

Halogen bonding matters: visible light-induced photoredox catalyst-free aryl radical formation and its applications

Rong Miao,^a Dan Wang,^a Jianliang Xiao,^a Jiani Ma,^b Dong Xue,^{*a} Fengyi Liu,^{*a} and Yu Fang^{*a}

^aKey Laboratory of Applied Surface and Colloid Chemistry of Ministry of Education

^aSchool of Chemistry and Chemical Engineering

^aShaanxi Normal University, Xi'an 710062, People's Republic of China.

^bCollege of Chemistry and Materials Science,

^bNorthwest University, Xi'an 710127, People's Republic of China.

Email: xuedong_welcome@snnu.edu.cn; FengyiLiu@snnu.edu.cn; yfang@snnu.edu.cn

Table of Contents

1. General Information.....	2
1.1 Materials.....	2
1.2 Characterization Details.....	2
2. Synthesis.....	2
2.1 Reactor.....	2
2.2 General Procedure for Visible-Light-Driven Synthesis.....	3
3. Computation Details.....	4
3.1 General Information for Computation.....	4
3.2 Photocleavage of C-X Bond in aryl-Cl and aryl-I without Et ₃ N.....	5
3.3 Photo Activation of C-X Bond in aryl-X···Et ₃ N Complex.....	6
4. Supplement Data.....	8
4.1 Supplementary Figures for Theoretical Calculations.....	8
4.2 Cartesian Coordinates of Important Stationary Points.....	13
4.3 Studies on Phosphorescence of 4-I-COMe with/without Et ₃ N.....	16
4.4 Ns-TA spectra of 4-I-COMe with/without Et ₃ N.....	17
4.5 Application of 4-I-COMe in ¹ O ₂ Photosensitizer.....	18
4.6 HRMS Analysis of TEMPO-Trapped Intermediate.....	19
4.7 GC-MS Analysis of Photoreduction of 4-Iodoacetophenone.....	20
4.8 Supplementary Data for Study on Reaction Condition.....	21
5. Characterization Data.....	23
6. NMR Spectra.....	31
7. References.....	49

1. General Information

1.1 Materials Commercial grade reagents (including aryl halides, pyrroles, and 2, 2, 6, 6-tetramethylpiperidinoxyl) were purchased from Sigma-Aldrich, Alfa Aesar, Tokyo Chemical Industry, J & K Chemicals, Macklin at the highest commercial quality and used without further purification, unless otherwise stated.

1.2 Characterization Details The NMR spectra were recorded at 600 MHz ^1H and 150 MHz ^{13}C . The chemical shift (δ) for ^1H and ^{13}C are given in ppm relative to residual signals of the solvents (CHCl_3 @ 7.26 ppm ^1H NMR and 77.16 ppm ^{13}C NMR, DMSO-d_6 @ 2.50 ppm ^1H NMR and 39.51 ppm ^{13}C NMR, tetramethylsilane @ 0 ppm). High resolution mass spectra (HRMS) were obtained from the liquid chromatography coupled time-of-flight mass spectrometer with electrospray ionization (ESI), MAXIS, Bruker. Gas chromatography coupled to mass spectrometry (GC-MS) analysis was performed on GCMS-QP2010Ultra (Hitachi) using N_2 gas as carrier. UV-vis measurements were carried out on a U-3900 (Hitachi) spectrophotometer.

2. Synthesis

2.1 Reactor Visible-light-driven C-C coupling reactions were performed on a homemade photochemical reactor (Figure S1) with purple LEDs (Tianhui, TH-UV395T3WL- 3535-60 purple LEDs, 3-4 V, 500 mA) as light source, except for reaction condition optimization under visible light of different wavelengths. Wavelength of the purple LEDs was checked on a UV-vis spectrometer as mentioned earlier, and the result is depicted in Figure S2. It is seen that the peak wavelength of

the emission from the LED is ~ 400 nm with a peak width of ~ 10 nm.

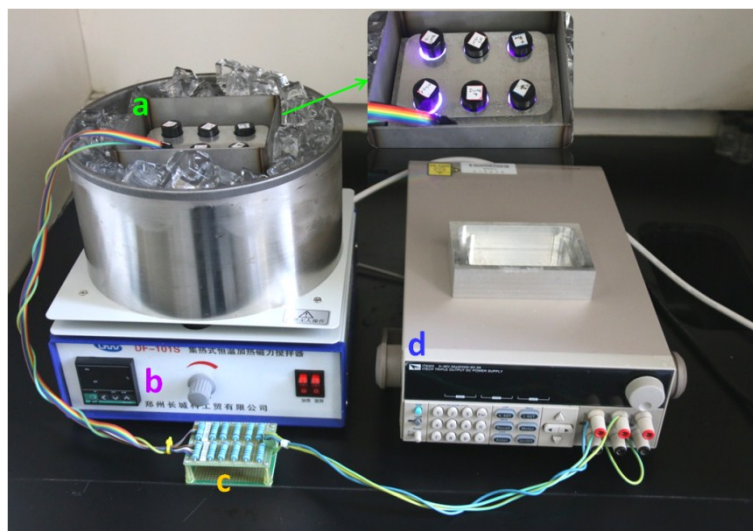


Figure S1. Photograph of the homemade photochemical reactor. The photochemical reactor as used contains four parts: the reactor with LEDs was kept around ice to avoid thermal effect of working LEDs (a), a magnetic stirring apparatus (b), a current control system made up of resistances (c), and a regulated power supply (d).

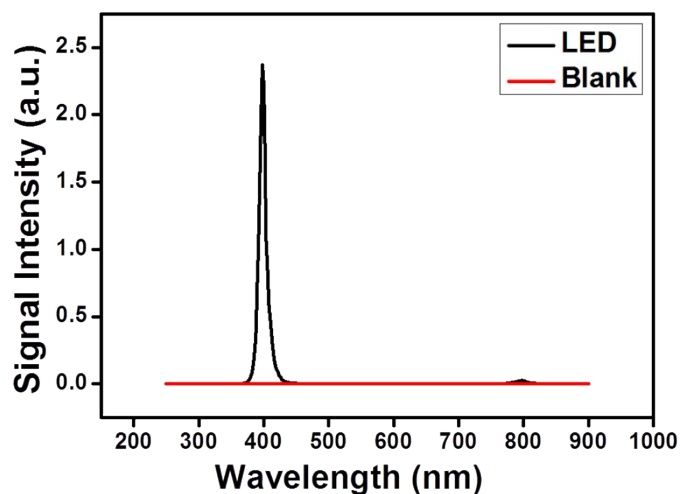


Figure S2. Emission spectra of the purple LED (black). Red: background.

2.2 General Procedure for Visible-Light-Driven Synthesis Respective aryl halide (0.1 mmol, 1 equiv) was dissolved in 2 mL MeCN in a 5 mL vial with magnetic stirring bar. The solution was degassed by N_2 via a syringe needle for 20 min, and 2 equiv Et_3N (30 μ L) was added during the degassing process. Corresponding pyrrole

was added into the mixture when the degassing is completed. Then, the vial was sealed up and the reaction mixture was irradiated through the bottom side of the vial using LED light. The reaction was monitored by thin-layer chromatography (TLC) analysis. When the reaction is completed, the reaction mixture was transferred into a 25 mL round-bottom flask and then concentrated in vacuum at 30 °C. Purification of the crude product was achieved by column chromatography using petrol ether/ethyl acetate on silica gel column.

3. Computation Details

3.1 General Information for Computation The singlet and triplet ground-state (S_0 and T_1 , respectively) minima and potential energy curves (PECs) were optimized at density functional theory (DFT)¹⁻³ level. A M062X⁴ functional with Grimme's D3 dispersion corrections⁵ (M062X-D3) were employed to consider both the weak interactions and the dispersion effects. For all atoms, the valent-splitting def2-SVPD basis sets⁶ from EMSL Basis Set Exchange Library⁷ were used in DFT calculations as well as Effective Core Potential (ECP) was applied for the I atom. The solvent contribution to energy and geometry was studied with SMD solvation model⁸ using acetonitrile as solvent ($\epsilon=35.69$). The S_0 - and T_1 -PECs were constructed from a series of constraint geometries along the C-I distance. The excited-state S_1 -PEC was obtained using the same strategy except for a time-dependent (TD)^{9,10} M062X-D3 functional was employed.

Multi-state (MS) CASPT2¹¹ single-point calculations with Douglas-Kroll Hamiltonian and ANO-RCC-VDZP¹² basis sets were carried out on top of the

(TD)DFT-optimized geometries, to provide the high-level energy correction for spin-free states, as well as to consider the spin-orbit coupling between singlet and triplet wave functions. In CASPT2 calculations, an active space of 14 electrons distributed in 10 orbitals, namely, CAS(14e,10o), were used. The active orbitals include the C-X σ/σ^* pair, lone-pair orbital on I atom, as well as the frontier π and π^* orbitals on the benzene moiety. The spin-orbit treatments were done using the RASSI(SO) algorithm¹³ implemented in MOLCAS 8.0 within the framework of Atomic Mean Filed Integrals (AMFI) approach¹⁴.

The (TD)DFT and MS-CASPT2/RASSI-SO calculations were carried out by Gaussian 09¹⁵ and MOLCAS 8.0 program¹⁴, respectively.

3.2 Photocleavage of C-X Bond in aryl-Cl and aryl-I without Et₃N: As discussed in the manuscript, previous multireference *ab initio* calculations suggested that the repulsive (π,π^*) and (π,σ^*) states, i.e., the S₁ and T₁ mentioned in this study, go downhill towards longer C-I distance, until energetically degenerate with the ground state (S₀), and neither S₁ nor T₁ intermediate has been located. While in our DFT calculations, as shown in Figure S3(a), the aryl-Cl does not show an evident downhill MEP with the elongation of C-Cl distance, therefore it is not able to support a favorable C-Cl bond cleavage process; for aryl-I in S3(c), the T₁-MEP shows a slight downhill trend, and in right ending of the investigated range, the optimized T₁- and S₀-PECs are not fully degenerate, instead, the T₁ becomes slightly energetically favorable than S₁ (It is possibly because the previous calculations were carried out with a C_{2v} symmetric constraints, therefore the full relaxation of T₁ towards an out-of-

plane bending structure, as seen in Figure 2, is not allowed). The MS-CASPT2 energy correction does not change the topology of the C-X bond dissociation path (Figure S4a and 4c). Moreover, for aryl-Cl, in the MS-CASPT2/RASSI(SO) calculations, the $S_1/S_0/T_1$ state mixing along the C-Cl energy profile (Figure S5a, bottom panel) is negligible, showing too weak spin-orbital coupling between the S_1/T_1 state to facilitate a $S_1 \rightarrow T_1$ intersystem crossing. For the case of aryl-I (shown in figure S5c), the S_1/T_1 state mixing is observed in rather long C-I distance of 3.2-3.6 Å, which is also too late for the efficient formation of radical complex. In both cases, although a minimum can be obtained on the flat T_1 -PEC, its rather low kinetic and thermodynamic stabilities do not support the aryl radical as a long lifetime intermediate that can be utilized in organic synthesis.

3.3 Photo Activation of C-X Bond in aryl-X...Et₃N Complex: Figure S3 and S4 also shows the DFT-optimized C-X dissociative PECs (S3b, S3d) and the corresponding energy corrections at the MS-CASPT2 level (S4b, S4d). At the DFT level, the T_1 -PECs are nearly degenerate with S_1 state in the (π, π^*) with short C-X distance, then goes downhill along the (π, σ^*) state at long C-X region. Comparisons with the base-free aryl-X case (Figure S3a and S3c) reveal that the Lewis acid Et₃N prefer to stabilize the T_1 state in both cases. Further explorations of T_1 -PEC find a triplet intermediate (T_1 -min). At T_1 -min, the atomic charge distributions beside the C-I bond does not change with respect to those in S_0 (see Table S1), thus a homolytic cleavage is supported.

It is also noted that after MS-CASPT2 energy correction, the aryl-Cl+Et₃N

energy profile (Figure S4b) show a barrier at 2.4 angstrom, which is unfavorable for the formation of the T₁-min; while for aryl-I+Et₃N, no barrier is observed. Meanwhile, from Figure S5b and 5d, it is seen that along the T₁-PEC, the S₁ and T₁ states are close in energy in an extended range, which may suggest a high probability of S₁ → T₁ intersystem crossing (ISC). The narrow S₁-T₁ energy gap, as well as the large magnitude of SOC, support an efficient S₁ → T₁ ISC process, as has been observed experimentally.

The frontier molecular orbital (FMO), natural transition orbitals (NTOs) and spin density of the singlet and triplet minima are plotted in Figure S6 and S7. The NTOs at S₀-min reveal the same (π, π^*) nature of both S₁ and T₁ states at short C-X distance, while the single-occupied MOs and spin density at T₁-min suggest the biradical nature of the formed complex.

4. Supplemental Data

4.1 Supplementary Figures for Theoretical Calculations

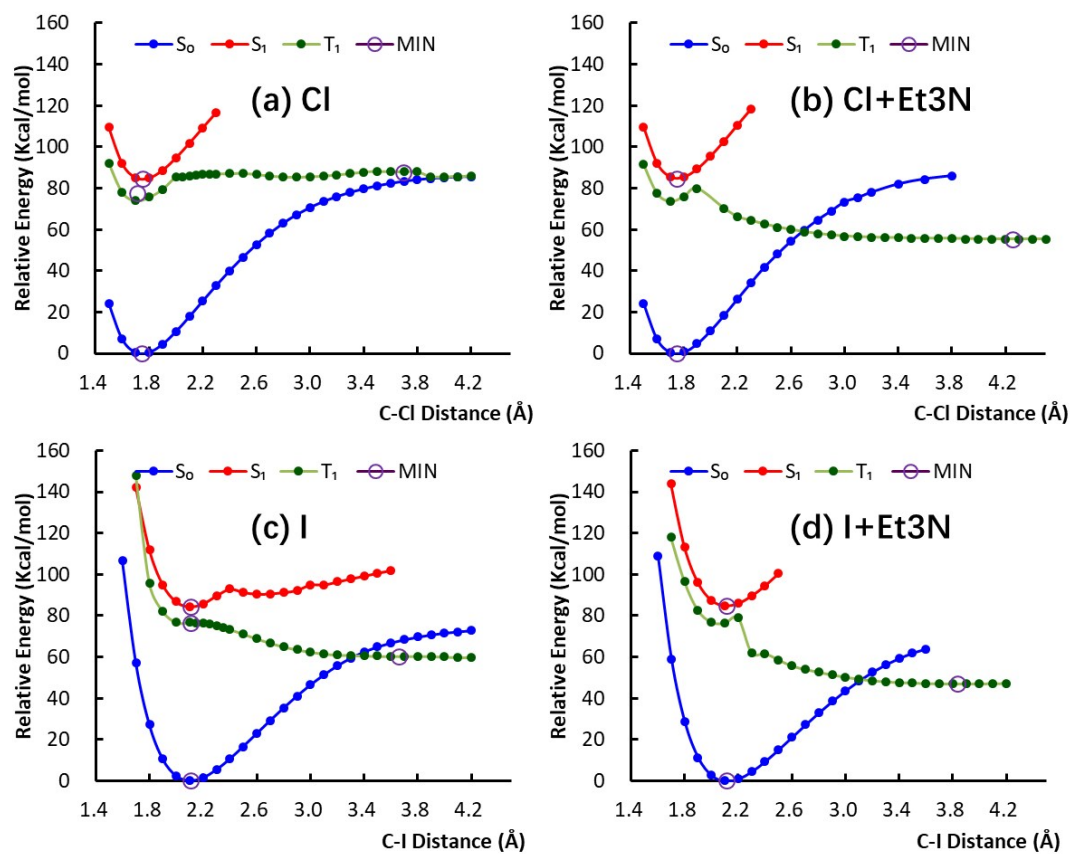


Figure S3. The S_1 , S_0 and T_1 energy profiles optimized at M062X-D3/def2-SVPD (ECP) level along the C-X distance in acetonitrile solution for (a) aryl-Cl, (b) aryl-Cl+Et₃N, (c) aryl-I and (d) aryl-I+Et₃N. The optimized minima on the MEPs are emphasized by purple circles.

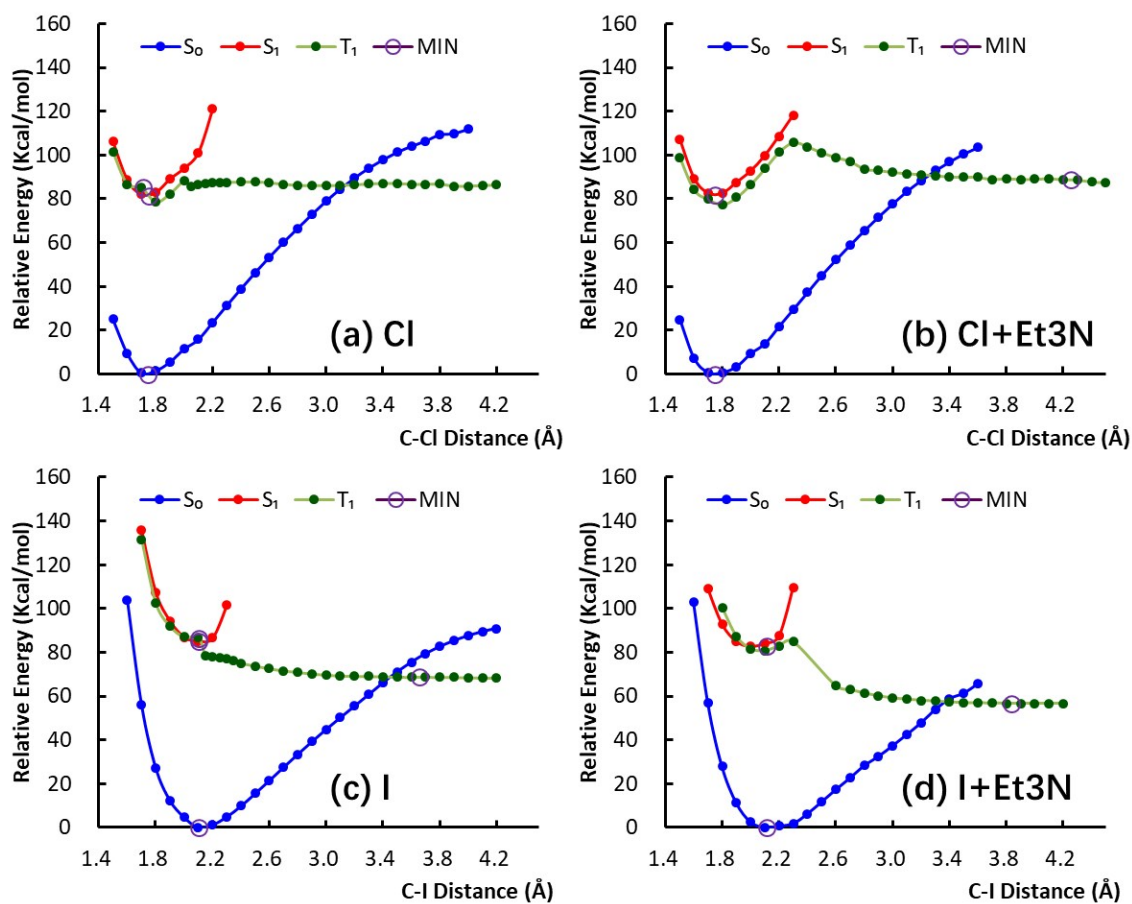


Figure S4. The MS-CASPT2/ANO-RCC-VDZP-calculated S₁, S₀ and T₁ energy profiles on top of the M062X-D3/def2-SVPD (ECP) optimized structures along the C-X distance in acetonitrile solution for (a) aryl-Cl, (b) aryl-Cl+Et₃N, (c) aryl-I and (d) aryl-I+Et₃N. The optimized minima on the MEPs are emphasized by purple circles.

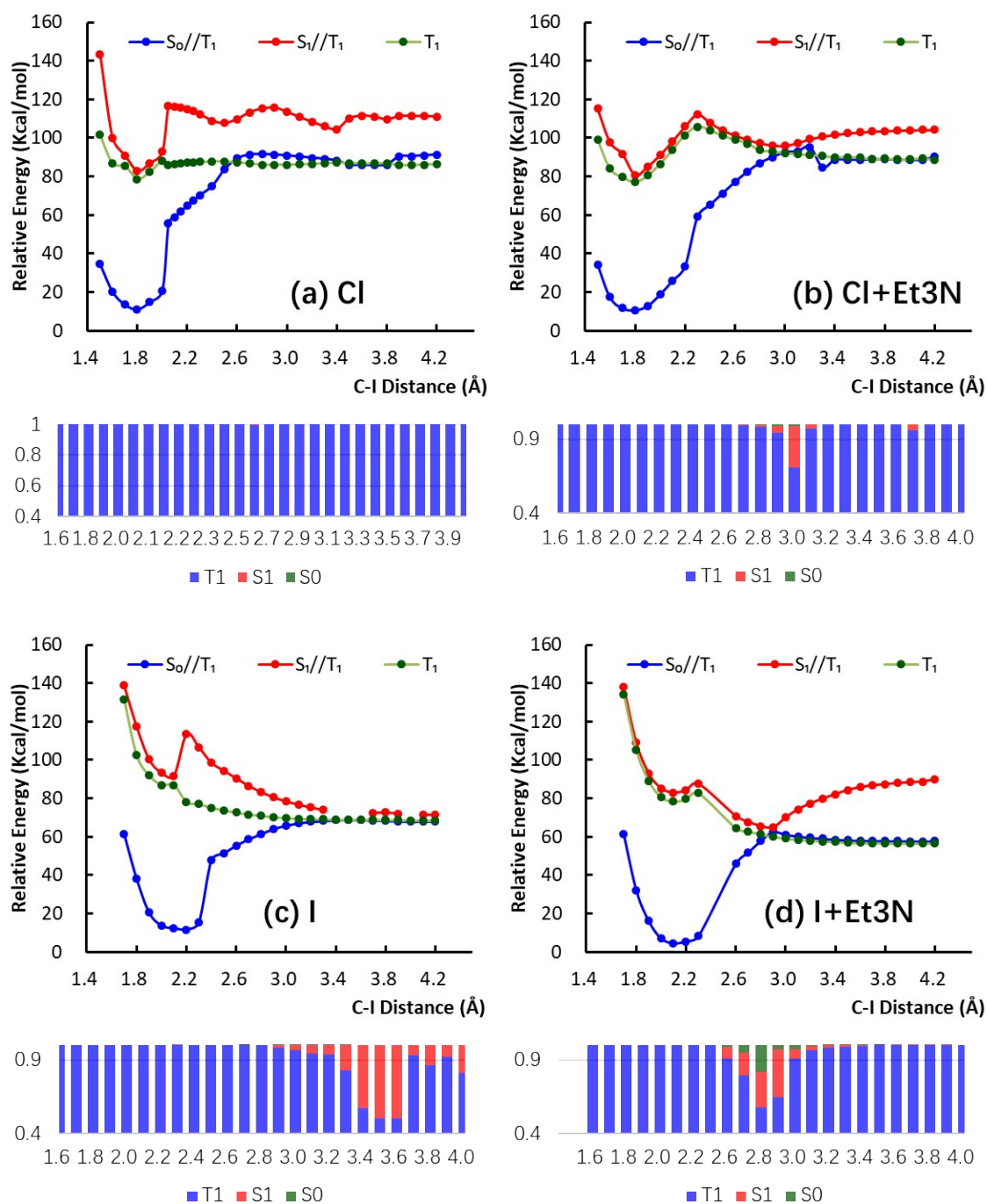


Figure S5. The MS-CASPT2-corrected T_1 energy profiles calculated on top of the M062X-optimized geometries and their vertical projection on S_0 and S_1 states ($S_0//T_1$ and $S_1//T_1$, respectively) for (a) aryl-Cl, (b) aryl-Cl+Et₃N, (c) aryl-I and (d) aryl-I+Et₃N. The weight of the spin-free S_0 , S_1 and T_1 states along the SOC T_1 -PECs are shown in the bottom of each figures.

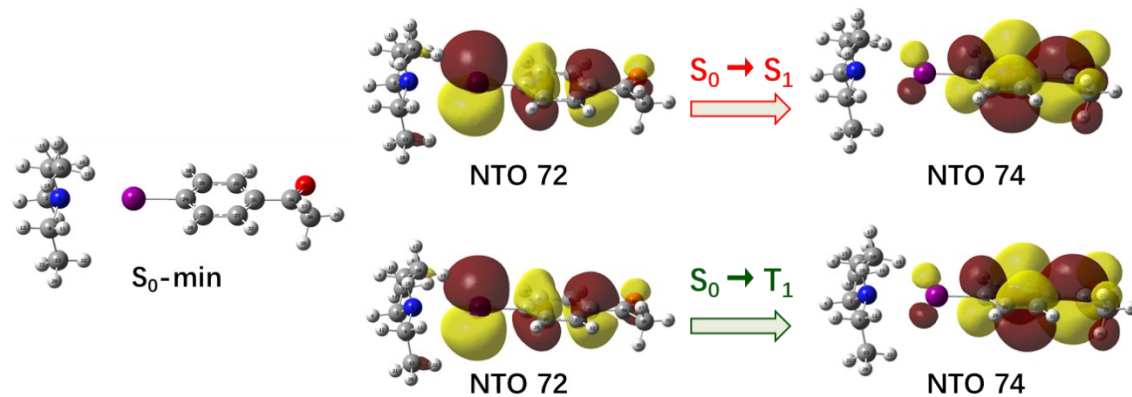


Figure S6. The natural transition orbitals (NTO) of S_0 -min. S_1 and T_1 states, both correspond to the electron transition from NTO 72 to NTO 74 and show a (π, π^*) nature.

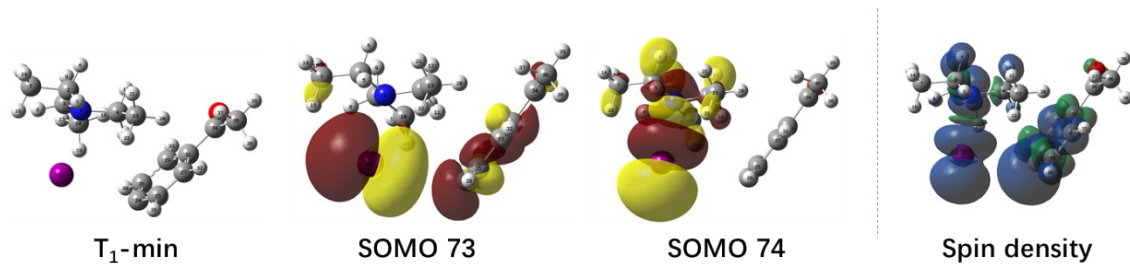


Figure S7. The singly occupied orbitals (SOMO 66 and SOMO 69) and spin density of T₁-min for aryl-I...Et₃N complex, which suggest that the two unpaired electrons are localized at the p orbital of I and aryl-C atoms, respectively.

Table S1. Natural Bond Orbital (NBO) charges distribution (in e) of S_0 -min and T_1 -min structures.

	$Q(S_0\text{-min})$	$Q(T_1\text{-min})$
The fragment partition method 1		
Et₃N	0.043	0.490
I-Benz	-0.043	-0.490
The fragment partition method 2		
Et₃N...I	0.231	0.000
·Benz	-0.231	0.000
The fragment partition method 3		
I	0.188	-0.491
Et₃	0.646	0.855
N	-0.603	-0.365

4.2 Cartesian Coordinates of Important Stationary Points

S_0-min (I+Et₃N)				T_1-min(I+Et₃N)			
-973.5680239				-973.493239			
N	-3.642672	-0.037080	0.003334	N	1.335447	1.385023	0.196393
C	-4.132631	1.130367	-0.728948	C	2.185979	2.264173	-0.611588
C	-4.075654	-0.006913	1.400263	C	1.510725	1.548680	1.642416
C	-4.042828	-1.283241	-0.650175	C	-0.066790	1.339287	-0.231845
H	-3.694436	1.105120	-1.733432	H	2.175741	1.882347	-1.637107
H	-5.234425	1.061412	-0.856317	H	1.705189	3.260052	-0.626247
C	-3.781762	2.465413	-0.088287	C	3.618491	2.390359	-0.126732
H	-3.644846	0.886571	1.867201	H	2.551542	1.307865	1.878529
H	-5.180139	0.104174	1.450906	H	1.360530	2.620468	1.870042
C	-3.655050	-1.221704	2.215215	C	0.583595	0.701475	2.493074
H	-3.543430	-2.109806	-0.131163	H	-0.524308	0.457383	0.229956
H	-5.136091	-1.440231	-0.528516	H	-0.567071	2.228730	0.195197
C	-3.685484	-1.361378	-2.127480	C	-0.276774	1.306711	-1.733884
H	-4.012451	3.273875	-0.792754	H	4.188219	2.945403	-0.880851
H	-4.350778	2.654157	0.829857	H	3.691087	2.938170	0.819531
H	-2.709834	2.512367	0.146883	H	4.078623	1.401118	-0.005861
H	-3.843567	-1.023186	3.277359	H	0.902936	0.782414	3.538540
H	-4.216134	-2.123409	1.942557	H	-0.459444	1.033739	2.431914
H	-2.582683	-1.423532	2.089247	H	0.640928	-0.352717	2.193193
H	-3.831414	-2.390526	-2.477539	H	-1.349917	1.202946	-1.929101

H	-4.313732	-0.709373	-2.745890	H	0.059598	2.229733	-2.219064
H	-2.633004	-1.091170	-2.289332	H	0.241609	0.451692	-2.188774
I	-0.646635	0.034385	-0.002493	I	2.309334	-1.155409	-0.309400
C	1.469748	0.050171	-0.002195	C	-1.279897	-2.252379	0.474756
C	2.168943	-1.157689	-0.005746	C	-1.634065	-1.983475	-0.829575
C	2.155623	1.268811	0.001874	C	-1.833851	-1.671590	1.596728
C	3.562532	-1.145226	-0.005082	C	-2.640818	-1.032168	-1.023269
H	1.632335	-2.105767	-0.009204	H	-1.154708	-2.470916	-1.678725
C	3.546126	1.270583	0.002534	C	-2.831995	-0.719119	1.378262
H	1.606318	2.209852	0.004526	H	-1.508078	-1.921125	2.606877
C	4.262806	0.066895	-0.000905	C	-3.234075	-0.392270	0.074798
H	4.098882	-2.093143	-0.007882	H	-2.944129	-0.784086	-2.039698
H	4.095122	2.211986	0.005871	H	-3.304012	-0.209882	2.218504
C	5.762834	0.113186	0.000184	C	-4.276335	0.672605	-0.107445
O	6.341002	1.182192	0.004543	O	-4.781629	1.206118	0.860842
C	6.518687	-1.187104	-0.003850	C	-4.661657	1.064666	-1.507238
H	6.250266	-1.782872	0.880013	H	-3.777568	1.425730	-2.051362
H	6.250618	-1.777539	-0.891367	H	-5.049514	0.193075	-2.052131
H	7.592405	-0.982393	-0.002974	H	-5.422262	1.848714	-1.467384

S₀-min (CI+Et3N)

-1135.994958

N	-3.699427	-0.027261	0.004772
C	-4.244122	1.072777	-0.781869
C	-4.157422	0.030521	1.388193
C	-3.992866	-1.321829	-0.600025
H	-3.830112	1.000652	-1.793840
H	-5.348073	0.970249	-0.880004
C	-3.910342	2.452719	-0.232349
H	-3.842266	0.992918	1.807613
H	-5.269660	0.013556	1.426199
C	-3.605148	-1.076630	2.274886
H	-3.478030	-2.091784	-0.013609
H	-5.081388	-1.543085	-0.531397
C	-3.543990	-1.451668	-2.049045
H	-4.160463	3.213639	-0.982037
H	-4.471027	2.691721	0.679379
H	-2.836398	2.527361	-0.012790
H	-3.821880	-0.843658	3.324818
H	-4.051297	-2.053896	2.054833
H	-2.515610	-1.153547	2.157178
H	-3.597225	-2.504532	-2.352578
H	-4.175014	-0.876793	-2.737367

T₁-min(CI+Et3N)

-1135.906914

N	-2.086727	-0.699272	0.510408
C	-3.000815	-1.677176	-0.046707
C	-2.553775	0.191883	1.553844
C	-0.661747	-0.844136	0.278392
H	-2.763610	-1.759753	-1.112886
H	-2.726259	-2.642246	0.417048
C	-4.472355	-1.381488	0.149664
H	-3.478308	0.650303	1.186463
H	-2.835756	-0.458837	2.401895
C	-1.567451	1.253440	1.988817
H	-0.258566	0.166777	0.139048
H	-0.238886	-1.225161	1.226548
C	-0.286810	-1.740412	-0.882613
H	-5.039023	-2.178515	-0.344162
H	-4.757877	-1.367584	1.207644
H	-4.739565	-0.426148	-0.318372
H	-2.055568	1.869043	2.752435
H	-0.659193	0.824298	2.427632
H	-1.297330	1.897049	1.142484
H	0.805491	-1.785202	-0.936338
H	-0.658076	-2.763317	-0.755003

H	-2.504658	-1.113592	-2.161402	H	-0.662413	-1.327686	-1.827480
C	1.120726	0.054304	-0.004204	C	1.280382	2.522548	-0.205329
C	1.816653	-1.152439	-0.009621	C	1.560614	1.832415	-1.364391
C	1.788195	1.280125	0.003515	C	1.647808	2.145415	1.069423
C	3.208746	-1.128399	-0.006555	C	2.286832	0.644494	-1.225540
H	1.276995	-2.098145	-0.015827	H	1.234401	2.177702	-2.345556
C	3.177236	1.288316	0.006660	C	2.359250	0.949118	1.184725
H	1.223044	2.211163	0.007541	H	1.390181	2.733846	1.950641
C	3.900543	0.088520	0.001645	C	2.682556	0.199706	0.043938
H	3.750828	-2.072662	-0.010673	H	2.529182	0.064193	-2.115173
H	3.720385	2.232660	0.013232	H	2.672910	0.584219	2.162645
C	5.400531	0.144703	0.005989	C	3.428418	-1.091333	0.221806
O	5.970193	1.217952	0.015088	O	3.650109	-1.520156	1.337410
C	6.164548	-1.150411	-0.000706	C	3.884167	-1.829365	-1.006709
H	5.898775	-1.750038	0.881362	H	3.014581	-2.133999	-1.606172
H	5.900963	-1.740180	-0.889996	H	4.502090	-1.174934	-1.636593
H	7.236964	-0.939137	0.001887	H	4.454410	-2.713166	-0.708934
Cl	-0.625302	0.034746	-0.006219	Cl	-2.502885	1.234977	-1.655051

S₀-min (I)

-681.497971

I	2.574171	-0.026287	-0.000007
C	0.467882	0.014475	0.000009
C	-0.243641	-1.184653	-0.000213
C	-0.190280	1.246669	0.000253
C	-1.636894	-1.146191	-0.000173
H	0.277725	-2.140643	-0.000427
C	-1.580428	1.269085	0.000243
H	0.375412	2.177426	0.000443
C	-2.316086	0.077405	0.000040
H	-2.187901	-2.085632	-0.000346
H	-2.113285	2.219661	0.000412
C	-3.816206	0.150612	0.000001
O	-4.372269	1.230787	-0.000558
C	-4.595253	-1.135205	0.000406
H	-4.337363	-1.732762	-0.885381
H	-4.336862	-1.732701	0.886077
H	-5.665221	-0.911612	0.000639

T₁-min(I)

-681.4017444

C	0.131028	2.401656	0.499594
C	0.214475	1.450414	1.494564
C	0.830387	2.388854	-0.689578
C	1.092636	0.380624	1.269555
H	-0.363207	1.513851	2.417413
C	1.698590	1.313553	-0.890259
H	0.718458	3.168311	-1.444032
C	1.832677	0.310171	0.081593
H	1.185521	-0.394606	2.029818
H	2.279900	1.238757	-1.809546
C	2.761443	-0.837896	-0.193664
O	3.430545	-0.851083	-1.207873
C	2.828926	-1.958622	0.806442
H	3.164176	-1.576537	1.780972
H	1.830717	-2.396013	0.950636
H	3.524104	-2.722416	0.448563
I	-2.040095	-0.466325	-0.169440

S₀-min (Cl)

-843.9300457

C	1.695267	-0.015121	0.000083
---	----------	-----------	----------

T₁-min(Cl)

-843.7899945

C	-1.713245	-0.010174	0.000012
---	-----------	-----------	----------

C	0.979575	-1.208779	-0.000128	C	-0.956059	-1.252838	0.000071
C	1.058137	1.225116	0.000212	C	-1.041044	1.267084	-0.000060
C	-0.411838	-1.155571	-0.000157	C	0.391387	-1.218692	0.000036
H	1.500293	-2.165032	-0.000258	H	-1.497332	-2.198432	0.000144
C	-0.330601	1.260669	0.000162	C	0.307629	1.312187	-0.000085
H	1.642239	2.144287	0.000357	H	-1.637735	2.178963	-0.000092
C	-1.077535	0.075620	-0.000025	C	1.110911	0.067150	-0.000053
H	-0.972284	-2.089072	-0.000314	H	0.958791	-2.147035	0.000085
H	-0.854690	2.215749	0.000269	H	0.843725	2.258376	-0.000135
C	-2.577194	0.164307	-0.000102	C	2.545647	0.155062	-0.000097
O	-3.121171	1.250391	-0.000373	O	3.094093	1.274552	-0.000118
C	-3.368883	-1.113547	0.000068	C	3.363053	-1.113176	0.000133
H	-3.116365	-1.713394	-0.885727	H	3.136313	-1.723929	0.886222
H	-3.116139	-1.713407	0.885783	H	3.136316	-1.724253	-0.885733
H	-4.436704	-0.879990	0.000172	H	4.425887	-0.855194	0.000094
Cl	3.442438	-0.070496	0.000119	Cl	-3.421670	-0.072031	0.000036

4.3 Studies on Phosphorescence of 4-I-COMe with/without Et₃N

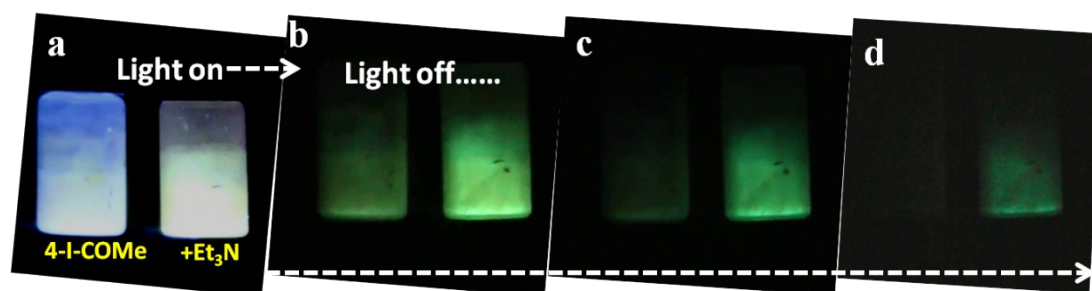


Figure S8. Pictures of frozen 4-I-COMe solution without (left in each picture)/with (right in each picture) Et₃N under 365 nm light (a) and after the light was turned off immediately (b-d).

Concentration of 4-I-COMe was 0.1 M and 2 eqv. Et₃N was added. The solution was frozen by immersing in liquid nitrogen for 5 min.

4.4 NS-TA spectra of 4-I-COMe with and without Et₃N

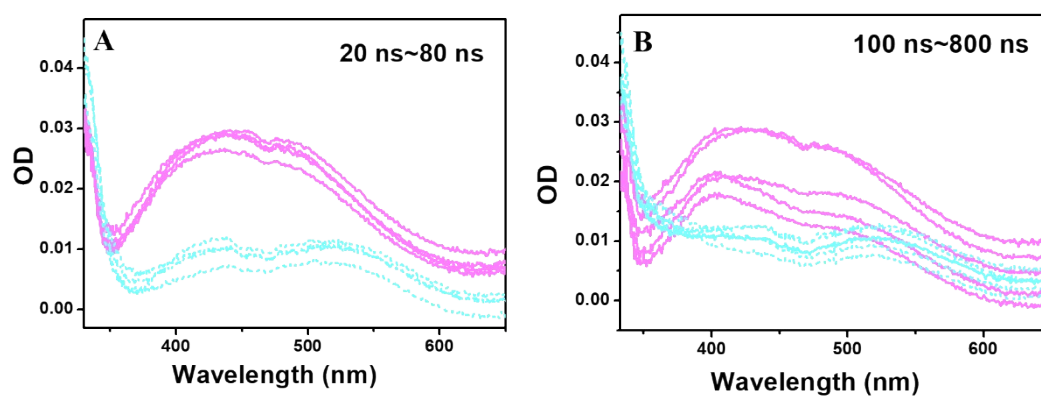


Figure S9. Ns-TA Spectra of 4-I-COMe with (purple) and without (blue) Et₃N. Excitation wavelength: 360 nm; Solvent: acetonitrile; concentration of 4-I-COMe: 0.1 M; Et₃N: 0.2 M.

4.5 Application of 4-I-COMe in $^1\text{O}_2$ Photosensitizer

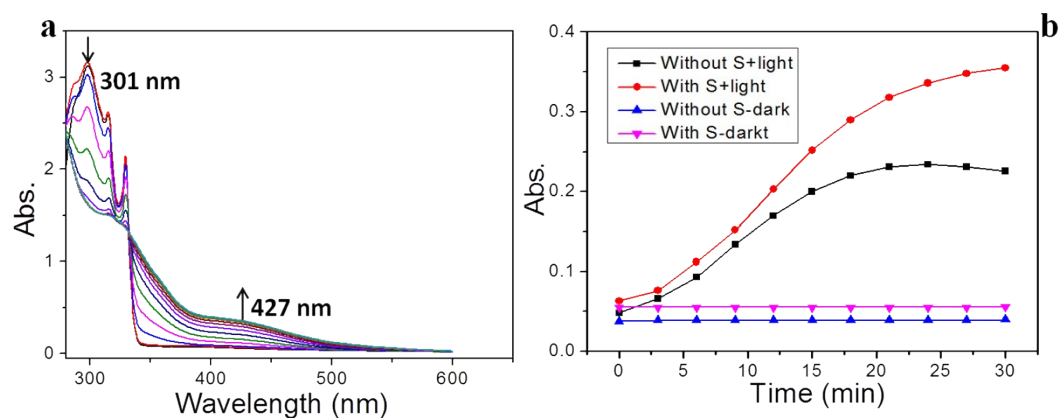


Figure S10. Photooxidation of DHN. a, UV-vis absorption changes during the oxidation of DHN with 4-I-COMe. b, Plots of absorbance at 427 nm vs photooxidation time under different conditions. $c(\text{DHN})=3.3\times 10^{-4}$ M; $c(4\text{-I-COMe})=3.3\times 10^{-5}$ M. Note: S represents 4-I-COMe.

4.6 High Resolution Mass Spectrum (HRMS) analysis of TEMPO-Trapped intermediate Procedure for coupling of TEMPO-trapped intermediate was similar as for 4-iodoacetophenone reduction, except that 4 equiv TEMPO was added together with 1 equiv 4-iodoacetophenone (Figure S4). After 12 h, the reaction mixture was analyzed by HRMS. Exact molecular ion was found, which proves formation of coupling product of TEMPO-trapped intermediate.

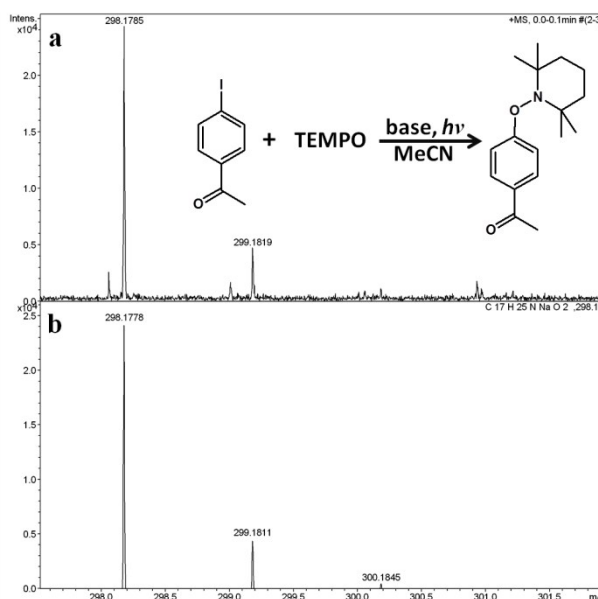


Figure S11. HRMS of TEMPO-trapped intermediate. **Note:** Experimental result (a, 298.1785) and calculated result (b, 298.1778) for the species of $[M+Na]^+$, $C_{17}H_{25}NO_2Na^+$.

4.7 GC-MS Analysis of Photoreduction of 4-iodoacetophenone 0.1 mmol of 4-iodoaceto-phenone was dissolved in 2 mL MeCN in a 5 mL vial with magnetic stirring bar. The solution was degassed by N_2 via a syringe needle for 25 min, and 2 equiv Et_3N was added during the degassing process. When degassing is completed, the vial was sealed up and the reaction mixture was irradiated through the bottom side of the vial using 400 nm LED light for 12 h. Afterwards, the reaction mixture was diluted and analyzed using GC-MS analysis. It was found that abundance of

dehalogenation product, acetophenone, was found by GC-MS analysis (Figure S13). Two groups of compounds were found in the GC result, which had retention time of 7.210 min and 12.855 min respectively (FigureS13a). Further MS analysis reveals that the compound with retention time of 7.210 min was acetophenone (FigureS13b) and the compound with retention time of 12.855 was 4-iodoaceto-phenone (FigureS31c).

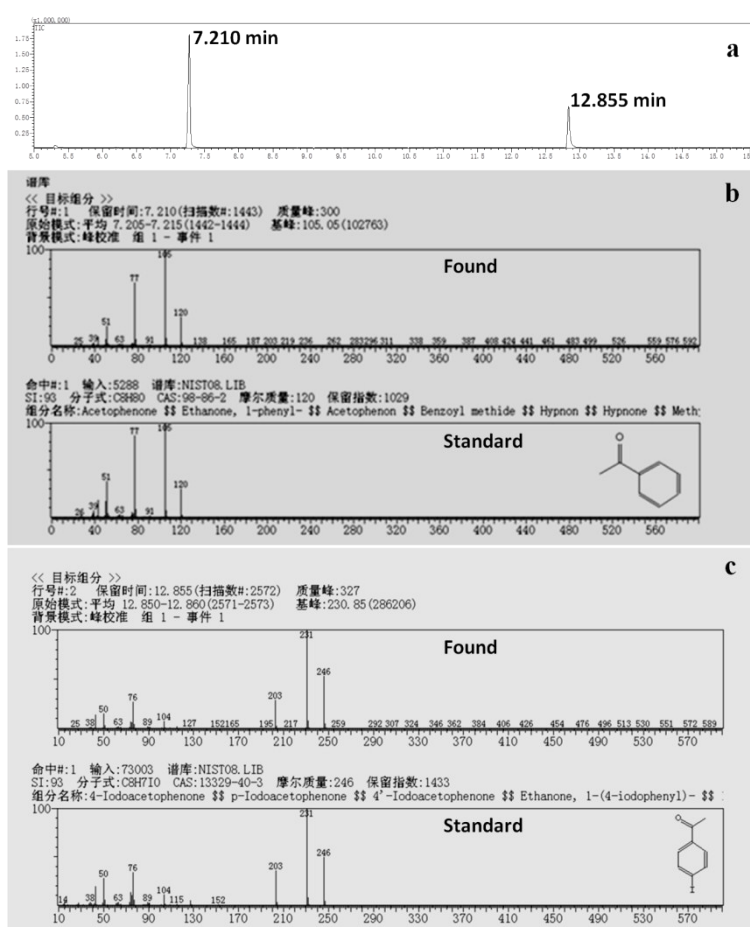
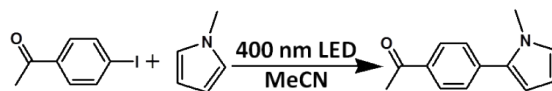


Figure S12. GC-MS analysis of photoreduction of 4-iodoacetophenone. a. GC result of the reaction mixture. b. MS result of the corresponding compounds showed in a with retention time of 7.210 min: the upper shows MS spectrum of the compound found; the lower shows the standard MS spectrum of acetophenone. c. MS result of the corresponding compounds showed in a with retention time of 12.855 min: the upper shows MS spectrum of the compound found; the lower shows the standard MS spectrum of 4-iodoacetophenone.

4.8 Supplementary Data for Study on Reaction Condition

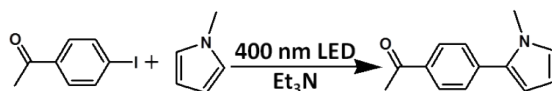
Table S2. Effect of Base on the reaction.



Entry	Base	Yield (%)
1	2 eqv. NaOH	73
2	2 eqv. NaAc	66
3	2 eqv. PrNH ₂	96
4	2 eqv. KO ^t Bu	23
5	2 eqv. Et ₃ N	99
6	None	0
7	1 eqv. Et ₃ N	50
8	4 eqv. Et ₃ N	45

Reaction time for all entries is 12 h and the yields were determined by ¹H NMR analysis of crude reaction mixture with internal standard after the reaction.

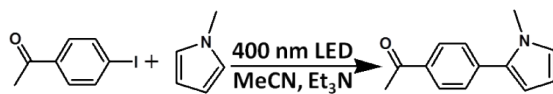
Table S3. Effect of solvent on the reaction.



Entry	Solvent	Yield (%)
1	toluene	75
2	dioxane	65
3	THF	70
4	DMF	96
6	MeCN	99

Reaction time for all entries is 12 h, 2 eqv. Et₃N was added and the yields were determined by ¹H NMR analysis of crude reaction mixture with internal standard after the reaction.

Table S4. Effect of trapping agent amount on the reaction.



Entry	N-methylpyrrole	Yield (%)
1	1 eqv.	15
2	8 eqv.	70
3	16 eqv.	85
4	24 eqv.	99
5	32 eqv.	99

Reaction time for all entries is 12 h, 2 eqv. Et₃N was added and the yields were determined by ¹H NMR analysis of crude reaction mixture with internal standard after the reaction.

5. Characterization Data

4-(1H-pyrrol-2-yl)acetophenone (1a). The compound was prepared according to a general procedure, using 4-iodoacetophenone (24.9 mg), pyrrole (167 μ L) and triethylamine (30 μ L). The crude product was purified by chromatography on silica gel and 16.7 mg 1a was obtained (yield: 90%). HRMS calculated for $[\text{C}_{12}\text{H}_{11}\text{NONa}]^+$: 208.0733; found: 208.0739.

^1H NMR (600 MHz, CDCl_3) δ 11.54 (1H), 8.00-7.93 (2H), 7.56-7.51 (2H), 6.94 (1H), 6.68 (1H), 6.34 (1H), 2.60 (3H).

^{13}C NMR (150 MHz, CDCl_3) δ 197.4, 137.1, 134.5, 130.8, 129.7, 123.4, 120.8, 110.8, 108.1, 26.2.

4-(1-Methyl-1H-pyrrol-2-yl)acetophenone (1b). The compound was prepared according to the procedures described already, using 4-iodoacetophenone (24.9 mg), N-methylpyrrole (226 μ L) and triethylamine (30 μ L). The crude product was purified by chromatography on silica gel and 16.9 mg 1b was obtained (yield: 85%). HRMS calculated for $[\text{C}_{13}\text{H}_{13}\text{NONa}]^+$:222.0889; found:222.0892.

^1H NMR (600 MHz, CDCl_3) δ 7.99-7.98 (2H), 7.49-7.51 (2H), 6.77 (1H), 6.35 (1H), 6.23 (1H), 3.72 (3H), 2.62 (3H).

^{13}C NMR (150 MHz, CDCl_3) δ 197.5, 138.0, 135.0, 133.4, 128.6, 128.0, 125.3, 110.3, 108.4, 35.6, 26.6.

4-(1-Phenyl-1H-pyrrol-2-yl)acetophenone (1c). The compound was prepared according to the procedures described already, using 4-iodoacetophenone (24.9 mg), N-phenylpyrrole (57 mg) and triethylamine (30 μ L). The crude product was purified

by chromatography on silica gel and 14.4 mg 1c was obtained (yield: 55%). HRMS calculated for $[C_{15}H_{15}NONa]^+$: 284.1046; found: 284.1059.

1H NMR (600 MHz, $CDCl_3$) δ 7.81-7.76 (2H), 7.37-7.33 (2H), 7.32-7.31 (1H), 7.20-7.17 (4H), 6.99 (1H), 6.57 (1H), 6.40 (1H), 2.55 (3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 197.6, 140.3, 137.6, 134.6, 132.6, 129.3, 128.3, 127.7, 126.0, 125.8, 112.3, 109.8, 26.5.

4-(1H-pyrrol-2-yl)methyl benzoate (2a). The compound was prepared according to the procedures described already, using methyl 4-iodobenzoate (26.2 mg), pyrrole (167 μ L) and triethylamine (30 μ L). The crude product was purified by chromatography on silica gel and 18.7 mg 2a was obtained (yield: 93%). HRMS calculated for $[C_{12}H_{11}NO_2Na]^+$: 224.0684; found: 224.0682.

1H NMR (600 MHz, $CDCl_3$) δ 8.52 (1H), 8.04-8.02 (2H), 7.53-7.52 (2H), 6.93 (1H), 6.66 (1H), 6.33 (1H), 3.92 (3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 170.0, 136.9, 131.0, 130.4, 127.3, 123.2, 120.3, 110.7, 108.0, 52.0.

4-(1-Methyl-1H-pyrrol-2-yl)methyl benzoate (2b). The compound was prepared according to the procedures described already, using methyl 4-iodobenzoate (26.2 mg), N-methylpyrrole (226 μ L) and triethylamine (30 μ L). The crude product was purified by chromatography on silica gel and 19.6 mg 2b was obtained (yield: 91%). HRMS calculated for $[C_{13}H_{13}NO_2Na]^+$: 238.0838; found: 238.0841.

1H NMR (600 MHz, $CDCl_3$) δ 8.06-8.05 (2H), 7.48-7.47 (2H), 6.76 (1H), 6.34(4H), 6.22 (1H), 3.93 (3H), 3.71 (3H).

¹³C NMR (150 MHz, CDCl₃) δ 167.0, 137.8, 133.5, 129.8, 128.0, 127.9, 125.1, 110.1, 108.3, 52.1, 35.4.

4-(1-Phenyl-1H-pyrrol-2-yl)methyl benzoate (2c). The compound was prepared according to the procedures described already, using methyl 4-iodobenzoate (26.2 mg), N-phenylpyrrole (57 mg) and triethylamine (30 μL). The crude product was purified by chromatography on silica gel and 16.6 mg 2c was obtained (yield: 60%). HRMS calculated for [C₁₈H₁₅NO₂Na]⁺: 300.0995; found: 300.1005.

¹H NMR (600 MHz, CDCl₃) δ 7.87-7.85 (2H), 7.35-7.33 (2H), 7.31-7.29 (2H), 7.18-7.16 (4H), 6.98 (1H), 6.55(4H), 6.38 (1H). 3.88 (3H).

¹³C NMR (150 MHz, CDCl₃) δ 166.7, 140.3, 137.4, 132.7, 129.4, 129.2, 127.6, 127.5, 127.0, 125.8, 125.7, 112.1, 109.7, 52.0.

4-(1H-pyrrol-2-yl)benzaldehyde (3a). The compound was prepared according to the procedures described already, using 4-iodobenzaldehyde (23.2 mg), pyrrole (167 μL) and triethylamine (30 μL). The crude product was purified by chromatography on silica gel and 15.6 mg 3a was obtained (yield: 88%). HRMS calculated for [C₁₁H₉NONa]⁺:194.1394; found:194.0976.

¹H NMR (600 MHz, CDCl₃) δ 9.96 (1H), 8.60 (1H), 7.88-7.87 (2H), 7.62-7.60 (2H), 6.96 (1H), 6.71 (1H), 6.36 (1H).

¹³C NMR (150 MHz, DMSO-d₆) δ 191.9, 138.5, 133.06, 130.3, 129.9, 123.2, 121.6, 109.9, 108.7.

4-(1-Methyl-1H-pyrrol-2-yl)benzaldehyde (3b). The compound was prepared according to the procedures described already, using 4-iodobenzaldehyde (23.2 mg),

N-methylpyrrole (226 μL) and triethylamine (30 μL). The crude product was purified by chromatography on silica gel and 15.7 mg 3b was obtained (yield: 85%). HRMS calculated for $[\text{C}_{12}\text{H}_{11}\text{NONa}]^+$: 208.0733; found: 208.0734.

^1H NMR (600 MHz, CDCl_3) δ 10.02 (1H), 7.91-7.89 (2H), 7.58-7.56 (2H), 6.79 (1H), 6.39 (1H), 6.24 (1H), 3.74 (3H).

^{13}C NMR (150 MHz, CDCl_3) δ 191.7, 139.3, 134.3, 133.3, 130.0, 128.2, 125.8, 110.8, 108.7, 35.5.

4-(1-Phenyl-1H-pyrrol-2-yl)benzaldehyde (3c). The compound was prepared according to the procedures described already, using 4-iodobenzaldehyde (23.2 mg), N-phenylpyrrole (57 mg) and triethylamine (30 μL). The crude product was purified by chromatography on silica gel and 13.2 mg 3c was obtained (yield: 53%). HRMS calculated for $[\text{C}_{17}\text{H}_{13}\text{NONa}]^+$: 270.0889; found: 270.0895.

^1H NMR (600 MHz, CDCl_3) δ 9.92 (1H), 7.71-7.69 (2H), 7.38-7.35 (2H), 7.33-7.31 (1H), 7.27 (1H), 7.25 (1H), 7.19-7.18 (2H), 7.00 (1H), 6.60 (1H), 6.40 (1H).

^{13}C NMR (150 MHz, CDCl_3) δ 191.7, 140.3, 138.9, 133.9, 132.4, 129.6, 129.3, 128.0, 127.2, 126.4, 125.8, 112.8, 109.9.

4-(1H-Pyrrol-2-yl)benzotrile (4a). The compound was prepared according to the procedures described already, using 4-iodophenylacetonitrile (24.3 mg), pyrrole (167 μL) and triethylamine (30 μL). The crude product was purified by chromatography on silica gel and 16.0 mg 4a was obtained (yield: 95%). HRMS calculated for $[\text{C}_{11}\text{H}_8\text{N}_2\text{Na}]^+$: 191.0580; found: 191.0583.

^1H NMR (600 MHz, CDCl_3) δ 8.56 (1H), 7.64-7.62 (2H), 7.54-7.52 (2H), 6.95 (1H),

6.77 (1H), 6.35 (1H).

^{13}C NMR (150 MHz, CDCl_3) δ 136.9, 132.8, 130.1, 123.7, 121.0, 119.2, 111.1, 108.8, 108.7.

4-(1-Methyl-1H-Pyrrol-2-yl)benzotrile (4b). The compound was prepared according to the procedures described already, using 4-iodophenylacetonitrile (24.3 mg), N-methylpyrrole (226 μL) and triethylamine (30 μL). The crude product was purified by chromatography on silica gel and 16.9 mg 4b was obtained (yield: 93%). HRMS calculated for $[\text{C}_{12}\text{H}_{10}\text{N}_2\text{Na}]^+$: 205.0736; found: 205.0739.

^1H NMR (600 MHz, CDCl_3) δ 7.67-7.66 (2H), 7.50-7.49 (2H), 6.78 (1H), 6.34(1H), 6.23 (1H), 3.71 (3H).

^{13}C NMR (150 MHz, CDCl_3) δ 137.8, 132.6, 132.3, 128.3, 125.9, 119.0, 110.8, 109.7, 108.6, 35.5.

4-(1-Phenyl-1H-Pyrrol-2-yl)benzotrile (4c). The compound was prepared according to the procedures described already, using 4-iodophenylacetonitrile (24.3 mg), N-phenylpyrrole (57 mg) and triethylamine (30 μL). The crude product was purified by chromatography on silica gel and 15.4 mg 4c was obtained (yield: 63%). HRMS calculated for $[\text{C}_{17}\text{H}_{12}\text{N}_2\text{Na}]^+$: 267.0893; found: 267.0898.

^1H NMR (600 MHz, CDCl_3) δ 7.46-7.45 (2H), 7.38-7.36 (2H), 7.34-7.32 (1H), 7.19-7.15 (4H), 6.99 (1H), 6.56(1H), 6.39 (1H).

^{13}C NMR (150 MHz, CDCl_3) δ 140.1, 137.3, 131.9, 131.8, 129.4, 128.0, 127.3, 126.4, 125.8, 119.1, 112.7, 109.9, 109.3.

3-(1-Methyl-1H-Pyrrol-2-yl)benzotrile (5a, 8a, 10a). The compound was

prepared according to the procedures described already, using 3-iodophenylacetonitrile (24.3 mg)/3-bromophenylacetonitrile (19.6 mg)/3-chlorophenylacetonitrile (15.1 mg), pyrrole (167 μ L) and triethylamine (30 μ L). The crude product was purified by chromatography on silica gel and 14.5 mg 5a (yield: 86%), 14.6 mg 8a (yield: 90%), 14.0 mg 10a (yield: 83%) was obtained, respectively. HRMS calculated for $[C_{11}H_8N_2Na]^+$: 191.0580; found: 191.0583.

1H NMR (600 MHz, DMSO- d_6) δ 11.46 (1H), 8.07 (1H), 7.95-7.93 (2H), 7.57-7.52 (2H), 6.93 (1H), 6.70 (1H), 6.16 (1H).

^{13}C NMR (150 MHz, DMSO- d_6) δ 134.1, 129.9, 128.9, 128.5, 127.6, 126.3, 120.6, 118.9, 111.9, 109.5, 107.4.

3-(1H-Pyrrol-2-yl)benzonitrile (5b, 8b, 10b). The compound was prepared according to the procedures described already, using 3-iodophenylacetonitrile (24.3 mg)/3-bromophenylacetonitrile (19.6 mg)/3-chlorophenylacetonitrile (15.1 mg), N-methylpyrrole (226 μ L) and triethylamine (30 μ L). The crude product was purified by chromatography on silica gel and 15.1 mg 5b (yield: 83%), 16.0 mg 8b (yield: 88%), 13.8 mg 10b (yield: 76%) was obtained, respectively. HRMS calculated for $[C_{12}H_{10}N_2Na]^+$: 205.0736; found: 205.0743.

1H NMR (600 MHz, DMSO- d_6) δ 7.90 (1H), 7.80-7.78 (1H), 7.74-7.72 (1H), 7.62-7.59 (1H), 6.91 (1H), 6.32 (1H), 6.10 (1H), 3.69 (3H).

^{13}C NMR (150 MHz, DMSO- d_6) δ 134.1, 132.3, 130.7, 128.5, 129.8, 129.7, 125.6, 118.7, 111.8, 109.8, 107.7, 35.0.

3-(1-Phenyl-1H-Pyrrol-2-yl)benzonitrile (5c, 8c, 10c). The compound was prepared

according to the procedures described already, using 3-iodophenylacetonitrile (24.3 mg)/3-bromophenylacetonitrile (19.6 mg)/3-chlorophenylacetonitrile (15.1 mg), N-phenylpyrrole (57 mg) and triethylamine (30 μ L). The crude product was purified by chromatography on silica gel and 14.4 mg 5c (yield: 59%), 12.9mg 8c (yield: 53%), 12.0 mg 10c (yield: 49%) was obtained, respectively. HRMS calculated for $[C_{17}H_{12}N_2Na]^+$: 267.0893; found: 267.0897..

1H NMR (600 MHz, DMSO- d_6) δ 7.62-7.61 (1H), 7.52 (1H), 7.43-7.40 (3H), 7.38-7.36 (1H), 7.31-7.30 (1H), 7.21-7.19 (2H), 7.15 (1H), 6.61(1H), 6.35 (1H).

^{13}C NMR (150 MHz, DMSO- d_6) δ 139.5, 133.7, 132.0, 130.6, 129.6, 129.4, 129.3, 127.2, 126.0, 125.7, 118.6, 112.2, 111.4, 109.7.

2-(1-Methyl -1H-Pyrrol-2-yl)benzonitrile (6a, 7a, 9a). The compound was prepared according to the procedures described already, using 2-iodophenylacetonitrile (24.3 mg)/2-bromophenylacetonitrile (19.6 mg)/2-chlorophenylacetonitrile (15.1 mg), pyrrole (167 μ L) and triethylamine (30 μ L). The crude product was purified by chromatography on silica gel and 16.1 mg 6a (yield: 96%), 14.5 mg 7a (yield: 86%), 15.6 mg 9a (yield: 93%) was obtained, respectively. HRMS calculated for $[C_{11}H_8N_2Na]^+$: 191.0580; found: 191.0587.

1H NMR (600 MHz, DMSO- d_6) δ 11.50 (1H), 7.82-7.81 (1H), 7.73-7.69 (2H), 7.37-7.34 (1H), 7.01 (1H), 6.85 (1H), 6.23 (1H).

^{13}C NMR (150 MHz, DMSO- d_6) δ 135.8, 134.1, 133.1, 128.2, 126.7, 125.9, 120.9, 120.2, 110.4, 110.3, 106.1.

2-(1H-Pyrrol-2-yl)benzonitrile (6b, 7b, 9b). The compound was prepared according

to the procedures described already, using 2-iodophenylacetonitrile (24.3 mg)/2-bromophenylacetonitrile (19.6 mg)/2-chlorophenylacetonitrile (15.1 mg), N-methylpyrrole (226 μ L) and triethylamine (30 μ L). The crude product was purified by chromatography on silica gel and 17.5 mg 6b (yield: 96%), 16.0 mg 7b (yield: 88%), 16.4 mg 9b (yield: 90%) was obtained, respectively. HRMS calculated for $[\text{C}_{12}\text{H}_{10}\text{N}_2\text{Na}]^+$: 205.0736; found: 205.0739.

^1H NMR (600 MHz, CDCl_3) δ 7.74-7.73 (1H), 7.62-7.59 (1H), 7.44-7.39 (2H), 6.79 (1H), 6.40 (1H), 6.25 (1H), 3.61 (3H).

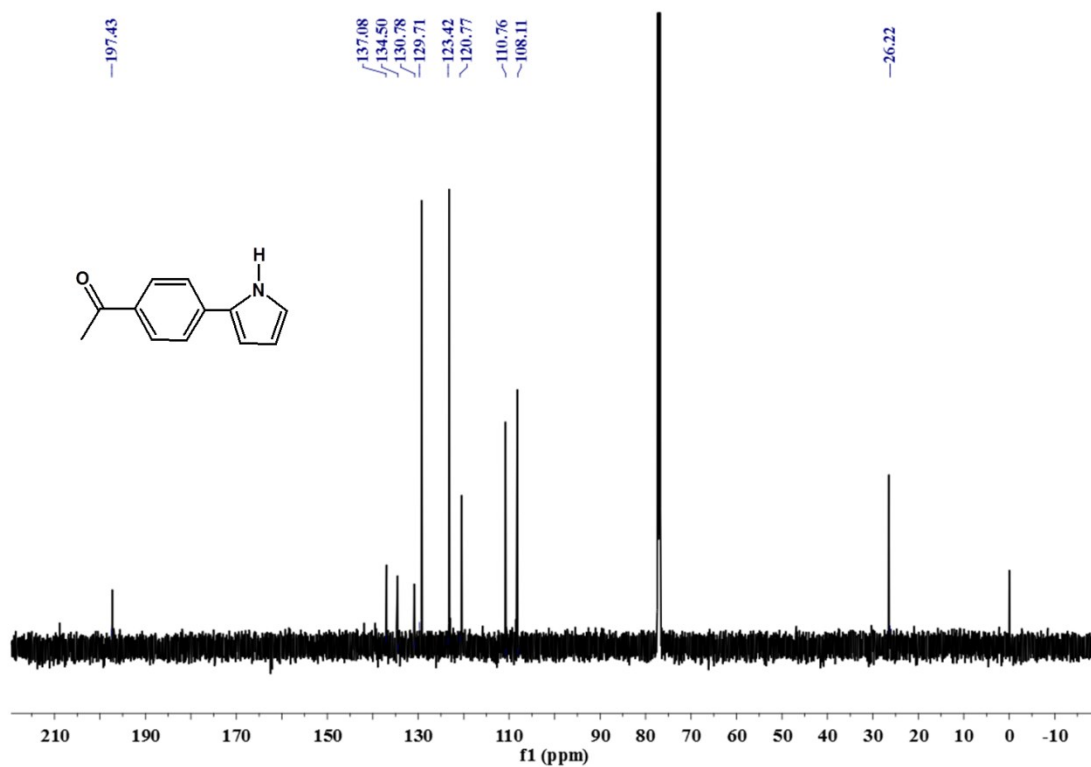
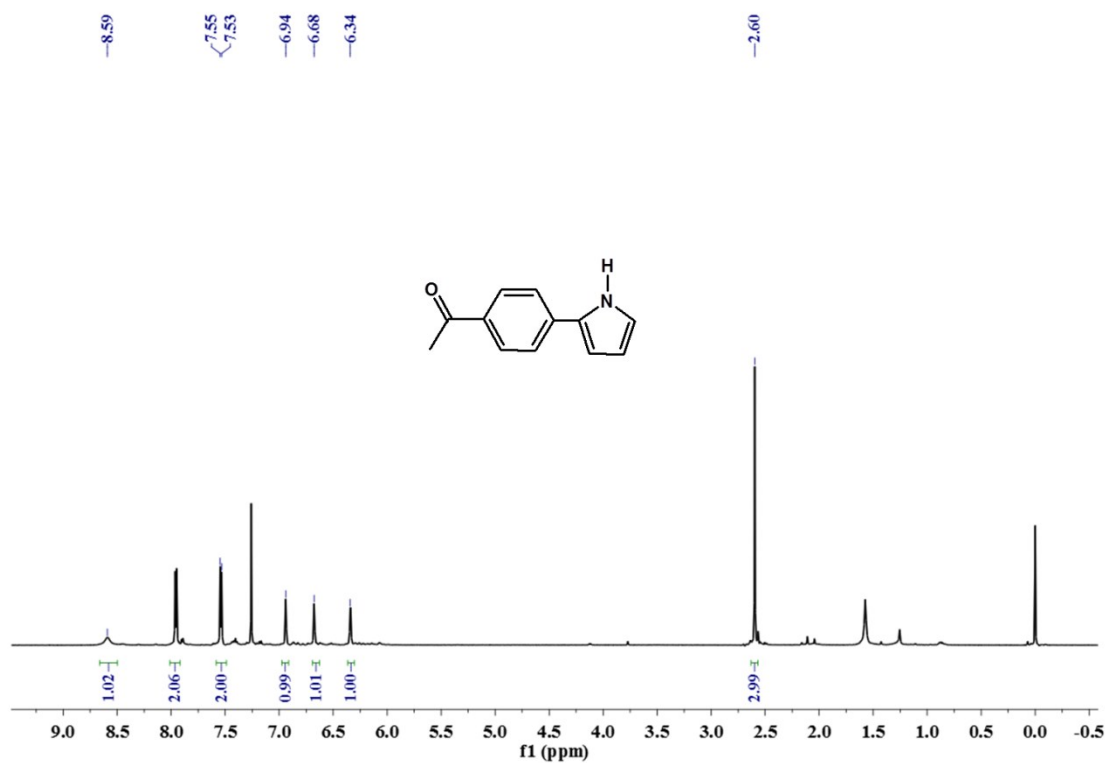
^{13}C NMR (150 MHz, CDCl_3) δ 137.0, 133.5, 132.3, 130.9, 130.0, 127.4, 124.8, 118.6, 112.9, 111.5, 108.3, 34.8.

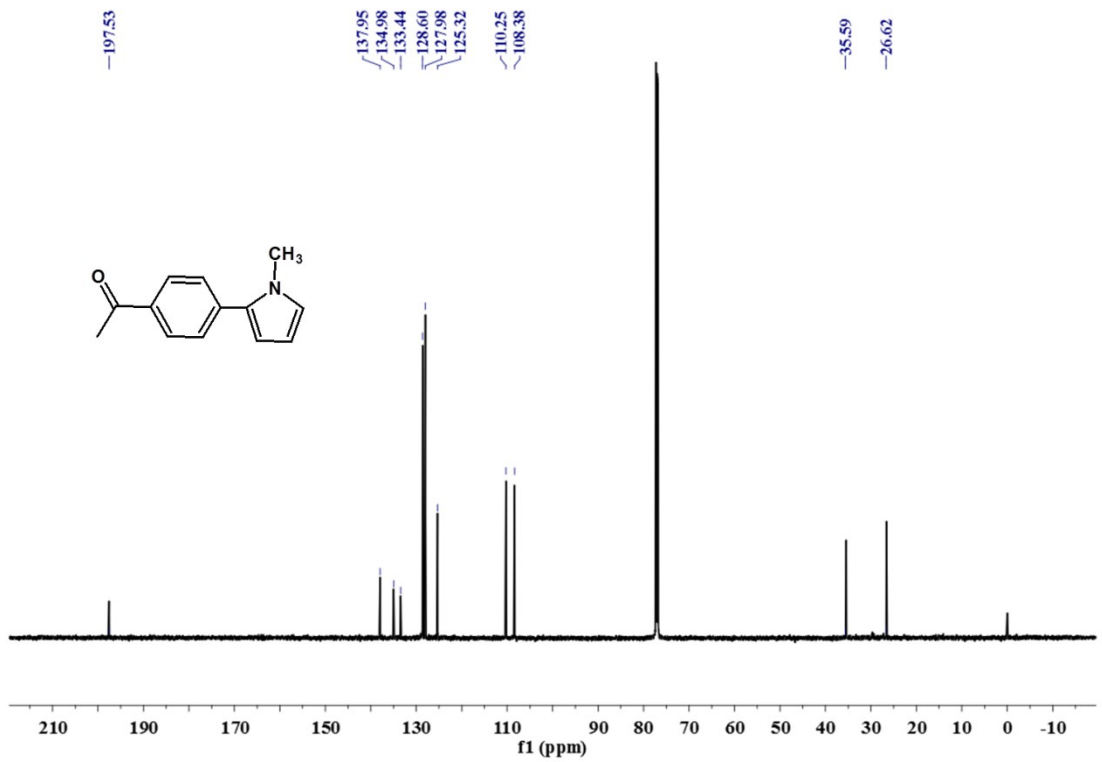
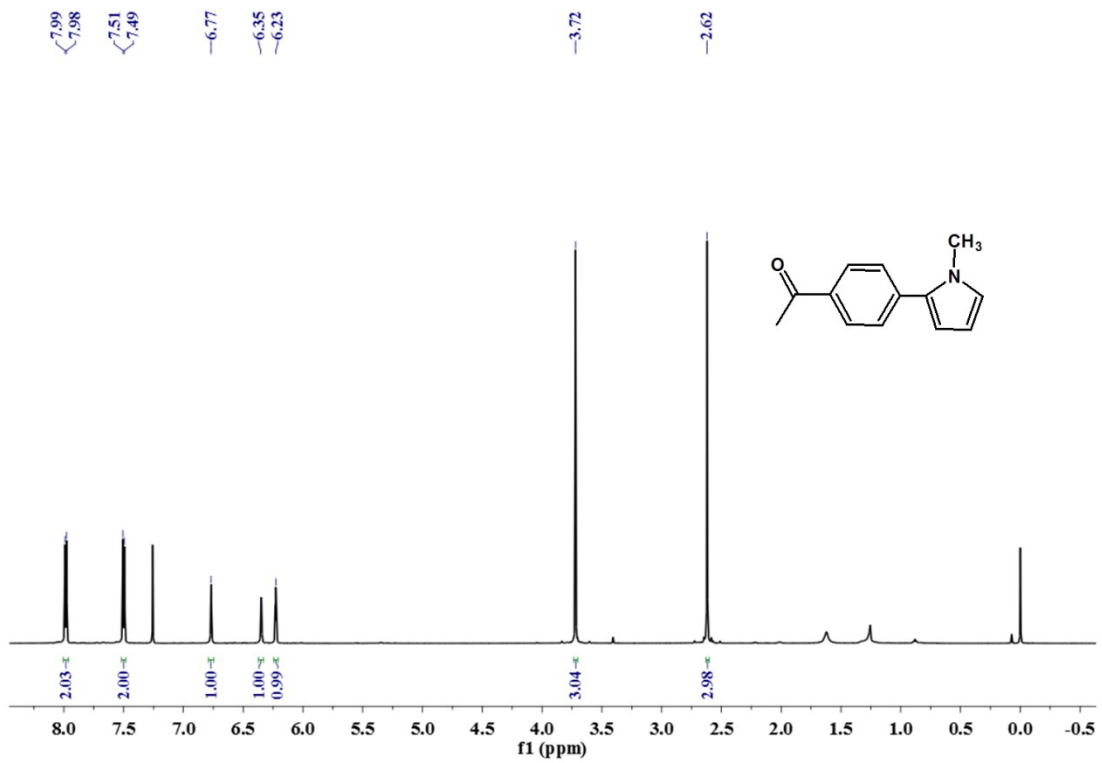
2-(1-Phenyl-1H-Pyrrol-2-yl)benzonitrile (6c, 7c, 9c). The compound was prepared according to the procedures described already, using 2-iodophenylacetonitrile (24.3 mg)/2-bromophenylacetonitrile (19.6 mg)/2-chlorophenylacetonitrile (15.1 mg), N-phenylpyrrole (57 mg) and triethylamine (30 μ L). The crude product was purified by chromatography on silica gel and 14.2 mg 6c (yield: 58%), 12.0 mg 7c (yield: 49%), 12.7 mg 9c (yield: 52%) was obtained, respectively. HRMS calculated for $[\text{C}_{17}\text{H}_{12}\text{N}_2\text{Na}]^+$: 267.0893; found: 267.0896..

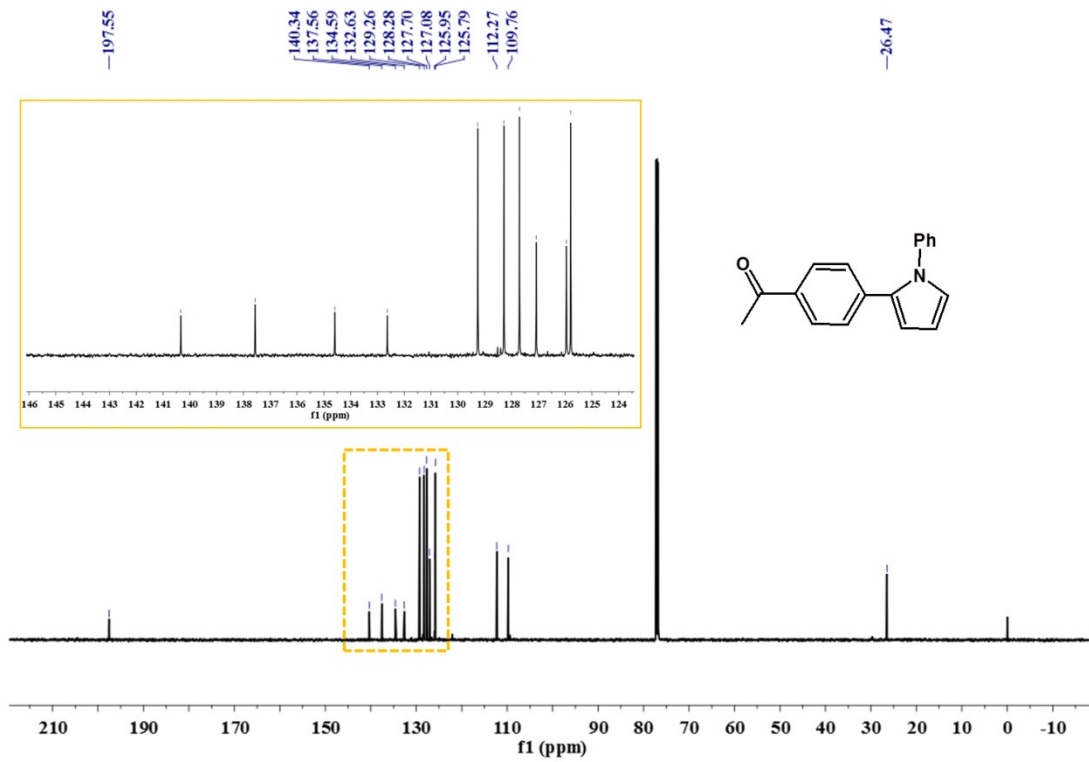
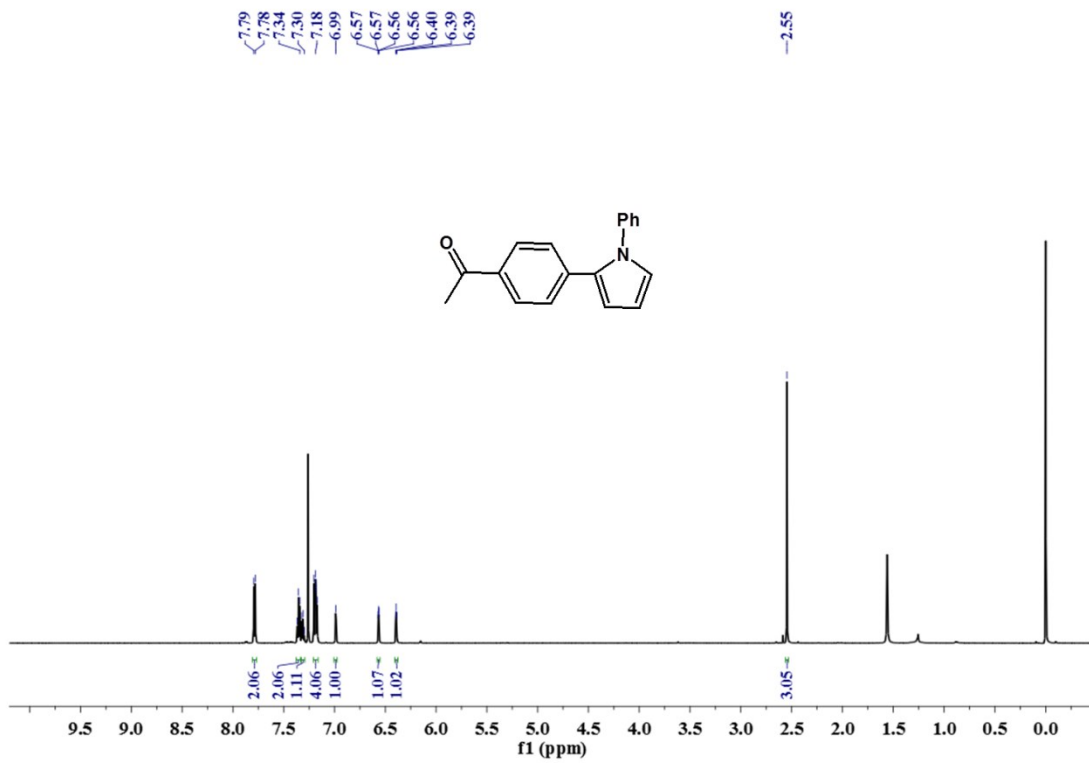
^1H NMR (600 MHz, DMSO-d_6) δ 7.82-7.81 (1H), 7.55-7.52 (1H), 7.43-7.41 (1H), 7.37-7.35 (2H), 7.30-7.27 (1H), 7.25 (1H), 7.14-7.11 (3H), 6.59(1H), 6.40 (1H).

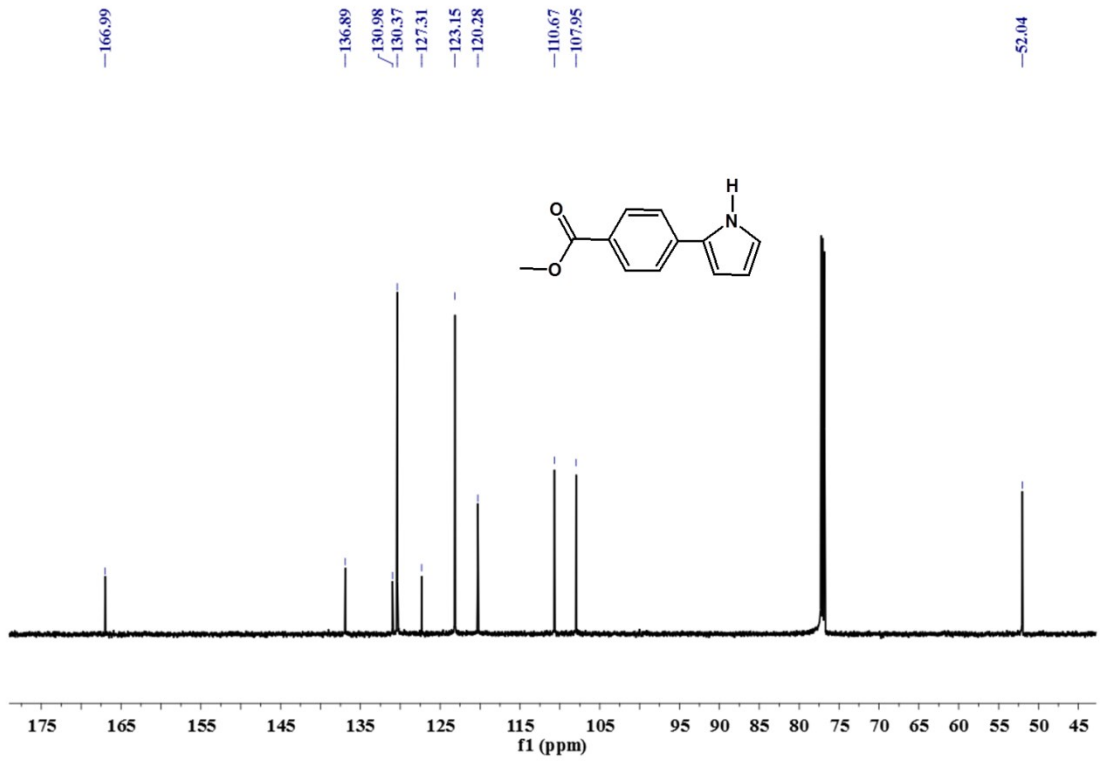
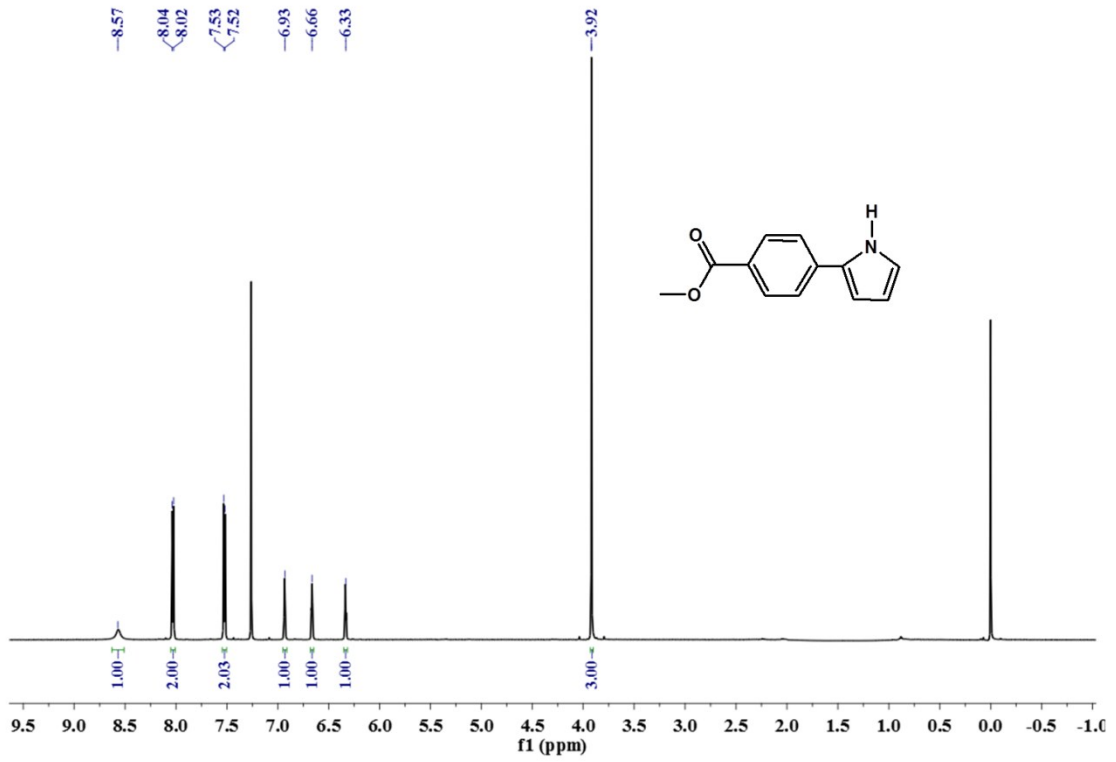
^{13}C NMR (150 MHz, DMSO-d_6) δ 139.2, 136.0, 133.5, 132.6, 130.8, 129.2, 128.6, 127.7, 126.8, 125.4, 125.1, 118.2, 113.4, 111.2, 109.5.

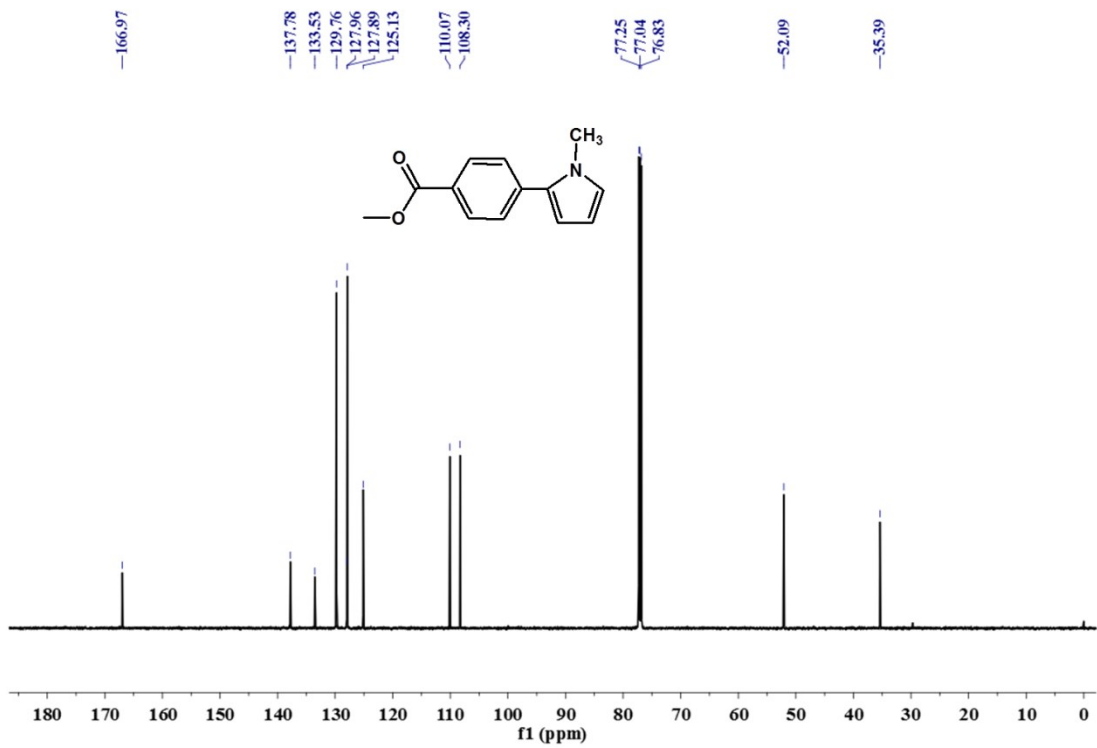
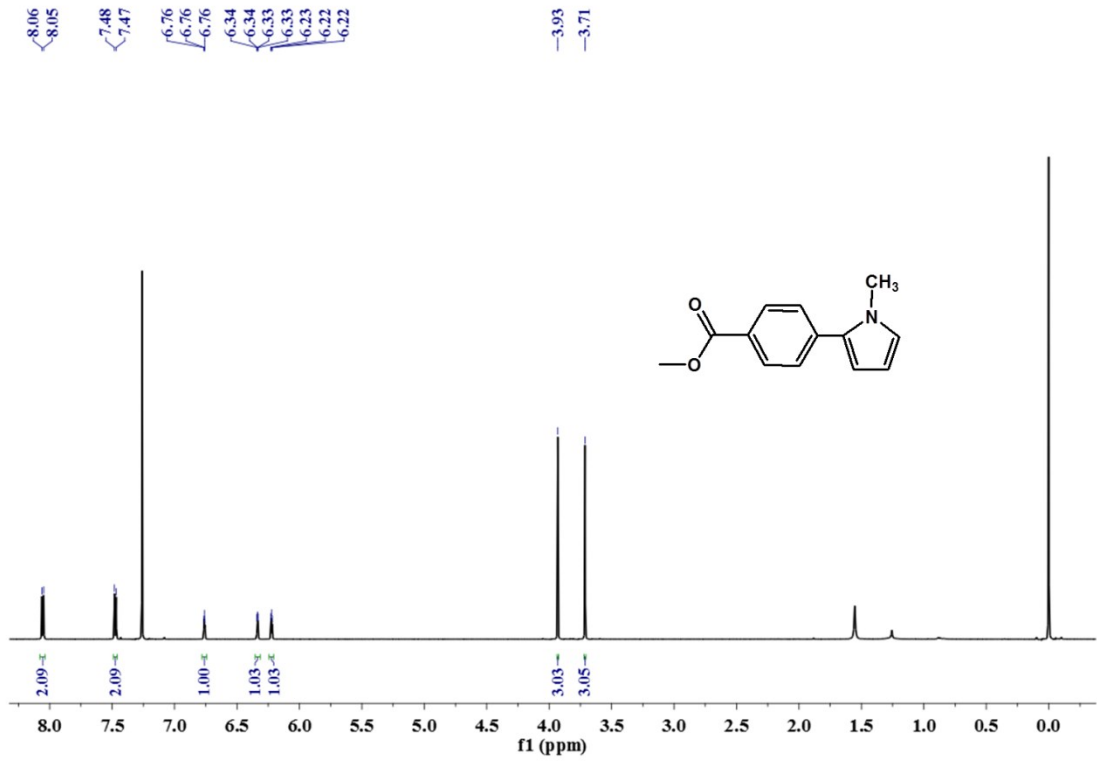
6. NMR Spectra

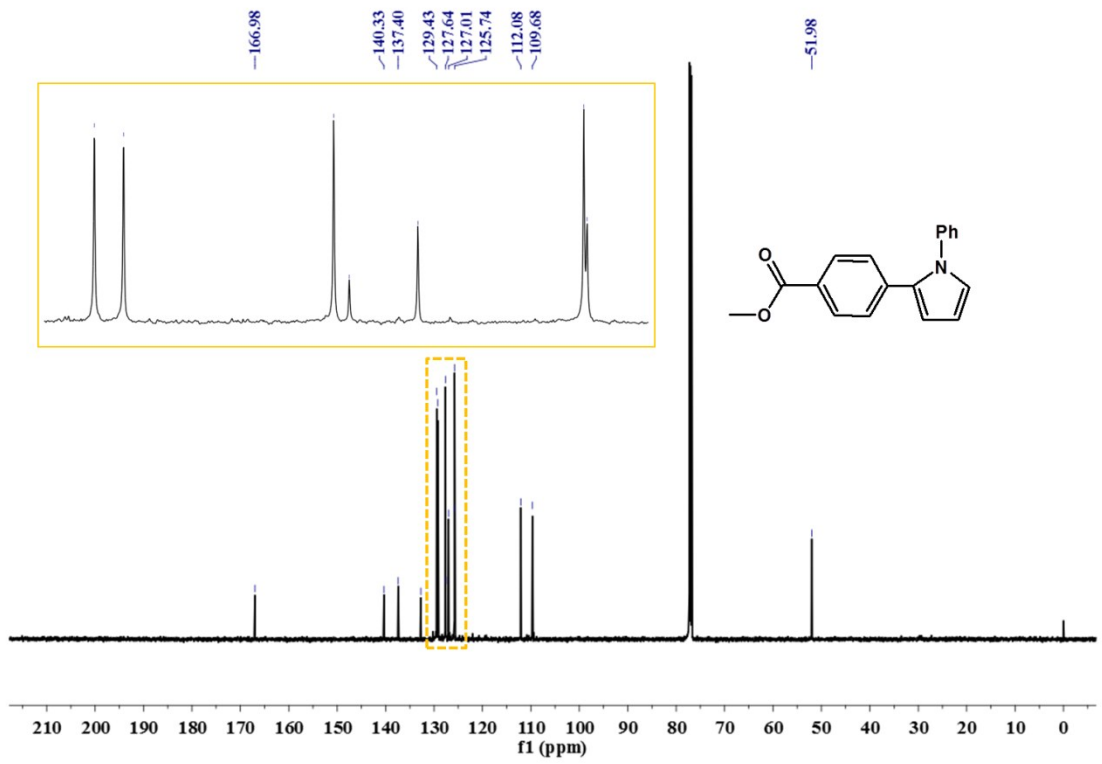
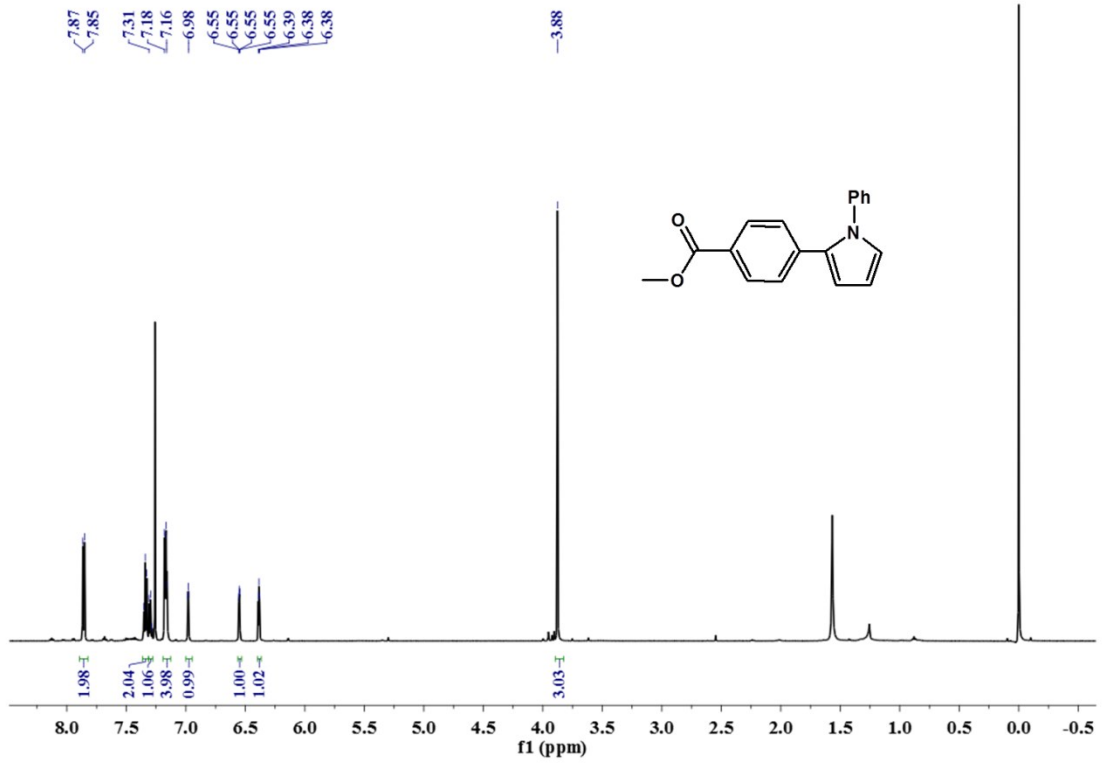


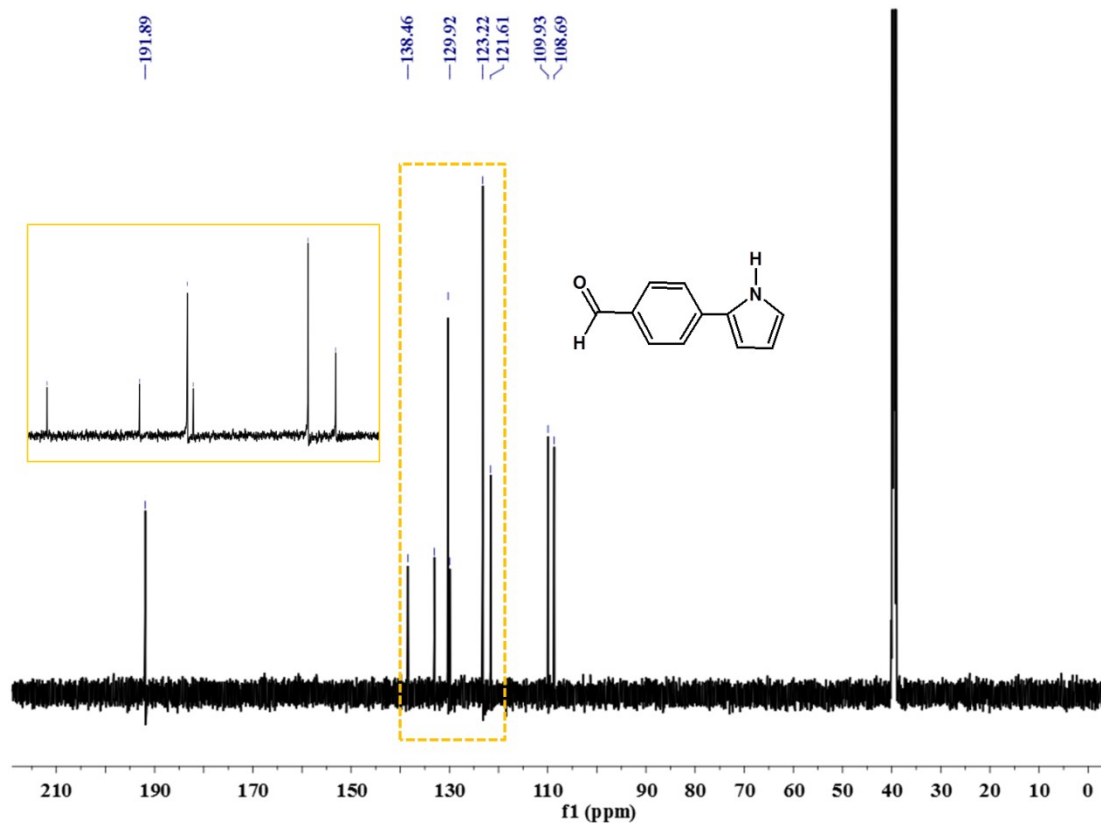
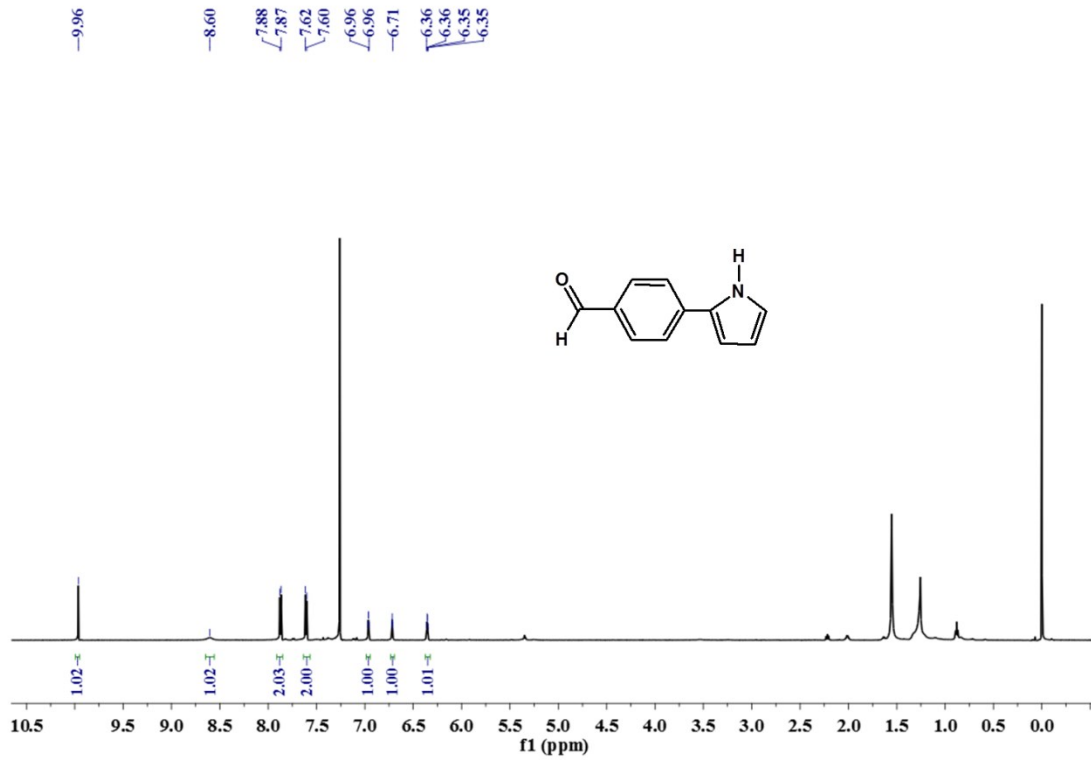


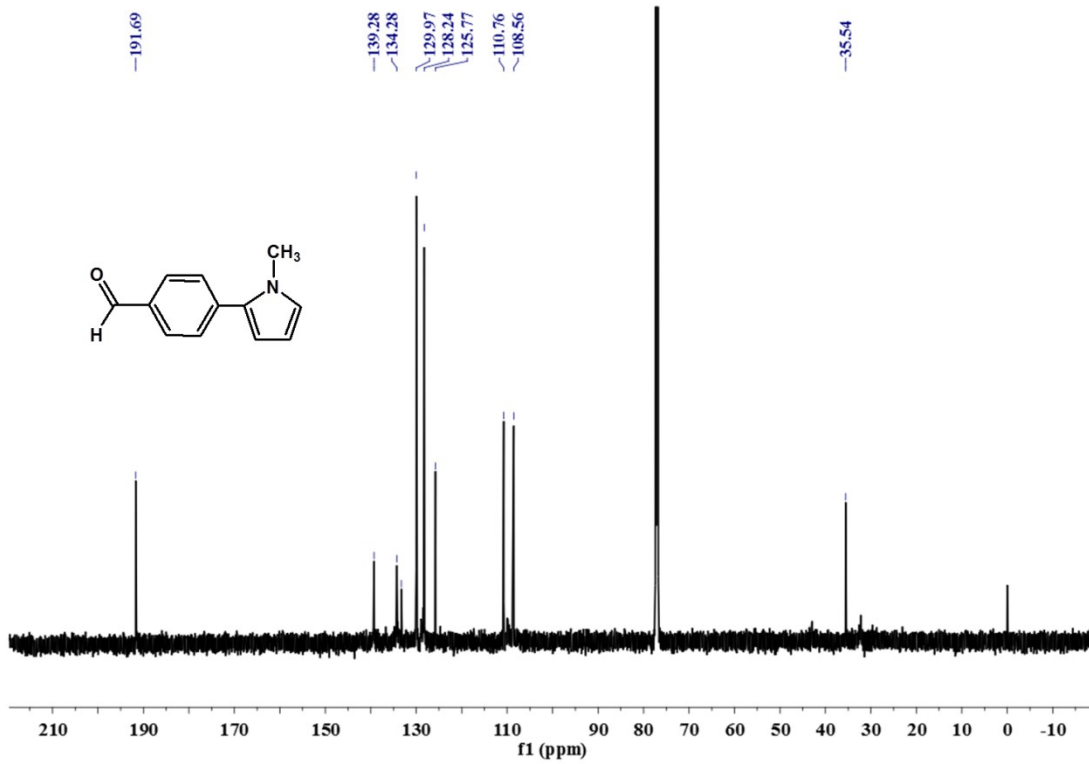
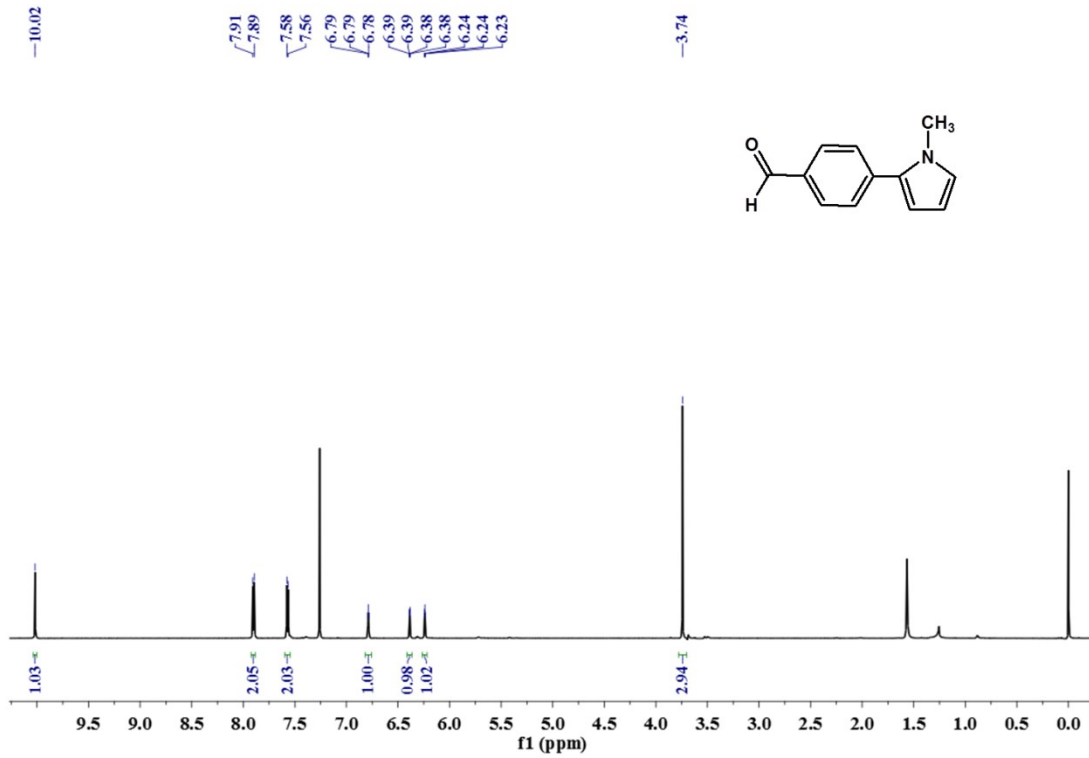


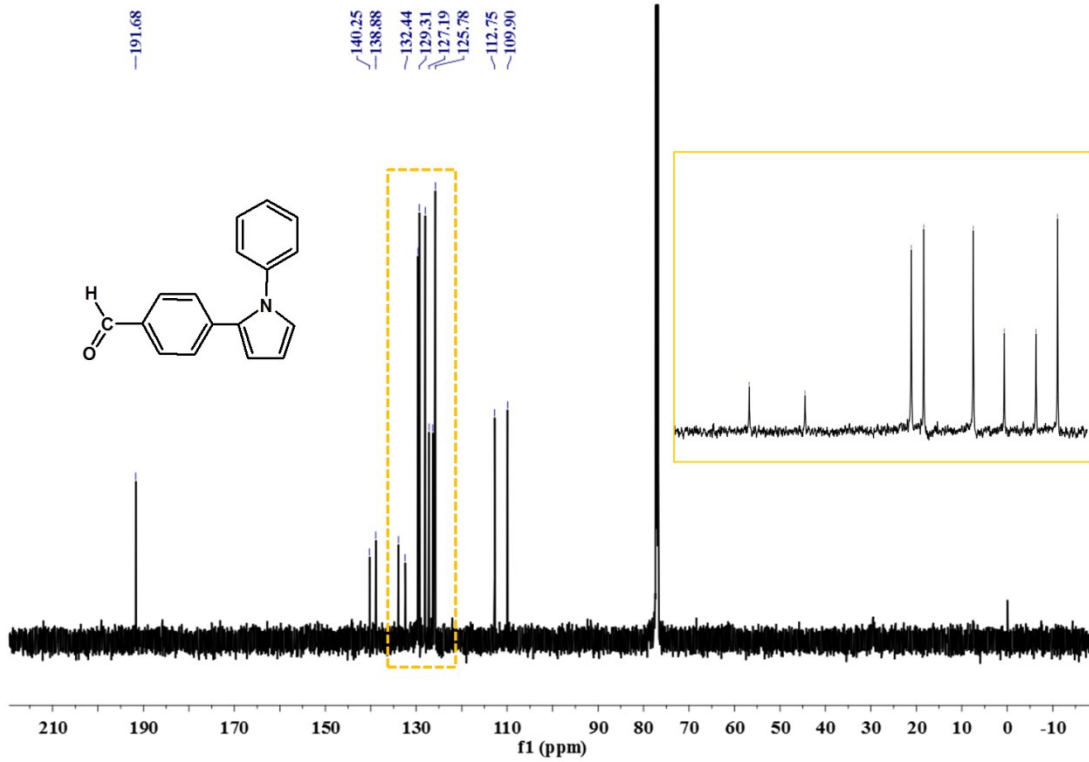
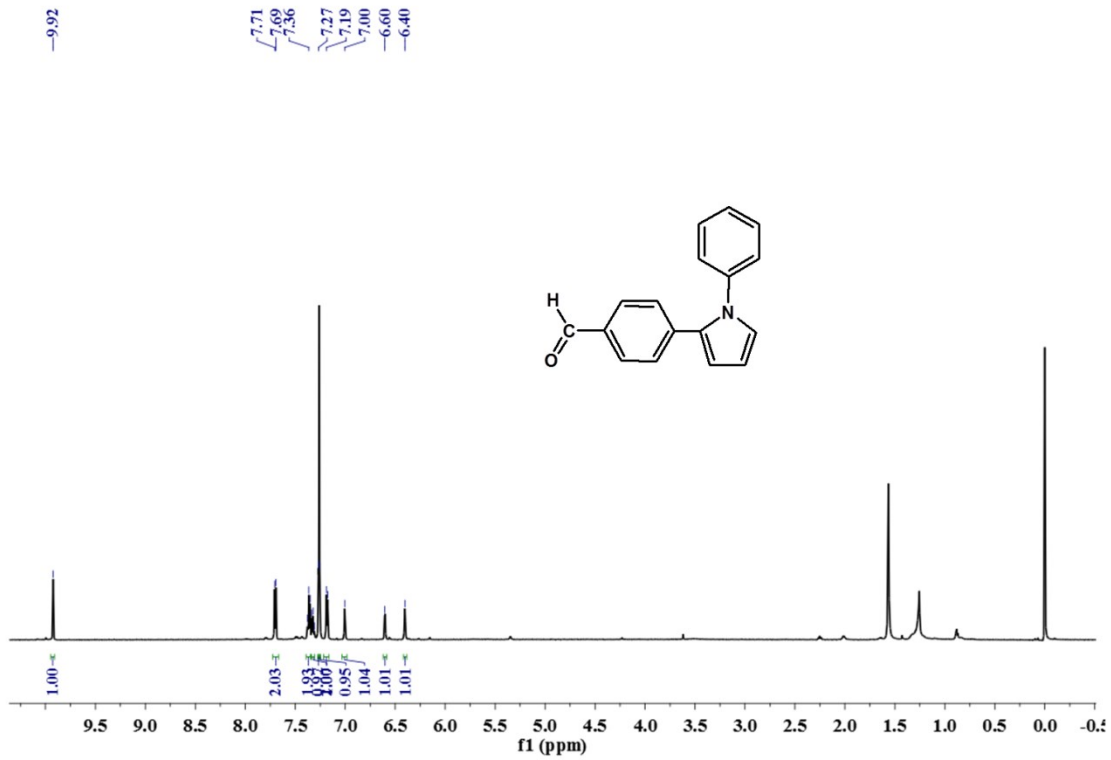


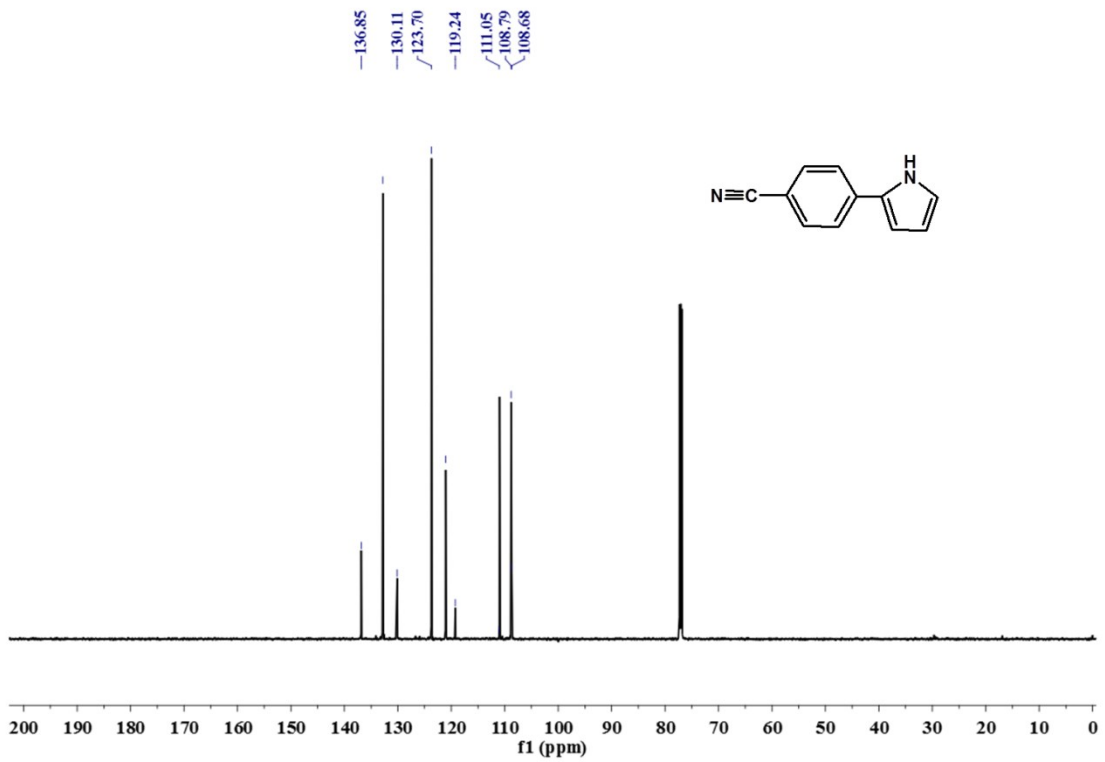
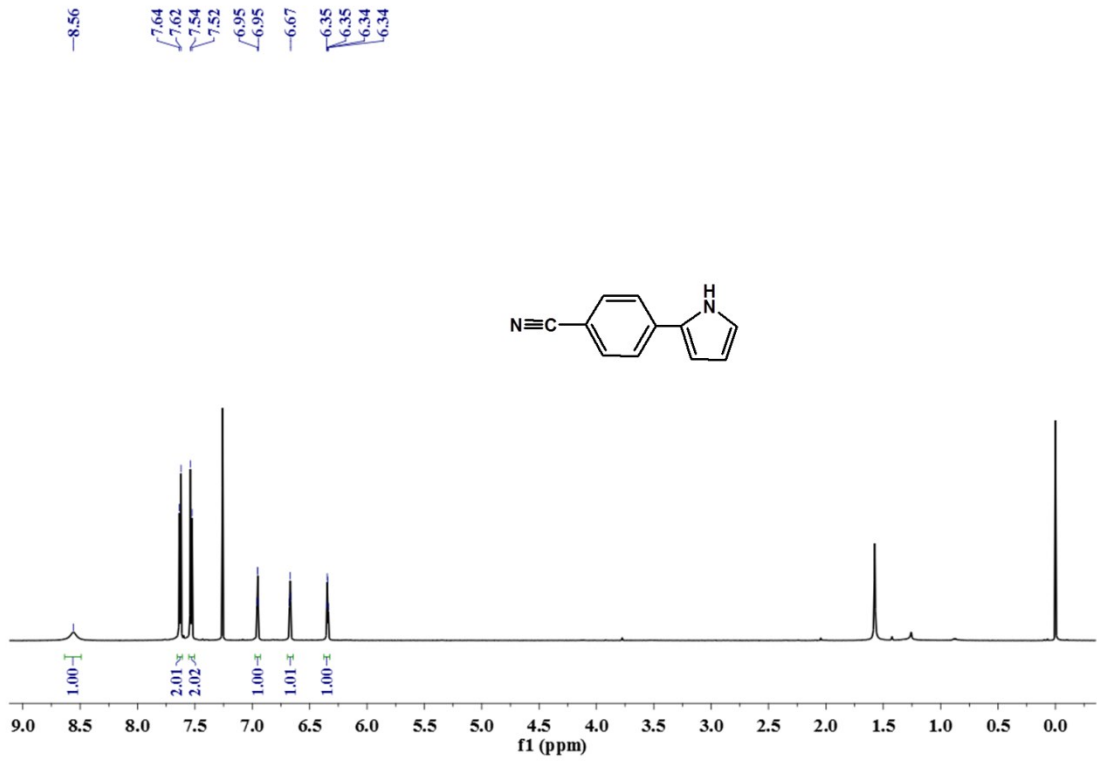


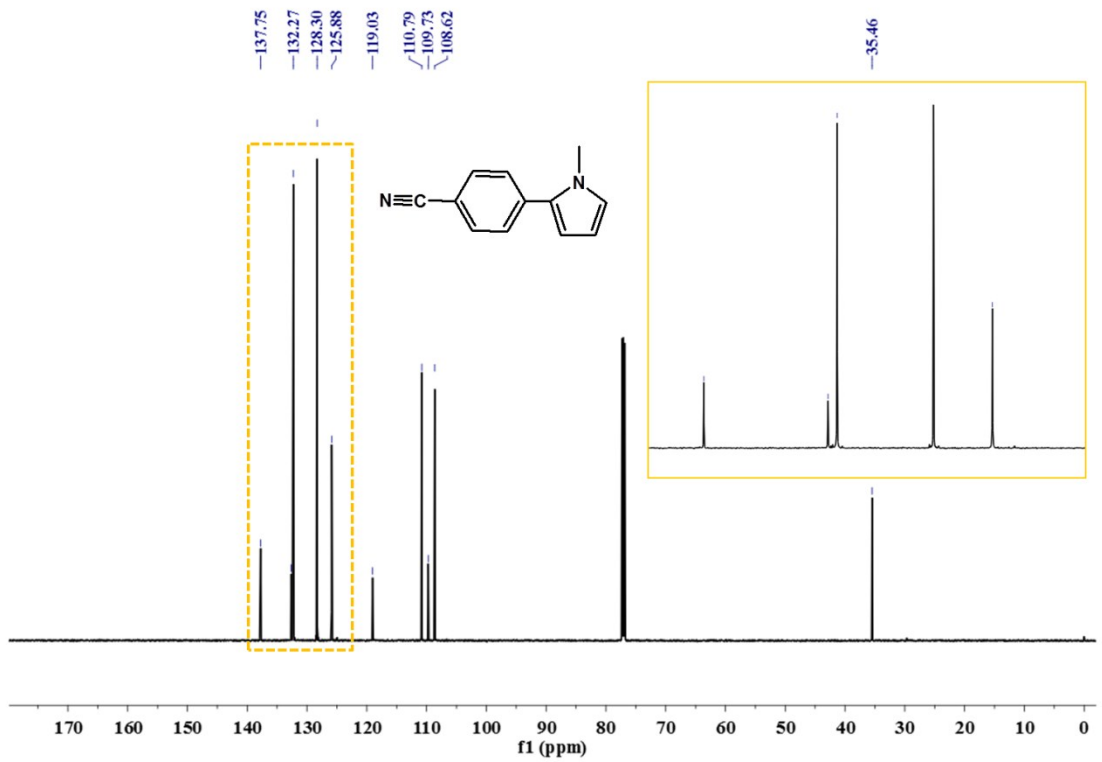
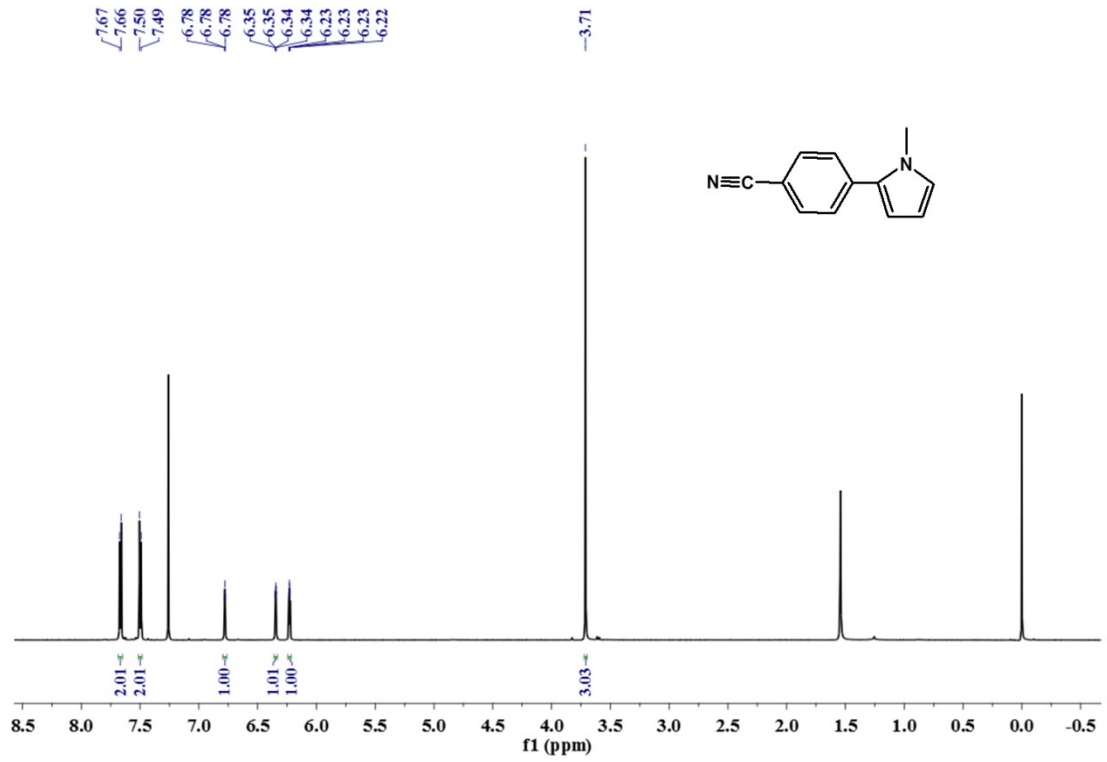


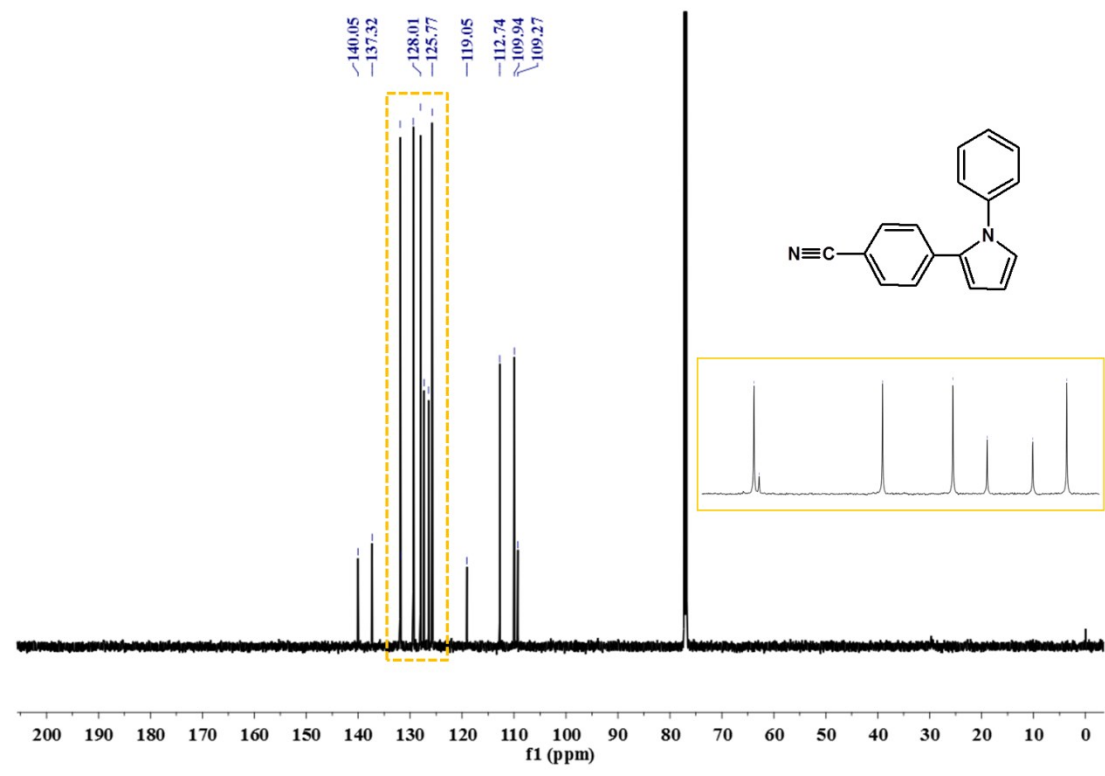
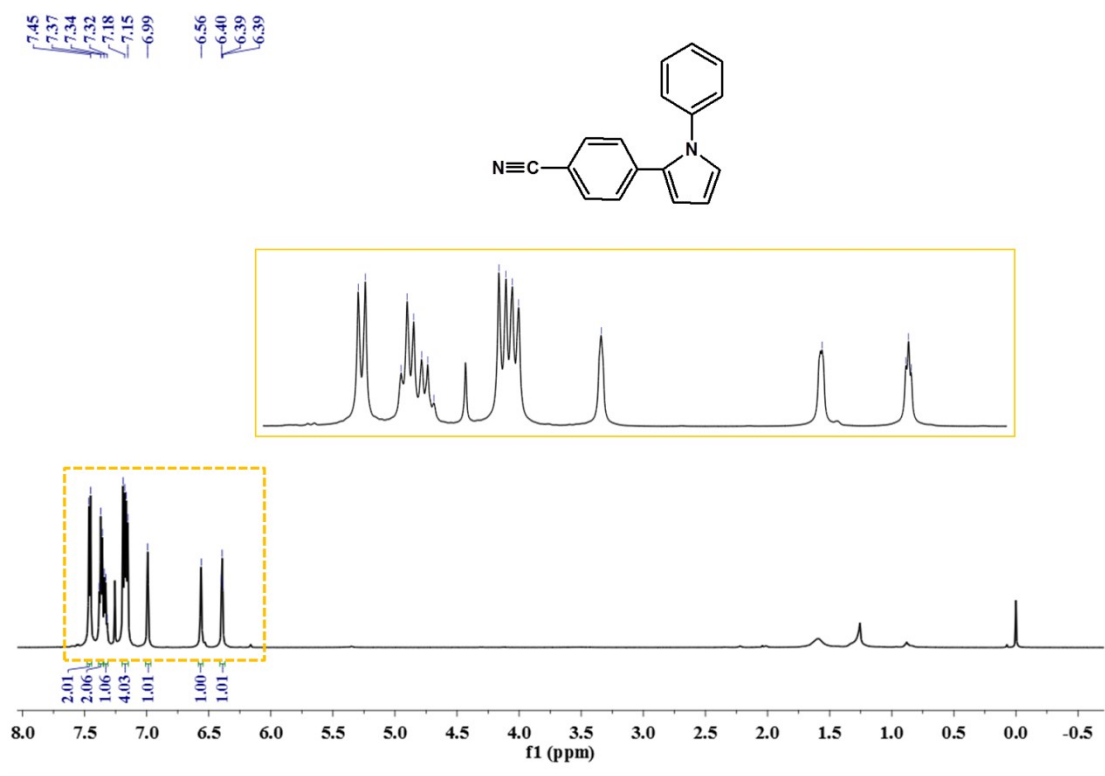


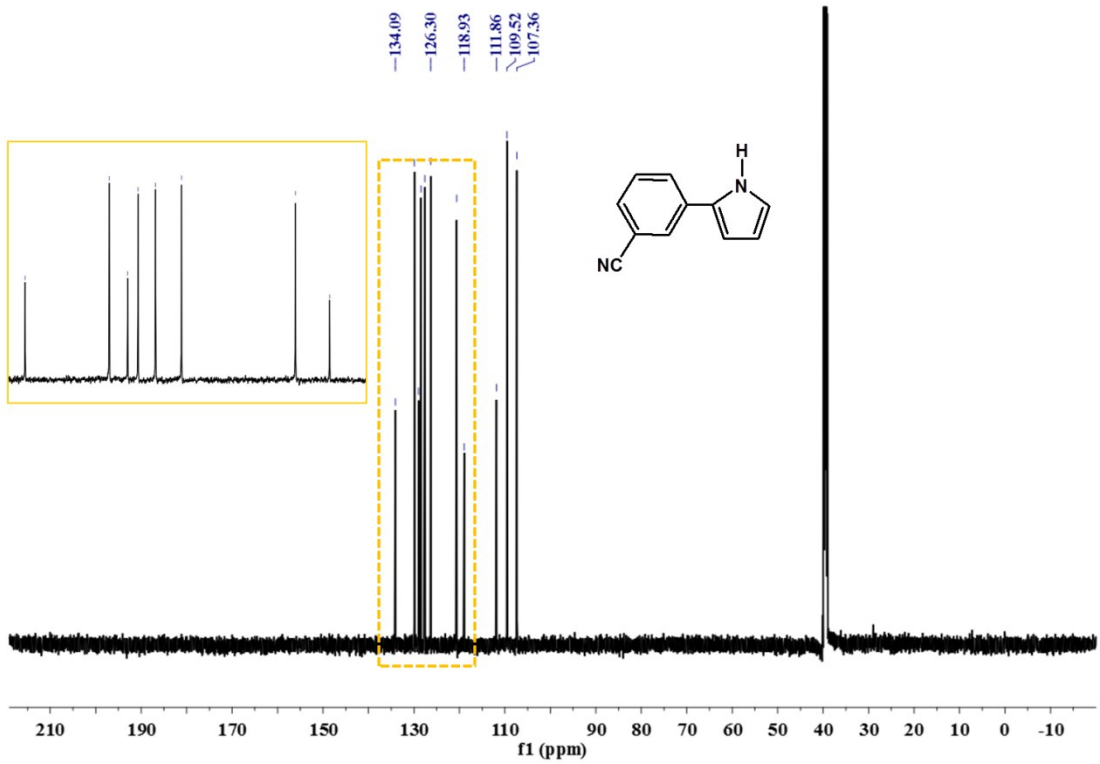
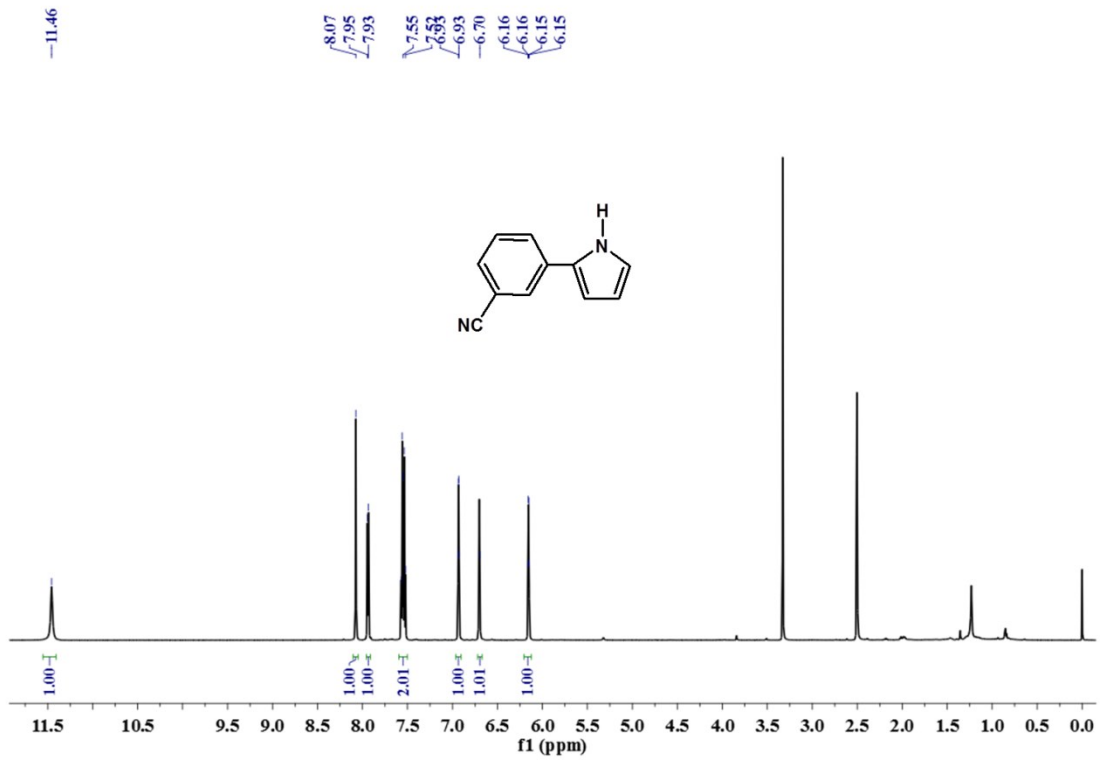


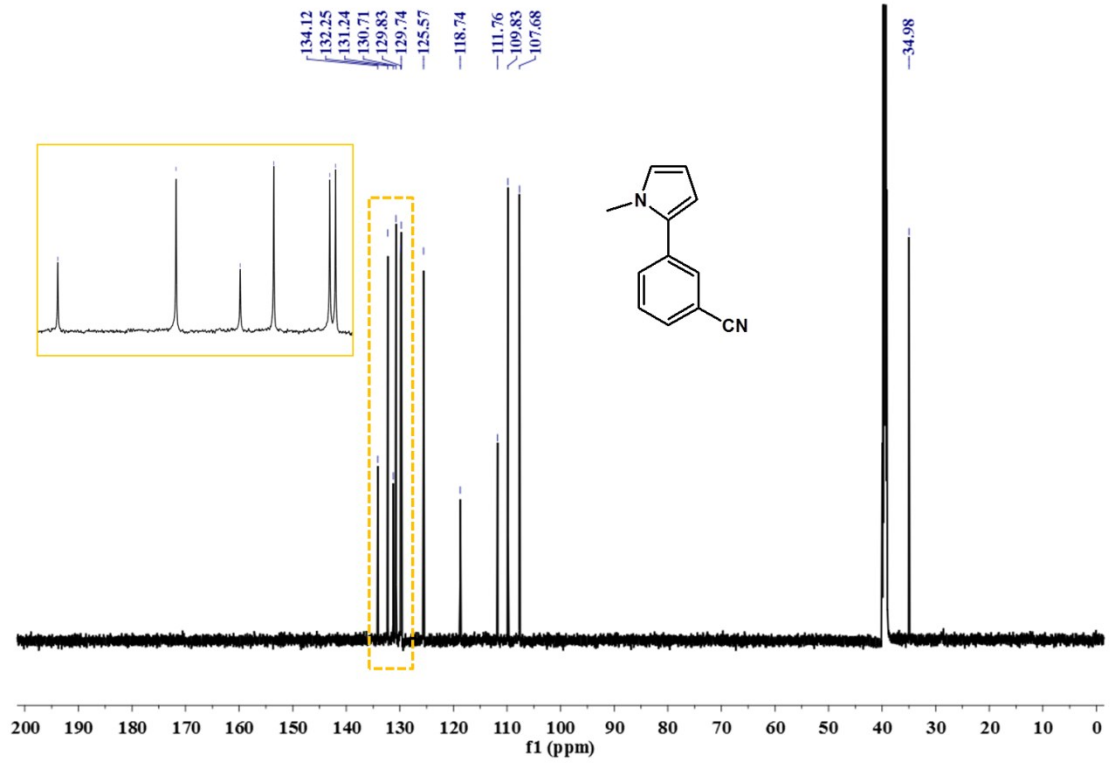
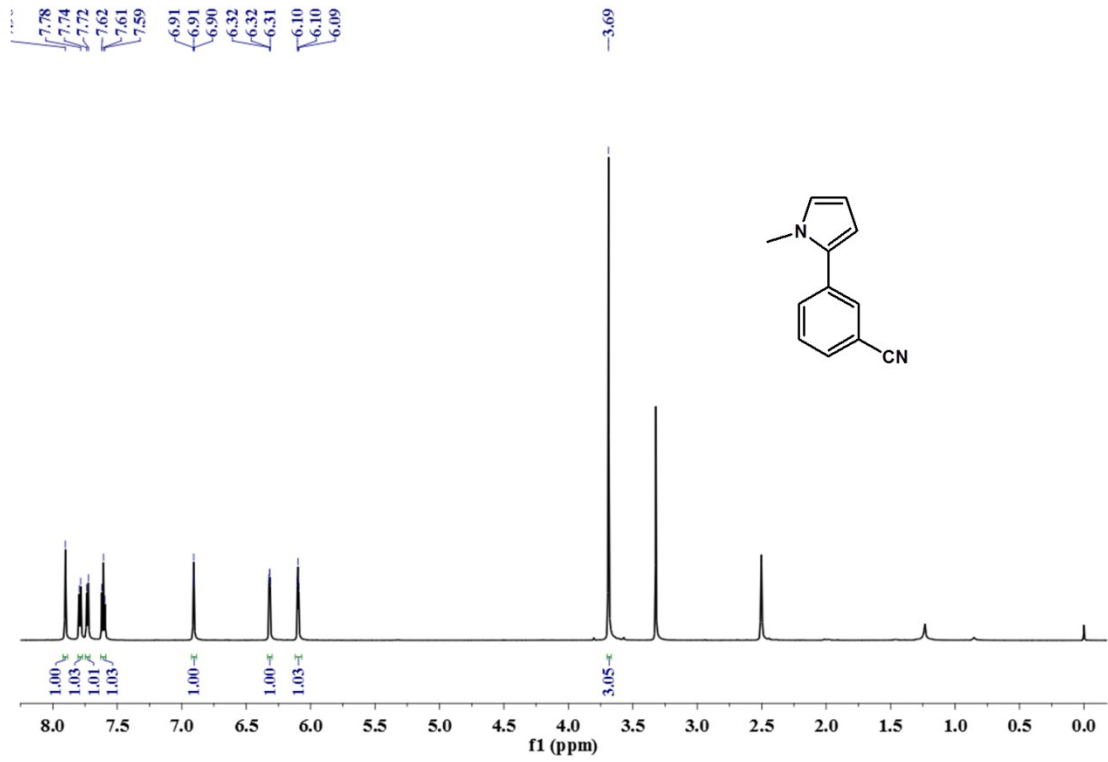


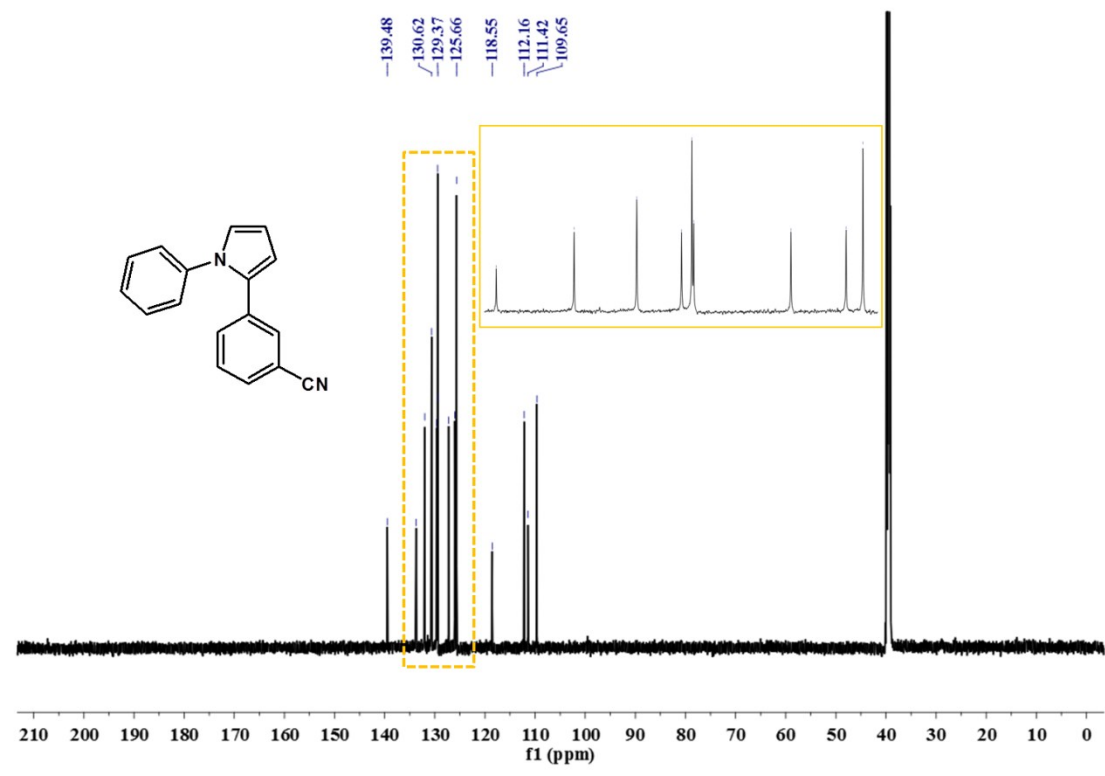
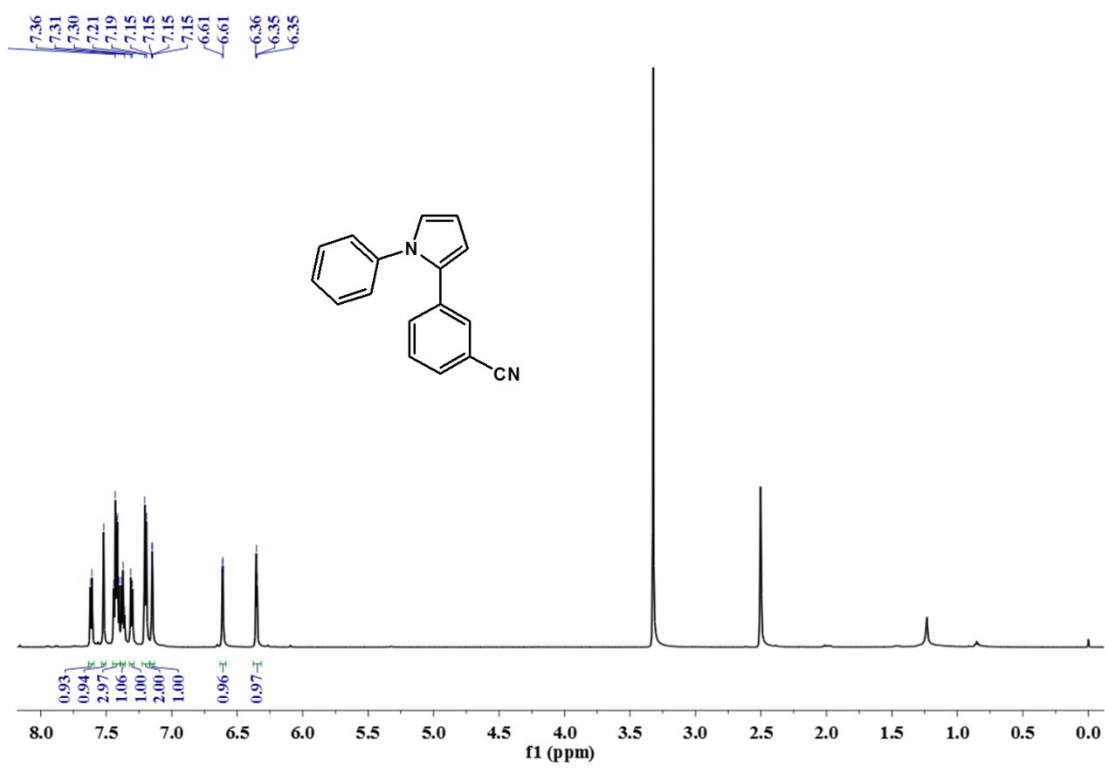


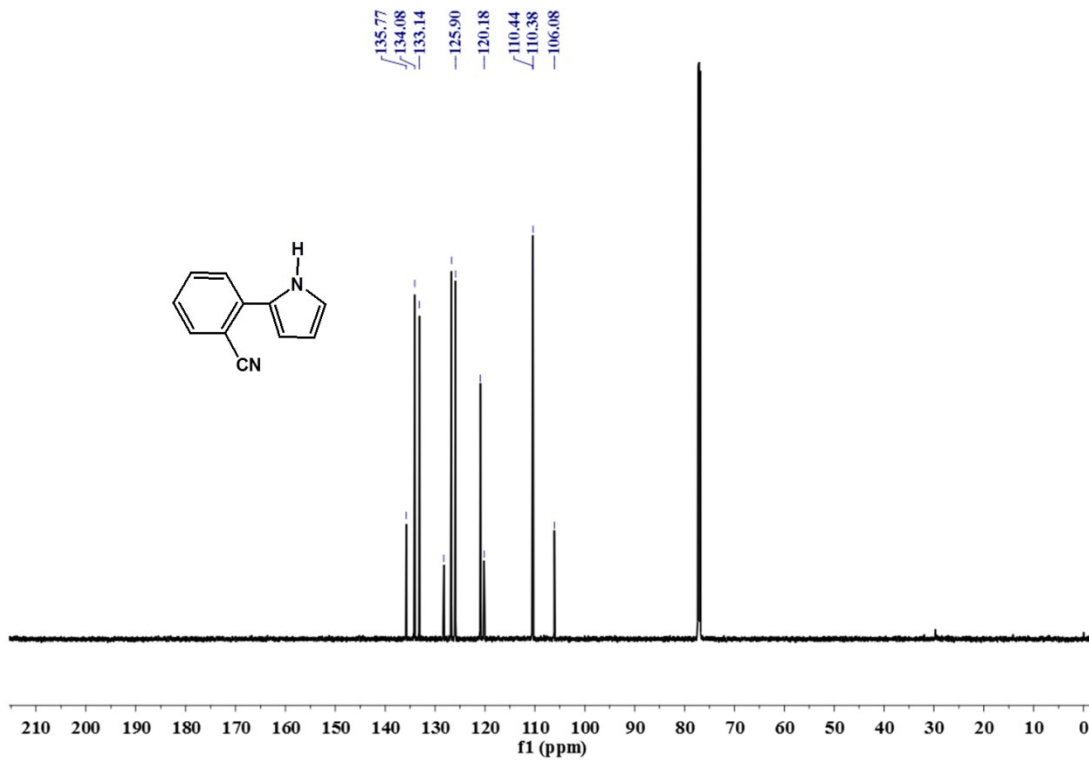
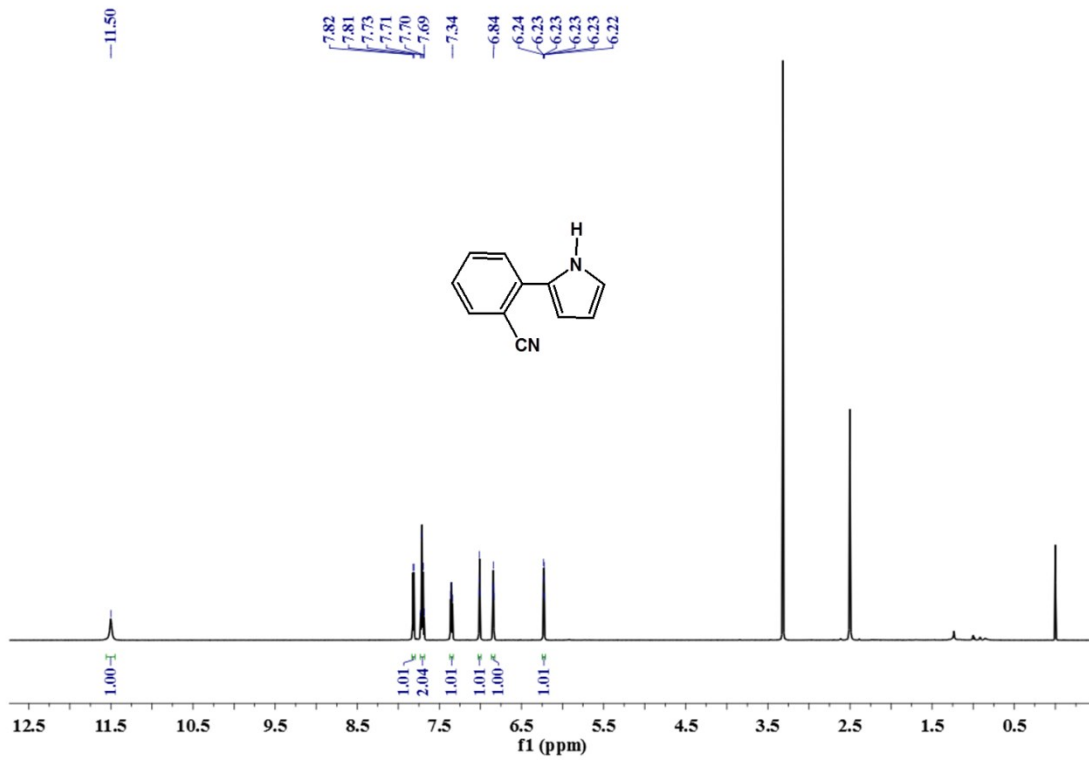


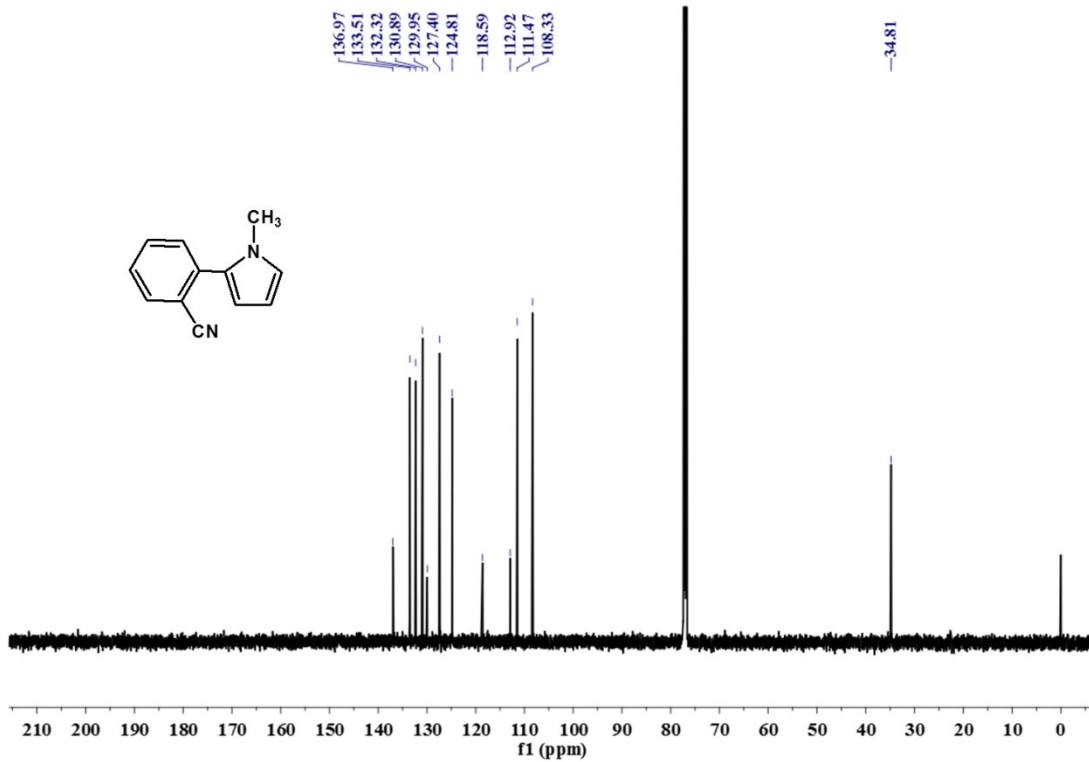
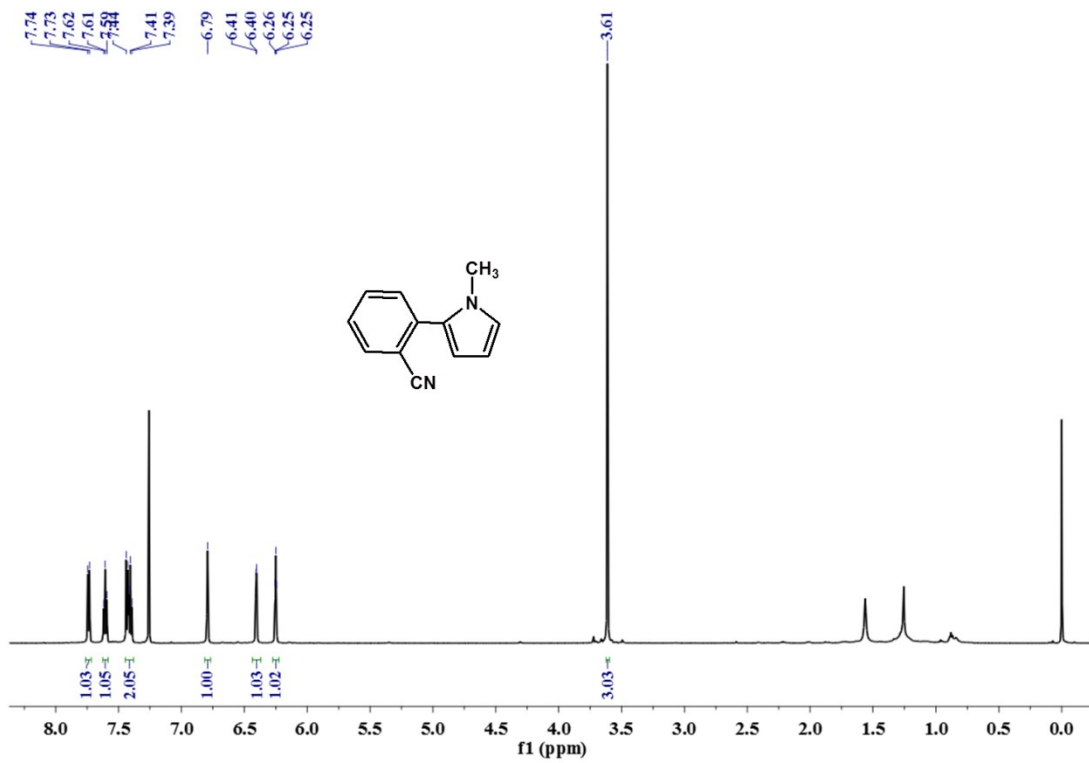


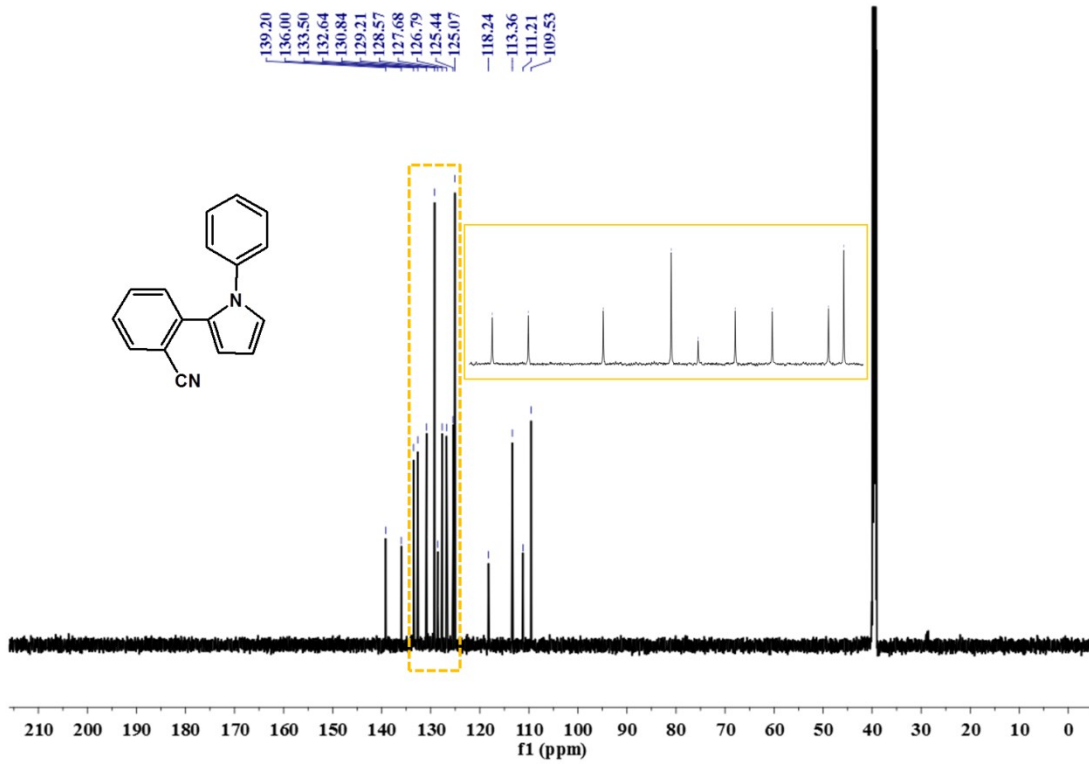
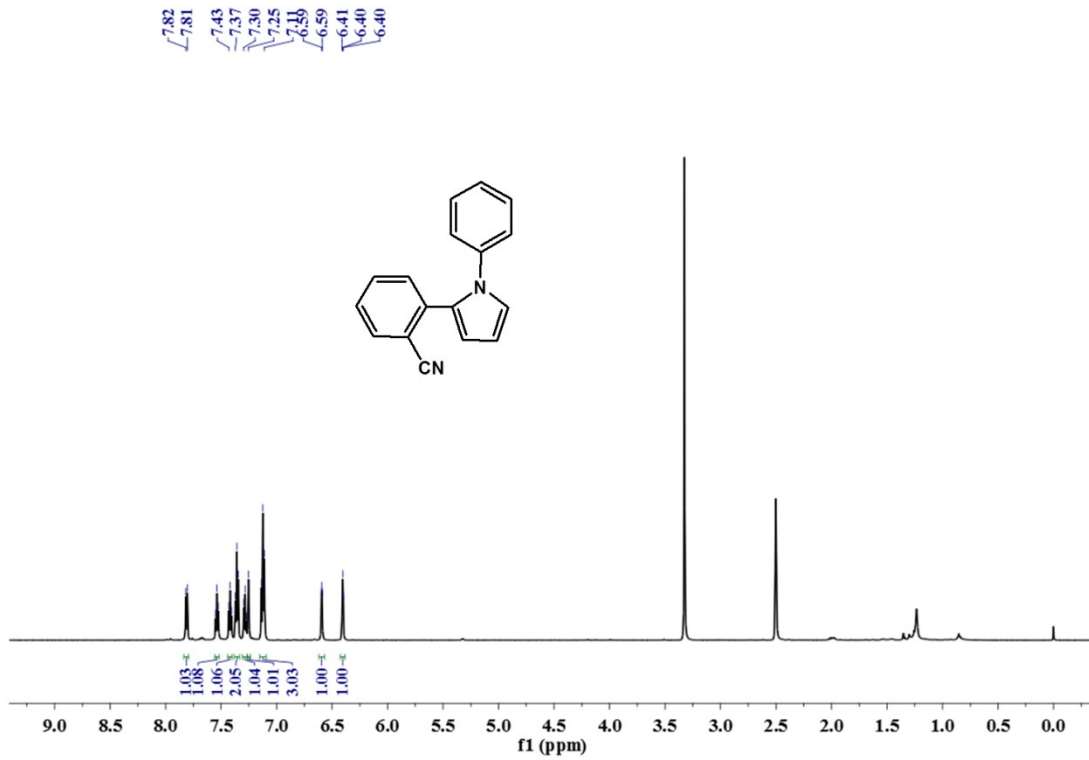












7. References

- (1) Dreizler, R. M.; Gross, E. U. *Density functional theory. Perspect. Electron. Struct. Theory* **1990**, 255-368.
- (2) Cohen, A. J.; Mori-Sánchez, P.; Yang, W. *Chem. Rev.* **2012**, 112, 289-320.
- (3) Zhao, Y.; Truhlar, D. G.; Spectus, C. O. N. *Acc. Chem. Res.* **2008**, 41, 157-167.
- (4) Zhao, Y.; Truhlar, D. G. *Theor. Chem. Acc.* **2007**, 120, 215-241.
- (5) Grimme, S. *Wiley Interdiscip. Rev. Comput. Mol. Sci.* **2011**, 1, 211-228.
- (6) Rappoport, D.; Furche, F. *J. Chem. Phys.* **2010**, 133, 134105.
- (7) Schuchardt, K. L.; Didier, B. T.; Elsethagen, T.; Sun, L.; Gurumoorthi, V.; Chase, J.; Li, J.; Windus, T. L. *J. Chem. Inf. Model.* **2007**, 47, 1045-1052.
- (8) Marenich, A. V.; Cramer, C. J.; Truhlar, D. G. *J. Phys. Chem. B* **2009**, 113, 6378-6396.
- (9) Marques, M. A. L. *et al. Phys. Chem. Chem. Phys.* **2009**, 11, 4436-4436.
- (10) Burke, K.; Werschnik, J.; Gross, E. K. U. *J. Chem. Phys.* **2005**, 123, 062206.
- (11) Finley, J.; Malmqvist, P.-Å.; Roos, B. O.; Serrano-Andrés, L. *Chem. Phys. Lett.* **1998**, 288, 299-306.
- (12) Roos, B. O.; Lindh, R.; Malmqvist, P. Å.; Veryazov, V.; Widmark, P. O. *J. Phys. Chem. A* **2004**, 108, 2851-2858.
- (13) Malmqvist, P. Å.; Roos, B. O.; Schimmelpfennig, B. *Chem. Phys. Lett.* **2002**, 357, 230-240.
- (14) Aquilante, F.; Autschbach, J.; Carlson, R. K.; Chibotaru, L. F.; Delcey, M. G.; Vico, L. D.; Galván, I. F.; Ferré, N.; Frutos, L. M.; Gagliardi, L.; Garavelli, M.;

Giussani, A.; Hoyer, C. E.; Manni, G. L.; Lischka H.; Ma, D.; Malmqvist, P. Å.; Müller, T.; Nenov, A.; Olivucci, M.; Pedersen, T. B.; Peng, D.; Plasser, F.; Pritchard, B.; Reiher, M.; Rivalta, I.; Schapiro, I.; Segarra-Martí, J.; Stenrup, M.; Truhlar, D. G.; Ungur, L.; Valentini, A.; Vancoillie, S.; Veryazov, V.; Vysotskiy, V. P.; Weingart, O.; Zapata, F.; Lindh, R. J. *Comput. Chem.* **2016**, *37*, 506-541.

(15)Frisch, M. J. *et al.* Gaussian 09, Revision C.01. **2009**.