

Synthesis of nicotinimidamides via a tandem CuAAC/ring-cleavage /cyclization/oxidation four-component reaction and its cytotoxicity

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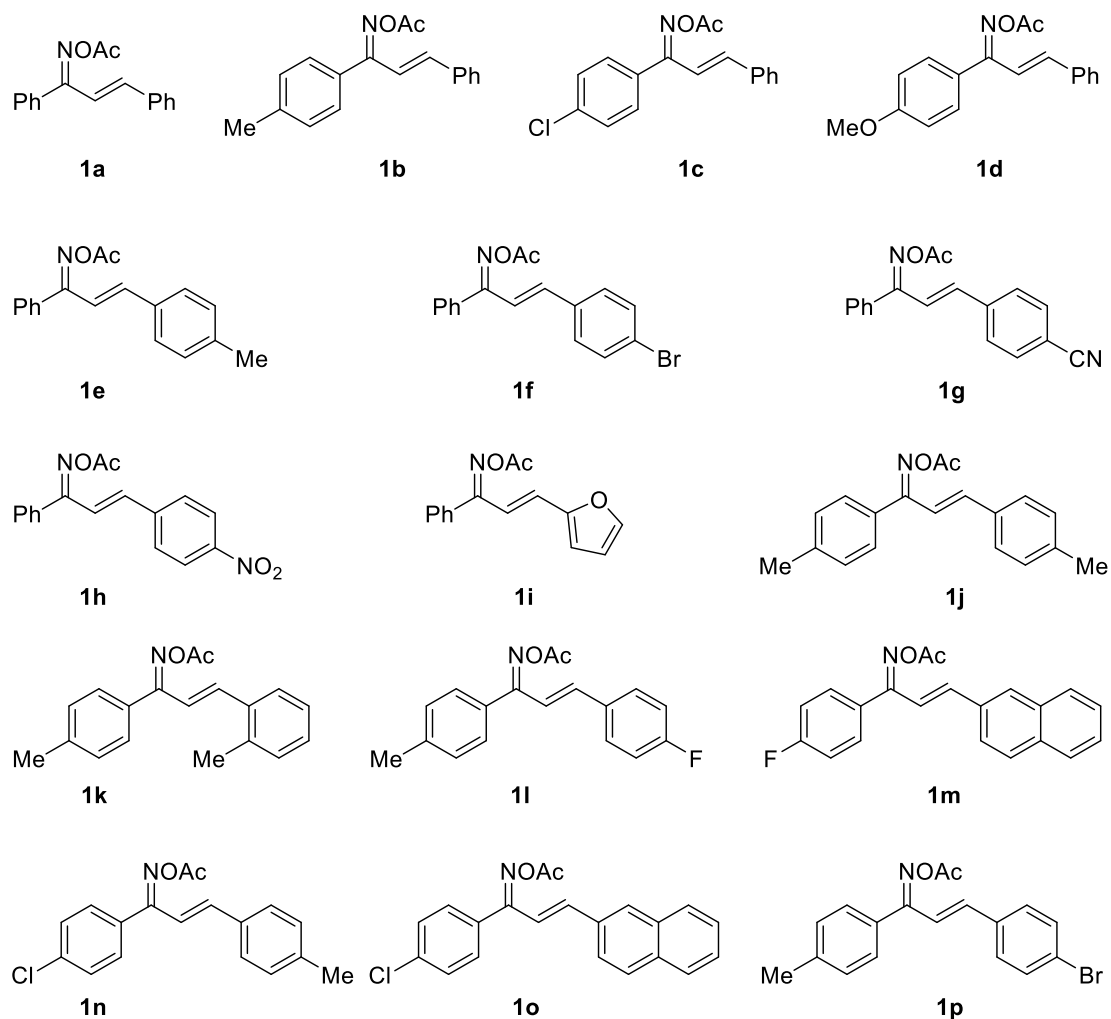
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1. General Information

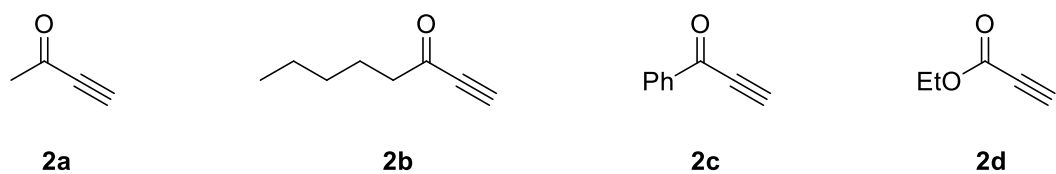
All melting points were determined on a Yanaco melting point apparatus (Kyoto, Japan) and were uncorrected. IR spectra were recorded as KBr pellets on a Nicolet FT-IR 5DX spectrometer (Waltham, MA, USA). All spectra of ^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) were recorded on a Bruker AVANCE NEO 400 MHz spectrometer (Berne, Switzerland) in $\text{DMSO-}d_6$ or CDCl_3 (unless otherwise indicated), with TMS used as an internal reference and the J values given in Hz. HRMS were obtained on a Thermo Scientific Q Exactive Focus Orbitrap LC-MS/MS spectrometer (Waltham, MA, USA). Optical rotations are measured on a P-2000, serial number: B209161232, JASCO corporation (Tokyo, Japan).

2. The structures of starting materials 1a-1p, 2a-2c and 3a-3j

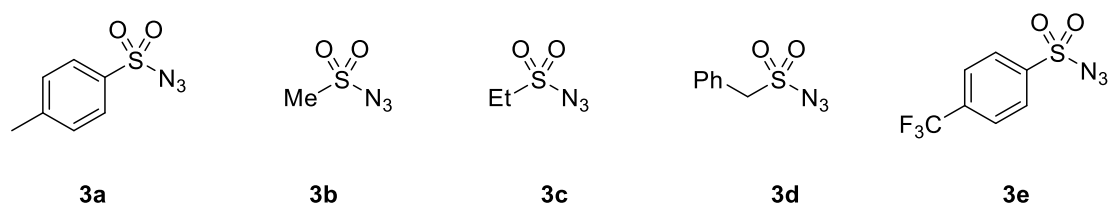
Scheme S1 Structures of the starting materials 1a-1p.



Scheme S2 Structures of the starting materials 2a-2d.



Scheme S3 Structures of the starting materials 3a-3e.



3. Copies of NMR spectra

Figure S1. ^1H NMR of **5a** (400 MHz, $\text{DMSO-}d_6$) and ^{13}C NMR of **5a** (100 MHz, $\text{DMSO-}d_6$).

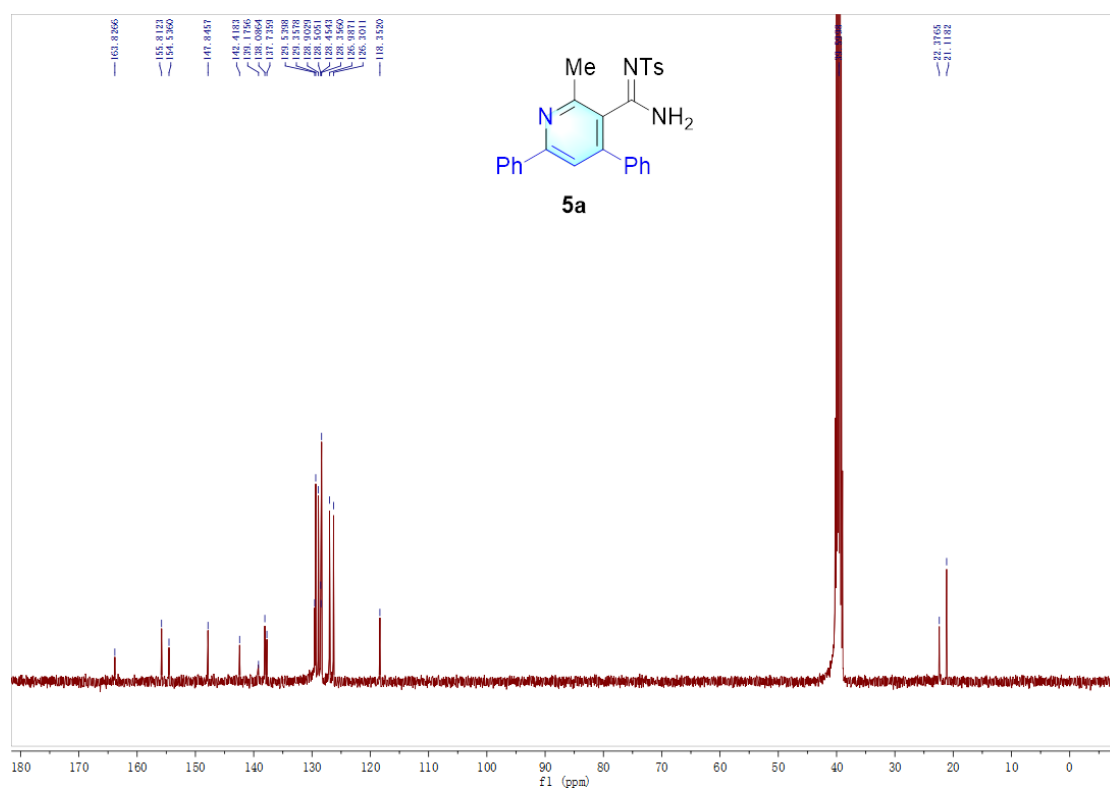
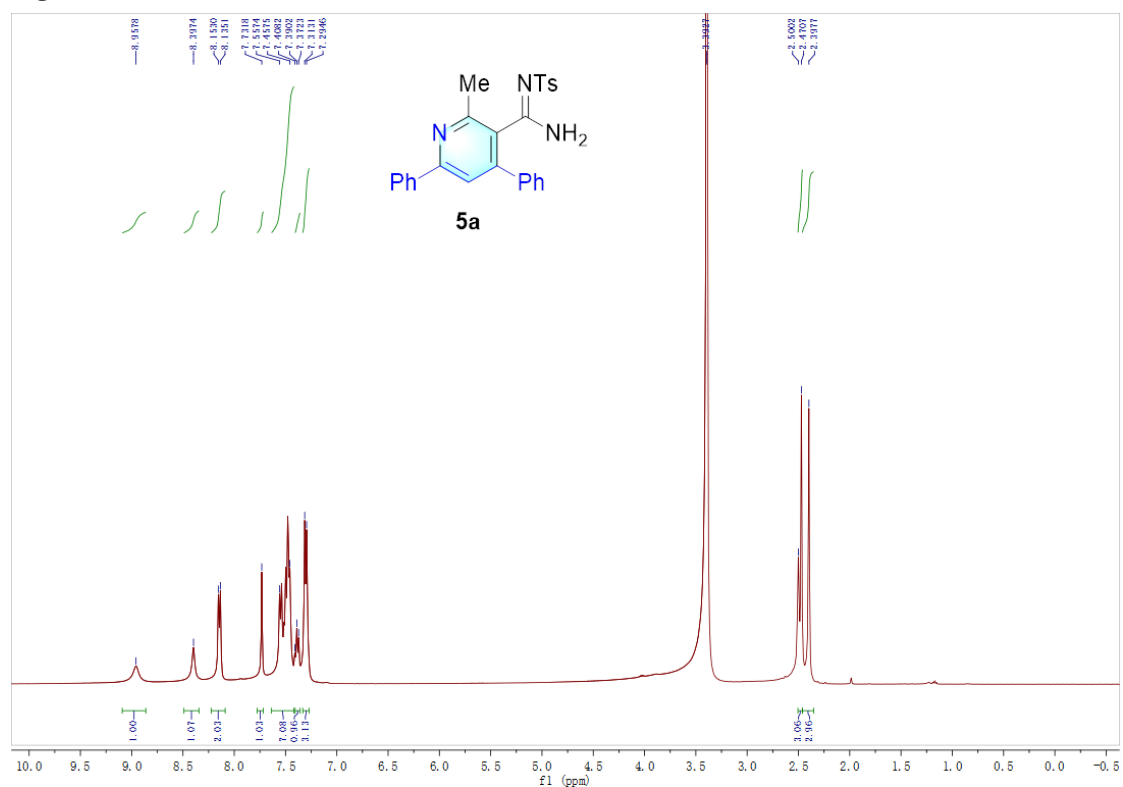


Figure S2. ^1H NMR of **5b** (400 MHz, $\text{DMSO-}d_6$) and ^{13}C NMR of **5b** (100 MHz, $\text{DMSO-}d_6$).

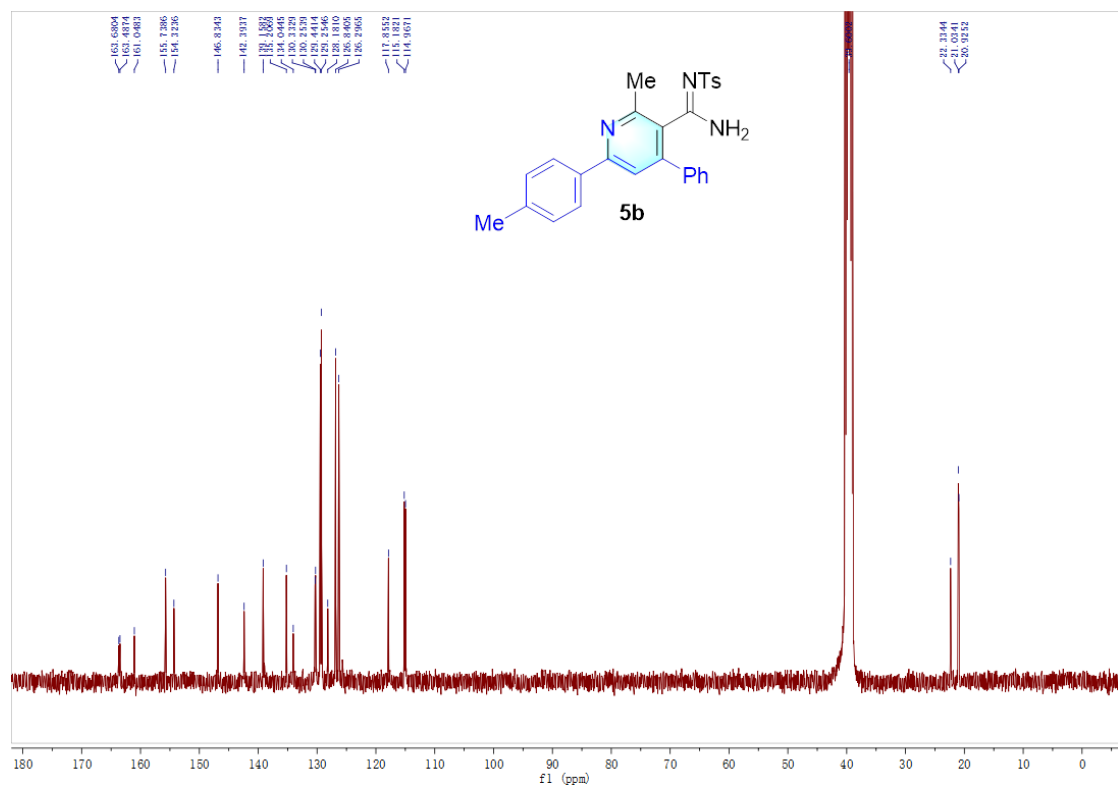
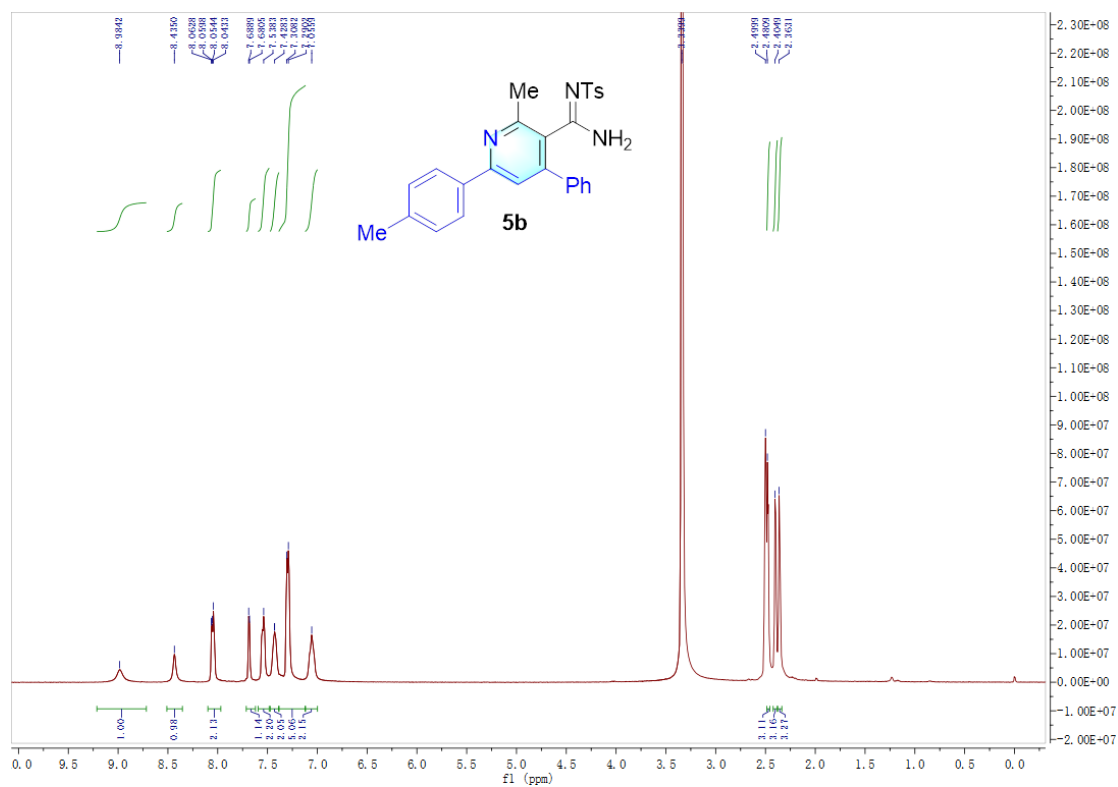


Figure S4. ^1H NMR of **5d** (400 MHz, $\text{DMSO-}d_6$) and ^{13}C NMR of **5d** (100 MHz, $\text{DMSO-}d_6$).

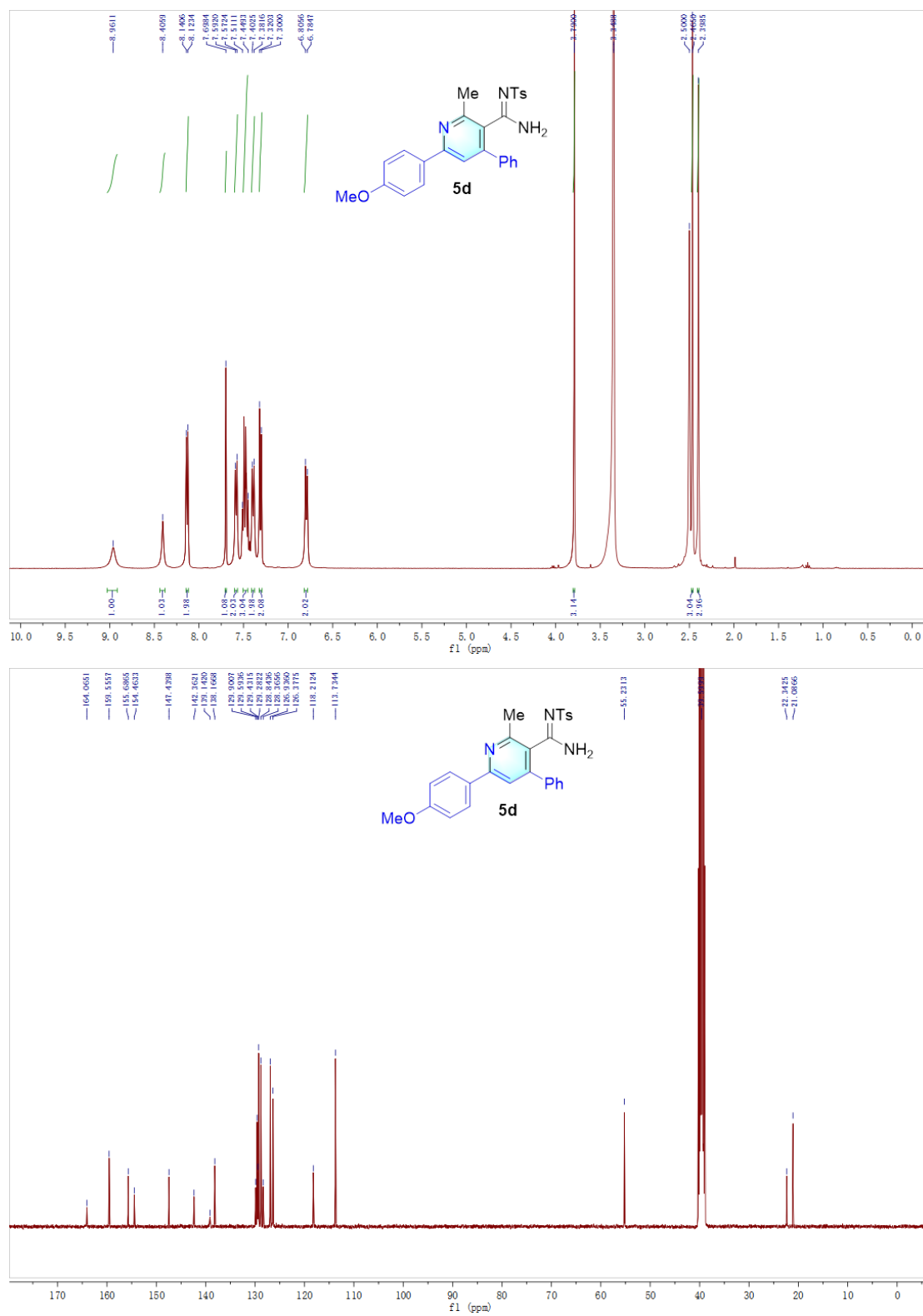


Figure S5. ^1H NMR of **5e** (400 MHz, $\text{DMSO-}d_6$) and ^{13}C NMR of **5e** (100 MHz, $\text{DMSO-}d_6$).

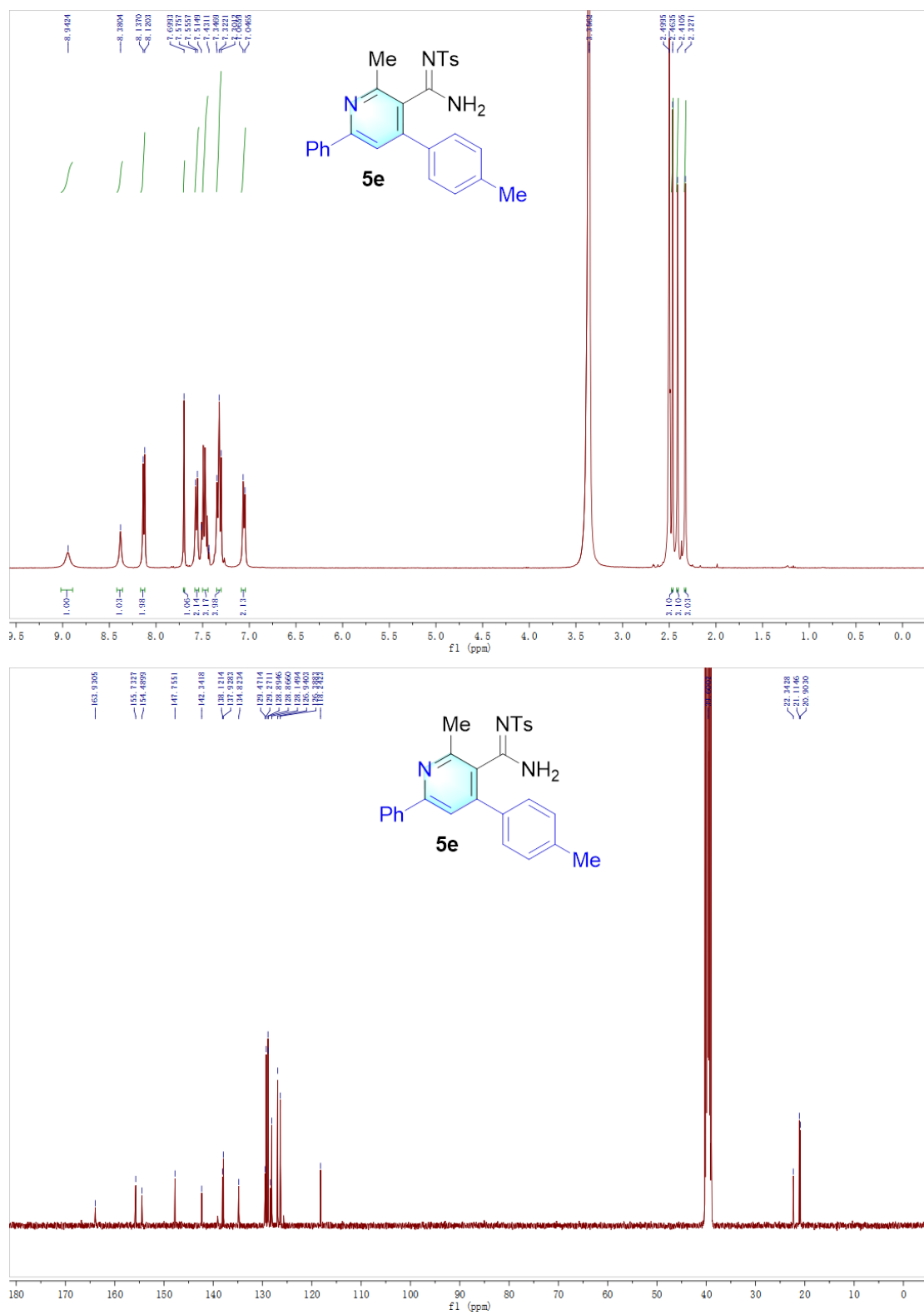


Figure S6. ^1H NMR of **5f** (400 MHz, $\text{DMSO-}d_6$) and ^{13}C NMR of **5f** (100 MHz, $\text{DMSO-}d_6$).

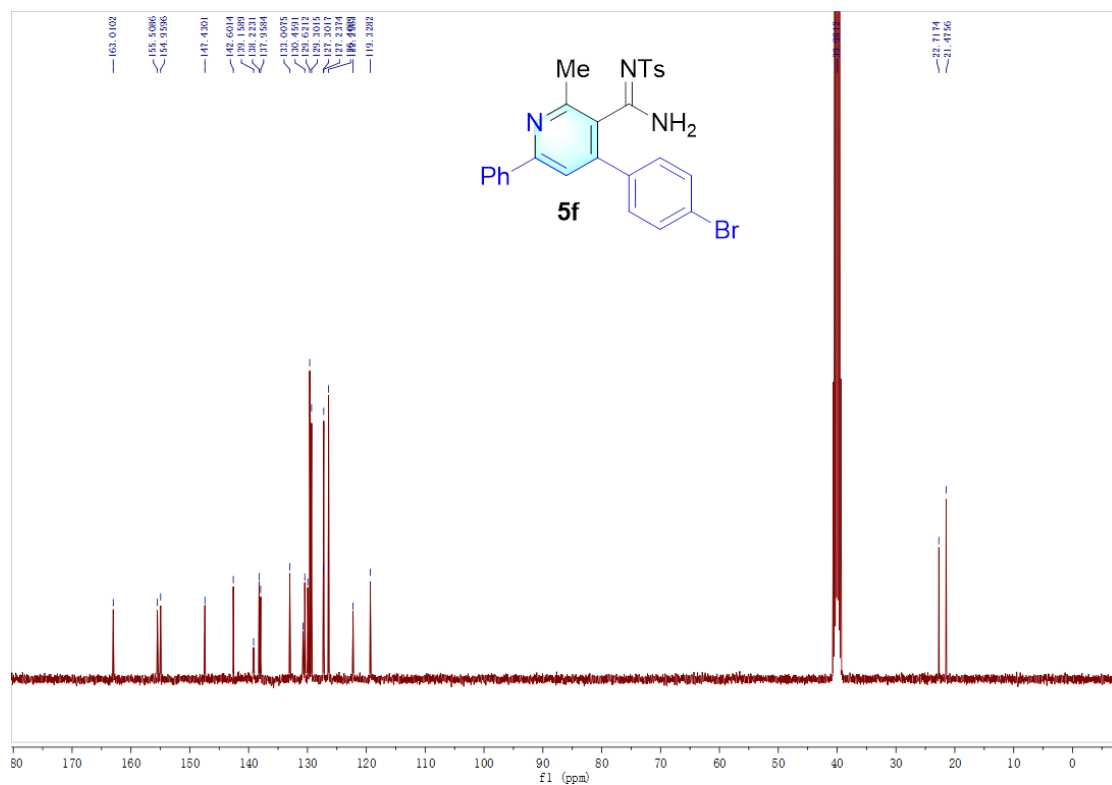
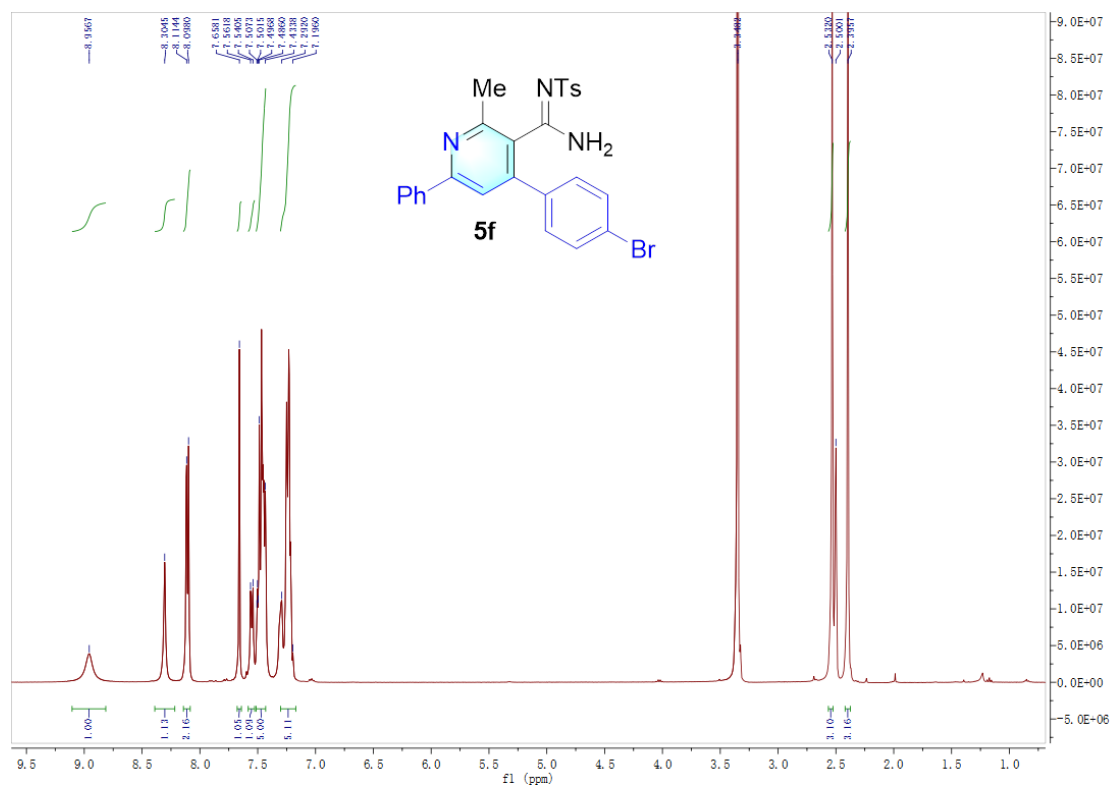


Figure S7. ^1H NMR of **5g** (400 MHz, $\text{DMSO-}d_6$) and ^{13}C NMR of **5g** (100 MHz, $\text{DMSO-}d_6$).

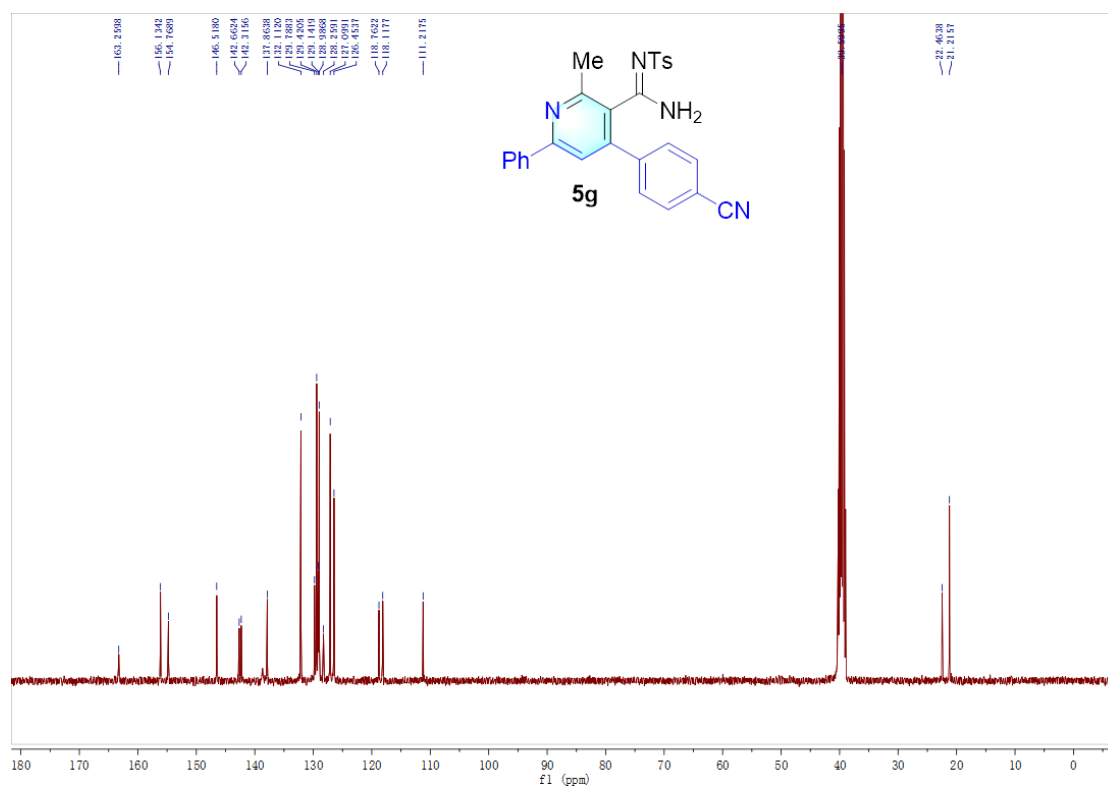
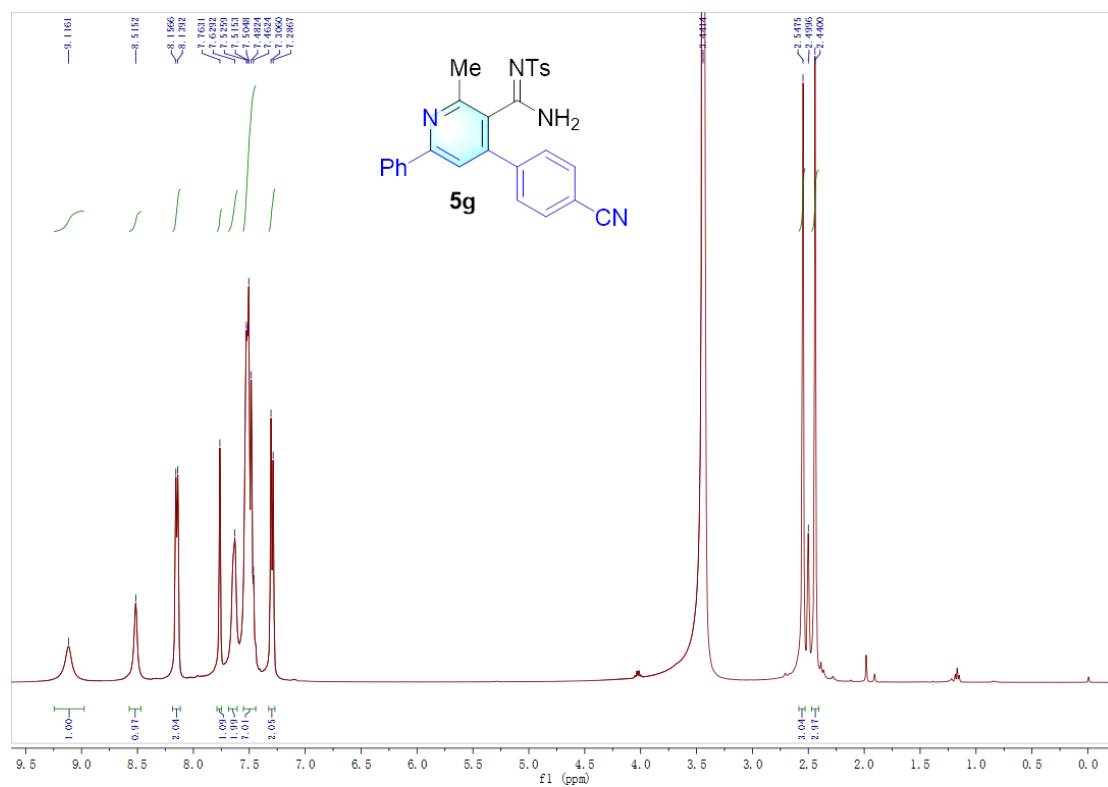


Figure S8. ^1H NMR of **5h** (400 MHz, $\text{DMSO-}d_6$) and ^{13}C NMR of **5h** (100 MHz, $\text{DMSO-}d_6$).

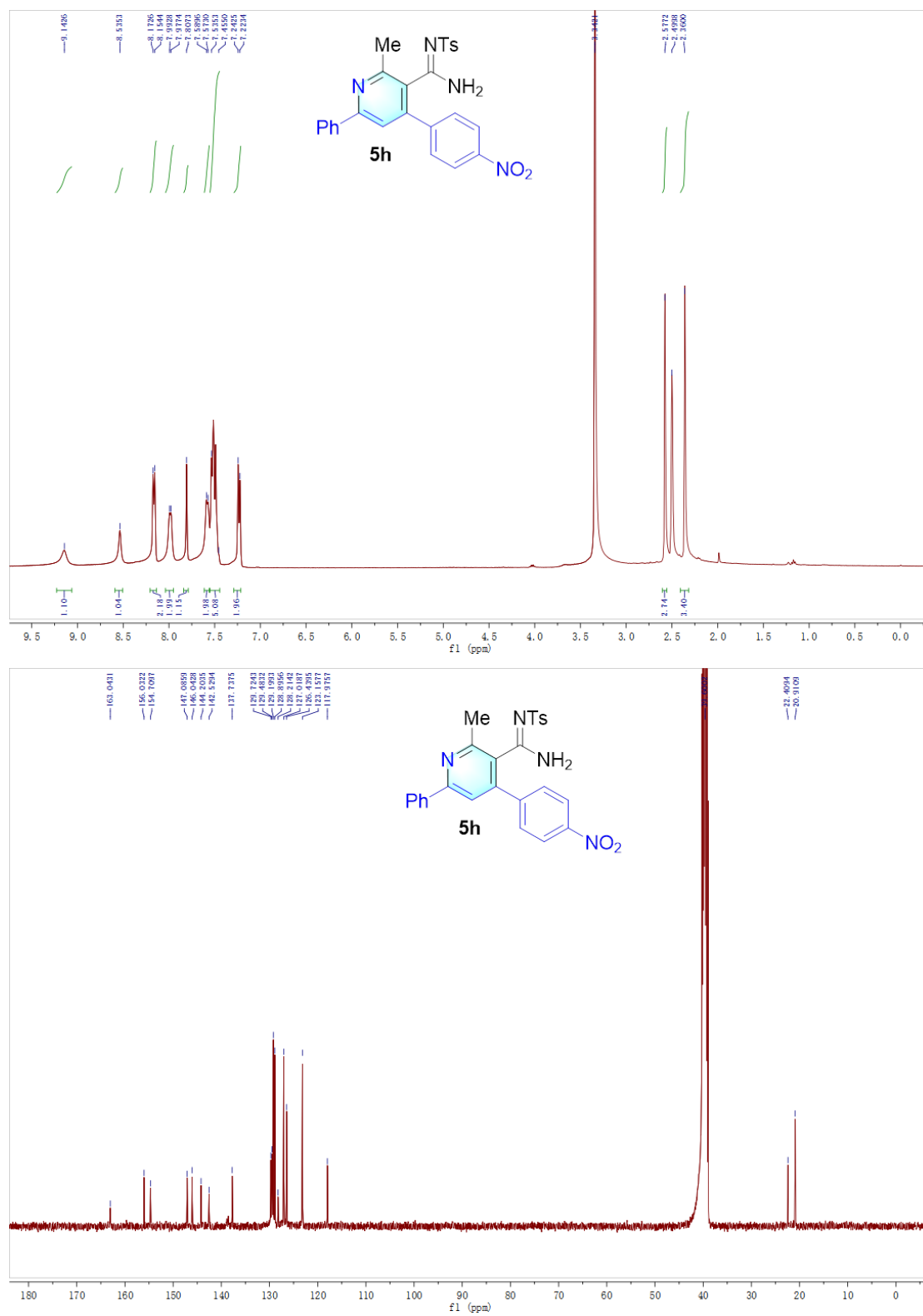


Figure S9. ^1H NMR of **5i** (400 MHz, $\text{DMSO-}d_6$) and ^{13}C NMR of **5i** (100 MHz, $\text{DMSO-}d_6$).

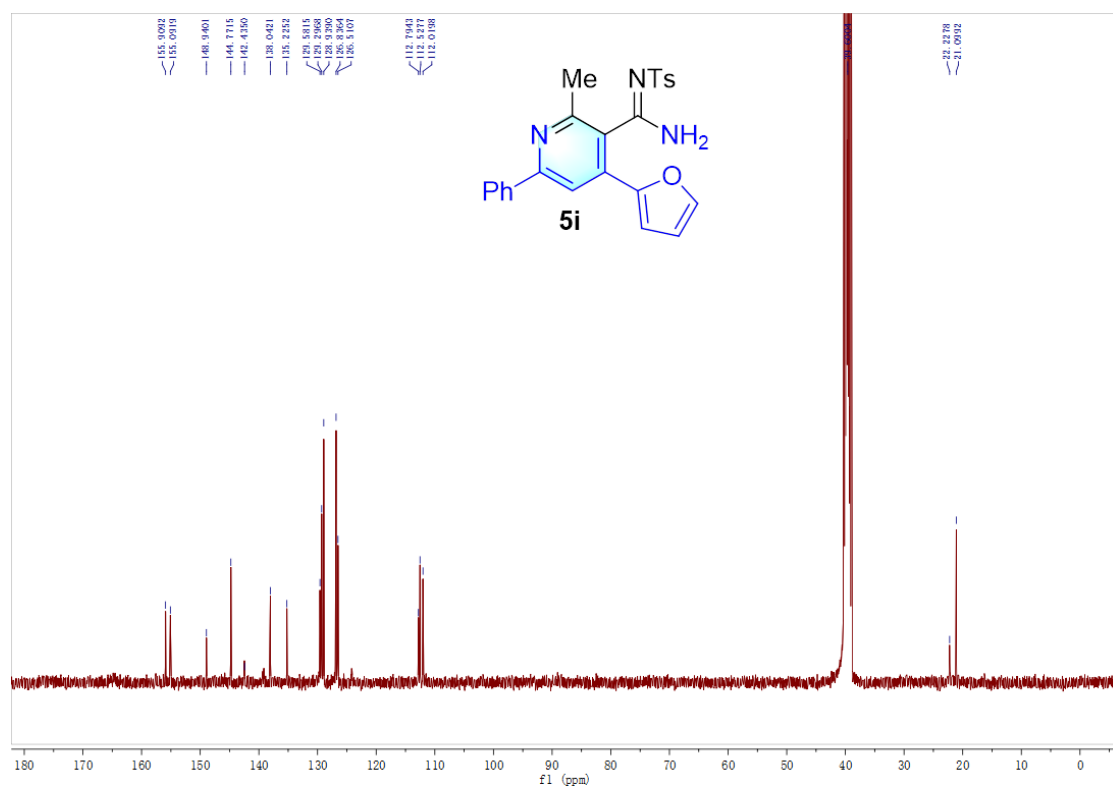
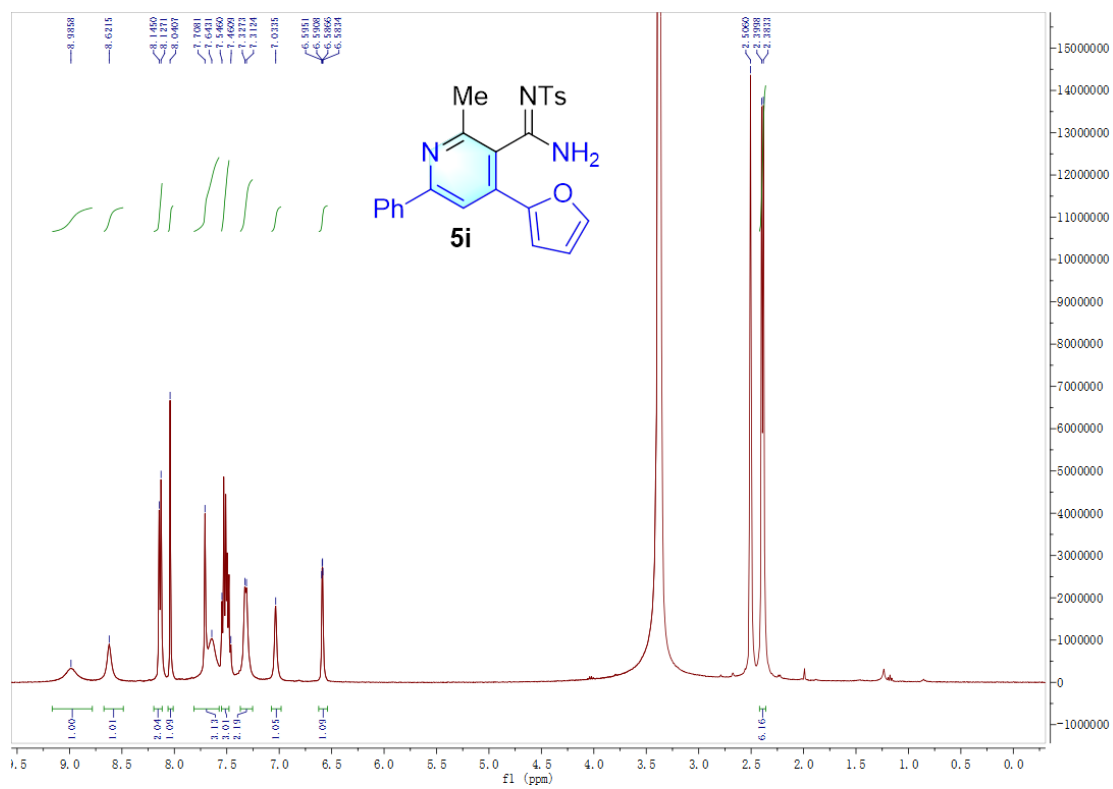


Figure S10. ^1H NMR of **5j** (400 MHz, $\text{DMSO-}d_6$) and ^{13}C NMR of **5j** (100 MHz, $\text{DMSO-}d_6$).

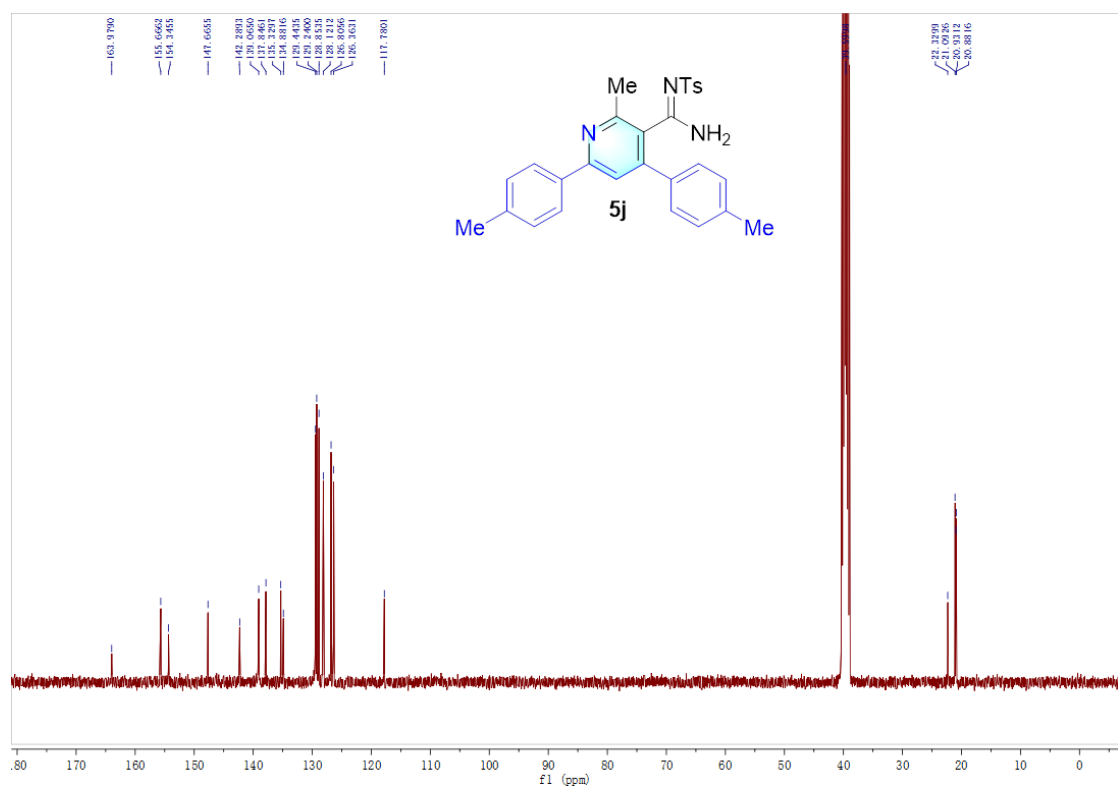
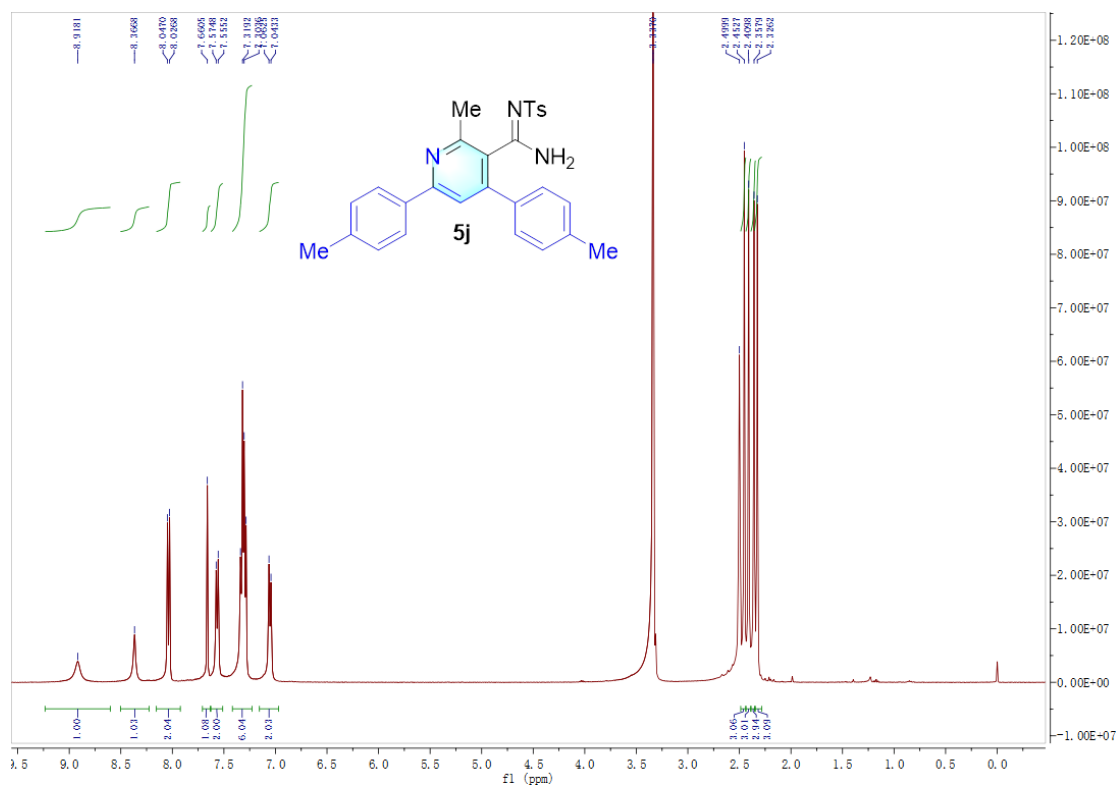


Figure S11. ^1H NMR of **5k** (400 MHz, $\text{DMSO-}d_6$) and ^{13}C NMR of **5k** (100 MHz, $\text{DMSO-}d_6$).

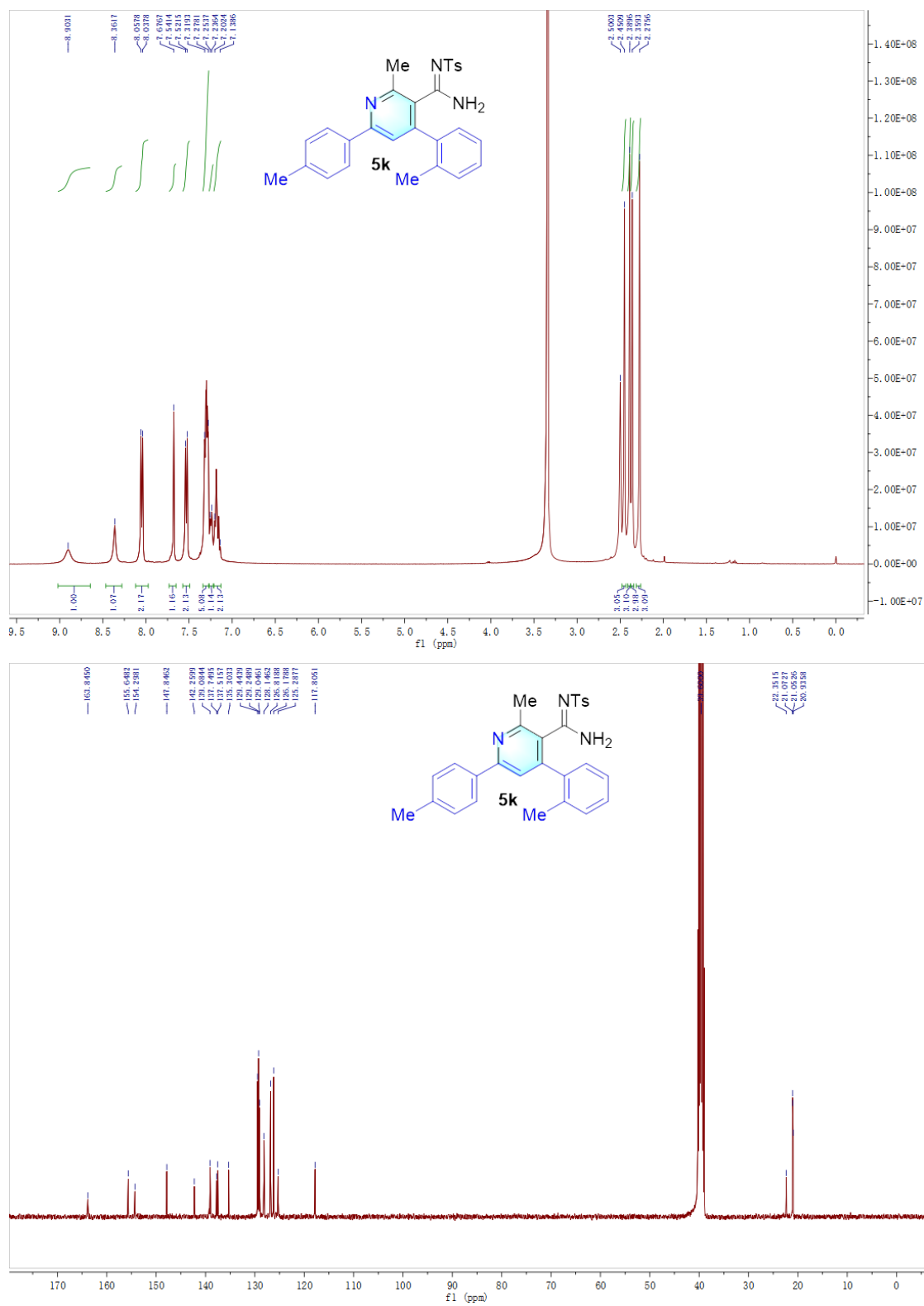


Figure S12. ^1H NMR of **5I** (400 MHz, $\text{DMSO-}d_6$) and ^{13}C NMR of **5I** (100 MHz, $\text{DMSO-}d_6$).

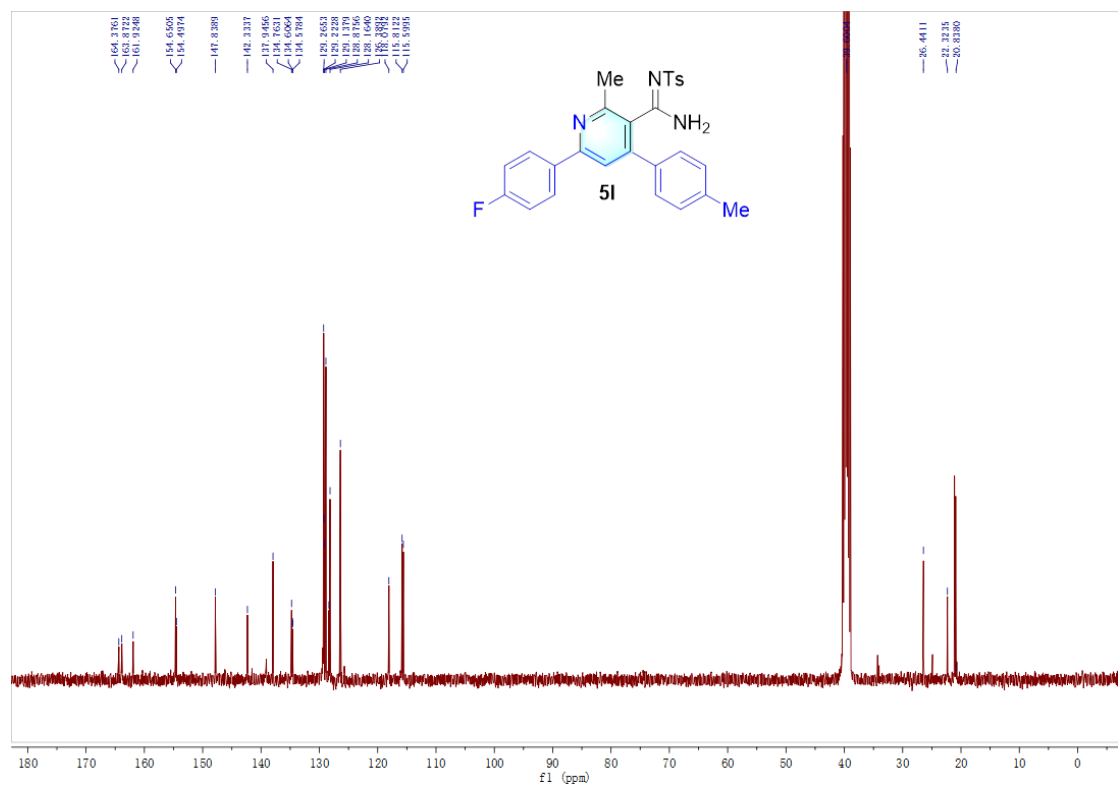
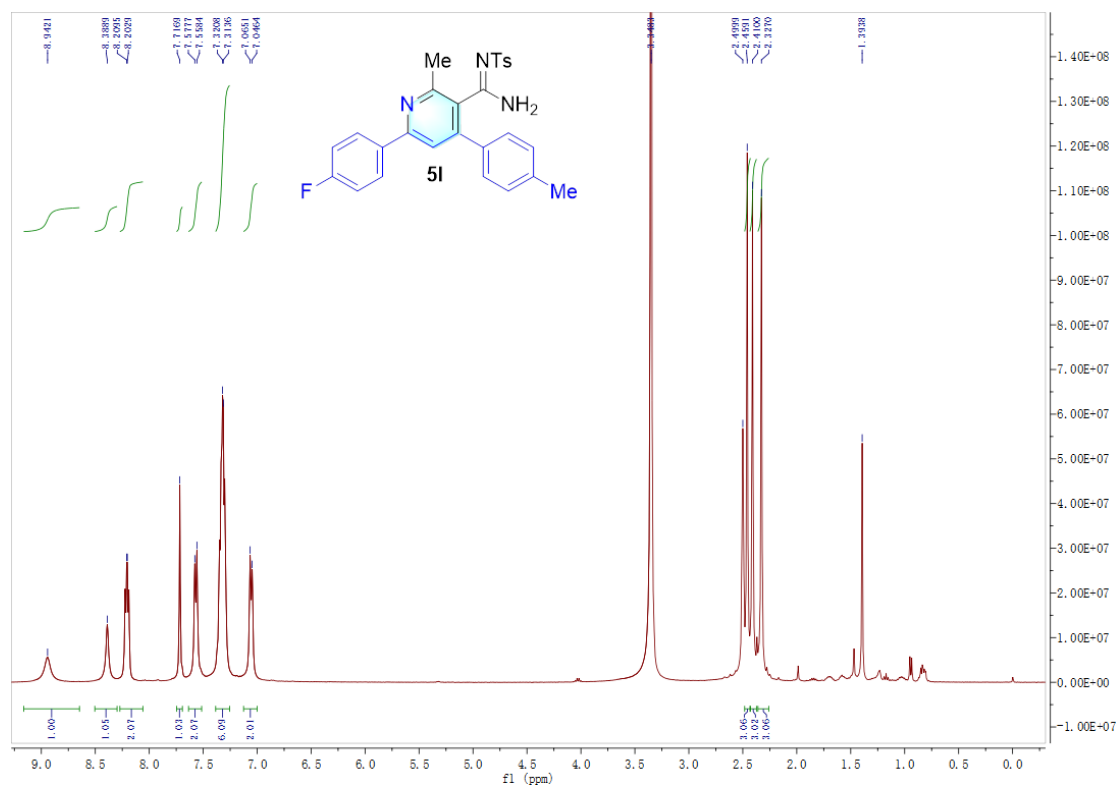


Figure S13. ^1H NMR of **5m** (400 MHz, $\text{DMSO-}d_6$) and ^{13}C NMR of **5m** (100 MHz, $\text{DMSO-}d_6$).

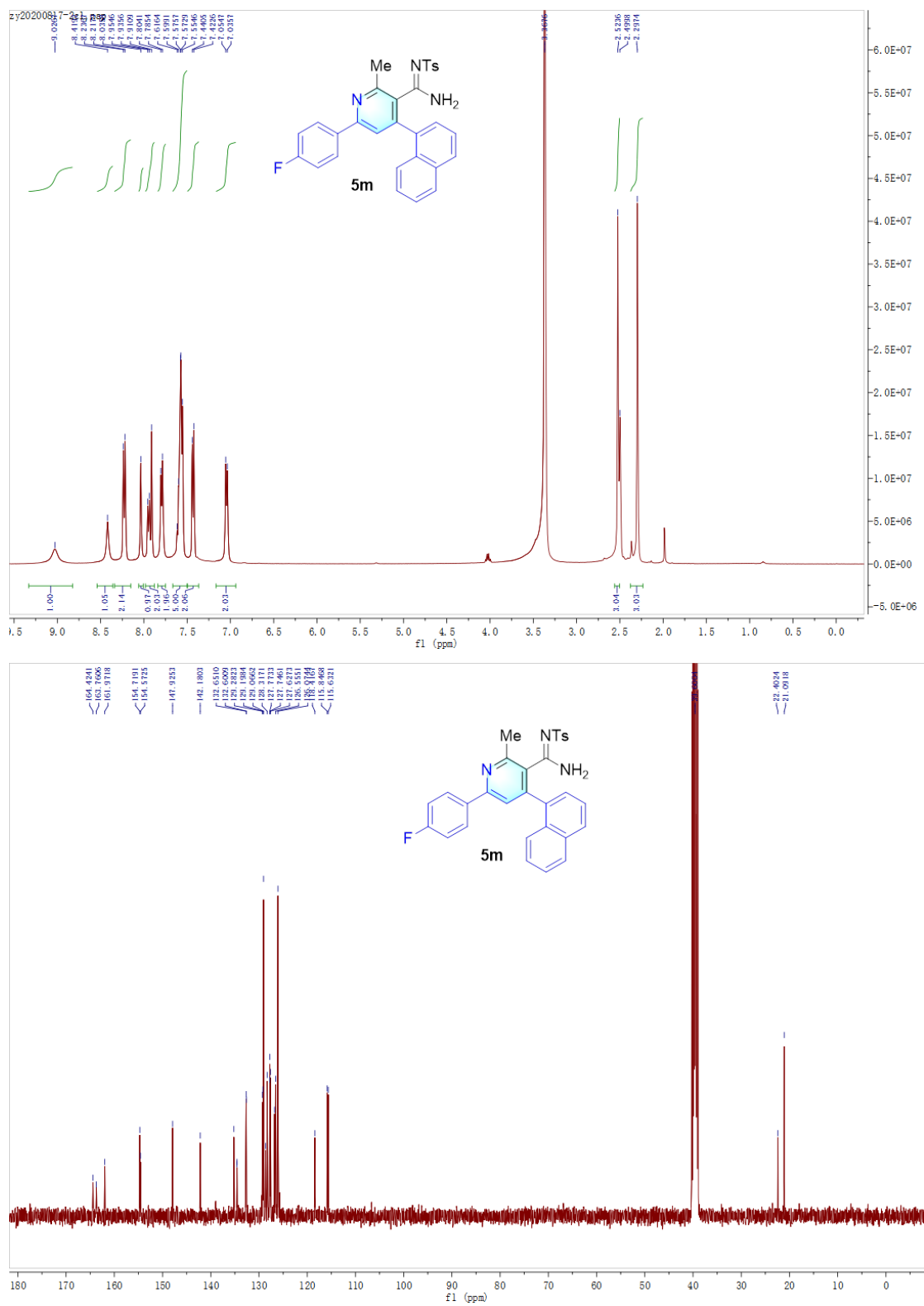


Figure S14. ^1H NMR of **5n** (400 MHz, $\text{DMSO-}d_6$) and ^{13}C NMR of **5n** (100 MHz, $\text{DMSO-}d_6$).

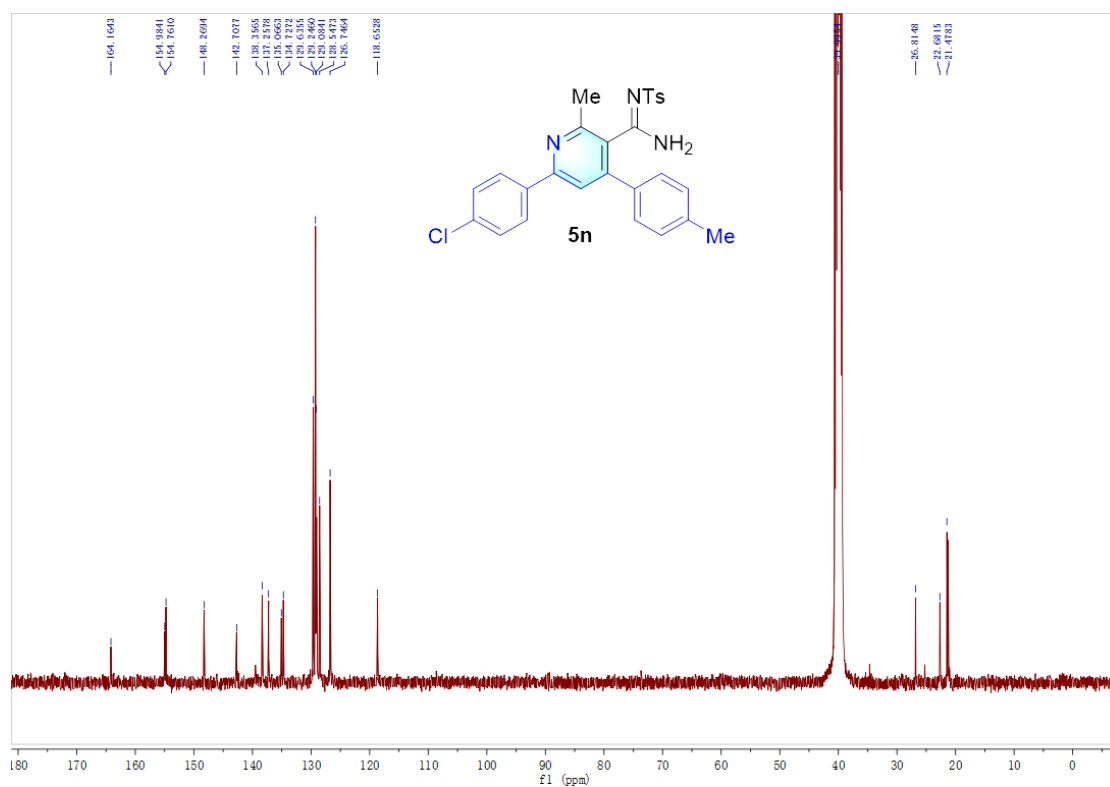
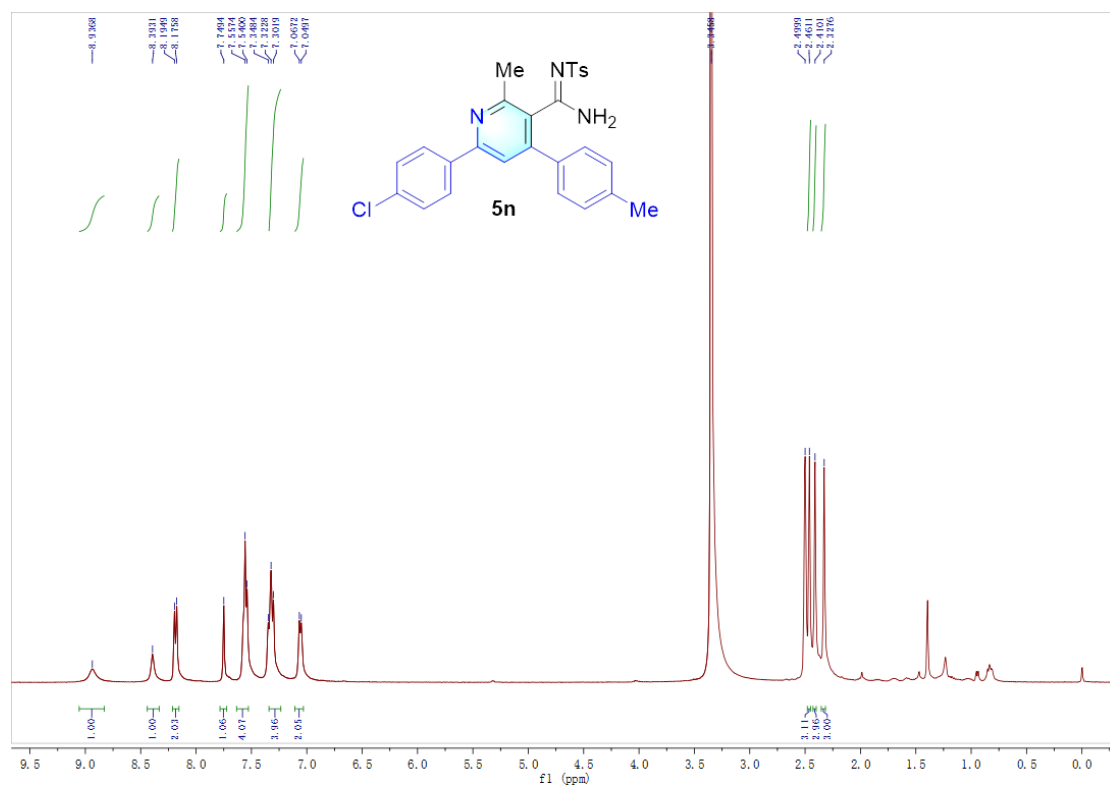


Figure S15. ^1H NMR of **5o** (400 MHz, $\text{DMSO-}d_6$) and ^{13}C NMR of **5o** (100 MHz, $\text{DMSO-}d_6$).

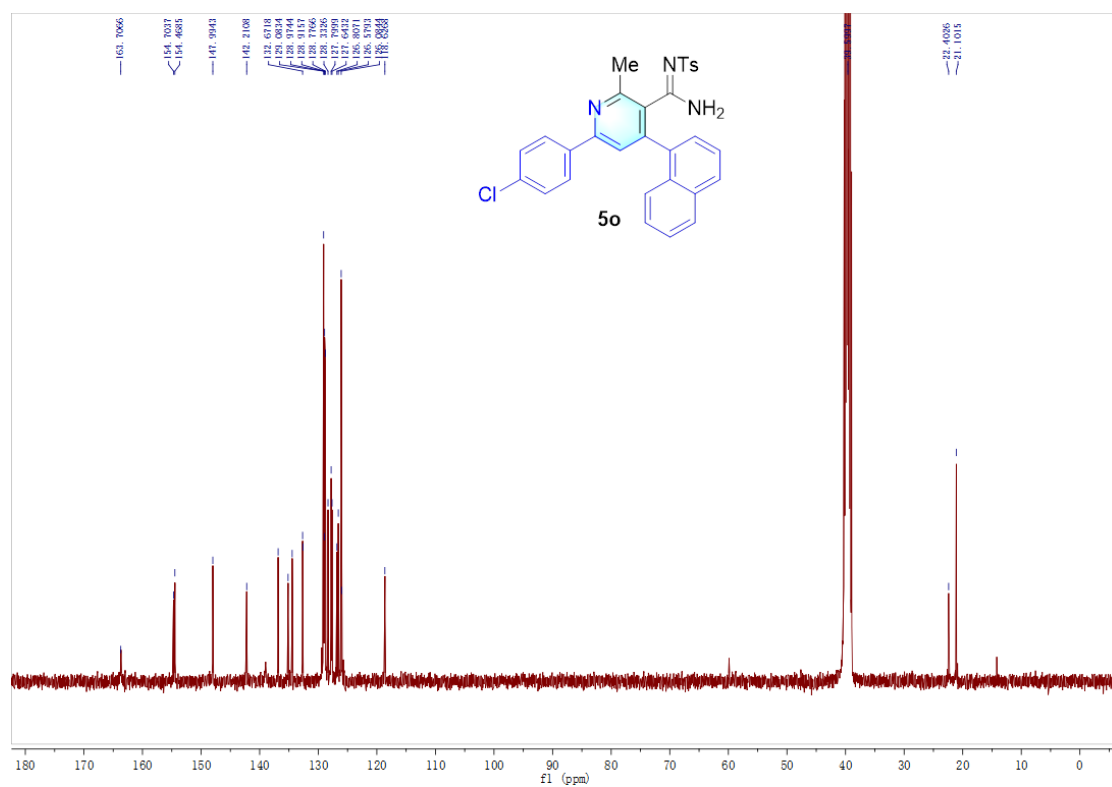
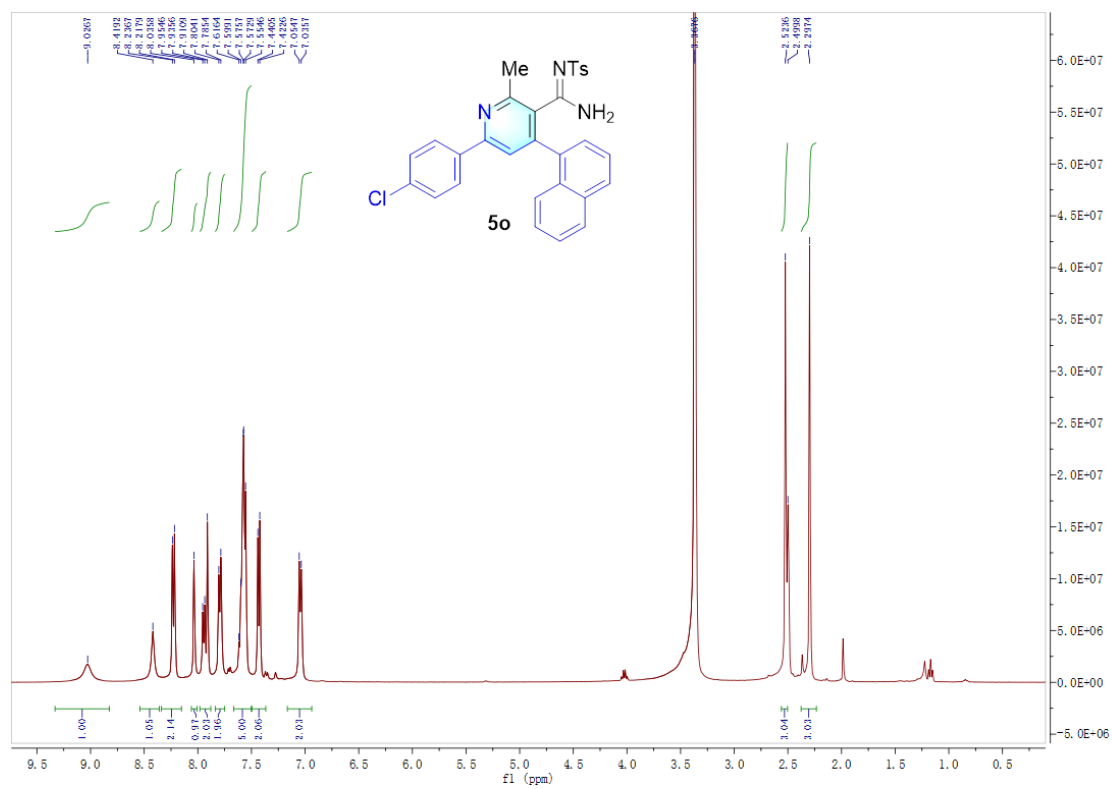


Figure S16. ^1H NMR of **5p** (400 MHz, $\text{DMSO-}d_6$) and ^{13}C NMR of **5p** (100 MHz, $\text{DMSO-}d_6$).

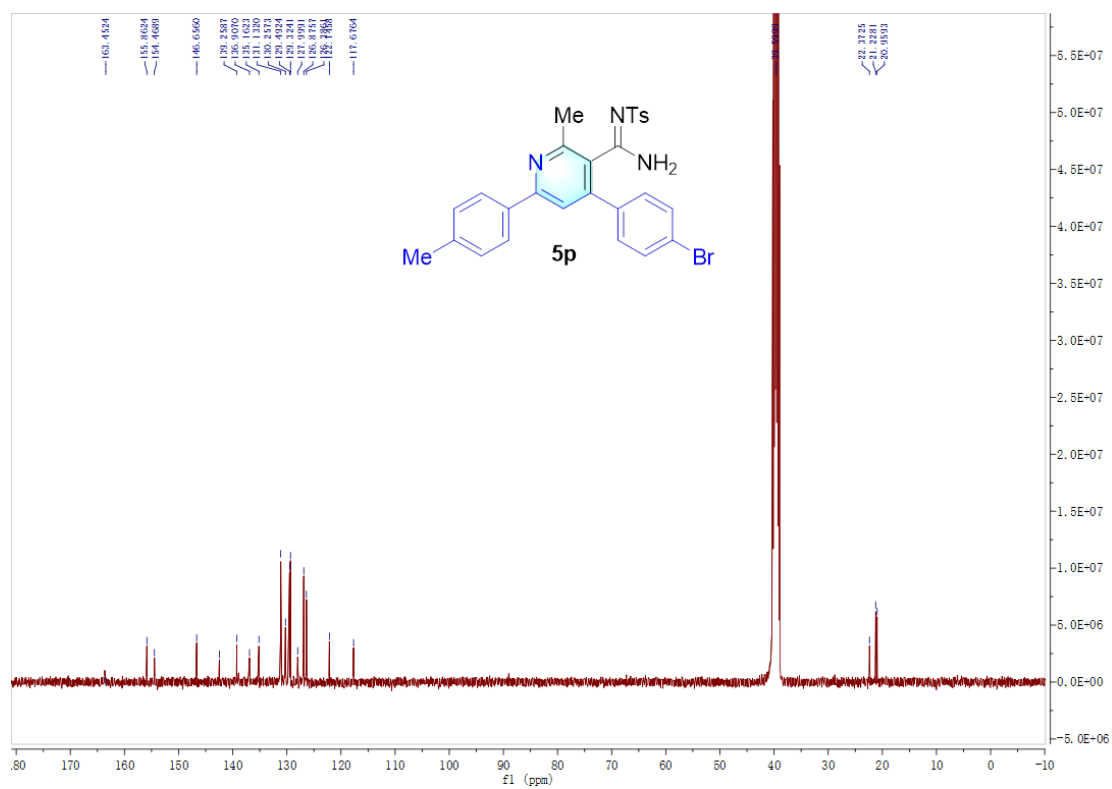
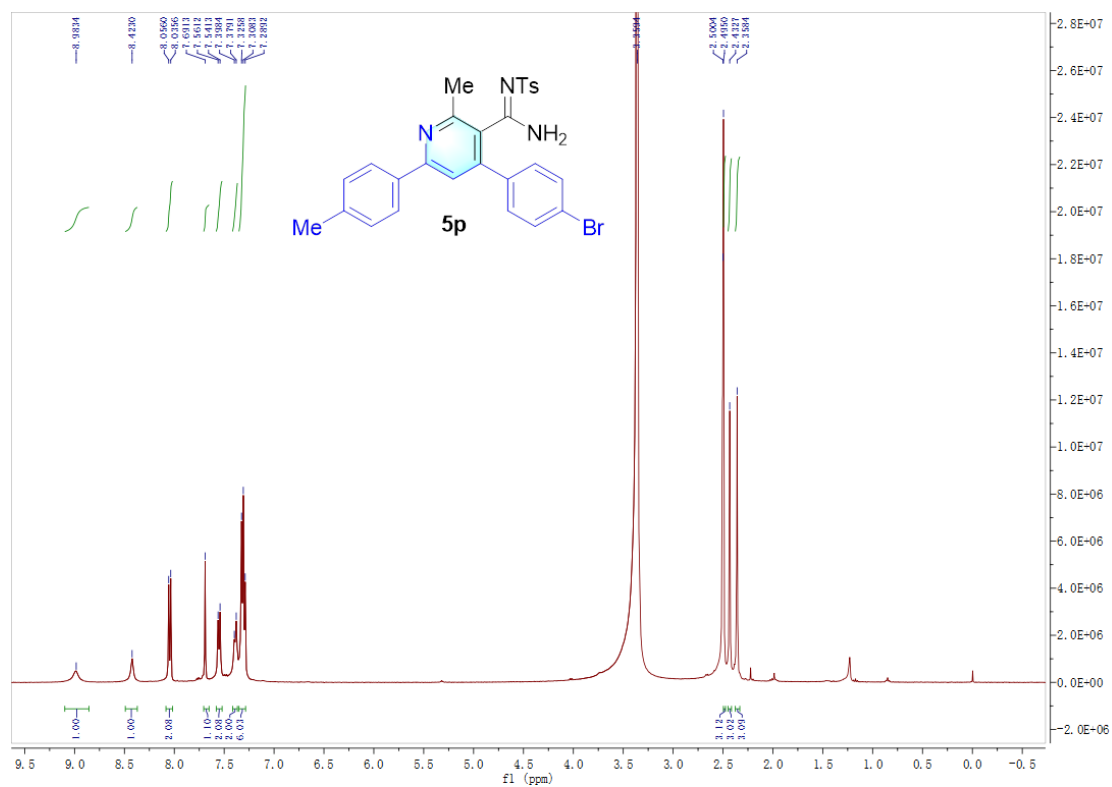


Figure S17. ^1H NMR of **5q** (400 MHz, $\text{DMSO-}d_6$) and ^{13}C NMR of **5q** (100 MHz, $\text{DMSO-}d_6$).

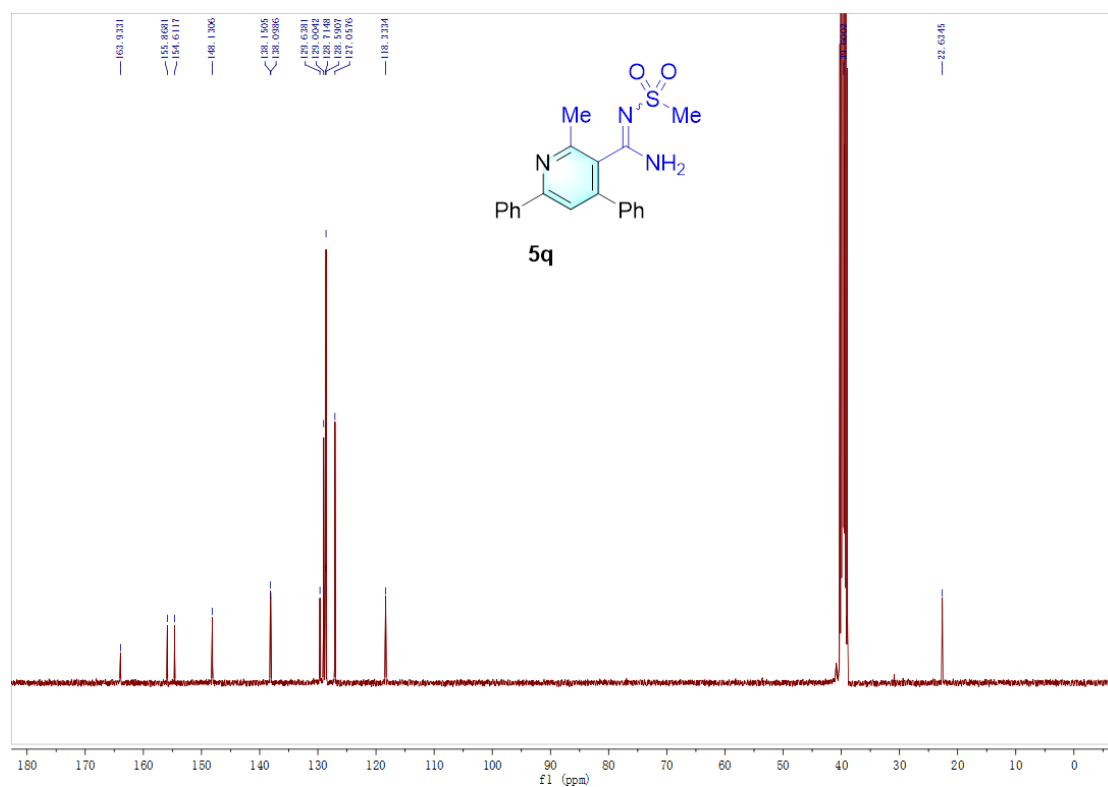
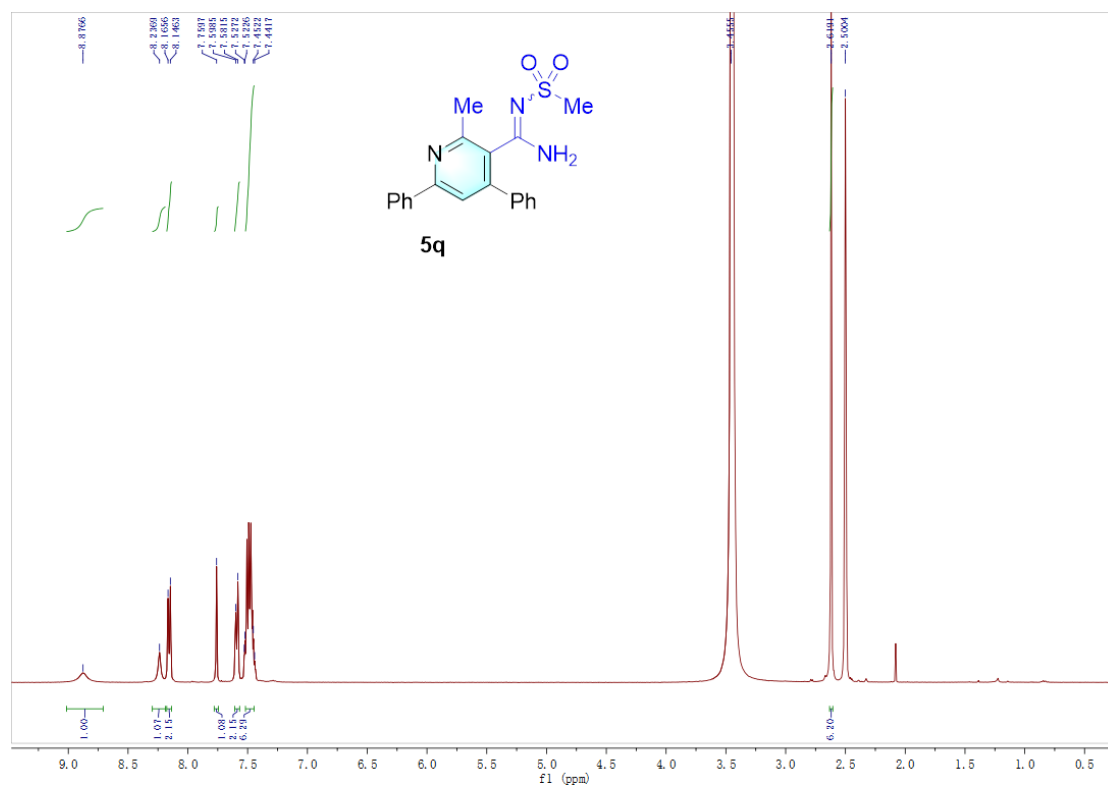


Figure S18. ^1H NMR of **5r** (400 MHz, $\text{DMSO-}d_6$) and ^{13}C NMR of **5r** (100 MHz, $\text{DMSO-}d_6$).

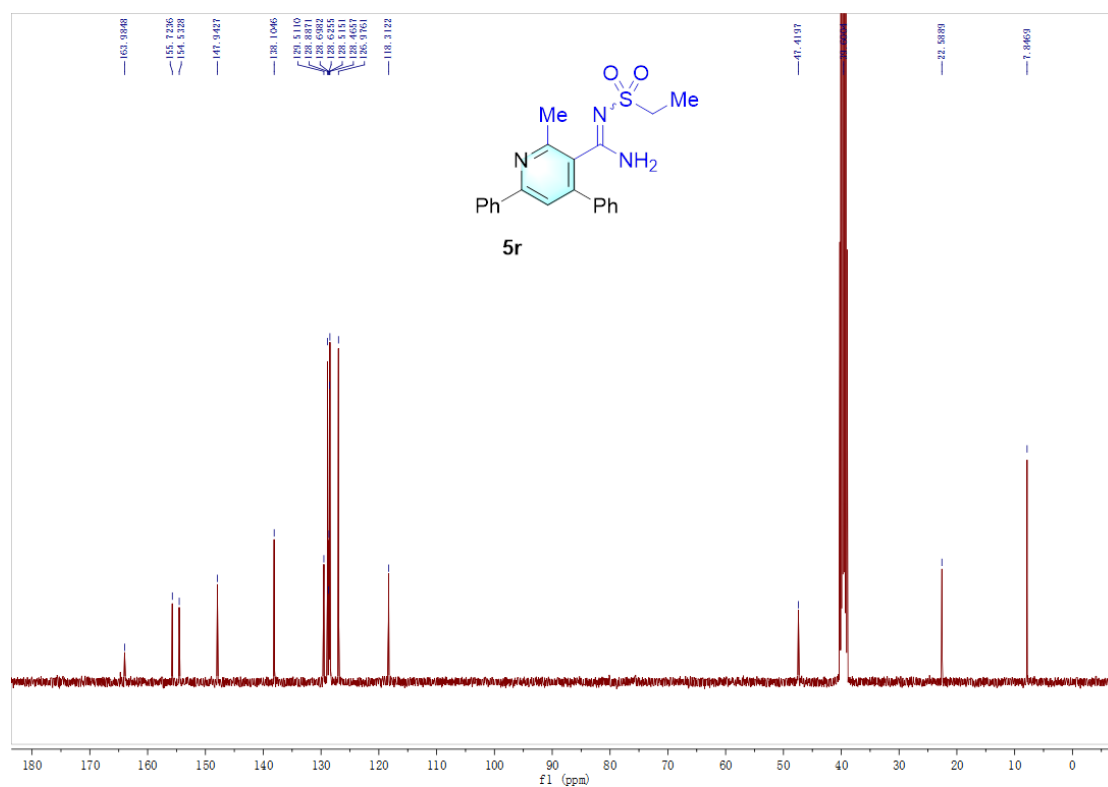
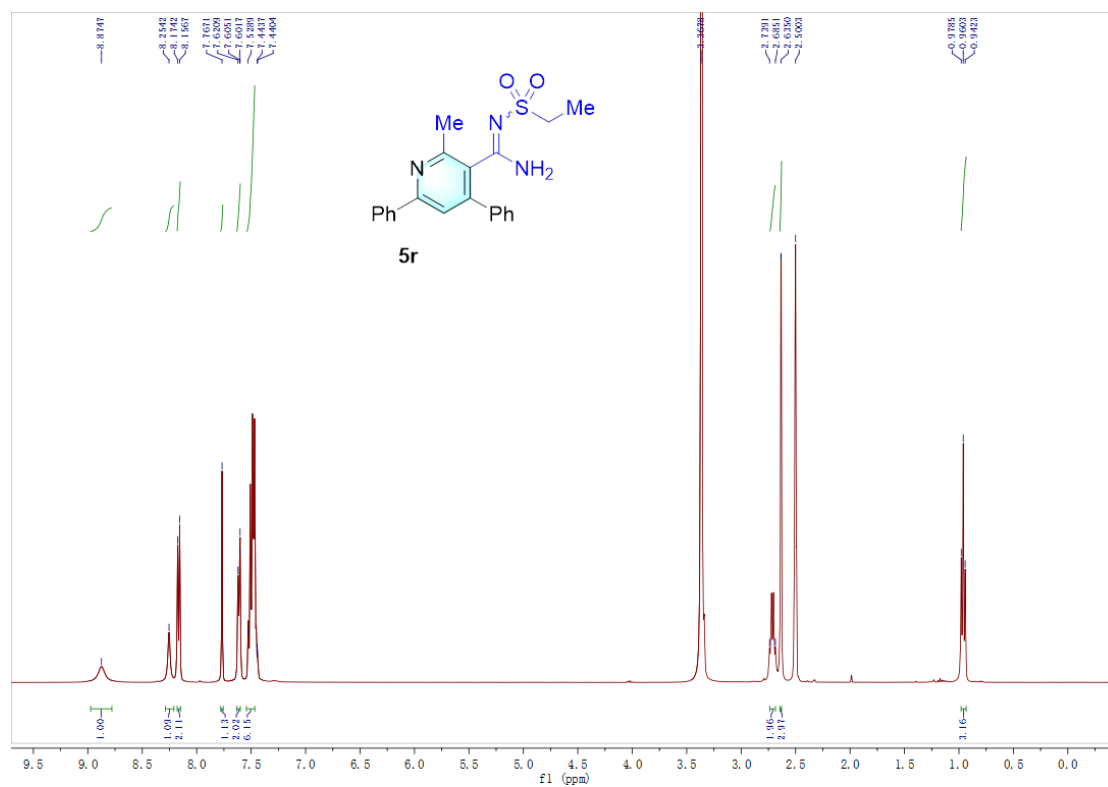


Figure S19. ^1H NMR of **5s** (400 MHz, $\text{DMSO-}d_6$) and ^{13}C NMR of **5s** (100 MHz, $\text{DMSO-}d_6$).

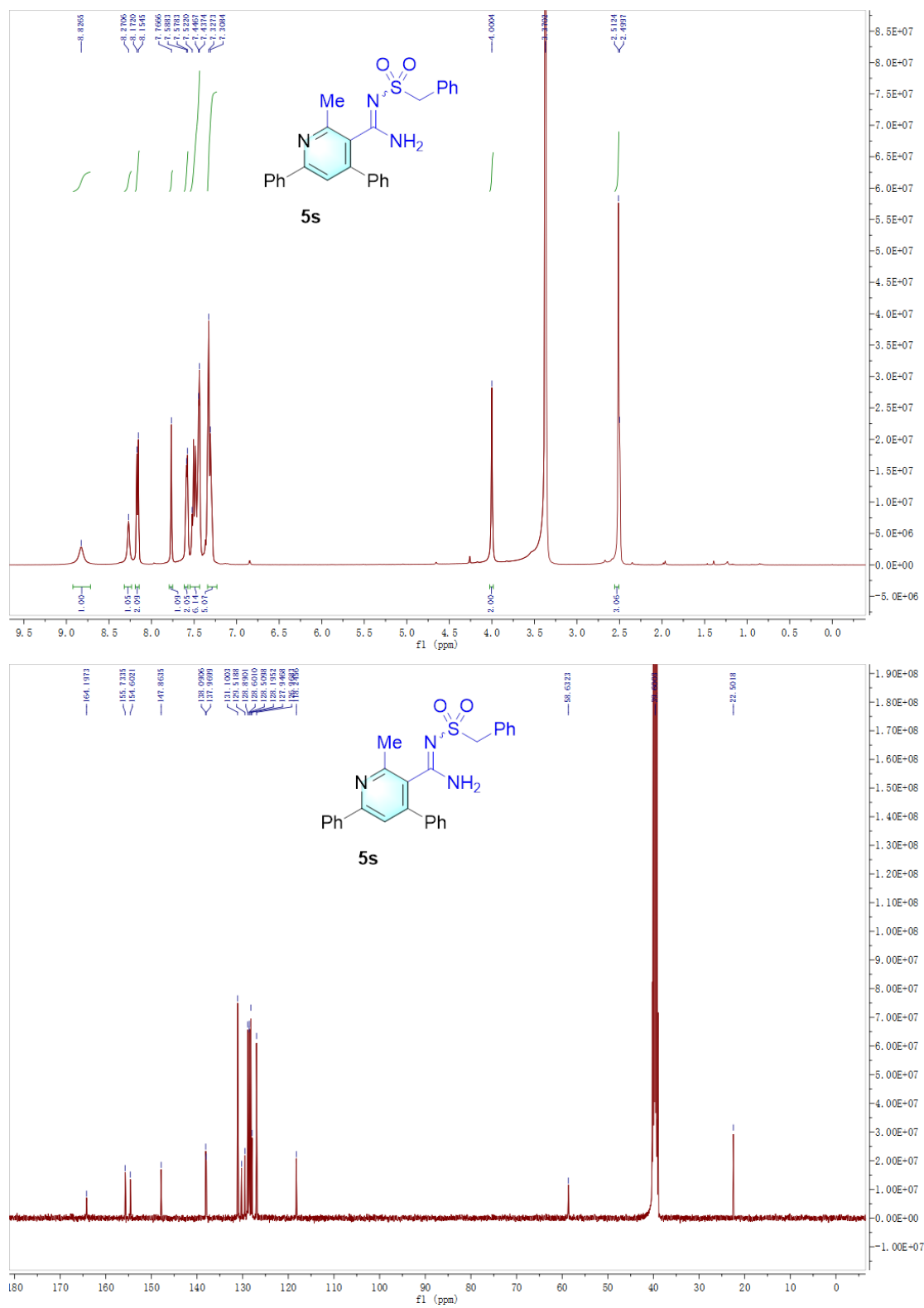


Figure S20. ^1H NMR of **5t** (400 MHz, $\text{DMSO-}d_6$) and ^{13}C NMR of **5t** (100 MHz, $\text{DMSO-}d_6$).

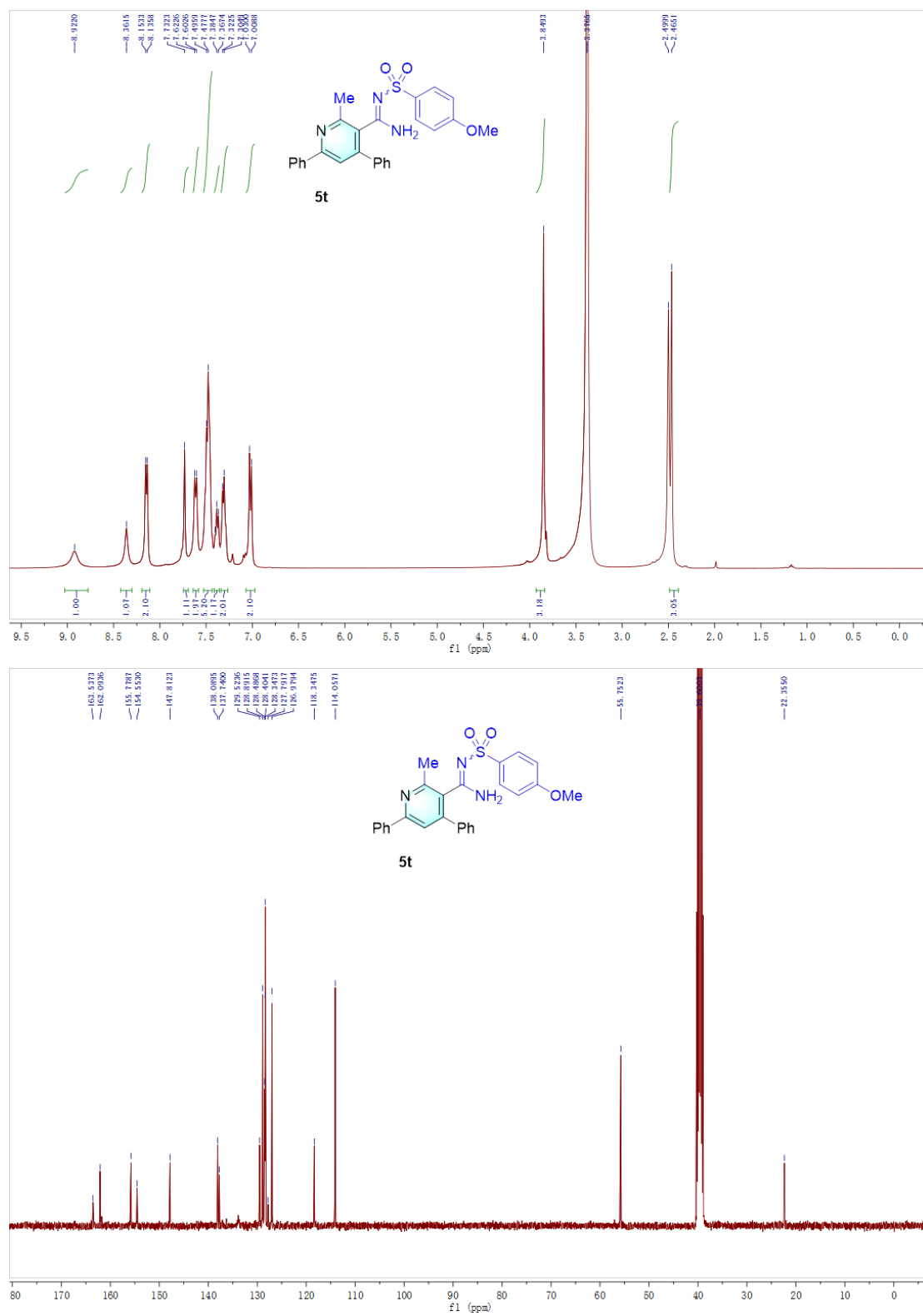


Figure S21. ^1H NMR of **5u** (400 MHz, $\text{DMSO-}d_6$) and ^{13}C NMR of **5u** (100 MHz, $\text{DMSO-}d_6$).

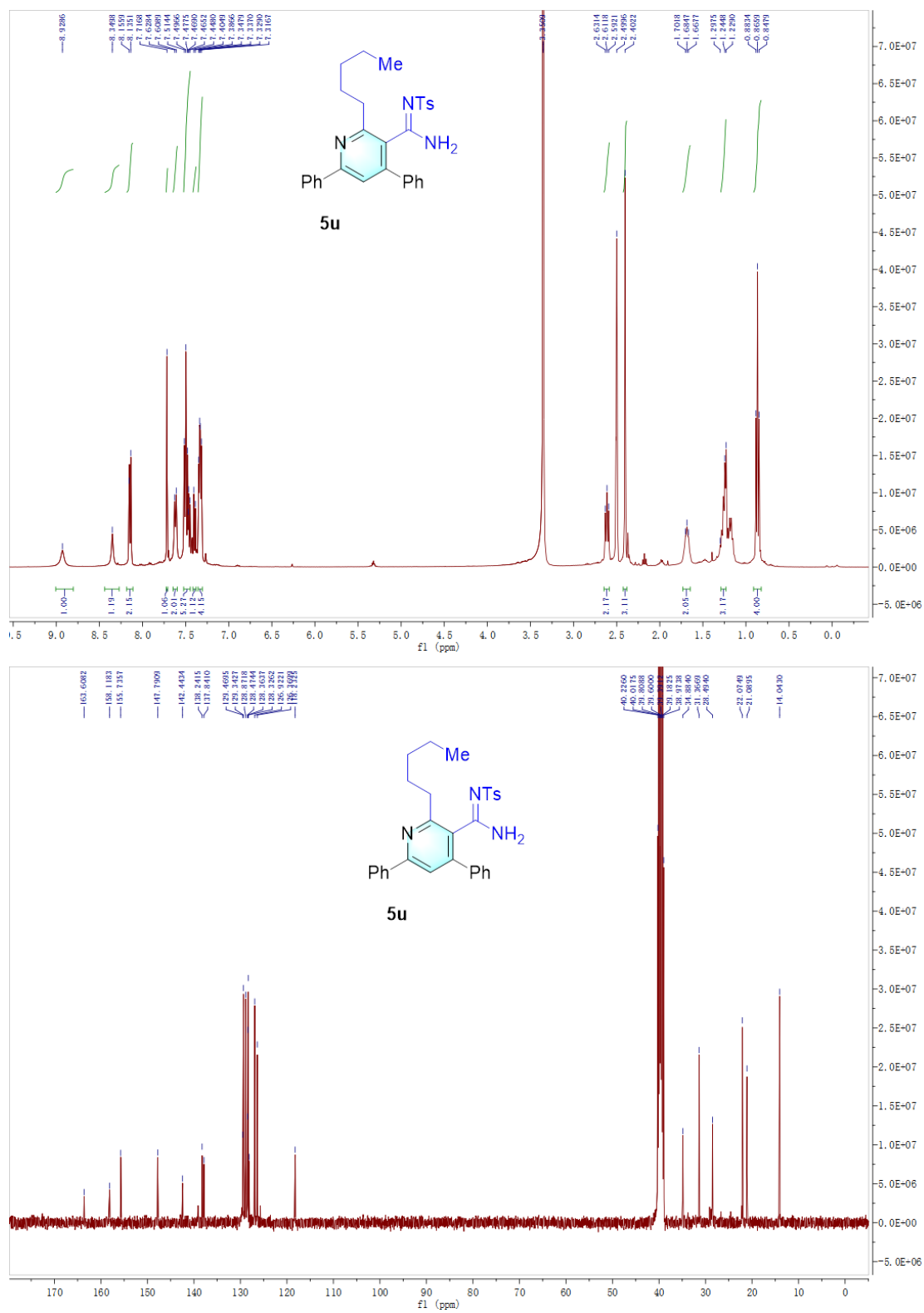


Figure S22. ^1H NMR of **6** (400 MHz, $\text{DMSO-}d_6$) and ^{13}C NMR of **6** (100 MHz, $\text{DMSO-}d_6$).

