Electronic Supporting Information

One-pot Synthesis of Benzotripyrrole Derivatives from 1H-pyrroles

Pandeeti Obaiah, B. Sathish Kumar and Pradeepta K. Panda*

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1. Instrumentation and reagents:

Melting points were determined by MR-Vis$^+$ visual melting point range apparatus from LABINDIA instruments private limited. IR spectra were recorded on NICOLET iS5. LCMS analysis were carried out by Shimadzu-LCMS-2010 mass spectrometer and HRMS data were obtained with Bruker Maxis spectrometer and XEVO-G2XSQTOF#YEA1155. NMR spectra were recorded on Bruker 400 and 500 MHz FT-NMR spectrometers operating at ambient temperature. TMS was used as internal standard for ^{1}H NMR spectra. UV-Visible spectrum was recorded on Perkin Elmer Lambda-35 spectrometer. Spectroscopic grade solvent was used for absorbance measurement. Cyclic voltammetric (CV) and differential pulse voltammetric (DPV) measurements were done using CH Instruments Electrochemical analyzer and electrodes were purchased from CH Instruments Inc. All measurements were performed in dichloromethane under flow of nitrogen and 0.1M tetrabutylammonium hexafluorophosphate ($TBAPF_6$) used as a supporting electrolyte. Glassy carbon as working electrode, platinum wire as counter electrode and Ag/AgCl in (1M) KCl as reference electrode were used. The redox potentials were referenced vs. sat. calomel electrode, SCE (0.48V for Fc^+ /Fc couple vs SCE). All cyclic voltammetric data were recorded at 100 mV/s scan rate.

Crystallographic data for **3a** and **8** were collected on BRUKER APEX-II CCD microfocus diffractometer, Mo-K_α (λ = 0.71073 Å) radiation was used to collect X-ray reflections from their single crystals. Data reduction was performed using Bruker SAINT software.[S1] Intensities for absorption were corrected using and SADABS 2014/5,[S2] refined using SHELXL-2014/7[S3] with anisotropic displacement parameters for non-H atoms. Hydrogen atoms on O and N were experimentally located in difference electron density maps. All C−H atoms were fixed geometrically using HFIX command in SHELX-TL. A check of the final CIF file using PLATON[S4] did not show any missed symmetry. DTA-TG analysis was done on Perkin Elmer STA-6000.

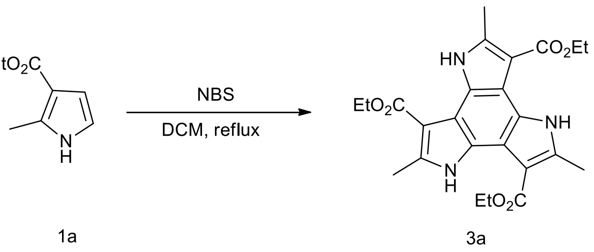
Crystallographic data (including the structure factor) for structures **3a** and **8** in this paper have been deposited in the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 1935235-1935236. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).

Commercially available solvents were distilled before use. Reagents were purchased from Sigma Aldrich, Merck and Spectrochem and used as received without further purification unless otherwise stated. Solvents for the reactions were dried according to literature methods.

2. Synthesis:

2.1) Synthesis of Triethyl 2,5,8-trimethyl-4,7-dihyro-1H-dipyrrolo[2,3-e:2',3'-g]indole-3,6,9-tricarboxylate (3a):

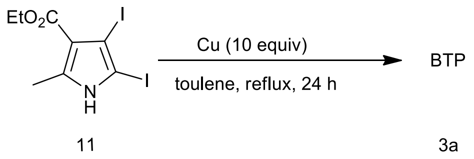
Protocol 1:



To ethyl 2-methyl-1H-pyrrole-3-carboxylate (**1a**)[S5a,S5d] (100 mg, 0.65 mmol) in DCM (5 mL), NBS (128 mg, 0.72 mmol) solution in DCM (10 mL) was added under N_2 atmosphere at room temperature and was refluxed for 24 h. The reaction mixture was cooled to room temperature and quenched by addition of aq. $NaHCO_3$ solution. Then the organic layer was separated and the aq. layer was extracted with DCM (2 x 10 mL). The combined organic layers were dried over anhyd. Na_2SO_4 and concentrated in rotary evaporator under reduced pressure. Finally the crude product was purified by silica gel column chromatography using EtOAc: hexane (5:95) as an eluent to obtain the desired product **3a** as white color solid after drying (12 mg, 12 %).

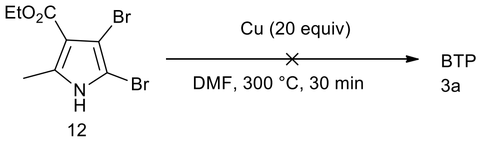
Melting point: 260-262 ^{o}C; IR (KBr) (cm^{-1}): 3320, 2956, 1659, 1431; ^{1}H NMR (500 MHz, $CDCl_3$, δ in ppm): 11.36 (s, 3H), 4.42 (q, *J* = 7.1 Hz, 6H), 2.77 (s, 9H), 1.46 (t, *J* = 7.1 Hz, 9H) ; ^{13}C NMR (125 MHz, $CDCl_3$, δ in ppm): 168.1, 137.8, 124.5, 109.1, 103.4, 15.3, 14.6; HRMS- (ESI+) m/z: calculated for $C_{24}H_{28}N_3O_6$ $[M+H]^+$: 454.1978; found: 454.1978.

Protocol 2:



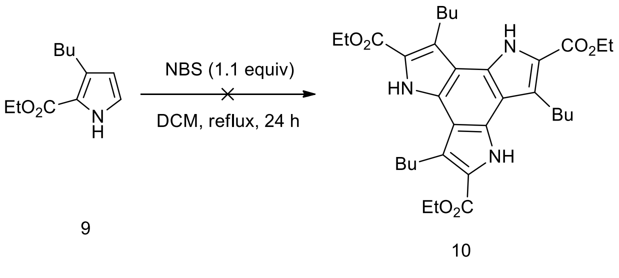
To ethyl 4,5-diiodo-2-methyl-1H-pyrrole-3-carboxylate (**11**) [S5b] (100 mg, 0.25 mmol) in toulene (15 mL), Cu (157 mg, 2.47 mmol) was added under N_2 atmosphere at room temperature and was refluxed for 24 h. After complete consumption of starting material, the reaction mixture was cooled to room temperature. The organic layer was separated and the residue was washed with DCM (2 x 10 mL). The combined organic layers were concentrated in rotary evaporator under reduced pressure. Finally the crude product was purified by silica gel column chromatography by using EtOAc: hexane (5:95) as an eluent, which resulted the product as white solid (2 mg, 2 %).

Protocol 3:



To ethyl 4,5-dibromo-2-methyl-1H-pyrrole-3-carboxylate (**12**) [S5c] (100 mg, 0.25 mmol) in DMF (1 mL), Cu (255 mg, 4.02 mmol) was added under N_2 atmosphere at room temperature and was heated for 30 min at 300 °C . The reaction mixture was cooled to room temperature and TLC confirmed the complete consumption of starting material, but there was no desired BTP **3a**.

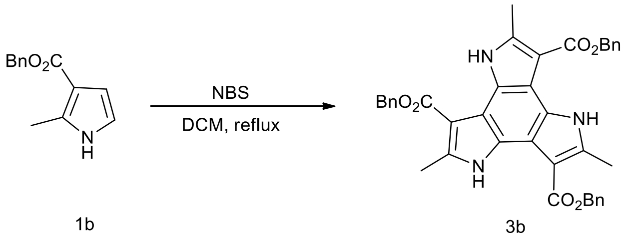
2.2) Attempted synthesis of Triethyl 3,6,9-tributyl-4,7-dihydro-1H-dipyrrolo[2,3-e:2',3'-g]indole-2,5,8-tricarboxylate (10):



To ethyl 3-butyl-1H-pyrrole-2-carboxylate (**9**)[S6] (100 mg, 0.51 mmol) in DCM (5 mL), NBS (128 mg, 0.72 mmol) solution in DCM (10 mL) was added under N_2 atmosphere at room temperature and was refluxed for 24 h. The reaction mixture was cooled to room temperature and quenched by addition of aq.$NaHCO_3$. TLC showed complete consumption of the starting material but there was no formation of desired BTP (**10**).

2.3) Synthesis of Tribenzyl 2,5,8-trimethyl-4,7-dihydrodipyrrolo[2,3-e:2',3'-g]indole-3,6,9-tricarboxylate (3b):

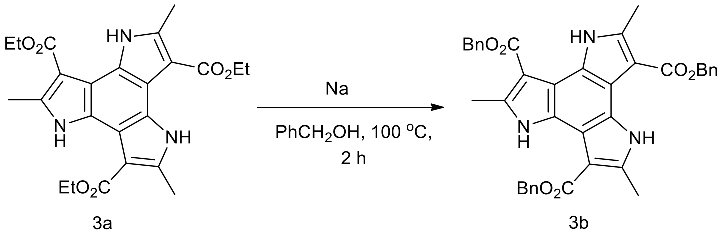
Protocol 1:



The same synthetic procedure for **3a** was followed; 5 mg product (**3b**) was obtained from 100 mg starting material (**1b**) [S5a] with 5% yield (white solid).

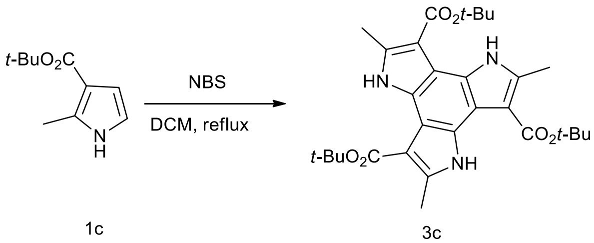
Melting point: 201-203 °C; IR (KBr) (cm^{-1}): 3345, 2929, 1671, 1424; ^{1}H NMR (400 MHz, CDCl$_3$, δ in ppm):11.25 (s, 3H), 7.49 (d, *J* = 7 Hz, 2H), 7.42(t, *J* = 7 Hz, 3H), 7.37 (d, *J* = 7 Hz, 2H) 5.43 (s, 6H), 2.67 (s, 9H); ^{13}C NMR (100 MHz, CDCl$_3$, δ in ppm):167.60, 138.7, 136.6, 128.8, 128.3, 128.2, 103.2, 66.2, 15.4; HRMS (ESI+) : m/z : calculated for $C_{39}H_{34}N_3O_6$ $[M+H]^+$: 640.2447; found: 640.2430.

Protocol 2:



To sodium metal (25 mg) in benzyl alcohol (2 mL), BTP **3a** (100 mg, 0.22 mmol) in benzyl alcohol (3 mL) was added under N_2 atmosphere at room temperature and was stirred at 100 °C for 2 h under ~10 mmHg pressure. Subsequently benzyl alcohol was removed under reduced pressure and residue was dissolved in DCM. The DCM layer was washed with water, passed through anhydrous Na_2SO_4 and evaporated to dryness under reduced pressure. Crude product was purified by silica-gel column chromatography by using EtOAc: hexane (3:7) as an eluent, which resulted the desired product as white solid (85 mg, 60 %).

2.4) Synthesis of Tri-tert-butyl 2,5,8-trimethyl-4,7-dihydro-1H-dipyrrolo[2,3-e:2', 3;-g]indole-3,6,9-tricarboxylate (3c):



1c

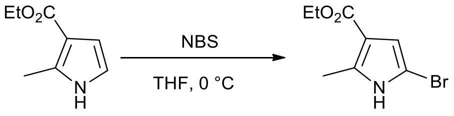
3c

The same synthetic procedure for **3a** was followed; 2 mg product (**3c**) was obtained from 100 mg of starting material **1c** [S5a] with 2% yield (white solid).

IR (KBr) (cm^{-1}): 3312, 2921, 1666, 1462; ^{1}H NMR (500 MHz, $CDCl_3$, δ in ppm):11.39 (s, 3H), 2.75 (s, 9H), 1.67 (s, 27H); HRMS (ESI+) : m/z : calculated for $C_{30}H_{40}N_3O_6$ $[M+H]^+$: 538.2917; found: 538.2918.

2.5) Synthesis of Ethyl 5-bromo-2-methyl-1H-pyrrole-3-carboxylate (5a):[S7]

(**[S7]** = The product **5a** was reported recently by different procedure).



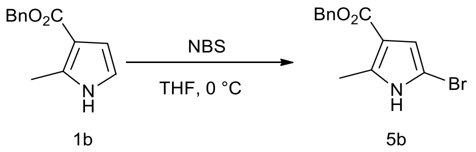
1a

5a

To ethyl 2-methyl-1Hpyrrole-3-carboxylate **1a** (100 mg, 0.65 mmol) in THF (50 mL), NBS (116 mg, 0.65 mmol) was added under N_2 atmosphere at 0 °C and stirred for 1 h. After complete consumption of starting material, the reaction was quenched by addition of aq.$NaHCO_3$ solution. Then the organic layer was separated and the aqueous layer was extracted with EtOAc (2 x 10 mL). Then organic layers were combined, dried over anhyd. Na_2SO_4, and concentrated using the rotary evaporator under reduced pressure. Finally, the crude product was purified by silica gel column chromatography by using EtOAc: hexane (15:85) as an eluent, which resulted the desired product as white solid (110 mg, 73 %).

IR (KBr) (cm^{-1}): 3256, 2980, 1673, 1445; ^{1}H NMR (500 MHz, CD_3CN δ in ppm): 9.68 (s, 1H), 6.38 (s, 1H), 4.18 (q, J = 7 Hz, 2H), 2.42 (s, 3H), 1.27 (t, J = 7 Hz, 3H); ^{13}C NMR (125 MHz, CD_3CN, δ in ppm): 164.0, 137.7, 114.1, 112.1, 96.9, 60.2, 14.7, 12.8; HRMS (ESI+) : m/z : calculated for $C_8H_{11}BrNO_2$ $[M+H]^+$: 231.9973; found: 231.9984.

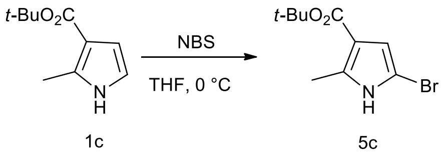
2.6) Synthesis of Benzyl 5-bromo-2-methyl-1Hpyrrole-3-carboxylate (5b):



The same synthetic procedure for **5a** was followed; 95 mg product (**5b**) was obtained from 100 mg starting material (**1b**) with 70% yield (white solid).

IR (KBr) (cm^{-1}): 3269, 3030, 1667, 1431; ^{1}H NMR (500 MHz, CDCl$_3$, δ in ppm): 8.34 (s, 1H), 7.4 (d, *J* = 7.2 Hz, 2H), 7.4 (t, *J* = 7 Hz, 3H), 7.3 (d, *J* = 7 Hz, 2H), 6.54 (d, *J* = 2.8 Hz, 1H), 5.27 (s, 2H), 2.5 (s, 3H); ^{13}C NMR (125 MHz, CDCl$_3$, δ in ppm): 164.4, 136.8, 136.7, 128.6, 128.1, 128.0, 113.4, 112.3, 96.5, 65.6, 13.2; HRMS (ESI+): m/z: calculated for $C_{13}H_{13}BrNO_2$ [M+H]$^+$: 294.0129; found: 294.0129.

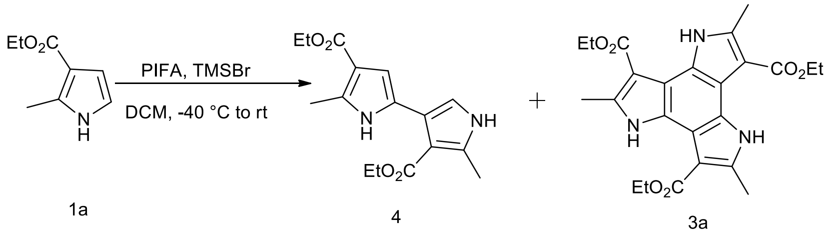
2.7) Synthesis of *t*ert-butyl 5-bromo-2-methyl-1Hpyrrole-3-carboxylate (5c):



The same synthetic procedure for **5a** was followed; 90 mg product (**5c**) was obtained from 100 mg starting material (**1c**) with 70% yield (white solid).

IR (KBr) (cm^{-1}): 3176, 2969, 1649, 1453; ^{1}H NMR (400 MHz, CDCl$_3$, δ in ppm): 8.35 (s, 1H), 6.44 (d, *J* = 2.9 Hz, 1H), 2.46 (s, 3H), 1.54 (s, 9H); ^{13}C NMR (100 MHz, CDCl$_3$, δ in ppm): 164.2, 135.8, 115.3, 112.3, 86.0, 79.9, 28.6, 13.4; HRMS (ESI+): m/z: calculated for $C_{10}H_{14}BrNNaO_2$ [M+Na]$^+$: 282.0105; found: 282.0100.

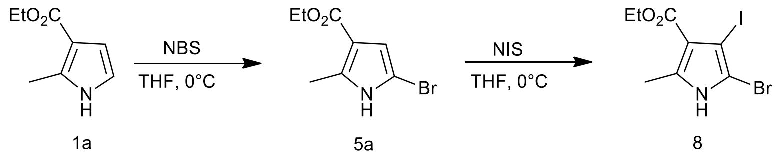
2.8) Attempted synthesis of bipyrrole 2:



To ethyl 2-methyl-1Hpyrrole- 3-carboxylate **1a** (100 mg, 0.65 mmol) in DCM (20 mL), PIFA (200 mg, 1.30 mmol) and TMSBr (0.11 mL, 0.87 mmol) were added under N_2 atmosphere at low temperature i.e. -40 ^{o}C and was stirred overnight. After complete consumption of starting material, the reaction was stopped by addition of aq.NaHCO$_3$ solution. Then the organic layer was separated and the remaining crude compound was extracted with DCM (2 x 10 mL). Then the organic layers were combined, dried over anhyd. Na_2SO_4, and concentrated using rotary evaporator under reduced pressure. Finally the crude product was purified by silica gel column chromatography using EtOAc: hexane (1:9) as an eluent, which resulted the 1st fraction as BTP **3a** 5 mg (5 %), along with the 2nd fraction as compound **4**, a white solid 60 mg (15 %).

Compound **4**: Melting point 266-267 °C; IR (KBr), (cm^{-1}): 3213, 2979, 1652, 1441; ^1H NMR (500 MHz, $CDCl_3$, δ in ppm): 11.51 (s, 1H), 8.30 (s, 1H), 6.90 (d, *J* = 2.15Hz, 1H), 6.64 (s, 1H), 4.33 (q, *J* = 7.1 Hz, 2H), 4.27 (q, *J* = 7.1 Hz, 2H), 2.6 (s, 3H), 2.5 (s, 3H), 1.39 (t, *J* = 7.1 Hz, 3H), 1.35 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$, δ in ppm): 167.6, 166.2, 136.4, 133.9, 125, 118.8, 113.7, 111.9, 105.8, 60.5, 59.3, 15.5, 14.7, 14.6, 13.7; HRMS (ESI+) : m/z : calculated for $C_{16}H_{21}N_2O_4$ $[M+H]^+$: 305.1501; found 305.1502.

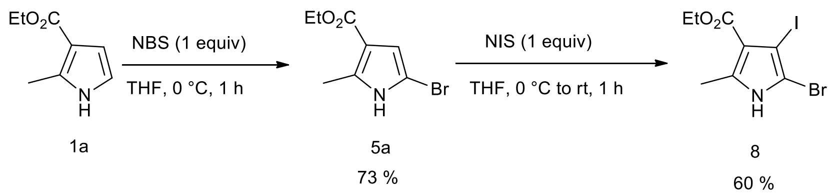
2.9) Synthesis of 5-bromo-4-iodo-2-methyl-1H-pyrrole-3-carboxylate (8):



To ethyl 2-methyl-1Hpyrrole-3-carboxylate **1a** (100 mg, 0.65 mmol), NBS (116 mg, 0.65 mmol) in THF (30 mL) was added at 0 °C under N_2 atmosphere and then stirred for 1 h. Subsequently, to the same reaction mixture NIS (146 mg, 0.65 mmol) was added, and stirred for additional 2 h. Then the reaction was quenched with aq. $NaHCO_3$ solution. The organic layer was separated and the aq. layer was extracted with EtOAc (2 x 10 mL). Then combined organic layer was dried over anhyd. Na_2SO_4, and concentrated using rotary evaporator under reduced pressure. Finally the crude product was purified on silica gel column using EtOAc : Hexane (1:9) as an eluent, which resulted the product as white solid (150 mg, 60 %).

IR (cm^{-1}): 3213, 2984, 1671, 1436; ^1H NMR data (500 MHz , $CDCl_3$, δ in ppm): 8.54 (s, 1H), 4.3 (q, *J* = 9 Hz, 2H), 2.5 (s, 3H), 1.37 (t, *J* = 9 Hz, 3H); ^{13}C NMR Data (500 MHz , $CDCl_3$, δ in ppm): 163.3, 137.8, 114.9, 105.8, 68.5, 60.2, 14.6, 14.6, 14.4; HRMS (ESI+) m/z: calculated for $C_8H_{10}BrINO_2[M+H]^+$: 357.8939; found: 357.8938.

Scheme S1:



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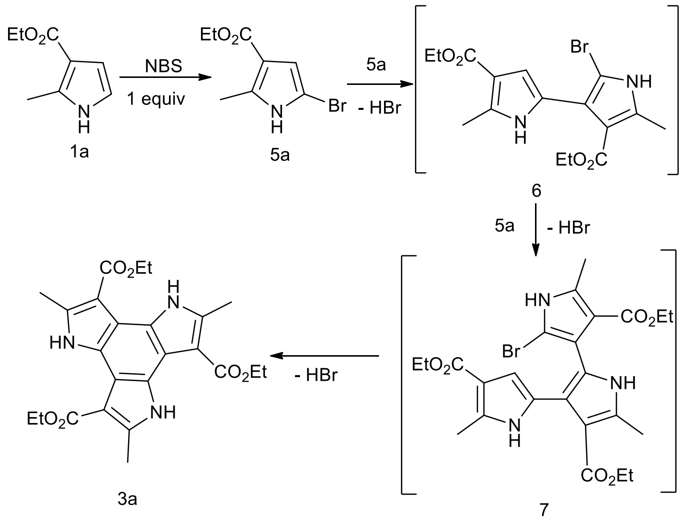

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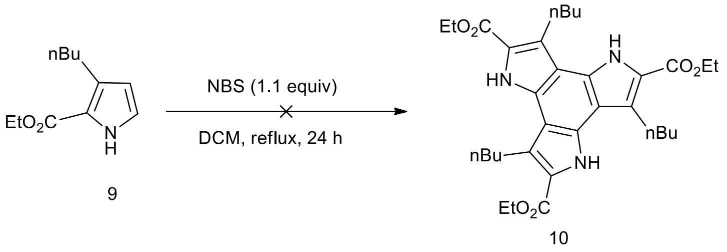


Scheme S4:

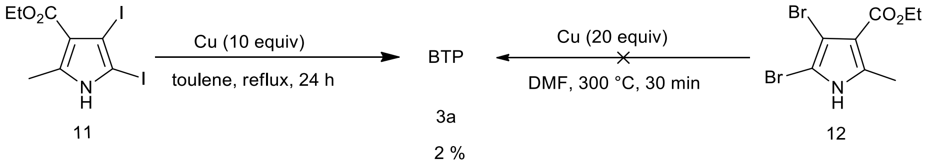


Table S1: Optimization of reaction conditions for BTPs formation.

entry	**substrate**	**Reagent (equiv)**	**solvent**	**Time (h)**	**Temp**	**compound**	**Yield (%)**
1	**1a**	NBS (1.1)	DCM	24	reflux	**3a**	12
2	**1a**	NBS (1.1)	$CHCl_3$	24	reflux	**3a**	10
3	**1a**	NBS (1.1)	DCE	24	reflux	**3a**	10
4	**1a**	NBS (1.1)	CCl_4	24	reflux	**3a**	2
5	**1b**	NBS (1.1)	DCM	24	reflux	**3b**	5
6	**1c**	NBS (1.1)	DCM	24	reflux	**3c**	2
7	**5a**	**-**	DCM	24	reflux	**3a**	10
8	**5b**	**-**	DCM	24	reflux	**3b**	5
9	**5c**	**-**	DCM	24	reflux	**3c**	trace

3. ^{1}H, ^{13}C NMR and HRMS spectra:

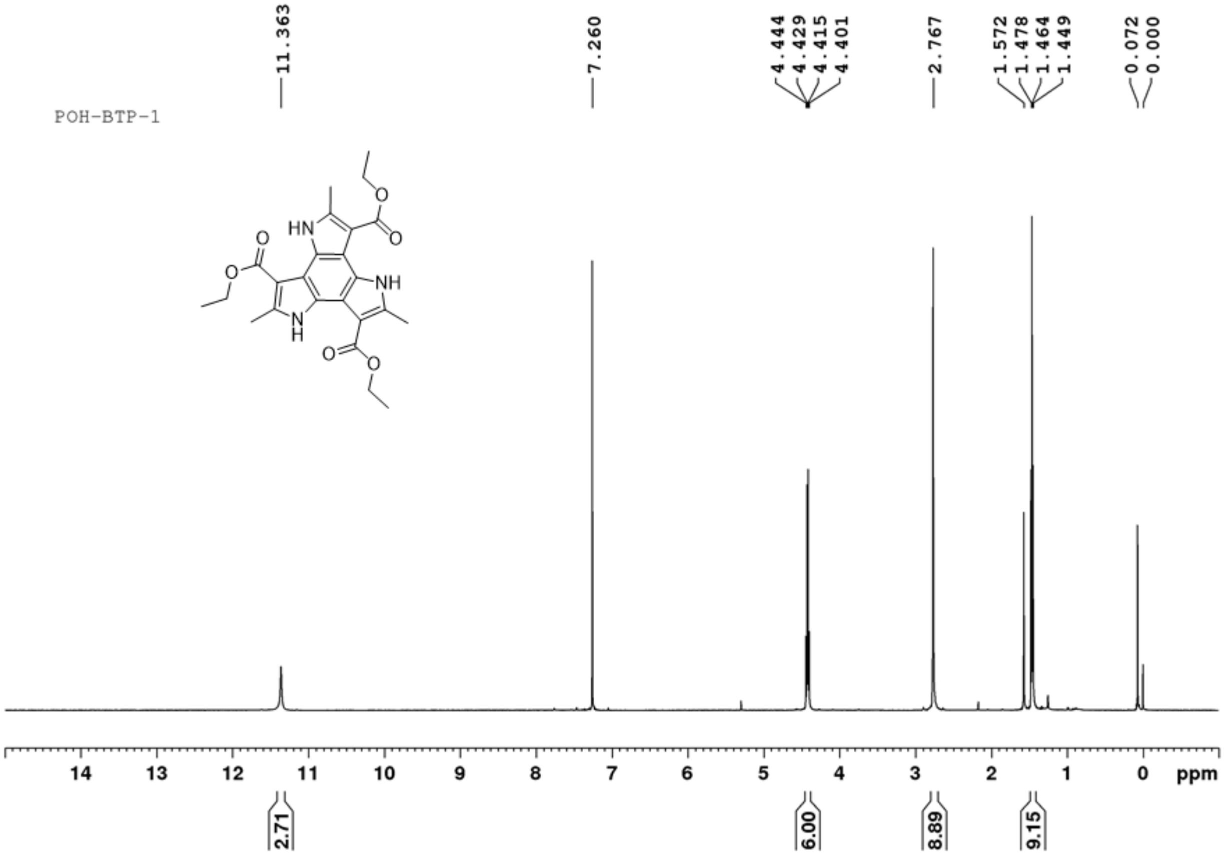


Fig. S1 ^{1}H NMR spectrum of **3a** in CDCl$_3$.

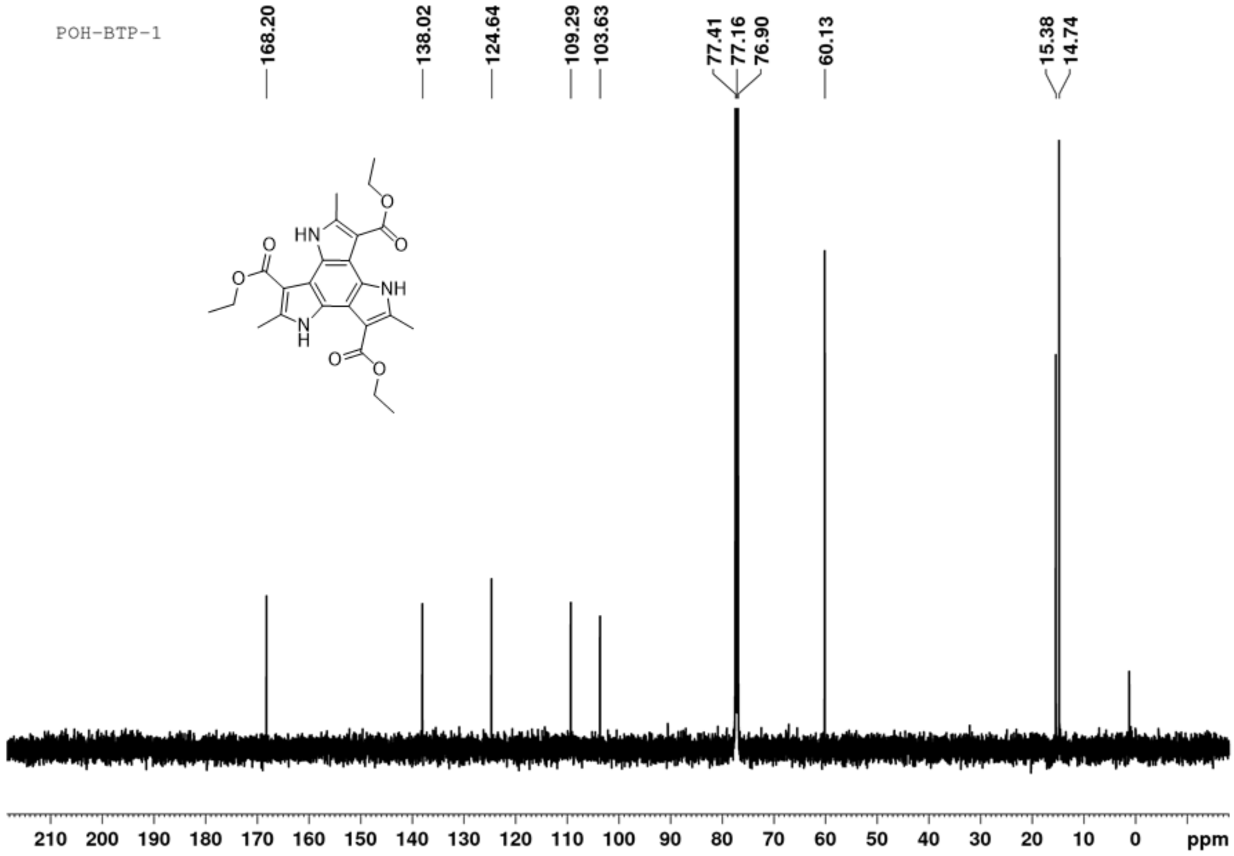
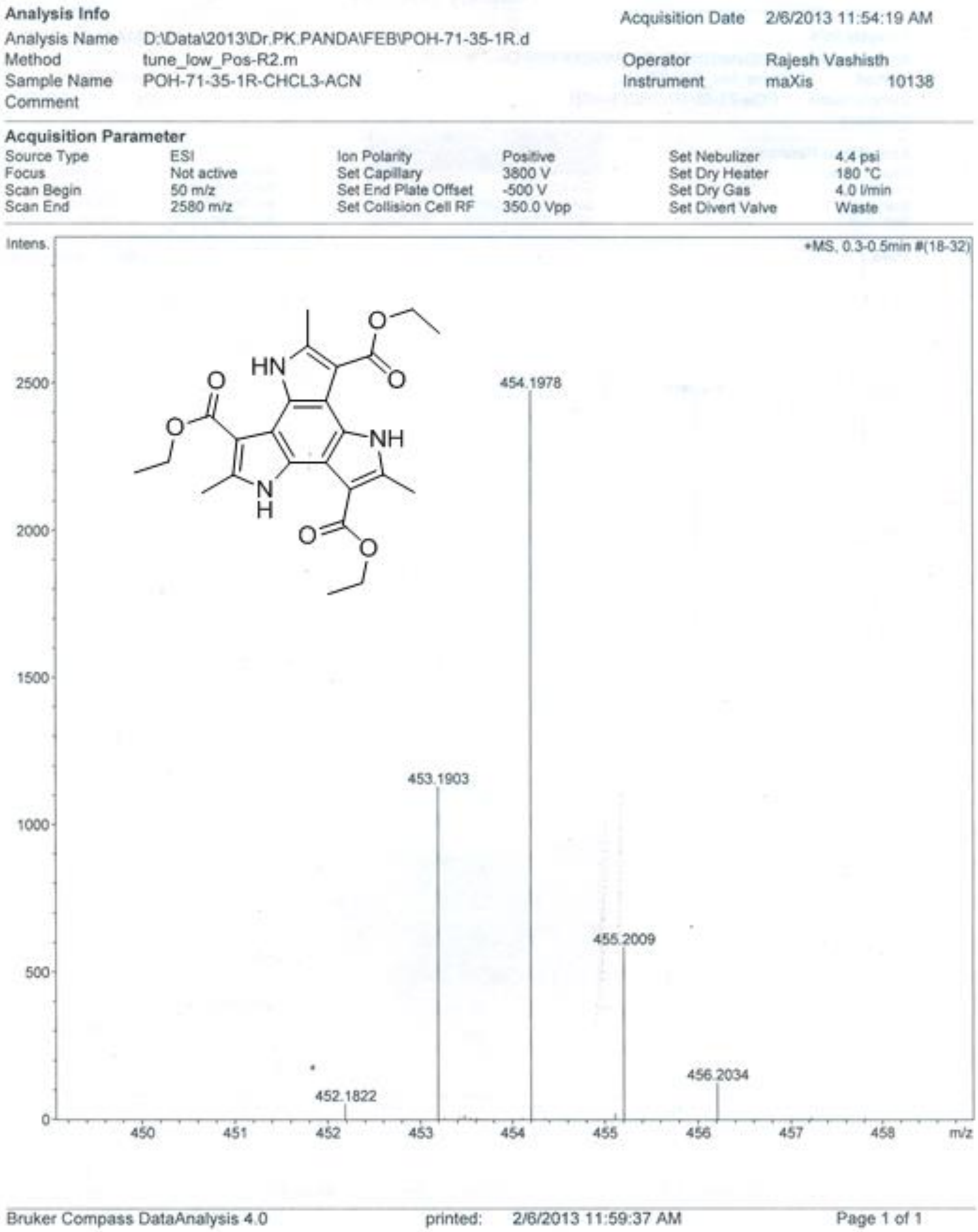


Fig. S2 ^{13}C NMR spectrum of **3a** in CDCl$_3$.



Analysis Info

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Sample Name	POH-71-35-1R-CHCL3-ACN	Instrument	maXis 10138
Comment			

Acquisition Parameter

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Scan End	2580 m/z	Set Collision Cell RF	350.0 Vpp	Set Divert Valve	Waste

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Fig. S3 HRMS spectrum of **3a** $(M+H)^+$; Calculated for $C_{24}H_{28}N_3O_6$: 454.1978; found: 454.1978.

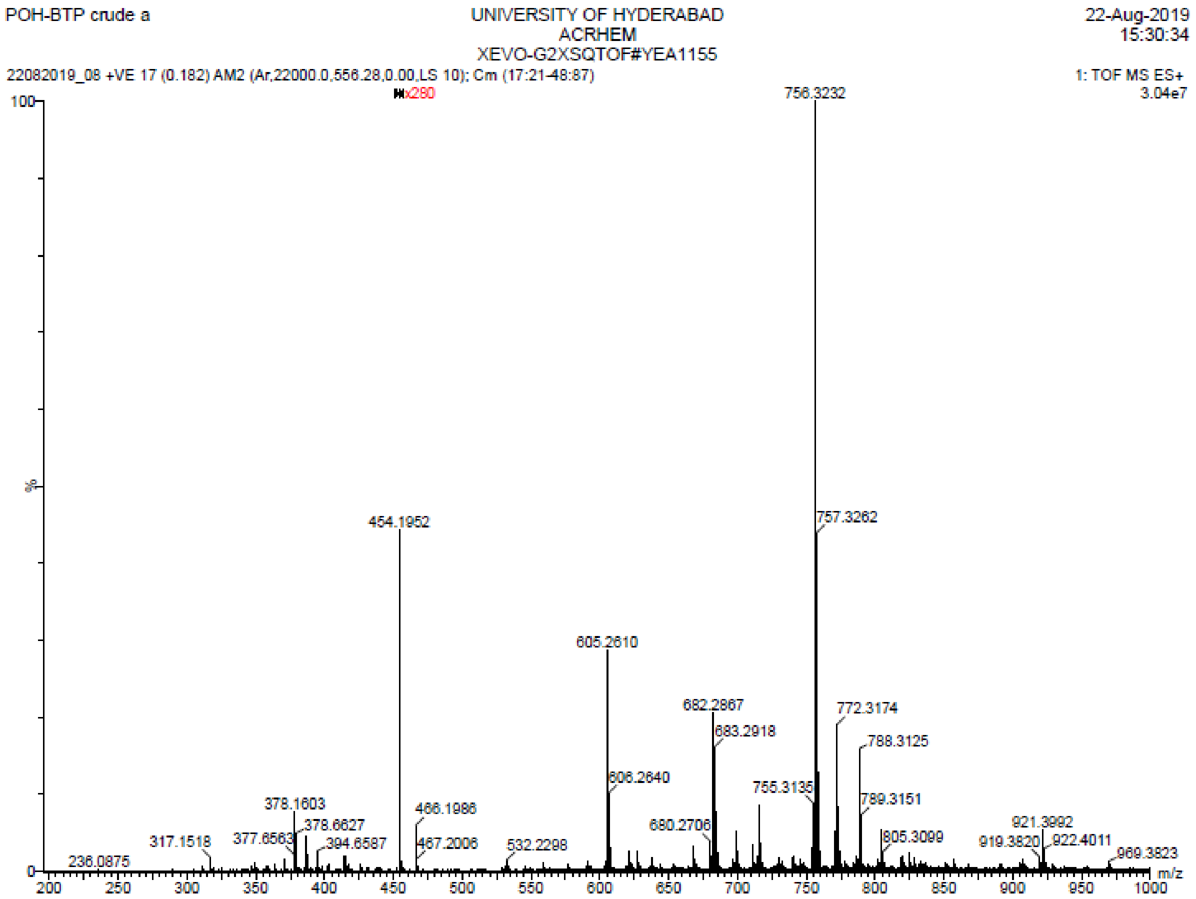


Fig. S4 HRMS spectrum of crude reaction mixture: Calculated mass $[M+H]^+$ for trimer BTP (**3a**), $C_{24}H_{28}N_3O_6$: 454.1978; found: 454.1978; calculated mass $[M+H]^+$ for Tetramer, $C_{32}H_{37}N_4O_8$: 605.2611; found: 605.2610; calculated mass $[M+H]^+$ for Pentamer, $C_{40}H_{46}N_5O_{10}$: 756.3245; found: 756.3232.

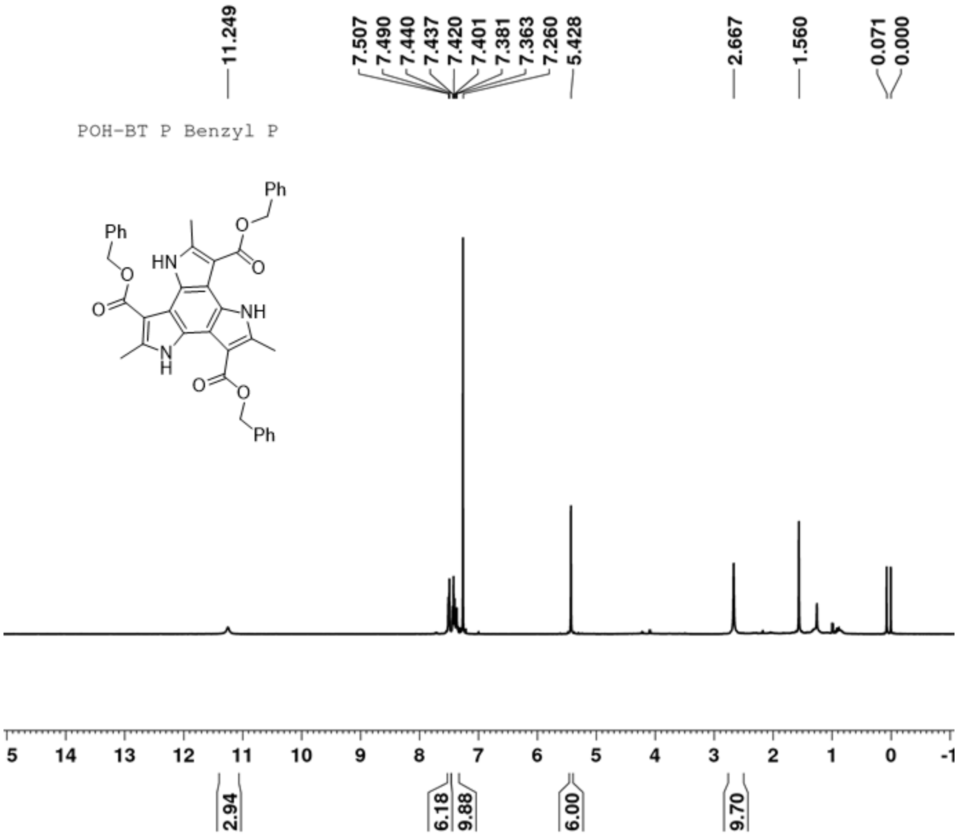


Fig. S5 ^{1}H NMR spectrum of **3b** in $CDCl_3$.

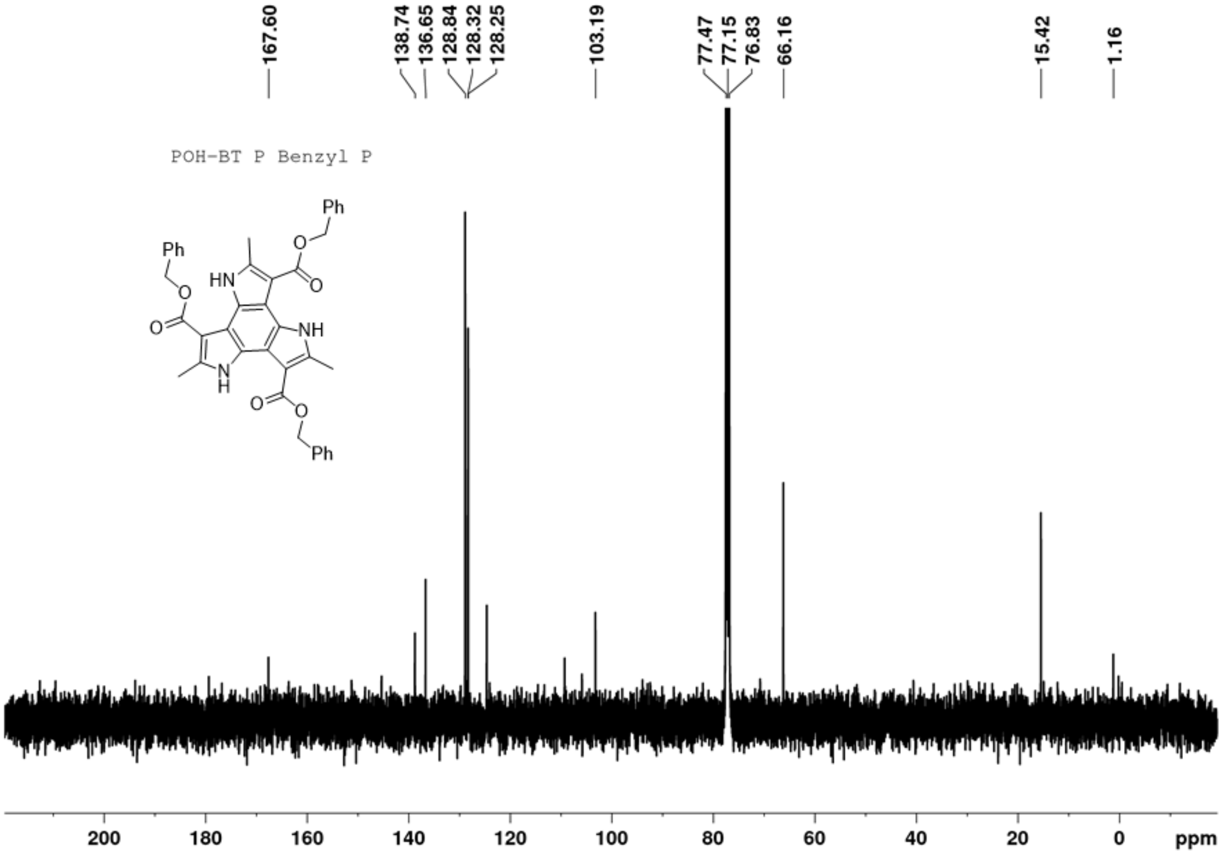
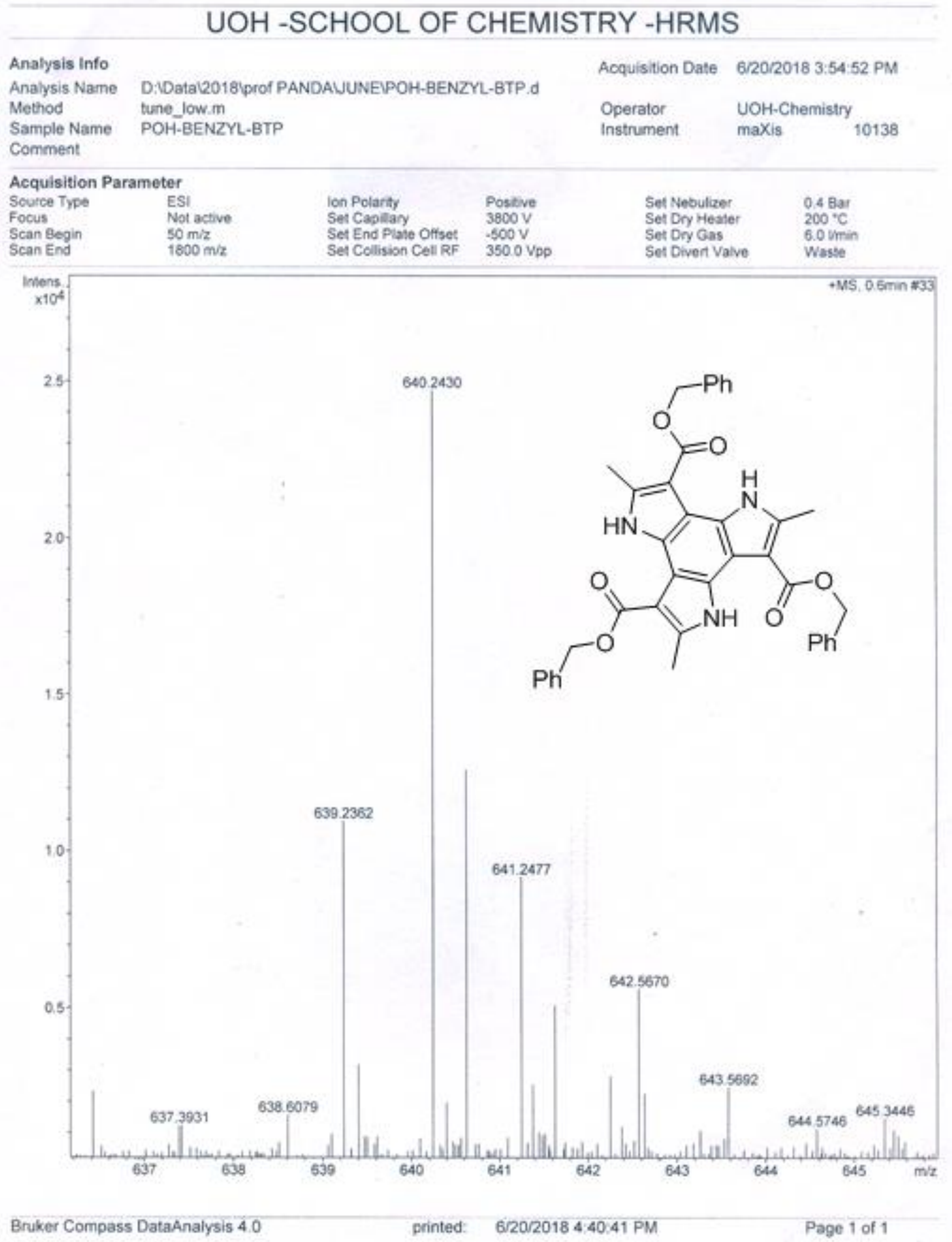


Fig. S6 ^{13}C NMR spectrum of **3b** in $CDCl_3$.



UOH -SCHOOL OF CHEMISTRY -HRMS

Analysis Info

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Comment			

Acquisition Parameter

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Scan End	1800 m/z	Set Collision Cell RF	350.0 Vpp	Set Divert Valve	Waste

Bruker Compass DataAnalysis 4.0 printed: 6/20/2018 4:40:41 PM Page 1 of 1

Fig. S7 HRMS spectrum of **3b** $(M+H)^+$; Calculated for $C_{39}H_{34}N_3O_6$ $[M+H]^+$: 640.2447; found: 640.2430.

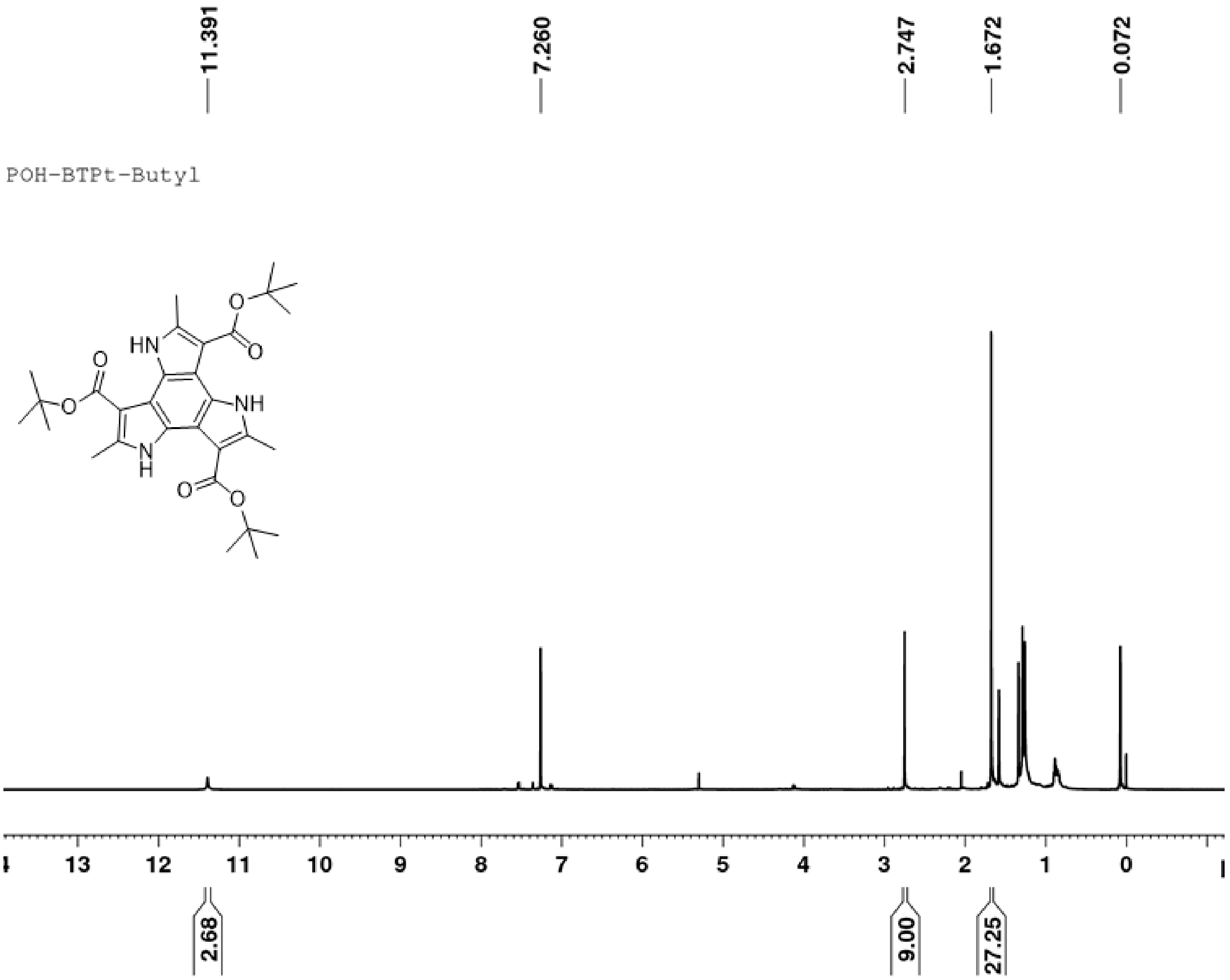
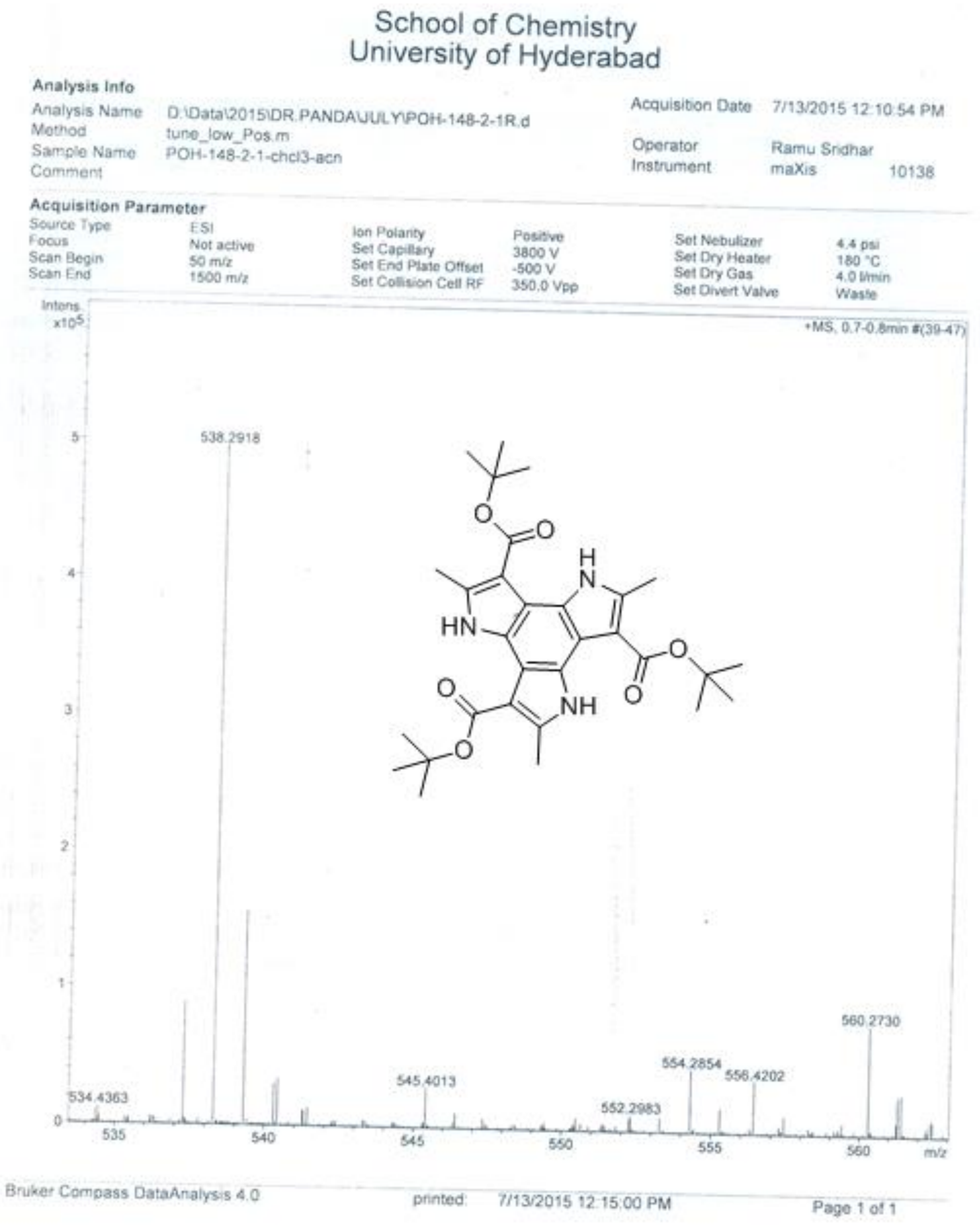


Fig. S8 ^{1}H NMR spectrum of **3c** in $CDCl_3$ (^{13}C NMR data could not be recorded due to lack of stability).



School of Chemistry
University of Hyderabad

Analysis Info

Analysis Name D:\Data\2015\DR.PANDA\JULY\POH-148-2-1R.d
Method tune_low_Pos.m
Sample Name POH-148-2-1-chcl3-acn
Comment

Acquisition Date 7/13/2015 12:10:54 PM
Operator Ramu Sridhar
Instrument maXis 10138

Acquisition Parameter

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Scan End 1500 m/z
Ion Polarity Positive
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Set End Plate Offset -500 V
Set Collision Cell RF 350.0 Vpp
Set Nebulizer 4.4 psi
Set Dry Heater 180 °C
Set Dry Gas 4.0 l/min
Set Divert Valve Waste

Bruker Compass DataAnalysis 4.0 printed: 7/13/2015 12:15:00 PM Page 1 of 1

Fig. S9 HRMS spectrum of **3c** $(M+H)^+$; Calculated for $C_{30}H_{40}N_3O_6$ $[M+H]^+$: 538.2917; found: 538.2918.

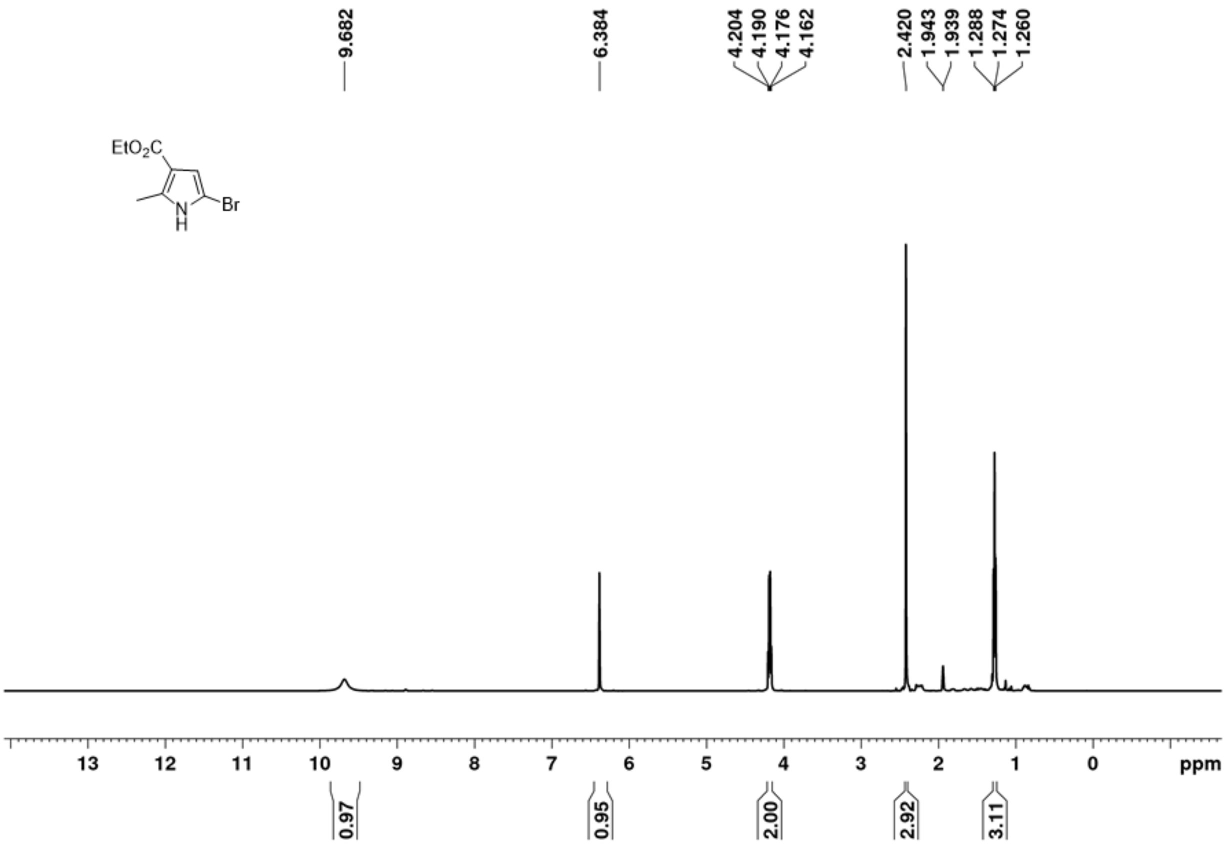


Fig. S10 ^{1}H NMR spectrum of **5a** in CD_3CN.

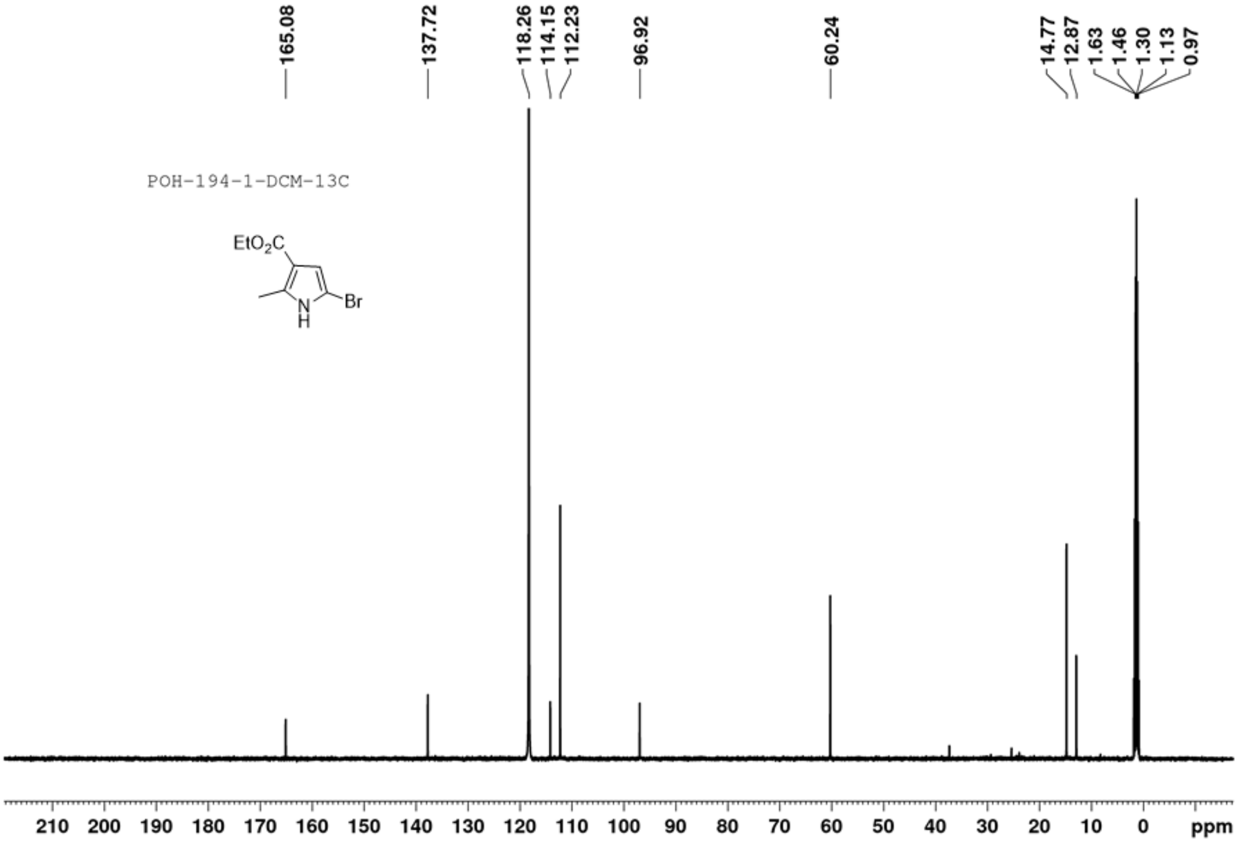
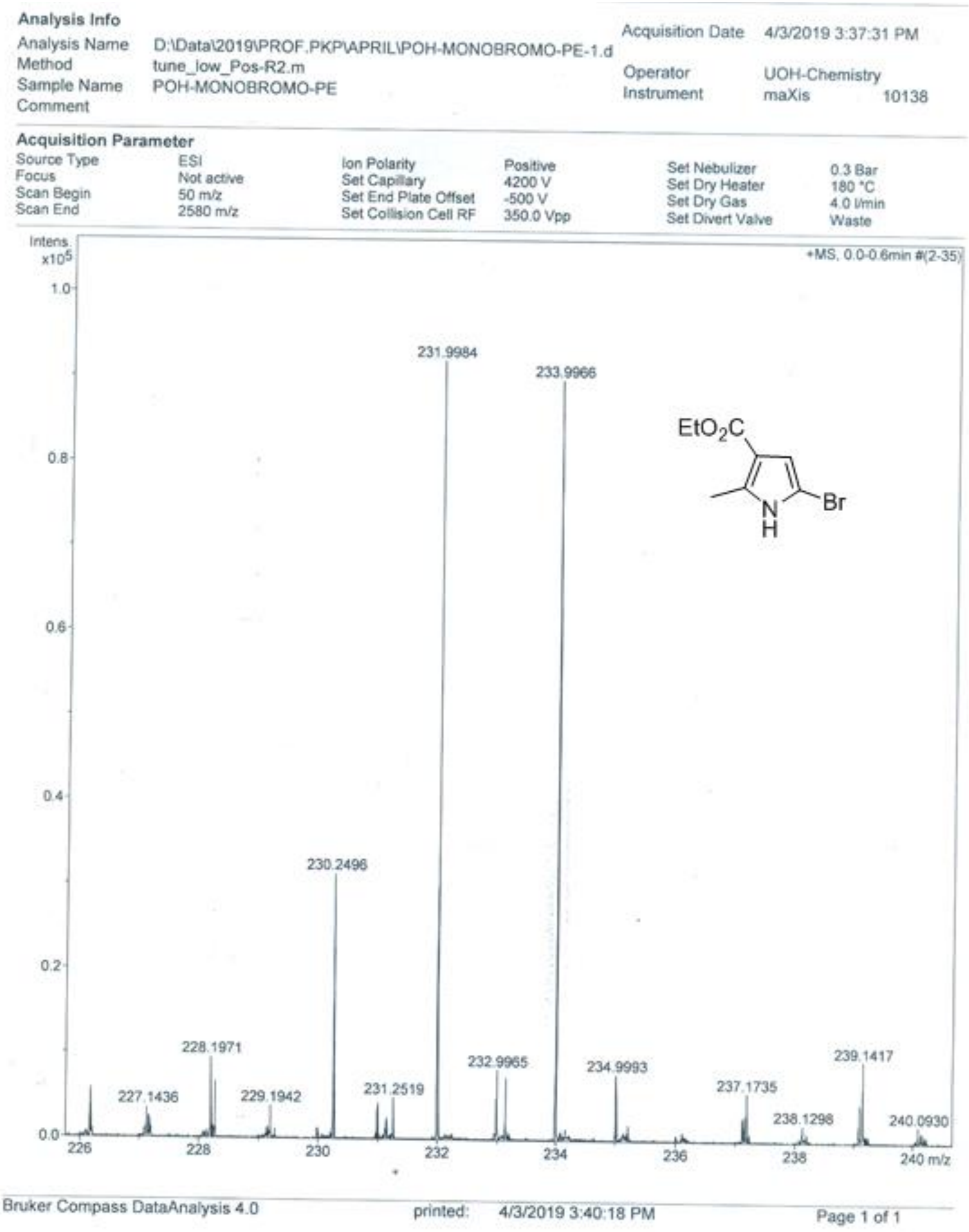


Fig. S11 ^{13}C NMR spectrum of **5a** in CD_3CN.



Analysis Info

Analysis Name D:\Data\2019\PROF.PKP\APRIL\POH-MONOBROMO-PE-1.d
Method tune_low_Pos-R2.m
Sample Name POH-MONOBROMO-PE
Comment

Acquisition Date 4/3/2019 3:37:31 PM
Operator UOH-Chemistry
Instrument maXis 10138

Acquisition Parameter

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Scan End 2580 m/z
Ion Polarity Positive
Set Capillary 4200 V
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Set Collision Cell RF 350.0 Vpp
Set Nebulizer 0.3 Bar
Set Dry Heater 180 °C
Set Dry Gas 4.0 l/min
Set Divert Valve Waste

Bruker Compass DataAnalysis 4.0 printed: 4/3/2019 3:40:18 PM Page 1 of 1

Fig. S12 HRMS spectrum of **5a** (M+H)$^+$; Calculated for $C_8H_{11}BrNO_2$ [M+H]$^+$: 231.9973; found: 231.9984.

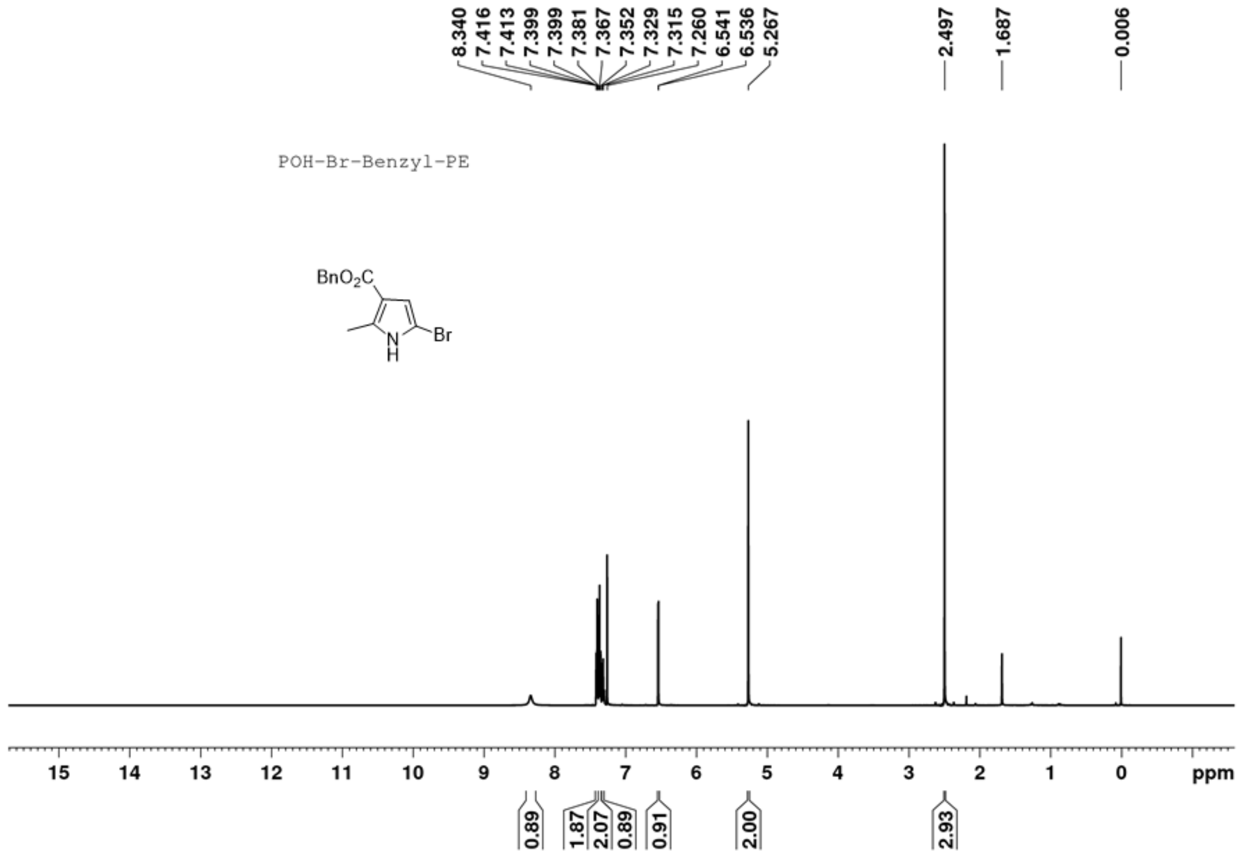


Fig. S13 ^{1}H NMR spectrum of **5b** in $CDCl_3$.

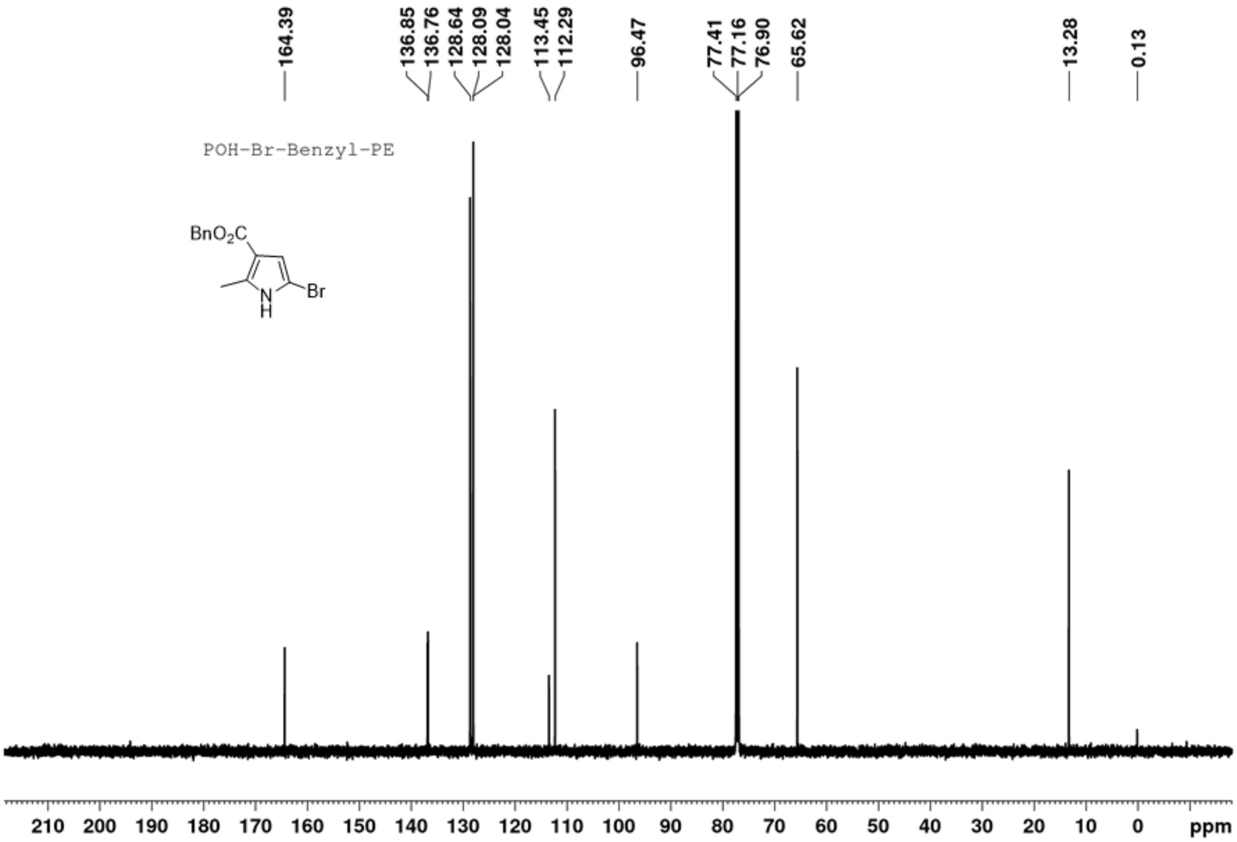
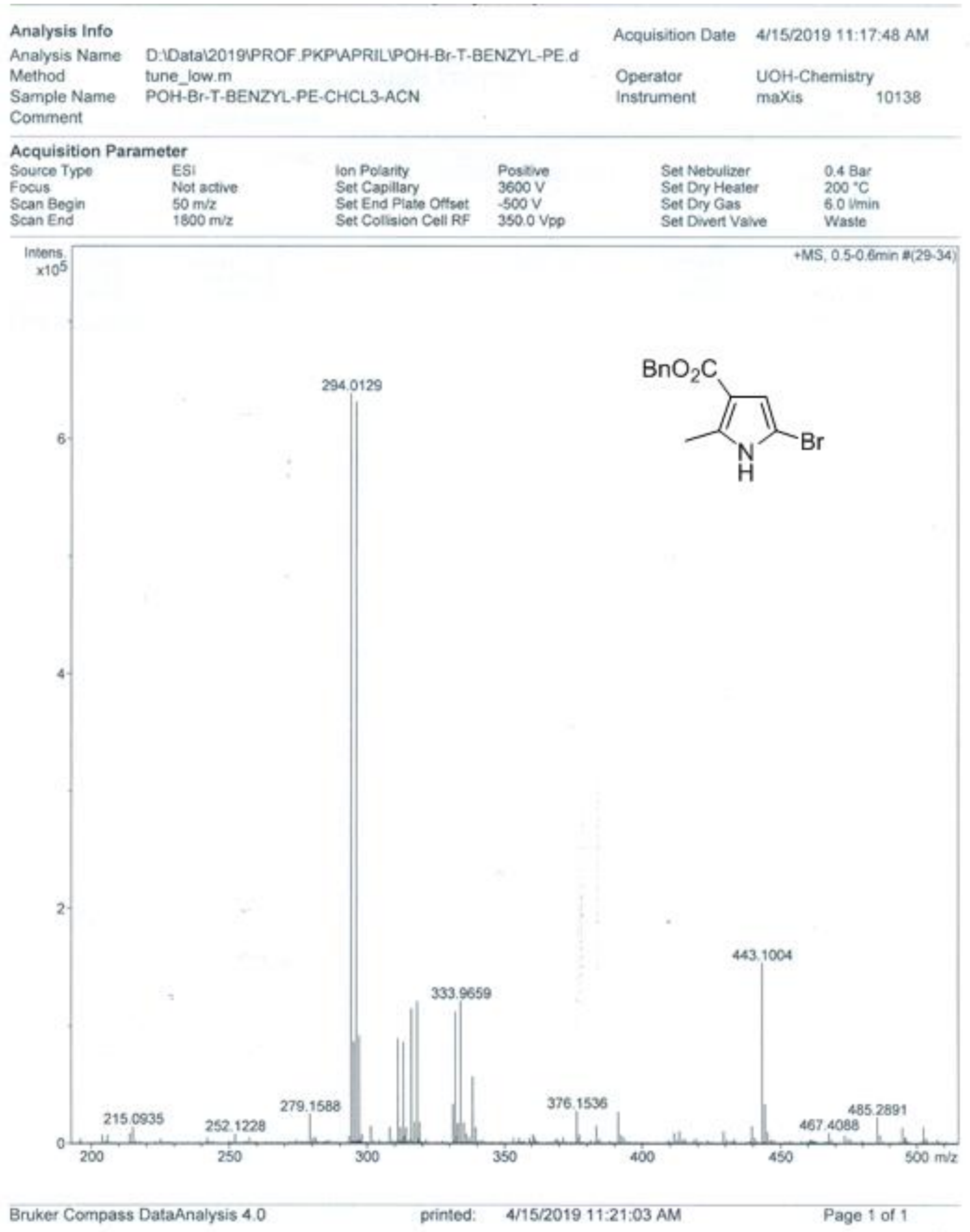


Fig. S14 ^{13}C NMR spectrum of **5b** in $CDCl_3$.



Analysis Info

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Method	tune_low.m	Operator	UOH-Chemistry
Sample Name	POH-Br-T-BENZYL-PE-CHCL3-ACN	Instrument	maXis 10138
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.4 Bar
Focus	Not active	Set Capillary	3600 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	6.0 l/min
Scan End	1800 m/z	Set Collision Cell RF	350.0 Vpp	Set Divert Valve	Waste

Bruker Compass DataAnalysis 4.0 printed: 4/15/2019 11:21:03 AM Page 1 of 1

Fig. S15 HRMS spectrum of **5b** (M+H)$^+$; Calculated for $C_{13}H_{13}BrNO_2$ [M+H]$^+$: 294.0129; found: 294.0129.

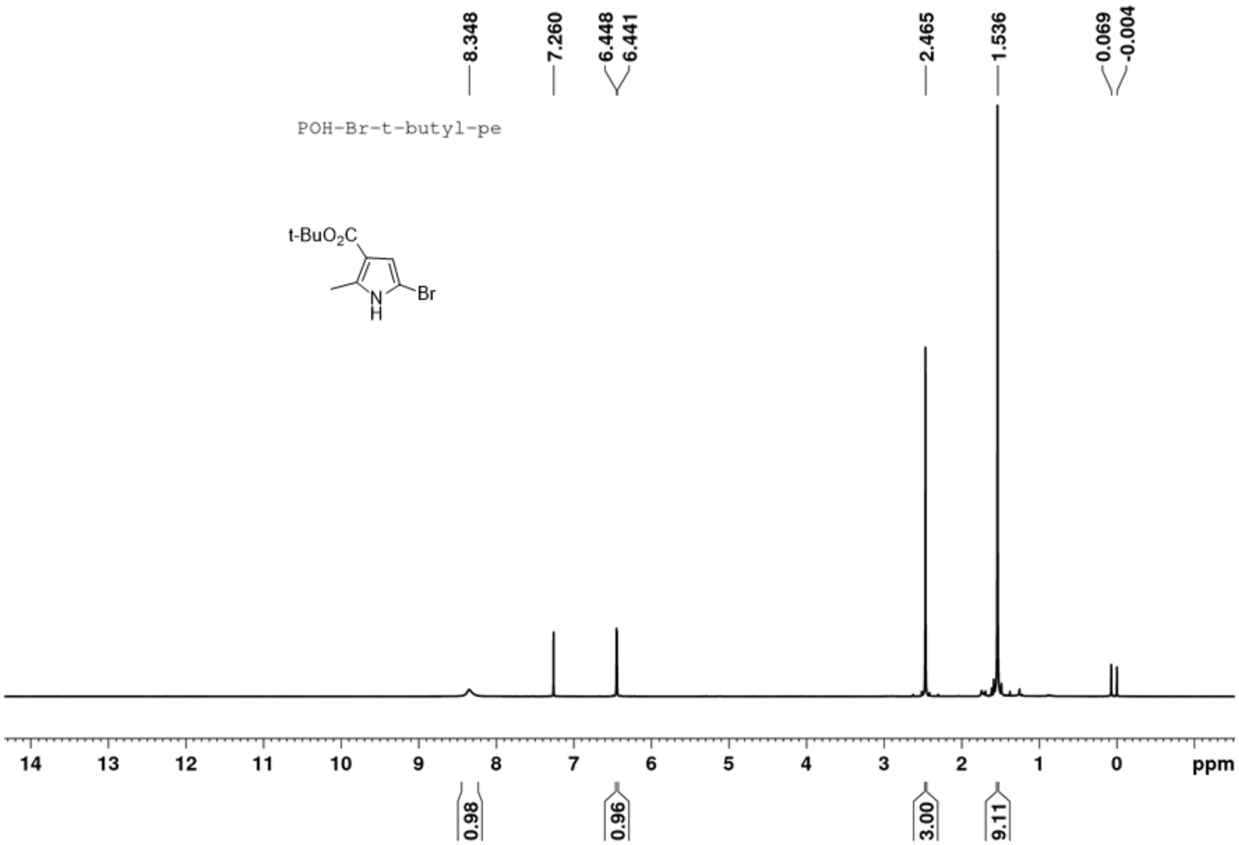


Fig. S16 ^{1}H NMR spectrum of **5c** in $CDCl_3$.

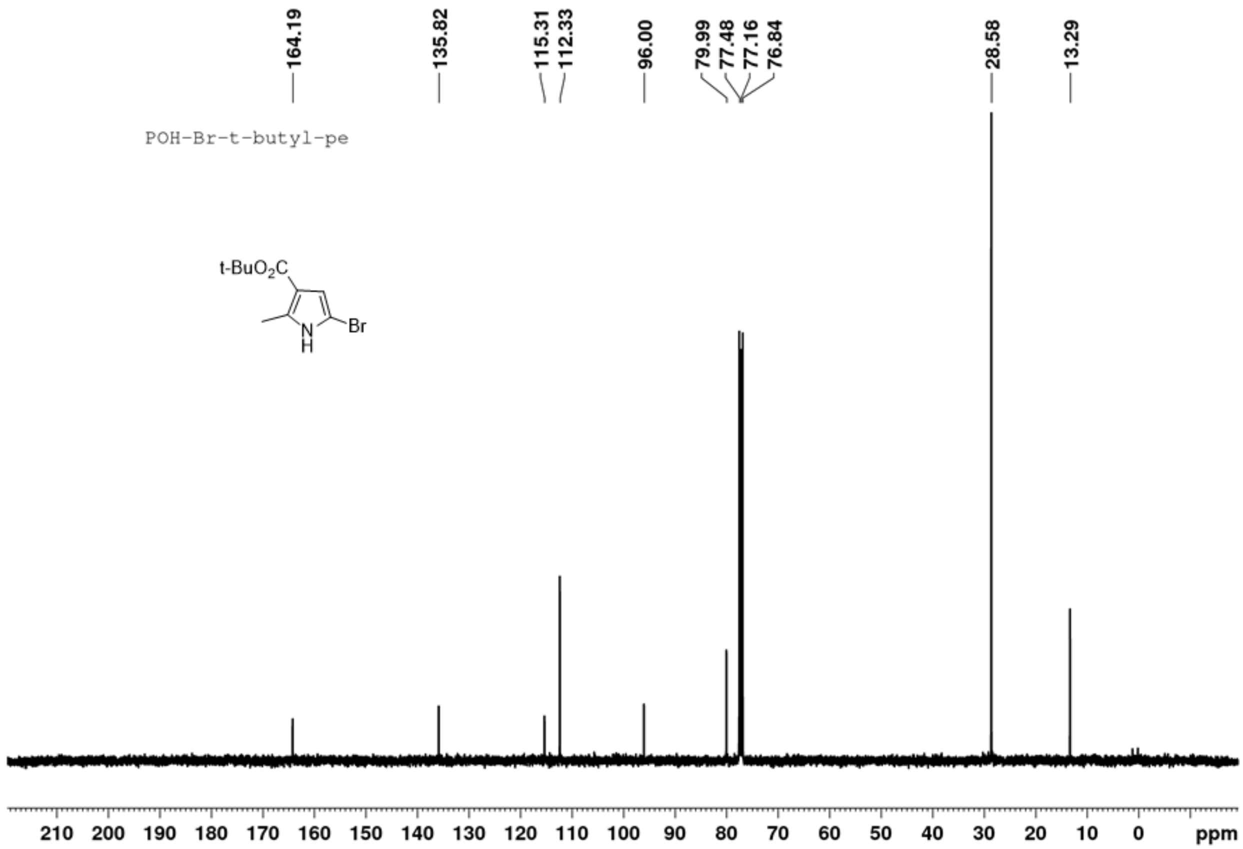
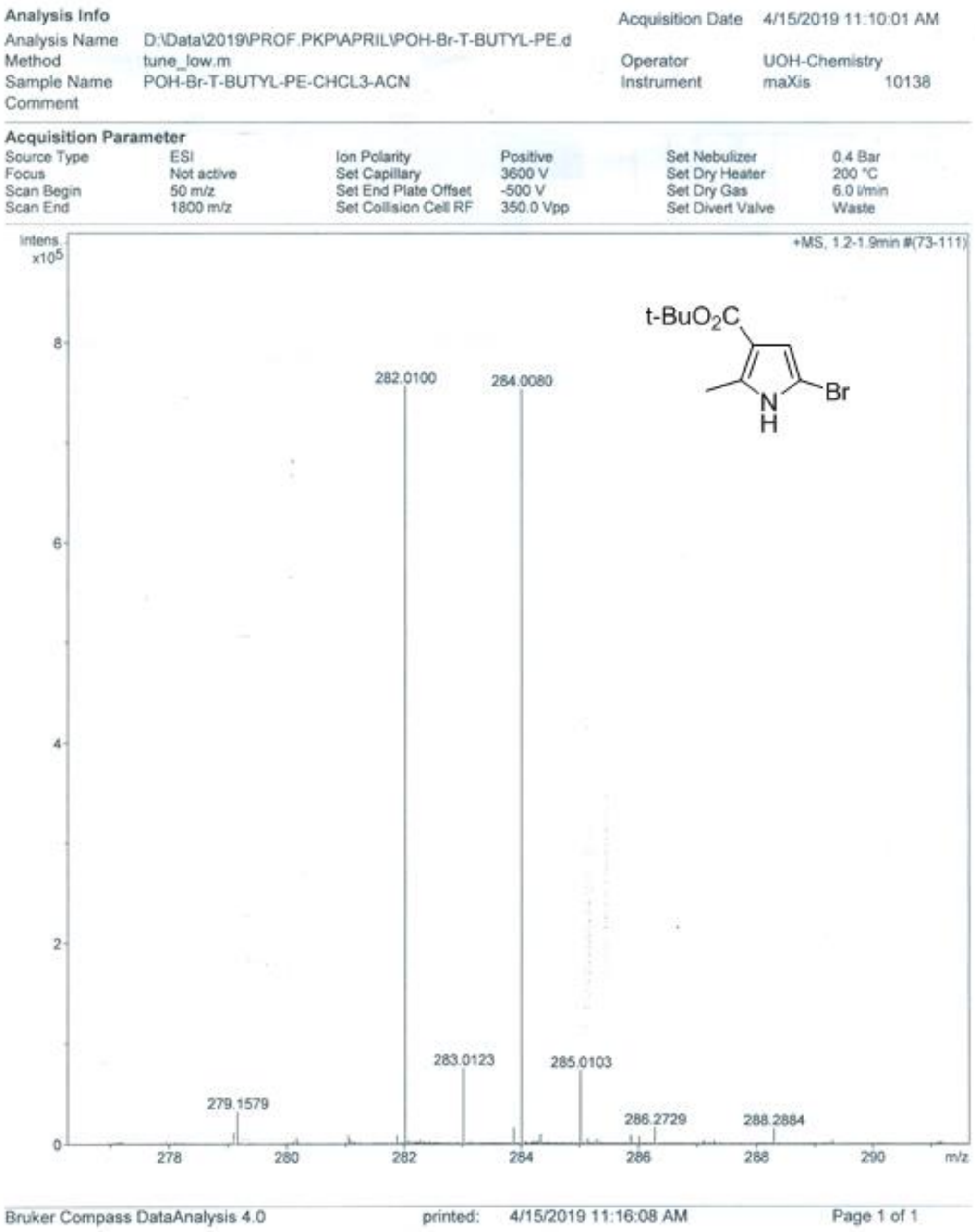


Fig. S17 ^{13}C NMR spectrum of **5c** in $CDCl_3$.



Analysis Info

Analysis Name	D:\Data\2019\PROF.PKP\APRIL\POH-Br-T-BUTYL-PE.d	Acquisition Date	4/15/2019 11:10:01 AM
Method	tune_low.m	Operator	UOH-Chemistry
Sample Name	POH-Br-T-BUTYL-PE-CHCL3-ACN	Instrument	maXis 10138
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.4 Bar
Focus	Not active	Set Capillary	3600 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	6.0 l/min
Scan End	1800 m/z	Set Collision Cell RF	350.0 Vpp	Set Divert Valve	Waste

Bruker Compass DataAnalysis 4.0 printed: 4/15/2019 11:16:08 AM Page 1 of 1

Fig. S18 HRMS spectrum of **5c** [M+Na]$^+$; Calculated for $C_{10}H_{14}BrNaNO_2$ [M+Na]$^+$: 282.0105; found: 282.0100.

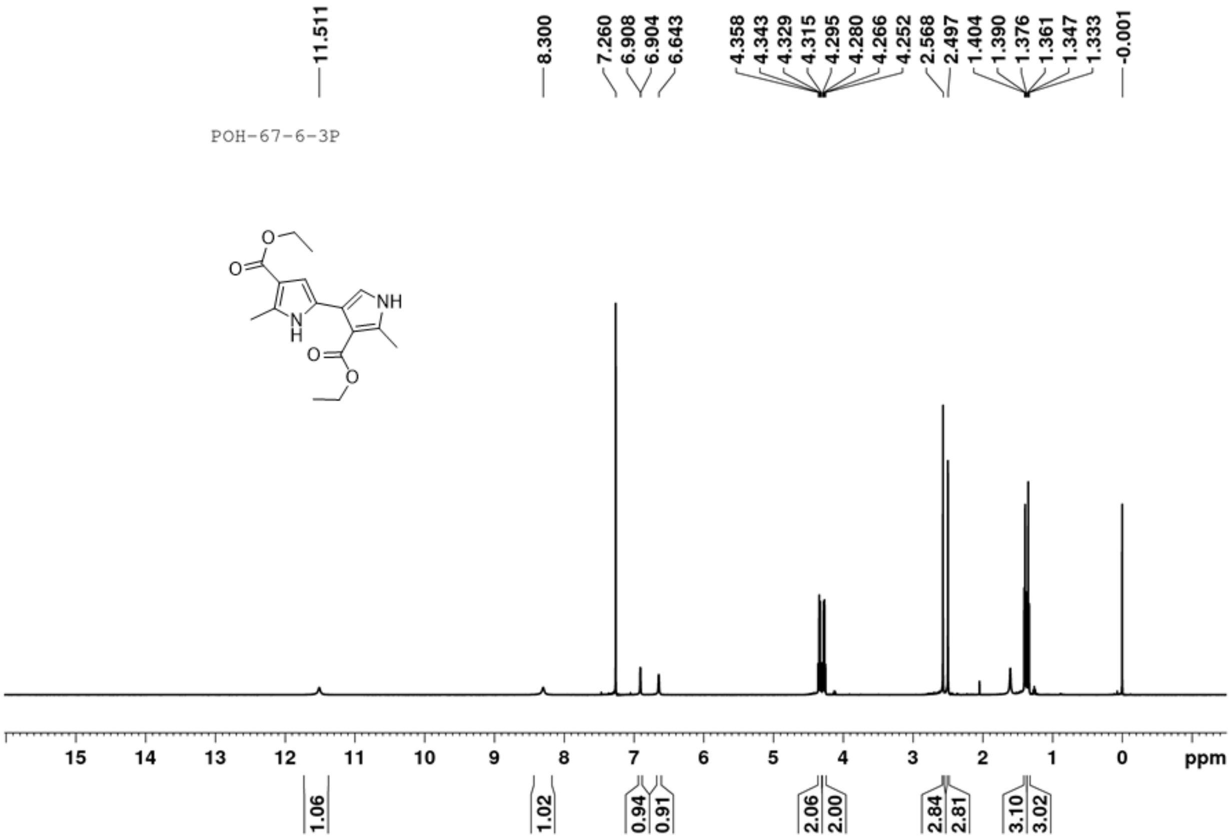


Fig. S19 ^{1}H NMR spectrum of **4** in $CDCl_3$.

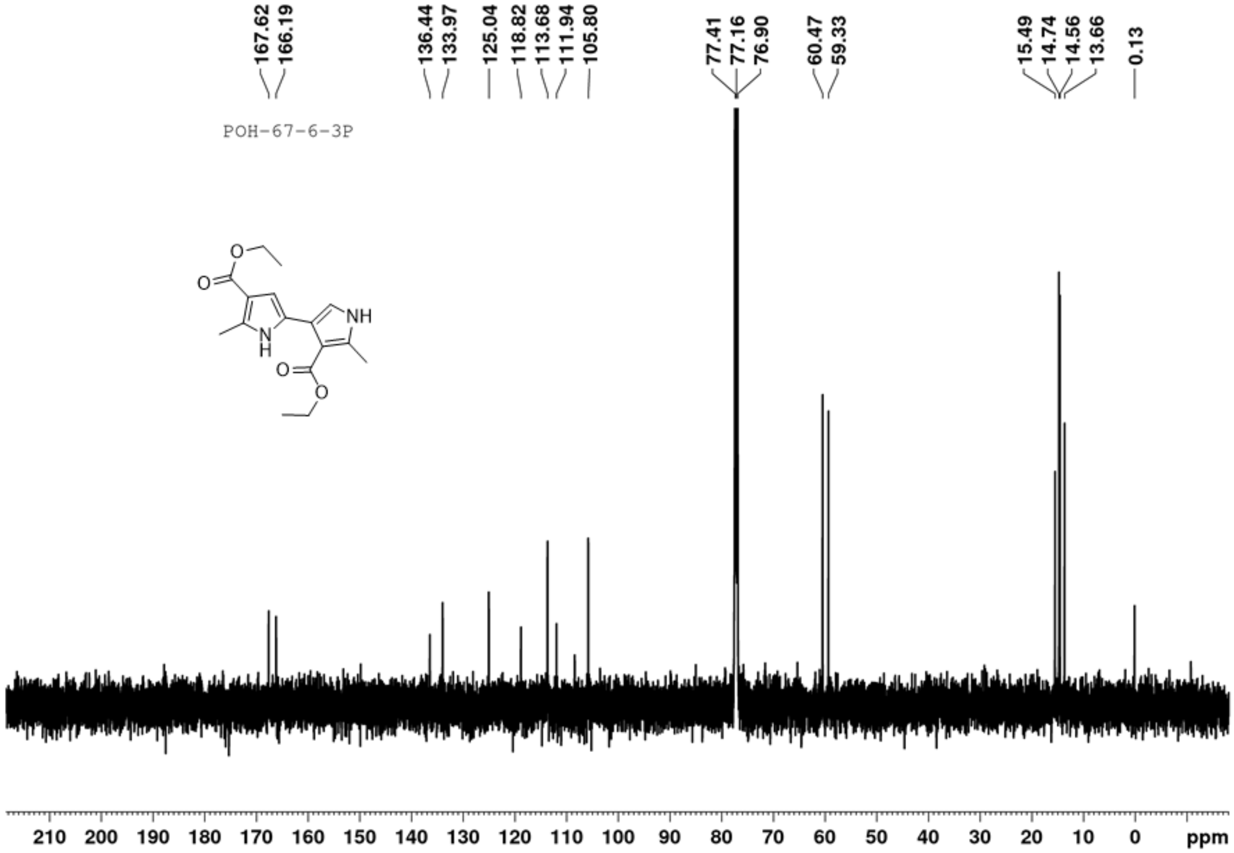
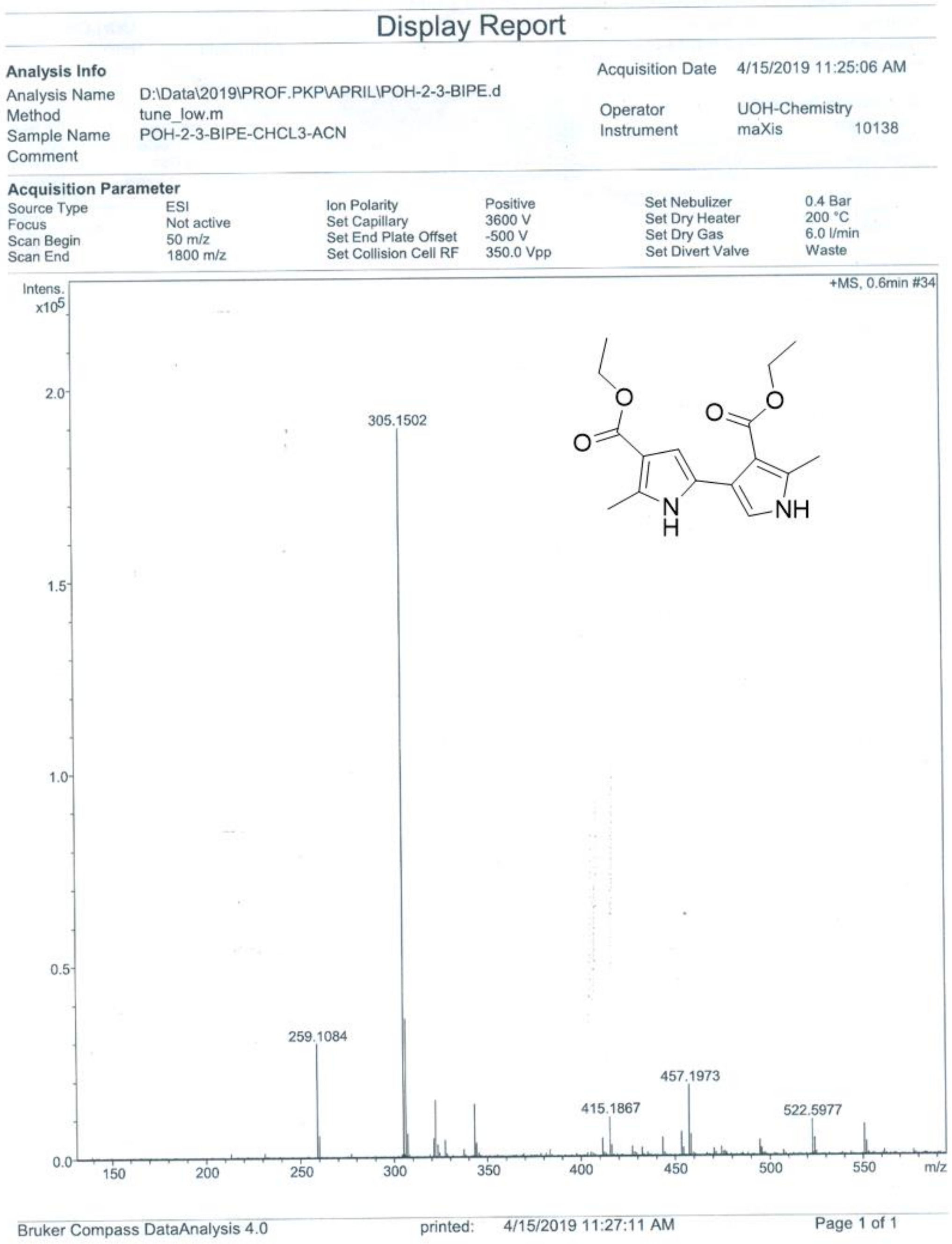


Fig. S20 ^{13}C NMR spectrum of **4** in CDCl$_3$.



Display Report

Analysis Info

Analysis Name	D:\Data\2019\PROF.PKP\APRIL\POH-2-3-BIPE.d	Acquisition Date	4/15/2019 11:25:06 AM
Method	tune_low.m	Operator	UOH-Chemistry
Sample Name	POH-2-3-BIPE-CHCL3-ACN	Instrument	maXis 10138
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.4 Bar
Focus	Not active	Set Capillary	3600 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	6.0 l/min
Scan End	1800 m/z	Set Collision Cell RF	350.0 Vpp	Set Divert Valve	Waste

Bruker Compass DataAnalysis 4.0 printed: 4/15/2019 11:27:11 AM Page 1 of 1

Fig. S21 HRMS spectrum of **4** $(M+H)^+$; Calculated for $C_{16}H_{21}N_2O_4$ $[M+H]^+$: 305.1501; found: 305.1502.

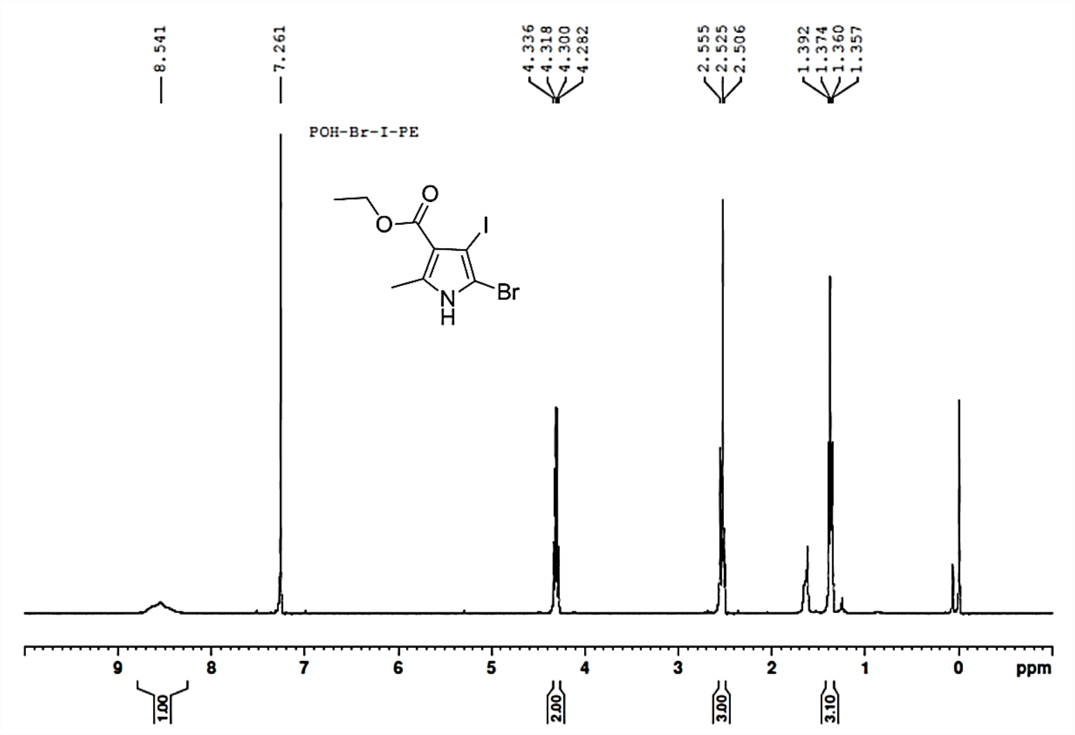


Fig. S22 ^{1}H NMR spectrum of **8** in $CDCl_3$.

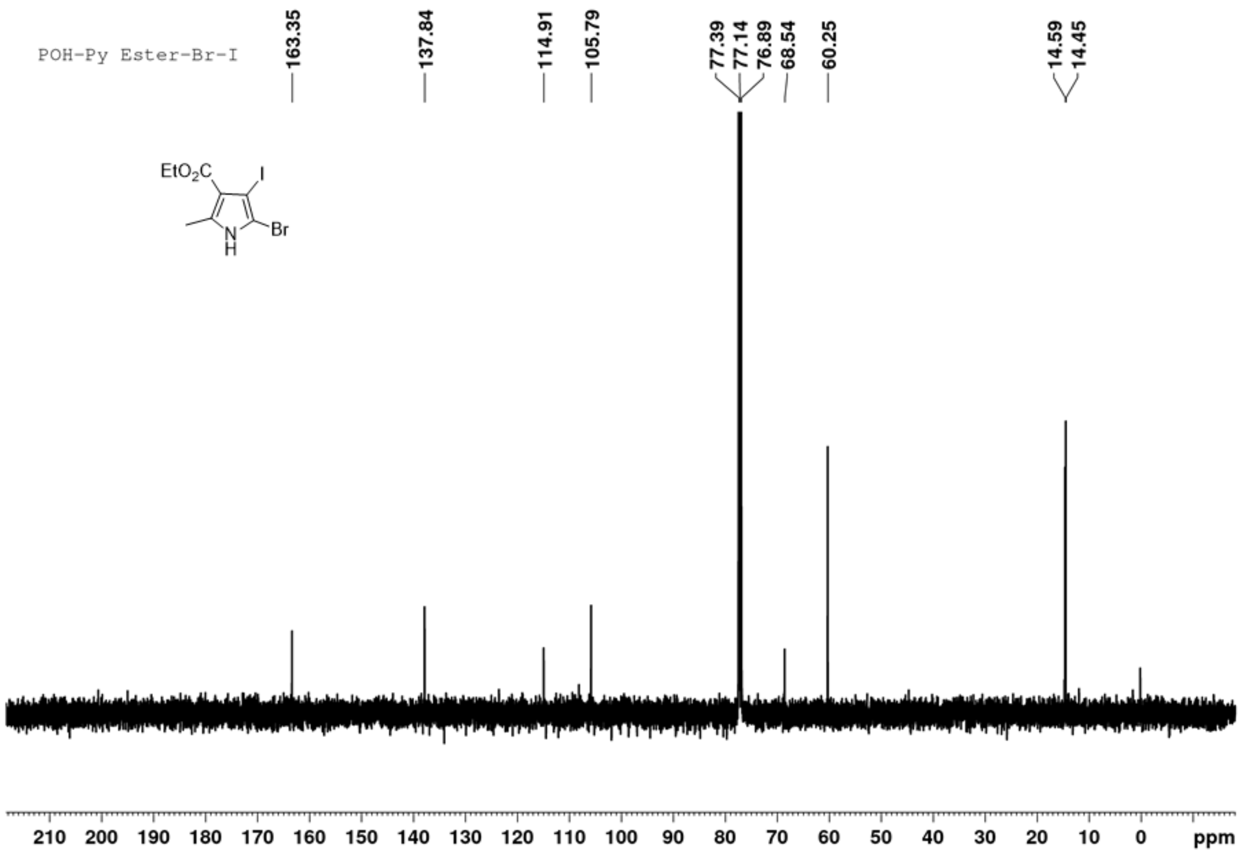
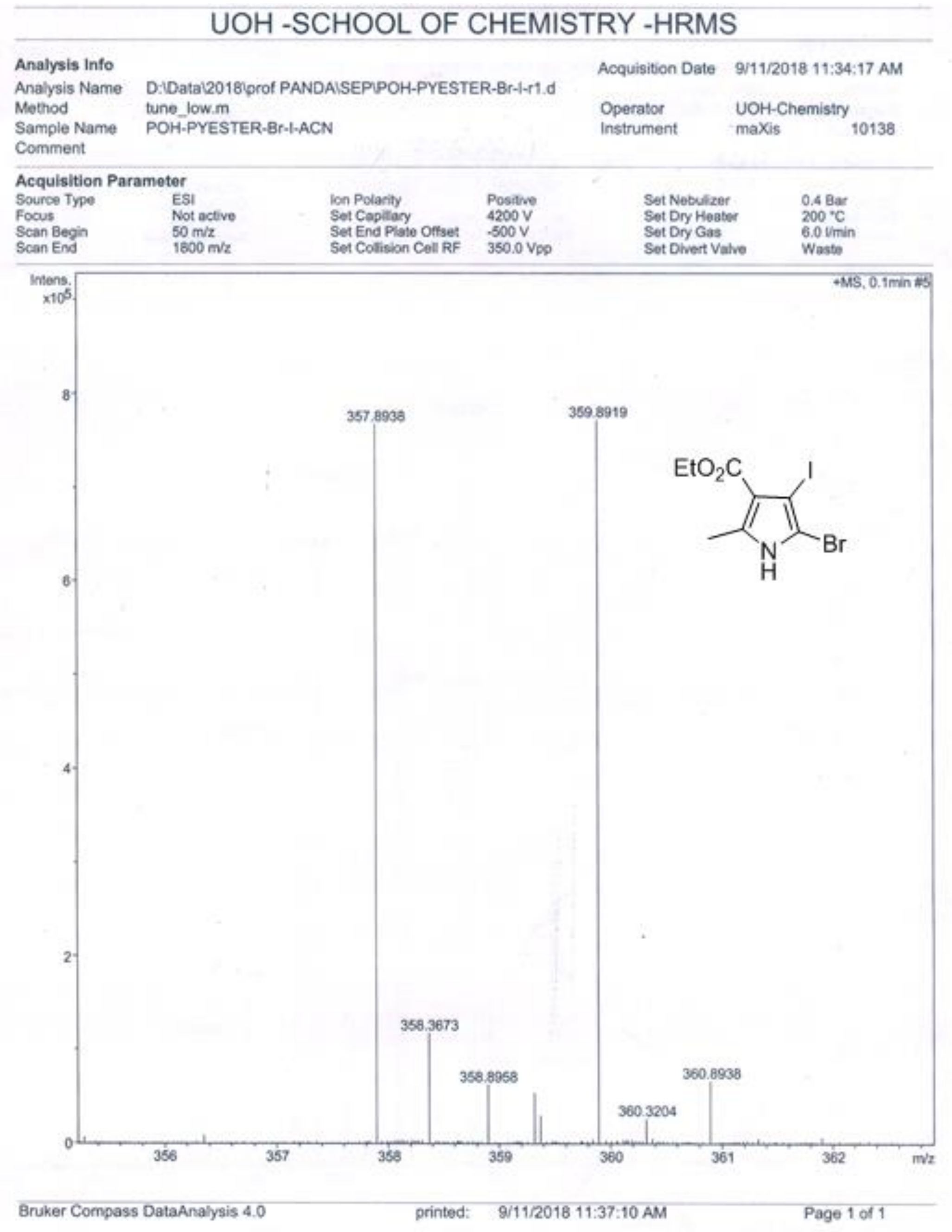


Fig. S23 ^{13}C NMR spectrum of **8** in CDCl$_3$.



UOH -SCHOOL OF CHEMISTRY -HRMS

Analysis Info

Analysis Name D:\Data\2018\prof PANDA\SEP\POH-PYESTER-Br-I-r1.d
Method tune_low.m
Sample Name POH-PYESTER-Br-I-ACN
Comment

Acquisition Date 9/11/2018 11:34:17 AM
Operator UOH-Chemistry
Instrument maXis 10138

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.4 Bar
Focus	Not active	Set Capillary	4200 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	6.0 l/min
Scan End	1800 m/z	Set Collision Cell RF	350.0 Vpp	Set Divert Valve	Waste

Bruker Compass DataAnalysis 4.0 printed: 9/11/2018 11:37:10 AM Page 1 of 1

Fig. S24 HRMS spectrum of **8** (M+H)$^+$; Calculated for $C_8H_{10}BrINO_2$ [M+H]$^+$: 357.8939; found: 357.8938.

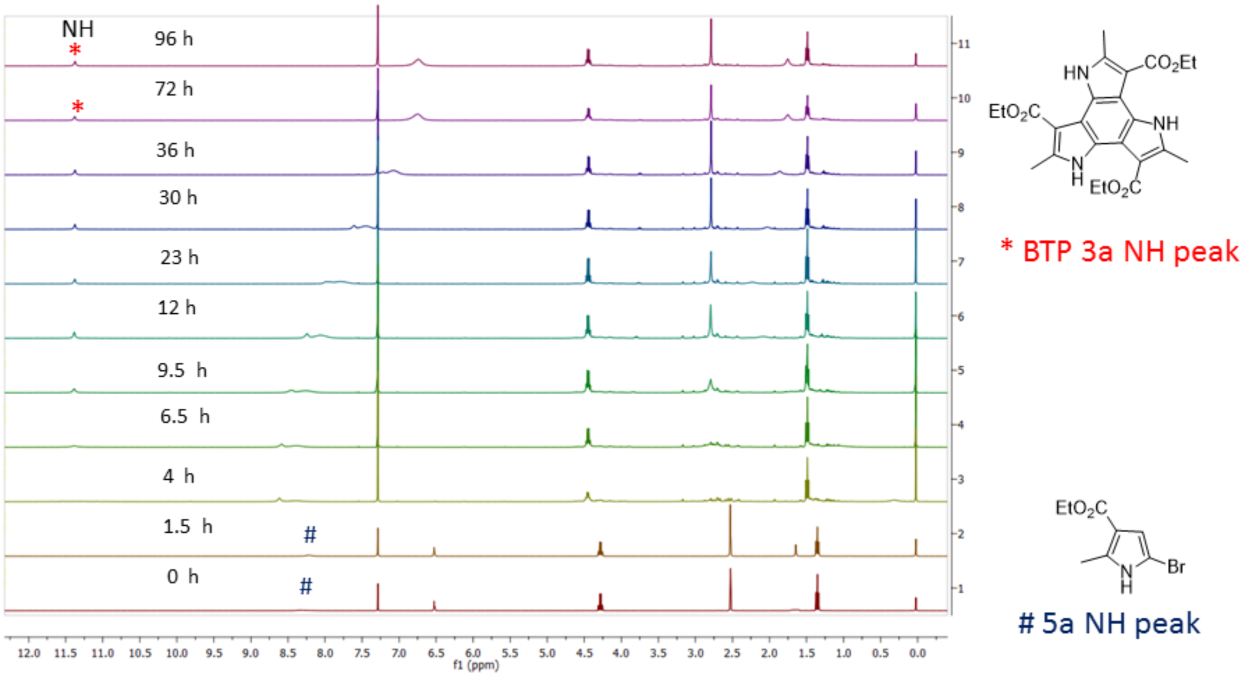


Fig. S25 Reaction monitoring of BTP **3a** in $CDCl_3$.

4. X-ray crystal structures and refinement data:

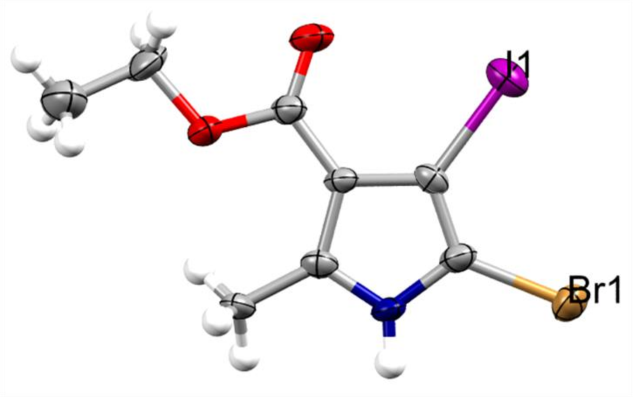


Fig. S26 ORTEP Pov-ray diagram of compound **8**; Thermal ellipsoids are scaled upto 35% probability level; Color code: grey: C, Blue: N, Red: O, Brown: Br, Violet: I and White: H.

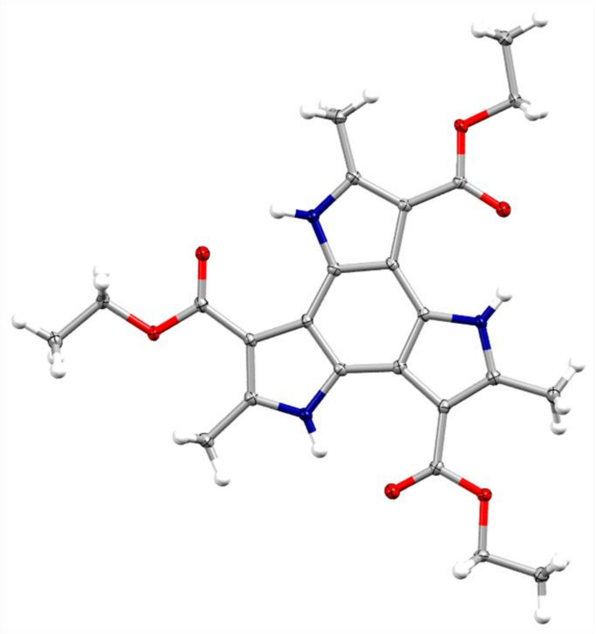


Fig. S27 ORTEP Pov-ray diagram of BTP **3a**; Thermal ellipsoids are scaled upto 50% probability level; Color code: grey: C, Blue: N, Red: O and White: H.

Table S2: Crystallographic data of compound **8**:

Identification code	**8**	
Empirical formula	$C_8 H_9 Br I N O_2$	
Formula weight	357.97	
Temperature	299(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P c	
Unit cell dimensions	a = 9.9046(5) Å	α = 90°.
	b = 8.2466(4) Å	β = 105.4160(10)°.
	c = 14.0533(6) Å	γ = 90°.
Volume	1106.56(9) $Å^3$	
Z	4	
Density (calculated)	2.149 Mg/m^3	
Absorption coefficient	6.475 mm^{-1}	
F(000)	672	
Crystal size	0.18 x 0.12 x 0.10 mm^3	
Theta range for data collection	3.825 to 25.108°.	
Index ranges	-11<=h<=11, -9<=k<=9, -15<=l<=16	
Reflections collected	18333	
Independent reflections	3616 [R(int) = 0.0455]	
Completeness to theta = 25.108°	96.2 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7459 and 0.7158	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3616 / 2 / 239	
Goodness-of-fit on F^2	1.185	
Final R indices [I>2sigma(I)]	R1 = 0.0424, wR2 = 0.1360	
R indices (all data)	R1 = 0.0432, wR2 = 0.1371	
Absolute structure parameter	0.5	
Extinction coefficient	n/a	
Largest diff. peak and hole	1.015 and -0.914 e.$Å^{-3}$	

Table S3: Crystallographic data of compound **3a**:

Identification code	**3a**	
Empirical formula	$C_{24} H_{27} N_3 O_6$	
Formula weight	453.48	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	*P* -1	
Unit cell dimensions	a = 7.5562(3) Å	α = 80.335(2)°.
	b = 7.5770(3) Å	β = 85.586(2)°.
	c = 19.0345(8) Å	γ = 86.0240(10)°.
Volume	1069.37(8) $Å^3$	
Z	2	
Density (calculated)	1.408 Mg/m^3	
Absorption coefficient	0.102 mm^{-1}	
F(000)	480	
Crystal size	0.28 x 0.24 x 0.18 mm^3	
Theta range for data collection	2.708 to 27.565°.	
Index ranges	-9<=h<=9, -9<=k<=9, -24<=l<=24	
Reflections collected	53415	
Independent reflections	4943 [R(int) = 0.0471]	
Completeness to theta = 25.242°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7459 and 0.7158	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4943 / 0 / 316	
Goodness-of-fit on F^2	0.810	
Final R indices [I>2sigma(I)]	R1 = 0.0419, wR2 = 0.1150	
R indices (all data)	R1 = 0.0535, wR2 = 0.1259	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.409 and -0.317 $e.Å^{-3}$	

5. Absorption Spectrum :

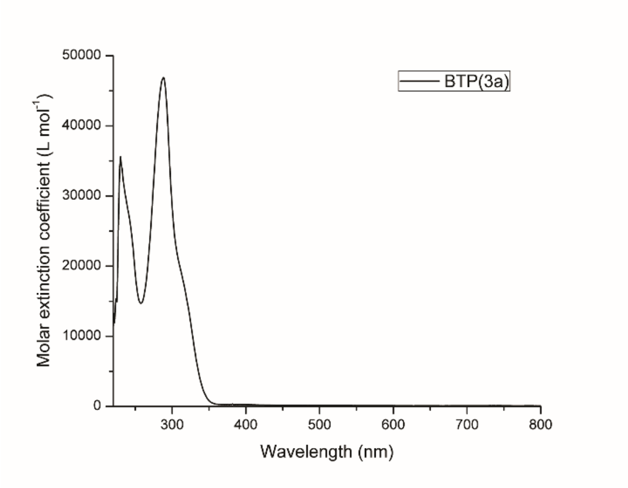


Fig. S28 UV -Vis absorption spectrum of BTP **3a** in DCM.

6. Electrochemical study:

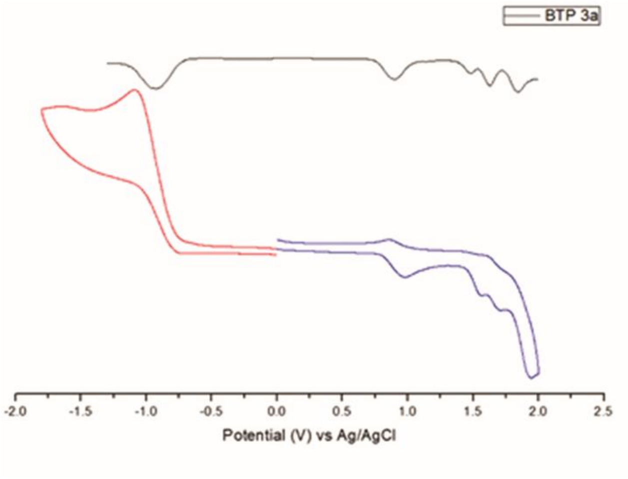


Fig. S29 CV and DPV of BTP **3a** vs Ag/AgCl at scan rate of 0.1 V/sec in DCM**.**

7. Computational study:

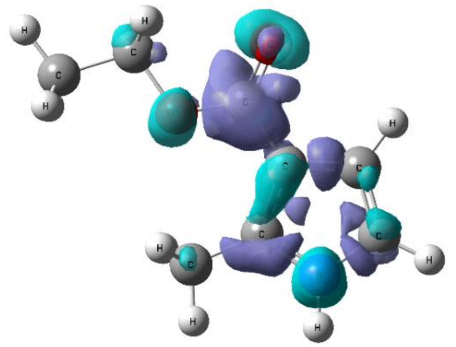
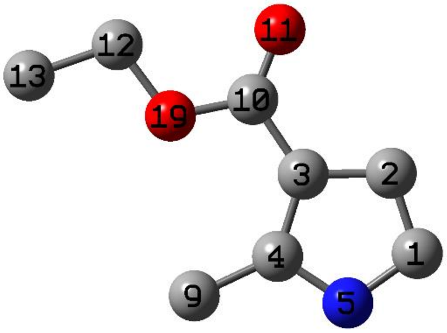
Quantum mechanical calculations were performed with Gaussian 09 program[S8] provided by CMSD facility of University of Hyderabad. All calculations were carried out by density functional theory (DFT) with Becke's three-parameter hybrid exchange functional and the Lee-Yang-Parr correlation functional (B3LYP) and the 6-311+G(d,p) basis set was used. The molecular orbitals were visualized using Gauss view 4.1 software. The theoretical excitation energies are obtained for the compound BTP **3a** by applying the TD-SCF method, which are visualized and tabulated by using GaussSum 3.0 software. Fukui function[S9] and dual descriptor study[S10] have been carried out by Multiwfn program,[S11] to generate electron density surfaces to understand the electrophilic and nucleophilic centers, and the corresponding electron density cubes were visualized by using the GaussView 4.1 software. The nucleus independent chemical shift, NICS(1) values were obtained with gauge independent atomic orbital (GIAO) method based on the optimized geometries.[S12] HOMA (Harmonic Oscillator Model of Aromaticity) was calculated by using Ropt (C-C) = 1.388 Å and Ropt (C-N) = 1.334 Å.[S13]

7.1 Visualization of iso-surface of dual descriptors of the compounds: where the cyan colored mesh (negative), which indicates about the more electron density (favorable for the electrophilic attack) and the violet colored mesh (positive) indicates the less electron density (favorable for nucleophilic attack).

7.1.1 Exact evaluation of dual descriptor based on electron density:[S11]

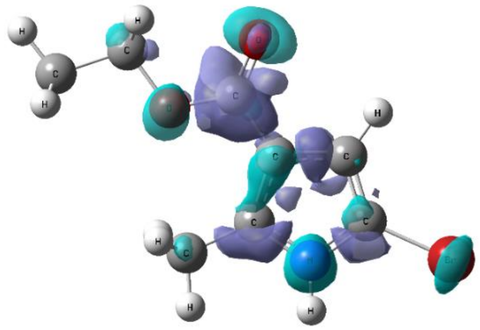
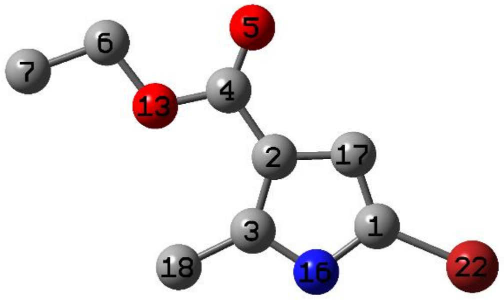
Electron densities have calculated for the electron systems N, N+1 and N-1; $\boldsymbol{f}^-$ **=** for electrophilic attack, $\boldsymbol{f}^+$ **=** for nucleophilic attack;

1. Compound 1a:

	
Electron density surfaces **Mesh color (cyan = - ve; violet = + ve)**	**Corresponding atomic labels**

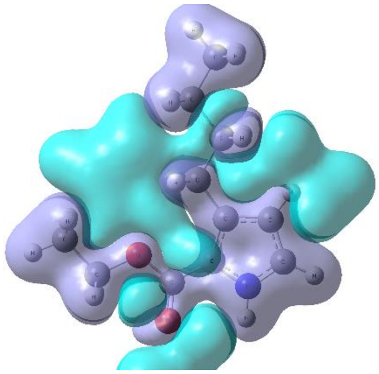
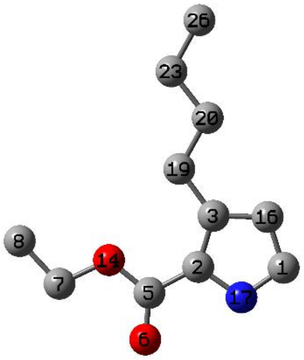
Symbol	Label	N	N-1	N+1	f^-	f^+	Δf
C	1	0.019486	0.132634	-0.093563	**0.113148**	0.113049	-0.00010
C	2	-0.002637	0.013405	-0.12303	**0.016042**	0.120393	0.10435

2. Compound 5a:

	
Electron density surfaces **Mesh color (cyan = - ve; violet = + ve)**	**Corresponding atomic labels**

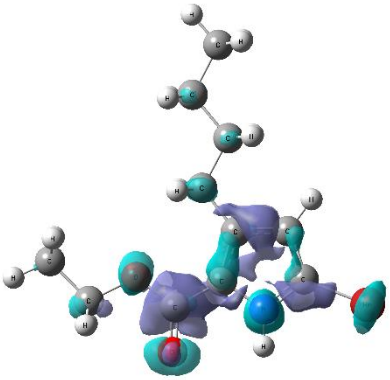
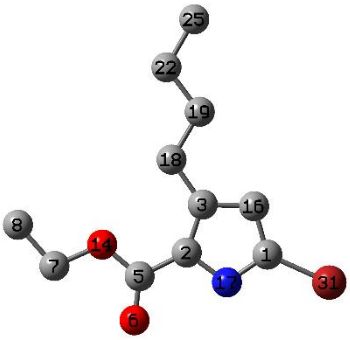
Symbol	Label	N	N-1	N+1	f^-	f^+	Δf
C	1	0.106572	0.109011	-0.033854	0.002439	0.140426	0.13799
C	17	0.027139	0.004871	-0.112539	-0.022268	**0.139678**	0.16195
Br	22	-0.101502	0.2037	-0.151827	**0.305202**	0.050325	-0.25488

3. Compound 9:

	
Electron density surfaces **Mesh color (cyan = - ve; violet = + ve)**	**Corresponding atomic labels**

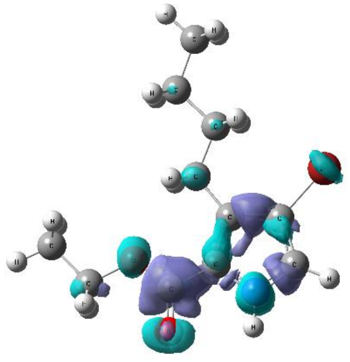
Symbol	**Label**	**N**	**N-1**	**N+1**	**f^-**	**f^+**	**Δf**
C	1	0.054083	0.135465	-0.114745	**0.081382**	**0.168828**	0.08745
C	16	-0.032076	-0.016716	-0.142837	**0.015360**	**0.110761**	0.09540

4. Compound 9a:

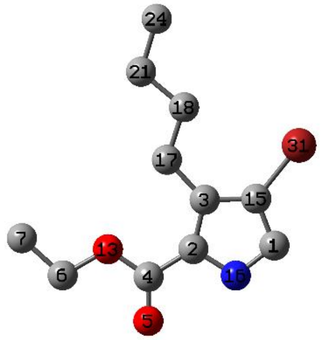
	
Electron density surfaces **Mesh color (cyan = - ve; violet = + ve)**	**Corresponding atomic labels**

Symbol	**Label**	**N**	**N-1**	**N+1**	**f^-**	**f^+**	**Δf**
C	1	0.136565	0.114857	-0.051147	**-0.021708**	**0.187712**	0.20942
C	16	0.00299	-0.022647	-0.133547	**-0.025637**	**0.136537**	0.16217
Br	31	-0.096586	0.198358	-0.152781	**0.294944**	**0.056195**	-0.23875

5. Compound 9b:



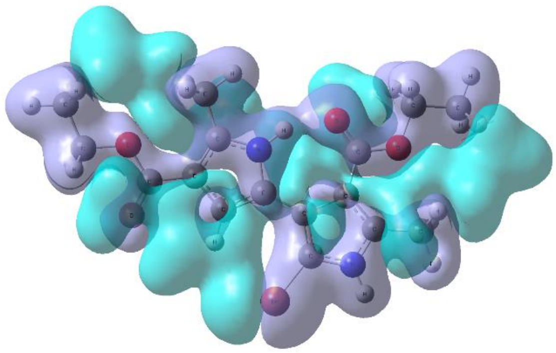
Electron density surfaces
Mesh color (cyan = - ve; violet = + ve)



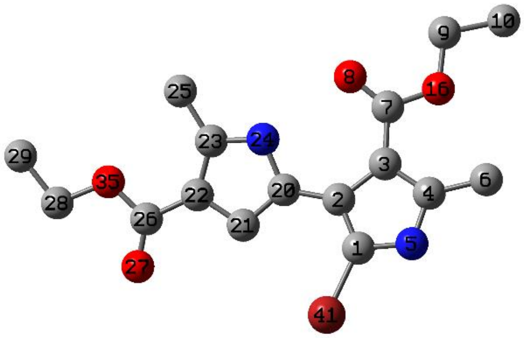
Corresponding atomic labels

Symbol	Label	N	N-1	N+1	f^-	f^+	Δf
C	1	0.08926	0.126615	-0.106996	**0.037355**	**0.196256**	0.15890
C	15	0.059488	0.021465	-0.076607	**-0.038023**	**0.136095**	0.17412
Br	31	-0.098893	0.175836	-0.131365	**0.274729**	**0.032472**	-0.24226

6. Compound 6:



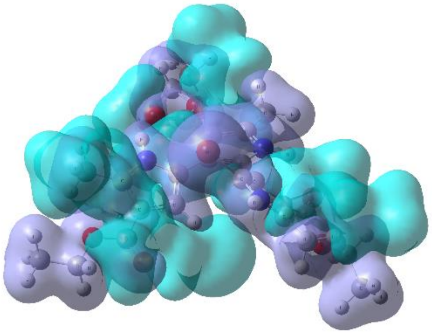
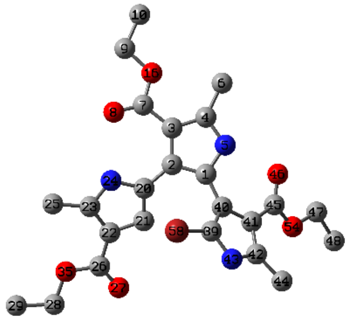
Electron density surfaces
Mesh color (cyan = - ve; violet = + ve)



Corresponding atomic labels

Symbol	Label	N	N-1	N+1	f^-	f^+	Δf
C	1	0.104927	0.067824	-0.019533	-0.037103	0.124460	0.16156
C	21	-0.003191	-0.018304	-0.121349	-0.015113	**0.118158**	0.13327
Br	41	-0.07848	0.113943	-0.076482	**0.192423**	-0.001998	-0.19442

7. Compound 7:

	
Electron density surfaces **Mesh color (cyan = - ve; violet = + ve)**	**Corresponding atomic labels**

Symbol	Label	N	N-1	N+1	f^-	f^+	Δf
C	21	-0.013466	-0.029369	-0.102527	-0.015903	**0.089061**	0.10496
C	39	0.125477	0.038207	-0.005638	-0.087270	0.131115	0.21839
Br	58	-0.081544	0.043173	-0.060569	**0.124717**	-0.020975	-0.14569

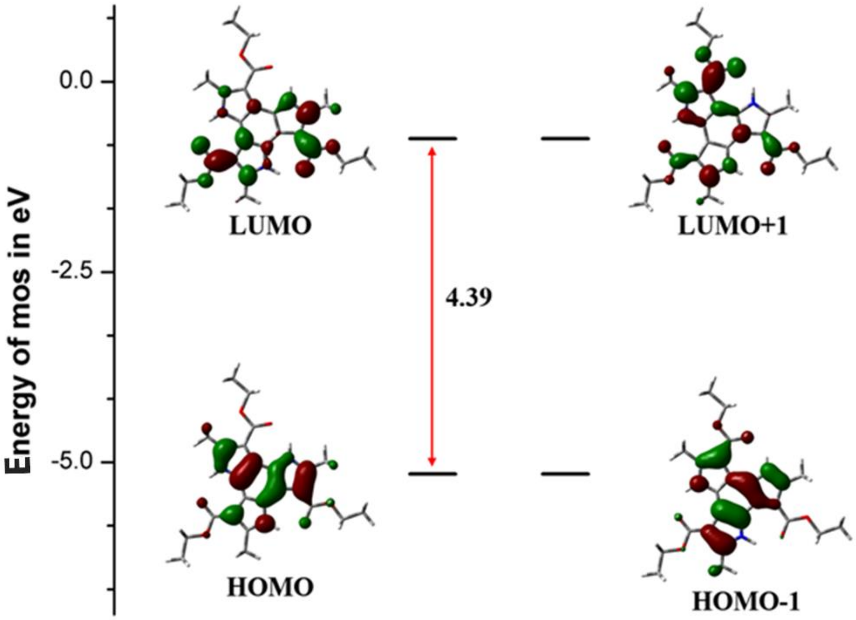


Fig. S 30 Selected molecular orbital diagram of the optimized structure of BTP **3a**.

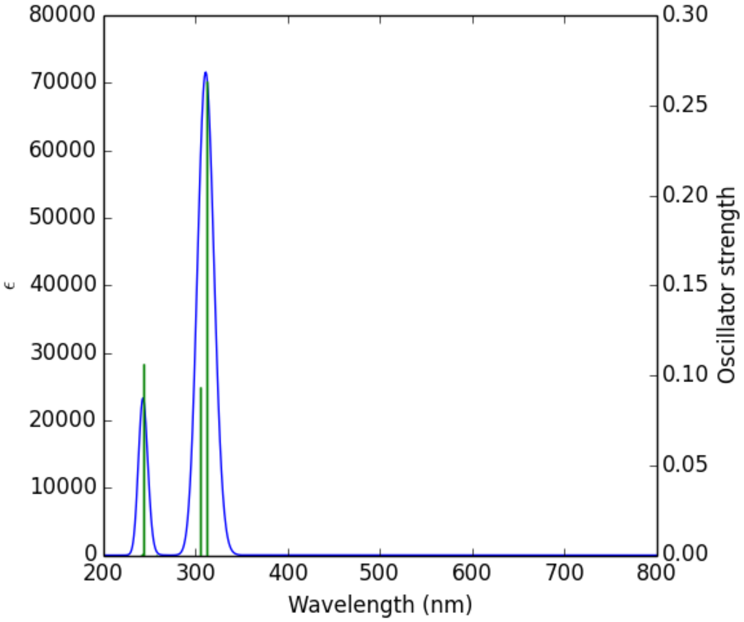


Fig. S31 Theoretical absorption spectrum (by TD-DFT) of BTP **3a**.

Table S4: Summary of theoretical excitation energies of BTP **3a**

Sl. No.	**Wavelength (nm)**	**Oscillator Strength**	**Major contributions**
1	312.87	0.2631	H-1 —> L+1 (22%), H-1 —> L+2 (16%), HOMO —> LUMO (21%), HOMO —> L+2 (20%)
2	312.84	0.2636	H-1 —> LUMO (22%), H-1 —> L+2 (20%), HOMO —> L+1 (22%), HOMO —> L+2 (16%)
3	305.27	0.0932	H-1 —> LUMO (10%), H-1 —> L+2 (25%), HOMO —> L+1 (10%), HOMO —> L+2 (38%)
4	305.25	0.0935	H-1 —> L+1 (10%), H-1 —> L+2 (38%), HOMO —> LUMO (10%), HOMO —> L+2 (25%)
5	243.22	0.1063	H-2 —> LUMO (91%), H-1 —> L+10 (2%), HOMO —> L+9 (2%)
6	243.21	0.1064	H-2 —> L+1 (91%), H-1 —> L+9 (2%), HOMO —> L+10 (2%)

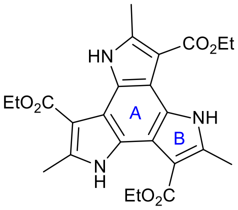
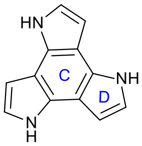
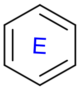
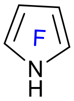
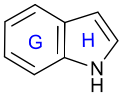
Table S5: Cartesian coordinates of the optimized structure BTP **3a**

Atom Label	Symbol	x	y	z	Atom Label	Symbol	x	y	z
1	O	-1.29239	4.988344	-6.6E-05	31	H	-5.52449	-3.29128	0.881703
2	O	-3.67434	-3.61336	-0.0001	32	C	-5.39367	-5.27444	0.00058
3	O	4.966564	-1.37532	-9.3E-05	33	H	-4.97304	-5.7553	-0.88561
4	O	3.19861	-2.76723	-0.0004	34	H	-6.47408	-5.44259	0.000271
5	O	-3.99509	-1.38629	-8.3E-05	35	H	-4.97366	-5.75446	0.887515
6	O	0.797036	4.153454	0.000216	36	C	-3.62164	3.252689	-7.1E-05
7	N	2.159736	1.713534	0.000154	37	H	-4.53542	2.654622	0.000798
8	N	-2.56389	1.01332	0.000001	38	H	-3.63157	3.902942	-0.87753
9	N	0.404338	-2.72743	-9.7E-05	39	H	-3.63072	3.904293	0.87637
10	C	-1.02532	-0.99568	-0.00005	40	C	-0.72446	6.318279	-0.00013
11	C	0.335994	-1.34813	-6.1E-05	41	H	-0.08977	6.430621	-0.8822
12	C	-3.21827	-2.3361	-5.4E-05	42	H	-0.08971	6.430702	0.88188
13	C	3.257675	0.913265	0.000076	43	C	5.834565	-2.5319	-0.00031
14	C	-2.41978	2.364294	0.000024	44	H	5.615043	-3.13742	-0.88272
15	C	-1.04794	2.653268	0.000066	45	H	5.61444	-3.13826	0.881355
16	C	2.822079	-0.41929	-4.6E-05	46	C	-1.00654	-4.76308	-0.00015
17	C	1.37494	-0.39044	0.000069	47	H	-0.03189	-5.25575	-0.0013
18	C	-1.33522	0.38293	0.000033	48	H	-1.56666	-5.09643	-0.87648
19	C	3.632501	-1.6195	-0.00016	49	H	-1.56462	-5.09665	0.877429
20	C	0.99948	0.964715	0.000151	50	C	-1.87265	7.307642	-0.00014
21	C	-0.41384	3.955197	0.000083	51	H	-2.49874	7.183821	-0.8868
22	C	-0.34935	1.385655	0.0001	52	H	-1.47845	8.327546	0.00001
23	C	-1.77376	-2.23449	-0.00004	53	H	-2.49887	7.183628	0.88641
24	C	-0.83771	-3.27807	-0.00015	54	C	7.265209	-2.03133	0.000401
25	C	4.627933	1.510014	0.00023	55	H	7.470597	-1.42641	-0.8858
26	H	5.19648	1.19238	-0.87648	56	H	7.952133	-2.88204	0.000336
27	H	5.195949	1.193069	0.87757	57	H	7.469919	-1.42709	0.887219
28	H	4.566653	2.600381	-0.00019	58	H	1.302794	-3.20466	-0.00014
29	C	-5.11018	-3.78556	-5.9E-05	59	H	2.123769	2.730242	0.000242
30	H	-5.52443	-3.29209	-0.88232	60	H	-3.42631	0.473648	-0.00018

Table S6: Cartesian coordinates of the optimized structure **BTP (free)**

Atom Label	Symbol	x	y	z
1	N	-0.95449	-2.58909	-0.00047
2	N	2.719318	0.468068	0.000166
3	N	-1.76502	2.121101	0.000007
4	C	0.354683	1.388403	0.000308
5	C	-0.99462	0.978997	0.000526
6	C	-2.32791	-2.43689	-0.00013
7	C	3.274451	-0.79733	0.000286
8	C	2.263801	-1.72491	0.00004
9	C	-2.62564	-1.09782	0.000456
10	C	-1.37974	-0.38707	0.000288
11	C	1.345045	0.371751	-0.00016
12	C	-0.35049	-1.35093	-0.0001
13	C	1.025131	-1.0016	-0.00035
14	C	0.362009	2.822795	-0.00039
15	C	-0.94655	3.234407	-0.00038
16	H	-2.77031	2.142882	0.00005
17	H	-0.47073	-3.47058	-0.00076
18	H	3.240594	1.327962	0.000568
19	H	-1.36495	4.227908	-0.00029
20	H	1.219853	3.477522	-0.00057
21	H	4.344081	-0.9315	0.000266
22	H	2.402442	-2.79513	-0.00026
23	H	-2.97906	-3.29604	0.000004
24	H	-3.62161	-0.6824	0.000713

Table S7: Summary of calculated NICS (1) and HOMA values.

Compounds		**NICS(1)**	**HOMA**
BTP (3a)		A = - 10.45 B = - 9.21	A = 0.847 B = 0.484
BTP free		C = -9.85 D = -9.38	C = 0.767 D = 0.534
Benzene		E = -10.20 *	E = 0.972
Pyrrole		F = -10.09 *	F = 0.693
Indole		G = -10.83 * H = -10.18 *	G = 0.894 H = 0.422

NICS values calculated by using B3LYP/6-311+G(d,p) by NMR GIAO method in Gaussian 09. ‘*’ = from ref S13.

8. TGA-DTA profiles: DTA-TG was measured at the scanning rate of 10 °C min^{-1} under nitrogen atmosphere.

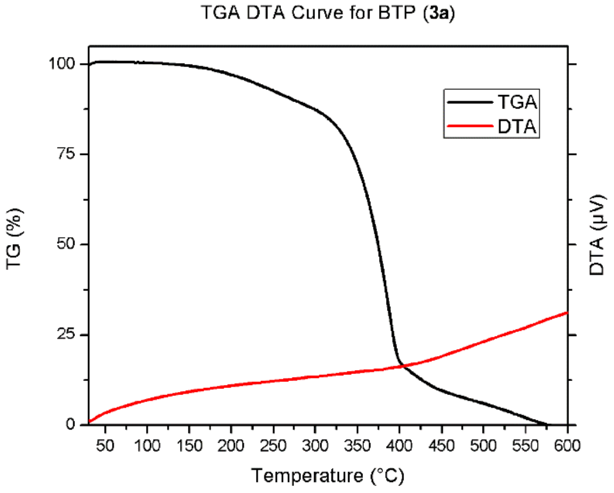


Fig. S32 TGA profile for BTP **3a**.

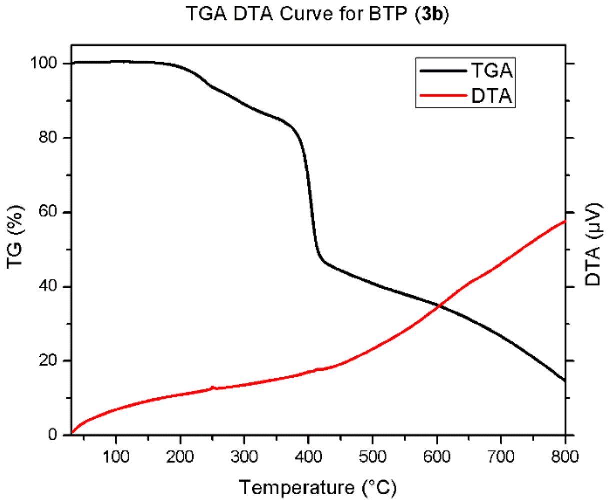


Fig. S33 TGA profile for BTP **3b**.

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