SUPPLEMENTARY INFORMATION

2-Amino-4,6-Diarylpyrimidines As Potential Chronic Myeloid Leukemia Cell Inhibitors Targeting Anti-ABL1 Kinase: Microwave-Assisted Synthesis, Biological Evaluation, Molecular Docking, And Dynamics Studies

Thi-Anh-Truc Phan, [a,b] Kim-Khanh-Huy Ngo, [a] Thi-Cam-Thu Nguyen, [a] Thanh-Tan Mai, [c] Hai-Dang Nguyen, [d] Thu-Trang Duong, [d] Le-Phu Tran, [a,b] Thanh-Tuyen Duong, [a,b] Thi-Kim-Chi Huynh, [a] Elena V. Koroleva, [e] Zhanna V. Ignatovich, [e] Anastasiya L. Ermolinskaya, [e] Hoang-Phuc Nguyen, [a] Thi-Hong-An Nguyen, [a] Anh-Khoa Ton, [a] Tuong-Ha Do, [b] Thi-Kim-Dung Hoang *[a]

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[e] *Institute of Chemistry of New Materials, National Academy of Sciences of Belarus, 36, F. Skorina St., Minsk, 220141, Republic of Belarus.*

FIGURE CAPTIONS

TABLE CAPTIONS

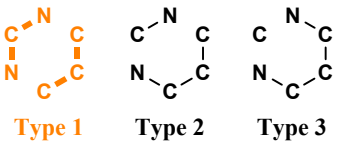

Figure S1. Synthetic approaches for pyrimidine nucleus

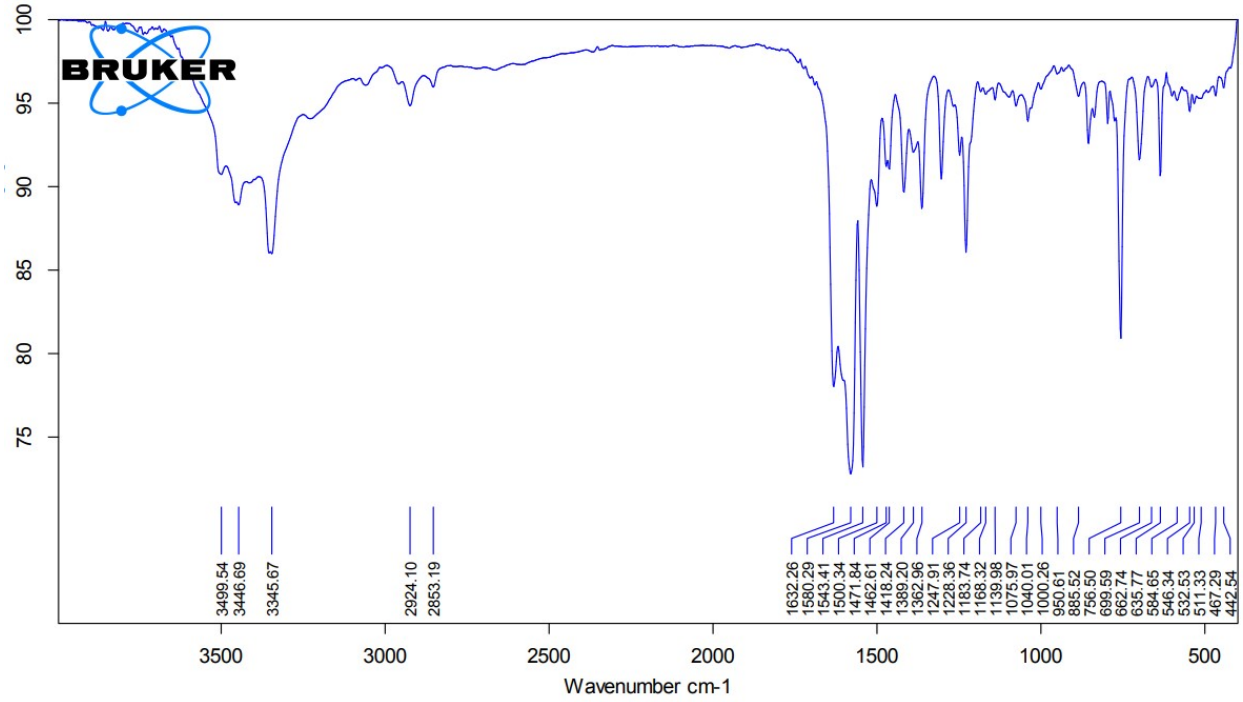

Figure S2. FTIR spectrum of compound **1a**

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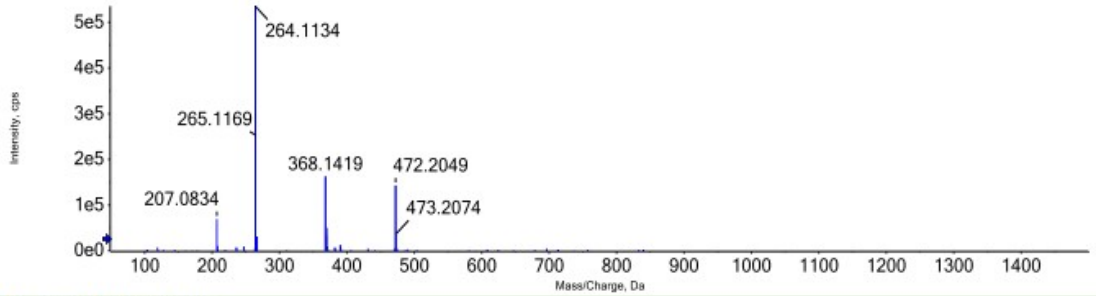
Injection details

Sample name	PH2HA	*Vial position*	5
Sample file name	SER. wiff2- HUY	*Inject volume*	2.00
Acquisition date	27/02/2024 11:30:14 AM	*Acquisition method*	**ESI _POS_SCAN**
Operator	CB21261708	*Instrument name*	X500R QTOF

Full mass spectrum

Spectrum from HUY_PH2HA_(+)ESI 2024-02-27-11-30-14.wiff2 (sample 1) - HUY_PH2HA_(+)E... 0.181 min, noise filtered (noise multiplier = 1.5), Gaussian smoothed (0.5 points)



Expanded spectrum

Spectrum from HUY_PH2HA_(+)ESI 2024-02-27-11-30-14.wiff2 (sample 1) - HUY_PH2HA_(+)E... 0.181 min, noise filtered (noise multiplier = 1.5), Gaussian smoothed (0.5 points)

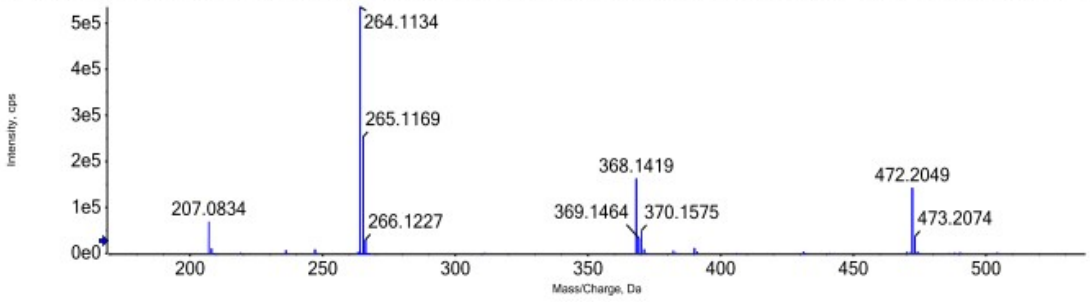


Figure S3. HRMS spectrum of compound **1a**

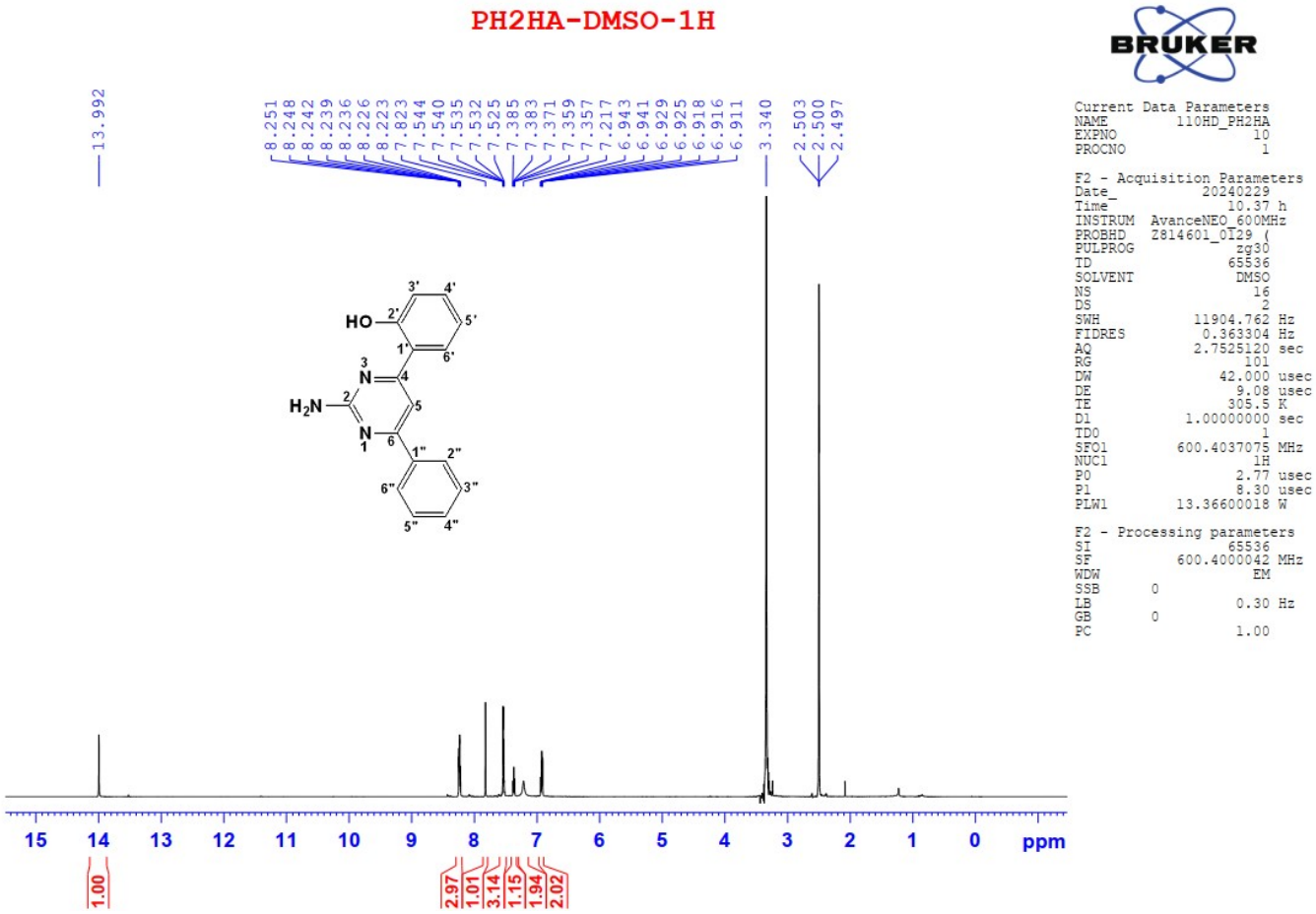


Figure S4. ^{1}H-NMR spectrum of compound **1a**

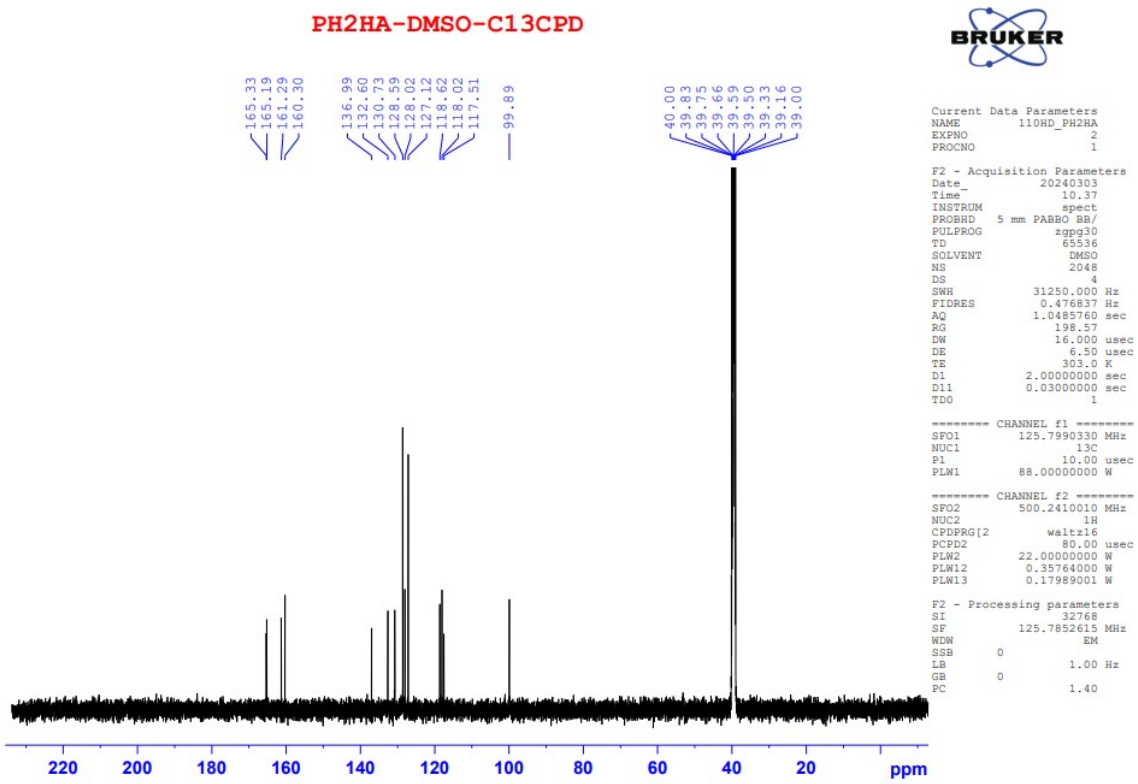


Figure S5. ^{13}C-NMR spectrum of compound **1a**

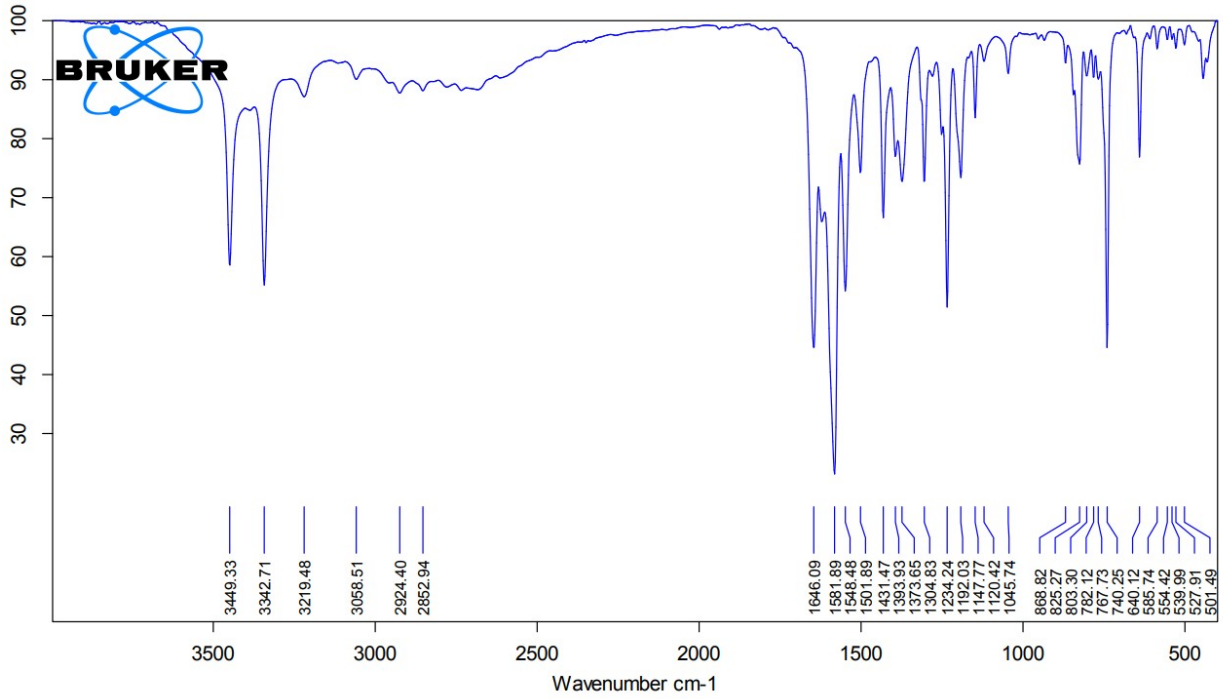


Figure S6. FTIR spectrum of compound **1b**

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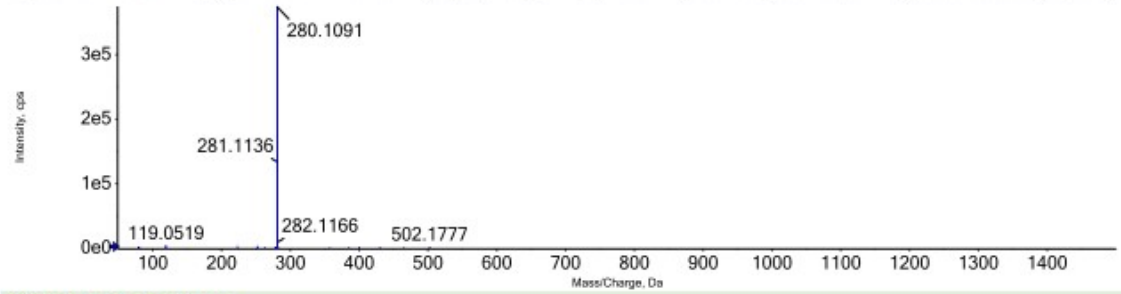
Injection details

Sample name	PH2H2H	*Vial position*	6
Sample file name	SER. wiff2- HUY	*Inject volume*	2.00
Acquisition date	27/02/2024 11:32:18 AM	*Acquisition method*	**ESI _POS_SCAN**
Operator	CB21261708	*Instrument name*	X500R QTOF

Full mass spectrum

Spectrum from HUY_PH2H2H_(+)ESI 2024-02-27-11-32-18.wiff2 (sample 1) - HUY_PH2H2H_(... 0.162 min, noise filtered (noise multiplier = 1.5), Gaussian smoothed (0.5 points)



Expanded spectrum

Spectrum from HUY_PH2H2H_(+)ESI 2024-02-27-11-32-18.wiff2 (sample 1) - HUY_PH2H2H_(... 0.162 min, noise filtered (noise multiplier = 1.5), Gaussian smoothed (0.5 points)

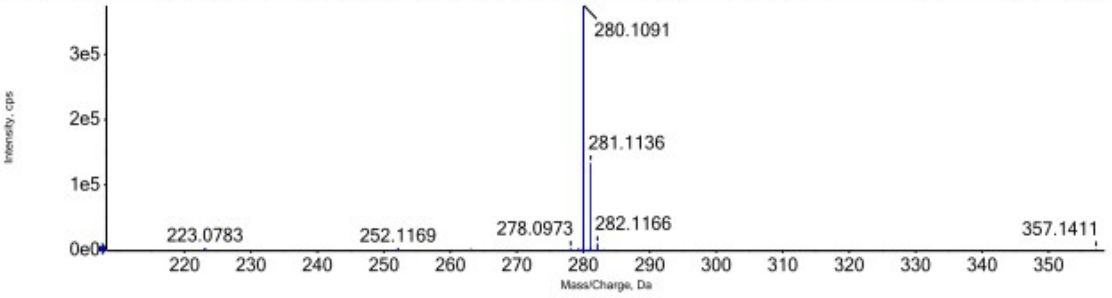


Figure S7. HRMS spectrum of compound **1b**

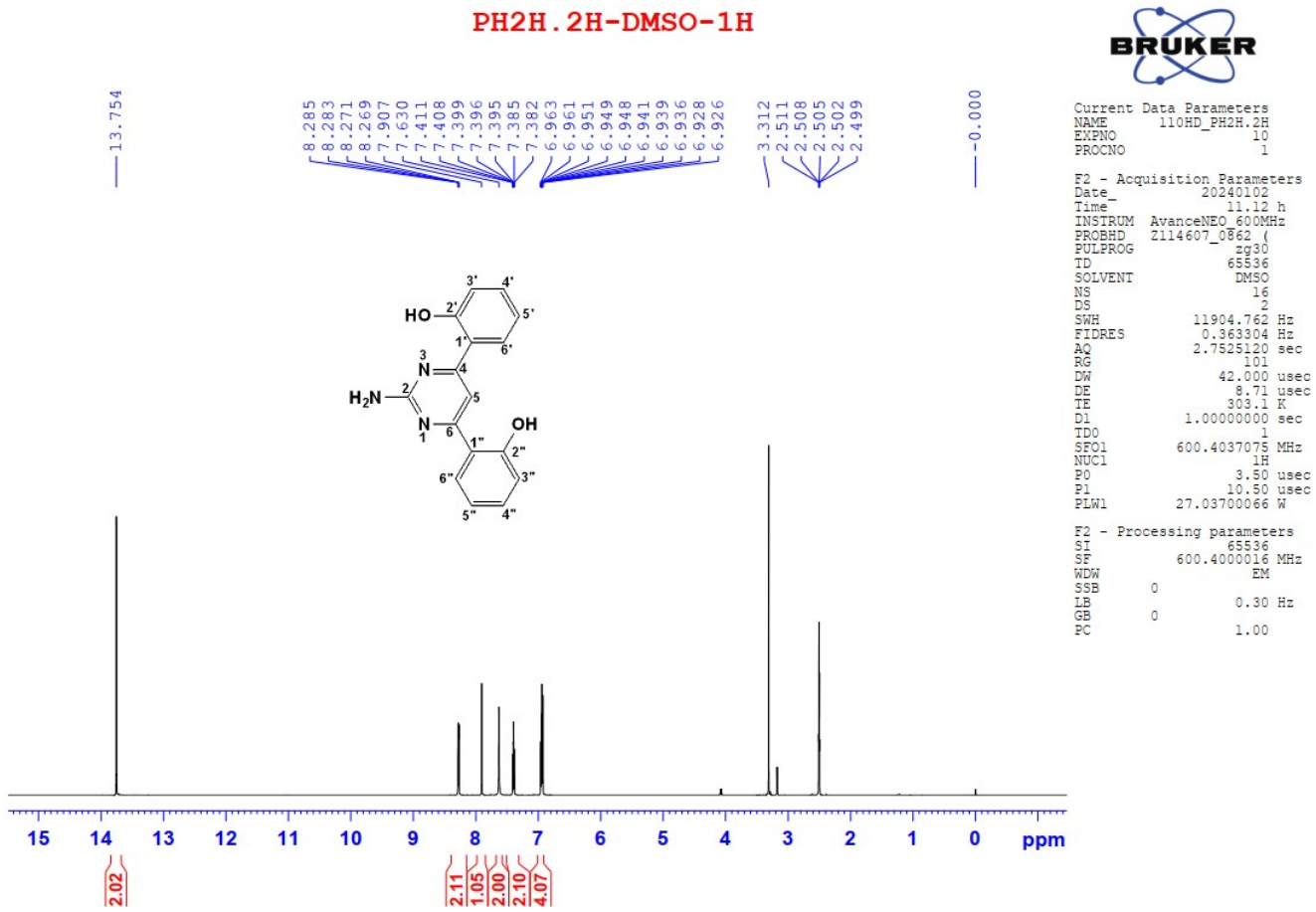


Figure S8. ^{1}H-NMR spectrum of compound **1b**

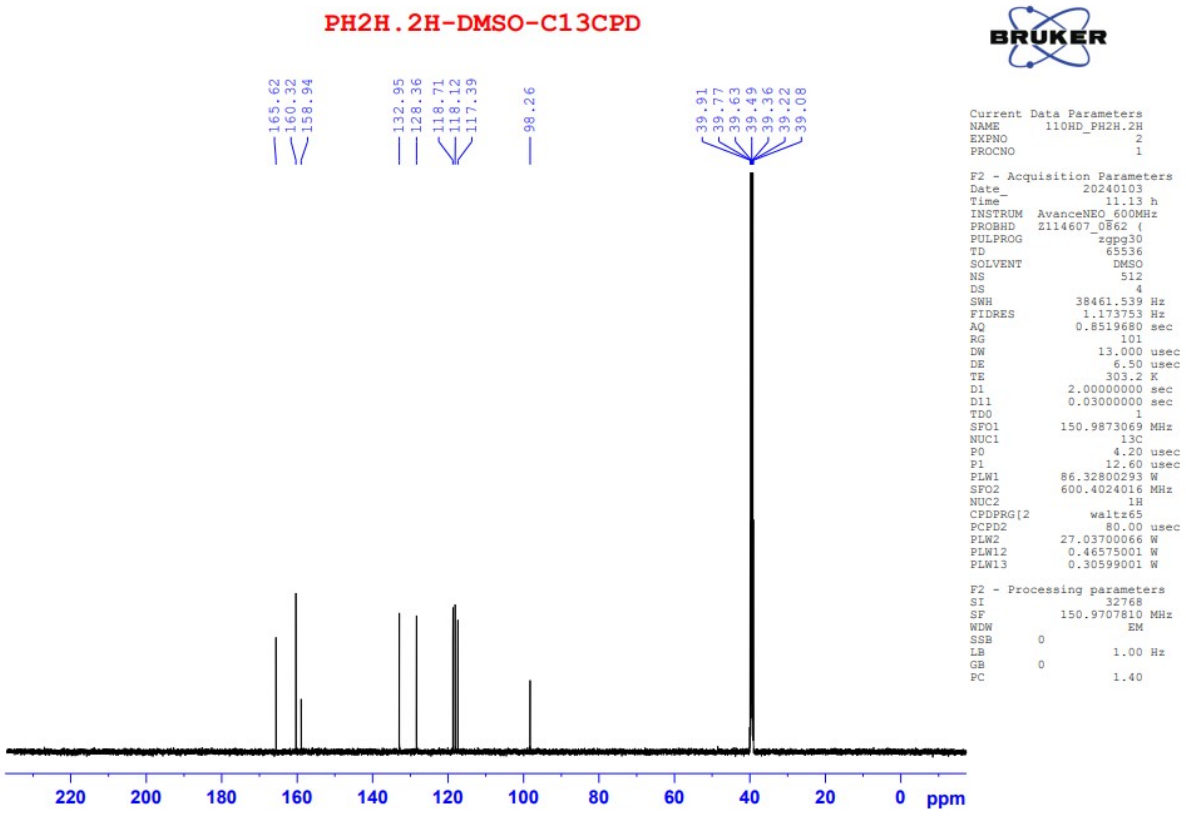


Figure S9. ^{13}C-NMR spectrum of compound **1b**

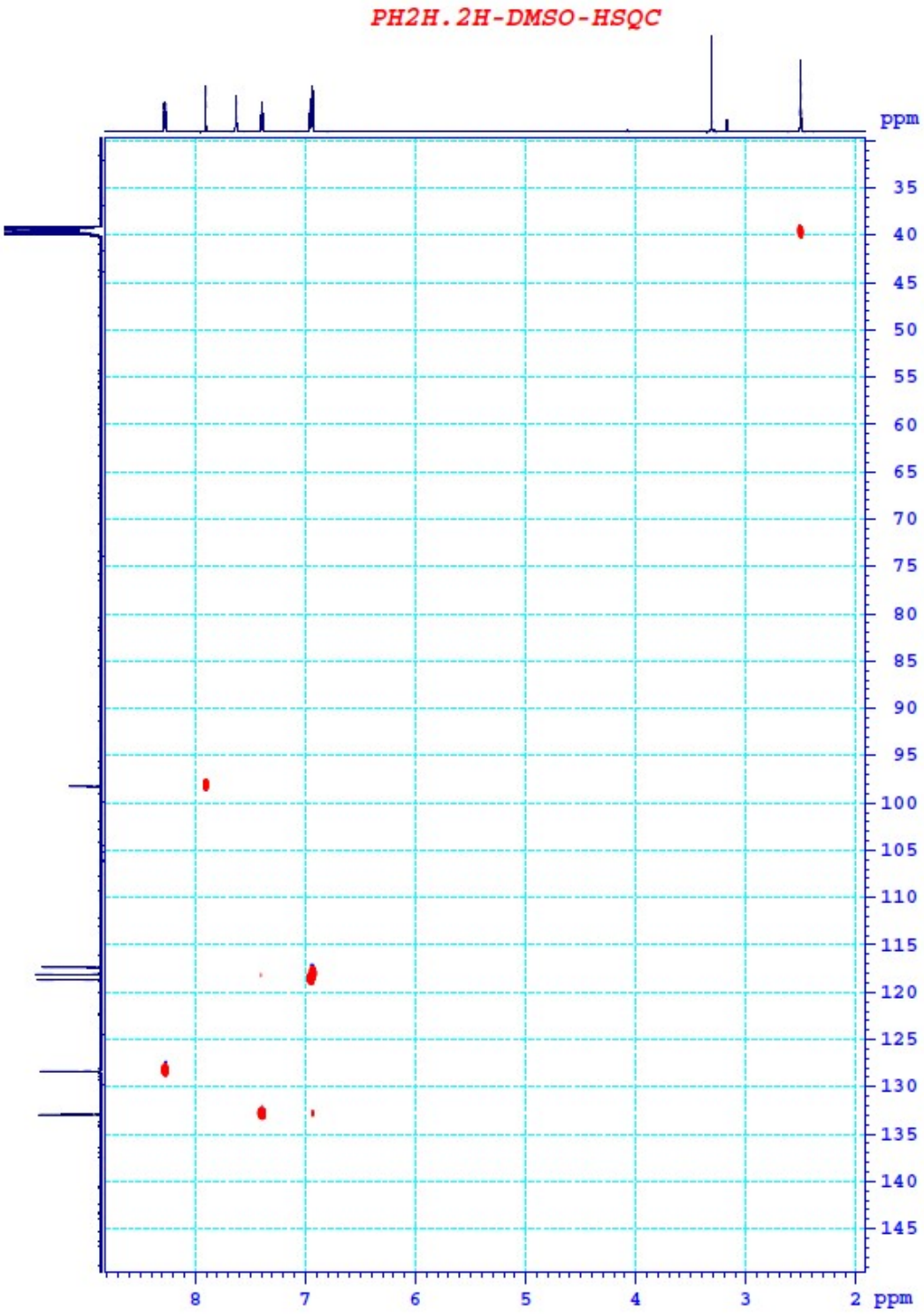


Figure S10. HSQC of compound **1b**

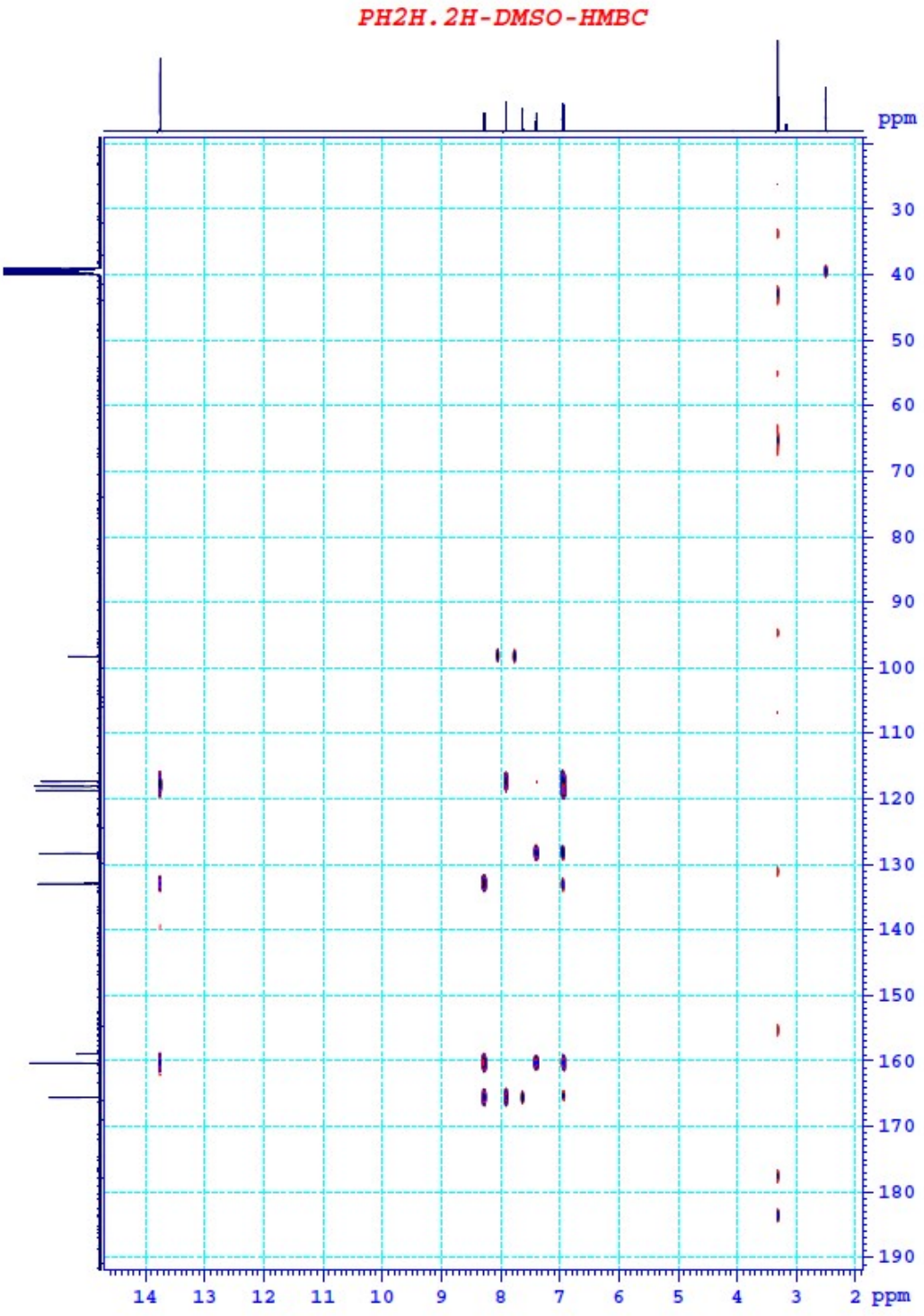


Figure S11. HMBC of compound **1b**

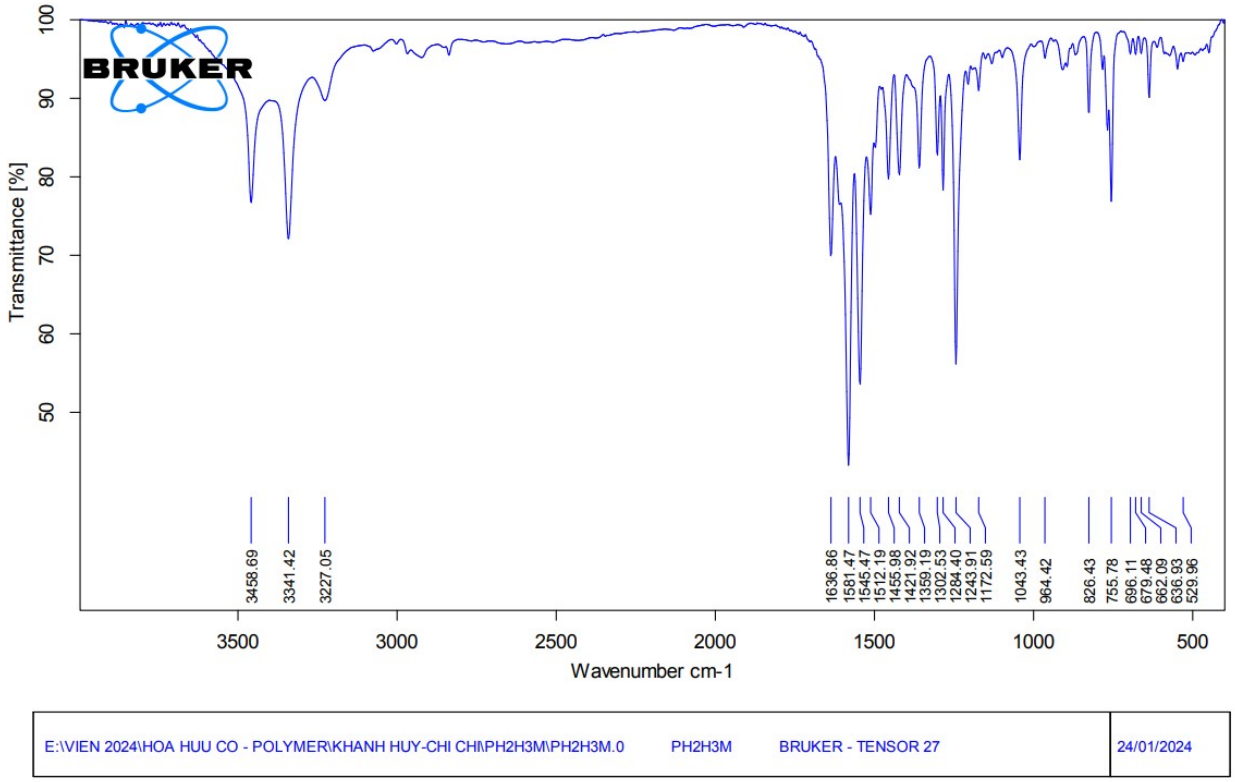


Figure S12. FTIR spectrum of compound **1c**

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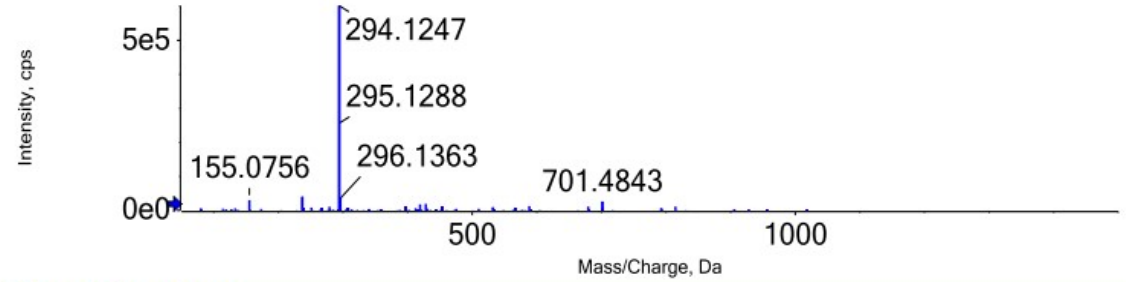
ANALYSIS REPORT

Injection details

Sample name	PH2H3M	*Vial position*	20
Sample file name	SER. wiff2- HUY	*Inject volume*	2.00
Acquisition date	19/01/2024 09:49:13 AM	*Acquisition method*	**ESI _POS_SCAN**
Operator	CB21261708	*Instrument name*	X500$_R$ QTOF

Full mass spectrum

Spectrum from HUY_PH2H3M_(+)ESI 2024-01-19-09-49-13...e multiplier = 1.5), Gaussian smoothed (0.5 points)



Expanded spectrum

Spectrum from HUY_PH2H3M_(+)ESI 2024-01-19-09-49-13...e multiplier = 1.5), Gaussian smoothed (0.5 points)

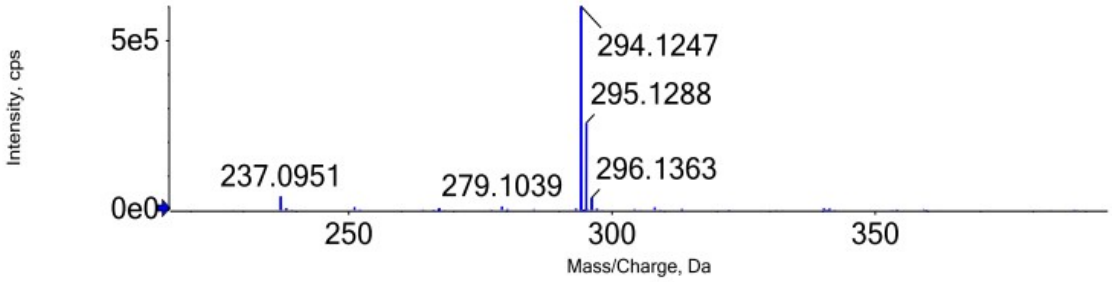


Figure S13. HRMS spectrum of compound **1c**

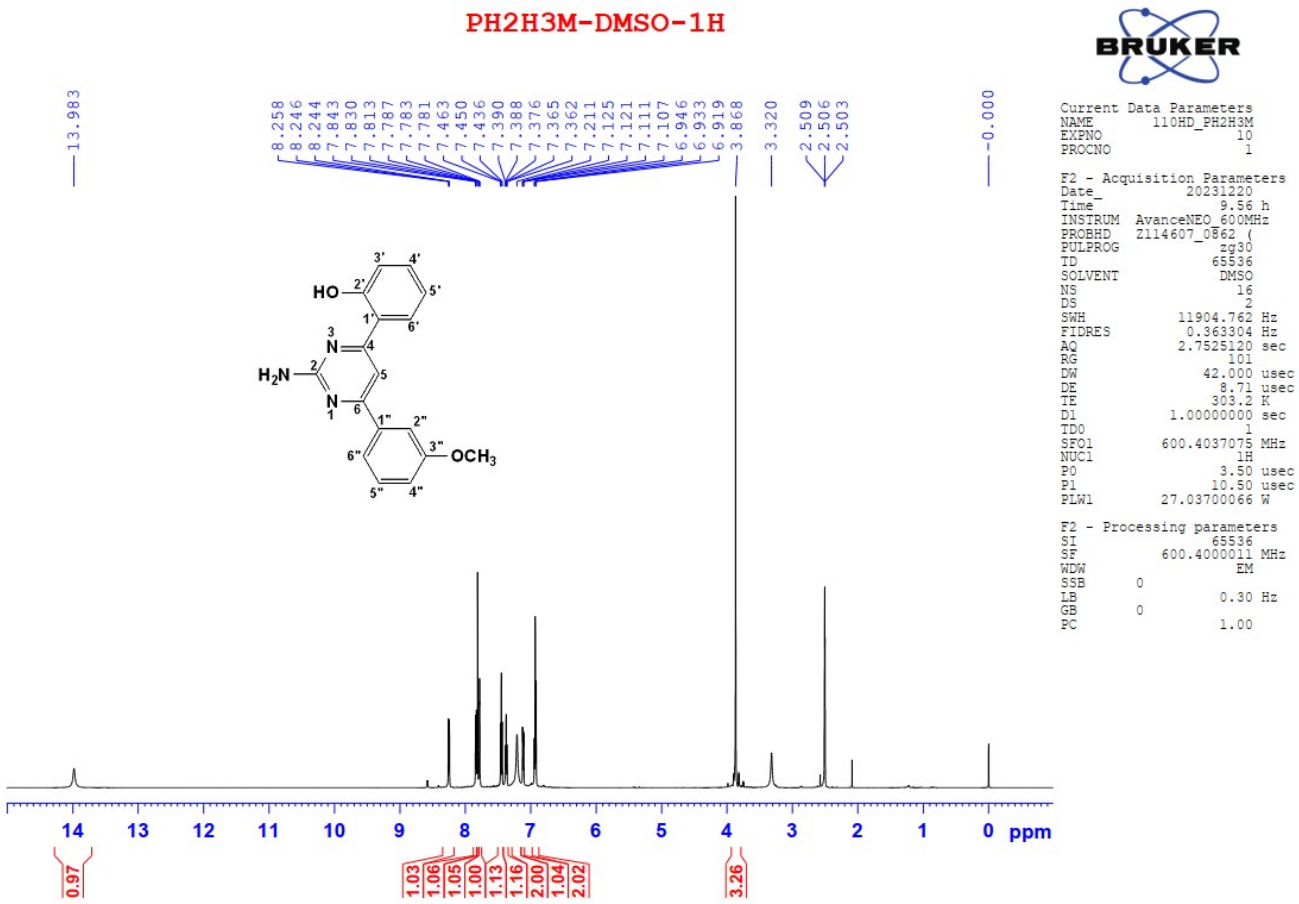


Figure S14. ^{1}H-NMR spectrum of compound **1c**

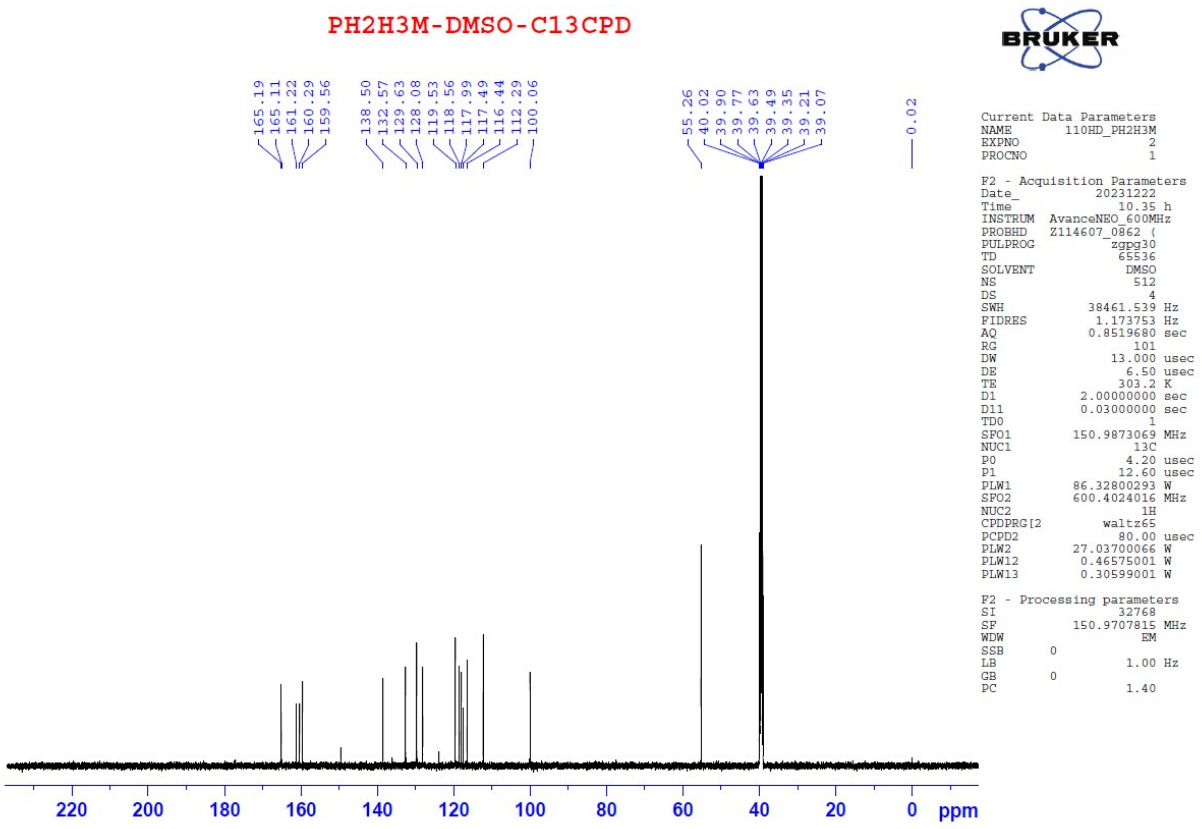


Figure S15. ^{13}C-NMR spectrum of compound **1c**

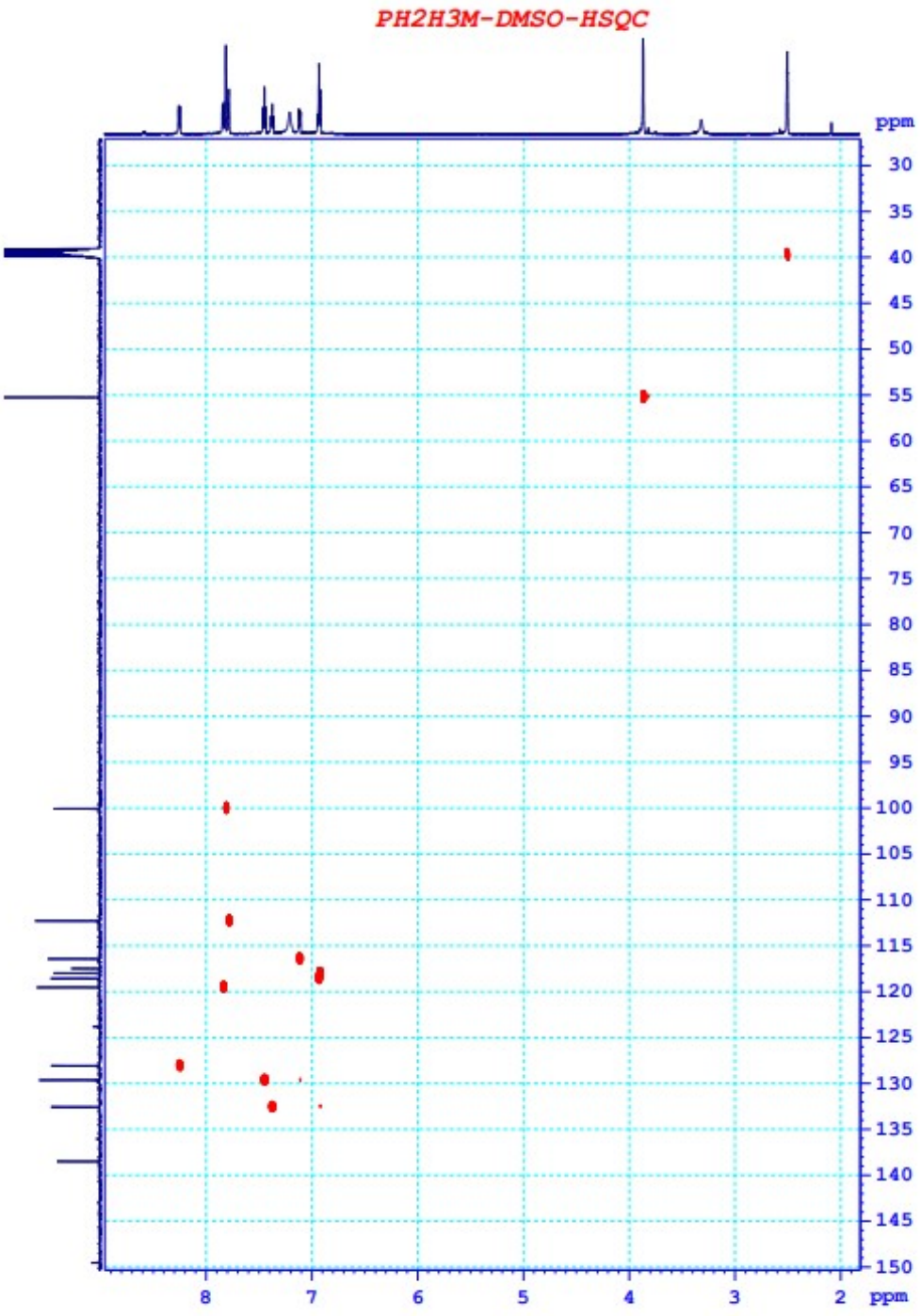


Figure S16. HSQC of compound **1c**

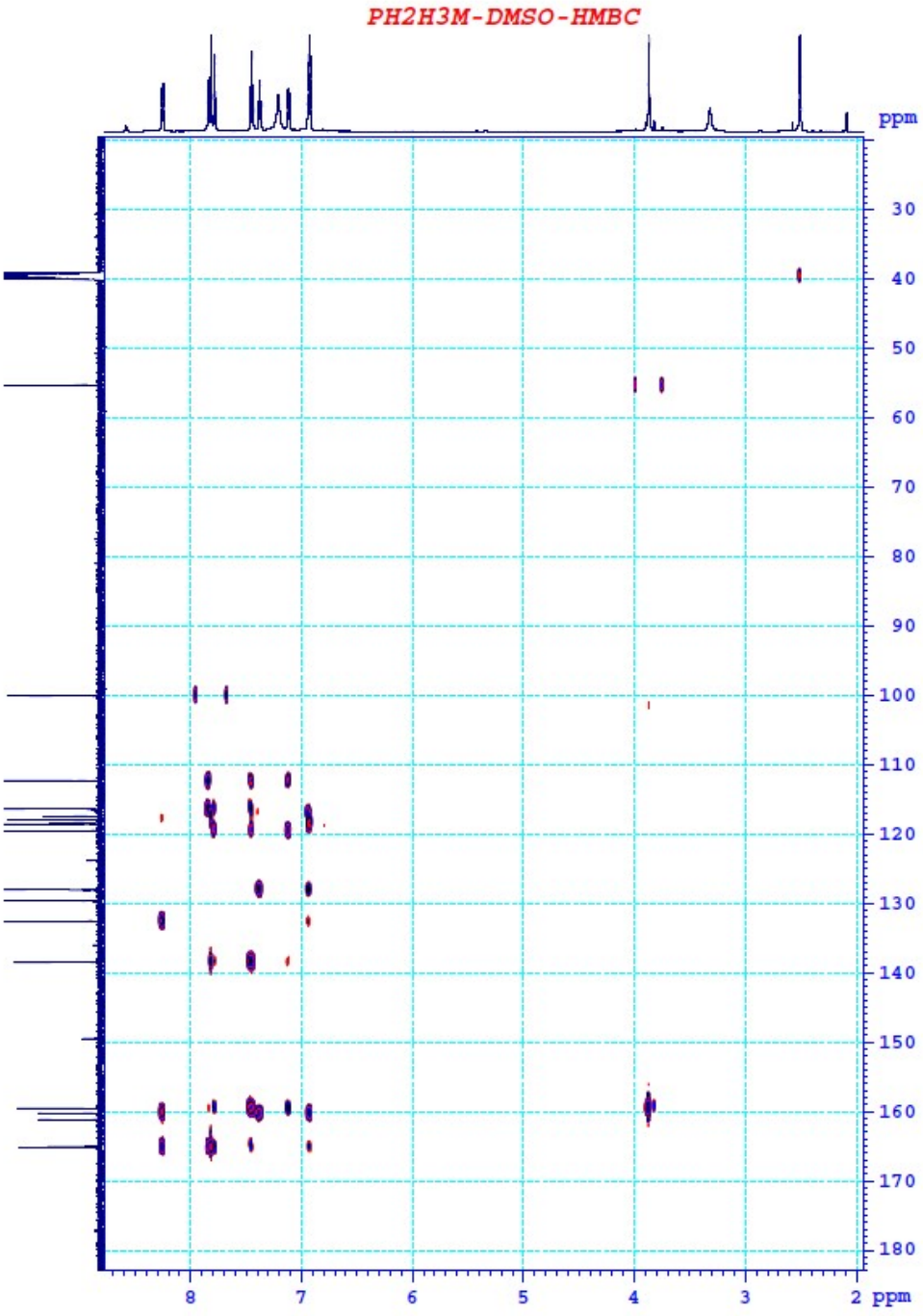


Figure S17. HMBC of compound **1c**

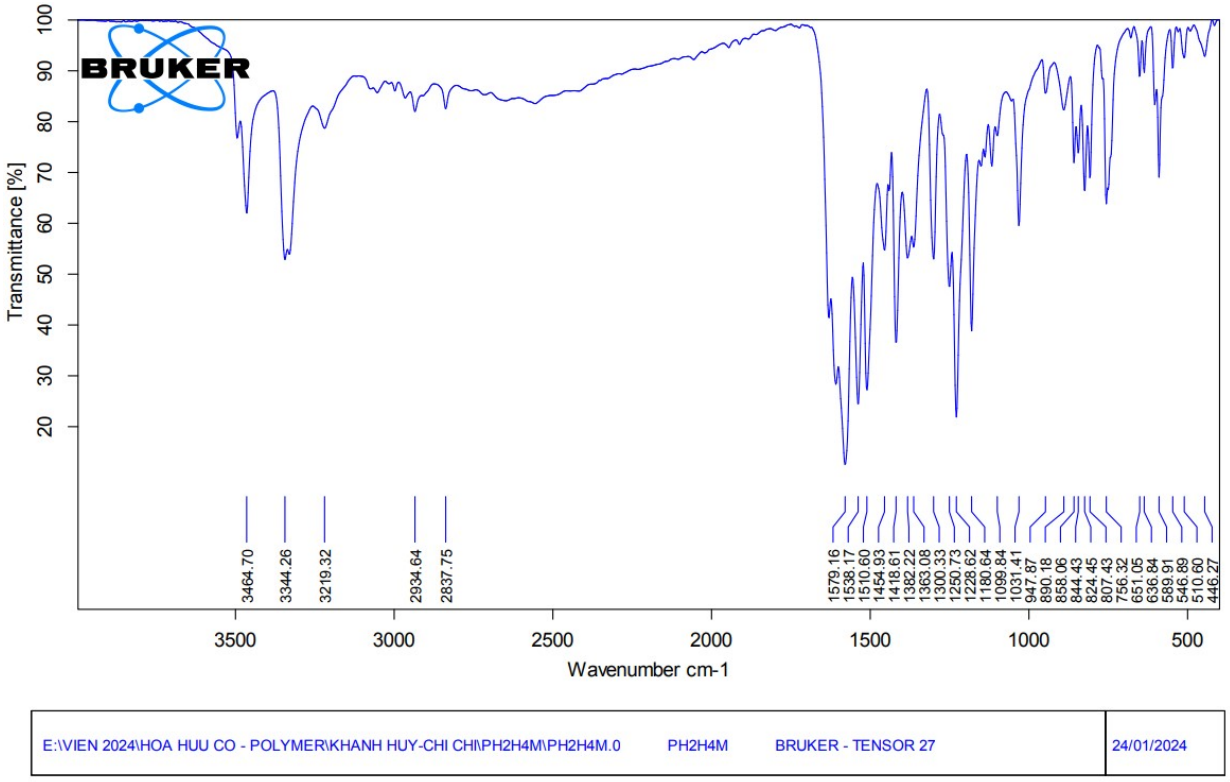


Figure S18. FTIR spectrum of compound **1d**

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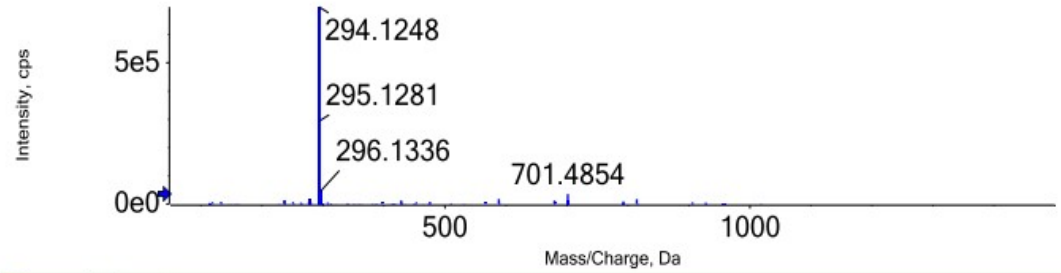
Injection details

Sample name	PH2H4M	*Vial position*	21
Sample file name	SER. wiff2- HUY	*Inject volume*	2.00
Acquisition date	19/01/2024 09:52:07 AM	*Acquisition method*	**ESI _POS_SCAN**
Operator	CB21261708	*Instrument name*	X500$_R$ QTOF

Full mass spectrum

Spectrum from HUY_PH2H4M_(+)ESI 2024-01-19-09-52-07...e multiplier = 1.5), Gaussian smoothed (0.5 points)



Expanded spectrum

Spectrum from HUY_PH2H4M_(+)ESI 2024-01-19-09-52-07...e multiplier = 1.5), Gaussian smoothed (0.5 points)

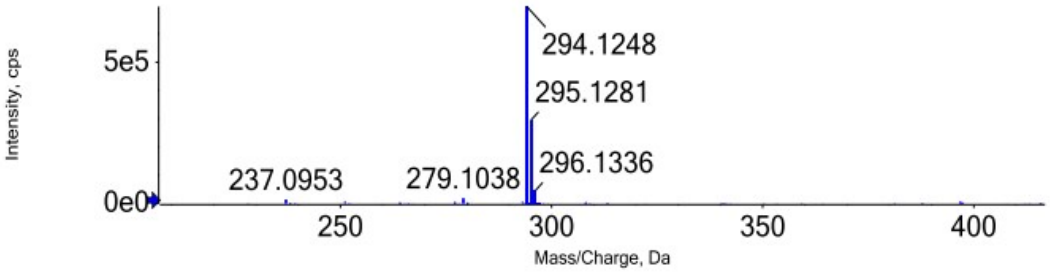


Figure S19. HRMS spectrum of compound **1d**

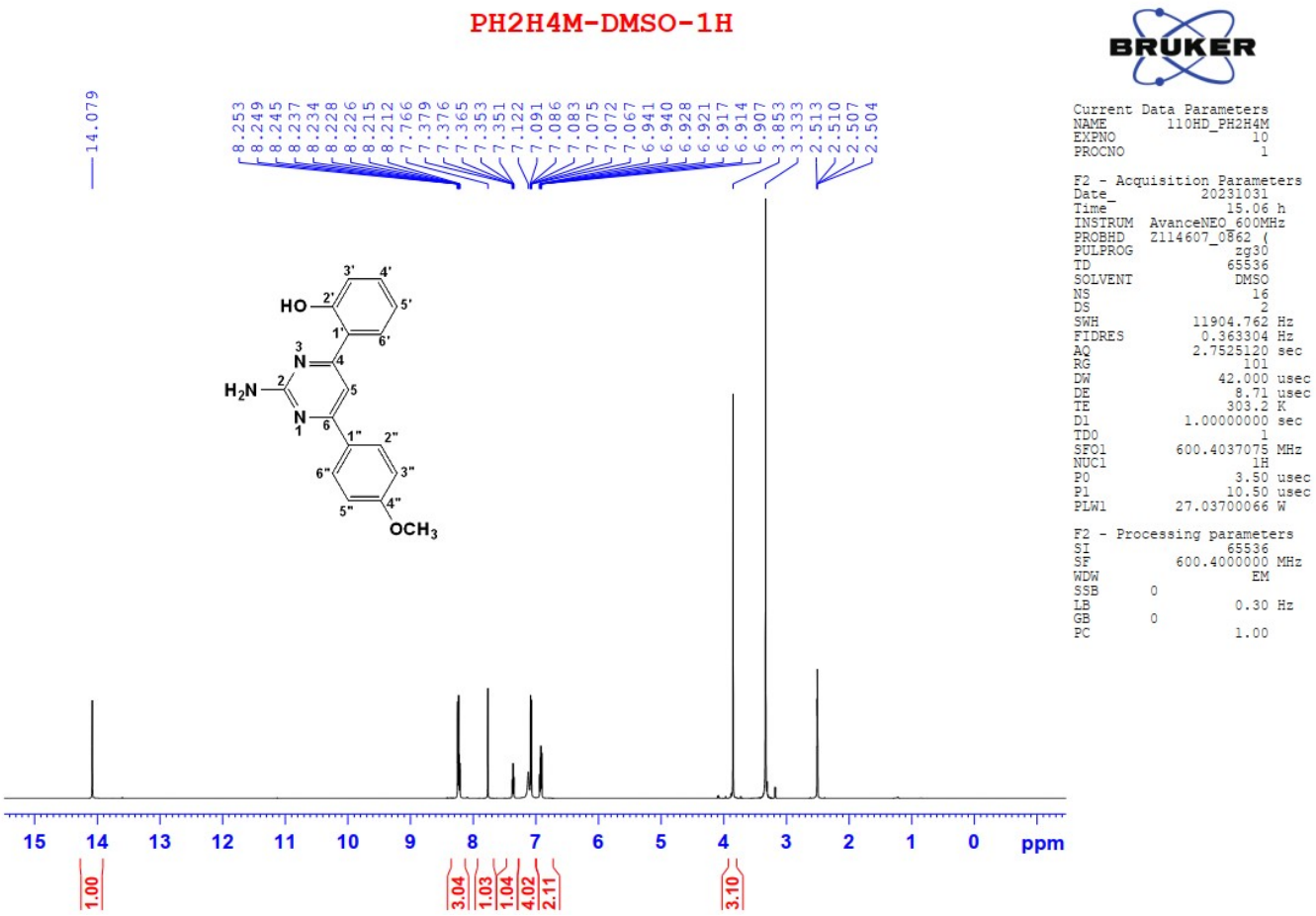


Figure S20. ^{1}H-NMR spectrum of compound **1d**

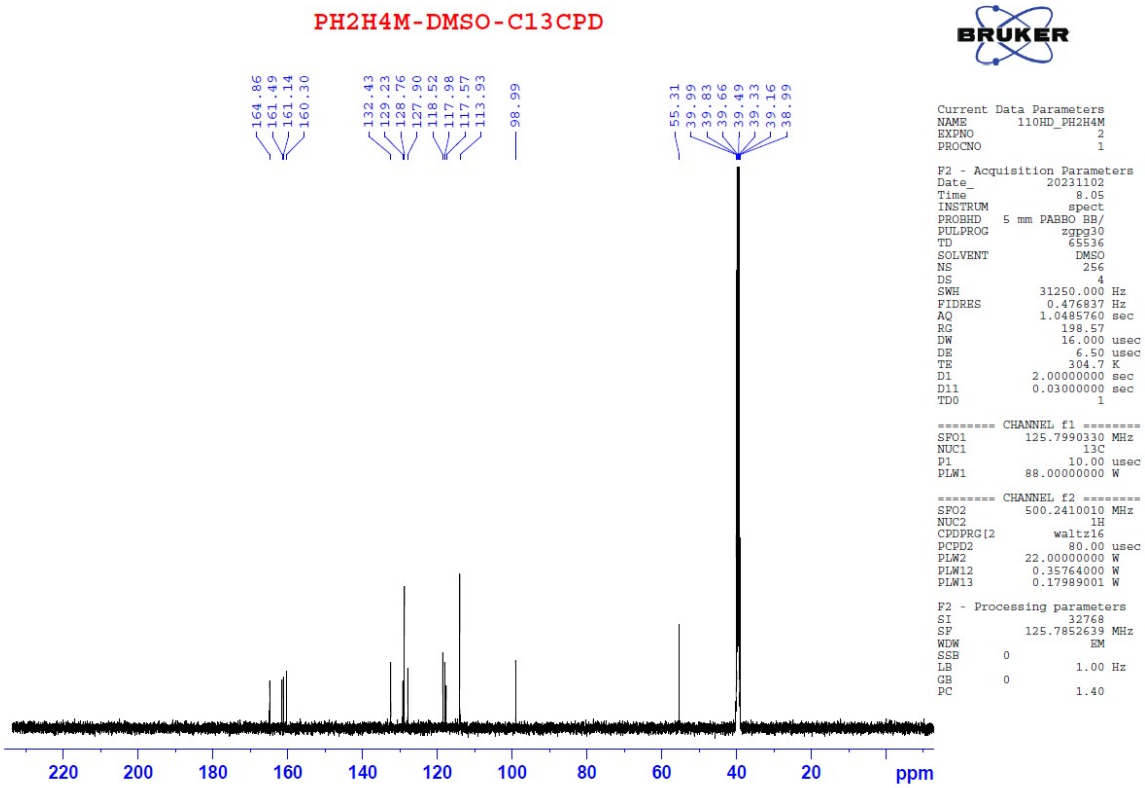


Figure S21. ^{13}C-NMR spectrum of compound **1d**

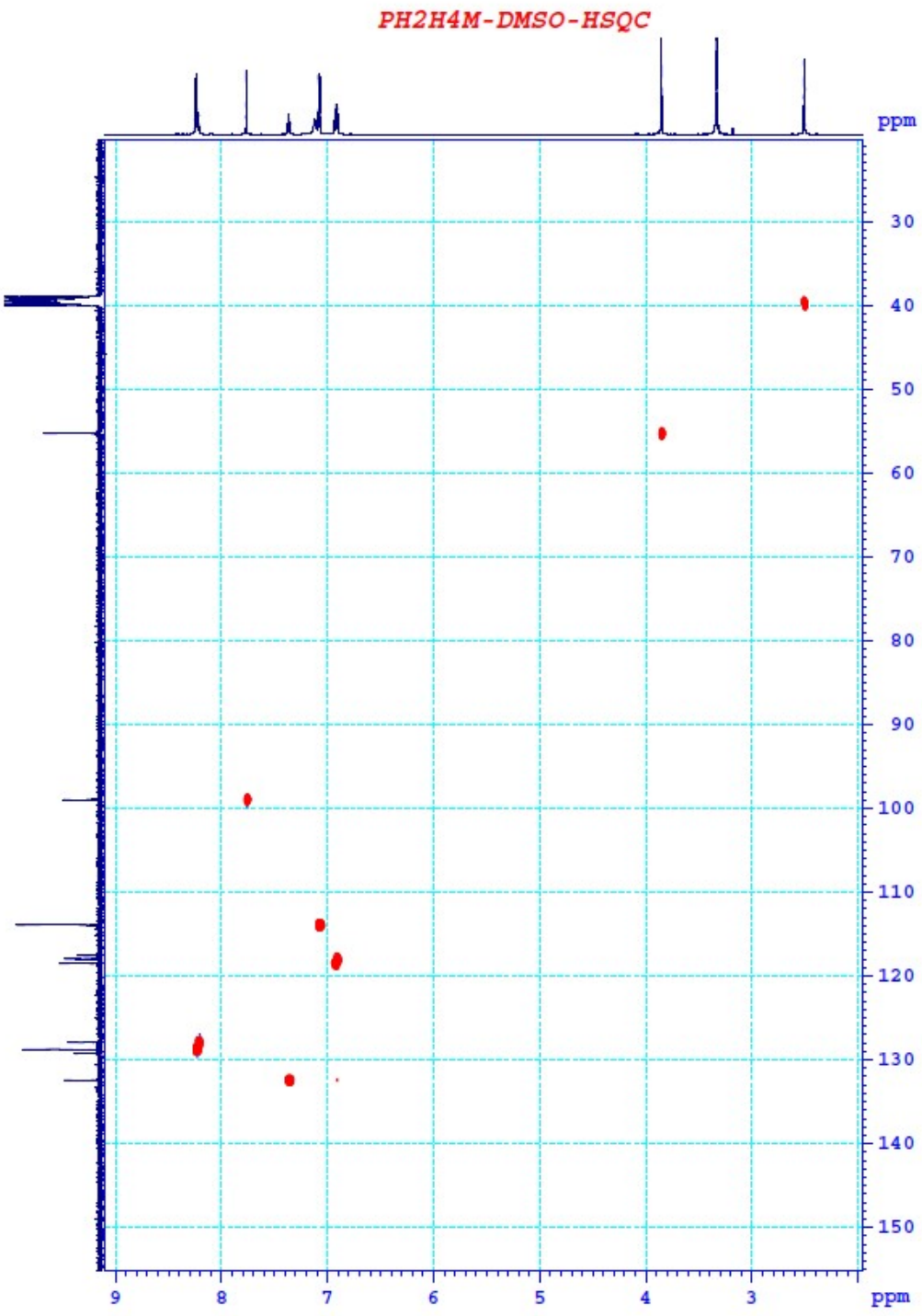


Figure S22. HSQC of compound **1d**

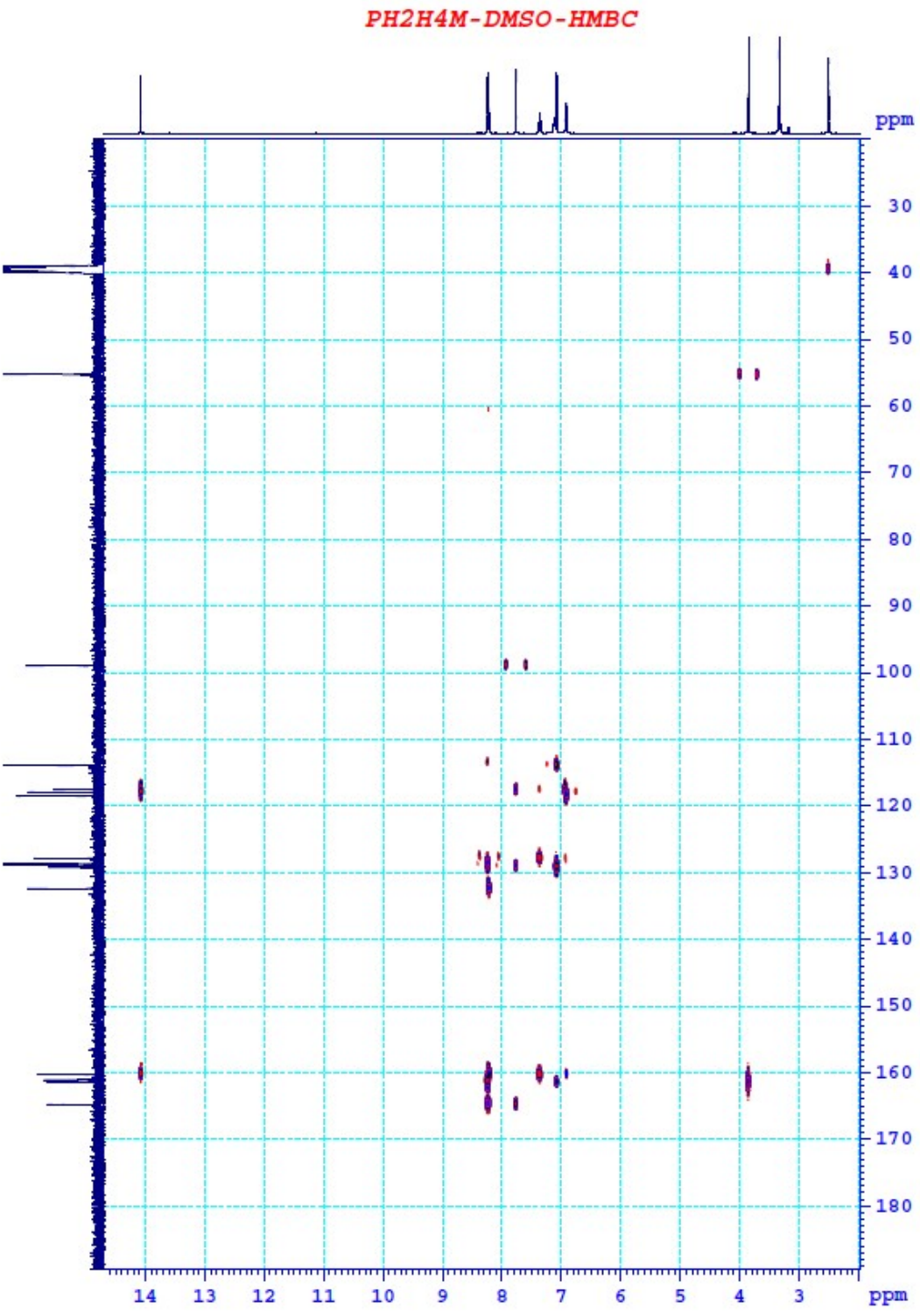


Figure S23. HMBC of compound **1d**

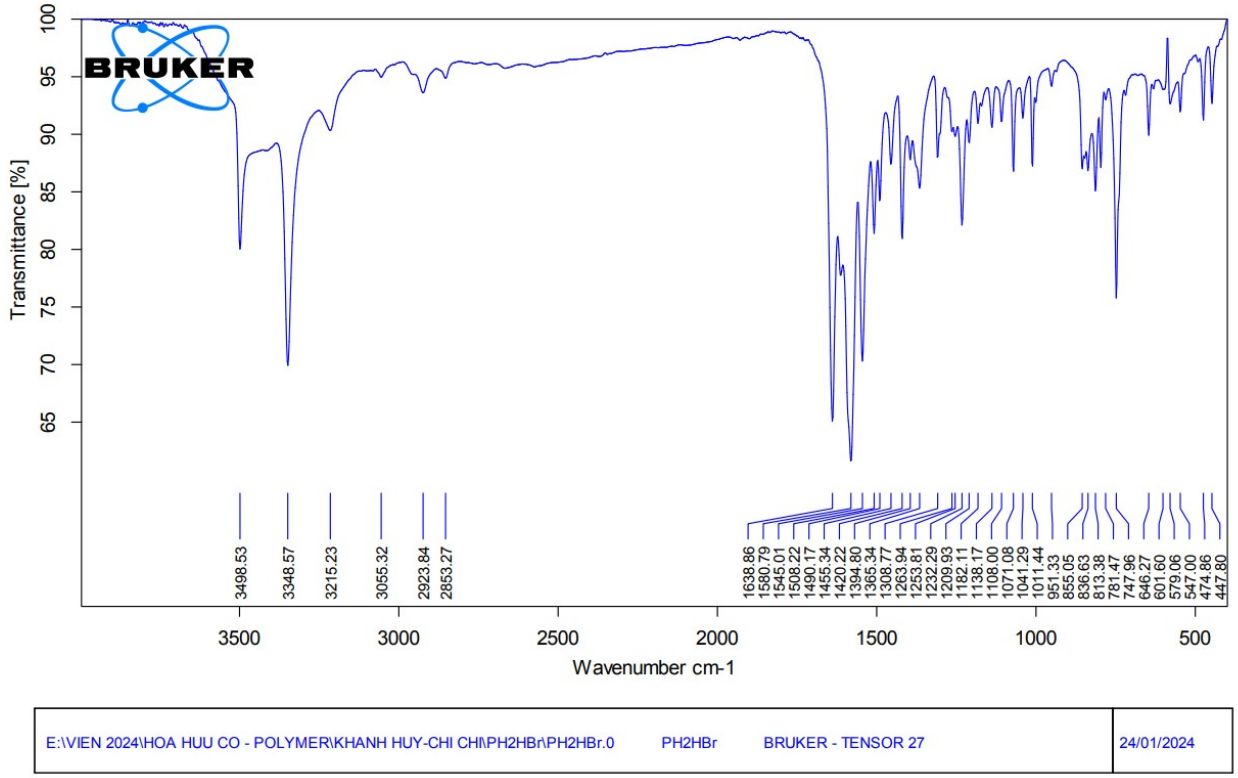


Figure S24. FTIR spectrum of compound **1e**

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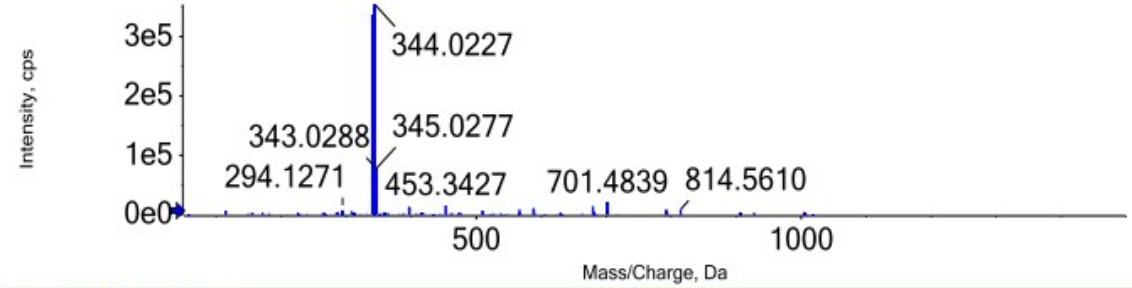
ANALYSIS REPORT

Injection details

Sample name	PH2HBr	*Vial position*	22
Sample file name	SER. wiff2- HUY	*Inject volume*	2.00
Acquisition date	19/01/2024 09:54:14 AM	*Acquisition method*	**ESI _POS_SCAN**
Operator	CB21261708	*Instrument name*	X500$_R$ QTOF

Full mass spectrum

Spectrum from HUY_PH2HBr_(+)ESI 2024-01-19-09-54-14....e multiplier = 1.5), Gaussian smoothed (0.5 points)



Expanded spectrum

Spectrum from HUY_PH2HBr_(+)ESI 2024-01-19-09-54-14....e multiplier = 1.5), Gaussian smoothed (0.5 points)

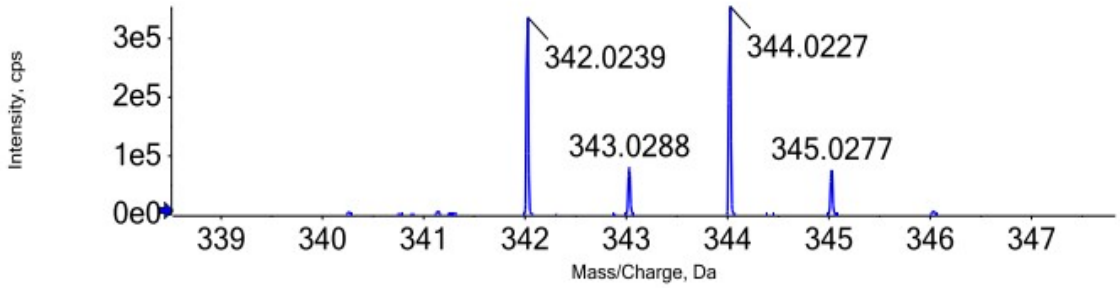


Figure S25. HRMS spectrum of compound **1e**

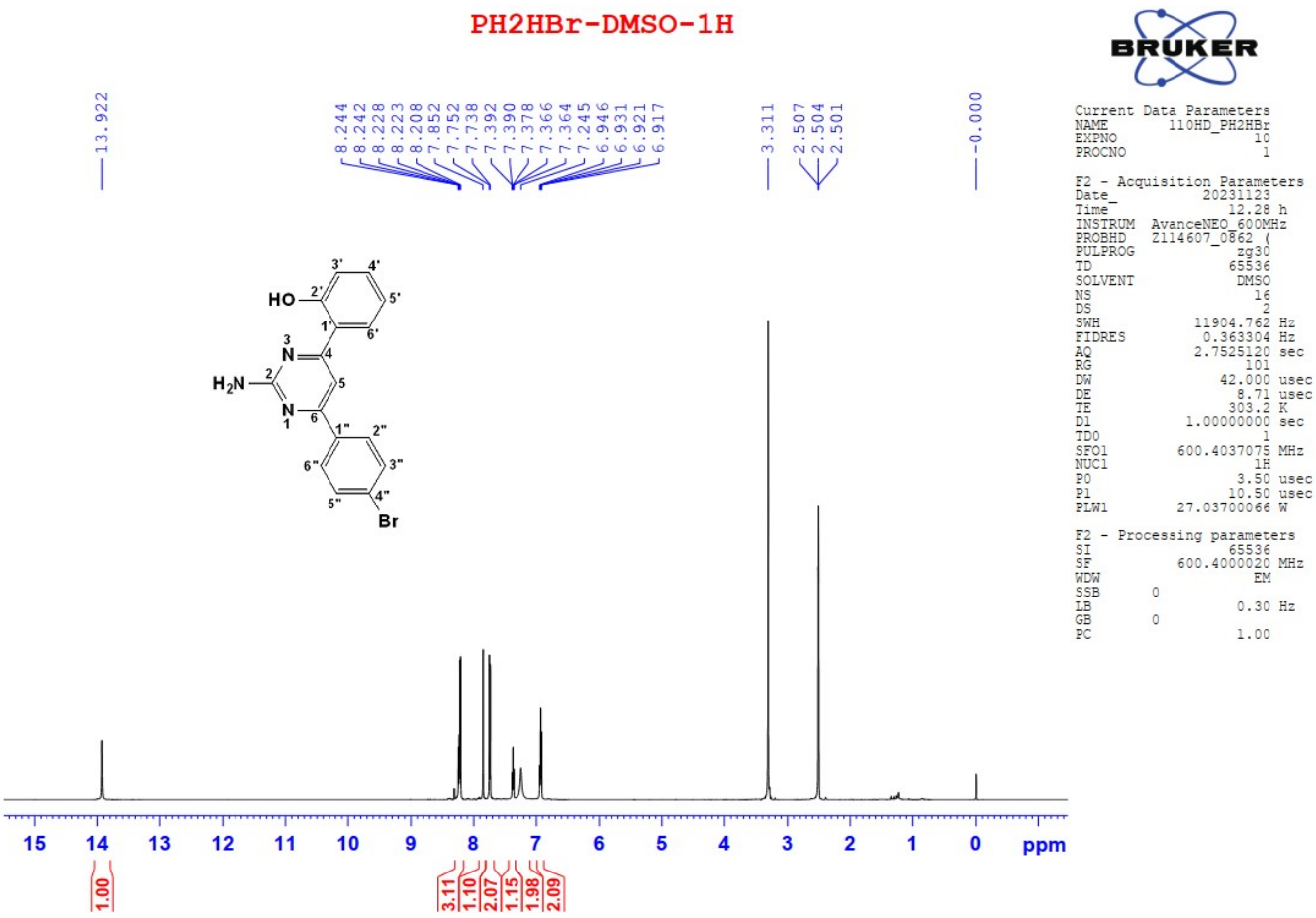


Figure S26. ^{1}H-NMR spectrum of compound **1e**

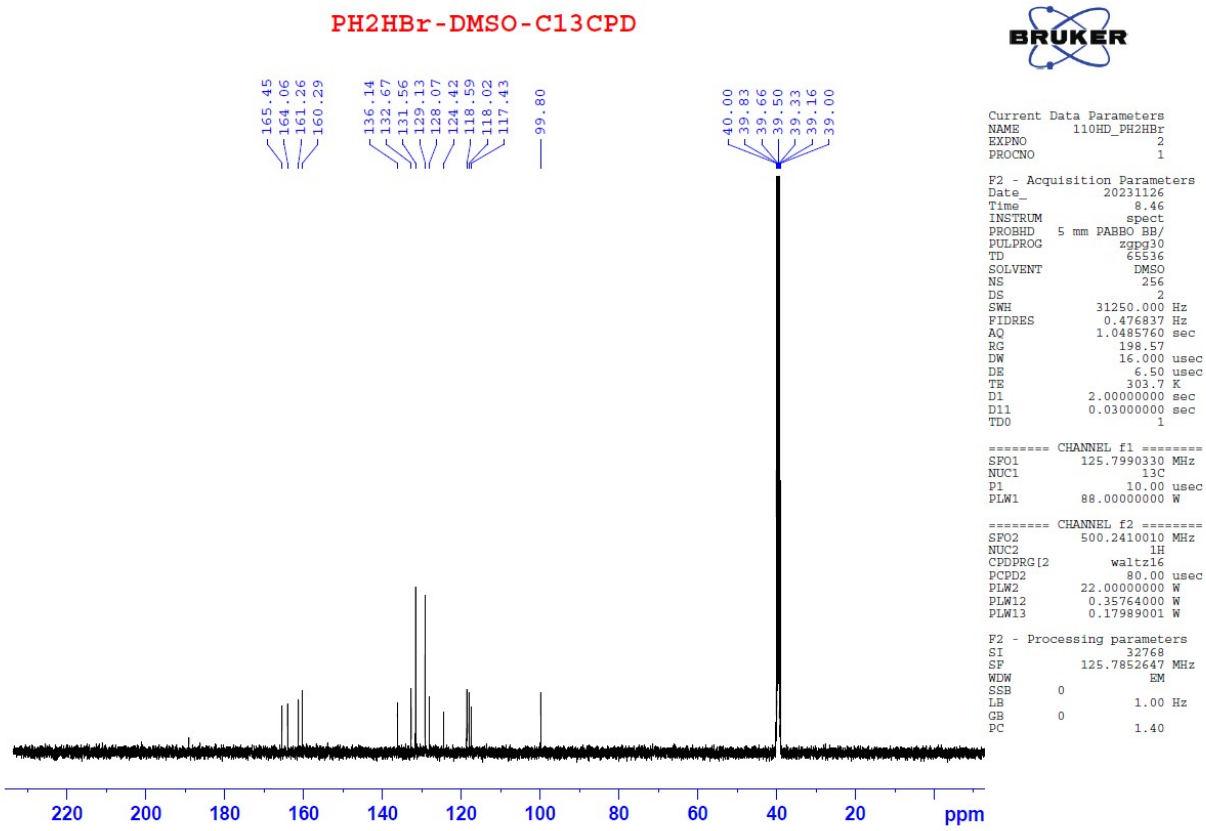


Figure S27. ^{13}C-NMR spectrum of compound **1e**

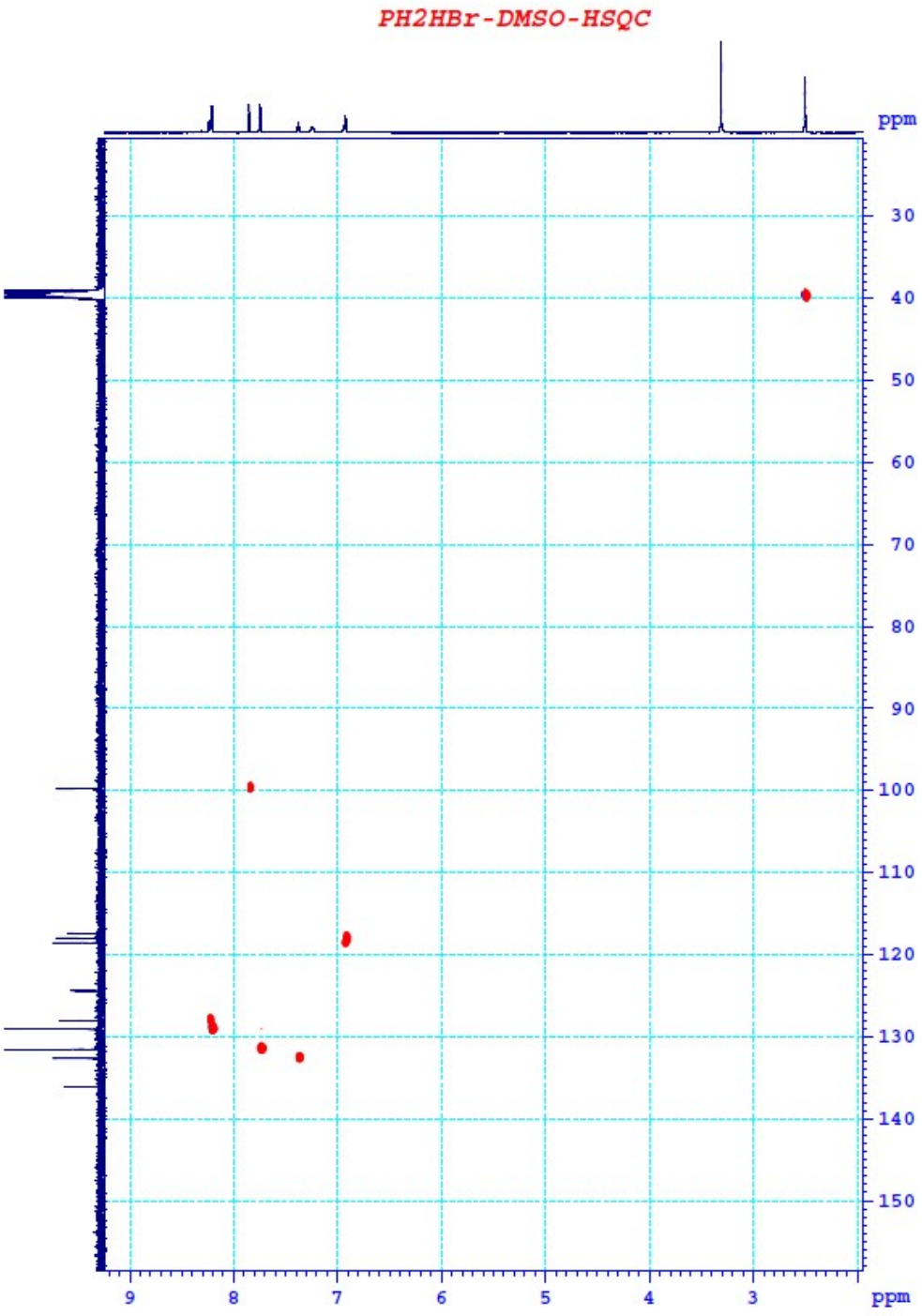


Figure S28. HSQC of compound **1e**

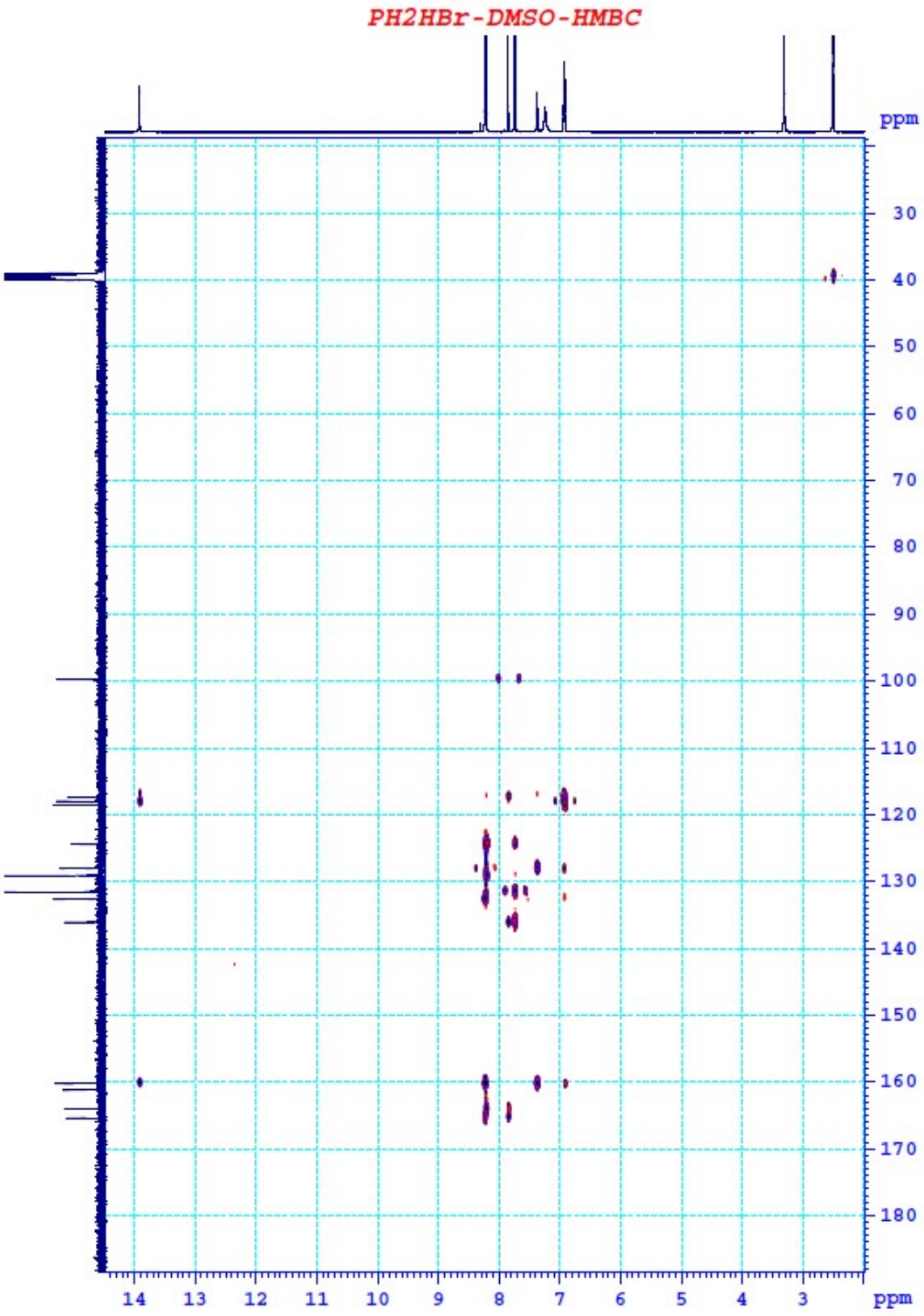


Figure S29. HMBC of compound **1e**

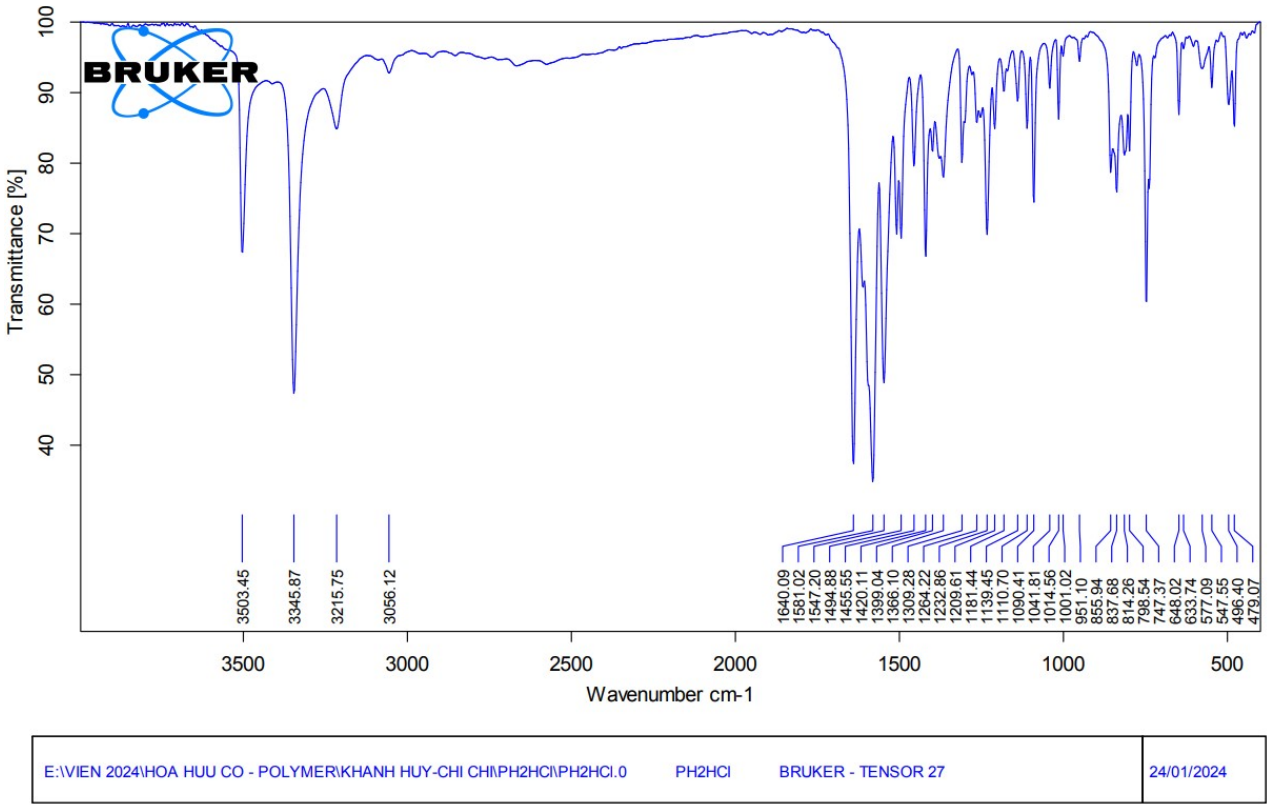


Figure S30. FTIR spectrum of compound **1f**

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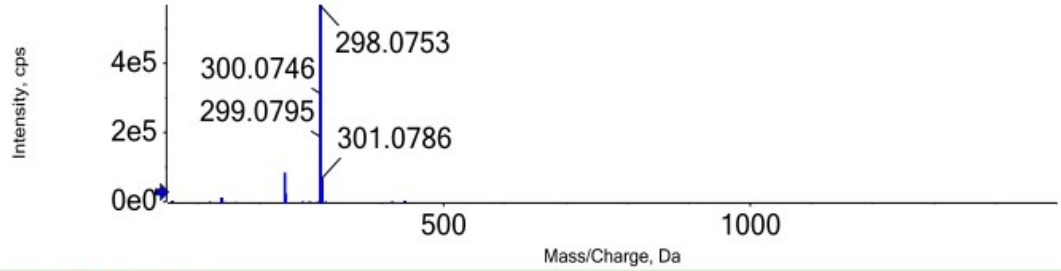
ANALYSIS REPORT

Injection details

Sample name	PH2HCl	*Vial position*	23
Sample file name	SER. wiff2- HUY	*Inject volume*	2.00
Acquisition date	19/01/2024 09:59:38 AM	*Acquisition method*	**ESI _POS_SCAN**
Operator	CB21261708	*Instrument name*	X500$_R$ QTOF

Full mass spectrum

Spectrum from HUY_PH2HCl_(+)ESI 2024-01-19-09-59-38....e multiplier = 1.5), Gaussian smoothed (0.5 points)



Expanded spectrum

Spectrum from HUY_PH2HCl_(+)ESI 2024-01-19-09-59-38....e multiplier = 1.5), Gaussian smoothed (0.5 points)

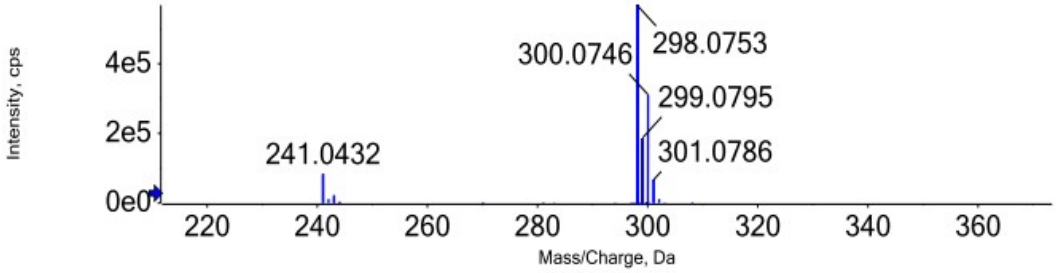


Figure S31. HRMS spectrum of compound **1f**

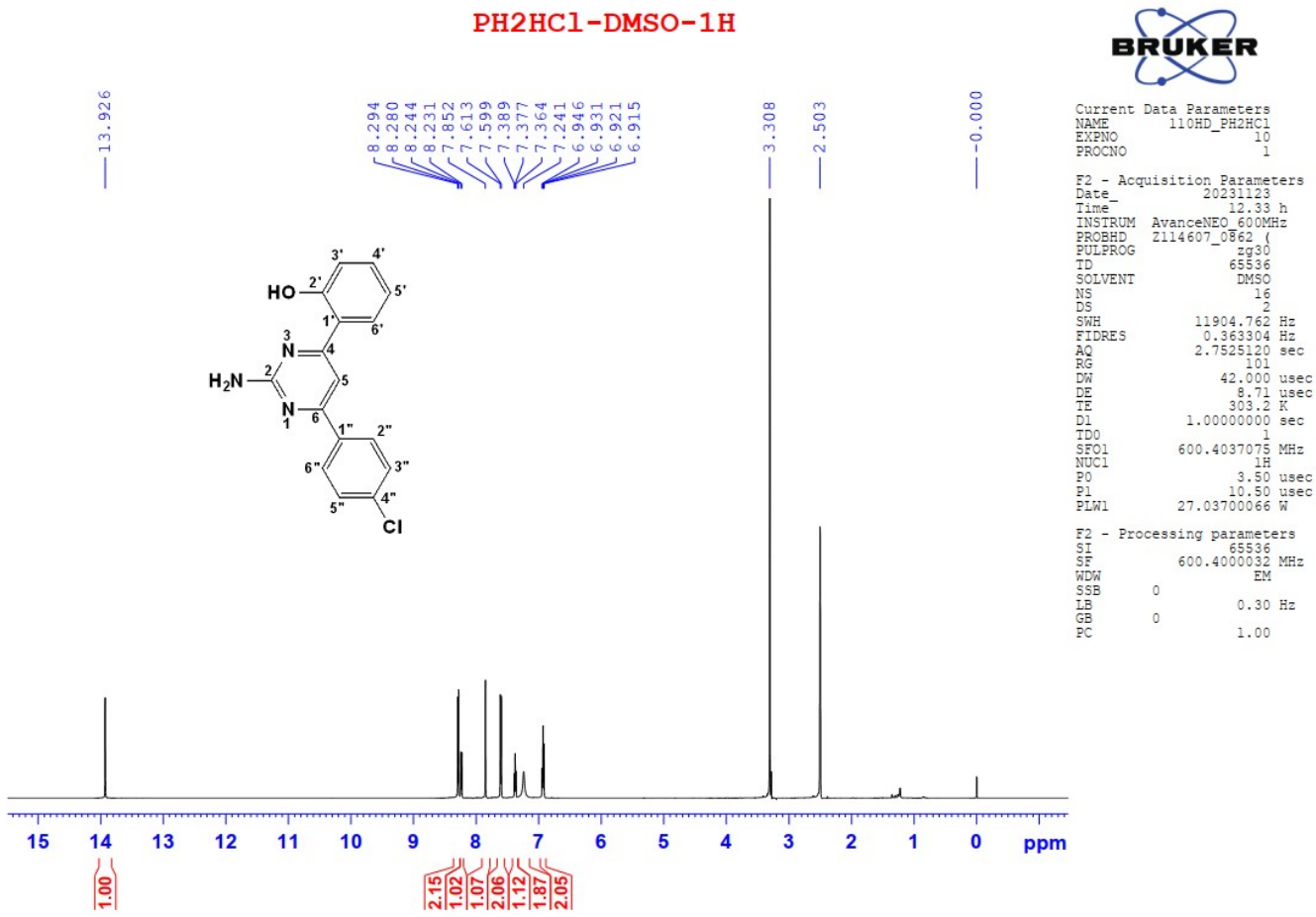


Figure S32. ^{1}H-NMR spectrum of compound **1f**

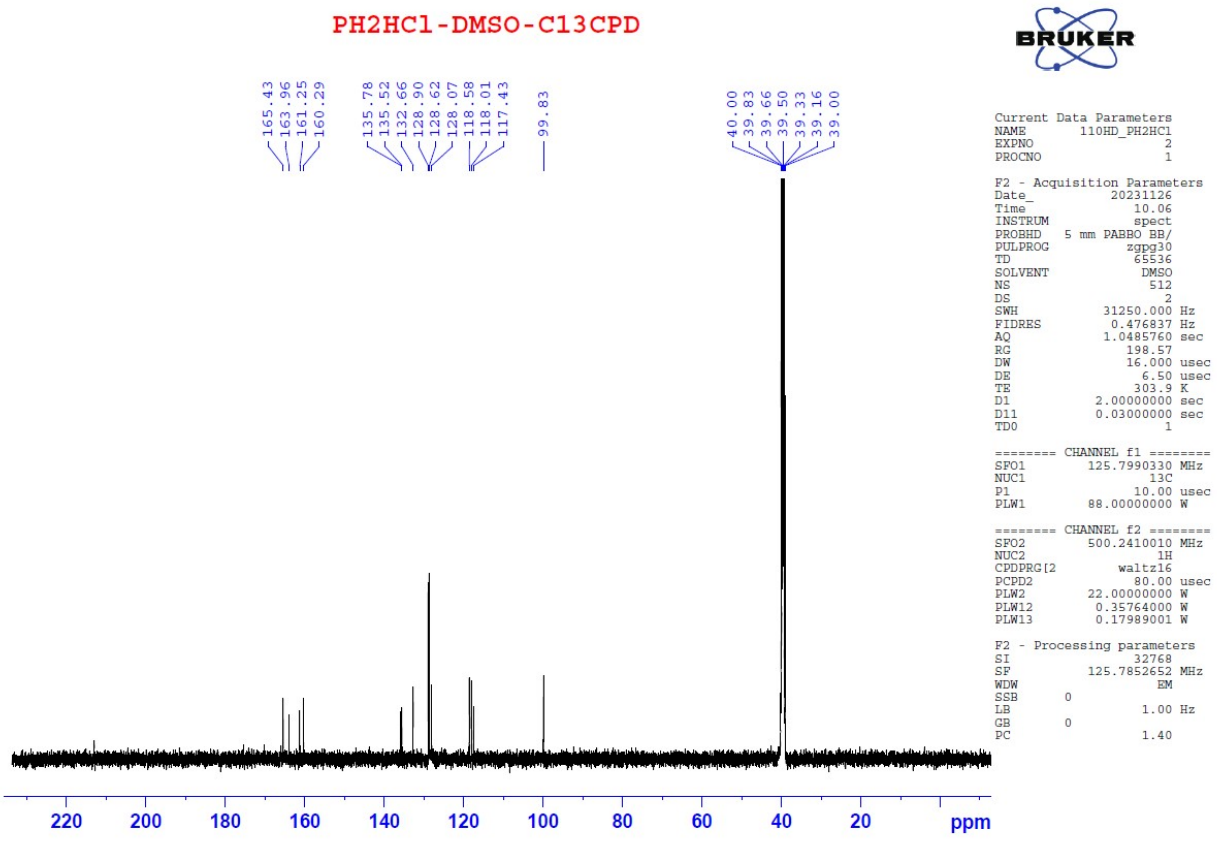


Figure S33. ^{13}C-NMR spectrum of compound **1f**

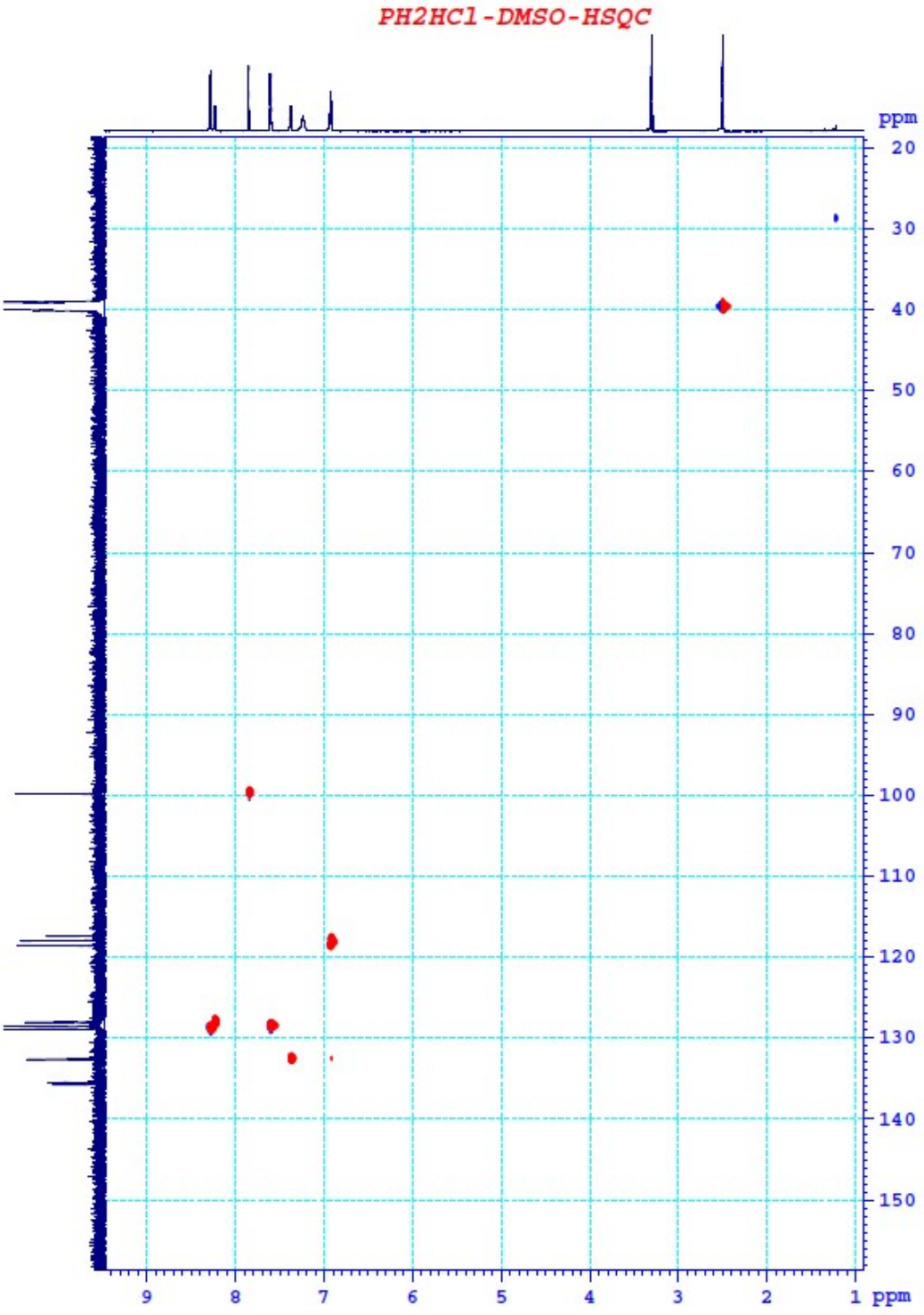


Figure S34. HSQC of compound **1f**

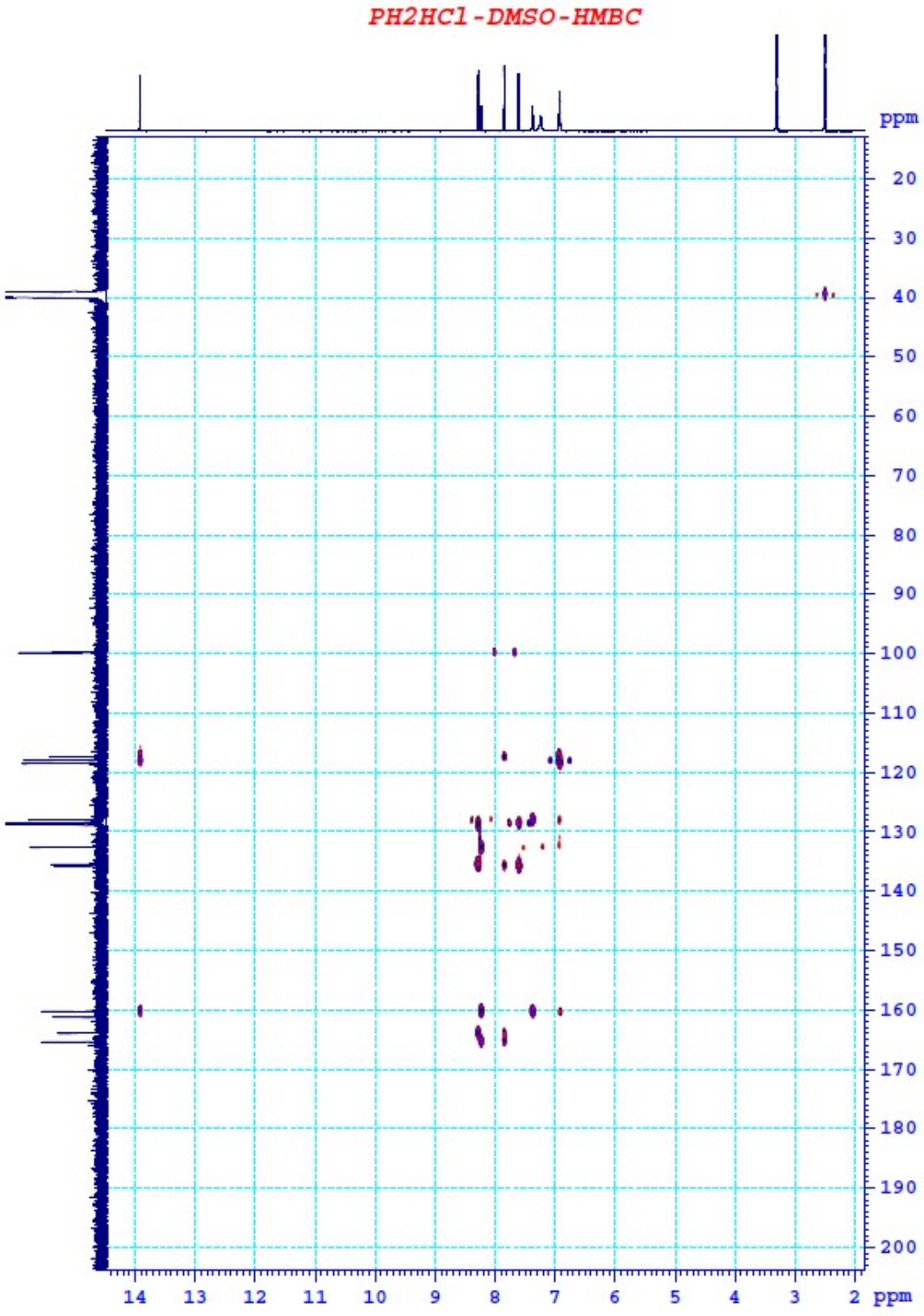


Figure S35. HMBC spectrum of compound **1f**

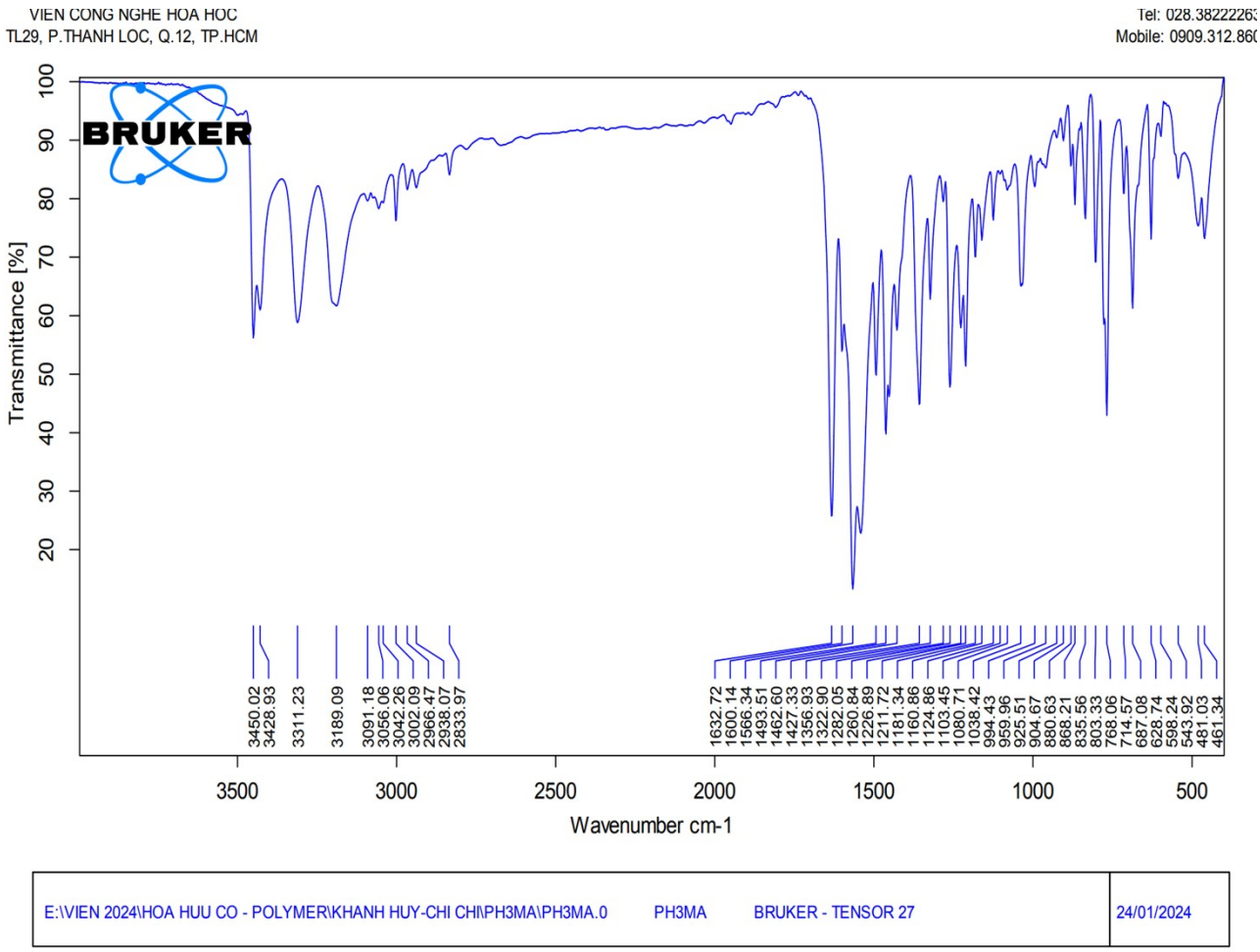


Figure S36. FTIR spectrum of compound **1g**

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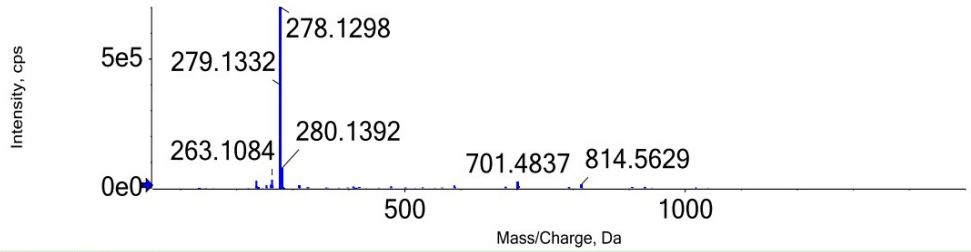
Injection details

Sample name	PH3MA	*Vial position*	26
Sample file name	SER. wiff2- HUY	*Inject volume*	2.00
Acquisition date	19/01/2024 10:09:13 AM	*Acquisition method*	**ESI _POS_SCAN**
Operator	CB21261708	*Instrument name*	X500$_R$ QTOF

Full mass spectrum

Spectrum from HUY_PH3MA_(+)ESI 2024-01-19-10-09-13....e multiplier = 1.5), Gaussian smoothed (0.5 points)



Expanded spectrum

Spectrum from HUY_PH3MA_(+)ESI 2024-01-19-10-09-13....e multiplier = 1.5), Gaussian smoothed (0.5 points)

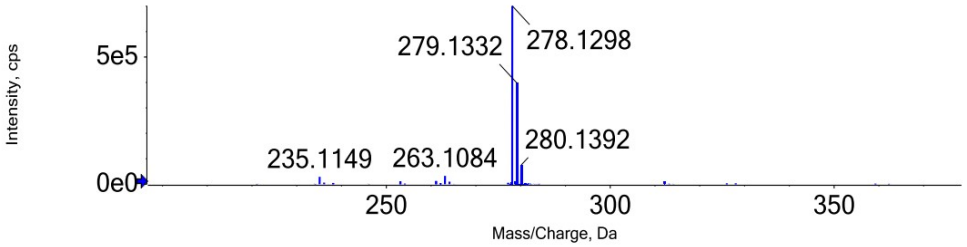


Figure S37. HRMS spectrum of compound **1g**

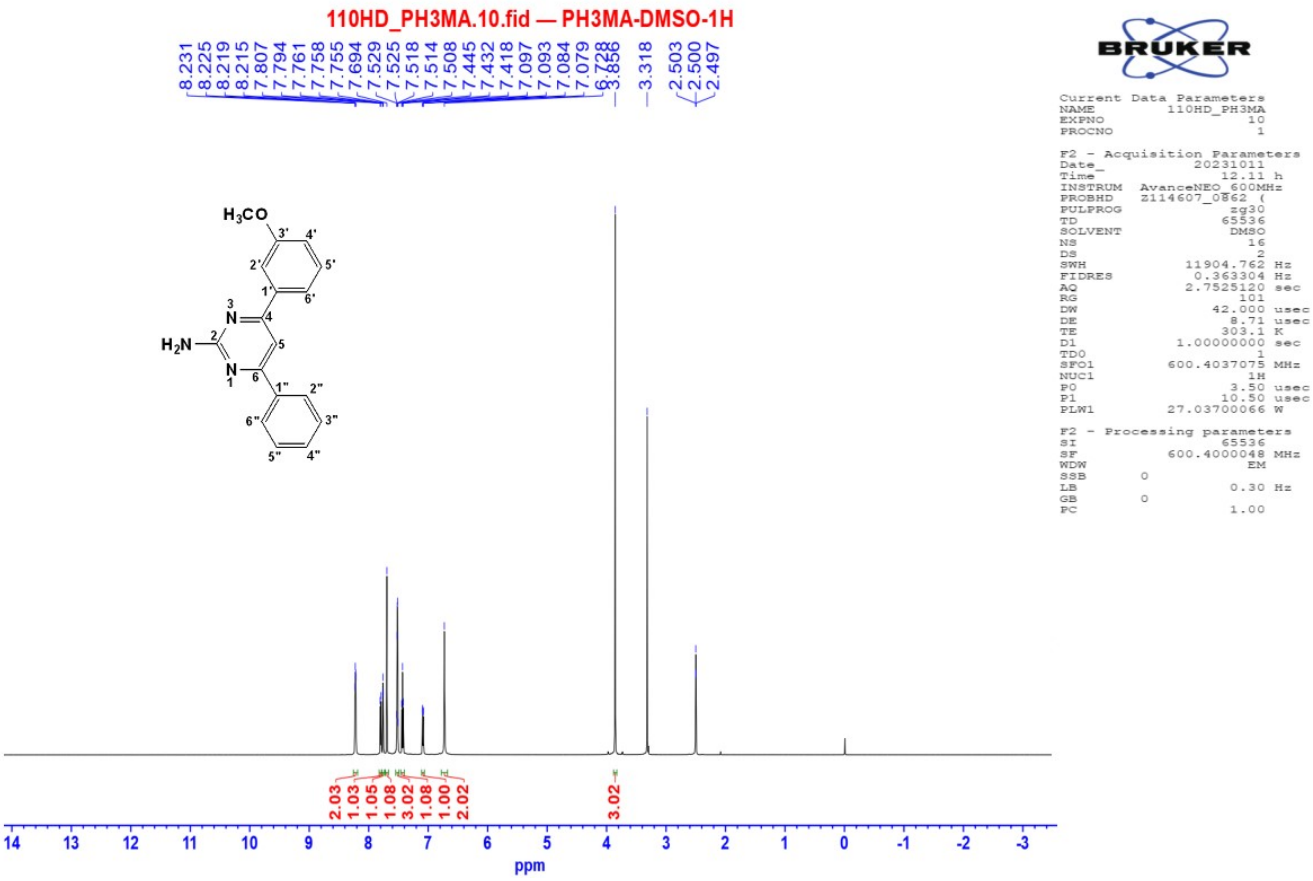


Figure S38. ^{1}H-NMR spectrum of compound **1g**

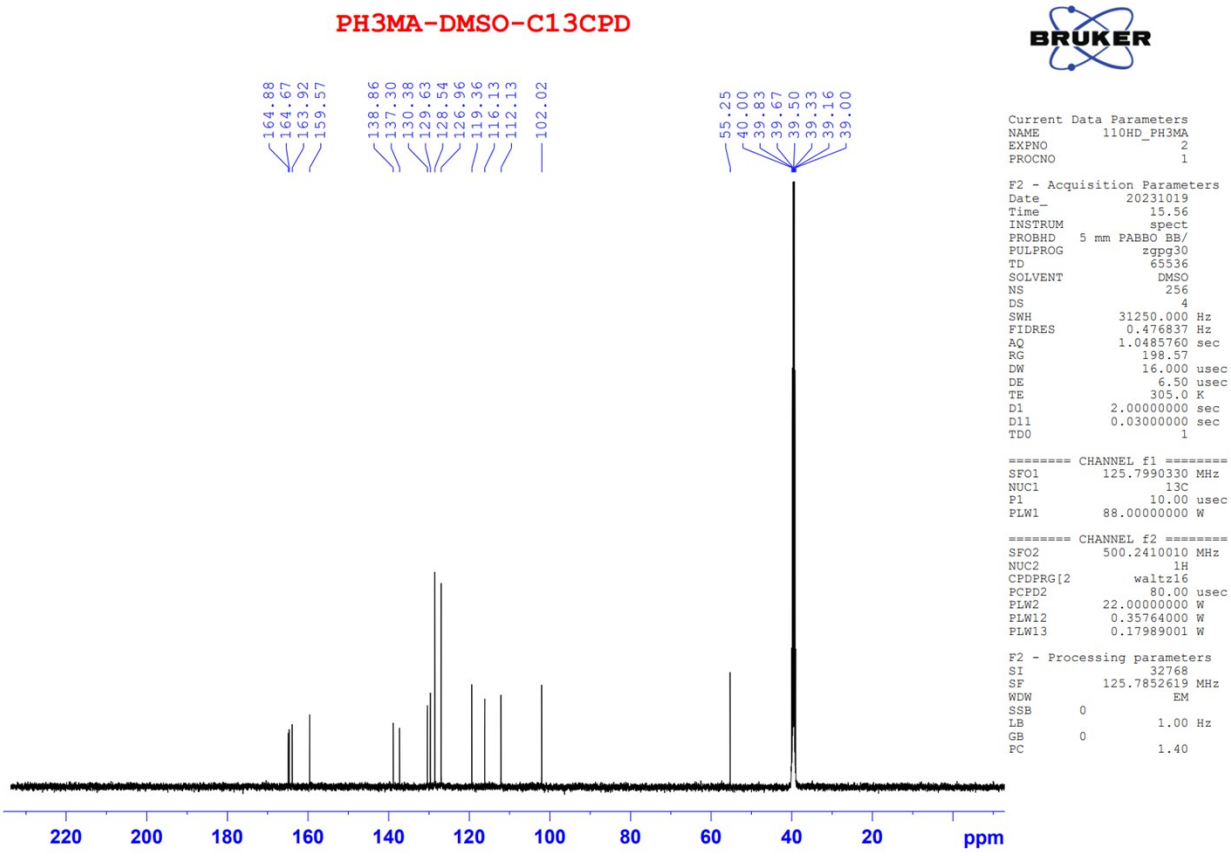


Figure S39. ^{13}C-NMR spectrum of compound **1g**

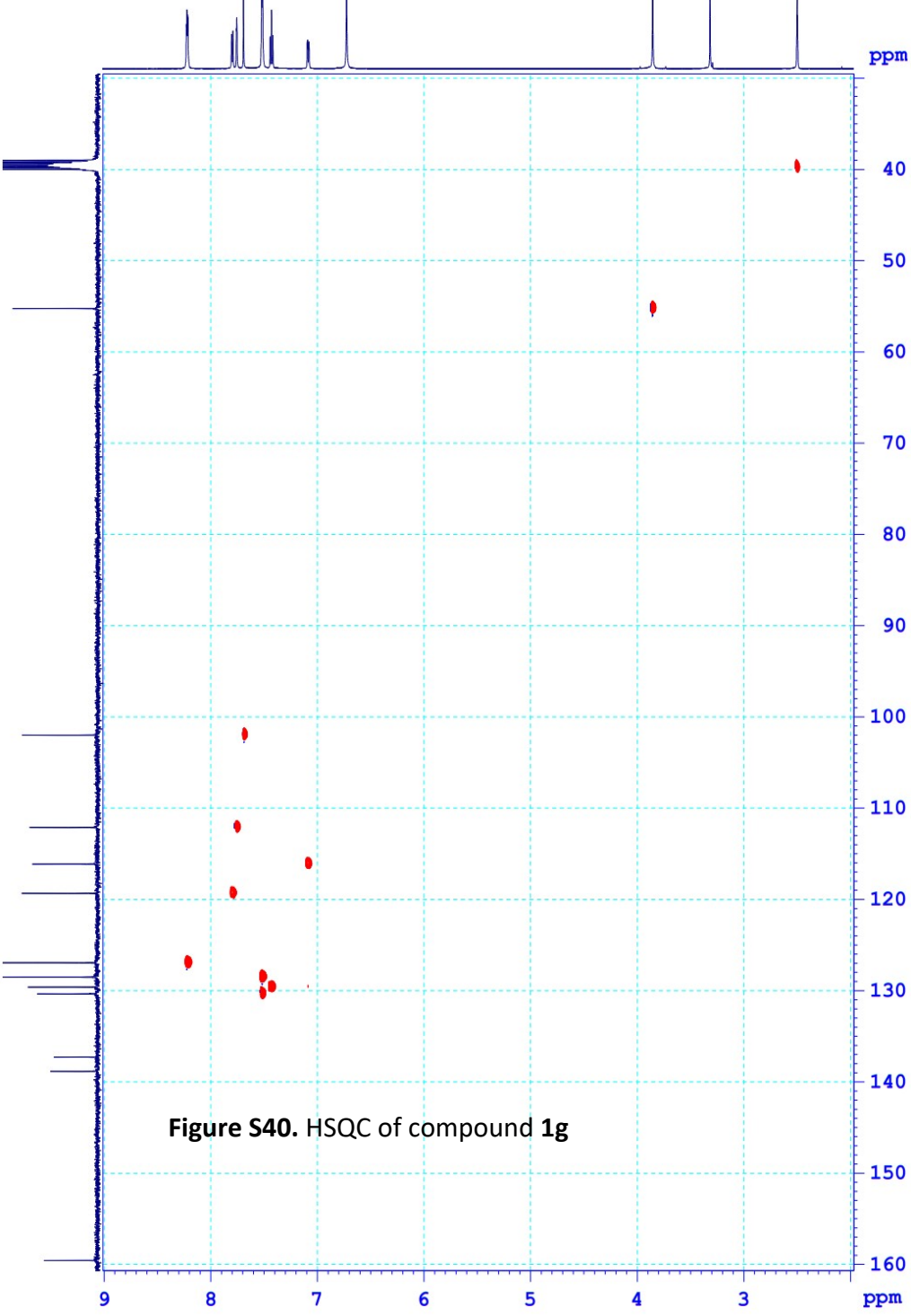


Figure S40. HSQC of compound **1g**

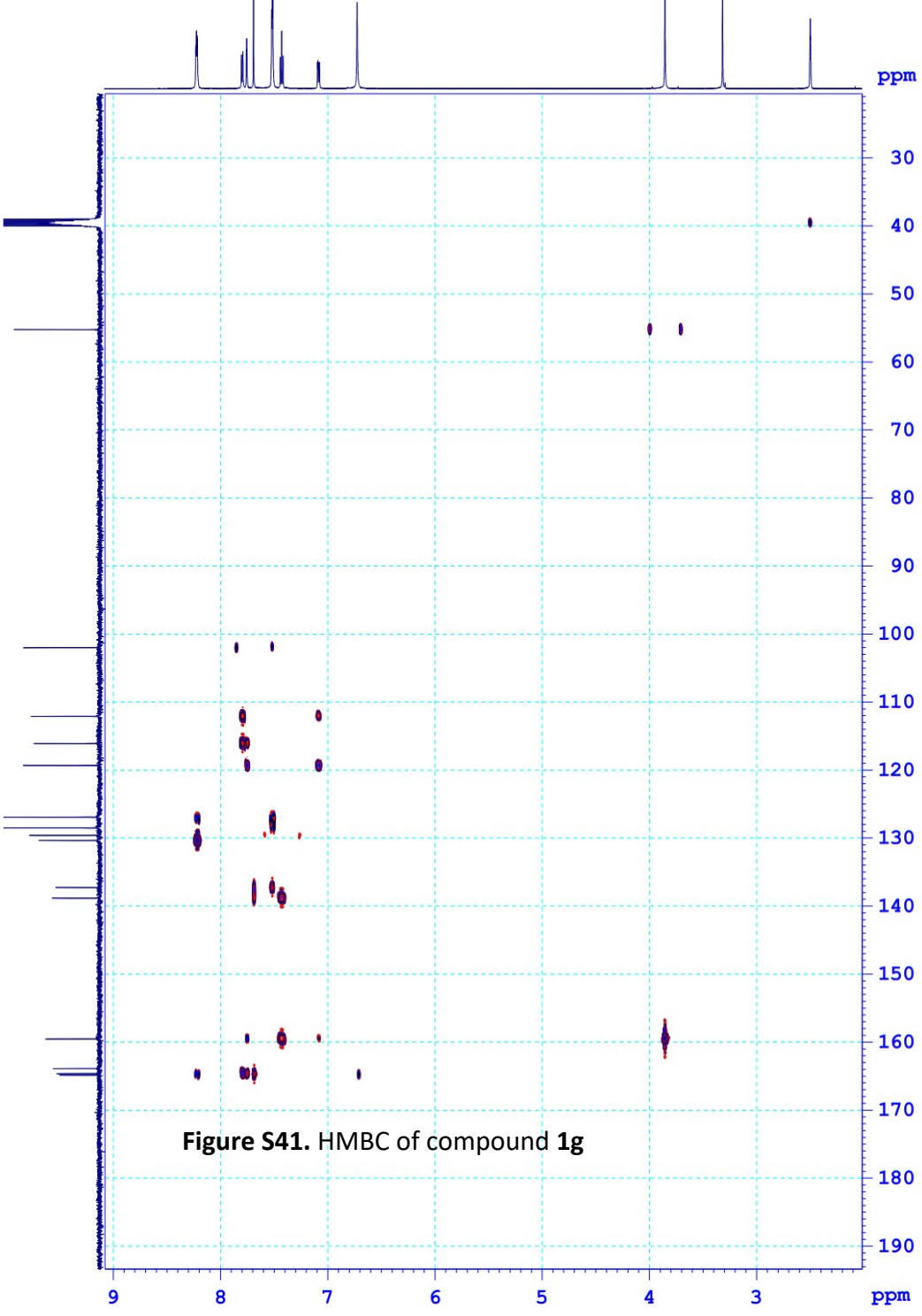


Figure S41. HMBC of compound **1g**

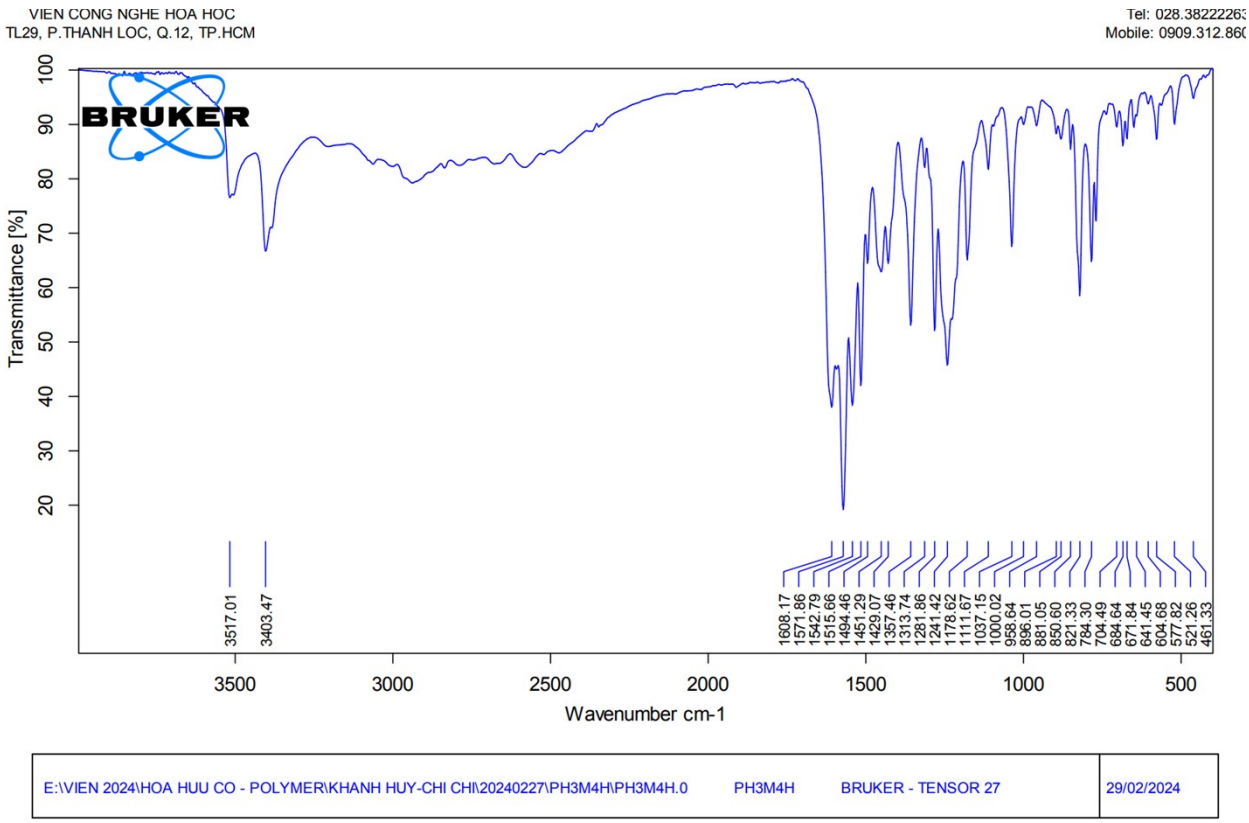


Figure S42. FTIR spectrum of compound **1h**

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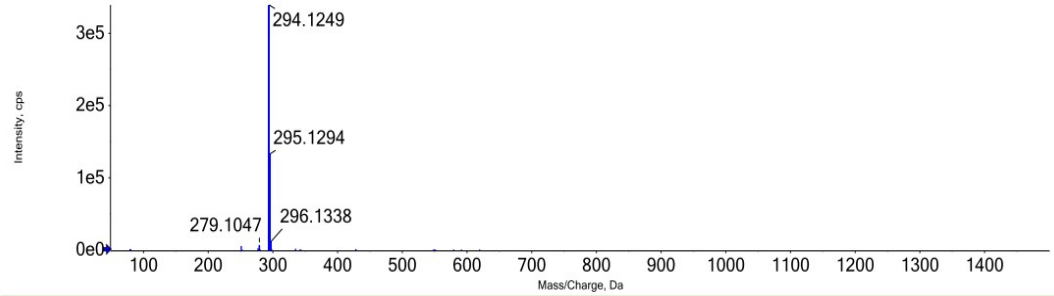
ANALYSIS REPORT

Injection details

Sample name	PH3M4H	*Vial position*	7
Sample file name	SER. wiff2- HUY	*Inject volume*	2.00
Acquisition date	27/02/2024 11:36:38 AM	*Acquisition method*	**ESI _POS_SCAN**
Operator	CB21261708	*Instrument name*	X500$_R$ QTOF

Full mass spectrum

Spectrum from HUY_PH3M4H_(+)ESI 2024-02-27-11-36-38.wiff2 (sample 1) - HUY_PH3M4H_(... 0.167 min, noise filtered (noise multiplier = 1.5), Gaussian smoothed (0.5 points)



Expanded spectrum

Spectrum from HUY_PH3M4H_(+)ESI 2024-02-27-11-36-38.wiff2 (sample 1) - HUY_PH3M4H_(... 0.167 min, noise filtered (noise multiplier = 1.5), Gaussian smoothed (0.5 points)

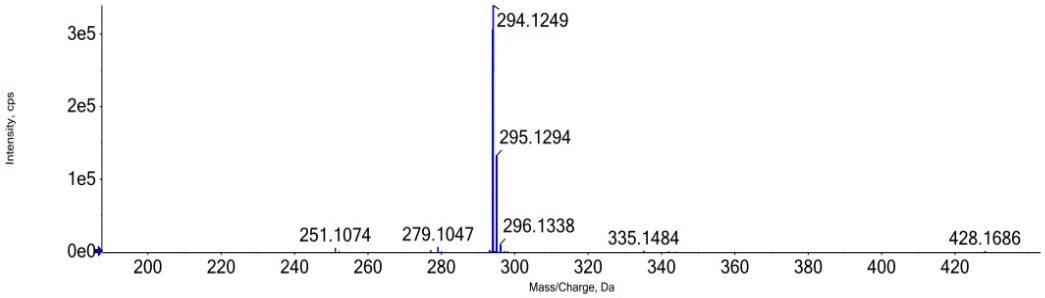


Figure S43. HRMS spectrum of compound **1h**

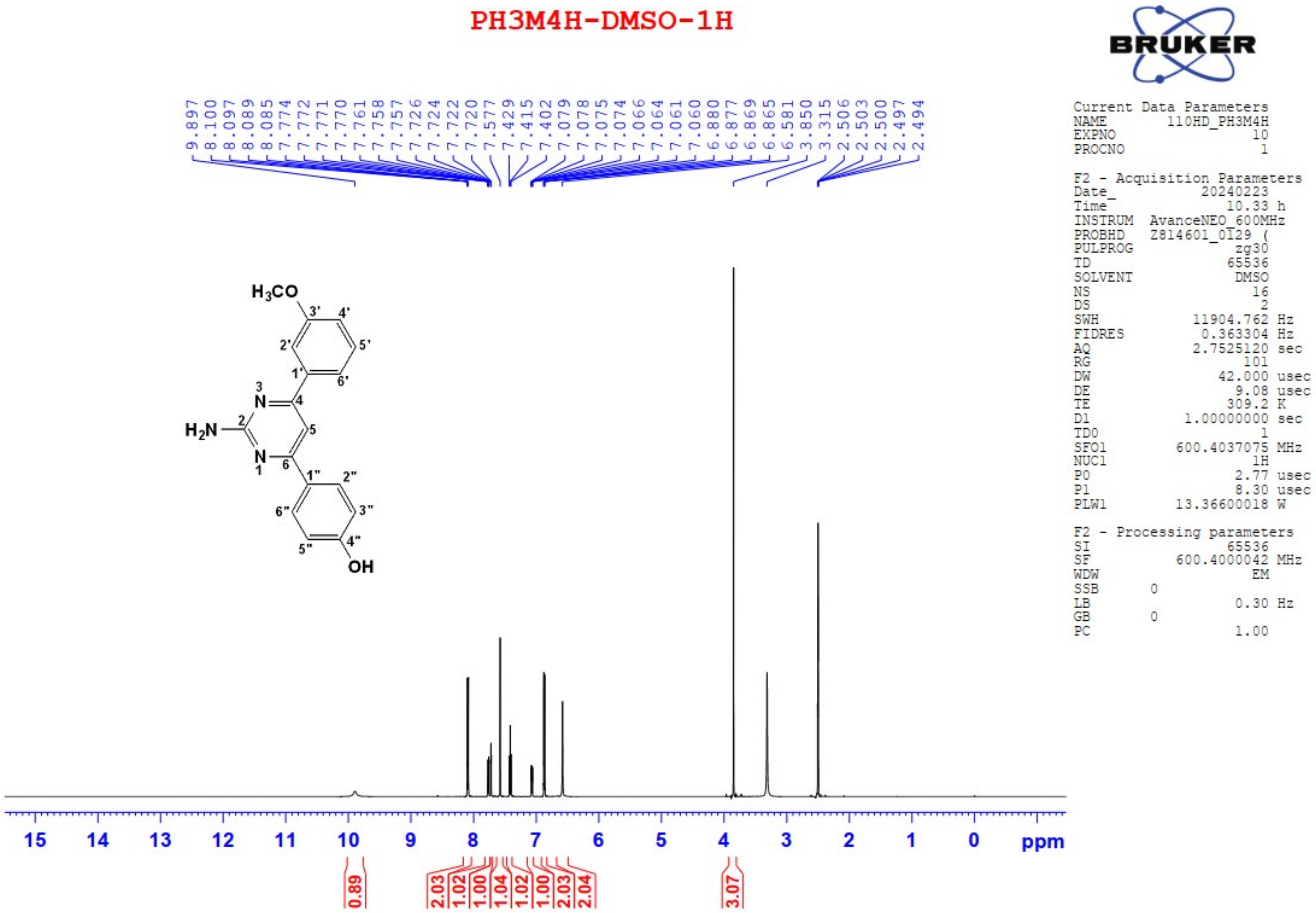


Figure S44. ^{1}H-NMR spectrum of compound **1h**

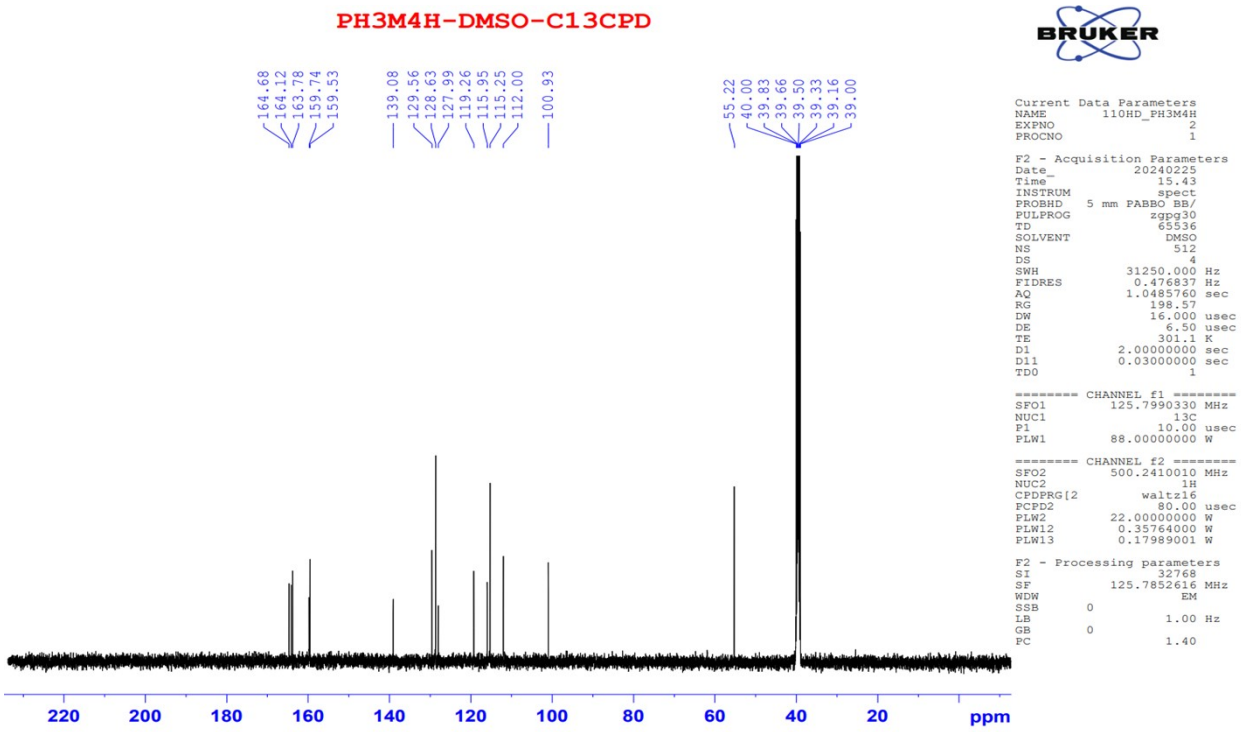


Figure S45. ^{13}C-NMR spectrum of compound **1h**

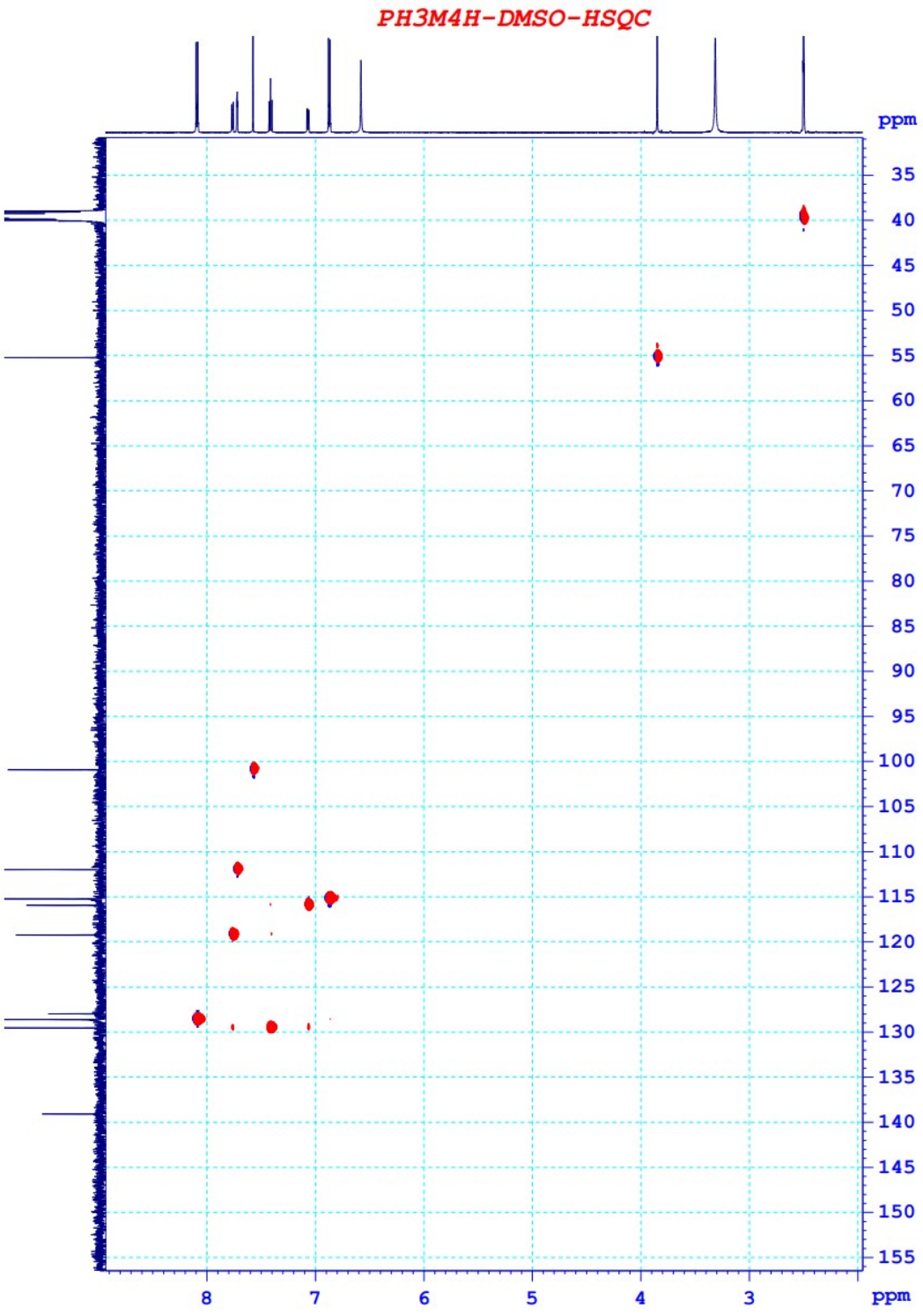


Figure S46. HSQC of compound 1h

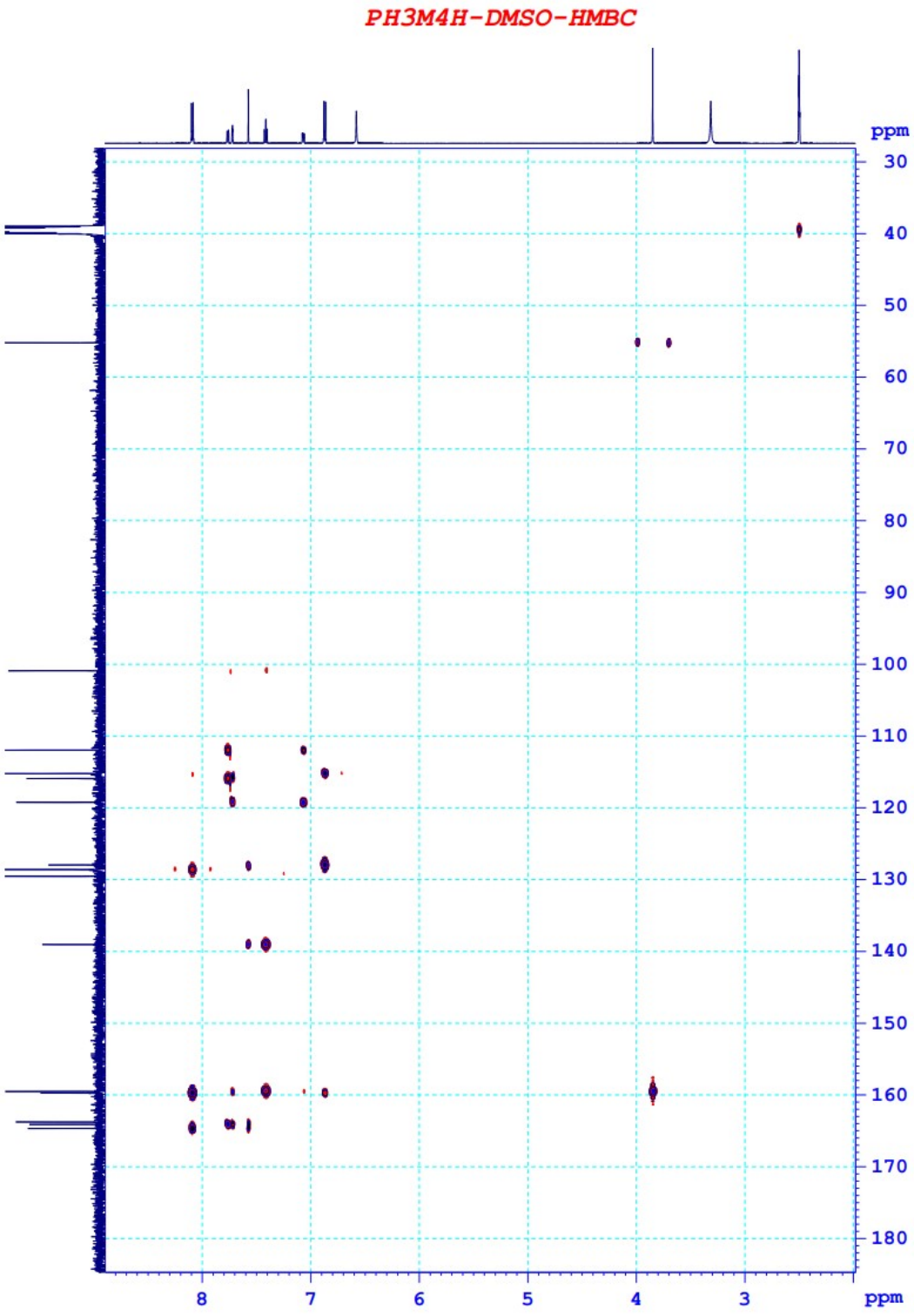


Figure S47. HMBC of compound 1h

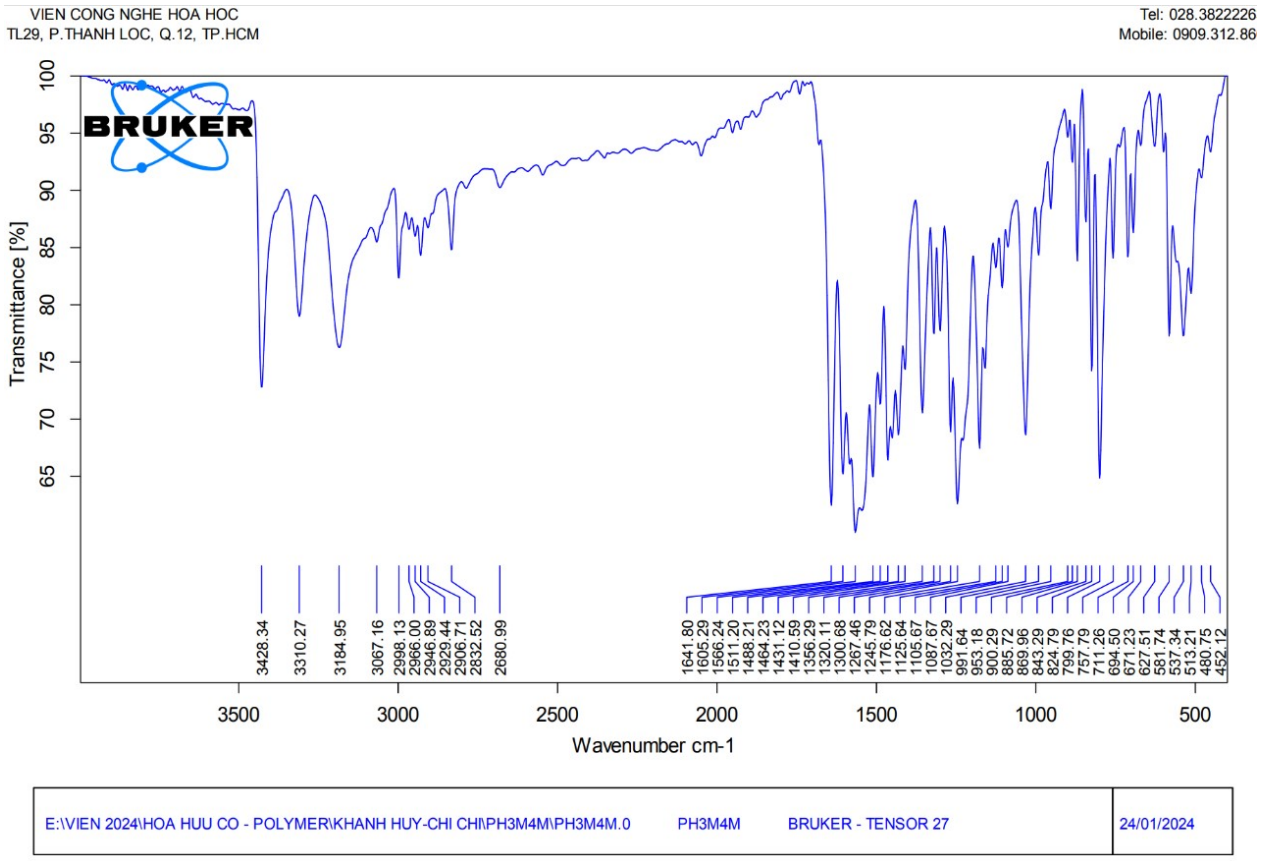


Figure S48. FTIR spectrum of compound **1i**

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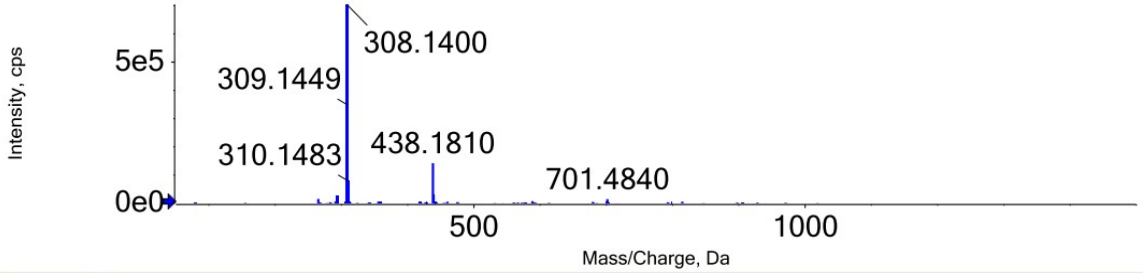
Injection details

Sample name	PH3M4M	*Vial position*	25
Sample file name	SER. wiff2- HUY	*Inject volume*	2.00
Acquisition date	19/01/2024 10:06:29 AM	*Acquisition method*	**ESI _POS_SCAN**
Operator	CB21261708	*Instrument name*	X500$_R$ QTOF

Full mass spectrum

Spectrum from HUY_PH3M4M_(+)ESI 2024-01-19-10-06-29...e multiplier = 1.5), Gaussian smoothed (0.5 points)



Expanded spectrum

Spectrum from HUY_PH3M4M_(+)ESI 2024-01-19-10-06-29...e multiplier = 1.5), Gaussian smoothed (0.5 points)

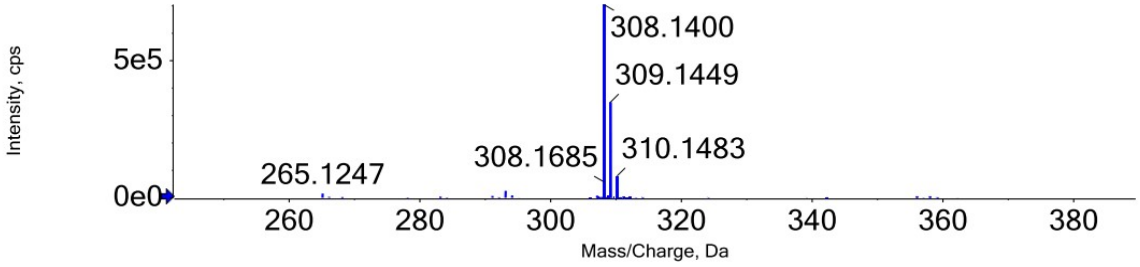


Figure S49. HRMS spectrum of compound **1i**

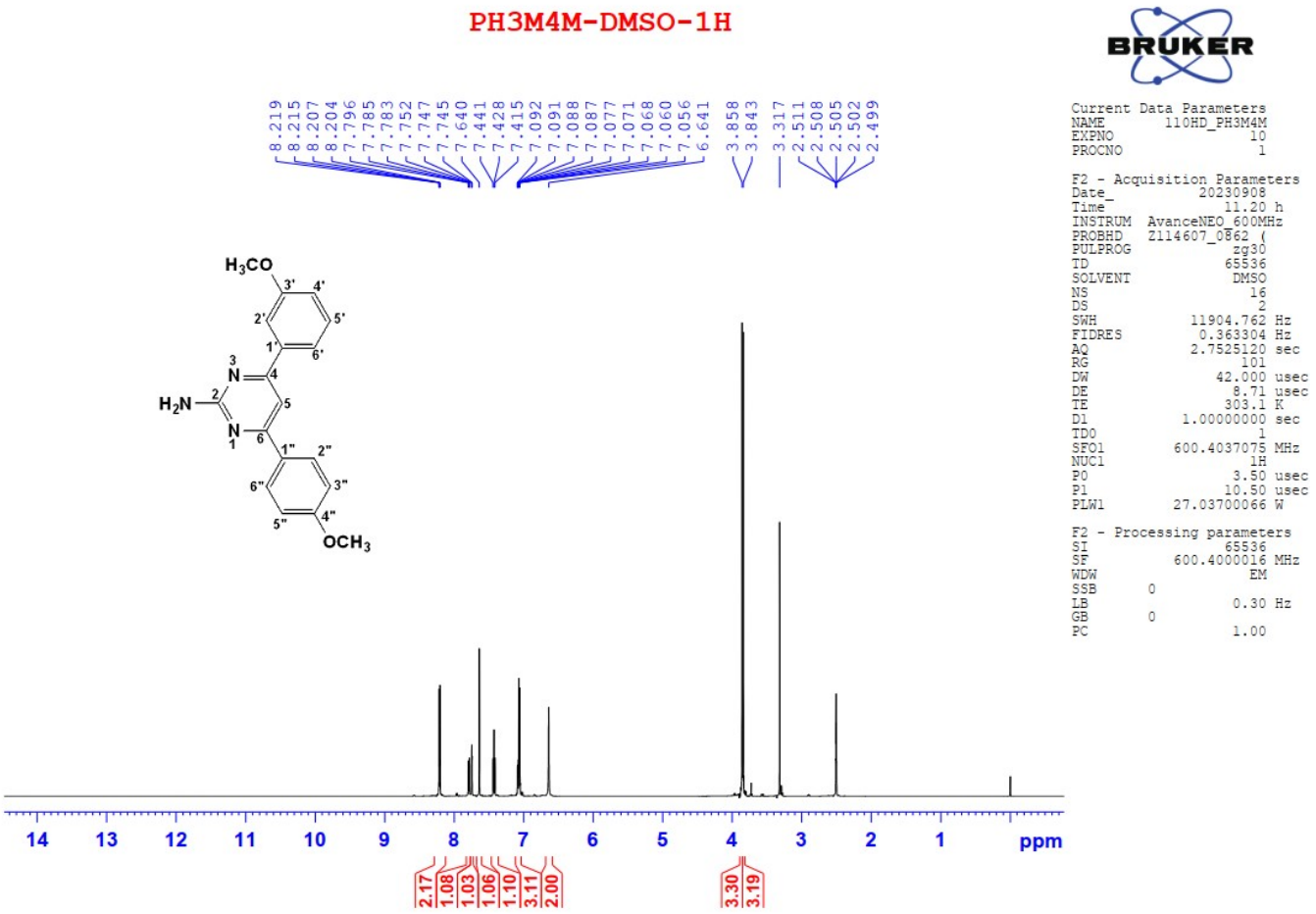


Figure S50. ^{1}H-NMR spectrum of compound **1i**

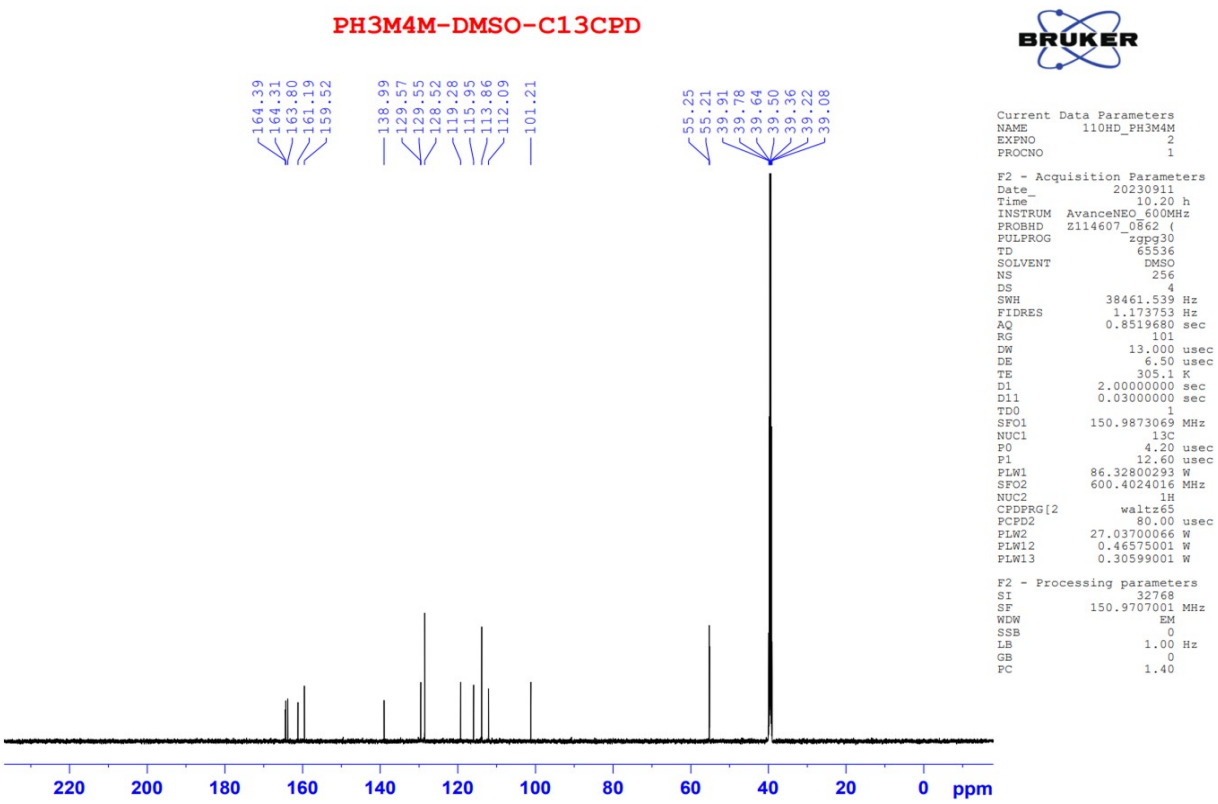


Figure S51. ^{13}C-NMR spectrum of compound **1i**

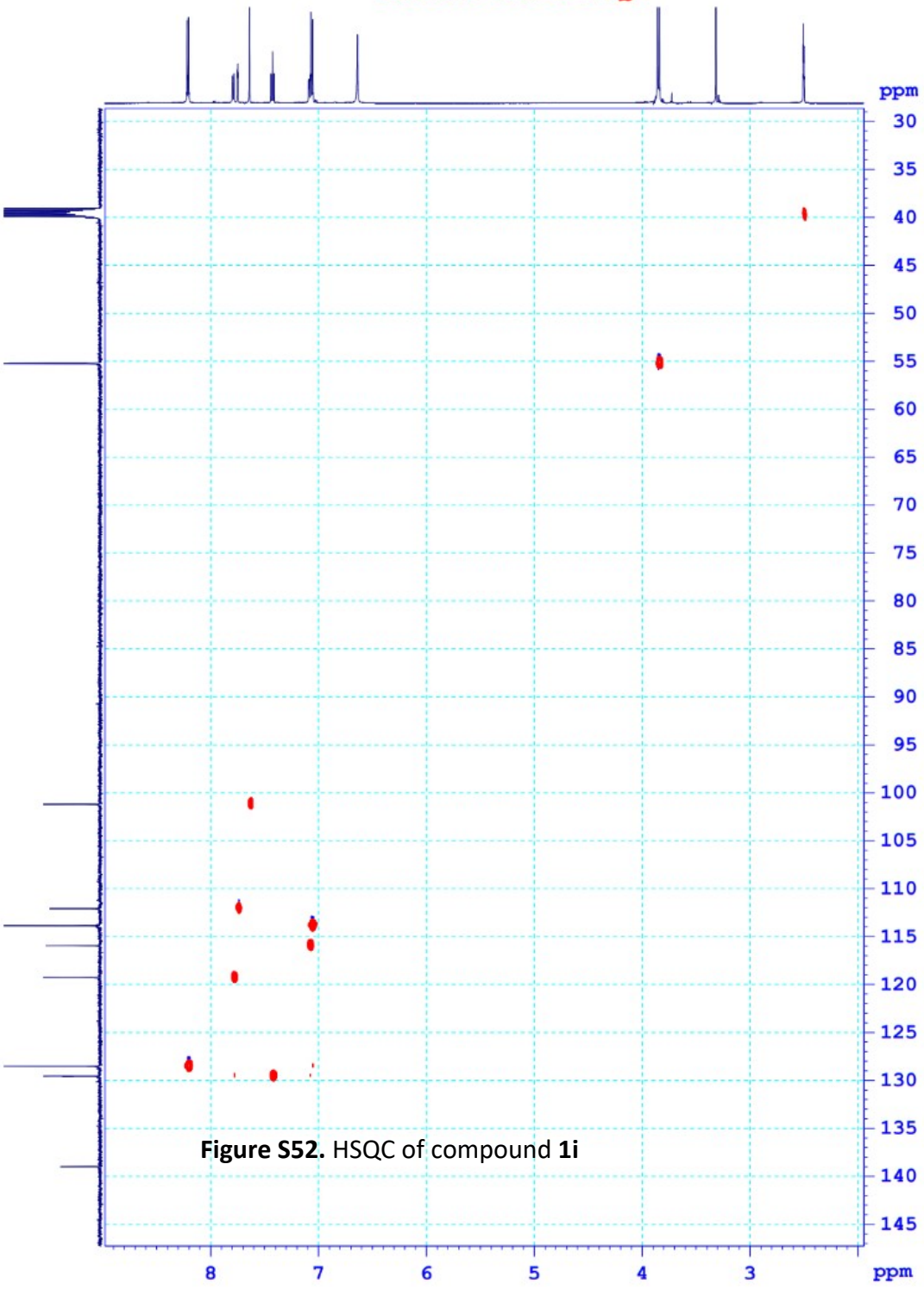


Figure S52. HSQC of compound **1i**

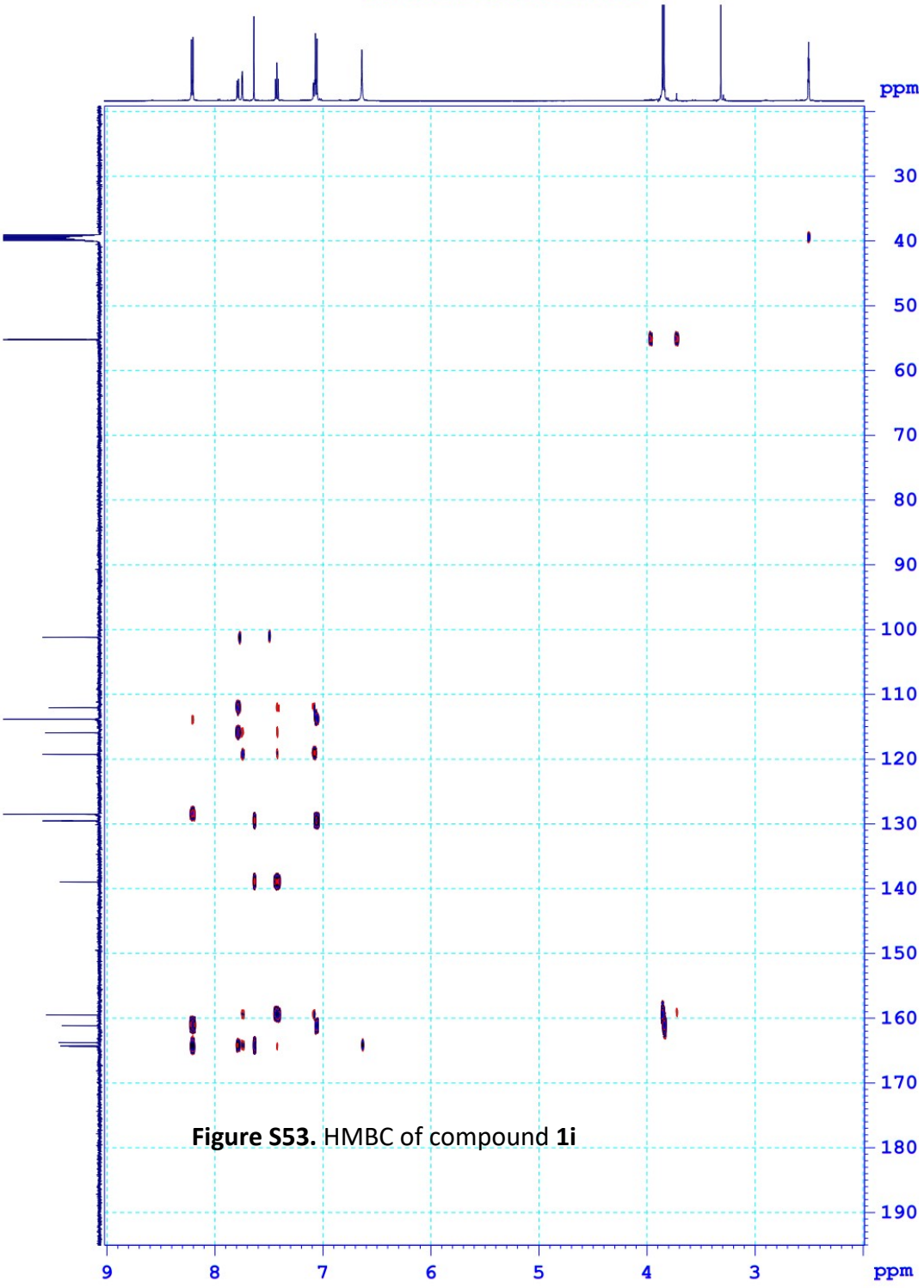


Figure S53. HMBC of compound **1i**

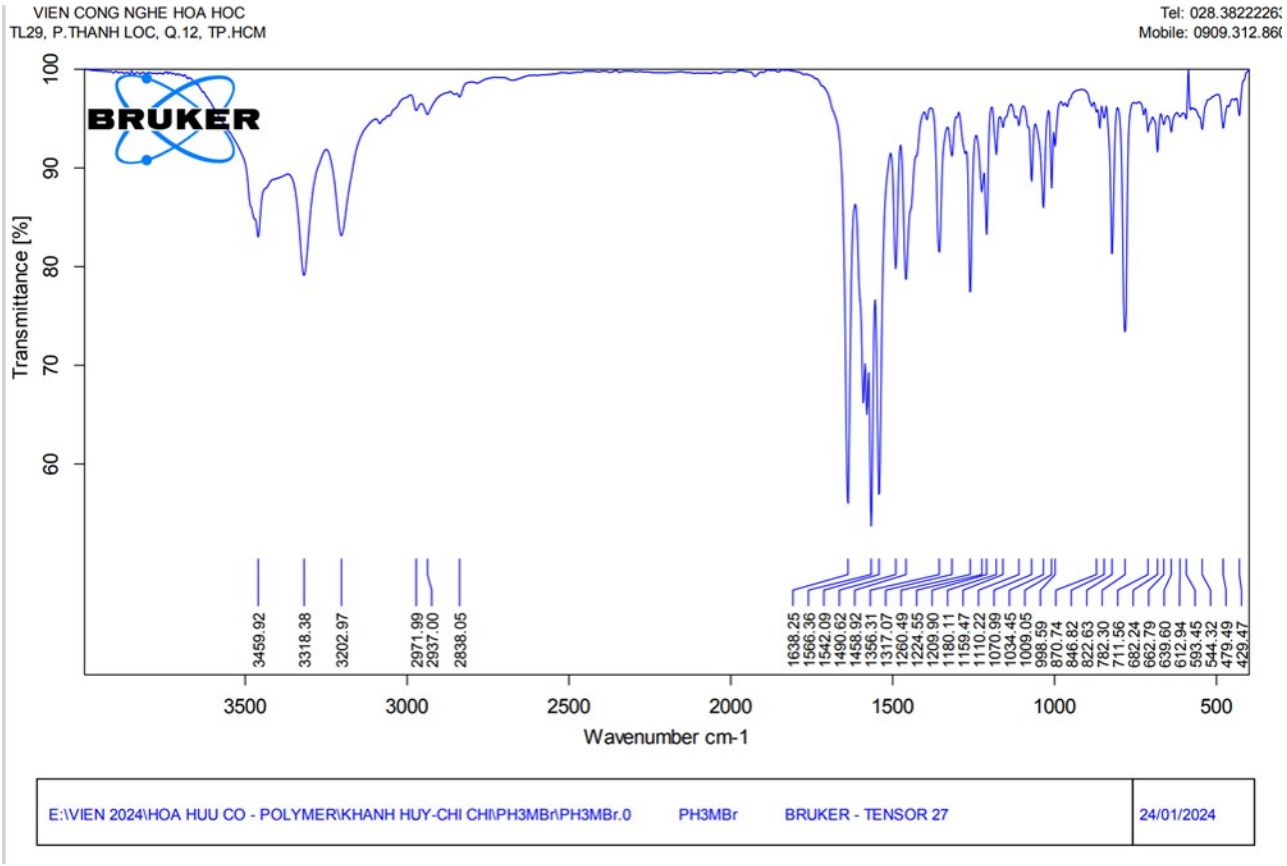


Figure S54. FTIR spectrum of compound **1j**

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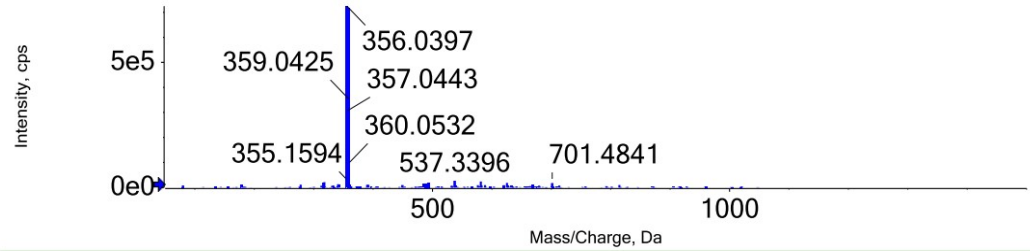
ANALYSIS REPORT

Injection details

Sample name	PH3MBr	*Vial position*	27
Sample file name	SER. wiff2- HUY	*Inject volume*	2.00
Acquisition date	19/01/2024 10:11:09 AM	*Acquisition method*	**ESI _POS_SCAN**
Operator	CB21261708	*Instrument name*	$X500_R$ QTOF

Full mass spectrum

Spectrum from HUY_PH3MBr_(+)ESI 2024-01-19-10-11-09....e multiplier = 1.5), Gaussian smoothed (0.5 points)



Expanded spectrum

Spectrum from HUY_PH3MBr_(+)ESI 2024-01-19-10-11-09....e multiplier = 1.5), Gaussian smoothed (0.5 points)

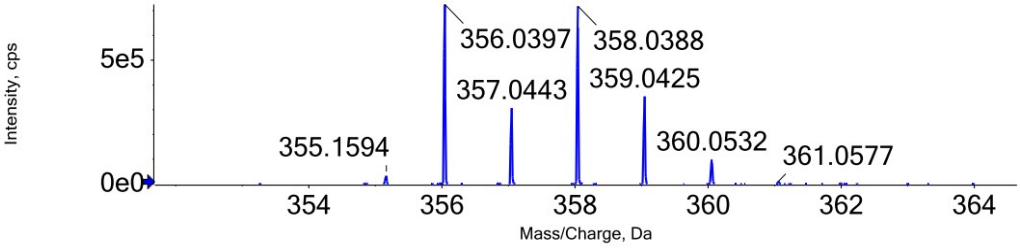


Figure S55. HRMS spectrum of compound **1j**

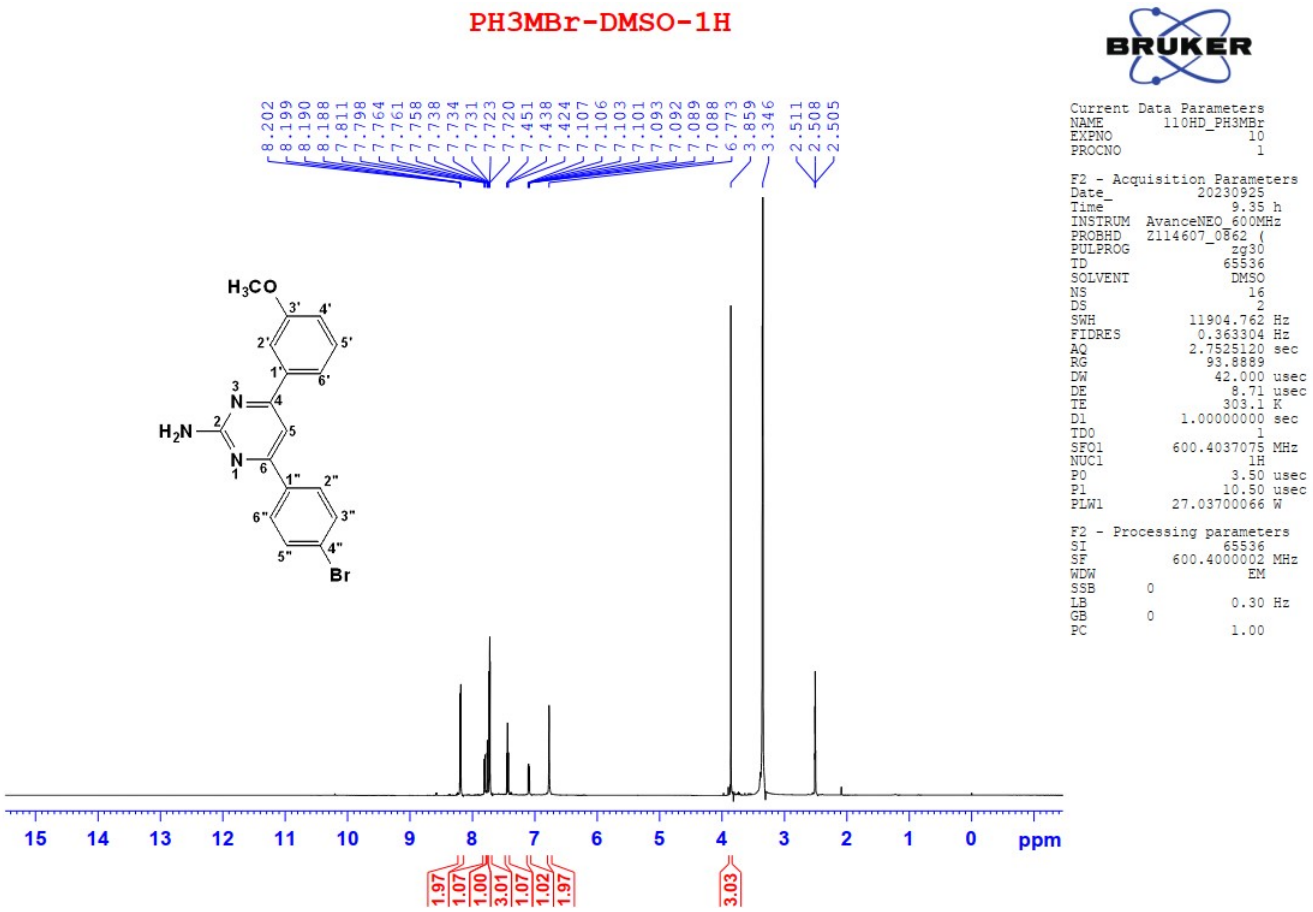


Figure S56. ^{1}H-NMR spectrum of compound **1j**

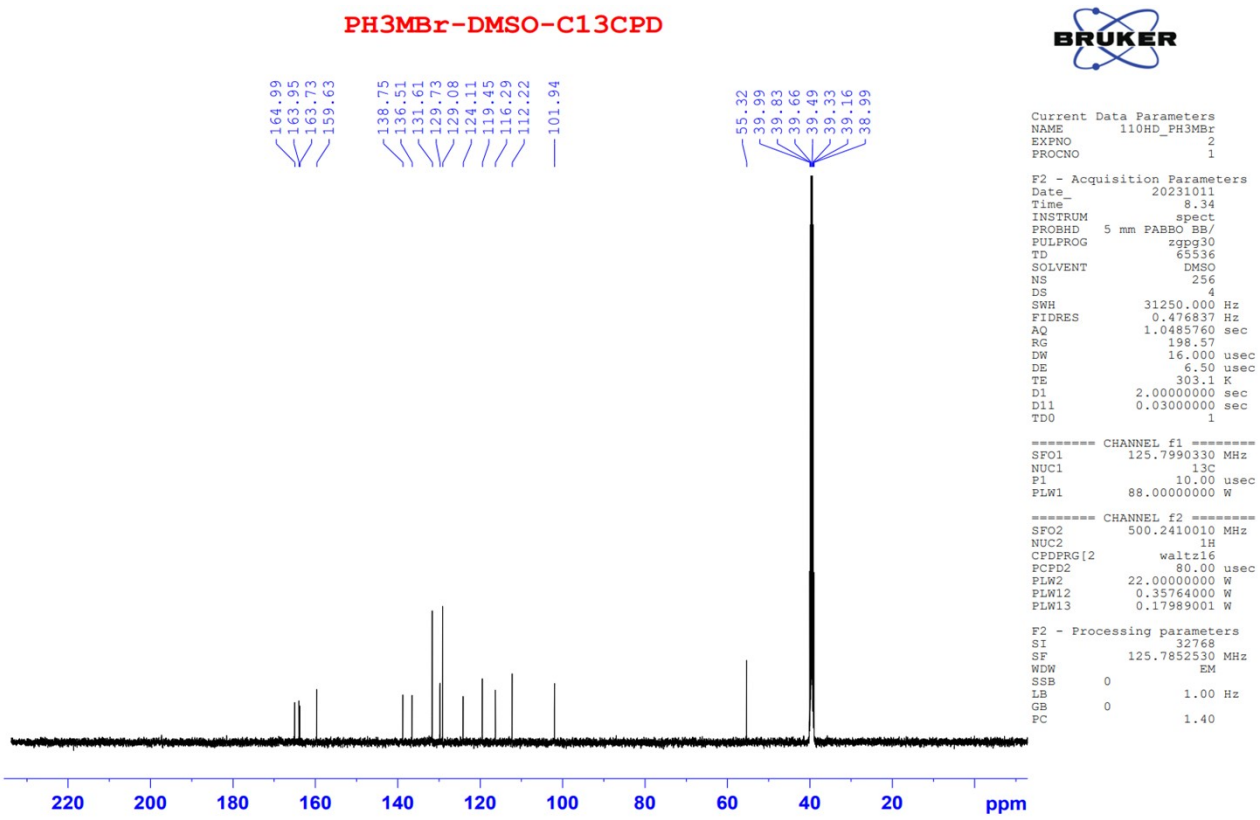


Figure S57. ^{13}C-NMR spectrum of compound **1j**

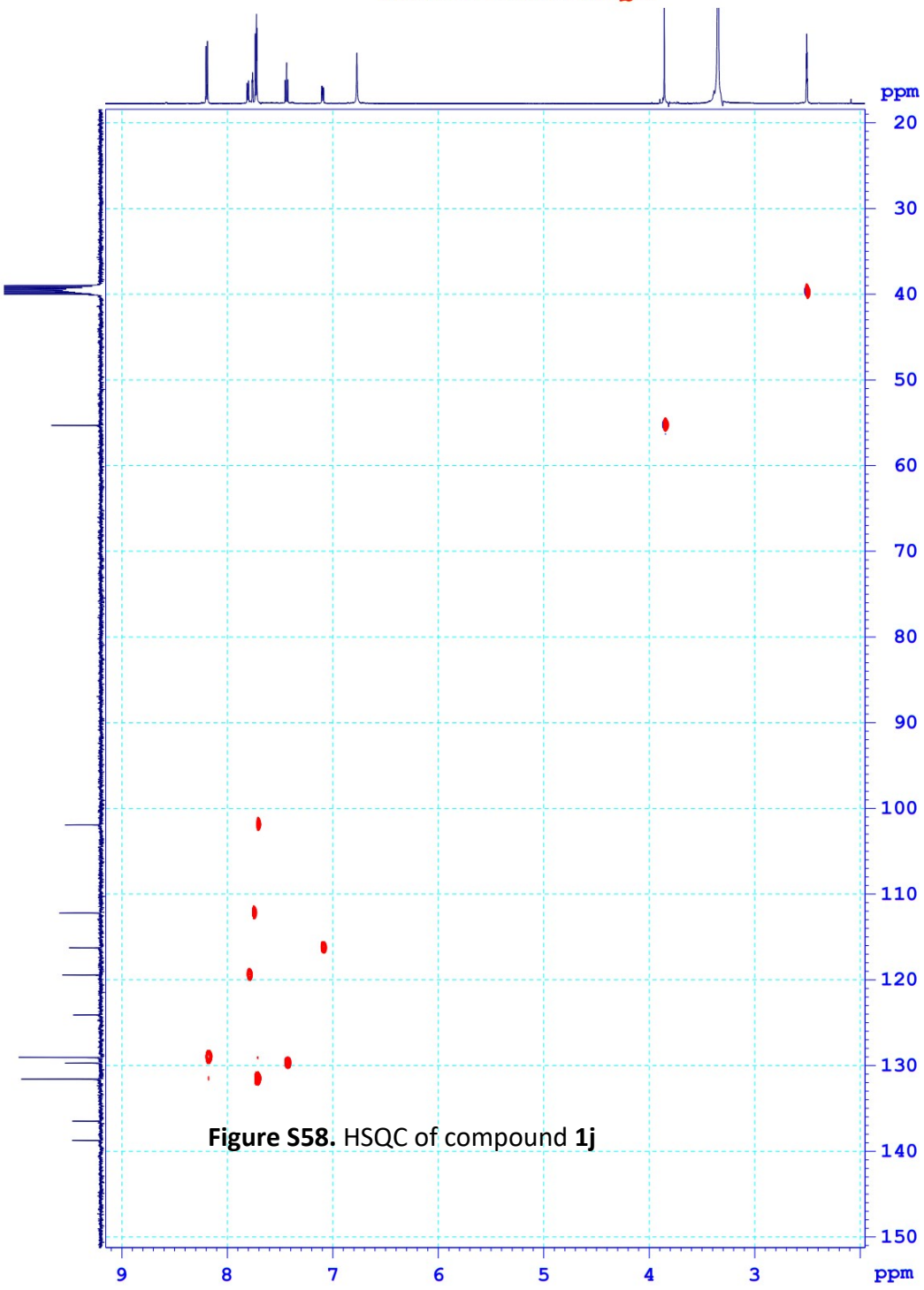


Figure S58. HSQC of compound **1j**

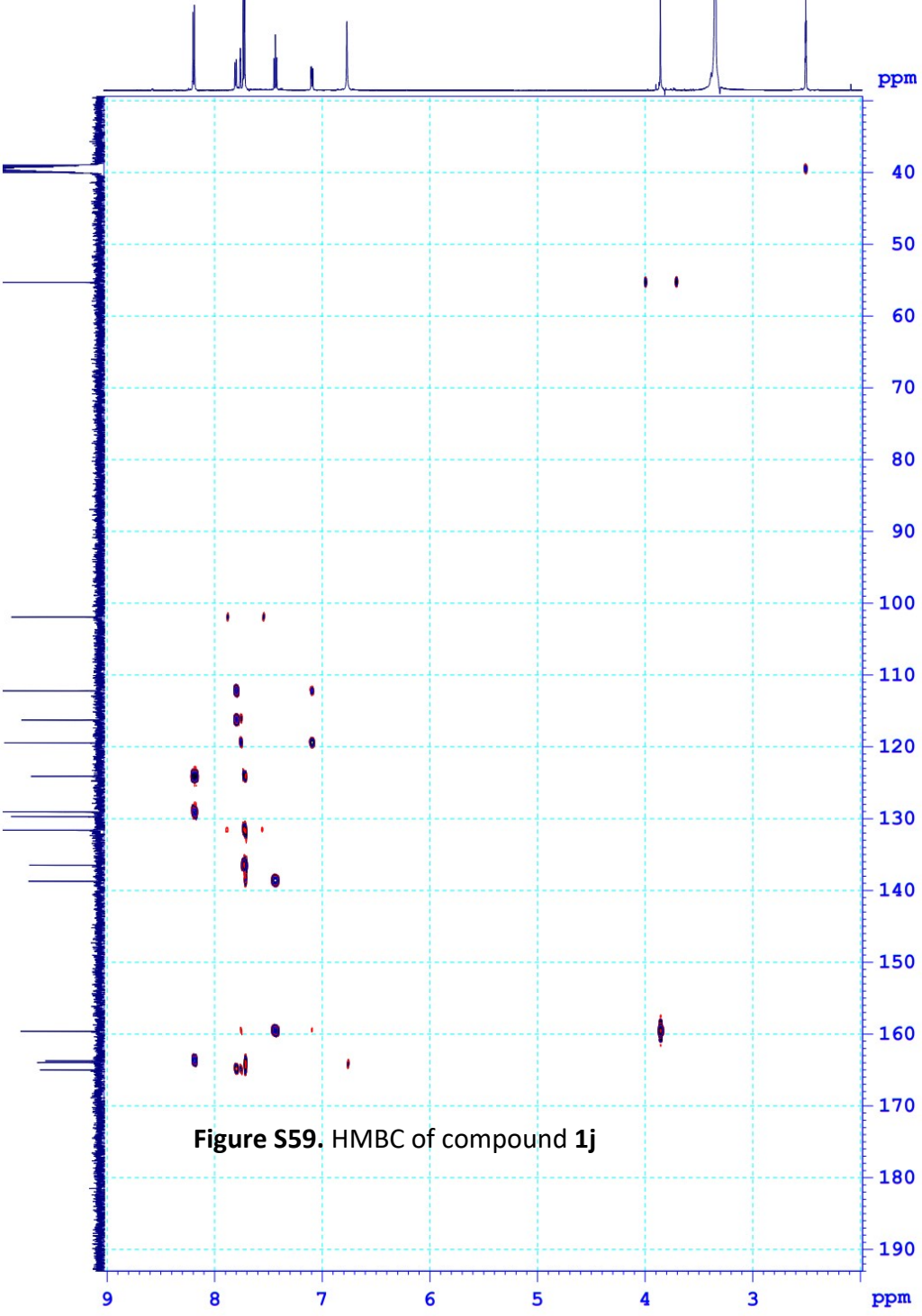


Figure S59. HMBC of compound **1j**

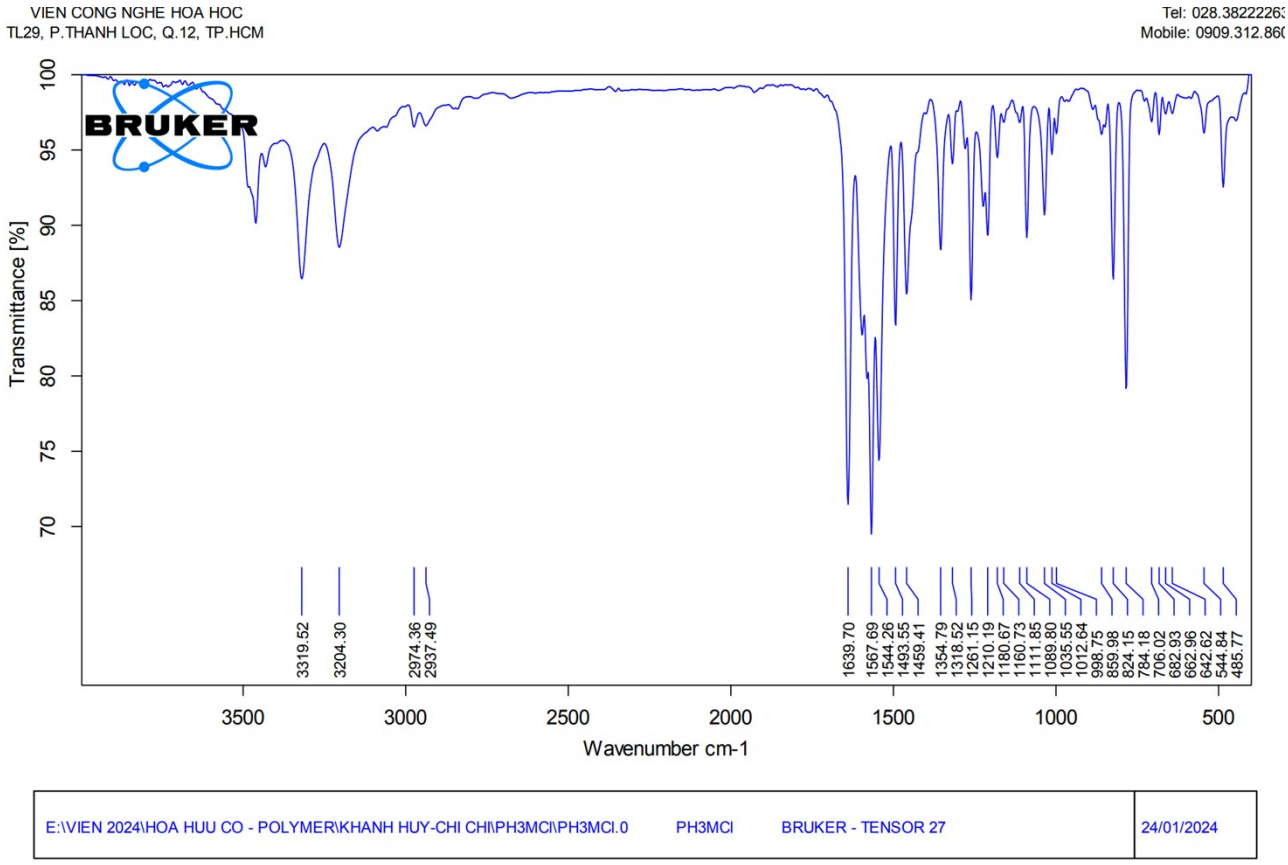


Figure S60. FTIR spectrum of compound **1k**

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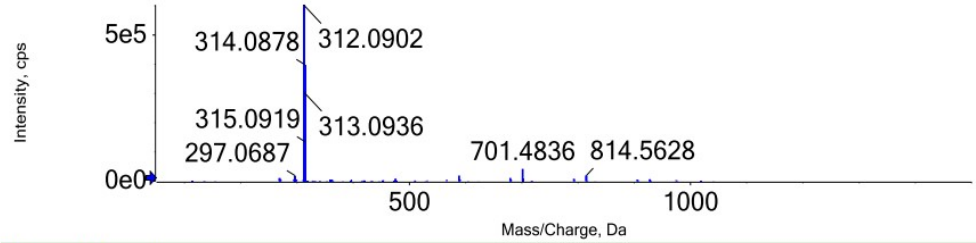
ANALYSIS REPORT

Injection details

Sample name	PH3MCl	*Vial position*	28
Sample file name	SER. wiff2- HUY	*Inject volume*	2.00
Acquisition date	19/01/2024 10:12:49 AM	*Acquisition method*	**ESI _POS_SCAN**
Operator	CB21261708	*Instrument name*	X500$_R$ QTOF

Full mass spectrum

Spectrum from HUY_PH3MCl_(+)ESI 2024-01-19-10-12-49....e multiplier = 1.5), Gaussian smoothed (0.5 points)



Expanded spectrum

Spectrum from HUY_PH3MCl_(+)ESI 2024-01-19-10-12-49....e multiplier = 1.5), Gaussian smoothed (0.5 points)

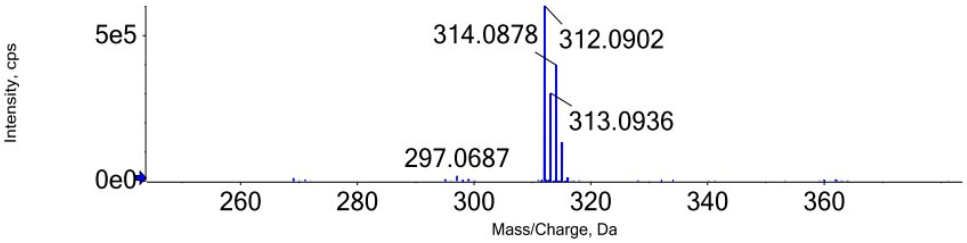


Figure S61. HRMS spectrum of compound **1k**

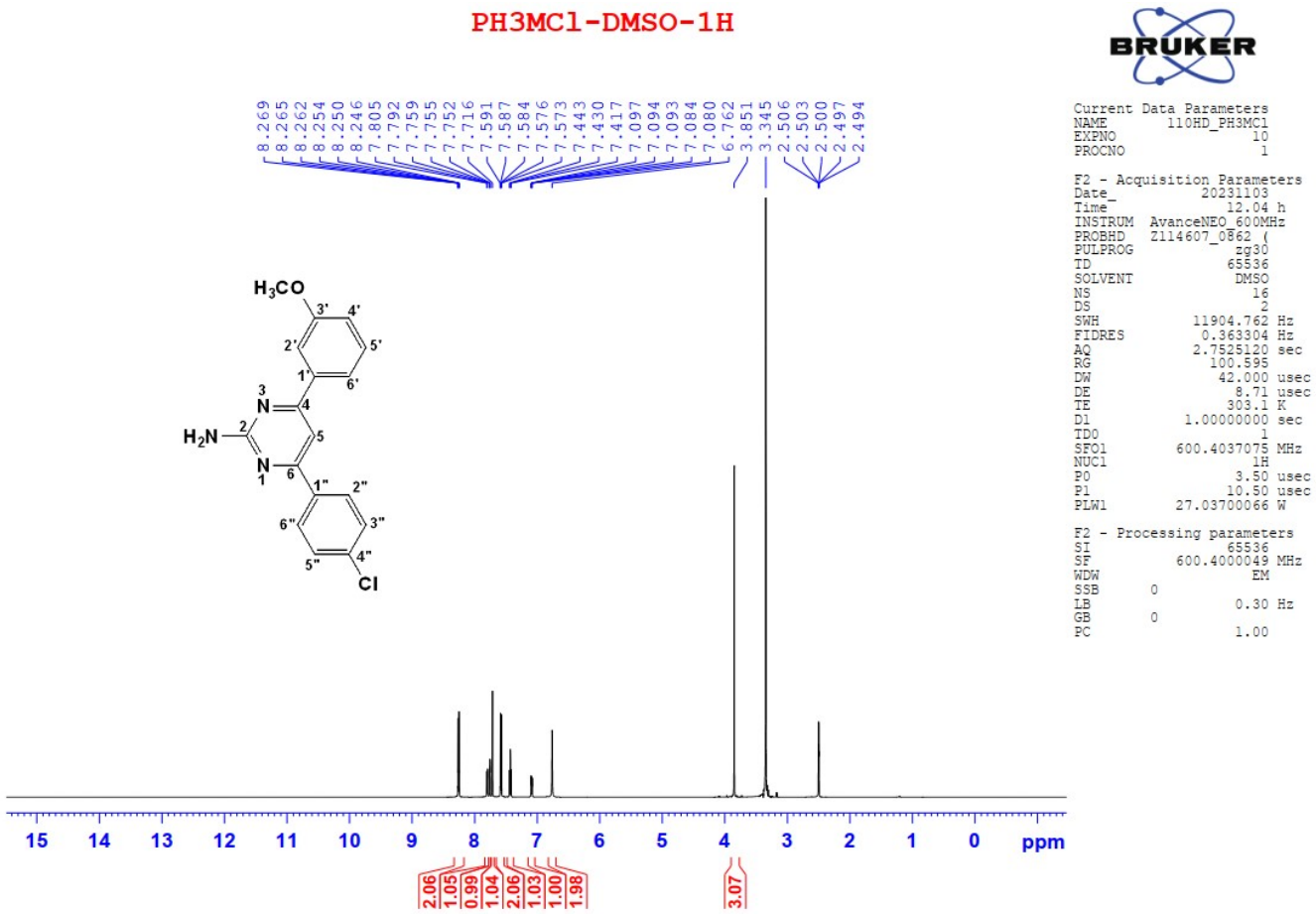


Figure S62. ^{1}H-NMR spectrum of compound **1k**

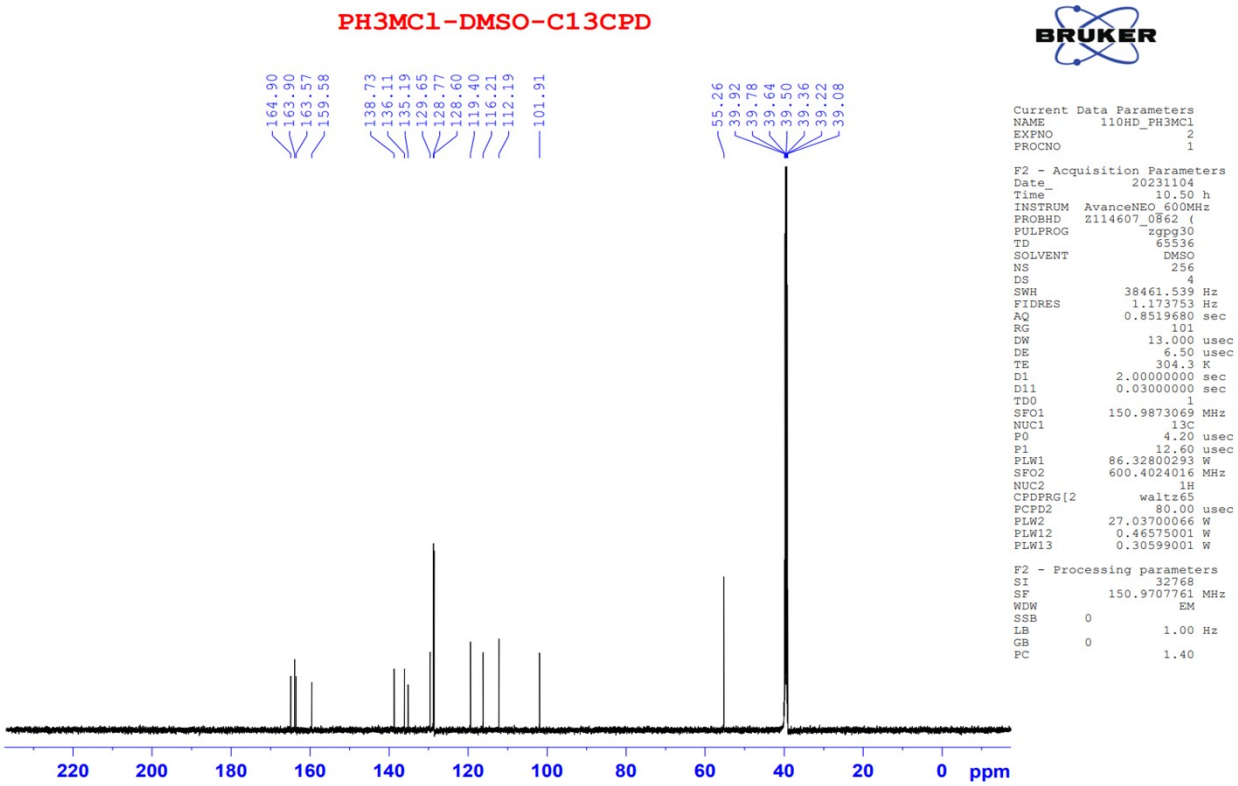


Figure S63. ^{13}C-NMR spectrum of compound **1k**

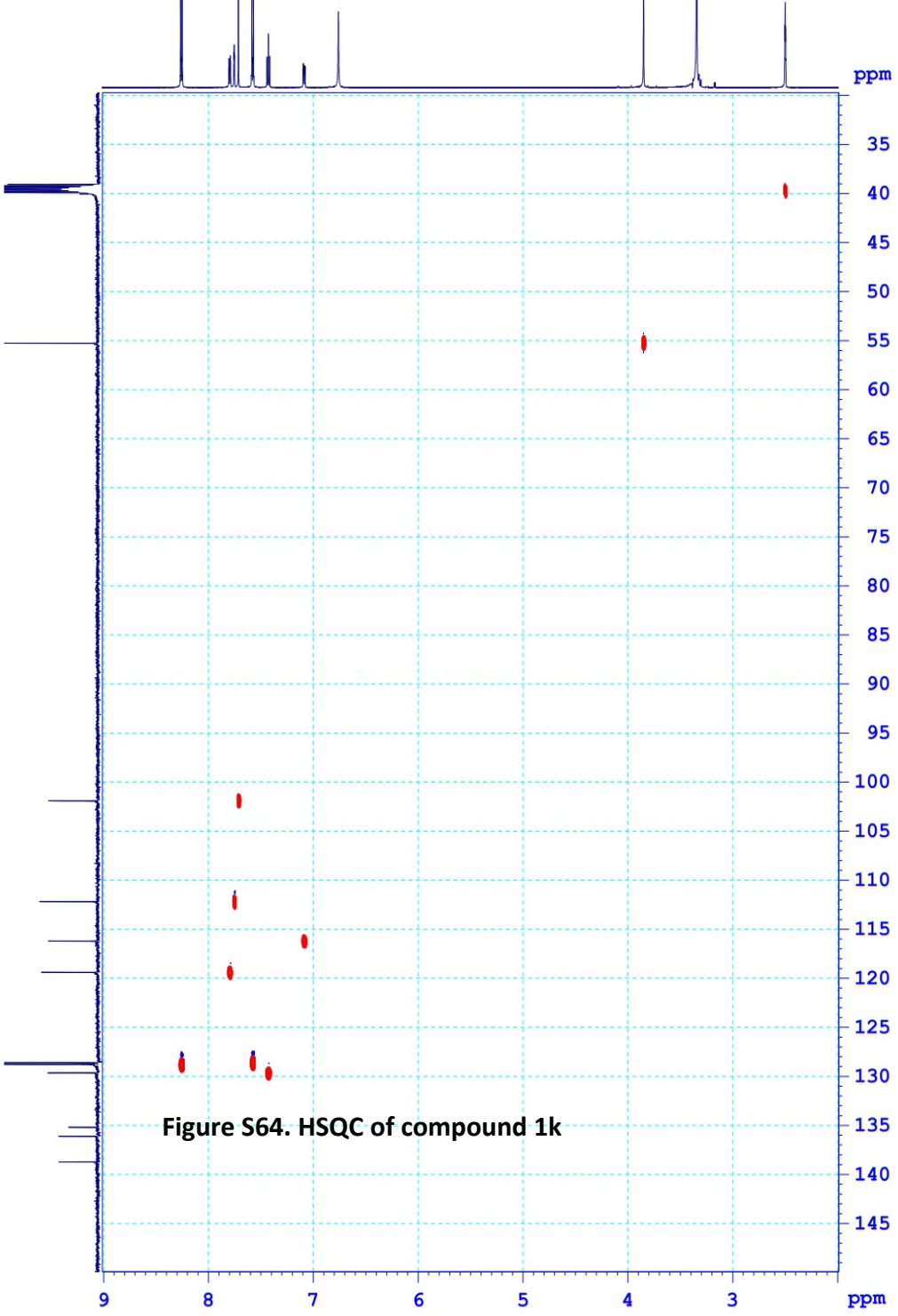


Figure S64. HSQC of compound 1k

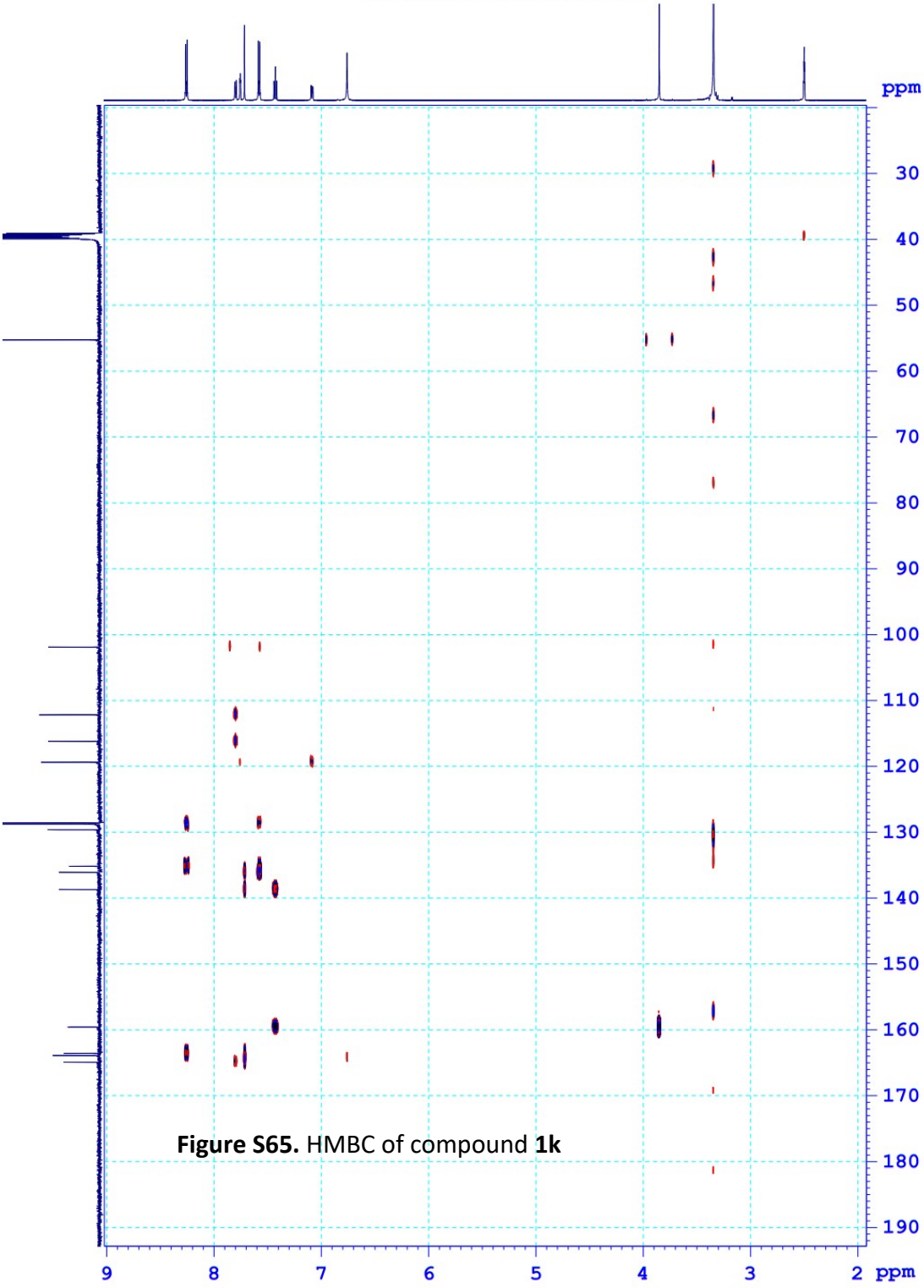


Figure S65. HMBC of compound **1k**

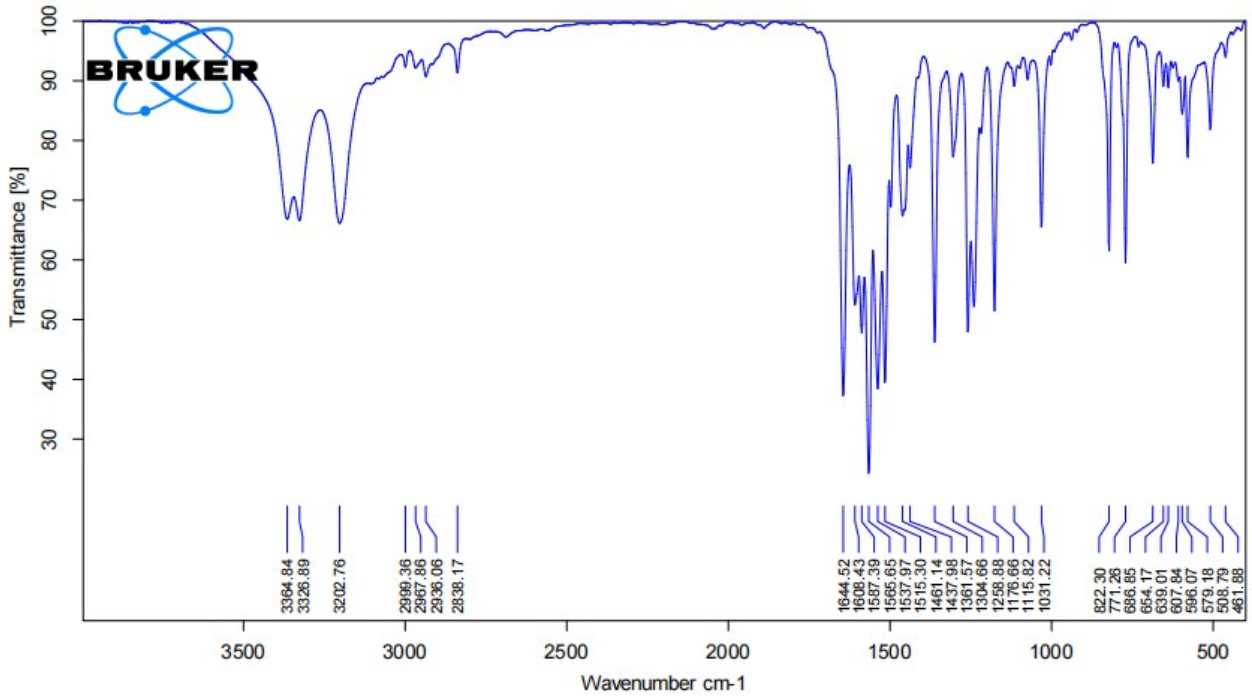


Figure S66. FTIR spectrum of compound **1l**

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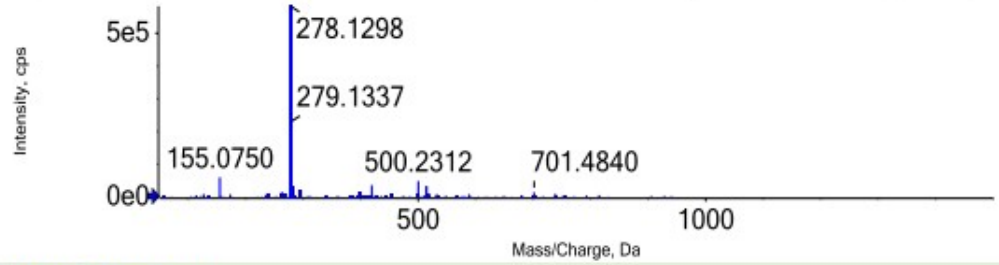
ANALYSIS REPORT

Injection details

Sample name	PH4MA	*Vial position*	32
Sample file name	SER. wiff2- HUY	*Inject volume*	2.00
Acquisition date	19/01/2024 10:20:38 AM	*Acquisition method*	**ESI _POS_SCAN**
Operator	CB21261708	*Instrument name*	X500$_R$ QTOF

Full mass spectrum

Spectrum from HUY_PH4MA_(+)ESI 2024-01-19-10-20-38....e multiplier = 1.5), Gaussian smoothed (0.5 points)



Expanded spectrum

Spectrum from HUY_PH4MA_(+)ESI 2024-01-19-10-20-38....e multiplier = 1.5), Gaussian smoothed (0.5 points)

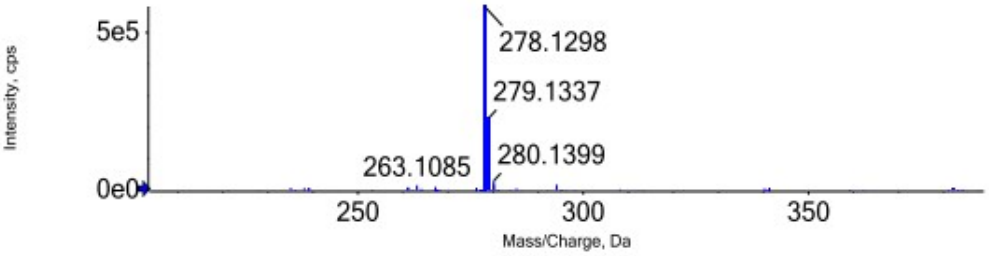


Figure S67. HRMS spectrum of compound **1l**

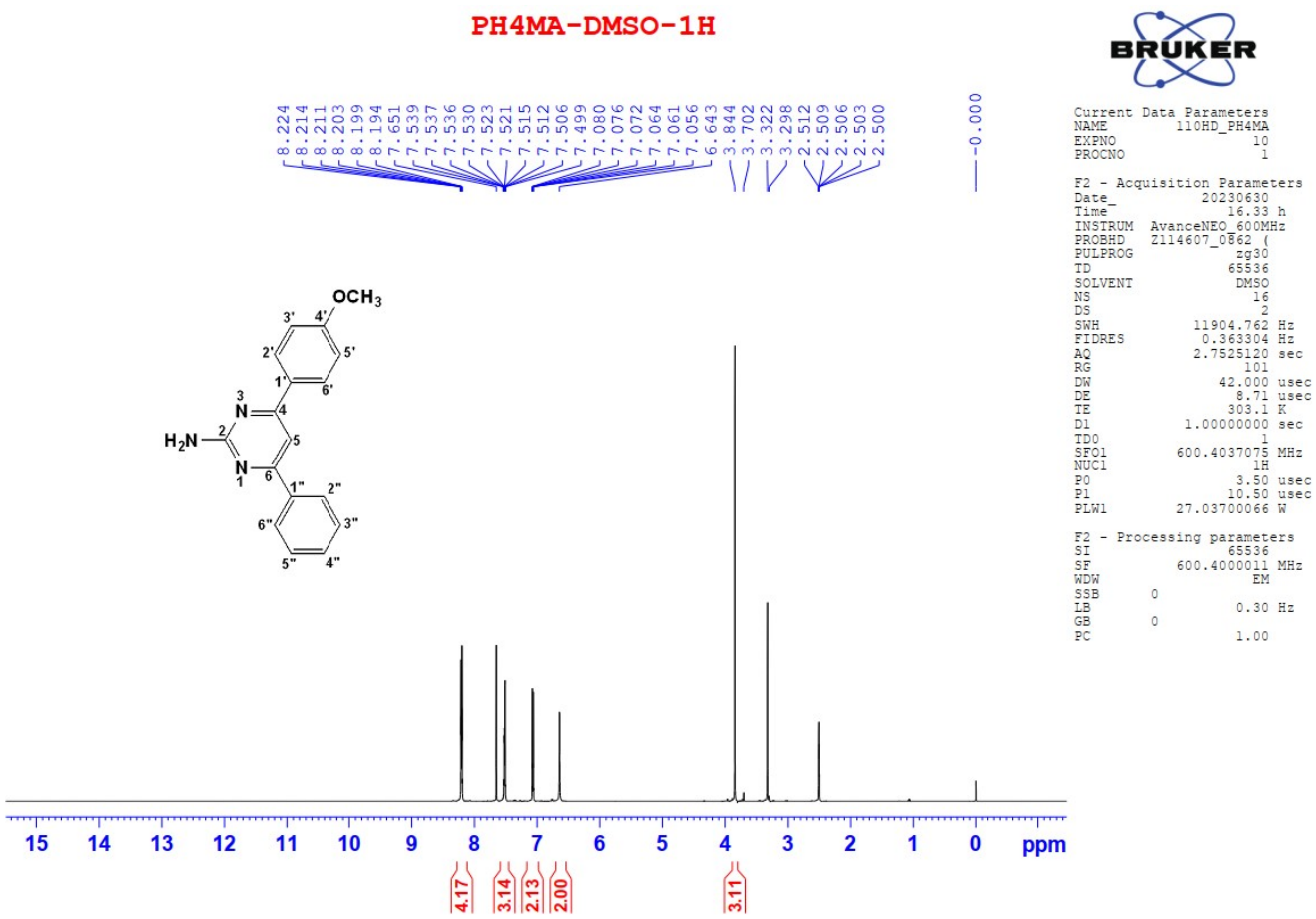


Figure S68. ^{1}H-NMR spectrum of compound **1l**

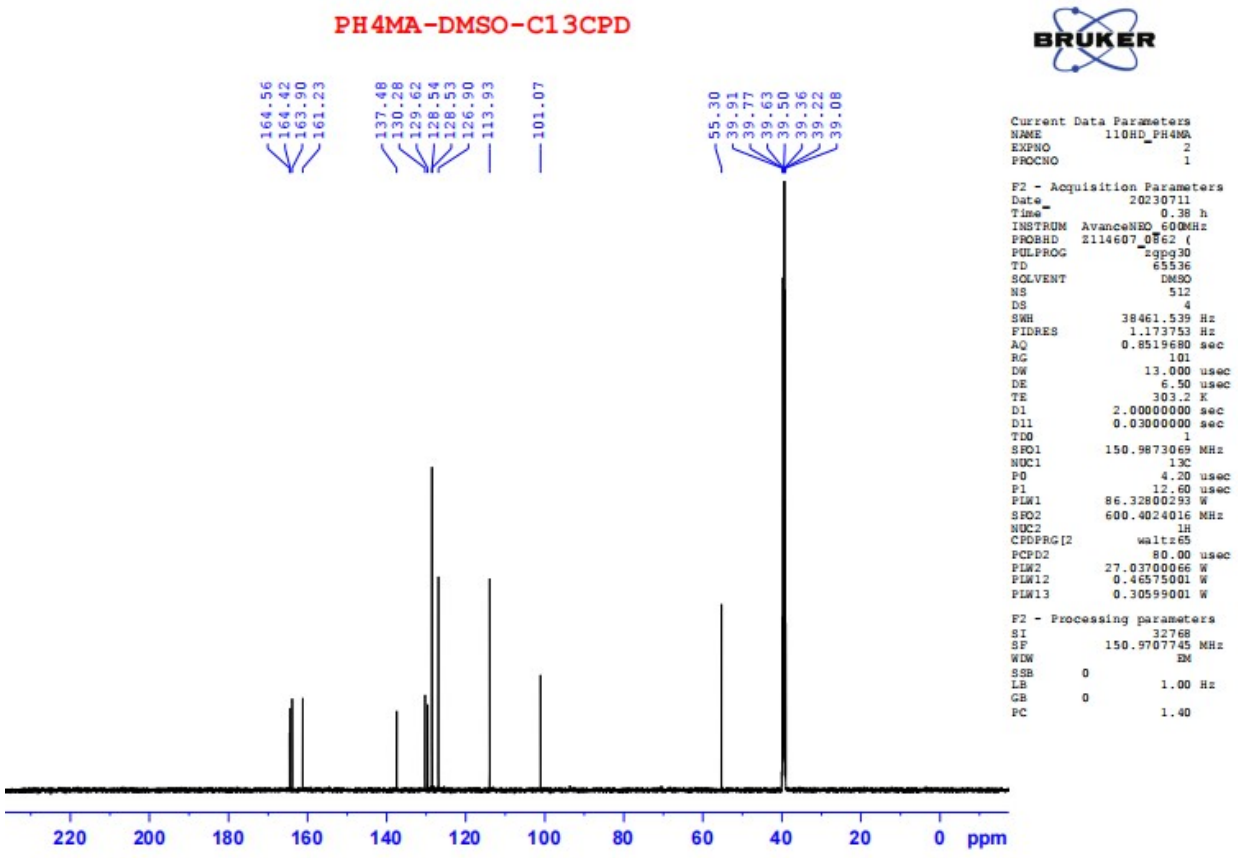


Figure S69. ^{13}C-NMR spectrum of compound **1l**

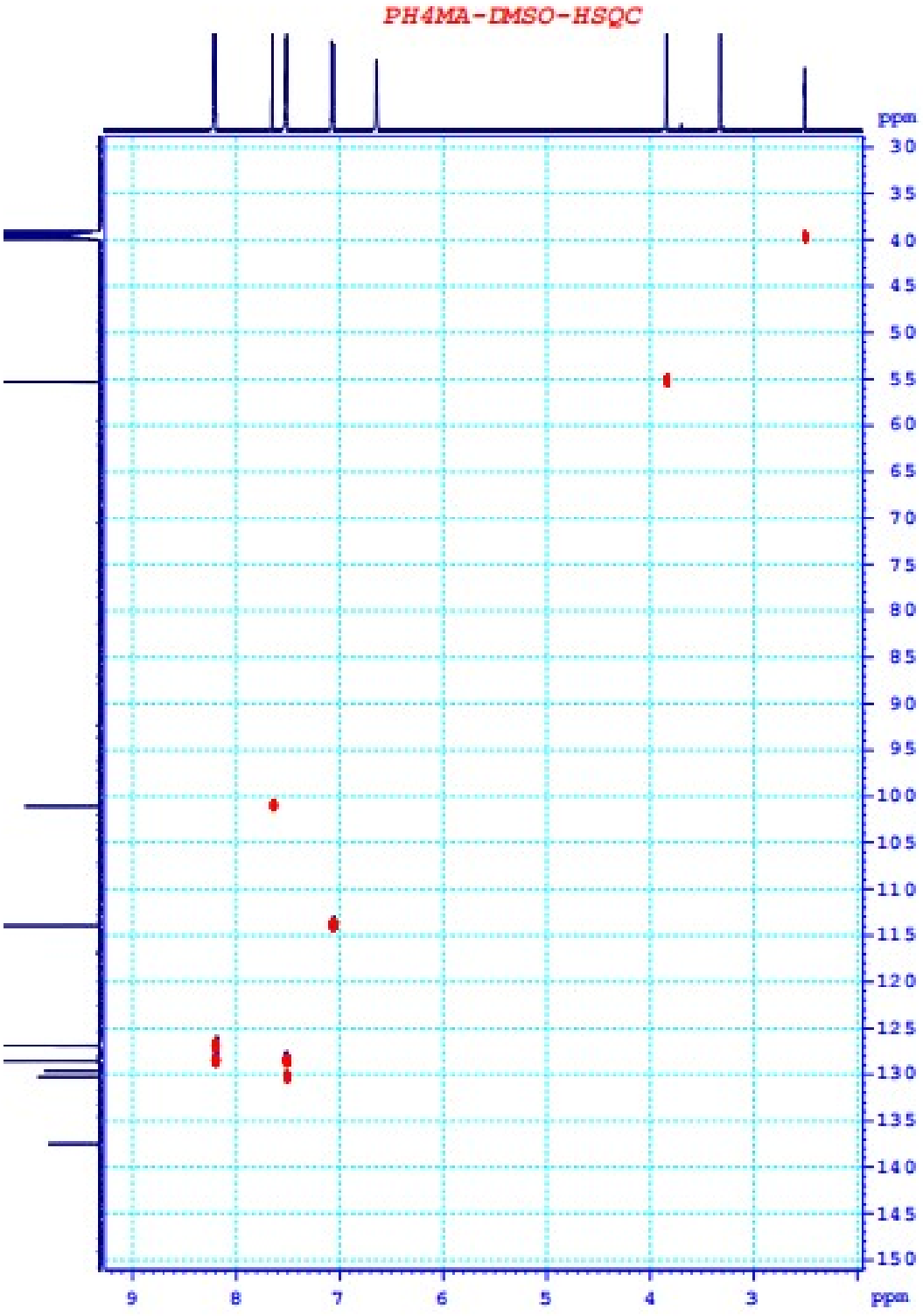


Figure S70. HSQC of compound 1l

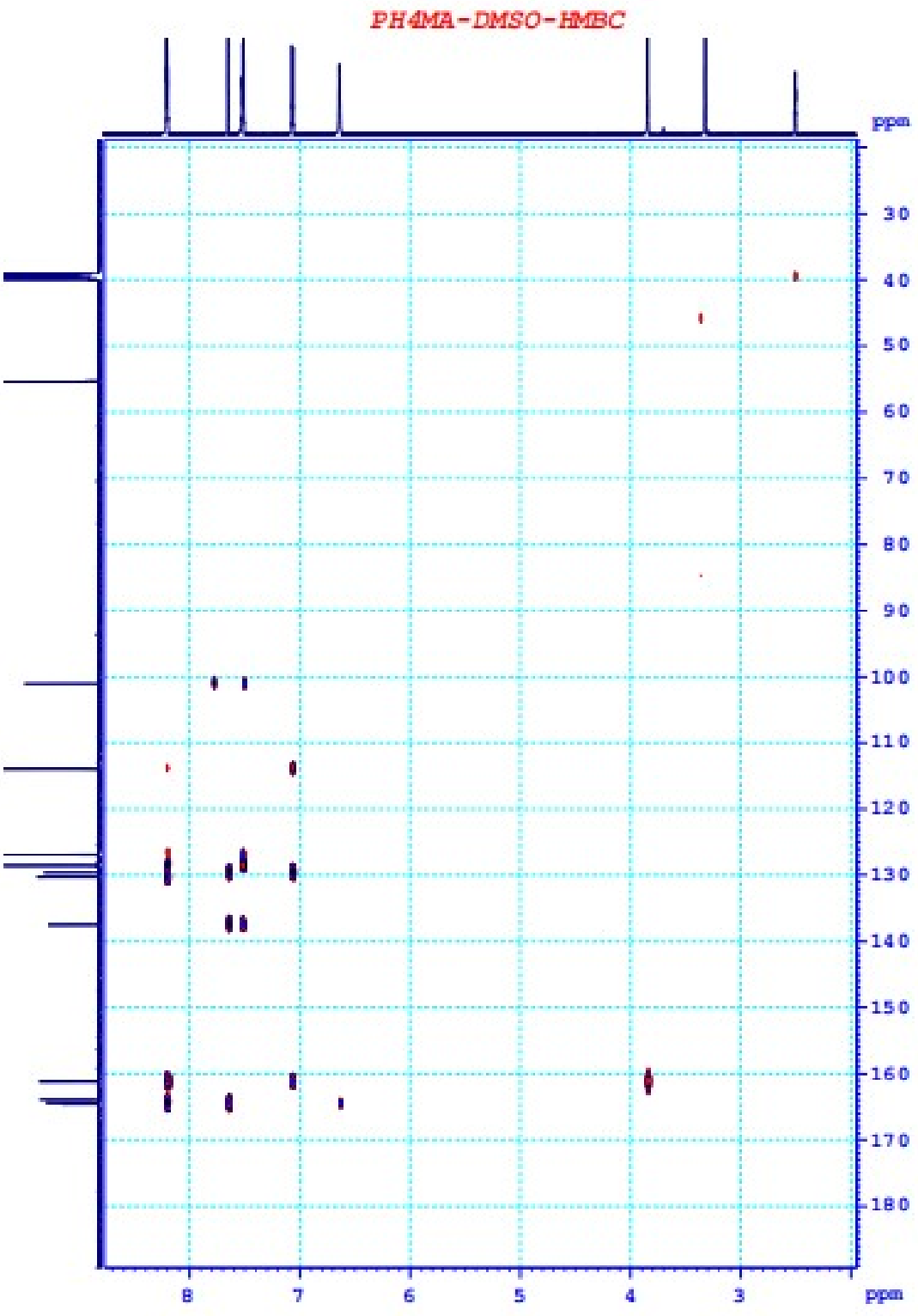


Figure S71. HMBC of compound **1l**

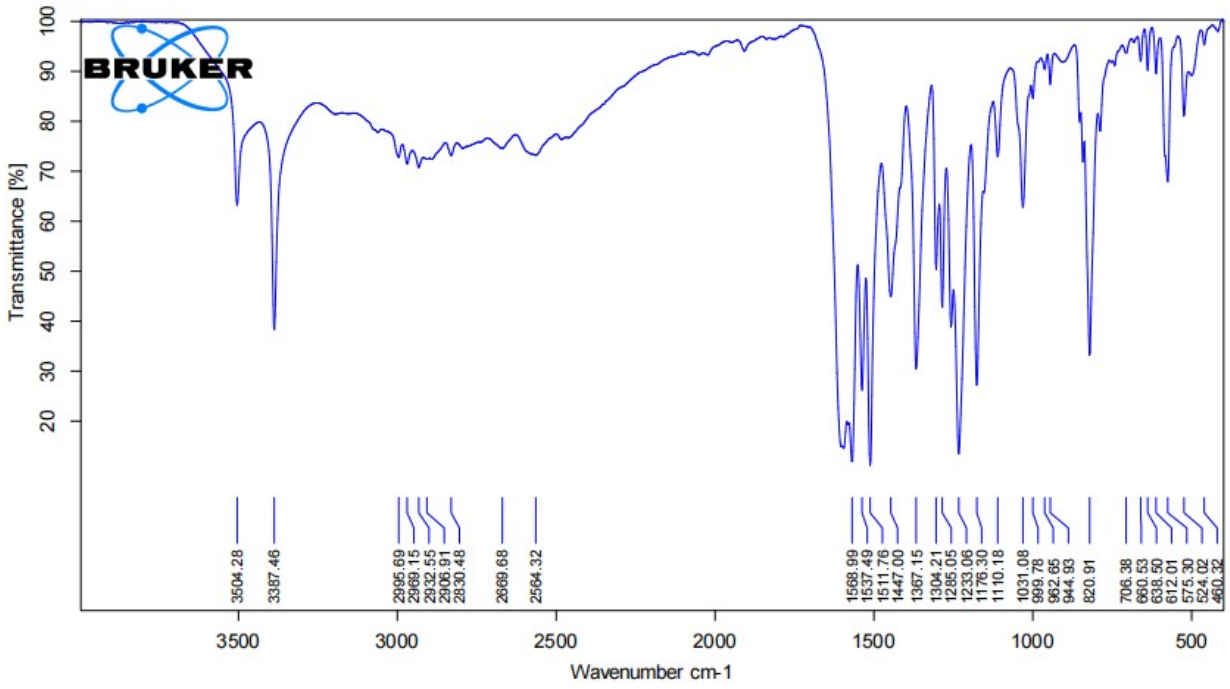


Figure S72. FTIR spectrum of compound **1m**

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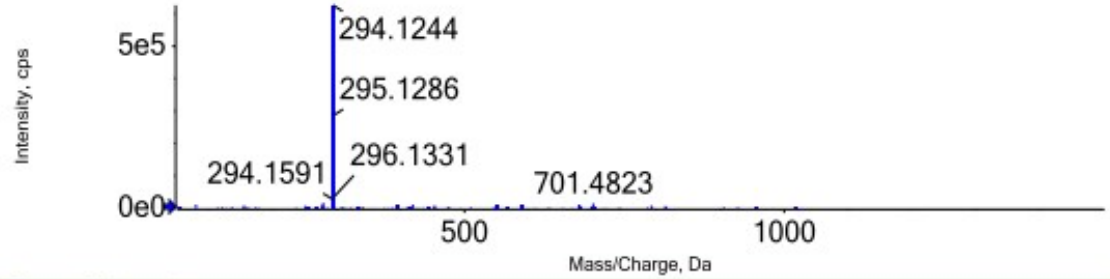
ANALYSIS REPORT

Injection details

Sample name	PH4M4H	*Vial position*	30
Sample file name	SER. wiff2- HUY	*Inject volume*	2.00
Acquisition date	19/01/2024 10:17:13 AM	*Acquisition method*	**ESI _POS_SCAN**
Operator	CB21261708	*Instrument name*	$X500_R$ QTOF

Full mass spectrum

Spectrum from HUY_PH4M4H_(+)ESI 2024-01-19-10-17-13...e multiplier = 1.5), Gaussian smoothed (0.5 points)



Expanded spectrum

Spectrum from HUY_PH4M4H_(+)ESI 2024-01-19-10-17-13...e multiplier = 1.5), Gaussian smoothed (0.5 points)

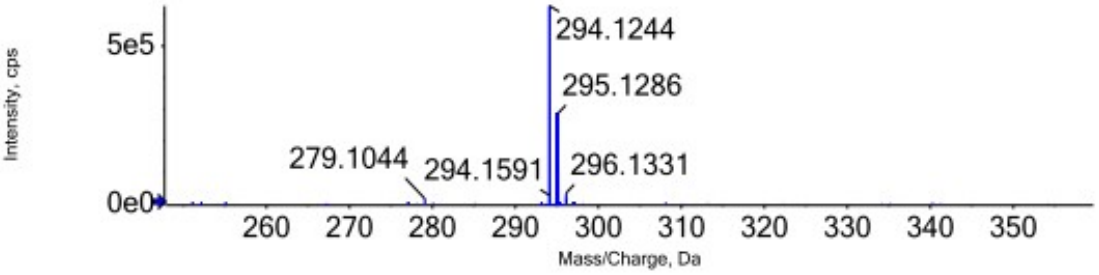


Figure S73. HRMS spectrum of compound **1m**

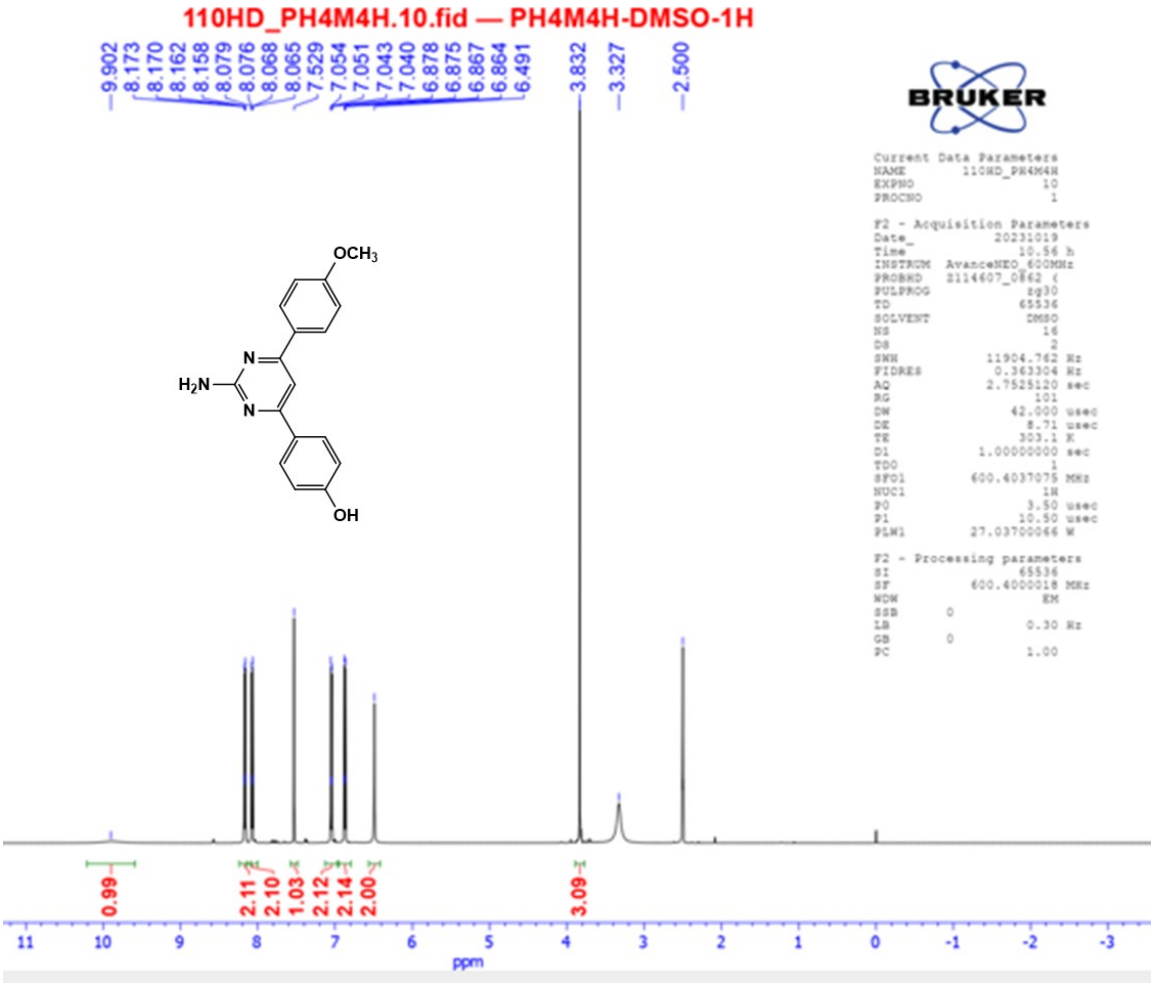


Figure S74. ^{1}H-NMR spectrum of compound **1m**

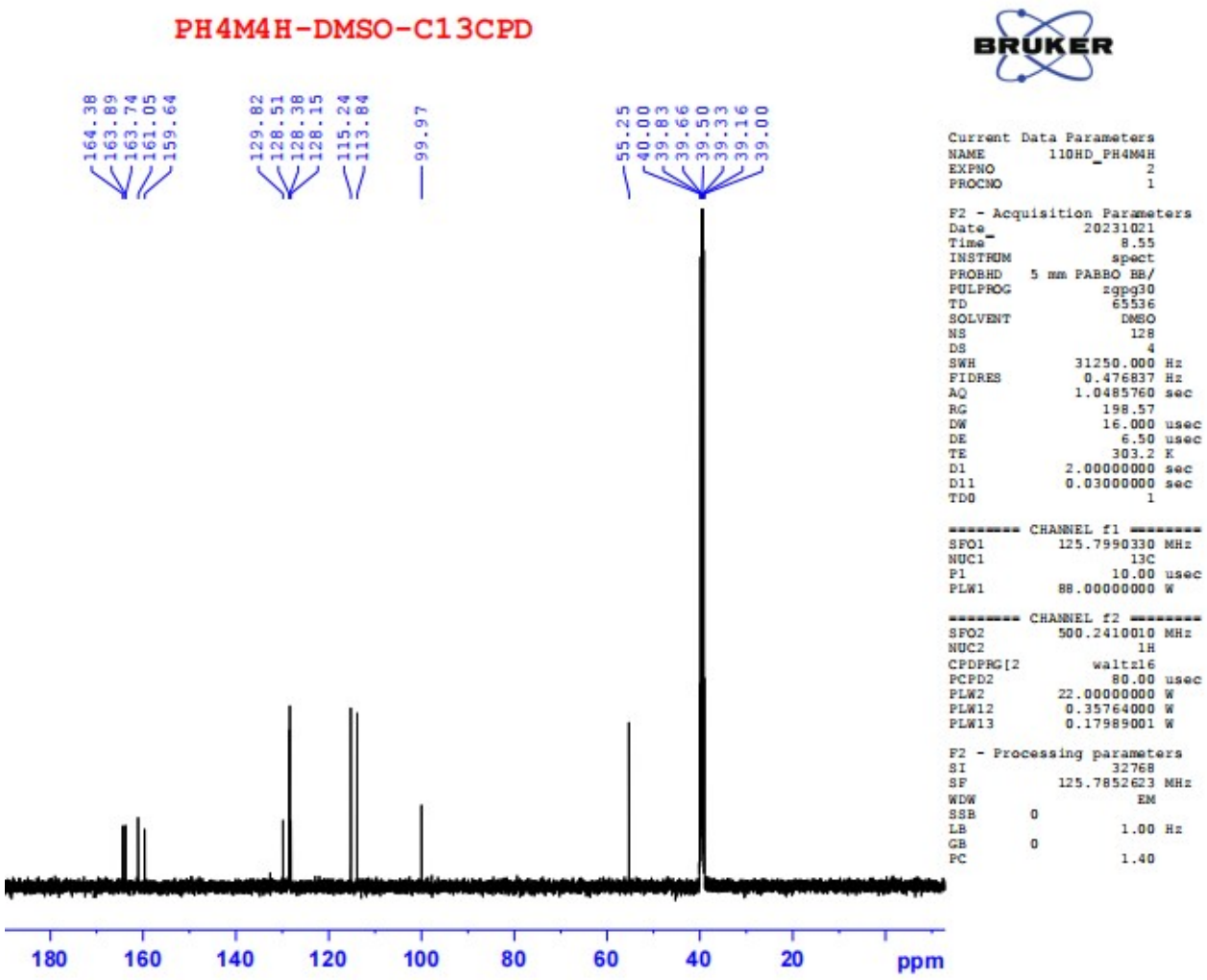


Figure S75. ^{13}C-NMR spectrum of compound **1m**

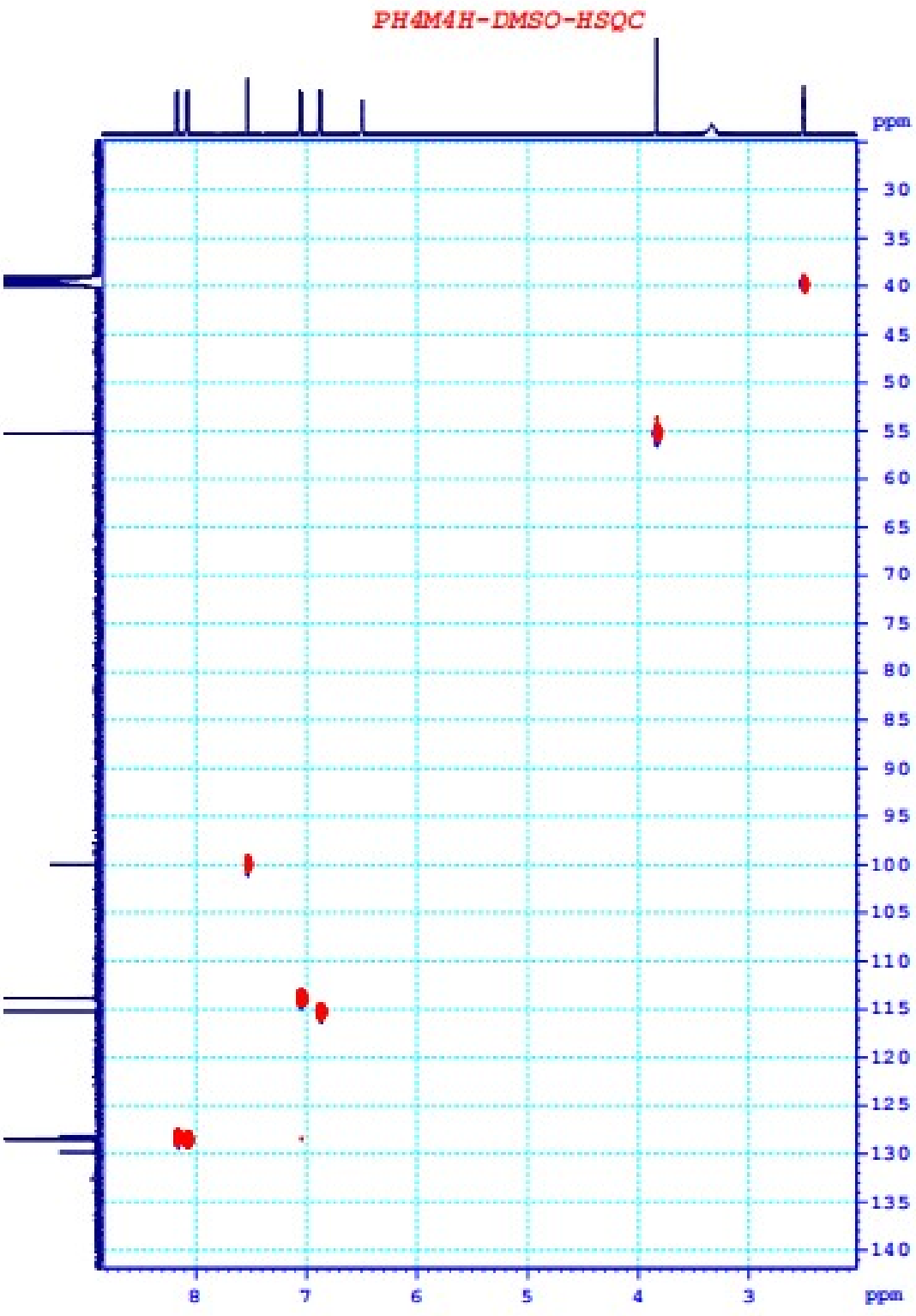


Figure S76. HSQC of compound **1m**

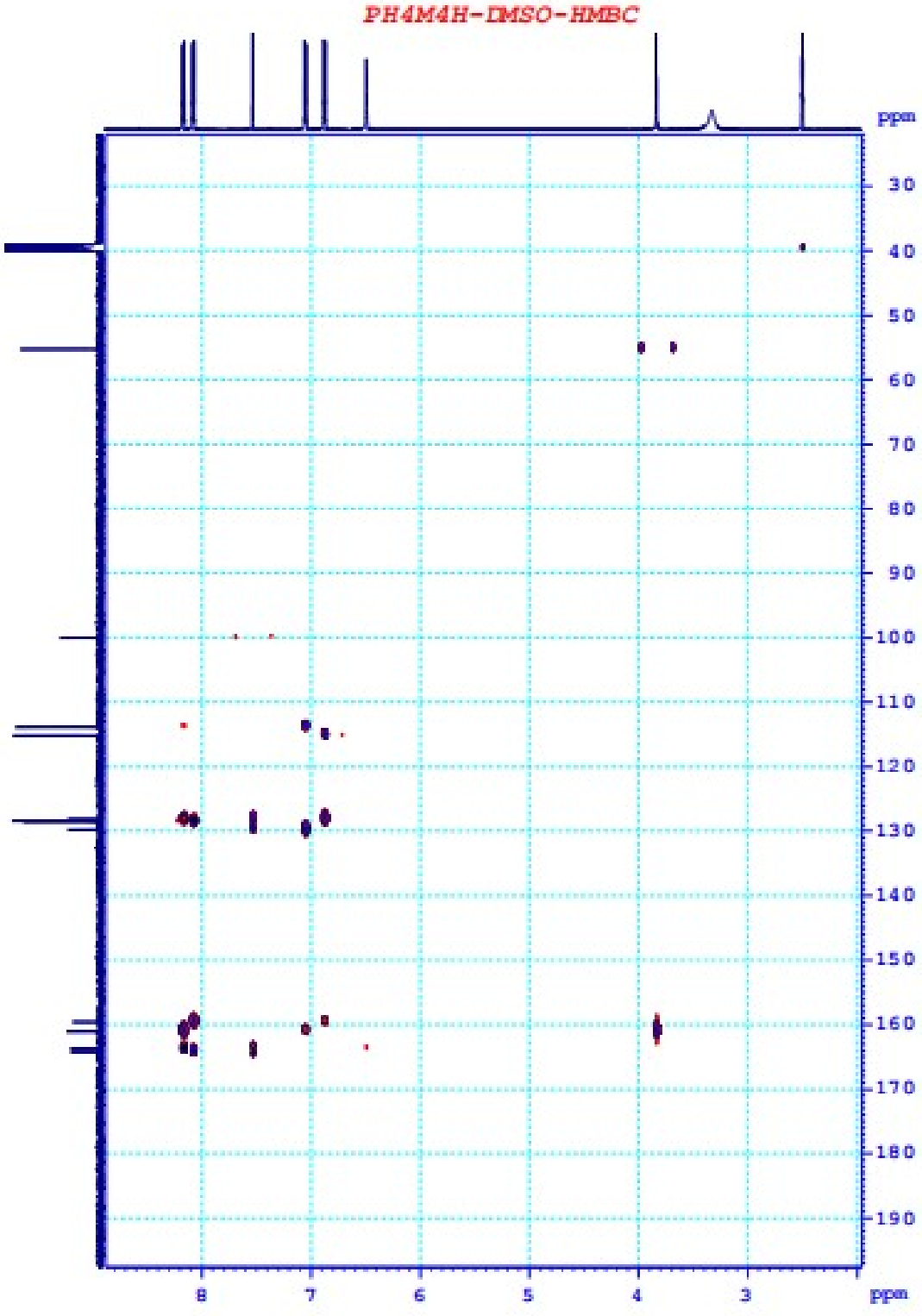


Figure S77. HMBC of compound **1m**

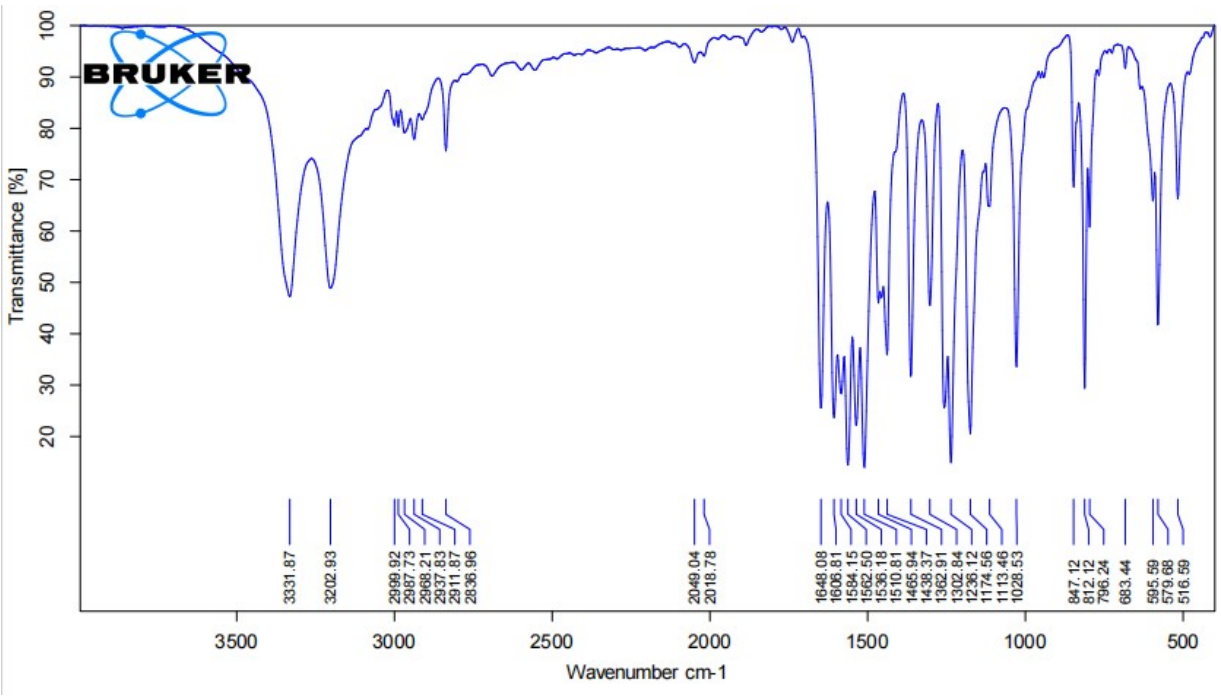


Figure S78. FTIR spectrum of compound **1n**

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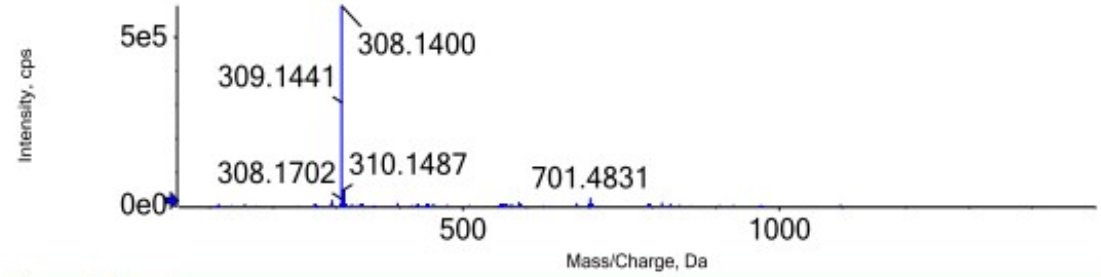
Injection details

Sample name	PH4M4M	*Vial position*	31
Sample file name	SER. wiff2- HUY	*Inject volume*	2.00
Acquisition date	19/01/2024 10:18:55 AM	*Acquisition method*	**ESI _POS_SCAN**
Operator	CB21261708	*Instrument name*	X500$_R$ QTOF

Full mass spectrum

Spectrum from HUY_PH4M4M_(+)ESI 2024-01-19-10-18-55...e multiplier = 1.5), Gaussian smoothed (0.5 points)



Expanded spectrum

Spectrum from HUY_PH4M4M_(+)ESI 2024-01-19-10-18-55...e multiplier = 1.5), Gaussian smoothed (0.5 points)

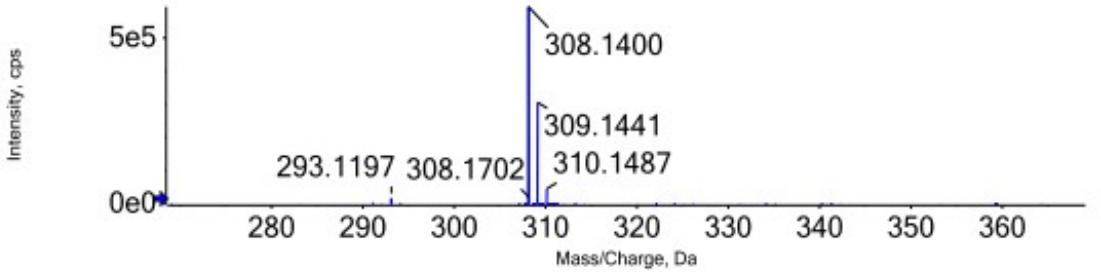


Figure S79. HRMS spectrum of compound **1n**

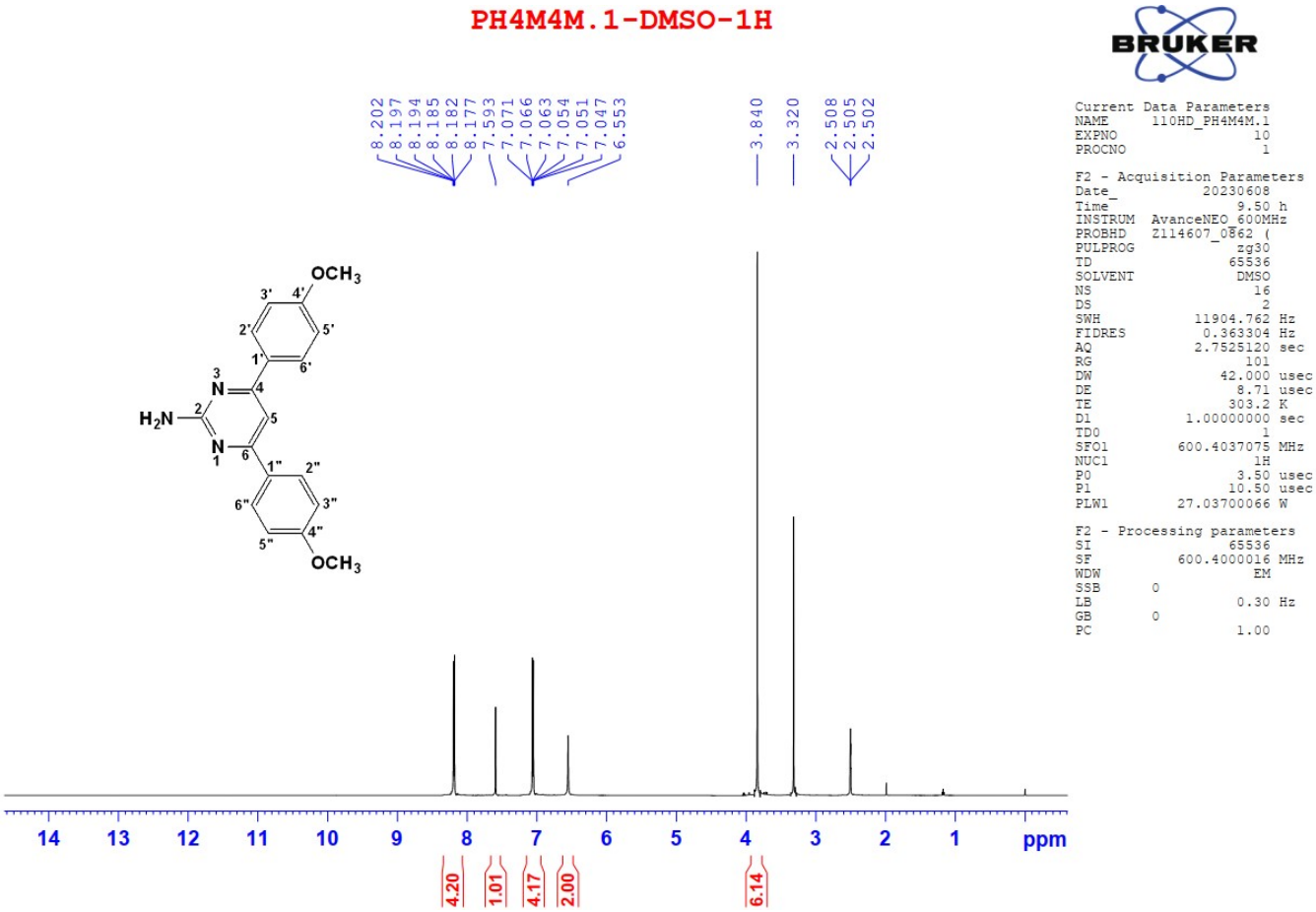


Figure S80. ^{1}H-NMR spectrum of compound **1n**

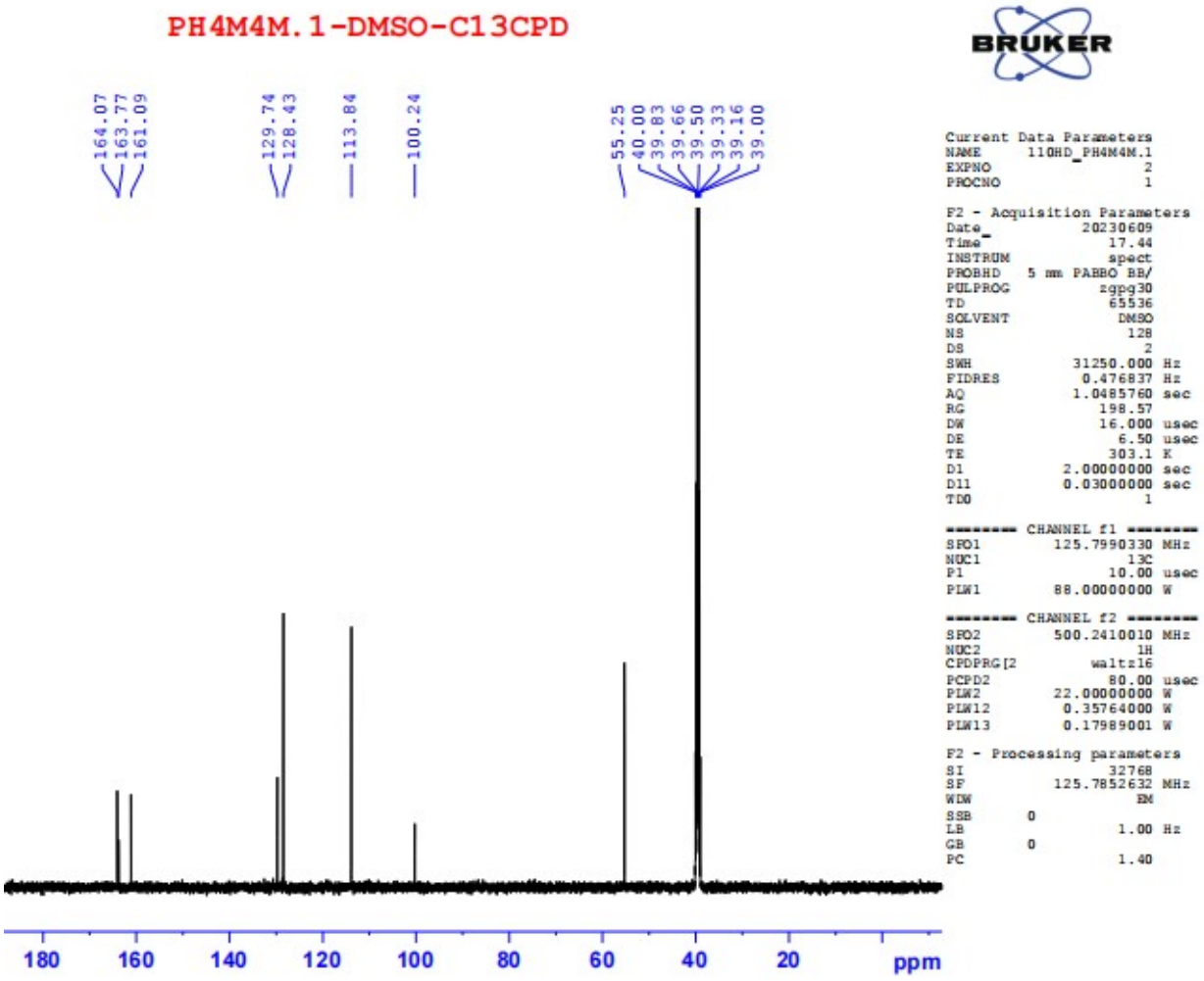


Figure S81. ^{13}C-NMR spectrum of compound **1n**

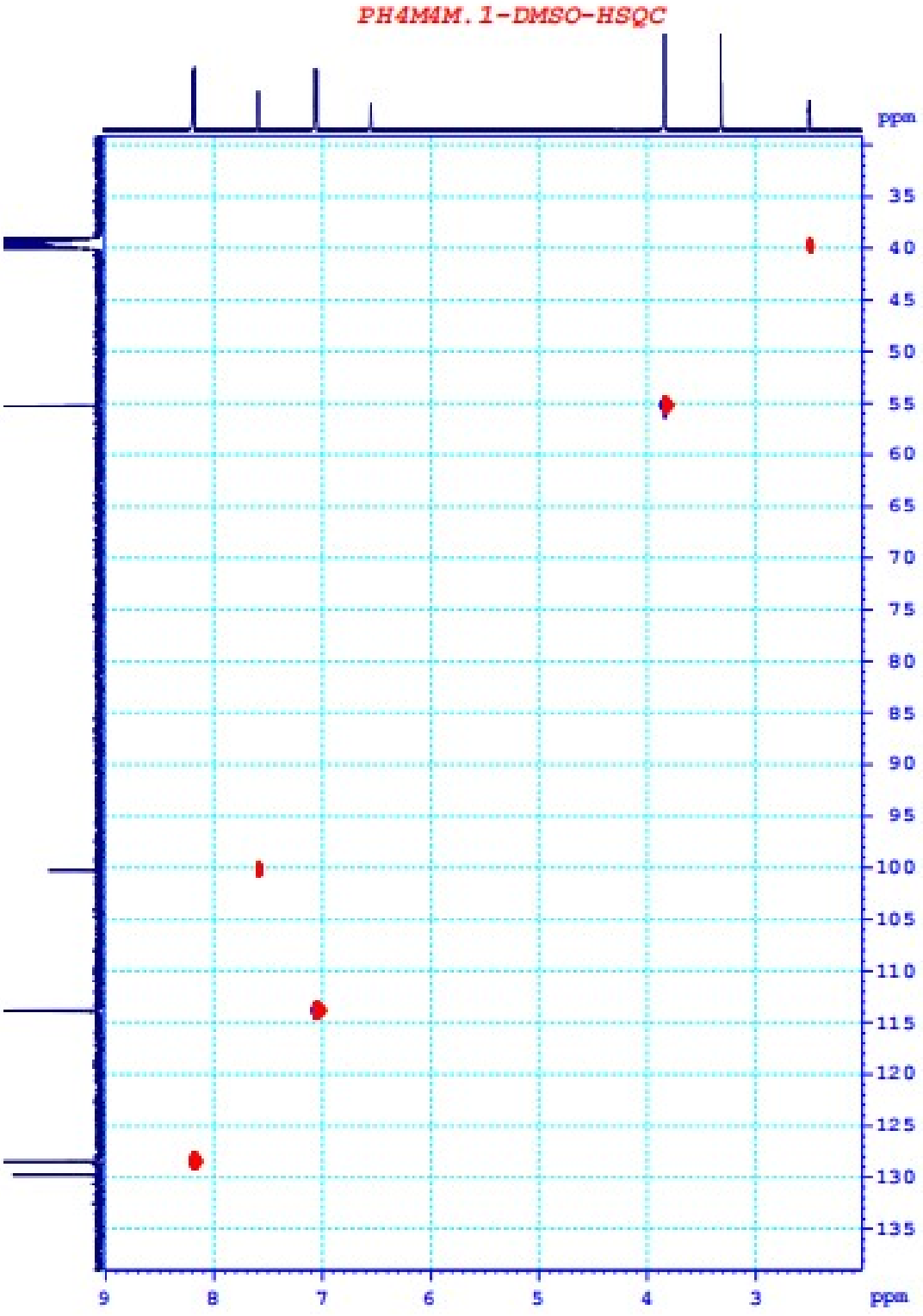


Figure S82. HSQC of compound **1n**

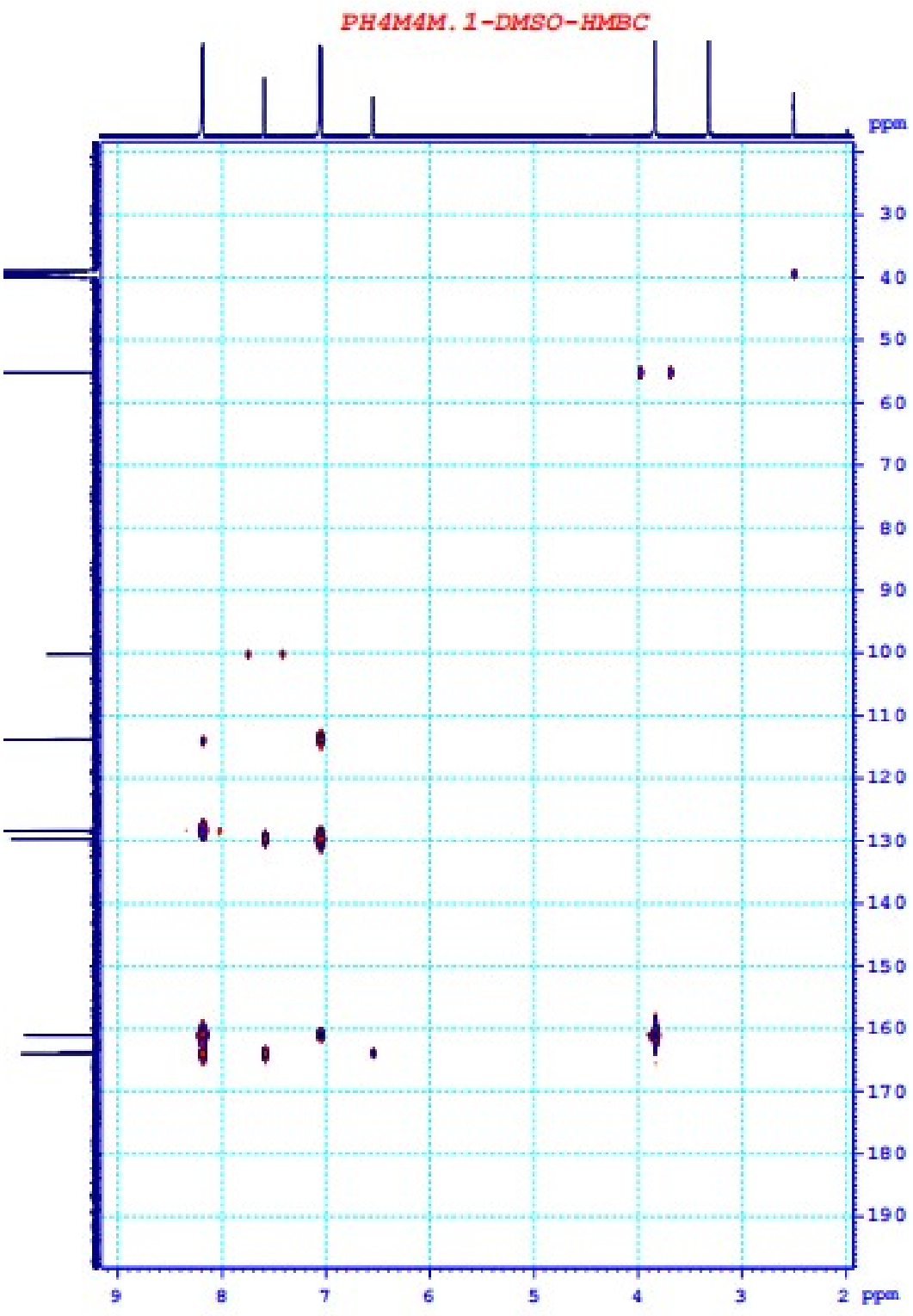


Figure S83. HMBC of compound **1n**

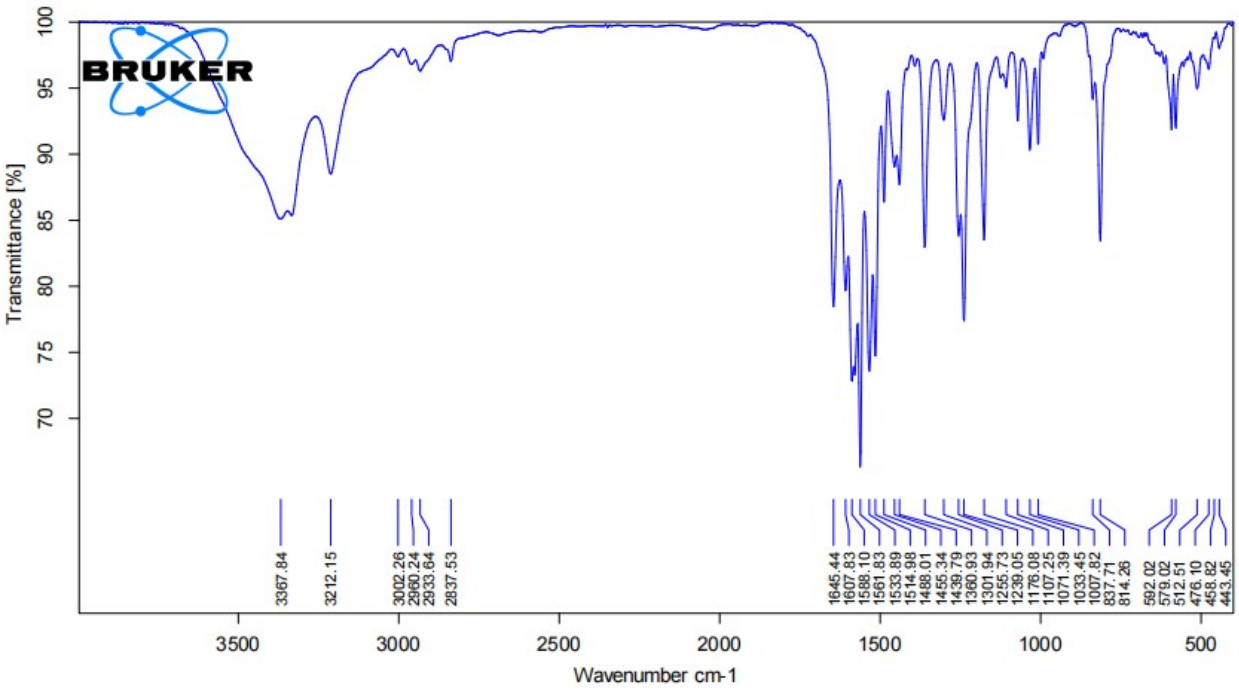


Figure S84. FTIR spectrum of compound **1o**

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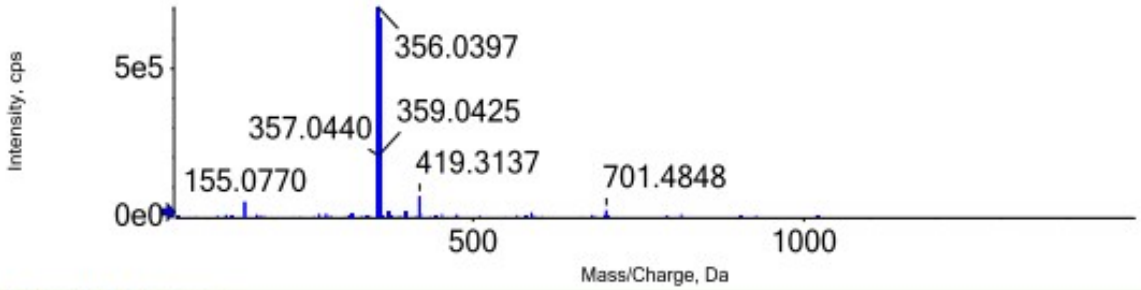
ANALYSIS REPORT

Injection details

Sample name	PH4MBr	*Vial position*	33
Sample file name	SER. wiff2- HUY	*Inject volume*	2.00
Acquisition date	19/01/2024 10:22:46 AM	*Acquisition method*	**ESI _POS_SCAN**
Operator	CB21261708	*Instrument name*	X500$_R$ QTOF

Full mass spectrum

Spectrum from HUY_PH4MBr_(+)ESI 2024-01-19-10-22-46....e multiplier = 1.5), Gaussian smoothed (0.5 points)



Expanded spectrum

Spectrum from HUY_PH4MBr_(+)ESI 2024-01-19-10-22-46....e multiplier = 1.5), Gaussian smoothed (0.5 points)

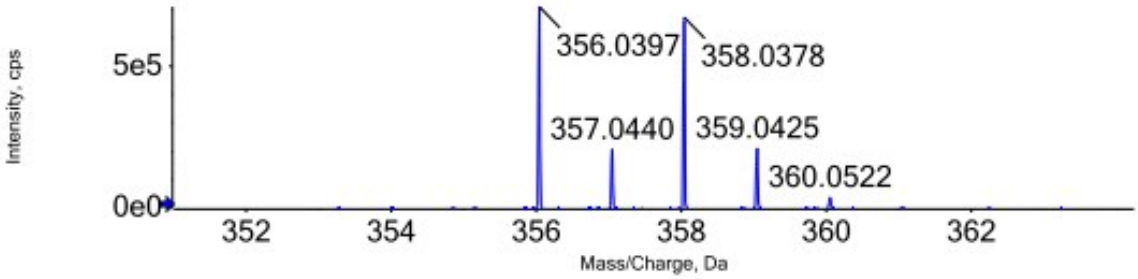


Figure S85. HRMS spectrum of compound **1o**

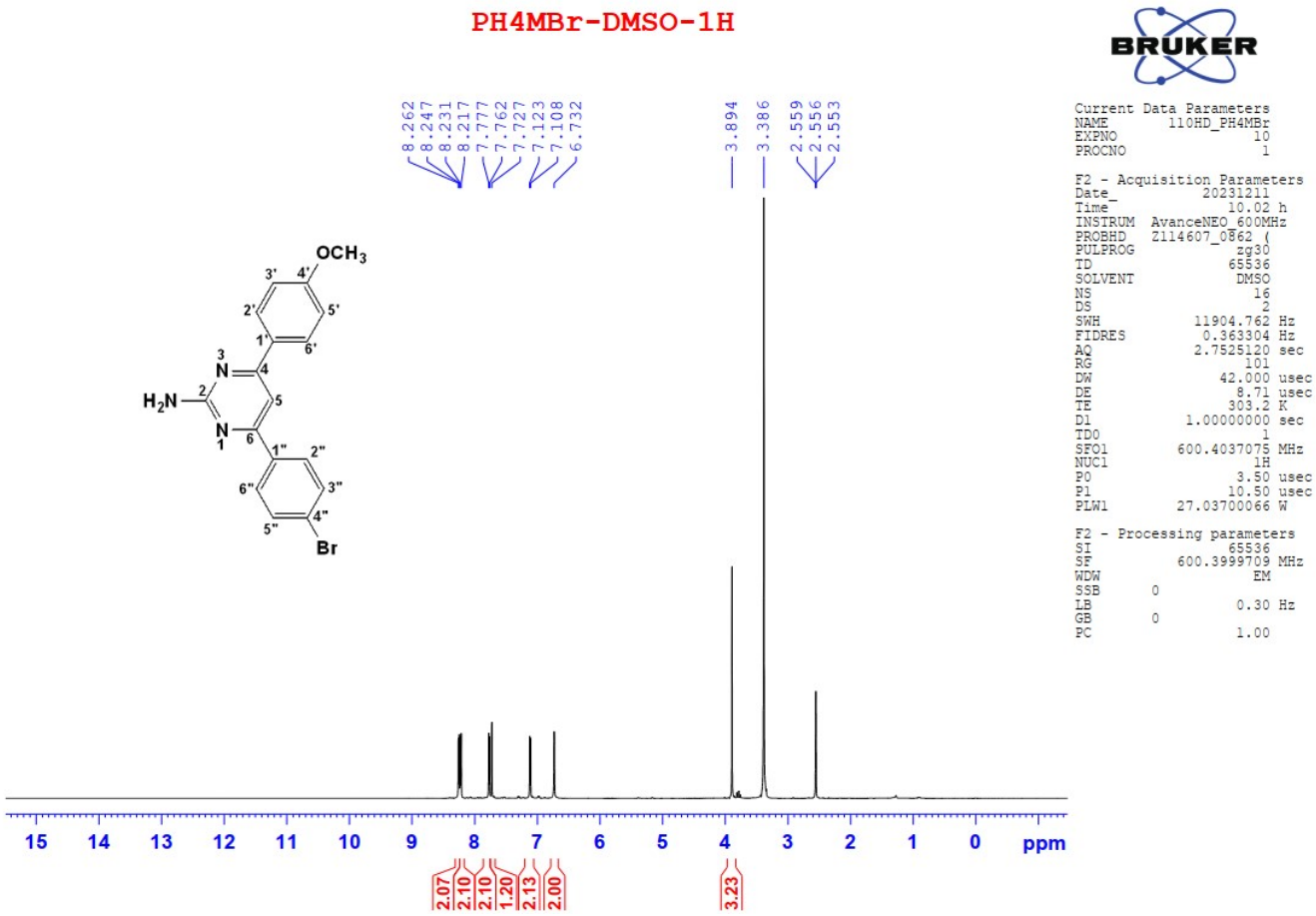


Figure S86. ^{1}H-NMR spectrum of compound **1o**

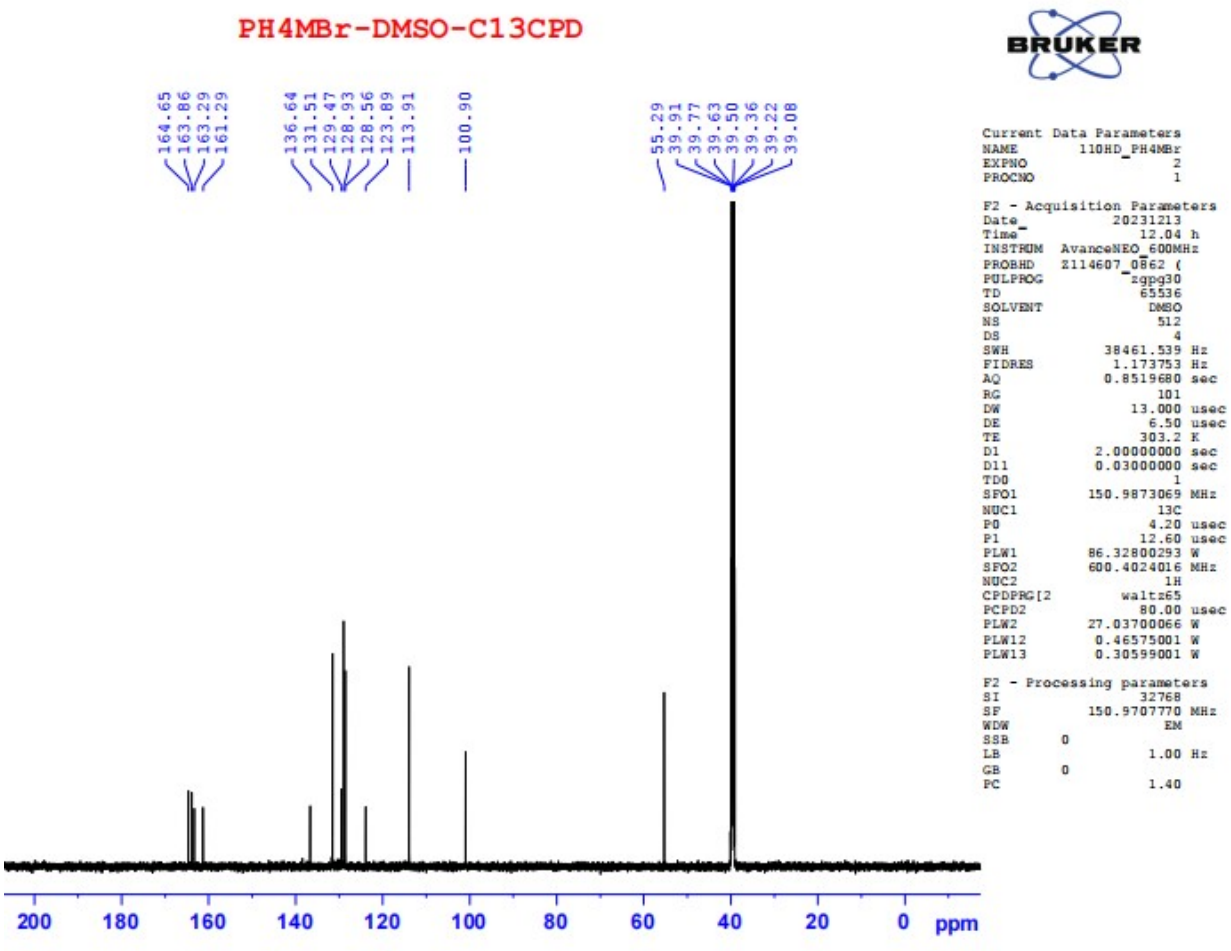


Figure S87. ^{13}C-NMR spectrum of compound **1o**

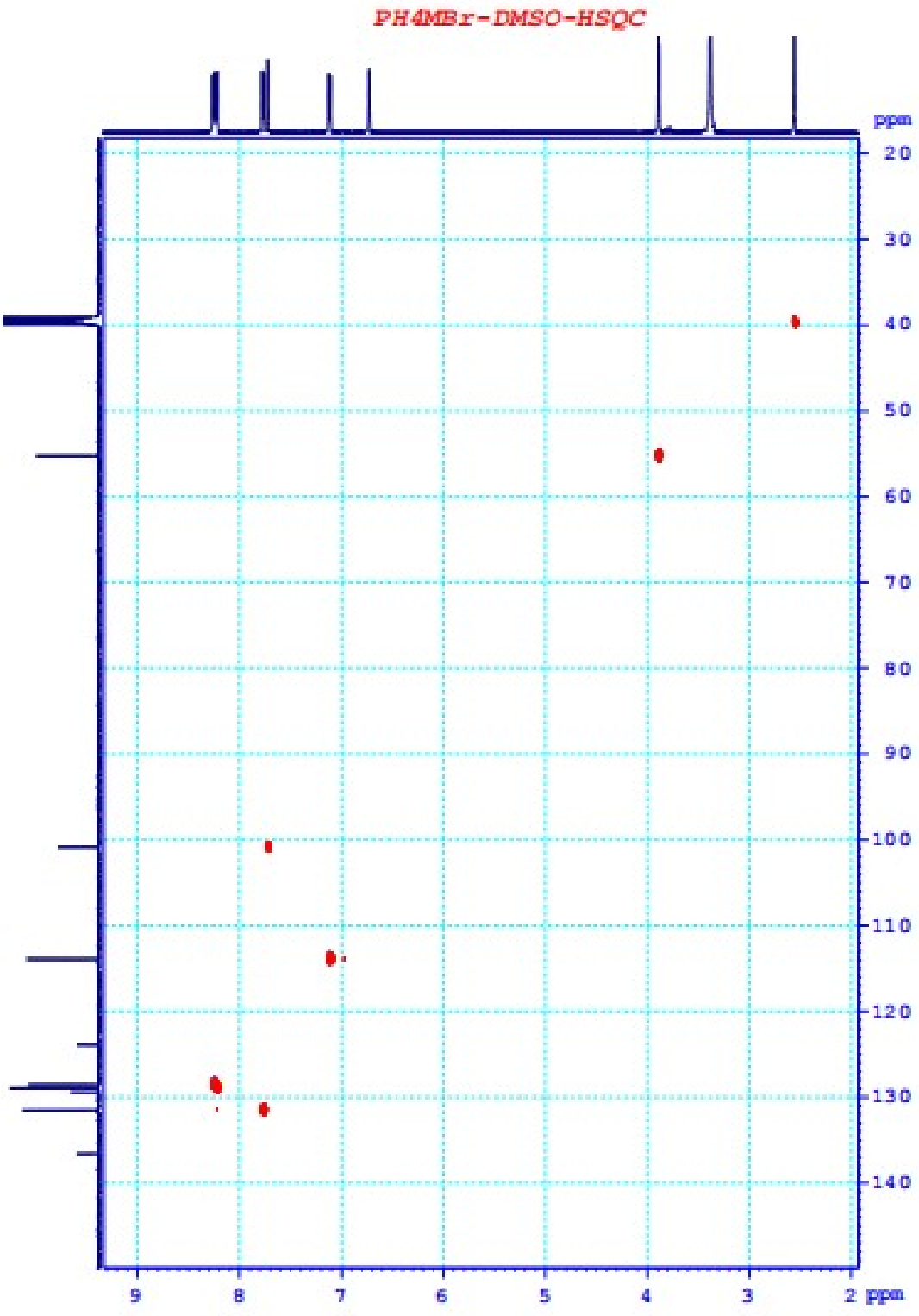


Figure S88. HSQC of compound **1o**

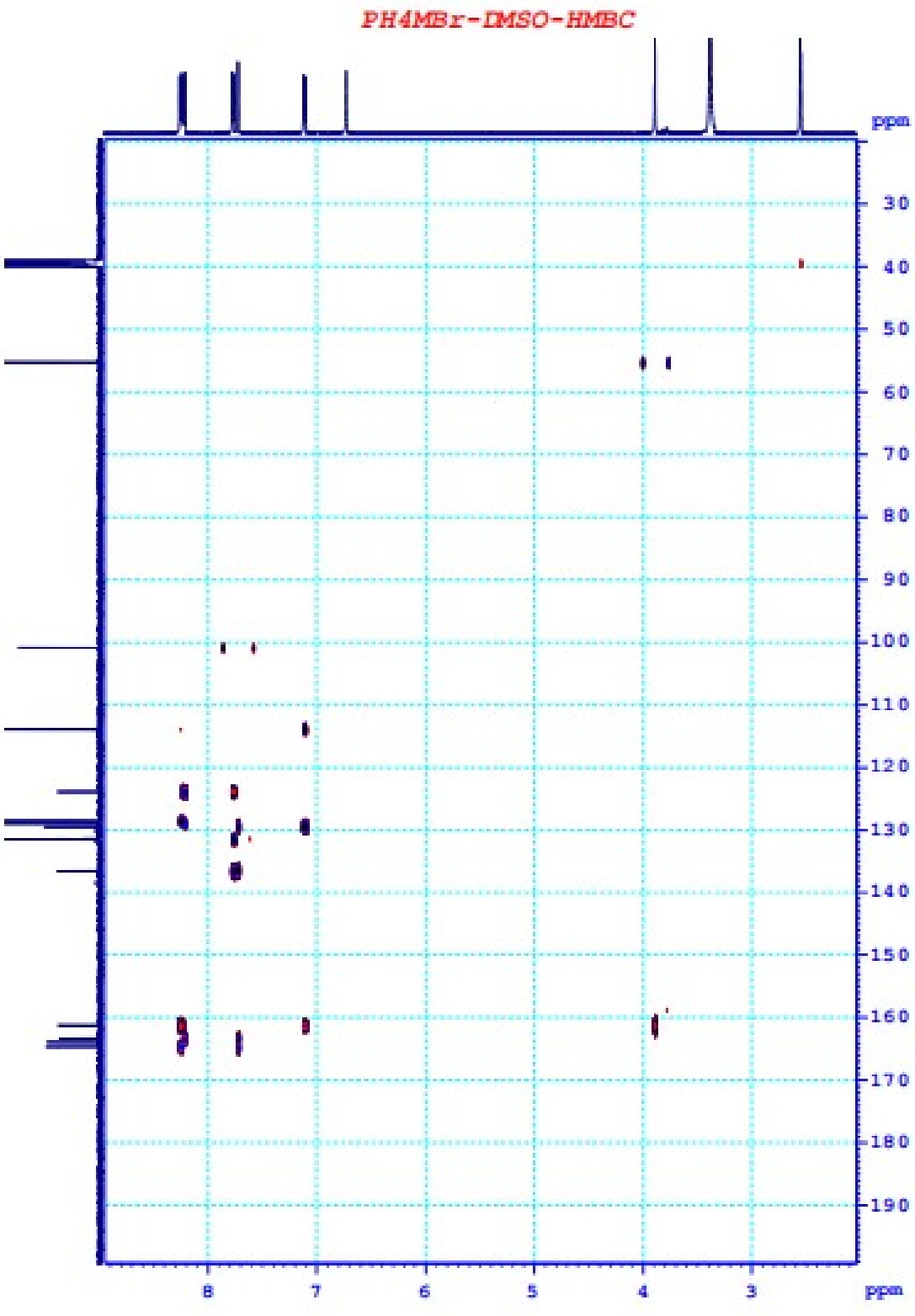


Figure S89. HMBC of compound **1o**

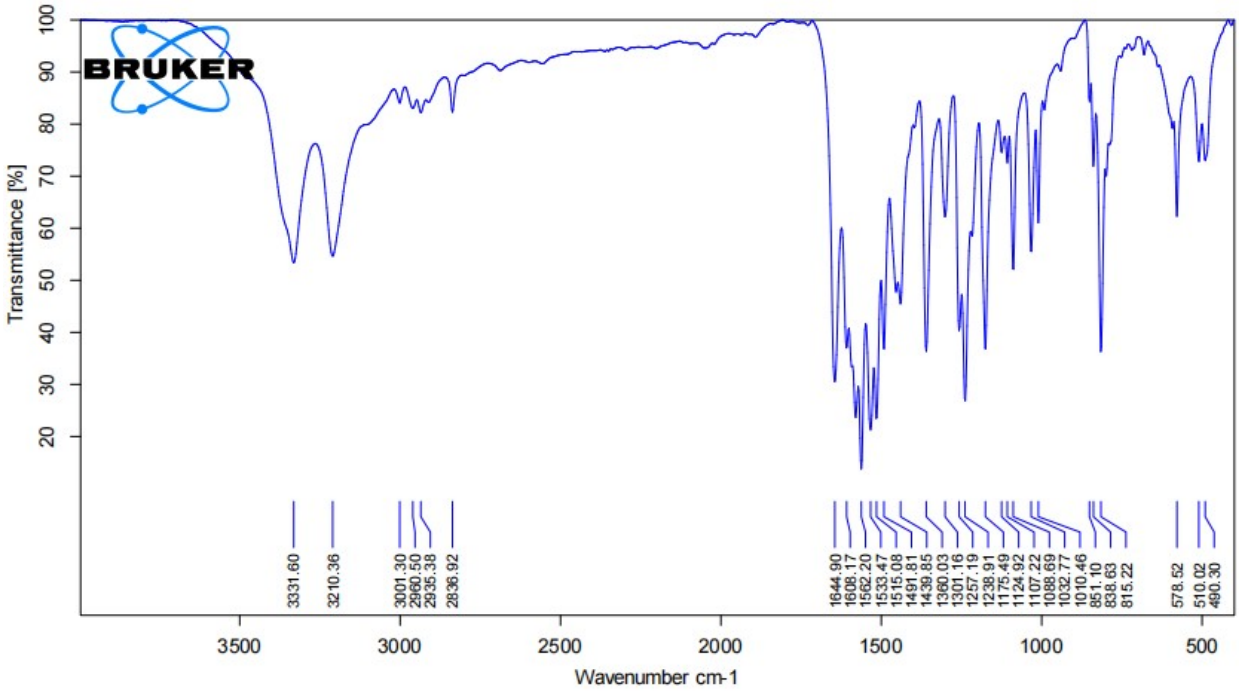


Figure S90. FTIR spectrum of compound **1p**

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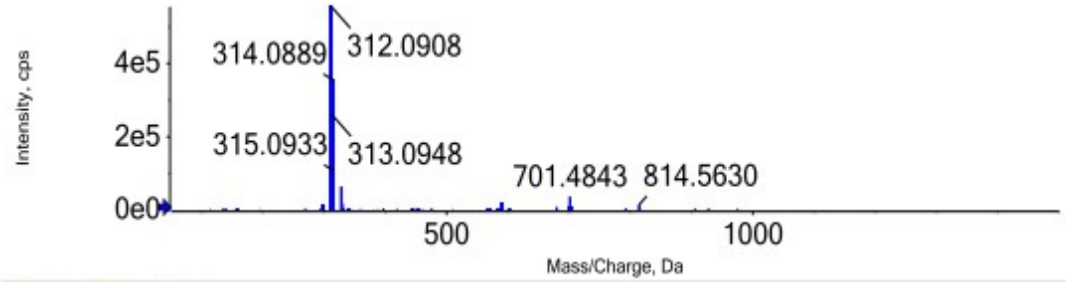
Injection details

Sample name	PH4MCl	*Vial position*	34
Sample file name	SER. wiff2- HUY	*Inject volume*	2.00
Acquisition date	19/01/2024 10:25:01 AM	*Acquisition method*	**ESI _POS_SCAN**
Operator	CB21261708	*Instrument name*	X500$_R$ QTOF

Full mass spectrum

Spectrum from HUY_PH4MCl_(+)ESI 2024-01-19-10-25-01....e multiplier = 1.5), Gaussian smoothed (0.5 points)



Expanded spectrum

Spectrum from HUY_PH4MCl_(+)ESI 2024-01-19-10-25-01....e multiplier = 1.5), Gaussian smoothed (0.5 points)

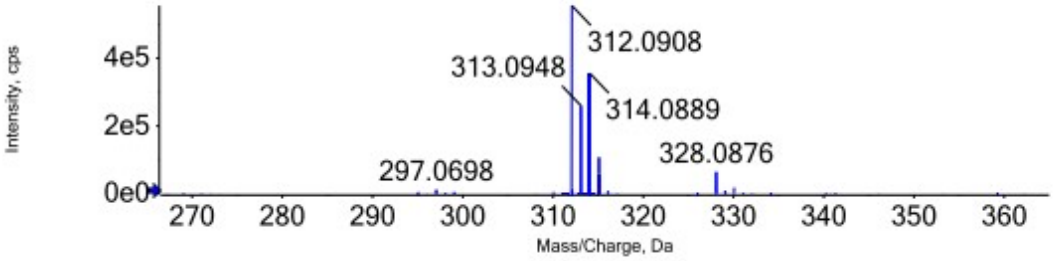


Figure S91. HRMS spectrum of compound **1p**

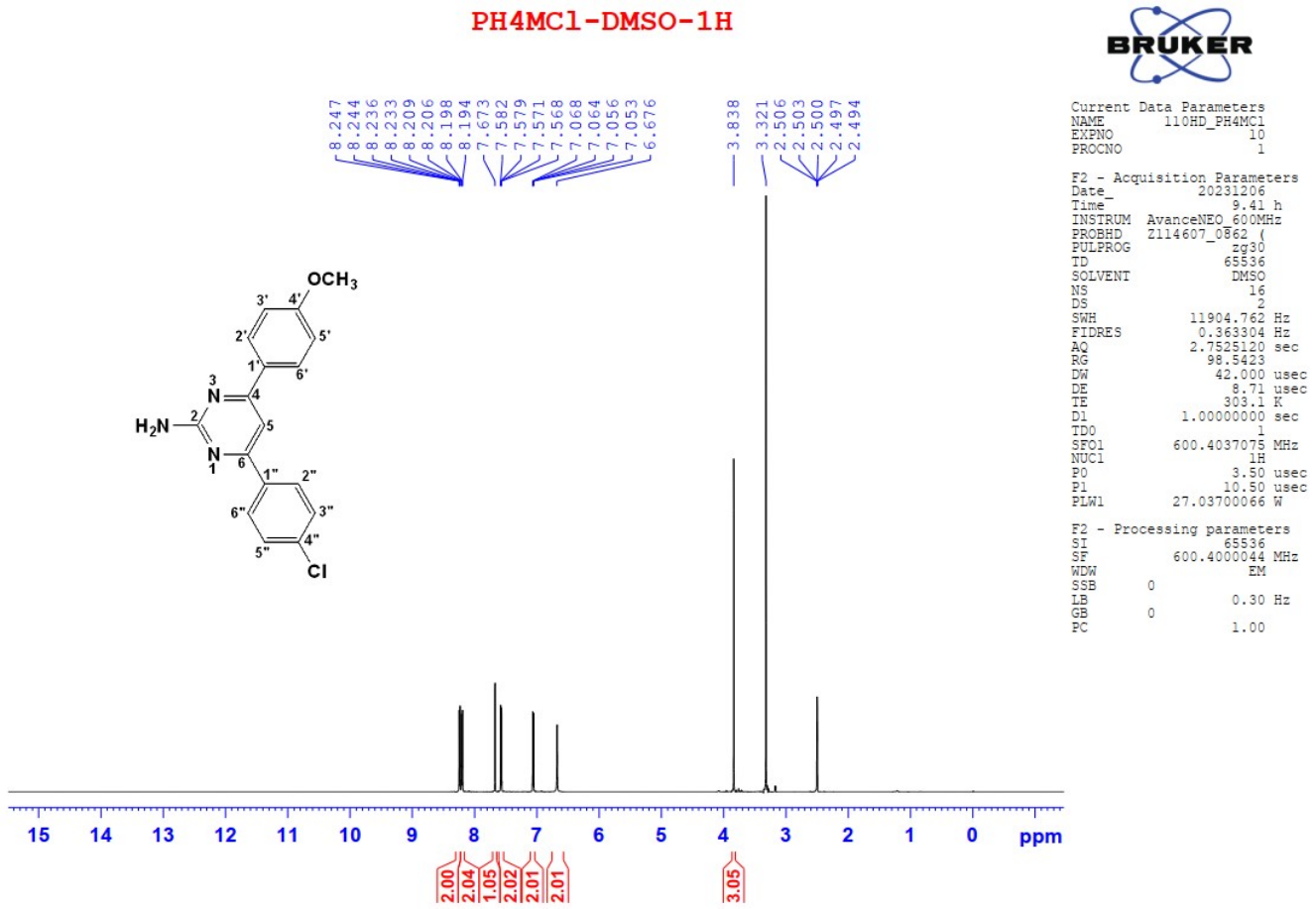


Figure S92. ^{1}H-NMR spectrum of compound **1p**

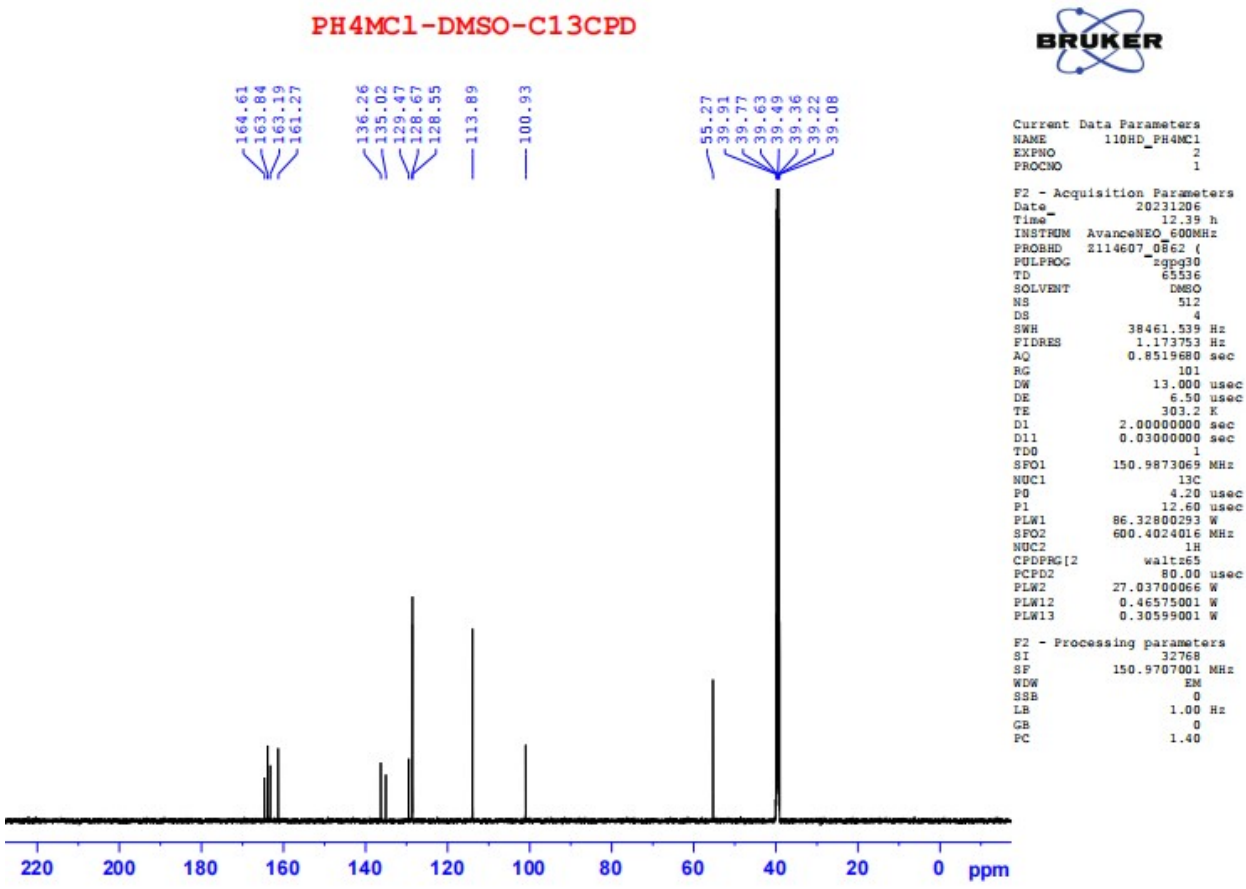


Figure S93. ^{13}C-NMR spectrum of compound **1p**

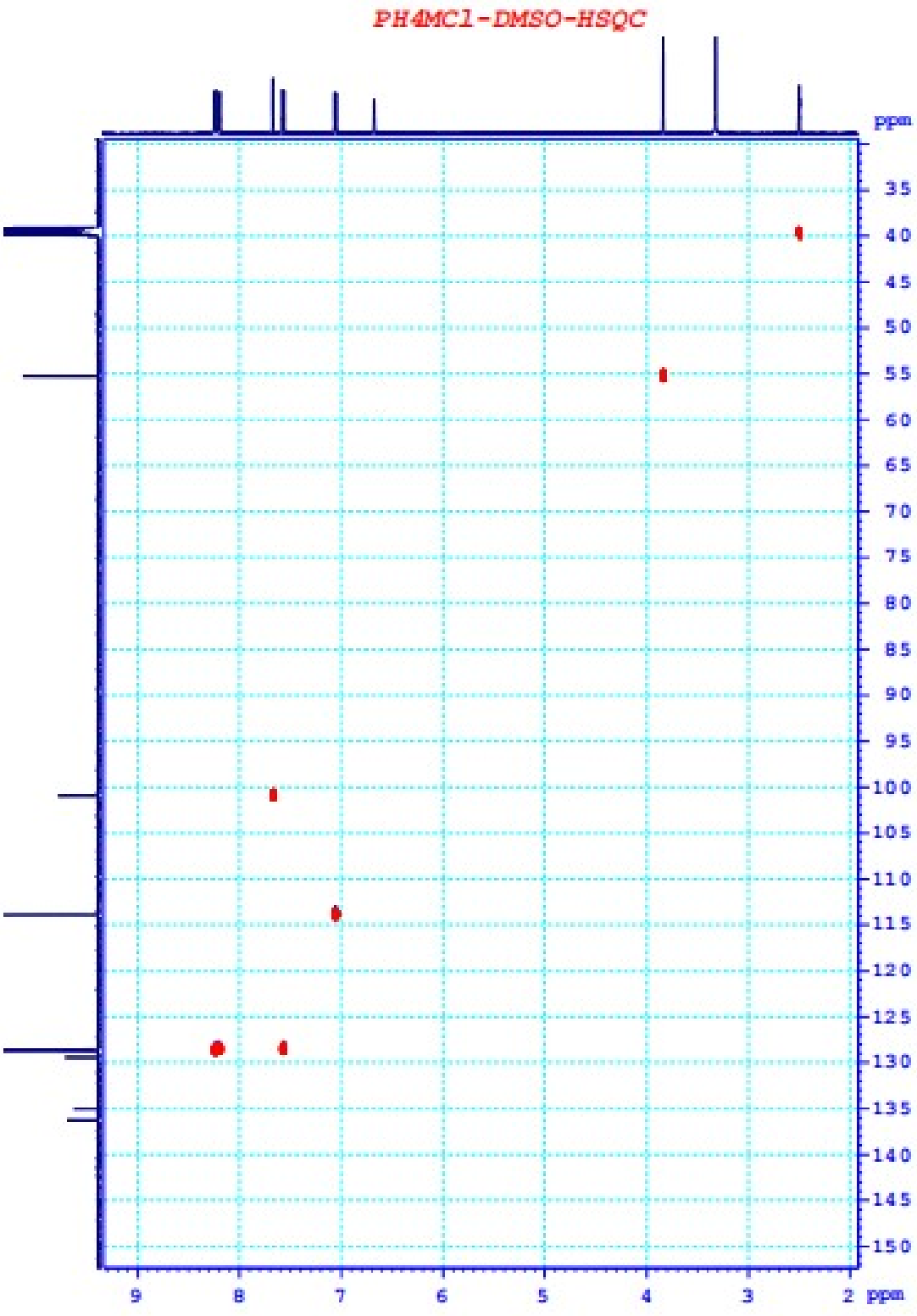


Figure S94. HSQC of compound **1p**

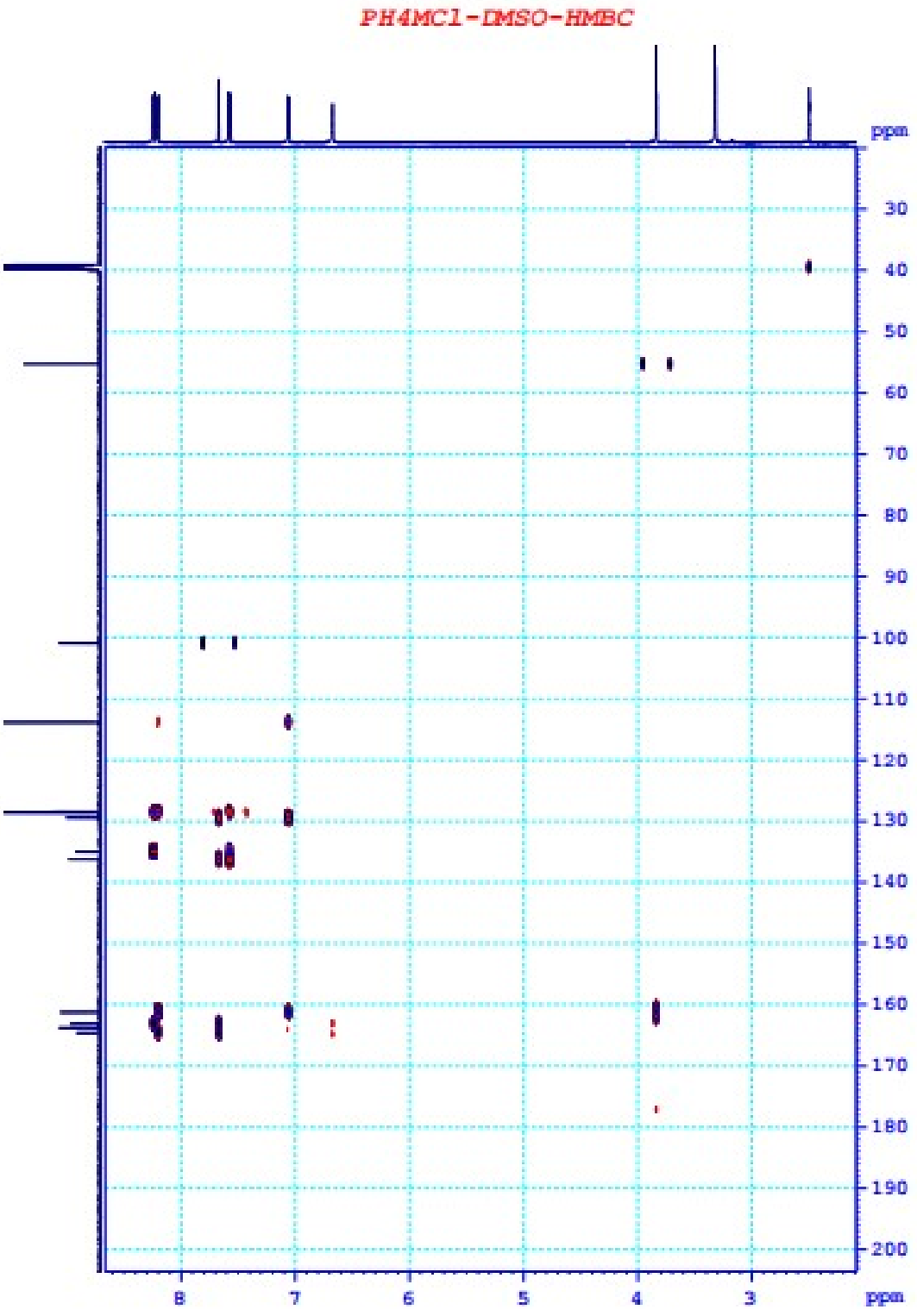


Figure S95. HMBC of compound **1p**

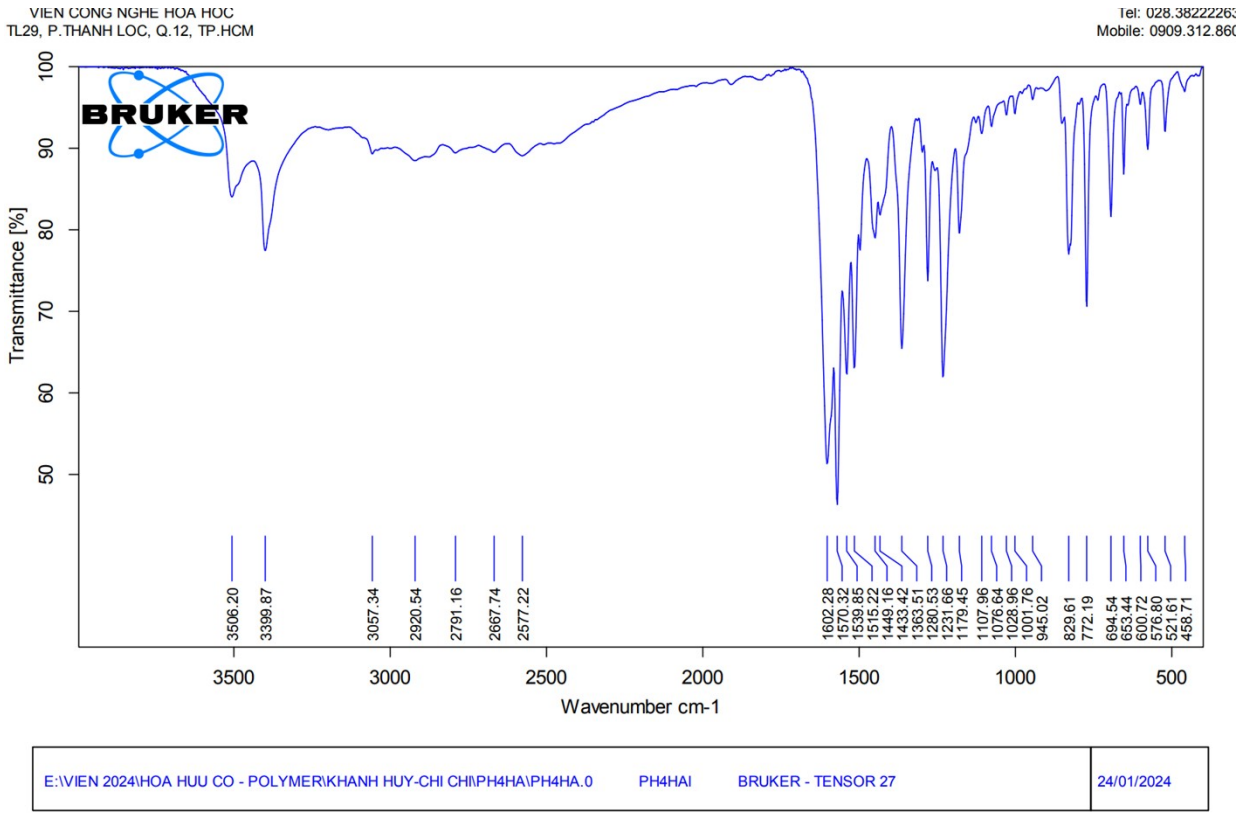


Figure S96. FTIR spectrum of compound **1q**

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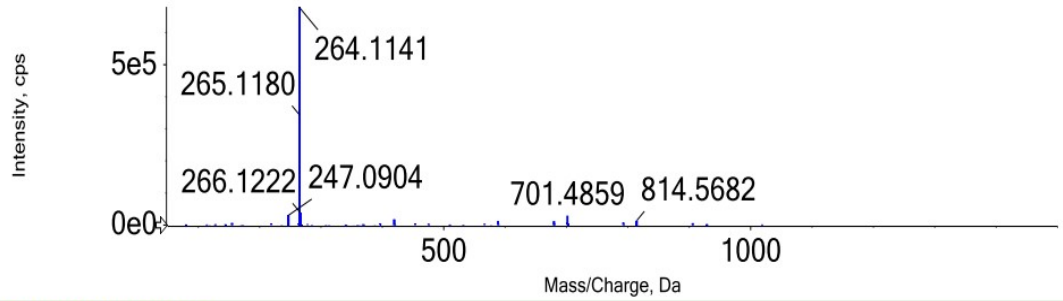
ANALYSIS REPORT

Injection details

Sample name	PH4HA	*Vial position*	29
Sample file name	SER. wiff2- HUY	*Inject volume*	2.00
Acquisition date	19/01/2024 10:15:19 AM	*Acquisition method*	**ESI _POS_SCAN**
Operator	CB21261708	*Instrument name*	$X500_R$ QTOF

Full mass spectrum

Spectrum from HUY_PH4HA_(+)ESI 2024-01-19-10-15-19....e multiplier = 1.5), Gaussian smoothed (0.5 points)



Expanded spectrum

Spectrum from HUY_PH4HA_(+)ESI 2024-01-19-10-15-19....e multiplier = 1.5), Gaussian smoothed (0.5 points)

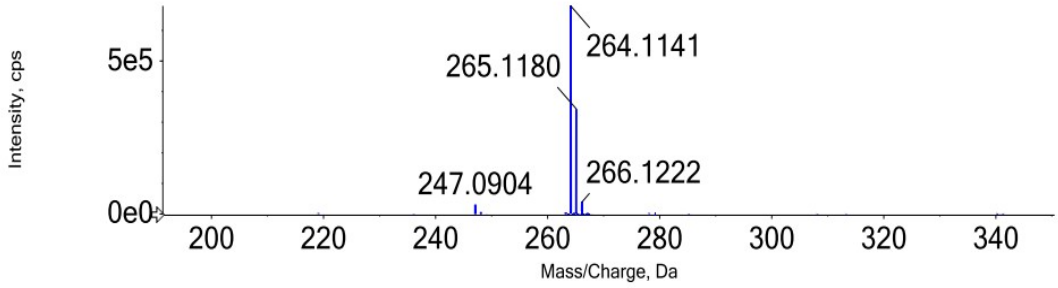


Figure S97. HRMS spectrum of compound **1q**

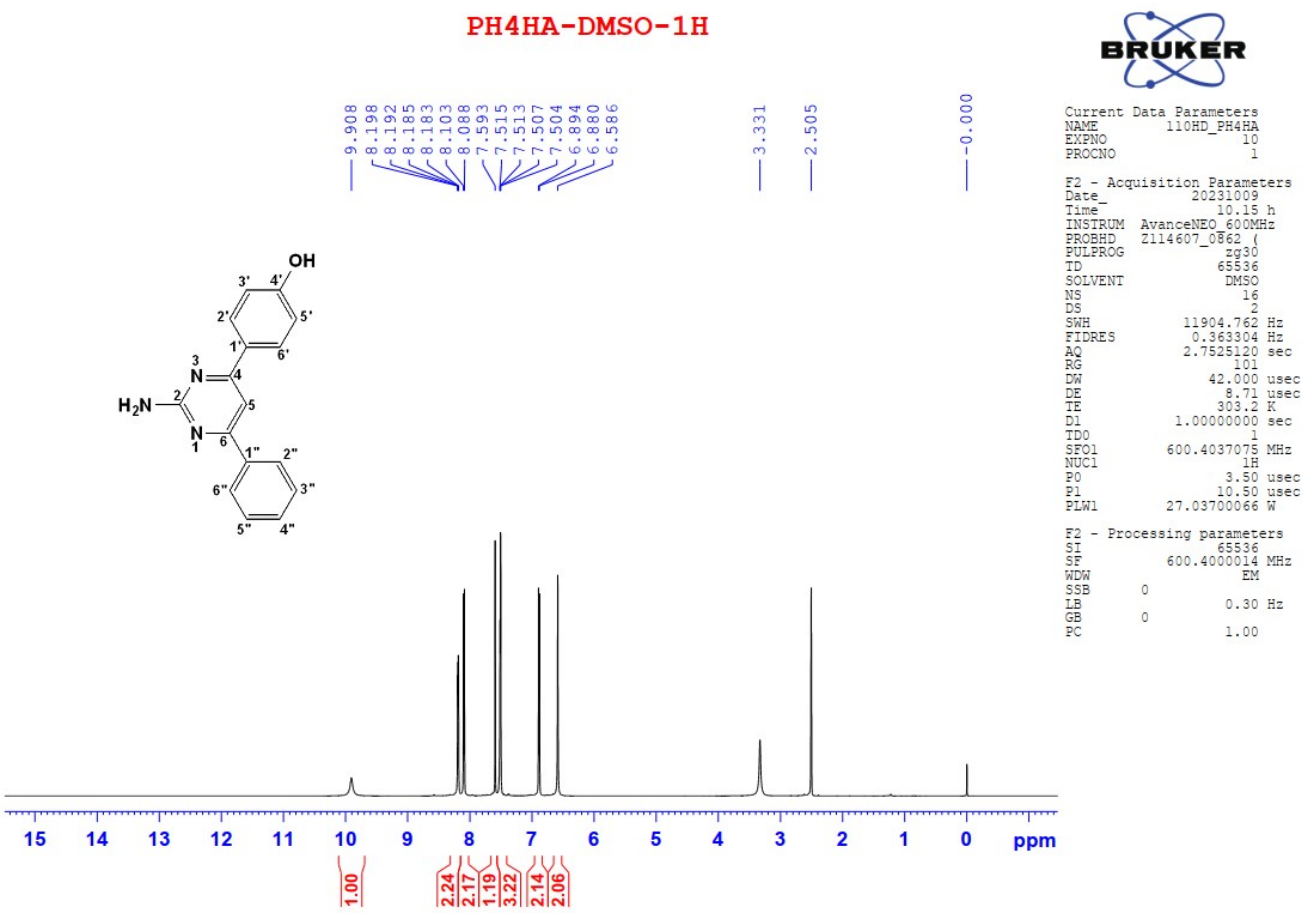


Figure S98. ^{1}H-NMR spectrum of compound **1q**

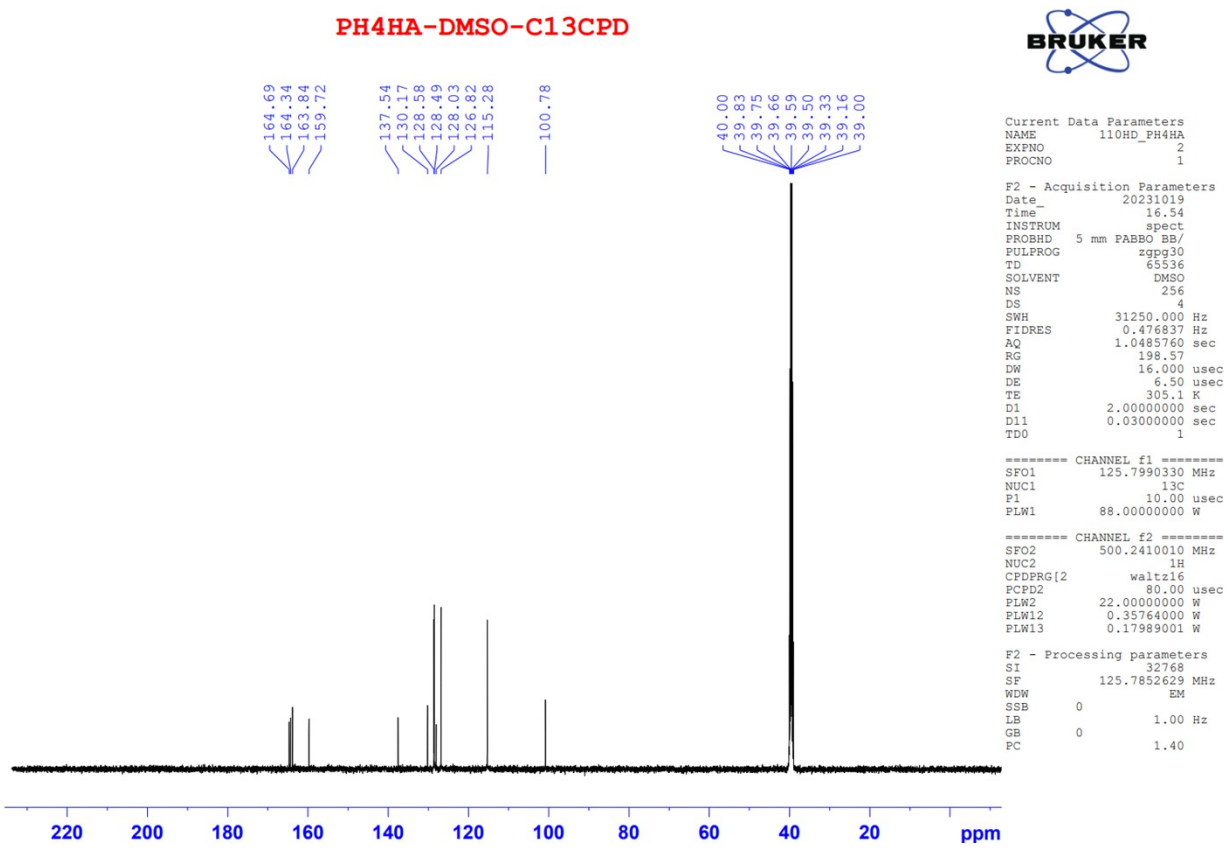


Figure S99. ^{13}C-NMR spectrum of compound **1q**

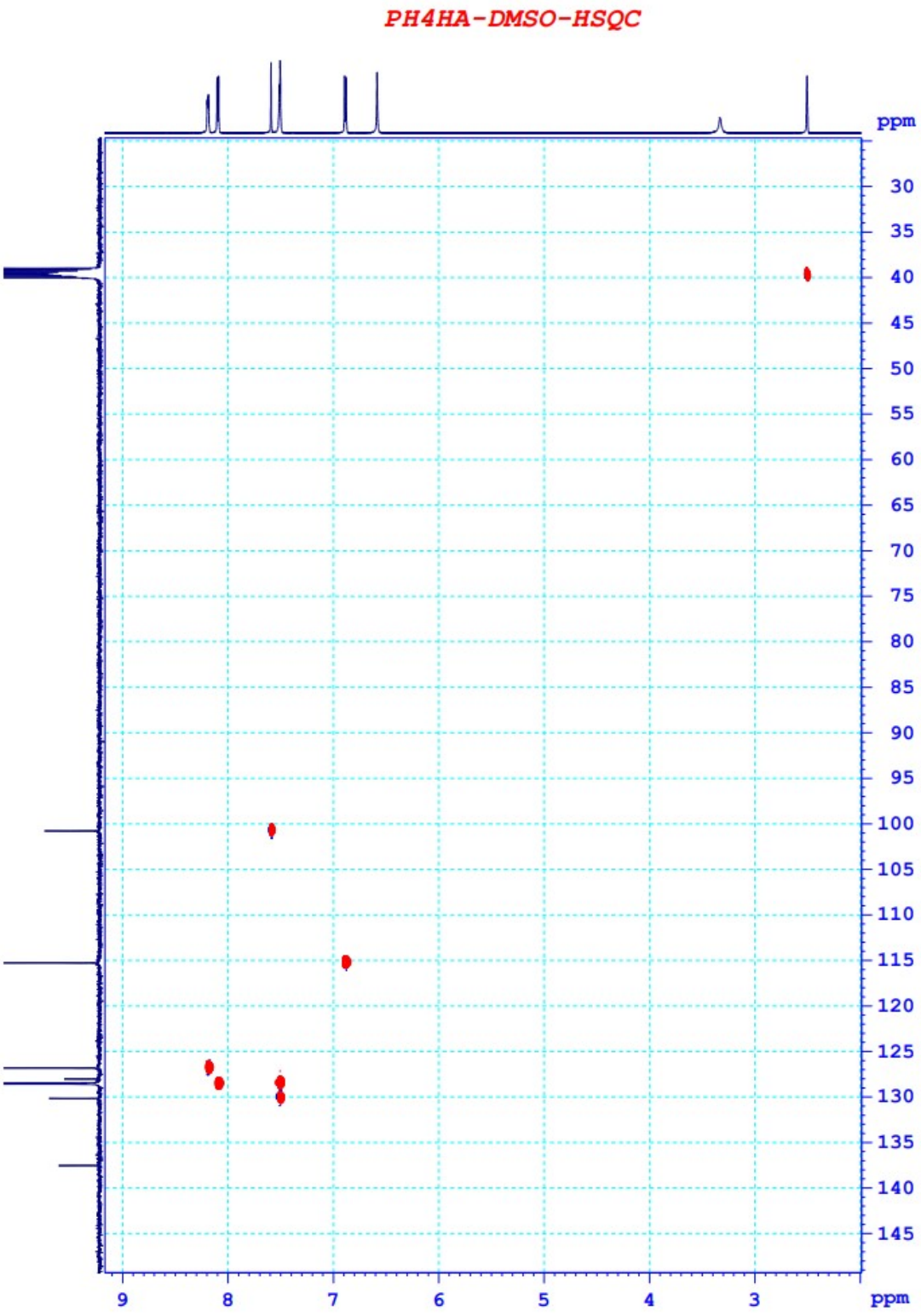


Figure S100. HSQC of compound **1q**

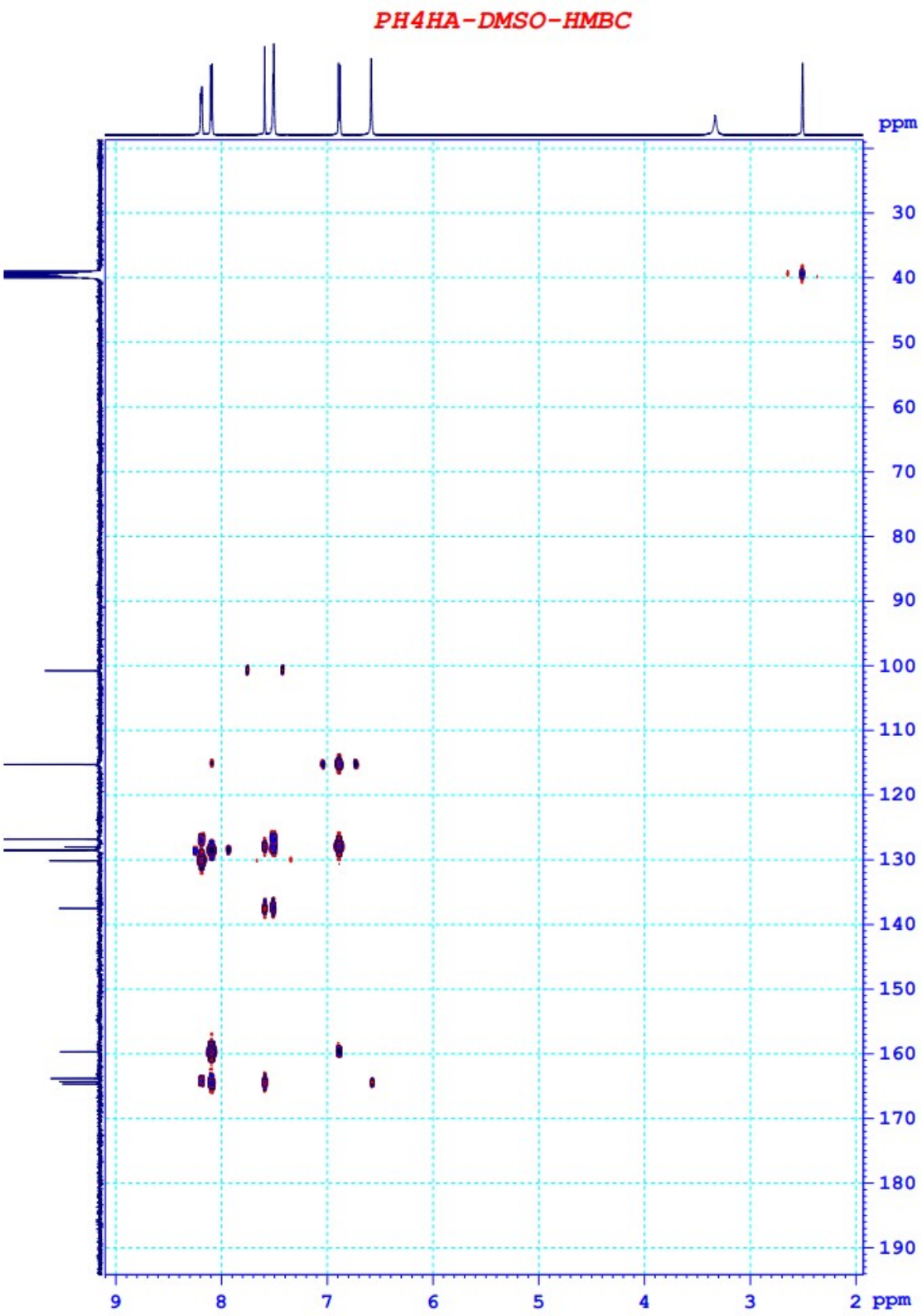


Figure S101. HMBC of compound **1q**

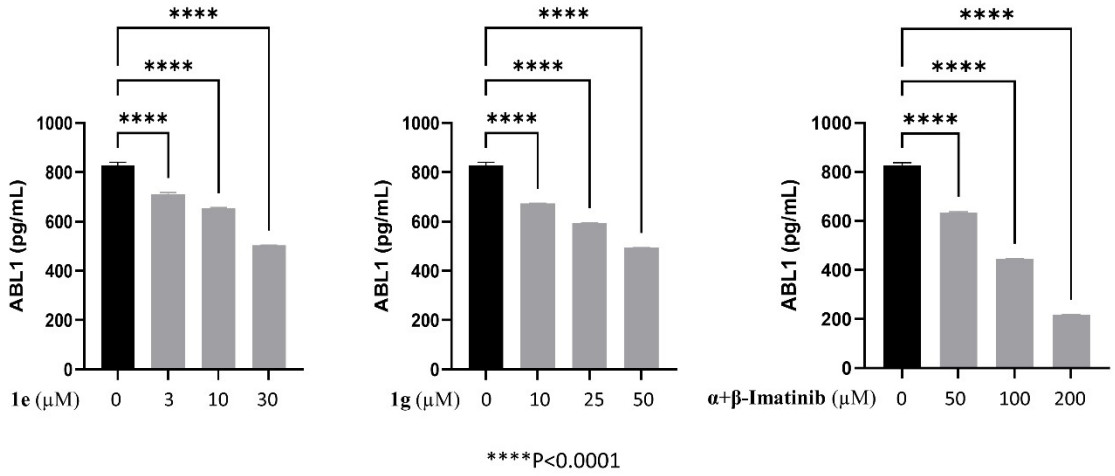
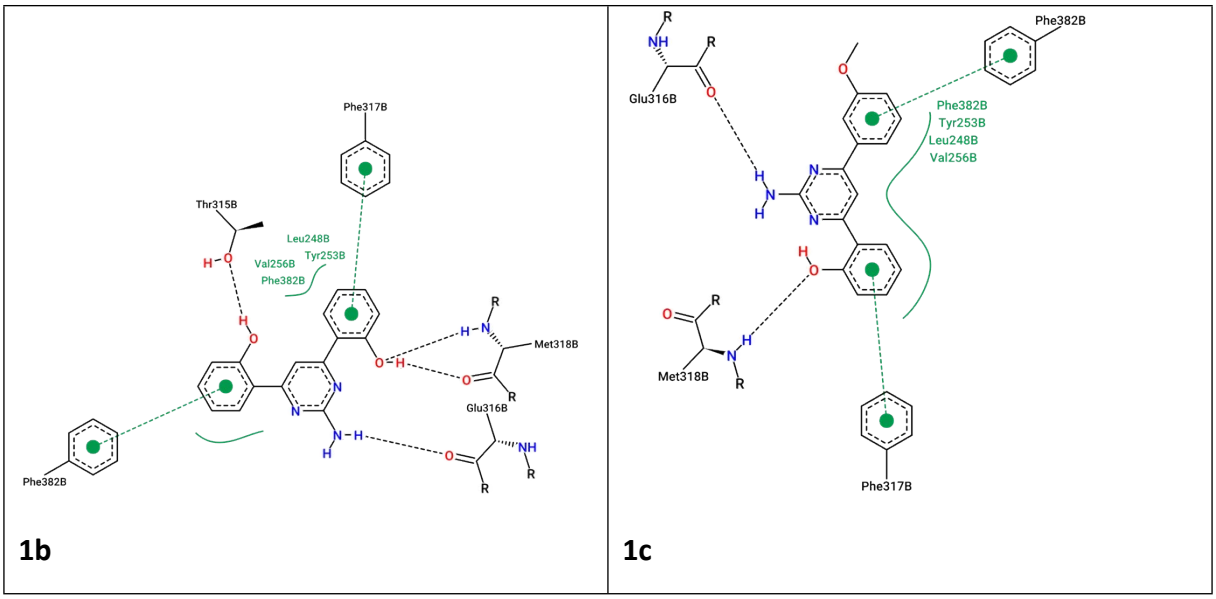
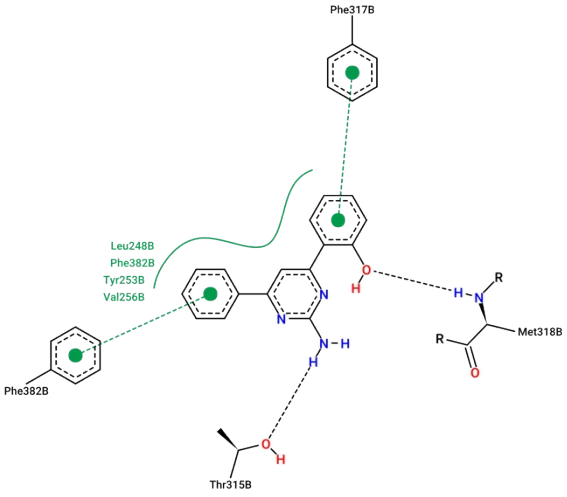
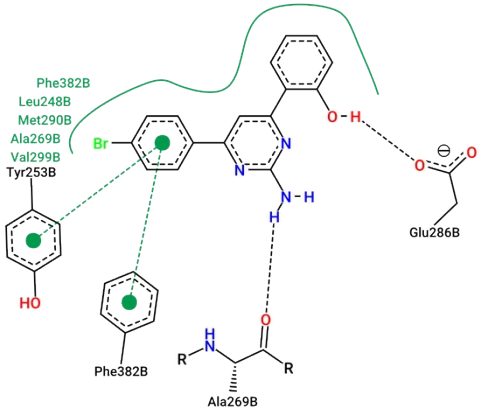


Figure S102. ABL1 tyrosine kinase inhibitory activity of compounds **1e**, **1g** and Imatinib

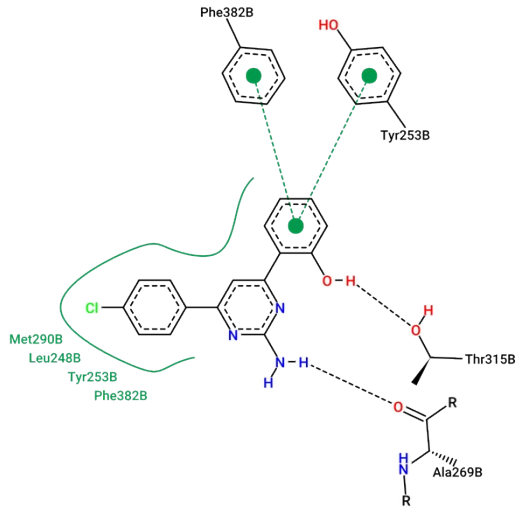



Phe317B
Leu248B
Phe382B
Tyr253B
Val256B
Met318B
Thr315B
Phe382B

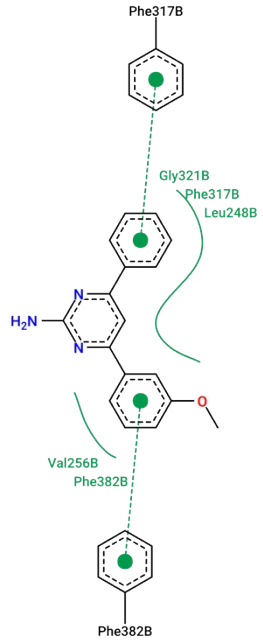
1a


Phe382B
Leu248B
Met290B
Ala269B
Val299B
Tyr253B
Br
Glu286B
HO
Phe382B
Ala269B

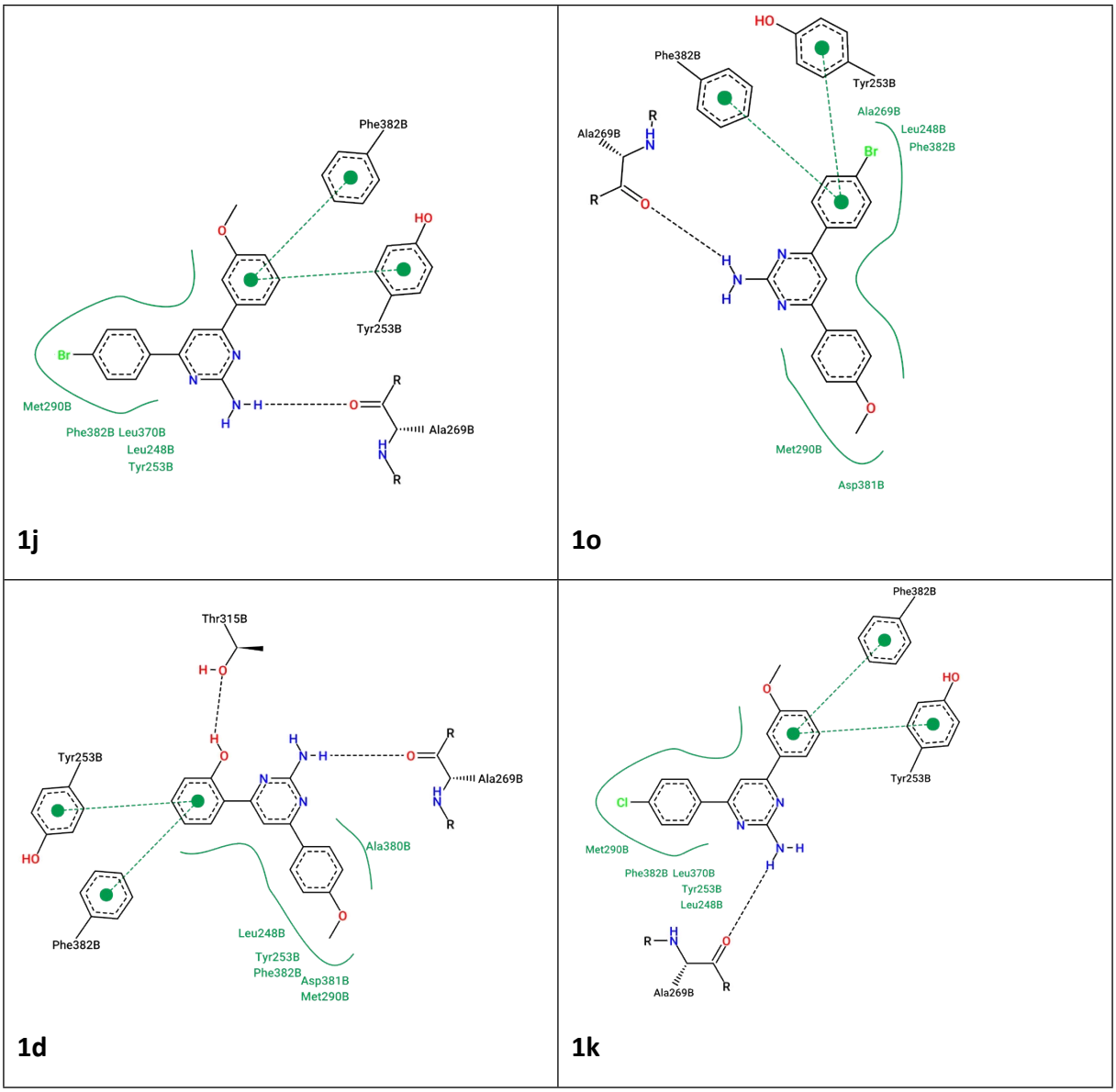
1e

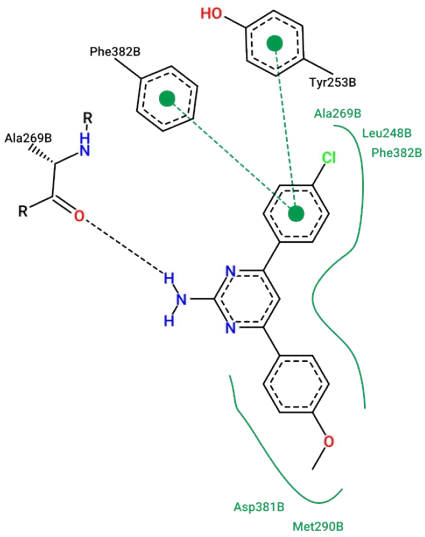

Phe382B
HO
Tyr253B
Cl
Met290B
Leu248B
Tyr253B
Phe382B
Thr315B
Ala269B

1f

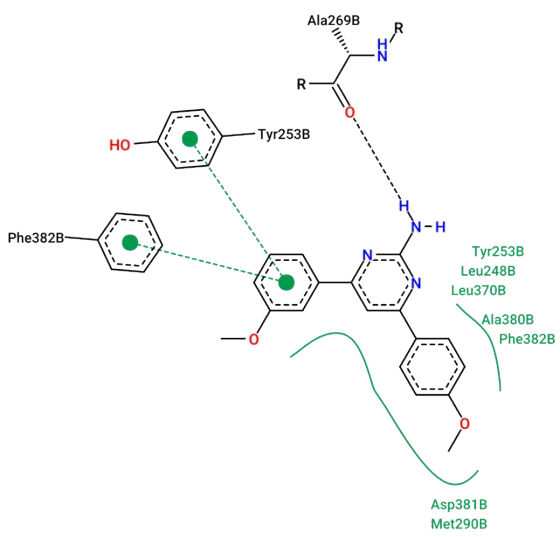

Phe317B
Gly321B
Phe317B
Leu248B
Val256B
Phe382B
Phe382B

1g

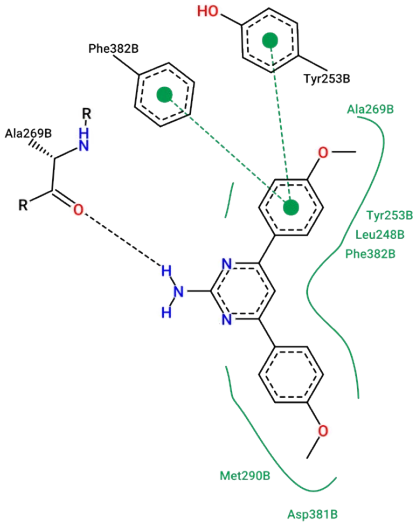

Phe382B
HO
Tyr253B
Br
Met290B
Phe382B Leu370B
Leu248B
Tyr253B
Ala269B
1j
HO
Phe382B
Tyr253B
Ala269B
Leu248B
Phe382B
Ala269B
Br
Met290B
Asp381B
1o
Thr315B
Tyr253B
Ala269B
Ala380B
Phe382B
Leu248B
Tyr253B
Phe382B
Asp381B
Met290B
1d
Phe382B
HO
Tyr253B
Met290B
Phe382B Leu370B
Tyr253B
Leu248B
Ala269B
1k


HO
Phe382B
Tyr253B
Ala269B
Leu248B
Phe382B
Cl
Ala269B
R
HN
R
O
H
N
H
N
N
N
O
Asp381B
Met290B

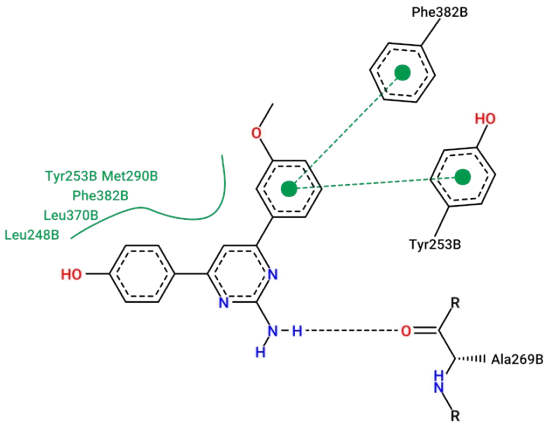
1p


Ala269B
R
HN
R
O
HO
Tyr253B
H
N-H
Phe382B
N
N
Tyr253B
Leu248B
Leu370B
Ala380B
Phe382B
O
O
Asp381B
Met290B

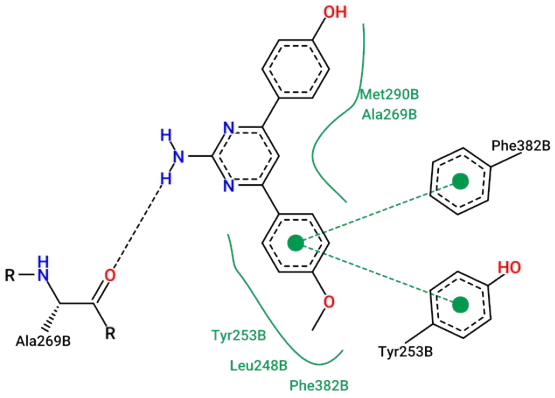
1i


HO
Phe382B
Tyr253B
Ala269B
R
HN
Ala269B
O
O
Tyr253B
Leu248B
Phe382B
H
N
H
N
N
O
Met290B
Asp381B

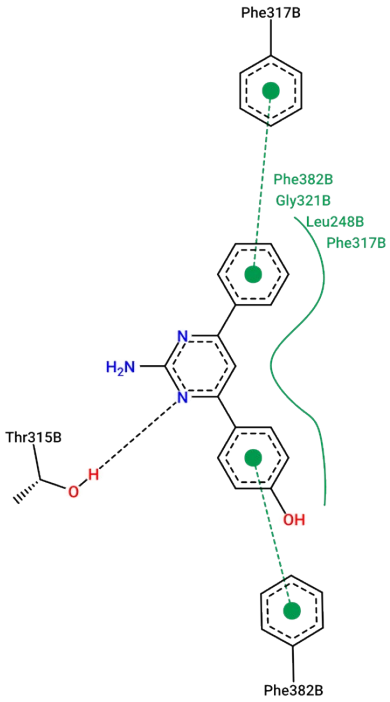
1n


Phe382B
HO
O
Tyr253B Met290B
Phe382B
Leu370B
Leu248B
Tyr253B
HO
N
N
N-H
H
O
R
Ala269B
HN
R

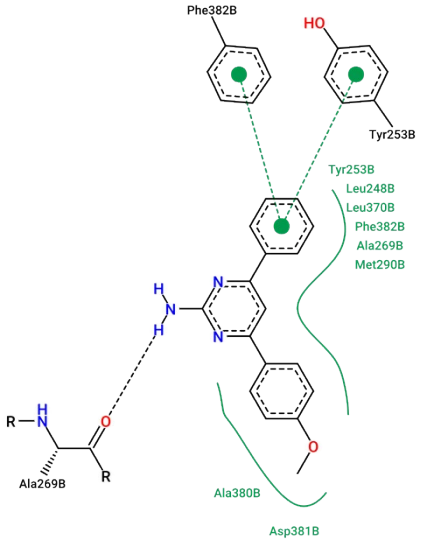
1h


OH
Met290B
Ala269B
Phe382B
HO
Tyr253B
Leu248B
Phe382B
Tyr253B
Ala269B

1m


Phe317B
Phe382B
Gly321B
Leu248B
Phe317B
Thr315B
OH
Phe382B

1q


Phe382B
HO
Tyr253B
Tyr253B
Leu248B
Leu370B
Phe382B
Ala269B
Met290B
Ala380B
Asp381B
Ala269B

1l

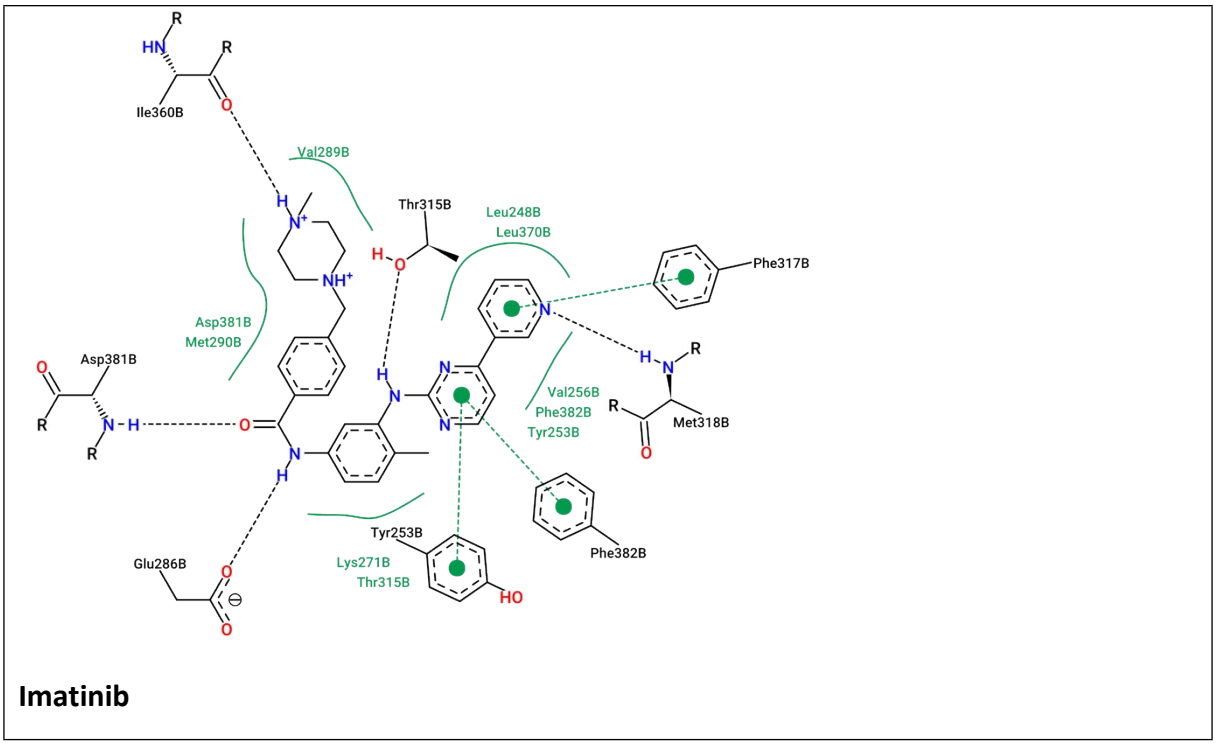


Figure S103. Interaction diagrams of the best docking pose of each 2-amino-4,6-diaryl-pyrimidine derivatives and Imatimib

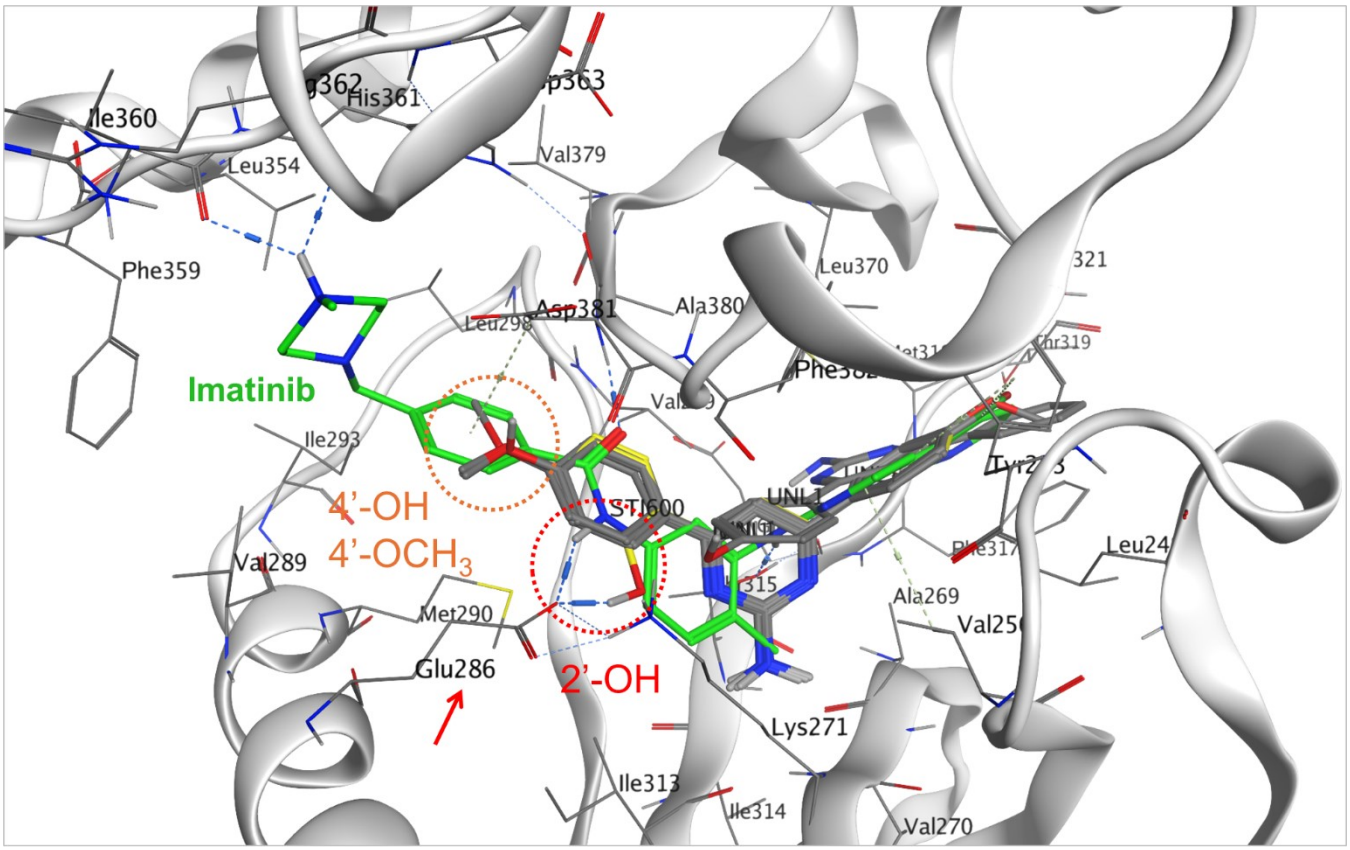


Figure S104. Docking conformation of 2-amino-4,6-diarylpyrimidines with R_1 substituents of -OH or -OCH_3 at 4'-position (ligands with gray carbon atoms) and R_1 substituents of -OH at 2'-position (compound **1e**, shown with yellow carbon atoms). The binding conformation of imatinib to wild-type ABL1 in the co-crystallized complex (PDB ID: 2HYY) is depicted as sticks with green carbon atoms.

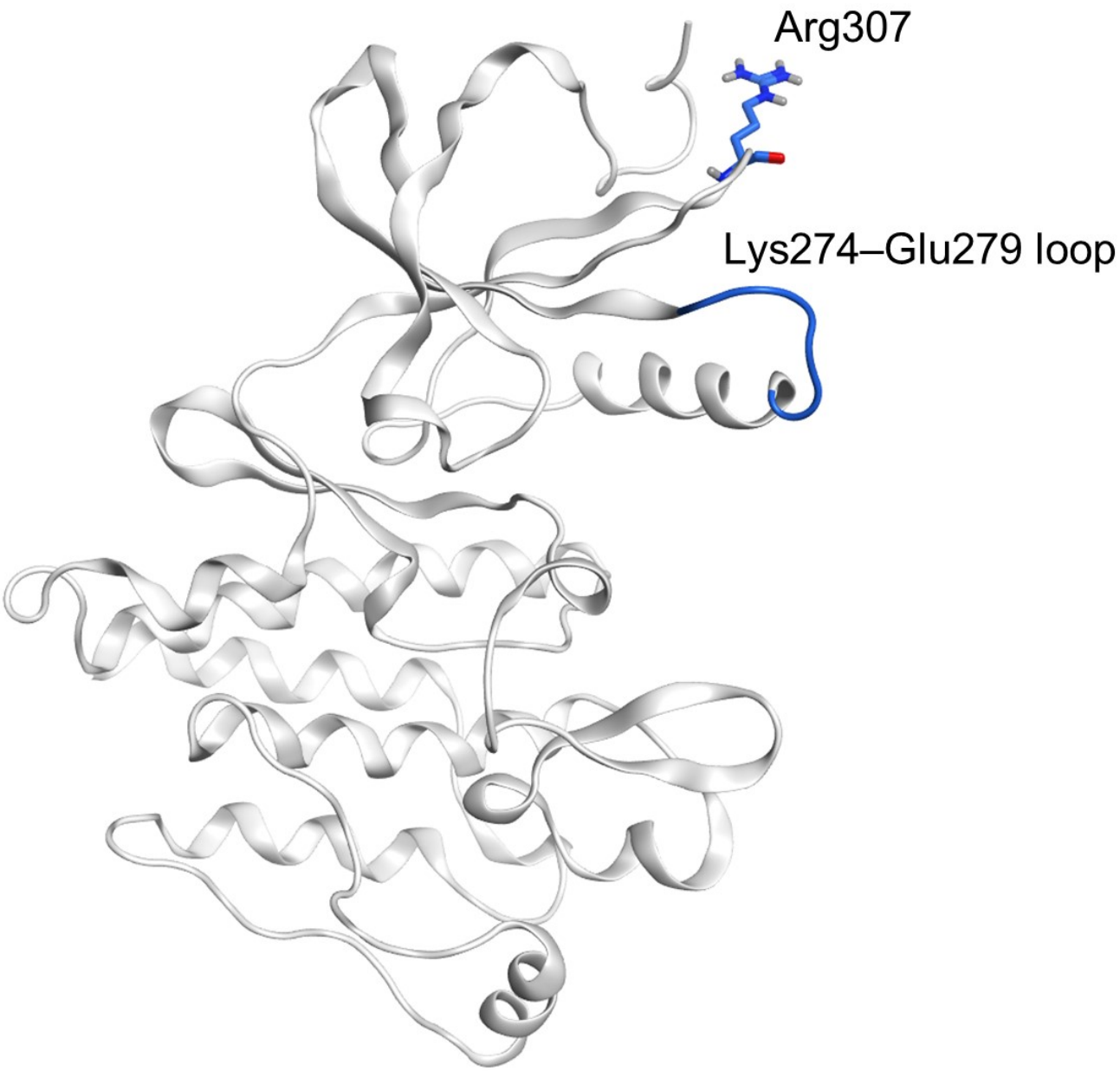


Figure S105. Flexible loops of ABL1 (in blue) were observed in 100 ns MD simulations.

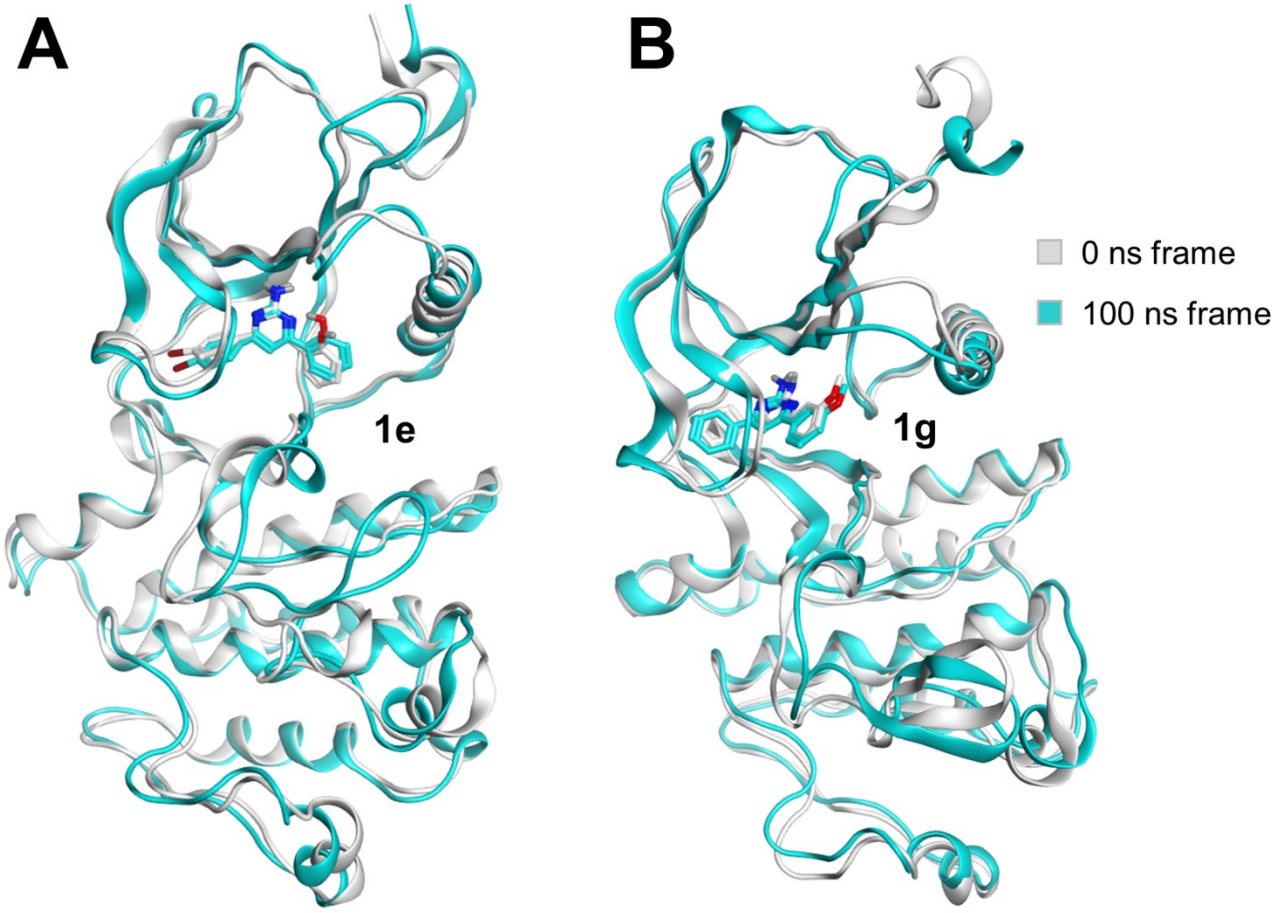


Figure S106. Conformations of ABL1 in complex with **1e** and **1g** at the first and last frames of the 100 ns MD simulation trajectories.

Table S1. Synthesis of intermediate chalcones and corresponding pyrimidines containing the electron-withdrawing groups

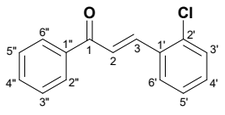
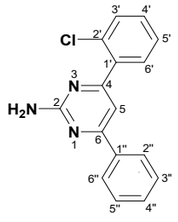
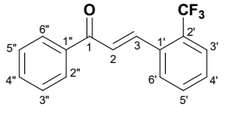
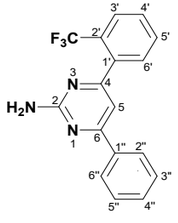
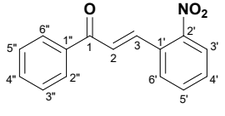
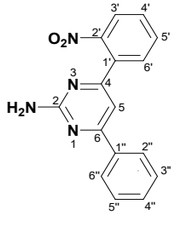
Intermediate chalcones	TLC perform of synthesis of intermediate chalcones	Corresponding pyrimidines	TLC perform of synthesis of corresponding pyrimidines
Ch-x 	Monitoring successfully	**1x** 	Monitoring unsuccessfully
Ch-y 	Monitoring successfully	**1y** 	Monitoring unsuccessfully
Ch-z 	Monitoring unsuccessfully	**1z** 	

Table S2. The ^{1}H-NMR spectra of 2-amino-4,6-diarylpyrimidine derivatives

Cpd./ Positions	1a	1b	1c	1d	1e	1f	1g	1h	1i	1j	1k	1l	1m	1n	1o	1p	1q
	^{1}H-NMR spectra (ppm)																
-OH	13.99 (s)	13.75 (s)	13.98 (s)	14.08 (s)	13.92 (s)	13.93 (s)	-	9.89 (s)	-	-	-	-	9.90 (s)	-	-	-	9.91 (s)
-OCH_3		-	3.87 (s)	3.85 (s)	-	-	3.85 (s)	3.85 (s)	3.84 (s); 3.85 (s)	3.86 (s)	3.85 (s)	3.84 (s)	3.83 (s)	3.84 (s)	3.89 (s)	3.84 (s)	-
-NH_2	7.22 (s)	7.63 (s)	7.21 (s)	7.12 (s)	7.25 (s)	7.24 (s)	6.73 (s)	6.58 (s)	6.64 (s)	6.77 (s)	6.76 (s)	6.64 (s)	6.49 (s)	6.55 (s)	6.73 (s)	6.68 (s)	6.59 (s)
1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2	-	-	-	-	-	-	-	-	7.75 (s)	7.76 (s)	-	-	-	-	-	-	-
5	7.82 (s)	7.91 (s)	7.81 (s)	7.77 (s)	7.85 (s)	7.85 (s)	7.69 (s)	7.57 (s)	7.64 (s)	7.73 (m)	7.72 (s)	7.65 (s)	7.53 (s)	7.59 (s)	7.73 (s)	7.67 (s)	7.59 (s)
6	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2’	-	-	-	-	-	-	7.76 (s)	7.72 (s)	-	-	7.76 (s)	8.22 (m)	8.17 (d, *J* = 6.6 Hz)	8.20 (d, *J* = 9.0 Hz)	8.26 (d, *J* = 9.0 Hz)	8.21 (d, *J* = 9.0 Hz)	8.10 (d, *J* = 9.0 Hz)
3’	6.94 (m)	6.96 (m)	6.95 (m)	6.94 (m)	6.95 (m)	6.95 (m)	-	-	-	-	-	7.08 (d, *J* = 9.0 Hz)	7.05 (d, *J* = 6.6 Hz)	7.07 (d, *J* = 9.0 Hz)	7.12 (d, *J* = 9.0 Hz)	7.07 (d, *J* = 9.0 Hz)	6.89 (d, *J* = 8.4 Hz)
4’	7.39 (dt, *J* = 1.2, *J* = 8.4 Hz)	7.41 (dt *J* = 1.8 Hz, *J* = 8.4 Hz)	7.39 (dt, *J* = 1.2 Hz, *J* = 8.4 Hz)	7.38 (dt, *J* = 1.8 Hz, *J* = 8.4 Hz)	7.39 (dt, *J* = 1.2 Hz, *J* = 8.4 Hz)	7.39 (t, *J* = 7.8 Hz)	7.09 (dd, *J* = 2.4 Hz, *J* = 7.8 Hz)	7.07 (dd, *J* = 2.4 Hz, *J* = 7.8 Hz)	7.09 (m)	7.10 (dd, *J* = 2.4 Hz, *J* = 6.0 Hz)	7.09 (dd, *J* = 2.4 Hz, *J* = 7.8 Hz)	-	-	-	-	-	-
5’	6.94 (m)	6.96 (m)	6.95 (m)	6.94 (m)	6.95 (m)	6.95 (m)	7.44 (t, *J* = 7.8 Hz)	7.42 (t, *J* = 7.8 Hz)	7.44 (t, *J* = 7.8 Hz)	7.45 (t, *J* = 7.8 Hz)	7.44 (t, *J* = 7.8 Hz)	7.08 (d, *J* = 9.0 Hz)	7.05 (d, *J* = 6.6 Hz)	7.07 (d, *J* = 9.0 Hz)	7.12 (d, *J* = 9.0 Hz)	7.07 (d, *J* = 9.0 Hz)	6.89 (d, *J* = 8.4 Hz)
6’	8.25 (m)	8.29 (dd, *J* = 1.2 Hz, *J* = 8.4 Hz)	8.26 (d, *J* = 8.4 Hz)	8.25 (m)	8.24 (m)	8.24 (d, *J* = 7.8 Hz)	7.80 (d, *J* = 7.8 Hz)	7.77 (d, *J* = 7.8 Hz)	7,79 (d, *J* = 7.8 Hz)	7.81 (d, *J* = 7.8 Hz)	7.80 (d, *J* = 7.8 Hz)	8.22 (m)	8.17 (d, *J* = 6.6 Hz)	8.20 (d, *J* = 9.0 Hz)	8.26 (d, *J* = 9.0 Hz)	8.21 (d, *J* = 9.0 Hz)	8.10 (d, *J* = 9.0 Hz)
2”	-	-	7.78 (s)	8.25 (m)	8.24 (m)	8.29 (d, *J* = 8.4 Hz)	8.23 (m)	8.09 (d, *J* = 9.0 Hz)	8,21 (d, *J* = 7.2 Hz)	8.20 (d, *J* = 7.2 Hz)	8.26 (d, *J* = 6.6 Hz)	8.22 (m)	8.08 (d, *J* = 6.6 Hz)	8.20 (d, *J* = 9.0 Hz)	8.23 (d, *J* = 8.4 Hz)	8.25 (d, *J* = 8.4 Hz)	8.19 (m)
3”	7.54 (m)	6.96 (m)		7.09 (m)	7.75 (d, *J* = 8.4 Hz)	7.61 (d, *J* = 8.4 Hz)	7.52 (m)	6.87 (d, *J* = 9.0 Hz)	7.09 (m)	7.73 (m)	7.59 (d, *J* = 6.6 Hz)	7.54 (m)	6.88 (d, *J* = 6.6 Hz)	7.07 (d, *J* = 9.0 Hz)	7.77 (d, *J* = 9.0 Hz)	7.58 (d, *J* = 8.4 Hz)	7.51 (m)
4”	7.54 (m)	7.41 (dt *J* = 1.8 Hz, *J* = 8.4 Hz)	7.12 (dd, *J* = 2.4, *J* = 8.4 Hz)	7.12 (dd, *J* = 2.4, *J* = 8.4 Hz)	-	-	7.52 (m)	-	-	-	-	7.54 (m)	-	-	-	-	7.51 (m)
5”	7.54 (m)	6.96 (m)	7.46 (t, *J* = 8.4 Hz)	7.09 (m)	7.75 (d, *J* = 8.4 Hz)	7.61 (d, *J* = 8.4 Hz)	7.52 (m)	6.87 (d, *J* = 9.0 Hz)	7.09 (m)	7.73 (m)	7.59 (d, *J* = 6.6 Hz)	7.54 (m)	6.88 (d, *J* = 6.6 Hz)	7.07 (d, *J* = 9.0 Hz)	7.77 (d, *J* = 9.0 Hz)	7.58 (d, *J* = 8.4 Hz)	7.51 (m)
6”	8.25 (m)	8.29 (dd, *J* = 1.2 Hz, *J* = 8.4 Hz)	7.84 (d, *J* = 7.8 Hz)	8.25 (m)	8.24 (m)	8.29 (d, *J* = 8.4 Hz)	8.23 (m)	8.09 (d, *J* = 9.0 Hz)	8,21 (d, *J* = 7.2 Hz)	8.20 (d, *J* = 7.2 Hz)	8.26 (d, *J* = 6.6 Hz)	8.22 (m)	8.08 (d, *J* = 6.6 Hz)	8.20 (d, *J* = 9.0 Hz)	8.23 (d, *J* = 8.4 Hz)	8.25 (d, *J* = 8.4 Hz)	8.19 (m)

Table S3. The ^{13}C-NMR spectra of 2-amino-4,6-diarylpyrimidine derivatives

Compounds/ Positions	1a	1b	1c	1d	1e	1f	1g	1h	1i	1j	1k	1l	1m	1n	1o	1p	1q
	^{13}C-NMR spectra (ppm)																
-OCH_3	-	-	55.26	55.31	-	-	55.25	55.22	55.21 – 55.25	55.32	55.26	55.30	55.25	55.25	55.29	55.27	-
2	161.29	158.94	161.22	161.49	161.26	161.25	163.92	163.78	163.80	163.95	163.90	163.90	164.38	163.77	163.86	163.84	163.84
4	165.33	165.62	165.19	164.86	165.45	165.43	164.88	164.12	164.31	164.99	164.90	164.56	163.74	164.07	164.65	164.61	164.69
5	99.89	98.26	100.06	98.99	98.90	99.83	102.02	100.93	101.21	101.94	101.91	101.07	99.97	100.24	100.09	100.93	100.78
6	165.19	165.62	165.11	161.14	164.06	163.96	164.67	164.68	164.39	163.73	163.57	164.42	163.89	164.07	163.29	163.19	164.34
1’	117.51	117.39	117.49	117.57	117.43	117.43	138.86	139.08	138.99	138.75	138.73	129.62	129.82	129.74	129.47	129.47	128.03
2’	160.30	160.32	160.29	160.30	160.29	160.29	112.13	112.00	112.09	112.22	112.19	126.90	128.38	128.43	128.56	128.67	128.58
3’	118.02	118.12	117.99	117.98	118.02	118.01	159.57	159.53	159.52	159.63	159.58	113.93	113.84	113.84	113.91	113.89	115.28
4’	132.60	132.95	132.57	132.43	132.67	132.66	116.13	115.95	115.95	116.29	116.21	161.23	161.05	161.09	161.29	161.27	159.72
5’	118.62	118.71	118.56	118.52	118.59	118.58	129.63	129.56	129.55	129.73	129.65	113.93	113.84	113.84	113.91	113.89	115.28
6’	130.73	128.36	128.08	127.90	128.07	128.07	119.36	119.26	119.28	119.45	119.40	126.90	128.38	128.43	128.56	128.67	128.58
1”	136.99	117.39	138.50	129.23	136.14	135.52	137.30	127.99	129.57	136.51	136.11	137.48	128.15	129.74	136.64	136.26	137.54
2”	127.12	160.32	112.29	128.76	129.13	128.90	126.96	128.63	128.52	129.08	128.77	128.53	128.51	128.43	128.93	128.55	126.82
3”	128.59	118.12	159.56	113.93	131.56	128.62	128.54	115.25	113.86	131.61	128.60	128.54	115.24	113.84	131.51	128.55	128.49
4”	128.02	132.95	116.44	161.49	124.42	135.78	130.38	159.74	161.19	124.11	135.19	130.28	159.64	161.09	123.89	135.02	130.17
5”	128.59	118.71	129.63	113.93	131.56	128.62	128.54	115.25	113.86	131.61	128.60	128.54	115.24	113.84	131.51	128.55	128.49
6”	127.12	128.36	119.53	128.76	129.13	128.90	126.96	128.63	128.52	129.08	128.77	128.53	128.51	128.43	128.93	128.55	126.82

Table S4. Results of cell survival for K562 cytotoxic activity

Entry	Compound	Concentration (mM)	% Cell survival (CS)
	Control		100.00 ± 0.60
1	**1a**	30	67.26 ± 0.63
		100	**41.72 ± 1.15**
2	**1b**	30	71.05 ± 1.73
		100	62.69 ± 0.70
3	**1c**	30	84.48 ± 0.85
		100	**36.71 ± 0.97**
4	**1d**	30	95.66 ± 0.80
		100	76.29 ± 0.70
5	**1e**	30	**5.59 ± 0.06**
		100	**4.37 ± 0.04**
6	**1f**	30	78.54 ± 0.74
		100	74.97 ± 0.51
7	**1g**	30	52.66 ± 1.27
		100	**11.87 ± 1.39**
8	**1h**	30	51.37 ± 0.61
		100	**36.74 ± 1.68**
8	**1i**	30	55.52 ± 1.19
		100	**42.24 ± 0.32**
9	**1j**	30	61.83 ± 0.92
		100	10.67 ± 1.12
10	**1k**	30	75.06 ± 0.82
		100	63.33 ± 1.09

11	**1l**	30	65.23 ± 1.99
		100	**46.95 ± 0.48**
12	**1m**	30	56.45 ± 0.75
		100	**44.33 ± 1.59**
13	**1n**	30	102.08 ± 0.92
		100	84.10 ± 0.91
14	**1o**	30	71.42 ± 0.61
		100	54.68 ± 0.70
15	**1p**	30	92.34 ± 0.21
		100	80.12 ± 1.08
16	**1q**	30	79.52 ± 0.87
		100	68.06 ± 1.08
17	**Imatinib**	200 nM	41.56 ± 0.92
		20 uM	23.90 ± 1.00

Table S5. Occupancy of interaction types between ABL1 and the ligands **1e** and **1g** during 100 ns MD simulations

1e	**1g**
Leu248 (Hyd 99%, VdW 36%)	Leu248 (Hyd 100%, VdW 59%)
Tyr253 (Hyd 92%, Pi-pi 61%, VdW 30%)	Tyr253 (Hyd 100%, Pi-pi 37%, VdW 48%)
Val256 (Hyd 100%, VdW 33%)	Val256 (Hyd 100%, VdW 69%)
Ala269 (Hyd 100%, HBD 72%, VdW 91%)	Ala269 (Hyd 100%)
Lys271 (Hyd 97%, VdW 73%)	Lys271 (Hyd 92%, VdW 49%)
Glu286 (Hyd 79%)	Val299 (Hyd 50%)
Met290 (Hyd 99%, VdW 65%)	Thr315 (HBD 85%, VdW 95%)
Val299 (Hyd 67%)	Glu316 (HBD 96%, VdW 99%)
Ile313 (Hyd 45%, HBD 38%, VdW 78%)	Phe317 (Hyd 93%, VdW 31%)
Thr315 (Hyd 100%, VdW 80%)	Gly321 (VdW 42%)
Phe317 (Hyd 32%)	Leu370 (Hyd 99%, VdW 31%)
Met318 (Hyd 88%, VdW 54%)	Phe382 (Hyd 100%, VdW 89%)
Gly321 (VdW 38%)	
Leu370 (Hyd 100%, VdW 52%)	
Ala380 (Hyd 62%)	
Asp381 (VdW 34%)	
Phe382 (Hyd 100%, VdW 67%)	