Supporting Information

Silver-Catalyzed Decarboxylative Radical Cascade Cyclization towards Benzimidazo[2,1-*a*]isoquinolin-6(5*H*)-ones

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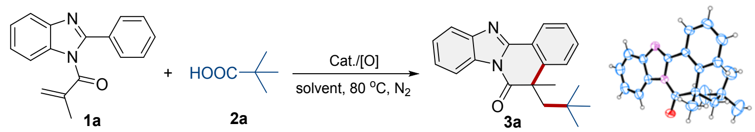
1. General Information

All the chemicals were purchased from commercial sources and used without treatment. Reactions were monitored by Thin Layer Chromatography (TLC) using silica gel F254 plates. Products were purified by column chromatography by using 200-300 mesh silica gel as the stationary phase. All the ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Ascend 400 spectrometer at 25 °C operating at 400.13 and 100.61 MHz, respectively. Proton chemical shifts δ were given in ppm using TMS as the internal standard. High-resolution mass spectra (HRMS) were obtained with 3000-mass spectrometer, using Waters Q-Tof MS/MS system (ESI).

2. Condition Optimization

We initiated our study by evaluating the model reaction of *N*-methacryloyl-2-phenylbenzoimidazole (**1a**) with pivalic acid (**2a**) under different reaction conditions (Table S1). To our delight, the treatment of **1a** with 2 equiv. of **2a** in the presence of 10 mol% of $AgNO_3$ and 2 equiv. of $K_2S_2O_8$ in CH_3CN/H_2O (v/v = 1/1) under a N_2 atmosphere at 80 °C for 8 h, afforded a desired benzimidazo[2,1-*a*]isoquinolin-6(5*H*)-one (**3a**) in 62% yield (entry 1). The structure of **3a** was further confirmed by X-ray crystallography. With this intriguing result in hand, we further examined other silver catalysts including AgOAc, $AgSbF_6$, Ag_2CO_3 and Ag_2O under identical conditions. It was found that these silver catalysts were active for this decarboxylative cascade reaction, giving **3a** in yields of 50-58% (entries 2-5). Then various transition metals such as CuI, CuCl, CuBr, $CuSO_4$, $Fe(NO_3)_3$, $FeSO_4$, $NiCl_2$ and $MnSO_4$ as catalysts were surveyed, and however, no desired product was detected (entries 6-13). Therefore, $AgNO_3$ was selected as the catalyst for further optimization. It was observed that the yield of **3a** increased from 40% to 79% as the dosage of $AgNO_3$ increased from 5 mol% to 15 mol% (entries 14 and 15). The screening of oxidants showed that $K_2S_2O_8$ was the best choice (entries 16-19). The experiments from entries 20-21 indicated that no product could be produced in the absence of $AgNO_3$ or $K_2S_2O_8$. Further increasing the amount of $K_2S_2O_8$ to 3 equivalents improved the yield to 82% (entry 22). The screening of solvents showed that CH_3CN/H_2O (v/v = 1:1) was the best choice among the solvents tested (entries 24-27). Therefore, the optimal reaction conditions were thus established as follows: **1a** (0.5 mmol), **2a** (1 mmol), $AgNO_3$ (15 mol%) and $K_2S_2O_8$ (3 equiv.) in the mixed solvent of CH_3CN/H_2O (v/v = 1/1) at 80 °C for 8 h under a N_2 atmosphere.

Table S1. Optimization of the reaction conditons[a]

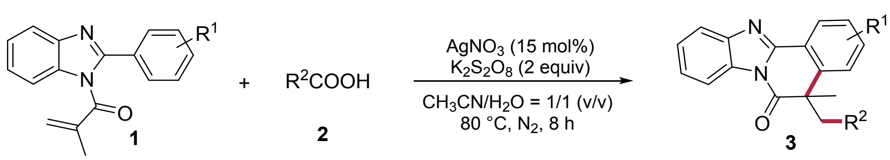


Entry	Cat. (mol%)	Oxidant (equiv)	Solvent (v/v= 1:1)	Yield[b] (%)
1	$AgNO_3$ (10)	$K_2S_2O_8$ (2)	CH_3CN/H_2O	62
2	AgOAc (10)	$K_2S_2O_8$ (2)	CH_3CN/H_2O	58
3	$AgSbF_6$ (10)	$K_2S_2O_8$ (2)	CH_3CN/H_2O	50
4	Ag_2CO_3 (10)	$K_2S_2O_8$ (2)	CH_3CN/H_2O	55
5	Ag_2O (10)	$K_2S_2O_8$ (2)	CH_3CN/H_2O	53
6	CuI (10)	$K_2S_2O_8$ (2)	CH_3CN/H_2O	N.D.
7	CuCl (10)	$K_2S_2O_8$ (2)	CH_3CN/H_2O	N.D.
8	CuBr (10)	$K_2S_2O_8$ (2)	CH_3CN/H_2O	N.D.
9	$CuSO_4$ (10)	$K_2S_2O_8$ (2)	CH_3CN/H_2O	N.D.
10	$Fe(NO_3)_3$ (10)	$K_2S_2O_8$ (2)	CH_3CN/H_2O	N.D.
11	$FeSO_4$ (10)	$K_2S_2O_8$ (2)	CH_3CN/H_2O	N.D.
12	$NiCl_2$ (10)	$K_2S_2O_8$ (2)	CH_3CN/H_2O	N.D.
13	$MnSO_4$ (10)	$K_2S_2O_8$ (2)	CH_3CN/H_2O	N.D.
14	$AgNO_3$ (5)	$K_2S_2O_8$ (2)	CH_3CN/H_2O	40
15	$AgNO_3$ (15)	$K_2S_2O_8$ (2)	CH_3CN/H_2O	79
16[c]	$AgNO_3$ (15)	TBHP (2)	CH_3CN/H_2O	N.D.
17	$AgNO_3$ (15)	DTBP (2)	CH_3CN/H_2O	N.D.
18	$AgNO_3$ (15)	Oxone (2)	CH_3CN/H_2O	N.D.
19	$AgNO_3$ (15)	O_2 (1 atm)	CH_3CN/H_2O	N.D.
20	$AgNO_3$ (15)	--	CH_3CN/H_2O	N.D.
21	-	$K_2S_2O_8$ (2)	CH_3CN/H_2O	N.D.
22	**$AgNO_3$ (15)**	**$K_2S_2O_8$ (3)**	**CH_3CN/H_2O**	**82**
23	$AgNO_3$ (15)	$K_2S_2O_8$ (4)	CH_3CN/H_2O	80
24	$AgNO_3$ (15)	$K_2S_2O_8$ (3)	DCE/H_2O	66
25	$AgNO_3$ (15)	$K_2S_2O_8$ (3)	DMF/H_2O	35
26	$AgNO_3$ (15)	$K_2S_2O_8$ (3)	$DMSO/H_2O$	56
27	$AgNO_3$ (15)	$K_2S_2O_8$ (3)	$EtOH/H_2O$	71

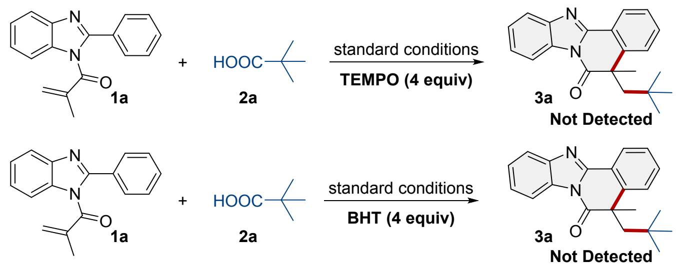
[a]Reaction conditions: **1a** (0.5 mmol), **2a** (1 mmol), catalyst (0-20 mol%), oxidant, mixed solvent (5 mL), N_2 atmosphere, 80 °C, 8 h. TBHP = *tert*-butyl hydroperoxide, DTBP = Di-*tert*-butyl peroxide. [b]Isolated yields were given. [c]CuI, CuBr, CuCl, and $CuSO_4$ were tested, respectively. [d]70 wt% aqueous solution was applied.

3. Experimental procedures

General Procedure for Synthesis of Benzo[4,5]imidazo[2,1-*a*]isoquinolin-6(5*H*)-ones (3)

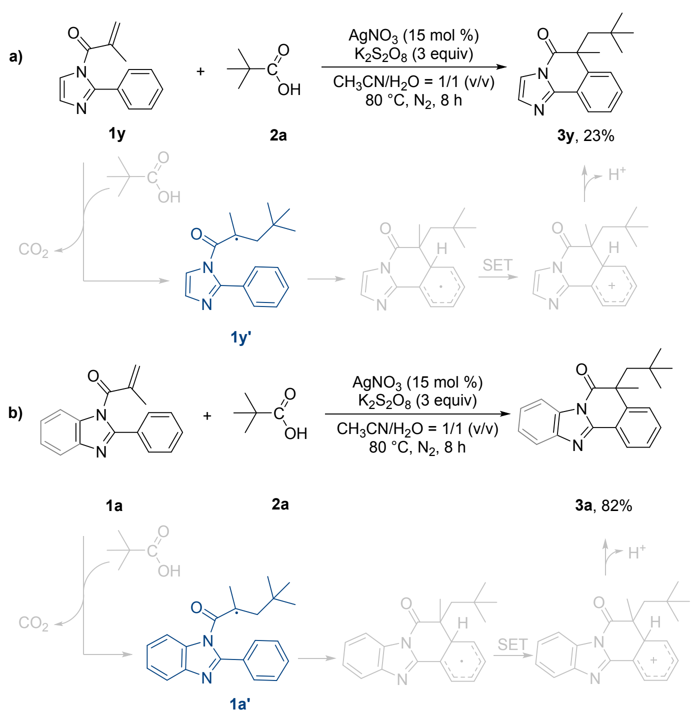


N-methacryloyl-2-aryl-benzoimidazole **1** (0.5 mmol), carboxylic acid **2** (1 mmol), $K_2S_2O_8$ (3 equiv) and $AgNO_3$ (15 mol%) in CH_3CN/H_2O (v/v =1/1) (5 mL) stirred at 80 °C under N_2 for 8 h. The solvent was evaporated under vacuum, and the residue was quenched with water (10 mL), extracted with ethyl acetate (3 × 10 mL). The combined organic layers were washed with brine (25 mL) and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated in vacuo. The crude product was purified by silica gel chromatography (petroleum ether: ethyl acetate = 10:1) to give the desired products.



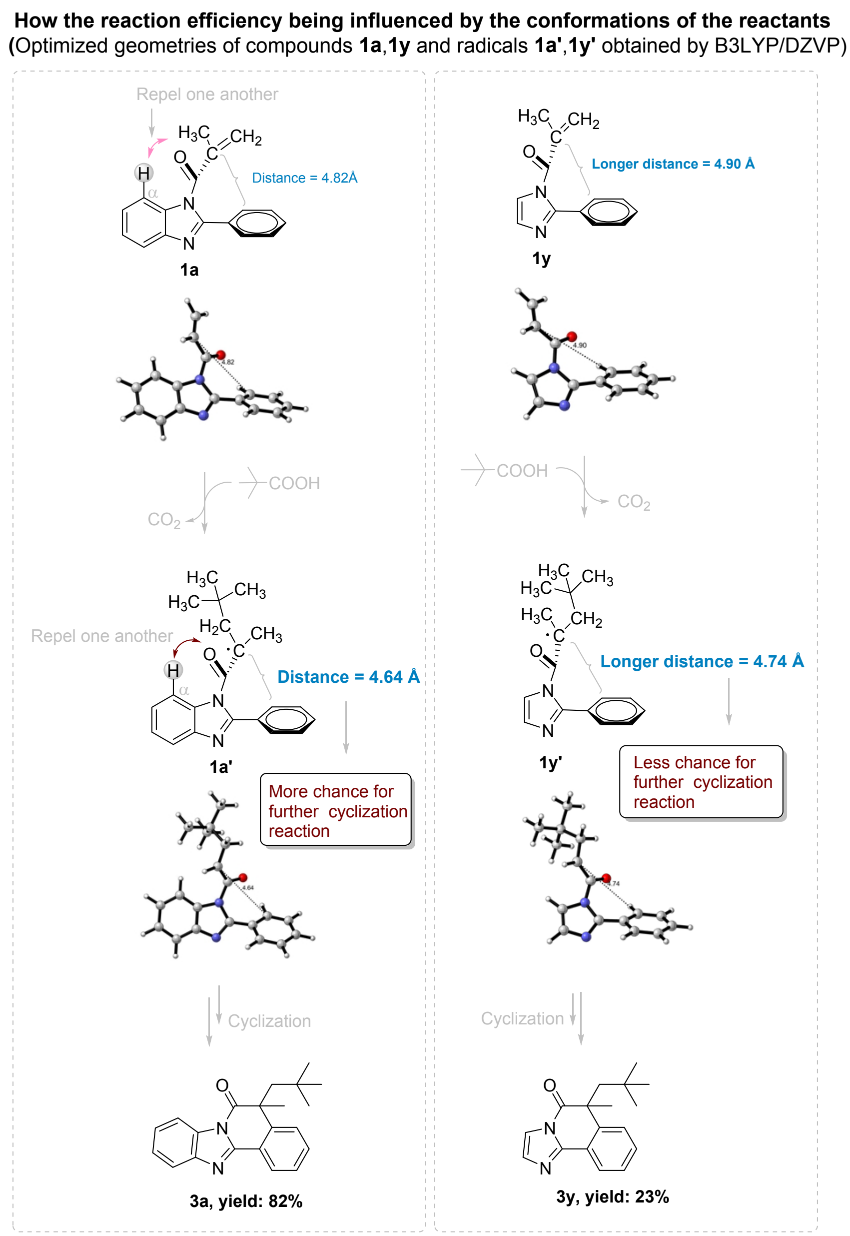
Scheme S1. Control experiments

We carried out a reaction starting form *N*-methacryloyl-2-phenylimidazole (**1y**) and pivalic acid under optimized reaction conditions, as illustrated in Scheme S2a. However, we only get 23% yield of the corresponding product (**3y**), a much low yield compared with that of **3a** when compound **1a** was employed as the reactant (Scheme S2b below). For further understanding this seemingly abnormal result, we then utilized computational methods to calculate the most stable conformations of *N*-methacryloyl-2-phenylimidazole (**1y**) and **1a** as well as their corresponding radical intermediates 1y' and 1a', as shown below in Scheme S3 (the most stable geometries of **1y**, **1a** and **1y'**, **1a'** were obtained by B3LYP/DZVP). As it can be seen from Scheme S3, the most stable conformation of **1y'** renders a longer distance between radical



Scheme S2

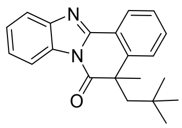
carbon and phenyl ortho carbon, two reaction sites of further cyclization reaction, in comparison with the relatively short distance in **1a'** which should be resulted from the repulsion from the nearby α-H. Thus, it is reasonably believed that reactant *N*-methacryloyl-2-phenylimidazole (**1y**) would own less chance to fulfill the cyclization process to access the final product **3y**, compared to the use of **1a** to access the corresponding product **3a**. The conformational analysis of **1a**, **1y** and **1a'**, **1y'** shown in Scheme 3 might provide an insight to the reason why a much low yield of **3y** was obtained**.**



Scheme S3

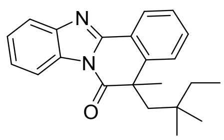
4. Characterization Data for Products

5-methyl-5-neopentylbenzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one (3a)



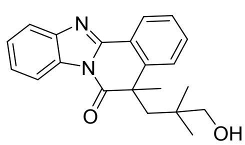
White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (d, J = 7.6 Hz, 1H), 8.40-8.38 (m, 1H), 7.85-7.83 (m, 1H), 7.56-7.40 (m, 5H), 2.63 (d, J = 14.4 Hz, 1H), 2.17 (d, J = 14.4 Hz, 1H), 1.71 (s, 3H), 0.54 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.5, 149.8, 144.1, 142.0, 131.4, 131.2, 127.6, 127.6, 125.9, 125.5, 122.4, 119.7, 115.8, 55.3, 47.6, 33.1, 32.0, 30.8. HRMS Calcd for $C_{21}H_{23}N_2O$ $[M + H]^+$: m/z 319.1805, Found: 319.1811

5-(2,2-dimethylbutyl)-5-methylbenzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one (3b)



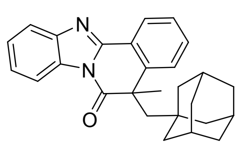
White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (d, J = 7.6 Hz, 1H), 8.40-8.38 (m, 1H), 7.84-7.82 (m, 1H), 7.55-7.50 (m, 2H), 7.48-7.40 (m, 3H), 2.61 (d, J = 14.4 Hz, 1H), 2.16 (d, J = 14.4 Hz, 1H), 1.71 (s, 3H), 1.00-0.86 (m, 2H), 0.68 (t, J = 7.6 Hz, 3H), 0.48 (s, 3H), 0.36 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 173.5, 149.8, 144.1, 142.1, 131.5, 131.1, 127.6, 127.5, 125.9, 125.8, 125.5, 122.4, 119.7, 115.8, 53.1, 47.5, 36.6, 34.4, 33.2, 27.6, 26.9, 8.3. HRMS Calcd for $C_{22}H_{25}N_2O$ $[M + H]^+$: m/z 333.1961, Found: 333.1965

5-(3-hydroxy-2,2-dimethylpropyl)-5-methylbenzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one (3c)



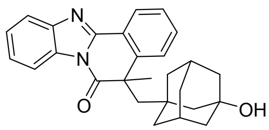
White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (d, J = 8.0 Hz, 1H), 8.39-8.37 (m, 1H), 7.83-7.81 (m, 1H), 7.57-7.53 (m, 2H), 7.50-7.41 (m, 3H), 2.94-2.84 (m, 2H), 2.69 (d, J = 14.8 Hz, 1H), 2.25 (d, J = 14.8 Hz, 1H), 1.96 (s, 1H), 1.71 (s, 3H), 0.60 (s, 3H), 0.42 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.0, 149.7, 144.0, 141.9, 131.3, 127.7, 127.2, 126.0, 125.9, 125.6, 122.1, 119.7, 115.8, 71.1, 48.5, 47.4, 36.6, 33.7, 26.3, 24.8. HRMS Calcd for $C_{21}H_{23}N_2O_2$ $[M + H]^+$: m/z 335.1754, Found: 335.1753

5-(adamantan-1-ylmethyl)-5-methylbenzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one (3d)



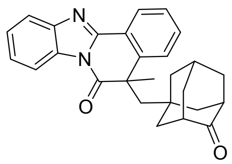
White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (d, J = 7.6 Hz, 1H), 8.41-8.39 (m, 1H), 7.85-7.83 (m, 1H), 7.52-7.49 (m, 2H), 7.48-7.40 (m, 3H), 2.50 (d, J = 14.4, 1H), 2.06 (d, J = 14.4 Hz, 1H), 1.66 (s, 3H),1.63-1.61(m, 3H), 1.42 (d, J = 12.0 Hz, 3H), 1.28 (d, J = 11.6 Hz, 3H), 1.15-1.07 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.4, 149.8, 144.1, 142.3, 131.5, 131.1, 127.6, 125.8, 125.8, 125.5, 122.1, 119.7, 115.9, 56.2, 46.8, 43.5, 36.4, 34.2, 33.7, 28.4. HRMS Calcd for $C_{27}H_{29}N_2O$ $[M + H]^+$: m/z 397.2274, Found: 397.2277

5-(3-hydroxyadamantan-1-yl)methyl)-5-methylbenzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one (3e)



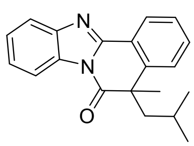
White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (d, J = 7.6 Hz, 1H), 8.39 (d, J = 7.2 Hz, 1H), 7.85-7.83 (m, 1H), 7.55-7.41 (m, 5H), 2.60 (d, J = 14.4 Hz, 1H), 2.14 (d, J = 14.4 Hz, 1H), 1.86 (d, J = 16.0 Hz, 2H), 1.67 (s, 3H), 1.45-1.25 (m, 5H), 1.17-0.87 (m, 7H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.2, 149.6, 144.1, 141.9, 131.4, 131.2, 127.8, 127.4, 126.0, 125.9, 125.6, 122.1, 119.8, 115.8, 68.3, 54.8, 51.6, 46.9, 44.1, 44.0, 41.9, 41.6, 37.7, 34.8, 33.7, 30.4, 30.4. HRMS Calcd for $C_{27}H_{29}N_2O_2$ $[M + H]^+$: m/z 413.2224, Found: 413.2230

5-methyl-5-(4-oxoadamantan-1-yl)methyl)benzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one (3f)



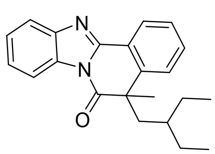
White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53-8.51 (m, 1H), 8.40-8.38 (m, 1H), 7.87-7.85 (m, 1H), 7.58-7.43 (m, 5H), 2.65 (d, J = 14.8 Hz, 1H), 2.26 (d, J = 14.8 Hz, 2H), 2.16 (d, J = 14.8 Hz, 1H), 1.81-1.75 (m, 2H), 1.72-1.70 (m, 2H), 1.69 (s, 3H), 1.63-1.55 (m, 2H), 1.51-1.39 (m, 3H), 1.36-1.25 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 217.3, 173.0, 149.4, 144.1, 141.4, 131.3, 128.0, 127.3, 126.2, 126.1, 125.7, 122.1, 119.9, 115.8, 53.6, 46.9, 46.3, 46.1, 44.9, 44.2, 41.7, 38.2, 38.2, 34.0, 33.8, 27.5. HRMS Calcd for $C_{27}H_{27}N_2O_2$ $[M + H]^+$: m/z 411.2067, Found: 411.2071

5-isobutyl-5-methylbenzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one (3g)



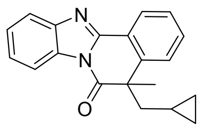
Yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (d, J = 7.6, 1H), 8.40-8.38 (m, 1H), 7.84-7.82 (m, 1H), 7.54 (td, J = 7.6, 1.6 Hz, 1H), 7.47-7.38 (m, 4H), 2.45 (dd, J = 14.4, 8.4 Hz, 1H), 2.07 (dd, J = 14.4, 5.2 Hz, 1H), 1.68 (s, 3H), 1.33-1.25 (m, 1H), 0.61 (d, J = 6.8 Hz, 3H), 0.56 (d, J = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.5, 149.8, 144.1, 141.8, 131.6, 131.4, 127.6, 126.6, 125.9, 125.8, 125.5, 122.7, 119.8, 115.8, 50.5, 48.5, 31.4, 25.6, 23.9, 22.4. HRMS Calcd for $C_{20}H_{21}N_2O$ $[M + H]^+$: m/z 305.1648, Found: 305.1651

5-(2-ethylbutyl)-5-methylbenzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one (3h)



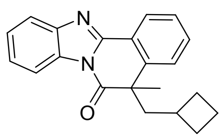
Yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50-8.48 (m, 1H), 8.38-8.36 (m, 1H), 7.83-7.81 (m, 1H), 7.54-7.50 (m, 1H), 7.45-7.39 (m, 4H), 2.39 (dd, J = 14.0, 6.4 Hz, 1H), 1.98 (dd, J = 14.4, 4.0 Hz, 1H), 1.72 (s, 3H), 0.97-0.84 (m, 5H), 0.54 (q, J = 7.6 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.4, 149.8, 144.1, 141.8, 131.4 (d, J = 13.8 Hz), 127.5, 126.6, 125.8, 125.7, 125.4, 122.9, 119.7, 115.6, 48.6, 46.4, 37.3, 29.8, 25.8, 25.2, 10.3, 10.0. HRMS Calcd for $C_{22}H_{25}N_2O$ [M + H]$^+$: m/z 333.1961, Found: 333.1966

5-(cyclopropylmethyl)-5-methylbenzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one (3i)



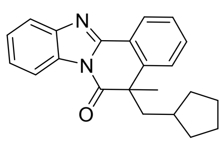
White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (d, J = 8.0, 1H), 8.38-8.36 (m, 1H), 7.83-7.81 (m, 1H), 7.59-7.55 (m, 1H), 7.50-7.40 (m, 4H), 2.18 (dd, J = 13.6, 5.2 Hz, 1H), 2.00 (dd, J = 13.6, 8.4 Hz, 1H), 1.77 (s, 3H), 0.17-0.06 (m, 2H), -0.04-0.10 (m, 2H), -0.20-0.24 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.6, 150.1, 144.0, 142.0, 131.7, 131.4, 127.6, 126.3, 125.8, 125.7, 125.5, 123.3, 119.7, 115.6, 49.7, 49.5, 26.9, 6.9, 3.9, 3.7. HRMS Calcd for $C_{20}H_{19}N_2O$ [M + H]$^+$: m/z 303.1492, Found: 303.1492

5-(cyclobutylmethyl)-5-methylbenzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one (3j)



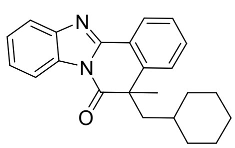
White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48-8.45 (m, 1H), 8.37-8.35 (m, 1H), 7.83-7.81 (m, 1H), 7.57-7.53 (m, 1H), 7.48-7.39 (m, 4H), 2.47 (dd, J = 13.6, 8.0 Hz, 1H), 2.07 (dd, J = 13.6, 8.0 Hz, 1H), 1.89-1.80 (m, 1H), 1.74 (s, 3H), 1.52-1.38 (m, 5H), 1.34-1.25 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3, 149.9, 144.0, 141.8, 131.6, 131.4, 127.6, 126.5, 125.8, 125.7, 125.5, 122.9, 119.7, 115.7, 51.3, 48.6, 32.9, 28.9, 28.5, 27.9, 18.6. HRMS Calcd for $C_{21}H_{21}N_2O$ [M + H]$^+$: m/z 317.1648, Found: 317.1654

5-(cyclopentylmethyl)-5-methylbenzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one (3k)



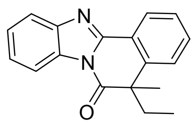
White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49-8.47 (m, 1H), 8.40-8.37 (m, 1H), 7.84-7.82 (m, 1H), 7.59-7.55 (m, 1H), 7.50-7.41 (m, 4H), 2.53 (dd, J = 13.6, 7.6 Hz, 1H), 2.19 (dd, J = 13.6, 7.2 Hz, 1H), 1.73 (s, 3H), 1.39-1.15 (m, 7H), 0.96-0.94 (m, 1H), 0.81-0.78 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.6, 149.9, 144.1, 142.1, 131.6, 131.4, 127.6, 126.6, 125.9, 125.8, 125.5, 122.8, 119.7, 115.8, 49.1, 49.1, 37.5, 33.6, 32.4, 30.1, 24.9, 24.6. HRMS Calcd for $C_{22}H_{23}N_2O$ [M + H]$^+$: m/z 331.1805, Found: 331.1805

5-(cyclohexylmethyl)-5-methylbenzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one (3l)



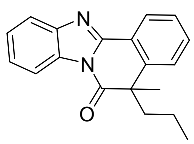
White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (d, J = 8.0, 1H), 8.39-8.37 (m, 1H), 7.84-7.82 (m, 1H), 7.58-7.54 (m, 1H), 7.49-7.40 (m, 4H), 2.48 (dd, J = 14.4, 8.0 Hz, 1H), 2.06 (dd, J = 14.4, 4.8 Hz, 1H), 1.66 (s, 3H), 1.46-1.36 (m, 3H), 1.27-1.16 (m, 2H), 1.00-0.75 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.5, 149.8, 144.1, 141.9, 131.6, 131.5, 127.6, 126.6, 125.9, 125.8, 125.5, 122.6, 119.7, 115.8, 48.8, 48.3, 34.9, 34.2, 32.9, 31.8, 26.0, 25.9. HRMS Calcd for $C_{23}H_{25}N_2O$ $[M + H]^+$: m/z 345.1961, Found: 345.1959

5-methyl-5-propylbenzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one (3m)



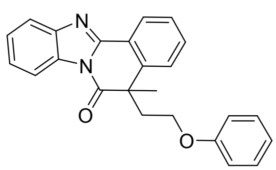
White oil, ^1H NMR (400 MHz, $CDCl_3$) δ 8.48 (d, J = 8.0 Hz, 1H), 8.38-8.36 (m, 1H), 7.83-7.80 (m, 1H), 7.54 (m, 1H), 7.48-7.40 (m, 4H), 2.47-2.38 (m, 1H), 2.04-1.95 (m, 1H), 1.72 (s, 3H), 0.57 (t, J = 7.6 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3, 149.9, 144.1, 141.5, 131.8, 131.3, 127.6, 126.1, 125.8, 125.8, 125.5, 123.2, 119.8, 115.7, 50.0, 36.4, 29.7, 28.3, 9.6. HRMS Calcd for $C_{18}H_{17}N_2O$ $[M + H]^+$: m/z 277.1335, Found: 277.1341

5-methyl-5-propylbenzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one (3n)



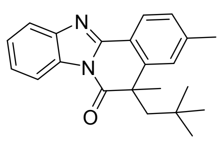
White oil, ^1H NMR (400 MHz, $CDCl_3$) δ 8.49-8.46 (m, 1H), 8.38-8.35 (m, 1H), 7.83-7.80 (m, 1H), 7.58-7.54 (m, 1H), 7.48-7.39 (m, 4H), 2.41-2.33 (m, 1H), 1.98-1.90 (m, 1H), 1.73 (s, 3H), 1.00-0.78 (m, 2H), 0.74 (t, J = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.4, 149.9, 144.1, 141.9, 131.8, 131.3, 127.6, 126.0, 125.8, 125.8, 125.5, 123.0, 119.8, 115.7, 49.5, 45.5, 28.6, 18.5, 14.0. HRMS Calcd for $C_{19}H_{19}N_2O$ $[M + H]^+$: m/z 291.1492, Found: 291.1497

5-methyl-5-(2-phenoxyethyl)benzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one (3o)



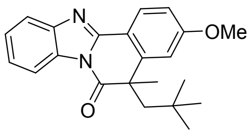
White solid, ^1H NMR (400 MHz, $CDCl_3$) δ 8.45-8.40 (m, 2H), 7.80-7.76 (m, 1H), 7.55 (t, J = 7.2 Hz, 1H), 7.48-7.42 (m, 4H), 6.91 (t, J = 7.6 Hz, 2H), 6.70 (t, J = 7.2 Hz, 1H), 6.12 (d, J = 8.4 Hz, 2H), 3.82-3.77 (m, 1H), 3.45-3.39 (m, 1H), 3.17-3.10 (m, 1H), 2.40-2.35 (m, 1H), 1.80 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.0, 157.6, 149.6, 144.0, 140.4, 131.7, 131.6, 129.1, 127.9, 126.2, 126.1, 125.8, 125.6, 123.2, 120.7, 119.8, 115.7, 113.6, 63.7, 47.0, 41.6, 29.7. HRMS Calcd for $C_{24}H_{21}N_2O_2$ $[M + H]^+$: m/z 369.1598, Found: 369.1596

3,5-dimethyl-5-neopentylbenzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one (3p)



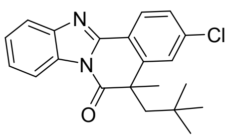
White solid, ^1H NMR (400 MHz, $CDCl_3$) δ 8.38-8.36 (m, 2H), 7.81 (d, J = 7.2 Hz, 1H), 7.43-7.36 (m, 2H), 7.29-7.25 (m, 2H), 2.61 (d, J = 14.4 Hz, 1H), 2.43 (s, 3H), 2.14 (d, J = 14.4, 1H), 1.69 (s, 3H), 0.54 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.5, 150.0, 144.2, 141.9, 141.6, 131.4, 128.7, 128.0, 125.8, 125.7, 125.2, 119.8, 119.5, 115.7, 55.2, 47.5, 33.0, 32.0, 30.8, 21.9. HRMS Calcd for $C_{22}H_{25}N_2O$ $[M + H]^+$: m/z 333.1961, Found: 333.1959

3-methoxy-5-methyl-5-neopentylbenzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one (3q)



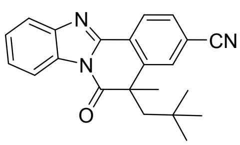
White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (d, *J* = 8.8 Hz, 1H), 8.33 (d, *J* = 8.0 Hz, 1H), 7.75 (d, *J* = 7.6 Hz, 1H), 7.39-7.31 (m, 2H), 7.00-6.95 (m, 2H), 3.84 (d, *J* = 2.8 Hz, 3H), 2.59 (d, *J* = 14.4 Hz, 1H), 2.09 (d, *J* = 14.4 Hz, 1H), 1.66 (s, 3H), 0.54 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3, 162.0, 149.9, 144.2, 144.0, 131.3, 127.8, 125.7, 125.0, 119.3, 115.6, 115.4, 113.6, 113.1, 55.5, 55.4, 47.7, 33.1, 32.0, 30.8. HRMS Calcd for $C_{22}H_{25}N_2O_2$ $[M + H]^+$: m/z 349.1911, Found: 349.1911

3-chloro-5-methyl-5-neopentylbenzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one (3r)



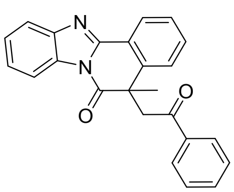
White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (d, *J* = 8.4 Hz, 1H), 8.38-8.36 (m, 1H), 7.83-7.81 (m, 1H), 7.49-7.41 (m, 4H), 2.64 (d, *J* = 14.4 Hz, 1H), 2.12 (d, *J* = 14.4 Hz, 1H), 1.71 (s, 3H), 0.56 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.7, 148.8, 144.0, 143.7, 137.5, 131.3, 128.2, 127.7, 127.3, 126.1, 125.8, 121.0, 119.8, 115.8, 55.3, 47.7, 33.0, 32.1, 30.8, 14.1. HRMS Calcd for $C_{21}H_{22}ClN_2O$ $[M + H]^+$: m/z 353.1415, Found: 353.1415

5-methyl-5-neopentyl-6-oxo-5,6-dihydrobenzo[4,5]imidazo[2,1-a]isoquinoline-3-carbonitrile (3s)



White solid, ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.60 (d, *J* = 8.0 Hz, 1H), 8.41 – 8.39 (m, 1H), 7.88 – 7.85 (m, 1H), 7.81 (s, 1H), 7.74 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.52 – 7.47 (m, 2H), 2.69 (d, *J* = 14.4, 1H), 2.15 (d, *J* = 14.4 Hz, 1H), 1.73 (s, 3H), 0.55 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.0, 147.7, 144.0, 142.9, 131.7, 131.4, 130.7, 126.6, 126.6, 126.4, 126.4, 120.3, 118.1, 116.0, 114.4, 55.4, 47.7, 32.9, 32.1, 30.8. HRMS Calcd for $C_{22}H_{22}N_3O$ $[M + H]^+$: m/z 344.1757, Found: 344.1760

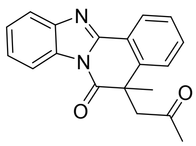
5-methyl-5-(2-oxo-2-phenylethyl)benzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one (3t)



Light yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65-8.47 (m, 1H), 8.34 (dd, *J* = 7.4, 1.6 Hz, 1H), 8.00-

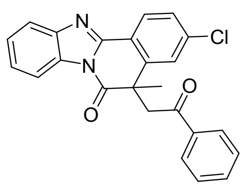
7.76 (m, 3H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.48-7.34 (m, 6H), 7.32 (dt, *J* = 5.0, 3.1 Hz, 1H), 4.29 (d, *J* = 18.3 Hz, 1H), 4.14 (d, *J* = 18.2 Hz, 1H), 1.70 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.2, 173.3, 150.1, 144.1, 142.0, 135.6, 133.7, 131.7, 131.6, 128.7, 128.1, 127.6, 126.4, 125.7, 125.4, 124.5, 123.0, 119.8, 115.7, 49.3, 46.2, 30.2. HRMS Calcd for $C_{24}H_{19}N_2O_2$ $[M + H]^+$: m/z 367.1441, Found: 367.1443

5-methyl-5-(2-oxopropyl)benzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one (3u)



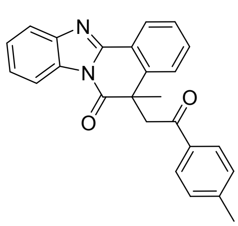
White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (d, *J* = 7.2, 1H), 8.32 (d, *J* = 7.6, 1H), 7.83 (d, *J* = 7.6, 1H), 7.46-7.37 (m, 4H), 7.27 (d, *J* = 7.6 Hz, 1H), 3.76 (d, *J* = 16.8 Hz, 1H), 3.48 (d, *J* = 16.8 Hz, 1H), 1.99 (s, 3H), 1.57 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 204.8, 173.2, 150.0, 144.0, 141.7, 131.6, 131.6, 130.0, 129.0, 127.6, 126.7, 126.3, 125.7, 125.4, 124.5, 123.0, 119.7, 115.6, 53.9, 45.9, 29.9, 29.5. HRMS Calcd for $C_{19}H_{17}N_2O_2$ $[M + H]^+$: m/z 305.1285, Found: 305.1286

3-chloro-5-methyl-5-(2-oxo-2-phenylethyl)benzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one (3v)



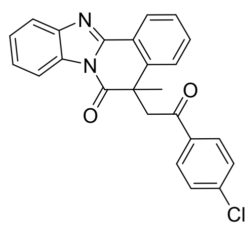
White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (d, *J* = 8.8 Hz, 1H), 8.36-8.34 (m, 1H), 7.90-7.85 (m, 3H), 7.55 (t, *J* = 7.2 Hz, 1H), 7.49-7.40 (m, 5H), 7.33 (d, *J* = 1.2 Hz, 1H), 4.35 (d, *J* = 18.0 Hz, 1H), 4.08 (d, *J* = 18.0 Hz, 1H), 1.73 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.0, 172.6, 149.2, 144.1, 143.8, 137.7, 135.4, 133.8, 131.6, 130.1, 128.7, 128.2, 128.1, 127.8, 125.8, 125.6, 124.8, 121.8, 119.9, 115.7, 49.4, 46.2, 30.0. HRMS Calcd for $C_{24}H_{18}ClN_2O_2$ $[M + H]^+$: m/z 401.1051, Found: 401.1055

5-methyl-5-(2-oxo-2-(p-tolyl)ethyl)benzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one (3w)



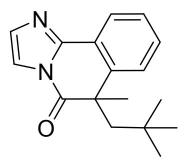
White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58-8.56 (m, 1H), 8.37-8.35 (m, 1H), 7.89 (d, *J* = 7.2 Hz, 1H), 7.77 (d, *J* = 8.0 Hz, 2H), 7.48-7.40 (m, 4H), 7.36-7.33 (m, 1H), 7.22 (d, *J* = 8.0 Hz, 2H), 4.30 (d, *J* = 18.0 Hz, 1H), 4.15 (d, *J* = 18.1 Hz, 1H), 2.40 (s, 3H), 1.74 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.6, 173.3, 150.1, 144.5, 144.0, 142.0, 133.2, 131.7, 131.6, 129.3, 128.1, 127.5, 126.4, 125.6, 125.3, 124.4, 123.0, 119.7, 115.6, 49.2, 46.2, 30.2, 21.6. HRMS Calcd for $C_{25}H_{21}N_2O_2$ $[M + H]^+$: m/z 381.1598, Found: 381.1601

5-(2-(4-chlorophenyl)-2-oxoethyl)-5-methylbenzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one (3x)



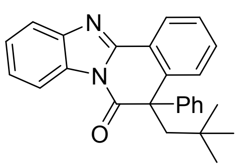
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58-8.56 (m, 1H), 8.37-8.35 (m, 1H), 7.90-7.88 (m, 1H), 7.75 (d, *J* = 8.8 Hz, 2H), 7.48-7.40 (m, 4H), 7.36-7.28 (m, 3H), 4.26 (d, *J* = 18.4 Hz, 1H), 4.08 (d, *J* = 18.4 Hz, 1H), 1.71 (s, 3H). ^{13}C NMR (101 MHz, CDCl3) δ 195.0, 173.2, 150.1, 144.1, 141.8, 140.1, 133.9, 131.7, 129.5, 129.0, 127.6, 126.4, 125.7, 125.4, 124.4, 123.1, 119.8, 115.6, 49.2, 46.2, 30.1. HRMS Calcd for $C_{24}H_{18}ClN_2O_2$ $[M + H]^+$: m/z 401.1051, Found: 401.1056

6-methyl-6-neopentylimidazo[2,1-a]isoquinolin-5(6H)-one (3y)



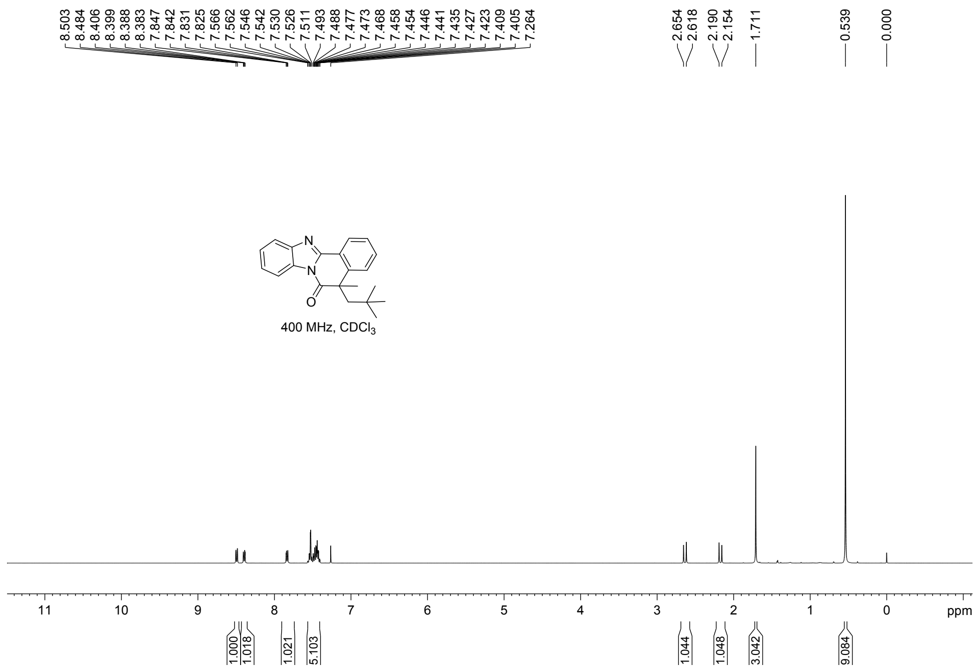
White oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35-8.22 (m, 2H), 7.65-7.20 (m, 4H), 2.51 (d, *J* = 14.4 Hz, 1H), 2.04 (d, *J* = 14.4 Hz, 1H), 1.59 (s, 3H), 0.60 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.6, 163.9, 145.1, 133.83, 133.82, 128.5, 127.3, 127.26, 127.25, 123.9, 53.4, 46.3, 33.4, 32.0, 30.8. HRMS Calcd for $C_{17}H_{21}N_2O$ $[M + H]^+$: m/z 269.1648, Found: 269.1646

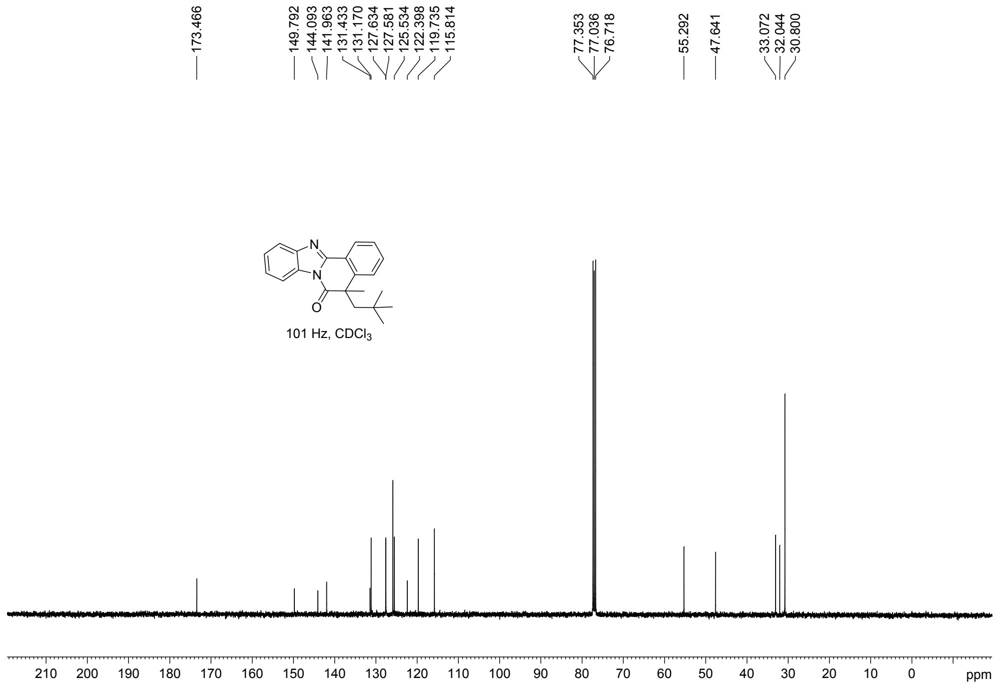
5-neopentyl-5-phenylbenzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one (3z)



White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (dd, *J* = 8.0, 1.6 Hz, 1H), 8.30-8.27 (m, 1H), 7.86-7.83 (m, 1H), 7.50-7.37 (m, 4H), 7.28 – 7.20 (m, 5H), 7.15 (dd, *J* = 8.0, 1.2 Hz, 1H), 3.30 (d, *J* = 13.6 Hz, 1H), 2.55 (d, *J* = 13.6 Hz, 1H), 0.63 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.4, 149.8, 145.0, 144.1, 142.0, 131.5, 131.2, 130.2, 128.8, 127.9, 127.5, 127.0, 126.0, 125.7, 125.6, 123.3, 119.7, 115.9, 55.4, 51.5, 31.9, 31.1. HRMS Calcd for $C_{26}H_{25}N_2O$ $[M + H]^+$: m/z 381.1961, Found: 381.1966

5. NMR Copies of Products


8.503 8.484 8.406 8.399 8.388 8.383 7.847 7.842 7.831 7.825 7.566 7.562 7.546 7.542 7.530 7.526 7.511 7.493 7.488 7.477 7.473 7.468 7.458 7.454 7.446 7.441 7.435 7.427 7.423 7.409 7.405 7.264
2.654 2.618 2.190 2.154 1.711 0.539 0.000
400 MHz, CDCl3
11 10 9 8 7 6 5 4 3 2 1 0 ppm
1.000 1.018 1.021 5.103 1.044 1.048 3.042 9.084


173.466 149.792 144.093 141.963 131.433 131.170 127.634 127.581 125.534 122.398 119.735 115.814
77.353 77.036 76.718 55.292 47.641 33.072 32.044 30.800
101 Hz, CDCl3
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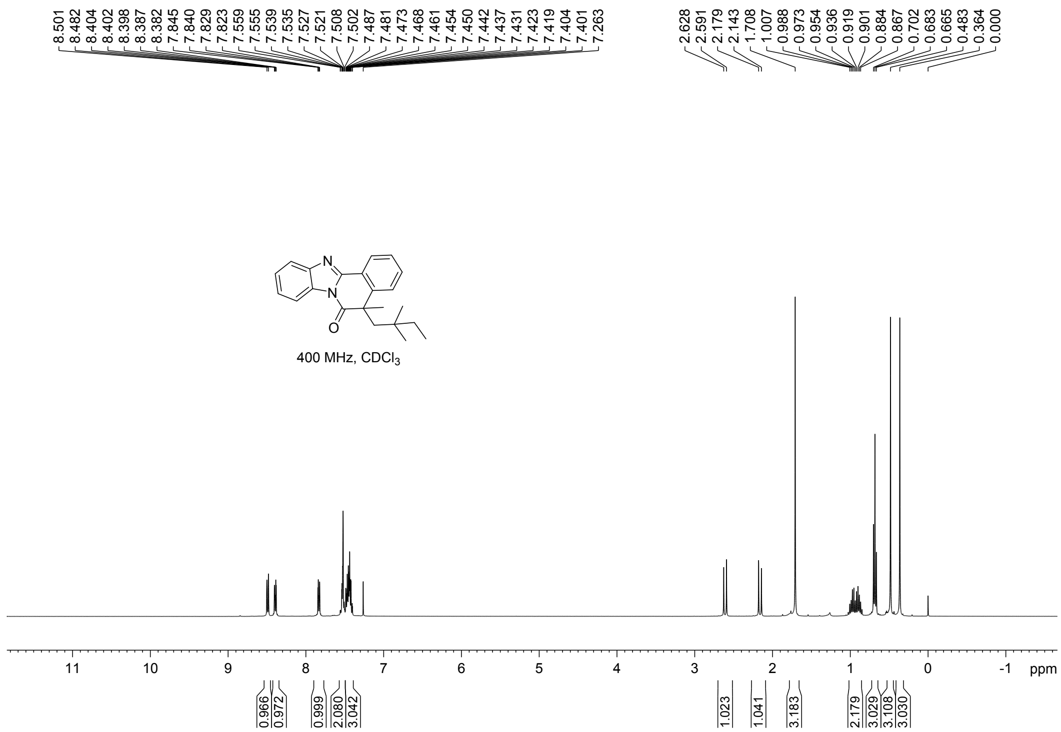
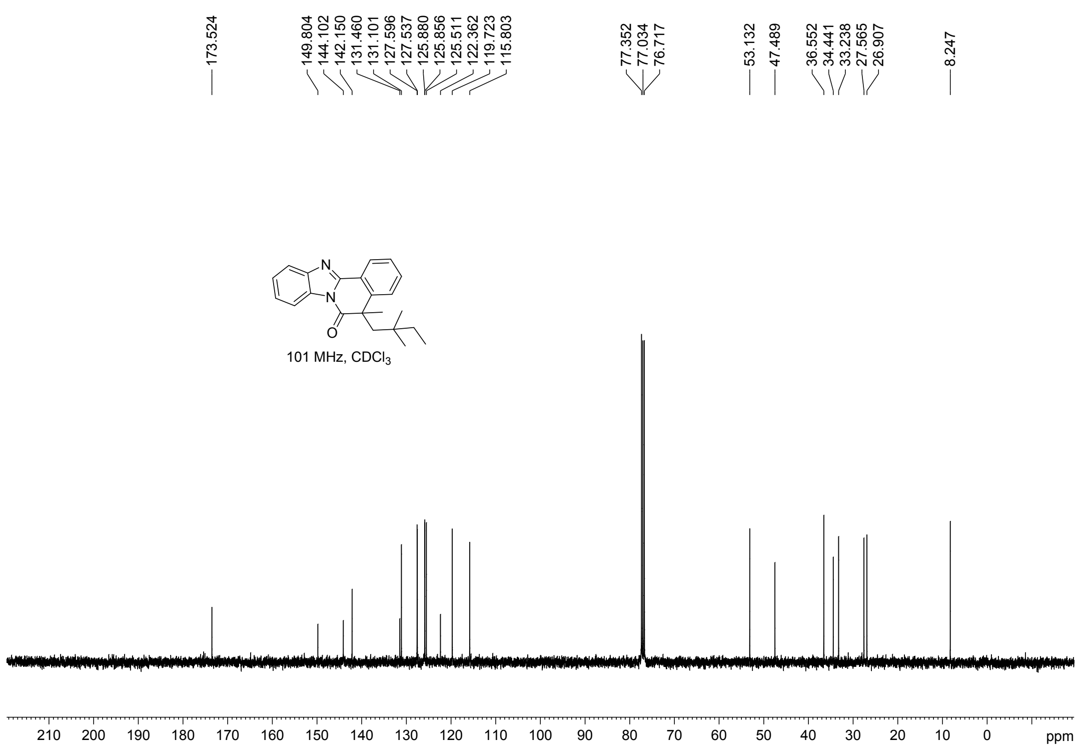
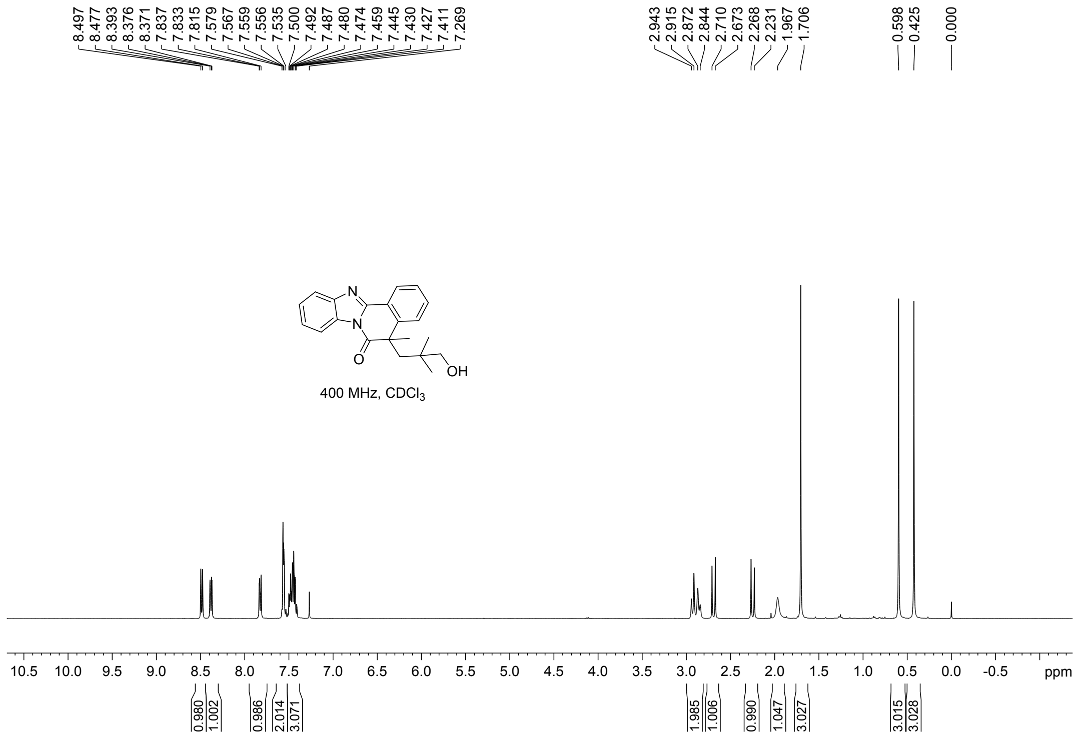
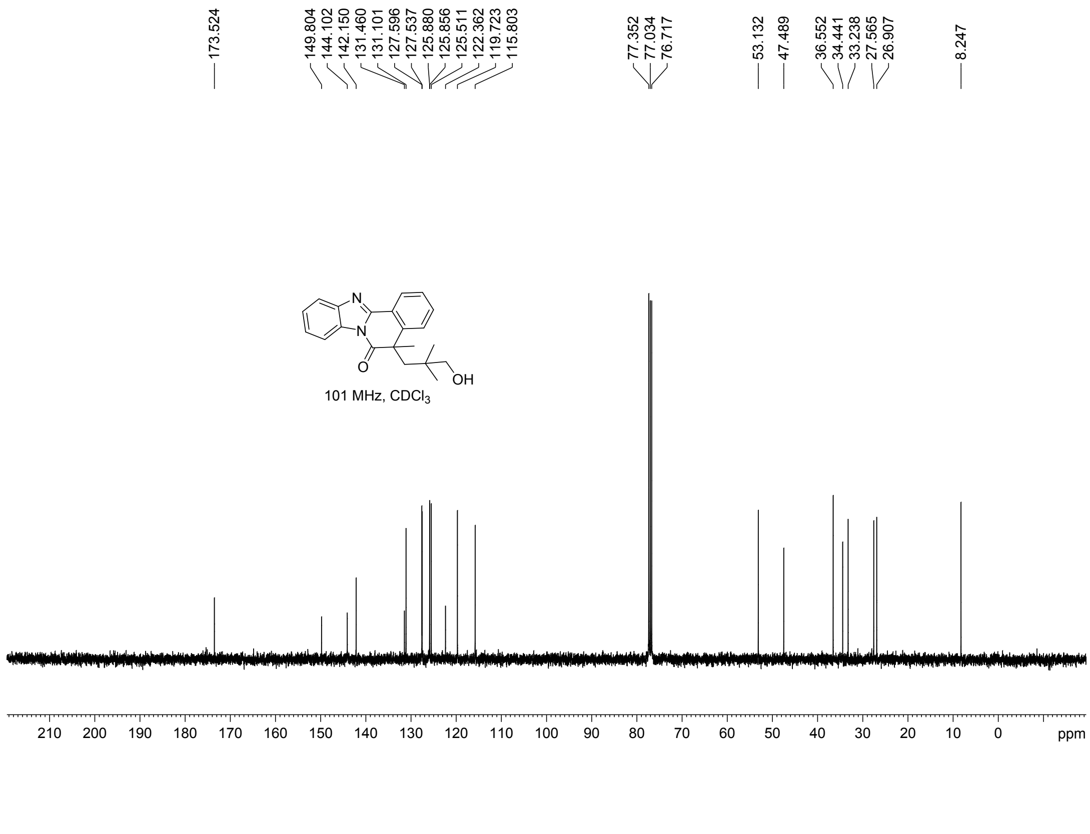
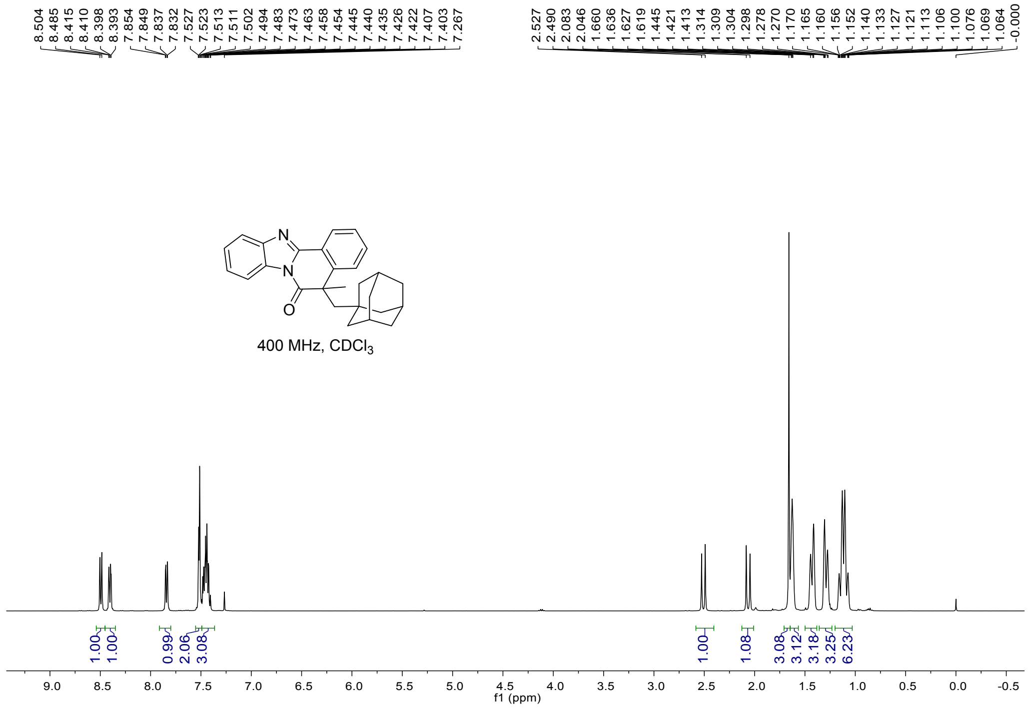
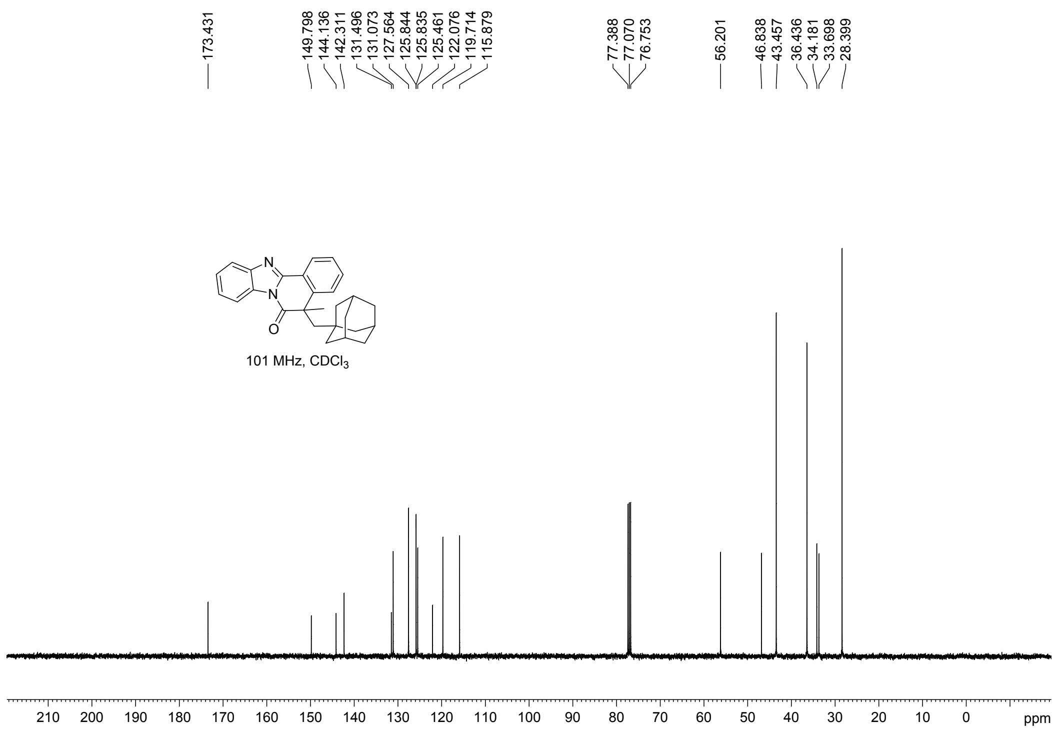

8.501 8.482 8.404 8.402 8.398 8.387 8.382 7.845 7.840 7.829 7.823 7.559 7.555 7.539 7.535 7.527 7.521 7.508 7.502 7.487 7.481 7.473 7.468 7.461 7.454 7.450 7.442 7.437 7.431 7.423 7.419 7.404 7.401 7.263
2.628 2.591 2.179 2.143 1.708 1.007 0.988 0.973 0.954 0.936 0.919 0.901 0.884 0.867 0.702 0.683 0.665 0.483 0.364 0.000
N
N
O
400 MHz, CDCl3
11 10 9 8 7 6 5 4 3 2 1 0 -1 ppm
0.966 0.972 0.999 2.080 3.042 1.023 1.041 3.183 2.179 3.029 3.108 3.030

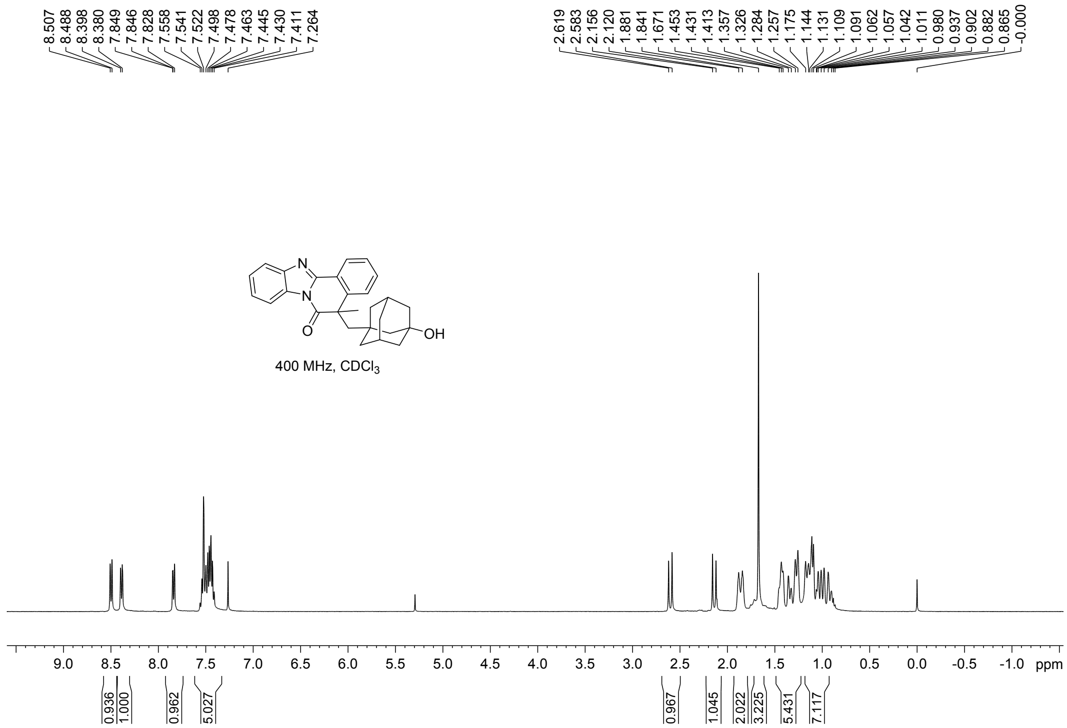

173.524
149.804 144.102 142.150 131.460 131.101 127.596 127.537 125.880 125.856 125.511 122.362 119.723 115.803
77.352 77.034 76.717
53.132 47.489 36.552 34.441 33.238 27.565 26.907 8.247
N
N
O
101 MHz, CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


8.497 8.477 8.393 8.376 8.371 7.837 7.833 7.815 7.579 7.567 7.559 7.556 7.535 7.500 7.492 7.487 7.480 7.474 7.459 7.445 7.430 7.427 7.411 7.269
2.943 2.915 2.872 2.844 2.710 2.673 2.268 2.231 1.967 1.706
0.598 0.425
0.000
N
N
O
OH
400 MHz, CDCl3
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 ppm
0.980 1.002 0.986 2.014 3.071
1.985 1.006 0.990 1.047 3.027 3.015 3.028

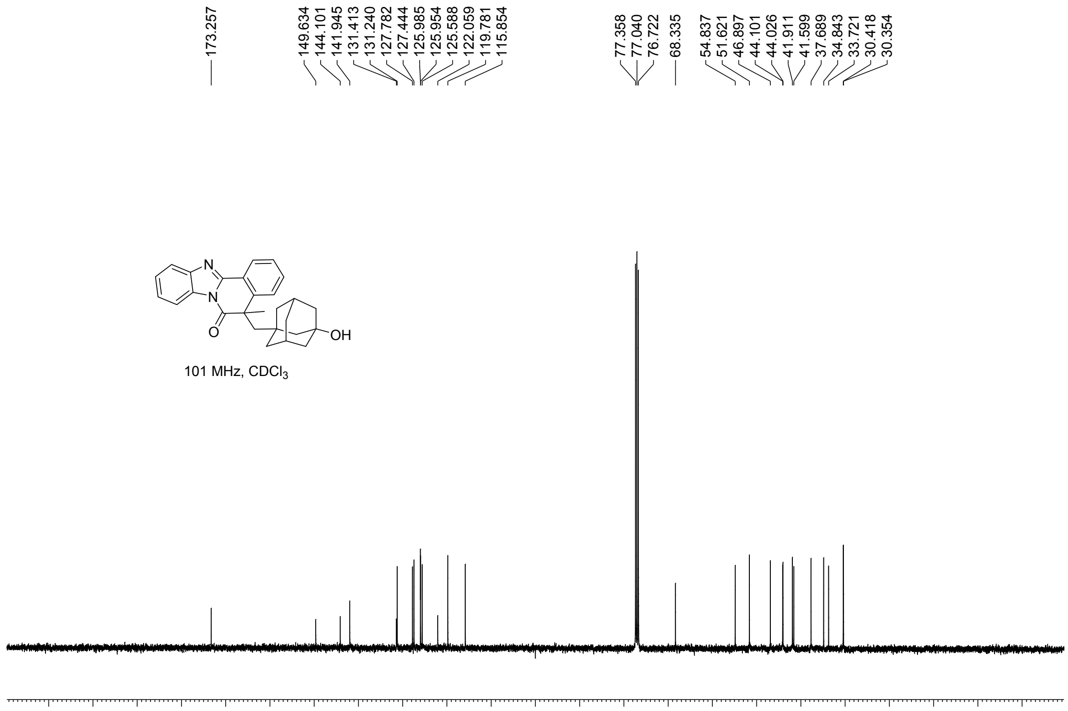

173.524
149.804 144.102 142.150 131.460 131.101 127.596 127.537 125.880 125.856 125.511 122.362 119.723 115.803
77.352 77.034 76.717
53.132 47.489
36.552 34.441 33.238 27.565 26.907
8.247
N
N
O
OH
101 MHz, CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


400 MHz, CDCl$_3$
8.504 8.485 8.415 8.410 8.398 8.393 7.854 7.849 7.837 7.832 7.527 7.523 7.513 7.511 7.502 7.494 7.483 7.473 7.463 7.458 7.454 7.445 7.440 7.435 7.426 7.422 7.407 7.403 7.267
2.527 2.490 2.083 2.046 1.660 1.636 1.627 1.619 1.445 1.421 1.413 1.314 1.309 1.304 1.298 1.278 1.270 1.170 1.165 1.160 1.156 1.152 1.140 1.133 1.127 1.121 1.113 1.106 1.100 1.076 1.069 1.064 -0.000
1.00 1.00 0.99 2.06 3.08 1.00 1.08 3.08 3.12 3.18 3.25 6.23
f1 (ppm)

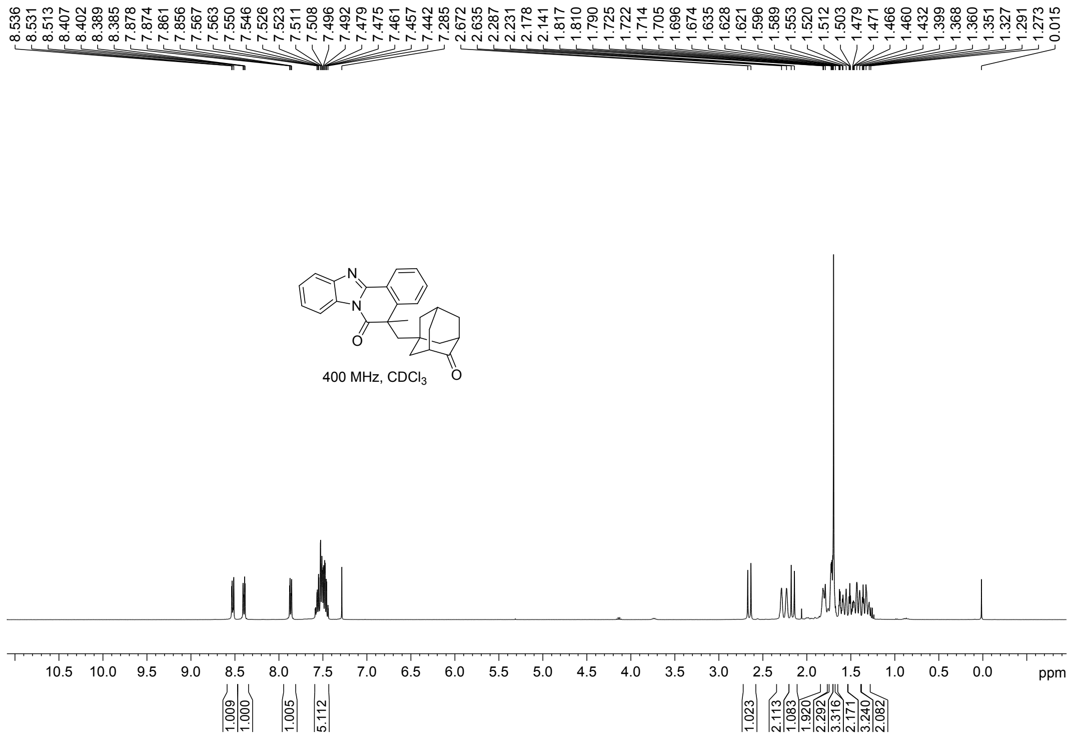

173.431
149.798 144.136 142.311 131.496 131.073 127.564 125.844 125.835 125.461 122.076 119.714 115.879
77.388 77.070 76.753
56.201
46.838 43.457 36.436 34.181 33.698 28.399
101 MHz, CDCl$_3$
ppm



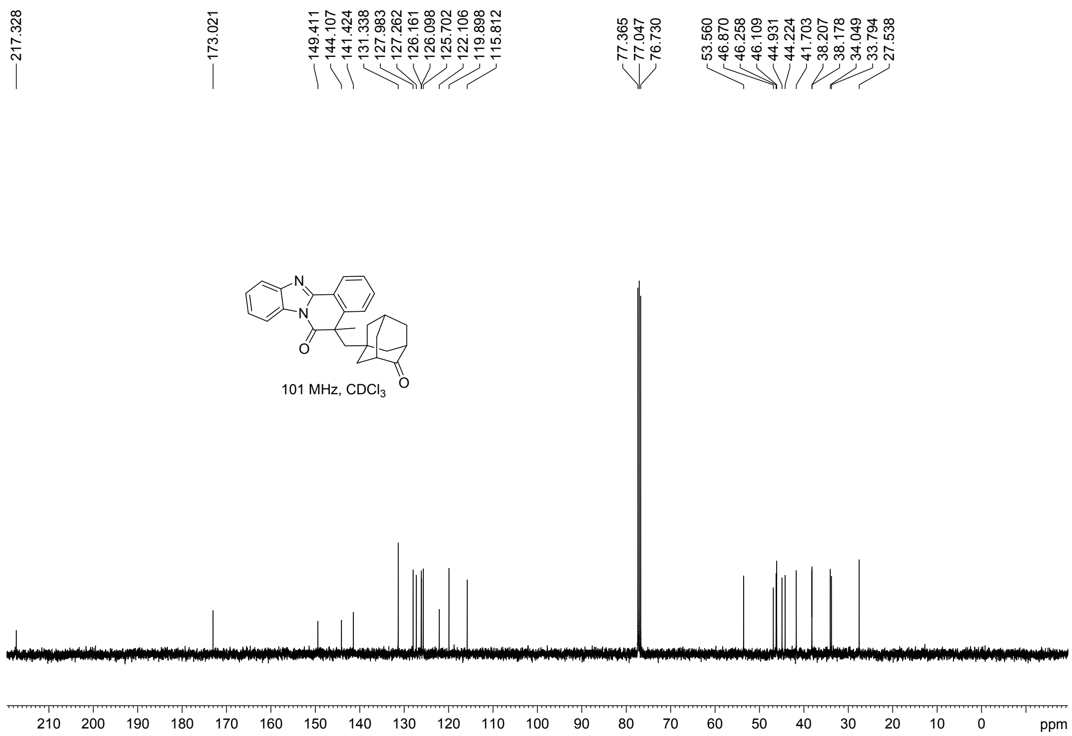
8.507 8.488 8.398 8.380 7.849 7.846 7.828 7.558 7.541 7.522 7.498 7.478 7.463 7.445 7.430 7.411 7.264
2.619 2.583 2.156 2.120 1.881 1.841 1.671 1.453 1.431 1.413 1.357 1.326 1.284 1.257 1.175 1.144 1.131 1.109 1.091 1.062 1.057 1.042 1.011 0.980 0.937 0.902 0.882 0.865 -0.000
OH
400 MHz, CDCl3
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 ppm
0.936 1.000 0.962 5.027 0.967 1.045 2.022 3.225 5.431 7.117



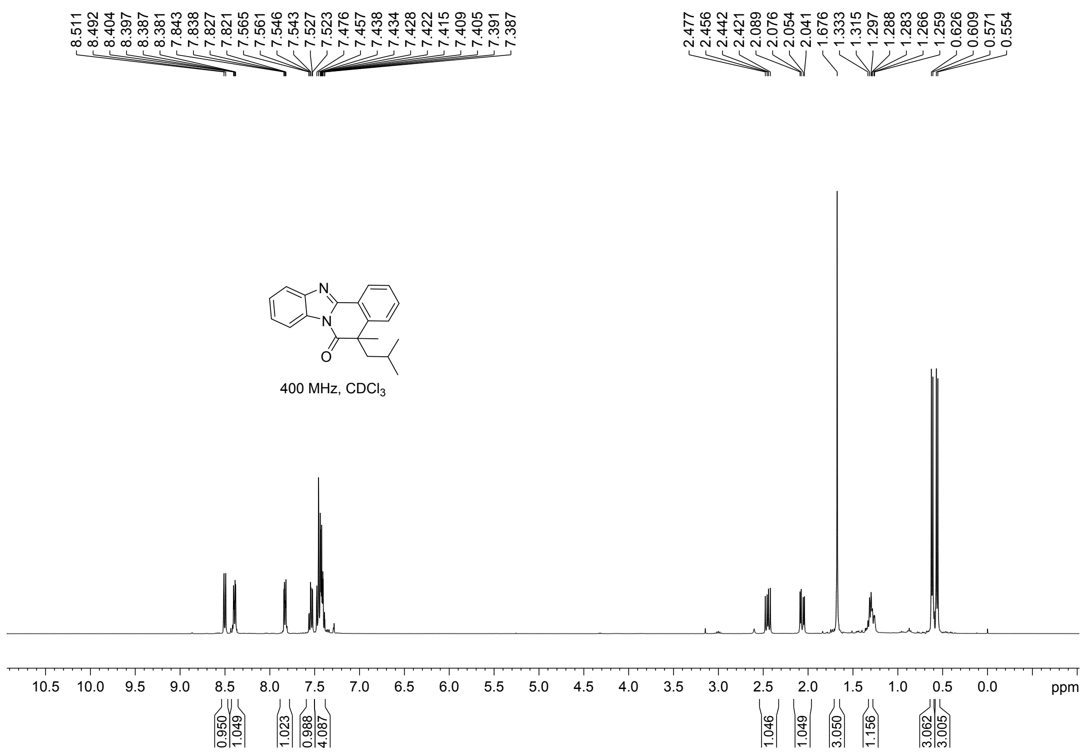
173.257
149.634 144.101 141.945 131.413 131.240 127.782 127.444 125.985 125.954 125.588 122.059 119.781 115.854
77.358 77.040 76.722 68.335
54.837 51.621 46.897 44.101 44.026 41.911 41.599 37.689 34.843 33.721 30.418 30.354
OH
101 MHz, CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

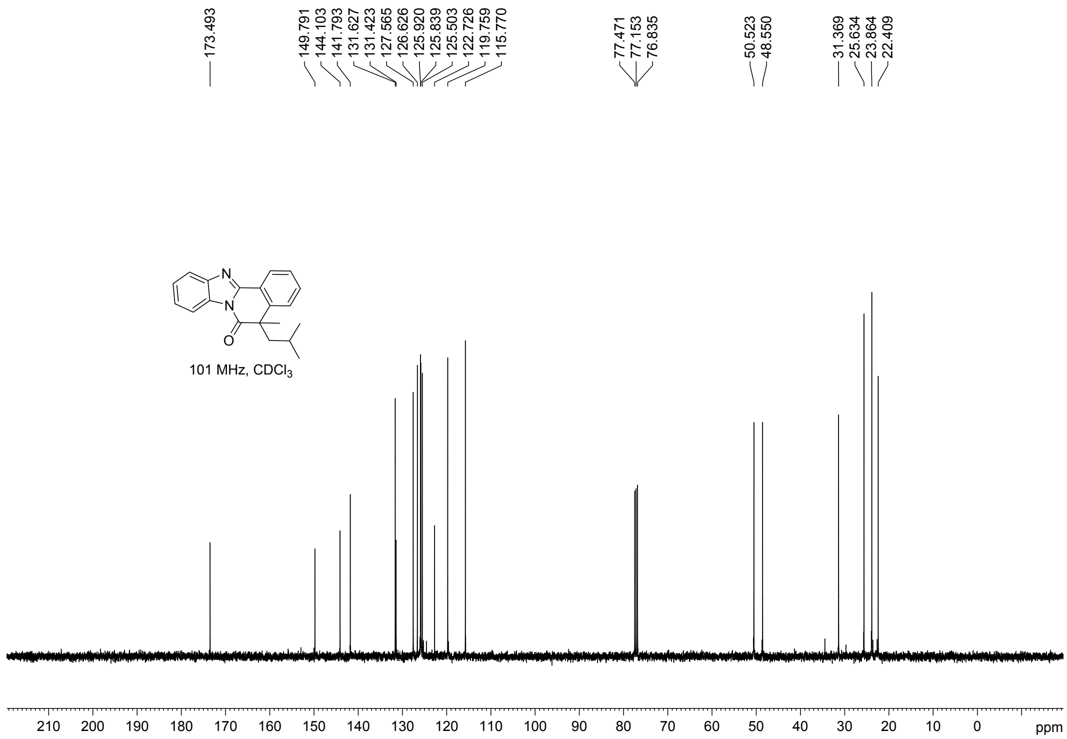


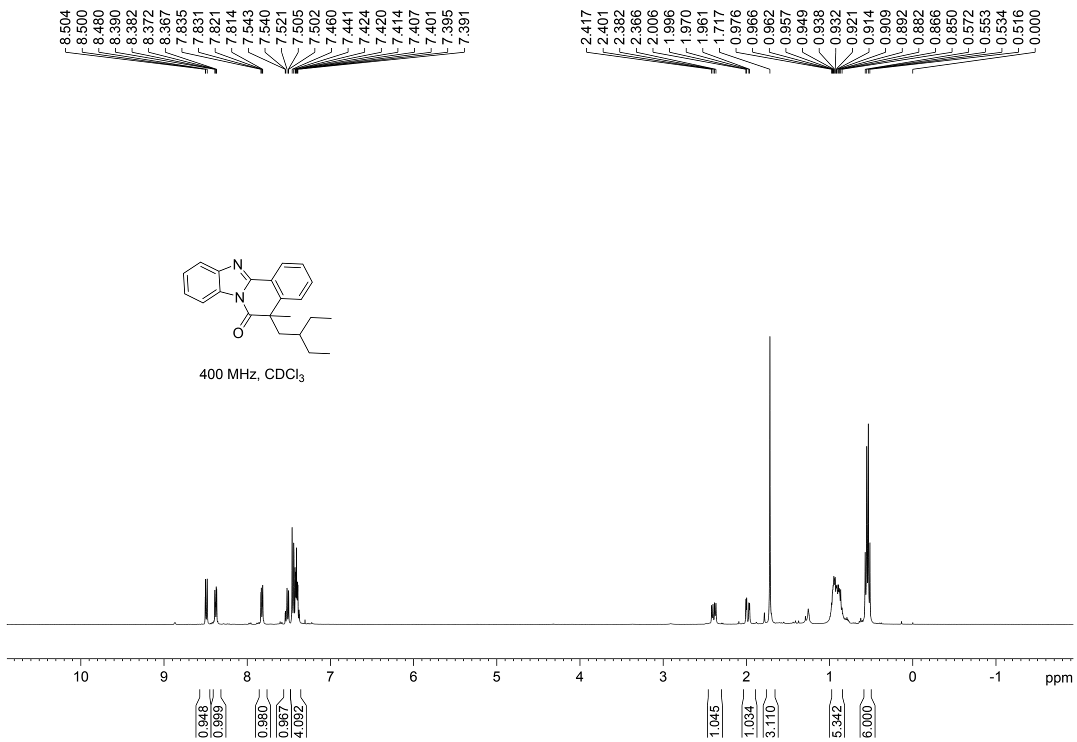
8.536 8.531 8.513 8.407 8.402 8.389 8.385 7.878 7.874 7.861 7.856 7.567 7.563 7.550 7.546 7.526 7.523 7.511 7.508 7.496 7.492 7.479 7.475 7.461 7.457 7.442 7.285 2.672 2.635 2.287 2.231 2.178 2.141 1.817 1.810 1.790 1.725 1.722 1.714 1.705 1.696 1.674 1.635 1.628 1.621 1.596 1.589 1.553 1.520 1.512 1.503 1.479 1.471 1.466 1.460 1.432 1.399 1.368 1.360 1.351 1.327 1.291 1.273 0.015
400 MHz, CDCl3
1.009 1.000 1.005 5.112 1.023 2.113 1.083 1.920 2.292 3.316 2.171 3.240 2.082
ppm

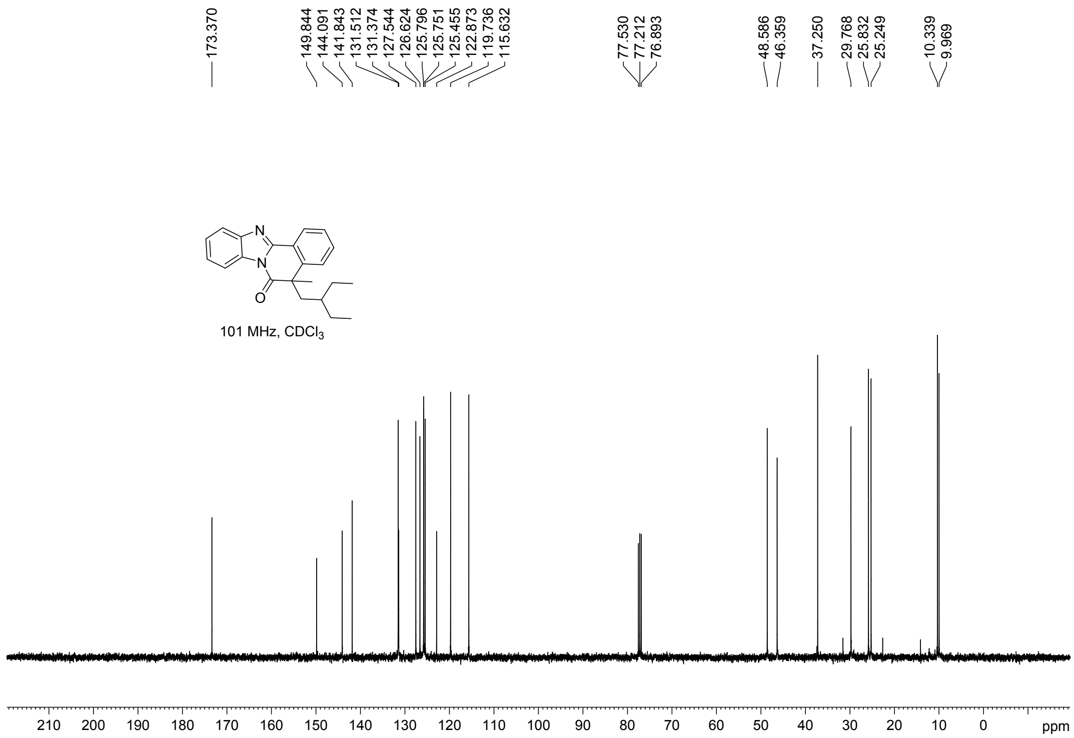


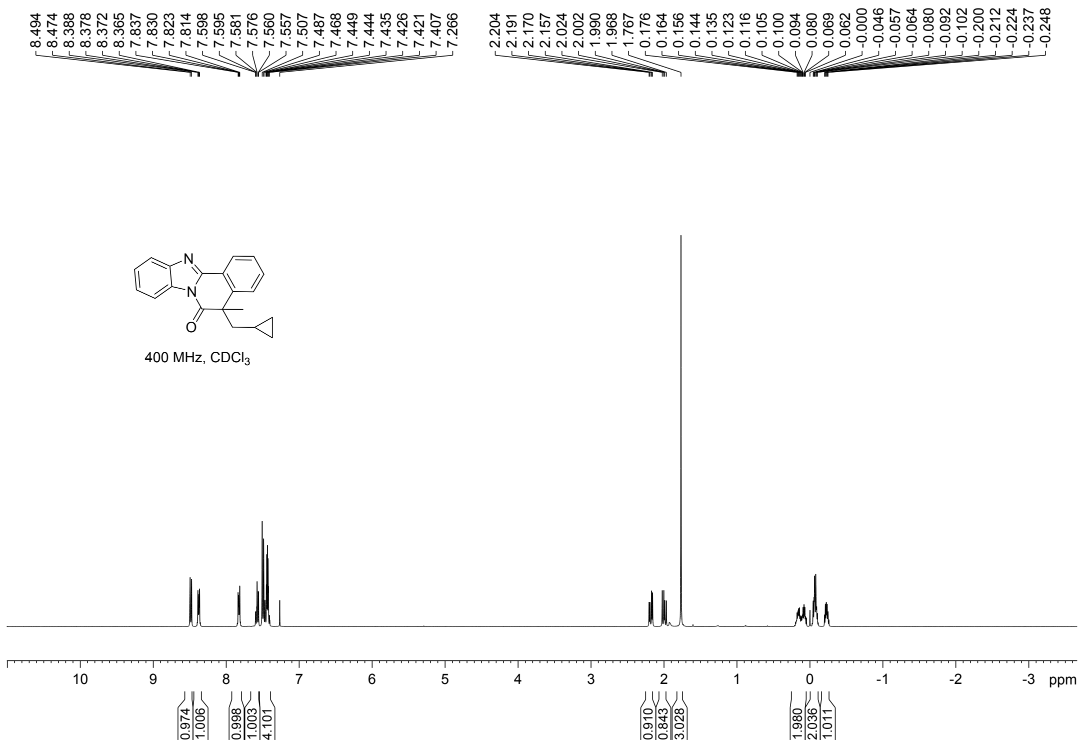
217.328 173.021 149.411 144.107 141.424 131.338 127.983 127.262 126.161 126.098 125.702 122.106 119.898 115.812 77.365 77.047 76.730 53.560 46.870 46.258 46.109 44.931 44.224 41.703 38.207 38.178 34.049 33.794 27.538
101 MHz, CDCl3
ppm

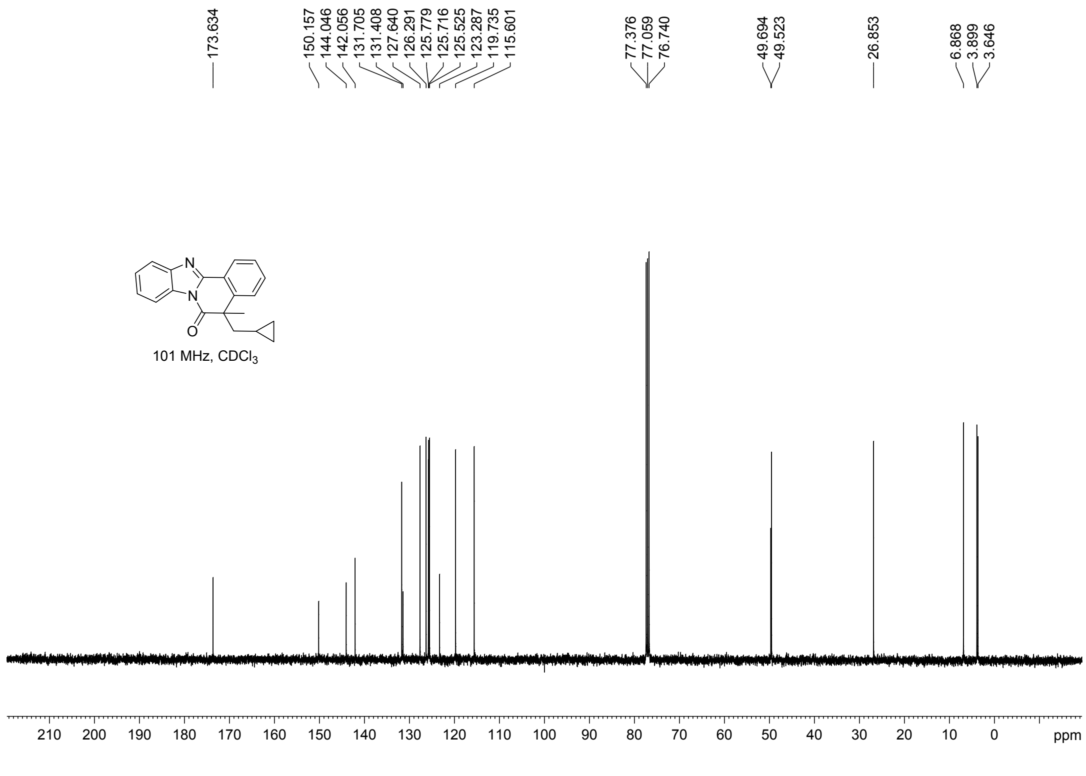

8.511 8.492 8.404 8.397 8.387 8.381 7.843 7.838 7.827 7.821 7.565 7.561 7.546 7.543 7.527 7.523 7.476 7.457 7.438 7.434 7.428 7.422 7.415 7.409 7.405 7.391 7.387
2.477 2.456 2.442 2.421 2.089 2.076 2.054 2.041 1.676 1.333 1.315 1.297 1.288 1.283 1.266 1.259 0.626 0.609 0.571 0.554
N
N
O
400 MHz, CDCl3
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
0.950 1.049 1.023 0.988 4.087 1.046 1.049 3.050 1.156 3.062 3.005

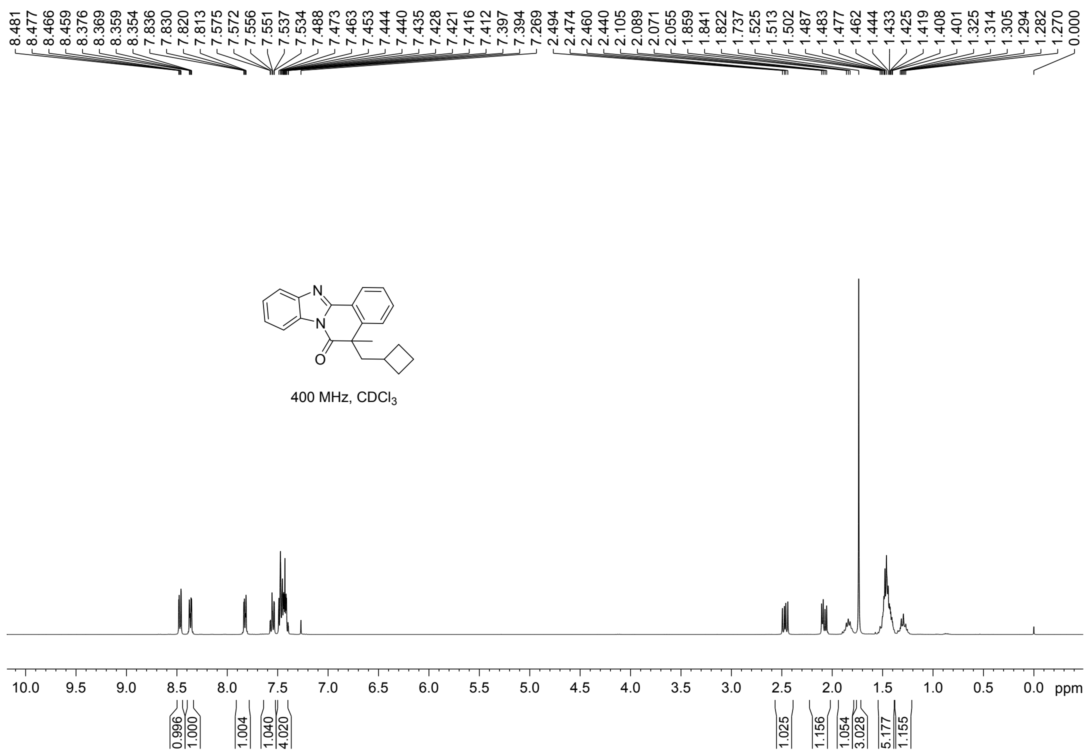

173.493
149.791 144.103 141.793 131.627 131.423 127.565 126.626 125.920 125.839 125.503 122.726 119.759 115.770
77.471 77.153 76.835
50.523 48.550
31.369 25.634 23.864 22.409
N
N
O
101 MHz, CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

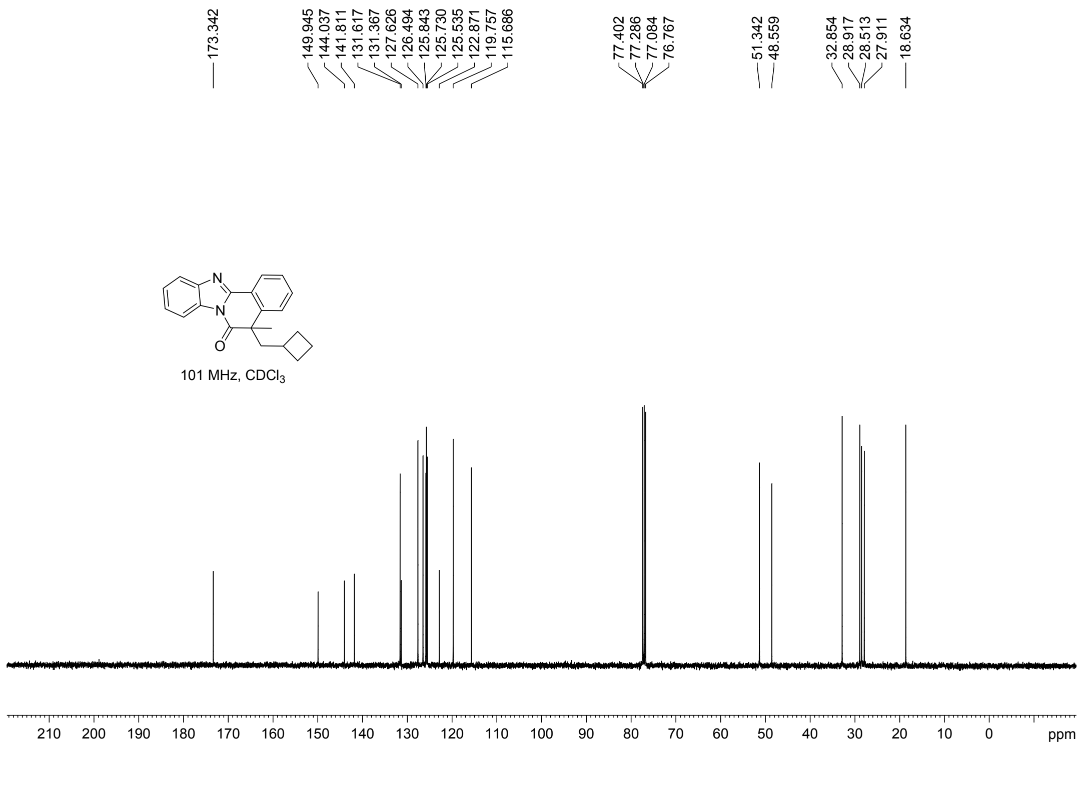

8.504 8.500 8.480 8.390 8.382 8.372 8.367 7.835 7.831 7.821 7.814 7.543 7.540 7.521 7.505 7.502 7.460 7.441 7.424 7.420 7.414 7.407 7.401 7.395 7.391
2.417 2.401 2.382 2.366 2.006 1.996 1.970 1.961 1.717 0.976 0.966 0.962 0.957 0.949 0.938 0.932 0.921 0.914 0.909 0.892 0.882 0.866 0.850 0.572 0.553 0.534 0.516 0.000
N
N
O
400 MHz, CDCl3
10 9 8 7 6 5 4 3 2 1 0 -1 ppm
0.948 0.999 0.980 0.967 4.092 1.045 1.034 3.110 5.342 6.000

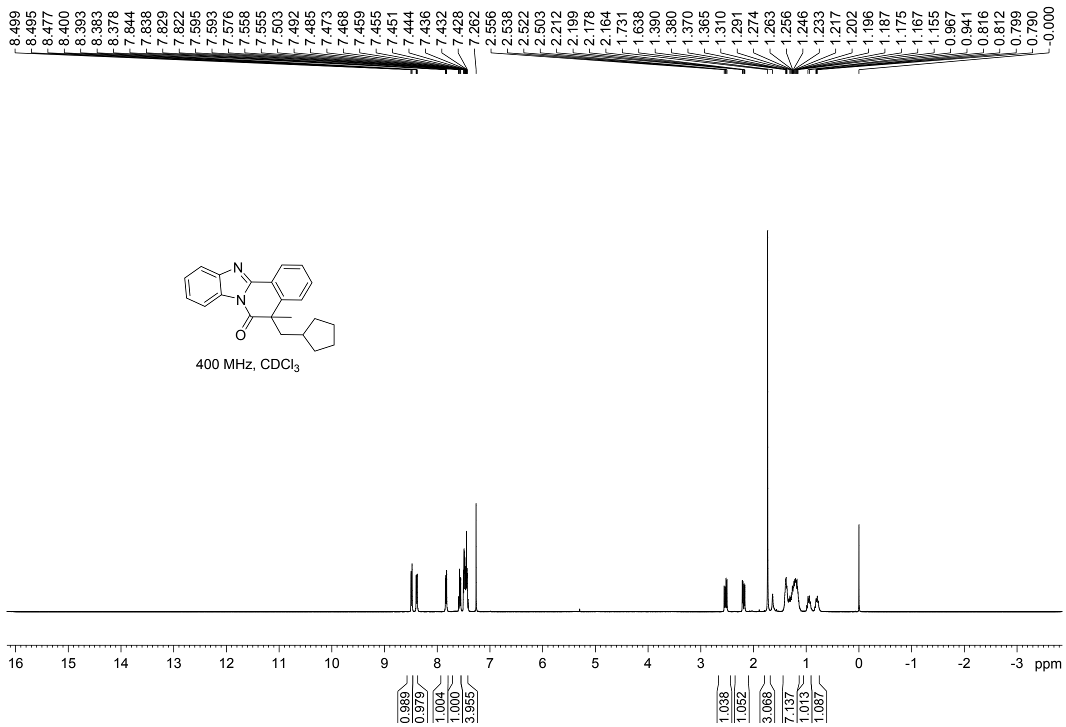

173.370
149.844 144.091 141.843 131.512 131.374 127.544 126.624 125.796 125.751 125.455 122.873 119.736 115.632
77.530 77.212 76.893
48.586 46.359 37.250 29.768 25.832 25.249 10.339 9.969
N
N
O
101 MHz, CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


8.494
8.474
8.388
8.378
8.372
8.365
7.837
7.830
7.823
7.814
7.598
7.595
7.581
7.576
7.560
7.557
7.507
7.487
7.468
7.449
7.444
7.435
7.426
7.421
7.407
7.266
2.204
2.191
2.170
2.157
2.024
2.002
1.990
1.968
1.767
0.176
0.164
0.156
0.144
0.135
0.123
0.116
0.105
0.100
0.094
0.080
0.069
0.062
-0.000
-0.046
-0.057
-0.064
-0.080
-0.092
-0.102
-0.200
-0.212
-0.224
-0.237
-0.248
400 MHz, CDCl3
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
ppm
0.974
1.006
0.998
1.003
4.101
0.910
0.843
3.028
1.980
2.036
1.011

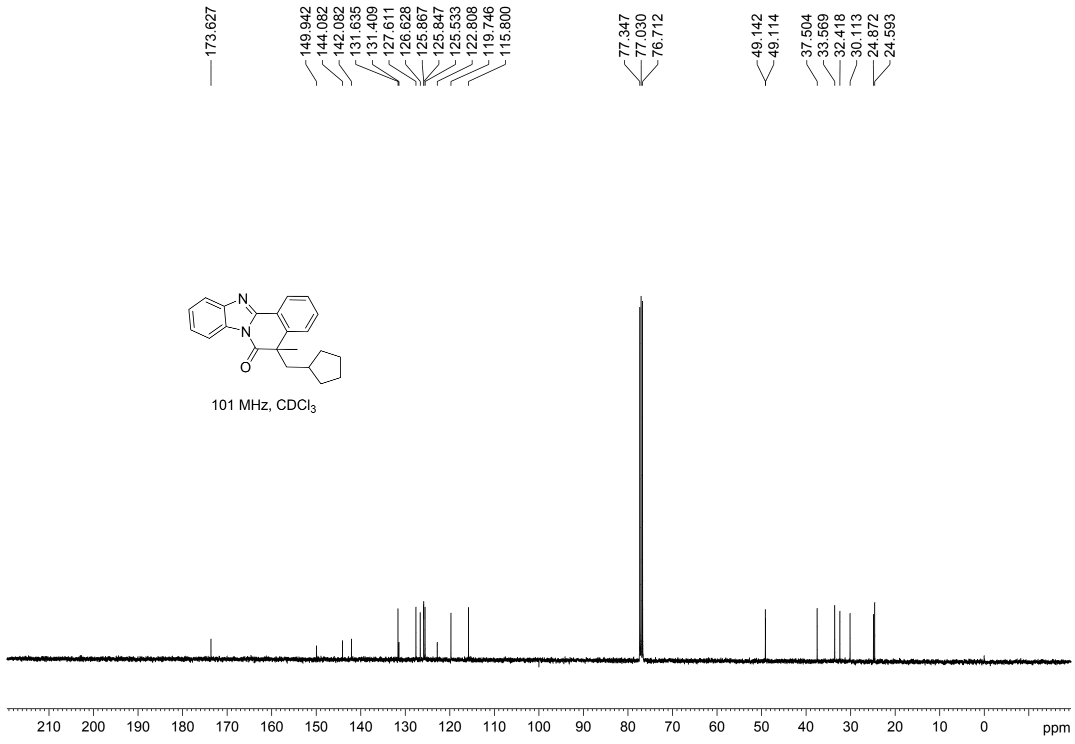

173.634
150.157
144.046
142.056
131.705
131.408
127.640
126.291
125.779
125.716
125.525
123.287
119.735
115.601
77.376
77.059
76.740
49.694
49.523
26.853
6.868
3.899
3.646
101 MHz, CDCl3
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


8.481 8.477 8.466 8.459 8.376 8.369 8.359 8.354 7.836 7.830 7.820 7.813 7.575 7.572 7.556 7.551 7.537 7.534 7.488 7.473 7.463 7.453 7.444 7.440 7.435 7.428 7.421 7.416 7.412 7.397 7.394 7.269 2.494 2.474 2.460 2.440 2.105 2.089 2.071 2.055 1.859 1.841 1.822 1.737 1.525 1.513 1.502 1.487 1.483 1.477 1.462 1.444 1.433 1.425 1.419 1.408 1.401 1.325 1.314 1.305 1.294 1.282 1.270 0.000
N
N
O
400 MHz, CDCl3
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
0.996 1.000 1.004 1.040 4.020 1.025 1.156 1.054 3.028 5.177 1.155

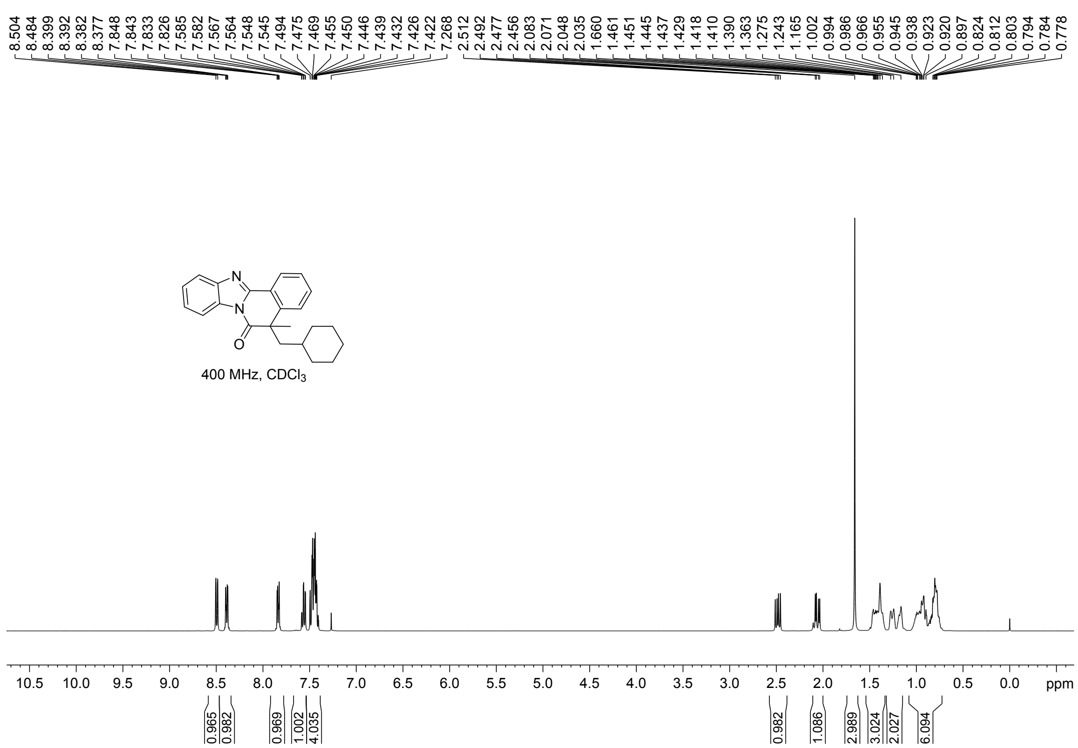

173.342
149.945 144.037 141.811 131.617 131.367 127.626 126.494 125.843 125.730 125.535 122.871 119.757 115.686
77.402 77.286 77.084 76.767
51.342 48.559
32.854 28.917 28.513 27.911
18.634
N
N
O
101 MHz, CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

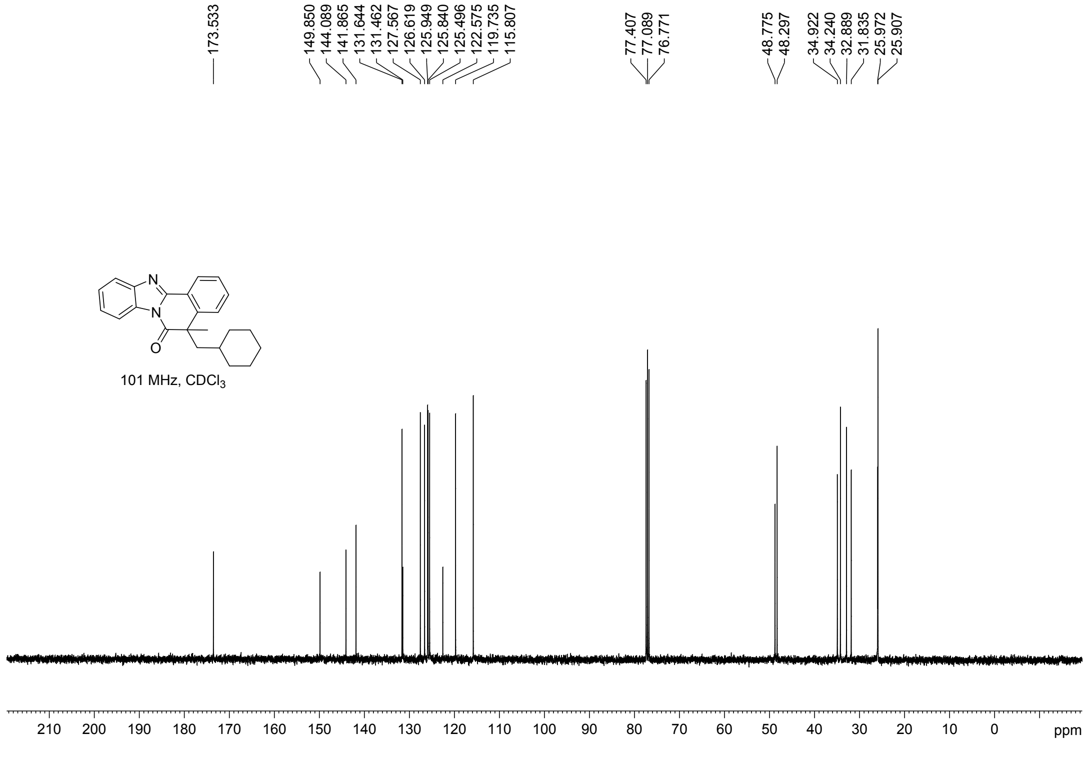


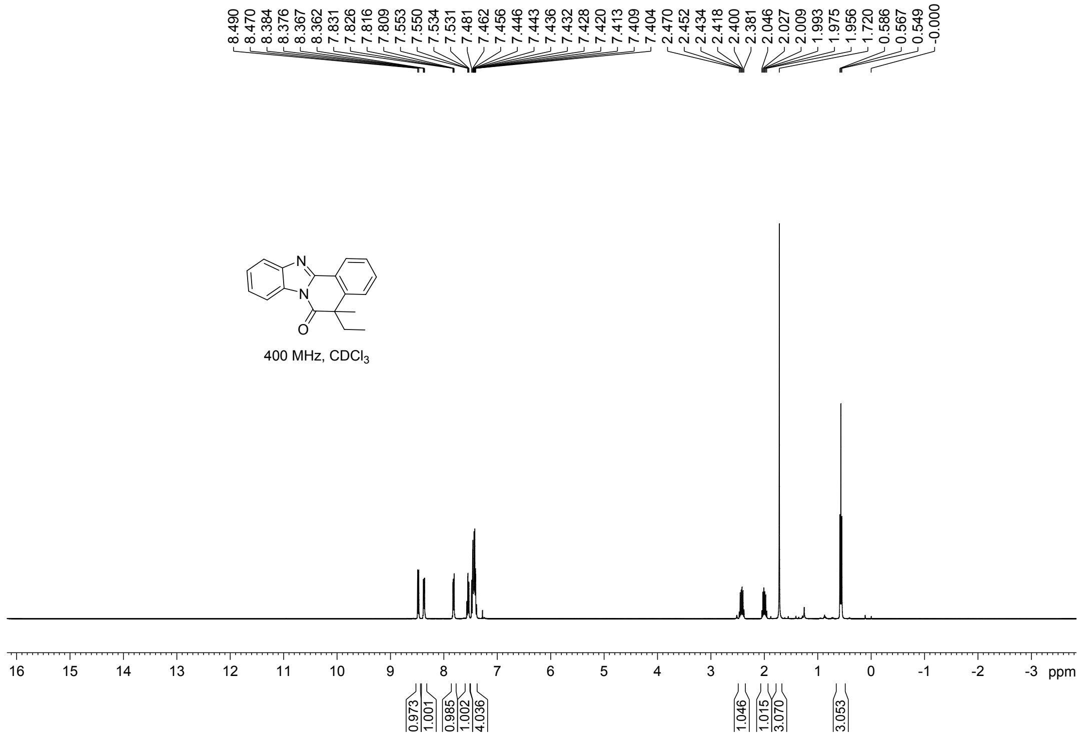
400 MHz, $CDCl_3$

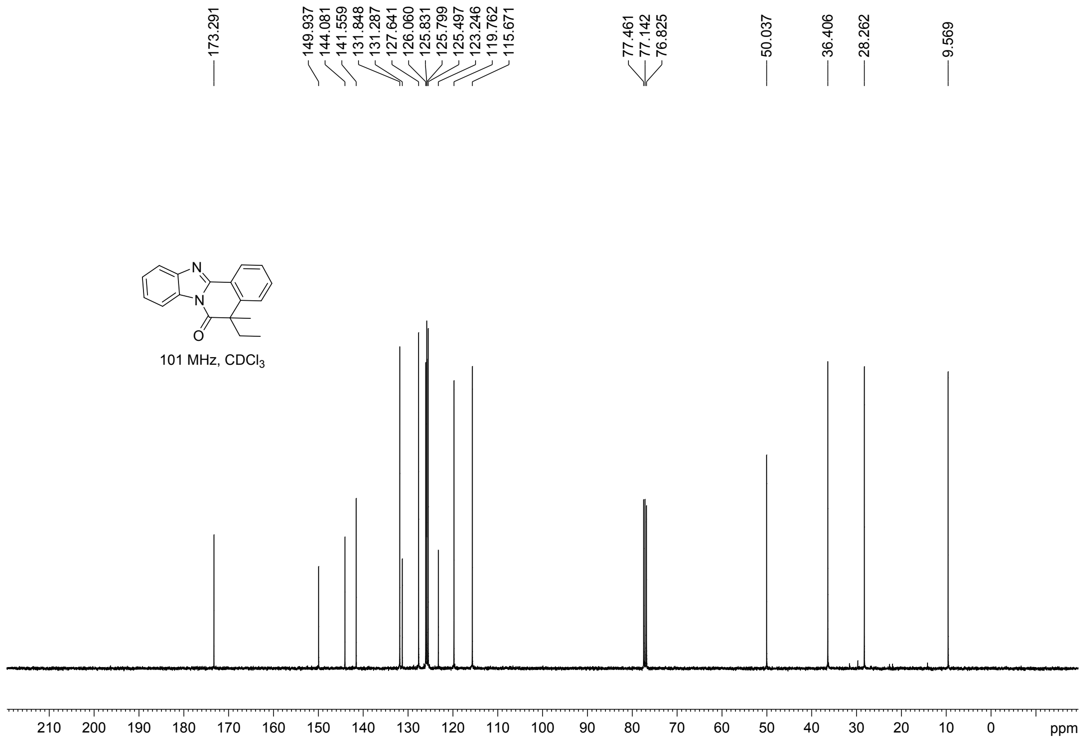


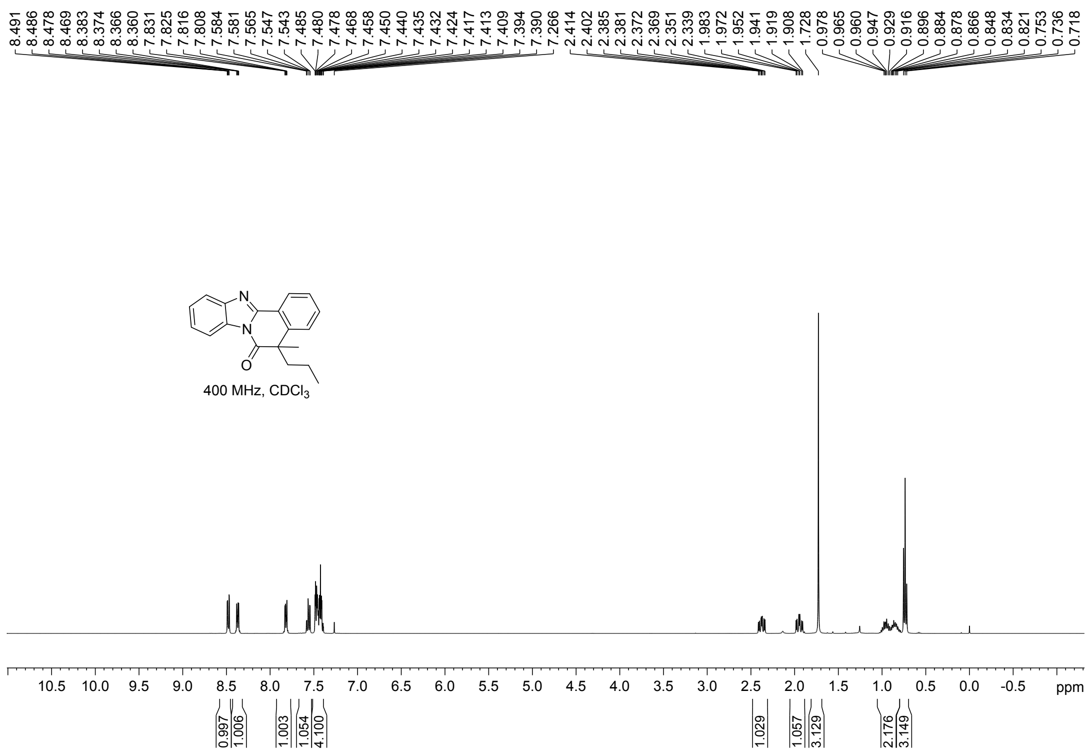
101 MHz, $CDCl_3$

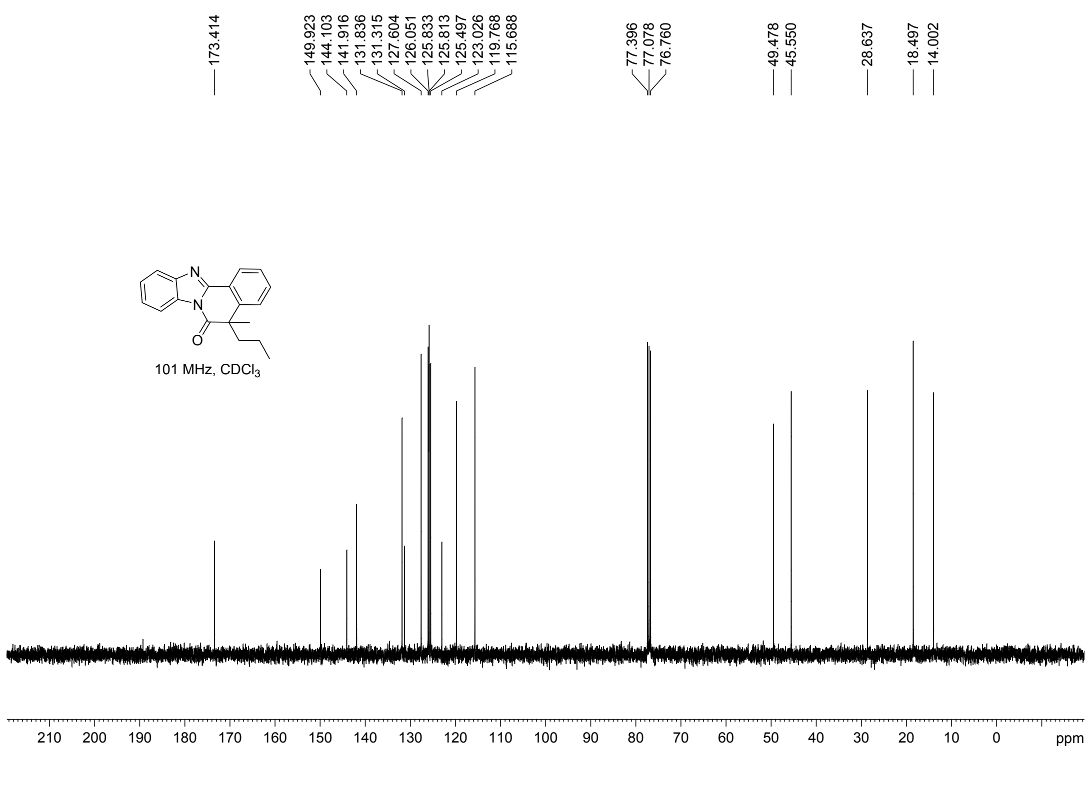

8.504
8.484
8.399
8.392
8.382
8.377
7.848
7.843
7.833
7.826
7.585
7.582
7.567
7.564
7.548
7.545
7.494
7.475
7.469
7.455
7.450
7.446
7.439
7.432
7.426
7.422
7.268
2.512
2.492
2.477
2.456
2.083
2.071
2.048
2.035
1.660
1.461
1.451
1.445
1.437
1.429
1.418
1.410
1.390
1.363
1.275
1.243
1.165
1.002
0.994
0.986
0.966
0.955
0.945
0.938
0.923
0.920
0.897
0.824
0.812
0.803
0.794
0.784
0.778
N
N
O
400 MHz, CDCl3
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
0.965
0.982
0.969
1.002
4.035
0.982
1.086
2.989
3.024
2.027
6.094

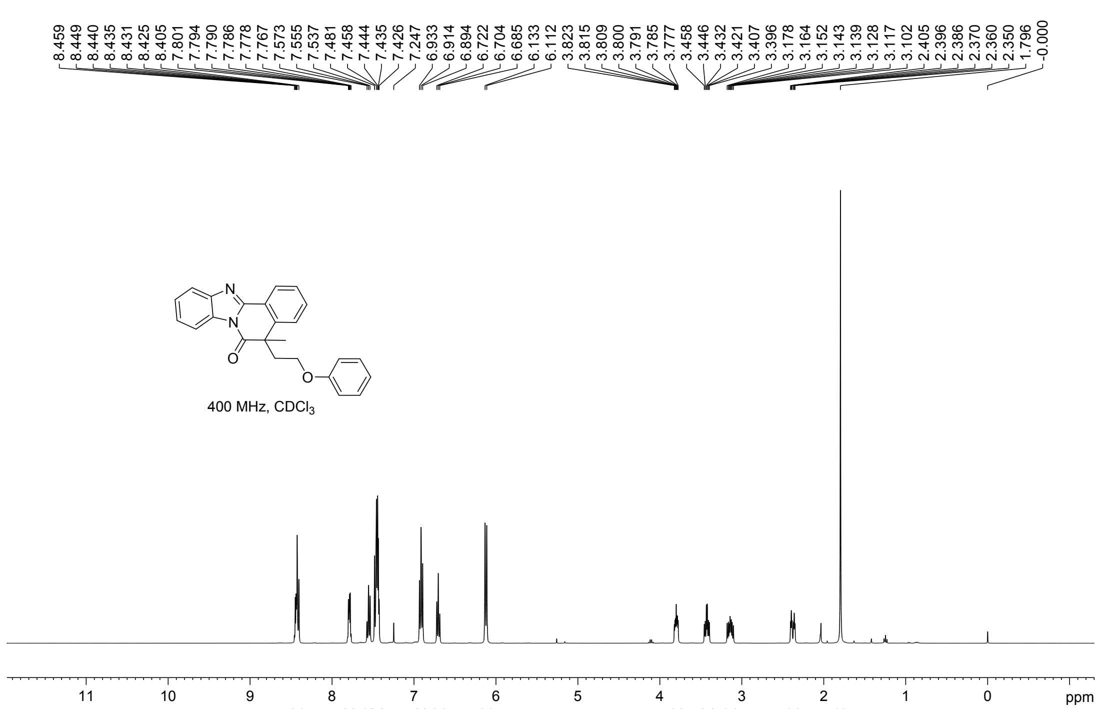

173.533
149.850
144.089
141.865
131.644
131.462
127.567
126.619
125.949
125.840
125.496
122.575
119.735
115.807
77.407
77.089
76.771
48.775
48.297
34.922
34.240
32.889
31.835
25.972
25.907
N
N
O
101 MHz, CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

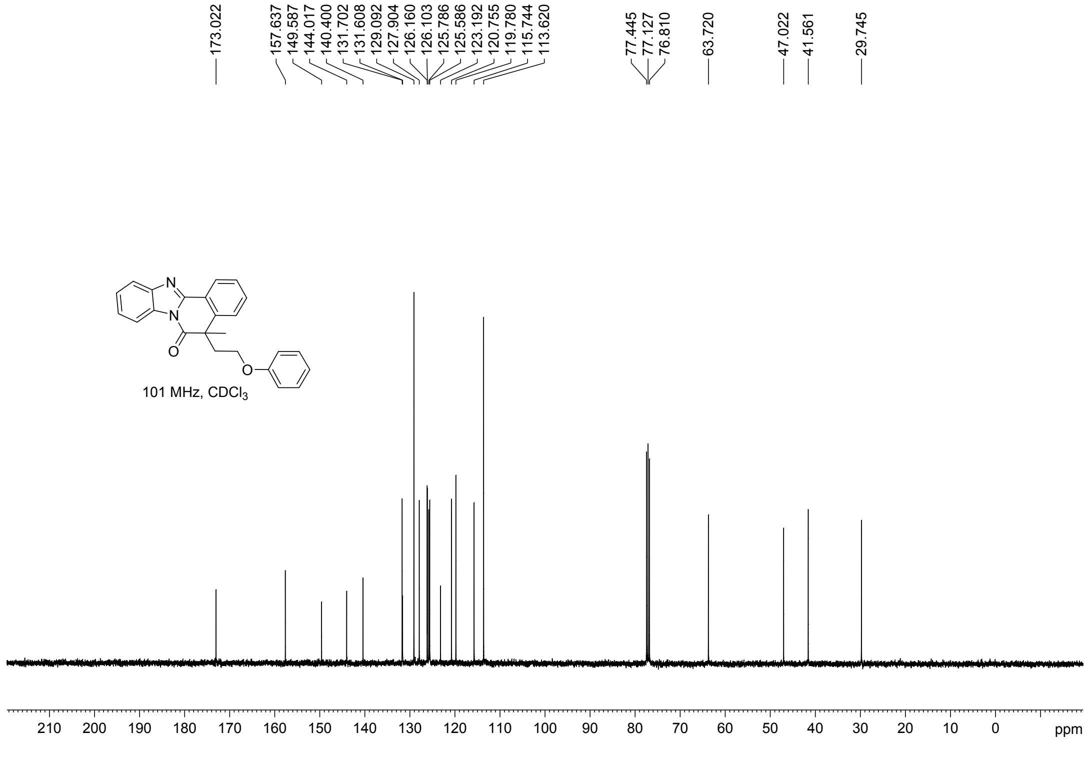

8.490 8.470 8.384 8.376 8.367 8.362 7.831 7.826 7.816 7.809 7.553 7.550 7.534 7.531 7.481 7.462 7.456 7.446 7.443 7.436 7.432 7.428 7.420 7.413 7.409 7.404 2.470 2.452 2.434 2.418 2.400 2.381 2.046 2.027 2.009 1.993 1.975 1.956 1.720 0.586 0.567 0.549 -0.000
N
N
O
400 MHz, CDCl3
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 ppm
0.973 1.001 0.985 1.002 4.036 1.046 1.015 3.070 3.053

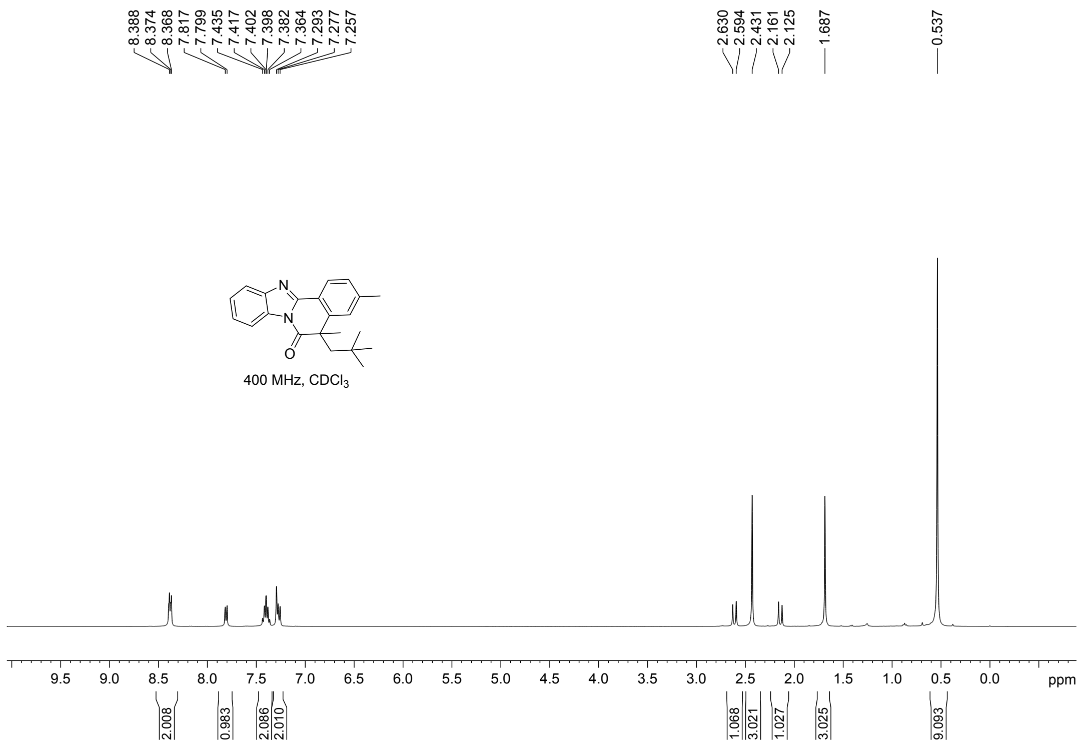

173.291
149.937 144.081 141.559 131.848 131.287 127.641 126.060 125.831 125.799 125.497 123.246 119.762 115.671
77.461 77.142 76.825
50.037
36.406
28.262
9.569
N
N
O
101 MHz, CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

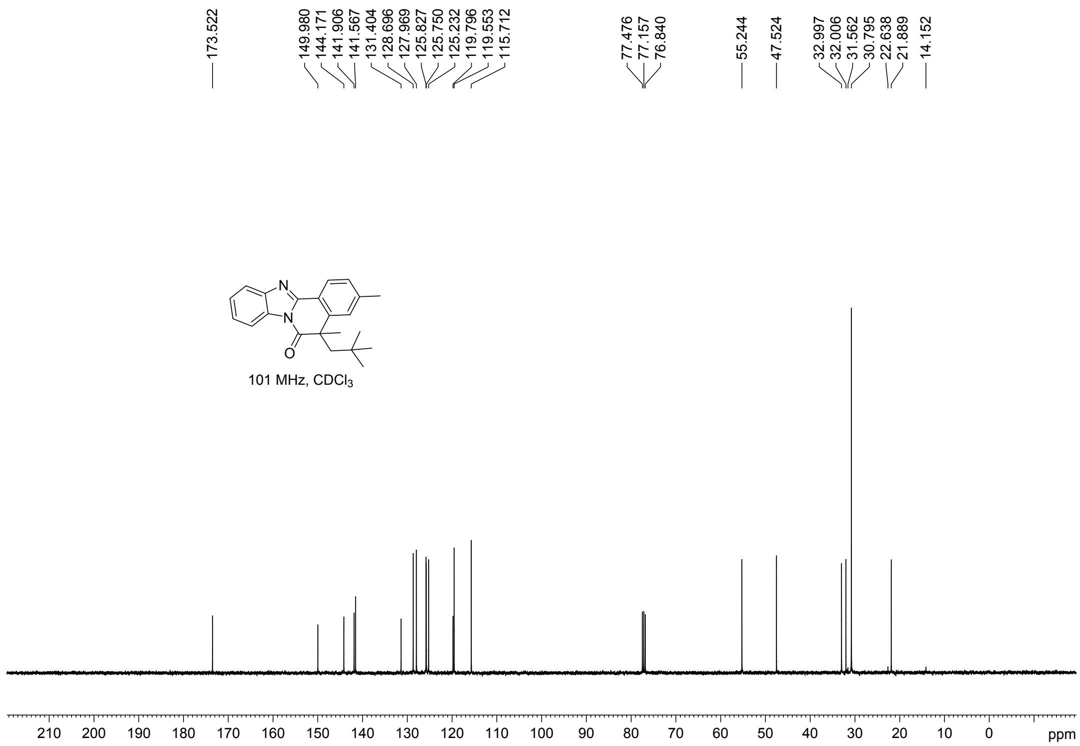

8.491
8.486
8.478
8.469
8.383
8.374
8.366
8.360
7.831
7.825
7.816
7.808
7.584
7.581
7.565
7.547
7.543
7.485
7.480
7.478
7.468
7.458
7.450
7.440
7.435
7.432
7.424
7.417
7.413
7.409
7.394
7.390
7.266
2.414
2.402
2.385
2.381
2.372
2.369
2.351
2.339
1.983
1.972
1.952
1.941
1.919
1.908
1.728
0.978
0.965
0.960
0.947
0.929
0.916
0.896
0.884
0.878
0.866
0.848
0.834
0.821
0.753
0.736
0.718
N
N
O
400 MHz, CDCl3
0.997
1.006
1.003
1.054
4.100
1.029
1.057
3.129
2.176
3.149
ppm

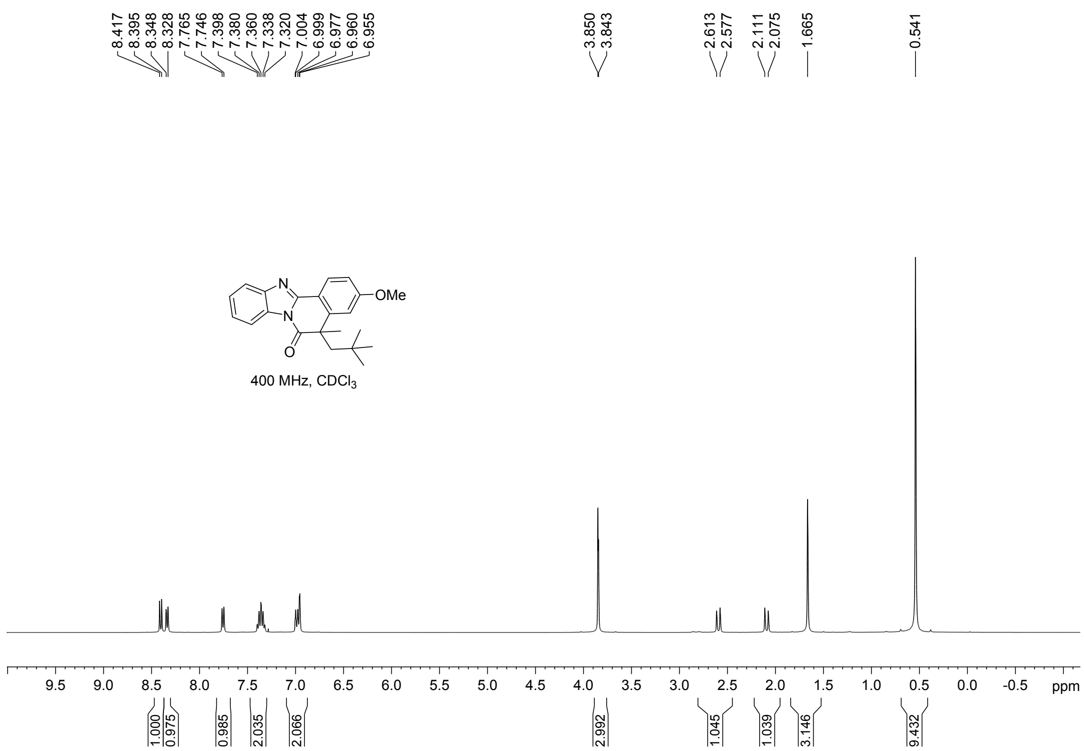

173.414
149.923
144.103
141.916
131.836
131.315
127.604
126.051
125.833
125.813
125.497
123.026
119.768
115.688
77.396
77.078
76.760
49.478
45.550
28.637
18.497
14.002
N
N
O
101 MHz, CDCl3
ppm

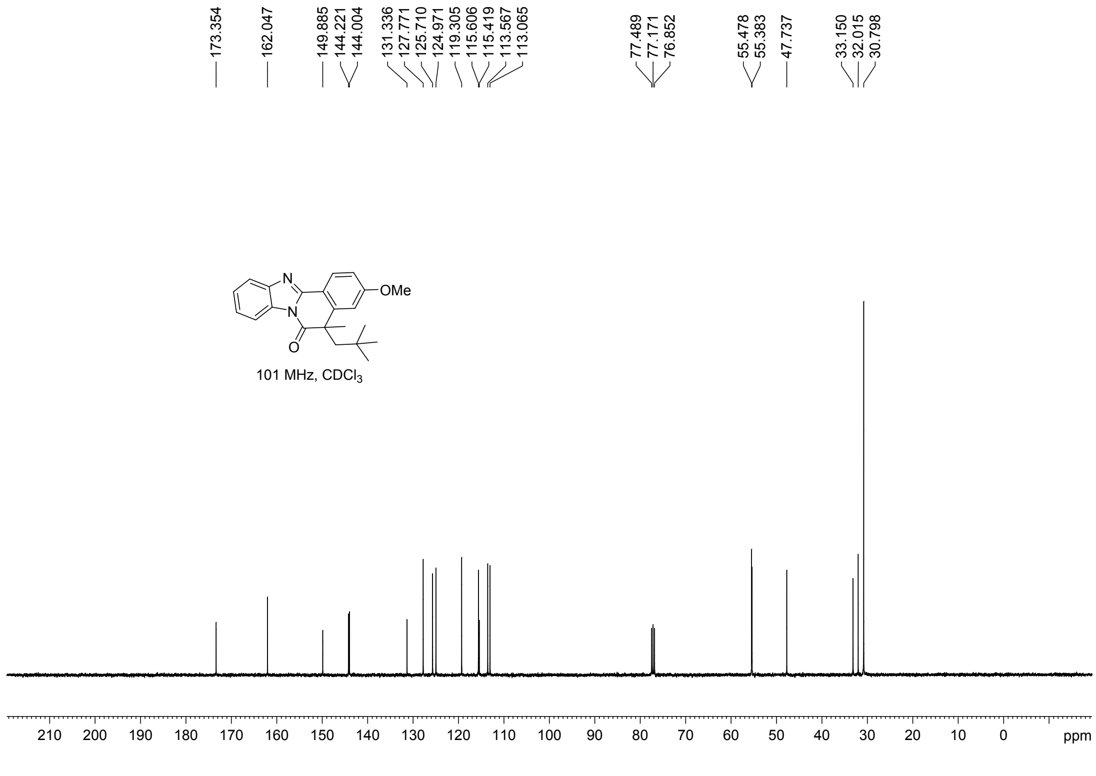

8.459 8.449 8.440 8.435 8.431 8.425 8.405 7.801 7.794 7.790 7.786 7.778 7.767 7.573 7.555 7.537 7.481 7.458 7.444 7.435 7.426 7.247 6.933 6.914 6.894 6.722 6.704 6.685 6.133 6.112 3.823 3.815 3.809 3.800 3.791 3.785 3.777 3.458 3.446 3.432 3.421 3.407 3.396 3.178 3.164 3.152 3.143 3.139 3.128 3.117 3.102 2.405 2.396 2.386 2.370 2.360 2.350 1.796 -0.000
400 MHz, CDCl3
11 10 9 8 7 6 5 4 3 2 1 0 ppm
1.981 0.992 1.021 4.023 2.014 0.999 1.995 0.999 0.995 0.995 0.996 2.995

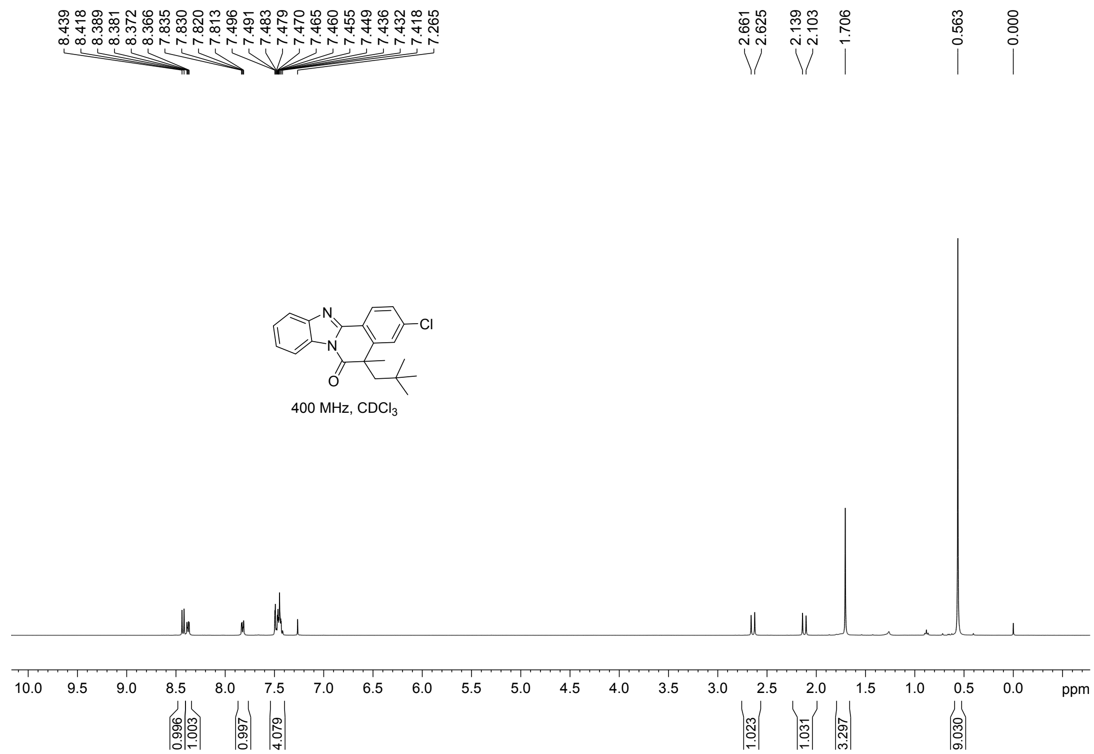

173.022 157.637 149.587 144.017 140.400 131.702 131.608 129.092 127.904 126.160 126.103 125.786 125.586 123.192 120.755 119.780 115.744 113.620 77.445 77.127 76.810 63.720 47.022 41.561 29.745
101 MHz, CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

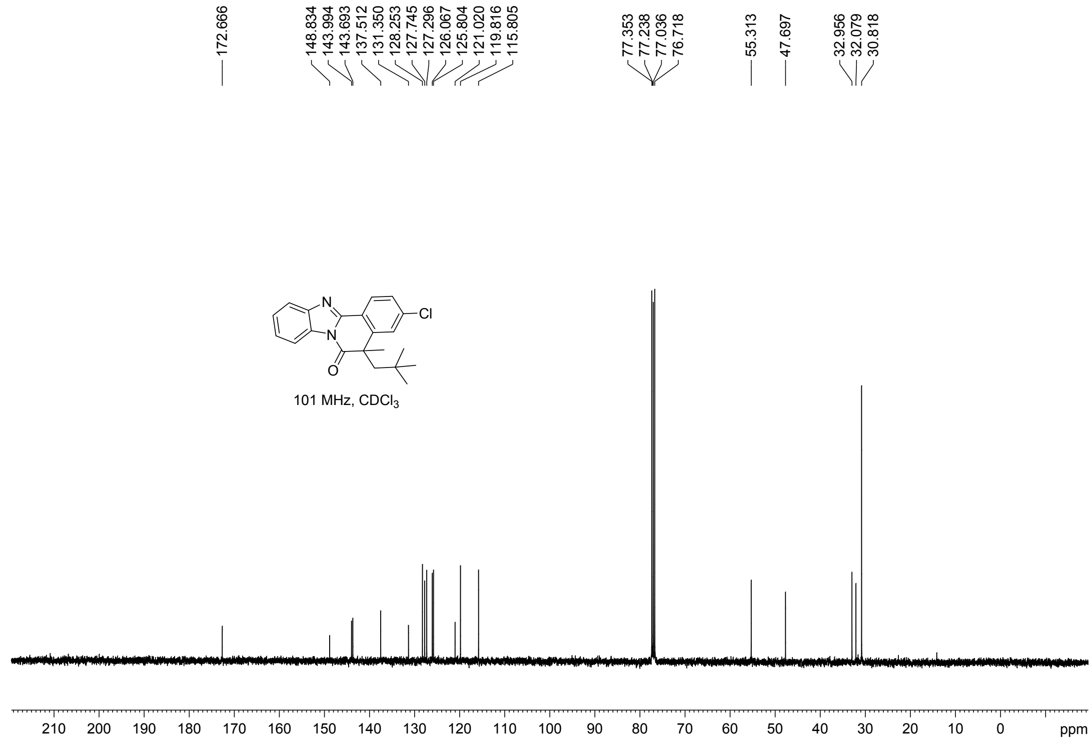

8.388
8.374
8.368
7.817
7.799
7.435
7.417
7.402
7.398
7.382
7.364
7.293
7.277
7.257
2.630
2.594
2.431
2.161
2.125
1.687
0.537
400 MHz, CDCl3
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
2.008
0.983
2.086
2.010
1.068
3.021
1.027
3.025
9.093

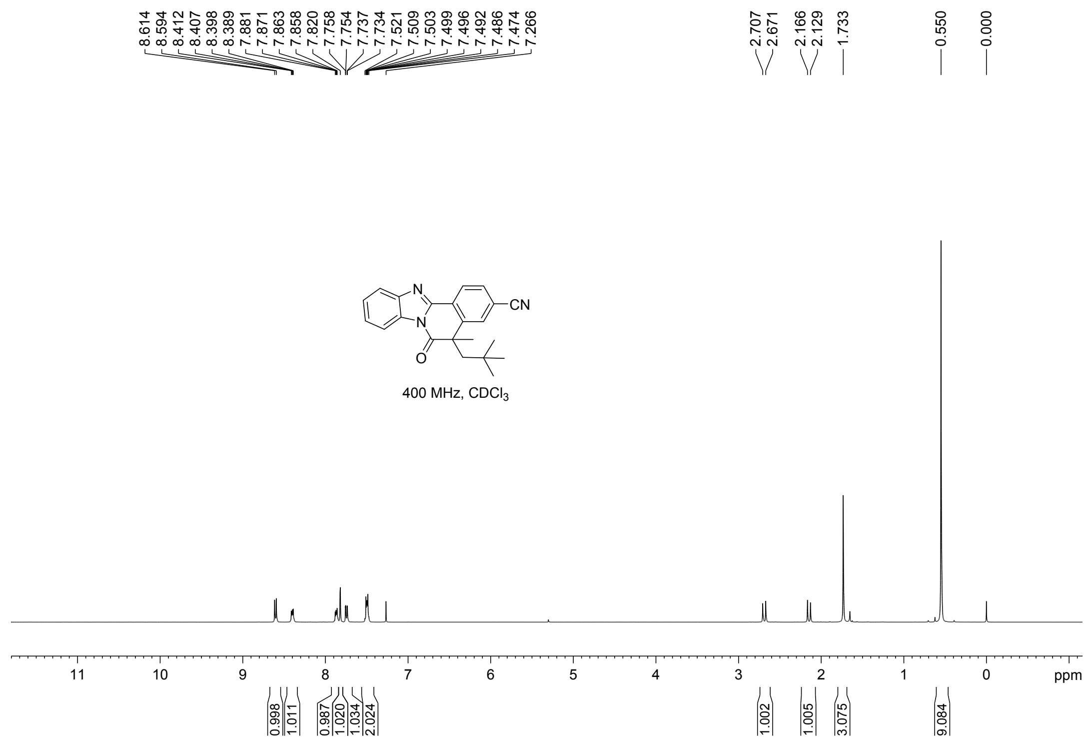

173.522
149.980
144.171
141.906
141.567
131.404
128.696
127.969
125.827
125.750
125.232
119.796
119.553
115.712
77.476
77.157
76.840
55.244
47.524
32.997
32.006
31.562
30.795
22.638
21.889
14.152
101 MHz, CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

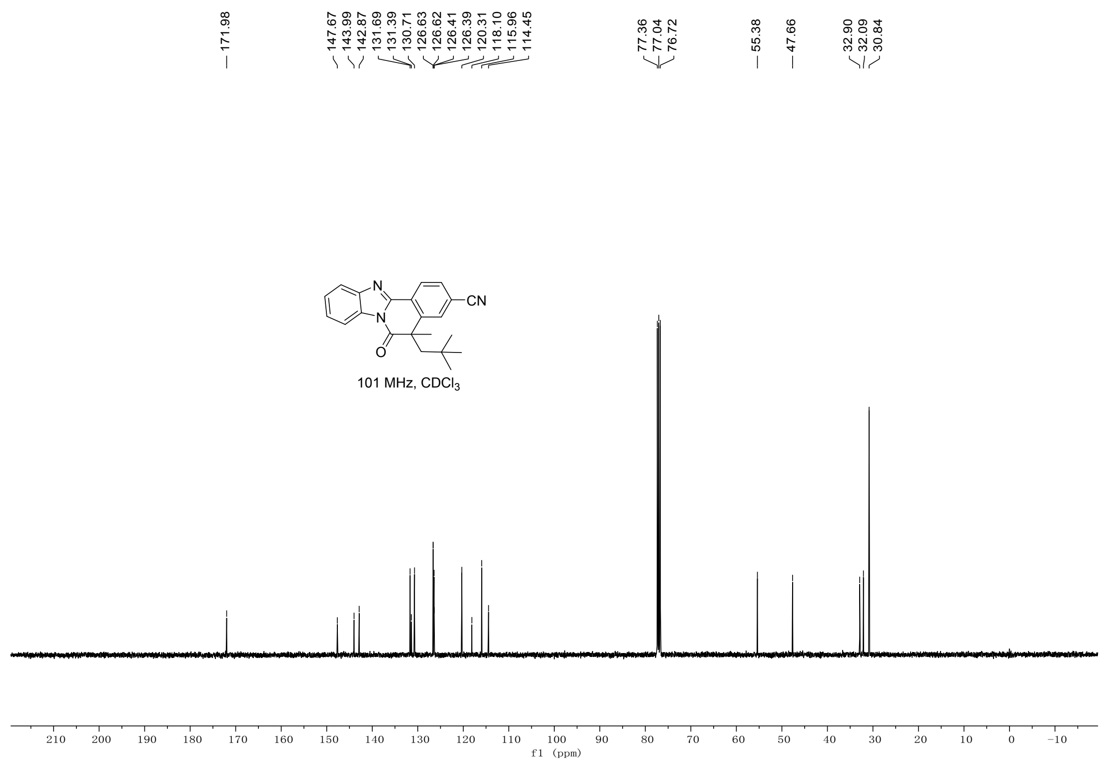

8.417
8.395
8.348
8.328
7.765
7.746
7.398
7.380
7.360
7.338
7.320
7.004
6.999
6.977
6.960
6.955
3.850
3.843
2.613
2.577
2.111
2.075
1.665
0.541
OMe
N
O
400 MHz, CDCl3
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
ppm
1.000
0.975
0.985
2.035
2.066
2.992
1.045
1.039
3.146
9.432

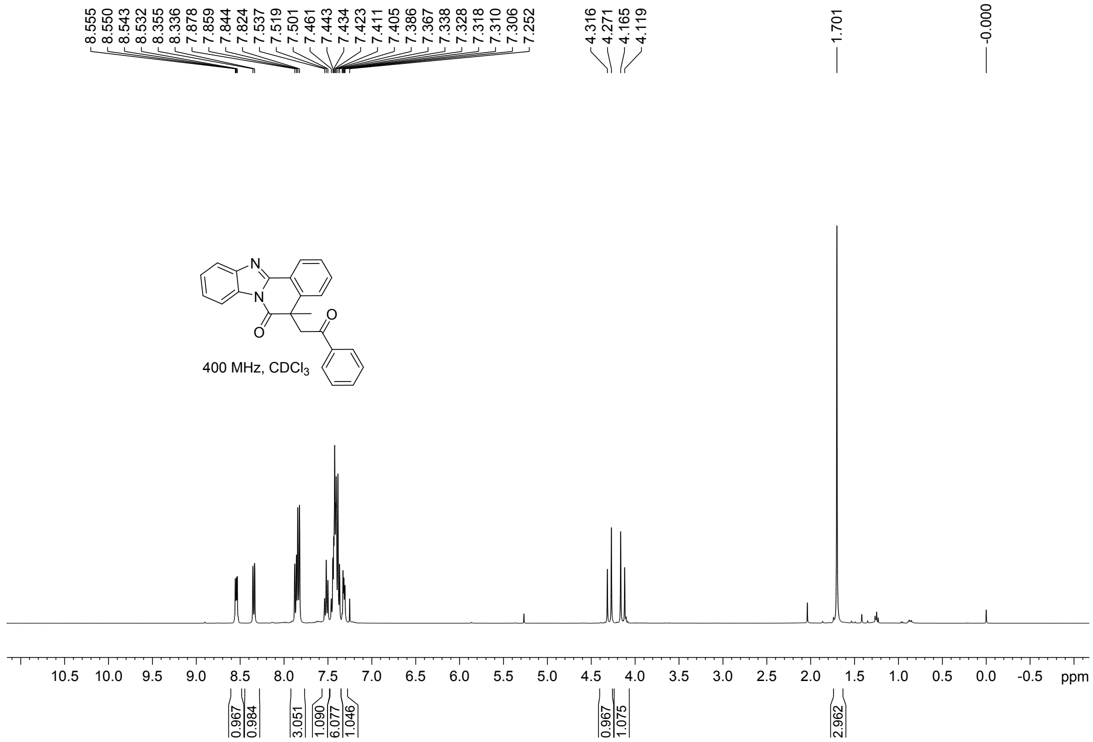

173.354
162.047
149.885
144.221
144.004
131.336
127.771
125.710
124.971
119.305
115.606
115.419
113.567
113.065
77.489
77.171
76.852
55.478
55.383
47.737
33.150
32.015
30.798
OMe
N
O
101 MHz, CDCl3
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

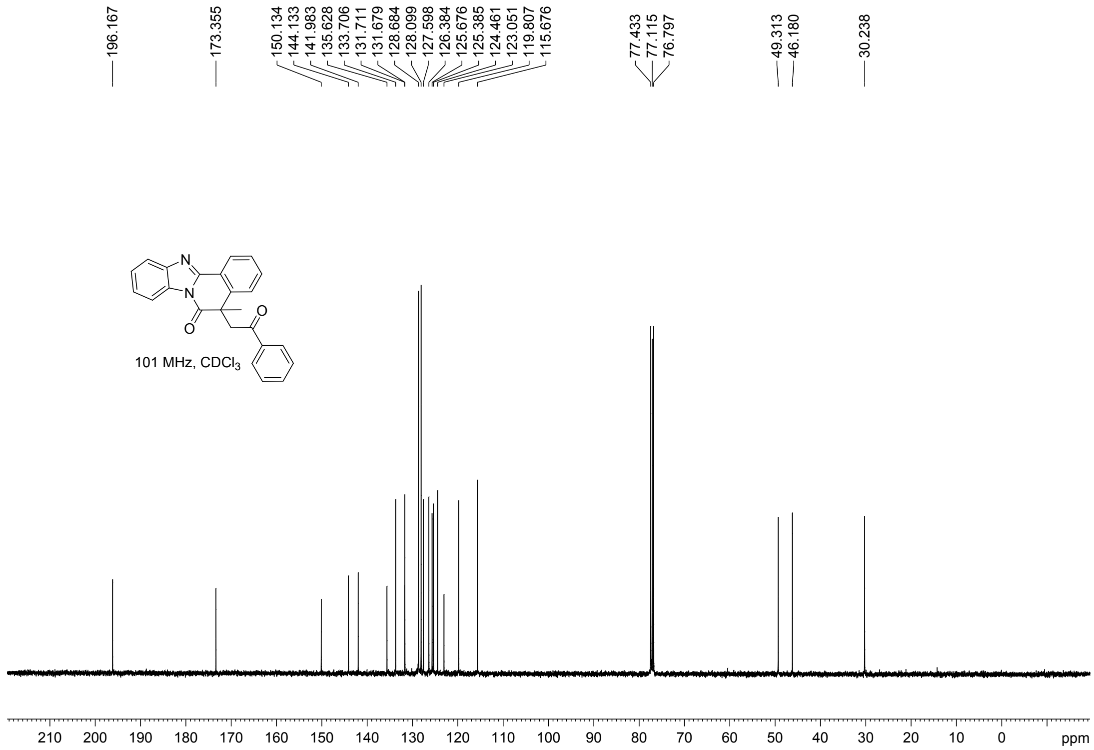

8.439
8.418
8.389
8.381
8.372
8.366
7.835
7.830
7.820
7.813
7.496
7.491
7.483
7.479
7.470
7.465
7.460
7.455
7.449
7.436
7.432
7.418
7.265
2.661
2.625
2.139
2.103
1.706
0.563
0.000
N
Cl
N
O
400 MHz, CDCl3
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
0.996
1.003
0.997
4.079
1.023
1.031
3.297
9.030

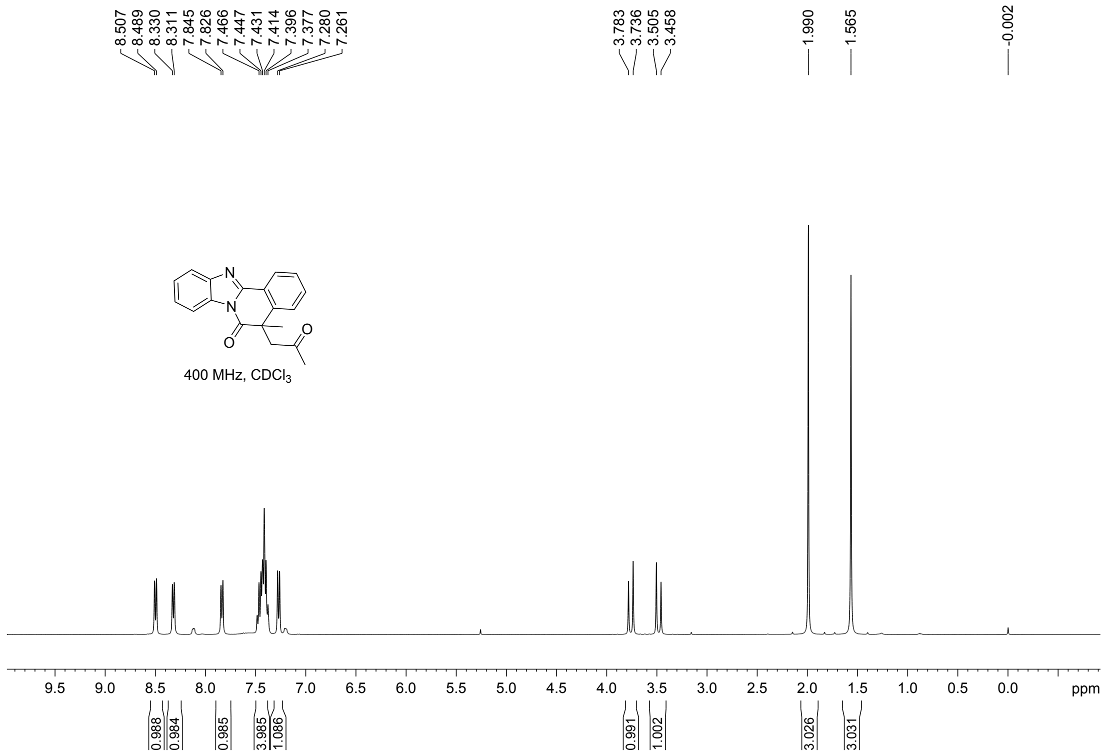

172.666
148.834
143.994
143.693
137.512
131.350
128.253
127.745
127.296
126.067
125.804
121.020
119.816
115.805
77.353
77.238
77.036
76.718
55.313
47.697
32.956
32.079
30.818
N
Cl
N
O
101 MHz, CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

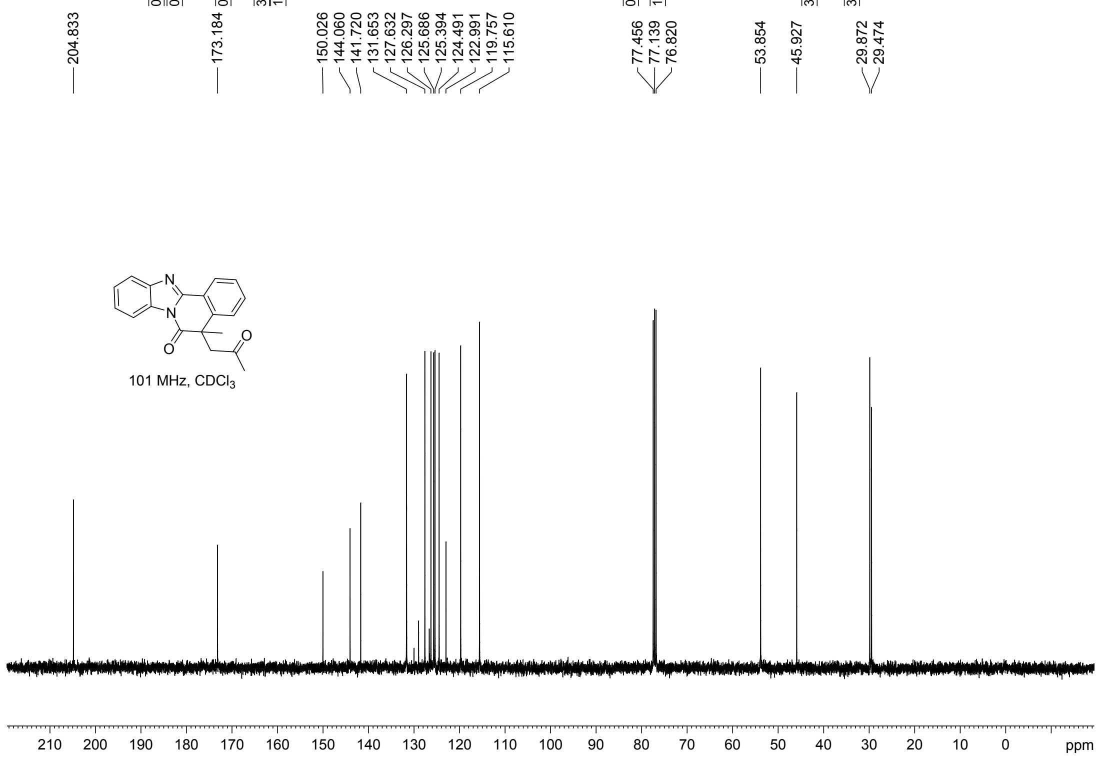

8.614
8.594
8.412
8.407
8.398
8.389
7.881
7.871
7.863
7.858
7.820
7.758
7.754
7.737
7.734
7.521
7.509
7.503
7.499
7.496
7.492
7.486
7.474
7.266
2.707
2.671
2.166
2.129
1.733
0.550
0.000
CN
N
O
400 MHz, CDCl3
ppm
0.998
1.011
0.987
1.020
1.034
2.024
1.002
1.005
3.075
9.084

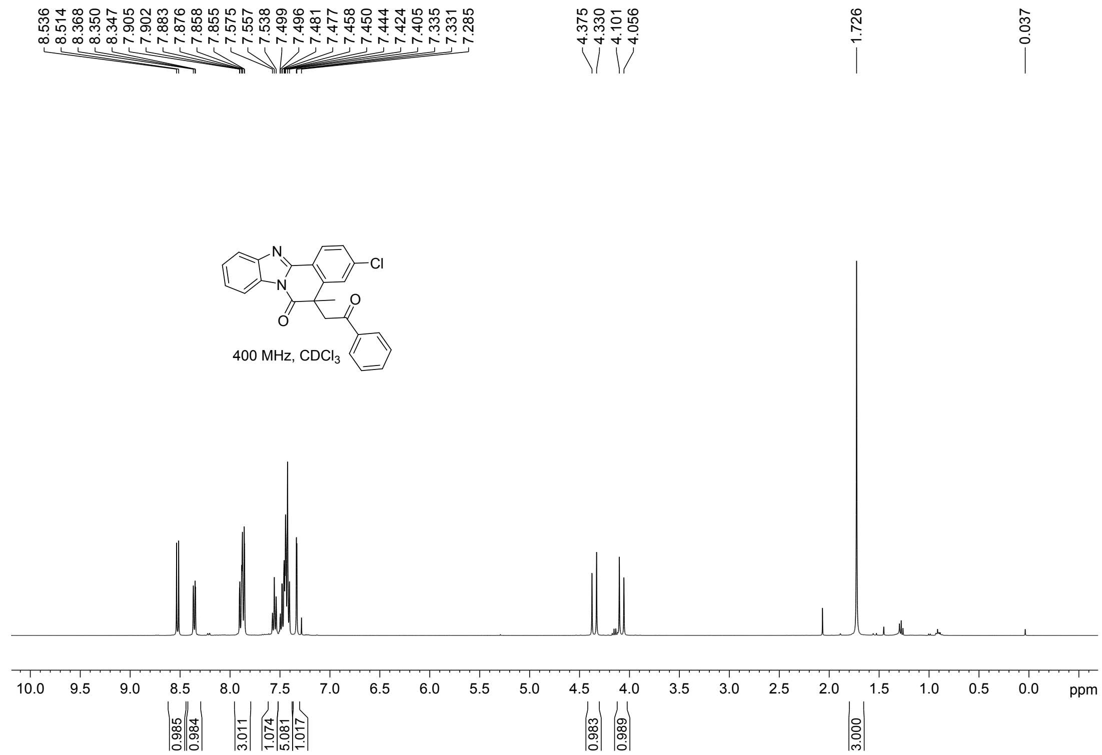

171.98
147.67
143.99
142.87
131.69
131.39
130.71
126.63
126.62
126.41
126.39
120.31
118.10
115.96
114.45
77.36
77.04
76.72
55.38
47.66
32.90
32.09
30.84
CN
N
O
101 MHz, CDCl3
f1 (ppm)


8.555
8.550
8.543
8.532
8.355
8.336
7.878
7.859
7.844
7.824
7.537
7.519
7.501
7.461
7.443
7.434
7.423
7.411
7.405
7.386
7.367
7.338
7.328
7.318
7.310
7.306
7.252
4.316
4.271
4.165
4.119
1.701
-0.000
400 MHz, CDCl3
0.967
0.984
3.051
1.090
6.077
1.046
0.967
1.075
2.962
ppm

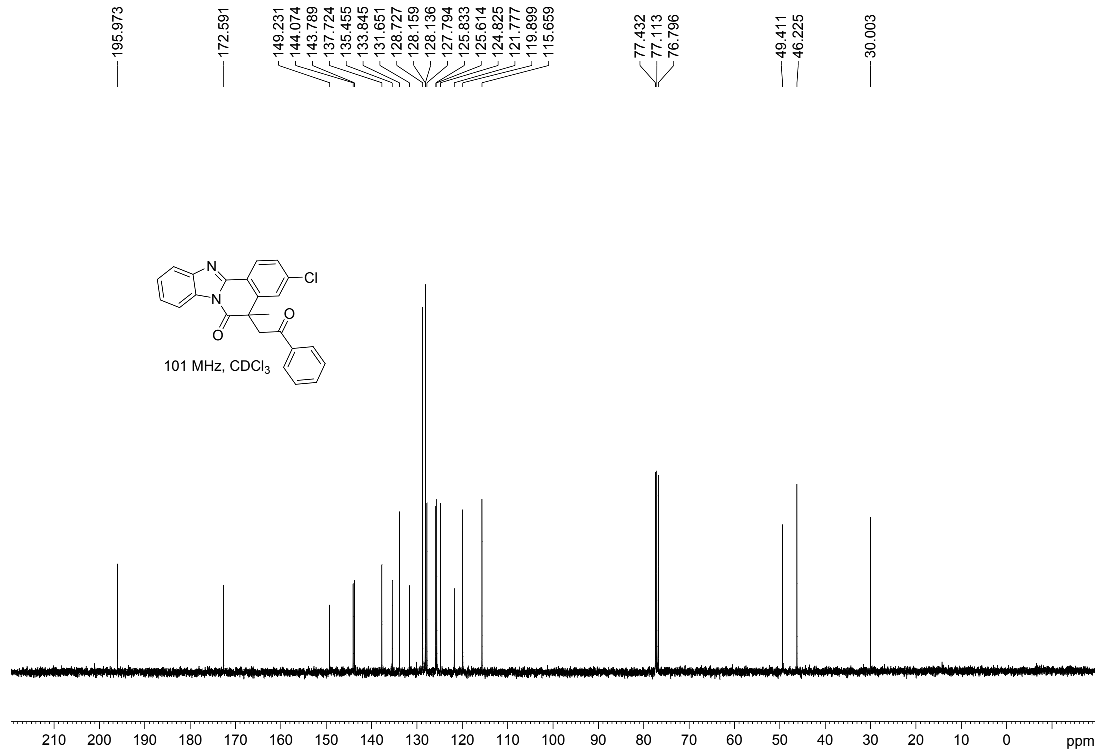

196.167
173.355
150.134
144.133
141.983
135.628
133.706
131.711
131.679
128.684
128.099
127.598
126.384
125.676
125.385
124.461
123.051
119.807
115.676
77.433
77.115
76.797
49.313
46.180
30.238
101 MHz, CDCl3
ppm


8.507
8.489
8.330
8.311
7.845
7.826
7.466
7.447
7.431
7.414
7.396
7.377
7.280
7.261
3.783
3.736
3.505
3.458
1.990
1.565
-0.002
N
N
O
O
400 MHz, CDCl3
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
0.988
0.984
0.985
3.985
1.086
0.991
1.002
3.026
3.031

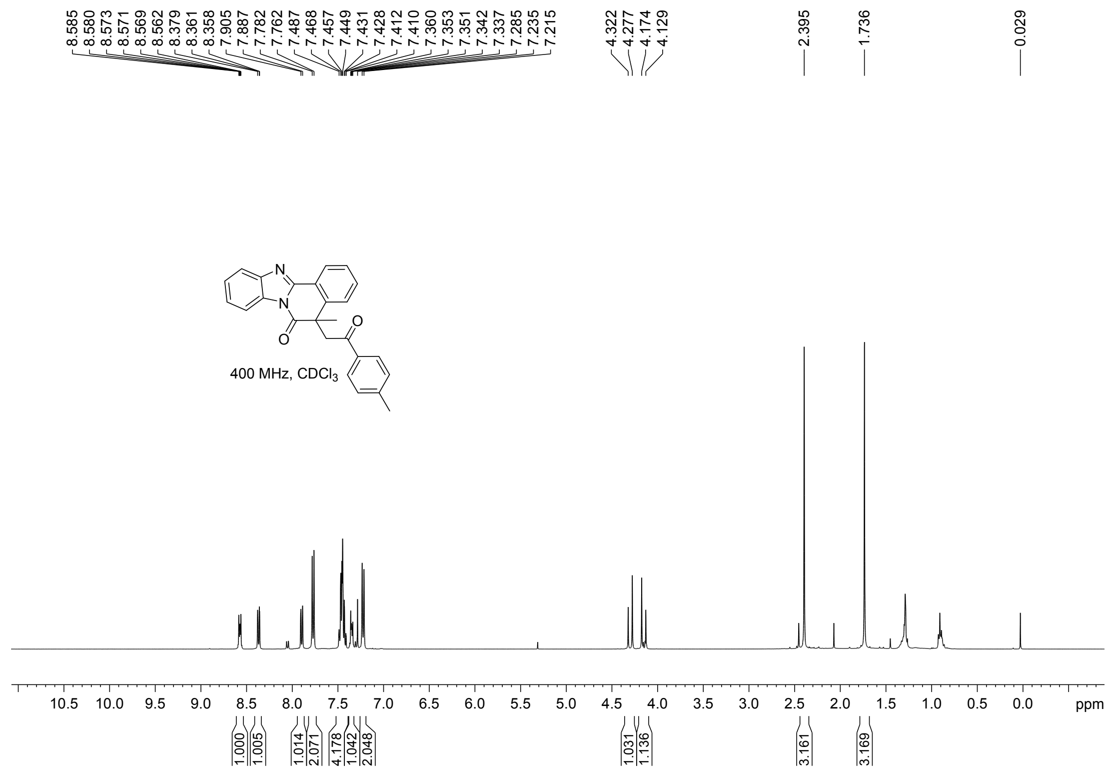

204.833
173.184
150.026
144.060
141.720
131.653
127.632
126.297
125.686
125.394
124.491
122.991
119.757
115.610
77.456
77.139
76.820
53.854
45.927
29.872
29.474
N
N
O
O
101 MHz, CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

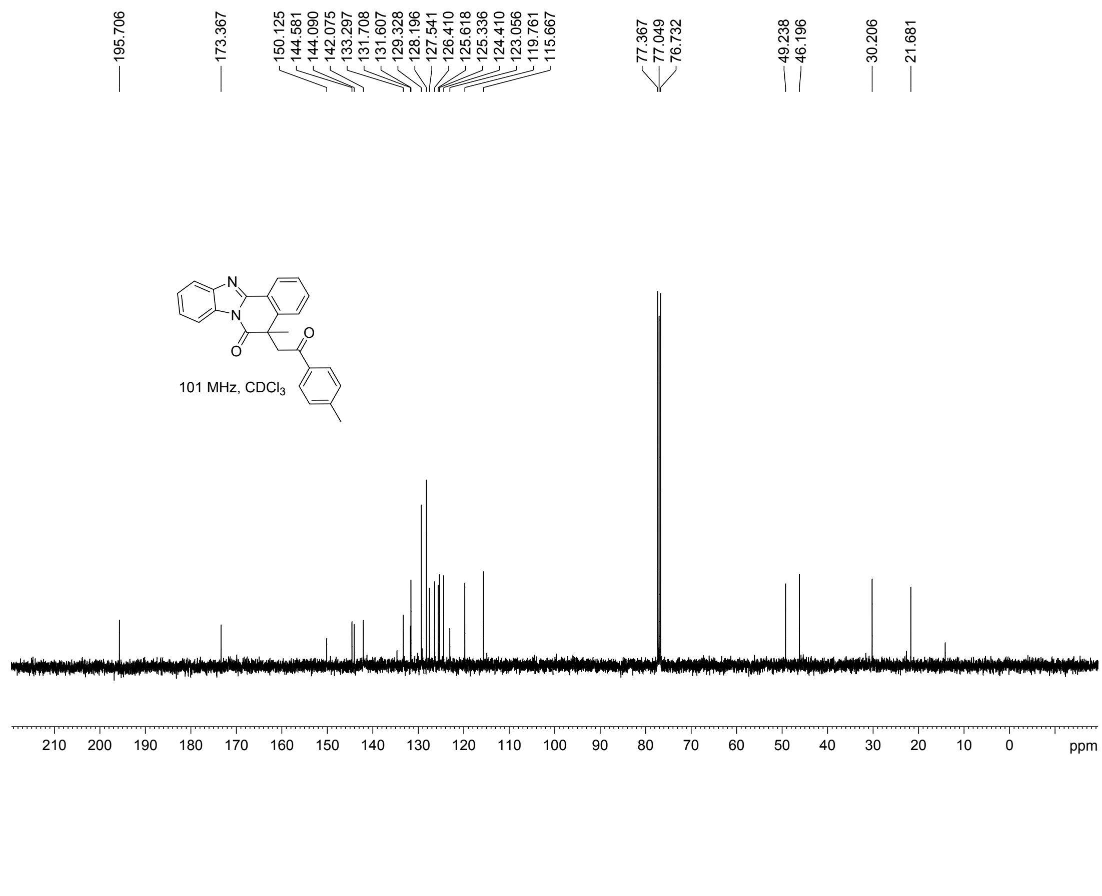


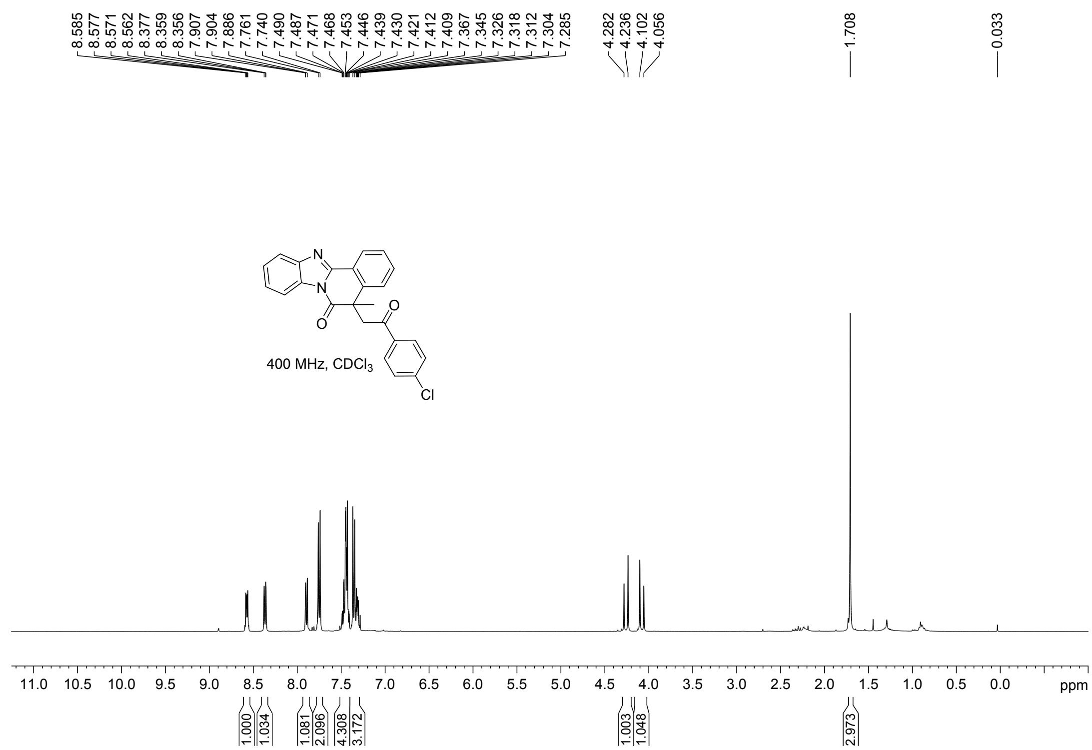
8.536 8.514 8.368 8.350 8.347 7.905 7.902 7.883 7.876 7.858 7.855 7.575 7.557 7.538 7.499 7.496 7.481 7.477 7.458 7.450 7.444 7.424 7.405 7.335 7.331 7.285
4.375 4.330 4.101 4.056
1.726
0.037
N
N
Cl
O
O
400 MHz, CDCl3
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
0.985 0.984 3.011 1.074 5.081 1.017 0.983 0.989 3.000

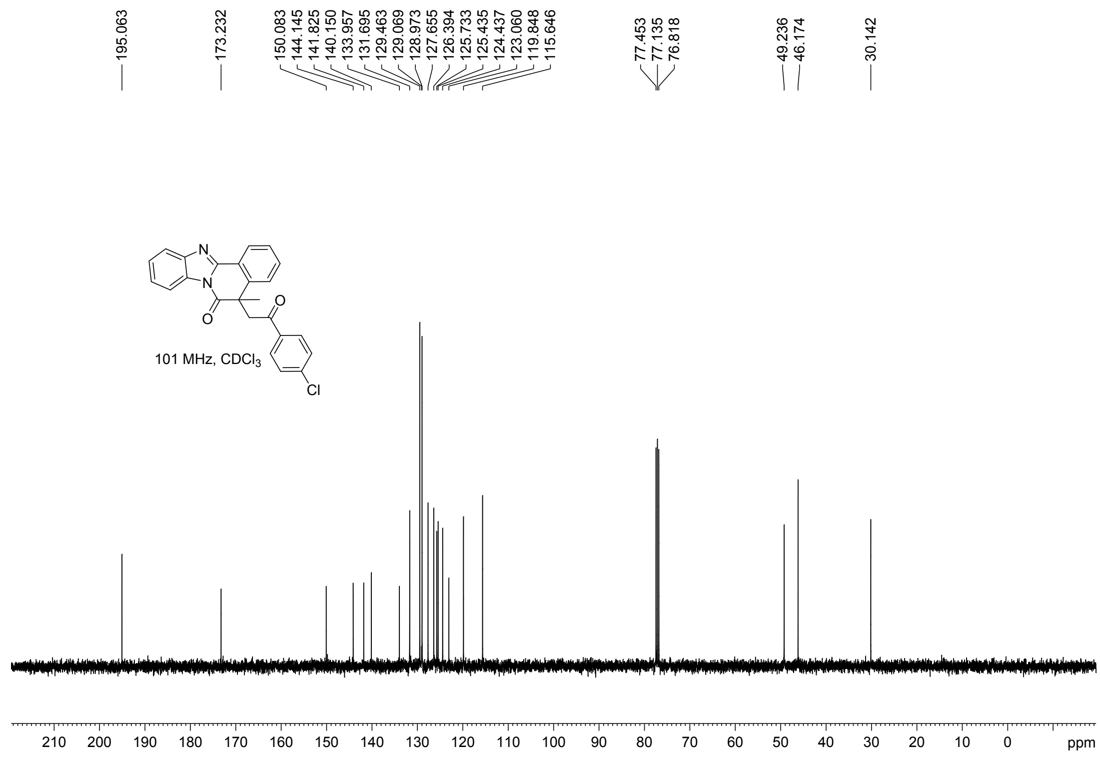


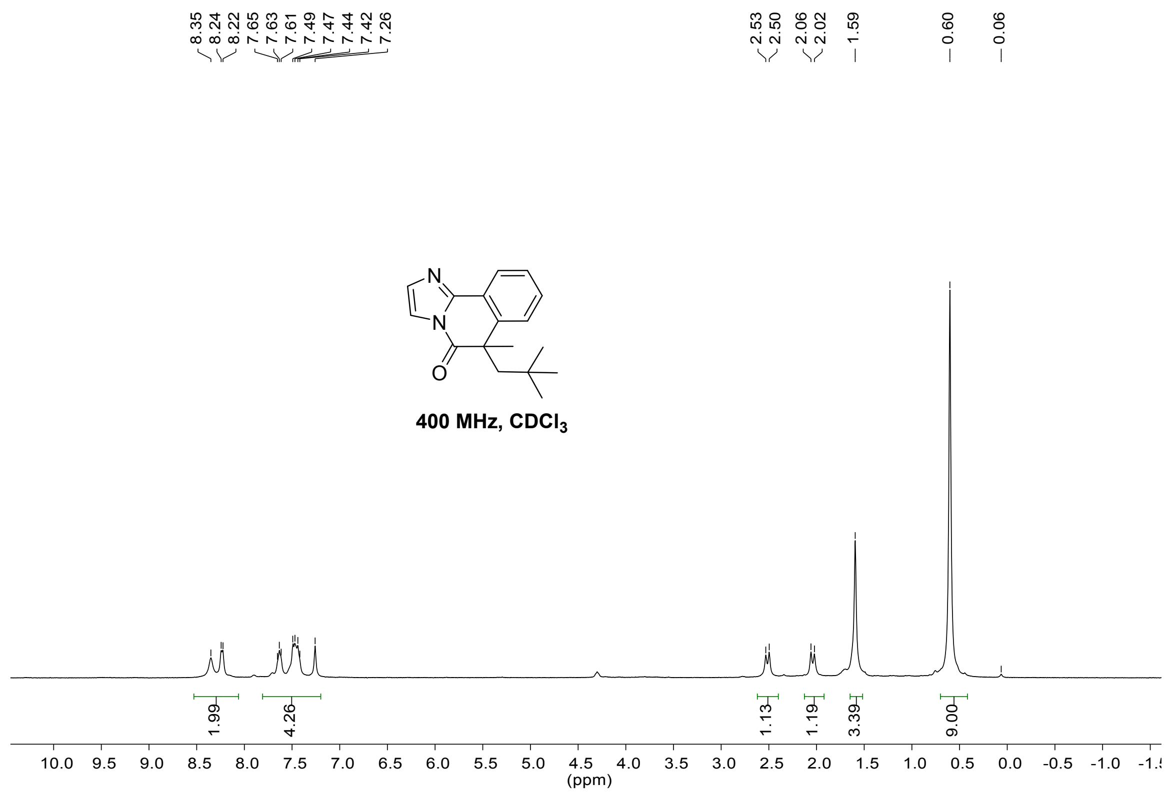
195.973
172.591
149.231 144.074 143.789 137.724 135.455 133.845 131.651 128.727 128.159 128.136 127.794 125.833 125.614 124.825 121.777 119.899 115.659
77.432 77.113 76.796
49.411 46.225
30.003
N
N
Cl
O
O
101 MHz, CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

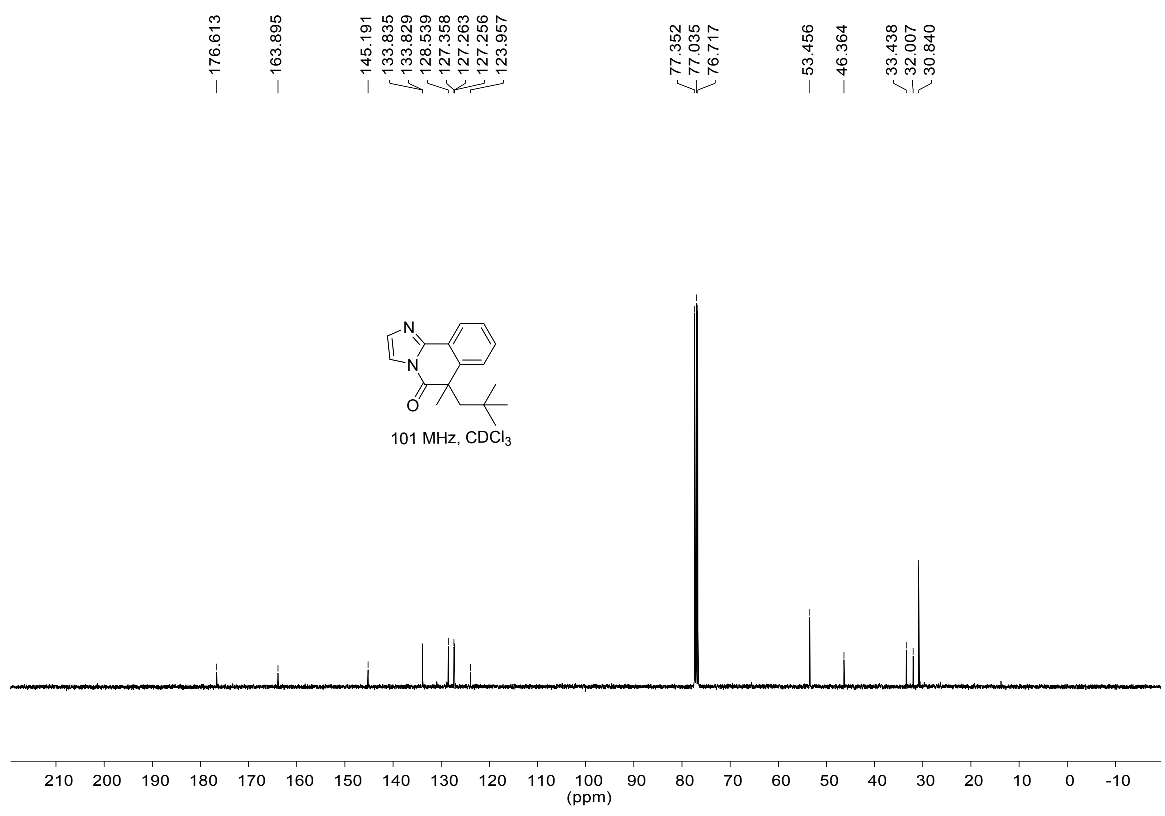

400 MHz, CDCl3
ppm

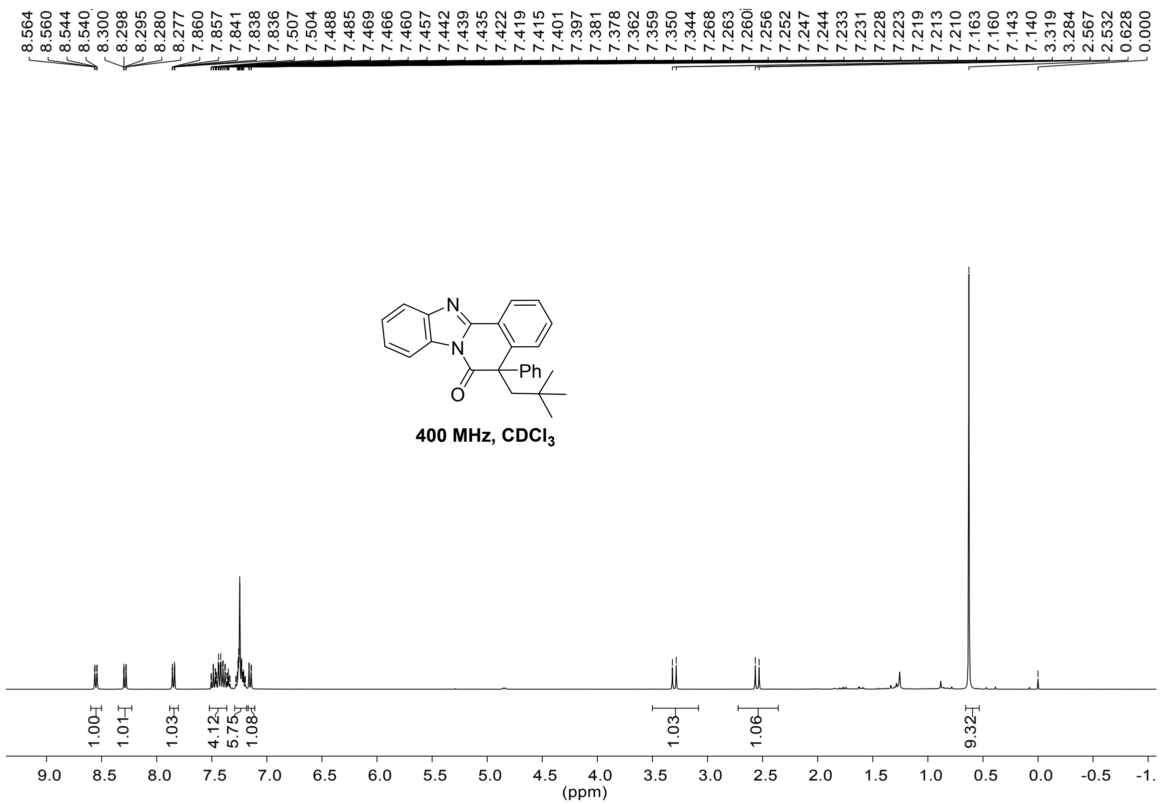

101 MHz, CDCl3
ppm

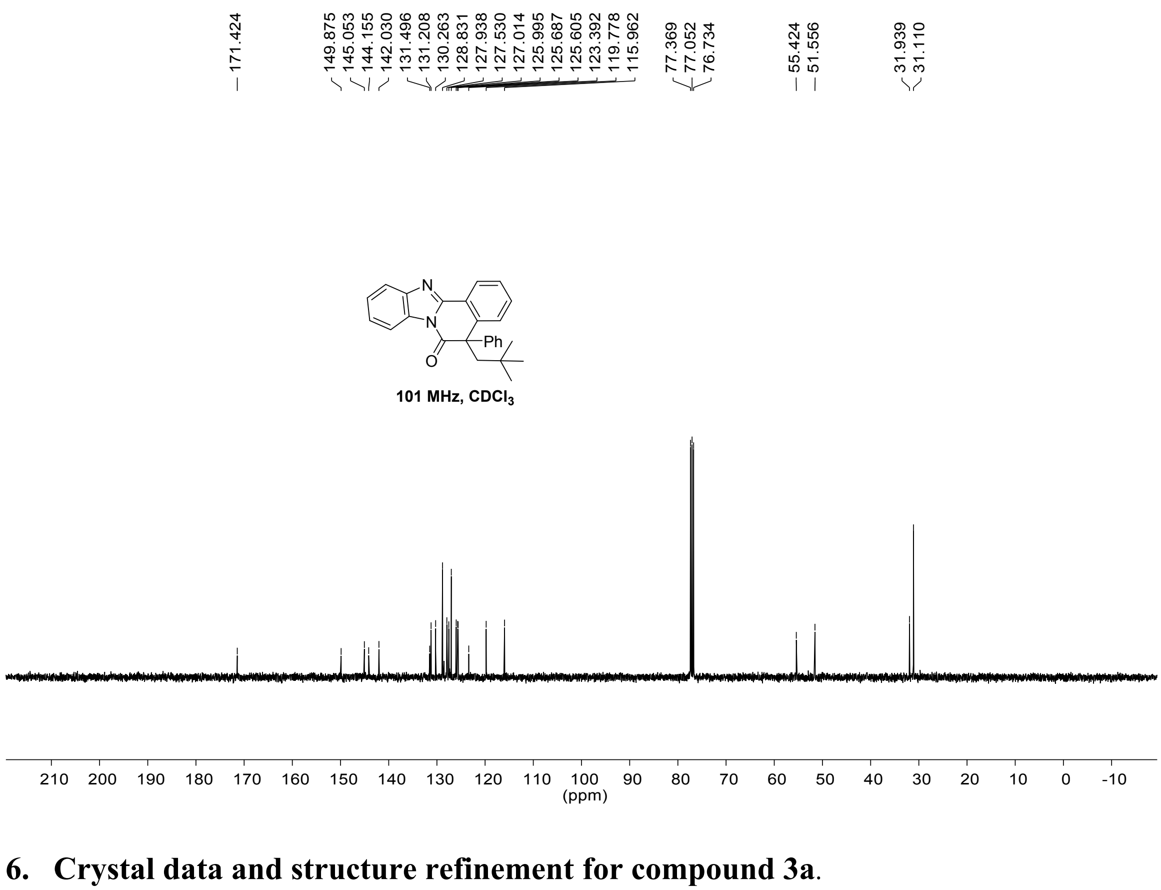

8.585
8.577
8.571
8.562
8.377
8.359
8.356
7.907
7.904
7.886
7.761
7.740
7.490
7.487
7.471
7.468
7.453
7.446
7.439
7.430
7.421
7.412
7.409
7.367
7.345
7.326
7.318
7.312
7.304
7.285
4.282
4.236
4.102
4.056
1.708
0.033
400 MHz, CDCl3
O
N
Cl
1.000
1.034
1.081
2.096
4.308
3.172
1.003
1.048
2.973
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm


195.063
173.232
150.083
144.145
141.825
140.150
133.957
131.695
129.463
129.069
128.973
127.655
126.394
125.733
125.435
124.437
123.060
119.848
115.646
77.453
77.135
76.818
49.236
46.174
30.142
101 MHz, CDCl3
O
N
Cl
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


8.35
8.24
8.22
7.65
7.63
7.61
7.49
7.47
7.44
7.42
7.26
2.53
2.50
2.06
2.02
1.59
0.60
0.06
N
N
O
400 MHz, CDCl3
1.99
4.26
1.13
1.19
3.39
9.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
(ppm)


176.613
163.895
145.191
133.835
133.829
128.539
127.358
127.263
127.256
123.957
77.352
77.035
76.717
53.456
46.364
33.438
32.007
30.840
N
N
O
101 MHz, CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
(ppm)





6. Crystal data and structure refinement for compound 3a.

Empirical formula	$C_{21}H_{22}N_2O$
Formula weight	318.40
Temperature/K	293(2)
Crystal system	orthorhombic
Space group	Pbca
a/Å	16.5024(4)
b/Å	11.1420(2)
c/Å	19.3013(5)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	3548.93(14)
Z	8
ρ_{calc}g/cm^3	1.192
μ/mm^{-1}	0.575
F(000)	1360.0
Crystal size/mm^3	0.21 × 0.2 × 0.15
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	9.164 to 135.468
Index ranges	-19 ≤ h ≤ 19, -10 ≤ k ≤ 13, -22 ≤ l ≤ 14
Reflections collected	13149
Independent reflections	3164 [R_{int} = 0.0242, R_{sigma} = 0.0169]
Data/restraints/parameters	3164/13/221
Goodness-of-fit on F^2	1.070
Final R indexes [I>=2σ (I)]	R_1 = 0.0468, wR_2 = 0.1327
Final R indexes [all data]	R_1 = 0.0564, wR_2 = 0.1428
Largest diff. peak/hole / e Å^{-3}	0.17/-0.18

7. Calculational Details

All the theoretical calculations in the study were performed using Gaussian16 program package[1]. All the geometries were optimized at the B3LYP[2]/DZVP[3] level, and the solvent effect was utilized the polarizable continuum model (PCM) in water solvent.[4] And the harmonic vibrational frequency calculations were performed at the same level to confirm the local minima and transition state.

The solution translational entropy correction has been calculated with THERMO program, [5] which is based on the free volume that a solute molecule could move along three axes within the cavity.

References:

[1] Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Petersson, G. A.; Nakatsuji, H.; Li, X.; Caricato, M.; Marenich, A. V.; Bloino, J.; Janesko, B. G.; Gomperts, R.; Mennucci, B.; Hratchian, H. P.; Ortiz, J. V.; Izmaylov, A. F.; Sonnenberg, J. L.; Williams-Young, D.; Ding, F.; Lipparini, F.; Egidi, F.; Goings, J.; Peng, B.; Petrone, A.; Henderson, T.; Ranasinghe, D.; Zakrzewski, V. G.; Gao, J.; Rega, N.; Zheng, G.; Liang, W.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Throssell, K.; Montgomery Jr., J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M. J.; Heyd, J. J.; Brothers, E. N.; Kudin, K. N.; Staroverov, V. N.; Keith, T. A.; Kobayashi ,R.; Normand, J.; Raghavachari, K.; Rendell, A. P.;Burant, J. C.;Iyengar, S. S.;Tomasi,J.; Cossi, M.; Millam, J. M.; Klene,M.:Adamo,C.:Cammi,R.:Ochterski, J. W.; Martin, R. L.;Morokuma,K.;Farkas,O.;Foresman, J. B.; Fox, D. J. *Gaussian16*, Gaussian, Inc., Wallingford, CT, **2016**.

[2] (a) Lee, C.; Yang, W.; Parr, R.G.; Development of the Colle-Salvetti Correlation-Energy Formula into a Functional of the Electron Density, Phys. Rev. B: Condens. Matter Mater. Phys. 1988, 37, 785-789; (b) Becke, A.D. Density-Functional Thermochemistry. III. The role of Exact Exchange, *J. Chem. Phys.* **1993**, *98*, 5648-5652.

[3] (a) Godbout, N.; Salahub, D. R.; Andzelm, J.; Wimmer, E. Optimization of Gaussian-Type Basis-Sets for Local Spin-Density Functional Calculations .1. Boron Through Neon, Optimization Technique and Validation, Can. J. Chem. 1992, 70, 560−571. (b) Sosa, C.; Andzelm, J.; Elkin, B. C.; Wimmer, E.; Dobbs, K. D.; Dixon, D. A. A Local Density Functional Study of the Structure and Vibrational Frequencies of Molecular Transition-Metal Compounds, *J. Phys. Chem.* **1992**, 96, 6630−6636.

[4] Scalmani, G.; Frisch, M. J. Continuous Surface Charge Polarizable Continuum Models of Solvation. I. General formalism, *J. Chem. Phys.***2010**, *132*, 114110-24.

[5] Fang, D.-C. THERMO; Beijing Normal University, Beijing, People's Republic of China, 2013.

7.1 The energies, entropies and Gibbs free energies of Stationary Points

Species	E(a.u.)	S(cal/mol/K)	G(a.u.)
1a	-841.04855	**104.2**	-840.81182
5	-157.81299	**54.0**	-157.71473
TS1	-998.85905	**137.4**	-998.51283
6	-998.90193	**129.3**	-998.54781
TS2	-998.87699	**123.2**	-998.52137
7	-998.89617	**121.6**	-998.53787
TS2'	-998.84741	**124.9**	-998.49324
7'	-998.86688	**125.2**	-998.51095

7.2 Coordinates of Stationary Points

1a			
C	-1.70165	-0.43418	-0.02832
C	-1.40539	-1.80902	0.10625
C	-2.43421	-2.75819	0.18458
C	-3.75091	-2.30208	0.10847
C	-4.03506	-0.93006	-0.05177
C	-3.01843	0.02746	-0.13013
C	0.51806	-0.82162	-0.00107
H	-2.20350	-3.81457	0.29215
H	-4.57124	-3.01250	0.16511
H	-5.06929	-0.60364	-0.11934
H	-3.26098	1.07504	-0.27032
N	-0.44519	0.20570	-0.09292
N	-0.02815	-2.00703	0.13388
C	1.97609	-0.59975	0.05187
C	2.54393	0.46220	0.77770
C	2.82261	-1.52502	-0.58454
C	3.93190	0.60065	0.85507
H	1.90951	1.17038	1.30261
C	4.21048	-1.38010	-0.51086
H	2.38724	-2.34964	-1.14127
C	4.77007	-0.31624	0.20779
H	4.35854	1.42140	1.42568
H	4.85414	-2.09653	-1.01468
H	5.84964	-0.20422	0.26638
C	-0.21155	1.53741	-0.56056
O	0.68073	1.75186	-1.36609
C	-1.08637	2.61345	0.00706
C	-1.48613	3.58259	-0.83290
H	-2.10974	4.40350	-0.48866
H	-1.21246	3.56767	-1.88423
C	-1.41042	2.59436	1.48431
H	-0.49380	2.67650	2.07947
H	-2.05714	3.43720	1.73931
H	-1.91151	1.67261	1.79205
5			
C	1.43745	-0.39179	0.01769
C	0.00008	0.00002	-0.17487
H	1.65422	-1.37390	-0.41943
H	2.12259	0.34032	-0.42646
H	1.69990	-0.45905	1.08972

C	-0.37936	1.44055	0.01769
C	-1.05807	-1.04872	0.01770
H	-1.35831	1.66595	-0.42207
H	-0.44760	1.70263	1.08973
H	0.35999	2.11964	-0.42385
H	-1.25167	-1.23930	1.08959
H	-2.01554	-0.74742	-0.42412
H	-0.76414	-2.00921	-0.42238
TS1			
C	2.06031	-1.30829	-0.05277
C	3.27973	-0.60302	0.07794
C	4.49946	-1.29604	0.12285
C	4.46605	-2.68674	0.01323
C	3.24434	-3.37653	-0.14620
C	2.02110	-2.70121	-0.18740
C	1.73331	0.90603	0.01997
H	5.43768	-0.75790	0.22973
H	5.39447	-3.25098	0.04241
H	3.25203	-4.45912	-0.24080
H	1.09141	-3.24485	-0.32394
N	1.06350	-0.32104	-0.07046
N	3.03865	0.76407	0.13157
C	1.05505	2.21413	0.07541
C	-0.16361	2.39259	0.75349
C	1.67459	3.32733	-0.52189
C	-0.75543	3.65659	0.82380
H	-0.64170	1.55371	1.25096
C	1.07837	4.58883	-0.45458
H	2.61747	3.19437	-1.04400
C	-0.13946	4.75815	0.21699
H	-1.69355	3.78149	1.35822
H	1.56263	5.43922	-0.92773
H	-0.60249	5.74013	0.27003
C	-0.28820	-0.53246	-0.56589
O	-0.64710	0.09429	-1.55947
C	-1.10330	-1.50996	0.16849
C	-2.16858	-2.05597	-0.49307
H	-2.72492	-2.87748	-0.05514
H	-2.31714	-1.85691	-1.54889
C	-0.80499	-1.83352	1.61715
H	-1.50069	-2.59304	1.98234

H	0.21038	-2.20914	1.77039
H	-0.91654	-0.94693	2.25277
C	-3.94575	0.58280	-0.12891
C	-4.36513	-0.85778	-0.08676
H	-3.23634	0.82173	0.66988
H	-3.49441	0.85166	-1.08822
H	-4.82510	1.23425	0.01606
C	-5.09337	-1.40550	-1.28204
C	-4.73337	-1.42120	1.25802
H	-5.11784	-2.50092	-1.28195
H	-6.14265	-1.06374	-1.27393
H	-4.65279	-1.06390	-2.22437
H	-5.70028	-1.00402	1.58830
H	-4.84849	-2.51004	1.23367
H	-3.99619	-1.16250	2.02512
6			
C	2.02561	-1.26242	-0.06560
C	3.22845	-0.53475	0.09656
C	4.45982	-1.20691	0.15123
C	4.45292	-2.59618	0.02116
C	3.24688	-3.30699	-0.16743
C	2.01244	-2.65376	-0.21829
C	1.64942	0.94011	0.04172
H	5.38676	-0.65452	0.28142
H	5.39096	-3.14389	0.05702
H	3.27701	-4.38771	-0.27739
H	1.09617	-3.21370	-0.37766
N	1.01096	-0.29819	-0.07783
N	2.95746	0.82534	0.16663
C	0.93897	2.23124	0.08904
C	-0.29178	2.38156	0.75255
C	1.53709	3.35742	-0.50635
C	-0.91571	3.63109	0.81030
H	-0.75244	1.53518	1.25384
C	0.90902	4.60373	-0.45086
H	2.48895	3.24572	-1.01701
C	-0.32059	4.74500	0.20585
H	-1.86238	3.73487	1.33398
H	1.37733	5.46420	-0.92179
H	-0.80848	5.71530	0.24943
C	-0.33696	-0.53703	-0.57436

O	-0.66829	-0.00764	-1.64458
C	-1.19903	-1.38880	0.20817
C	-2.47928	-1.87062	-0.41083
H	-2.63529	-2.90342	-0.07399
H	-2.35550	-1.88966	-1.49778
C	-0.81499	-1.87480	1.57085
H	-1.66150	-1.79780	2.25917
H	-0.56049	-2.94359	1.53046
H	0.03522	-1.33936	1.99531
C	-4.13166	-1.03783	1.39160
C	-3.81546	-1.08852	-0.11549
H	-4.13252	-2.03848	1.83958
H	-3.41775	-0.41551	1.94106
H	-5.12611	-0.60449	1.54918
C	-3.75691	0.34405	-0.67648
C	-4.93844	-1.86620	-0.83452
H	-3.55266	0.34336	-1.75188
H	-4.71620	0.84932	-0.51251
H	-2.97951	0.94108	-0.18996
H	-5.90303	-1.36721	-0.68752
H	-4.75316	-1.92688	-1.91306
H	-5.02701	-2.88806	-0.44791
TS2			
C	2.45259	0.12385	-0.04190
C	2.72810	1.36219	-0.67045
C	3.96514	1.58039	-1.29368
C	4.89833	0.54186	-1.27325
C	4.60794	-0.68916	-0.64722
C	3.37963	-0.92203	-0.01901
C	0.72031	1.54859	0.10080
H	4.18172	2.52857	-1.77836
H	5.86652	0.68118	-1.74692
H	5.35779	-1.47580	-0.64732
H	3.16317	-1.86560	0.46789
N	1.13868	0.24447	0.43256
N	1.63872	2.22337	-0.55281
C	-0.60087	2.00669	0.50435
C	-1.21761	1.34549	1.63387
C	-1.32000	2.91758	-0.26874
C	-2.56626	1.71865	1.95597
H	-0.58219	1.09611	2.48206

C	-2.64983	3.22767	0.05088
H	-0.84670	3.36238	-1.13973
C	-3.26945	2.60910	1.15965
H	-3.02812	1.30491	2.84793
H	-3.20330	3.93676	-0.55791
H	-4.29505	2.86547	1.41374
C	0.38263	-0.75833	1.10344
O	0.98028	-1.62719	1.73305
C	-1.10478	-0.65987	1.03499
C	-1.75627	-0.66386	-0.34562
H	-1.17831	-0.01190	-1.00614
H	-2.74489	-0.19851	-0.24436
C	-1.79317	-1.41051	2.15375
H	-2.87445	-1.25818	2.11163
H	-1.59964	-2.48642	2.08710
H	-1.43198	-1.08601	3.13516
C	-2.36178	-1.62668	-2.55813
C	-1.95230	-2.01465	-1.11848
H	-3.27682	-1.02250	-2.56284
H	-1.57390	-1.04898	-3.05518
H	-2.55033	-2.52353	-3.15931
C	-0.65006	-2.83613	-1.17838
C	-3.08467	-2.87522	-0.51911
H	-0.34290	-3.19305	-0.19022
H	-0.78777	-3.71604	-1.81758
H	0.17536	-2.24970	-1.59977
H	-4.01448	-2.30090	-0.43194
H	-3.28493	-3.73536	-1.16877
H	-2.83725	-3.26759	0.47011
7			
C	2.50231	-0.12172	0.28821
C	2.83416	1.04302	-0.44758
C	4.15036	1.24834	-0.88819
C	5.10238	0.27386	-0.58057
C	4.75591	-0.88144	0.14984
C	3.44669	-1.10182	0.59796
C	0.72082	1.23101	-0.02128
H	4.41202	2.13973	-1.45176
H	6.12976	0.40576	-0.90975
H	5.52082	-1.62067	0.37201
H	3.18087	-1.99020	1.15665

N	1.12862	0.00745	0.56373
N	1.72054	1.85359	-0.62485
C	-0.63615	1.65277	0.10614
C	-1.48864	0.90276	1.10494
C	-1.11842	2.78542	-0.55216
C	-2.94383	1.28631	1.02688
H	-1.14908	1.28978	2.08741
C	-2.45238	3.17597	-0.43135
H	-0.44225	3.34483	-1.19279
C	-3.36576	2.38448	0.34042
H	-3.65687	0.70913	1.60819
H	-2.81132	4.05397	-0.96022
H	-4.41733	2.66053	0.36037
C	0.28254	-0.96883	1.09808
O	0.74266	-2.04925	1.44837
C	-1.21677	-0.64363	1.22146
C	-2.03820	-1.59440	0.27206
H	-3.09170	-1.41715	0.51807
H	-1.81527	-2.60011	0.64477
C	-1.61094	-1.06836	2.66522
H	-2.67448	-0.88469	2.83953
H	-1.41962	-2.13118	2.82079
H	-1.04210	-0.50478	3.41189
C	-2.51659	-0.43742	-1.99388
C	-1.93937	-1.67664	-1.28322
H	-3.54487	-0.23883	-1.67272
H	-1.92523	0.46157	-1.80818
H	-2.53119	-0.60053	-3.07841
C	-0.50553	-1.93975	-1.78709
C	-2.81070	-2.89477	-1.67926
H	-0.04807	-2.79314	-1.27474
H	-0.52292	-2.16553	-2.85961
H	0.14770	-1.07213	-1.65686
H	-3.84482	-2.77432	-1.33562
H	-2.83205	-3.01221	-2.76856
H	-2.41880	-3.82401	-1.24940
TS2'			
C	-0.09981	1.71305	-0.71543
C	-0.96442	2.60572	-0.10621
C	-0.46739	3.87544	0.28129
C	0.91620	4.08567	0.11061

C	1.77986	3.14156	-0.47002
C	1.29991	1.86039	-0.92870
C	-1.99790	0.68247	-0.16512
H	-1.10026	4.62839	0.74147
H	1.33429	5.04263	0.41448
H	2.82145	3.40586	-0.63102
H	1.77323	1.44507	-1.81726
N	-0.69442	0.46245	-0.69812
N	-2.17029	1.94675	0.16776
C	-3.02310	-0.35943	-0.04803
C	-3.01679	-1.50177	-0.87025
C	-4.06646	-0.19065	0.88539
C	-4.03284	-2.45543	-0.75740
H	-2.22600	-1.63868	-1.59963
C	-5.07621	-1.14672	0.99521
H	-4.07173	0.68923	1.52151
C	-5.06347	-2.28359	0.17408
H	-4.02133	-3.33089	-1.40150
H	-5.87249	-1.00890	1.72214
H	-5.85136	-3.02756	0.25996
C	0.28654	-0.55930	-0.41113
O	0.05307	-1.74738	-0.51066
C	1.60320	0.06468	0.04205
C	2.88089	-0.53435	-0.53842
H	3.58587	0.30014	-0.65466
H	2.64972	-0.87231	-1.55572
C	1.56315	0.46256	1.50887
H	1.53786	-0.42040	2.15811
H	2.44875	1.04987	1.76587
H	0.67958	1.06372	1.74347
C	4.41090	-1.19039	1.43457
C	3.68702	-1.68358	0.16240
H	5.00488	-0.29108	1.23275
H	3.72038	-0.96245	2.24990
H	5.09586	-1.96555	1.79810
C	2.81436	-2.90471	0.50608
C	4.76628	-2.11980	-0.85611
H	2.31331	-3.30034	-0.38261
H	3.43812	-3.70137	0.92962
H	2.03939	-2.66200	1.23928
H	5.40231	-2.90437	-0.43040

H	4.31344	-2.51542	-1.77269
H	5.41363	-1.27986	-1.13572
7'			
C	-0.11114	1.61802	-0.65850
C	-1.01697	2.58244	-0.31035
C	-0.51002	3.87974	0.01178
C	0.91198	3.98552	0.11252
C	1.80743	2.95325	-0.12347
C	1.35349	1.61330	-0.66226
C	-2.06307	0.65934	-0.21414
H	-1.15335	4.71406	0.27244
H	1.32115	4.94603	0.41946
H	2.87344	3.13708	-0.01632
H	1.75003	1.50285	-1.68611
N	-0.70542	0.38474	-0.54476
N	-2.25756	1.96147	-0.09481
C	-3.10487	-0.36338	-0.08222
C	-2.96942	-1.63901	-0.66162
C	-4.28961	-0.05030	0.61597
C	-3.99599	-2.58027	-0.54184
H	-2.06848	-1.89305	-1.20943
C	-5.30985	-0.99431	0.73398
H	-4.39730	0.93255	1.06455
C	-5.16763	-2.26414	0.15591
H	-3.88118	-3.56021	-0.99793
H	-6.21584	-0.74268	1.27933
H	-5.96352	-2.99869	0.24847
C	0.29820	-0.56116	-0.13565
O	0.08210	-1.73149	0.08655
C	1.64375	0.22172	0.06923
C	2.87633	-0.45260	-0.60614
H	3.57331	0.36960	-0.81152
H	2.53818	-0.79363	-1.59308
C	1.74906	0.44909	1.59414
H	1.77355	-0.49856	2.13573
H	2.65536	1.01199	1.82878
H	0.89409	1.02650	1.96178
C	4.60031	-1.09935	1.20144
C	3.74749	-1.59363	0.01026
H	5.14816	-0.18429	0.94619
H	4.00334	-0.89784	2.09357

H	5.33885	-1.86309	1.47192
C	2.94633	-2.83939	0.43375
C	4.72462	-2.01225	-1.11644
H	2.35105	-3.23303	-0.39644
H	3.63525	-3.62799	0.76033
H	2.25978	-2.63016	1.25765
H	5.41016	-2.79043	-0.76206
H	4.18530	-2.41056	-1.98379
H	5.33024	-1.16384	-1.45713