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Supporting Information

Photocyclization of Coumarinoyl Enamides Revisited: [2+2+2]Cycloreversion/Cycloaddition Mechanism

Sivanna Chithanna[a] and Ding-Yah Yang[a,b]*

[a]Department of Chemistry, Tunghai University
[b]Graduate Program for Biomedical and Materials Science, Tunghai University
No. 1727, Sec. 4, Taiwan Boulevard, Xitun District, Taichung 407224, Taiwan
*Corresponding author; Tel: 886-4-2359-7613; Fax: 886-4-2359-0426;
Email: yang@thu.edu.tw

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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 **10a** (CCDC-1900621)

Single crystal of **10a** 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.

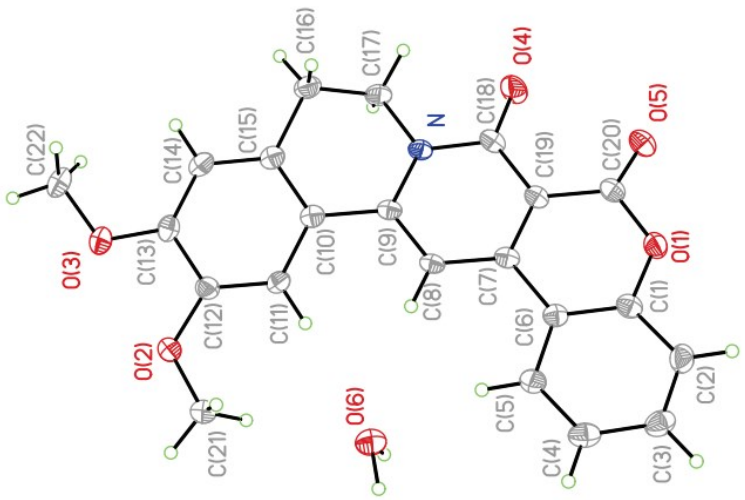


Figure S1: ORTEP diagram of compound **10a**. The ellipsoid contour probability levels: 50%

Table S1. Crystal data and structure refinement of compound **10a**.

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 **10b** (CCDC-2012710)

Single crystal of **10b** 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.

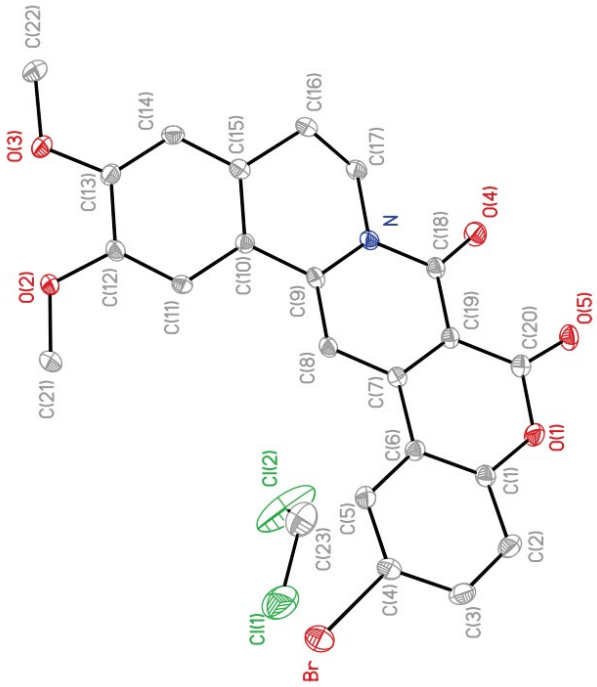


Figure S2: ORTEP diagram of compound **10b**. The ellipsoid contour probability levels: 50%

Table S2. Crystal data and structure refinement for compound **10b**.

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 **11b** (CCDC-2003732)

Single crystal of **11b** 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.

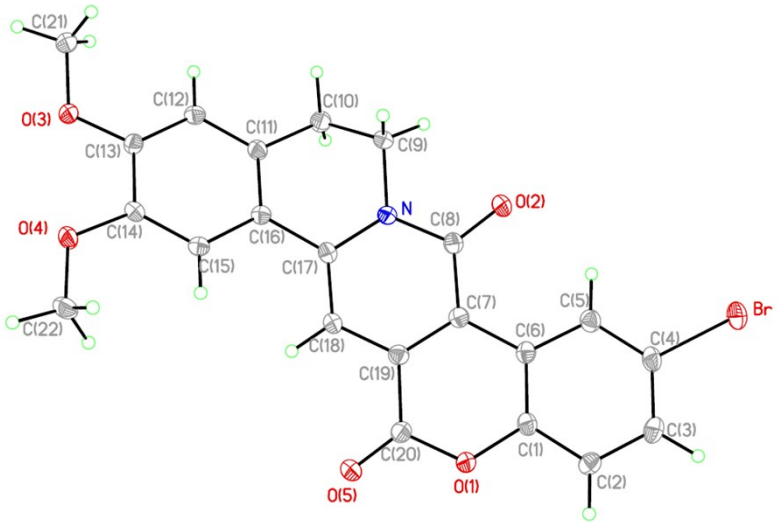


Figure S3: ORTEP diagram of compound **11b**. The ellipsoid contour probability levels: 50%

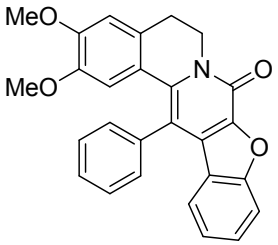
Table S3. Crystal data and structure refinement for compound **11b**.

Identification code	CS-479	
Empirical formula	C_{22} H_{16} Br N O_5	
Formula weight	454.27	
Temperature	150(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 9.3236(3) Å	a= 74.6908(16)°.
	b = 10.0313(3) Å	b= 65.4310(11)°.
	c = 11.2021(5) Å	g = 70.1382(11)°.
Volume	886.89(6) $Å^3$	
Z	2	
Density (calculated)	1.701 Mg/m^3	
Absorption coefficient	2.355 mm^{-1}	
F(000)	460	
Crystal size	0.370 x 0.350 x 0.210 mm^3	
Theta range for data collection	3.179 to 27.905°.	
Index ranges	-12<=h<=12, -13<=k<=13, -14<=l<=14	
Reflections collected	18511	
Independent reflections	4204 [R(int) = 0.0285]	
Completeness to theta = 25.242°	99.3 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9281 and 0.7477	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4204 / 0 / 262	
Goodness-of-fit on F^2	1.058	
Final R indices [I>2sigma(I)]	R1 = 0.0218, wR2 = 0.0560	
R indices (all data)	R1 = 0.0256, wR2 = 0.0575	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.384 and -0.308 $e.Å^{-3}$	

General procedure A for the preparation of compounds **1a**–**j**.

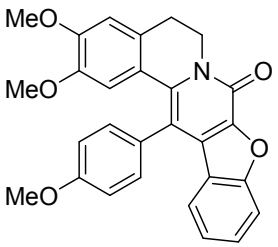
A sealed tube with Teflon screw-stopper was charged with compounds (**6a** or **6b**, 1.0 eq), appropriate boronic acid (1.1 eq), $Pd(PPh_3)_4$ (0.2 eq), and aqueous Na_2CO_3 (2 M, 0.5 mL) in DME/EtOH (3:1, 5 mL) and mixture was degassed with argon for 10 min and then heated to 110 ^oC for 12 h. After completion of the reaction, the reaction mixture was diluted with EtOAc (100 mL), washed with water (30 mL) and brine (30 mL). The organic layer was then dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuum* to give the crude product which was further purified by column chromatography to obtain the desired compound.

2,3-Dimethoxy-14-phenyl-5*H*-benzofuro[3',2':4,5]pyrido[2,1-*a*]isoquinolin-8(6*H*)-one (1a).



The title compound **1a** was synthesized by following general procedure A from compound **6a** (100 mg, 0.23 mmol), phenylboronic acid (32 mg, 0.25 mmol) and $Pd(PPh_3)_4$ (54 mg, 0.047 mmol), and purified by flash column chromatography (0.5% MeOH in DCM) to give a white solid (86 mg, 86% yield). R_f = 0.4 (3% MeOH/DCM). mp 288–290 ℃. ^1H NMR ($CDCl_3$, 400 MHz) δ: 7.67 (d, J = 8.0 Hz, 1H), 7.55–7.48 (m, 3H), 7.47–7.42 (m, 3H), 7.08 (td, J = 8.0, 1.2 Hz, 1H), 6.76 (t, J = 8.0 Hz, 1H), 6.72 (s, 1H), 6.59 (s, 1H), 4.47 (t, J = 6.4 Hz, 2H), 3.89 (s, 3H), 3.18 (s, 3H), 2.94 (t, J = 6.4 Hz, 2H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ: 157.0, 153.3, 149.8, 147.5, 146.7, 145.1, 142.5, 136.3, 132.5 (2C), 131.7, 128.8, 127.6, 124.8 (2C), 123.5, 122.8, 122.6, 120.9, 113.9, 113.0, 111.0, 110.2, 56.0, 55.3, 41.3, 28.8. IR $_{vmax}$ (neat): 2945, 2832, 1666, 1506, 1275, 1206, 1109, 1035, 877, 720 cm^{-1}. HRMS (EI) m/z: [M^+] calcd for $C_{27}H_{21}NO_4$, 423.1471; found, 423.1473.

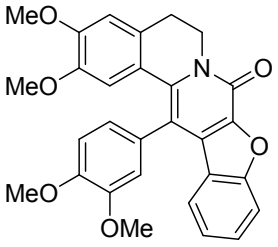
2,3-Dimethoxy-14-(4-methoxyphenyl)-5*H*-benzofuro[3',2':4,5]pyrido[2,1-*a*]isoquinolin-8(6*H*)-one (1b).



The title compound **1b** was synthesized by following general procedure A from compound **6a** (100 mg, 0.23 mmol), 4-methoxyphenylboronic acid (39 mg, 0.25 mmol) and $Pd(PPh_3)_4$ (54 mg, 0.047 mmol), and purified by flash column chromatography (0.5% MeOH in DCM) to give a white solid (98 mg, 92% yield). R_f= 0.35 (3% MeOH/DCM). mp 220–222 ℃. ^1H NMR ($CDCl_3$, 400 MHz) δ: 7.67 (d, J = 8.0 Hz, 1H), 7.46 (td, J = 8.0, 1.2 Hz, 1H), 7.34–7.31 (m, 2H), 7.11 (td, J = 8.0, 1.2 Hz, 1H), 7.07–7.03 (m, 2H), 6.88 (d, J = 8.0 Hz, 1H), 6.71 (s, 1H), 6.62 (s, 1H), 4.46 (t, J = 6.4 Hz, 2H), 3.89 (s, 6H), 3.26 (s, 3H), 2.93 (t, J = 6.4 Hz, 2H).$^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz) δ: 159.4, 157.0, 153.5, 148.9, 146.3, 142.2, 135.6, 132.0 (2C), 130.9, 129.7, 129.6, 128.4, 123.6, 123.3, 123.1, 121.9, 114.8 (2C), 113.6, 133.3, 112.7, 109.6, 55.8, 55.4, 55.2, 41.4, 28.8. IR $_{vmax}$ (neat): 3044, 2832, 1670, 1501,

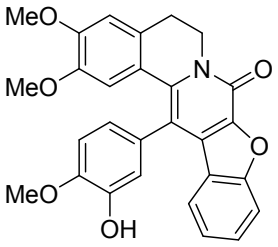
1220, 1106, 1032, 833, 730 cm^{-1}. HRMS (EI) m/z: [M^+] calcd for $C_{28}H_{23}NO_5$, 453.1576; found, 453.1574.

14-(3,4-Dimethoxyphenyl)-2,3-dimethoxy-5*H*-benzofuro[3',2':4,5]pyrido[2,1-*a*]isoquinolin-8(6*H*)-one (1c).



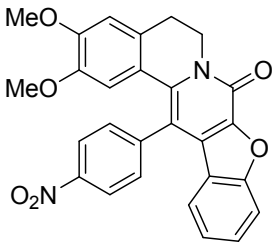
The title compound **1c** was synthesized by following general procedure A from compound **6a** (100 mg, 0.23 mmol), 3,4-dimethoxyphenylboronic acid (47 mg, 0.25 mmol) and $Pd(PPh_3)_4$ (54 mg, 0.047 mmol), and purified by flash column chromatography (0.5% MeOH in DCM) to give a white solid (98 mg, 92% yield). R_f = 0.33 (3% MeOH/DCM). mp 308–310 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.67 (d, J = 8.4 Hz, 1H), 7.49–7.44 (m, 1H), 7.11 (td, J = 8.4, 1.2 Hz, 1H), 7.00 (d, J = 8.4 Hz, 1H), 6.97–6.92 (m, 2H), 6.87 (d, J = 8.4 Hz, 1H), 6.72 (s, 2H), 4.63–4.56 (m, 1H), 4.36–4.30 (m, 1H), 3.97 (s, 3H), 3.90 (s, 3H), 3.80 (s, 3H), 3.28 (s, 3H), 2.94 (t, J = 6.0 Hz, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz) δ: 157.0, 153.5, 149.8, 149.0, 148.9, 146.4, 142.2, 135.6, 130.9, 130.0, 129.1, 128.4, 123.6, 123.3, 123.1 (3C), 121.9, 113.7, 113.3, 112.7, 112.0, 109.6, 56.1, 56.0, 55.8, 55.2, 41.3, 28.8. IR $_{vmax}$ (neat): 2940, 2833, 1655, 1501, 1255, 1140, 1021, 876, 744 cm^{-1}. HRMS (EI) m/z: [M^+] calcd for $C_{29}H_{25}NO_6$, 483.1682; found, 483.1685.

14-(3-Hydroxy-4-methoxyphenyl)-2,3-dimethoxy-5*H*-benzofuro[3',2':4,5]pyrido[2,1-*a*]isoquinolin-8(6*H*)-one (1d).



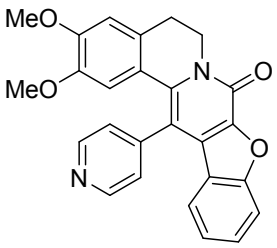
The title compound **1d** was synthesized by following general procedure A from compound **6a** (100 mg, 0.23 mmol), 3-hydroxy-4-methoxyphenylboronic acid (43 mg, 0.25 mmol) and $Pd(PPh_3)_4$ (54 mg, 0.047 mmol), and purified by flash column chromatography (1% MeOH in DCM) to give a white solid (88 mg, 80% yield). R_f = 0.3 (3% MeOH/DCM). mp 282–284 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.65 (d, J = 8.0 Hz, 1H), 7.48–7.43 (m, 1H), 7.12 (td, J = 8.0, 0.8 Hz, 1H), 7.00 (d, J = 2.0 Hz, 1H), 6.97 (d, J = 8.0 Hz, 1H), 6.94 (d, J = 8.0 Hz, 1H), 6.86 (dd, J = 8.0, 0.8 Hz, 1H), 6.72 (s, 1H), 6.71 (s, 1H), 5.81 (s, 1H), 4.56–4.39 (m, 1H), 4.39–4.33 (m, 1H), 3.99 (s, 3H), 3.90 (s, 3H), 3.31 (s, 3H), 2.92 (t, J = 6.4 Hz, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ: 157.0, 153.5, 149.0, 146.5, 146.43, 146.40, 142.2, 135.6, 130.9, 130.7, 129.1, 128.4, 123.6, 123.4, 123.1, 122.5, 122.0, 117.1, 113.5, 113.3, 112.6, 111.3, 109.6, 56.1, 55.8, 55.2, 41.4, 28.8. IR $_{vmax}$ (neat): 2941, 2830, 1654, 1502, 1254, 1141, 1023, 876, 742 cm^{-1}. HRMS (EI) m/z: [M^+] calcd for $C_{28}H_{23}NO_6$, 469.1525; found, 469.1522.

2,3-Dimethoxy-14-(4-nitrophenyl)-5*H*-benzofuro[3',2':4,5]pyrido[2,1-*a*]isoquinolin-8(6*H*)-one (1e).



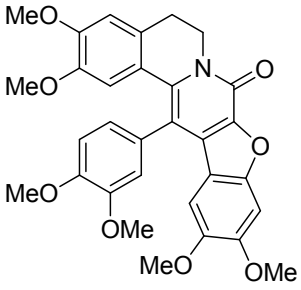
The title compound **1e** was synthesized by following general procedure A from compound **6a** (100 mg, 0.23 mmol), 4-nitrophenylboronic acid (43 mg, 0.25 mmol) and $Pd(PPh_3)_4$ (54 mg, 0.047 mmol), and purified by flash column chromatography (1% MeOH in DCM) to give a yellow solid (93 mg, 85% yield). R_f = 0.3 (3% MeOH/DCM). mp 260–262 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.40 (d, J = 8.8 Hz, 2H), 7.70 (d, J = 8.8 Hz, 1H), 7.66 (d, J = 8.8 Hz, 2H), 7.50 (td, J = 8.8, 1.2 Hz, 1H), 7.19 (td, J = 8.8, 1.2 Hz, 1H), 6.79 (d, J = 8.8 Hz, 1H), 6.76 (s, 1H), 6.33 (s, 1H), 4.44 (t, J = 6.4 Hz, 2H), 3.91 (s, 3H), 3.18 (s, 3H), 2.96 (t, J = 6.4 Hz, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ: 157.0, 153.3, 149.8, 147.5, 146.7, 145.1, 142.5, 136.3, 132.5 (2C), 131.7, 128.8, 127.6, 124.5 (2C), 123.5, 122.8, 122.6, 120.9, 113.9, 113.0, 111.0, 110.2, 56.0, 55.3, 41.3, 28.8. IR $_{vmax}$ (neat): 2999, 2849, 1655, 1516, 1463, 1237, 1142, 1022, 805,723 cm^{-1}. HRMS (EI) m/z: [M$^+$] calcd for $C_{27}H_{20}N_2O_6$, 468.1321; found, 468.1325.

2,3-Dimethoxy-14-(pyridin-4-yl)-5*H*-benzofuro[3',2':4,5]pyrido[2,1-*a*]isoquinolin-8(6*H*)-one (1f).



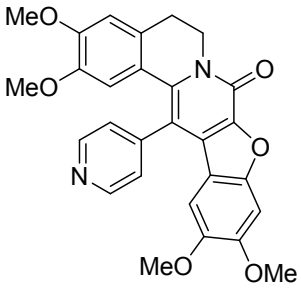
The title compound **1f** was synthesized by following general procedure A from compound **6a** (100 mg, 0.23 mmol), 4-pyridinylboronic acid (32 mg, 0.25 mmol) and $Pd(PPh_3)_4$ (54 mg, 0.047 mmol), and purified by flash column chromatography (3% MeOH in DCM) to give a white solid (88 mg, 88% yield). R_f = 0.3 (10% MeOH/DCM). mp 290–292 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.80 (dd, J = 8.4, 1.2 Hz, 2H), 7.70 (d, J = 8.4 Hz, 1H), 7.49 (td, J = 8.4, 1.2 Hz, 1H), 7.43 (dd, J = 8.4, 1.2 Hz, 2H), 7.13 (td, J = 8.4, 1.2 Hz, 1H), 6.86 (d, J = 8.4 Hz, 1H), 6.75 (s, 1H), 6.40 (s, 1H), 4.46 (t, J = 6.4 Hz, 2H), 3.89 (s, 3H), 3.26 (s, 3H), 2.93 (t, J = 6.4 Hz, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz) δ: 157.0, 153.4, 150.9 (2C), 149.6, 146.6, 146.4, 142.5, 135.9, 131.4, 128.8, 127.4, 126.3 (2C), 123.4, 122.8, 122.7, 120.8, 113.6, 113.0, 110.5, 110.0, 55.9, 55.2, 41.3, 28.7. IR $_{vmax}$ (neat): 2974, 2833, 1627, 1507, 1343, 1257, 1103, 1030, 872, 791 cm^{-1}. HRMS (EI) m/z: [M$^+$] calcd for $C_{26}H_{20}N_2O_4$, 424.1423; found, 424.1425.

14-(3,4-Dimethoxyphenyl)-2,3,11,12-tetramethoxy-5*H*-benzofuro[3',2':4,5]pyrido[2,1-*a*]isoquinolin-8(6*H*)-one (1g).



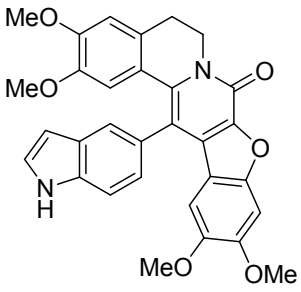
The title compound **1g** was synthesized by following general procedure A from compound **6b** (100 mg, 0.20 mmol), 3,4-dimethoxyphenylboronic acid (41 mg, 0.22 mmol) and $Pd(PPh_3)_4$ (48 mg, 0.041 mmol), and purified by flash column chromatography (2% MeOH in DCM) to give a white solid (100 mg, 89% yield). R_f = 0.3 (5% MeOH/DCM). mp 254–256 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.14 (s, 1H), 7.03–6.95 (m, 3H), 6.75 (s, 1H), 6.72 (s, 1H), 6.23 (s, 1H), 4.60–4.54 (m, 1H), 4.34–4.27 (m, 1H), 3.95 (s, 6H), 3.90 (s, 3H), 3.82 (s, 3H), 3.59 (s, 3H), 3.28 (s, 3H), 2.93 (t, J = 6.4 Hz, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ: 153.1, 152.6, 151.2, 150.0, 149.1, 149.0, 146.5, 146.4, 141.9, 135.4, 131.0, 130.4, 129.8, 123.5, 122.1, 115.1, 114.1, 113.5, 113.0, 112.0, 109.8, 103.7, 95.5, 56.4 (2C), 56.3, 56.0, 55.9, 55.4, 41.2, 28.9. IR $_{vmax}$ (neat): 2932, 2855, 1661, 1600, 1453, 1272, 1134, 1001, 925, 771 cm^{-1}. HRMS (EI) m/z: [M$^+$] calcd for $C_{31}H_{29}NO_8$, 543.1893; found, 543.1897.

2,3,11,12-Tetramethoxy-14-(pyridin-4-yl)-5*H*-benzofuro[3',2':4,5]pyrido[2,1-*a*]isoquinolin-8(6*H*)-one (1h).



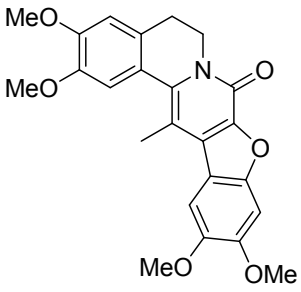
The title compound **1h** was synthesized by following general procedure A from compound **6b** (100 mg, 0.20 mmol), 4-pyridinylboronic acid (28 mg, 0.22 mmol) and $Pd(PPh_3)_4$ (48 mg, 0.041 mmol), and purified by flash column chromatography (5% MeOH in DCM) to give a white solid (80 mg, 80% yield). R_f = 0.3 (10% MeOH/DCM). mp 296–298 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.80 (d, J = 5.6 Hz, 2H), 7.46 (d, J = 5.6 Hz, 2H), 7.14 (s, 1H), 6.75 (s, 1H), 6.43 (s, 1H), 6.16 (s, 1H), 4.21 (t, J = 6.0 Hz, 2H), 3.95 (s, 3H), 3.91 (s, 3H), 3.59 (s, 3H), 3.21 (s, 3H), 2.95 (t, J = 6.0 Hz, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz) δ: 153.0, 152.6, 151.3, 150.7 (2C), 149.5, 146.6 (3C), 142.0, 135.7, 131.3, 128.0, 126.5 (2C), 121.0, 114.1, 113.6, 110.0, 109.9, 102.8, 95.5, 56.2, 55.9, 55.8, 55.2, 41.0, 28.7. IR $_{vmax}$ (neat): 2939, 2860, 1669, 1593, 1478, 1354, 1212, 1181, 1034, 837 cm^{-1}. HRMS (EI) m/z: [M$^+$] calcd for $C_{28}H_{24}N_2O_6$, 484.1634; found, 484.1631.

14-(1*H*-indol-5-yl)-2,3,11,12-tetramethoxy-5*H*-benzofuro[3',2':4,5]pyrido[2,1-*a*]isoquinolin-8(6*H*)-one (1i).



The title compound **1i** was synthesized by following general procedure A from compound **6b** (100 mg, 0.20 mmol), (1*H*-indol-5-yl) boronic acid (36 mg, 0.22 mmol) and $Pd(PPh_3)_4$ (48 mg, 0.041 mmol), and purified by flash column chromatography (3% MeOH in DCM) to give a white solid (106 mg, 99% yield). R_f = 0.4 (10% MeOH/DCM). mp 310–312 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 11.28 (s, 1H), 7.60 (d, J = 8.4 Hz, 1H), 7.58 (s, 1H), 7.45–7.44 (m, 1H), 7.42 (s, 1H), 7.12 (dd, J = 8.4, 1.2 Hz, 1H), 6.92 (s, 1H), 6.68 (s, 1H), 6.48 (s, 1H), 5.92 (s, 1H), 4.38–4.32 (m, 1H), 4.24–4.18 (m, 1H), 3.83 (s, 3H), 3.75 (s, 3H), 3.17 (s, 3H), 2.94 (t, J = 6.0 Hz, 2H), 2.75 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ: 153.2, 152.7, 151.1, 148.8, 146.3, 146.1, 141.4, 135.6, 135.2, 131.0, 128.7, 128.1, 125.7, 124.2, 122.6, 122.2, 115.4, 115.2, 113.9, 112.0, 109.6, 104.0, 102.2, 95.3, 56.1, 55.7, 55.5, 54.8, 41.3, 28.7. IR ν_{max} (neat): 2939, 2860, 1669, 1593, 1478, 1354, 1212, 1181, 1034, 837 cm^{-1}. HRMS (EI) m/z: [M$^+$] calcd for $C_{31}H_{26}N_2O_6$, 522.1791; found, 522.1795.

2,3,11,12-Tetramethoxy-14-methyl-5H-benzofuro[3',2':4,5]pyrido[2,1-a]isoquinolin-8(6H)-one (1j).



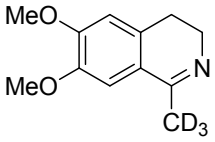
The title compound **1j** was synthesized by following general procedure B from 1-ethyl-6,7-dimethoxy-3,4-dihydroisoquinoline (**2a**, 100 mg, 0.45 mmol), triethylamine (92 mg, 0.92 mmol), and 5,6-dimethoxybenzofuran-2-carbonyl chloride (**3b**, 1,029 mg, 0.50 mmol), and purified by flash column chromatography (1.5% MeOH in DCM) to give a yellow solid (108 mg, 56% yield). R_f = 0.5 (3% MeOH/DCM). mp 254–256 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.45 (s, 1H), 7.20 (s, 1H), 7.19 (s, 1H), 6.83 (s, 1H), 4.33 (s, 2H), 4.01 (s, 3H), 4.00 (s, 3H), 3.97 (s, 3H), 3.96 (s, 3H), 2.89–2.86 (m, 2H), 2.87 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz) δ: 152.8, 152.5, 151.2, 149.2, 146.8, 146.7, 142.0, 135.8, 131.7, 130.3, 122.3, 115.5, 113.3, 110.2, 107.3, 104.0, 95.8, 56.6, 56.3, 56.2, 56.0, 41.2, 29.1, 18.1. IR ν_{max} (neat): 2920, 2845, 1660, 1512, 1480, 1335, 1210, 1111, 1015, 928 cm^{-1}. HRMS (EI) m/z: [M$^+$] calcd for $C_{24}H_{23}NO_6$, 421.1525; found, 421.1523.

General procedure for the preparation of deuterated **2b**.

To a stirred solution of imine **2a** (1.0 eq) in deuterium oxide (D_2O, 5.0 mL) was added Na_2CO_3 (0.3 eq) at room temperature. The resulting mixture was stirred at 80 ℃ for 18 h. After

completion of the reaction, the crude mixture was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuum* to yield the desired product **2b**.

6,7-Dimethoxy-1-(methyl-d_3)-3,4-dihydroisoquinoline (**2b**)

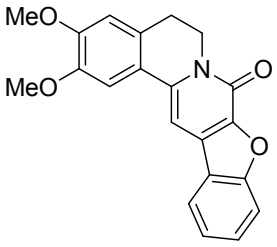


Brown solid. R_f = 0.3 (5% MeOH/DCM). 300 mg. Yield 98%. mp 92−94 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 6.99 (s, 1H), 6.69 (s, 1H), 3.92 (s, 3H), 3.91 (s, 3H), 3.63 (t, J = 7.6 Hz, 3H), 2.64 (t, J = 7.6 Hz, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz) δ: 163.5, 150.8, 147.4, 131.1, 122.5, 110., 109.0, 56.2, 55.9, 47.0, 25.7, 22.6 (sept, $J_{C\text{-}D}$ = 19.3 Hz). HRMS (EI) m/z: [M^+] calcd for $C_{12}H_{12}D_3NO_2$, 208.1291; found, 208.1293.

General procedure B for the preparation of compounds **5a**–**b**.

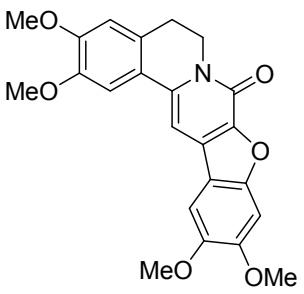
To a stirred solution of imine **2a** (1.0 eq) and triethylamine (2.0 eq) in dry toluene (10 mL) was added acid chloride **3a** or **3b** (1.1 eq) at 0 ℃. The resulting mixture was stirred at room temperature for 1 h. The mixture was then diluted with degassed dry acetonitrile (100 mL) and irradiated with UV light (352 nm) in a Rayonet photoreactor for 2 h at room temperature. After completion of the reaction, the solution was concentrated and the residue was diluted with dichloromethane (100 mL), washed with 5 N HCl (30 mL), water (30 mL) and brine (30 mL). The organic layer was then dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuum* to give the crude product which was further purified by column chromatography to obtain the desired compound.

2,3-Dimethoxy-5*H*-benzofuro[3',2':4,5]pyrido[2,1-*a*]isoquinolin-8(6*H*)-one (5a).



The title compound **5a** was synthesized by following general procedure B from imine **2** (1,000 mg, 4.87 mmol), triethylamine (986 mg, 9.74 mmol), and benzofuran-2-carbonyl chloride (**3a**, 968 mg, 5.36 mmol), and purified by flash column chromatography (1% MeOH in DCM) to give a yellow solid (1,400 mg, 82% yield). R_f = 0.5 (3% MeOH/DCM). mp 248–250 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.96 (d, J = 8.0 Hz, 1H), 7.69 (d, J = 8.0 Hz, 1H), 7.56 (td, J = 8.0, 1.2 Hz, 1H), 7.41 (td, J = 8.0, 1.2 Hz, 1H), 7.30 (s, 1H), 7.14 (s, 1H), 6.78 (s, 1H), 4.45 (t, J = 6.4 Hz, 2H), 4.03 (s, 3H), 3.96 (s, 3H), 2.97 (t, J = 6.4 Hz, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz) δ: 157.0, 153.8, 150.5, 148.6, 142.9, 139.0, 128.8, 128.5, 128.4, 123.4, 123.3, 122.3, 121.7, 112.9, 110.4, 108.0, 94.7, 56.3, 56.1, 39.8, 27.9. IR $_{vmax}$ (neat): 2920, 2838, 1665, 1515, 1472, 1338, 1200, 1111, 1020, 920 cm^{-1}. HRMS (EI) m/z: [M^+] calcd for $C_{21}H_{17}NO_4$, 347.1158; found, 347.1155.

2,3,11,12-Tetramethoxy-5*H*-benzofuro[3',2':4,5]pyrido[2,1-*a*]isoquinolin-8(6*H*)-one (5b).

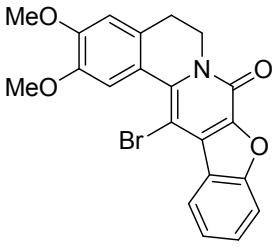


The title compound **5b** was synthesized by following general procedure B from imine **2a** (1,000 mg, 4.87 mmol), triethylamine (986 mg, 9.74 mmol), and 5,6-dimethoxybenzofuran-2-carbonyl chloride (**3b**, 1,029 mg, 5.36 mmol), and purified by flash column chromatography (1.5% MeOH in DCM) to give a yellow solid (1,100 mg, 55% yield). R_f = 0.45 (3% MeOH/DCM). mp 264–266 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.31 (s, 1H), 7.30 (s, 1H), 7.27 (s, 1H), 7.14 (s, 1H), 6.77 (s, 1H), 4.41 (t, J = 6.4 Hz, 2H), 4.04 (s, 3H), 4.02 (s, 3H), 3.97 (s, 3H), 3.96 (s, 3H), 2.95 (t, J = 6.4 Hz, 2H).^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ: 152.8, 152.4, 151.2, 149.5, 146.8 (2C), 141.9, 135.7, 131.7, 130.3, 122.3, 115.4, 113.5, 110.2, 107.4, 104.0, 95.8, 56.6, 56.3, 56.2, 56.0, 41.2, 29.0. IR $_{\nu max}$ (neat): 2919, 2842, 1661, 1511, 1484, 1335, 1211, 1112, 1015, 928 cm^{-1}. HRMS (EI) m/z: [M$^+$] calcd for $C_{23}H_{21}NO_6$, 407.1369; found, 407.1365.

General procedure C for the preparation of compounds **6a**–**b**.

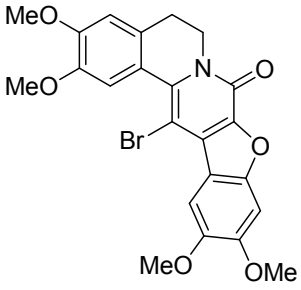
To a stirred solution of compounds (**5a** or **5b**, 1.0 eq) in dry THF (10 mL) was added *N*-bromosuccinimide (1.2 eq) at 0 ℃. The resulting mixture was stirred at 0 ℃ for 15 min. After completion of the reaction, the reaction mixture was diluted with EtOAc (100 mL), washed with saturated sodium bicarbonate solution (30 mL), water (30 mL) and brine (30 mL). The organic layer was then dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuum* to give the crude product which was further purified by column chromatography to obtain the desired compound.

14-Bromo-2,3-dimethoxy-5*H*-benzofuro[3',2':4,5]pyrido[2,1-*a*]isoquinolin-8(6*H*)-one (6a).



The title compound **6a** was synthesized by following general procedure C from compound **5a** (1,000 mg, 2.88 mmol) and *N*-bromosuccinimide (615 mg, 3.45 mmol), and purified by flash column chromatography (0.5% MeOH in DCM) to give a yellow solid (1,140 mg, 93% yield). R_f = 0.6 (3% MeOH/DCM). mp 258–260 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.58 (d, J = 8.0 Hz, 1H), 7.94 (s, 1H), 7.72 (d, J = 8.0 Hz, 1H), 7.60 (td, J = 8.0, 1.2 Hz, 1H), 7.45 (td, J = 8.0, 1.2 Hz, 1H), 6.81 (s, 1H), 4.38 (s, 2H), 3.98 (s, 3H), 3.97 (s, 3H), 2.90 (t, J = 6.0 Hz, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ: 157.0, 153.8, 150.5, 148.6, 142.9, 139.0, 128.8, 128.5, 128.4, 123.4, 123.3, 122.3, 121.7, 112.9, 110.5, 108.1, 94.6, 56.4, 56.1, 39.8, 27.9. IR $_{\nu max}$ (neat): 2918, 2828, 1665, 1509, 1462, 1318, 1232, 1109, 1022, 927 cm^{-1}. HRMS (EI) m/z: [M$^+$] calcd for $C_{21}H_{16}BrNO_4$, 425.0263; found, 425.0265.

14-Bromo-2,3,11,12-tetramethoxy-5*H*-benzofuro[3',2':4,5]pyrido[2,1-*a*]isoquinolin-8(6*H*)-one (6b).



The title compound **6b** was synthesized by following general procedure C from compound **5b** (1,000 mg, 2.45 mmol) and *N*-bromosuccinimide (524 mg, 2.95 mmol), and purified by flash column chromatography (1% MeOH in DCM) to give a yellow solid (1,100 mg, 92% yield). R_f = 0.5 (3% MeOH/DCM). mp 264–266 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.94 (s, 1H), 7.93 (s, 1H), 7.18 (s, 1H), 6.81 (s, 1H), 4.35 (s, 2H), 4.01 (s, 6H), 3.98 (s, 3H), 3.97 (s, 3H), 2.89 (t, J = 6.0 Hz, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ: 152.8, 152.5, 151.2, 150.7, 149.6, 146.7, 146.6, 142.0, 135.6, 131.4, 121.0, 114.1, 113.9, 110.1, 110.0, 102.9, 95.4, 56.1, 55.93, 55.91, 55.3, 40.9, 28.7. IR $_{vmax}$ (neat): 2919, 2842, 1661, 1511, 1484, 1335, 1211, 1112, 1015, 928 cm^{-1}. HRMS (EI) m/z: [M$^+$] calcd for $C_{23}H_{20}BrNO_6$, 485.0474; found, 485.0477.

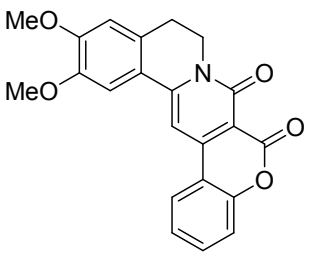
General procedure D for the preparation of compounds **10a**–**b** and **11a**–**b**.

To a stirred solution of imine **2a** (0.5 mmol) and triethylamine (1.0 mmol) in dry toluene (3 mL) was added acid chloride **3a** or **3b** (0.55 mmol) at -60 ℃. The resulting mixture was stirred at 0 ℃ for 1 h. The mixture was then 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 concentrated and the residue was diluted with dichloromethane (100 mL), washed with 5 N HCl (30 mL), water (30 mL) and brine (30 mL). The organic layer was then dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuum* to give the crude product which was further purified by column chromatography to obtain the desired compound.

Procedure E for the preparation of compound **11a** from **2a** and **12**.

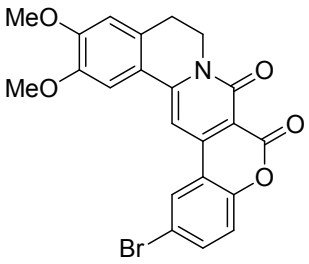
To a stirred solution of imine **2a** (0.5 mmol) and triethylamine (1.0 mmol) in dry toluene (3 mL) was added acid chloride **12** (0.55 mmol) at 0 ℃. The resulting mixture was stirred at room temperature for 1 h. The reaction mixture was diluted with degassed dry acetonitrile (100 mL) and irradiated with 352 nm UV light in a Rayonet photoreactor for 2 h at room temperature. After completion of the reaction, the solvent was concentrated and the residue was diluted with dichloromethane (100 mL), washed with 5 N HCl (30 mL), water (30 mL) and brine (30 mL). The organic layer was then dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuum* to provide the crude product. The crude product 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 (10a).



The title compound **10a** was synthesized by following general procedure D from imine **2a** (103 mg, 0.5 mmol), triethylamine (101 mg, 1.0 mmol), and 2-oxo-2*H*-chromene-3-carbonyl chloride (**8a**, 115 mg, 0.55 mmol), and purified by flash column chromatography (3% MeOH in DCM) to give a yellow solid (96 mg, 51% 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 $_{vmax}$ (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.

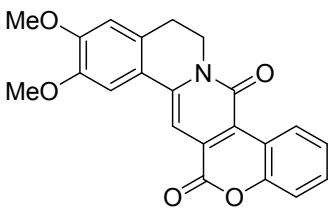
2-Bromo-12,13-dimethoxy-9,10-dihydrochromeno[4',3':4,5]pyrido[2,1-*a*]isoquinoline-6,7-dione (10b).



The title compound **10b** was synthesized by following general procedure D from imine **2a** (103 mg, 0.5 mmol), triethylamine (101 mg, 1.0 mmol), and 6-bromo-2-oxo-2*H*-chromene-3-carbonyl chloride (**8b**, 158 mg, 0.55 mmol), and purified by flash column chromatography (2% MeOH in DCM) to give a yellow solid (119 mg, 52% 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 = 8.8 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 $_{vmax}$ (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, 453.0215.

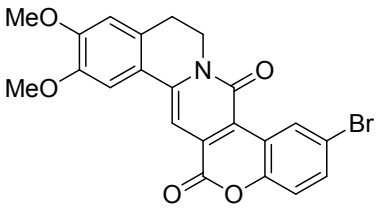
9,10-Dimethoxy-12,13-dihydrochromeno[3',4':4,5]pyrido[2,1-*a*]isoquinoline-6,15-dione (11a).

The title compound **11a** was synthesized by following general procedure D from imine **2a** (103 mg, 0.5 mmol), triethylamine (101 mg, 1.0 mmol), and 2-oxo-2*H*-chromene-3-carbonyl chloride (**8a**, 115 mg, 0.55 mmol), and purified by flash column chromatography (40% EtOAc in hexanes) to give a yellow solid (60 mg, 32% yield). The title compound **11a** was also synthesized by



following general procedure E from imine **2a** (103 mg, 0.5 mmol), triethylamine (101 mg, 1.0 mmol) and 2-oxo-2*H*-chromene-4-carbonyl chloride (**12**, 115 mg, 0.55 mmol), and purified by flash column chromatography (40% EtOAc in hexanes) to give a yellow solid (124 mg, 66% yield). R_f = 0.5 (50% EtOAc in hexanes). mp 228–230 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 9.49 (dd, J = 8.0, 1.6 Hz, 1H), 7.49 (td, J = 8.0, 1.6 Hz, 1H), 7.44 (s, 1H), 7.41–7.35 (m, 2H), 7.31 (s, 1H), 6.77 (s, 1H), 4.43 (t, J = 6.4 Hz, 2H), 4.00 (s, 3H), 3.96 (s, 3H), 3.01 (t, J = 6.4 Hz, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ: 160.7, 160.2, 151.8, 151.1, 149.0, 143.2, 130.0, 128.9, 128.8, 127.5, 125.2, 122.7, 121.0, 117.7, 116.6, 110.4, 108.2, 99.1, 56.5, 56.2, 40.2, 27.5. IR $_{vmax}$ (neat): 2907, 1739, 1647, 1565, 1325, 1217, 780, 650 cm^{-1}. HRMS (EI) m/z: [M$^+$] calcd for $C_{22}H_{17}NO_5$, 375.1107; found, 375.1104.

2-Bromo-9,10-dimethoxy-12,13-dihydrochromeno[3',4':4,5]pyrido[2,1-*a*]isoquinoline-6,15-dione (11b).

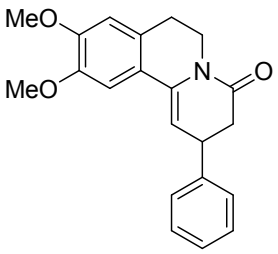


The title compound **11b** was synthesized by following general procedure D from imine **2a** (103 mg, 0.5 mmol), triethylamine (101 mg, 1.0 mmol), and 6-bromo-2-oxo-2*H*-chromene-3-carbonyl chloride (**8b**, 158 mg, 0.55 mmol), and purified by flash column chromatography (30% EtOAc in hexanes) to give a yellow solid (82 mg, 36% yield). R_f = 0.5 (40% EtOAc in hexanes). mp 292–294 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 9.67 (d, J = 2.0 Hz, 1H), 7.58 (dd, J = 8.4, 2.0 Hz, 1H), 7.43 (s, 1H), 7.30 (s, 1H), 7.23 (d, J = 8.4 Hz, 1H), 6.77 (s, 1H), 4.42 (t, J = 6.4 Hz, 2H), 4.00 (s, 3H), 3.97 (s, 3H), 3.02 (t, J = 6.4 Hz, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ: 160.0, 159.9, 152.0, 149.8, 148.9, 144.0, 132.6, 129.8, 129.2, 129.0, 121.0, 120.7, 119.1, 118.2, 118.0, 110.3, 108.2, 99.0, 56.4, 56.2, 40.2, 27.3. IR $_{vmax}$ (neat): 2915, 1720, 1659, 1525, 1425, 1211, 875, 659 cm^{-1}. HRMS (EI) m/z: [M$^+$] calcd for $C_{22}H_{16}BrNO_5$, 453.0212; found, 453.0216.

Procedure for preparation of compound **16a**.

To a stirred solution of imine **2a** (103 mg, 0.5 mmol) and triethylamine (101 mg, 1.0 mmol) in dry toluene (3 mL) was added acid chloride **14** (92 mg, 0.55 mmol) at 0 ℃. The resulting mixture was stirred at room temperature for 1 h, diluted with degassed dry acetonitrile (100 mL), and then irradiated with 352 nm UV lamp in a Rayonet photoreactor at room temperature for 20 min. After completion of the reaction, the solvent was concentrated and the crude product was purified by column chromatography to obtain the desired compound.

9,10-Dimethoxy-2-phenyl-6,7-dihydro-2*H*-pyrido[2,1-*a*]isoquinolin-4(3*H*)-one (16a).

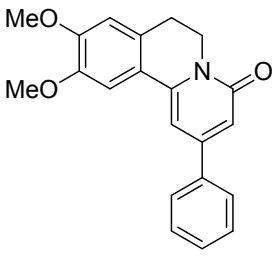


Yellow liquid. R_f = 0.5 (50% EtOAc/hexanes). 37 mg. Yield 22%. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.38–7.34 (m, 2H), 7.31–7.27 (m, 3H), 7.05 (s, 1H), 6.65 (s, 1H), 5.75 (d, J = 4.0 Hz, 1H), 4.20–4.14 (m, 1H), 3.90 (s, 3H), 3.89–3.86 (m, 4H), 3.78–3.72 (m, 1H), 2.90 (dd, J = 16.0, 6.8 Hz, 1H), 2.85–2.81 (m, 2H), 2.74 (dd, J = 16.0, 11.2 Hz, 1H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ: 168.9, 149.5, 148.2, 143.2, 135.5, 128.9 (2C), 127.7, 127.2 (2C), 127.0, 122.0, 110.7, 107.0, 104.8, 56.1, 56.0, 39.5, 378.5, 37.5, 28.8. IR $_{vmax}$ (neat): 2939, 1716, 1649, 1565, 1425, 1217, 845, 650 cm^{-1}. HRMS (EI) m/z: [M$^+$] calcd for $C_{21}H_{21}NO_3$, 335.1521; found, 335.1525.

Procedure for preparation of compound **18a**.

The solution of compound **16a** (30 mg) in degassed dry acetonitrile (100 mL) was irradiated with UV light (352 nm) in a Rayonet photoreactor for 2 h at room temperature. After completion of the reaction, the acetonitrile was evaporated and the crude residue 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 (18a).



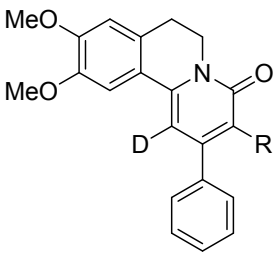
Yellow solid (29.8 mg, 99% yield). R_f = 0.3 (50% EtOAc/hexanes). mp 156–158 ℃. ^{1}H NMR ($CDCl_3$, 400 MH) δ: 7.66–7.63 (m, 2H), 7.52–7.45 (m, 3H), 7.23 (s, 1H), 6.79 (d, J = 2.0 Hz, 1H), 6.77 (s, 1H), 6.75 (d, J = 2.0 Hz, 1H), 4.31 (t, J = 6.0 Hz, 2H), 3.96 (s, 3H), 3.95 (s, 3H), 2.96 (t, J = 6.0 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, 333.1363.

Procedure for preparation of compound **18b**.

To a stirred solution of imine **2b** (103 mg, 0.5 mmol) and triethylamine (101 mg, 1.0 mmol) in dry toluene (3 mL) was added acid chloride **14** (92 mg, 0.55 mmol) at 0 ℃. The resulting mixture was stirred at room temperature for 1 h, diluted with degassed dry acetonitrile (100 mL), and then irradiated with UV lamps (352 nm) in a Rayonet photoreactor at room temperature for 3 h. After completion of the reaction, the solution was concentrated and the residue was diluted with dichloromethane (100 mL), washed with 5 N HCl (30 mL), water (30 mL) and brine (30 mL). The organic layer was then dried over anhydrous $MgSO_4$, filtered and concentrated *in*

vacuum to give 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-1,3-d_2 (18b).



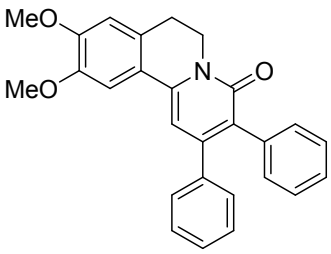
R = H, 16%, R = D, 84%

Brown solid (68.0 mg, 42% yield). R_f = 0.3 (50% EtOAc/hexanes). mp 156–158 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.67–7.65 (m, 2H), 7.55–7.53 (m, 3H), 7.17 (s, 1H), 6.79 (s, 1H), 4.35 (t, J = 6.4 Hz, 2H), 3.97 (s, 3H), 3.94 (s, 3H), 3.00 (t, J = 6.4 Hz, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ: 160.9, 158.4, 158.3, 152.6, 148.8, 147.2 (d, $J_{C\text{-}D}$ = 4.9 Hz), 136.3 (d, $J_{C\text{-}D}$ = 3.7 Hz), 130.4, 130.37, 128.9 (2C), 128.0 (2C), 120.0, 116.5, 110.6, 108.7, 103.3, 56.4, 56.3, 39.8, 27.1. IR $_{\nu max}$ (neat): 2941, 1718, 1653, 1561, 1211, 871, 755 cm^{-1}. HRMS (EI) m/z: [M$^+$] calcd for $C_{21}H_{17}D_2NO_3$, 335.1490; found, 335.1492.

Procedure for the preparation of compound **19**.

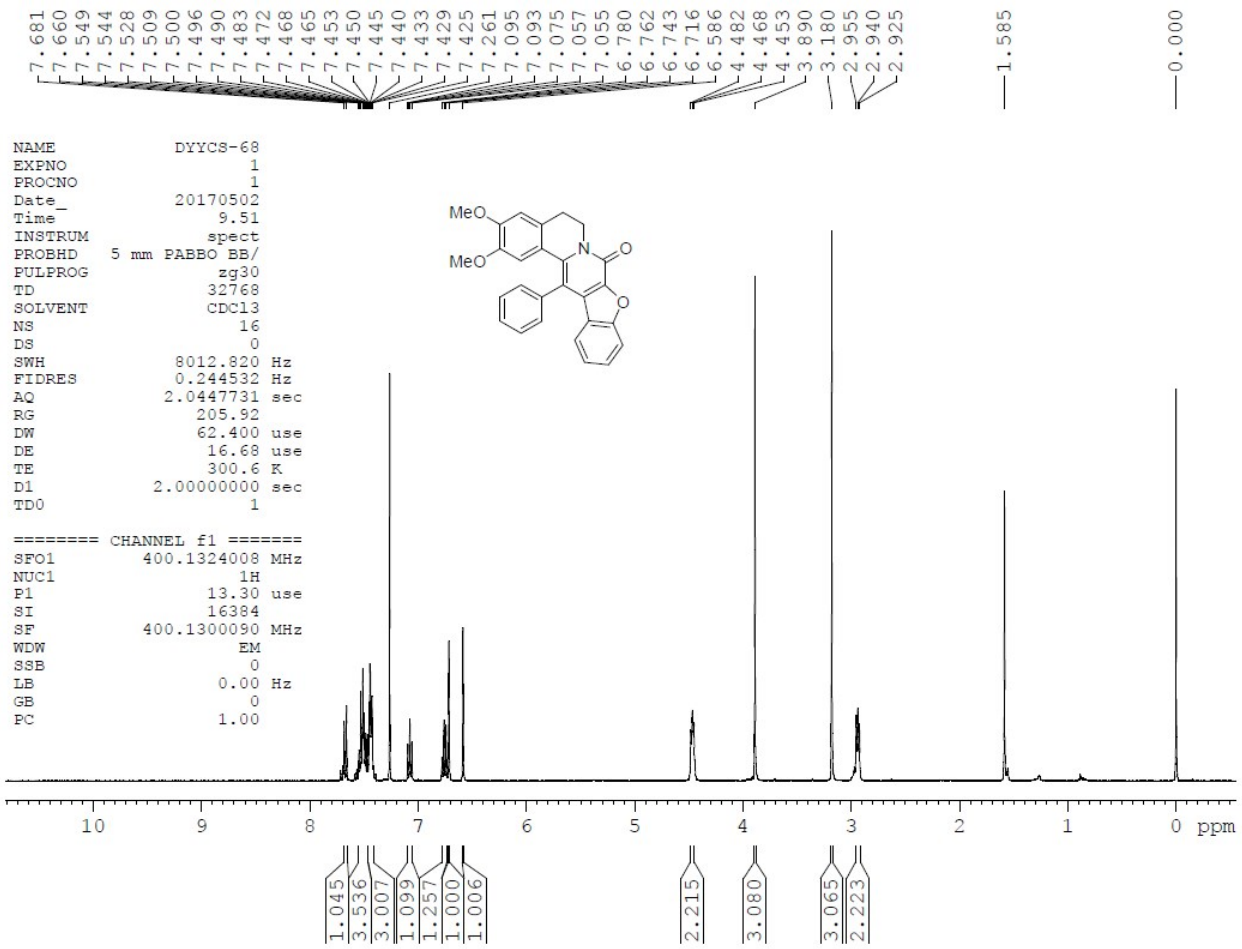
To a stirred solution of imine **2a** (103 mg, 0.5 mmol), *cis*-stilbene (1,035 mg, 7.5 mmol) and triethylamine (101 mg, 1.0 mmol) in dry toluene (3 mL) was added acid chloride **8a** (0.55 mmol) at -60 ℃. The resulting mixture was stirred at 0 ℃ for 1 h. The mixture was then diluted with degassed dry acetonitrile (300 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 concentrated and the residue was diluted with dichloromethane (100 mL), washed with 5 N HCl (30 mL), water (30 mL) and brine (30 mL). The organic layer was then dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuum* to give the crude product which was further purified by column chromatography to obtain the desired compound.

9,10-Dimethoxy-2,3-diphenyl-6,7-dihydro-4*H*-pyrido[2,1-*a*]isoquinolin-4-one (19).

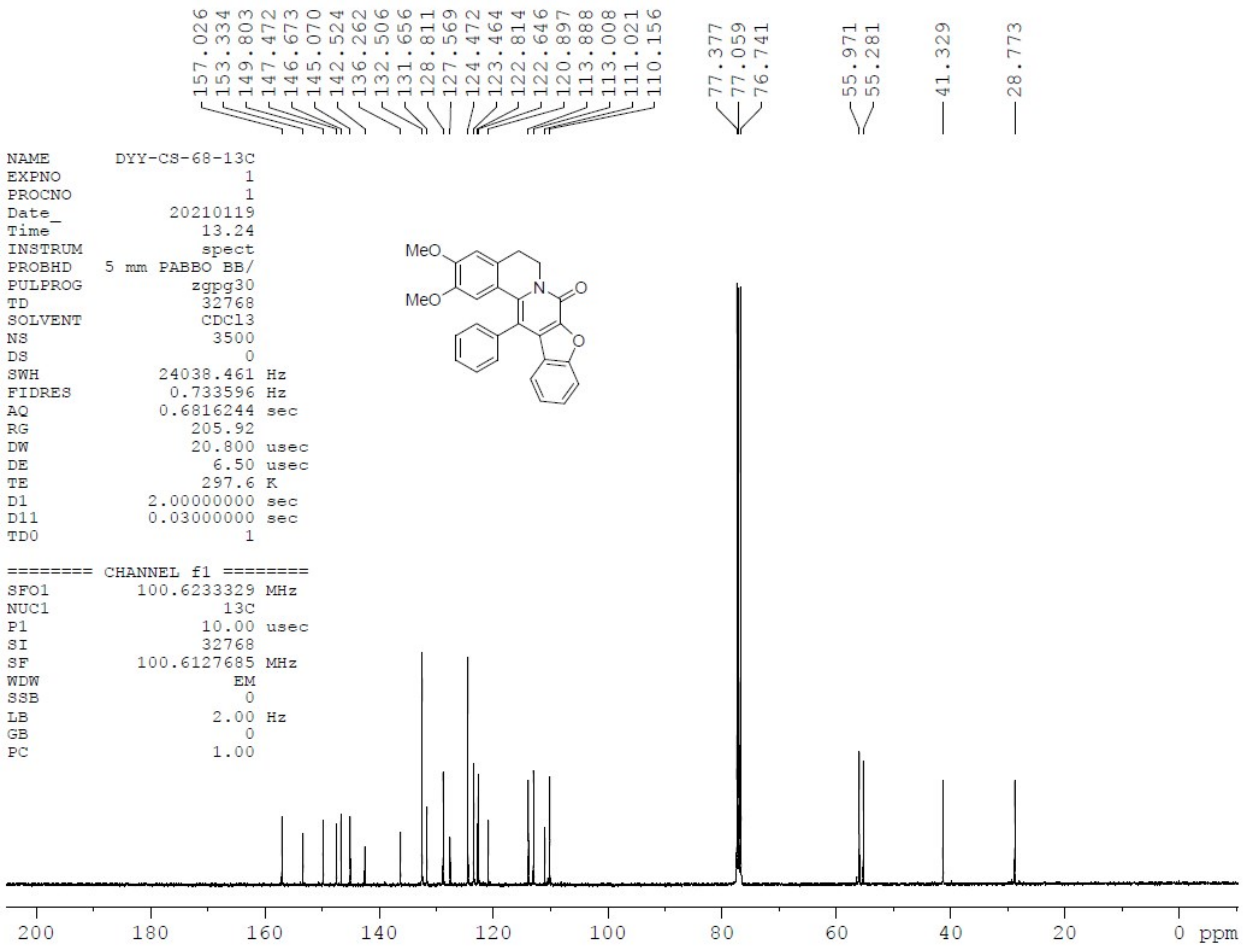


Yellow solid (11 mg, 5% yield). R_f = 0.6 (50% EtOAc/hexanes). mp 196–198 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.64 (dd, J = 8.4, 1.2 Hz, 2H), 7.36–7.32 (m, 1H), 7.28–7.24 (m, 2H), 7.22–7.17 (m, 6H), 6.80 (s, 1H), 6.48 (s, 1H), 4.44 (t, J = 6.4 Hz, 2H), 3.97 (s, 3H), 3.92 (s, 3H), 3.07 (t, J = 6.4 Hz, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ: 156.6, 152.2, 150.3, 148.8, 144.9, 138.4, 137.7, 133.3, 129.9, 129.5 (2C), 129.3, 128.7 (2C), 128.5 (2C), 128.4 (2C), 120.6, 120.5, 110.5, 108.5, 104.0, 56.5, 56.3, 42.6, 27.5. IR $_{\nu max}$ (neat): 2958, 1744, 1650, 1555, 1209, 865, 752 cm^{-1}. HRMS (EI) m/z: [M$^+$] calcd for $C_{27}H_{23}NO_3$, 409.1678; found, 409.1675.

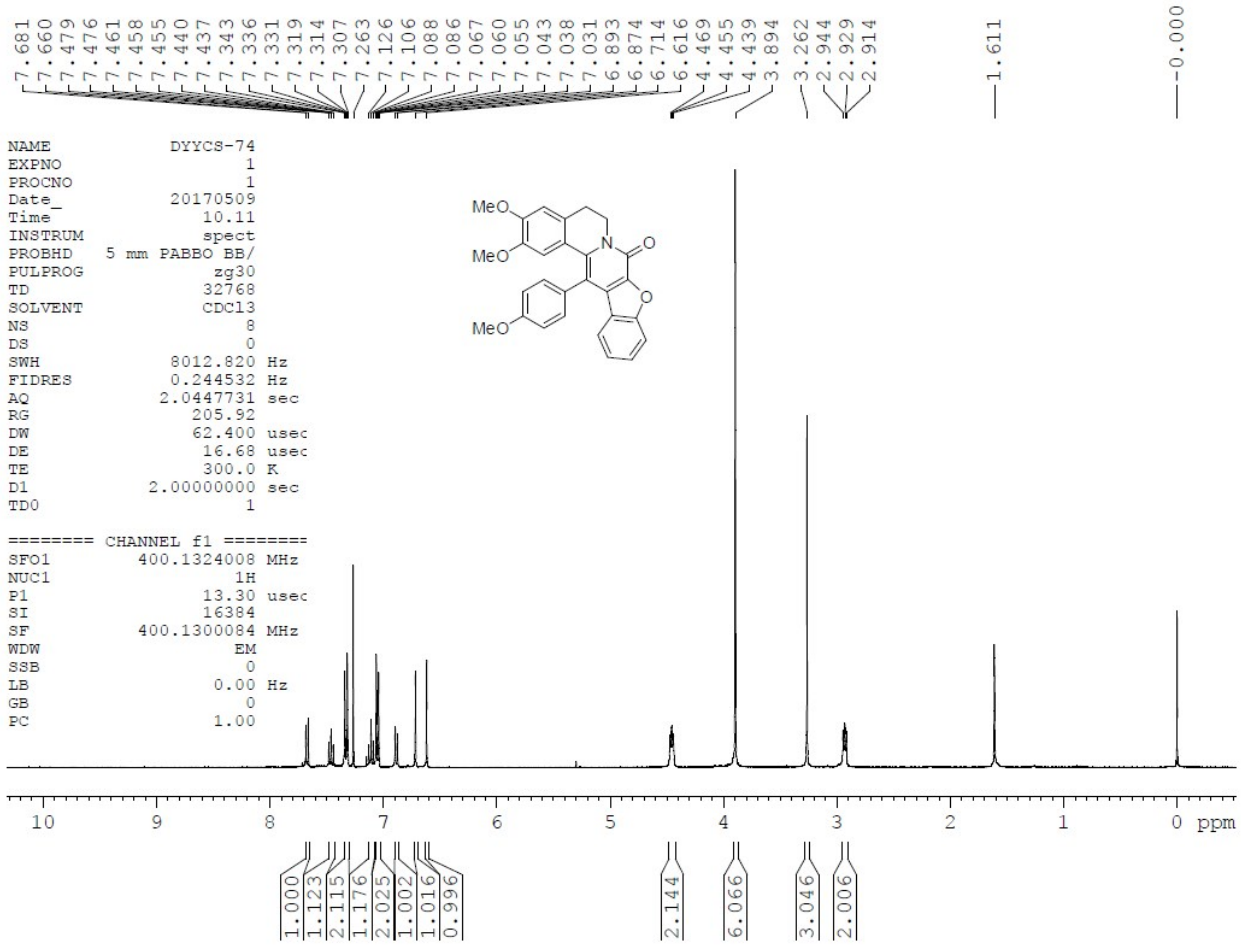
^{1}H NMR of compound **1a** ($CDCl_3$)



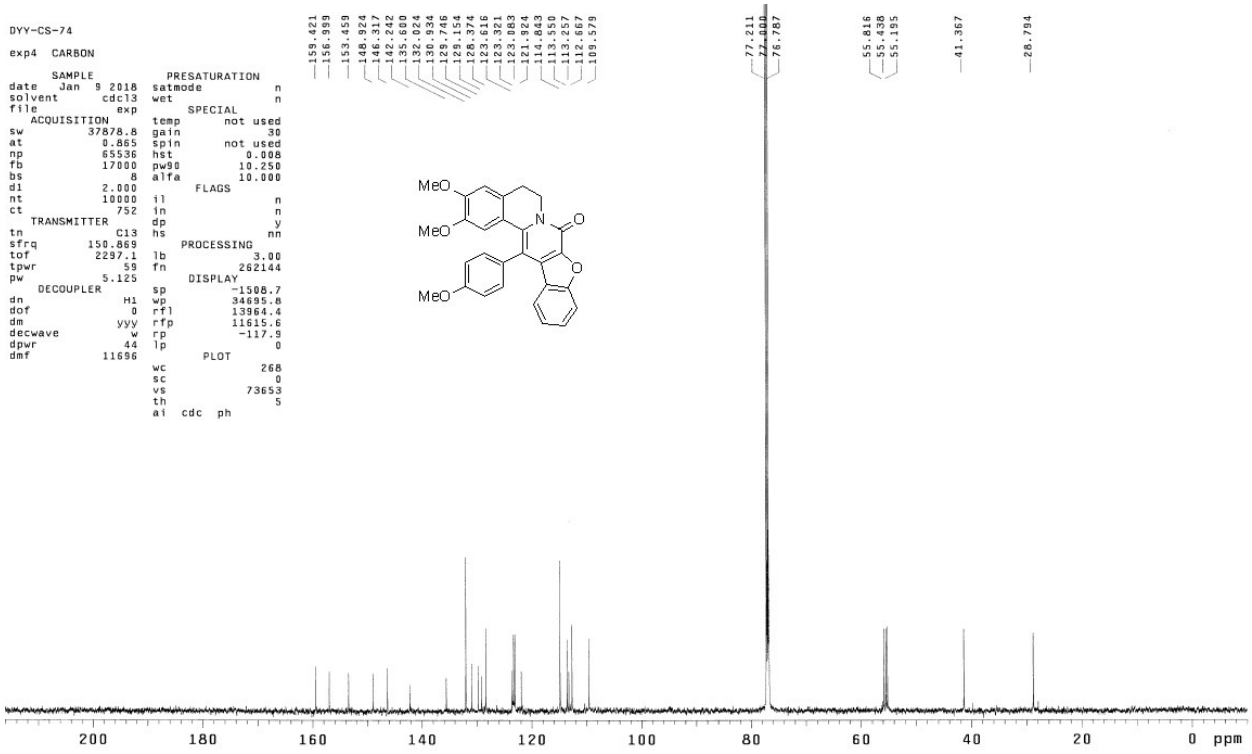
^{13}C NMR of compound **1a** ($CDCl_3$)



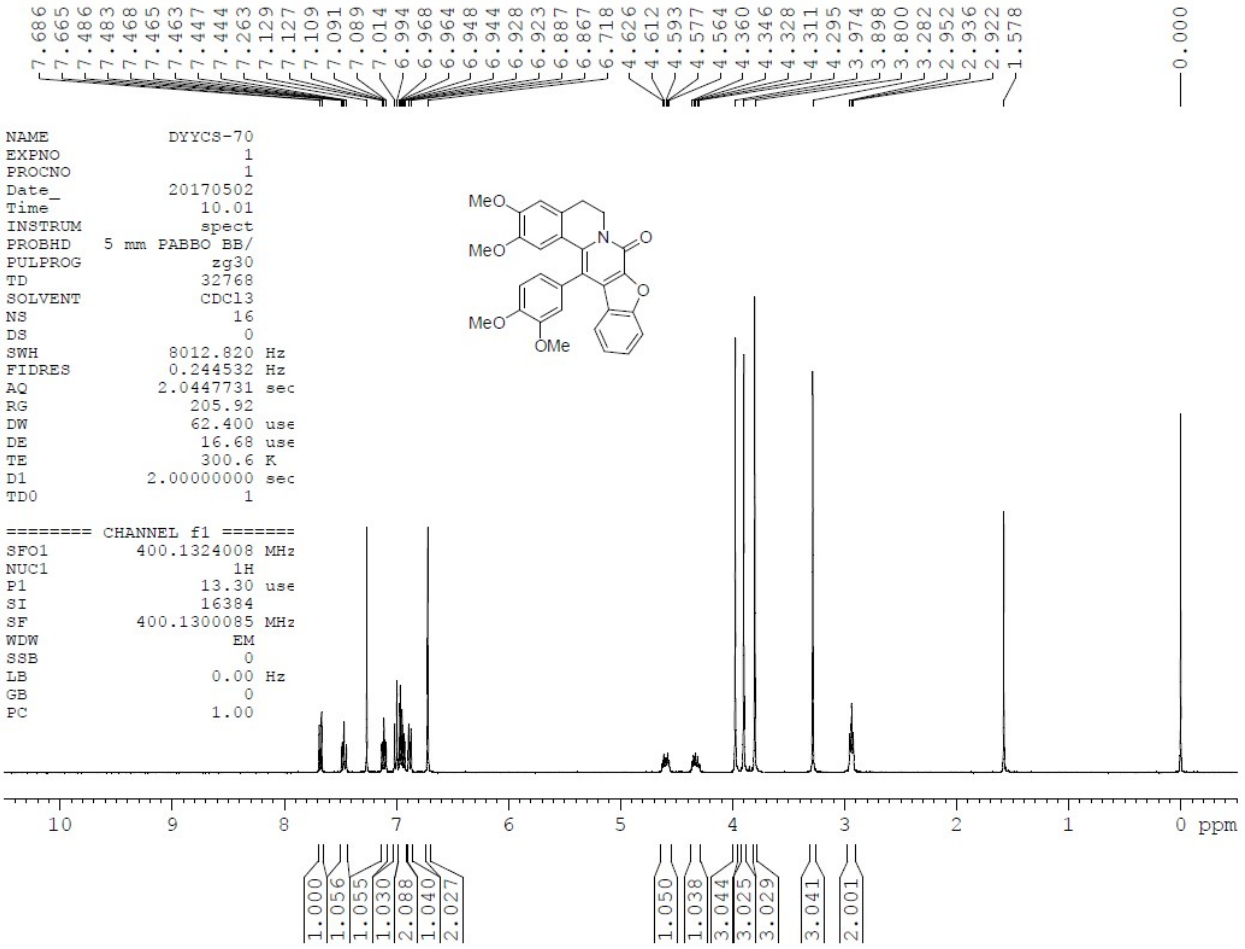
^{1}H NMR of compound **1b** ($CDCl_3$)



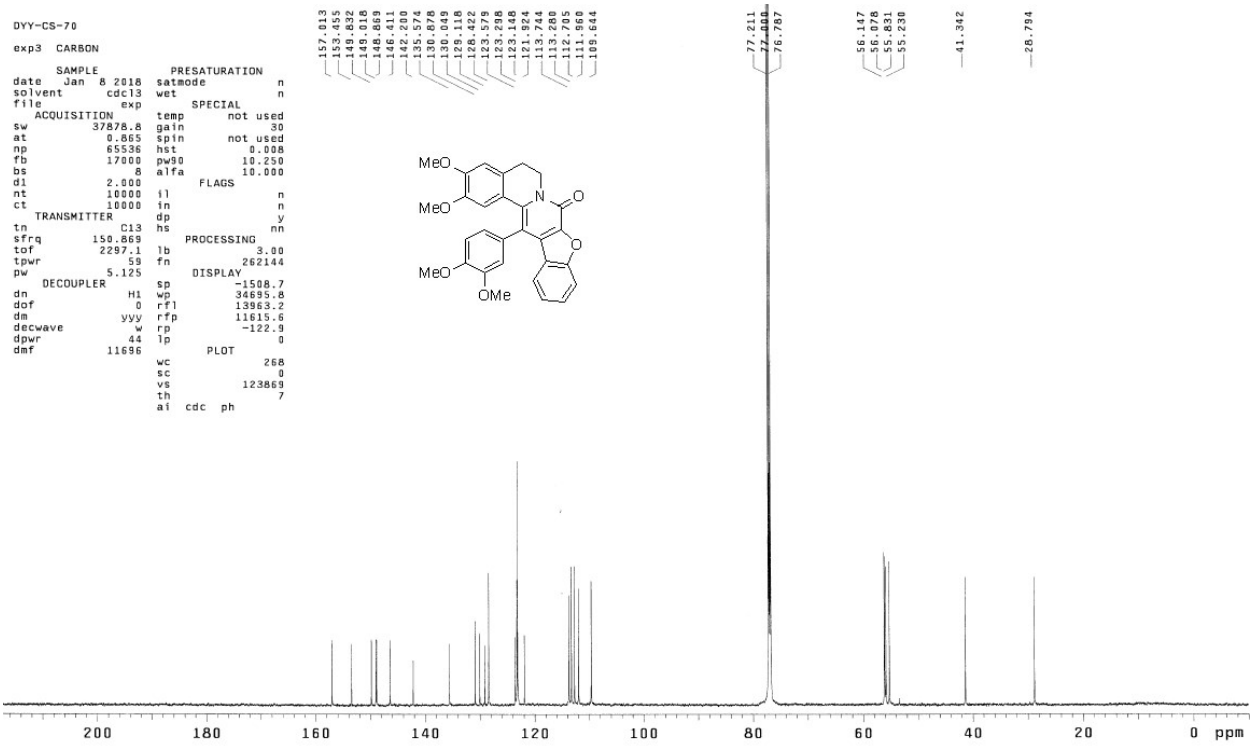
^{13}C NMR of compound **1b** ($CDCl_3$)



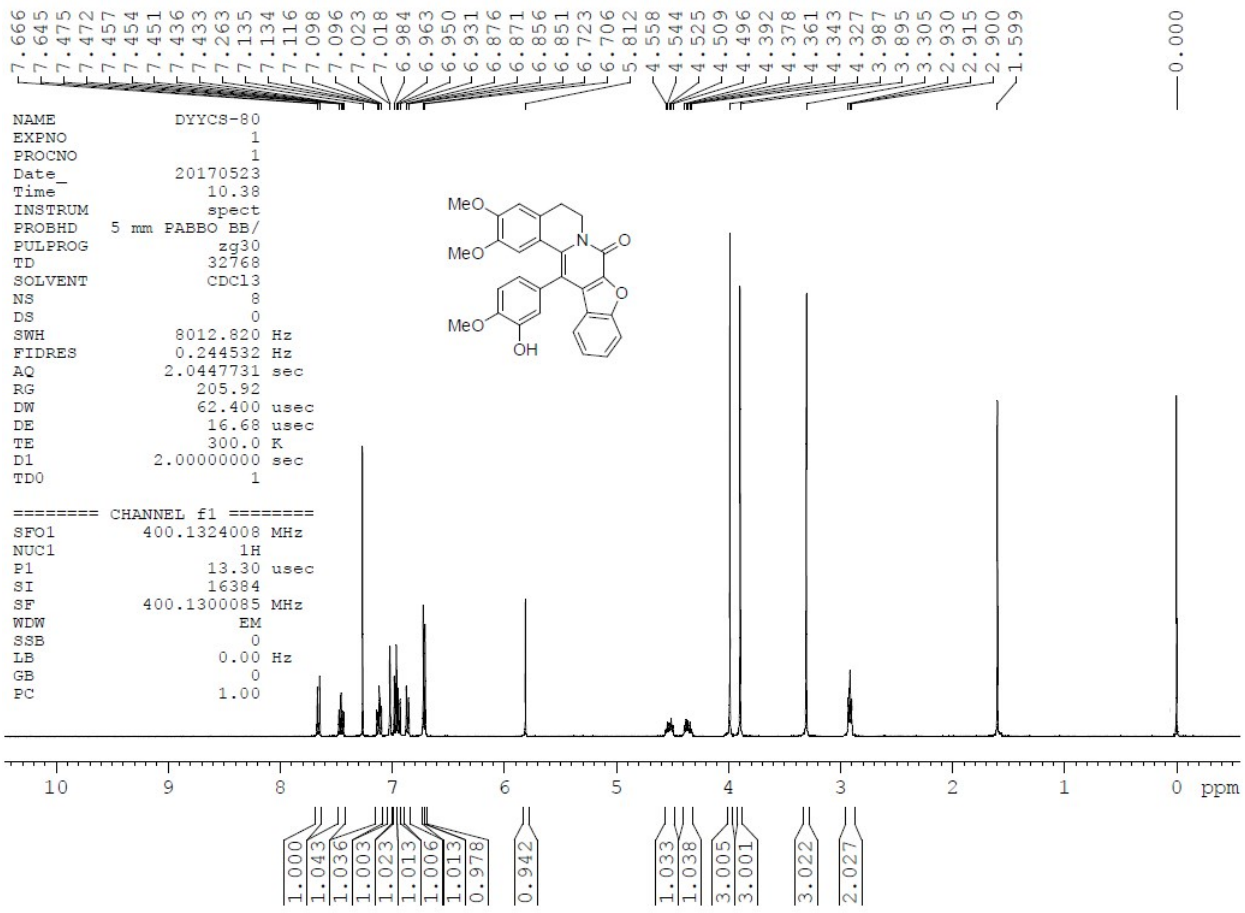
^{1}H NMR of compound **1c** ($CDCl_3$)



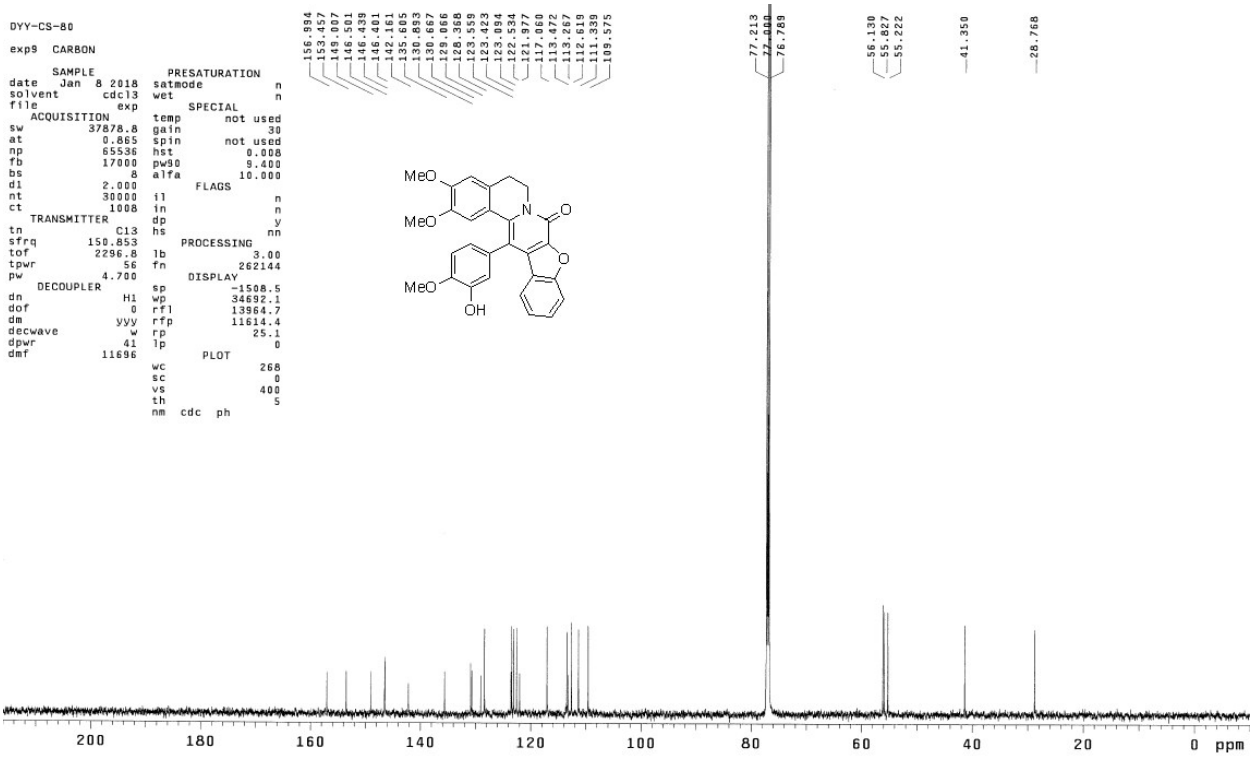
^{13}C NMR of compound **1c** ($CDCl_3$)



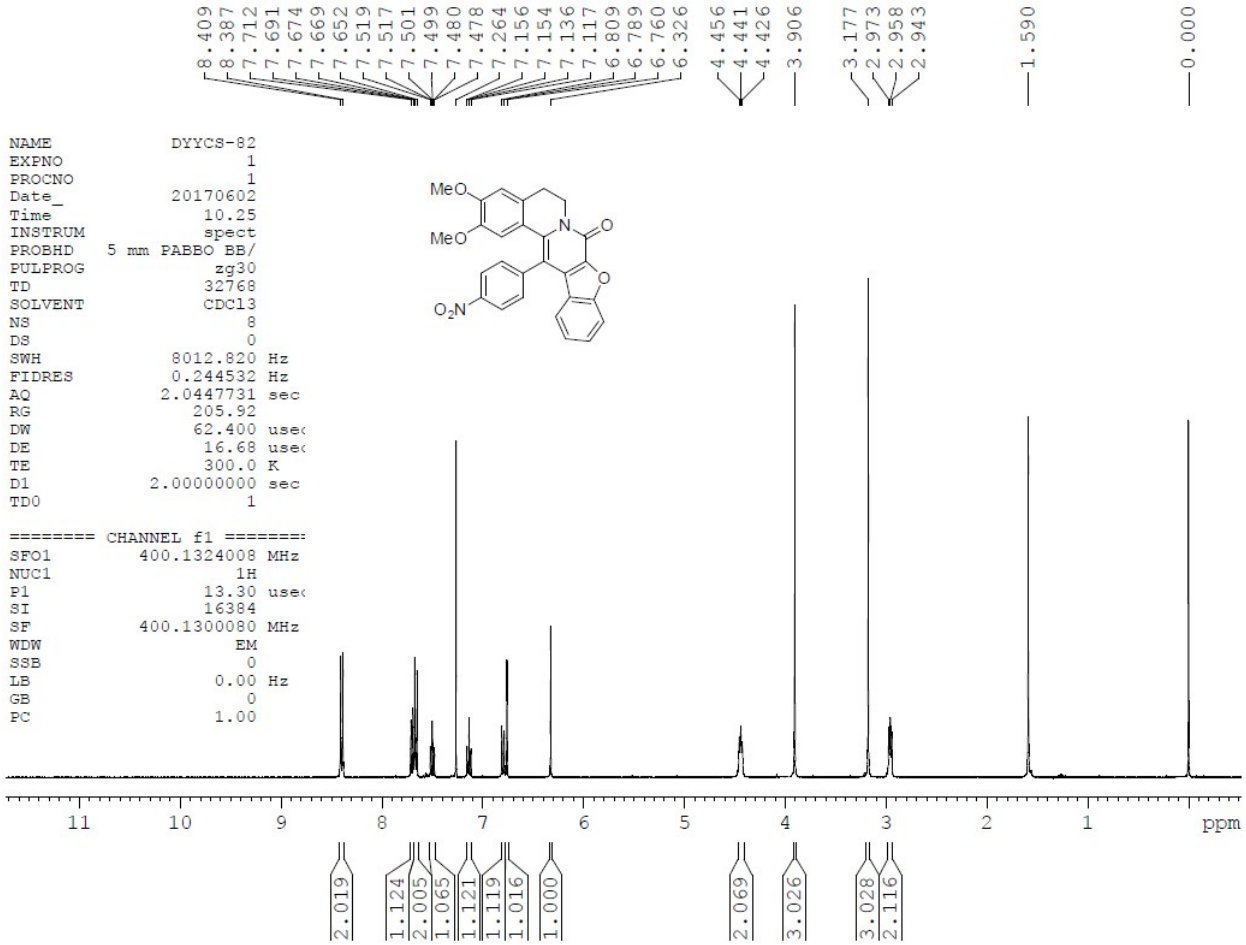
^{1}H NMR of compound **1d** ($CDCl_3$)



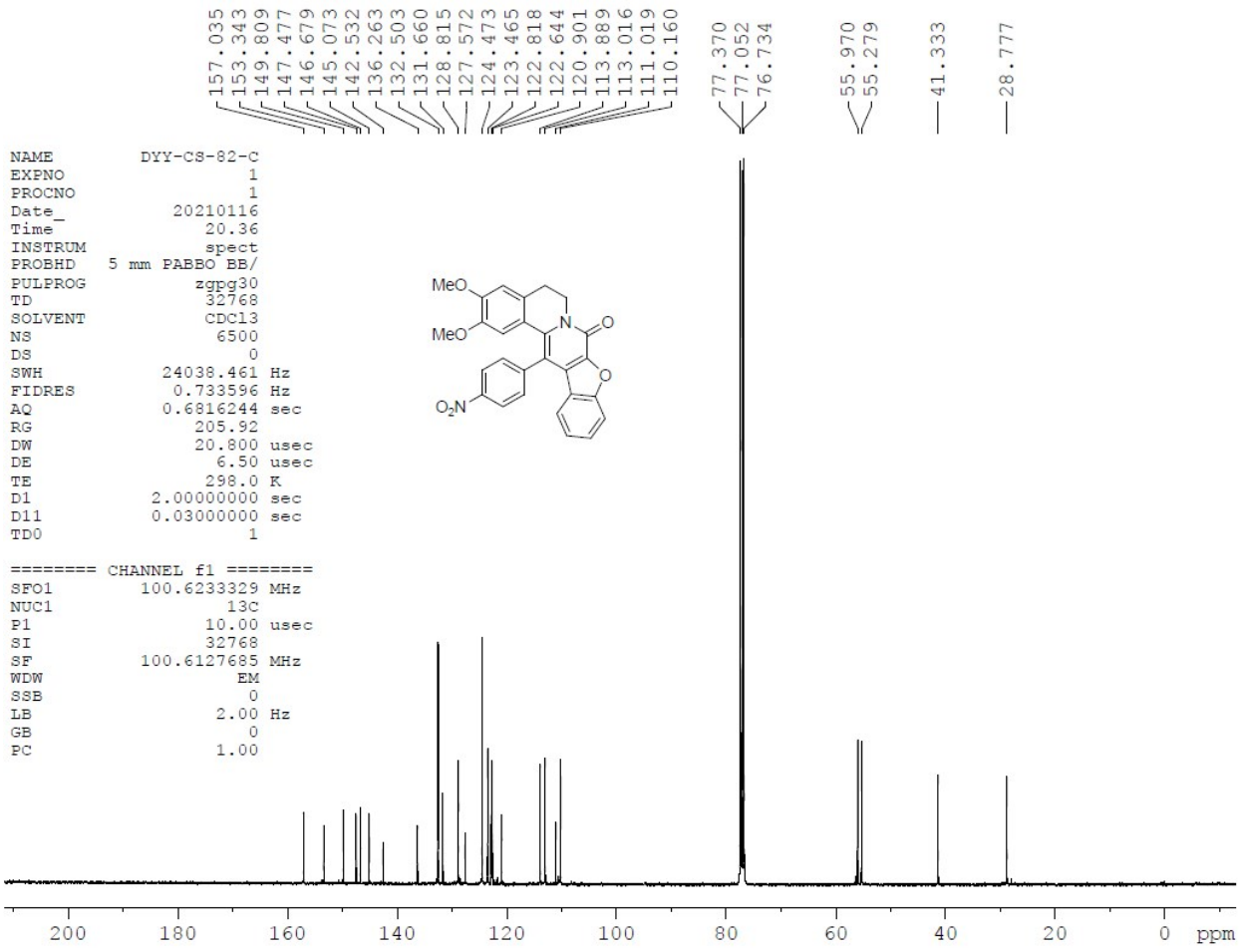
^{13}C NMR of compound **1d** ($CDCl_3$)



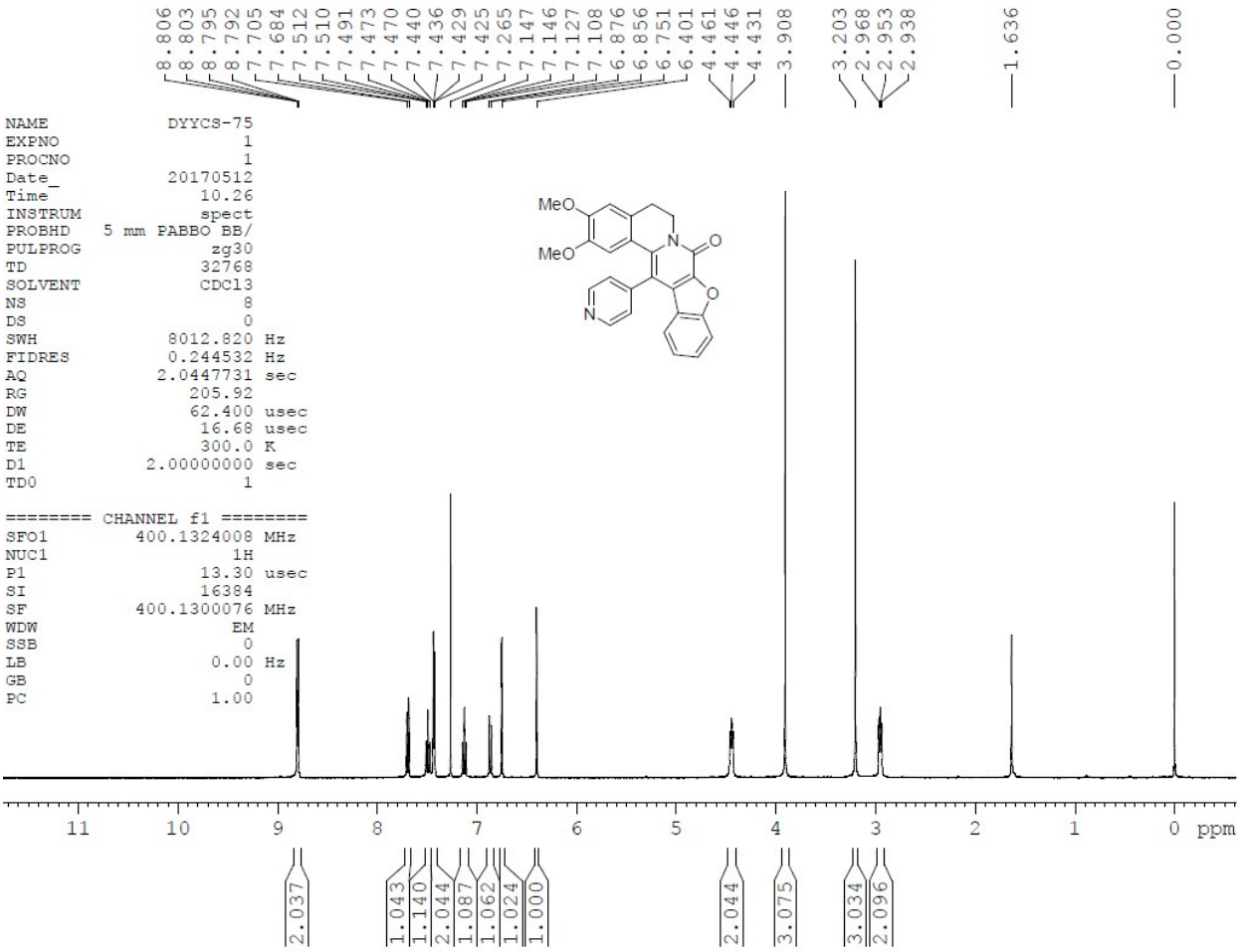
^{1}H NMR of compound **1e** ($CDCl_3$)



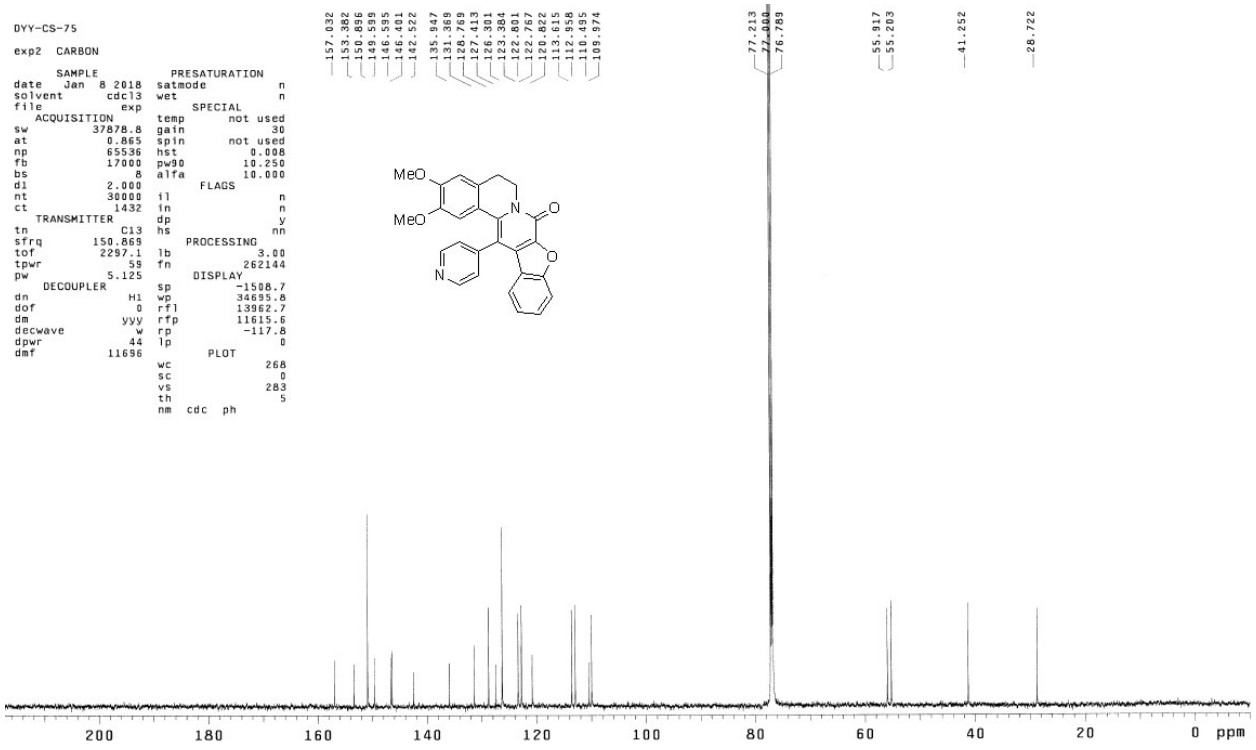
^{13}C NMR of compound **1e** ($CDCl_3$)



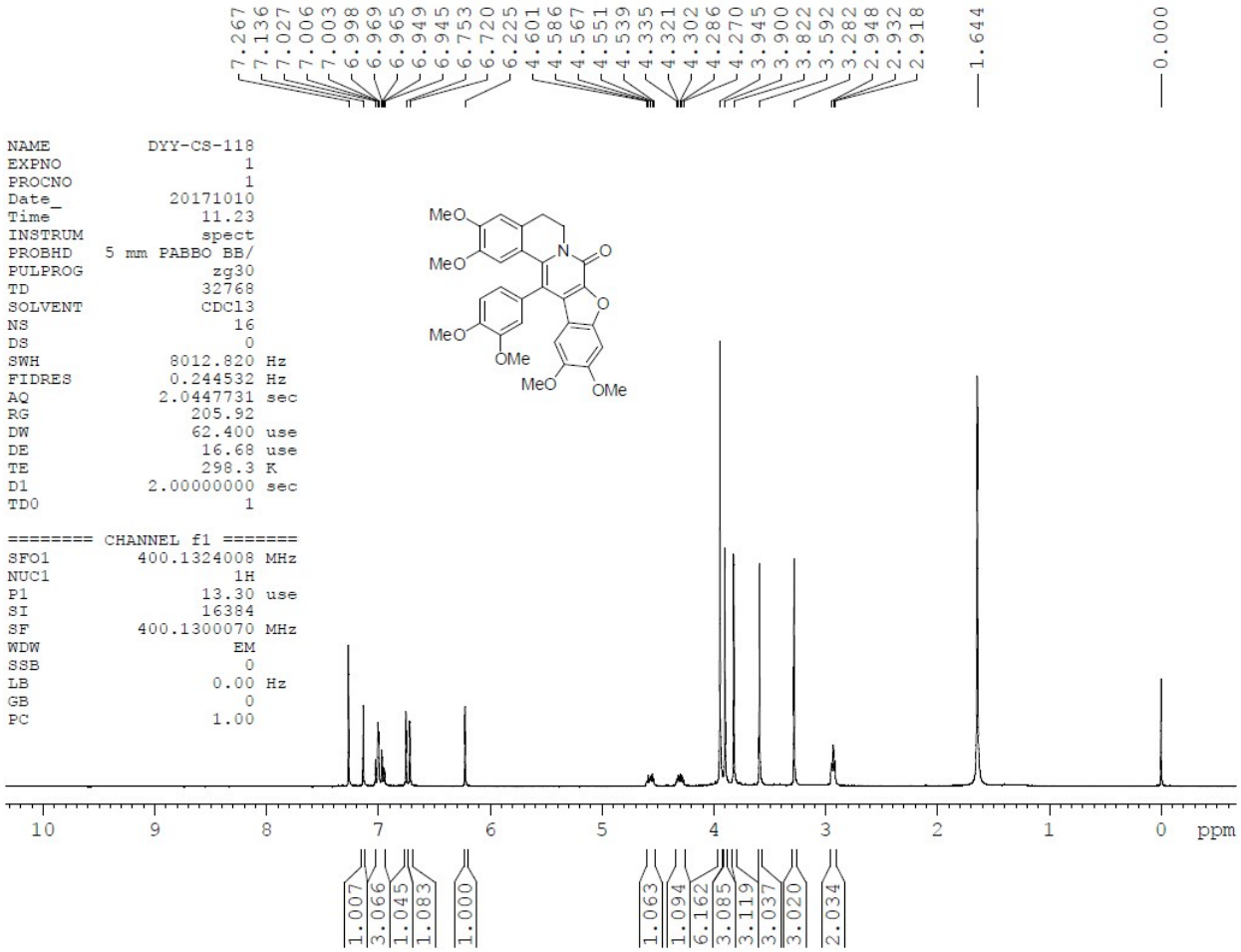
^{1}H NMR of compound **1f** ($CDCl_3$)



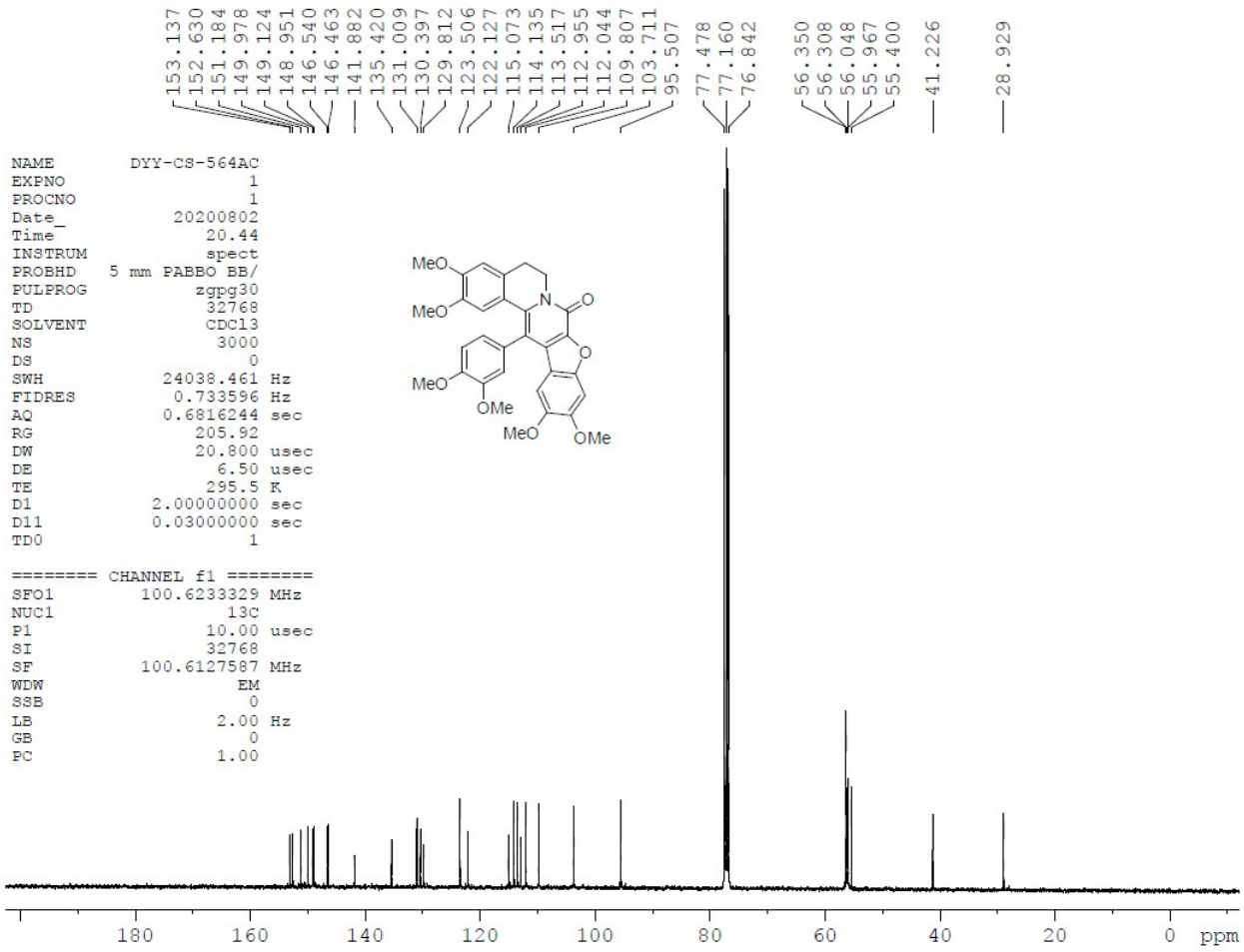
^{13}C NMR of compound **1f** ($CDCl_3$)



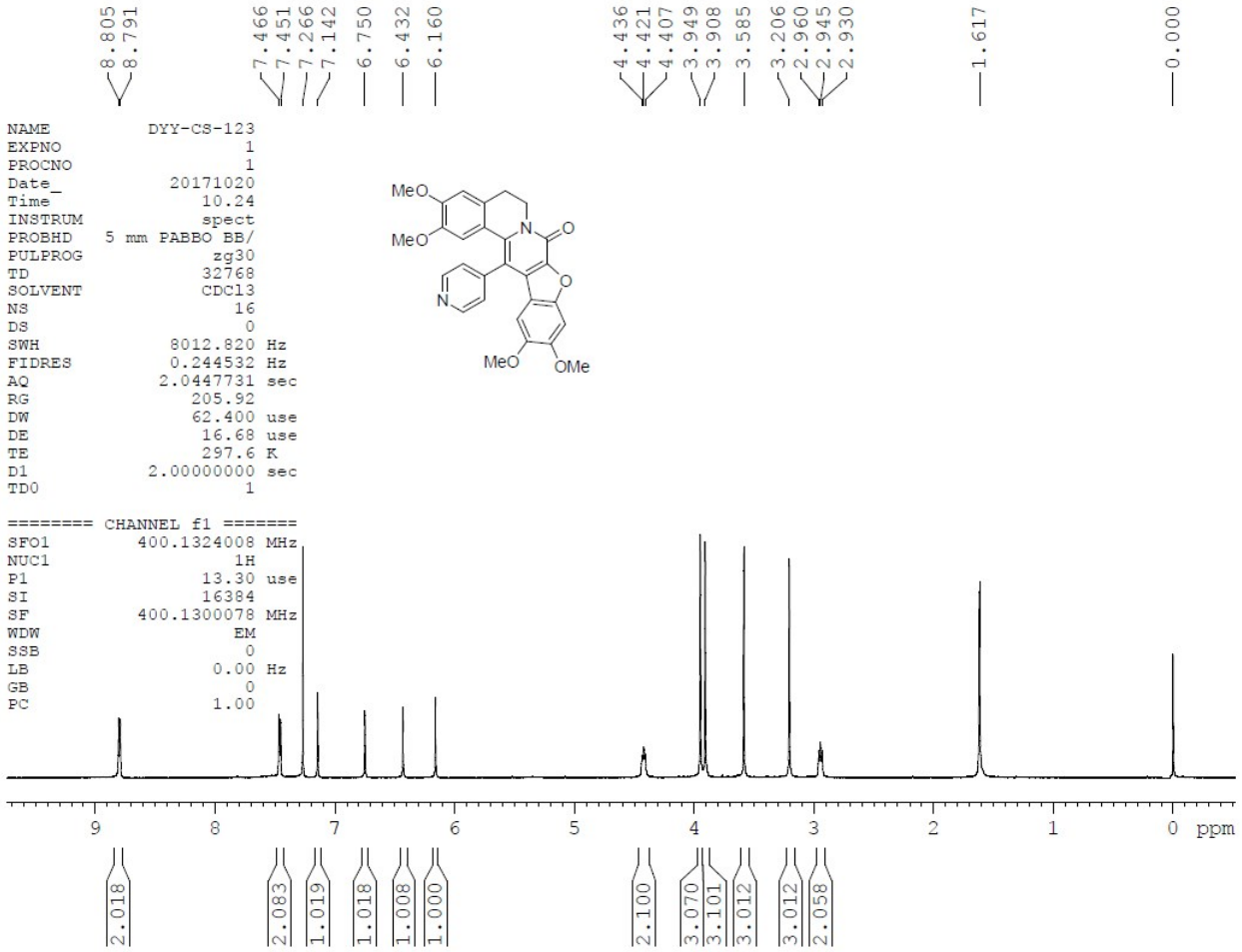
^{1}H NMR of compound **1g** ($CDCl_3$)



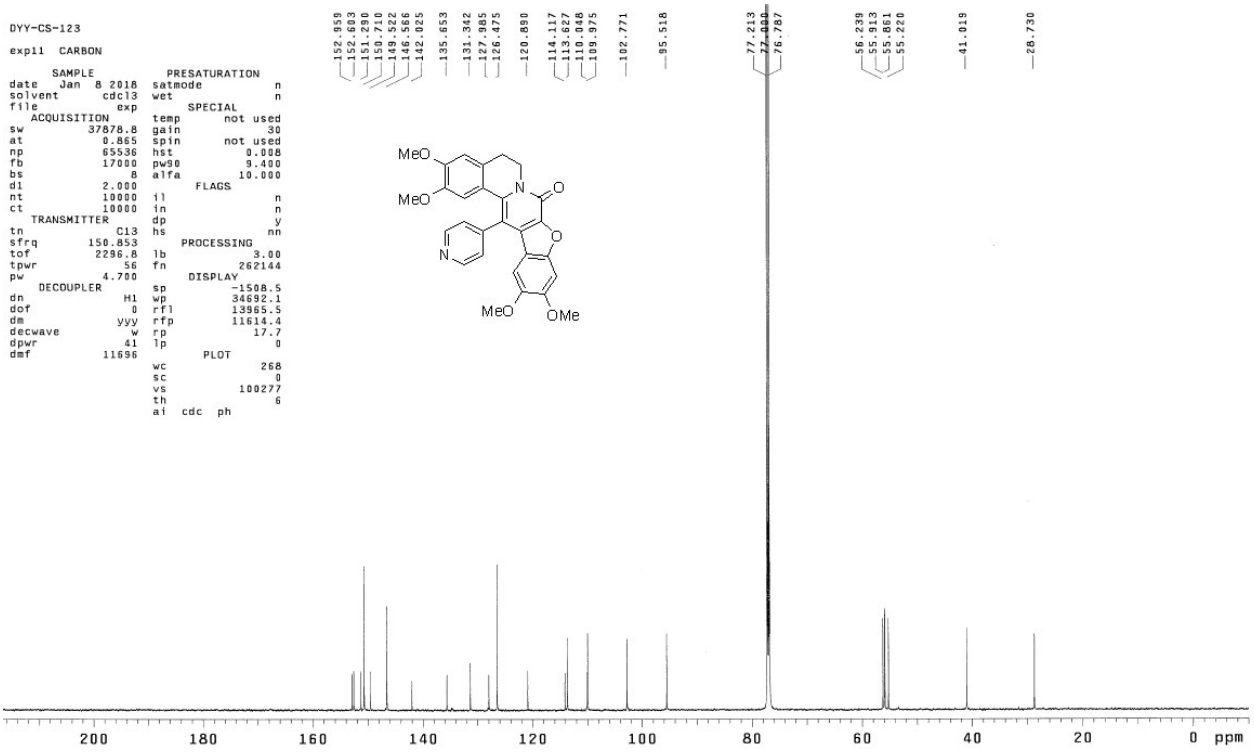
^{13}C NMR of compound **1g** ($CDCl_3$)



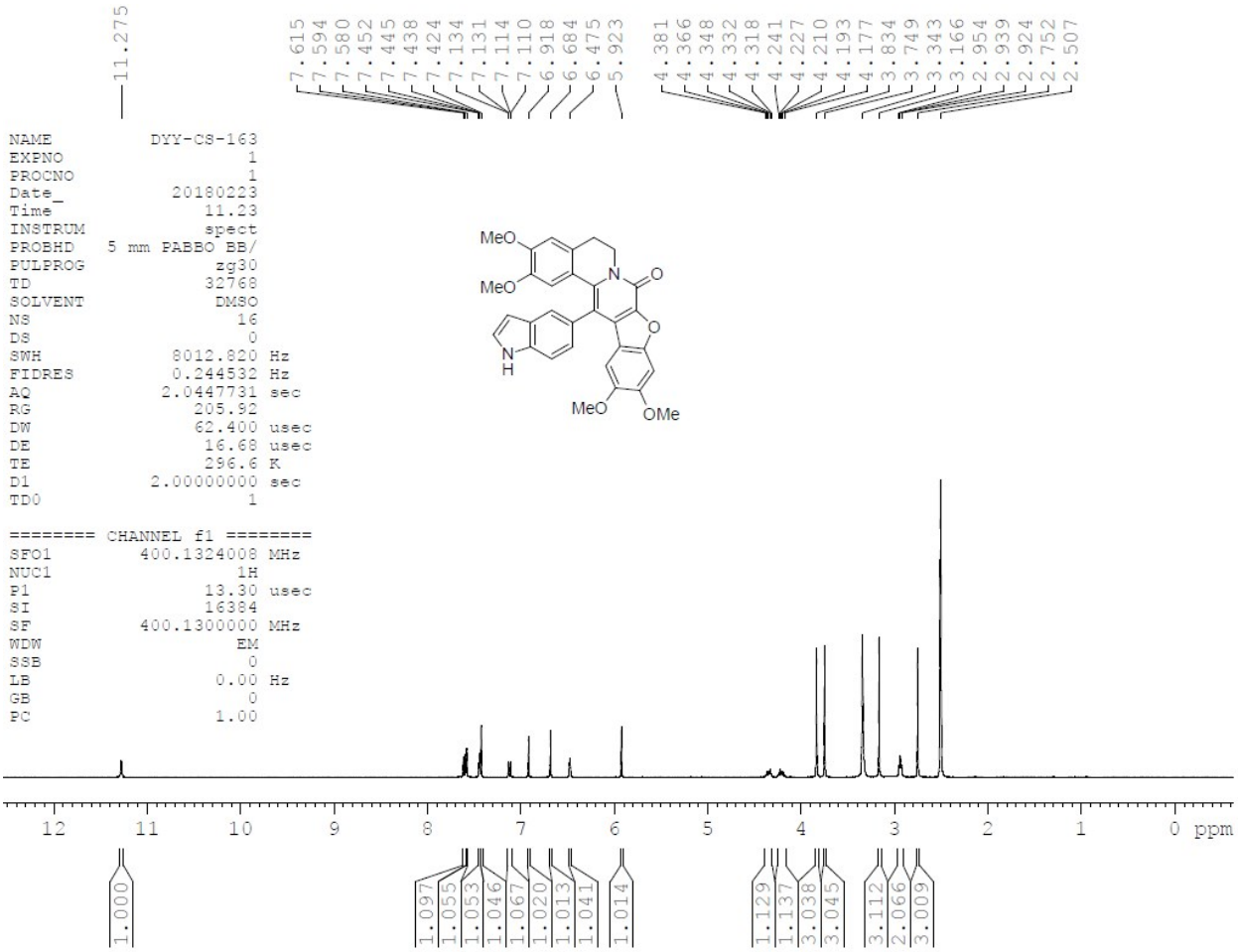
^{1}H NMR of compound **1h** ($CDCl_3$)



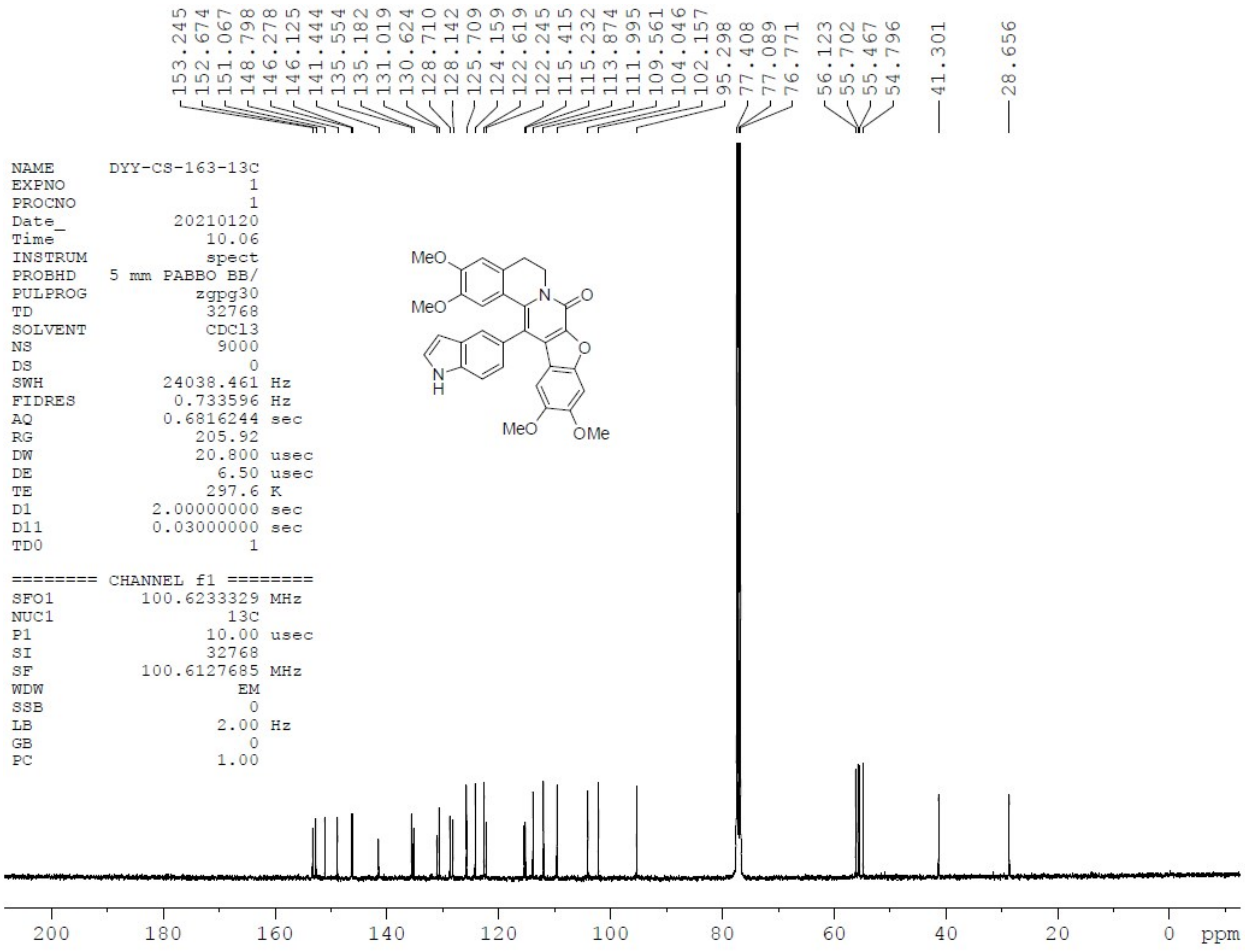
^{13}C NMR of compound **1h** ($CDCl_3$)



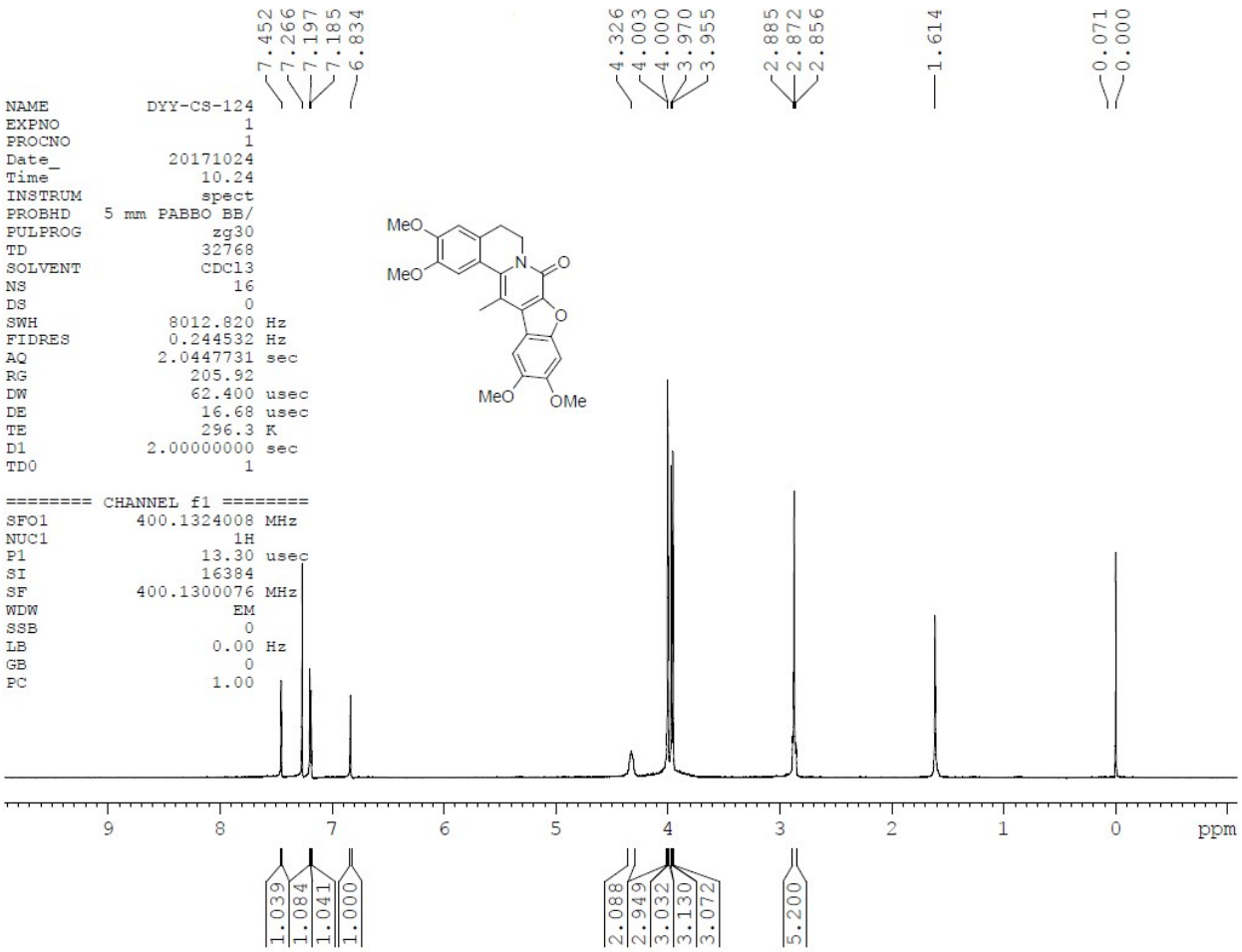
^{1}H NMR of compound **1i** ($CDCl_3$)



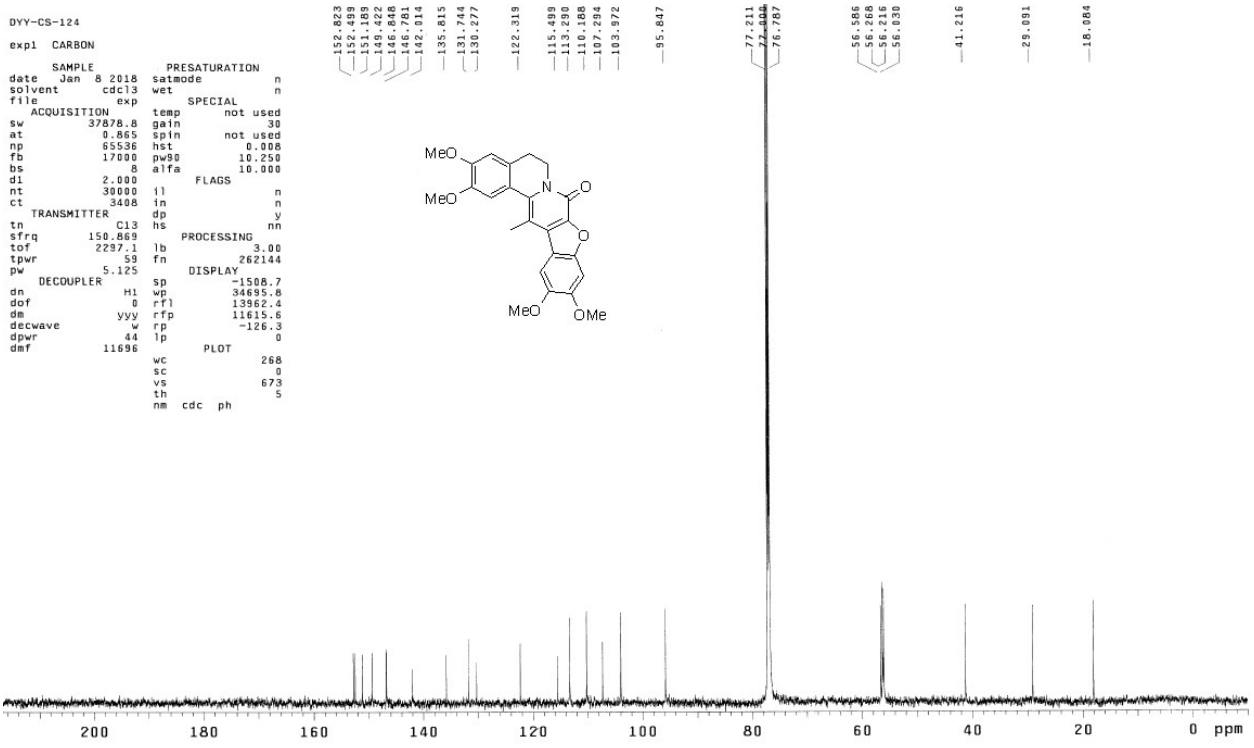
^{13}C NMR of compound **1i** ($CDCl_3$)



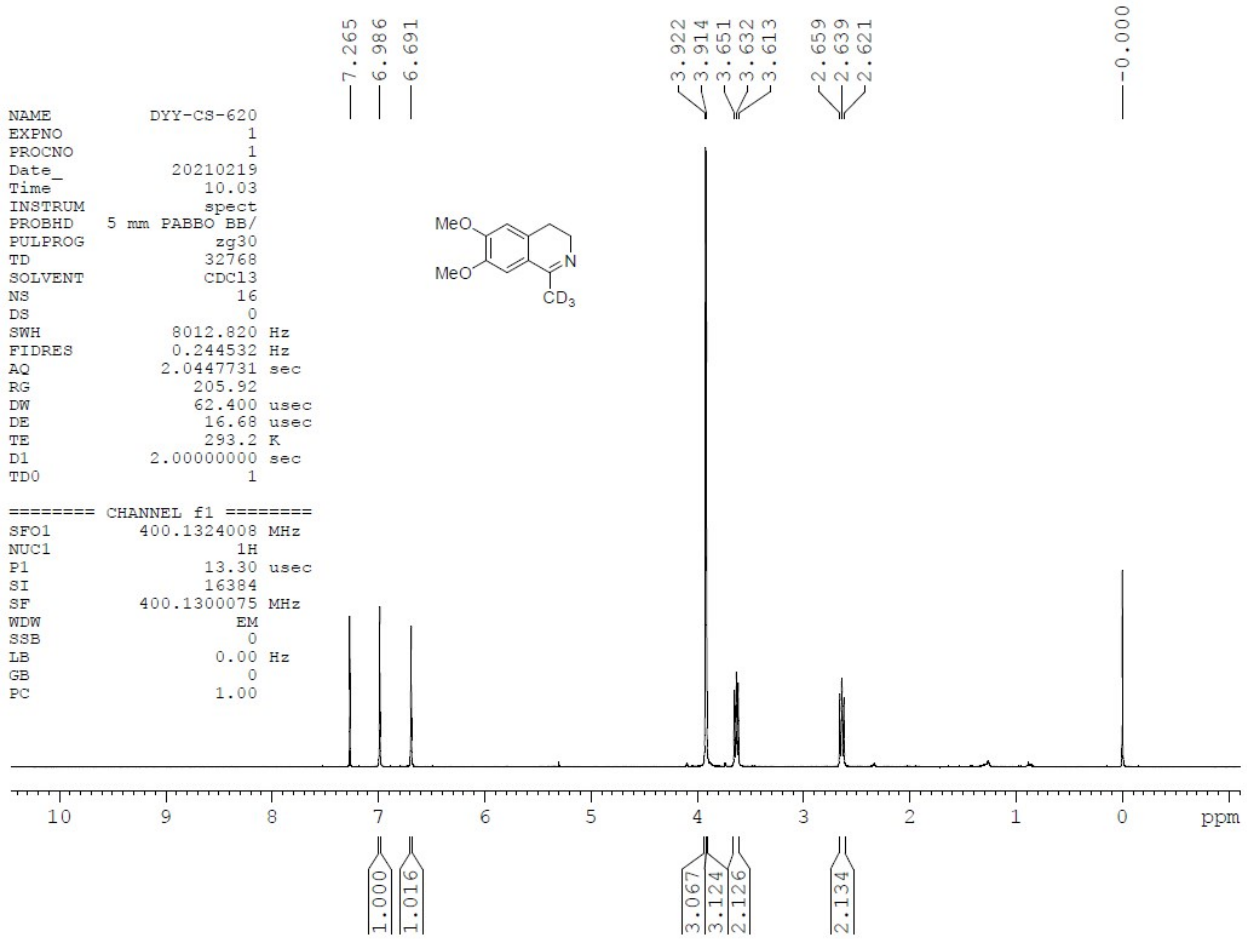
^{1}H NMR of compound **1j** ($CDCl_3$)



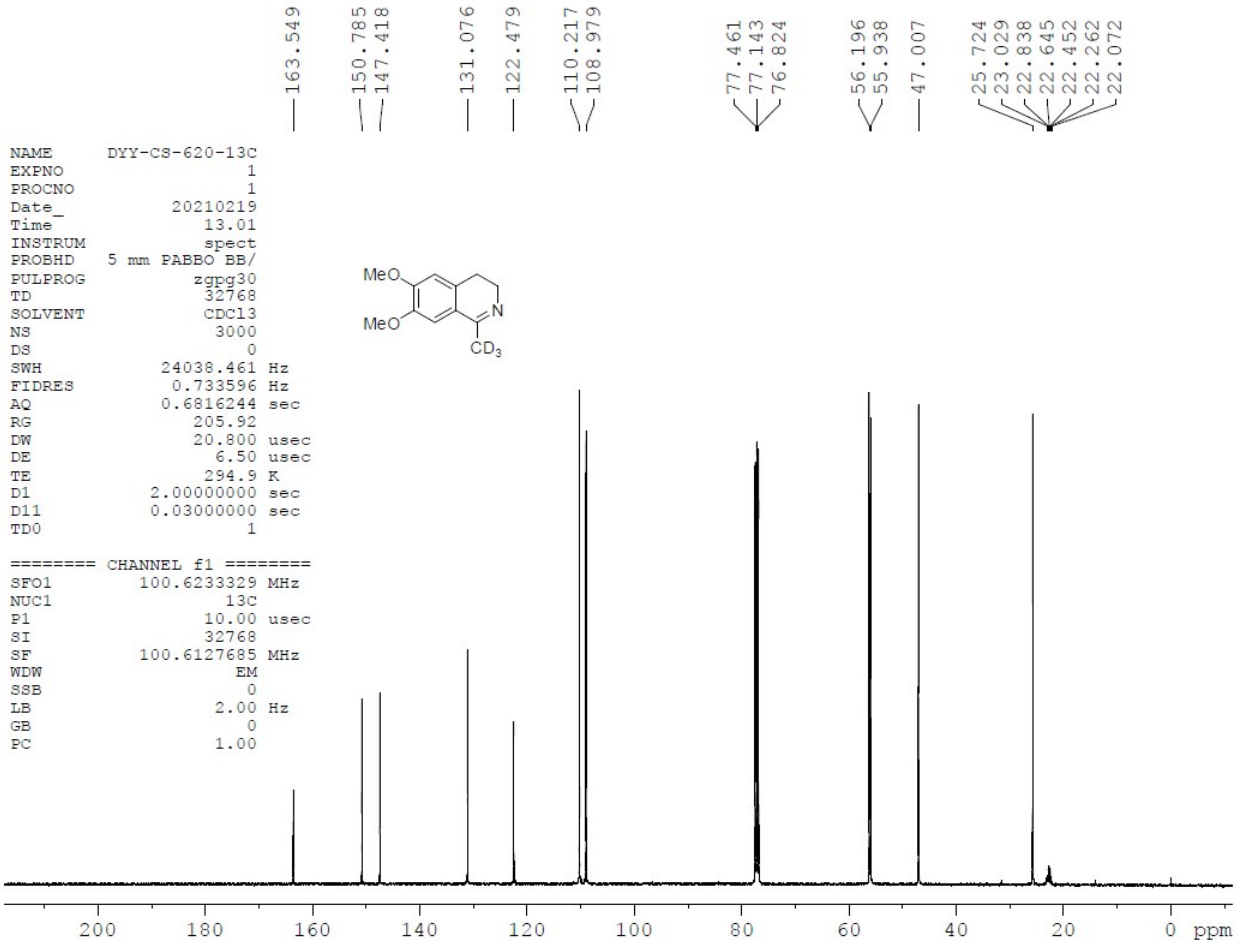
^{13}C NMR of compound **1j** ($CDCl_3$)



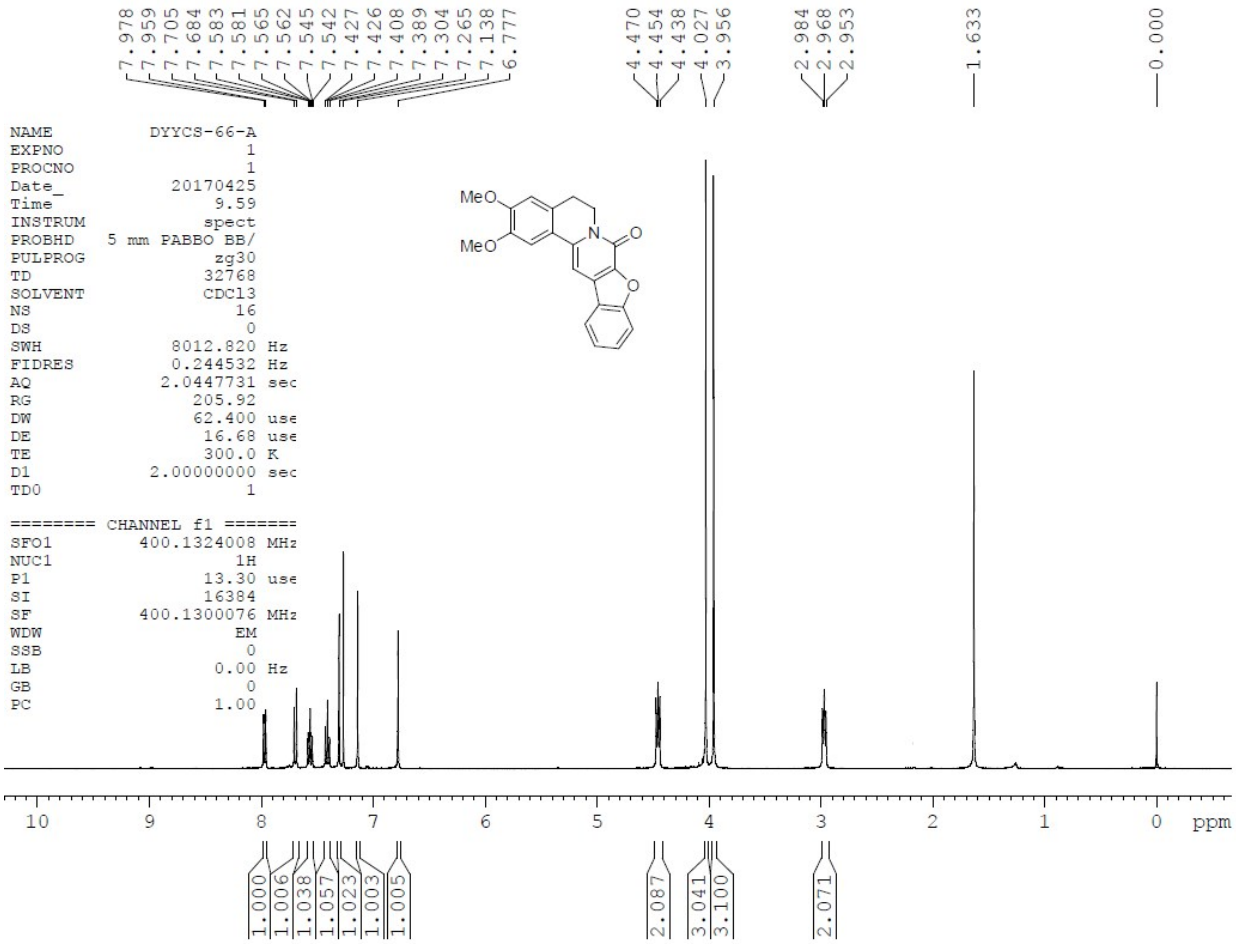
^{1}H NMR of compound **2b** ($CDCl_3$)



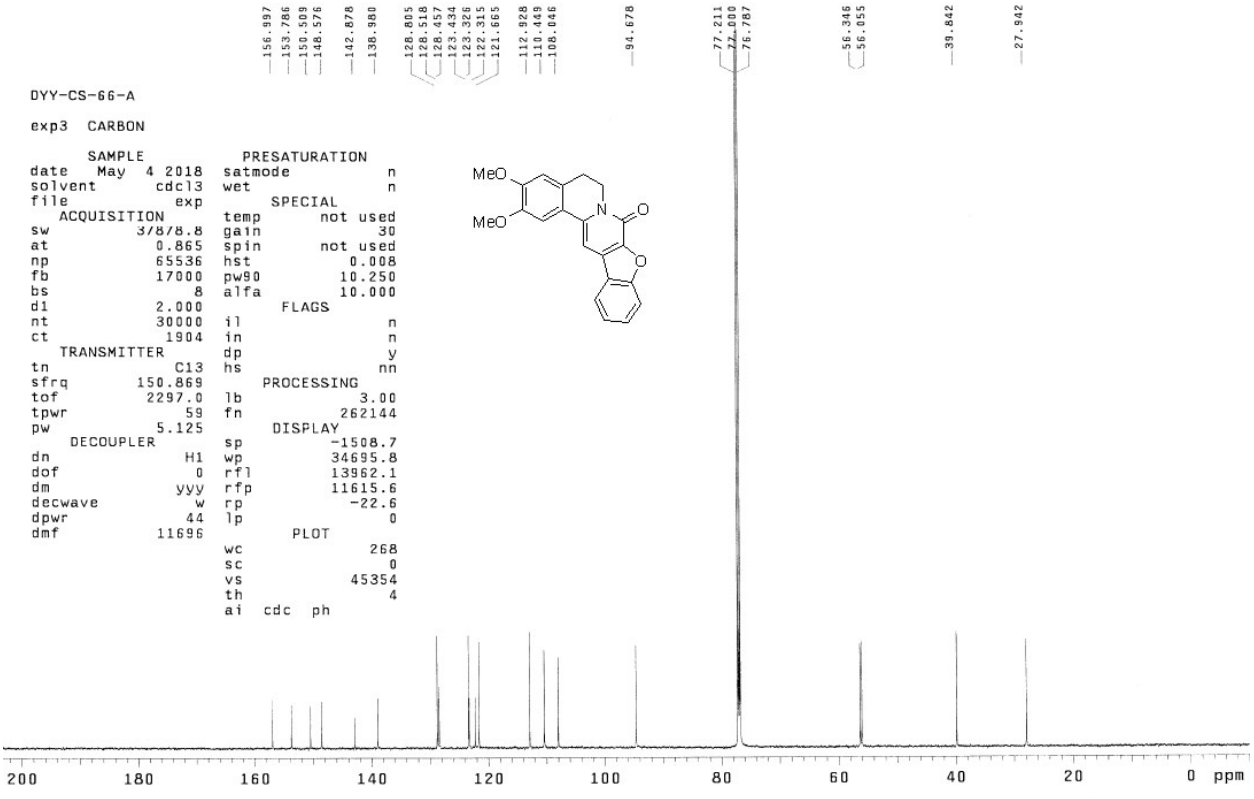
^{13}C NMR of compound **2b** ($CDCl_3$)



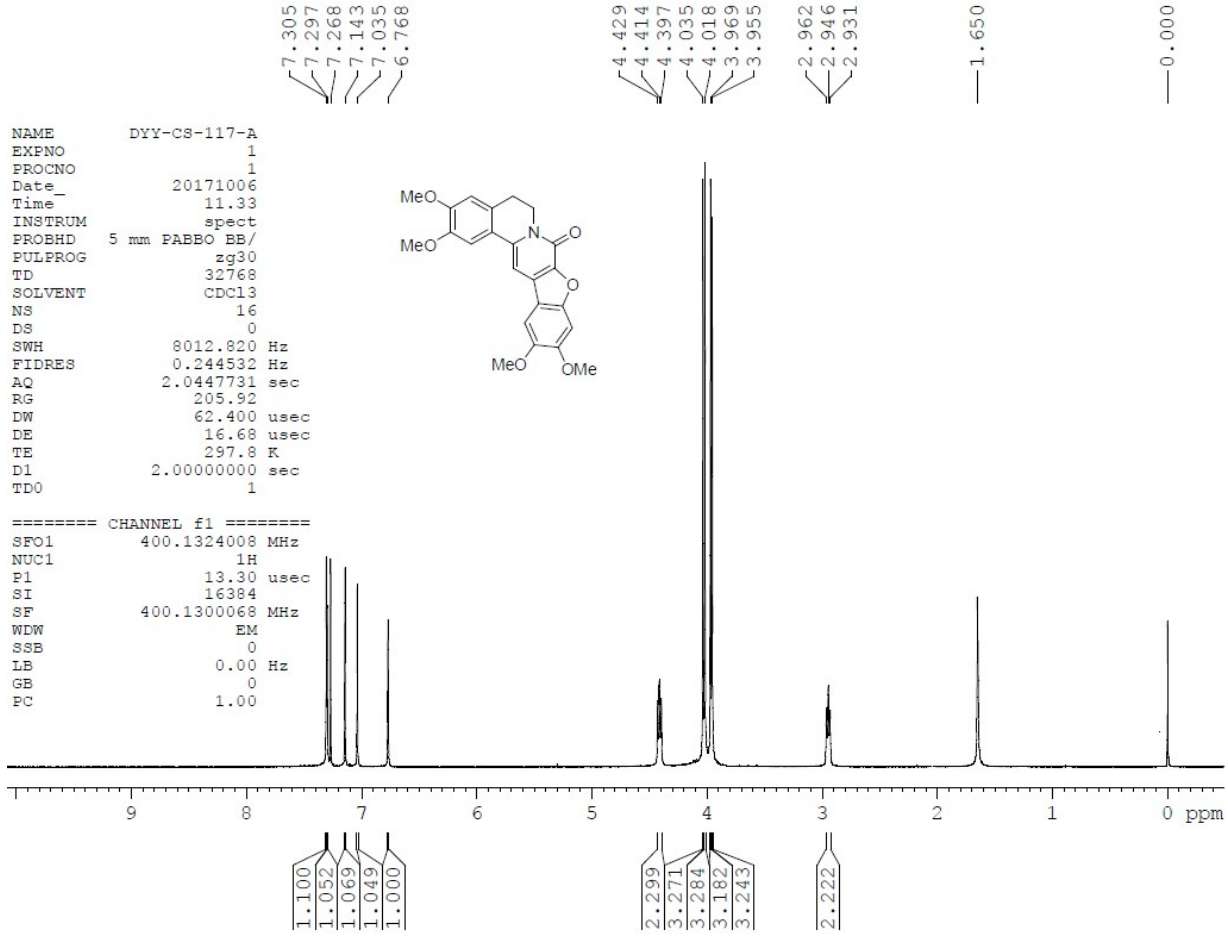
^{1}H NMR of compound **5a** ($CDCl_3$)



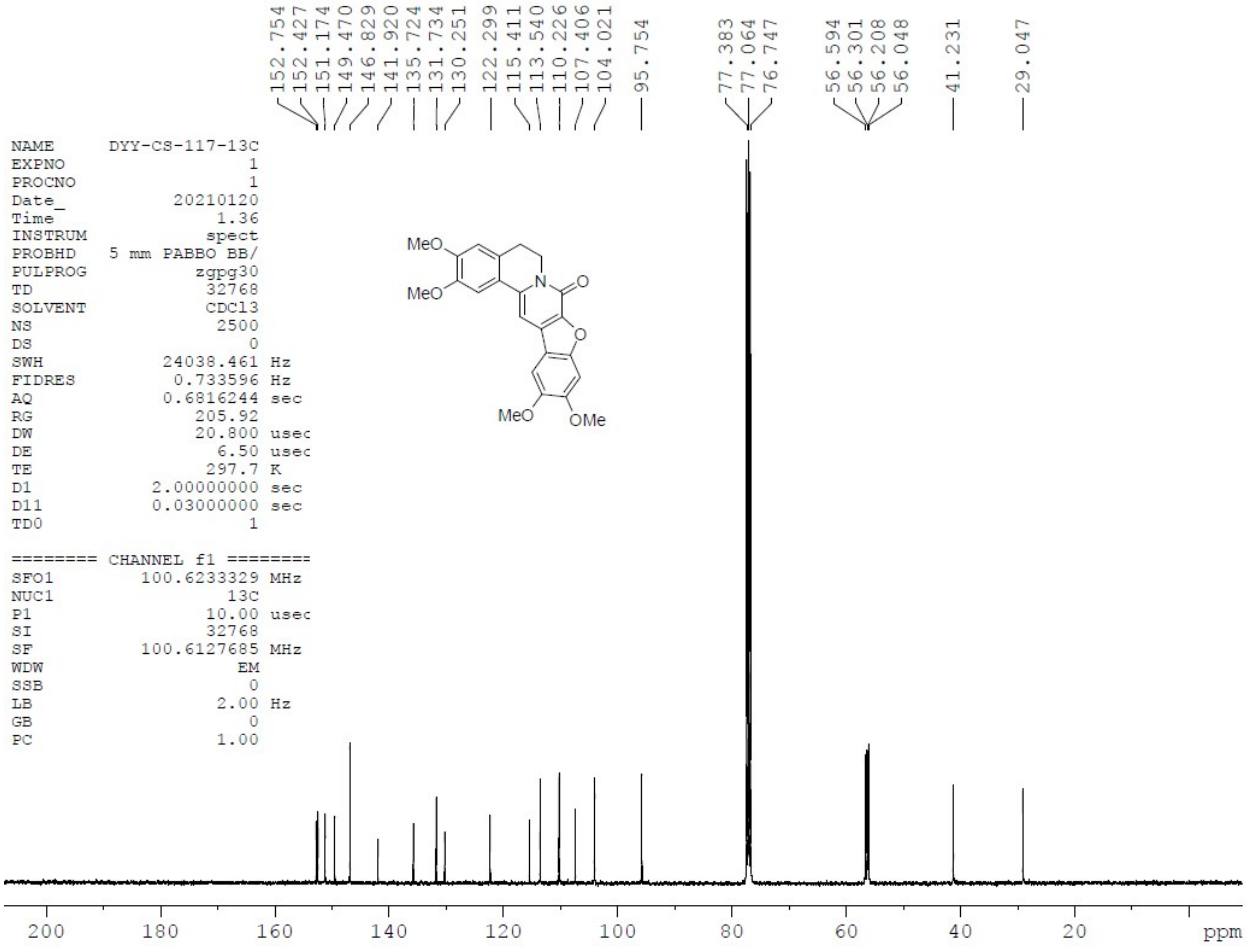
^{13}C NMR of compound **5a** ($CDCl_3$)



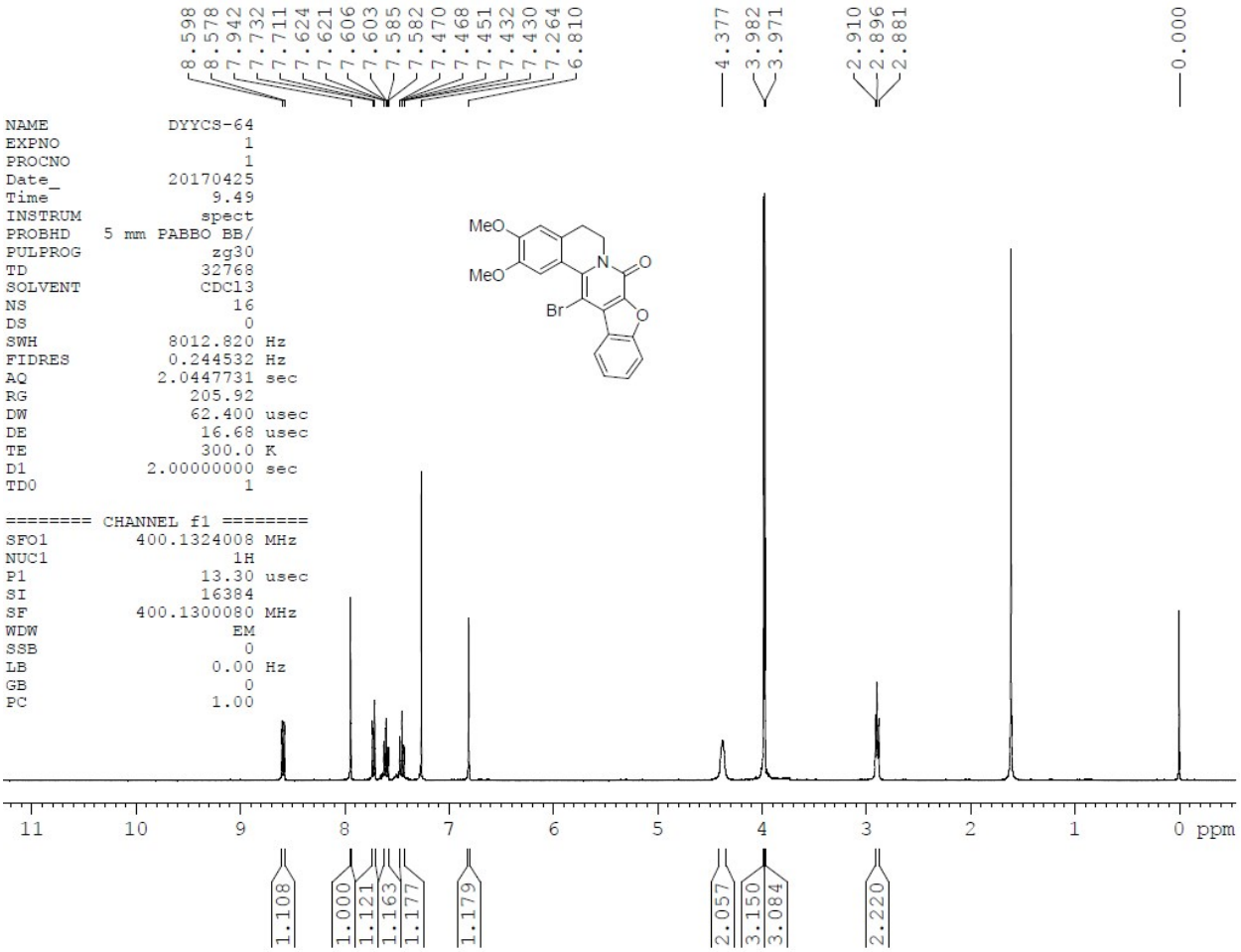
^{1}H NMR of compound **5b** ($CDCl_3$)



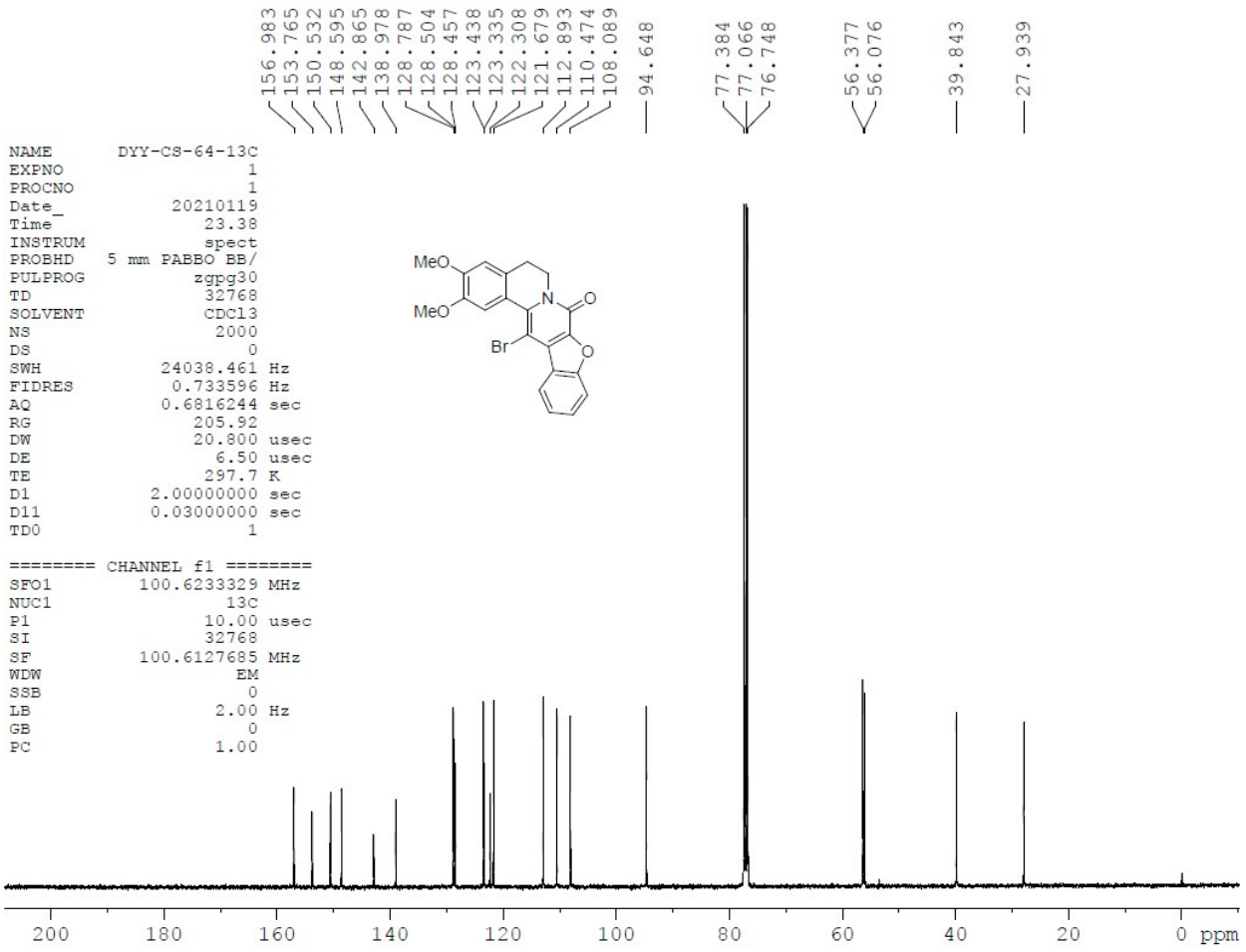
^{13}C NMR of compound **5b** ($CDCl_3$)



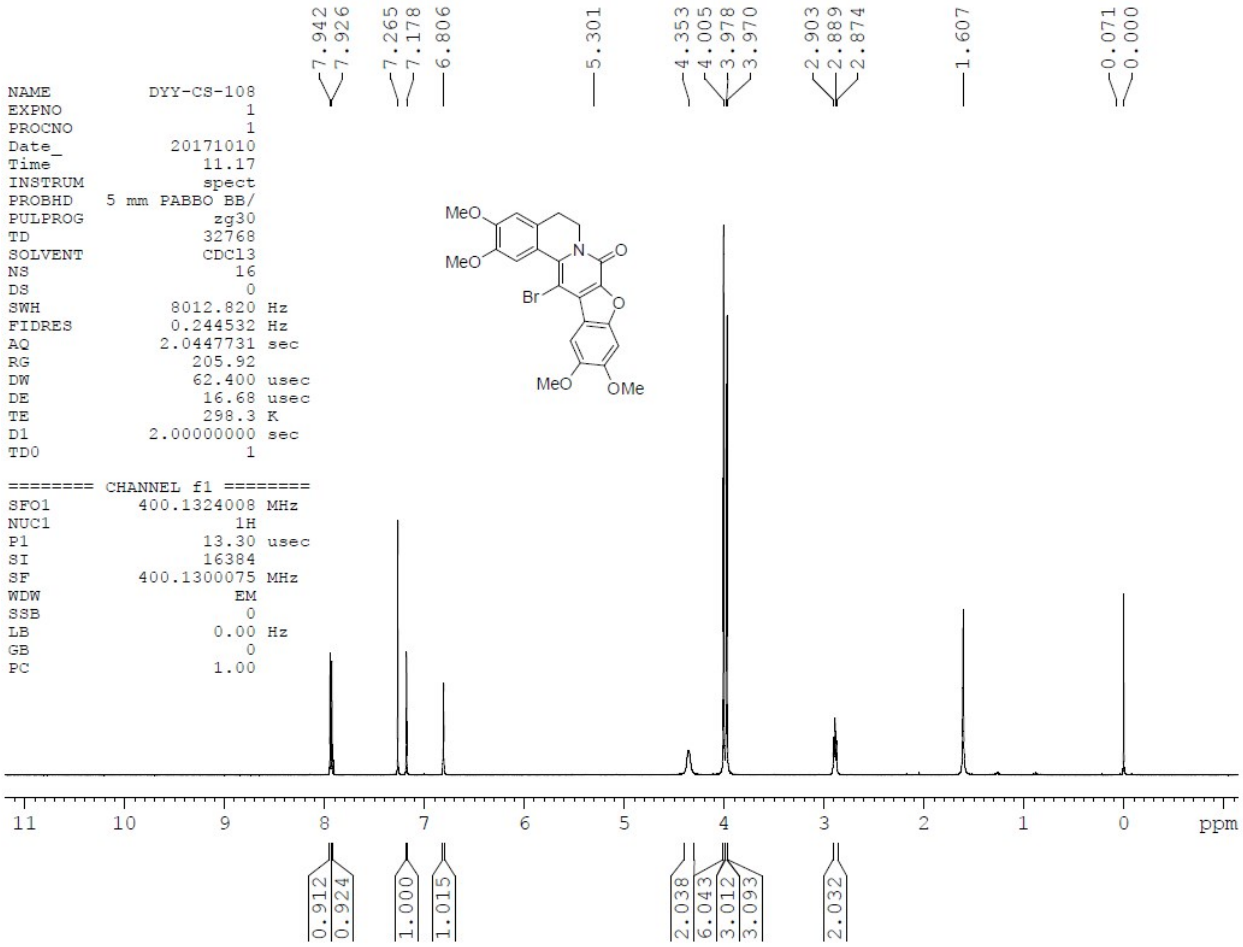
^{1}H NMR of compound **6a** ($CDCl_3$)



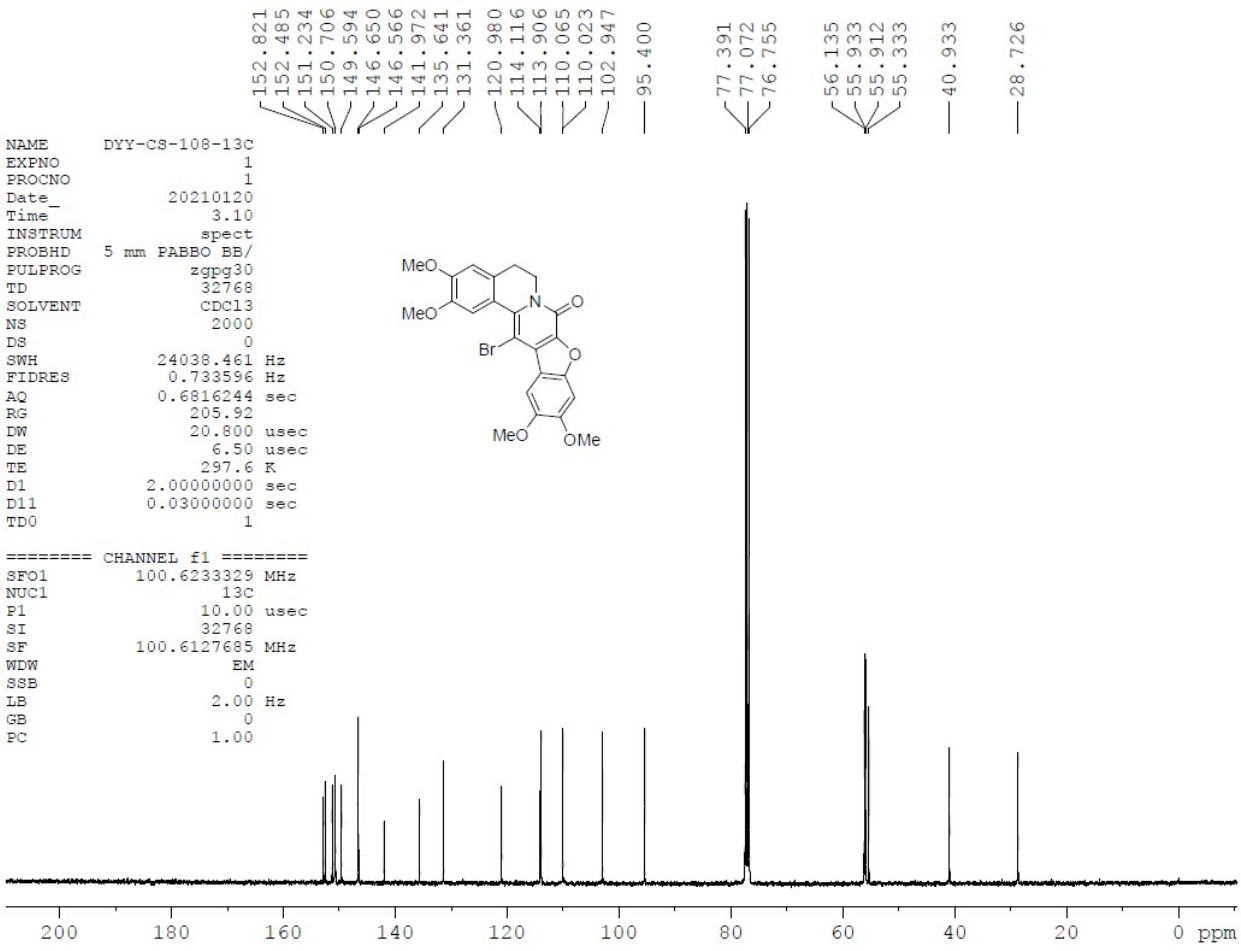
^{13}C NMR of compound **6a** ($CDCl_3$)



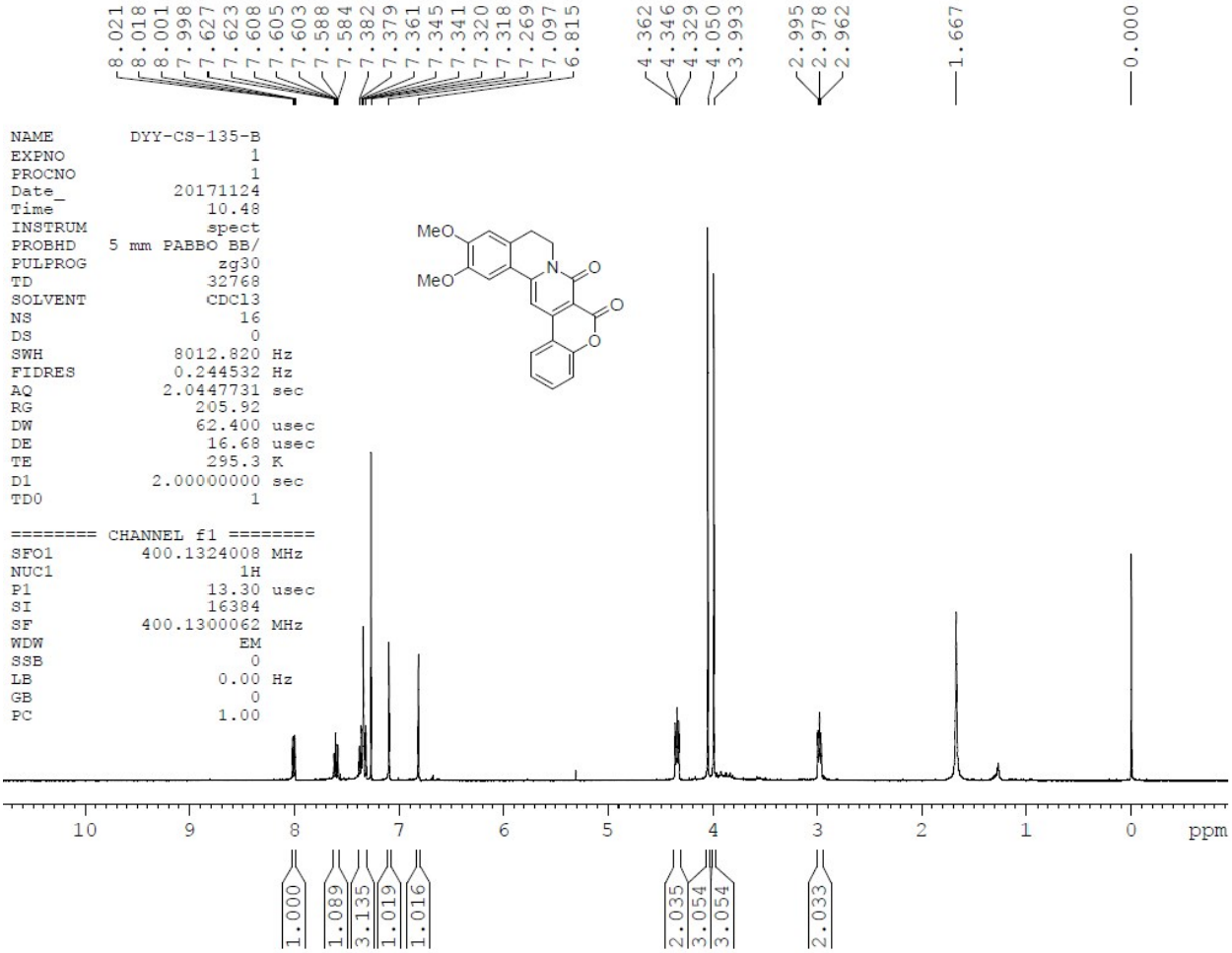
^{1}H NMR of compound **6b** ($CDCl_3$)



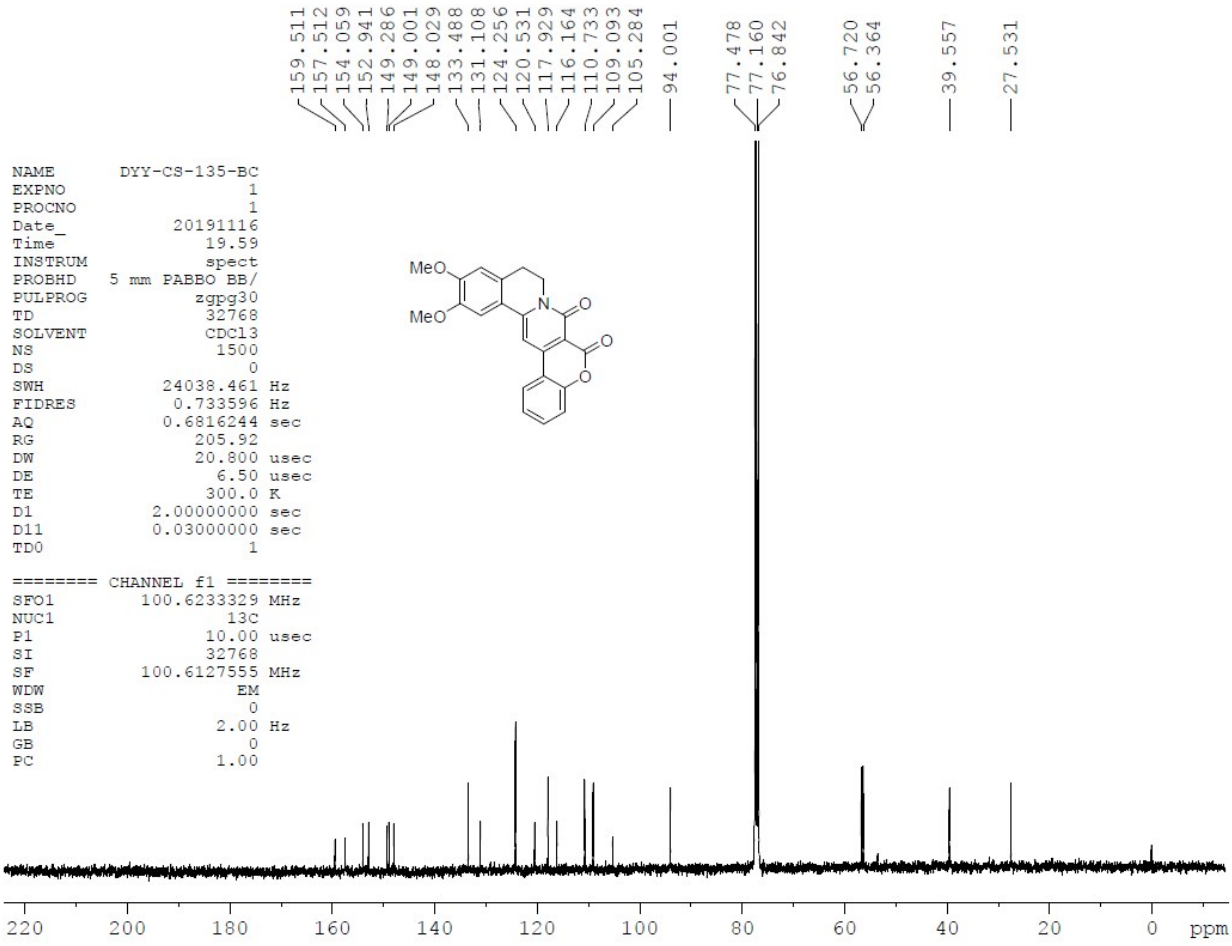
^{13}C NMR of compound **6b** ($CDCl_3$)



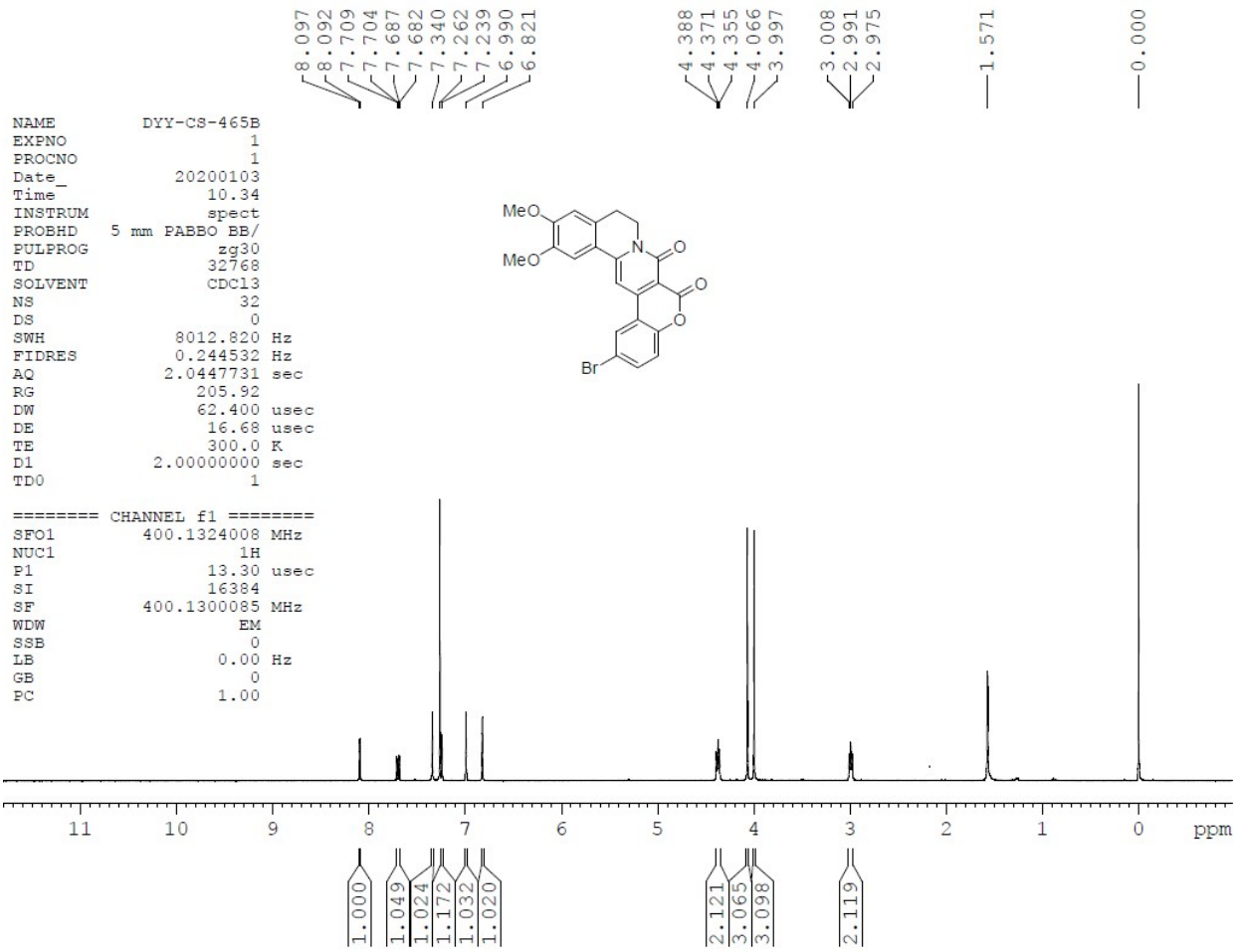
^{1}H NMR of compound **10a** ($CDCl_3$)



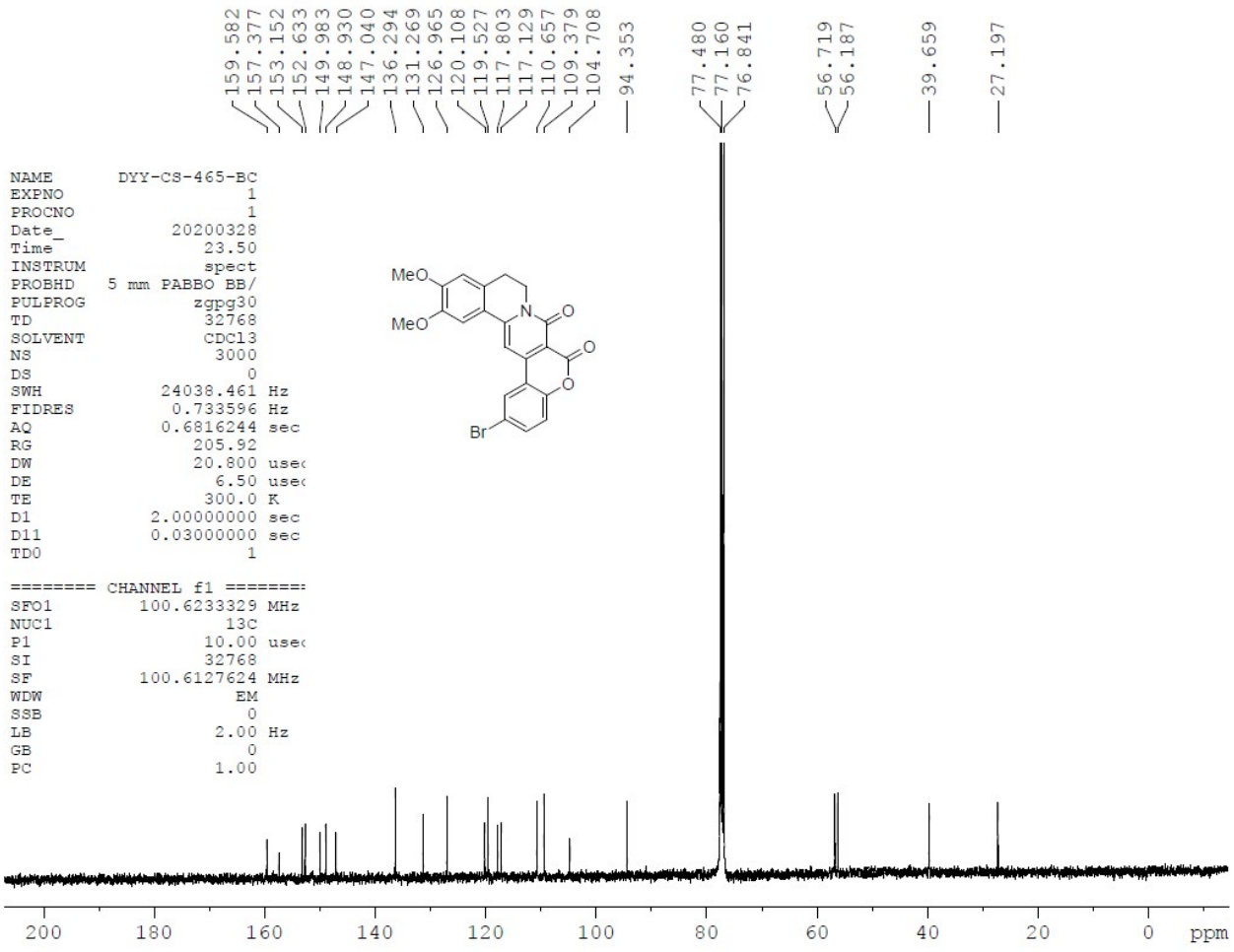
^{13}C NMR of compound **10a** ($CDCl_3$)



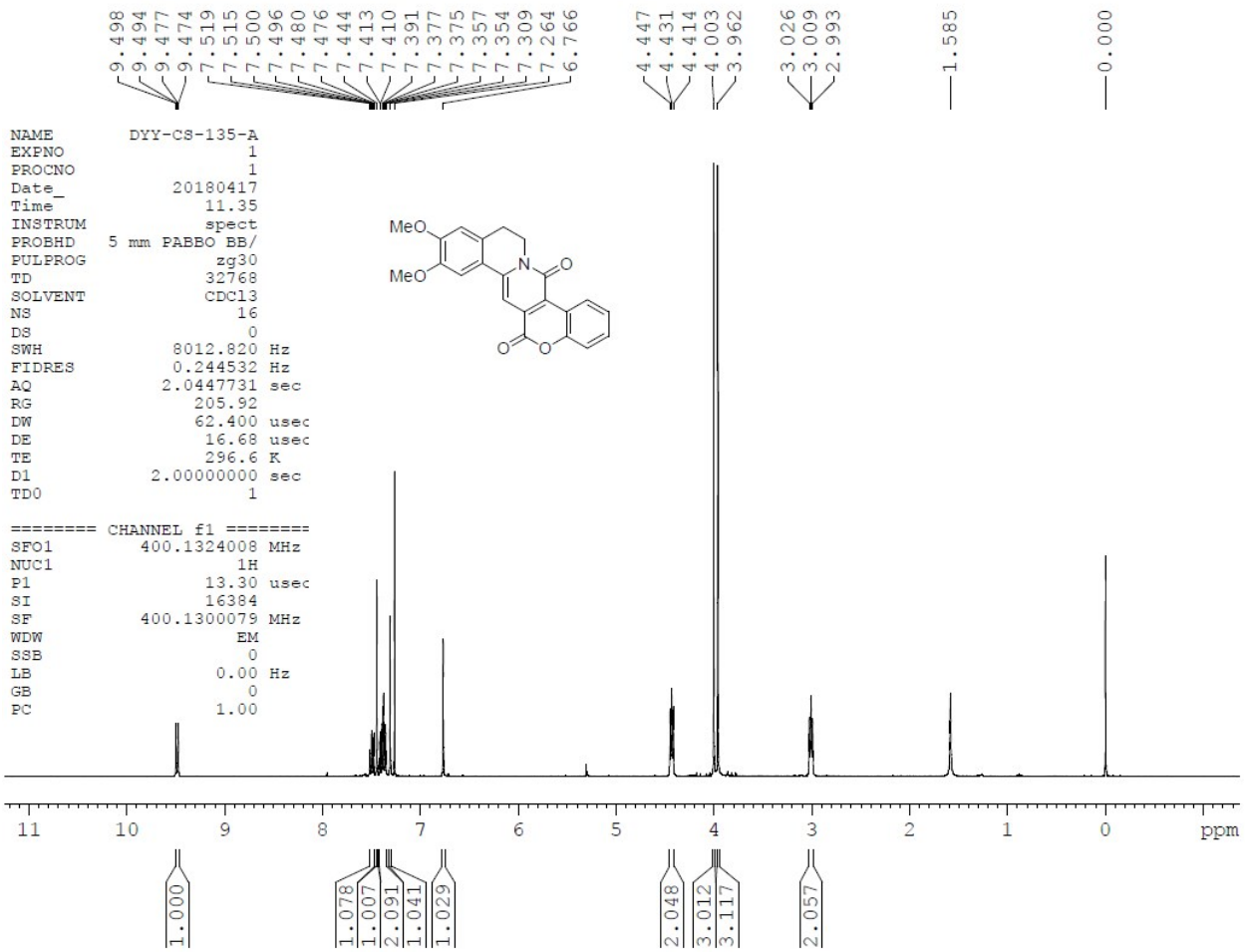
^{1}H NMR of compound **10b** ($CDCl_3$)



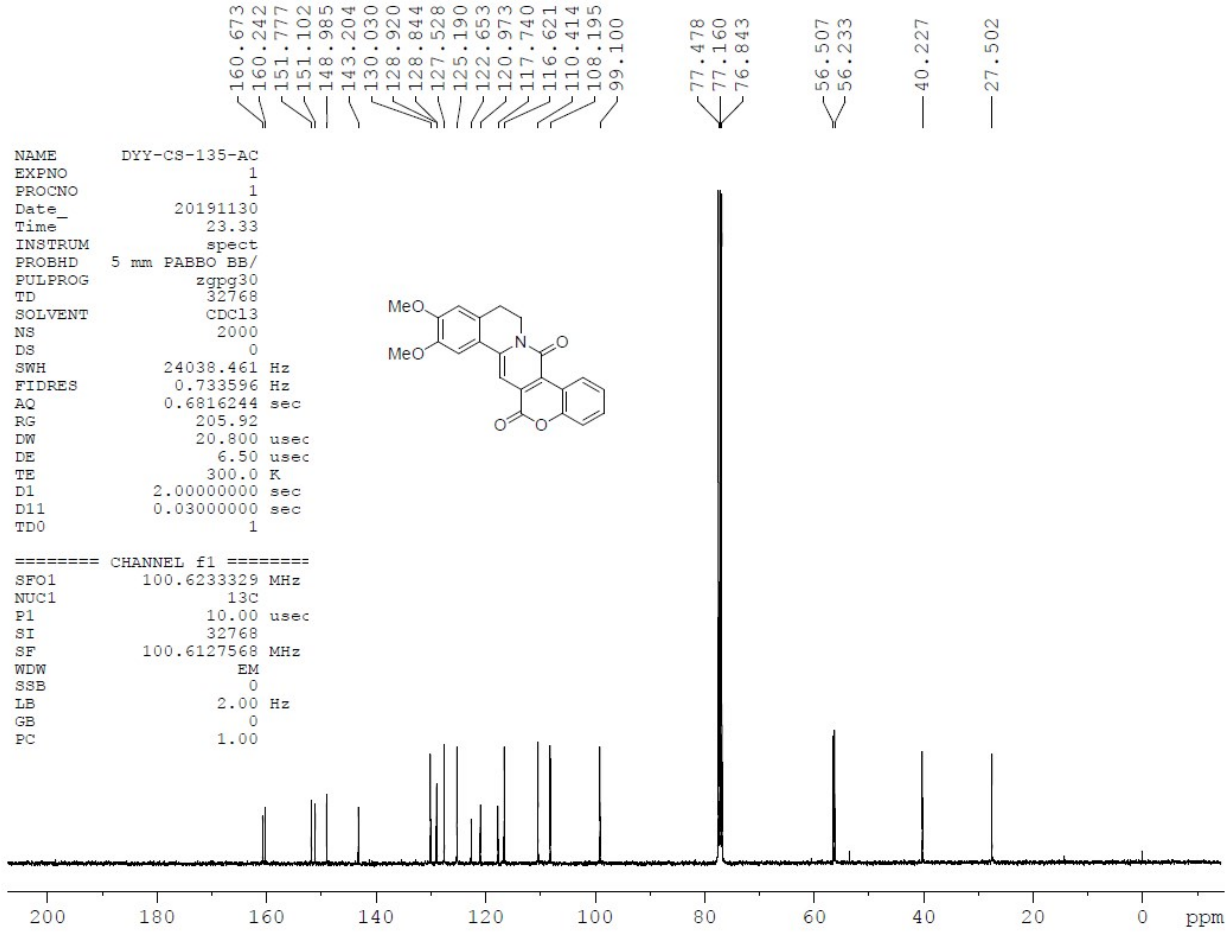
^{13}C NMR of compound **10b** ($CDCl_3$)



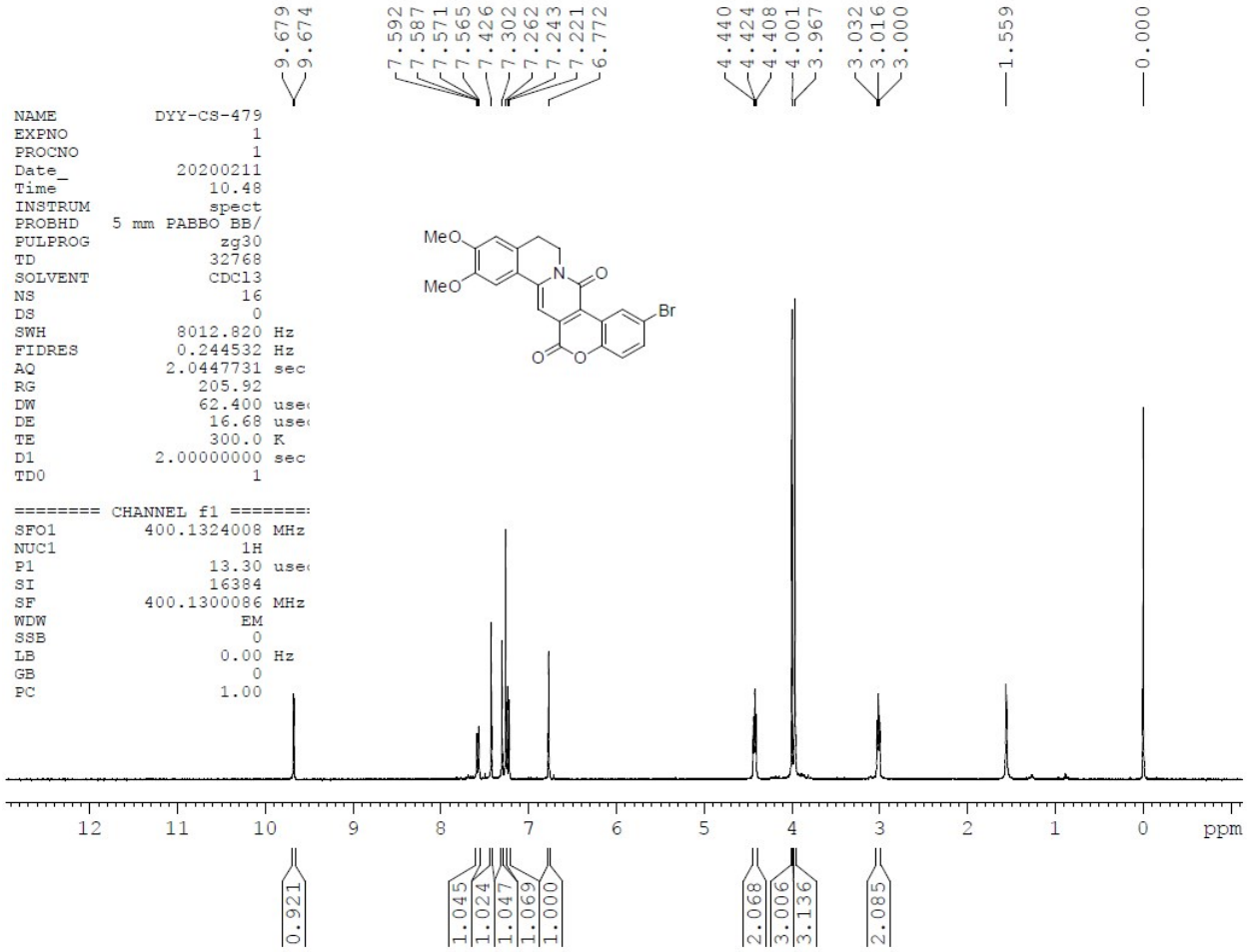
^{1}H NMR of compound **11a** ($CDCl_3$)



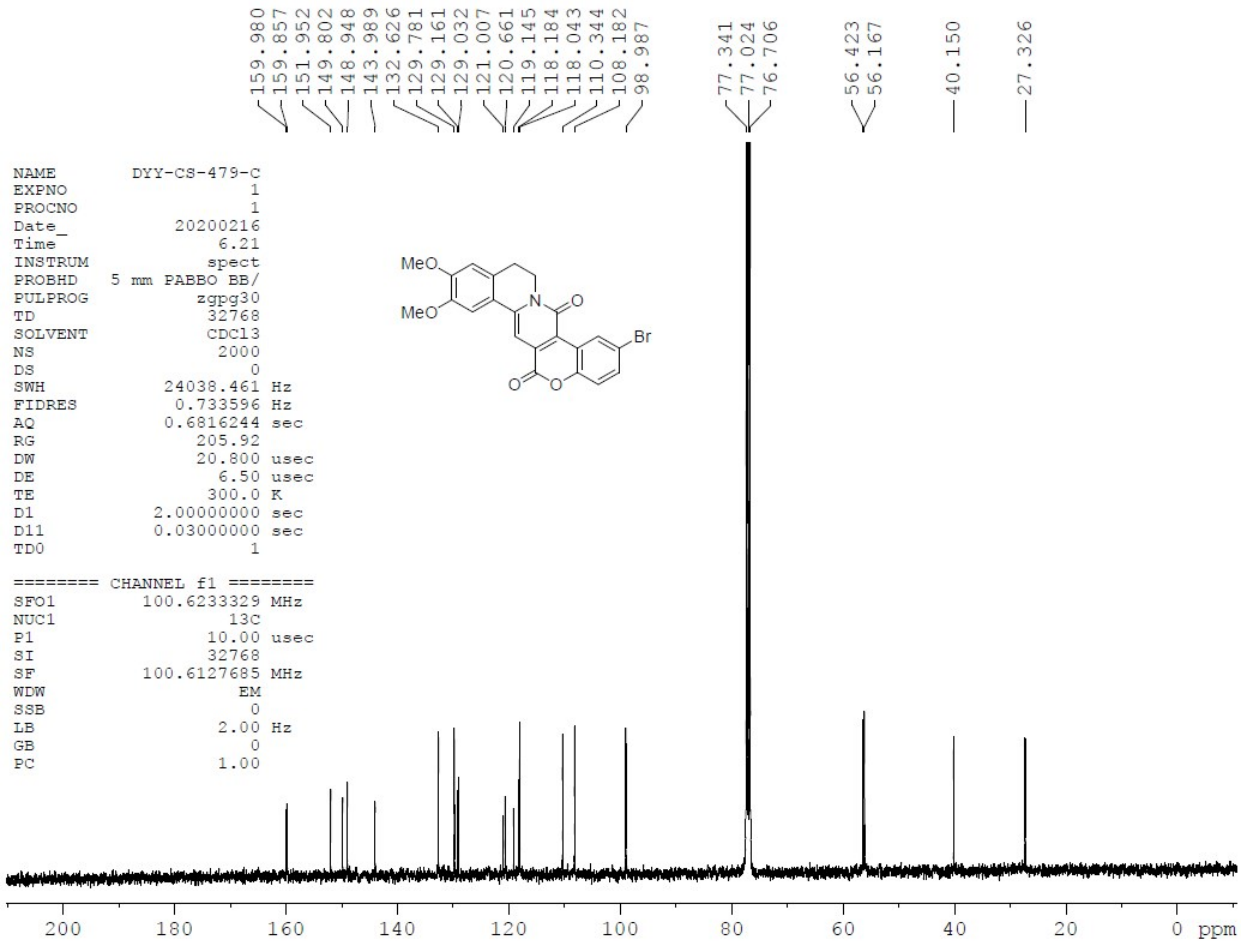
^{13}C NMR of compound **11a** ($CDCl_3$)



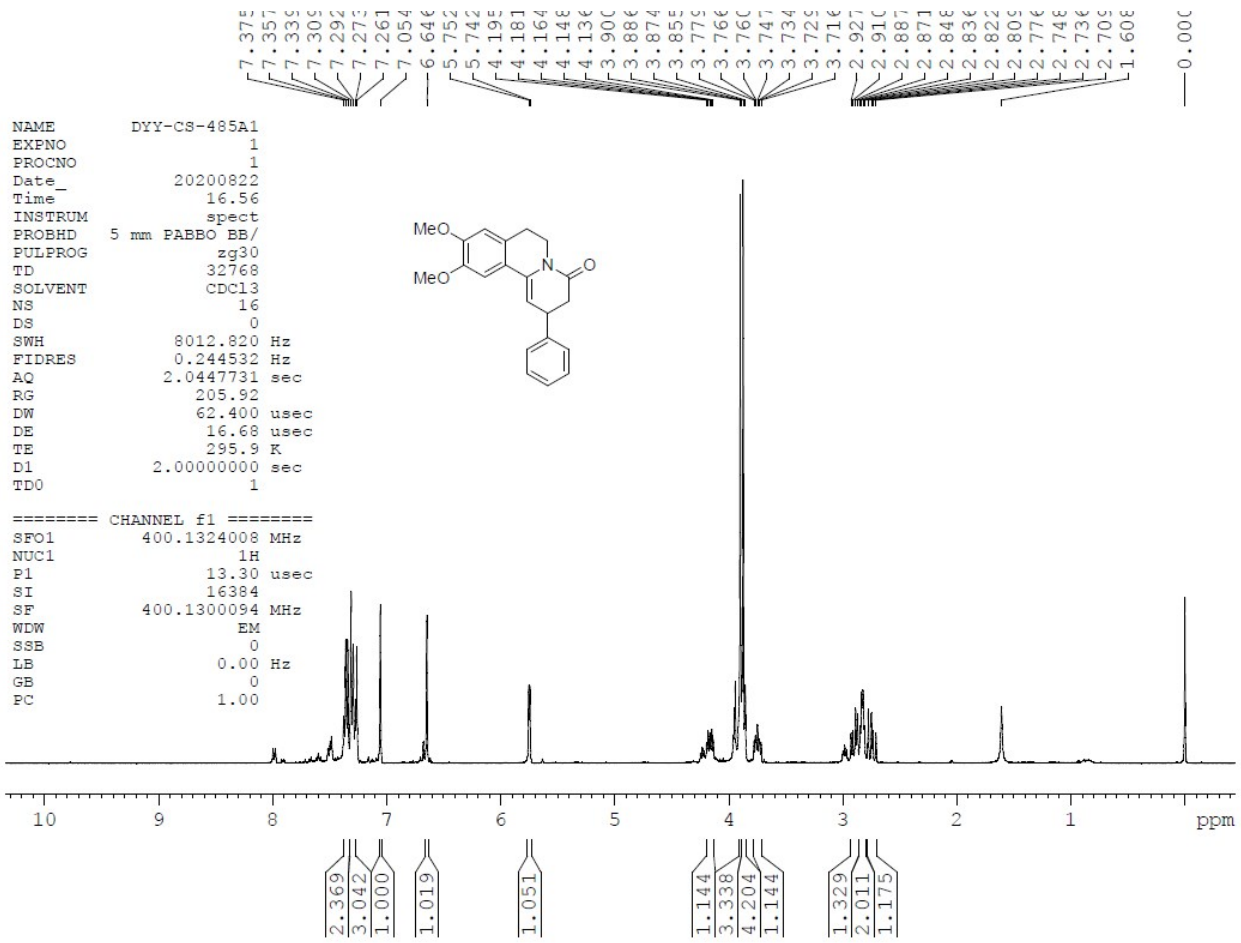
^{1}H NMR of compound **11b** ($CDCl_3$)



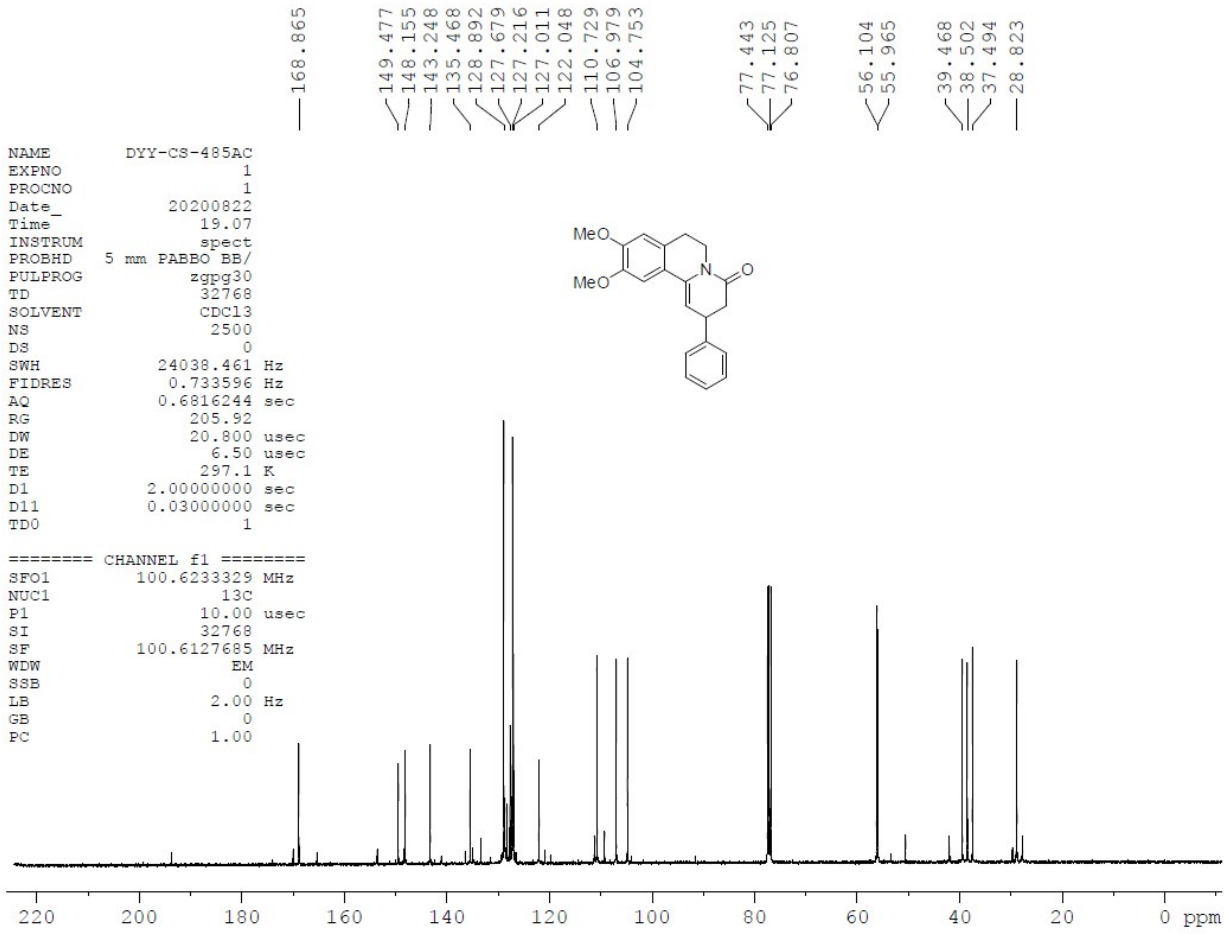
^{13}C NMR of compound **11b** ($CDCl_3$)



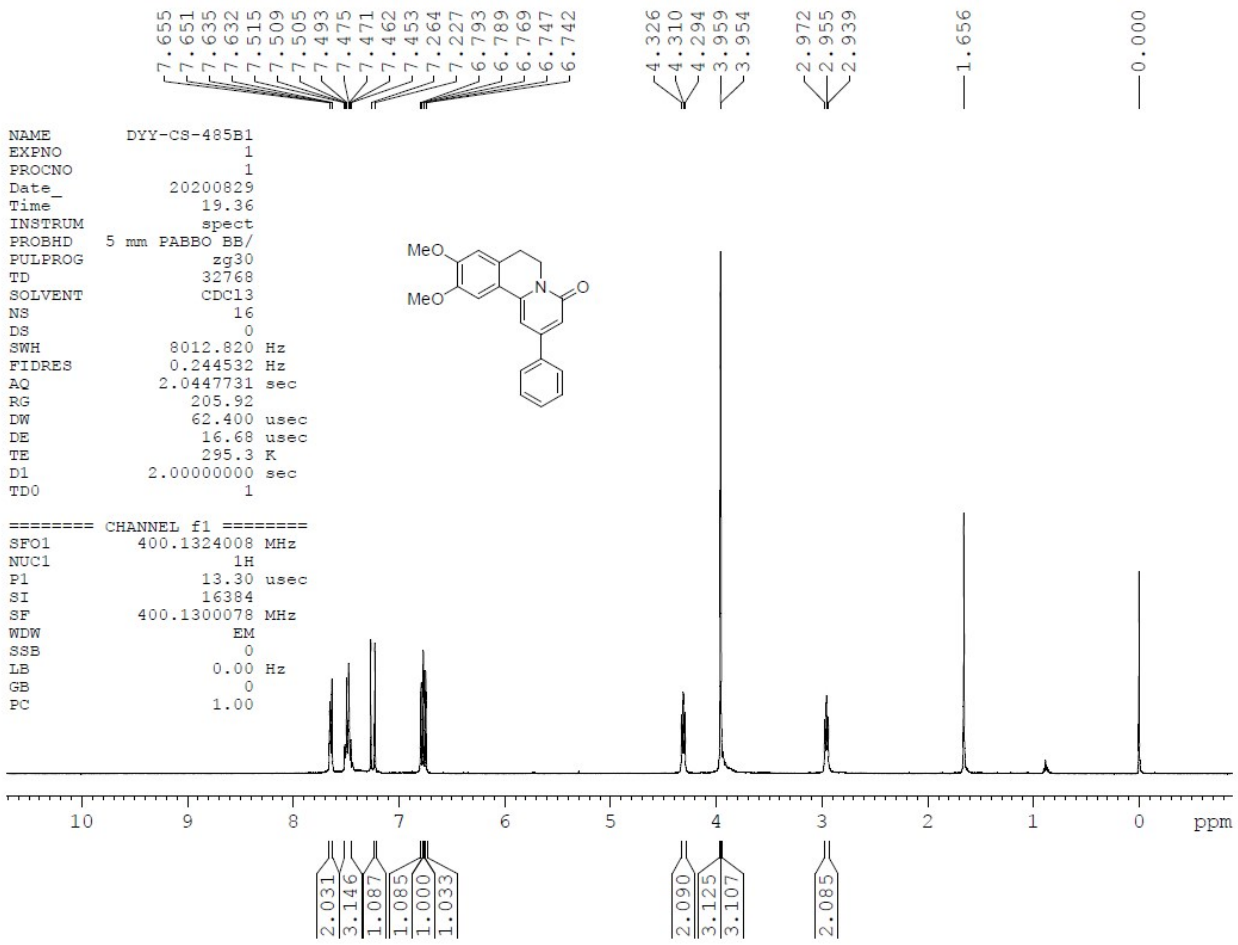
^{1}H NMR of compound **16a** ($CDCl_3$)



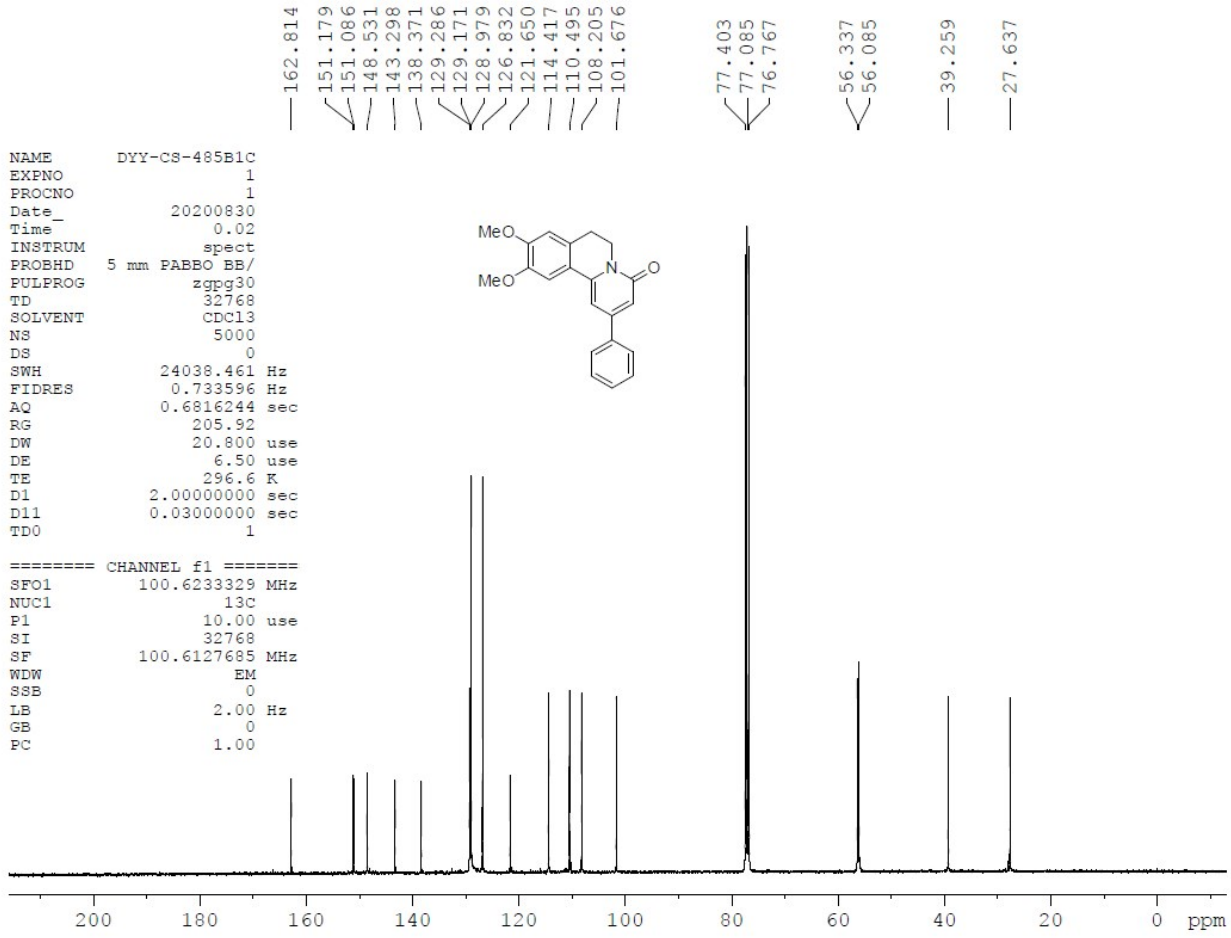
^{13}C NMR of compound **16a** ($CDCl_3$)



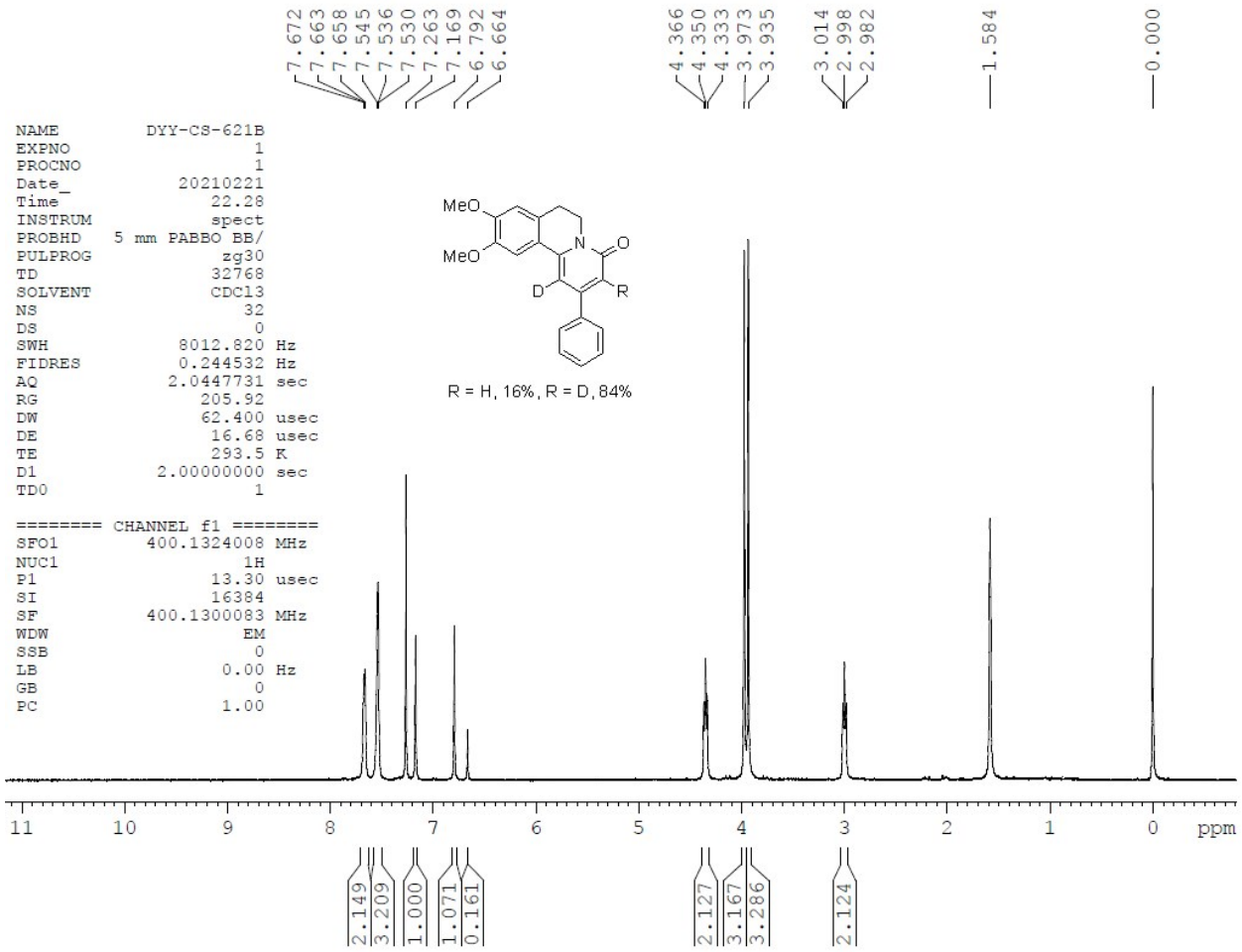
^{1}H NMR of compound **18a** ($CDCl_3$)



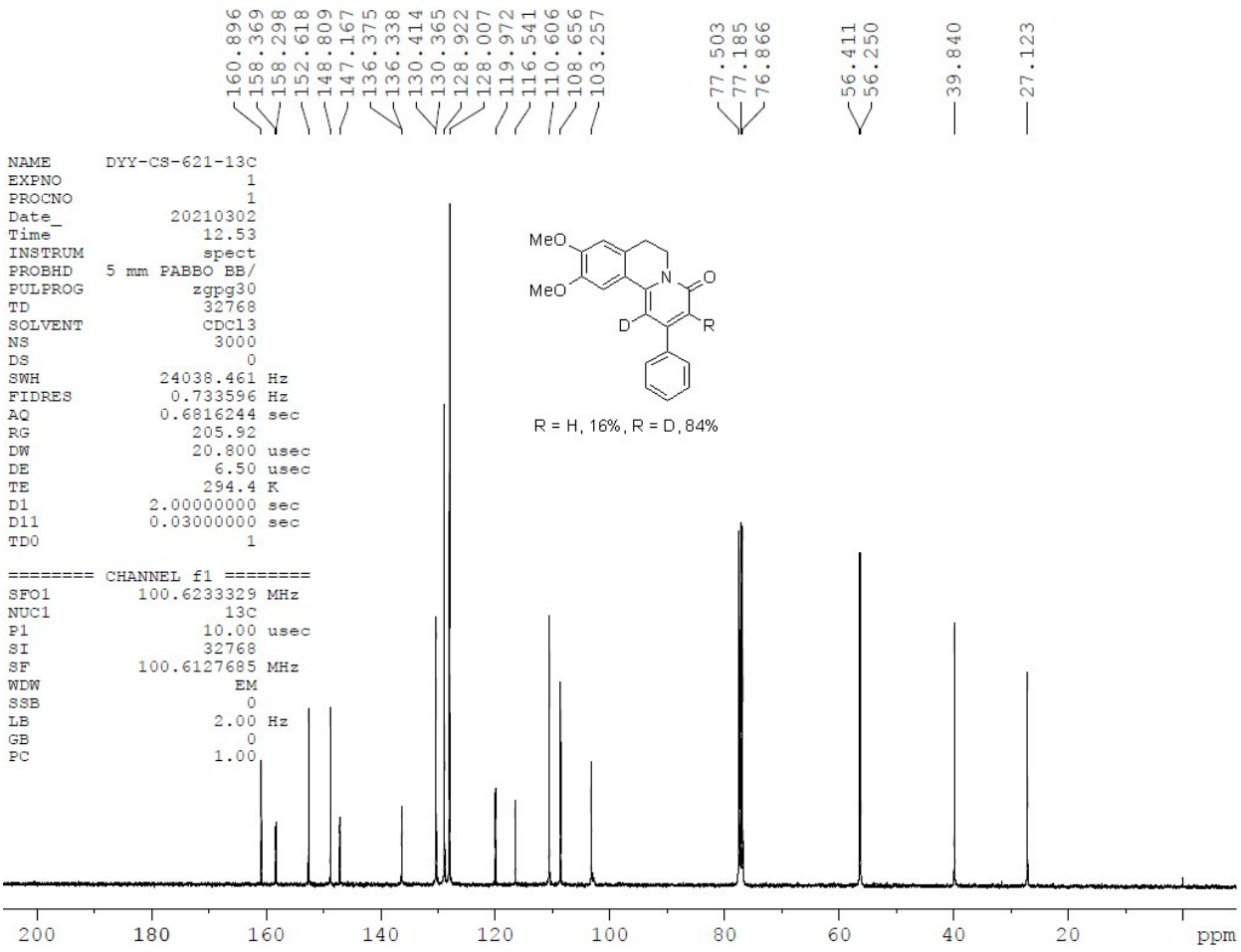
^{13}C NMR of compound **18a** ($CDCl_3$)



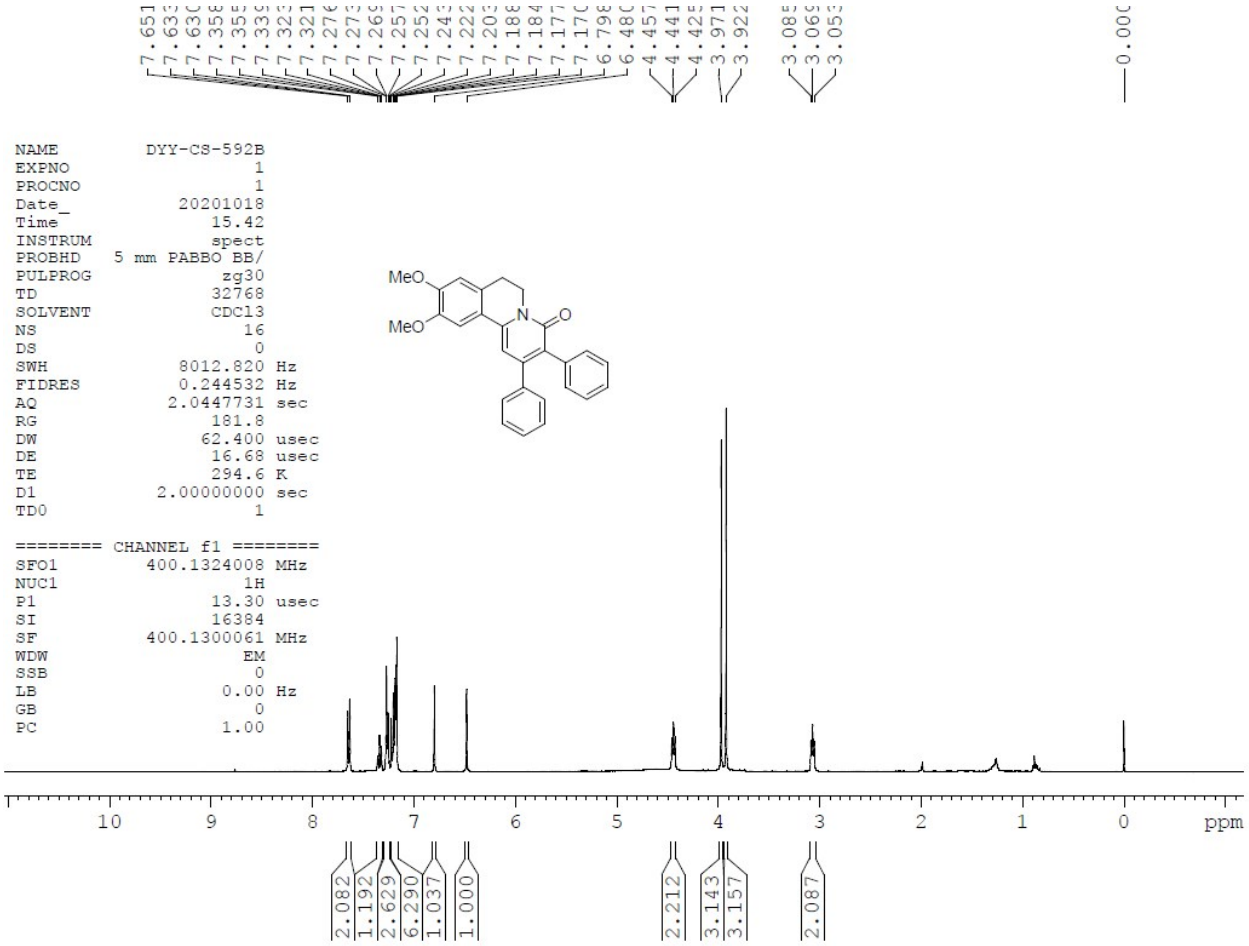
^{1}H NMR of compound **18b** ($CDCl_3$)



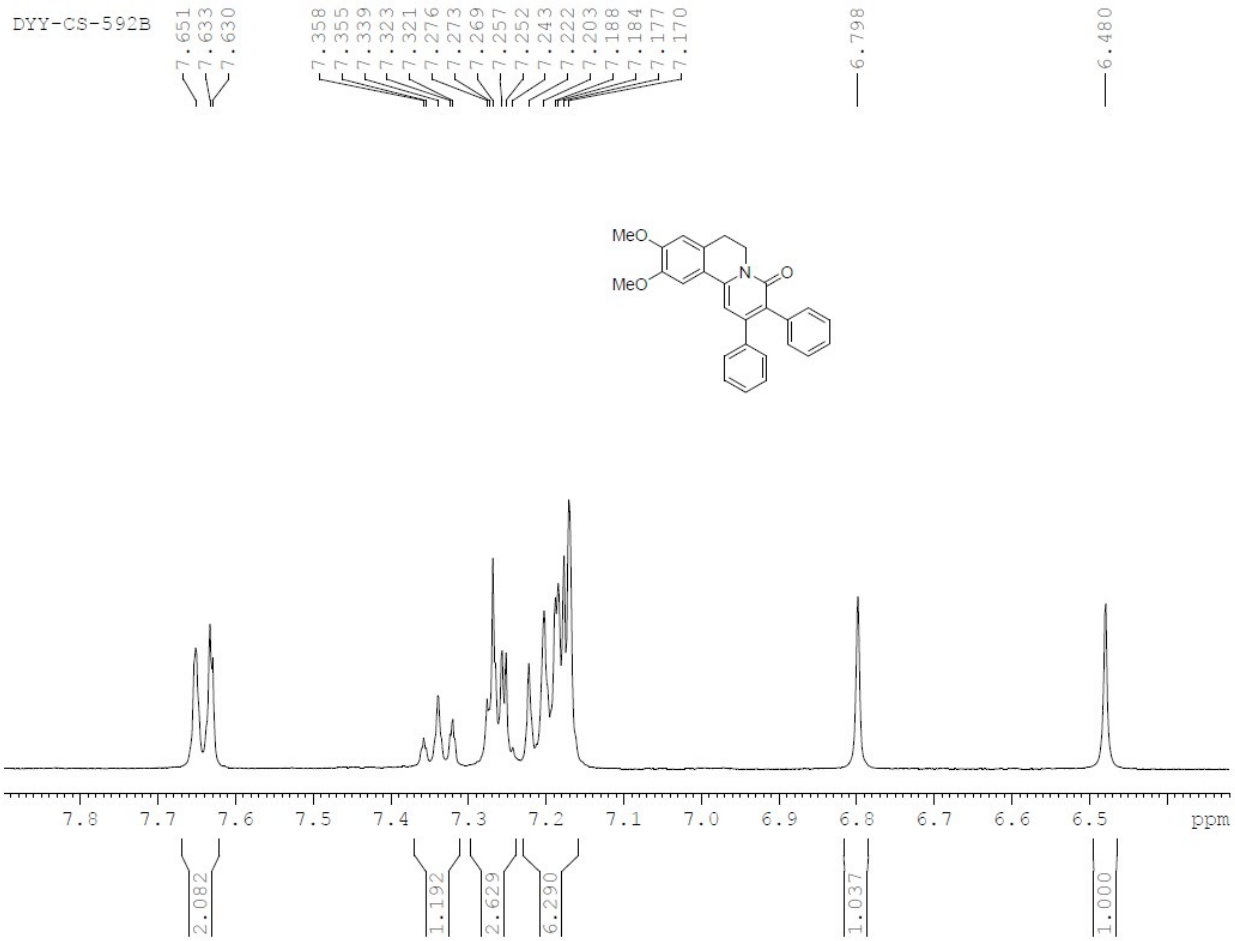
^{13}C NMR of compound **18b** ($CDCl_3$)



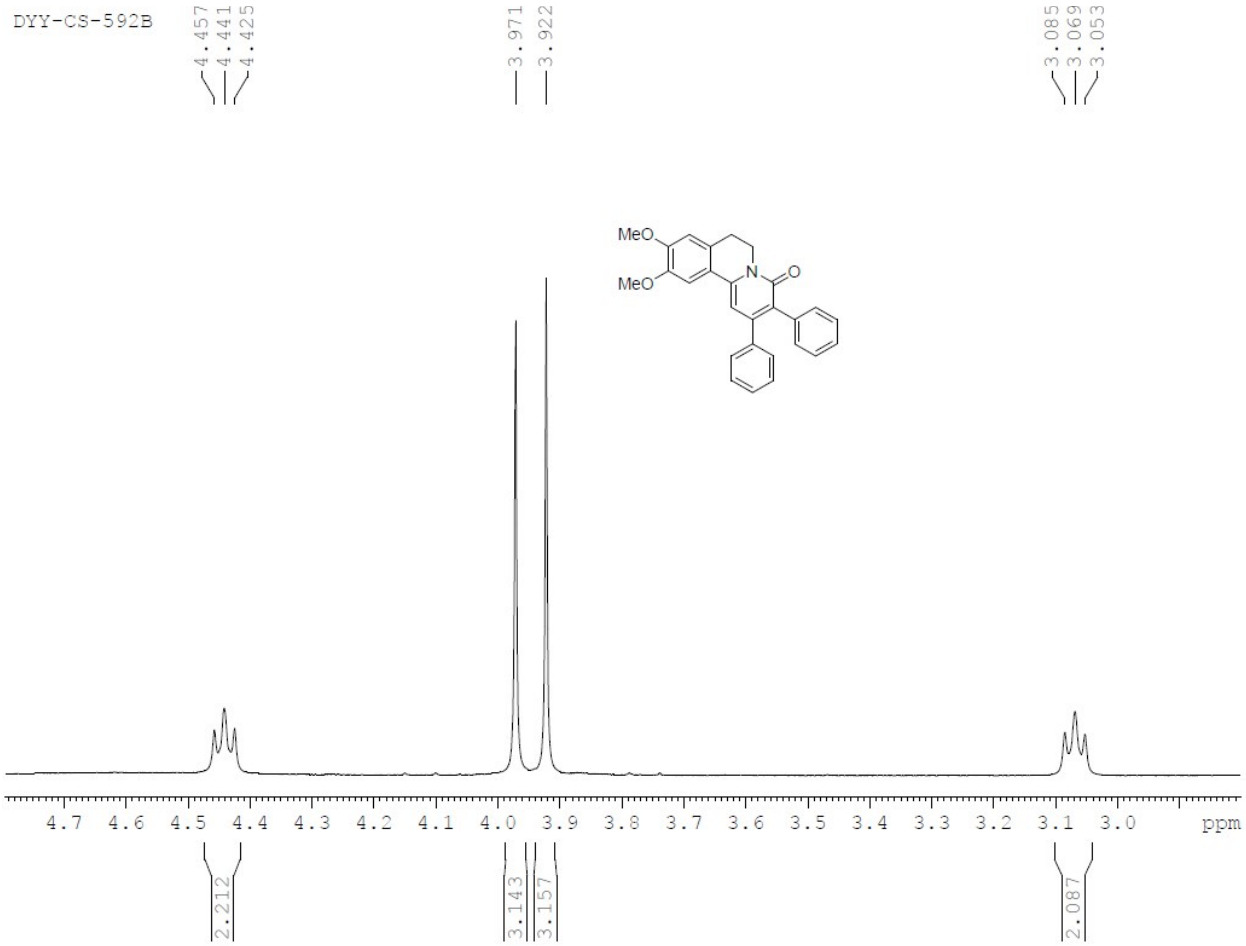
^{1}H NMR of compound **19** ($CDCl_3$)



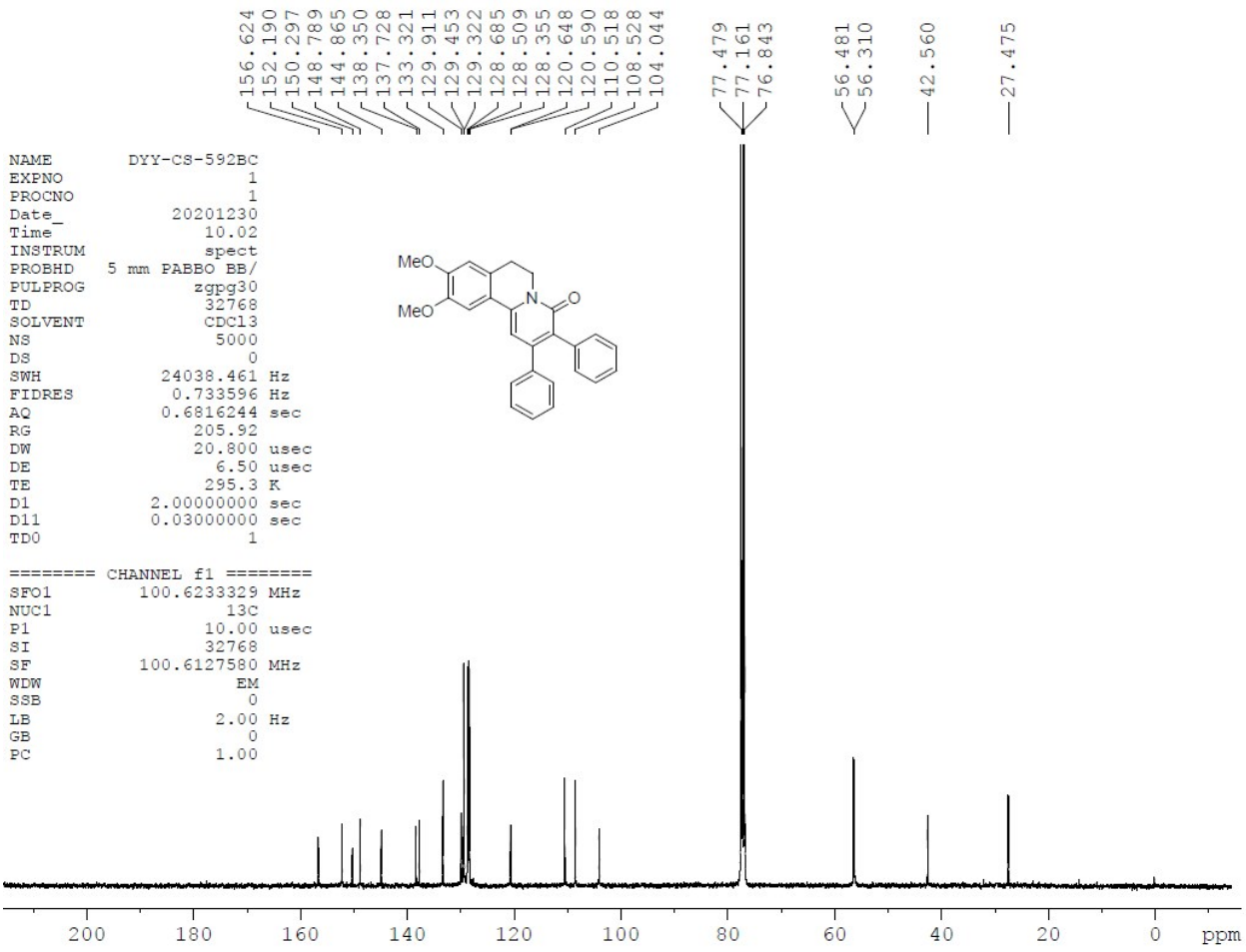
^{1}H NMR of compound **19** ($CDCl_3$)



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



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



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