

## **A multicomponent reaction-initiated synthesis of imidazopyridine-fused isoquinolinones**

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## 1. General Information

All the GBB reactions were conducted in a sealed Biotage microwave reaction vial unless stated otherwise. Flash column chromatography was performed utilizing silica gel (200–300 mesh) under elevated pressure. The  $^1\text{H}$ -NMR, and  $^{13}\text{C}$ -NMR spectroscopic data were acquired using Bruker Mercury Plus 400 MHz or Bruker AVANCE NEO 500 MHz NMR spectrometers. Chemical shifts were expressed in parts per million (ppm) relative to internal TMS for  $^1\text{H}$  NMR data and deuterated solvent for  $^{13}\text{C}$ -NMR data.  $^1\text{H}$  NMR coupling constants were expressed in Hz, with multiplicity denoted as follows: s (singlet); d (doublet); t (triplet); q (quartet); m (multiplet); dd (doublet of doublets); and td (triplet of doublets). LC-MS were performed on an Agilent 2100 system with  $\text{C}_{18}$  column (5.0  $\mu\text{m}$ , 6.0 x 50 mm). The mobile phases were ACN and  $\text{H}_2\text{O}$  both containing 0.05% trifluoroacetic acid. A linear gradient was used to increase from 25:75 MeOH/ $\text{H}_2\text{O}$  to 100% MeOH in 7.0 min at a flow rate of 0.7 mL/min. UV detections were conducted at 210 nm, 254 nm and 280 nm.

## 2. General procedures for the synthesis of GBB products 4

The GBB reactions for making imidazo[1,2-*a*] pyridines 4 were conducted using aminopyridines 1 (0.5 mmol), isocyanides 3 (0.6 mmol, 1.2 equiv.), and furfuraldehyde 2 (0.6 mmol, 1.2 equiv.) in 3:1 DCM/MeOH (4 mL) using  $\text{Yb}(\text{OTf})_3$  (0.04 mmol, 0.08 equiv.) as a Lewis acid catalyst under microwave irradiation at 100 °C for 1 h (Scheme 2, Table S1). Nineteen distinct adducts 4 were obtained in 89–98% yields. The reaction of GBB adducts 4 with acryloyl chloride 5 (1.5 equiv.) in the presence of  $\text{Et}_3\text{N}$  (2 equiv.) at room temperature in anhydrous  $\text{CH}_2\text{Cl}_2$  for 6 h afforded 19 *N*-acylated compounds 6 in 80–90% yields after flash chromatography with 1:6 EtOAc/hexanes Scheme 2, Table S2) [10].

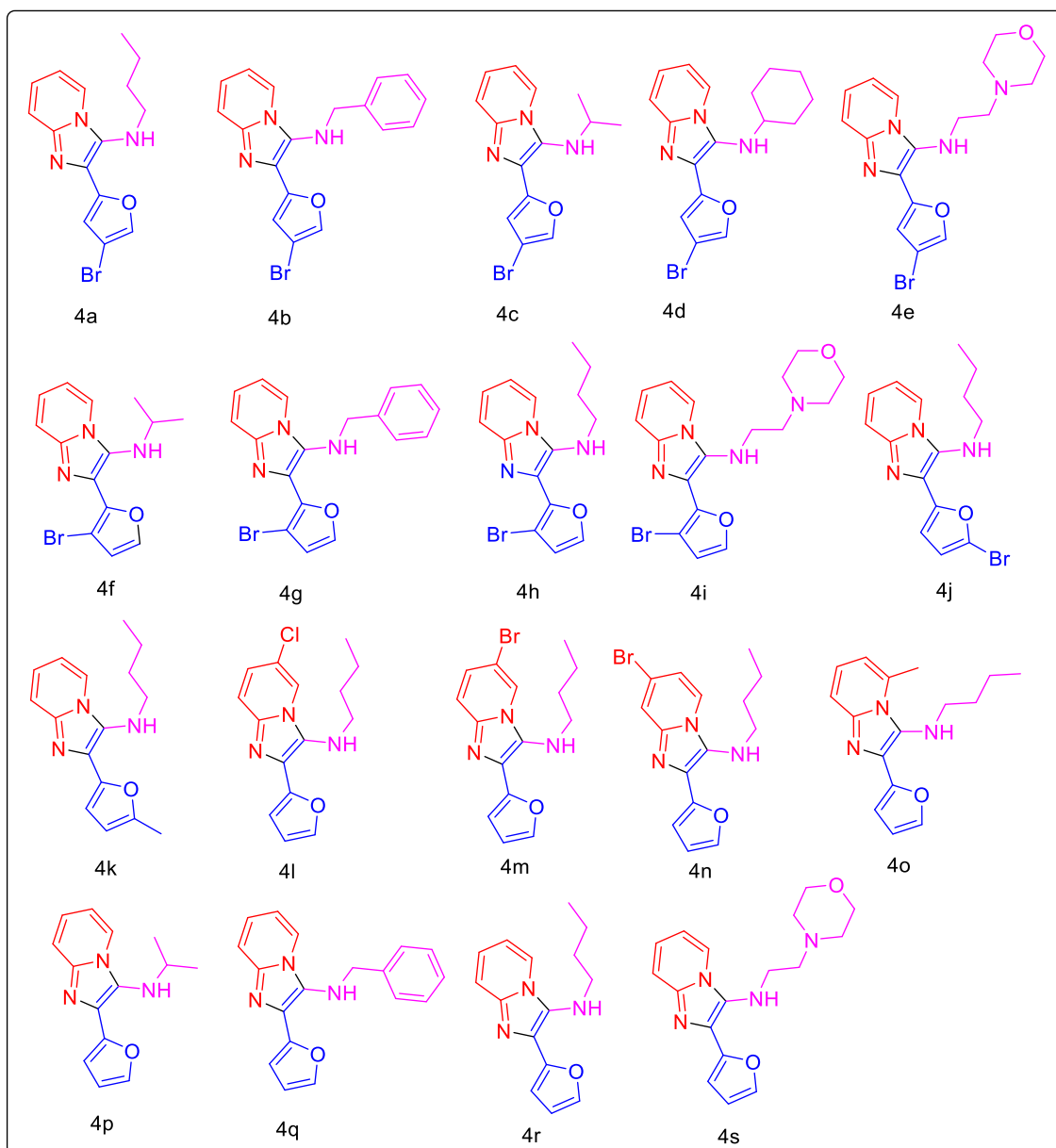
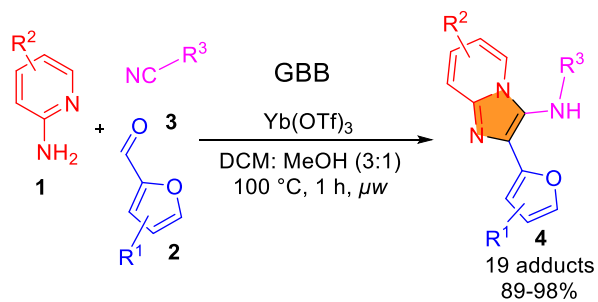
## 3. General procedures of *N*-acylation for the synthesis of products 6

Reactions of 4 with acryloyl chloride 5 (1.5 equiv.) in the presence of  $\text{Et}_3\text{N}$  (2 equiv.) at room temperature in anhydrous  $\text{CH}_2\text{Cl}_2$  for 6 h afforded 19 *N*-acylated compounds 6 in 80–90% yields (Table S2) [10]. Further purification was conducted by flash chromatography with 1:6 EtOAc/hexanes.

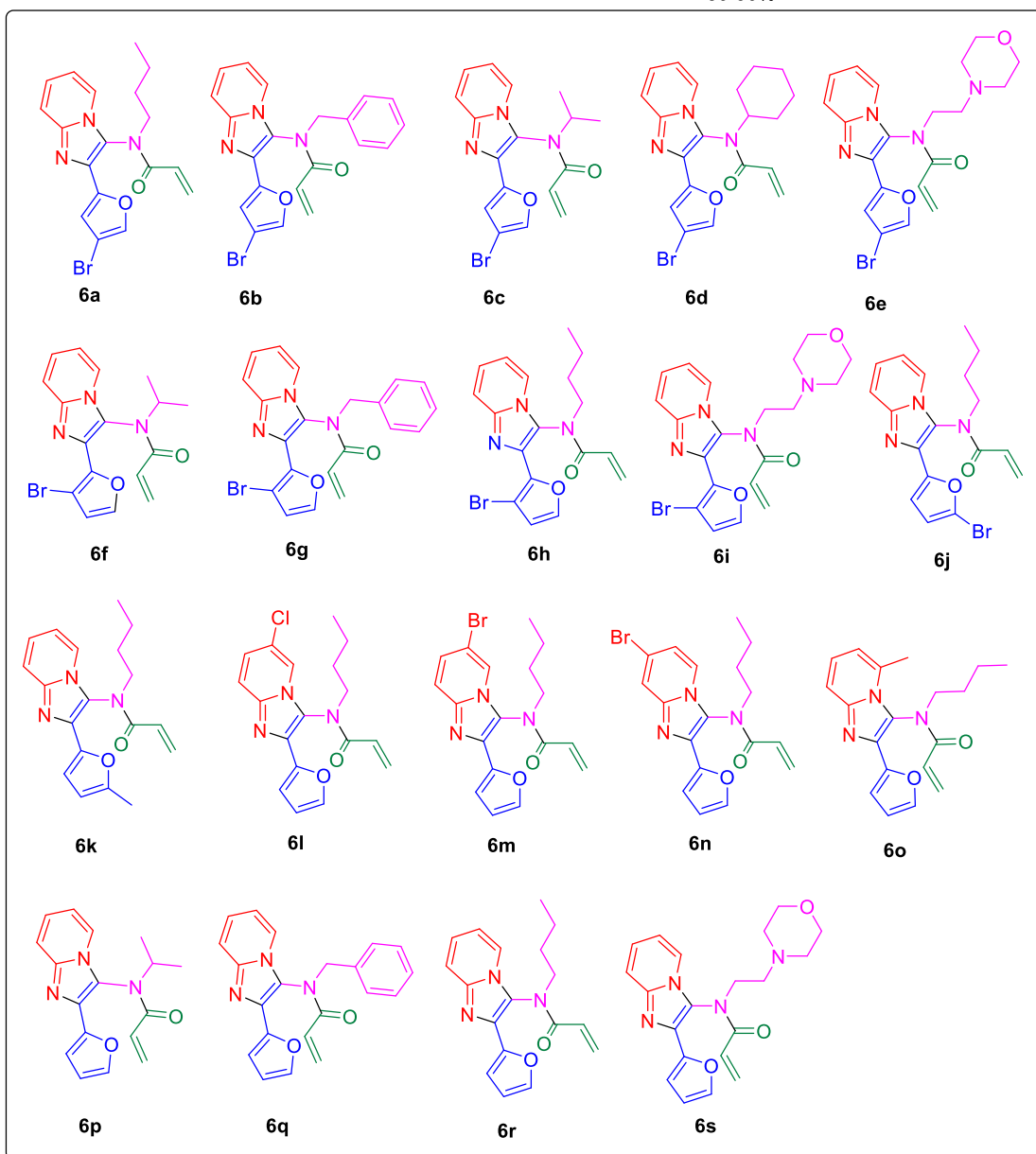
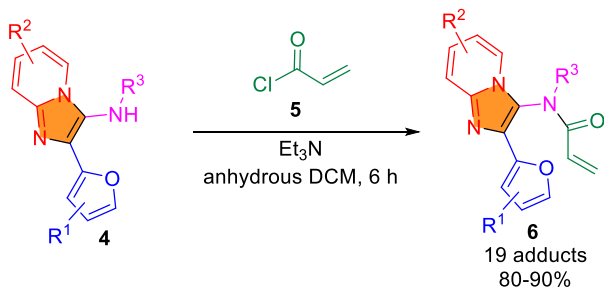
## 4. General procedures for IMDA and dehydrative re-aromatization for making products 8

In the presence of 0.08 equiv. Lewis's acid  $\text{AlCl}_3$ , *N*-acylation products 6 (0.1 mmol) in dichlorobenzene were heated at 180 °C for 4 h (Table 2). The reaction mixtures were checked by LC-MS to follow the formation of DA adducts 7 and the ring opening products 8 (Figure S1). After 4 h, the reaction mixtures were worked up and the crude products were purified 30:70 EtOAc/hexanes. Product structures were confirmed by  $^1\text{H}$ -,  $^{13}\text{C}$ -NMR analysis and x-ray crystal structure analysis of 8a.

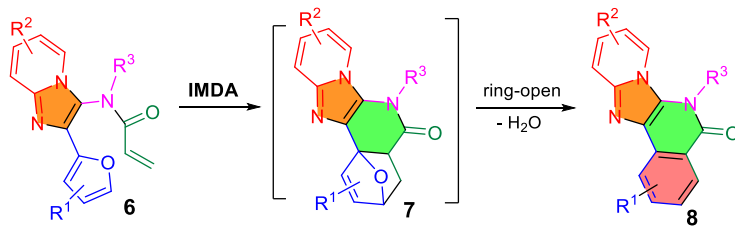
**Table S1.** Three-component GBB cycloaddition for the syntheses of **4**



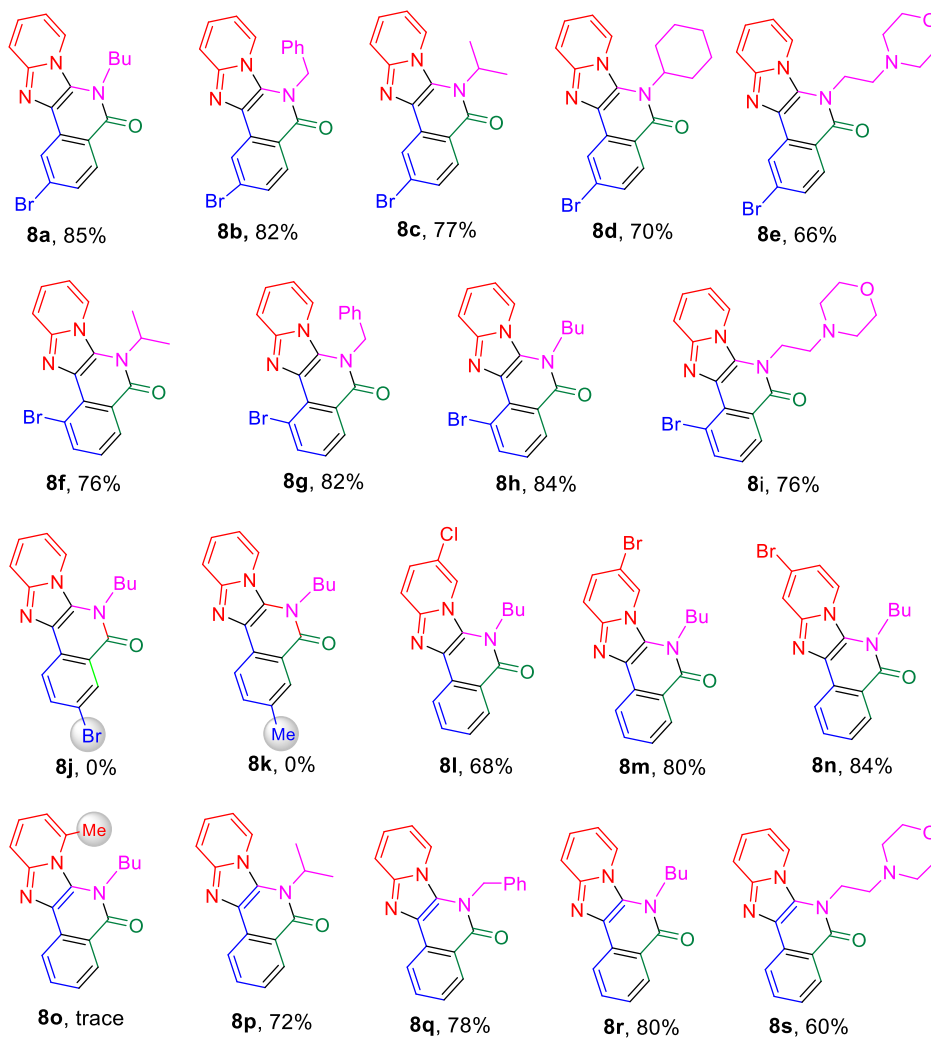
**Table S2.** *N*-acylation of fused imidazo[1,2-*a*]pyridines



**Table S3.** Substrate scope for the reaction of imidazopyridine-fused isoquinolinones **8**<sup>a</sup>



*Substrate scope of various imidazopyridine-fused isoquinolinones*



<sup>a</sup> Reactions of **6** were carried out using AlCl<sub>3</sub> (10 mol%) in 1,2-dichlorobenzene at 180 °C for 4 h.

## 5. LC-MS detection IMDA adduct 7a

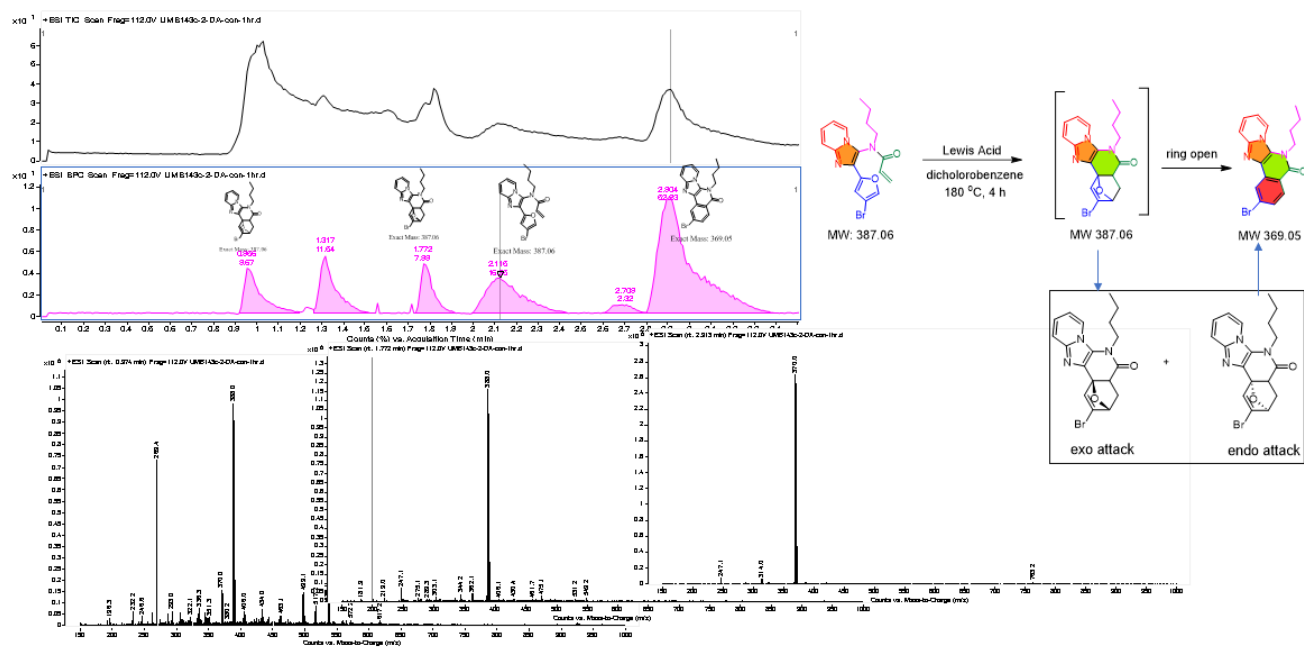
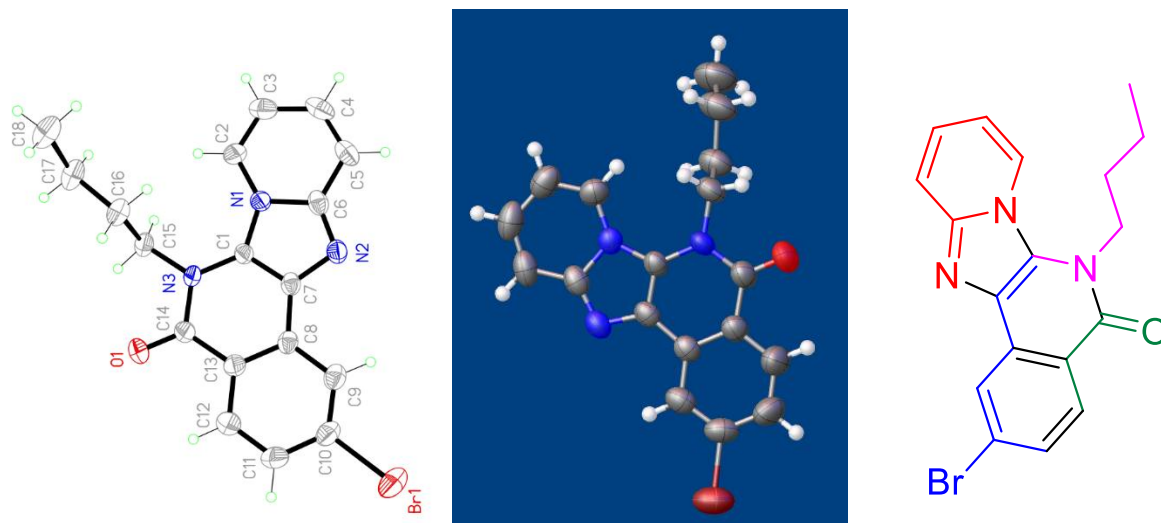


Figure S1: LC-MS of overserving IMDA adduct 7a

## 6. X-ray crystallography report of 8a and 6t

### X-ray Crystallographic Analysis of 8a (CCDC: 2429172)



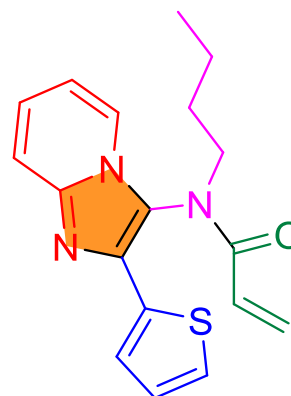
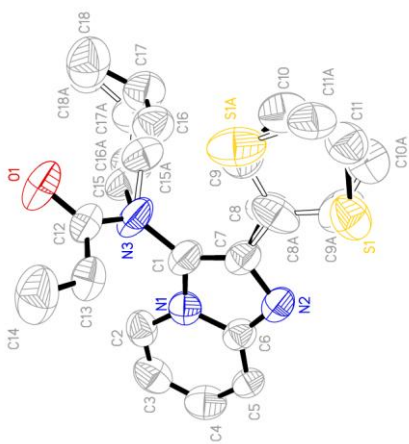
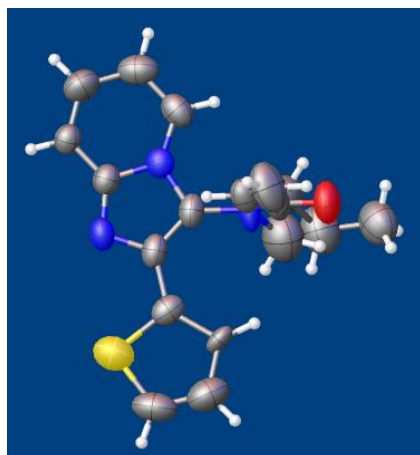
**8a**

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Cell	a = 19.882(3) Å; b = 7.8944(9) Å; c = 20.396(3) Å a = 90°; b = 90°; g = 90°.	
Temperature	300(2) K	
Volume	Calculated 3201.3(7) Å <sup>3</sup>	Reported 3201.3(7) Å <sup>3</sup>
Space group	Pbca	Pbca
Moiety formula	C <sub>18</sub> H <sub>16</sub> BrN <sub>3</sub> O	C <sub>18</sub> H <sub>16</sub> BrN <sub>3</sub> O
Sum formula	C <sub>18</sub> H <sub>16</sub> BrN <sub>3</sub> O	C <sub>18</sub> H <sub>16</sub> BrN <sub>3</sub> O
Z	8	8
μ (mm <sup>-1</sup> )	2.576	2.576
F000	1504	1504
<b>CCDC: 2429172</b>		

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## X-ray Crystallographic Analysis of 6t (CCDC: 2429579)



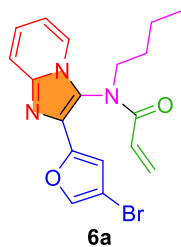
6t

Cell	a = 11.5629(12) Å; b = 11.0333(12) Å; c = 14.0321(16) Å	
Temperature	a = 90°; b = 106.650°; g = 90°. 300(2) K	
Volume	Calculated 1715.1(3) Å <sup>3</sup>	Reported 1715.1(3) Å <sup>3</sup>
Space group	P2 <sub>1</sub> /n	P2 <sub>1</sub> /n
Moiety formula	C <sub>18</sub> H <sub>19</sub> N <sub>3</sub> OS	C <sub>18</sub> H <sub>19</sub> N <sub>3</sub> OS
Sum formula	C <sub>18</sub> H <sub>19</sub> N <sub>3</sub> OS	C <sub>18</sub> H <sub>19</sub> N <sub>3</sub> OS
Z	4	4
μ (mm <sup>-1</sup> )	2.576	2.576
F000	1504	1504
<b>CCDC: 2429579</b>		



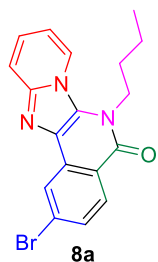
## 7. Analytical characterization data of products 6a and 8.

### *N*-(2-(4-bromofuran-2-yl)imidazo[1,2-*a*]pyridin-3-yl)-*N*-butylacrylamide (**6a**)



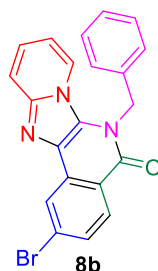
Light yellow solid (90% yield), Chemical Formula:  $C_{18}H_{18}BrN_3O_2$   $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.79 (d,  $J = 6.8$  Hz, 1H), 7.63 (d,  $J = 9.1$  Hz, 1H), 7.48 (s, 1H), 7.36 – 7.26 (m, 1H), 6.92 (t,  $J = 6.8$  Hz, 1H), 6.81 (s, 1H), 6.43 (d,  $J = 16.7$  Hz, 1H), 5.80 (dd,  $J = 16.7, 10.3$  Hz, 1H), 5.50 (d,  $J = 10.4$  Hz, 1H), 3.87 (ddd,  $J = 15.5, 10.1, 5.7$  Hz, 1H), 3.67 (td,  $J = 13.3, 11.9, 5.9$  Hz, 1H), 1.45 – 1.20 (m, 5H), 0.97 – 0.81 (m, 3H).

### 2-bromo-6-butylpyrido[2',1':2,3]imidazo[4,5-*c*]isoquinolin-5(6*H*)-one (**8a**)



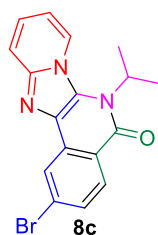
Yellow solid (85% yield), Chemical Formula:  $C_{18}H_{16}BrN_3O$ .  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  8.57 (d,  $J = 1.9$  Hz, 1H), 8.37 – 8.30 (m, 2H), 7.69 (d,  $J = 9.2$  Hz, 1H), 7.63 (dd,  $J = 8.7, 1.9$  Hz, 1H), 7.26 – 7.15 (m, 2H), 6.87 (t,  $J = 7.0$  Hz, 1H), 4.63 (t,  $J = 7.9$  Hz, 2H), 1.88 (q,  $J = 7.9$  Hz, 2H), 1.59 – 1.50 (m, 2H), 1.02 (t,  $J = 7.4$  Hz, 3H).  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  158.49, 136.25, 134.18, 127.15, 124.05, 122.95, 122.55, 120.08, 118.14, 188.01, 116.2, 114.42, 111.95, 107.15, 41.19, 29.84, 17.89, 11.70. HRMS (ESI) calcd for  $C_{18}H_{16}BrN_3O$   $m/z$ : 369.0477, found 369.0480.

### 6-benzyl-2-bromopyrido[2',1':2,3]imidazo[4,5-*c*]isoquinolin-5(6*H*)-one (**8b**)



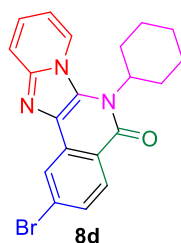
Light yellow solid (82% yield),  $C_{21}H_{14}BrN_3O$ .  $^1H$  NMR (399 MHz,  $CDCl_3$ )  $\delta$  8.55 (d,  $J = 2.0$  Hz, 1H), 8.40 – 8.31 (m, 5H), 7.70 – 7.61 (m, 4H), 7.17 (dd,  $J = 9.6, 1.8$  Hz, 2H), 4.61 (t,  $J = 7.9$  Hz, 2H).  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  150.11, 137.22, 130.26, 130.15, 128.91, 128.83, 126.34, 126.27, 125.09, 121.78, 120.76, 119.89, 105.06, 104.92, 46.57. HRMS (ESI) calcd for  $C_{21}H_{14}BrN_3O$   $m/z$ : 403.0320, found 403.0341.

### 2-bromo-6-isopropylpyrido[2',1':2,3]imidazo[4,5-*c*]isoquinolin-5(6*H*)-one (**8c**)



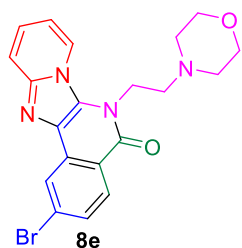
Off-white solid (77% yield), Chemical Formula:  $C_{17}H_{14}BrN_3O$ .  $^1H$  NMR (399 MHz,  $CDCl_3$ )  $\delta$  8.57 (d,  $J = 1.9$  Hz, 1H), 8.37 – 8.30 (m, 2H), 7.69 (d,  $J = 9.2$  Hz, 1H), 7.63 (dd,  $J = 8.7, 1.9$  Hz, 1H), 7.26 – 7.15 (m, 1H), 6.87 (t,  $J = 7.0$  Hz, 1H), 5.09 – 4.75 (m, 1H), 1.89 – 1.83 (m, 6H).  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  168.31, 148.22, 131.85, 125.07, 124.08, 120.93, 120.05, 111.53, 110.24, 108.22, 106.30, 44.92, 20.05. HRMS (ESI) calcd for  $C_{17}H_{14}BrN_3O$   $m/z$ : 355.0320, found 355.0612.

### 2-bromo-6-cyclohexylpyrido[2',1':2,3]imidazo[4,5-*c*]isoquinolin-5(6*H*)-one (**8d**)



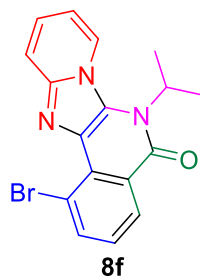
Off-white solid (70% yield), Chemical Formula:  $C_{20}H_{18}BrN_3O$ .  $^1H$  NMR (399 MHz,  $CDCl_3$ )  $\delta$  8.38 – 8.31 (m, 1H), 8.26 (d,  $J = 8.5$  Hz, 0H), 8.14 (d,  $J = 7.4$  Hz, 1H), 7.69 (d,  $J = 9.3$  Hz, 1H), 7.50 – 7.43 (m, 1H), 7.18 (s, 0H), 6.89 (t,  $J = 7.0$  Hz, 1H), 4.39 (d,  $J = 12.1$  Hz, 1H), 2.95 – 2.85 (m, 2H), 1.99 (dd,  $J = 26.2, 11.4$  Hz, 5H), 0.85 (d,  $J = 17.3$  Hz, 3H).  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  167.43, 143.08, 135.90, 135.21, 130.56, 128.03, 126.58, 126.32, 125.90, 124.90, 121.56, 117.85, 113.39, 48.17, 30.63, 20.31, 13.70.

*2-bromo-6-(2-morpholinoethyl)pyrido[2',1':2,3]imidazo[4,5-c]isoquinolin-5(6H)-one (8e)*



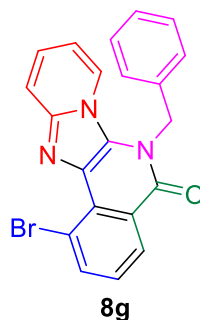
Yellow solid (66% yield), Chemical Formula:  $C_{20}H_{19}BrN_4O_2$ ,  $^1H$  NMR (399 MHz,  $CDCl_3$ )  $\delta$  8.72 (d,  $J = 7.9$  Hz, 1H), 8.01 (s, 1H), 7.69 (s, 1H), 7.25 (d,  $J = 2.0$  Hz, 4H), 4.74 (d,  $J = 24.6$  Hz, 2H), 3.64 (s, 2H), 3.34 (s, 4H), 2.95 (d,  $J = 1.9$  Hz, 4H).  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  167.19, 147.17, 143.47, 130.29, 126.68, 121.92, 120.14, 119.91, 117.40, 111.64, 109.15, 63.15, 45.38, 44.68, 35.23, 28.69.

*1-bromo-6-isopropylpyrido[2',1':2,3]imidazo[4,5-c]isoquinolin-5(6H)-one (8f)*



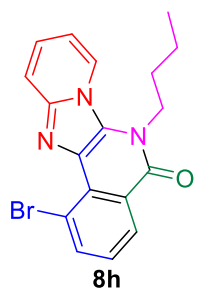
Off-white solid (70% yield), Chemical Formula:  $C_{17}H_{14}BrN_3O$ .  $^1H$  NMR (399 MHz,  $CDCl_3$ )  $\delta$  8.52 – 8.46 (m, 1H), 8.23 (d,  $J = 7.2$  Hz, 1H), 8.03 (d,  $J = 8.4$  Hz, 1H), 7.80 (d,  $J = 9.2$  Hz, 1H), 7.36 (t,  $J = 7.9$  Hz, 1H), 7.25 (d,  $J = 1.2$  Hz, 1H), 6.88 (t,  $J = 7.0$  Hz, 1H), 5.09 – 4.75 (m, 1H), 1.89 – 1.83 (m, 6H).  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  143.09, 129.30, 128.13, 125.96, 122.10, 118.48, 115.95, 113.54, 49.56, 20.76, 19.81. HRMS (ESI) calcd for  $C_{17}H_{14}BrN_3O$  m/z): 355.0320, found 355.0718.

*6-benzyl-1-bromopyrido[2',1':2,3]imidazo[4,5-c]isoquinolin-5(6H)-one (8g)*



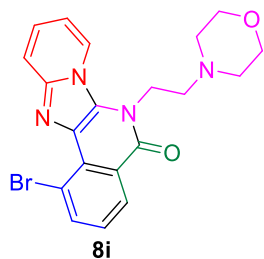
Light yellow solid (82% yield), Chemical Formula:  $C_{21}H_{14}BrN_3O$ .  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.53 (dt,  $J = 9.1, 1.2$  Hz, 1H), 7.42 (dd,  $J = 3.7, 1.1$  Hz, 1H), 7.36 (dd,  $J = 5.1, 1.1$  Hz, 1H), 7.21 – 7.04 (m, 6H), 7.01 (dt,  $J = 6.8, 1.2$  Hz, 1H), 6.55 – 6.44 (m, 2H), 4.61 (t,  $J = 7.9$  Hz, 2H).  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  139.46, 135.54, 129.48, 129.45, 127.99, 127.36, 125.39, 123.62, 122.99, 119.63, 112.92, 47.40. HRMS (ESI) calcd for  $C_{21}H_{14}BrN_3O$  m/z): 403.0320, found 403.0568.

*1-bromo-6-butylpyrido[2',1':2,3]imidazo[4,5-c]isoquinolin-5(6H)-one (8h)*



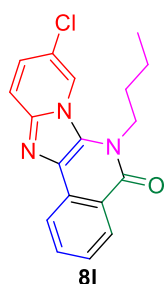
Yellow solid (84% yield), Chemical Formula:  $C_{18}H_{16}BrN_3O$ .  $^1H$  NMR (399 MHz,  $CDCl_3$ )  $\delta$  8.57 (dd,  $J = 8.0, 1.4$  Hz, 1H), 8.36 (d,  $J = 7.3$  Hz, 1H), 8.09 – 8.02 (m, 1H), 7.80 (d,  $J = 9.3$  Hz, 1H), 7.42 – 7.33 (m, 1H), 7.25 (d,  $J = 1.2$  Hz, 1H), 7.22 – 7.13 (m, 1H), 6.91 – 6.83 (m, 1H), 4.67 (t,  $J = 7.8$  Hz, 2H), 1.92 (t,  $J = 8.0$  Hz, 2H), 1.56 (q,  $J = 7.5$  Hz, 2H), 1.04 (t,  $J = 7.4$  Hz, 3H).  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  160.61, 141.77, 139.13, 131.05, 130.28, 129.15, 127.23, 126.55, 123.31, 122.58, 120.05, 117.10, 113.25, 43.26, 31.91, 19.96, 13.78. HRMS (ESI) calcd for  $C_{18}H_{16}BrN_3O$  m/z): 369.0477, found 369.0424.

*1-bromo-6-(2-morpholinoethyl)pyrido[2',1':2,3]imidazo[4,5-c]isoquinolin-5(6H)-one (8i)*



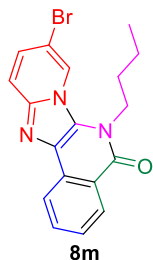
Deep yellow solid (76% yield), Chemical Formula: C<sub>20</sub>H<sub>19</sub>BrN<sub>4</sub>O<sub>2</sub>. <sup>1</sup>H NMR (399 MHz, CDCl<sub>3</sub>) δ 8.57 (dd, *J* = 8.0, 1.4 Hz, 1H), 8.36 (d, *J* = 7.3 Hz, 1H), 8.09 – 8.02 (m, 1H), 7.80 (d, *J* = 9.3 Hz, 1H), 7.42 – 7.33 (m, 1H), 7.22 – 7.13 (m, 1H), 6.91 – 6.83 (m, 1H), 4.45 (ddd, *J* = 14.0, 7.3, 4.5 Hz, 2H), 3.61 – 3.50 (m, 3H), 3.45 (d, *J* = 7.1 Hz, 4H), 2.62 – 2.52 (m, 3H), 2.29 (ddd, *J* = 12.7, 7.1, 4.1 Hz, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 149.03, 132.73, 123.27, 118.21, 117.97, 117.02, 116.28, 115.91, 115.54, 115.26, 114.10, 106.98, 111.05, 100.31, 54.55, 43.29, 41.83, 35.27.

*6-butyl-9-chloropyrido[2',1':2,3]imidazo[4,5-c]isoquinolin-5(6H)-one (8l)*



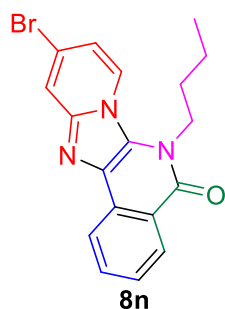
White solid (76% yield), Chemical Formula: C<sub>18</sub>H<sub>16</sub>ClN<sub>3</sub>O. <sup>1</sup>H NMR (399 MHz, CDCl<sub>3</sub>) δ 8.52 (dd, *J* = 14.1, 8.1 Hz, 2H), 8.32 (d, *J* = 7.1 Hz, 1H), 7.86 – 7.77 (m, 1H), 7.58 (t, *J* = 7.5 Hz, 1H), 7.32 – 7.22 (m, 1H), 7.25 (s, 2H), 7.25 (s, 2H), 6.82 (t, *J* = 7.2 Hz, 1H), 4.65 (t, *J* = 7.9 Hz, 2H), 1.95 – 1.86 (m, 2H), 1.64 – 1.55 (m, 2H), 1.04 (t, *J* = 7.4 Hz, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 132.99, 129.22, 127.54, 124.76, 122.46, 121.53, 112.29, 43.05, 32.15, 19.97, 13.80. HRMS (ESI) calcd for C<sub>18</sub>H<sub>16</sub>ClN<sub>3</sub>O: 325.0982, found 325.0915.

*9-bromo-6-butylpyrido[2',1':2,3]imidazo[4,5-c]isoquinolin-5(6H)-one (8m)*



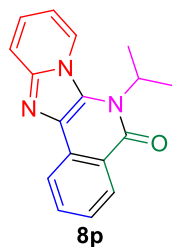
White solid (80% yield), Chemical Formula: C<sub>18</sub>H<sub>16</sub>BrN<sub>3</sub>O. <sup>1</sup>H NMR (399 MHz, CDCl<sub>3</sub>) δ 8.51 (d, *J* = 8.7 Hz, 2H), 8.39 (d, *J* = 7.9 Hz, 1H), 7.81 (t, *J* = 7.7 Hz, 1H), 7.64 – 7.50 (m, 2H), 7.23 (dd, *J* = 13.4, 3.7 Hz, 2H), 4.63 (t, *J* = 7.8 Hz, 2H), 1.91 (q, *J* = 7.8 Hz, 2H), 1.12 – 1.03 (m, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 133.13, 129.38, 127.53, 126.73, 122.63, 121.93, 119.50, 42.61, 29.69, 19.91, 13.76. HRMS (ESI) calcd for C<sub>18</sub>H<sub>16</sub>BrN<sub>3</sub>O m/z: 369.0477, found 369.0432.

*10-bromo-6-butylpyrido[2',1':2,3]imidazo[4,5-c]isoquinolin-5(6H)-one (8n)*



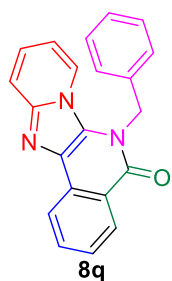
White solid (84% yield), Chemical Formula: C<sub>18</sub>H<sub>16</sub>BrN<sub>3</sub>O. <sup>1</sup>H NMR (399 MHz, CDCl<sub>3</sub>) δ 8.55 – 8.48 (m, 1H), 8.45 – 8.32 (m, 2H), 7.85 – 7.76 (m, 1H), 7.75 – 7.68 (m, 1H), 7.61 – 7.52 (m, 1H), 7.23 – 7.14 (m, 1H), 4.67 (t, *J* = 7.9 Hz, 2H), 1.92 (t, *J* = 7.7 Hz, 2H), 1.58 (h, *J* = 7.4 Hz, 2H), 1.16 (s, 2H), 1.08 – 1.00 (m, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 167.19, 147.17, 143.47, 130.29, 129.38, 126.68, 122.36, 121.92, 120.14, 119.91, 117.40, 111.64, 109.15, 48.15, 30.38, 20.23, 13.69. HRMS (ESI) calcd for C<sub>18</sub>H<sub>16</sub>BrN<sub>3</sub>O m/z: 369.0477, found 369.0425.

6-isopropylpyrido[2',1':2,3]imidazo[4,5-c]isoquinolin-5(6H)-one (**8p**)



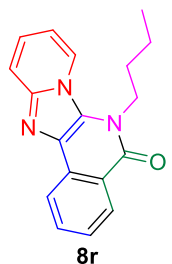
White solid (84% yield), Chemical Formula: C<sub>17</sub>H<sub>15</sub>N<sub>3</sub>O. <sup>1</sup>H NMR (399 MHz, CDCl<sub>3</sub>) δ 8.51 (d, 1H), 8.40 (d, 1H), 8.37 (d, 1H), 7.84 – 7.81 (m, 1H), 7.74 – 7.72 (m, 1H), 7.57 – 7.54 (m, 1H), 7.19 (t, 1H), 6.86 (t, *J* = 7.7 Hz, 1H), 4.93 (m, 1H), 1.87 (d, 6H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 143.05, 136.29, 130.21, 128.49, 128.42, 126.14, 122.38, 117.62, 115.35, 112.07, 51.15, 24.22. HRMS (ESI) calcd for C<sub>17</sub>H<sub>15</sub>N<sub>3</sub>O. *m/z*: 277.1215, found 277.1205.

6-benzylpyrido[2',1':2,3]imidazo[4,5-c]isoquinolin-5(6H)-one (**8q**)



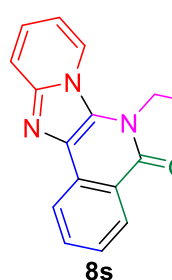
Light yellow solid (82% yield), Chemical Formula: C<sub>21</sub>H<sub>15</sub>N<sub>3</sub>O. <sup>1</sup>H NMR (399 MHz, CDCl<sub>3</sub>) δ 8.57 (d, *J* = 8.0 Hz, 1H), 8.48 (dd, *J* = 16.3, 8.0 Hz, 1H), 8.37 (d, *J* = 8.0 Hz, 1H), 8.26 (d, *J* = 7.8 Hz, 1H), 8.19 – 8.12 (m, 1H), 7.90 – 7.77 (m, 1H), 7.72 – 7.60 (m, 1H), 7.62 – 7.53 (m, 1H), 7.40 – 7.22 (m, 3H), 7.12 – 7.04 (m, 1H), 6.89 – 6.82 (m, 1H), 6.60 (t, *J* = 7.0 Hz, 1H), 4.62 (d, *J* = 7.9 Hz, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 133.36, 133.12, 129.61, 129.44, 129.35, 127.90, 127.44, 127.32, 125.45, 123.17, 122.94, 121.93, 117.64, 114.57, 46.85. HRMS (ESI) calcd for C<sub>21</sub>H<sub>15</sub>N<sub>3</sub>O *m/z*: 325.1215, found 325.1232.

6-butylpyrido[2',1':2,3]imidazo[4,5-c]isoquinolin-5(6H)-one (**8r**)



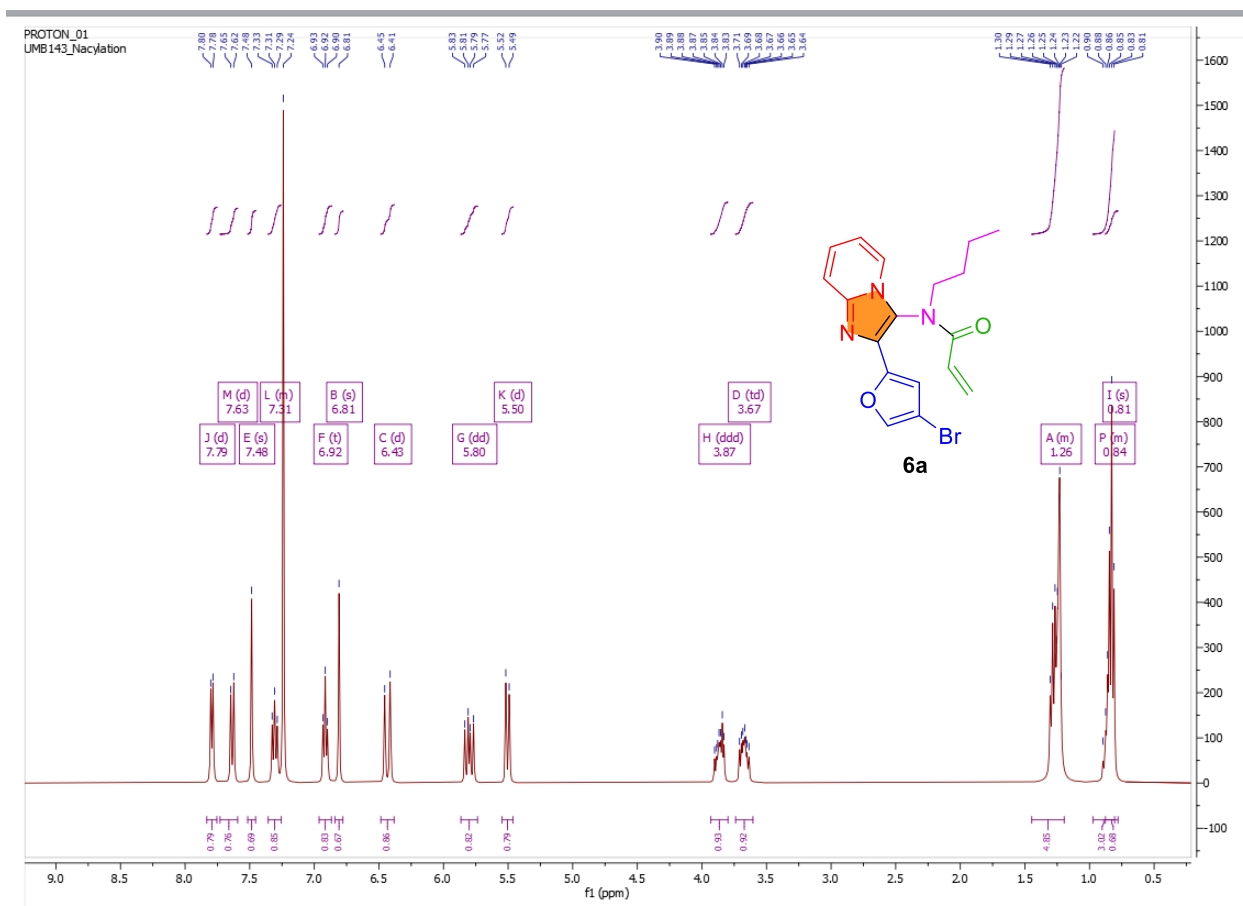
Deep yellow solid (80% yield), Chemical Formula: C<sub>18</sub>H<sub>17</sub>N<sub>3</sub>O. <sup>1</sup>H NMR (399 MHz, CDCl<sub>3</sub>) δ 8.55 – 8.48 (m, 1H), 8.45 – 8.32 (m, 2H), 7.85 – 7.76 (m, 1H), 7.75 – 7.68 (m, 1H), 7.61 – 7.52 (m, 1H), 7.28 – 7.14 (m, 1H), 6.92 – 6.83 (m, 1H), 4.67 (t, *J* = 7.9 Hz, 2H), 1.92 (t, *J* = 7.7 Hz, 2H), 1.58 (h, *J* = 7.4 Hz, 2H), 1.08 – 1.00 (m, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 161.38, 143.03, 132.97, 131.60, 129.30, 127.15, 124.13, 123.46, 122.88, 122.77, 121.85, 119.15, 112.90, 42.77, 32.17, 20.00, 13.82. HRMS (ESI) calcd for C<sub>18</sub>H<sub>17</sub>N<sub>3</sub>O *m/z*: 291.1372, found 291.1369.

6-(2-morpholinoethyl)pyrido[2',1':2,3]imidazo[4,5-c]isoquinolin-5(6H)-one (**8s**)

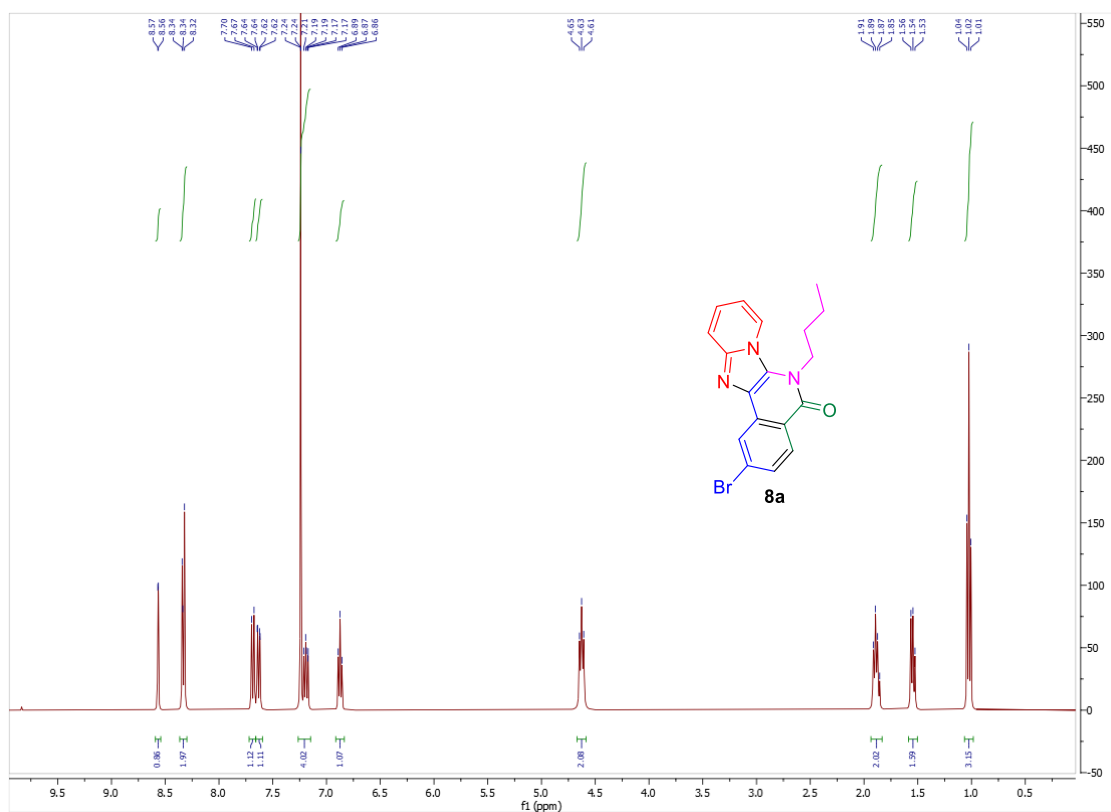


Yellow solid (60% yield), Chemical Formula: C<sub>20</sub>H<sub>20</sub>N<sub>4</sub>O<sub>2</sub>. <sup>1</sup>H NMR (399 MHz, CDCl<sub>3</sub>) δ 8.77 (s, 1H), 8.50 (d, *J* = 8.2 Hz, 1H), 8.42 (d, *J* = 8.0 Hz, 1H), 7.82 (t, *J* = 7.5 Hz, 1H), 7.72 (d, *J* = 9.4 Hz, 1H), 7.57 (t, *J* = 7.7 Hz, 1H), 7.25 (s, 2H), 6.89 (t, *J* = 6.7 Hz, 1H), 4.82 (s, 2H), 3.72 (s, 5H), 3.63 (s, 2H), 2.95 (s, 2H), 2.88 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 168.07, 149.27, 143.22, 132.67, 131.59, 126.98, 126.41, 123.56, 117.06, 111.83, 111.22, 108.31, 66.58, 56.52, 52.12, 44.23.

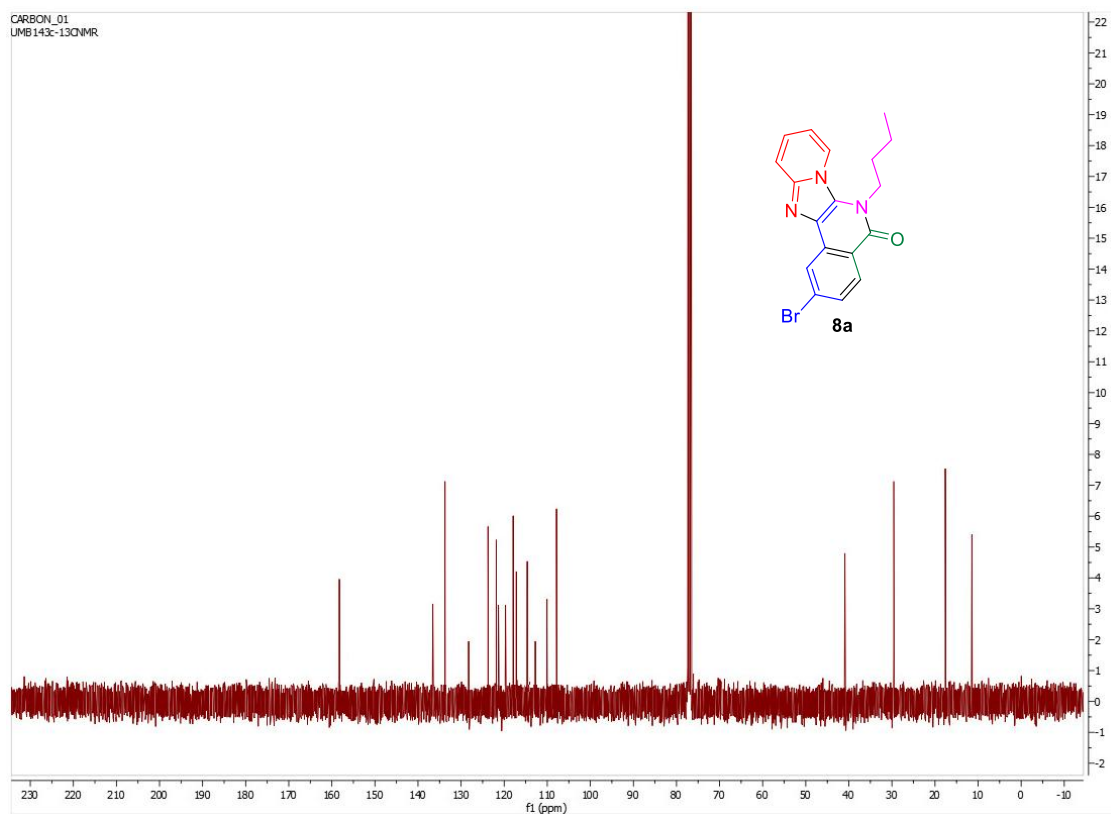
## 8. $^1\text{H-NMR}$ , $^{13}\text{C-NMR}$ spectra of products 6a and 8



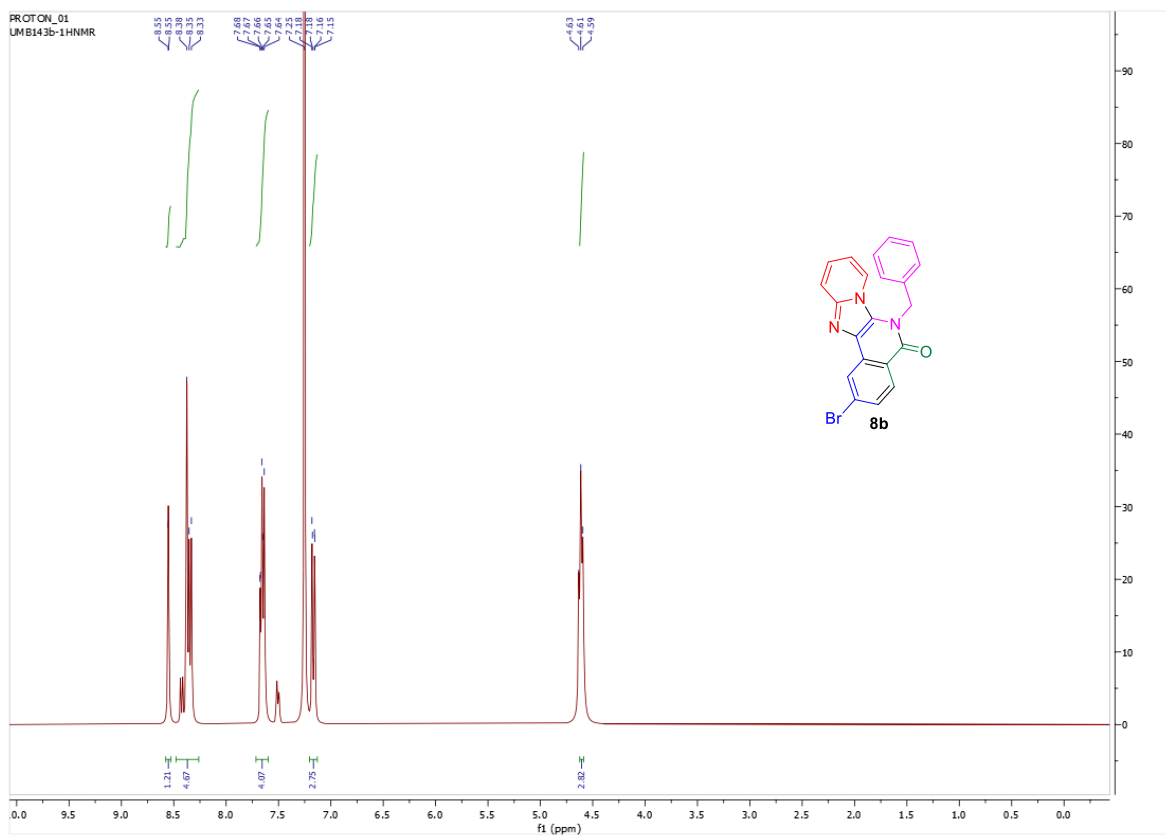
$^1\text{H NMR}$  of **6a**



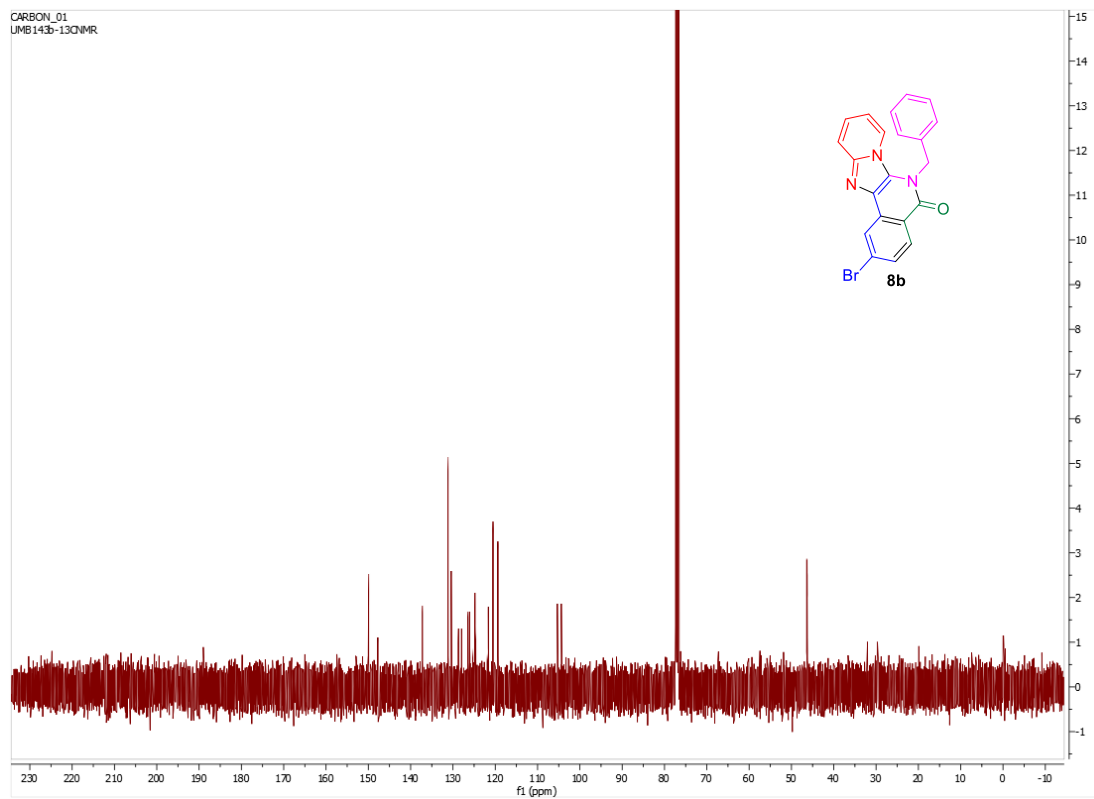
**<sup>1</sup>H NMR of 8a**



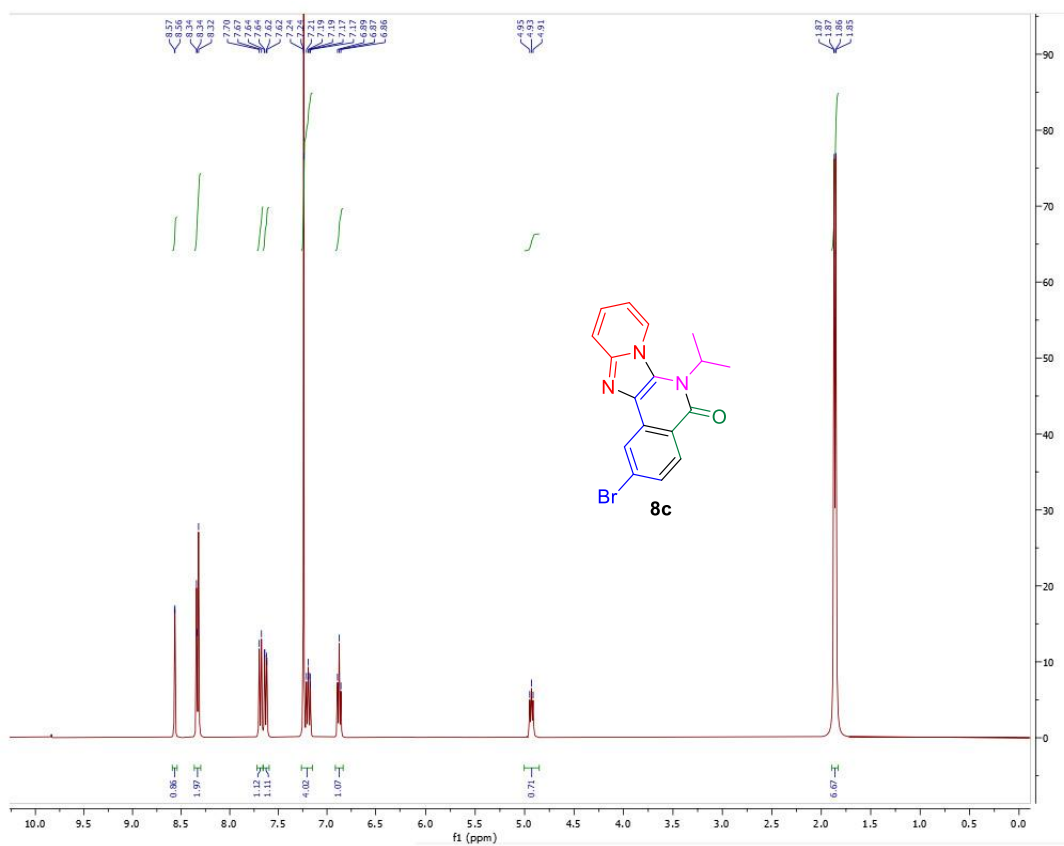
**<sup>13</sup>C NMR of 8a**



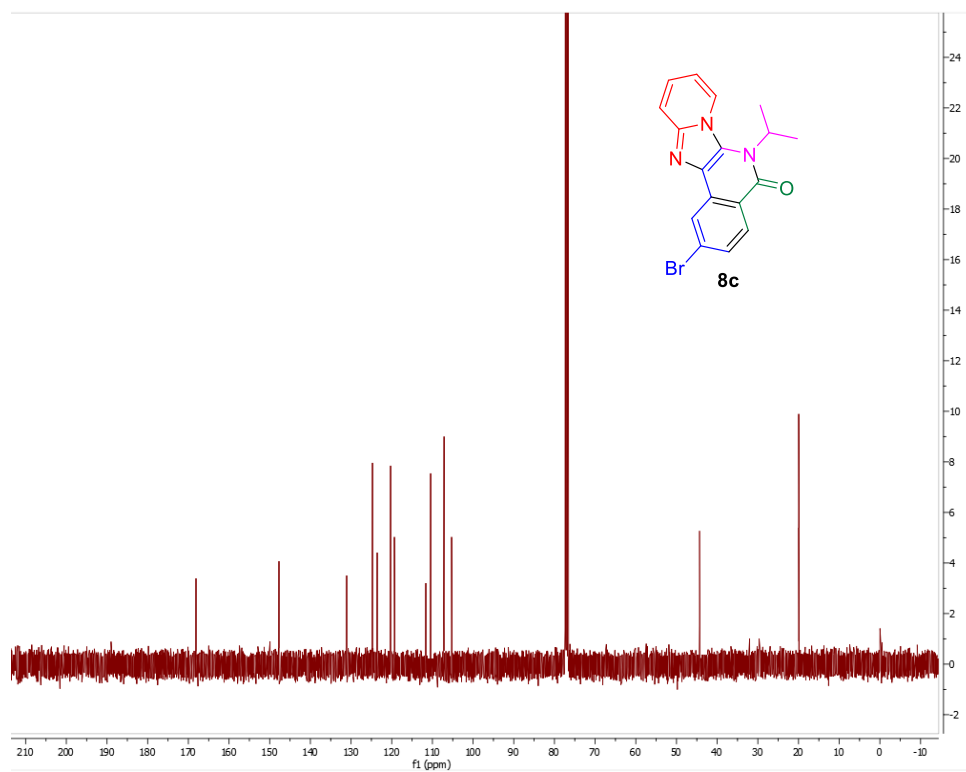
<sup>1</sup>H NMR of **8b**



<sup>13</sup>C NMR of **8b**

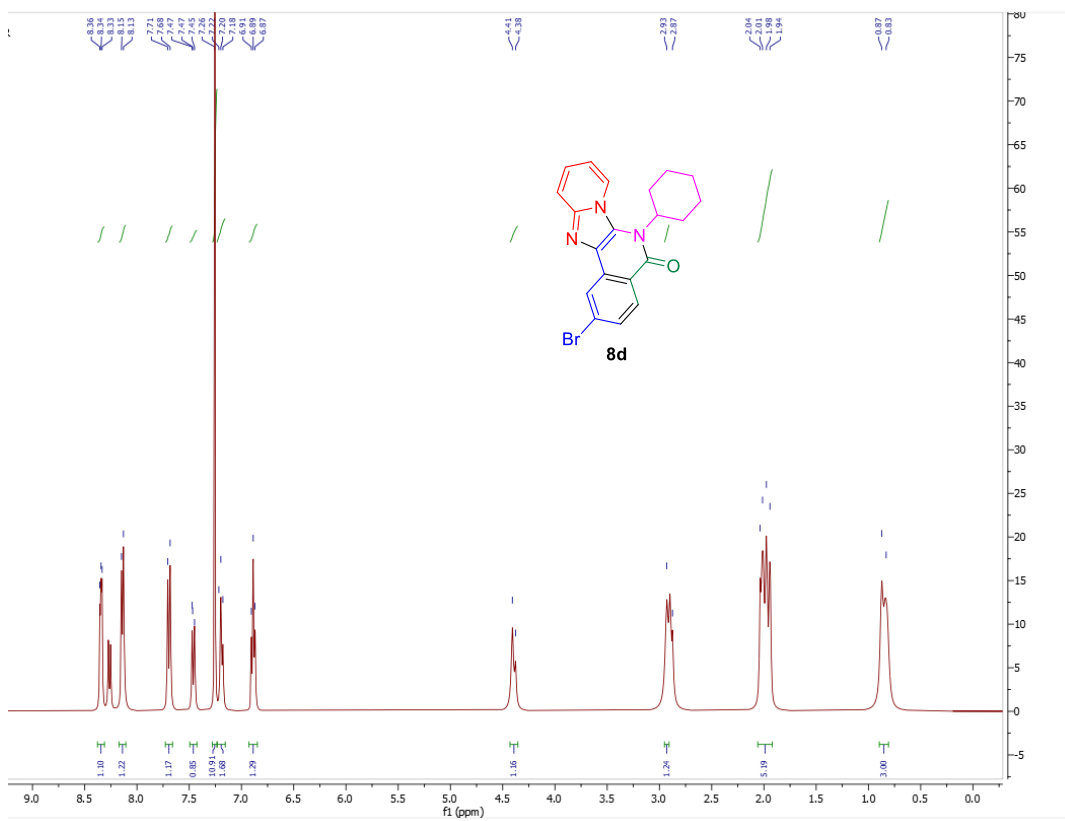


**<sup>1</sup>H NMR of 8c**

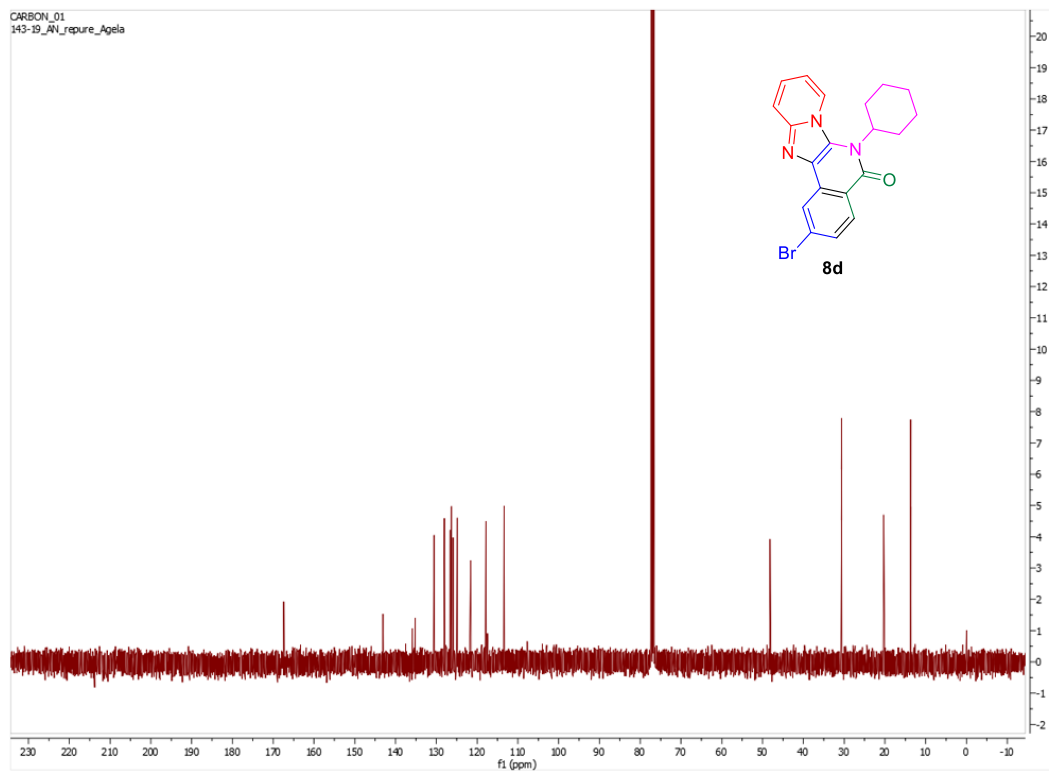


**<sup>13</sup>C NMR of 8c**

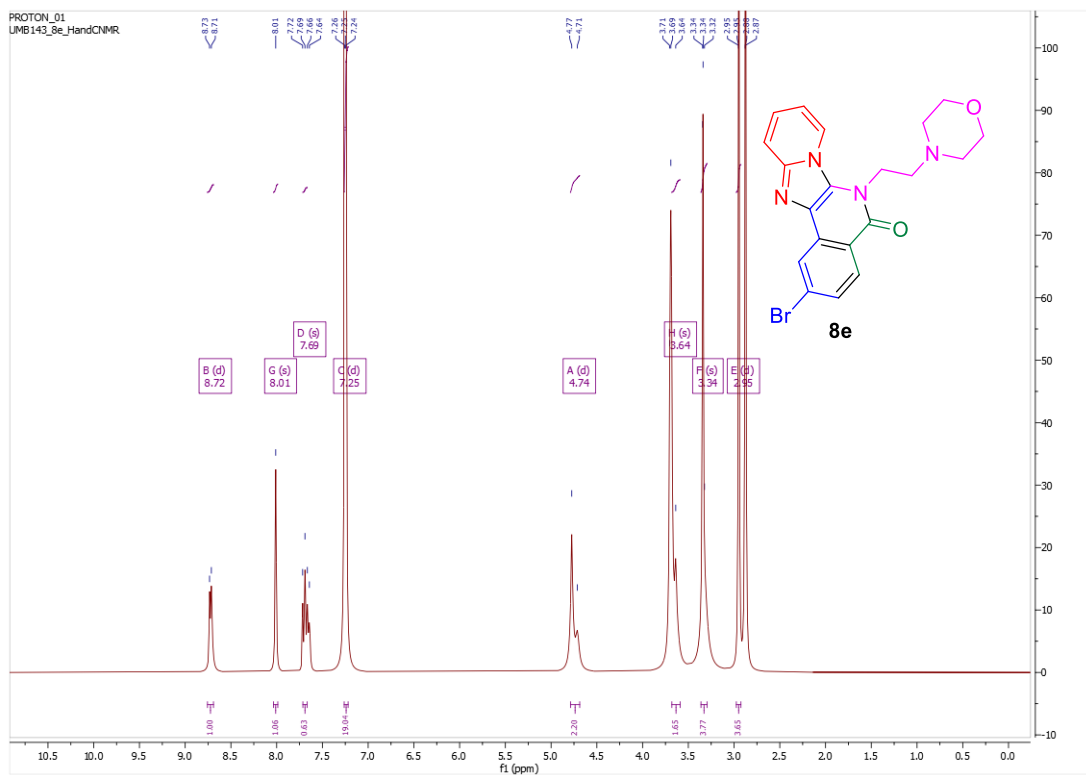




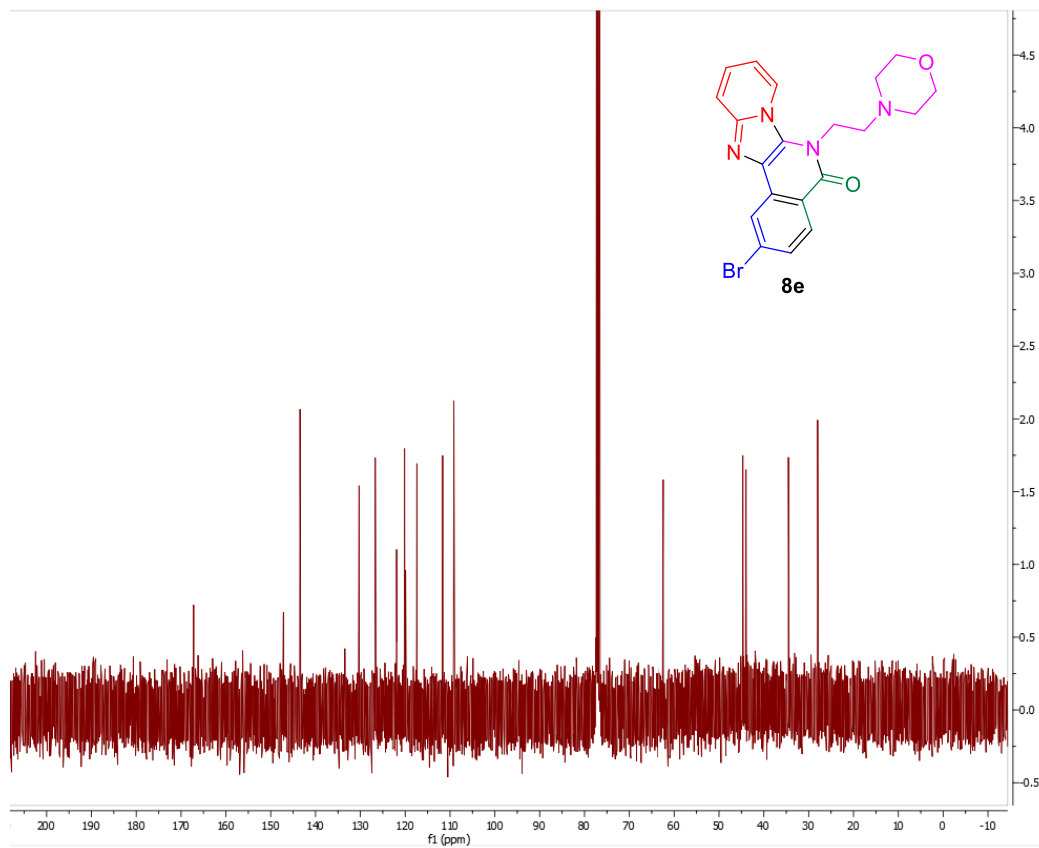
**<sup>1</sup>H NMR of 8d**



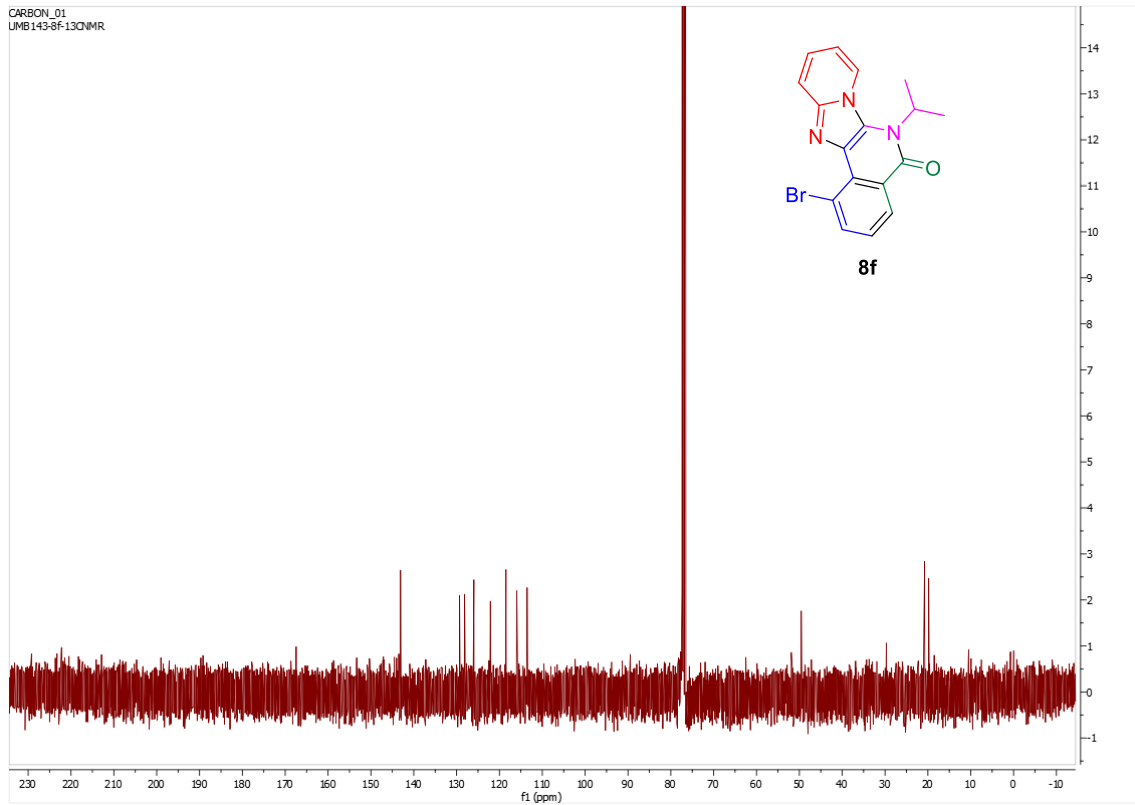
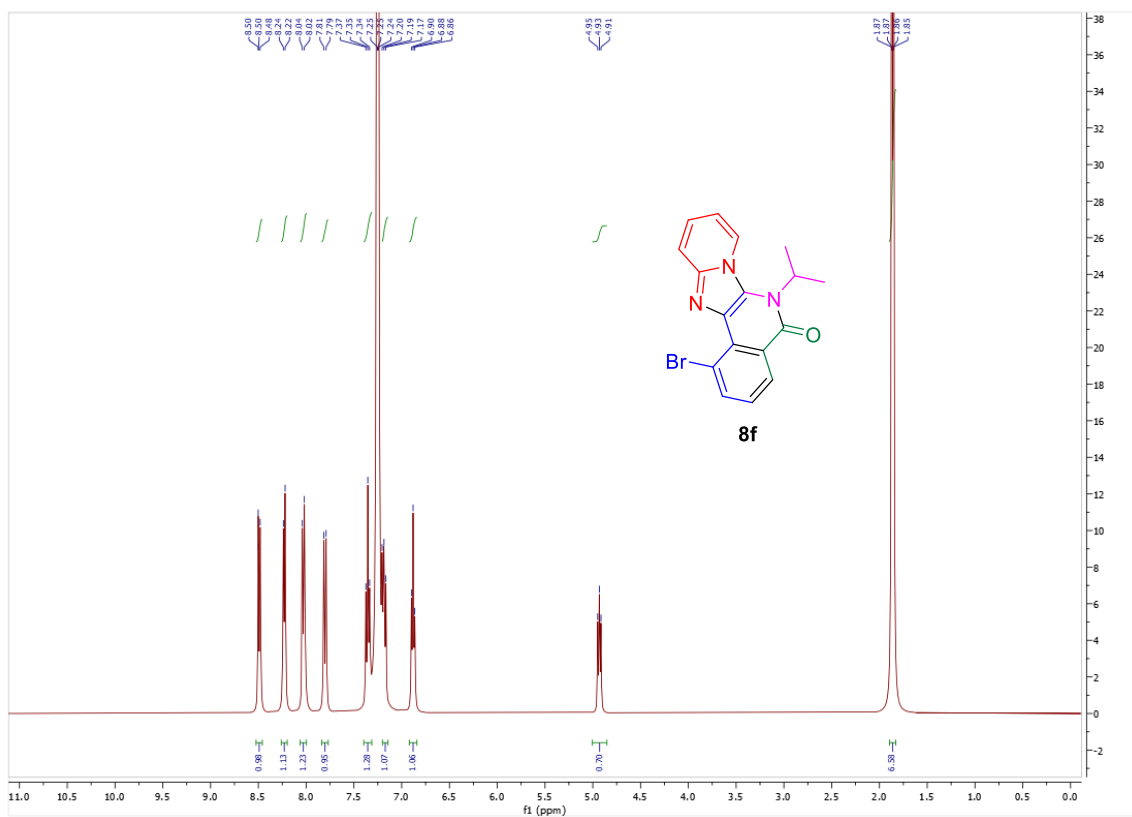
**<sup>13</sup>C NMR of 8d**



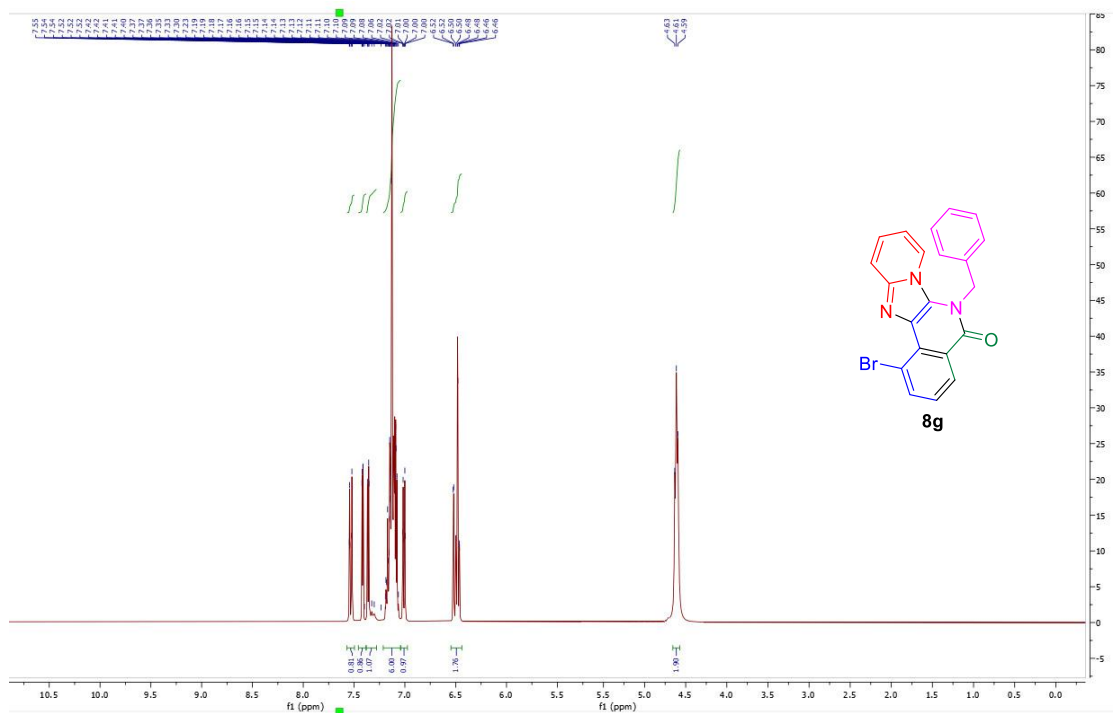
$^1\text{H}$  NMR of **8e**



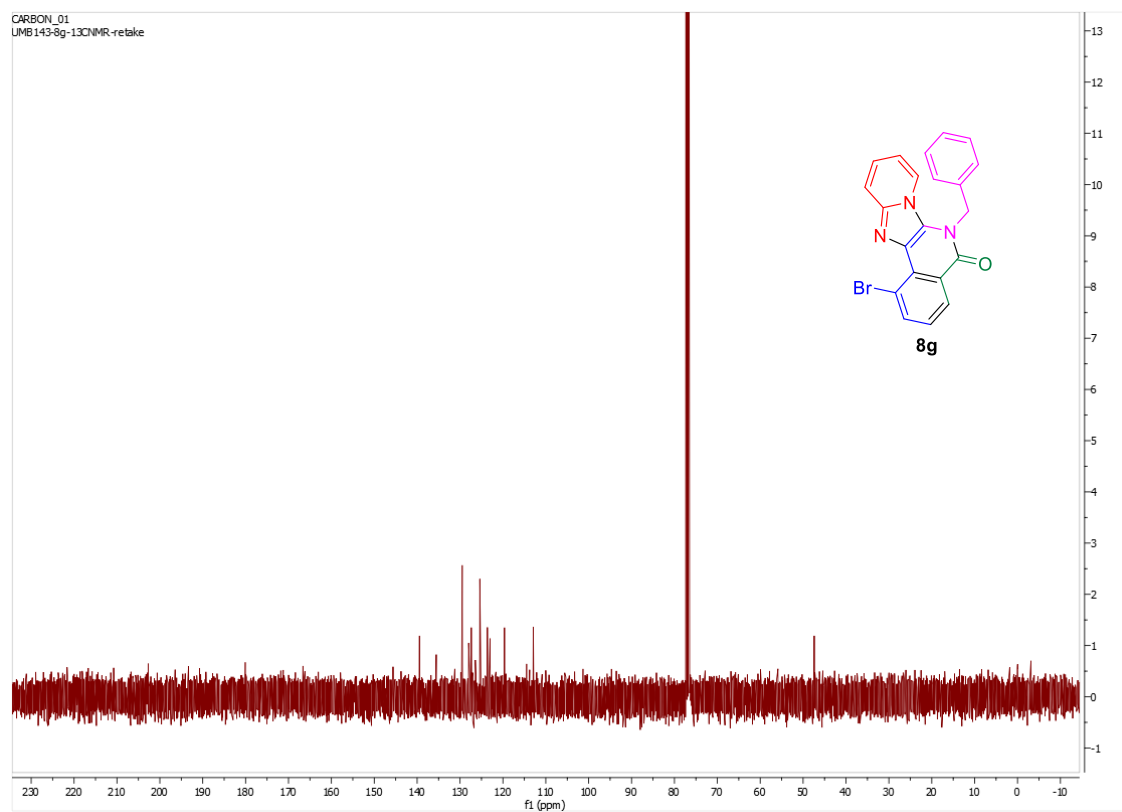
$^{13}\text{C}$  NMR of **8e**



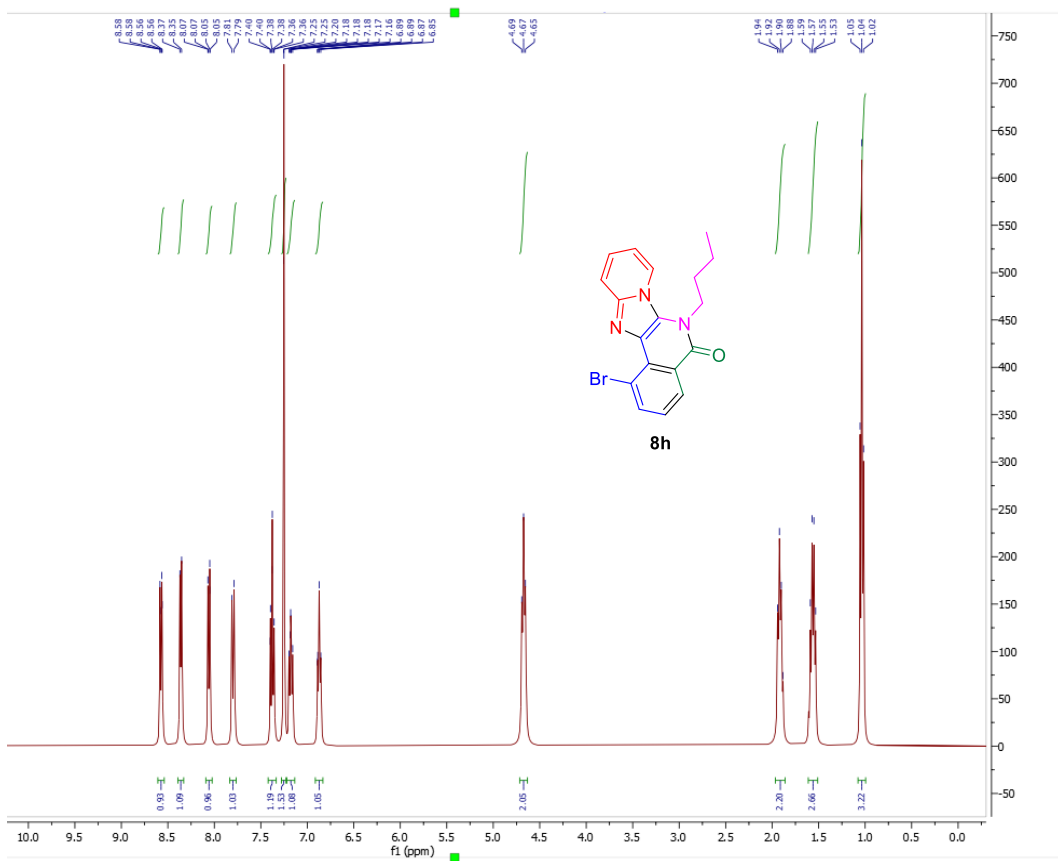
**<sup>13</sup>C NMR of 8f**



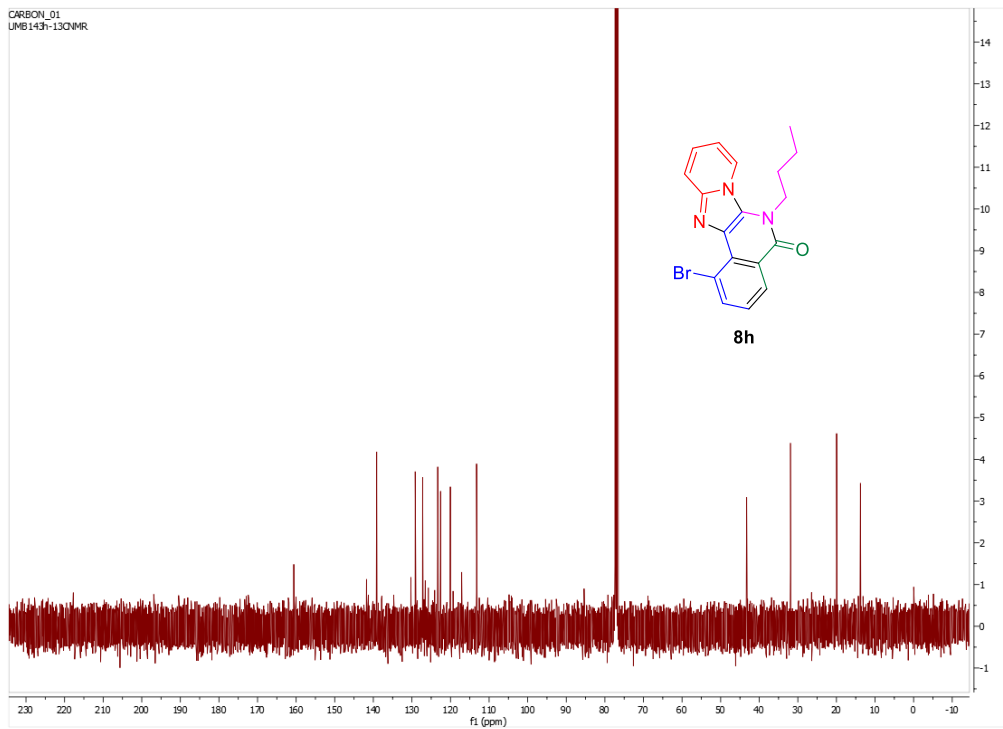
<sup>1</sup>H NMR of **8g**



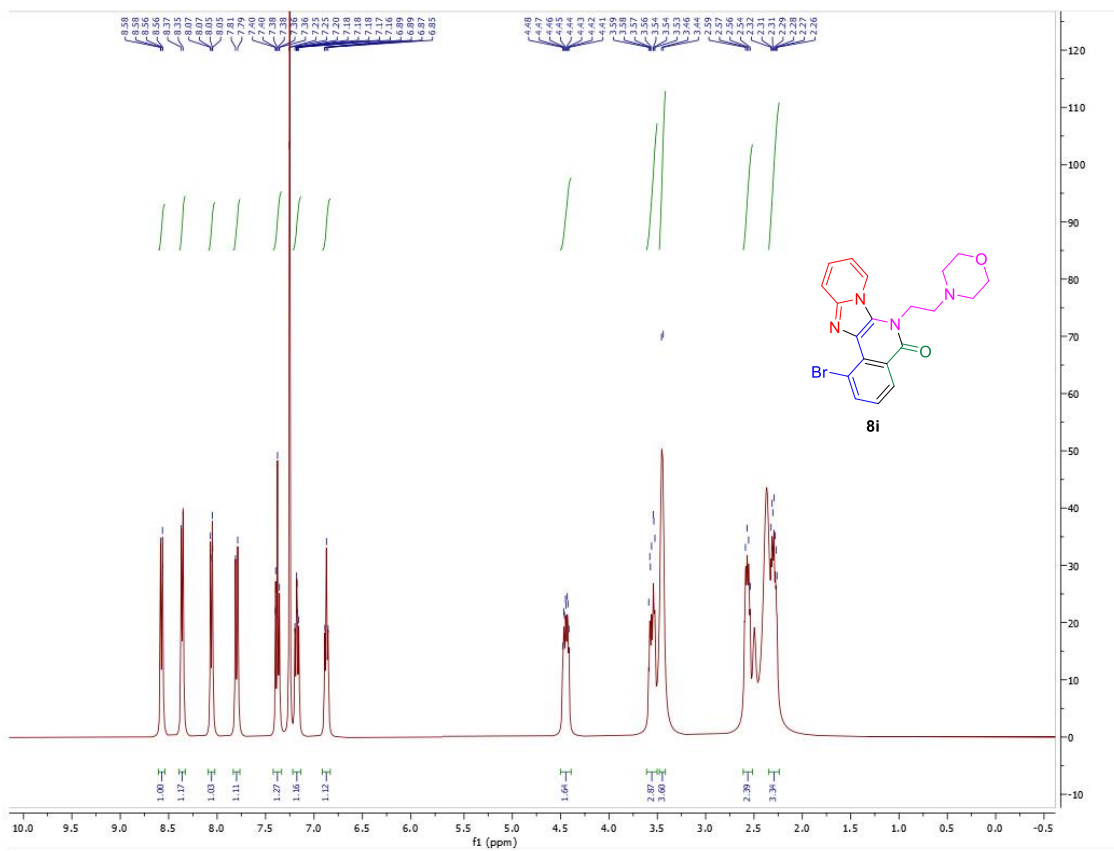
<sup>13</sup>C NMR of **8g**



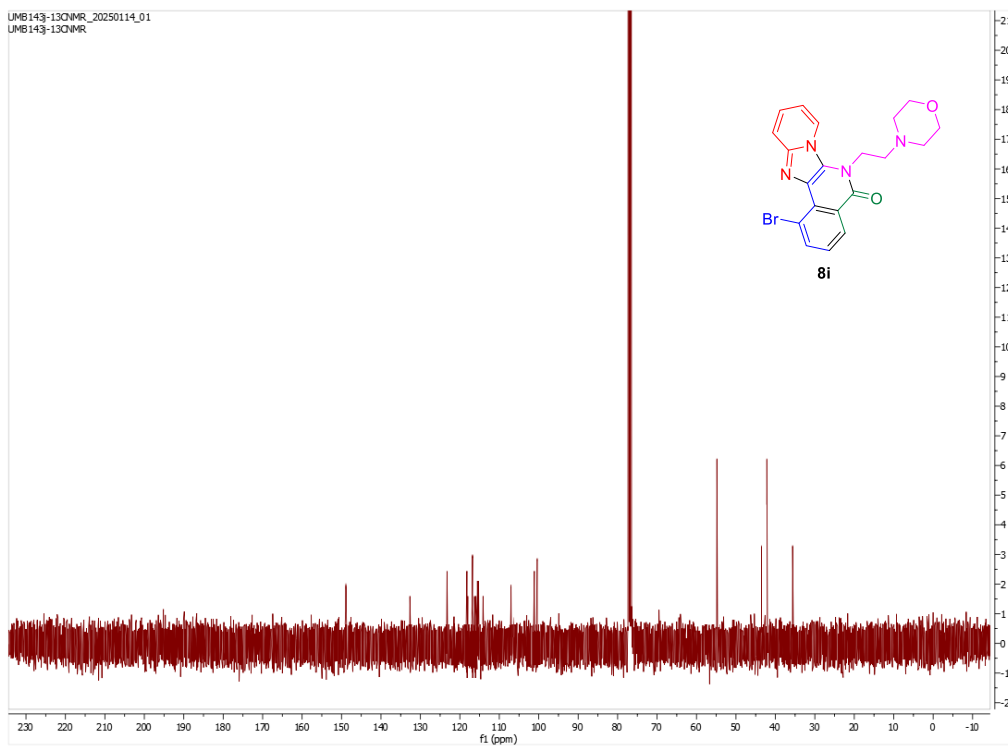
**<sup>1</sup>H NMR of 143**



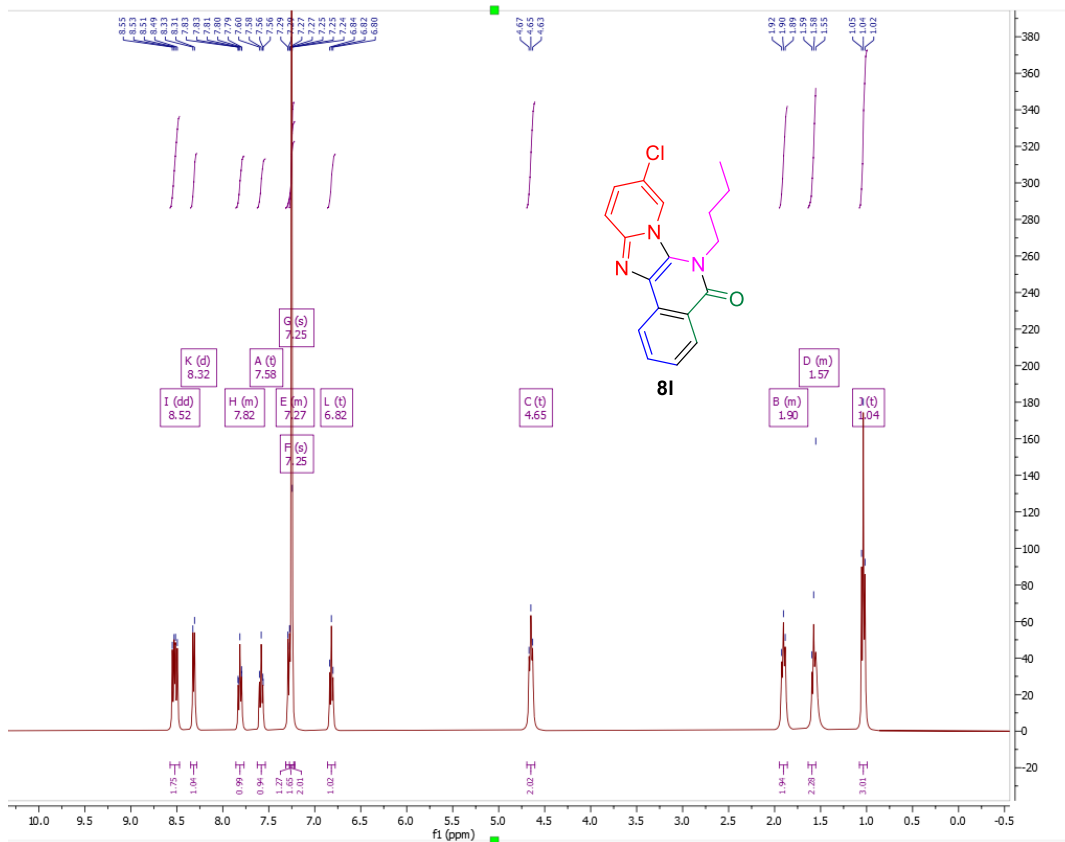
**<sup>13</sup>C NMR of 8h**



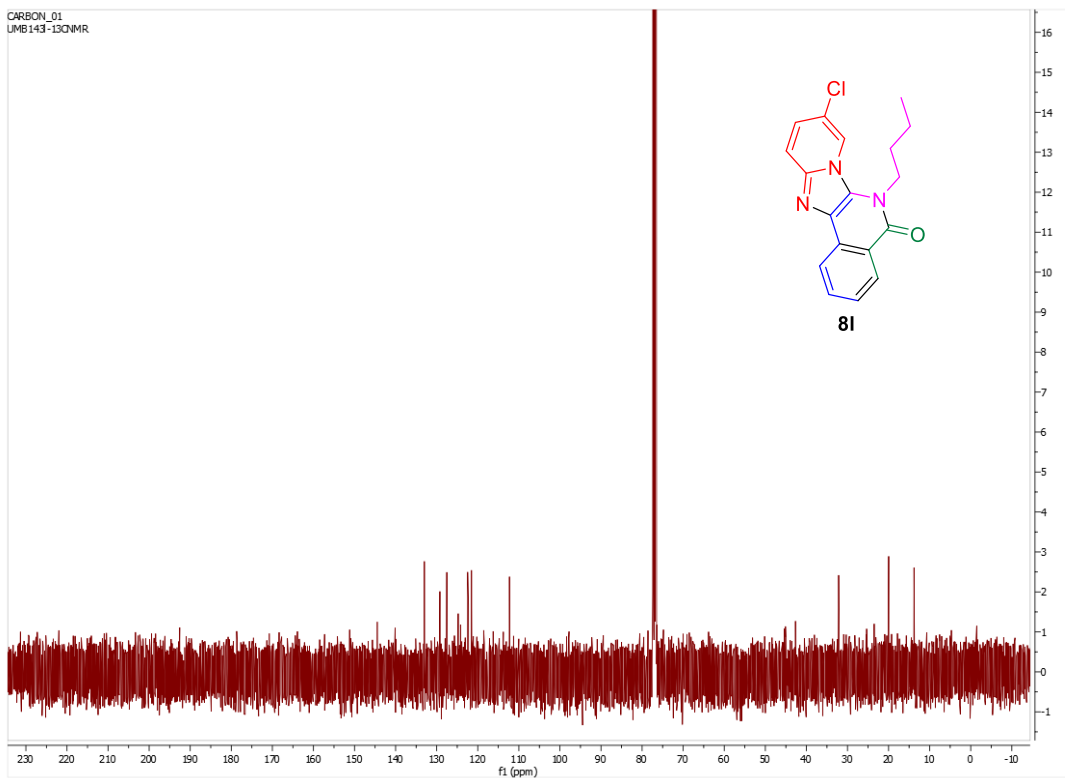
**1H NMR of 8i**



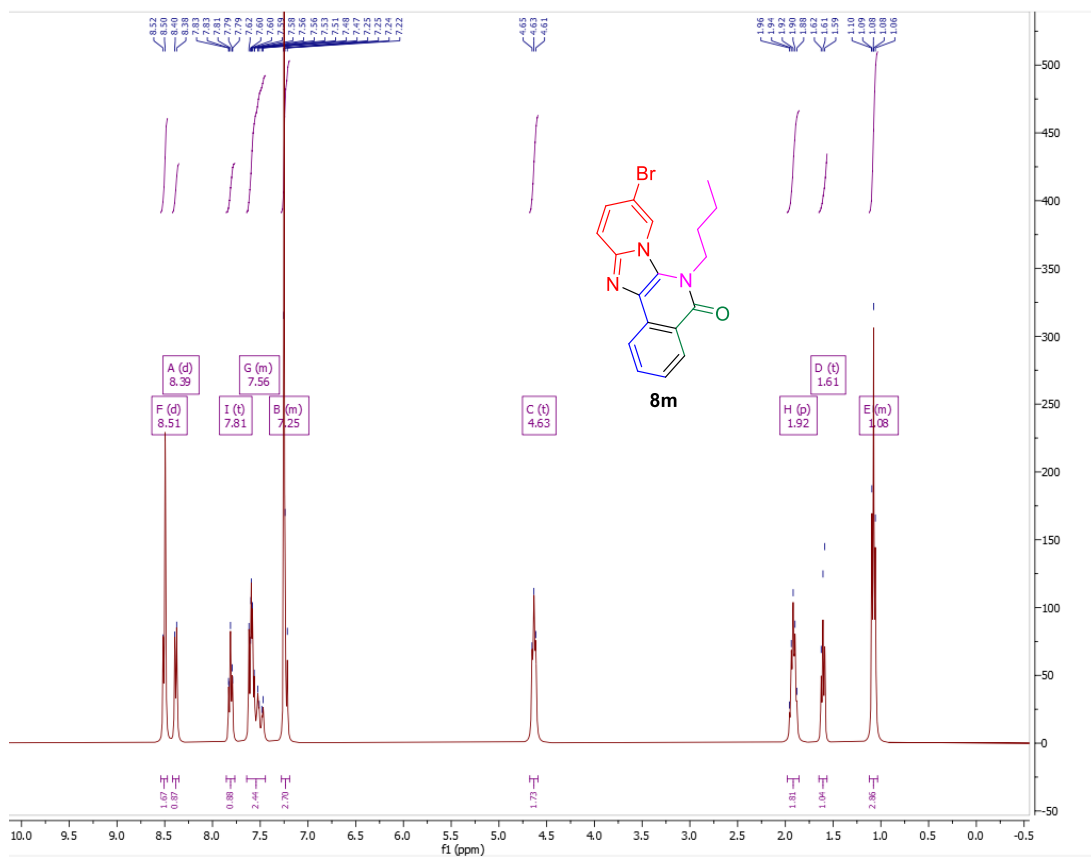
**13C NMR of 8i**



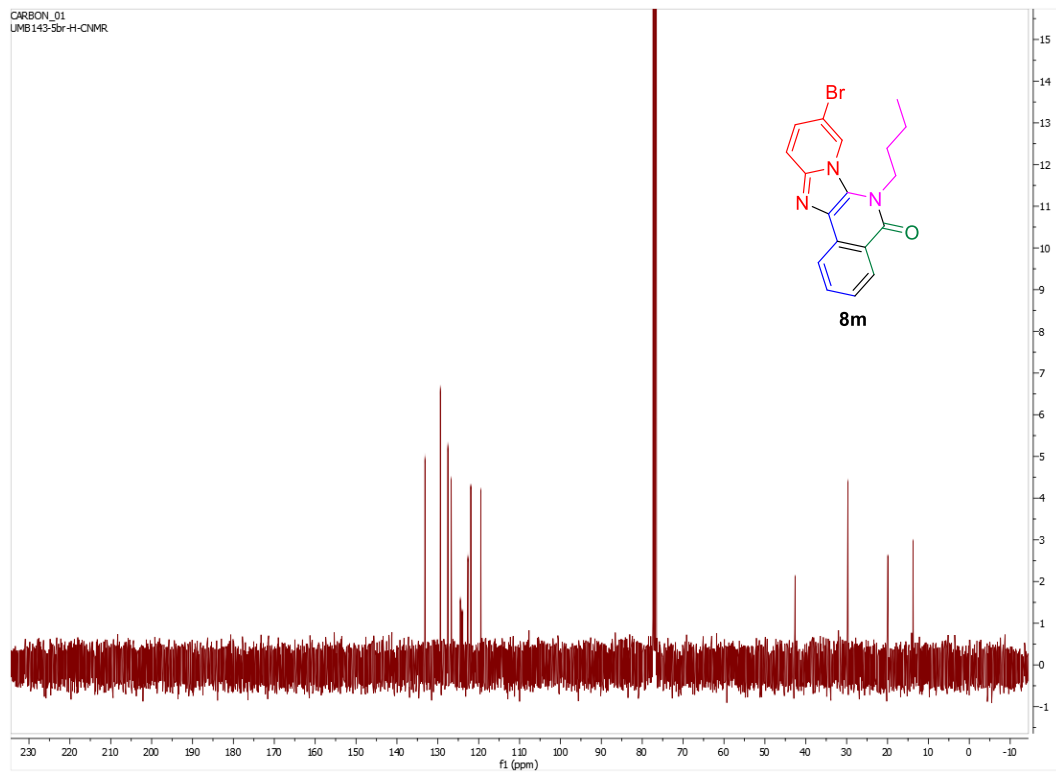
**<sup>1</sup>H NMR of 8I**



**<sup>13</sup>C NMR of 8I**

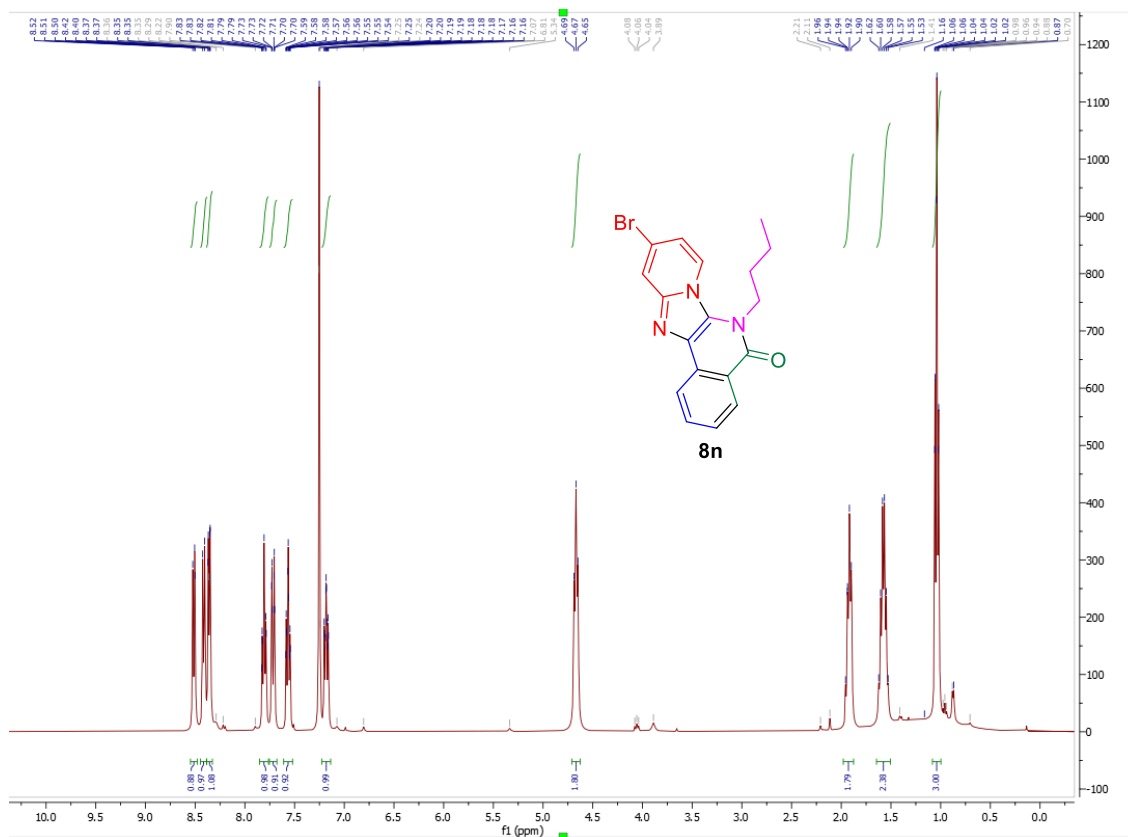


**1H NMR of 8m**

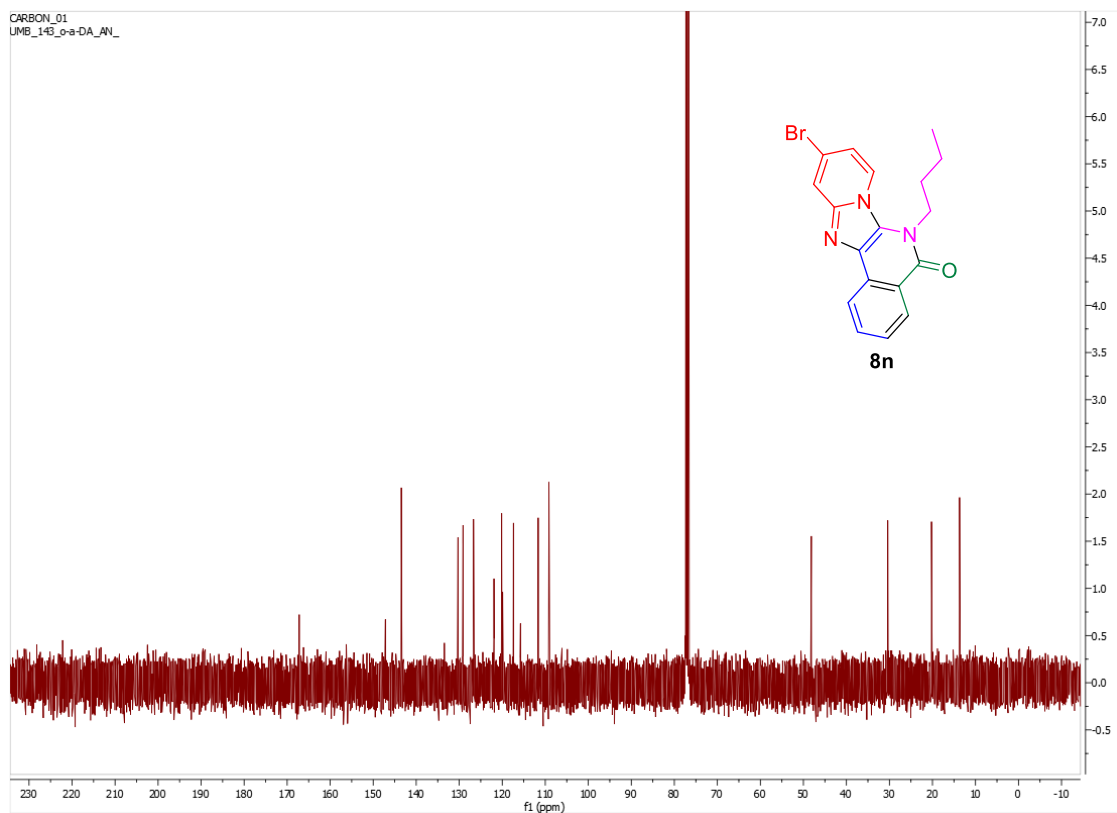


**13C NMR of 8m**

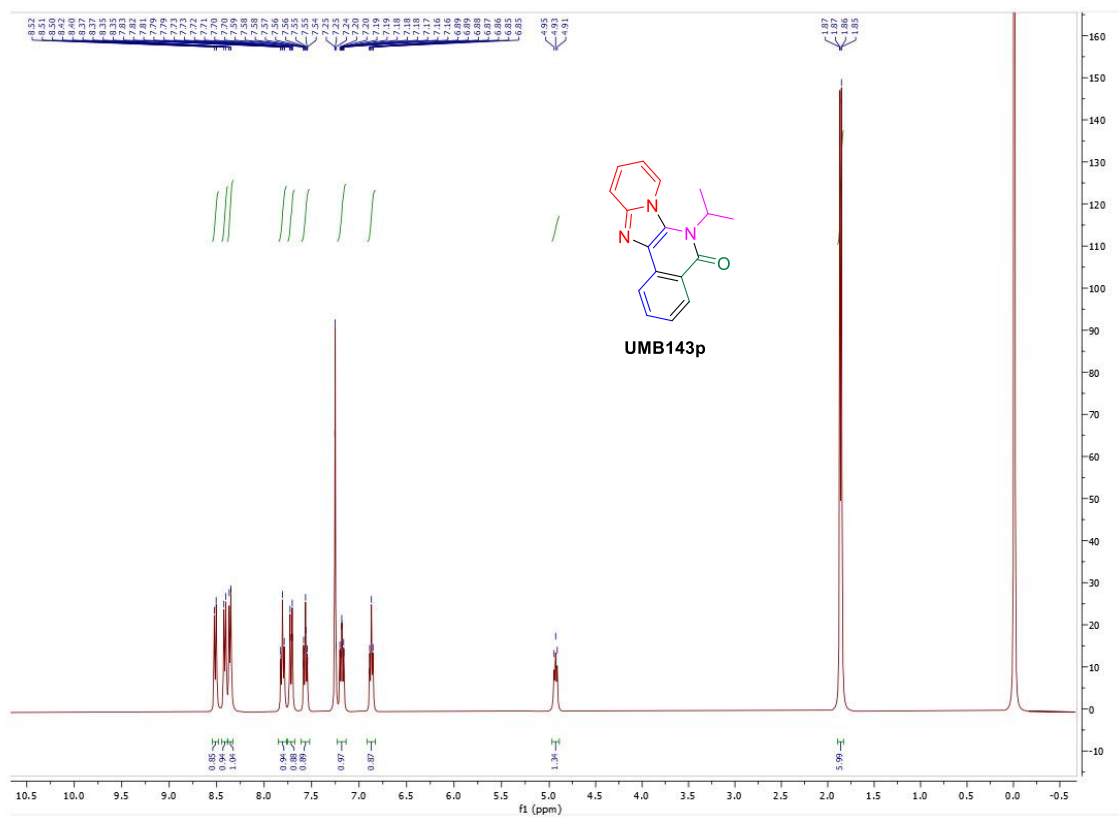




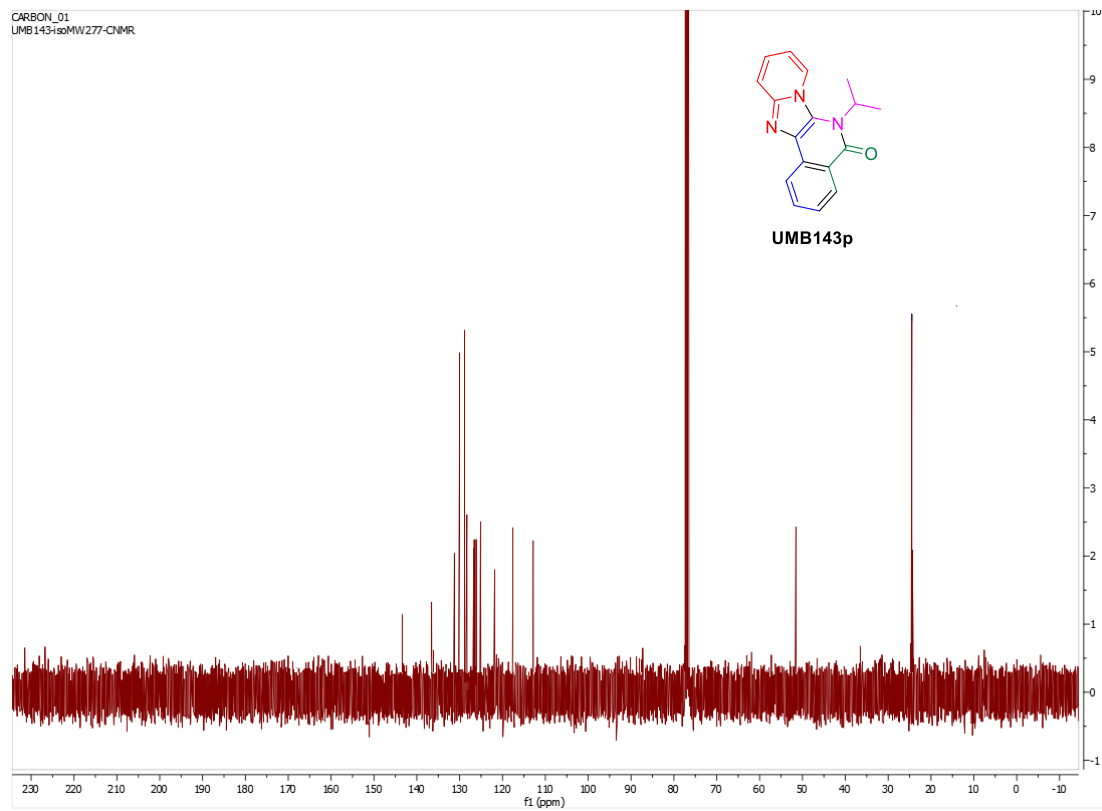
**$^1\text{H}$  NMR of 8n**



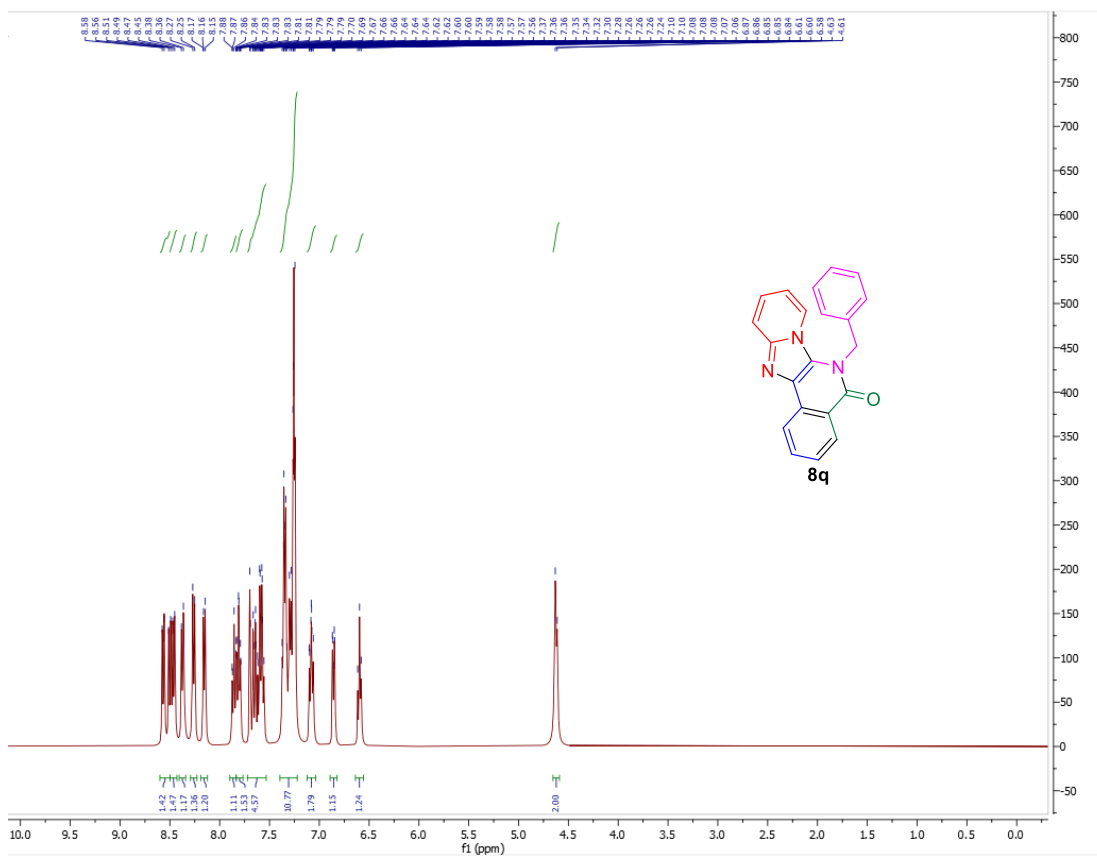
**$^{13}\text{C}$  NMR of 8n**



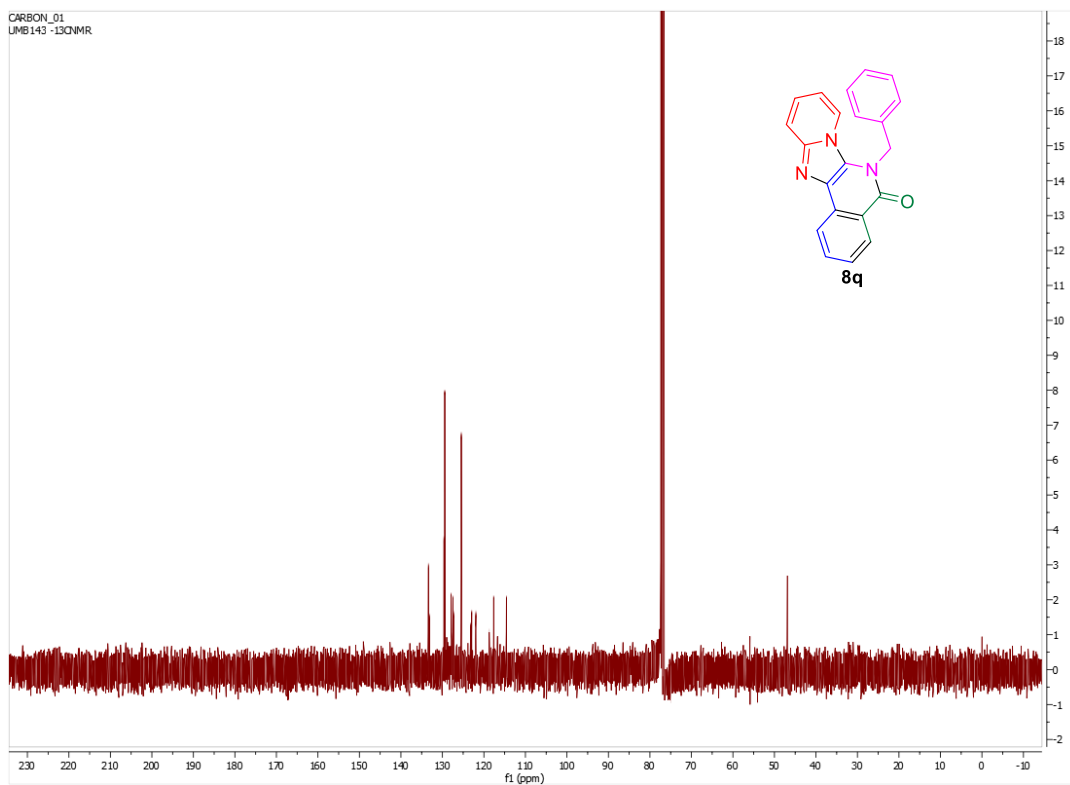
**<sup>1</sup>H NMR of 8p**



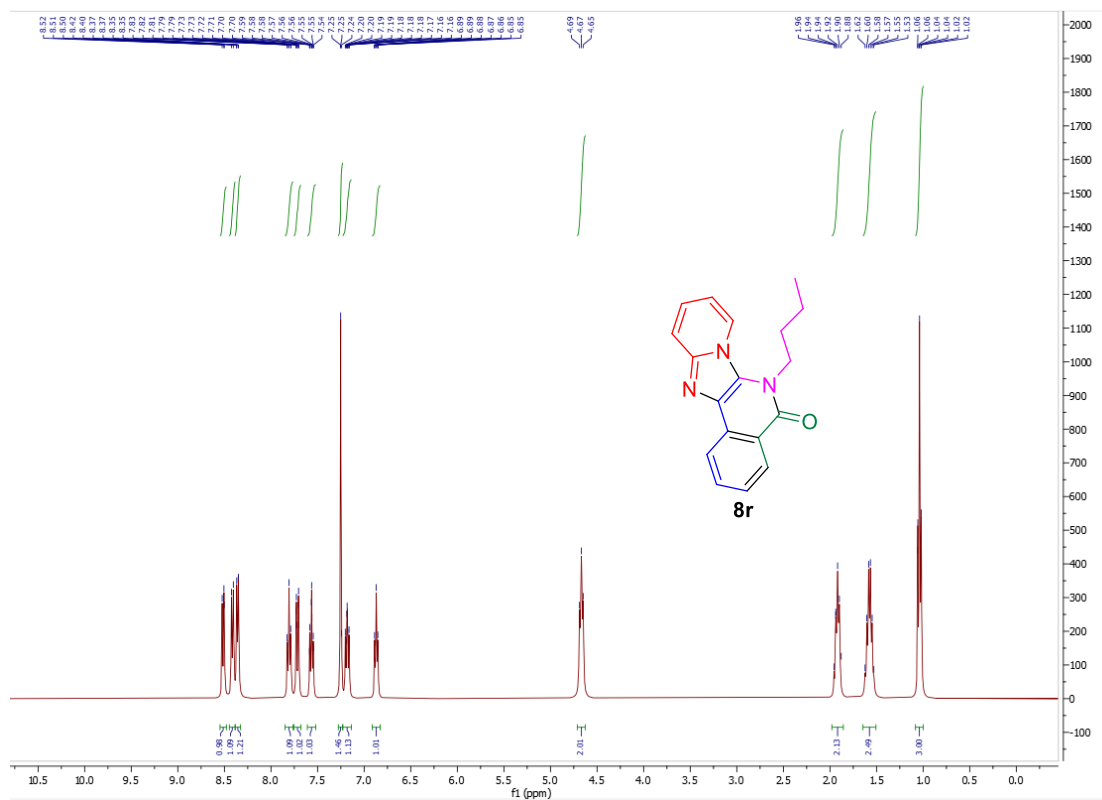
**<sup>13</sup>C NMR of 8p**



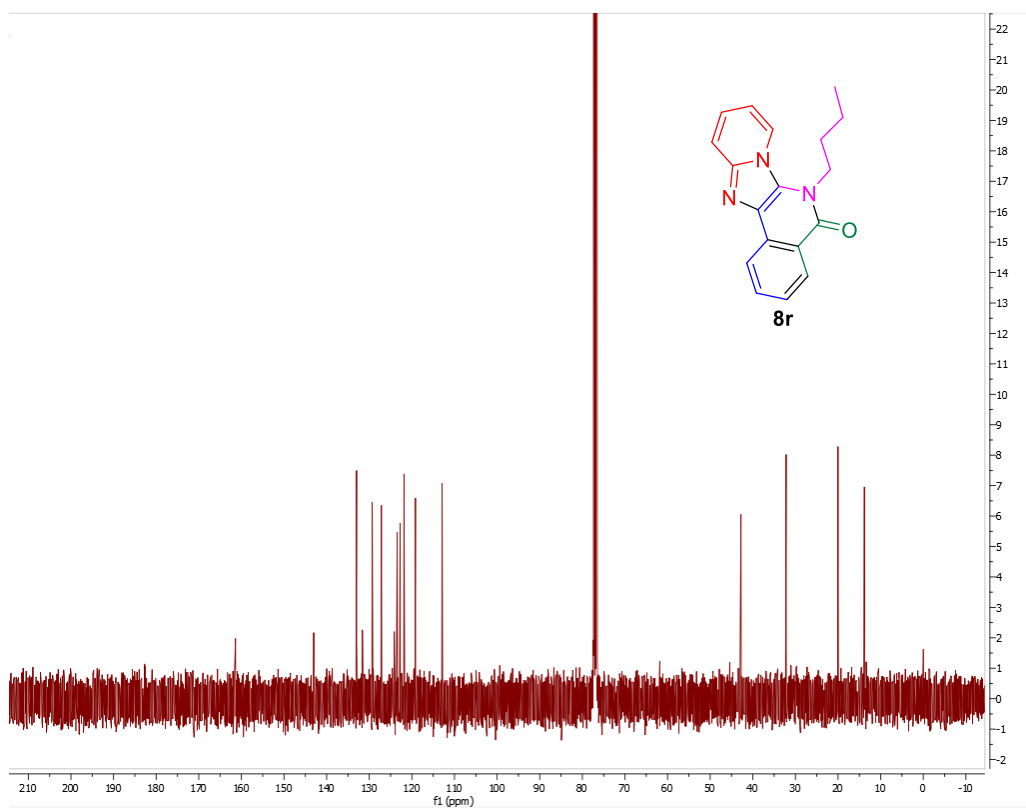
**<sup>1</sup>H NMR of 8q**



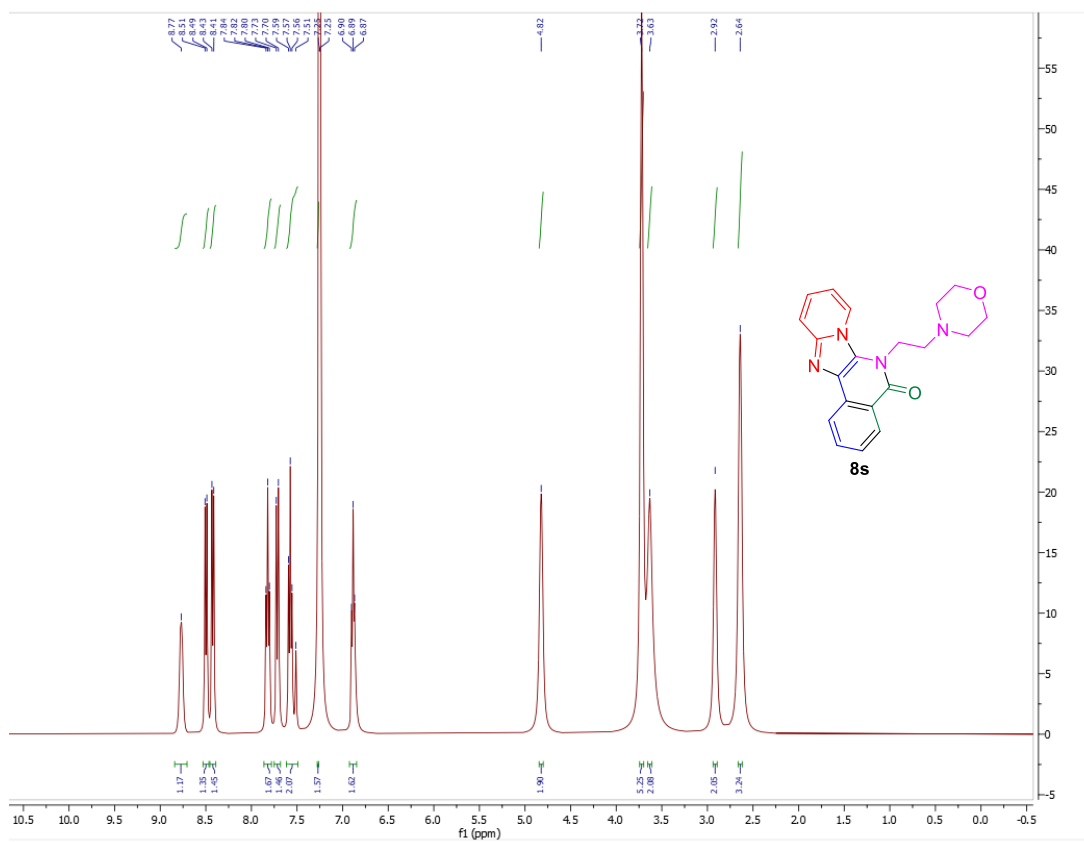
**<sup>13</sup>C NMR of 8q**



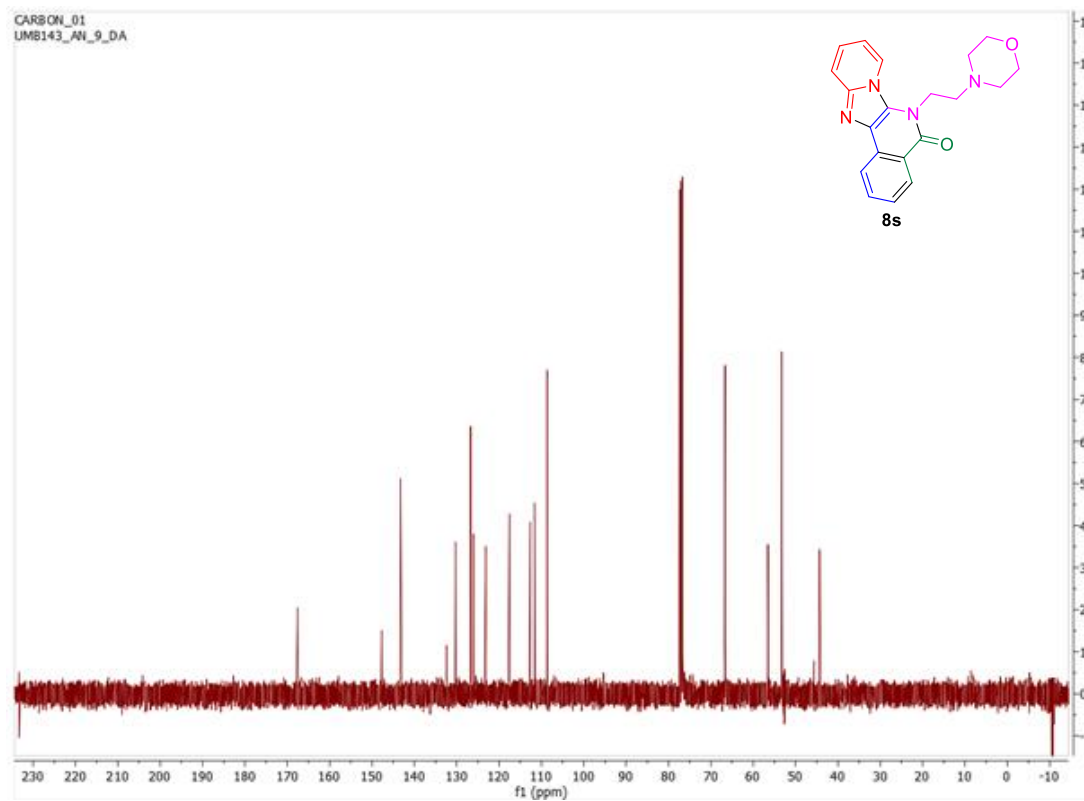
**<sup>1</sup>H NMR of 8r**



**<sup>13</sup>C NMR of 8r**



**<sup>1</sup>H NMR of 8s**



**<sup>13</sup>C NMR of 8s**