

Supplementary data

Diversity Oriented Multi-Component (DOS-MCR) approach to access Natural Product Analogues: Regio- and Chemo- Selective Synthesis of Polyheterocyclic Scaffolds via one pot Cascade Reaction

Lakshmanan Pazhanivel ^a and Vasuki Gnanasambandam ^{a*}

Department of Chemistry, Pondicherry University, RV Nagar, Kalapet Pondicherry-605014,
India.

Corresponding author E-mail: vasukig@gmail.com

General procedure for the synthesis aza-cyclopenta (*cd*) diindene S₁

Synthesis of 5-amino-2-imino-10c-phenyl-2,10c-dihydro-1-oxa-4,6,10b-triazacyclopenta[1,2-a:5,4,3-c'd']diinden-3(4H)-one S₁:

Initially, a three component reaction was performed between 4-methyl phenylglyoxal (1mmol) (**A₁**), benzimidazole acetonitrile (1mmol) (**C₁**) and malononitrile (1mmol) (**C₅**) in the presence of Triflic acid medium at room temperature in an open atmosphere. The progress of the reaction was monitored by TLC for completion of the reaction. The reaction mixture turned to a pale yellow precipitate to afford the required product in 1 h. Subsequently, the crude product was washed in CH₃CN solvent several times and a white solid was obtained (Yield of 87%). Then, the product was confirmed by ¹H NMR, ¹³C NMR and HRMS spectra.

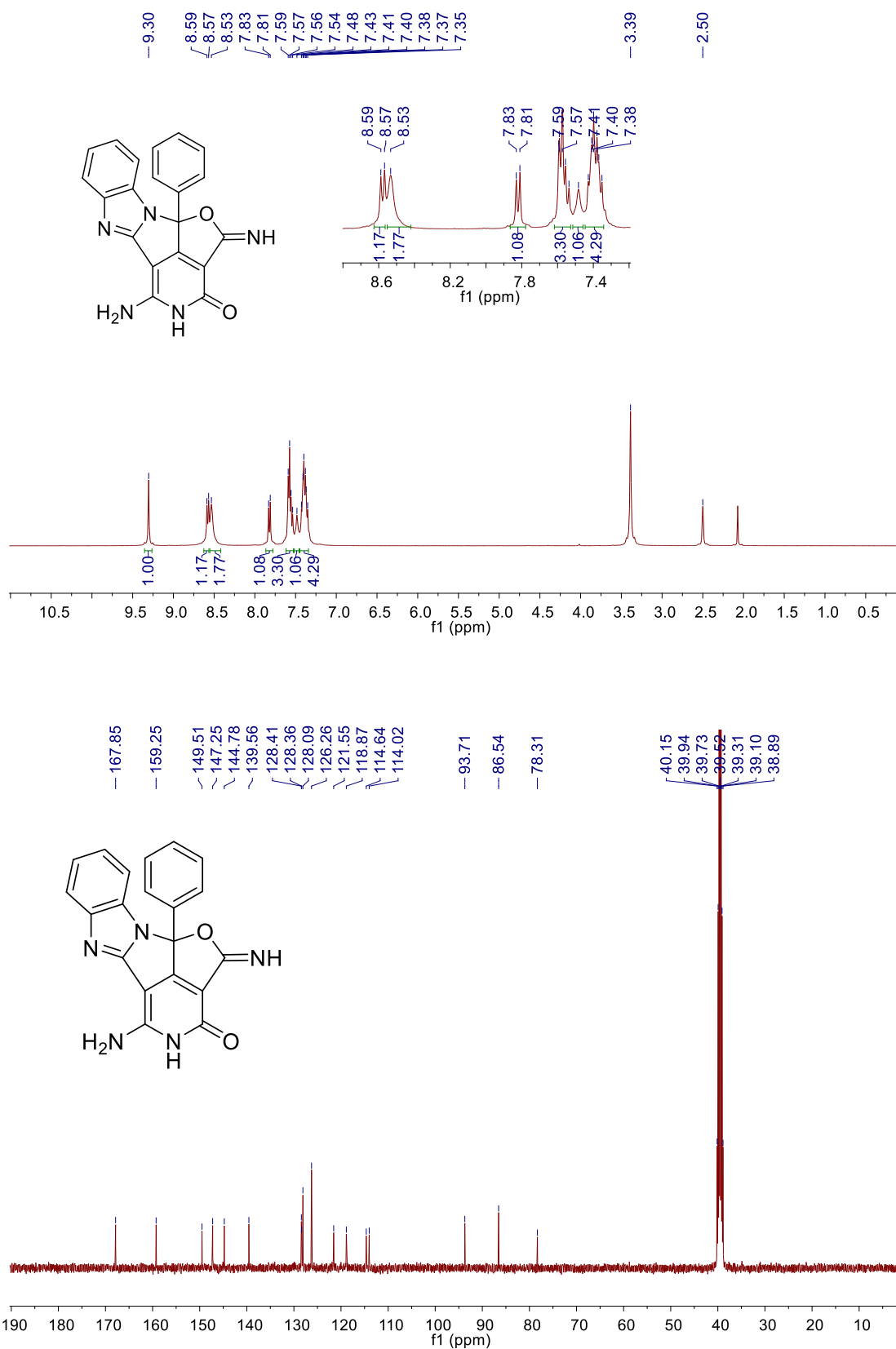


Fig. 1 ¹H, ¹³C spectrum of 5-amino-2-imino-10c-phenyl-2,10c-dihydro-1-oxa-4,6,10b-triazacyclopenta[1,2-a:5,4,3-c'd']diinden-3(4H)-one **S1a**

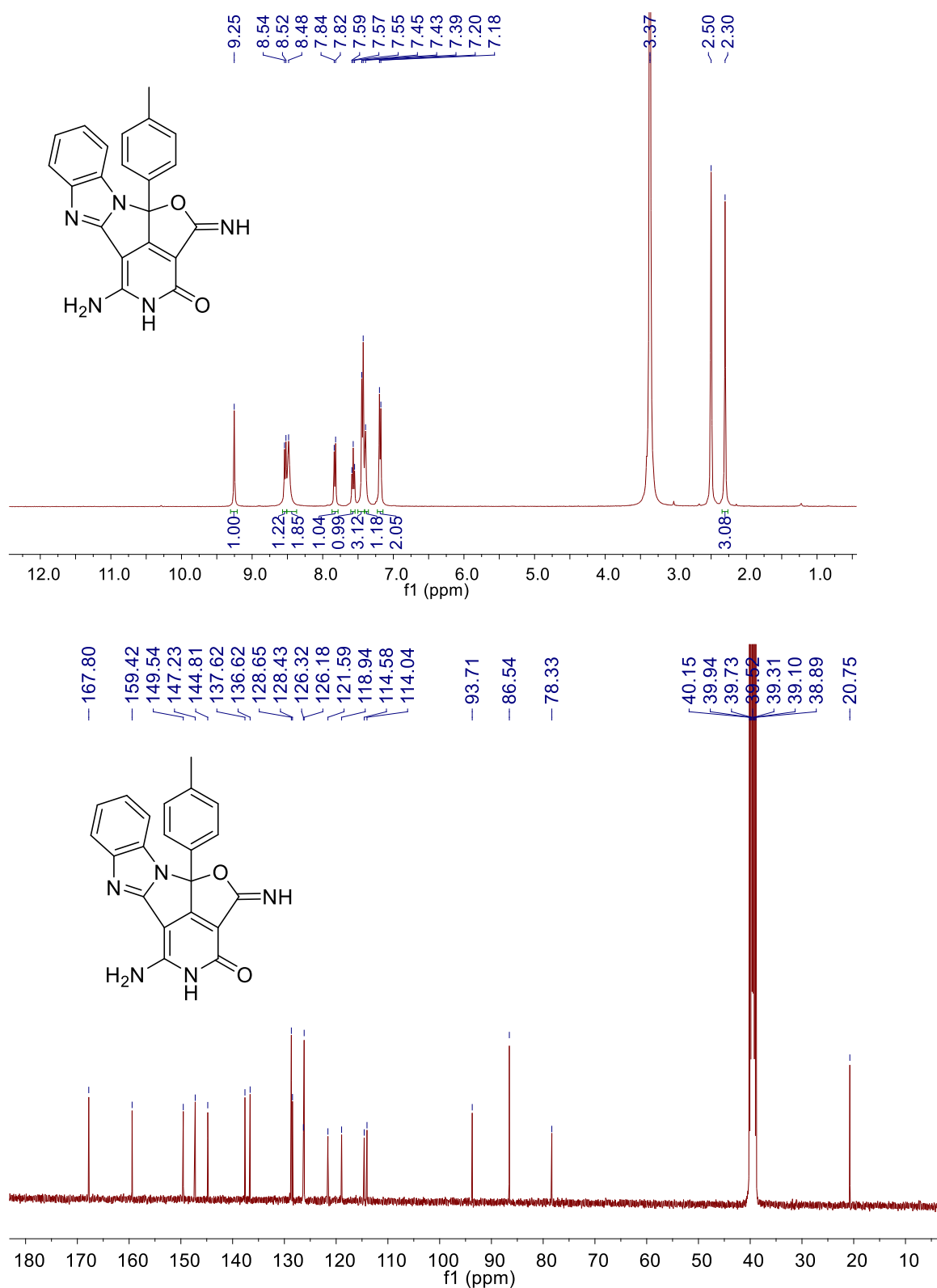


Fig. 2 ¹H, ¹³C spectrum of **5-amino-2-imino-10c-(p-tolyl)-2,10c-dihydro-1-oxa-4,6,10b-triazacyclopenta[1,2-a:5,4,3-c'd']diinden-3(4H)-one S1b**

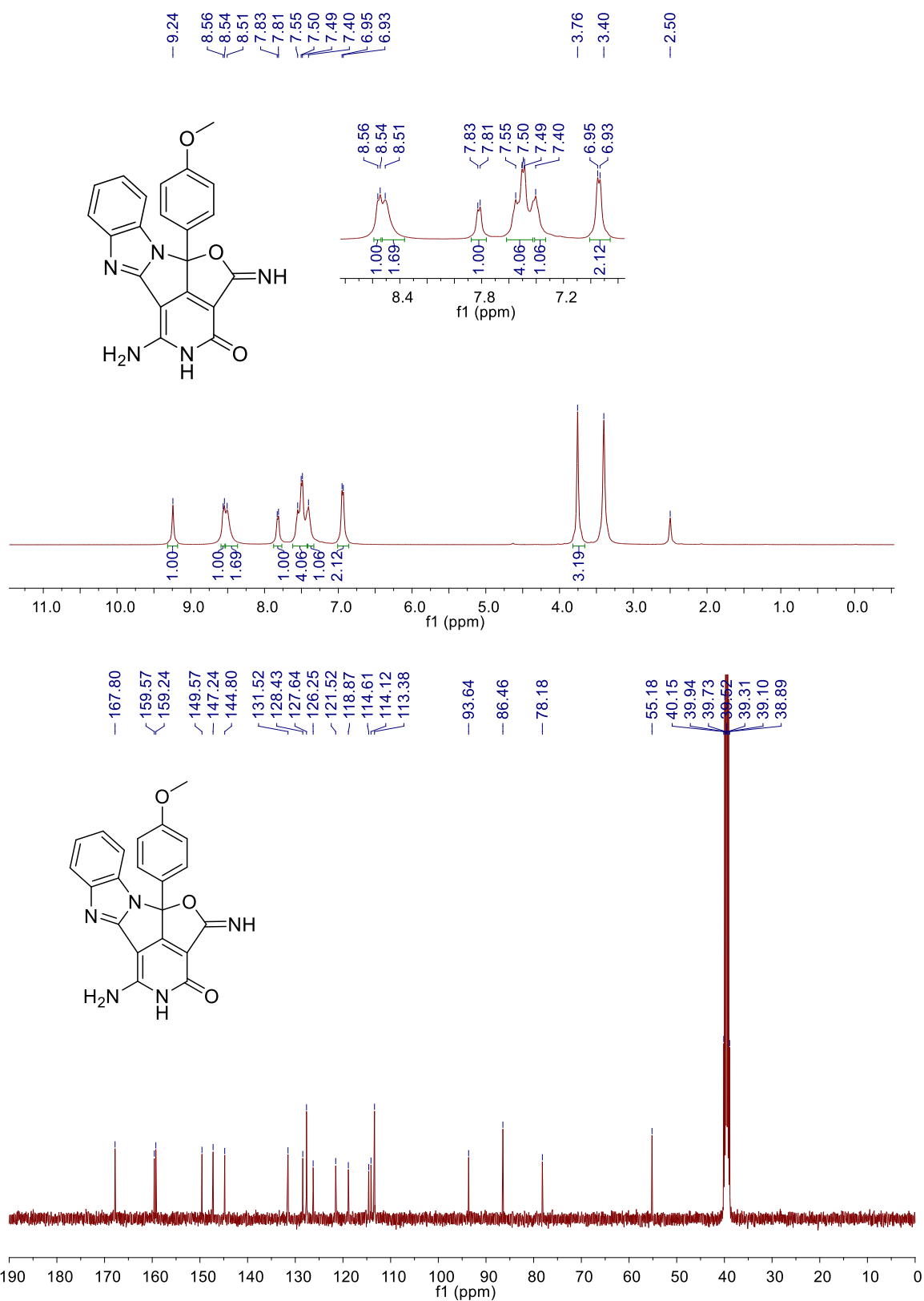


Fig. 3 ¹H, ¹³C spectrum of 5-amino-2-imino-10c-(4-methoxyphenyl)-2,10c-dihydro-1-oxa-4,6,10b-triazacyclopenta[1,2-a:5,4,3-c'd']diinden-3(4H)-one **S_{1c}**

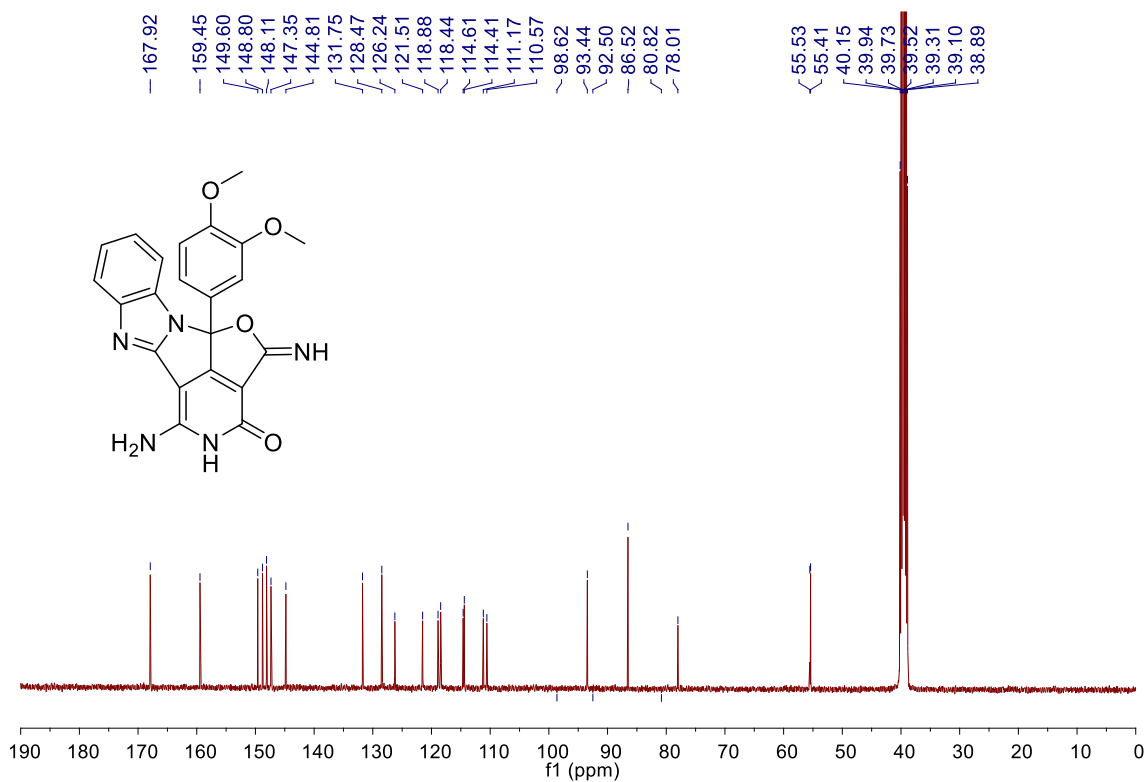
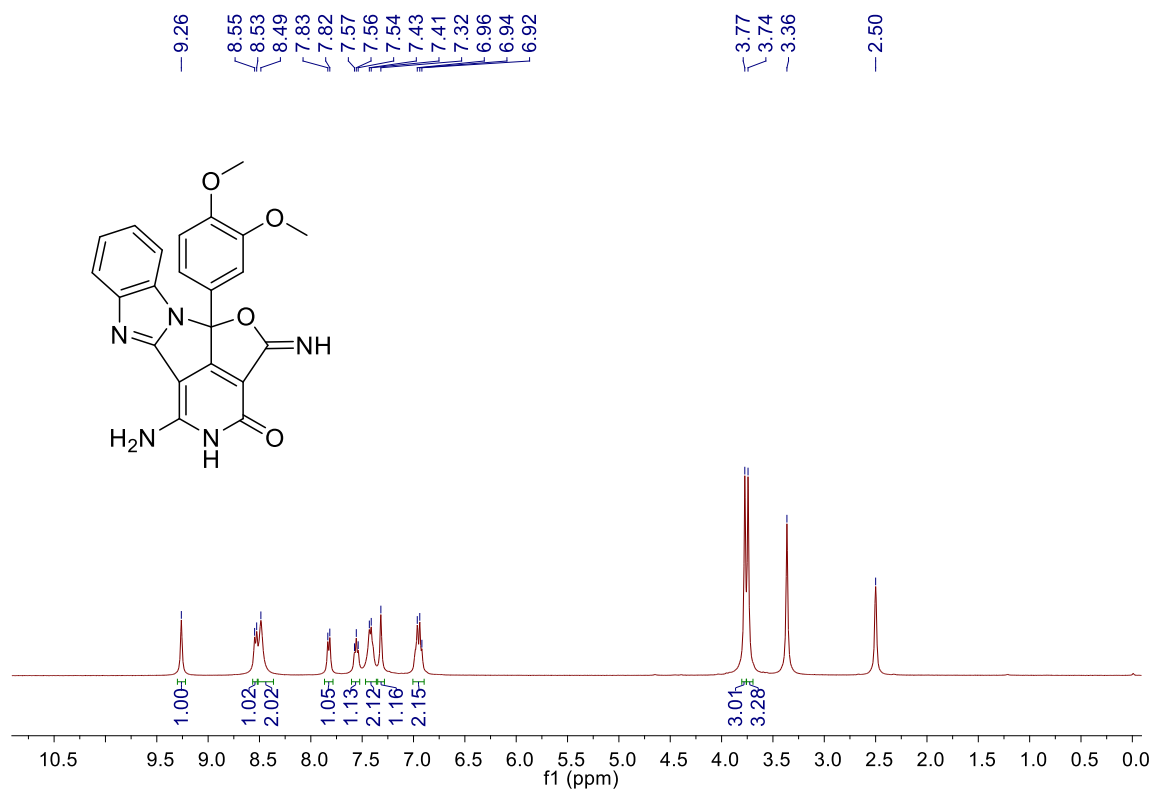


Fig. 4 ¹H, ¹³C spectrum of 5-amino-10c-(3,4-dimethoxyphenyl)-2-imino-2,10c-dihydro-1-oxa-4,6,10b-triazacyclo penta[1,2-a:5,4,3-c'd']diinden-3(4H)-one **S1a**

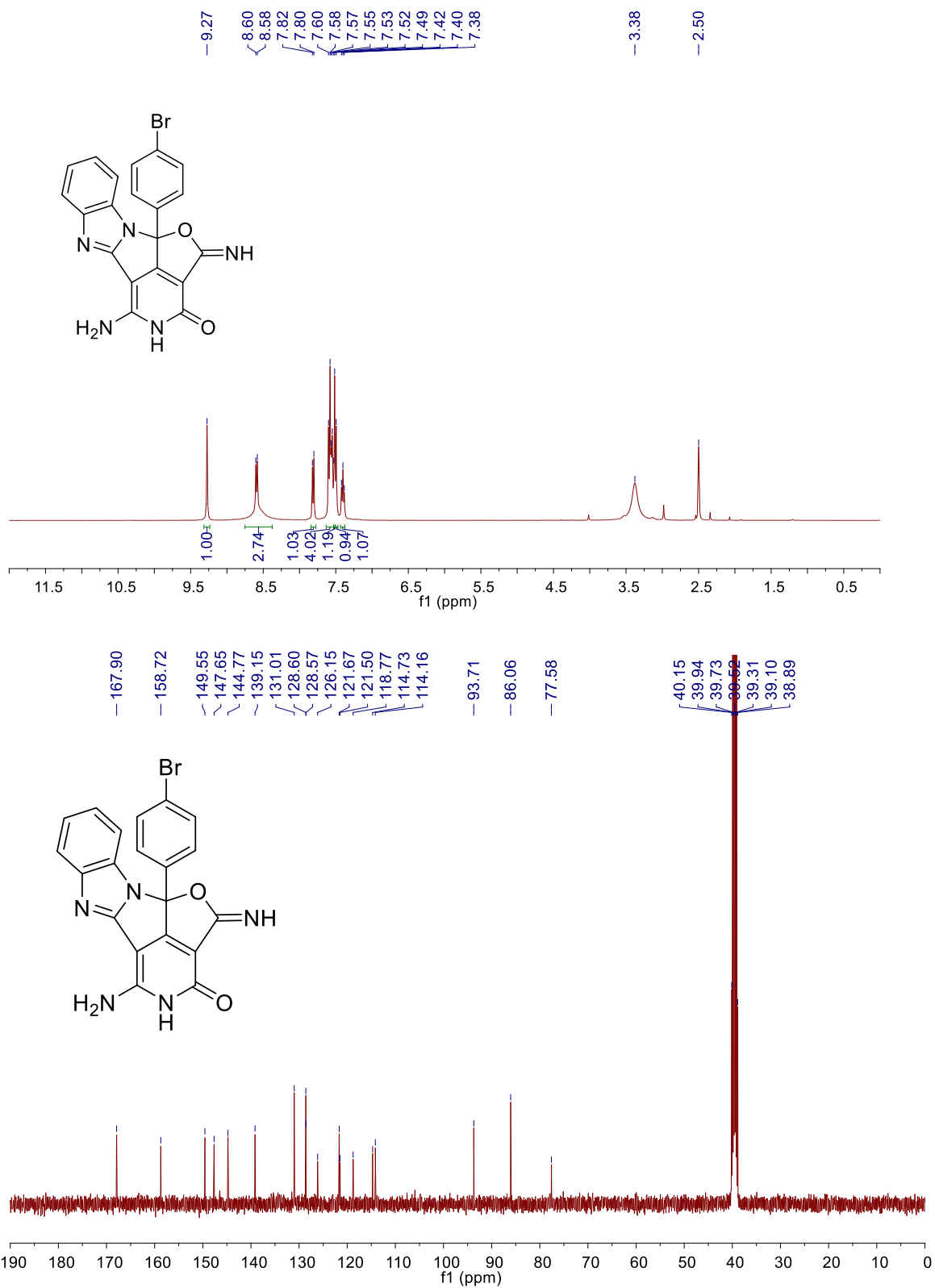


Fig. 5 ¹H, ¹³C spectrum of 5-amino-10c-(4-bromophenyl)-2-imino-2,10c-dihydro-1-oxa-4,6,10b-triazacyclopenta[1,2-a:5,4,3-c'-d']diinden-3(4H)-one **S_{1e}**

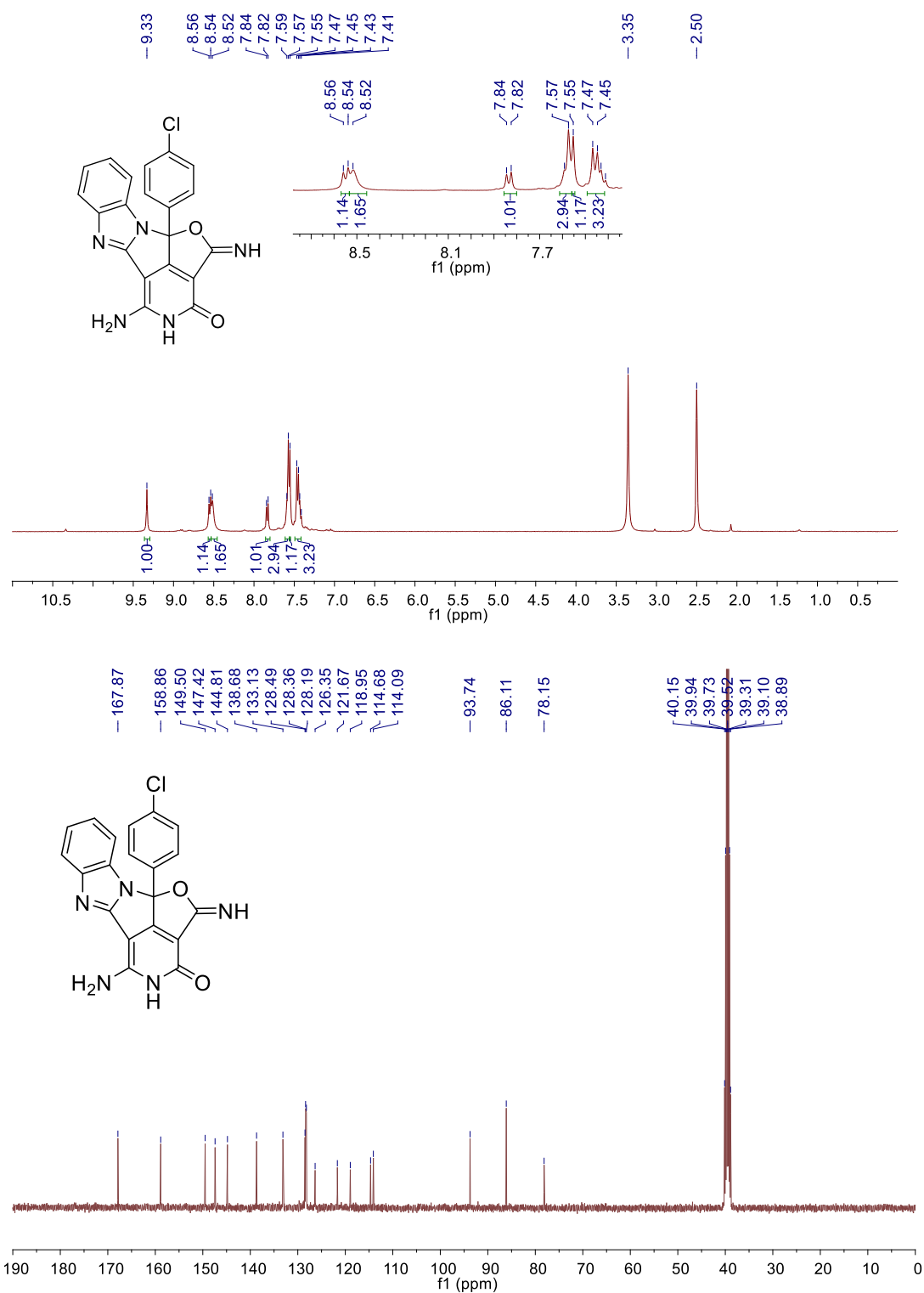


Fig. 6 ^1H , ^{13}C spectrum of 5-amino-10c-(4-chlorophenyl)-2-imino-2,10c-dihydro-1-oxa-4,6,10b-triazacyclopenta[1,2-a:5,4,3-c'd']diinden-3(4H)-one **S1r**

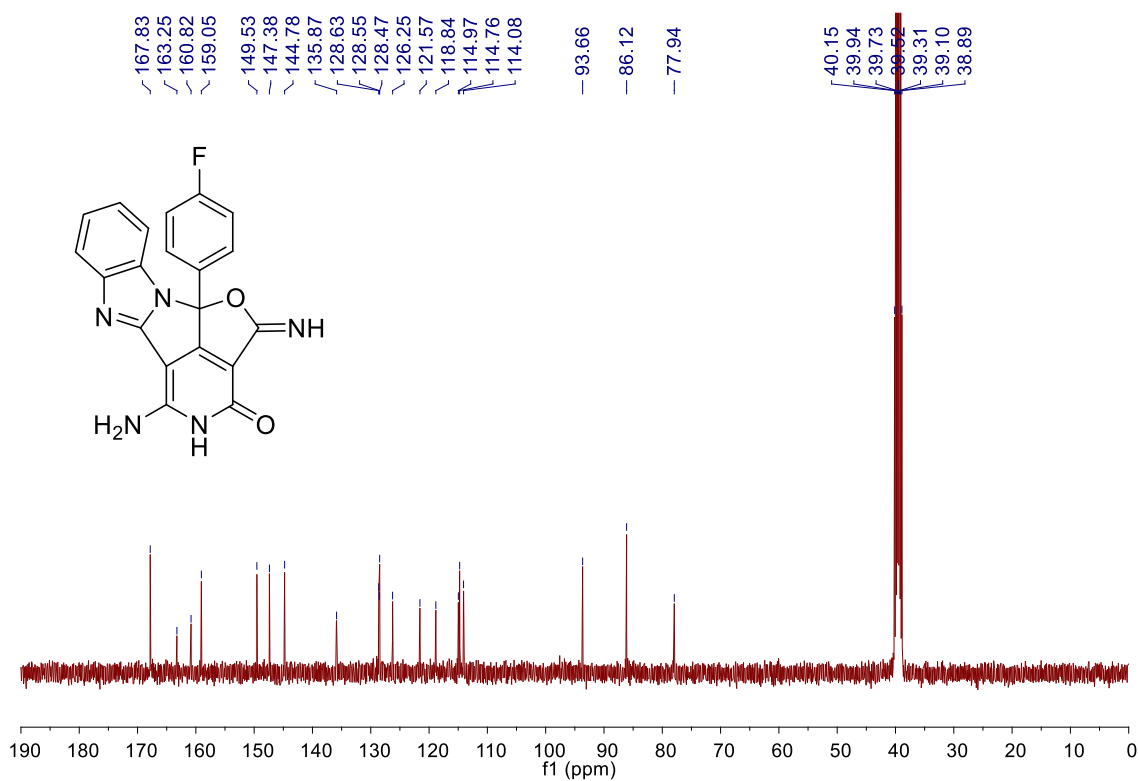
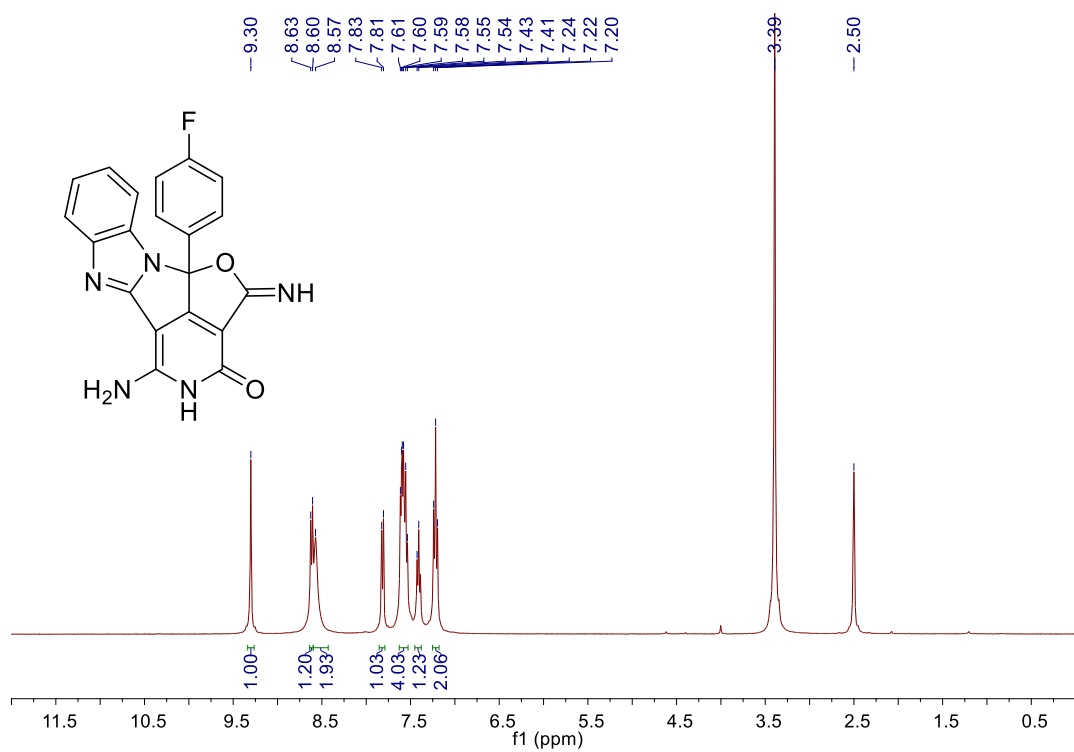


Fig.7 ¹H, ¹³C spectrum of 5-amino-10c-(4-fluorophenyl)-2-imino-2,10c-dihydro-1-oxa-4,6,10b-triazacyclopenta[1,2-a:5,4,3-c'd']diinden-3(4H)-one **S_{1g}**

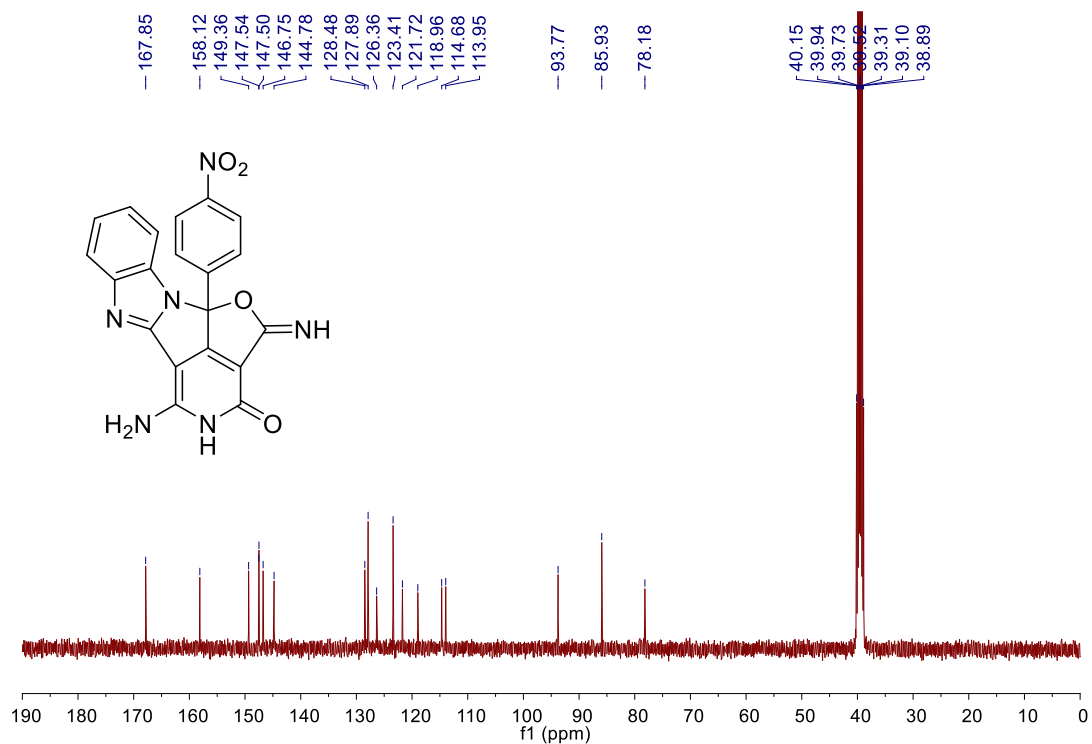
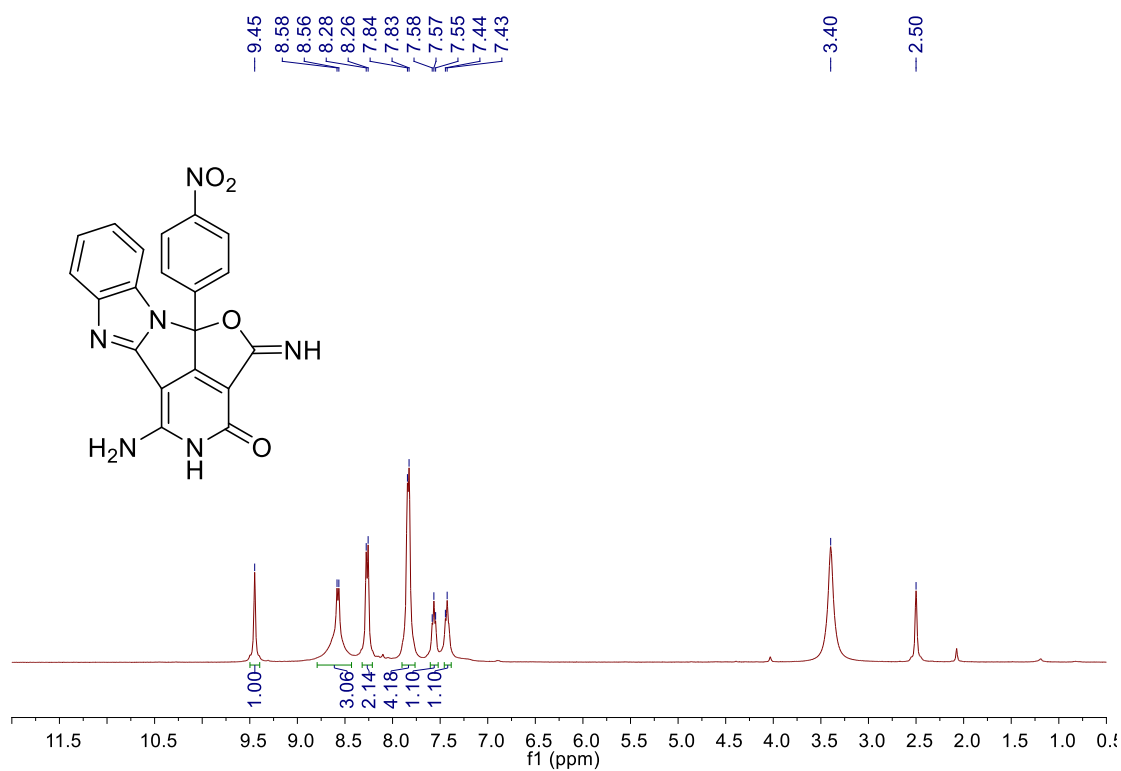


Fig. 8 ¹H, ¹³C spectrum of 5-amino-2-imino-10c-(4-nitrophenyl)-2,10c-dihydro-1-oxa-4,6,10b-triazacyclopenta[1,2-a:5,4,3-c'd']diinden-3(4H)-one **S1h**

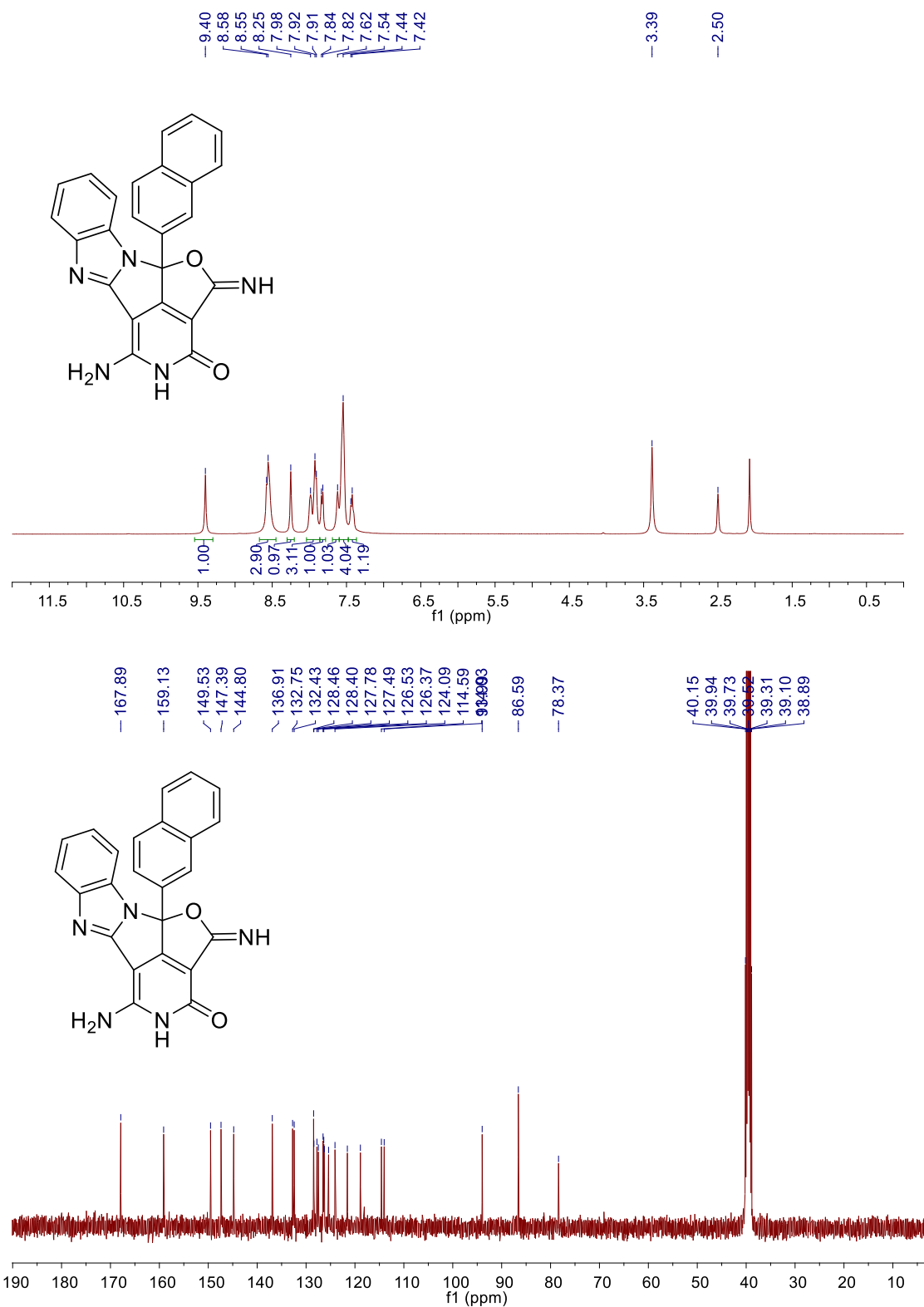


Fig. 9 ¹H, ¹³C spectrum of 5-amino-2-imino-10c-(naphthalen-2-yl)-2,10c-dihydro-1-oxa-4,6,10b-triazacyclopenta[1,2-a:5,4,3-c'd']diinden-3(4H)-one **S₁₁**

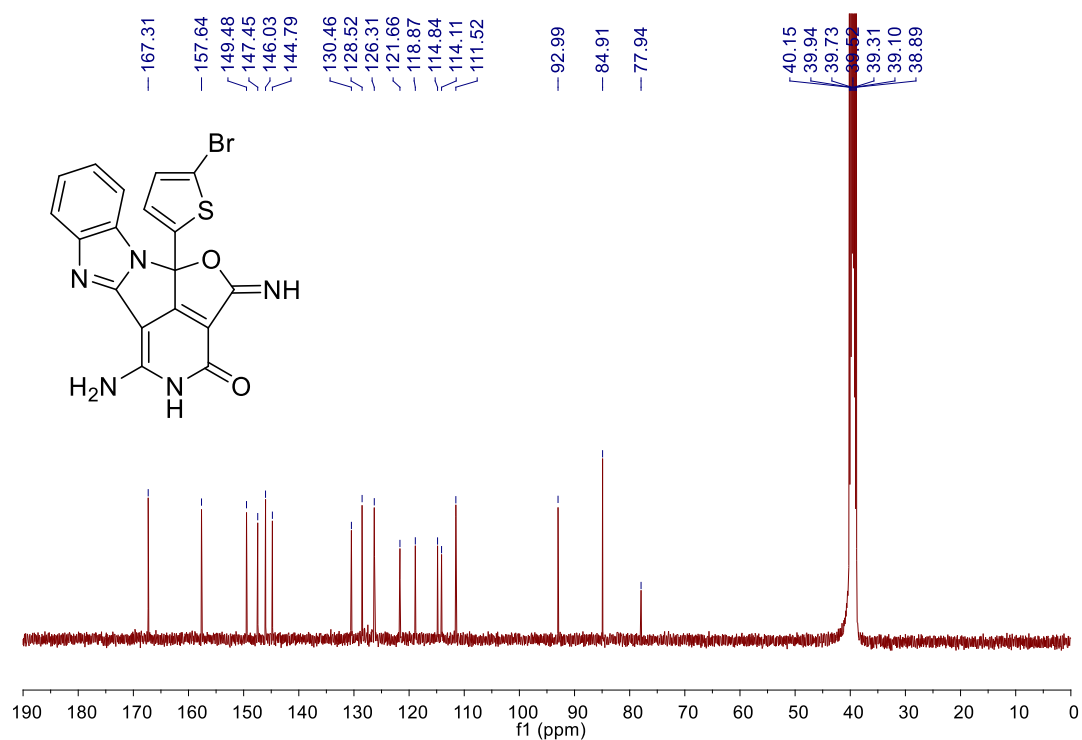
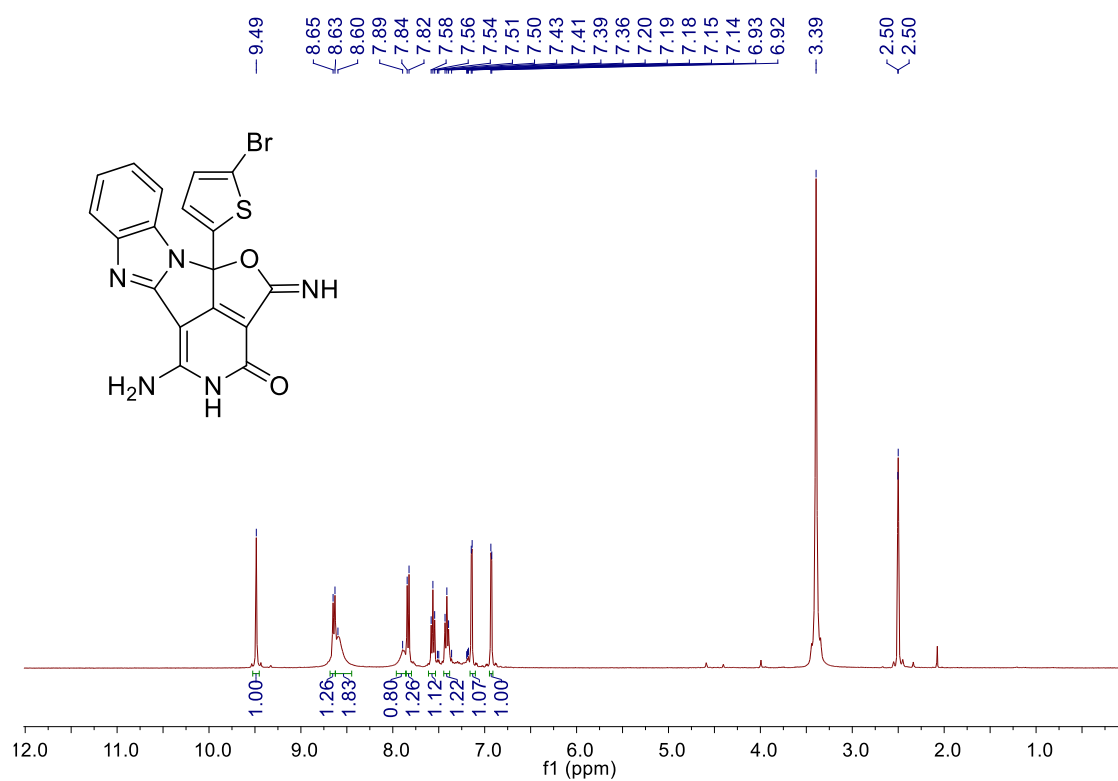


Fig. 10 ¹H, ¹³C spectrum of 5-amino-10c-(5-bromothiophen-2-yl)-2-imino-2,10c-dihydro-1-oxa-4,6,10b-triazacyclopenta[1,2-a:5,4,3-c'd']diinden-3(4H)-one **S_{1j}**

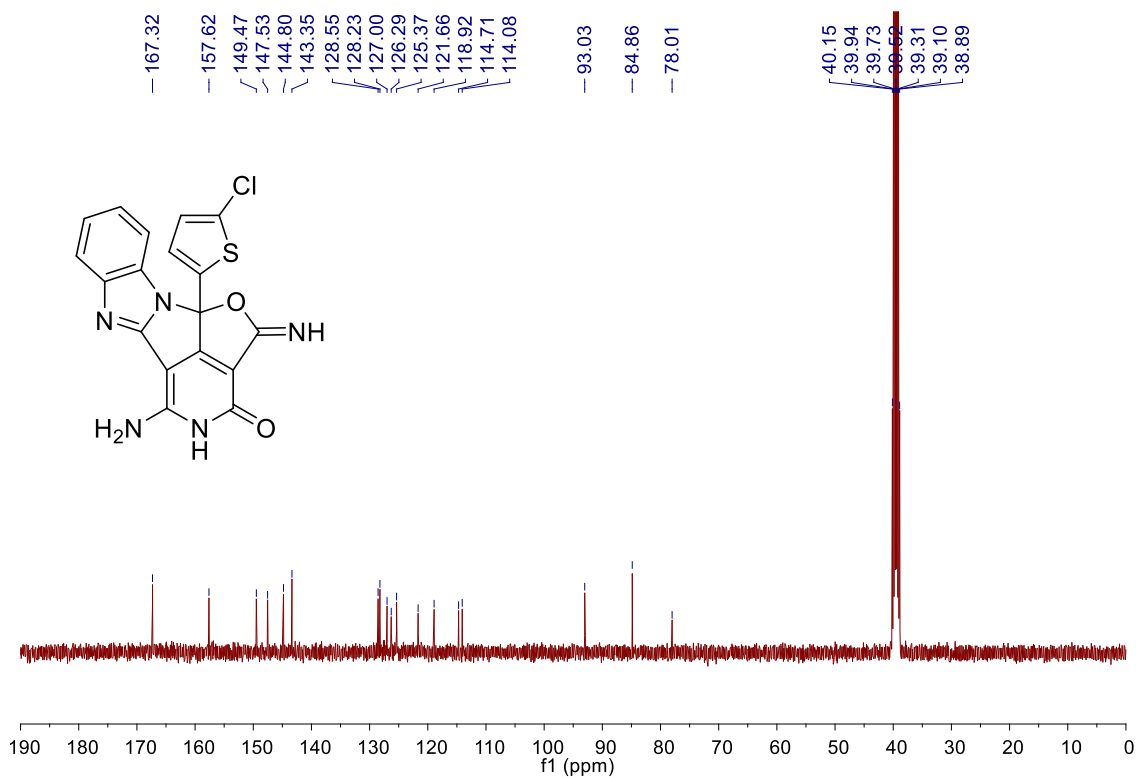
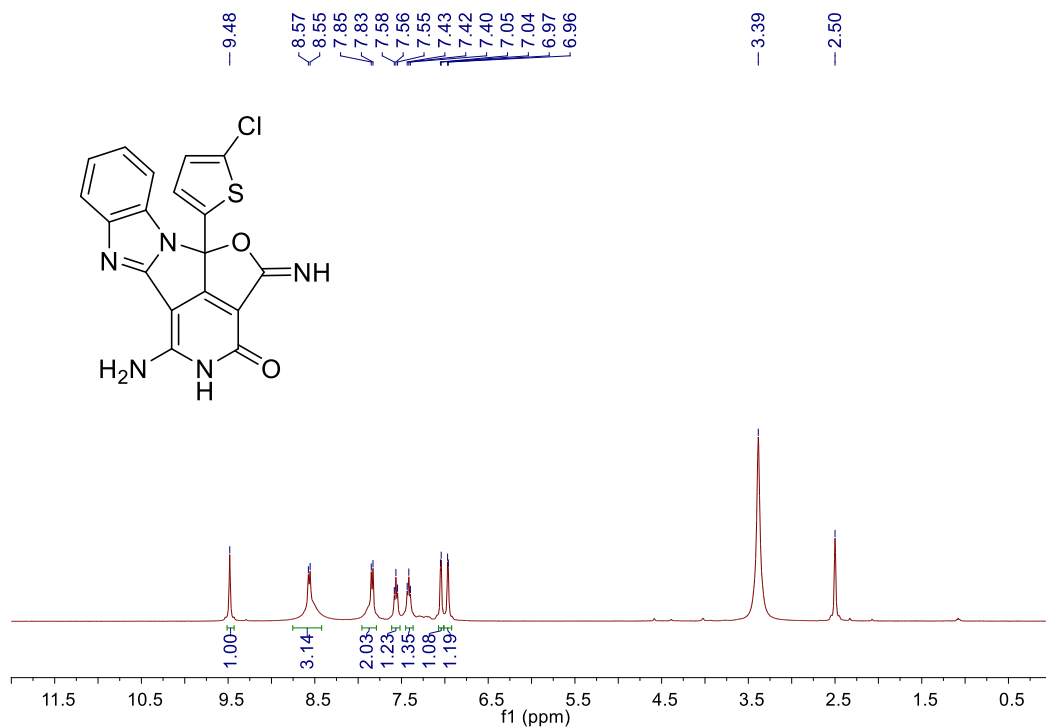


Fig. 11 ¹H, ¹³C spectrum of 5-amino-10c-(5-chlorothiophen-2-yl)-2-imino-2,10c-dihydro-1-oxa-4,6,10b-triazacyclopenta[1,2-a:5,4,3-c'd']diinden-3(4H)-one **S_{1k}**

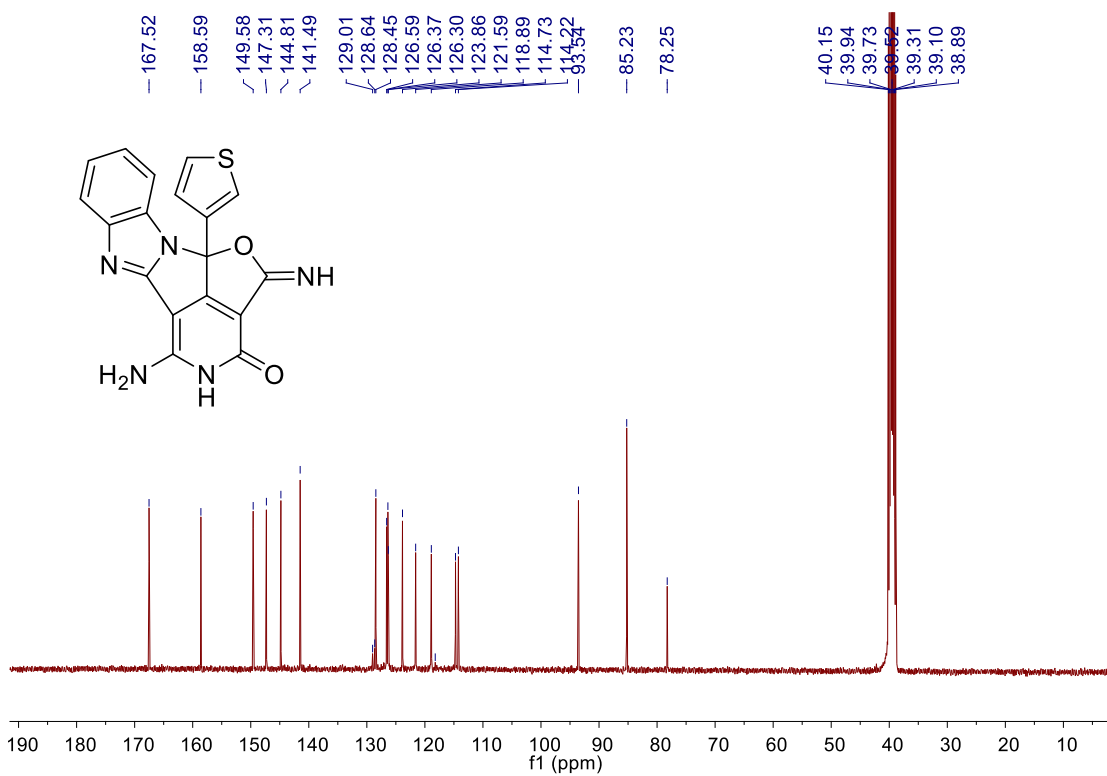
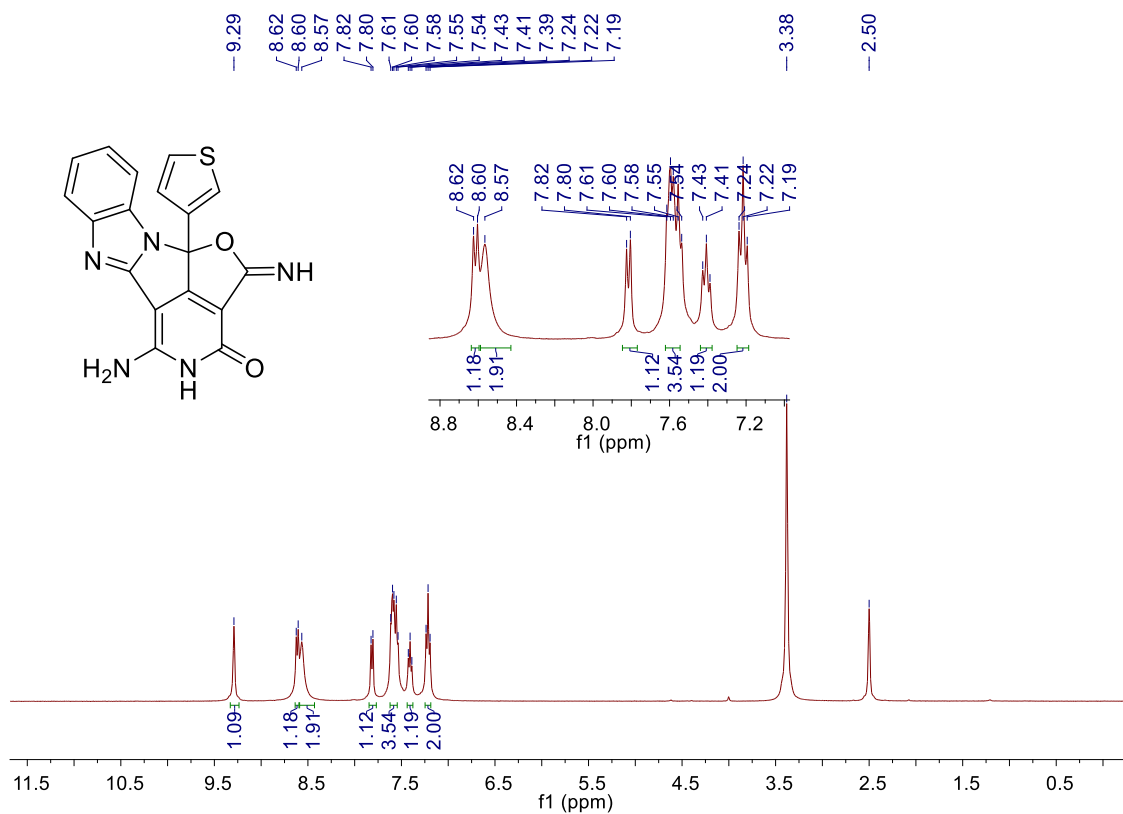


Fig. 12 ^1H , ^{13}C spectrum of 5-amino-2-imino-10c-(thiophen-3-yl)-2,10c-dihydro-1-oxa-4,6,10b-triazacyclopenta[1,2-a:5,4,3-c'd']diinden-3(4H)-one **S₁₁**

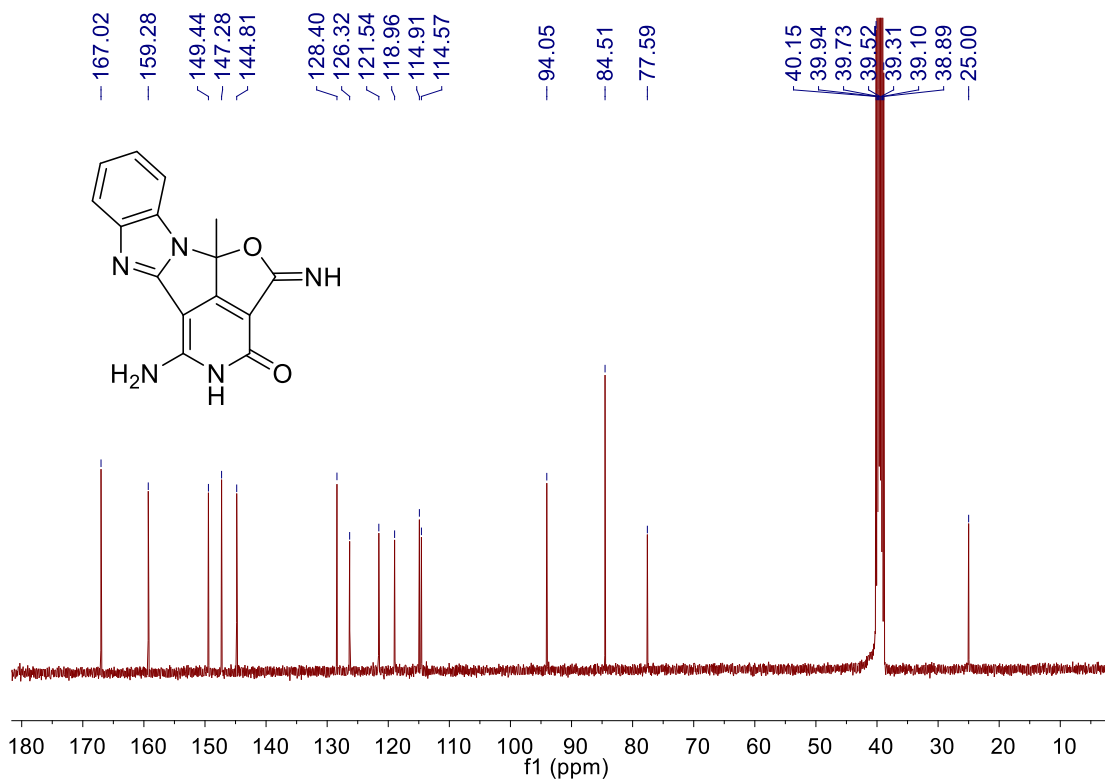
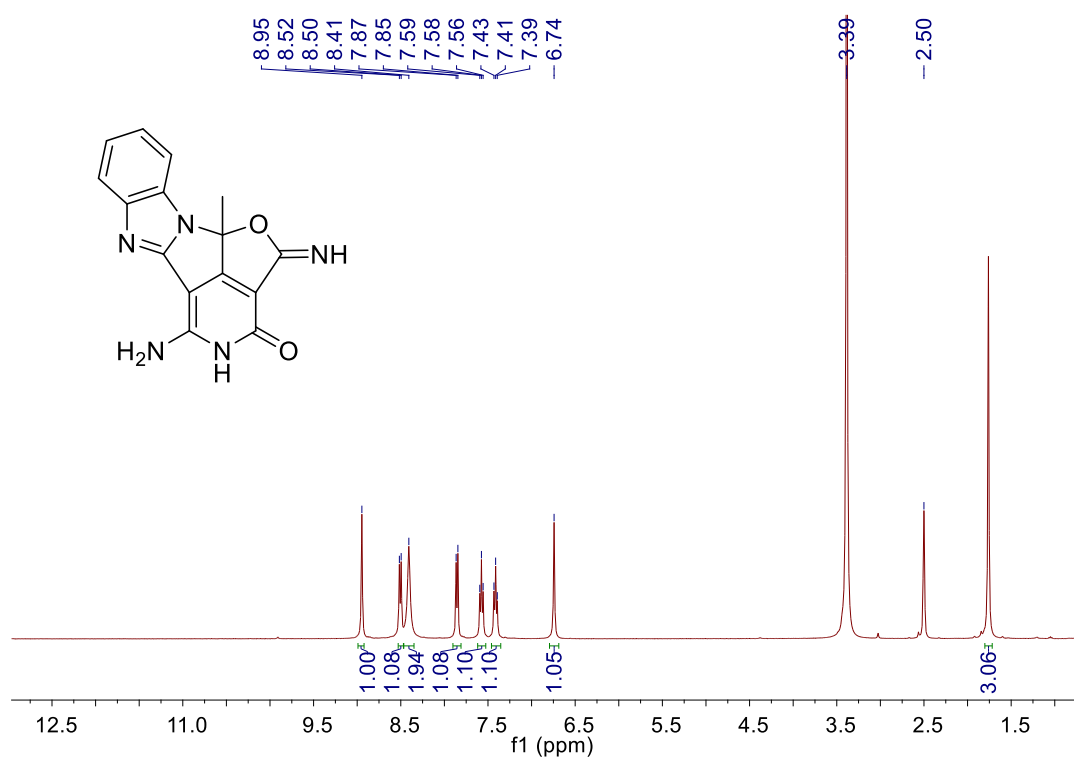


Fig. 13 ^1H , ^{13}C spectrum of 5-amino-2-imino-10c-methyl-2,10c-dihydro-1-oxa-4,6,10b-triazacyclopenta[1,2-a:5,4,3-c'd']diinden-3(4H)-one **S_{1m}**

Synthetic procedure for the synthesis of pyrrolo[3,4-d]pyridine-13-carboxamide S₂

A three component reaction was performed between 4-methyl phenylglyoxal (1mmol) (**A₂**), benzimidazole acetonitrile (**B₁**) (2mmol) in the presence of mild base catalyst as DABCO at room temperature in ethanol were taken in round bottom flask. The progress of the reaction was monitored by TLC for completion of the reaction. The reaction mixture formed yellow precipitate to afford the required product in 30 min. The precipitate washed with 10 mL of EtOH solvent to remove unreacted starting material and finally observed yellow solid yield of 80%. It was showed single spot in checking TLC and the crude product was confirmed by ¹H NMR, ¹³C NMR and HRMS spectra without further purification.

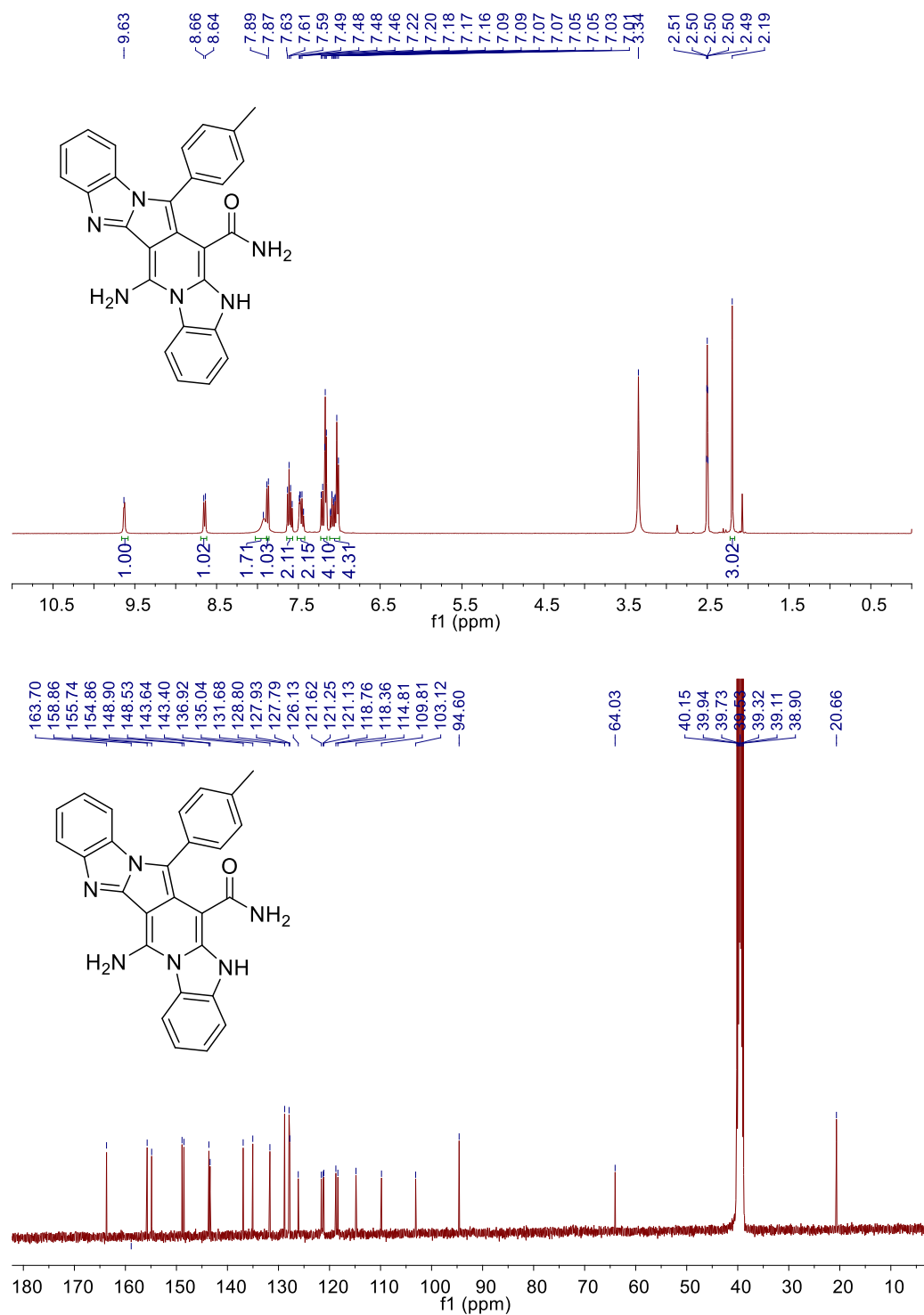


Fig. 14 ¹H, ¹³C spectrum of 6-amino-14-(p-tolyl)-12H-benzo[4',5']imidazo[1',2':1,5]pyrrolo[3,4-d]benzo[4,5]imidazo [1,2-a]pyridine-13-carboxamide **S_{2a}**

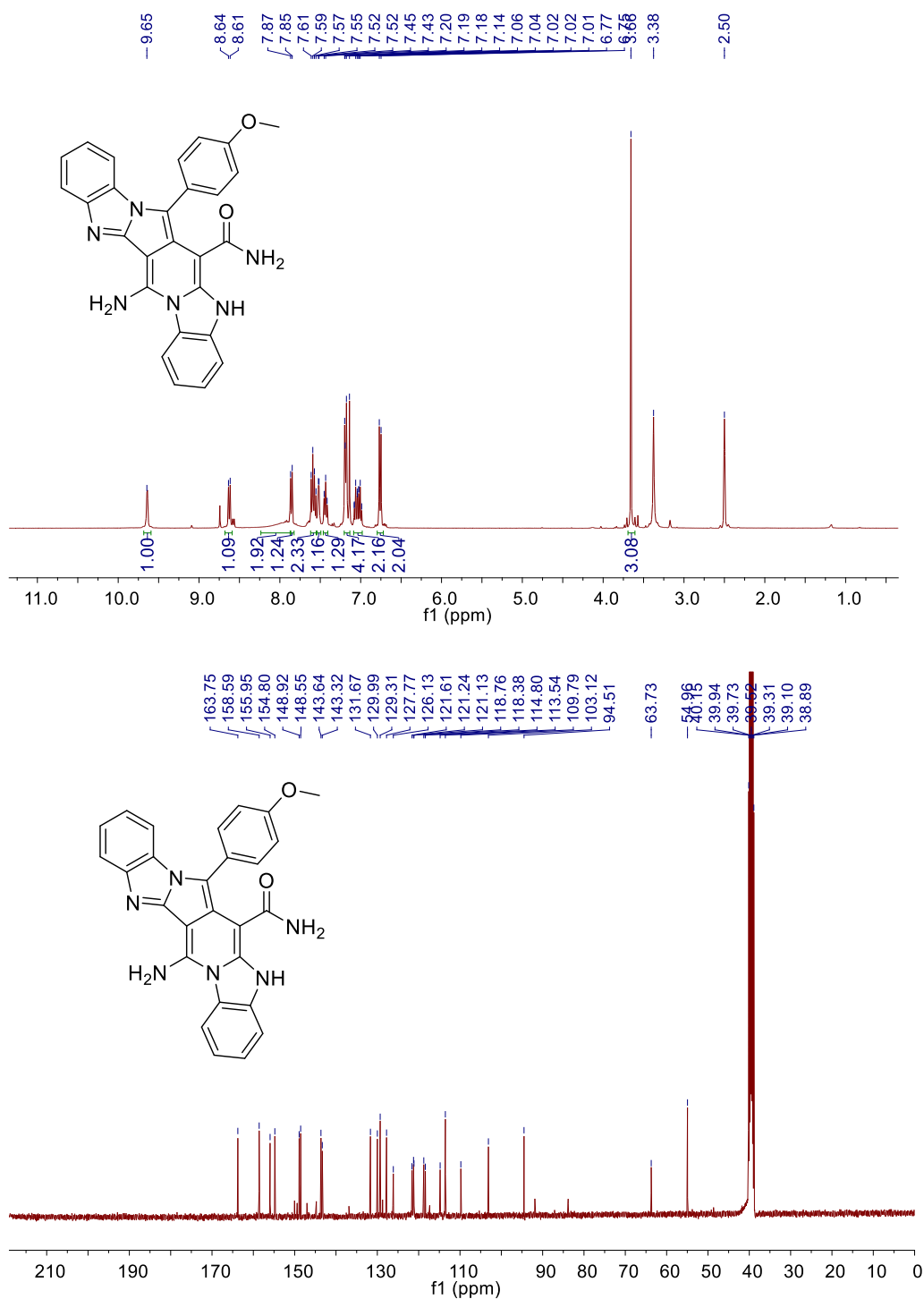


Fig. 15 ¹H, ¹³C spectrum of 6-amino-14-(4-methoxyphenyl)-12H-benzo[4',5']imidazo[1',2':1,5] pyrrolo[3,4-d]benzo[4,5] imidazo[1,2-a]pyridine-13-carboxamide **S2b**

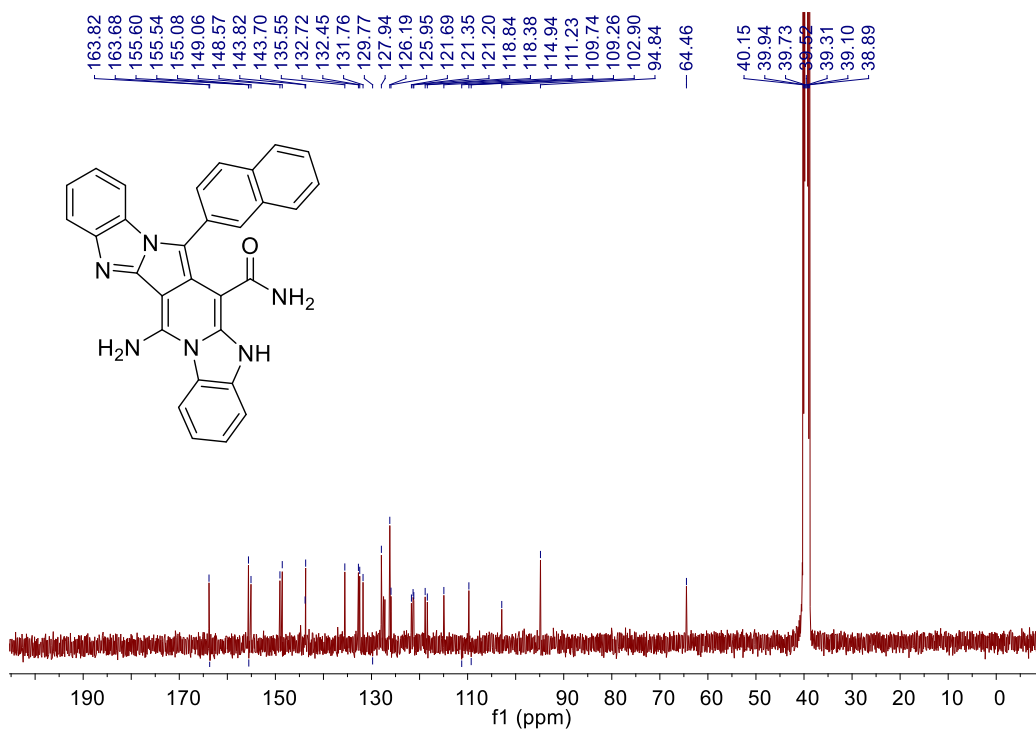
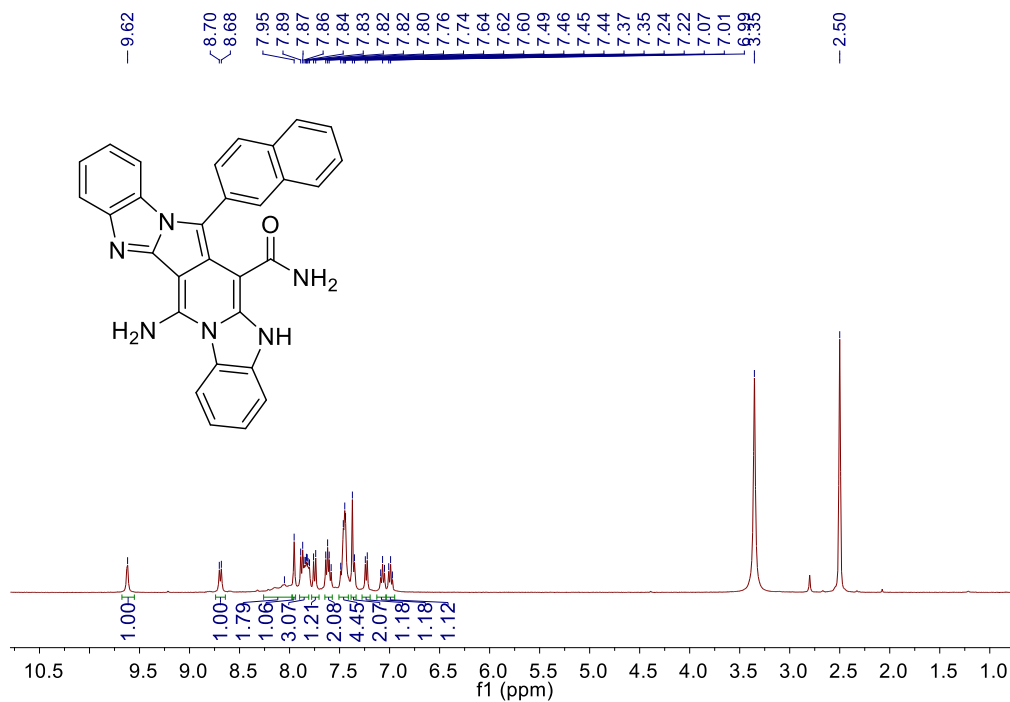


Fig. 16 ¹H, ¹³C spectrum of 6-amino-14-(naphthalen-2-yl)-12H-benzo[4',5']imidazo[1',2':1,5]pyrrolo[3,4-d]benzo[4,5]imidazo[1,2-a]pyridine-13-carboxamide **S**_{2c}

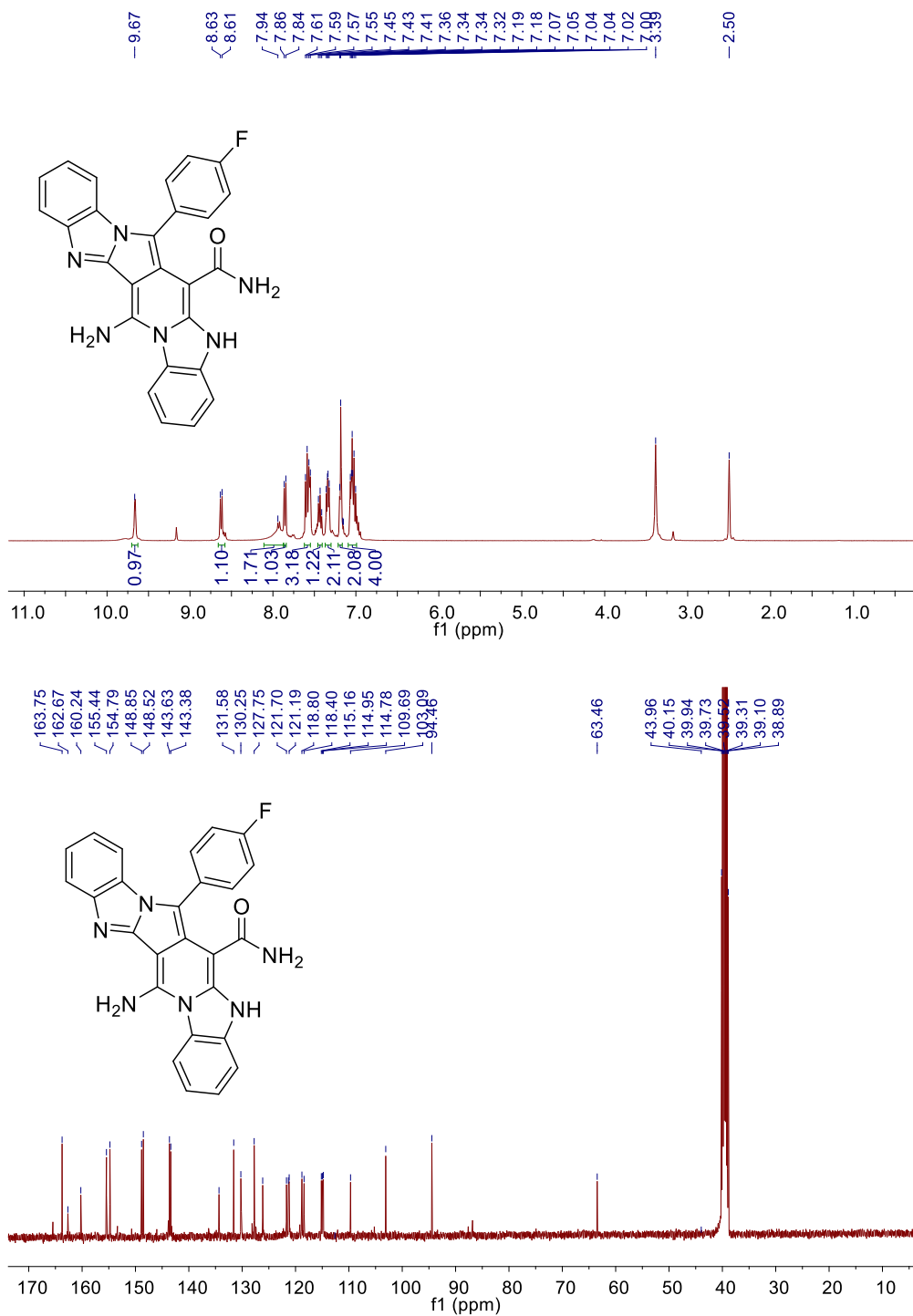


Fig. 17 ¹H, ¹³C spectrum of 6-amino-14-(4-fluorophenyl)-12H-benzo[4',5']imidazo[1',2':1,5]pyrrolo[3,4-d]benzo[4,5]imidazo[1,2-a]pyridine-13-carboxamide **S_{2a}**

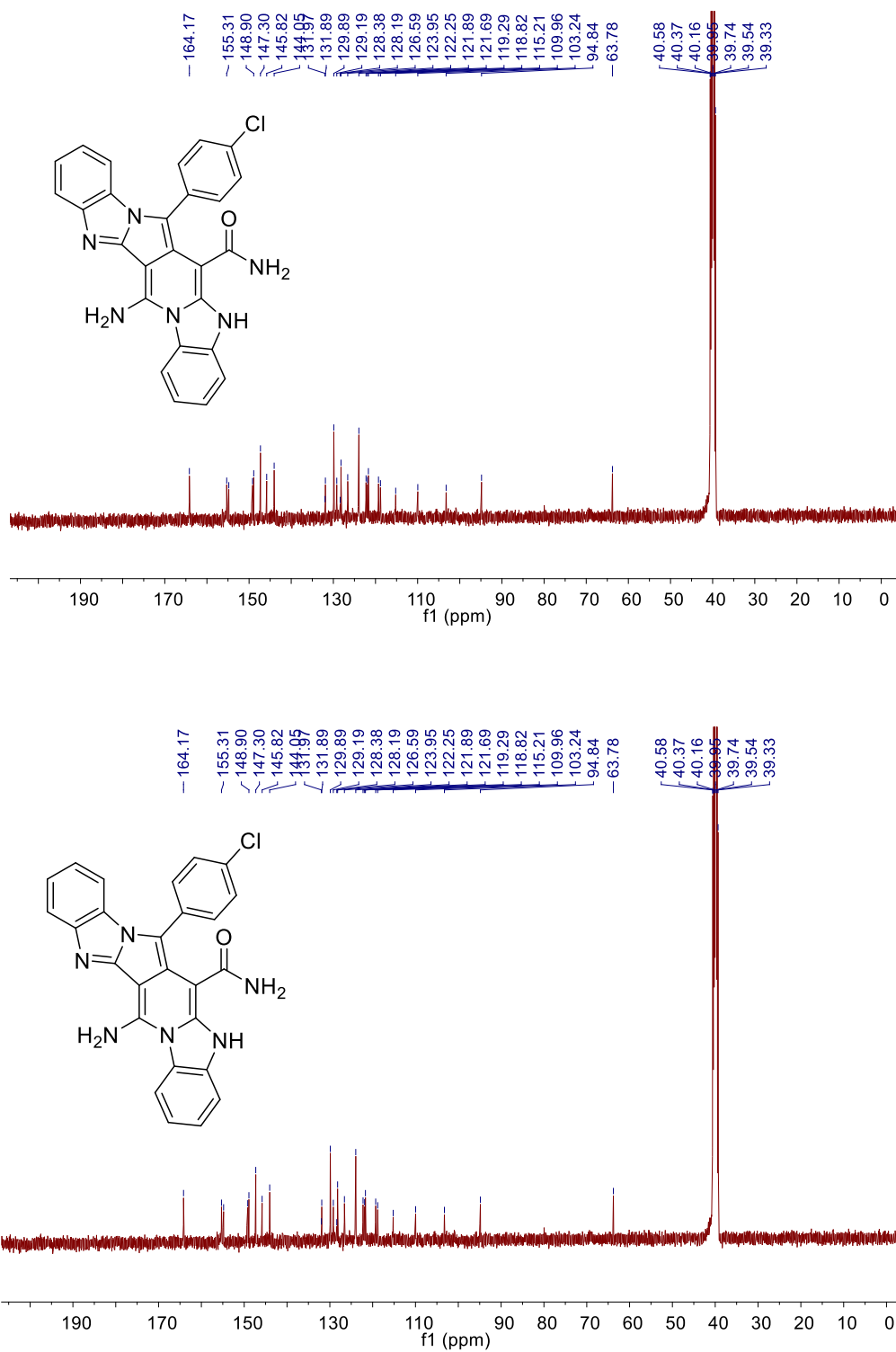


Fig. 18 ^1H , ^{13}C spectrum of 6-amino-14-(4-chlorophenyl)-12H-benzo[4,5']imidazo[1',2':1,5]pyrrolo[3,4-d]benzo[4,5]imidazo[1,2-a]pyridine-13-carboxamide **S_{2e}**

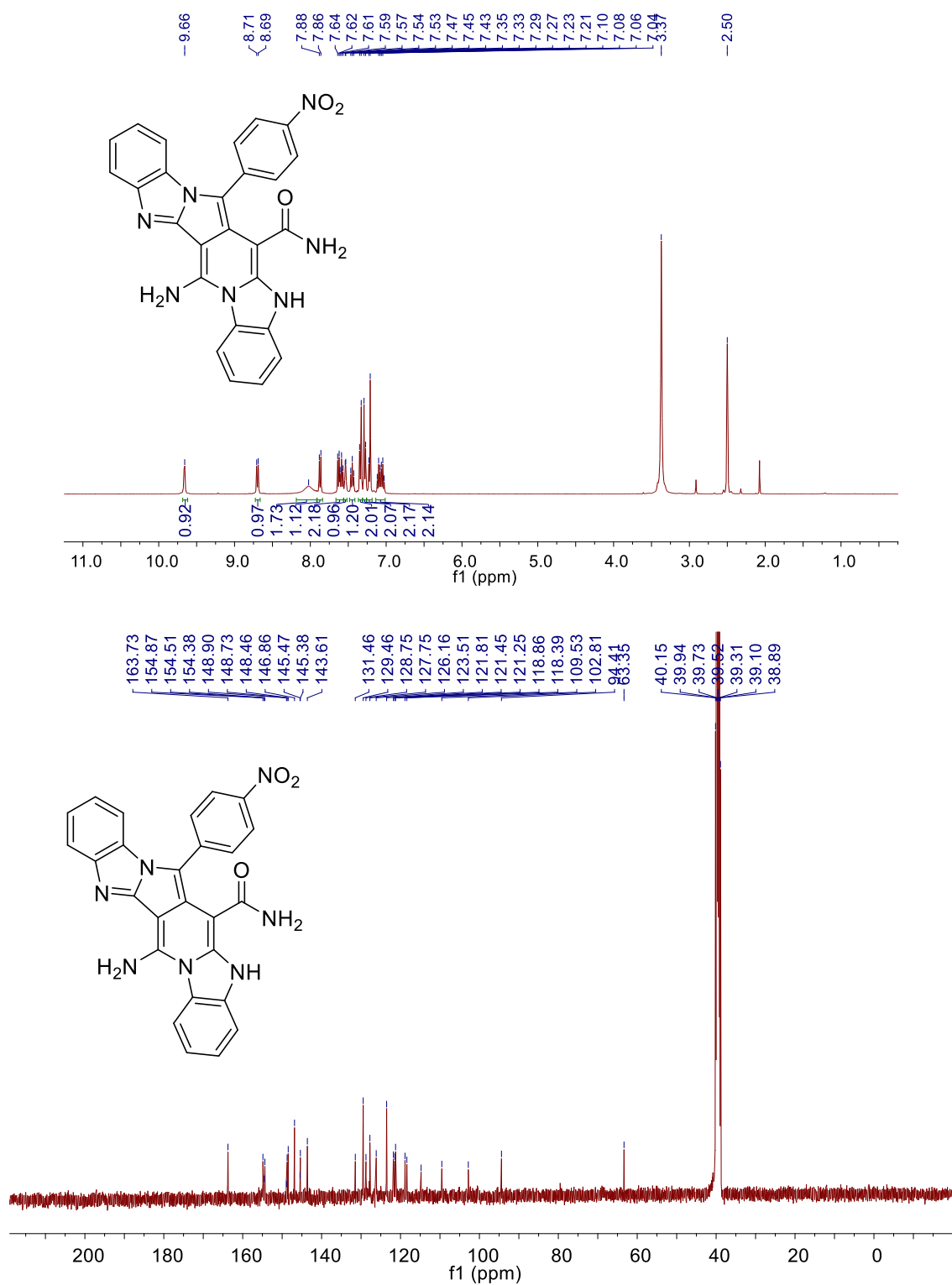


Fig. 19 ¹H, ¹³C spectrum of 6-amino-14-(4-nitrophenyl)-12H-benzo[4',5']imidazo[1',2':1,5]pyrrolo[3,4-d]benzo[4,5]imidazo[1,2-a]pyridine-13-carboxamide **S_{2f}**

Synthetic procedure for the synthesis of 2-amino-3-(1H-benzo[d]imidazol-2-yl)-10a-phenyl-10aH-benzo[d]furo[3',2':4,5] pyrrolo[1,2-a]imidazole-4-carboxamide **S₃**

Initially, the reaction was carried out between 4-methyl phenylglyoxal (1 mmol) (**A₂**), benzimidazole acetonitrile (2 mmol) (**B₁**) in the presence of NaO^tBu catalyst at room temperature in open atmosphere in the round bottom flask. The progress of the reaction was monitored by TLC for completion of the reaction. The reaction mixture turned to pale yellow precipitate in 1h and the solid washed with suitable EtOH solvent 5x3 mL for removal of unreacted starting material. Finally observed pale yellow solid with good yield of 85% **S_{3a}**. The product was confirmed by ¹H NMR, ¹³C NMR, FTIR and HRMS spectra.

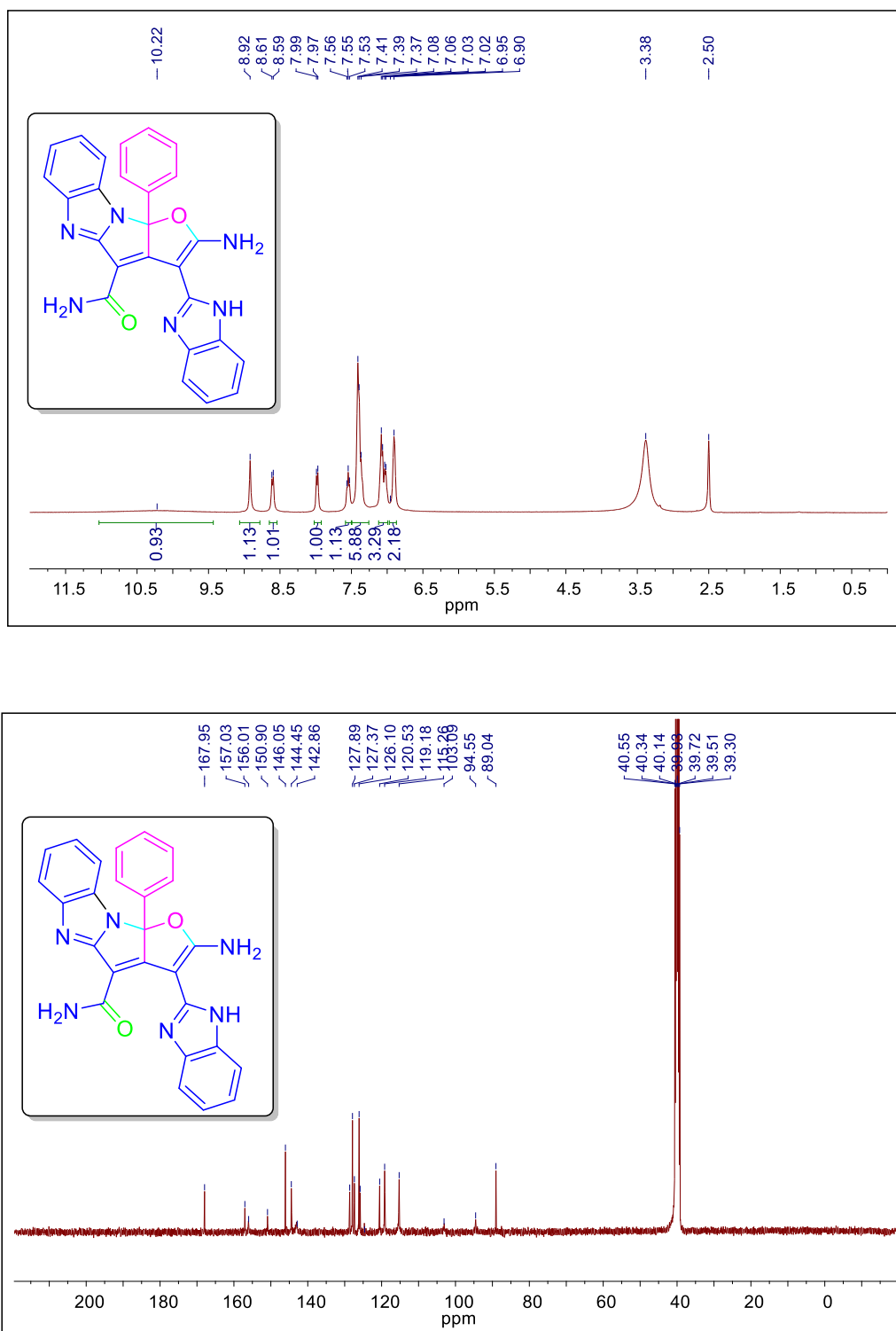


Fig. 20 ¹H, ¹³C spectrum of 2-amino-3-(1H-benzo[d]imidazol-2-yl)-10a-phenyl-10aH-benzo[d]furo[3',2':4,5]pyrrolo [1,2-a]imidazole-4-carboxamide **S_{3a}**

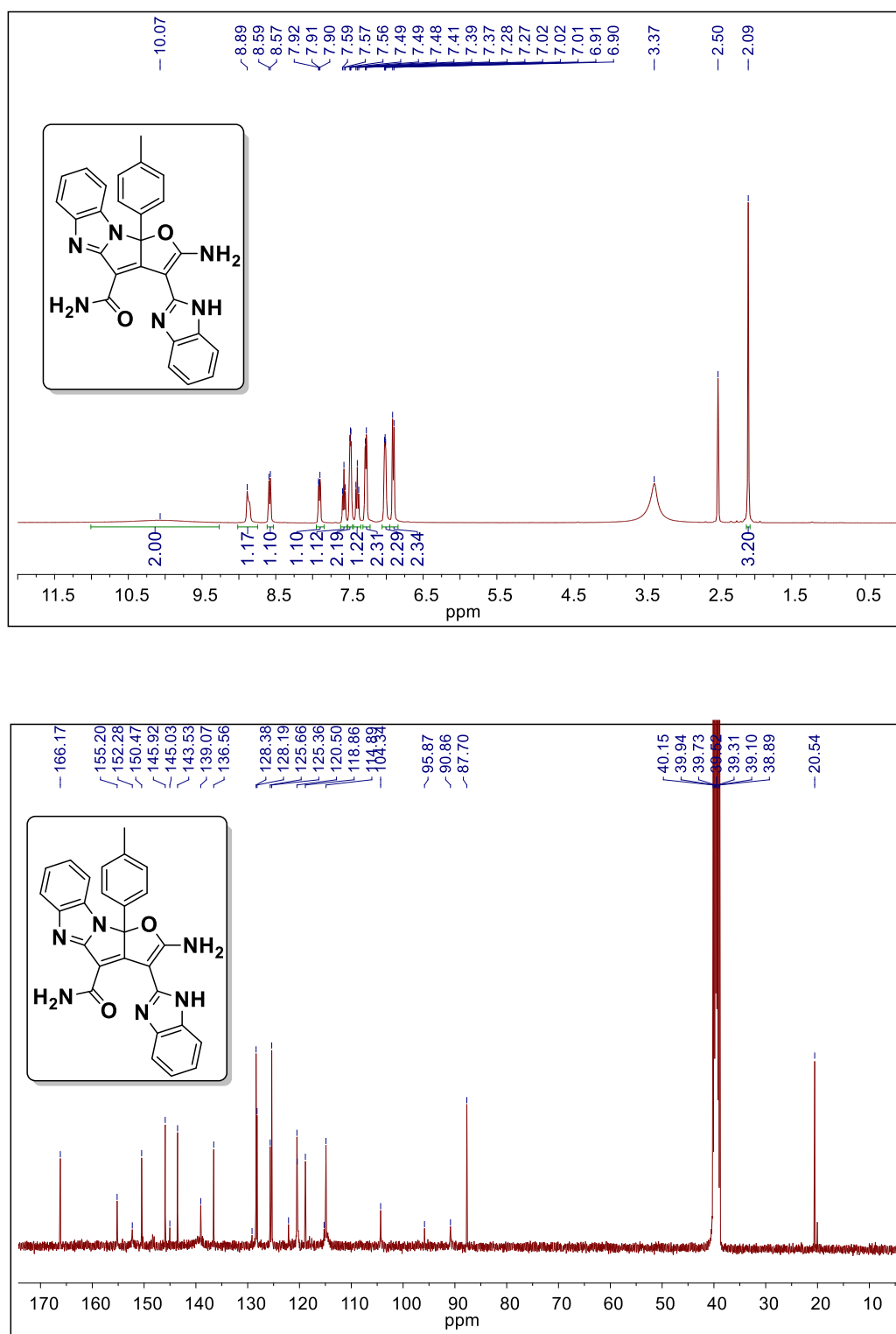


Fig. 21 ¹H, ¹³C spectrum of 2-amino-3-(1H-benzo[d]imidazol-2-yl)-10a-(p-tolyl)-10aH-benzo[d]furo[3',2':4,5] pyrrolo [1,2-a]imidazole-4-carboxamide **S_{3b}**

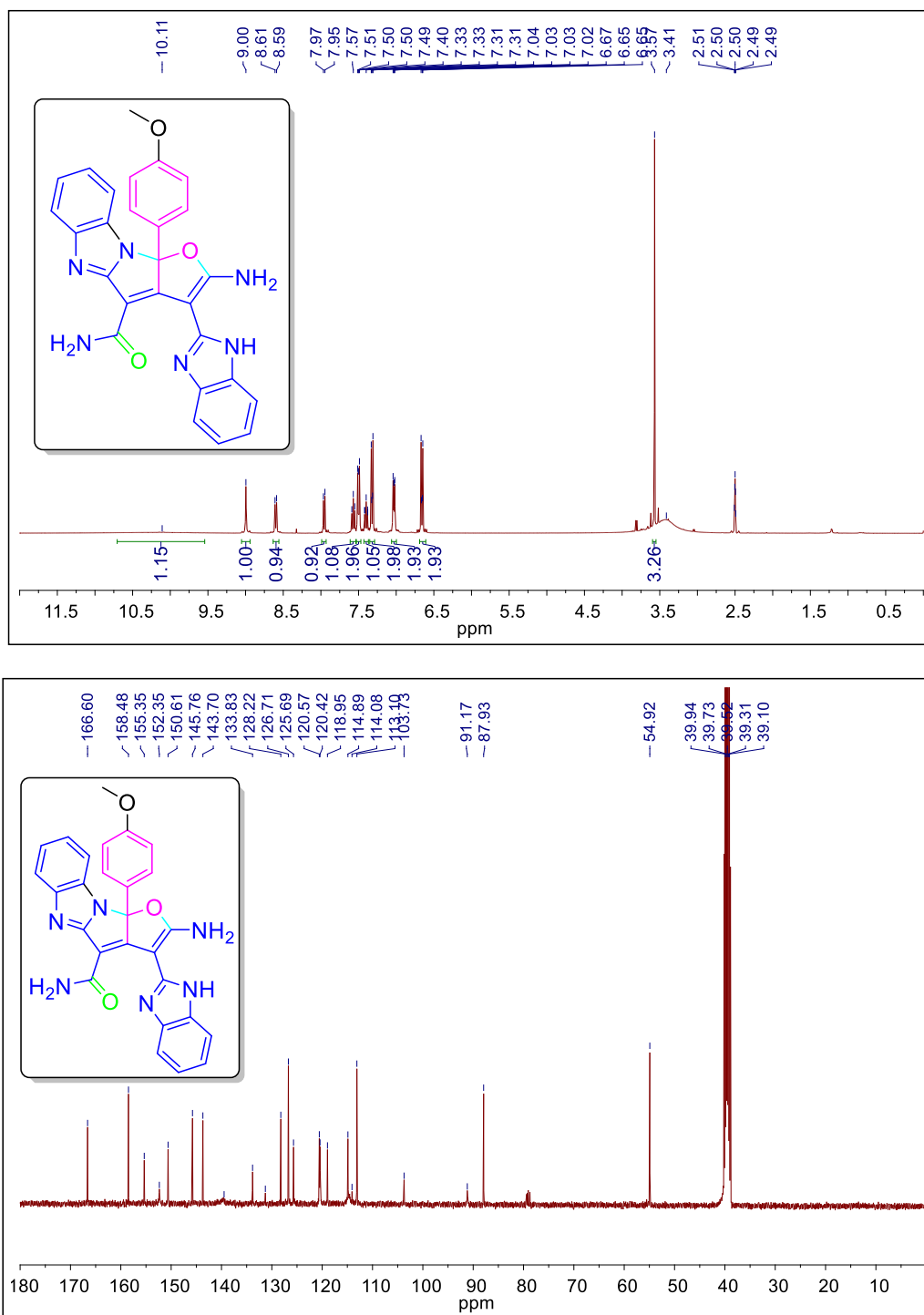


Fig. 22 ¹H, ¹³C spectrum of 2-amino-3-(1H-benzo[d]imidazol-2-yl)-10a-(4-methoxyphenyl)-10aH-benzo[d]furo [3',2':4,5]pyrrolo[1,2-a]imidazole-4-carboxamide **3c**

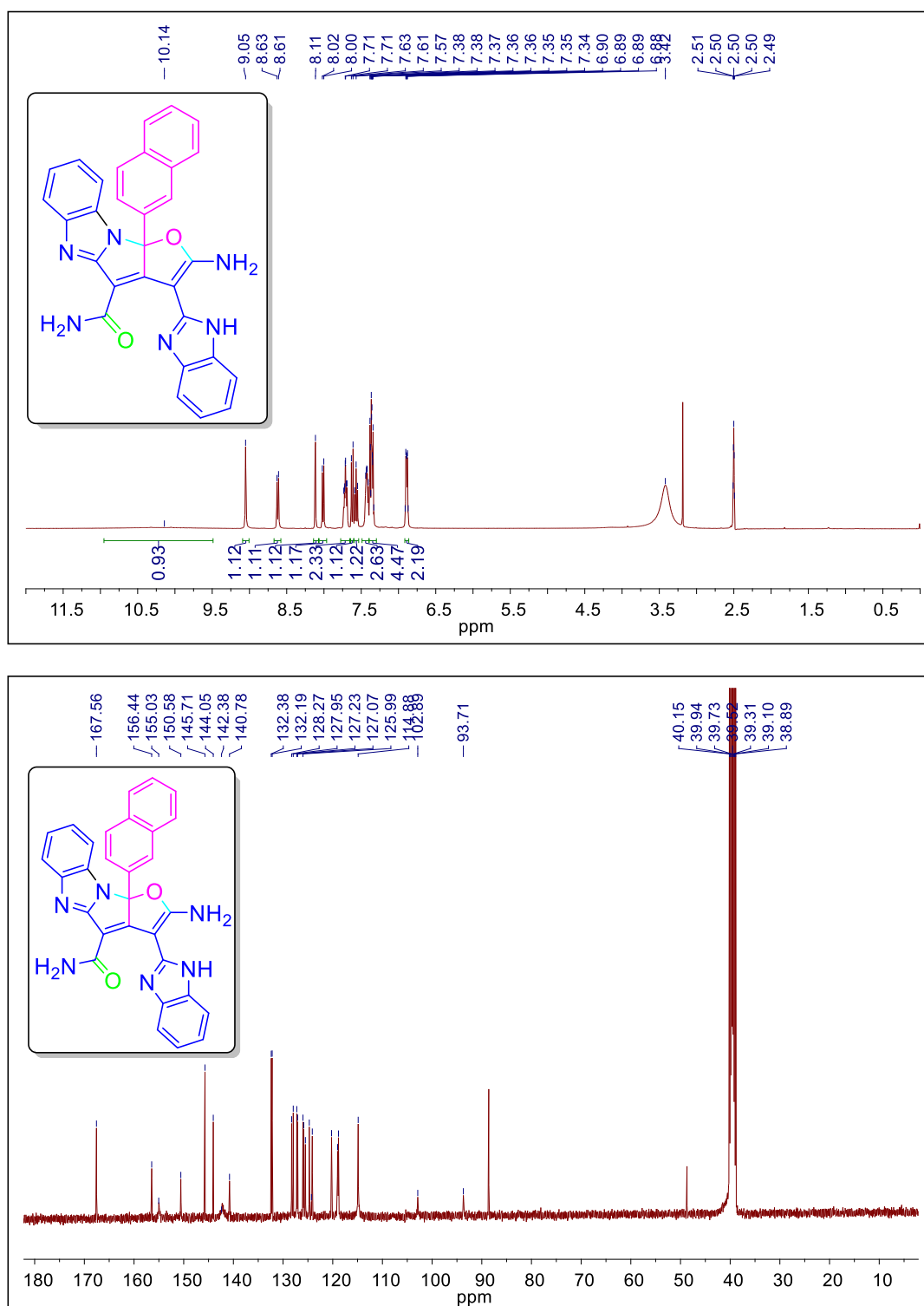


Fig. 23 ¹H, ¹³C spectrum of 2-amino-3-(1H-benzo[d]imidazol-2-yl)-10a-(naphthalen-2-yl)-10aH-benzo[d]furo [3',2':4,5] pyrrolo[1,2-a]imidazole-4-carboxamide **S3a**

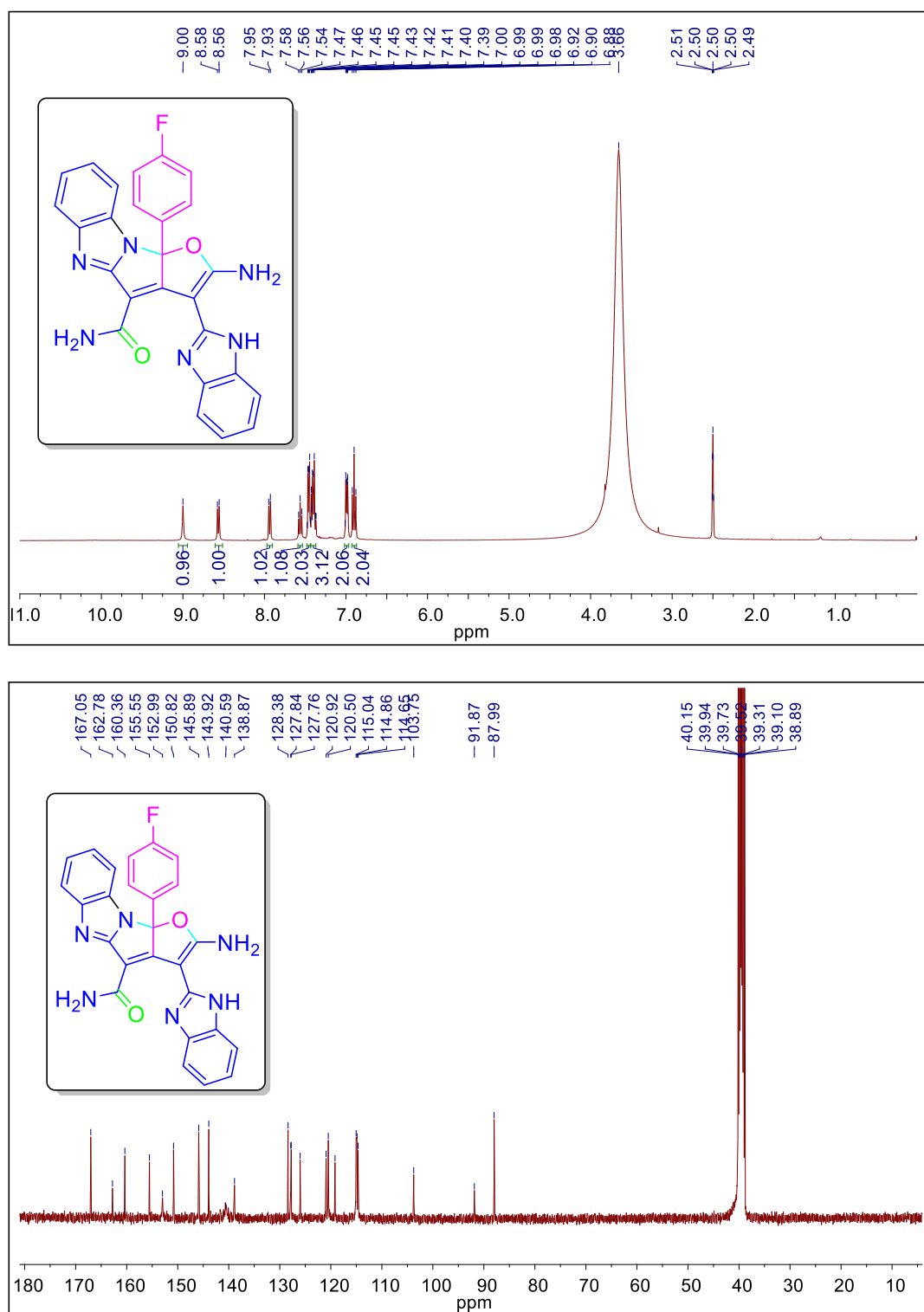


Fig. 24 ¹H, ¹³C spectrum of 2-amino-3-(1H-benzo[d]imidazol-2-yl)-10a-(4-fluorophenyl)-10aH-benzo[d]furo[3',2':4,5] pyrrolo[1,2-a]imidazole-4-carboxamide **S_{3e}**

Synthetic procedure for the synthesis of 5-amino-4-(benzo[d]thiazol-2-yl)-6a-methyl-2-phenyl-3a,6a-dihydrofuro[2,3-b]furan-3-carbonitrile **S₄**

Initially, a three component reaction was performed between methylglyoxal (**A₁₃**), benzoyl acetonitrile (**C₃**) and benzothiazole acetonitrile (**B₂**) in EtOH/H₂O in the presence of DABCO at room temperature. The reaction was monitored by TLC for completion of the reaction. The reaction mixture turned to white precipitate and showed single spot in TLC. Therefore, the precipitate was filtered and washed with 5x3 mL of CH₃CN solution observed white solid yield of 90% **S_{4a}**. The entire product formed was characterized by FTIR, ¹H NMR, ¹³C NMR, and HRMS spectra.

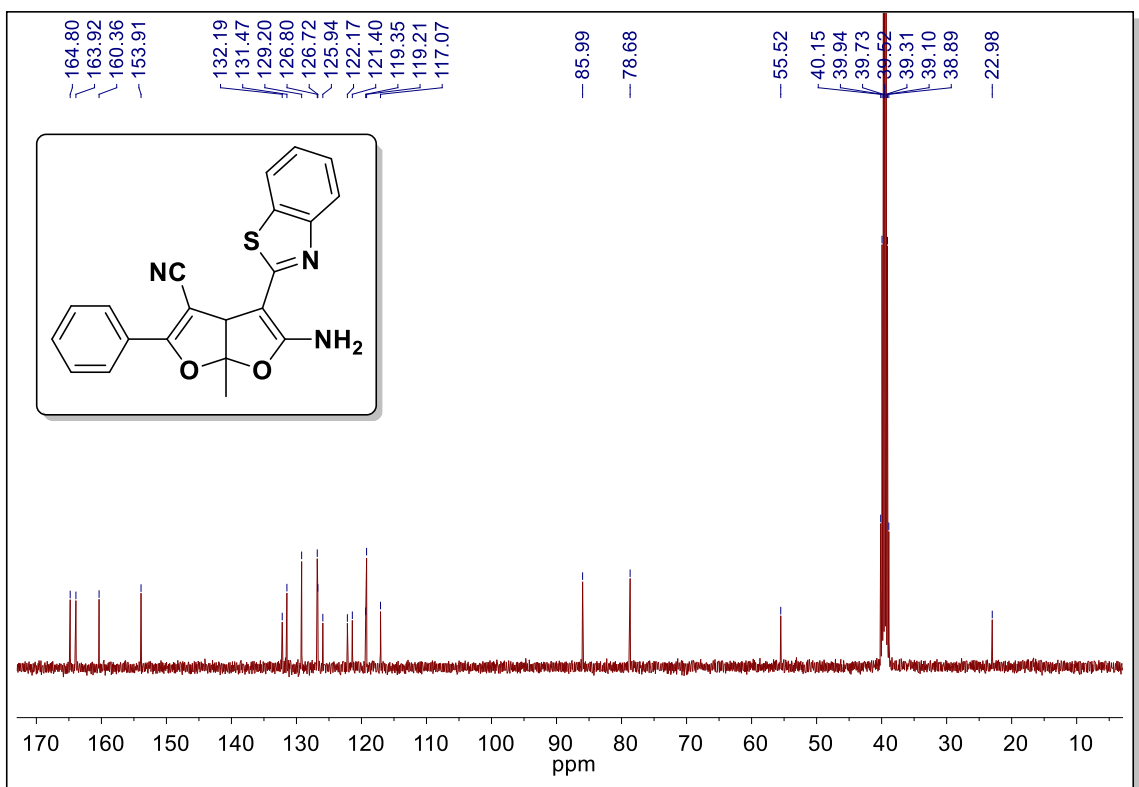
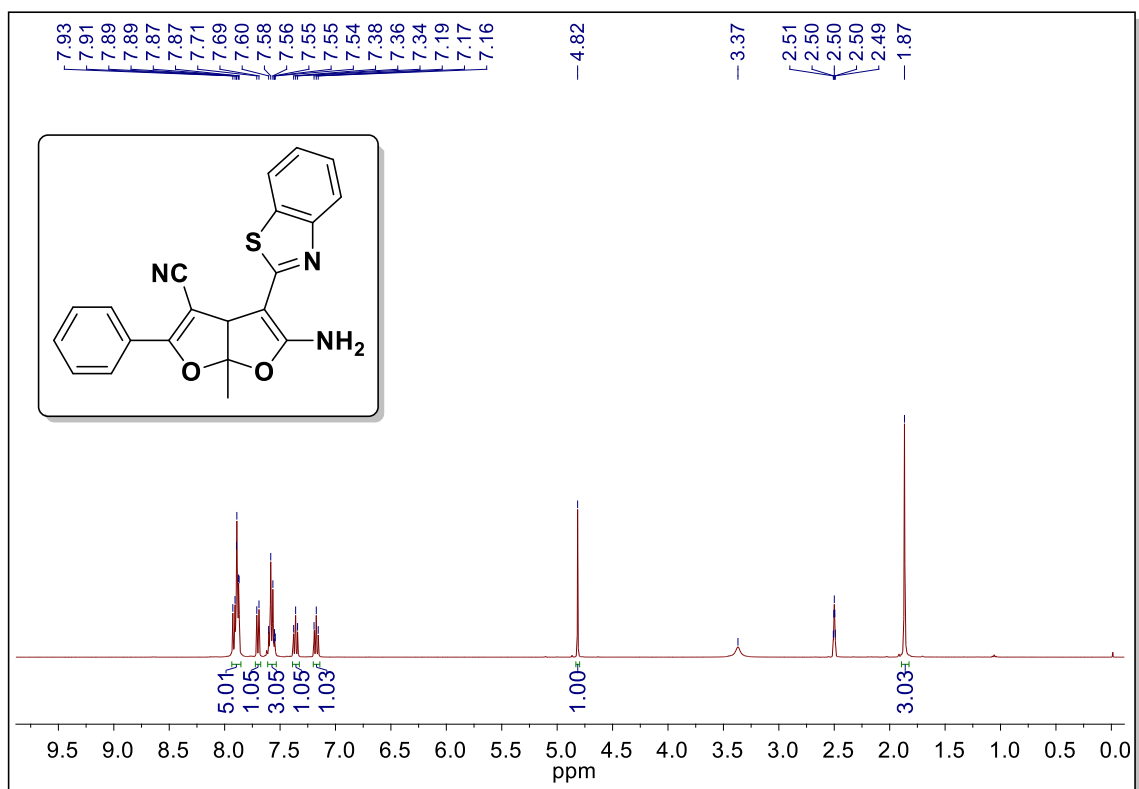


Fig. 25 ¹H, ¹³C spectrum of 5-amino-4-(benzo[d]thiazol-2-yl)-6a-methyl-2-phenyl-3a,6a-dihydrofuro[2,3-b]furan-3-carbonitrile **S**_{4a}

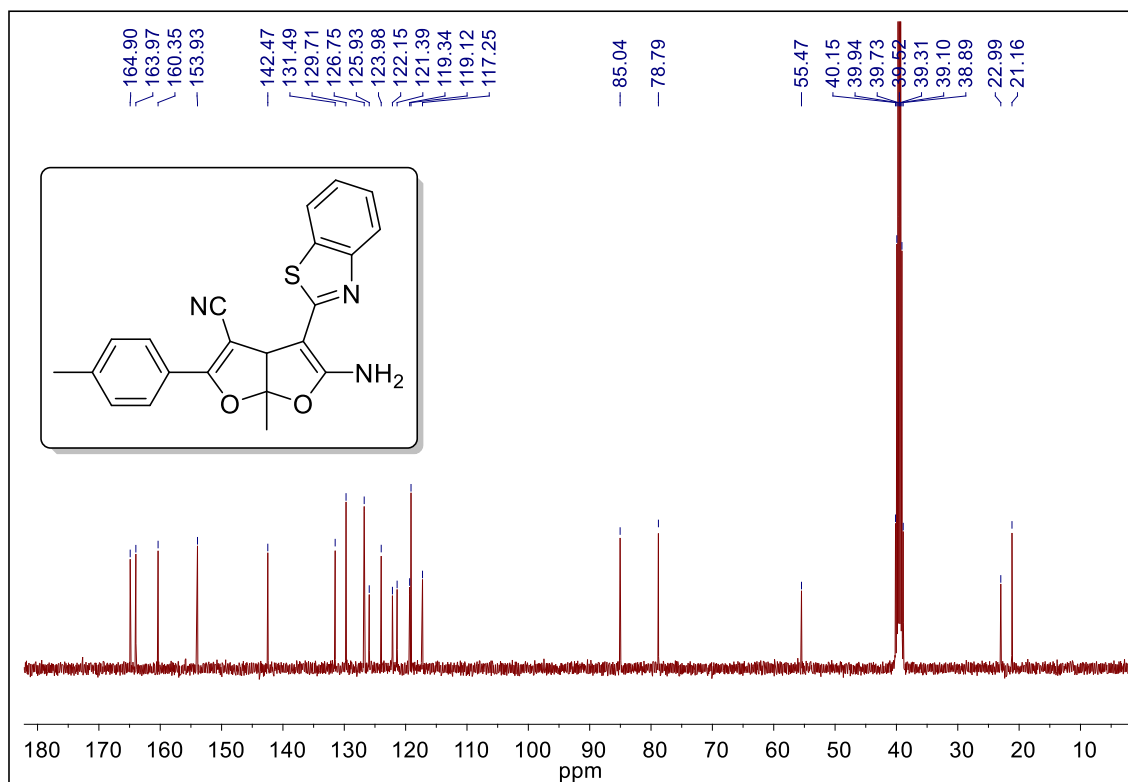
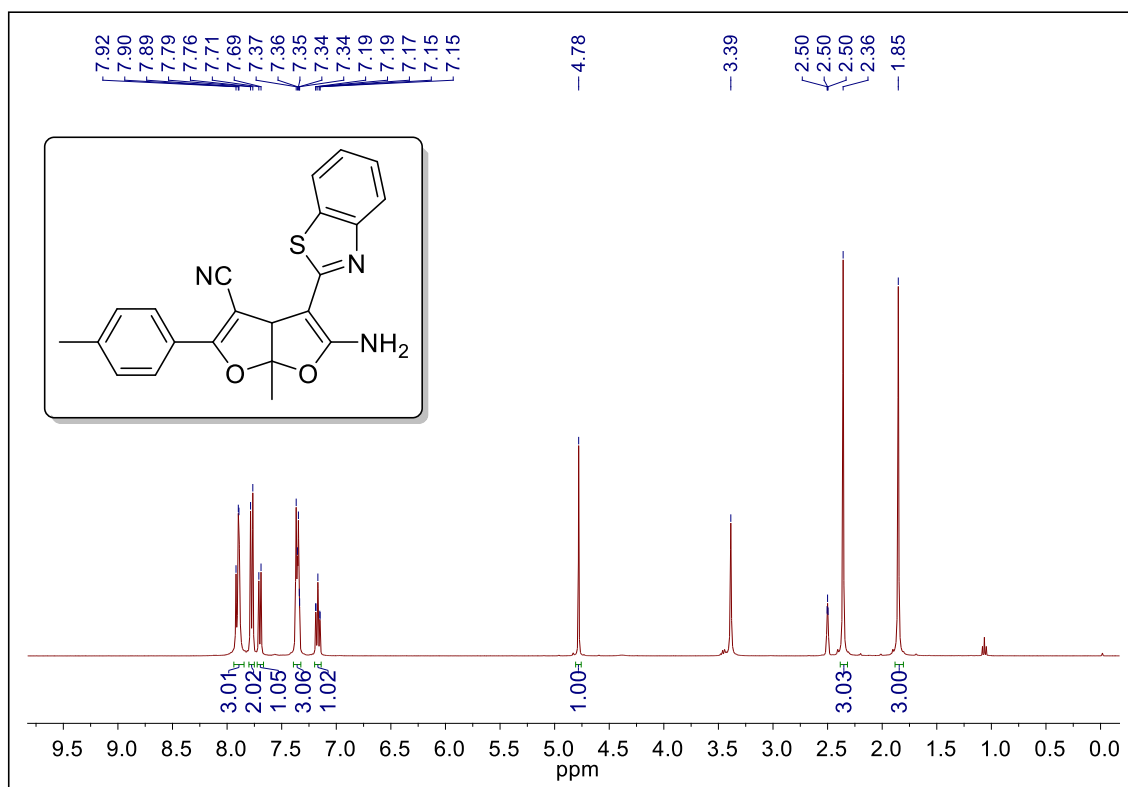


Fig. 26 ¹H, ¹³C spectrum of 5-amino-4-(benzo[d]thiazol-2-yl)-6a-methyl-2-(p-tolyl)-3a,6a-dihydrofuro[2,3-b]furan-3-carbonitrile **S_{4b}**

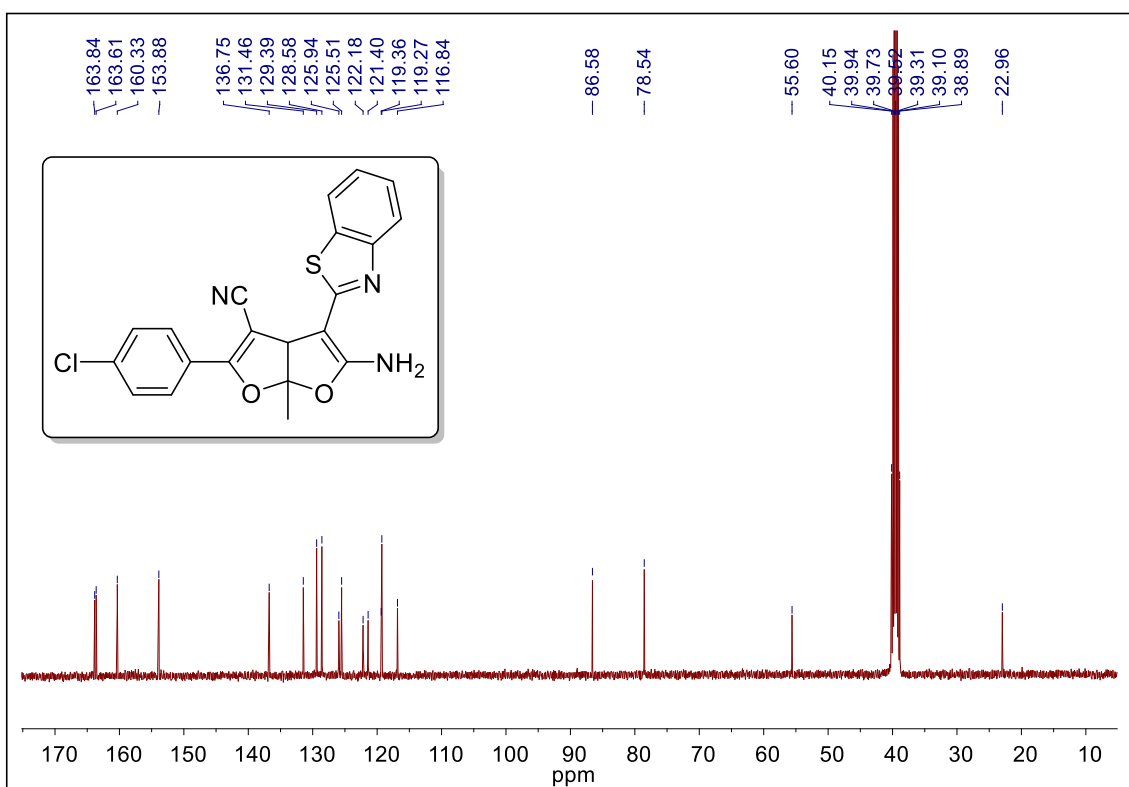
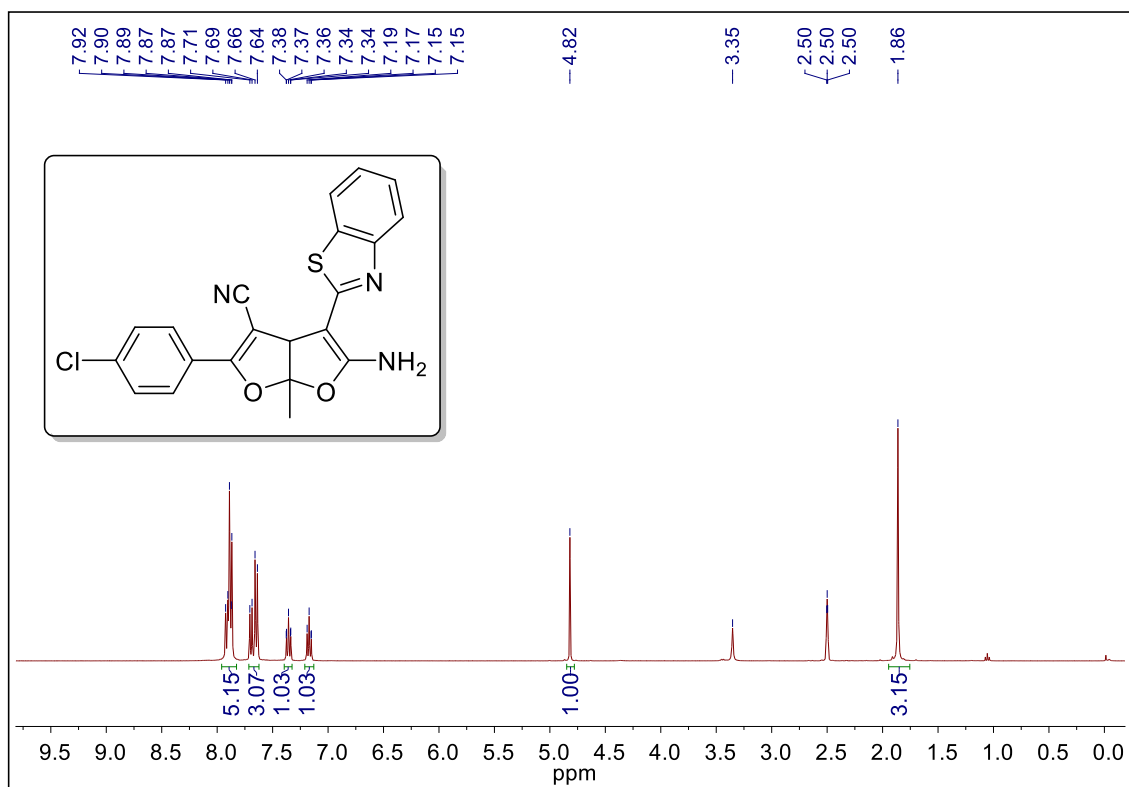


Fig. 27 ¹H, ¹³C spectrum of 5-amino-4-(benzo[d]thiazol-2-yl)-2-(4-chlorophenyl)-6a-methyl-3a,6a-dihydrofuro[2,3-b] furan-3-carbonitrile **S_{4c}**

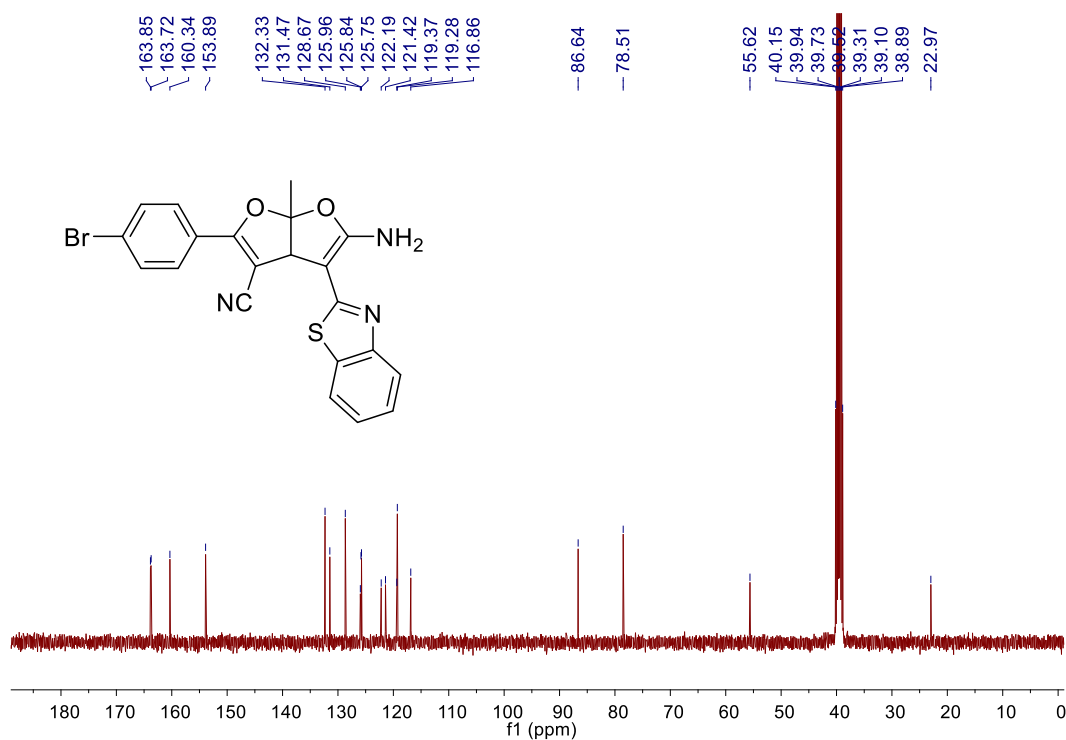
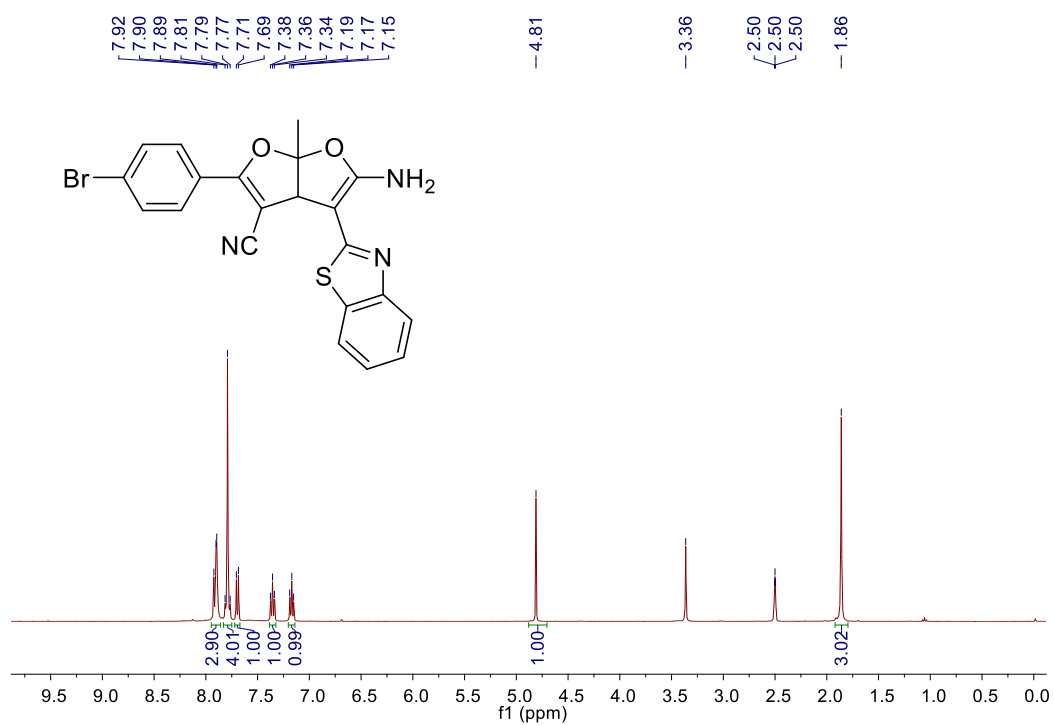


Fig. 28 ¹H, ¹³C spectrum of 5-amino-4-(benzo[d]thiazol-2-yl)-2-(4-bromophenyl)-6a-methyl-3a,6a-dihydrofuro[2,3-b]furan-3-carbonitrile **S_{4d}**

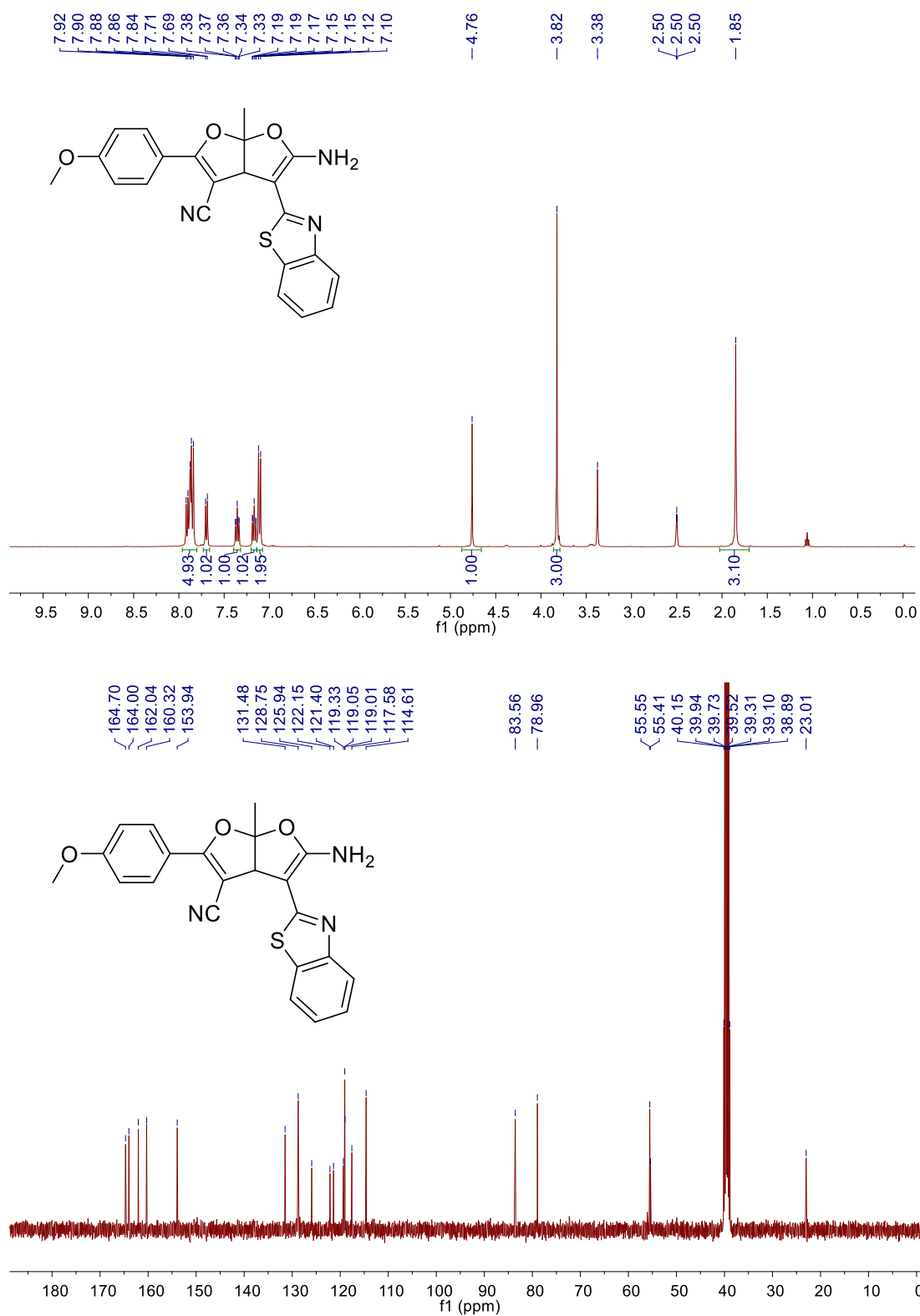


Fig. 29 ¹H, ¹³C spectrum of 5-amino-4-(benzo[d]thiazol-2-yl)-2-(4-methoxyphenyl)-6a-methyl-3a,6a-dihydrofuro[2,3-b]furan-3-carbonitrile **S_{4e}**

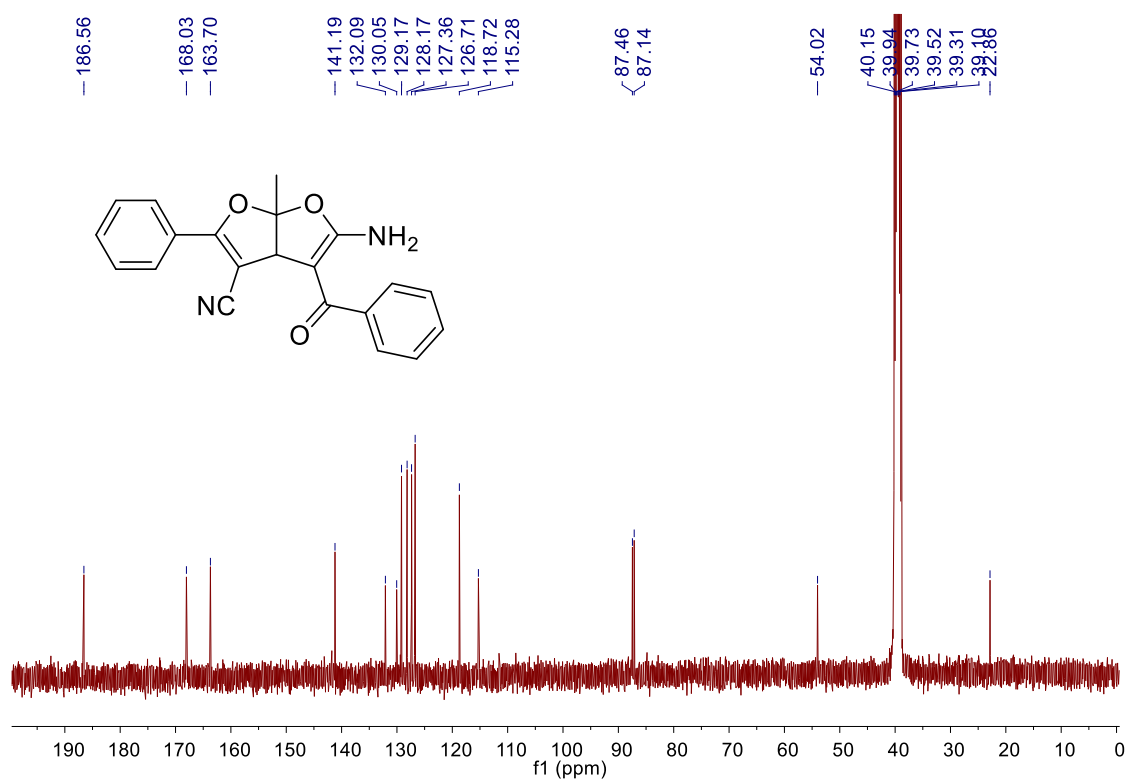
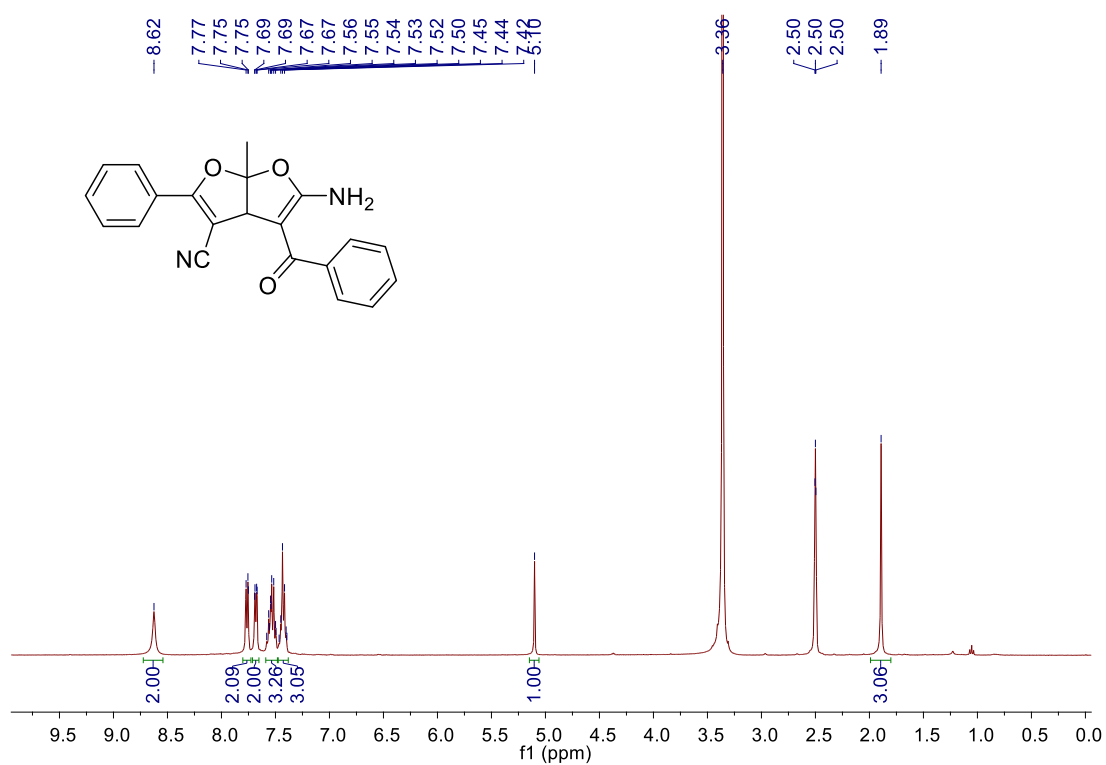


Fig. 30 ¹H, ¹³C spectrum of 5-amino-4-benzoyl-6a-methyl-2-phenyl-3a,6a-dihydrofuro[2,3-b]furan-3-carbonitrile **54f**

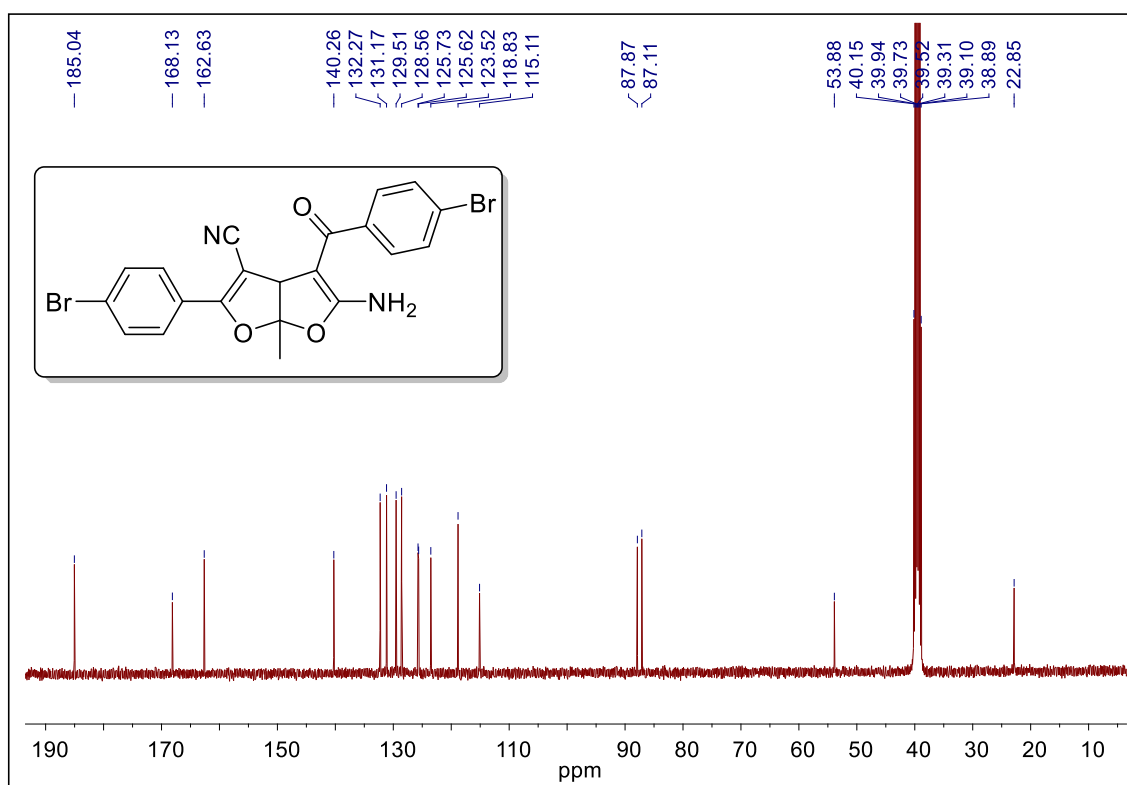
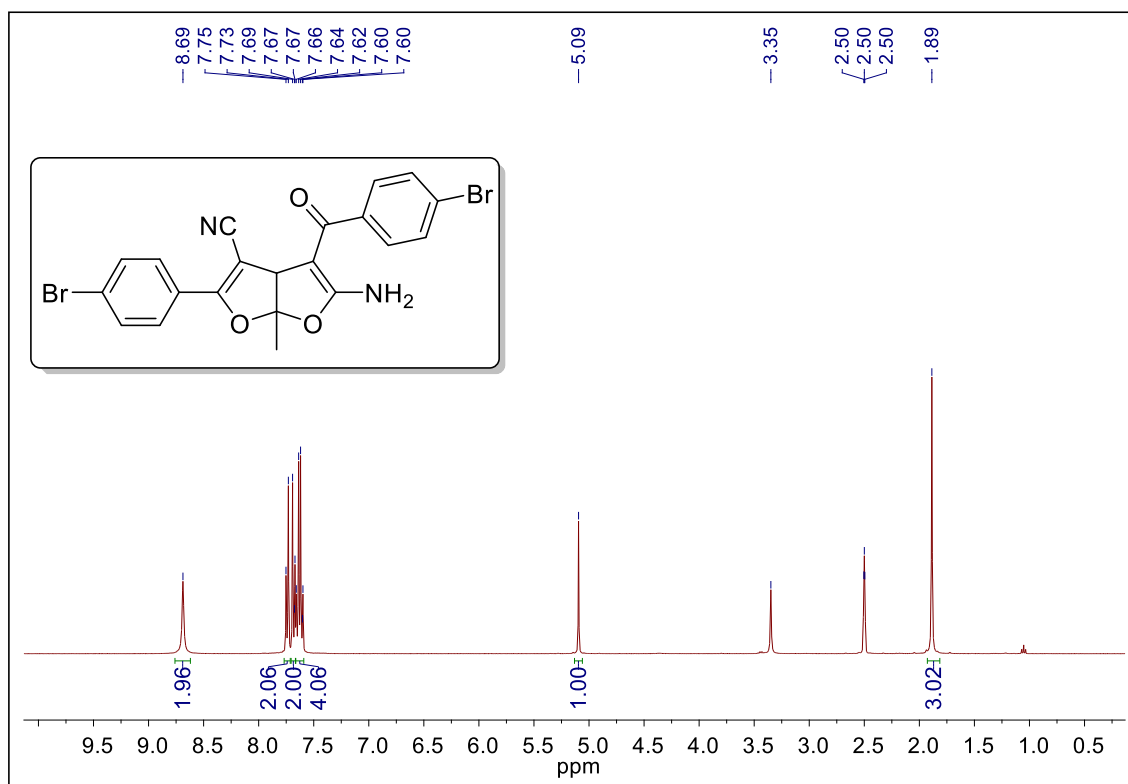


Fig. 31 ¹H, ¹³C spectrum of 5-amino-4-(4-bromobenzoyl)-2-(4-bromophenyl)-6a-methyl-3a,6a-dihydrofuro[2,3-b]furan-3-carbonitrile **S_{4g}**

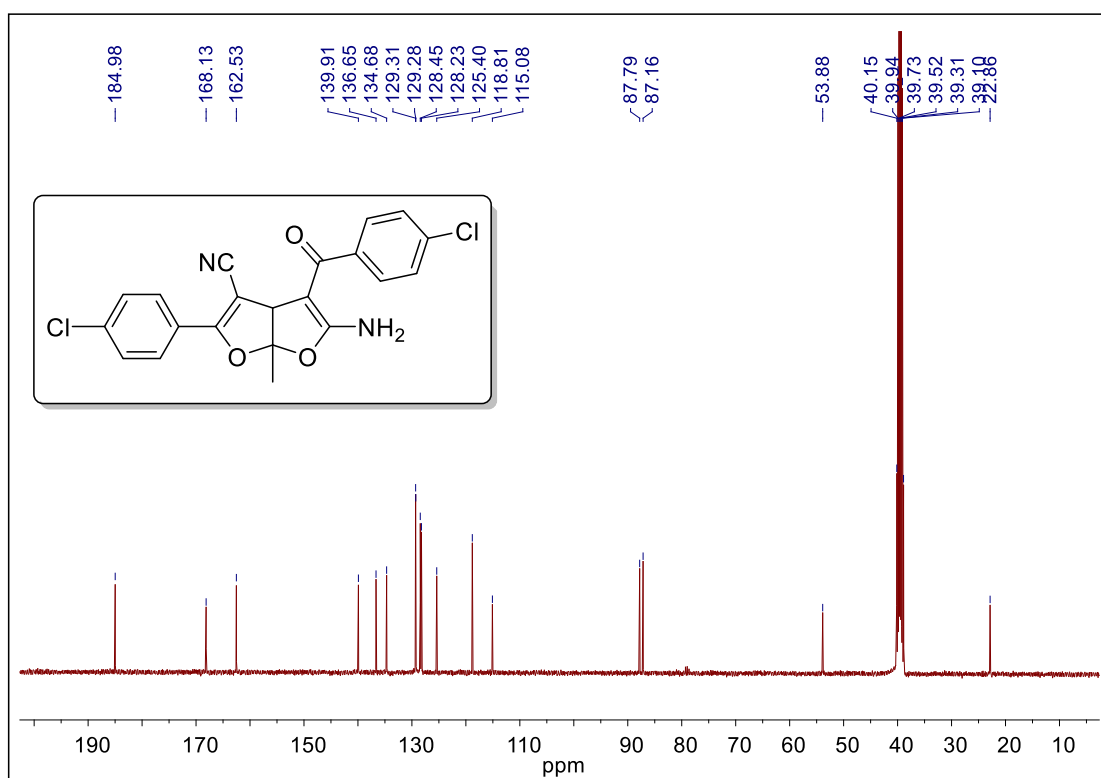
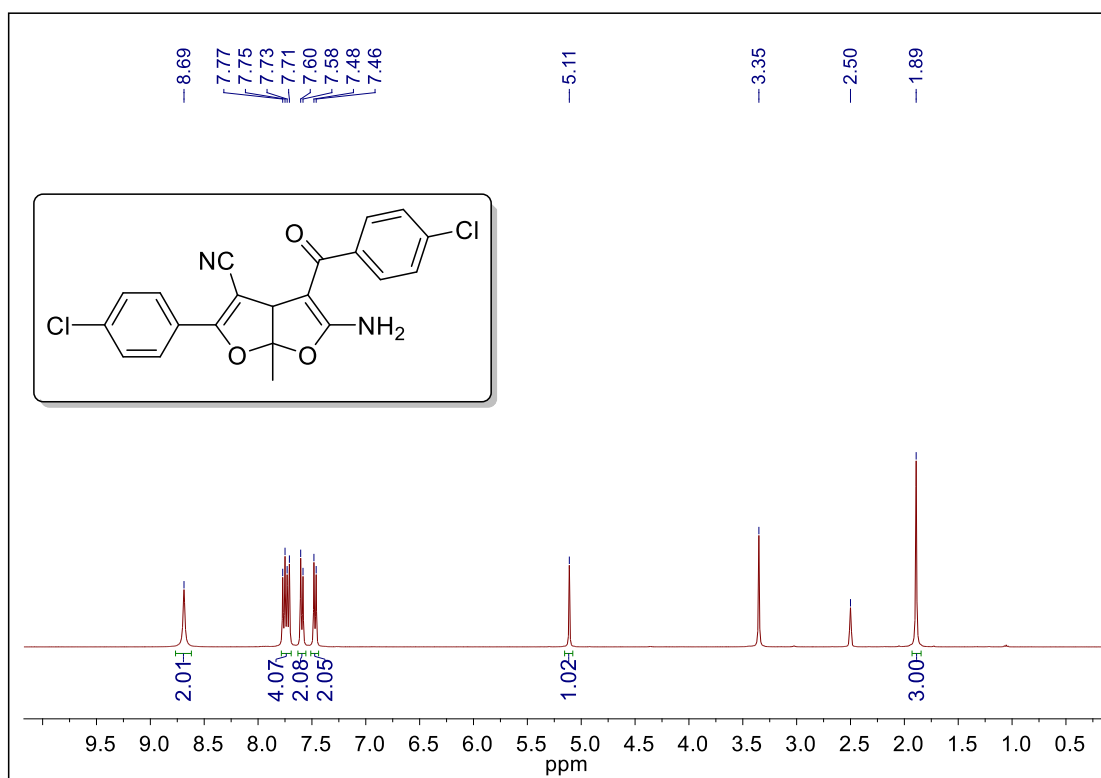


Fig. 32 ¹H, ¹³C spectrum of 5-amino-4-(4-chlorobenzoyl)-2-(4-chlorophenyl)-6a-methyl-3a,6a-dihydrofuro[2,3-b]furan-3-carbonitrile **S_{4h}**

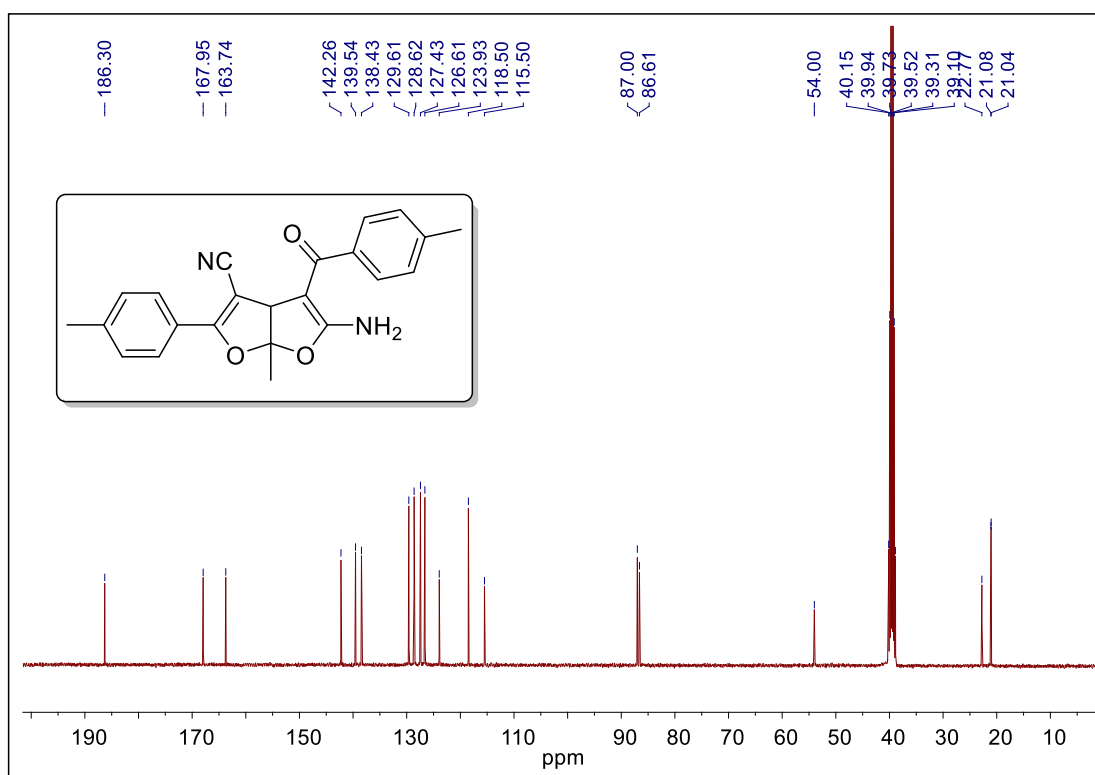
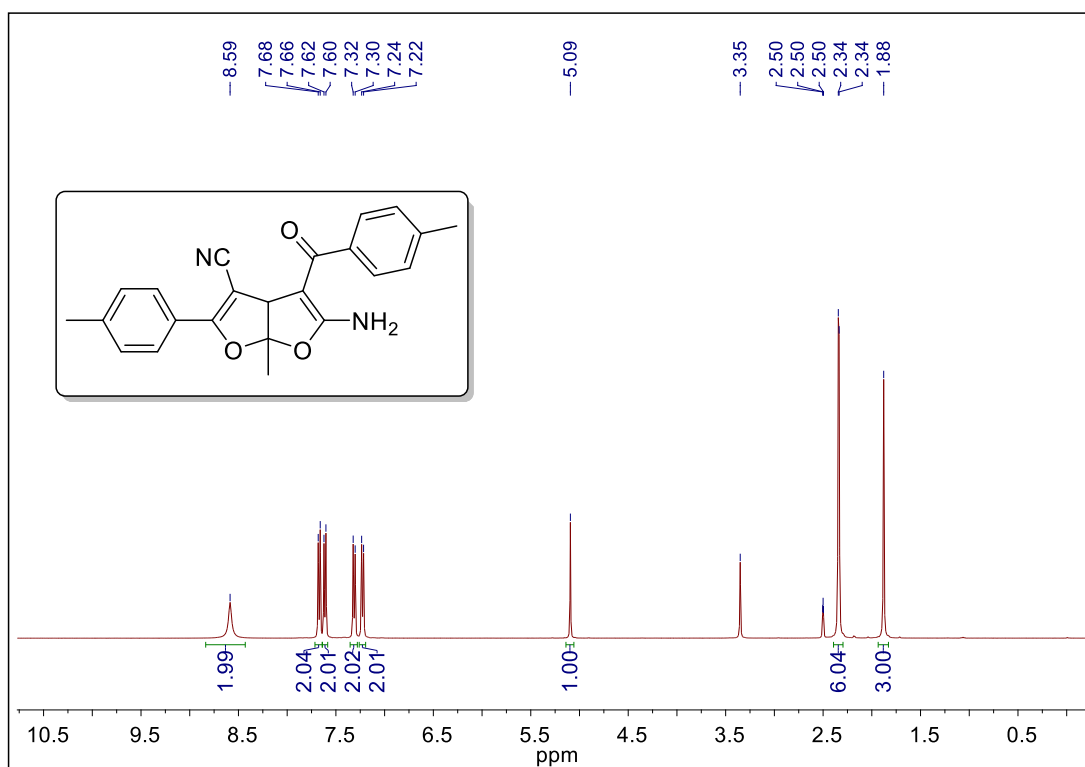


Fig. 33 ¹H, ¹³C spectrum of 5-amino-6a-methyl-4-(4-methylbenzoyl)-2-(p-tolyl)-3a,6a-dihydrofuro[2,3-b]furan-3-carbonitrile **S_{4i}**

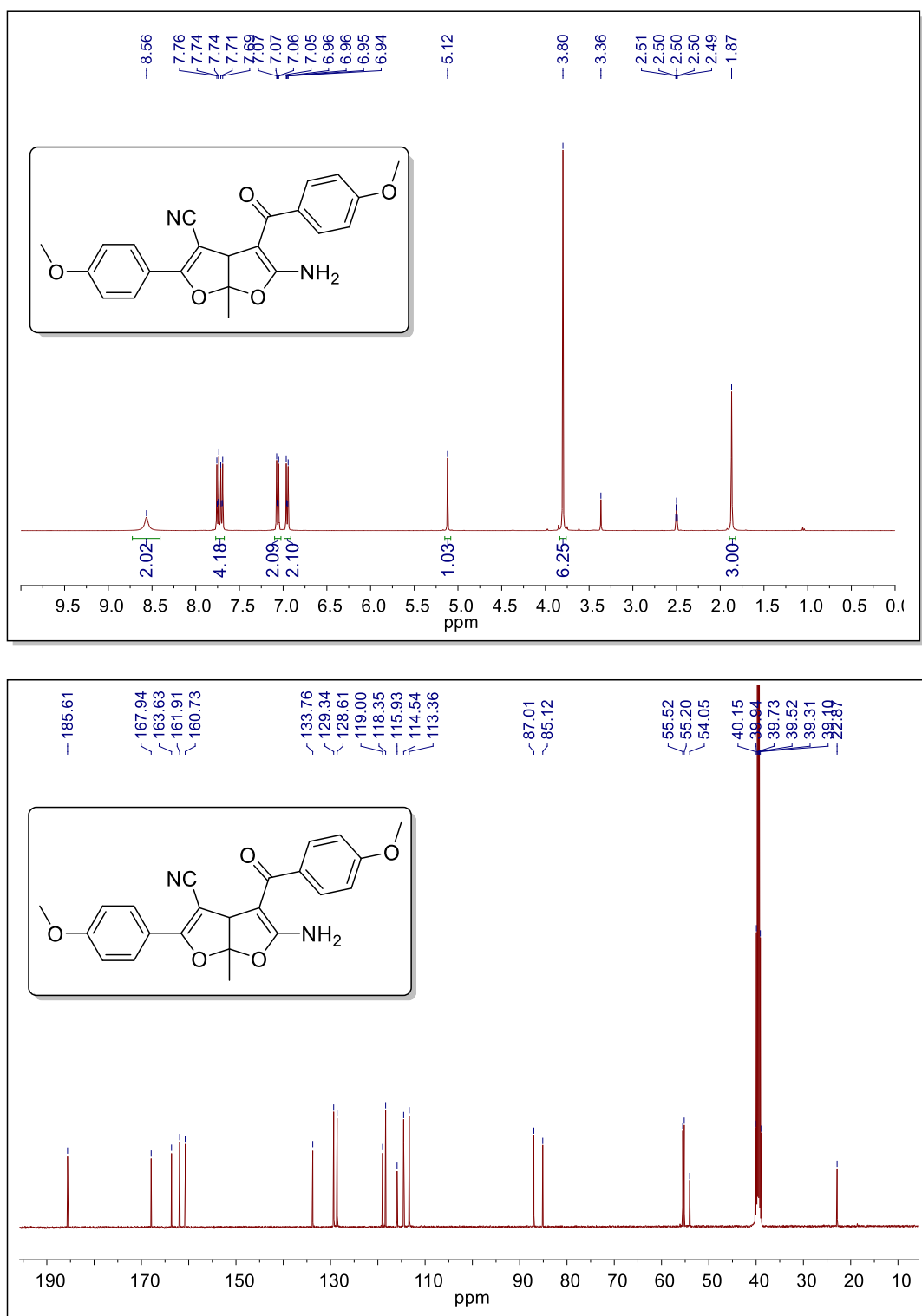


Fig. 34 ¹H, ¹³C spectrum of 5-amino-4-(4-methoxybenzoyl)-2-(4-methoxyphenyl)-6a-methyl-3a,6a-dihydrofuro[2,3-b]furan-3-carbonitrile **S_{4j}**

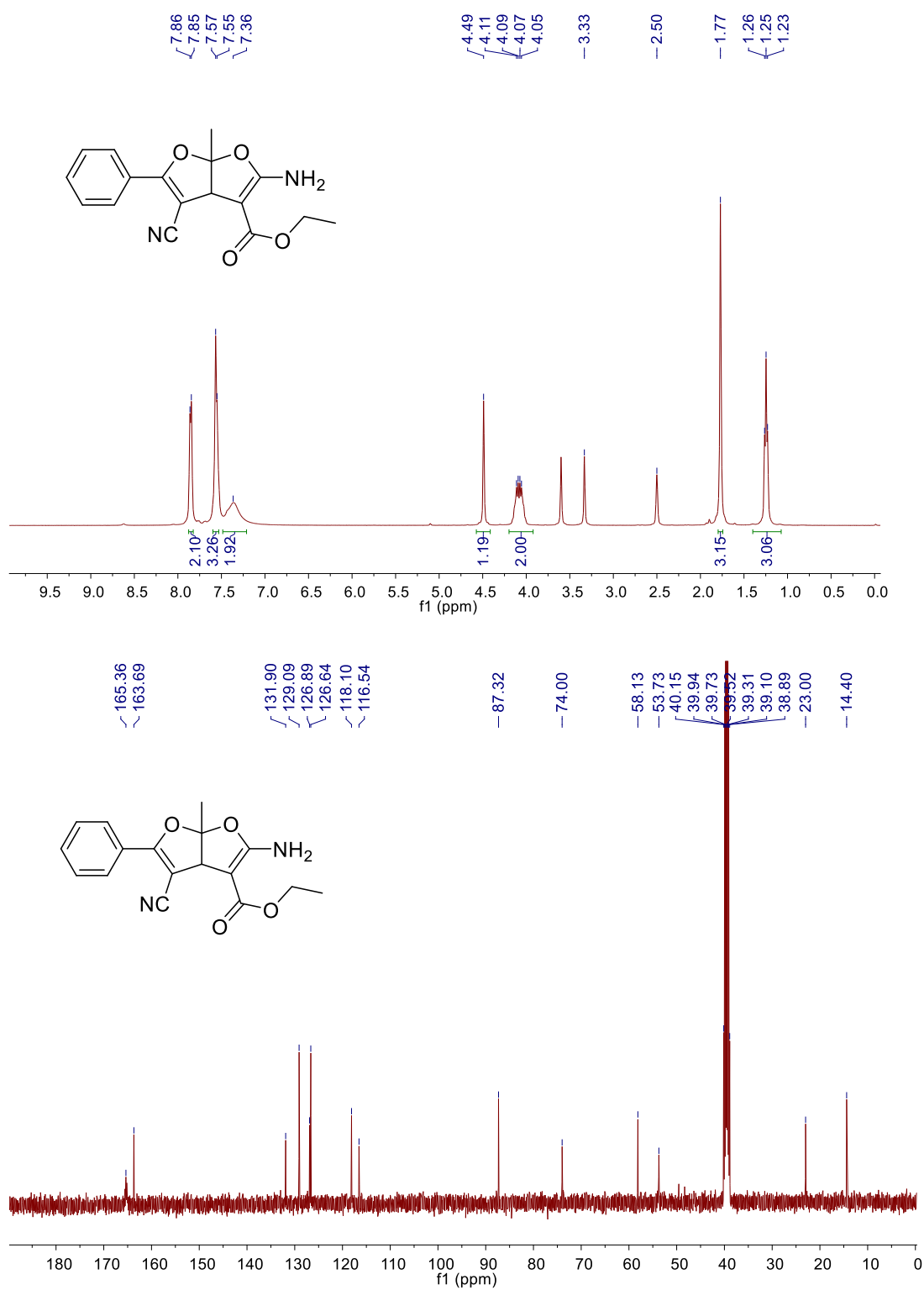


Fig. 35 ¹H, ¹³C spectrum of ethyl 2-amino-4-cyano-6a-methyl-5-phenyl-3a,6a-dihydrofuro[2,3-b]furan-3-carboxylate **S4k**

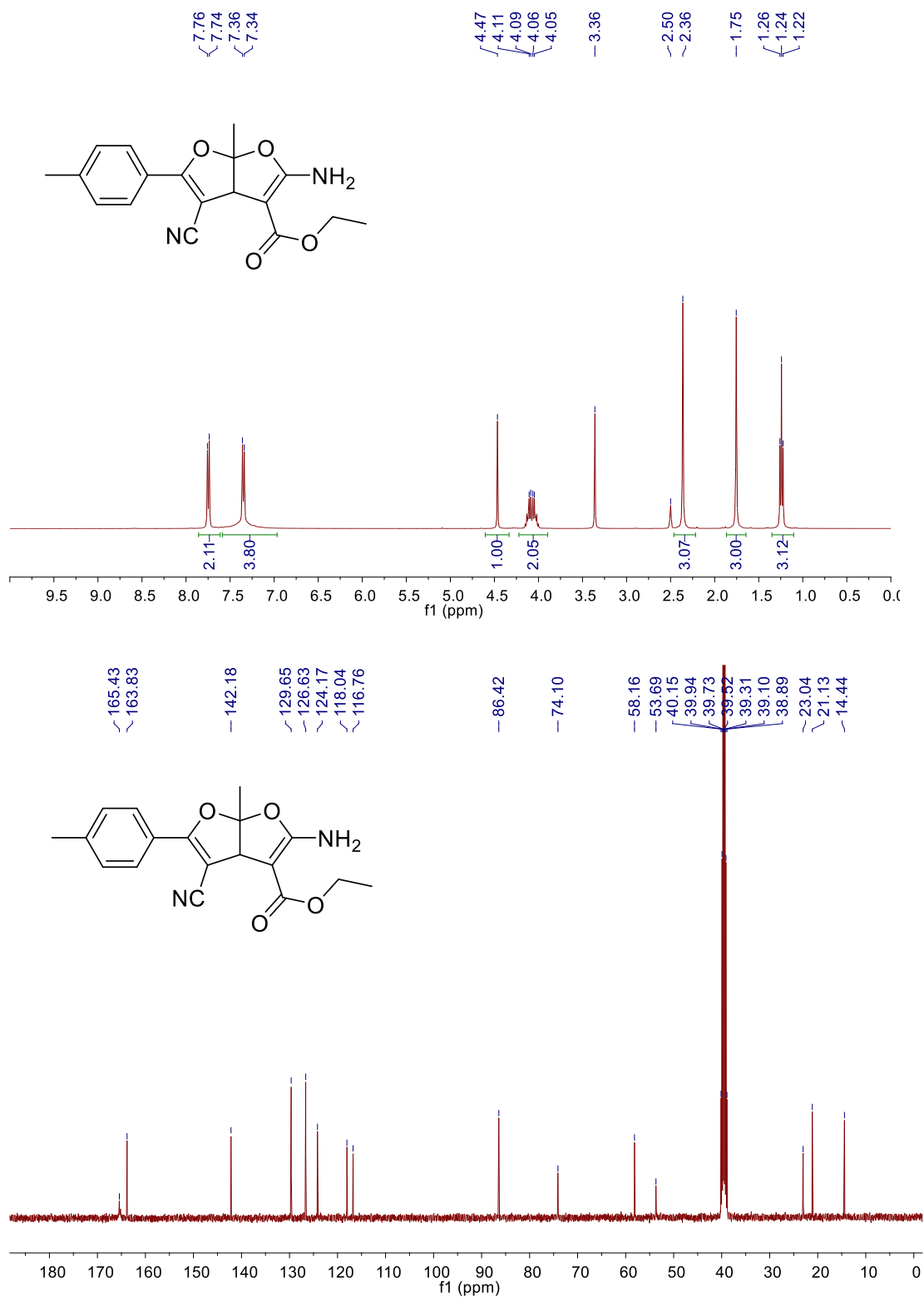


Fig. 36 ¹H, ¹³C spectrum of ethyl 2-amino-4-cyano-6a-methyl-5-(p-tolyl)-3a,6a-dihydrofuro[2,3-b]furan-3-carboxylate **S₄₁**

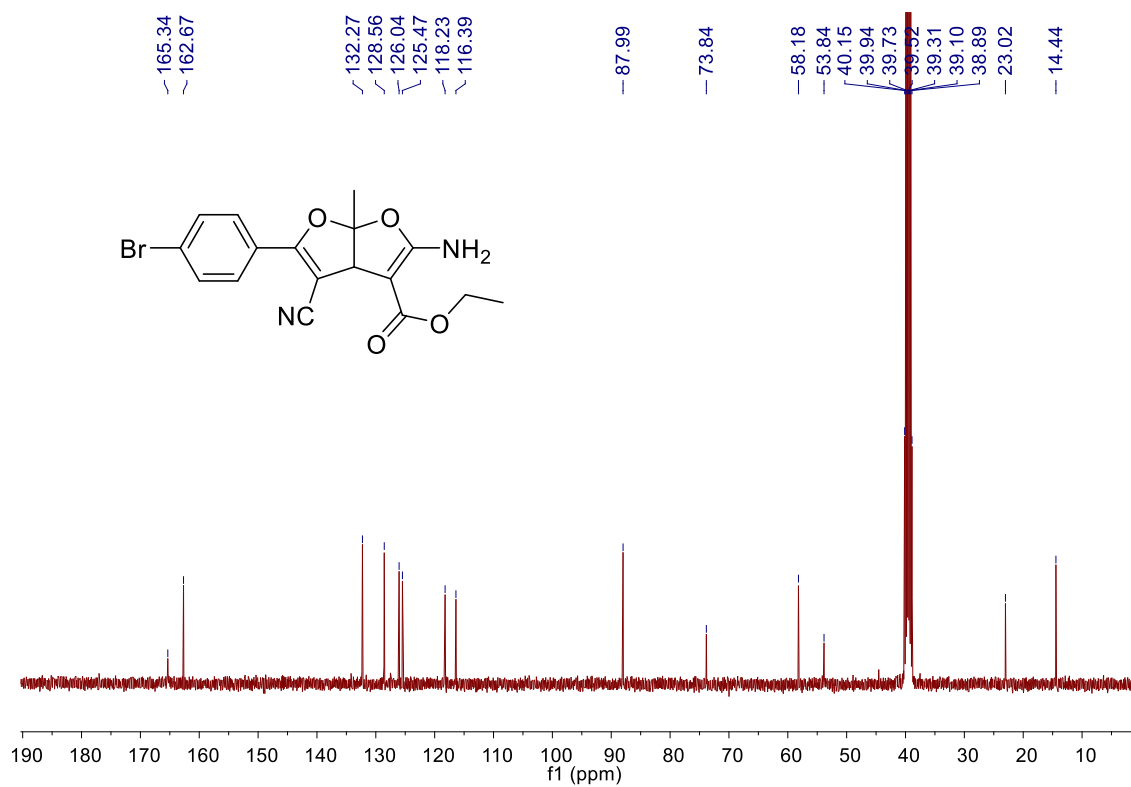
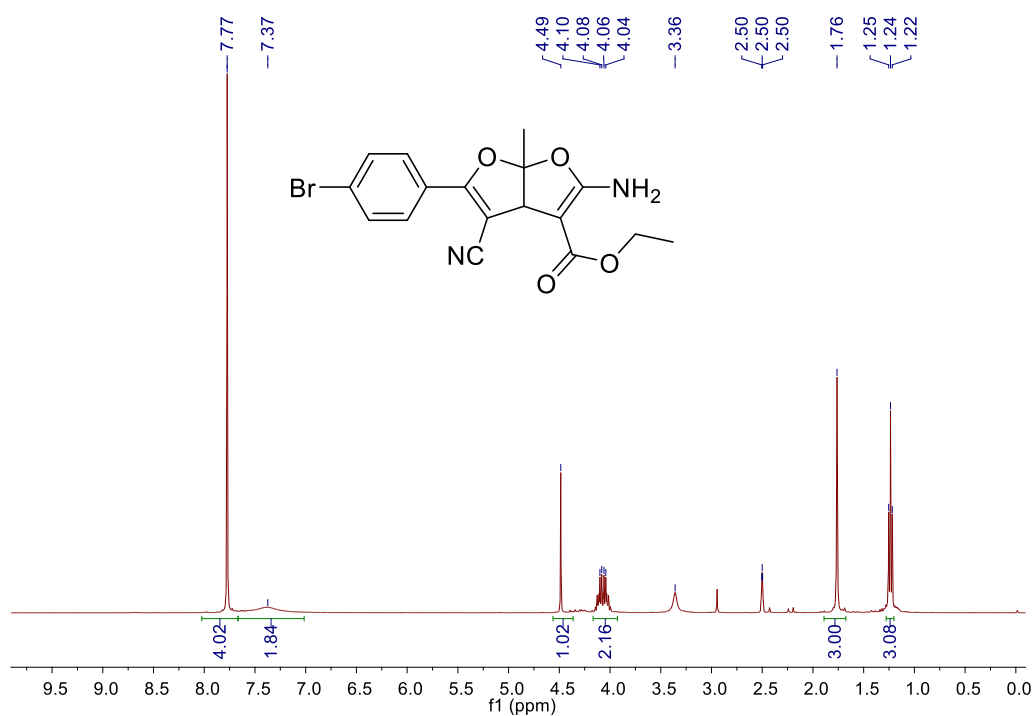


Fig. 37 ¹H, ¹³C spectrum of ethyl 2-amino-5-(4-bromophenyl)-4-cyano-6a-methyl-3a,6a-dihydrofuro[2,3-b]furan-3-carboxylate **S_{4m}**

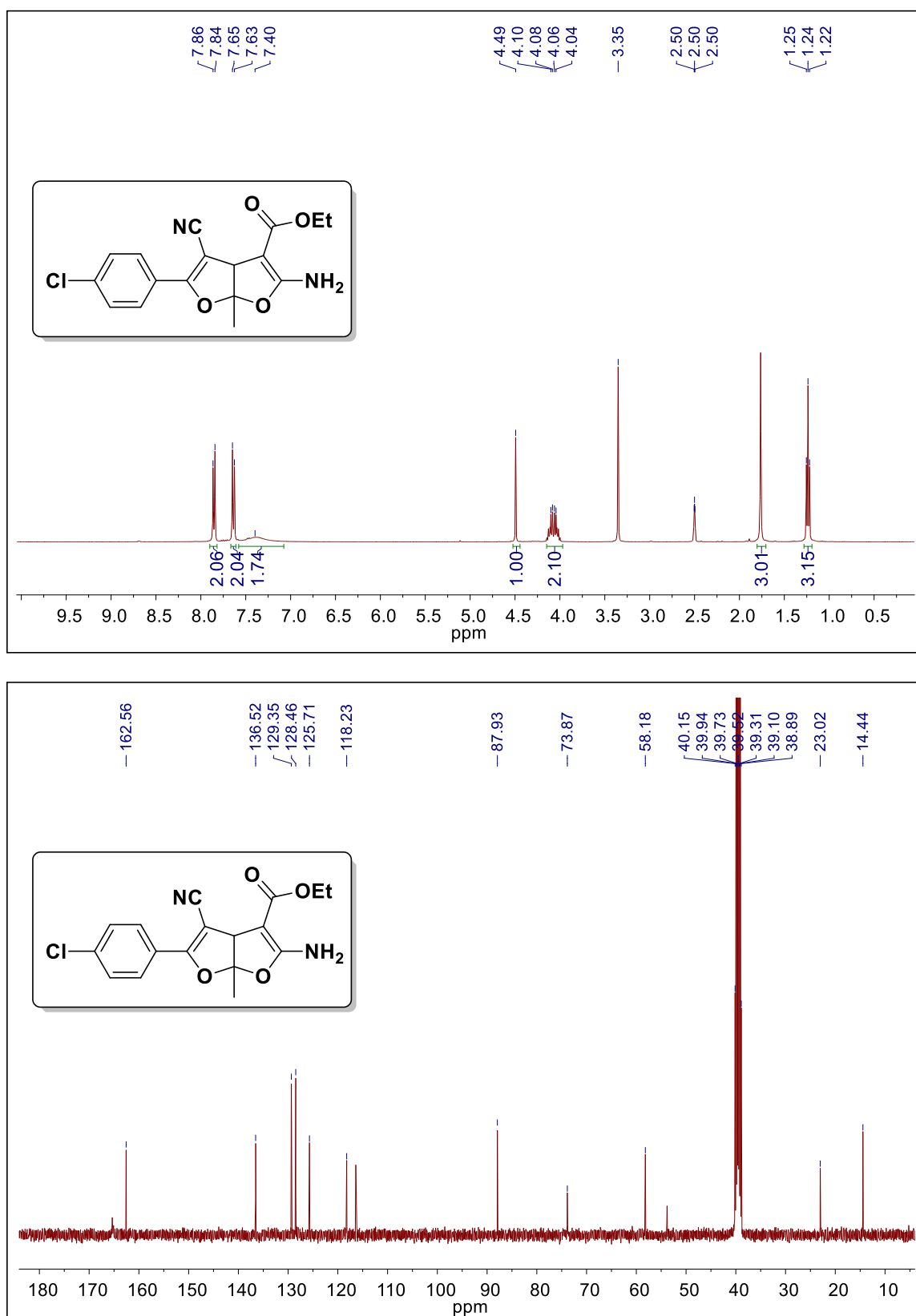


Fig. 38 ¹H, ¹³C spectrum of ethyl 2-amino-5-(4-chlorophenyl)-4-cyano-6a-methyl-3a,6a-dihydrofuro[2,3-b]furan-3-carboxylate **S_{4n}**

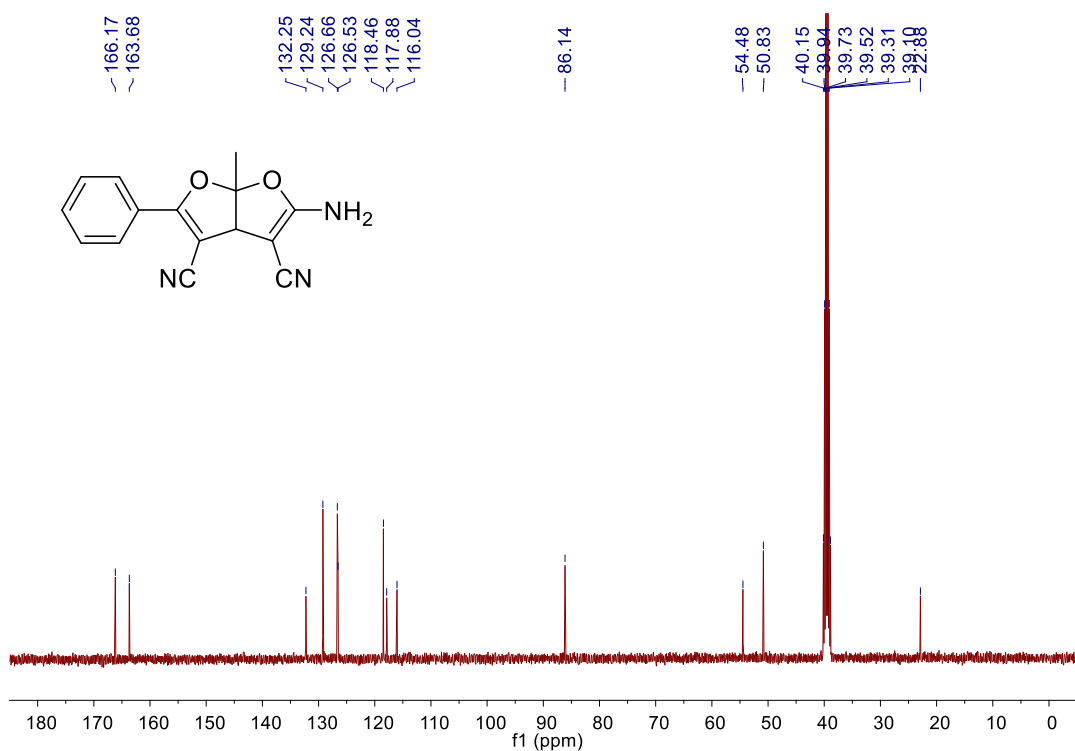
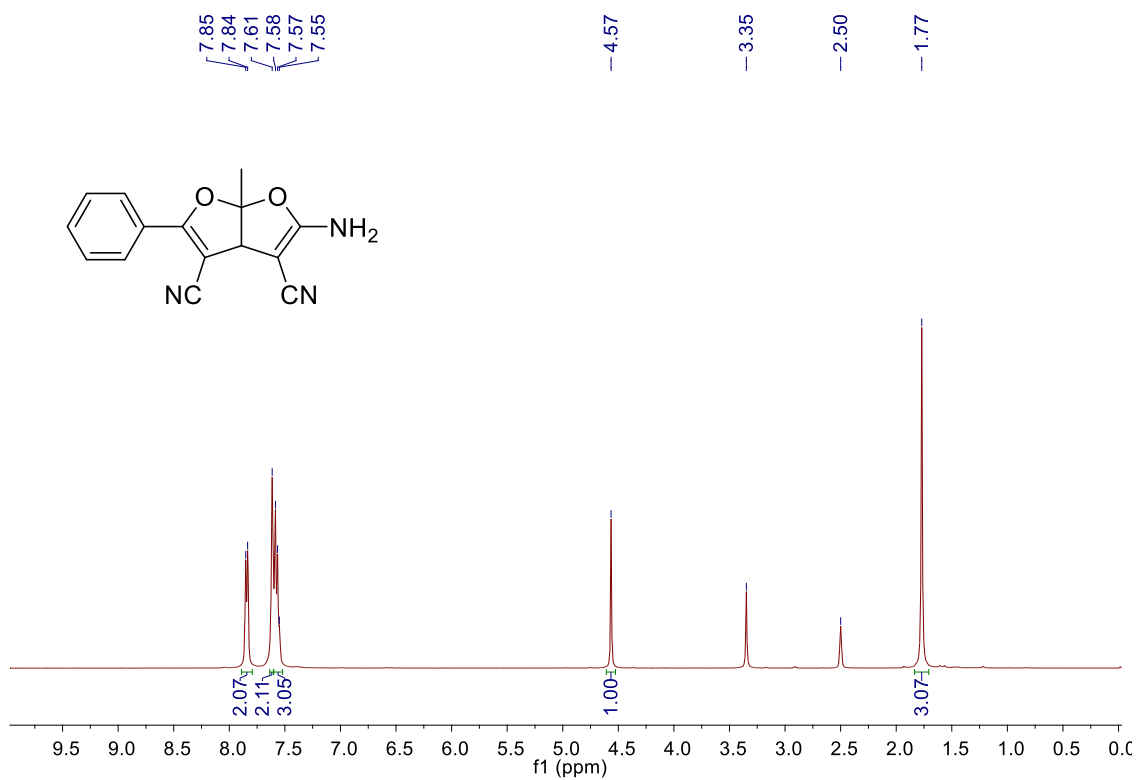


Fig. 39 ¹H, ¹³C spectrum of 2-amino-6a-methyl-5-phenyl-3a,6a-dihydrofuro[2,3-b]furan-3,4-dicarbonitrile **S**₄₀