Supporting Information

Rh-Catalyzed Chemo-, Stereo- and Regioselective C-H Cascade Annulation of indolyloxopropanenitriles for Pyranoindoles

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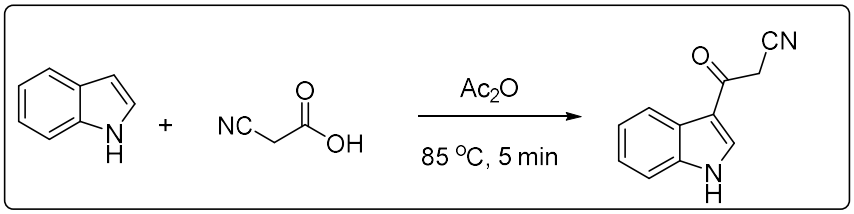
1. General Information and methods.

All reagents and solvents were purchased from commercial sources and used without purification. NMR spectra were recorded with a 300, 400 or 500 MHz spectrometer for ^{1}H NMR, 100 or 125 MHz for ^{13}C NMR spectroscopy. Chemical shifts are reported relative to the residual signals of tetramethyl silane in $CDCl_3$ or deuterated solvent $CDCl_3$ and DMSO for 1H and 13C NMR spectroscopy. Multiplicities are reported as follows: singlet (s), doublet (d), doublet of doublets (dd), doublet of triplets (dt), triplet (t), quartet (q), multiplet (m). HRMS were recorded by using ORBITRAP and ESI mass spectrometer. Column chromatography was performed with silica gel (100–200 mesh) as the stationary phase. All reactions were monitored by using TLC.

Following the known procedure, 3-cyanoacetylindoles[1] and 4-hydroxy-2-alkynoate Derivatives[2] were prepared (Table S1 and S2).

2. Experimental Procedures

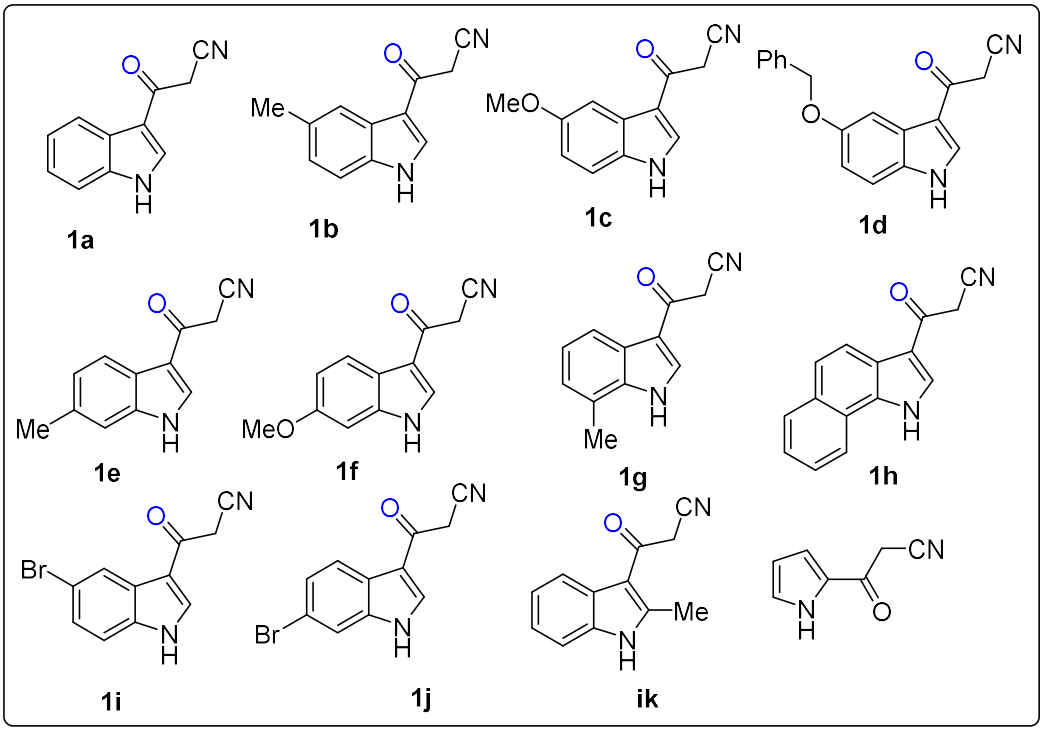
2.1. Preparation of substituted 3-cyanoacetylindoles: General Procedure (GP-1):



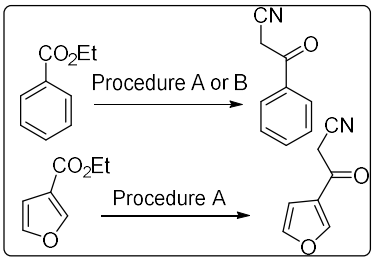
General Procedure for the Synthesis of 3-cyanoacetylindoles(1a-1k):

3-cyanoacetylindoles were prepared according to the reported procedures.[1] Indole (5.85 g, 50 mmol) was added to a solution of cyanoacetic acid (5.0 g, 50 mmol) in Ac_2O (50 mL) preheated to 50 °C. The solution was heated at 85 °C and stirred for 5 minutes. 3-cyanoacetylindole started to crystallize slowly. After 5 more minutes, the mixture was slowly allowed to cool and the solid was collected through filtration and washed with MeOH before drying. For pyrrole derivative reaction time 4h, cool to room temperature, neutral with saturated aqueous $NaHCO_3$ and extracted with DCM. The combined organic extracts were washed with brine, dried over sodium sulfate and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel with EtOAc/petroleum ether to give the corresponding 3-oxo-3-(1H-pyrrol-2-yl)propanenitrile.

Table S1: List of 3-cyanoacetylindoles.



2.3 Preparation of 3-Oxo-nitrile Substrates

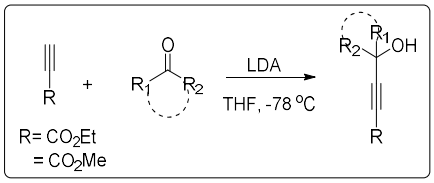


Procedure A:[6a] Ethyl ester (6.65 mmol, 1 equiv) was dissolved in THF (30 mL) with stirring at ambient temperature. Potassium tert-butoxide (1.57 g, 14.0 mmol, 95%, 2 equiv) was added to the above THF solution. After stirring enough the flask, acetonitrile (6.65 mmol, 1 equiv) was then added. The resulting mixture was stirred at ambient temperature for 3 h. The reaction mixture was quenched by addition of water (50 mL) and then stirred for 5 min. After adding ethyl acetate (40 mL) and then HCl solution (1 mL, 12 M), the organic layer was separated and dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure and the resulting residue was purified by flash column chromatography on silica gel with EtOAc/petroleum ether to give the corresponding β-ketonitriles

Procedure B:[6b]To a solution of ester (10 mmol, 1.0 equiv) in THF (20 mL) under a nitrogen atmosphere was added NaH (15 mmol, 60 % dispersion in mineral oil, 1.5 equiv) at r.t and the mixture was stirred for 30 min. Acetonitrile (20 mL) was added dropwise and the reaction mixture was stirred at 60 °C for 12 h. The reaction was quenched with H_2O and the solvent was removed in vacuo. The water phase was extracted with ethyl acetate (3×25 mL). The combined organic phase was dried over anhydrous Na_2SO_4 and then concentrated in vacuo.

The residue was purified by column chromatography on silica gel (petroleum ether: ethyl acetate = 3:1) to obtain the corresponding 3-oxo-3-propanenitrile.

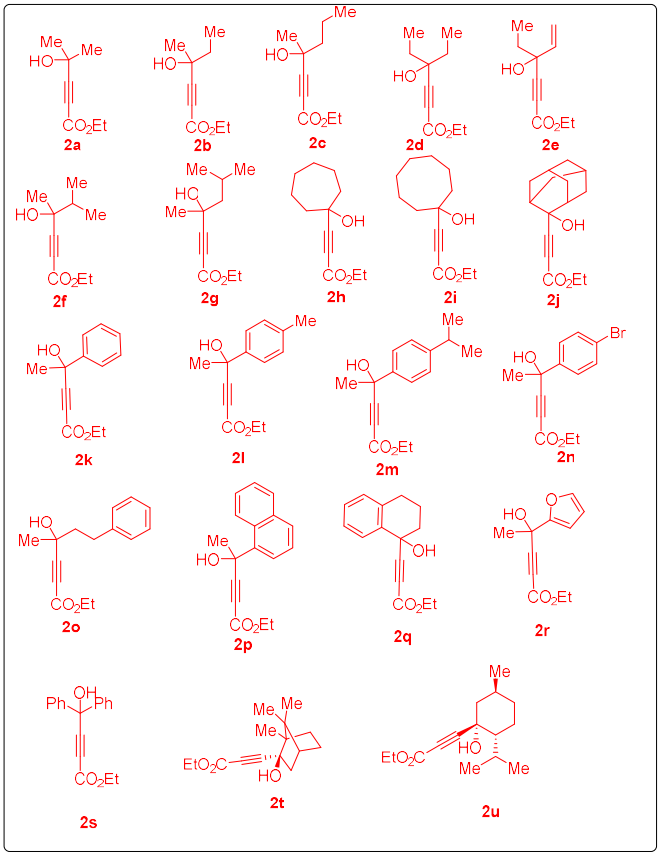
2.2. Preparation of 4-hydroxy-2-alkynoates:



General Procedure for the Synthesis of 4-hydroxy-2-alkynoates(2a-2u)[2]:

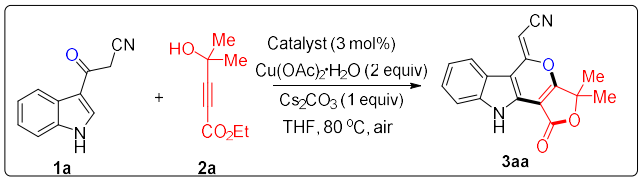
To a solution of alkyl propiolate (4.5 mmol) in tetrahydrofuran (20 mL), lithium diisopropylamide (1.6 M in hexane, 4.5 mmol) was added drop wise by syringe at -78 °C. After stirring for 1 h, a solution of ketone (3 mmol) in THF (5 mL) was added drop wise and the mixture was stirred at the same temperature for 2h. The solution was then allowed to warm to room temperature, quenched with saturated aqueous NH_4Cl and extracted with ethyl acetate. The combined organic extracts were washed with brine, dried over sodium sulfate and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (EtOAc:Hexanes) to get the expected 4-hydroxy-2-alkynoates.

Table S2: List of 4-hydroxy-2-alkynoates.



3. Optimization Studies:

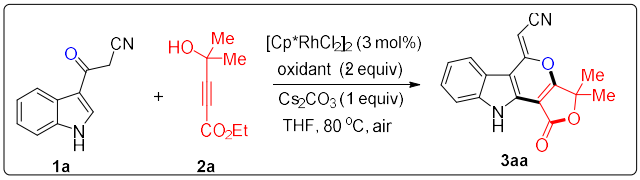
Table S1: Optimization of Metal Catalyst.[a]



Entry	Metal Catalyst	Yield of **3aa**
1	$Pd(OAc)_2$	--
2	--	--
3	$[RuCl_2(p\text{-cymene})]_2$	trace
4	**$[Cp^*RhCl_2]_2$**	**73%**
5	$[Cp^*Co(CO)I_2]$	--
6	$MnBr(CO)_5$	--
7	$Co(OAc)_2$	--

[a]Reactionconditons:**1a** (0.3 mmol), **2a** (0.3 mmol), catalyst (3 mol%), $Cu(OAc)_2.H_2O$ (2 equiv), Cs_2CO_3(1 equiv), THF, 80 °C, 5 hours under an air balloon. n.r. = no reaction.

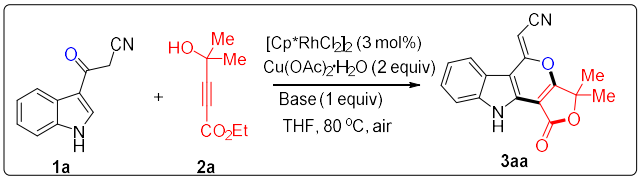
Table S2: Optimization of Oxidant.[a]



Entry	Oxidant	Yield of **3aa**
1	$Zn(OAc)_2.2H_2O$	44%
2	AgOAc	38%
3	$Cu(OAc)_2.H_2O$	73%
4	---	---
5	Ag_2CO_3	22%
6	$PhI(OAc)_2$	n.r.

[a]Reaction conditions: **1a** (0.3 mmol), **2a** (0.3 mmol), $[RhCp^*Cl_2]_2$ (3 mol %), Oxidant (2 equiv), Cs_2CO_3 (1 equiv), THF, 80 °C, 5 hours under an air balloon. n.r. = no reaction.

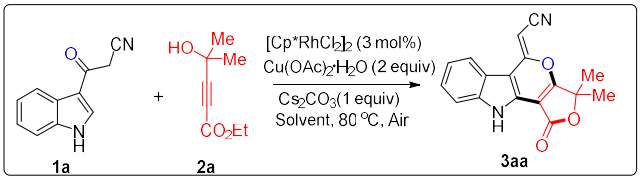
Table S3: Optimization of base.[a]



Entry	base	Yield of **3aa**
1	CsOAc	---
2	---	---
3	Cs_2CO_3	**73%**
4	K_2CO_3	35%
5	$(C_2H_5)_3N$ instead of Cs_2CO_3	30%

[a]Reaction conditions: **1a** (0.3 mmol), **2a** (0.3 mmol), $[RhCp^*Cl_2]_2$ (3 mol %), $Cu(OAc)_2.H_2O$ (2equiv), base (1 equiv), THF, 80 °C, 5 hours under an air balloon. n.r. = no reaction.

Table S4: Optimization of Solvent.[a]



Entry	Solvent	Yield of **3aa**
1	DCE	68%
2	*t*-AmOH	---
3	MeCN	n.r.
4	THF	73%
5	DMF	n.r.
6	1,4-Dioxan	n.r.

[a]Reaction conditions: **1a** (0.3 mmol), **2a** (0.3 mmol), $[RhCp^*Cl_2]_2$ (3 mol %), $Cu(OAc)_2.H_2O$ (2equiv), Cs_2CO_3 (1 equiv), solvent, 80 °C, 5 hours under an air balloon. n.r. = no reaction

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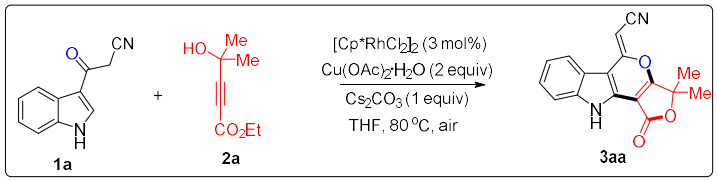
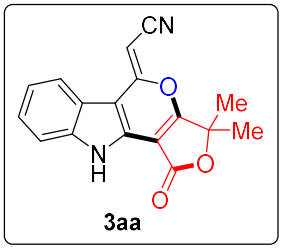
4. General Procedure for title compounds 3 and Characteristic data:

General Procedure for title compounds taking 3aa as an example:



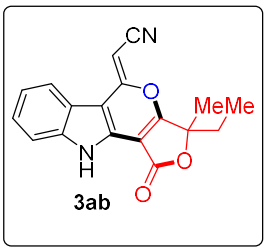
To a mixture of 3-(1H-indol-3-yl)-3-oxopropanenitrile **1a** (55 mg, 0.3 mmol) and 4-hydroxyalkynoate derivative **2a** (46.8mg, 0.3 mmol) in THF, $[RhCp^*Cl_2]_2$ (5.6 mg, 3 mol %), $Cu(OAc)_2.H_2O$ (119 mg, 2 equiv), Cs_2CO_3 (97.5 mg, 1 equiv) were introduced and the reaction mixture was stirred at 80 °C (oil bath) for 5 hours under air balloon. After completion of reaction (monitored by TLC), THF was evaporated, water was added and the contents were extracted with ethyl acetate (2×10 mL). The organic layer was evaporated and the residue was purified by column chromatography (R_f = 0.50) (SiO_2, EtOAc:Hexane, 14:86) to get **3aa** as white solid in 73% (63.7mg) yield; mp 193-198 °C.

(Z)-2-(3,3-dimethyl-1-oxo-3,10-dihydrofuro[3',4':5,6]pyrano[4,3-b]indol-5(1H)-ylidene)acetonitrile (3aa):



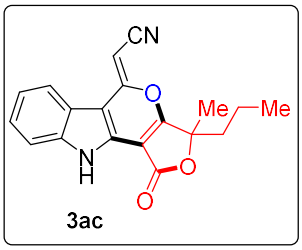
^{1}H NMR (400 MHz, DMSO) δ 12.91 (s, 1H), 7.93 (d, *J* = 5.1 Hz, 1H), 7.60 (d, *J* = 5.5 Hz, 1H), 7.34 (dd, *J* = 18.4, 6.5 Hz, 2H), 5.42 (s, 1H), 1.68 (s, 6H). ^{13}C NMR (100 MHz, DMSO) δ 177.0, 164.4, 162.7, 138.3, 130.6, 124.6, 122.6, 119.7, 113.2, 101.3, 98.0, 82.7, 64.8, 24.0. HRMS (ESI) calcd for $C_{17}H_{11}N_2O_3$ $[M-H]^-$ 291.0769, found 291.0771.

(Z)-2-(3-ethyl-3-methyl-1-oxo-3,10-dihydrofuro[3',4':5,6]pyrano[4,3-b]indol-5(1H)-ylidene)acetonitrile (3ab):



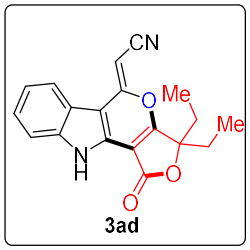
The title compound was prepared from **1a** (55 mg, 0.3 mmol) and **2b** (51 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.50, SiO_2, EtOAc:Hexane, 15:85) gave pure product as an off-white solid (64, 70% yield), mp 242-247 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 1H), 7.66 (d, *J* = 7.5 Hz, 1H), 7.57 (d, *J* = 7.9 Hz, 1H), 7.46 – 7.36 (m, 2H), 4.99 (s, 1H), 2.11 (dd, *J* = 7.3, 2.6 Hz, 2H), 1.76 (s, 3H), 0.98 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.0, 165.8, 163.1, 137.6, 130.2, 125.5, 123.5, 119.6, 112.9, 102.6, 99.0, 86.8, 66.9, 30.61, 23.0, 7.90. HRMS (ESI) calcd for $C_{18}H_{13}O_3N_2$ $[M-H]^-$ 305.0926, found 305.0926.

(Z)-2-(3-methyl-1-oxo-3-propyl-3,10-dihydrofuro[3',4':5,6]pyrano[4,3-b]indol-5(1H)-ylidene)acetonitrile (3ac):



The title compound was prepared from **1a** (55 mg, 0.3 mmol) and **2c** (55 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.51, SiO_2, EtOAc:Hexane, 14:86) gave pure product as a pale yellow solid (67 mg, 70% yield), mp 195-198 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 7.65 (d, *J* = 7.2 Hz, 1H), 7.59 (d, *J* = 7.5 Hz, 1H), 7.47 – 7.36 (m, 2H), 4.99 (s, 1H), 2.03 (dd, *J* = 12.1, 7.2 Hz, 2H), 1.75 (s, 3H), 1.33 – 1.24 (m, 2H), 0.96 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.2, 165.8, 163.1, 137.7, 130.2, 125.5, 123.4, 121.7, 119.6, 113.0, 102.6, 98.9, 86.6, 66.8, 39.4, 23.3, 16.9, 14.0. HRMS (ESI) calcd for $C_{19}H_{17}N_2O_3$ $[M+H]^+$ 321.1239, found 321.1223.

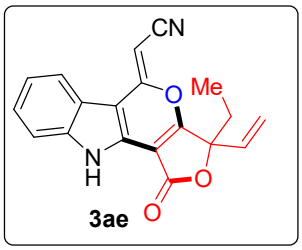
(Z)-2-(3,3-diethyl-1-oxo-3,10-dihydrofuro[3',4':5,6]pyrano[4,3-b]indol-5(1H)-ylidene)acetonitrile (3ad):



The title compound was prepared from **1a** (55 mg, 0.3 mmol) and **2d** (55 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.52, SiO_2, EtOAc:Hexane, 14:86) gave pure product as a pale yellow solid (68.8 mg, 72% yield), mp 179-184 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.97 (s, 1H), 7.65 (d, *J* = 7.5 Hz, 1H),

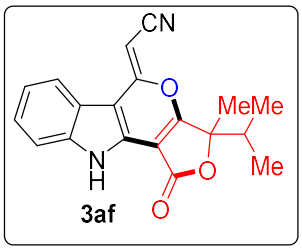
7.57 (d, J = 7.4 Hz, 1H), 7.41 (tt, J = 7.3, 6.1 Hz, 2H), 4.98 (s, 1H), 2.12 (qd, J = 7.4, 2.4 Hz, 4H), 0.95 (t, J = 7.4 Hz, 6H).^{13}C NMR (100 MHz, $CDCl_3$) δ 176.0, 166.2, 163.2, 137.7, 130.0, 125.5, 123.5, 121.7, 119.6, 113.0, 102.5, 100.2, 90.0, 7.7, 29.2, 7.7. HRMS (ESI) calcd for $C_{19}H_{17}N_2O_3$ $[M+H]^+$321.1233, found 321.1227.

(Z)-2-(3-ethyl-1-oxo-3-vinyl-3,10-dihydrofuro[3',4':5,6]pyrano[4,3-b]indol-5(1H)-ylidene)acetonitrile (3ae):



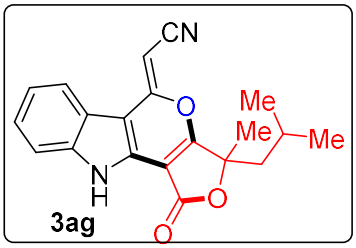
The title compound was prepared from **1a** (55 mg, 0.3 mmol) and **2e** (54.6 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.51, SiO_2, EtOAc:Hexane, 13:87) gave pure product as a off-white solid (64.6 mg, 68% yield), mp 186-189 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.98 (s, 1H), 7.64 (d, J = 7.7 Hz, 1H), 7.58 (d, J = 7.8 Hz, 1H), 7.46 – 7.36 (m, 2H), 6.10 (dd, J = 17.2, 10.9 Hz, 1H), 5.64 (d, J = 17.2 Hz, 1H), 5.44 (d, J = 10.9 Hz, 1H), 4.99 (s, 1H), 2.25 – 2.07 (m, 2H), 1.01 (t, J = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.3, 165.8, 163.1, 137.7, 132.6, 130.0, 125.5, 123.5, 119.6, 118.7, 112.9, 102.7, 98.6, 88.3, 67.0, 29.9, 7.7. HRMS (ESI) calcd for $C_{19}H_{13}N_2O_3$ $[M-H]^-$ 317.0920, found 317.0928.

(Z)-2-(3-isopropyl-3-methyl-1-oxo-3,10-dihydrofuro[3',4':5,6]pyrano[4,3-b]indol-5(1H)-ylidene)acetonitrile (3af):



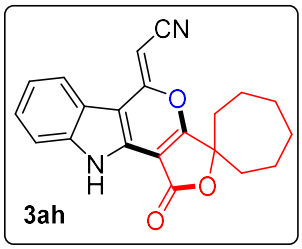
The title compound was prepared from **1a** (55 mg, 0.3 mmol) and **2f** (55 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.55, SiO_2, EtOAc:Hexane, 14:86) gave pure product as a pale yellow solid (61.2 mg, 64% yield), mp 196-200 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.07 (s, 1H), 7.65 (d, J = 7.3 Hz, 1H), 7.56 (d, J = 7.4 Hz, 1H), 7.45 – 7.36 (m, 2H), 4.98 (s, 1H), 2.32 (dd, J = 13.7, 6.9 Hz, 1H), 1.75 (s, 3H), 1.12 (d, J = 6.8 Hz, 3H), 1.07 (d, J = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.4, 166.1, 163.2, 137.8, 130.2, 125.4, 123.4, 121.7, 119.6, 113.0, 102.5, 99.1, 89.1, 66.7, 35.2, 21.4, 17.3, 16.9. HRMS (ESI) calcd for $C_{19}H_{17}O_3N_2$ $[M+H]^+$321.1233, found 321.1234.

(Z)-2-(3-isobutyl-3-methyl-1-oxo-3,10-dihydrofuro[3',4':5,6]pyrano[4,3-b]indol-5(1H)-ylidene)acetonitrile (3ag):



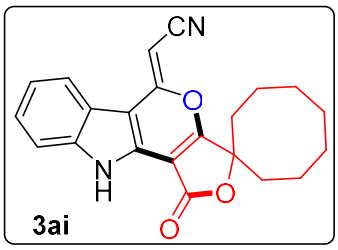
The title compound was prepared from **1a** (55 mg, 0.3 mmol) and **2g** (59.4 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.55, SiO_2, EtOAc:Hexane, 15:85) gave pure product as a white solid (67 mg, 67% yield), mp 190-193 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.84 (s, 1H), 7.66 (d, *J* = 7.7 Hz, 1H), 7.55 (d, *J* = 7.5 Hz, 1H), 7.43 – 7.39 (m, 2H), 4.99 (s, 1H), 2.11 – 2.07 (m, 1H), 1.90 – 1.85 (m, 2H), 1.75 (s, 3H), 0.99 (d, *J* = 6.7 Hz, 3H), 0.90 (d, *J* = 6.6 Hz, 3H).^{13}C NMR (125 MHz, $CDCl_3$) δ 177.5, 165.8, 163.0, 137.7, 130.2, 125.5, 123.5, 119.6, 116.6, 112.9, 102.6, 98.8, 86.5, 66.8, 45.7, 24.4, 24.2, 24.0, 23.3. HRMS (ESI) calcd for $C_{20}H_{17}O_3N_2$ $[M-H]^-$ 333.1233, found 333.1241.

(Z)-2-(1'-oxo-1'H-spiro[cycloheptane-1,3'-furo[3',4':5,6]pyrano[4,3-b]indol]-5'(10'H)-ylidene)acetonitrile (3ah):



The title compound was prepared from **1a** (55 mg, 0.3 mmol) and **2h** (63 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.50 SiO_2, EtOAc:Hexane, 16:84) gave pure product as a off-white solid (66.1 mg, 64% yield), mp 290-293 °C. ^{1}H NMR (500 MHz, DMSO) δ 12.89 (s, 1H), 7.92 (d, *J* = 6.3 Hz, 1H), 7.60 (d, *J* = 6.6 Hz, 1H), 7.33 (dd, *J* = 24.0, 6.6 Hz, 2H), 5.42 (s, 1H), 2.11 (d, *J* = 12.7 Hz, 4H), 1.75 (s, 4H), 1.68 (s, 4H). ^{13}C NMR (125 MHz, DMSO) δ 178.0, 164.5, 162.9, 138.2, 130.7, 124.6, 122.6, 121.3, 119.7, 117.5, 113.2, 101.3, 97.3, 9.7, 64.8, 36.5, 29.3, 22.3. HRMS (ESI) calcd for $C_{21}H_{19}O_3N_2$ $[M+H]^+$ 347.1390, found 347.1382.

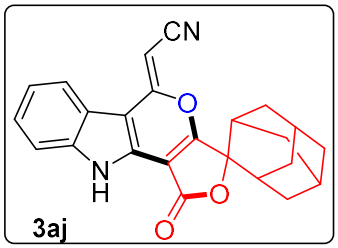
(Z)-2-(1'-oxo-1'H-spiro[cyclooctane-1,3'-furo[3',4':5,6]pyrano[4,3-b]indol]-5'(10'H)-ylidene)acetonitrile (3ai):



The title compound was prepared from **1a** (55 mg, 0.3 mmol) and **2i** (67.2 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.50, SiO_2, EtOAc:Hexane, 17:83) gave pure product as a white solid (66.7 mg, 62% yield), mp 288-292 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.90 (s, 1H), 7.64 (d, *J* = 7.3 Hz, 1H), 7.55 (d,

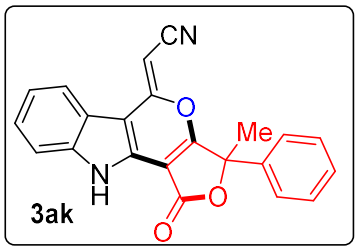
J = 7.5 Hz, 1H), 7.42 – 7.37 (m, 2H), 4.97 (s, 2H), 2.22 – 2.10 (m, 4H), 1.96 (t, *J* = 14.1 Hz, 2H), 1.87 – 1.78 (m, 8H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.1, 165.9, 163.3, 137.6, 130.5, 125.4, 123.4, 121.8, 119.6, 112.9, 102.6, 97.9, 89.3, 66.6, 33.3, 27.7, 24.8, 22.1. HRMS (ESI) calcd for $C_{22}H_{19}O_3N_2$ $[M-H]^-$ 359.1390, found 359.1395.

(Z)-2-(1'-oxo-1'H-spiro[adamantane-2,3'-furo[3',4':5,6]pyrano[4,3-b]indol]-5'(10'H)-ylidene)acetonitrile (3aj):



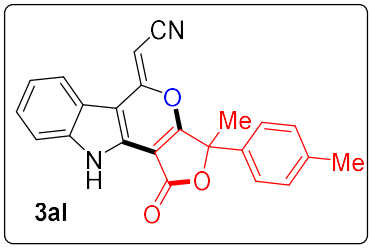
The title compound was prepared from **1a** (55 mg, 0.3 mmol) and **2j** (74.4 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.50, SiO_2, EtOAc:Hexane 16:84) gave pure product as a off-white solid (46 mg, 40% yield), mp 183-188 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.76 (s, 1H), 7.64 (d, *J* = 7.8 Hz, 1H), 7.54 (d, *J* = 7.8 Hz, 1H), 7.42 – 7.38 (m, 2H), 4.94 (s, 1H), 2.65 (d, *J* = 13.1 Hz, 2H), 2.36 (d, *J* = 12.6 Hz, 2H), 2.15 (d, *J* = 23.2 Hz, 2H), 1.98 (d, *J* = 14.1 Hz, 2H), 1.87 – 1.79 (m, 6H).^{13}C NMR (100 MHz, $CDCl_3$) δ 177.9, 165.6, 163.7, 137.6, 130.7, 125.5, 123.4, 119.7, 117.2, 112.8, 102.6, 98.7, 90.8, 66.4, 37.5, 36.8, 34.3, 33.6, 29.9, 26.5, 26.1. HRMS (ESI) calcd for $C_{24}H_{19}O_3N_2[M-H]^-$383.1395, found 383.1398.

(Z)-2-(3-methyl-1-oxo-3-phenyl-3,10-dihydrofuro[3',4':5,6]pyrano[4,3-b]indol-5(1H)-ylidene)acetonitrile (3ak):



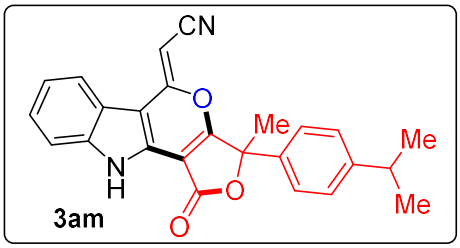
The title compound was prepared from **1a** (55 mg, 0.3 mmol) and **2k** (65.4 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.55, SiO_2, EtOAc:Hexane, 16:84) gave pure product as a pale yellow solid (65.6 mg, 62 % yield), mp 294-297 °C. ^{1}H NMR (400 MHz, DMSO) δ 13.00 (s, 1H), 7.92 (d, *J* = 4.6 Hz, 1H), 7.58 (s, 3H), 7.48 (d, *J* = 4.3 Hz, 3H), 7.34 (d, *J* = 26.4 Hz, 2H), 5.45 (s, 1H), 2.08 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ 175.3, 164.4, 162.7, 138.4, 136.9, 130.3, 129.4, 129.3, 125.2, 124.8, 122.7, 121.2, 119.8, 117.3, 113.3, 101.5, 98.2, 84.8, 65.2, 24.0. HRMS (ESI) calcd for $C_{22}H_{13}O_3N_2$ $[M-H]^-$ 353.0921, found 353.0929.

(Z)-2-(3-methyl-1-oxo-3-(p-tolyl)-3,10-dihydrofuro[3',4':5,6]pyrano[4,3-b]indol-5(1H)-ylidene)acetonitrile (3al):



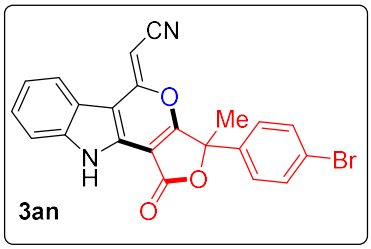
The title compound was prepared from **1a** (55 mg, 0.3 mmol) and **2l** (69.6 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.50, SiO_2, EtOAc:Hexane, 15:85) gave pure product as a sticky solid (60.5 mg, 55% yield). ^{1}H NMR (400 MHz, DMSO) δ 12.99 (s, 1H), 7.92 (d, *J* = 7.9 Hz, 1H), 7.62 (d, *J* = 8.1 Hz, 1H), 7.44 (d, *J* = 8.2 Hz, 2H), 7.38 (t, *J* = 7.6 Hz, 1H), 7.30 (t, *J* = 8.8 Hz, 3H), 5.44 (s, 1H), 2.32 (s, 3H), 2.06 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ 175.5, 164.5, 162.7, 139.1, 138.4, 133.8, 129.8, 125.2, 124.8, 122.7, 121.2, 119.8, 117.3, 113.3, 101.4, 98.1, 84.8, 65.2, 23.7, 20.7. HRMS (ESI) calcd for $C_{23}H_{15}O_3N_2$ $[M-H]^-$ 367.1077, found 367.1086.

(Z)-2-(3-(4-isopropylphenyl)-3-methyl-1-oxo-3,10-dihydrofuro[3',4':5,6]pyrano[4,3-b]indol-5(1H)-ylidene)acetonitrile (3am):



The title compound was prepared from **1a** (55 mg, 0.3 mmol) and **2m** (78 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.53, SiO_2, EtOAc:Hexane, 16:84) gave pure product as a pale yellow gel 55.6 mg, 47% yield). ^{1}H NMR (400 MHz, DMSO) δ 12.99 (s, 1H), 7.93 (d, *J* = 7.8 Hz, 1H), 7.62 (d, *J* = 8.0 Hz, 1H), 7.48 (d, *J* = 8.3 Hz, 2H), 7.37 (d, *J* = 5.4 Hz, 2H), 7.32 (d, *J* = 7.8 Hz, 2H), 5.45 (s, 1H), 2.93 – 2.89 (m, 1H), 2.06 (s, 3H), 1.20 (s, 3H), 1.18 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ 175.4, 164.4, 162.7, 149.8, 138.4, 134.3, 130.3, 127.2, 125.2, 124.8, 122.7, 119.8, 113.3, 101.5, 98.2, 84.9, 65.2, 33.2, 24.0, 23.8, 23.8. HRMS (ESI) calcd for $C_{25}H_{19}O_3N_2$ $[M-H]^-$ 395.1390, found 395.1399.

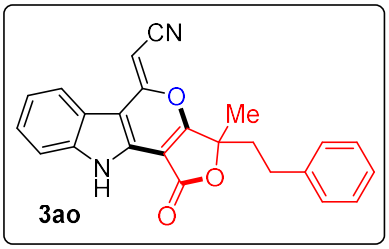
(Z)-2-(3-(4-bromophenyl)-3-methyl-1-oxo-3,10-dihydrofuro[3',4':5,6]pyrano[4,3-b]indol-5(1H)-ylidene)acetonitrile (3an):



The title compound was prepared from **1a** (55 mg, 0.3 mmol) and **2n** (88.8 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.50, SiO_2, EtOAc:Hexane, 16:84) gave pure product as a yellowish gel (58 mg, 45% yield).

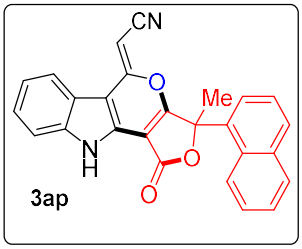
^{1}H NMR (400 MHz, DMSO) δ 13.01 (s, 1H), 7.93 (d, *J* = 7.4 Hz, 1H), 7.69 (d, *J* = 8.0 Hz, 2H), 7.62 (d, *J* = 8.2 Hz, 1H), 7.53 (d, *J* = 8.1 Hz, 2H), 7.40 – 7.35 (m, 1H), 7.33 – 7.28 (m, 1H), 5.45 (s, 1H), 2.07 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ 174.8, 164.3, 162.7, 138.4, 136.2, 132.2, 127.6, 124.8, 122.9, 122.8, 121.2, 119.8, 117.3, 113.3, 101.5, 98.4, 84.3, 65.3, 23.7. HRMS (ESI) calcd for $C_{22}H_{12}O_3N_2Br$ $[M-H]^-$ 431.0025, found 431.0037.

(Z)-2-(3-methyl-1-oxo-3-phenethyl-3,10-dihydrofuro[3',4':5,6]pyrano[4,3-b]indol-5(1H)-ylidene)acetonitrile (3ao):



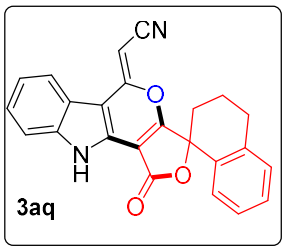
The title compound was prepared from **1a** (55 mg, 0.3 mmol) and **2o** (73.8 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.50, SiO_2, EtOAc:Hexane,17:83) gave pure product as a yellow solid (66.2 mg, 58% yield), mp 234-238 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.76 (s, 1H), 7.60 (dd, *J* = 11.7, 8.0 Hz, 2H), 7.45 – 7.36 (m, 2H), 7.13 (q, *J* = 7.4 Hz, 4H), 7.01 (t, *J* = 6.6 Hz, 1H), 4.90 (s, 1H), 2.86 – 2.80 (m, 1H), 2.64 – 2.55 (m, 1H), 2.44 (t, *J* = 7.6 Hz, 2H), 1.79 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.6, 165.8, 162.9, 139.4, 137.6, 130.0, 128.6, 128.4, 126.4, 125.4, 123.4, 121.7, 119.6, 112.9, 102.7, 99.2, 85.8, 66.8, 38.4, 29.8,24.0. HRMS (ESI) calcd for $C_{24}H_{19}O_3N_2[M+H]^+$383.1390, found 383.1385.

(Z)-2-(3-methyl-3-(naphthalen-1-yl)-1-oxo-3,10-dihydrofuro[3',4':5,6]pyrano[4,3-b]indol-5(1H)-ylidene)acetonitrile (3ap):



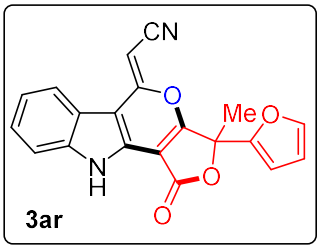
The title compound was prepared from **1a** (55 mg, 0.3 mmol) and **2p** (80.4 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.55, SiO_2, EtOAc:Hexane, 18:82) gave pure product as a pale yellow gum (50.7, 42% yield). ^{1}H NMR (500 MHz, DMSO) δ 8.53 (d, *J* = 8.6 Hz, 1H), 8.04 (d, *J* = 7.4 Hz, 2H), 8.00 (d, *J* = 7.9 Hz, 1H), 7.71 (d, *J* = 6.4 Hz, 2H), 7.63 (d, *J* = 7.8 Hz, 2H), 7.54 (t, *J* = 7.8 Hz, 1H), 7.40 (t, *J* = 7.5 Hz, 1H), 7.34 (t, *J* = 7.5 Hz, 1H), 5.56 (s, 1H), 2.31 (s, 3H).^{13}C NMR (125 MHz, DMSO) δ 175.0, 164.1, 162.8, 138.4, 134.5, 133.0, 130.6, 130.2, 129.6, 129.4, 127.1, 126.2, 125.6, 125.1, 124.9, 124.0, 122.8, 121.2, 119.9, 117.5, 113.3, 101.8, 99.7, 87.1, 65.5, 25.6. HRMS (ESI) calcd for $C_{26}H_{17}O_3N_2$ $[M+H]^+$405.1233, found 405.1225.

(Z)-2-(1-oxo-3',4'-dihydro-1H,2'H-spiro[furo[3',4':5,6]pyrano[4,3-b]indole-3,1'-naphthalen]-5(10H)-ylidene)acetonitrile (3aq):



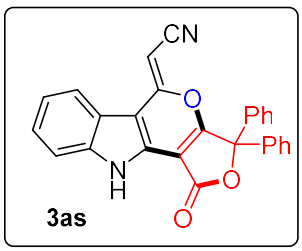
The title compound was prepared from **1a** (55 mg, 0.3 mmol) and **2q** (73.2 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.50, SiO_2, EtOAc:Hexane, 17:83) gave pure product as a colourless solid (54.5 mg, 48% yield). mp 278-283 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.17 (s, 1H), 7.64 (d, *J* = 7.4 Hz, 1H), 7.60 (d, *J* = 7.5 Hz, 1H), 7.44 – 7.39 (m, 2H), 7.36 – 7.31 (m, 1H), 7.26 (s, 1H), 7.19 – 7.15 (m, 1H), 7.01 (d, *J* = 7.3 Hz, 1H), 4.94 (s, 1H), 3.01 (t, *J* = 18.0 Hz, 2H), 2.54 – 2.45 (m, 1H), 2.38 – 2.25 (m, 2H), 2.20 (d, *J* = 13.7 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.9, 163.1, 139.0, 137.8, 130.4, 130.2, 129.2, 127.1, 126.4, 125.5, 123.5, 121.7, 119.6, 113.1, 102.9, 99.3, 85.5, 66.9, 33.6, 28.8, 19.3. HRMS (ESI) calcd for $C_{24}H_{17}O_3N_2$ $[M+H]^+$381.1234, found 381.1225.

(Z)-2-(3-(furan-2-yl)-3-methyl-1-oxo-3,10-dihydrofuro[3',4':5,6]pyrano[4,3-b]indol-5(1H)-ylidene)acetonitrile (3ar):



The title compound was prepared from **1a** (55 mg, 0.3 mmol) and **2r** (62.4 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.60, SiO_2, EtOAc:Hexane, 18:82) gave pure product as a yellow gum (57.6 mg, 56% yield). ^{1}H NMR (400 MHz, DMSO) δ 13.05 (s, 1H), 7.95 (d, *J* = 7.4 Hz, 1H), 7.78 (s, 1H), 7.64 (d, *J* = 7.5 Hz, 1H), 7.42 – 7.37 (m, 1H), 7.36 – 7.31 (m, 1H), 6.92 (s, 1H), 6.59 (s, 1H), 5.46 (s, 1H), 2.08 (s, 3H).^{13}C NMR (100 MHz, DMSO) δ 172.8, 164.1, 162.6, 147.8, 145.1, 138.4, 129.9, 124.9, 122.8, 121.2, 119.9, 117.2, 113.4, 111.5, 111.3, 101.8, 99.5, 80.3, 65.4, 20.7. HRMS (ESI) calcd for $C_{20}H_{11}O_4N_2$ $[M-H]^-$ 343.0713, found 343.0721.

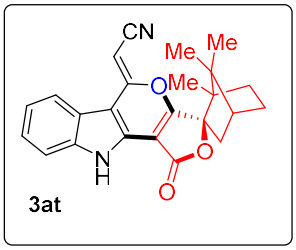
(Z)-2-(1-oxo-3,3-diphenyl-3,10-dihydrofuro[3',4':5,6]pyrano[4,3-b]indol-5(1H)-ylidene)acetonitrile (3as):



The title compound was prepared from **1a** (55 mg, 0.3 mmol) and **2s** (84 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f =

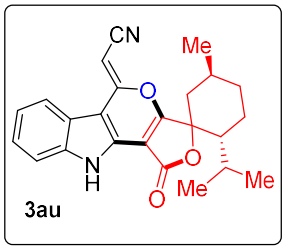
0.60, SiO_2, EtOAc:Hexane, 18:82) gave pure product as a pale yellow gum (54.7 mg, 44% yield). ^{1}H NMR (400 MHz, DMSO) δ 13.05 (s, 1H), 7.93 (d, *J* = 7.9 Hz, 1H), 7.62 (d, *J* = 8.1 Hz, 1H), 7.51 (d, *J* = 2.4 Hz, 2H), 7.49 (s, 4H), 7.48 (s, 3H), 7.45 (d, *J* = 1.9 Hz, 1H), 7.37 (t, *J* = 7.4 Hz, 1H), 7.30 (t, *J* = 7.4 Hz, 1H), 5.49 (s, 1H).^{13}C NMR (100 MHz, DMSO) δ 172.8, 164.0, 162.8, 138.5, 137.0, 129.7, 129.2, 126.6, 124.9, 122.8, 121.2, 119.8, 117.3, 113.3, 101.7, 99.5, 88.1, 65.7. HRMS (ESI) calcd for $C_{27}H_{15}O_3N_2$ $[M-H]^-$ 415.1077, found 415.1086.

(Z)-2-((1R)-1,7,7-trimethyl-1'-oxo-1'H-spiro[bicyclo[2.2.1]heptane 2,3'furo[3',4':5,6]pyrano[4,3-b]indol]-5'(10'H)-ylidene)acetonitrile (3at):



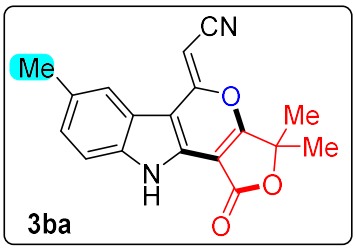
The title compound was prepared from **1a** (55 mg, 0.3 mmol) and **2t** (75 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.50, SiO_2, EtOAc:Hexane, 15:85) gave pure product as a white solid (58.8 mg, 51% yield), mp 176-180 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.58 (s, 1H), 7.65 (d, *J* = 7.5 Hz, 1H), 7.55 (d, *J* = 7.5 Hz, 1H), 7.43 – 7.40 (m, 2H), 4.95 (s, 1H), 2.55 – 2.49 (m, 1H), 2.16 – 2.12 (m, 2H), 2.04 (t, *J* = 4.4 Hz, 1H), 1.72 – 1.66 (m, 2H), 1.26 (d, *J* = 5.6 Hz, 1H), 1.19 (s, 3H), 0.99 (s, 3H), 0.87 (s, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 175.6, 165.9, 163.5, 137.6, 130.5, 125.5, 123.4, 121.7, 119.7, 116.9, 112.8, 102.5, 100.1, 95.0, 66.6, 56.0, 51.0, 45.4, 41.8, 29.0, 26.9, 20.6, 20.3, 10.4. HRMS (ESI) calcd for $C_{24}H_{23}O_3N_2$ $[M+H]^+$ 387.1703 found 387.1697.

(Z)-2-(2-isopropyl-5-methyl-1'-oxo-1'H-spiro[cyclohexane-1,3'furo[3',4':5,6]pyrano[4,3-b]indol]-5'(10'H)-ylidene)acetonitrile (3au):



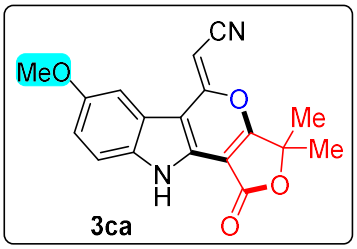
The title compound was prepared from **1a** (55 mg, 0.3 mmol) and **2u**(75.6 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.50, SiO_2, EtOAc:Hexane, 16:84) gave pure product as a pale yellow solid (63.8 mg, 55% yield), mp 229-234 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.08 (s, 1H), 7.65 (d, *J* = 6.7 Hz, 1H), 7.60 (d, *J* = 6.7 Hz, 1H), 7.44 – 7.38 (m, 2H), 4.97 (s, 1H), 1.95 (d, *J* = 0.5 Hz, 3H), 1.82 – 1.73 (m, 3H), 1.35 – 1.23 (m, 2H), 1.17 (d, *J* = 12.2 Hz, 1H), 0.98 (d, *J* = 5.6 Hz, 3H), 0.90 (d, *J* = 6.4 Hz, 3H), 0.83 (d, *J* = 6.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.9, 166.2, 163.1, 137.8, 130.3, 125.4, 123.4, 121.8, 119.6, 113.0, 102.6, 99.1, 90.1, 66.6, 46.6, 44.1, 33.9, 28.8, 28.2, 23.2, 22.2, 21.8, 18.6. HRMS (ESI) calcd for $C_{24}H_{25}O_3N_2$ $[M+H]^+$389.1859, found 389.1855.

(Z)-2-(3,3,7-trimethyl-1-oxo-3,10-dihydrofuro[3',4':5,6]pyrano[4,3-b]indol-5(1H)-ylidene)acetonitrile (3ba):



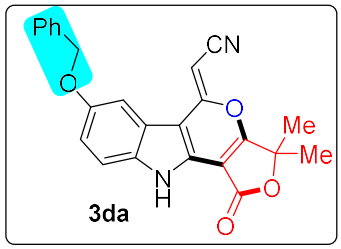
The title compound was prepared from **1b** (59 mg, 0.3 mmol) and **2a** (46.8 mg, 0.3 mmol) according to general procedure**A**. Purification using column chromatography (R_f = 0.55, SiO_2, EtOAc:Hexane, 16:84) gave pure product as a pale brown solid (63 mg, 69% yield), mp 258-263 °C. ^{1}H NMR (500 MHz, DMSO) δ 12.79 (s, 1H), 7.75 (s, 1H), 7.48 (s, 1H), 7.19 (s, 1H), 5.41 (s, 1H), 2.45 (s, 3H), 1.67 (s, 6H).^{13}C NMR (125 MHz, DMSO) δ 176.8, 164.4, 162.8, 136.5, 131.9, 130.4, 126.1, 121.5, 119.5, 117.5, 112.9, 101.0, 98.0, 82.7, 64.5, 24.0, 21.3. HRMS (ESI) calcd for $C_{18}H_{13}N_2O_3$ [M-H]$^-$ 305.0920, found 305.0931.

(Z)-2-(7-methoxy-3,3-dimethyl-1-oxo-3,10-dihydrofuro[3',4':5,6]pyrano[4,3-b]indol-5(1H)-ylidene)acetonitrile (3ca):



The title compound was prepared from **1c** (64 mg, 0.3 mmol) and **2a** (46.8 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.60, SiO_2, EtOAc:Hexane, 20:80) gave pure product as a pale brown solid (62.6 mg, 65% yield), mp 267-272 °C. ^{1}H NMR (400 MHz, DMSO) δ 12.77 (s, 1H), 7.49 (d, *J* = 8.6 Hz, 1H), 7.31 (s, 1H), 6.99 (d, *J* = 8.0 Hz, 1H), 5.47 (s, 1H), 3.85 (s, 3H), 1.67 (s, 6H). ^{13}C NMR (100 MHz, DMSO) δ 176.6, 164.4, 162.7, 156.0, 132.9, 130.5, 127.5, 122.0, 117.6, 114.3, 114.0, 101.9, 101.2, 97.9, 82.7, 64.9, 55.9, 24.0. HRMS (ESI) calcd for$C_{18}H_{13}O_4N_2$[M-H]$^-$ 321.0869, found 321.0879.

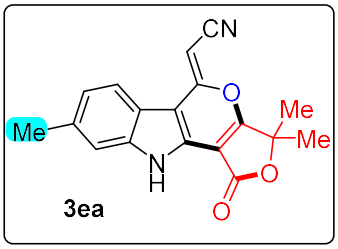
(Z)-2-(7-(benzyloxy)-3,3-dimethyl-1-oxo-3,10-dihydrofuro[3',4':5,6]pyrano[4,3-b]indol-5(1H)-ylidene)acetonitrile (3da):



The title compound was prepared from **1d** (87 mg, 0.3 mmol) and **2a** (46.8 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.6, SiO_2, EtOAc:Hexane, 22:78)) gave pure product as a white solid (69.2 mg, 58% yield),

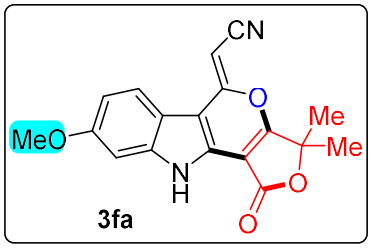
mp 249-253 °C. ^{1}H NMR (500 MHz, DMSO) δ 12.78 (s, 1H), 7.50 (d, *J*= 6.3 Hz, 3H), 7.46 (s, 1H), 7.40 (t, *J* = 7.4 Hz, 2H), 7.33 (t, *J* = 7.1 Hz, 1H), 7.06 (d, *J* = 7.3 Hz, 1H), 5.48 (s, 1H), 5.19 (s, 2H), 1.67 (s, 6H).^{13}C NMR (125 MHz, DMSO) δ 176.7, 164.4, 162.7, 155.0, 137.4, 133.1, 130.6, 128.5, 128.0, 122.0, 117.6, 114.9, 114.0, 103.3, 101.2, 97.9, 82.7, 70.1, 64.8, 24.0. HRMS (ESI) calcd for $C_{24}H_{17}O_4N_2$ [M-H]$^-$397.1182, found 397.1191.

(Z)-2-(3,3,8-trimethyl-1-oxo-3,10-dihydrofuro[3',4':5,6]pyrano[4,3-b]indol-5(1H)-ylidene)acetonitrile (3ea):



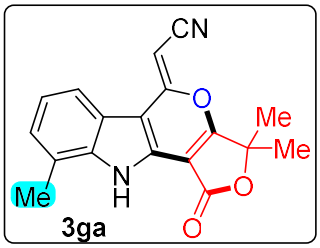
The title compound was prepared from **1e** (59 mg, 0.3 mmol) and **2a** (46.8 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.50, SiO_2, EtOAc:Hexane, 18:82) gave pure product as a pale yellow solid (60 mg, 66% yield), mp 290-294 °C. ^{1}H NMR (400 MHz, DMSO) δ 12.78 (s, 1H), 7.81 (d, *J* = 7.3 Hz, 1H), 7.39 (s, 1H), 7.14 (d, *J* = 8.5 Hz, 1H), 5.37 (s, 1H), 2.44 (s, 3H), 1.67 (s, 6H).^{13}C NMR (100 MHz, DMSO) δ 176.6, 164.4, 162.8, 138.7, 134.3, 130.2, 124.3, 119.4, 119.1, 117.5, 113.0, 101.4, 98.0, 82.7, 64.4, 24.0, 21.4. HRMS (ESI) calcd for $C_{18}H_{13}O_3N_2$ [M-H]$^-$ 305.0920, found 305.0927.

(Z)-2-(8-methoxy-3,3-dimethyl-1-oxo-3,10-dihydrofuro[3',4':5,6]pyrano[4,3-b]indol-5(1H)-ylidene)acetonitrile (3fa):



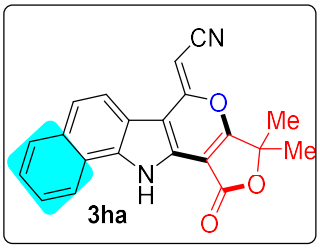
The title compound was prepared from **1f** (64 mg, 0.3 mmol) and **2a** (46.8 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.50, SiO_2, EtOAc:Hexane, 21:79) gave pure product as off-white solid (53 mg, 55% yield), mp 282-288°C. ^{1}H NMR (500 MHz, DMSO) δ 12.72 (s, 1H), 7.80 (s, 1H), 7.07 (s, 1H), 6.92 (s, 1H), 5.33 (s, 1H), 3.81 (s, 3H), 1.67 (s, 6H).^{13}C NMR (125 MHz, DMSO) δ 176.0, 164.4, 162.7, 157.5, 139.6, 129.8, 120.5, 117.6, 115.2, 112.1, 101.6, 98.7, 96.4, 82.7, 64.1, 55.5, 24.1. HRMS (ESI) calcd for $C_{18}H_{15}O_4N_2$ [M+H]$^+$323.1026, found 323.1015.

(Z)-2-(3,3,9-trimethyl-1-oxo-3,10-dihydrofuro[3',4':5,6]pyrano[4,3-b]indol-5(1H)-ylidene)acetonitrile (3ga):



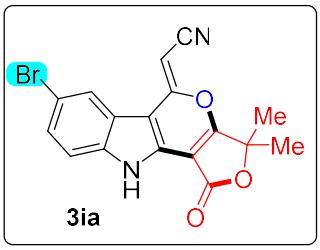
The title compound was prepared from **1g** (59 mg, 0.3 mmol) and **2a** (46.8 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.55, SiO_2, EtOAc:Hexane, 19:81) gave pure product as a white solid (47.4 mg, 52% yield), mp 288-293 °C. ^{1}H NMR (400 MHz, DMSO) δ 12.67 (s, 1H), 7.66 (d, *J* = 6.2 Hz, 1H), 7.17 – 7.06 (m, 2H), 5.34 (s, 1H), 2.42 (s, 3H), 1.59 (s, 6H). ^{13}C NMR (100 MHz, DMSO) δ 177.0, 164.3, 162.7, 137.6, 130.8, 125.7, 123.2, 122.9, 121.4, 117.5, 117.2, 101.9, 97.9, 82.3, 64.8, 24.1, 17.5. HRMS (ESI) calcd for $C_{18}H_{15}O_3N_2$ $[M+H]^+$307.1077, found 307.1068.

(Z)-2-(3,3-dimethyl-1-oxo-3,12-dihydrobenzo[g]furo[3',4':5,6]pyrano[4,3-b]indol-5(1H)-ylidene)acetonitrile (3ha):



The title compound was prepared from **1h** (70 mg, 0.3 mmol) and **2a** (46.8 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.50, SiO_2, EtOAc:Hexane, 17:83) gave pure product as a sticky pale brown gel (41 mg, 40% yield). ^{1}H NMR (400 MHz, DMSO) δ 13.62 (s, 1H), 8.89 (d, *J* = 7.9 Hz, 1H), 8.05 (t, *J* = 8.3 Hz, 2H), 7.79 (d, *J* = 8.6 Hz, 1H), 7.64 (s, 1H), 7.57 (d, *J* = 7.5 Hz, 1H), 5.63 (s, 1H), 1.70 (s, 6H). ^{13}C NMR (100 MHz, DMSO) δ 176.1, 164.3, 162.8, 133.7, 130.8, 128.8, 128.6, 126.6, 125.6, 123.6, 122.2, 121.8, 118.5, 117.9, 103.2, 98.8, 82.4, 65.6, 24.1. HRMS (ESI) calcd forC_{21} H_{15} O_3 N_2 $[M+H]^+$343.1077, found 343.1073.

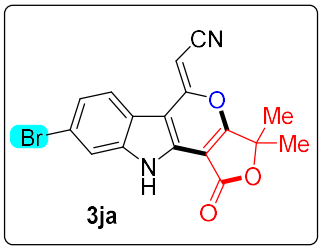
(Z)-2-(7-bromo-3,3-dimethyl-1-oxo-3,10-dihydrofuro[3',4':5,6]pyrano[4,3-b]indol-5(1H)-ylidene)acetonitrile (3ia):



The title compound was prepared from **1i** (78 mg, 0.3 mmol) and **2a** (46.8 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.6, SiO_2, EtOAc:Hexane, 19:81)gave pure product as a white solid (55 mg, 50% yield), mp 304-307 °C. ^{1}H NMR (400 MHz, DMSO) δ 13.07 (s, 1H), 8.17 (s, 1H), 7.51 (d, *J* = 9.3 Hz, 2H), 5.58 (s, 1H), 1.67 (s, 6H).^{13}C NMR (100 MHz, DMSO) δ 177.5, 164.2, 162.1, 137.0,

131.6, 127.3, 123.0, 121.9, 117.2, 115.5, 115.0, 100.8, 97.8, 82.8, 66.0, 24.0. HRMS (ESI) calcd for $C_{17}H_{12}O_3N_2Br$ $[M+H]^+$371.0025, found 371.0020.

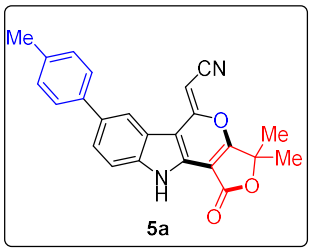
(Z)-2-(8-bromo-3,3-dimethyl-1-oxo-3,10-dihydrofuro[3',4':5,6]pyrano[4,3-b]indol-5(1H)-ylidene)acetonitrile (3ja):



The title compound mixture was prepared from **1j** (78 mg, 0.3mmol) and **2a** (46.8 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.55, SiO_2, EtOAc:Hexane, 19:81) gave pure product as a pale yellow solid (49.6 mg, 45% yield), mp 297-300 °C. ^{1}H NMR (400 MHz, DMSO) δ 13.03 (s, 1H), 7.91 (d, *J* = 8.6 Hz, 1H), 7.73 (d, *J* = 1.5 Hz, 1H), 7.43 (dd, *J* = 8.5, 1.6 Hz, 1H), 5.47 (s, 1H), 1.68 (s, 6H).^{13}C NMR (100 MHz, DMSO) δ 177.4, 164.2, 162.3, 139.1, 131.4, 127.5, 125.4, 121.4, 120.4, 117.1, 117.0, 115.7, 114.0, 101.4, 97.9, 82.9, 65.7, 23.9. HRMS (ESI) calcd for $C_{17}H_{10}O_3N_2Br$ $[M-H]^-$368.9869, found 368.9876.

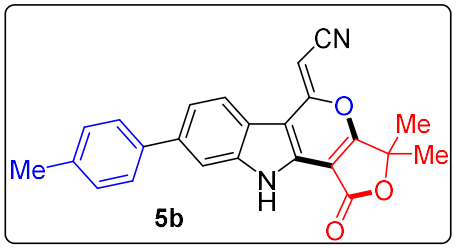
Synthetic utility:

(Z)-2-(3,3-dimethyl-1-oxo-7-(p-tolyl)-3,10-dihydrofuro[3',4':5,6]pyrano[4,3-b]indol-5(1H)-ylidene)acetonitrile



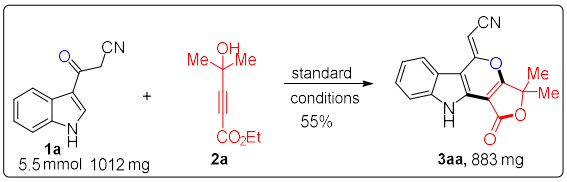
The bromo pyrano indole **3ia** (55 mg, 0.15 mmol) in H_2O (3 ml) was added p-tolylboronic acid (30 mg, 1.5 equiv), $Pd(OAc)_2$ (1.7 mg, 5 mol%) DIPA (0.05 ml, 1.5 equiv) and the reaction mixture was stirred at reflux (oil bath). After completion (monitored by TLC) of the conversion, reaction mixture was quenched with H_2O and extracted with ethyl acetate. The combined organic layers were dried over anhydrous sodium sulphate, filtered and concentrated under reduced pressure and the product was purified through a short silica gel column using EtOAc:Hexane (15:85) as the eluent to get pure product as a yellow solid (44 mg, 78% yield), mp 290-293 °C. ^{1}H NMR (400 MHz, DMSO) δ 12.94 (s, 1H), 8.08 (s, 1H), 7.70 (s, 2H), 7.65 (s, 2H), 7.28 (s, 2H), 5.65 (s, 1H), 2.35 (s, 3H), 1.68 (s, 6H).^{13}C NMR (100 MHz, DMSO) δ 177.1, 164.4, 162.5, 137.6, 136.4, 135.1, 131.0, 129.5, 127.1, 123.7, 122.0, 117.5, 117.0, 113.6, 101.5, 97.9, 82.8, 65.5, 24.0, 20.8. HRMS (ESI) calcd for $C_{24}H_{19}O_3N_2$ $[M+H]^+$ 383.1396, found 383.1388.

(Z)-2-(3,3-dimethyl-1-oxo-8-(p-tolyl)-3,10-dihydrofuro[3',4':5,6]pyrano[4,3-b]indol-5(1H)-ylidene)acetonitrile



The bromo pyrano indole **3ja** (55 mg, 0.15 mmol) in H_2O (3 ml) was added p-tolylboronic acid (30 mg, 1.5 equiv), $Pd(OAc)_2$ (1.7 mg, 5 mol%) DIPA (0.05 ml, 1.5 equiv) and the reaction mixture was stirred at reflux (oil bath). After completion (monitored by TLC) of the conversion, reaction mixture was quenched with H_2O and extracted with ethyl acetate. The combined organic layers were dried over anhydrous sodium sulphate, filtered and concentrated under reduced pressure and the product was purified through a short silica gel column using EtOAc:Hexane (16:84) as the eluent to get the pure product as a yellow solid (39.7 mg, 70% yield), mp 300-305 °C. ^{1}H NMR (400 MHz, DMSO) δ 12.96 (s, 1H), 7.98 (s, 1H), 7.77 (s, 1H), 7.58 (s, 3H), 7.30 (s, 2H), 5.46 (s, 1H), 2.35 (s, 3H), 1.69 (s, 6H). ^{13}C NMR (101 MHz, DMSO) δ 177.01, 164.37, 162.63, 139.06, 137.45, 136.83, 131.14, 129.77, 126.82, 121.69, 120.41, 120.12, 117.45, 110.60, 101.38, 98.00, 82.80, 64.93, 24.03, 20.78. HRMS (ESI) calcd for $C_{24}H_{19}O_3N_2$ $[M+H]^+$383.1396, found 383.1388.

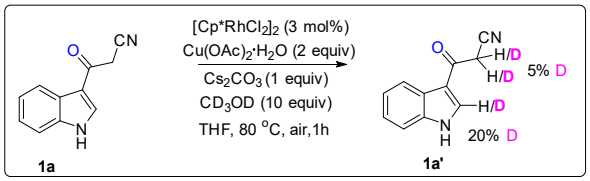
Scale-up Experiments:

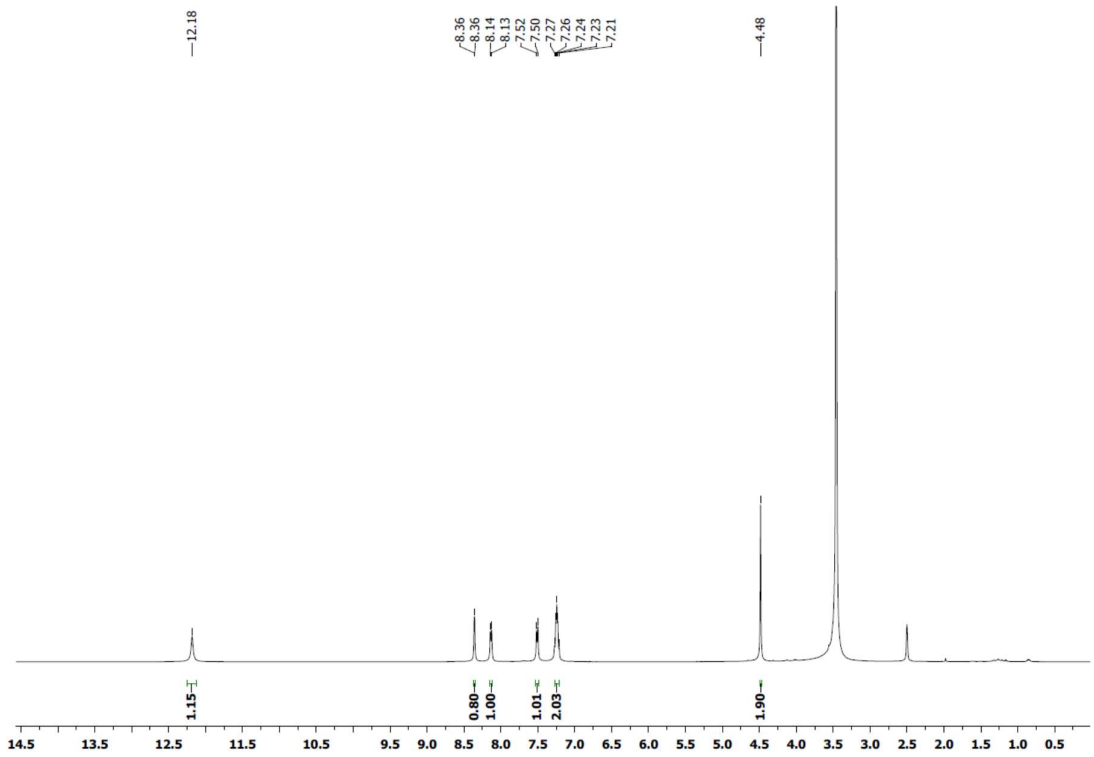


To a mixture of 3-(1H-indol-3-yl)-3-oxopropanenitrile **1a** (1012 mg, 5.5 mmol) and 4-hydroxyalkynoate derivative **2a** (858 mg, 5.5 mmol) in THF, $[RhCp^*Cl_2]_2$ (102 mg, 3 mol %), $Cu(OAc)_2.H_2O$ (2189 mg, 2 equiv), Cs_2CO_3 (1788 mg, 1 equiv) were introduced and the reaction mixture was stirred at 80 °C (oil bath) for 8 hours under air balloon. After completion of reaction (monitored by TLC), THF was evaporated, water was added and the contents were extracted with ethyl acetate (2×10 mL). The organic layer was evaporated and the residue was purified by column chromatography (R_f = 0.50) (SiO_2, EtOAc:Hexane, 14:86) to get **3aa** in 55% (883 mg) yield.

Deuterium labelling studies:

An oven-dried reaction vessel was charged with $[Cp^*RhCl2]_2$ (5.6 mg, 3 mol%), $Cu(OAc)_2 \cdot H_2O$ (119 mg, 2 equiv), Cs_2CO_3 (97.5 mg, 1 equiv) 3-(1H-indol-3-yl)-3-oxopropanenitrile **1a** (55 mg, 0.3mmol), THF (0.5 ml), and CD_3OD (10equiv) under Ar. The vessel was sealed and heated at 80 °C (oil bath) for 1 h. After removal of solvents, the residue was purified by flash column chromatography on silica gel (eluent: EtOAc/ petroleum ether = 32:68). **1a'** was recovered in 88% yield.

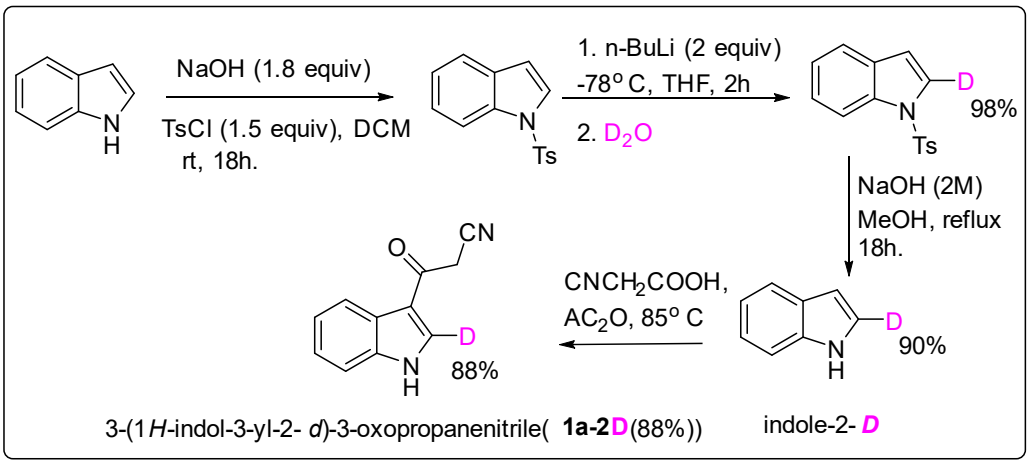




KIE studies:

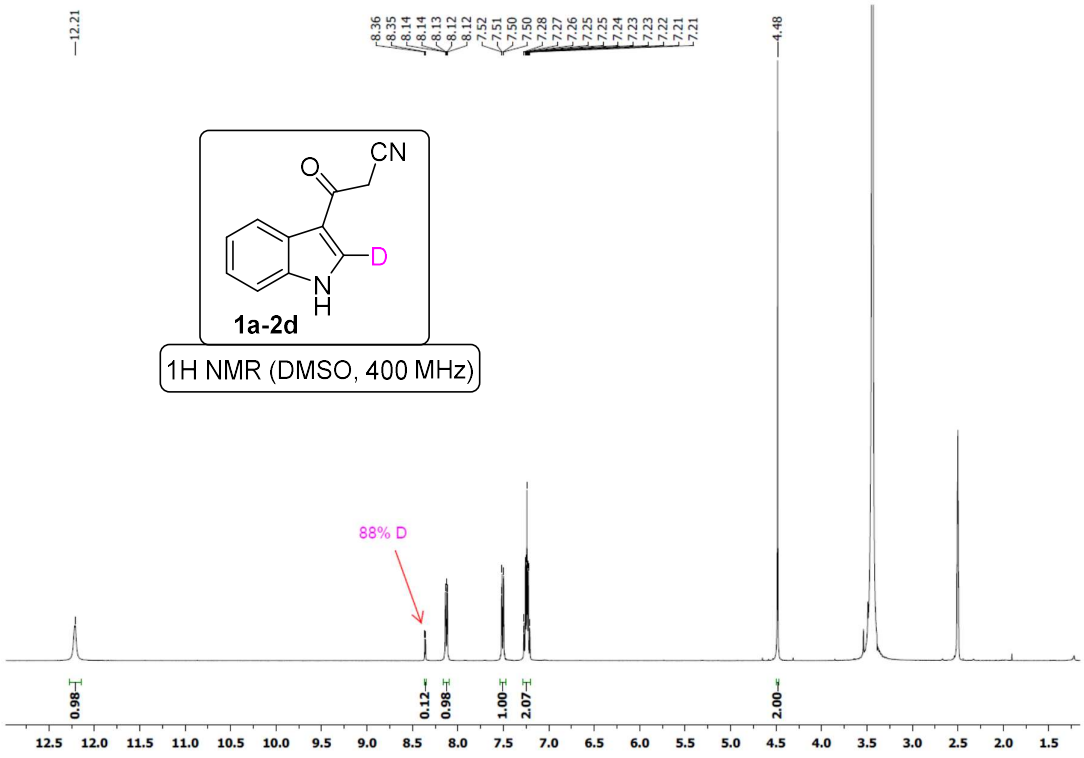
Preparation of indole-2-d and 3-(1H-indol-3-yl-2-d)-3-oxopropanenitrile(1a-2D)

indole-2-D is prepared according the literature procedure.[7a]

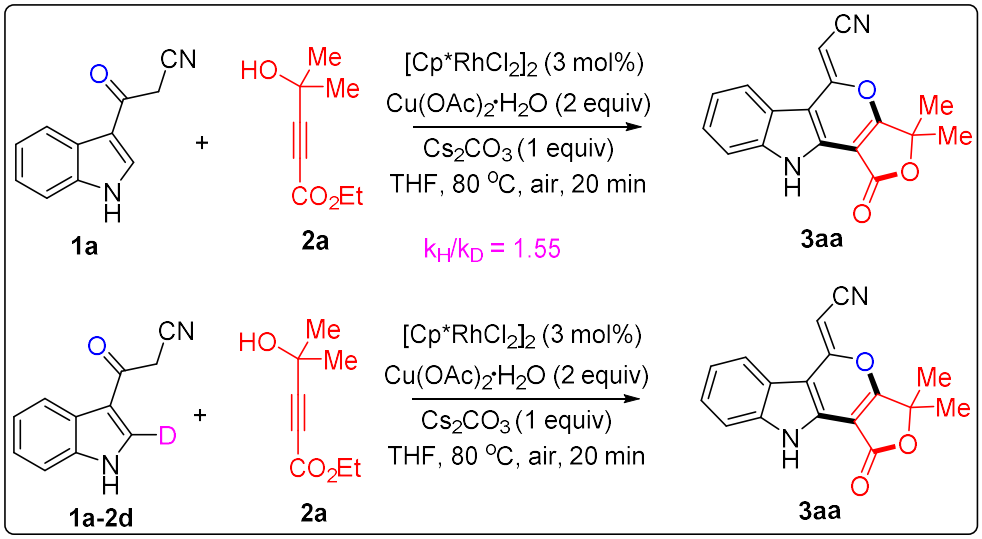


3-(1H-indol-3-yl-2-d)-3-oxopropanenitrile(1a-2d):

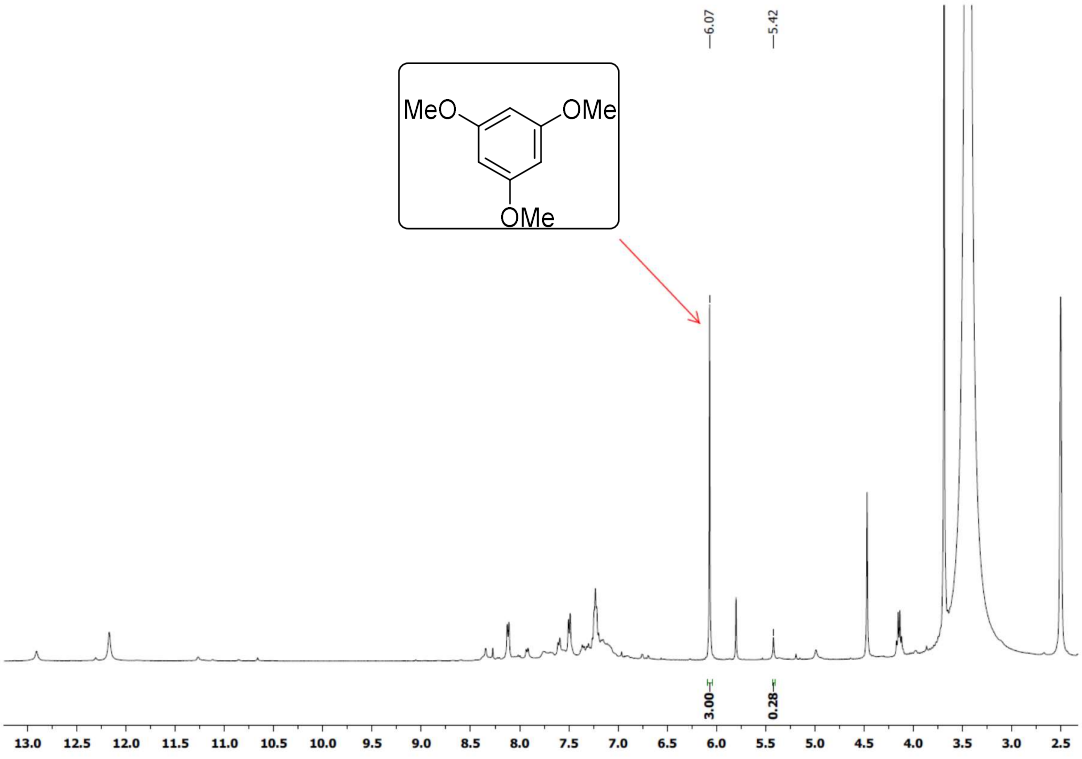
^{1}H NMR (400 MHz, DMSO) δ 12.21 (s, 1H), 8.36 (d, *J* = 3.2 Hz, 0.12H), 8.15 – 8.11 (m, 1H), 7.51 (dd, *J* = 6.4, 1.9 Hz, 1H), 7.28 – 7.20 (m, 2H), 4.48 (s, 2H).

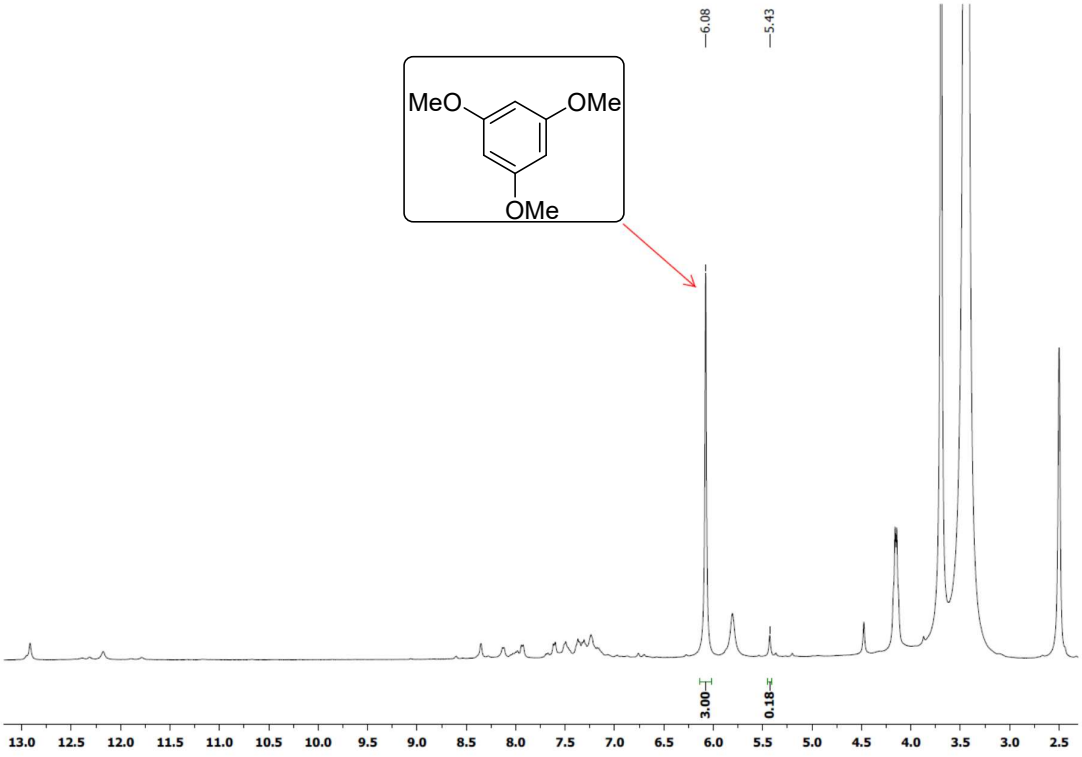


Parallel experiments Study:[7b]

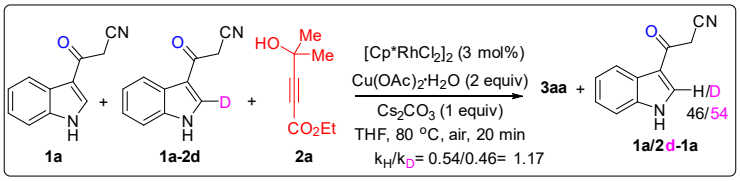


To a mixture of 3-(1H-indol-3-yl)-3-oxopropanenitrile **1a** (27.6 mg, 0.15 mmol) or **2d-1a** (27.5 mg, 0.15 mmol) and 4-hydroxyalkynoate derivative **2a** (23.5 mg, 0.15 mmol) in THF, $[RhCp^*Cl_2]_2$ (2.8 mg, 3 mol %), $Cu(OAc)_2.H_2O$ (60 mg, 2 equiv), Cs_2CO_3 (48.7 mg, 1 equiv) were introduced and the reaction mixtures was stirred at 80 °C (Pre-heated oil bath) for 20 minutes under air balloon. From the resulting solution of reaction mixture THF was evaporated. The ^1H NMR yields of **3aa** for each reaction were given using 1,3,5trimethoxybenze as an internal standard. A KIE value of 1.55 was determined on the basis of the ^1H NMR analysis.

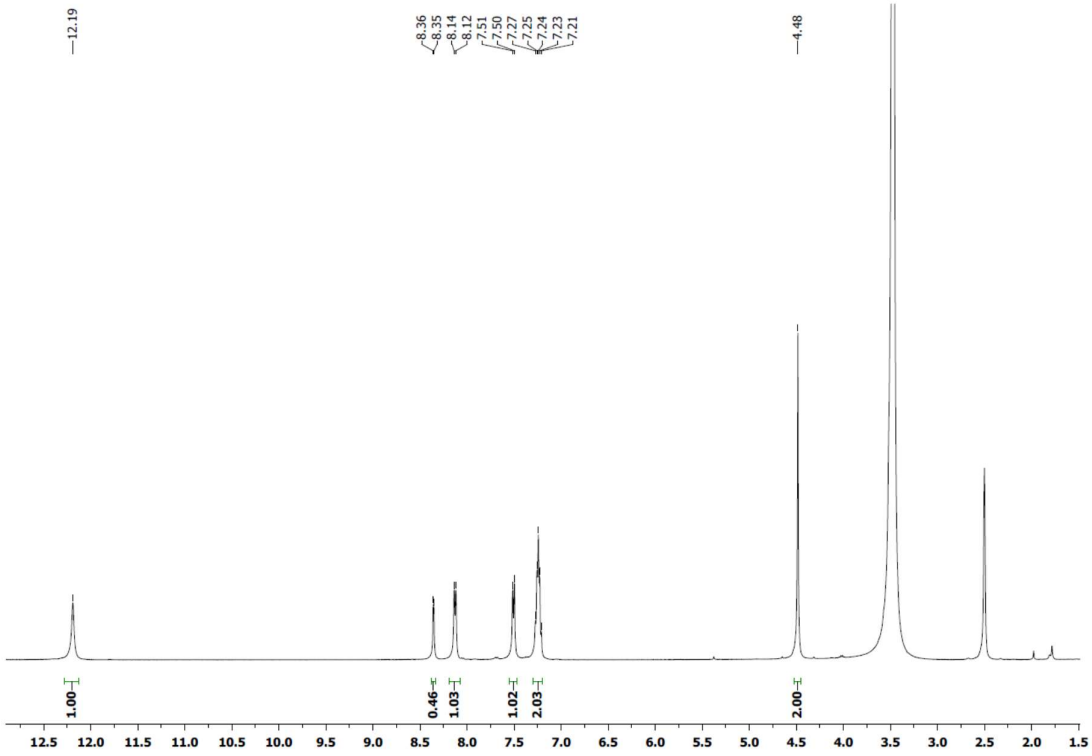




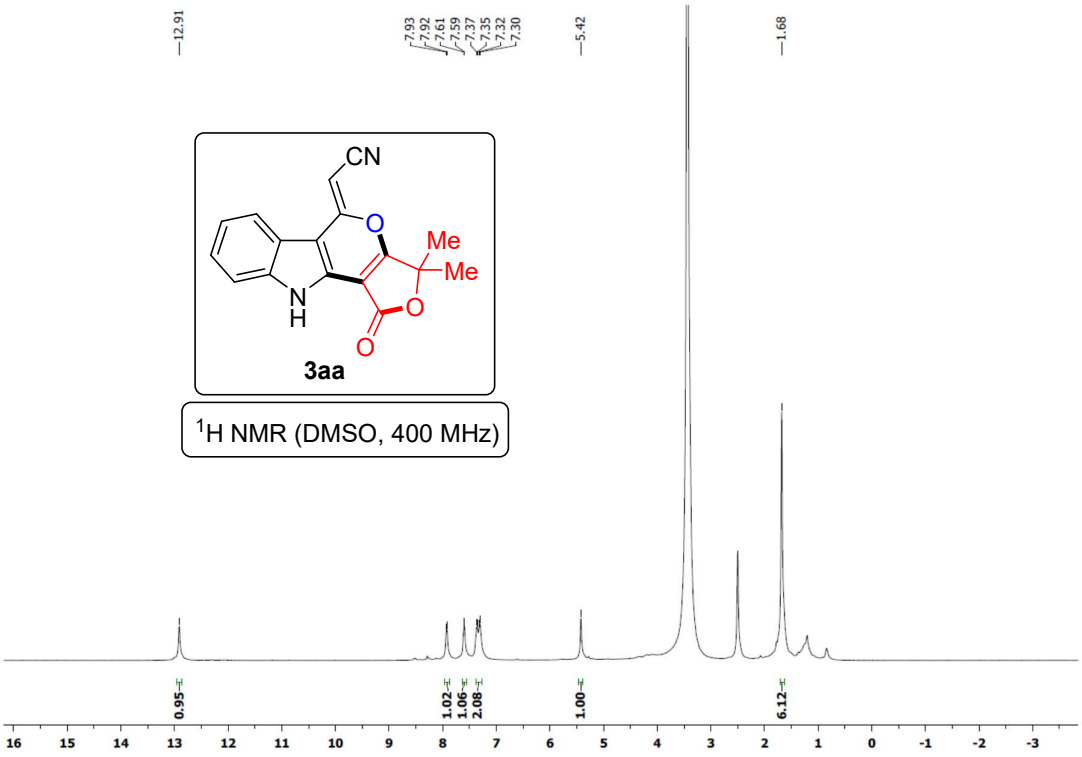
Combined experiments Study:[7c]



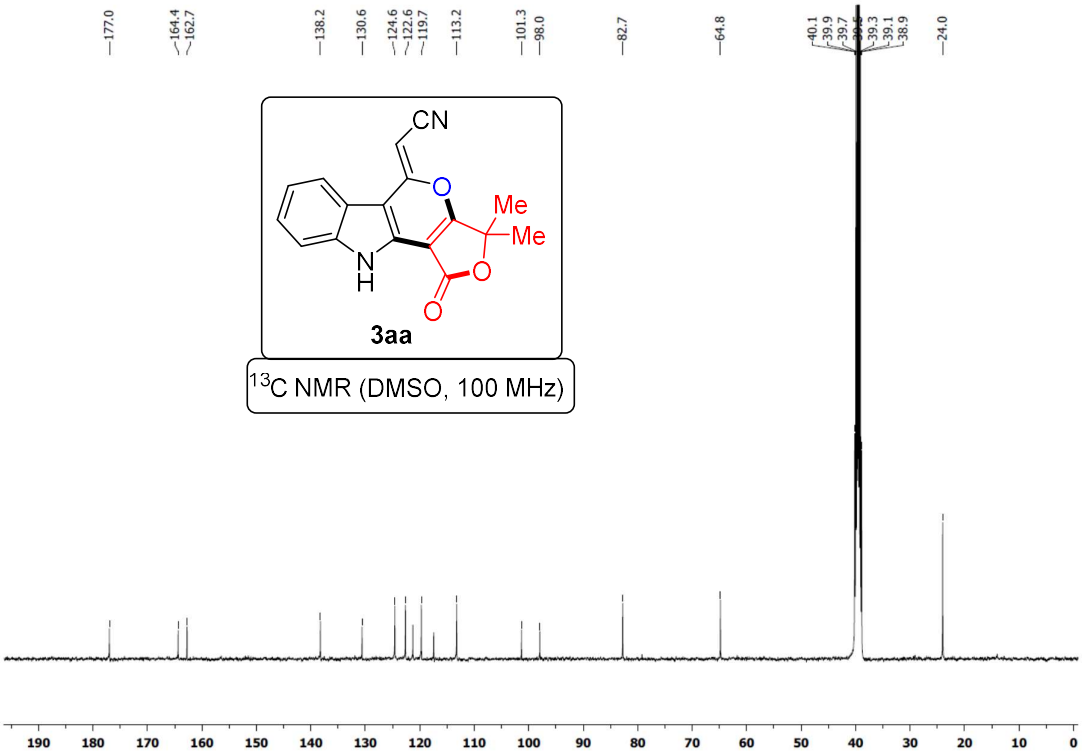
To an equimolar mixture of 3-(1H-indol-3-yl)-3-oxopropanenitrile **1a** (27.6 mg, 0.15 mmol) or **2d-1a** (27.5 mg, 0.15 mmol) and 4-hydroxyalkynoate derivative **2a** (23.5 mg, 0.15 mmol) in THF, $[RhCp^*Cl_2]_2$ (2.8 mg, 3 mol %), $Cu(OAc)_2.H_2O$ (60 mg, 2 equiv), Cs_2CO_3 (48.7 mg, 1 equiv) were introduced and the reaction mixtures was stirred at 80 °C (Pre-heated oil bath) for 20 minutes under air balloon. From the resulting solution of reaction mixture THF was evaporated. Then the crude reaction mixture was directly subjected to column chromatography, and best of the recovered **1a**/**1a-2d** calculated the KIE. The observed KIE = 0.54/0.46= (1.17), suggested initial rate of the reaction does not depend on the CH cleavage step.



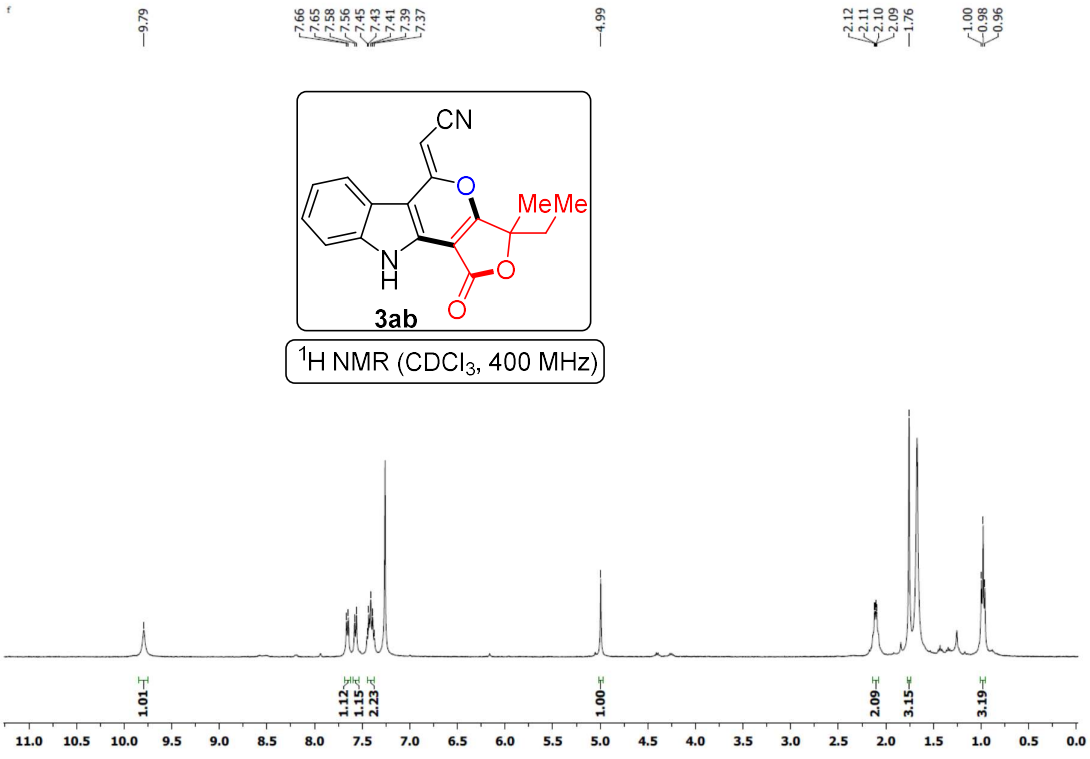
Copies of ^1H and ^{13}C NMR spectras:



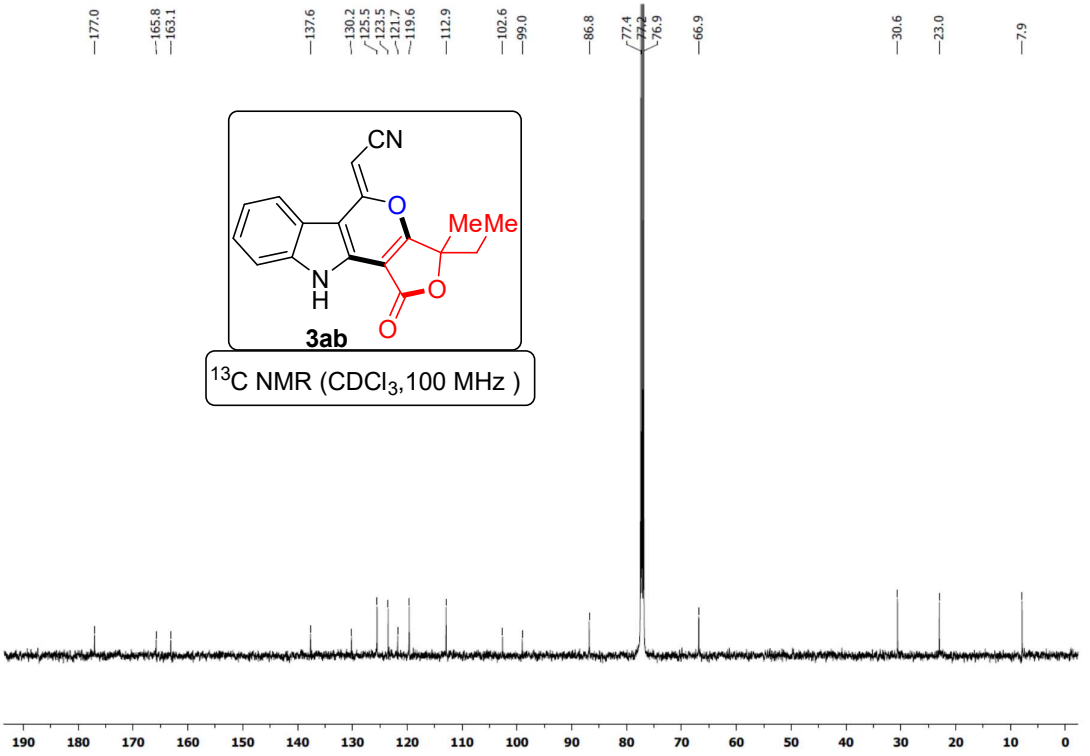
^{1}H NMR (DMSO, 400 MHz)



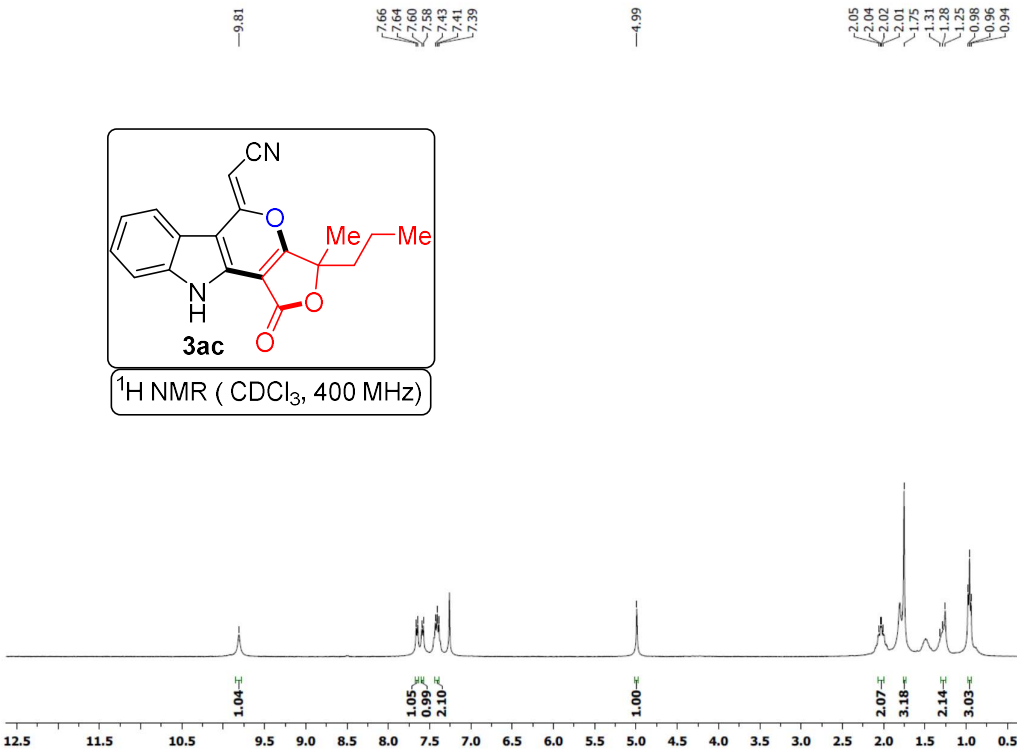
^{13}C NMR (DMSO, 100 MHz)

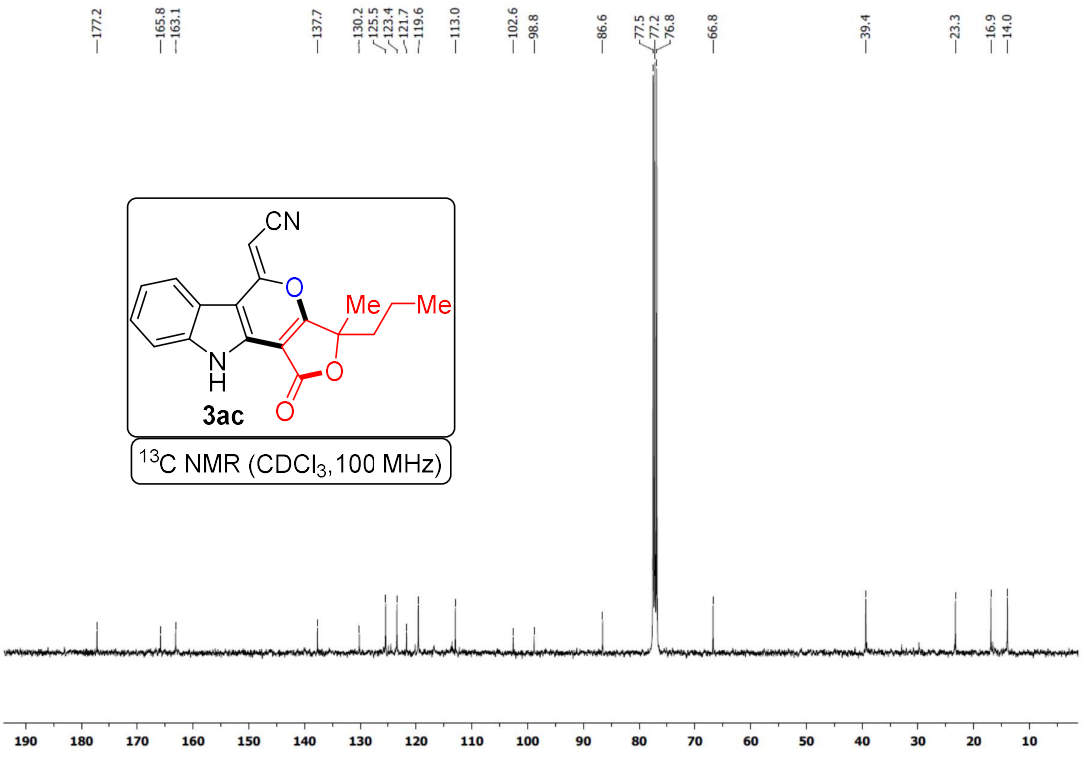


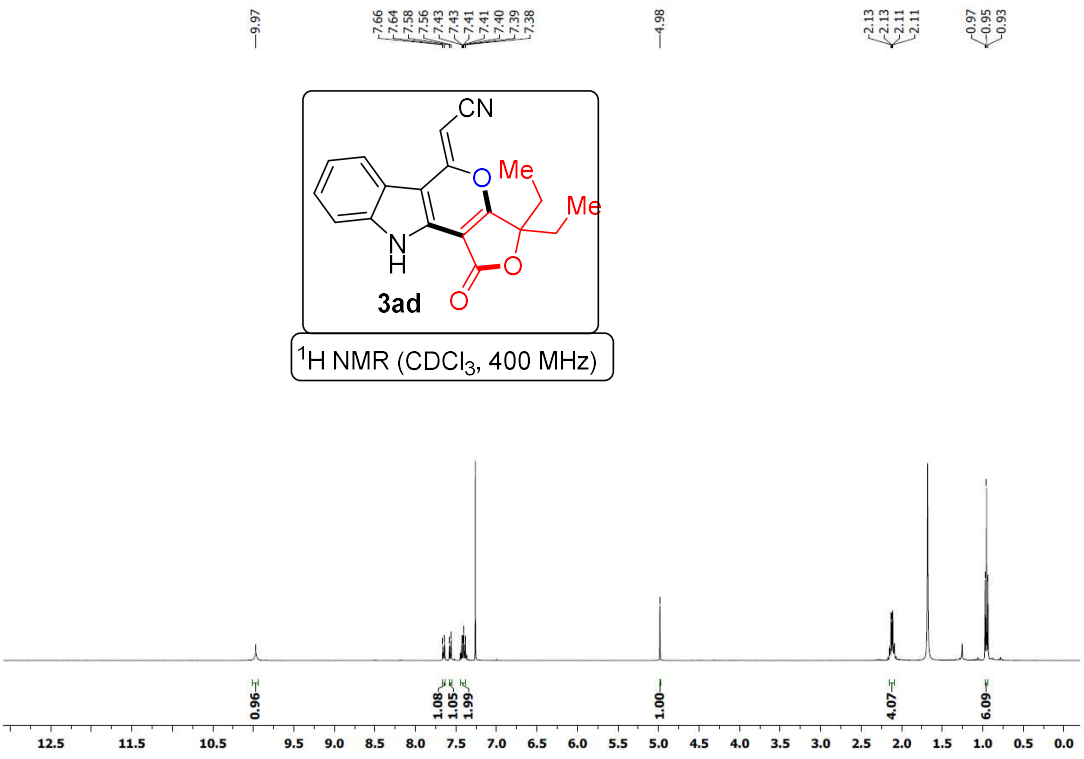
^{1}H NMR ($CDCl_3$, 400 MHz)

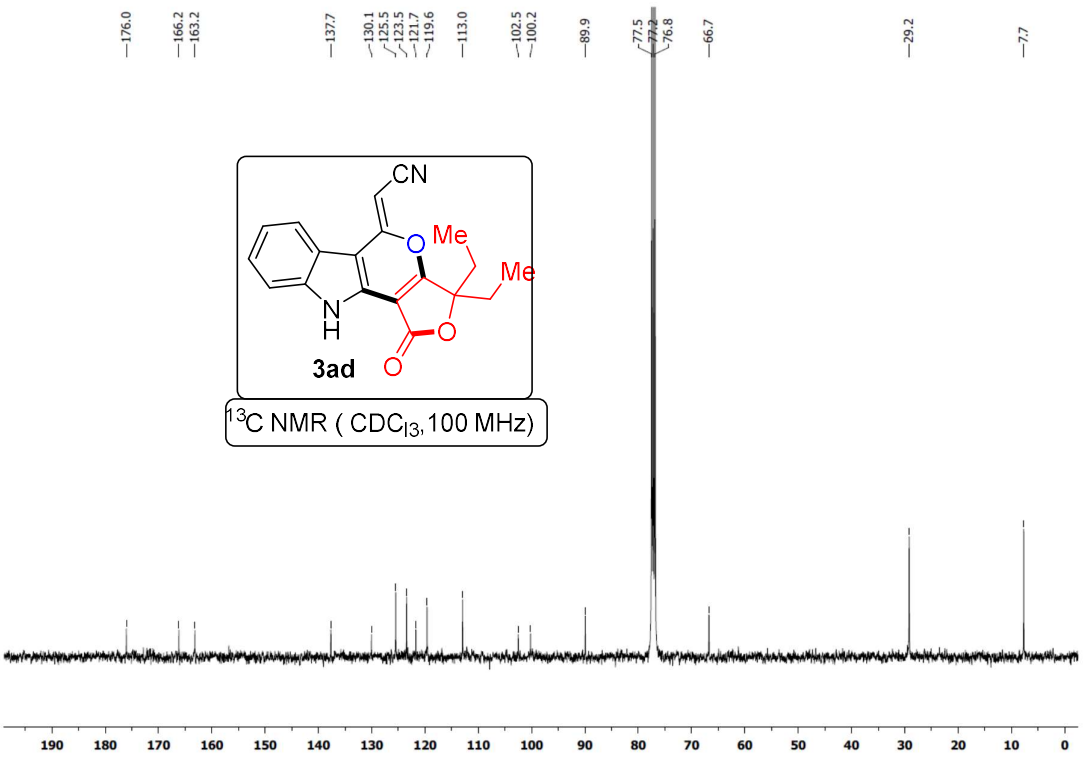


^{13}C NMR ($CDCl_3$,100 MHz)

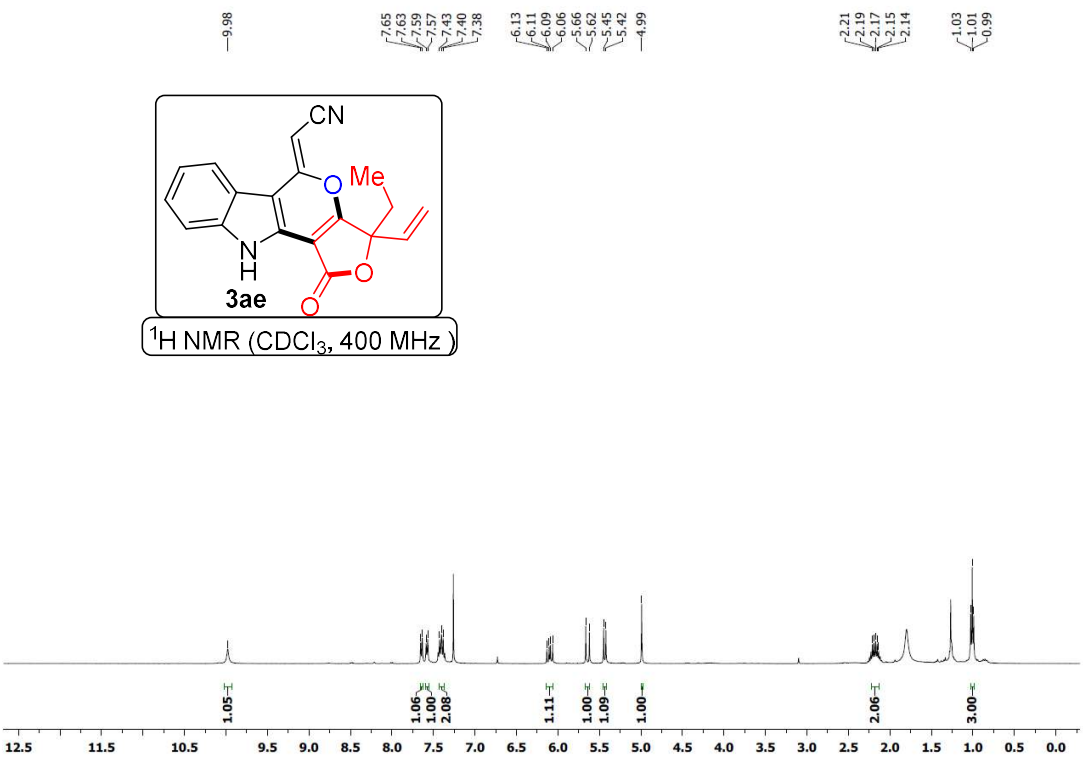

9.81
7.66
7.64
7.60
7.58
7.43
7.41
7.39
4.99
2.05
2.04
2.02
2.01
1.75
1.31
1.28
1.25
0.98
0.96
0.94
CN
O
Me
Me
N
H
O
O
3ac
1H NMR (CDCl3, 400 MHz)
1.04
1.05
0.99
2.10
1.00
2.07
3.18
2.14
3.03
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0


177.2
165.8
163.1
137.7
130.2
125.5
123.4
121.7
119.6
113.0
102.6
98.8
86.6
77.5
77.2
76.8
66.8
39.4
23.3
16.9
14.0
CN
O
Me
Me
N
H
O
O
3ac
13C NMR (CDCl3, 100 MHz)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10

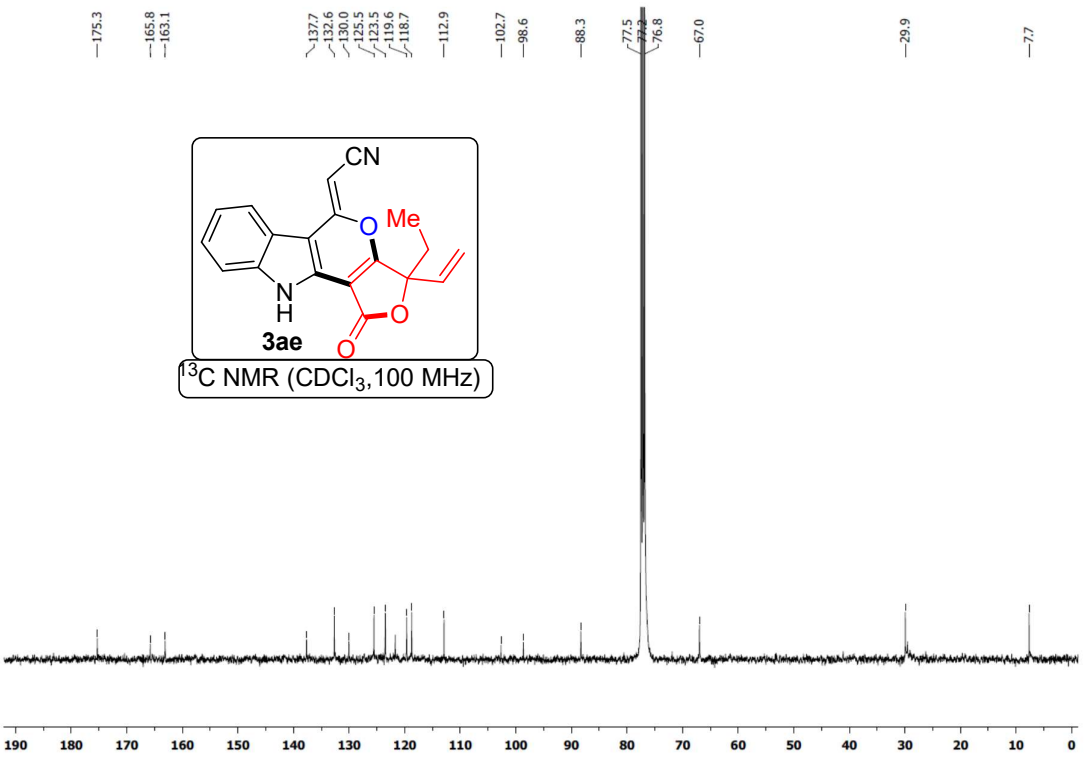

9.97
7.66
7.64
7.58
7.56
7.43
7.43
7.41
7.41
7.40
7.39
7.38
4.98
2.13
2.13
2.11
2.11
0.97
0.95
0.93
CN
O
Me
Me
N
H
O
O
3ad
1H NMR (CDCl3, 400 MHz)
0.96
1.08
1.05
1.99
1.00
4.07
6.09
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0



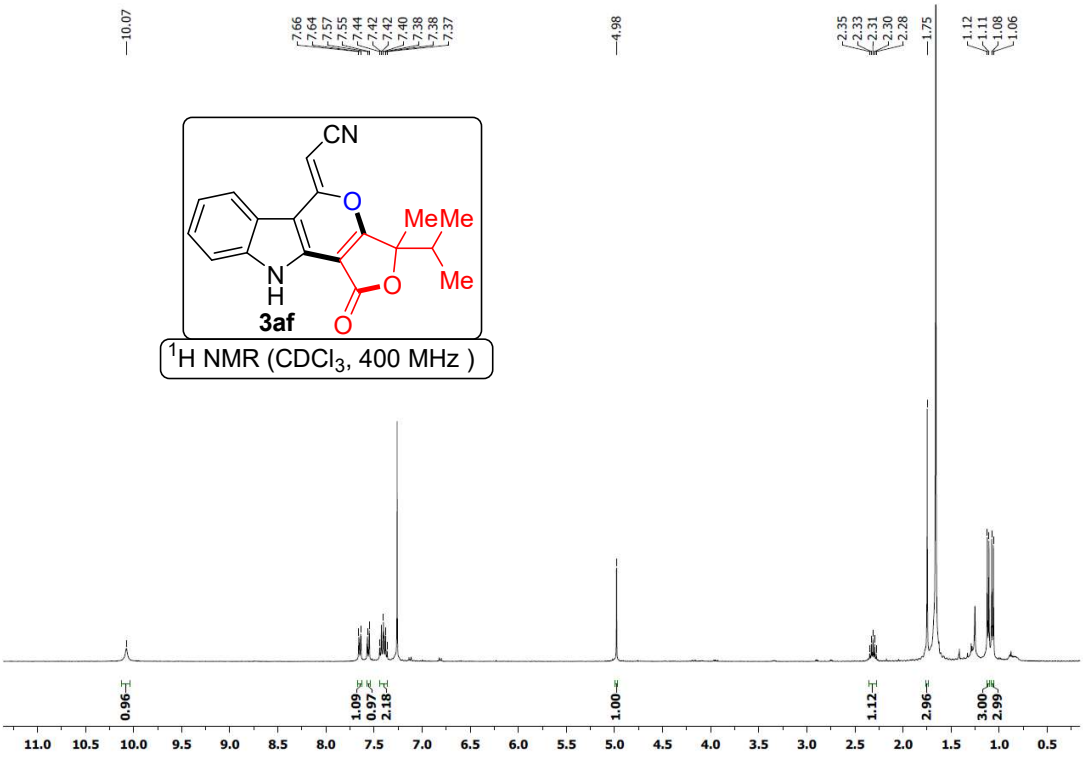
^{13}C NMR (CDC_{l3}, 100 MHz)



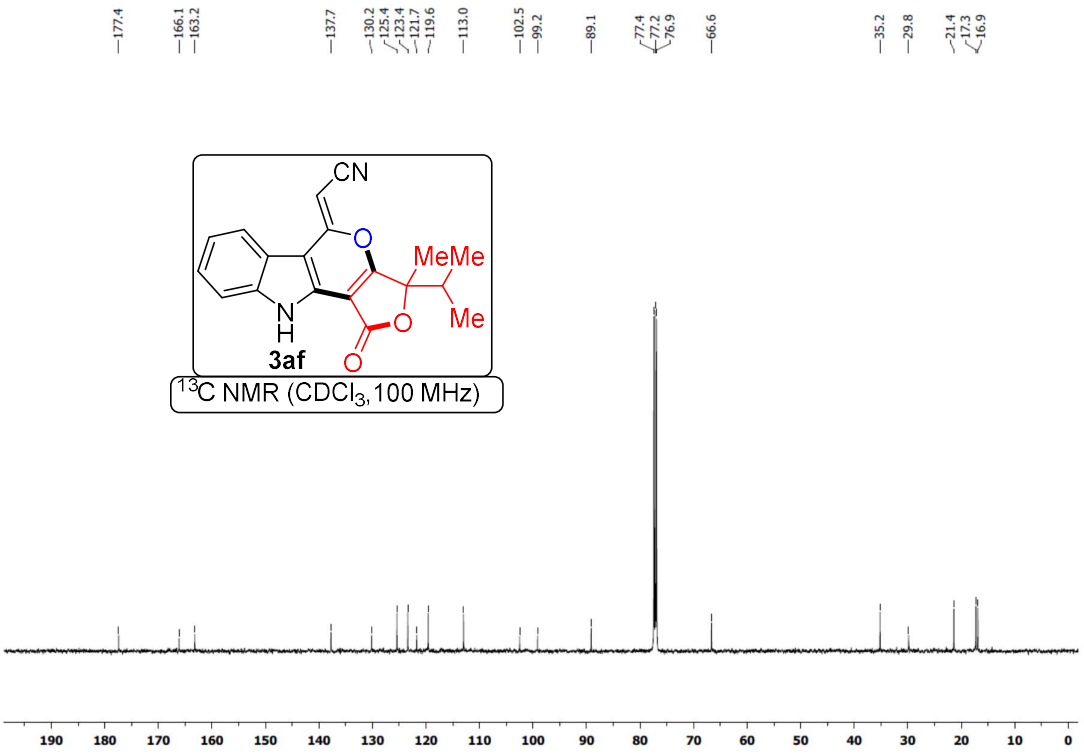
^{1}H NMR ($CDCl_3$, 400 MHz)

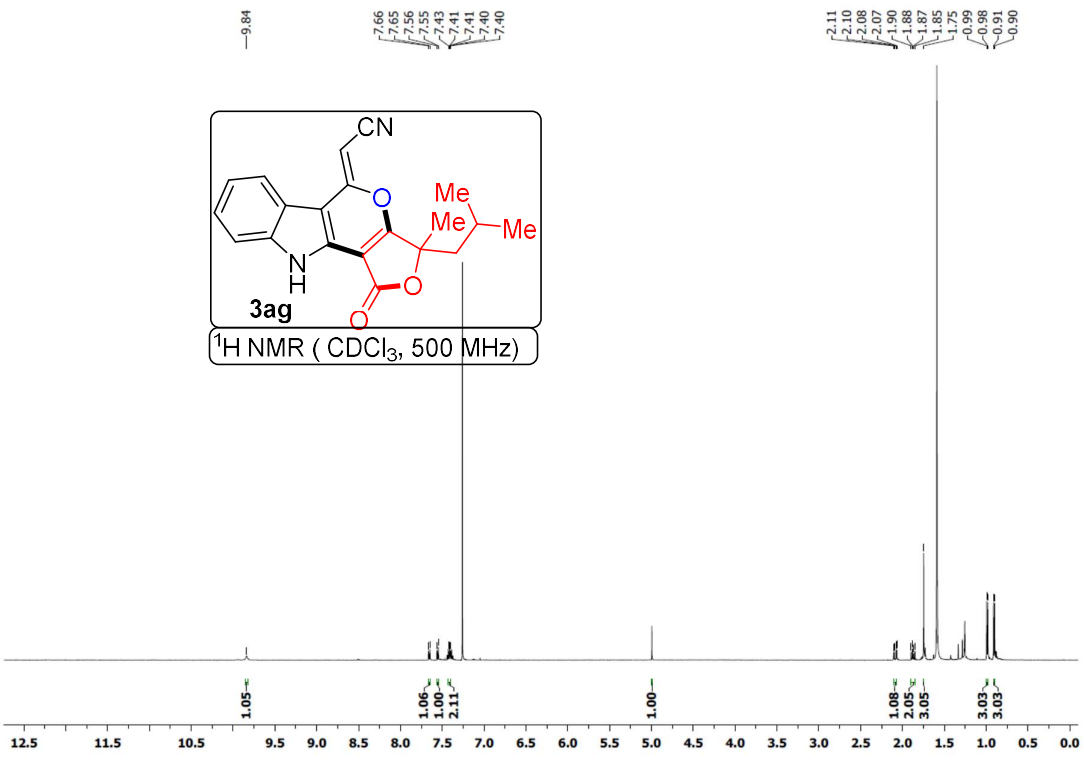


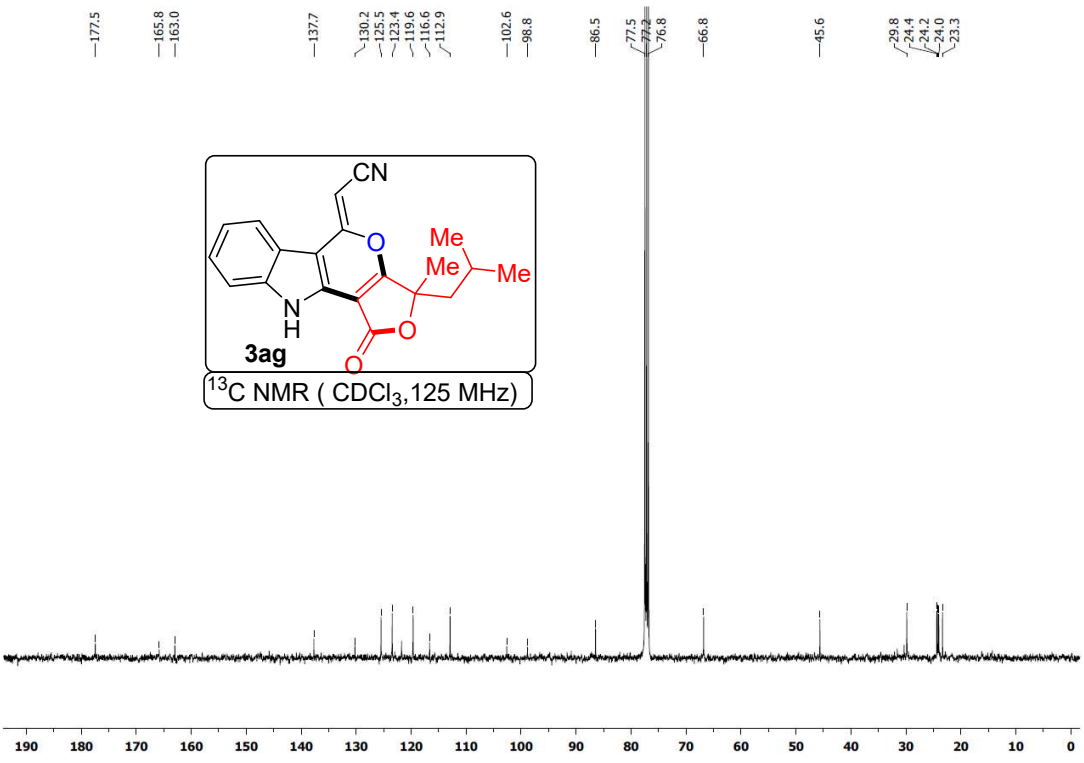
^{13}C NMR ($CDCl_3$,100 MHz)

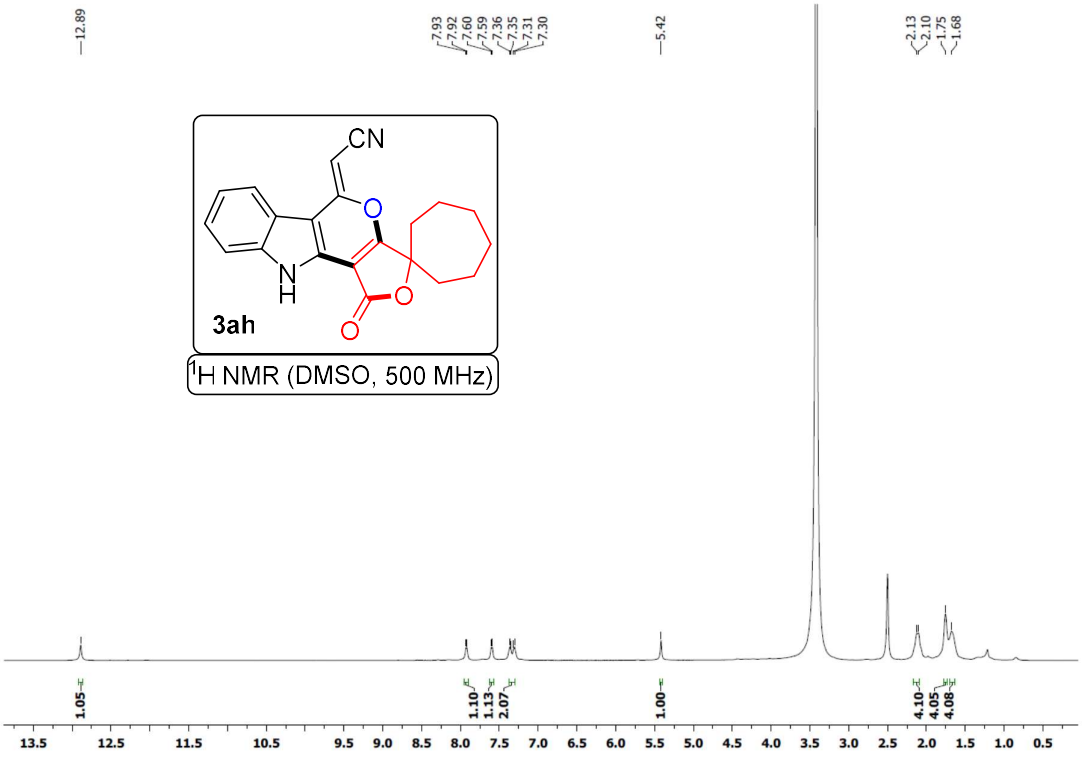


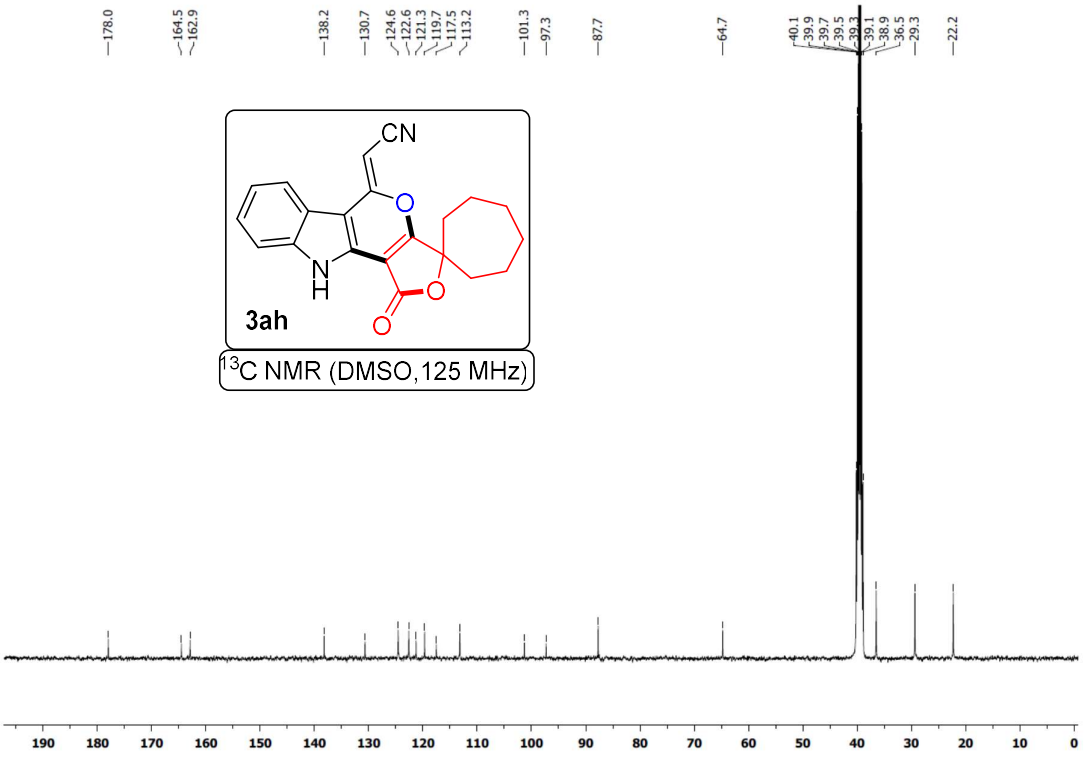
^{1}H NMR ($CDCl_3$, 400 MHz)

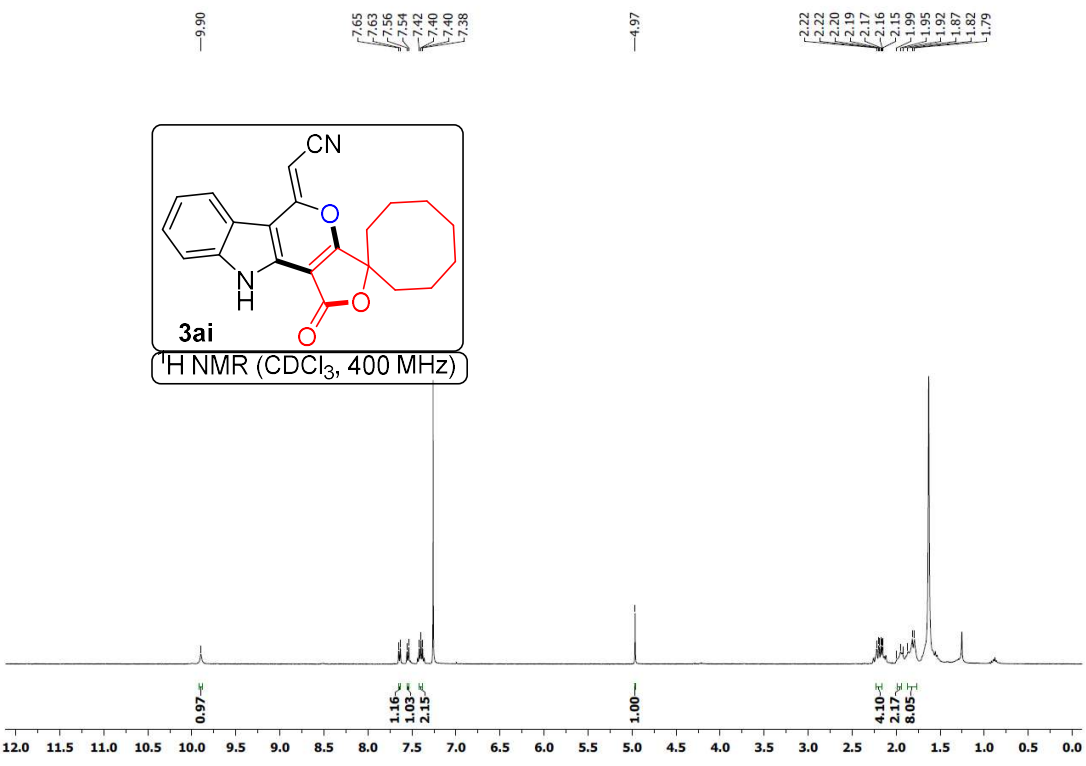

177.4
166.1
163.2
137.7
130.2
125.4
123.4
121.7
119.6
113.0
102.5
99.2
89.1
77.4
77.2
76.9
66.6
35.2
29.8
21.4
17.3
16.9
CN
O
MeMe
Me
N
H
O
O
3af
13C NMR (CDCl3,100 MHz)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

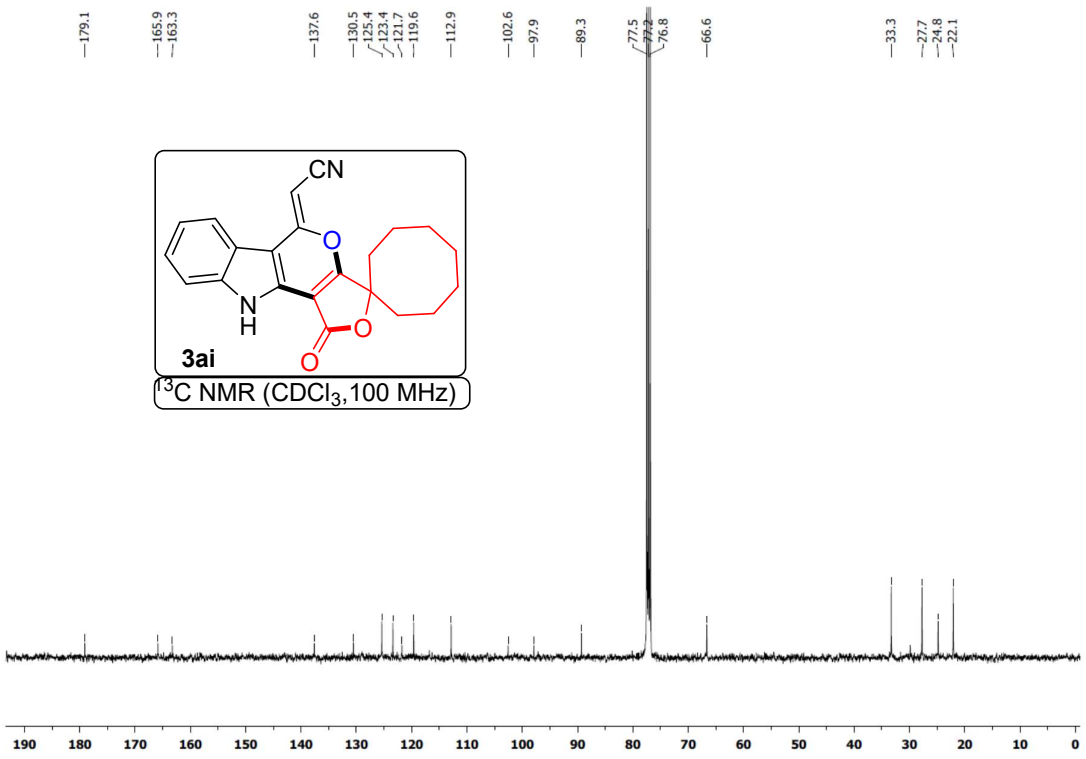

9.84
7.66
7.65
7.56
7.55
7.43
7.41
7.41
7.40
7.40
2.11
2.10
2.08
2.07
1.90
1.88
1.87
1.85
1.75
0.99
0.98
0.91
0.90
CN
O
Me
Me
Me
N
H
O
O
3ag
1H NMR (CDCl3, 500 MHz)
1.05
1.06
1.00
2.11
1.00
1.08
2.05
3.05
3.03
3.03
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

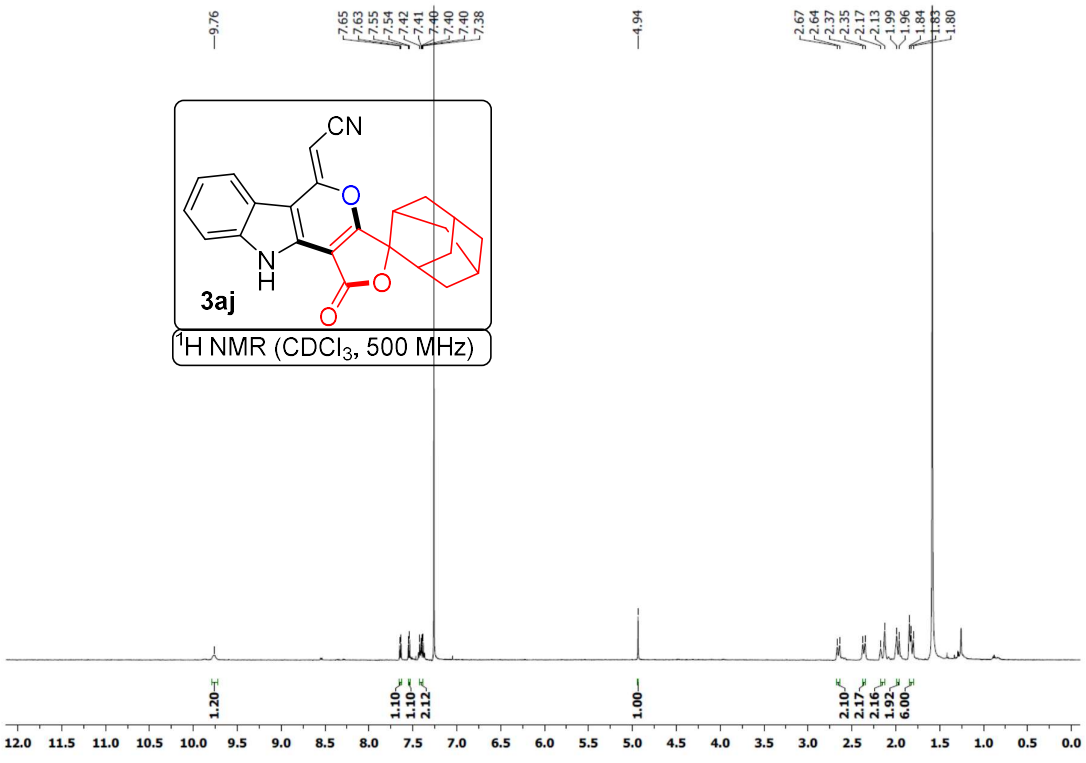

177.5
165.8
163.0
137.7
130.2
125.5
123.4
119.6
116.6
112.9
102.6
98.8
86.5
77.5
77.2
76.8
66.8
45.6
29.8
24.4
24.2
24.0
23.3
CN
O
Me
Me
Me
N
H
O
O
3ag
13C NMR (CDCl3,125 MHz)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

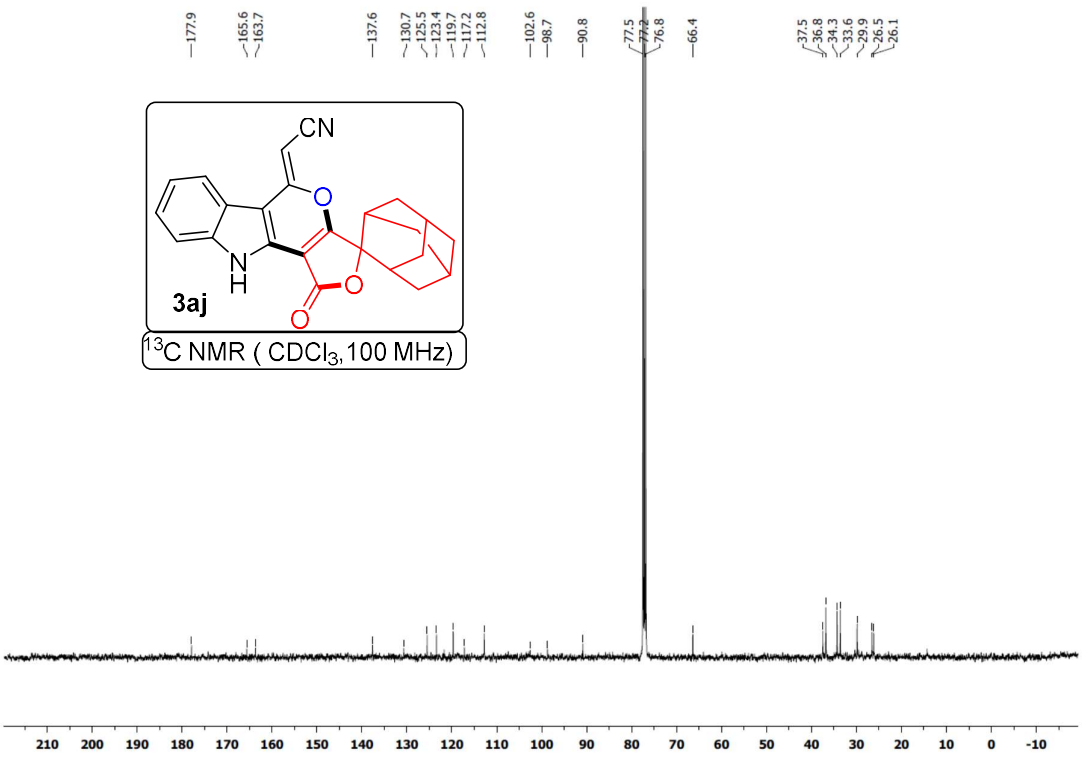

12.89
7.93
7.92
7.60
7.59
7.36
7.35
7.31
7.30
5.42
2.13
2.10
1.75
1.68
CN
O
N
H
O
O
3ah
1H NMR (DMSO, 500 MHz)
1.05
1.10
1.13
2.07
1.00
4.10
4.05
4.08
13.5
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5


178.0
164.5
162.9
138.2
130.7
124.6
122.6
121.3
119.7
117.5
113.2
101.3
97.3
87.7
64.7
40.1
39.9
39.7
39.5
39.3
39.1
38.9
36.5
29.3
22.2
CN
O
N
H
O
O
3ah
^{13}C NMR (DMSO,125 MHz)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

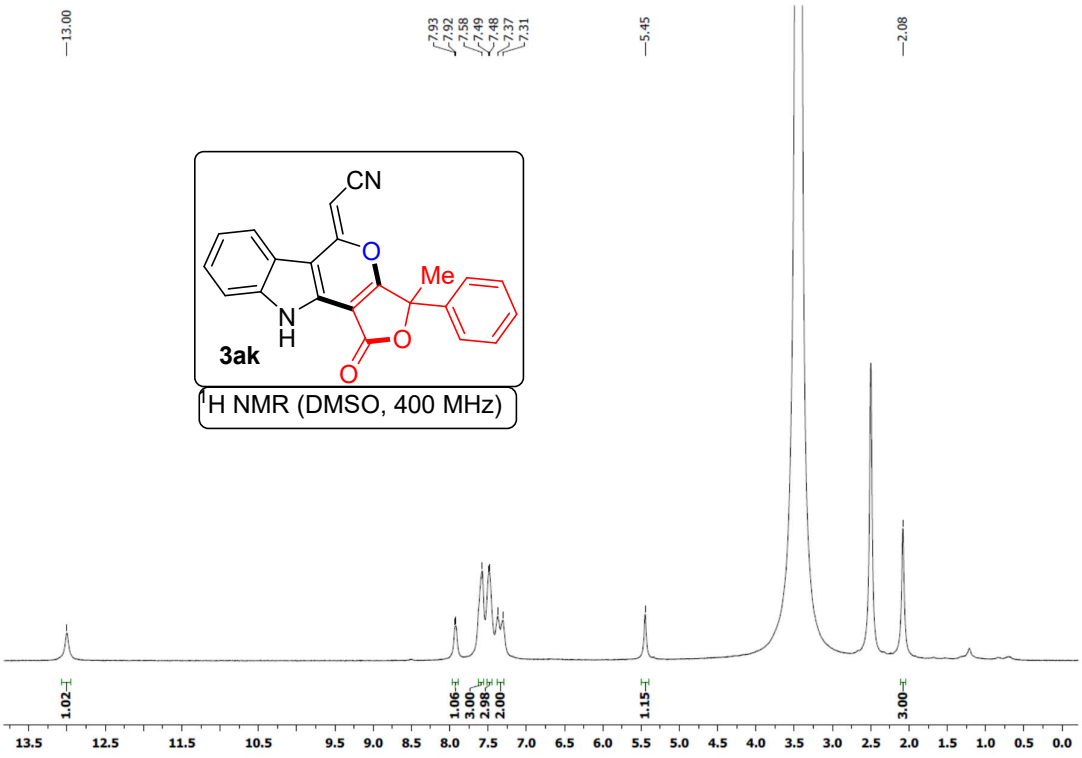

9.90
7.65
7.63
7.56
7.54
7.42
7.40
7.40
7.38
4.97
2.22
2.22
2.20
2.19
2.17
2.16
2.15
1.99
1.95
1.92
1.87
1.82
1.79
CN
O
N
H
O
O
3ai
^{1}H NMR ($CDCl_3$, 400 MHz)
0.97
1.16
1.03
2.15
1.00
4.10
2.17
8.05
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0


179.1
165.9
163.3
137.6
130.5
125.4
123.4
121.7
119.6
112.9
102.6
97.9
89.3
77.5
77.2
76.8
66.6
33.3
27.7
24.8
22.1
CN
O
N
H
O
O
3ai
^{13}C NMR (CDCl$_3$,100 MHz)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

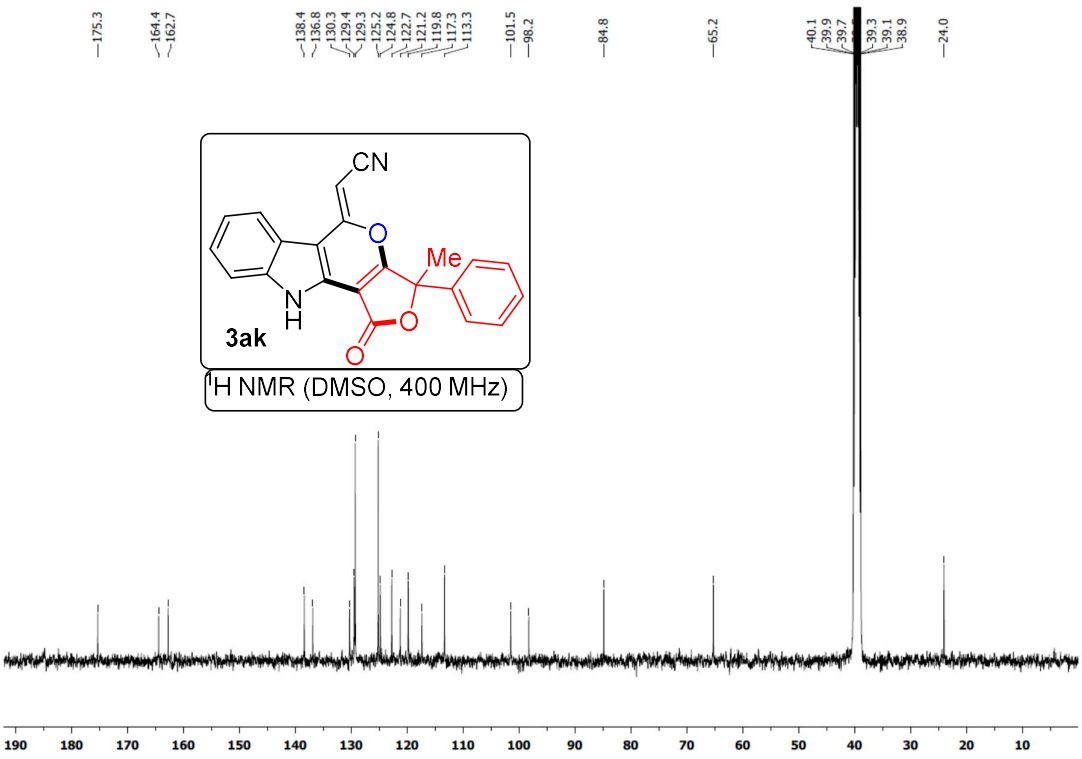

9.76
7.65
7.63
7.55
7.54
7.42
7.41
7.40
7.40
7.40
7.38
4.94
2.67
2.64
2.37
2.35
2.17
2.13
1.99
1.96
1.84
1.83
1.80
CN
O
N
H
O
O
3aj
^{1}H NMR (CDCl$_3$, 500 MHz)
1.20
1.10
1.10
2.12
1.00
2.10
2.17
2.16
1.92
6.00
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

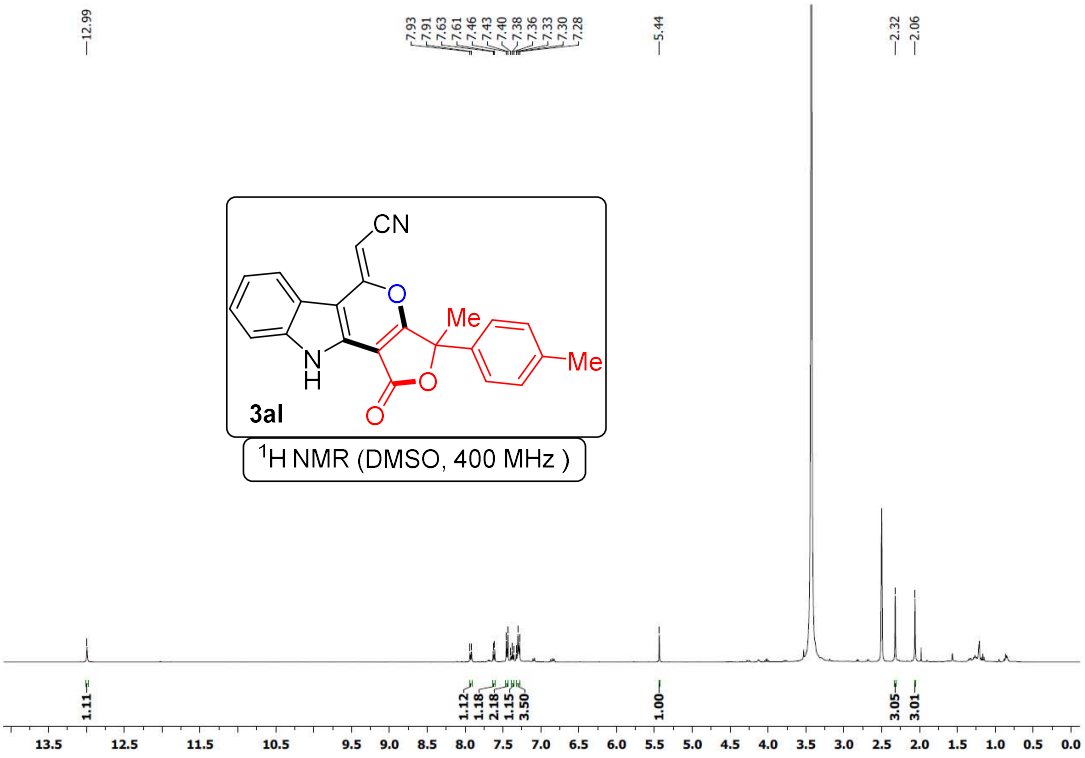


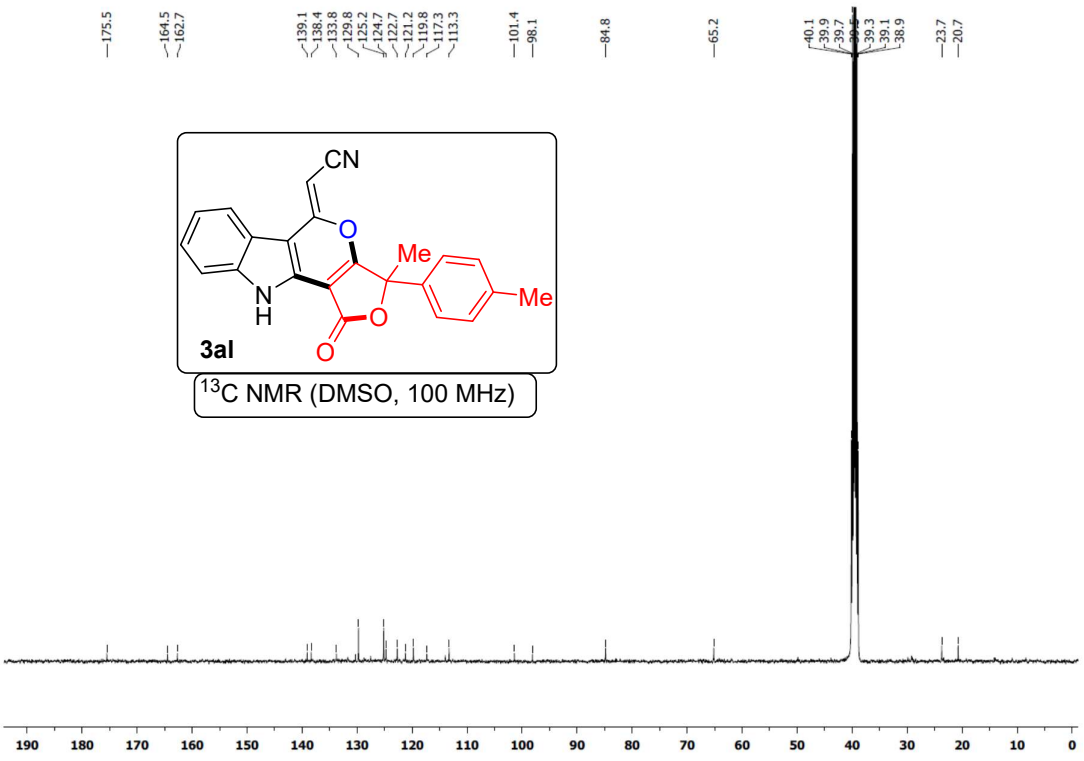
^{13}C NMR ($CDCl_3$, 100 MHz)



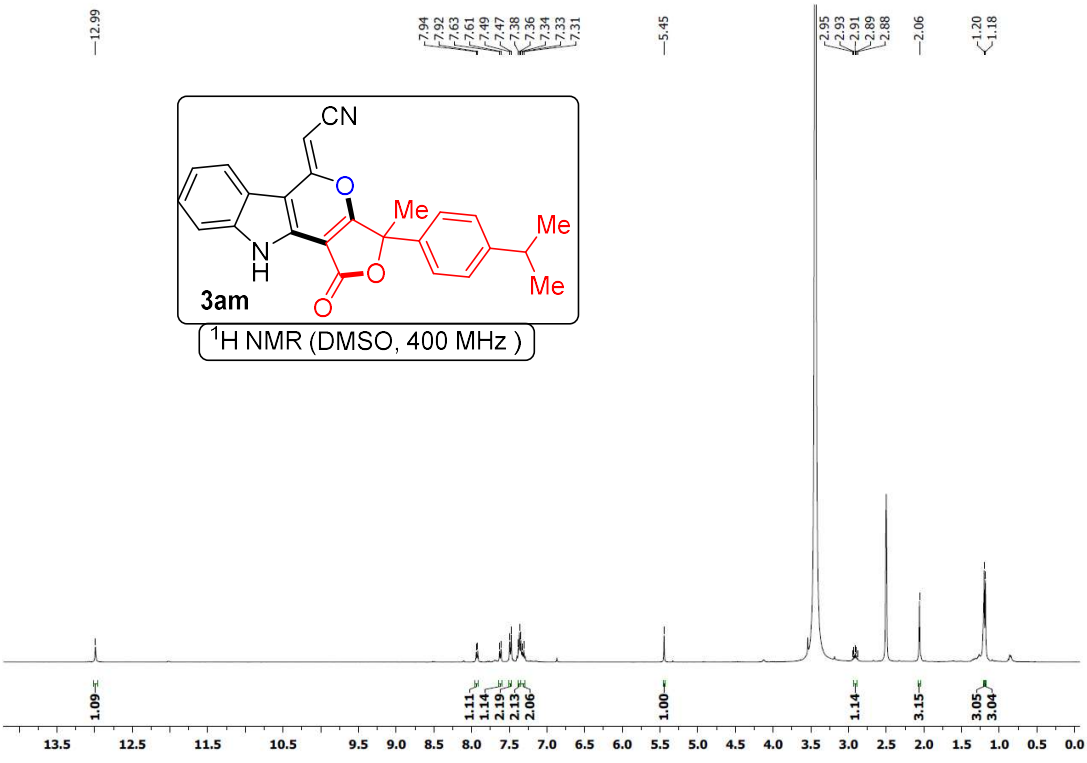
^{1}H NMR (DMSO, 400 MHz)


175.3
164.4
162.7
138.4
136.8
130.3
129.4
129.3
125.2
124.8
122.7
121.2
119.8
117.3
113.3
101.5
98.2
84.8
65.2
40.1
39.9
39.7
39.3
39.1
38.9
24.0
CN
O
Me
N
H
O
O
3ak
1H NMR (DMSO, 400 MHz)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10

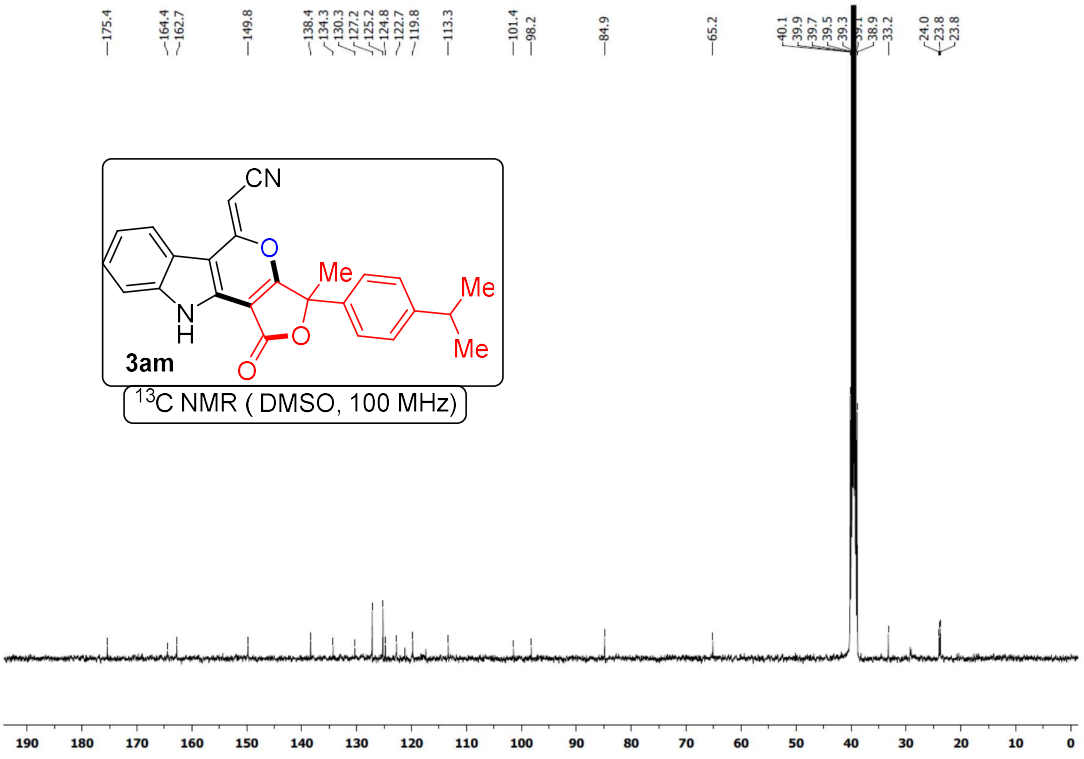

12.99
7.93
7.91
7.63
7.61
7.46
7.43
7.40
7.38
7.36
7.33
7.30
7.28
5.44
2.32
2.06
CN
O
Me
Me
N
H
O
O
3al
1H NMR (DMSO, 400 MHz)
1.11
1.12
1.18
2.18
1.15
3.50
1.00
3.05
3.01
13.5
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

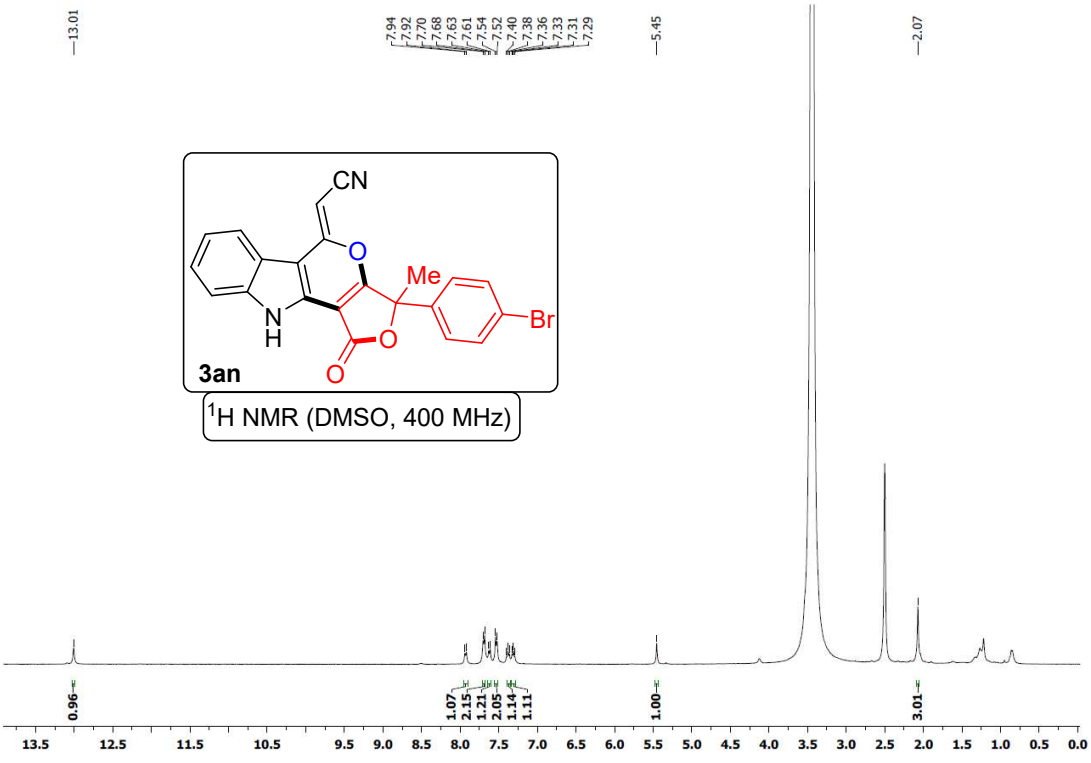


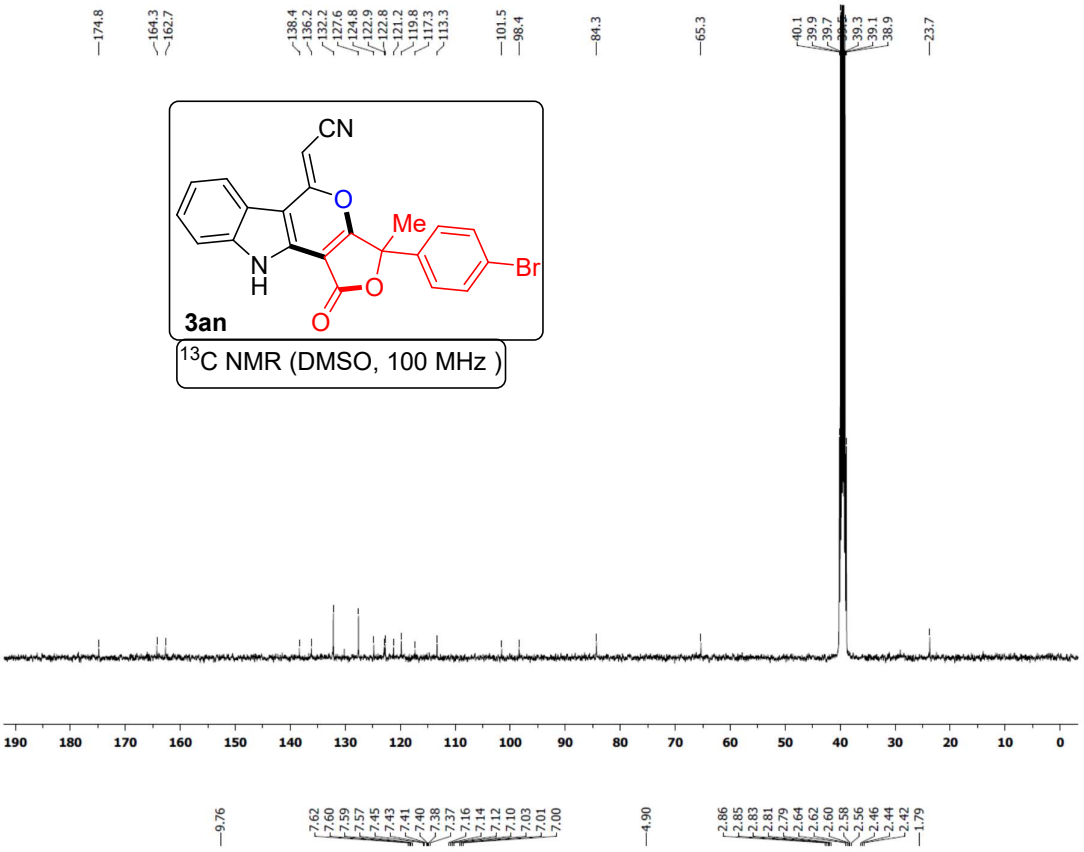
^{13}C NMR (DMSO, 100 MHz)



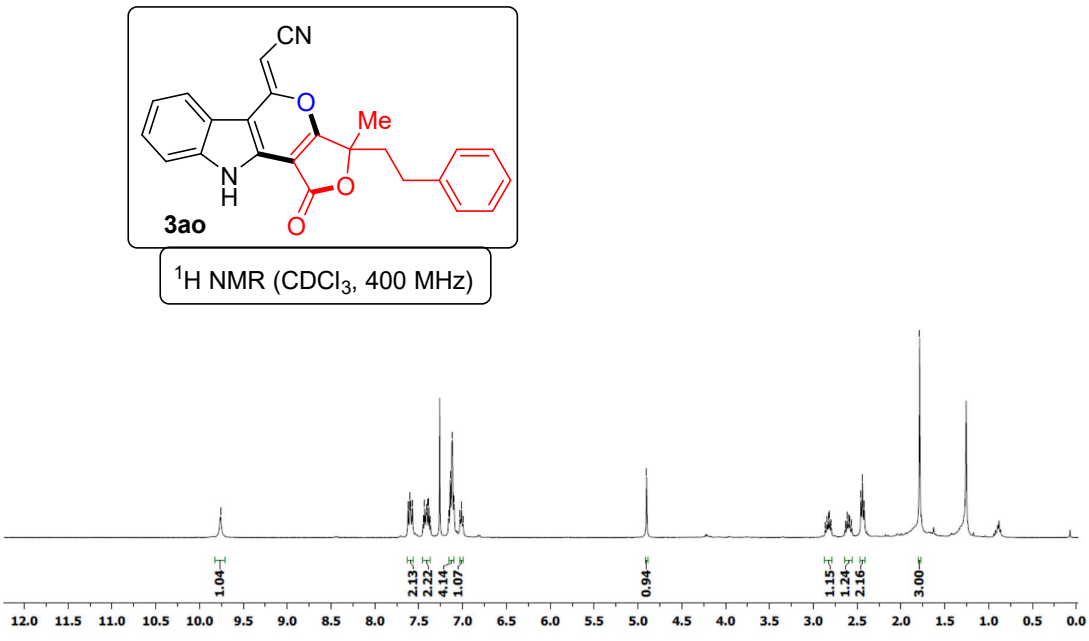
^{1}H NMR (DMSO, 400 MHz)


175.4
164.4
162.7
149.8
138.4
134.3
130.3
127.2
125.2
124.8
122.7
119.8
113.3
101.4
98.2
84.9
65.2
40.1
39.9
39.7
39.5
39.3
38.9
33.2
24.0
23.8
23.8
CN
O
Me
Me
Me
N
H
O
O
3am
13C NMR (DMSO, 100 MHz)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

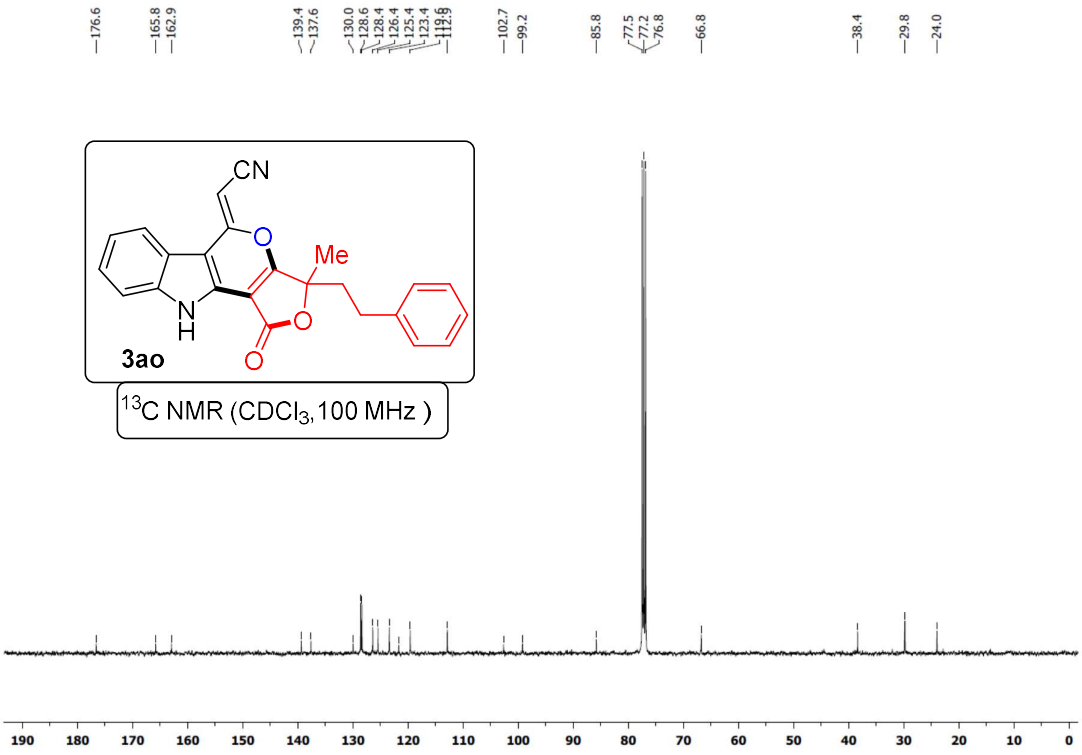

13.01
7.94
7.92
7.70
7.68
7.63
7.61
7.54
7.52
7.40
7.38
7.36
7.33
7.31
7.29
5.45
2.07
CN
O
Me
Br
N
H
O
O
3an
1H NMR (DMSO, 400 MHz)
0.96
1.07
2.15
1.21
2.05
1.14
1.11
1.00
3.01
13.5
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

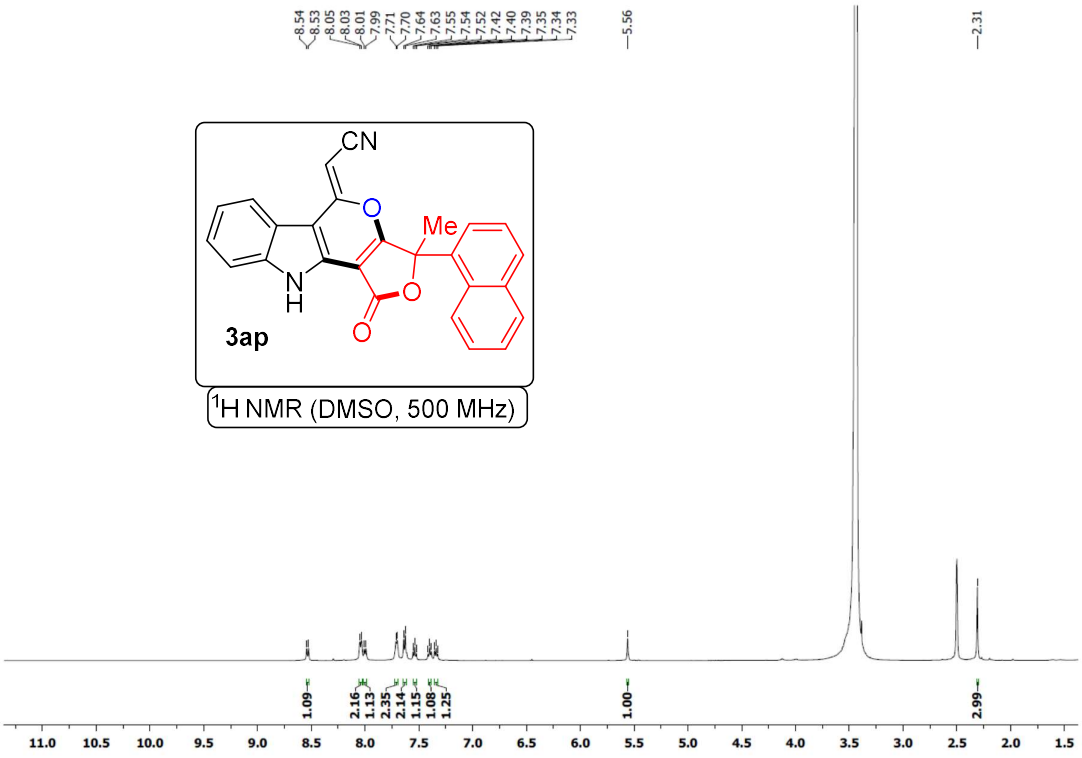


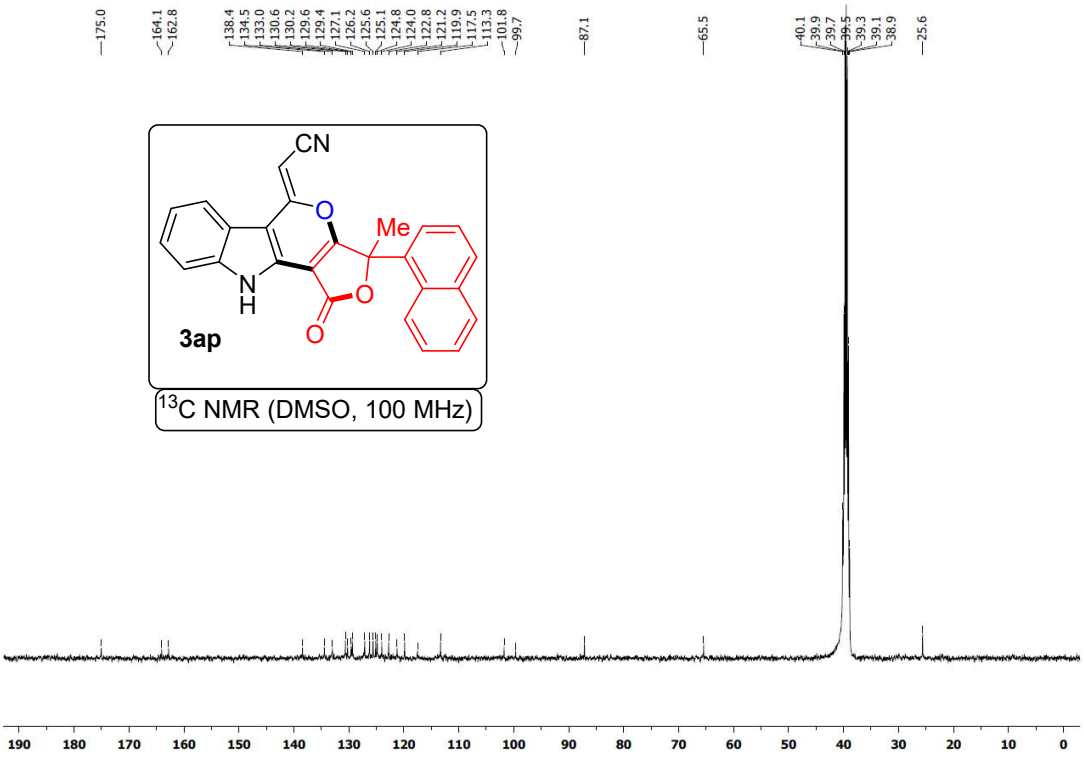
^{13}C NMR (DMSO, 100 MHz)



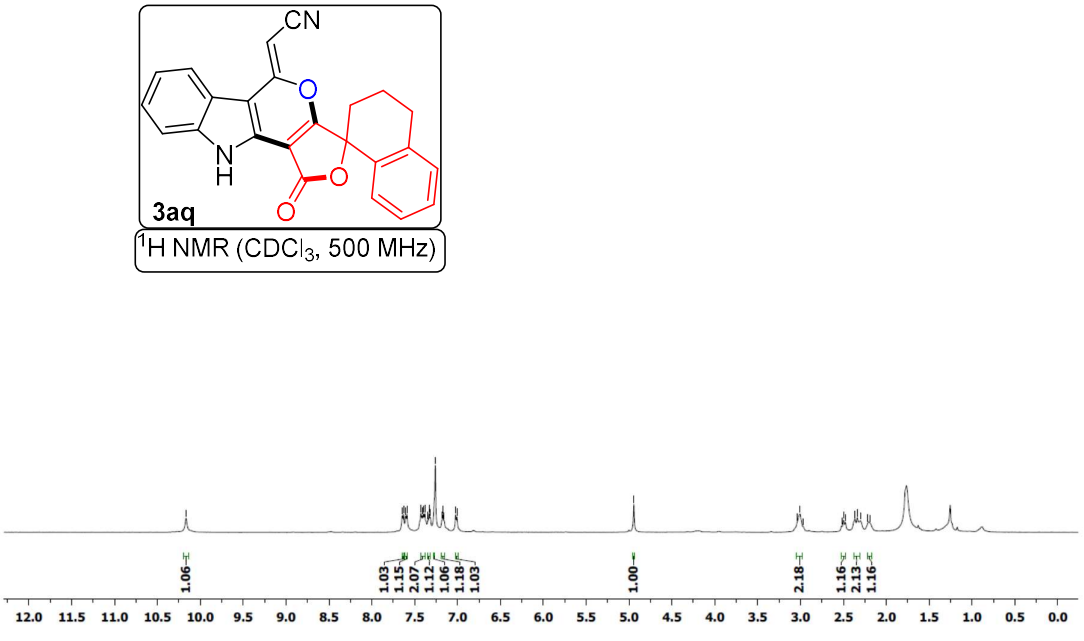
^{1}H NMR ($CDCl_3$, 400 MHz)


176.6
165.8
162.9
139.4
137.6
130.0
128.6
128.4
126.4
125.4
123.4
119.6
112.9
102.7
99.2
85.8
77.5
77.2
76.8
66.8
38.4
29.8
24.0
CN
O
Me
N
H
O
O
3ao
13C NMR (CDCl3, 100 MHz)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

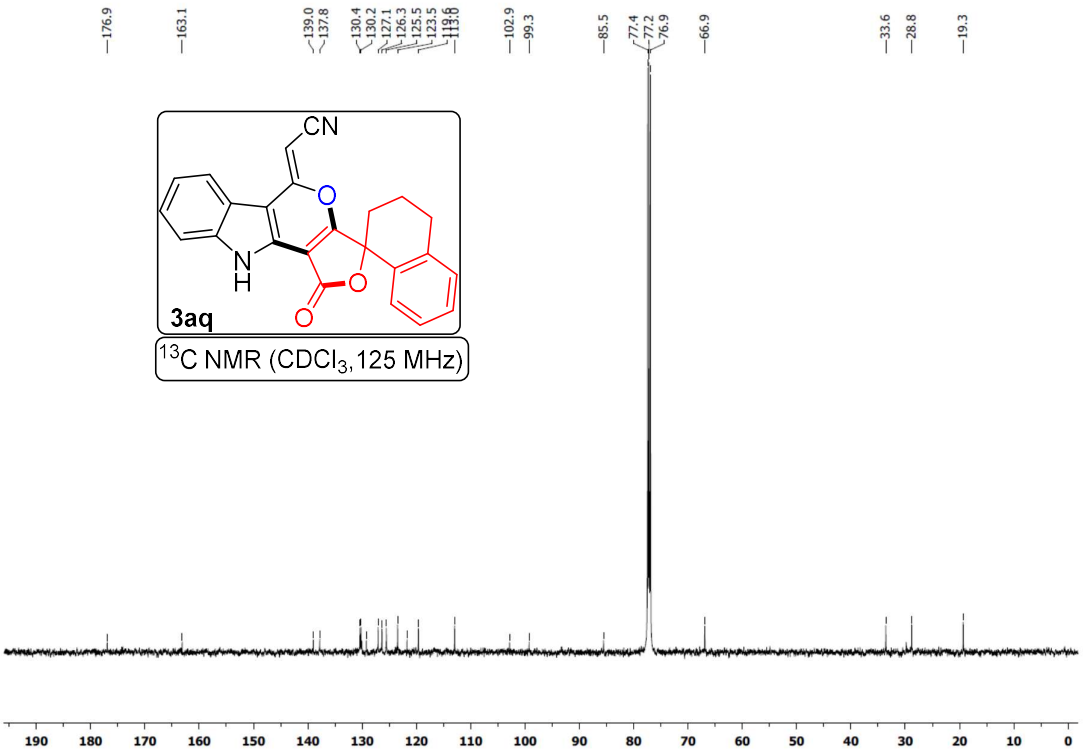

8.54
8.53
8.05
8.03
8.01
7.99
7.71
7.70
7.64
7.63
7.55
7.54
7.52
7.42
7.40
7.39
7.35
7.34
7.33
5.56
2.31
CN
O
Me
N
H
O
O
3ap
1H NMR (DMSO, 500 MHz)
1.09
2.16
1.13
2.35
2.14
1.15
1.08
1.25
1.00
2.99
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5

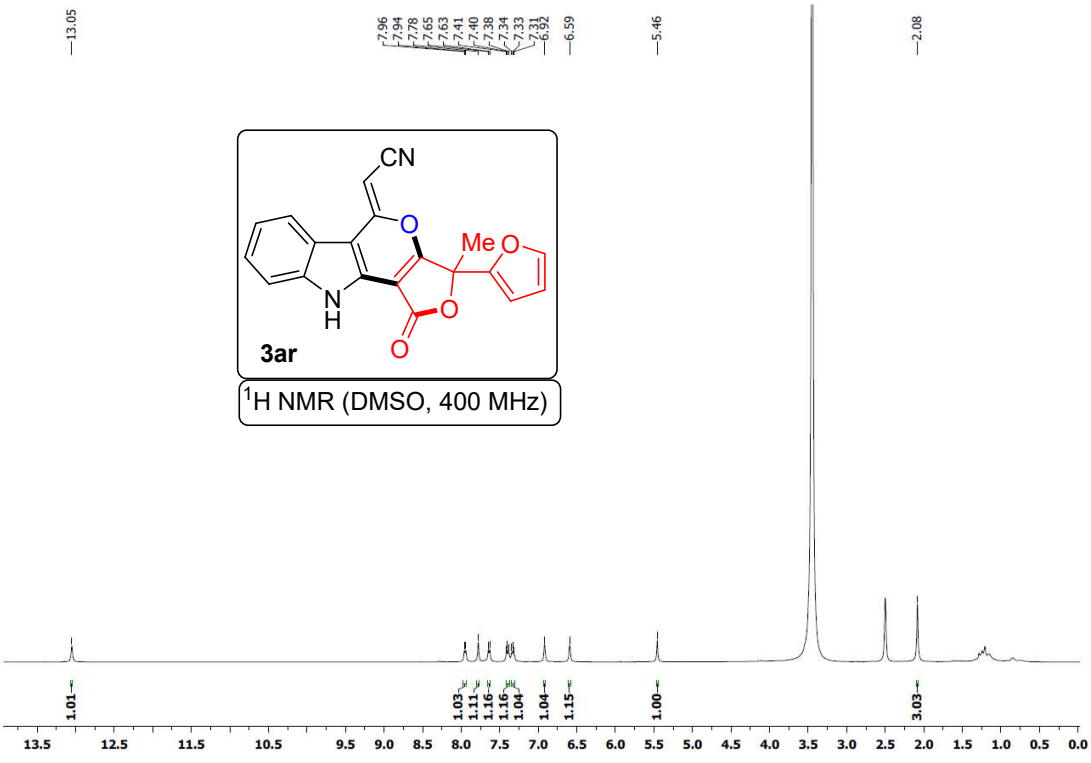


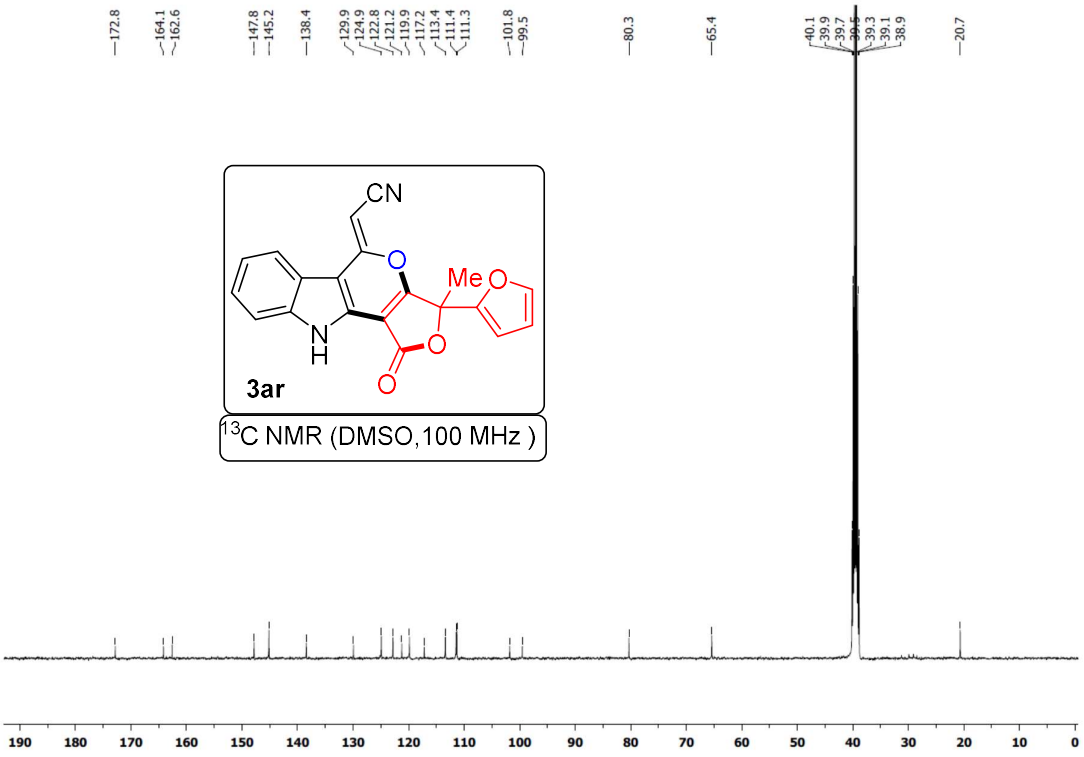
^{13}C NMR (DMSO, 100 MHz)

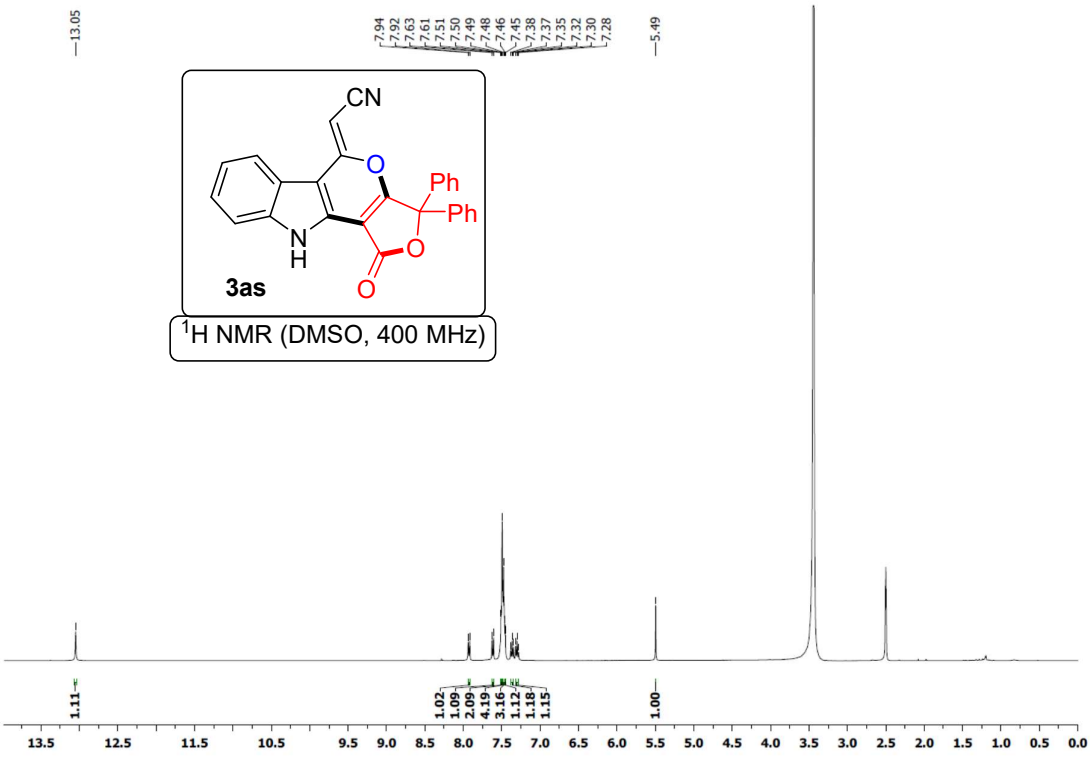


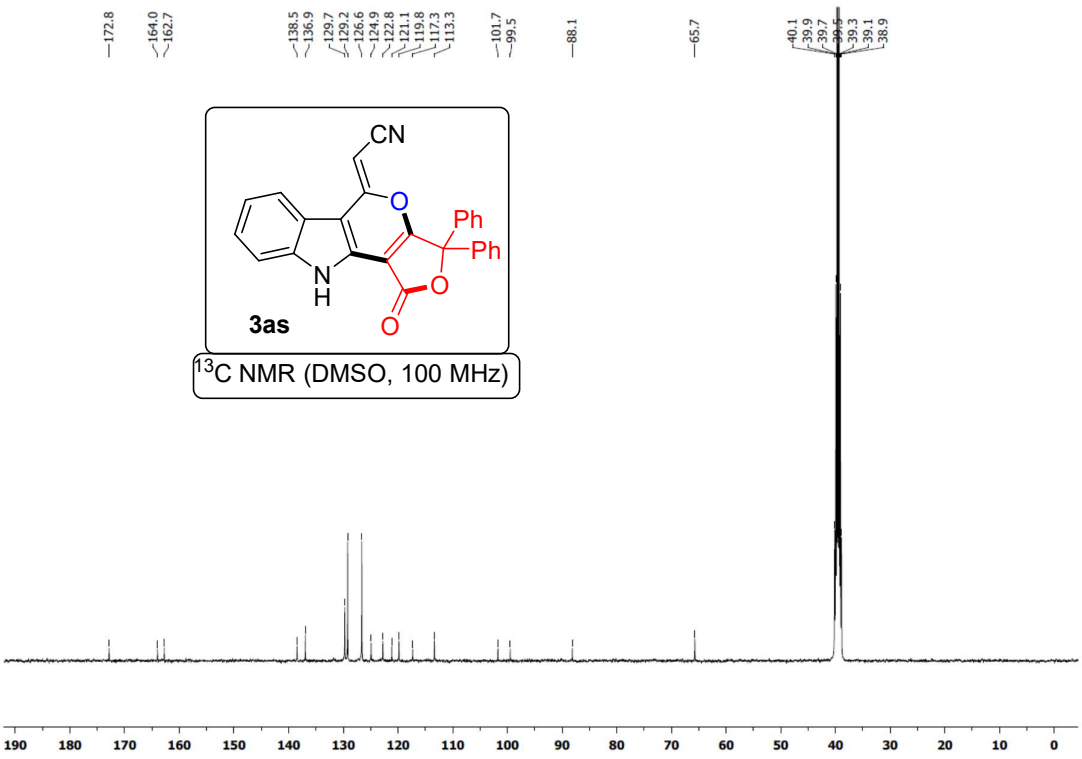
^{1}H NMR ($CDCl_3$, 500 MHz)

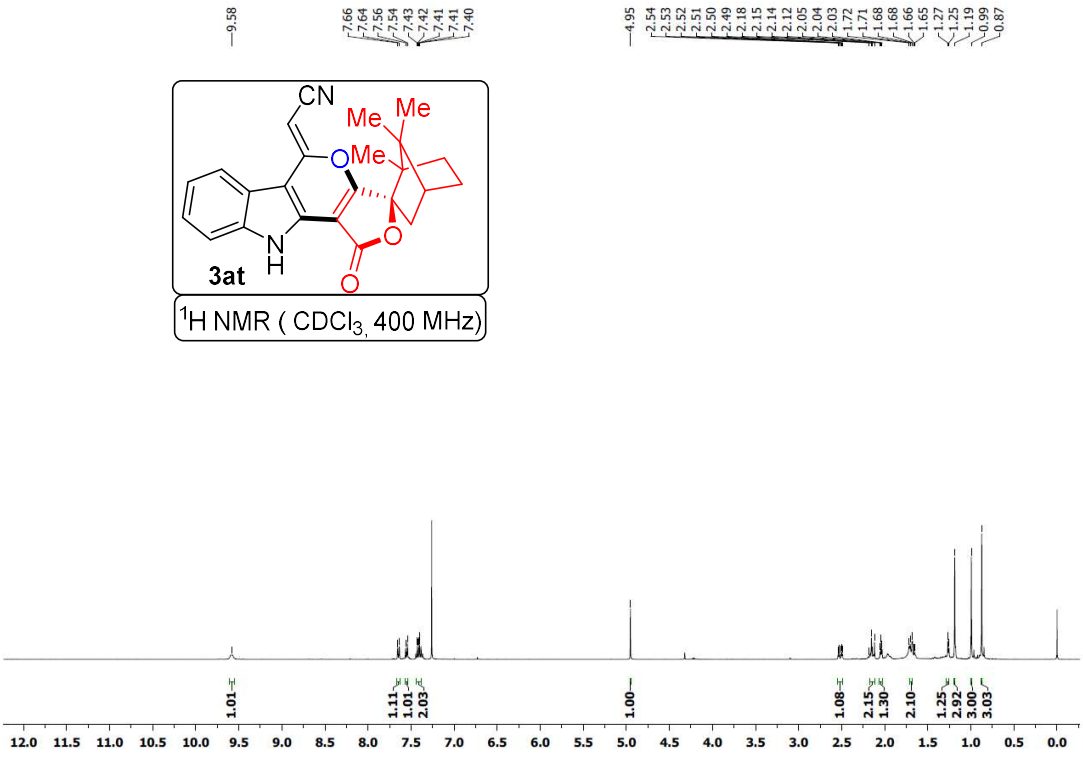

CN
O
N
H
O
O
3aq
^{13}C NMR ($CDCl_3$, 125 MHz)

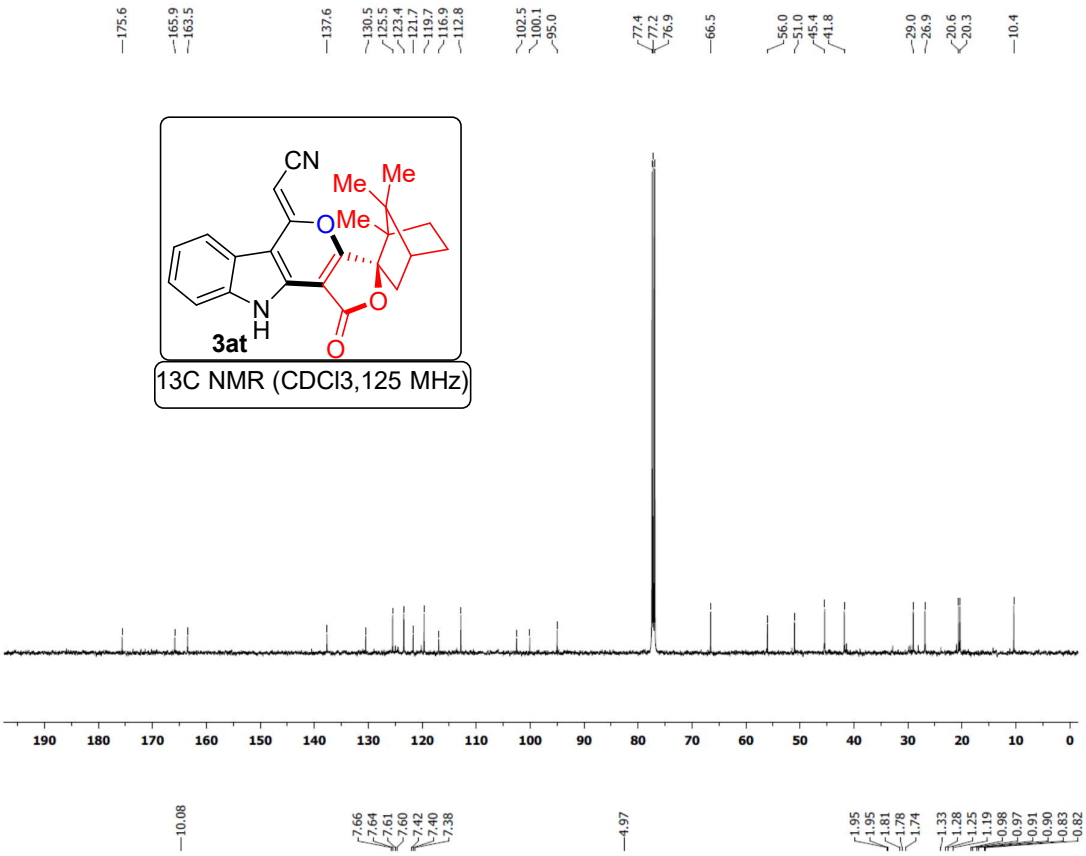

CN
O
Me
O
N
H
O
O
3ar
^{1}H NMR (DMSO, 400 MHz)

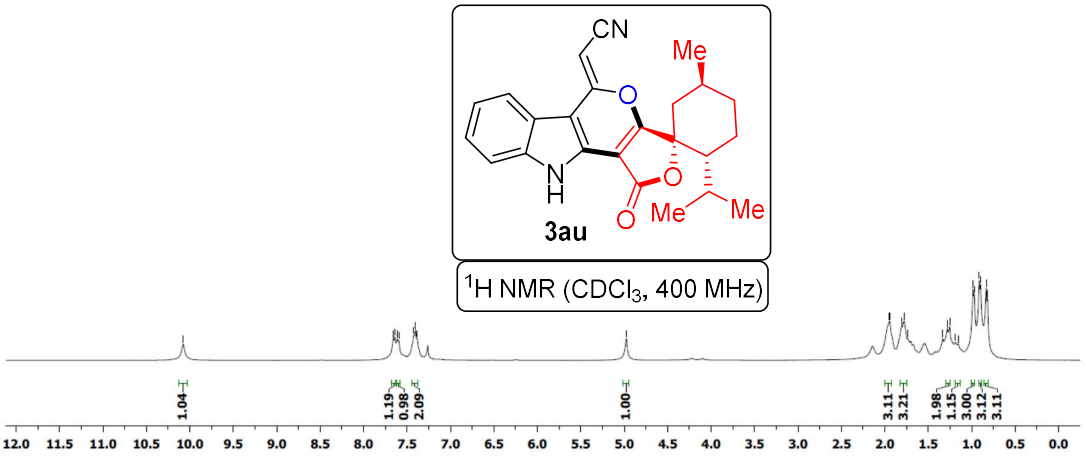

172.8
164.1
162.6
147.8
145.2
138.4
129.9
124.9
122.8
121.2
119.9
117.2
113.4
111.4
111.3
101.8
99.5
80.3
65.4
40.1
39.9
39.7
39.5
39.3
39.1
38.9
20.7
CN
O
Me
O
N
H
O
O
3ar
13C NMR (DMSO,100 MHz)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

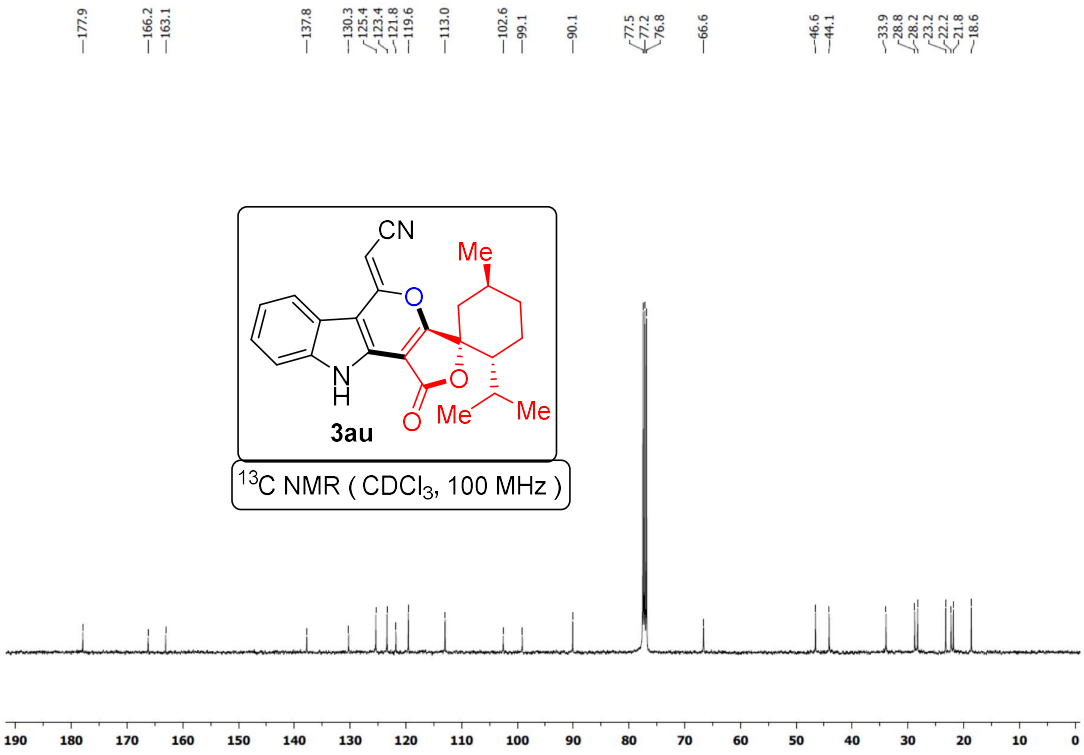

13.05
7.94
7.92
7.63
7.61
7.51
7.50
7.49
7.48
7.46
7.45
7.38
7.37
7.35
7.32
7.30
7.28
5.49
CN
O
Ph
Ph
N
H
O
O
3as
1H NMR (DMSO, 400 MHz)
1.11
1.02
1.09
2.09
4.19
3.16
1.12
1.18
1.15
1.00
13.5
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

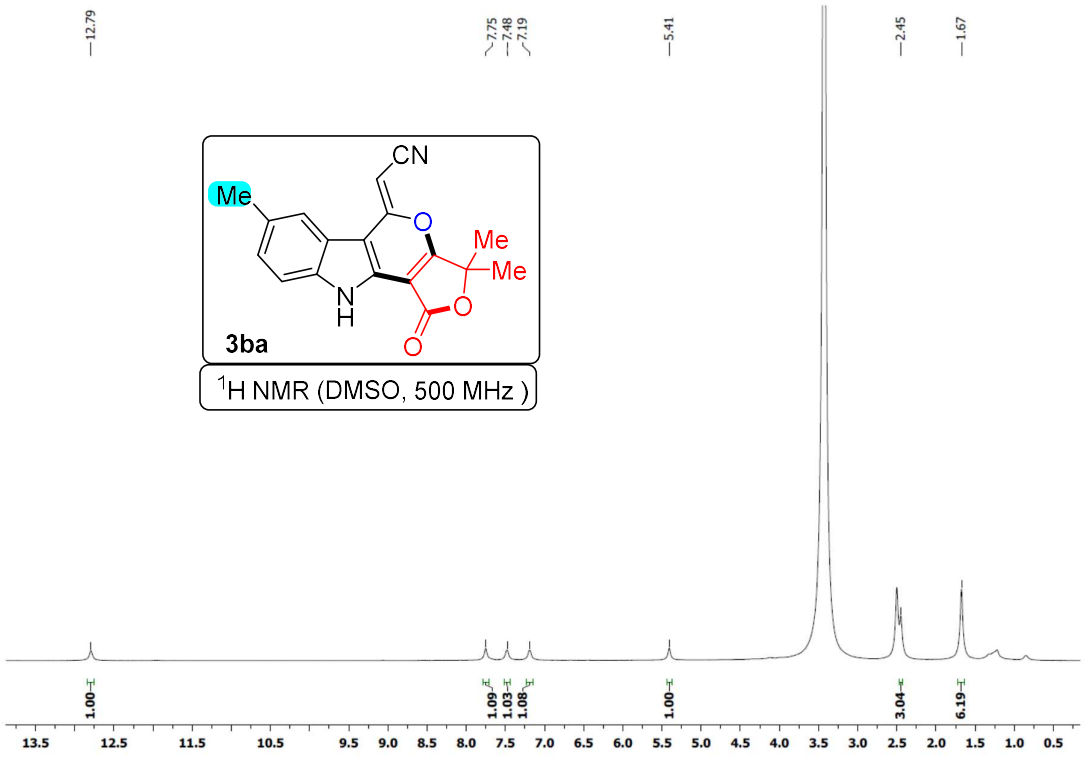

172.8
164.0
162.7
138.5
136.9
129.7
129.2
126.6
124.9
122.8
121.1
119.8
117.3
113.3
101.7
99.5
88.1
65.7
40.1
39.9
39.7
39.5
39.3
39.1
38.9
CN
O
Ph
Ph
N
H
O
O
3as
13C NMR (DMSO, 100 MHz)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

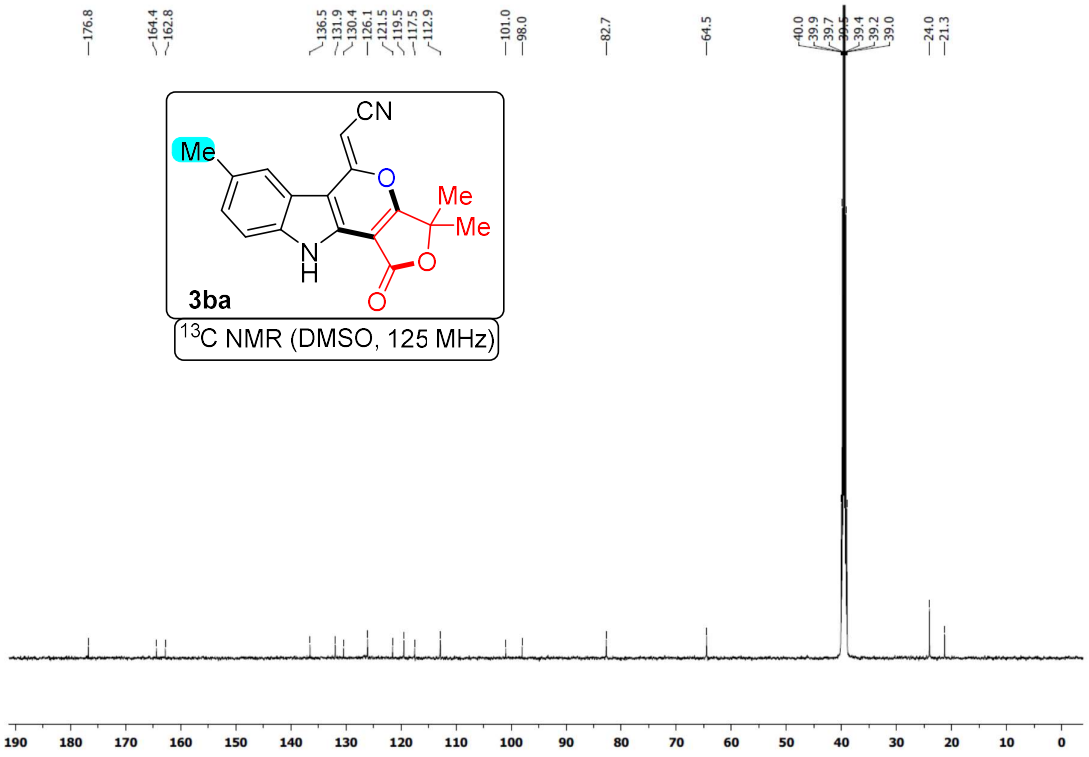

9.58
7.66
7.64
7.56
7.54
7.43
7.42
7.41
7.41
7.40
4.95
2.54
2.53
2.52
2.51
2.50
2.49
2.18
2.15
2.14
2.12
2.05
2.04
2.03
1.72
1.71
1.68
1.68
1.66
1.65
1.27
1.25
1.19
0.99
0.87
CN
Me
Me
O
Me
N
H
O
O
3at
1H NMR (CDCl3, 400 MHz)
1.01
1.11
1.01
2.03
1.00
1.08
2.15
1.30
2.10
1.25
2.92
3.00
3.03
12.0
11.5
11.0
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

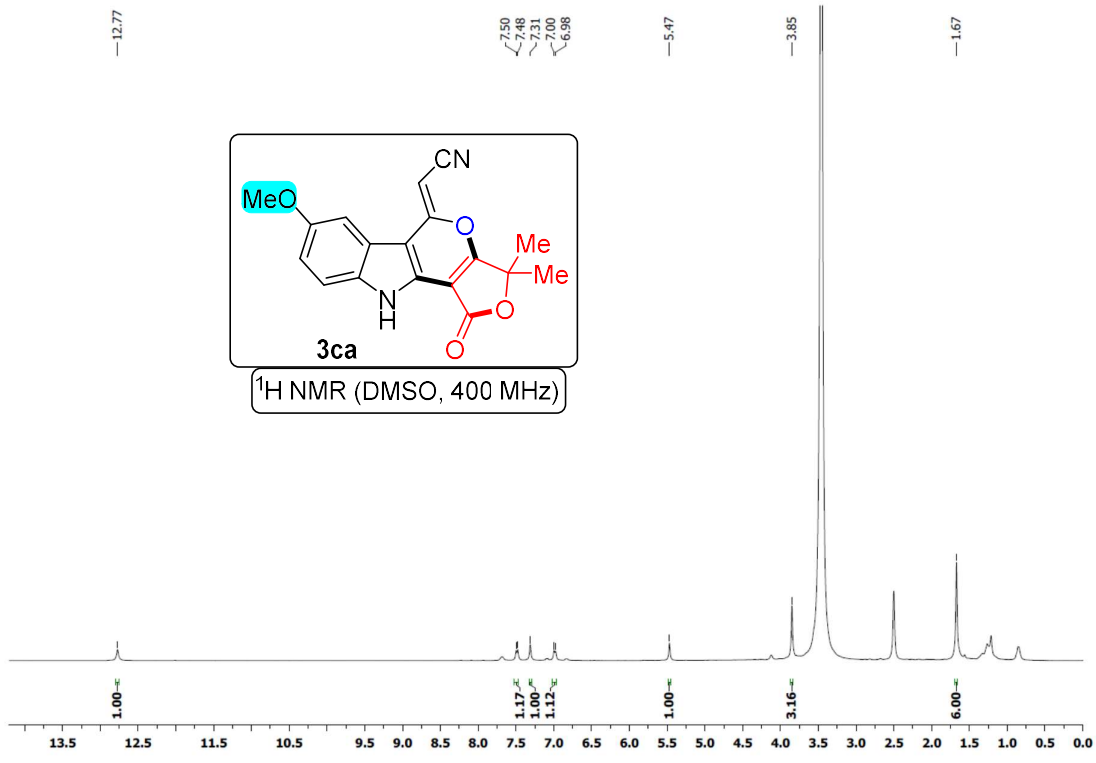

175.6
165.9
163.5
137.6
130.5
125.5
123.4
121.7
119.7
116.9
112.8
102.5
100.1
95.0
77.4
77.2
76.9
66.5
56.0
51.0
45.4
41.8
29.0
26.9
20.6
20.3
10.4
CN
Me
Me
O
Me
N
H
O
O
3at
13C NMR (CDCl3,125 MHz)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
10.08
7.66
7.64
7.61
7.60
7.42
7.40
7.38
4.97
1.95
1.95
1.81
1.78
1.74
1.33
1.28
1.25
1.19
0.98
0.97
0.91
0.90
0.83
0.82

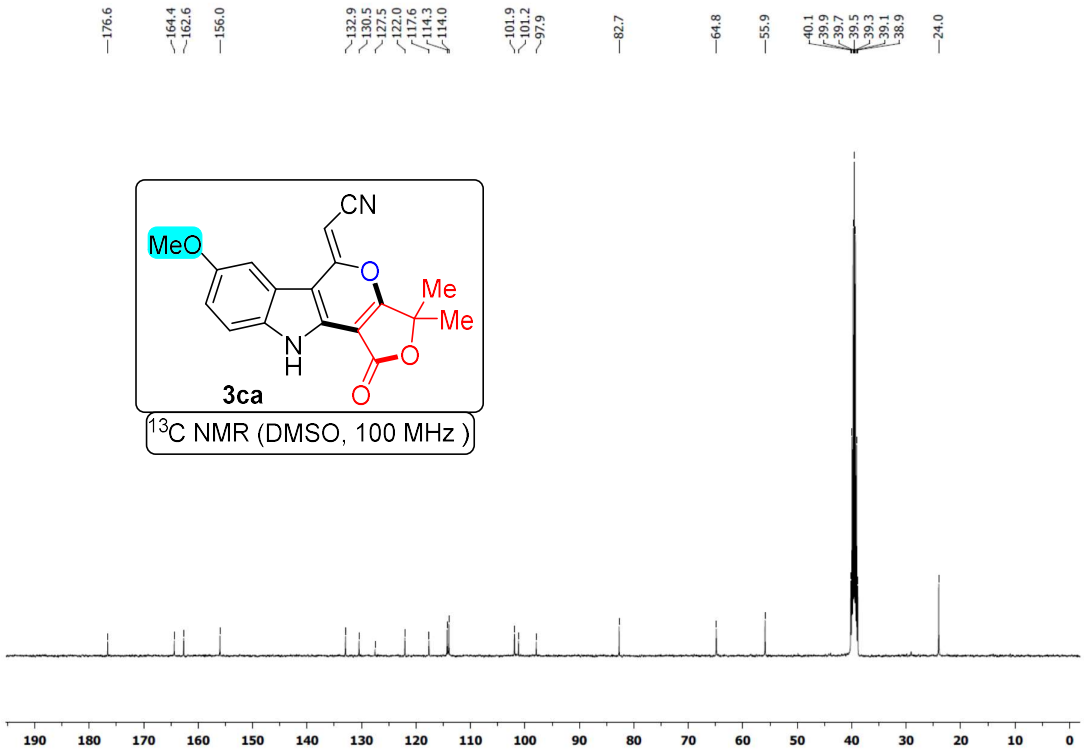

CN
Me
O
N
H
O
O
Me
Me
3au
1H NMR (CDCl3, 400 MHz)
1.04
1.19
0.98
2.09
1.00
3.11
3.21
1.98
1.15
3.00
3.12
3.11
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

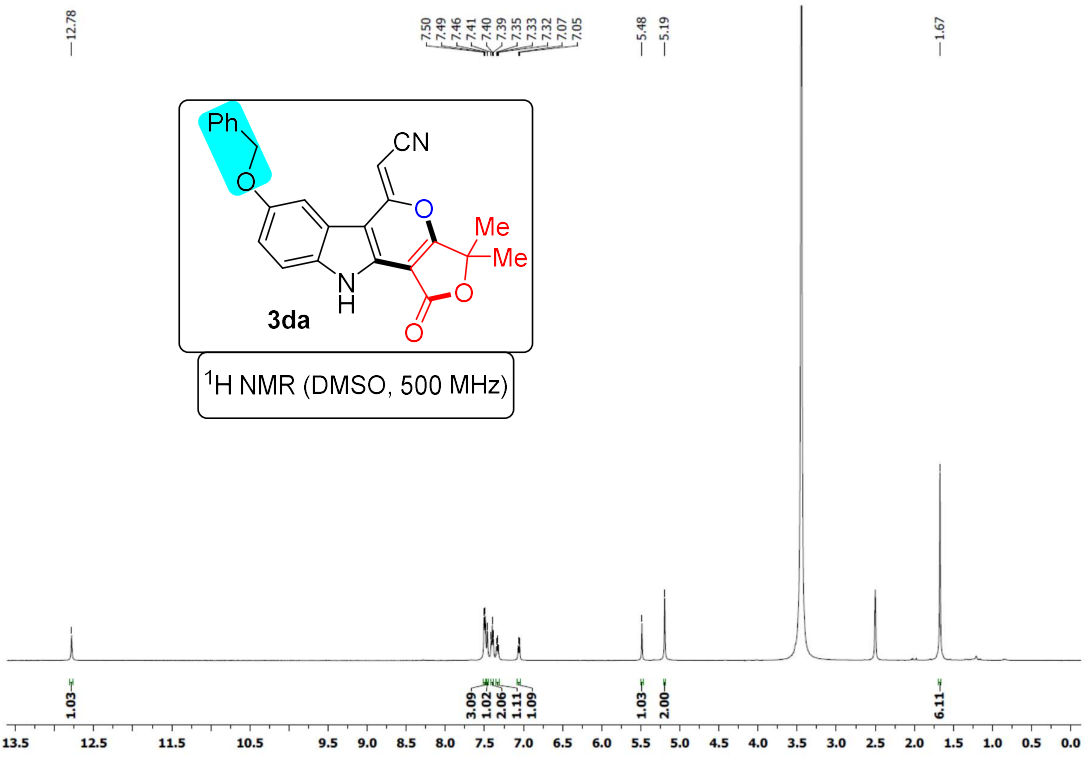

177.9
166.2
163.1
137.8
130.3
125.4
123.4
121.8
119.6
113.0
102.6
99.1
90.1
77.5
77.2
76.8
66.6
46.6
44.1
33.9
28.8
28.2
23.2
22.2
21.8
18.6
CN
Me
O
N
H
O
O
Me
Me
3au
^{13}C NMR ($CDCl_3$, 100 MHz)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

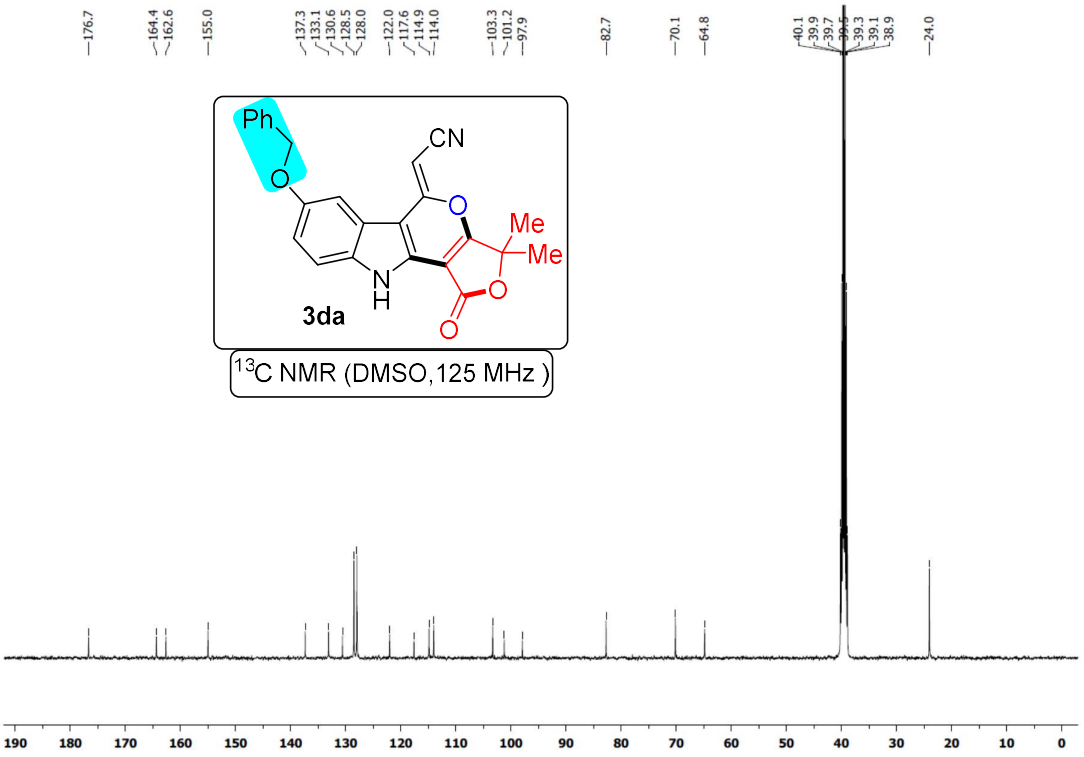

12.79
7.75
7.48
7.19
5.41
2.45
1.67
CN
Me
O
Me
Me
N
H
O
O
3ba
^{1}H NMR (DMSO, 500 MHz)
1.00
1.09
1.03
1.08
1.00
3.04
6.19
13.5 12.5 11.5 10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5

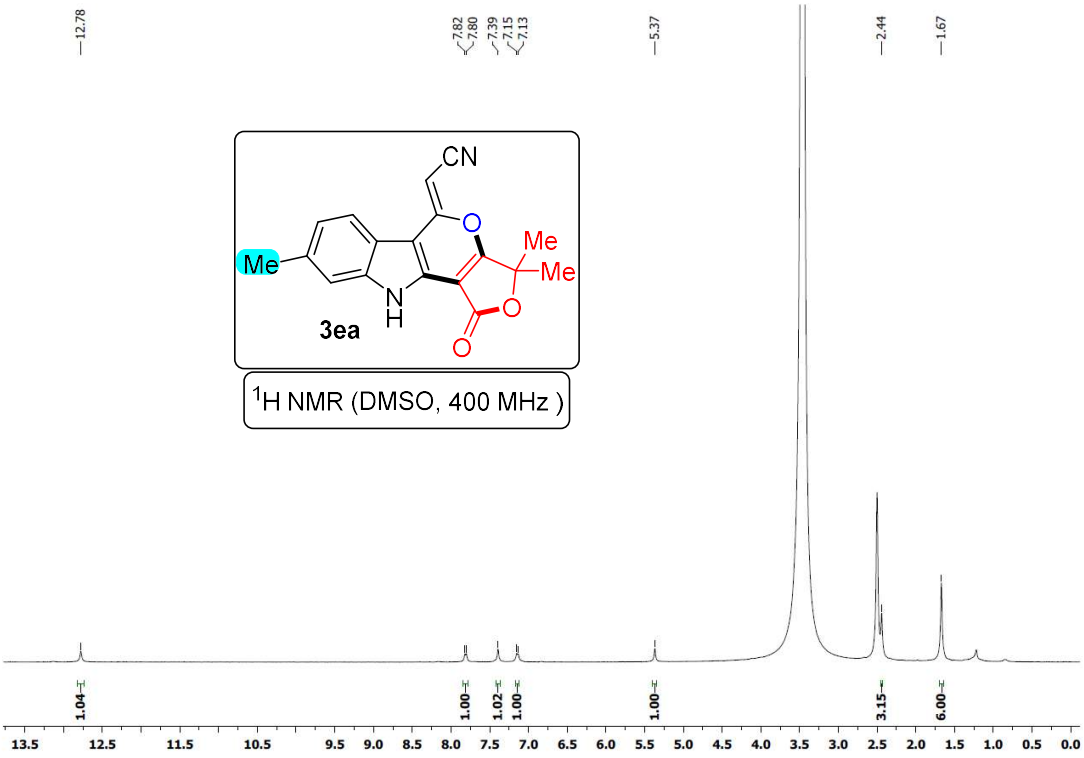

176.8
164.4
162.8
136.5
131.9
130.4
126.1
121.5
119.5
117.5
112.9
101.0
98.0
82.7
64.5
40.0
39.9
39.7
39.5
39.4
39.2
39.0
24.0
21.3
CN
Me
O
Me
Me
N
H
O
O
3ba
13C NMR (DMSO, 125 MHz)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

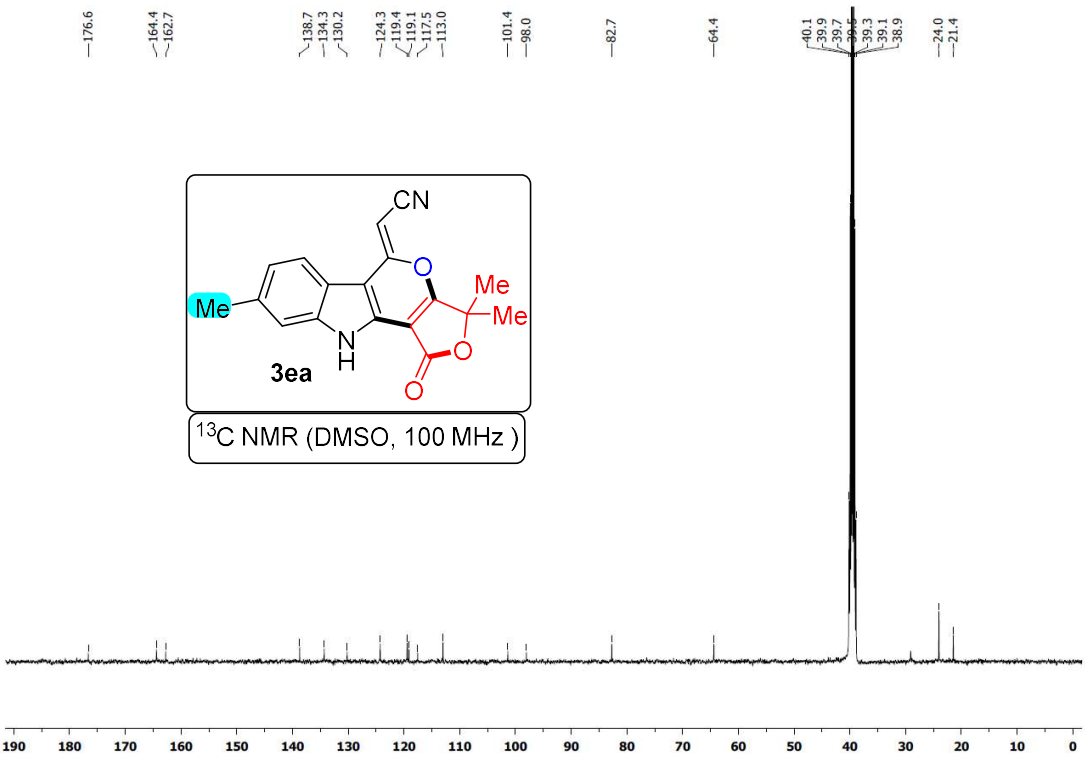

12.77
7.50
7.48
7.31
7.00
6.98
5.47
3.85
1.67
CN
MeO
O
Me
Me
N
H
O
O
3ca
1H NMR (DMSO, 400 MHz)
1.00
1.17
1.00
1.12
1.00
3.16
6.00
13.5 12.5 11.5 10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0


176.6
164.4
162.6
156.0
132.9
130.5
127.5
122.0
117.6
114.3
114.0
101.9
101.2
97.9
82.7
64.8
55.9
40.1
39.9
39.7
39.5
39.3
39.1
38.9
24.0
CN
MeO
O
Me
Me
N
H
O
O
3ca
13C NMR (DMSO, 100 MHz)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

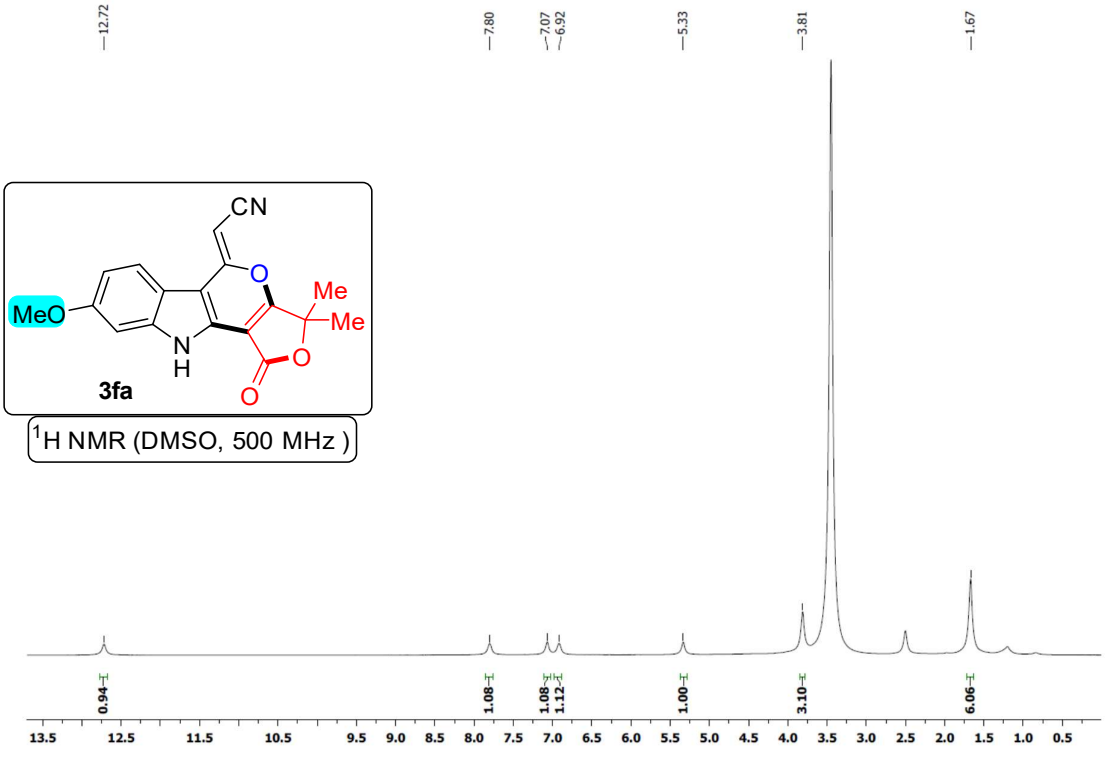

12.78
7.50
7.49
7.46
7.41
7.40
7.39
7.35
7.33
7.32
7.07
7.05
5.48
5.19
1.67
Ph
O
CN
O
Me
Me
N
H
O
O
3da
1H NMR (DMSO, 500 MHz)
1.03
3.09
1.02
2.06
1.11
1.09
1.03
2.00
6.11
13.5
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0


Ph
O
CN
O
Me
Me
N
H
O
O
3da
^{13}C NMR (DMSO,125 MHz)

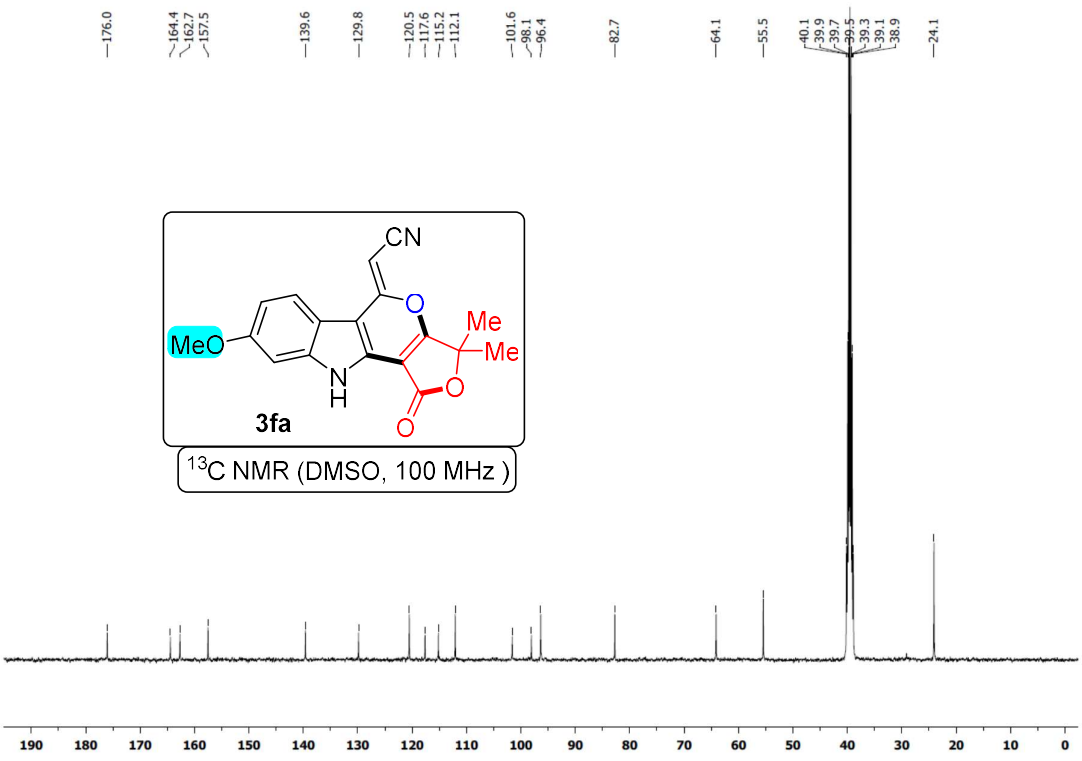

CN
O
Me
Me
Me
N
H
O
O
3ea
^{1}H NMR (DMSO, 400 MHz)

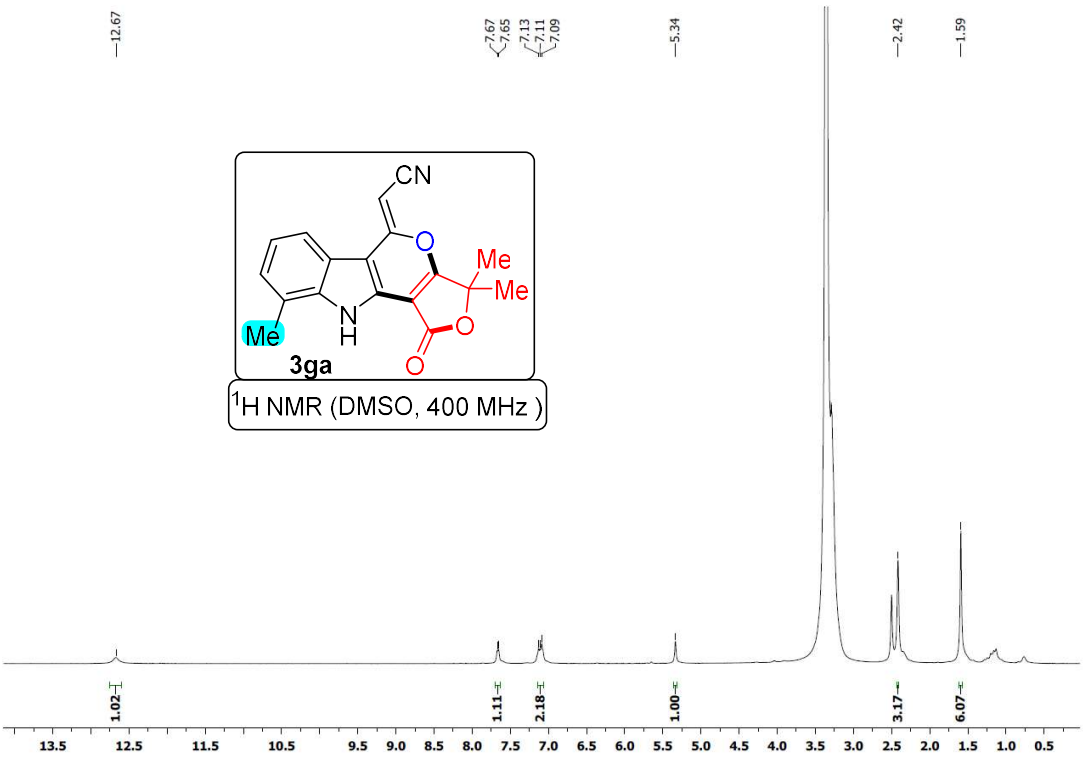


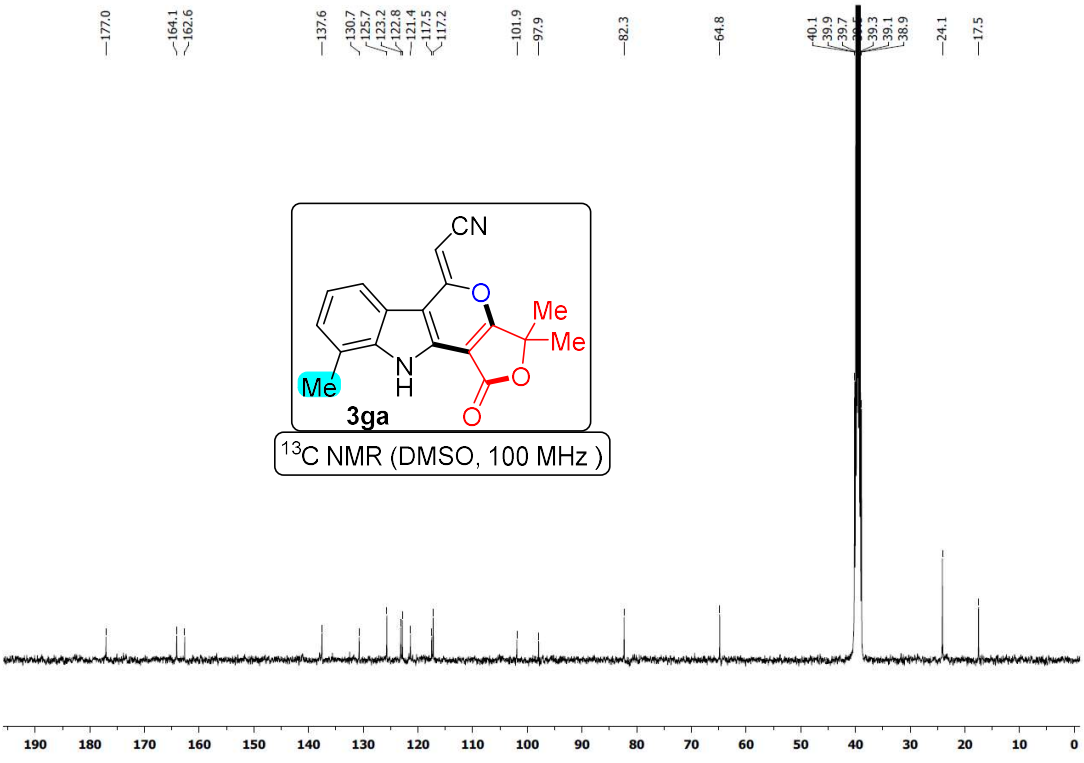
^{13}C NMR (DMSO, 100 MHz)

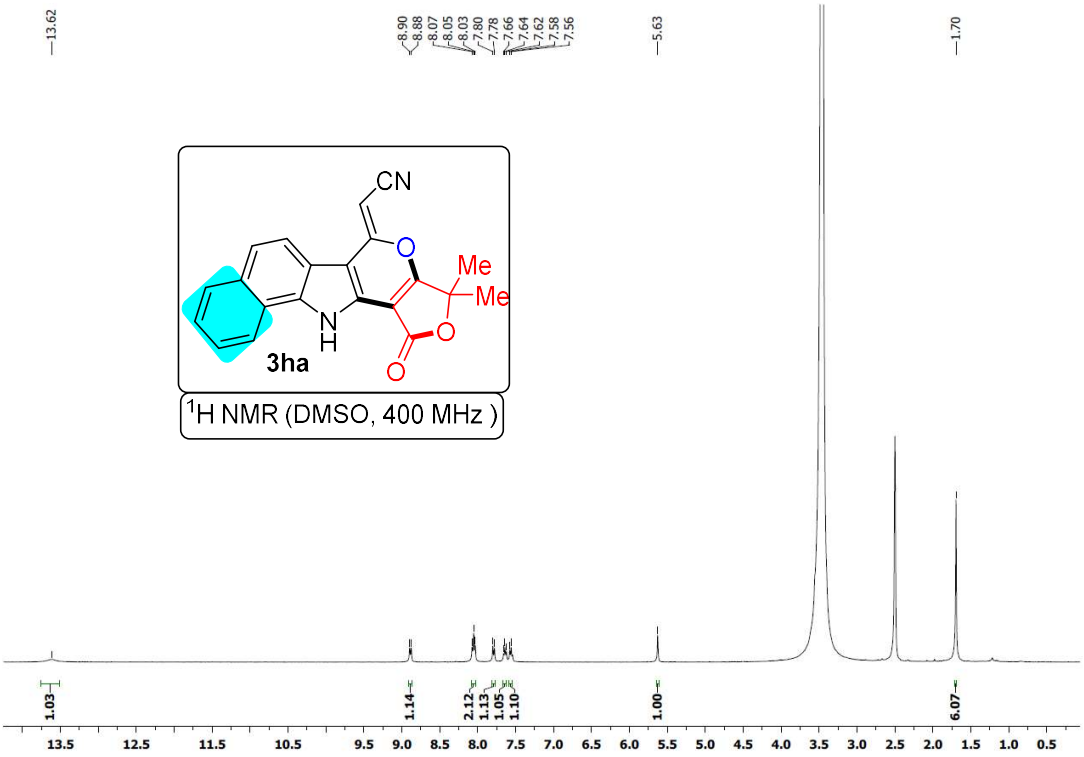


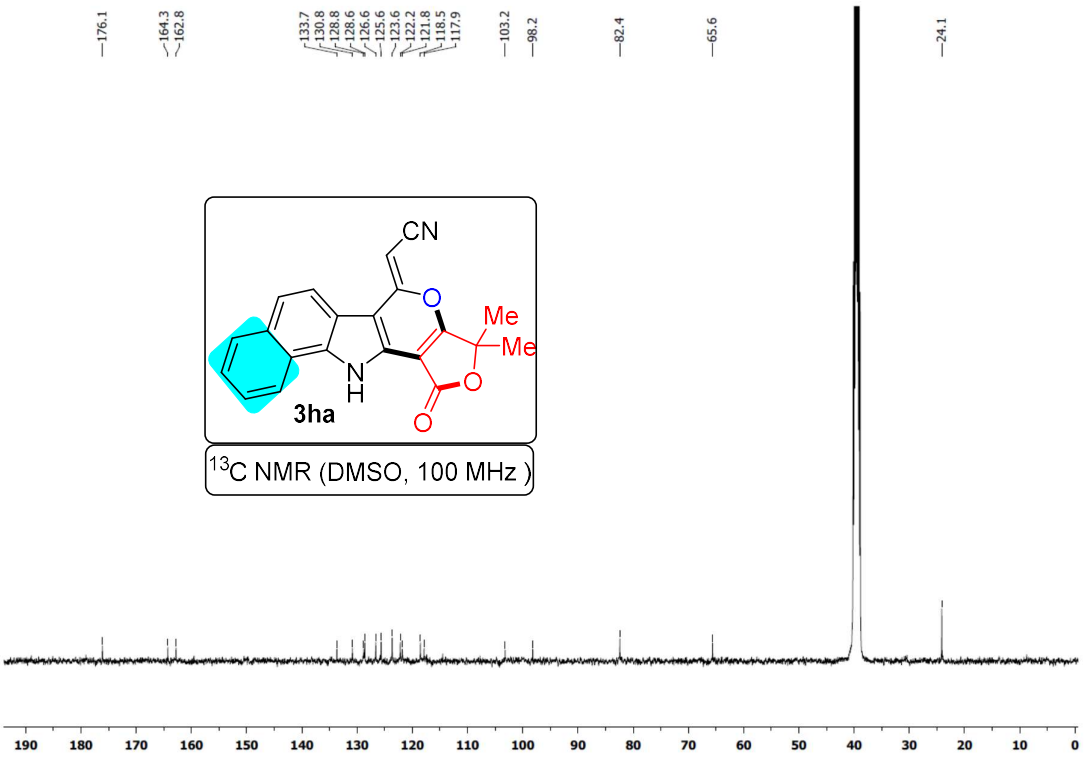
^{1}H NMR (DMSO, 500 MHz)

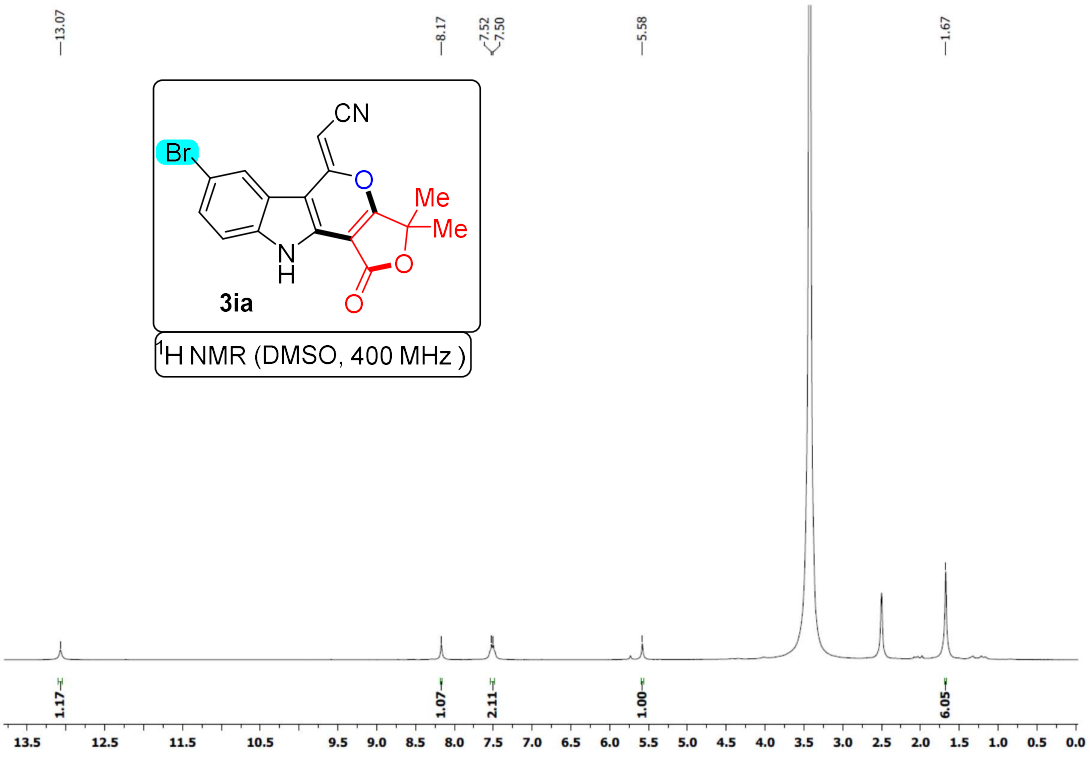

176.0
164.4
162.7
157.5
139.6
129.8
120.5
117.6
115.2
112.1
101.6
98.1
96.4
82.7
64.1
55.5
40.1
39.9
39.7
39.5
39.3
39.1
38.9
24.1
CN
O
Me
Me
MeO
N
H
O
O
3fa
13C NMR (DMSO, 100 MHz)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


12.67
7.67
7.65
7.13
7.11
7.09
5.34
2.42
1.59
CN
O
Me
Me
N
H
Me
O
O
3ga
1H NMR (DMSO, 400 MHz)
1.02
1.11
2.18
1.00
3.17
6.07
13.5
12.5
11.5
10.5
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

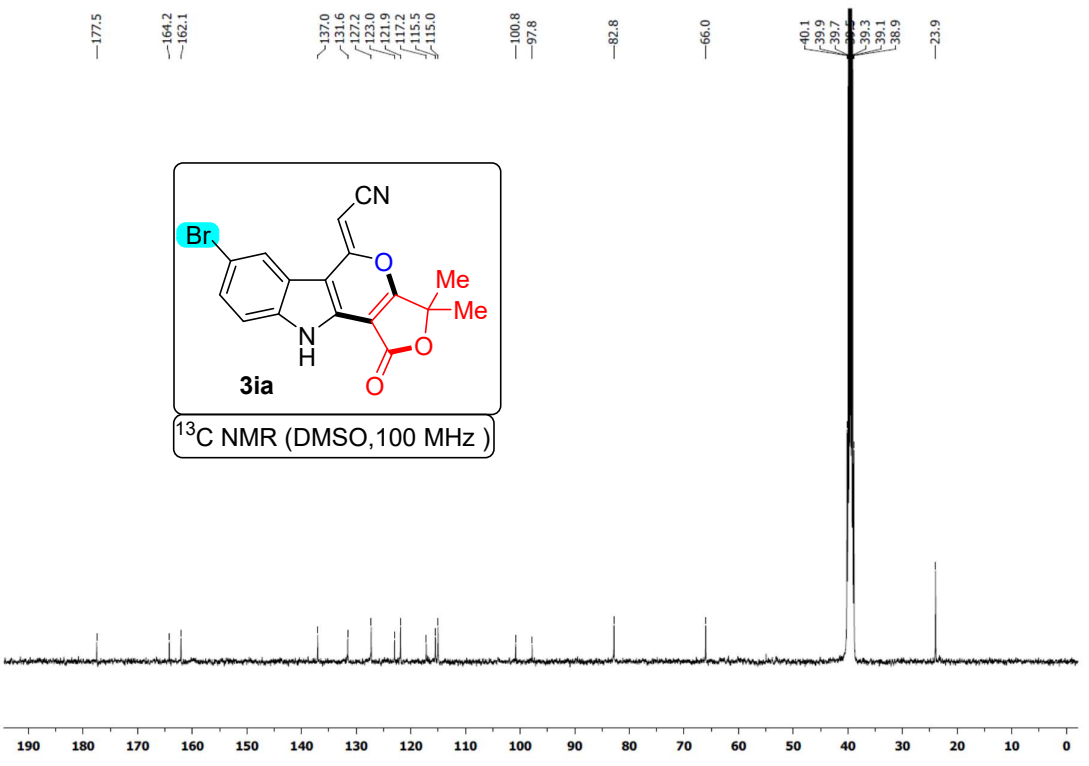

177.0
164.1
162.6
137.6
130.7
125.7
123.2
122.8
121.4
117.5
117.2
101.9
97.9
82.3
64.8
40.1
39.9
39.7
39.3
39.1
38.9
24.1
17.5
CN
O
Me
Me
N
H
Me
O
O
3ga
13C NMR (DMSO, 100 MHz)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


13.62
8.90
8.88
8.07
8.05
8.03
7.80
7.78
7.66
7.64
7.62
7.58
7.56
5.63
1.70
CN
O
Me
Me
N
H
O
O
3ha
1H NMR (DMSO, 400 MHz)
1.03
1.14
2.12
1.13
1.05
1.10
1.00
6.07
13.5
12.5
11.5
10.5
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

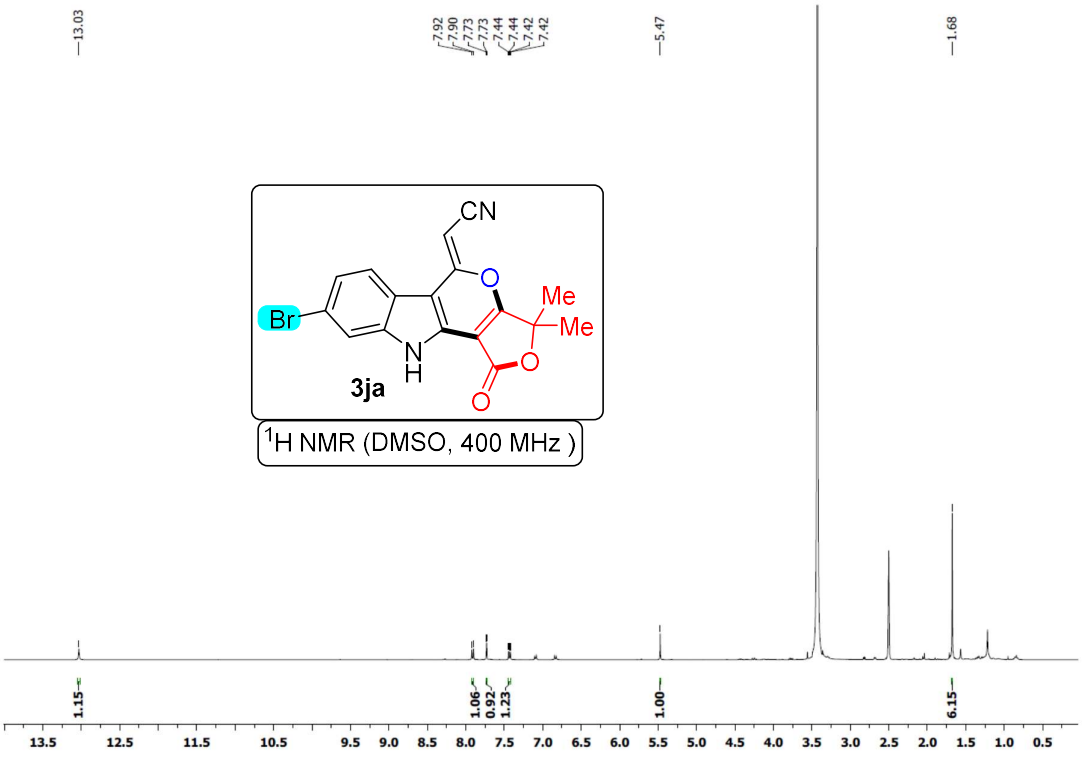

176.1
164.3
162.8
133.7
130.8
128.8
128.6
126.6
125.6
123.6
122.2
121.8
118.5
117.9
103.2
98.2
82.4
65.6
24.1
CN
O
Me
Me
N
H
O
O
3ha
13C NMR (DMSO, 100 MHz)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0



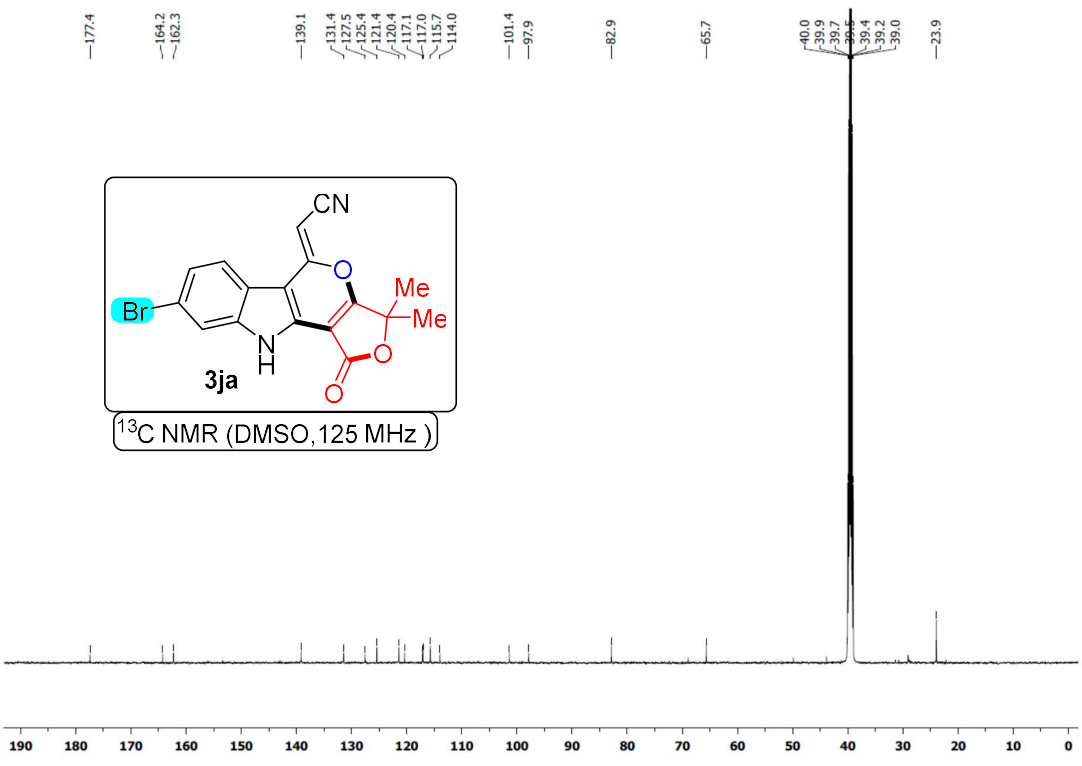
^{1}H NMR (DMSO, 400 MHz)



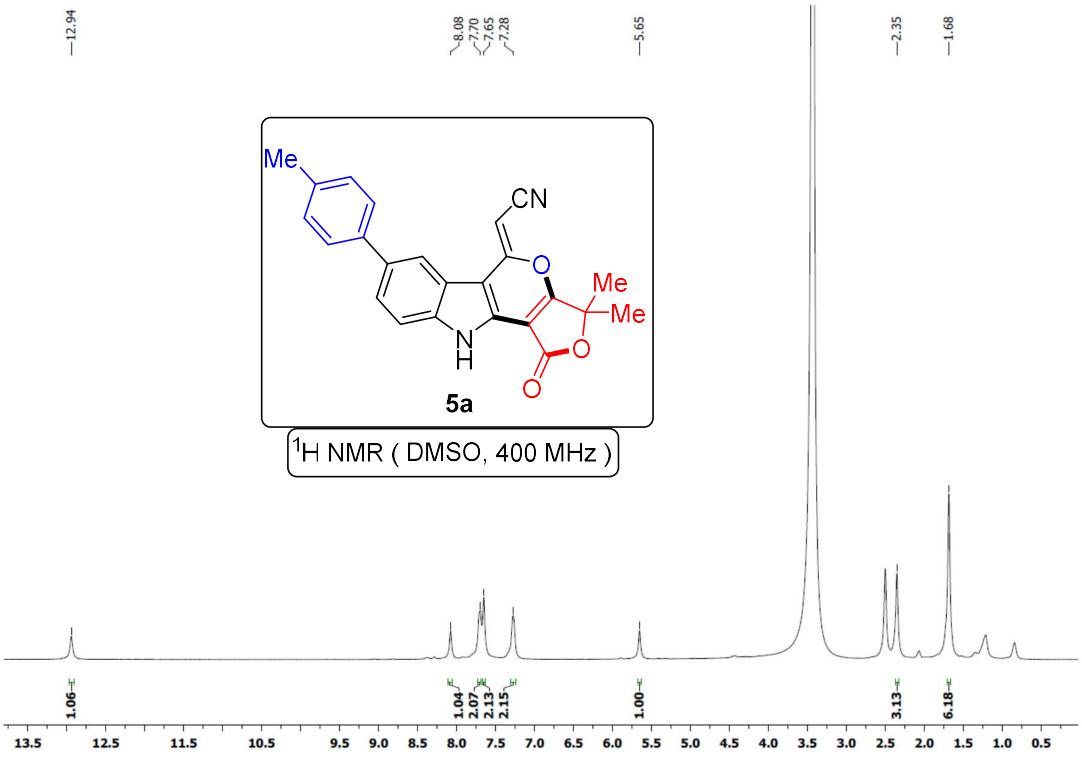
^{13}C NMR (DMSO,100 MHz)

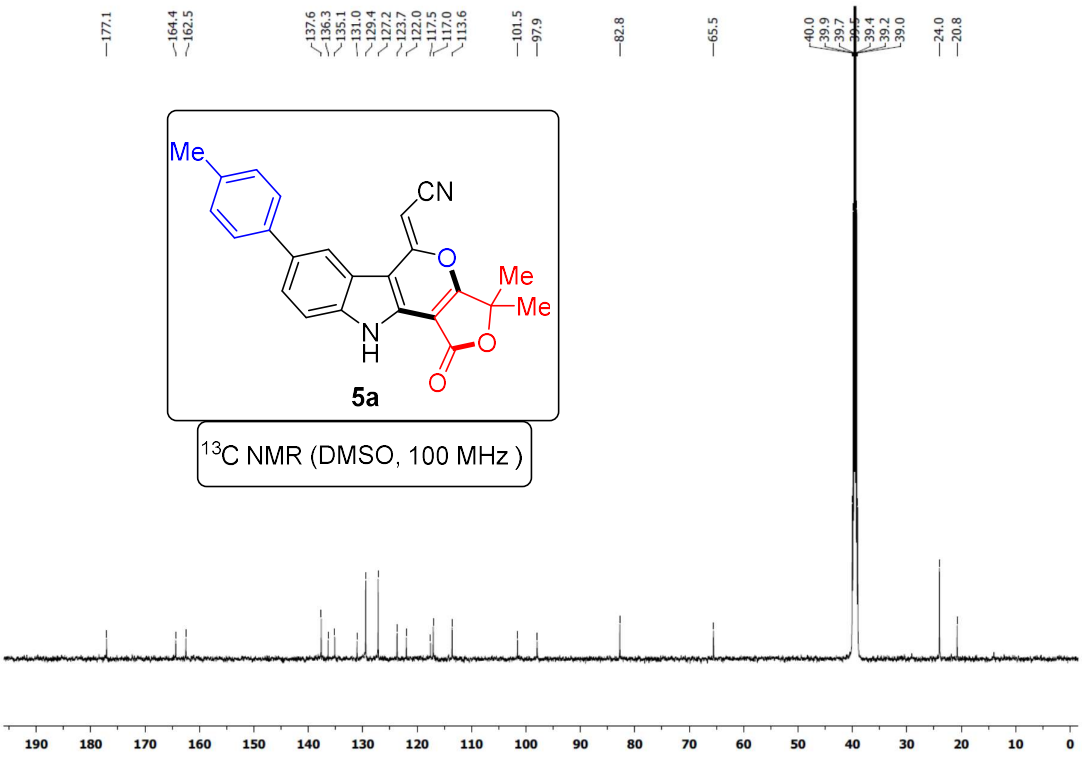


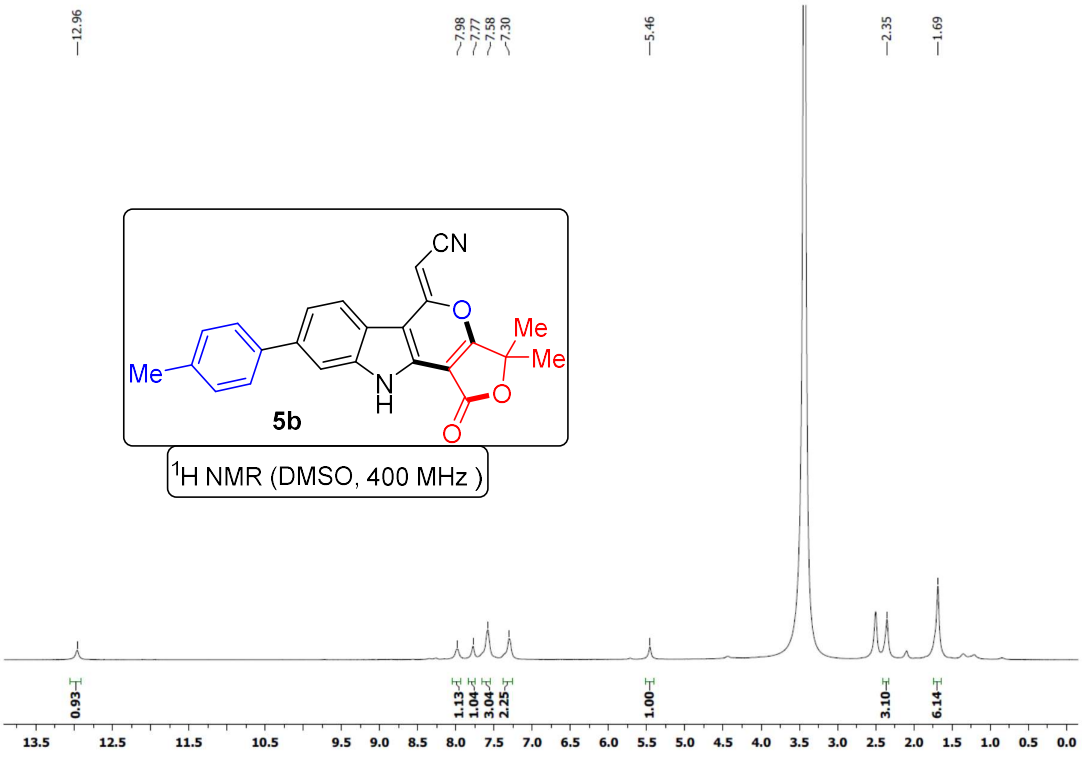
^{1}H NMR (DMSO, 400 MHz)



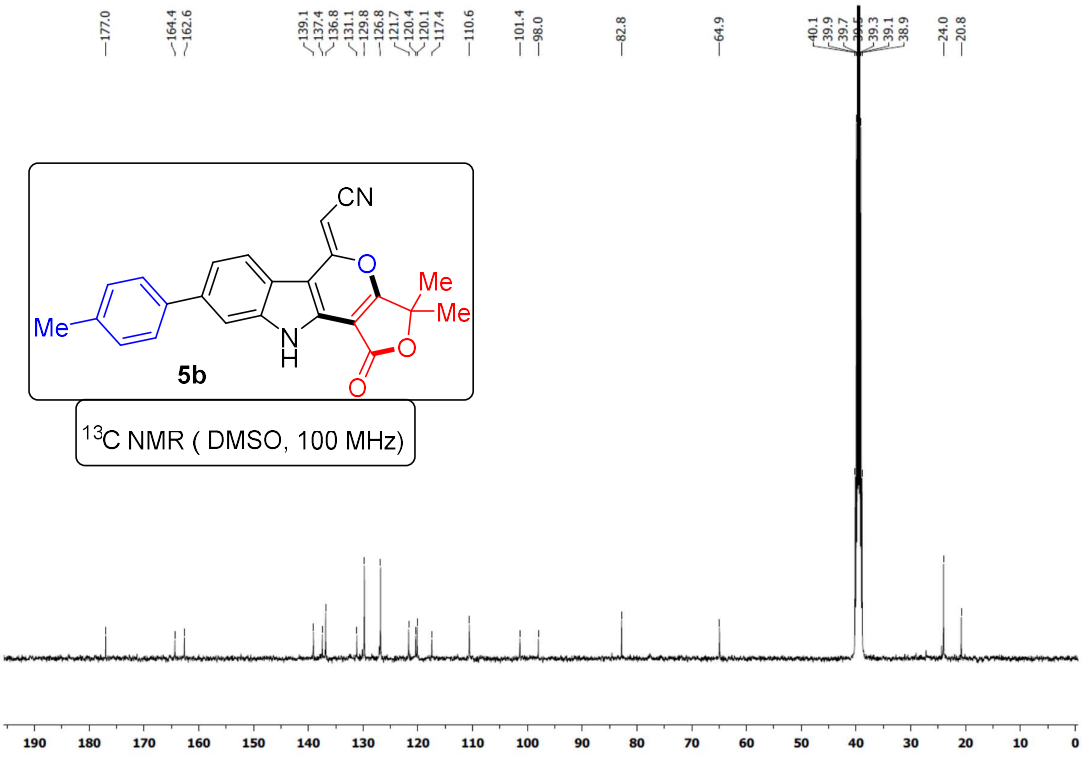
^{13}C NMR (DMSO,125 MHz)


12.94
8.08
7.70
7.65
7.28
5.65
2.35
1.68
Me
CN
O
Me
Me
N
H
O
O
5a
1H NMR (DMSO, 400 MHz)
1.06
1.04
2.07
2.13
2.15
1.00
3.13
6.18
13.5
12.5
11.5
10.5
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


177.1
164.4
162.5
137.6
136.3
135.1
131.0
129.4
127.2
123.7
122.0
117.5
117.0
113.6
101.5
97.9
82.8
65.5
40.0
39.9
39.7
39.5
39.4
39.2
39.0
24.0
20.8
Me
CN
O
Me
Me
N
H
O
O
5a
13C NMR (DMSO, 100 MHz)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

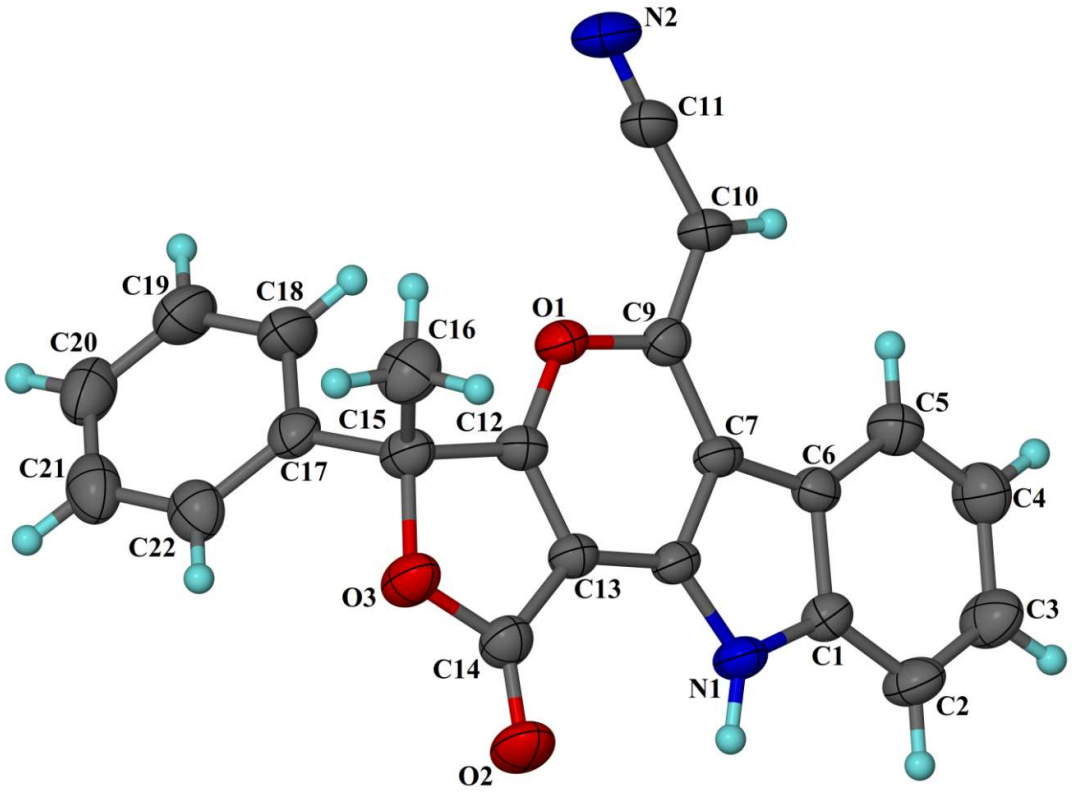


^{1}H NMR (DMSO, 400 MHz)



^{13}C NMR (DMSO, 100 MHz)

8. X-ray crystallography data:



Sample Preparation for Crystal Growth: The compound **3aa** was dissolved in acetone in beaker and kept for slow evaporation at room temperature. Formation of needle shape crystals was observed after three days. The single crystals were then subjected to X-ray diffraction analysis.

Figure caption: ORTEP diagram of KB658 compound with the atom-numbering. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radius. **CCDC deposition number 2234910** contains the supplementary crystallographic data for this paper which can be obtained free of charge at https://www.ccdc.cam.ac.uk/structures/

Crystal data for KB658: $C_{22}H_{14}N_2O_3$, M = 354.35, Monoclinic, Space group *Cc* (No. 9), a = 9.8625(12)Å, b = 24.973(3)Å, c = 7.5384(10)Å, α = 90°, β = 111.143(4)°, γ = 90°, V = 1731.7(4)Å^3, Z = 4, D_c = 1.359 g/cm^3, F_{000} = 736, Bruker D8 QUEST PHOTON-III-C7 detector, Mo-Kα radiation, λ = 0.71073 Å, T = 293(2)K, $2\theta_{max}$ = 55º, μ = 0.092 mm^{-1}, 22582 reflections collected, 3617 unique (R_{int} = 0.0651), 249 parameters, *R1* = 0.0394, *wR2* =

0.0738, *R* indices based on 2539 reflections with I > 2σ(I) (refinement on F^2), Final *GooF* = 1.012, largest difference hole and peak = -0.179 and 0.133 e.Å^{-3}.

Data collection and Structure solution details:

X-ray data for the compound were collected at room temperature on a Bruker D8 QUEST instrument with an IμS Mo microsource (λ = 0.7107Å) and a PHOTON-III C7 HPAD detector. The raw data frames were reduced and corrected for absorption effects using the Bruker Apex 3 software suite programs [1]. The structure was solved using intrinsic phasing method [2] and further refined with the SHELXL [2-4] program and expanded using Fourier techniques. Anisotropic displacement parameters were included for all non-hydrogen atoms. All C bound H atoms were positioned geometrically and treated as riding on their parent C atoms [C-H = 0.93-0.97 Å, and Uiso(H) = 1.5Ueq(C) for methyl H or 1.2Ueq(C) for other H atoms]. The N bound H atom was located in the difference Fourier map. **CCDC deposition number 2234910** contains the supplementary crystallographic data for this paper which can be obtained free of charge at https://www.ccdc.cam.ac.uk/structures/

1. Bruker (2016). APEX3, SAINT and SADABS. Bruker AXS, Inc., Madison, Wisconsin, USA.
2. G. M. Sheldrick, Acta Crystallogr., 2015, C71: 3-8.
3. C. B. Hübschle, G. M. Sheldrick and B. Dittrich, ShelXle: a Qt graphical user interface for SHELXL, *J. Appl. Cryst.*, 2011, 44, 1281-1284.
4. Muller, P, Herbst-Imer, R, Spek, A. L, Schneider, T. R, and Sawaya, M. R. Crystal Structure Refinement: A Crystallographer's Guide to SHELXL. Muller, P. Ed. 2006 Oxford University Press: Oxford, New York, pp. 57–91.

checkCIF/PLATON report

Structure factors have been supplied for datablock(s) KB658_0m_a

THIS REPORT IS FOR GUIDANCE ONLY. IF USED AS PART OF A REVIEW PROCEDURE FOR PUBLICATION, IT SHOULD NOT REPLACE THE EXPERTISE OF AN EXPERIENCED CRYSTALLOGRAPHIC REFEREE.

No syntax errors found. CIF dictionary Interpreting this report

Datablock: KB658_0m_a

```
Bond precision:   C-C = 0.0046 A          Wavelength=0.71073

Cell:             a=9.8625(12)     b=24.973(3)         c=7.5384(10)
                  alpha=90         beta=111.143(4)     gamma=90
Temperature:      293 K

                  Calculated                Reported
Volume            1731.7(4)                 1731.7(4)
Space group       C c                       C c
Hall group        C -2yc                    C -2yc
Moiety formula    C22 H14 N2 O3             C22 H14 N2 O3
Sum formula       C22 H14 N2 O3             C22 H14 N2 O3
Mr                354.35                    354.35
Dx,g cm-3         1.359                     1.359
Z                 4                         4
Mu (mm-1)         0.092                     0.092
F000              736.0                     736.0
F000'             736.34
h,k,lmax          12,32,9                   12,32,9
Nref              3966[ 1991]               3617
Tmin,Tmax         0.970,0.976               0.637,0.746
Tmin'             0.969

Correction method= # Reported T Limits: Tmin=0.637 Tmax=0.746
AbsCorr = MULTI-SCAN

Data completeness= 1.82/0.91        Theta(max)= 27.500

R(reflections)= 0.0394( 2359)                    wR2(reflections)=
                                                 0.0892( 3617)
S = 1.012                 Npar= 249
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The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

Alert level C

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STRVA01_ALERT_4_C           Flack test results are meaningless.
          From the CIF: _refine_ls_abs_structure_Flack   -0.100
          From the CIF: _refine_ls_abs_structure_Flack_su    0.600
PLAT340_ALERT_3_C Low Bond Precision on  C-C Bonds ..............    0.00461 Ang.
PLAT767_ALERT_4_C INS Embedded LIST 6 Instruction Should be LIST 4     Please Check
```

Alert level G

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PLAT032_ALERT_4_G Std. Uncertainty on Flack Parameter Value High .      0.600 Report
PLAT199_ALERT_1_G Reported _cell_measurement_temperature ..... (K)        293 Check
PLAT200_ALERT_1_G Reported   _diffrn_ambient_temperature ..... (K)        293 Check
PLAT792_ALERT_1_G Model has Chirality at C15         (Polar  SPGR)          R Verify
PLAT883_ALERT_1_G No Info/Value for _atom_sites_solution_primary .     Please Do !
PLAT910_ALERT_3_G Missing # of FCF Reflection(s) Below Theta(Min).          2 Note
PLAT913_ALERT_3_G Missing # of Very Strong Reflections in FCF ....         1 Note
PLAT916_ALERT_2_G Hooft y and Flack x Parameter Values Differ by .      0.20 Check
PLAT933_ALERT_2_G Number of HKL-OMIT Records in Embedded .res File         2 Note
PLAT967_ALERT_5_G Note: Two-Theta Cutoff Value in Embedded .res ..      55.0 Degree
PLAT978_ALERT_2_G Number C-C Bonds with Positive Residual Density.         0 Info
```

```
  0 ALERT level A = Most likely a serious problem - resolve or explain
  0 ALERT level B = A potentially serious problem, consider carefully
  3 ALERT level C = Check. Ensure it is not caused by an omission or oversight
 11 ALERT level G = General information/check it is not something unexpected

  4 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
  3 ALERT type 2 Indicator that the structure model may be wrong or deficient
  3 ALERT type 3 Indicator that the structure quality may be low
  3 ALERT type 4 Improvement, methodology, query or suggestion
  1 ALERT type 5 Informative message, check
```

It is advisable to attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so attention to these fine details can be worthwhile. In order to resolve some of the more serious problems it may be necessary to carry out additional measurements or structure refinements. However, the purpose of your study may justify the reported deviations and the more serious of these should normally be commented upon in the discussion or experimental section of a paper or in the "special_details" fields of the CIF. checkCIF was carefully designed to identify outliers and unusual parameters, but every test has its limitations and alerts that are not important in a particular case may appear. Conversely, the absence of alerts does not guarantee there are no aspects of the results needing attention. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.

Publication of your CIF in IUCr journals

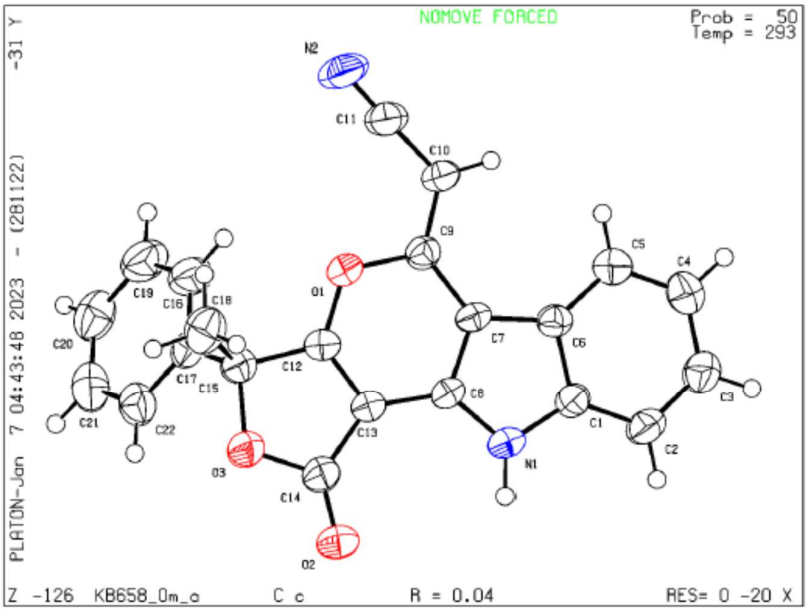
A basic structural check has been run on your CIF. These basic checks will be run on all CIFs submitted for publication in IUCr journals (*Acta Crystallographica*, *Journal of Applied Crystallography*, *Journal of Synchrotron Radiation*); however, if you intend to submit to *Acta Crystallographica Section C* or *E* or *IUCrData*, you should make sure that full publication checks are run on the final version of your CIF prior to submission.

Publication of your CIF in other journals

Please refer to the *Notes for Authors* of the relevant journal for any special instructions relating to CIF submission.

PLATON version of 28/11/2022; check.def file version of 28/11/2022

Datablock KB658_0m_a - ellipsoid plot



References:

1. (a) J. Slätt, I. Romero and J. Bergman, Synthesis., 2004, **16**, 2760; (b) Y. Xiao, H. Xiong, S. Sun, J. Yu and J. Cheng, *Org. Biomol. Chem.*, 2018, **16**, 8715.
2. (a) Y. Xu, B. Li, X. Zhang and X. Fan, *Adv. Synth. Catal.*, 2018, **360**, 2613; (b) G. Liao, H. Song, X.-S. Yin and B.-F. Shi, *Chem. Commun.*, 2017, **53**, 7824.
3. C. Palomo, A. Gonzalez, J. M. García, C. Landa, M. Oiarbide, S. Rodríguez and A. Linden, *Angew. Chem*., *Int. Ed. Engl*., 1998, **37**, 180.
4. (a) C. Spino and C. Beaulieu, *J. Am. Chem. Soc*., 1998, **120**, 11832; (b) C. Spino, C. Beaulieu and J. Lafreniere, *J. Org. Chem.*, 2000, **65**, 7091.
5. (a) K. Yan, B. Li and B. Wang, Adv. Synth. Catal., 2018, **360**, 2272; (b) K. Xu, H. Liu, Y. Hou, J. Shen, D. Liu and W. Zhang, Chem. Commun., 2019, **55**, 13295.
6. (a). L. Cooper, J. M. Alonso, L. Eagling , H. Newson, S. Herath, C. Thomson, A. Lister, C. Howsham, B. Cox and M. P. Muñoz, Chem.–Eur. J., 2018, **24**, 6105; (b) H. Sun, Y. Cheng, H. Teng, X. Chen, X. Niu, H. Yang, Y.-M. Cui, L.-W. Xu and L. Yang, J. Org. Chem., 2022, **87**, 13346; (c) M. Kumar, A. Rastogi, Raziullah, A. Ahmad, M. K. Gangwar, and D. Koley, Org. Lett. 2022, **48**, 8729.
7. K. Wei, T. Yang, Q. Chen, S. Liang and W. Yu, Chem. Commun., 2020, **56**, 11685.