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Metal-free protocol for the synthesis of novel 6-(het)aryl-5-aryl-5*H*-imidazo[4,5-*b*][1,2,5]oxadiazolo[3,4-*e*]pyrazines

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All reagents and solvents were obtained from commercial sources and dried according to the standard procedures before use. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DRX-400 (400 MHz for 1H and 100 MHz for 13C spectra) and AVANCE-500 (500 MHz for 1H and 125 MHz for 13C spectra) instruments in DMSO-d_6, $CDCl_3$ and CD_3CN using Me_4Si as an internal standard. Elemental analysis was carried on a Eurovector EA 3000 automated analyzer. Mass spectrometry data were obtained by using a Bruker maXis Impact HD spectrometer. UV spectra were recorded for a 2×10^{-5} *M* $CHCl_3$ solution with Shimadzu UV-2401PC spectrophotometer. Melting points were determined on Boetius combined heating stages, and were not corrected.Flash-column chromatography was carried out using Alfa Aesar silica gel 0.040-0.063 mm (230–400 mesh), eluting with ethyl acetate-hexane or $CHCl_3$. The progress of reactions and the purity of compounds were checked by TLC on Sorbfil plates (Russia), in which the spots were visualized with UV light (λ 254 or 365 nm). X-ray diffraction analysis was performed on an automated X-ray diffractometer "Xcalibur E" on standard procedure. CCDC 1840270 (for compound **6**), 1840272 (for compound **7a**) and 1840271 (for compound **9**). These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

General procedure for the synthesis of 6-(het)aryl-5-(*p*-tolyl)-5*H*-imidazo[4,5-*b*][1,2,5]-oxadiazolo[3,4-*e*]pyrazines 3a-c from amidines 2a-c and 5,6-dichloro[1,2,5]oxadiazolo-[3,4-*b*]pyrazine 1

A solution of amidine **2a-c** (1 mmol) in acetonitrile (5 ml) was added to a stirred and cooled solution of 5,6-dichloro[1,2,5]oxadiazolo[3,4-*b*]pyrazine **1** (191 mg, 1 mmol) in acetonitrile (10 ml). Without cooling, triethylamine (278 μl, 2 mmol) was added dropwise with stirring. After 1 h, water (30 ml) was added, and the mixture was cooled in the refrigerator. The solid formed was filtered off, washed with water, dried and purified by silica gel column chromatography ($CHCl_3$).

General procedure for the synthesis of N^5-aryl[1,2,5]oxadiazolo[3,4-*b*]pyrazine-5,6-diamines (4a,b).

A solution of aniline or *p*-toluidine (5 mmol) in acetonitrile (10 ml) was added dropwise to a solution of 5,6-dichloro[1,2,5]oxadiazolo[3,4-*b*]pyrazine **1** (0.954 g, 5 mmol) in acetonitrile (20 ml). The mixture was stirred for the 0.5 h. Then a solution of triethylamine (693 μl, 5 mmol) in acetonitrile (10 ml) was added. The mixture was stirred for 0.5 h, the solid precipitate was filtered off and washed with acetonitrile (10 ml). Through the obtained yellow filtrate ammonia gas was bubbled with stirring for 0.5 h. The solid was filtered off, the filtrate was concentrated under reduced pressure to leave solid crude diamine. This material was washed with diethyl ether and purified by crystallization from acetonitrile.

General procedure for the synthesis of 6-ethoxy-5-aryl-6,7-dihydro-5*H*-imidazo-[4,5-*b*][1,2,5]oxadiazolo [3,4-*e*]pyrazines (5a,b).

N^5-Aryl[1,2,5]oxadiazolo[3,4-*b*]pyrazin-5,6-diamine (1 mmol) **4a,b** was added to triethyl orthoformate (1 ml), and AcOH (100 μl) acetic acid was added to the resulting solution. The mixture was stirred under reflux for 10 minutes. Excess triethyl orthoformate was removed under reduced pressure, the solid residue was purified by crystallization from ethanol.

Synthesis of 5-phenyl-6-trifluoromethyl-6,7-dihydro-5*H*-imidazo-[4,5-*b*][1,2,5]oxadiazolo[3,4-*e*]pyrazin-6-ol (6)

Trifluoroacetic anhydride (155 μl, 1.1 mmol) was added to a solution of N^5-phenyl-[1,2,5]oxadiazolo[3,4-*b*]pyrazin-5,6-diamine **4a** (228 mg, 1 mmol) in acetonitrile (5 ml). The mixture was stirred for 1 h, and the solvent was removed under vacuum. The solid residue was purified by silica gel column chromatography (hexane-ethyl acetate, 2:1).

General procedure for the synthesis of 6-(het)aryl-5-aryl-5*H*-imidazo-[4,5-*b*][1,2,5]oxadiazolo[3,4-*e*]pyrazines 7a-n.

5-Aryl-6-ethoxy-6,7-dihydro-5*H*-imidazo[4,5-*b*][1,2,5]oxadiazolo [3,4-*e*]pyrazine **5a,b** (0.2 mmol) was added to trifluoroacetic acid (5 ml), and to this mixture the corresponding nucleophile (0.3 mmol) was added. The mixture was heated at 50 °C for 24 h, then trifluoroacetic acid was removed. The solid residue was purified by silica gel column chromatography ($CHCl_3$).

General procedure for the synthesis of *(E)*-*N'*-(6-phenylamino[1,2,5]oxadiazolo-[3,4-*b*]pyrazin-5-yl)-*N*-(*p*-tolyl)formamidine 8 and *(E)*-*N*-phenyl-6-[(pyrrolydin-1-yl)methylidenamino][1,2,5]oxadiazolo[3,4-*b*]pyrazin-5-amine 9

Amine (1.1 mmol) was added to a solution of 6-ethoxy-5-phenyl-6,7-dihydro-5*H*-imidazo[4,5-*b*][1,2,5]oxadiazolo[3,4-*e*]pyrazine **7a** (1 mmol) in acetonitrile (5 ml). The mixture was heated at 50 °C for 2 h. Then the mixture was cooled, the yellow solid was collected by filtration and purified by crystallization from acetonitrile

6-Phenyl-5-(*p*-tolyl)-5*H*-imidazo[4,5-*b*][1,2,5]oxadiazolo[3,4-*e*]pyrazine (3a).

Yield: 128 mg (39%); yellow crystals; mp 298°C

^{1}H NMR (500 MHz, DMSO-d_6): δ= 7.79 – 7.74 (m, 2H), 7.67 (td, *J* = 7.2, 1.3 Hz, 1H), 7.56 – 7.50 (m, 2H), 7.46 – 7.40 (m, 4H), 2.44 (s, 3H).

^{13}C NMR (126 MHz, DMSO-d_6): δ =171.04, 158.39, 153.16, 152.44, 151.47, 139.72, 133.63, 131.04, 130.37, 130.36, 128.90, 127.78, 127.15, 20.81.

Anal.Calcd for $C_{18}H_{12}N_6O$: C, 65,85; H, 3,68; N,25,60. Found: C, 65,75; H, 3,71; N, 25,75.

6-(4-Chlorophenyl)-5-(*p*-tolyl)-5*H*-imidazo[4,5-*b*][1,2,5]oxadiazolo[3,4-*e*]pyrazine (3b).

Yield: 154 mg (42%); yellow crystals; mp 261°C

^{1}H NMR (500 MHz, DMSO-d_6): δ =7.78 – 7.73 (m, 2H), 7.66 – 7.62 (m, 2H), 7.47 – 7.41 (m, 5H), 2.44 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d_6): δ= 170.11, 158.24, 153.16, 152.30, 151.47, 139.88, 138.76, 132.09, 130.83, 130.48, 129.19, 127.76, 126.04, 20.84.

Anal.Calcd for $C_{18}H_{11}N_6OCl$: C, 59.60; H, 3,06; N,23.17. Found: C, 59.54; H, 3.02; N, 23.22.

6-(2-Thienyl)-5-(*p*-tollyl)-5*H*-imidazo[4,5-*b*][1,2,5]oxadiazolo[3,4-*e*]pyrazine (3c).

Yield: 91 mg (27%); bright yellow crystals; mp 352°C decomposition.

^{1}H NMR (400 MHz, DMSO-d_6): δ= 8.25 (dd, J = 4.9, 1.2 Hz, 1H), 7.63 – 7.52 (m, 6H), 7.43 (dd, J = 4.0, 1.2 Hz, 1H), 7.30 (dd, J = 4.8, 4.1 Hz, 1H), 2.44 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d_6): δ= 165.74, 158.95, 153.78, 153.36, 152.00, 141.54, 139.36, 136.59, 131.32, 130.83, 130.15, 129.19, 100.00, 21.47.

Anal.Calcd for $C_{16}H_{10}N_6OS$: C, 57.48; H, 3.01; N,25.14. Found: C, 57.55; H, 2.84; N, 25.24.

***N*^{5}-Phenyl[1,2,5]oxadiazolo[3,4-*e*]pyrazine-5,6-diamine (4a).**

Yield: 1.06 g (92%); yellowish crystals; mp 239 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ= 9.72 (s, 1H), 8.32 (s, 2H), 7.87 – 7.77 (m, 2H), 7.49 – 7.39 (m, 2H), 7.28 – 7.16 (m, 1H).;

^{13}C NMR (101 MHz, DMSO- d_6): δ= 151.10, 150.56, 150.01, 146.66, 137.77, 128.77, 125.03, 122.40.

Anal. Calcd for $C_{10}H_8N_6O$: C, 52.63; H, 3.53; N, 36.83. Found: C, 52.81; H, 3.63; N, 37.01.

***N*^{5}-*p*-Tolyl[1,2,5]oxadiazolo[3,4-*e*]pyrazine-5,6-diamine (4b).**

Yield: 1.14 g (94%); yellowish solid; mp 237 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ= 9.80 (s, 1H), 8.37 (s, 2H), 7.73 (d, J = 8.4 Hz, 2H), 7.24 (d, J = 8.2 Hz, 2H), 2.32 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d_6): δ= 150.00, 149.44, 148.96, 145.47, 134.21, 133.05, 128.01, 121.25, 19.41.

Anal. Calcd for $C_{11}H_{10}N_6O$: C, 54.54; H, 4.16; N, 34.69. Found: C, 54.82; H, 4.25; N, 34.89.

6-Ethoxy-5-phenyl-6,7-dihydro-5*H*-imidazo[4,5-*b*][1,2,5]oxadiazolo[3,4-*e*]pyrazine (5a) .

Yield: 241 mg (84%); white crystals; mp 159 °C.

^{1}H NMR (500 MHz, DMSO-d_6): δ= 10.85 (s, 1H), 7.91 – 7.83 (m, 2H), 7.58 – 7.50 (m, 2H), 7.39 – 7.31 (m, 1H), 7.28 (s, 1H), 3.58 (dq, J = 9.7, 7.0 Hz, 1H), 3.41 (dq, J = 9.8, 7.1 Hz, 1H), 1.03 (t, J = 7.0 Hz, 3H).

^{13}C NMR (126 MHz, DMSO-d_6): δ= 152.74, 151.66, 151.28, 149.81, 135.09, 129.18, 126.52, 122.04, 94.53, 57.47, 14.65.

Anal. Calcd for $C_{13}H_{12}N_6O_2$: C, 54.93; H, 4.25; N, 29,56. Found: C, 54.75; H, 4.18; N, 29.40.

6-Ethoxy-5-*p*-tolyl-6,7-dihydro-5*H*-imidazo[4,5-*b*][1,2,5]oxadiazolo[3,4-*e*]pyrazine (5b).

Yield: 254 mg (85%); white crystals; mp 168 °C

^{1}H NMR (400 MHz, DMSO-d_6): δ= 10.80 (s, 1H), 7.74 (d, *J* = 8.6 Hz, 2H), 7.34 (d, *J* = 8.3 Hz, 2H), 7.23 (s, 1H), 3.56 (dq, *J* = 9.8, 7.0 Hz, 1H), 3.39 (dq, *J* = 9.7, 7.1 Hz, 1H), 2.35 (s, 3H), 1.03 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (126 MHz, DMSO-d_6): δ= 152.76, 151.68, 151.34, 149.72, 136.03, 132.50, 129.60, 122.05, 94.54, 57.44, 20.60, 14.66.

Anal. Calcd for $C_{14}H_{14}N_6O_2$: C, 56.37; H, 4.73; N, 28.17. Found : C, 56.19; H, 4.78; N, 27.98.

5-Phenyl-6-trifluoromethyl-6,7-dihydro-5*H*-imidazo[4,5-*b*][1,2,5]oxadiazolo-[3,4-*e*]pyrazin-6-ol (6).

Yield: 231 mg (67%); white solid; mp 214 °C

^{1}H NMR (500 MHz, DMSO-d_6): δ= 11.74 (s, 1H), 10.02 (s, 1H), 7.67 – 7.40 (m, 5H).

^{13}C NMR (101 MHz, CD_3CN): δ= 152.66, 152.56, 152.20, 152.13, 133.66, 130.76, 129.51, 121.78(q, J=288.1), 101.07, 98.95(q, J=35.1).

^{19}F NMR(470.5 MHz, DMSO-d_6): δ= 81.77

Anal.Calcd for $C_{12}H_9F_3N_6O_3$: C, 42.11; H, 2.65; N, 24.56. Found: C, 42.06; H, 2.52; N, 24.53.

2,6-Di-*tert*-butyl-6-(5-phenyl-5*H*-imidazo[4,5-*b*][1,2,5]oxadiazolo[3,4-*e*]-pyrazin-6-yl)phenol (7a).

Yield: 61 mg (69%); yellow crystals; mp 338°C decomposition

^{1}H NMR (400 MHz, DMSO-d_6): δ= 8.37 (s, 1H), 7.75 – 7.63 (m, 5H), 7.62 – 7.56 (m, 2H), 1.24 (s, 18H).

^{13}C NMR (101 MHz, DMSO-d_6): δ= 153.34, 152.94, 151.49, 138.54, 134.66, 130.16, 129.92, 128.56, 128.26, 34.43, 29.57.

Anal.Calcd for $C_{25}H_{26}N_6O_2$:C, 67.86; H, 5.92; N,18.99. Found: C, 67,71; H, 5.98; N, 19.19.

2,6-Di-*tert*-butyl-6-(5-*p*-tolyl-5*H*-imidazo[4,5-*b*][1,2,5]oxadiazolo[3,4-*e*]-pyrazin-6-yl)phenol (7h).

Yield: 52 mg (57%); yellow crystals; mp 299°C

^{1}HNMR (500 MHz, DMSO-d_6): δ= 8.37 (s, 1H), 7.72 (s, 2H), 7.53 – 7.44 (m, 4H), 2.44 (s, 3H), 1.25 (s, 18H).

^{13}CNMR (126 MHz, DMSO-d_6): δ= 153.34, 153.00, 151.53, 139.86, 138.47, 132.04, 130.57, 128.62, 128.04, 34.46, 29.54, 20.77.

Anal.Calcd for $C_{26}H_{28}N_6O_2$:C, 68.40; H, 6.18; N,18.41. Found: C, 68.48; H, 6.51; N, 18.20.

2,4-Di-*tert*-butyl-6-(5-phenyl-5*H*-imidazo[4,5-*b*][1,2,5]oxadiazolo[3,4-*e*]-pyrazine-6-yl)phenol (7b).

Yield: 54 mg (61%); red crystals; mp 332 °C

^{1}H NMR (500 MHz, DMSO-d_6): δ= 13.27 (s, 1H), 7.78 – 7.68 (m, 2H), 7.67 – 7.63 (m, 2H), 7.53 (d, *J* = 2.4 Hz, 1H), 7.04 (d, *J* = 2.3 Hz, 1H), 1.44 (s, 9H), 0.92 (s, 9H).

^{13}C NMR (126 MHz, DMSO-d_6): δ= 169.67, 159.51, 156.00, 153.05, 151.62, 151.55, 140.17, 137.87, 134.61, 131.34, 130.47, 130.44, 128.24, 123.95, 109.41, 35.13, 33.67, 30.44, 29.17.

Anal.Calcd for $C_{25}H_{26}N_6O_2$:C, 67.86; H, 5.92; N 18.99. Found: C, 67.55; H, 6.05; N, 18.88.

2,4-di-*tert*-butyl-6-(5-*p*-tollyl-5*H*-imidazo[4,5-*b*][1,2,5]oxadiazolo[3,4-*e*]-pyrazine-6-yl)phenol (7i).

Yield: 51 mg (56%); red crystals; mp 255 °C

^{1}H NMR (500 MHz, $CDCl_3$): δ =13.22 (s, 1H), 7.55 (d, *J* = 2.4 Hz, 1H), 7.49 (d, *J* = 8.0 Hz, 2H), 7.37 (d, *J* = 8.2 Hz, 2H), 7.03 (d, *J* = 2.4 Hz, 1H), 2.51 (s, 3H), 1.47 (s, 9H), 0.95 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$): δ= 169.54, 161.54, 154.79, 152.97, 151.26, 150.19, 141.17, 140.56, 139.14, 132.65, 131.90, 131.35, 127.59, 123.81, 108.60, 35.59, 34.02, 30.57, 29.34, 21.30.

Anal.Calcd for $C_{26}H_{28}N_6O_2$:C, 68.40; H, 6.18; N, 18.41.Found: C, 68.28; H, 6.35; N, 18.26.

5-Phenyl-6-(2,4,6-trimethoxyphenyl)-5*H*-imidazo[4,5-*b*][1,2,5]oxadiazolo-[3,4-*e*]pyrazine (7c).

Yield: 42 mg (52%); yellow solid; mp 226°C

^{1}H NMR (400 MHz, DMSO-d_6): δ= 7.54 – 7.47 (m, 3H), 7.33 – 7.28 (m, 2H), 6.28 (s, 2H), 3.83 (s, 3H), 3.62 (s, 6H).

^{13}C NMR (101 MHz, DMSO-d_6): δ= 169.93, 164.70, 159.41, 158.14, 153.10, 151.58, 150.18, 133.03, 129.06, 129.00, 126.29, 98.42, 91.02, 55.92, 55.69.

Anal.Calcd for $C_{20}H_{16}N_6O_4$:C, 59.40; H, 3.99; N, 20.78. Found: C, 59.16; H, 4.10; N, 20.68.

5-(*p*-Tolyl)-6-(2,4,6-trimethoxyphenyl)-5*H*-imidazo[4,5-*b*][1,2,5]oxadiazolo-[3,4-*e*]pyrazine (7j).

Yield: 38 mg (45%); yellow solid; mp 229°C

^{1}H NMR (500 MHz, $CDCl_3$): δ= 7.23 (d, *J* = 8.2 Hz, 2H), 7.18 (d, *J* = 8.3Hz, 2H), 6.07 (s, 2H), 3.84 (s, 3H), 3.65 (s, 6H), 2.38 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ= 170.27, 165.04, 159.83, 157.56, 152.91, 151.26, 149.56, 139.20, 130.60, 129.69, 125.78, 99.24, 90.58, 55.81, 55.54, 21.23.

Anal.Calcd for $C_{21}H_{18}N_6O_4$:C, 60.28; H, 4.34; N, 20.09. Found: C, 59.94; H, 4.20; N, 19.91.

6-(2-Methoxynaphthalene-1-yl)-5-phenyl-5*H*-imidazo[4,5-*b*][1,2,5]oxadiazolo-[3,4-*e*]pyrazine (7d).

Yield: 49 mg (62%); yellow solid; mp 252°C

^{1}H NMR (500 MHz, $CDCl_3$): δ= 8.11 – 8.05 (m, 1H), 8.04 (d, *J* = 9.1 Hz, 1H), 7.90 – 7.86 (m, 1H), 7.61 (ddd, *J* = 8.4, 6.8, 1.3 Hz, 1H), 7.49 (ddd, *J* = 8.1, 6.8, 1.1 Hz, 1H), 7.37 – 7.31 (m, 3H), 7.25 – 7.20 (m, 2H), 7.10 (d, *J* = 9.2 Hz, 1H), 3.53 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ =171.28, 157.24, 155.74, 152.96, 151.32, 149.41, 135.05, 133.10, 132.31, 129.17, 129.09, 129.05, 128.72, 128.64, 125.78, 124.92, 123.65, 111.79, 110.06, 55.81.

Anal.Calcd for $C_{22}H_{14}N_6O_2$:C, 67.00; H, 3.58; N, 21.31. Found: C, 66.87; H, 3.47; N, 21.12.

6-(2-methoxynaphthalene-1-yl)-5-(*p*-tollyl)-5*H*-imidazo[4,5-*b*][1,2,5]-oxadiazolo[3,4-*e*]pyrazine (7k).

Yield: 44 mg (53%); yellow solid; mp 211°C

^{1}H NMR (500 MHz, $CDCl_3$): δ= 8.07 – 8.01 (m, 2H), 7.87 (d, *J* = 8.2 Hz, 1H), 7.59 (ddd, *J* = 8.3, 6.8, 1.3 Hz, 1H), 7.47 (ddd, *J* = 7.9, 6.7, 1.0 Hz, 1H), 7.15 – 7.06 (m, 4H), 3.57 (s, 3H), 2.32 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ= 171.52, 157.25, 155.68, 152.91, 151.30, 149.54, 139.40, 134.91, 132.24, 130.32, 129.69, 128.94, 128.62, 128.59, 125.56, 124.82, 123.58, 111.84, 110.05, 55.86, 21.16.

Anal.Calcd for $C_{23}H_{16}N_6O_2$:C, 67.64; H, 3.95; N, 20.58. Found: C, 67.60; H, 3.84; N, 20.48.

***N*,*N*-Diphenyl-4-(5-phenyl-5*H*-imidazo[4,5-*b*][1,2,5]oxadiazolo[3,4-*e*]-pyrazin-6-yl)aniline (7e).**

Yield: 60 mg (62%); dark lilac crystals; mp 318°C

^{1}H NMR (500 MHz, DMSO-d_6): δ =7.70 – 7.55 (m, 7H), 7.48 – 7.39 (m, 4H), 7.32 – 7.20 (m, 6H), 6.73 – 6.66 (m, 2H).

^{13}CNMR (126 MHz, DMSO-d_6): δ= 169.36, 158.43, 153.39, 153.05, 152.60, 151.48, 144.65, 134.31, 132.57, 130.12, 130.09, 129.44, 128.20, 126.90, 126.24, 116.68, 116.52.$C_{29}H_{19}N_7O$.

HRMS (APCI) m/z Calcd for $C_{29}H_{20}N_7O$: 482.1724 $[M+H]^+$; Found: 482.1726.

***N*,*N*-Diphenyl-4-(5-*p*-tolyl-5*H*-imidazo[4,5-*b*][1,2,5]oxadiazolo[3,4-*e*]-pyrazin-6-yl)aniline (7l).**

Yield: 59 mg (60%); dark lilac crystals; mp 309°C

^{1}H NMR (500 MHz, $CDCl_3$): δ =7.74 – 7.69 (m, 2H), 7.42 – 7.31 (m, 8H), 7.24 – 7.16 (m, 6H), 6.86 – 6.82 (m, 2H), 2.48 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ =169.32, 157.50, 153.39, 153.32, 151.92, 151.36, 145.30, 140.65, 132.90, 131.60, 131.07, 129.91, 127.48, 126.76, 125.97, 118.15, 117.02, 21.41.$C_{30}H_{21}N_7O$.

HRMS (APCI) m/z Calcd for $C_{20}H_{22}N_7O$: 496.1881 $[M+H]^+$; Found: 496.1880.

5-Phenyl-6-(5-phenyl-1*H*-pyrrol-2-yl)-5*H*-imidazo[4,5-*b*][1,2,5]oxadiazolo-[3,4-*e*]pyrazine (7f).

Yield: 58 mg (76%); dark red crystals; mp 380°C

^{1}H NMR (500 MHz, DMSO-d_6): δ =13.29 (s, 1H), 8.09 – 7.95 (m, 2H), 7.82 – 7.67 (m, 5H), 7.50 – 7.42 (m, 2H), 7.41 – 7.35 (m, 1H), 6.81 (d, J = 4.3 Hz, 1H), 5.82 (d, J = 4.3 Hz, 1H).

^{13}C NMR (126 MHz, DMSO): δ= 161.36, 159.00, 153.56, 153.17, 151.59, 143.24, 133.84, 130.73, 130.29, 129.83, 128.95, 128.83, 128.78, 126.44, 121.71, 121.02, 112.19.

Anal.Calcd for $C_{21}H_{13}N_7O$: C, 66.48; H, 3.45; N, 25.84. Found: C, 66.29; H, 3.36; N, 25.69

6-(5-Phenyl-1*H*-pyrrol-2-yl)-5-(*p*-tolyl)-5*H*-imidazo[4,5-*b*][1,2,5]-oxadiazolo[3,4-*e*]pyrazine (7m).

Yield: 62 mg (78%); dark red crystals; mp 373-375°C

^{1}H NMR (500 MHz, DMSO-d_6): δ= 13.27 (s, 1H), 8.09 – 7.95 (m, 2H), 7.61 – 7.51 (m, 4H), 7.49 – 7.43 (m, 2H), 7.42 – 7.35 (m, 1H), 6.82 (d, J = 4.4 Hz, 1H), 5.88 (d, J = 4.3 Hz, 1H).

^{13}C NMR (126 MHz, DMSO): δ =161.46, 158.99, 153.55, 153.20, 151.60, 143.19, 140.54, 131.18, 130.72, 129.85, 128.93, 128.82, 128.46, 126.43, 121.78, 121.05, 112.17, 20.97.

Anal.Calcd for $C_{22}H_{15}N_7O$: C, 67.17; H, 3.84; N, 24.92. Found: C, 66.07; H, 3.67; N, 24.78.

6-(1-Ethyl-1*H*-indol-3-yl)-5-phenyl-5*H*-imidazo[4,5-*b*][1,2,5]oxadiazolo-[3,4-*e*]pyrazine (7g).

Yield: 49 mg (64%); red crystals; mp 354°C

^{1}H NMR (400 MHz, DMSO-d_6): δ= 8.73 – 8.65 (m, 1H), 7.82 – 7.68 (m, 6H), 7.53 – 7.37 (m, 2H), 6.79 (s, 1H), 4.16 (q, J = 7.2 Hz, 2H), 1.21 (t, J = 7.3 Hz, 3H).

The^{13}C NMR could not be recordeded due to the poor solubility of this compound in deuteriated solvents.

Anal. Calcd for $C_{21}H_{15}N_7O$:C, 66.13; H, 3.96; N, 25.71. Found: C, 65.98; H, 3.93; N, 25.58.

6-(1-Ethyl-1*H*-indol-3-yl)-5-(*p*-tolyl)-5*H*-imidazo[4,5-*b*][1,2,5]oxadiazolo-[3,4-*e*]pyrazine (7n).

Yield: 55 mg (69%); red crystals; mp 338°C

^{1}H NMR (500 MHz, DMSO-d_6): δ= 8.68 (d, *J* = 7.4 Hz, 1H), 7.69 (d, *J* = 7.6 Hz, 1H), 7.62 – 7.54 (m, 4H), 7.51 – 7.38 (m, 2H), 6.83 (s, 1H), 4.16 (q, *J* = 7.2 Hz, 2H), 2.53 (s, 3H), 1.21 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (126 MHz, DMSO-d_6): δ= 166.72, 159.33, 153.41, 152.62, 151.58, 140.51, 136.15, 135.26, 131.32, 130.82, 128.42, 126.94, 124.23, 123.46, 122.87, 111.49, 103.14, 41.57, 20.95, 14.29.

Anal.Calcd for $C_{22}H_{17}N_7O$:C, 66.82; H, 4.33; N, 24.80. Found: C, 66.67; H, 4.37; N, 24.65.

***(E)*-*N'*-(6-Phenylamino[1,2,5]oxadiazolo[3,4-*b*]pyrazin-5-yl)-*N*-(*p*-tolyl)formimidamide (8).**

Yield: 42 mg (61%); light yellow crystals; mp 218°C

^{1}H NMR (400 MHz, DMSO-d_6): δ= 10.70 (s, 1H), 7.72 – 7.66 (m, 2H), 7.49 – 7.41 (m, 3H), 7.33 – 7.26 (m, 1H), 6.93 (d, *J* = 8.2 Hz, 2H), 6.87 – 6.77 (m, 1H), 6.61 (d, *J* = 8.4 Hz, 2H), 2.14 (s, 3H).;

^{13}C NMR (126 MHz, DMSO-d_6): δ= 152.74, 151.43, 150.31, 141.00, 134.87, 129.54, 128.88, 127.62, 126.64, 123.55, 122.26, 114.69, 113.99, 20.00.

Anal.Calcd for $C_{18}H_{15}N_7O$:C, 62.60; H, 4.38; N, 28.39. Found: C, 62.45; H, 4.50; N, 28.12.

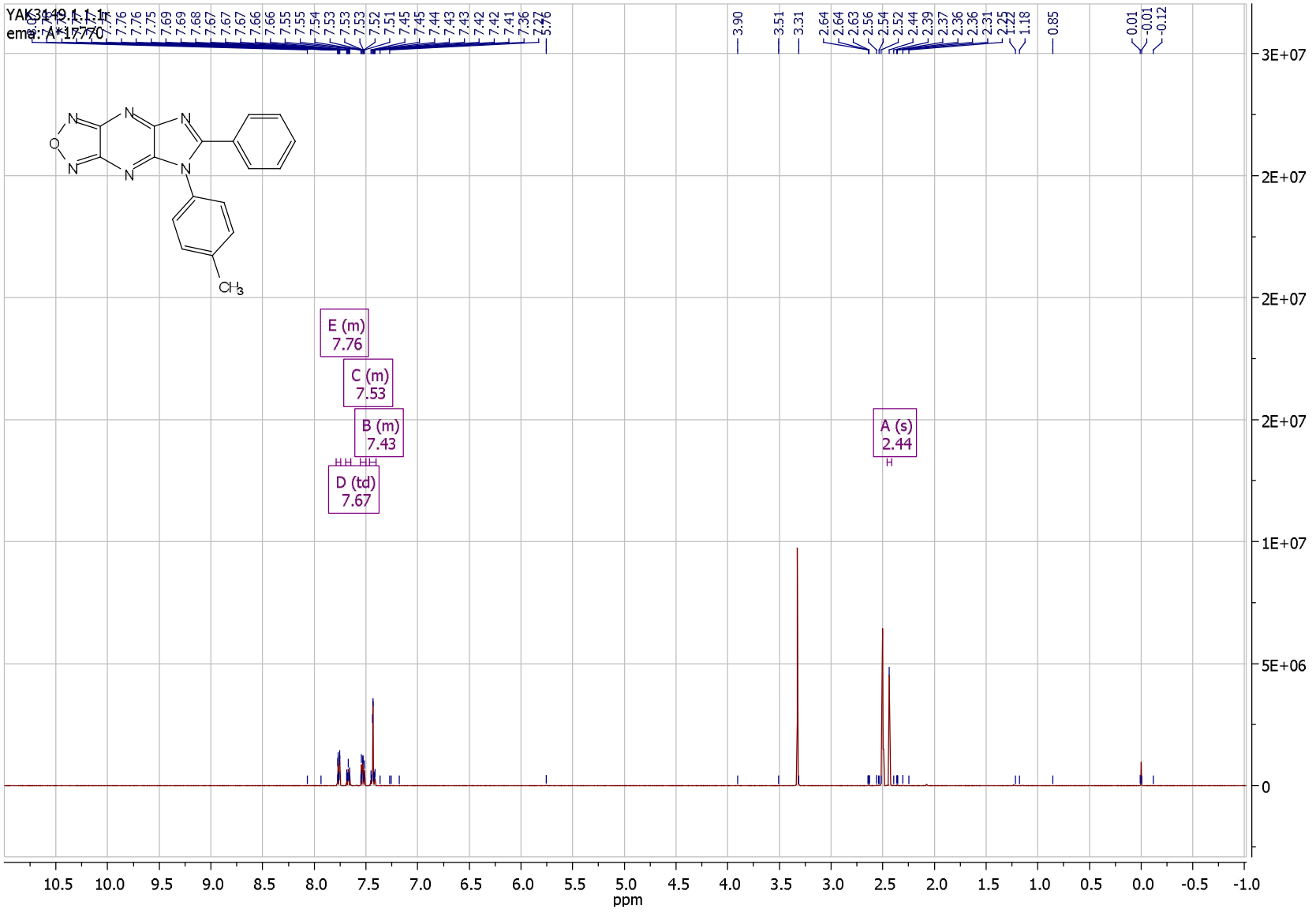
***(E)*-*N*-Phenyl-6-(pyrrolidin-1-ylmethylidenamino)[1,2,5]oxadiazolo[3,4-*e*]pyrazin-5-amine (9).**

Yield: 45 mg (72%); light yellow crystals; mp 282°C decomposition.

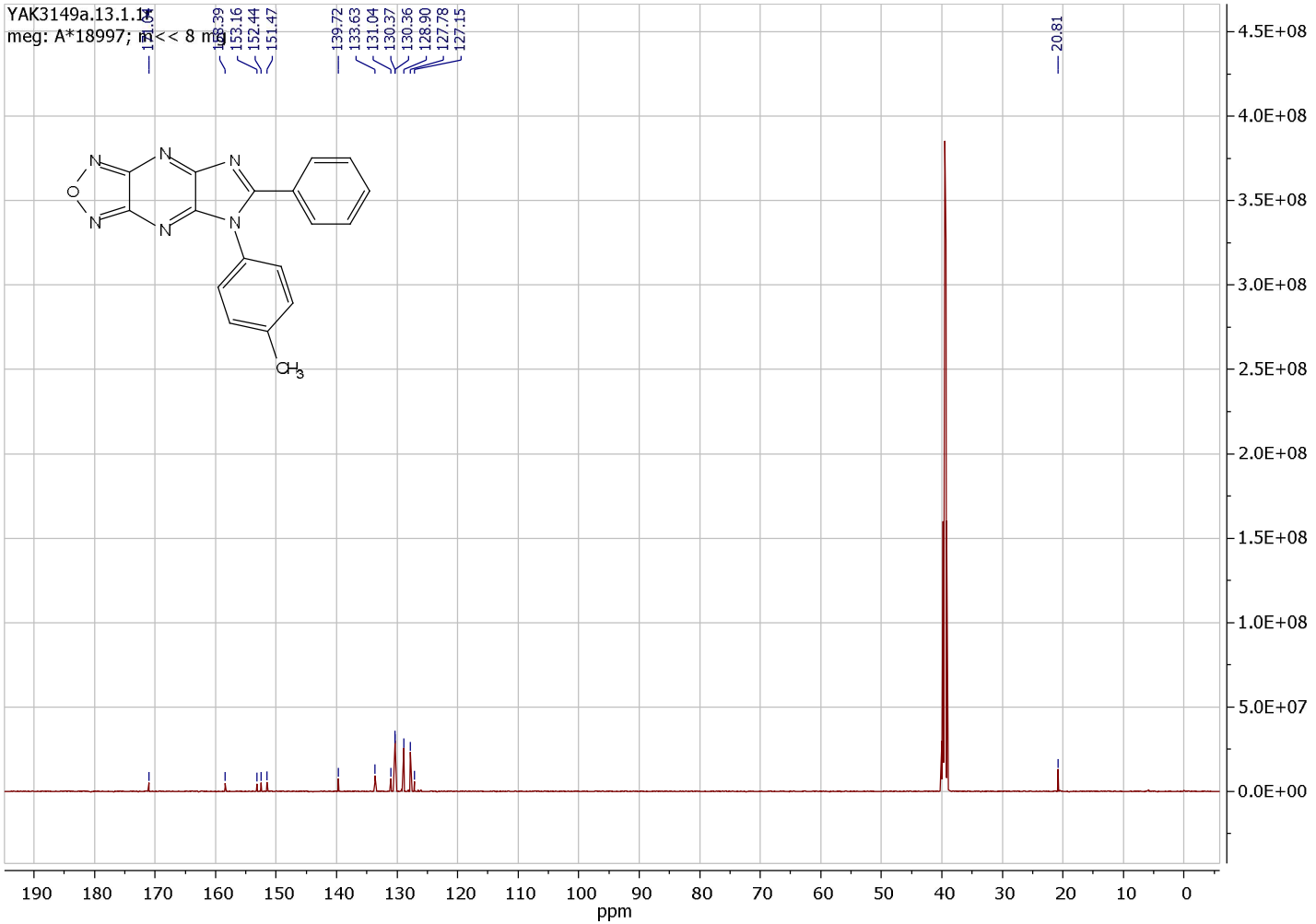
^{1}H NMR (500 MHz, DMSO-d_6): δ= 9.84 (s, 1H), 9.06 (s, 1H), 7.99 – 7.94 (m, 2H), 7.48 – 7.42 (m, 2H), 7.23 – 7.18 (m, 1H), 3.88 – 3.82 (m, 4H), 1.98 (dq, *J* = 13.0, 6.7 Hz, 4H).

^{13}C NMR (126 MHz, DMSO): δ= 155.28, 154.78, 150.91, 150.75, 150.12, 137.60, 128.75, 124.57, 121.36, 50.27, 46.90, 24.47, 23.76.

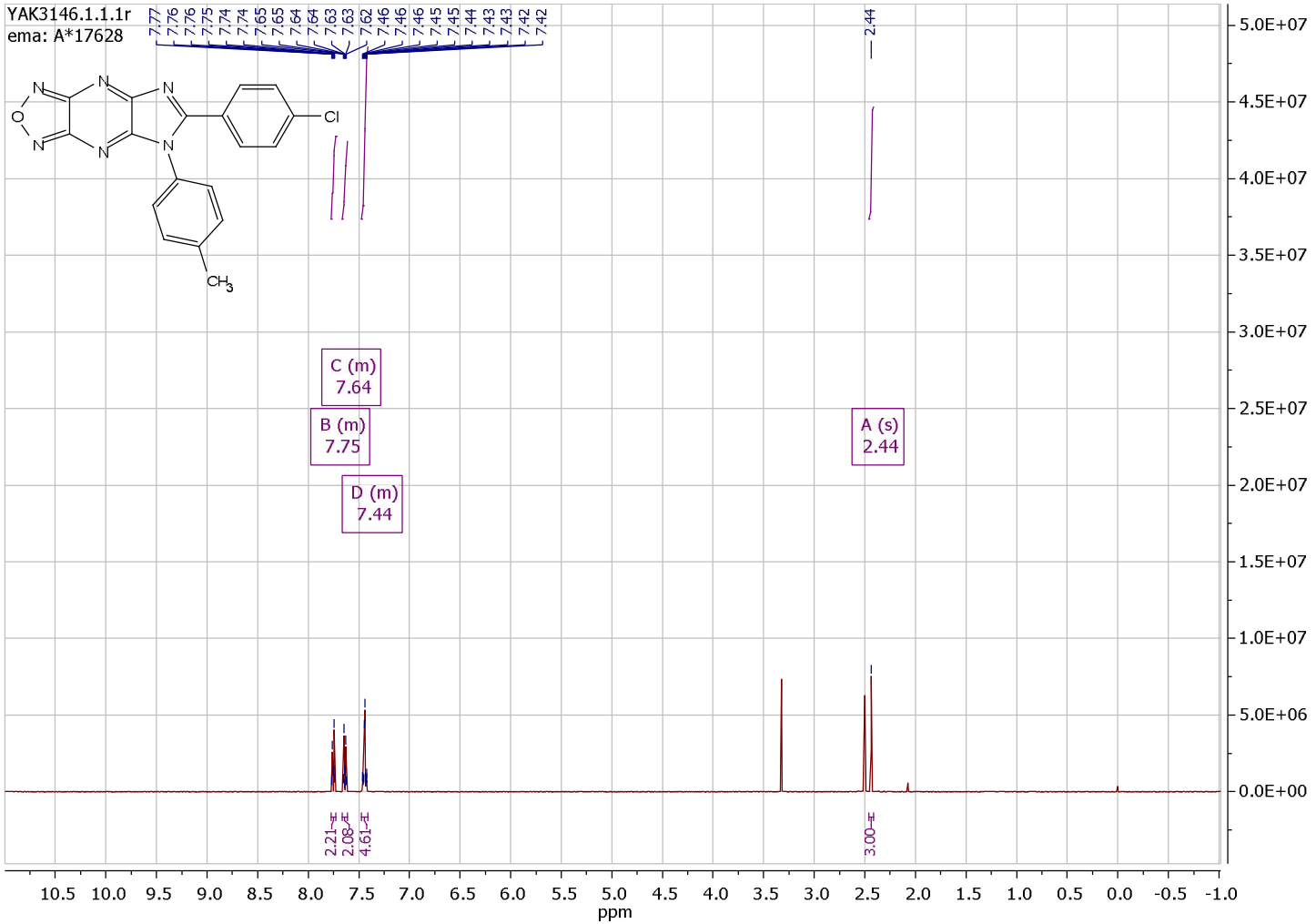
Anal.Calcd for $C_{15}H_{15}N_7O$:C, 58.24; H, 4.89; N, 31.70. Found: C, 58.09; H, 5.01; N, 31.61.



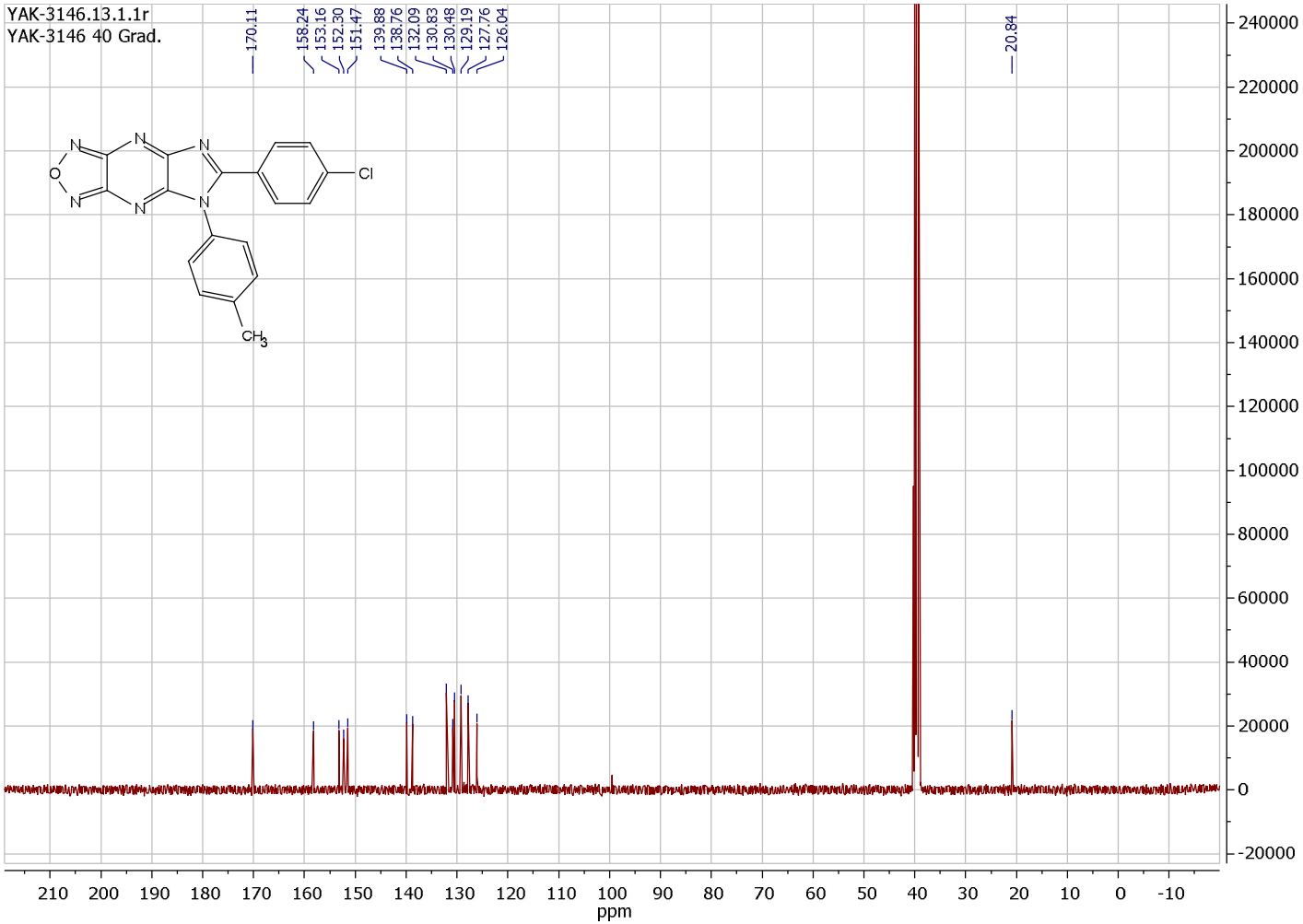
^{1}H NMR of compound **3a**



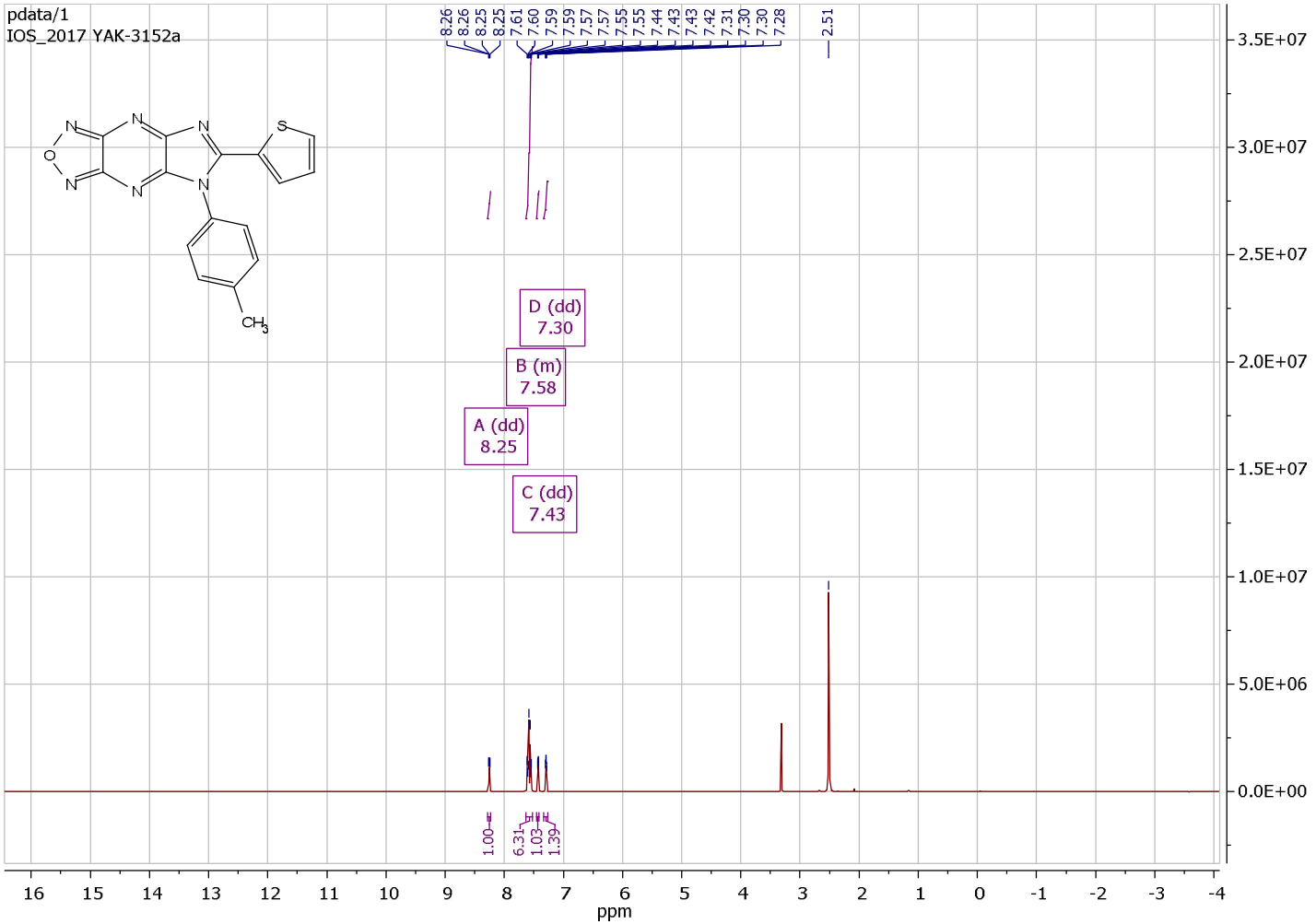
^{13}C NMR ofcompound **3a**



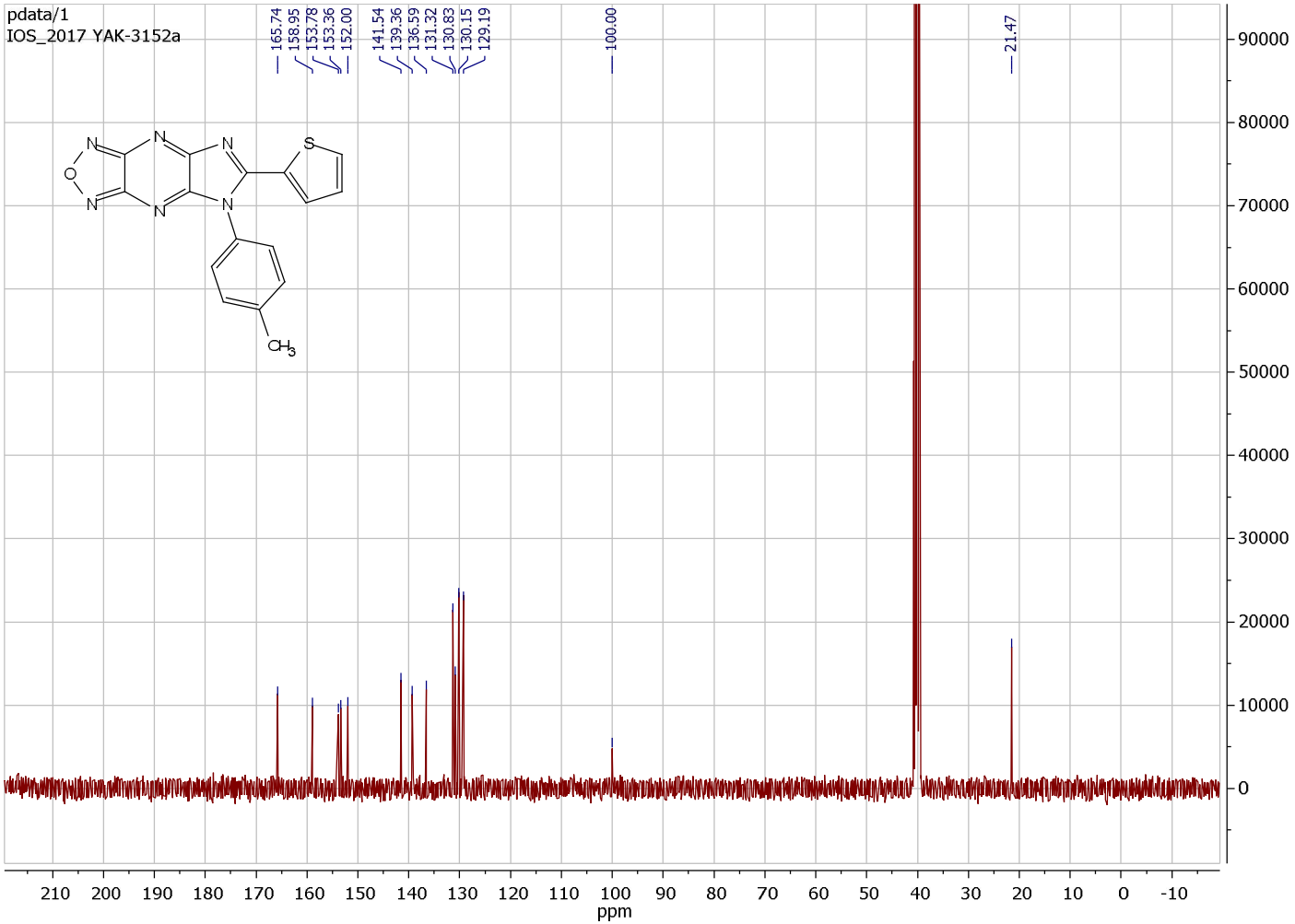
^{1}H NMR of compound **3b**



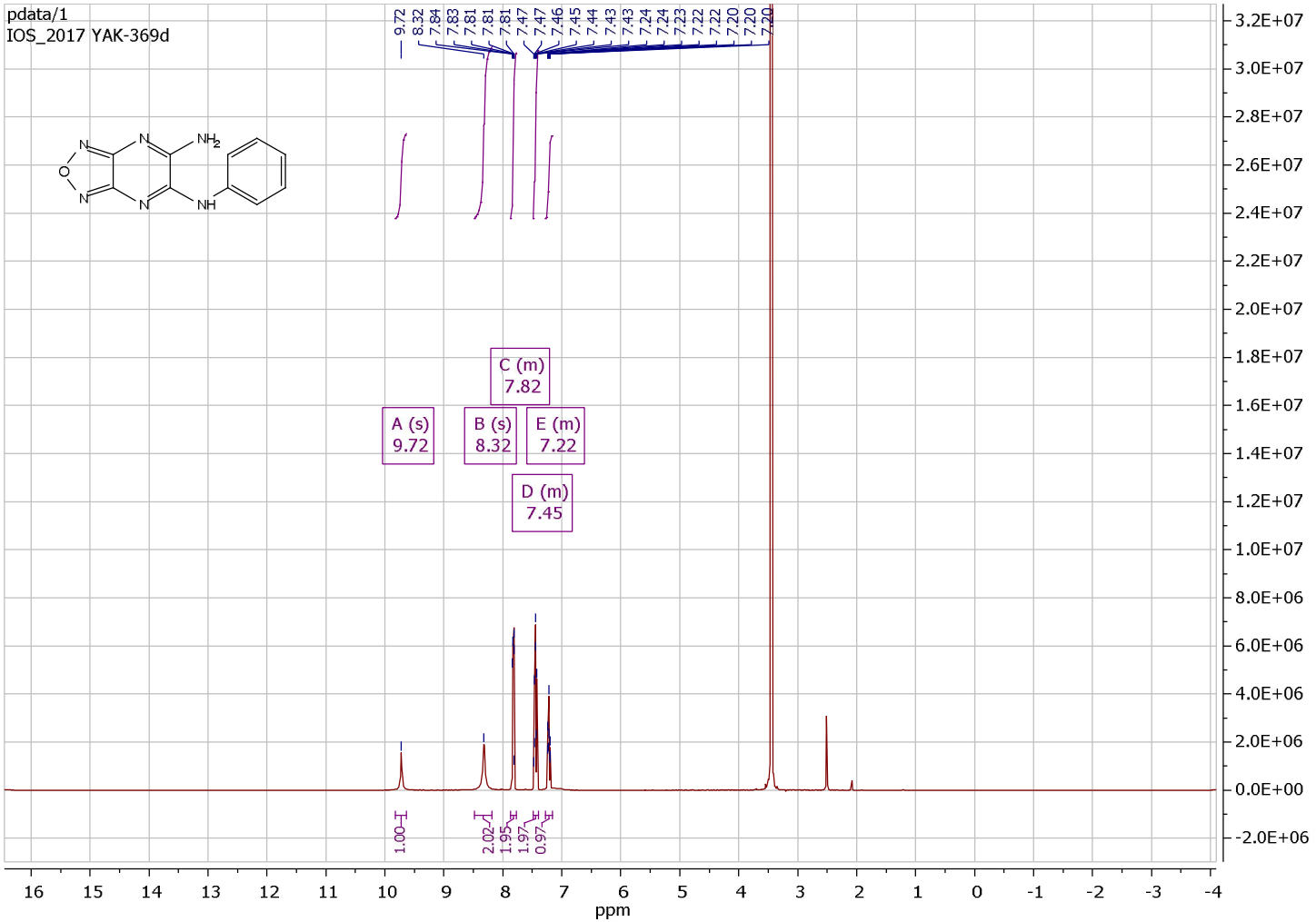
^{13}C NMR of compound **3b**



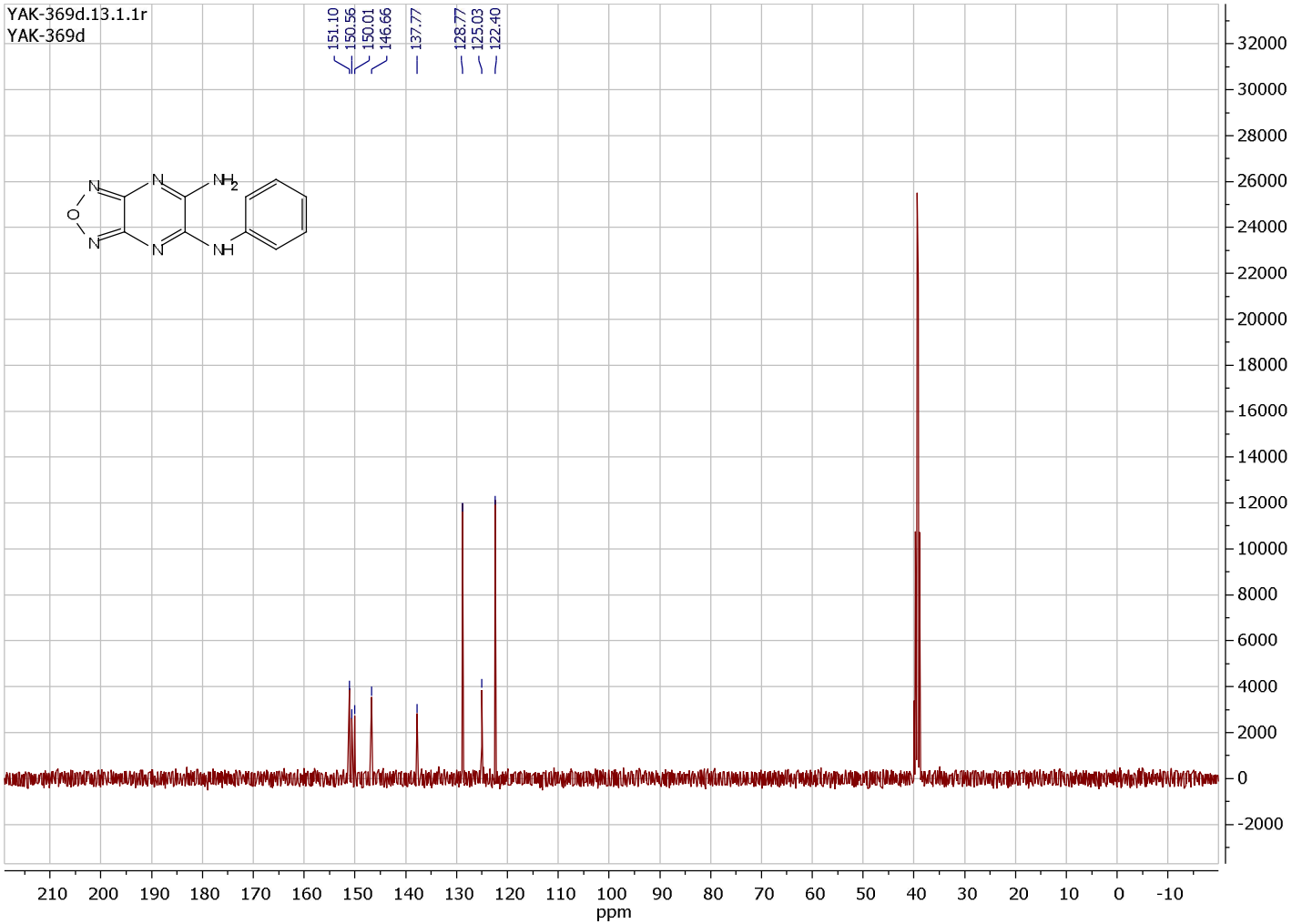
^{1}H NMR of compound **3c**



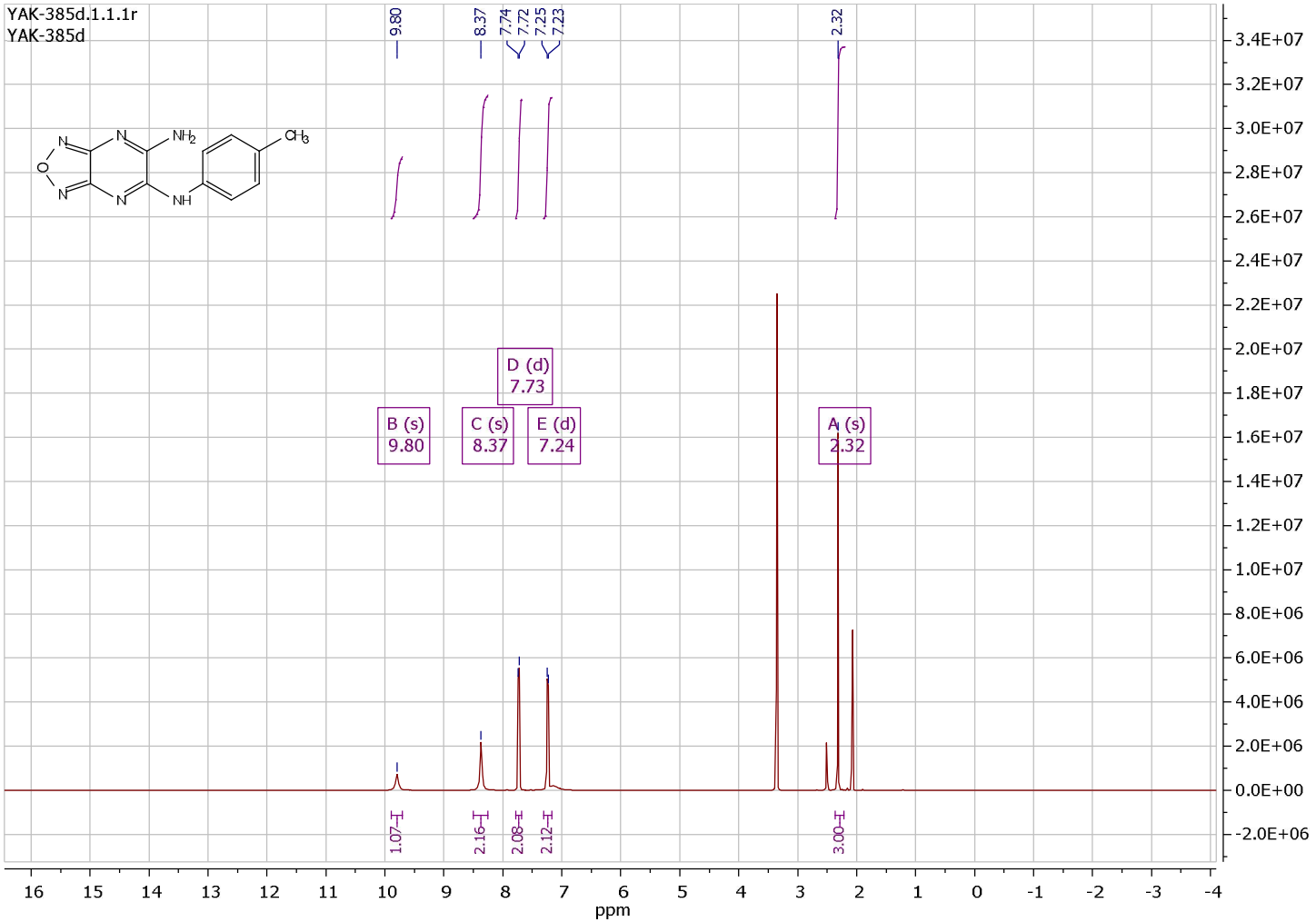
^{13}C NMR of compound **3c**



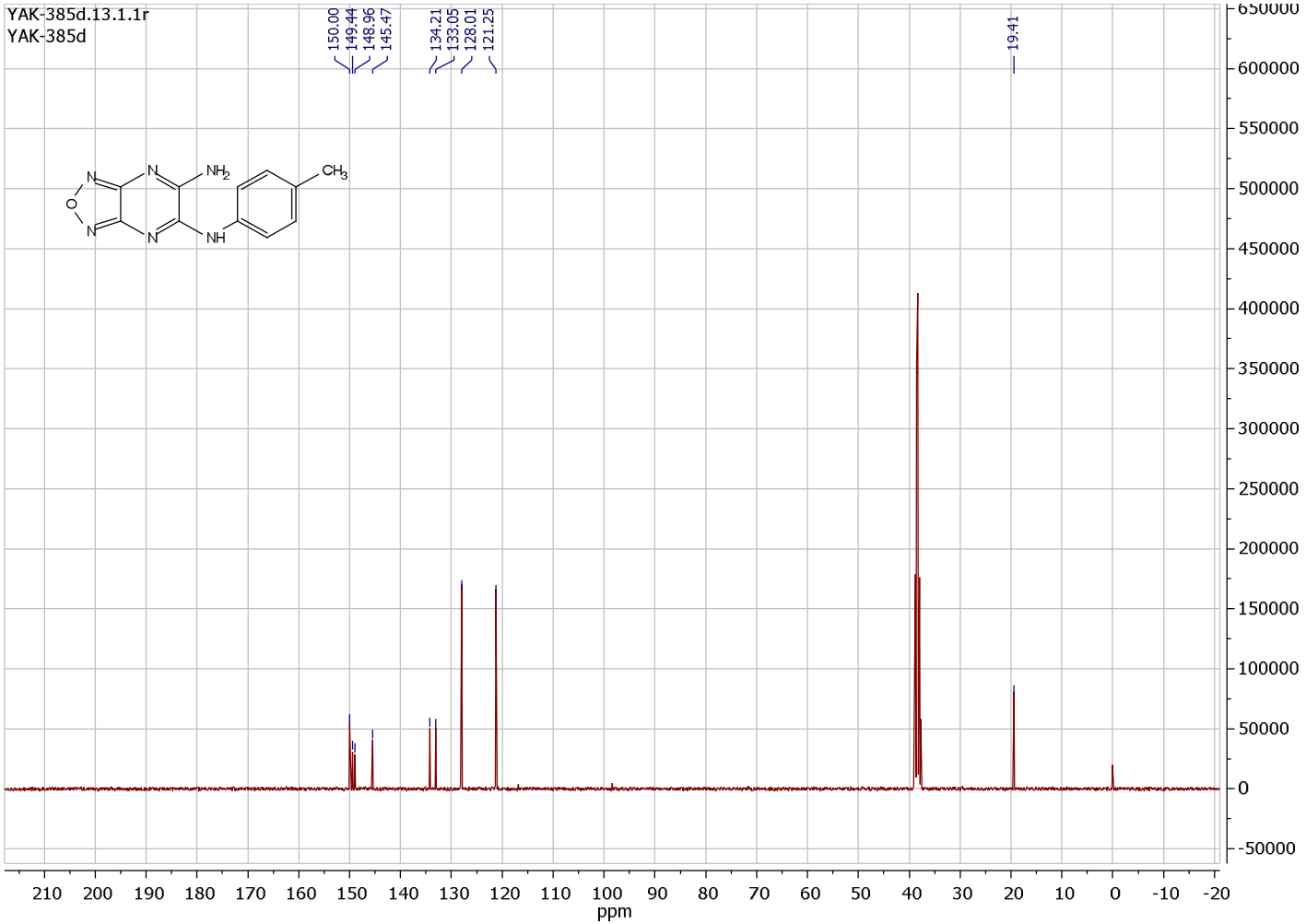
[1]H NMR of compound **4a**



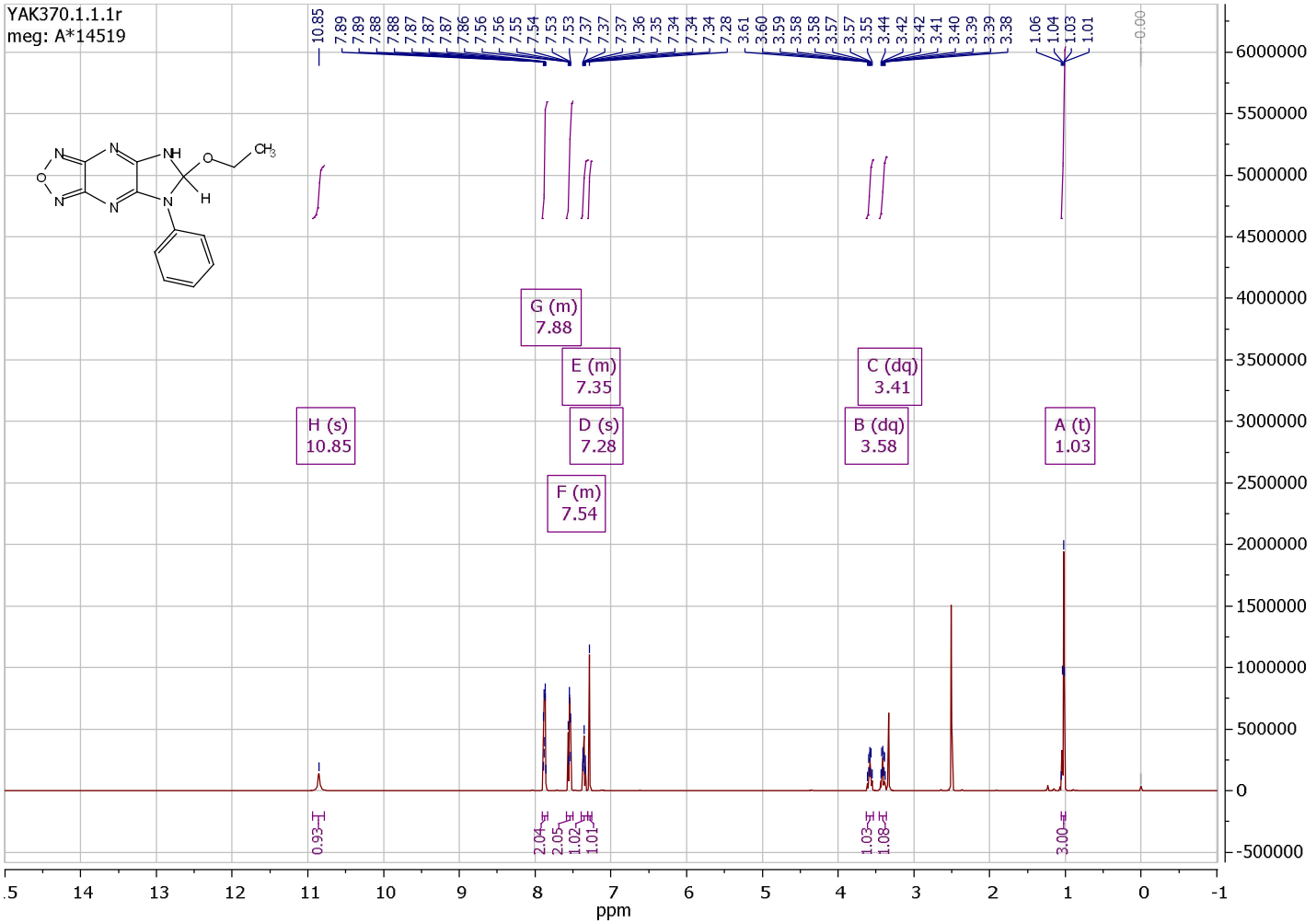
^{13}C NMR ofcompound **4a**



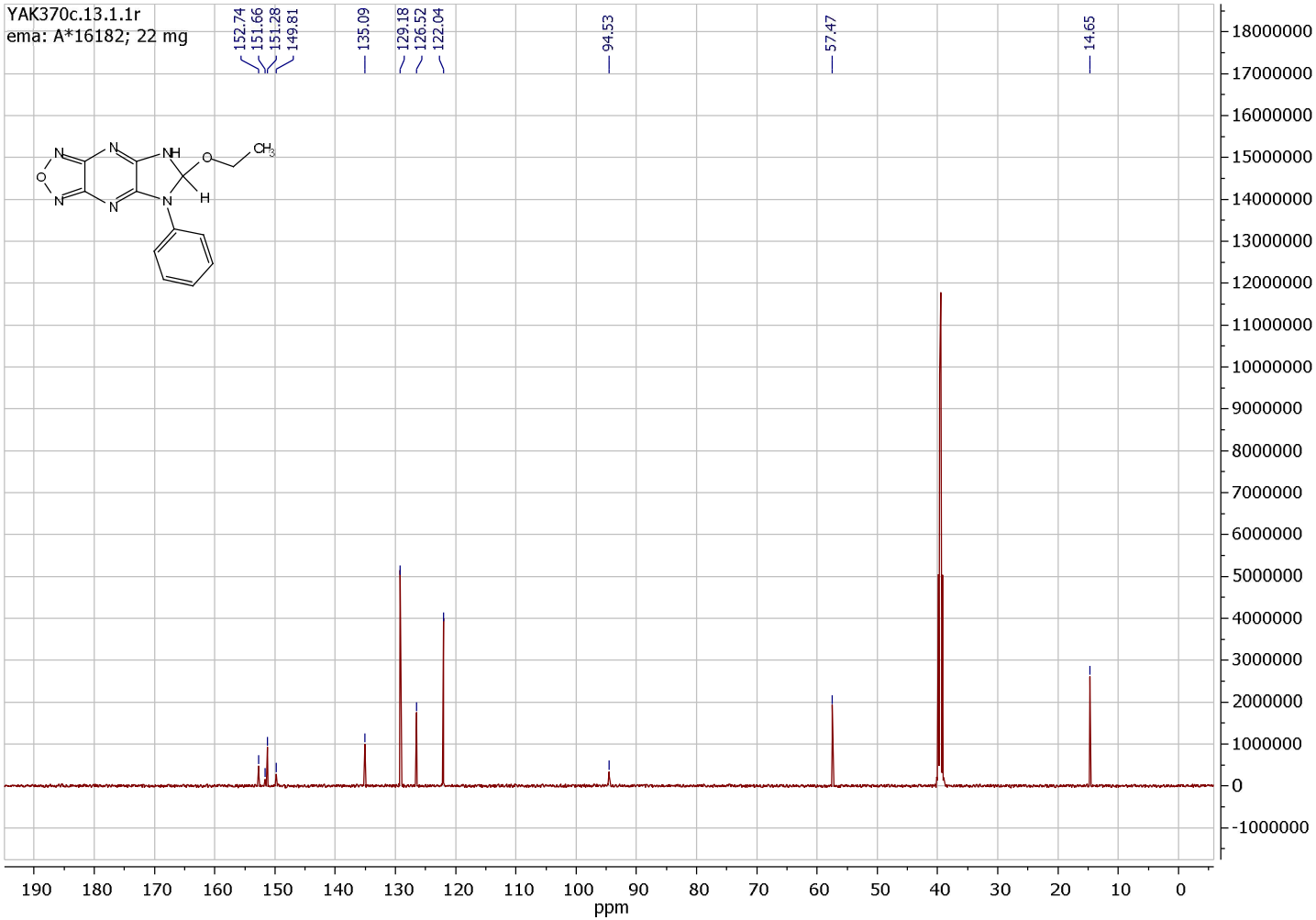
[1]H NMR of compound **4b**



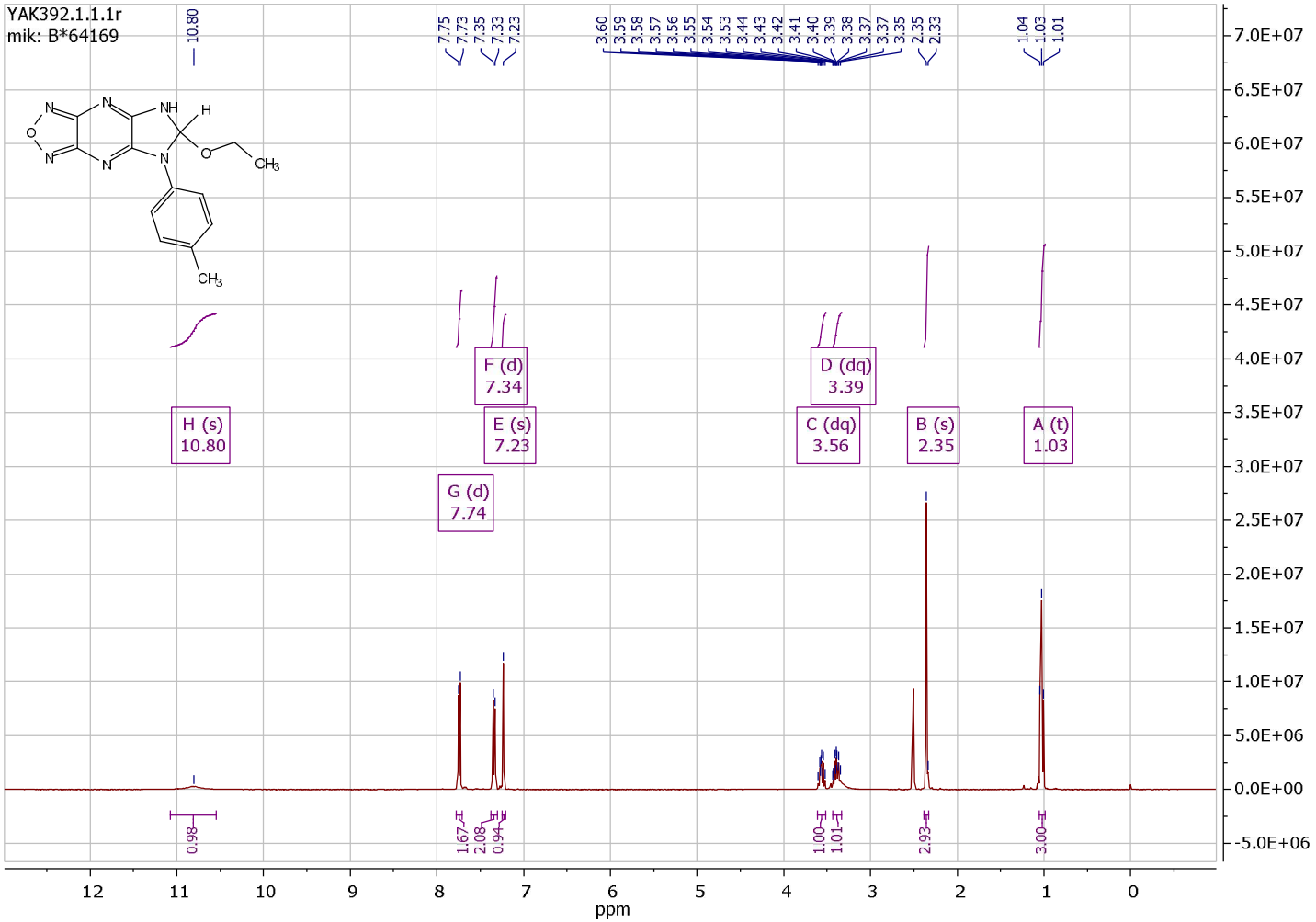
^{13}C NMR ofcompound **4b**



^{1}H NMR of compound **5a**



^{13}C NMR ofcompound **5a**



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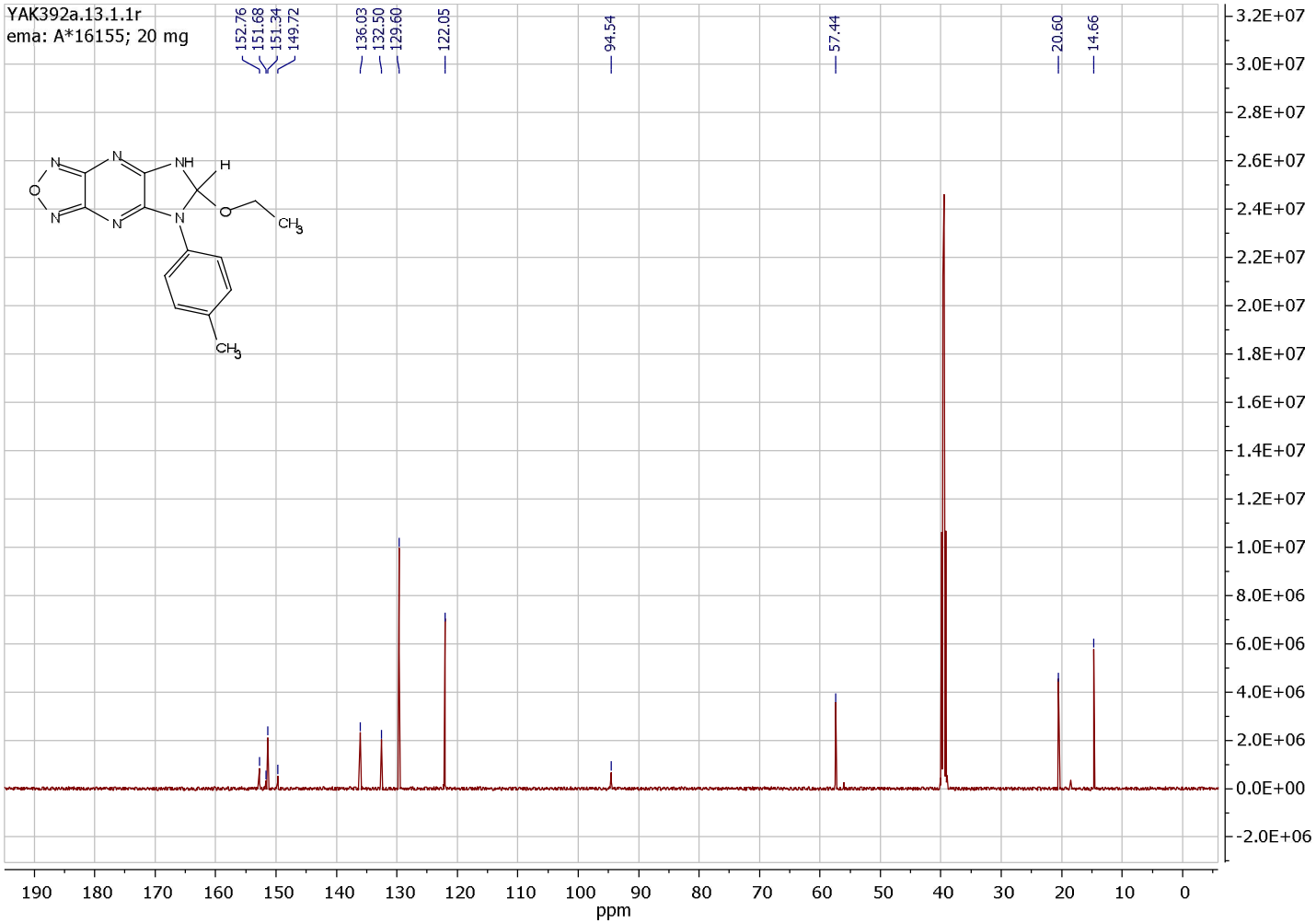
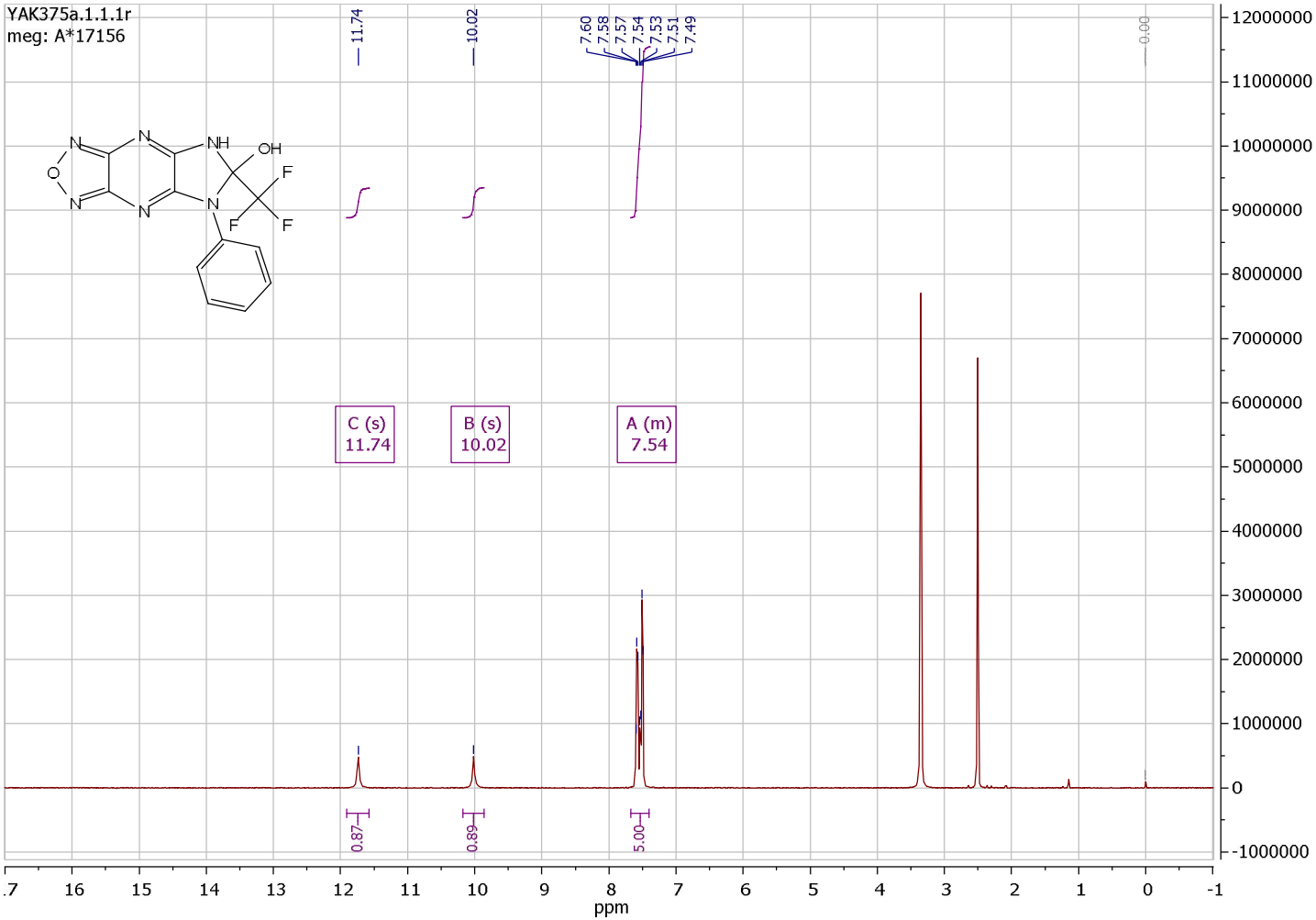
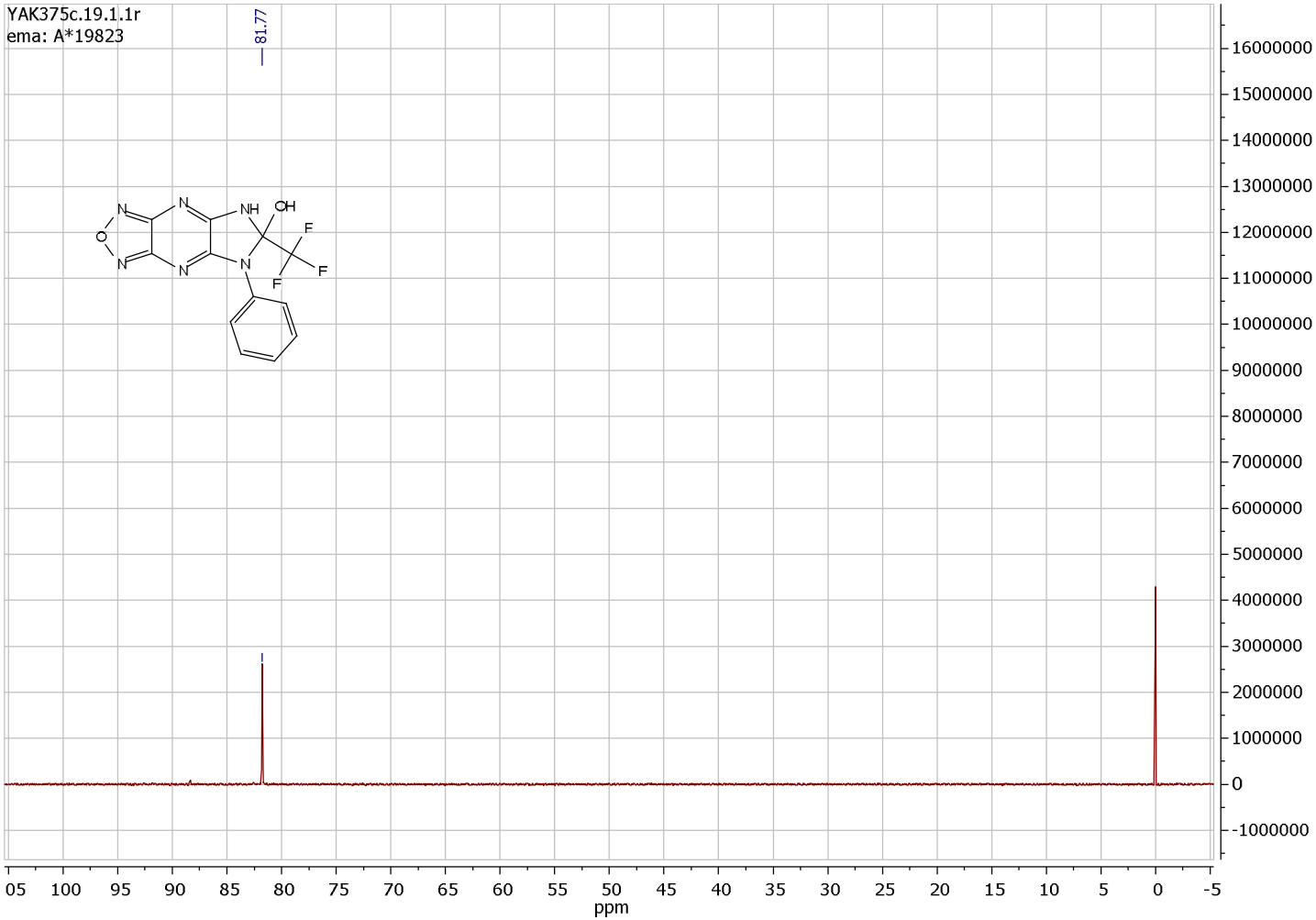


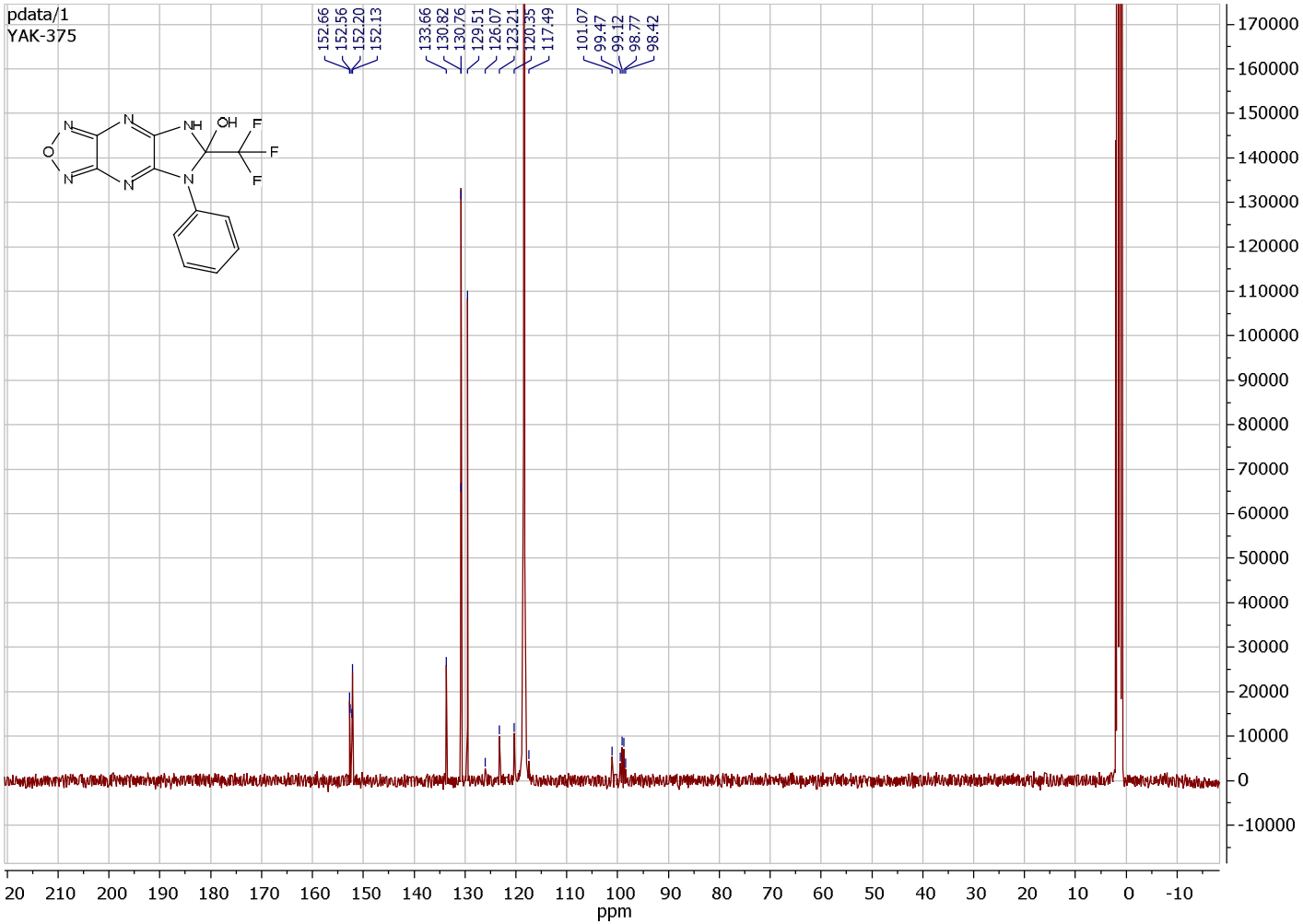
^{13}C NMR of compound **5b**



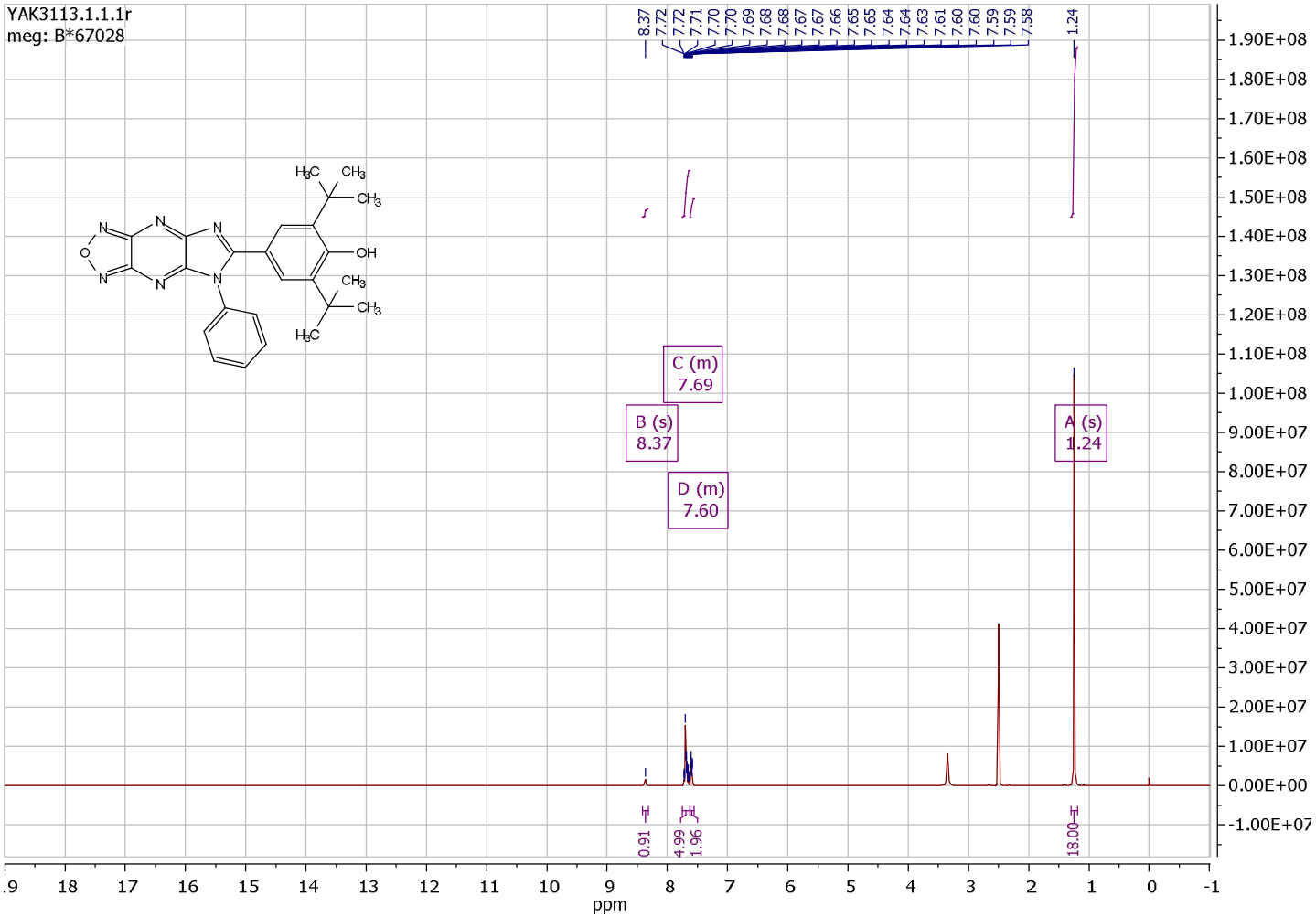
^{1}H NMR ofcompound **6**



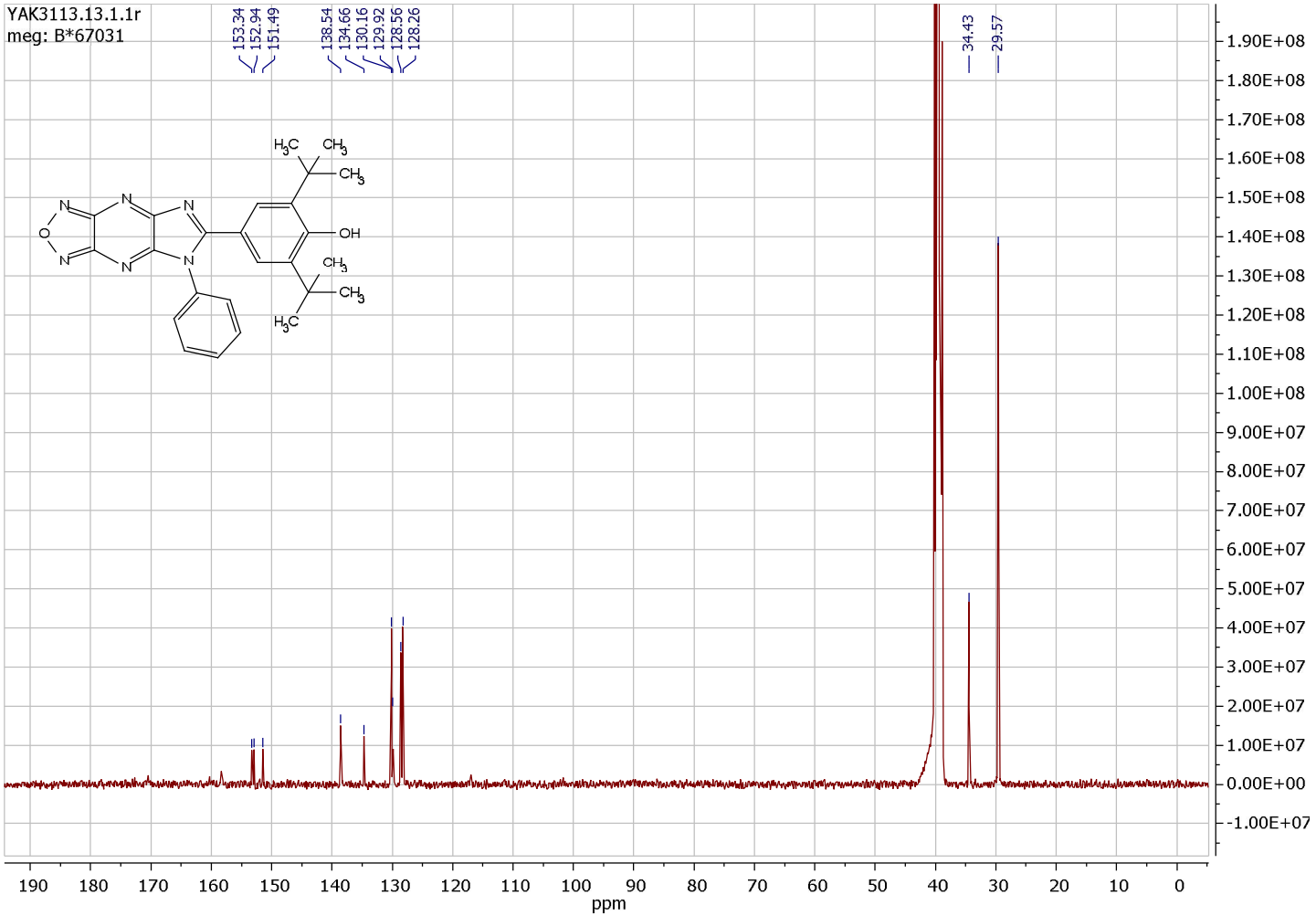
^{19}F NMR ofcompound **6**



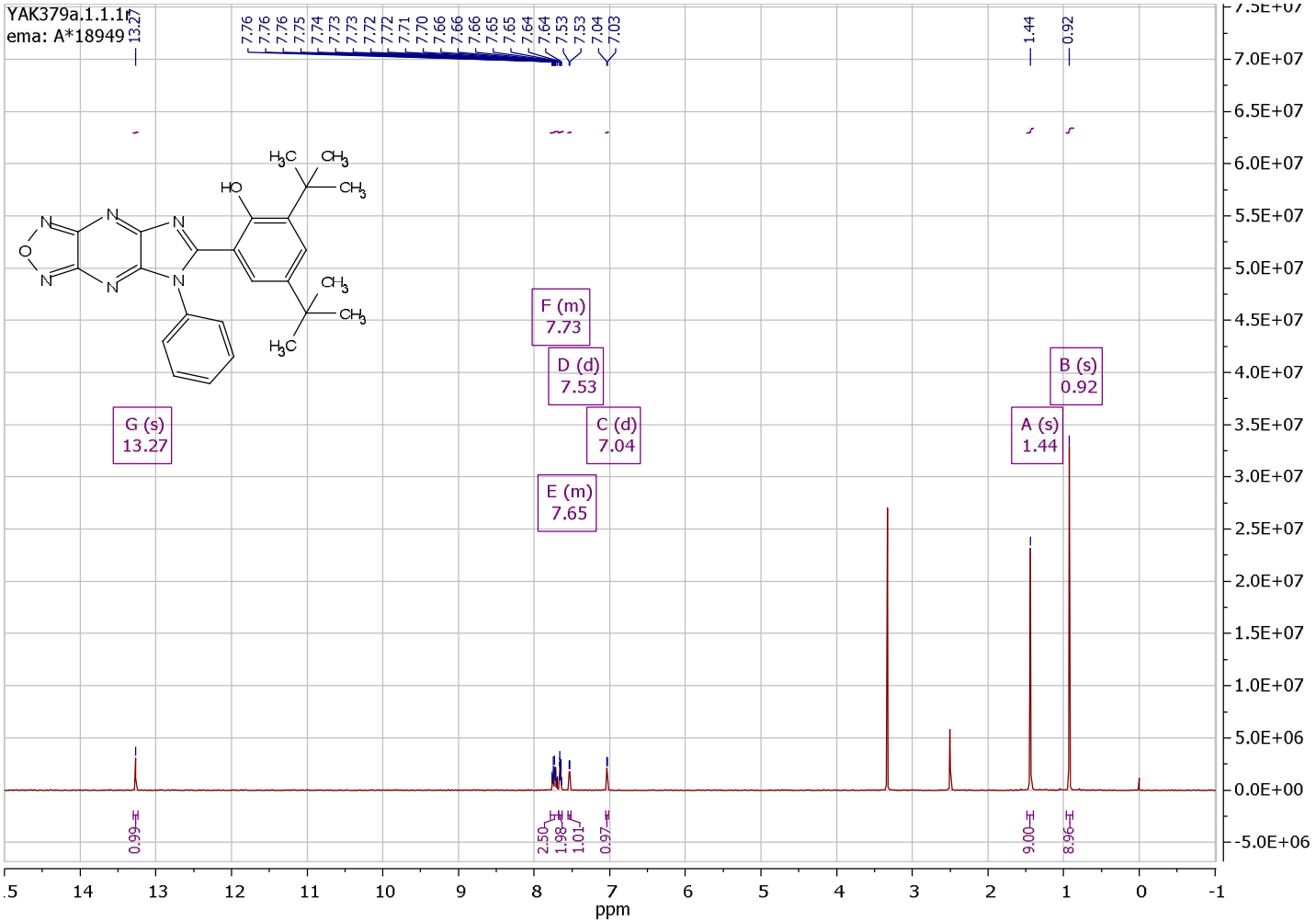
^{13}C NMR ofcompound **6**



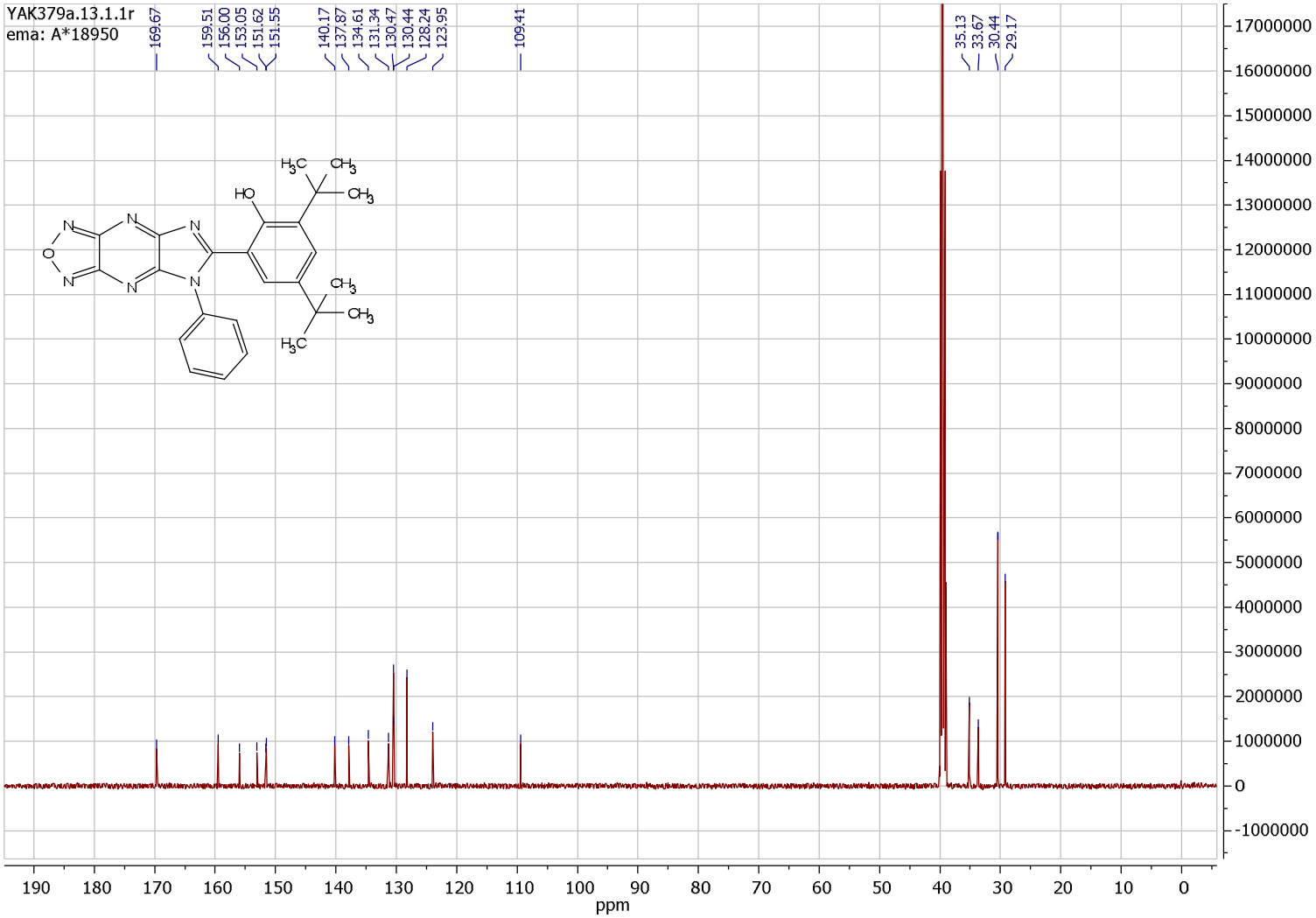
^{1}H NMR of compound **7a**



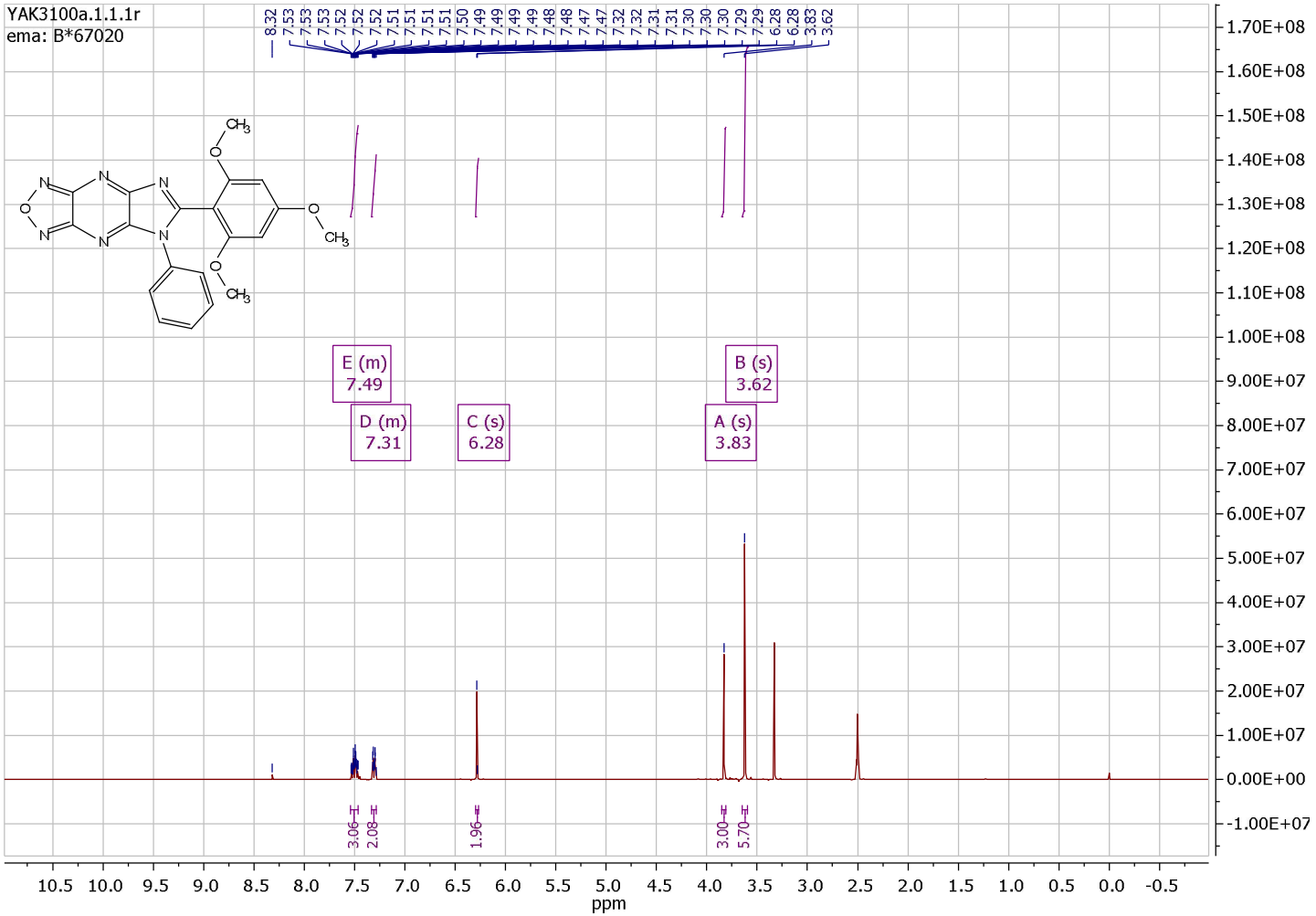
^{13}C NMR of compound **7a**



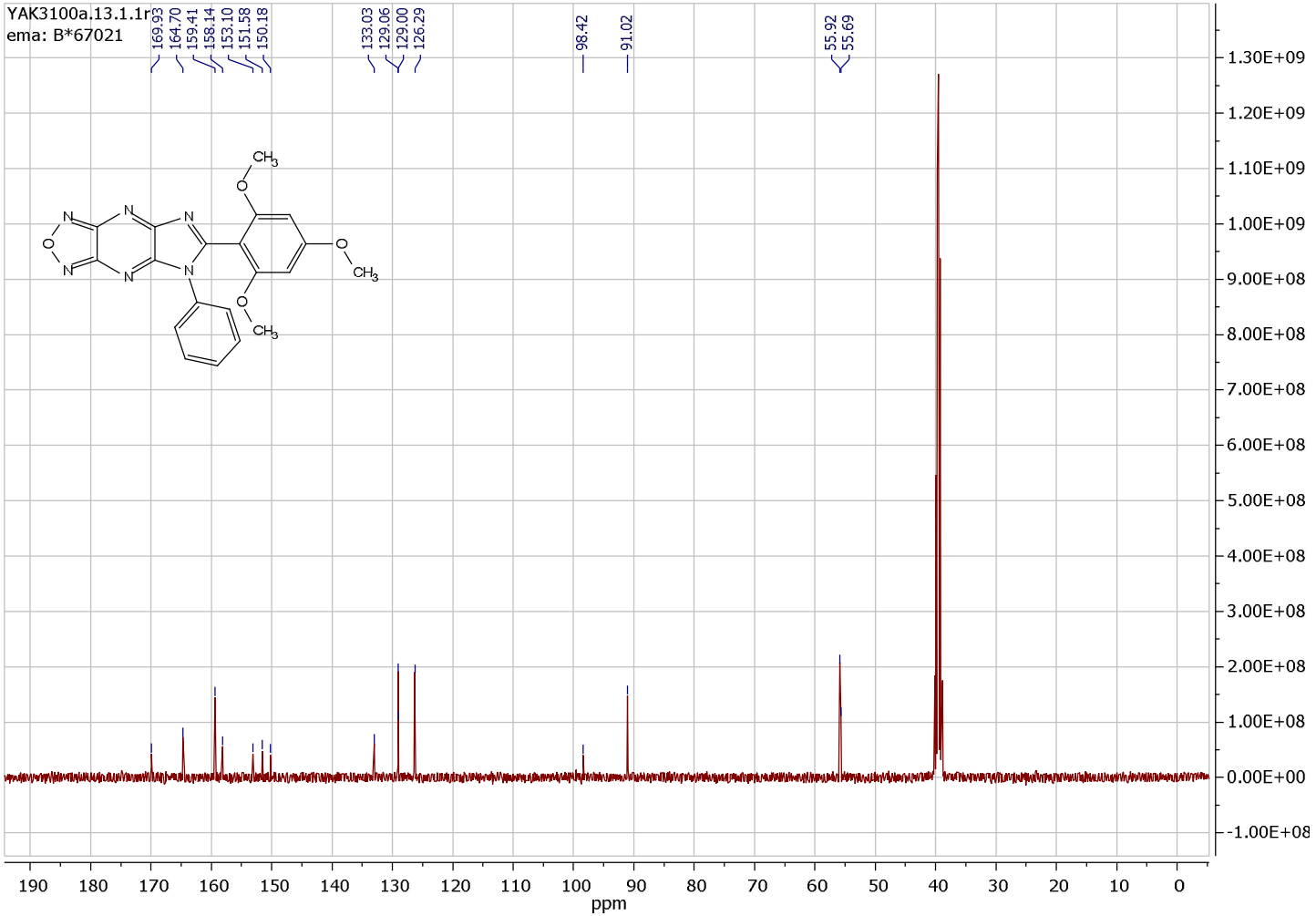
^{1}H NMR of compound **7b**



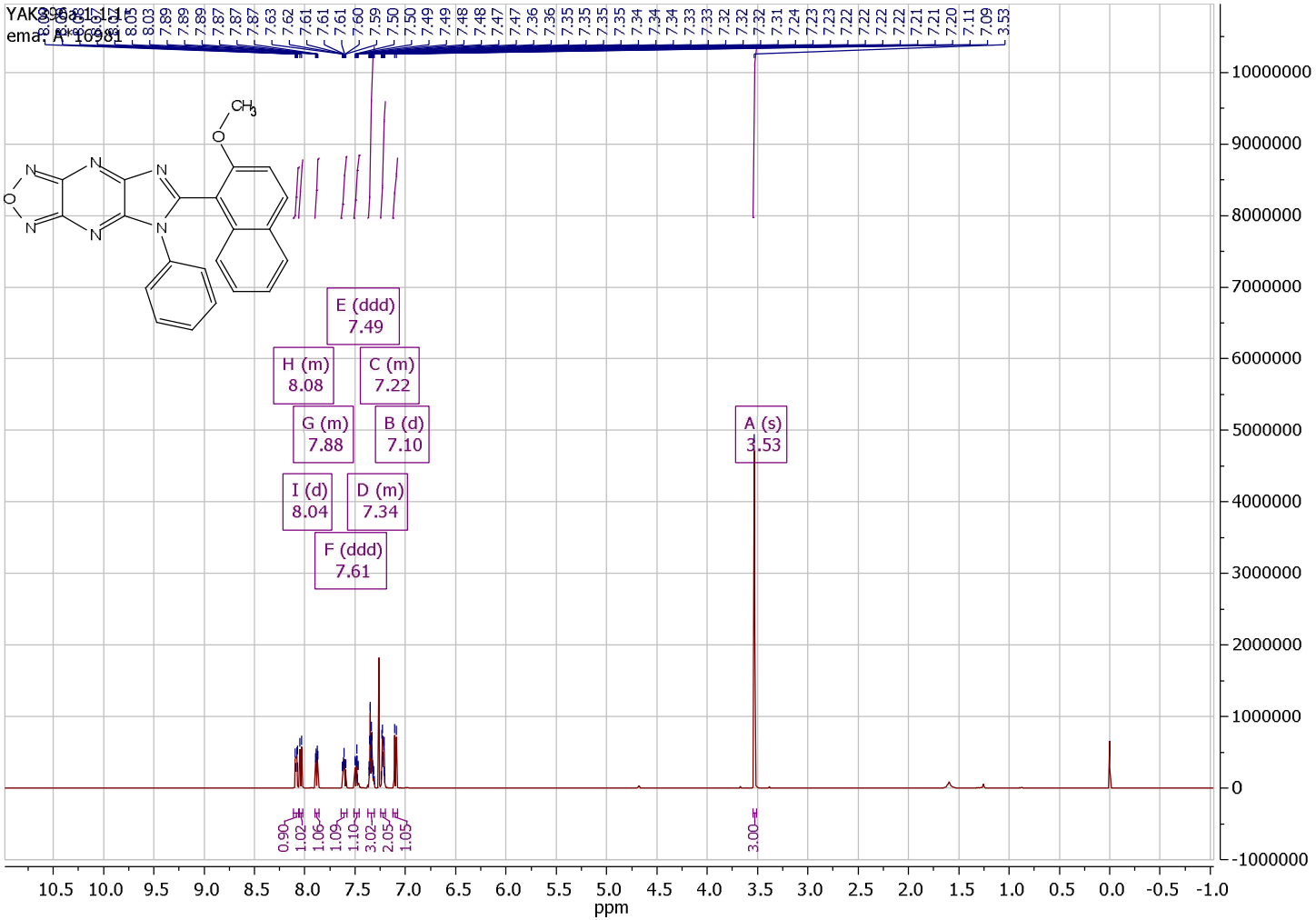
^{13}C NMR ofcompound **7b**



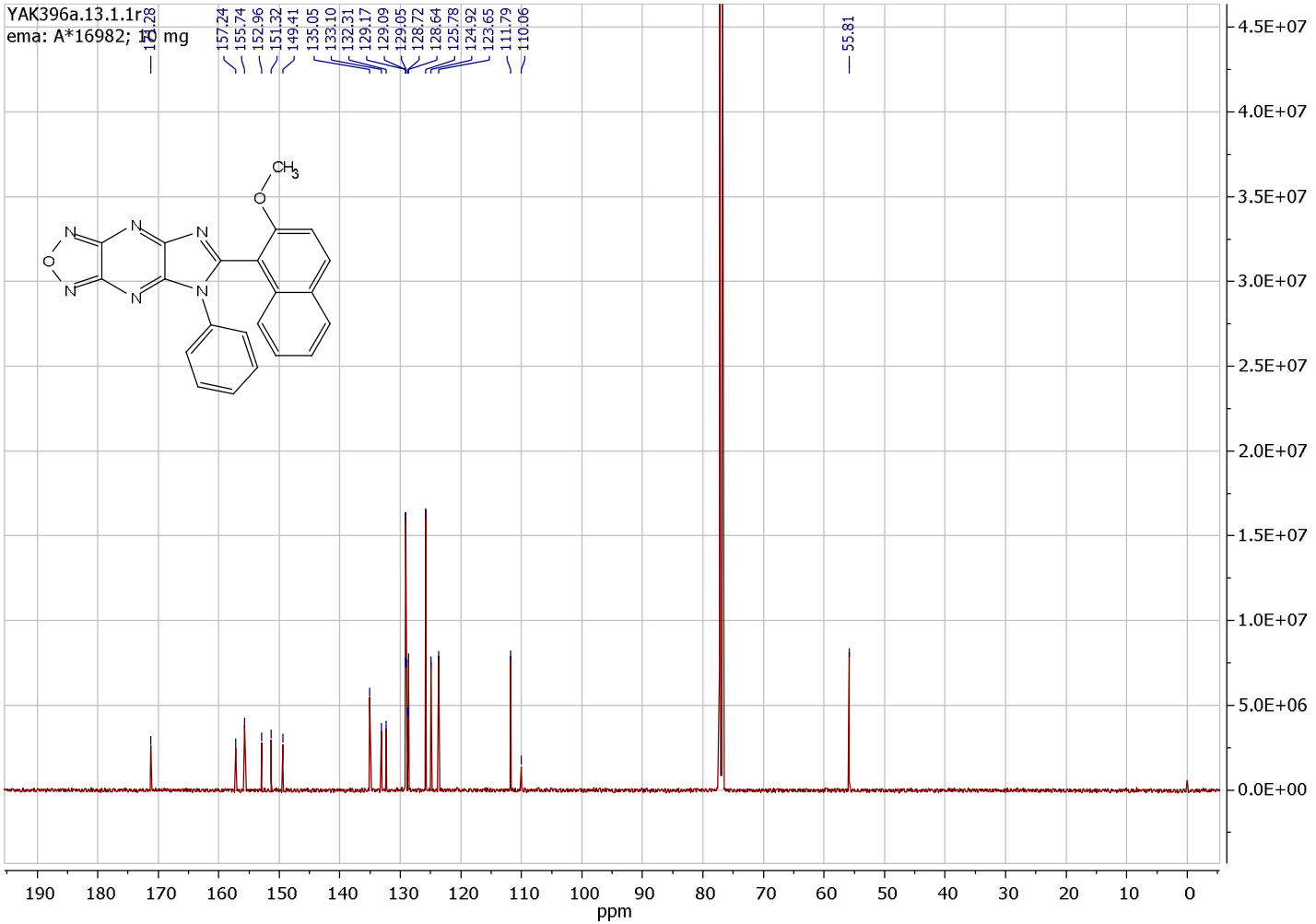
^{1}H NMR of compound **7c**



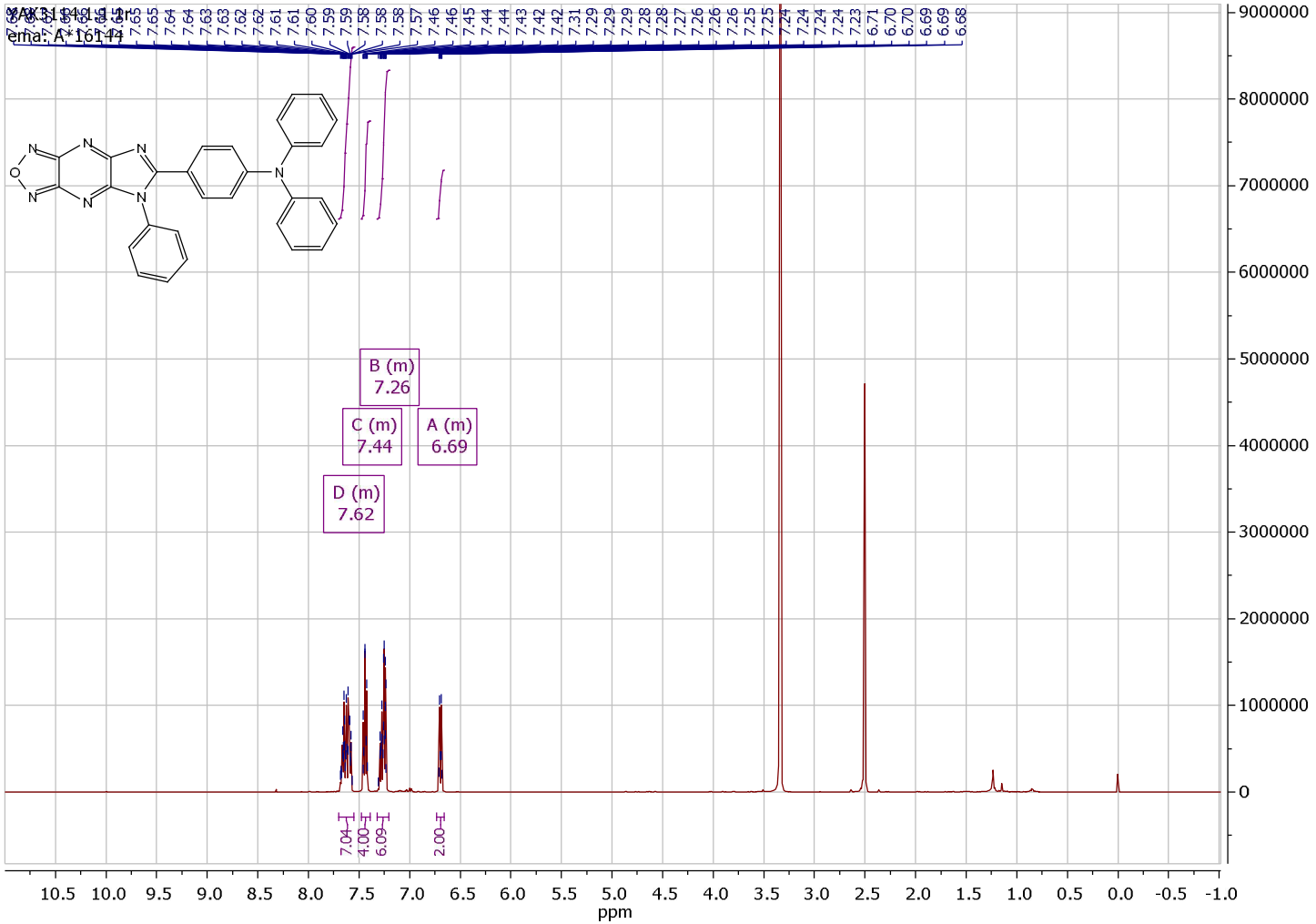
^{13}C NMR of compound **7c**



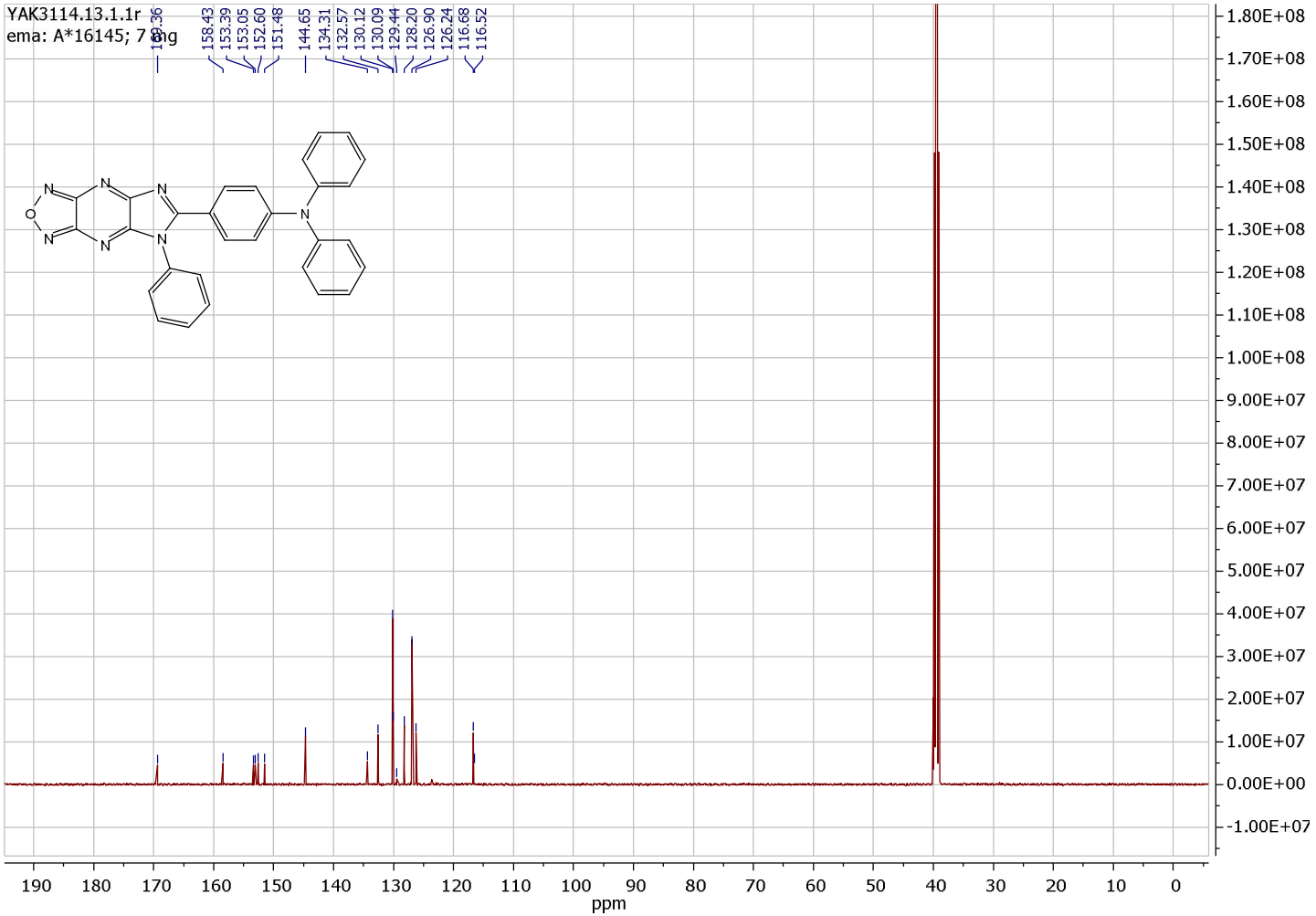
[1]H NMR of compound **7d**



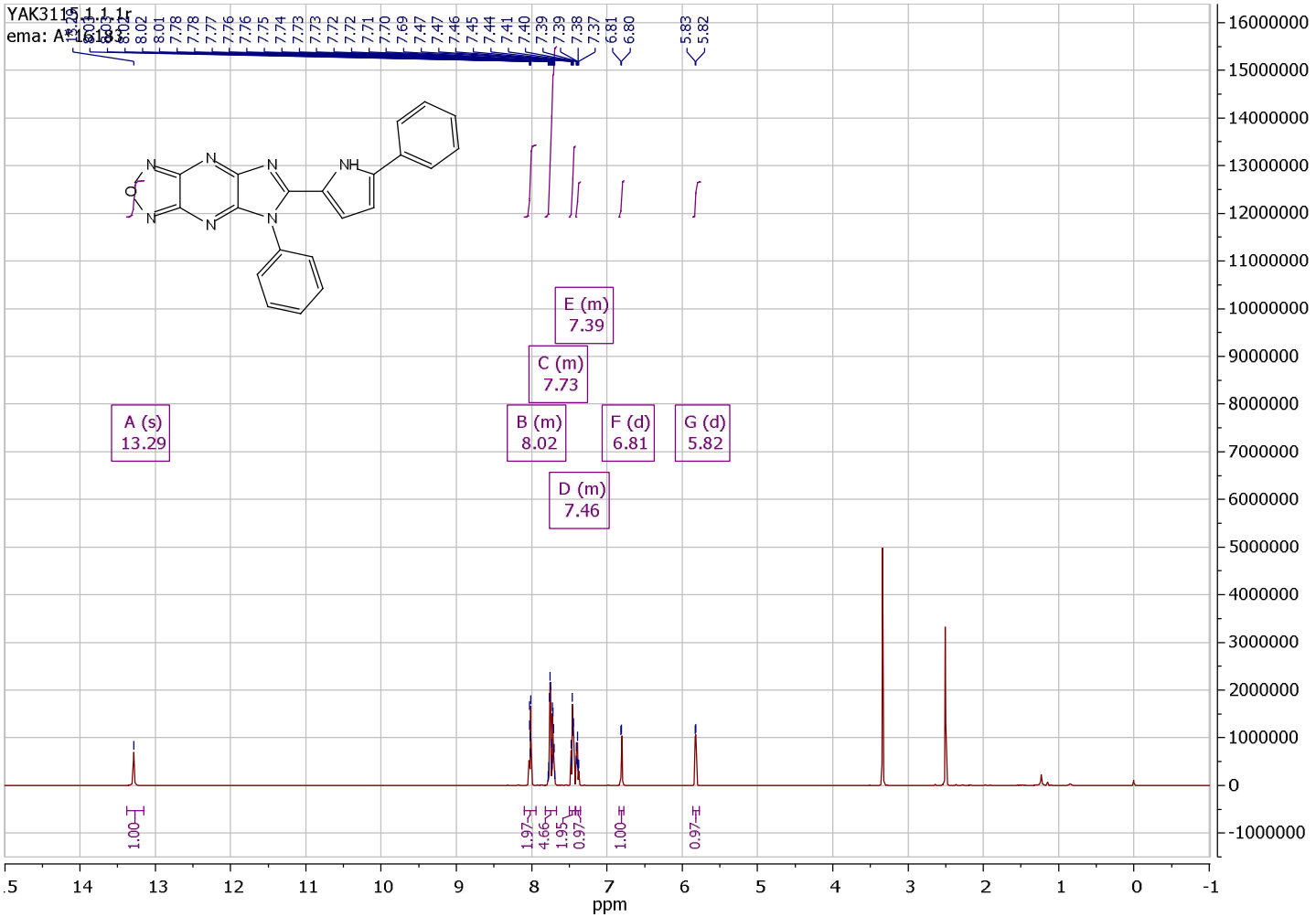
^{13}C NMR ofcompound **7d**



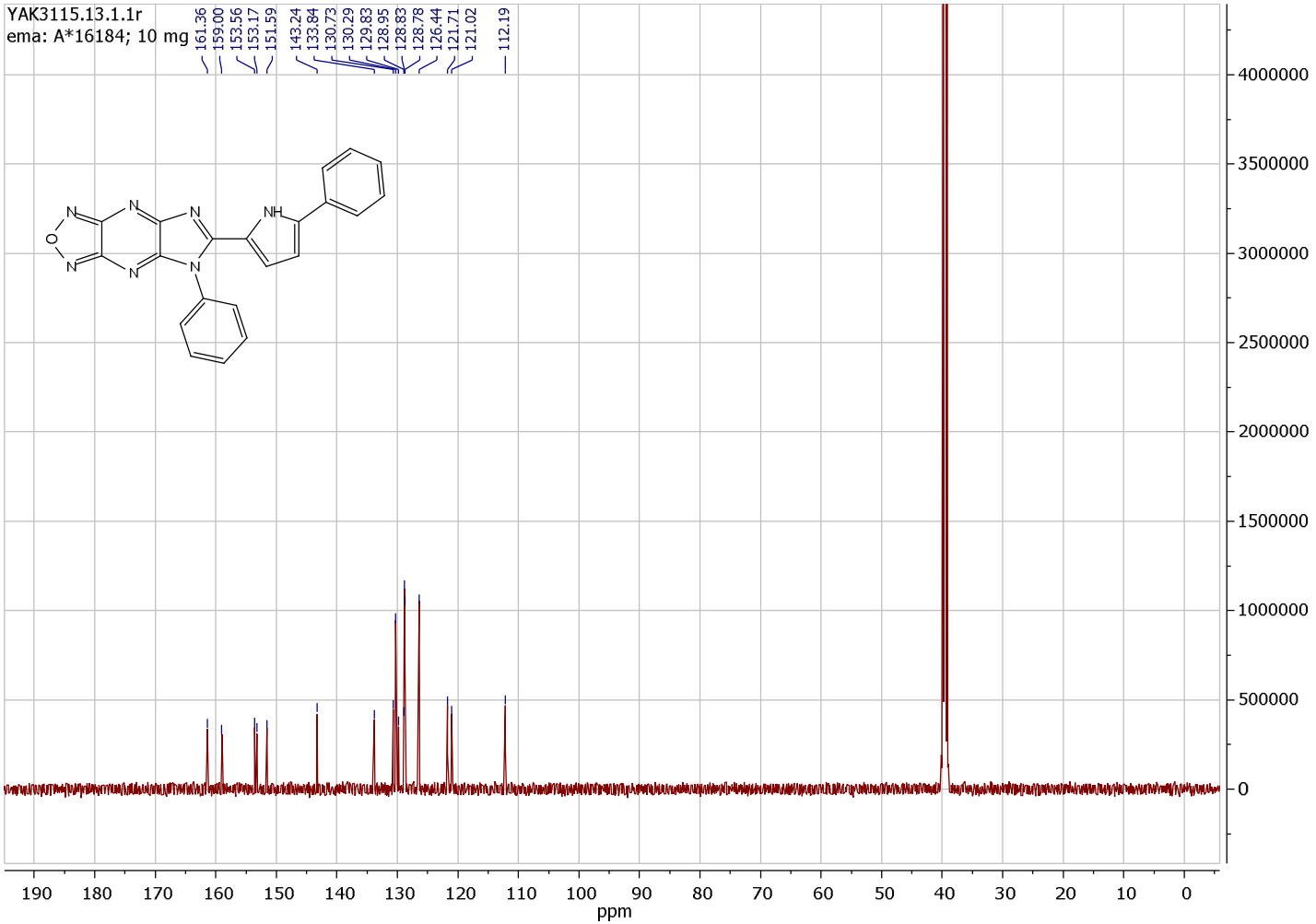
^{1}H NMR ofcompound **7e**



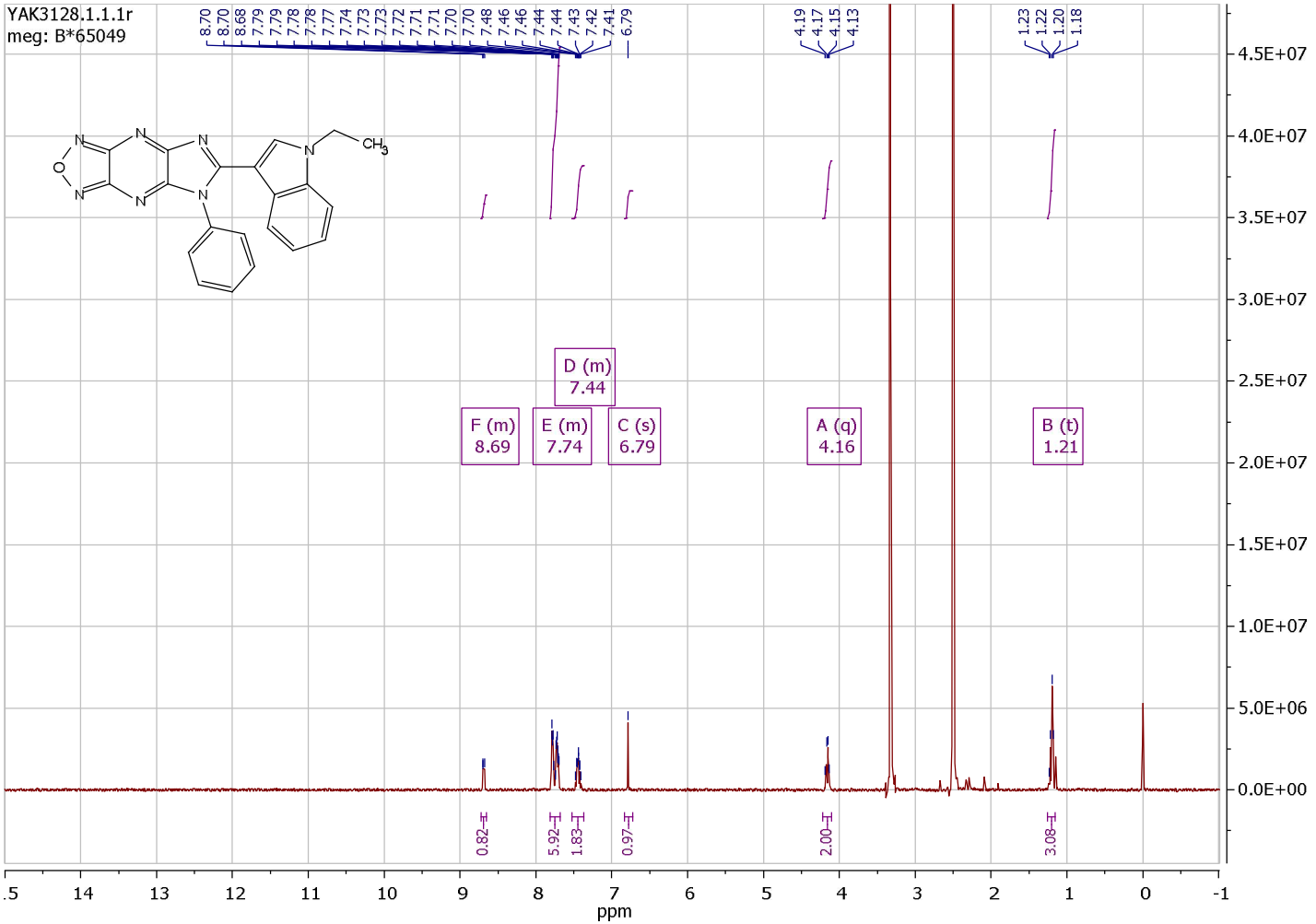
^{13}C NMR ofcompound **7e**



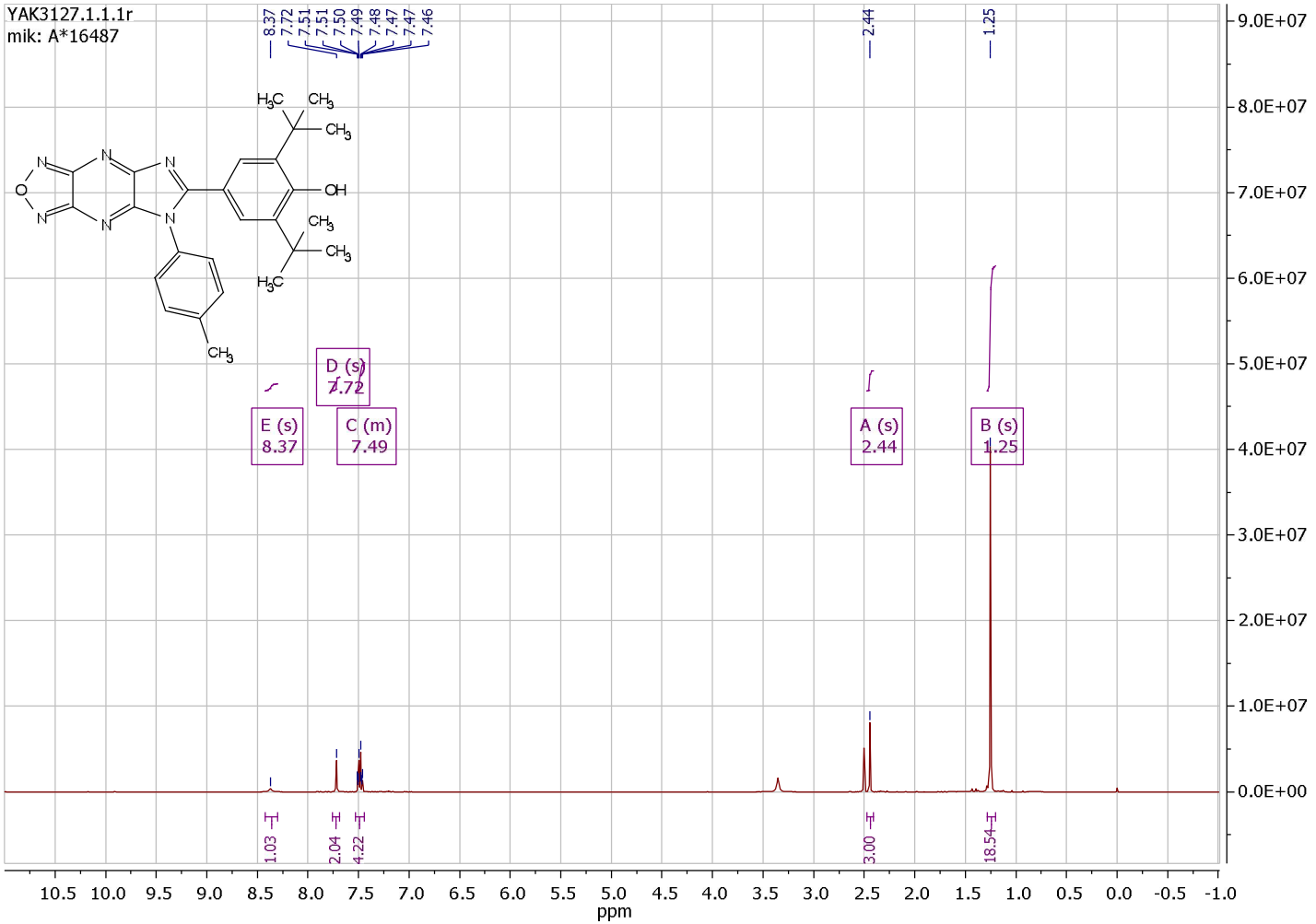
^{1}H NMR of compound **7f**



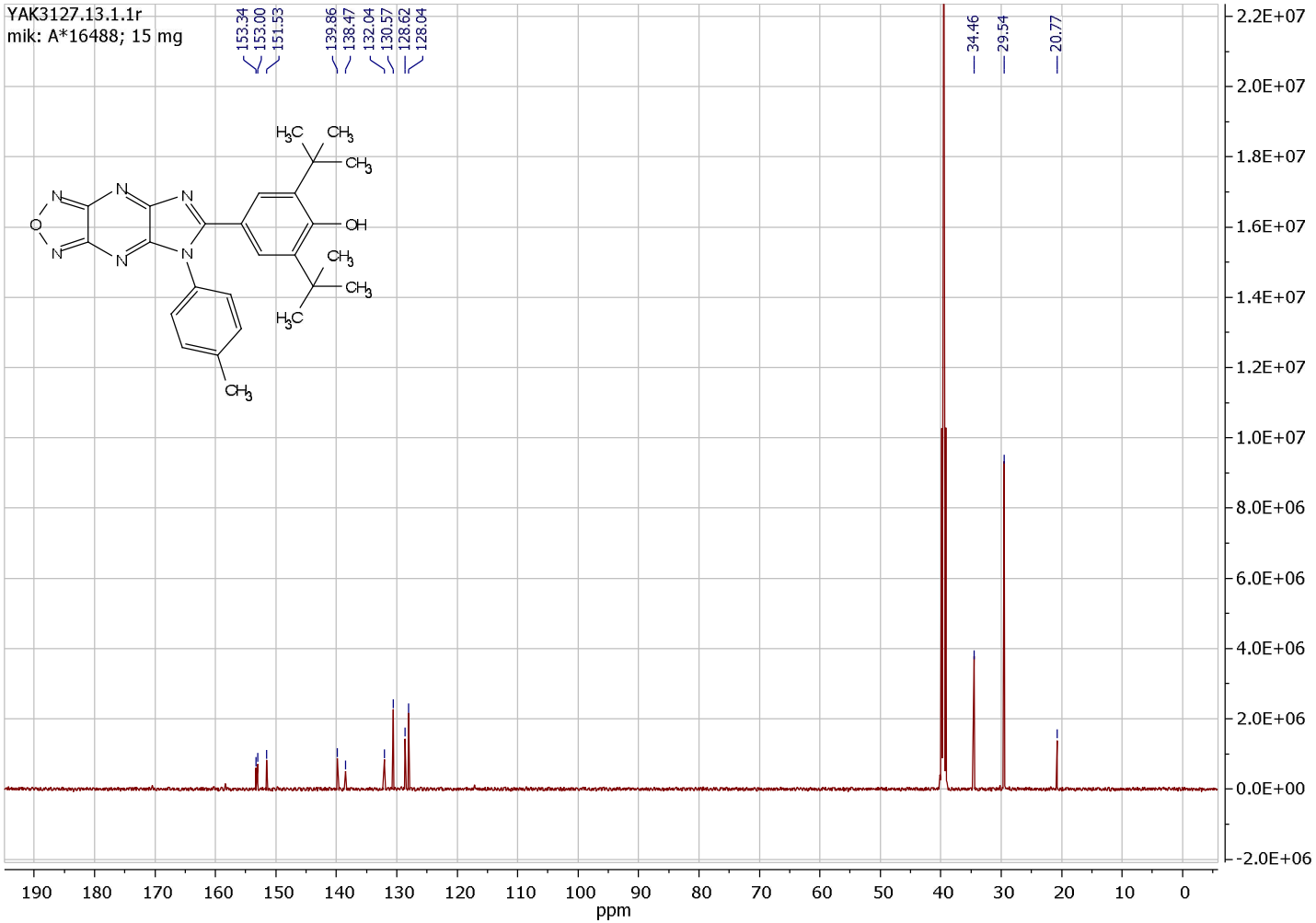
^{13}C NMR of compound **7f**



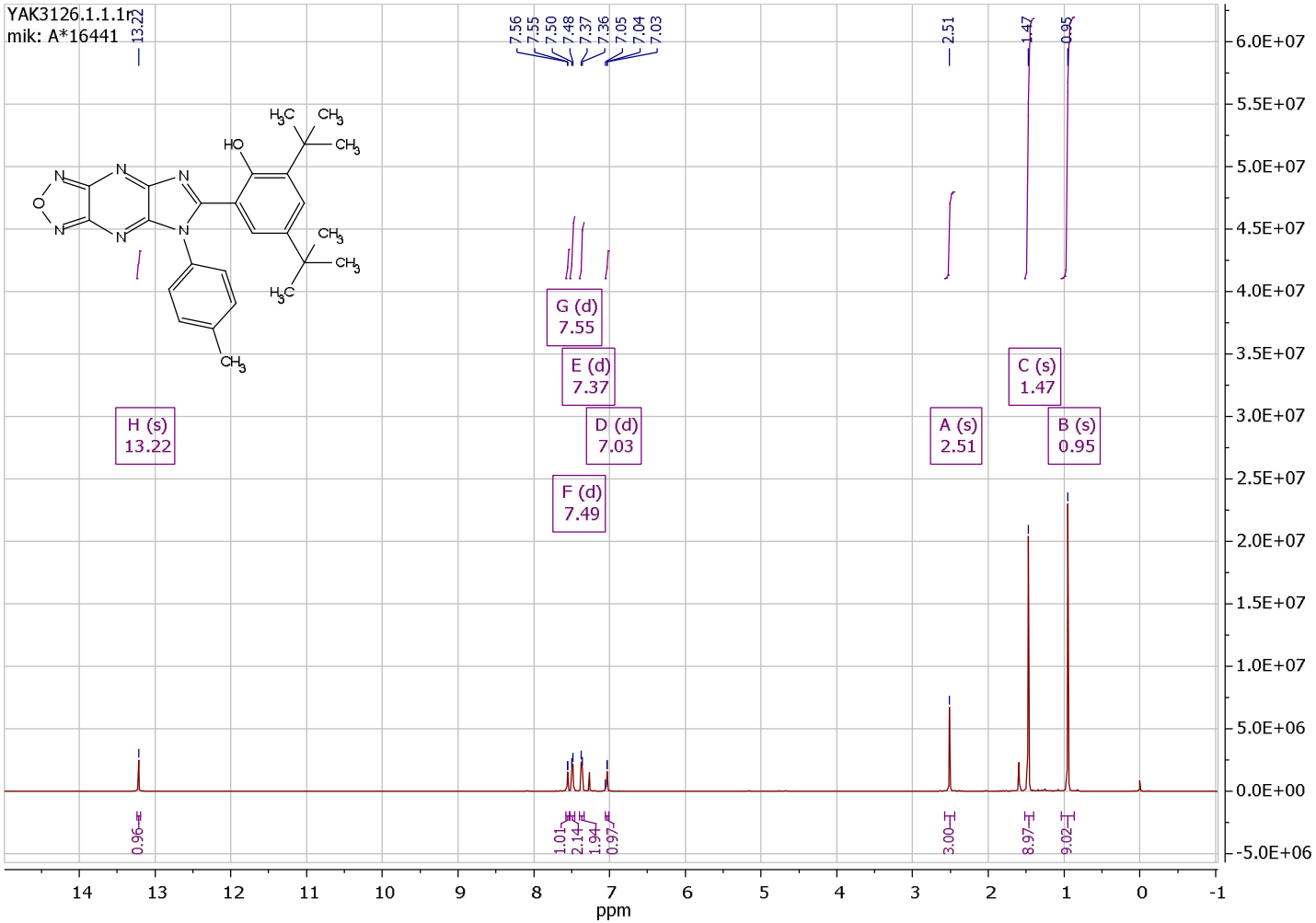
^{1}H NMR of compound **7g**



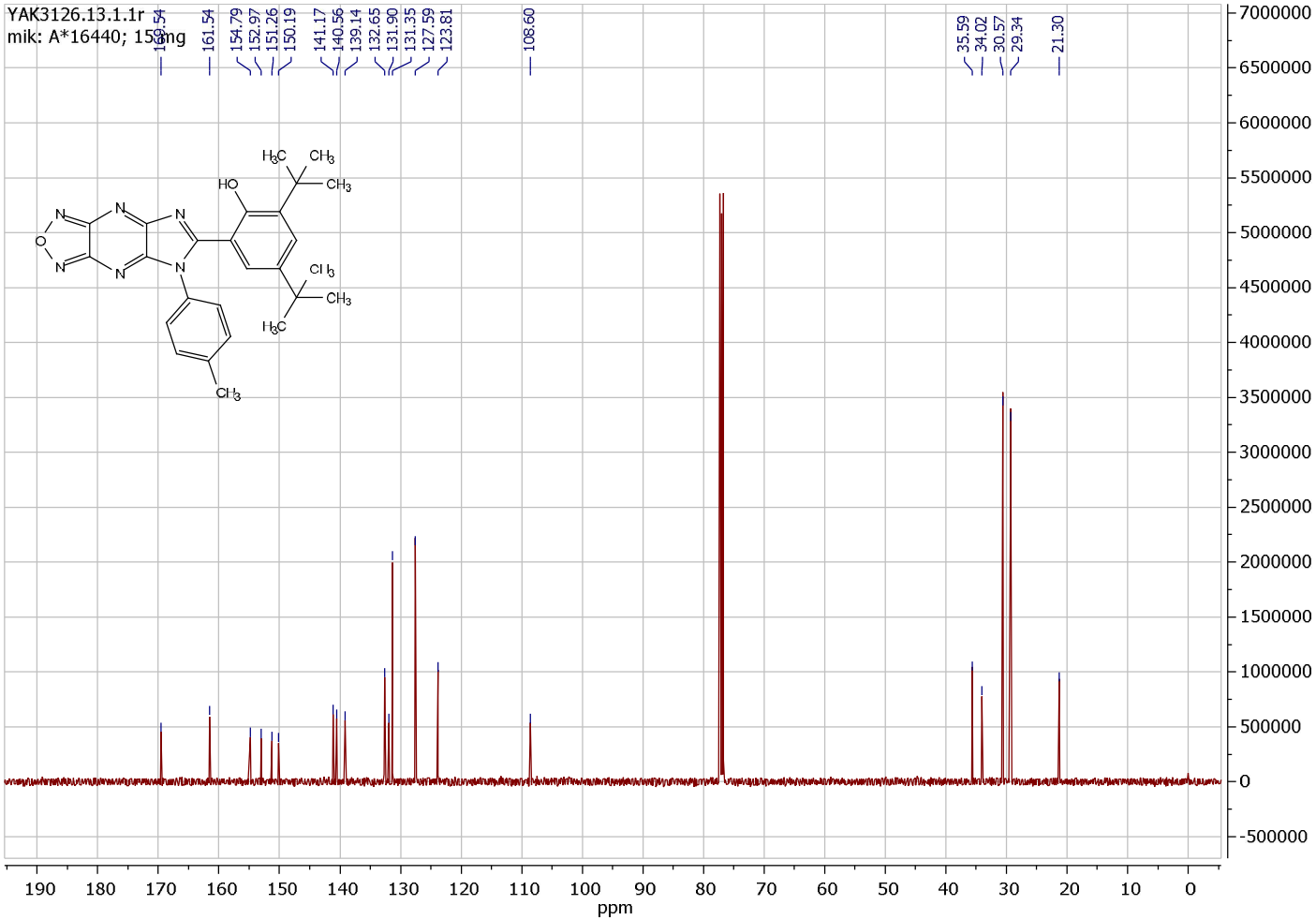
^{1}H NMR of compound **7h**



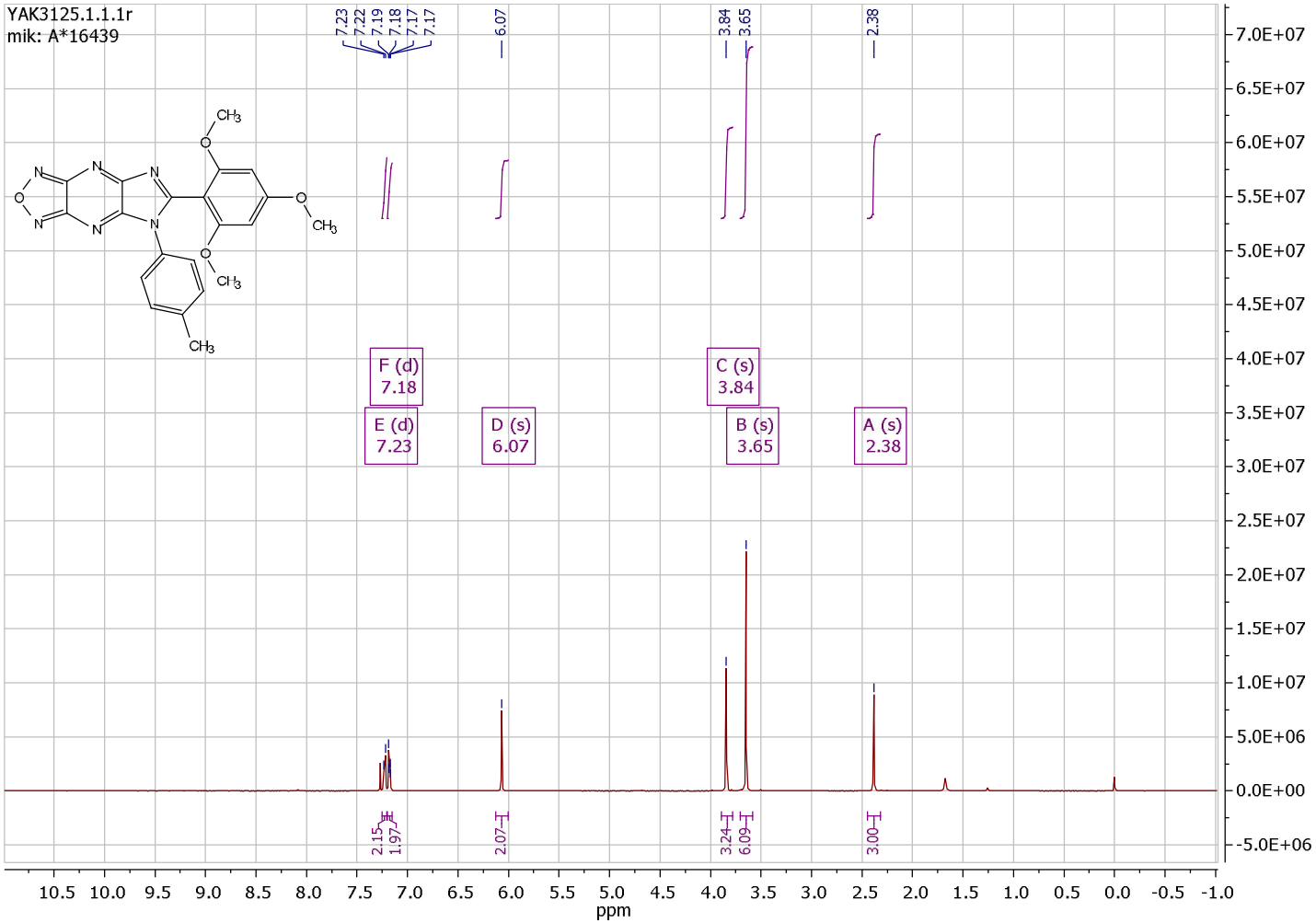
^{13}C NMR of compound **7h**



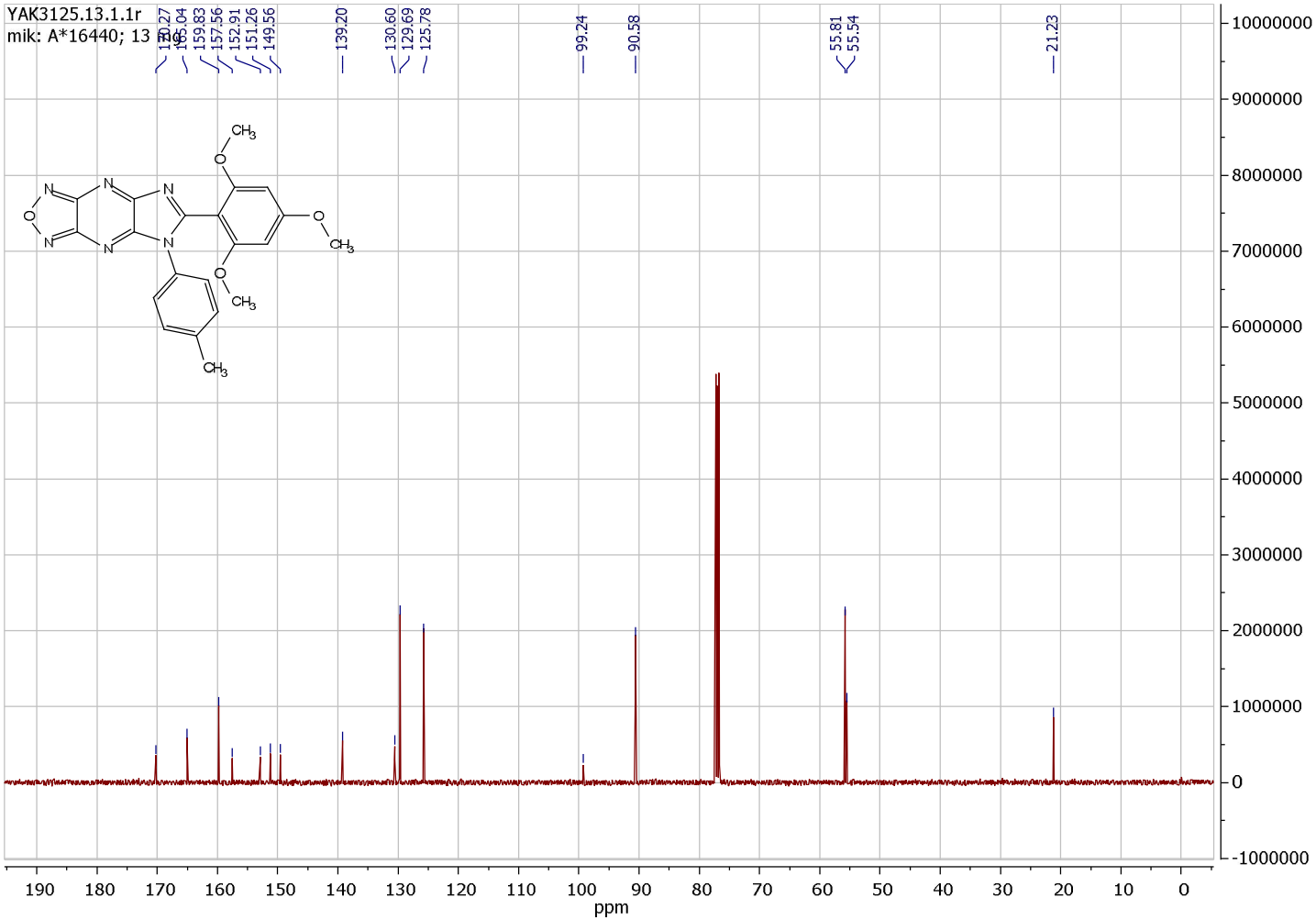
^{1}H NMR of compound **7i**



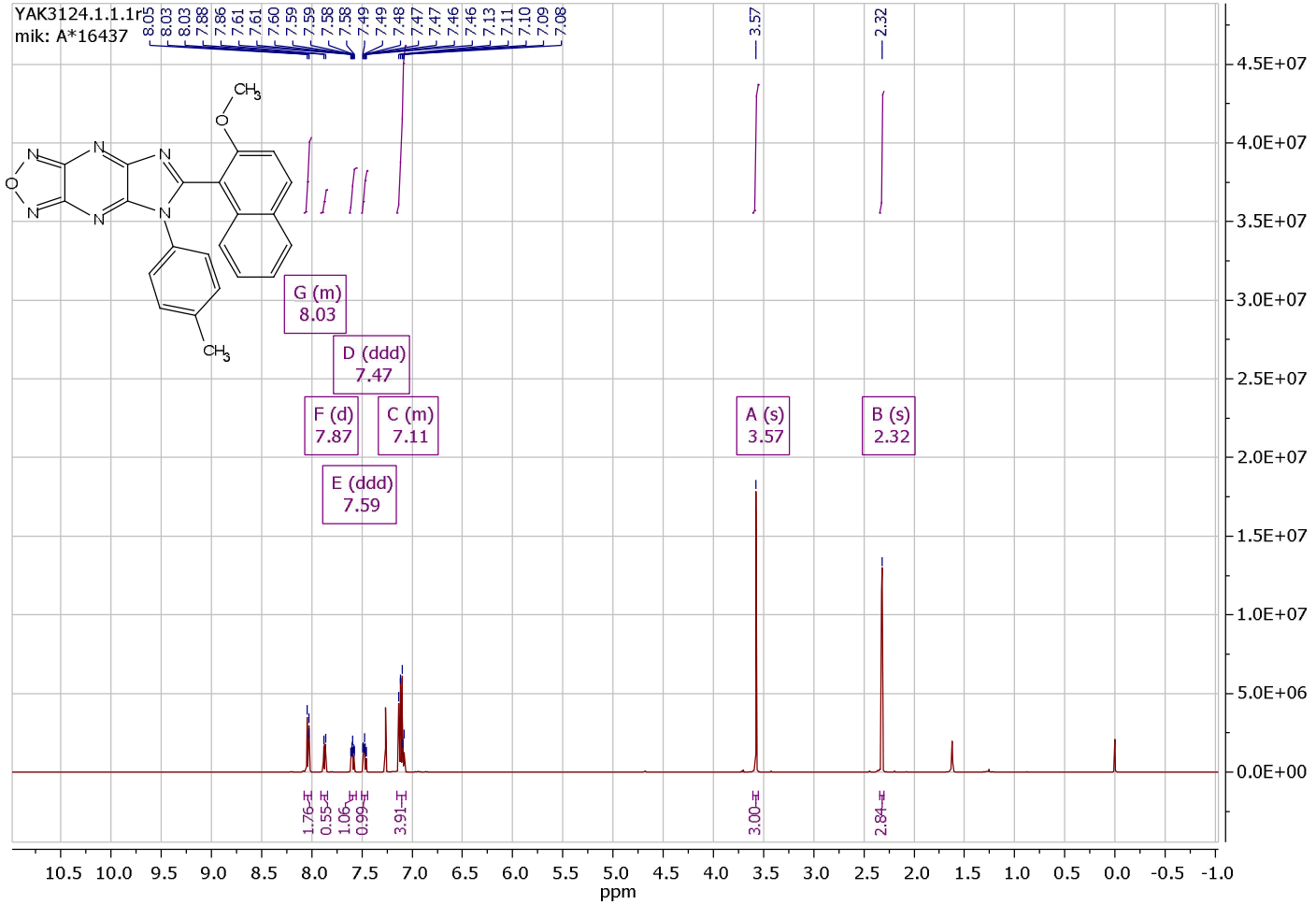
^{13}C NMR of compound **7i**



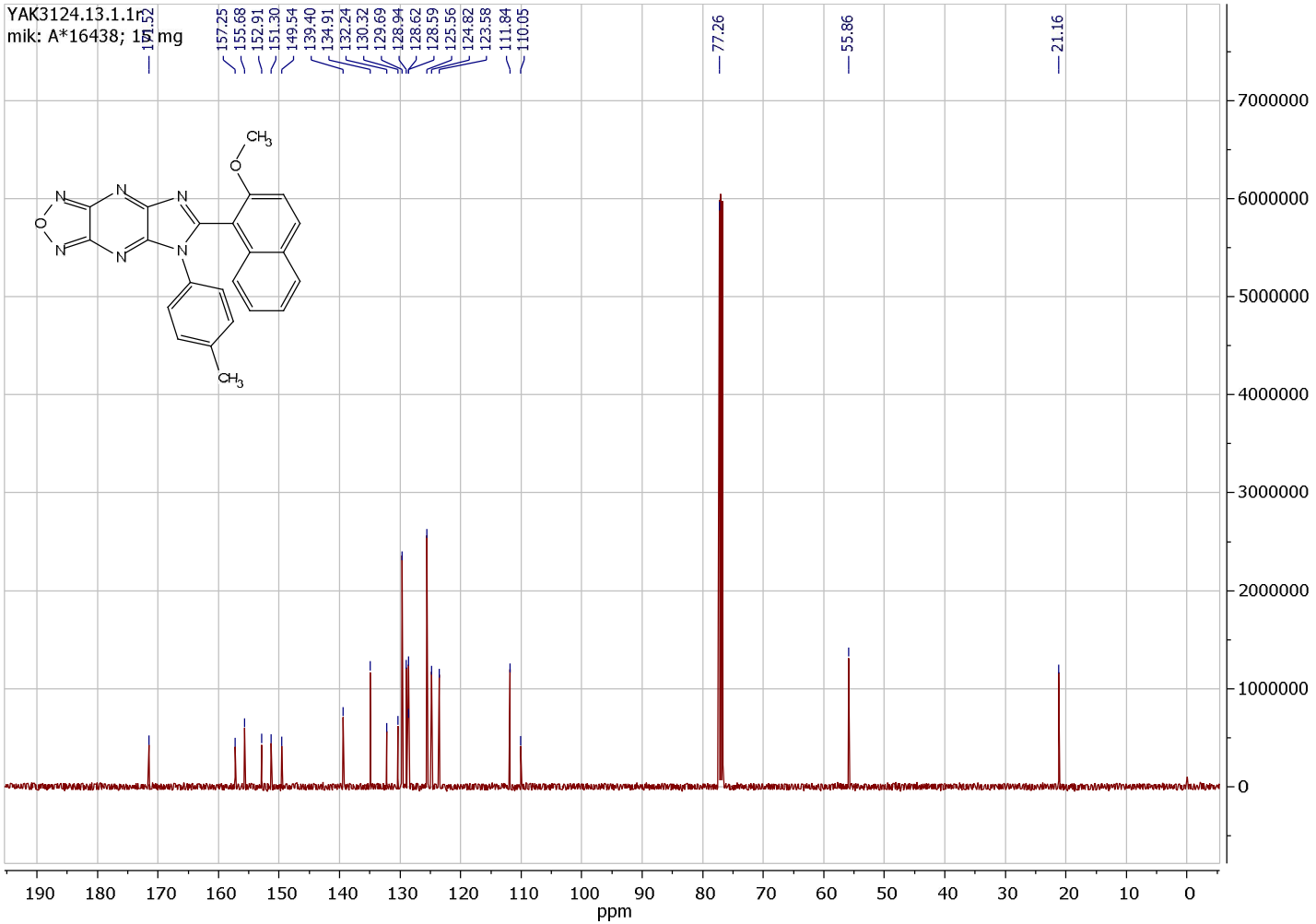
^{1}H NMR of compound **7j**



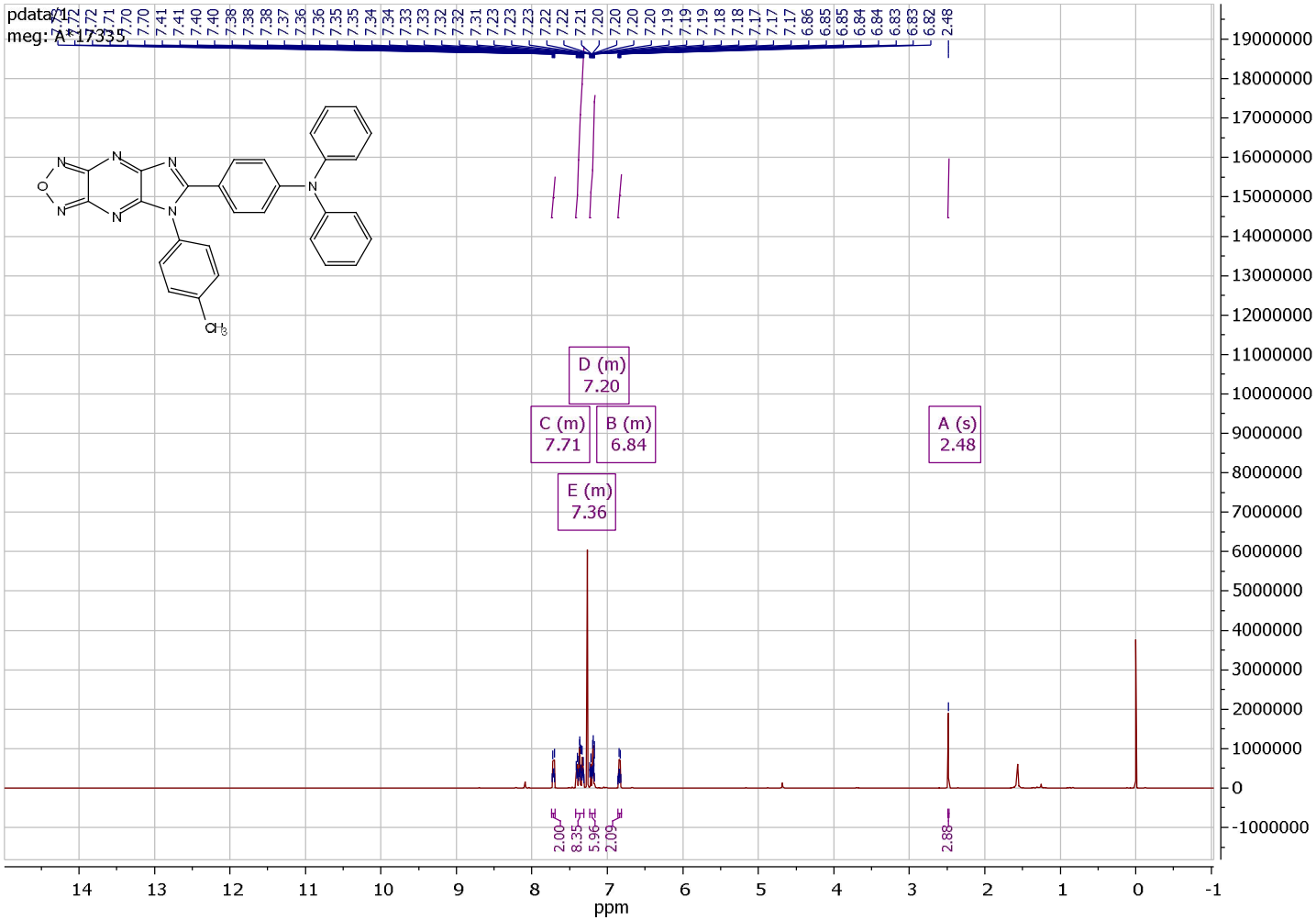
^{13}C NMR ofcompound **7j**



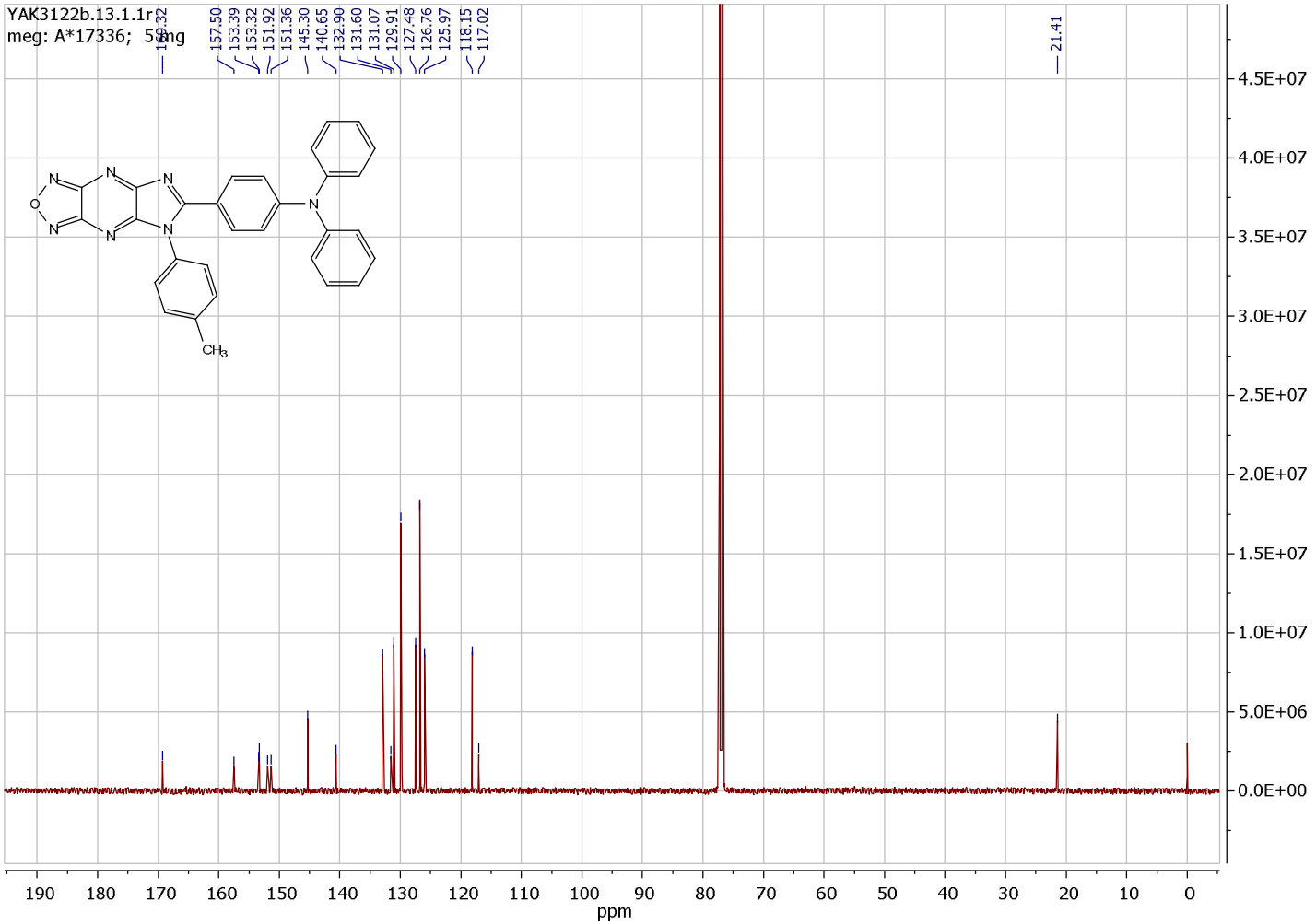
^{1}H NMR of compound **7k**



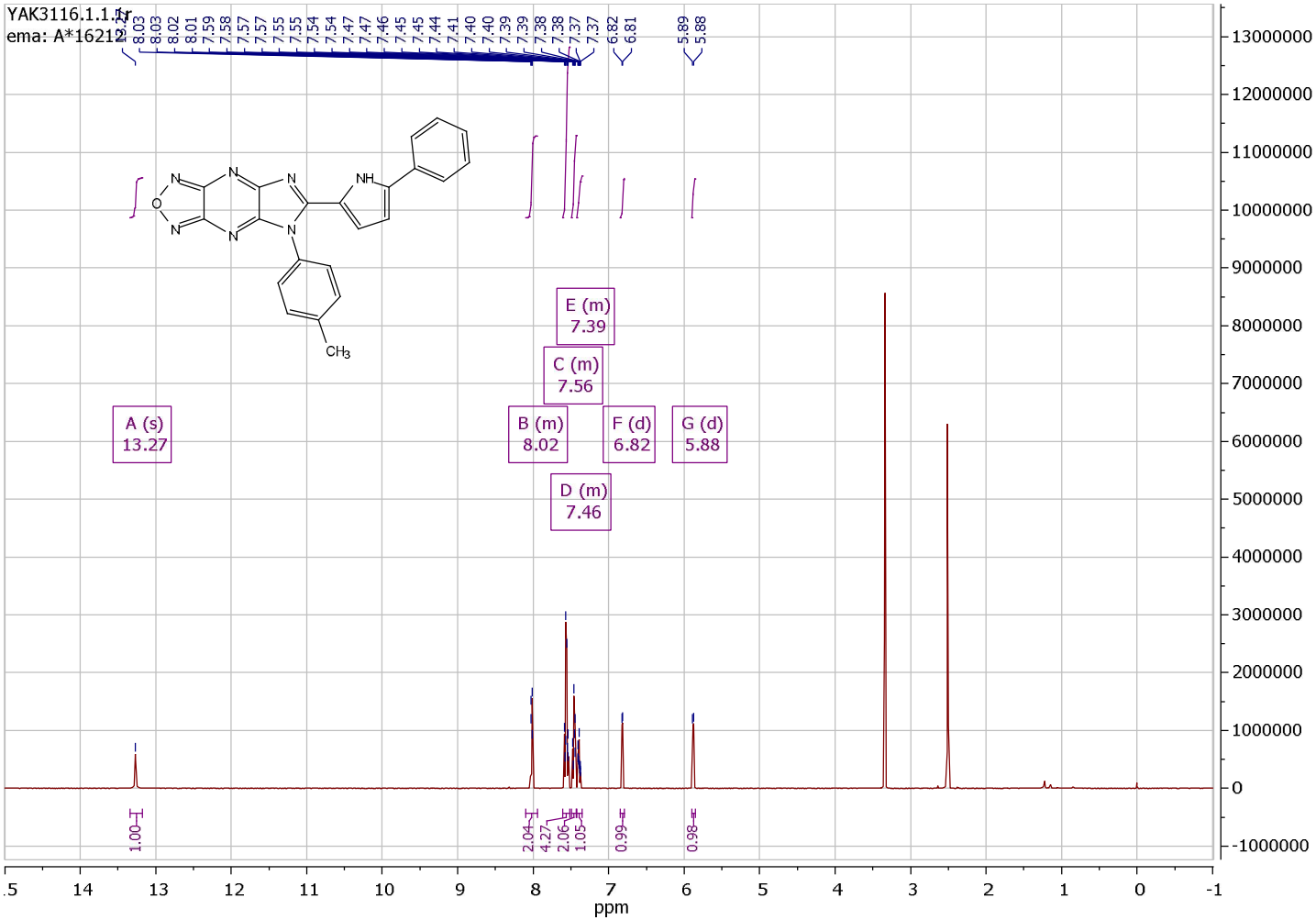
^{13}C NMR of compound **7k**



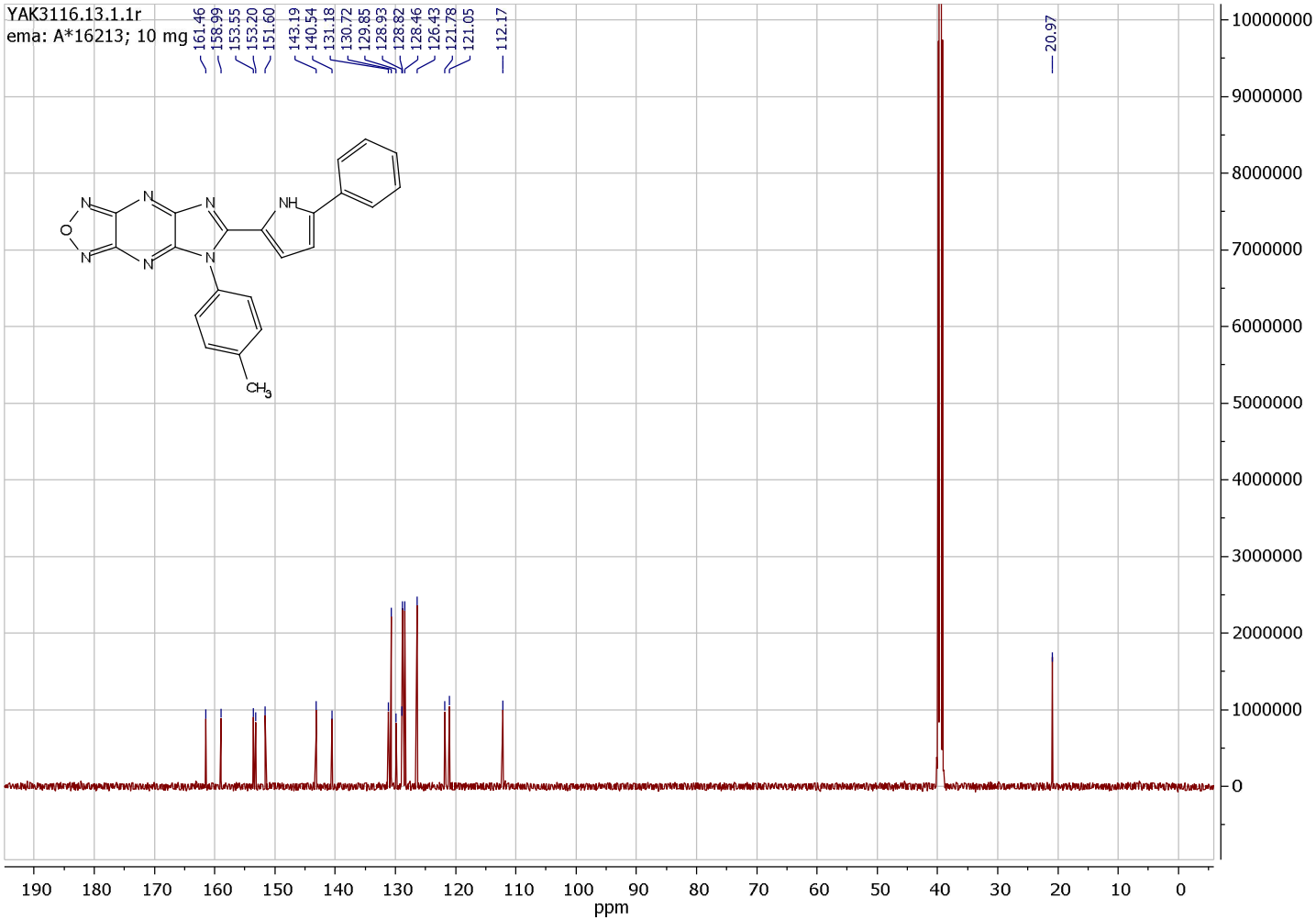
^{1}H NMR of compound **7l**



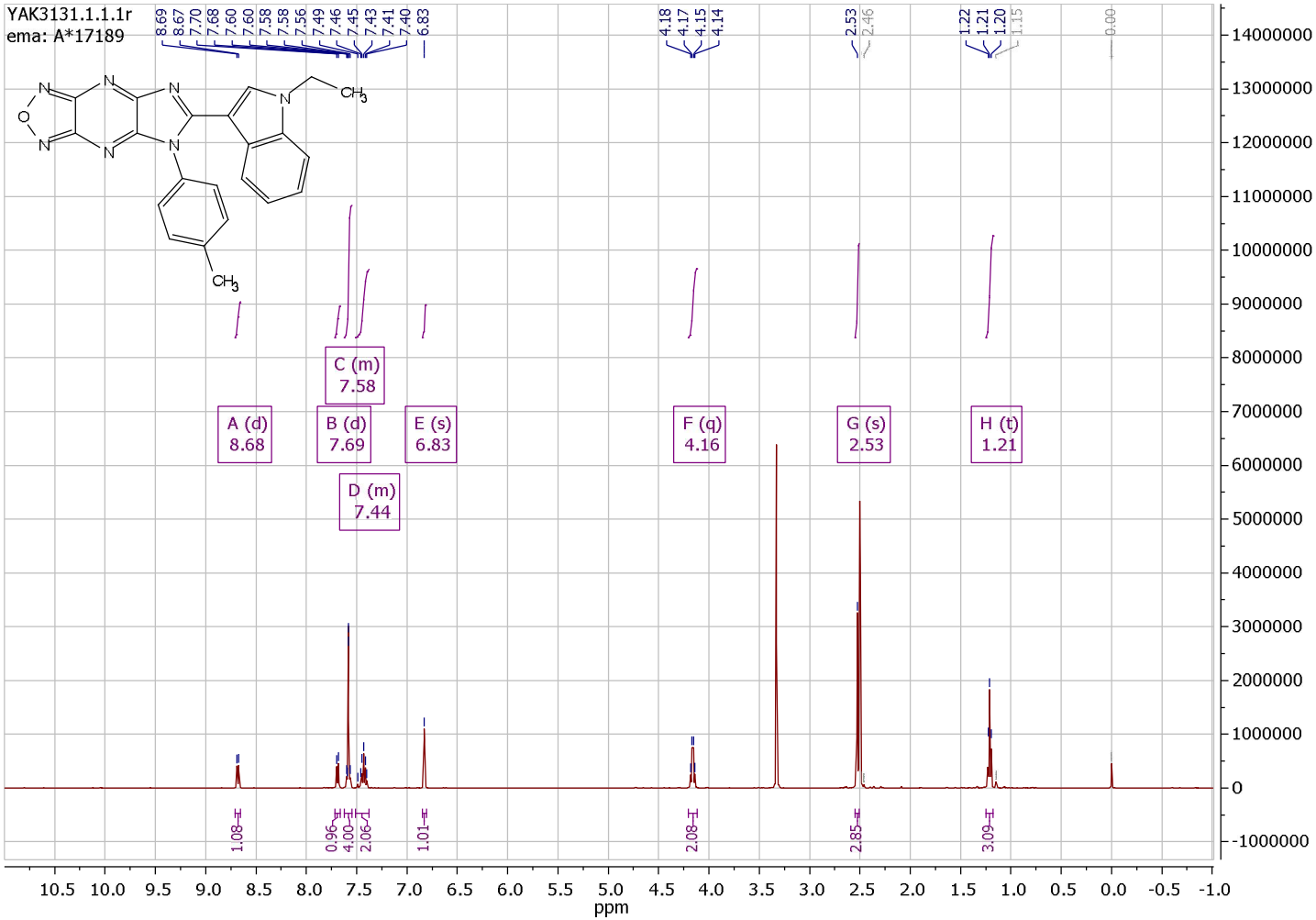
^{13}C NMR of compound **7l**



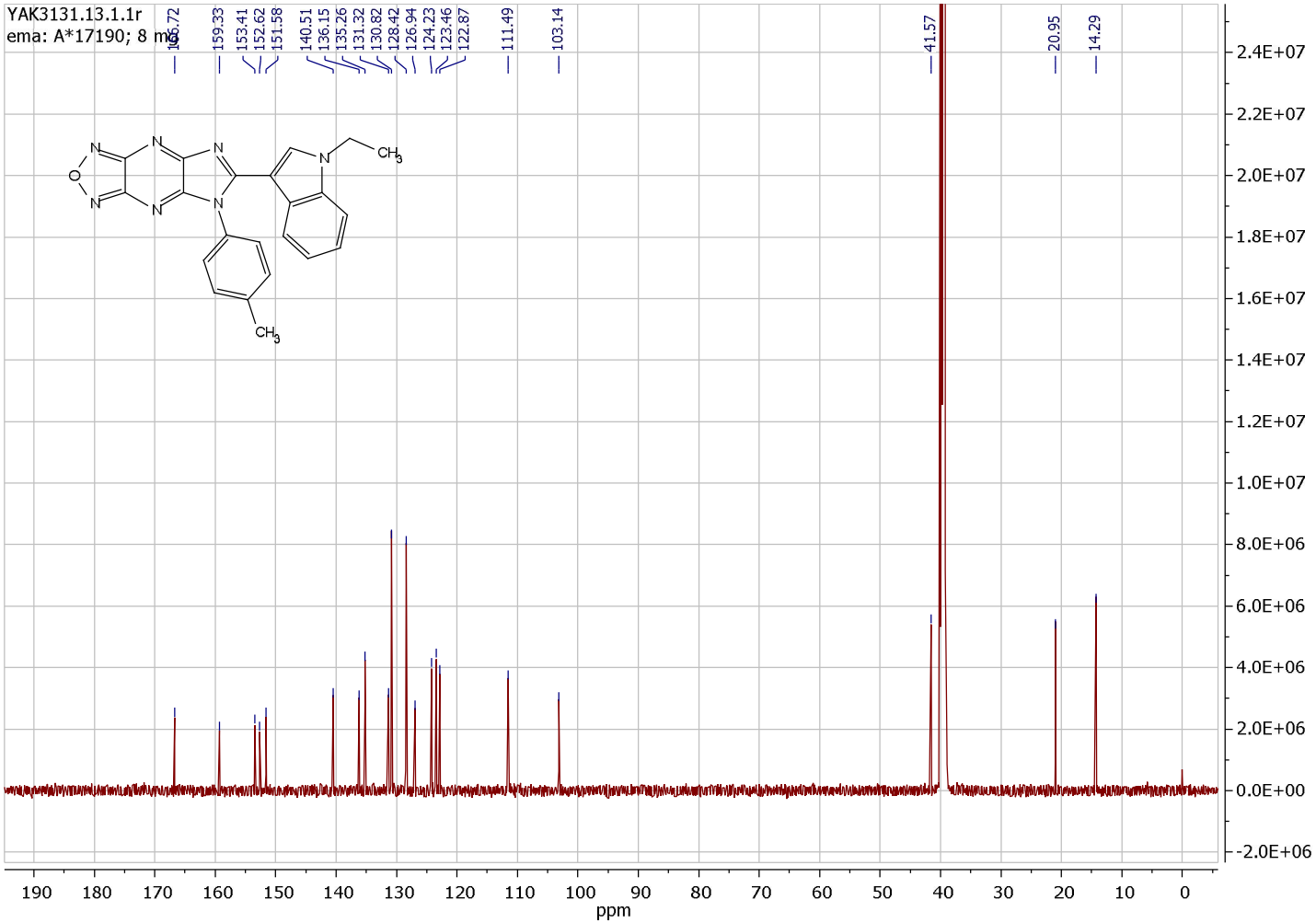
^{1}H NMR of compound **7m**



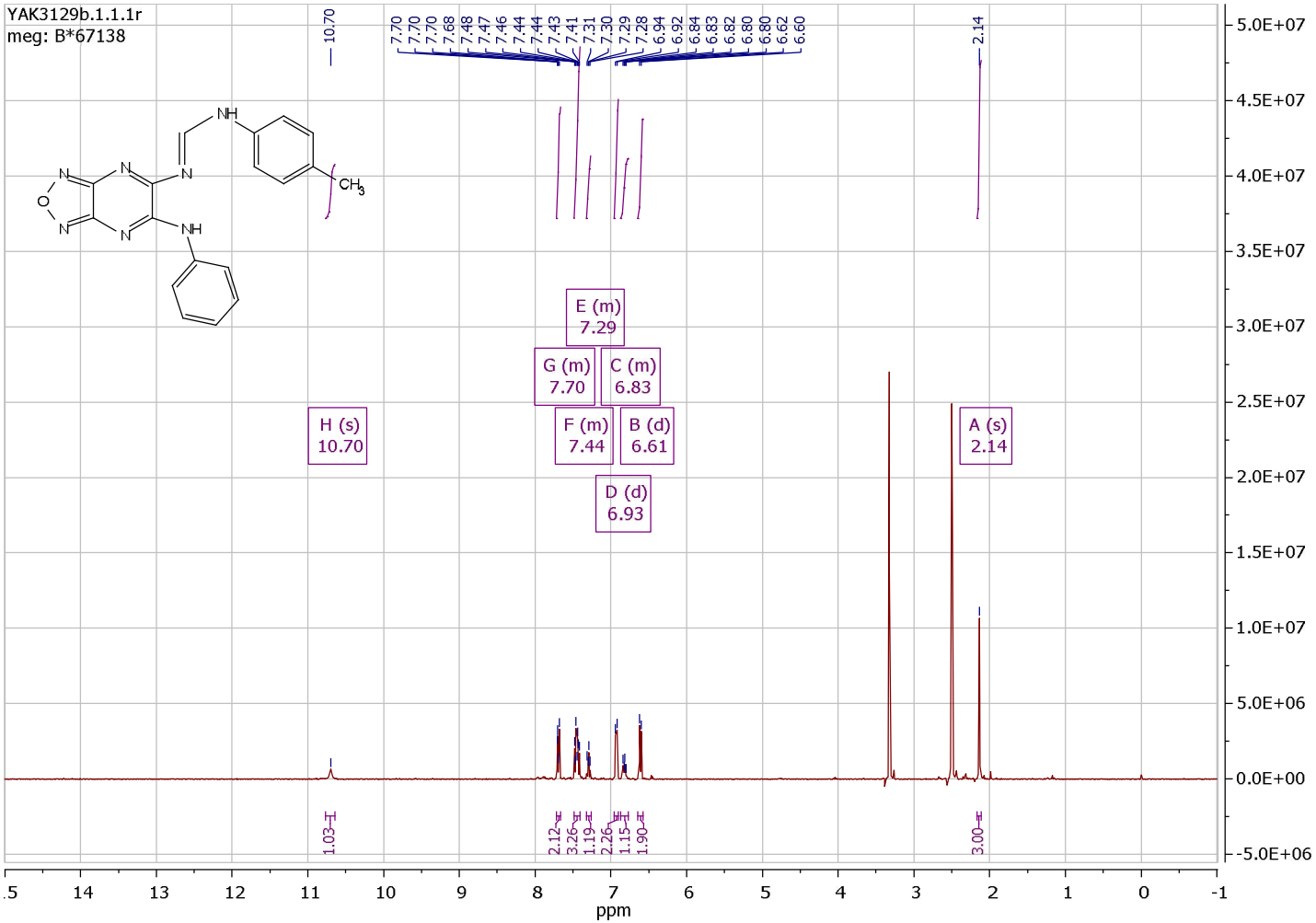
^{13}C NMR of compound **7m**



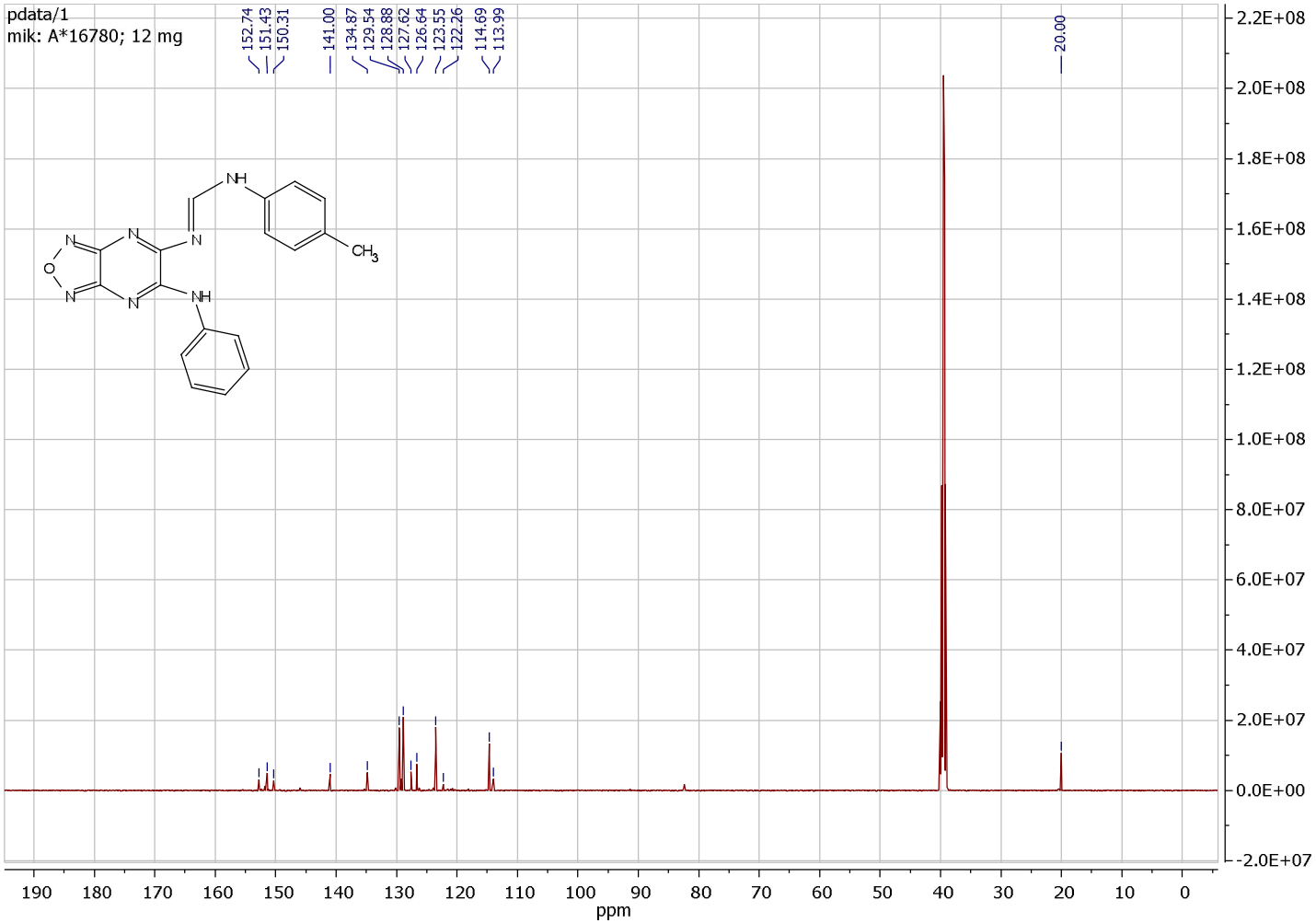
^{1}H NMR of compound **7n**



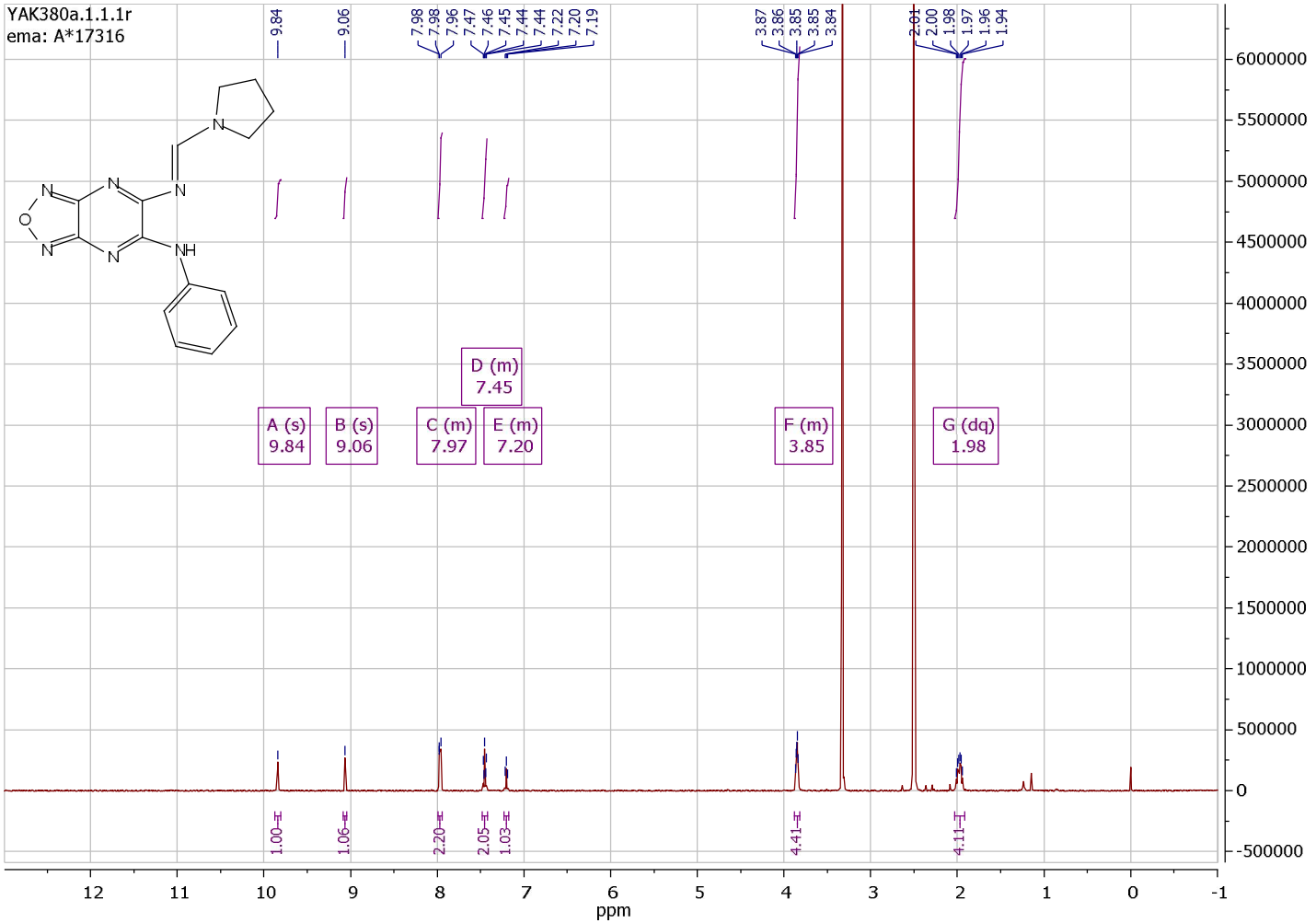
^{13}C NMR of compound **7n**



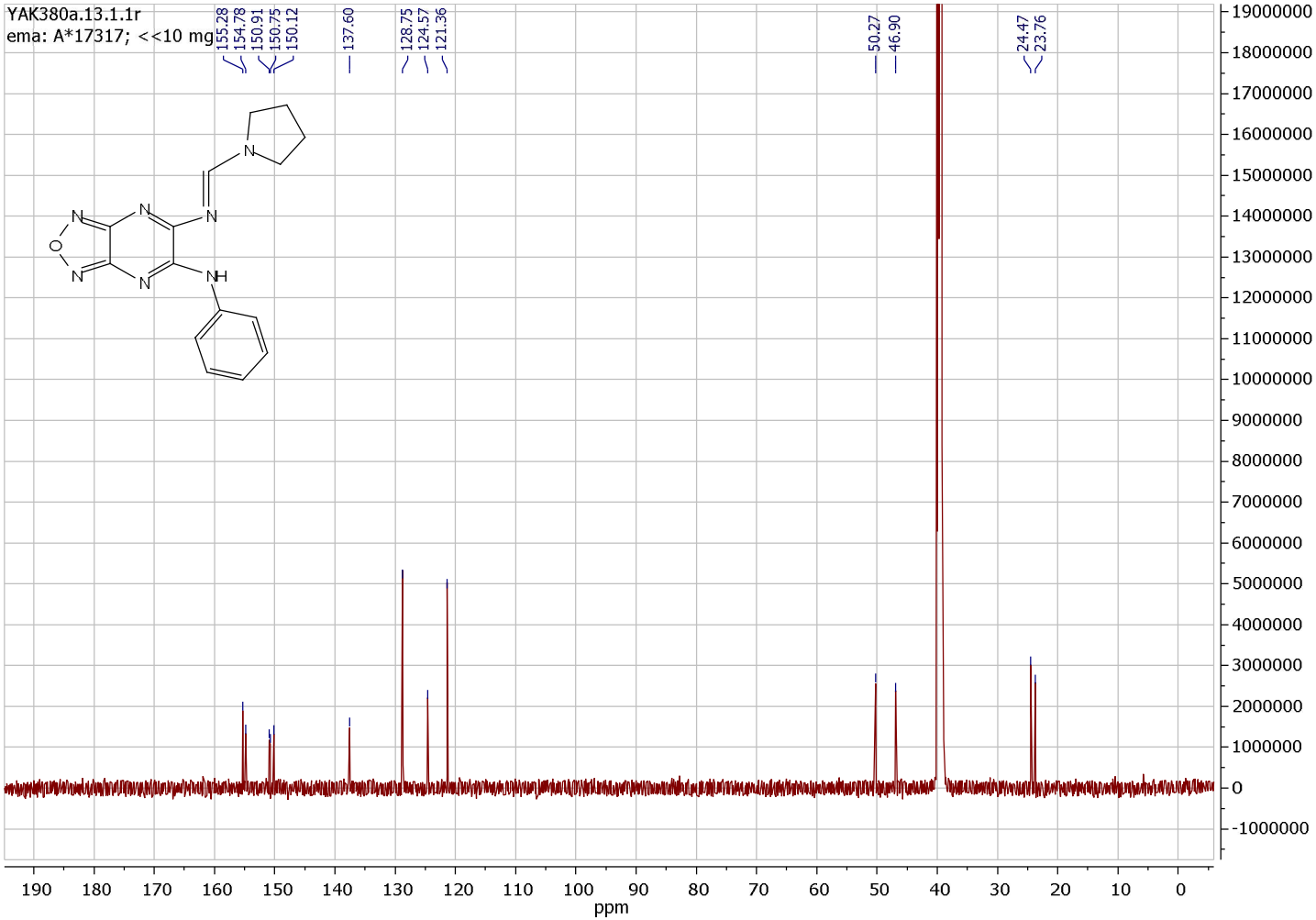
^{1}H NMR ofcompound **8**



^{13}C NMR ofcompound **8**

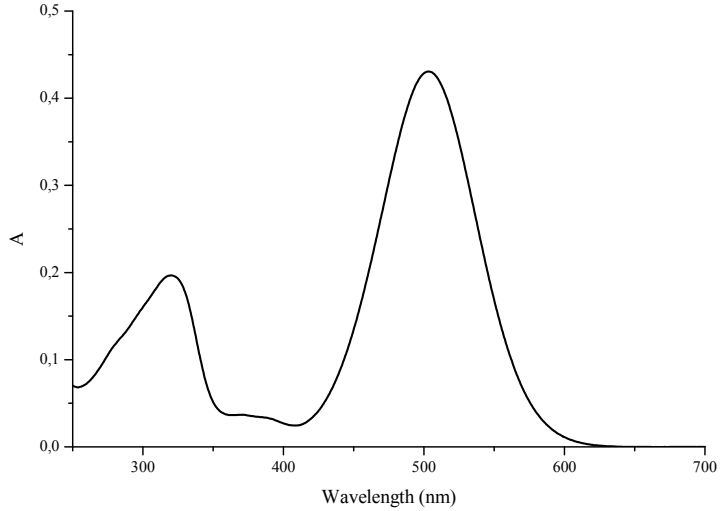


^{1}H NMR ofcompound **9**

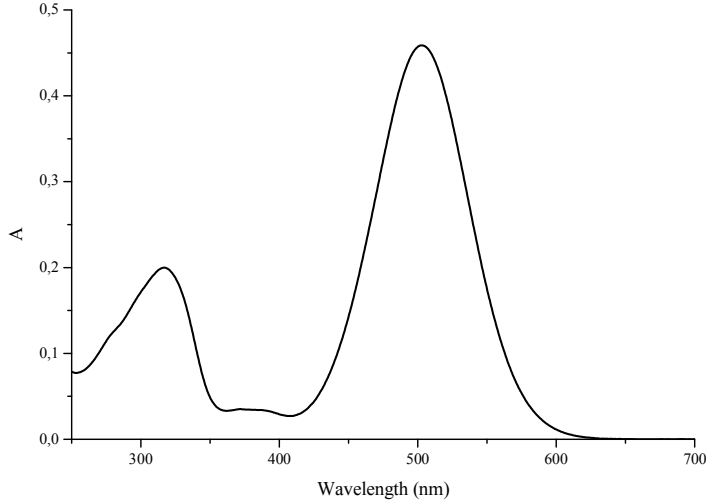


^{13}C NMR of compound **9**

UV spectra of compound **7e**

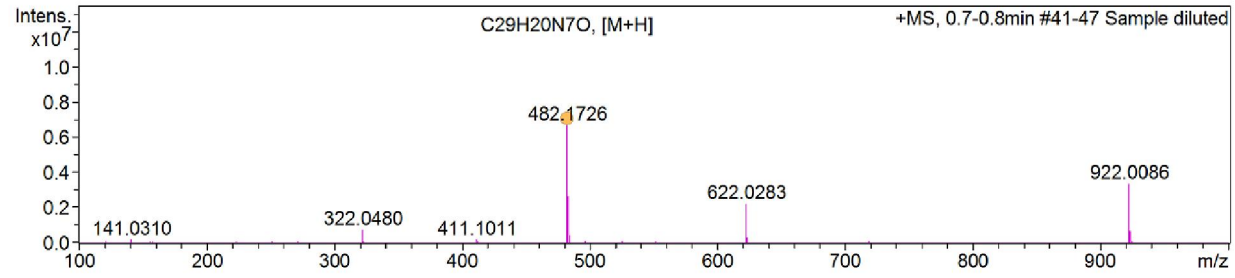


UV spectra of compound **7l**



HRMS for compound **7e**

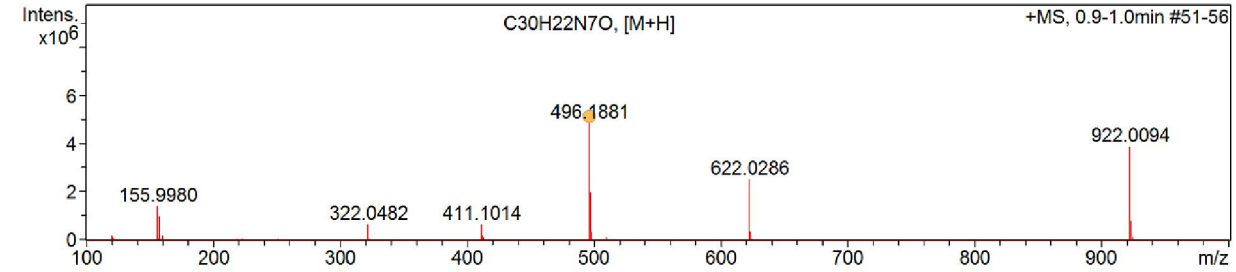
+MS, 0.7-0.8min #41-47 Sample diluted



Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdb	e¯ Conf	N-Rule
482.1726	1	C29H20N7O	482.1724	-0.4	33.0	1	100.00	23.5	even	ok

HRMS for compound **7l**

+MS, 0.9-1.0min #51-56



Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdb	e¯ Conf	N-Rule
496.1881	1	C30H22N7O	496.1880	-0.1	29.3	1	100.00	23.5	even	ok
	2	C29H26N3O5	496.1867	-2.8	41.0	2	36.89	18.5	even	ok
	3	C17H30N5O12	496.1885	1.0	101.1	3	6.37	5.5	even	ok
	4	C18H26N9O8	496.1899	3.7	103.5	4	1.91	10.5	even	ok
	5	C15H18N19O2	496.1885	0.9	104.2	5	4.13	16.5	even	ok
	6	C16H34NO16	496.1872	-1.7	112.6	6	2.94	0.5	even	ok
	7	C14H22N15O6	496.1872	-1.8	117.2	7	1.72	11.5	even	ok