

SUPPORTING INFORMATION

Novel base-initiated cascade reactions of hemiindigos to produce dipolar γ -Carbolines and indole-fused pentacycles

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1. General Information.

All chemicals and solvents were purchased from commercial sources and were used without further purification. IR spectra were run as KBr disks on a IR-Fourier-spectrometer Magna 750 IR Nicolet. ^1H NMR (300, 400 or 600 MHz), ^{13}C NMR (75, 101 or 151 MHz) and ^{19}F NMR (282 MHz) spectra were recorded on a Bruker AvanceTM - 300, Bruker AvanceTM - 400 or Bruker AvanceTM - 600 spectrometers. NMR spectra were recorded in solutions of DMSO- d_6 , CF_3COOD , CD_3COOD . Chemical shifts were reported in the δ scale relative to residual signal of solvent DMSO (2.50 ppm), CF_3COOH (11.50 ppm) and CH_3COOH (2.04 ppm) for ^1H -NMR and to the central line of DMSO- d_6 (39.5 ppm), CF_3COOD (116.6, 164.2 ppm), CD_3COOD (20.0, 179.0 ppm) for ^{13}C -NMR, respectively. ^{19}F -NMR spectra were recorded using CD_3COOD , DMSO- d_6 as a lock solvent. COSY-HH, NOESY-HH, HMBC-HC and HMQC-HC were used where necessary in assigning NMR spectra. Multiplicities are indicated by s (singlet), d (doublet), t (triplet), and m (multiplet). Coupling constants J are reported in Hertz. Among all chromatographically homogenous γ -carbolines **2**, 3-aryl and 2,3-diaryl substituted carbolines **2e** and **2g-i** featured the ^1H and ^{13}C NMR spectra with the increased number of aromatic, or aromatic and aliphatic proton, and carbon signals, probably, due to the hindered rotation of the C1-aryl ring around the Ar-C1 bond. Mass spectra were recorded on a Finnigan LCQ Advantage for ESI, on a Finnigan LTQ FT Ultra for HRMS (ICR) and on a Finnigan Polaris Q for EI. Elemental analyses were performed at the laboratory of microanalysis of A. N. Nesmeyanov Institute of Organoelement Compounds, Moscow. Melting points were uncorrected. X-Ray diffraction experiments for compounds **2a**, **3**, **4**, and **7** were carried out with a Bruker SMART APEX 1000 CCD area detector, using graphite monochromated Mo-K α radiation ($\lambda = 0.71073 \text{ \AA}$, ω -scans) at temperature 100 °K. Flash Column chromatography was performed on Silica gel Merck 60 (Merck, 230 mesh). Starting materials 2-arylidene-1*H*-indol-3(2*H*)-ones (indogenides) **1** were prepared by literature procedures.¹⁻³

Biological evaluation. A series of compounds were tested for their in vitro antimycobacterial activity against a laboratory strain *M. tuberculosis* H37Rv and against a clinical isolate of INH-resistant *M. tuberculosis* with selective single INH resistance, designated as CN-40. *M. tuberculosis* strain H37Rv (museum strain) was originally obtained from the Institute Pasteur, Paris, France (a kind gift of G. Marchal). The CN-40 strain was isolated from a TB patient at the TB Research Institute of the Russian Academy of Medical Sciences. MICs against *M. tuberculosis* were determined by standard microdilution in microtubes using Dubos medium containing 0.05% Tween 80.

***M. tuberculosis* strains.** *M. tuberculosis* strain H37Rv (Pasteur) was maintained and prepared for in vitro infection exactly as described previously.^{7,8} Briefly, following 3 weeks of growth on Loewenstein-Jensen medium at 37°C, mycobacteria were suspended in sterile saline containing 0.05% Tween 20 and 0.1% bovine serum albumin (BSA; Sigma), washed, aliquoted (10 mg of semidry bacterial mass in 1 ml), and stored at -80°C. To obtain the log-phase bacteria for challenge, 50 μl from a thawed aliquot was added to 5 ml of Dubos broth (Difco, Detroit, Mich.) supplemented with 0.5% BSA and incubated for 1 week at 37°C. The mycobacterial suspension (0.5 ml) was diluted in 20 ml of fresh warm Dubos-BSA medium and further cultured for 1 week. The resulting suspension was washed three times at $3,000 \times g$ and 4°C with 0.02% EDTA-phosphate-buffered saline (PBS) (Ca^{2+} - and Mg^{2+} -free) solution, resuspended in medium 2, and filtered through a 4- μm -pore-size filter (Sigma) to remove clumps. To estimate the CFU content in the filtrate, 10 μl from each fivefold serial dilution was plated onto Dubos agar (Difco), and the total number of microcolonies in the spot was calculated under an inverted CK-2 microscope (Olympus, Osaka, Japan) after being cultured for 3 days at 37°C. The bulk of the filtered culture was stored at 4°C, and it was found that no change in the CFU content occurred during this period.

The lowest concentration of a compound resulting in no visible growth of *M. tuberculosis* for 2 weeks was considered the MIC. All samples were tested twice in triplicate. We also used a micro method developed in our laboratory based on measurement under a microscope of the volume of growing compact mycobacterial culture in the wells of round-bottom 96-well plates in the presence or absence of a tested compound (K. Majorov, unpublished data).

2. Experimental procedures and spectral data.

General Methods for the Synthesis of γ -Carbolines (**2a-i**).

Method A: To a solution of the corresponding 2-arylidene-1*H*-indol-3(2*H*)-ones **1** (0.6 mmol) in *tert*-BuOH (1.6 mL) was added KOH (130 mg, 2.0 mmol), and the reaction mixture was refluxed for 24 h. After cooling of the solution to room temperature, the solvent was evaporated in vacuo. Water (2-5 mL) was added to a precipitate and the mixture was acidified with 5% hydrochloric acid to pH 5.0-6.0. The precipitate of cude **2** was filtered off, dried on air and recrystallized from MeOH or MeOH/AcOH.

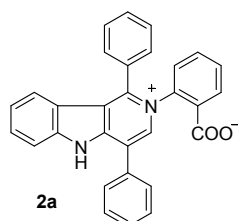
Method B: To a solution of 2-benzylidene-1,2-dihydro-3*H*-indol-3-one **1a** (0.6 mmol) in DMSO (2 mL) was added EtONa (2 mmol) and the reaction mixture was heated to 50 °C for 6 h. Water (2 mL) was added, the precipitate formed was filtered off, washed with water and dried on air. Compound **2a** was obtained as a white powder (5 % yield): m.p. 355-357 °C (MeOH).

Method C: To a suspension of the corresponding 2-arylidene-1H-indol-3(2H)-ones **1e**, **1f** and **1i** (0.6 mmol) in *tert*-BuOH (7 mL), was added potassium hydroxide (388 mg, 6.0 mmol) and the mixture was refluxed. Work-up of the reaction mixture was performed as described above.

Method B: To a solution of 5,12-diphenyl-11H-pyrido[1,2-a:4,5-b']diindol-11-one **7** (20 mg, 0.047 mmol) in methanol (9 mL) under reflux was added potassium hydroxide (929 mg, 14.27 mmol) and the mixture was refluxed for 80 h. After evaporation of methanol from a reaction mixture, to a residue was added water (3-5 mL) and the mixture was acidified with 5% hydrochloric acid to pH 5.0-6.0. The precipitate formed was filtered off, washed with water and dried on air. Compound **2a** was obtained as a white powder (11 mg, 53% yield): m.p. 355-357 °C (MeOH).

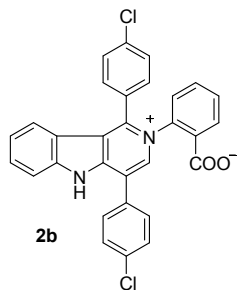
Method E: To a solution of 5,12-diphenyl-5,13-dihydro-11H-pyrido[1,2-a:4,5-b']diindol-11-one **6** (60 mg, 0.142 mmol) in ethanol (6 mL) potassium hydroxide (107 mg, 1.64 mmol) was added and the mixture was refluxed for 135 h. After evaporation of ethanol from a reaction mixture, to a residue was added water (3-5 mL) and the mixture was acidified with 5% hydrochloric acid to pH 5.0-6.0. The precipitate formed was filtered off, washed with water and dried on air. Compound **2a** was obtained as a white powder (30 mg, 48% yield): m.p. 355-357 °C (MeOH).

2-(1,4-Diphenyl-5H-pyrido[4,3-b]indol-2-ium-2-yl)benzoate (**2a**).



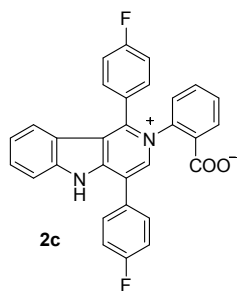
Compound **2a** was synthesized from (Z)-2-benzylidene-1,2-dihydro-3H-indol-3-one **1a** (130 mg, 0.6 mmol) according to the method A to give a white powder (54 mg, 42% yield): m.p. 355-357 °C (MeOH); ¹H NMR (400 MHz, DMSO-d₆) δ 6.61 (d, *J* = 8.2 Hz, 1H), 7.15 (t, *J* = 7.6 Hz, 1H), 7.27 (t, *J* = 7.6 Hz, 1H), 7.33-7.59 (m, 11H), 7.67 (d, *J* = 7.0 Hz, 1H), 7.75 (br s, 2H), 7.81 (d, *J* = 6.8 Hz, 1H), 7.88 (d, *J* = 8.2 Hz, 1H), 8.56 (s, 1H); ¹³C NMR (101 MHz, CD₃COOD) δ 166.45, 164.07, 147.41, 143.69, 140.78, 139.22, 136.64, 131.52, 130.58, 130.10, 129.57, 129.40, 129.08, 128.50, 128.18, 128.02, 127.60, 127.50, 126.77, 123.60, 121.71, 121.00, 120.61, 119.95, 118.95, 112.20; IR (KBr, cm⁻¹) 3059, 1610, 1595, 1587, 1560, 1489, 1474, 1445, 1424, 1342, 1276, 1230, 1120, 793, 759, 700; MS, *m/z* [M]⁺: 440; Anal. Calcd. for C₃₀H₂₀N₂O₂: C, 81.80; H, 4.58; N, 6.36. Found: C, 81.67; H, 4.73; N, 6.24.

2-[1,4-Bis(4-chlorophenyl)-5H-pyrido[4,3-b]indol-2-ium-2-yl]benzoate (**2b**).



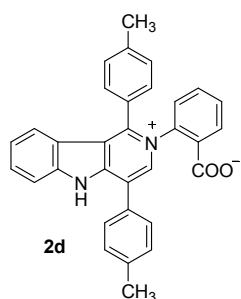
Compound **2b** was synthesized from (Z)-2-(4-chlorobenzylidene)-1,2-dihydro-3H-indol-3-one **1b** (150 mg, 0.6 mmol) according to the method A to give a white powder (46 mg, 31% yield): m.p. 351-353 °C (MeOH); ¹H NMR (600 MHz, CF₃COOD) δ 6.57 (d, *J* = 8.2 Hz, 1H), 6.81 (t, *J* = 7.6 Hz, 1H), 6.91 (t, *J* = 9.0 Hz, 2H), 7.03 (t, *J* = 7.6 Hz, 2H), 7.14-7.24 (m, 8H), 7.34 (t, *J* = 7.1 Hz, 1H), 7.81 (d, *J* = 6.8 Hz, 1H), 7.93 (s, 1H); ¹³C NMR (151 MHz, CF₃COOD) δ 168.66, 147.58, 144.64, 144.49, 140.99, 140.85, 140.33, 138.07, 137.01, 136.14, 134.74, 132.67, 131.00, 129.94, 129.86, 129.53, 129.23, 129.15, 128.96, 128.85, 128.74, 128.04, 127.06, 124.28, 123.45, 121.75, 121.46, 120.34, 120.03, 112.16; IR (KBr, cm⁻¹) 3397, 3064, 2954, 2604, 1610, 1598, 1557, 1491, 1476, 1455, 1431, 1397, 1346, 1231, 1093, 1016, 1007, 848, 826, 760, 743, 731; MS, *m/z* [M]⁺: 509; Anal. Calcd. for C₃₀H₁₈Cl₂N₂O₂: C, 70.74; H, 3.56; N, 5.50; Cl, 13.92. Found: C, 70.70; H, 3.56; N, 5.42; Cl, 13.77.

2-[1,4-Bis(4-fluorophenyl)-5H-pyrido[4,3-b]indol-2-ium-2-yl]benzoate (**2c**).



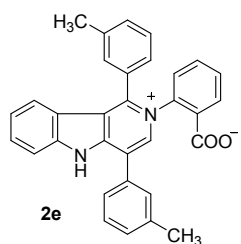
Compound **2c** was synthesized from (Z)-2-(4-fluorobenzylidene)-1,2-dihydro-3H-indol-3-one **1c** (141 mg, 0.6 mmol) according to the method A to give a white powder (49 mg, 35% yield): m.p. 337-339 °C (MeOH); ¹H NMR (600 MHz, CD₃COOD) δ 6.98 (d, *J* = 7.7 Hz, 1H), 7.28-7.88 (m, 14H), 8.12 (d, *J* = 6.3 Hz, 1H), 8.77 (s, 1H); ¹³C NMR (151 MHz, CF₃COOD) δ 168.63, 164.06 (d, *J* = 153 Hz), 163.85 (d, *J* = 153 Hz), 147.73, 144.66, 140.89, 140.48, 136.23, 134.76, 132.66, 130.96, 130.10, 130.05, 129.90, 129.68, 129.62, 128.92, 125.85, 125.83, 124.92, 124.89, 124.35, 123.42, 121.91, 121.48, 120.48, 120.20, 112.21; ¹⁹F NMR (300 MHz, CD₃COOD) δ -30.92 (s, 1F), -33.83 (s, 1F); IR (KBr, cm⁻¹) 3435, 3059, 2920, 2851, 1606, 1562, 1501, 1476, 1455, 1431, 1404, 1351, 1305, 1278, 1229, 1160, 1121, 1098, 1017, 838, 776, 760, 671, 531; MS, *m/z* [M]⁺: 476; Anal. Calcd. for C₃₀H₁₈F₂N₂O₂: C, 75.62; H, 3.81; N, 5.88; F, 7.97. Found: C, 75.26; H, 3.68; N, 5.85; F, 7.61.

2-[1,4-Bis(4-methylphenyl)-5H-pyrido[4,3-b]indol-2-yl]benzoate (**2d**).



Compound **2d** was synthesized from (Z)-2-(4-methylbenzylidene)-1,2-dihydro-3H-indol-3-one **1d** (138 mg, 0.6 mmol) according to the method A to give a white powder (53 mg, 39% yield): m.p. 335-337 °C (MeOH); ¹H NMR (600 MHz, CD₃COOD) δ 2.42 (s, 3H), 2.46 (s, 3H), 6.95 (d, *J* = 7.6 Hz, 1H), 7.23-7.81 (m, 14H), 8.12 (d, *J* = 6.9 Hz, 1H), 8.68 (s, 1H); ¹³C NMR (151 MHz, CD₃COOD) δ 167.99, 148.93, 144.92, 141.93, 141.37, 140.67, 140.08, 137.87, 132.62, 131.84, 130.61, 130.11, 129.98, 129.53, 129.47, 129.22, 128.89, 128.82, 128.54, 127.60, 122.93, 122.29, 122.05, 121.41, 120.23, 113.44, 20.44, 20.33; IR (KBr, cm⁻¹) 3428, 3063, 3028, 2918, 2859, 1617, 1598, 1588, 1561, 1500, 1476, 1454, 1428, 1344, 1313, 1276, 1257, 1232, 1219, 1120, 1022, 881, 843, 821, 758, 671, 617, 522; MS, *m/z* [*M*]⁺: 468; Anal. Calcd. for C₃₂H₂₄N₂O₂: C, 82.03; H, 5.16; N, 5.98. Found: C, 81.75; H, 5.39; N, 5.78.

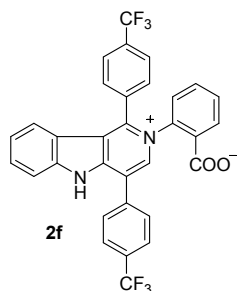
2-[1,4-Bis(3-methylphenyl)-5H-pyrido[4,3-b]indol-2-yl]benzoate (**2e**).



Compound **2e** was synthesized from (Z)-2-(3-methylbenzylidene)-1,2-dihydro-3H-indol-3-one **1e** (138 mg, 0.6 mmol) according to the method A to give a white powder (68 mg, 49% yield): m.p. 327-329 °C (MeOH); ¹H NMR (600 MHz, CF₃COOD) δ 1.81 (s, 3H), 1.95 (s, 3H), 6.53 (d, *J* = 6.4 Hz, 1H), 6.64-7.29 (m, 14H), 7.72 (br s, 1H), 7.87 (s, 1H); ¹³C NMR (151 MHz, CF₃COOD) δ 168.88, 168.73, 148.79, 148.73, 144.56, 140.64, 140.62, 140.58, 140.50, 140.08, 139.63, 139.61, 135.87, 135.80, 134.47, 134.30, 132.37, 132.16, 131.32, 131.31, 130.59, 130.57, 130.54, 129.77, 129.45, 128.97, 128.87, 128.78, 128.73, 128.66, 128.59, 127.99, 127.83, 125.26, 124.56, 124.45, 124.31, 123.03, 122.76, 122.75, 121.67, 121.63, 120.34, 119.94, 111.85, 18.90, 18.69, 18.65; IR (KBr, cm⁻¹) 3393, 3058, 2921, 2852, 1608, 1592, 1563, 1528, 1476, 1454, 1432, 1342, 1287, 1258, 1240, 1223, 1118, 1043, 877, 830, 794, 757, 721, 705, 680, 651, 623; MS, *m/z* [*M*]⁺: 468; Anal. Calcd. for C₃₂H₂₄N₂O₂: C, 82.03; H, 5.16; N, 5.98. Found: C, 81.85; H, 5.20; N, 6.07.

Compound **2e** was obtained from **1e** (138 mg, 0.6 mmol) by method B and reflux for 40 h to give 79 mg (57%) of a target product.

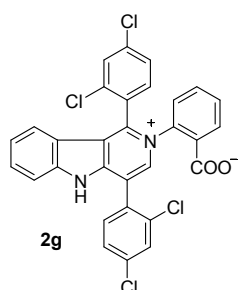
2-[1,4-Bis[4-(trifluoromethyl)phenyl]-5H-pyrido[4,3-b]indol-2-yl]benzoate (**2f**).



Compound **2f** was synthesized from (Z)-2-[4-(trifluoromethyl)benzylidene]-1,2-dihydro-3H-indol-3-one **1f** (170 mg, 0.6 mmol) according to the method A to give a white powder (31 mg, 18% yield): m.p. 360-362 °C (MeOH); ¹H NMR (600 MHz, CF₃COOD) δ 6.41 (d, *J* = 7.9 Hz, 1H), 6.77 (t, *J* = 7.6 Hz, 1H), 7.13-7.44 (m, 13H), 7.78 (d, *J* = 7.7 Hz, 1H), 8.00 (s, 1H); ¹³C NMR (151 MHz, CF₃COOD) δ 168.57, 147.22, 144.47, 141.00, 140.06, 136.51, 134.80, 133.77 (q, *J* = 33 Hz), 133.26, 132.90 (q, *J* = 33 Hz), 132.73, 132.38, 131.20, 130.20, 129.37, 128.90, 128.32, 128.16, 126.17 (q, *J* = 3 Hz), 125.87 (q, *J* = 4 Hz), 125.78 (q, *J* = 3 Hz), 124.31, 123.64, 122.79 (q, *J* = 272 Hz), 122.42 (q, *J* = 272 Hz), 121.59, 121.55, 121.29, 120.51, 120.46, 119.83, 119.80, 112.35; IR (KBr, cm⁻¹) 3438, 3067, 2918, 2850, 1618, 1600, 1563, 1498, 1476, 1454, 1433, 1407, 1325, 1278, 1231, 1171, 1121, 1110, 1090, 1067, 1020, 845, 707; MS, *m/z* [*M*]⁺: 576; Anal. Calcd. for C₃₂H₁₈F₆N₂O₂: C, 66.67; H, 3.15; N, 4.86; F, 19.77. Found: C, 66.53; H, 3.23; N, 4.99; F, 19.53.

Compound **2f** was obtained from **1f** (170 mg, 0.6 mmol) by method B and reflux for 38 h to give 48 mg (28%) of a target product.

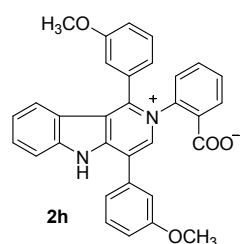
2-[1,4-Bis(2,4-dichlorophenyl)-5H-pyrido[4,3-b]indol-2-yl]benzoate (**2g**).



Compound **2g** was synthesized from (Z)-2-(2,4-dichlorobenzylidene)-1,2-dihydro-3H-indol-3-one **1g** (171 mg, 0.6 mmol) according to the method A to give a white powder (45 mg, 26% yield): m.p. 277-279 °C (MeOH); ¹H NMR (600 MHz, CF₃COOD) δ 6.61 (d, *J* = 8.2 Hz, 1H), 7.00-7.52 (m, 12H), 8.04 (d, *J* = 7.4 Hz, 1H), 7.97 (s, 1H); ¹³C NMR (151 MHz, CF₃COOD) δ 160.05, 159.76, 144.88, 144.74, 144.48, 141.06, 140.92, 139.84, 139.15, 137.94, 137.81, 134.80, 133.46, 132.58, 131.38, 131.11, 130.26, 129.84, 129.81, 129.37, 127.86, 127.59, 126.86, 126.62, 126.49, 123.75, 120.91, 119.51, 119.33, 112.22; IR (KBr, cm⁻¹) 3390, 3066, 2928, 2817, 1612, 1585, 1563, 1504, 1471, 1454,

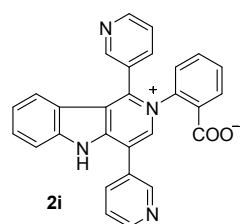
1435, 1381, 1347, 1278, 1227, 1144, 1101, 1041, 949, 887, 862, 812, 797, 768, 710; MS, m/z $[M]^+$: 578; Anal. Calcd. for $C_{30}H_{16}Cl_4N_2O_2$: C, 62.31; H, 2.79; N, 4.84; Cl, 24.52. Found: C, 62.42; H, 2.76; N, 4.73; Cl, 24.34.

2-[1,4-Bis(3-methoxyphenyl)-5H-pyrido[4,3-b]indol-2-ium-2-yl]benzoate (2h).



Compound **2h** was synthesized from (Z)-2-(3-methoxybenzylidene)-1,2-dihydro-3H-indol-3-one **1h** (148 mg, 0.6 mmol) according to the method A to give a white powder (27 mg, 17% yield): m.p. 313-315 °C (MeOH); 1H NMR (600 MHz, CF_3COOD) δ 3.36 (d, J = 15.3 Hz, 3H), 3.55 (s, 3H), 6.51 (d, J = 8.1 Hz, 1H), 6.59-6.70 (m, 3H), 6.73 (t, J = 7.6 Hz, 1H), 6.80 (d, J = 8.1 Hz, 1H), 6.89 (d, J = 7.6 Hz, 1H), 6.96-7.31 (m, 8H), 7.76 (t, J = 7.0 Hz, 1H), 7.95 (d, J = 2.8 Hz, 1H); ^{13}C NMR (151 MHz, CF_3COOD) δ 168.69, 168.60, 158.61, 158.46, 158.18, 149.62, 149.30, 147.69, 144.26, 140.86, 140.38, 140.31, 136.02, 134.54, 132.49, 132.40, 131.47, 130.96, 130.81, 130.80, 130.49, 130.42, 130.22, 129.78, 128.85, 128.83, 124.37, 124.33, 123.26, 123.24, 121.93, 121.70, 121.57, 121.46, 121.14, 120.19, 120.03, 112.21, 54.97, 54.63, 54.54; IR (KBr, cm^{-1}) 3407, 3066, 2937, 2839, 1609, 1587, 1561, 1536, 1501, 1479, 1464, 1430, 1348, 1307, 1295, 1274, 1254, 1230, 1182, 1120, 1112, 1029, 873, 763, 680; MS, m/z $[M]^+$: 500; Anal. Calcd. for $C_{32}H_{24}N_2O_4$: C, 76.78; H, 4.83; N, 5.60. Found: C, 76.80; H, 4.81; N, 5.55.

2-(1,4-Dipyridin-3-yl-5H-pyrido[4,3-b]indol-2-ium-2-yl)benzoate (2i).



Compound **2i** was synthesized from (Z)-2-(pyridin-3-ylmethylene)-1,2-dihydro-3H-indol-3-one **1i** (131 mg, 0.6 mmol) according to the method A to give a white powder (31 mg, 24% yield): m.p. 359-361 °C (MeOH); 1H NMR (300 MHz, $DMSO-d_6$) δ 6.61 (t, J = 7.0 Hz, 1H), 7.22 (t, J = 7.6 Hz, 1H), 7.41-8.16 (m, 11H), 8.69 (d, J = 3.7 Hz, 1H), 8.73 (d, J = 3.5 Hz, 1H), 8.85 (d, J = 9.7 Hz, 2H), 8.98 (s, 1H); ^{13}C NMR (151 MHz, CD_3COOD) δ 171.28, 150.32, 148.33, 147.43, 146.59, 145.85, 145.68, 145.17, 145.13, 142.46, 142.35, 140.18, 139.94, 139.55, 139.27, 133.97, 133.41, 132.32, 132.09, 131.47, 131.36, 130.33, 129.99, 129.85, 129.49, 127.80, 126.48, 125.25, 125.05, 123.79, 121.81, 121.77, 121.29, 121.22, 120.73, 120.70, 117.85, 113.96; IR (KBr, cm^{-1}) 3413, 3062, 2919, 2850, 1611, 1596, 1590, 1563, 1533, 1501, 1474, 1453, 1430, 1412, 1352, 1315, 1282, 1234, 1220, 1195, 1123, 1027, 840, 812, 758, 710, 657, 619; MS, m/z $[M]^+$: 442; Anal. Calcd. for $C_{28}H_{18}N_4O_2$: C, 76.01; H, 4.10; N, 12.66. Found: C, 76.19; H, 3.93; N, 12.60.

Compound **2i** was obtained from **1i** (131 mg, 0.6 mmol) by method B and reflux for 30 h to give 104 mg (80%) of a target product.

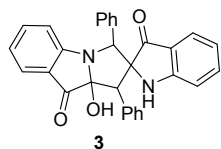
2-(1,4-Diphenyl-5H-pyrido[4,3-b]indol-2-ium-2-yl)benzoate (2a), 9a'-hydroxy-1',3'-diphenyl-1'H-spiro[indole-2,2'-pyrrolo[1,2-a]indole]-3,9'(1H,9a'H)-dione (3), 3-benzyl-3-hydroxy-1,3-dihydro-2H-indol-2-one (4), 3-hydroxy-3-[methoxy(phenyl)methyl]-1,3-dihydro-2H-indol-2-one (5).

Method A: To a solution of **1a** (1.0 g, 4.5 mmol) in ethanol (45 mL) was added potassium hydroxide (2.96 g, 45 mmol) under reflux for 6 h, then the reaction mixture was concentrated in vacuo and water (90 mL) was added. Solid precipitate was filtered off and washed with water to give compound 9a'-hydroxy-1',3'-diphenyl-1'H-spiro[indole-2,2'-pyrrolo[1,2-a]indole]-3,9'(1H,9a'H)-dione **3** and other mixtures. The residue was purified by flash column chromatography on silica gel (C_6H_6 /MeOH, 5/1, v/v) to give **3** (144 mg, 14% yield) as a yellow crystalline: m.p. 258-260 °C. The mother liquor was extracted with ether (4×20mL). The organic phases were combined and the solvent was removed in vacuo. The residue was purified by flash column chromatography on silica gel (C_6H_6 /acetone, 5/2, v/v) to give 3-benzyl-3-hydroxy-1,3-dihydro-2H-indol-2-one **4** (54 mg, 5% yield) as a white powder: m.p. 163-165 °C (C_6H_6) (lit.⁴ 162-164 °C). The aqueous phase was acidified with 5% hydrochloric acid to pH 5.0-6.0, the precipitate formed was filtered off and washed with water to give **2a** (16 mg, 2% yield).

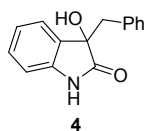
Method B: To a solution of **1a** (1.0 g, 4.5 mmol) in methanol (45 mL) was added potassium hydroxide (2.96 g, 45 mmol) under reflux, then the reaction mixture was concentrated in vacuo and water (90 mL) was added. Solid precipitate was filtered

off and washed with water to give compound 9a'-hydroxy-1',3'-diphenyl-1'H-spiro[indole-2,2'-pyrrolo[1,2-a]indole]-3,9'(1H,9a'H)-dione **3** and other mixtures. The residue was purified by flash column chromatography on silica gel (C₆H₆/MeOH, 5/1, v/v) to give **3** (144 mg, 14% yield) as a yellow crystalline: m.p. 258-260 °C. The mother liquor was extracted with ether (4×20mL). The organic phases were combined and the solvent was removed in vacuo. The residue was purified by flash column chromatography on silica gel (C₆H₆/acetone, 5/2, v/v) to give 3-hydroxy-3-[methoxy(phenyl)methyl]-1,3-dihydro-2H-indol-2-one **5** (151 mg, 12% yield) as a white powder: m.p. 214-216 °C (C₆H₆). **5** was obtained as a mixture of isomers, single isomer was isolated after recrystallization from methanol. The aqueous layer was acidified with 5% hydrochloric acid, the precipitate formed was filtered off and washed with water to give **2a** (150 mg, 7% yield).

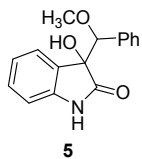
Data of compounds 3-5.



¹H NMR (600 MHz, DMSO-d₆) δ 3.22 (s, 1H), 4.72 (s, 1H), 6.40 (t, *J* = 7.3 Hz, 1H), 6.61 (d, *J* = 8.2 Hz, 1H), 6.69 (d, *J* = 8.2 Hz, 1H), 7.07-7.11 (m, 4H), 7.13 (t, *J* = 7.5 Hz, 1H), 7.16 (d, *J* = 7.7 Hz, 1H), 7.23 (t, *J* = 7.0 Hz, 1H), 7.26-7.31 (m, 4H), 7.43 (d, *J* = 5.9 Hz, 2H), 7.47 (s, 1H), 7.58-7.63 (m, 3H); ¹³C NMR (151 MHz, DMSO-d₆) δ 199.39, 197.69, 161.70, 161.58, 138.77, 138.26, 138.02, 132.43, 131.21, 128.57, 128.09, 127.82, 127.71, 127.16, 125.07, 123.78, 121.98, 121.83, 118.36, 117.15, 113.17, 112.30, 98.09, 83.45, 74.86, 57.10; IR (KBr, cm⁻¹) 3382, 3288, 3063, 3026, 1686, 1605, 1585, 1491, 1464, 1322, 1299, 1260, 1150, 1096, 1077, 1020, 935, 750, 698; MS, *m/z* [M]⁺: 458; Anal. Calcd. for C₃₀H₂₂N₂O₃: C, 78.59; H, 4.84; N, 6.11. Found: C, 78.31; H, 4.74; N, 6.06.

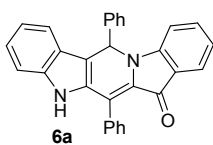


¹H NMR (400 MHz, DMSO-d₆) δ 3.01 (d, *J* = 12.6 Hz, 1H), 3.14 (d, *J* = 12.6 Hz, 1H), 6.60 (d, *J* = 7.8 Hz, 1H), 6.89-7.12 (m, 8H), 10.04 (s, 1H); ¹³C NMR (101 MHz, DMSO-d₆) δ 179.21, 142.12, 135.54, 131.41, 130.58, 129.31, 127.93, 126.78, 125.03, 121.64, 109.73, 77.03, 43.92; IR (KBr, cm⁻¹) 3338, 3178, 3085, 3030, 1709, 1670, 1625, 1608, 1473, 1217, 1180, 1112, 756, 700; MS, *m/z* [M]⁺: 239; Anal. Calcd. for C₁₅H₁₃NO₂: C, 75.30; H, 5.48; N, 5.85. Found: C, 75.08; H, 5.31; N, 5.98.



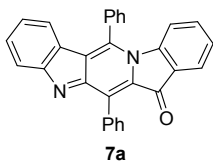
¹H NMR (400 MHz, DMSO-d₆) δ 3.07 (s, 3H), 4.54 (s, 1H), 6.05 (d, *J* = 7.2 Hz, 1H), 6.18 (s, 1H), 6.70 (t, *J* = 7.5 Hz, 1H), 6.77 (d, *J* = 7.6 Hz, 1H), 7.12-7.36 (m, 6H), 10.24 (s, 1H); ¹³C NMR for mixture of isomers (75 MHz, DMSO-d₆) δ 179.55, 177.46, 143.75, 142.54, 136.67, 136.51, 129.50, 129.31, 128.76, 128.42, 128.20, 127.75, 126.79, 126.30, 121.58, 120.80, 109.74, 109.39, 87.34, 87.22, 85.55, 85.46, 79.49, 77.37, 57.94, 57.43; IR (KBr, cm⁻¹) 3326, 3276, 3059, 1708, 1624, 1489, 1472, 1453, 1359, 1350, 1214, 1185, 1132, 1101, 1077, 975, 754, 727, 699, 674, 599; MS, *m/z* [M]⁺: 269; Anal. Calcd. for C₁₆H₁₅NO₃: C, 71.36; H, 5.61; N, 5.20. Found: C, 71.64; H, 5.49; N, 5.11.

5,12-Diphenyl-5,13-dihydro-11H-pyrido[1,2-a:4,5-b']diindol-11-one (6a).



To a solution of **1a** (260 mg, 1.18 mmol) in *tert*-BuOH (3.2 mL) was added potassium hydroxide (260 mg, 4.02 mmol) and the mixture was stirred at room temperature for 17 h. Water (3-5 mL) was added to a precipitate, the aqueous layer was extracted with benzene (3×20 mL) or ethyl acetate (2×50 mL), the organic layers were combined and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (C₆H₆/MeOH, 5/1, v/v) to give 5,12-diphenyl-5,13-dihydro-11H-pyrido[1,2-a:4,5-b']diindol-11-one **6** (177 mg, 83% yield) as a blue powder: m.p. 207-209 °C (C₆H₆/MeOH). ¹H NMR (600 MHz, DMSO-d₆) δ 6.88 (t, *J* = 7.4 Hz, 1H), 6.98 (t, *J* = 7.5 Hz, 1H), 7.02 (s, 1H), 7.08-7.58 (m, 12H), 7.61 (d, *J* = 7.0 Hz, 2H), 7.64 (d, *J* = 7.6 Hz, 2H), 10.89 (s, 1H); ¹³C NMR (151 MHz, DMSO-d₆) δ 182.29, 150.70, 143.05, 139.51, 135.70, 131.86, 130.52, 130.42, 130.17, 129.32, 128.98, 128.87, 128.34, 127.07, 124.82, 124.19, 123.84, 123.19, 120.61, 120.10, 119.29, 118.55, 113.02, 112.90, 111.39, 56.66; IR (KBr, cm⁻¹) 3431, 3281, 2921, 2851, 1651, 1614, 1584, 1566, 1511, 1474, 1435, 1346, 1326, 1295, 1270, 1239, 1189, 1153, 1134, 1101, 1063, 980, 744, 721, 560, 475, 429, 403; MS, *m/z* [M]⁺: 424; Anal. Calcd. for C₃₀H₂₀N₂O: C, 84.88; H, 4.75; N, 6.60. Found: C, 84.74; H, 4.98; N, 6.43.

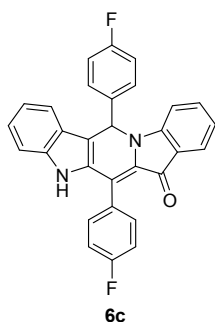
5,12-Diphenyl-11H-pyrido[1,2-a:4,5-b']diindol-11-one (7a).



To a solution of **6** (84 mg, 0.198 mmol) in ethanol (10 mL) under reflux was added potassium hydroxide (150 mg, 2.3 mmol) and the mixture was refluxed for 32h. Reaction mixture was acidified with hydrochloric acid to pH 2.0-3.0. The solid precipitate was filtered off. The organic layer was diluted with water (10-20 mL) and was added 86 % potassium hydroxide to pH 8.0-10.0. The precipitate was filtered off, washed with water, dried on air. The residue was purified by flash column

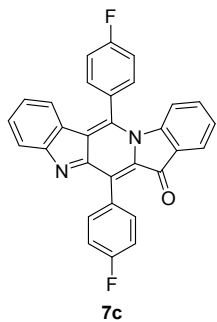
chromatography on silica gel (C₆H₆/MeOH, 5/1, v/v) to give 5,12-diphenyl-11*H*-pyrido[1,2-*a*:4,5-*b'*]diindol-11-one **7** (68 mg, 81% yield) as a red powder: m.p. 317-319 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ 6.02 (d, *J* = 8.6 Hz, 1H), 6.56 (d, *J* = 7.6 Hz, 1H), 6.98 (t, *J* = 7.1 Hz, 1H), 7.31 (t, *J* = 7.2 Hz, 1H), 7.35-7.96 (m, 14H); ¹³C NMR (101 MHz, DMSO-*d*₆) δ 182.62, 162.80, 158.07, 154.83, 147.72, 141.90, 136.37, 132.37, 131.84, 131.81, 131.14, 130.68, 129.44, 129.14, 129.01, 128.04, 127.92, 127.41, 126.82, 126.64, 125.16, 122.79, 122.22, 121.54, 120.66, 116.24; IR (KBr, cm⁻¹) 3050, 1703, 1608, 1582, 1541, 1466, 1443, 1362, 1346, 1297, 1221, 1209, 1094, 996, 769, 755, 737, 697; MS, *m/z* [M]⁺: 422; Anal. Calcd for C₃₀H₁₈N₂O: C, 85.29; H, 4.29; N, 6.63. Found: C, 85.37; H, 4.33; N, 6.54.

5,12-Bis(4-fluorophenyl)-5,13-dihydro-11*H*-pyrido[1,2-*a*:4,5-*b'*]diindol-11-one (6c**).**



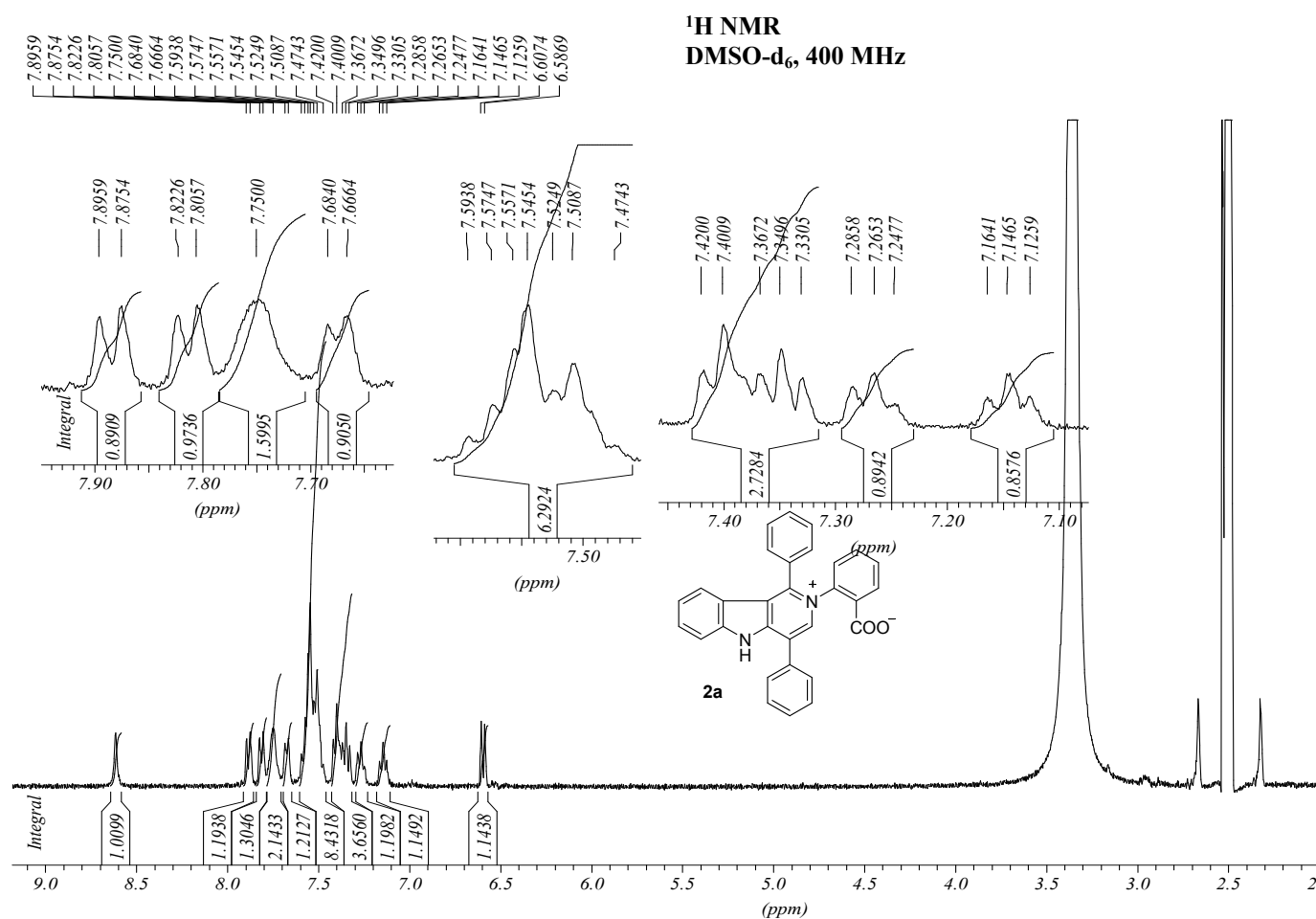
To a solution of **1a** (740 mg, 3.10 mmol) in *tert*-BuOH (8.5 mL) was added potassium hydroxide (647 mg, 11.55 mmol) and the mixture was stirred at room temperature for 21 h. After reaction completion, the water (15 mL) was added, the mixture was acidified with CH₃COOH to pH 7. The resulting solid precipitate was filtered off, washed with water and dried. The residue was recrystallized from MeOH to give 5,12-bis(4-fluorophenyl)-5,13-dihydro-11*H*-pyrido[1,2-*a*:4,5-*b'*]diindol-11-one **6c** (330 mg, 46% yield) as a purple powder: m.p. 243-246 °C (MeOH). ¹H NMR (600 MHz, DMSO-*d*₆) δ 6.88 (t, *J* = 7.2 Hz, 1H), 6.98 (br s, 2H), 7.10 (t, *J* = 7.8 Hz, 4H), 7.34 (q, *J* = 8.7 Hz, 3H), 7.42-7.49 (m, 3H), 7.64 (t, *J* = 6.1 Hz, 4H), 10.93 (s, 1H); ¹³C NMR (126 MHz, DMSO-*d*₆) δ 182.50, 163.80, 162.95, 161.85, 161.00, 150.57, 139.46, 139.16, 139.14, 135.96, 132.59, 130.48, 130.02, 129.20, 127.92, 127.90, 124.70, 123.07, 120.85, 120.40, 119.25, 117.69, 116.19, 115.99, 115.75, 113.04, 112.81, 111.40; MS, *m/z* [M]⁺: 460.

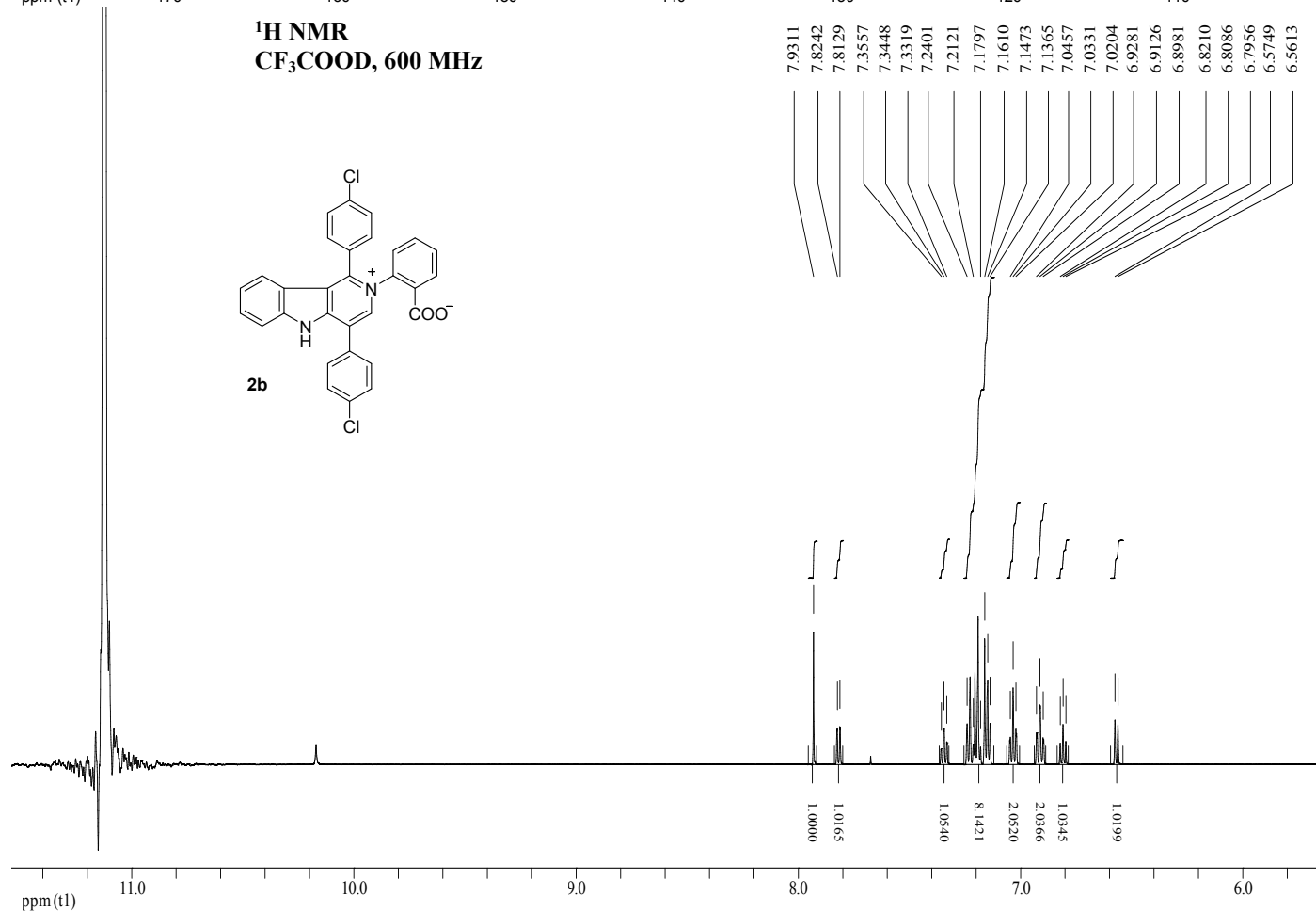
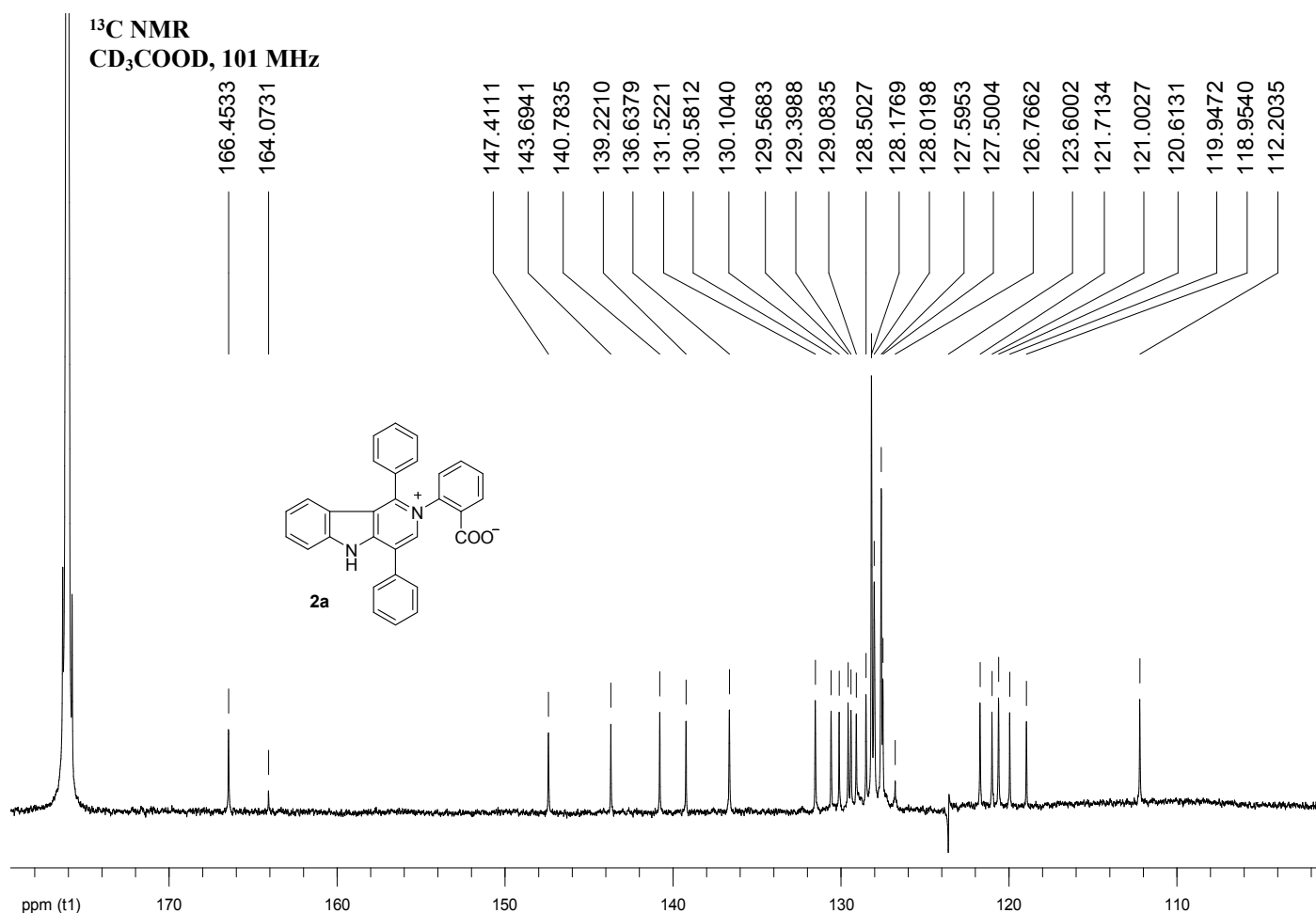
5,12-Bis(4-fluorophenyl)-11*H*-pyrido[1,2-*a*:4,5-*b'*]diindol-11-one (7c**).**

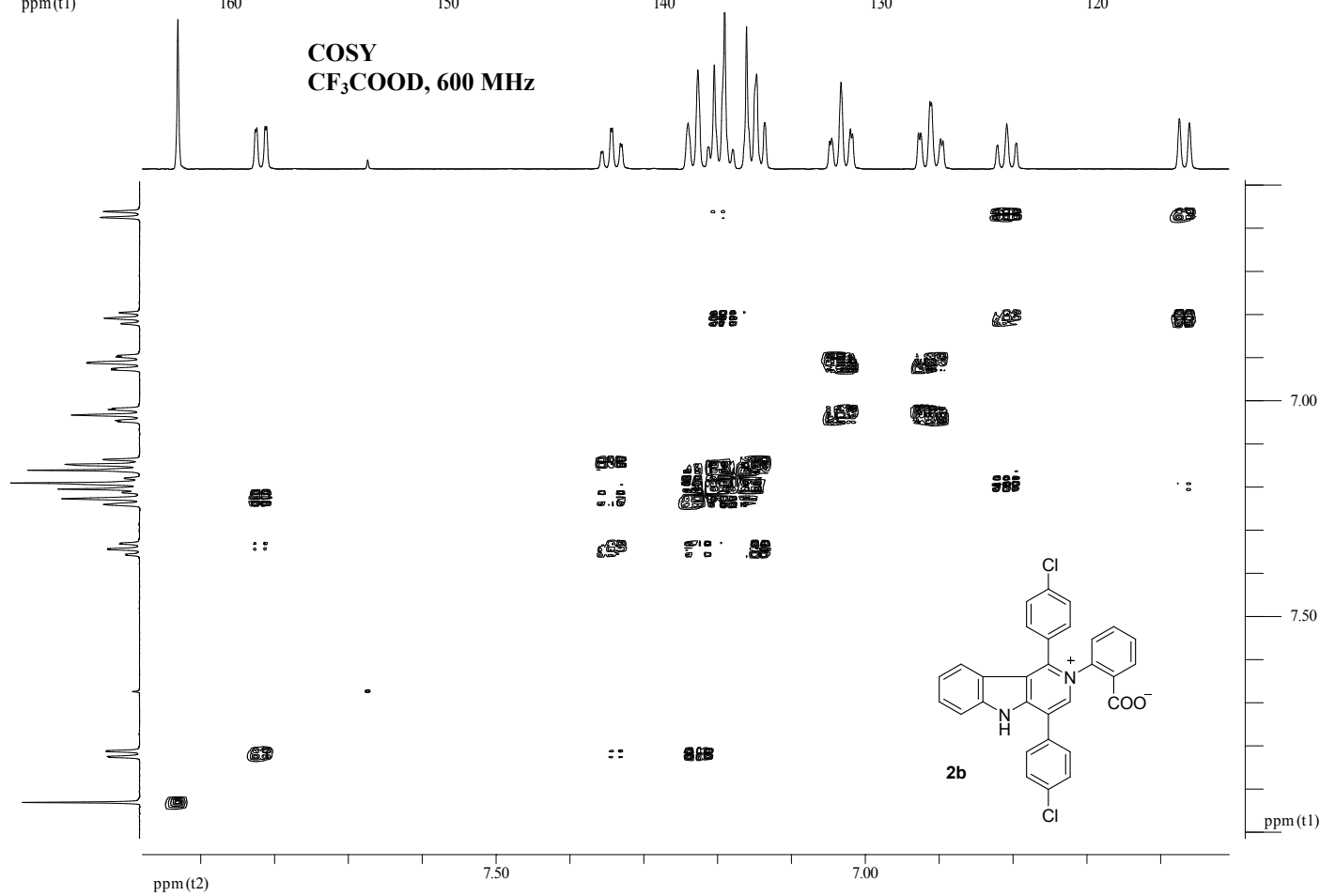
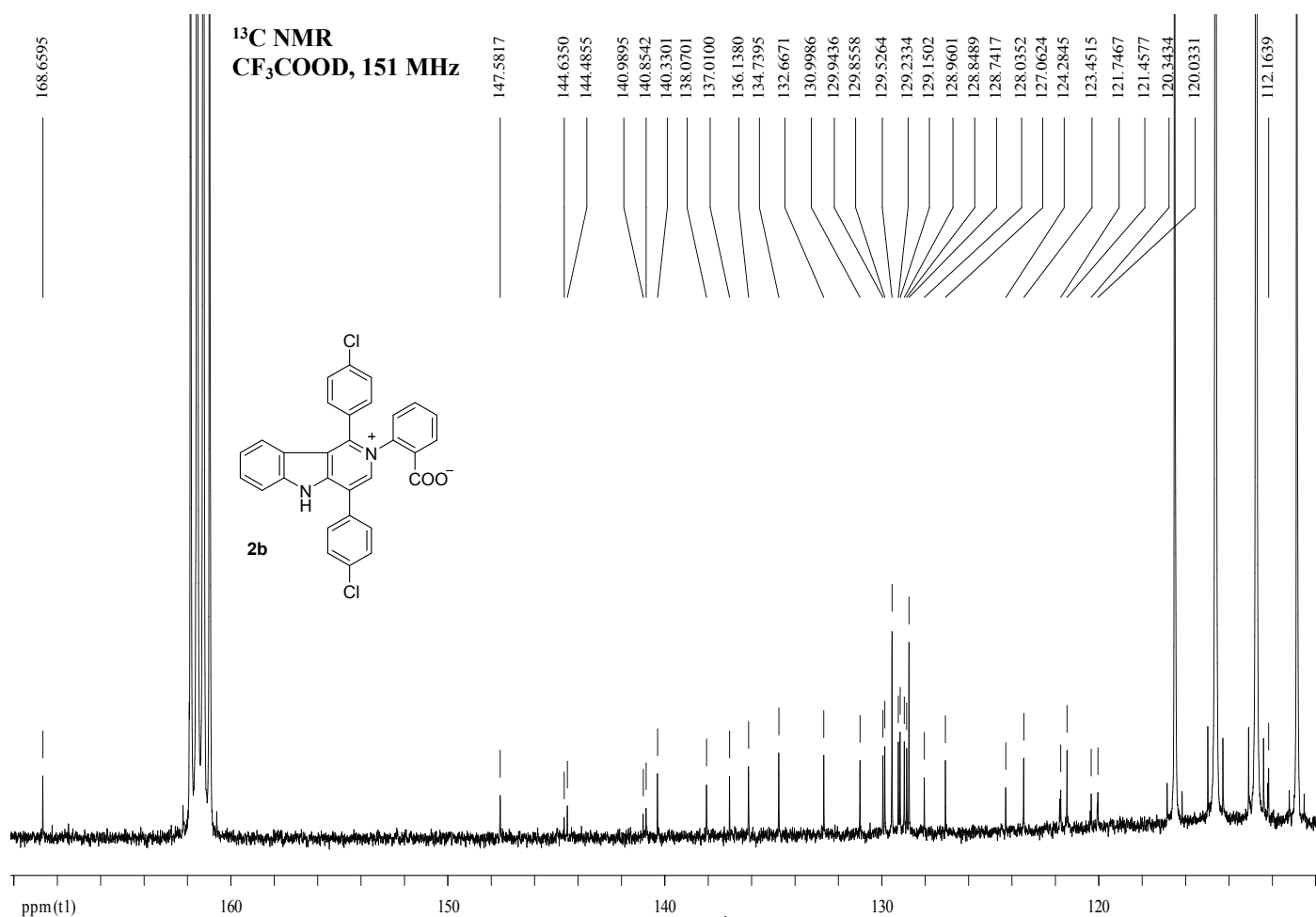


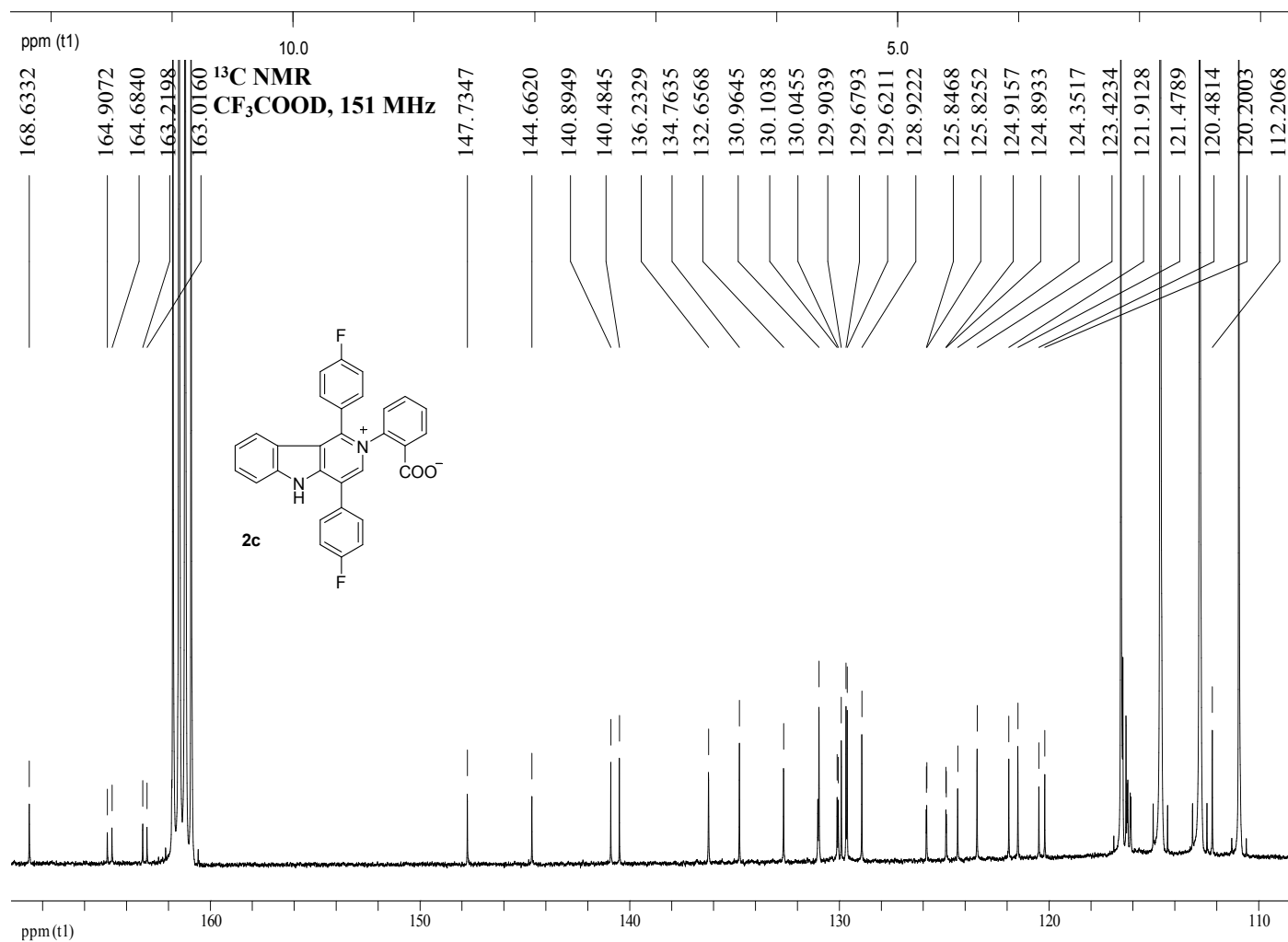
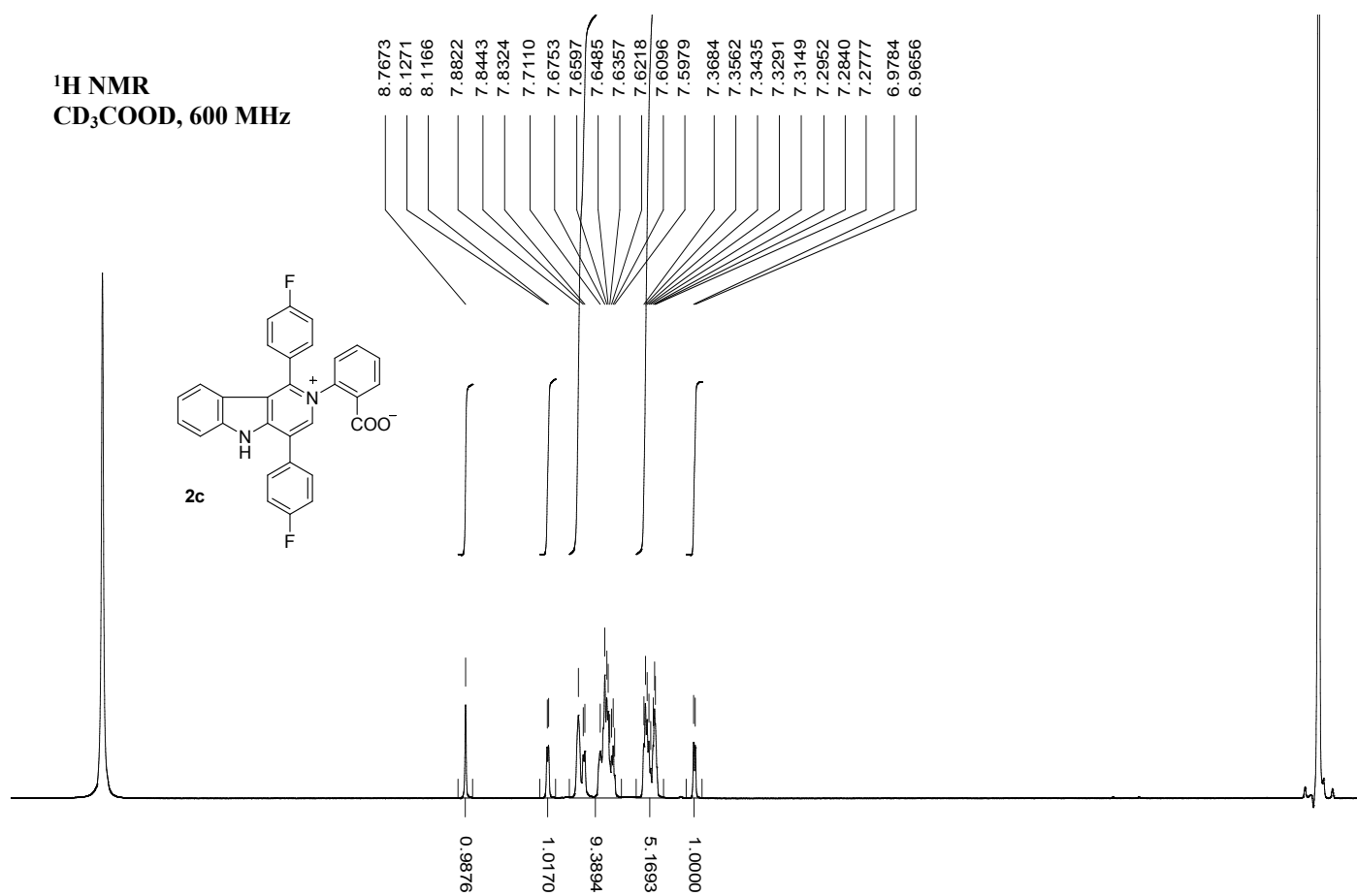
To a solution of **6c** (106 mg, 0.25 mmol) in ethanol (10 mL) under reflux was added potassium hydroxide (205 mg, 4.4 mmol) and the mixture was refluxed for 40h. Reaction mixture was acidified with hydrochloric acid to pH 2.0. The solid precipitate was filtered off. The organic layer was diluted with water (10-20 mL) and was added 86 % potassium hydroxide to pH 8.0-10.0. The precipitate was filtered off, washed with water, dried on air. The residue was recrystallized from DMF/EtOH to give 5,12-bis(4-fluorophenyl)-11*H*-pyrido[1,2-*a*:4,5-*b'*]diindol-11-one **7c** (42 mg, 40% yield) as a red powder: m.p. 395 °C (decomp.). ¹H NMR (600 MHz, DMSO-*d*₆) δ 6.07 (d, *J* = 8.6, 1H), 6.57 (d, *J* = 8.1, 1H), 7.02 (t, *J* = 7.5, 1H), 7.31-7.44 (m, 6H), 7.69-7.73 (m, 6H), 7.92 (q, *J* = 2.9Hz, 2H); ¹³C NMR (126 MHz, DMSO-*d*₆) δ 182.83, 165.12, 163.94, 163.14, 161.99, 158.15, 157.79, 154.64, 147.60, 141.18, 136.68, 133.38, 133.32, 131.80, 131.73, 129.35, 128.54, 128.52, 128.26, 128.21, 127.76, 127.66, 126.60, 126.52, 125.34, 123.02, 122.54, 121.50, 120.63, 118.11, 117.94, 116.31, 115.24, 115.06; MS, *m/z* [M]⁺: 458.

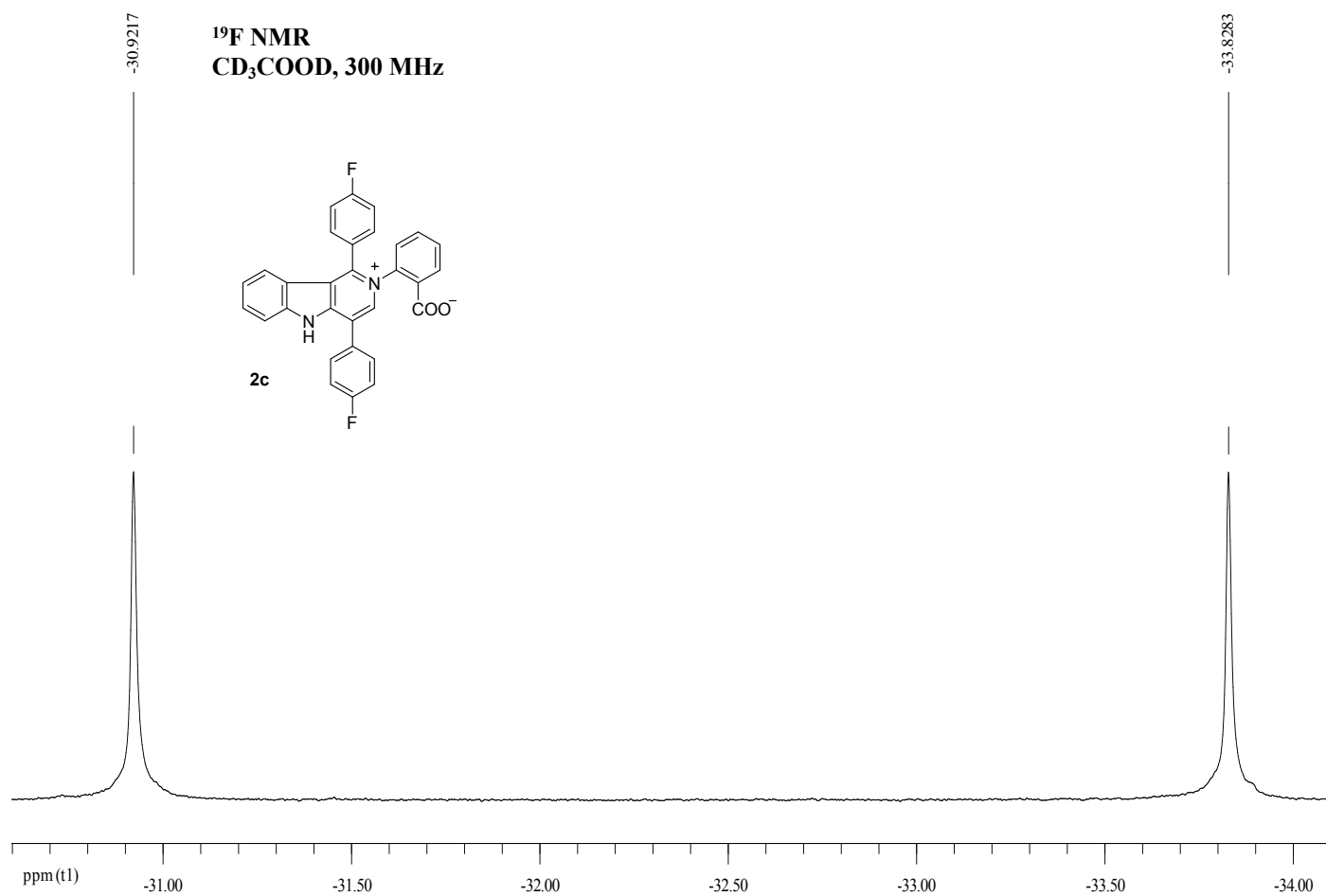
3. Copies of NMR Spectra

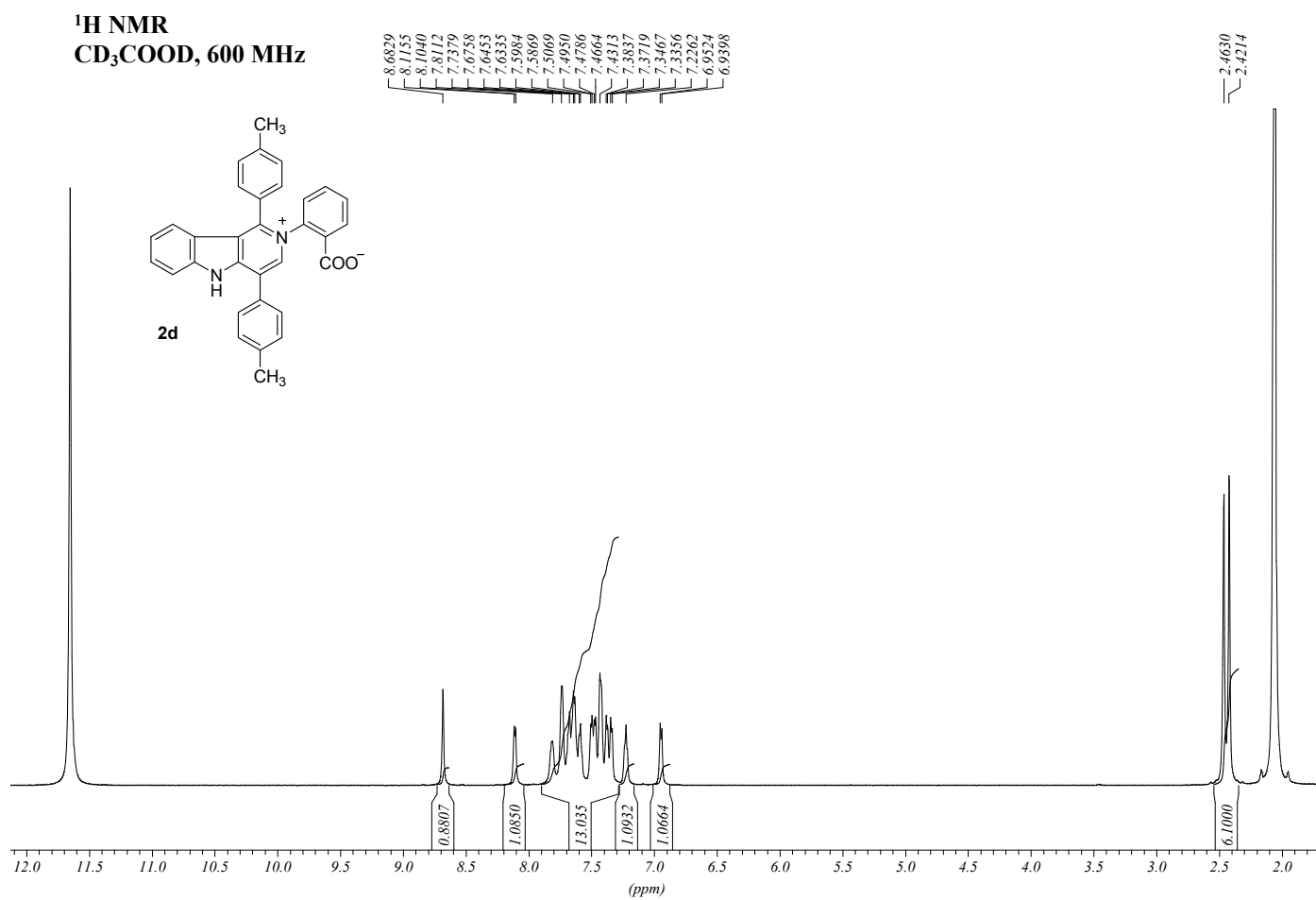
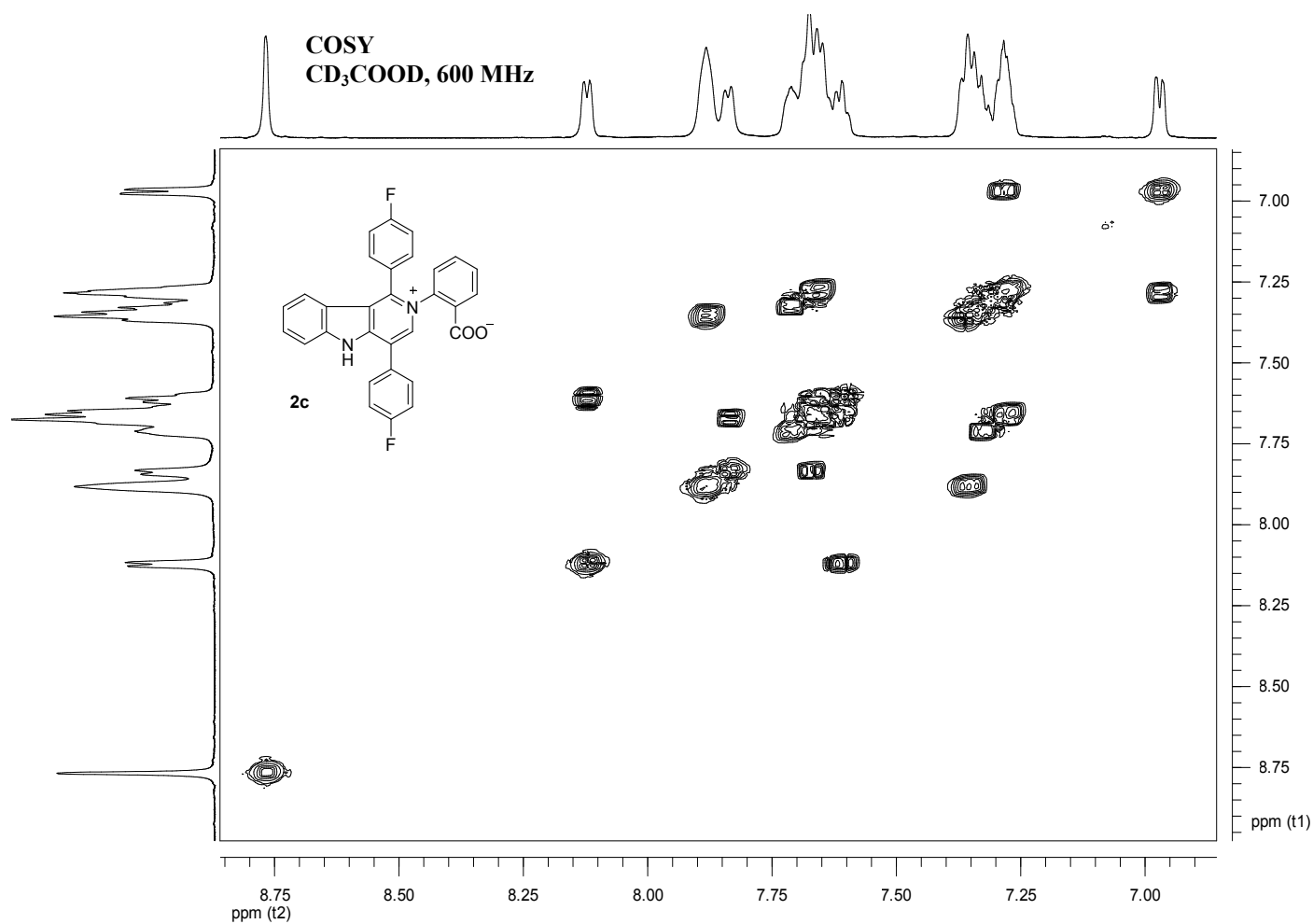


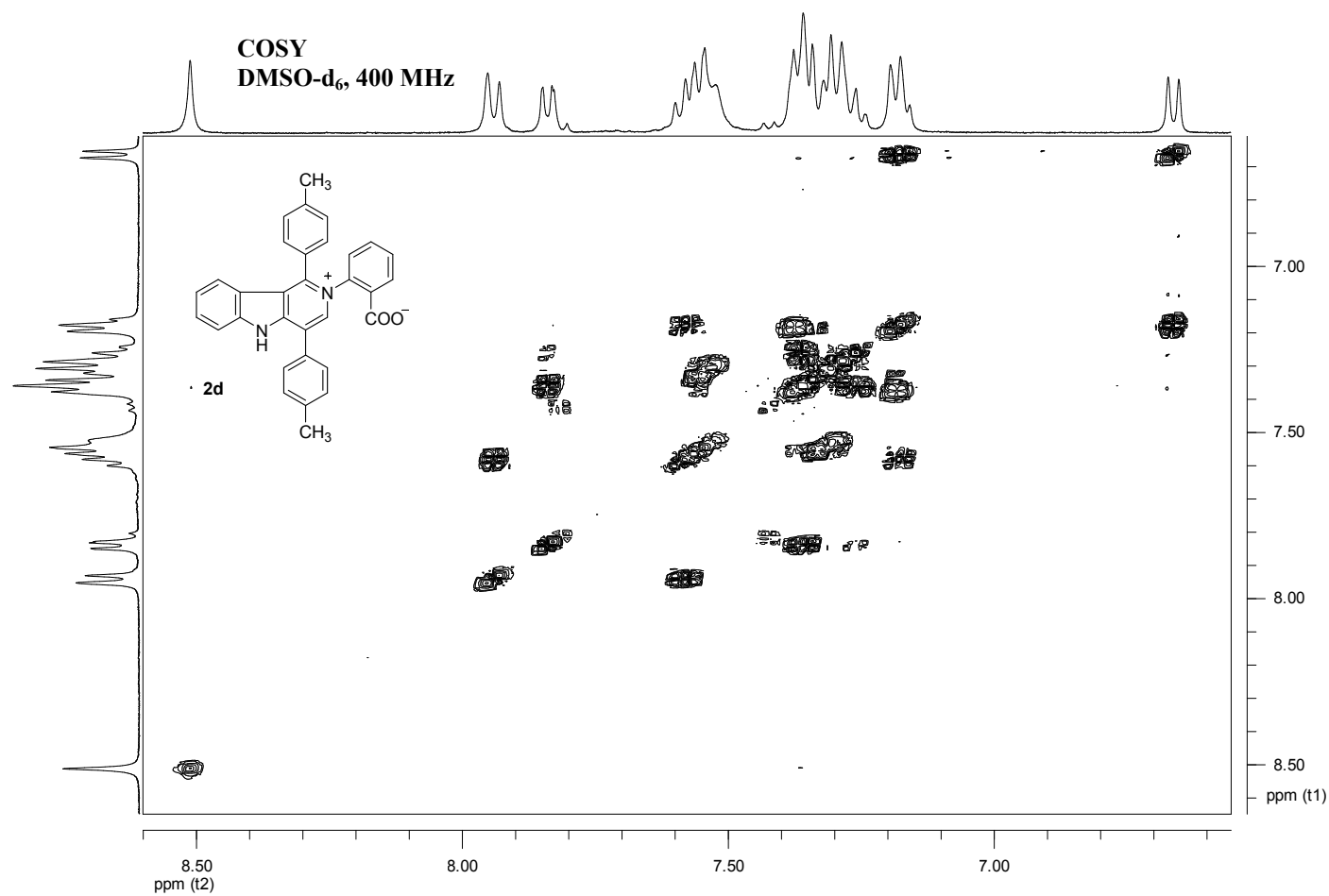
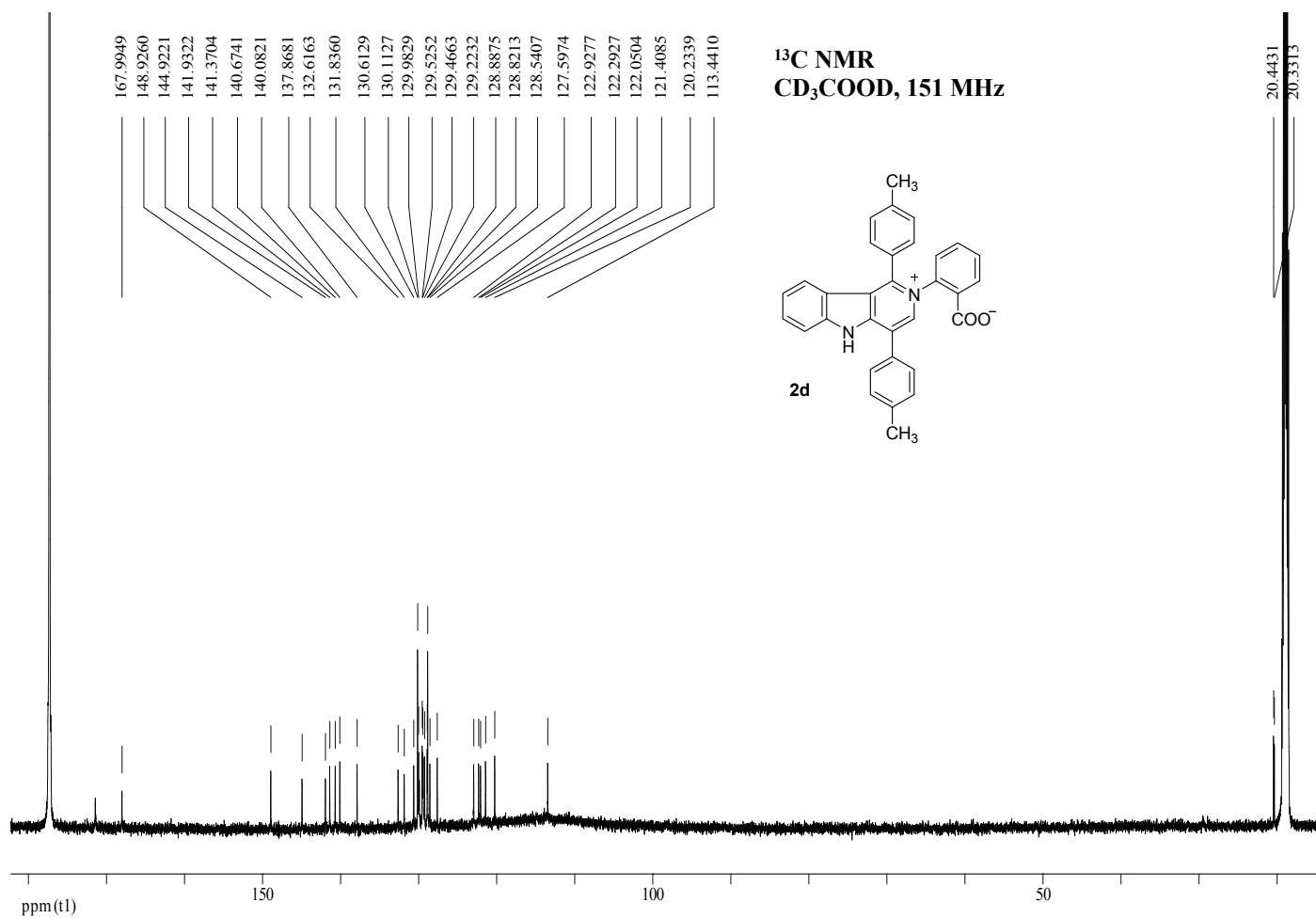




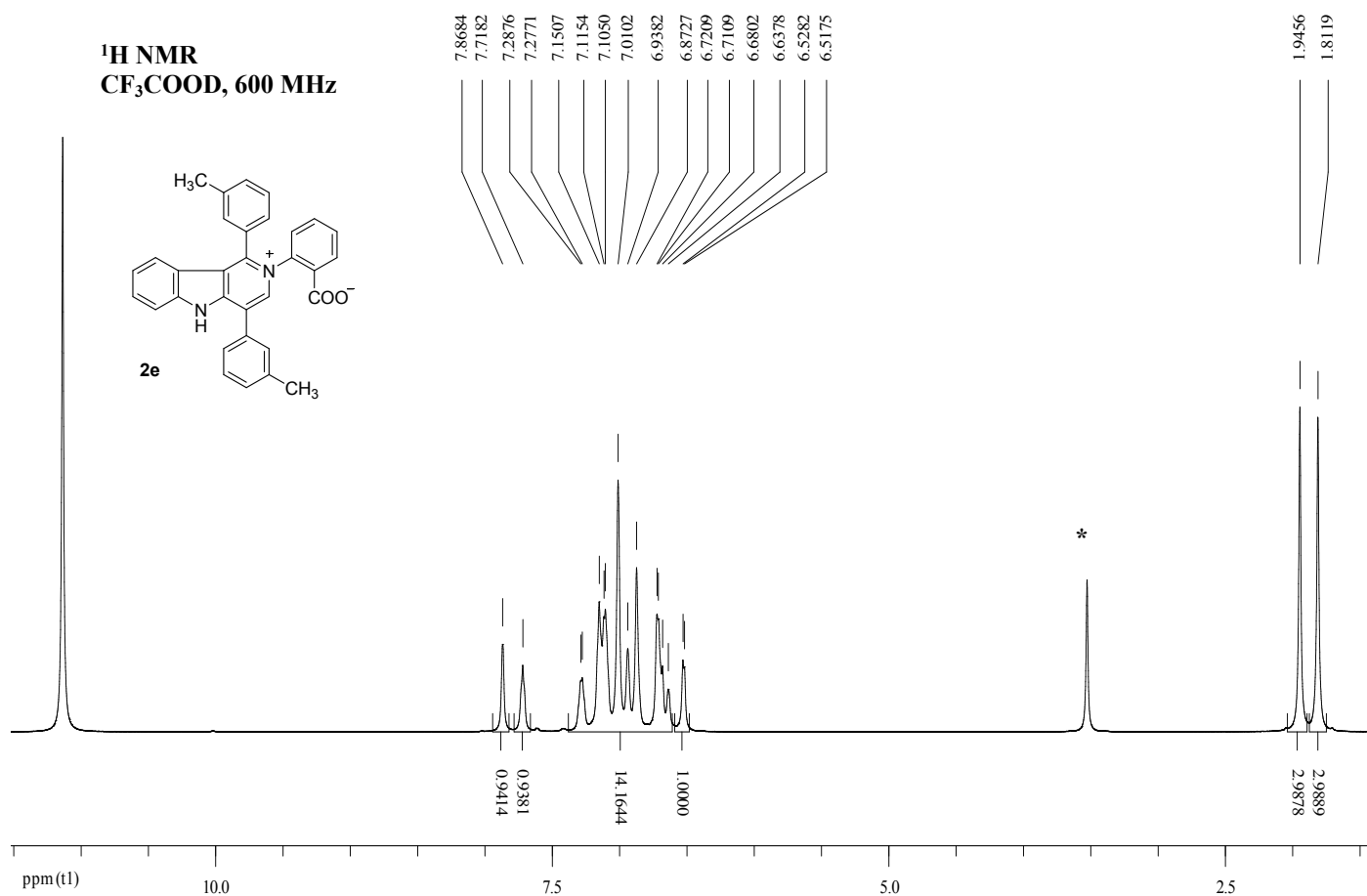






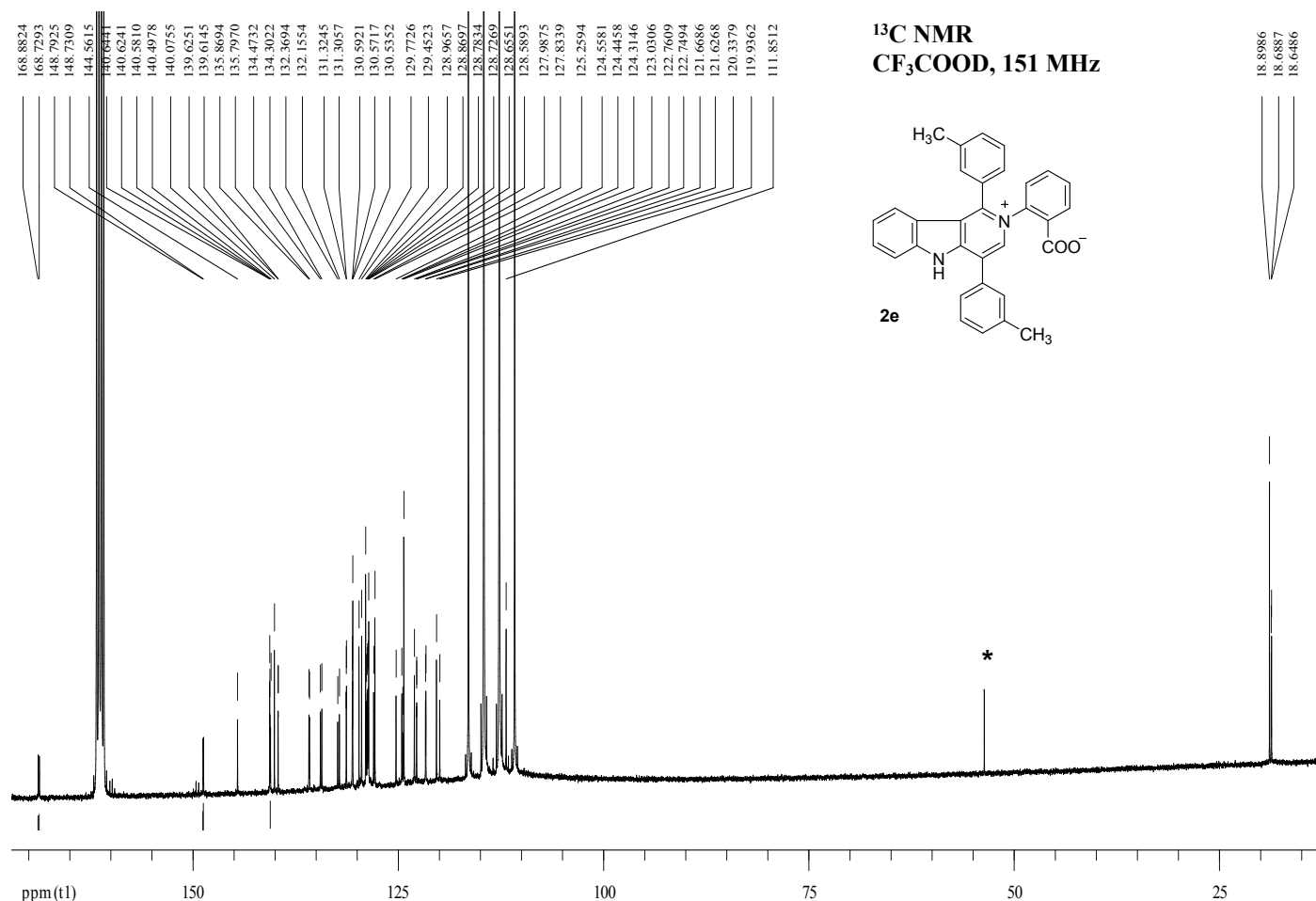


¹H NMR
CF₃COOD, 600 MHz

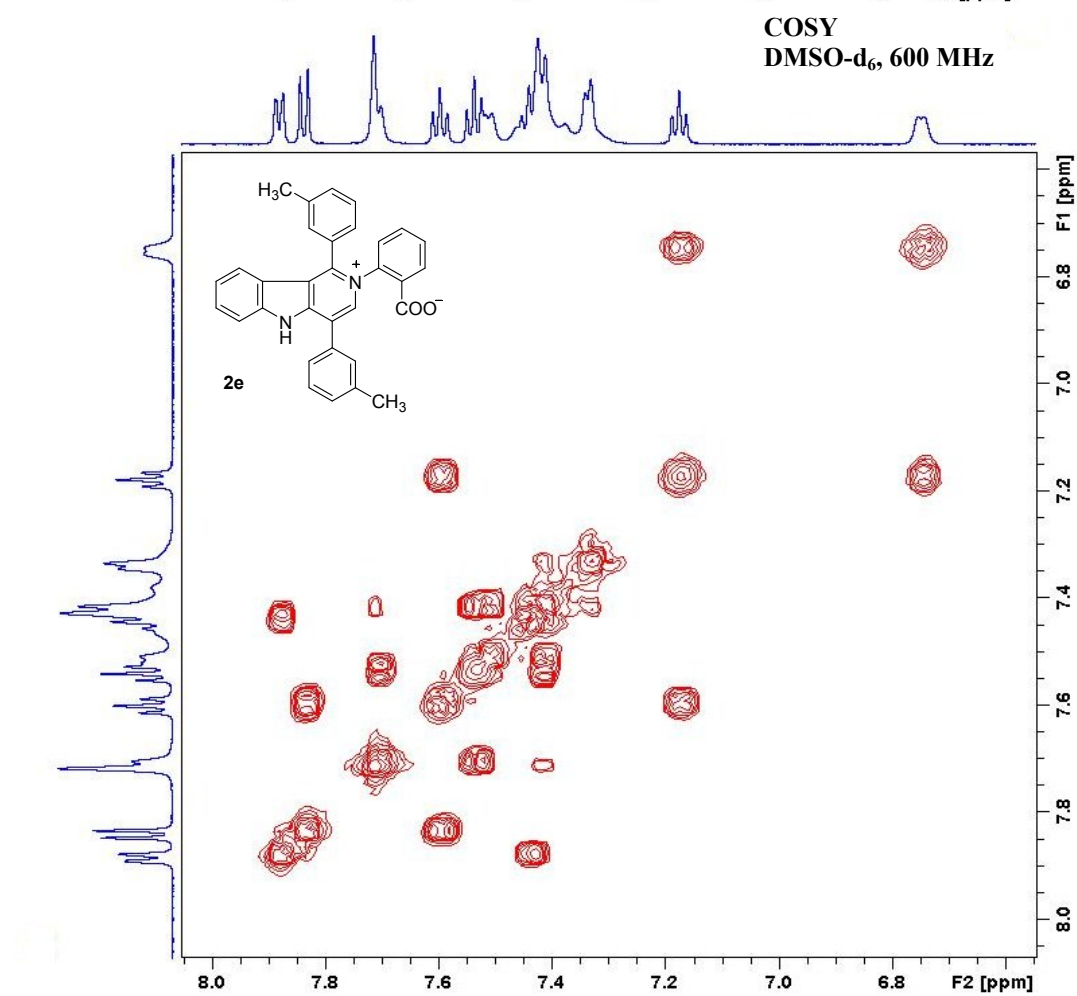
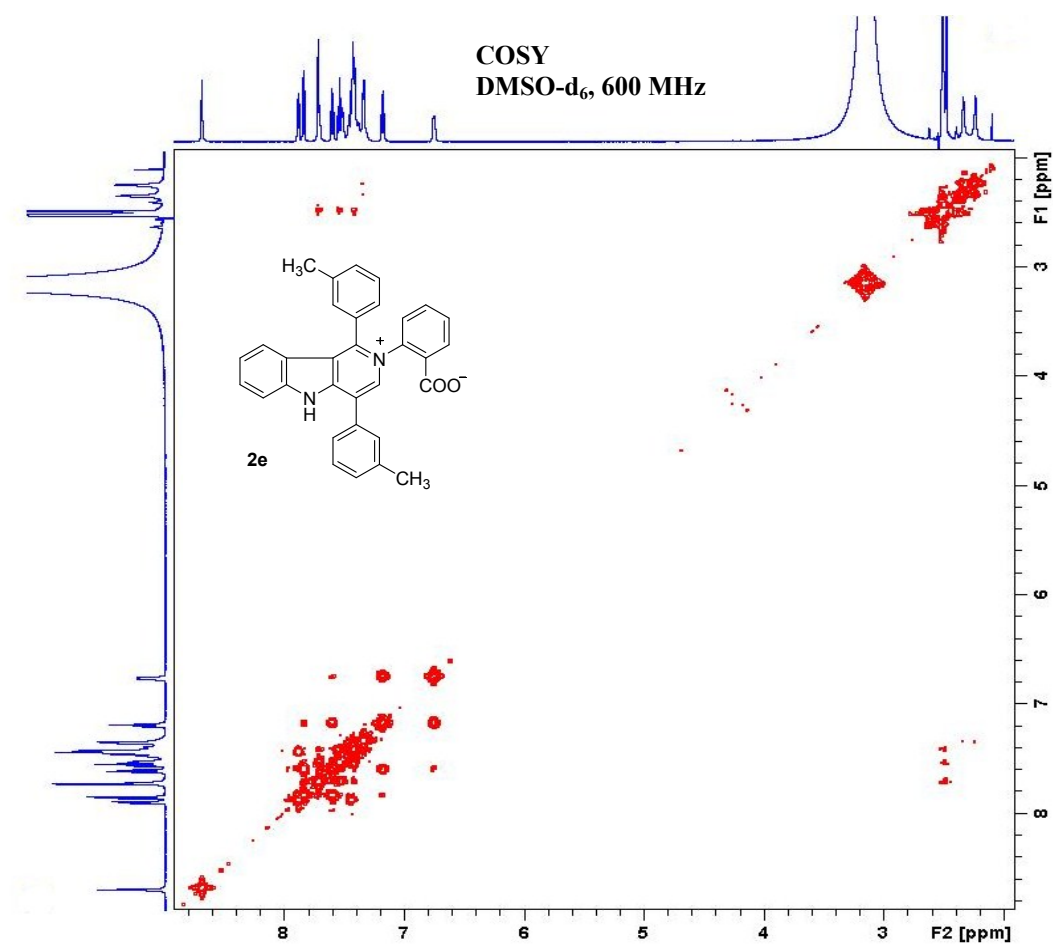


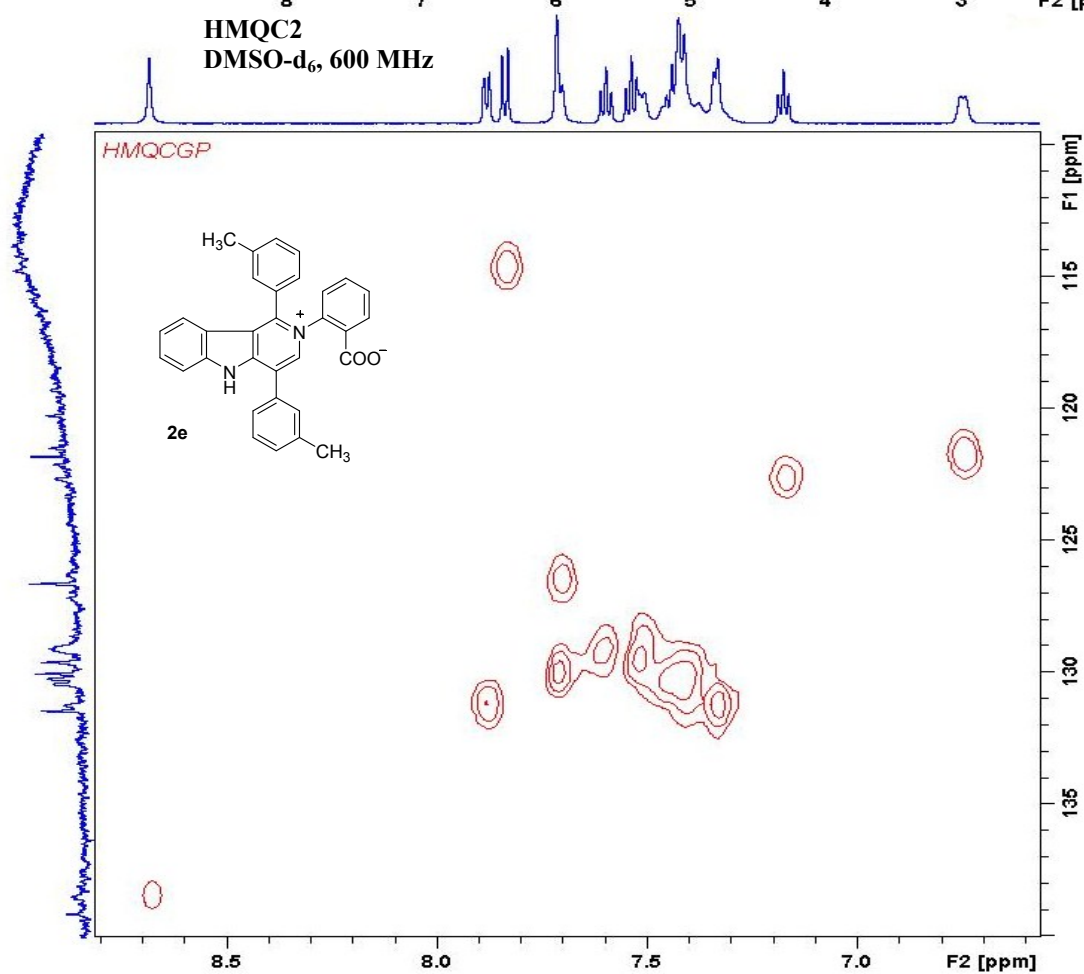
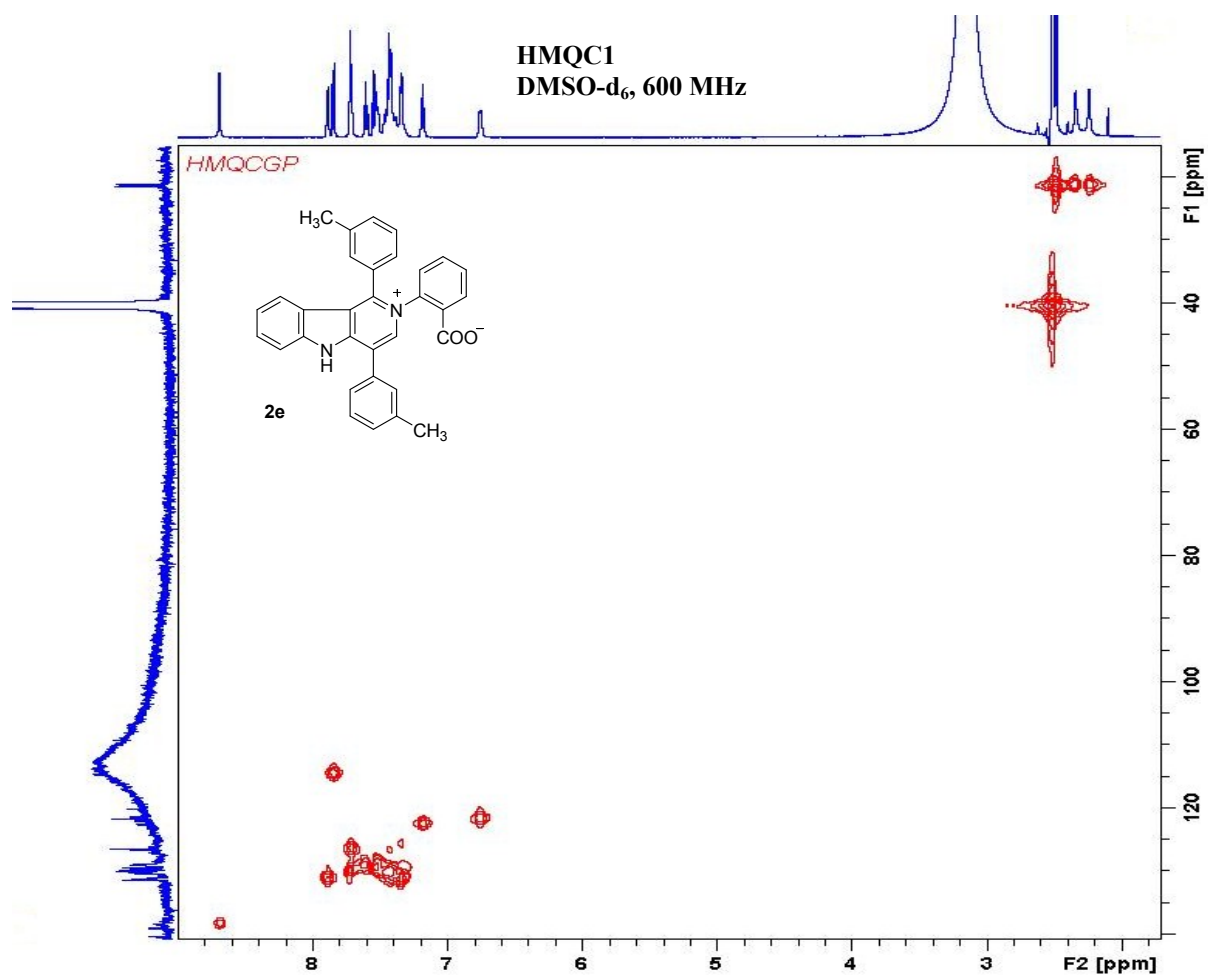
*) from CF₃COOD

¹³C NMR
CF₃COOD, 151 MHz

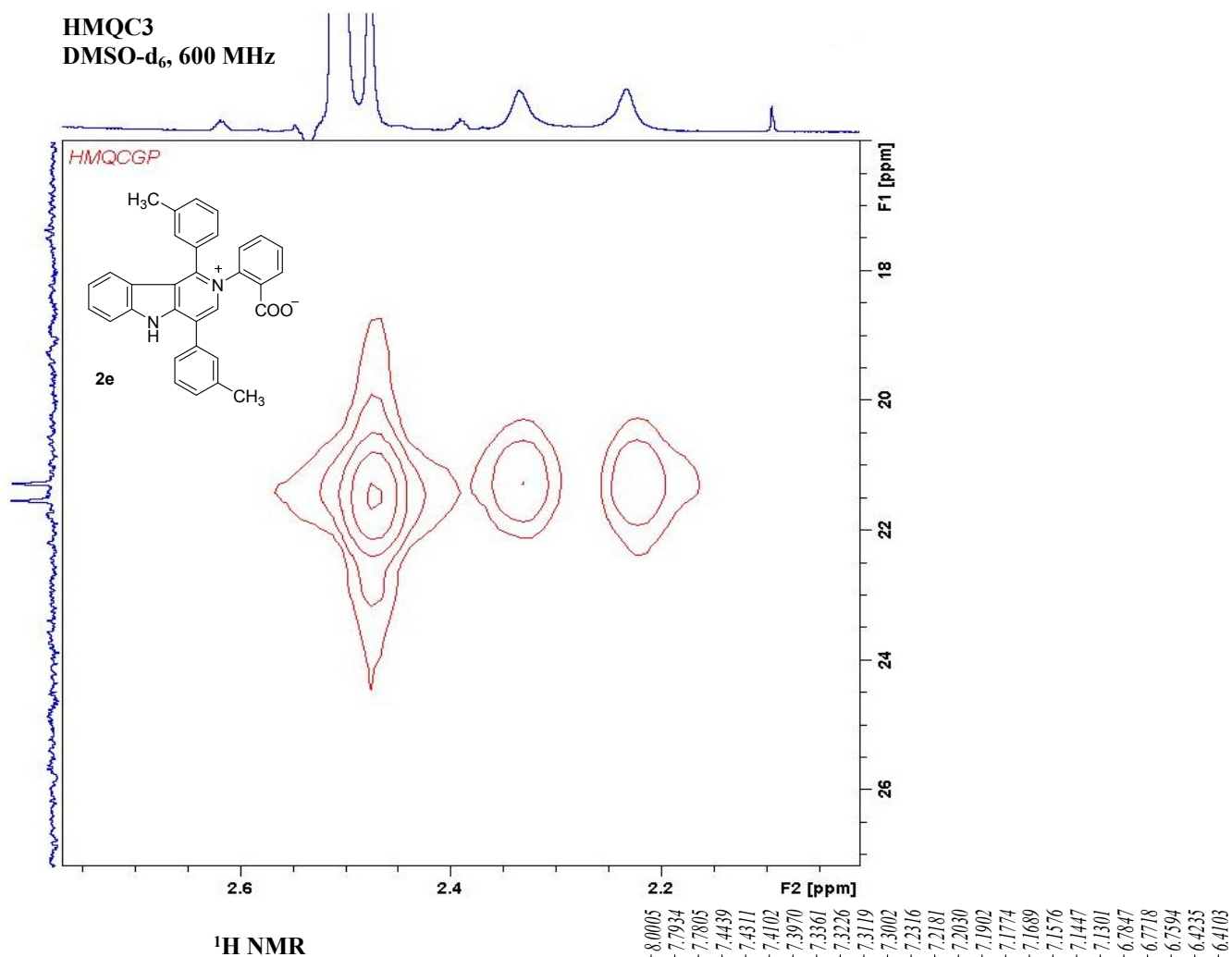


*) from CF₃COOD

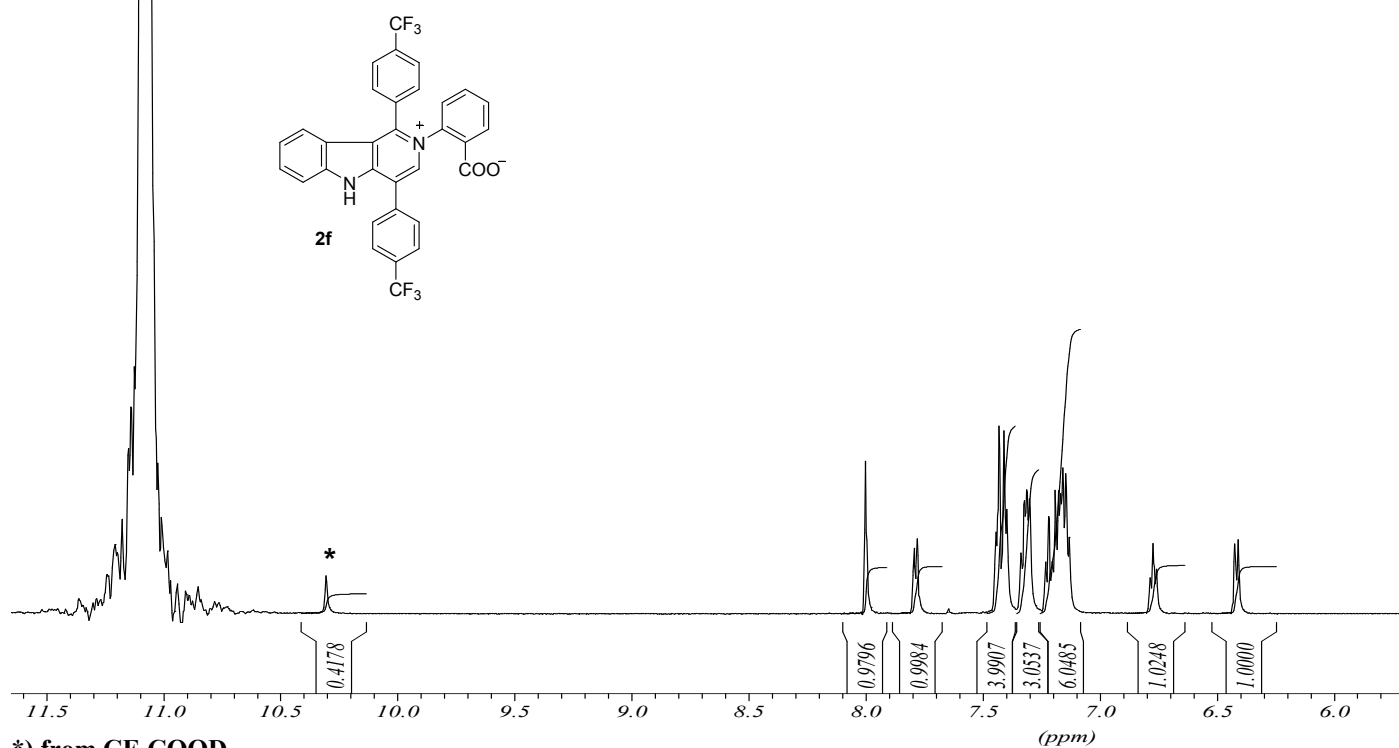




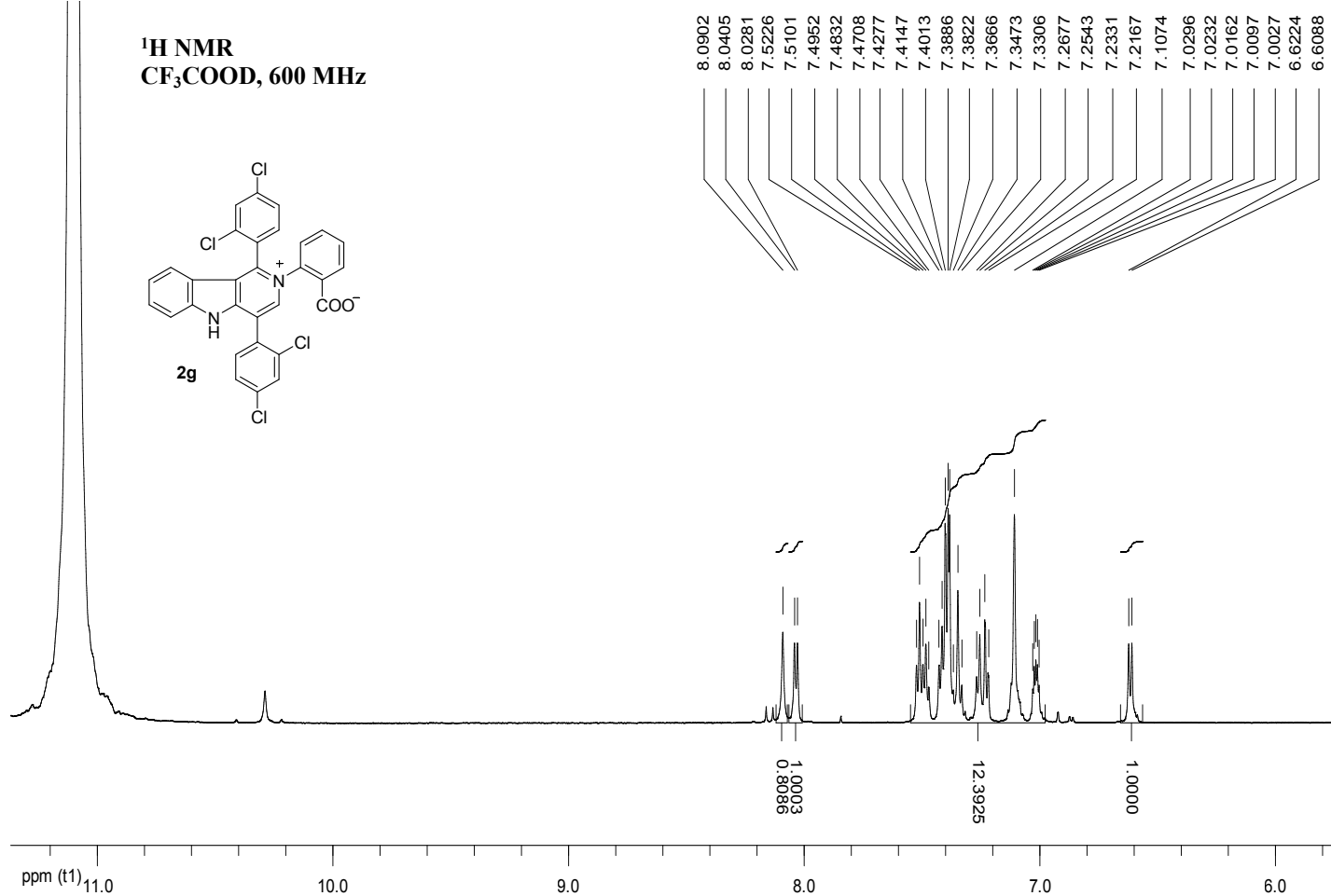
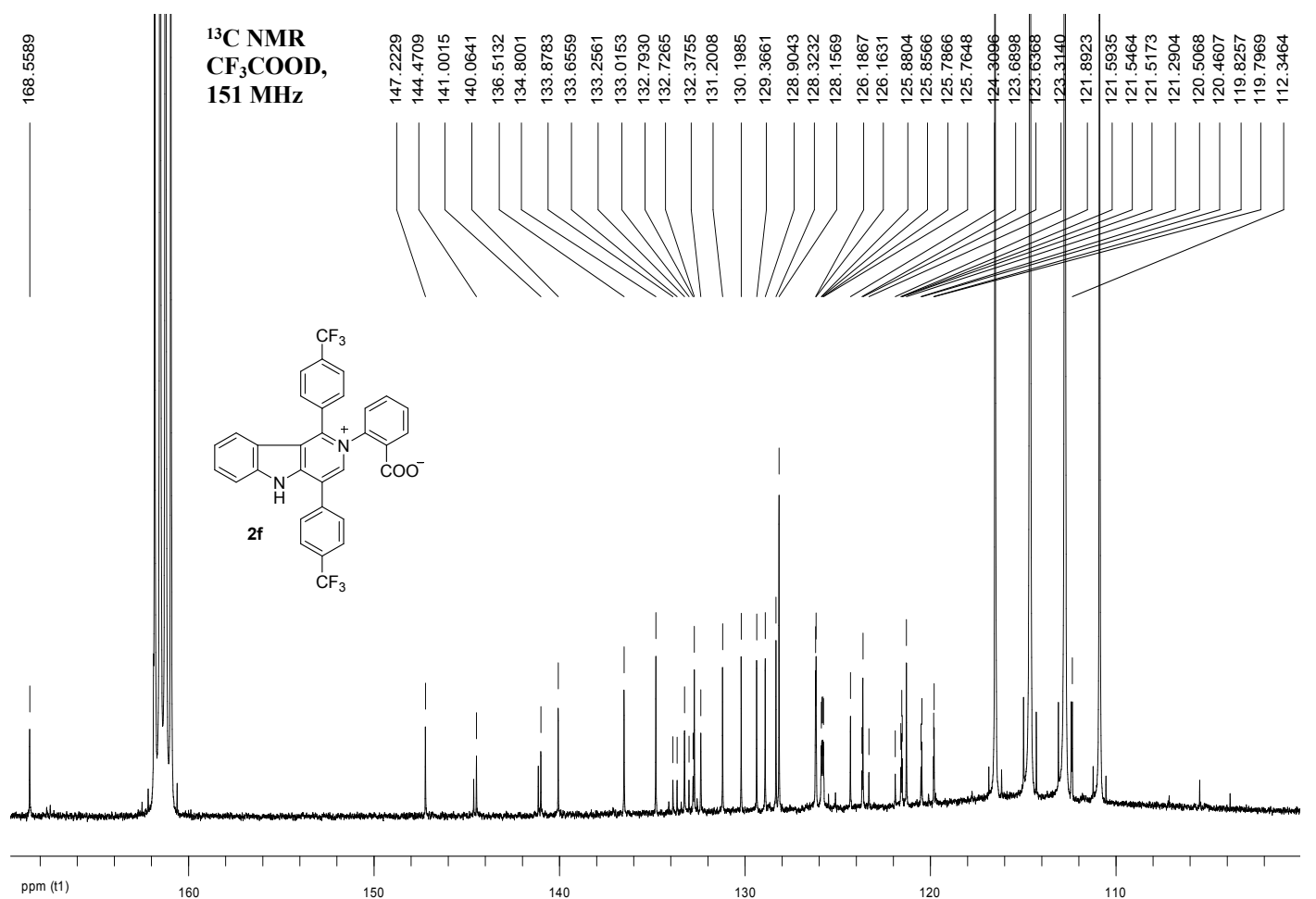
HMQC3
DMSO-d₆, 600 MHz

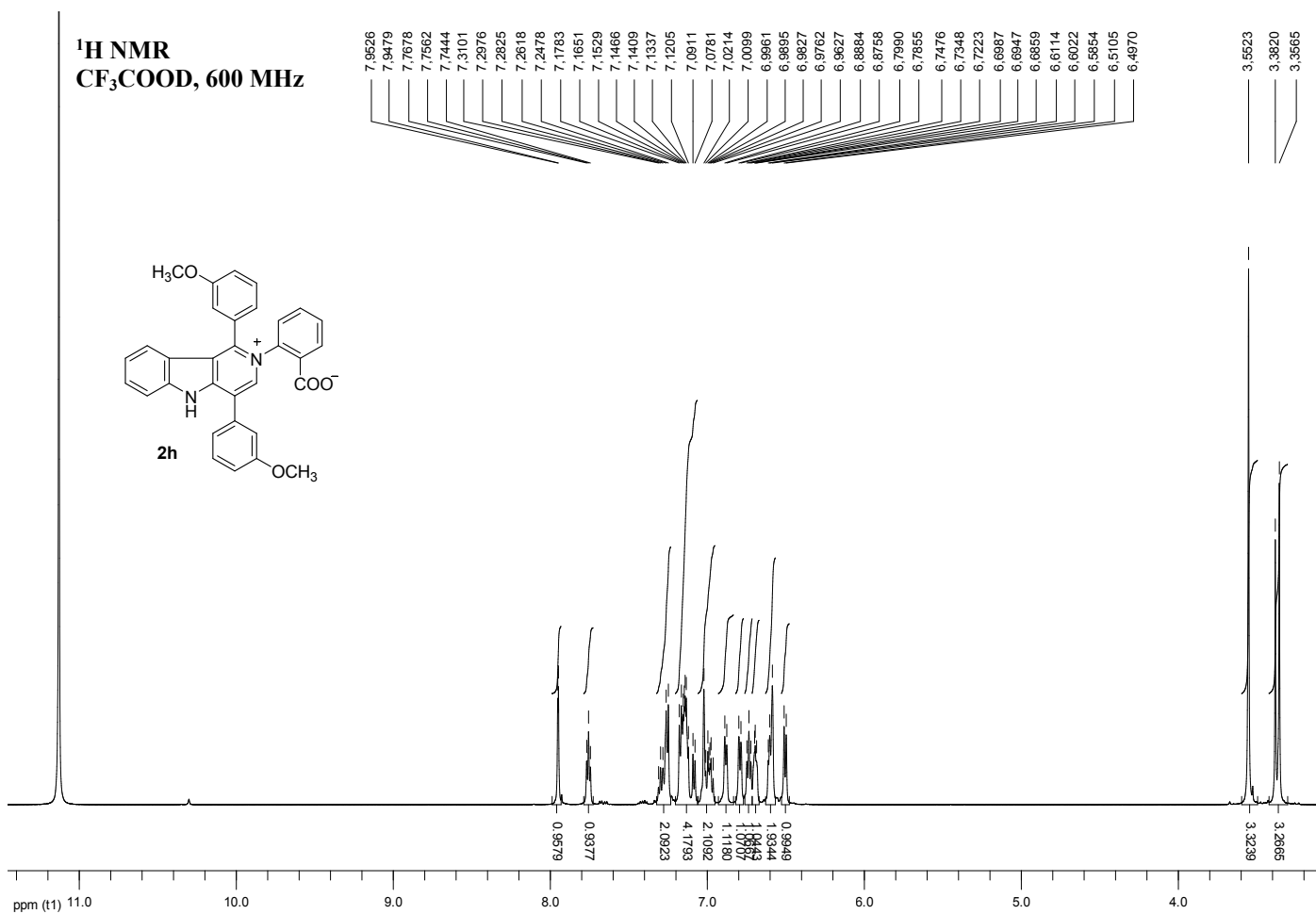
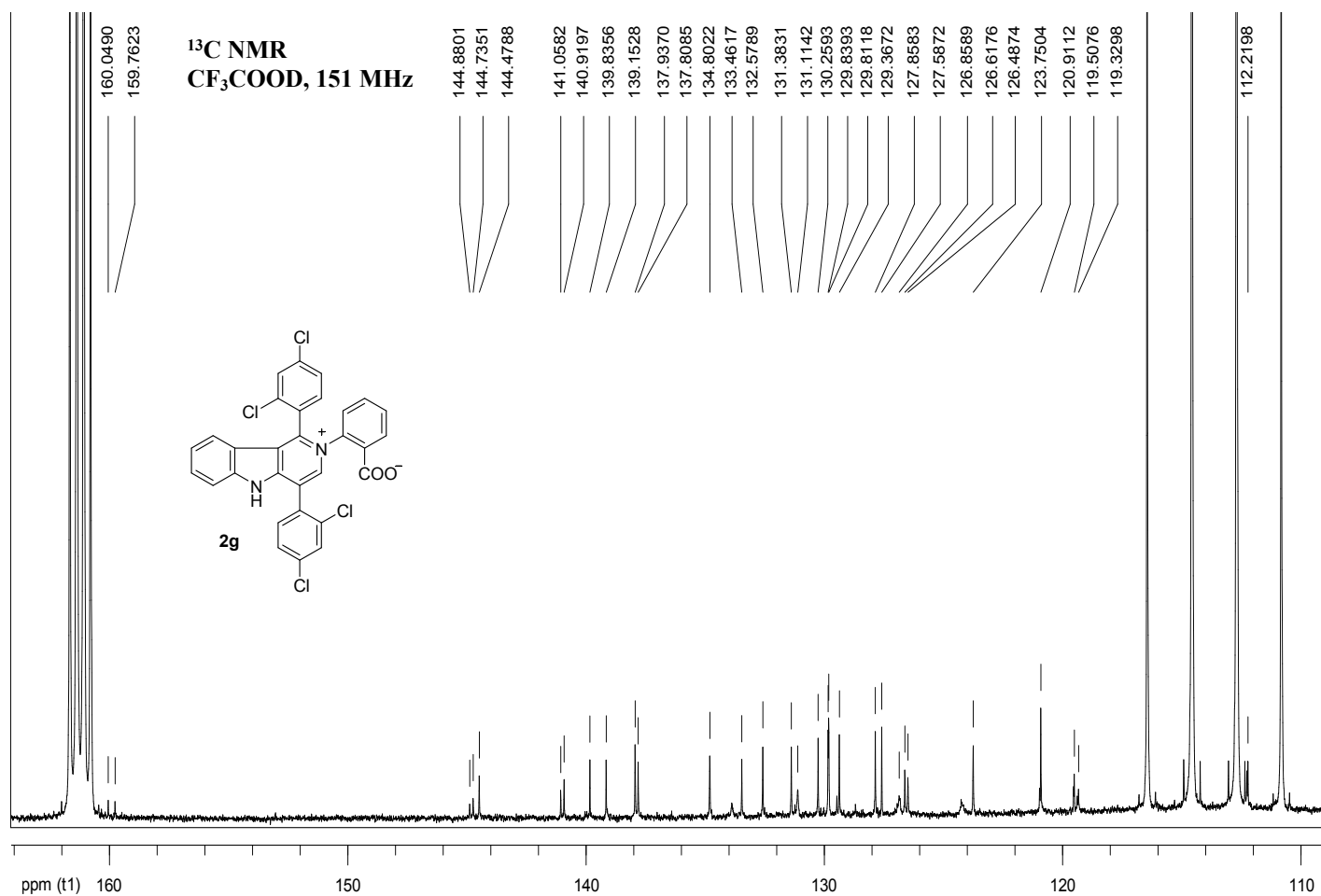


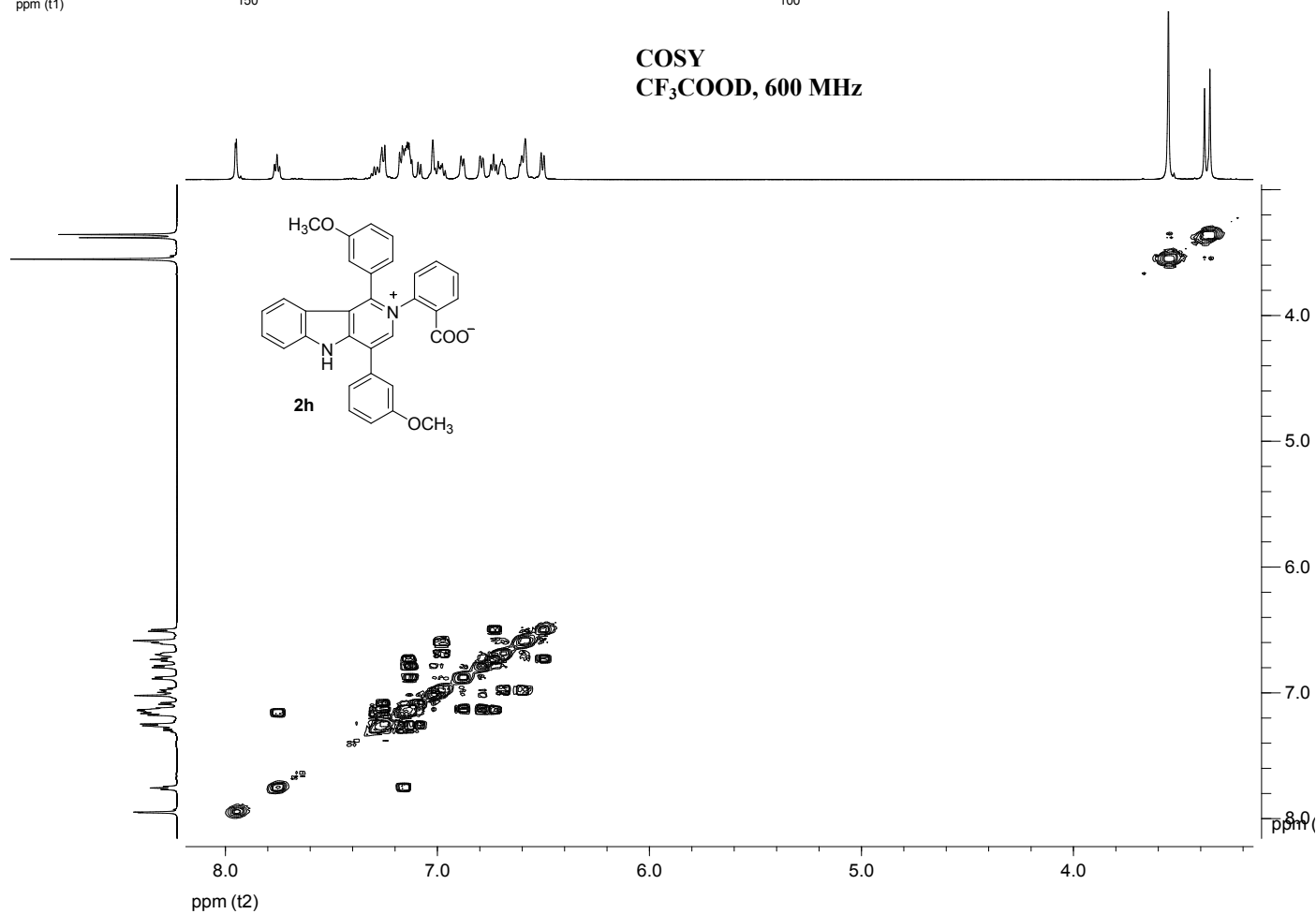
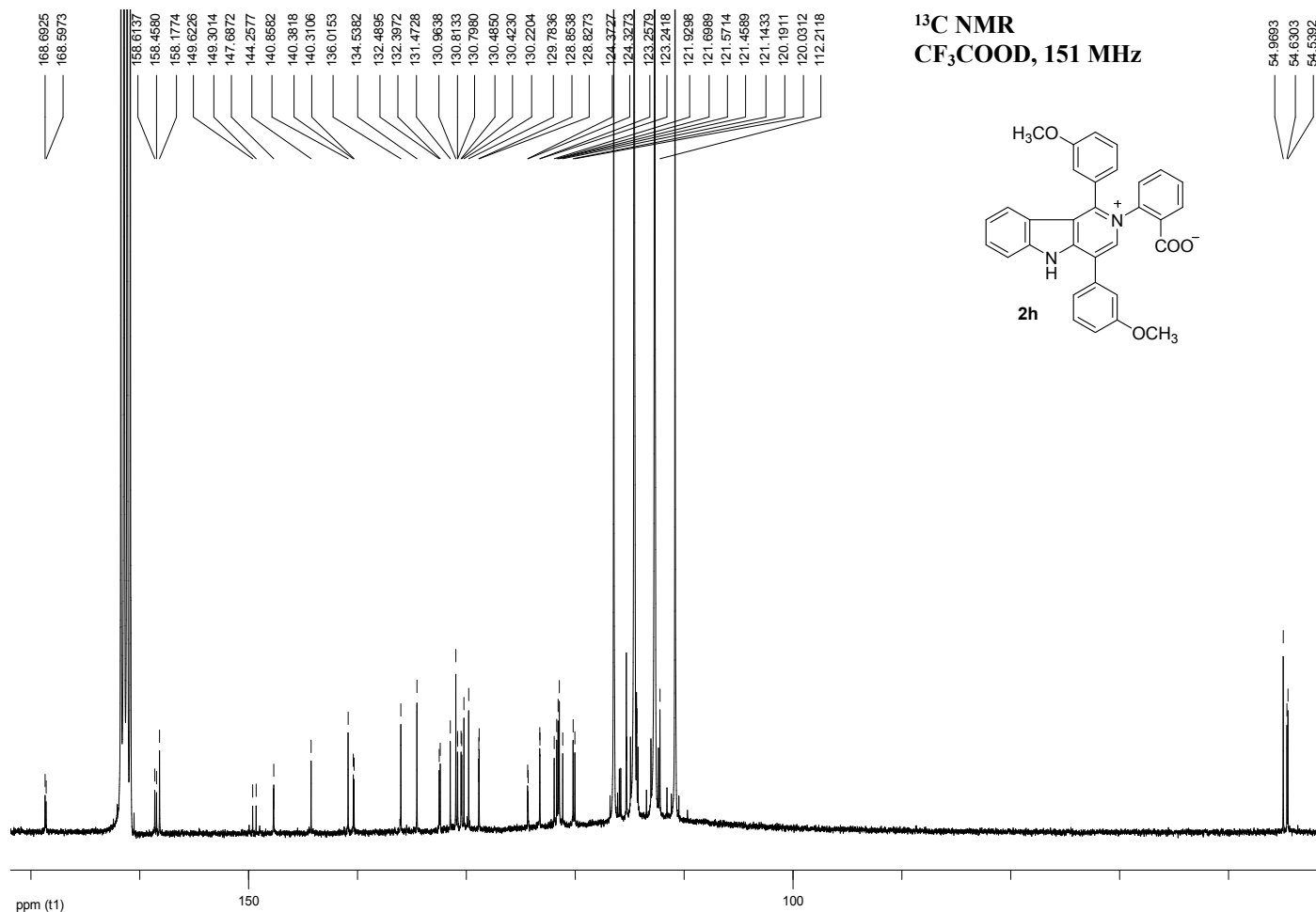
¹H NMR
CF₃COOD, 600 MHz

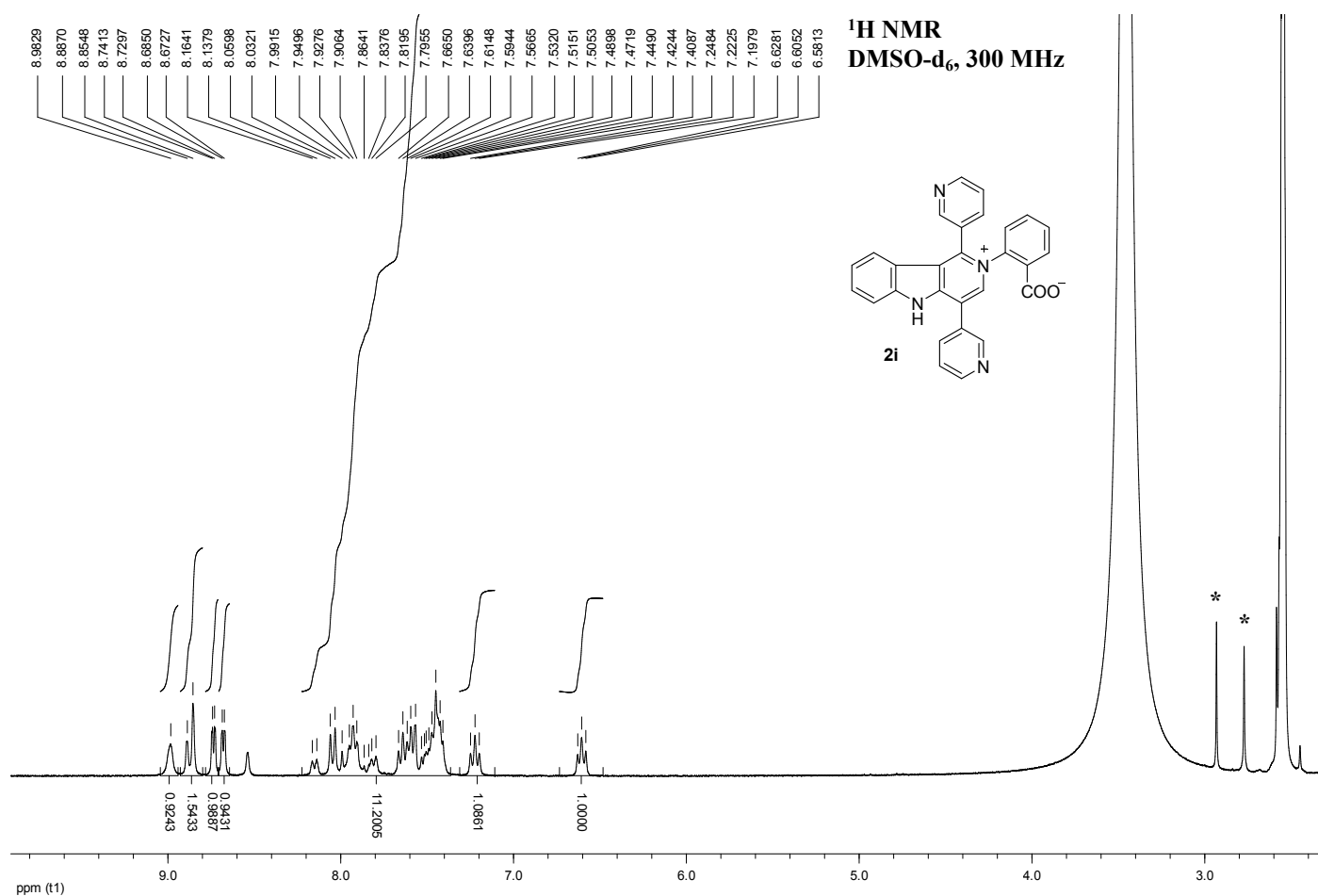


*) from CF₃COOD

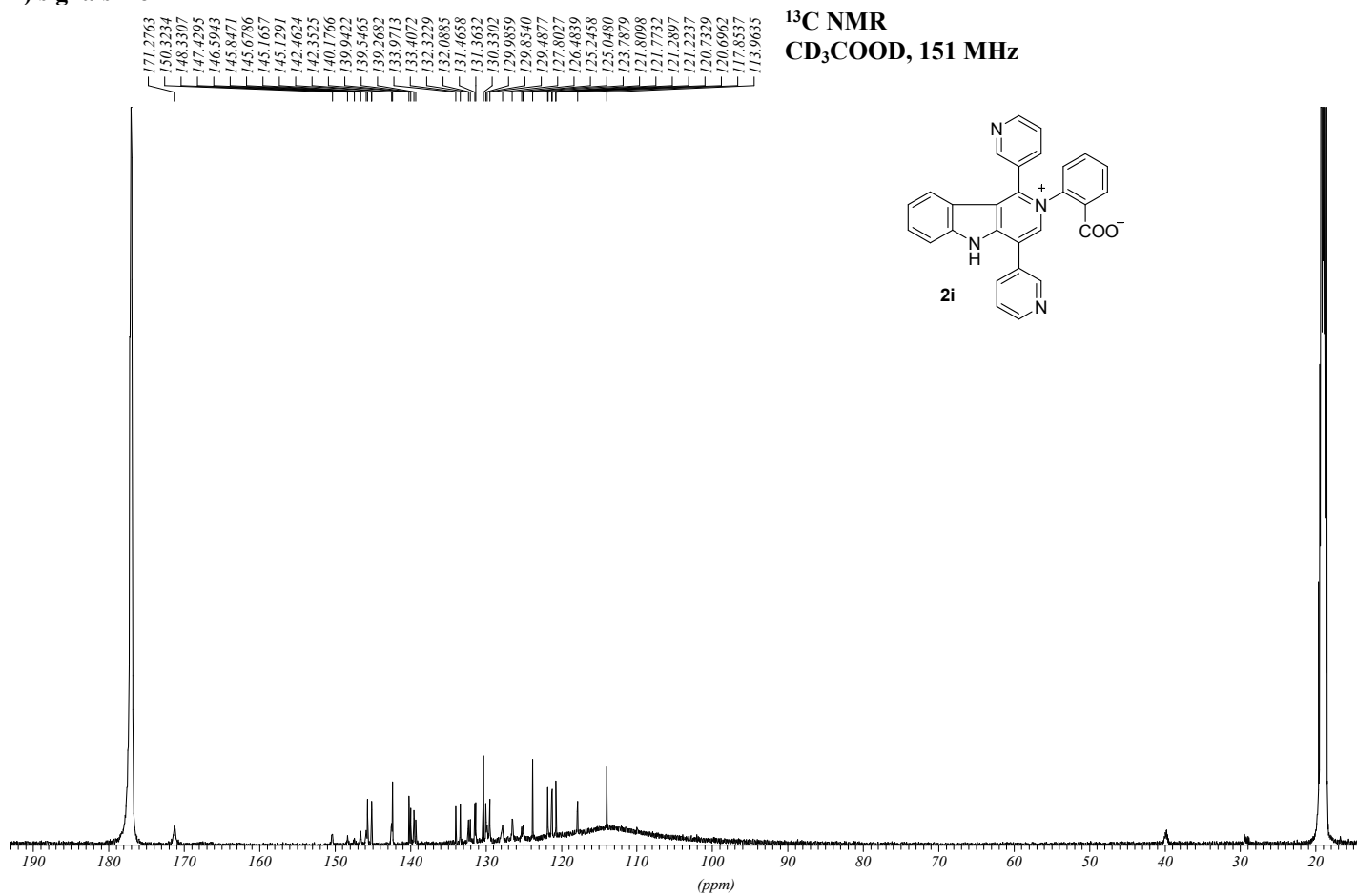


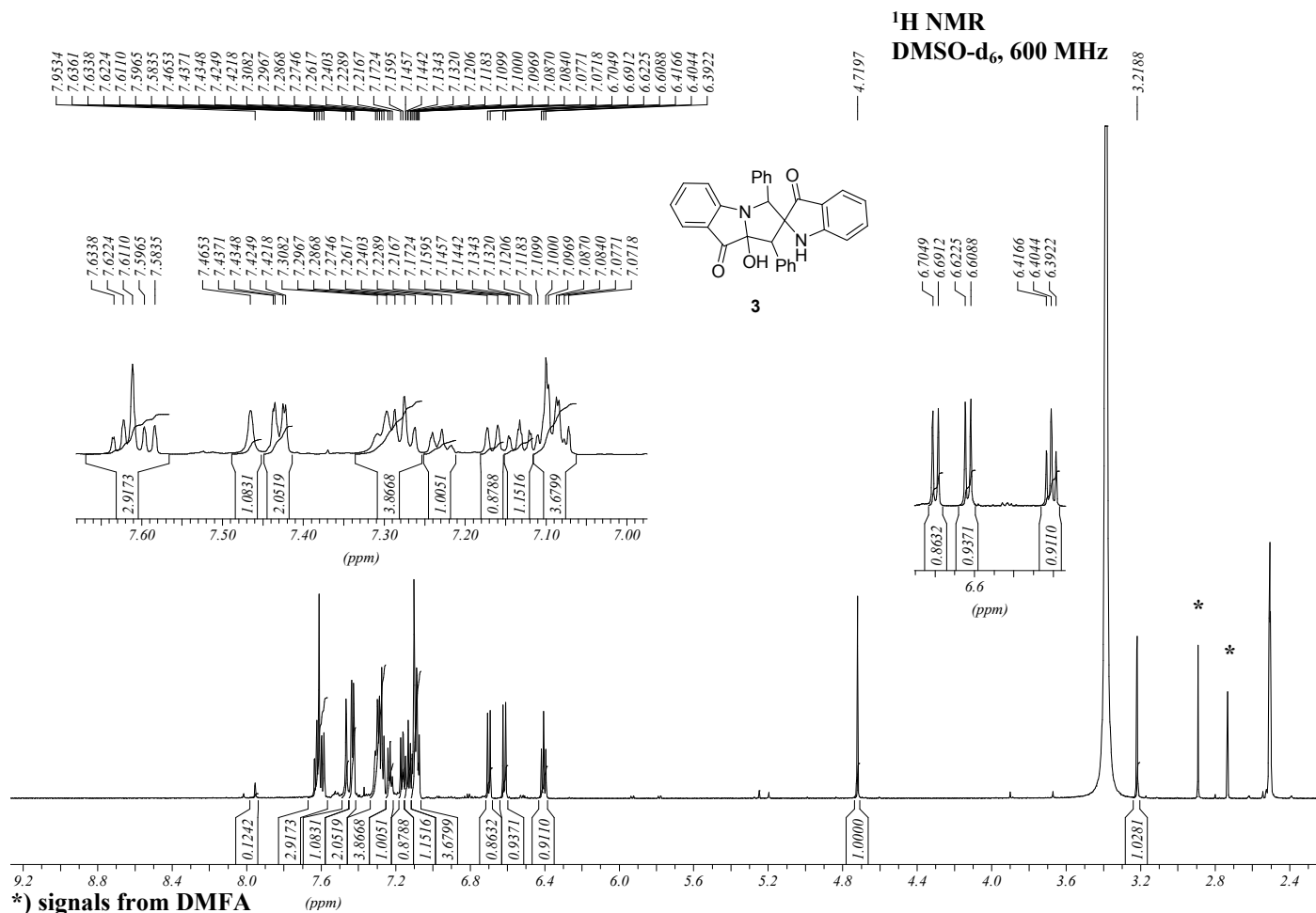




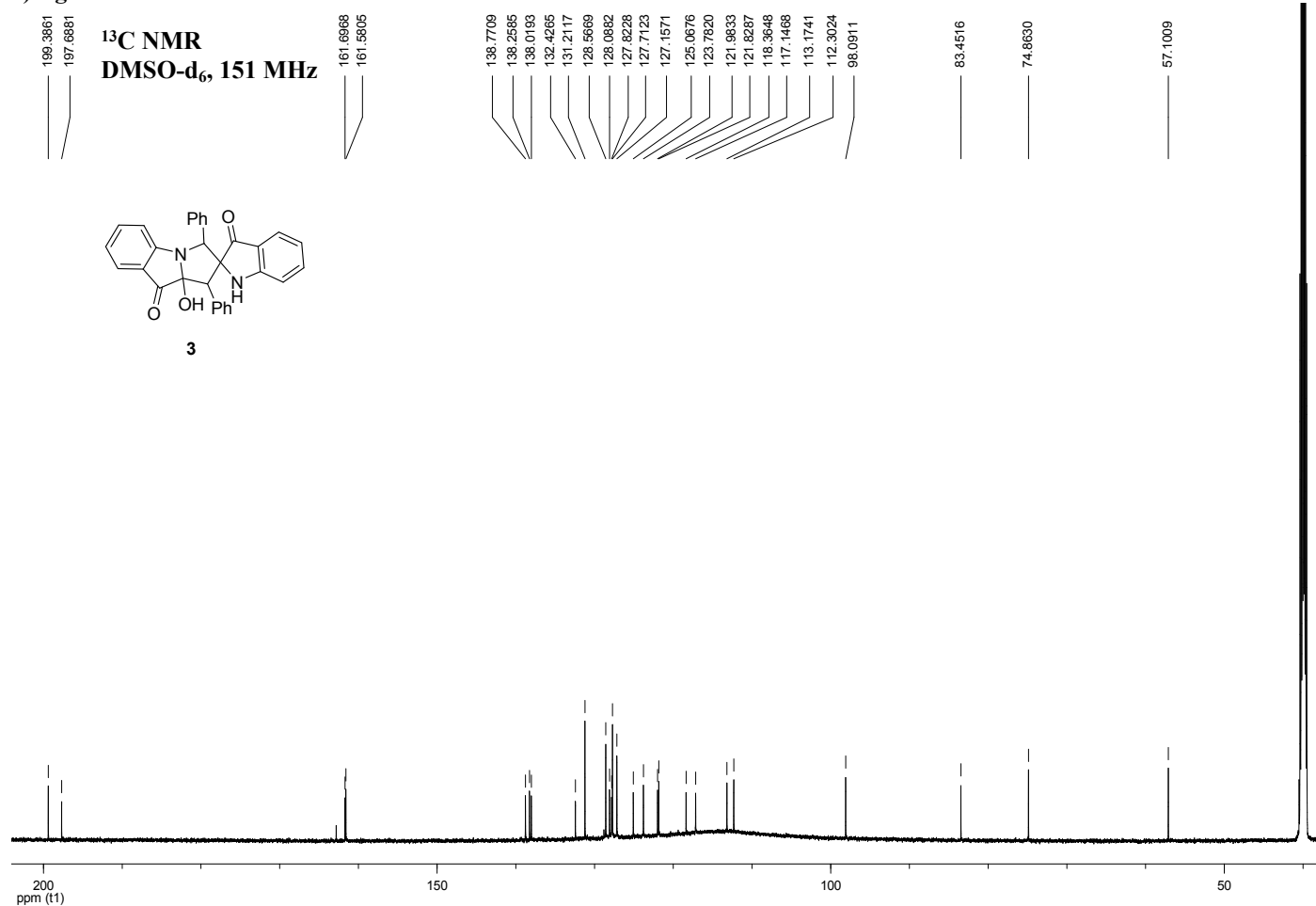


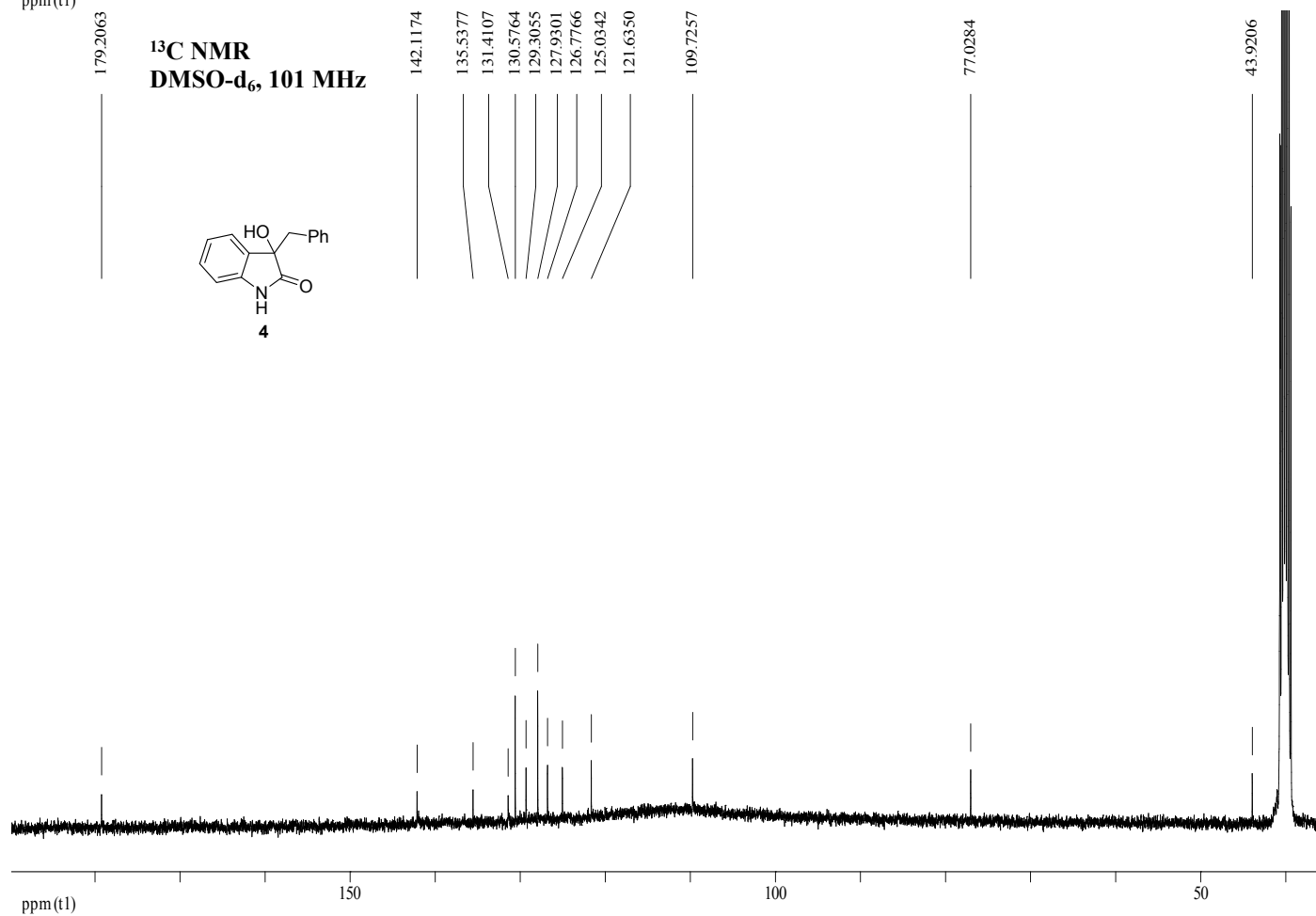
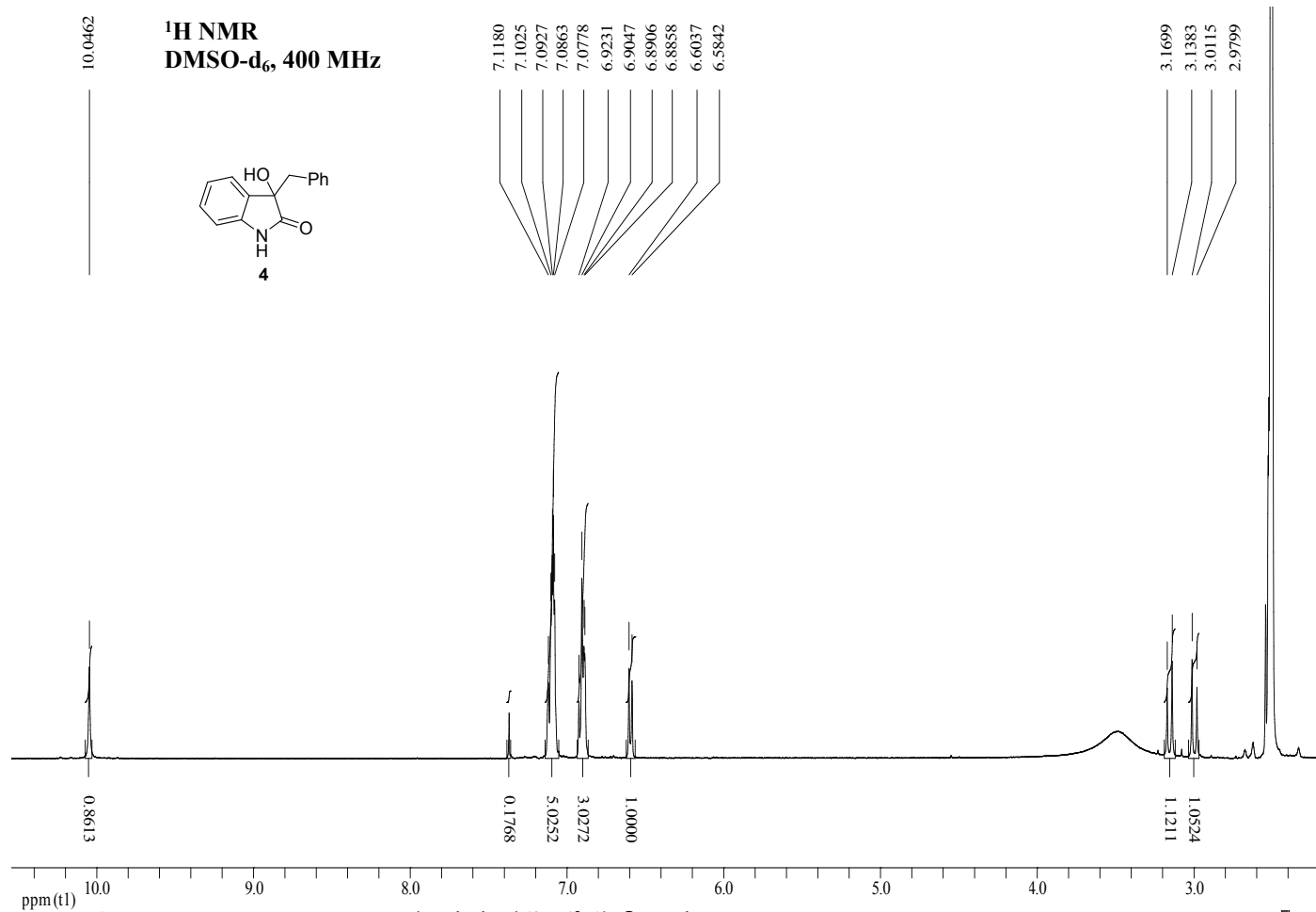
*) signals from DMFA

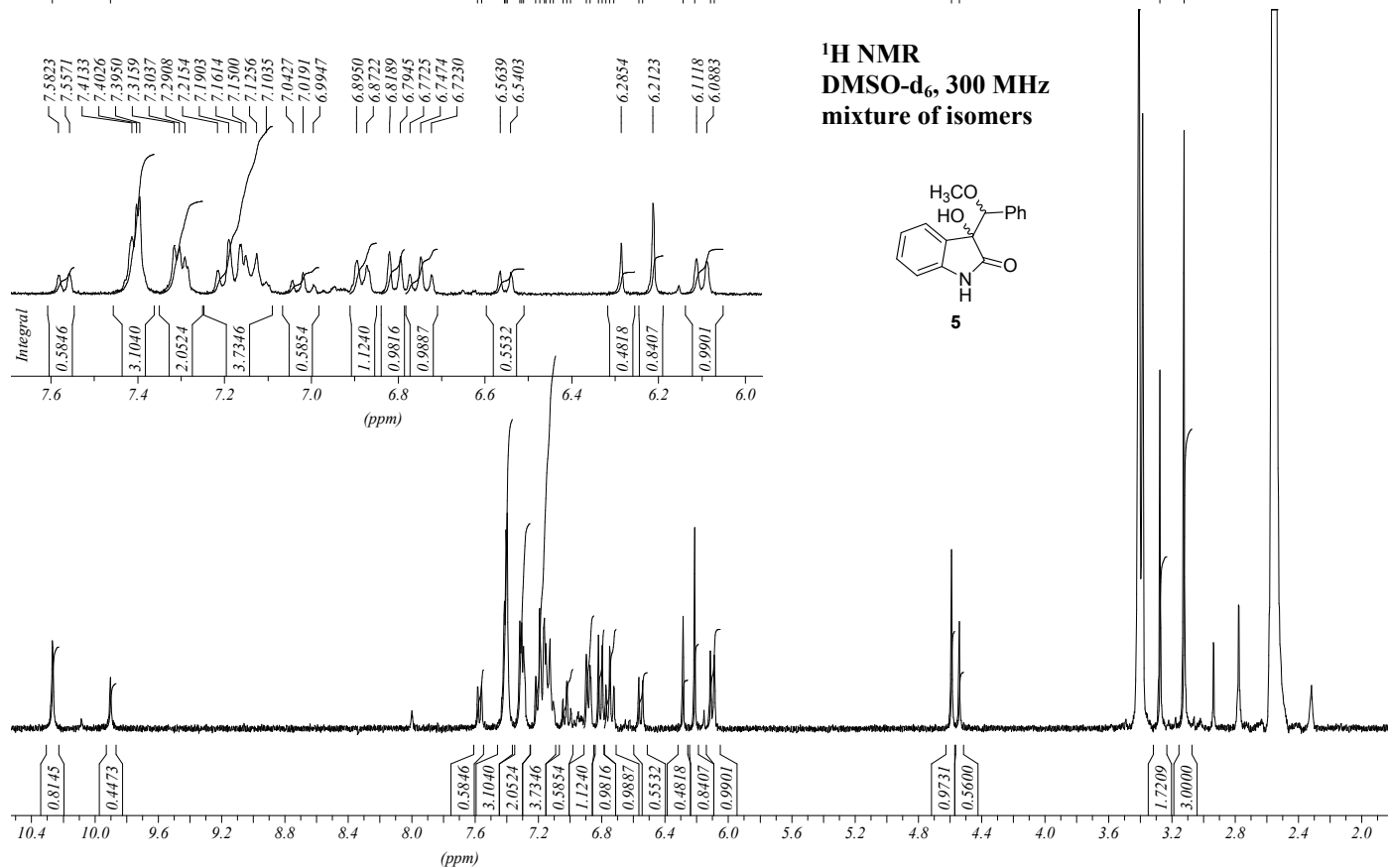
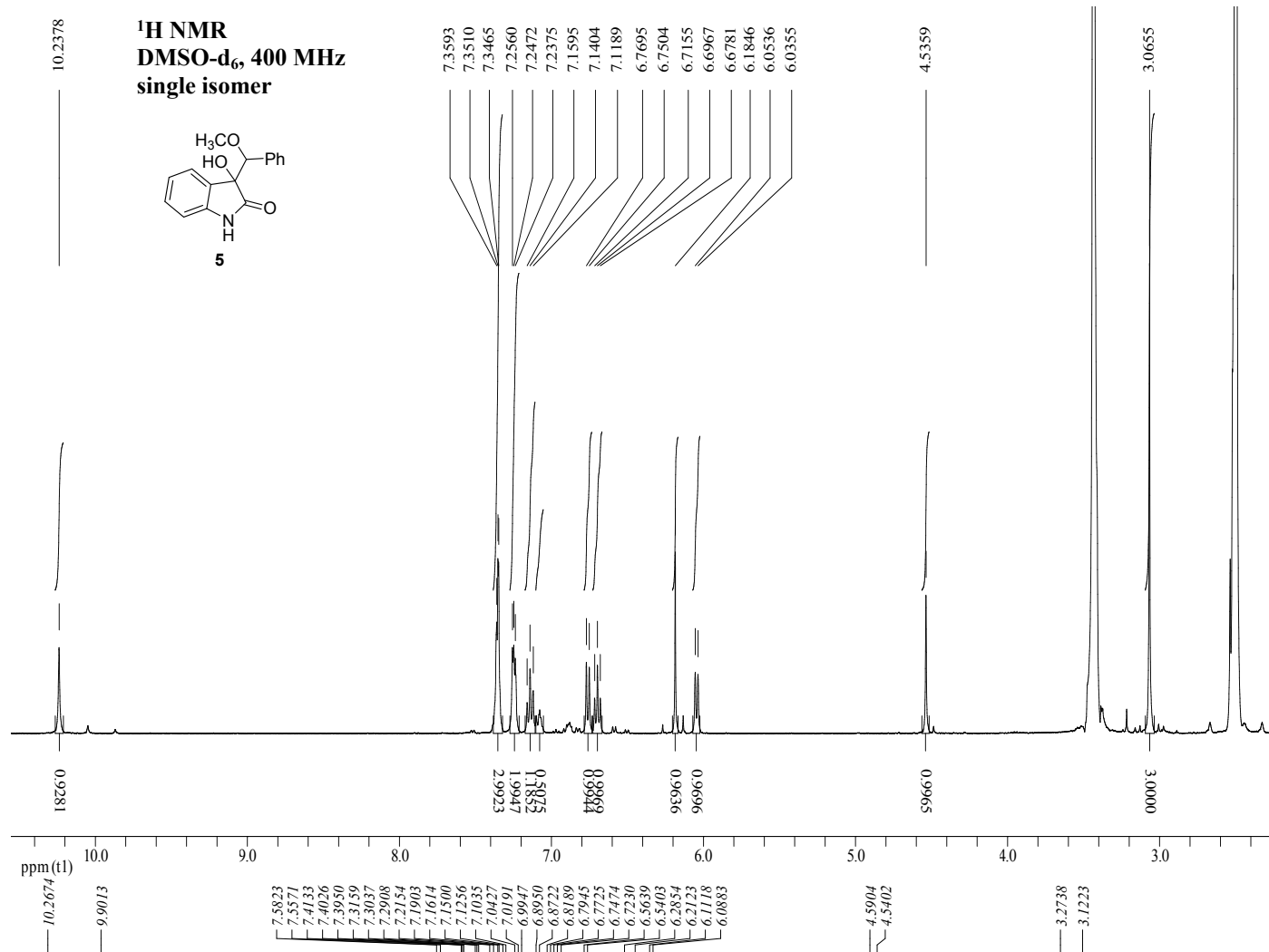




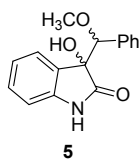
*) signals from DMFA







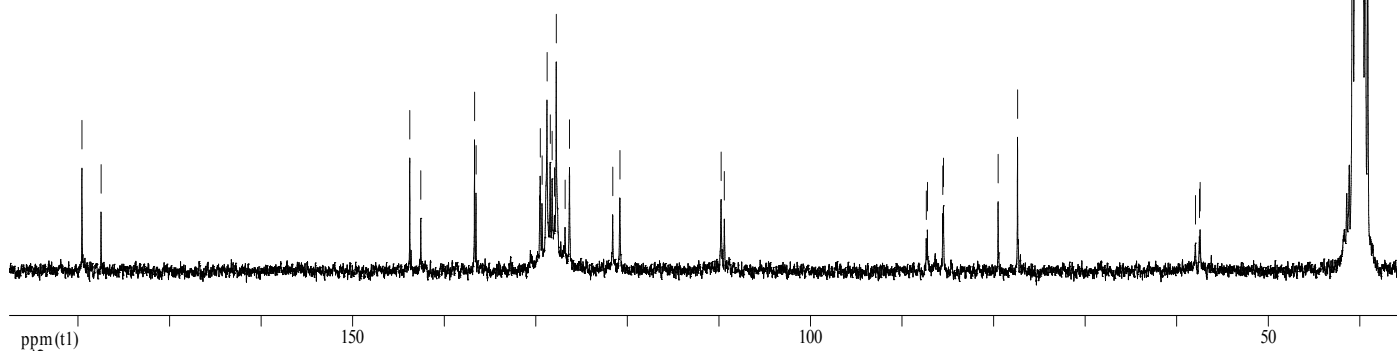
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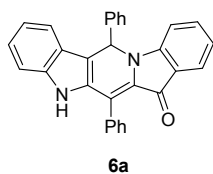
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127.9463
127.7526
126.7867
126.3043
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109.7436
109.3940

87.3428
87.2171
85.5470
85.4608
79.4927
77.3713

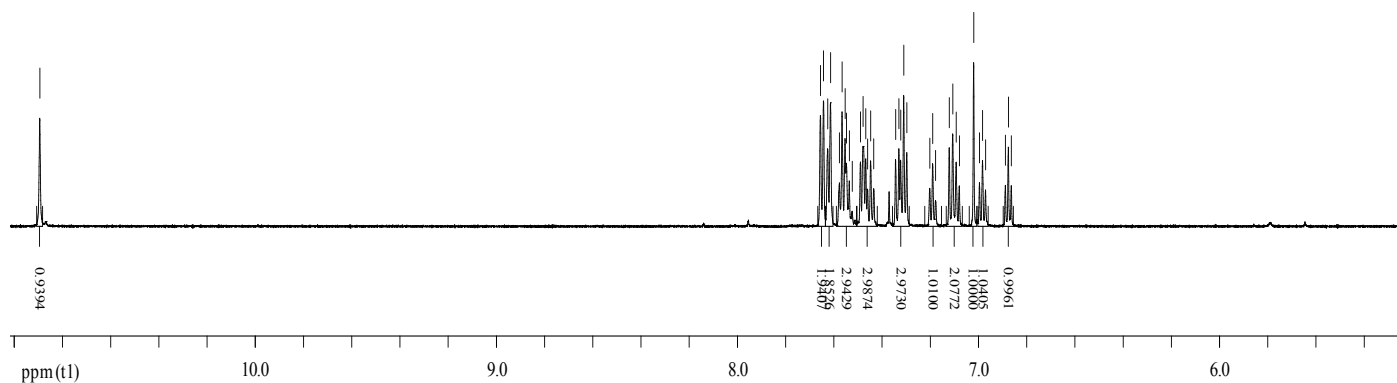
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57.5092
57.4315

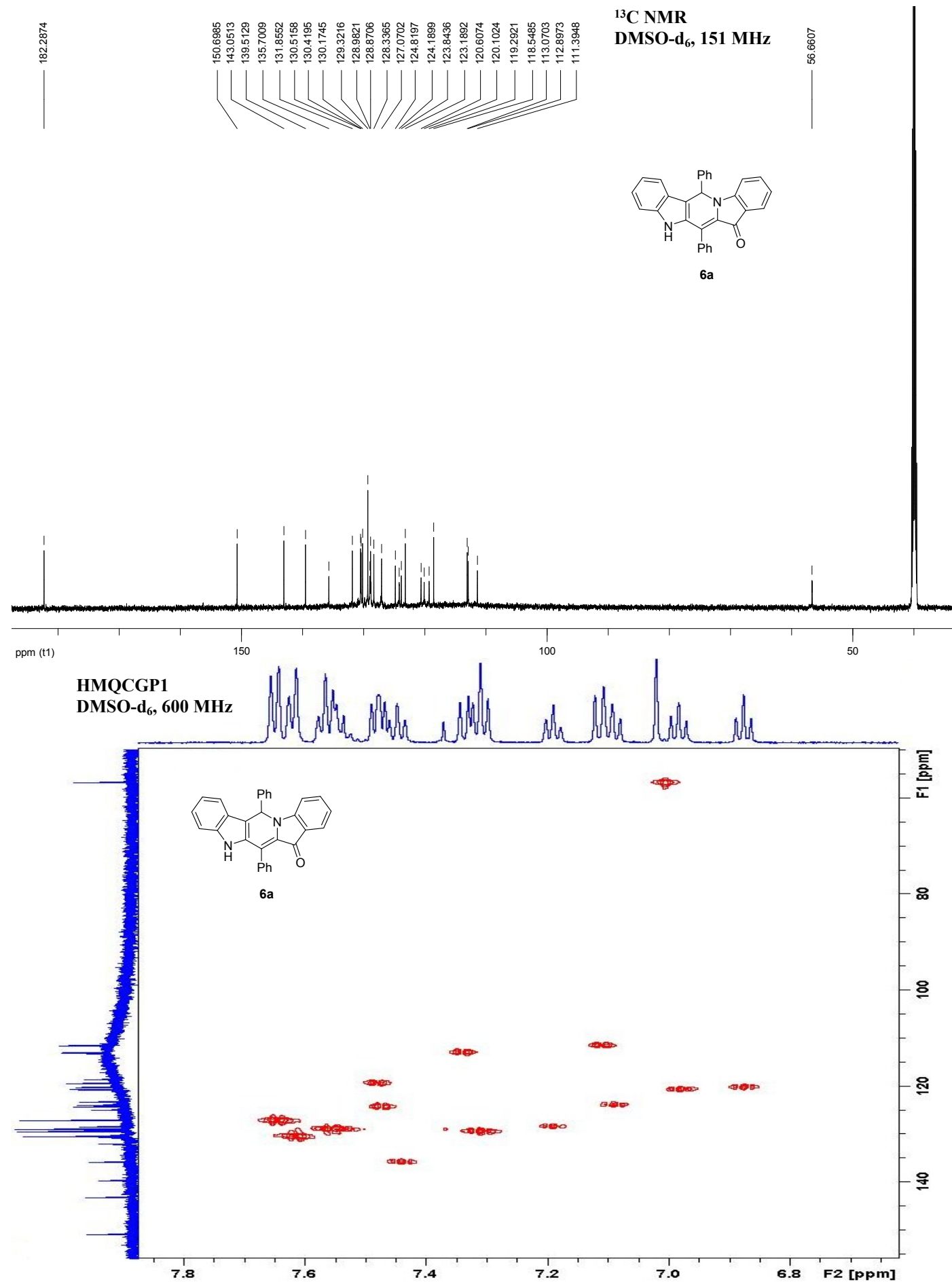


¹H NMR
DMSO-d₆, 600 MHz

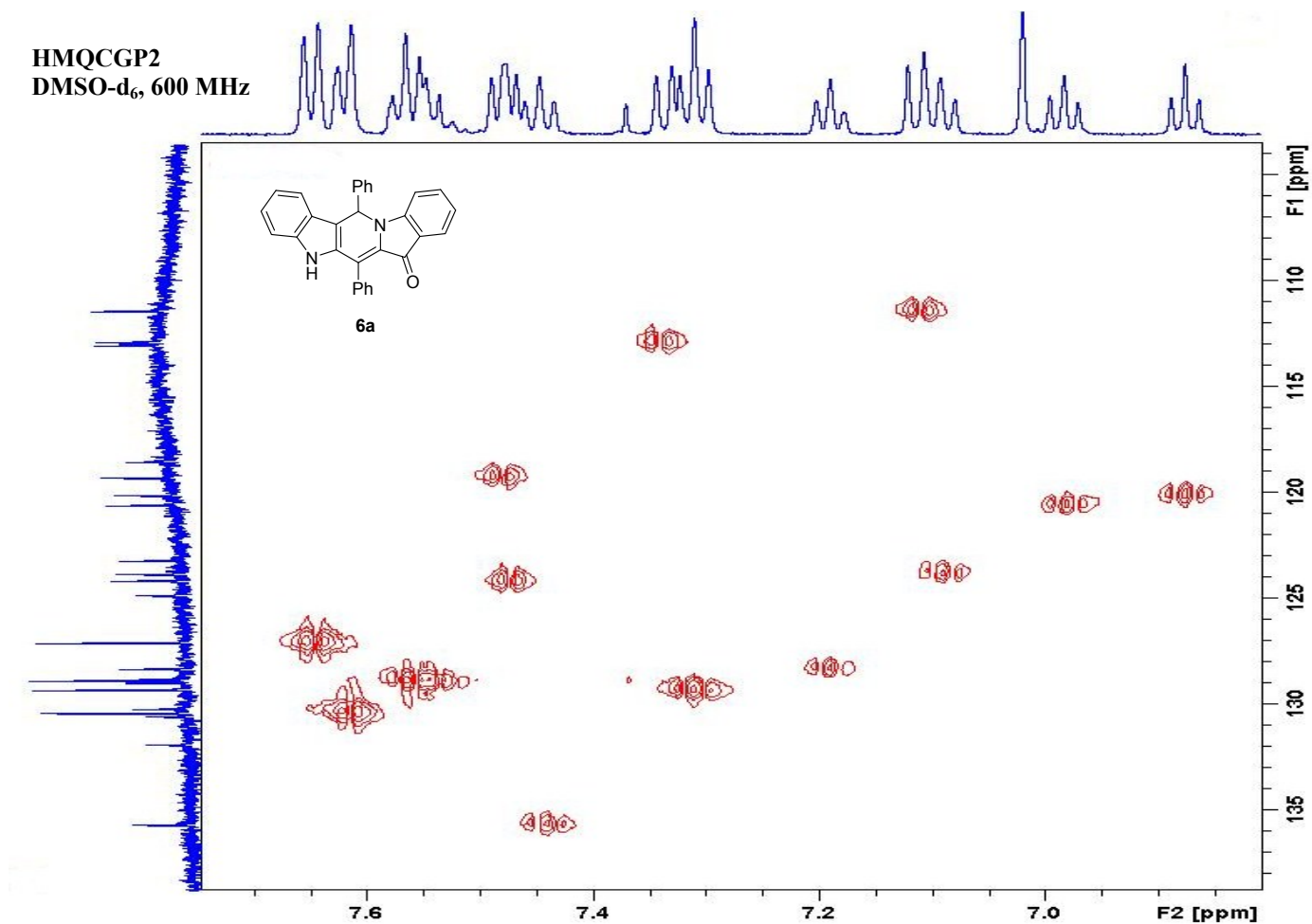


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7.5236
7.4890
7.4781
7.4673
7.4596
7.4468
7.4340
7.3433
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7.3224
7.3097
7.2969
7.2017
7.1895
7.1774
7.1207
7.1065
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6.8633

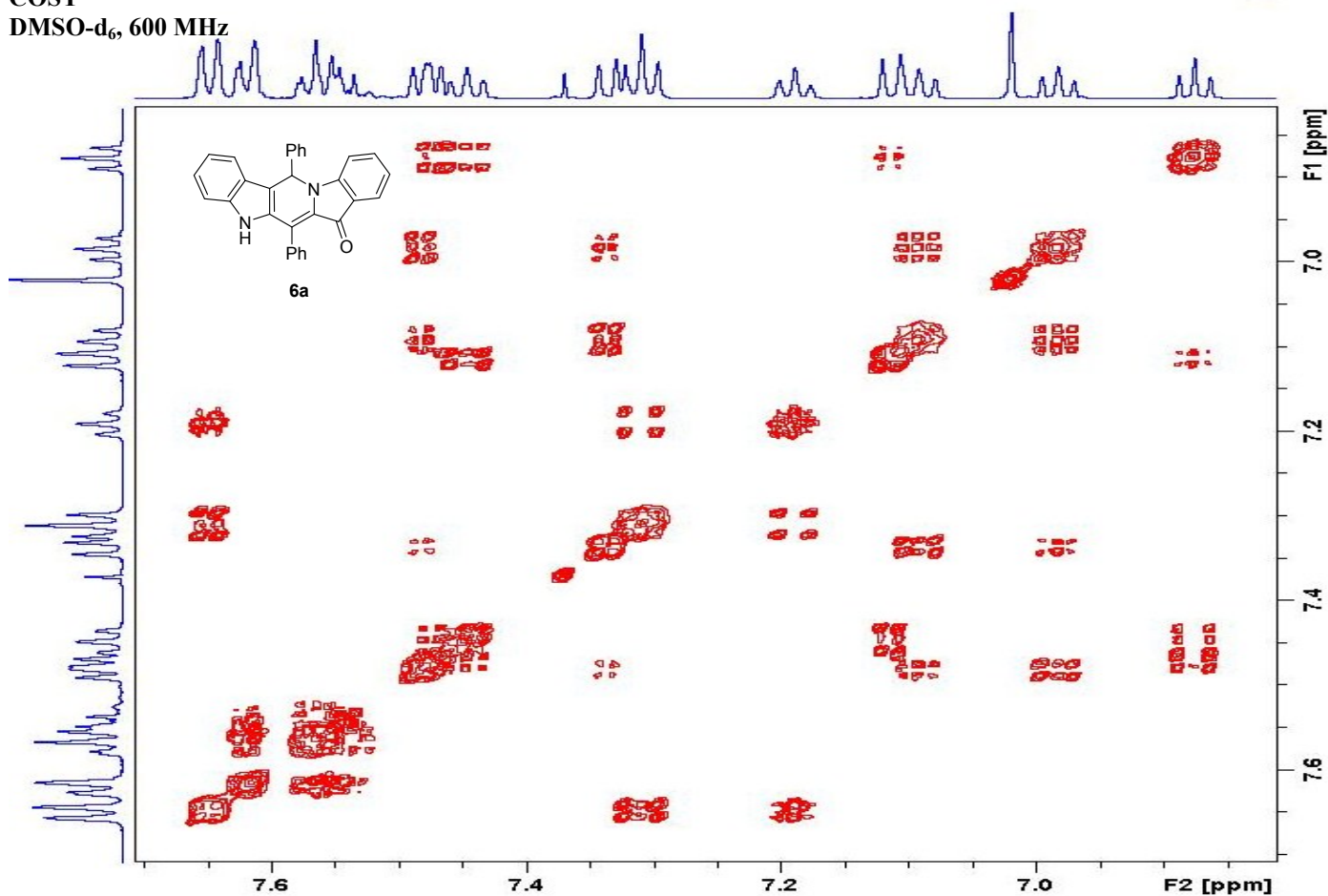




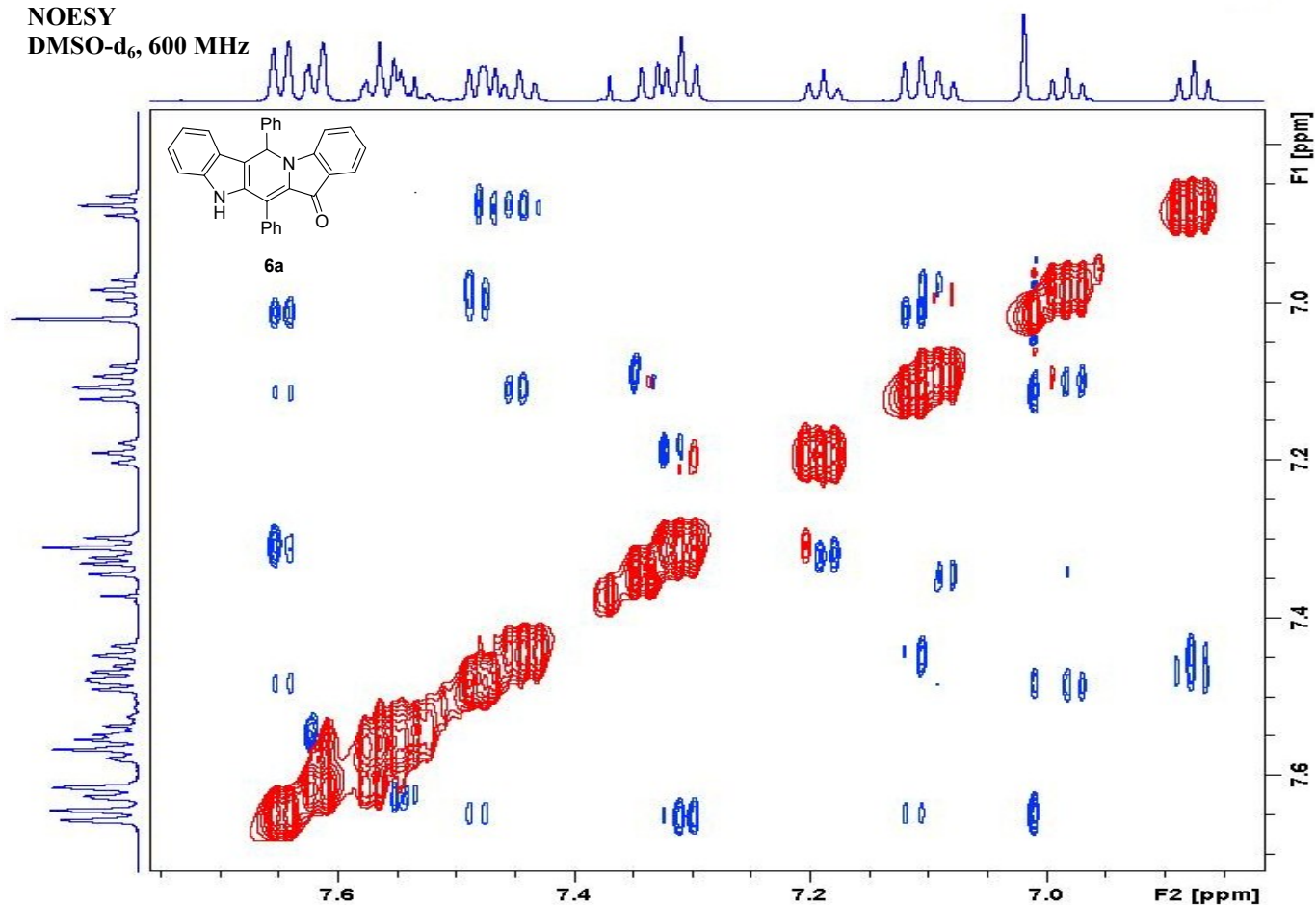
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DMSO-d₆, 600 MHz



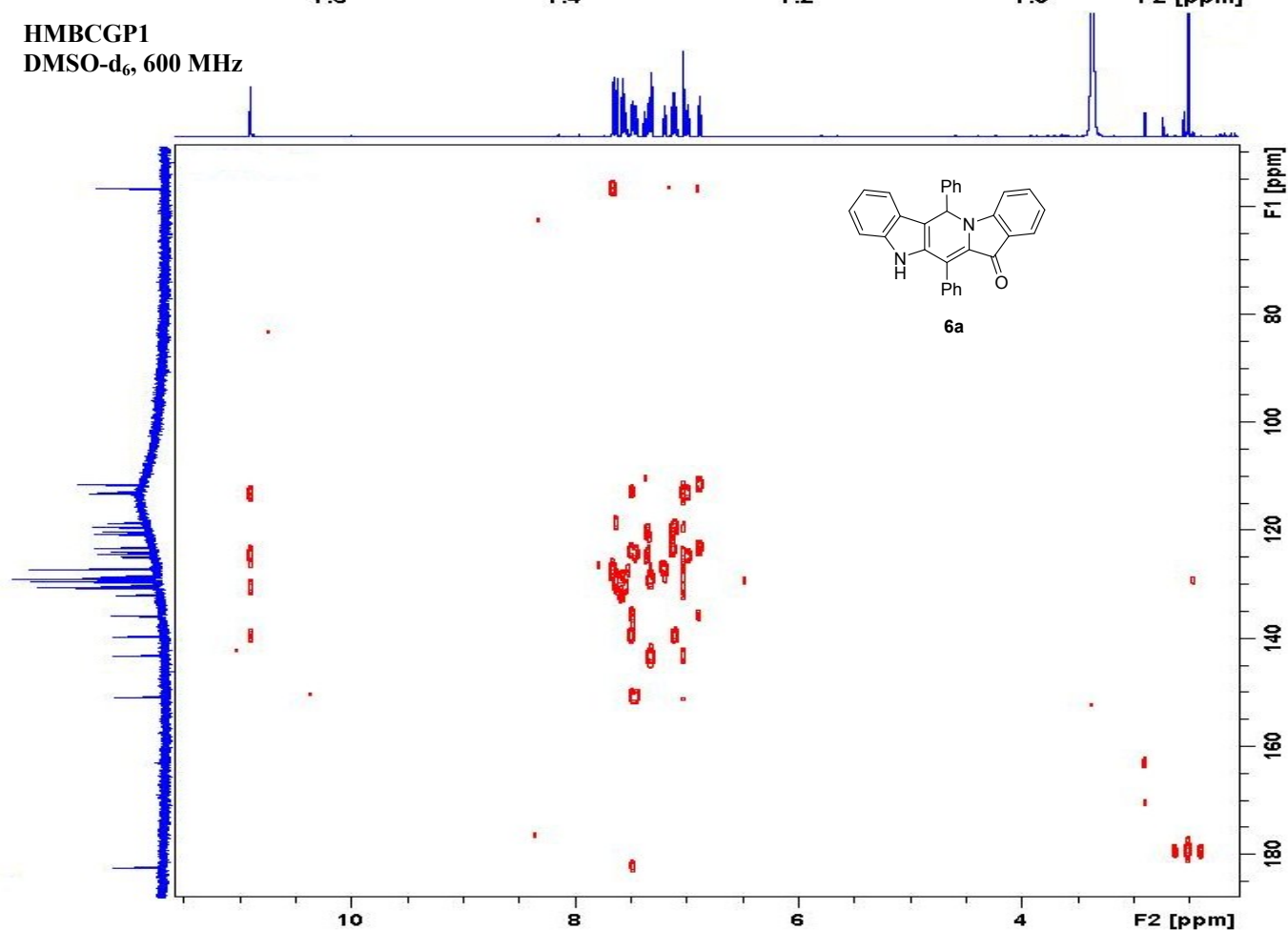
COSY
DMSO-d₆, 600 MHz

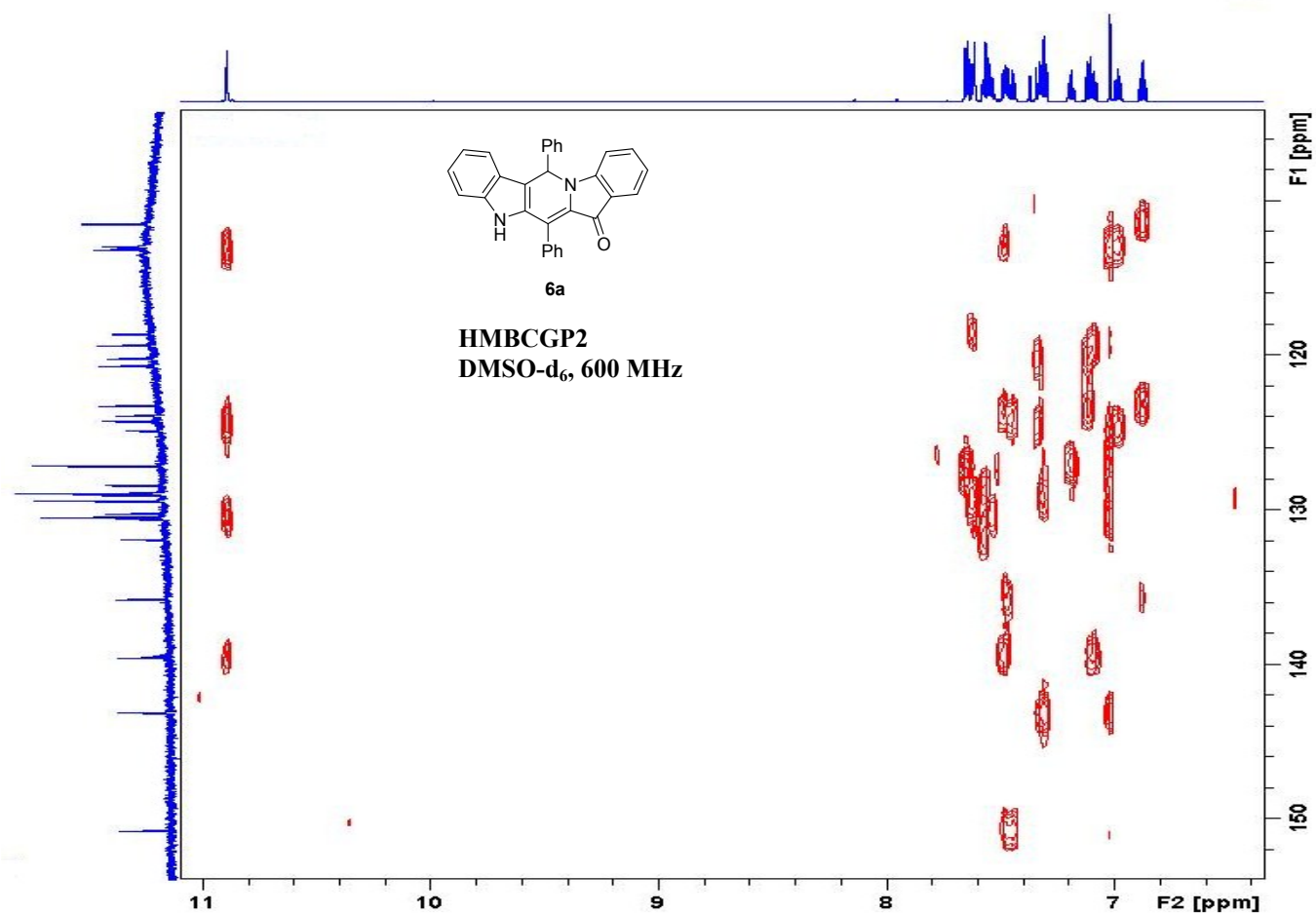


NOESY
DMSO-d₆, 600 MHz

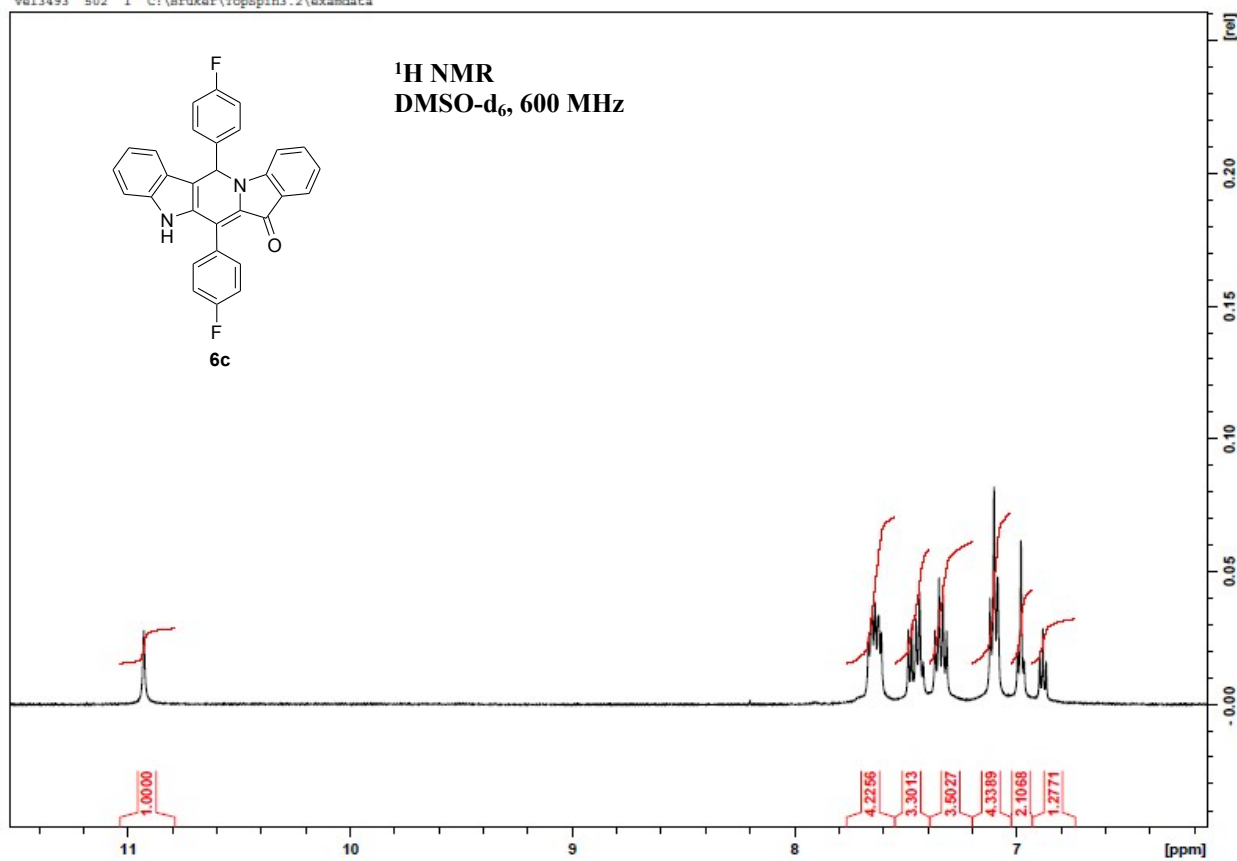


HMBCGP1
DMSO-d₆, 600 MHz

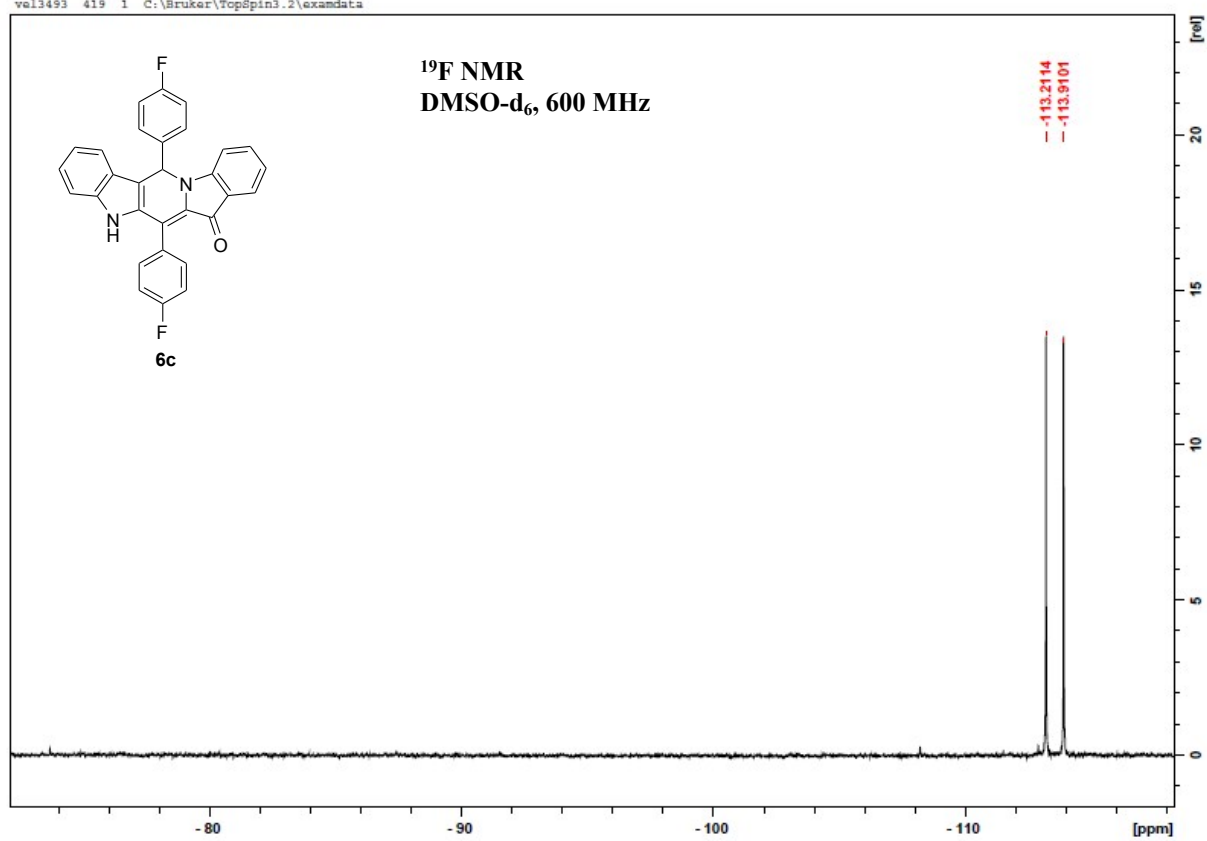




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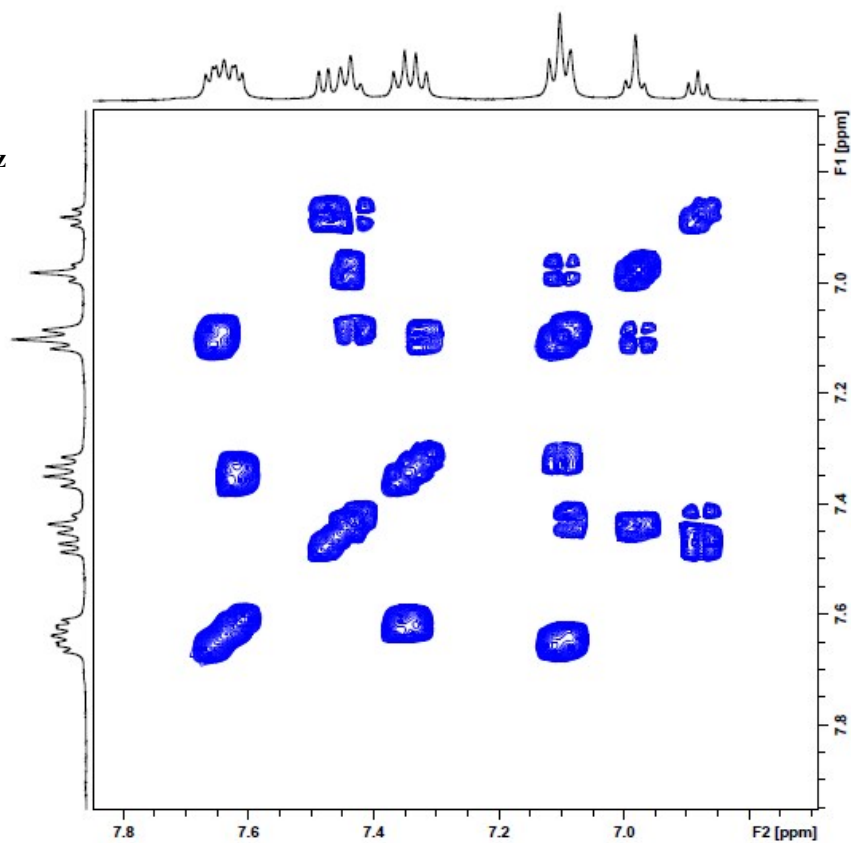
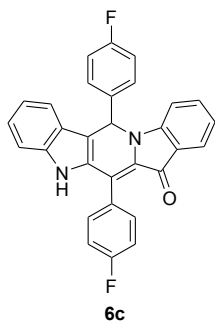


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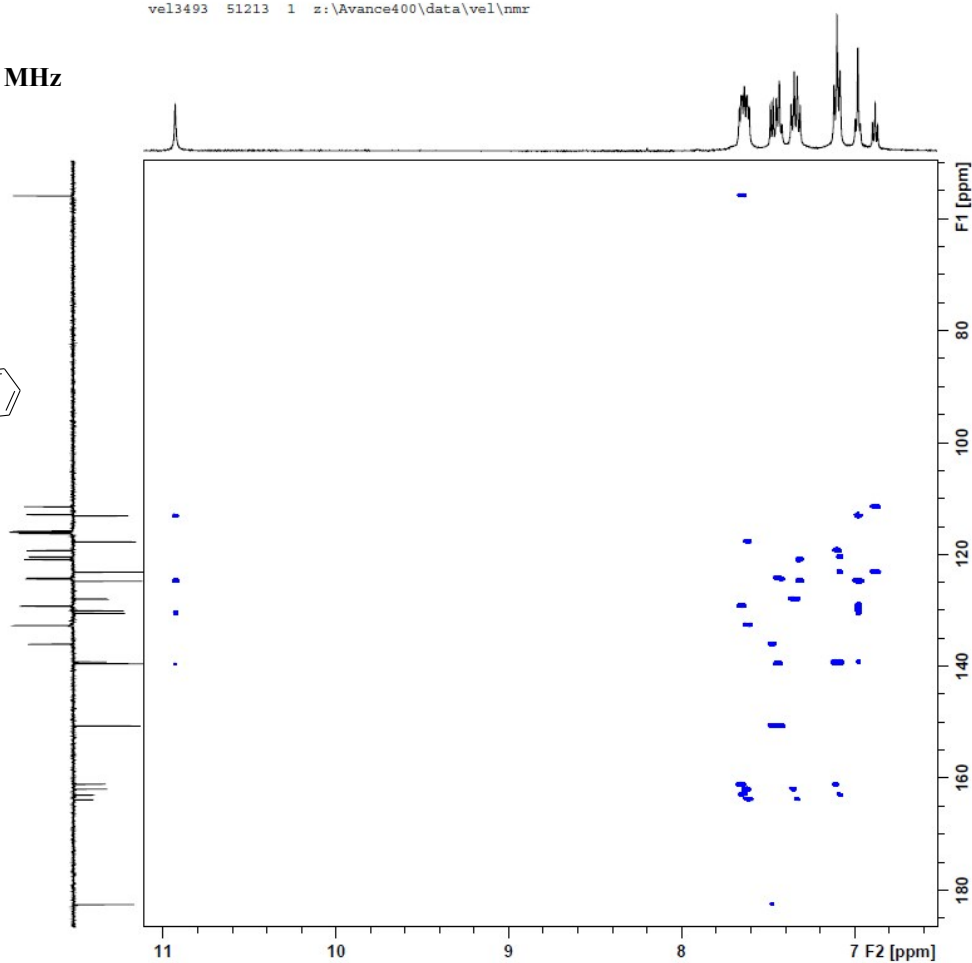
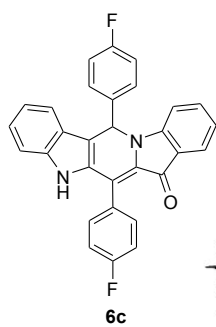
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COSY
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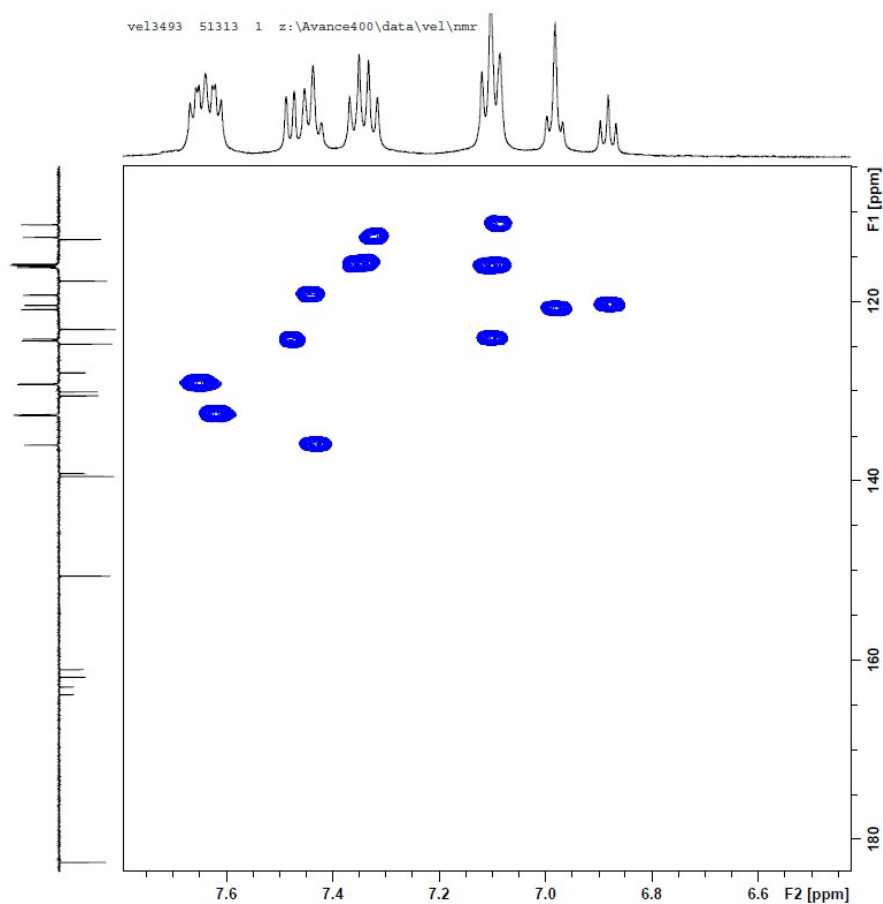
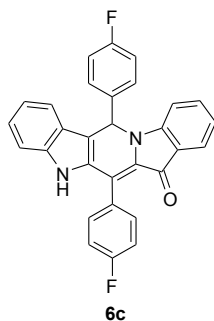


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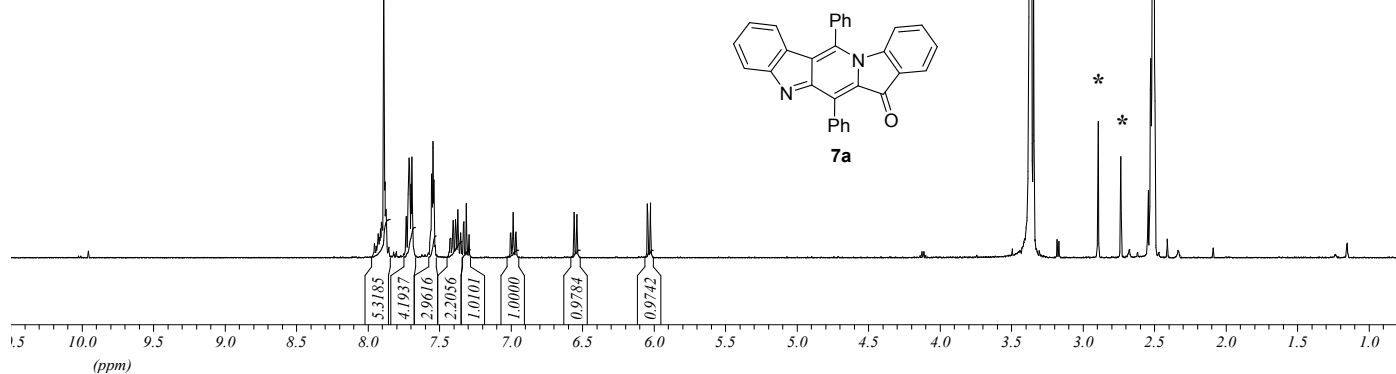
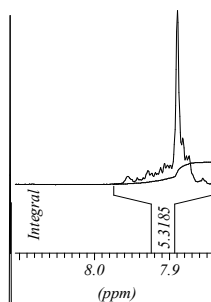
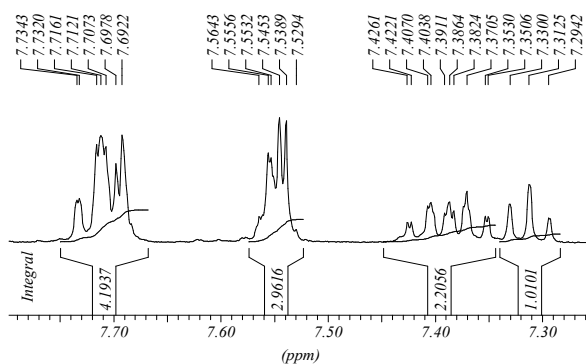
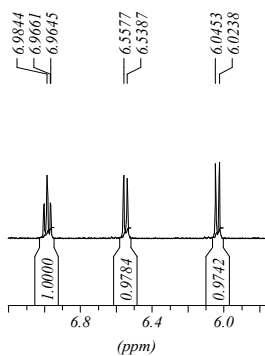
HMBC
DMSO-d₆, 600 MHz



HSQC
DMSO-d₆, 600 MHz

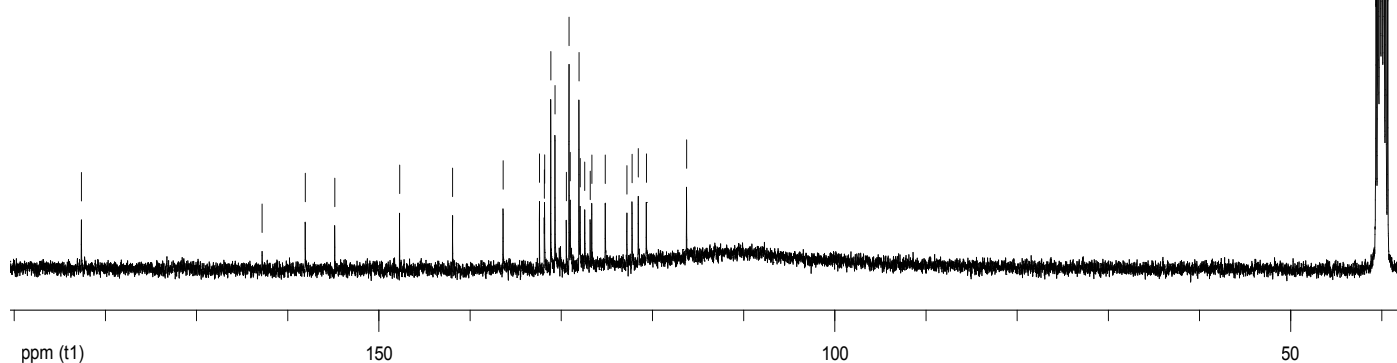
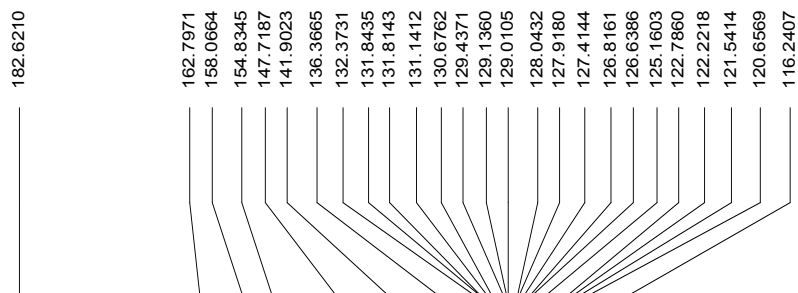
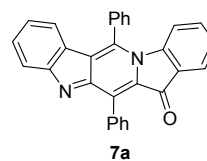


¹H NMR
DMSO-d₆, 400 MHz

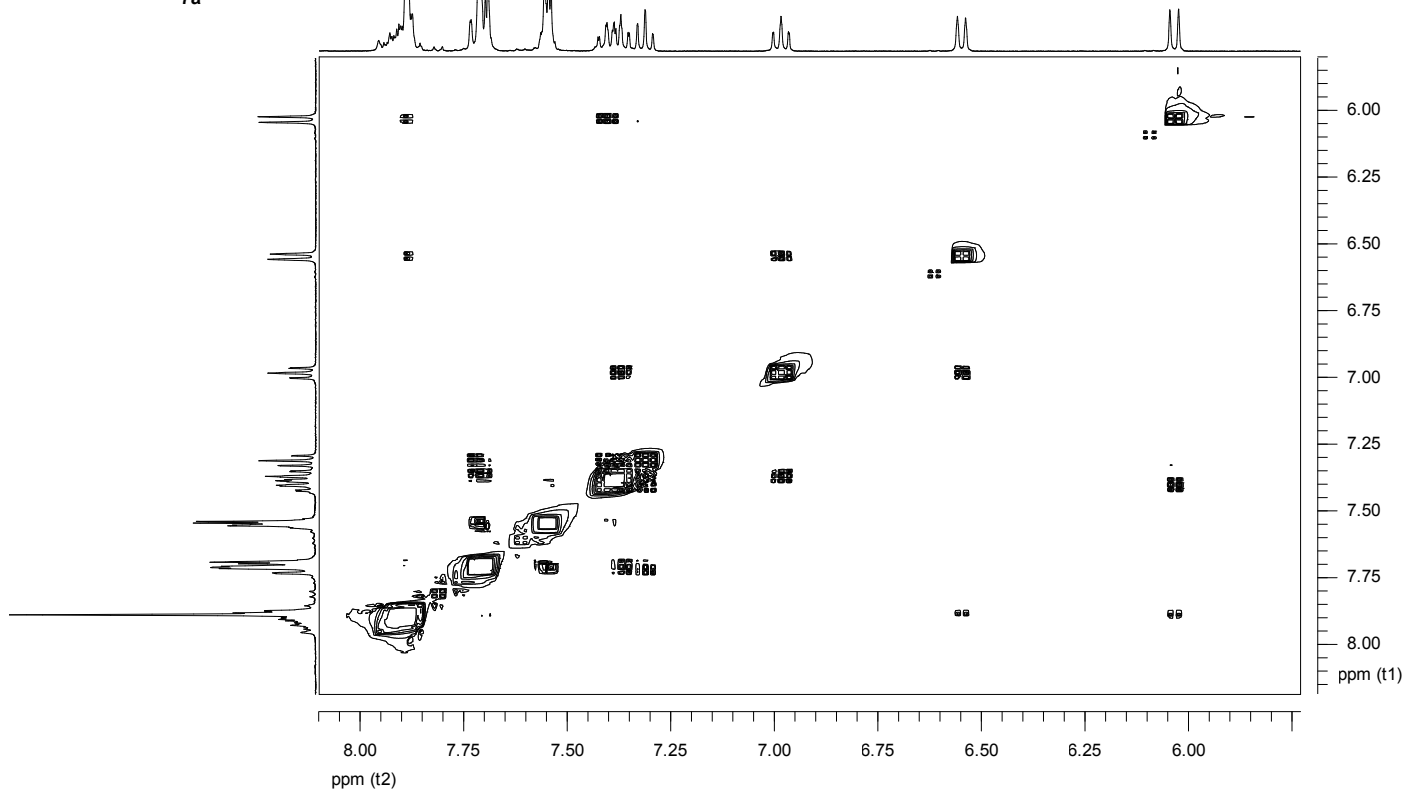
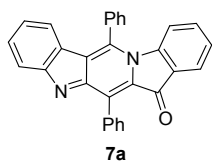


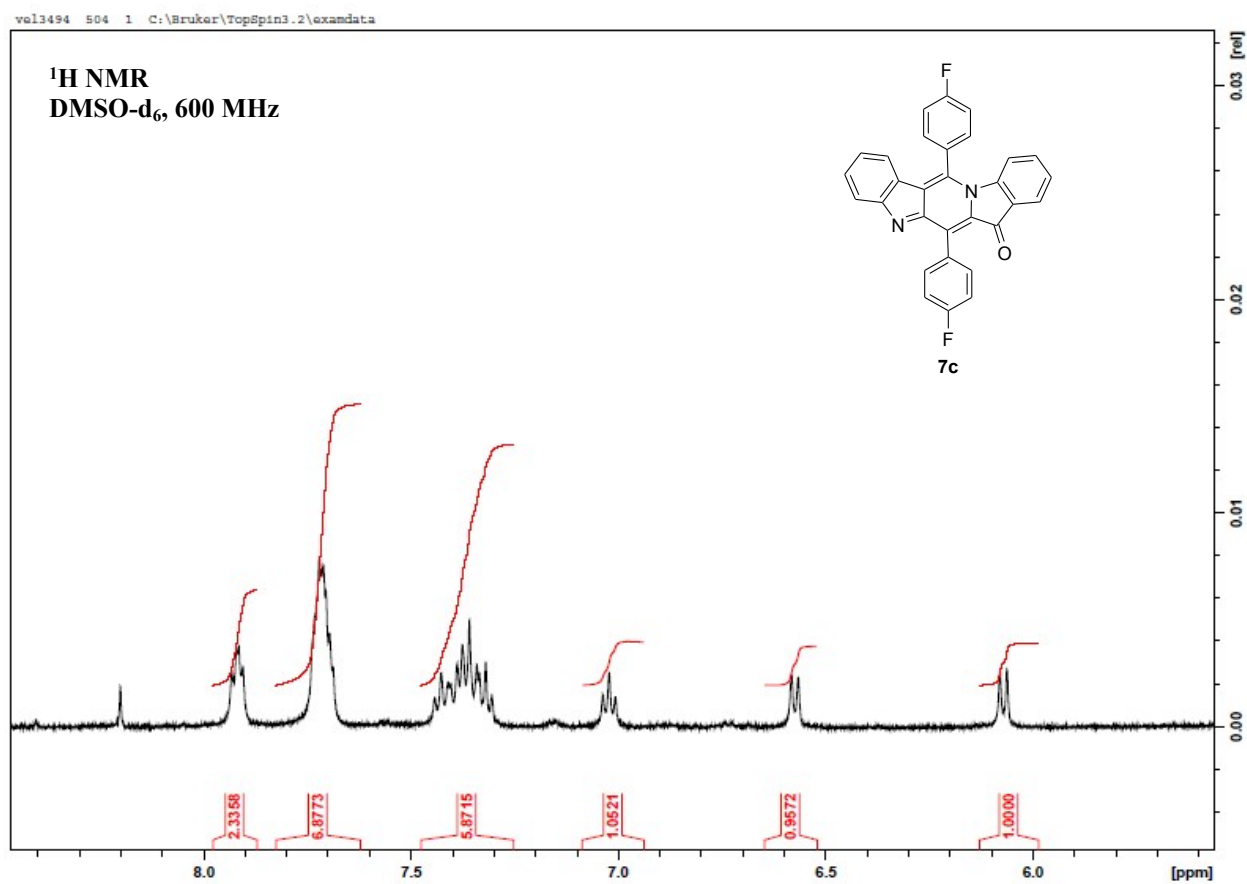
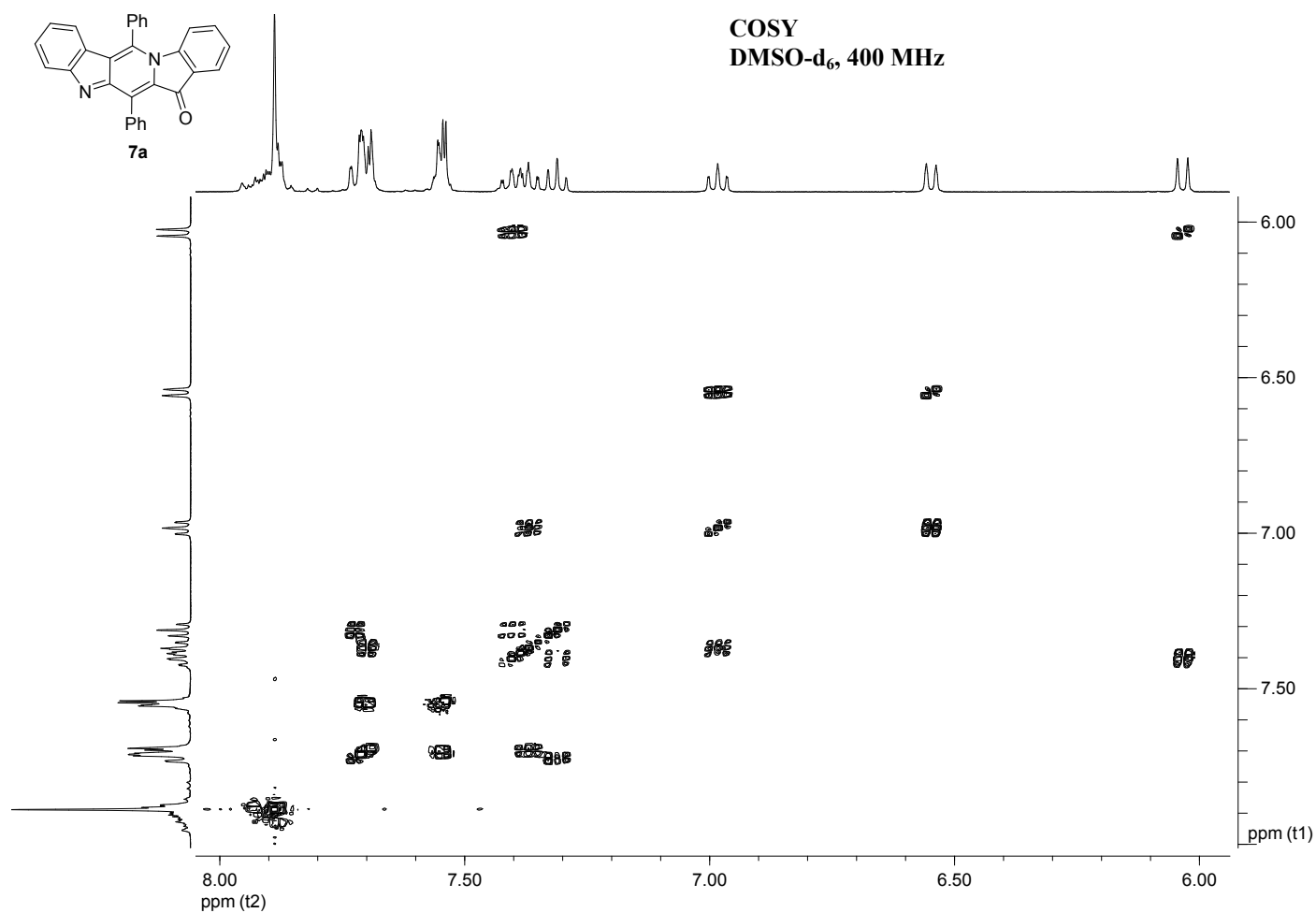
*) signals from DMFA

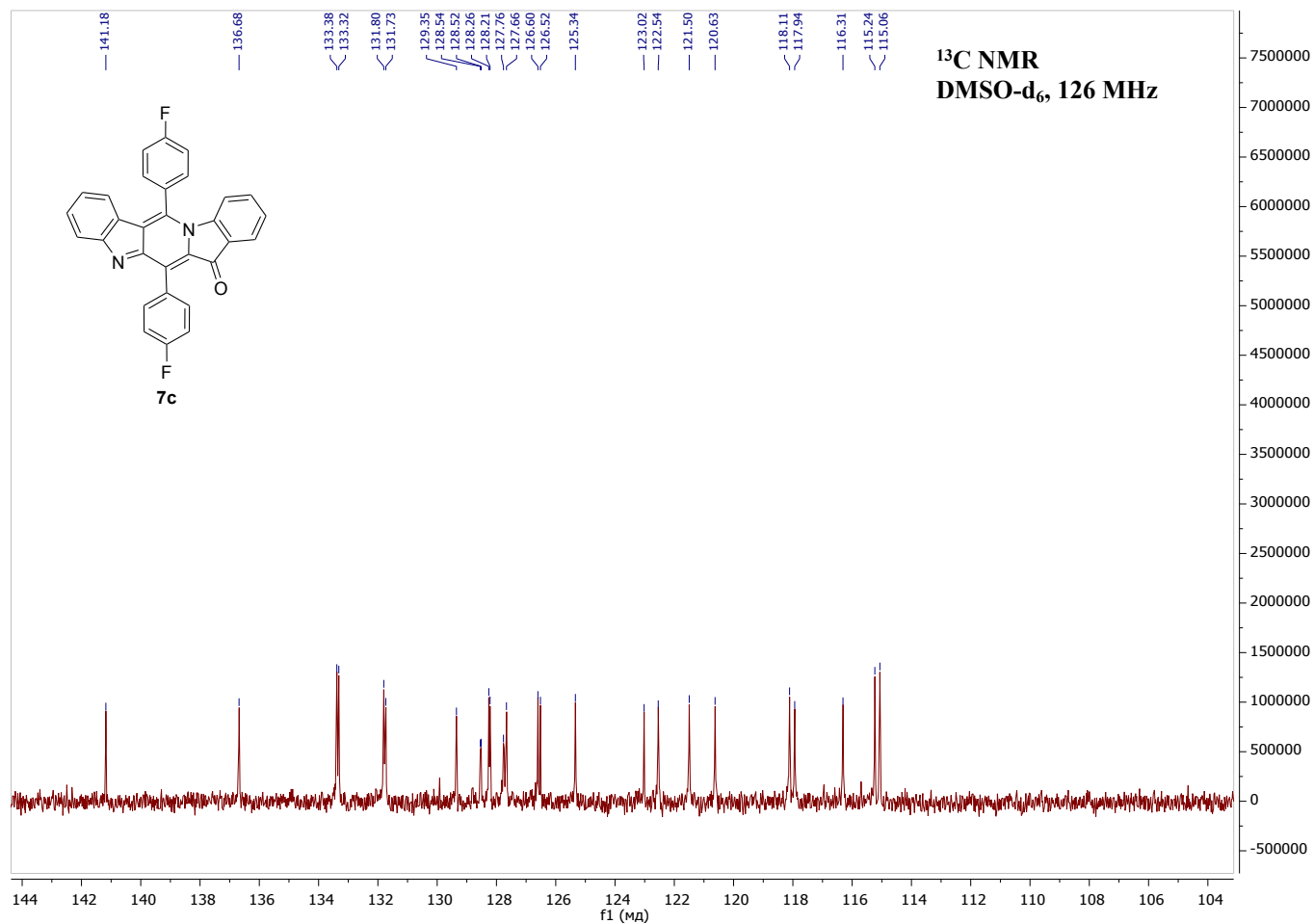
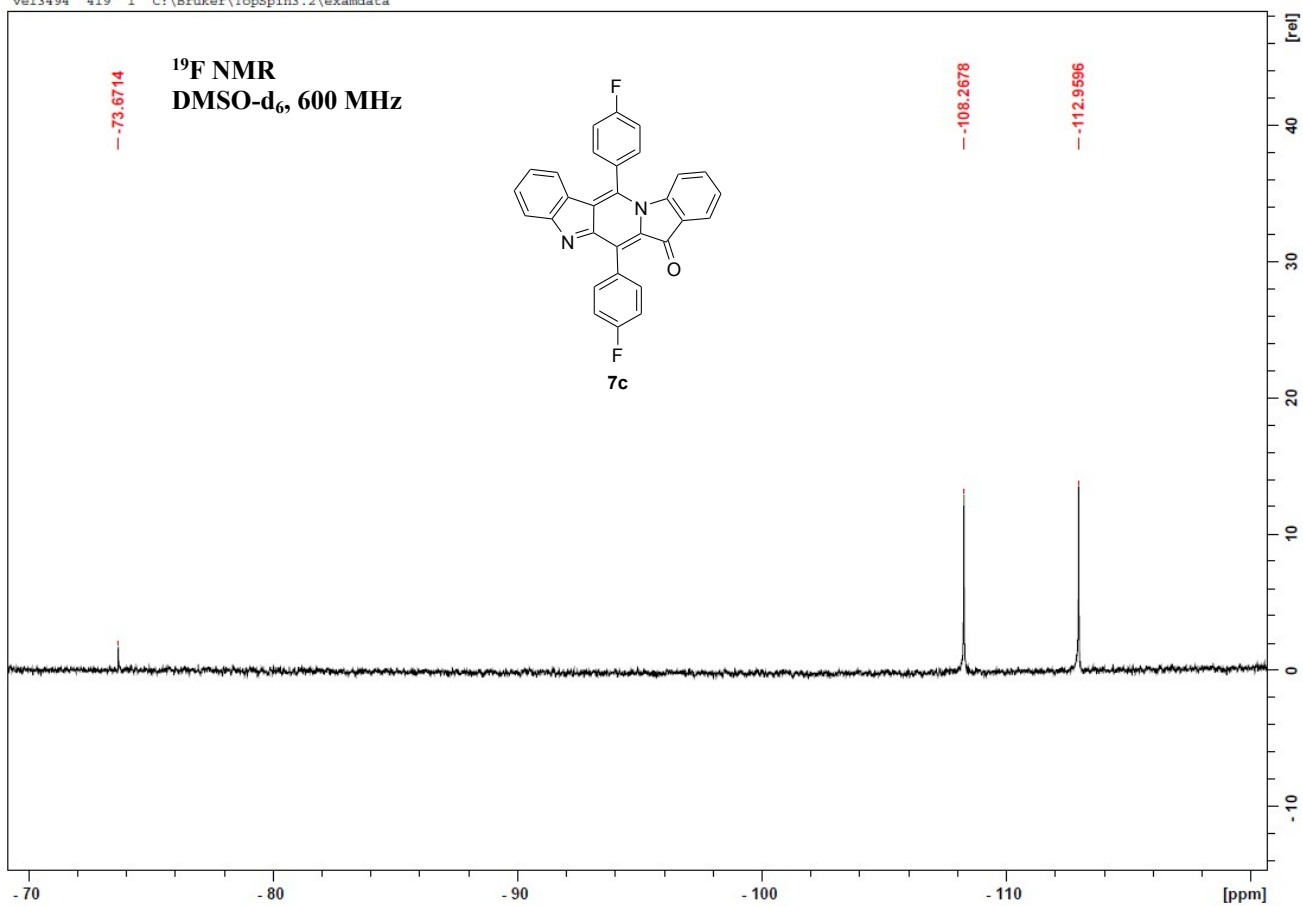
¹³C NMR
DMSO-d₆, 101 MHz



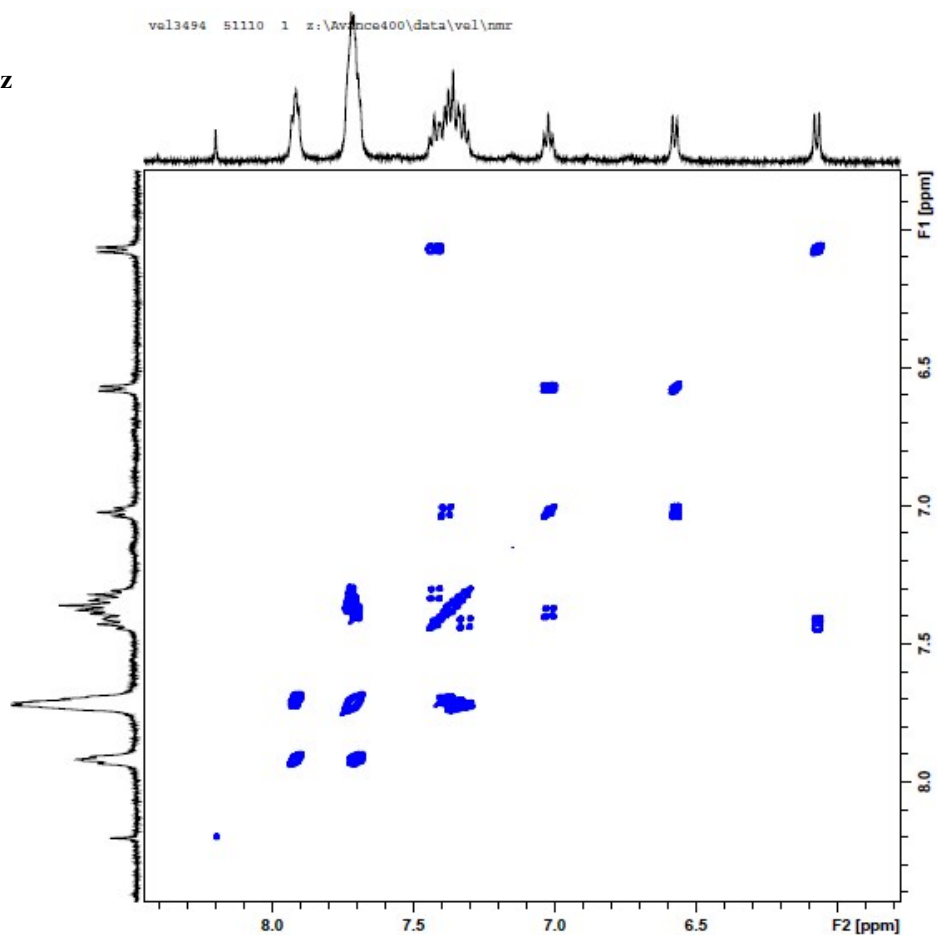
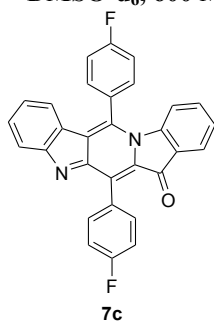
NOESY
DMSO-d₆, 400 MHz



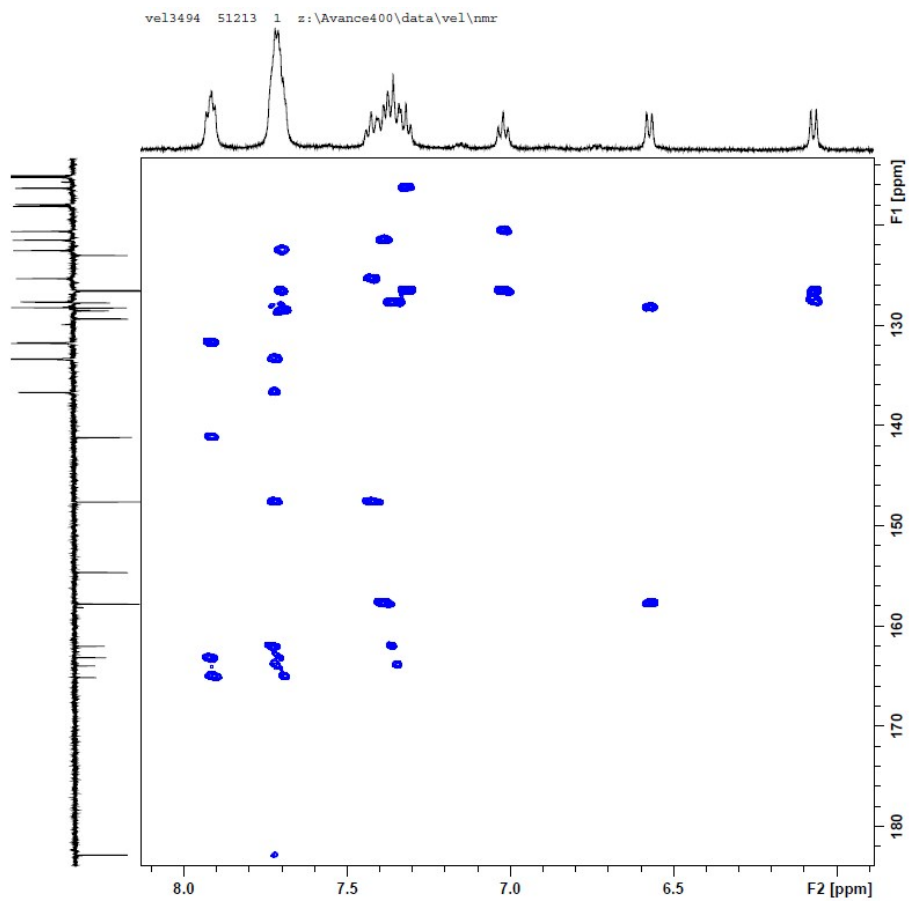
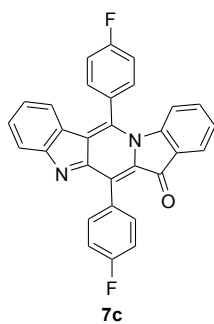




COSY
DMSO-d₆, 600 MHz



HMBC
DMSO-d₆, 600 MHz



4. X-ray diffraction

X-ray diffraction experiments were carried out at 120 K with a Bruker SMART APEX2 CCD diffractometer for the compound **3** and with a Bruker SMART 1000 CCD diffractometer for all others, using graphite monochromated Mo-K α radiation ($\lambda = 0.71073$ Å, ω -scans). The structures were solved with the ShelXS⁵ structure solution program using Direct methods and refined with the olex2.refine⁶ refinement package using Gauss-Newton minimisation. Hydrogen atoms of the NH and OH groups in **2a** and **3** were found in difference Fourier synthesis while the positions of other hydrogen atoms were calculated. All of them were refined in the isotropic approximation within the riding model. Crystal data and structure refinement parameters for **2a**, **3** and **7** are given in Table S1.

All calculations were performed using the SHELXTL⁵ and Olex2⁶ software. CCDC 1947196 (for **2a**), 1947197 (for **3**) and (for **7**) contain the supplementary crystallographic data for this paper.

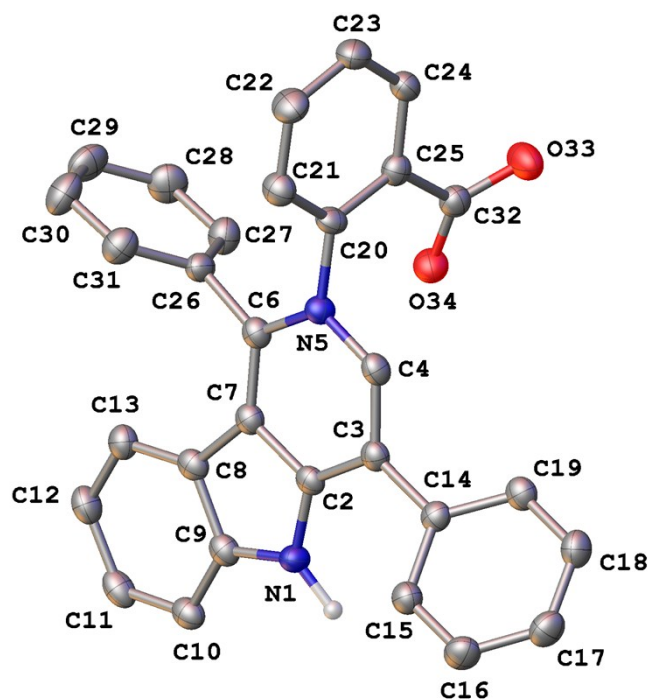


Fig. S1. General view of the compound **2a** in representation of atoms *via* thermal ellipsoids at 50% probability level. Solvate methanol molecules and hydrogen atoms except belonging to the NH group are omitted for clarity.

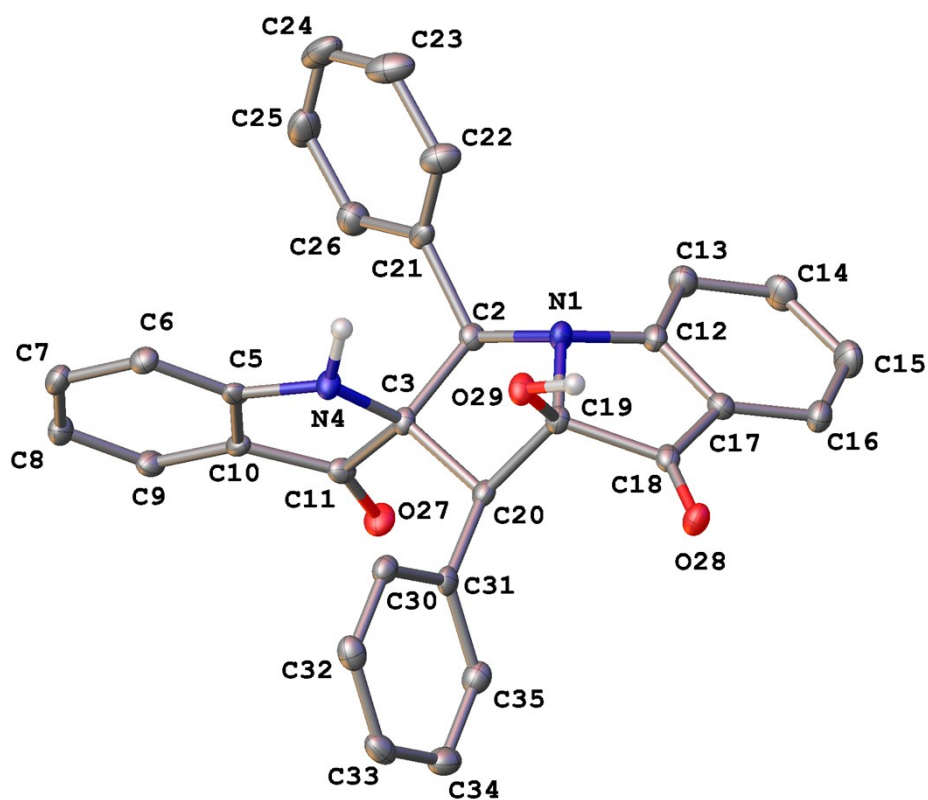


Fig. S2. General view of the compound **3** in representation of atoms *via* thermal ellipsoids at 50% probability level. Hydrogen atoms except those of NH and OH groups are omitted for clarity.

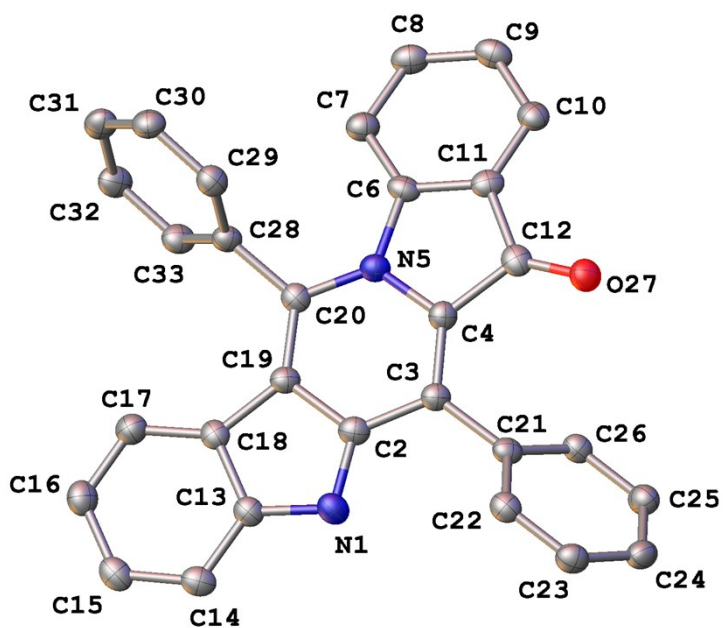


Fig. S3. General view of one of the two symmetry-independent molecules of **7** in representation of atoms *via* thermal ellipsoids at 50% probability level. Hydrogen atoms are omitted for clarity.

Table S1. Crystal data and structure refinement parameters for **2a**, **3** and **7**.

	2a	3	7
Empirical formula	C ₃₂ H ₂₈ N ₂ O ₄	C ₃₀ H ₂₂ N ₂ O ₃	C ₃₀ H ₁₈ N ₂ O
Formula weight	504.59	458.52	422.46
Crystal system	Triclinic	Monoclinic	Triclinic
Space group	P-1	P2 ₁	P-1
Z	2	2	4
a, Å	8.9151(10)	11.3360(8)	9.8297(9)
b, Å	9.6712(11)	6.3863(4)	11.1714(10)
c, Å	15.8118(17)	15.8956(11)	20.2818(18)
α , °	72.760(3)	90	100.752(2)
β , °	83.325(3)	95.678(2)	98.996(3)
γ , °	76.504(3)	90	106.440(2)
V, Å ³	1264.5(2)	1145.12(13)	2046.3(3)
D_{calc} (g cm ⁻³)	1.325	1.330	1.371
Linear absorption, μ (cm ⁻¹)	0.88	0.87	0.84
F(000)	532	480	880
2 θ_{max} , °	52	58	56
Reflections measured	14904	13219	20875
Independent reflections	4953	6010	9818
Observed reflections [$I > 2\sigma(I)$]	2543	4389	4536
Parameters	356	316	595
R1	0.0592	0.0521	0.0468
wR2	0.1645	0.1016	0.0800
GOF	0.875	1.034	1.006
$\Delta\rho_{\text{max}}/\Delta\rho_{\text{min}}$ (e Å ⁻³)	0.787/-0.575	0.366/-0.360	0.720/-0.204

5. References

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