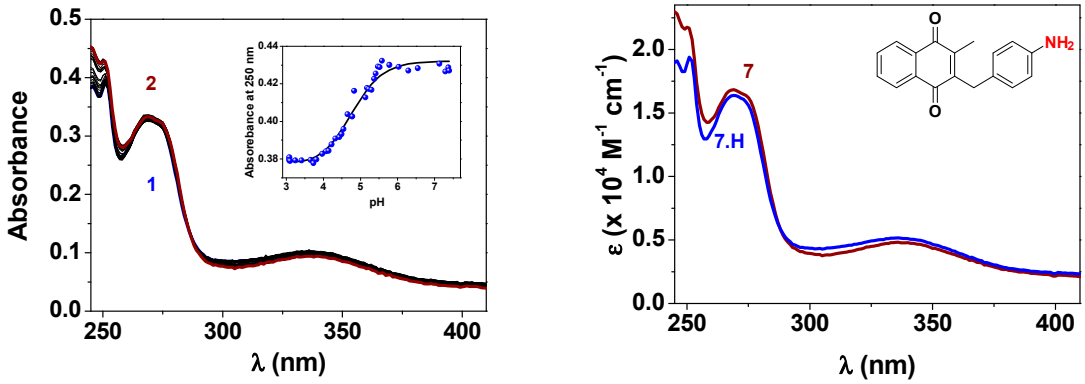
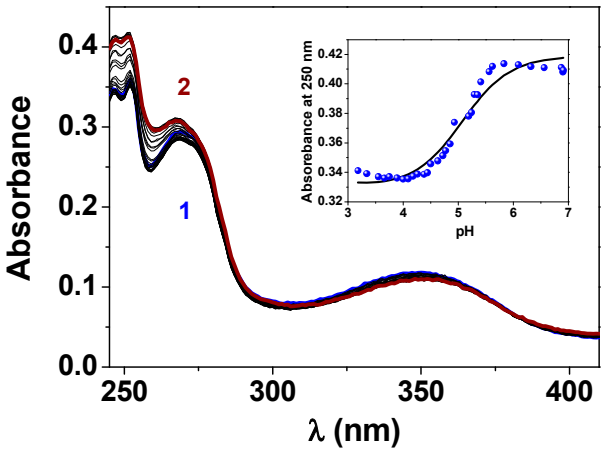
Supplementary materials: Pharmacomodulation of the Antimalarial Plasmodione: Synthesis of Biaryl- and *N*-Arylalkylamine Analogues, Antimalarial Activities and Physicochemical Properties

Karène Urgin, Mouhamad Jida, Katharina Ehrhardt, Tobias Müller, Michael Lanzer, Louis Maes, Mourad Elhabiri, and Elisabeth Davioud-Charvet

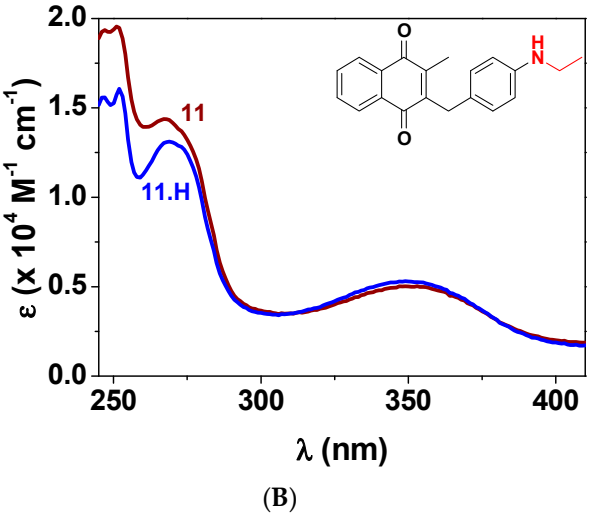


(**A**) (**B**)

Figure S1. (**A**) Absorption spectrophotometric titration of compound 7 as a function of pH and (**B**) electronic spectra of 7 and its protonated species 7.H. Solvent: Water; I = 0.1 M $NaClO_4$; T = 25.0 ± 0.2 °C; l = 1 cm; $[7]_{tot}$ = 2.00 × 10^{-5} M; (1) pH = 3.08; (2) pH = 7.39. The charges have been omitted for the sake of clarity. The inset of (**A**) shows the spectral variation at 250 nm as a function of pH. The UV-visible absorption spectra have not been corrected from dilution effects.

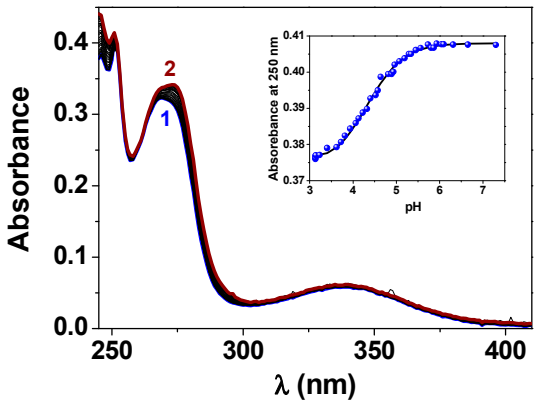


(**A**)

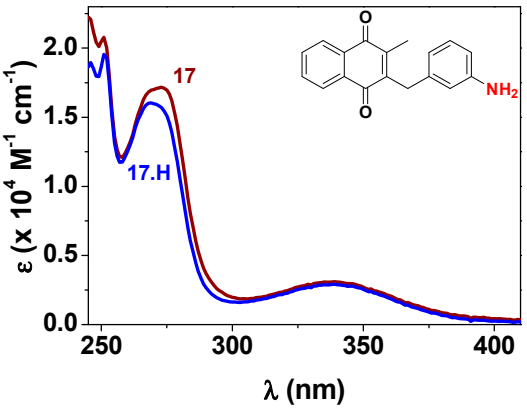


(**B**)

Figure S2. (**A**) Absorption spectrophotometric titration of compound 11 as a function of pH and (**B**) electronic spectra of 11 and its protonated species 11.H. Solvent: Water/DMSO (91/9 v/v); I = 0.1 M $NaClO_4$; T = 25.0 ± 0.2 °C; l = 1 cm; $[11]_{tot} = 2.18 \times 10^{-5}$ M; (1) pH = 3.18; (2) pH = 6.91. The charges have been omitted for the sake of clarity. The inset of (**A**) shows the spectral variation at 250 nm as a function of pH. The UV-visible absorption spectra have not been corrected from dilution effects.



(**A**)



(**B**)

Figure S3. (**A**) Absorption spectrophotometric titration of compound 17 as a function of pH and (**B**) electronic spectra of 17 and its protonated species 17.H. Solvent: Water; I = 0.1 M $NaClO_4$; T = 25.0 ± 0.2 °C; l = 1 cm; $[17]_{tot} = 2.00 \times 10^{-5}$ M; (1) pH = 3.13; (2) pH = 7.30. The charges have been omitted for the sake of clarity. The inset of (**A**) shows the spectral variation at 250 nm as a function of pH. The UV-visible absorption spectra have not been corrected from dilution effects.

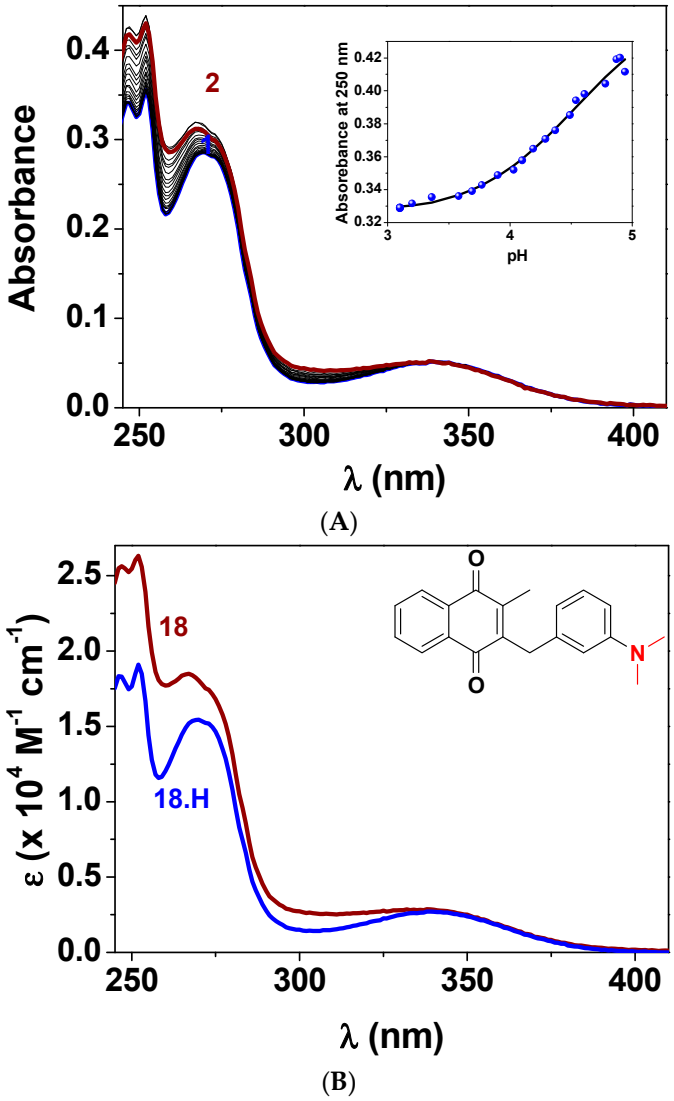


Figure S4. (**A**) Absorption spectrophotometric titration of compound 18 as a function of pH and (**B**) electronic spectra of 18 and its protonated species 18.H. Solvent: Water; I = 0.1 M $NaClO_4$; T = 25.0 ± 0.2 °C; l = 1 cm; $[18]_{tot} = 1.84 \times 10^{-5}$ M; (1) pH = 3.10; (2) pH = 4.94. The charges have been omitted for the sake of clarity. The inset of (**A**) shows the spectral variation at 250 nm as a function of pH. The UV-visible absorption spectra have not been corrected from dilution effects.

2. ^{1}H-NMR and ^{13}C-NMR spectra

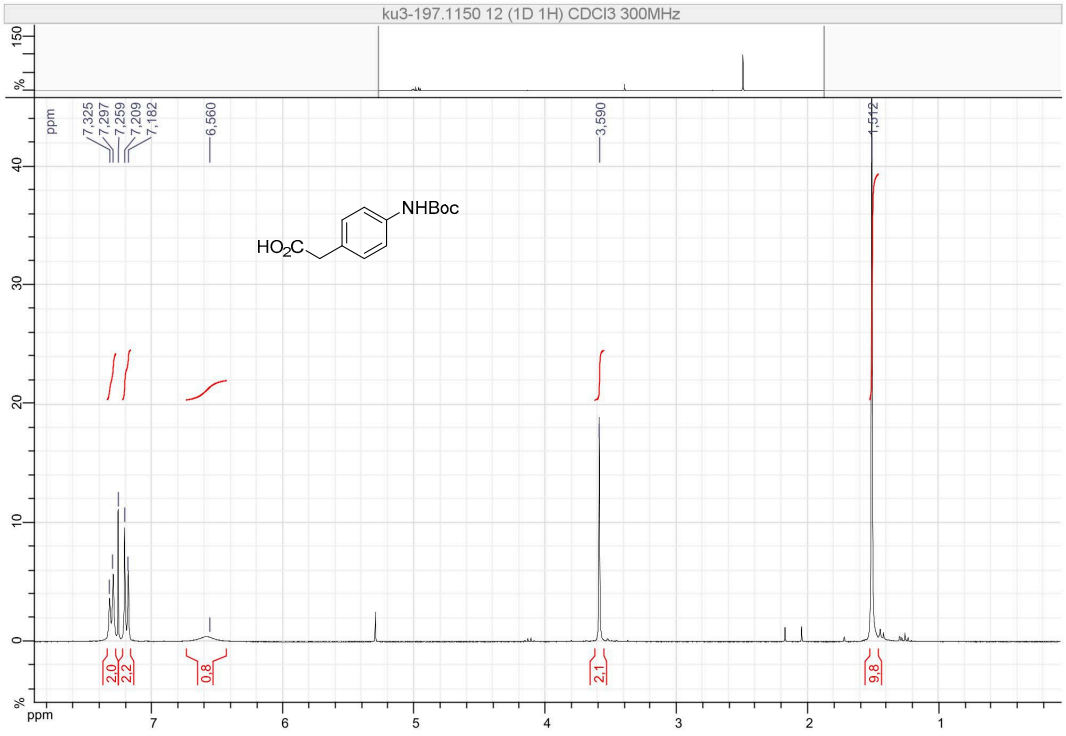


Figure S5. ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of compound **5**.

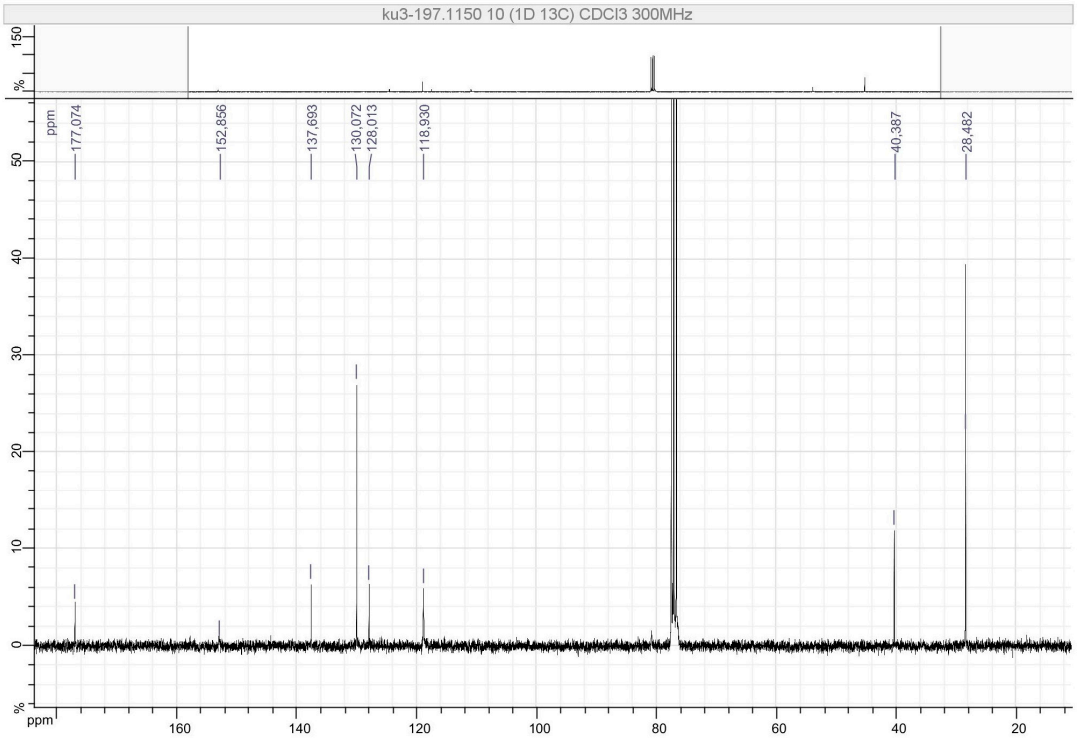


Figure S6. ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of compound **5**.

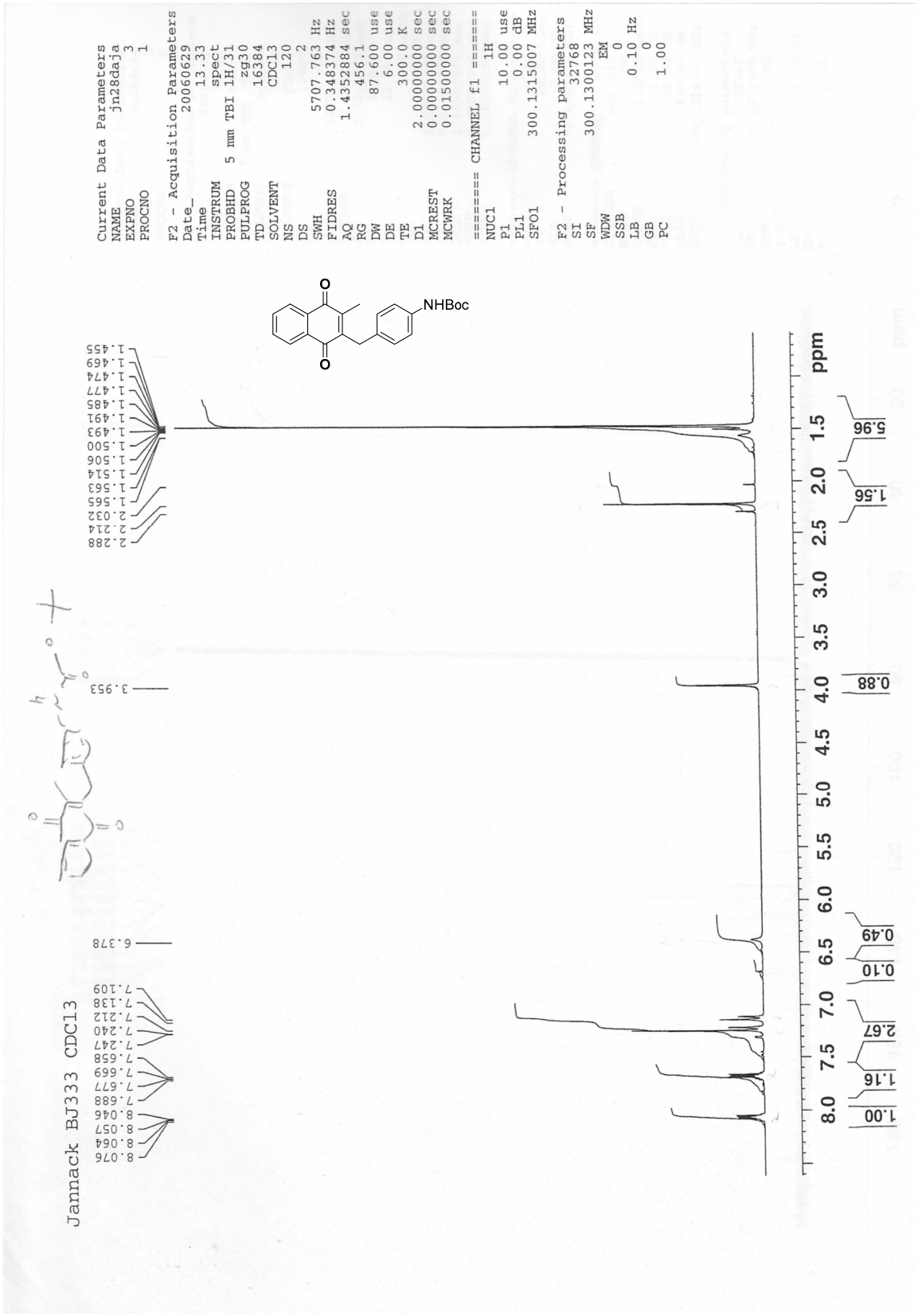


Figure S7. ^{1}H NMR (300 MHz, $CDCl_3$) spectrum of compound **6**.

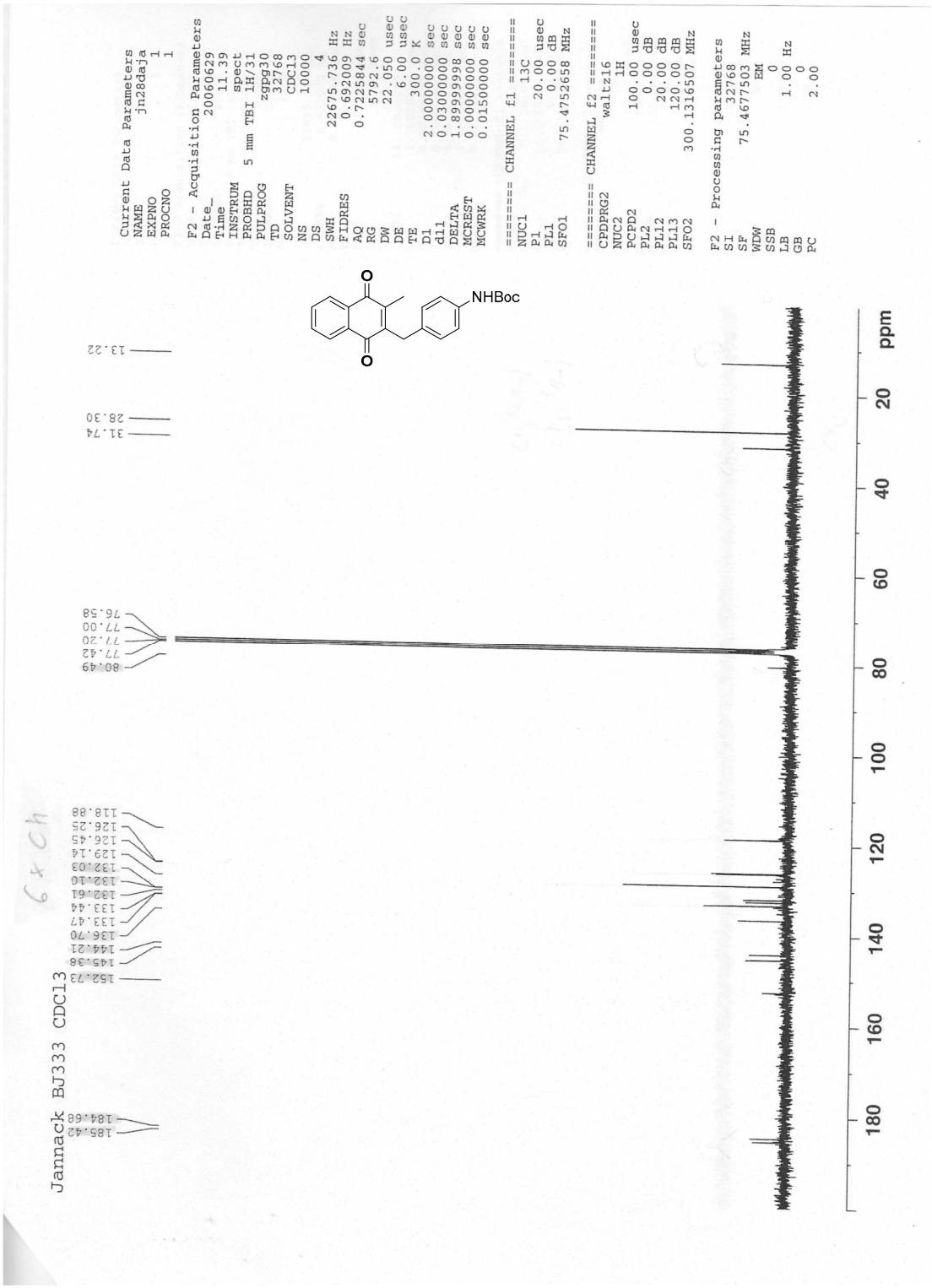


Figure S8. $^{13C\text{-}NMR}$ (75 MHz, $CDCl_3$) spectrum of compound **6**.

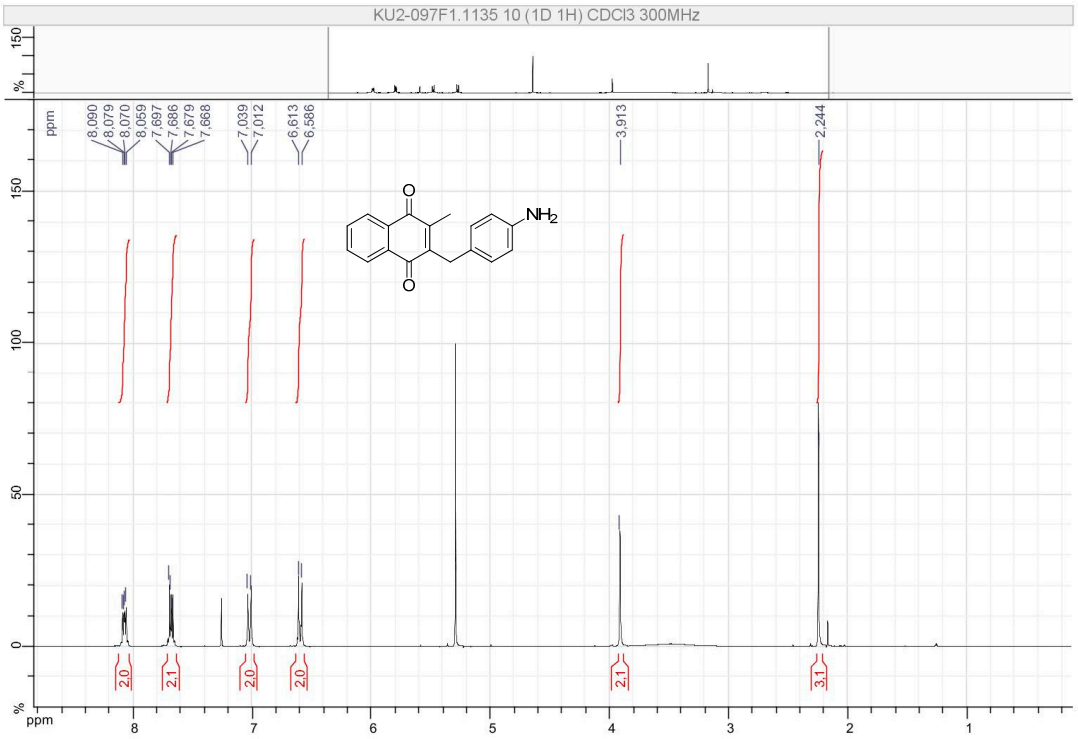


Figure S9. ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of compound **7**.

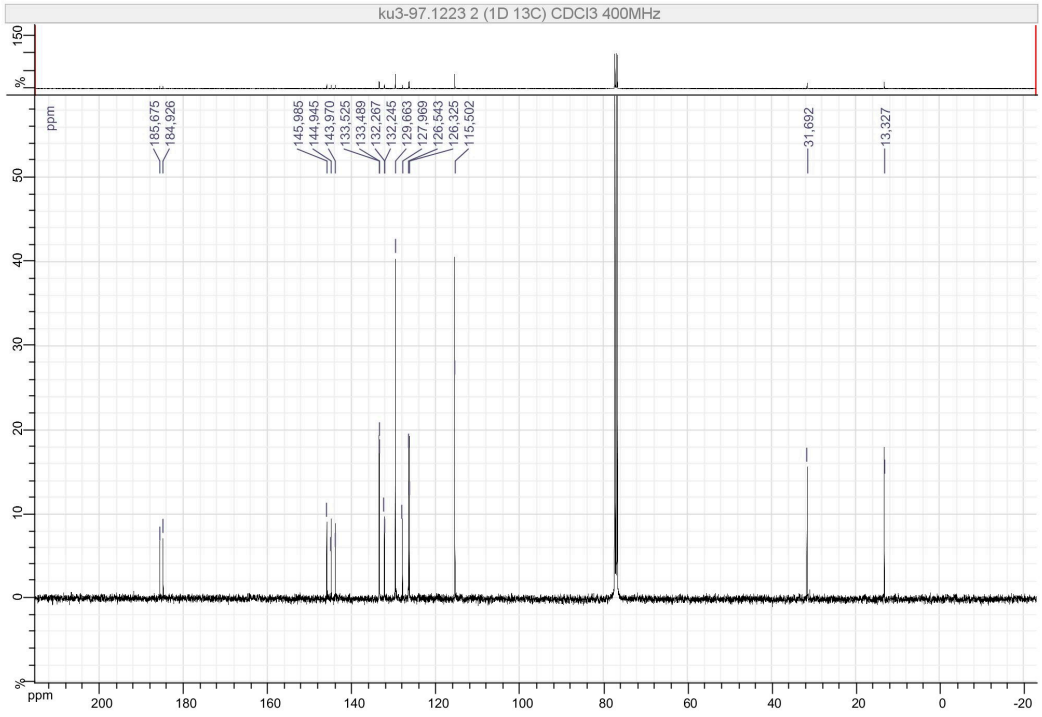


Figure S10. ^{13}C-NMR (100 MHz, $CDCl_3$) spectrum of compound **7**.

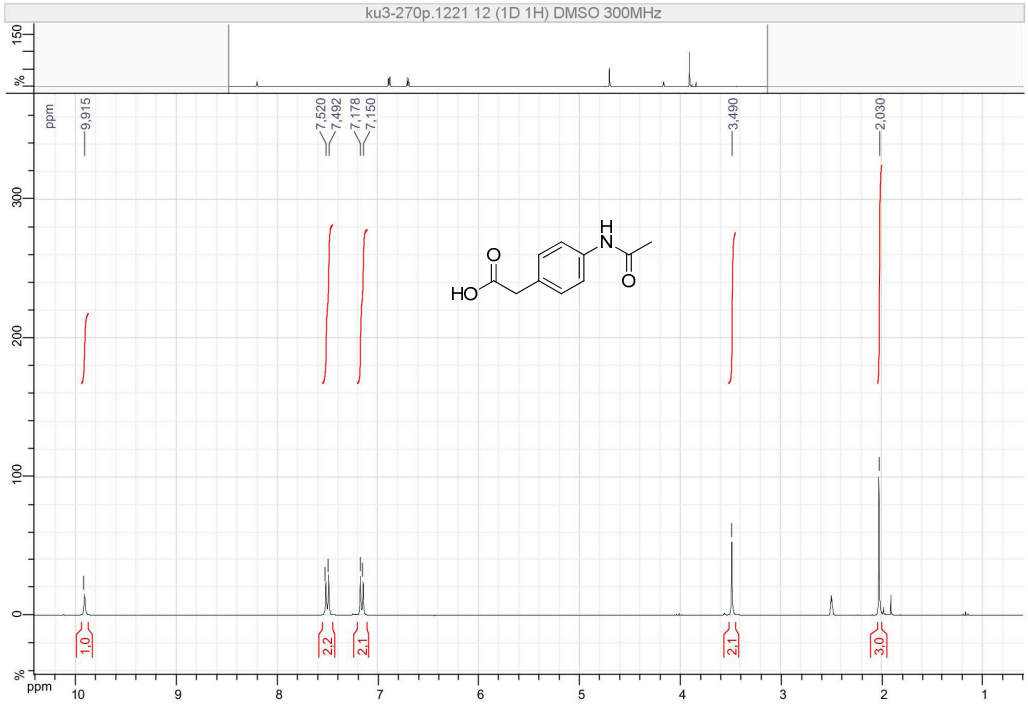


Figure S11. ^{1}H-NMR (300 MHz, DMSO-d$_6$) spectrum of compound **8**.

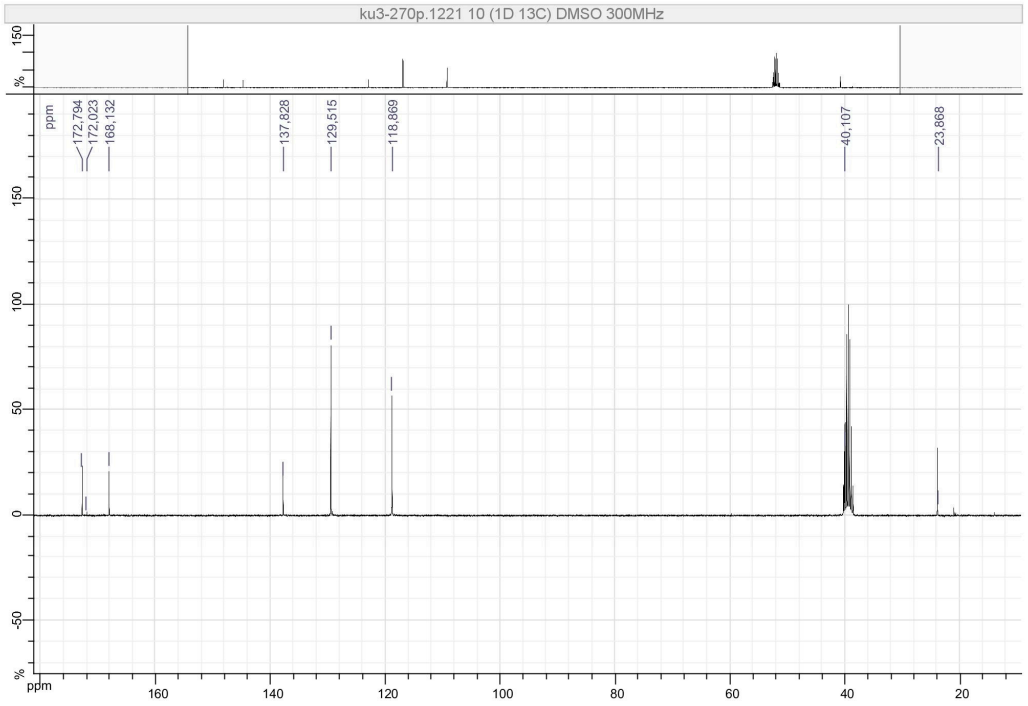


Figure S12. ^{13}C-NMR (75 MHz, DMSO-d$_6$) spectrum of compound **8**.

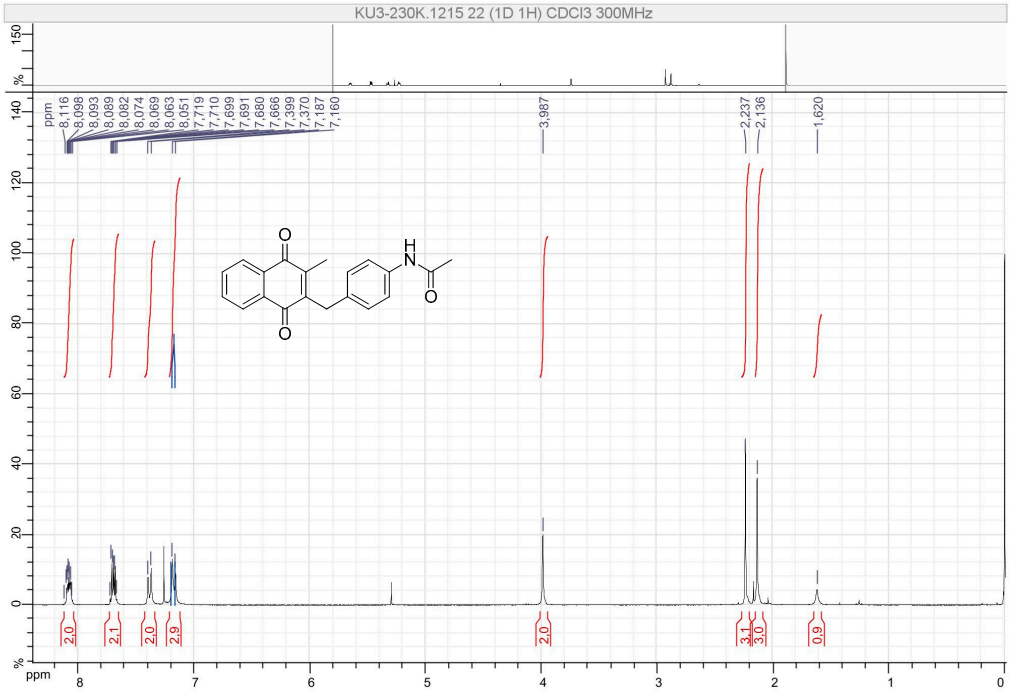


Figure S13. ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of compound **9**.

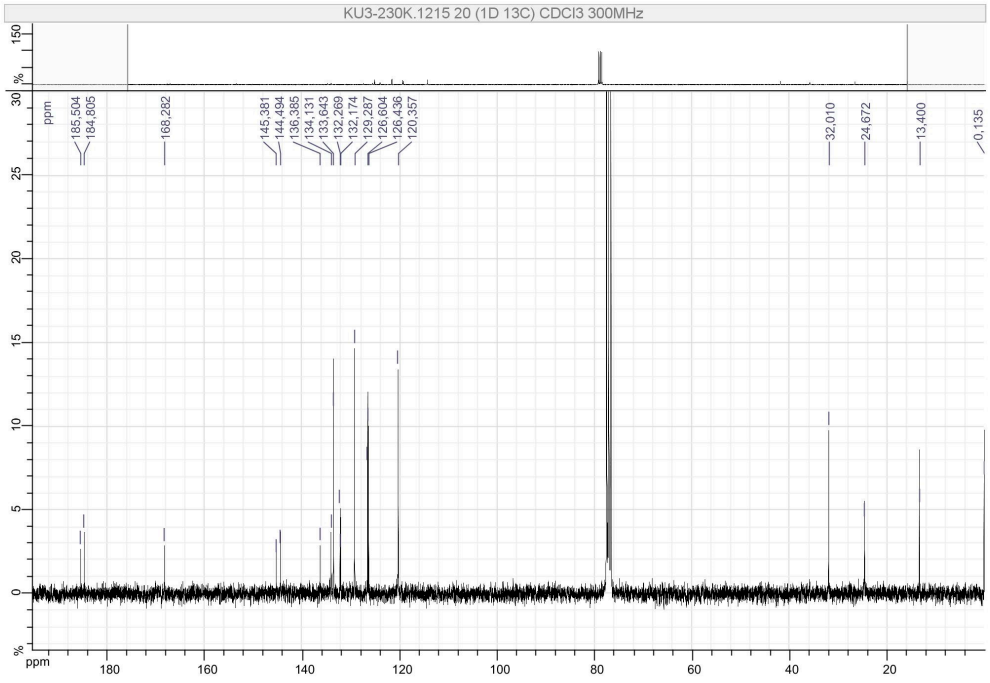


Figure S14. ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of compound **9**.

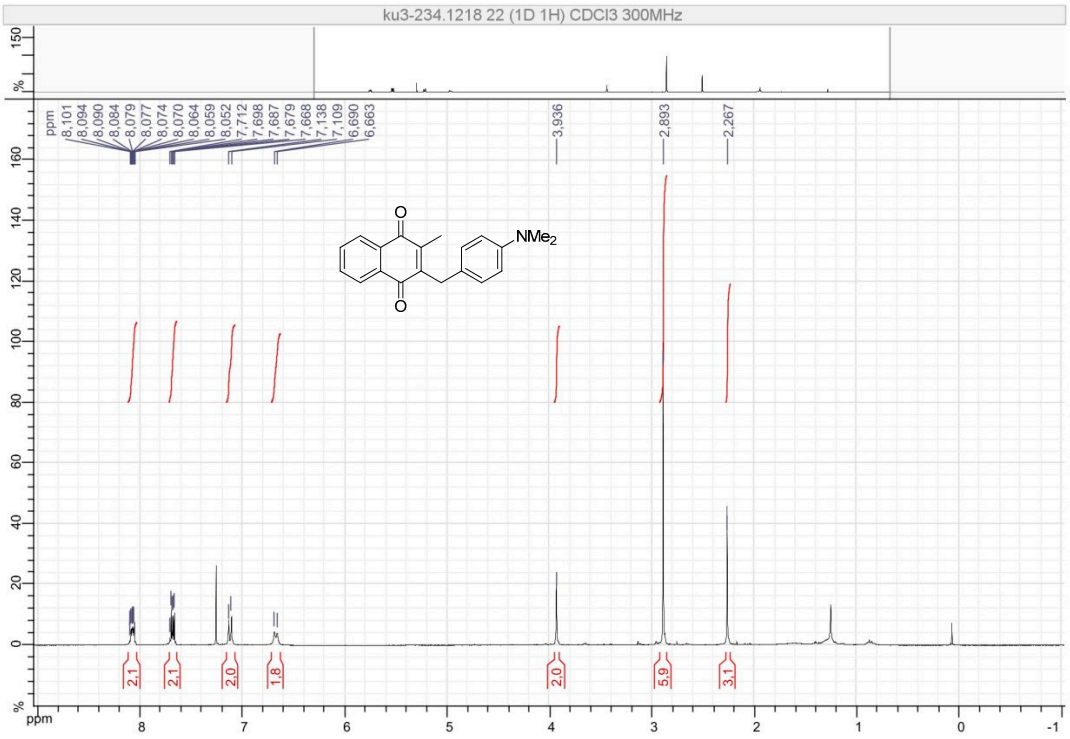


Figure S15. ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of compound **3**.

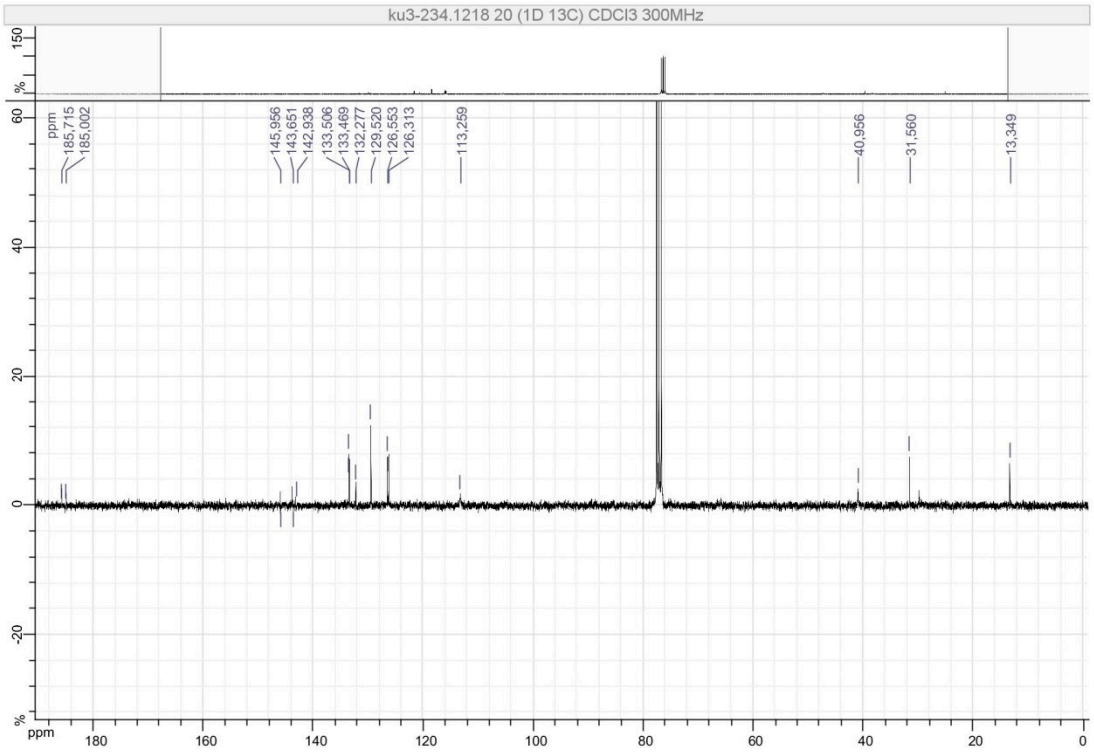


Figure S16. ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of compound **3**.

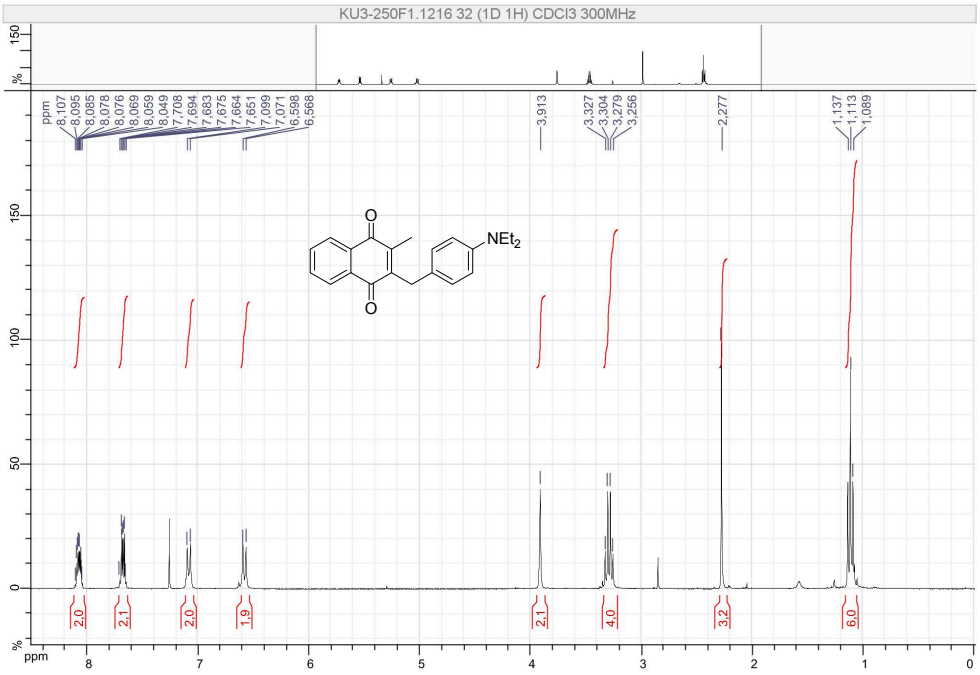


Figure S17. ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of compound **11**.

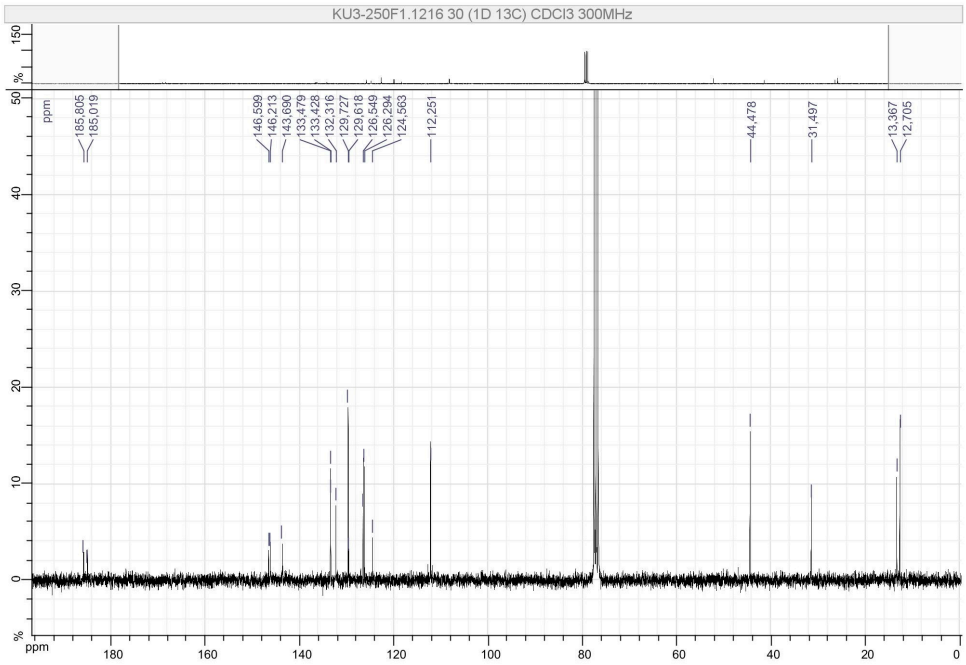


Figure S18. ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of compound **11**.

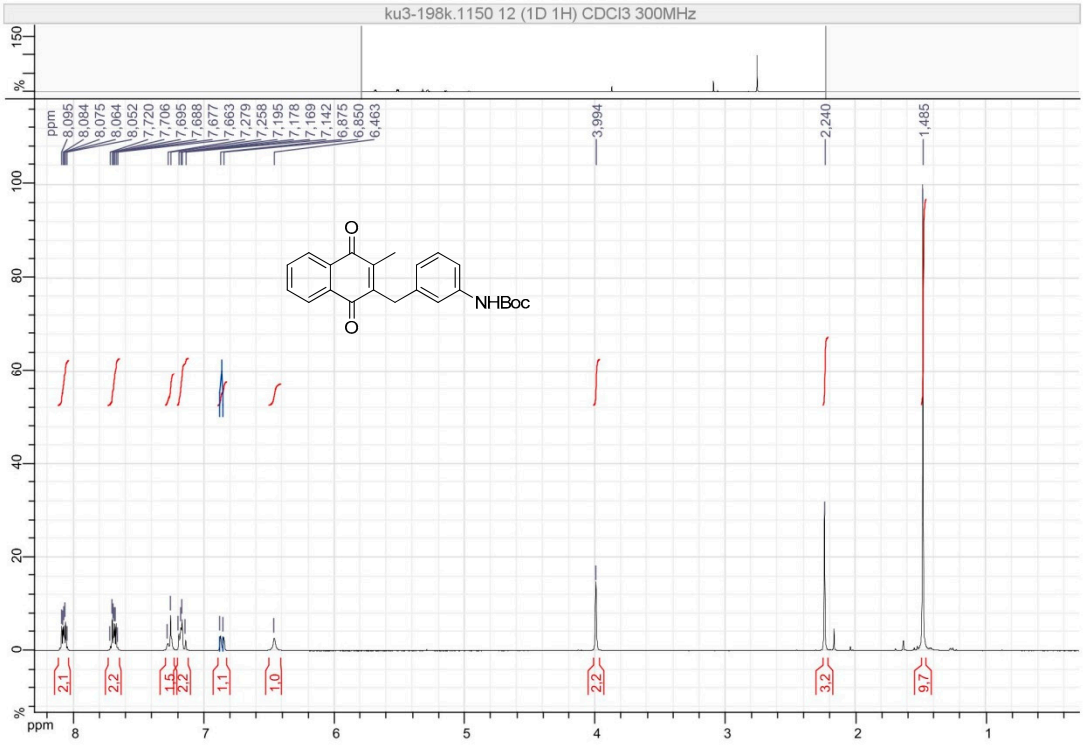


Figure S19. ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of compound **14**.

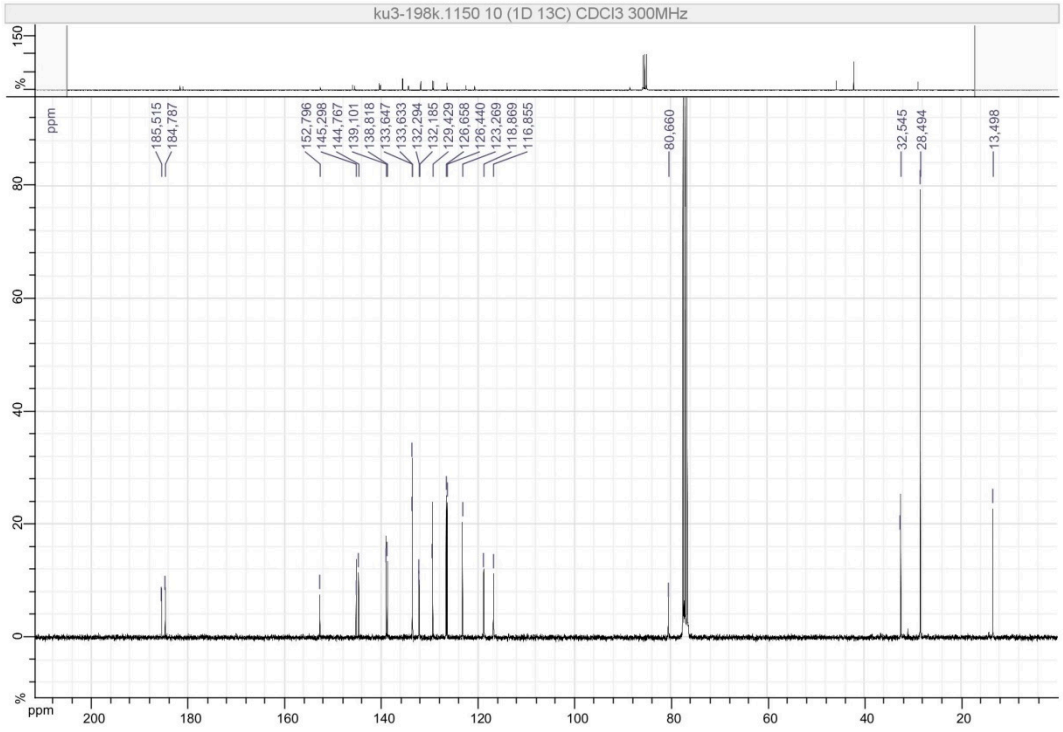


Figure S20. ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of compound **14**.

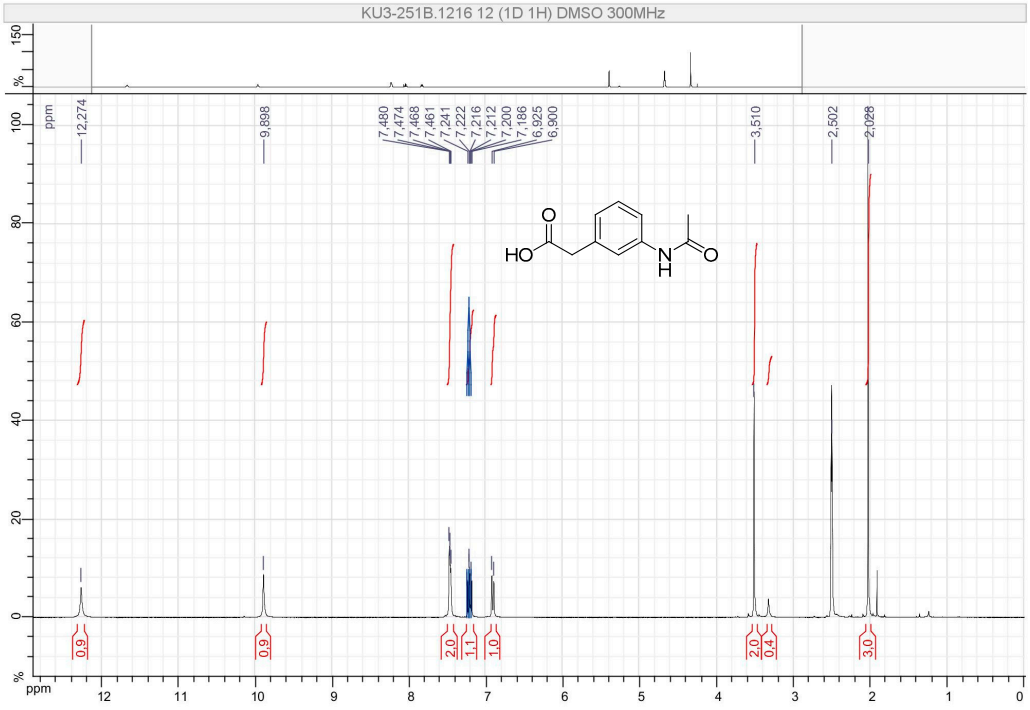


Figure S21. ^{1}H-NMR (300 MHz, DMSO-d$_6$) spectrum of compound **15**.

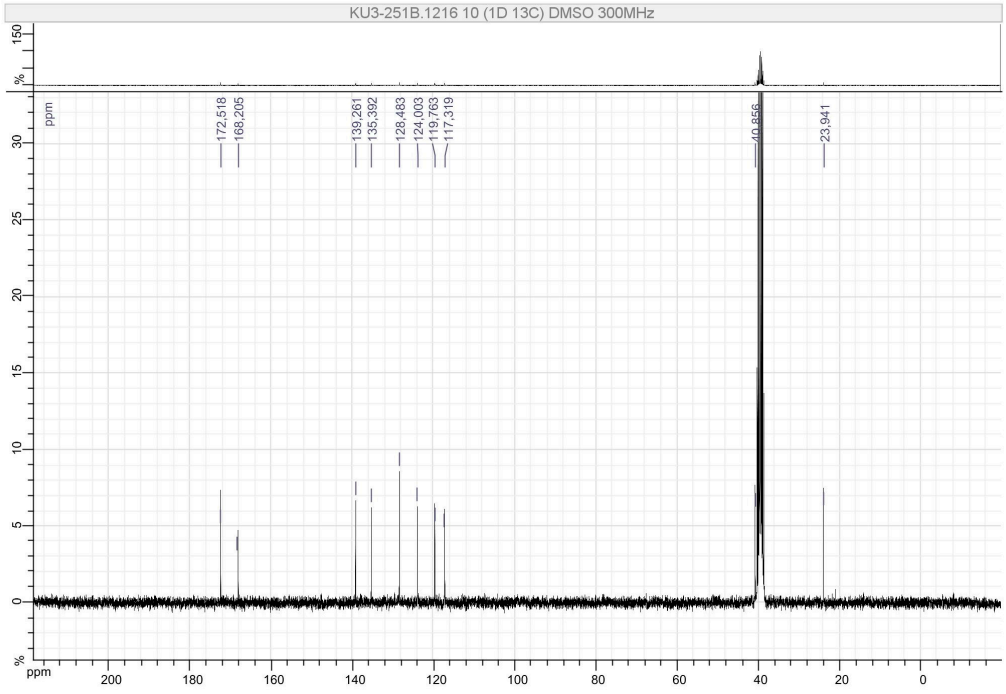


Figure S22. ^{13}C-NMR (75 MHz, DMSO-d$_6$) spectrum of compound **15**.

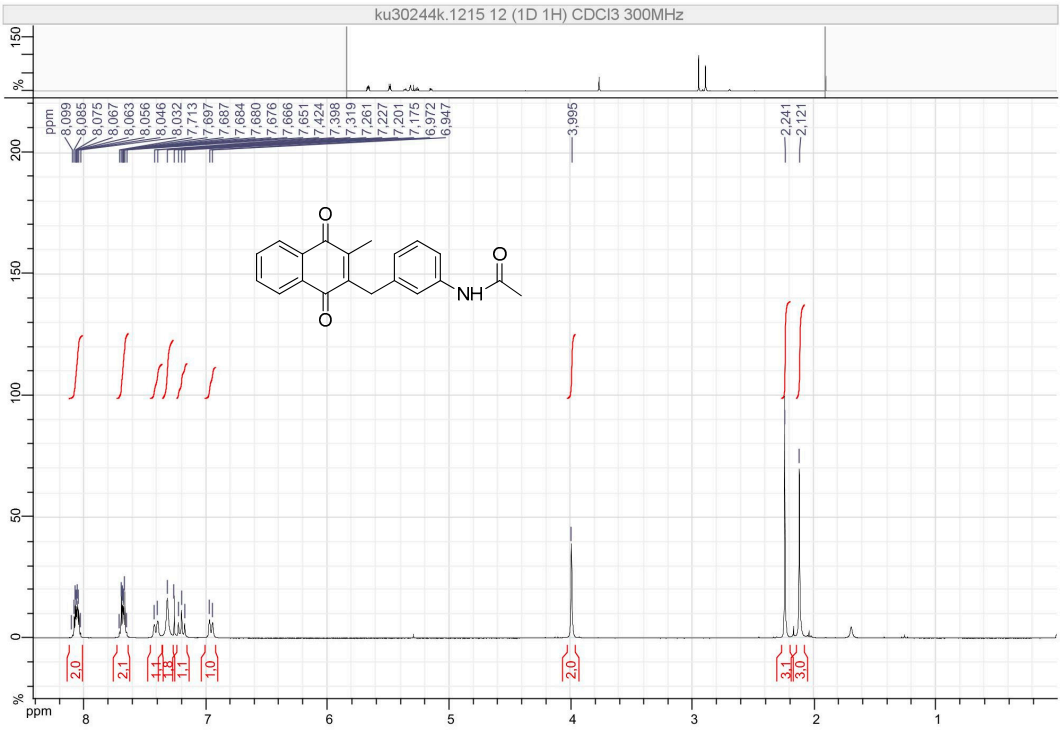


Figure S23. ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of compound **16**.

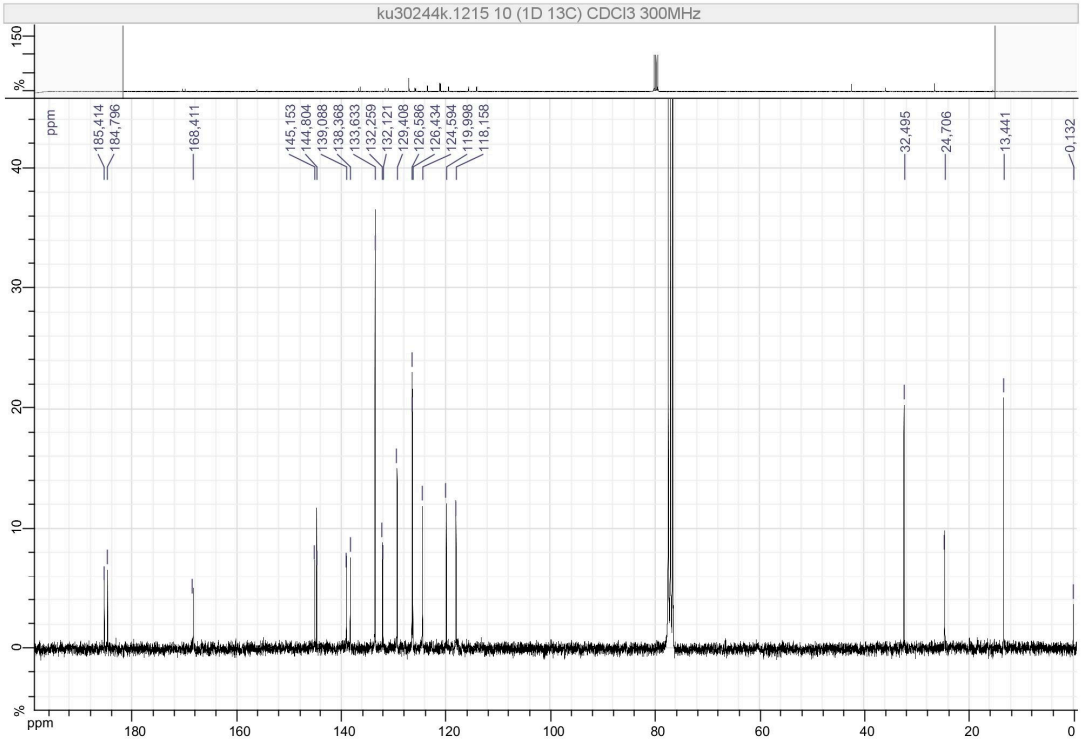


Figure S24. ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of compound **16**.

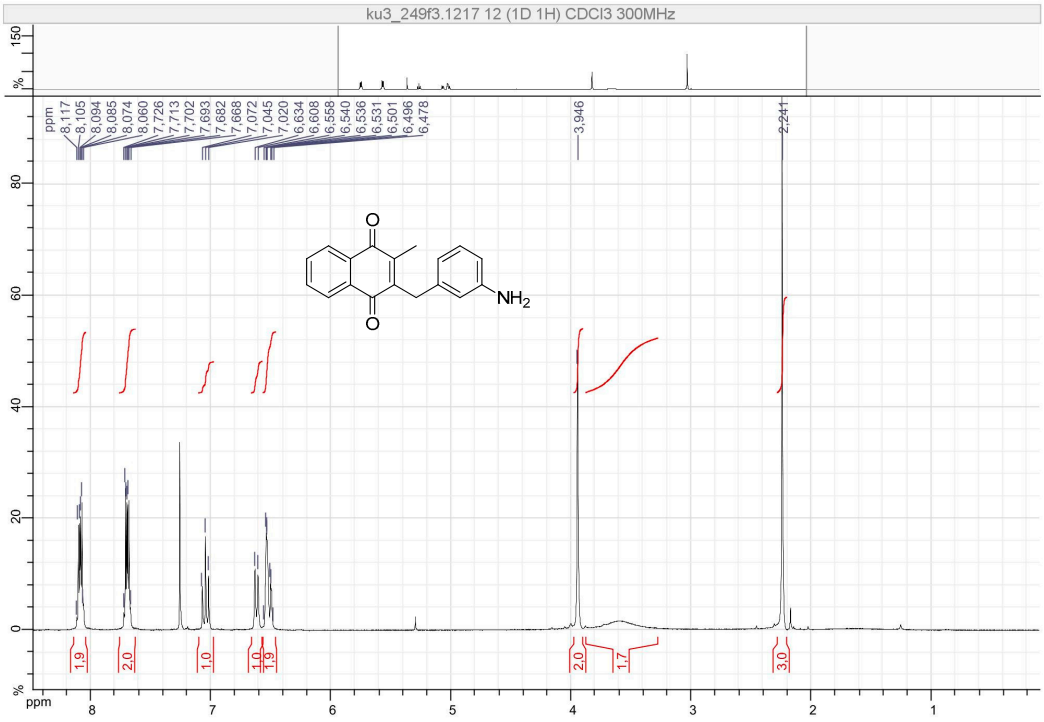


Figure S25. ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of compound **17**.

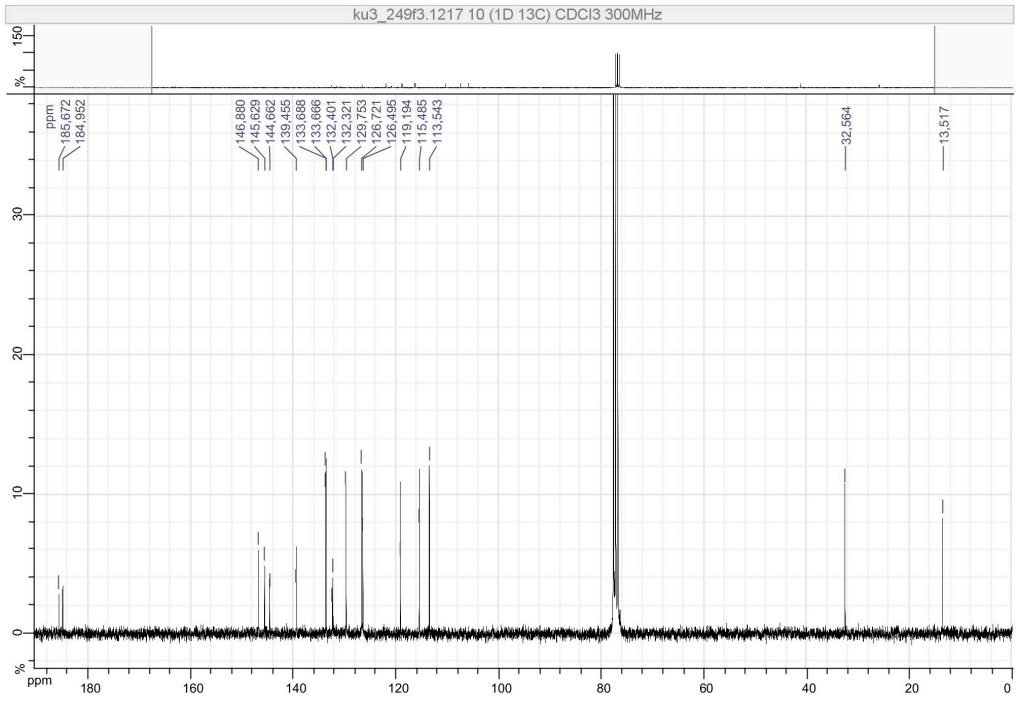


Figure S26. ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of compound **17**.

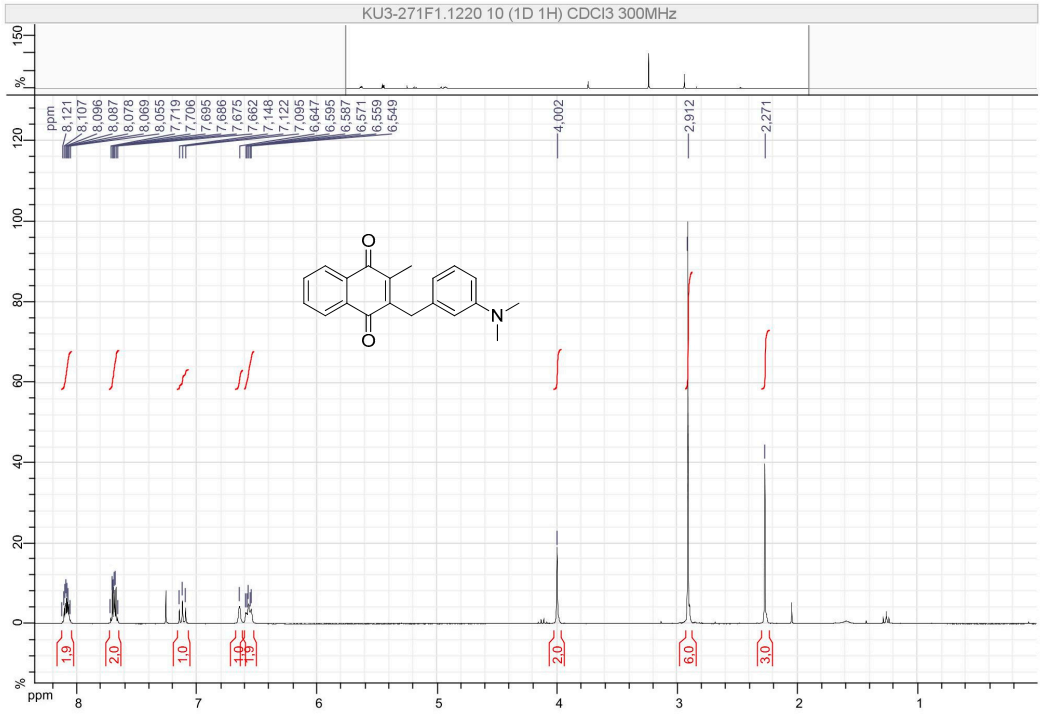


Figure S27. ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of compound **18**.

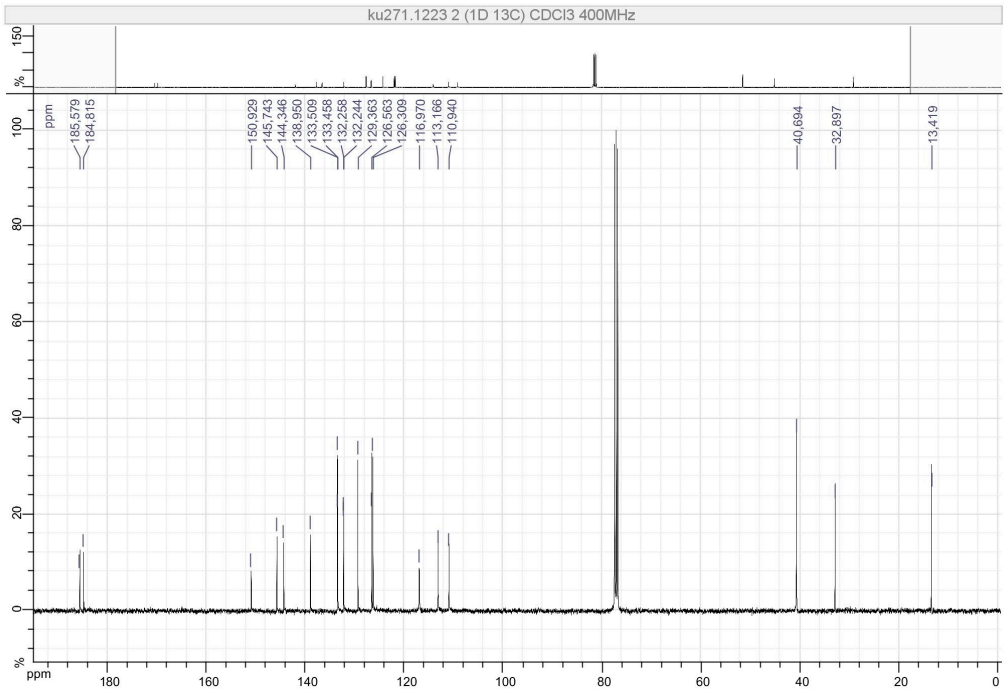


Figure S28. ^{13}C-NMR (100 MHz, $CDCl_3$) spectrum of compound **18**.

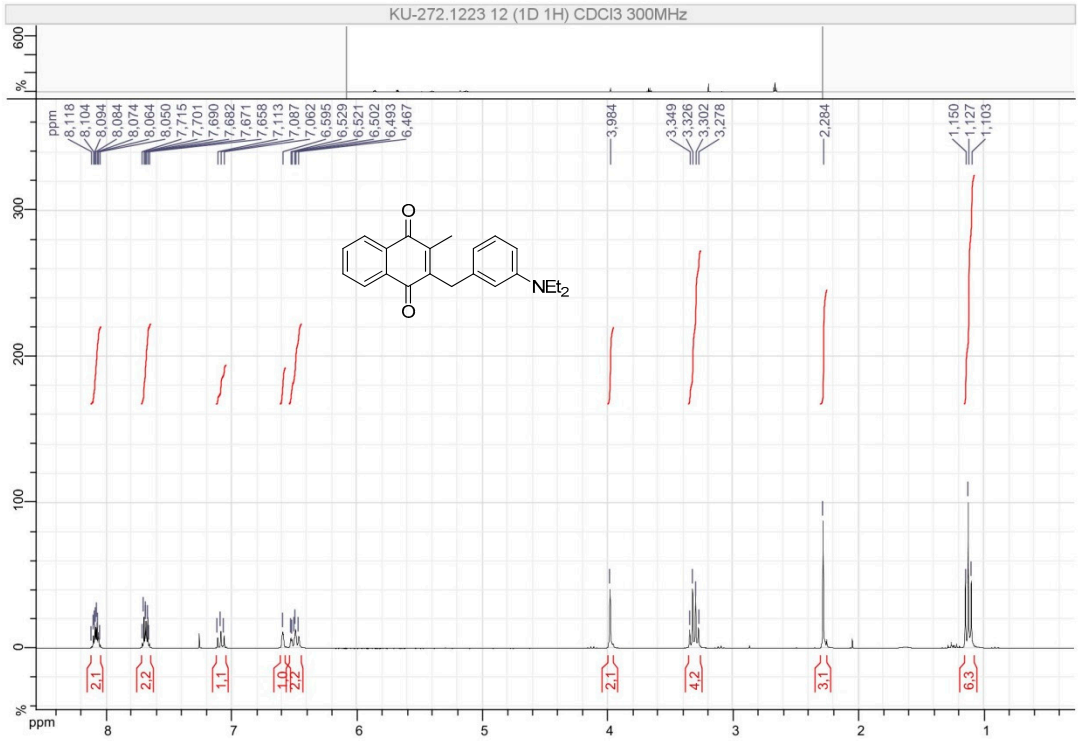


Figure S29. ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of compound **19**.

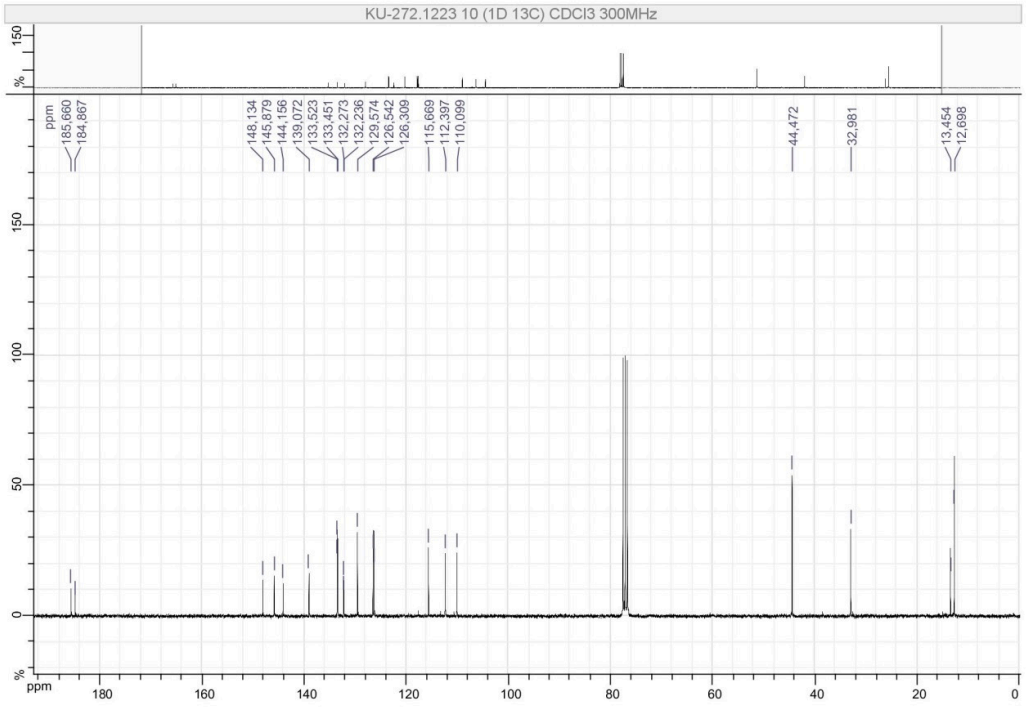


Figure S30. ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of compound **19**.

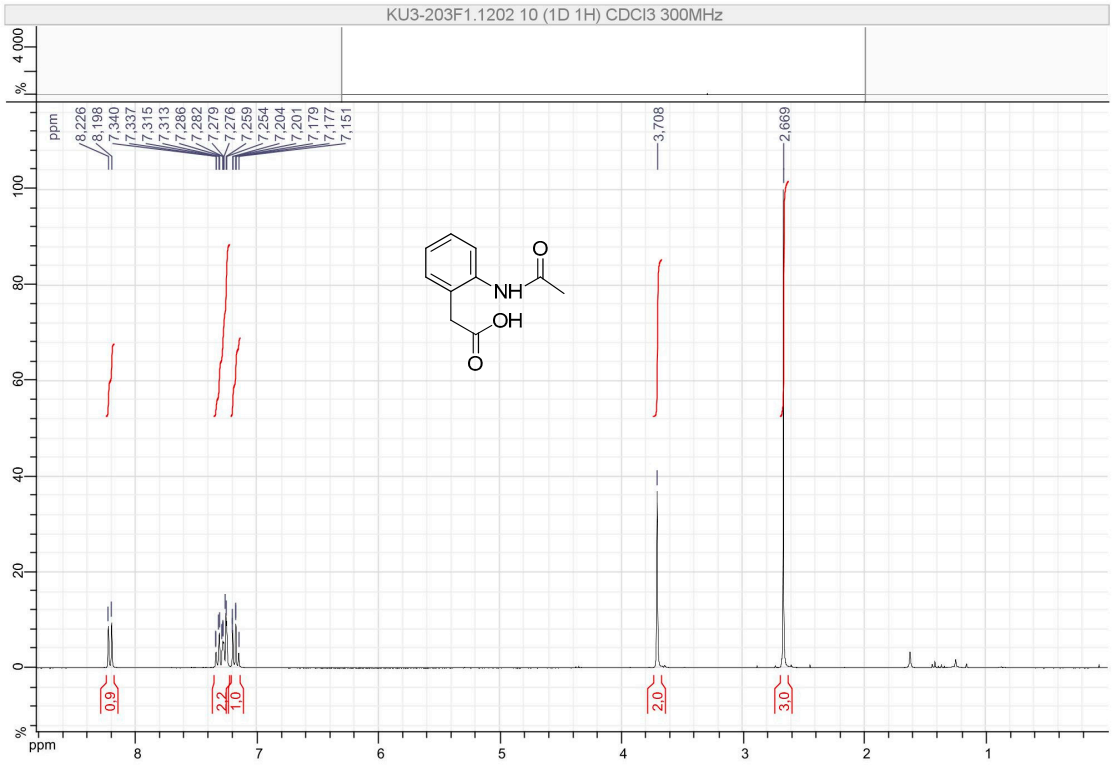


Figure S31. ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of compound **21a**.

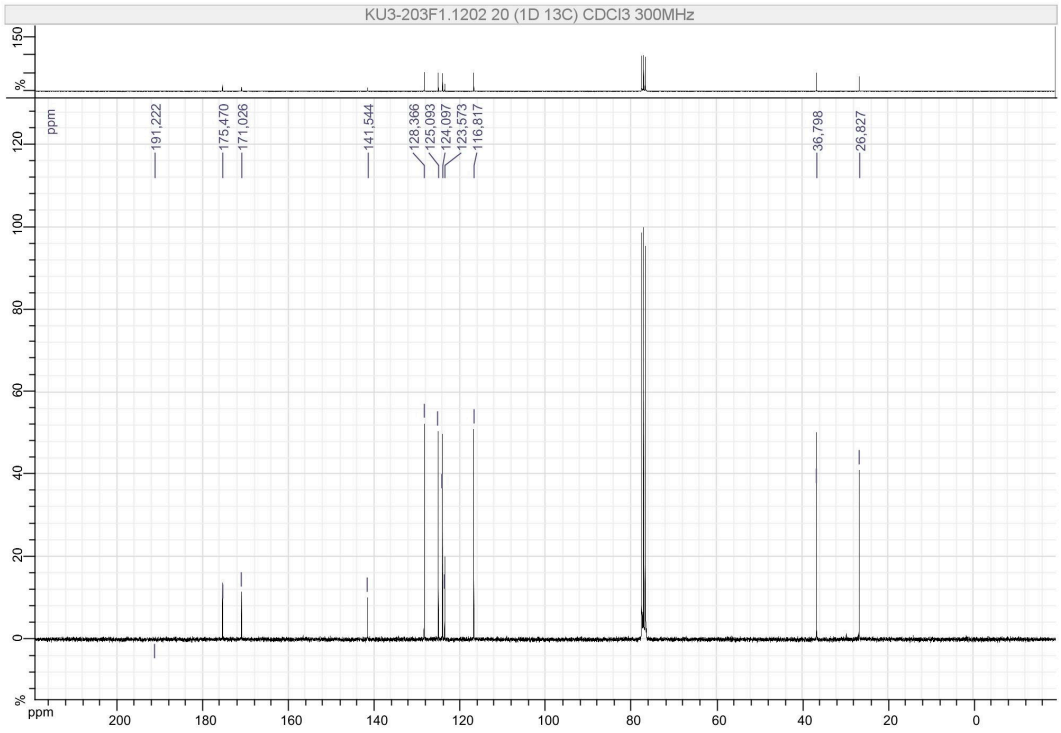


Figure S32. ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of compound **21a**.

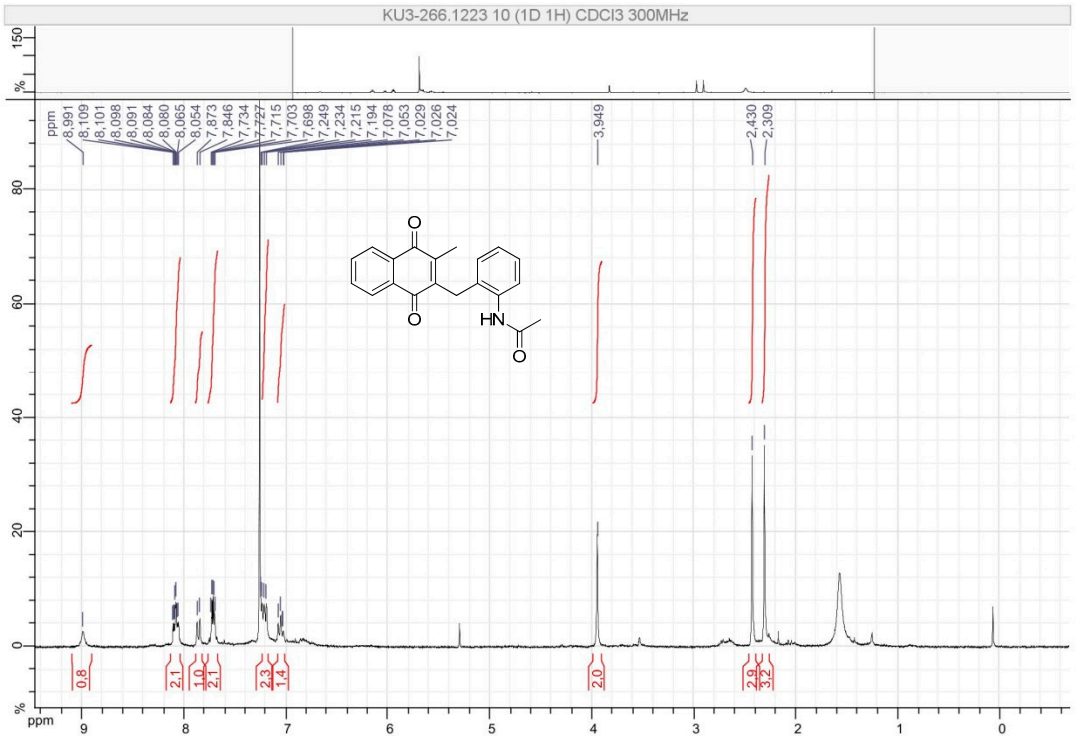


Figure S33. ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of compound **22**.

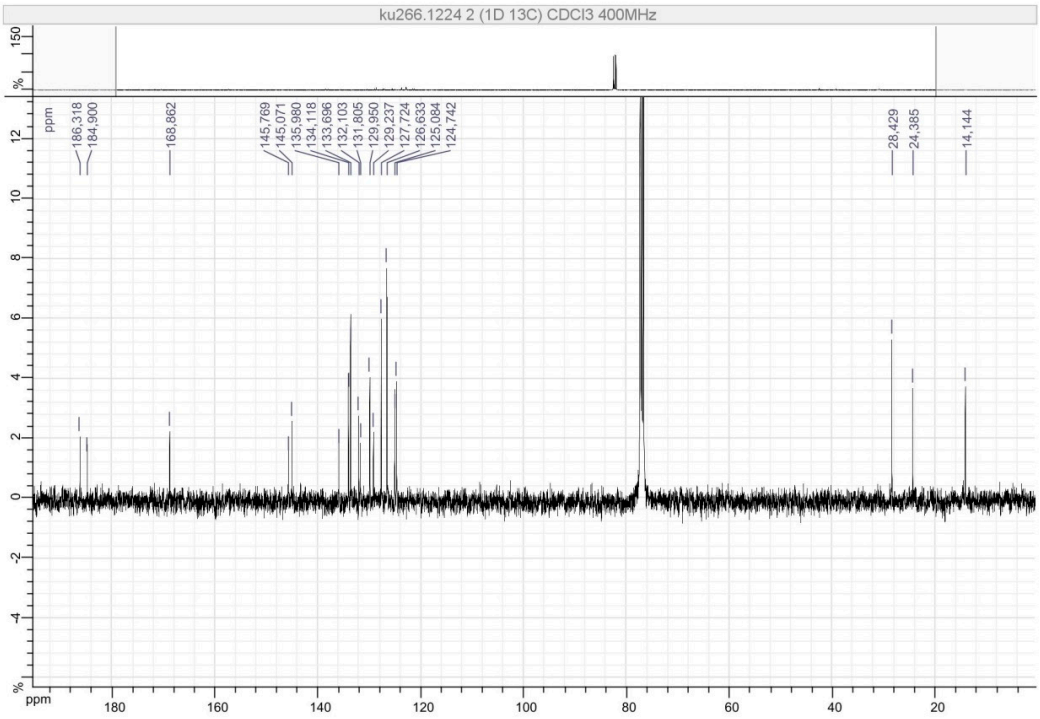


Figure S34. ^{13}C-NMR (100 MHz, $CDCl_3$) spectrum of compound **22**.

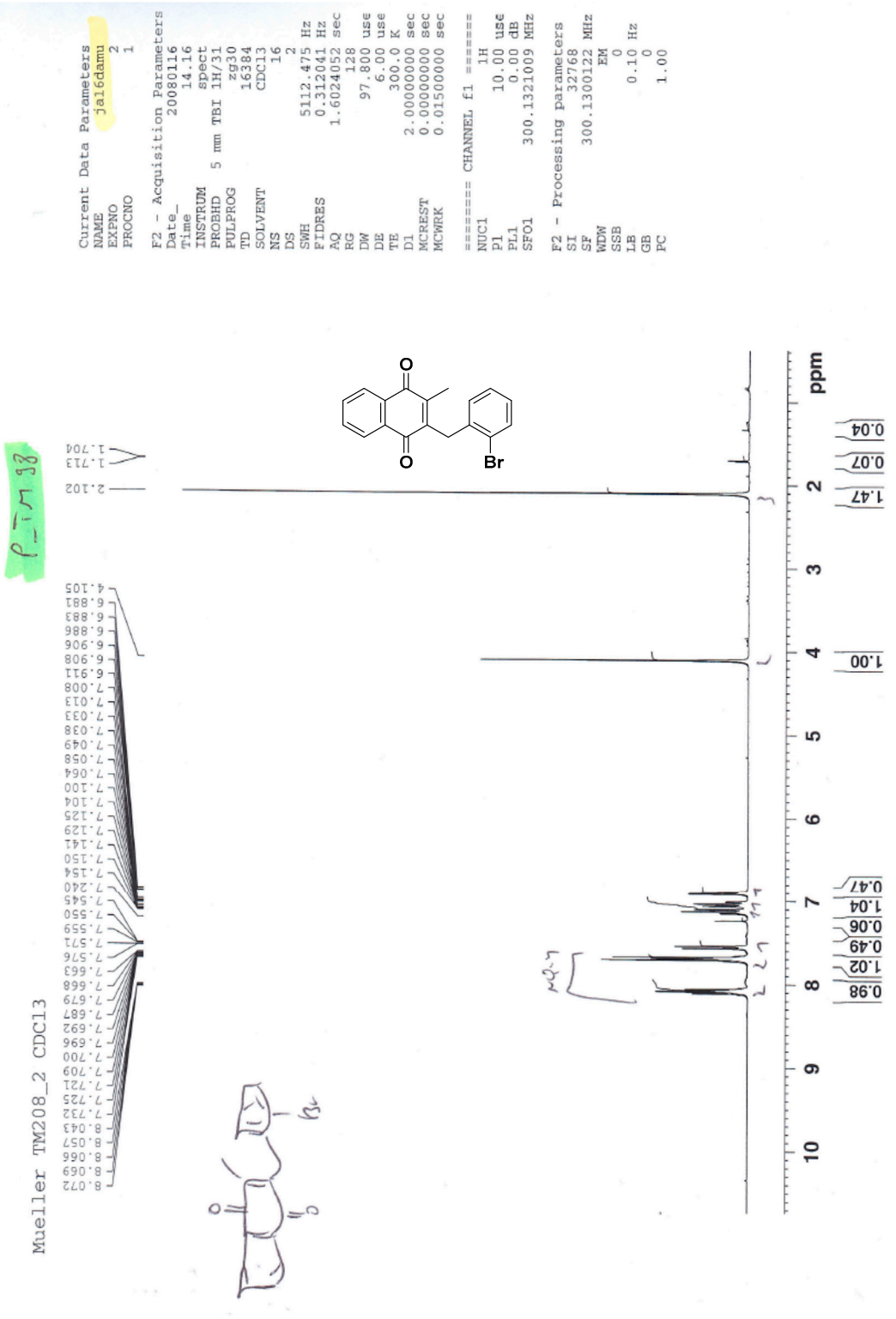


Figure S35. ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of compound **25a**.

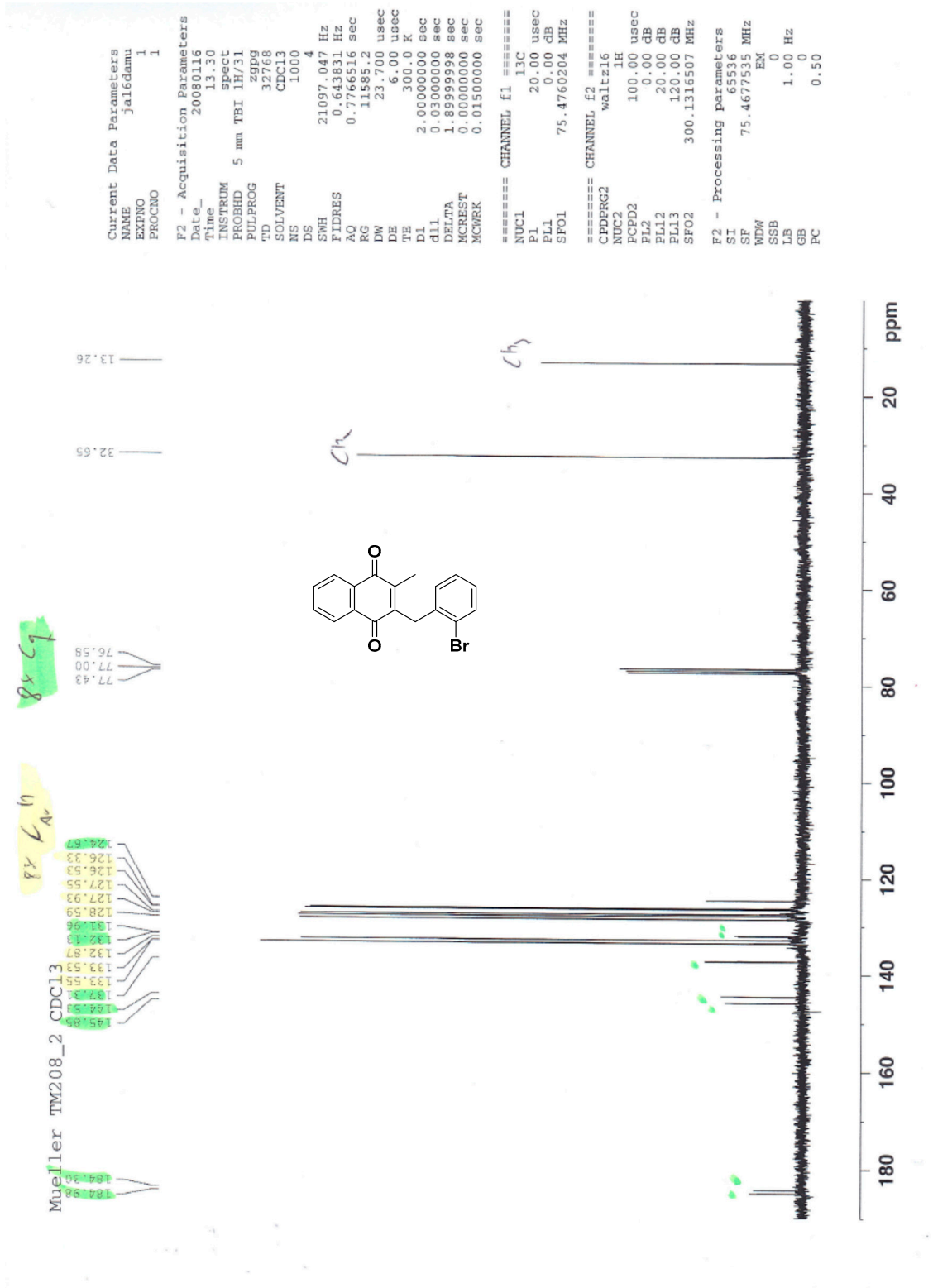


Figure S36. ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of compound **25a**.

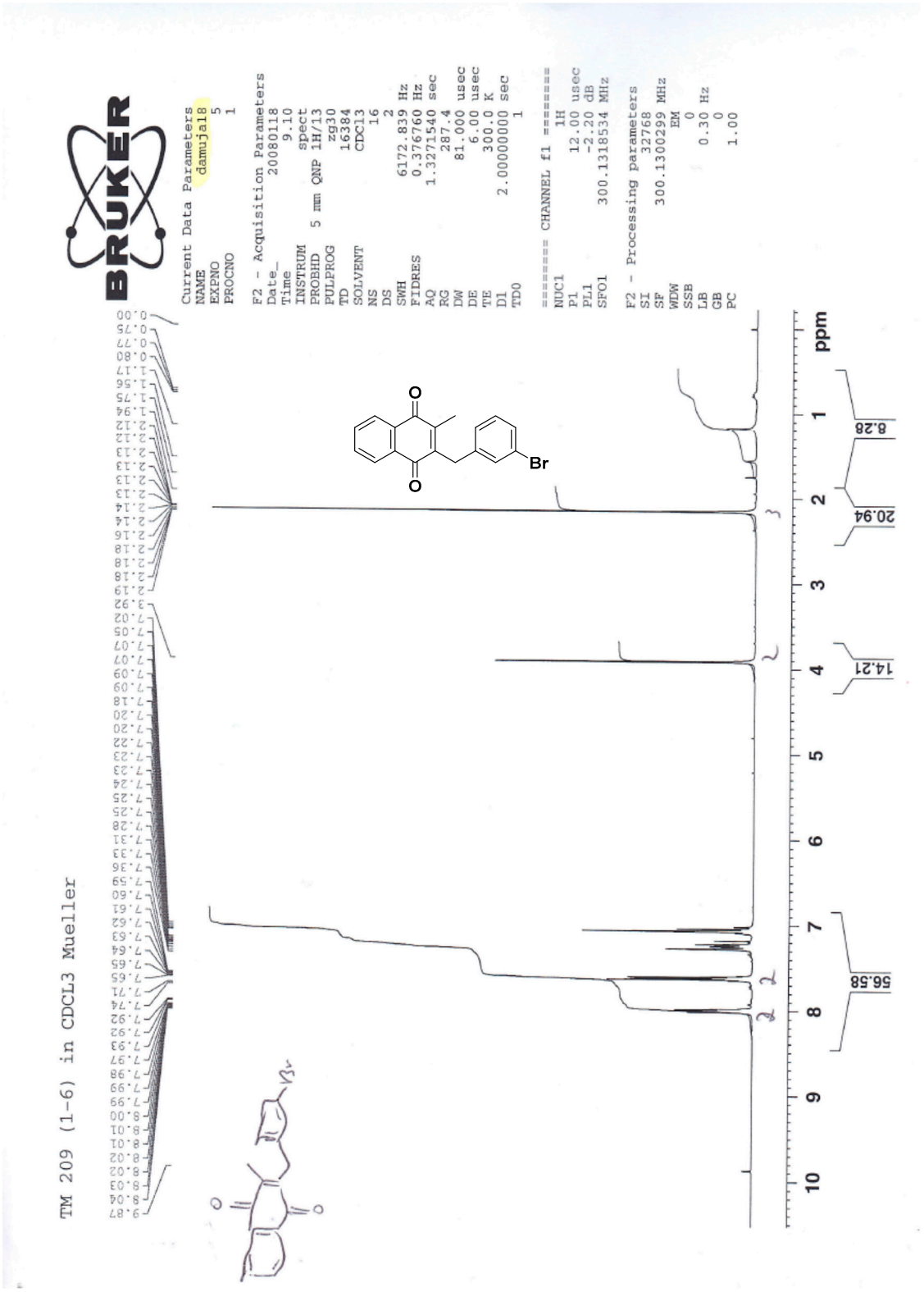


Figure S37. ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of compound **25b**.

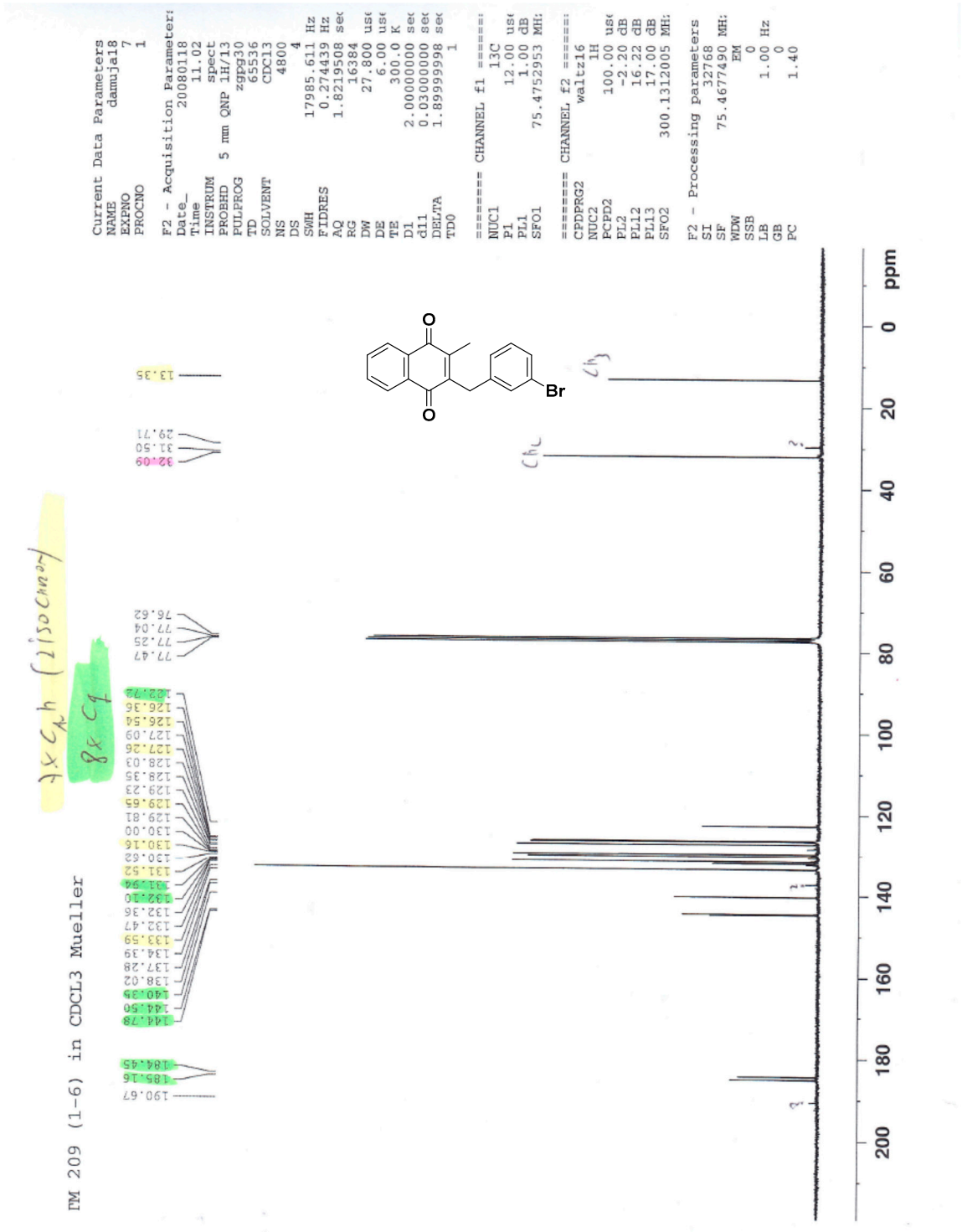


Figure S38. ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of compound **25b**.

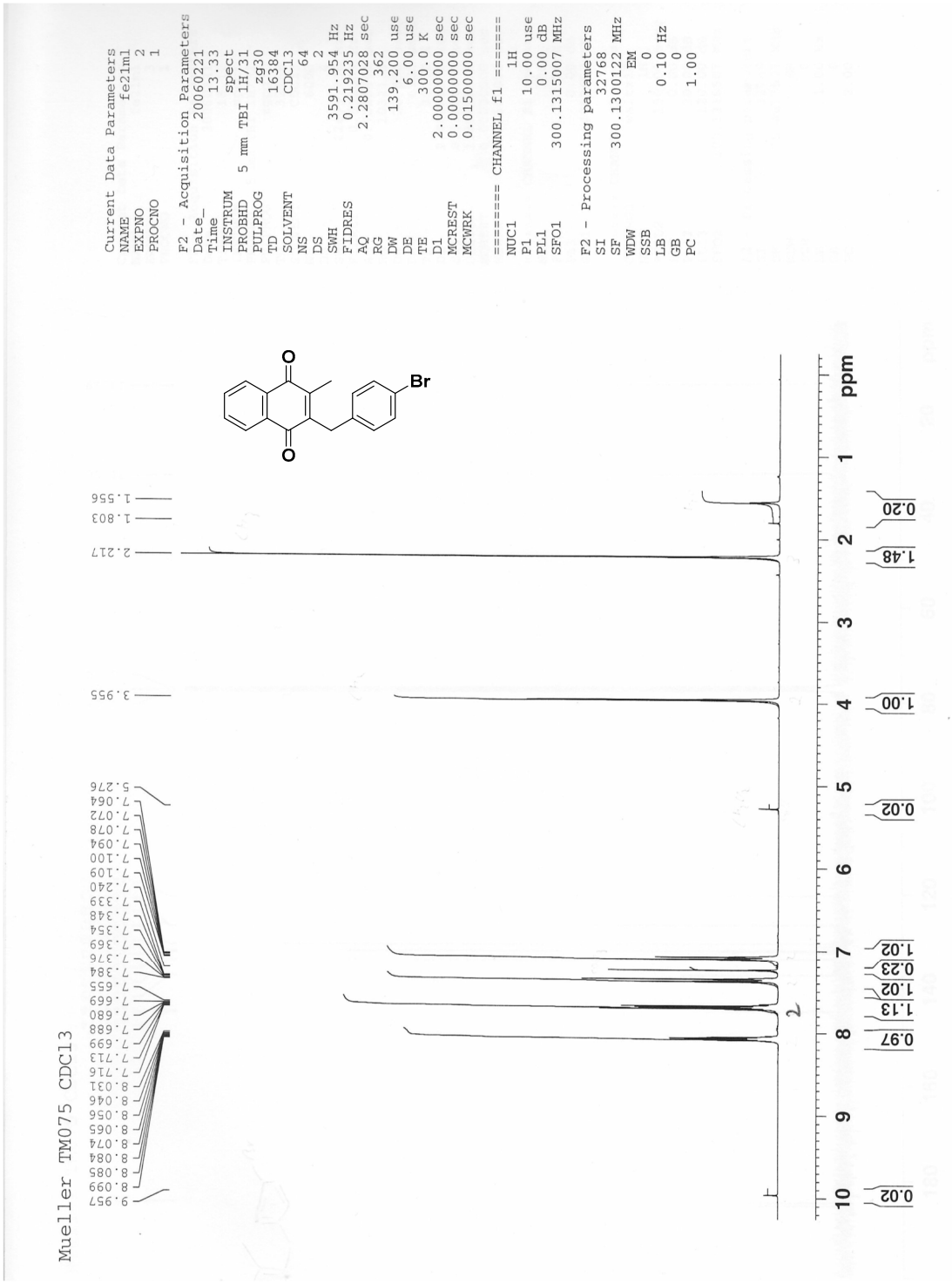


Figure S39. ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of compound **25c**.

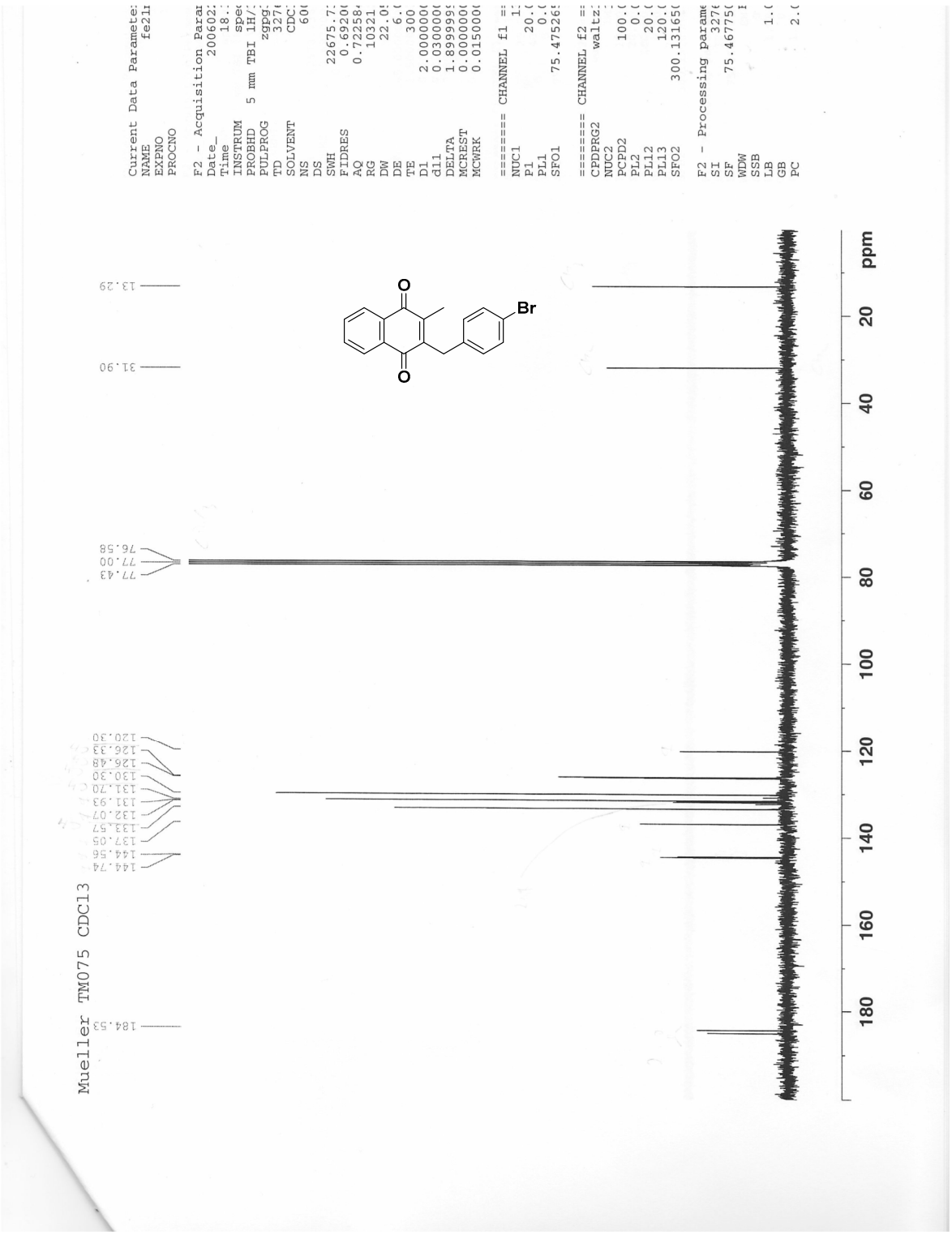


Figure S40. ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of compound **25c**.

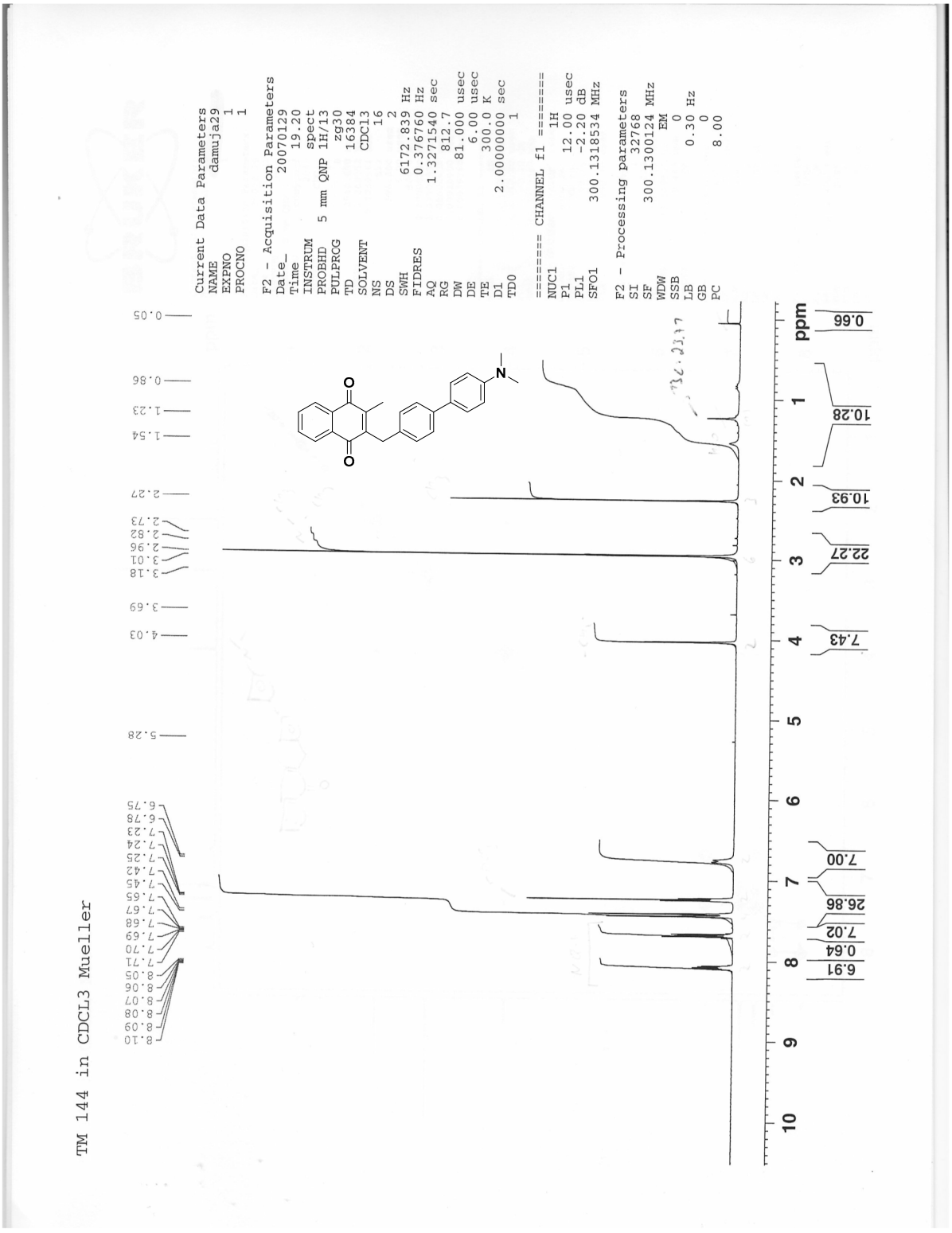


Figure S41. ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of compound **26**.

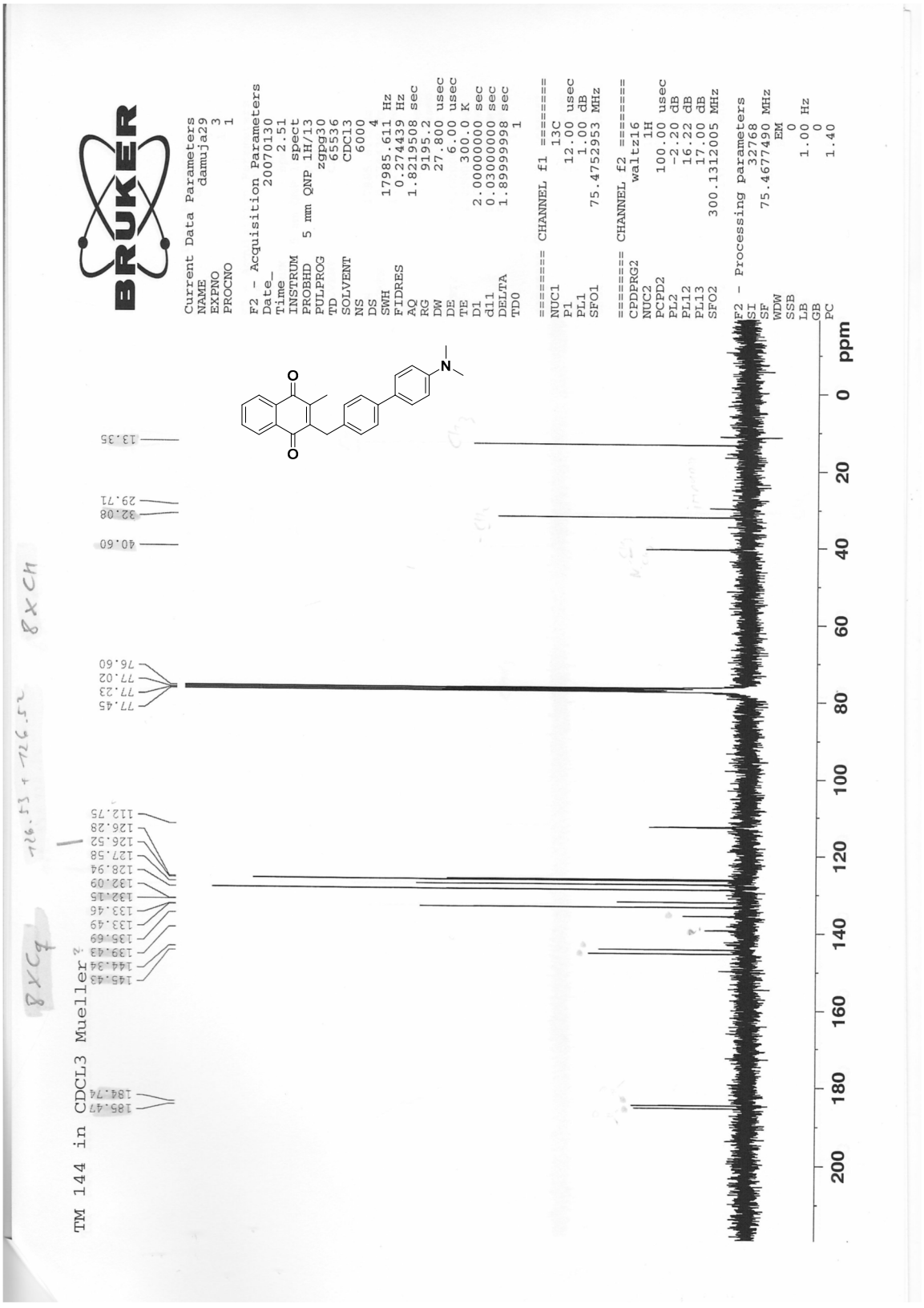


Figure S42. ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of compound **26**.

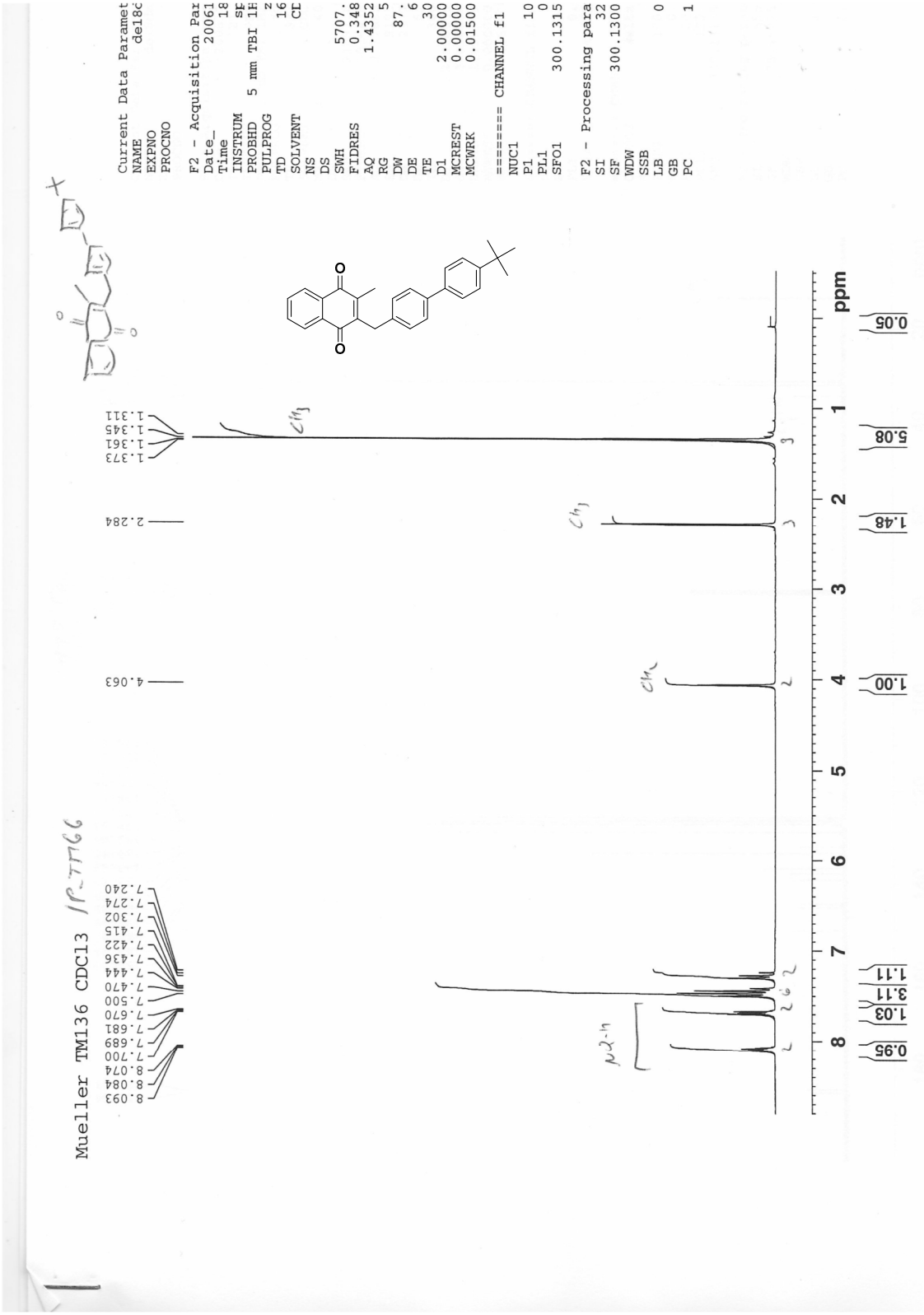


Figure S43. ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of compound **27**.

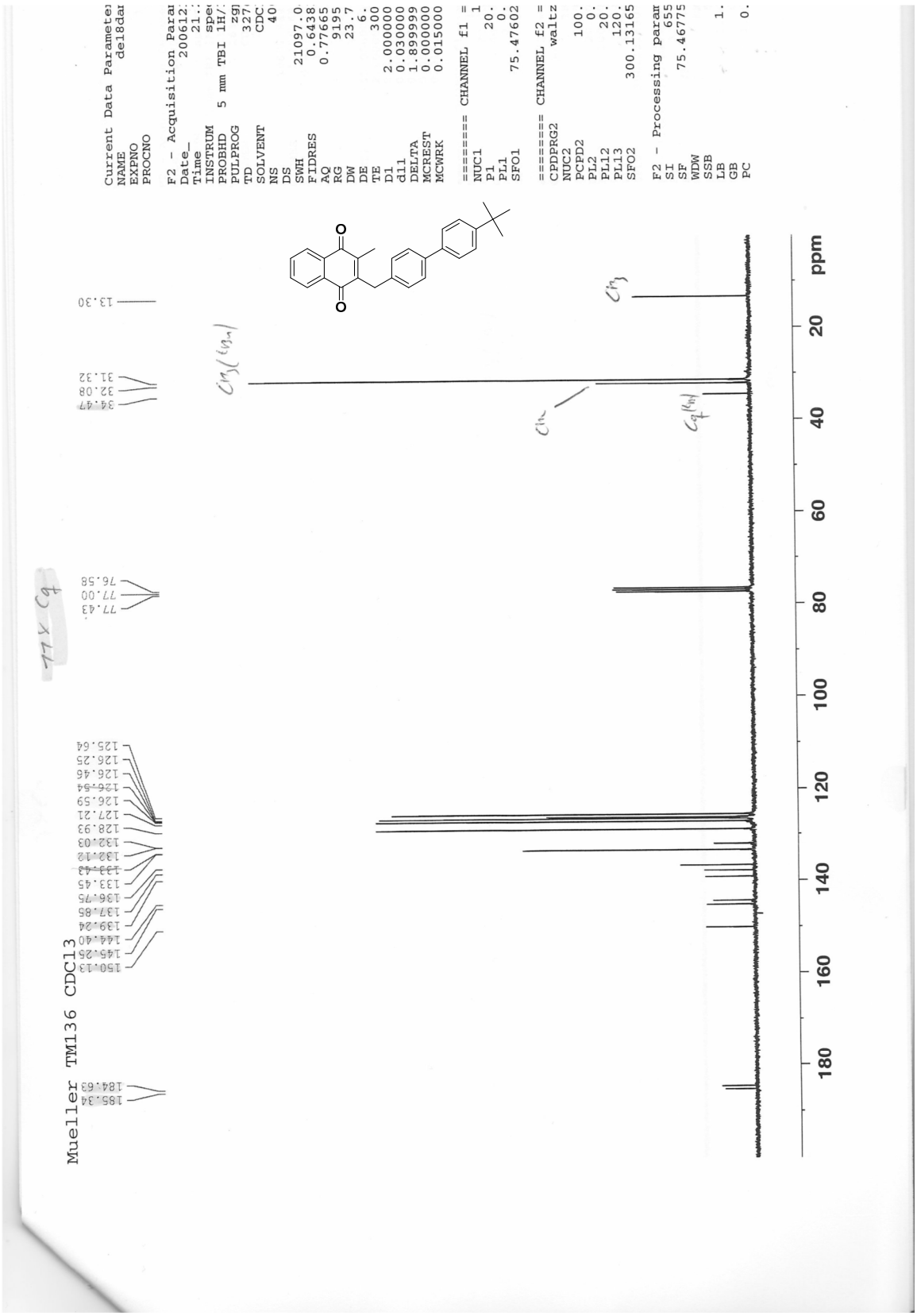


Figure S44. ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of compound **27**.

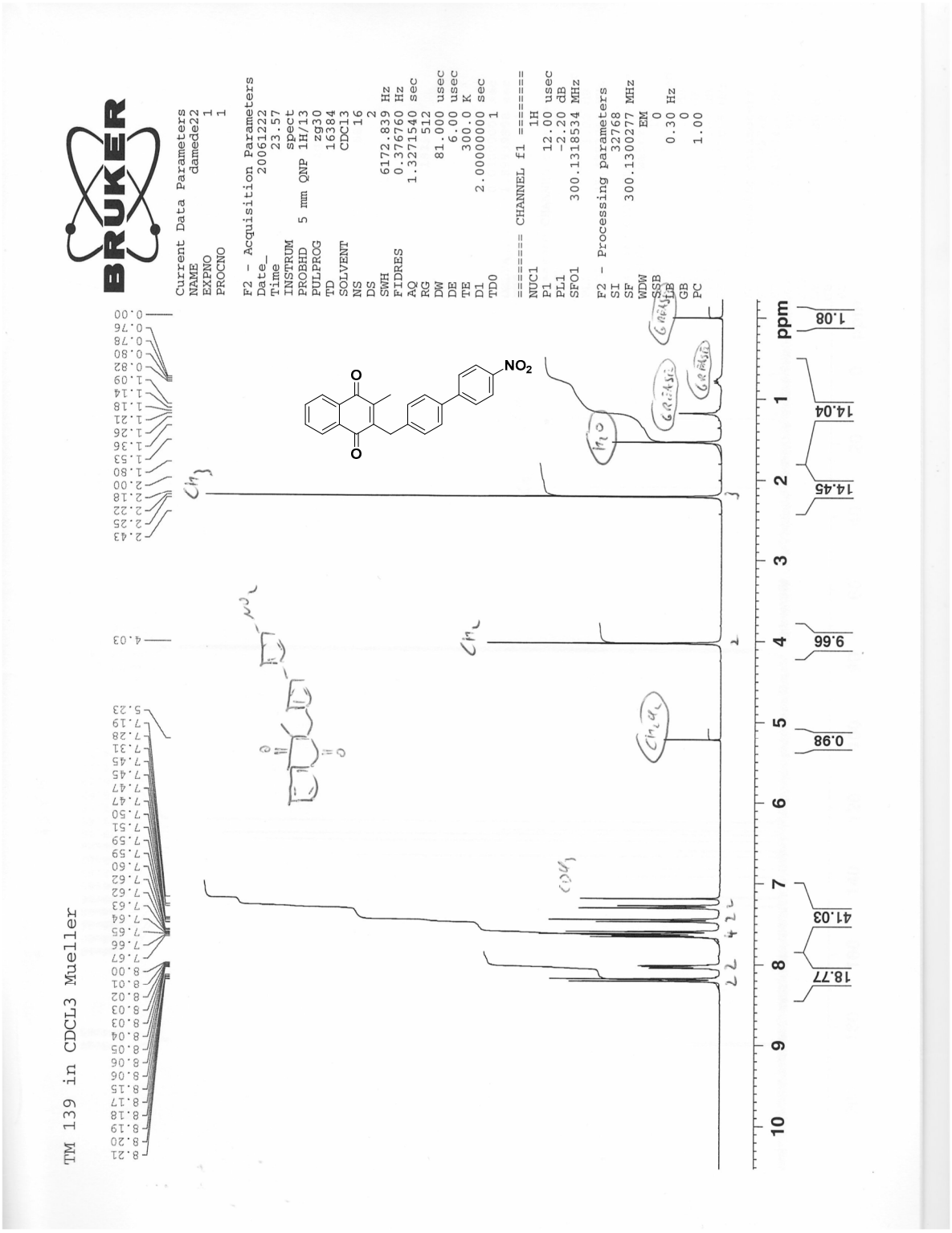


Figure S45. ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of compound **28**.

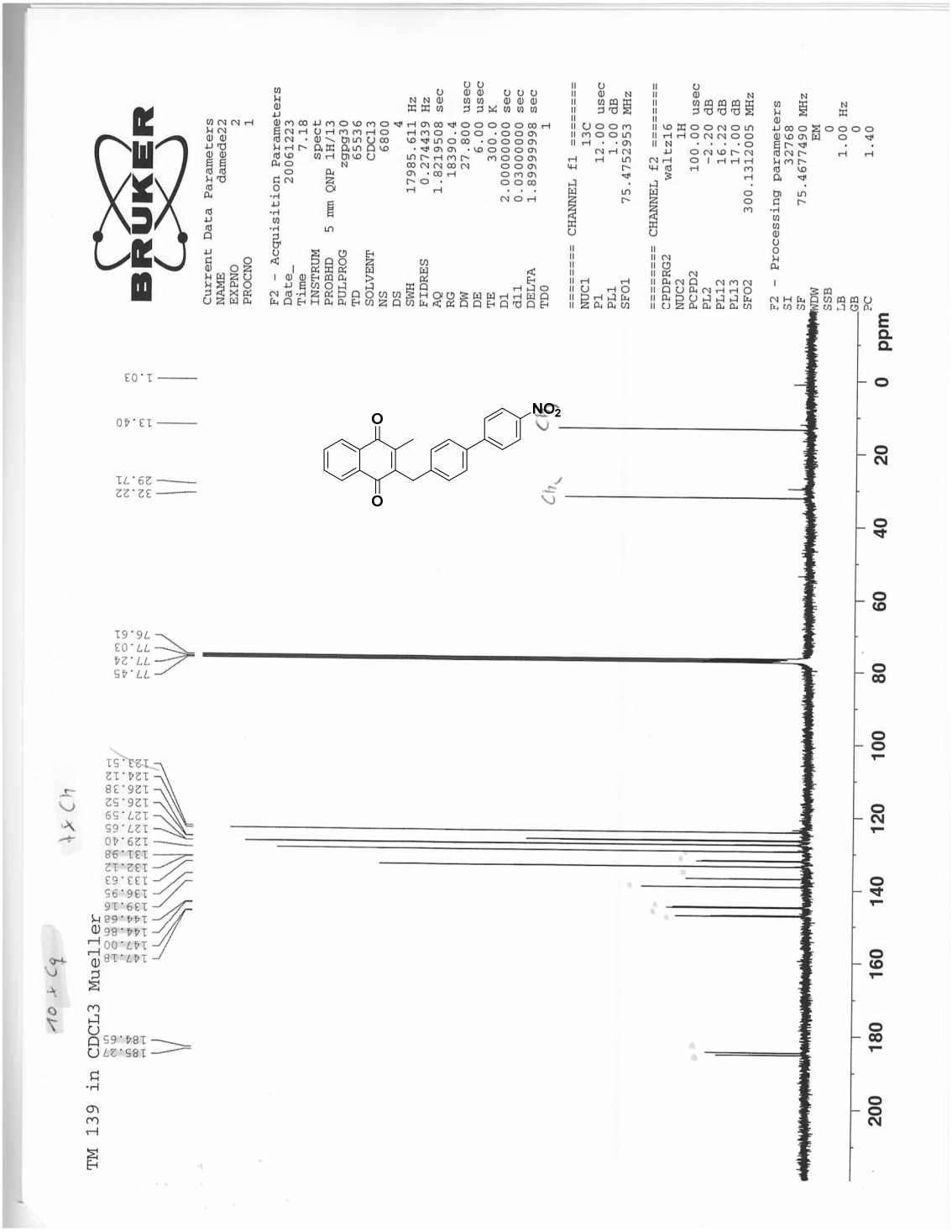


Figure S46. ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of compound **28**.