Supporting Information

Carboamination and Olefination: *Ortho* C-H Functionalization of Phenoxyacetamide

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1. General Information:[1a]

Reactions were performed using borosil seal tube vial under N_2 atmosphere. Column chromatography was done by using 100-200 & 230-400 mesh size silica gel of Acme Chemicals. A gradient elution was performed by using distilled petroleum ether and ethyl acetate. TLC plates detected under UV light at 254 nm. ^{1}H NMR and ^{13}C NMR were recorded on Bruker AV 400, 700 MHz spectrometer using $CDCl_3$ and DMSO-d_6 as NMR solvents. The residual $CHCl_3$ and DMSO-H_6 for ^{1}H NMR (δ = 7.26 ppm and 2.54 ppm respectively) were used as reference. The deuterated solvent signal for ^{13}C NMR (δ = 77.36 ppm 40.45 ppm) is used as reference.[1b] Multiplicity (s = single, d = doublet, t = triplet, q = quartet, m = multiplet, dd = double doublet), integration, and coupling constants (*J*) in hertz (Hz). HRMS signal analysis was performed using micro TOF Q-II mass spectrometer. X-ray analysis was conducted using Rigaku Smartlab X-ray diffractometer at SCS, NISER. Reagents and starting materials were purchased from Sigma Aldrich, Alfa Aesar, TCI, Avra, Spectrochem and other commercially available sources and used without further purification unless otherwise noted. Structurally diverse maleimide were synthesized according to literature procedure.[2]

Abbreviations:

$NaHCO_3$ = Sodium bicarbonate, Na_2CO_3 = Sodium carbonate, K_3PO_4 = Tripotassium phosphate, CsOAc = Cesium acetate, Na_2SO_4 = Sodium sulfate, $Zn(OAc)_2$ = Zinc acetate, $AgBF_4$ = Silver tetrafluoroborate, TEMPO = 2,2,6,6-Tetramethylpiperidine 1-oxyl, BHT = Butylated hydroxytoluene, TLC = Thin layer chromatography, EtOAc = Ethyl acetate, TFE = Trifluoroethanol, DCM = Dichloromethane, MeOH = Methanol, D_2O = Deuterium oxide.

(2) Experimental procedure:

(2.1) General procedure for the synthesis of *N*-phenoxyacetamides 1:[3]

Method A: *O*-mesitylsulfonylhydroxylamine (MSH) was prepared according to the literature.[4] Phenol (1.5 equiv) was dissolved in methanol (0.7 M), and then potassium tert-butoxide (1.5 equiv) was added. The mixture was allowed to stir for 0.5 h under argon atmosphere. Then methanol was removed under vacuum, and DMF was added into the residue (1.3 M). Then the freshly prepared *O*-mesitylsulfonylhydroxylamine (1.0 equiv, 0.9 M in DMF) was added under ice cold bath. The mixture was allowed to stir for 2 h, diluted with ethylacetate, and washed with brine. The aqueous layer was extracted with EtOAc, which was then removed under reduced pressure to afford the corresponding *N*-aryloxyamine. Na_2CO_3 (1.5 equiv) and H_2O/EtOAc (v/v 1/2, 1.0 M) was next added to the reaction flask. The resulting solution was kept under ice bath followed by dropwise addition of acyl chloride (1.2 equiv). After stirring at 0 ºC for 2 h, the reaction was quenched with saturated $NaHCO_3$ and diluted with EtOAc. The organic phase was washed twice with saturated $NaHCO_3$, dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel to provide the desired product.

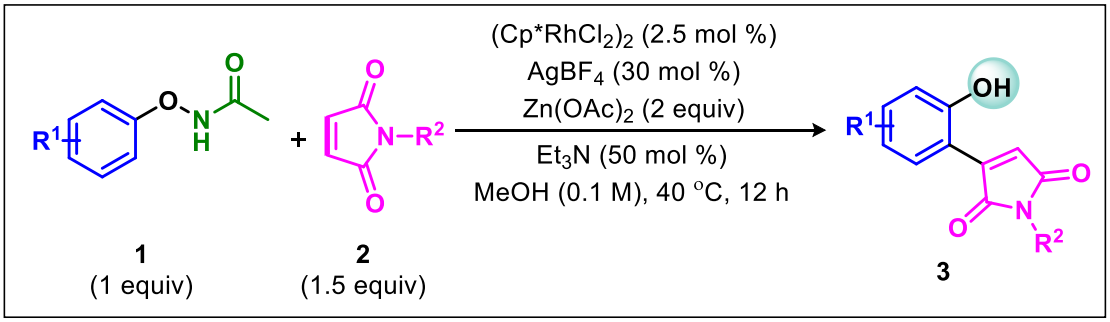
Method B:[5] A mixture of *N*-hydroxyphthalimide (1.0 equiv), arylboronic acid (2.0 equiv), CuCl (1.0 equiv), freshly activated 4Å molecular sieves (250mg/mmol) and pyridine (1.1 equiv.) were dissolved in 1,2-dichloroethane (0.25 M) and stirred at room temperature under air. After 48-120 hours, the reaction mixture turned green. Silica gel was added to the flask and the solvent was evaporated under reduced pressure. The purification was performed by flash column chromatography on silica gel to afford desired *N*-aryloxyphthalimides. The product was directly used for the next step.

Hydrazine monohydrate (4.00 equiv., 51- 64%) was added to the solution of *N*-aryloxyphthalimide (1.0 equiv) in DCM (0.25 M). The reaction was stirred at room temperature overnight. $MgSO_4$ was added to the mixture and the suspension was stirred for additional 10 minutes. The precipitate was filtered off and washed with DCM followed by EtOAc. The filtrate was concentrated and the resulting oil was directly used without further purification. *N*-aryloxyamine (1.0 equiv.) was

dissolved in DCM (0.2 M). The resulting solution was cooled to 0 °C and acetic anhydride (1.10 equiv.) was added dropwise to the mixture. After stirring at room temperature for 3 h the reaction was quenched with saturated $NaHCO_3$ and extracted with DCM. The organic phase was washed three times with saturated $NaHCO_3$ and dried over anhydrous Na_2SO_4, followed by filtration. The solvent was evaporated under reduced pressure. The crude product was purified by recrystallization from EtOAc/pentane to afford the desired *N*-aryloxyacetamide **2**.

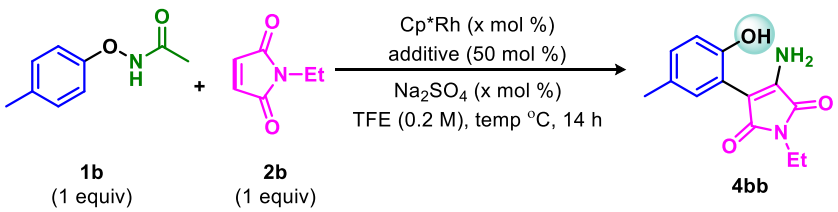
(3) Catalysis reactions:

(3.1) General procedure for the Cp*Rh catalyzed C-H olefination of aryloxyacetamide 1 with maleimide 2:



To an oven-dried seal tube charged with a stir bar, aryloxy acetamide **1** (0.1 mmol, 1 equiv), maleimide **2** (0.15 mmol, 1.5 equiv), $(Cp^*RhCl_2)_2$ (0.0025 mmol, 2.5 mol %), $Zn(OAc)_2$ (0.2 mmol, 2.0 equiv), Et_3N (0.05 mmol, 50 mol %) and MeOH (1.0 mL, 0.1 M with respect to **1)** were added under nitrogen atmosphere. The seal tube was taken inside the glove box and $AgBF_4$ (0.03 mmol, 30 mol %) was added. The reaction mixture was stirred (700 rpm) in a preheated aluminum block at 40 ℃ for 12 h. After completion of the reaction (monitored by TLC), the solvent was evaporated under reduced pressure, and the crude was purified by column chromatography using EtOAc/hexane as eluent to get the corresponding *ortho*-olefinated product **3**.

(3.2) Table S1: Optimization table for Cp*Rh catalyzed C-H olefination of aryloxyacetamide **1** followed by intermolecular C-H amination of maleimide **2**.

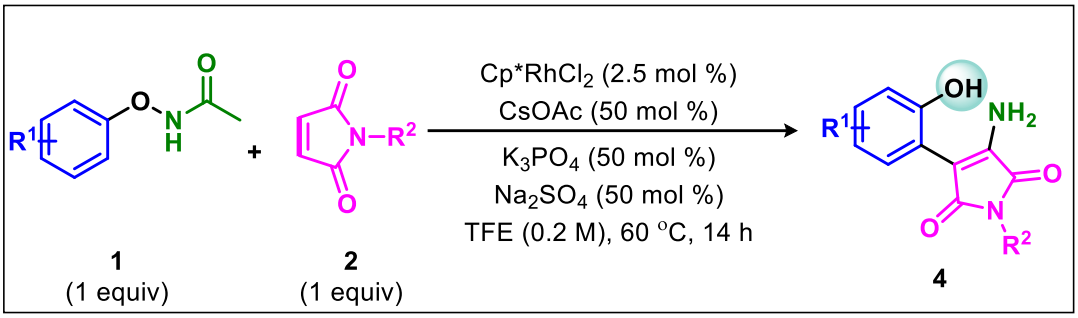


1b (1 equiv) + **2b** (1 equiv) → **4bb**

entry	catalyst	additive (50 mol %)	solvent (0.2 M)	temp °C	yield of **4bb** (%)[b]
1	Cp*[Rh] (5 mol %)	CsOAc + K_3PO_4	TFE	60	11
2	Cp*[Rh] (5 mol %)	CsOAc + K_3PO_4	TFE	rt	nd
3	Cp*[Rh] (5 mol %)	CsOAc + K_3PO_4	TFE	40	6
4	Cp*[Rh] (5 mol %)	CsOAc + K_3PO_4	TFE	80	30
5	Cp*[Rh] (2.5 mol %)	CsOAc + K_3PO_4	TFE	60	36
6	Cp*$RhCl_2$ (2.5 mol %)	CsOAc + K_3PO_4	TFE	60	48
7	Cp*$RhCl_2$ (2.5 mol %)	LiOAc + K_3PO_4	TFE	60	28
8	Cp*$RhCl_2$ (2.5 mol %)	NaOAc + K_3PO_4	TFE	60	40
9	Cp*$RhCl_2$ (2.5 mol %)	KOAc + K_3PO_4	TFE	60	43
10	Cp*$RhCl_2$ (2.5 mol %)	Cs_2CO_3 + K_3PO_4	TFE	60	19
11	**Cp*$RhCl_2$ (2.5 mol %)**	**CsOAc + K_3PO_4 + Na_2SO_4 (50 mol %)**	TFE	**60**	**65[c]**
12	Cp*$RhCl_2$ (2.5 mol %)	CsOAc + K_3PO_4 + $MgSO_4$ (50 mol %)	TFE	60	50
13	Cp*$RhCl_2$ (2.5 mol %)	CsOAc + K_3PO_4 + 4A MS (50 mol %)	TFE	60	38
14	Cp*$RhCl_2$ (2.5 mol %)	CsOAc + K_3PO_4 + Na_2SO_4 (50 mol %)	MeOH	60	15
15	Cp*$RhCl_2$ (2.5 mol %)	CsOAc + K_3PO_4 + Na_2SO_4 (50 mol %)	EtOH	60	10
16	Cp*$RhCl_2$ (2.5 mol %)	CsOAc + K_3PO_4 + Na_2SO_4 (50 mol %)	HFIP	60	nd
17	Cp*$RhCl_2$ (2.5 mol %)	CsOAc + K_3PO_4 + Na_2SO_4 (50 mol %)	DCM	60	nd
18	Cp*$RhCl_2$ (2.5 mol %)	CsOAc + K_3PO_4 + Na_2SO_4 (50 mol %)	CH_3CN	60	nd
19	Cp*$RhCl_2$ (2.5 mol %)	CsOAc + K_3PO_4 + Na_2SO_4 (100 mol %)	TFE	60	30
20	--	CsOAc + K_3PO_4 + Na_2SO_4 (50 mol %)	TFE	60	nd

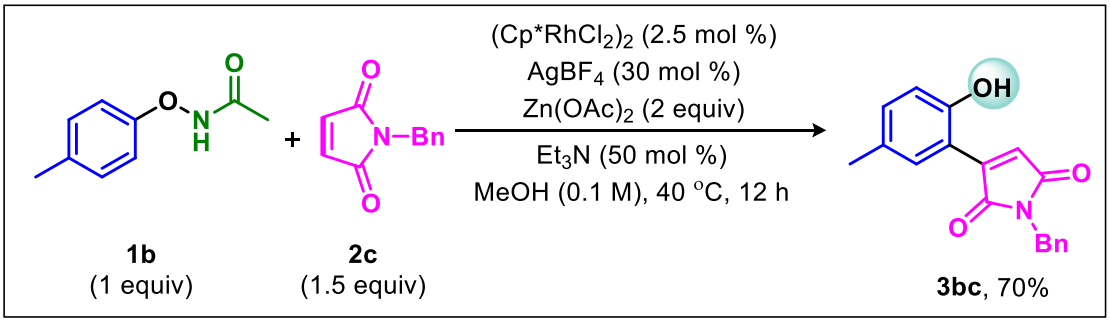
[a]Reaction conditions: **1b** (0.1 mmol), **2b** (0.15 mmol), Cp*[Rh] = $[Cp^*Rh(CH_3CN)_3]$ $(SbF_6)_2$, $(Cp^*RhCl_2)_2$ (2.5 mol %), additives (50 mol %), TFE (0.5 mL), temp °C, N_2. [b]NMR yield (1,3,5-trimethoxy benzene was used as internal standard), [c]Isolated yield.

(3.3) General procedure for the Cp*Rh catalyzed C-H olefination of aryloxyacetamide 1 followed by intermolecular C-H amination of maleimide 2.



To an oven-dried seal tube charged with a stir bar, aryloxy acetamide **1** (0.1 mmol, 1 equiv), maleimide **2** (0.1 mmol, 1.0 equiv), $(Cp^*RhCl_2)_2$ (0.0025 mmol, 2.5 mol %), Na_2SO_4 (0.05 mmol, 50 mol %), and TFE (0.5 mL, 0.2 M with respect to **1)** were added under nitrogen atmosphere. The seal tube was taken inside the glove box and CsOAc (0.05 mmol, 50 mol %), and K_3PO_4 (0.05 mmol, 50 mol %), were added. The reaction mixture was stirred (700 rpm) in a preheated aluminum block at 60 °C for 14 h. After completion of the reaction (monitored by TLC), the solvent was evaporated under reduced pressure and the crude was purified by column chromatography using EtOAc/hexane as eluent to get the corresponding product **4**.

(3.4) General procedure for the Cp*Rh catalyzed olefination reaction of aryloxy acetamide 1b in 1 mmol scale:



To an oven-dried seal tube charged with a stir bar, *N*-(*p*-tolyloxy)acetamide **1b** (1.0 mmol, 1 equiv), *N*-benzyl maleimide **2c** (1.5 mmol, 1.5 equiv), $(Cp^*RhCl_2)_2$ (0.025 mmol, 2.5 mol %), $Zn(OAc)_2$ (2.0 mmol, 2.0 equiv), Et_3N (0.5 mmol, 50 mol %) and MeOH (10.0 mL, 0.1 M with

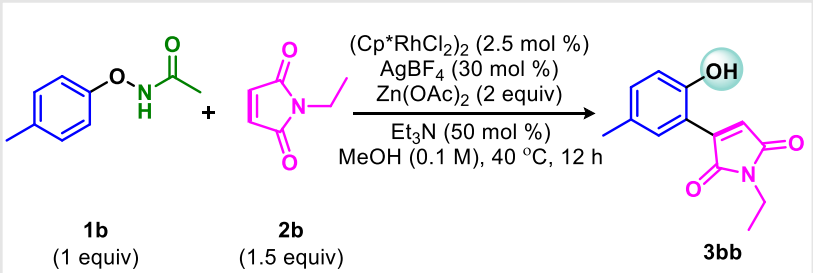
respect to **1**) were added under nitrogen atmosphere. The seal tube was taken inside the glove box and $AgBF_4$ (0.3 mmol, 30 mol %) was added. The reaction mixture was stirred (700 rpm) in a preheated aluminum block at 40 ℃ for 12 h. After completion of the reaction (monitored by TLC), the solvent was evaporated under reduced pressure, and the crude was purified by column chromatography using EtOAc/hexane as eluent to get the corresponding *ortho*-olefinated product **3bd** in 70% (205 mg).

(3.5) RESULTS AND DISCUSSION

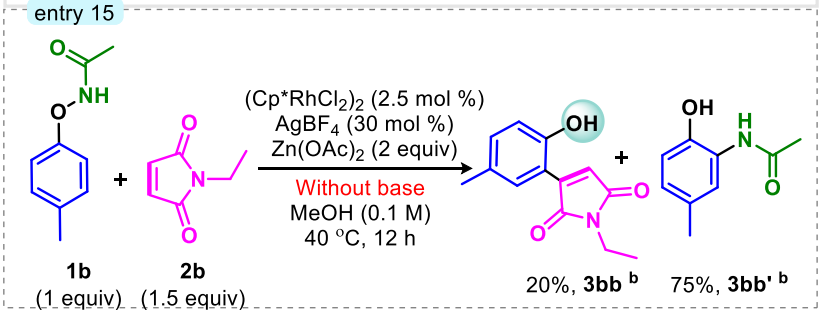
We began our investigation by taking *p*-tolyl phenoxyacetamide **1b** as the model substrate and *N*-Et maleimide **2b** as the coupling partner. After an extensive screening of various parameters, a catalytic condition comprising of $(Cp^*RhCl_2)_2$ (2.5 mol %), $AgBF_4$ (30 mol %), $Zn(OAc)_2$ (2 equiv), Et_3N (50 mol %), and MeOH solvent (0.1M) at 40 °C in 12 h provided the desired product **3bb** in 74 % yield (Table S2, entry 1). To ascertain the working limits of this condition, we varied different parameters. At first, the reaction temperature was changed to room temperature, 60 °C, and 80 °C (Table S2, entry 2-4).

yield (Table S2, entries 5, 6). The effect of various silver salt in the reaction has been tested, and sulphate was found to be a suitable counter anion to stabilize the active catalyst after tetrafluoroborate (Table S2, entries 7-9). As the base plays a very crucial role, carbonate and acetate bases have been employed; however, we have not observed any superior results (Table S2, entries 10, 11). Next, the catalyst loading was increased from 2.5 mol % to 5 mol %, and in this case, only a 50% yield of the desired product was observed (Table S2, entry 12). May be the availability of excess rhodium catalyst is consuming the substrate by undergoing oxidative addition between the O-N bond leading to the deactivation of the directing group. The control experiment without Rh catalyst and $Zn(OAc)_2$ suggested that they play a very crucial role (Table S2, entry 13, 14). While $(Cp^*RhCl_2)_2$ acts as a catalyst to activate the C-H bond, $Zn(OAc)_2$ may serve as a Lewis acid[6] to activate the maleimide double bond to undergo effective olefin insertion. The role of the base can be explained from the control experiment (Table S2, entry 15).

Table S2. Optimization of Reaction Conditions[a,b,c]



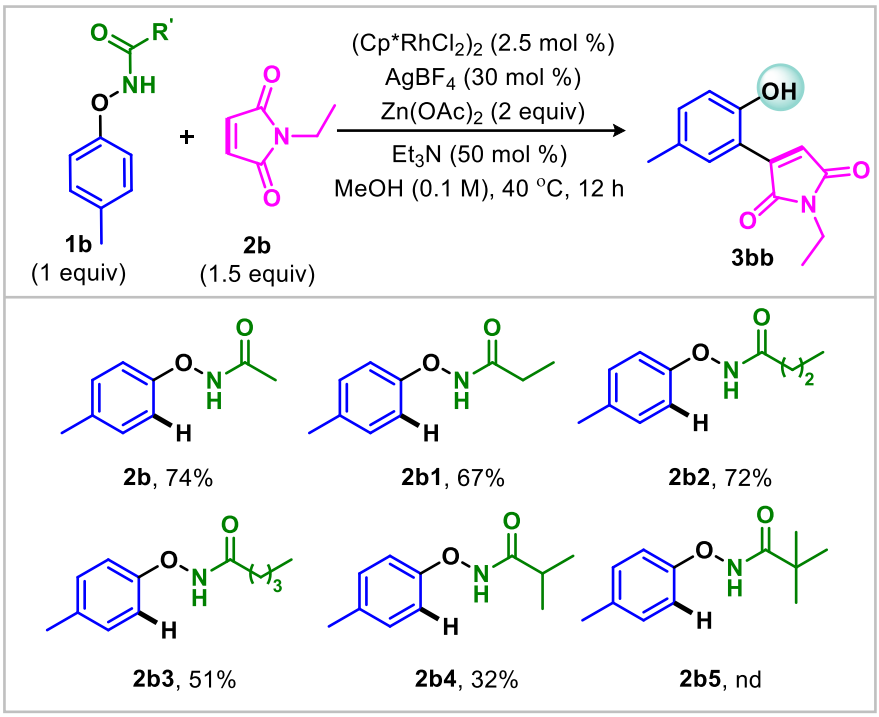
entry	deviation from the standard conditions	yield of **3bb** (%)[b]
1	**none**	**74[c]**
2	Room temprature	62
3	60 °C	45
4	80 °C	26
5	**2c**, 1 equiv	61
6	**2c**, 2 equiv	44
7	Ag_2SO_4	55
8	$AgSbF_6$	40
9	AgOAc	45
10	Instead of Et_3N, K_2CO_3	37
11	Instead of Et_3N, KOAc	29
12	5 mol % of $(Cp^*RhCl_2)_2$	50
13	Without $(Cp^*RhCl_2)_2$	0
14	Without $Zn(OAc)_2$	0



[a]Reaction conditions: **1a** (0.1 mmol), **2b** (0.15 mmol), $(Cp^*RhCl_2)_2$ (2.5 mol %), Ag salt (30 mol %), Base (50 mol %), $Zn(OAc)_2$ (2 equiv), MeOH (1 mL), 40 °C, N_2, [b]NMR yield (1,3,5-trimethoxy benzene was used as internal standard), [c]Isolated yield.

It shows that without a base (Et_3N), only 20% of the olefination product and 75% of the *ortho*-amidated product was formed, which means without an adequate base, the restricted *β*-hydride elimination makes maleimide an effective olefin mediator rather a coupling partner. In the absence of Et_3N, acetate might be helping in the E2-elimination, albeit inefficiently, leading to a 20% yield of olefination product **3bb**. However, all these variations in temperature failed to increase the yield of the desired product. The variation in equivalence of the maleimide (coupling partner) also did not result in an improved

Table S3. Screening of various direction groups.[a]



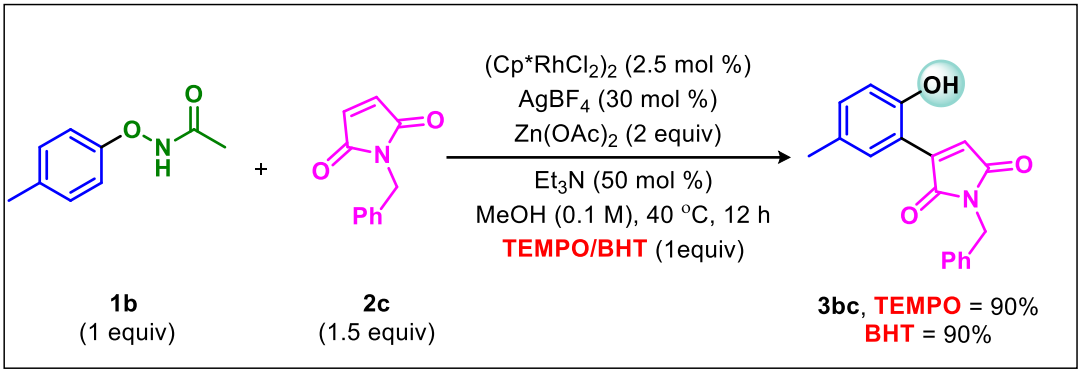
[a]Reaction conditions: **1a** (0.1 mmol), **2b** (0.15 mmol), $(Cp^*RhCl_2)_2$ (2.5 mol %), $AgBF_4$ (30 mol %), Et_3N (50 mol %), $Zn(OAc)_2$ (2 equiv), MeOH (1 mL), 40 °C, N_2, Isolated yields are mentioned.

After screening the reaction parameters, we varied the substituent in the directing group. We found a good range *N*-substitution with an alkyl chain of up to four carbons working efficiently under the reaction condition giving 51%-74% yield of the desired product **3bb** (Table S3, **2b**-**2b3**). However, with an increase in the steric around the directing group, the reactivity decreases and

further ceases when the *N*-pivaloyl group has been employed (Table S3, **2b4**-**2b5**). Thus, we sticked to *N*-acetamide as our directing group as it is delivering 74% yield of the desired product **3bb**.

(4) Control and mechanistic experiments:

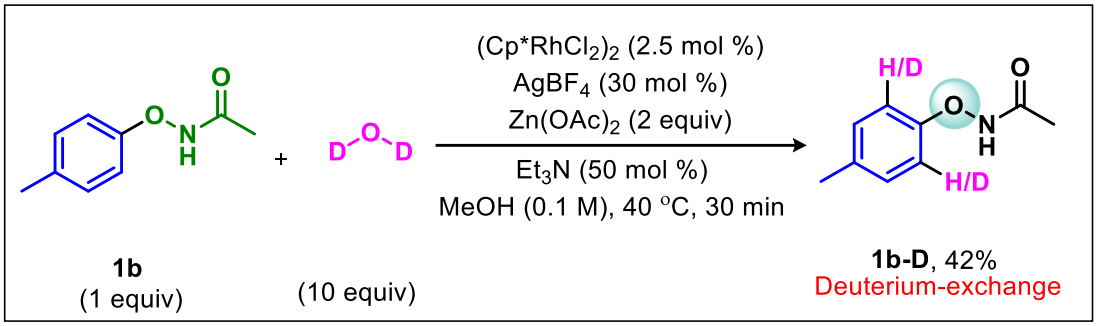
(4.1) The effect of radical scavenger:



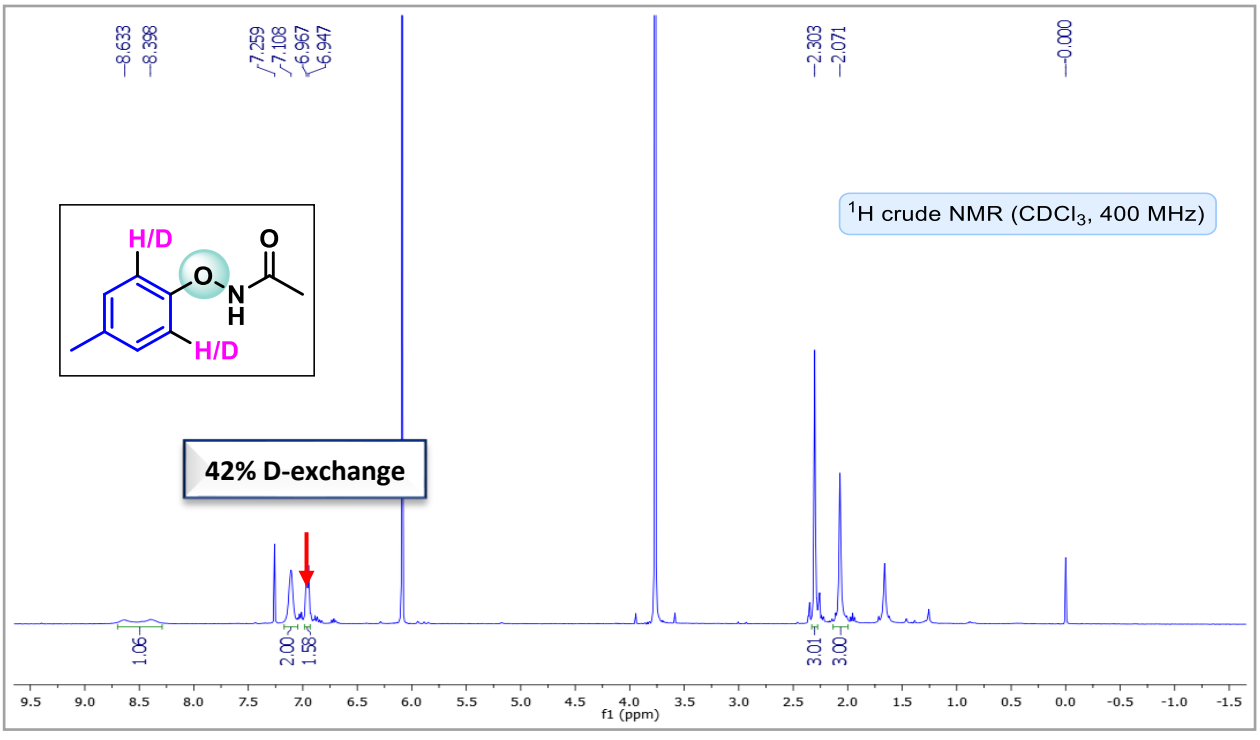
To an oven-dried seal tube charged with a stir bar, *N*-(*p*-tolyloxy)acetamide **1b** (0.1 mmol, 1 equiv), *N*-benzyl maleimide **2c** (0.15 mmol, 1.5 equiv), $(Cp^*RhCl_2)_2$ (0.0025 mmol, 2.5 mol %), $Zn(OAc)_2$ (0.2 mmol, 2.0 equiv), Et_3N (0.05 mmol, 50 mol %), radical scavenger (1 equiv) and MeOH (1.0 mL, 0.1 M with respect to **1b**) were added under nitrogen atmosphere. The seal tube was taken inside the glove box, and $AgBF_4$ (0.03 mmol, 30 mol %) was added. The reaction mixture was stirred (700 rpm) in a preheated aluminum block at 40 ℃ for 12 h. After completion of the reaction (monitored by TLC), the reaction mixture was passed through a short silica pad, washed with ethyl acetate, and evaporated under reduced pressure. The crude was submitted for NMR analysis. The product yield was calculated from crude NMR spectra (1,3,5-Trimethoxy benzene was used as an internal standard).

N.B: **Reaction is not following a radical pathway.**

(4.2) Deuterium exchange study:

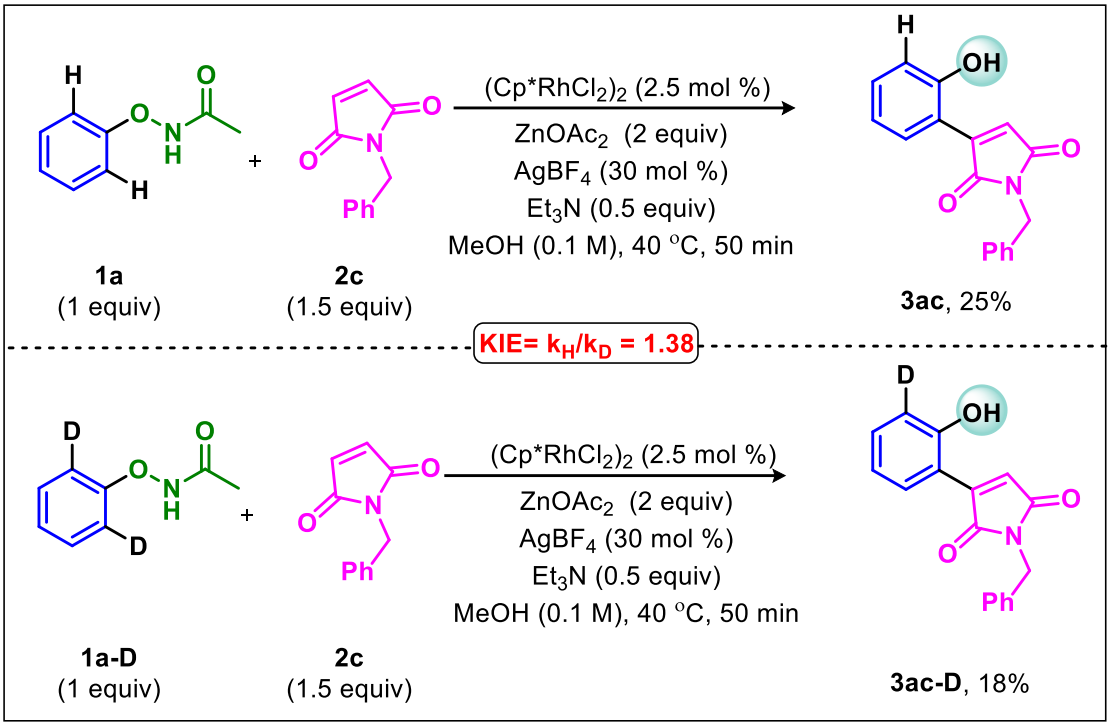


To an oven-dried seal tube charged with a stir bar, *N*-(*p*-tolyloxy)acetamide **1b** (0.1 mmol, 1 equiv), $(Cp^*RhCl_2)_2$ (0.0025 mmol, 2.5 mol %), $Zn(OAc)_2$ (0.2 mmol, 2.0 equiv), Et_3N (0.05 mmol, 50 mol %), and MeOH (1.0 mL, 0.1 M with respect to **1b**) were added under nitrogen atmosphere. The seal tube was taken inside the glove box, and $AgBF_4$ (0.03 mmol, 30 mol %) was added. Finally, D_2O (10 equiv) was added and the seal tube was sealed. The reaction mixture was stirred (700 rpm) in a preheated aluminum block at 40 °C for 30 min. Then, the reaction mixture was passed through a short silica pad washed with ethyl acetate, and evaporated under reduced

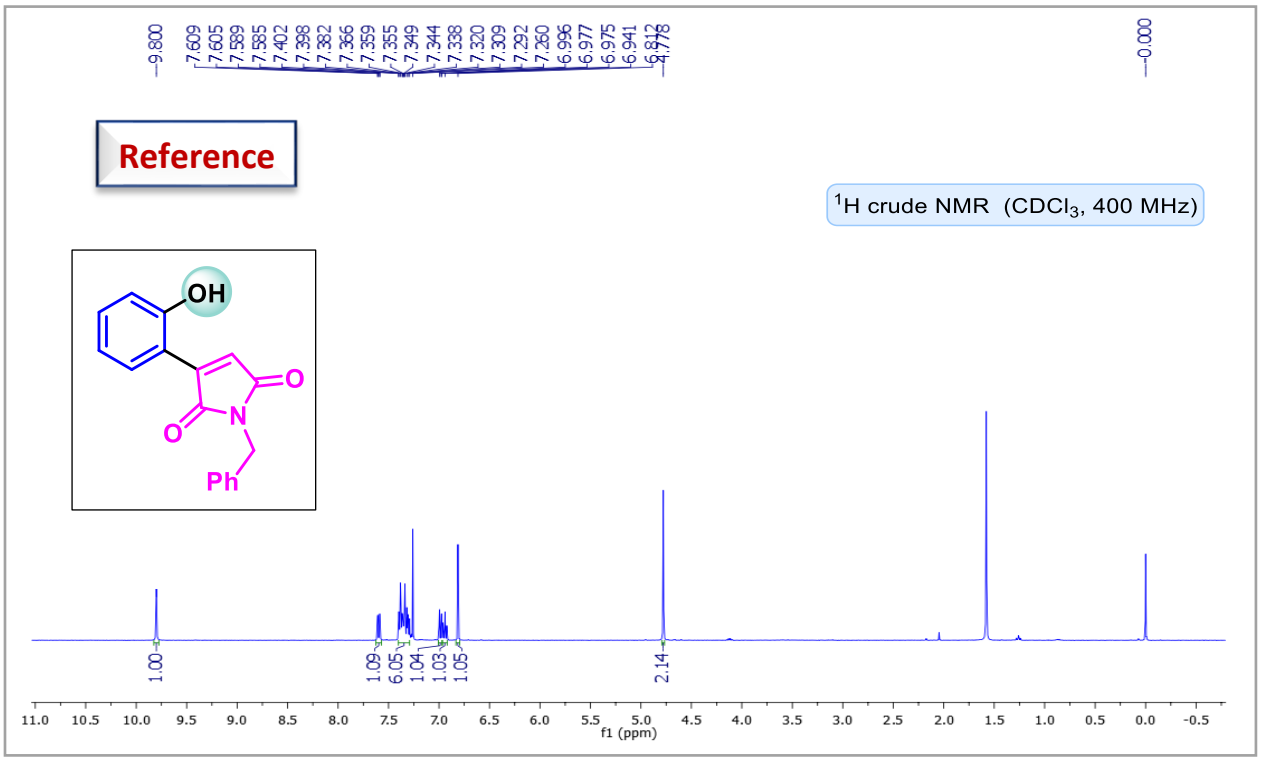


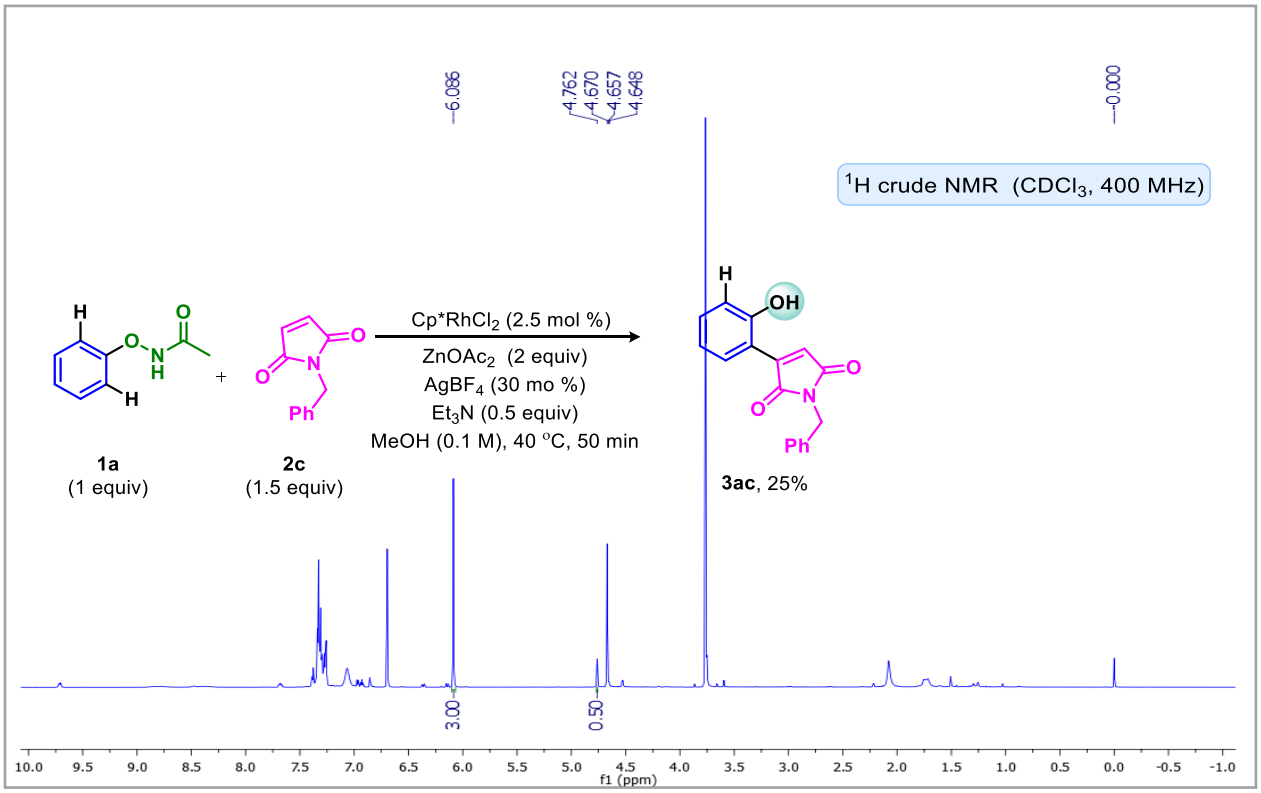
pressure. The crude was submitted for NMR analysis. The percentage of H/D exchange was calculated from the crude ^{1}H-NMR spectrum as shown below.

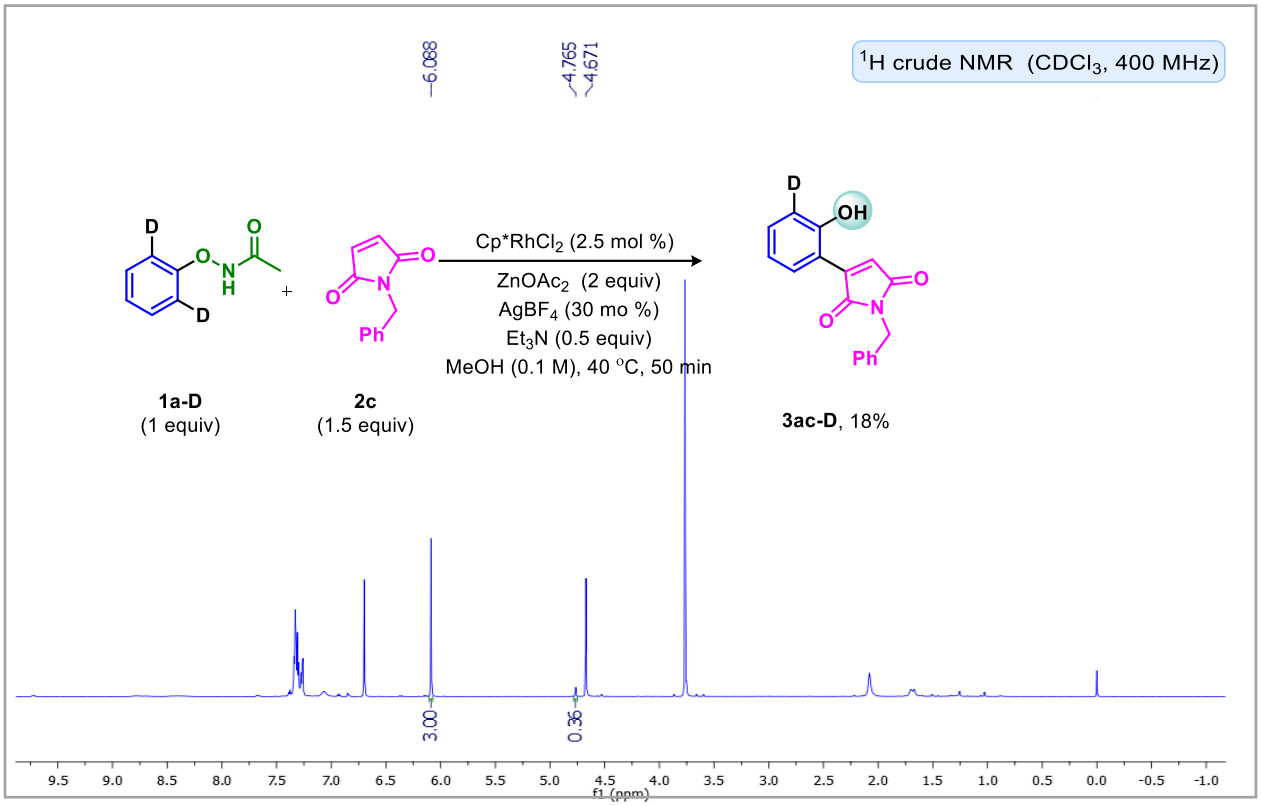
(4.3) Kinetic isotope effect (KIE):



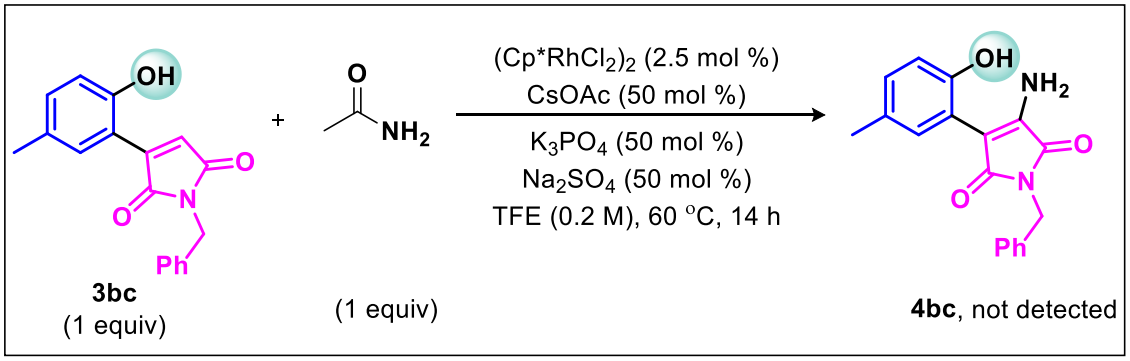
In a parallel set of reaction, to an oven-dried seal tube charged with a stir bar, *N*-phenoxy acetamide **1a/1a-D** [3] (0.1 mmol, 1 equiv), *N*-benzyl maleimide **2d** (0.15 mmol, 1.5 equiv), $(Cp^*RhCl_2)_2$ (0.0025 mmol, 2.5 mol %), $Zn(OAc)_2$ (0.2 mmol, 2.0 equiv), Et_3N (0.05 mmol, 50 mol %), and MeOH (1.0 mL, 0.1 M with respect to **1a/1a-D**) were added under nitrogen atmosphere. The seal tube was taken inside the glove box, and $AgBF_4$ (0.03 mmol, 30 mol %) was added. The reaction mixture was stirred (700 rpm) in a preheated aluminum block at 40 °C for 50 min. Then, the reaction mixture was passed through a short silica pad, washed with ethyl acetate, and evaporated under reduced pressure. The crude was submitted for NMR analysis. The percentage of H/D exchange was calculated from the crude ^{1}H-NMR spectrum as shown below.


Reference
^{1}H crude NMR (CDCl$_3$, 400 MHz)
OH
O
N
O
Ph
f1 (ppm)


^{1}H crude NMR (CDCl$_3$, 400 MHz)
Cp*RhCl$_2$ (2.5 mol %)
ZnOAc$_2$ (2 equiv)
AgBF$_4$ (30 mo %)
Et$_3$N (0.5 equiv)
MeOH (0.1 M), 40 °C, 50 min
1a
(1 equiv)
2c
(1.5 equiv)
3ac, 25%
f1 (ppm)



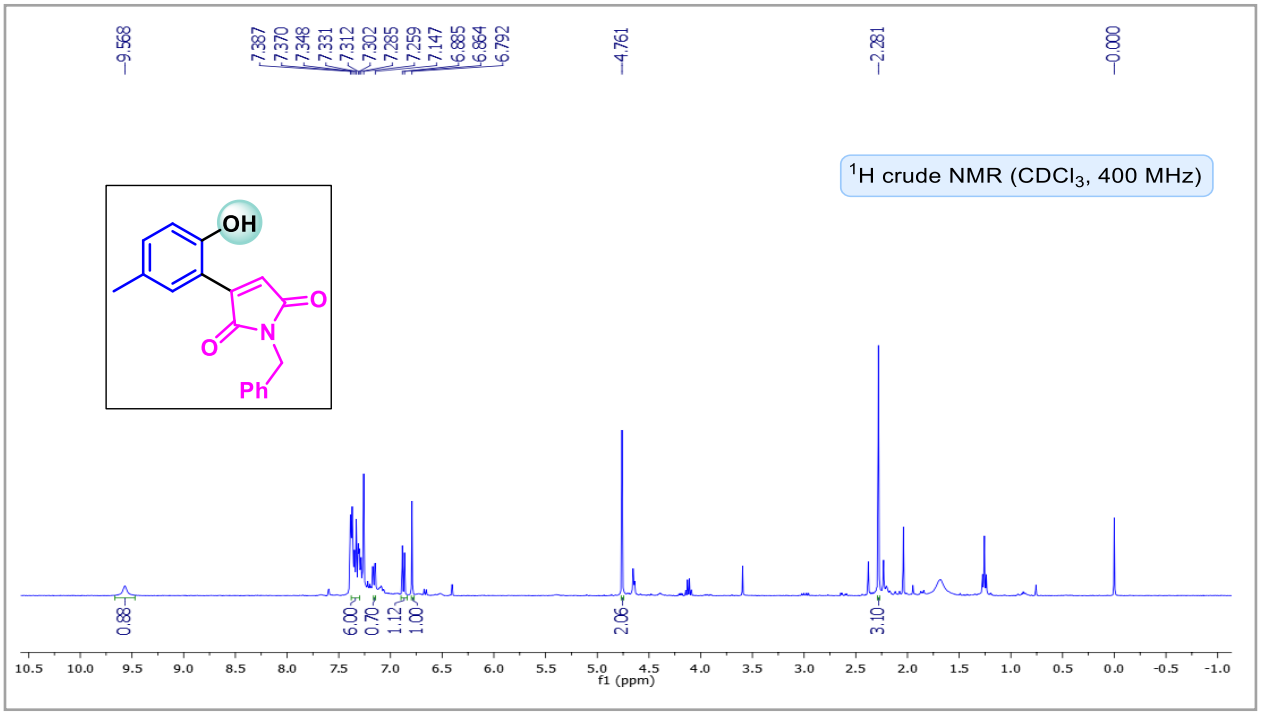
(4.4) Reaction of 3bc with acetamide under standard reaction conditions:



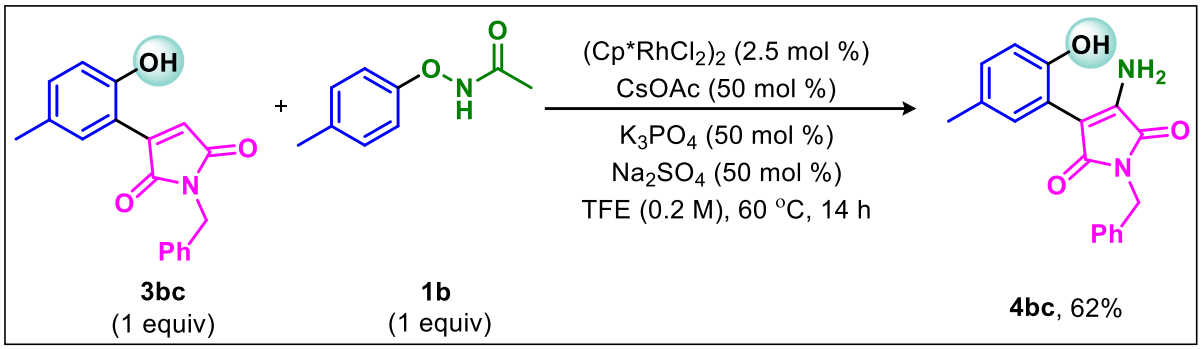
To an oven-dried seal tube charged with a stir bar, 1-benzyl-3-(2-hydroxy-5-methylphenyl)-1*H*-pyrrole-2,5-dione **3bc** (0.1 mmol, 1 equiv), acetamide (0.15 mmol, 1.5 equiv), $(Cp^*RhCl_2)_2$ (0.0025 mmol, 2.5 mol %), Na_2SO_4 (0.05 mmol, 50 mol %), and TFE (0.5 mL, 0.2 M with respect

to **3bc**) were added under nitrogen atmosphere. The seal tube was taken inside the glove box, and CsOAc (0.05 mmol, 50 mol %), K_3PO_4 (0.05 mmol, 50 mol %), were added. The reaction mixture was stirred (700 rpm) in a preheated aluminum block at 60 °C for 14 h. After completion of the reaction (monitored by TLC), the reaction mixture was passed through a short silica pad, washed with ethyl acetate, and evaporated under reduced pressure. The crude was submitted for NMR analysis. The product was not formed in this reaction.

N.B: **Acetamide is not the amine source.**



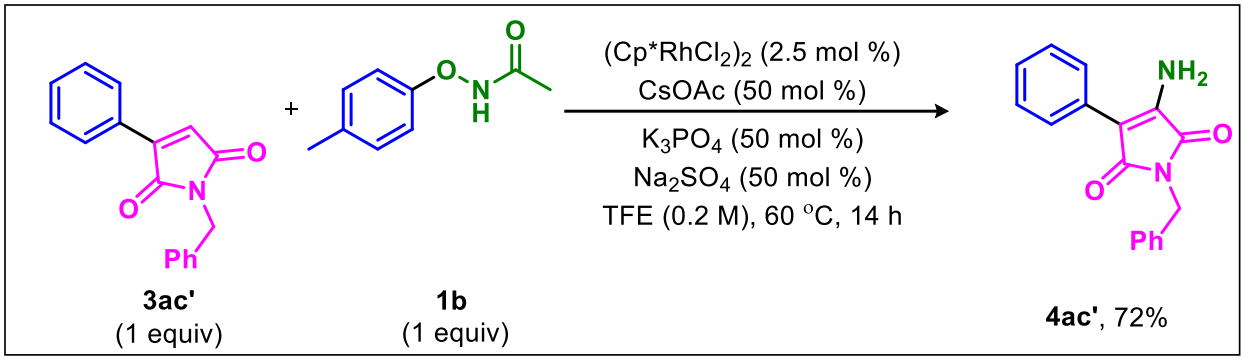
(4.5) Reaction of 3bc with *p*-tolyl phenoxy acetamide 1b:



To an oven-dried seal tube charged with a stir bar, 1-benzyl-3-(2-hydroxy-5-methylphenyl)-1*H*-pyrrole-2,5-dione **3bc** (0.1 mmol, 1 equiv), *N*-(*p*-tolyloxy)acetamide **1b** (0.1 mmol, 1 equiv), $(Cp^*RhCl_2)_2$ (0.0025 mmol, 2.5 mol %), Na_2SO_4 (0.05 mmol, 50 mol %), and TFE (0.5 mL, 0.2 M with respect to **1b**) were added under nitrogen atmosphere. The seal tube was taken inside the glove box, and CsOAc (0.05 mmol, 50 mol %), K_3PO_4 (0.05 mmol, 50 mol %), were added. The reaction mixture was stirred (700 rpm) in a preheated aluminum block at 60 °C for 14 h. After completion of the reaction (monitored by TLC), the solvent was evaporated under reduced pressure and the crude was purified by column chromatography using EtOAc/hexane as eluent to get the corresponding product **4bc** in 62% (19 mg) yield.

N.B: **Rhodium nitrenoid species is forming *insitu* from phenoxy acetamide.**

(4.6) Reaction of 3bc' with *p*-tolyl phenoxy acetamide 1b:



To an oven-dried seal tube charged with a stir bar, 1-benzyl-3-phenyl-1H-pyrrole-2,5-dione **3ac'** (0.1 mmol, 1 equiv), *N*-(*p*-tolyloxy)acetamide **1b** (0.1 mmol, 1 equiv), $(Cp^*RhCl_2)_2$ (0.0025 mmol, 2.5 mol %), Na_2SO_4 (0.05 mmol, 50 mol %), and TFE (0.5 mL, 0.2 M with respect to **1b**) were added under nitrogen atmosphere. The seal tube was taken inside the glove box, and CsOAc (0.05 mmol, 50 mol %), K_3PO_4 (0.05 mmol, 50 mol %), were added. The reaction mixture was stirred (700 rpm) in a preheated aluminum block at 60 °C for 14 h. After completion of the reaction (monitored by TLC), the solvent was evaporated under reduced pressure and the crude was purified by column chromatography using EtOAc/hexane as eluent to get the corresponding product **4ac'** in 72% (20 mg) yield.

(4.7) Mass analysis of carboamination reaction:

To an oven-dried seal tube charged with a stir bar, 1-benzyl-3-(2-hydroxy-5-methylphenyl)-1*H*-pyrrole-2,5-dione **3bc** (0.1 mmol, 1 equiv), *N*-(*p*-tolyloxy)acetamide **1b** (0.1 mmol, 1 equiv), $(Cp^*RhCl_2)_2$ (0.0025 mmol, 2.5 mol %), Na_2SO_4 (0.05 mmol, 50 mol %), and TFE (0.5 mL, 0.2 M with respect to **1b**) were added under nitrogen atmosphere. The seal tube was taken inside the glove box, and CsOAc (0.05 mmol, 50 mol %), K_3PO_4 (0.05 mmol, 50 mol %), were added. The reaction mixture was stirred (700 rpm) in a preheated aluminum block at 60 °C for 6 h. After 6 h, the residue was filtered through a nylon filter and evaporated under reduced pressure. It was then submitted for mass analysis.

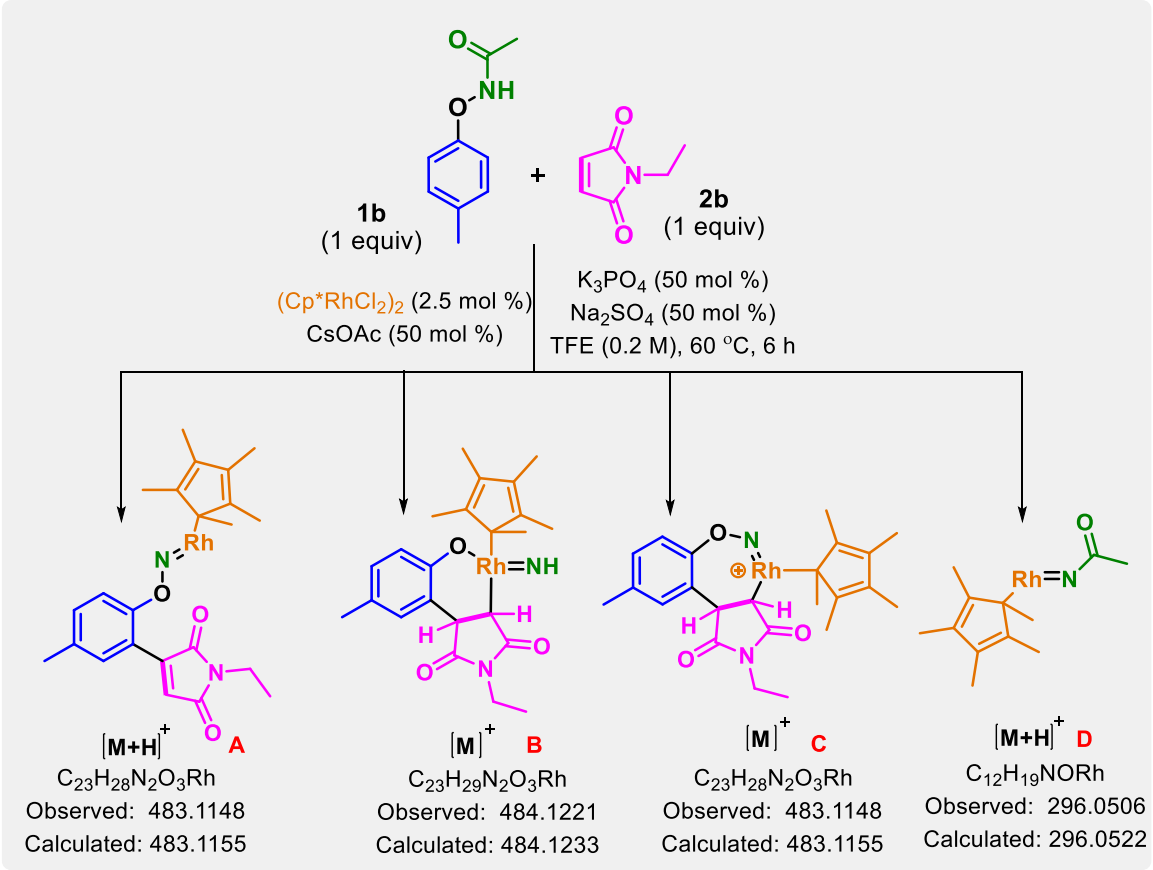
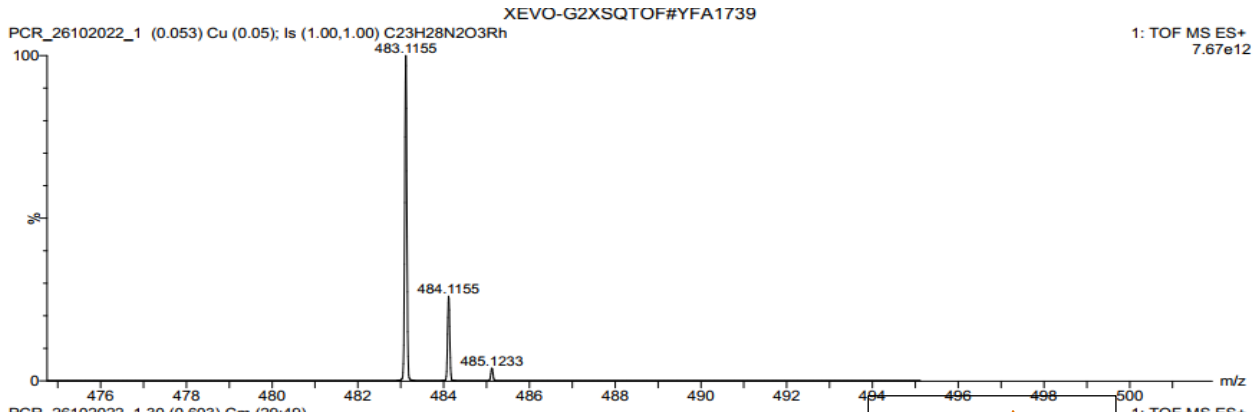
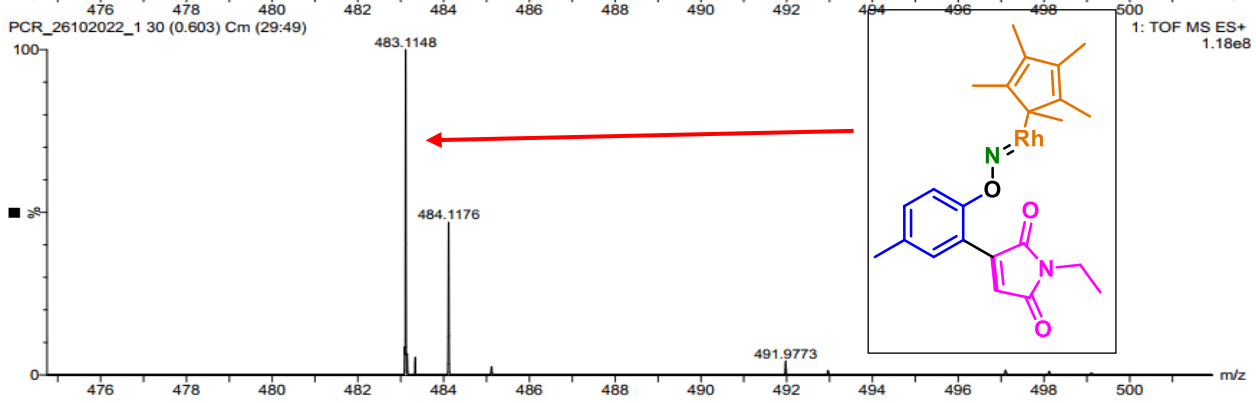
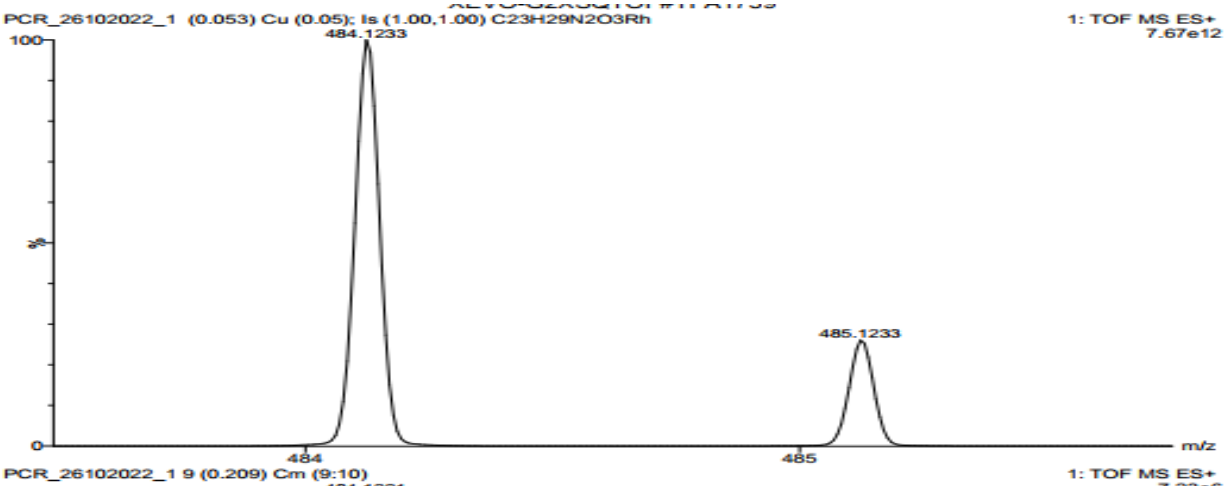
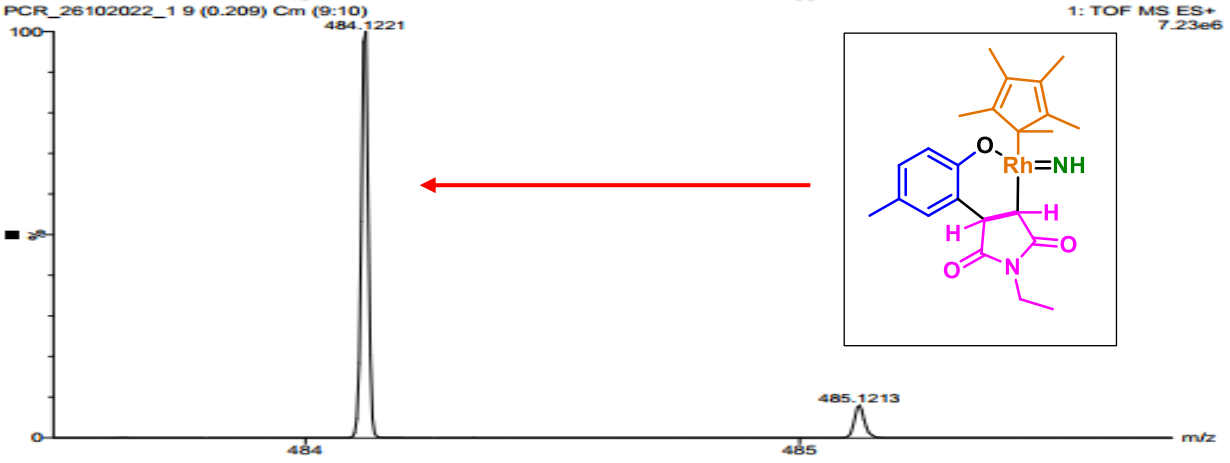


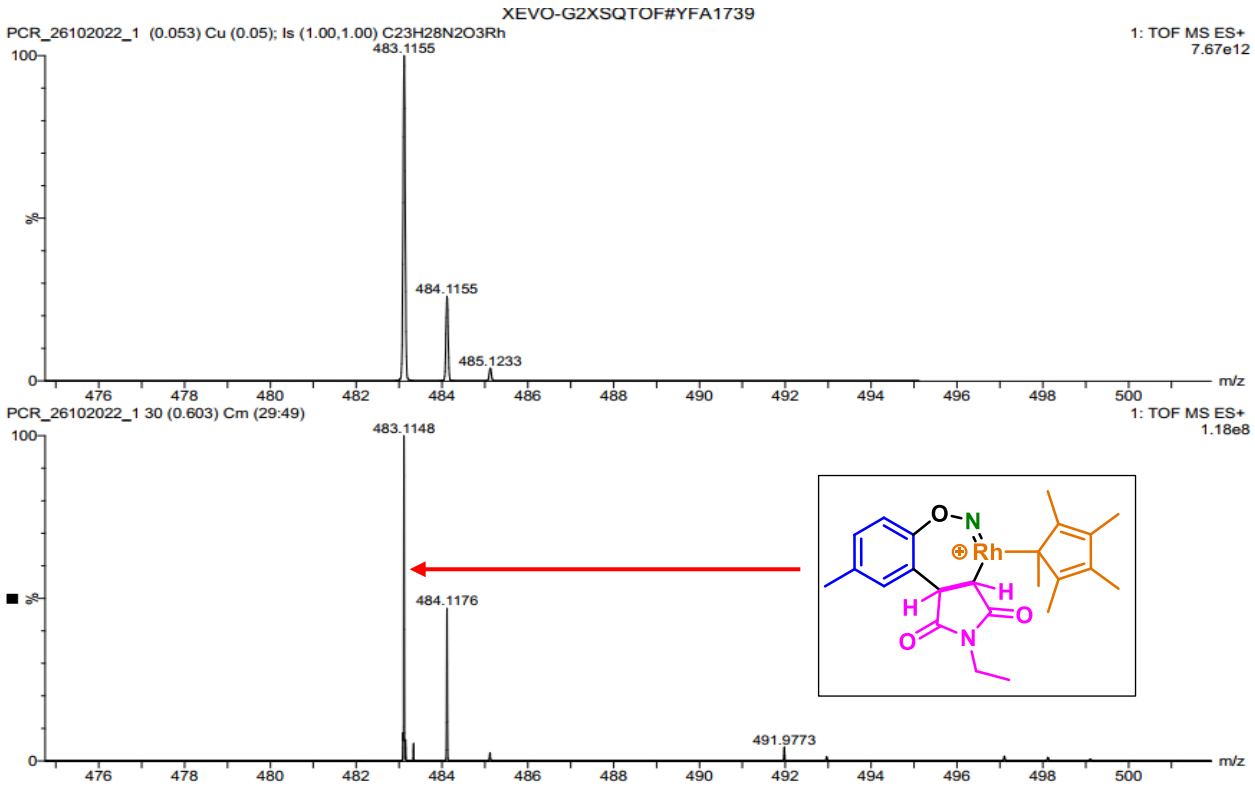
Figure S1. Mass analysis for reaction of **1b** with **2b**.

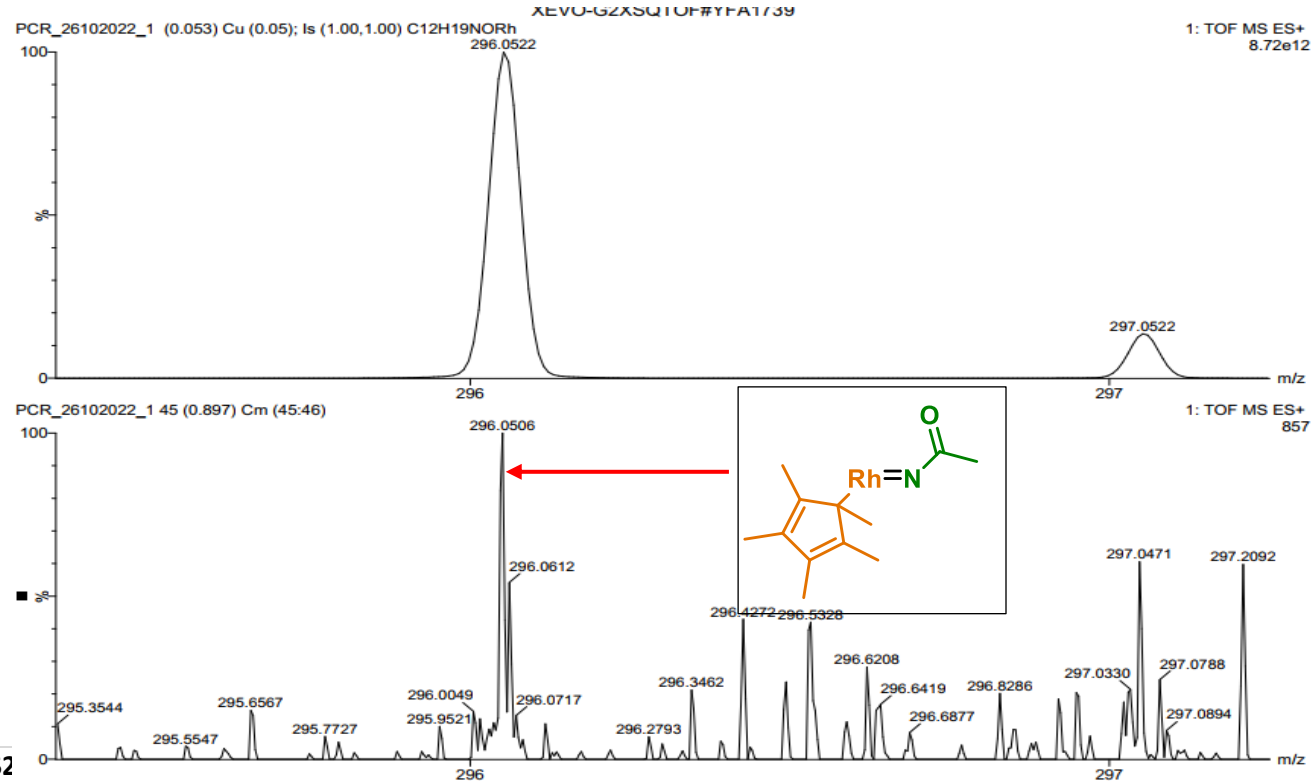

XEVO-G2XSQTOF#YFA1739
PCR_26102022_1 (0.053) Cu (0.05); Is (1.00,1.00) C23H28N2O3Rh
1: TOF MS ES+
7.67e12
483.1155
484.1155
485.1233
m/z


PCR_26102022_1 30 (0.603) Cm (29:49)
1: TOF MS ES+
1.18e8
483.1148
484.1176
491.9773
Rh
N
O
O
N
O
m/z


PCR_26102022_1 (0.053) Cu (0.05); Is (1.00,1.00) C23H29N2O3Rh
1: TOF MS ES+
7.67e12
484.1233
485.1233
m/z


PCR_26102022_1 9 (0.209) Cm (9:10)
1: TOF MS ES+
7.23e6
484.1221
485.1213
O
Rh=NH
H
H
O
O
N
m/z


XEVO-G2XSQTOF#YFA1739
PCR_26102022_1 (0.053) Cu (0.05); Is (1.00,1.00) C23H28N2O3Rh
1: TOF MS ES+
7.67e12
483.1155
484.1155
485.1233
PCR_26102022_1 30 (0.603) Cm (29:49)
1: TOF MS ES+
1.18e8
483.1148
484.1176
491.9773
m/z


XEVO-G2XSQTOF#YFA1739
PCR_26102022_1 (0.053) Cu (0.05); Is (1.00,1.00) C12H19NORh
1: TOF MS ES+
8.72e12
296.0522
297.0522
PCR_26102022_1 45 (0.897) Cm (45:46)
1: TOF MS ES+
857
296.0506
296.0612
296.0049
296.0717
295.9521
295.3544
295.5547
295.6567
295.7727
296.2793
296.3462
296.4272
296.5328
296.6208
296.6419
296.6877
296.8286
297.0330
297.0471
297.0788
297.0894
297.2092
m/z

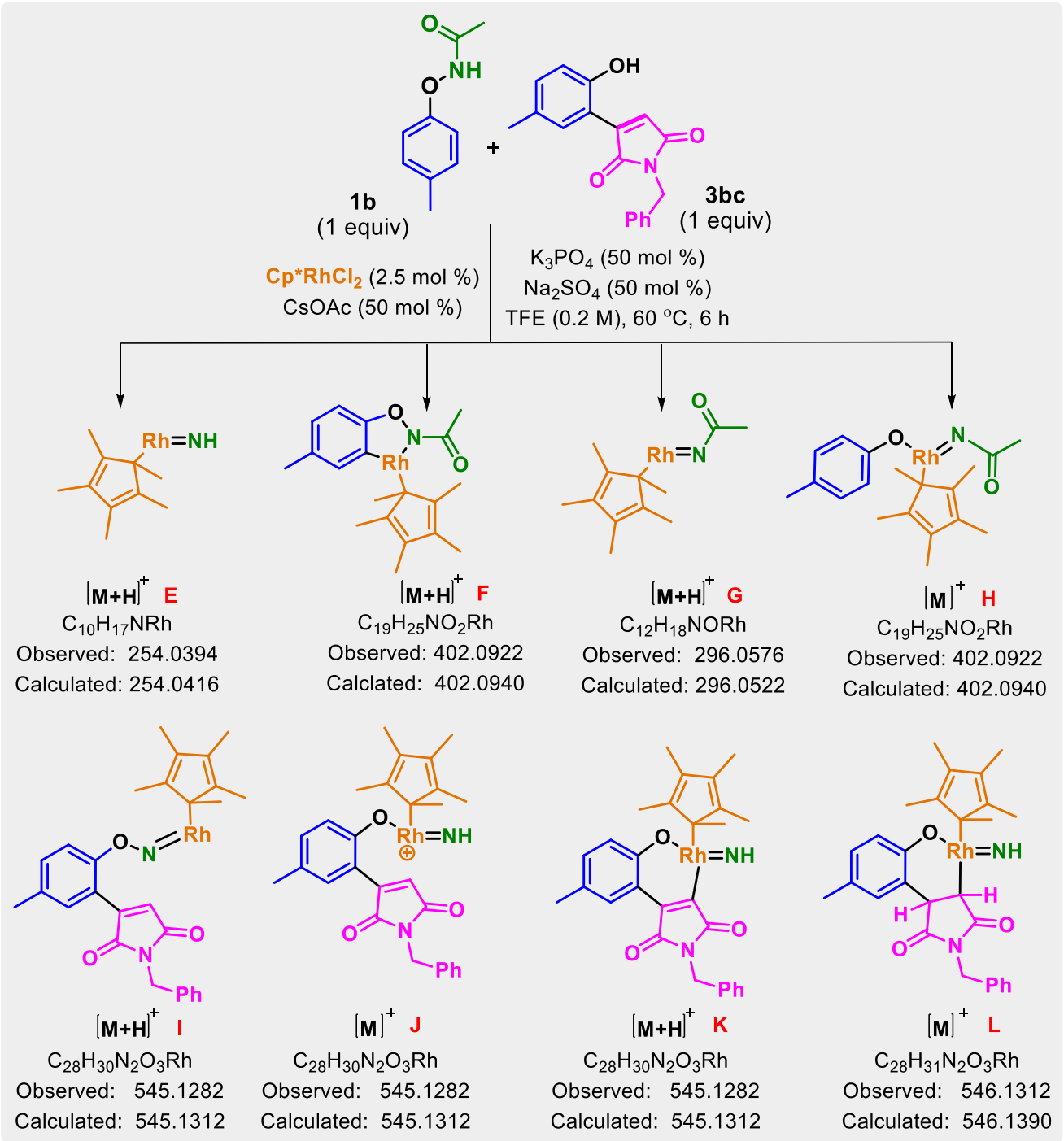
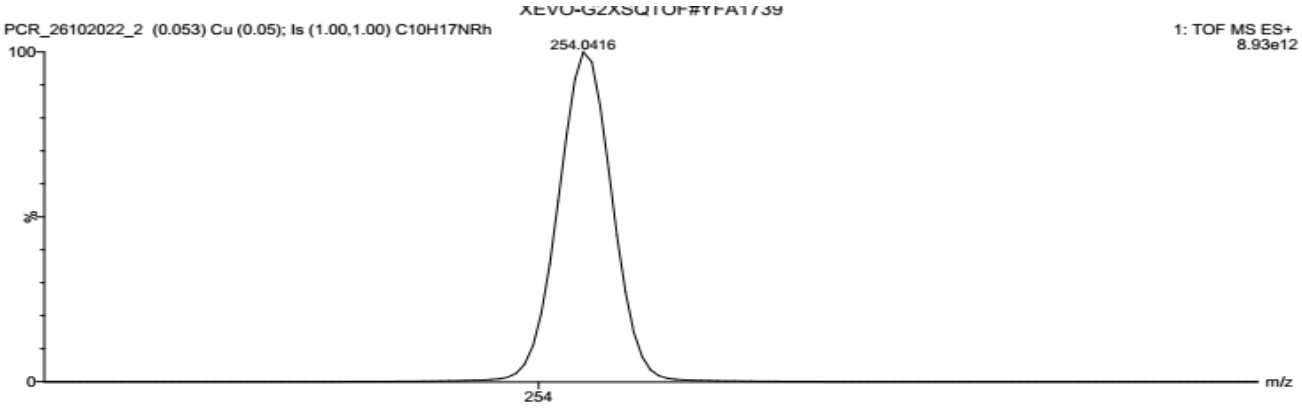
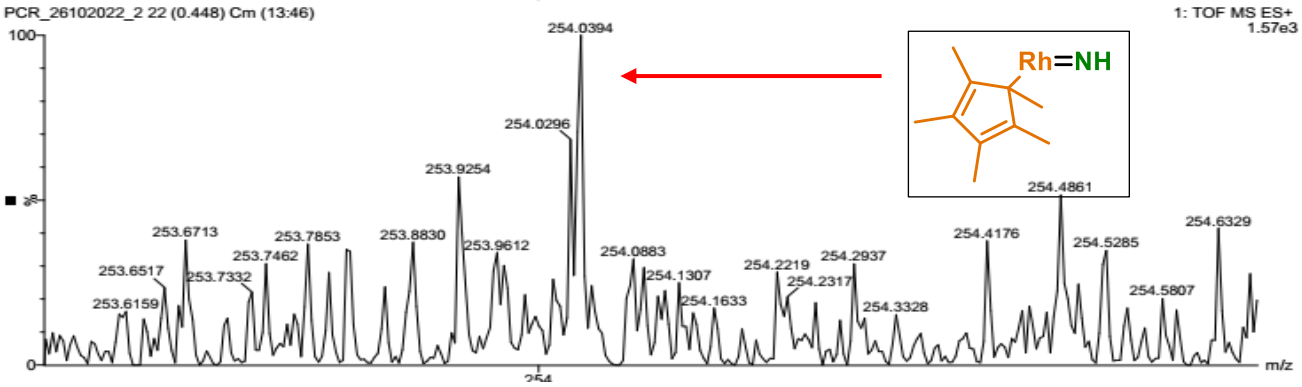
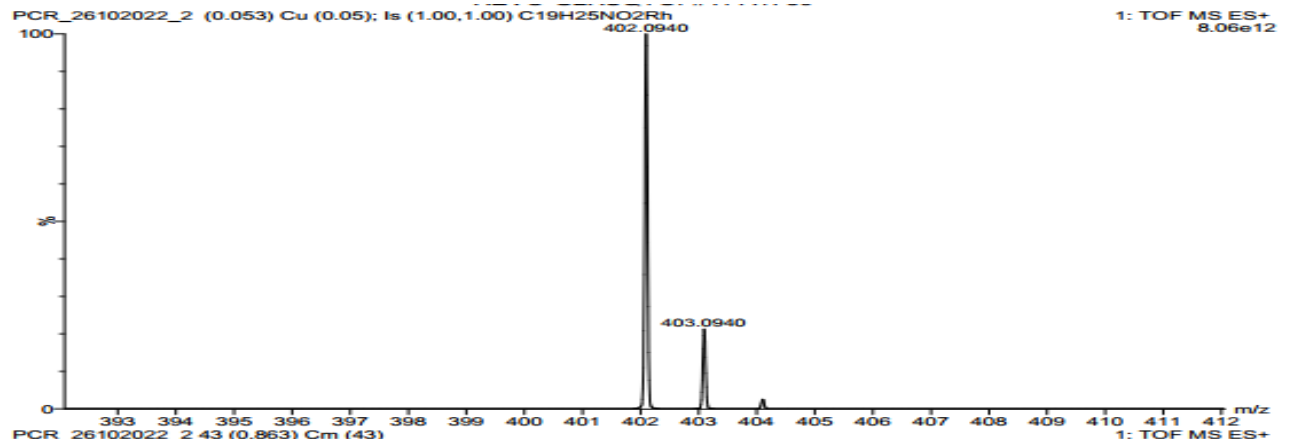
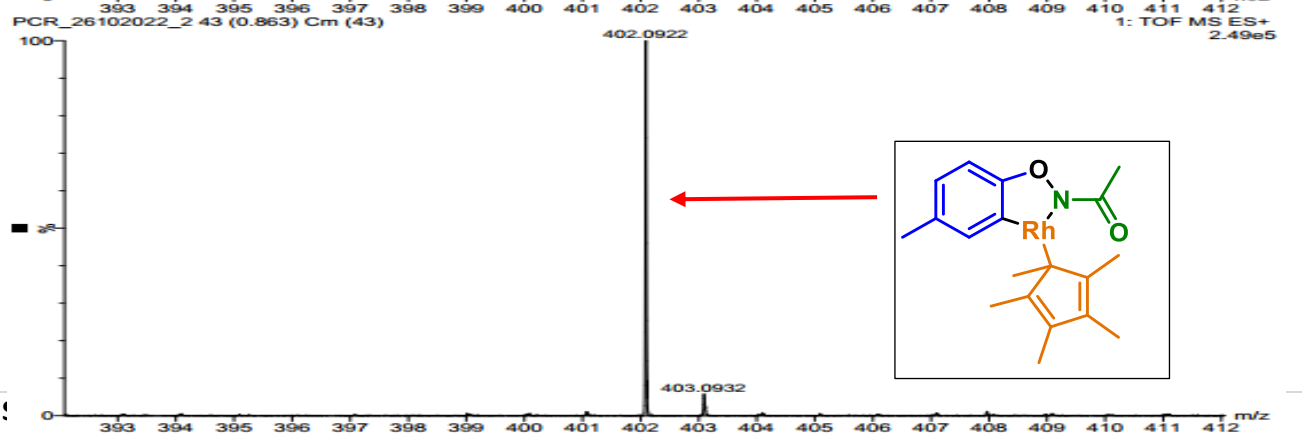


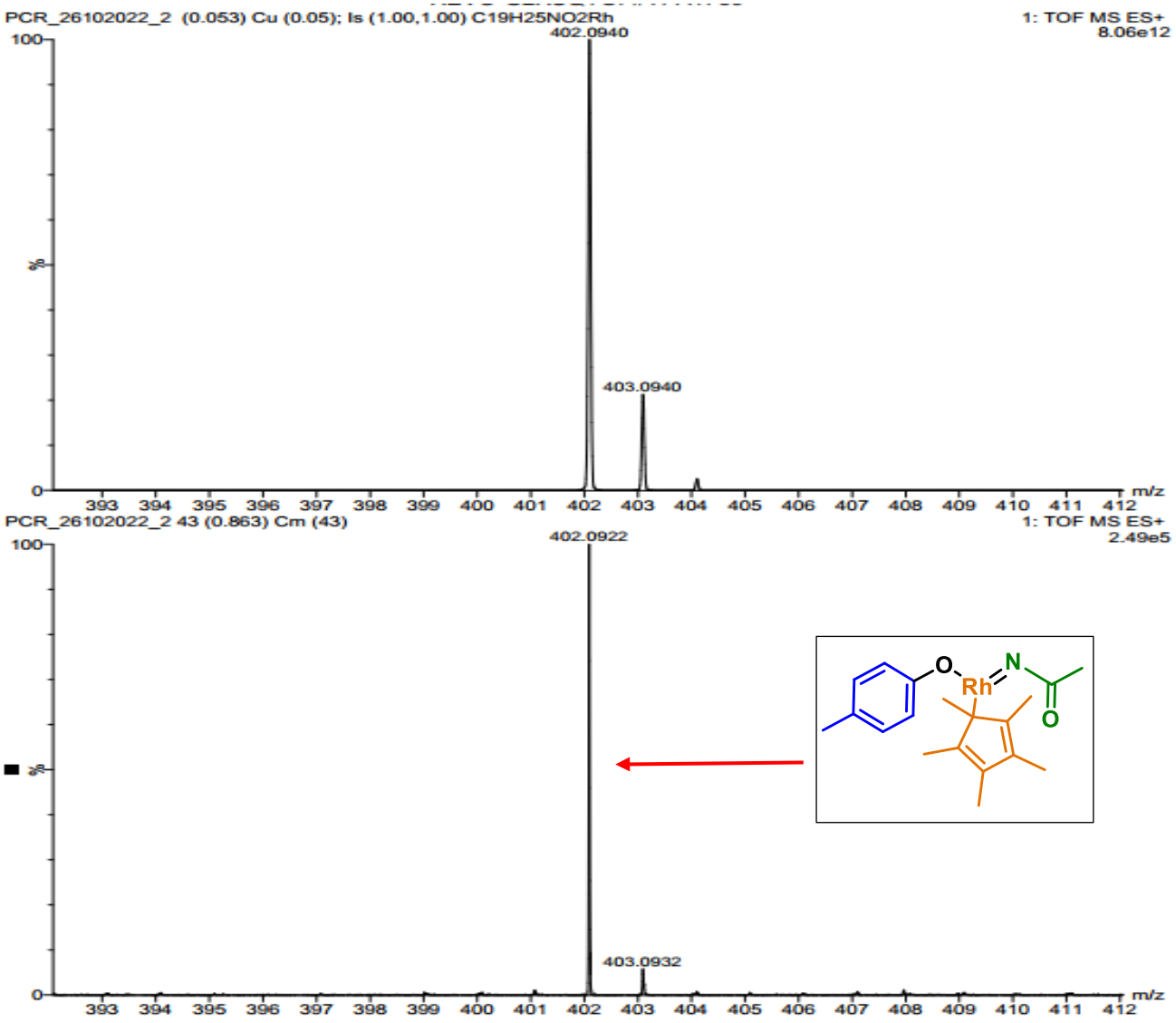
Figure S2. Mass analysis for reaction of **1b** with **3bc**.

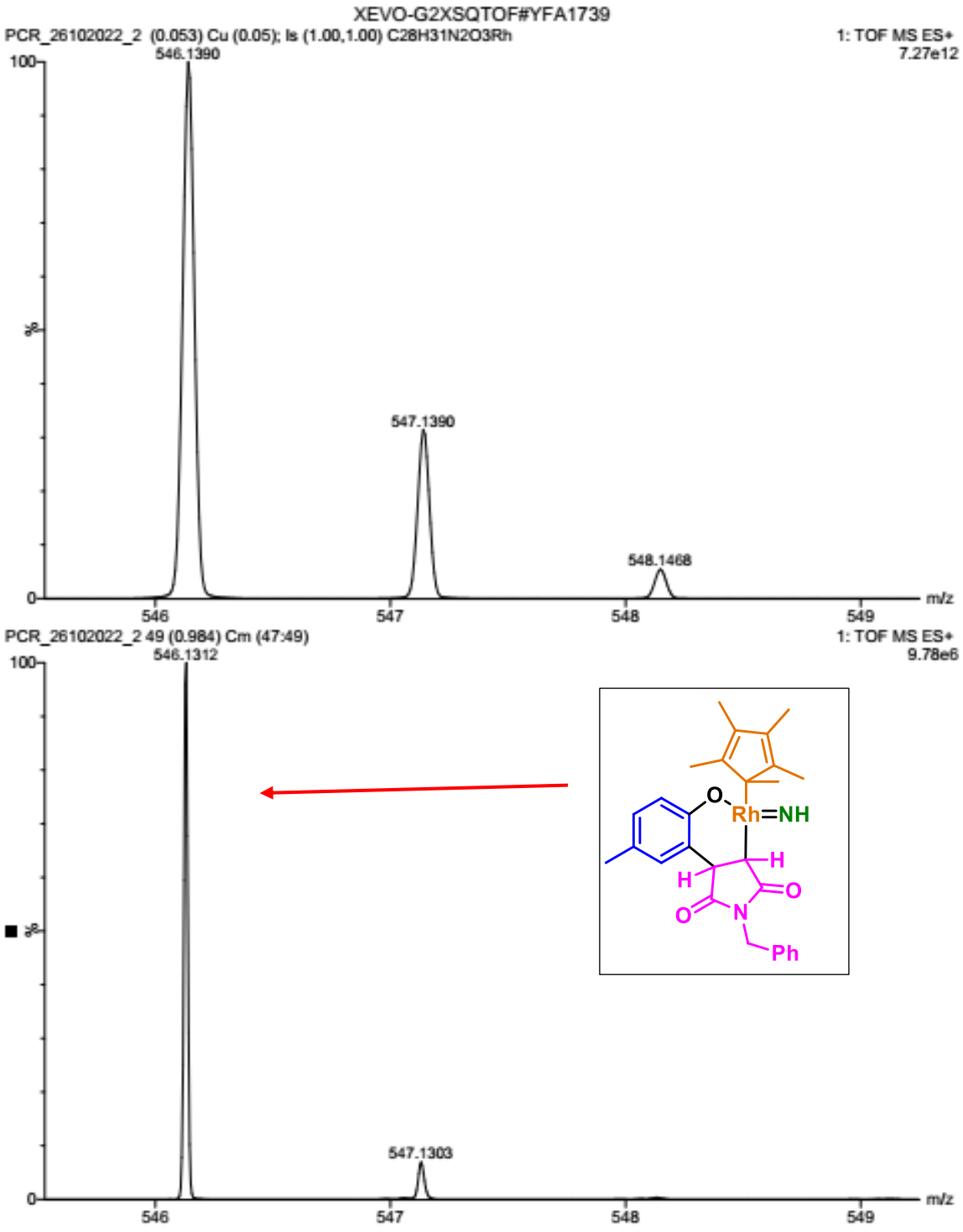

PCR_26102022_2 (0.053) Cu (0.05); Is (1.00,1.00) C10H17NRh
1: TOF MS ES+
8.93e12
254.0416
100
%
0
254
m/z

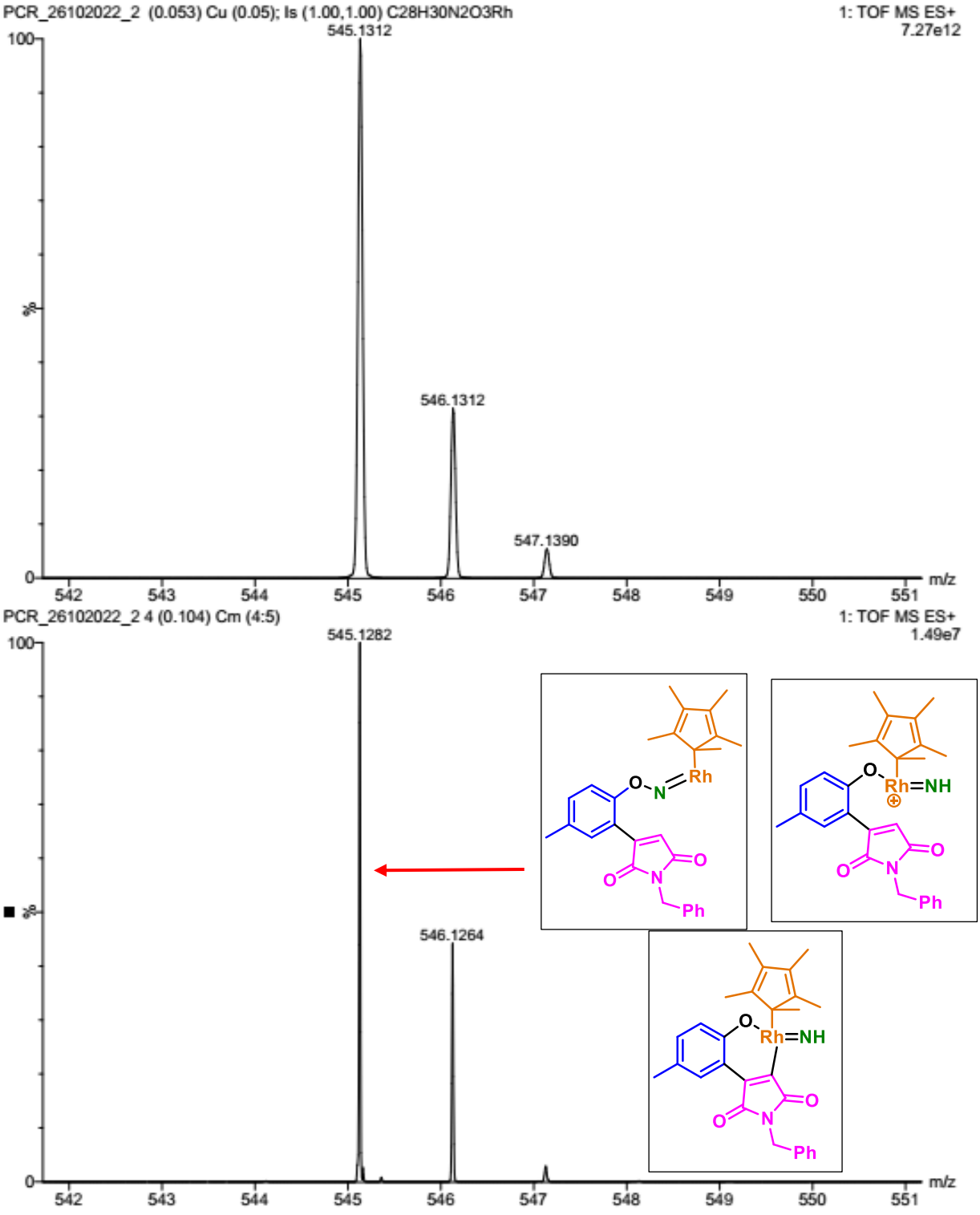

PCR_26102022_2 22 (0.448) Cm (13:46)
1: TOF MS ES+
1.57e3
254.0394
254.0296
253.9254
253.6713
253.7853
253.8830
253.7462
253.9612
253.6517
253.7332
253.6159
254.0883
254.1307
254.1633
254.2219
254.2317
254.2937
254.3328
254.4176
254.4861
254.5285
254.5807
254.6329
Rh=NH
100
%
0
254
m/z

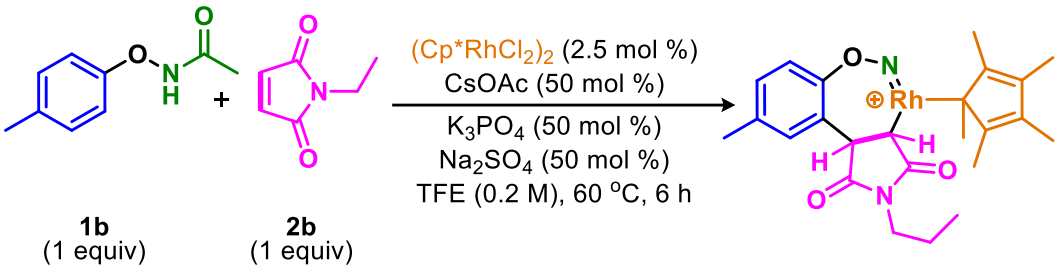

PCR_26102022_2 (0.053) Cu (0.05); Is (1.00,1.00) C19H25NO2Rh
1: TOF MS ES+
8.06e12
402.0940
403.0940
100
%
0
393 394 395 396 397 398 399 400 401 402 403 404 405 406 407 408 409 410 411 412
m/z


PCR_26102022_2 43 (0.863) Cm (43)
1: TOF MS ES+
2.49e5
402.0922
403.0932
O
N
Rh
O
100
%
0
393 394 395 396 397 398 399 400 401 402 403 404 405 406 407 408 409 410 411 412
m/z


PCR_26102022_2 (0.053) Cu (0.05); Is (1.00,1.00) C19H25NO2Rh
1: TOF MS ES+
8.06e12
402.0940
403.0940
100
%
0
393 394 395 396 397 398 399 400 401 402 403 404 405 406 407 408 409 410 411 412
m/z
PCR_26102022_2 43 (0.863) Cm (43)
1: TOF MS ES+
2.49e5
402.0922
403.0932
O
Rh
N
O


XEVO-G2XSQTOF#YFA1739
PCR_26102022_2 (0.053) Cu (0.05); Is (1.00,1.00) C28H31N2O3Rh
1: TOF MS ES+
7.27e12
546.1390
547.1390
548.1468
%
m/z
PCR_26102022_2 49 (0.984) Cm (47:49)
1: TOF MS ES+
9.78e6
546.1312
547.1303
Rh=NH
H
H
O
O
N
Ph

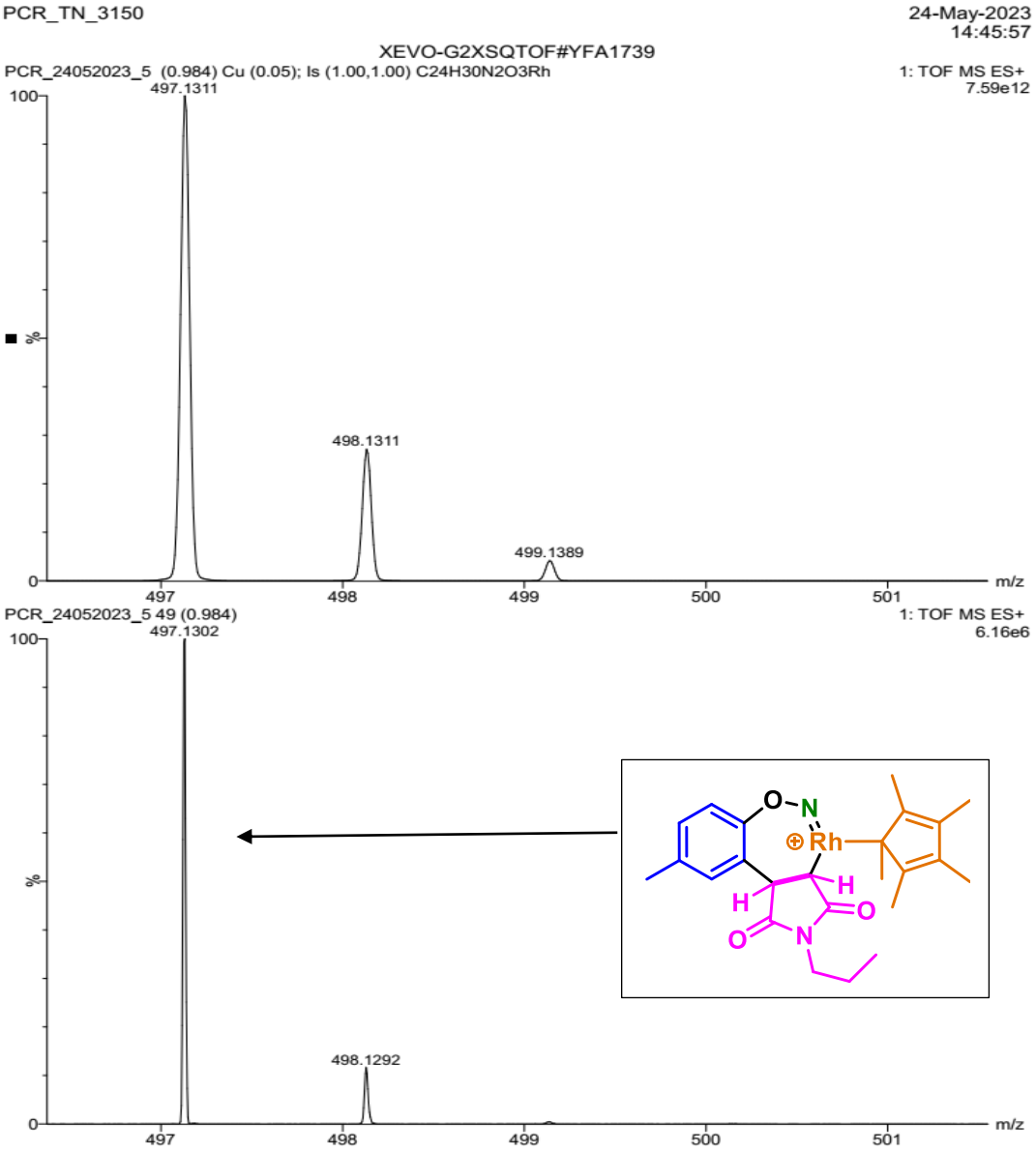

PCR_26102022_2 (0.053) Cu (0.05); Is (1.00,1.00) C28H30N2O3Rh
1: TOF MS ES+
7.27e12
545.1312
546.1312
547.1390
100
%
0
542
543
544
545
546
547
548
549
550
551
m/z
PCR_26102022_2 4 (0.104) Cm (4:5)
1: TOF MS ES+
1.49e7
545.1282
546.1264
Rh
N
O
Ph
Rh=NH

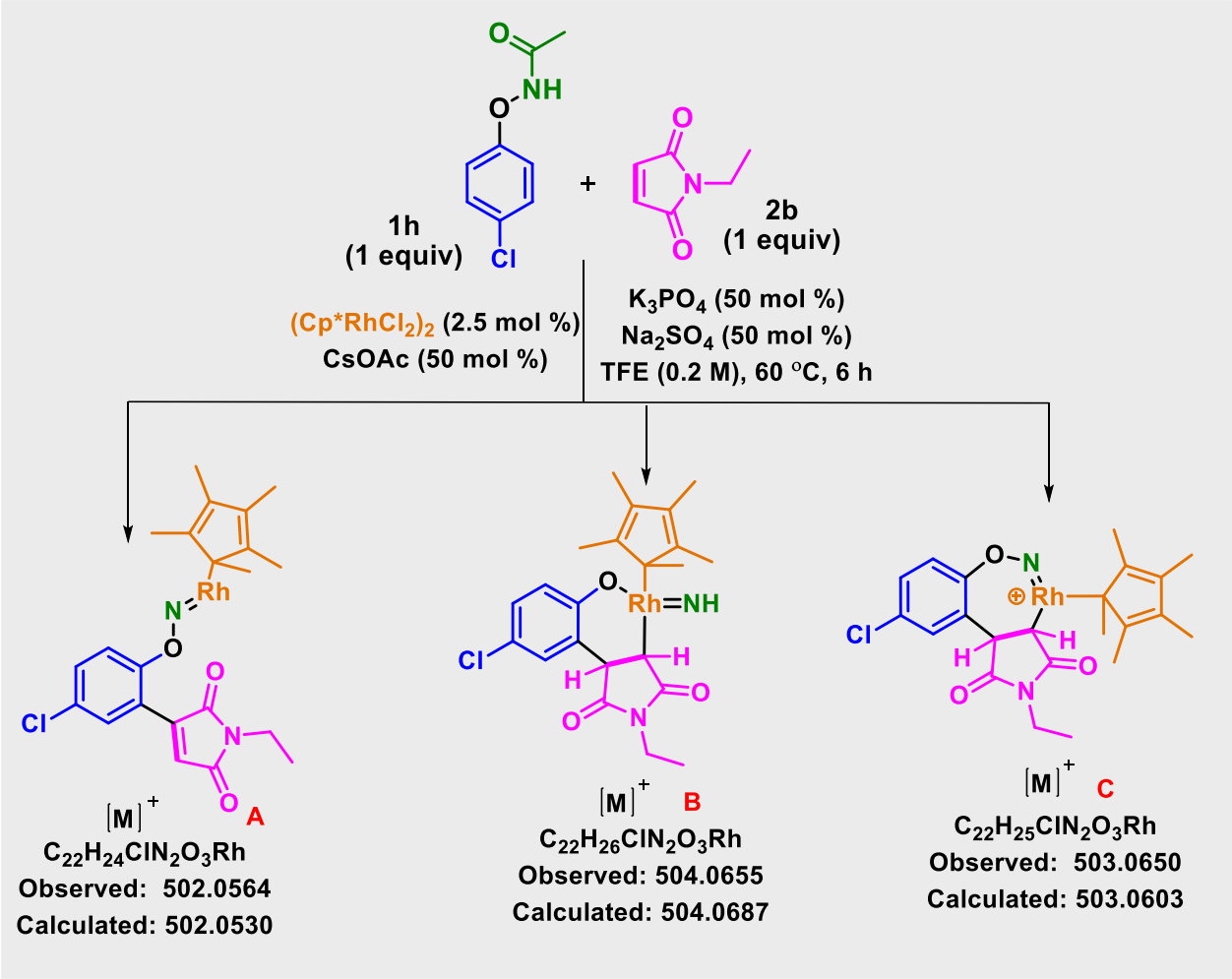


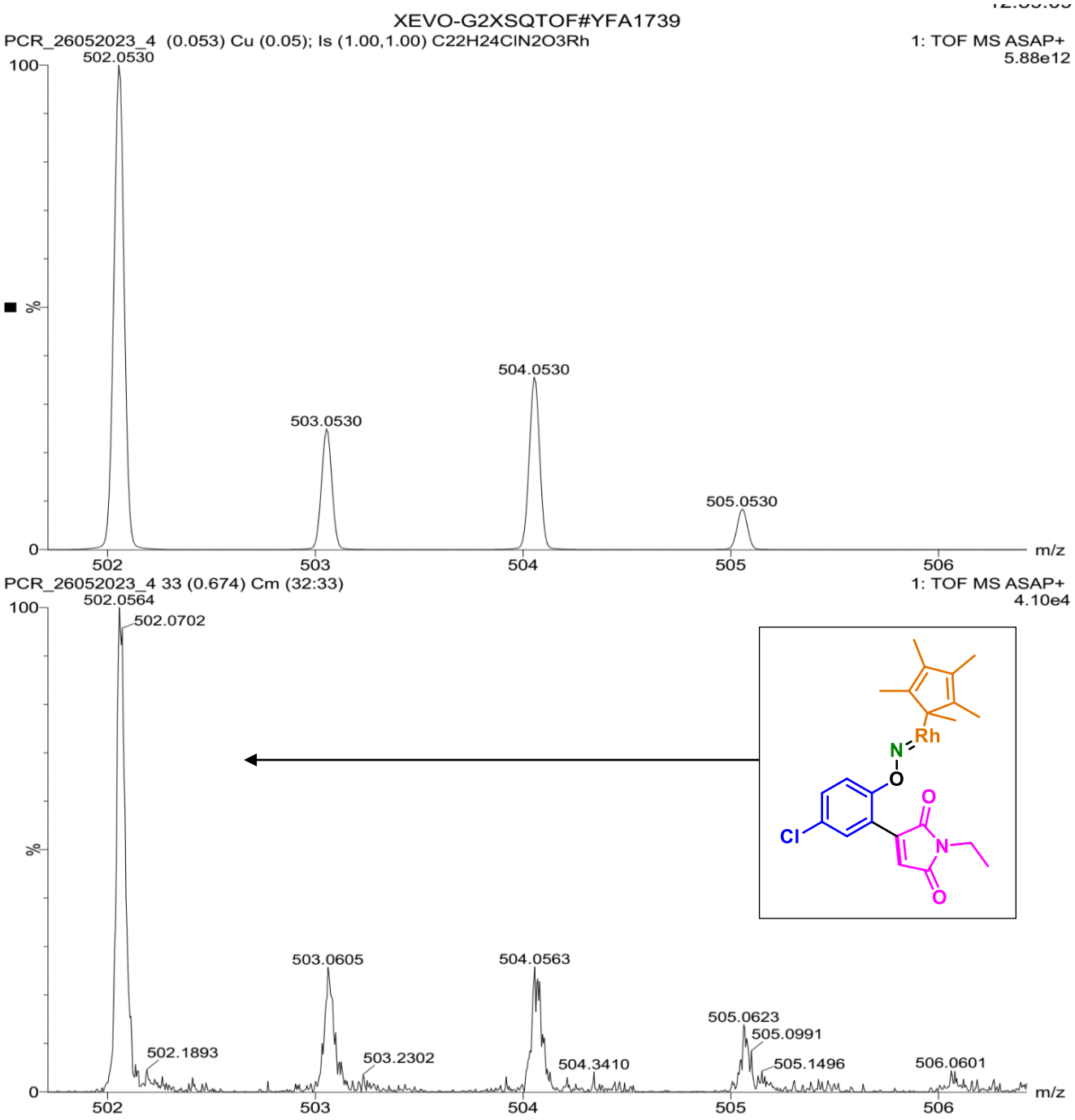
1b (1 equiv) + **2b** (1 equiv)

$[M]^+$ = $C_{24}H_{30}N_2O_3Rh$

Detected in HRMS
Observed: 497.1311
Calculated: 497.1306



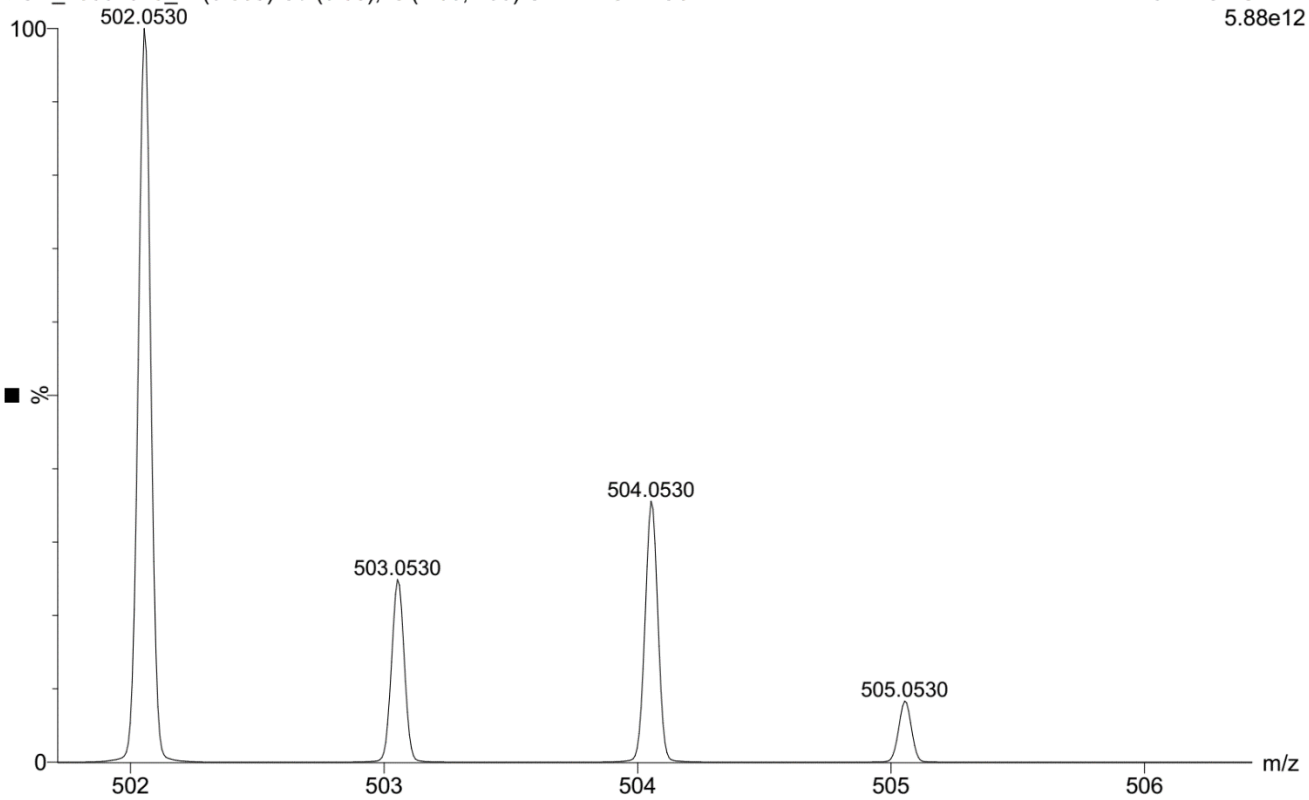

1h
(1 equiv)
2b
(1 equiv)
(Cp*RhCl2)2 (2.5 mol %)
CsOAc (50 mol %)
K3PO4 (50 mol %)
Na2SO4 (50 mol %)
TFE (0.2 M), 60 °C, 6 h
[M]+ A
C22H24ClN2O3Rh
Observed: 502.0564
Calculated: 502.0530
[M]+ B
C22H26ClN2O3Rh
Observed: 504.0655
Calculated: 504.0687
[M]+ C
C22H25ClN2O3Rh
Observed: 503.0650
Calculated: 503.0603


XEVO-G2XSQTOF#YFA1739
PCR_26052023_4 (0.053) Cu (0.05); Is (1.00,1.00) C22H24ClN2O3Rh
1: TOF MS ASAP+
5.88e12
502.0530
503.0530
504.0530
505.0530
m/z
PCR_26052023_4 33 (0.674) Cm (32:33)
1: TOF MS ASAP+
4.10e4
502.0564
502.0702
502.1893
503.0605
503.2302
504.0563
504.3410
505.0623
505.0991
505.1496
506.0601
Rh
N
O
Cl
O
N
O
m/z

XEVO-G2XSQTOF#YFA1739

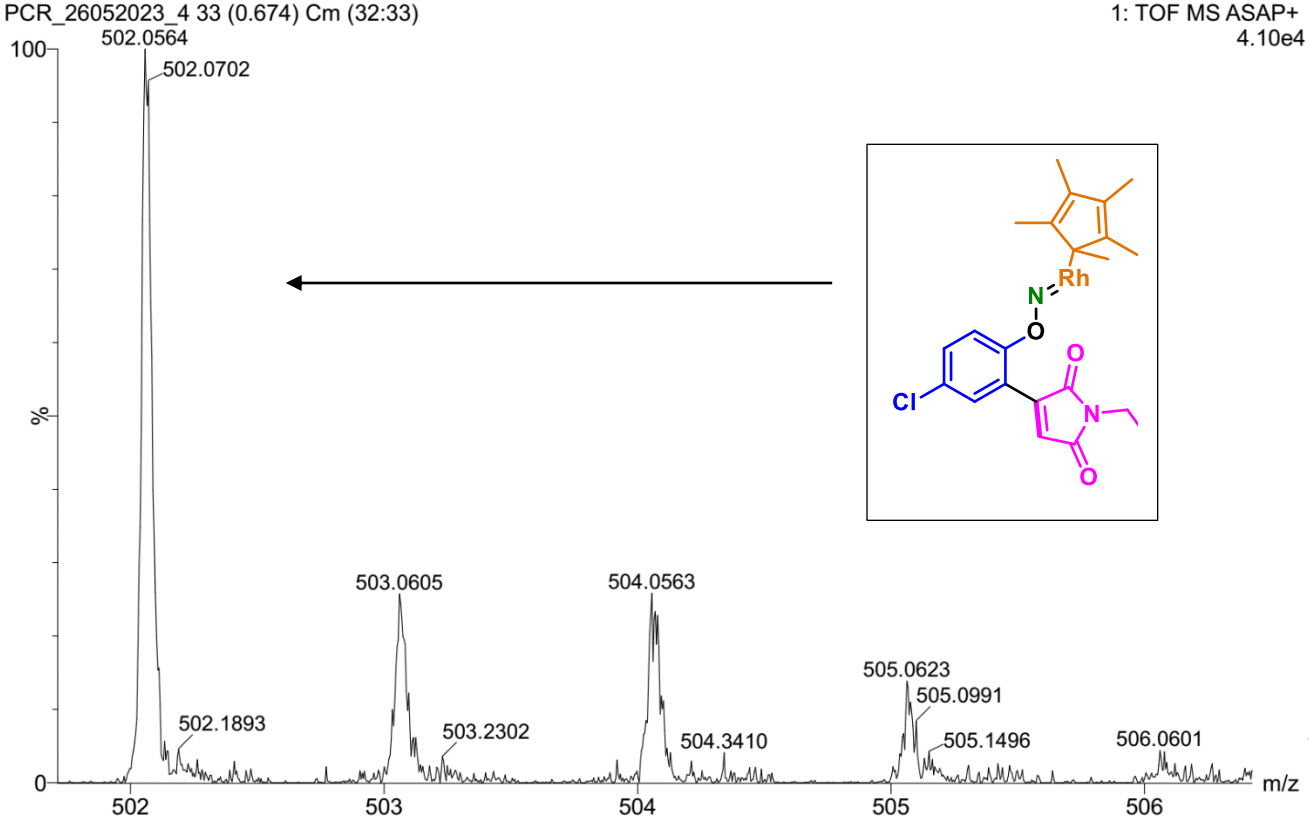
PCR_26052023_4 (0.053) Cu (0.05); Is (1.00,1.00) C22H24ClN2O3Rh

1: TOF MS ASAP+
5.88e12



PCR_26052023_4 33 (0.674) Cm (32:33)

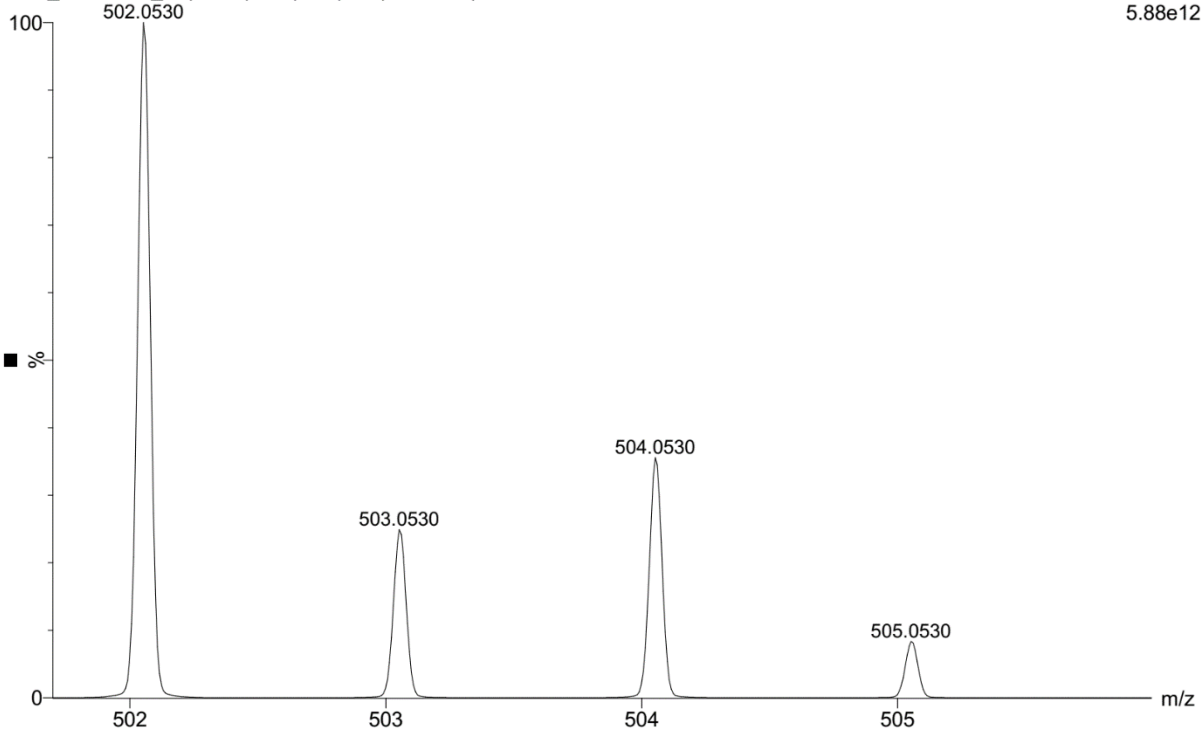
1: TOF MS ASAP+
4.10e4



XEVO-G2XSQTOF#YFA1739

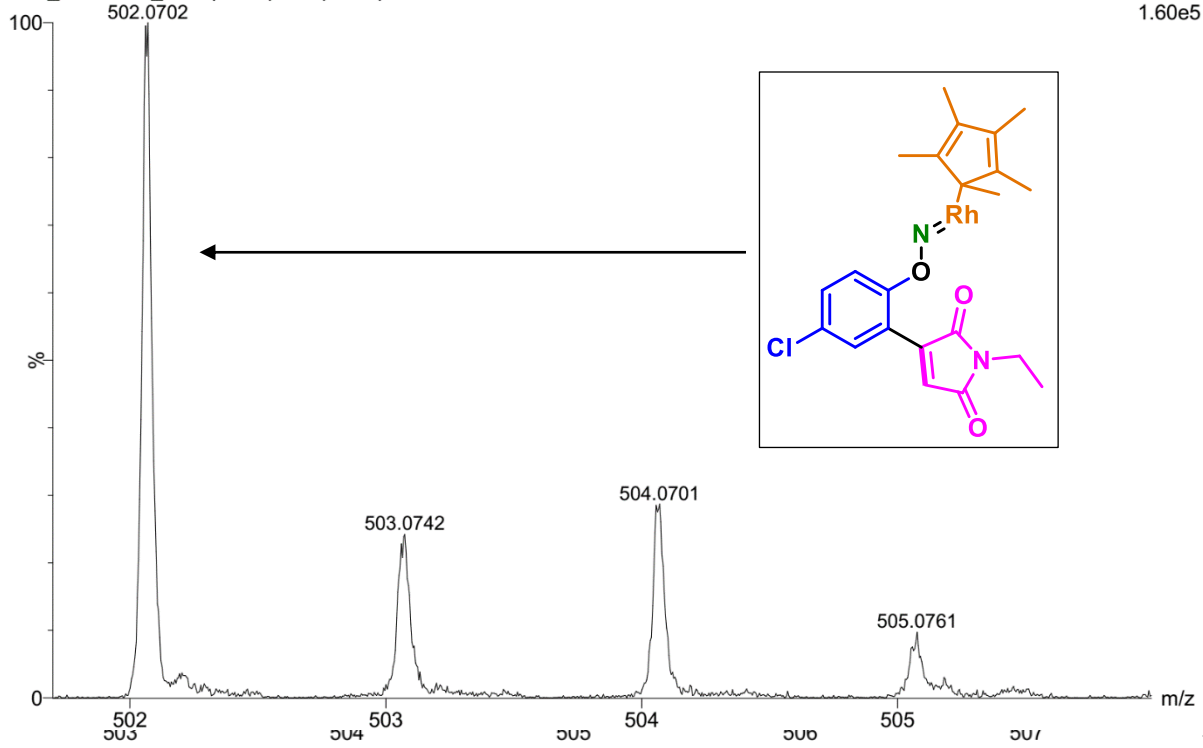
PCR_26052023_4 (0.053) Cu (0.05); Is (1.00,1.00) C22H24ClN2O3Rh

1: TOF MS ASAP+
5.88e12



PCR_26052023_4 41 (0.829) Cm (40:48)

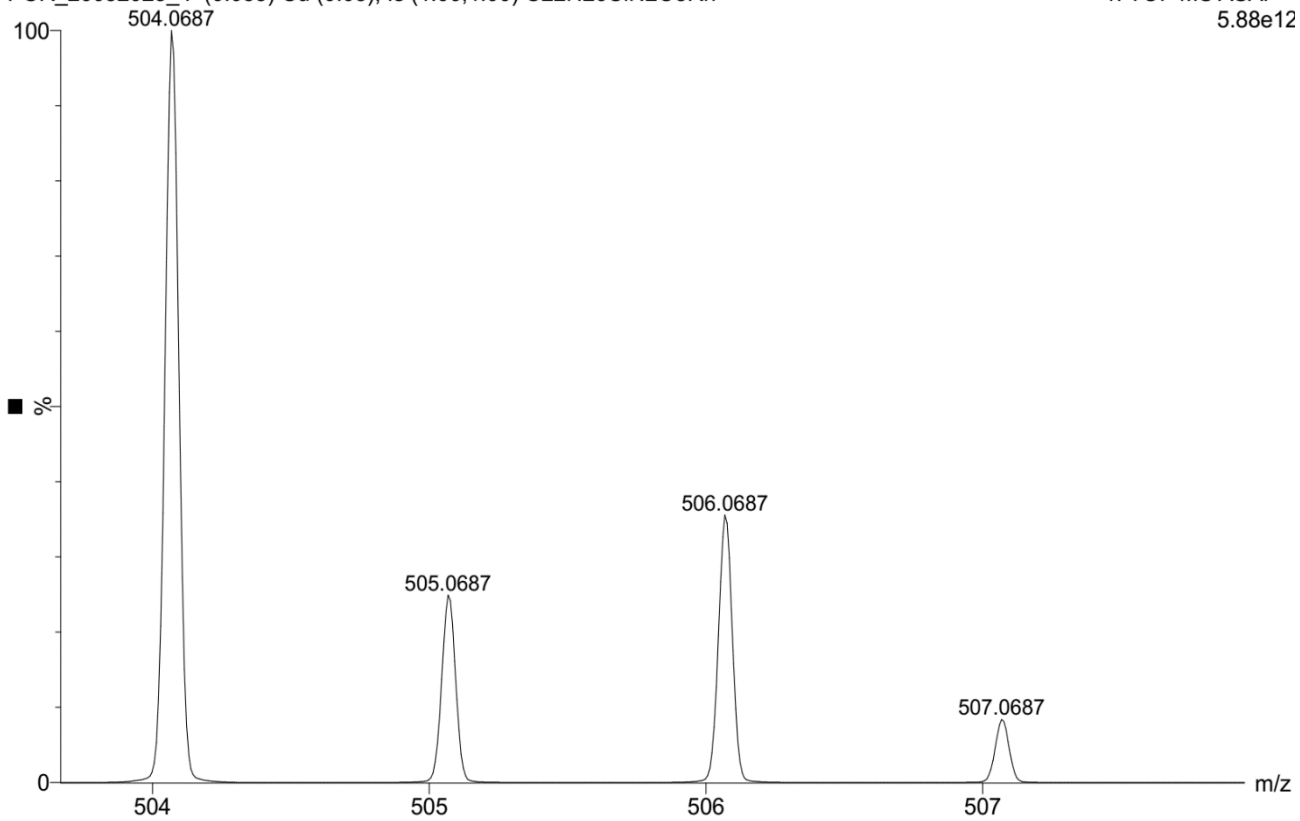
1: TOF MS ASAP+
1.60e5



XEVO-G2XSQTOF#YFA1739

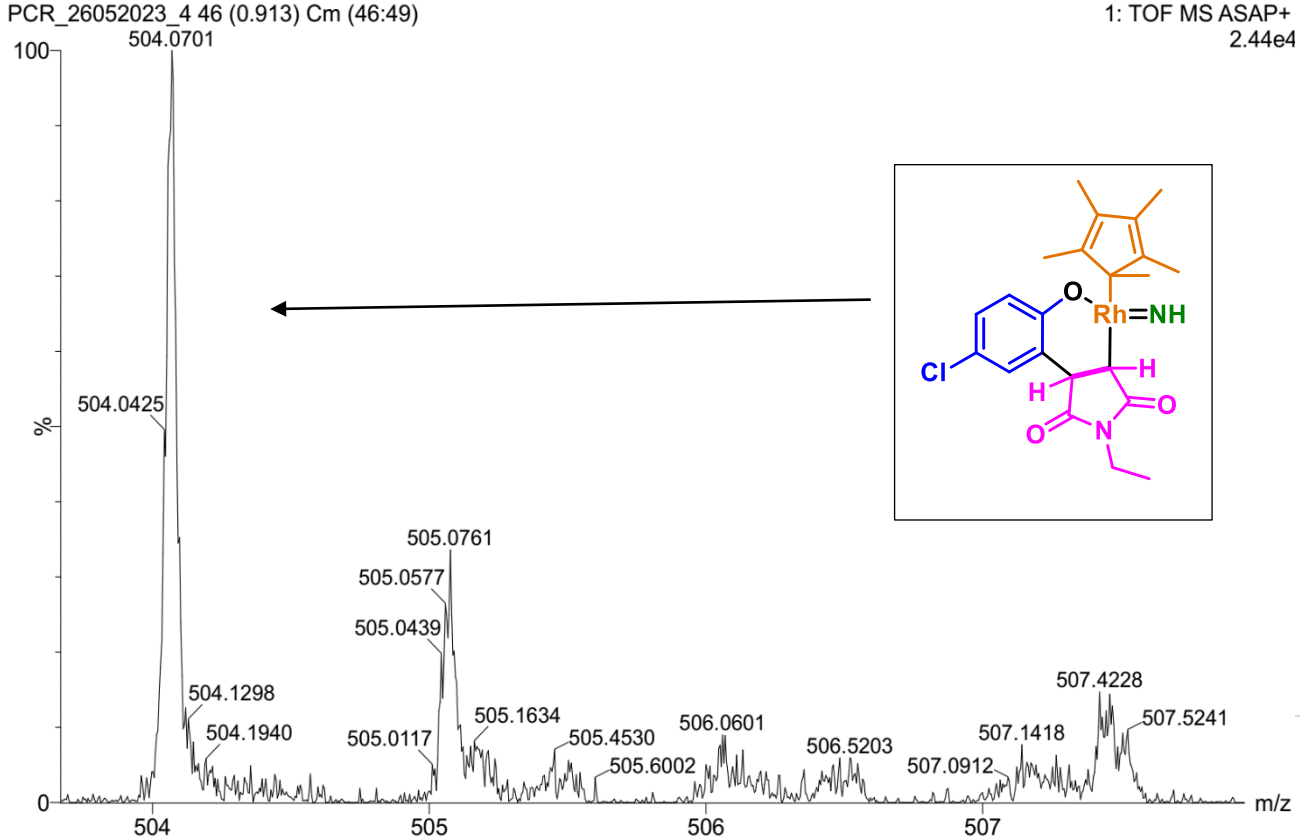
PCR_26052023_4 (0.053) Cu (0.05); Is (1.00,1.00) C22H26ClN2O3Rh

1: TOF MS ASAP+
5.88e12



PCR_26052023_4 46 (0.913) Cm (46:49)

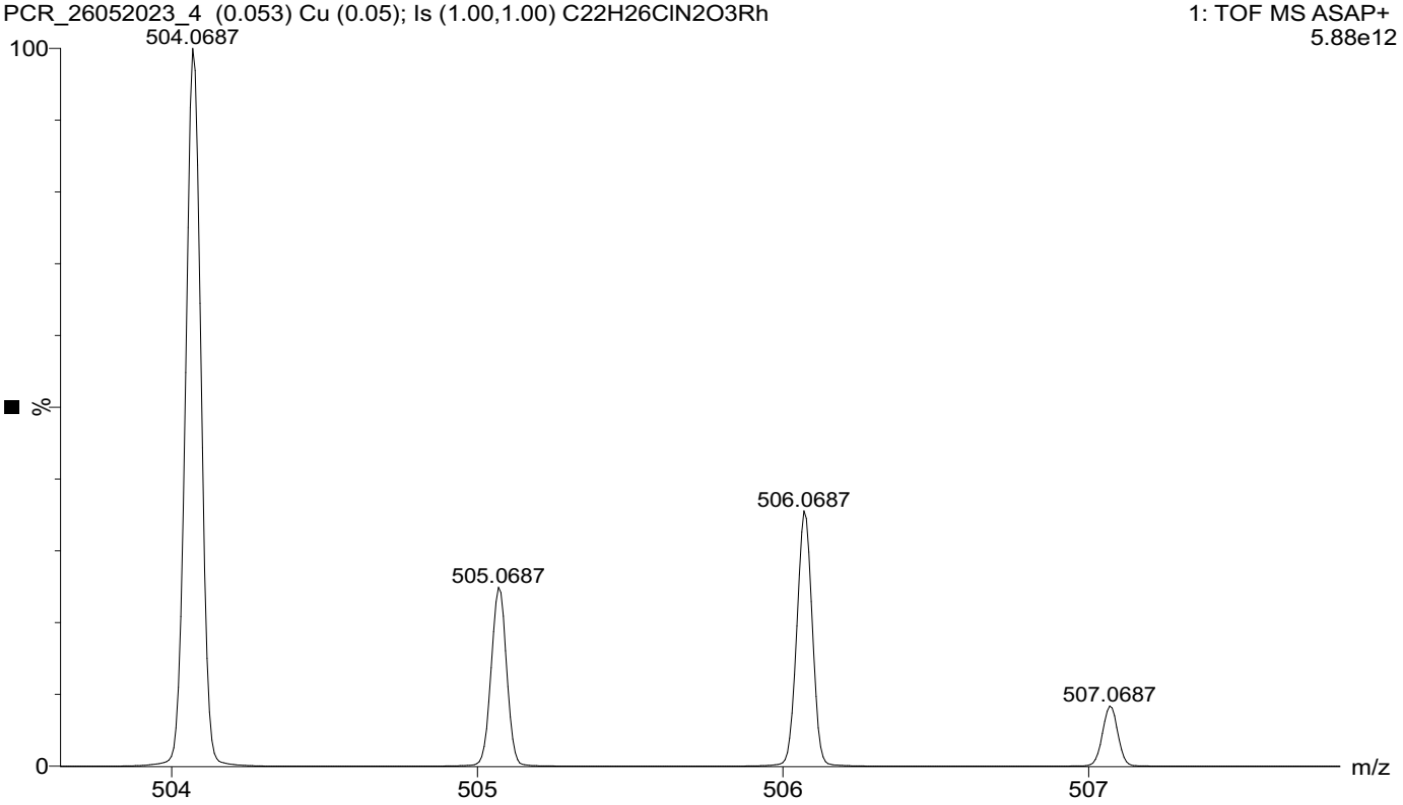
1: TOF MS ASAP+
2.44e4



XEVO-G2XSQTOF#YFA1739

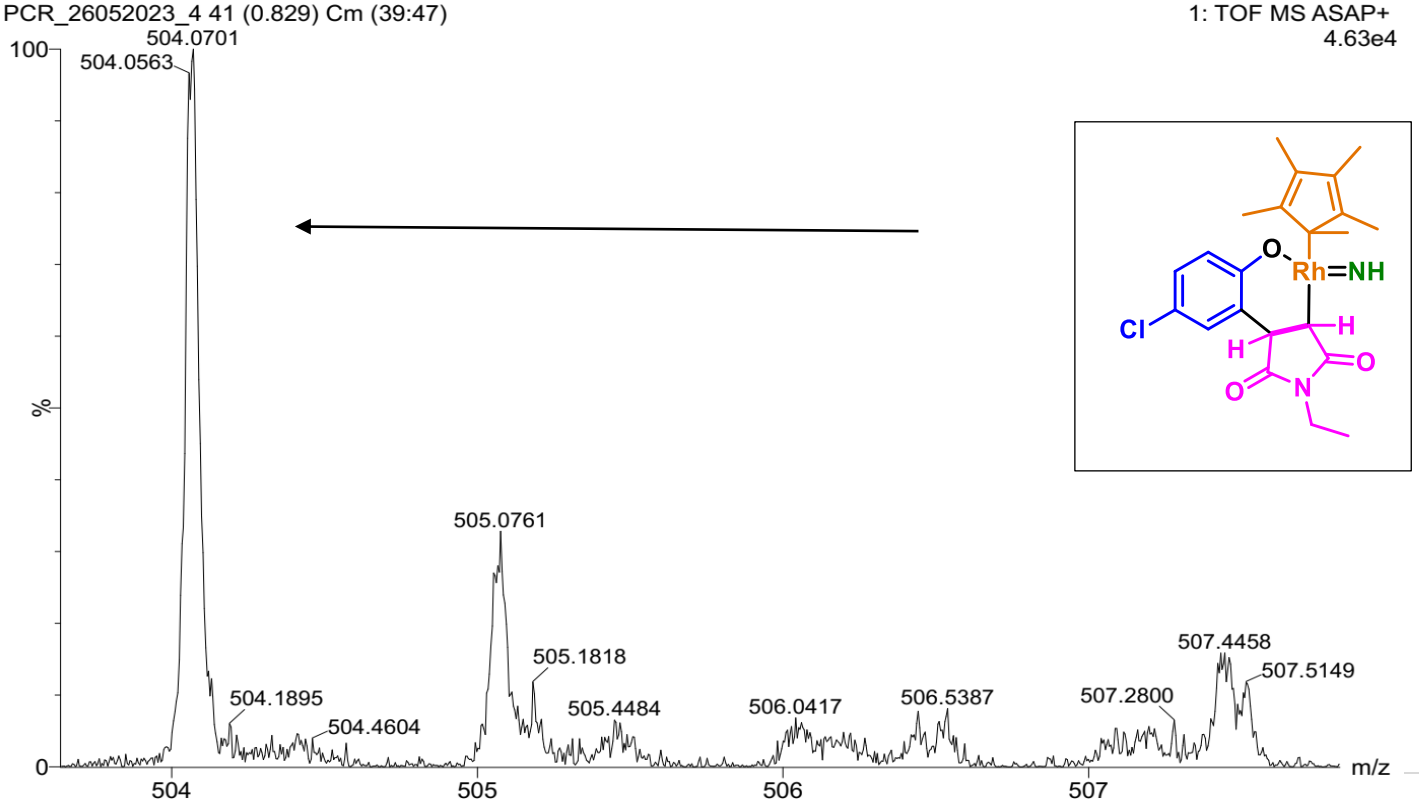
PCR_26052023_4 (0.053) Cu (0.05); Is (1.00,1.00) C22H26ClN2O3Rh

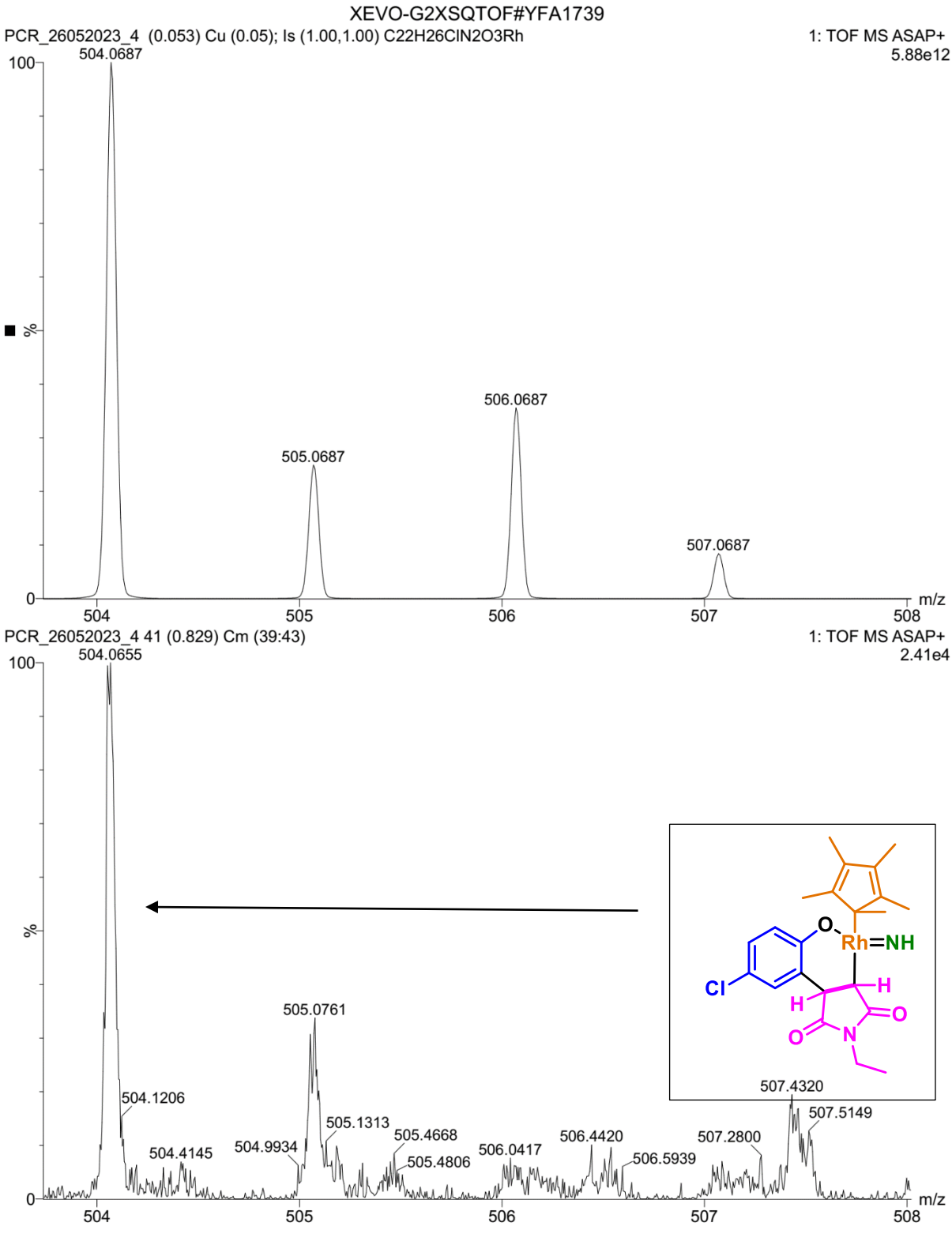
1: TOF MS ASAP+
5.88e12

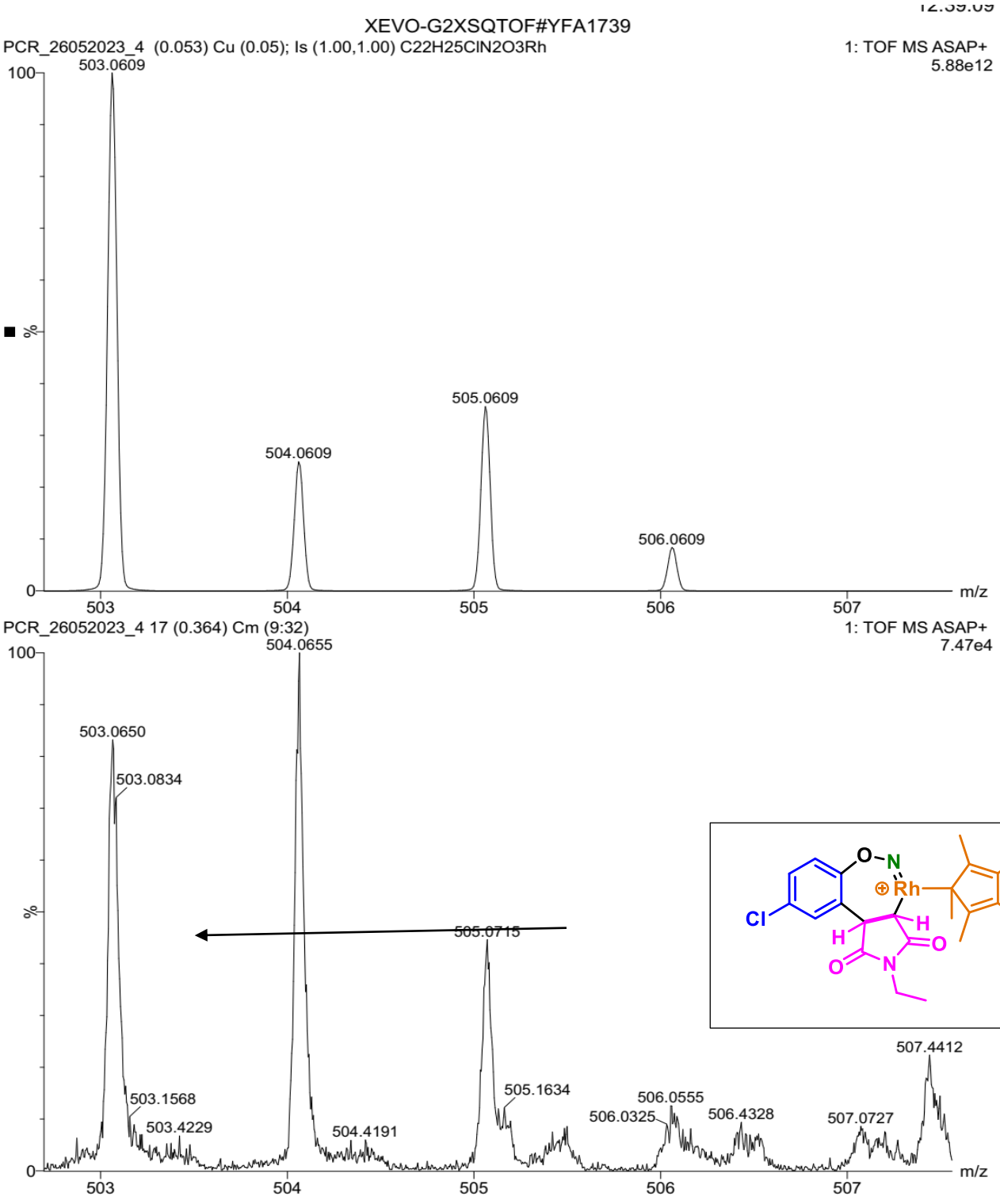


PCR_26052023_4 41 (0.829) Cm (39:47)

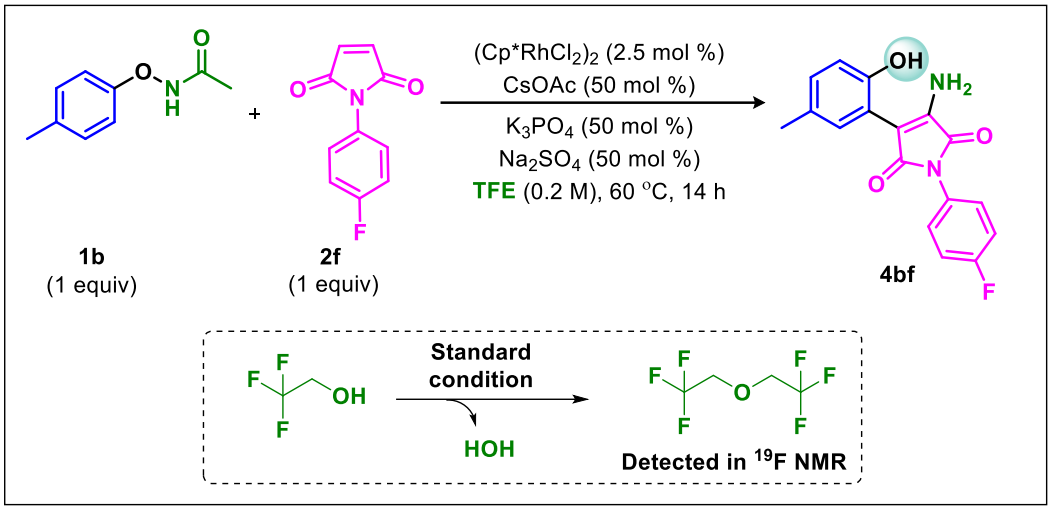
1: TOF MS ASAP+
4.63e4



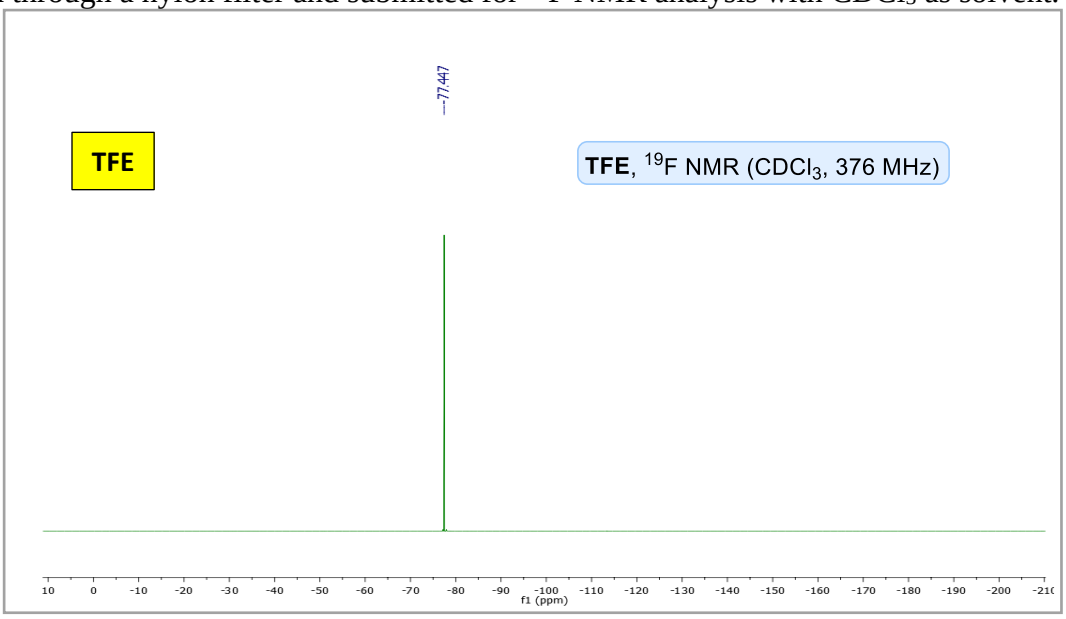

XEVO-G2XSQTOF#YFA1739
PCR_26052023_4 (0.053) Cu (0.05); Is (1.00,1.00) C22H26ClN2O3Rh
1: TOF MS ASAP+
5.88e12
504.0687
505.0687
506.0687
507.0687
PCR_26052023_4 41 (0.829) Cm (39:43)
1: TOF MS ASAP+
2.41e4
504.0655
505.0761
504.1206
504.4145
504.9934
505.1313
505.4668
505.4806
506.0417
506.4420
506.5939
507.2800
507.4320
507.5149
Rh=NH
Cl
m/z

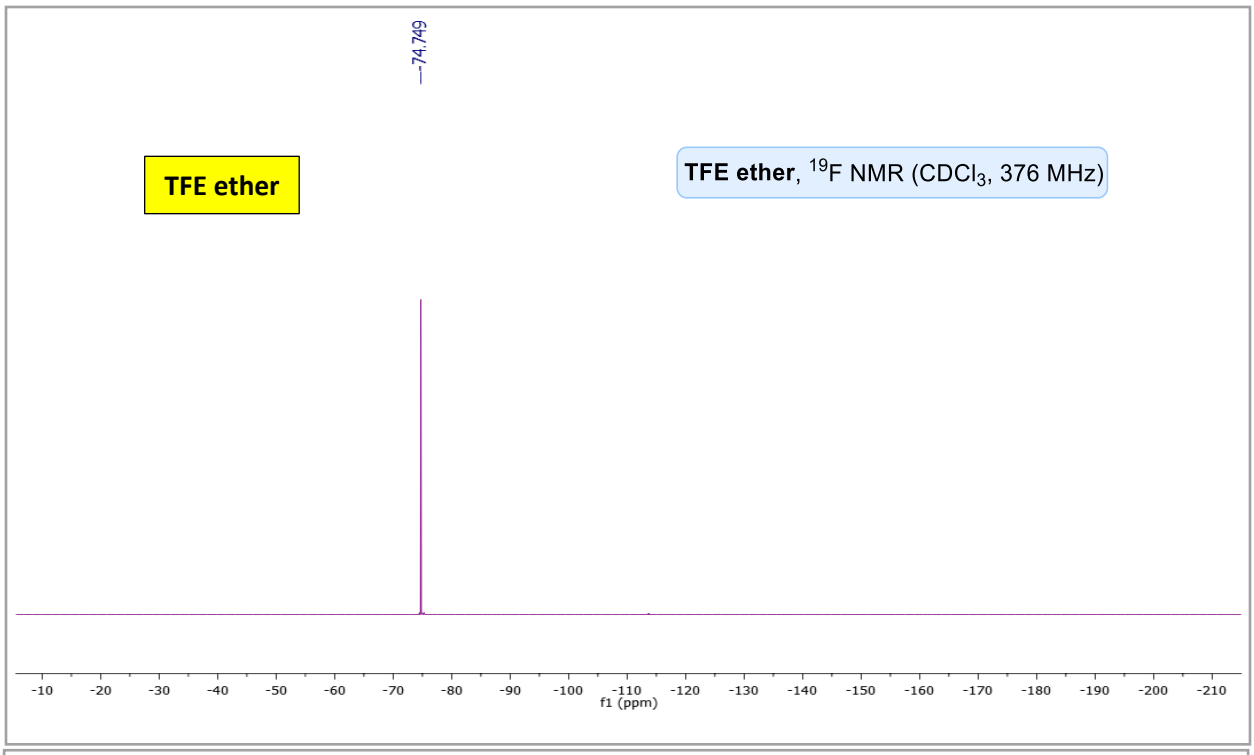

XEVO-G2XSQTOF#YFA1739
PCR_26052023_4 (0.053) Cu (0.05); Is (1.00,1.00) C22H25ClN2O3Rh
1: TOF MS ASAP+
5.88e12
503.0609
504.0609
505.0609
506.0609
m/z
PCR_26052023_4 17 (0.364) Cm (9:32)
1: TOF MS ASAP+
7.47e4
504.0655
503.0650
503.0834
505.0715
503.1568
503.4229
504.4191
505.1634
506.0325
506.0555
506.4328
507.0727
507.4412
Cl
Rh
H
O
N

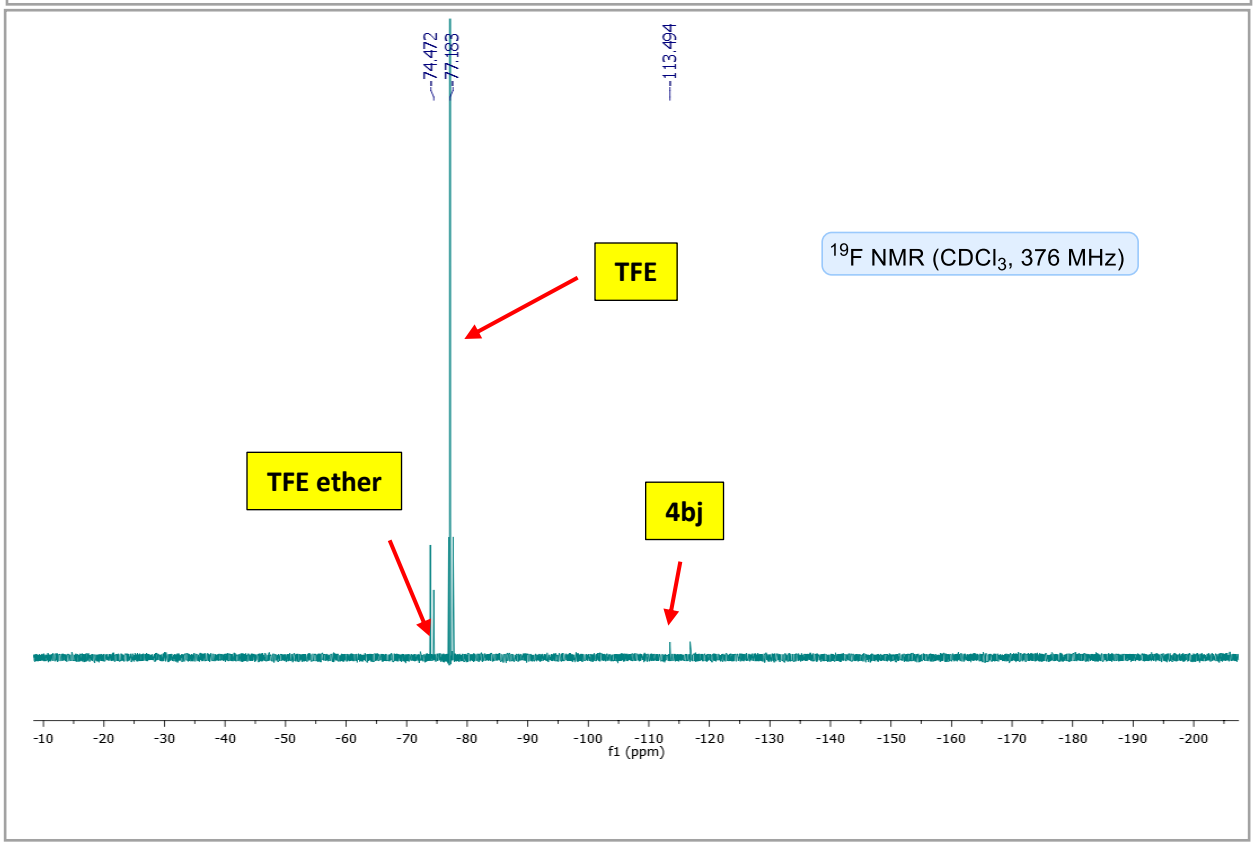
(4.8) ^{19}F NMR experiment:



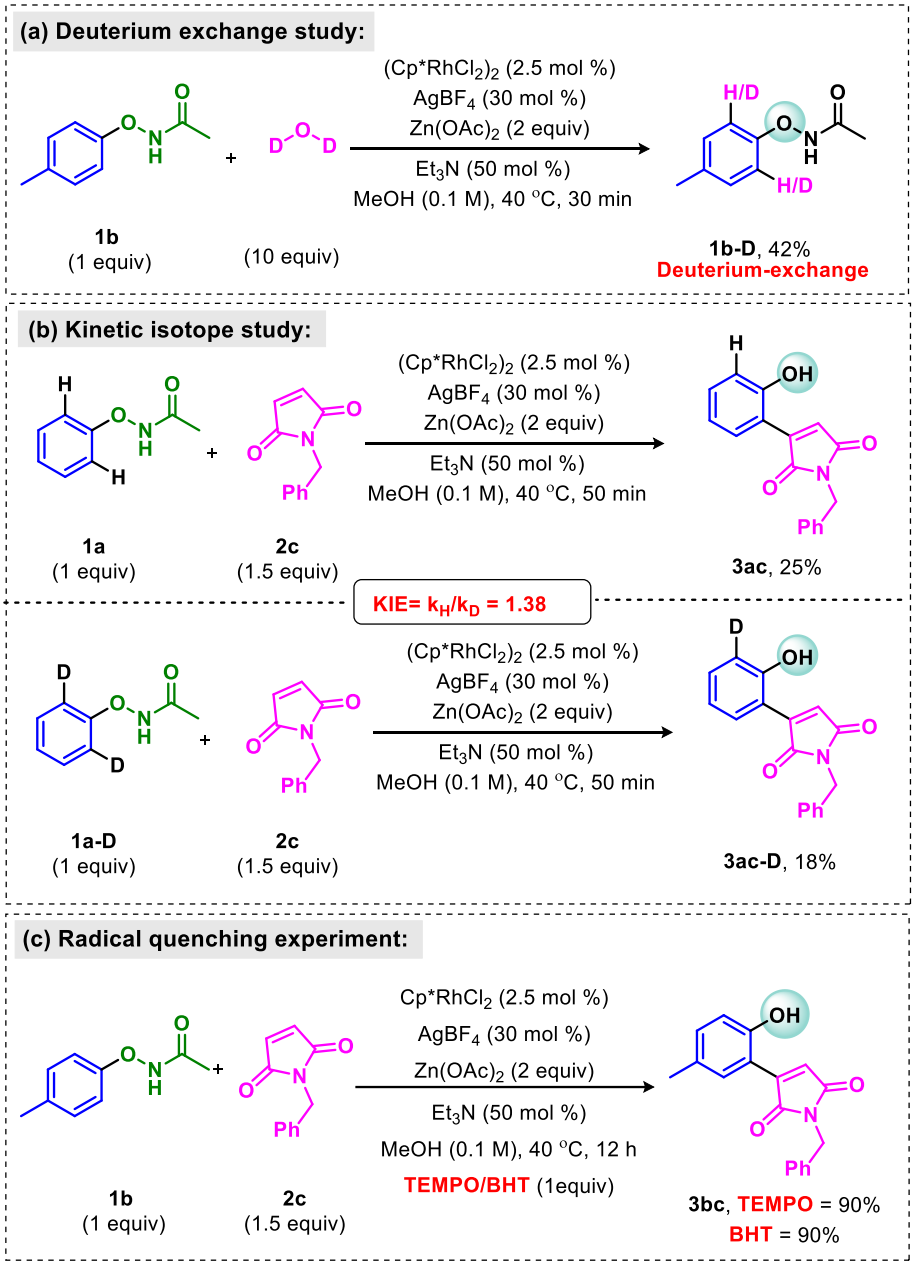
To an oven-dried seal tube charged with a stir bar, *N*-(*p*-tolyloxy)acetamide **1b** (0.1 mmol, 1 equiv), 1-(4-fluorophenyl)-1H-pyrrole-2,5-dione **2f** (0.1 mmol, 1 equiv), $(Cp^*RhCl_2)_2$ (0.0025 mmol, 2.5 mol %), Na_2SO_4 (0.05 mmol, 50 mol %), and TFE (0.5 mL, 0.2 M with respect to **1b**) were added under nitrogen atmosphere. The seal tube was taken inside the glove box, and CsOAc (0.05 mmol, 50 mol %), K_3PO_4 (0.05 mmol, 50 mol %), were added. The reaction mixture was stirred (700 rpm) in a preheated aluminum block at 60 °C for 14 h. After 14 h, the residue was filtered through a nylon filter and submitted for ^{19}F NMR analysis with $CDCl_3$ as solvent.




-74.749
TFE ether
TFE ether, ^{19}F NMR ($CDCl_3$, 376 MHz)
-10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)


-74.472
-77.183
-113.494
TFE
^{19}F NMR ($CDCl_3$, 376 MHz)
TFE ether
4bj
-10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)

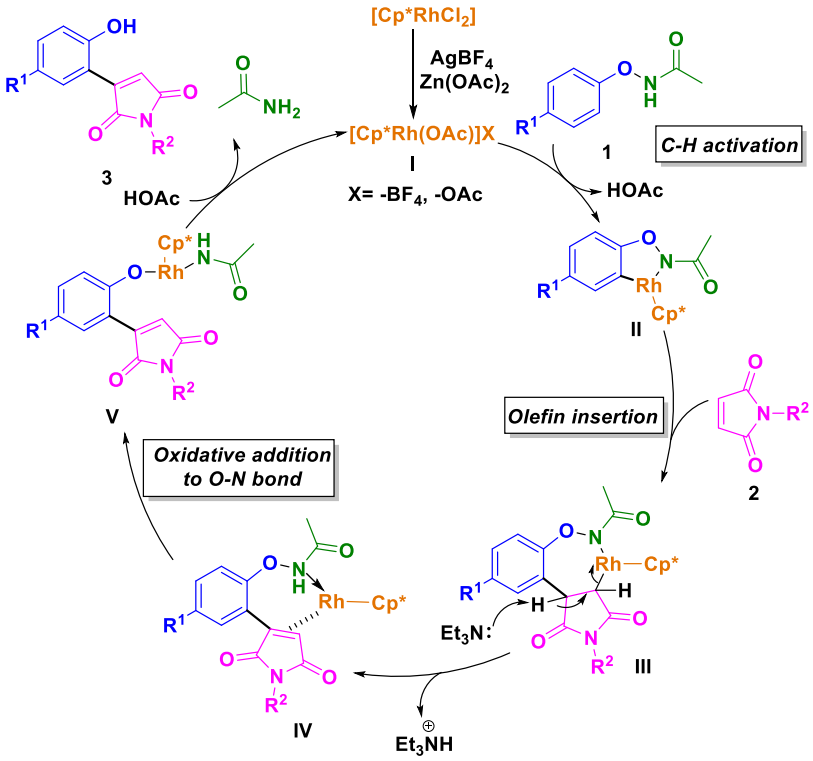
(4.9) Discussion on mechanistic study of *ortho*-olefination reaction



Scheme S1. Mechanistic studies for olefination reaction.

After synthesizing a wide range of *ortho*-olefination product, we performed various mechanistic studies to understand the mechanism. We have done an H-D exchange that resulted in 42% deuterium exchanged in the *ortho* position (Scheme S1a). This implies cyclometallation step is reversible. A kinetic isotope study has been performed, which resulted in a KIE value of 1.38 (Scheme S1b). This result indicates that C-H bond cleavage is not involved in the rate-determining step. A reaction in the presence of a radical quencher such as TEMPO or BHT resulted in a 90% yield of the desired product **3bc** (Scheme S1c). This implies that the reaction proceeds through non-radical pathway.

(4.10) Discussion on mechansim of *ortho*-olefination reaction.

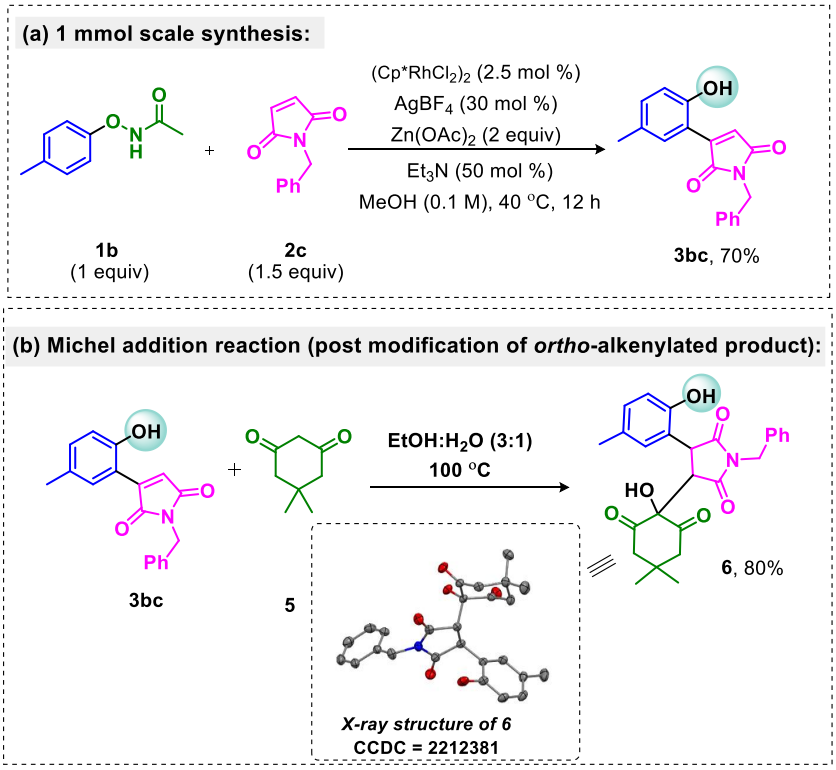


Scheme S2. Proposed catalytic cycle for olefination reaction.

From the mechanistic studies and literature precedences,[7] we proposed a plausible catalytic cycle for ortho-olefination reaction (Scheme S2). The olefination reaction proceeded after forming an active rhodium catalyst **I**. Rh(III) catalyst undergoes cyclometallation with phenoxyacetamide **1** to form the five-membered metallacycle **II**. Then, olefin insertion followed by base-mediated E2-

elimination gives rise to intermediate **IV** with the generation of Rh(I) intermediate. Then, Rh(I) oxidatively inserts into the O-N bond to form Rh(III) intermediate **V,** which on protonation, delivered the desired product **3** with the formation of acetamide and regenerated active Rh(III) catalyst.

(5) Discussion on synthetic utility

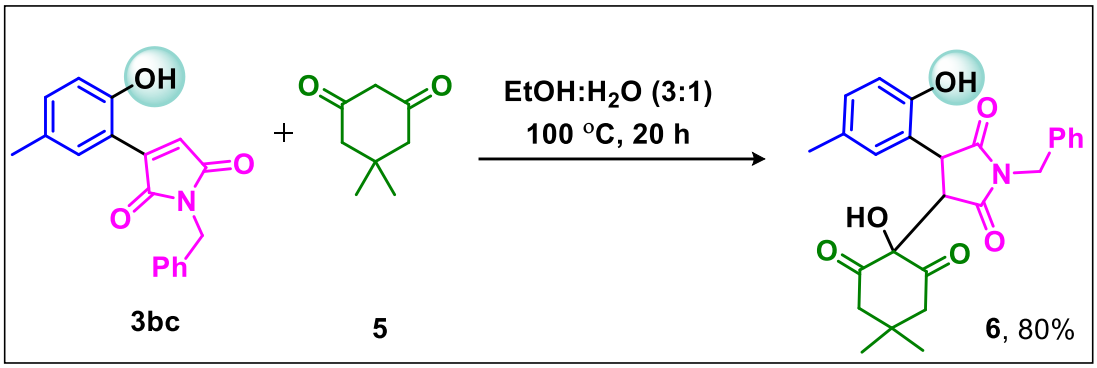


Scheme S4. Synthetic utility.

The synthetic utility of the demonstrated protocol has been further explored (Scheme S3). A reaction was performed at a 1 mmol scale and successfully delivered the *ortho*-olefinated product in 70% yield (Scheme S3a). The olefinated product generated through this protocol could be used as a Michael acceptor.[8] With this thought, we have treated the olefinated product with dimedone **5** that delivered the desired Michael addition product **6** in 80% yield with a quaternary center having a hydroxy group (Scheme S3b). The product formed has been characterized by the X-ray

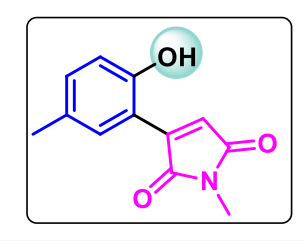
crystallographic study. However, the origin of the hydroxy group and the mechanism involved in this reaction is yet to be studied.

(5.1) Procedure for Michael addition reaction (post modification of *ortho*-olefinated product):



To an oven-dried seal tube charged with a stir bar, 1-benzyl-3-(2-hydroxy-5-methylphenyl)-1*H*-pyrrole-2,5-dione **3bc** (0.1 mmol, 1 equiv), 5,5-dimethylcyclohexane-1,3-dione **5** (0.1 mmol, 1 equiv), and EtOH:H_2O (0.33 M) were added in 3:1 ratio under air. The reaction mixture was stirred (700 rpm) in a preheated aluminum block at 100 °C for 20 h. After completion of the reaction (monitored by TLC), the solvent was evaporated under reduced pressure, and the crude was purified by column chromatography using EtOAc/hexane as eluent to get the corresponding *ortho*-olefinated product **6** in 80% yield (36 mg).

6. Experimental characterization data for products:



3-(2-hydroxy-5-methylphenyl)-1-methyl-1H-pyrrole-2,5-dione (3ba): was prepared according to general procedure (3.1). The crude reaction mixture was purified by column chromatography using silica gel (100-200 mesh size) giving (13 mg) 60% yield.

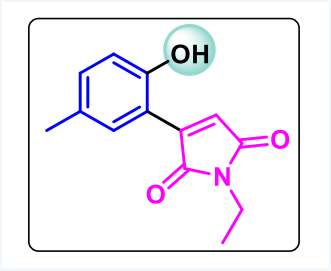
Physical State: yellow solid
Melting point: 223-224 ℃
R_f-value: 0.5 (10% EtOAc/hexane)

^{1}H NMR ($CDCl_3$, 700 MHz): δ 9.74 (s, 1H), 7.35 (s, 1H), 7.18 (dd, J = 8.4 Hz, 1.4 Hz, 1H), 6.90 (d, J = 8.4 Hz, 1H), 6.77 (s, 1H), 3.12 (s, 3H), 2.29 (s, 3H).

^{13}C NMR ($CDCl_3$, 175 MHz): δ 174.5, 170.2, 154.0, 146.0, 135.3, 130.3, 130.0, 124.0, 119.9, 115.1, 24.5, 20.7.

IR (KBr, cm^{-1}): 3438, 1635.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{12}H_{12}NO_3$: 218.0817; Found: 218.0833.



1-ethyl-3-(2-hydroxy-5-methylphenyl)-1H-pyrrole-2,5-dione (3bb): was prepared according to general procedure (3.1). The crude reaction mixture was purified by column chromatography using silica gel (100-200 mesh size) giving (17 mg) 74% yield.

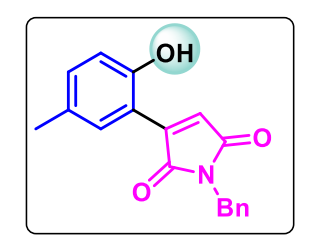
Physical State: yellow solid
Melting point: 147 -148 ℃
R_f-value: 0.5 (10% EtOAc/hexane)

^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.85 (s, 1H), 7.34 (brs, 1H), 7.18 (dd, J = 8.4 Hz, 1.6 Hz, 1H), 6.90 (d, J = 8.4Hz, 1H), 6.75 (s, 1H), 3.67 (q, J = 7.2 Hz, 2H), 2.29 (s, 3H), 1.25 (t, J = 7.2 Hz, 3H).

^{13}C NMR ($CDCl_3$, 175 MHz): δ 174.3, 170.0, 154.8, 145.9, 135.3, 130.3, 130.0, 123.9, 119.9, 115.1, 33.7, 20.7, 14.1.

IR (KBr, cm^{-1}): 3438, 1683, 1635.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{13}H_{14}NO_3$: 232.0974; Found: 232.0984.



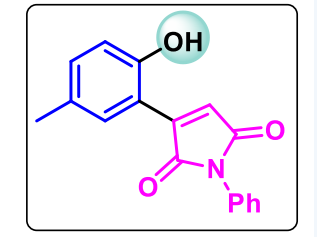
1-benzyl-3-(2-hydroxy-5-methylphenyl)-1H-pyrrole-2,5-dione (3bc): was prepared according to general procedure (3.1). The crude reaction mixture was purified by column chromatography using silica gel (100-200 mesh size) giving (28 mg) 95% yield.

Physical State: yellow solid
Melting point: 167-168 ℃
R_f-value: 0.5 (10% EtOAc/hexane)

^{1}H NMR ($CDCl_3$, 700 MHz): δ 9.56 (s, 1H), 7.38-7.36 (m, 3H), 7.33 (t, J = 7.7 Hz, 2H), 7.29 (d, J = 7 Hz, 1H), 7.16 (d, J = 8.4 Hz, 1H), 6.88 (d, J = 8.4 Hz, 1H), 6.79 (s, 1H), 4.76 (s, 2H), 2.28 (s, 3H).

^{13}C NMR ($CDCl_3$, 175 MHz): δ 174.1, 169.9, 154.0, 145.7, 136.0, 135.3, 130.3, 130.0, 129.1, 128.8, 128.4, 124.1, 119.8, 115.1, 42.2, 20.7.

IR (KBr, cm^{-1}): 3438, 1682, 1634.
HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{16}NO_3$: 294.1130; Found: 294.1147.



3-(2-hydroxy-5-methylphenyl)-1-phenyl-1H-pyrrole-2,5-dione (3bd): was prepared according to general procedure (3.1). The crude reaction mixture was purified by column chromatography using silica gel (100-200 mesh size) giving (17 mg) 61% yield.

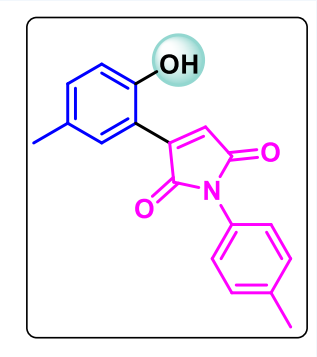
Physical State: yellow solid
Melting point: 173 ℃
R_f-value: 0.5 (10% EtOAc/hexane)

^{1}H NMR ($CDCl_3$, 700 MHz): δ 9.27 (s, 1H), 7.50 (t, J = 7 Hz, 2H), 7.47 (s, 1H), 7.41 (t, J = 7 Hz, 1H), 7.38 (d, J = 7 Hz, 2H), 7.21 (d, J = 8.4 Hz, 1H), 6.95 (s, 1H), 6.91 (d, J = 8.4 Hz, 1H), 2.32 (s, 3H).

^{13}C NMR ($CDCl_3$, 175 MHz): δ 173.2, 169.2, 154.1, 145.3, 135.3, 131.2, 130.5, 130.4, 129.5, 128.7, 126.7, 124.6, 119.7, 115.2, 20.7.

IR (KBr, cm^{-1}): 3423, 1700, 1617.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{17}H_{14}NO_3$: 280.0974; Found: 280.0958.



3-(2-hydroxy-5-methylphenyl)-1-(*p*-tolyl)-1H-pyrrole-2,5-dione (3be): was prepared according to general procedure (3.1). The crude reaction mixture was purified by column chromatography using silica gel (100-200 mesh size) giving (16 mg) 55% yield.

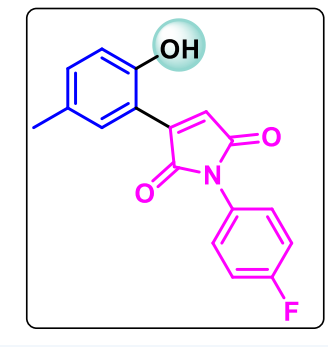
Physical State: yellow solid
Melting point: 193-194 ℃
R_f-value: 0.5 (10% EtOAc/hexane)

^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.38 (s, 1H), 7.45 (s, 1H), 7.30 (d, J = 8.4 Hz, 2H), 7.25-7.19 (m, 3H), 6.92-6.90 (m, 2H), 2.40 (s, 3H), 2.31 (s, 3H)

^{13}C NMR ($CDCl_3$, 175 MHz): δ 173.4, 169.3, 154.1, 145.4, 138.8, 135.4, 130.5, 130.3, 132.2, 128.5, 126.6, 124.4, 119.8, 115.2, 21.5, 20.7.

IR (KBr, cm^{-1}): 3421, 1693, 1611.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{16}NO_3$: 294.1130; Found: 294.1132.

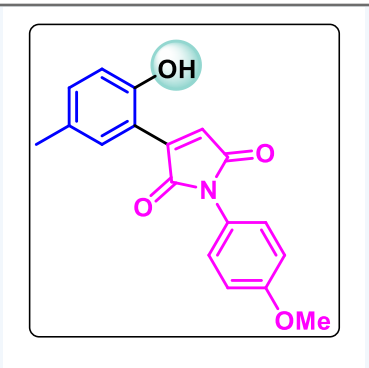


1-(4-fluorophenyl)-3-(2-hydroxy-5-methylphenyl)-1H-pyrrole-2,5-dione (3bf): was prepared according to general procedure (3.1). The crude reaction mixture was purified by column chromatography using silica gel (100-200 mesh size) giving (20 mg) 67% yield.

Physical State: orange solid
Melting point: 189-190 ℃
R_f-value: 0.5 (10% EtOAc/hexane)
^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.05 (s, 1H), 7.48 (brs, 1H), 7.39-7.35 (m, 2H), 7.22-7.19 (m, 3H), 6.96 (s, 1H), 6.91 (d, J = 8.4 Hz, 1H), 2.32 (s, 3H).

^{13}C NMR ($CDCl_3$, 175 MHz): δ 173.0, 169.0, 162.4 (d, J_{C-F} =247.1 Hz), 154.1, 145.2, 135.4, 130.6, 130.4, 128.5 (d, J_{C-F} = 8.7 Hz), 127.2 (d, J_{C-F} = 2.6 Hz), 124.6, 119.7, 116.6 (d, J_{C-F} = 22.7 Hz), 115.1, 20.7.

^{19}F NMR ($CDCl_3$, 376 MHz): δ -112.5.
IR (KBr, cm^{-1}): 3437, 1709, 1636.
HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{17}H_{13}NO_3F$: 298.0879; Found: 298.0896.



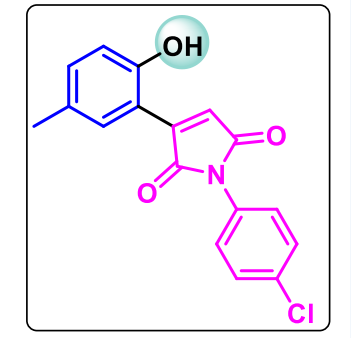
3-(2-hydroxy-5-methylphenyl)-1-(4-methoxyphenyl)-1H-pyrrole-2,5-dione (3bg) was prepared according to general procedure (3.1). The crude reaction mixture was purified by column chromatography using silica gel (100-200 mesh size) giving (18 mg) 58% yield.

Physical State: orange solid
Melting point: 154-155 ℃
R_f-value: 0.5 (10% EtOAc/hexane)

^{1}H NMR ($CDCl_3$, 700 MHz): δ 9.41 (s, 1H), 7.45 (s, 1H), 7.27 (d, J = 8.4 Hz, 2H), 7.20 (d, J = 8.4 Hz, 1H), 7.01 (d, J = 9.1 Hz, 2H) 6.92-6.90 (m, 2H), 3.84 (s, 3H), 2.31 (s, 3H).

^{13}C NMR ($CDCl_3$, 175 MHz): δ 173.5, 169.5, 159.8, 154.1, 145.4, 135.4, 130.5, 130.3, 128.1, 124.3, 123.8, 119.8, 115.2, 114.9, 55.8, 20.7.
IR (KBr, cm^{-1}): 3438, 1697, 1633.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{16}NO_4$: 310.1079; Found: 310.1062.

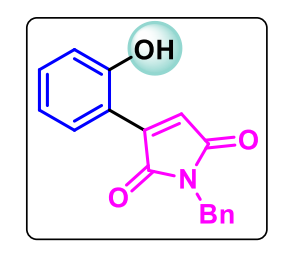


1-(4-chlorophenyl)-3-(2-hydroxy-5-methylphenyl)-1H-pyrrole-2,5-dione (3bh): was prepared according to general procedure (3.1). The crude reaction mixture was purified by column chromatography using silica gel (100-200 mesh size) giving (22 mg) 70% yield.

Physical State: light orange solid
Melting point: 210-211 ℃
R_f-value: 0.5 (30% EtOAc/hexane)

^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.93 (s, 1H), 7.49-7.45 (m, 3H), 7.37-7.34 (m, 2H), 7.21 (dd, J = 8.4 Hz, 2 Hz, 1H), 6.97 (s, 1H), 6.91 (d, J= 8.4 Hz, 1H), 2.32 (s, 3H).

^{13}C NMR ($CDCl_3$, 175 MHz): δ 172.7, 168.9, 154.1, 145.1, 135.4, 134.4, 130.7, 130.4, 129.8, 129.7, 127.7, 124.7, 119.6, 115.1, 20.7.
IR (KBr, cm^{-1}): 3420, 1684, 1635.
HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{17}H_{13}NO_3Cl$: 314.0584; Found: 314.0578.



1-benzyl-3-(2-hydroxyphenyl)-1H-pyrrole-2,5-dione (3ac): was prepared according to general procedure (3.1). The crude reaction mixture was purified by column chromatography using silica gel (100-200 mesh size) giving (24 mg) 86% yield.

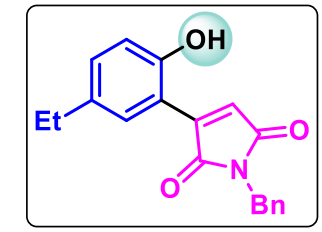
Physical State: yellow solid
Melting point: 171-172 ℃
R_f-value: 0.5 (10% EtOAc/hexane)

^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.80 (s, 1H), 7.59 (dd, J = 8.0 Hz, 1.6 Hz, 1H), 7.40-7.29 (m, 6H), 6.98 (dd, J = 8.0 Hz, 1.6 Hz, 1H), 6.94 (t, J = 8.0 Hz, 1H), 6.81 (s, 1H), 4.77 (s, 2H).

^{13}C NMR ($CDCl_3$, 175 MHz): δ 174.1, 169.8, 156.1, 145.7, 136.0, 134.3, 130.2, 129.1, 128.8, 128.4, 124.3, 121.1, 120.0, 115.4, 42.3.

IR (KBr, cm^{-1}): 3438, 1698, 1606.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{17}H_{13}NO_3Na$: 302.0793; Found: 302.0803.

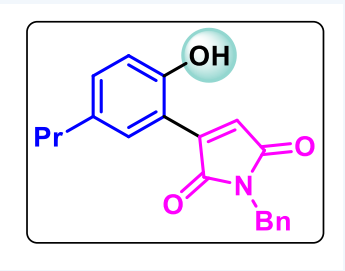


1-benzyl-3-(5-ethyl-2-hydroxyphenyl)-1H-pyrrole-2,5-dione (3cc): was prepared according to general procedure (3.1). The crude reaction mixture was purified by column chromatography using silica gel (100-200 mesh size) giving (26 mg) 85% yield.

Physical State: yellow solid
Melting point: 147-148 ℃
R_f-value: 0.5 (10% EtOAc/hexane)

^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.59 (s, 1H),), 7.38-7.37 (m, 3H), 7.33 (t, J = 7.0 Hz, 2H), 7.29 (t, J = 7.0 Hz, 1H), 7.20 (dd, J = 8.4 Hz, 2.1, Hz, 1H), 6.91 (d, J = 8.4 Hz, 1H), 6.80 (s, 1H), 4.77 (s, 2H), 2.58 (q, J = 7.7 Hz, 2H), 1.20 (t, J = 7.7 Hz, 3H).

^{13}C NMR ($CDCl_3$, 175 MHz): δ 174.1, 169.9, 154.2, 145.8, 136.8, 136.0, 134.2, 129.1, 128.9, 128.8, 128.3, 124.0, 119.9, 115.1, 42.2, 28.2, 15.9.
IR (KBr, cm^{-1}): 3437, 1684, 1635.
HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{19}H_{18}NO_3$: 308.1287; Found: 308.1274.



1-benzyl-3-(2-hydroxy-5-propylphenyl)-1H-pyrrole-2,5-dione (3dc): was prepared according to general procedure (3.1). The crude reaction mixture was purified by column chromatography using silica gel (100-200 mesh size) giving (28 mg) 87% yield.

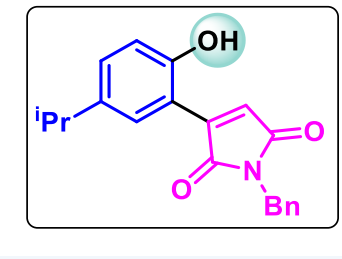
Physical State: yellow solid
Melting point: 136-137 ℃
R_f-value: 0.5 (10% EtOAc/hexane)

^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.59 (s, 1H), 7.39-728 (m, 6H), 7.17 (dd, J = 8.4 Hz, 2.0 Hz, 1H), 6.90 (d, J = 8.4 Hz, 1H), 6.80 (s, 1H), 4.76 (s, 2H), 2.51 (t, J = 7.2 Hz, 2H), 1.62-1.55 (m, 2H), 0.92 (t, J = 7.2 Hz, 3H).

^{13}C NMR ($CDCl_3$, 175 MHz): δ 174.1, 169.9, 154.2, 145.7, 136.0, 135.3, 134.7, 129.6, 129.1, 128.8, 128.3, 124.0, 119.8, 115.1, 42.2, 37.2, 24.8, 13.9.

IR (KBr, cm^{-1}): 3438, 1685, 1635.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{20}H_{20}NO_3$: 322.1443; Found: 322.1429.



1-benzyl-3-(2-hydroxy-5-isopropylphenyl)-1H-pyrrole-2,5-dione (3ec): was prepared according to general procedure (3.1). The crude reaction mixture was purified by column chromatography using silica gel (100-200 mesh size) giving (27 mg) 84% yield.

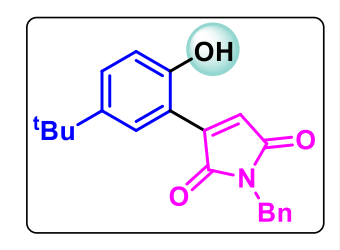
Physical State: yellow solid
Melting point: 136-137 ℃
R_f-value: 0.5 (10% EtOAc/hexane)

^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.58 (s, 1H), 7.40-7.28 (m, 6H), 7.25-7.23 (m, 1H), 6.92 (d, J = 8.4 Hz, 1H), 6.80 (s, 1H), 4.77 (s, 2H), 2.85 (sept, J = 6.8 Hz, 1H), 1.22 (d, J = 7.2 Hz, 6H).

^{13}C NMR ($CDCl_3$, 175 MHz): δ 174.1, 169.9, 154.2, 145.9, 141.5, 136.0, 132.7, 129.1, 128.8, 128.3, 127.6, 124.0, 119.9, 115.1, 42.2, 33.5, 24.3.

IR (KBr, cm^{-1}): 3438, 1682, 1641.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{20}H_{20}NO_3$: 322.1443; Found: 322.1423.

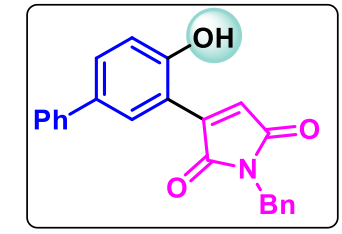


1-benzyl-3-(5-(tert-butyl)-2-hydroxyphenyl)-1H-pyrrole-2,5-dione (3fc): was prepared according to general procedure (3.1). The crude reaction mixture was purified by column chromatography using silica gel (100-200 mesh size) giving (30 mg) 90% yield.

Physical State: yellow solid
Melting point: 123-124 ℃
R_f-value: 0.5 (10% EtOAc/hexane)

^{1}H NMR ($CDCl_3$, 700 MHz): δ 9.57 (s, 1H), 7.54 (d, J = 2.1 Hz, 1H), 7.41 (dd, J = 9.1 Hz, 2.8 Hz, 1H), 7.37 (d, J = 7.7 Hz, 2H), 7.33 (t, J = 7.7Hz, 2H), 7.29 (d, J = 7.0 Hz, 1H), 6.92 (d, J =9.1 Hz, 1H), 6.80 (s, 1H), 4.77 (s, 2H), 1.29 (s, 9H).

^{13}C NMR ($CDCl_3$, 175 MHz): δ 174.1, 169.9, 153.9, 146.1, 143.8, 136.0, 132.0, 129.1, 128.8, 128.3, 126.4, 124.0, 119.6, 114.7, 42.2, 34.4, 31.6.
IR (KBr, cm^{-1}): 3437, 1689, 1613.
HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{21}H_{22}NO_3$: 336.1600; Found: 336.1632.



1-benzyl-3-(4-hydroxy-[1,1'-biphenyl]-3-yl)-1H-pyrrole-2,5-dione (3gc) was prepared according to general procedure (3.1). The crude reaction mixture was purified by column chromatography using silica gel (100-200 mesh size) giving (22 mg) 62% yield.

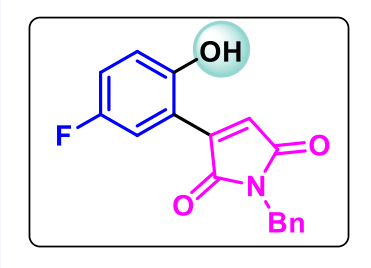
Physical State: yellow solid
Melting point: 169-170 ℃
R_f-value: 0.5 (10% EtOAc/hexane)

^{1}H NMR ($CDCl_3$, 700 MHz): δ 9.88 (s, 1H), 7.78 (d, J = 2.1 Hz, 1H), 7.60 (dd, J = 9.1 Hz, 2.8 Hz, 1H), 7.52 (d, J = 7.0 Hz, 2H), 7.43 (t, J = 7.7 Hz, 2H), 7.40 (d, J = 7.0 Hz, 2H), 7.35-7.34 (m, 3H), 7.30 (d, J = 7 Hz, 1H), 7.06 (d, J = 8.4 Hz, 1H), 6.88 (s, 1H), 4.79 (s, 2H).

^{13}C NMR ($CDCl_3$, 175 MHz): δ 174.1, 169.7, 155.6, 149.5, 145.7, 140.1, 135.9, 134.4, 133.2, 129.2, 129.1, 128.9, 128.6, 127.6, 127.0, 124.5, 120.5, 115.7, 42.3.

IR (KBr, cm^{-1}): 3438, 1683, 1639.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{23}H_{18}NO_3$: 356.1287; Found: 356.1294.



1-benzyl-3-(5-fluoro-2-hydroxyphenyl)-1H-pyrrole-2,5-dione (3hc): was prepared according to general procedure (3.2). The crude reaction mixture was purified by column chromatography using silica gel (100-200 mesh size) giving (24 mg) 81 % yield.

Physical State: yellow solid
Melting point: 192-193 ℃
R_f-value: 0.4 (20% EtOAc/hexane)

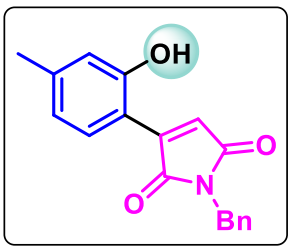
^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.49 (s, 1H), 7.39-7.29 (m, 6H), 7.08 (td, J = 10.0 Hz, 3.2 Hz, 1H), 6.95-6.91 (m, 1H), 6.83 (s, 1H), 4.77 (s, 2H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.4, 169.4, 156.9 (d, J = 237.3 Hz) 152.5, 144.3, 135.8, 129.0 (d, J = 25.5 Hz), 128.5, 125.5, 121.5, 121.2 (d, J = 4.1 Hz), 121.1, 115.9 (d, J = 7.7 Hz), 115. 3 (d, J = 24.2 Hz), 42.4.

^{19}F NMR ($CDCl_3$, 376 MHz): δ -123.37.

IR (KBr, cm^{-1}): 3438, 1684, 1634.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{17}H_{13}NO_3F$: 298.0879; Found: 298.0884.

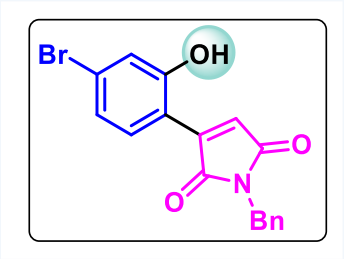


1-benzyl-3-(2-hydroxy-4-methylphenyl)-1H-pyrrole-2,5-dione (3jc): was prepared according to general procedure (3.2). The crude reaction mixture was purified by column chromatography using silica gel (100-200 mesh size) giving (25 mg) 84% yield.

Physical State: yellow solid
Melting point: 168-169 ℃
R_f-value: 0.5 (10% EtOAc/hexane)

^{1}H NMR ($CDCl_3$, 700 MHz): δ 9.96 (s, 1H), 7.47 (d, J = 7.0 Hz, 1H), 7.36 (d, J = 7.0 Hz, 2H), 7.33 (t, J = 7.0 Hz, 2H), 7.28 (t, J = 7.0 Hz, 1H), 6.79 (s, 1H), 6.75 (d, J = 8.4 Hz, 1H), 6.73 (s, 1H), 4.76 (s, 2H), 2.32 (s, 3H).

^{13}C NMR ($CDCl_3$, 175 MHz): δ 174.2, 170.0, 156.1, 145.8, 145.6, 136.0, 130.0, 129.1, 128.8, 128.4, 122.7, 122.5, 120.2, 112.7, 42.2, 21.7.
IR (KBr, cm^{-1}): 3438, 1682, 1634.
HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{16}NO_3$: 294.1130; Found: 294.1097.



3-(4-bromo-2-hydroxyphenyl)-1-ethyl-1H-pyrrole-2,5-dione) (3kc): was prepared according to general procedure (3.2). The crude reaction mixture was purified by column chromatography using silica gel (100-200 mesh size) giving (15 mg) 42 % yield.

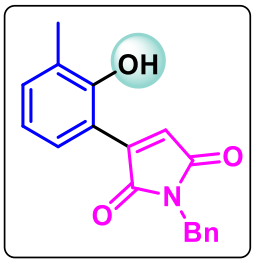
Physical State: yellow solid
Melting point: 172-173 ℃
R_f-value: 0.4 (20% EtOAc/hexane)

^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.23 (s,1H), 7.43 (d, J = 8.4 Hz, 1H), 7.39-7.29 (m, 5H), 7.18 (d, J = 2.0 Hz, 1H), 7.06 (dd, J = 8.8 Hz, 2.0 Hz, 1H), 6.80 (s, 1H), 4.77 (s, 2H).

^{13}C NMR ($CDCl_3$, 175 MHz): δ 174.0, 169.5, 156.7, 145.1, 135.8, 131.1, 129.1, 128.9, 128.5, 128.29, 124.5, 124.2, 123.2, 114.5, 42.4.

IR (KBr, cm^{-1}): 3438, 1634.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{17}H_{13}NO_3Br$: 358.0079; Found: 358.0072.



1-benzyl-3-(2-hydroxy-3-methylphenyl)-1H-pyrrole-2,5-dione (3lc): was prepared according to general procedure (3.2). The crude reaction mixture was purified by column chromatography using silica gel (100-200 mesh size) giving (9 mg) 31% yield.

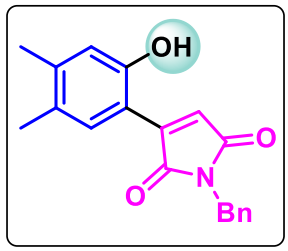
Physical State: yellow solid
Melting point: 153-154 ℃
R_f-value: 0.5 (10% EtOAc/hexane)

^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.03 (s, 1H), 7.39-7.28 (m, 6H), 7.26-7.24 (m, 1H), 6.84 (t, J = 7.6 Hz,1H), 6.75 (s, 1H), 4.77 (s, 2H), 2.27 (s, 3H).

^{13}C NMR ($CDCl_3$, 175 MHz): δ 174.3, 169.7, 154.3, 146.5, 136.0, 135.2, 129.1, 128.9, 128.4, 127.9, 124.2, 120.8, 115.3, 115.1, 42.3, 17.0.

IR (KBr, cm^{-1}): 3422, 1684.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{16}NO_3$: 294.1130; Found: 294.1132.

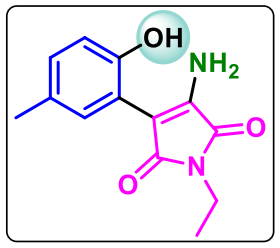


1-benzyl-3-(2-hydroxy-4,5-dimethylphenyl)-1H-pyrrole-2,5-dione (3nc): was prepared according to general procedure (3.2). The crude reaction mixture was purified by column chromatography using silica gel (100-200 mesh size) giving (26 mg) 85% yield.

Physical State: yellow solid
Melting point: 174-175 °C
R_f-value: 0.5 (10% EtOAc/hexane)

^{1}H NMR ($CDCl_3$, 700 MHz): δ 9.86 (s, 1H), 7.38 (d, J = 7.0 Hz, 2H), 7.33 (t, J = 7.0 Hz, 2H), 7.29-7.27 (m, 2H), 6.78 (s, 1H), 6.71 (s, 1H), 4.76 (s, 2H), 2.23 (s, 3H), 2.19 (s, 3H).

^{13}C NMR ($CDCl_3$, 175 MHz): δ 174.3, 170.0, 154.3, 145.9, 144.6, 136.1, 130.3, 129.5, 129.1, 128.8, 128.3, 122.3, 120.2, 112.7, 42.2, 20.3, 19.1.
IR (KBr, cm^{-1}): 3438, 1680, 1634.
HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{19}H_{18}NO_3$: 308.1287; Found: 308.1300.



3-amino-1-ethyl-4-(2-hydroxy-5-methylphenyl)-1H-pyrrole-2,5-dione (4bb): was prepared according to general procedure (3.2). The crude reaction mixture was purified by column chromatography using silica gel (230-400 mesh size) giving (16 mg) 65% yield.

Physical State: light yellow solid
Melting point: 179-180 °C
R_f-value: 0.3 (20% EtOAc/hexane)

^{1}H NMR ($CDCl_3$, 700 MHz): δ 7.38 (s, 1H), 7.16 (s, 1H), 7.04 (d, J = 8.4 Hz, 1H), 6.91 (d, J = 7.7 Hz, 1H), 5.37 (s, 2H), 3.64 (q, J = 7.7 Hz, 2H), 2.31 (s, 3H), 1.26 (t, J = 7.0 Hz, 3H).

^{13}C NMR ($CDCl_3$ 175 MHz): δ 174.5, 167.5, 151.3, 142.9, 130.7, 130.5, 129.1, 118.8, 117.5, 100.1, 33.4, 20.9, 14.3.
IR (KBr, cm^{-1}): 3429, 1642.
HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{13}H_{15}N_2O_3$: 247.1083; Found: 247.1092.

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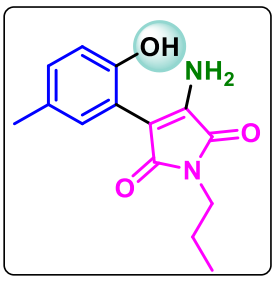


3-amino-4-(2-hydroxy-5-methylphenyl)-1-propyl-1H-pyrrole-2,5-dione (4bb'): was prepared according to general procedure (3.2). The crude reaction mixture was purified by column chromatography using silica gel (230-400 mesh size) giving (15 mg) 58% yield.

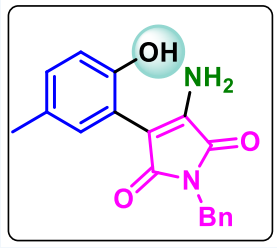
Physical State: orange liquid
R_f-value: 0.3 (20% EtOAc/Hexane)

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.39 (s, 1H), 7.14 (s, 1H), 7.02 (d, J = 8.0 Hz, 1H), 6.89 (d, J = 8.0 Hz, 1H), 5.36 (s, 2H), 3.52 (t, J = 8.0 Hz, 2H), 2.29 (s, 3H), 1.70-1.63 (m, 2H), 0.93 (t, J = 8.0 Hz, 3H).

^{13}C NMR ($CDCl_3$, 175 MHz): δ 174.8, 167.7, 151.3, 142.8, 130.6, 130.5, 129.1, 118.9, 117.5, 100.0, 40.1, 22.3, 20.9, 11.6.

IR (KBr, cm^{-1}): 3438, 1649.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{14}H_{17}N_2O_3$: 261.1239; Found: 261.1225.



3-amino-1-benzyl-4-(2-hydroxy-5-methylphenyl)-1H-pyrrole-2,5-dione (4bc): was prepared according to general procedure (3.2). The crude reaction mixture was purified by column chromatography using silica gel (230-400 mesh size) giving (17 mg) 55% yield.

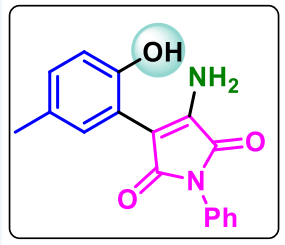
Physical State: orange liquid
R_f-value: 0.3 (20% EtOAc/hexane)

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.39-7.37 (m, 2H), 7.34-7.27 (m, 3H), 7.15 (d, J = 1.6 Hz, 2H), 7.01 (dd, J = 8.0 Hz, 1.6 Hz, 1H), 6.86 (d, J = 8.4 Hz, 1H), 5.36 (s, 2H), 4.71 (s, 2H), 2.28 (s, 3H).

^{13}C NMR ($CDCl_3$, 176 MHz): δ 174.0, 167.3, 151.2, 143.0, 136.6, 130.7, 130.5, 129.3, 129.0, 128.8, 128.1, 118.6, 117.3, 100.1, 42.0, 20.9.

IR (KBr, cm^{-1}): 3438, 1643.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{17}N_2O_3$: 309.1239; Found: 309.1252.



3-amino-1-benzyl-4-(2-hydroxy-5-methylphenyl)-1H-pyrrole-2,5-dione (4bd): was prepared according to general procedure (3.2). The crude reaction mixture was purified by column chromatography using silica gel (230-400 mesh size) giving (13 mg) 44% yield.

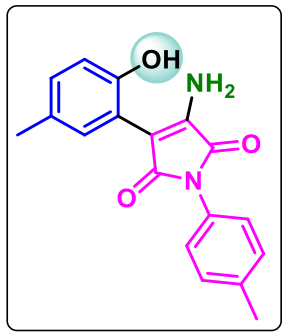
Physical State: orange liquid
R_f-value: 0.3 (20% EtOAc/hexane)

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.49- 7.40 (m, 4H), 7.38-7.34 (m, 1H), 7.24 (s, 1H), 7.05 (dd, *J* = 8.0 Hz, 1.6 Hz, 1H), 7.00 (s, 1H), 6.90 (d, *J* = 8.0 Hz, 1H), 5.50 (s, 2H), 2.31 (s, 3H).

^{13}C NMR ($CDCl_3$, 175 MHz): *δ* 172.9, 166.5, 151.3, 142.9, 131.8, 130.9, 130.7, 129.6, 129.4, 128.0, 126.2, 118.7, 117.2, 100.1, 20.9.

IR (KBr, cm^{-1}): 3439, 1702, 1649.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{17}H_{15}N_2O_3$: 295.1083; Found: 295.1099.



3-amino-4-(2-hydroxy-5-methylphenyl)-1-(*p*-tolyl)-1H-pyrrole-2,5-dione (4be): was prepared according to general procedure (3.2). The crude reaction mixture was purified by column chromatography using silica gel (230-400 mesh size) giving (14 mg) 45% yield.

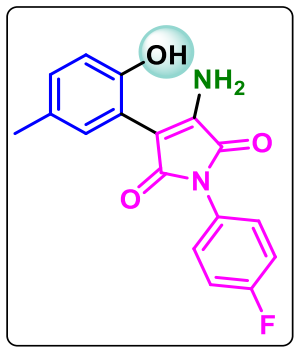
Physical State: orange liquid
R_f-value: 0.3 (10% EtOAc/hexane)

^{1}H NMR ($CDCl_3$, 400 MHz): *δ* 7.27-7.24 (m, 4H), 7.22 (d, J = 1.6 Hz, 1H), 7.11 (s, 1H), 7.04 (dd, *J* = 8.4 Hz, 2.0 Hz, 1H), 6.90 (d, *J* = 8.4 Hz, 1H), 5.49 (s, 2H), 2.38 (s, 3H), 2.31 (s, 3H)

^{13}C NMR ($CDCl_3$, 175 MHz): *δ* 173.2, 166.6, 151.3, 143.0, 138.1, 130.8, 130.7, 130.0, 129.5, 129.0, 126.2, 118.7, 117.3, 100.1, 21.5, 20.9.

IR (KBr, cm^{-1}): 3439, 1701, 1653.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{17}N_2O_3$: 309.1239; Found: 309.1245.



3-amino-1-(4-fluorophenyl)-4-(2-hydroxy-5-methylphenyl)-1H-pyrrole-2,5-dione (4bf): was prepared according to general procedure (3.2). The crude reaction mixture was purified by column chromatography using silica gel (230-400 mesh size) giving (11 mg) 35% yield.

Physical State: orange solid

Melting point: 166-167℃

R_f-value: 0.3 (10% EtOAc/hexane)

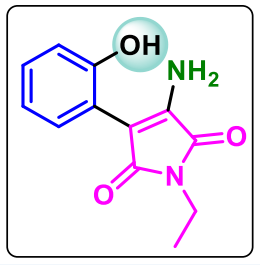
^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.41-7.37 (m, 2H), 7.24 (d, J = 1.6 Hz, 1H), 7.18-7.12 (m, 2H), 7.05 (dd, J = 8.0 Hz, 1.6 Hz, 1H), 6.89 (d, J = 8.0 Hz, 1H), 6.86 (s, 1H), 5.51 (s, 2H), 2.31 (s, 3H).

^{13}C NMR ($CDCl_3$, 175 MHz): δ 172.6, 166.4, 161.9 (d, J_{C-F} = 246.4 Hz), 151.2, 142.9, 131.0, 130.7, 129.8, 128.0 (d, J_{C-F} = 8.7 Hz), 127.7 (d, J_{C-F} = 3.1 Hz), 118.5, 117.0, 116.3 (d, J_{C-F} = 22.5 Hz), 100.0, 20.9.

^{19}F NMR ($CDCl_3$, 376 MHz): δ -113.5.

IR (KBr, cm^{-1}): 3438, 1652.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{17}H_{13}FN_2O_3$: 313.0988; Found: 313.1009.



3-amino-1-ethyl-4-(2-hydroxyphenyl)-1H-pyrrole-2,5-dione (4ab): was prepared according to general procedure (3.2). The crude reaction mixture was purified by column chromatography using silica gel (230-400 mesh size) giving (13 mg) 56% yield.

Physical State: yellow solid

Melting point: 190-191℃

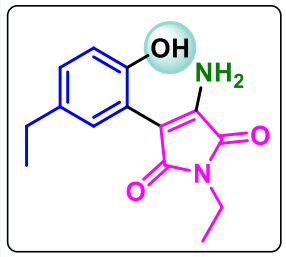
R_f-value: 0.3 (10% EtOAc/hexane)

^{1}H NMR ($CDCl_3$, 700 MHz): δ 7.74 (s, 1H), 7.33 (dd, J = 7.7 Hz, 1.4 Hz, 1H), 7.22 (td, J = 8.4 Hz, 1.4 Hz, 1H), 7.00 (d, J = 7.7 Hz, 1H), 6.98 (td, J = 7.7 Hz, 1.4 Hz, 1H), 5.37 (s, 2H), 3.62 (q, J = 7 Hz, 2H), 1.24 (t, J = 7.0 Hz, 3H).

^{13}C NMR ($CDCl_3$, 175 MHz): δ 174.7, 167.4, 153.6, 143.1, 129.8, 128.9, 121.4, 119.1, 117.8, 100.0, 33.4, 14.3.

IR (KBr, cm^{-1}): 3440, 1645.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{12}H_{13}N_2O_3$: 233.0926; Found: 233.0914.



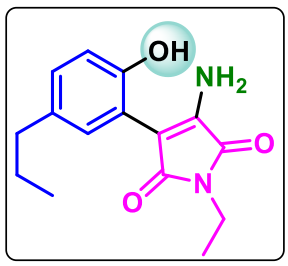
3-amino-1-ethyl-4-(5-ethyl-2-hydroxyphenyl)-1H-pyrrole-2,5-dione (4cb): was prepared according to general procedure (3.2). The crude reaction mixture was purified by column chromatography using silica gel (230-400 mesh size) giving (12 mg) 46% yield.

Physical State: orange liquid
R_f-value: 0.3 (20% EtOAc/hexane)

^{1}H NMR ($CDCl_3$, 700 MHz): δ 7.37 (s, 1H), 7.16 (d, J = 2.1 Hz, 1H), 7.05 (dd, J = 4.2 Hz, 2.1 Hz, 1H), 6.91 (d, J = 7.7 Hz, 1H), 5.34 (s, 2H), 3.62 (q, J = 7.0 Hz, 2H), 2.59 (q, J = 7.7 Hz, 2H), 1.25-1.20 (m, 6H).
^{13}C NMR ($CDCl_3$, 175 MHz): δ 174.5, 167.5, 151.5, 142.9, 137.2, 129.3, 128.1, 118.8, 117.5, 100.2, 33.4, 28.3, 16.1, 14.3.

IR (KBr, cm^{-1}): 3438, 1645.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{14}H_{17}N_2O_3$: 261.1239; Found: 261.1246.

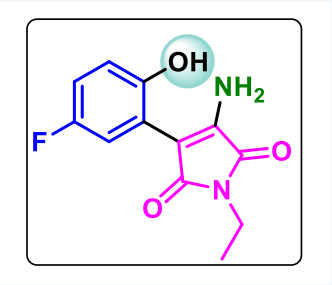


3-amino-1-ethyl-4-(2-hydroxy-5-propylphenyl)-1H-pyrrole-2,5-dione (4db) was prepared according to general procedure (3.2). The crude reaction mixture was purified by column chromatography using silica gel (230-400 mesh size) giving (14 mg) 51% yield.

Physical State: orange liquid
R_f-value: 0.3 (20% EtOAc/hexane)

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.36 (s, 1H), 7.14 (d, J = 2.0 Hz, 1H), 7.03 (dd, J = 8.0 Hz, 2.0 Hz, 1H), 6.91 (d, J = 8.0 Hz, 1H), 5.33 (s, 2H), 3.63 (q, J = 7.2 Hz, 2H), 2.53 (t, J = 7.6 Hz, 2H) 1.62 (q, J = 7.6 Hz, 2H), 1.24 (t, J = 7.2 Hz, 3H), 0.93 (t, J = 7.2 Hz, 3H).

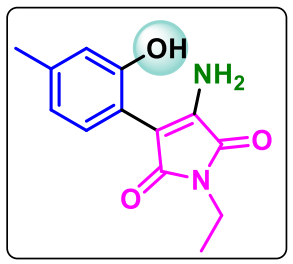
^{13}C NMR ($CDCl_3$, 175 MHz): δ 174.5, 167.5, 151.5, 142.9, 135.6, 129.8, 128.7, 118.8, 117.4, 100.2, 37.5, 33.4, 25.1, 14.3, 14.1.
IR (KBr, cm^{-1}): 3439, 2958, 1699, 1649.
HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{15}H_{19}N_2O_3$: 275.1396; Found: 275.1409.



3-amino-1-ethyl-4-(5-fluoro-2-hydroxyphenyl)-1H-pyrrole-2,5-dione (4hb): was prepared according to general procedure (3.2). The crude reaction mixture was purified by column chromatography using silica gel (230-400 mesh size) giving (17 mg) 68% yield.

Physical State: orange liquid
R_f-value: 0.3 (20% EtOAc/hexane)

^{1}H NMR (DMSO-d_6, 700 MHz): δ 9.77 (s, 1H), 7.12 (dd, J = 10.5 Hz, 3.5 Hz, 1H), 6.99-6.96 (m, 3H), 6.90-6.88 (m, 1H), 3.48 (q, J = 7.0 Hz, 2H), 1.13 (t, J = 7.0 Hz, 3H).
^{13}C NMR (DMSO-d_6, 175 MHz): δ 172.1, 167.7, 155.9 (d, J_{C-F} = 231.5 Hz), 151.7, 145.6, 119.5 (d, J_{C-F} = 8.7 Hz), 117.2 (d, J_{C-F} = 8.4 Hz), 117.04 (d, J_{C-F} = 23.2 Hz), 115.0 (d, J_{C-F} = 22.5 Hz), 95.2, 32.9, 14.8,
^{19}F NMR (DMSO-d_6, 376 MHz): δ -121.4.
IR (KBr, cm^{-1}): 3437, 1647.
HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{12}H_{12}FN_2O_3$: 309.1239; Found: 309.1246.



3-amino-1-ethyl-4-(2-hydroxy-4-methylphenyl)-1H-pyrrole-2,5-dione (4lb) was prepared according to general procedure (3.2). The crude reaction mixture was purified by column chromatography using silica gel (230-400 mesh size) giving (10 mg) 41% yield.

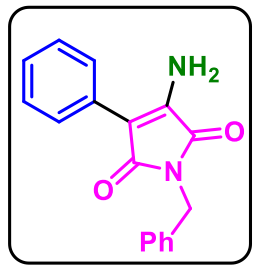
Physical State: orange liquid
R_f-value: 0.3 (20% EtOAc/hexane)

^{1}H NMR ($CDCl_3$, 700 MHz): δ 7.75 (s, 1H), 7.23(d, J = 7.7 Hz, 1H), 6.84 (s, 1H), 6.81 (d, J = 7.7 Hz, 1H), 5.33 (s, 2H), 3.63 (q, J = 7.0 Hz, 2H), 2.34 (s, 3H), 1.25 (t, J = 7.0 Hz, 3H).

^{13}C NMR ($CDCl_3$, 175 MHz): δ 174.8, 167.6, 153.5, 142.6, 140.3, 129.2, 122.3, 119.6, 114.8, 100.3, 33.4, 21.5, 14.3.

IR (KBr, cm^{-1}): 3443, 1760, 1650.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{13}H_{15}N_2O_3$: 247.1083; Found: 247.1092.



3-amino-1-benzyl-4-phenyl-1H-pyrrole-2,5-dione (4ac'): was prepared according to general procedure (4.6). The crude reaction mixture was purified by column chromatography using silica gel (100-200 mesh size) giving (20 mg) 72% yield.

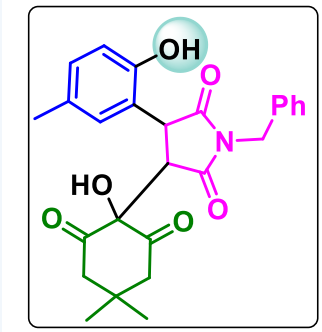
Physical State: yellow liquid
R_f-value: 0.4 (10% EtOAc/hexane)

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.53 (d, J = 7.2 Hz, 2H), 7.43-7.38 (m, 4H), 7.34-7.26 (m, 4H), 5.18 (s, 2H), 4.70 (s, 2H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 171.5, 167.6, 142.0, 136.9, 130.4, 129.2, 128.9, 128.8, 128.0, 127.7, 127.6, 102.1, 41.7.

IR (KBr, cm^{-1}): 3447, 3344, 1762, 1700, 1647.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{17}H_{15}N_2O_2$: 279.1133; Found: 279.1149 .



1-benzyl-3-(1-hydroxy-4,4-dimethyl-2,6-dioxocyclohexyl)-4-(2-hydroxy-5-methylphenyl)pyrrolidine-2,5-dione (6): was prepared according to general procedure (5). The crude reaction mixture was purified by column chromatography using silica gel (230-400 mesh size) giving (36 mg) 80% yield.

Physical State: pale yellow liquid
R_f-value: 0.3 (50% EtOAc/hexane)

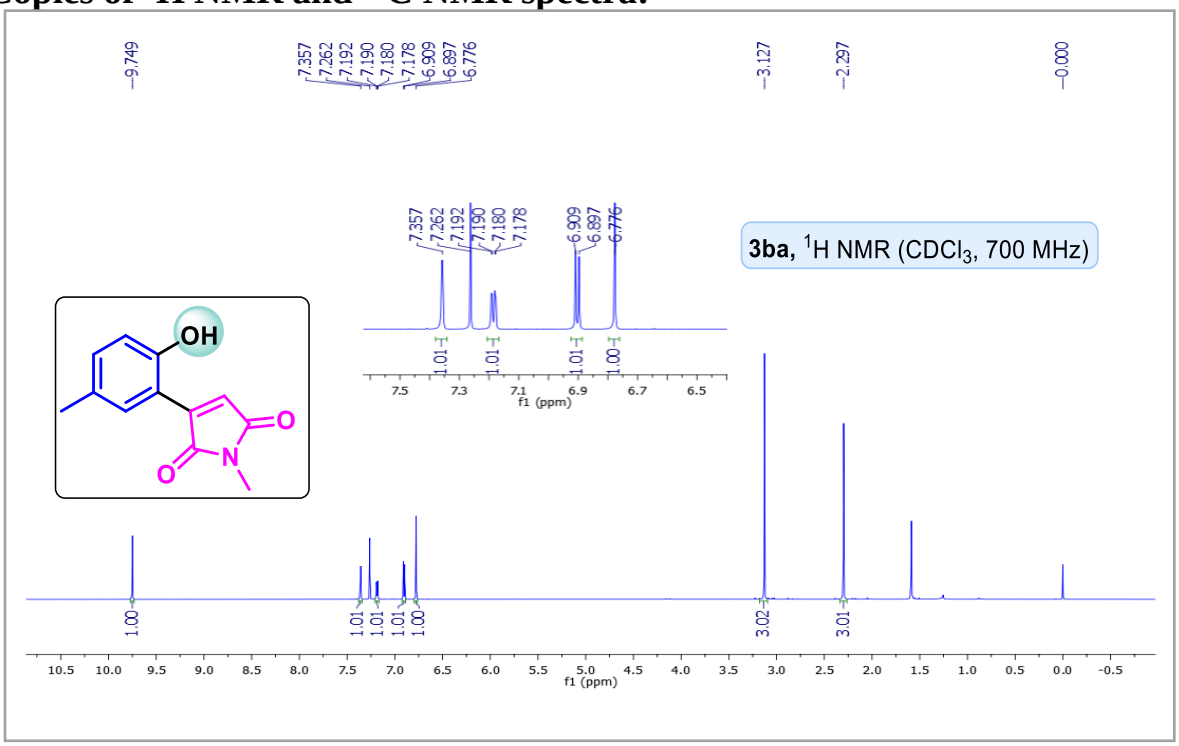
^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.64 (s, 1H), 7.38-7.31 (m, 5H), 6.96 (d, J = 8.0 Hz, 1H), 6.73 (d, J = 8.0 Hz, 1H), 6.65 (s, 1H), 4.71 (d, J = 15.2 Hz, 1H), 4.55 (d, J = 15.2 Hz, 1H), 4.12 (d, J = 4.0 Hz, 1H), 4.06 (d, J = 4.0 Hz, 1H), 3.82 (d, J = 3.6 Hz, 1H), 3.35-3.31 (m, 1H), 2.47-2.39 (m, 2H), 2.18-2.14 (m, 4H), 1.07 (s, 3H), 0.70 (s, 3H).

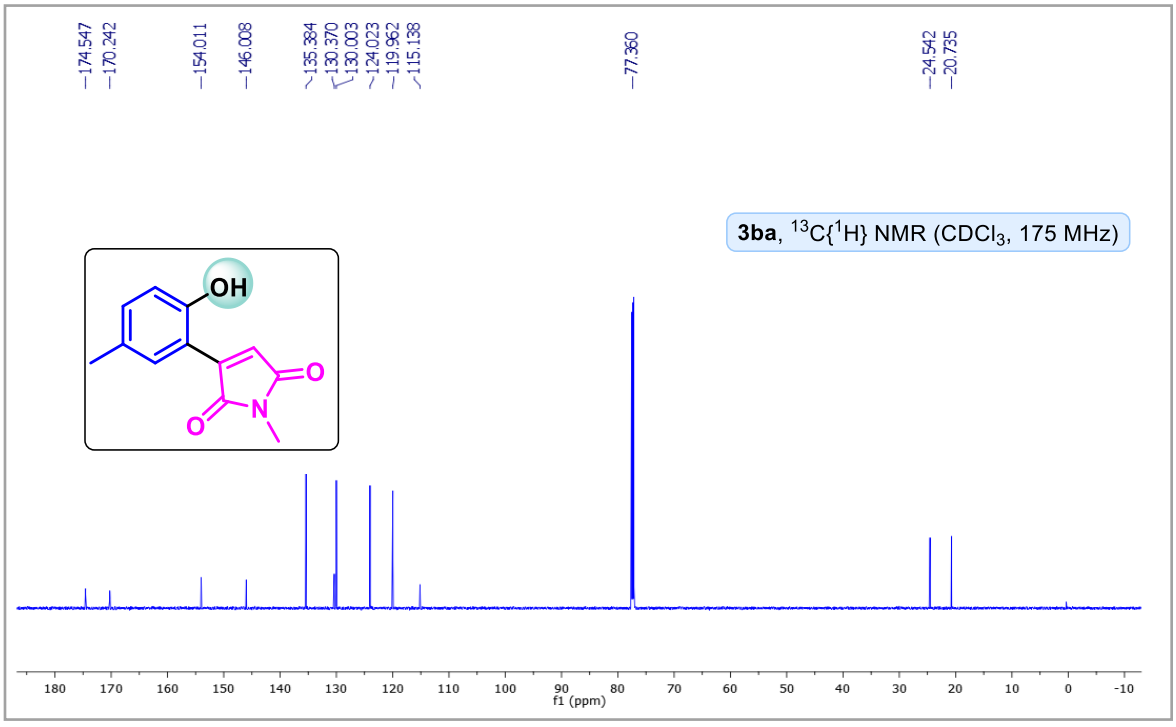
^{13}C NMR ($CDCl_3$, 100 MHz): δ 205.3, 204.2, 177.8, 175.2, 153.5, 136.7, 132.5, 130.2, 129.2, 128.2, 128.1, 128.0, 123.7, 116.1, 89.3, 52.9, 51.6 (2C), 45.5, 42.6, 32.0, 29.7, 27.0, 20.9.

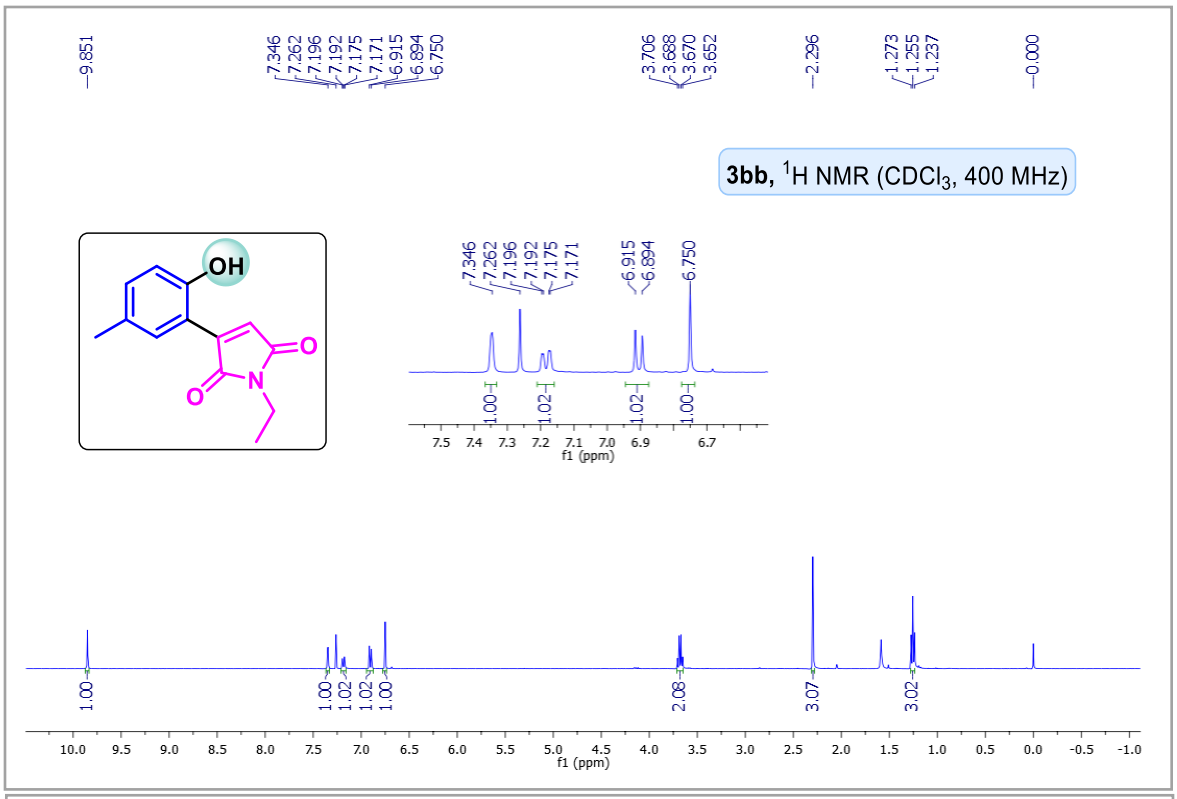
IR (KBr, cm^{-1}): 3422, 2922, 2852, 1700, 1635.

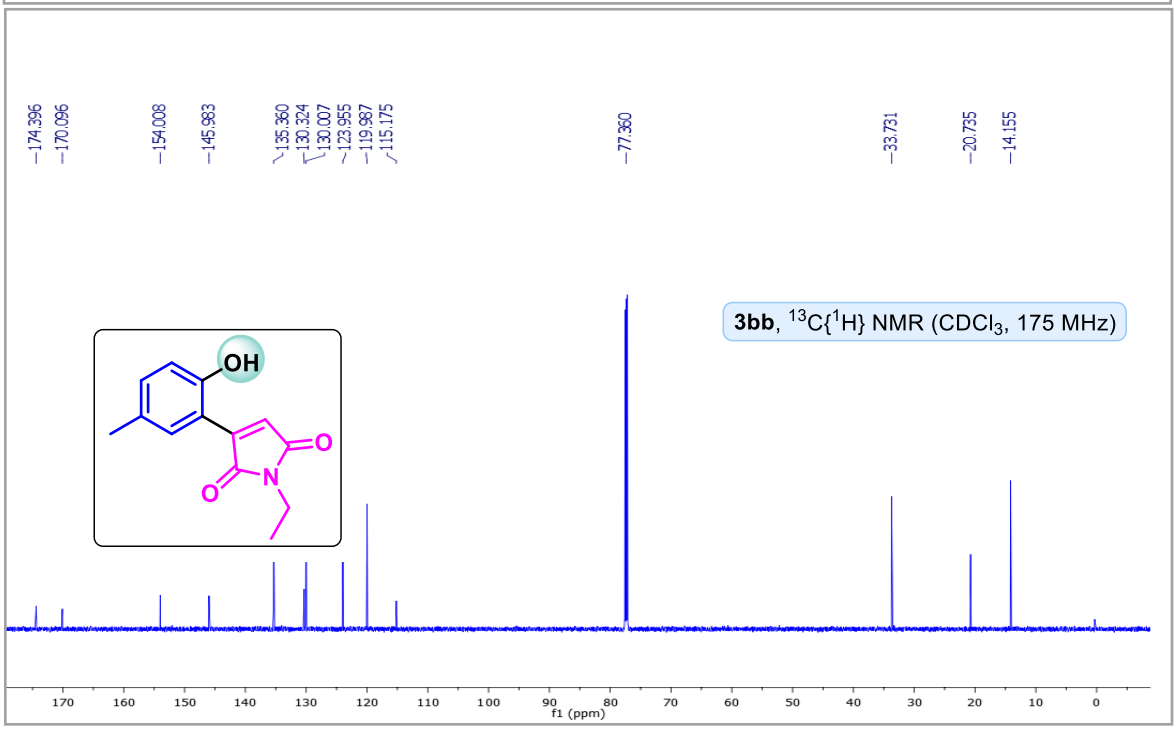
HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{26}H_{27}NO_6Na$: 472.1736; Found: 472.1743.

7. Copies of ^{1}H NMR and ^{13}C NMR spectra:






9.851
7.346
7.262
7.196
7.192
7.175
7.171
6.915
6.894
6.750
3.706
3.688
3.670
3.652
2.296
1.273
1.255
1.237
0.000
3bb, 1H NMR (CDCl3, 400 MHz)
OH
O
O
N
1.00
1.02
1.02
1.00
f1 (ppm)
1.00
1.00
1.02
1.02
1.00
2.08
3.07
3.02
f1 (ppm)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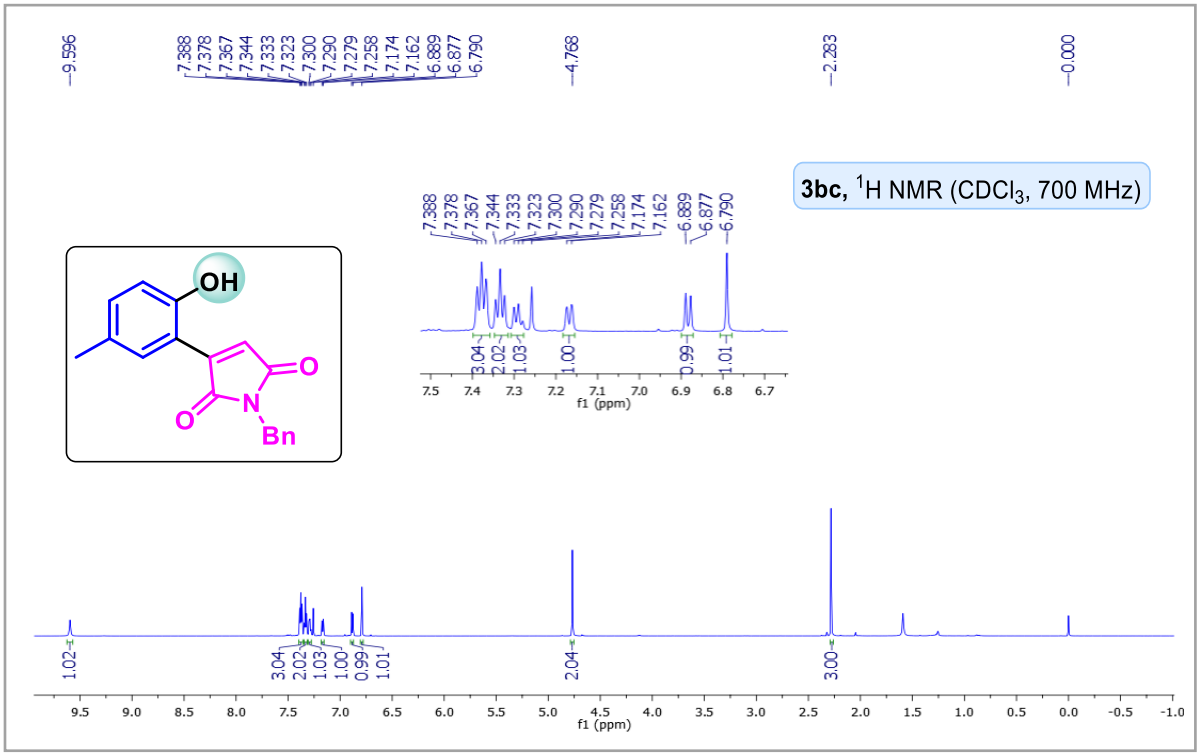
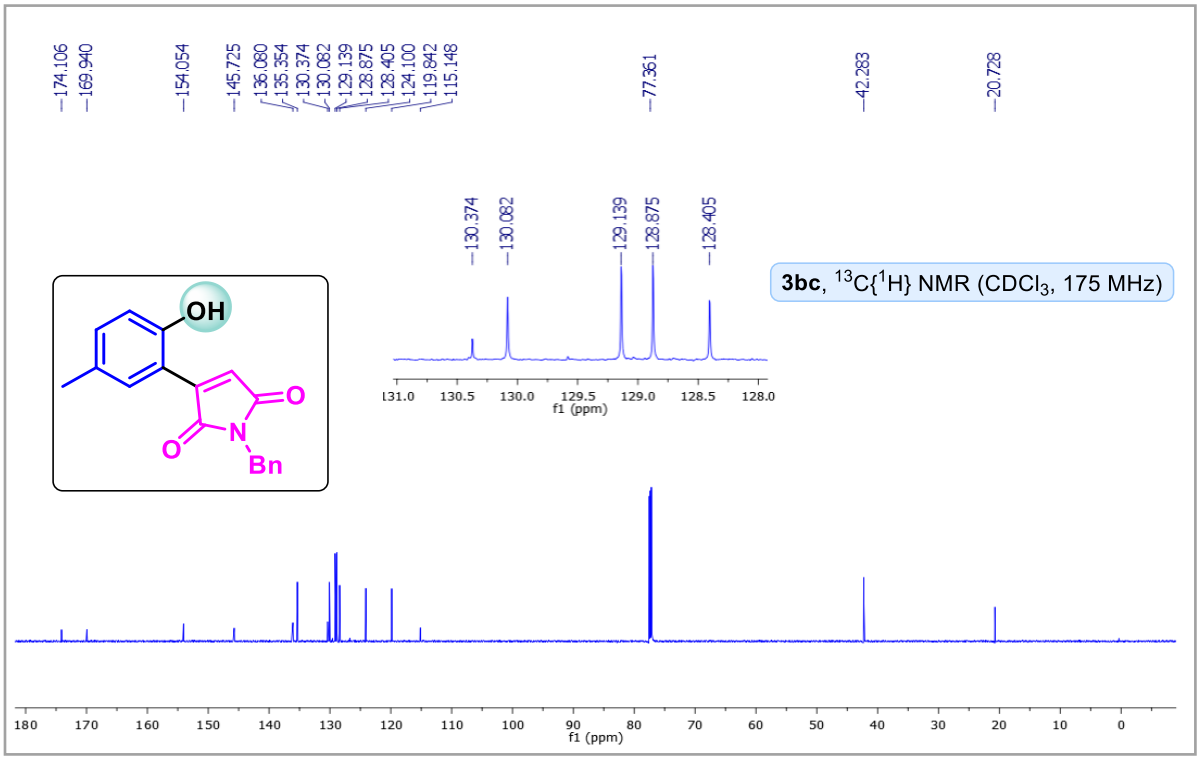
170.096
154.008
145.983
135.360
130.324
130.007
123.955
119.987
115.175
77.360
33.731
20.735
14.155
3bb, 13C{1H} NMR (CDCl3, 175 MHz)
OH
O
O
N
f1 (ppm)


9.596
7.388
7.378
7.367
7.344
7.333
7.323
7.300
7.290
7.279
7.258
7.174
7.162
6.889
6.877
6.790
4.768
2.283
0.000
3bc, 1H NMR (CDCl3, 700 MHz)
OH
O
O
N
Bn
1.02
3.04
2.02
1.03
1.00
0.99
1.01
2.04
3.00
f1 (ppm)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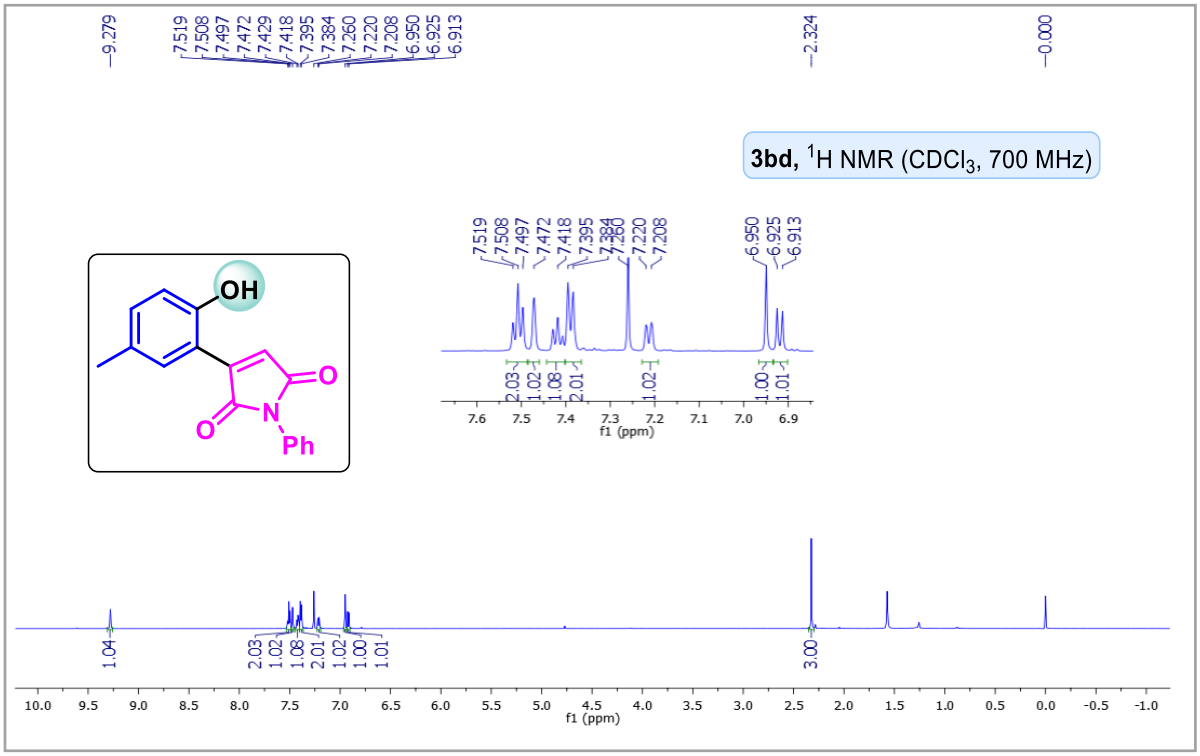
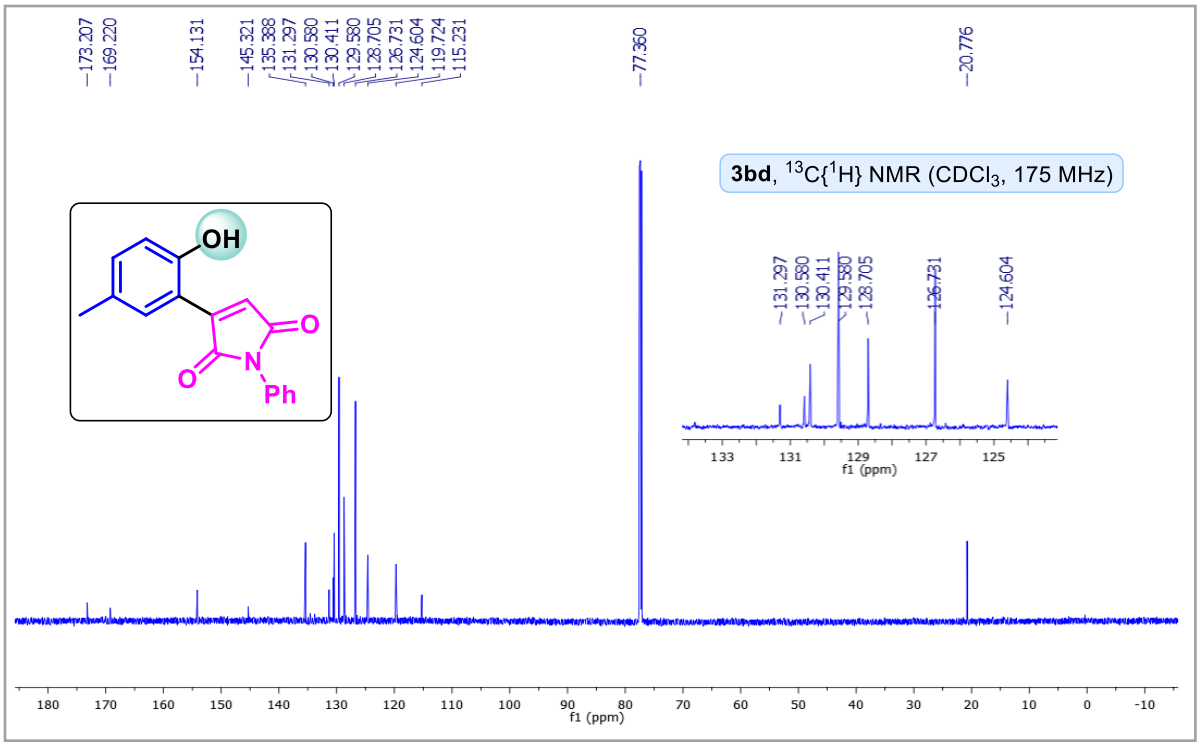
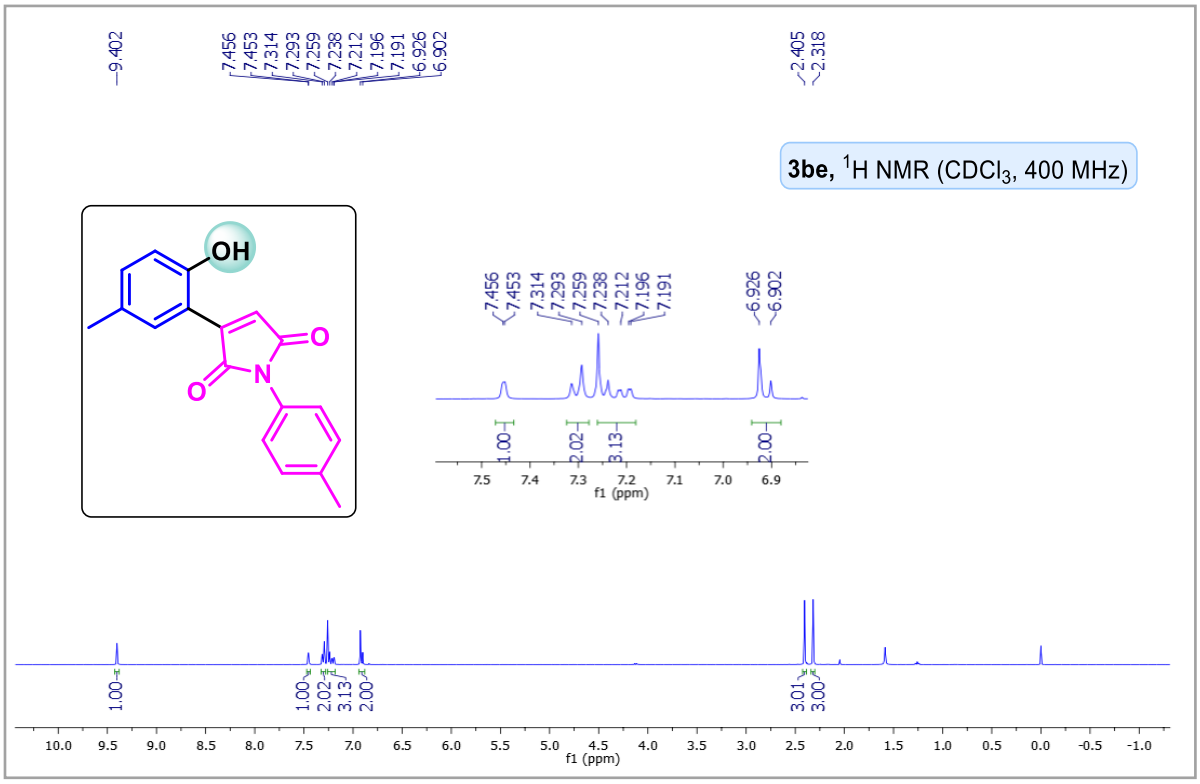
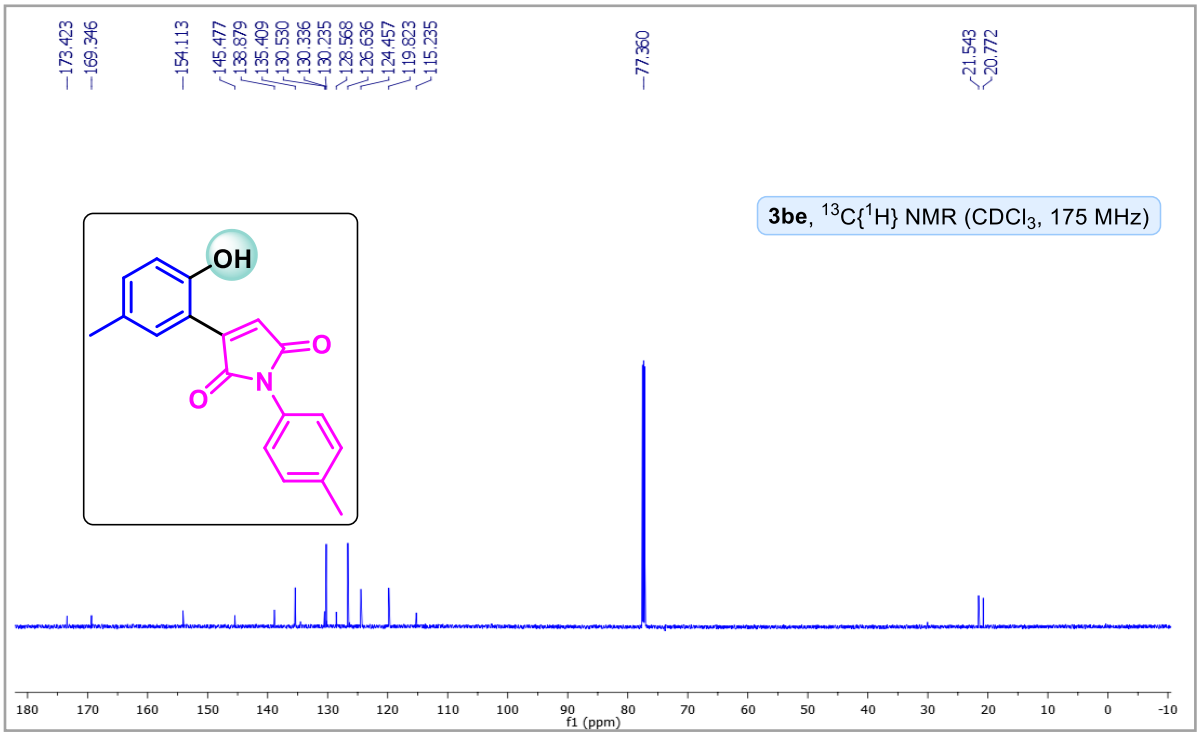
169.940
154.054
145.725
136.080
135.354
130.374
130.082
129.139
128.875
128.405
124.100
119.842
115.148
77.361
42.283
20.728
3bc, 13C{1H} NMR (CDCl3, 175 MHz)
OH
O
O
N
Bn
f1 (ppm)


3bd, ^{1}H NMR ($CDCl_3$, 700 MHz)
OH
O
N
Ph
f1 (ppm)


3bd, $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 175 MHz)
OH
O
N
Ph
f1 (ppm)


9.402
7.456
7.453
7.314
7.293
7.259
7.238
7.212
7.196
7.191
6.926
6.902
2.405
2.318
3be, 1H NMR (CDCl3, 400 MHz)
OH
O
N
O
1.00
2.02
3.13
2.00
f1 (ppm)
1.00
1.00
2.02
3.13
2.00
3.01
3.00
f1 (ppm)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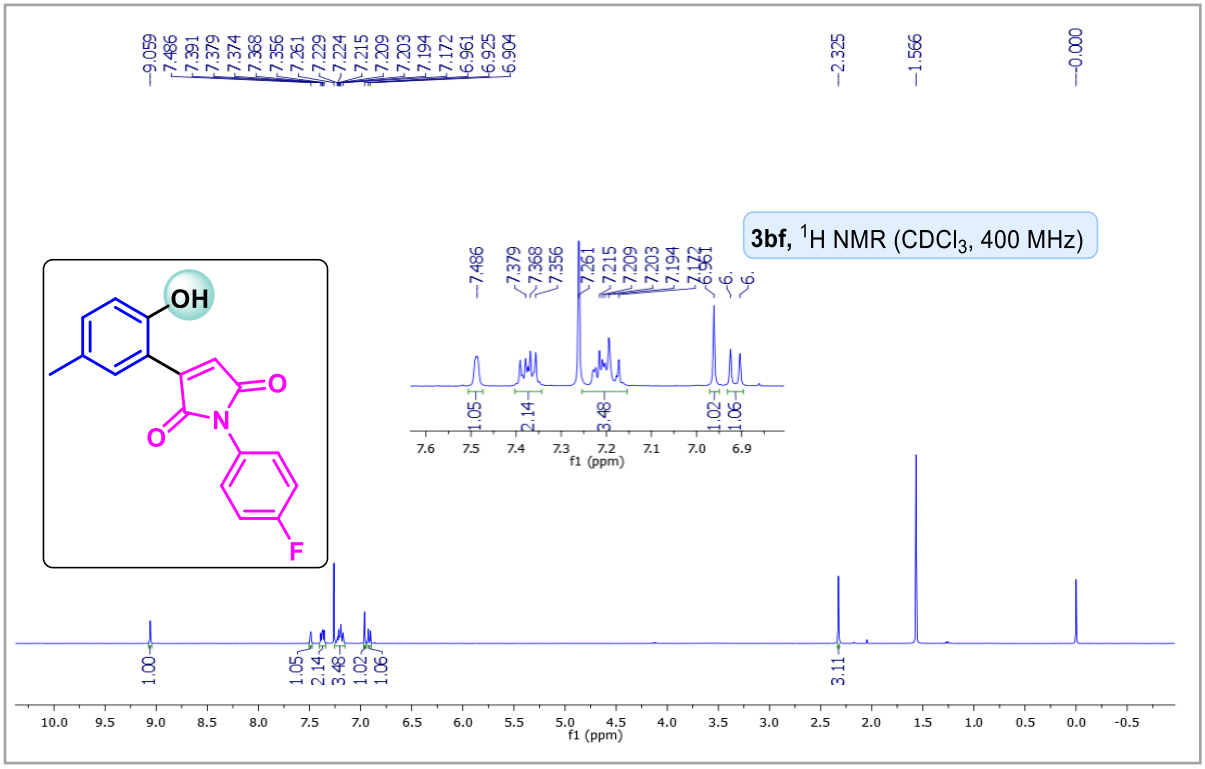
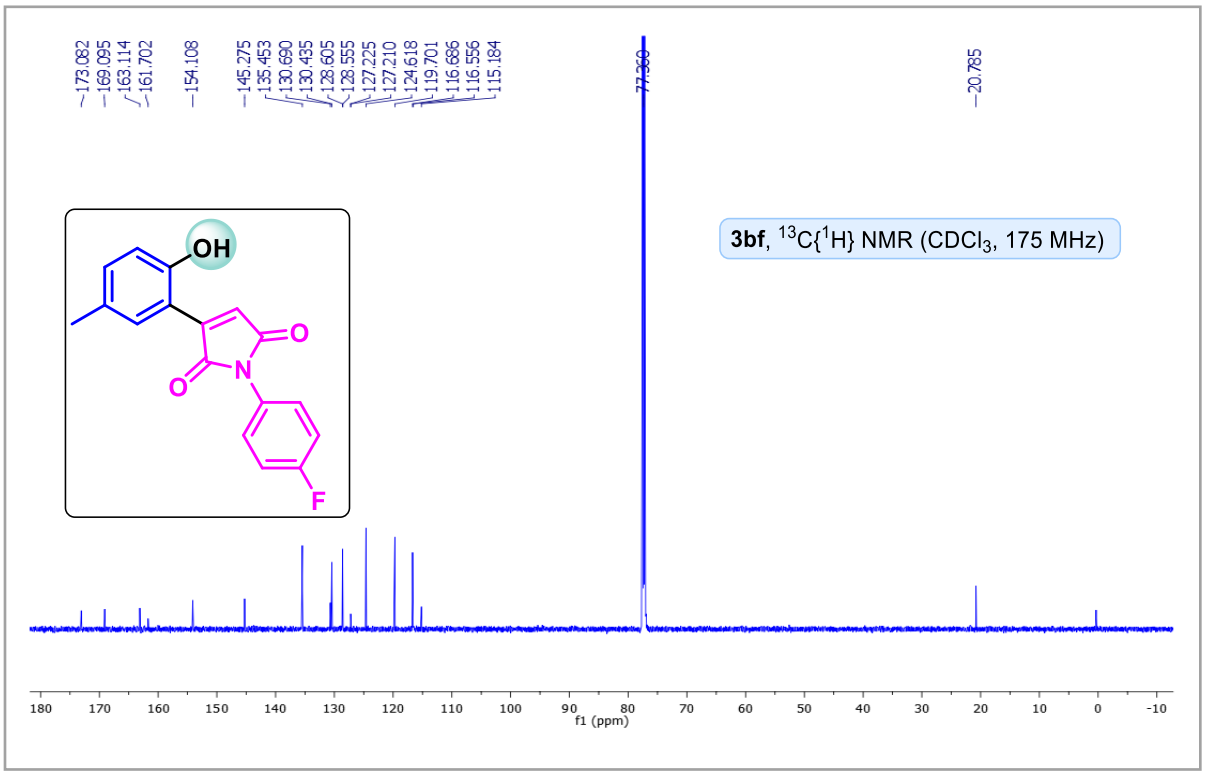
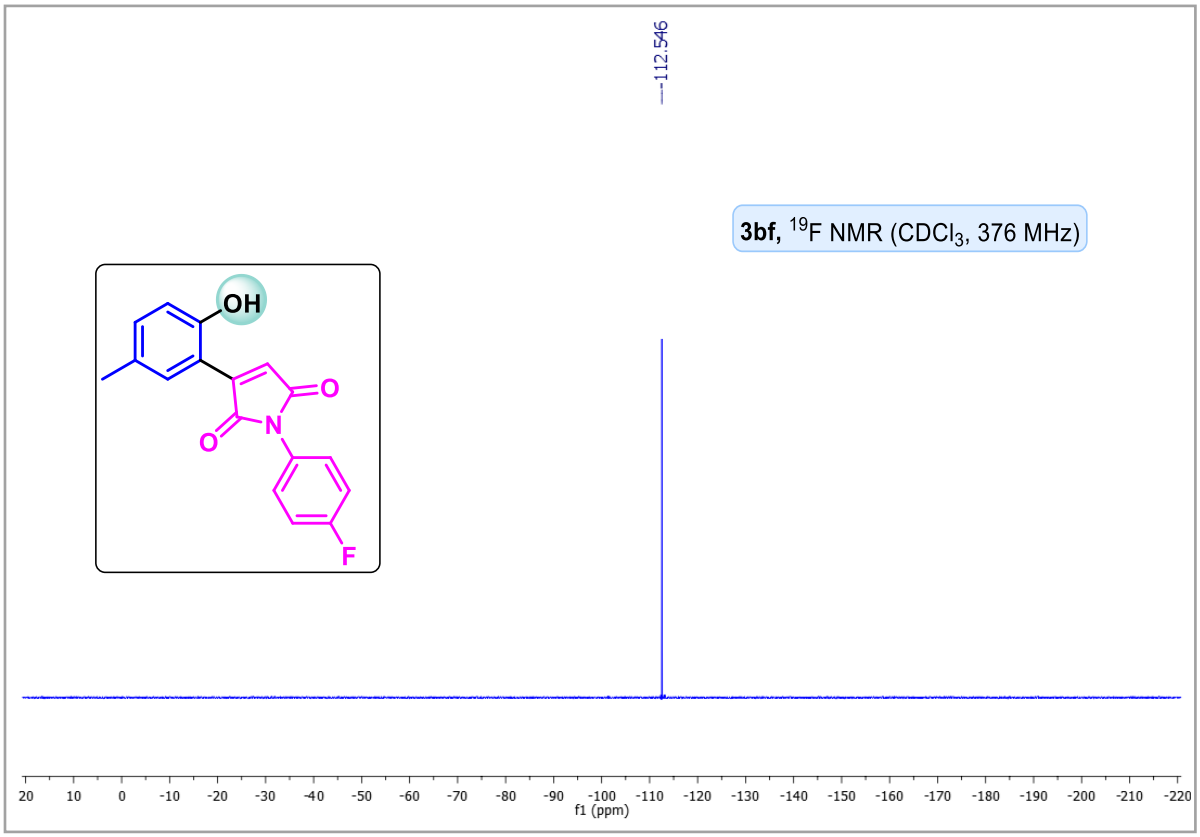
169.346
154.113
145.477
138.879
135.409
130.530
130.336
130.235
128.568
126.636
124.457
119.823
115.235
77.360
21.543
20.772
3be, 13C{1H} NMR (CDCl3, 175 MHz)
OH
O
N
O
f1 (ppm)


9.059
7.486
7.391
7.379
7.374
7.368
7.356
7.261
7.229
7.224
7.215
7.209
7.203
7.194
7.172
6.961
6.925
6.904
2.325
1.566
0.000
OH
O
N
O
F
3bf, ^{1}H NMR (CDCl$_3$, 400 MHz)
1.00
1.05
2.14
3.48
1.02
1.06
3.11
f1 (ppm)


173.082
169.095
163.114
161.702
154.108
145.275
135.453
130.690
130.435
128.605
128.555
127.225
127.210
124.618
119.701
116.686
116.556
115.184
77.360
20.785
OH
O
N
O
F
3bf, ^{13}C{^{1}H} NMR (CDCl$_3$, 175 MHz)
f1 (ppm)


-112.546
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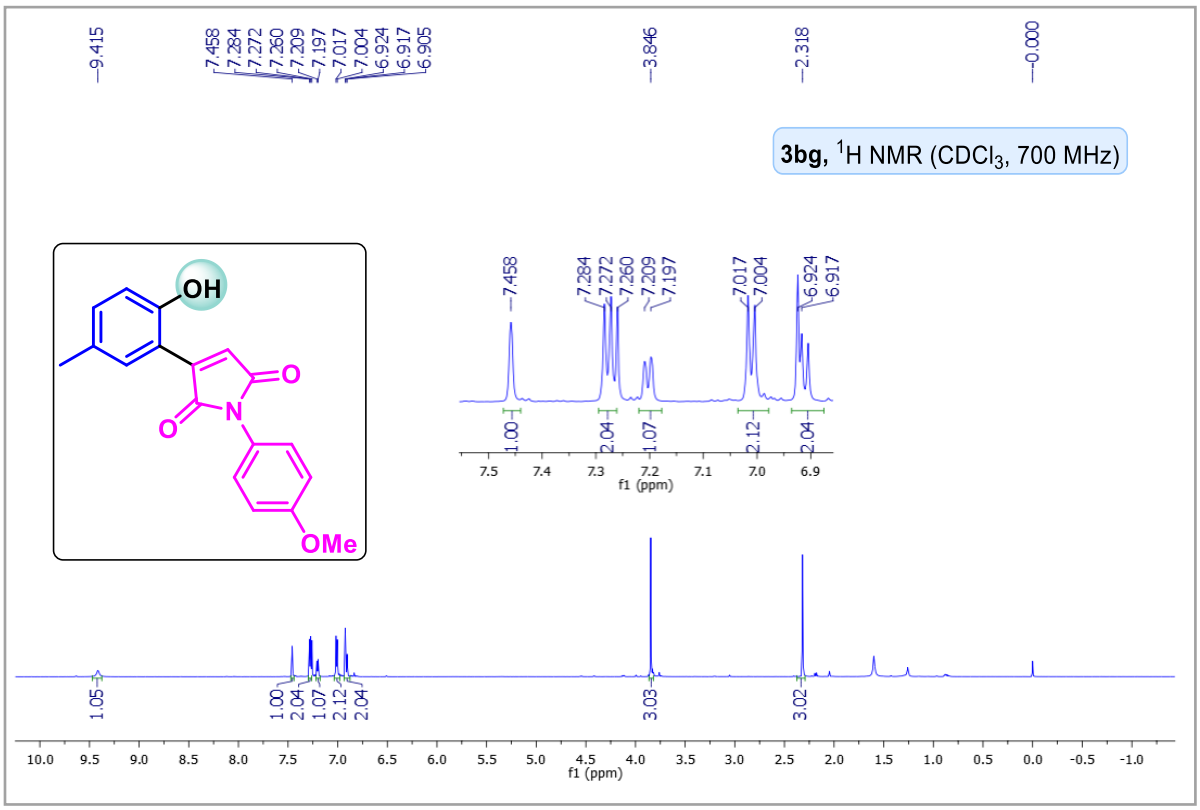
OH
O
N
O
F
20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)


9.415
7.458
7.284
7.272
7.260
7.209
7.197
7.017
7.004
6.924
6.917
6.905
3.846
2.318
0.000
3bg, 1H NMR (CDCl3, 700 MHz)
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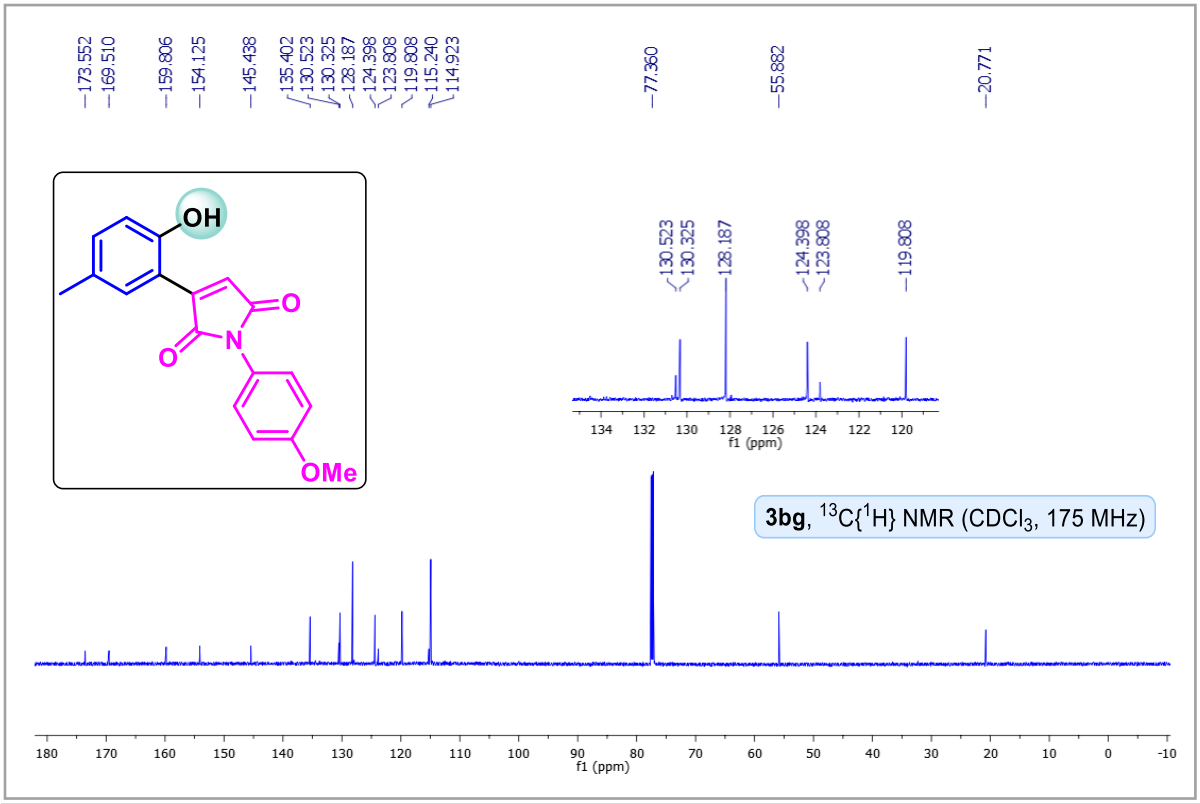
O
N
O
OMe
1.05
1.00
2.04
1.07
2.12
2.04
3.03
3.02
f1 (ppm)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159.806
154.125
145.438
135.402
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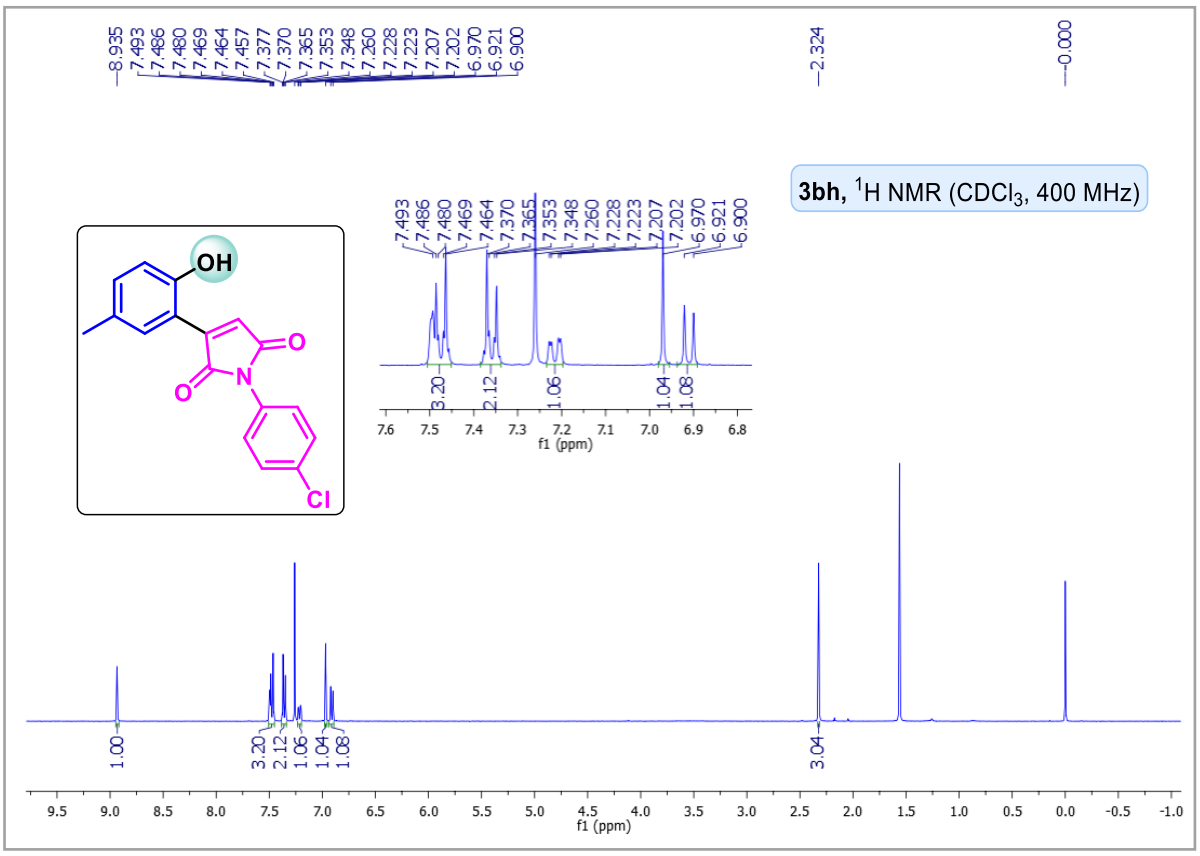
130.325
128.187
124.398
123.808
119.808
115.240
114.923
77.360
55.882
20.771
OH
O
N
O
OMe
3bg, 13C{1H} NMR (CDCl3, 175 MHz)
f1 (ppm)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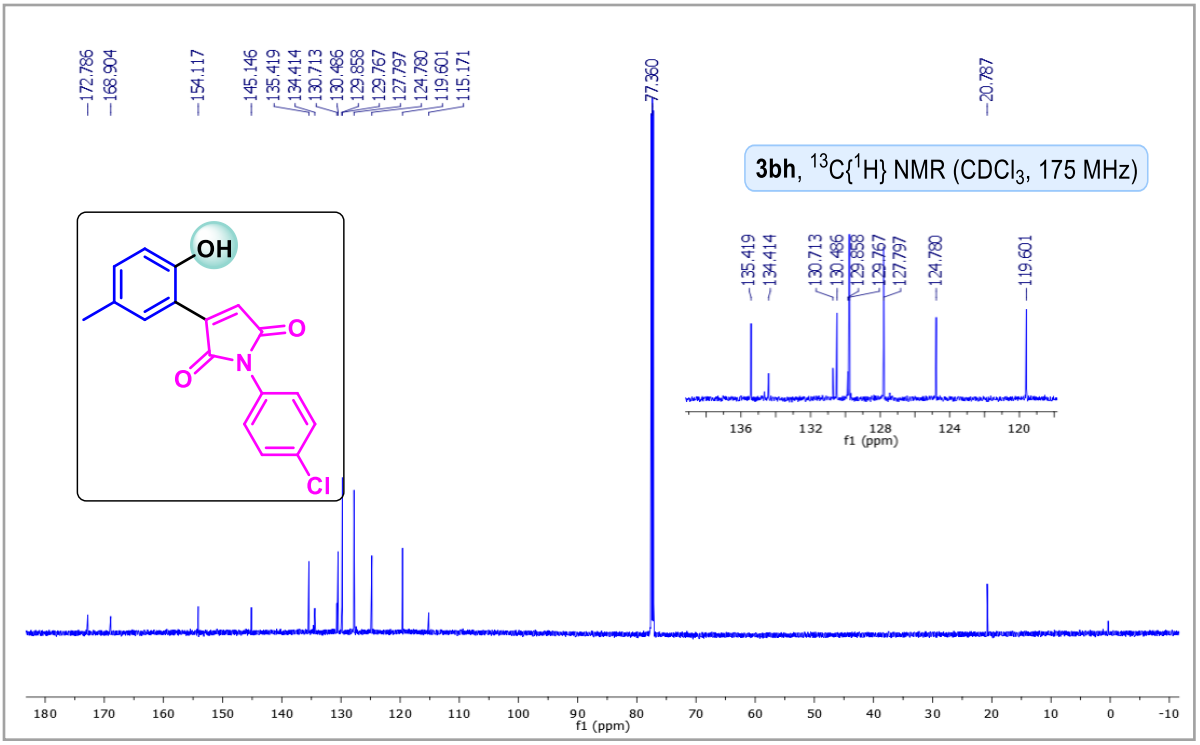
7.480
7.469
7.464
7.457
7.377
7.370
7.365
7.353
7.348
7.260
7.228
7.223
7.207
7.202
6.970
6.921
6.900
2.324
0.000
3bh, 1H NMR (CDCl3, 400 MHz)
OH
O
O
N
Cl
3.20
2.12
1.06
1.04
1.08
f1 (ppm)
1.00
3.04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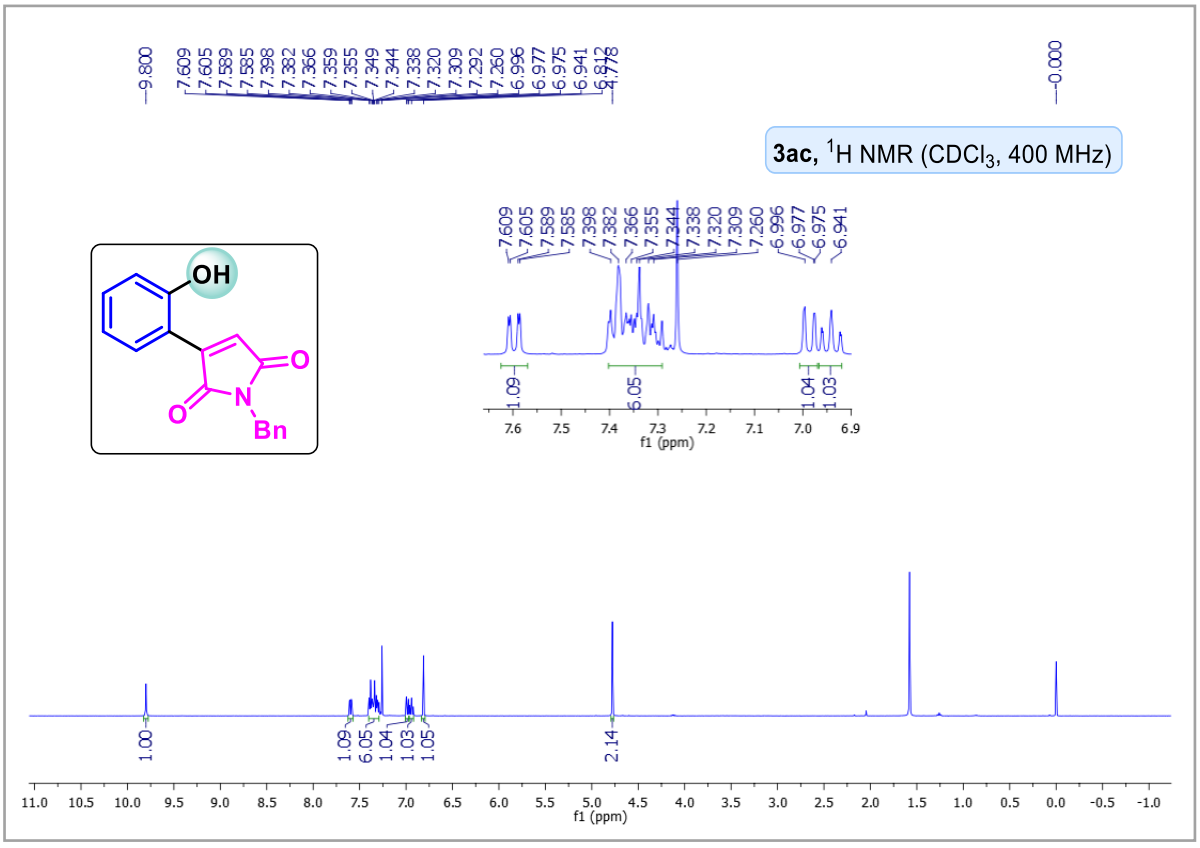
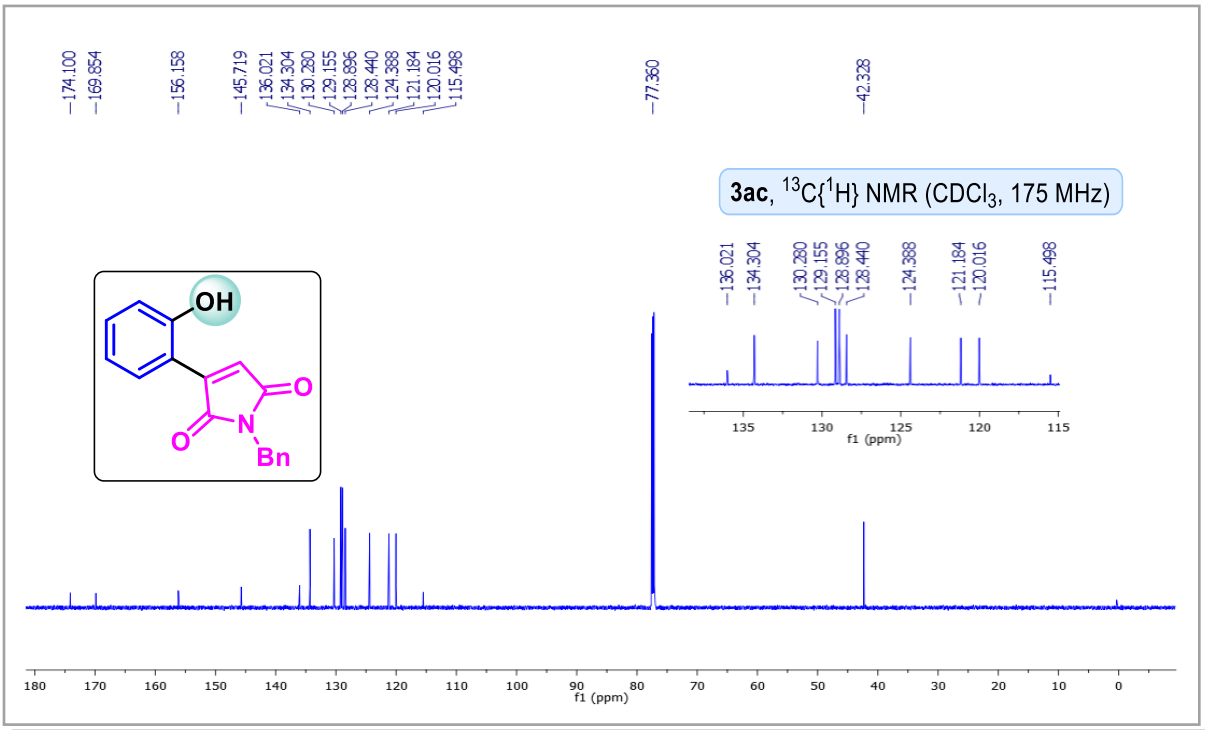
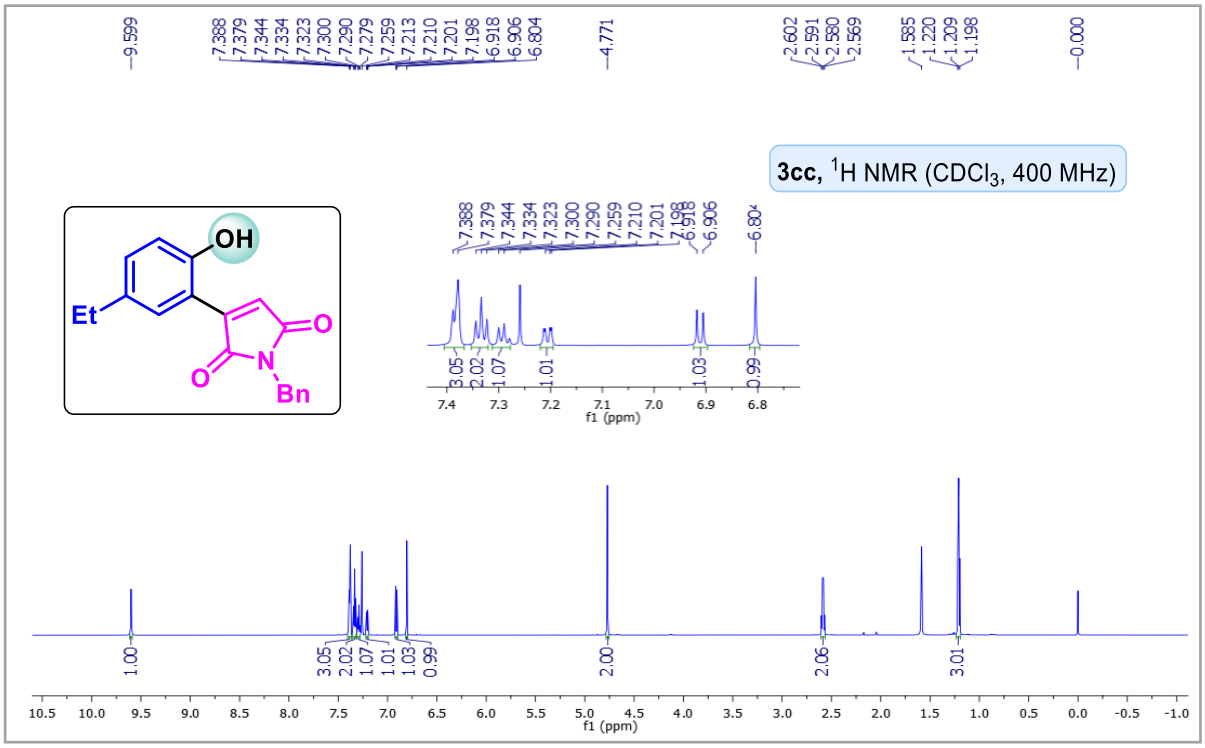
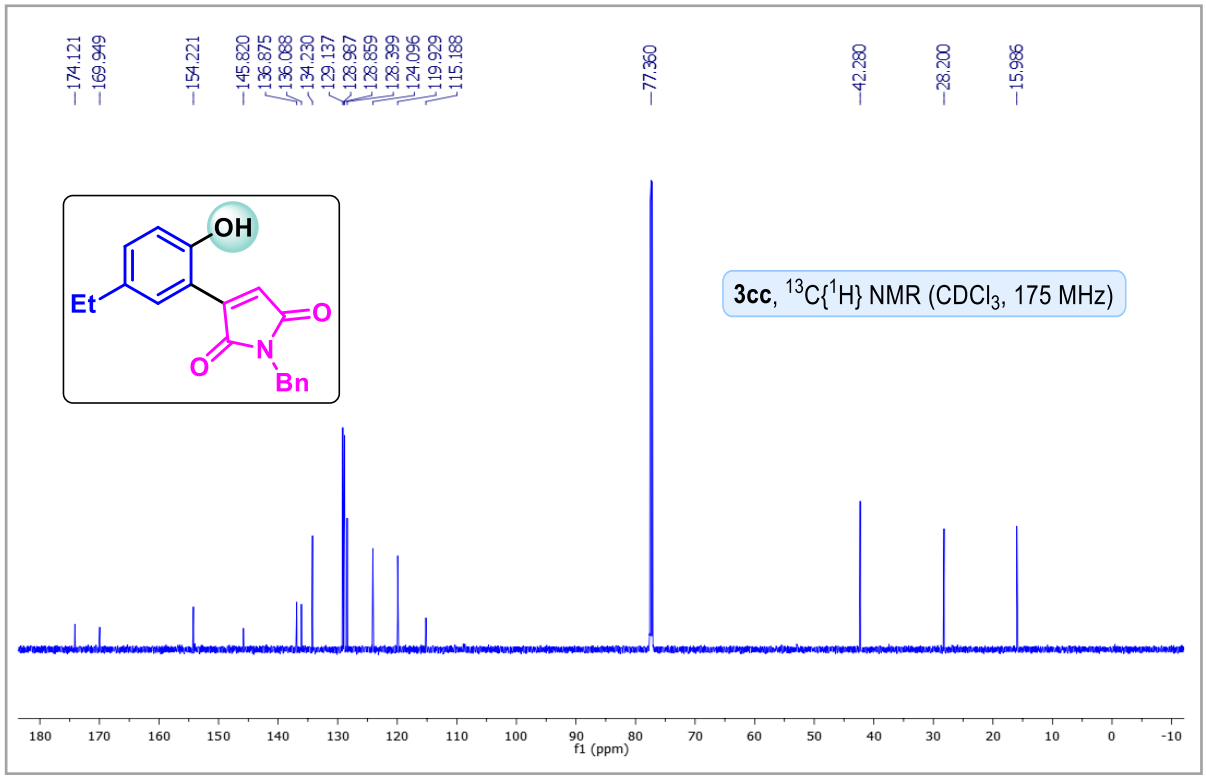
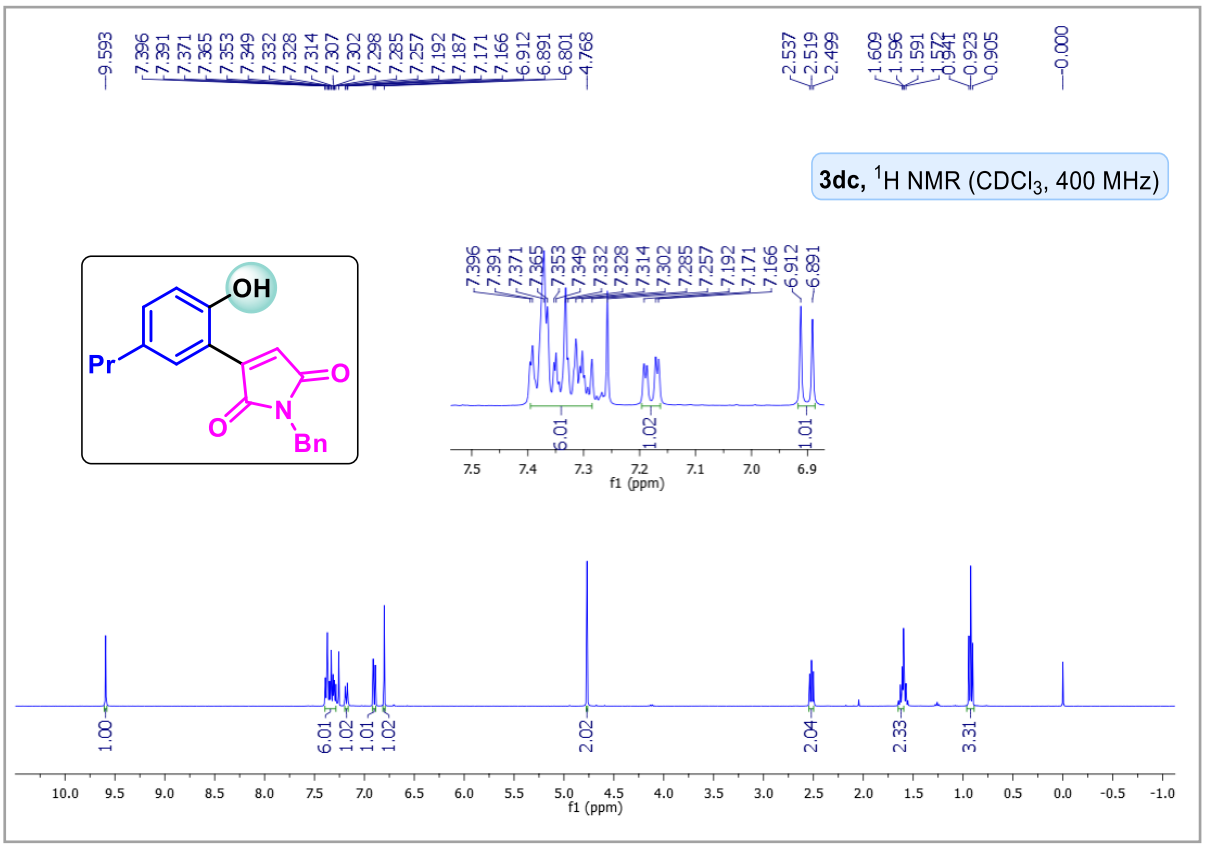
154.117
145.146
135.419
134.414
130.713
130.486
129.858
129.767
127.797
124.780
119.601
115.171
77.360
20.787
3bh, 13C{1H} NMR (CDCl3, 175 MHz)
OH
O
O
N
Cl
f1 (ppm)

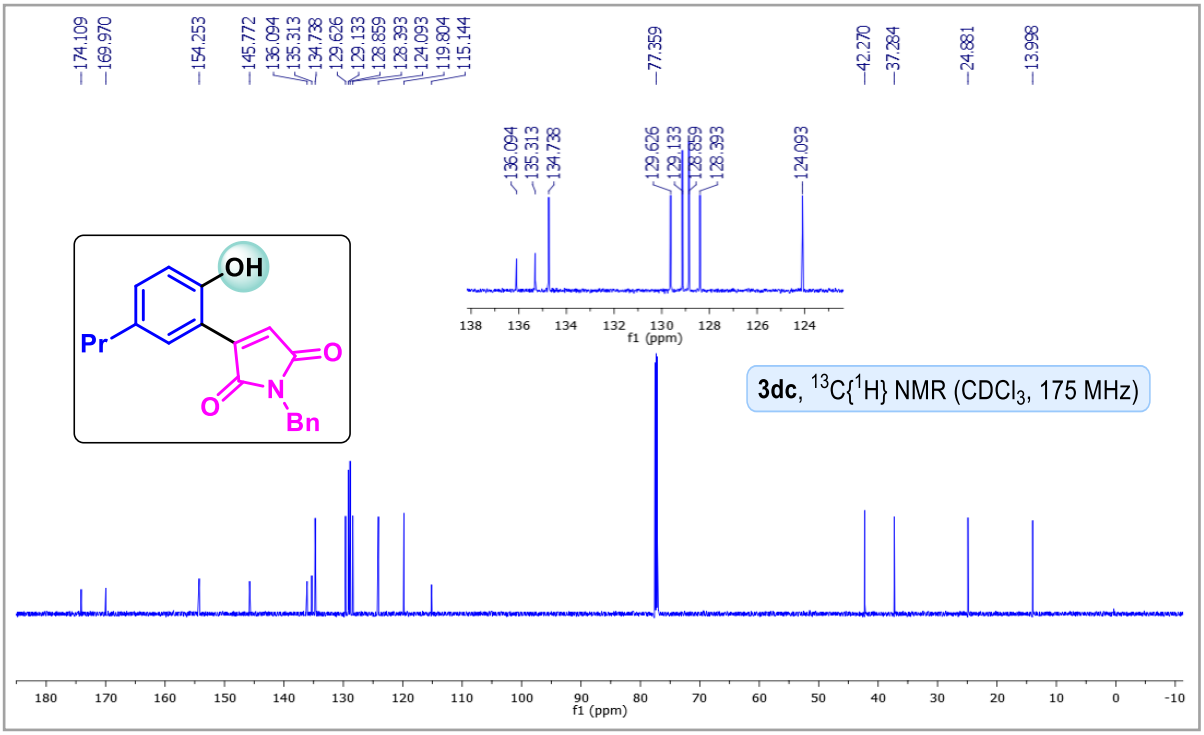

3ac, ^{1}H NMR ($CDCl_3$, 400 MHz)
OH
O
O
N
Bn
f1 (ppm)

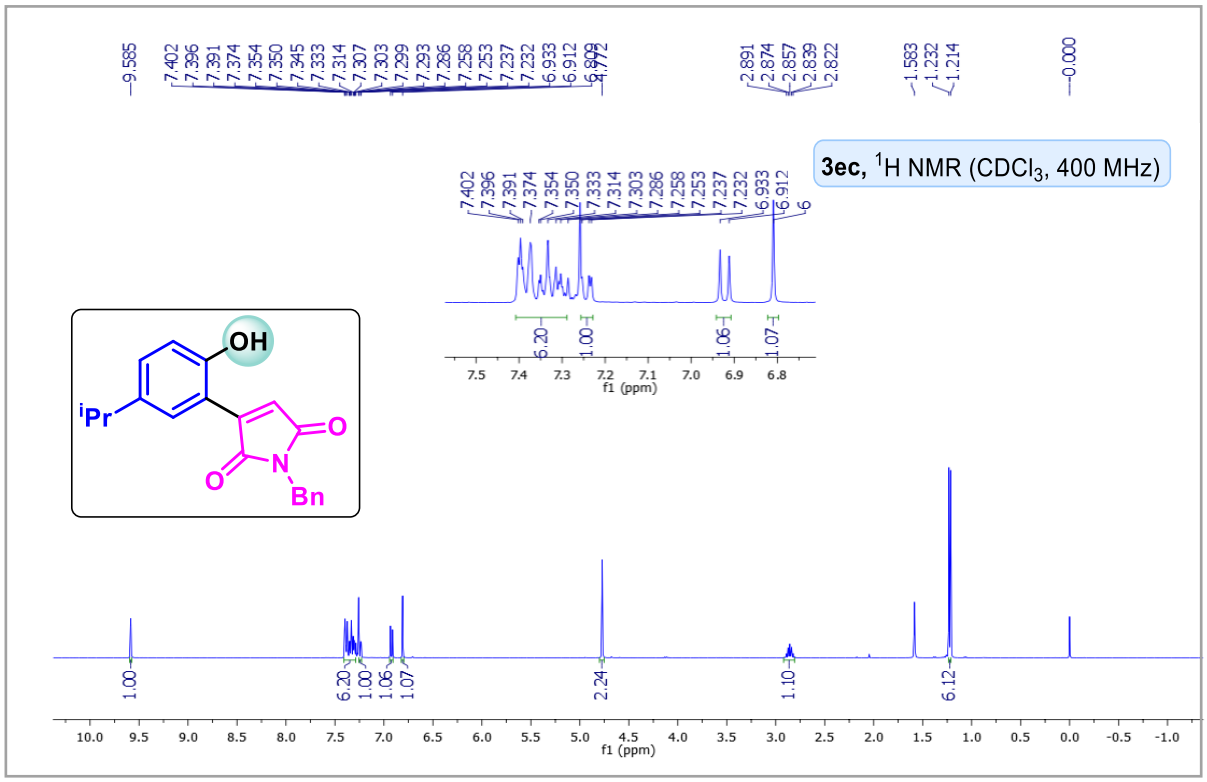

3ac, $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 175 MHz)
OH
O
O
N
Bn
f1 (ppm)

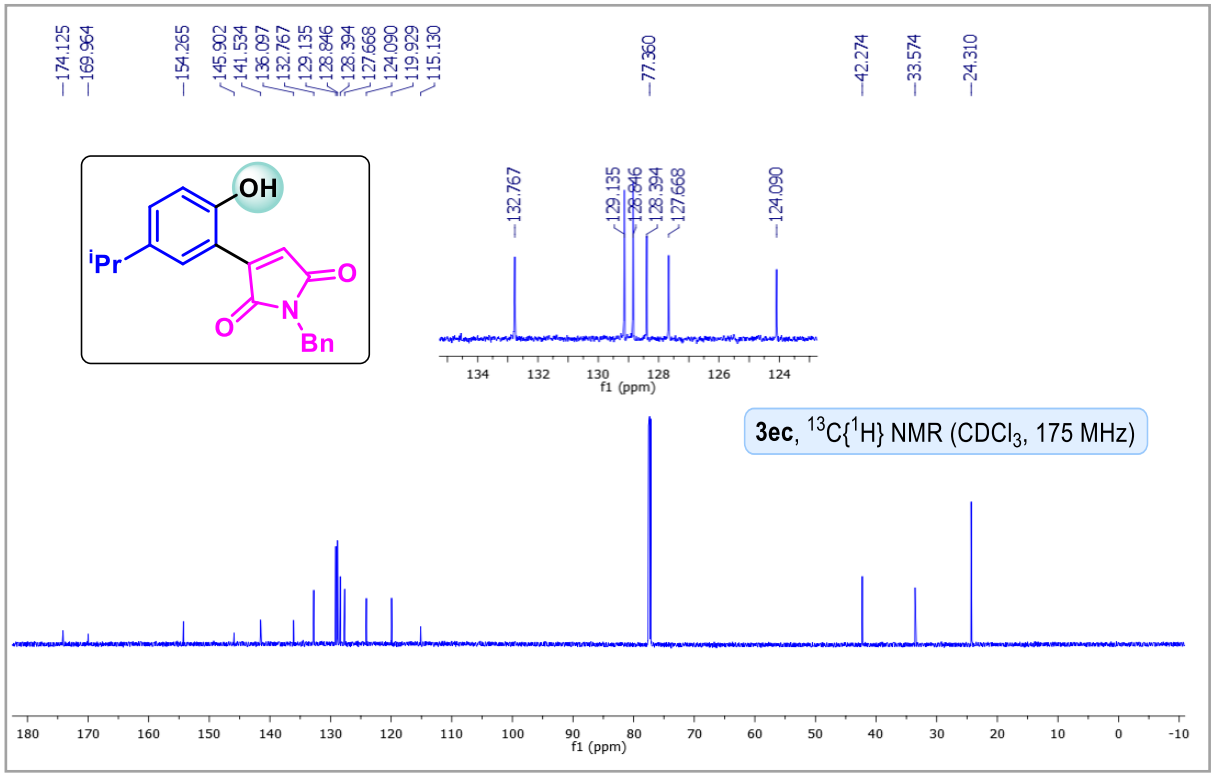

3cc, ^{1}H NMR ($CDCl_3$, 400 MHz)
OH
Et
O
N
O
Bn
f1 (ppm)

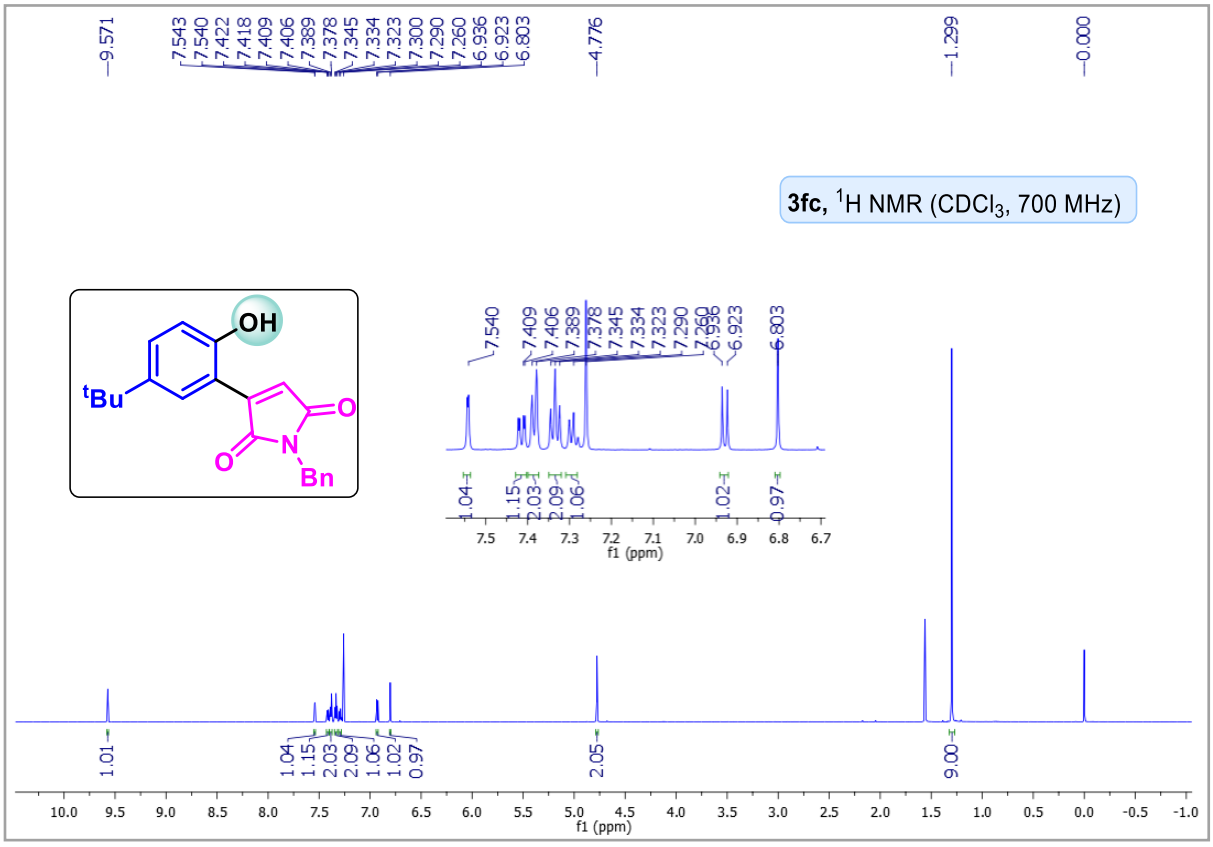

3cc, $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 175 MHz)
OH
Et
O
N
O
Bn
f1 (ppm)

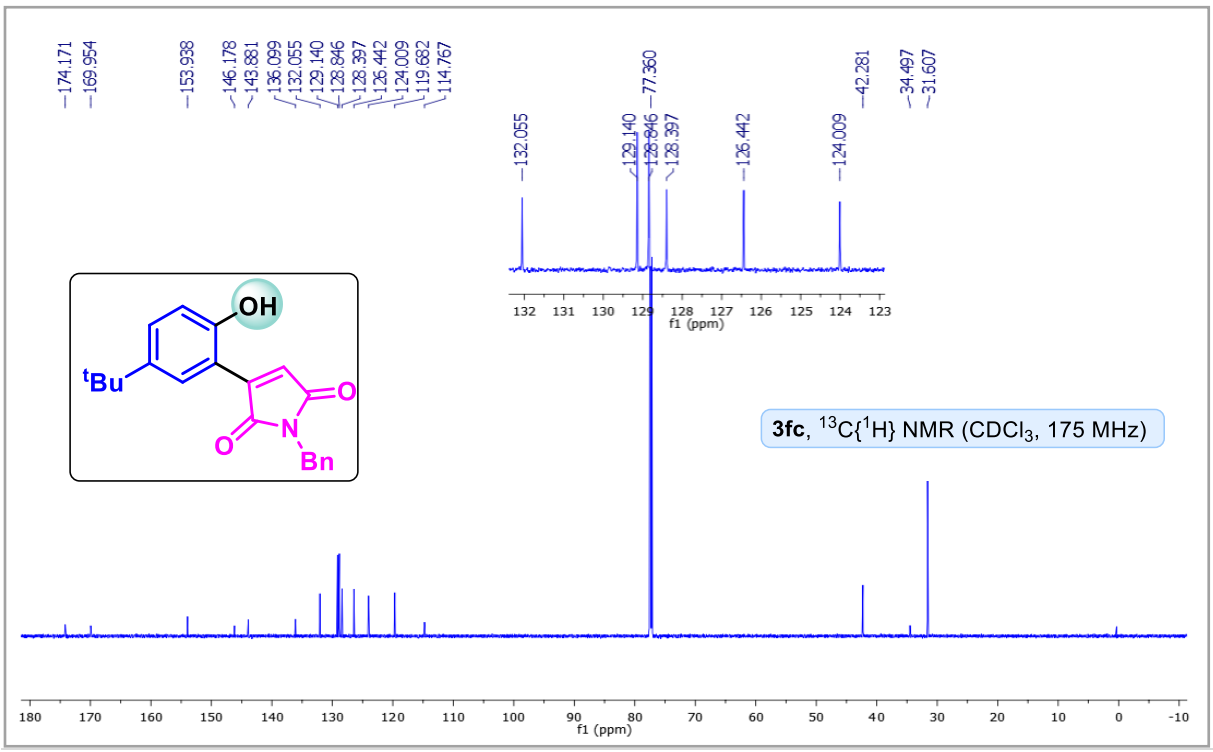

3dc, ^{1}H NMR ($CDCl_3$, 400 MHz)
OH
Pr
O
N
O
Bn
f1 (ppm)

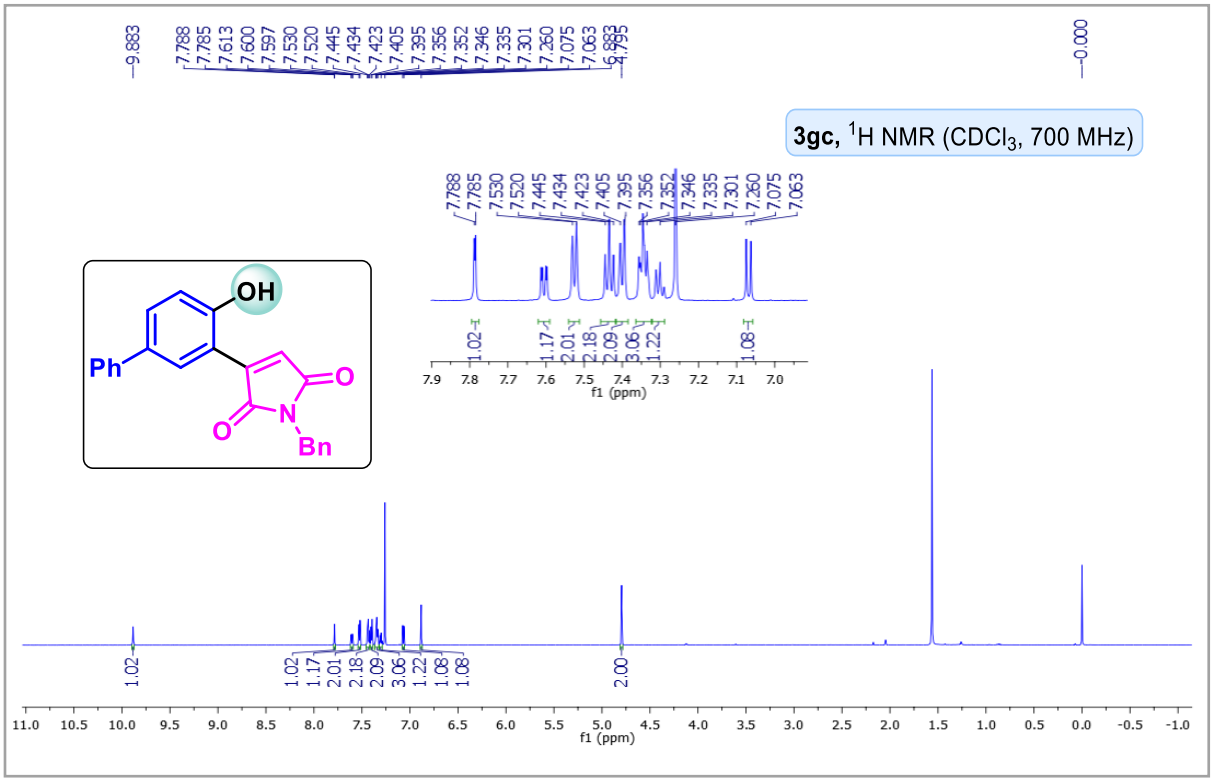

3dc, $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 175 MHz)
OH
Pr
O
N
O
Bn
f1 (ppm)

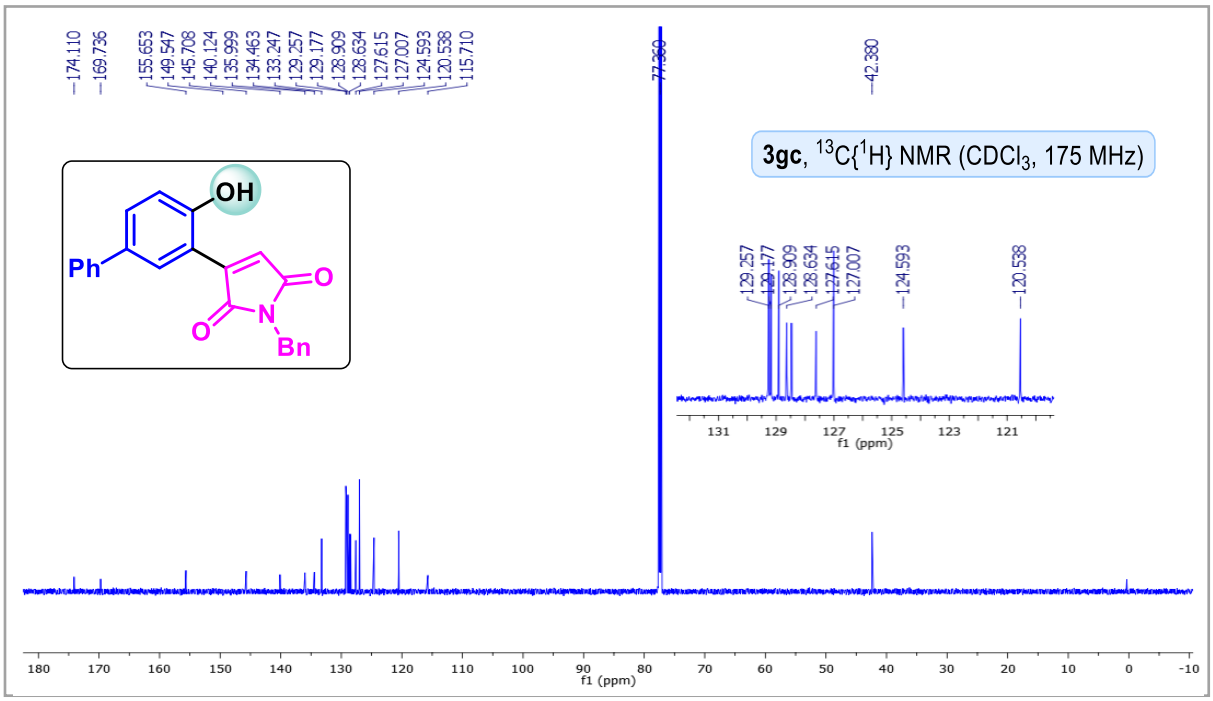

3ec, ^{1}H NMR ($CDCl_3$, 400 MHz)
OH
iPr
O
N
Bn
f1 (ppm)

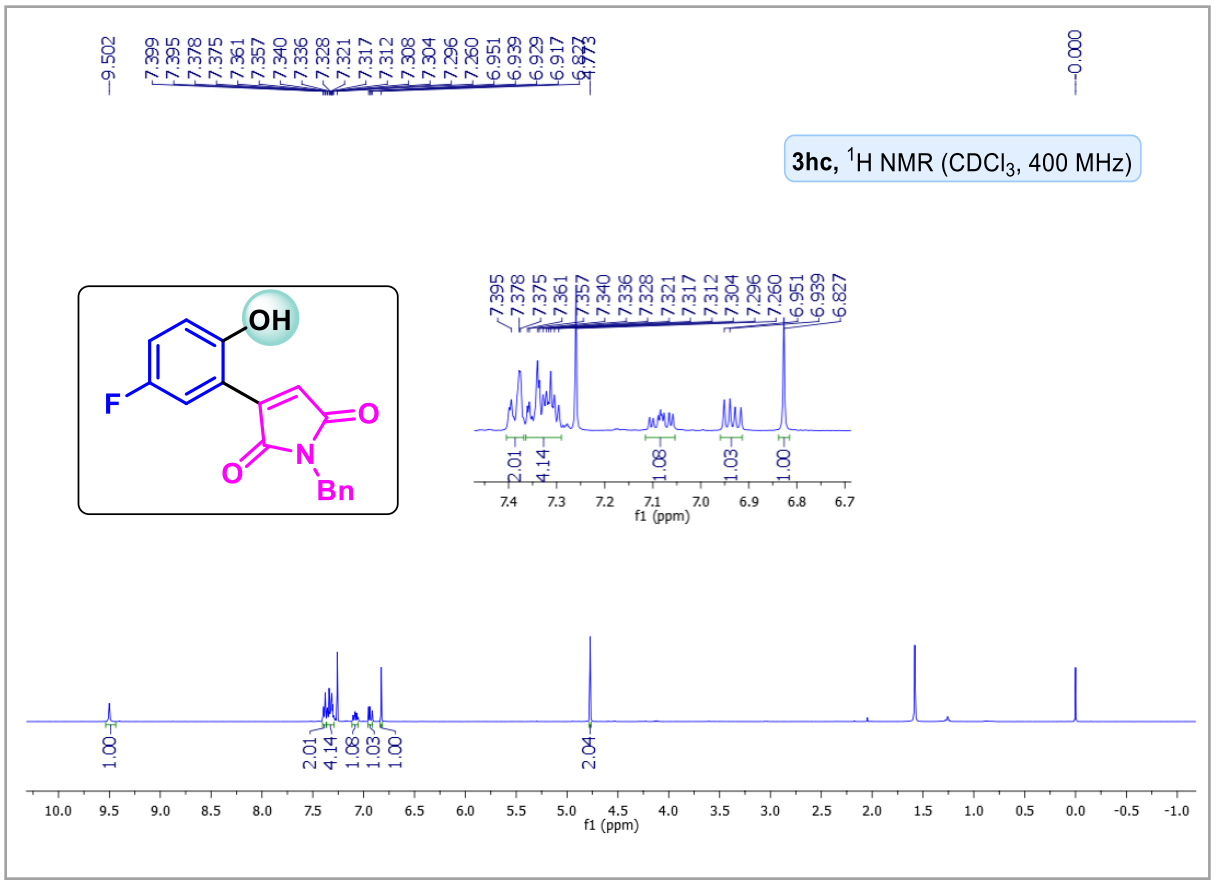

3ec, $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 175 MHz)
OH
iPr
O
N
Bn
f1 (ppm)

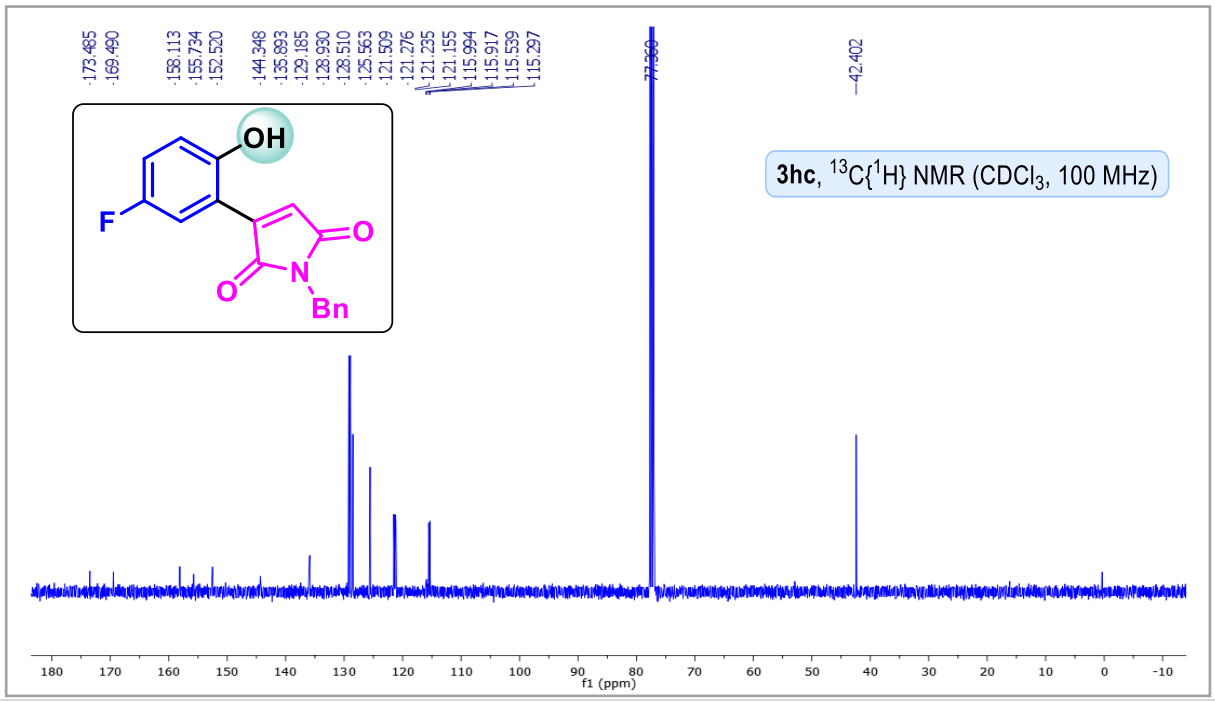

9.571
7.543
7.540
7.422
7.418
7.409
7.406
7.389
7.378
7.345
7.334
7.323
7.300
7.290
7.260
6.936
6.923
6.803
4.776
1.299
0.000
3fc, 1H NMR (CDCl3, 700 MHz)
OH
tBu
O
N
O
Bn
1.01
1.04
1.15
2.03
2.09
1.06
1.02
0.97
2.05
9.00
f1 (ppm)

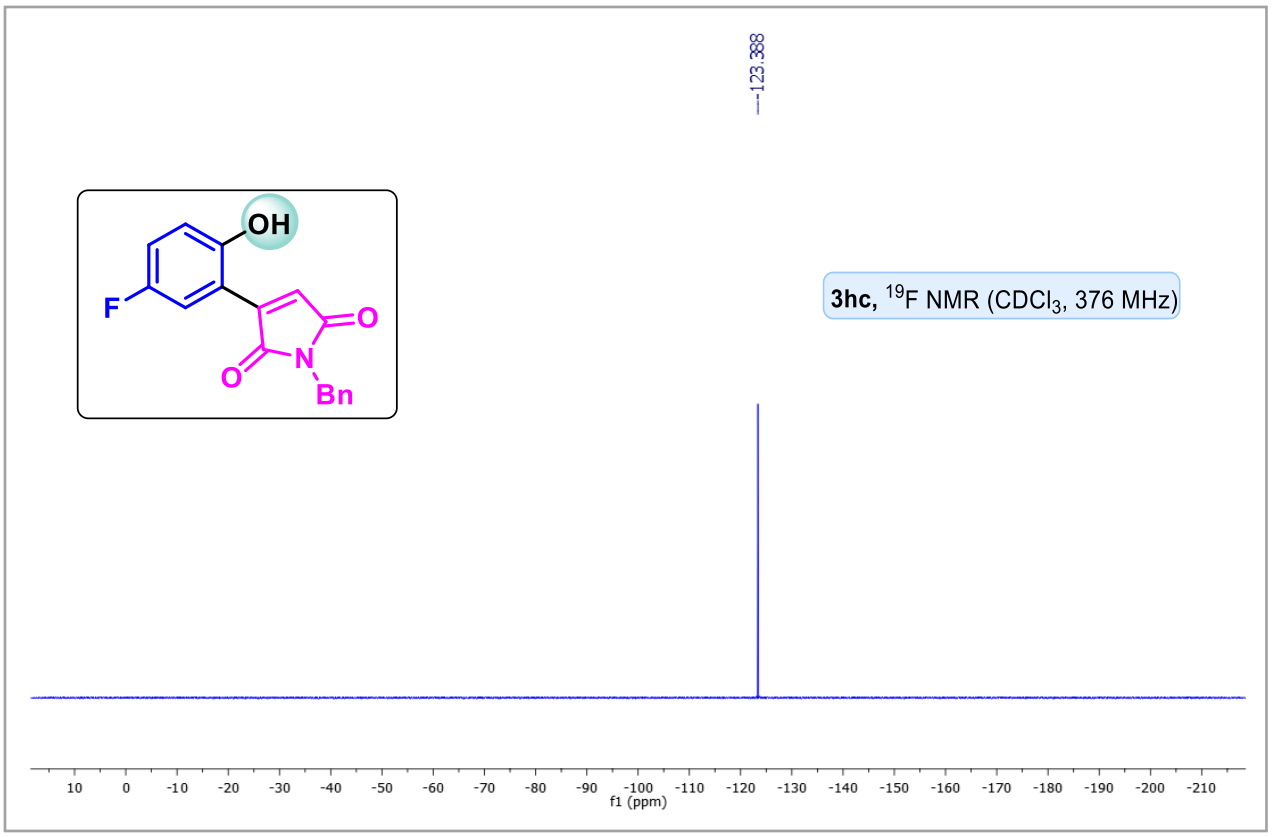

174.171
169.954
153.938
146.178
143.881
136.099
132.055
129.140
128.846
128.397
126.442
124.009
119.682
114.767
77.360
42.281
34.497
31.607
OH
tBu
O
N
O
Bn
3fc, 13C{1H} NMR (CDCl3, 175 MHz)
f1 (ppm)

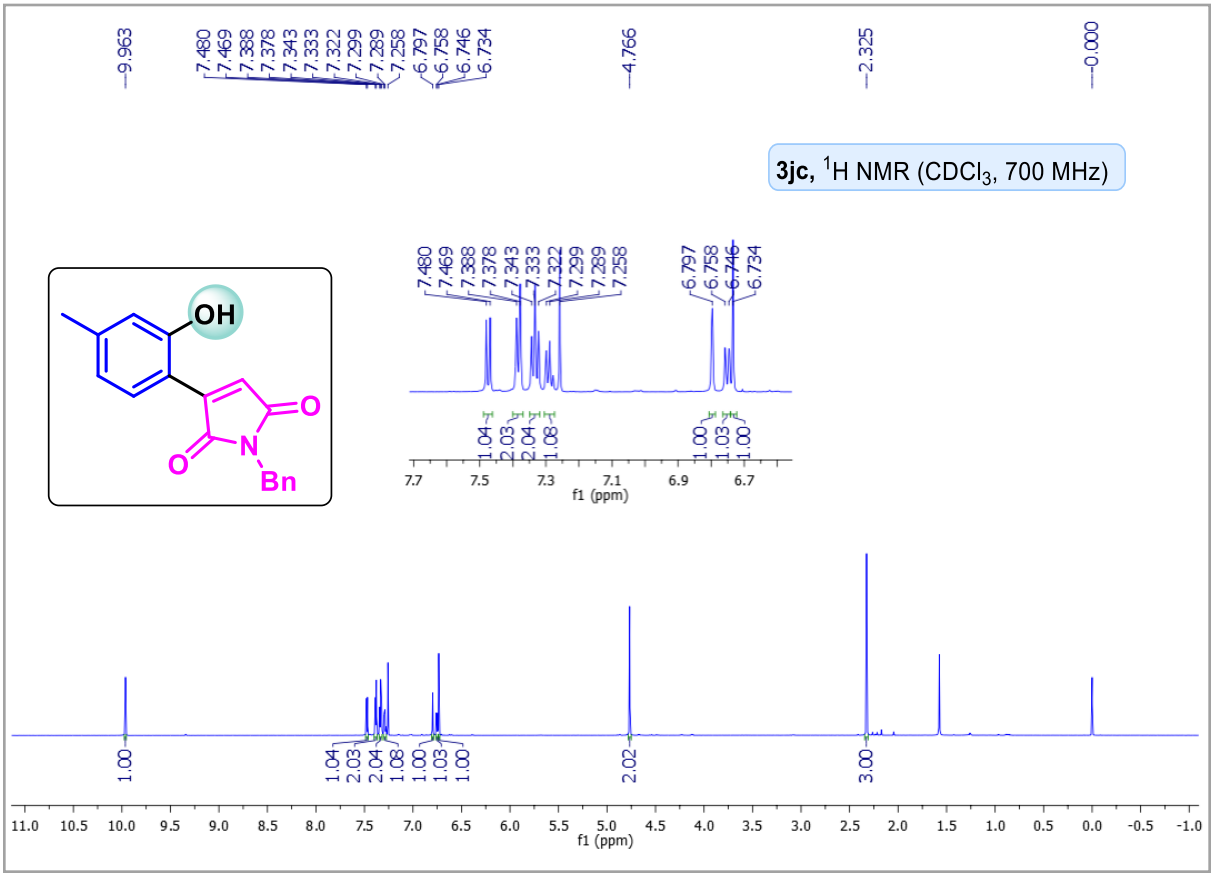

3gc, ^{1}H NMR ($CDCl_3$, 700 MHz)
OH
Ph
O
N
O
Bn
f1 (ppm)

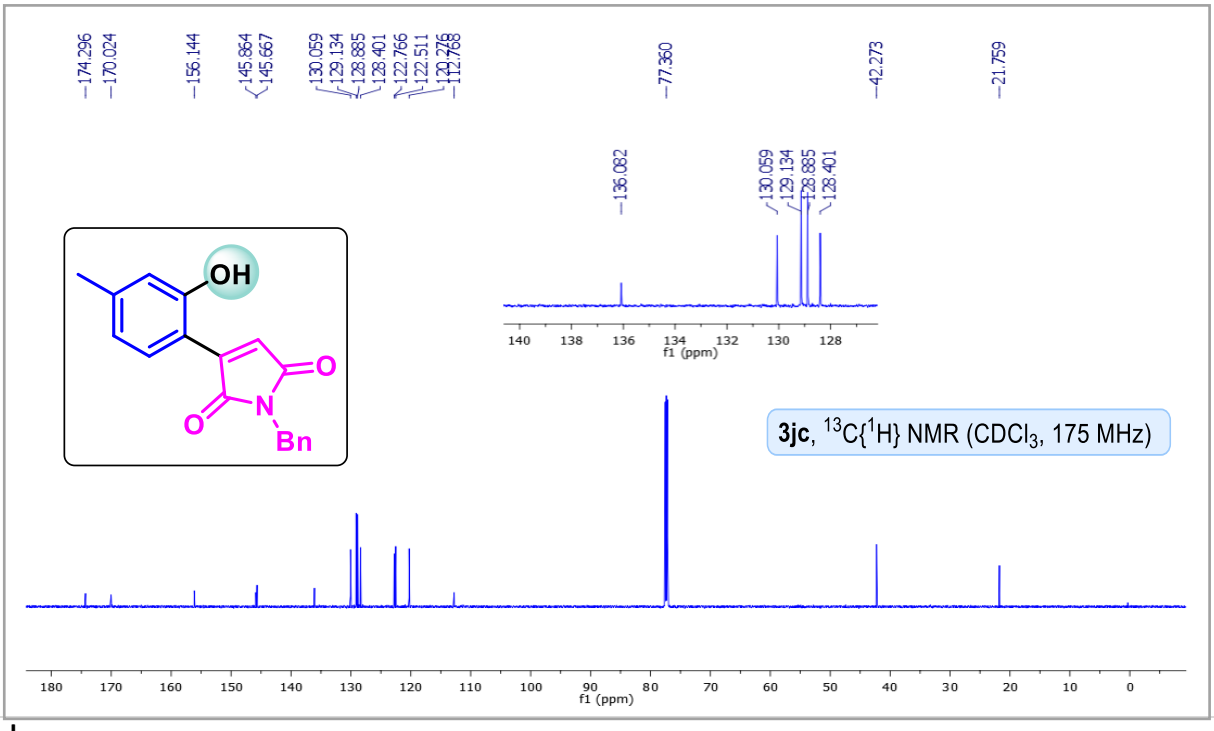

3gc, $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 175 MHz)
OH
Ph
O
N
O
Bn
f1 (ppm)

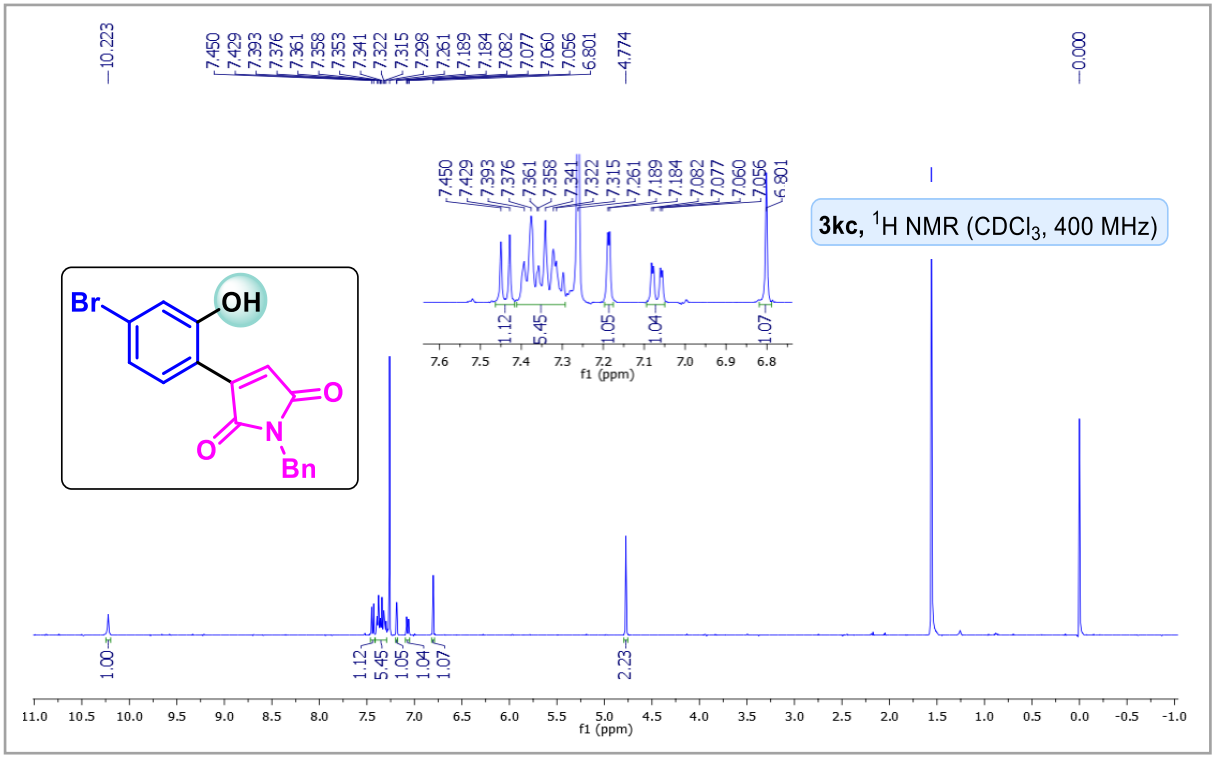

9.502
7.399
7.395
7.378
7.375
7.361
7.357
7.340
7.336
7.328
7.321
7.317
7.312
7.308
7.304
7.296
7.260
6.951
6.939
6.929
6.917
6.827
4.773
0.000
3hc, 1H NMR (CDCl3, 400 MHz)
OH
F
O
N
O
Bn
2.01
4.14
1.08
1.03
1.00
f1 (ppm)
1.00
2.01
4.14
1.03
1.03
1.00
2.04
f1 (ppm)

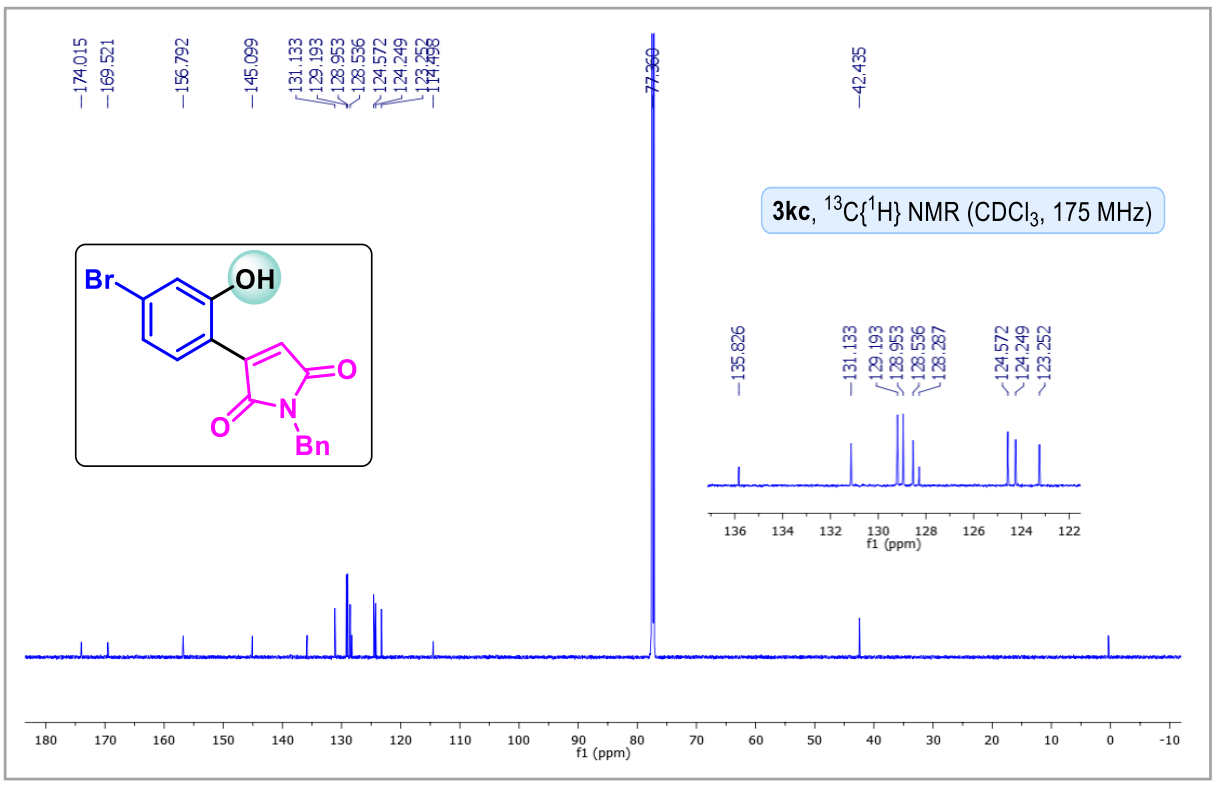

173.485
169.490
158.113
155.734
152.520
144.348
135.893
129.185
128.930
128.510
125.563
121.509
121.276
121.235
121.155
115.994
115.917
115.539
115.297
77.360
42.402
3hc, 13C{1H} NMR (CDCl3, 100 MHz)
OH
F
O
N
O
Bn
f1 (ppm)

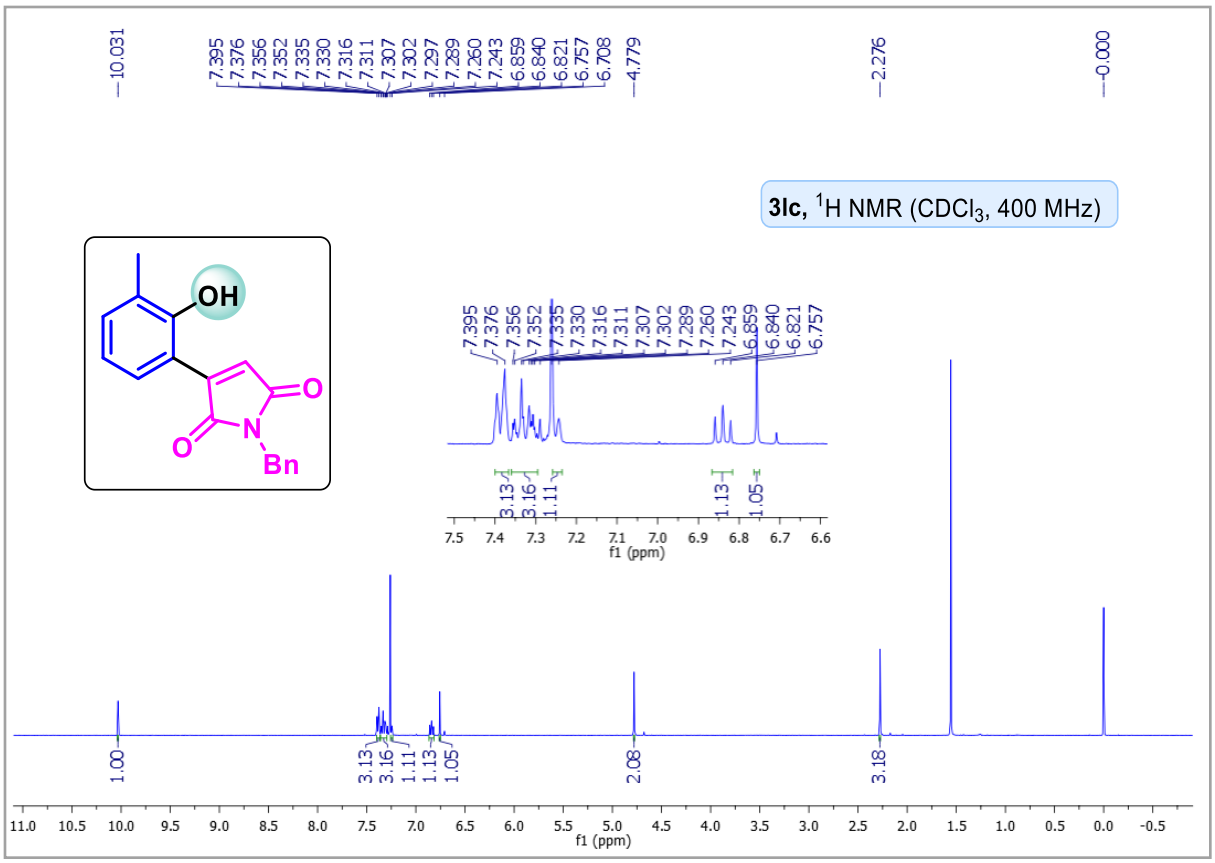

-123.388
OH
F
O
O
N
Bn
3hc, 19F NMR (CDCl3, 376 MHz)
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

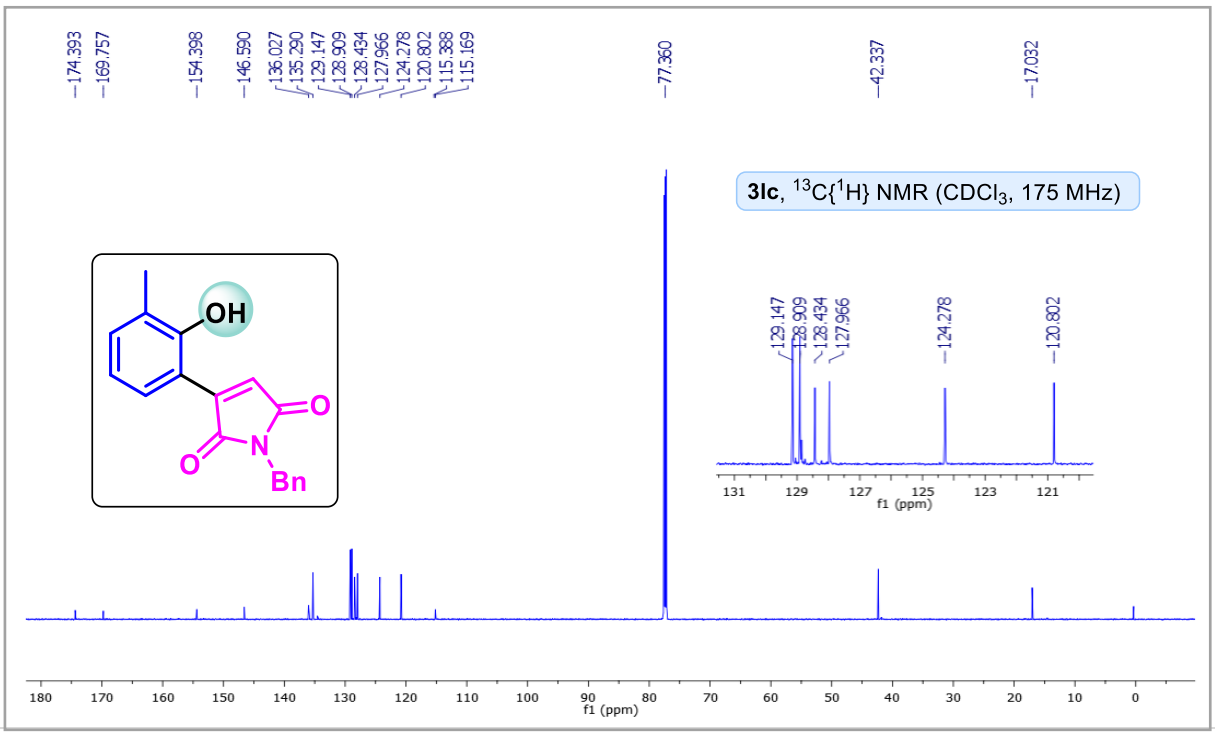

3jc, ^{1}H NMR ($CDCl_3$, 700 MHz)
OH
O
N
Bn
f1 (ppm)

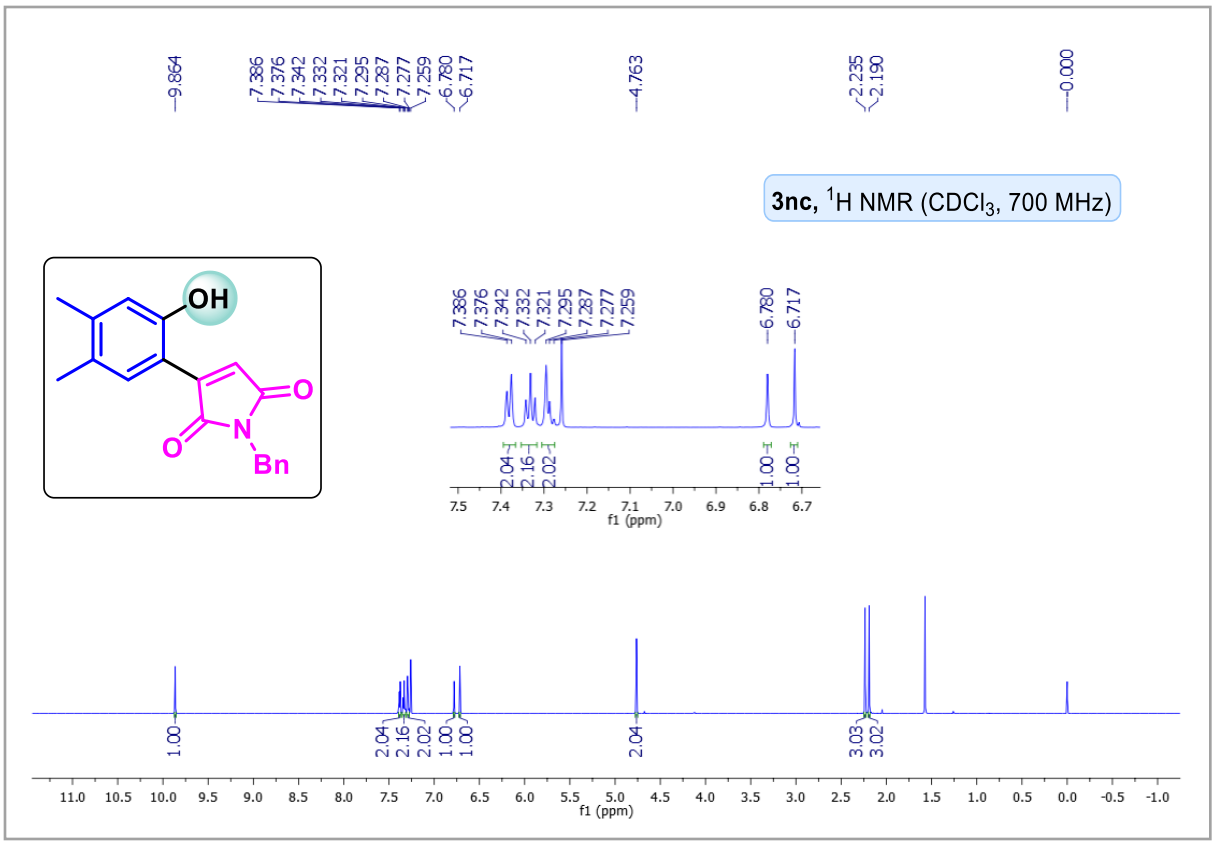

3jc, $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 175 MHz)
OH
O
N
Bn
f1 (ppm)

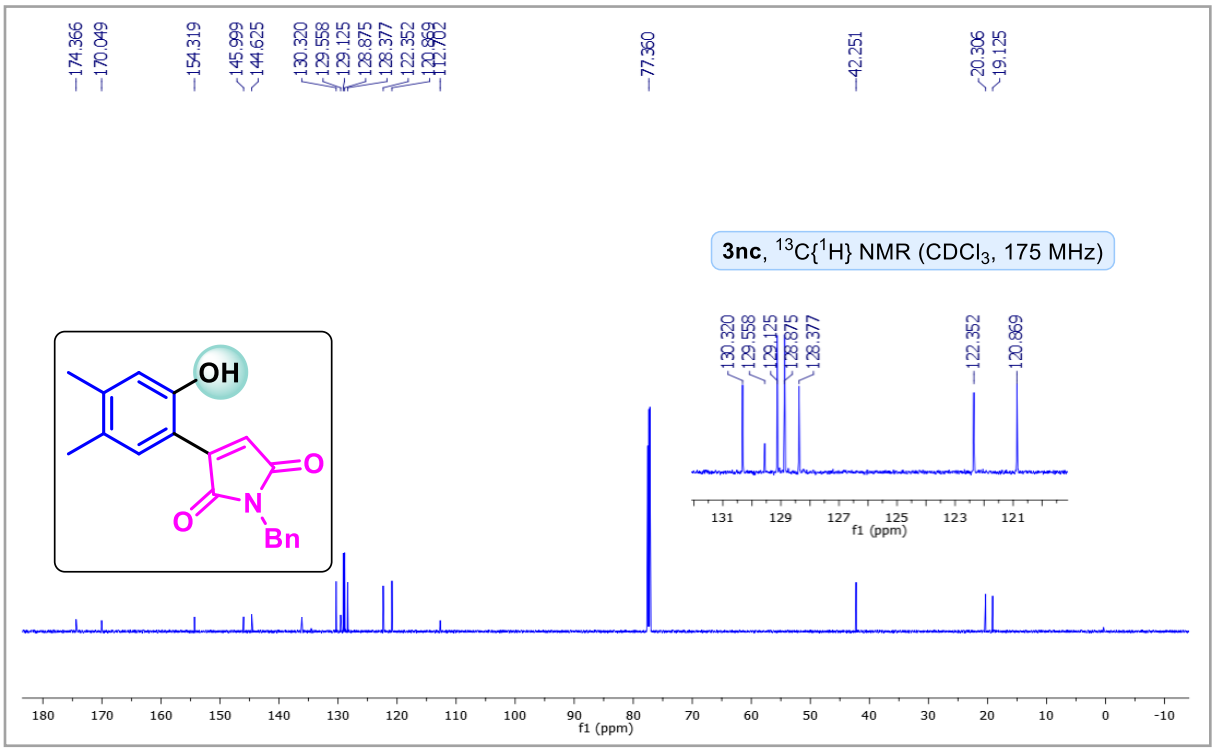

3kc, ^{1}H NMR ($CDCl_3$, 400 MHz)
Br
OH
O
O
N
Bn
f1 (ppm)

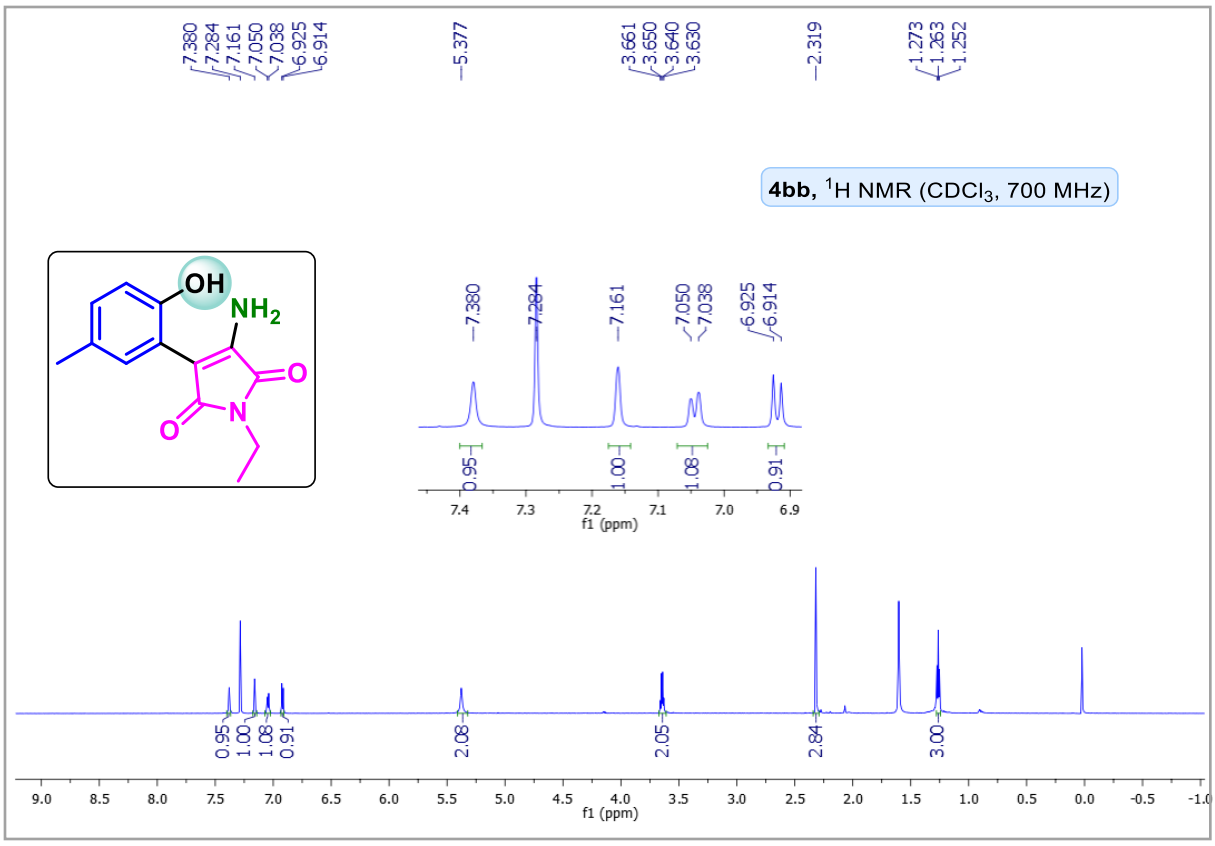

3kc, $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 175 MHz)
Br
OH
O
O
N
Bn
f1 (ppm)

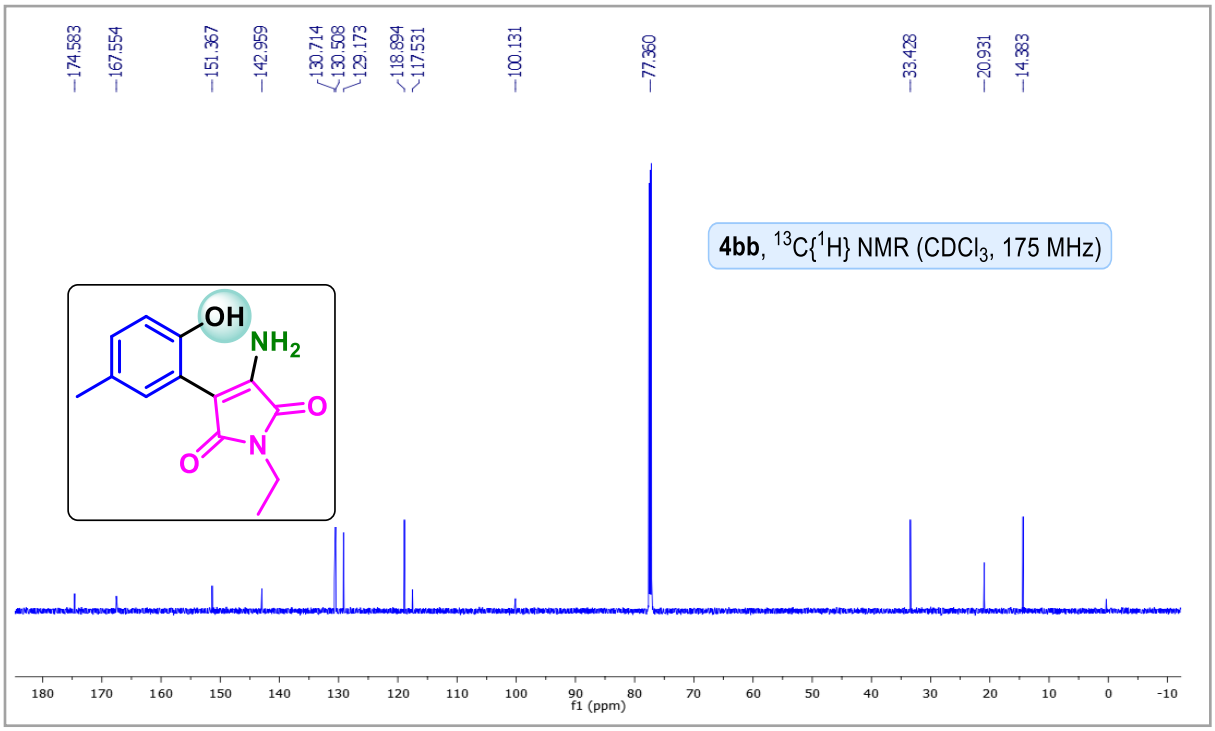

10.031
7.395
7.376
7.356
7.352
7.335
7.330
7.316
7.311
7.307
7.302
7.297
7.289
7.260
7.243
6.859
6.840
6.821
6.757
6.708
4.779
2.276
0.000
3lc, 1H NMR (CDCl3, 400 MHz)
OH
O
O
N
Bn
3.13
3.16
1.11
1.13
1.05
1.00
2.08
3.18
f1 (ppm)

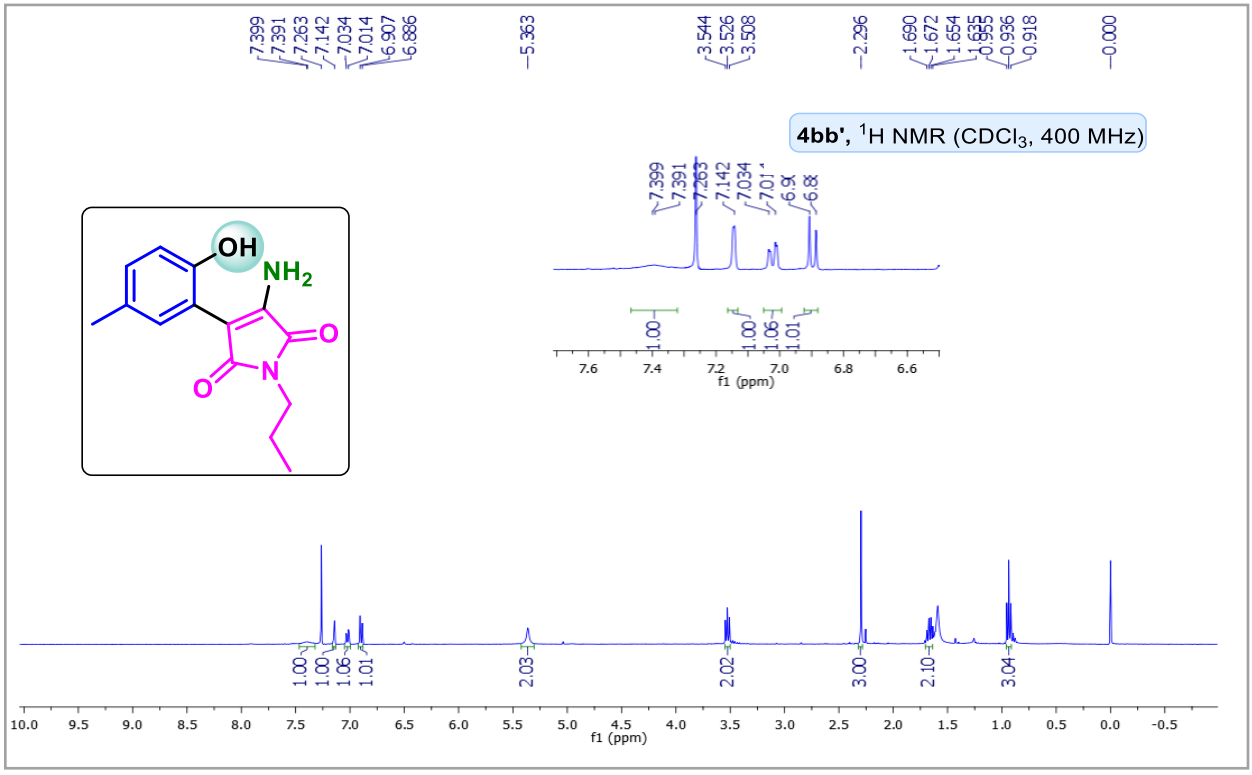

174.393
169.757
154.398
146.590
136.027
135.290
129.147
128.909
128.434
127.966
124.278
120.802
115.388
115.169
77.360
42.337
17.032
3lc, 13C{1H} NMR (CDCl3, 175 MHz)
OH
O
O
N
Bn
f1 (ppm)

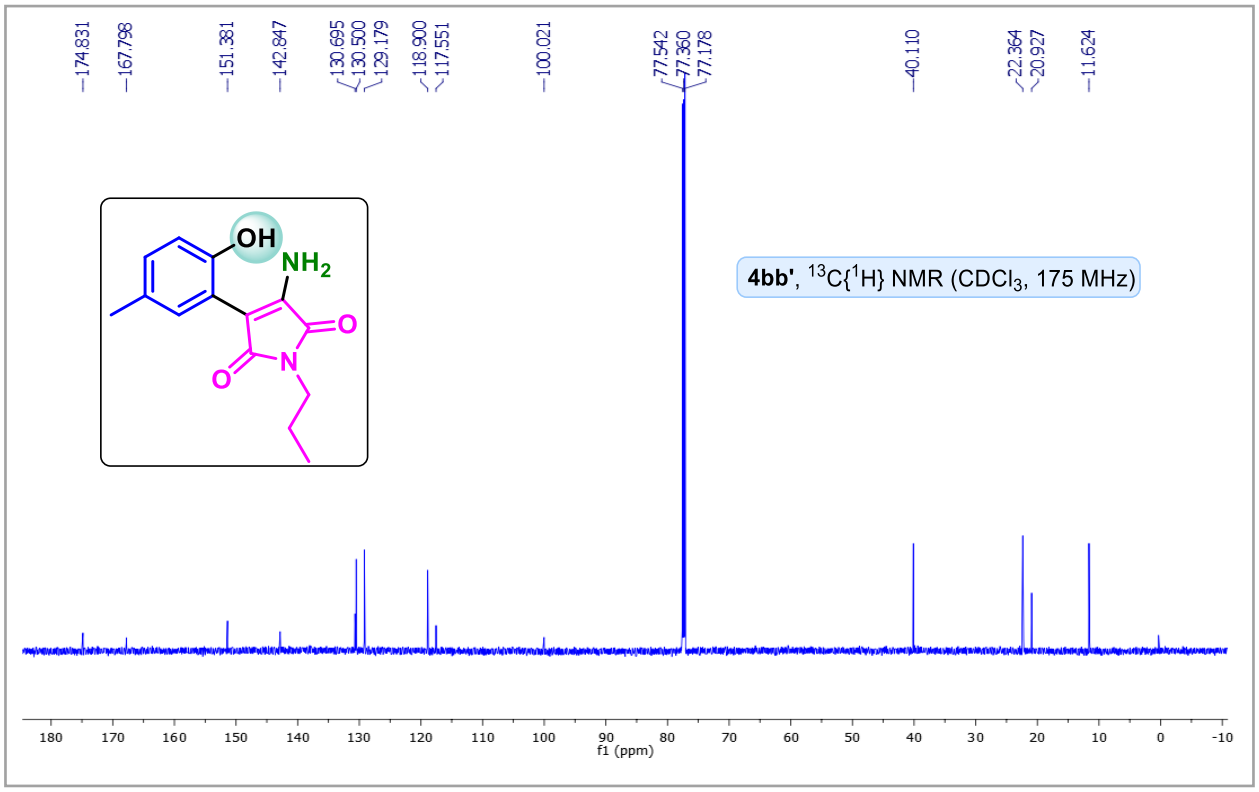

9.864
7.386
7.376
7.342
7.332
7.321
7.295
7.287
7.277
7.259
6.780
6.717
4.763
2.235
2.190
0.000
3nc, 1H NMR (CDCl3, 700 MHz)
OH
O
N
O
Bn
f1 (ppm)

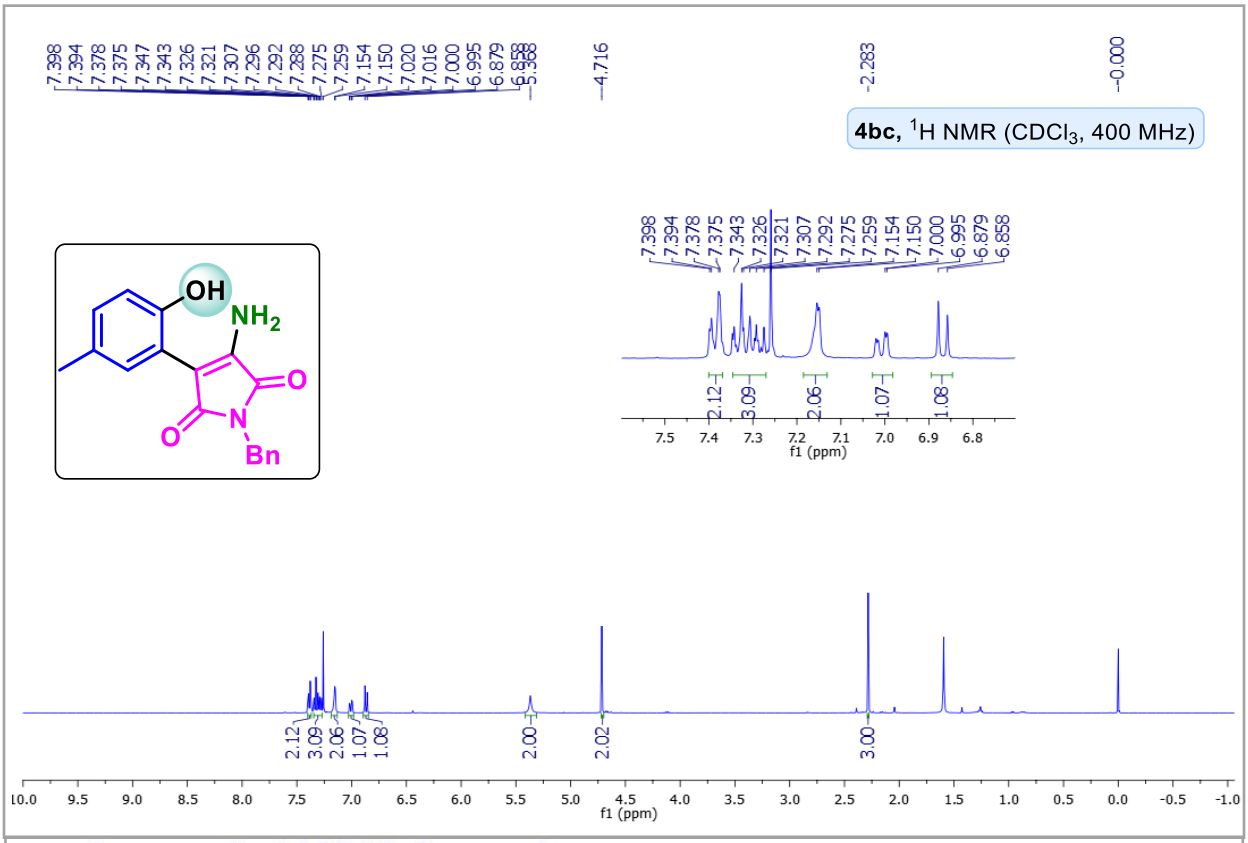

174.366
170.049
154.319
145.999
144.625
130.320
129.558
129.125
128.875
128.377
122.352
120.869
112.702
77.360
42.251
20.306
19.125
3nc, 13C{1H} NMR (CDCl3, 175 MHz)
OH
O
N
O
Bn
f1 (ppm)

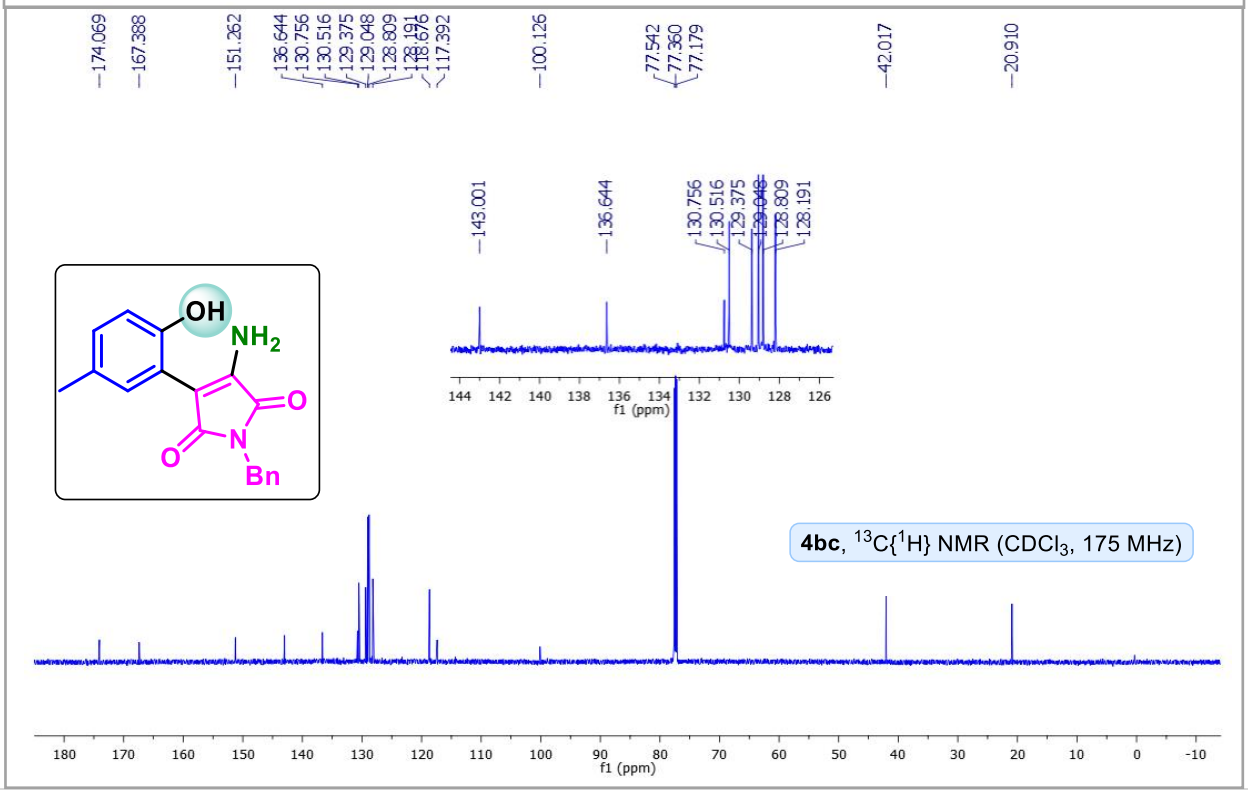

7.380
7.284
7.161
7.050
7.038
6.925
6.914
5.377
3.661
3.650
3.640
3.630
2.319
1.273
1.263
1.252
4bb, 1H NMR (CDCl3, 700 MHz)
OH
NH2
O
O
N
0.95
1.00
1.08
0.91
2.08
2.05
2.84
3.00
f1 (ppm)

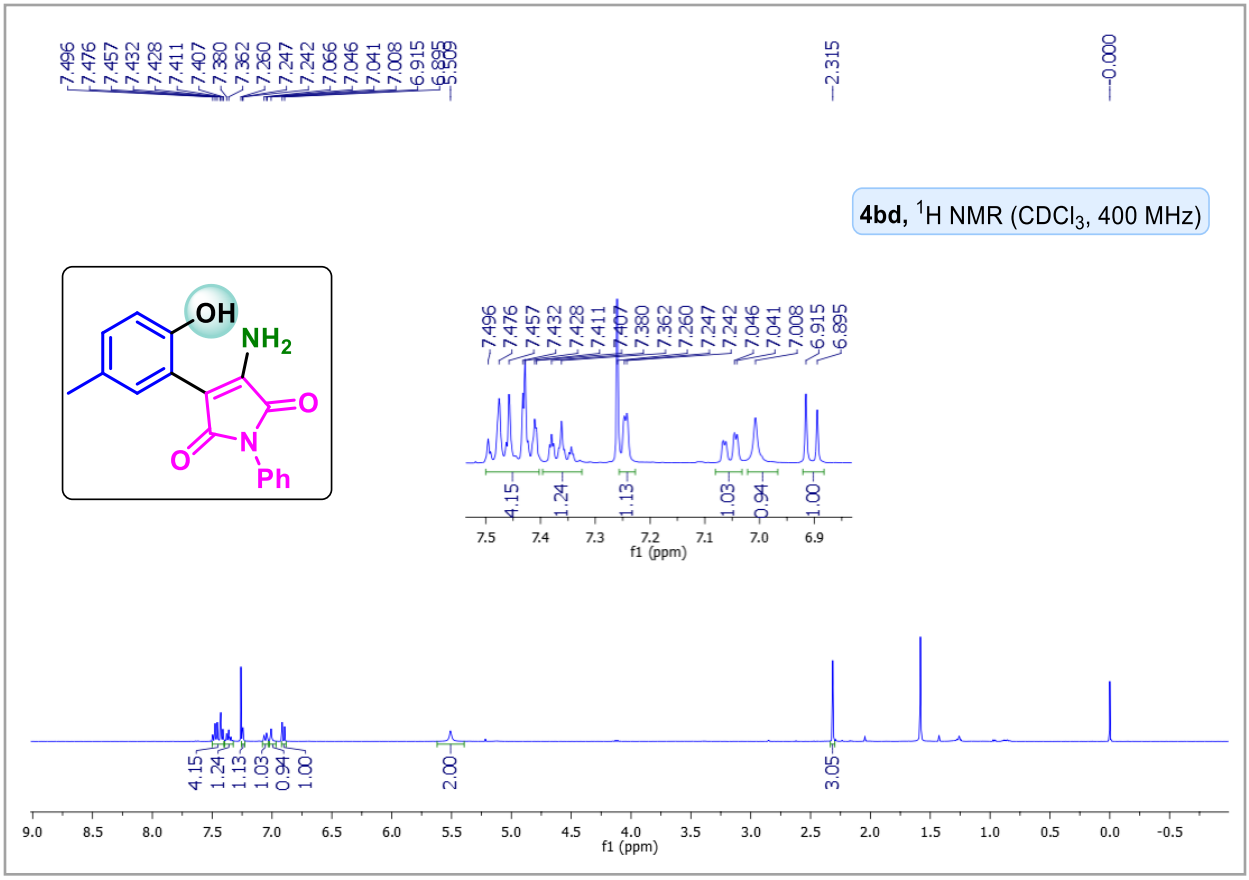

174.583
167.554
151.367
142.959
130.714
130.508
129.173
118.894
117.531
100.131
77.360
33.428
20.931
14.383
4bb, 13C{1H} NMR (CDCl3, 175 MHz)
OH
NH2
O
O
N
f1 (ppm)

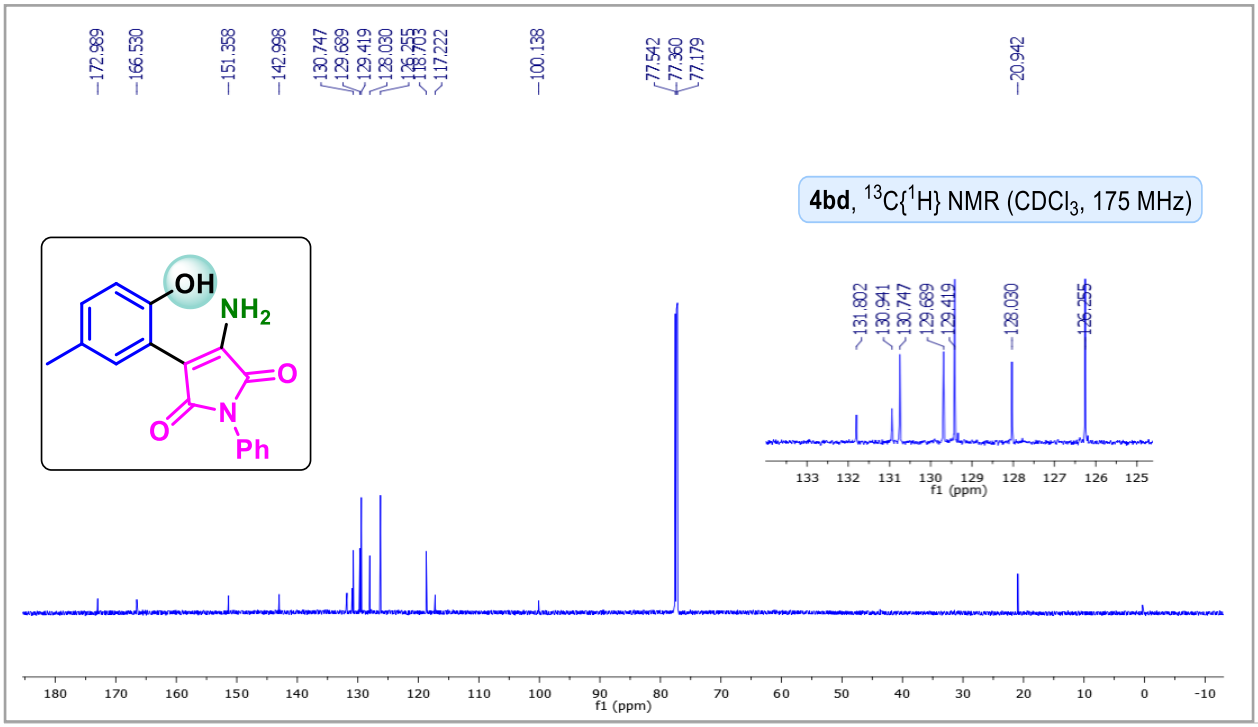

7.399
7.391
7.263
7.142
7.034
7.014
6.907
6.886
5.363
3.544
3.526
3.508
2.296
1.690
1.672
1.654
1.635
0.955
0.936
0.918
0.000
4bb', ^{1}H NMR ($CDCl_3$, 400 MHz)
OH
NH2
O
N
O
1.00
1.00
1.06
1.01
2.03
2.02
3.00
2.10
3.04
f1 (ppm)

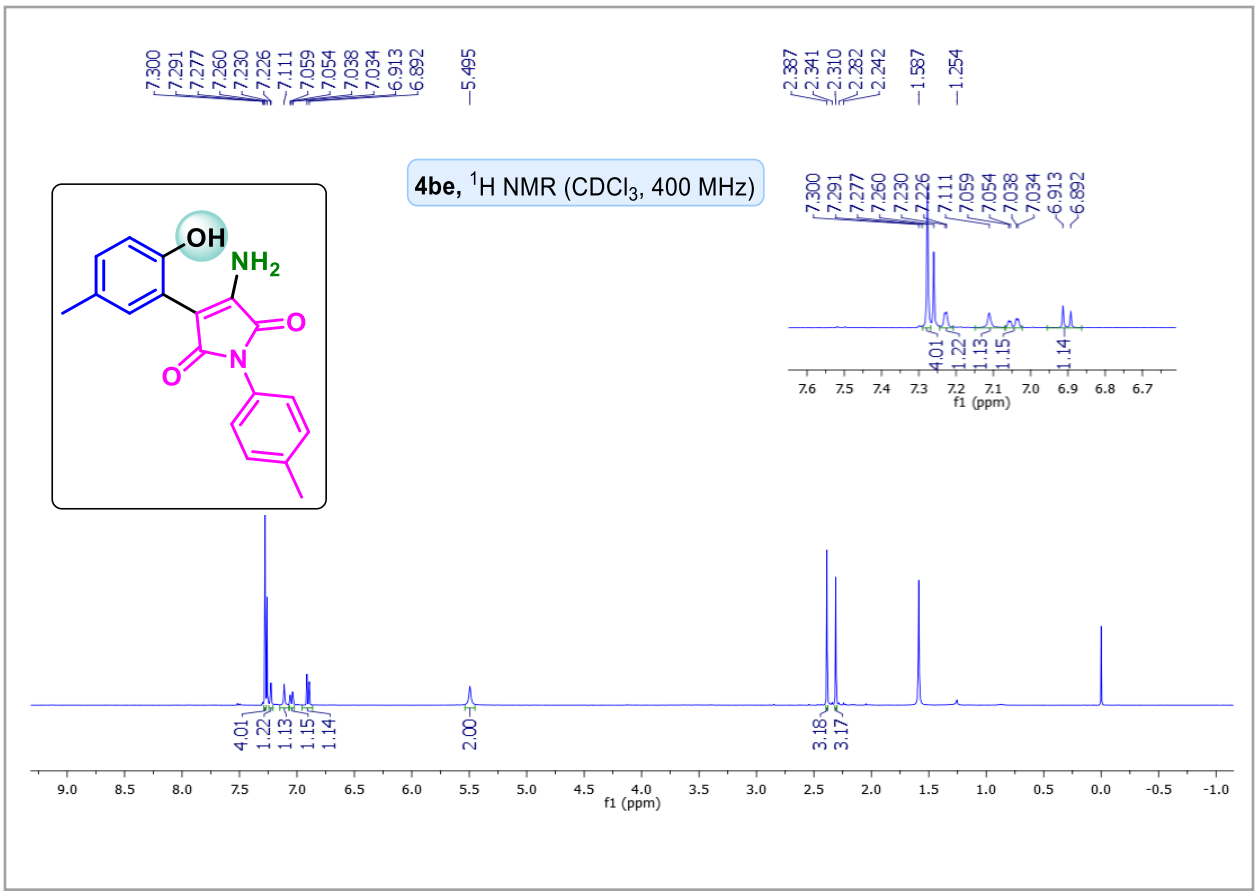

174.831
167.798
151.381
142.847
130.695
130.500
129.179
118.900
117.551
100.021
77.542
77.360
77.178
40.110
22.364
20.927
11.624
4bb', $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 175 MHz)
OH
NH2
O
N
O
f1 (ppm)

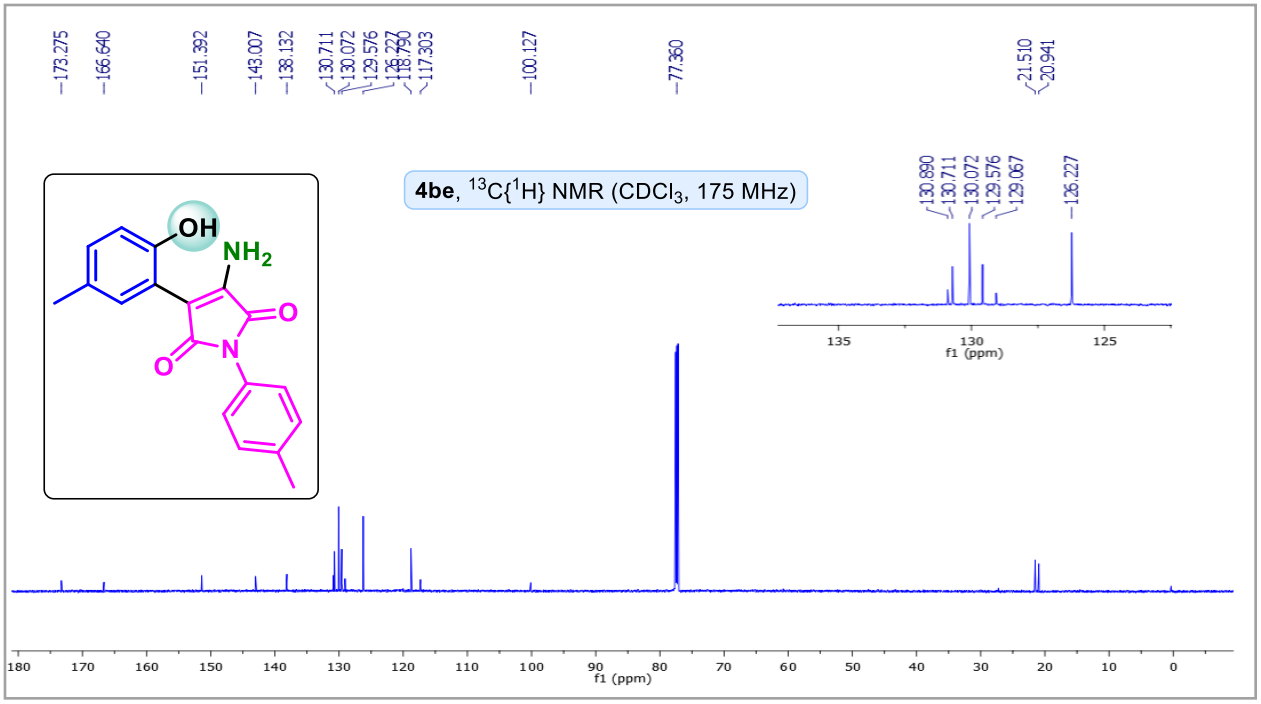

4bc, ^{1}H NMR ($CDCl_3$, 400 MHz)
OH
NH2
O
O
N
Bn
f1 (ppm)

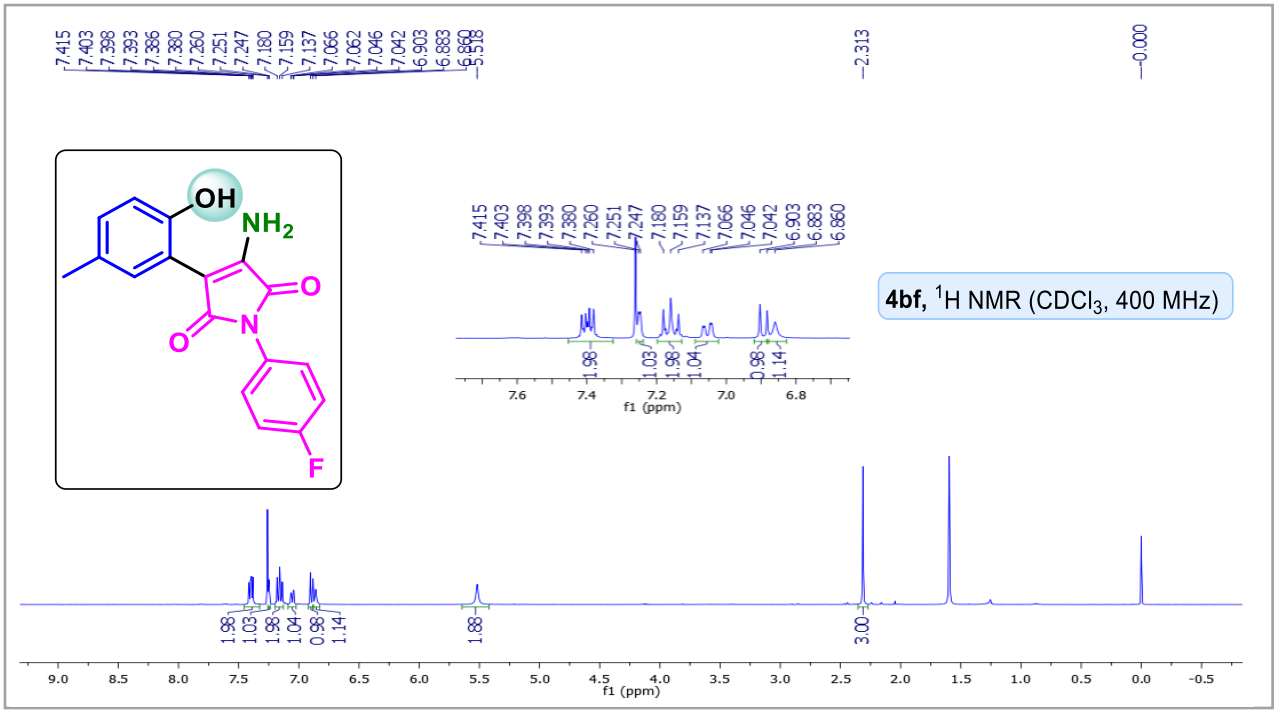

4bc, $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 175 MHz)
OH
NH2
O
O
N
Bn
f1 (ppm)

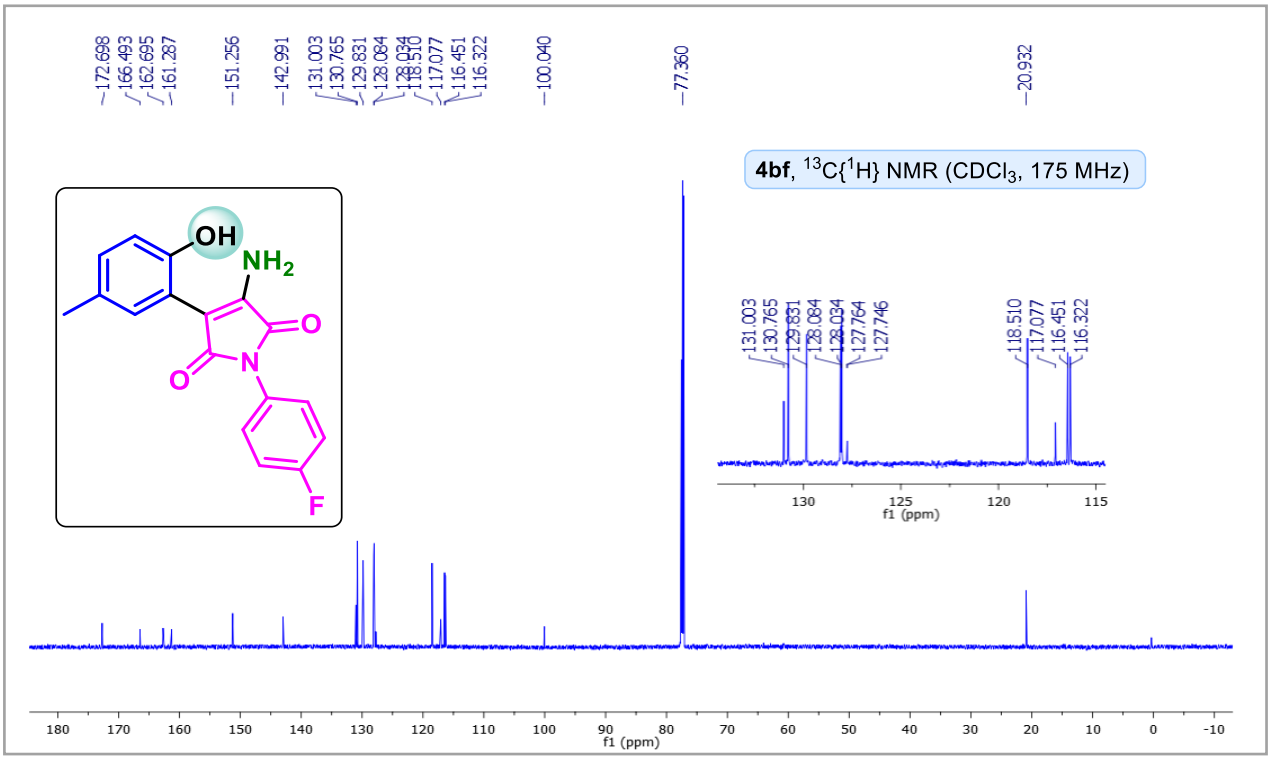

7.496
7.476
7.457
7.432
7.428
7.411
7.407
7.380
7.362
7.260
7.247
7.242
7.066
7.046
7.041
7.008
6.915
6.895
5.309
2.315
0.000
4bd, 1H NMR (CDCl3, 400 MHz)
OH
NH2
O
N
O
Ph
4.15
1.24
1.13
1.03
0.94
1.00
2.00
3.05
f1 (ppm)

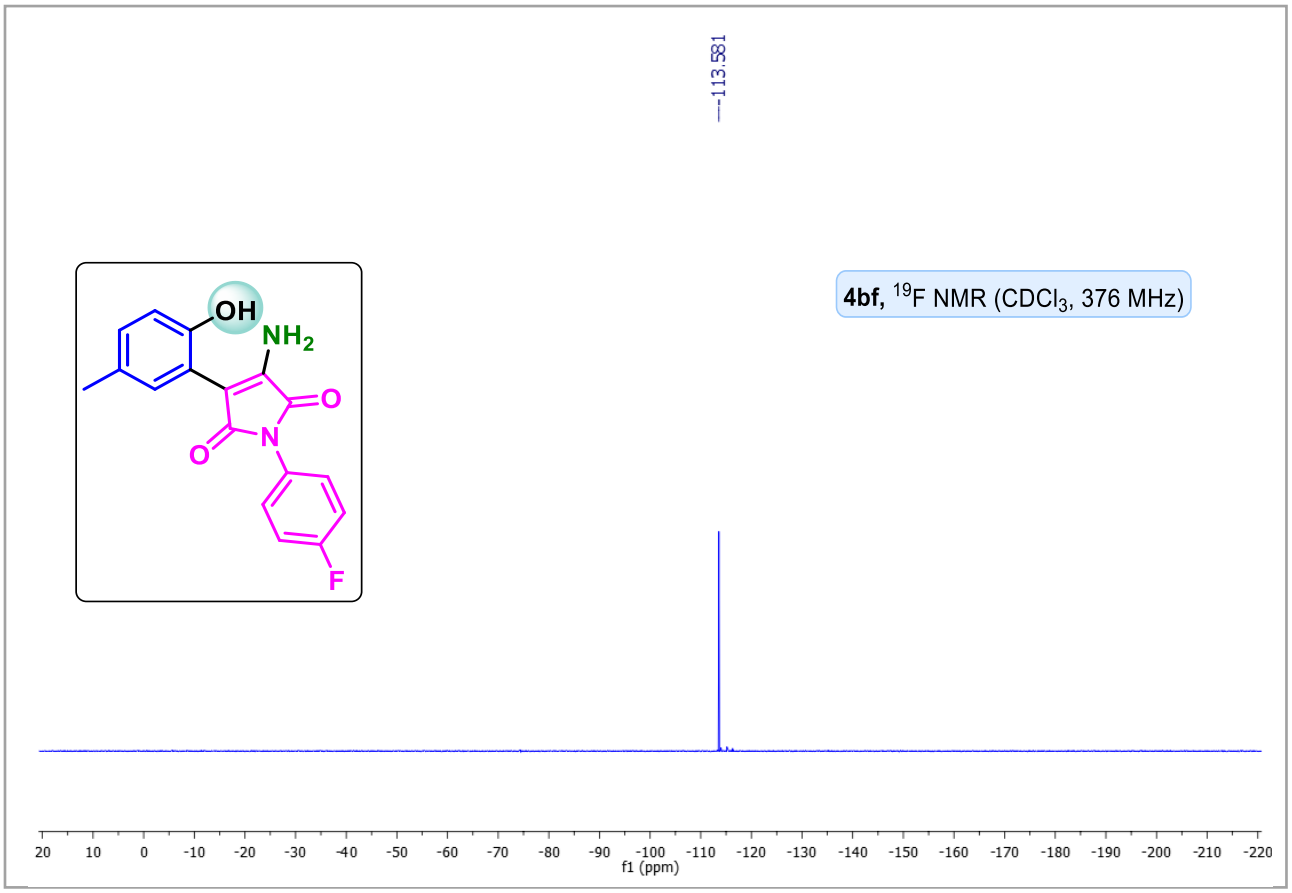

172.989
166.530
151.358
142.998
130.747
129.689
129.419
128.030
126.255
118.703
117.222
100.138
77.542
77.360
77.179
20.942
4bd, 13C{1H} NMR (CDCl3, 175 MHz)
OH
NH2
O
N
O
Ph
131.802
130.941
130.747
129.689
129.419
128.030
126.255
f1 (ppm)

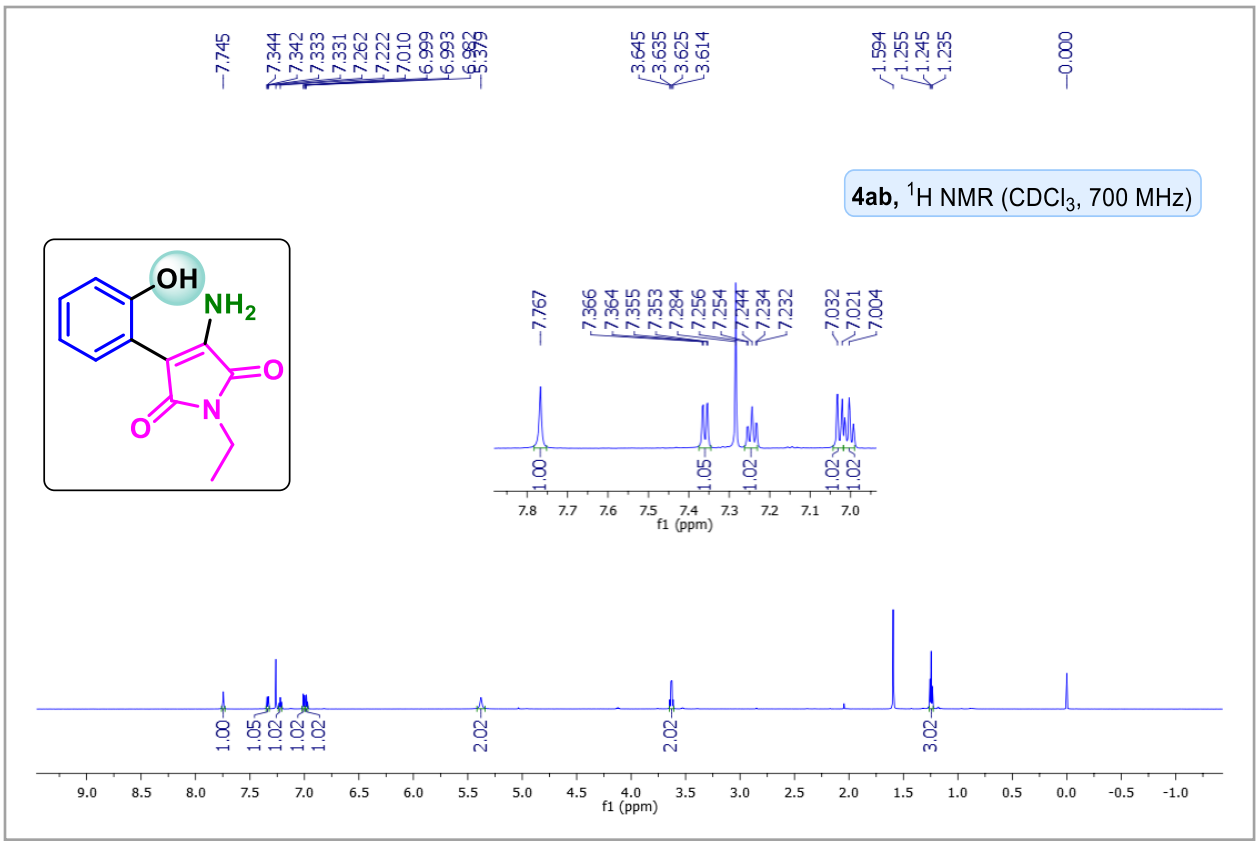

4be, ^{1}H NMR ($CDCl_3$, 400 MHz)
OH
NH2
O
N
O
f1 (ppm)

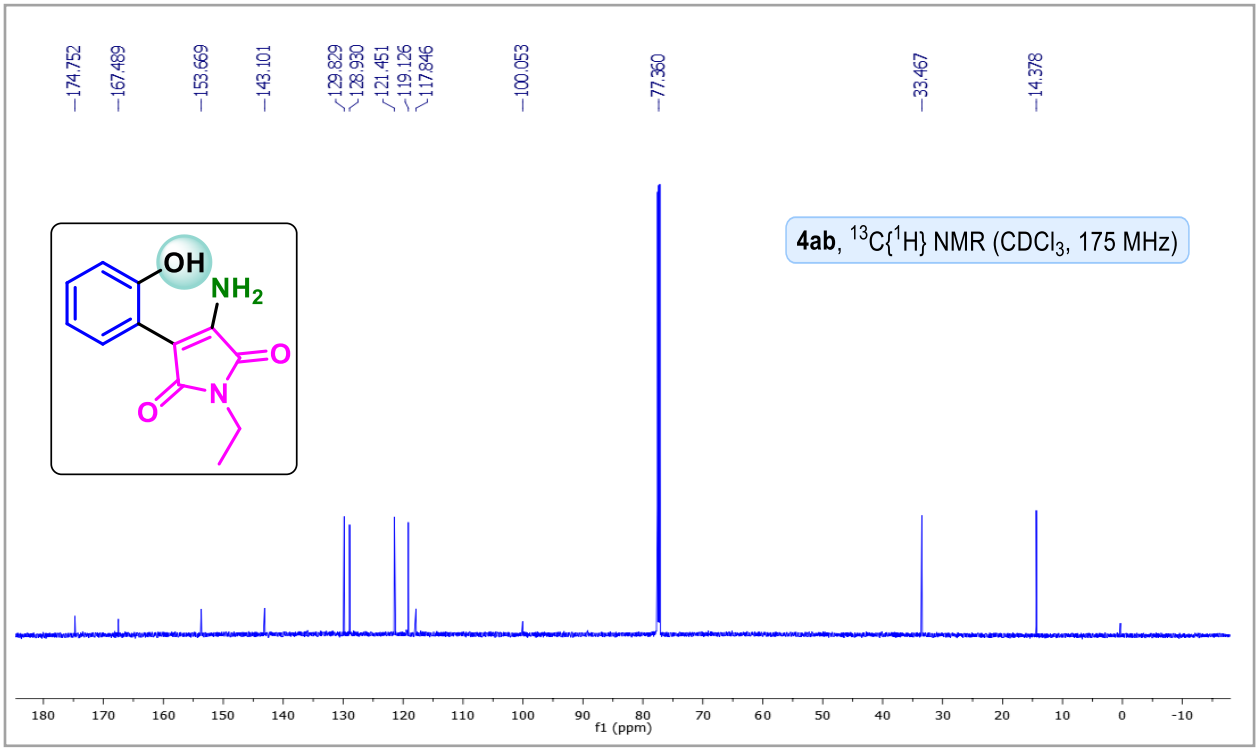

4be, $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 175 MHz)
OH
NH2
O
N
O
f1 (ppm)

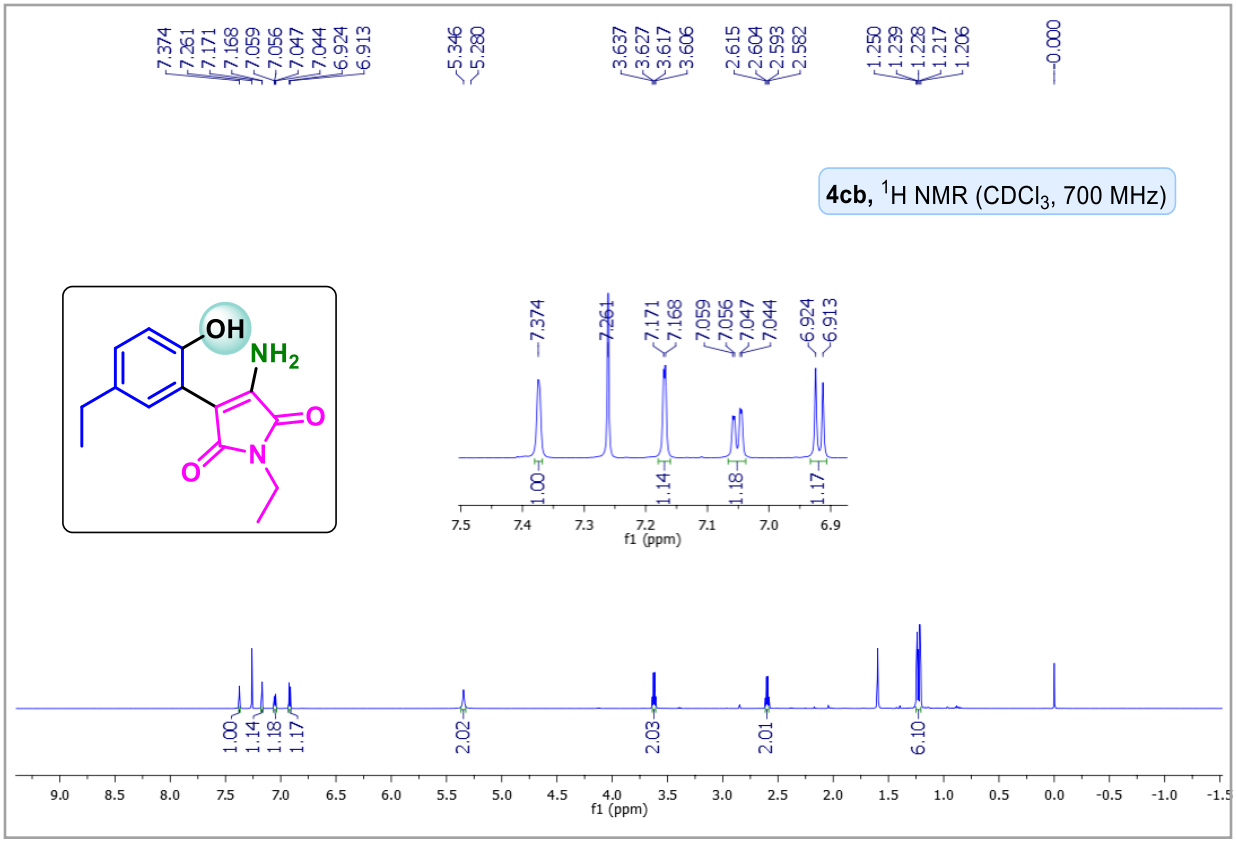

OH
NH2
O
N
O
F
4bf, 1H NMR (CDCl3, 400 MHz)
f1 (ppm)


OH
NH2
O
N
O
F
4bf, 13C{1H} NMR (CDCl3, 175 MHz)
f1 (ppm)


-113.581
OH
NH2
O
O
N
F
4bf, 19F NMR (CDCl3, 376 MHz)
20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)


7.745
7.344
7.342
7.333
7.331
7.262
7.222
7.010
6.999
6.993
5.379
3.645
3.635
3.625
3.614
1.594
1.255
1.245
1.235
0.000
4ab, 1H NMR (CDCl3, 700 MHz)
OH
NH2
O
O
N
7.767
7.366
7.364
7.355
7.353
7.284
7.256
7.254
7.244
7.234
7.232
7.032
7.021
7.004
1.00
1.05
1.02
1.02
1.02
f1 (ppm)
1.00
1.05
1.02
1.02
2.02
2.02
3.02
f1 (ppm)


174.752
167.489
153.669
143.101
129.829
128.930
121.451
119.126
117.846
100.053
77.360
33.467
14.378
4ab, 13C{1H} NMR (CDCl3, 175 MHz)
OH
NH2
O
O
N
f1 (ppm)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7.261
7.171
7.168
7.059
7.056
7.047
7.044
6.924
6.913
5.346
5.280
3.637
3.627
3.617
3.606
2.615
2.604
2.593
2.582
1.250
1.239
1.228
1.217
1.206
-0.000
4cb, 1H NMR (CDCl3, 700 MHz)
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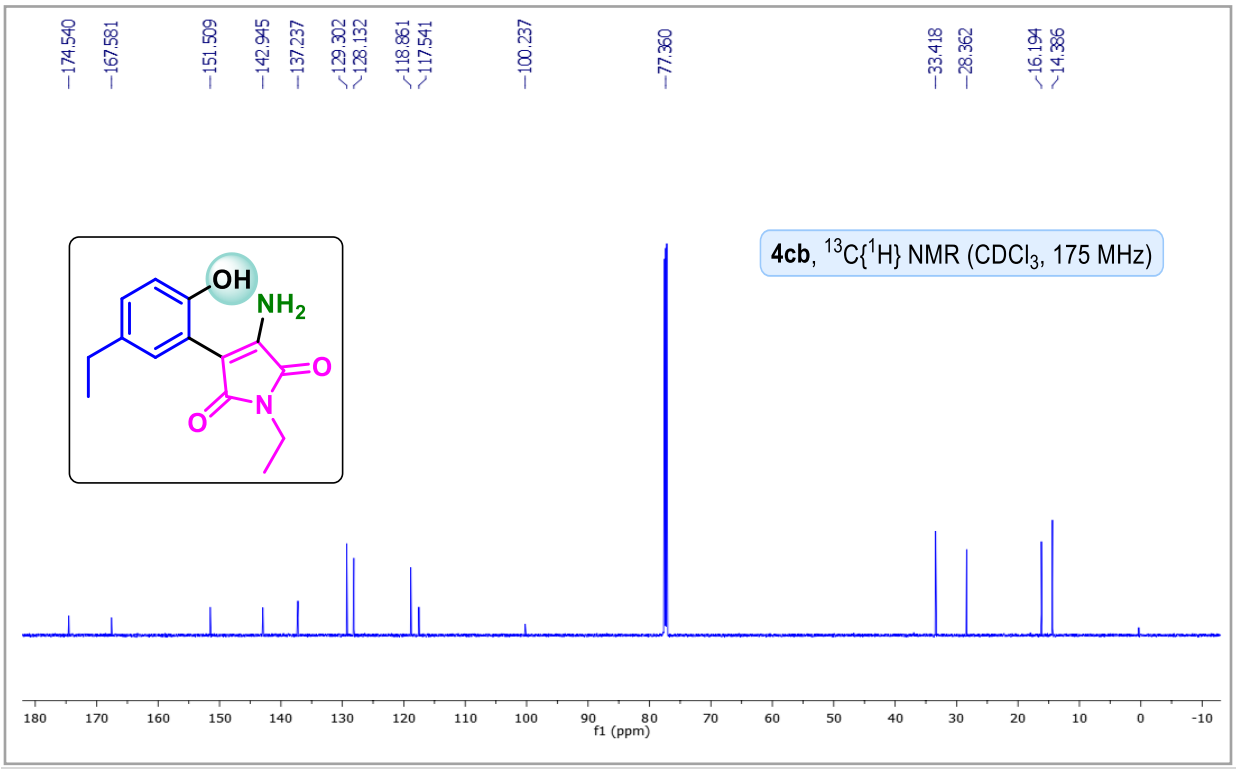
NH2
O
O
N
1.00
1.14
1.18
1.17
2.02
2.03
2.01
6.10
f1 (ppm)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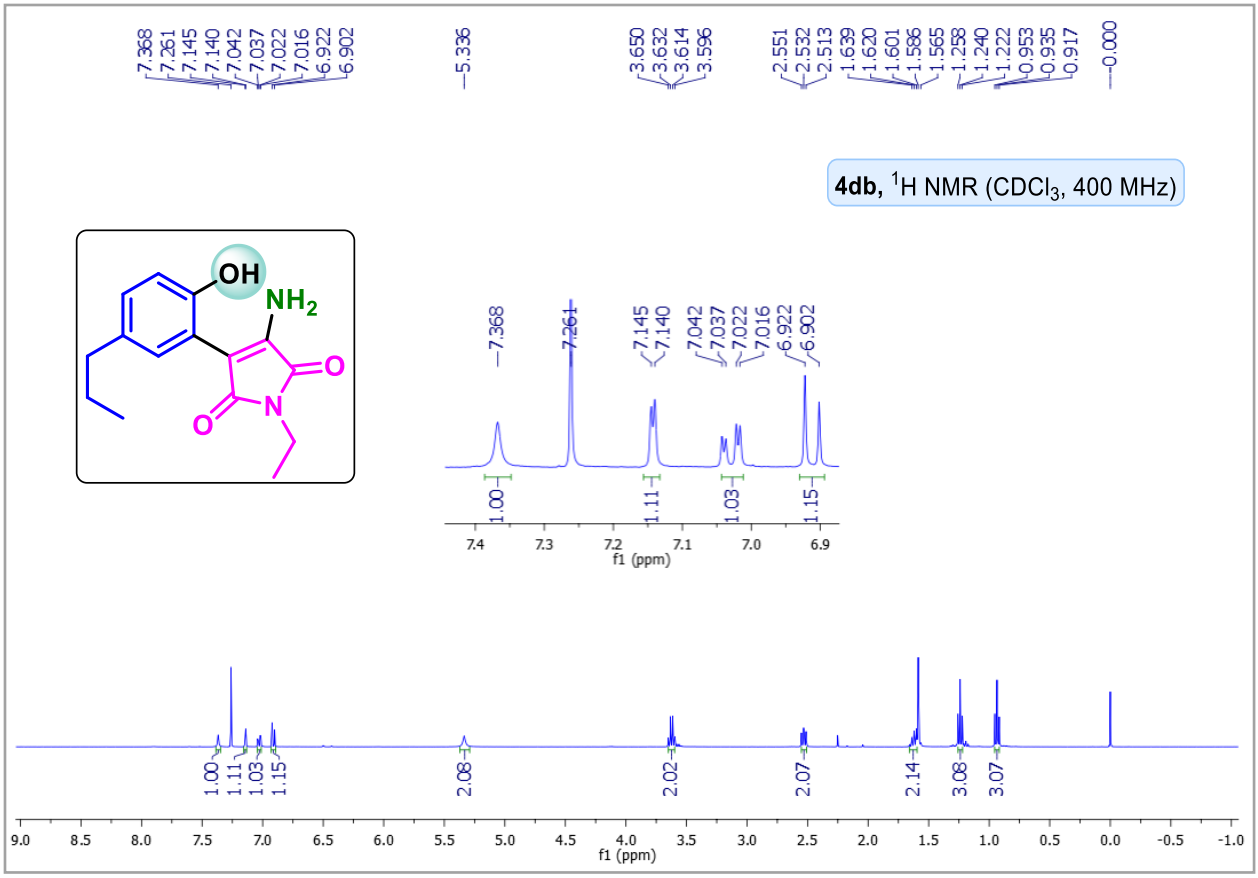
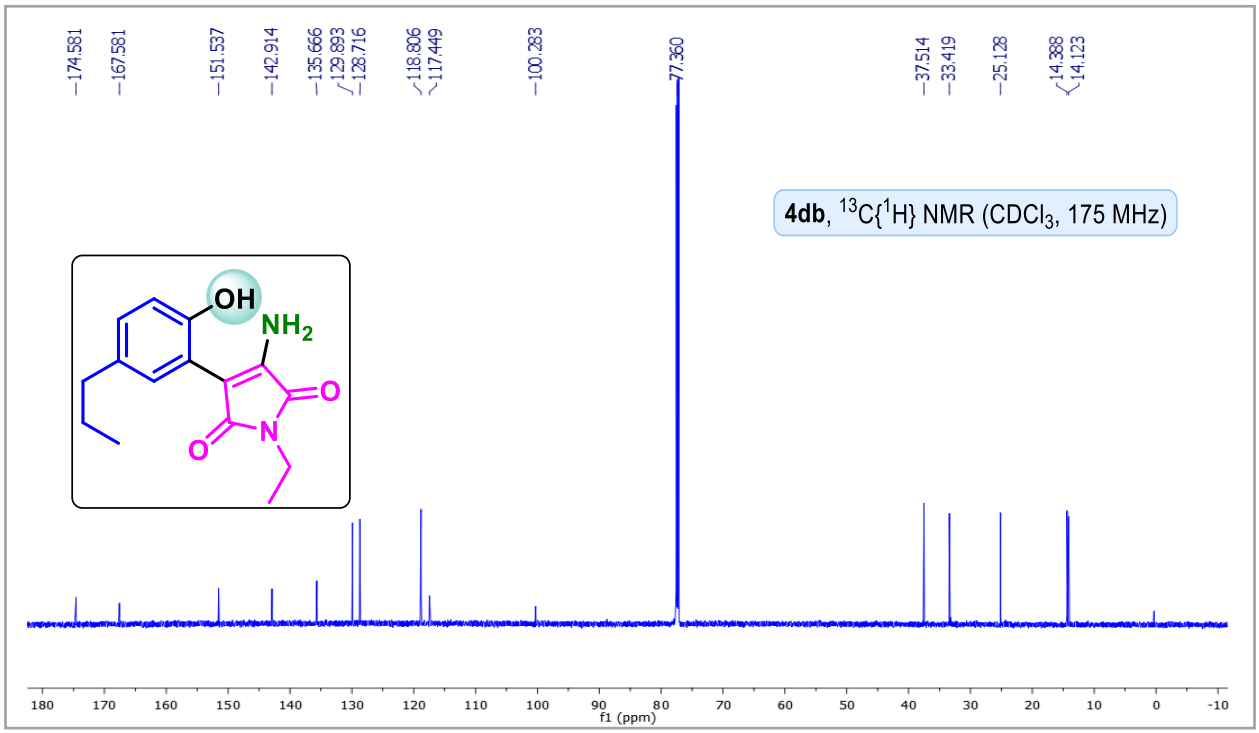
167.581
151.509
142.945
137.237
129.302
128.132
118.861
117.541
100.237
77.360
33.418
28.362
16.194
14.386
4cb, 13C{1H} NMR (CDCl3, 175 MHz)
OH
NH2
O
O
N
f1 (ppm)


7.368
7.261
7.145
7.140
7.042
7.037
7.022
7.016
6.922
6.902
5.336
3.650
3.632
3.614
3.596
2.551
2.532
2.513
1.639
1.620
1.601
1.586
1.565
1.258
1.240
1.222
0.953
0.935
0.917
0.000
4db, 1H NMR (CDCl3, 400 MHz)
OH
NH2
O
O
N
1.00
1.11
1.03
1.15
2.08
2.02
2.07
2.14
3.08
3.07
f1 (ppm)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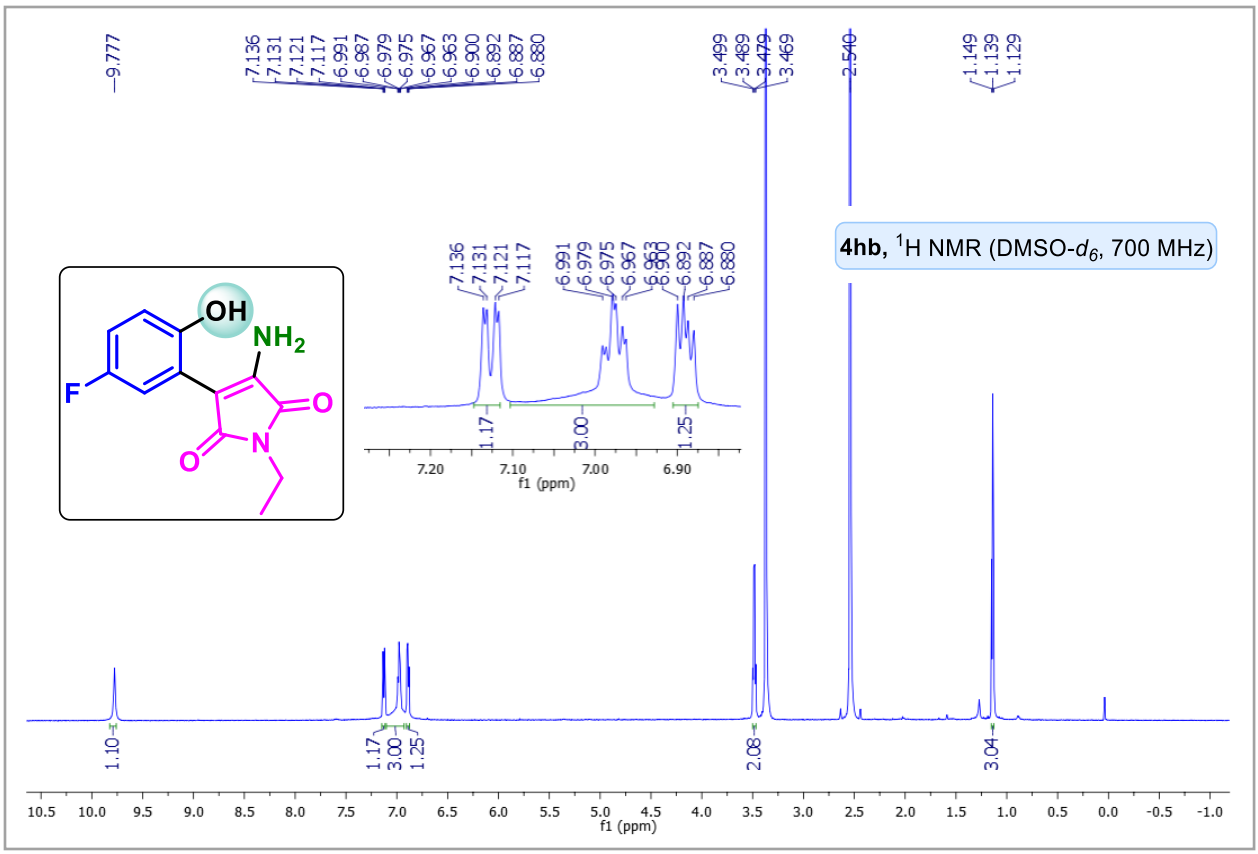
151.537
142.914
135.666
129.893
128.716
118.806
117.449
100.283
77.360
37.514
33.419
25.128
14.388
14.123
4db, 13C{1H} NMR (CDCl3, 175 MHz)
OH
NH2
O
O
N
f1 (ppm)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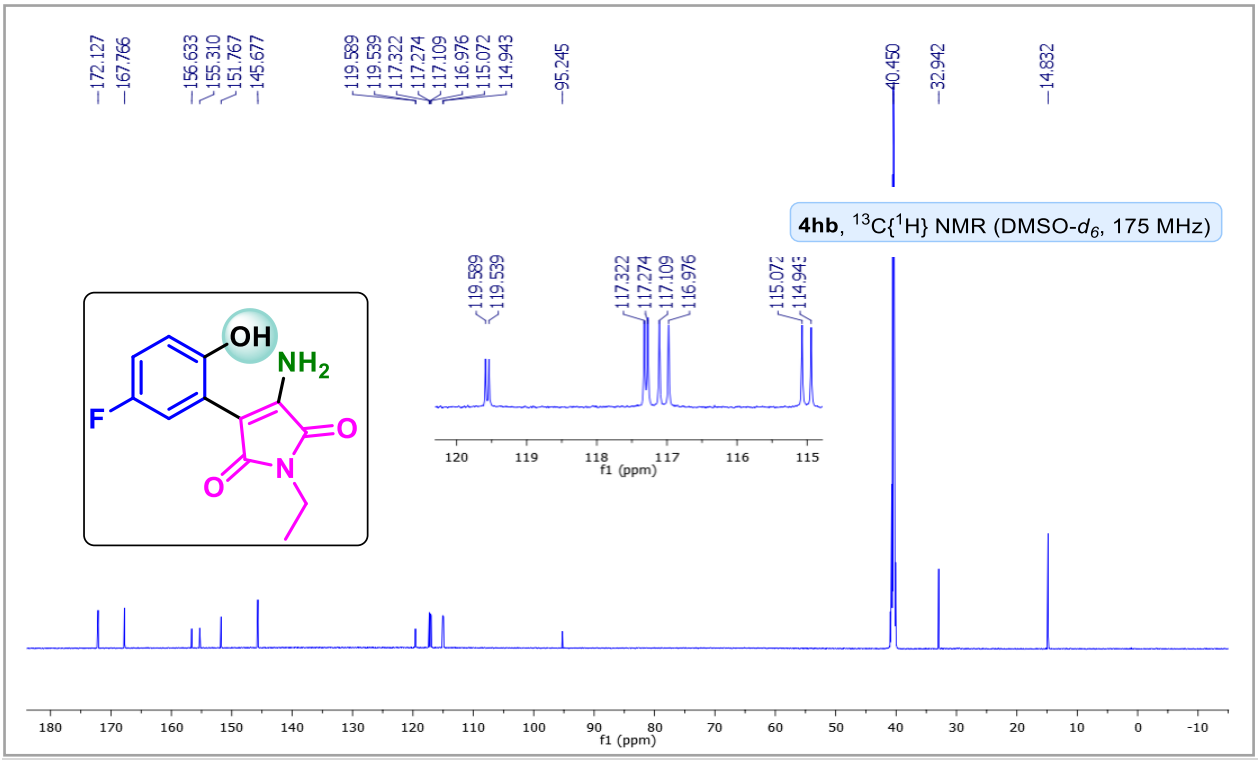
7.136
7.131
7.121
7.117
6.991
6.987
6.979
6.975
6.967
6.963
6.900
6.892
6.887
6.880
3.499
3.489
3.479
3.469
2.540
1.149
1.139
1.129
4hb, ^{1}H NMR (DMSO-d_6, 700 MHz)
OH
NH2
F
O
N
O
1.17
3.00
1.25
7.20
7.10
7.00
6.90
f1 (ppm)
1.10
1.17
3.00
1.25
2.08
3.04
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)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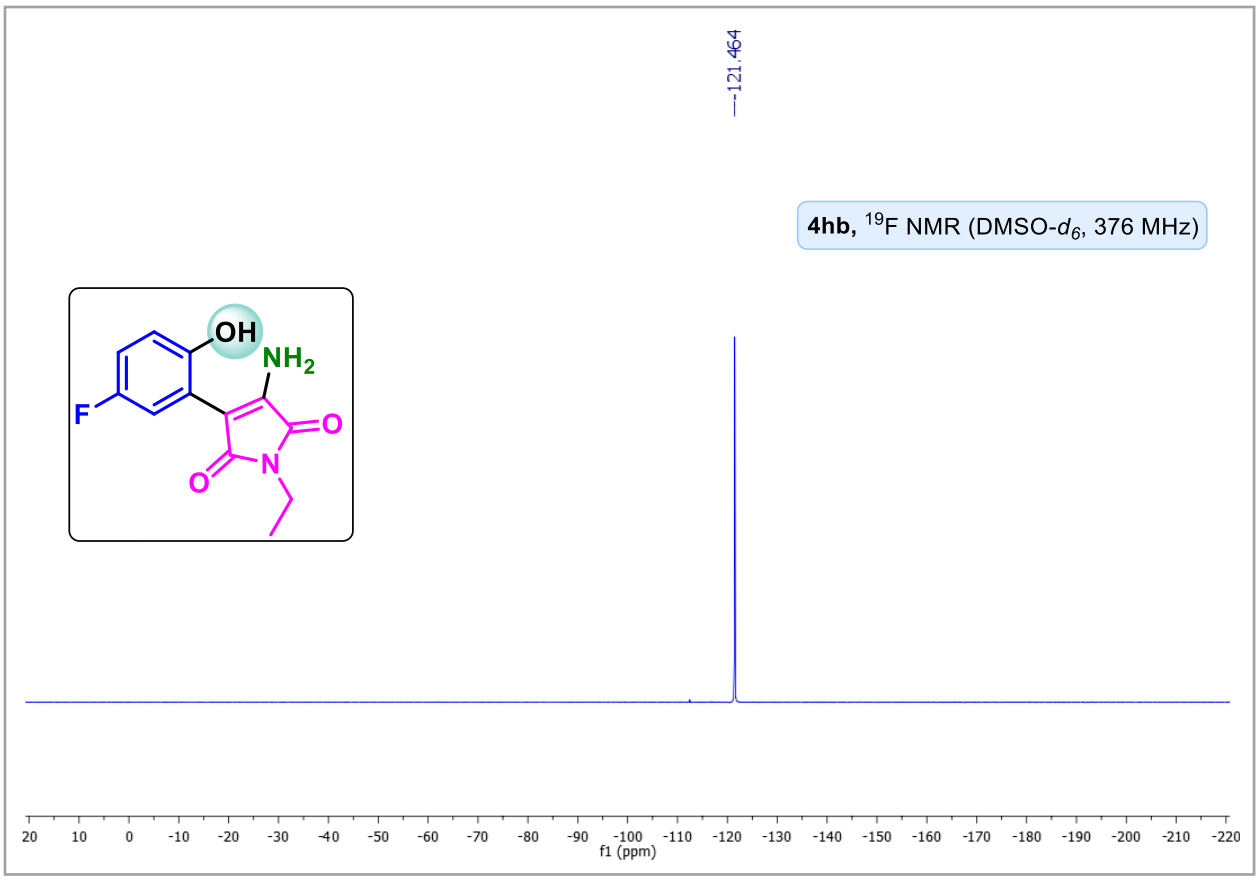
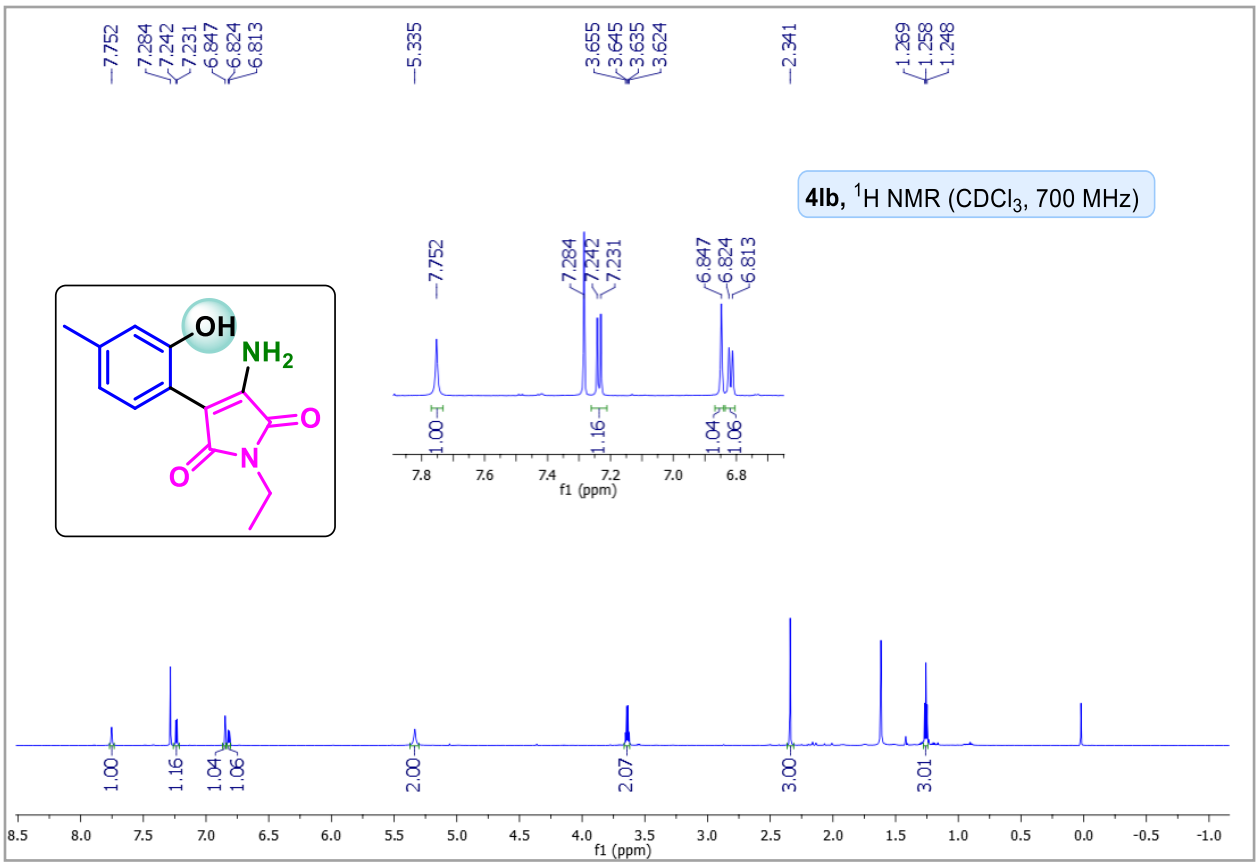
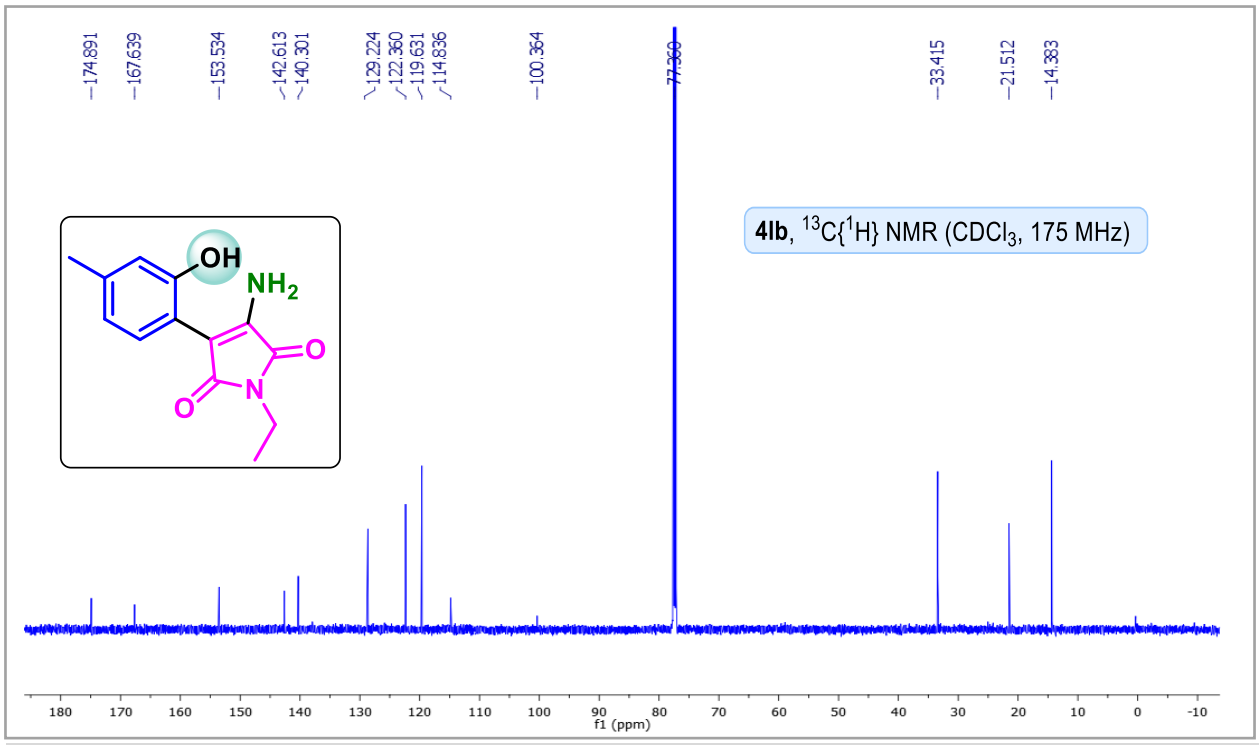
167.766
156.633
155.310
151.767
145.677
119.589
119.539
117.322
117.274
117.109
116.976
115.072
114.943
95.245
40.450
32.942
14.832
4hb, ^{13}C{^{1}H} NMR (DMSO-d_6, 175 MHz)
OH
NH2
F
O
N
O
120
119
118
117
116
115
f1 (ppm)
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


-121.464
4hb, 19F NMR (DMSO-d6, 376 MHz)
OH
NH2
F
O
O
N
20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)


7.752
7.284
7.242
7.231
6.847
6.824
6.813
5.335
3.655
3.645
3.635
3.624
2.341
1.269
1.258
1.248
4lb, 1H NMR (CDCl3, 700 MHz)
OH
NH2
O
O
N
1.00
1.16
1.04
1.06
2.00
2.07
3.00
3.01
f1 (ppm)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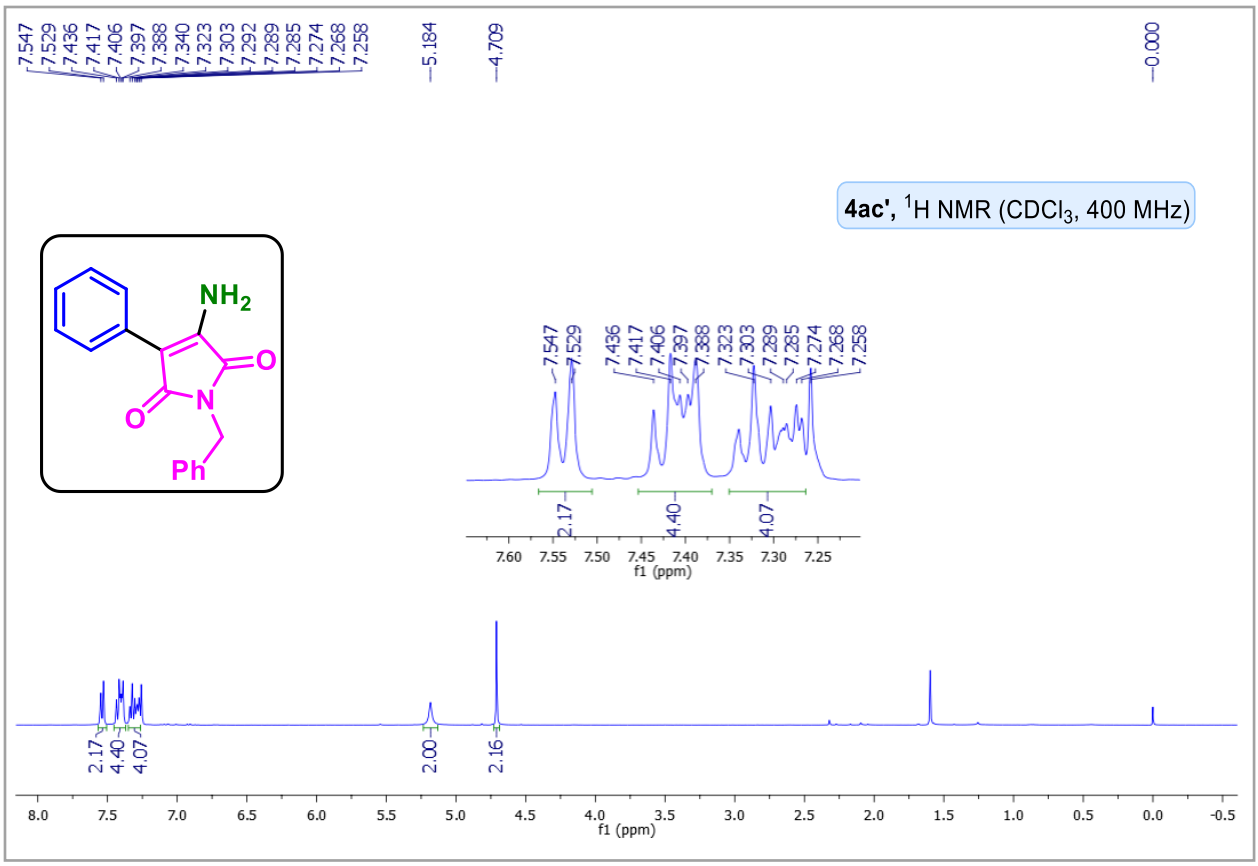
153.534
142.613
140.301
129.224
122.360
119.631
114.836
100.364
77.360
33.415
21.512
14.383
4lb, 13C{1H} NMR (CDCl3, 175 MHz)
OH
NH2
O
O
N
f1 (ppm)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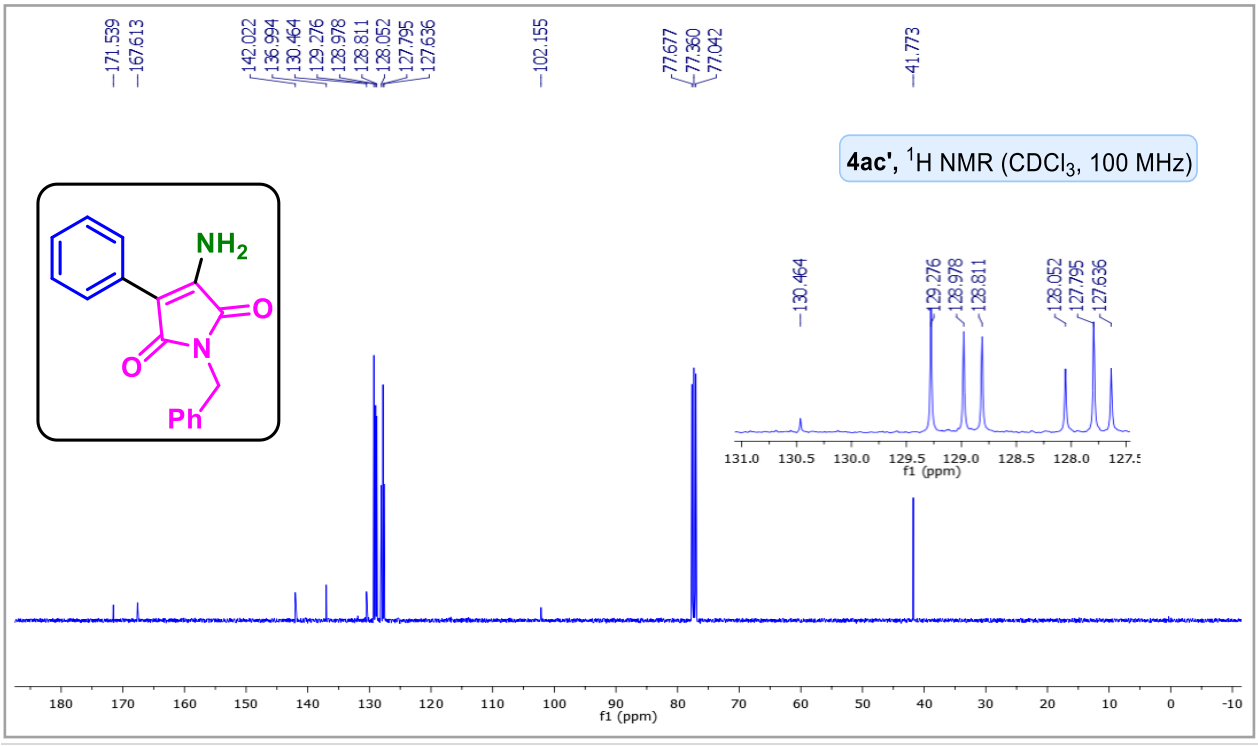
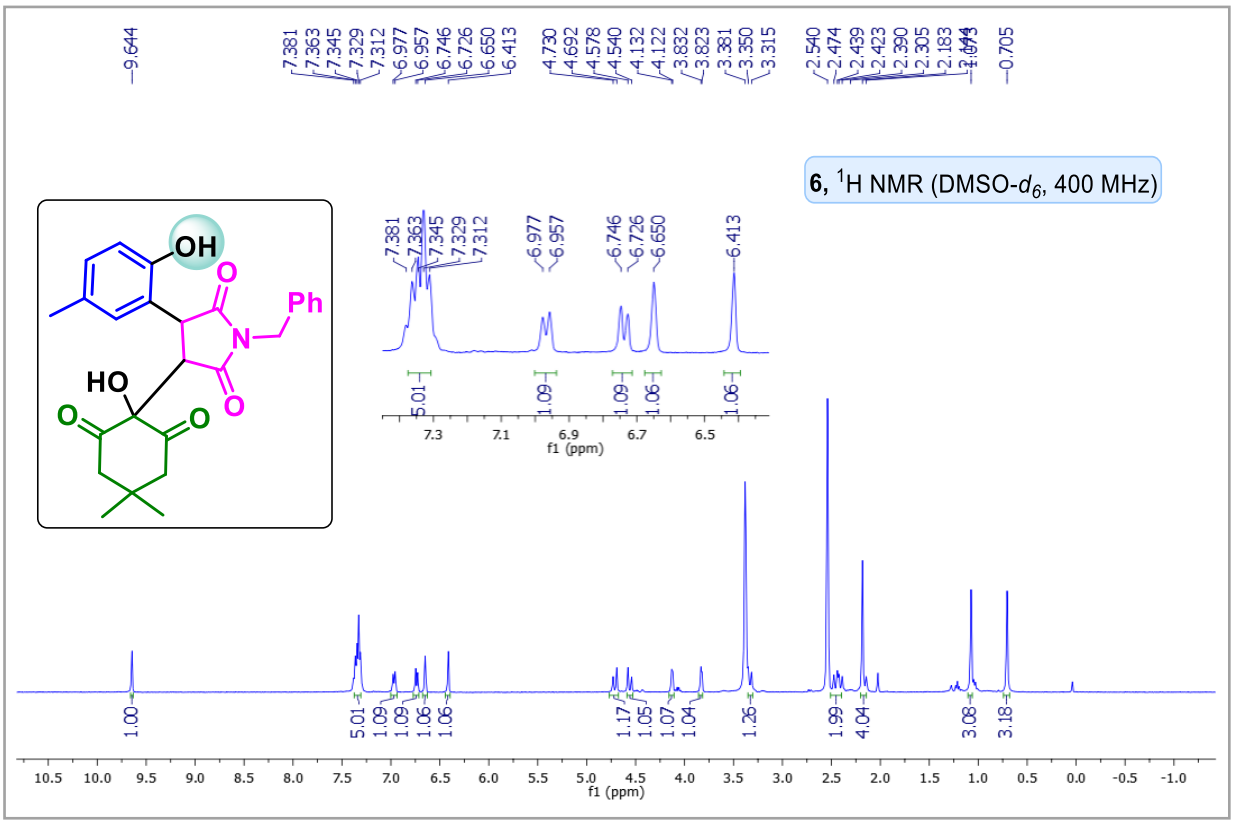
7.529
7.436
7.417
7.406
7.397
7.388
7.340
7.323
7.303
7.292
7.289
7.285
7.274
7.268
7.258
5.184
4.709
0.000
4ac', 1H NMR (CDCl3, 400 MHz)
NH2
O
O
N
Ph
2.17
4.40
4.07
2.00
2.16
f1 (ppm)


171.539
167.613
142.022
136.994
130.464
129.276
128.978
128.811
128.052
127.795
127.636
102.155
77.677
77.360
77.042
41.773
4ac', 1H NMR (CDCl3, 100 MHz)
NH2
O
O
N
Ph
f1 (ppm)


6, ^{1}H NMR (DMSO-d_6, 400 MHz)
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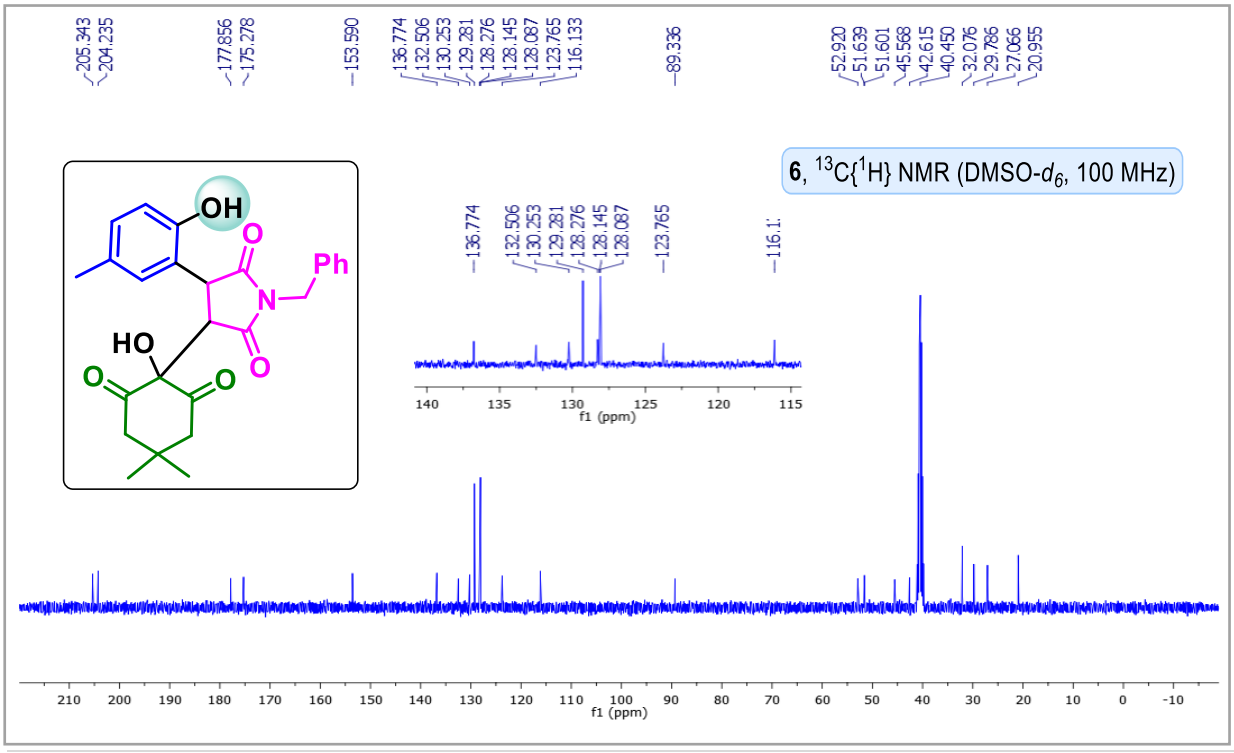
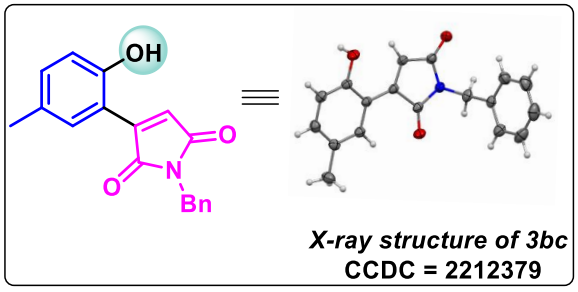
O
Ph
N
HO
O
O
O
f1 (ppm)


6, ^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz)
OH
O
Ph
N
HO
O
O
O
f1 (ppm)

8. Crystallographic data:

(a) X-ray data of 1-benzyl-3-(2-hydroxy-5-methylphenyl)-1H-pyrrole-2,5-dione (3bc): Crystals of the compound 1-benzyl-3-(2-hydroxy-5-methylphenyl)-1H-pyrrole-2,5-dione (**3bc**) were obtained after slow evaporation of ethyl acetate. Crystals suited for single crystal X-Ray diffraction measurements were mounted on a glass fiber. Geometry and intensity data were collected with a Rigaku Smartlab X-ray diffractometer equipped with graphite-monochromated Mo-Kα radiation (λ = 0.71073 Å, multilayer optics). Temperature was controlled using an Oxford Cryostream 700 instrument. Intensities were integrated with SAINT and SMART software packages and corrected for absorption with SADABS. The structure was solved by direct methods and refined on F2 with SHELXL-97 using Olex-2 software.



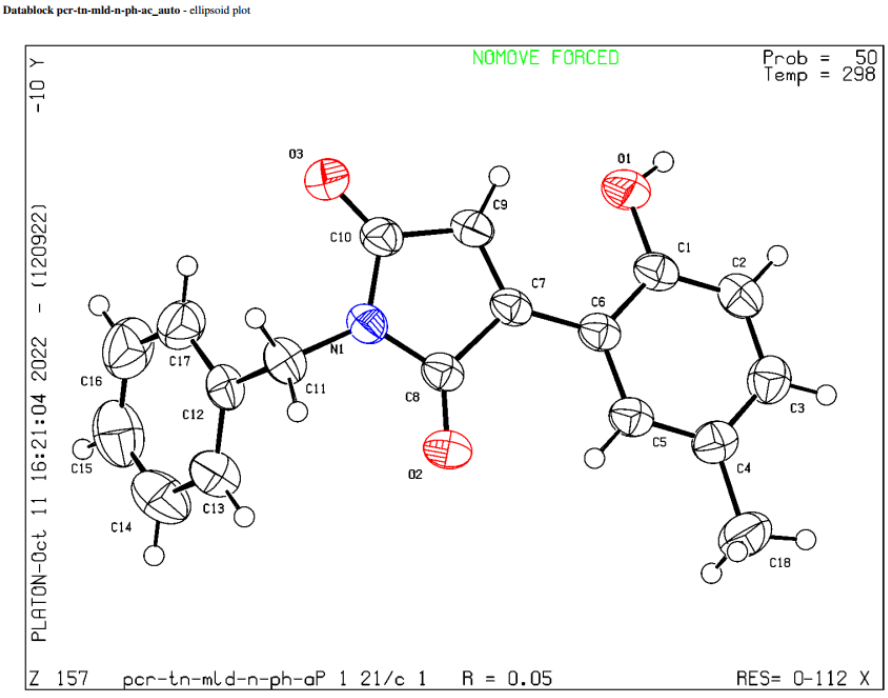


Figure S3. ORTEP diagram of **3bc** with 50% ellipsoid probability

Datablock: pcr-tn-mld-n-ph-ac_auto

Bond precision: C-C = 0.0022 A Wavelength=0.71073

Cell: a=12.9319(9) b=8.3942(7) c=14.1421(9)
alpha=90 beta=106.907(7) gamma=90
Temperature: 298 K

	Calculated	Reported
Volume	1468.81(19)	1468.81(19)
Space group	P 21/c	P 1 21/c 1
Hall group	-P 2ybc	-P 2ybc
Moiety formula	C18 H15 N O3	C18 H15 N O3
Sum formula	C18 H15 N O3	C18 H15 N O3
Mr	293.31	293.31
Dx,g cm-3	1.326	1.326
Z	4	4
Mu (mm-1)	0.091	0.091
F000	616.0	616.0
F000'	616.30	
h,k,lmax	18,11,20	16,11,19
Nref	4385	3624
Tmin,Tmax	0.989,0.991	0.324,1.000
Tmin'	0.982	

Correction method= # Reported T Limits: Tmin=0.324 Tmax=1.000
AbsCorr = MULTI-SCAN

Data completeness= 0.826 Theta(max)= 30.304

R(reflections)= 0.0456(2686) wR2(reflections)= 0.1256(3624)

S = 1.035 Npar= 201

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

PLAT906_ALERT_3_C	Large K Value in the Analysis of Variance	2.759 Check
PLAT910_ALERT_3_C	Missing # of FCF Reflection(s) Below Theta(Min).	7 Note

Alert level G

PLAT007_ALERT_5_G	Number of Unrefined Donor-H Atoms	1 Report
PLAT912_ALERT_4_G	Missing # of FCF Reflections Above STh/L= 0.600	684 Note
PLAT941_ALERT_3_G	Average HKL Measurement Multiplicity	4.5 Low
PLAT950_ALERT_5_G	Calculated (ThMax) and CIF-Reported Hmax Differ	2 Units
PLAT956_ALERT_1_G	Calculated (ThMax) and Actual (FCF) Hmax Differ	2 Units
PLAT978_ALERT_2_G	Number C-C Bonds with Positive Residual Density.	12 Info
PLAT992_ALERT_5_G	Repd & Actual _reflns_number_gt Values Differ by	3 Check

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

1 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
1 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
1 ALERT type 4 Improvement, methodology, query or suggestion
3 ALERT type 5 Informative message, check

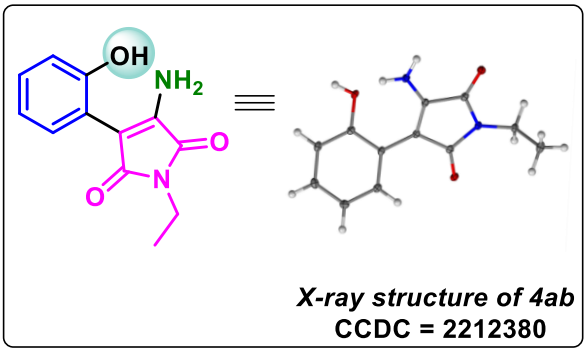
Table S1. Crystal data and structure refinement for **1-benzyl-3-(2-hydroxy-5-methylphenyl)-1H-pyrrole-2,5-dione (3bc):**

Crystal data and structure refinement for PCR-TN-MLD-N-Bn-AC_auto.

Identification code	PCR-TN-MLD-N-PH-AC_auto
Empirical formula	$C_{18}H_{15}NO_3$
Formula weight	293.31
Temperature/K	298(1)
Crystal system	monoclinic

Space group	$P2_1/c$
a/Å	12.9319(9)
b/Å	8.3942(7)
c/Å	14.1421(9)
α/°	90
β/°	106.907(7)
γ/°	90
Volume/Å^3	1468.81(19)
Z	4
ρ_{calc}g/cm^3	1.326
μ/mm^{-1}	0.091
F(000)	616.0
Crystal size/mm^3	0.2 × 0.1 × 0.1
Radiation	Mo Kα (λ = 0.71073)
2Θ range for data collection/°	7.018 to 60.608
Index ranges	$-16 \leq h \leq 16$, $-11 \leq k \leq 8$, $-15 \leq l \leq 19$
Reflections collected	16488
Independent reflections	3624 [R_{int} = 0.0371, R_{sigma} = 0.0291]
Data/restraints/parameters	3624/0/201
Goodness-of-fit on F^2	1.035
Final R indexes [I>=2σ (I)]	R_1 = 0.0456, wR_2 = 0.1161
Final R indexes [all data]	R_1 = 0.0658, wR_2 = 0.1256
Largest diff. peak/hole / e Å^{-3}	0.20/-0.16

(b) X-ray data of 3-amino-1-ethyl-4-(2-hydroxyphenyl)-1H-pyrrole-2,5-dione (4ab): Crystals of the compound 3-amino-1-ethyl-4-(2-hydroxyphenyl)-1H-pyrrole-2,5-dione (**4ab**) were obtained after slow evaporation of ethyl acetate. Crystals suited for single crystal X-Ray diffraction measurements were mounted on a glass fiber. Geometry and intensity data were collected with a Rigaku Smartlab X-ray diffractometer equipped with graphite-monochromated Mo-Kα radiation (λ = 0.71073 Å, multilayer optics). Temperature was controlled using an Oxford Cryostream 700 instrument. Intensities were integrated with SAINT and SMART software packages and corrected for absorption with SADABS. The structure was solved by direct methods and refined on F2 with SHELXL-97 using Olex-2 software.



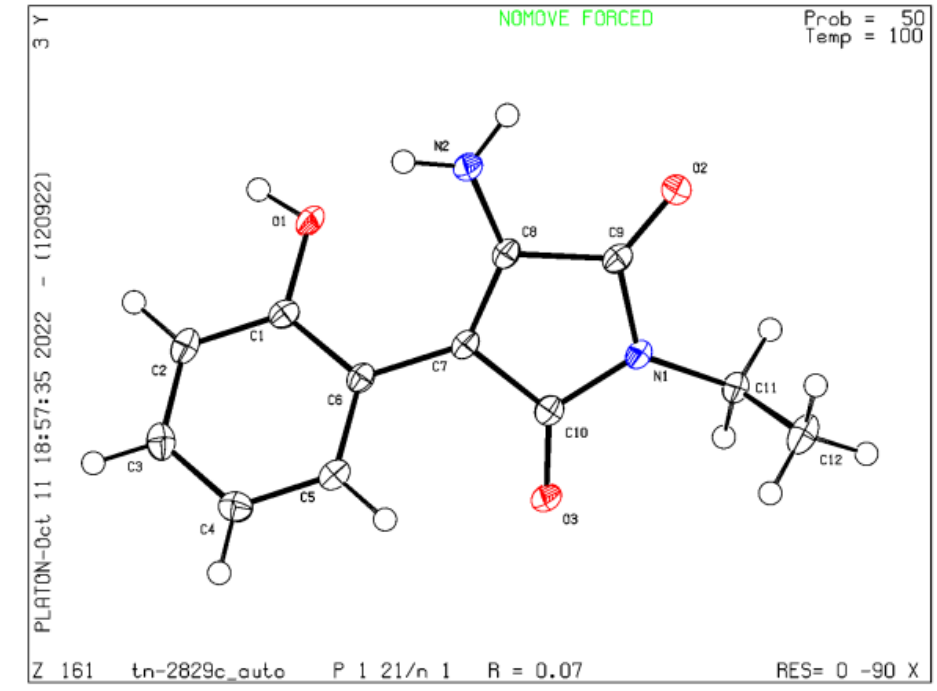


Figure S4. ORTEP diagram of **4ab** with 50% ellipsoid probability

Datablock: tn-2829c_auto

Bond precision: C-C = 0.0033 A Wavelength=0.71073

Cell: a=11.1398(14) b=7.1583(9) c=14.2695(19)
alpha=90 beta=110.123(14) gamma=90
Temperature: 100 K

	Calculated	Reported
Volume	1068.4(3)	1068.4(3)
Space group	P 21/n	P 1 21/n 1
Hall group	-P 2yn	-P 2yn
Moiety formula	C12 H12 N2 O3	C12 H12 N2 O3
Sum formula	C12 H12 N2 O3	C12 H12 N2 O3
Mr	232.24	232.24
Dx,g cm-3	1.444	1.444
Z	4	4
Mu (mm-1)	0.106	0.106
F000	488.0	488.0
F000'	488.24	
h,k,lmax	15,10,20	14,8,19
Nref	3264	2586
Tmin,Tmax	0.987,0.989	0.390,1.000
Tmin'	0.979	

Correction method= # Reported T Limits: Tmin=0.390 Tmax=1.000
AbsCorr = MULTI-SCAN

Data completeness= 0.792 Theta(max)= 30.521

R(reflections)= 0.0715(2119) wR2(reflections)= 0.1709(2586)

S = 1.119 Npar= 156

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

```
PLAT906_ALERT_3_C Large K Value in the Analysis of Variance ......      9.957 Check
PLAT906_ALERT_3_C Large K Value in the Analysis of Variance ......      2.301 Check
PLAT910_ALERT_3_C Missing # of FCF Reflection(s) Below Theta(Min).         5 Note
PLAT934_ALERT_3_C Number of (Iobs-Icalc)/Sigma(W) > 10 Outliers ..         1 Check
PLAT976_ALERT_2_C Check Calcd Resid. Dens.  1.02Ang From N2      .     -0.40 eA-3
PLAT977_ALERT_2_C Check Negative Difference Density on H2A       .     -0.39 eA-3
```

Alert level G

```
PLAT007_ALERT_5_G Number of Unrefined Donor-H Atoms ..............         3 Report
PLAT912_ALERT_4_G Missing # of FCF Reflections Above STh/L=  0.600       499 Note
PLAT941_ALERT_3_G Average HKL Measurement Multiplicity ...........       4.2 Low
PLAT951_ALERT_5_G Calculated (ThMax) and CIF-Reported Kmax Differ         2 Units
PLAT957_ALERT_1_G Calculated (ThMax) and Actual (FCF) Kmax Differ         2 Units
PLAT978_ALERT_2_G Number C-C Bonds with Positive Residual Density.        8 Info
```

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

   1 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
   5 ALERT type 3 Indicator that the structure quality may be low
   1 ALERT type 4 Improvement, methodology, query or suggestion
   2 ALERT type 5 Informative message, check
```

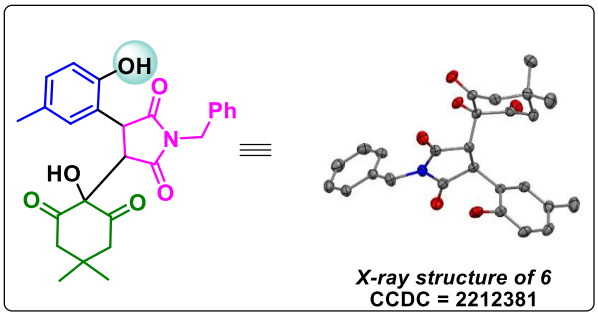
Table S2. Crystal data and structure refinement for **3-amino-1-ethyl-4-(2-hydroxyphenyl)-1H-pyrrole-2,5-dione (4ab):**

Crystal data and structure refinement for tn-2829c_auto.

Identification code	tn-2829c_auto
Empirical formula	$C_{12}H_{12}N_2O_3$
Formula weight	232.24
Temperature/K	99.99(10)
Crystal system	monoclinic

Space group	$P2_1/n$
a/Å	11.1398(14)
b/Å	7.1583(9)
c/Å	14.2695(19)
α/°	90
β/°	110.123(14)
γ/°	90
Volume/Å^3	1068.4(3)
Z	4
ρ_{calc}g/cm^3	1.444
μ/mm^{-1}	0.106
F(000)	488.0
Crystal size/mm^3	0.2 × 0.1 × 0.1
Radiation	Mo Kα (λ = 0.71073)
2Θ range for data collection/°	6.976 to 61.042
Index ranges	$-14 \leq h \leq 14$, $-8 \leq k \leq 7$, $-19 \leq l \leq 17$
Reflections collected	10741
Independent reflections	2586 [R_{int} = 0.0799, R_{sigma} = 0.0520]
Data/restraints/parameters	2586/0/156
Goodness-of-fit on F^2	1.119
Final R indexes [I>=2σ (I)]	R_1 = 0.0715, wR_2 = 0.1655
Final R indexes [all data]	R_1 = 0.0857, wR_2 = 0.1709
Largest diff. peak/hole / e Å^{-3}	0.40/-0.41

(c) X-ray data of 1-benzyl-3-(1-hydroxy-4,4-dimethyl-2,6-dioxocyclohexyl)-4-(2-hydroxy-5-methylphenyl)pyrrolidine-2,5-dione (6): Crystals of the compound 1-benzyl-3-(1-hydroxy-4,4-dimethyl-2,6-dioxocyclohexyl)-4-(2-hydroxy-5-methylphenyl)pyrrolidine-2,5-dione (**6**) were obtained after slow evaporation of ethyl acetate. Crystals suited for single crystal X-Ray diffraction measurements were mounted on a glass fiber. Geometry and intensity data were collected with a Rigaku Smartlab X-ray diffractometer equipped with graphite-monochromated Mo-Kα radiation (λ = 0.71073 Å, multilayer optics). Temperature was controlled using an Oxford Cryostream 700 instrument. Intensities were integrated with SAINT and SMART software packages and corrected for absorption with SADABS. The structure was solved by direct methods and refined on F2 with SHELXL-97 using Olex-2 software.



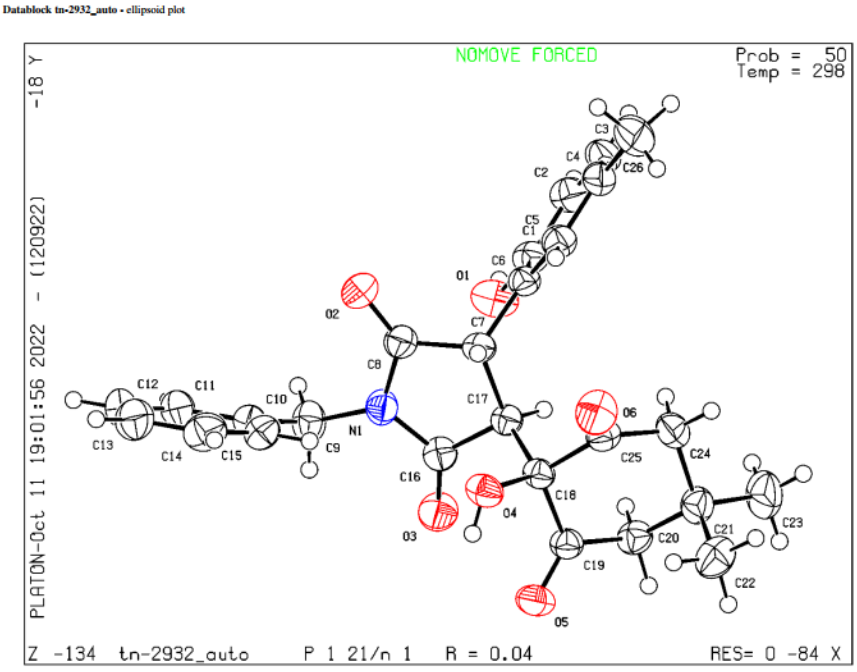


Figure S5. ORTEP diagram of **6** with 50% ellipsoid probability

Datablock: tn-2932_auto

Bond precision: C-C = 0.0018 A Wavelength=0.71073

Cell: a=14.1511(6) b=11.6784(4) c=14.2759(6)
alpha=90 beta=104.905(4) gamma=90
Temperature: 298 K

	Calculated	Reported
Volume	2279.89(16)	2279.89(16)
Space group	P 21/n	P 1 21/n 1
Hall group	-P 2yn	-P 2yn
Moiety formula	C26 H27 N O6	C26 H27 N O6
Sum formula	C26 H27 N O6	C26 H27 N O6
Mr	449.49	449.48
Dx,g cm-3	1.309	1.310
Z	4	4
Mu (mm-1)	0.093	0.093
F000	952.0	952.0
F000'	952.50	
h,k,lmax	20,16,20	20,16,18
Nref	6939	6015
Tmin,Tmax	0.989,0.991	0.711,1.000
Tmin'	0.982	

Correction method= # Reported T Limits: Tmin=0.711 Tmax=1.000
AbsCorr = MULTI-SCAN

Data completeness= 0.867 Theta(max)= 30.469

R(reflections)= 0.0415(4340) wR2(reflections)= 0.1194(6015)

S = 1.051 Npar= 303

```
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
PLAT905_ALERT_3_C Negative K value in the Analysis of Variance ...     -0.530 Report
PLAT910_ALERT_3_C Missing # of FCF Reflection(s) Below Theta(Min).          8 Note

 Alert level G
PLAT007_ALERT_5_G Number of Unrefined Donor-H Atoms ..............          2 Report
PLAT793_ALERT_4_G Model has Chirality at C7          (Centro SPGR)          S Verify
PLAT793_ALERT_4_G Model has Chirality at C17         (Centro SPGR)          S Verify
PLAT912_ALERT_4_G Missing # of FCF Reflections Above STh/L=  0.600        832 Note
PLAT952_ALERT_5_G Calculated (ThMax) and CIF-Reported Lmax Differ.          2 Units
PLAT958_ALERT_1_G Calculated (ThMax) and Actual (FCF) Lmax Differ.          2 Units
PLAT978_ALERT_2_G Number C-C Bonds with Positive Residual Density.         13 Info

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

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

Table S3. Crystal data and structure refinement for **1-benzyl-3-(1-hydroxy-4,4-dimethyl-2,6-dioxocyclohexyl)-4-(2-hydroxy-5-methylphenyl)pyrrolidine-2,5-dione (6):**

Crystal data and structure refinement for TN-2932_auto.

Identification code	TN-2932_auto
Empirical formula	$C_{26}H_{27}NO_6$
Formula weight	449.48
Temperature/K	297.6(7)
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	14.1511(6)
b/Å	11.6784(4)

c/Å	14.2759(6)
α/°	90
β/°	104.905(4)
γ/°	90
Volume/Å^3	2279.89(16)
Z	4
ρ_{calc}g/cm^3	1.310
μ/mm^{-1}	0.093
F(000)	952.0
Crystal size/mm^3	0.2 × 0.1 × 0.1
Radiation	Mo Kα (λ = 0.71073)
2Θ range for data collection/°	6.848 to 60.938
Index ranges	-18 ≤ h ≤ 20, -16 ≤ k ≤ 16, -18 ≤ l ≤ 18
Reflections collected	50828
Independent reflections	6015 [R_{int} = 0.0461, R_{sigma} = 0.0287]
Data/restraints/parameters	6015/0/303
Goodness-of-fit on F^2	1.051
Final R indexes [I>=2σ (I)]	R_1 = 0.0415, wR_2 = 0.1092
Final R indexes [all data]	R_1 = 0.0632, wR_2 = 0.1194
Largest diff. peak/hole / e Å^{-3}	0.23/-0.18

9. References:

(1) (a) Similar information was reported in Banjare, S. K.; Nanda, T.; Ravikumar, P. C. Cobalt-Catalyzed Regioselective Direct C-4 Alkenylation of 3-Acetylindole with Michael Acceptors Using a Weakly Coordinating Functional Group. *Org. Lett.* **2019**, *21*, 8138−8143. (b) Gottlieb, H. E.; Kotlyar, V.; Nudelman, A. NMR chemical shifts of common laboratory solvents as trace impurities. *J. Org. Chem.* **1997**, *62*, 7512.

(2) Yuan, Y. C.; Kamaraj, R.; Bruneau, C.; Labasque, T.; Roisnel, T.; Gramage-Doria, R. Unmasking Amides: Ruthenium-Catalyzed Protodecarbonylation of N-Substituted Phthalimide Derivatives. *Org. Lett.* **2017**, *19*, 6404−6407.

(3) Li, B.; Lan, J.; Wu, D.; You, J. Rhodium(III)-Catalyzed orthoHeteroarylation of Phenols through Internal Oxidative C−H Activation: Rapid Screening of Single-Molecular White-Light-Emitting Materials. *Angew. Chem., Int. Ed.* **2015**, *54*, 14008−14012.

(4) Bernardes, G. J. L.; Chalker, J. M.; Errey, J. C.; Davis, B. G. Facile Conversion of Cysteine and Alkyl Cysteines to Dehydroalanine on Protein Surfaces: Versatile and Switchable Access to Functionalized Proteins. *J. Am. Chem. Soc.* **2008**, *130*, 5052-5053.

(5) Liu, G.; Shen, Y.; Zhou, Z.; Lu, X. Rhodium(III)-Catalyzed Redox-Neutral Coupling of N-Phenoxyacetamides and Alkynes with Tunable Selectivity. *Angew. Chem., Int. Ed.* **2013**, *52*, 6033-6037.

(6) (a) Calvin, J. R.; Frederick, M. O.; Laird, D. L. T.; Remacle, J. R.; May, S. A. Rhodium-Catalyzed and Zinc(II)-Triflate-Promoted Asymmetric Hydrogenation of Tetrasubstituted *α,β*-Unsaturated Ketones. *Org. Lett.* **2012**, *14*, 1038−1041. (b) Zhang, G-. Y.; Zhang, P.; Li, B-. W.; Liu, K.; Li, J.; Yu, Z-. X. Dual Activation Strategy to Achieve C–C Cleavage of Cyclobutanes: Development and Mechanism of Rh and Zn Cocatalyzed [4 + 2] Cycloaddition of Yne-Vinylcyclobutanones. *J. Am. Chem. Soc.* **2022**, *144*, 21457–21469.

(7) Shen, Y.; Liu, G.; Zhou, Z.; Lu, X. Rhodium(III)-Catalyzed C− H Olefination for the Synthesis of ortho-Alkenyl Phenols Using an Oxidizing Directing Group. *Org. Lett.* **2013**, *15*, 3366−3369.

(8) Wang, S.; Lin, J-. J.; Cui, X.; Li, J-. P.; Huang, C. Controllable Synthesis of Two Isomers 4H-Chromene and 2,8-Dioxabicyclo[3.3.1]nonane Derivatives under Catalyst-Free Conditions. *J. Org. Chem.* **2021**, *86*, 16396−16408.