (CH_2, C-15), 29.8 (CH_2, C-2), 28.8 (CH_2, C-7), 27.6 (CH, C-23), 24.1 (CH_2, C-1), 21.1 (CH_3, C-12), 20.2 (CH_3, C-24, C-25), 18.8 (CH_3, C-13), 18.0 (CH_3, C-14); HRESIMS m/z 398.2702 $[M-H]^-$ (calcd for $C_{25}H_{36}NO_3$, 398.2686).

Smenodiol. White solid; UV (MeOH) λ_{max} (log ε) 219 (4.32), 267 (3.93) nm; IR (neat) ν_{max} 3469, 3338, 1679, 1439, 1297, 1234, 1002 cm^{-1}; ^{1}H NMR (C_6D_6, 500 MHz) δ 7.96 (1H, brs, H-17), 7.41 (1H, brs, H-19), 5.77 (1H, brs, 21-OH), 5.41 (1H, brs, H-7), 5.01 (1H, brs, 20-OH), 3.51 (3H, s, 22-OCH_3), 2.89 (1H, dd, J = 15.4, 9.4 Hz, H-15a), 2.69 (1H, dd, J = 15.4, 2.5 Hz, H-15b), 2.56 (1H, brd, J = 9.4 Hz, H-9), 1.94 (1H, brd, J =13.0 Hz, H-6eq), 1.86 (2H, overlapped, H-1eq, H-6ax), 1.64 (3H, dd, J = 2.2, 1.2 Hz, H3-13), 1.47 (1H, ddd, J = 13.0, 3.3, 3.3 Hz, H-2eq), 1.35 (2H, ddd, J = 13.0, 5.6, 3.3 Hz, H-2ax, H-3eq), 1.20 (1H, dd, J = 11.8, 5.1 Hz, H-5), 1.12 (1H, ddd, J = 13.0, 10.1, 3.3 Hz, H-1ax), 1.10 (1H, ddd, J = 13.0, 10.1, 3.3 Hz, H-3ax), 0.90 (3H, s, H3-14), 0.86 (3H, s, H3-11), 0.83 (3H, s, H3-12); ^{13}C NMR (C_6D_6, 125 MHz) δ 167.4 (C, C-22), 147.8 (C, C-21), 143.0 (C, C-20), 135.8 (C, C-8), 131.1 (C, C-16), 124.9 (CH, C-17), 123.2 (CH, C-7), 122.4 (C, C-18), 114.3 (CH, C-19), 54.7 (CH, C-9), 51.9 (CH_3, 22-OCH_3), 50.6 (CH, C-5), 42.7 (CH_2, C-3), 40.1 (CH_2, C-1), 37.6 (C, C-10), 33.7 (CH_3, C-12), 33.5 (C, C-4), 26.9 (CH_2, C-15), 24.5 (CH_2, C-6), 23.1 (CH_3, C-13), 22.5 (CH_3, C-11), 19.7 (CH_2, C-2), 14.5 (CH_3, C-14); HRESIMS m/z 373.2369 $[M+H]^+$ (calcd for $C_{23}H_{33}O_4$, 373.2370).

Cyclospongiaquinone-1 (5). Yellow solid; UV (MeOH) λ_{max} (log ε) 215 (3.56), 283 (3.83) nm; IR (neat) ν_{max} 3433, 2928, 1657, 1602, 1245, 1223 cm^{-1}; ^{1}H NMR (C_6D_6, 500 MHz) δ 5.41 (1H, s, H-19), 2.88 (3H, s, 20-OCH_3), 2.45 (1H, dd, J = 18, 4.7 Hz, H-15a), 1.97 (1H, ddd, J = 12.7, 3.3, 3.3 Hz, H-7eq), 1.91 (1H, dd, J = 18, 12.9 Hz, H-15b), 1.57 (1H, ddd, J = 12.7, 12.7, 4.4 Hz, H-7ax), 1.37 (1H, ddd, J = 13.8, 7.1, 3.6 Hz, H-2eq), 1.32 (1H, ddd, J = 12.8, 7.2, 3.4 Hz, H-1eq), 1.27 (1H, ddd, J = 13.1, 4.3, 2.9 Hz, H-6eq), 1.25 (1H, ddd, J = 13.9, 5.2, 3.2 Hz, H-3eq), 1.22 (1H, ddd, J = 13.1, 7.1, 3.5 Hz, H-6ax), 1.07 (1H, dd, J = 12.9, 4.7 Hz, H-9), 0.97 (1H, ddd, J = 13.9, 13.9, 3.8 Hz, H-3ax), 0.90 (1H, ddd, J = 13.8, 13.8, 3.4 Hz, H-2ax), 0.90 (3H, s, H3-13), 0.74 (3H, s, H3-12), 0.66 (3H, s, H3-11), 0.62 (1H, dd, J = 12.4, 2.2 Hz, H-5), 0.54 (1H,

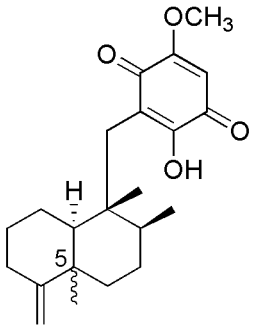
ddd, J = 12.8, 3.3, 3.3 Hz, H-1ax), 0.49 (3H, s, H3-14); ^{13}C NMR (C_6D_6, 125 MHz) δ 181.9 (C, C-18), 181.2 (C, C-21), 159.9 (C, C-20), 153.0 (C, C-17), 116.7 (C, C-16), 105.3 (CH, C-19), 81.2 (C, C-8), 56.1 (CH, C-5), 55.6 (CH_3, 20-OCH_3), 51.5 (CH, C-9), 42.3 (CH_2, C-3), 40.7 (CH_2, C-7), 39.4 (CH_2, C-1), 37.3 (C, C-10), 33.8 (CH_3, C-12), 33.5 (C, C-4), 21.9 (CH_3, C-11), 20.8 (CH_3, C-13), 20.1 (CH_2, C-2), 19.0 (CH_2, C-6), 17.0 (CH_2, C-15), 15.2 (CH_3, C-14); ESIMS m/z 381.2037 $[M+Na]^+$ (calcd for $C_{22}H_{30}O_4Na$, 381.2034).

Dactylospontriol. Pale green solid, UV (MeOH) λ_{max} (log ε) 220 (4.31) 276 (3.98) nm; IR (KBr) ν_{max} 3450, 2920, 2850, 1680, 1620, 1500, 1440, 1290 cm^{-1}; (C_6D_6, 500 MHz) δ 11.29 (1H, s, 19-OH), 7.55 (1H, s, H-17), 5.78 (1H, s, 20-OH), 5.42 (1H, s, H-7), 3.31 (3H, s, 22-OCH_3), 2.82 (1H, d, J = 15.5 Hz, H-15a), 2.65 (1H, dd, J = 15.5, 9.6 Hz, H-15b), 2.51 (1H, brs, H-9), 1.94 (1H, overlapped, H-6eq), 1.87 (1H, overlapped, H-6ax), 1.85 (1H, overlapped, H-1eq), 1.66 (3H, s, H3-13), 1.48 (1H, overlapped, H-2eq), 1.35 (1H, overlapped, H-2ax), 1.33 (1H, overlapped, H-3eq), 1.21 (1H, dd, J = 11.7, 5.0 Hz, H-5), 1.08 (1H, overlapped, H-1ax), 1.05 (1H, overlapped, H-3ax), 0.89 (3H, s, H3-14), 0.85 (3H, s, H3-11), 0.82 (3H, s, H3-12); ^{13}C NMR (C_6D_6, 125 MHz) δ 171.0 (C, C-22), 148.2 (C, C-21), 147.9 (C, C-19), 135.5 (C, C-8), 131.2 (C, C-20), 122.7 (CH, C-7), 122.6 (C, C-16), 121.4 (CH, C-17), 105.1 (C, C-18), 54.2 (CH, C-9), 51.6 (CH_3, 22-OCH_3), 50.3 (CH, C-5), 42.4 (CH_2, C-3), 39.6 (CH_2, C-1), 37.1 (C, C-10), 33.3 (CH_3, C-12), 33.1 (C, C-4), 25.9 (CH_2, C-15), 24.1 (CH_2, C-6), 22.8 (CH_3, C-13), 22.1 (CH_3, C-11), 19.3 (CH_2, C-2), 14.0 (CH_3, C-14); EIMS m/z (% relative intensity): 388 ($[M]^+$, 36), 197 (100), 164 (40).

Nakijiquinone L and smenospongiarine. Red solid; UV (MeOH) λ_{max} (log ε) 325 (3.98) nm; IR (neat) ν_{max} 3272, 2925, 2857, 1588, 1513, 1382, 1350, 1217, 1205 cm^{-1}; ^{1}H NMR (C_6D_6, 500 MHz) for nakijiquinone L δ 6.05 (1H, brs, -NH), 5.20 (1H, s, H-19), 4.60 (1H, dd, J = 1.6, 1.6

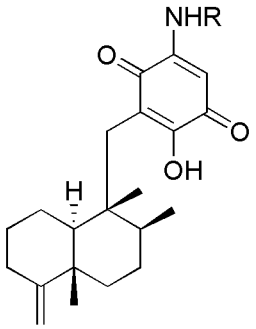
Hz, H-11a), 4.56 (1H, d, J = 1.6 Hz, H-11b), 2.67 (1H, d, J = 13.8 Hz, H-15a), 2.57 (1H, d, J = 13.8 Hz, H-15b), 2.37 (1H, overlapped, H-3ax), 2.35 (1H, overlapped, H-1eq), 2.21 (1H, dd, J = 13.5, 5.7 Hz, H-22a), 2.17 (1H, dd, J = 13.7, 5.9 Hz, H-3eq), 2.05 (1H, ddd, J = 13.5,13.5, 7.7 Hz, H-22b), 1.95 (1H, ddd, J = 12.3, 6.0, 3.8 Hz, H-2eq), 1.53 (1H, dd, J = 13.5, 4.5 Hz, H-6eq), 1.44 (1H, overlapped, H-2ax), 1.43 (2H, overlapped, H-1ax, H-6ax), 1.42 (1H, dd, J = 5.7, 3.1 Hz, H-8), 1.40 (2H, H2-7), 1.20 (3H, d, J =5.7 Hz, H3-13), 1.06 (3H, s, H3-12), 1.04 (1H, dd, J = 11.1, 1.8 Hz, H-10), 0.93 (1H, dd, J = 12.4, 6.6 Hz, H-23), 0.89 (3H, s, H3-14), 0.81 (1H, ddd, J = 13.1, 6.6, 2.0 Hz, H-24a), 0.65 (1H, ddd, J = 13.1, 12.4, 6.6 Hz, H-24b), 0.53 (3H, dd, J = 6.6, 6.6 Hz, H3-25), 0.42 (3H, d, J = 6.6 Hz, H3-26), for smenospongiarine δ 5.87 (1H, brs, -NH), 5.17 (1H, s, H-19), 4.60 (1H, dd, J = 1.6, 1.6 Hz, H-11a), 4.56 (1H, d, J = 1.6 Hz, H-11b), 2.68 (1H, d, J = 13.8 Hz, H-15a), 2.58 (1H, d, J = 13.8 Hz, H-15b), 2.38 (1H, overlapped, H-3ax), 2.37 (1H, overlapped, H-1eq), 2.19 (2H, H2-22), 2.16 (1H, dd, J = 13.7, 5.9 Hz, H-3eq), 1.95 (1H, ddd, J = 12.3, 6.0, 3.8 Hz, H-2eq), 1.53 (1H, dd, J = 13.5, 4.5 Hz, H-6eq), 1.44 (1H, overlapped, H-2ax), 1.43 (2H, overlapped, H-1ax, H-6ax), 1.42 (1H, dd, J = 5.7, 3.1 Hz, H-8), 1.40 (2H, H2-7), 1.21 (3H, d, J = 5.8 Hz, H3-13), 1.06 (3H, s, H3-12), 1.06 (1H, overlapped, H-24), 1.04 (1H, dd, J = 11.1, 1.8 Hz, H-10), 0.90 (3H, s, H3-14), 0.68 (2H, H2-23), 0.55 (6H, d, J = 6.6 Hz, H3-25, H3-26); ^{13}C NMR (C_6D_6, 125 MHz) for nakijiquinone L δ 183.7 (C, C-21), 178.4 (C, C-18), 160.4 (C, C-4), 157.9 (C, C-17), 150.5 (C, C-20), 113.9 (C, C-16), 103.7 (CH_2, C-11), 92.4 (CH, C-19), 51.0 (CH, C-10), 48.6 (CH_2, C-22), 43.5 (C, C-9), 41.2 (C, C-5), 38.8 (CH, C-8), 37.5 (CH_2, C-6), 34.0 (CH, C-23), 33.9 (CH_2, C-3), 33.3 (CH_2, C-15), 29.8 (CH_2, C-2), 28.8 (CH_2, C-7), 27.4 (CH_2, C-24), 24.1 (CH_2, C-1), 21.1 (CH_3, C-12), 18.8 (CH_3, C-13), 18.0 (CH_3, C-14), 17.3 (CH_3, C-26), 11.5 (CH_3, C-25), for smenospongiarine δ 183.7 (C, C-21), 178.4 (C, C-18), 160.4 (C, C-4), 157.9 (C, C-17), 150.3 (C, C-20), 113.9 (C, C-16), 103.8 (CH_2,

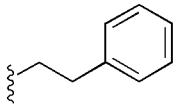
C-11), 92.3 (CH, C-19), 50.9 (CH, C-10), 43.5 (C, C-9), 41.2 (CH_2, C-22), 41.1 (C, C-5), 38.8 (CH, C-8), 37.6 (CH_2, C-6), 36.7 (CH_2, C-23), 34.0 (CH_2, C-3), 33.3 (CH_2, C-15), 29.8 (CH_2, C-2), 28.8 (CH_2, C-7), 26.3 (CH, C-24), 24.1 (CH_2, C-1), 22.6 (CH_3, C-25, C-26), 21.1 (CH_3, C-12), 18.8 (CH_3, C-13), 18.0 (CH_3, C-14); HRESIMS m/z 412.2856 $[M-H]^-$ (calcd for $C_{26}H_{38}NO_3$, 412.2842).

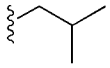


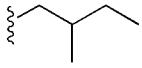
5*S* ilimaquinone

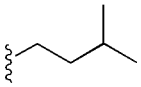
5*R* 5-*epi*-ilimaquinone

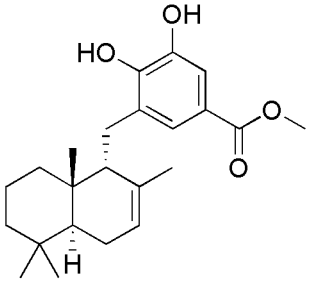


R =  smenospongidine

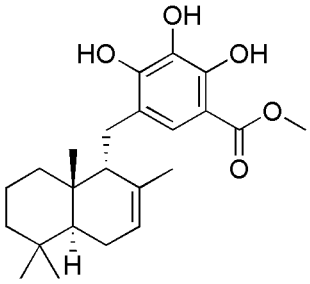
R =  smenospongorine

R =  nakijiquinone L

R =  smenospongiarine



smenodiol



dactylospontriol

Table S1. Anti-proliferative activity of isolated compounds

compounds	IC_{50} (μM)		
	PC-3	HeLa	MCF-7
1	6.7	7.6	12
2	16	ND	ND
4	20	ND	ND
5	10	27	ND
mixture of **3** and **6**	11	ND	ND
5-*epi*-ilimaquinone	14	ND	ND
smenospongidine	8.4	ND	ND
smenospongorine	5.2	ND	ND
smenodiol	17	4.5	6.0
dactylospontriol	ND	3.5	4.8
mixture of nakijiquinone L and smenospongiarine	3.1	ND	ND

Note: ND = not determined

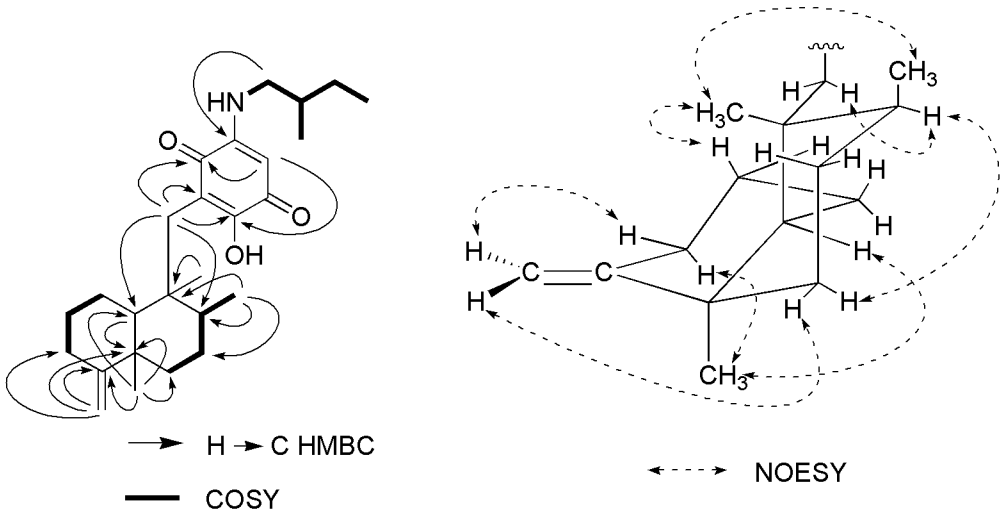


Figure S3 HMBC, COSY, and NOESY correlations of compound **3**

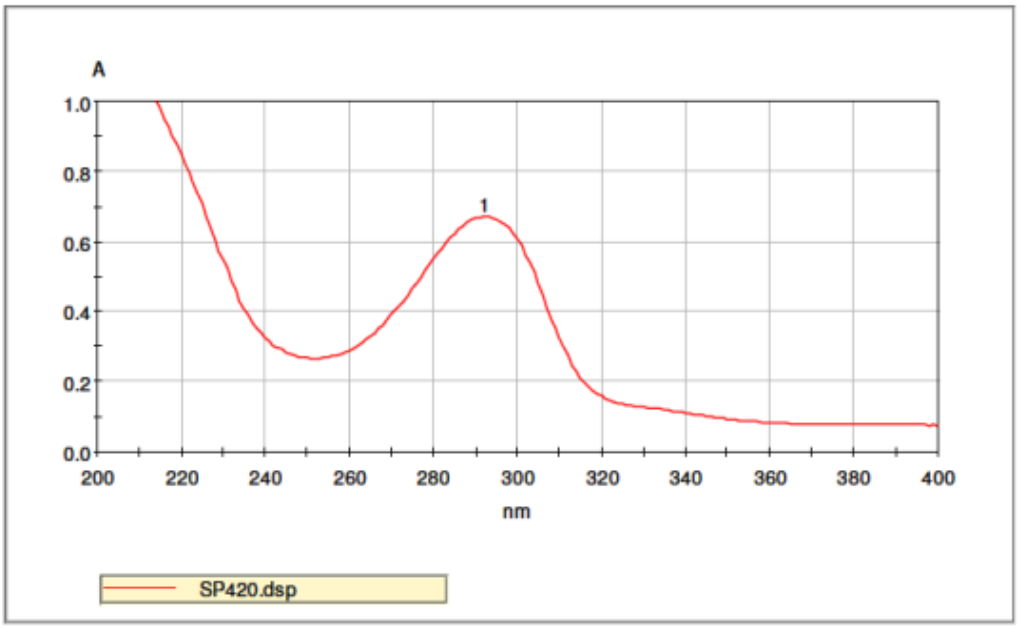


Figure S4. UV spectrum of **2** (MeOH)

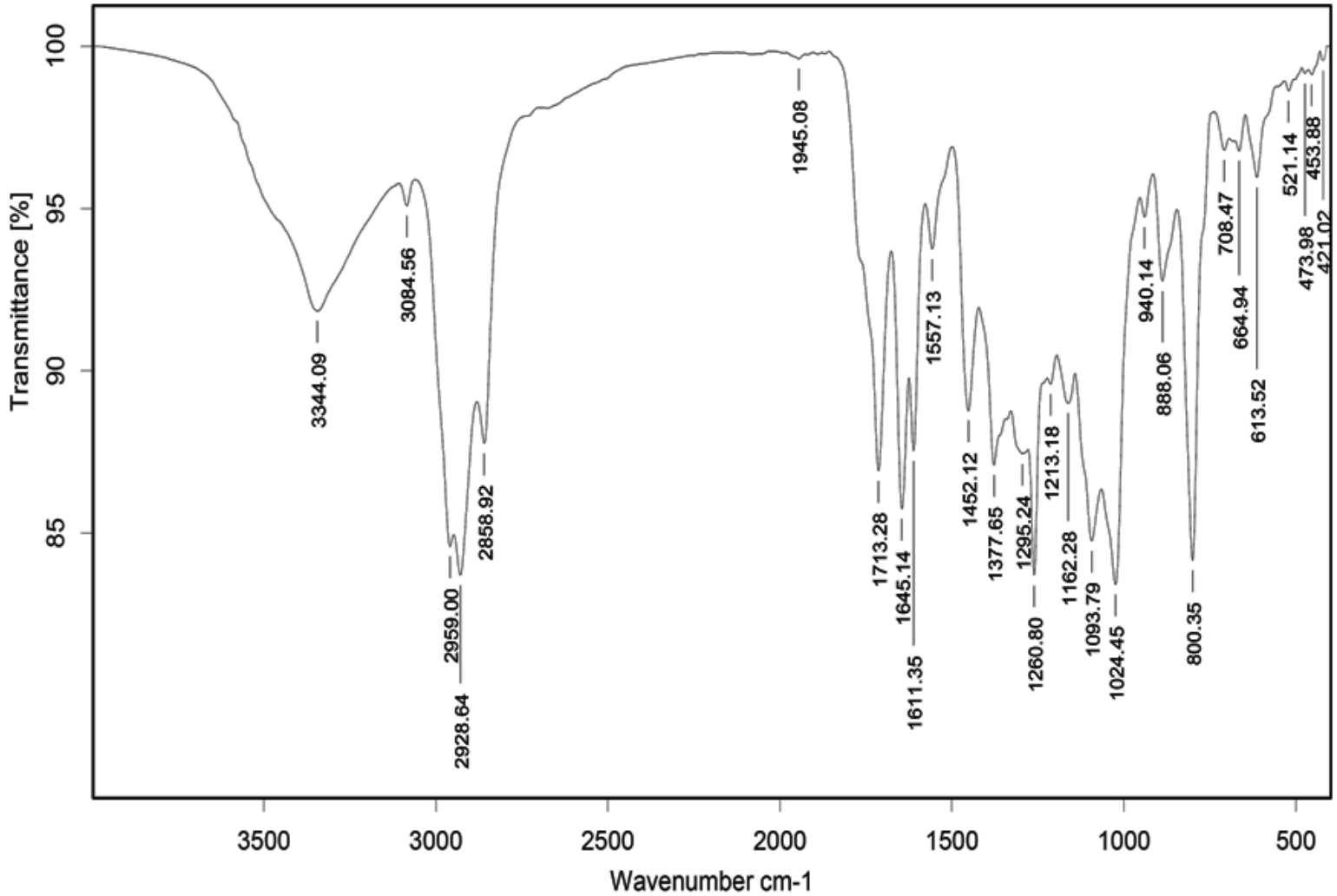


Figure S5. IR spectrum of **2** (neat)

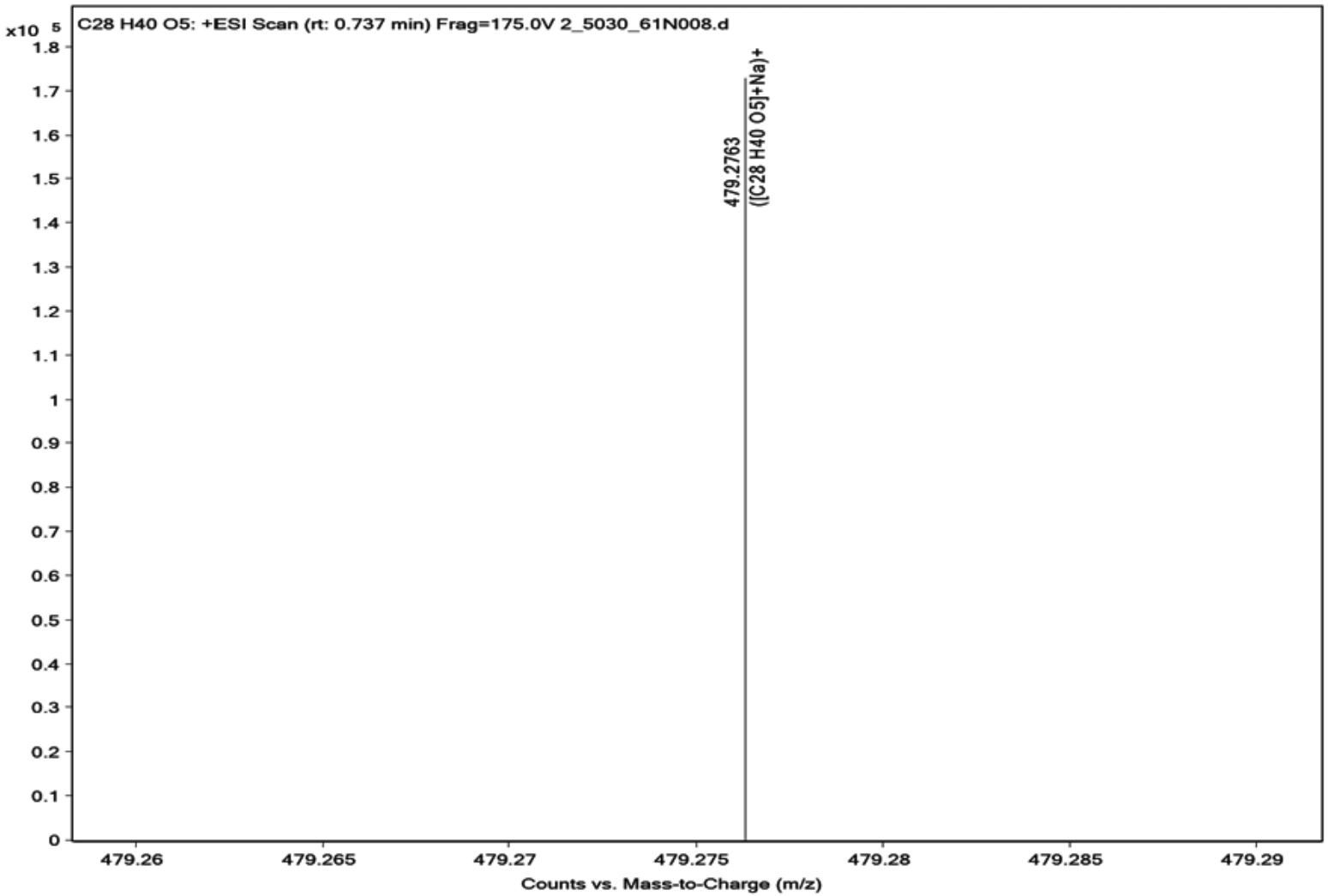


Figure S6. HR ESI mass spectrum of **2**

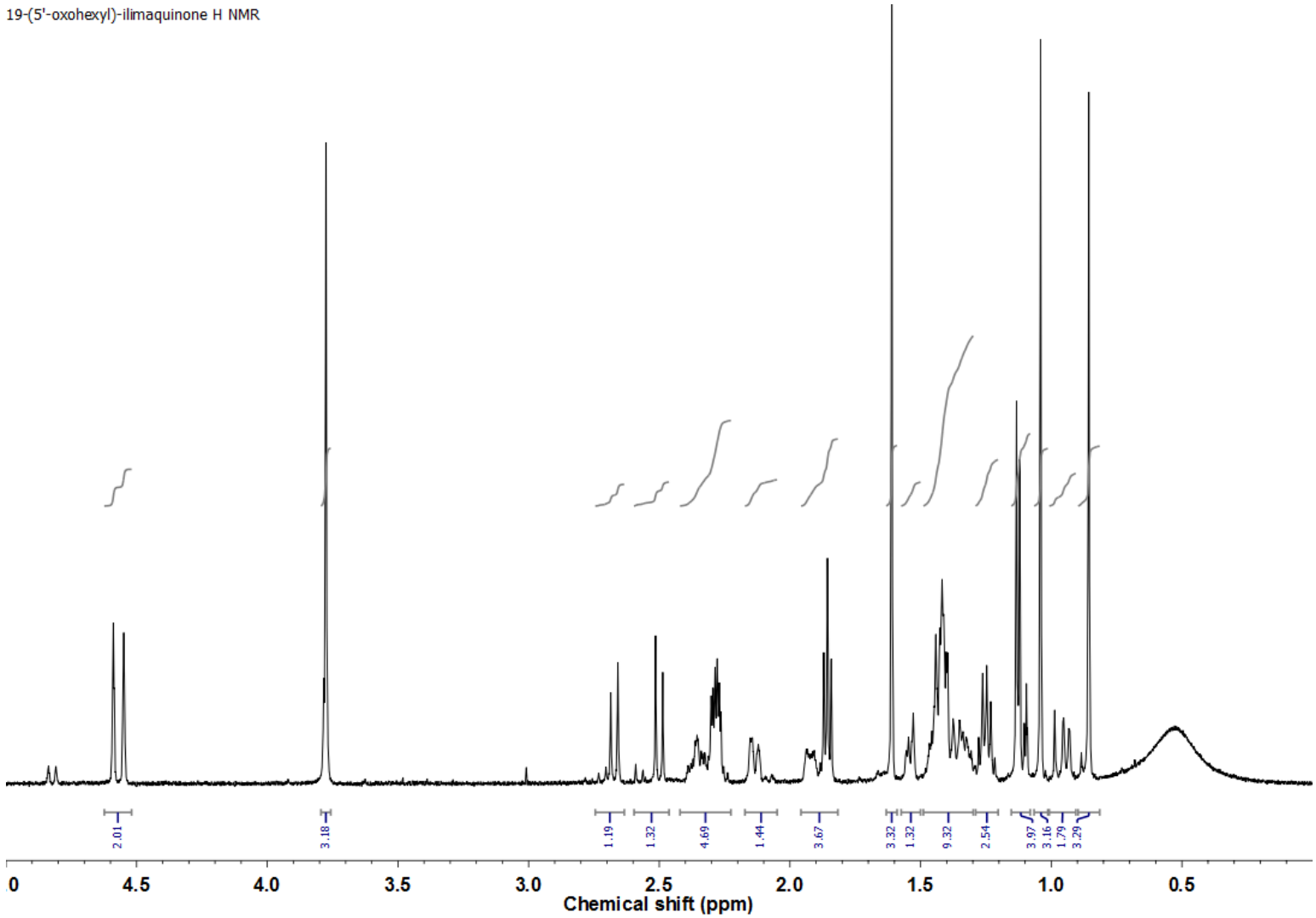


Figure S7. ^{1}H NMR spectrum of spectrum of **2** (500 MHz, C_6D_6)

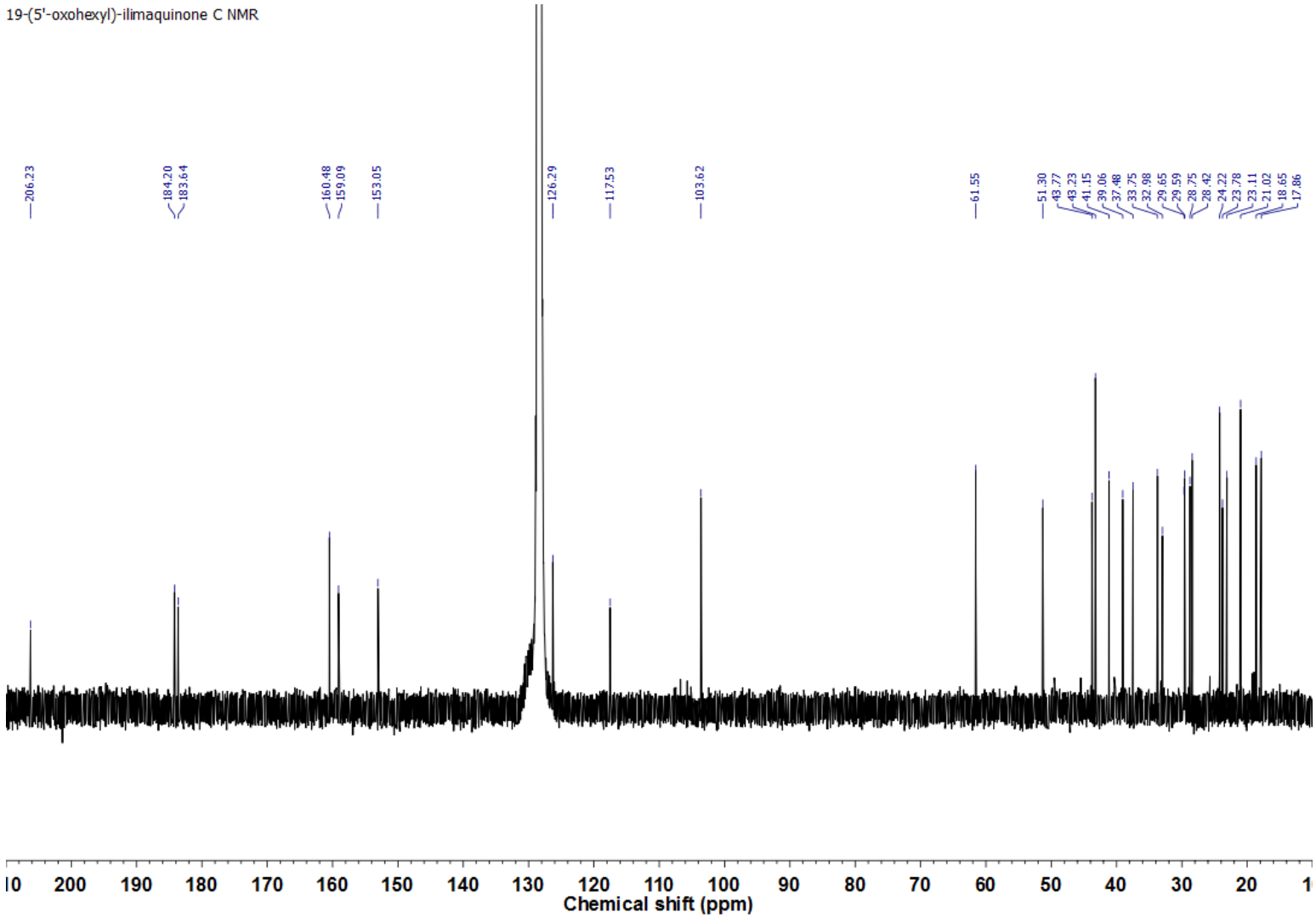


Figure S8. ^{13}C NMR spectrum of spectrum of **2** (125 MHz, C_6D_6)

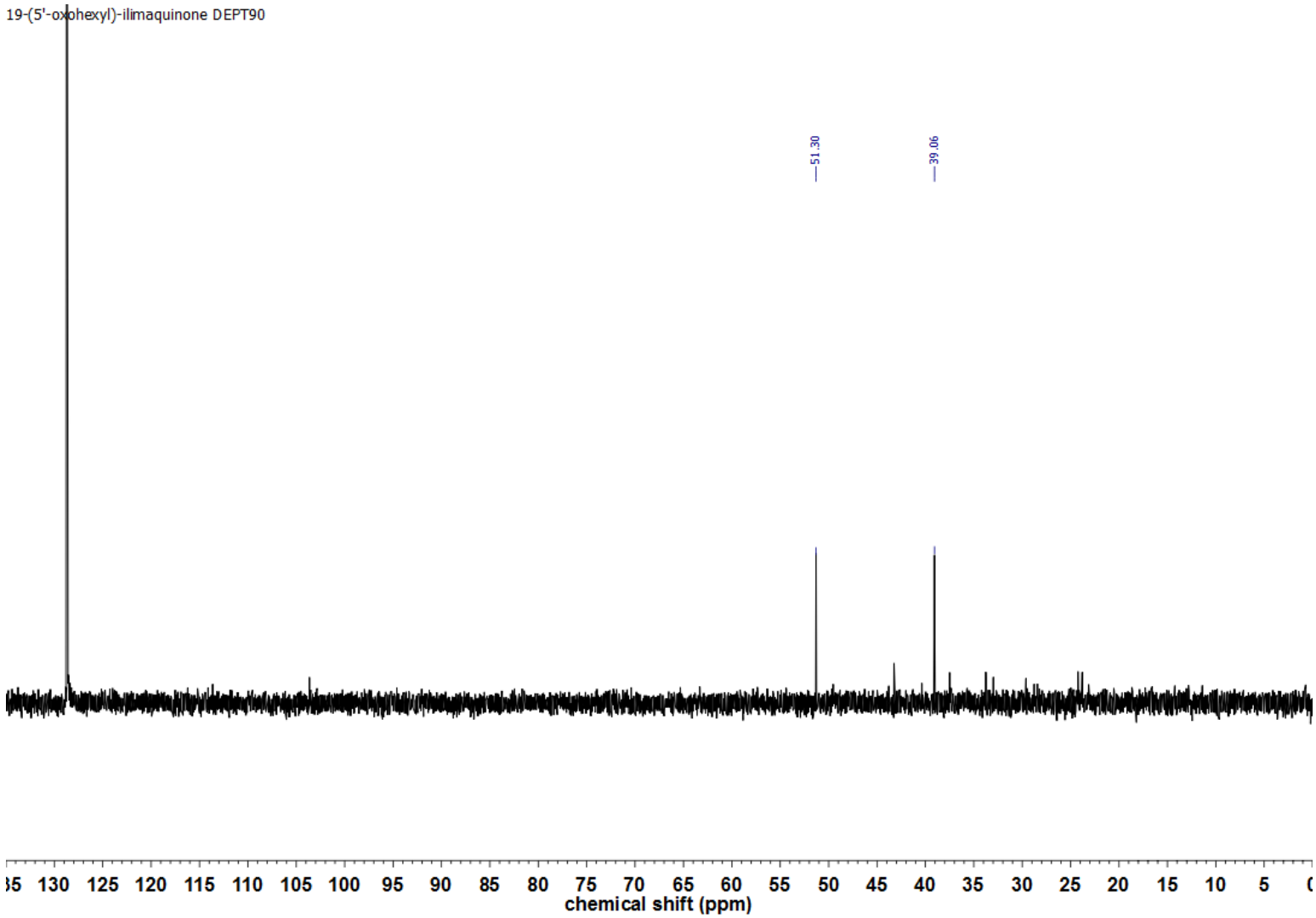


Figure S9. DEPT 90° spectrum of **2** (125 MHz, C_6D_6)

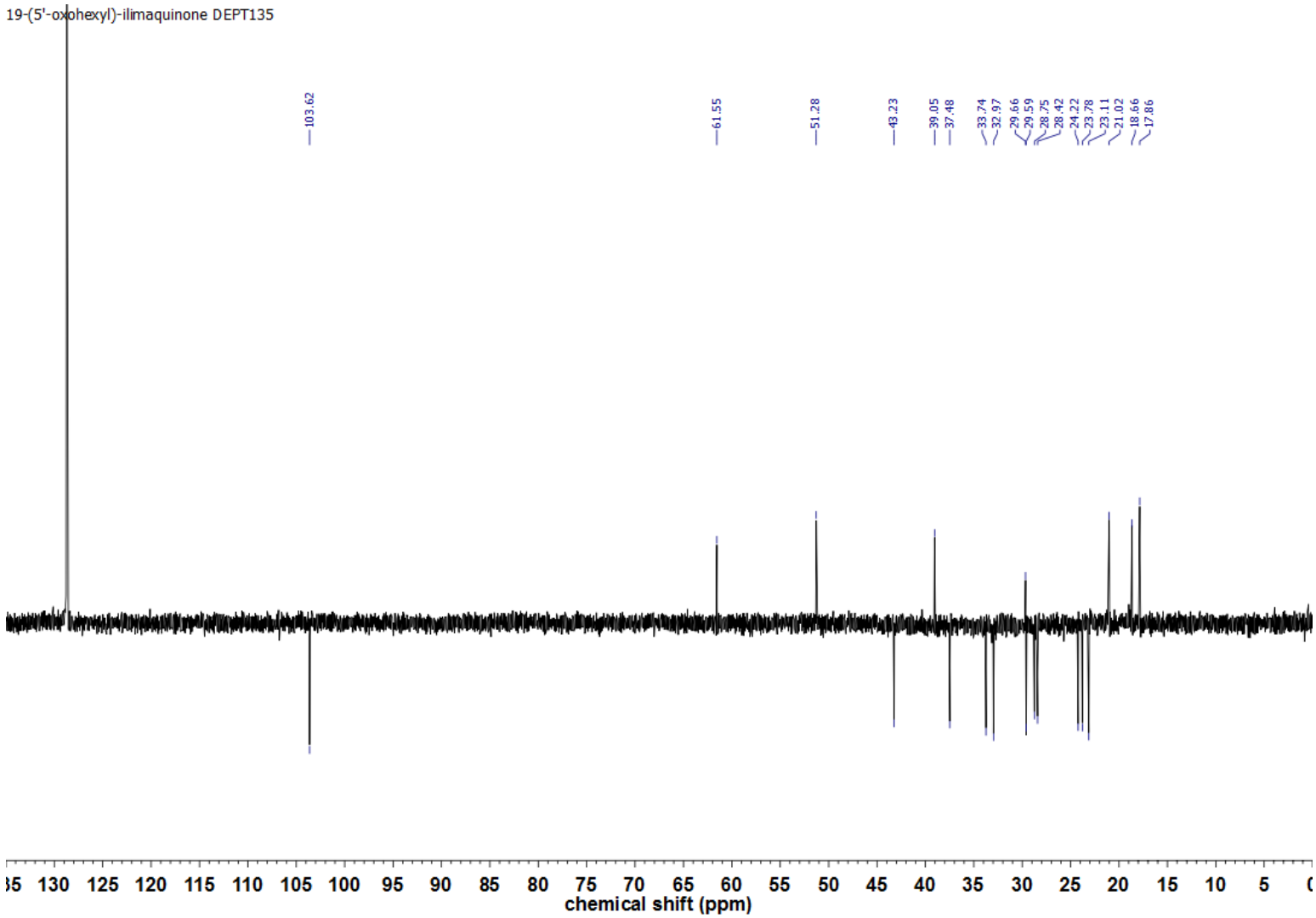


Figure S10. DEPT 135° spectrum of **2** (125 MHz, C_6D_6)

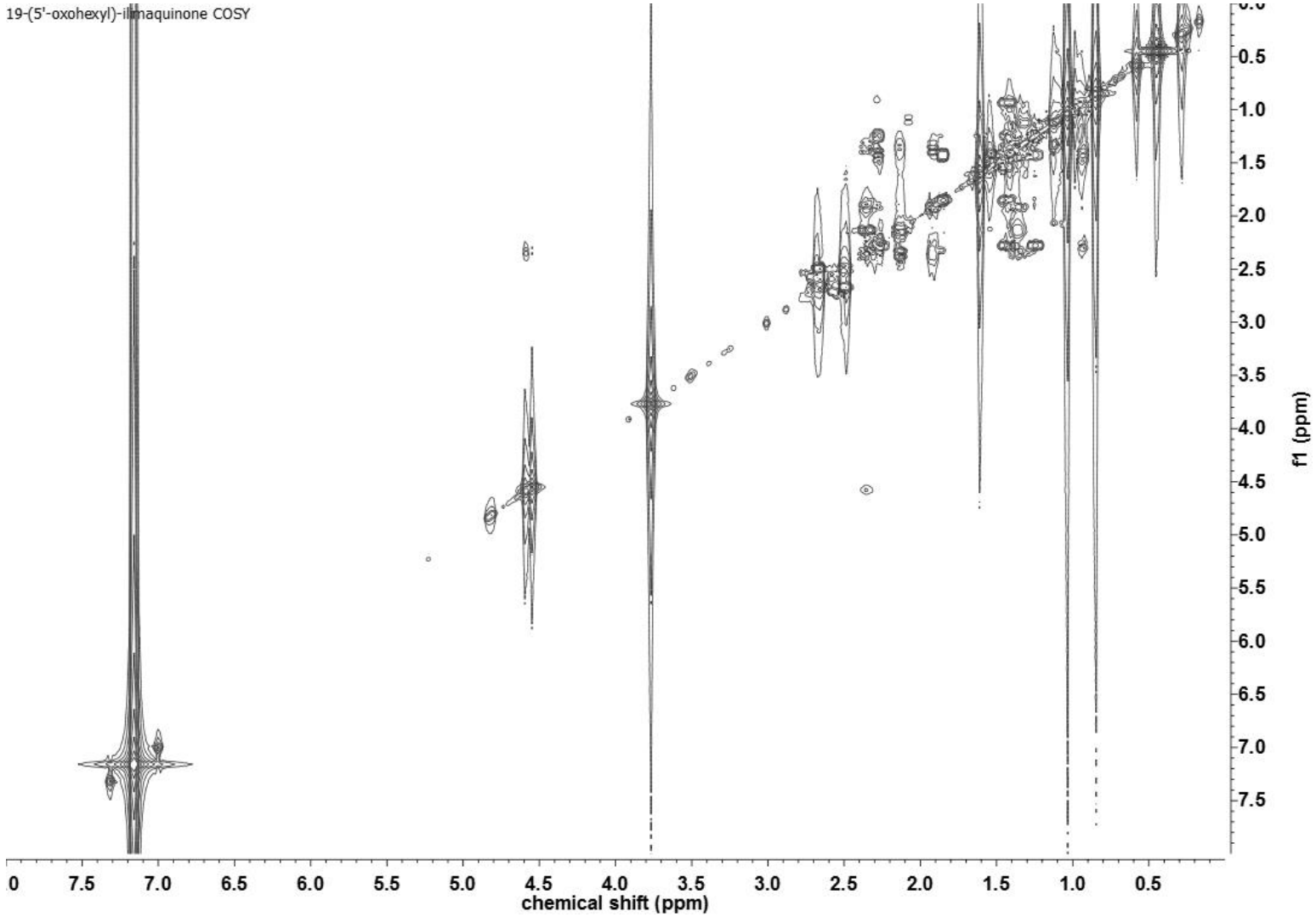


Figure S11. ^{1}H-^{1}H COSY spectrum of **2** (500 MHz, C_6D_6)

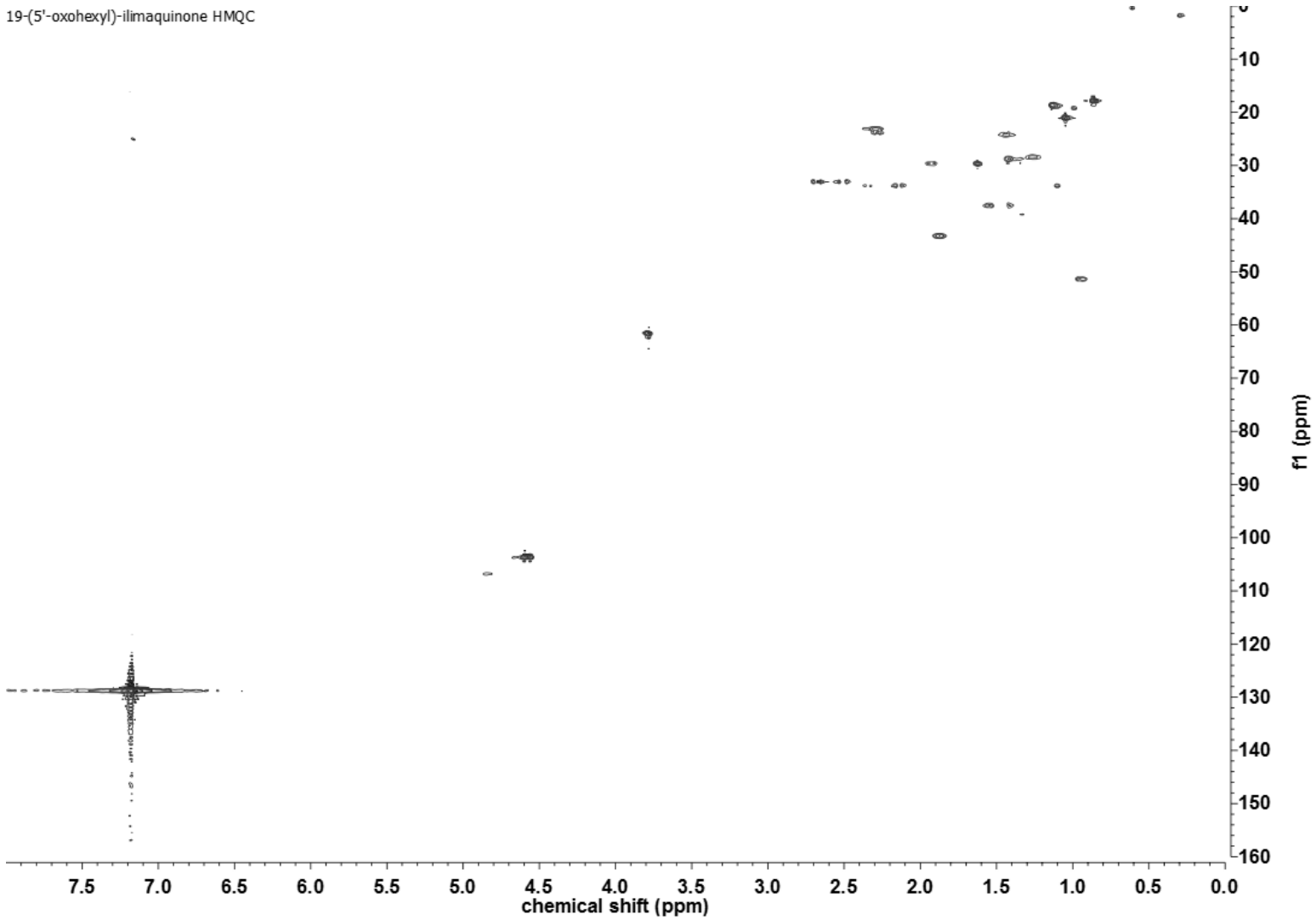


Figure S12. HMQC spectrum of **2** (500 MHz, C_6D_6)

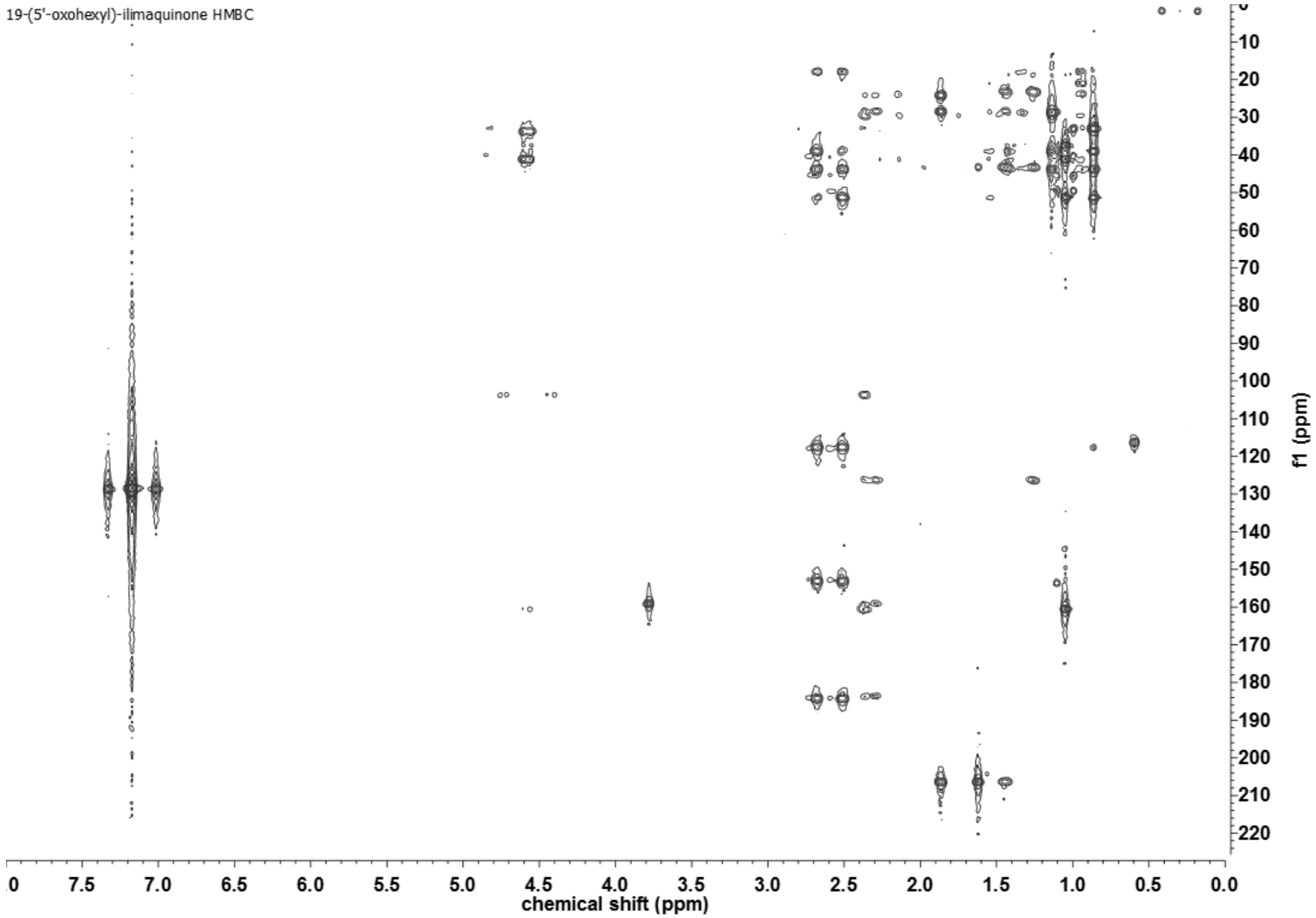


Figure S13. HMBC spectrum of **2** (500 MHz, C_6D_6)

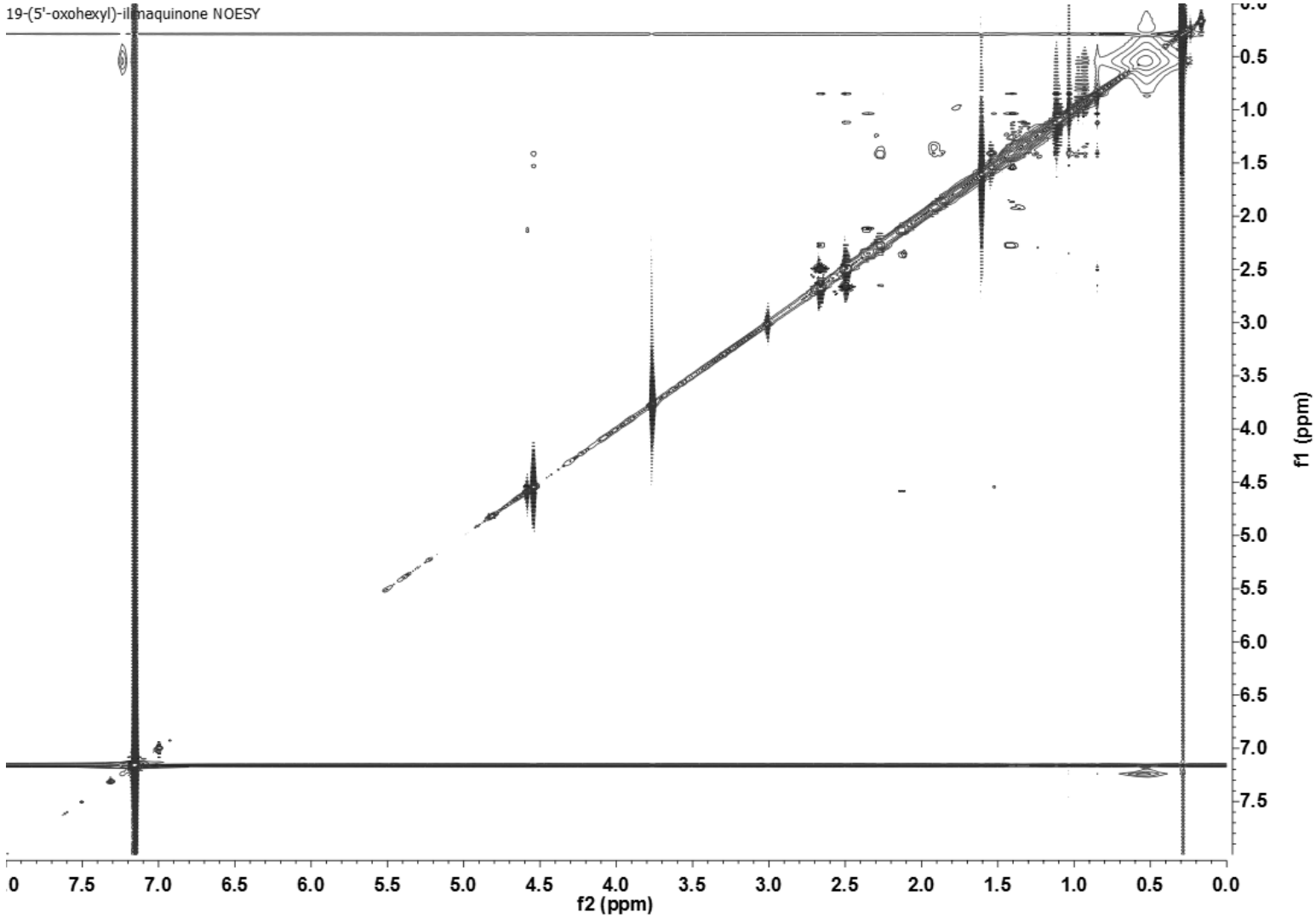


Figure S14. NOESY spectrum of **2** (500 MHz, C_6D_6)

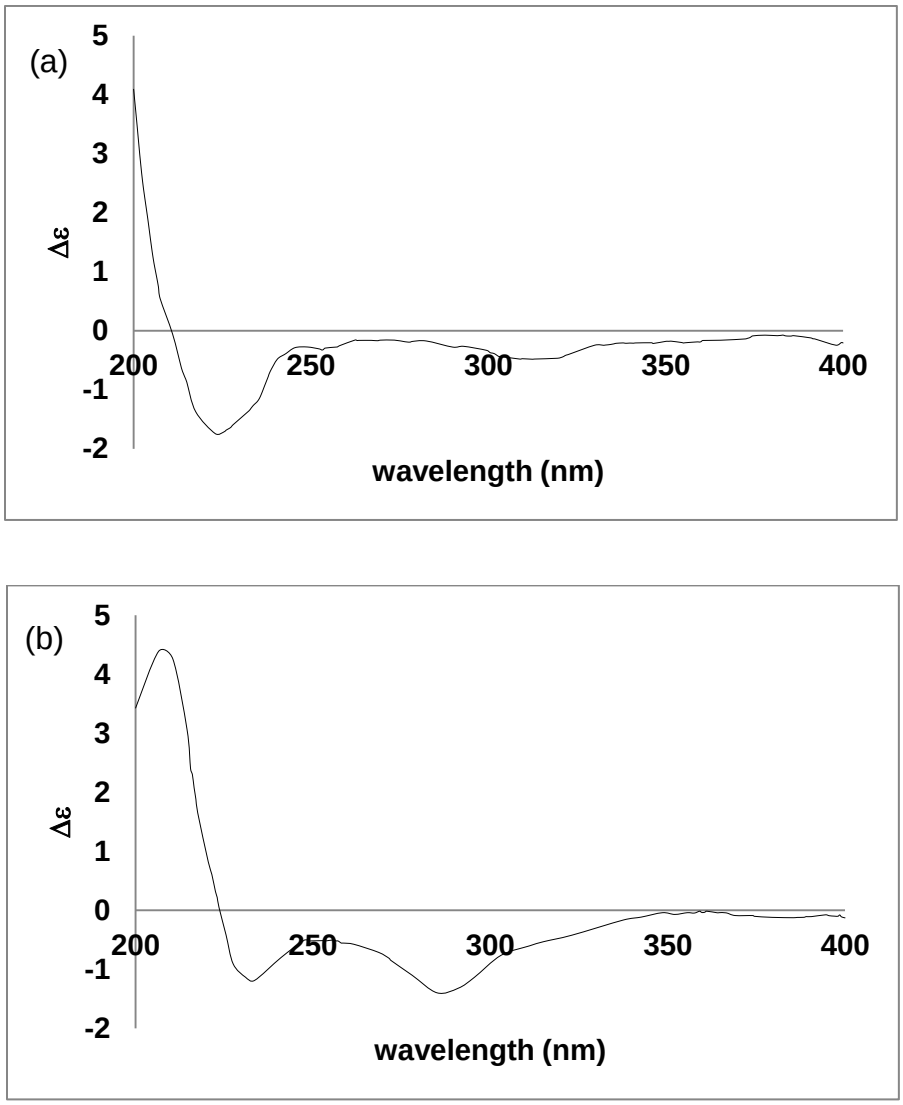


Figure S15. ECD spectra of (a) compound **2** (*c* 0.37 mM, MeOH) and (b) **1** (*c* 0.34 mM, MeOH)

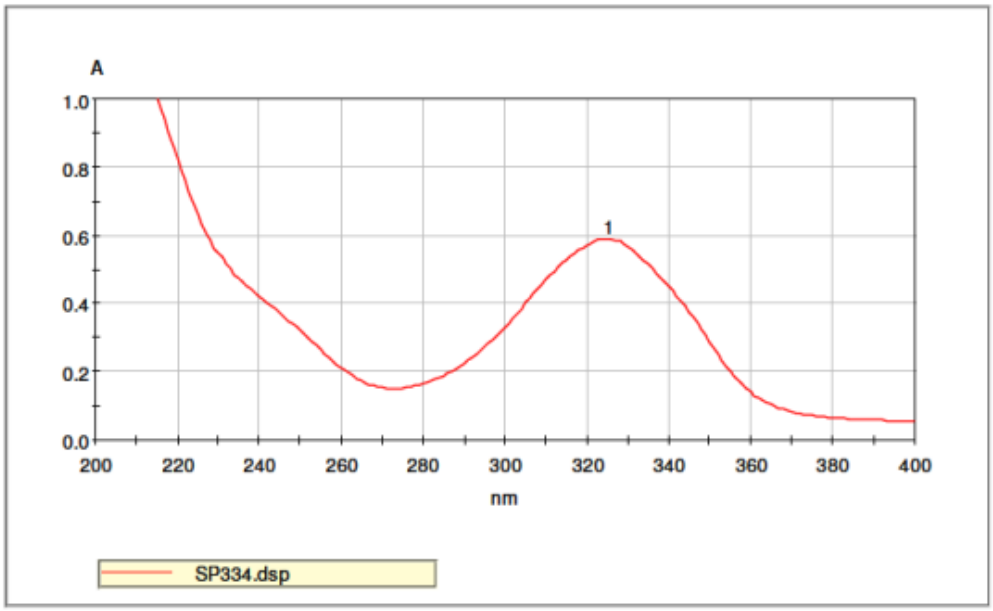


Figure S16. UV spectrum of mixture of **3** and **6**

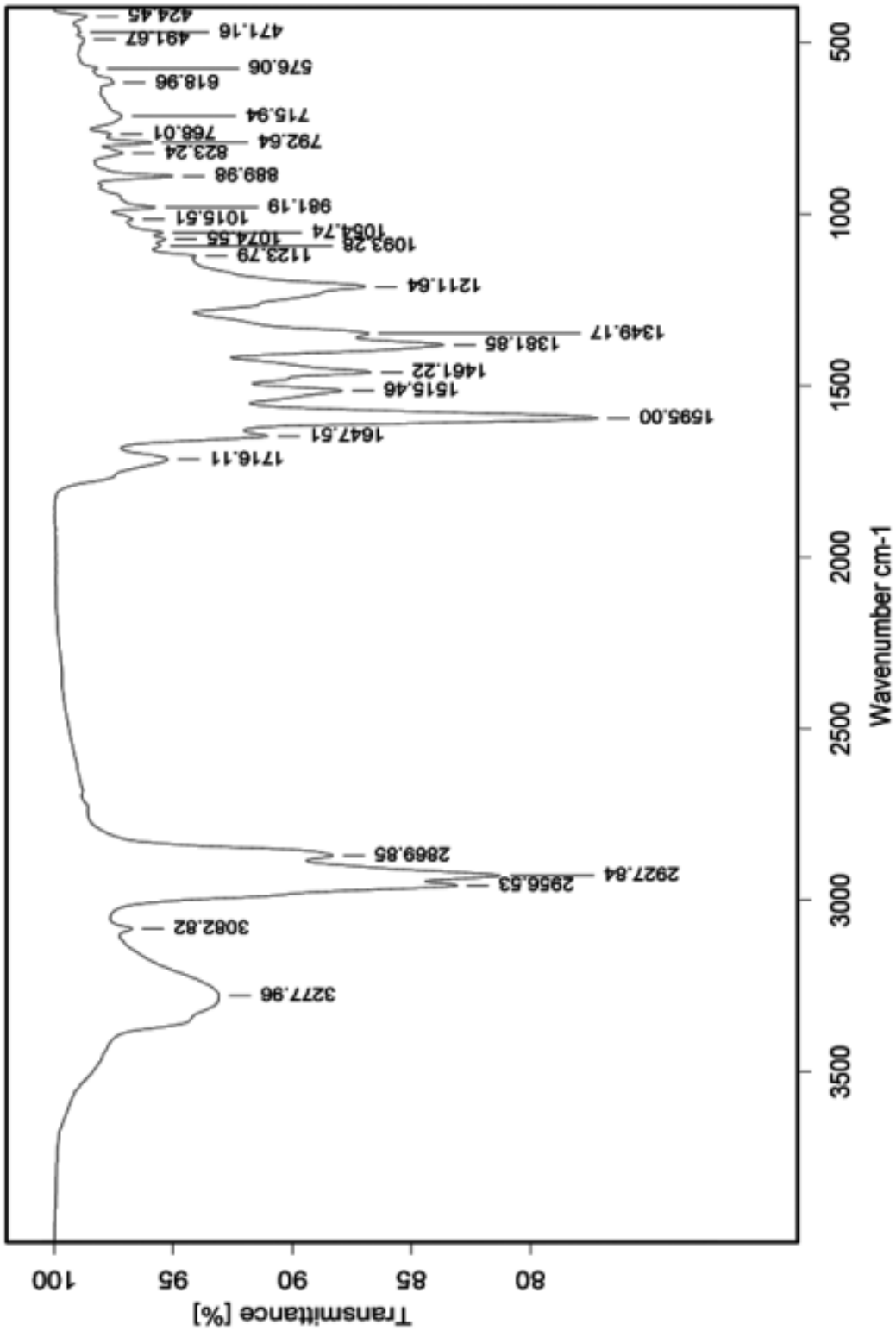


Figure S17. IR spectrum of mixture of **3** and **6** (neat)

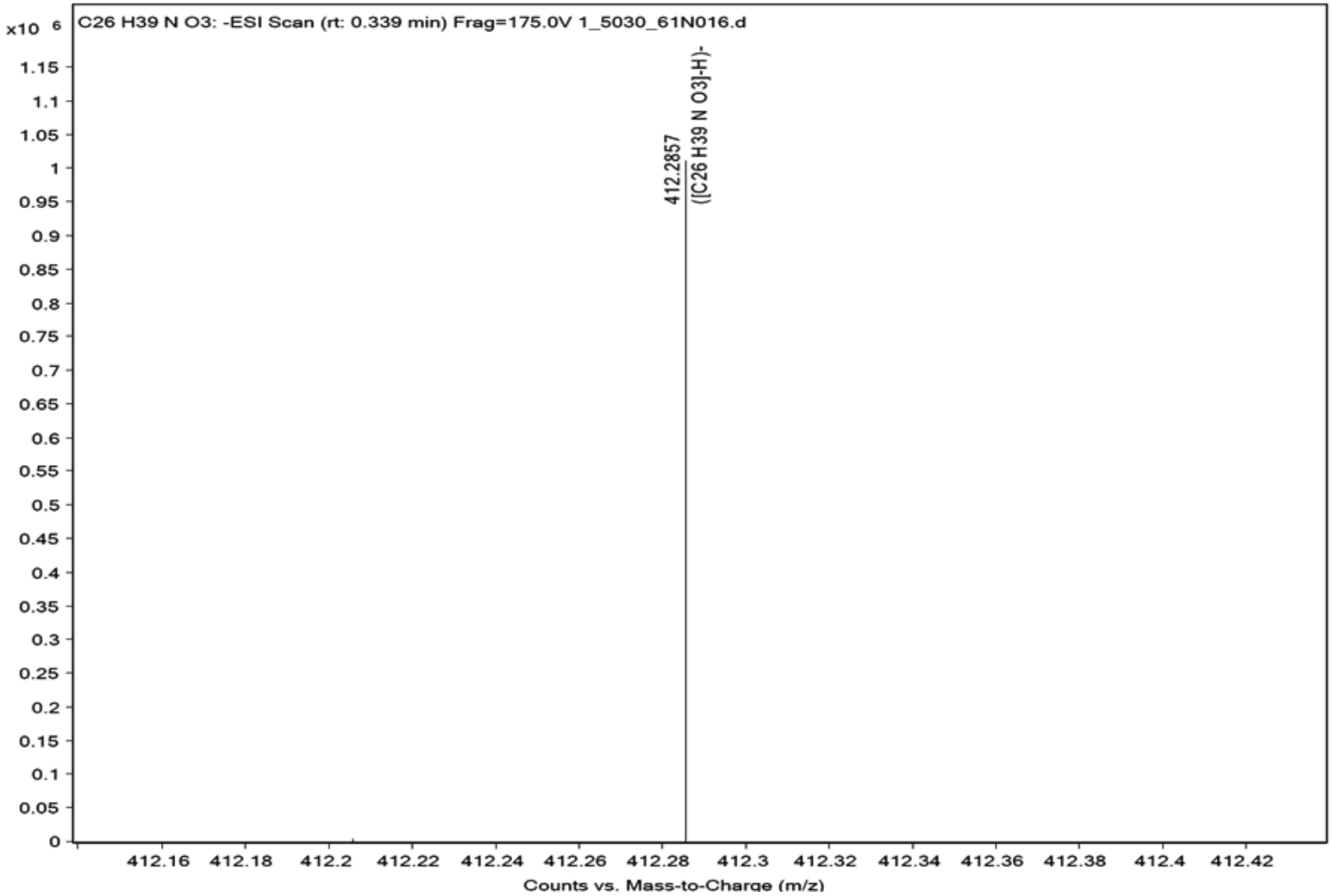


Figure S18 HR-ESI mass spectrum mixture of**3** and **6**

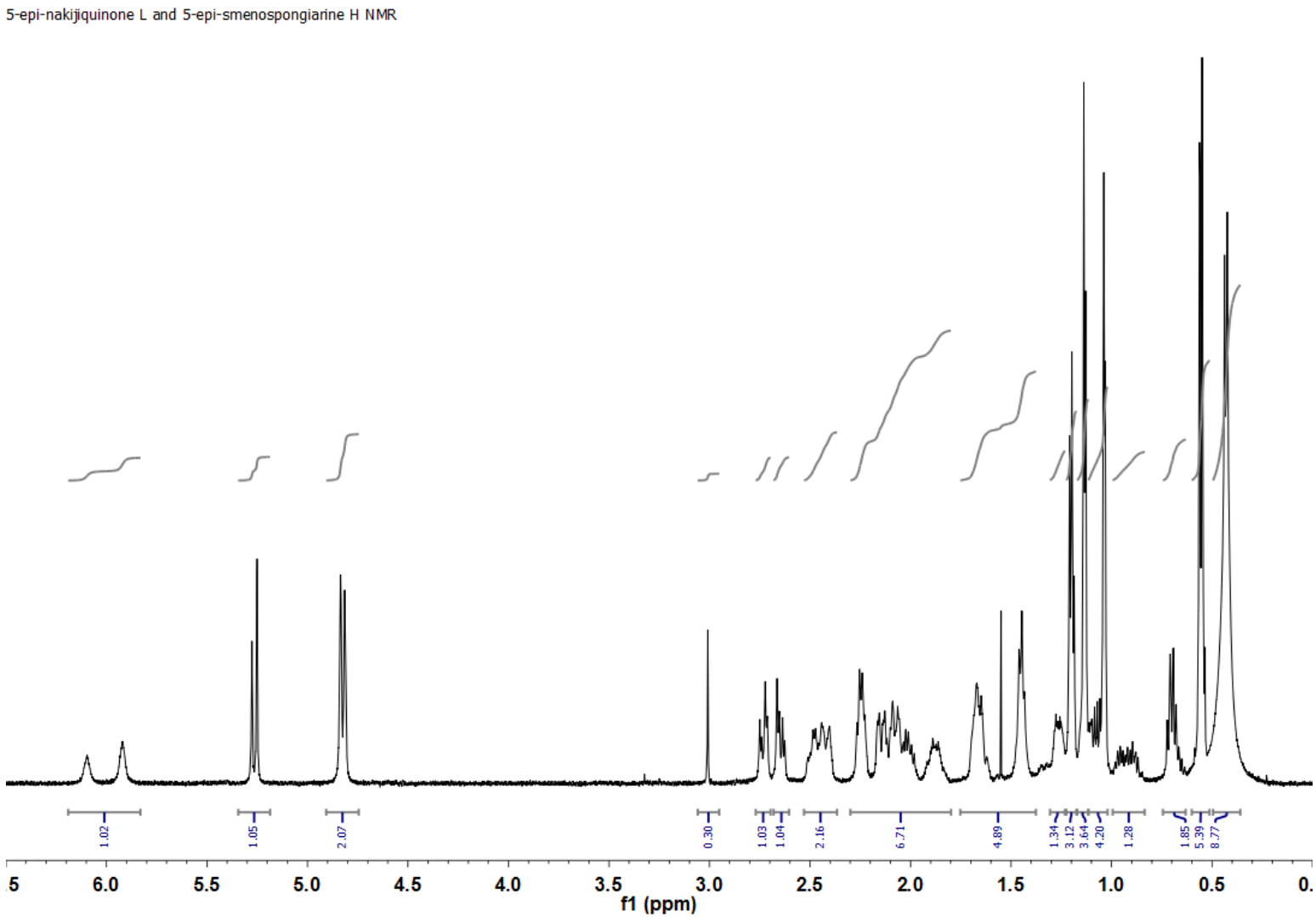


Figure S19. ^{1}H NMR spectrum of mixture of **3** and **6** (500 MHz, C_6D_6)

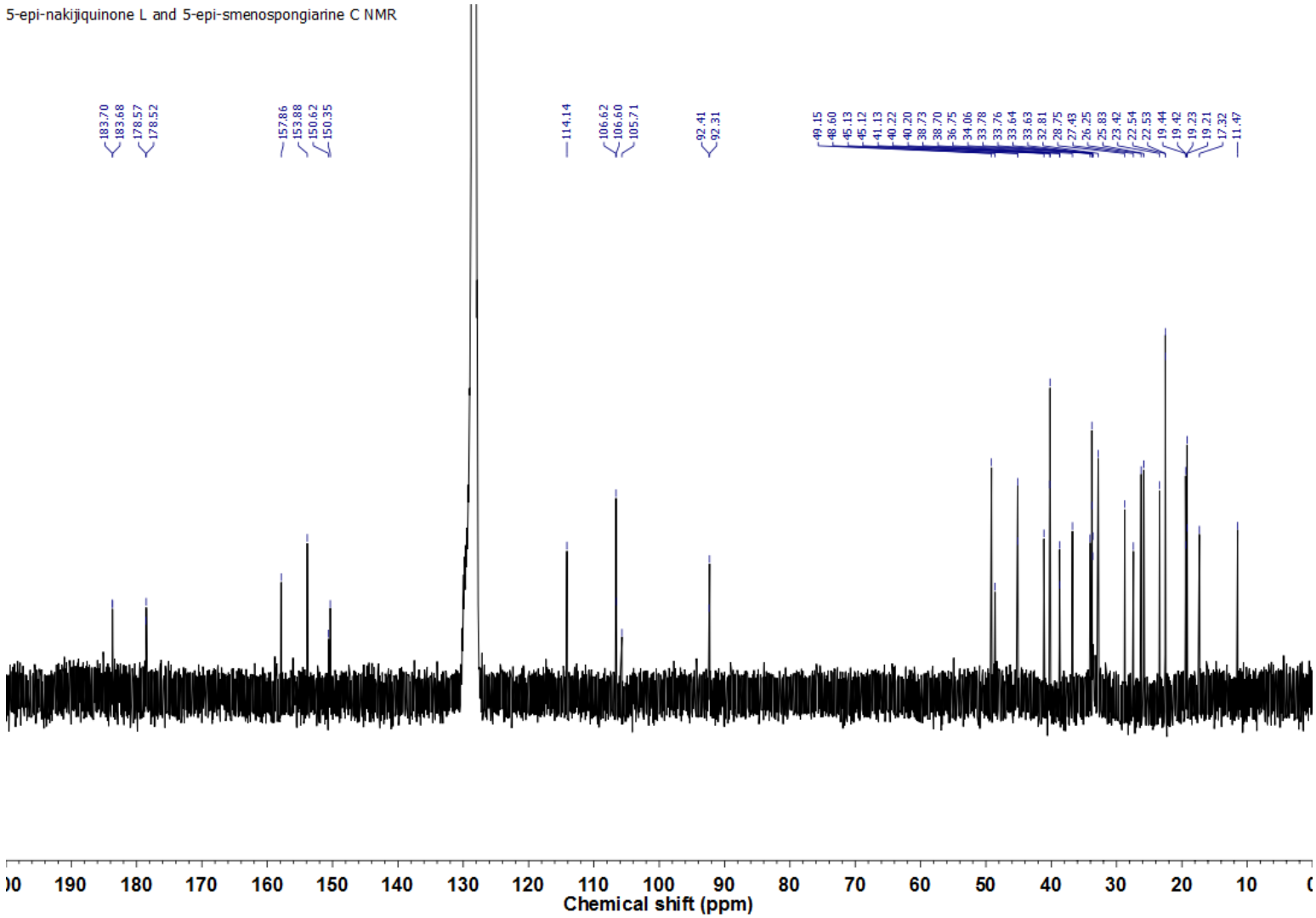


Figure S20. ^{13}C NMR spectrum of mixture of **3** and **6** (125 MHz, C_6D_6)

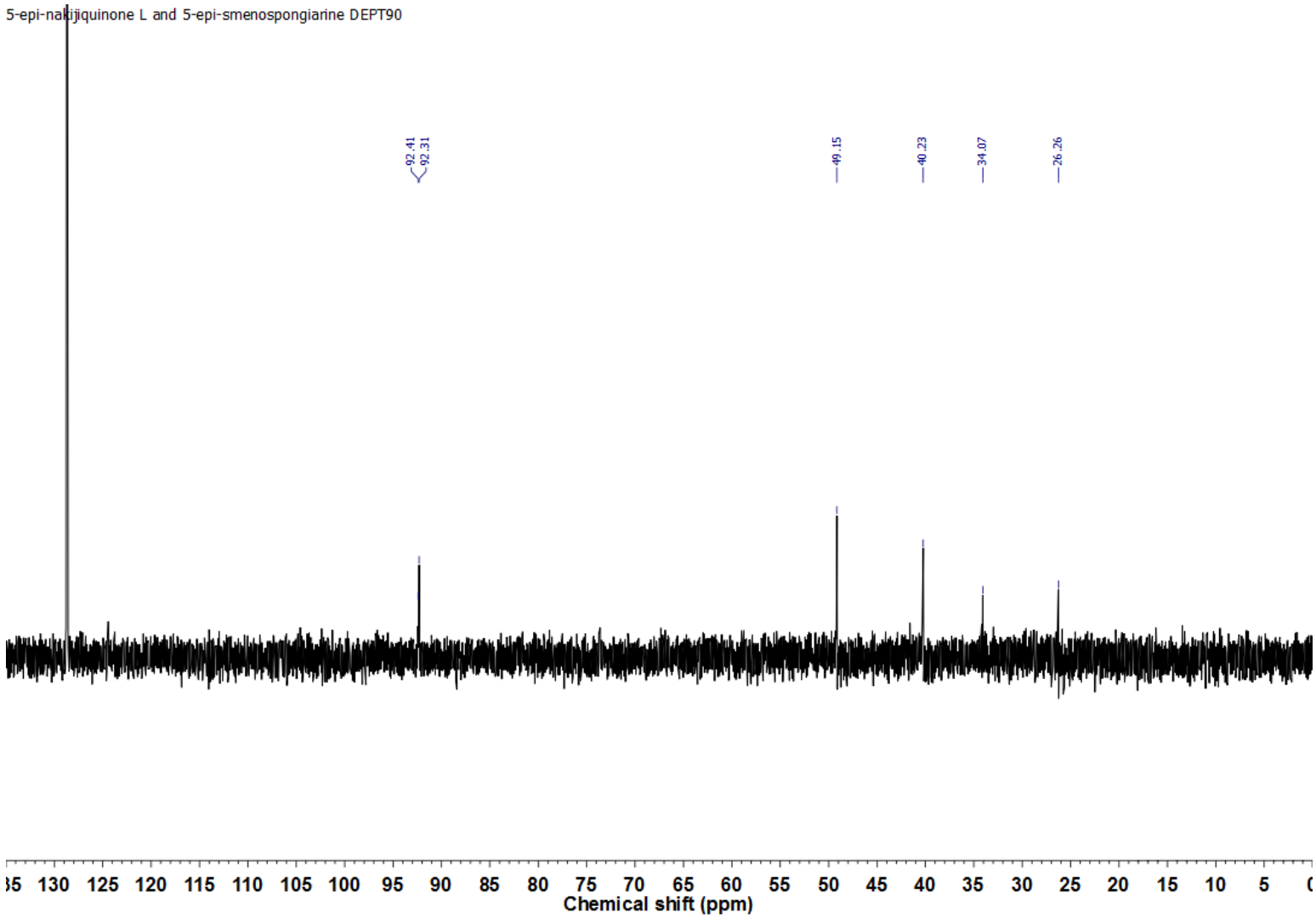


Figure S21 DEPT 90° spectrum of mixture of **3** and **6** (125 MHz, C_6D_6)

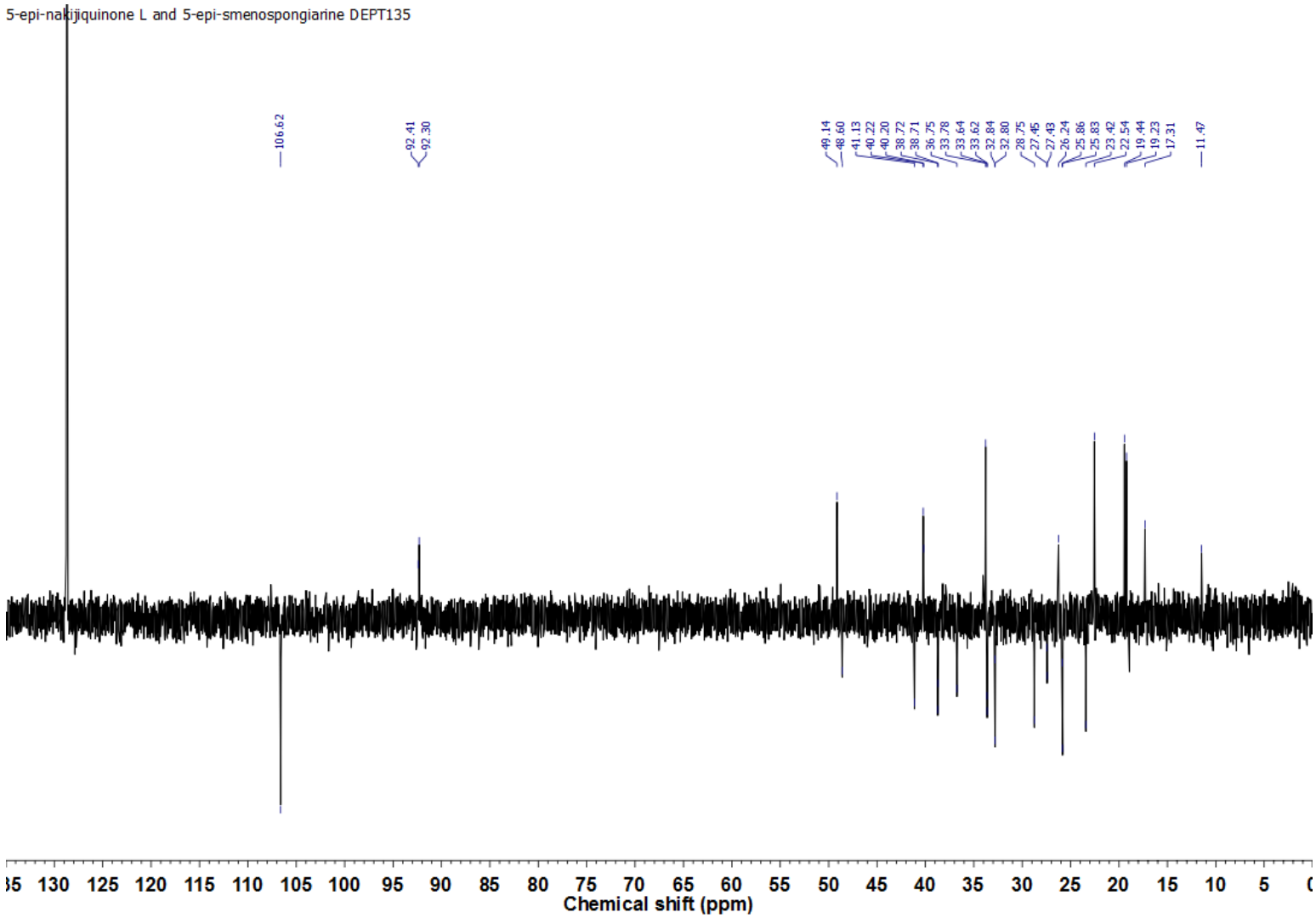


Figure S22 DEPT 135° spectrum of mixture of **3** and **6** (125 MHz, C_6D_6)

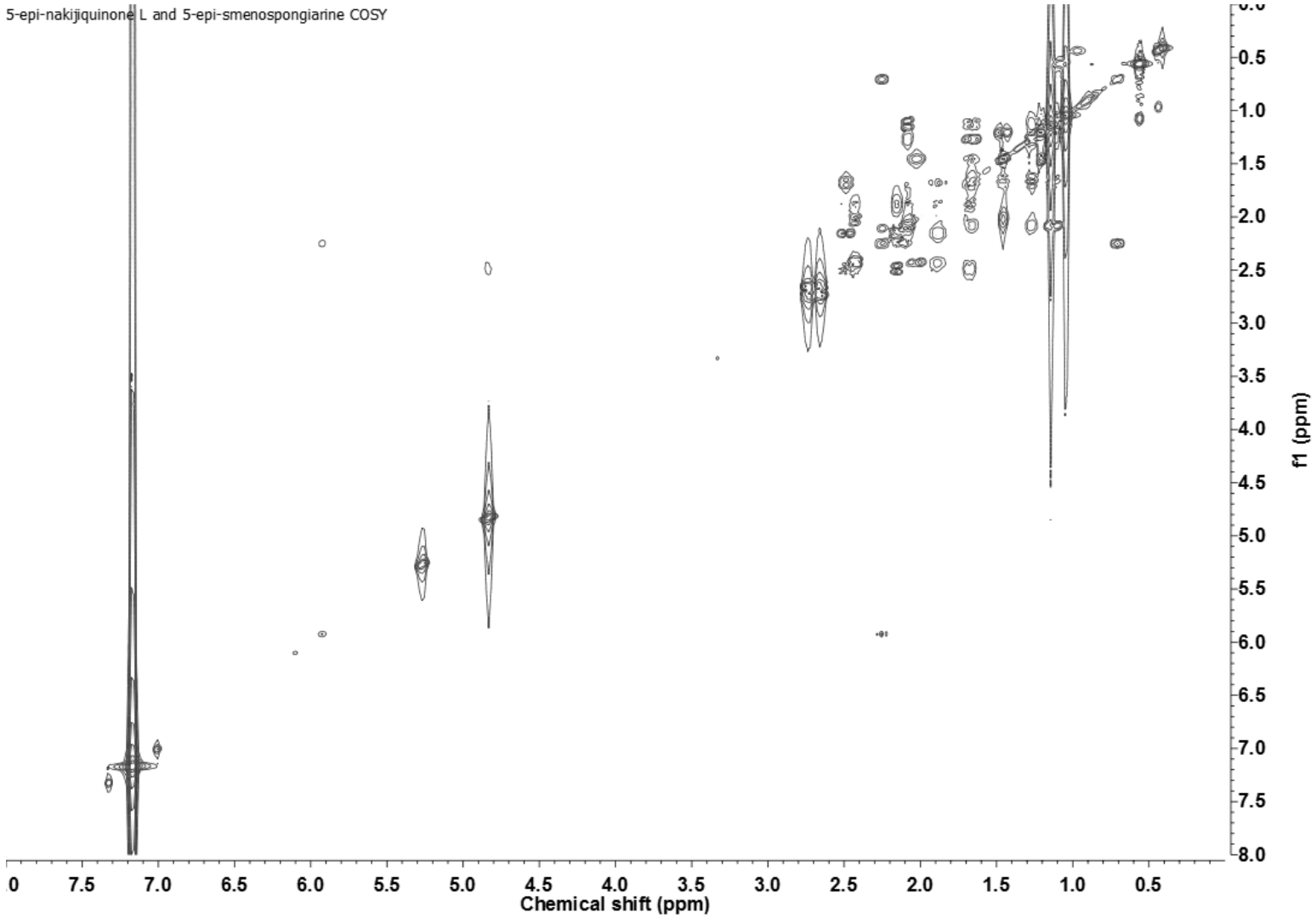


Figure S23 ^{1}H-^{1}H COSY spectrum of mixture of **3** and **6** (500 MHz, C_6D_6)

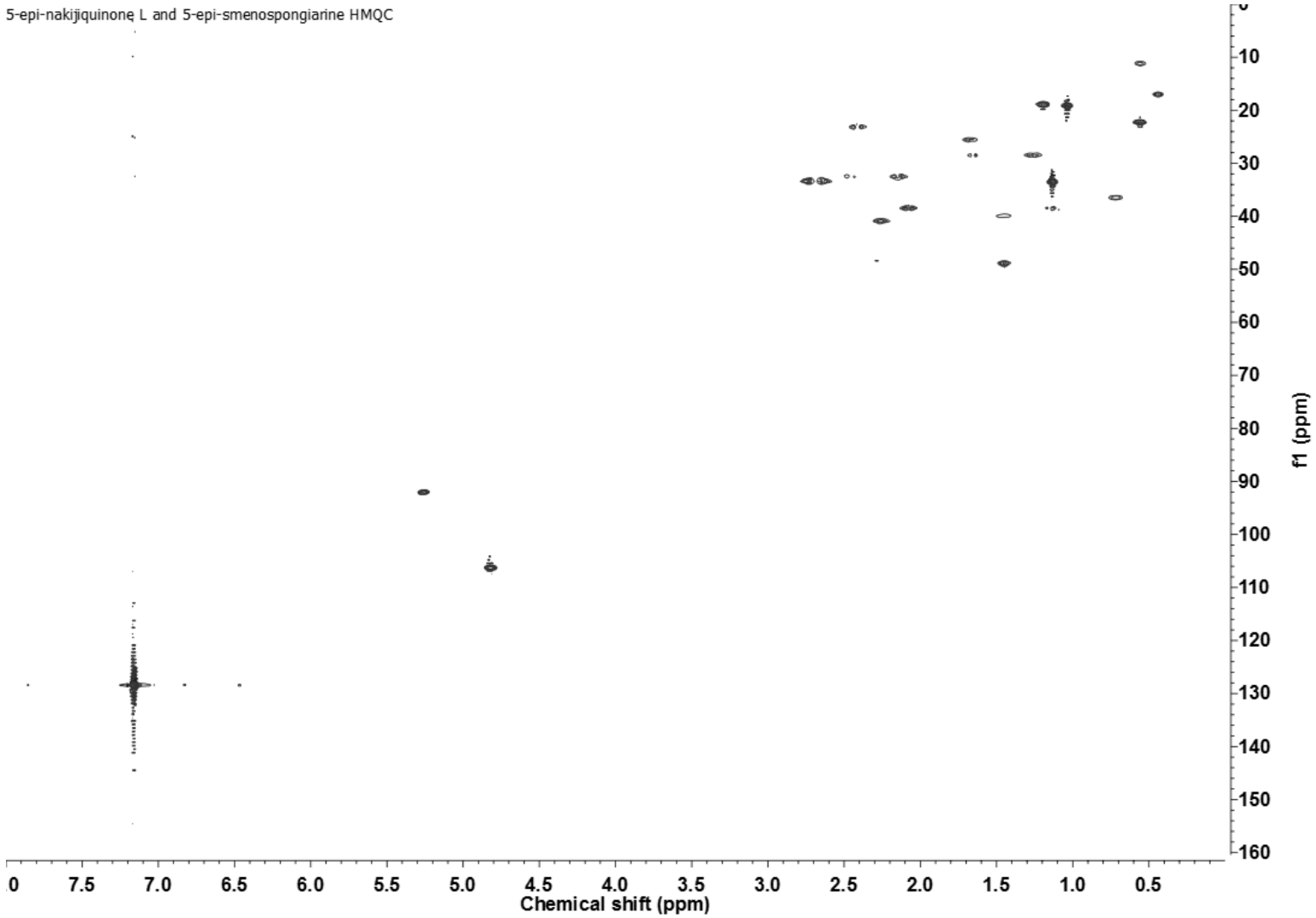


Figure S24 HMQC spectrum of mixture of **3** and **6** (500 MHz, C_6D_6)

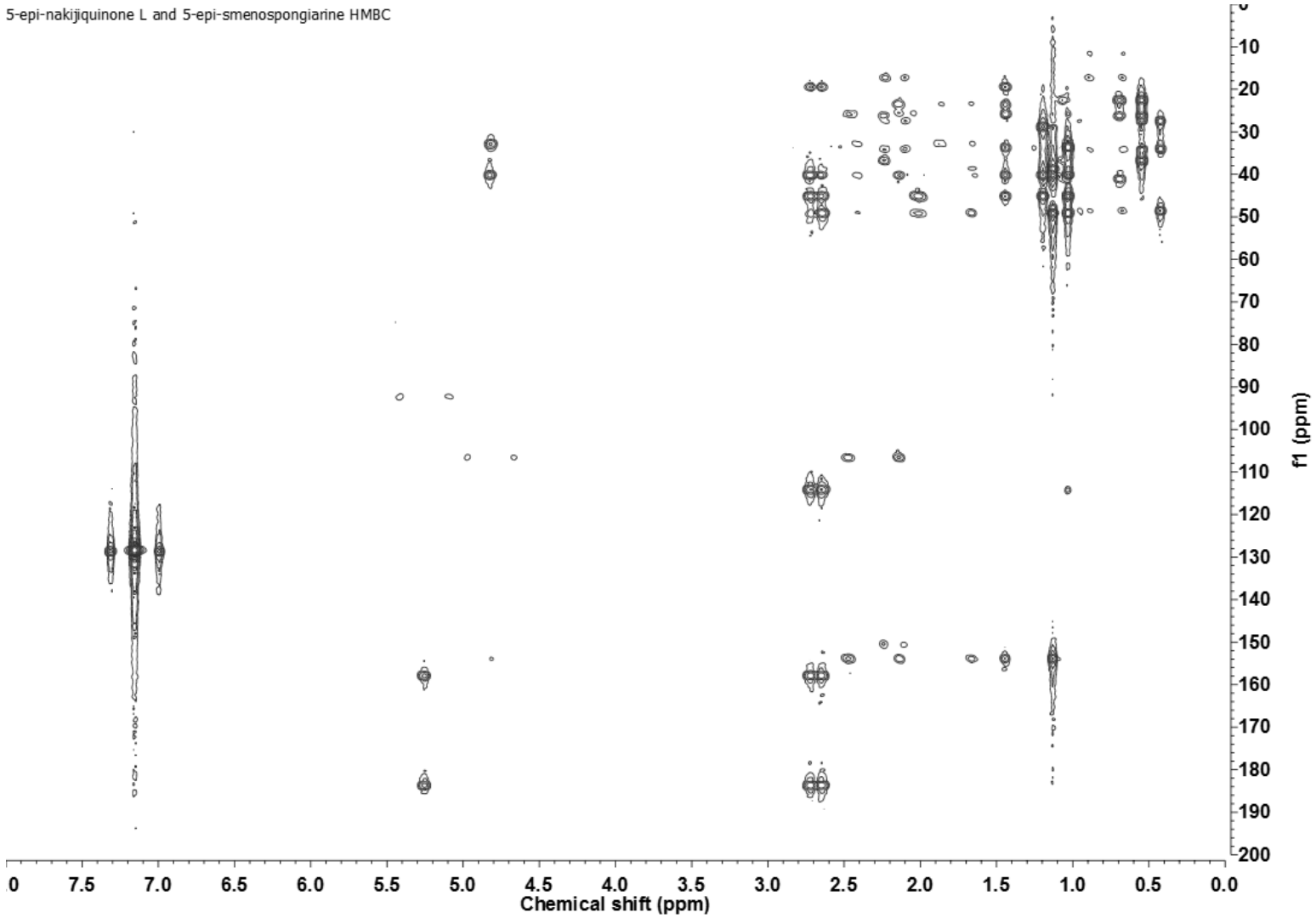


Figure S25 HMBC spectrum of mixture of **3** and **6** (500 MHz, C_6D_6)

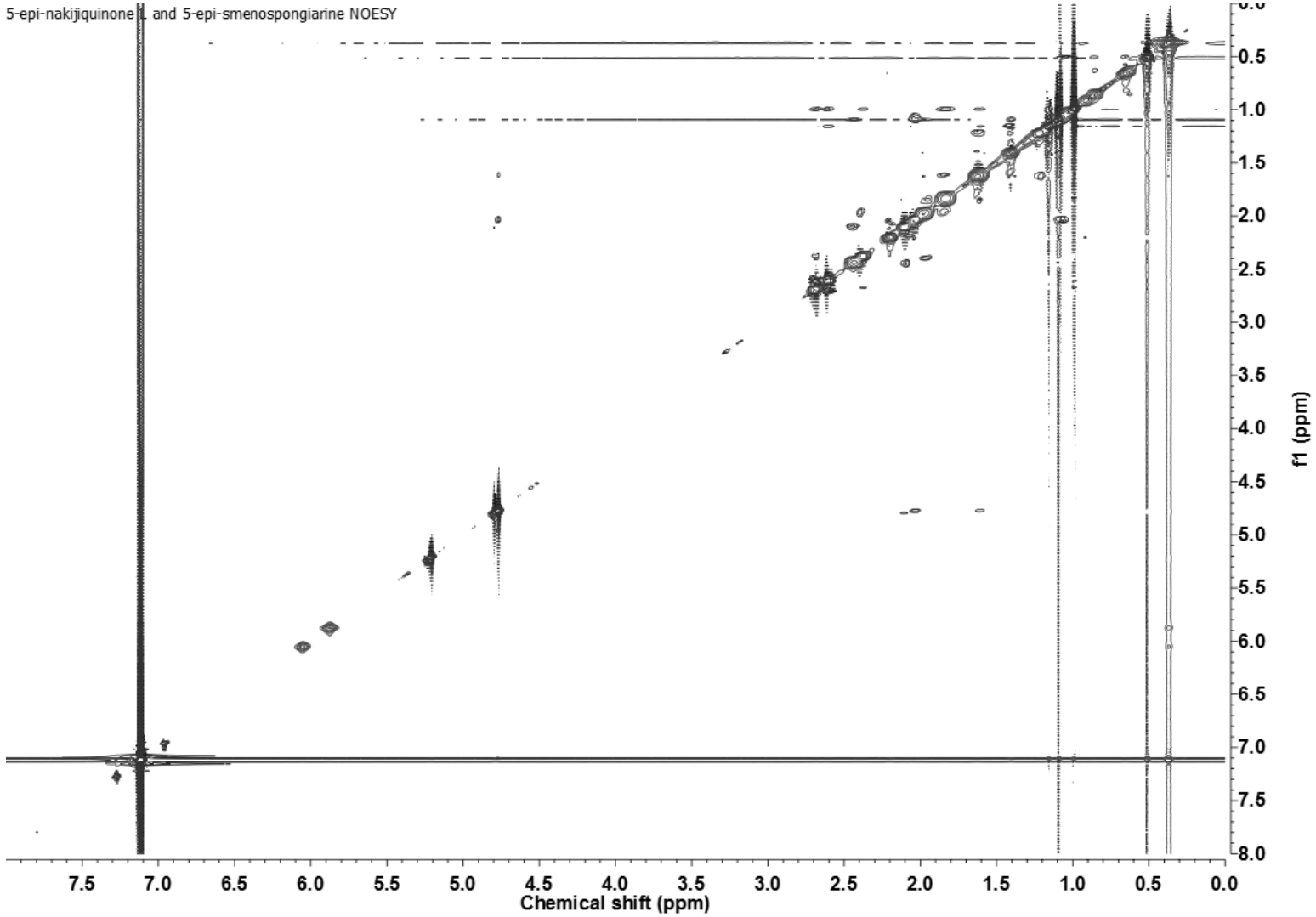
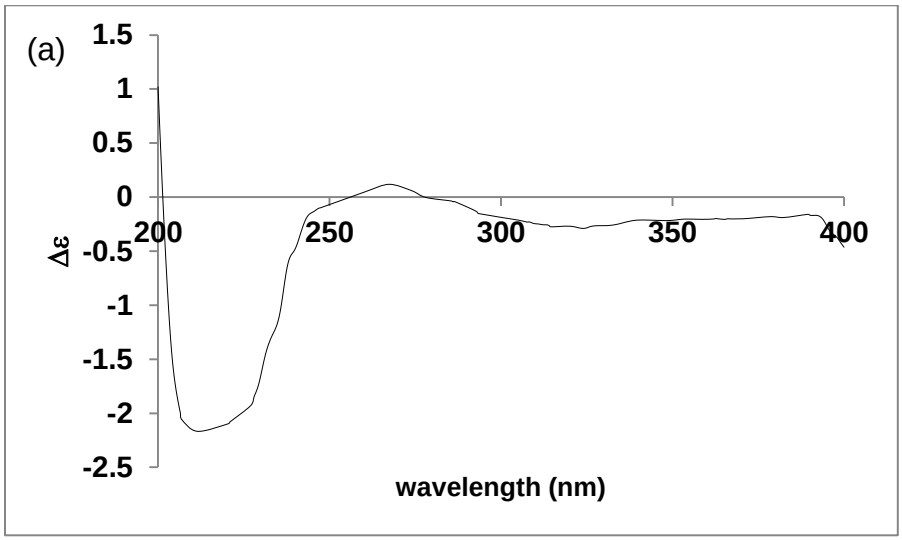


Figure S26 NOESY spectrum of mixture of **3** and **6** (500 MHz, C_6D_6)



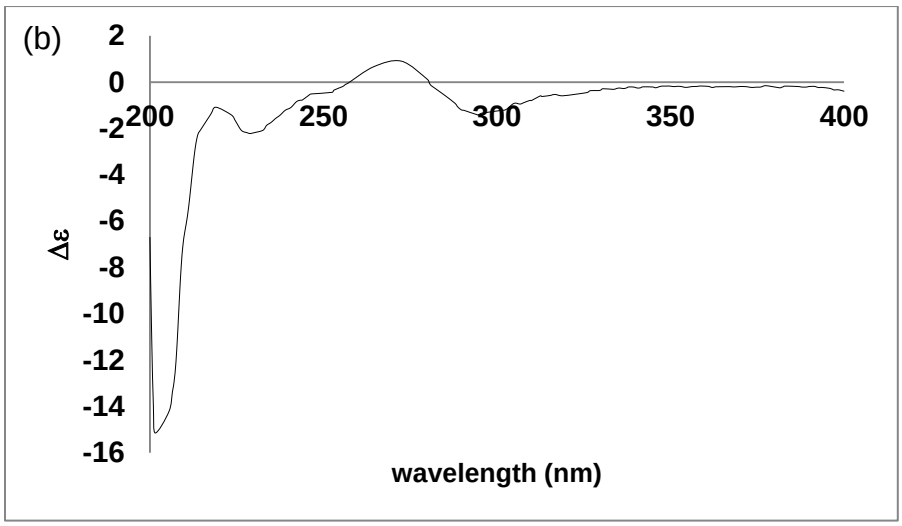


Figure S27. ECD spectra of (a) mixture of **3** and **6** (*c* 0.8 mM, MeOH) and (b) 5-*epi*-ilimaquinone (*c* 1.2 mM, MeOH)

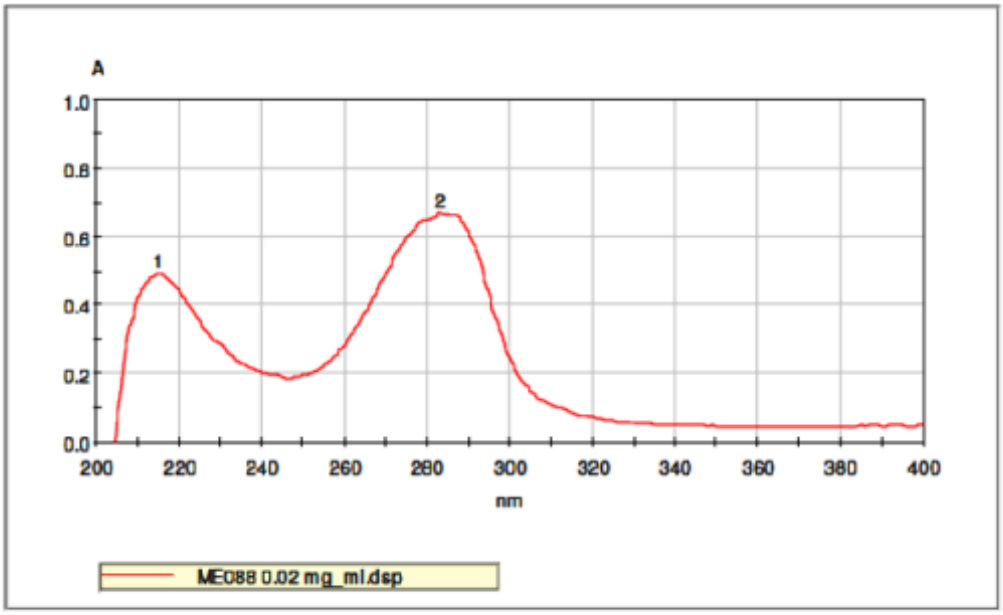


Figure S28. UV spectrum of **4** (MeOH)

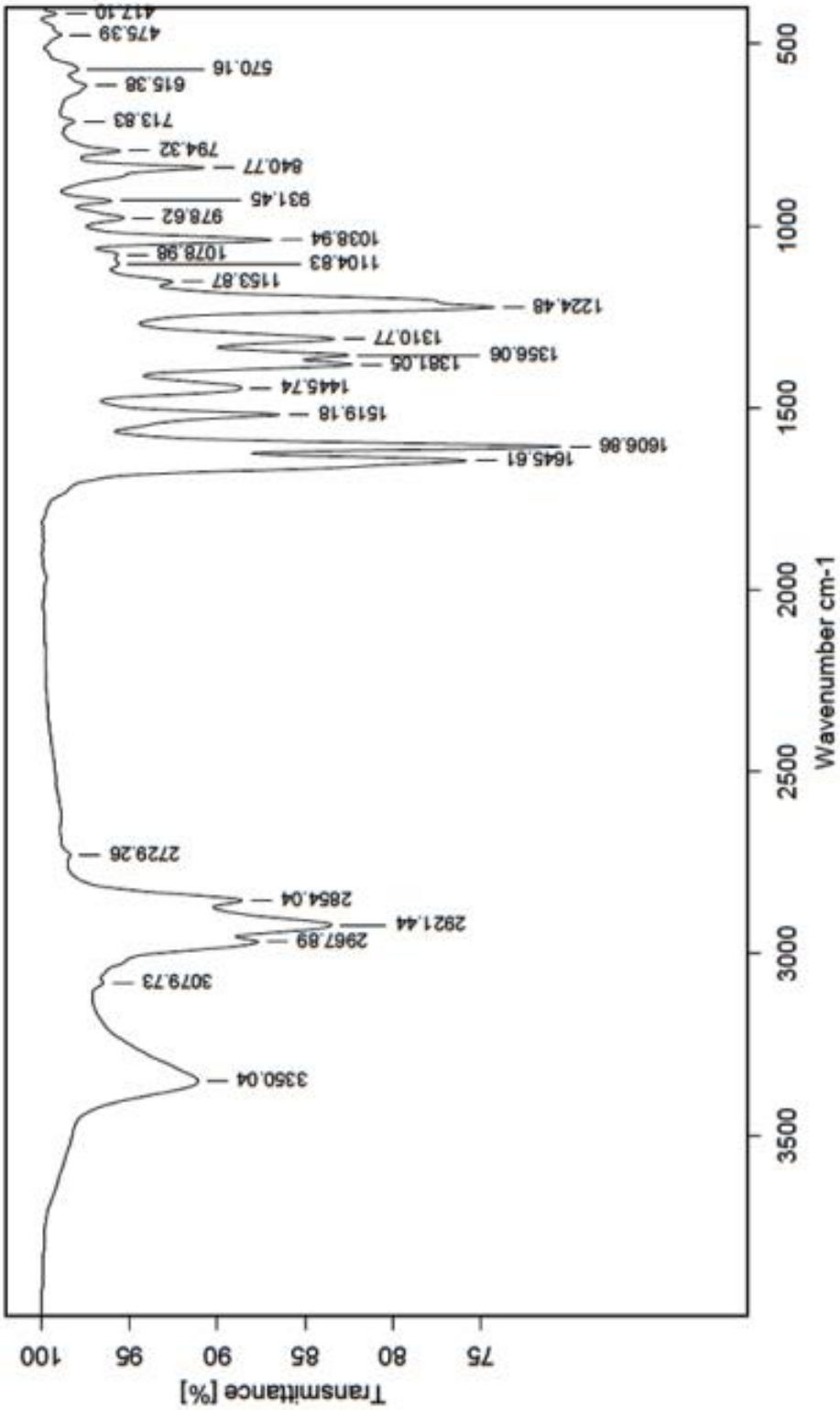


Figure S29 IR spectrum of **4** (neat)

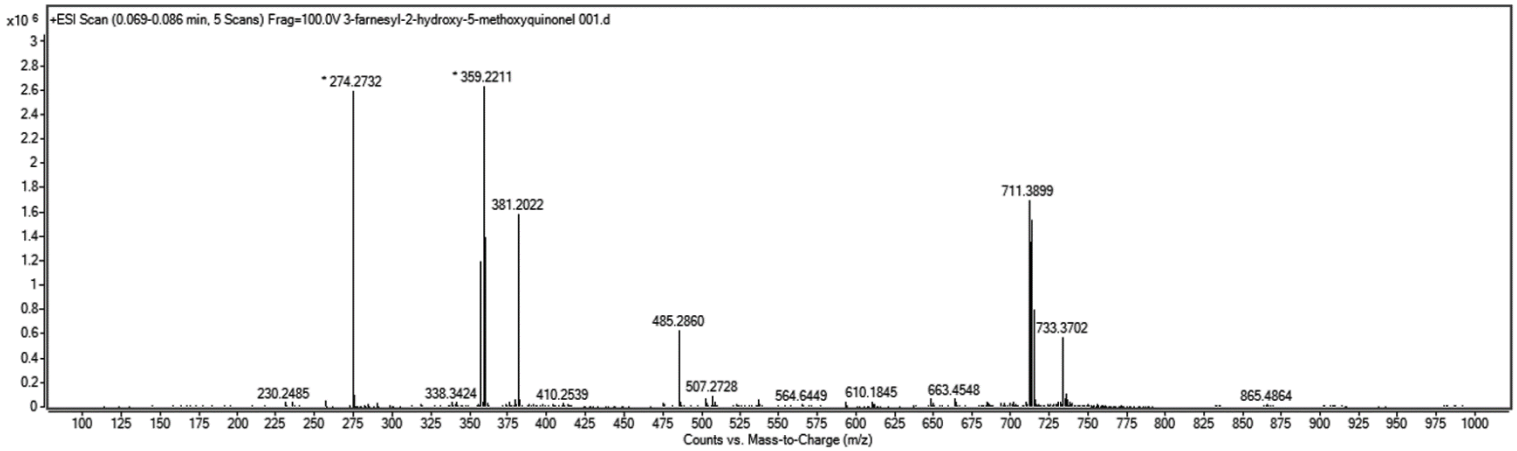


Figure S30 HR-ESI mass spectrum of **4**

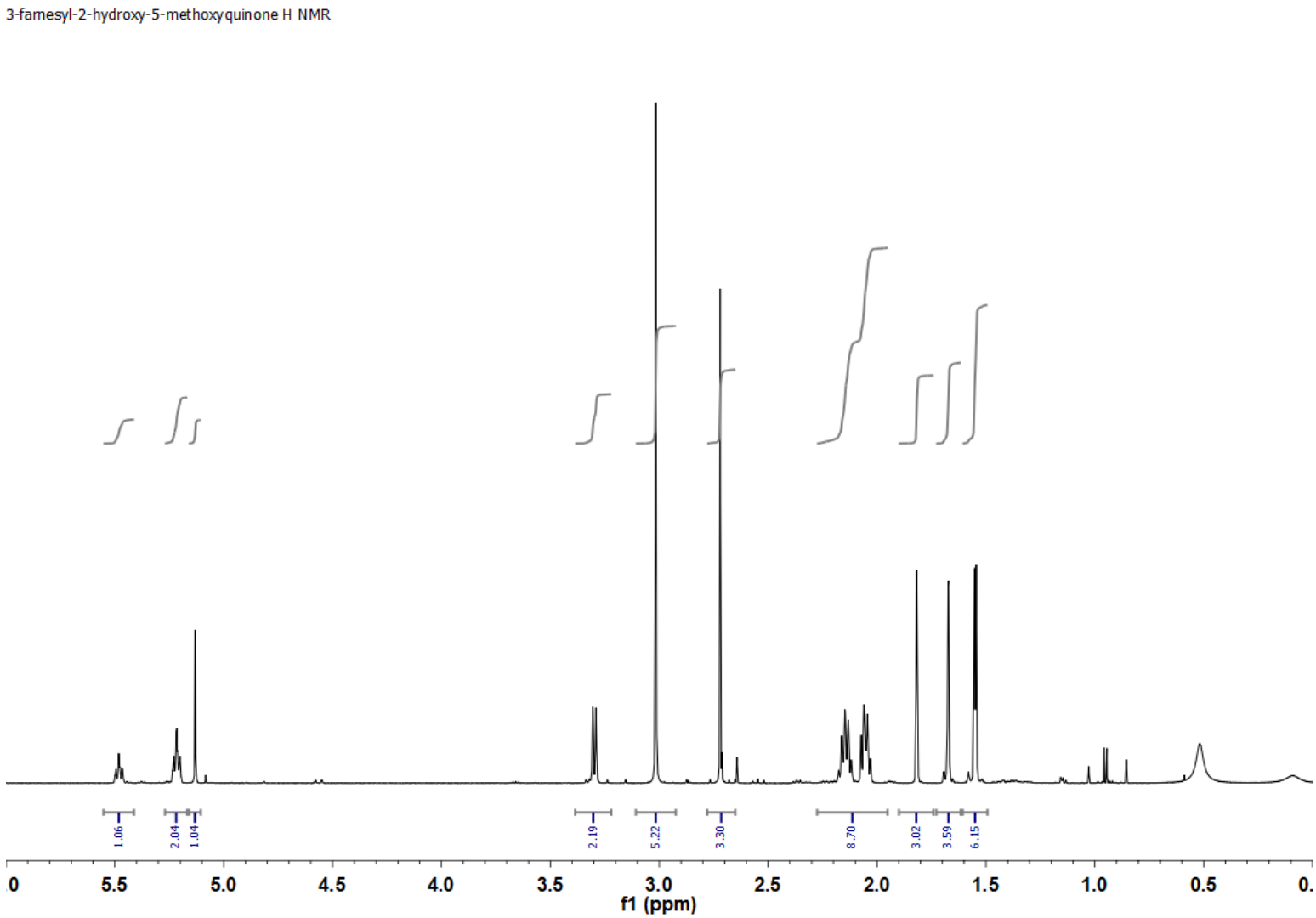


Figure S31 ^{1}H NMR spectrum of **4** (500 MHz, C_6D_6)

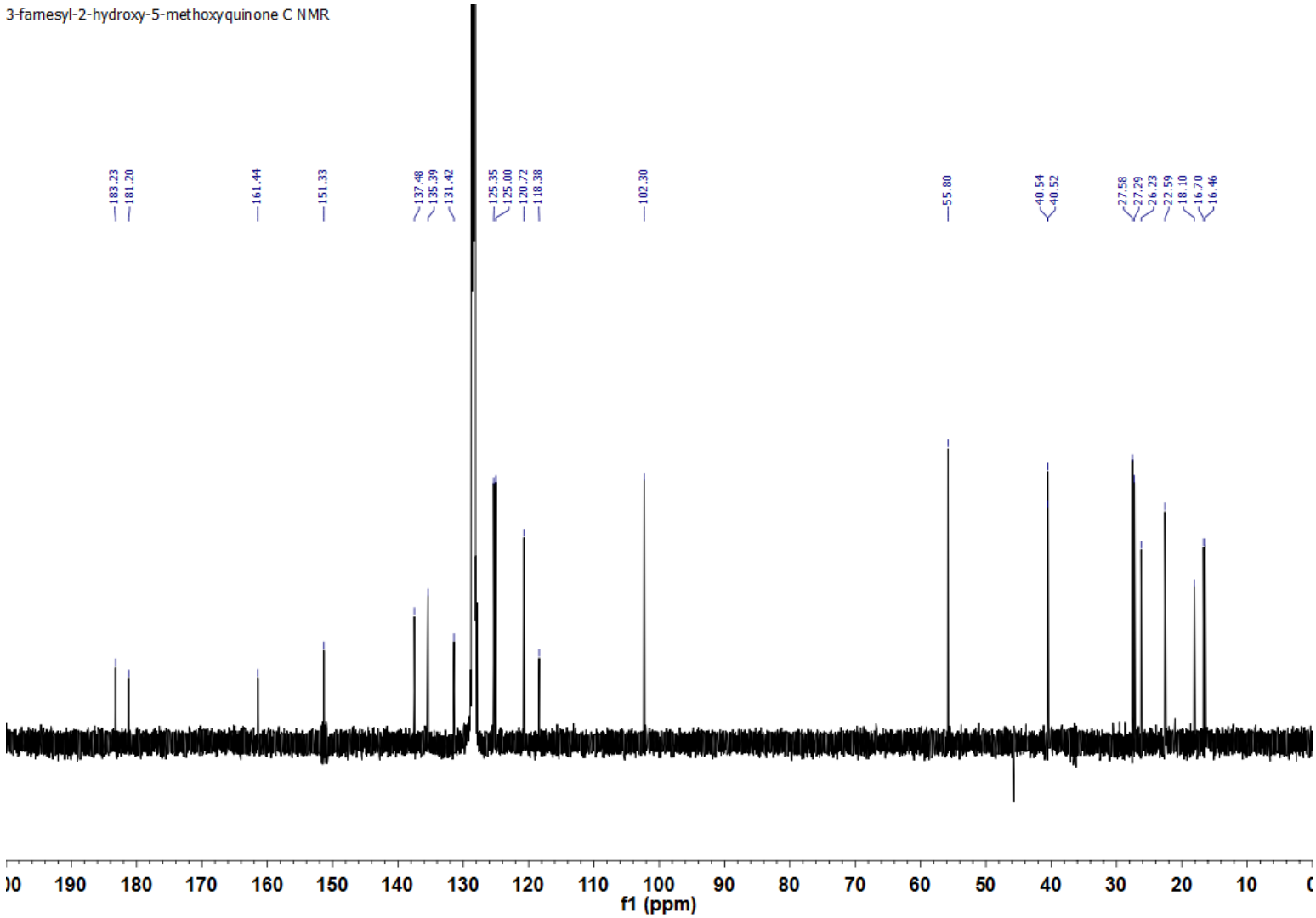


Figure S32 ^{13}C NMR spectrum of **4** (125 MHz, C_6D_6)

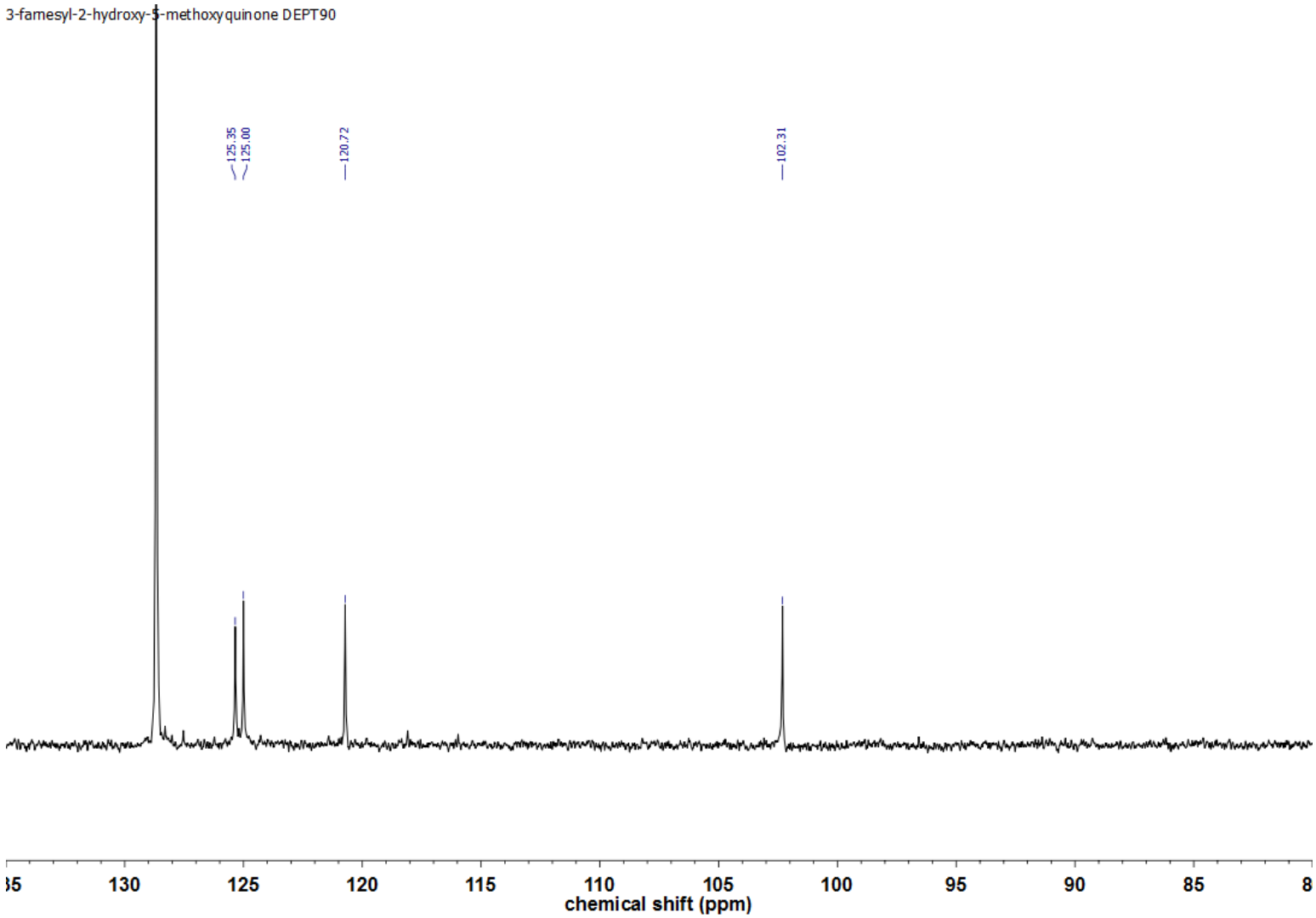


Figure S33 DEPT 90° spectrum of **4** (125 MHz, C_6D_6)

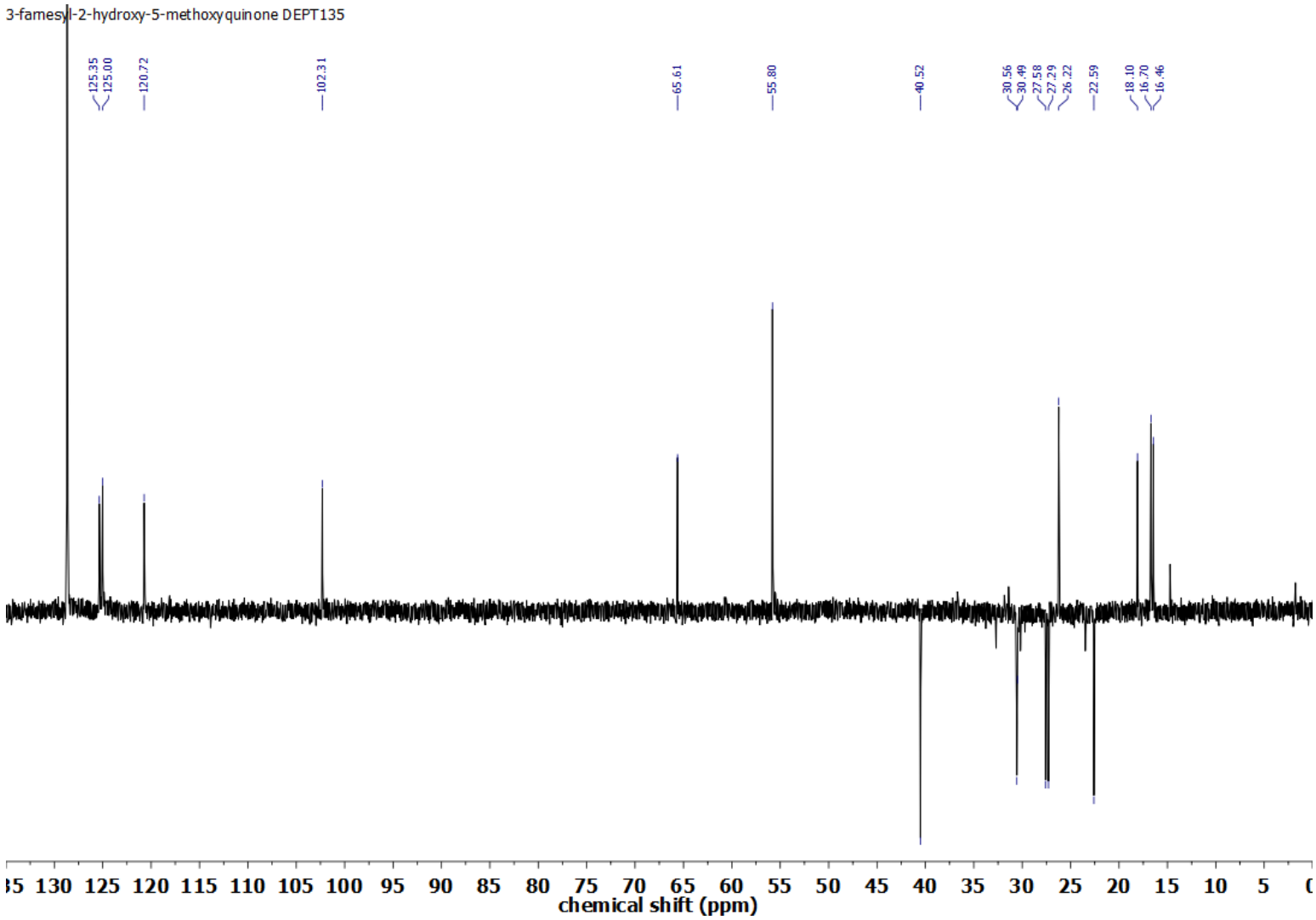


Figure S34 DEPT 135° spectrum of **4** (125 MHz, C_6D_6)

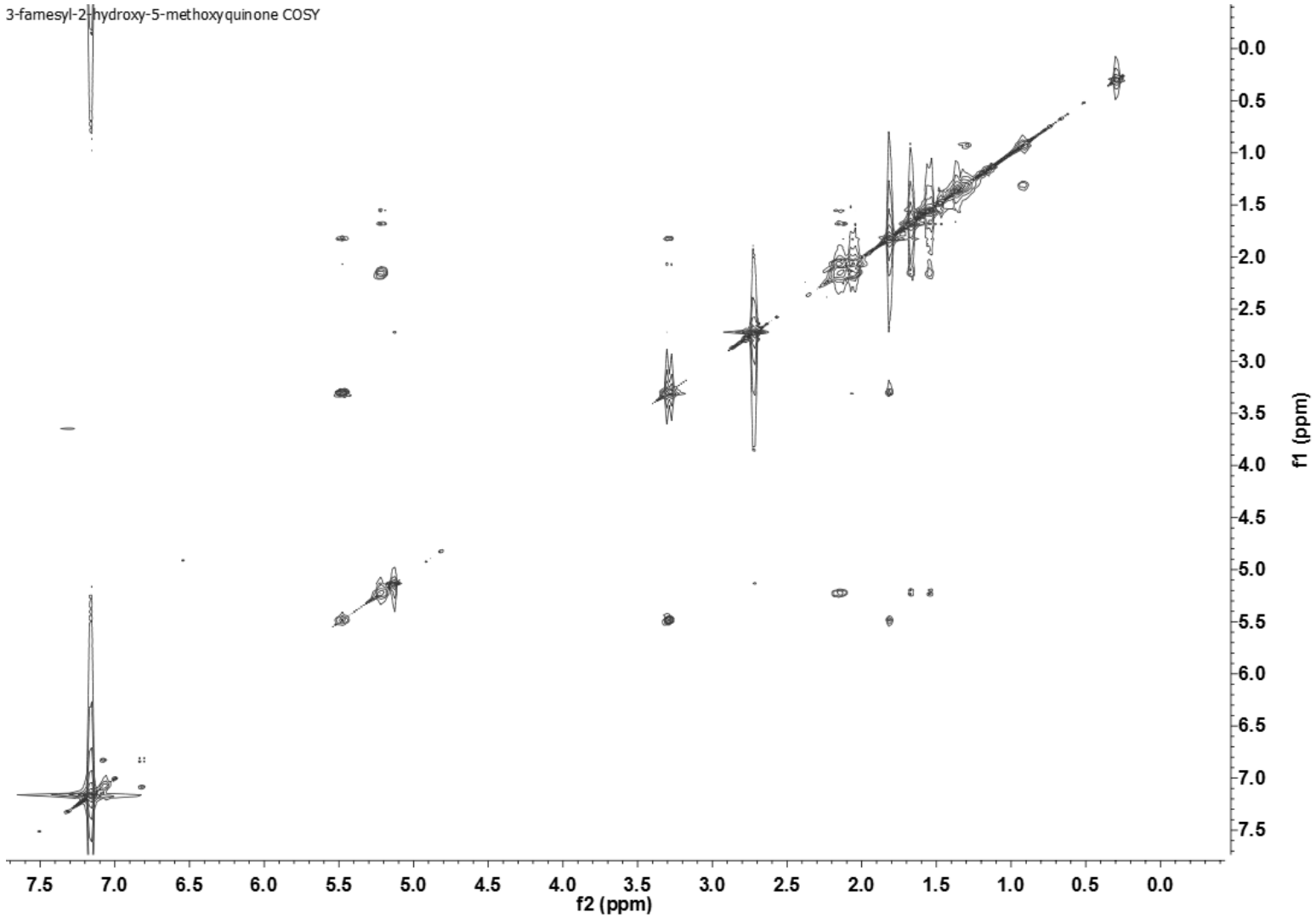


Figure S35 ^{1}H-^{1}H COSY spectrum of **4** (500 MHz, C_6D_6)

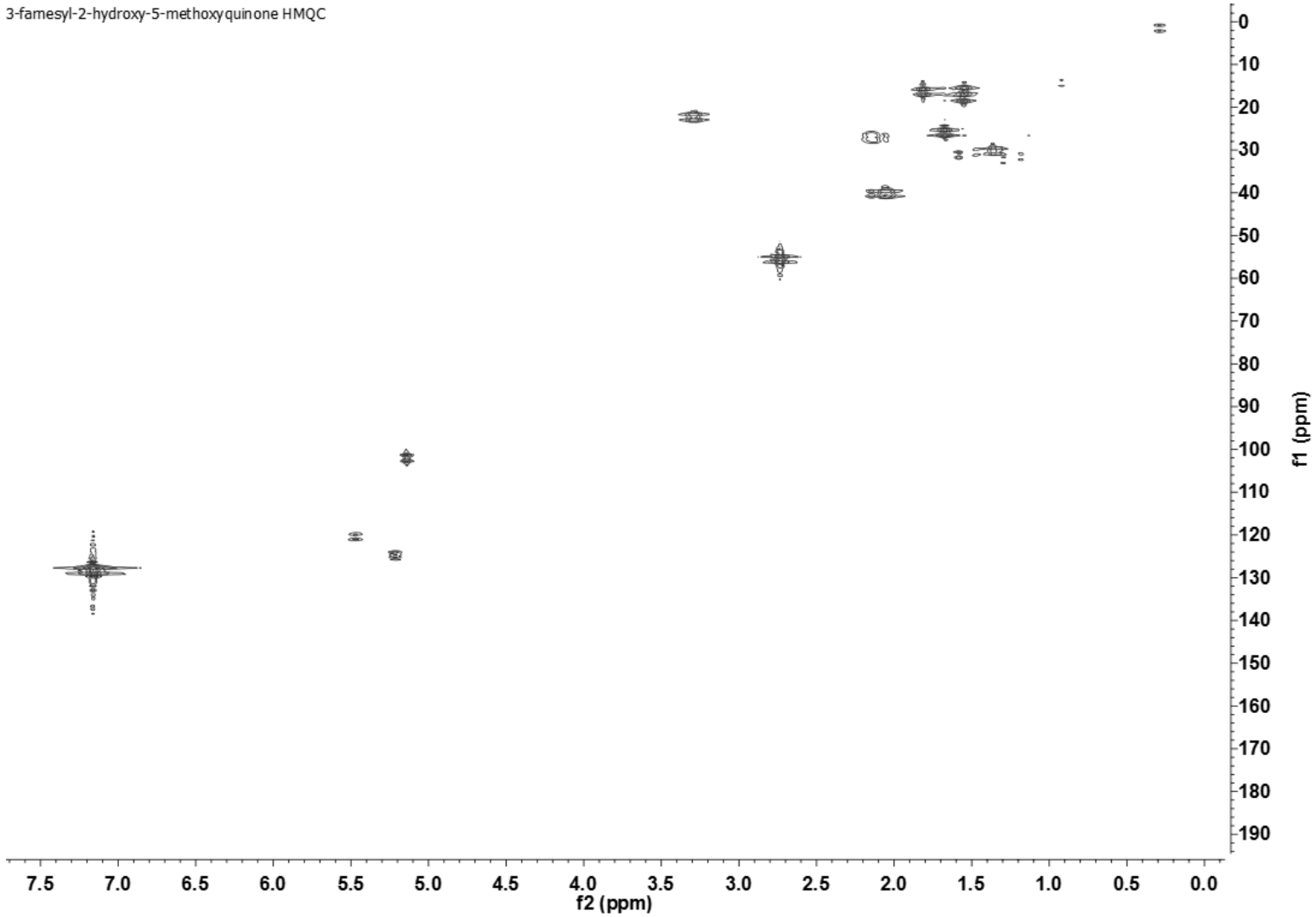


Figure S336 HMQC spectrum of **4** (500 MHz, C_6D_6)

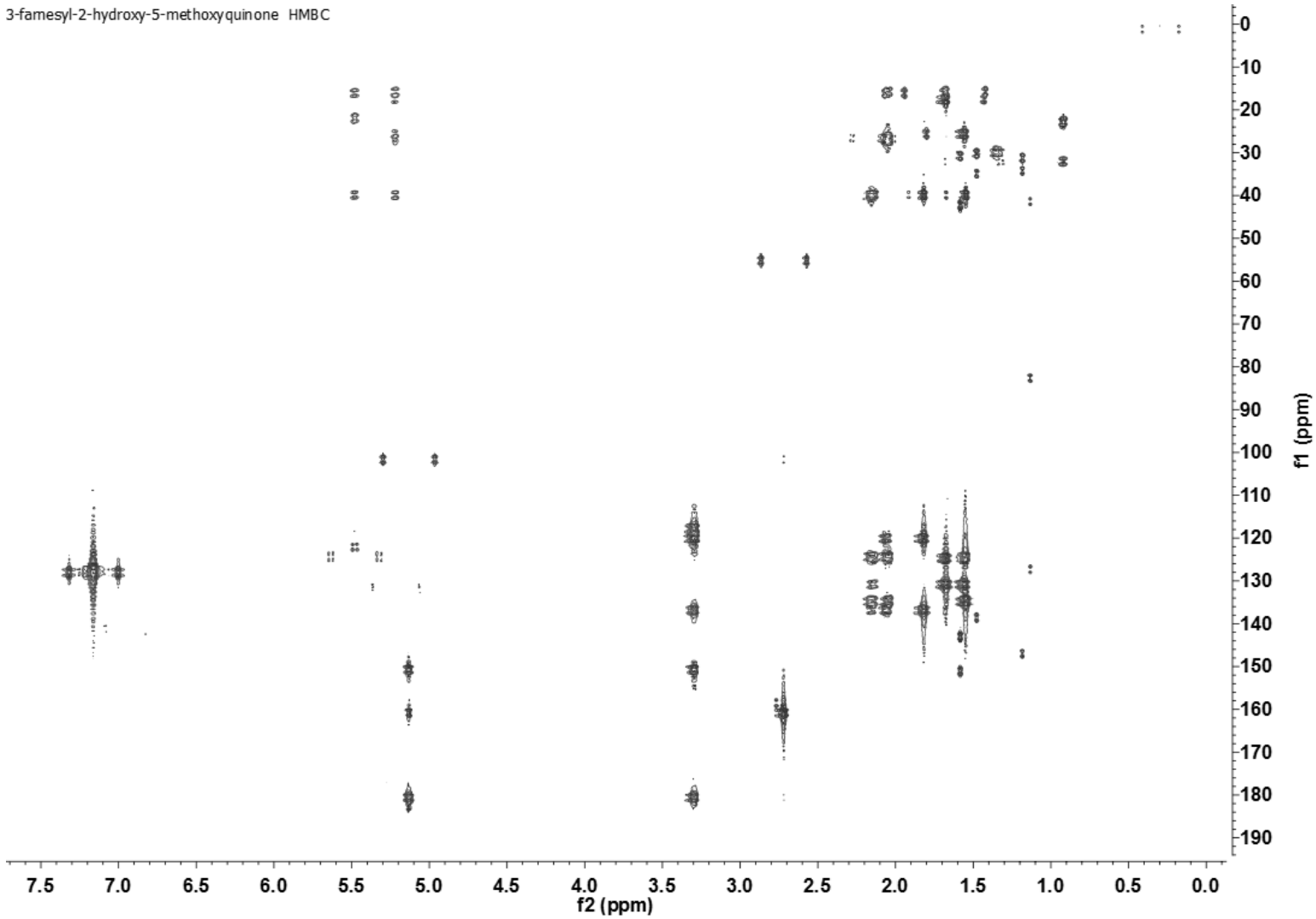


Figure S37 HMBC spectrum of **4** (500 MHz, C_6D_6)

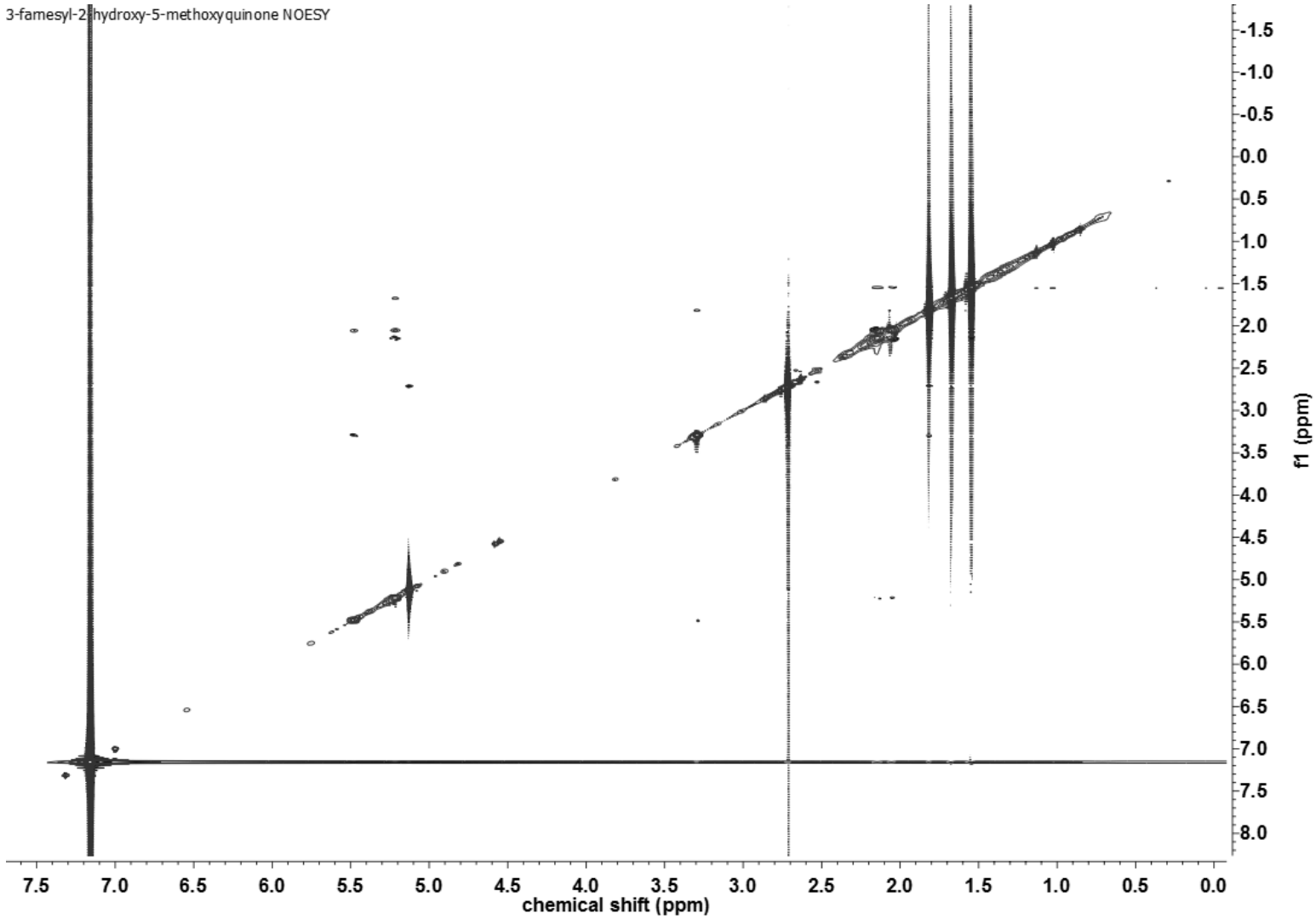


Figure S38 NOESY spectrum of **4** (500 MHz, C_6D_6)