Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting Information

Construction of 2-Pyridones via Oxidative Cyclization of Enamides: Access to Pechmann Dye Derivatives

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Instrumentation: Melting points were determined on a Mel-Temp melting point apparatus in open capillaries and are uncorrected. Infrared (IR) spectra were recorded using 1725XFT-IR spectrophotometer. High resolution mass spectra (HRMS) were obtained on a Thermo Fisher Scientific Finnigan MAT95XL spectrometer using magnetic sector analyzer. ^{1}H NMR (400 MHz) and ^{13}C NMR (100) spectra were recorded on a Bruker 400 spectrometer. Chemical shifts were reported in parts per million on the scale relative to an internal standard (tetramethylsilane, or appropriate solvent peaks) with coupling constants given in hertz. ^{1}H NMR multiplicity data are denoted by s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet). The photochemical reaction was carried out in a Rayonet photoreactor with 352 nm UV lamps. Analytical thin-layer chromatography (TLC) was carried out on Merck silica gel 60G-254 plates (25 mm) and developed with the solvents mentioned. Visualization was accomplished by using portable UV light, ninhydrin spray, or iodine chamber. Flash chromatography was performed in columns of various diameters with Merck silica gel (230–400 mesh ASTM 9385 kieselgel 60H) by elution with the solvent systems. Solvents, unless otherwise specified, were reagent grade and distilled once prior to use. All new compounds exhibited satisfactory spectroscopic and analytical data.

X-ray crystallographic data of compound **6a** (CCDC-1900621)

Single crystal of **6a** was obtained by slow evaporation from a mixture of dichloromethane and *n*-hexane at 25 ℃. Single-crystal X-ray data were collected at 150 K on a Bruker APEX-II CCD diffractometer using graphite-monochromated Mo KR radiation (λ = 0.71073A°). The crystal structures were solved by using SHELXS-97 and the structures were refined using SHELXL-97 2014. All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were fixed at geometrically calculated positions and were refined using riding model.

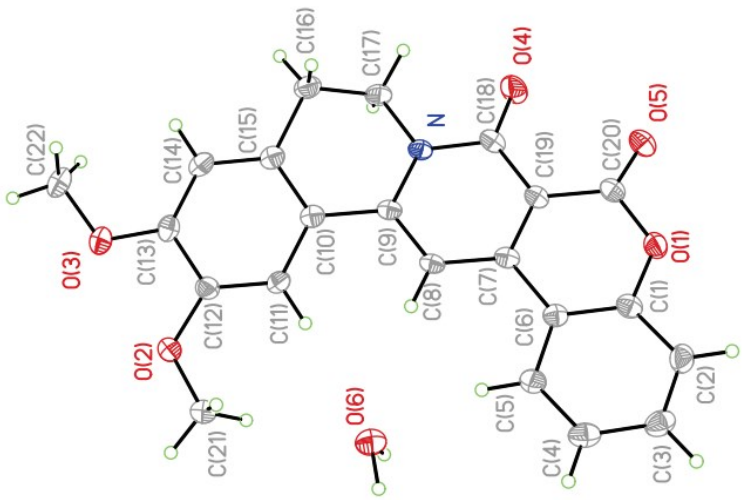


Figure S1: ORTEP diagram of compound **6a**. The ellipsoid contour probability levels: 50%

Table S1. Crystal data and structure refinement of compound **6a**.

Identification code	CS-140	
Empirical formula	C_{22} H_{19} N O_6	
Formula weight	393.38	
Temperature	150(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1/c$	
Unit cell dimensions	a = 9.0475(10) Å	a= 90°.
	b = 20.289(3) Å	b= 101.000(5)°.
	c = 9.7241(13) Å	g = 90°.
Volume	1752.2(4) $Å^3$	
Z	4	
Density (calculated)	1.491 Mg/m^3	
Absorption coefficient	0.109 mm^{-1}	
F(000)	824	
Crystal size	0.560 x 0.200 x 0.110 mm^3	
Theta range for data collection	2.930 to 26.411°.	
Index ranges	-11<=h<=11, -25<=k<=25, -12<=l<=12	
Reflections collected	29436	
Independent reflections	3569 [R(int) = 0.0513]	
Completeness to theta = 25.242°	99.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9281 and 0.8106	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3569 / 0 / 270	
Goodness-of-fit on F^2	1.010	
Final R indices [I>2sigma(I)]	R1 = 0.0411, wR2 = 0.1007	
R indices (all data)	R1 = 0.0610, wR2 = 0.1156	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.231 and -0.255 $e.Å^{-3}$	

X-ray crystallographic data of compound **6b** (CCDC-2012710)

Single crystal of **6b** was obtained by slow evaporation from a mixture of dichloromethane and *n*-hexane at 25 ℃. Single-crystal X-ray data were collected at 150 K on a Bruker APEX-II CCD diffractometer using graphite-monochromated Mo KR radiation (λ = 0.71073A°). The crystal structures were solved by using SHELXS-97 and the structures were refined using SHELXL-97 2014. All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were fixed at geometrically calculated positions and were refined using riding model.

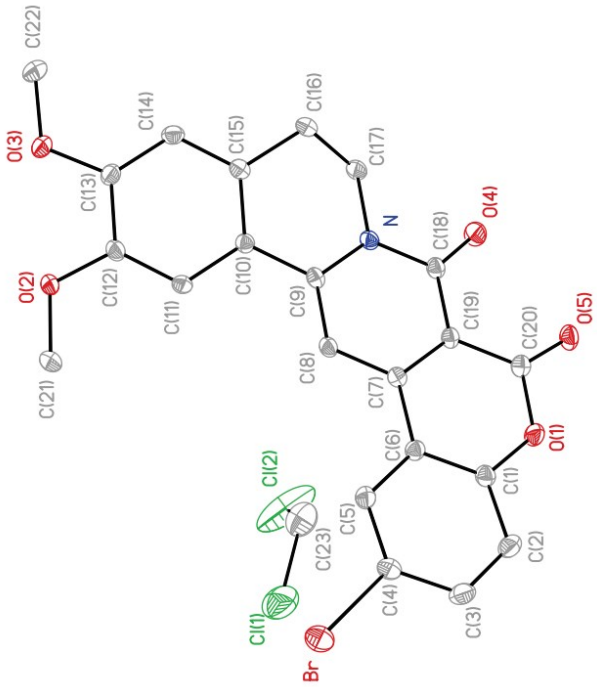


Figure S2: ORTEP diagram of compound **6b**. The ellipsoid contour probability levels: 50%

Table S2. Crystal data and structure refinement for compound **6b**.

Identification code	CS-465	
Empirical formula	C_{23} H_{18} Br Cl_2 N O_5	
Formula weight	539.19	
Temperature	150(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1/c$	
Unit cell dimensions	a = 15.9528(6) Å	a= 90°.
	b = 9.8435(4) Å	b= 110.3485(16)°.
	c = 14.8269(5) Å	g = 90°.
Volume	2182.99(14) $Å^3$	
Z	4	
Density (calculated)	1.641 Mg/m^3	
Absorption coefficient	2.165 mm^{-1}	
F(000)	1088	
Crystal size	0.480 x 0.340 x 0.290 mm^3	
Theta range for data collection	2.931 to 27.880°.	
Index ranges	-20<=h<=20, -12<=k<=12, -19<=l<=19	
Reflections collected	39472	
Independent reflections	5168 [R(int) = 0.0386]	
Completeness to theta = 25.242°	99.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9281 and 0.7973	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5168 / 0 / 289	
Goodness-of-fit on F^2	1.017	
Final R indices [I>2sigma(I)]	R1 = 0.0332, wR2 = 0.0837	
R indices (all data)	R1 = 0.0397, wR2 = 0.0879	
Extinction coefficient	n/a	
Largest diff. peak and hole	1.274 and -0.989 $e.Å^{-3}$	

X-ray crystallographic data of compound **6j** (CCDC-2036791)

Single crystal of **6j** was obtained by slow evaporation from a mixture of dichloromethane and *n*-hexane at 25 ℃. Single-crystal X-ray data were collected at 150 K on a Bruker APEX-II CCD diffractometer using graphite-monochromated Mo KR radiation (λ = 0.71073A°). The crystal structures were solved by using SHELXS-97 and the structures were refined using SHELXL-97 2014. All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were fixed at geometrically calculated positions and were refined using riding model.

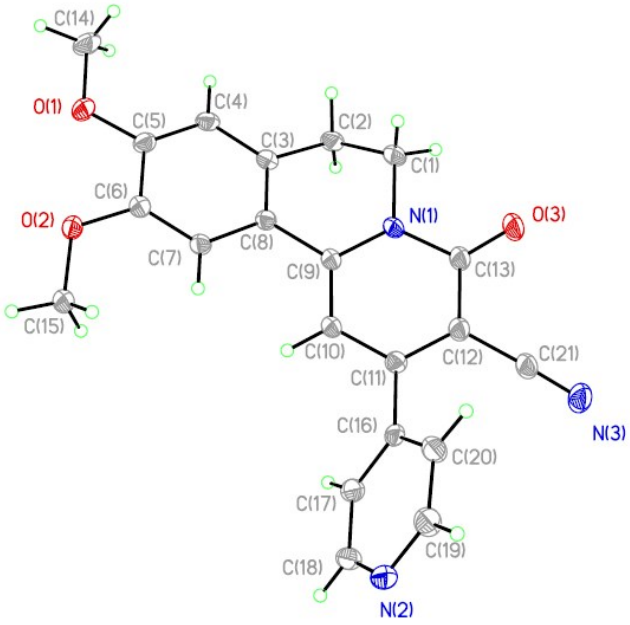


Figure S3: ORTEP diagram of compound **6j**. The ellipsoid contour probability levels: 50%

Table S3. Crystal data and structure refinement for compound **6j**.

Identification code	CS-565	
Empirical formula	$C_{21}H_{17}N_3O_3$	
Formula weight	359.38	
Temperature	150(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1/c$	
Unit cell dimensions	a = 12.4264(5) Å	a= 90°.
	b = 14.8397(5) Å	b= 111.5859(14)°.
	c = 9.9773(4) Å	g = 90°.
Volume	1710.82(11) $Å^3$	
Z	4	
Density (calculated)	1.395 Mg/m^3	
Absorption coefficient	0.095 mm^{-1}	
F(000)	752	
Crystal size	0.480 x 0.310 x 0.150 mm^3	
Theta range for data collection	3.263 to 27.905°.	
Index ranges	-16<=h<=16, -17<=k<=19, -13<=l<=13	
Reflections collected	21544	
Independent reflections	4076 [R(int) = 0.0465]	
Completeness to theta = 25.242°	99.6 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9281 and 0.8662	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4076 / 0 / 244	
Goodness-of-fit on F^2	1.017	
Final R indices [I>2sigma(I)]	R1 = 0.0433, wR2 = 0.1114	
R indices (all data)	R1 = 0.0523, wR2 = 0.1177	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.344 and -0.228 $e.Å^{-3}$	

X-ray crystallographic data of compound **8b** (CCDC- 2012685)

Single crystal of **8b** was obtained by slow evaporation of methanol from a mixture at 25 ℃. Single-crystal X-ray data were collected at 150 K on a Bruker APEX-II CCD diffractometer using graphite-monochromated Mo KR radiation (λ = 0.71073A°). The crystal structures were solved by using SHELXS-97 and the structures were refined using SHELXL-97 2014. All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were fixed at geometrically calculated positions and were refined using riding model.

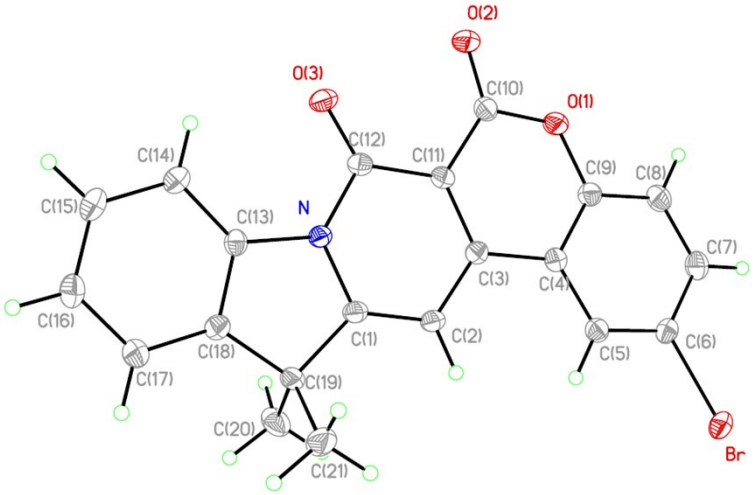


Figure S4: ORTEP diagram of compound **8b**. The ellipsoid contour probability levels: 50%

Table S4. Crystal data and structure refinement for compound **8b**.

Identification code	CS-509	
Empirical formula	C_{21} H_{14} Br N O_3	
Formula weight	408.24	
Temperature	150(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 8.4713(4) Å	a= 94.9324(17)°.
	b = 10.0832(5) Å	b= 105.5420(17)°.
	c = 10.7844(5) Å	g = 108.9946(16)°.
Volume	823.87(7) $Å^3$	
Z	2	
Density (calculated)	1.646 Mg/m^3	
Absorption coefficient	2.517 mm^{-1}	
F(000)	412	
Crystal size	0.500 x 0.370 x 0.330 mm^3	
Theta range for data collection	3.658 to 27.949°.	
Index ranges	-11<=h<=11, -13<=k<=13, -14<=l<=13	
Reflections collected	17024	
Independent reflections	3911 [R(int) = 0.0286]	
Completeness to theta = 25.242°	99.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9281 and 0.8156	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3911 / 0 / 235	
Goodness-of-fit on F^2	1.059	
Final R indices [I>2sigma(I)]	R1 = 0.0210, wR2 = 0.0535	
R indices (all data)	R1 = 0.0233, wR2 = 0.0546	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.331 and -0.285 $e.Å^{-3}$	

X-ray crystallographic data of compound **11** (CCDC-2012684)

Single crystal of **11** was obtained by slow evaporation from a mixture of dichloromethane and *n*-hexane at 25 ℃. Single-crystal X-ray data were collected at 150 K on a Bruker APEX-II CCD diffractometer using graphite-monochromated Mo KR radiation (λ = 0.71073A°). The crystal structures were solved by using SHELXS-97 and the structures were refined using SHELXL-97 2014. All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were fixed at geometrically calculated positions and were refined using riding model.

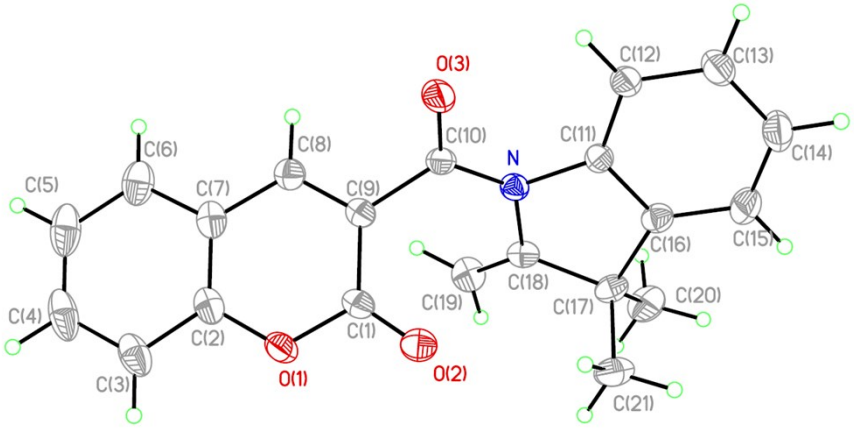


Figure S5: ORTEP diagram of compound **11**. The ellipsoid contour probability levels: 50%

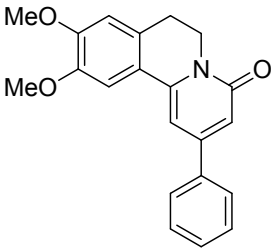
Table S5. Crystal data and structure refinement of compound **11**.

Identification code	CS-506A	
Empirical formula	C_{21} H_{17} N O_3	
Formula weight	331.36	
Temperature	150(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1/c$	
Unit cell dimensions	a = 8.9048(2) Å	a= 90°.
	b = 19.0917(5) Å	b= 106.2045(12)°.
	c = 10.2276(3) Å	g = 90°.
Volume	1669.69(8) $Å^3$	
Z	4	
Density (calculated)	1.318 Mg/m^3	
Absorption coefficient	0.088 mm^{-1}	
F(000)	696	
Crystal size	0.470 x 0.310 x 0.180 mm^3	
Theta range for data collection	3.198 to 27.881°.	
Index ranges	-11<=h<=11, -25<=k<=25, -13<=l<=13	
Reflections collected	28812	
Independent reflections	3965 [R(int) = 0.0356]	
Completeness to theta = 25.242°	99.2 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9281 and 0.8741	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3965 / 0 / 234	
Goodness-of-fit on F^2	1.004	
Final R indices [I>2sigma(I)]	R1 = 0.0392, wR2 = 0.1044	
R indices (all data)	R1 = 0.0486, wR2 = 0.1126	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.323 and -0.188 $e.Å^{-3}$	

General procedure A for preparation of compound **4**.

To a stirred solution of commercially available imine **1** (0.5 mmol) and triethylamine (1.5 mmol) in dry toluene (3 mL) was added dropwise acid chloride **2** (0.55 mmol) at 0 ℃. The resulting mixture was stirred at room temperature for 1 h. After that, the mixture was diluted with degassed dry acetonitrile (100 mL) and irradiated with UV light (352 nm) in a Rayonet photoreactor for 2 h at room temperature. After completion of the reaction, the solution was evaporated and the residue was diluted with ethyl acetate (100 mL), washed with 5 N HCl (30 mL), water (30 mL) and brine (30 mL). The organic layer was then dried over anhydrous $MgSO_4$ and concentrated under reduced pressure to provide the crude product which was further purified by column chromatography to obtain the desired compound.

9, 10-Dimethoxy-2-phenyl-6,7-dihydro-4*H*-pyrido[2, 1-*a*]isoquinolin-4-one (4).

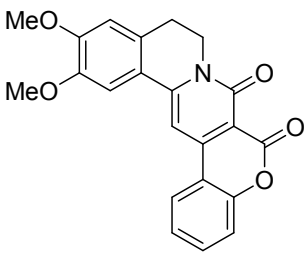


The title compound **4** was synthesized following general procedure A from imine **1** (103 mg, 0.5 mmol), triethylamine (101 mg, 1.5 mmol) and cinnamoyl chloride (**2**, 92 mg, 0.55 mmol), and purified by flash column chromatography (50% EtOAc in hexanes) to give a yellow solid (64 mg, 38% yield). R_f = 0.3 (50% EtOAc/hexanes). mp 156−158 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.66–7.63 (m, 2H), 7.52–7.45 (m, 3H), 7.23 (s, 1H), 6.79 (d, J = 2.0 Hz, 1H), 6.77 (s, 1H), 6.75 (d, J = 2.0 Hz, 1H), 4.31 (t, J = 6.0 Hz, 2H), 3.96 (s, 3H), 3.95 (s, 3H), 2.96 (t, J = 6.0 Hz, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ: 162.8, 151.2, 151.1, 148.5, 143.3, 138.4, 129.3, 129.2, 129.0 (2C), 126.8 (2C), 121.7, 114.4, 110.5, 108.2, 101.7, 56.3, 56.1, 39.3, 27.6. IR $_{vmax}$ (neat): 2947, 1716, 1655, 1565, 1217, 875, 750 cm^{-1}. HRMS (EI) m/z: [M$^+$] calcd for $C_{21}H_{19}NO_3$, 333.1365; found, 333.1357.

General procedure B for preparation of compounds **6a**–**m**.

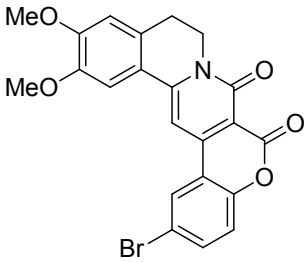
To a stirred solution of commercially available imine **1** (0.5 mmol) and triethylamine (1.5 mmol) in dry toluene (5 mL) was added acid chloride **5** (0.55 mmol) at 0 ℃. The resulting mixture was stirred at room temperature for 1 h and then refluxed for 2 h in oil bath. After completion of the reaction, the mixture was cooled to room temperature and diluted with dichloromethane (100 mL). The solution was washed sequentially with 5 N HCl (30 mL), water (30 mL) and brine (30 mL). The organic phase was then dried over anhydrous $MgSO_4$ and concentrated *in vacuum* to provide the crude product which was further purified by column chromatography to obtain the desired compound.

12,13-Dimethoxy-9,10-dihydrochromeno[4',3':4,5]pyrido[2,1-*a*]isoquinoline-6,7-dione (6a).



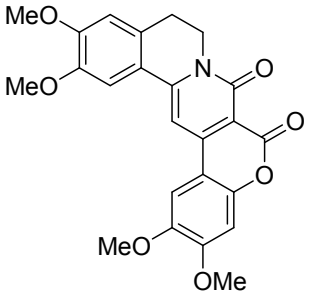
The title compound **6a** was synthesized following general procedure B from imine **1** (103 mg, 0.5 mmol), triethylamine (101 mg, 1.5 mmol), and 2-oxo-2*H*-chromene-3-carbonyl chloride (**5a**, 115 mg, 0.55 mmol), and purified by flash column chromatography (3% MeOH in DCM) to give a yellow solid (136 mg, 72% yield). R_f = 0.5 (5% MeOH/DCM). mp 252−254 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.01 (dd, J = 8.0, 1.2 Hz, 1H), 7.61 (td, J = 8.0, 1.2 Hz, 1H), 7.38–7.32 (m, 3H), 7.10 (s, 1H), 6.82 (s, 1H), 4.35 (t, J = 6.4 Hz, 2H), 4.10 (s, 3H), 3.99 (s, 3H), 2.98 (t, J = 6.4 Hz, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ: 159.5, 157.5, 154.1, 152.9, 149.3, 149.0, 148.0, 133.5, 131.1, 124.3 (2C), 120.5, 117.9, 116.2, 110.7, 109.1, 105.3, 94.0, 56.7, 56.4, 39.6, 27.5. IR $_{\nu max}$ (neat): 2898, 1745, 1647, 1565, 1425, 1217, 875, 750 cm^{-1}. HRMS (EI) m/z: [M$^+$] calcd for $C_{22}H_{17}NO_5$, 375.1107; found, 375.1104.

2-Bromo-12,13-dimethoxy-9,10-dihydrochromeno[4',3':4,5]pyrido[2,1-*a*]isoquinoline-6,7-dione (6b).



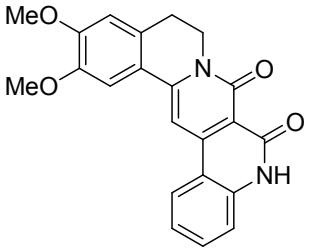
The title compound **6b** was synthesized following general procedure B from imine **1** (103 mg, 0.5 mmol), triethylamine (101 mg, 1.5 mmol), and 6-bromo-2-oxo-2*H*-chromene-3-carbonyl chloride (**5b**, 158 mg, 0.55 mmol), and purified by flash column chromatography (2% MeOH in DCM) to give a yellow solid (189 mg, 83% yield). R_f = 0.6 (5% MeOH/DCM). mp 306−308 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.09 (d, J = 2.0 Hz, 1H), 7.67 (dd, J = 8.8, 2.0 Hz, 1H), 7.34 (s, 1H), 7.25 (d, J = 9.2 Hz, 1H), 6.99 (s, 1H), 6.82 (s, 1H), 4.37 (t, J = 6.8 Hz, 2H), 4.07 (s, 3H), 4.00 (s, 3H), 2.99 (t, J = 6.8 Hz, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ: 159.6, 157.4, 153.2, 152.6, 150.0, 148.9, 147.0, 136.3, 131.3, 127.0, 120.1, 119.5, 117.8, 117.1, 110.7, 109.4, 104.7, 94.4, 56.7, 56.2, 39.7, 27.2. IR $_{\nu max}$ (neat): 2897, 1716, 1620, 1565, 1425, 1217, 875, 650 cm^{-1}. HRMS (EI) m/z: [M$^+$] calcd for $C_{22}H_{16}BrNO_5$, 453.0212; found, 453.0217.

2,3,12,13-Tetramethoxy-9,10-dihydrochromeno[4',3':4,5]pyrido[2,1-*a*]isoquinoline-6,7-dione (6c).



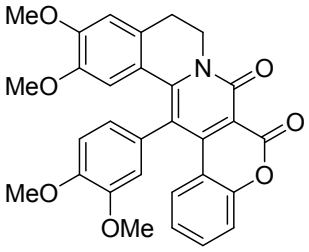
The title compound **6c** was synthesized following general procedure B from imine **1** (103 mg, 0.5 mmol), triethylamine (101 mg, 1.5 mmol), and 6,7-dimethoxy-2-oxo-2*H*-chromene-3-carbonyl chloride (**5c**, 148 mg, 0.55 mmol), and purified by flash column chromatography (5% MeOH in DCM) to give a yellow solid (138 mg, 63% yield). R_f = 0.3 (5% MeOH/DCM). mp 298−300 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.36 (s, 1H), 7.28 (s, 1H), 6.88 (s, 1H), 6.81 (s, 1H), 6.79 (s, 1H), 4.31 (t, J = 6.4 Hz, 2H), 4.04 (s, 3H), 4.02 (s, 3H), 3.99 (s, 3H), 3.95 (s, 3H), 2.96 (t, J = 6.4 Hz, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ: 160.0, 158.5, 154.5, 152.9, 150.0, 149.0, 148.8, 148.2, 146.5, 131.2, 120.4, 110.6, 109.8, 108.0, 105.6, 103.3, 100.4, 94.3, 56.9, 56.8, 56.4, 56.2, 39.4, 27.3. IR $_{vmax}$ (neat): 2942, 1738, 1687, 1565, 1425, 1217, 785, 632 cm^{-1}. HRMS (EI) m/z: [M$^+$] calcd for $C_{24}H_{21}NO_7$, 435.1318; found, 435.1313.

12,13-Dimethoxy-9,10-dihydro-5*H*-benzo[*f*]isoquinolino[2,1-*b*][2,7]naphthyridine-6,7-dione (6d).



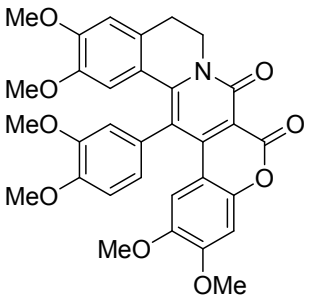
The title compound **6d** was synthesized following general procedure B from imine **1** (103 mg, 0.5 mmol), triethylamine (101 mg, 1.5 mmol), and 2-oxo-1,2-dihydroquinoline-3-carbonyl chloride (**5d**, 114 mg, 0.55 mmol), and purified by flash column chromatography (10% MeOH in DCM) to give a yellow solid (135 mg, 72% yield). R_f = 0.4 (10% MeOH/DCM). mp 382−384 ℃. ^{1}H NMR (CD_3OD, 400 MHz) δ: 8.68 (d, J = 8.0 Hz, 1H), 7.95 (s, 1H), 7.78–7.75 (m, 2H), 7.52–7.47 (m, 2H), 7.05 (s, 1H), 4.47 (t, J = 6.4 Hz, 2H), 4.05 (s, 3H), 3.97 (s, 3H), 3.10 (t, J = 6.4 Hz, 2H). ^{13}C{^{1}H} NMR (CD_3OD, 100 MHz) δ: 161.9, 161.8, 153.0, 149.1, 148.0, 147.3, 138.4, 133.2, 131.0, 125.4, 123.6, 120.1, 116.4, 116.2 110.5 (2C), 109.8, 97.8, 55.8, 55.3, 40.2, 26.6. IR $_{vmax}$ (neat): 3025, 2912, 1722, 1667, 1515, 1392, 1217, 812, 742 cm^{-1}. HRMS (EI) m/z: [M$^+$] calcd for $C_{22}H_{18}N_2O_4$, 374.1267; found, 374.1261.

15-(3,4-Dimethoxyphenyl)-12,13-dimethoxy-9,10-dihydrochromeno[4',3':4,5]pyrido[2,1-*a*]isoquinoline-6,7-dione (6e).



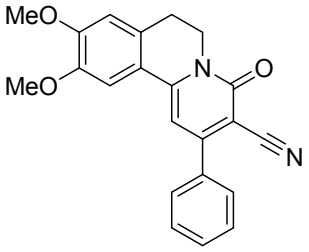
The title compound **6e** was synthesized following general procedure B from imine **1e** (171 mg, 0.5 mmol), triethylamine (101 mg, 1.5 mmol), and 2-oxo-2*H*-chromene-3-carbonyl chloride (**5e**, 115 mg, 0.55 mmol), and purified by flash column chromatography (5% MeOH in DCM) to give a yellow solid (175 mg, 68% yield). R_f = 0.4 (7% MeOH/DCM). mp 230−232 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.39–7.35 (m, 1H), 7.28 (d, J = 8.0 Hz, 1H), 6.90 (d, J = 8.0 Hz, 1H), 6.78–6.70 (m, 5H), 6.88 (s, 1H), 6.33 (s, 1H), 4.46–4.42 (m, 1H), 4.18–4.08 (m, 1H), 3.94 (s, 3H), 3.92 (s, 3H), 3.68 (s, 3H), 3.25 (s, 3H), 2.94 (t, J = 6.0 Hz, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ: 158.8, 157.5, 153.8, 150.7, 150.4, 149.5, 149.2, 148.0, 146.4, 132.8, 132.2, 131.1, 128.9, 124.8, 122.6, 121.0, 117.6, 117.0, 115.2, 114.6, 114.0, 112.4, 109.5, 107.2, 56.3, 56.1, 56.0, 55.3, 41.8, 28.2. IR $_{vmax}$ (neat): 2980, 1721, 1660, 1512, 1405, 1209, 844, 630 cm^{-1}. HRMS (EI) m/z: [M$^+$] calcd for $C_{30}H_{25}NO_7$, 511.1631; found, 511.1633.

15-(3,4-Dimethoxyphenyl)-2,3,12,13-tetramethoxy-9,10-dihydrochromeno[4',3':4,5]pyrido[2,1-*a*]isoquinoline-6,7-dione (6f).



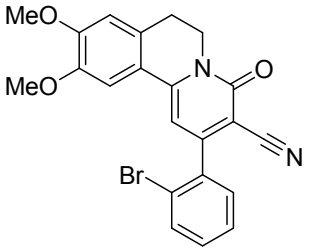
The title compound **6f** was synthesized following general procedure B from imine **1e** (171 mg, 0.5 mmol), triethylamine (101 mg, 1.5 mmol), and 6,7-dimethoxy-2-oxo-2*H*-chromene-3-carbonyl chloride (**5f**, 148 mg, 0.55 mmol), and purified by flash column chromatography (3% MeOH in DCM) to give a yellow solid (190 mg, 66% yield). R_f = 0.4 (10% MeOH/DCM). mp 270−272 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 6.92 (d, J = 8.0 Hz, 1H), 6.81 (d, J = 8.0 Hz, 1H), 6.80 (s, 1H), 6.76 (s, 1H), 6.73 (s, 1H), 6.73 (s, 1H), 6.37 (s, 1H), 6.31 (s, 1H), 4.43–4.40 (m, 1H), 4.10–4.05 (m, 1H), 3.92 (s, 3H), 3.90 (s, 6H), 3.72 (s, 3H), 3.26 (s, 3H), 3.22 (s, 3H), 2.93 (t, J = 6.4 Hz, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ: 159.0, 157.0, 152.7, 150.7, 150.5, 150.1, 149.4, 149.1, 147.5, 146.3, 144.2, 132.8, 131.5, 125.0, 121.0, 115.5, 113.9, 113.8, 112.5, 109.8, 109.5, 108.9, 105.7, 99.9, 56.4, 56.2 (2C), 56.0, 55.3, 55.2, 41.8, 28.3. IR $_{vmax}$ (neat): 2912, 1712, 1647, 1565, 1212, 812, 752 cm^{-1}. HRMS (EI) m/z: [M$^+$] calcd for $C_{32}H_{29}NO_9$, 571.1842; found, 571.1845.

9,10-Dimethoxy-4-oxo-2-phenyl-6,7-dihydro-4*H*-pyrido[2,1-*a*]isoquinoline-3-carbonitrile (6g).



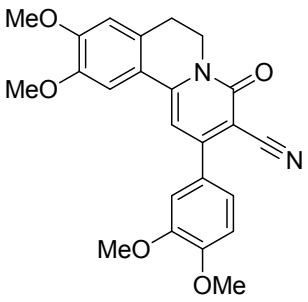
The title compound **6g** was synthesized following general procedure B from imine **1** (103 mg, 0.5 mmol), triethylamine (101 mg, 1.5 mmol) and (*E*)-2-cyano-3-phenylacryloyl chloride (**5g**, 105 mg, 0.55 mmol), and purified by flash column chromatography (40% EtOAc in hexanes) to give a yellow solid (122 mg, 68% yield). R_f = 0.3 (50% EtOAc/hexanes). mp 184−186 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.67–7.65 (m, 2H), 7.53–7.52 (m, 3H), 7.18 (s, 1H), 6.80 (s, 1H), 6.67 (s, 1H), 4.33 (t, J = 6.4 Hz, 2H), 3.97 (s, 3H), 3.93 (s, 3H), 3.00 (t, J = 6.4 Hz, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ: 161.0, 158.5, 152.7, 149.0, 147.2, 136.6, 130.5 (2C), 129.1 (2C), 128.1 (2C), 120.2, 116.5, 110.7, 108.8, 103.3, 98.7, 56.5, 56.3, 40.0, 27.3. IR $_{vmax}$ (neat): 2910, 2205, 1716, 1645, 1501, 1211, 809, 710 cm^{-1}. HRMS (EI) m/z: [M$^+$] calcd for $C_{22}H_{18}N_2O_3$, 358.1317; found, 358.1309.

2-(2-Bromophenyl)-9,10-dimethoxy-4-oxo-6,7-dihydro-4*H*-pyrido[2,1-*a*]isoquinoline-3-carbonitrile (6h).



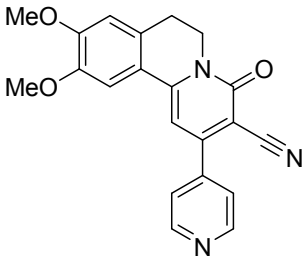
The title compound **6h** was synthesized following general procedure B from imine **1** (103 mg, 0.5 mmol), triethylamine (101 mg, 1.5 mmol) and (*E*)-3-(2-bromophenyl)-2-cyanoacryloyl chloride (**5h**, 149 mg, 0.55 mmol), and purified by flash column chromatography (35% EtOAc in hexanes) to give a yellow solid (182 mg, 83% yield). R_f = 0.45 (50% EtOAc/hexanes). mp 210−212 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.73 (d, J = 7.6 Hz, 1H), 7.47 (t, J = 7.6 Hz, 1H), 7.40 (dd, J = 7.6, 1.6 Hz, 1H), 7.32 (td, J = 7.6, 1.6 Hz, 1H), 7.14 (s, 1H), 6.79 (s, 1H), 6.59 (s, 1H), 4.36 (bs, 2H), 3.97 (s, 3H), 3.91 (s, 3H), 3.02 (t, J = 6.4 Hz, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ: 160.4, 158.0, 152.7, 148.9, 147.0, 137.5, 133.5, 131.1, 130.4, 129.8, 127.8, 121.2, 120.0, 115.4, 110.6, 108.6, 103.9, 100.8, 56.3, 56.2, 39.9, 27.1. IR $_{vmax}$ (neat): 2911, 2215, 1738, 1656, 1535, 1250, 875, 550 cm^{-1}. HRMS (EI) m/z: [M$^+$] calcd for $C_{22}H_{17}BrN_2O_3$, 436.0423; found, 436.0426.

2-(3,4-Dimethoxyphenyl)-9,10-dimethoxy-4-oxo-6,7-dihydro-4*H*-pyrido[2,1-*a*]isoquinoline-3-carbonitrile (6i).



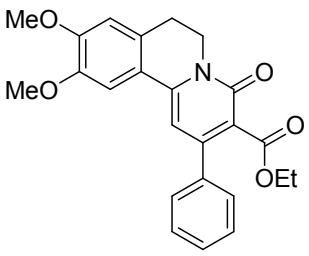
The title compound **6i** was synthesized following general procedure B from imine **1** (103 mg, 0.5 mmol), triethylamine (101 mg, 1.5 mmol) and (*E*)-2-cyano-3-(3,4-dimethoxyphenyl)acryloyl chloride (**5i**, 138 mg, 0.55 mmol), and purified by flash column chromatography (50% EtOAc in hexanes) to give a yellow solid (132 mg, 63% yield). R_f = 0.4 (60% EtOAc/hexanes). mp 262−264 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.28–7.26 (m, 2H), 7.20 (s, 1H), 7.01 (d, J = 8.8 Hz, 1H), 6.79 (s, 1H), 6.67 (s, 1H), 4.33 (t, J = 6.4 Hz, 2H), 3.97 (s, 3H), 3.96 (s, 3H), 3.95 (s, 3H), 3.94 (s, 3H), 3.00 (t, J = 6.4 Hz, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ: 161.1, 157.9, 152.7, 151.1, 149.1, 148.9, 146.9, 130.5, 128.8, 121.3, 120.2, 117.0, 111.4, 111.3, 110.7, 108.8, 103.1, 97.9, 56.5, 56.33, 56.31, 56.1, 39.9, 27.3. IR $_{vmax}$ (neat): 2999, 2225, 1728, 1641, 1565, 1217, 820, 716 cm^{-1}. HRMS (EI) m/z: [M$^+$] calcd for $C_{24}H_{22}N_2O_5$, 418.1529; found, 418.1519.

9,10-Dimethoxy-4-oxo-2-(pyridin-4-yl)-6,7-dihydro-4*H*-pyrido[2,1-*a*]isoquinoline-3-carbonitrile (6j).



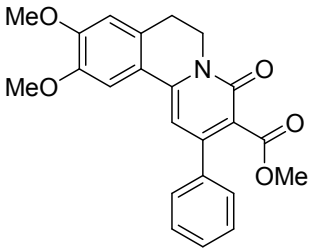
The title compound **6j** was synthesized following general procedure B from imine **1** (103 mg, 0.5 mmol), triethylamine (101 mg, 1.5 mmol) and (*E*)-2-cyano-3-(pyridin-4-yl)acryloyl chloride (**5j**, 106 mg, 0.55 mmol), and purified by flash column chromatography (1% MeOH in DCM) to give a yellow solid (139 mg, 77% yield). R_f = 0.5 (5% MeOH/DCM). mp 306−308 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.80 (d, J = 6.0 Hz, 2H), 7.55 (d, J = 6.0 Hz, 2H), 7.28 (s, 1H), 6.81 (s, 1H), 6.62 (s, 1H), 4.35 (t, J = 6.4 Hz, 2H), 3.98 (s, 3H), 3.94 (s, 3H), 3.01 (t, J = 6.4 Hz, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ: 160.4, 155.5, 153.0, 150.6 (3C), 149.0, 148.1, 144.0, 130.6, 122.2, 119.7, 115.6, 110.6, 108.7, 102.1, 98.6, 56.4, 56.3 40.0, 27.1. IR $_{vmax}$ (neat): 2928, 2245, 1739, 1652, 1515, 1217, 885, 550 cm^{-1}. HRMS (EI) m/z: [M$^+$] calcd for $C_{21}H_{17}N_3O_3$, 359.1270; found, 359.1277.

Ethyl 9,10-dimethoxy-4-oxo-2-phenyl-6,7-dihydro-4*H*-pyrido[2,1-*a*]isoquinoline-3-carboxylate (6k).



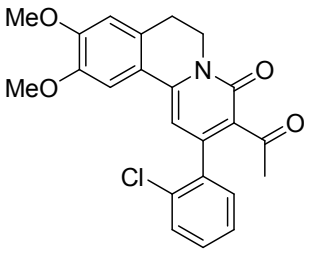
The title compound **6k** was synthesized following general procedure B from imine **1** (103 mg, 0.5 mmol), triethylamine (101 mg, 1.5 mmol) and (*E*)-ethyl 2-(chlorocarbonyl)-3-phenylacrylate (**5k**, 131 mg, 0.55 mmol), and purified by flash column chromatography (30% EtOAc in hexanes) to give a yellow solid (128 mg, 63% yield). R_f = 0.5 (50% EtOAc/hexanes). mp 156−158 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.48–7.43 (m, 5H), 7.16 (s, 1H), 6.76 (s, 1H), 6.58 (s, 1H), 4.33 (t, J = 6.4 Hz, 2H), 4.16 (q, J = 6.4 Hz, 2H), 3.95 (s, 3H), 3.92 (s, 3H), 2.95 (t, J = 6.4 Hz, 2H), 1.05 (t, J = 6.4 Hz, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ: 166.7, 159.7, 151.6, 150.5, 148.6, 143.9, 138.4, 129.5, 128.9, 128.6 (2C), 127.5 (2C), 120.9, 120.8, 110.5, 108.2, 103.1, 61.2, 56.3, 56.1, 39.4, 27.4, 13.8. IR $_{vmax}$ (neat): 2941, 1708, 1655, 1480, 1217, 808, 655 cm^{-1}. HRMS (EI) m/z: [M$^+$] calcd for $C_{24}H_{23}NO_5$, 405.1576; found, 405.1567.

Methyl 9,10-dimethoxy-4-oxo-2-phenyl-6,7-dihydro-4H-pyrido[2,1-*a*]isoquinoline-3-carboxylate (6l).



The title compound **6l** was synthesized following general procedure B from imine **1** (103 mg, 0.5 mmol), triethylamine (101 mg, 1.5 mmol) and (*E*)-methyl 2-(chlorocarbonyl)-3-phenylacrylate (**5l**, 124 mg, 0.55 mmol), and purified by flash column chromatography (30% EtOAc in hexanes) to give a yellow solid (122 mg, 62% yield). R_f = 0.45 (50% EtOAc/hexanes). mp 152−154 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.46–7.45 (m, 5H), 7.16 (s, 1H), 6.77 (s, 1H), 6.58 (s, 1H), 4.33 (t, J = 6.4 Hz, 2H), 3.95 (s, 3H), 3.92 (s, 3H), 3.69 (s, 3H), 2.96 (t, J = 6.4 Hz, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ: 167.3, 159.7, 151.6, 150.6, 148.6, 144.0, 138.3, 129.6, 129.1, 128.7 (2C), 127.5, 127.4 (2C), 120.8, 110.5, 108.2, 103.2, 56.3, 56.1, 52.3, 39.4, 27.2. IR $_{vmax}$ (neat): 2922, 1754, 1638, 1532, 1311, 880, 690 cm^{-1}. HRMS (EI) m/z: [M$^+$] calcd for $C_{23}H_{21}NO_5$, 391.1420; found, 391.1423.

3-Acetyl-2-(2-chlorophenyl)-9,10-dimethoxy-6,7-dihydro-4*H*-pyrido[2,1-*a*]isoquinolin-4-one (6m).

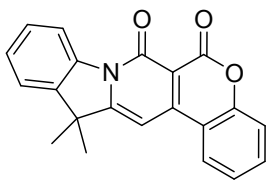


The title compound **6m** was synthesized following general procedure B from imine **1** (103 mg, 0.5 mmol), triethylamine (101 mg, 1.5 mmol) and (*E*)-2-(2-chlorobenzylidene)-3-oxobutanoyl chloride (**5m**, 134 mg, 0.55 mmol), and purified by flash column chromatography (25% EtOAc in hexanes) to give a yellow solid (134 mg, 65% yield). R_f = 0.55 (50% EtOAc/hexanes). mp 308−310 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.01 (d, J = 8.0 Hz, 1H), 7.61 (t, J = 8.0 Hz, 1H), 7.37 (t, J = 8.0 Hz, 1H), 7.36 (s, 1H), 7.31 (d, J = 8.0 Hz, 1H), 7.10 (s, 1H), 6.82 (s, 1H), 4.34 (t, J = 6.4 Hz, 2H), 4.07 (s, 3H), 4.00 (s, 3H), 2.98 (t, J = 6.4 Hz, 2H), 1.77 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ: 159.5, 157.5, 154.0, 152.9, 149.3, 148.9, 148.0, 133.5, 131.1, 124.3 (2C), 120.5, 117.9, 116.1, 110.7, 109.0, 105.2, 94.0, 56.7, 56.4, 39.5. 31.7, 27.5. IR $_{vmax}$ (neat): 2947, 2345, 1738, 1649, 1565, 1425, 1217, 810, 659 cm^{-1}. HRMS (EI) m/z: [M$^+$] calcd for $C_{23}H_{20}ClNO_4$, 409.1081; found, 409.1085.

General procedure C for preparation of compounds **8a**–**d**.

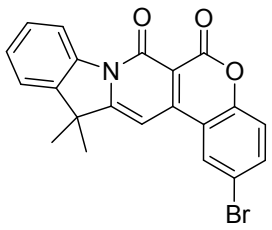
To a stirred solution of 2-methyl indole **7** (0.5 mmol) and triethylamine (1.5 mmol) in dry toluene (3 mL) was added acid chloride **5** (0.55 mmol) at 0 ℃. The resulting mixture was stirred at room temperature for 1 h and then refluxed in oil bath for 2 h. After completion of the reaction, the mixture was cooled to room temperature and diluted with ethyl acetate (100 mL). The solution was washed with 5 N HCl (30 mL), water (30 mL) and brine (30 mL). The organic phase was dried over anhydrous $MgSO_4$, filtered and evaporated under reduced pressure to give the crude product which was further purified by column chromatography to obtain the desired compound.

13,13-Dimethyl-6*H*-chromeno[4',3':4,5]pyrido[1,2-*a*]indole-6,7(13*H*)-dione (8a).



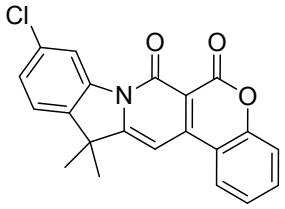
The title compound **8a** was synthesized following general procedure C from imine **7a** (80 mg, 0.5 mmol), triethylamine (101 mg, 1.5 mmol), and 2-oxo-2*H*-chromene-3-carbonyl chloride (**5a**, 115 mg, 0.55 mmol), and purified by flash column chromatography (40% EtOAc in hexanes) to give a white solid (135 mg, 82% yield). R_f= 0.3 (50% EtOAc/hexanes). mp 306−308 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.84 (d, J = 8.0 Hz, 1H), 8.00 (d, J = 8.0 Hz, 1H), 7.65–7.61 (m, 1H), 7.48–7.35 (m, 5H), 6.95 (s, 1H), 1.66 (s, 6H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ: 164.9, 158.3, 157.2, 154.0, 149.0, 140.0, 139.0, 133.8, 128.9, 127.2, 124.7, 124.4, 122.1, 118.8, 117.8, 116.1, 107.6, 93.3, 46.8, 27.9 (2C). IR $_{vmax}$ (neat): 2998, 1740, 1655, 1425, 1217, 835, 750 cm^{-1}. HRMS (EI) m/z: [M$^+$] calcd for $C_{21}H_{15}NO_3$, 329.1052; found, 329.1056.

2-Bromo-13,13-dimethyl-6*H*-chromeno[4',3':4,5]pyrido[1,2-*a*]indole-6,7(13*H*)-dione (8b).



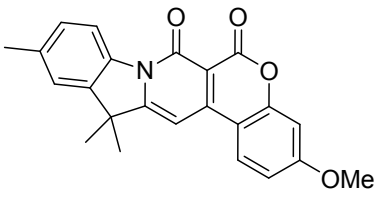
The title compound **8b** was synthesized following general procedure C from imine **7b** (80 mg, 0.5 mmol), triethylamine (101 mg, 1.5 mmol), and 6-bromo-2-oxo-2*H*-chromene-3-carbonyl chloride (**5b**, 158 mg, 0.55 mmol), and purified by flash column chromatography (35% EtOAc in hexanes) to give a white solid (190 mg, 93% yield). R_f = 0.4 (50% EtOAc/hexanes). mp 318−320 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz, δ): 8.80 (d, J = 7.6 Hz, 1H), 8.11 (d, J = 2.0 Hz, 1H), 7.69 (dd, J = 8.8, 2.0 Hz, 1H), 7.47–7.37 (m, 3H), 7.23 (d, J = 8.8 Hz, 1H), 6.89 (s, 1H), 1.68 (s, 6H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ: 165.5, 158.0, 156.5, 152.9, 147.7, 139.9, 139.0, 136.4, 129.0, 127.5, 127.3, 122.1, 119.6, 118.9, 117.9, 117.1, 107.7, 93.1, 47.0, 27.8 (2C). IR $_{\nu max}$ (neat): 2922, 1718, 1652, 1438, 1212, 880, 751 cm^{-1}. HRMS (EI) m/z: [M$^+$] calcd for $C_{21}H_{14}BrNO_3$, 407.0157; found, 407.0150.

10-Chloro-13,13-dimethyl-6*H*-chromeno[4',3':4,5]pyrido[1,2-*a*]indole-6,7(13*H*)-dione (8c).



The title compound **8c** was synthesized following general procedure C from imine **7c** (97 mg, 0.5 mmol), triethylamine (101 mg, 1.5 mmol), and 2-oxo-2*H*-chromene-3-carbonyl chloride (**5a**, 115 mg, 0.55 mmol), and purified by flash column chromatography (35% EtOAc in hexanes) to give a white solid (140 mg, 77% yield). R_f = 0.45 (50% EtOAc/hexanes). mp 340−342 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.77 (d, J = 8.4 Hz, 1H), 8.00 (d, J = 8.4 Hz, 1H), 7.65 (td, J = 8.4, 1.2 Hz, 1H), 7.43 (dd, J = 8.4, 2.0 Hz, 1H), 7.41–7.36 (m, 3H), 6.95 (s, 1H), 1.66 (s, 6H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ: 164.3, 158.0, 157.0, 154.1, 149.2, 140.9, 138.5, 134.0, 132.9, 129.1, 124.7, 124.5, 122.7, 119.8, 117.9, 116.0, 107.7, 93.5, 46.8, 27.8 (2C). IR $_{\nu max}$ (neat): 2977, 1733, 1660, 1420, 1217, 875, 733 cm^{-1}. HRMS (EI) m/z: [M$^+$] calcd for $C_{21}H_{14}ClNO_3$, 363.0662; found, 363.0671.

3-Methoxy-11,13,13-trimethyl-6*H*-chromeno[4',3':4,5]pyrido[1,2-*a*]indole-6,7(13*H*)-dione (8d).



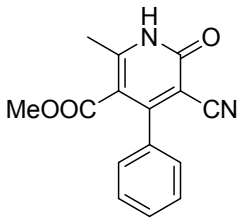
The title compound **8d** was synthesized following general procedure C from imine **7d** (87 mg, 0.5 mmol), triethylamine (101 mg, 1.5 mmol), and 7-methoxy-2-oxo-2*H*-chromene-3-carbonyl chloride (131 mg, 0.55 mmol), and purified by flash column chromatography (50% EtOAc in hexanes) to give a white solid (137 mg, 73% yield). R_f= 0.5 (80% EtOAc/hexanes). mp 298−300 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.68 (d, J = 8.4 Hz, 1H), 7.87 (d, J = 9.2 Hz, 1H), 7.24 (d, J = 8.4 Hz, 1H), 7.19 (s, 1H), 6.92 (dd, J = 8.4, 2.4 Hz, 1H), 6.81–6.80 (m, 2H),

3.90 (s, 3H), 2.44 (s, 3H), 1.62 (s, 6H). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100 MHz) δ: 165.3, 164.3, 157.8, 156.7, 155.7, 149.6, 140.1, 138.0, 136.8, 129.1, 127.8, 123.7, 117.4, 113.0, 109.7, 104.7, 101.1, 94.7, 56.5, 46.7, 27.3 (2C), 21.4. IR $_{vmax}$ (neat): 2944, 1740, 1647, 1425, 1280, 888, 650 cm^{-1}. HRMS (EI) m/z: [M^+] calcd for $C_{23}H_{19}NO_4$, 373.1314; found, 373.1315.

General procedure D for preparation of compounds **10a**–**d**.

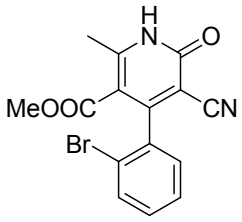
To a stirred solution of enamine **9** (0.5 mmol) and triethylamine (1.5 mmol) in dry toluene (3 mL) was added acid chloride **5** (0.55 mmol) at 0 ℃. The resulting mixture was stirred at room temperature for 1 h and then refluxed in oil bath for 2 h. After completion of the reaction, the mixture was cooled to room temperature and diluted with ethyl acetate (100 mL). The solution was washed with 5 N HCl (30 mL), water (30 mL) and brine (30 mL). The organic phase was dried over anhydrous $MgSO_4$, filtered and evaporated under reduced pressure to give the crude product which was further purified by column chromatography to obtain the desired compound.

Methyl 5-cyano-2-methyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxylate (10a).



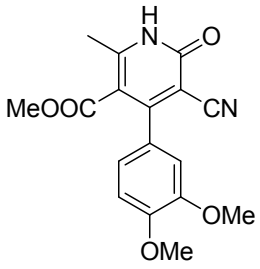
The title compound **10a** was synthesized following general procedure D from enamine **9** (58 mg, 0.5 mmol), triethylamine (101 mg, 1.5 mmol), and (*E*)-2-cyano-3-phenylacryloyl chloride (**5g**, 105 mg, 0.55 mmol), and purified by flash column chromatography (60% EtOAc in hexanes) to give a white solid (57 mg, 42% yield). R_f = 0.3 (80% EtOAc/hexanes). mp 300−302 ℃. ^1H NMR (DMSO-d_6, 400 MHz) δ: 13.02 (s, 1H), 7.53–7.50 (m, 3H), 7.35–7.30 (m, 2H), 3.35 (s, 3H), 2.39 (s, 3H), $^{13}C\{^{1}H\}$ NMR (DMSO-d_6, 100 MHz) δ: 165.9, 160.3, 159.8, 153.5, 136.2, 130.0, 129.0 (2C), 127.6 (2C), 115.9, 112.4, 101.0, 52.4, 18.7. IR $_{vmax}$ (neat): 2983, 1745, 1622, 1415, 1271, 790, 630 cm^{-1}. HRMS (EI) m/z: [M^+] calcd for $C_{15}H_{12}N_2O_3$, 268.0848; found, 268.0850.

Methyl 4-(2-bromophenyl)-5-cyano-2-methyl-6-oxo-1,6-dihydropyridine-3-carboxylate (10b).



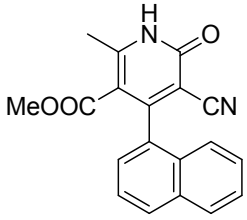
The title compound **10b** was synthesized following general procedure D from enamine **9** (58 mg, 0.5 mmol), triethylamine (101 mg, 1.5 mmol), and (*E*)-3-(2-bromophenyl)-2-cyanoacryloyl chloride (**5h**, 149 mg, 0.55 mmol), and purified by flash column chromatography (50% EtOAc in hexanes) to give a white solid (84 mg, 48% yield). R_f = 0.5 (80% EtOAc/hexanes). mp 228−230 ℃. ^1H NMR ($CDCl_3$, 400 MHz) δ: 13.55 (s, 1H), 7.69 (d, J = 8.0 Hz, 1H), 7.44 (t, J = 8.0 Hz, 1H), 7.33 (td, J = 8.0, 1.2 Hz, 1H), 7.22 (dd, J = 8.0, 1.2 Hz, 1H), 3.48 (s, 3H), 2.71 (s, 3H), $^{13}C\{^{1}H\}$ NMR (DMSO-d_6, 100 MHz) δ: 164.8, 160.0, 159.5, 155.7, 137.6, 132.8, 131.3, 129.4, 128.2, 120.8, 115.1, 111.5, 102.3, 52.4, 19.5. IR $_{vmax}$ (neat): 2998, 1741, 1660, 1425, 1213, 860, 622 cm^{-1}. HRMS (EI) m/z: [M^+] calcd for $C_{15}H_{11}BrN_2O_3$, 345.9953; found, 345.9950.

Methyl 5-cyano-4-(3,4-dimethoxyphenyl)-2-methyl-6-oxo-1,6-dihydropyridine-3-carboxylate (10c).



The title compound **10c** was synthesized following general procedure D from enamine **9** (58 mg, 0.5 mmol), triethylamine (101 mg, 1.5 mmol), and (*E*)-2-cyano-3-(3,4-dimethoxyphenyl)acryloyl chloride (**5i**, 138 mg, 0.55 mmol), and purified by flash column chromatography (2% MeOH in DCM) to give a white solid (70 mg, 43% yield). R_f = 0.35 (80% EtOAc/hexanes). mp 182−184 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 13.59 (s, 1H), 7.00 (dd, J = 8.4, 2.0 Hz, 1H), 6.95 (d, J = 8.4 Hz, 1H), 6.90 (d, J = 2.0 Hz, 1H), 3.94 (s, 3H), 3.91 (s, 3H), 3.53 (s, 3H), 2.59 (s, 3H), ^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz) δ: 166.4, 160.5, 159.4, 152.5, 150.4, 148.8, 128.0, 120.8, 116.3, 112.8, 112.0, 111.1, 100.7, 56.1, 56.0, 52.7, 18.6. IR $_{vmax}$ (neat): 2992, 1740, 1632, 1414, 1270, 795, 630 cm^{-1}. HRMS (EI) m/z: [M$^+$] calcd for $C_{17}H_{16}N_2O_5$, 328.1059; found, 328.1055.

Methyl 5-cyano-2-methyl-4-(naphthalen-1-yl)-6-oxo-1,6-dihydropyridine-3-carboxylate (10d).

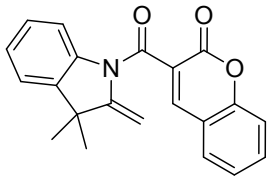


The title compound **10d** was synthesized following general procedure D from enamine **9** (58 mg, 0.5 mmol), triethylamine (101 mg, 1.5 mmol), and (*E*)-2-cyano-3-(naphthalen-1-yl)acryloyl chloride (**5n**, 133 mg, 0.55 mmol), and purified by flash column chromatography (1% MeOH in DCM) to give a white solid (89 mg, 56% yield). R_f = 0.4 (80% EtOAc/hexanes). mp 262−264 ℃. ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 13.13 (s, 1H), 8.03 (t, J = 7.6, Hz, 2H), 7.63–7.57 (m, 3H), 7.56–7.51 (m, 1H), 7.41 (dd, J = 7.6, J = 0.8 Hz, 1H), 3.02 (s, 3H), 2.47 (s, 3H), ^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz) δ: 165.4, 160.3, 159.4, 154.5, 134.1, 133.2, 130.0, 129.8, 128.8, 127.3, 126.8, 125.8, 125.6, 125.1, 115.7, 113.0, 102.8, 52.4, 19.2. IR $_{vmax}$ (neat): 2988, 1738, 1628, 1416, 1279, 792, 635 cm^{-1}. HRMS (EI) m/z: [M$^+$] calcd for $C_{19}H_{14}N_2O_3$, 318.1004; found, 318.1006.

Procedure for preparation of compound **11**.

To a stirred solution of 2-methyl indole **7a** (80 mg, 0.5 mmol) and triethylamine (101 mg, 1.5 mmol) in dry toluene (3 mL) was added acid chloride **5a** (115 mg, 0.55 mmol) at 0 ℃. The resulting mixture was stirred at room temperature for 1 h. After completion of the reaction, the reaction mixture was diluted with ethyl acetate (100 mL). The organic phase was washed with 5 N HCl (30 mL), water (30 mL), brine (30 mL), dried over anhydrous $MgSO_4$, filtered and evaporated under reduced pressure to provide the crude product. The crude product was further purified by column chromatography to obtain the desired compound.

3-(3,3-Dimethyl-2-methyleneindoline-1-carbonyl)-2*H*-chromen-2-one (11).

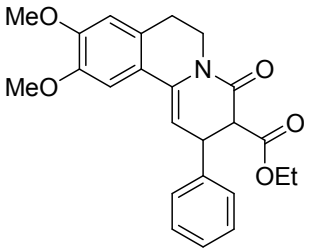


Yellow solid. R_f = 0.6 (50% EtOAc/hexanes). 54 mg. Yield 32%. mp 136−138 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.18 (s, 1H), 7.93 (d, J = 8.0 Hz, 1H), 7.64–7.60 (m, 2H), 7.38–7.33 (m, 2H), 7.24–7.20 (m, 2H), 7.17–7.13 (m, 1H), 4.89 (d, J = 2.0 Hz, 1H), 4.66 (d, J = 2.0 Hz, 1H), 1.48 (s, 6H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz, δ): 162.8, 157.1, 156.8, 154.3, 144.7, 140.6, 139.0, 133.2, 128.9, 127.5, 126.4, 125.0, 124.9, 122.1, 118.2, 116.7, 115.6, 93.8, 44.4 (2C), 23.0. IR $_{vmax}$ (neat): 2998, 1720, 1643, 1421, 1215, 835, 720 cm^{-1}. HRMS (EI) m/z: [M$^+$] calcd for $C_{21}H_{17}NO_3$, 331.1208; found, 331.1202.

Procedure for preparation of compound **12**.

To a stirred solution of imine **1** (103 mg, 0.5 mmol) and triethylamine (101 mg, 1.5 mmol) in dry toluene (3 mL) was added acid chloride **5k** (131 mg, 0.55 mmol) at 0 ℃. The resulting mixture was stirred at room temperature for 1 h and then stirred at 60 ℃ for another 1 h. After completion of the reaction, the reaction mixture was diluted with ethyl acetate (100 mL). The organic phase was washed with 5 N HCl (30 mL), water (30 mL), brine (30 mL), dried over anhydrous $MgSO_4$, filtered and evaporated under reduced pressure to provide the crude product. The crude product was further purified by column chromatography to obtain the desired compound.

Ethyl 9,10-dimethoxy-4-oxo-2-phenyl-3,4,6,7-tetrahydro-2H-pyrido[2,1-*a*]isoquinoline-3-carboxylate (12).



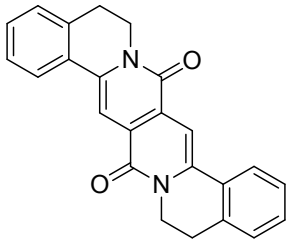
Yellow liquid. R_f = 0.4 (50% EtOAc/hexanes). 78 mg. Yield 38%. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.36–7.25 (m, 5H), 7.03 (s, 1H), 6.72 (s, 1H), 5.71 (d, J = 4.0 Hz, 1H), 4.28 (dd, J = 10.8, 4.0 Hz,, 1H), 4.21–4.08 (m, 3H), 3.89 (s, 3H), 3.86 (s, 3H), 3.79–3.73 (m, 1H), 3.70 (d, J = 10.8 Hz, 1H), 2.86–2.82 (m, 2H), 1.13 (t, J = 7.2, Hz, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ: 169.1, 165.4, 149.7, 148.3, 141.0, 135.1, 128.9 (2C), 127.7 (2C), 127.6, 127.4, 121.4, 110.8, 106.9, 103.6, 61.4, 56.1, 56.0, 55.7, 40.9, 39.0, 28.7, 14.0. IR $_{vmax}$ (neat): 2939, 1716, 1649, 1565, 1425, 1217, 845, 650 cm^{-1}. HRMS (EI) m/z: [M$^+$] calcd for $C_{24}H_{25}NO_5$, 407.1733; found, 407.1730.

Procedure E for preparation of compounds **19a**–**b**.

To a stirred solution of imine **1** (2.0 eq) and triethylamine (3.0 eq) in dry toluene (5 mL) was added furmaroyl chloride **18** (1.0 eq) at 0 ℃. The resulting mixture was stirred at room temperature for 2 h. After completion of the reaction, toluene was evaporated and the crude compound was diluted with dichloromethane (200 mL). The organic phase was washed with 5 N HCl (50 mL), water (50 mL), brine (50 mL), dried over anhydrous $MgSO_4$, filtered and

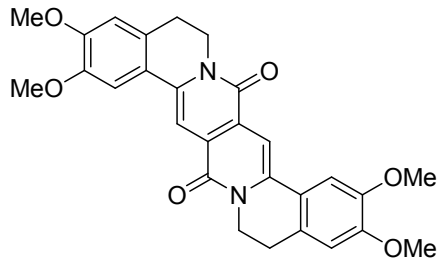
evaporated under reduced pressure to provide the crude product. The crude product was further purified by column chromatography to obtain the desired compound.

5,6,14,15-tetrahydrodiisoquinolino[2,1-b:2',1'-*g*][2,6]naphthyridine-8,17-dione (19a).



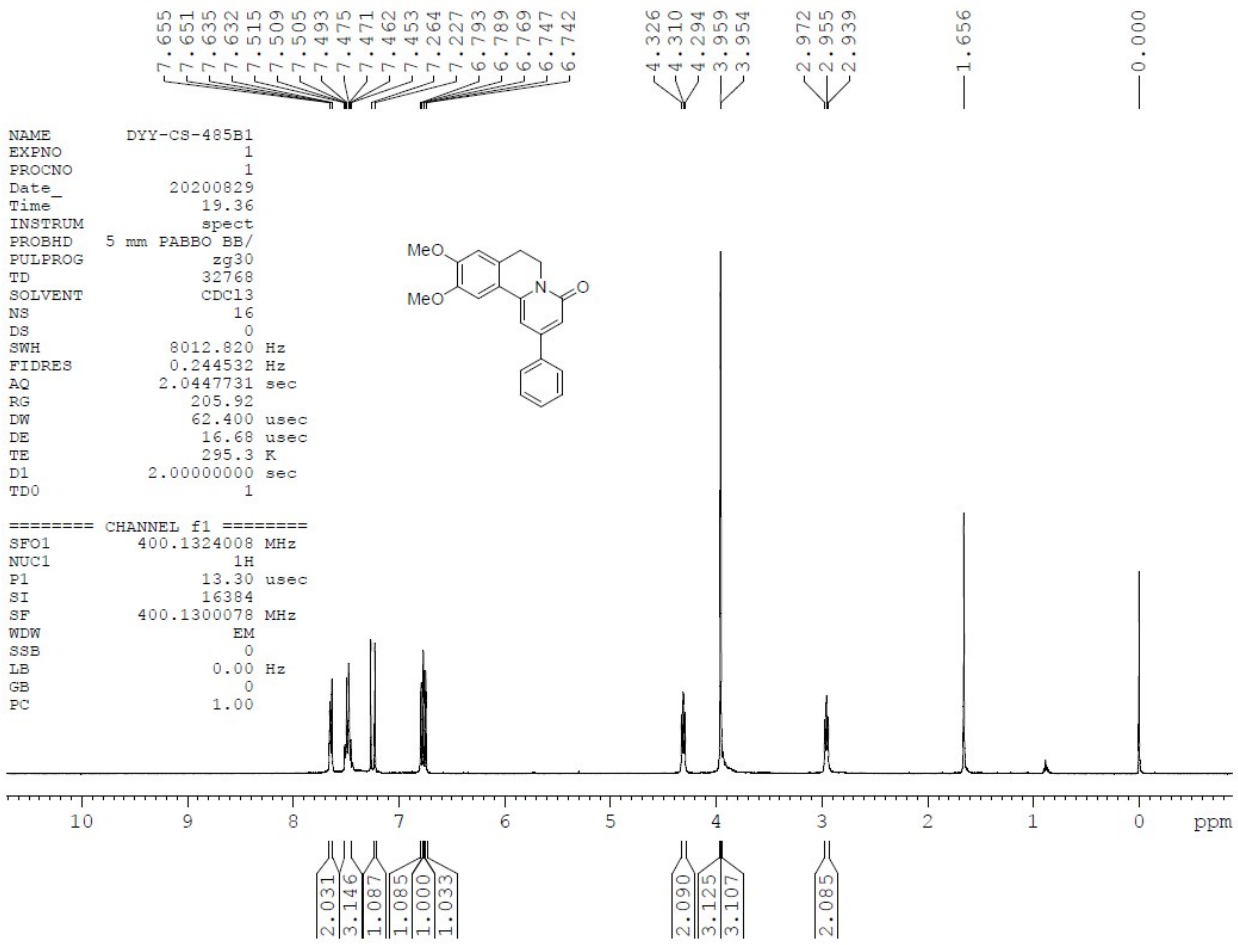
The title compound **19a** was synthesized following general procedure E from imine **1a** (1.0 g, 6.89 mmol), triethylamine (1.1 g, 10.33 mmol), and fumaroyl chloride (**18**, 527 mg, 3.44 mmol), and purified by flash column chromatography (0.5% MeOH in DCM) to give a blue solid (970 mg. Yield 77%). R_f = 0.5 (50% EtOAc/hexanes). mp 314−316 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.83–7.79 (m, 2H), 7.37–7.32 (m, 4H), 7.28–7.25 (m, 4H), 3.85 (t, J = 6.4 Hz, 4H), 3.06 (t, J = 6.4 Hz, 4H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ: 169.4, 145.1, 135.0, 130.4, 129.9, 128.7, 127.4, 126.5, 125.8, 97.7, 36.4, 28.8. IR $_{\nu max}$ (neat): 2948, 1732, 1655, 1570, 1420, 1217, 815, 757 cm^{-1}. HRMS (EI) m/z: [M$^+$] calcd for $C_{24}H_{18}N_2O_6$, 366.1368; found, 366.1365.

2,3,11,12-Tetramethoxy-5,6,14,15-tetrahydrodiisoquinolino[2,1-b:2',1'-*g*][2,6]naphthyridine-8,17-dione (19b).

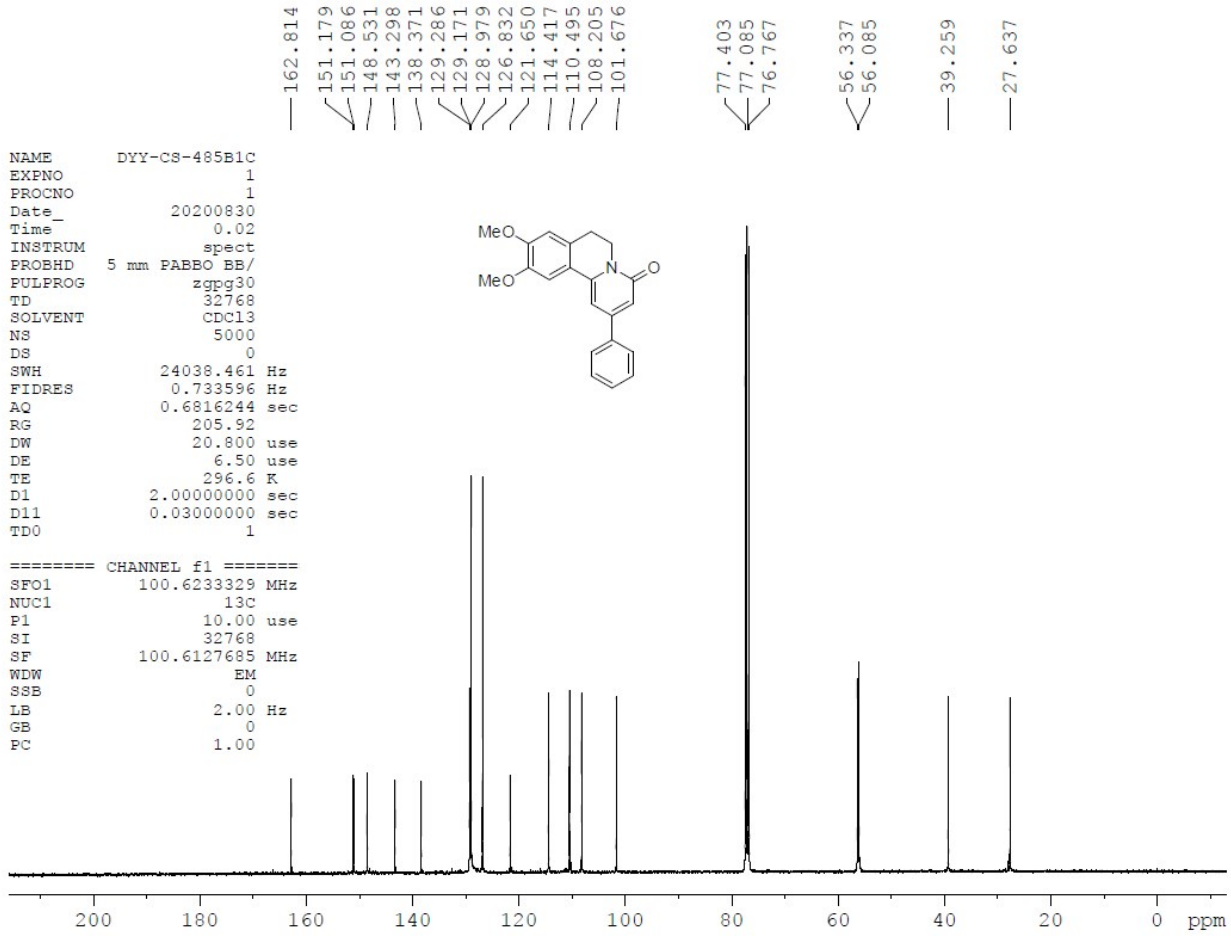


The title compound **19b** was synthesized following general procedure E from imine **1b** (103 mg, 0.5 mmol), triethylamine (76 mg, 0.75 mmol), and fumaroyl chloride (**18**, 38 mg, 0.25 mmol), and purified by flash column chromatography (1% MeOH in DCM) to give a blue solid (154 mg. Yield 63%). R_f = 0.5 (80% EtOAc/hexanes). mp 310−312 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.21 (s, 2H), 7.17 (s, 2H), 6.73 (s, 2H), 3.96 (s, 6H), 3.93 (s, 6H), 3.83 (t, J = 6.4 Hz, 4H), 3.00 (t, J = 6.4 Hz, 4H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ: 169.9, 151.4, 148.8, 144.5, 129.3, 129.0, 119.2, 111.2, 107.6, 96.5, 56.4, 56.2, 36.6, 28.5. IR $_{\nu max}$ (neat): 2955, 1720, 1652, 1569, 1425, 1211, 810, 777 cm^{-1}. HRMS (EI) m/z: [M$^+$] calcd for $C_{28}H_{26}N_2O_6$, 486.1791; found, 486.1786.

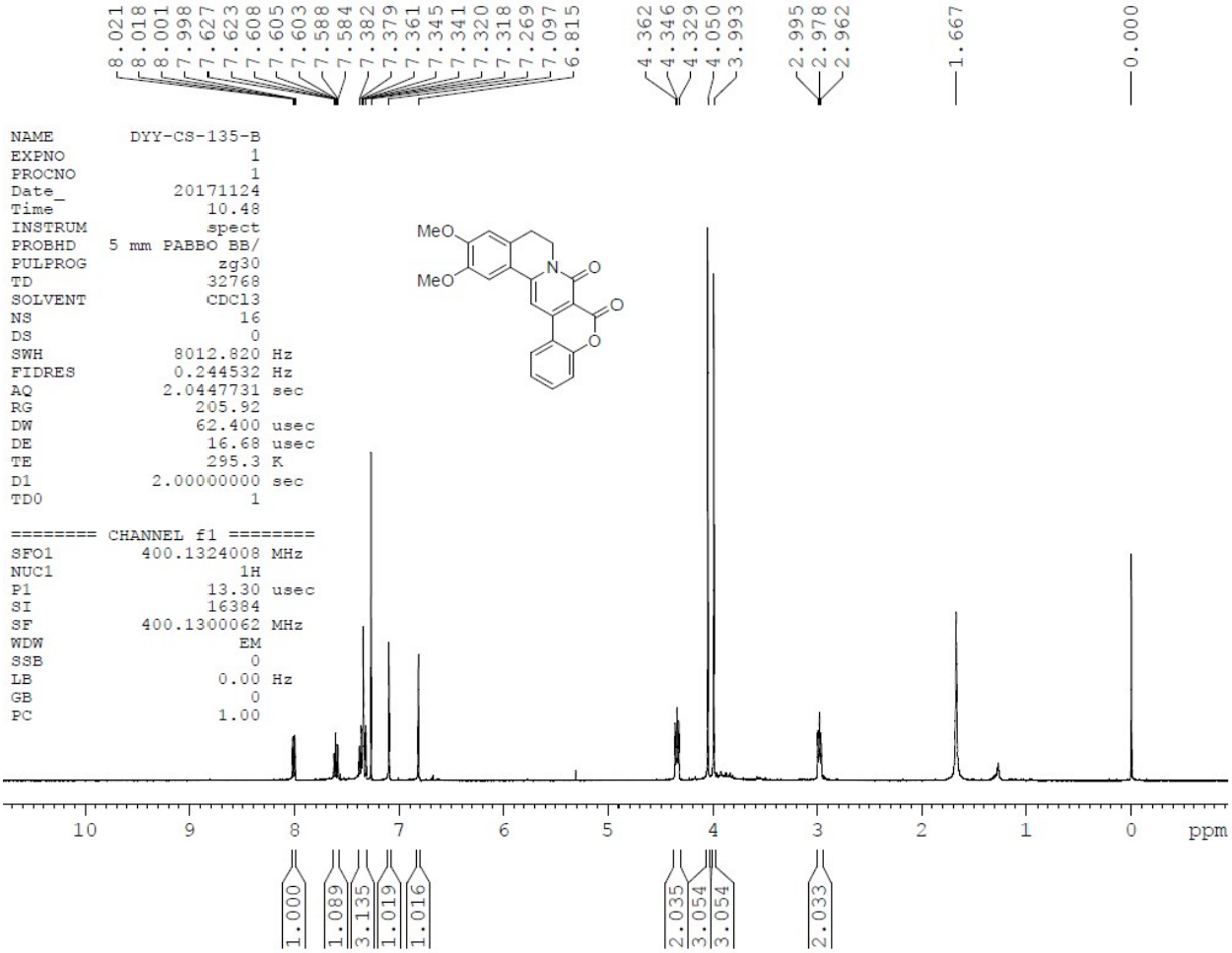
^{1}HNMR of compound **4a** ($CDCl_3$)



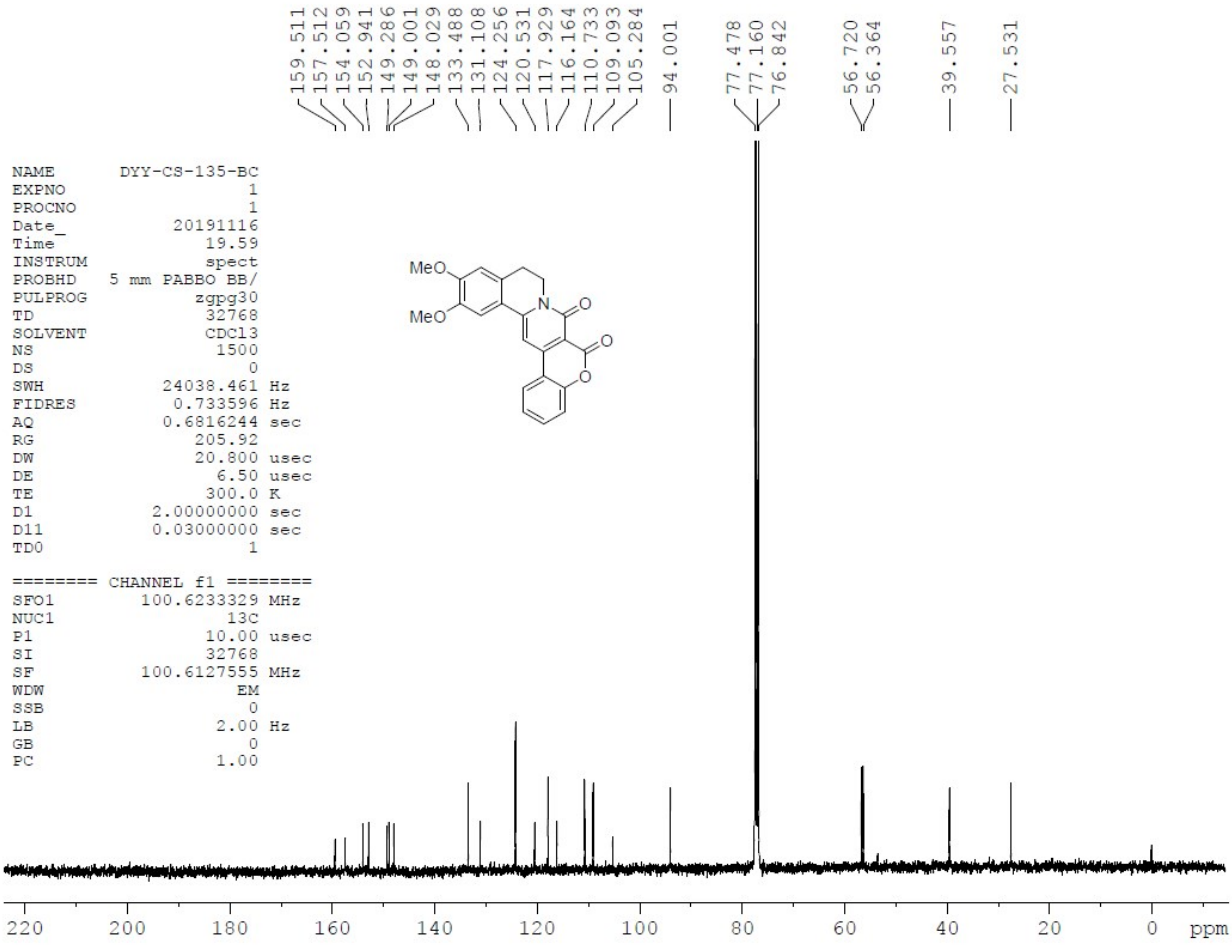
^{13}C NMR of compound **4a** ($CDCl_3$)



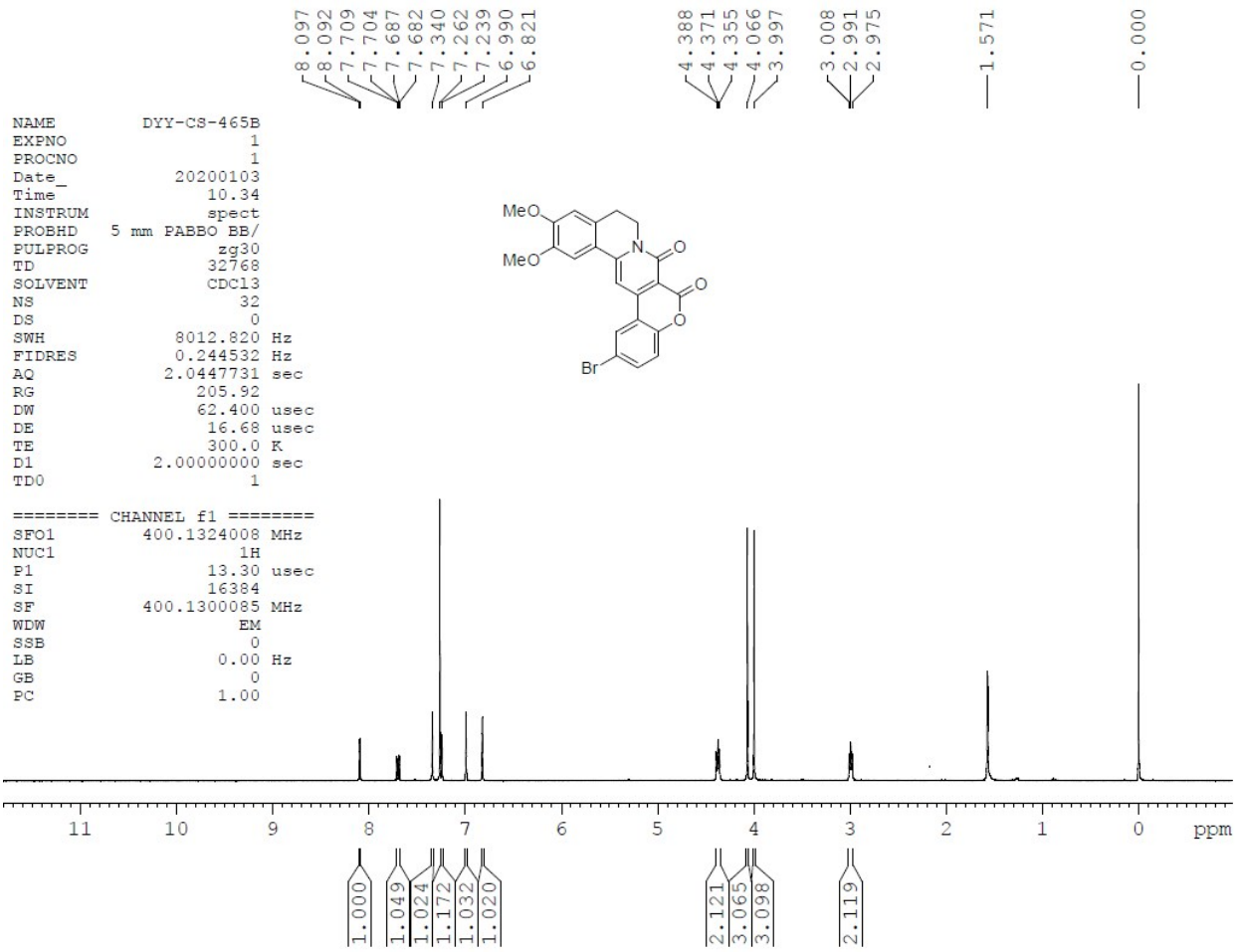
^{1}HNMR of compound **6a** ($CDCl_3$)



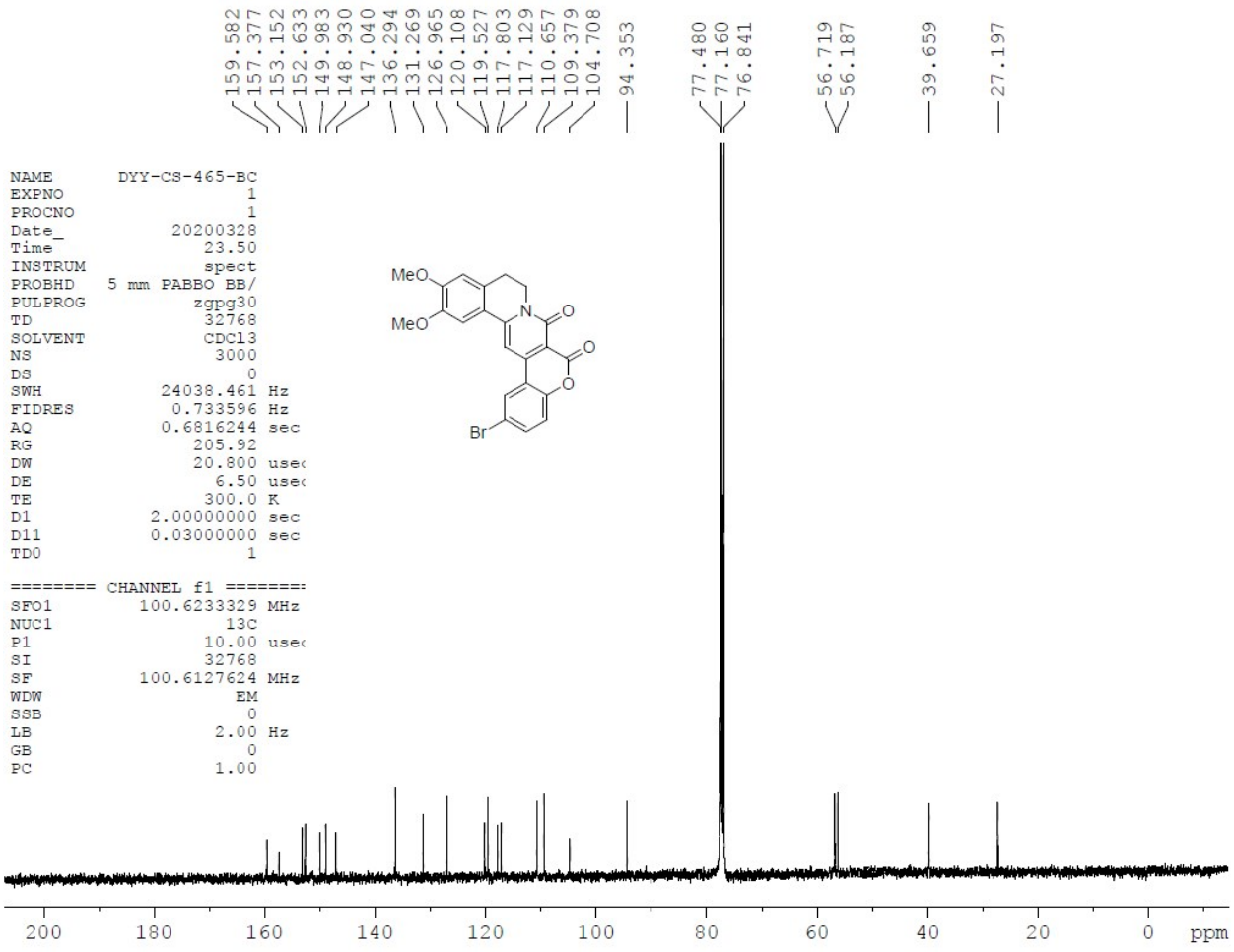
^{13}C NMR of compound **6a** ($CDCl_3$)



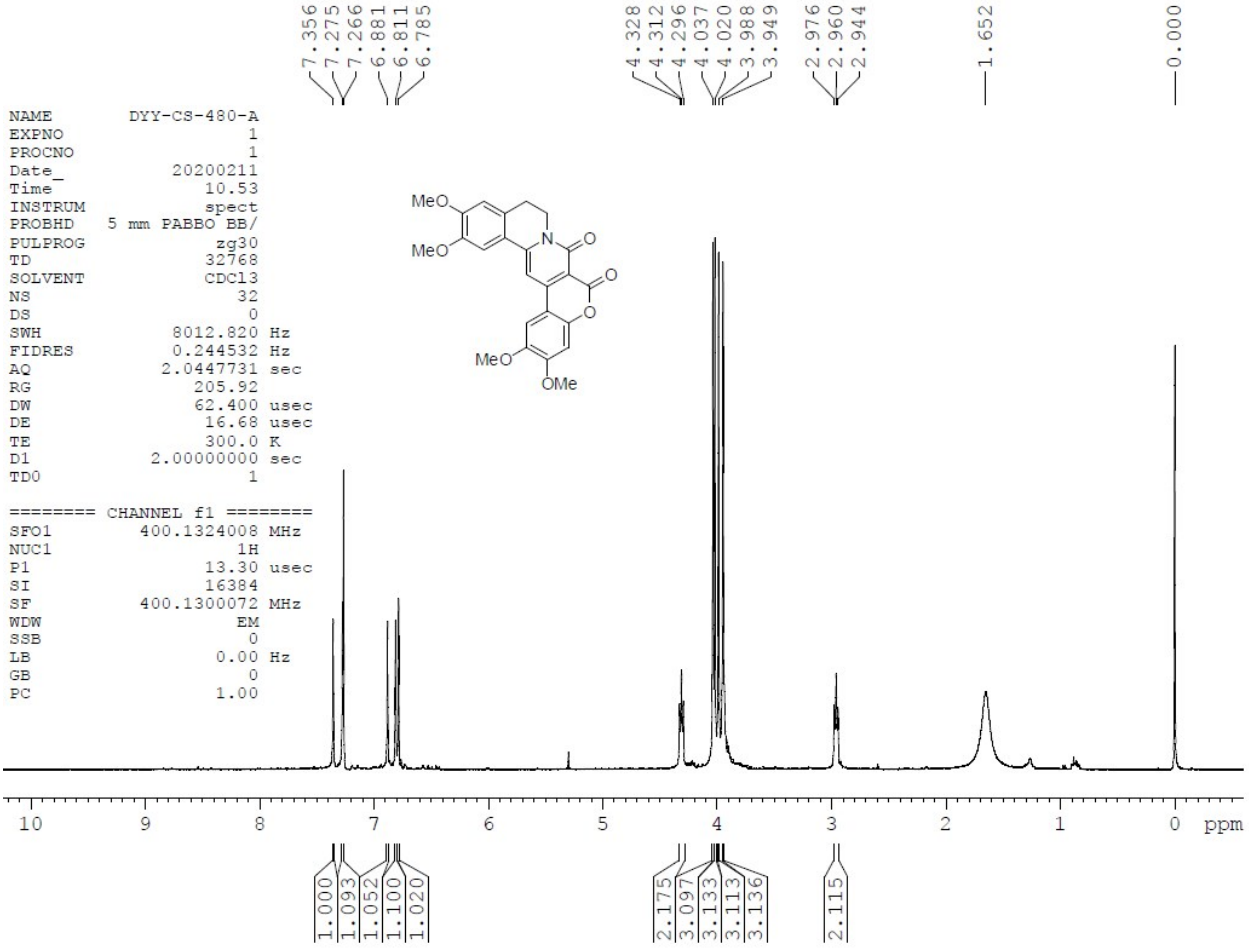
^{1}H NMR of compound **6b** ($CDCl_3$)



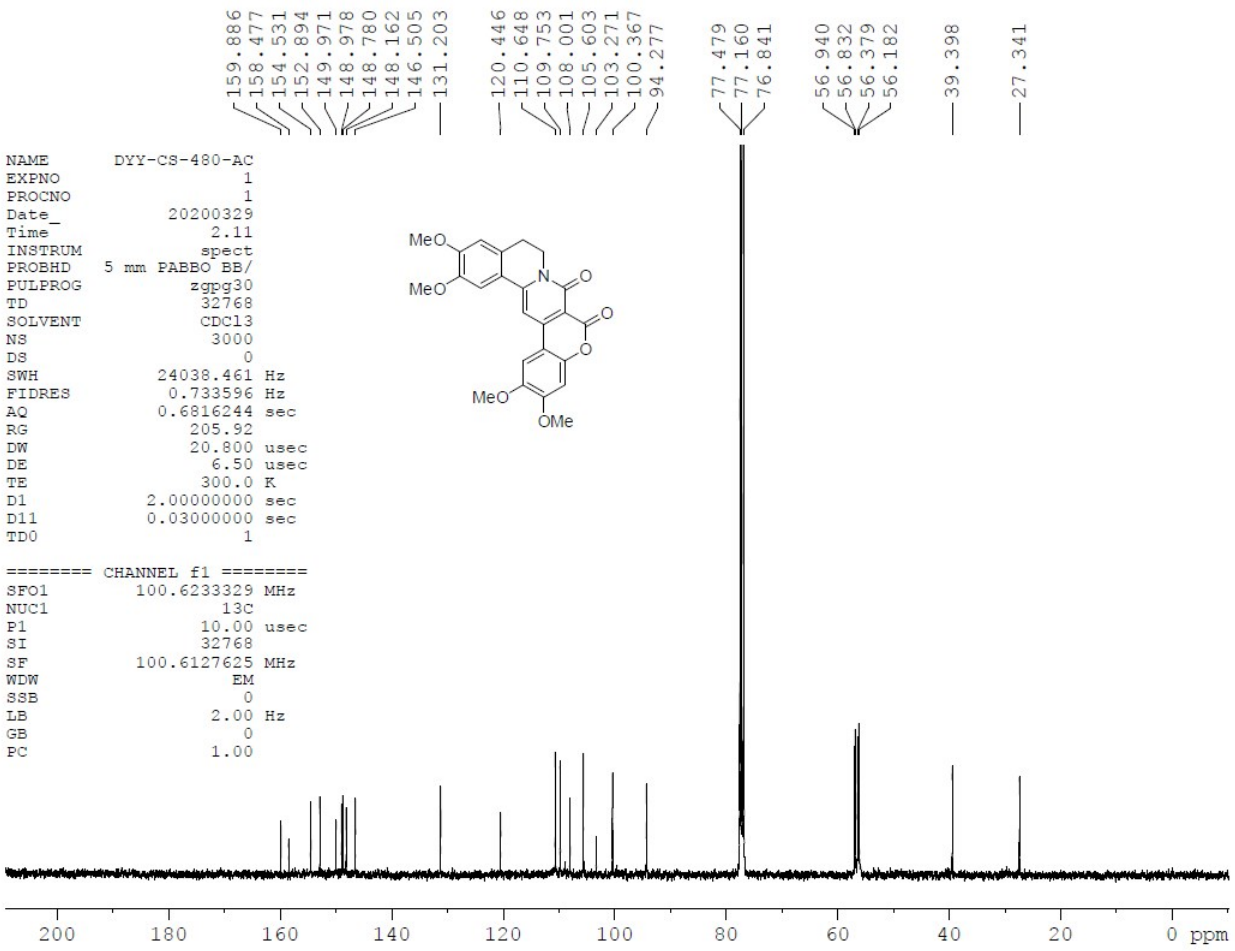
^{13}C NMR of compound **6b** ($CDCl_3$)



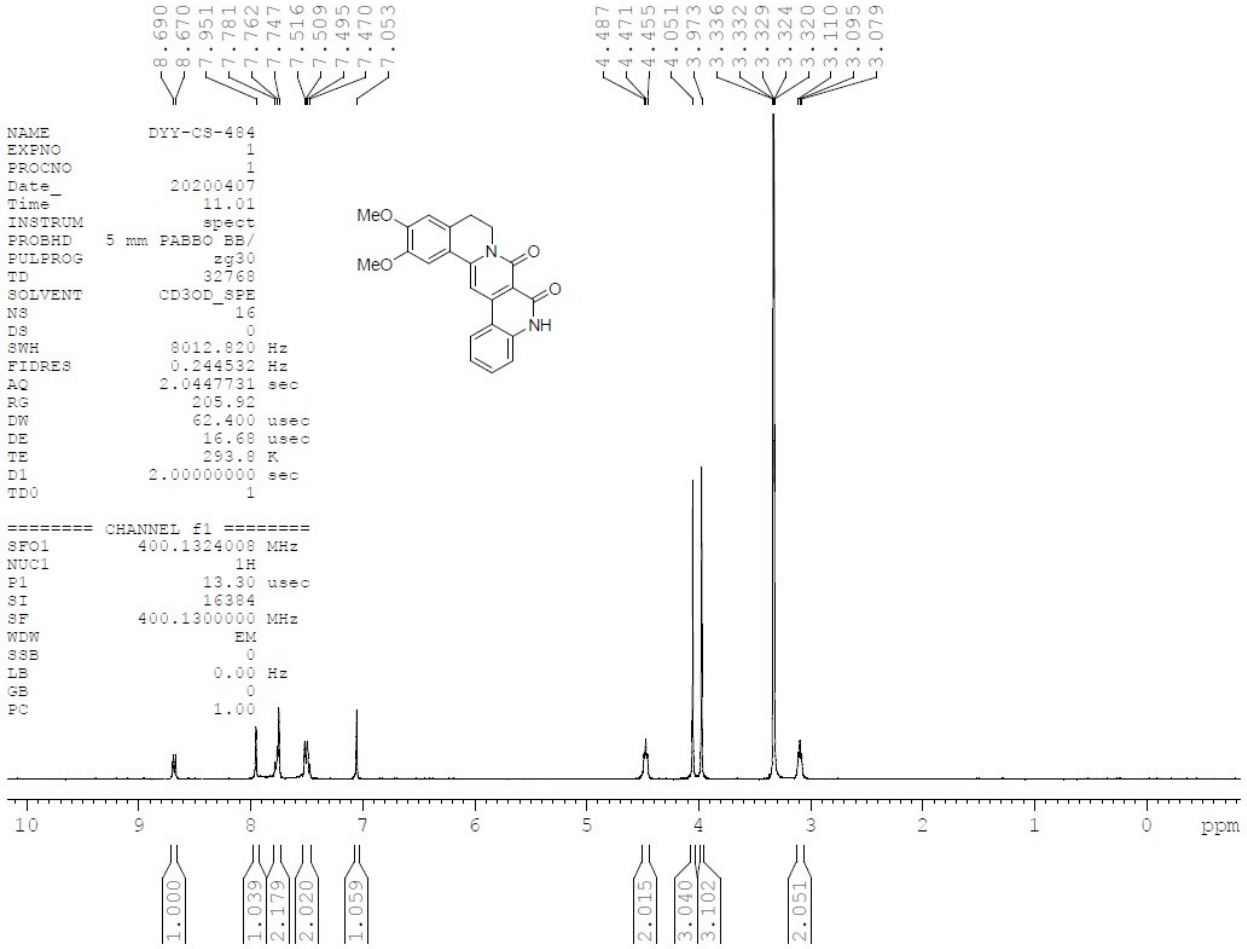
^{1}H NMR of compound **6c** ($CDCl_3$)



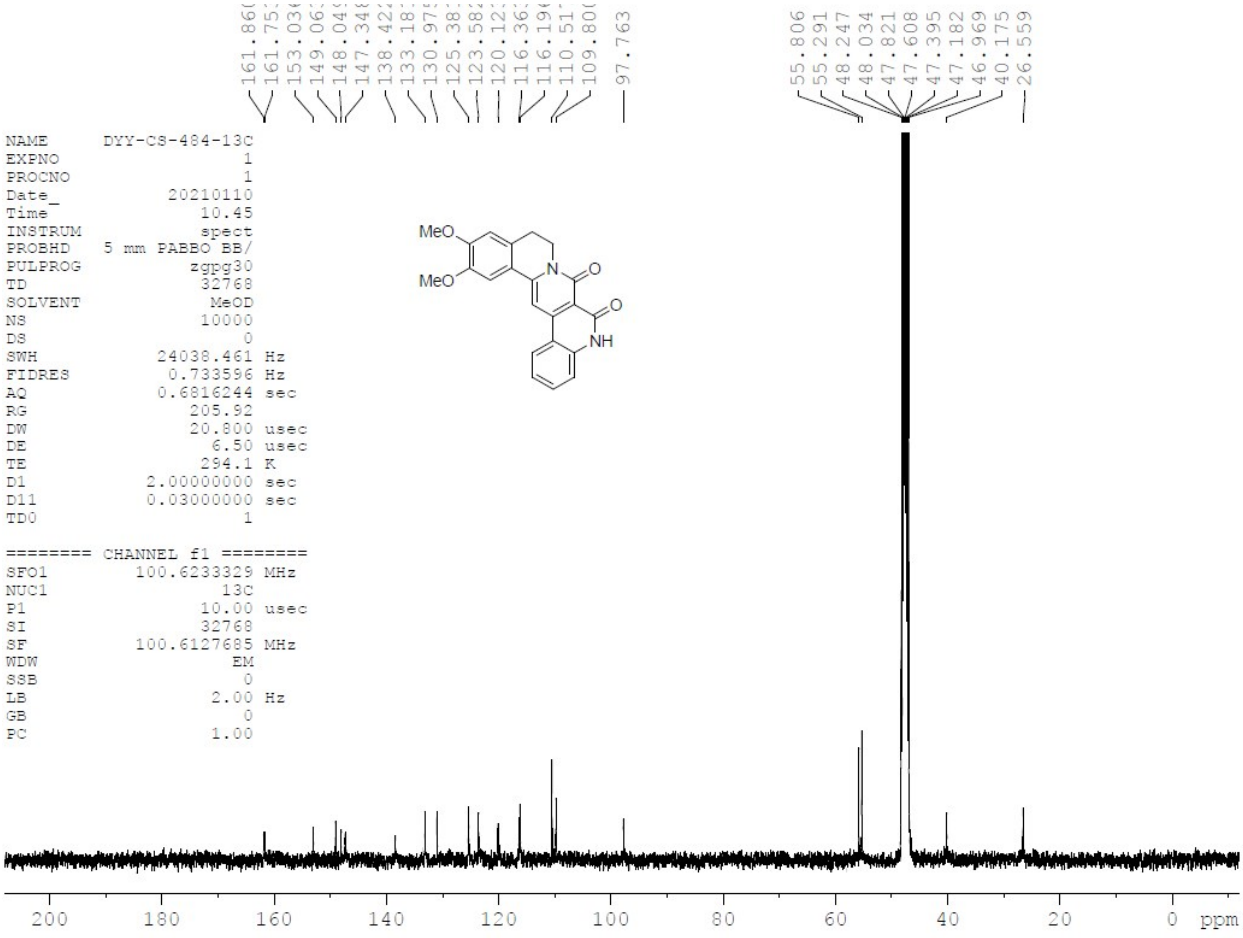
^{13}C NMR of compound **6c** ($CDCl_3$)



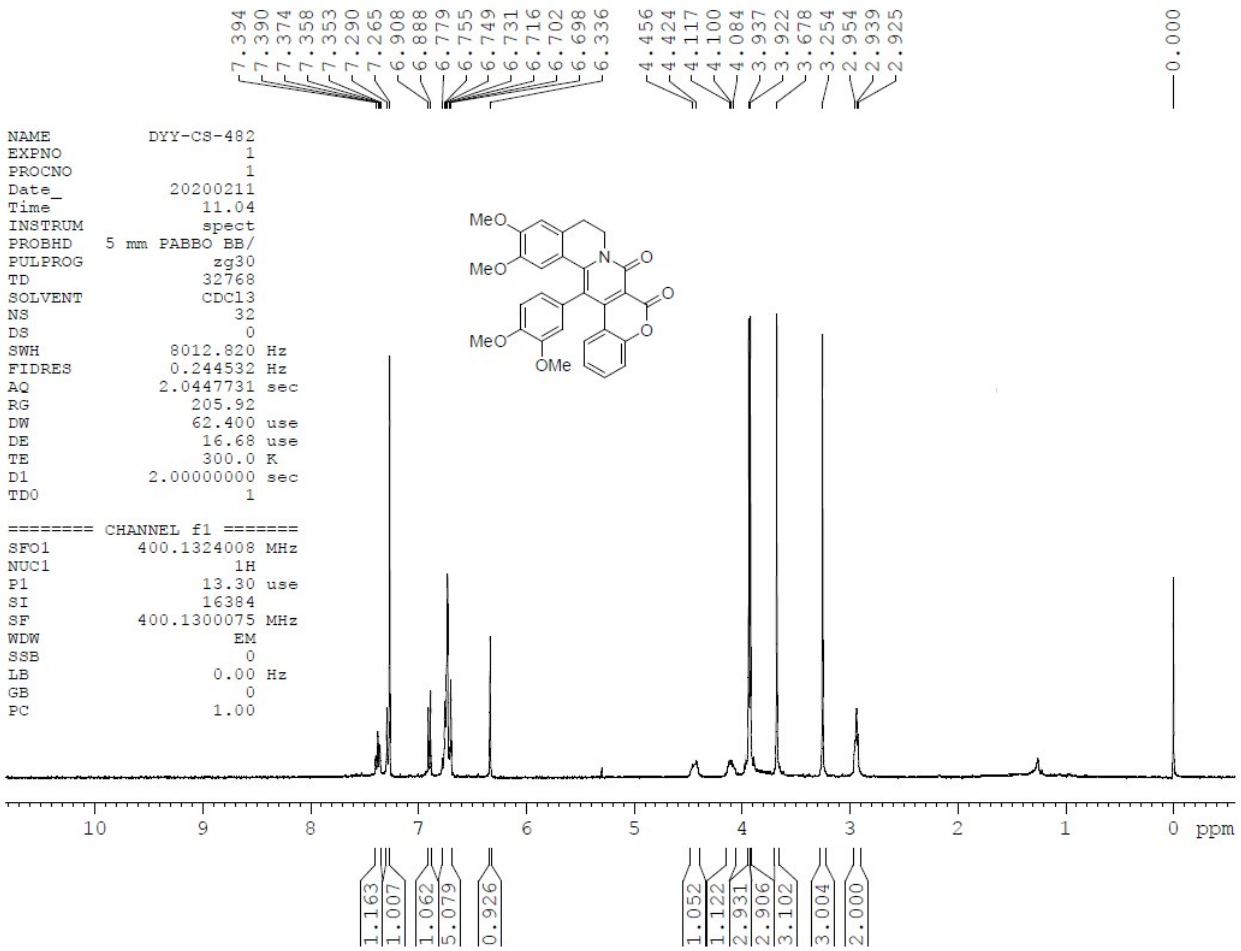
^{1}H NMR of compound **6d** (CD_3OD)



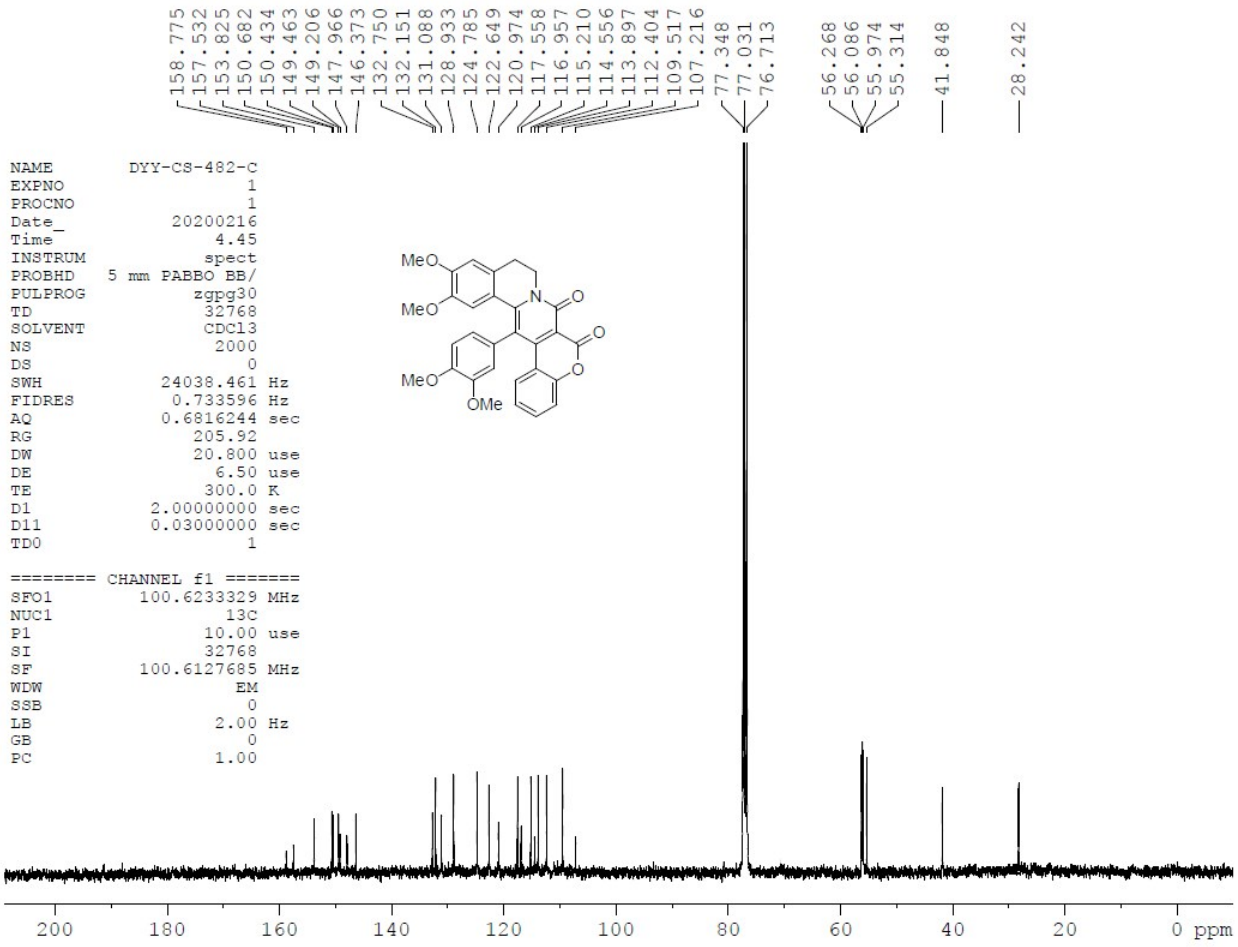
^{13}C NMR of compound **6d** (CD_3OD)



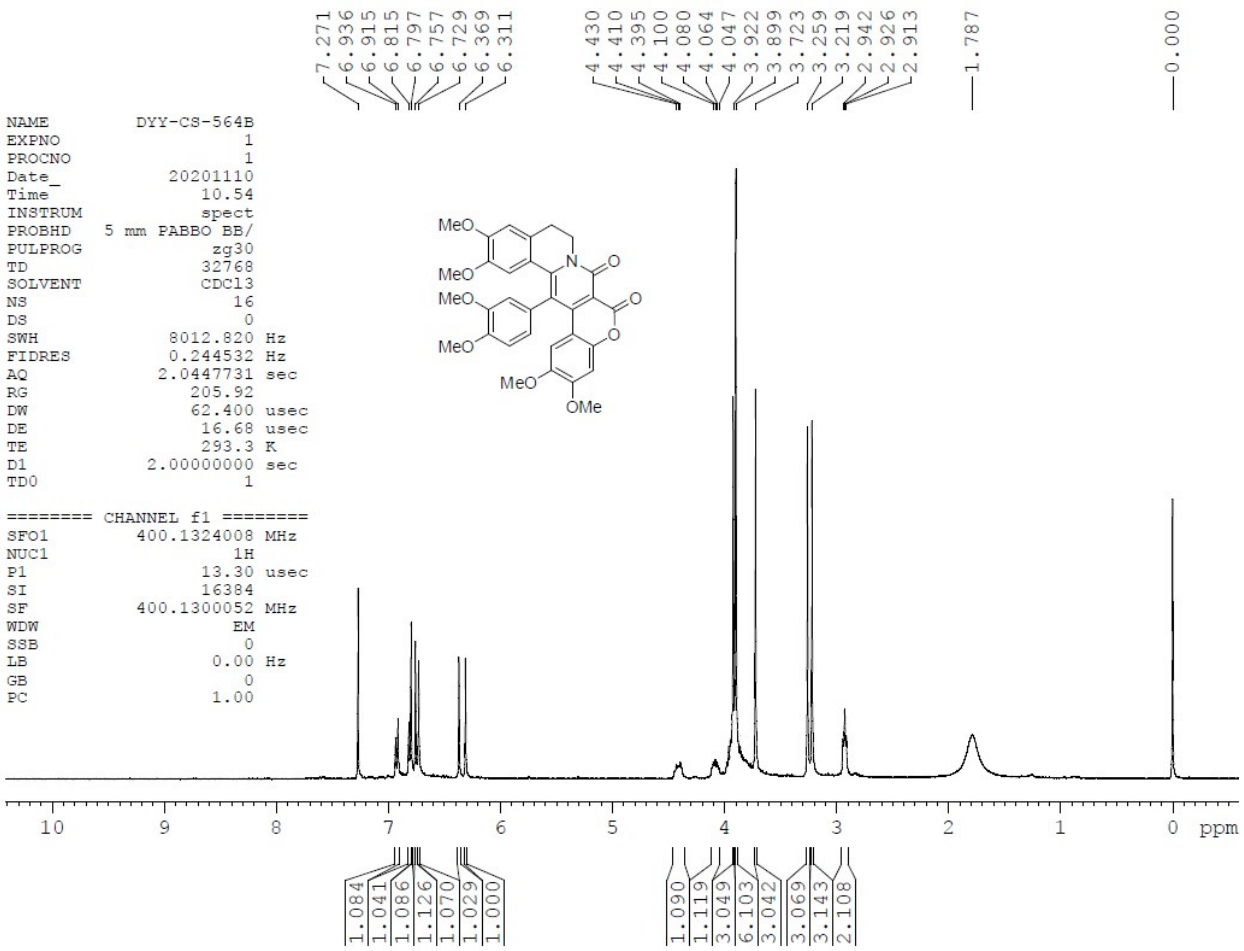
^{1}H NMR of compound **6e** ($CDCl_3$)



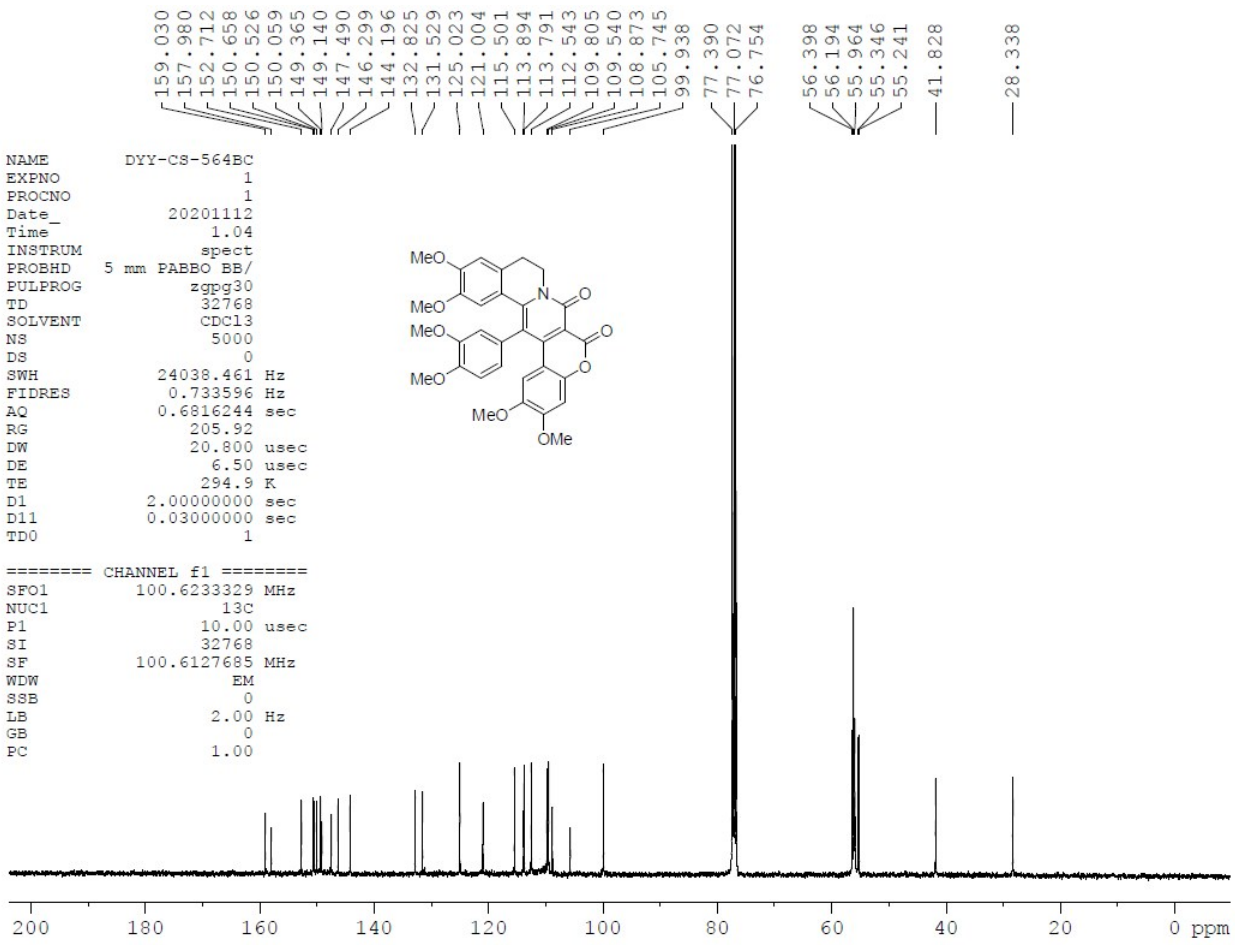
^{13}C NMR of compound **6e** ($CDCl_3$)



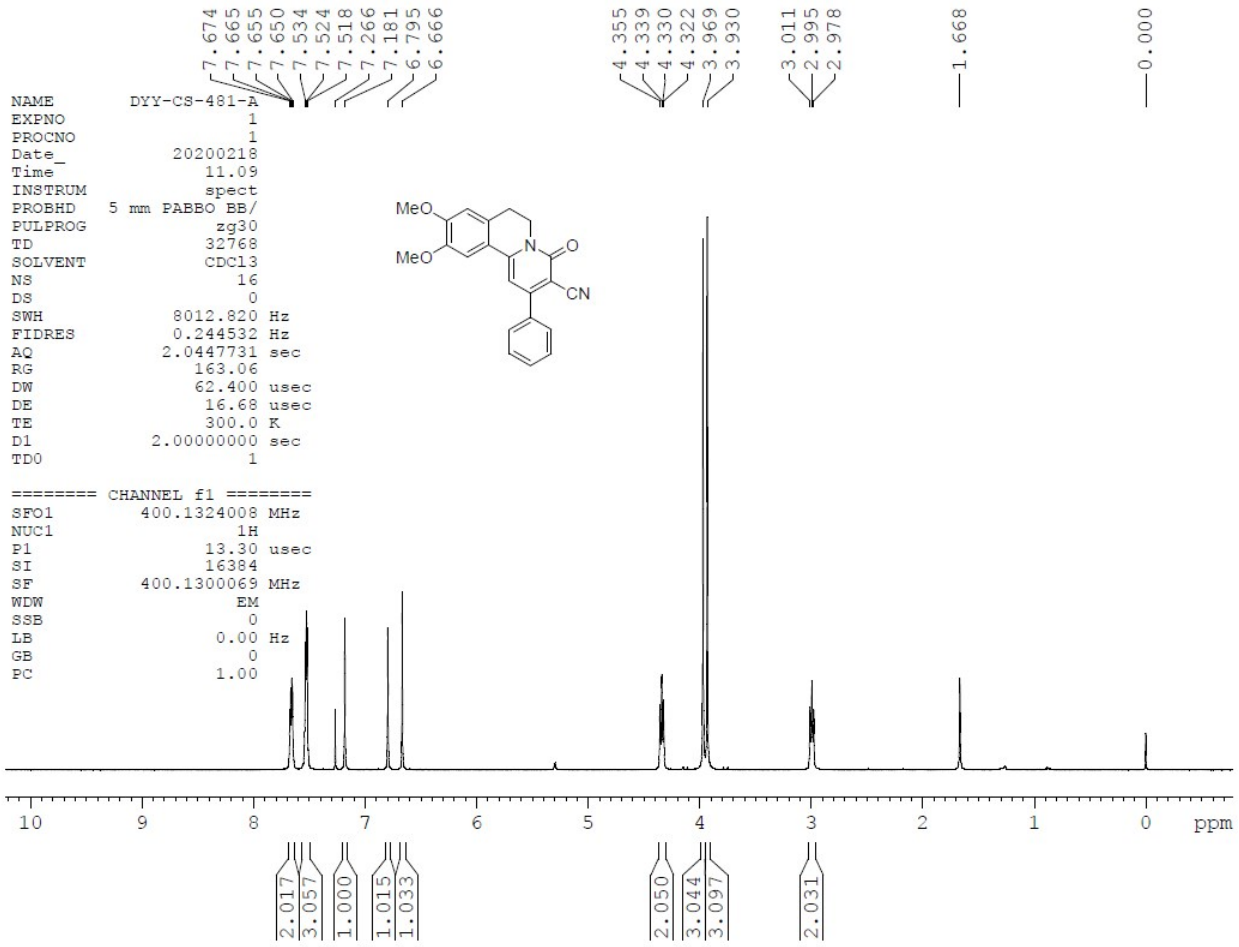
^{1}H NMR of compound **6f** ($CDCl_3$)



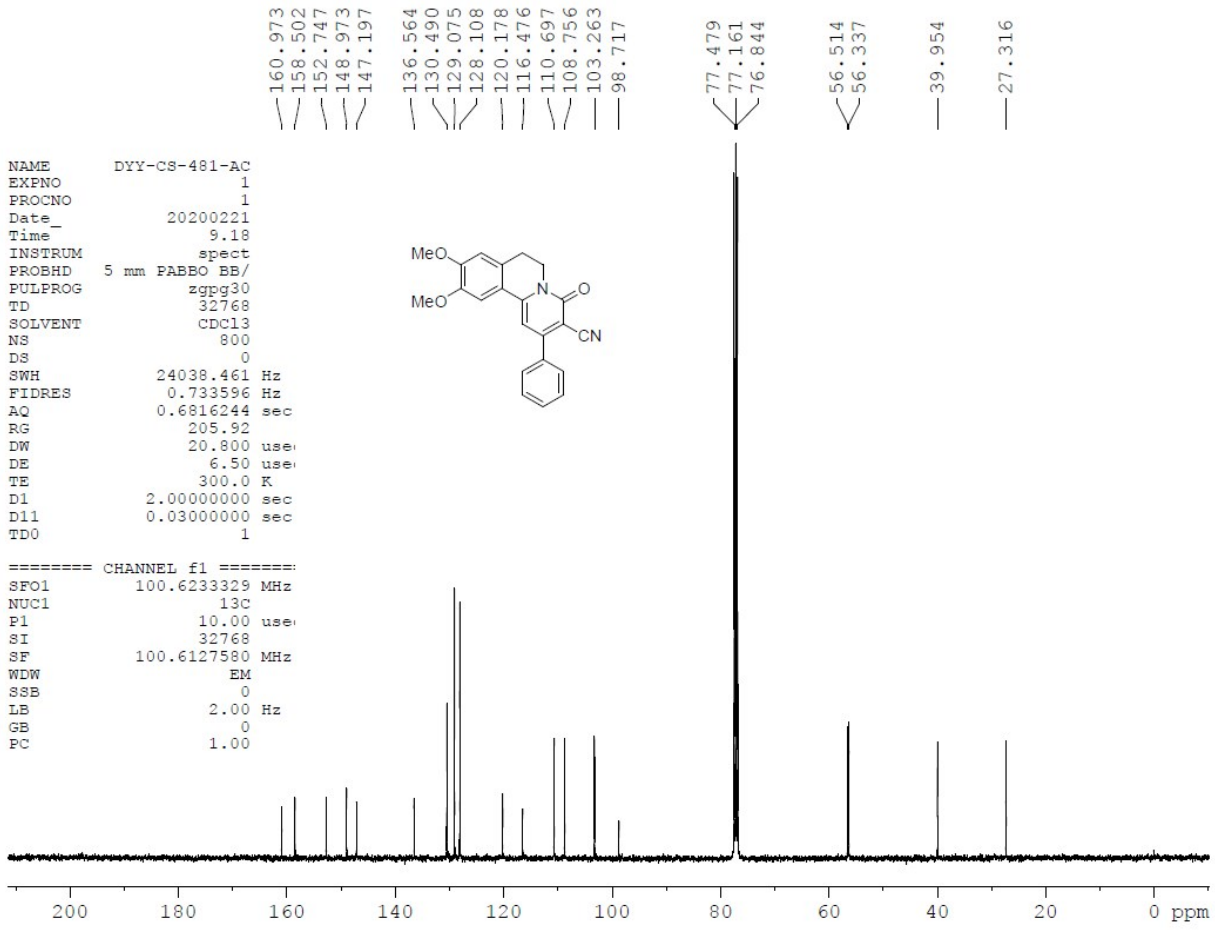
^{13}C NMR of compound **6f** ($CDCl_3$)



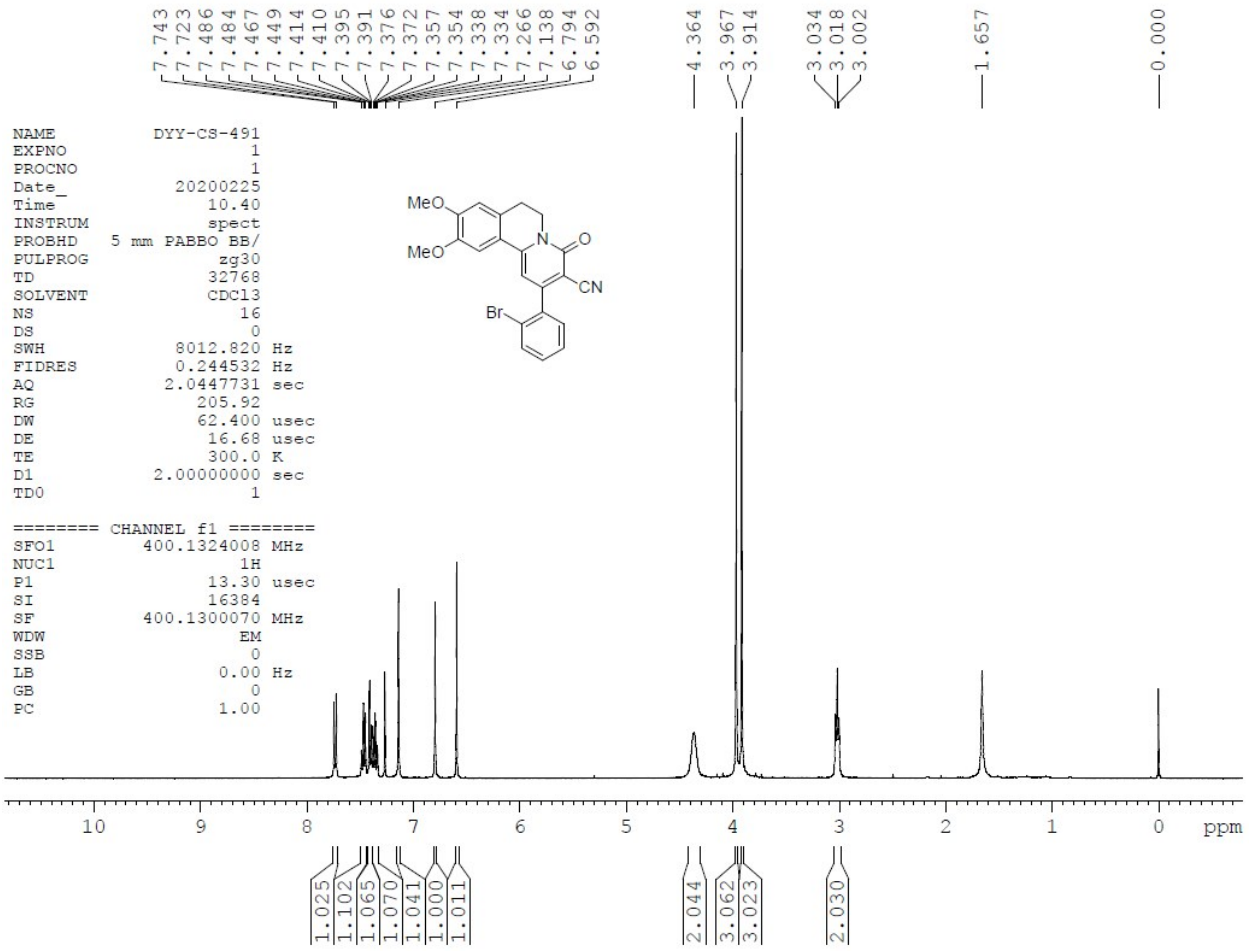
^{1}H NMR of compound **6g** ($CDCl_3$)



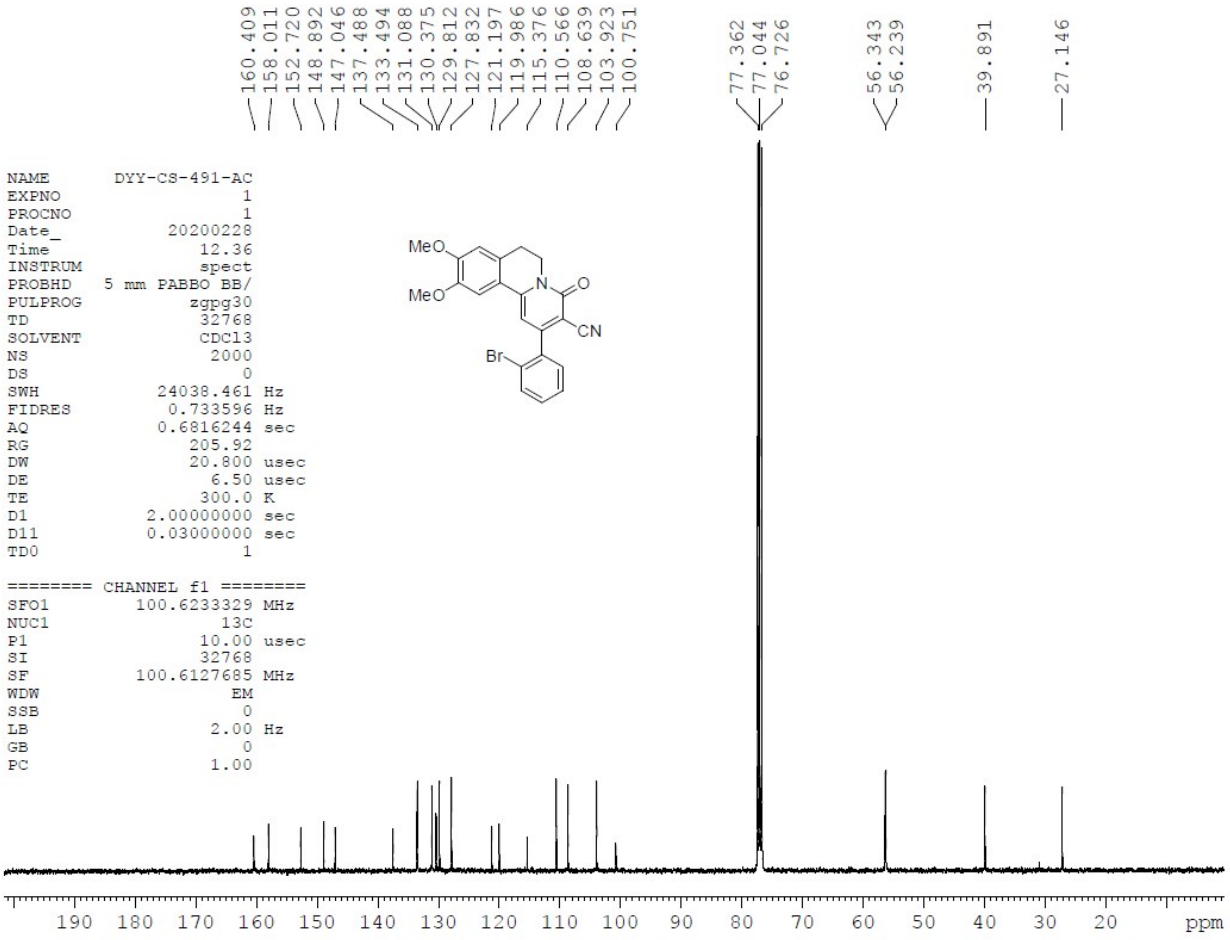
^{13}C NMR of compound **6g** ($CDCl_3$)



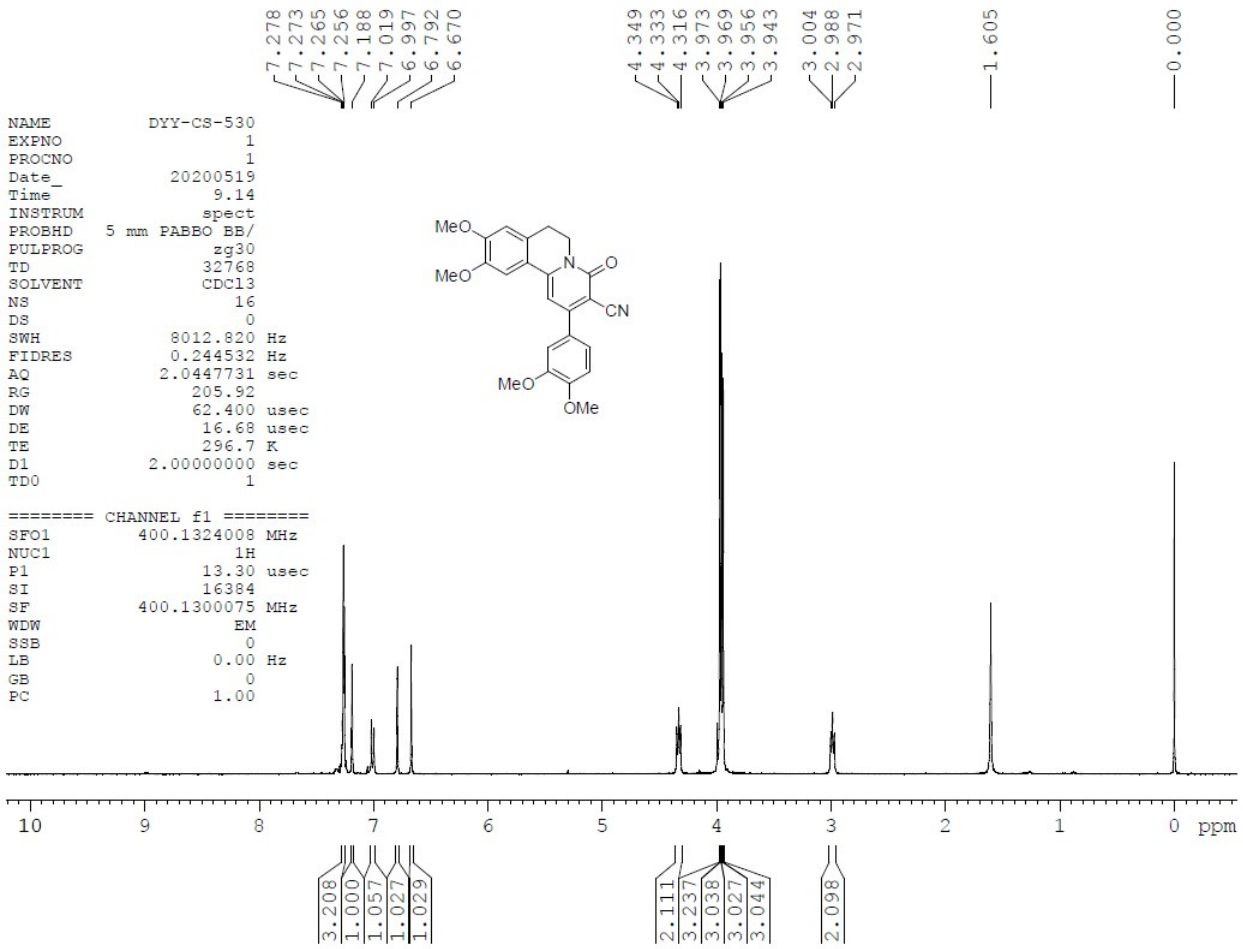
^{1}H NMR of compound **6h** ($CDCl_3$)



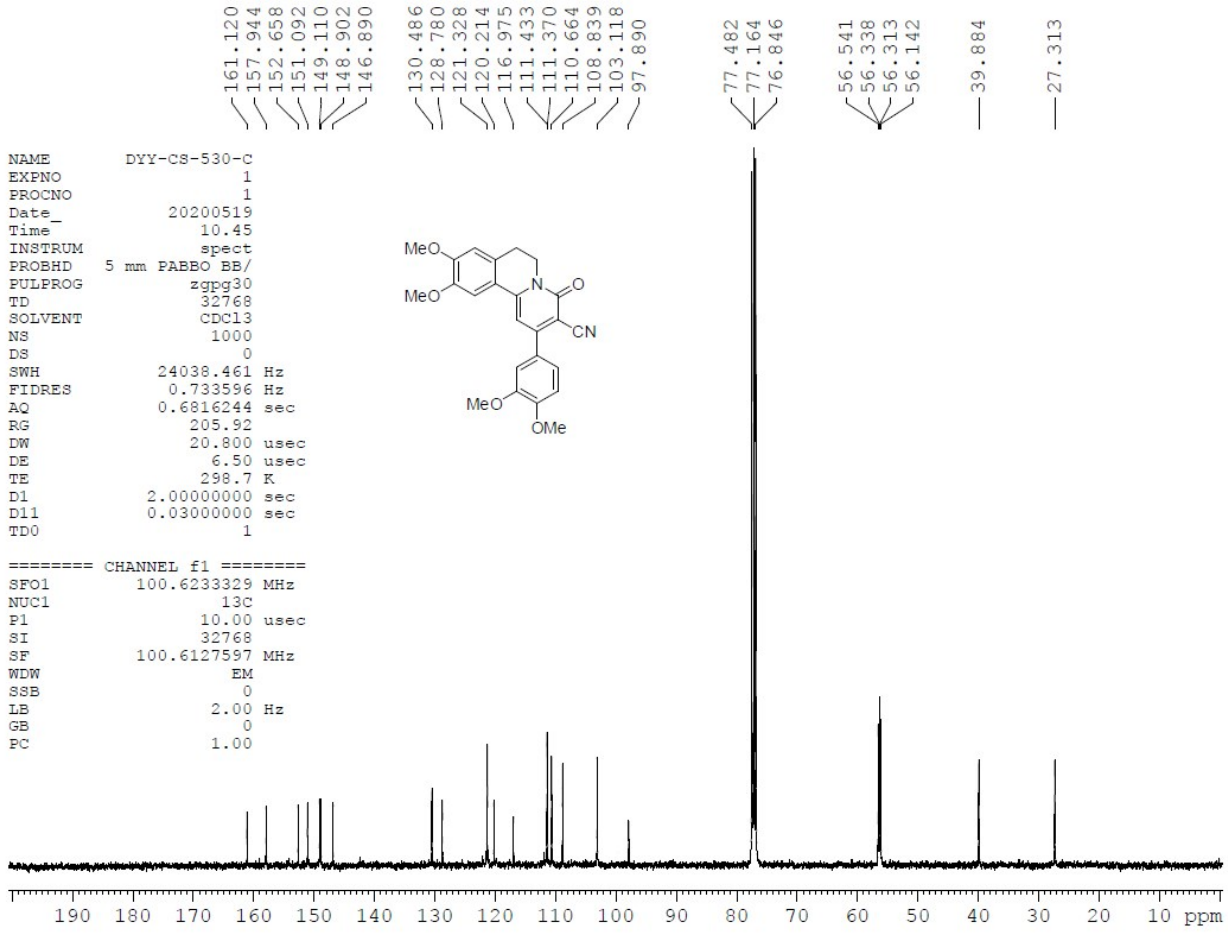
^{13}C NMR of compound **6h** ($CDCl_3$)



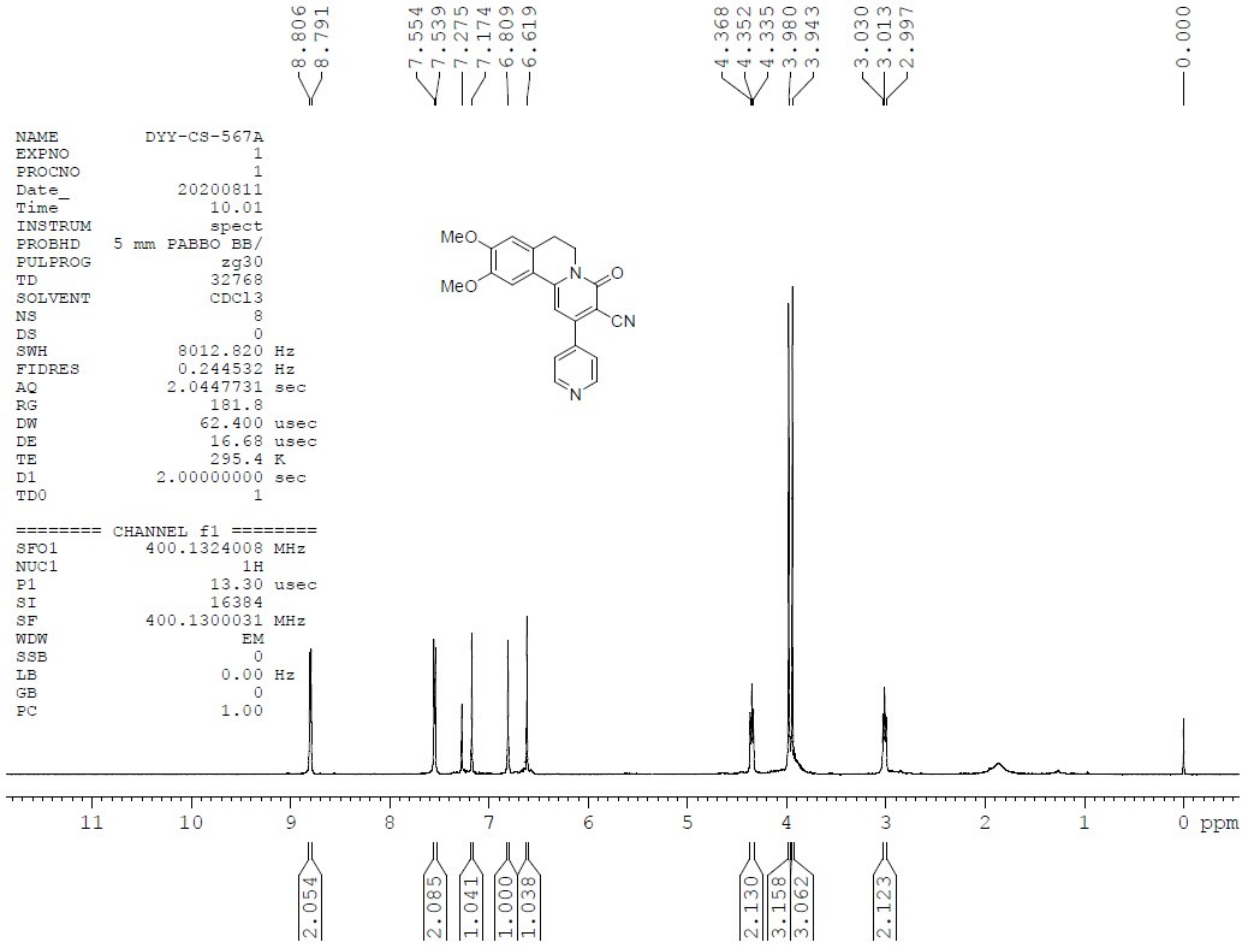
^{1}H NMR of compound **6i** ($CDCl_3$)



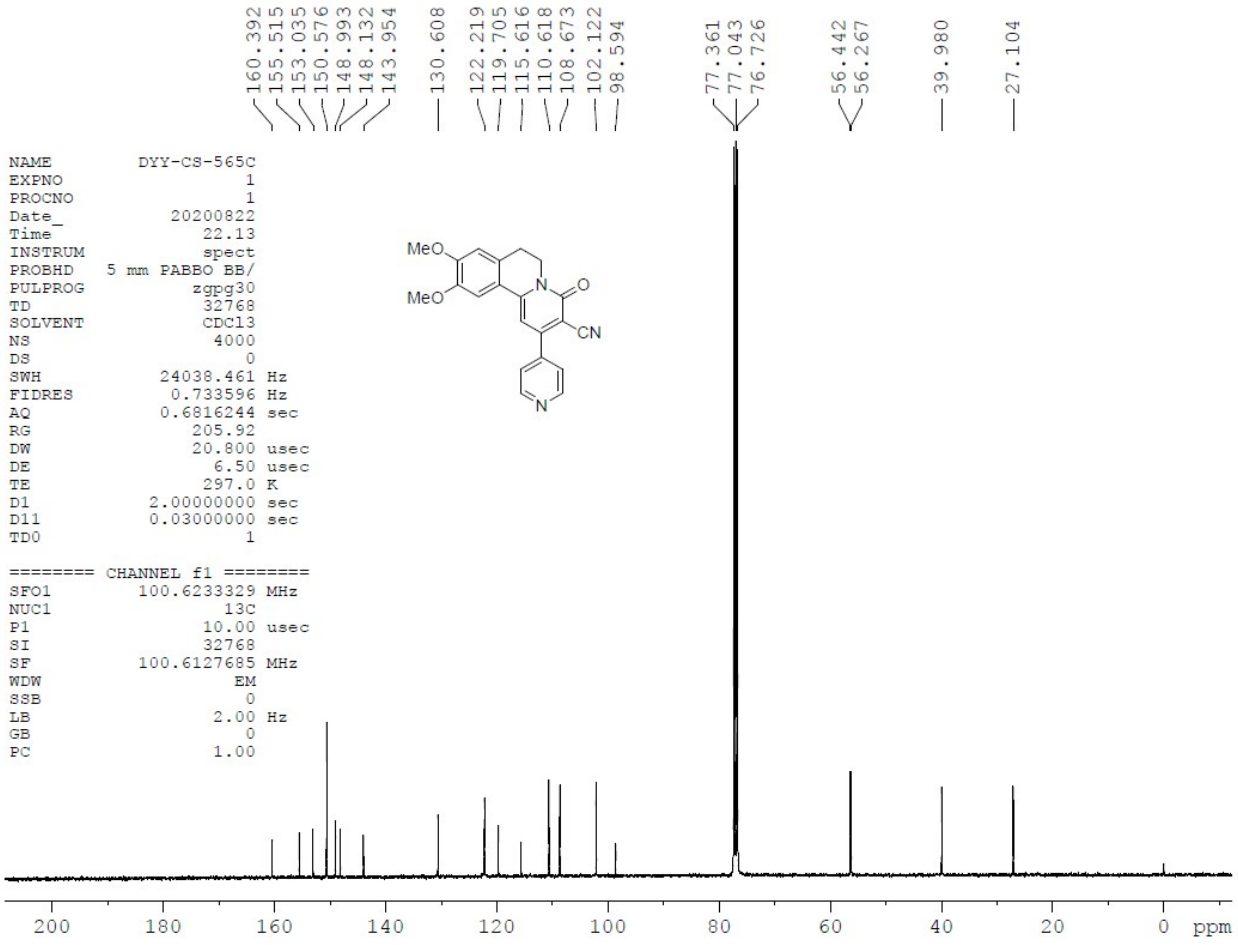
^{13}C NMR of compound **6i** ($CDCl_3$)



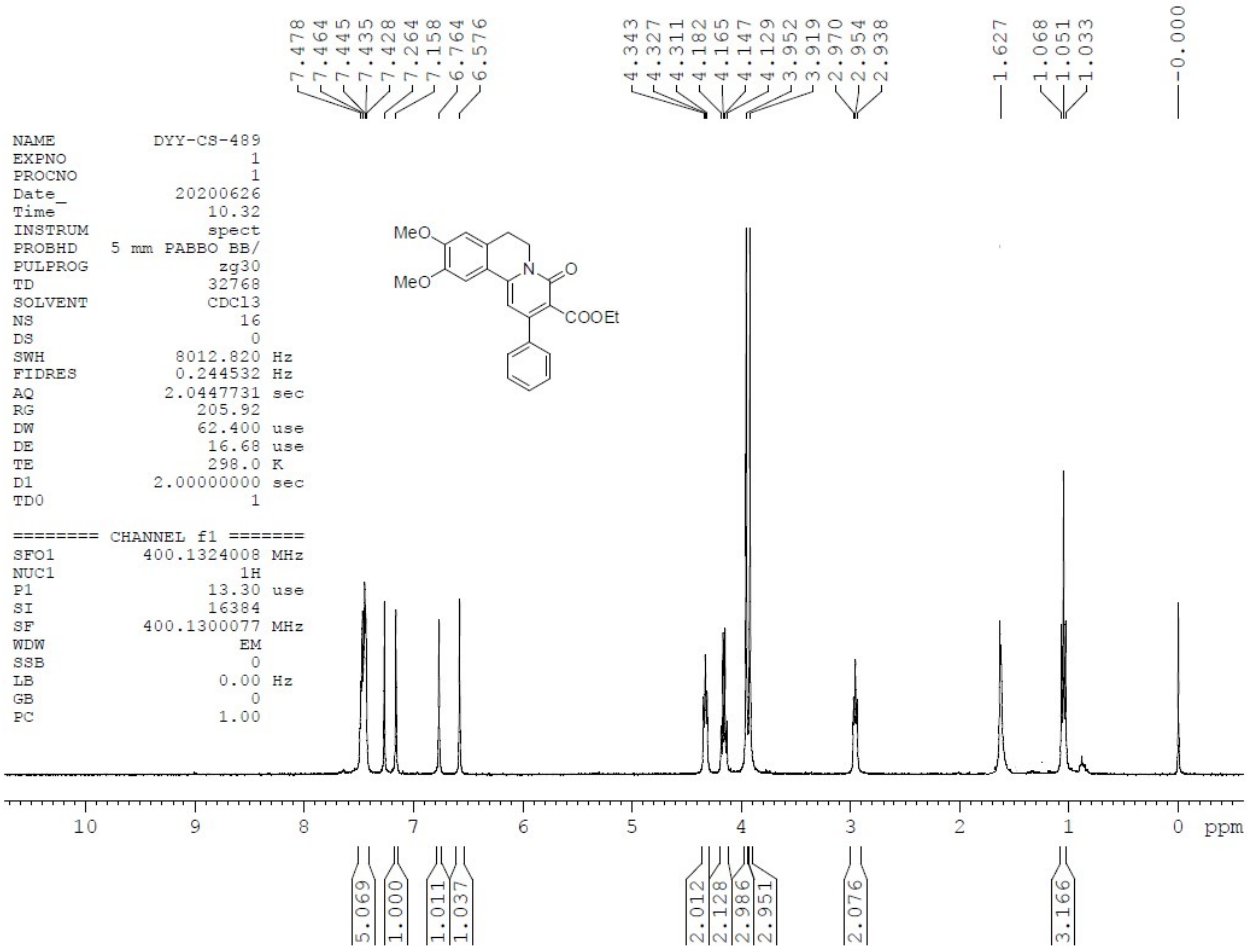
^{1}H NMR of compound **6j** ($CDCl_3$)



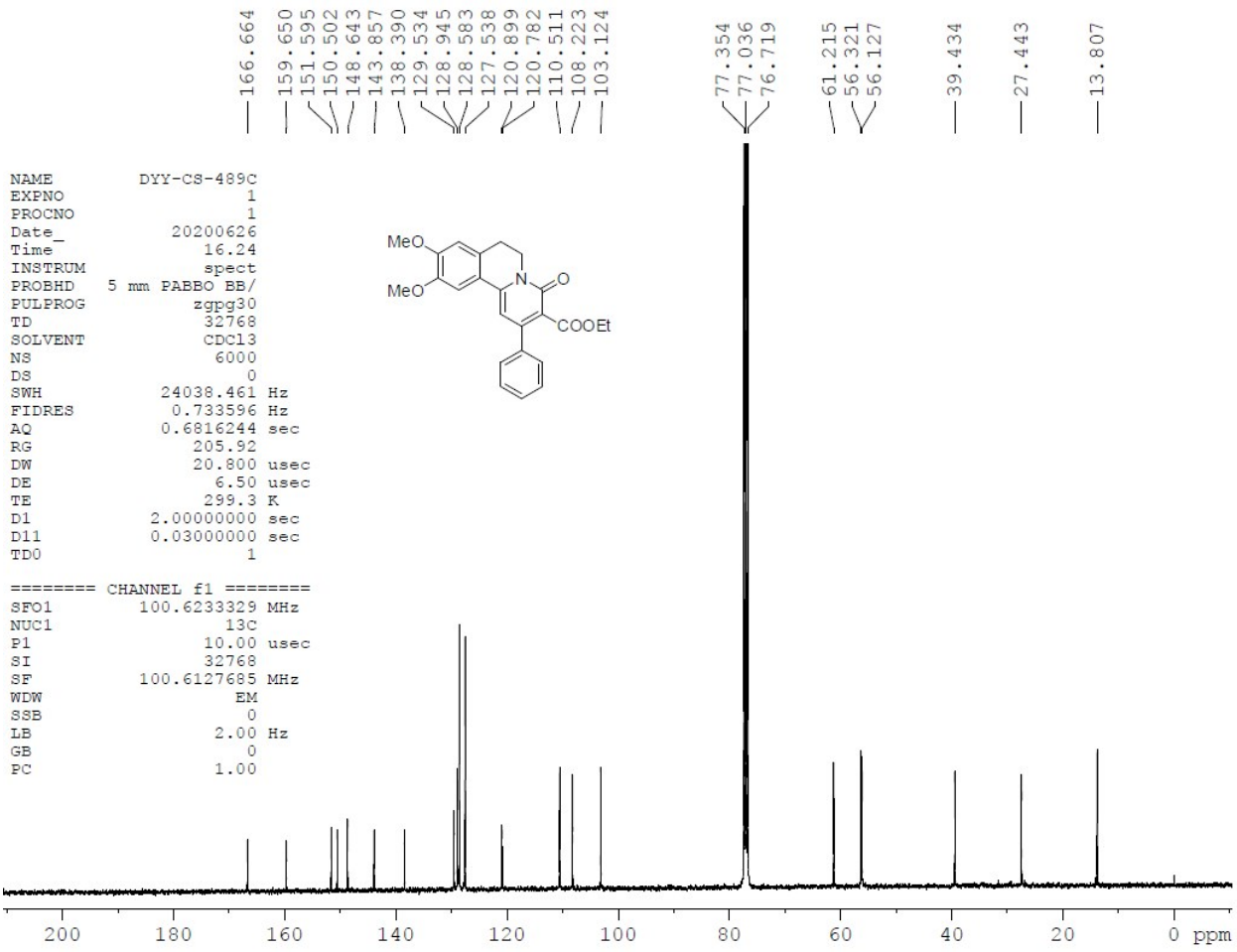
^{13}C NMR of compound **6j** ($CDCl_3$)



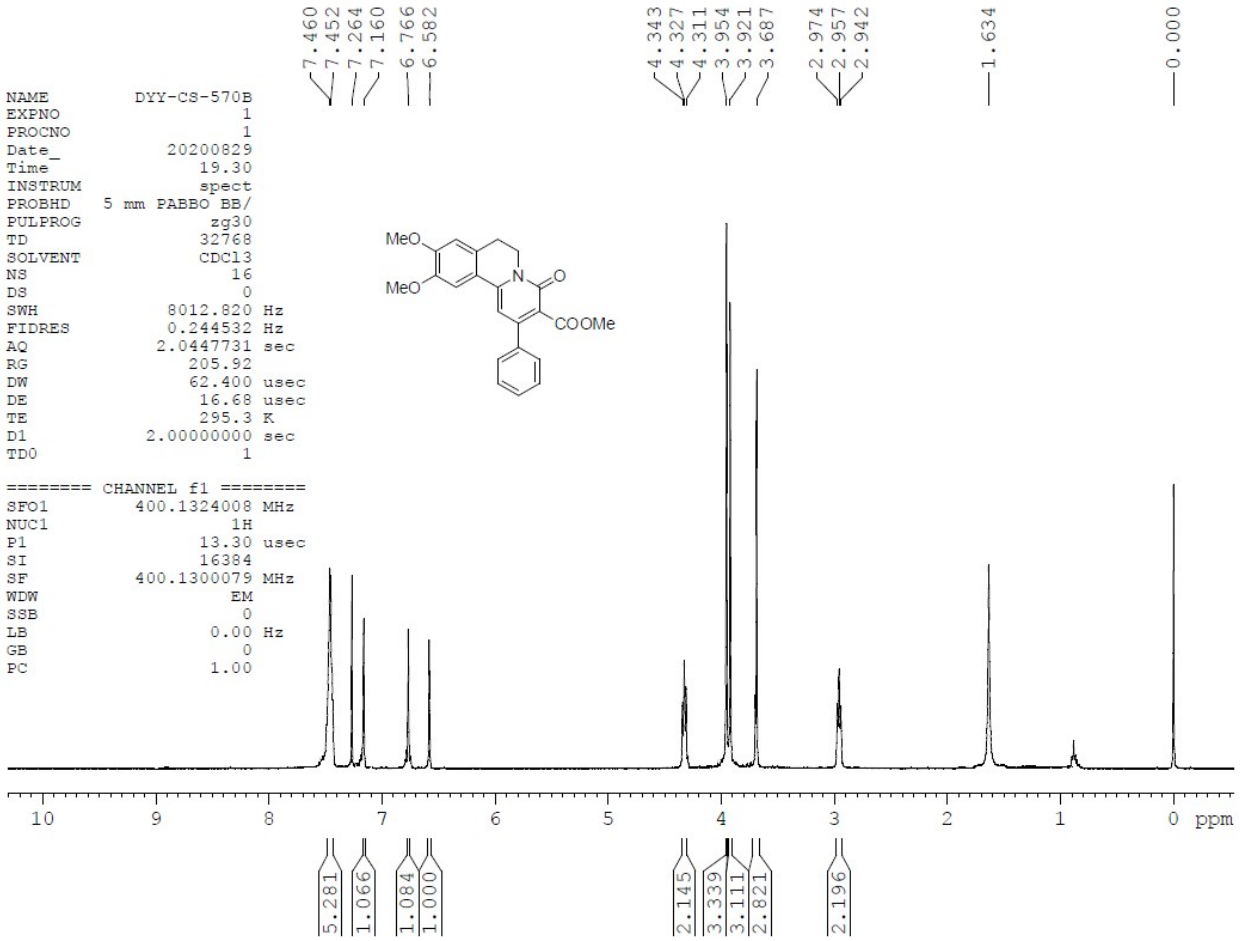
^{1}H NMR of compound **6k** ($CDCl_3$)



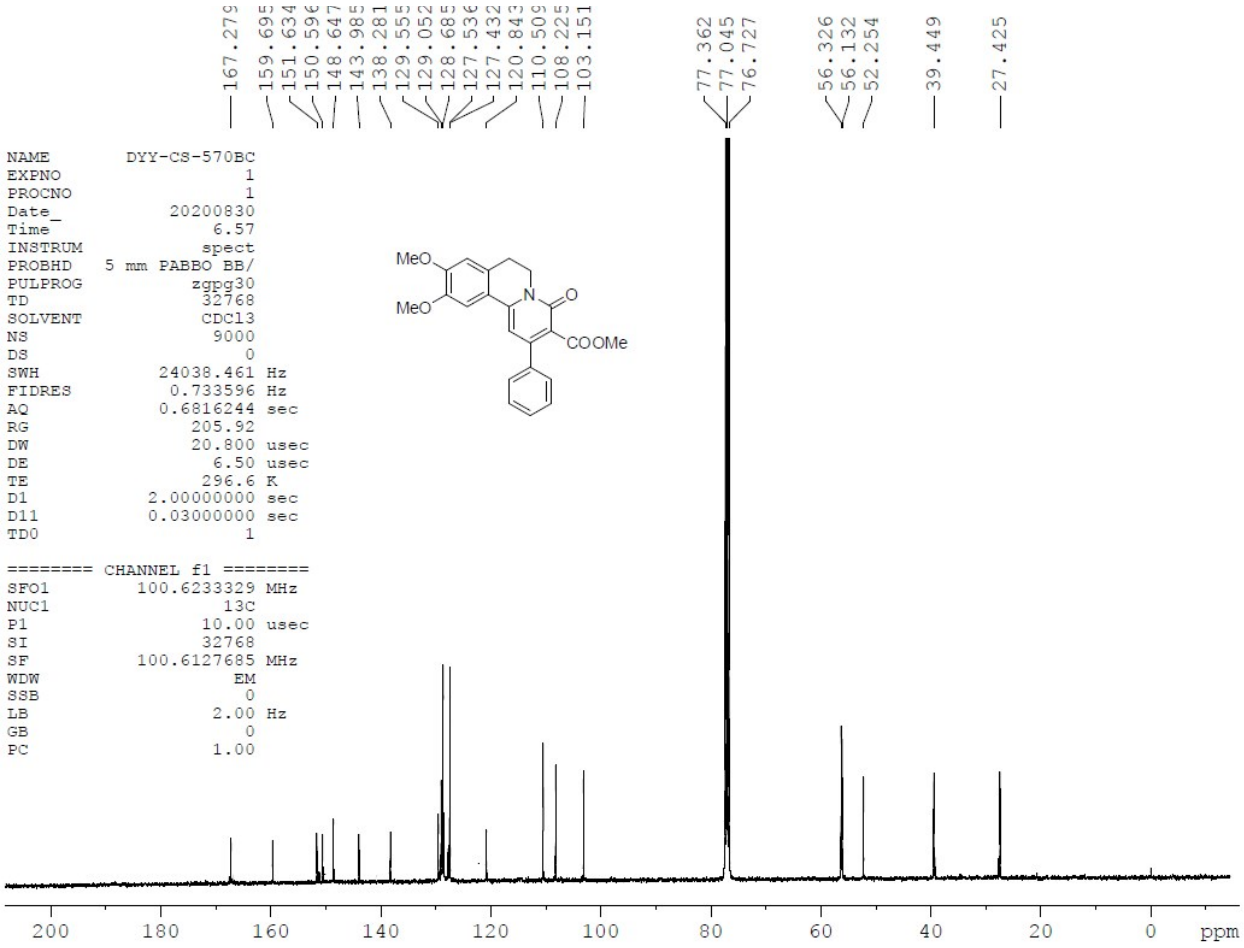
^{13}C NMR of compound **6k** ($CDCl_3$)



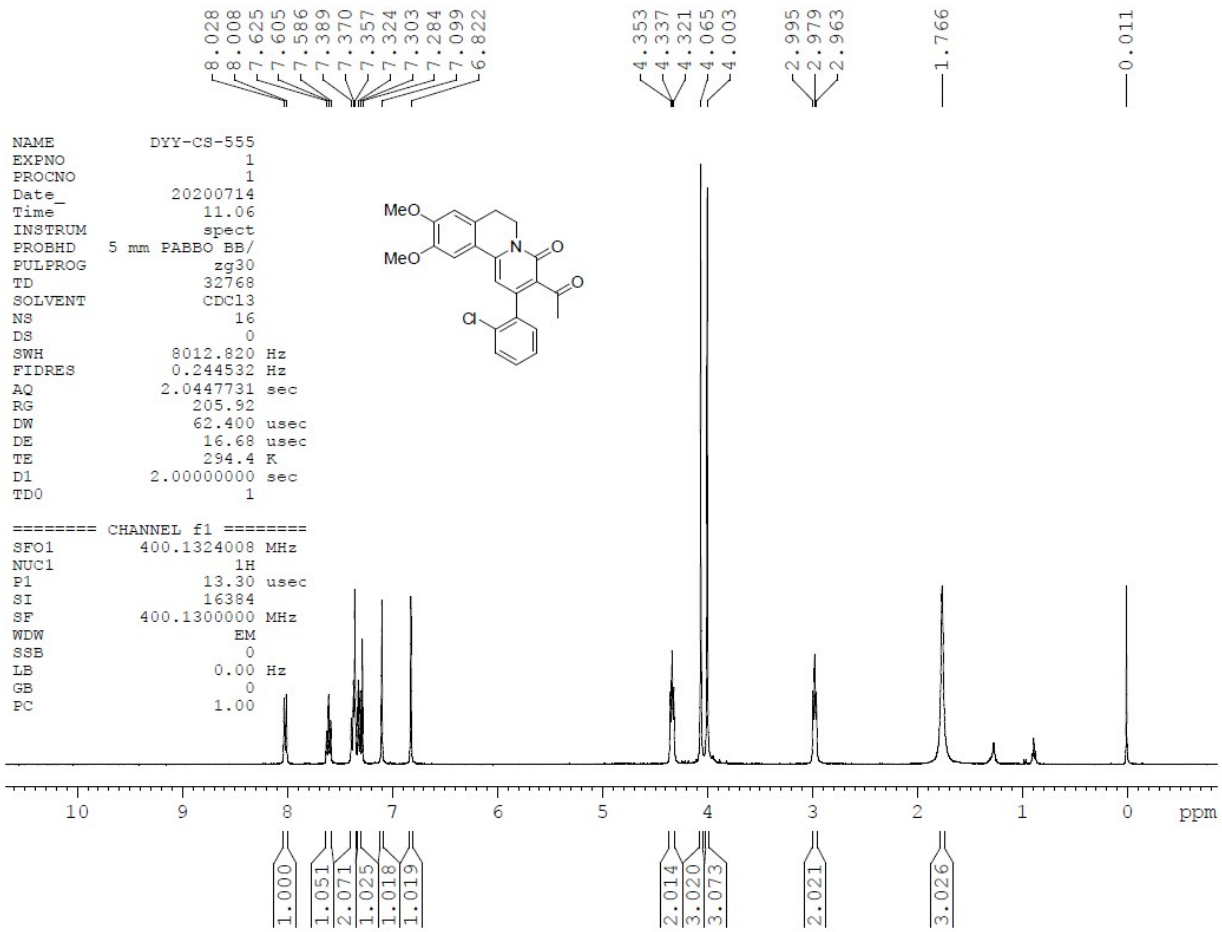
^{1}H NMR of compound **6l** ($CDCl_3$)



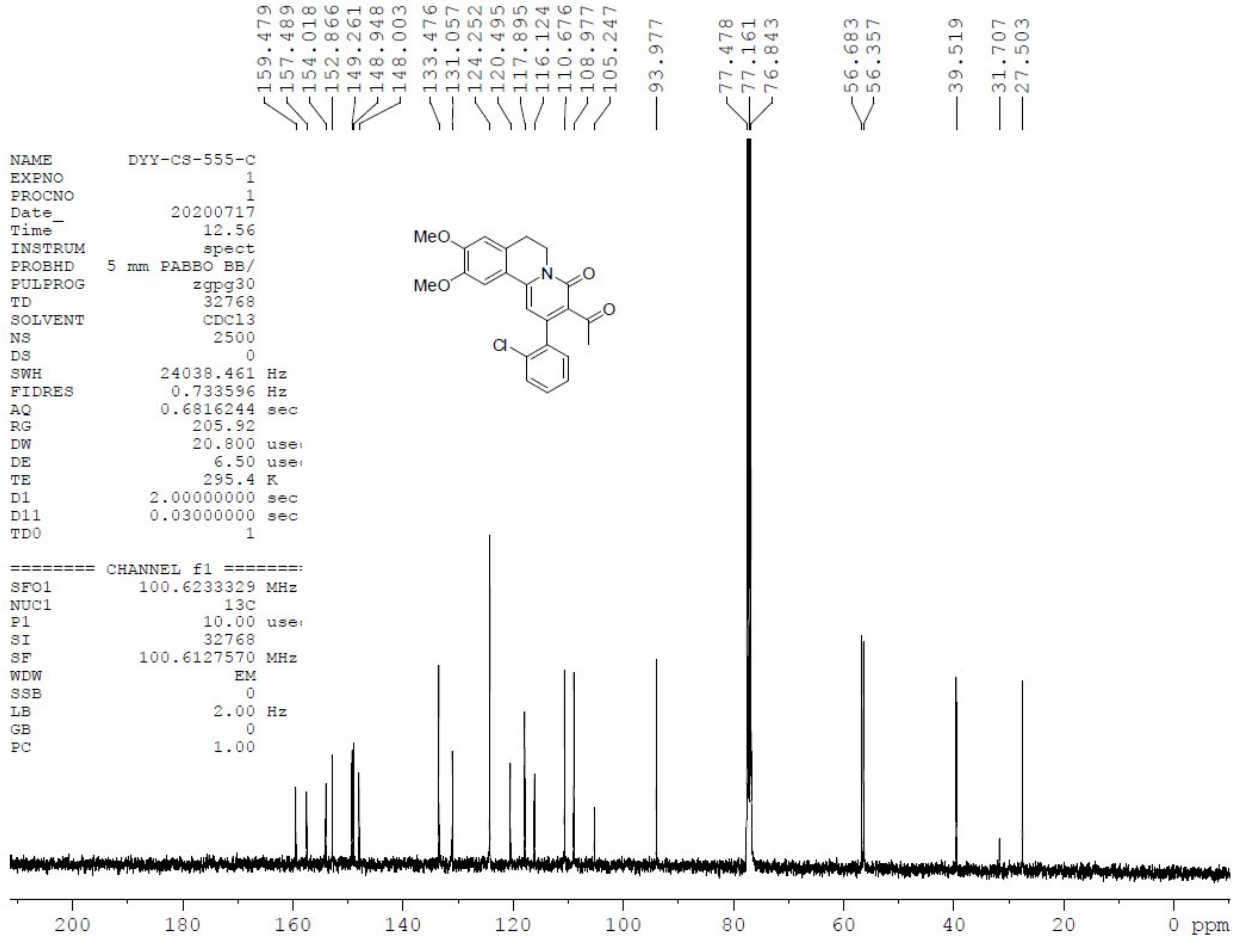
^{13}C NMR of compound **6l** ($CDCl_3$)



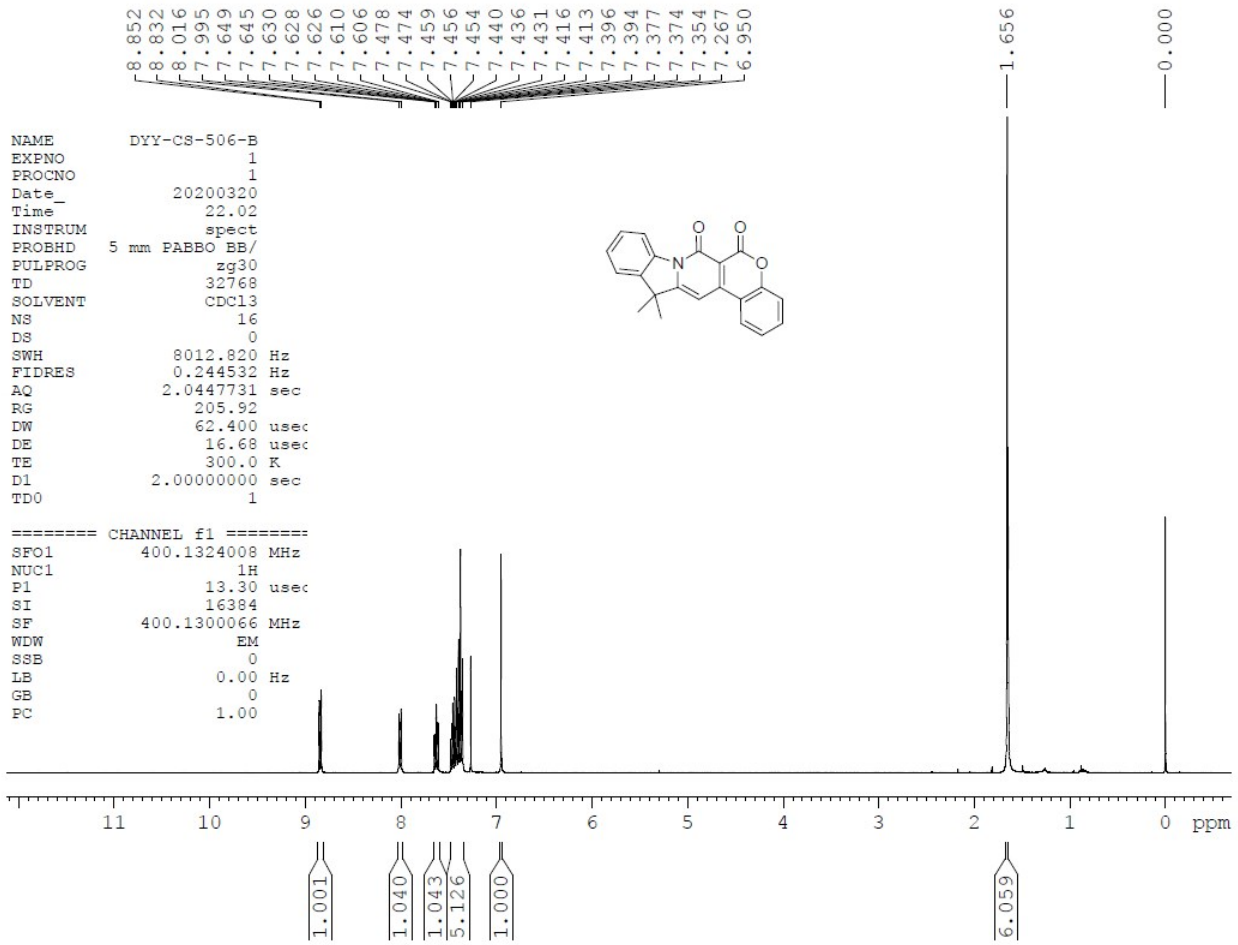
^{1}H NMR of compound **6m** ($CDCl_3$)



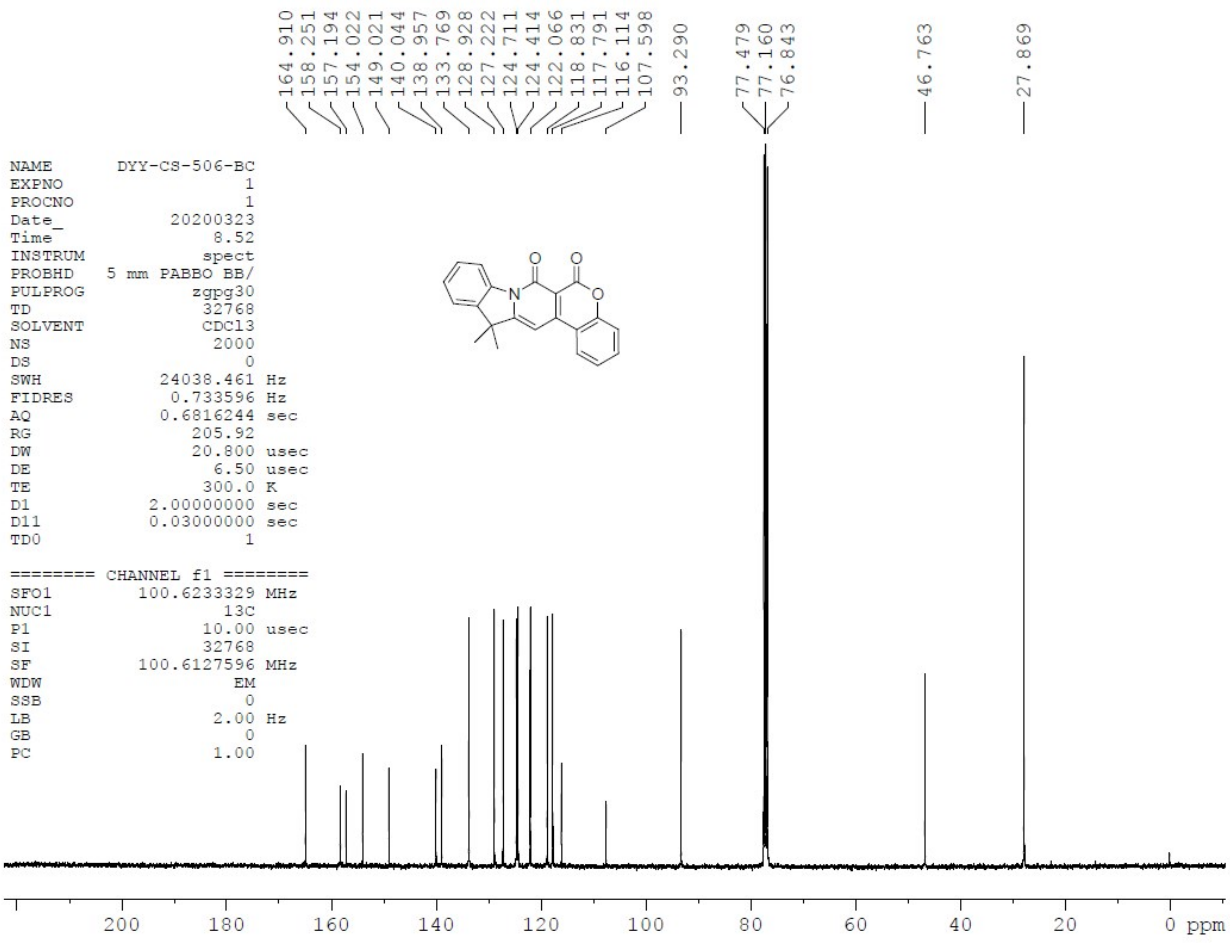
^{13}C NMR of compound **6m** ($CDCl_3$)



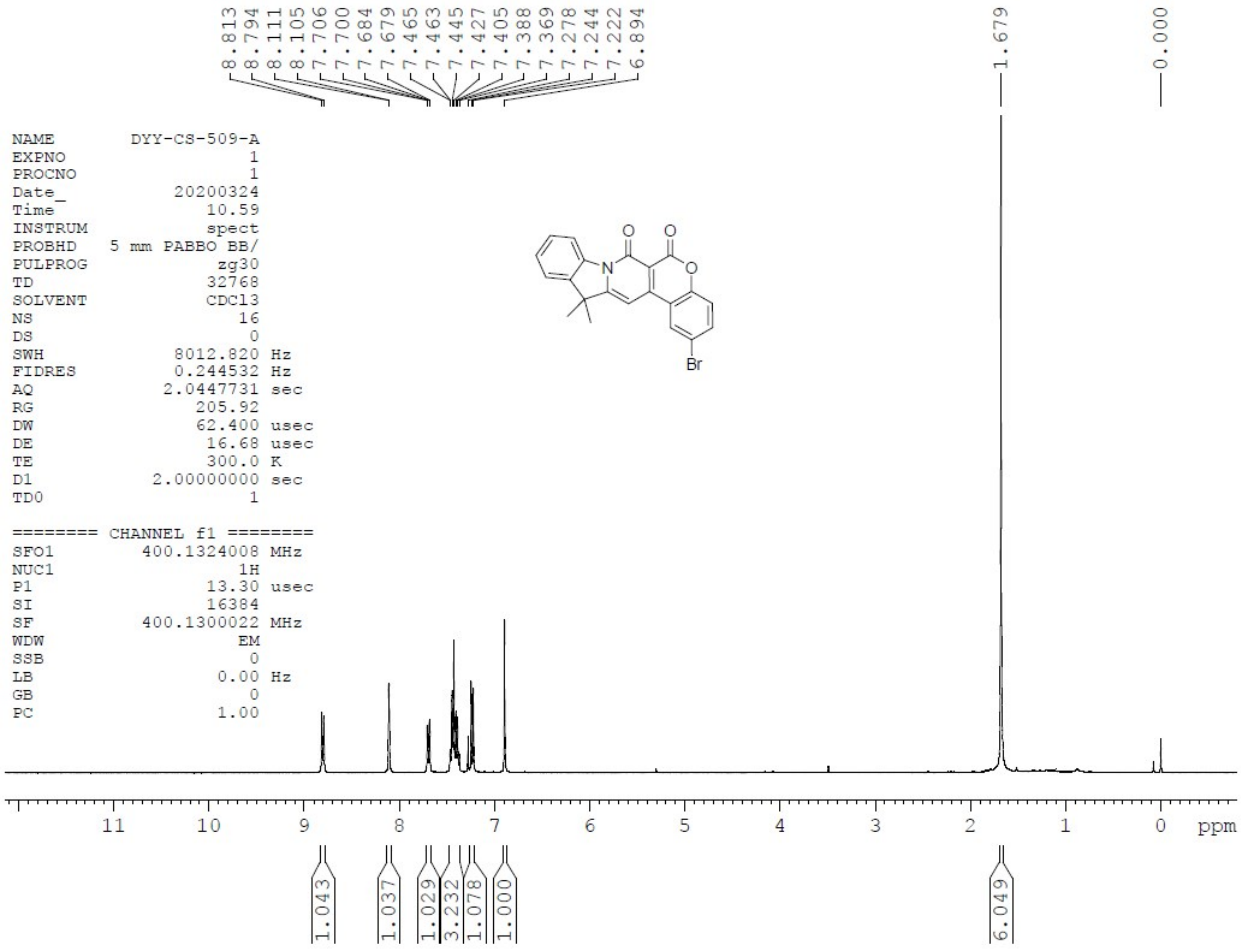
^{1}H NMR of compound **8a** ($CDCl_3$)



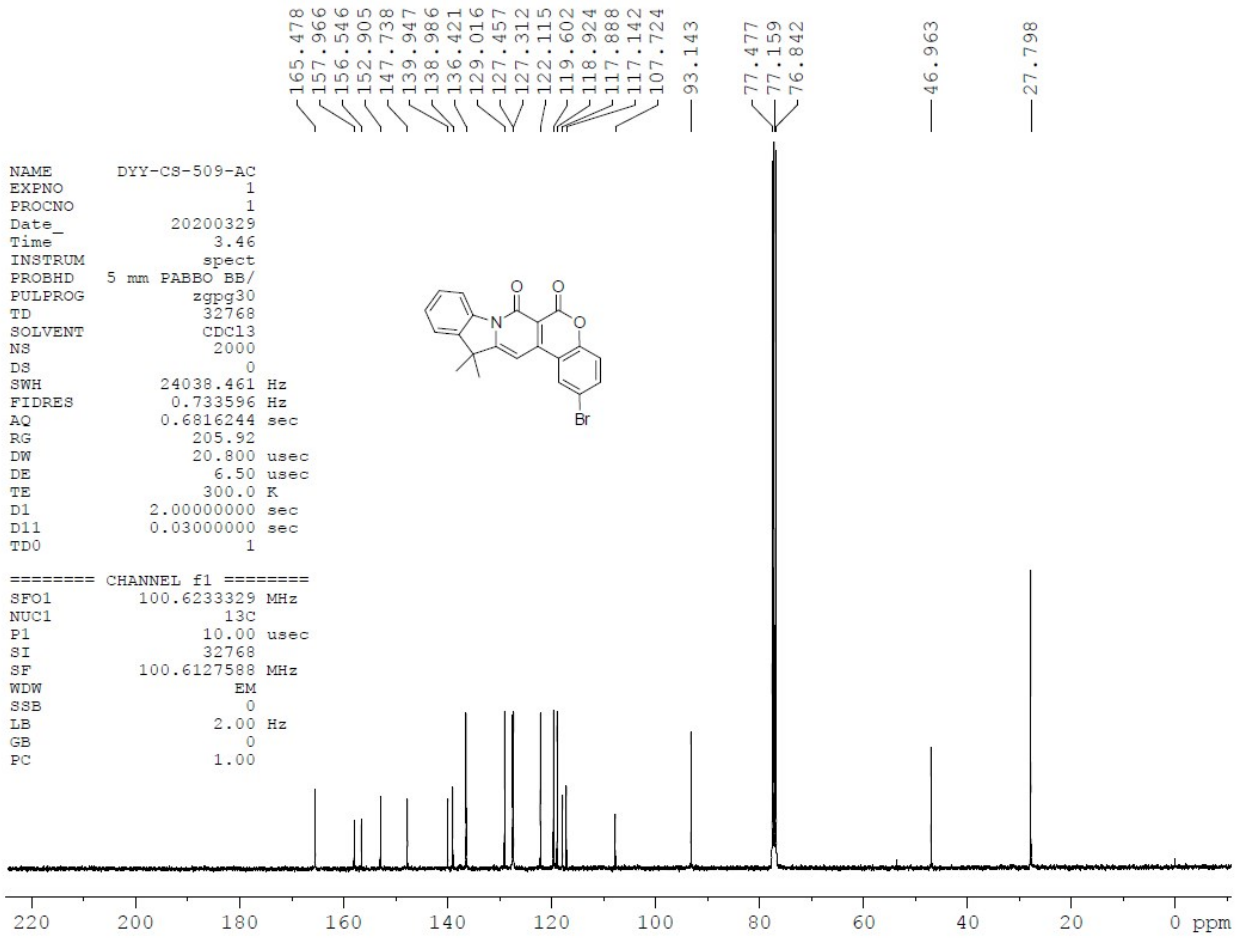
^{13}C NMR of compound **8a** ($CDCl_3$)



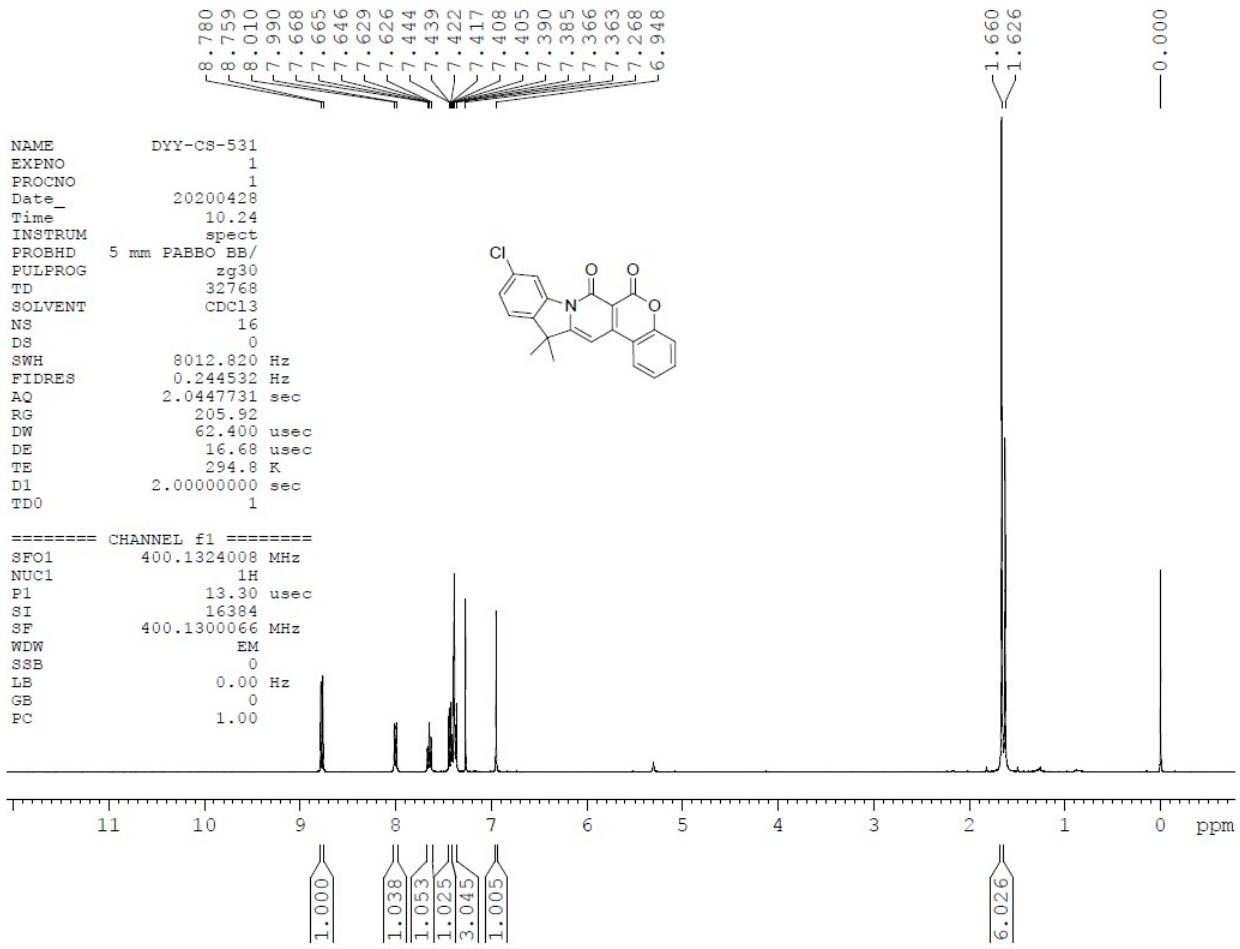
^{1}H NMR of compound **8b** ($CDCl_3$)



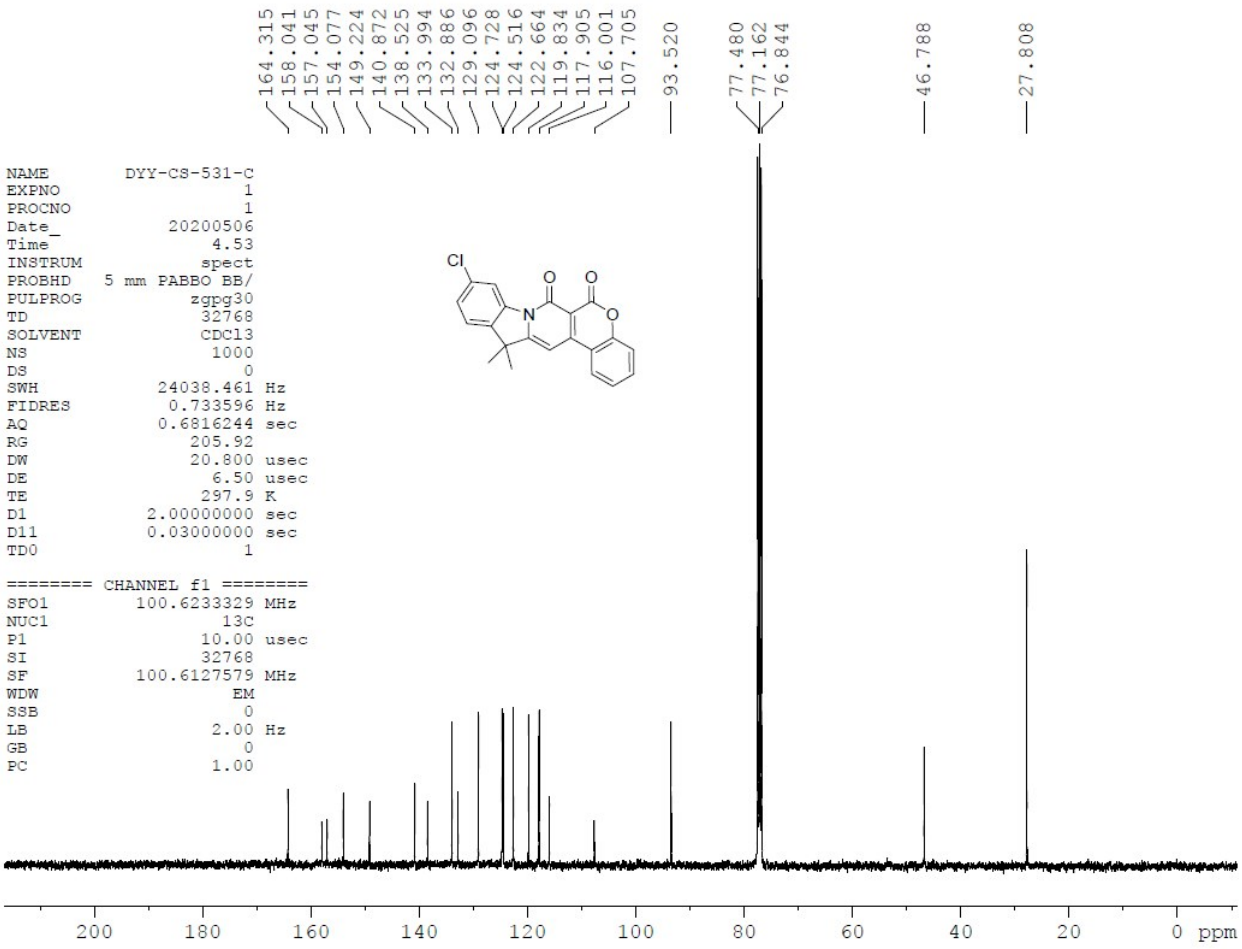
^{13}C NMR of compound **8b** ($CDCl_3$)



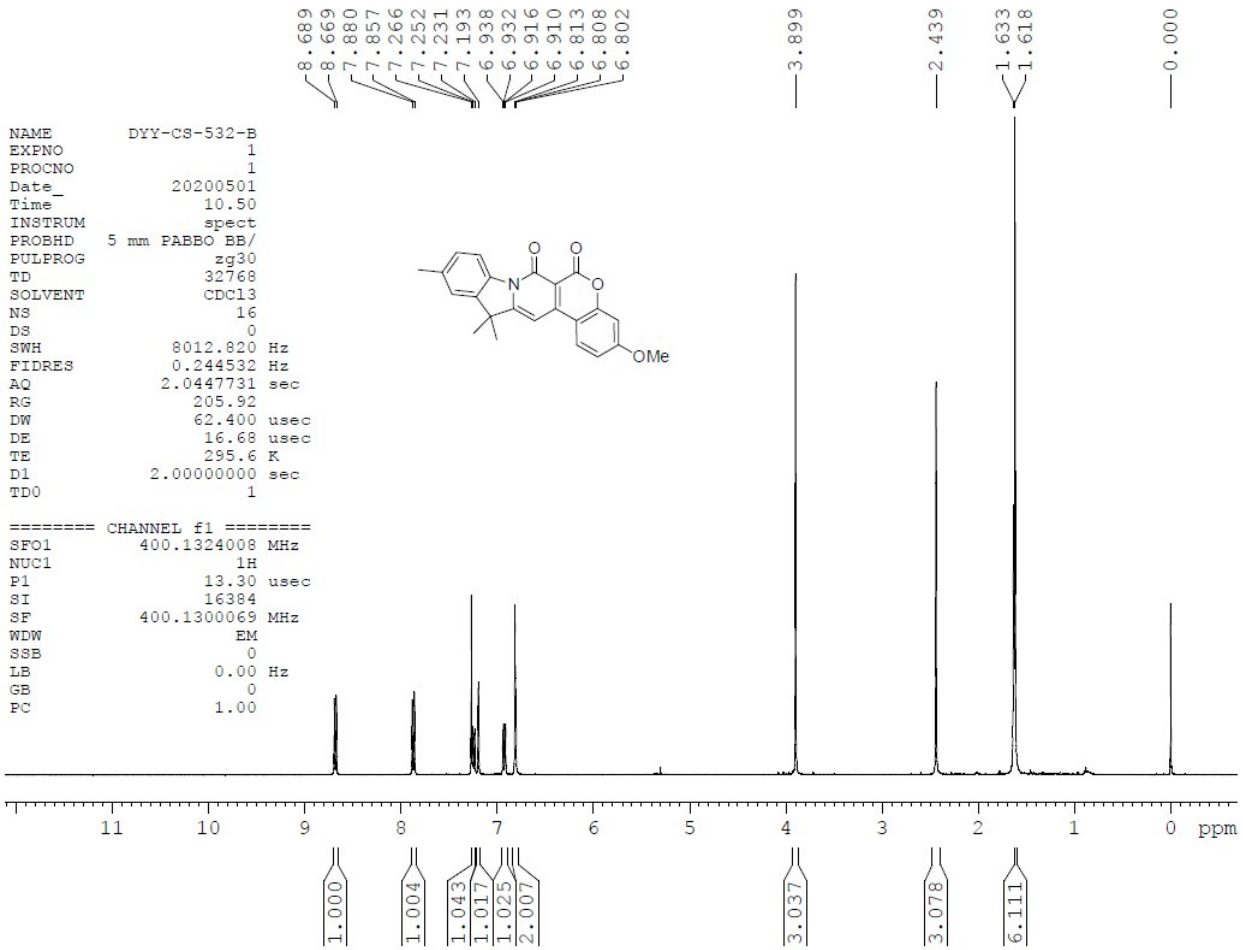
^{1}H NMR of compound **8c** ($CDCl_3$)



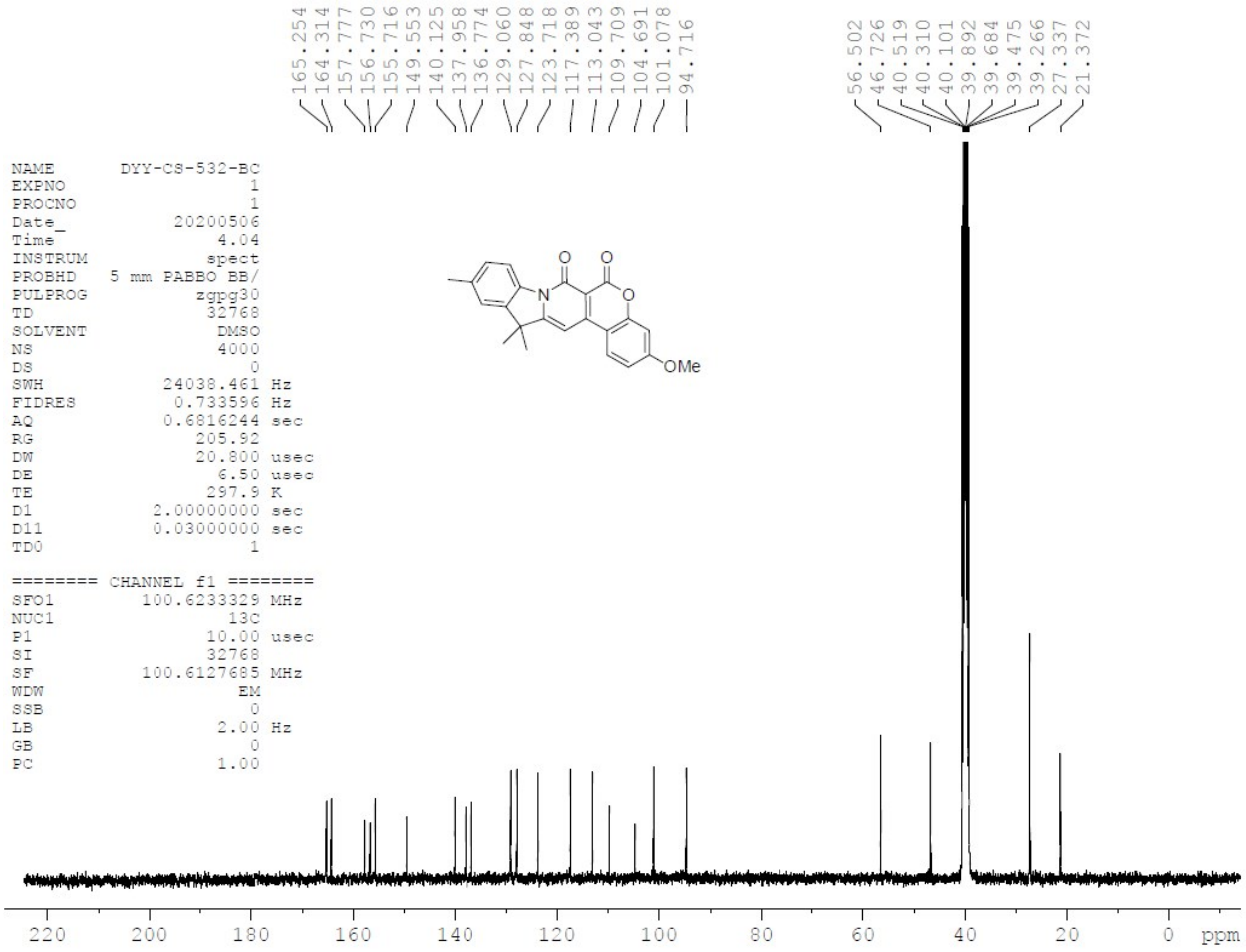
^{13}C NMR of compound **8c** ($CDCl_3$)



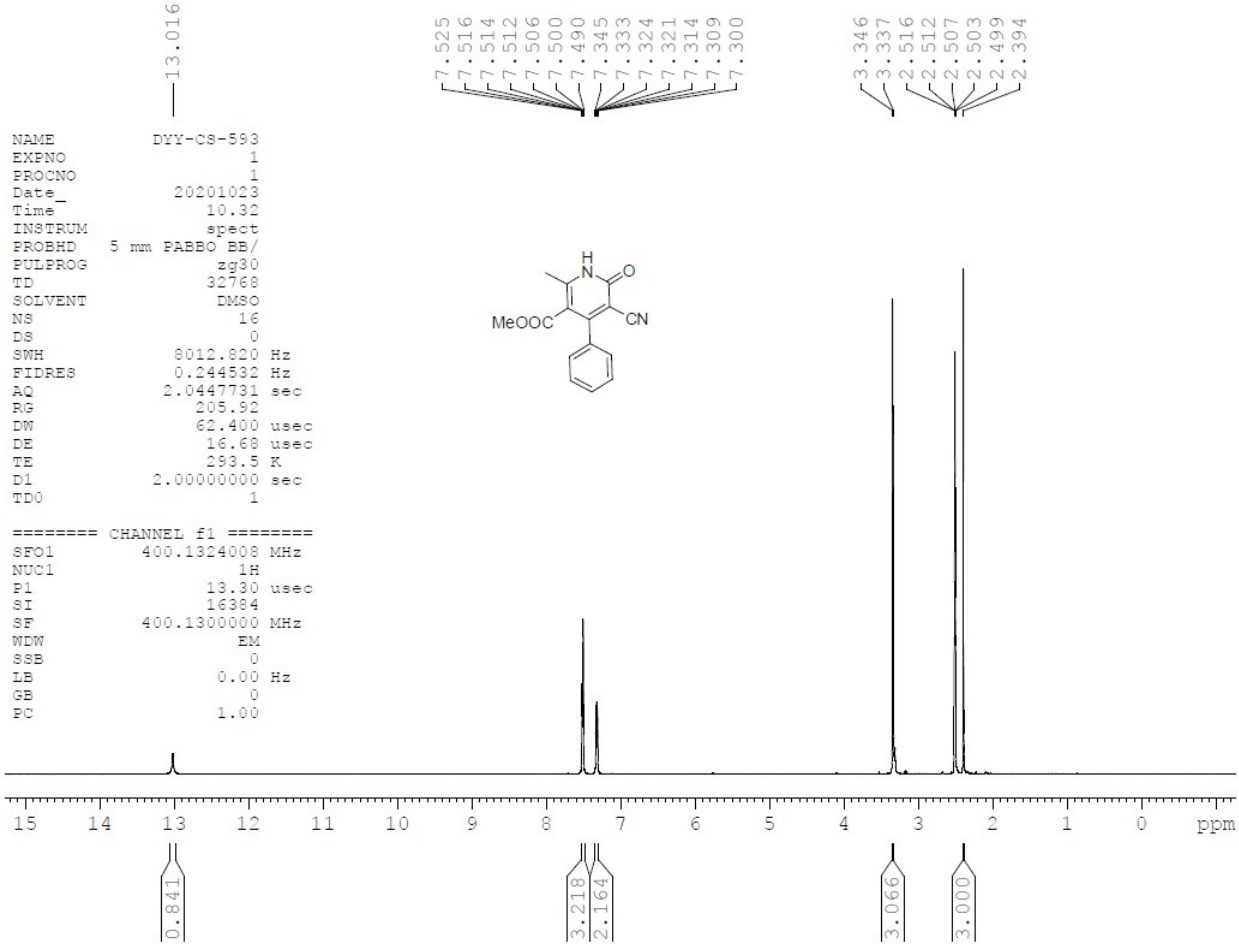
^{1}H NMR of compound **8d** ($CDCl_3$)



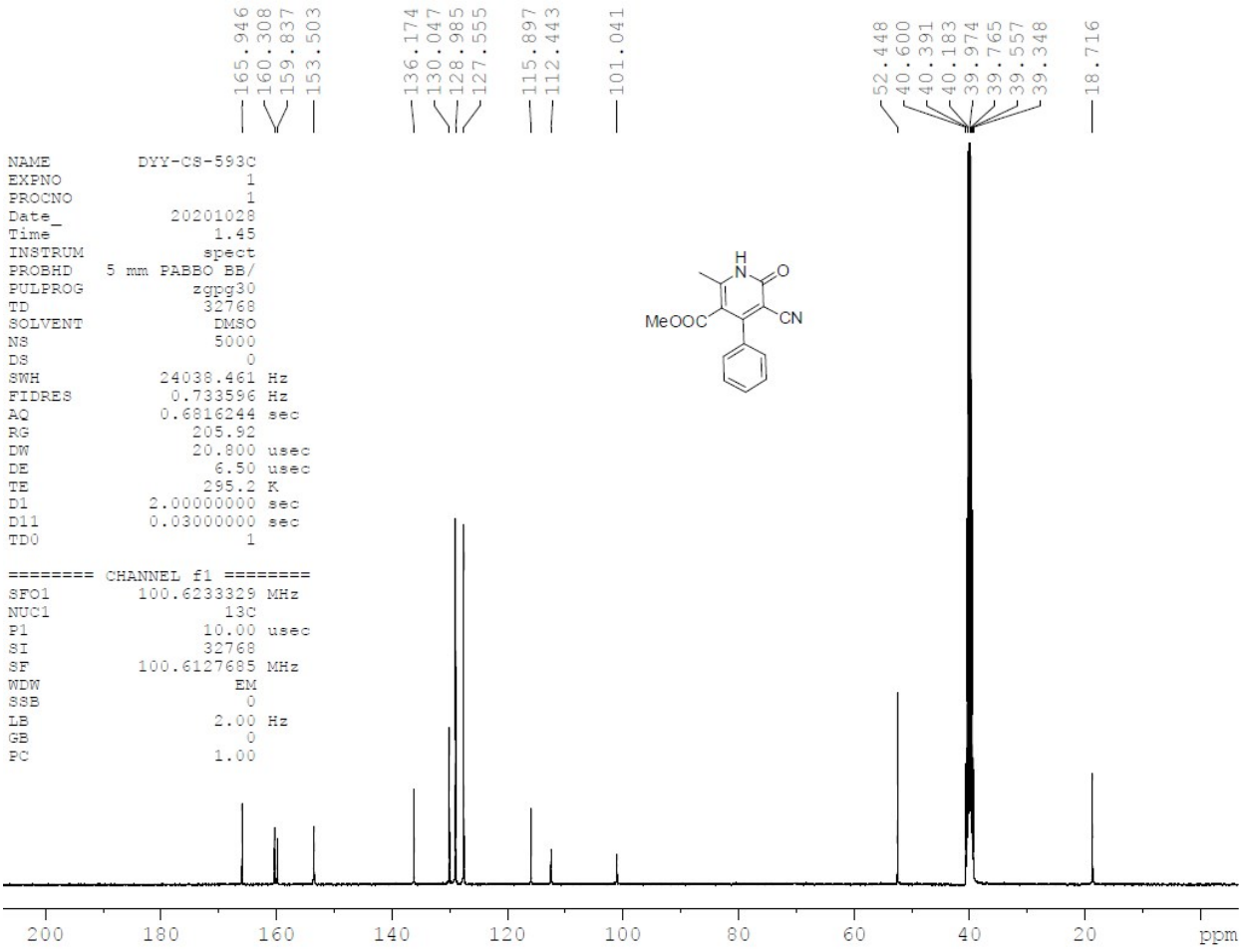
^{13}C NMR of compound **8d** (DMSO-d_6)



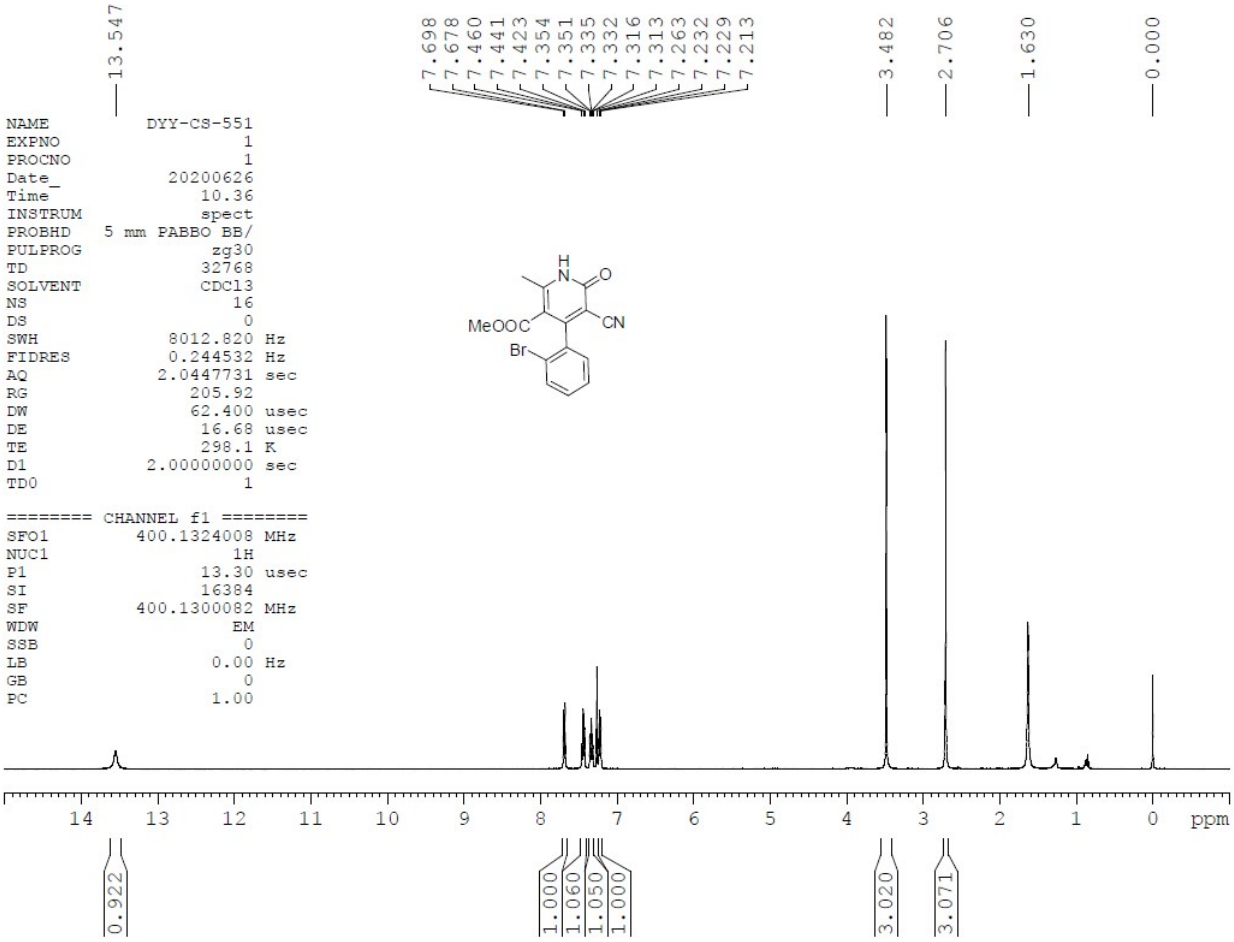
[1]HNMR of compound **10a** (DMSO-d_6)



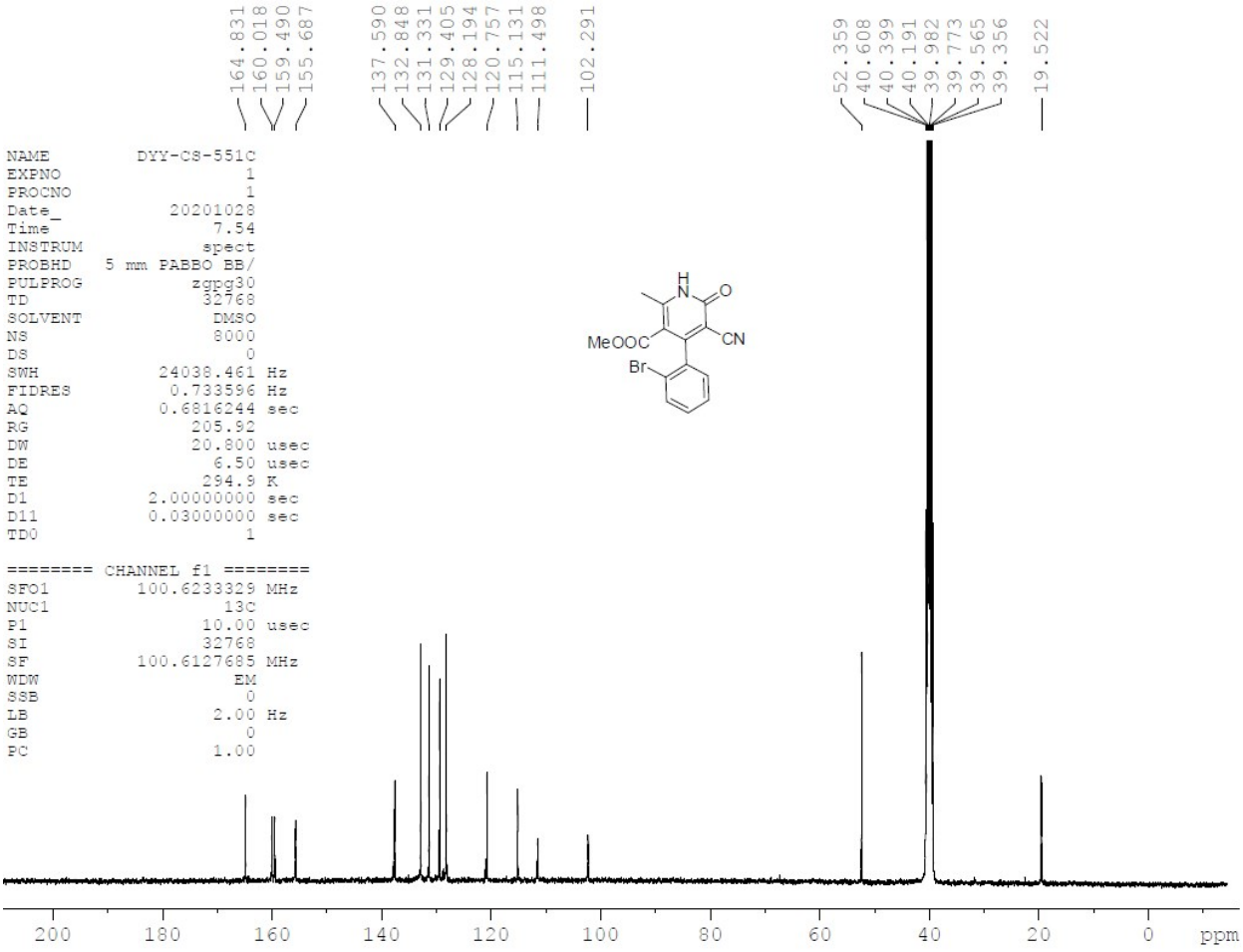
^{13}C NMR of compound **10a** (DMSO-d_6)



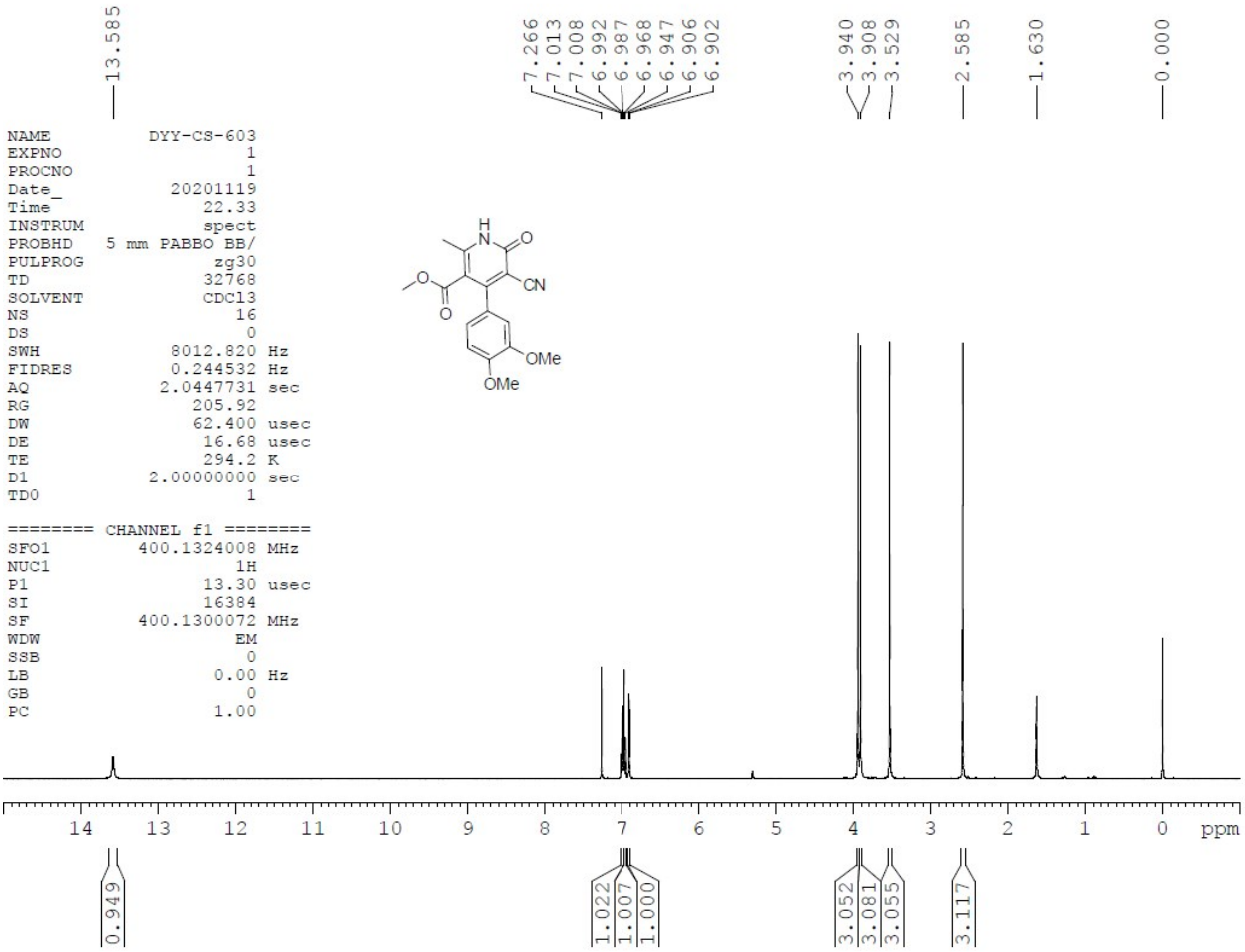
[1]HNMR of compound **10b** ($CDCl_3$)



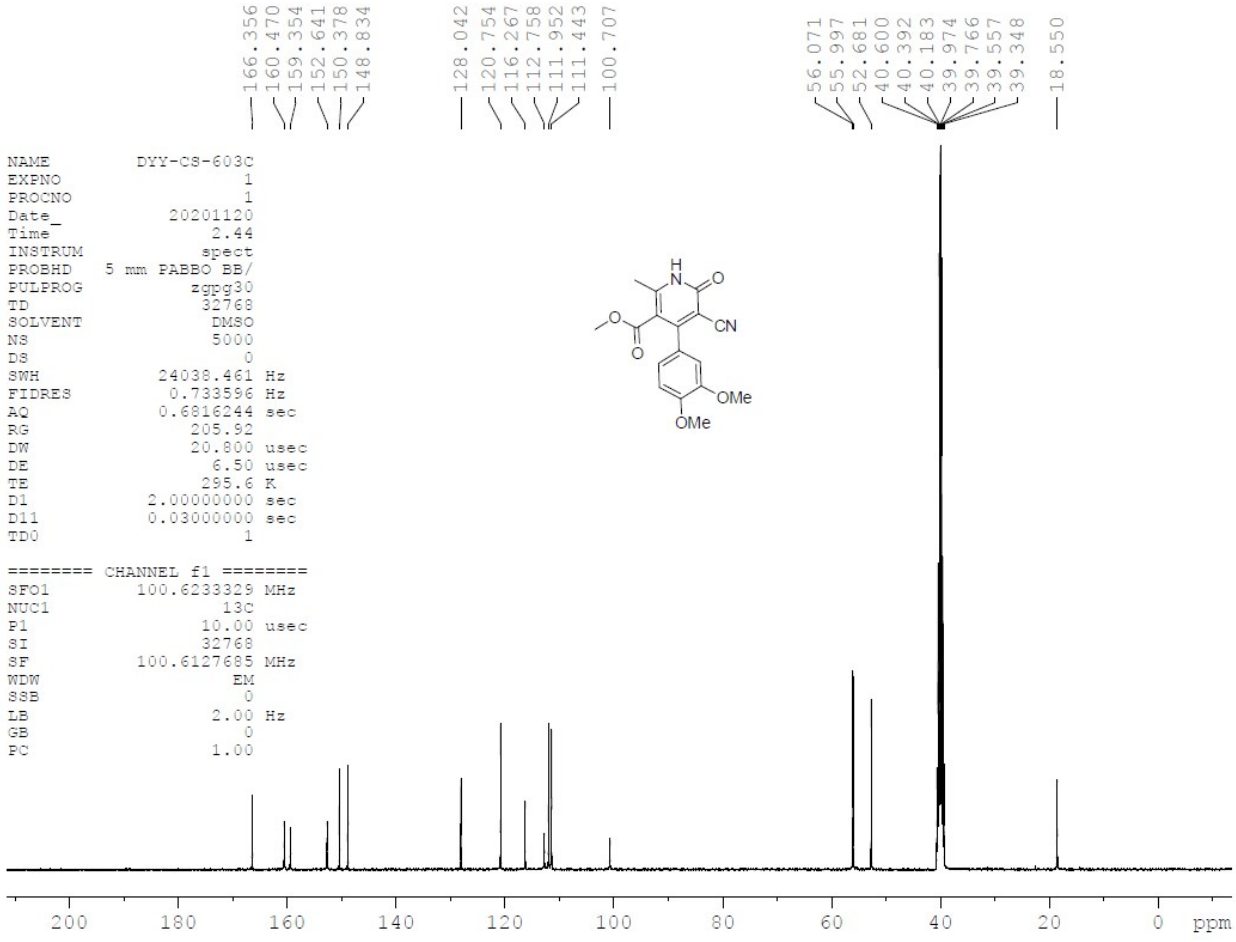
^{13}C NMR of compound **10b** (DMSO-d_6)



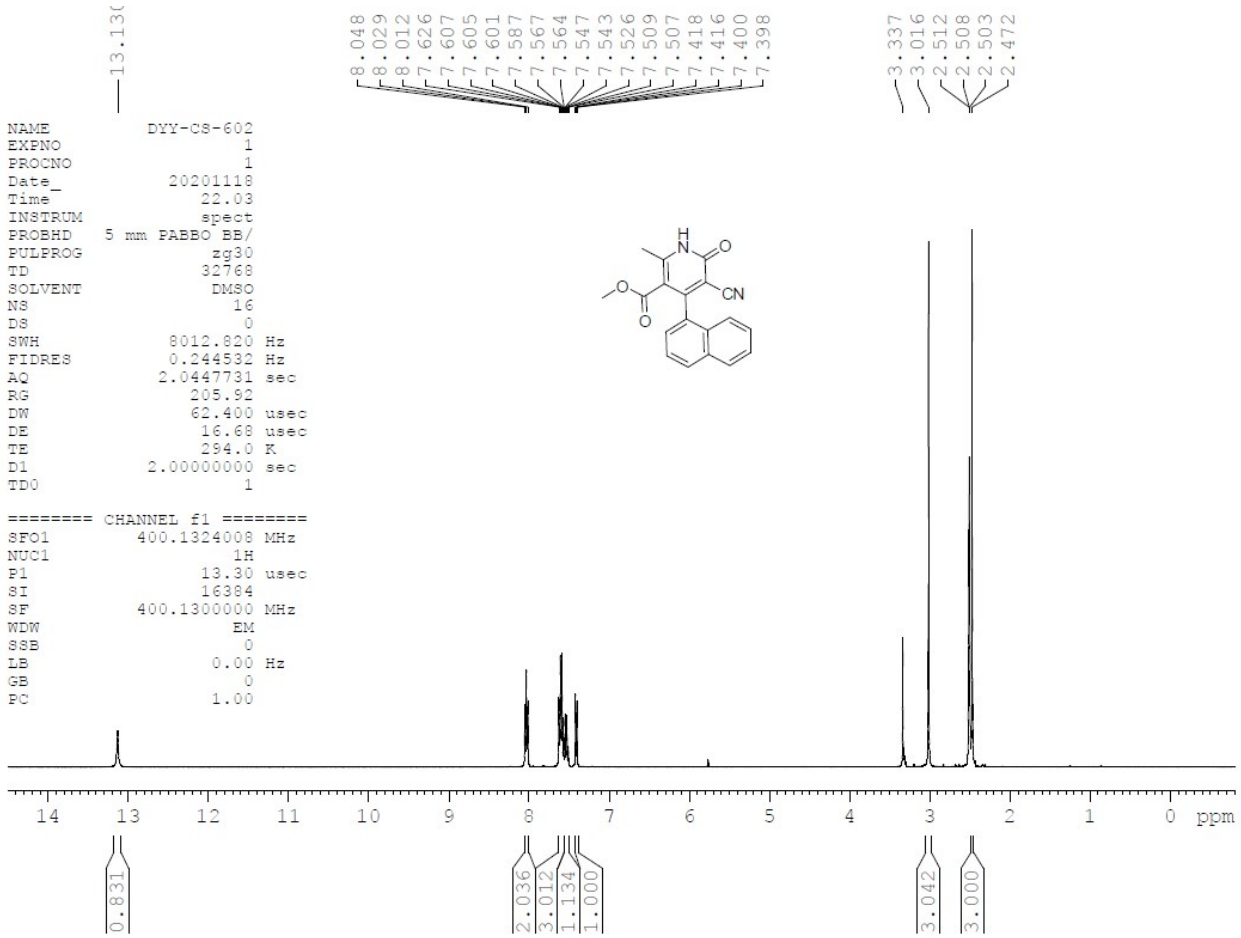
^{1}HNMR of compound **10c** ($CDCl_3$)



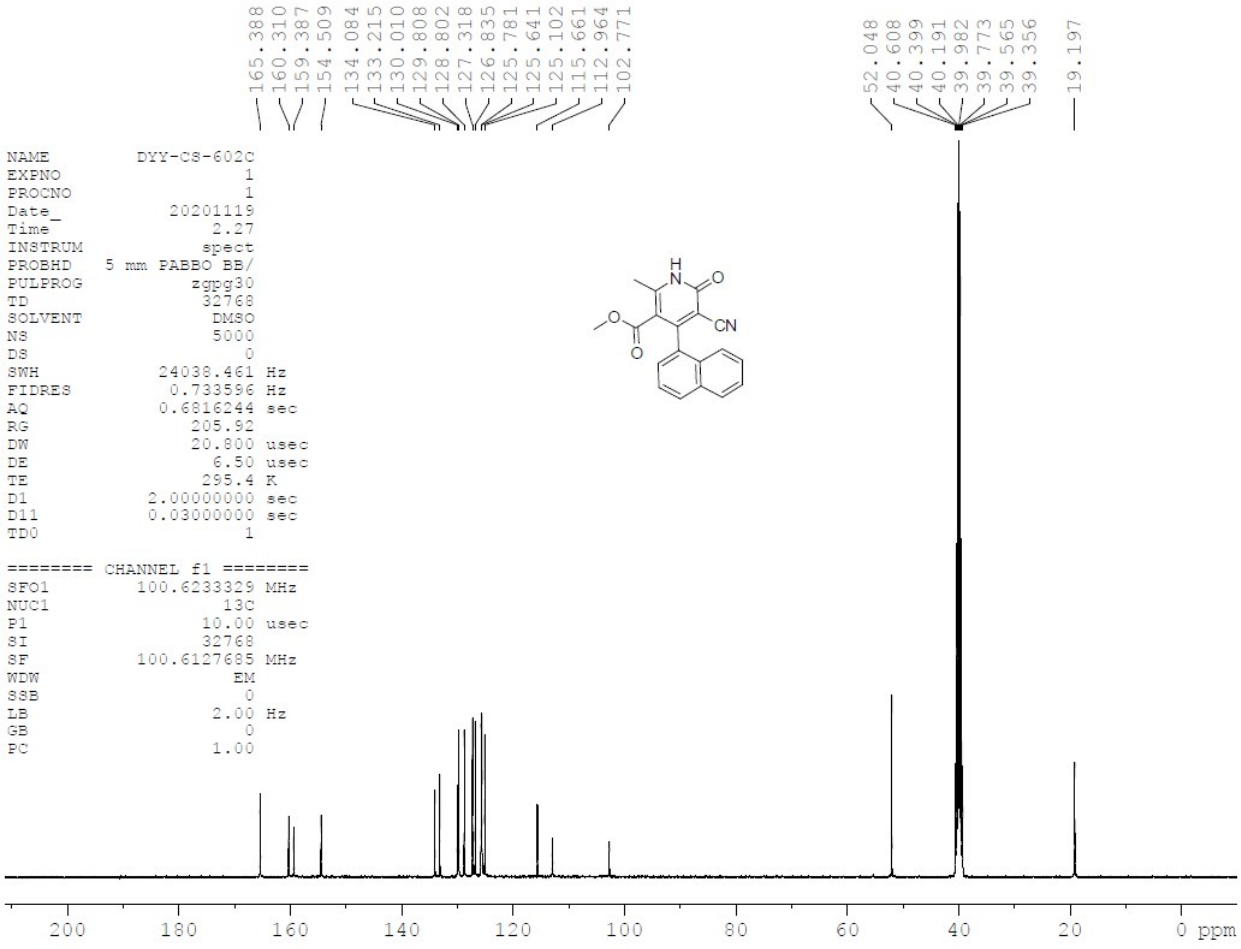
^{13}C NMR of compound **10c** (DMSO-d_6)



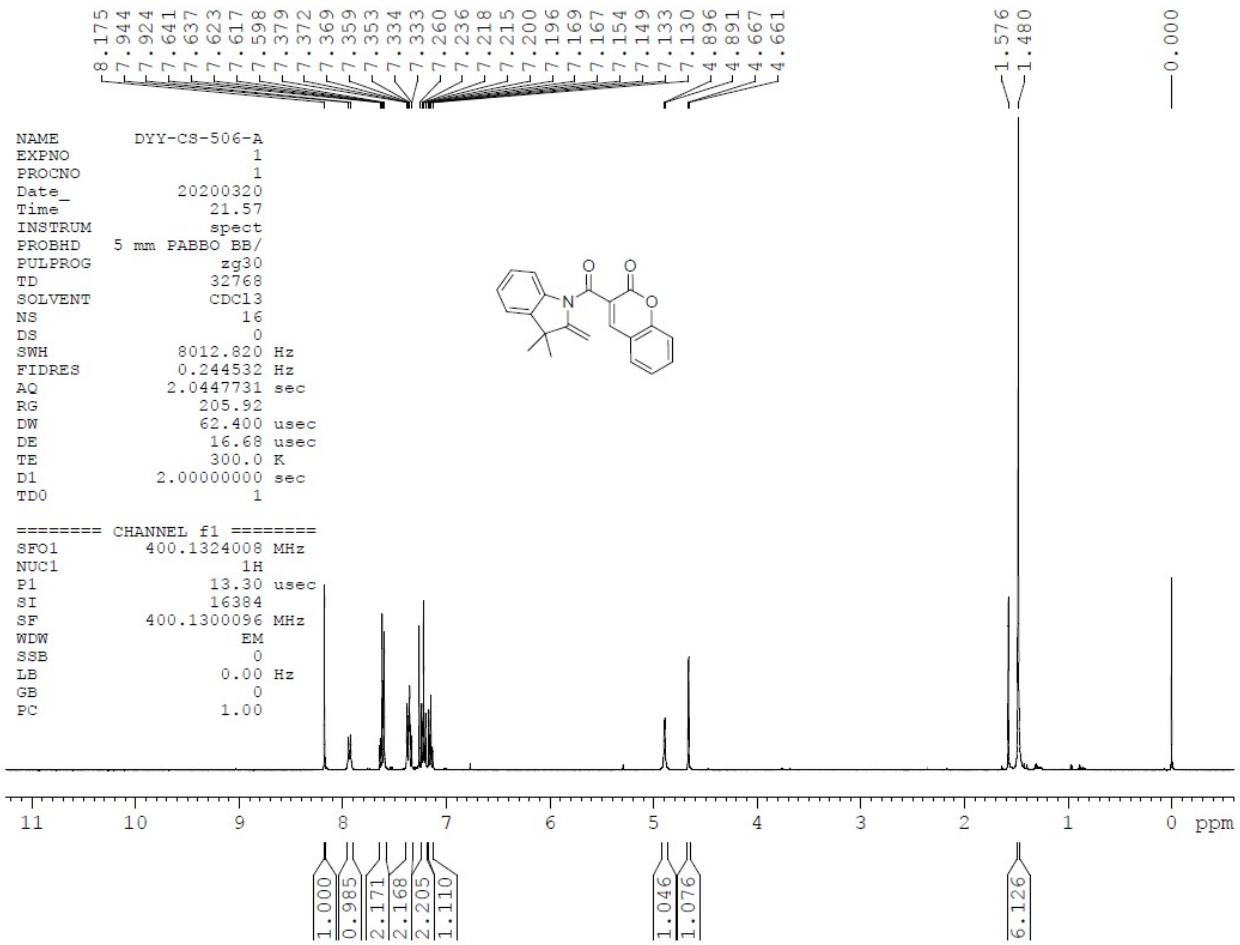
[1]HNMR of compound **10d** (DMSO-d_6)



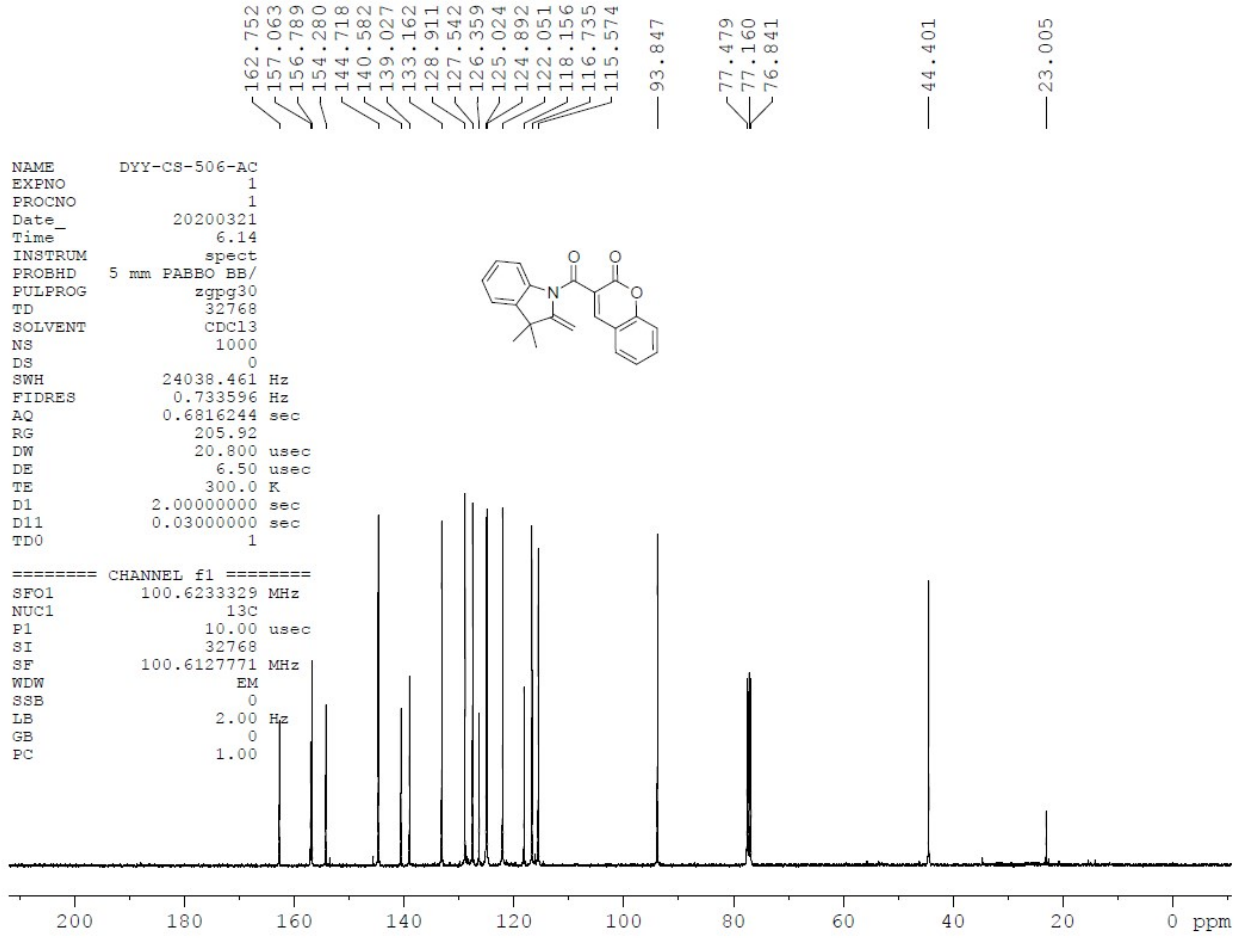
^{13}C NMR of compound **10d** (DMSO-d_6)



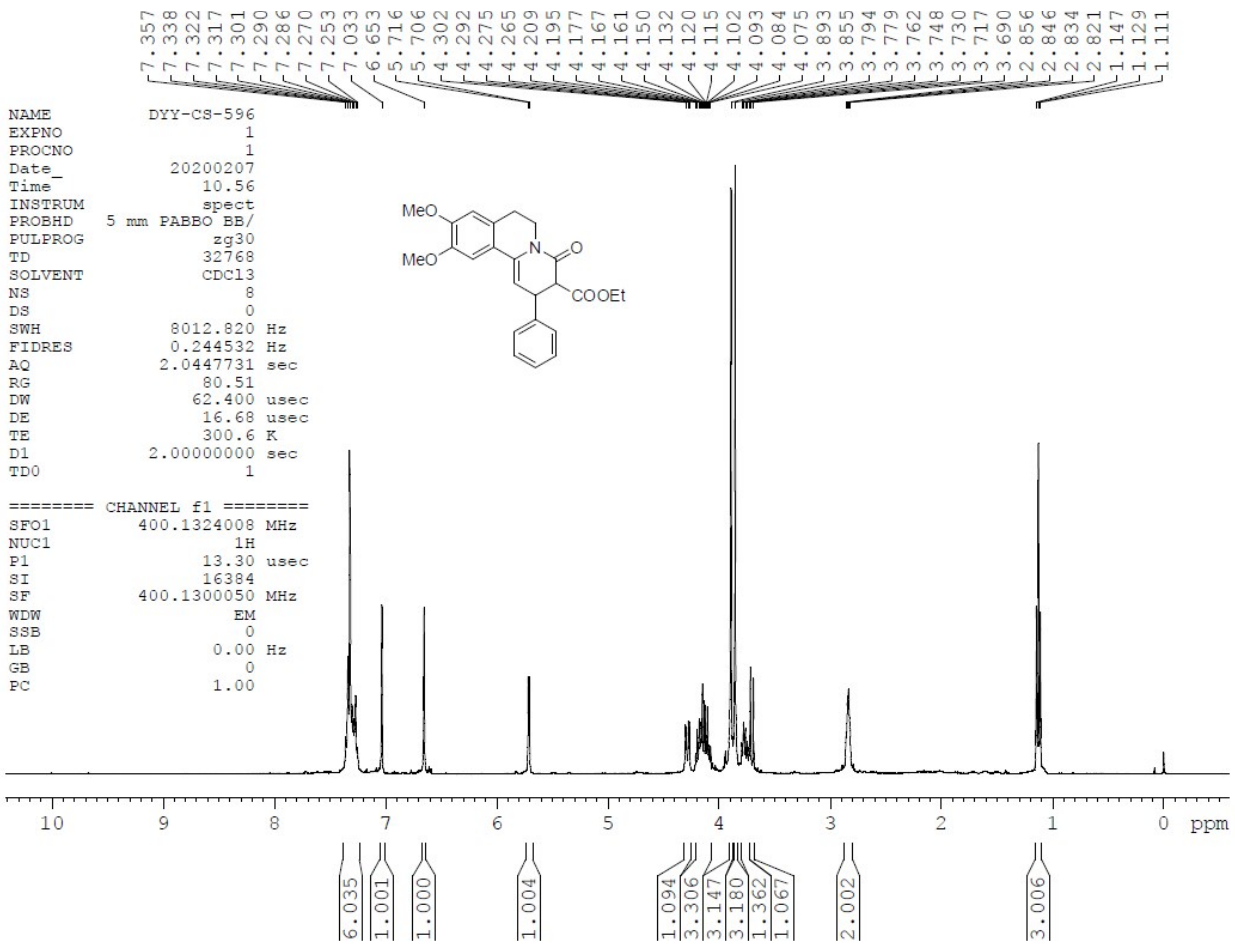
[1]HNMR of compound **11** ($CDCl_3$)



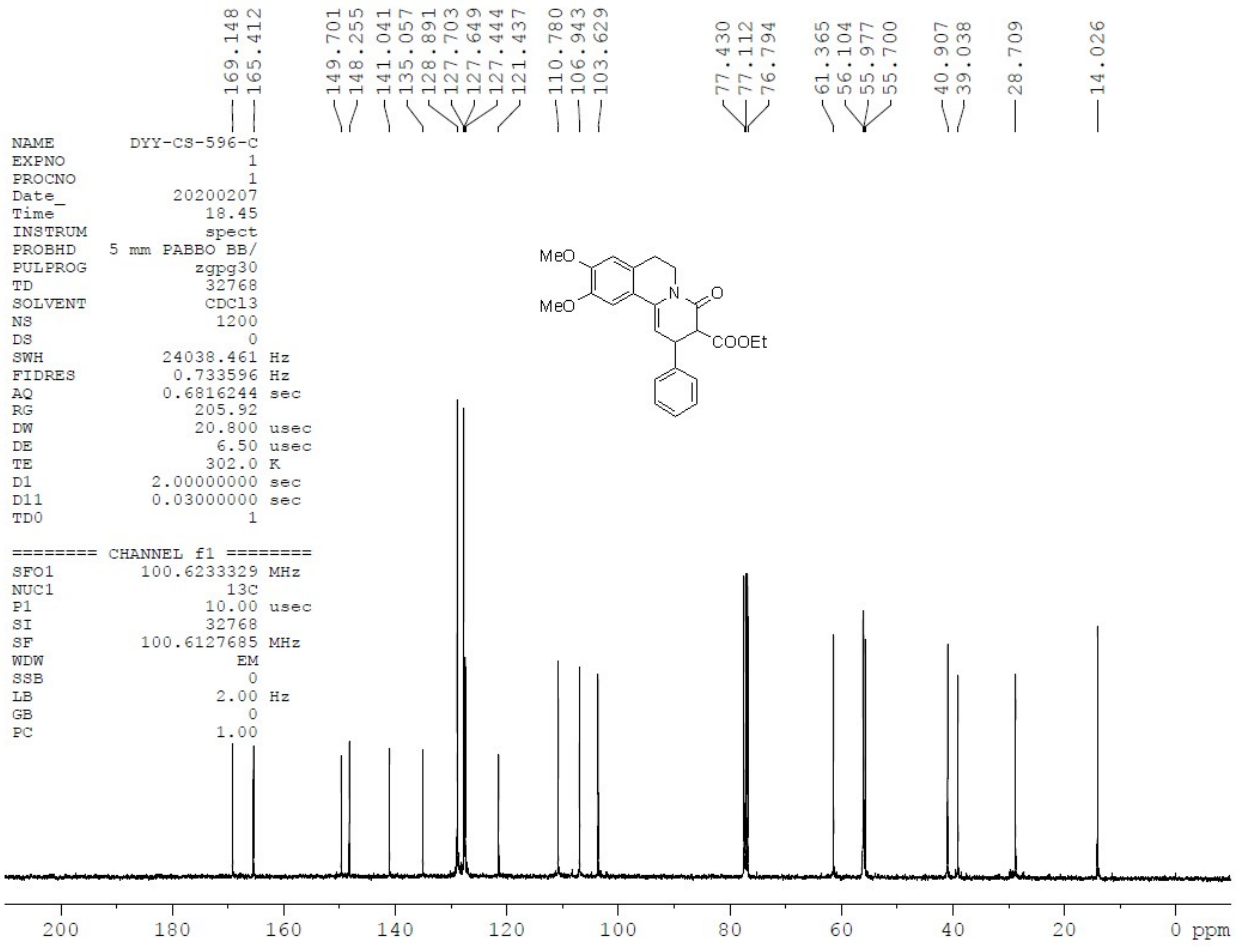
^{13}C NMR of compound **11** ($CDCl_3$)



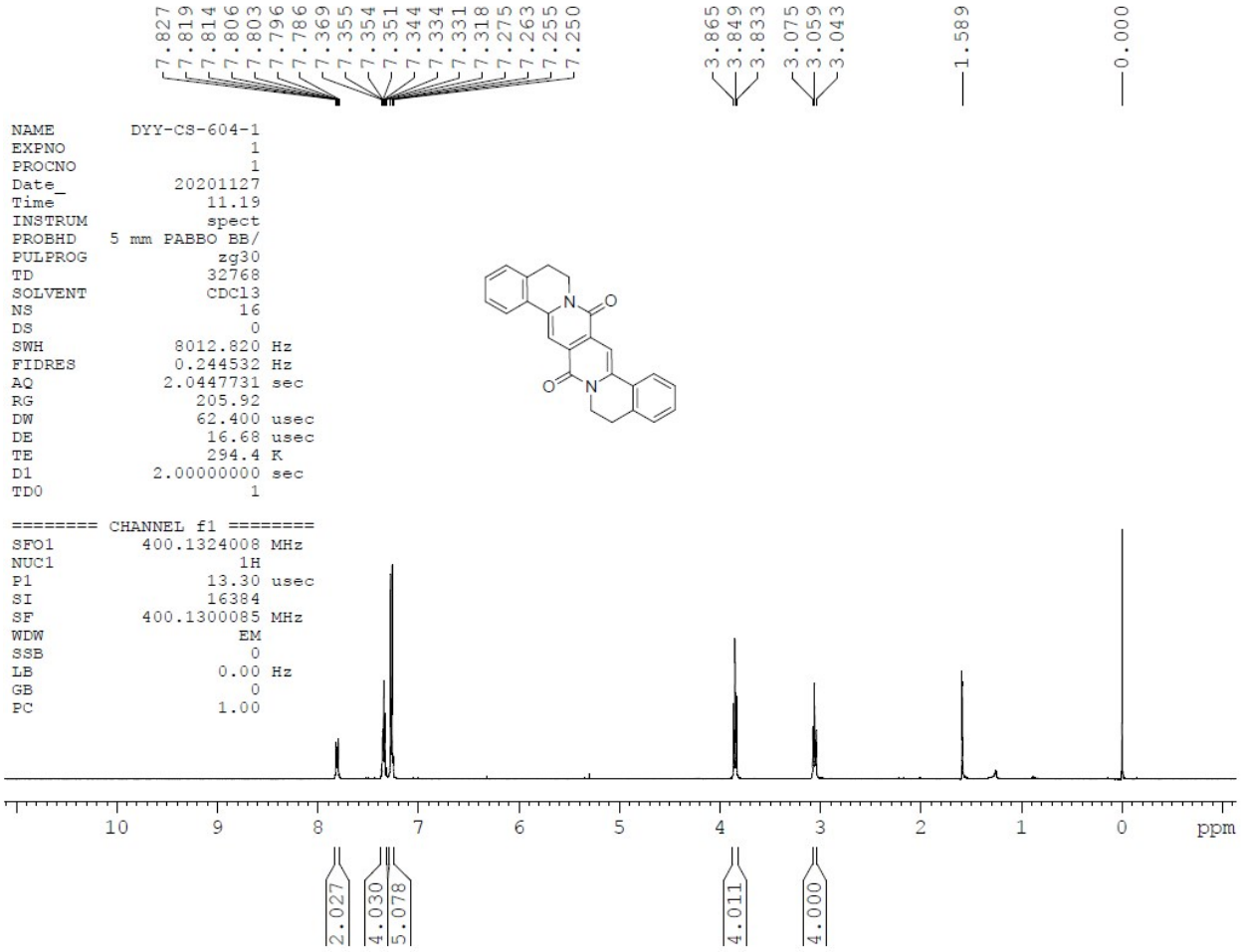
^{1}H NMR of compound **12** ($CDCl_3$)



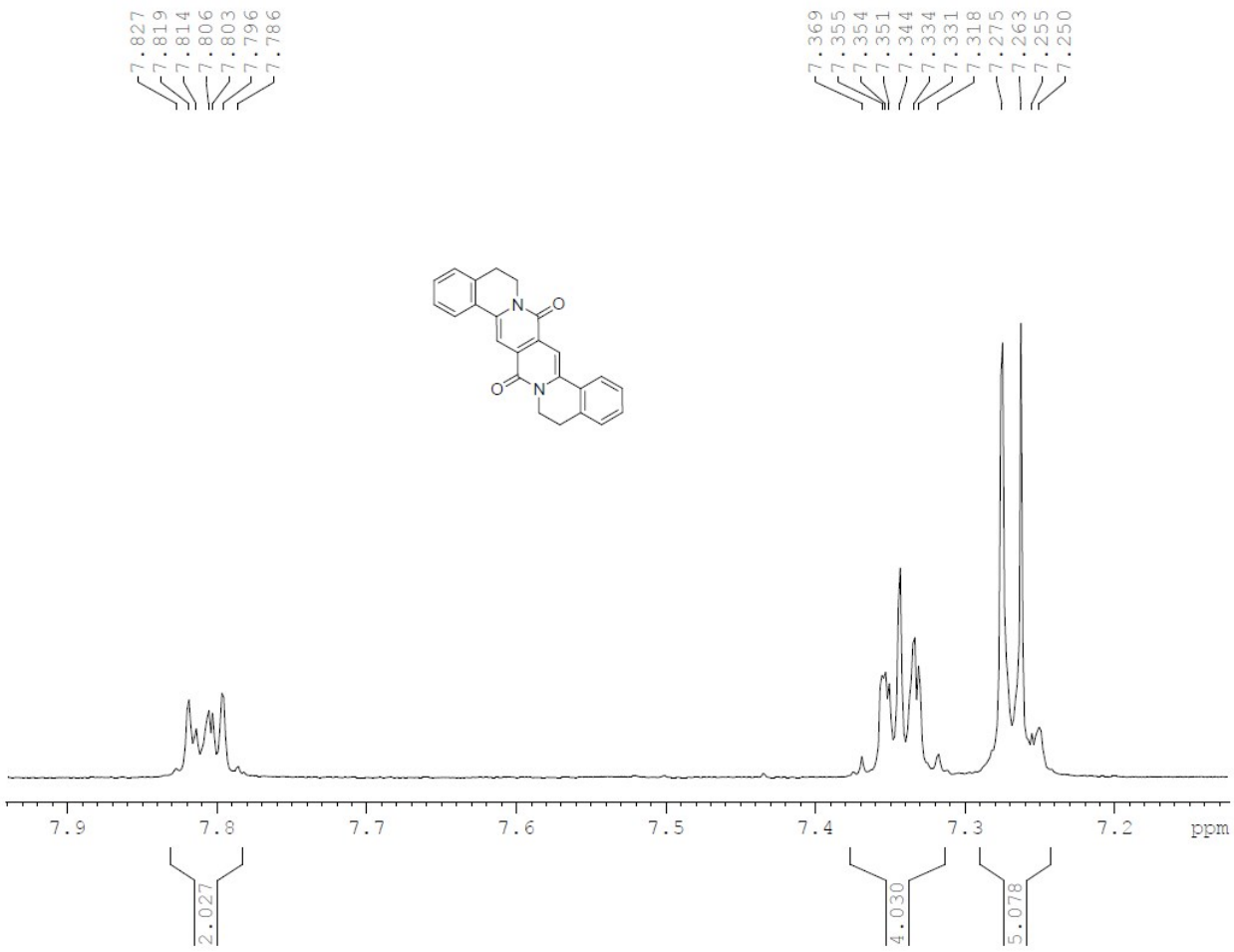
^{13}C NMR of compound **12** ($CDCl_3$)



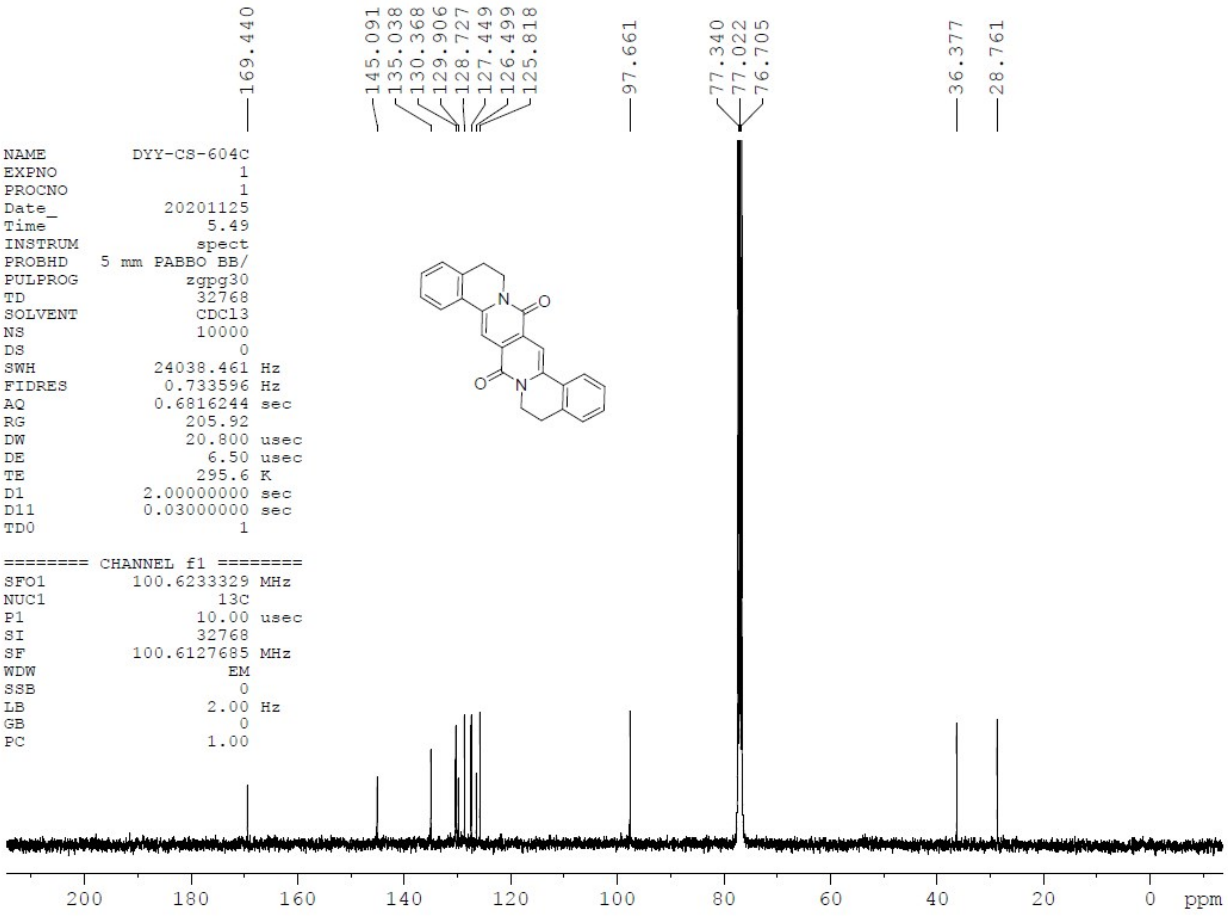
^{1}H NMR of compound **19a** ($CDCl_3$)



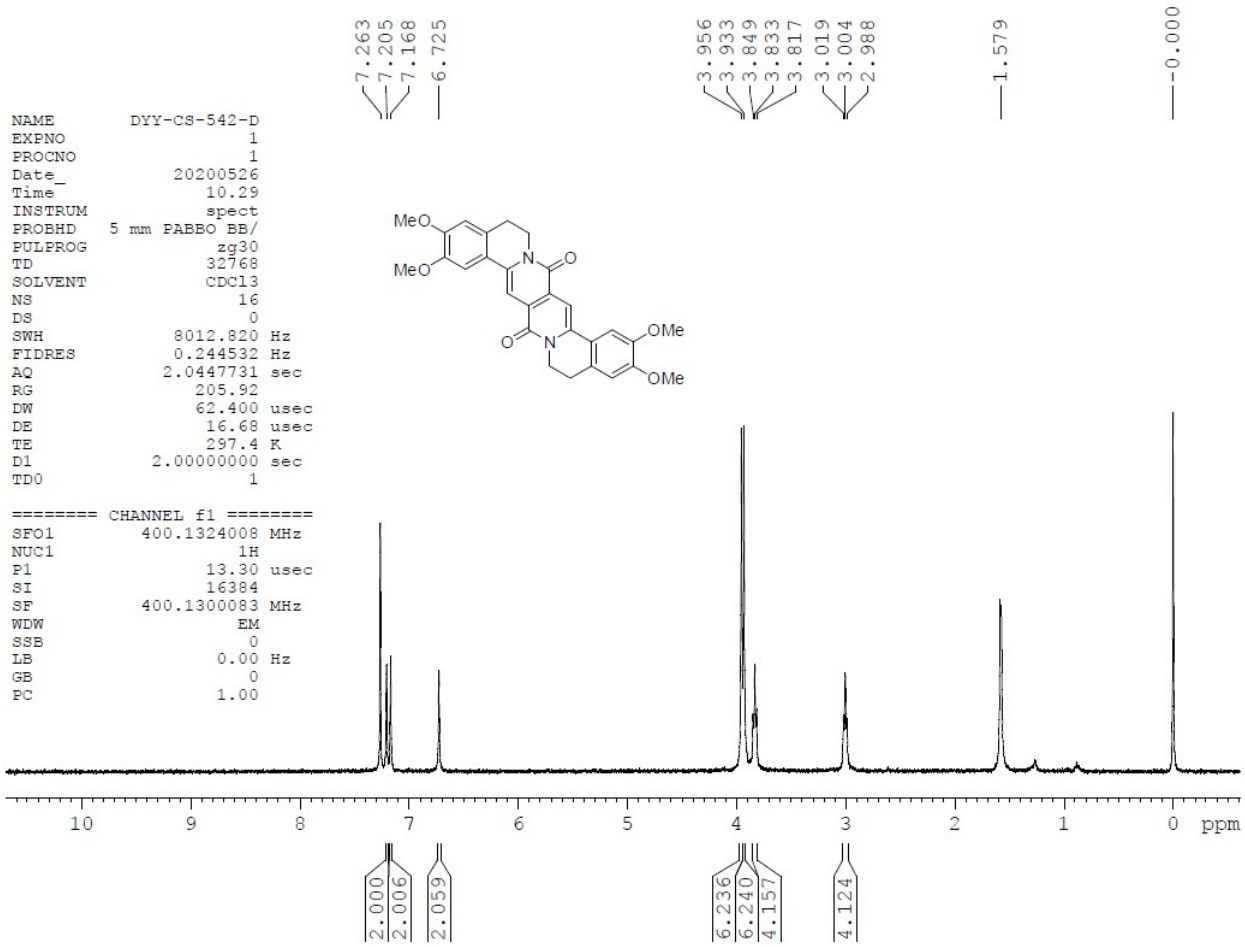
^{1}H NMR of compound **19a** ($CDCl_3$)



^{13}C NMR of compound **19a** ($CDCl_3$)



^{1}H NMR of compound **19b** ($CDCl_3$)



^{13}C NMR of compound **19b** ($CDCl_3$)