Supplementary Information

Aryl-O reductive elimination from well-defined aryl-Cu^{III} species with phenolates: the importance of ligand reactivity

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CONTENTS

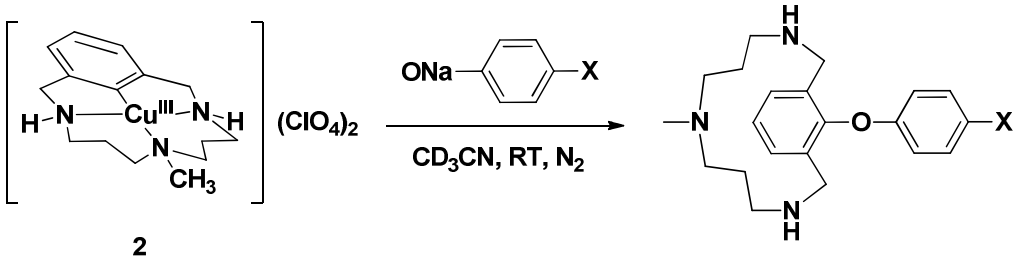
1. Synthesis of complex 2

Arylcopper(III) complex **2** was prepared following procedures described in the literature previously.[1, 2]

2. Synthesis of *para*-substituted phenolates

Para-substituted sodium phenolates *p*-X-phenolate (X= OCH_3, Cl, F, CN and NO_2) were prepared following procedures described in the literature previously.[3]

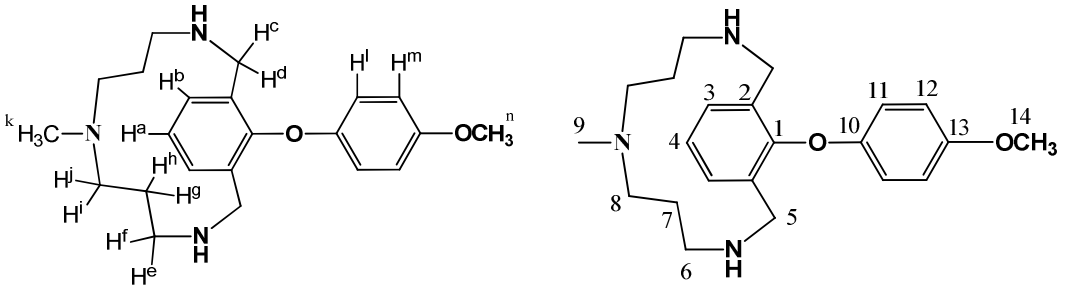
3. Stoichiometric reactions of complex 2 and phenolates



2 **4a-e (100 %)**

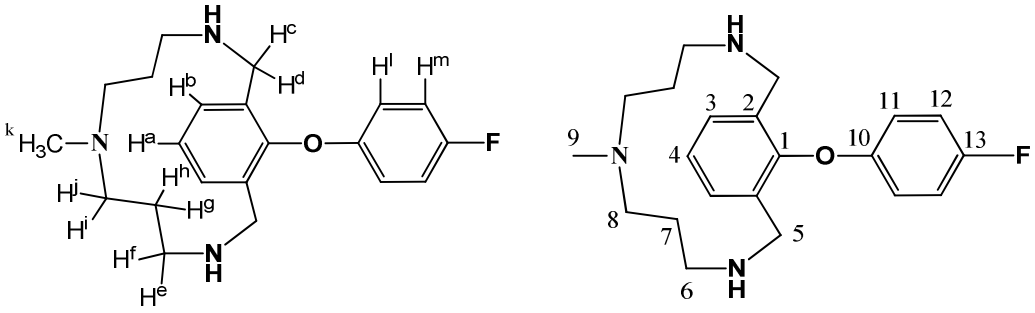
(X = OCH_3 (a), F (b), Cl (c), CN (d), NO_2 (e))

In an inert-atmosphere glove box, stock solutions of complex **2**/1,3,5-trimethoxybenzene (10/1.8 mM) and sodium para-substituted phenolates (X= OCH_3, F, Cl) (10 mM) were prepared in CD_3CN. The **2**/1,3,5-trimethoxybenzene stock solution (0.3 mL) was loaded into an NMR tube. Then 0.3 mL of p-X-phenolate was added to the NMR tube obtaining a deep violet solution that remains for 10 minutes. ^{1}H-NMR spectroscopy of the colourless solution showed that reaction was completed. Quantitative NMR yield of the corresponding C-O coupling product was obtained using 1,3,5-trimethoxybenzene as internal standard. The final concentrations were as follows: [**2**] = 5 mM, [4-X-phenolate] (X= OCH_3, F, Cl) = 5 mM. The same procedure was performed using sodium *p*-cyanophenolate and sodium *p*-nitrophenolate but due to their low solubility in CD_3CN, lower concentrations were used. In the case of p-cyanophenolate final concentrations were [**2**] = 2.5 mM and [*p*-CN-phenolate] = 2.5 mM. In the case of *p*-nitrophenolate final concentrations were [**2**] = 1.25 mM and [*p*-CN-phenolate] = 1.25 mM.

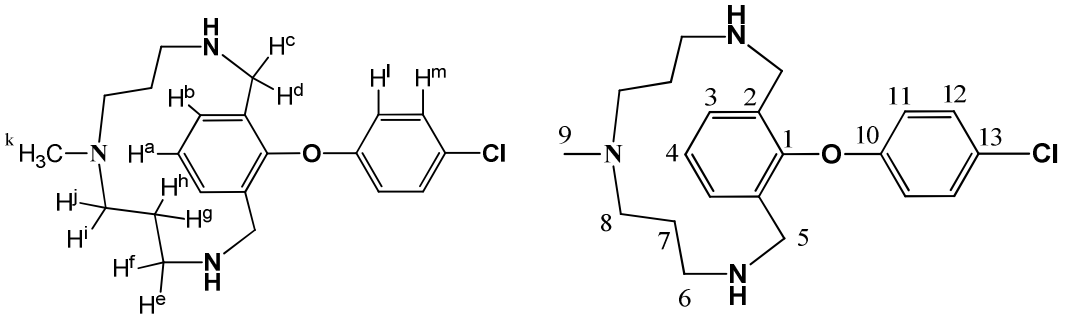


4a. **^{1}H-NMR** (CD_3CN, 400 MHz) δ, ppm: 7.20 (m, 3 H, H^a, H^b), 6.86 (dt, J = 9 Hz, J = 2 Hz, 2 H, H^m), 6.75 (dt, J = 9 Hz, J = 2 Hz, 2 H, H^l), 3.87 (d, J=14 Hz, 2 H, H^c or H^d), 3.73 (s, 3 H, H^n), 3.31 (d, J= 14 Hz, 2H, H^c or H^d), 2.50 (m, 2 H, H^e or H^f), 2.38 (m, 2

H, H^i or H^j), 2.26 (m, 2H, H^i or H^j), 2.15 (under water solvent peak, 2 H, H_{amines}), 2.03 (m, 2 H, H^e or H^f), 1.89 (s, 3 H, H^k), 1.56 (m, 4 H, H^g and H^h); **^{13}C-NMR** (CD_3CN, 100 MHz) δ, ppm: 154.90 (C_{13}), 152.47 (C_{10}), 151.07 (C_1), 134.40 (C_2), 131.02 (C_3), 124.90 (C_4), 115.57 (C_{11}), 114.91 (C_{12}), 55.58 (C_8), 55.27 (C_{14}), 50.15 (C_5), 44.72 (C_6), 39.48 (C_9), 25.99 (C_7); **ESI-MS** (CH_3CN, m/z): 370.3(100) $[C_{22}H_{32}N_3O_2]^+$.

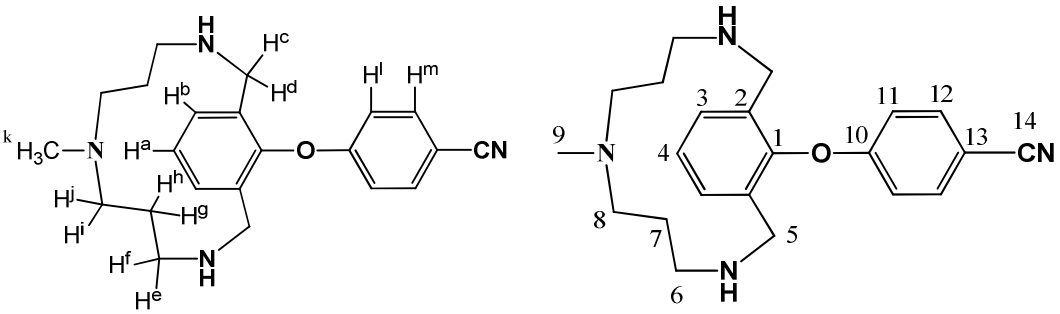


4b. **^{1}H-NMR** (CD_3CN, 400MHz) δ, ppm: 7.22 (m, 3 H, H^a, H^b), 7.04 (t, J = 9 Hz, 2 H, H^m), 6.82 (m, 2 H, H^l), 3.85 (d, J = 14 Hz, 2 H, H^c or H^d), 3.31 (d, J = 14 Hz, 2 H, H^c or H^d), 2.52 (m, 2 H, H^e or H^f), 2.40 (m, 2 H, H^i or H^j), 2.27 (m, 2 H, H^i or H^j), 2.15 (under water solvent peak, 2 H, H_{amines}), 2.04 (m, 2 H, H^e or H^f), 1.92 (s, 3 H, H^k), 1.54 (m, 4 H, H^g, H^h); **^{13}C-NMR** (CD_3CN, 100MHz) δ, ppm: 158.36 (d, J_{C-F} = 145.8 Hz, C_{13}), 153.49 (C_{10}), 152.08 (C_1), 134.57 (C_2), 130.88 (C_3), 125.02 (C_4), 116.36 (C_{11}), 116.03 (d, J_{C-F} = 8.9 Hz, C_{12}), 55.49 (C_8), 50.13 (C_5), 44.23 (C_6), 39.56 (C_9), 26.48 (C_7); **ESI-MS** (CH_3CN, m/z): 358.3(100) $[C_{21}H_{29}FN_3O]^+$.

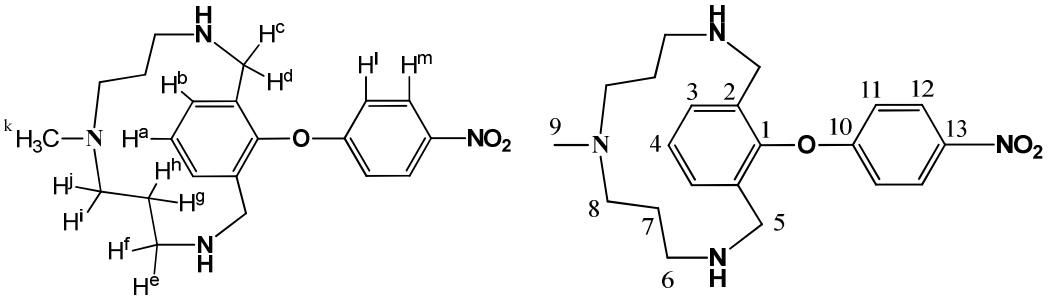


4c. **^{1}H-NMR** (CD_3CN, 400MHz) δ, ppm: 7.31 (dt, J = 9 Hz, J = 3 Hz, 2 H, H^m), 7.23 (m, 3 H, H^a, H^b), 6.81 (dt, J = 9 Hz, J = 2 Hz, 2 H, H^l), 3.84 (d, J = 14 Hz, 2 H, H^c or H^d), 3.31 (d, J = 14 Hz, 2 H, H^c or H^d), 2.50 (m, 2 H, H^e or H^f), 2.38 (m, 2 H, H^i or H^j), 2.28 (m, 2 H, H^i or H^j), 2.15 (under water solvent peak, 2 H, H_{amines}), 2.01 (m, 2 H, H^e or H^f), 1.90 (s, 3 H, H^k), 1.53 (m, 4 H, H^g, H^h); **^{13}C-NMR** (CD_3CN, 100MHz) δ, ppm:

156.07 (C_{10}), 151.70 (C_1), 134.64 (C_2), 130.89 (C_3), 129.78 (C_{12}), 126.62 (C_{13}), 125.18 (C_4), 116.37 (C_{11}), 55.49 (C_8), 50.07 (C_5), 44.22 (C_6), 39.57 (C_9), 26.40 (C_7); ESI-MS (CH_3CN, m/z): 374.2 (100) $[C_{21}H_{29}ClN_3O]^+$.

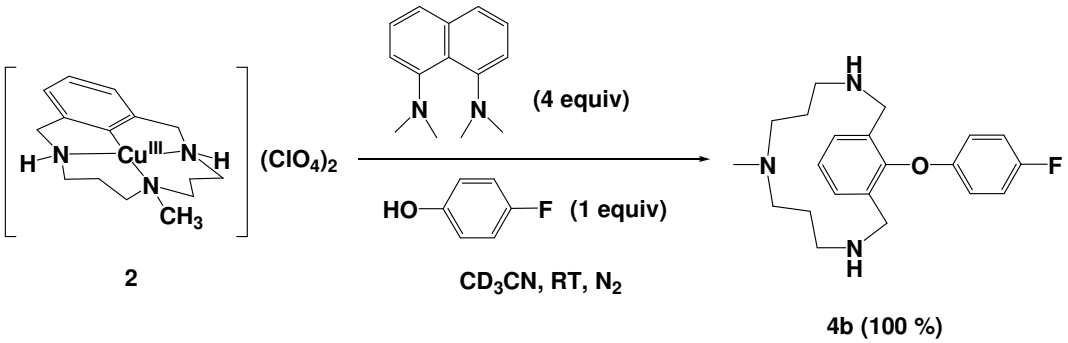


4d. ^{1}H-NMR (CD_3CN, 400MHz) δ, ppm: 7.68 (d, J = 9 Hz, 2 H, H^m), 7.25 (m, 3 H, H^a, H^b), 6.96 (d, J = 9 Hz, 2H, H^l), 3.78 (d, J=14 Hz, 2 H, H^c or H^d), 3.34 (d, J = 14 Hz, 2 H, H^c or H^d), 2.52 (m, 2 H, H^e or H^f), 2.39 (m, 2 H, H^i or H^j), 2.29 (m, 2 H, H^i or H^j), 2.15 (under water solvent peak, 2 H, H_{amines}), 2.04 (m, 2 H, H^e or H^f), 1.93 (s, 3 H, H^k), 1.50 (m, 4 H, H^g, H^h); **^{13}C-NMR** (CD_3CN, 100MHz) δ, ppm: 160.54 (C_{10}), 151.05 (C_1), 134.65 (C_{12}), 134.63 (C_2), 131.20 (C_3), 125.74 (C_4), 118.59 (C_{14}), 115.90 (C_{11}), 105.44 (C_{13}), 55.56 (C_8), 49.78 (C_5), 44.57 (C_6), 39.68 (C_9), 26.24 (C_7); **ESI-MS** (CH_3CN, m/z): 365.3 (100) $[C_{22}H_{29}N_4O]^+$.



4e. ^{1}H-NMR (CD_3CN, 400MHz) δ, ppm: 8.20 (d, J = 9 Hz, 2 H, H^m), 7.27 (m, 3 H, H^a, H^b), 6.97 (d, J = 9 Hz, 2 H, H^l), 3.79 (d, J = 14 Hz, 2 H, H^c or H^d), 3.35 (d, J = 14 Hz, 2 H, H^c or H^d), 2.54 (m, 2 H, H^e or H^f), 2.35 (m, 2 H, H^i or H^j), 2.29 (m, 2 H, H^i or H^j), 2.04 (m, 2 H, H^e or H^f), 1.90 (s, 3H, H^k), 1.48 (m, 4 H, H^g, H^h). **^{13}C-NMR** (CD_3CN, 100MHz) δ, ppm: 162.03 (C_{10}), 151.19 (C_1), 142.84 (C_{13}), 134.00 (C_2), 131.49 (C_3), 126.20 (C_{12}), 125.96 (C_4), 115.47 (C_{11}), 55.68 (C_8), 49.95 (C_5), 45.25 (C_6), 39.75 (C_9), 25.71 (C_7); ESI-MS (CH_3CN, m/z): 385.3 (100) $[C_{21}H_{29}N_4O_3]^+$.

4. Stoichiometric reaction of complex 2 and ProtonSponge® and 4-fluorophenol



2 **4b (100 %)**

In an inert-atmosphere glove box, stock solutions of complex **2**/1,3,5-trimethoxybenzene (10/1 mM), Protonsponge® (240 mM) and 4-fluorophenol (60 mM) were prepared in dry CD_3CN at room temperature. The **2**/1,3,5-trimethoxybenzene stock solution (0.3 mL) and 0.2 mL of CD_3CN were loaded into an NMR tube and sealed with a septum. 50 μL of ProtonSponge® stock solution was added to the NMR tube obtaining a deep violet solution. Then 50 μL of 4-fluorophenol stock solution was added into the NMR tube. ^{1}H-NMR spectroscopy of the colourless solution showed that reaction was completed. Quantitative NMR yield of the corresponding C-O coupling product was obtained using 1,3,5-trimethoxybenzene as internal standard. The final concentrations were as follows: [**2**] = 5 mM, [ProtonSponge®] = 20 mM and [4-fluorophenol] = 5 mM.

5. Procedures for monitoring kinetics by UV-vis spectroscopy

*a) Reaction of complex **2** with Protonsponge®*

A UV-Visible cuvette (1 cm) equipped with a Teflon stopcock was dried in an oven and cooled under vacuum. Stock solutions of complex **2** (1 mM) and Protonsponge® (24 mM) were prepared in dry CH_3CN in an inert glove box. Then 1.2 mL of stock solution of complex **2** and the corresponding volume of CH_3CN were loaded into the cuvette. The cuvette was inserted into the spectrometer and the temperature was allowed to equilibrate at 25ºC. The reaction was initiated by adding the corresponding volume of Protonsponge® stock solution (50 μL-0.6 mL) into the cuvette (3 mL of final volume). Final concentrations: [**2**] = 0.6 mM, [Protonsponge®] = 0.6-7.2 mM. ESI-MS of reaction mixture with 6 equiv. of Protonsponge added shows a major copper-containing signal corresponding to species **3:** m/z = 308.1.

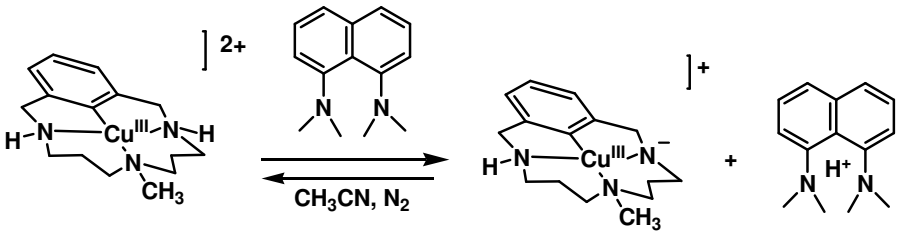


Figure S1. Formation of violet intermediates upon addition of 7 equiv of Protonsponge®complex to complex **2** at -30ºC in CH_3CN under N_2. Spectrum trace *a* corresponds to initial complex **2**, [**2**] = 0.73 mM. Conditions: [**2**] = 0.6 mM, [Protonsponge®] = 4.2 mM. Inset: Kinetic profile of absorbance at 550 nm.

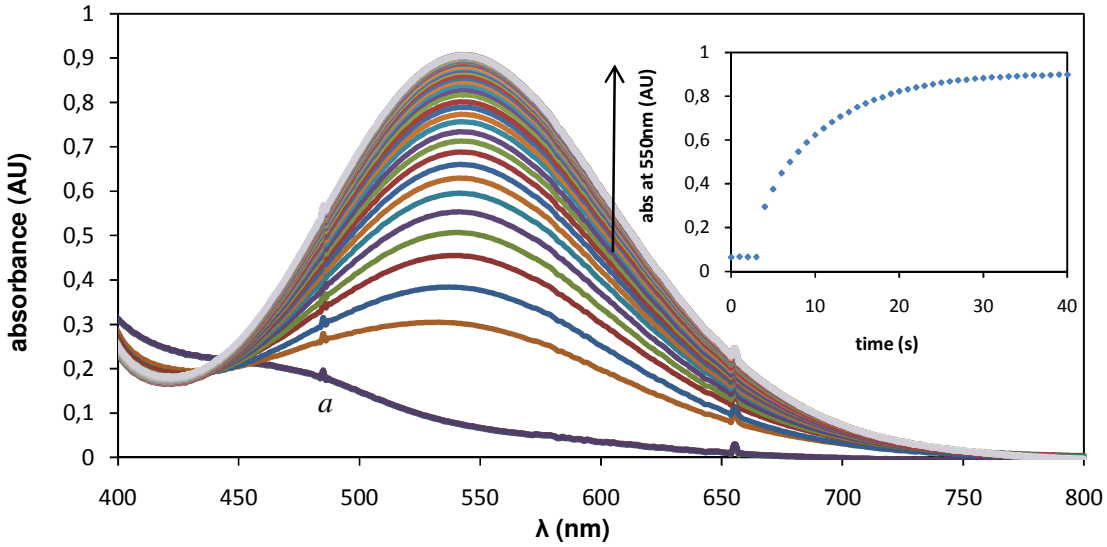
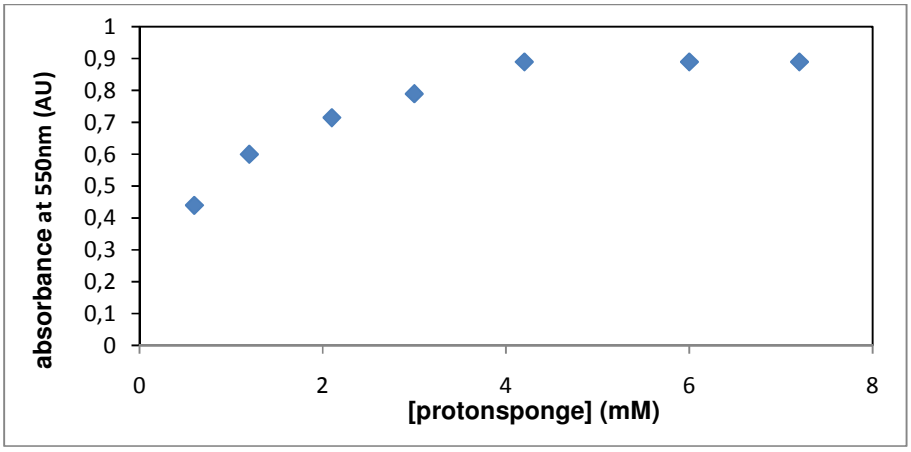


Figure S2. Plot of the maximum absorbance at 550 nm for reaction of complex **2** with several equivalents of Protonsponge® in CH_3CN at -30ºC under N_2, [**2**] = 0.6 mM, [Protosnponge®] = 0.6-7.2 mM (1-12 equiv).



*b) Reaction of complex **2** with p-X-phenolate substrates*

A UV-Visible cuvette (1cm) equipped with a Teflon stopcock was dried in an oven and cooled under vacuum. Stock solutions of complex **2** (0.7 mM) and sodium p-substituted phenolate (4.5 mM) (X= OCH_3, F, Cl, CN) were prepared in dry CH_3CN in an inert glove box. Then 2.6 mL of stock solution of complex **1** was loaded into the cuvette. The cuvette was inserted into the spectrometer and the temperature was allowed to equilibrate at 25ºC. The reaction was initiated by adding 0.4 mL of the *p*X-phenolate stock solution into the cuvette. Final concentrations: [**2**] = 0.6 mM, [*p*-fluorophenolate] = 0.6 mM. Due to low solubility of sodium *p*-nitrophenolate salt, reaction of complex **2** and *p*-nitrophenolate were achieved mixing 2 mL of stock solution of complex **2** (0.9 mM) and 1 mL of *p*-nitrophenolate (1.8 mM) which is cooled previously with an ice bath.

Figure S3. Reaction of complex **2** with 1 equiv of sodium *p*-fluorophenolate in CH_3CN at 10ºC, [**2**] = 0.6 mM, [4-fluorophenolate] = 0.6 mM.

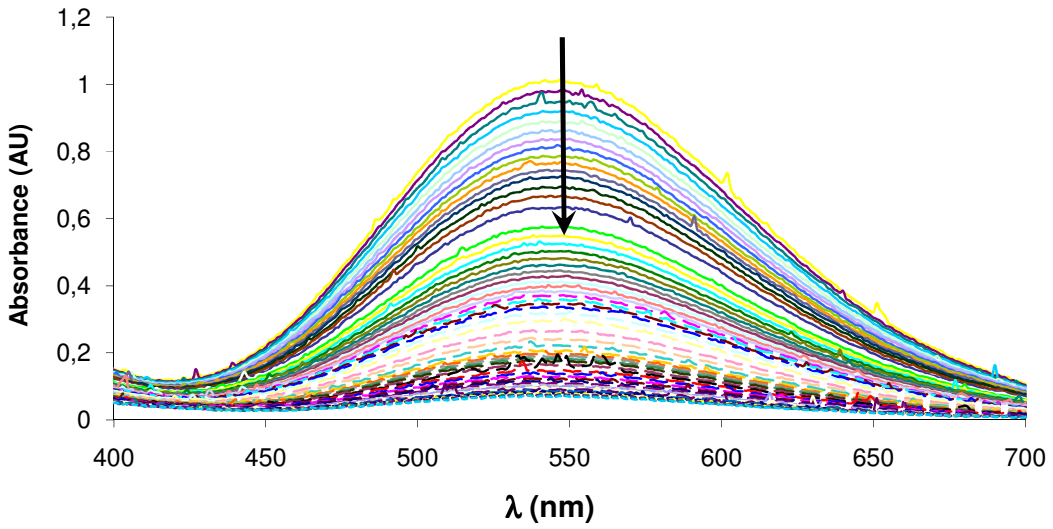
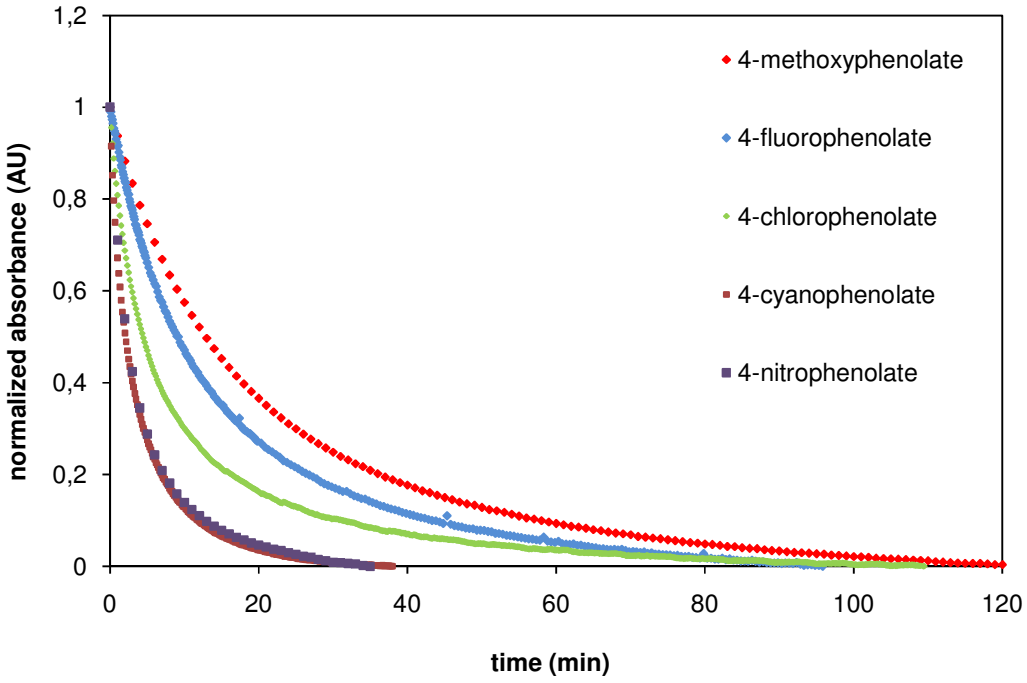


Figure S4. Decay profile plot of reaction of complex **2** with 1 equiv of several p-substituted sodium phenolates at 550 nm in CH_3CN at 10º C under N_2. [**2**] = 0.6 mM and [4-X-phenolate] = 0.6 mM.



c) Comparison between p-X-phenol and p-X-phenolate reactivity

A UV-Visible cuvette (0.5 cm) equipped with a Teflon stopcock was dried in an oven and cooled under vacuum. Stock solutions of complex **2** (6 mM) and sodium *p*-X-phenolate (24 mM) (X= OCH_3, F, CN) were prepared in dry CH_3CN in an inert glove box. Then 0.2 mL of stock solution of complex **2** and 0.75 mL of CH_3CN were loaded into the cuvette. The cuvette was inserted into the spectrometer and the temperature was allowed to equilibrate at 25ºC. The reaction was initiated by adding 50 µL of the *p*-X-phenolate stock solution into the cuvette. Final concentrations: [**2**] = 1.2 mM, [*p*-X-phenolate] = 1.2 mM.

For performing reactions with the corresponding *para*-substituted phenols, stock solutions of *p*X-phenols (24 mM) (X= OCH_3, F, CN) were prepared in dry CH_3CN in an inert glove box. Then, 0.4 mL of stock solution of complex **2** and 1.5 mL of CH_3CN were loaded into the cuvette (1 cm). The cuvette was inserted into the spectrometer and the temperature was allowed to equilibrate at 25ºC. The reaction was initiated by adding

100 µL of the 4-X-phenol stock solution into the cuvette. Final concentrations: [**2**] = 1.2 mM, [*p*-X-phenol] = 1.2 mM.

In order to compare the reaction rate between 4-fluorophenolate and 4-fluorophenol/Protonsponge®, stock solution of Protonsponge® (4.8 mM) was prepared in dry CH_3CN in an inert glove box. Then, 0.2 mL of stock solution of complex **2** was loaded into the cuvette (0.5 cm). The cuvette was inserted into the spectrometer and 0.75 mL of stock solution of Protonsponge® was also loaded into the cuvette. After formation of the corresponding band at 550 nm, 50 µL of the 4-fluorophenol stock solution was loaded into the cuvette. Final concentrations: [**2**] = 1.2 mM, [4-fluorophenol] = 1.2 mM, [Protonsponge®] = 3.6 mM (3 equiv).

Figure S5. Decay profile plot of reaction of complex **2** with a) 1 equiv of *p*-fluorophenol (450 nm), b) sodium *p*-fluorophenolate (decay of 550 nm band corresponding to **3**) and c) 3 equiv of Protonsponge® and 1 equiv of 4-fluorophenol (decay of 550 nm band corresponding to **3**). Conditions: CH_3CN solvent, N_2 atmosphere, 25ºC, [**2**] = 1.2 mM, [4-fluorophenolate] = 1.2 mM, [4-fluorophenol] = 1.2 mM and [Protonsponge®] = 3.6 mM.

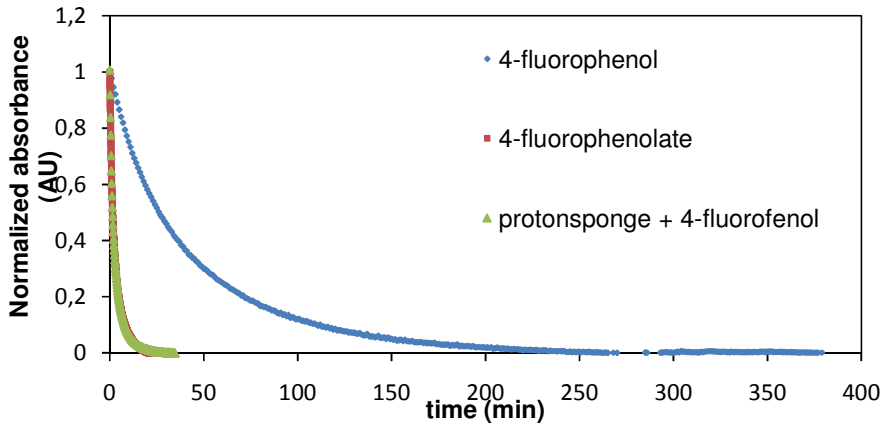


Figure S6. Decay profile plot of reaction of complex **2** with 1 equiv of 4-methoxyphenol (450 nm) and sodium *p*-methoxyphenolate (decay of 550 nm band corresponding to **3**) in CH_3CN at 25ºC under N_2. [**2**] = 1.2 mM and [4-methoxyphenolate] = 1.2 mM.

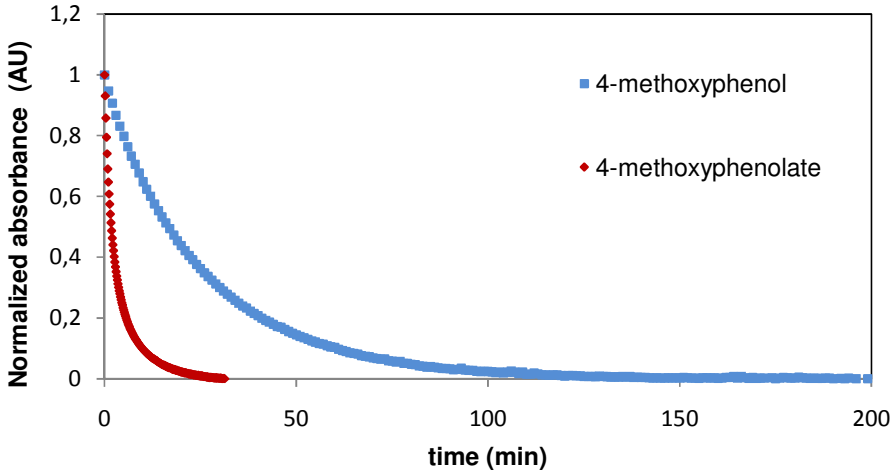
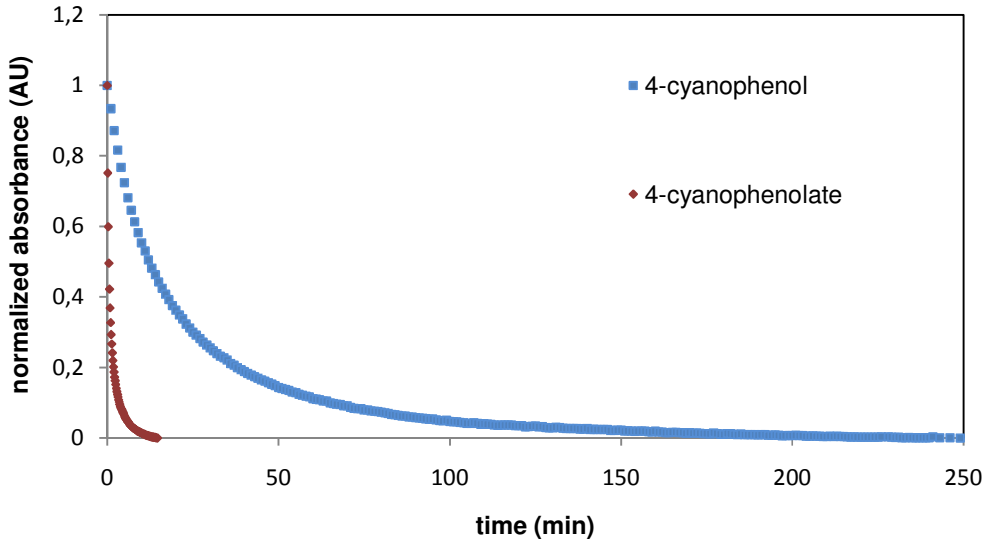


Figure S7. Decay profile plot of reaction of complex **2** with 1 equiv of 4-cyanophenol (450 nm) and sodium 4-cyanophenolate (decay of 550 nm band corresponding to **3**). Conditions: CH_3CN, 25º C, N_2 atmosphere, [**2**] = 1.2 mM and [*p*CN-PhONa] = 1.2 mM.



*d) Reaction of complex **2** with 4-flurorophenolate and CF_3SO_3H*

A UV-Visible cuvette (1 cm) equipped with a Teflon stopcock was dried in an oven and cooled under vacuum. Stock solutions of complex **2** (1 mM), sodium 4-fluorophenolate (24 mM) and trifluoromethanesulfonic acid (22 mM) were prepared in dry CH_3CN in an inert glove box. Then 2 mL of stock solution of complex **2** was loaded into the cuvette. The cuvette was inserted into the spectrometer and the temperature was allowed to equilibrate at 25ºC. The reaction was initiated by adding 0.1 mL of the 4-fluorophenolate stock solution (1 equiv) into the cuvette obtaining a deep violet intermediate. Then 0.1 mL of the trifluoromethanesulfonic acid (1 equiv) was added into the cuvette. This cycle was done two times more increasing the equivalents of base or acid in 0.5 equivalents each time in order to obtain the desired pH.

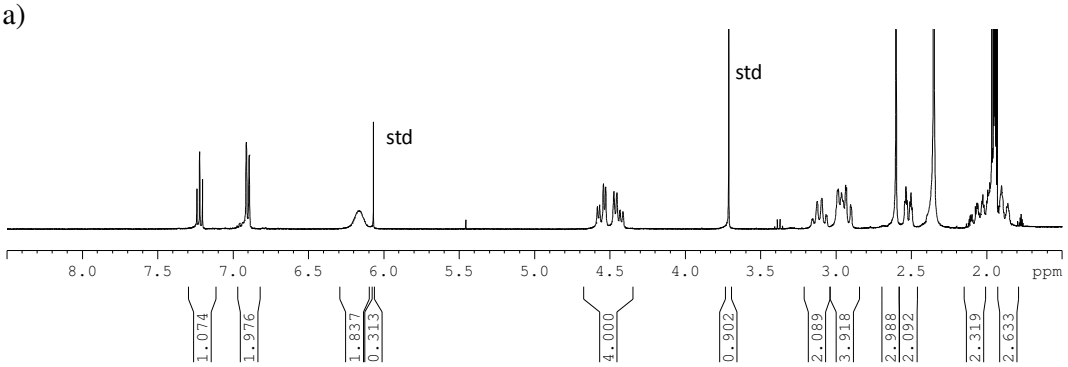
6. Procedures for monitoring kinetics by NMR spectroscopy

*a) Reaction of complex **2** with Protonsponge®*

In an inert-atmosphere glove box, a stock solution of the arylCu^{III} complex **2** and 1,3,5-trimethoxybenzene as an internal standard was prepared in CD_3CN (10/1 mM). A stock solution of Protonsponge (180 mM) was prepared in CD_3CN. Then, 0.3 mL of the stock solution of complex **2/**1,3,5-trimethoxybenzene and 0.2 mL of CD_3CN were loaded into an NMR tube and sealed with a septum. The sample was placed in the NMR probe for 5 min to allow temperature equilibration at -30ºC. ^{1}H-NMR spectra of complex **2** was obtained at -30ºC. Protonsponge® stock solution was cooled to -30ºC using a $CH_3CN/N_{2(l)}$ bath and 0.1 mL was added by syringe to the NMR tube. Final concentrations: [**2**] = 5 mM. [Protonsponge®] = 30 mM. The solution was mixed rapidly and formation of violet intermediate was observed. The tube was inserted into the probe to begin data acquisition.

Figure S9. ^{1}H-NMR spectra of reaction of complex **2** with 6 equiv of protonsponge in CD_3CN at 243 K. a) 0.5 mL of complex **2**, [**2**] = 6 mM; b) addition of 0.1 mL of protonsponge 180 mM, [**2**] = 5 mM, [Protonsponge®] = 30 mM (6 equiv).

a)



b)

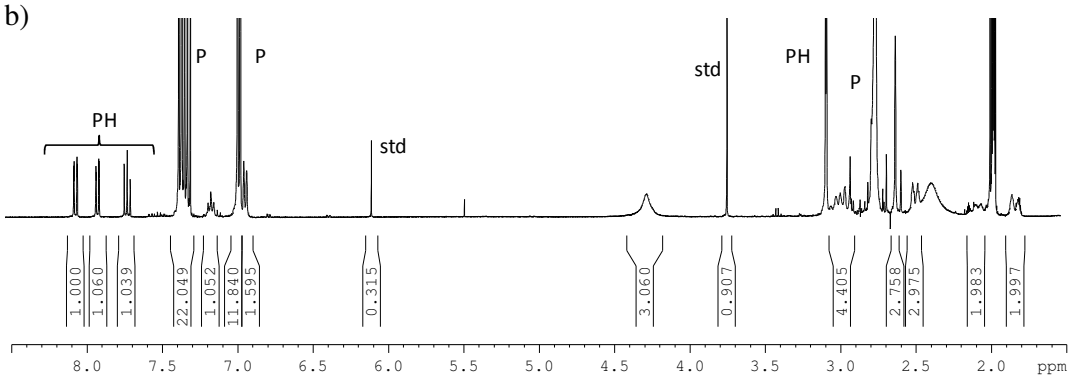
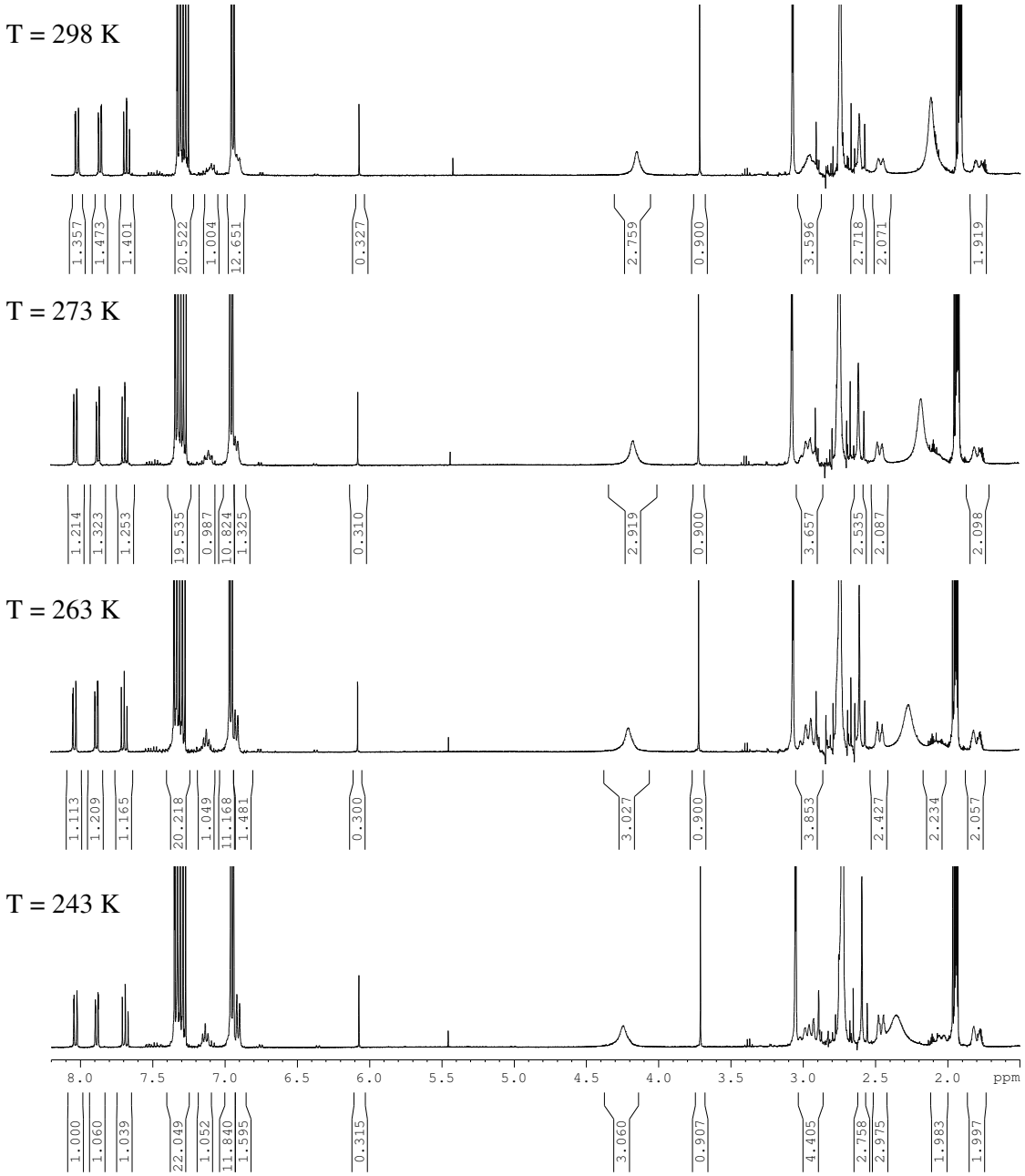


Figure S10. ^{1}H-NMR spectra of reaction of complex **2** with 6 equiv of protonsponge in CD_3CN at several temperatures (243-298 K) in CD_3CN, [**2**] = 5 mM, [Protonsponge®] = 30 mM (6 equiv). Cooling the sample at 298 K down to 243 k again restores the same spectrum (see spectrum at the bottom).



*b) Reaction of complex **2** with pF-PhONa*

In an inert-atmosphere glove box, a stock solution of the arylCu^{III} complex **2** and 1,3,5-trimethoxybenzene as an internal standard was prepared in CD_3CN (10/1 mM). A stock solution of 4-fluorophenolate (30 mM) was prepared in CD_3CN. Then, 0.3 mL of the stock solution of complex **2/**1,3,5-trimethoxybenzene and 0.2 mL of CD_3CN were loaded into an NMR tube and sealed with a septum. The sample was placed in the NMR probe for 5 min to allow temperature equilibration at -30ºC. ^{1}H-NMR spectra of complex **2** was obtained at -30ºC. Sodium 4-fluorophenolate stock solution was cooled to -30ºC using a $CH_3CN/N_{2(l)}$ bath and 0.1 mL was added by syringe to the NMR tube. Final concentrations: [**2**] = 5 mM. [4-fluorophenolate] = 5 mM. The solution was mixed rapidly and formation of violet intermediate was observed. The tube was inserted into the probe to begin data acquisition.

Figure S11. Monitoring the reaction of complex **2** with 1 equiv of *p*F-PhONa in CD_3CN at 243 K by ^{1}H-NMR spectroscopy, [**2**] = 5 mM, [*p*F-PhONa] = 5 mM. Disappearence of signals corresponding to **3** (bottom spectrum, t = 5 min) is observed concomitantly to the growth of signals corresponding to the aryl-O coupling product.

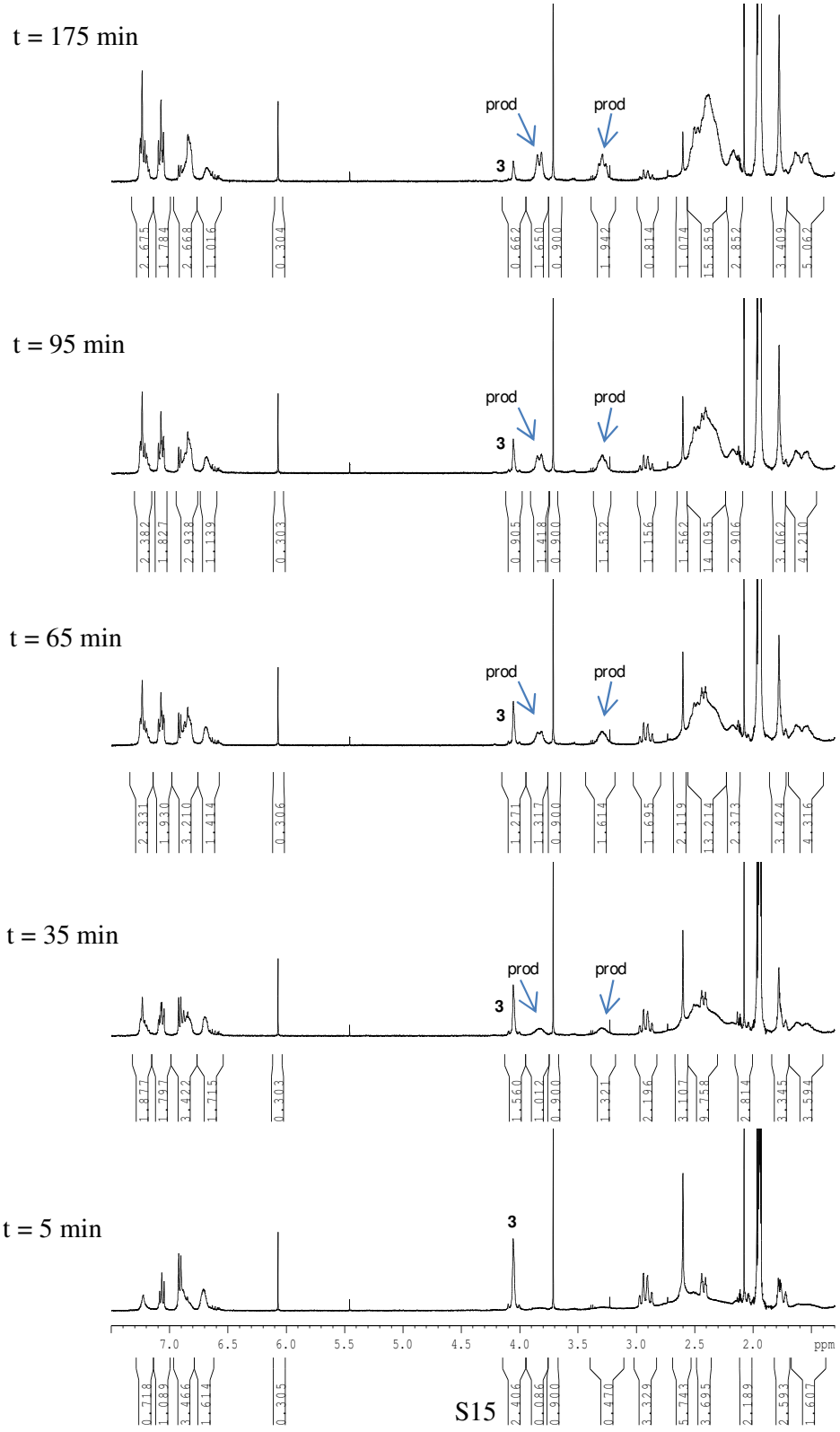


Figure S12. ^{1}H NMR spectrum of compound **4a** in CD_3CN at 298K.

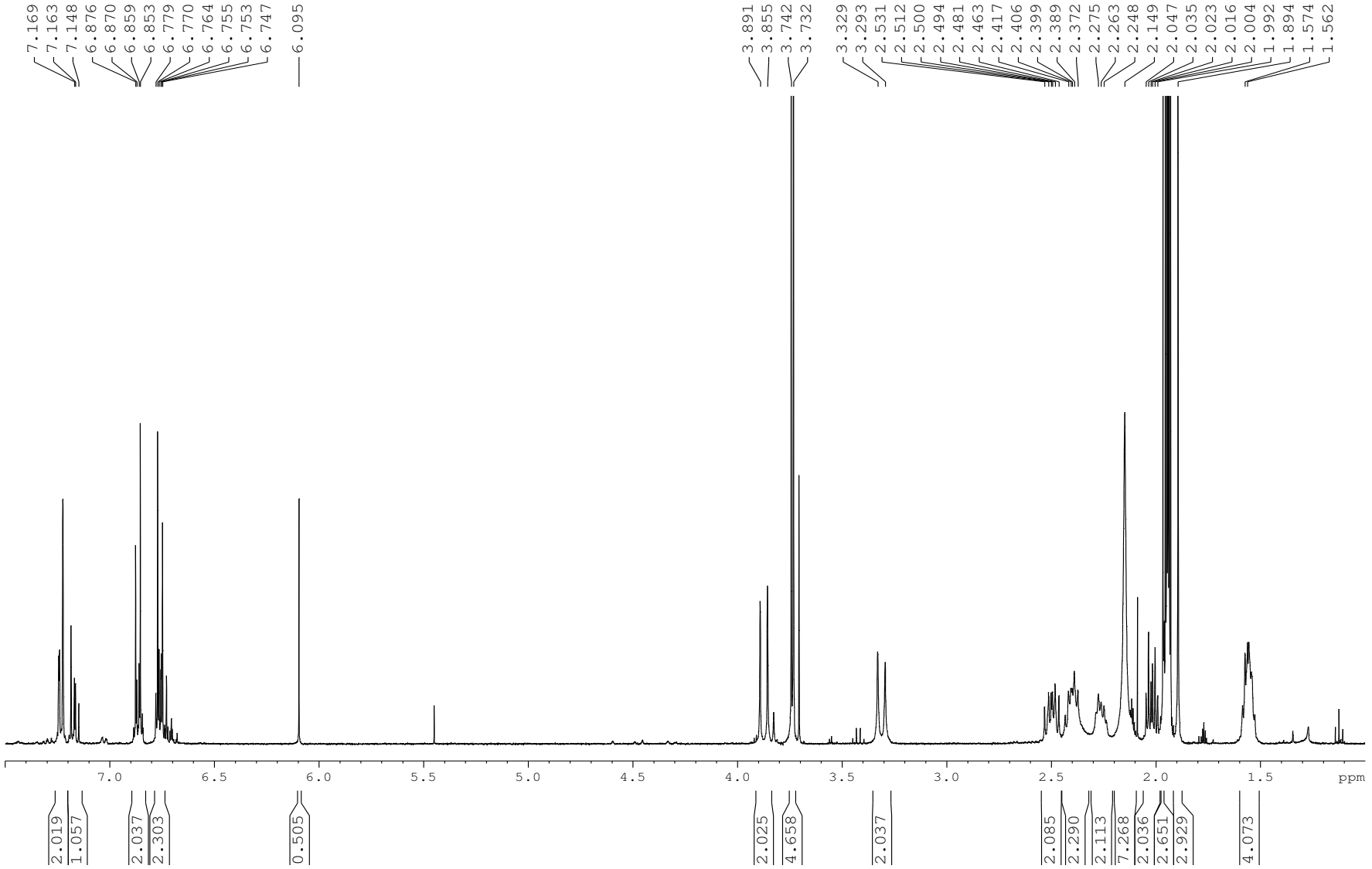


Figure S13. ^{13}C NMR spectrum of compound **4a** in CD_3CN at 298K.

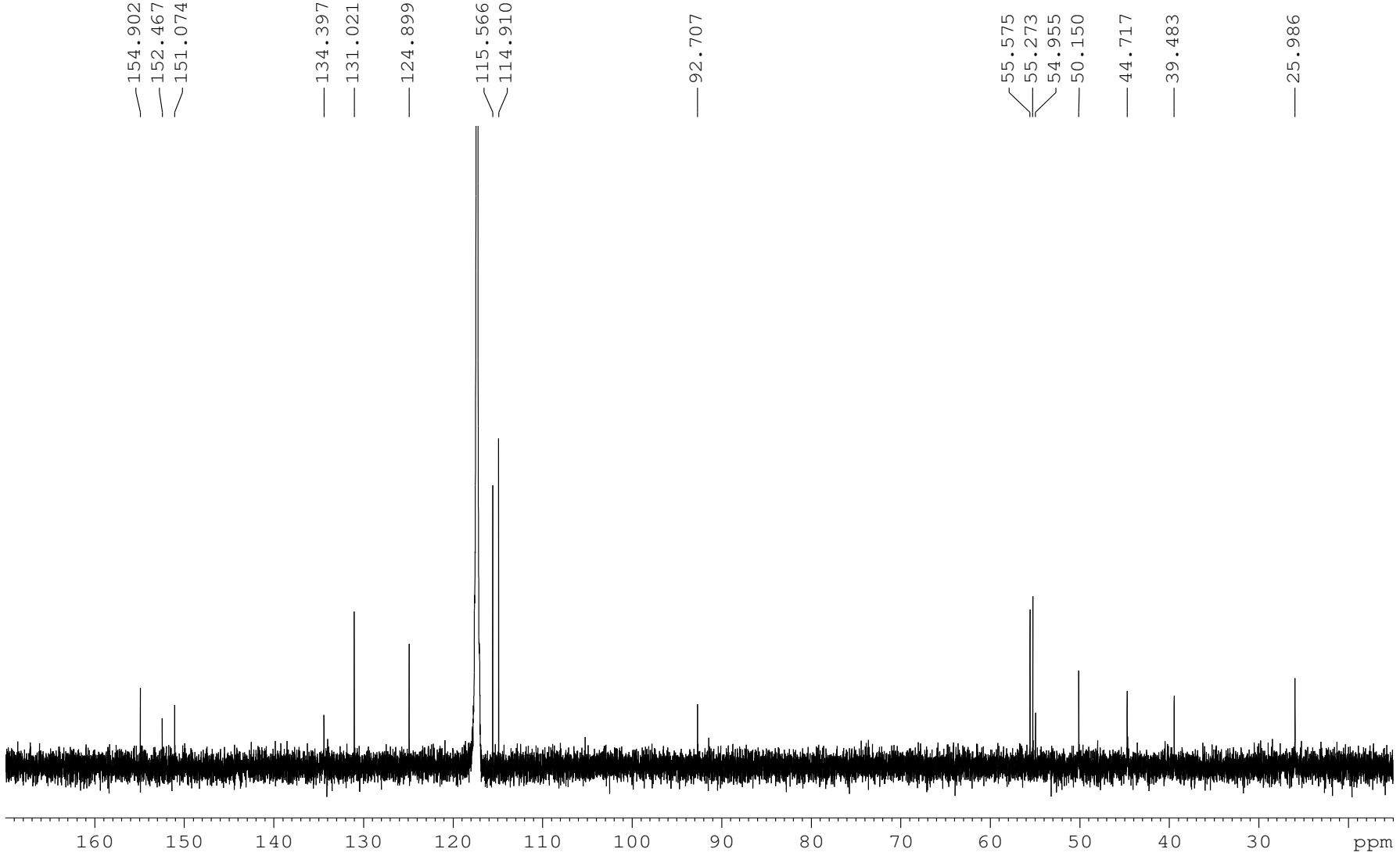


Figure S14. ^{1}H NMR spectrum of compound **4b** in CD_3CN at 298K.

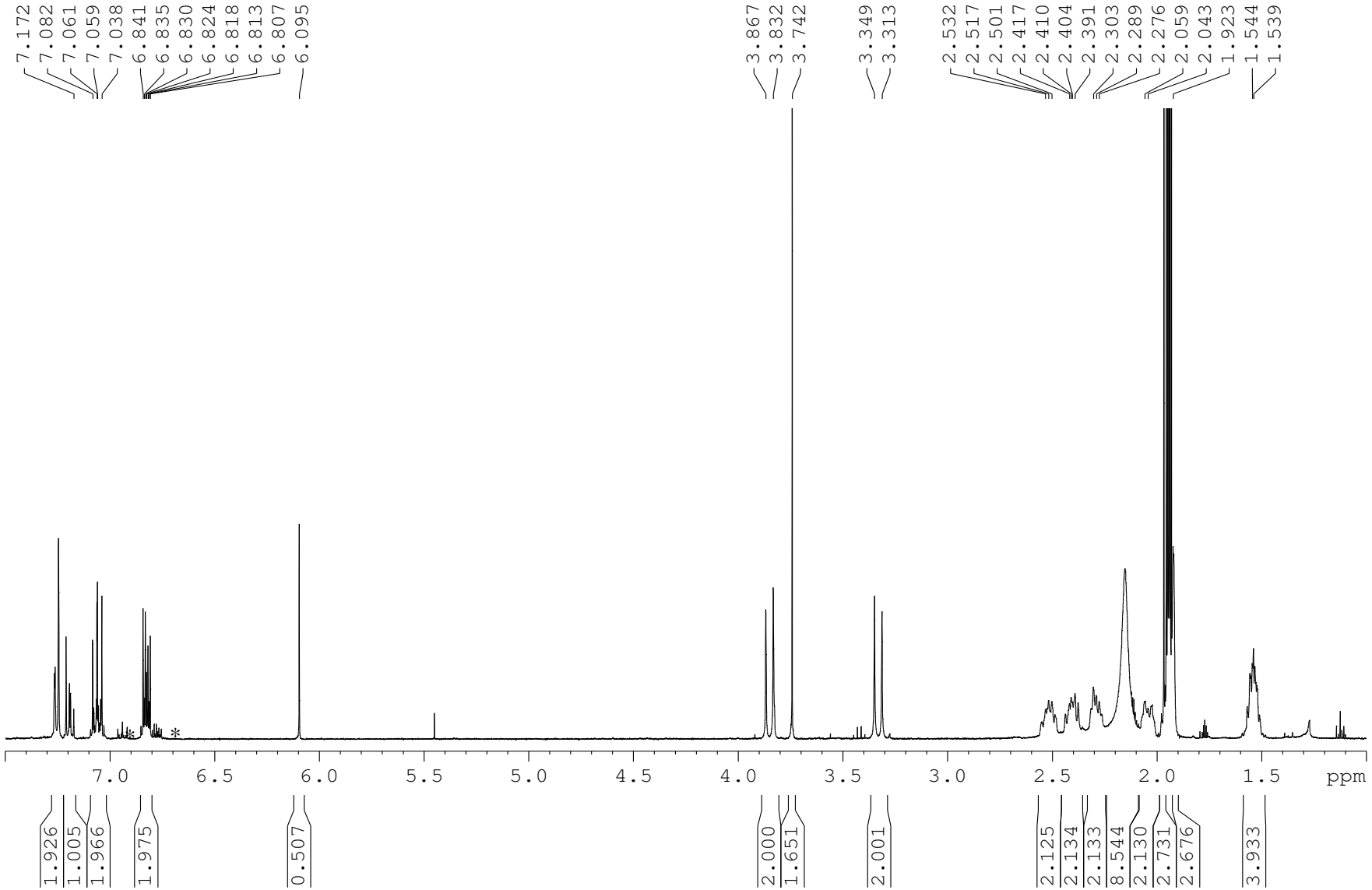


Figure S15. ^{13}C NMR spectrum of compound **4b** in CD_3CN at 298K.

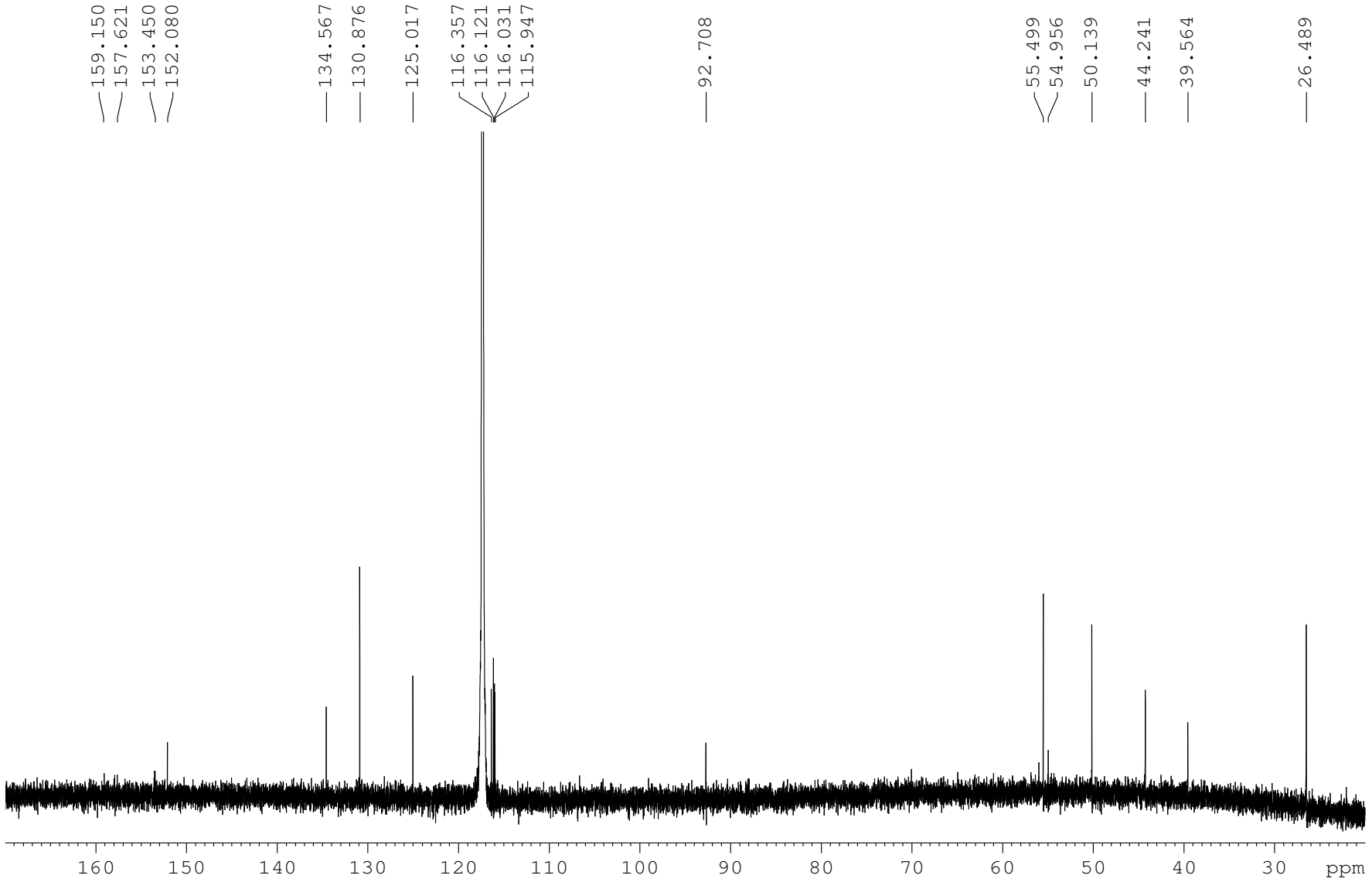


Figure S16. ^{1}H NMR spectrum of compound **4c** in CD_3CN at 298K.

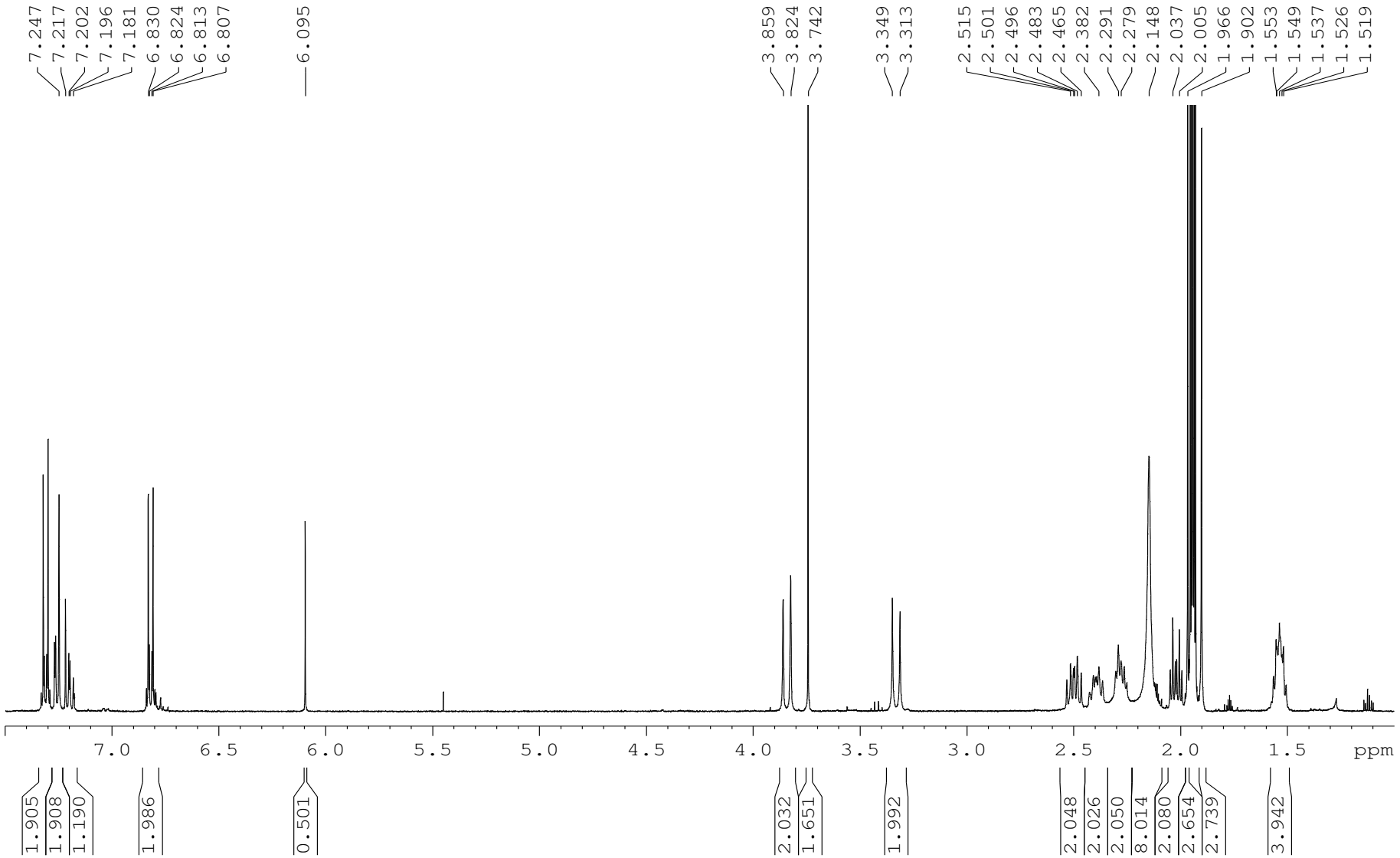


Figure S17. ^{13}C NMR spectrum of compound **4c** in CD_3CN at 298K.

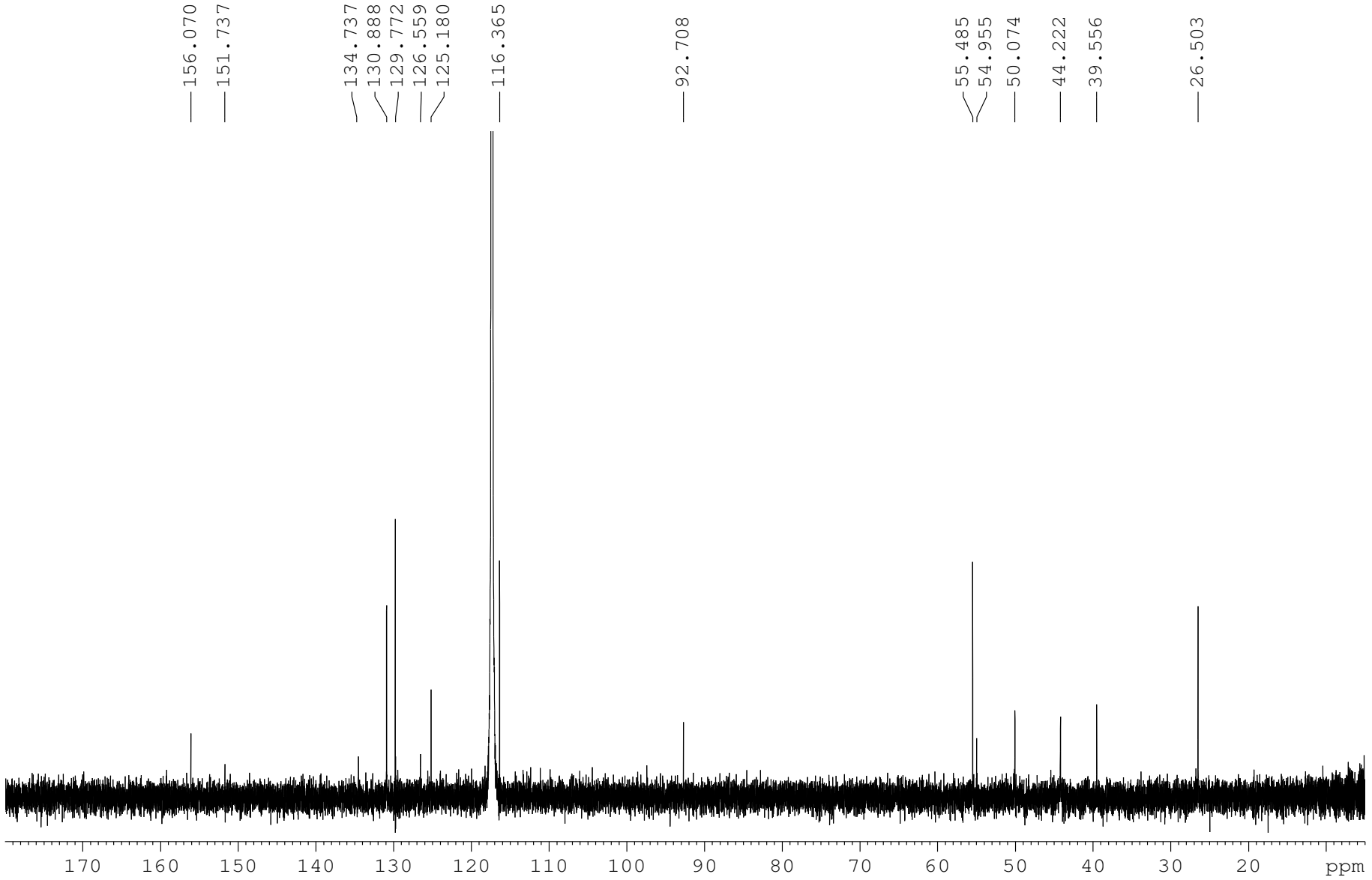


Figure S18. ^{1}H NMR spectrum of compound **4d** in CD_3CN at 298K.

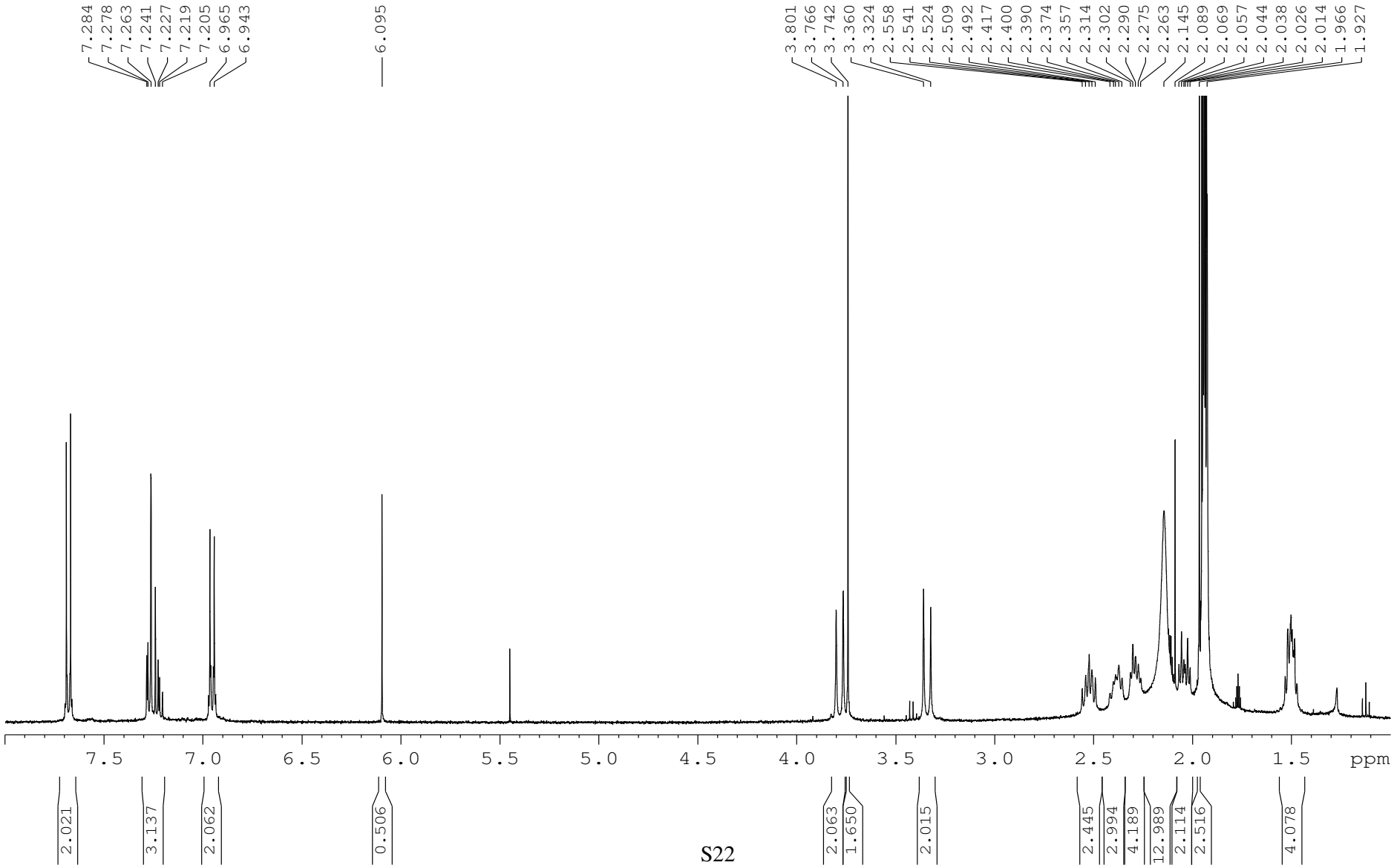


Figure S19. ^{13}C NMR spectrum of compound **4d** in CD_3CN at 298K.

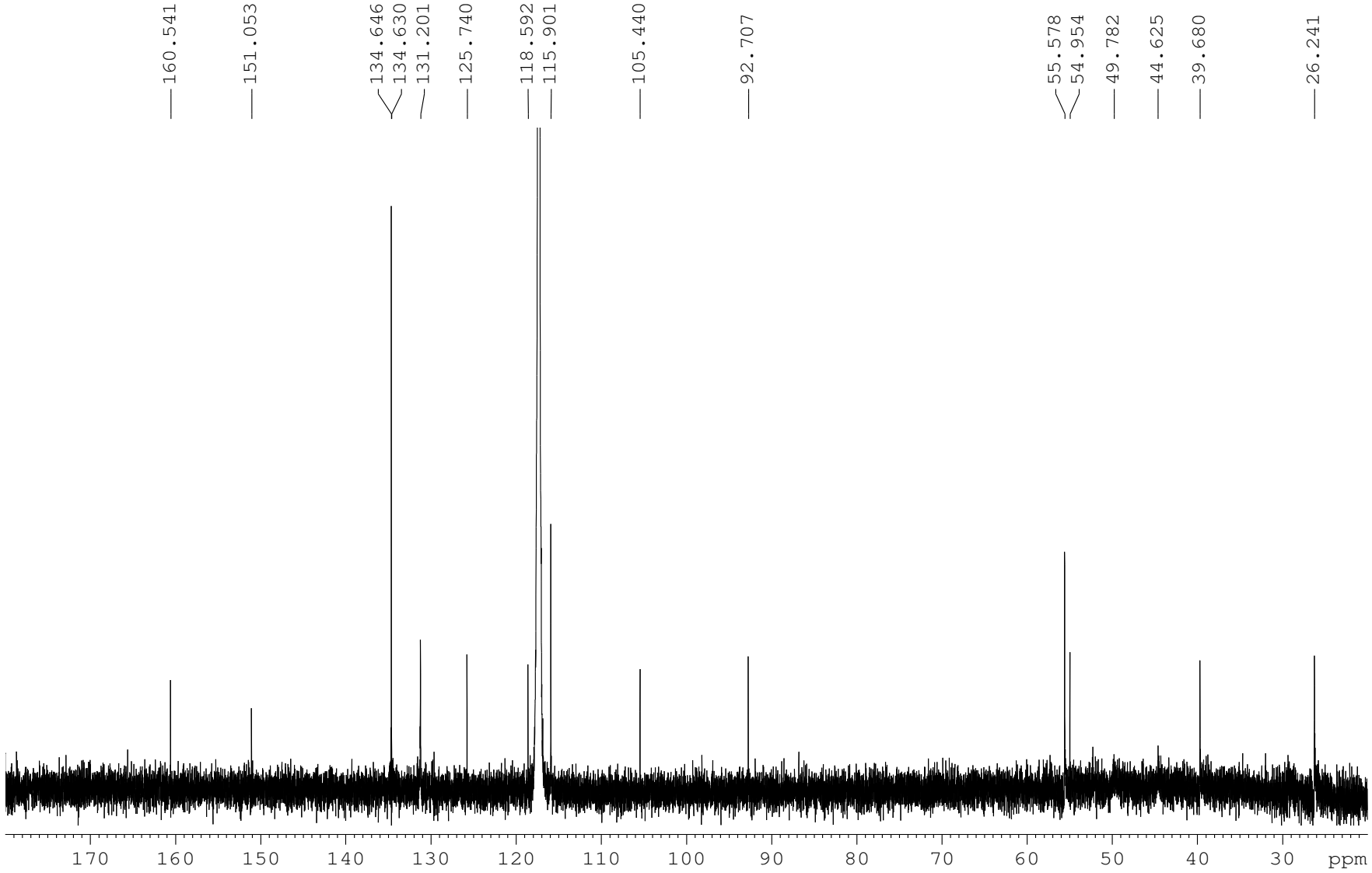


Figure S20. ^{1}H NMR spectrum of compound **4e** in CD_3CN at 298K.

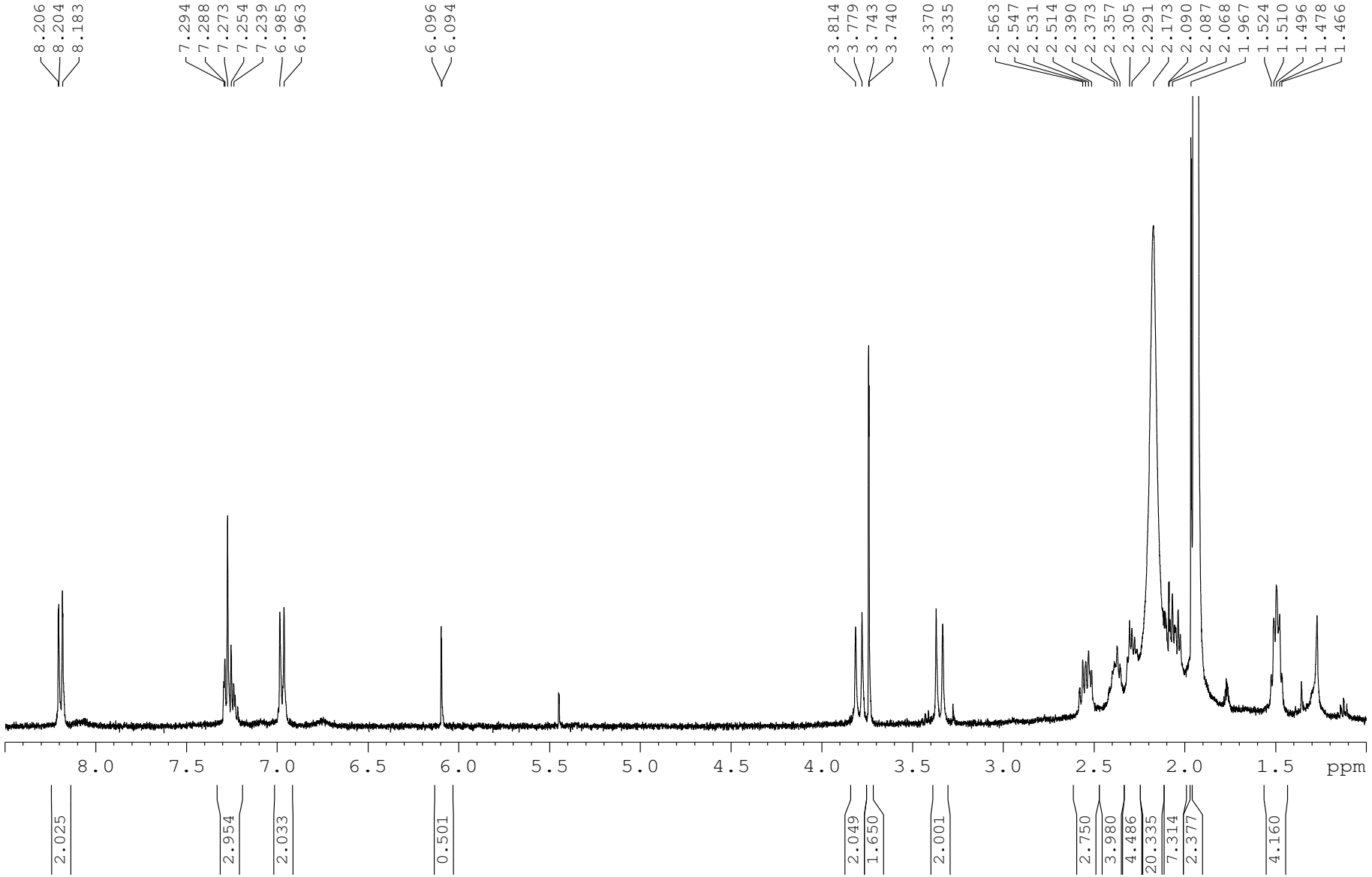


Figure S21. ^{13}C NMR spectrum of compound **4e** in CD_3CN at 298K.

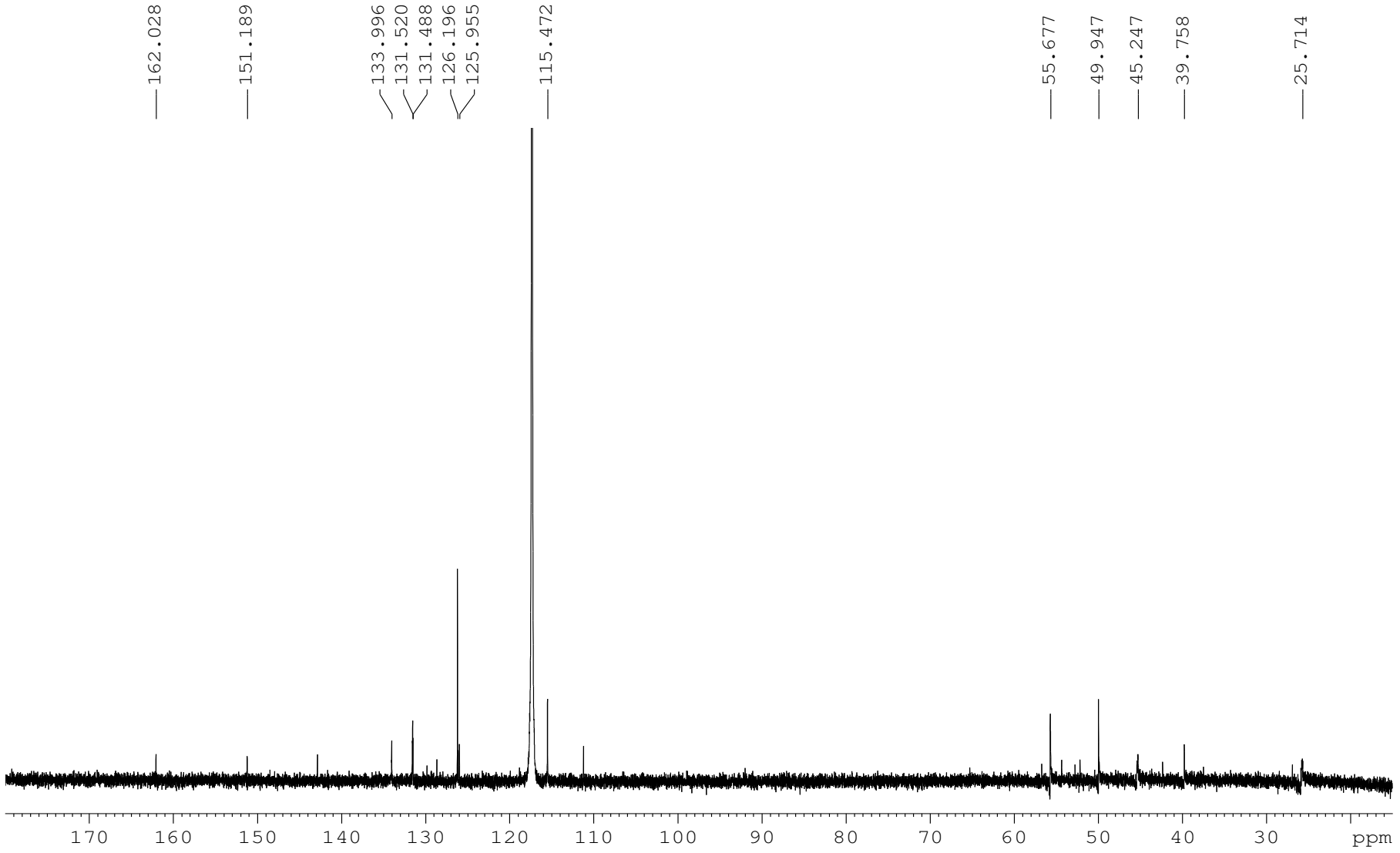
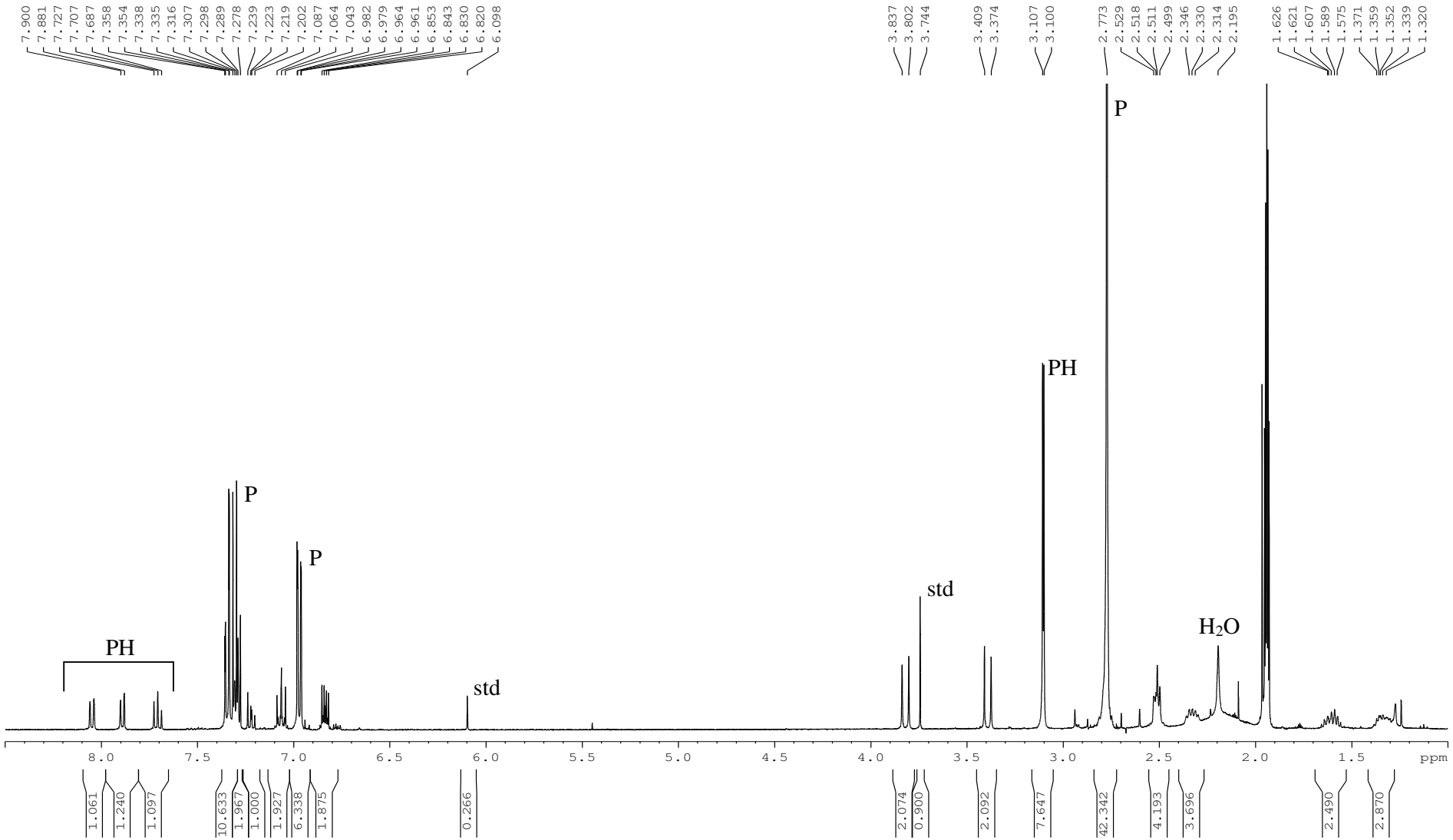


Figure S22. ^{1}H NMR spectrum of reaction of complex **2** with 4 equiv of protonsponge and 1 equiv of 4-fluorophenol in CD_3CN at 298K. (P = ProtonSponge® and PH = protonated ProtonSponge®, std = standard)



7. CW and Pulse-EPR experiments

7.1. Sample Preparation

a) Reaction with Protonsponge®

Stock solutions of complex **2** (10 mM) and Protonsponge® (50 mM) in CH_3CN were prepared under N_2. In vial sealed with a septum under N_2 atmosphere 1 mL of stock solution of complex **2** was added by syringe and 0.2 mL of acetonitrile. The solution mixture is cooled with a ice bath. Then 0.8 mL of stock solution of Protonsponge® and color solution from orange to deep violet. Several aliquots of 0.3mL were extracted from the reaction mixture at 2 min, 30 min, 1.5 h and 2.5 h and added into an EPR tube under N_2 atmosphere. Finally the EPR sample was frozen with N_2 liquid. Final concentrations were [**2**] = 5 mM and [Protonsponge®] = 20 mM.

For obtaining samples at higher concentrations the following procedure was done. Solution of complex **2** (39.2 mg, 0.08 mmols) in 1.55 mL of CH_3CN was prepared in a vial sealed with a septum and under N_2 atmosphere. Then solution of Protonsponge® (96.3 mg, 0.41mmols) was prepared also under N_2 atmosphere. The Protonsponge® solution was then added by syringe to a solution of **2** and stirred over time. Several aliquots of 0.3 mL were extracted from the reaction mixture at 2 min, 10 min and 20 min and added into an EPR tube under N_2 atmosphere. Finally the EPR sample was frozen with N_2 liquid. Final concentrations were [**2**] = 44 mM and [Protonsponge®] = 220 mM.

b) Reaction with triethylenediamine

Stock solutions of complex **2** (10 mM) and *triethylenediamine* (100 mM) in CH_3CN were prepared under N_2. In vial sealed with a septum under N_2 atmosphere 1 mL of stock solution of complex **2** was added by syringe and 0.6 mL of acetonitrile. The solution mixture is cooled with an ice bath. Then 0.4 mL of stock solution of *triethylenediamine* were added and color solution changed from orange to deep violet. An aliquot of 0.3 mL was extracted from the reaction mixture at 2 min and added into an EPR tube under N_2 atmosphere. Finally the EPR sample was frozen with N_2 liquid. Final concentrations were [**2**] = 5 mM and [*triethylenediamine*] = 20 mM.

c) Reaction with pF-PhONa

Stock solutions of complex **2** (10 mM) and sodium *p*-fluorophenolate (10 mM) in CH_3CN were prepared under N_2. In vial sealed with a septum under N_2 atmosphere 1 mL of stock solution of complex **2** was added by syringe and cooled with an ice bath. Then 1 mL of stock solution of *p*-fluorophenolate was added and color solution changed from orange to deep violet. An aliquot of 0.3 mL was extracted from the reaction mixture immediately and added into an EPR tube under N_2 atmosphere. Finally the EPR sample was frozen with N_2 liquid. Final concentrations were [**2**] = 5 mM and [*p*F-PhONa] = 5 mM.

7.2. EPR spectroscopy details

CW EPR measurements at X-band were carried out on a Bruker ESP 380E spectrometer equipped with a rectangular ER 4102ST cavity. Experimental conditions: microwave (mw) frequency, 9.429 GHz; mw power incident to the cavity, 0.2 mW; modulation frequency, 100 kHz; modulation amplitude, 0.1 mT. Cooling of the sample was performed with a liquid-nitrogen finger Dewar (T = 120 K).

CW EPR measurements at Q-band were carried out on a home-built spectrometer (at IMS Demokritos) equipped with an ER 5106 QT Bruker resonator. Experimental conditions: mw frequency, 34.6 GHz; mw power, 0.05 mW; modulation frequency, 100 kHz; modulation amplitude, 1 mT; temperature, 30 K.

Pulse EPR measurements at X-band (mw frequency 9.717 GHz) were performed at 30 K with a Bruker ESP 380E spectrometer equipped with an EN 4118X-MD4 Bruker resonator. The field-swept EPR spectrum (Figure **EPR2**, top trace) was recorded via the free induction decay (FID) following a pulse length of 500 ns. Davies electron-nuclear double resonance (ENDOR) experiments were carried out with the pulse sequence $\pi - T - \pi/2 - \tau - \pi - \tau - \text{echo}$, with selective ($\Delta t_\pi$ = 192 ns) or strong (Δt_π = 32 ns) mw pulses and a radio-frequency (rf) pulse of length 10 μs. HYSCORE experiments[4] were performed with the pulse sequence $\pi/2$ - τ - $\pi/2$ - t_1 - π - t_2 - $\pi/2$ - τ - echo using the following parameters : $t_{\pi/2}$ = 16 ns; starting values of the two variable times t_1 and t_2, 56 ns; time increment, Δt = 16 ns (data matrix 256 × 256). To avoid blind spots, spectra with different τ values were recorded and added. A four-step phase cycle was used to remove unwanted echoes. The data were processed with the program MATLAB 7.0 (The MathWorks, Natick, MA). The time traces were baseline corrected with a two-

order exponential, apodized with a gaussian window and zero filled. After a two-dimensional Fourier transform the absolute-value spectra were calculated.

The CW EPR and ENDOR spectra were simulated with the EasySpin packag.[5] HYSCORE spectra were simulated with a program written in-house.[6]

7.3. Quantification of the paramagnetic species

In order to quantify the paramagnetic species appeared after the reaction start, the cw EPR signal intensity (double integral) was compared to a standard Cu^{II} sample, namely $Cu^{II}(acac)_2$ in chloroform.

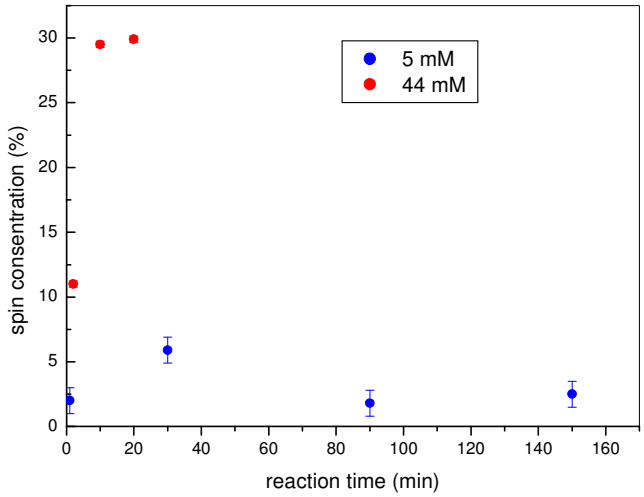


Fig. EPR1. Relative concentration of paramagnetic species to the initial concentration of **2** at different reaction times with protonsponge.

7.4. Identification of the paramagnetic species

ENDOR

All pulsed ENDOR spectra show proton (^1H) couplings ranging from 5 to 15 MHz. Spectrum (e) of Figure **EPR2**: there are clearly two sets of protons with couplings A_1=6 MHz and A_2=13.5 MHz. Using strong pulses two peaks at low frequencies appear. They are centered around 6 MHz and separated by approx. 2.5 MHz ($\approx 2\nu_{14N}$=2.4 MHz). This is consistent with a strongly coupled ^{14}N with A=12 MHz. This assignment is also supported by the fact that we don't observe the symmetric peak of the 5 MHz peak about ν_H (expected around 26 MHz if this was a proton peak). Moreover, HYSCORE measurements showed a strongly coupled N with identical parameters (see Fig. **EPR3**).

Finally, the high frequency proton peak from the A_2=13.5 MHz set (higher intensity peak) is broader than its low-frequency counterpart and this implies an overlap with another peak, possibly arising from another strongly-coupled nucleus. This is in agreement with the spectrum (b) of Fig. **EPR2** showing two sets of proton couplings with an additional peak at 23 MHz. The counterpart of this peak is missing; therefore it cannot be assigned to protons. A possible assignment is a strongly-coupled nitrogen with A=46 MHz. This value is typical for directly coordinated N ligands in copper complexes, for example equatorially coordinated N ligands in square-planar Cu(II) complexes. Overall, the ENDOR study shows at least two different sets of weakly coupled protons and presumably two strongly-coupled nitrogens, one with A=12 MHz and another one with A=46 MHz.

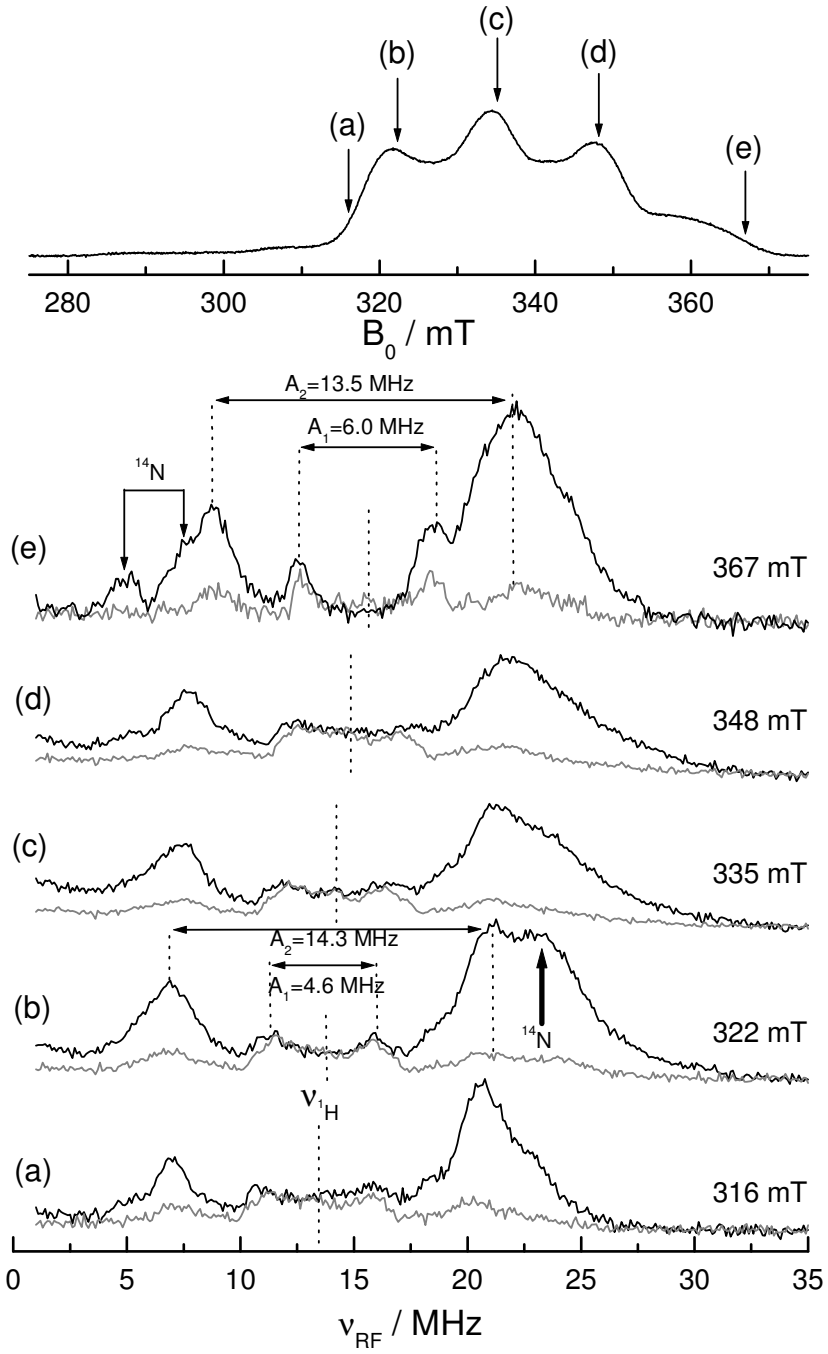


Fig. EPR2. ENDOR spectra at different observer positions. Black traces: strong mw pulses in order to suppress weak hf couplings (A<10 MHz). Gray traces: selective (soft) mw pulses. Top trace: FID-detected field swept EPR spectrum.

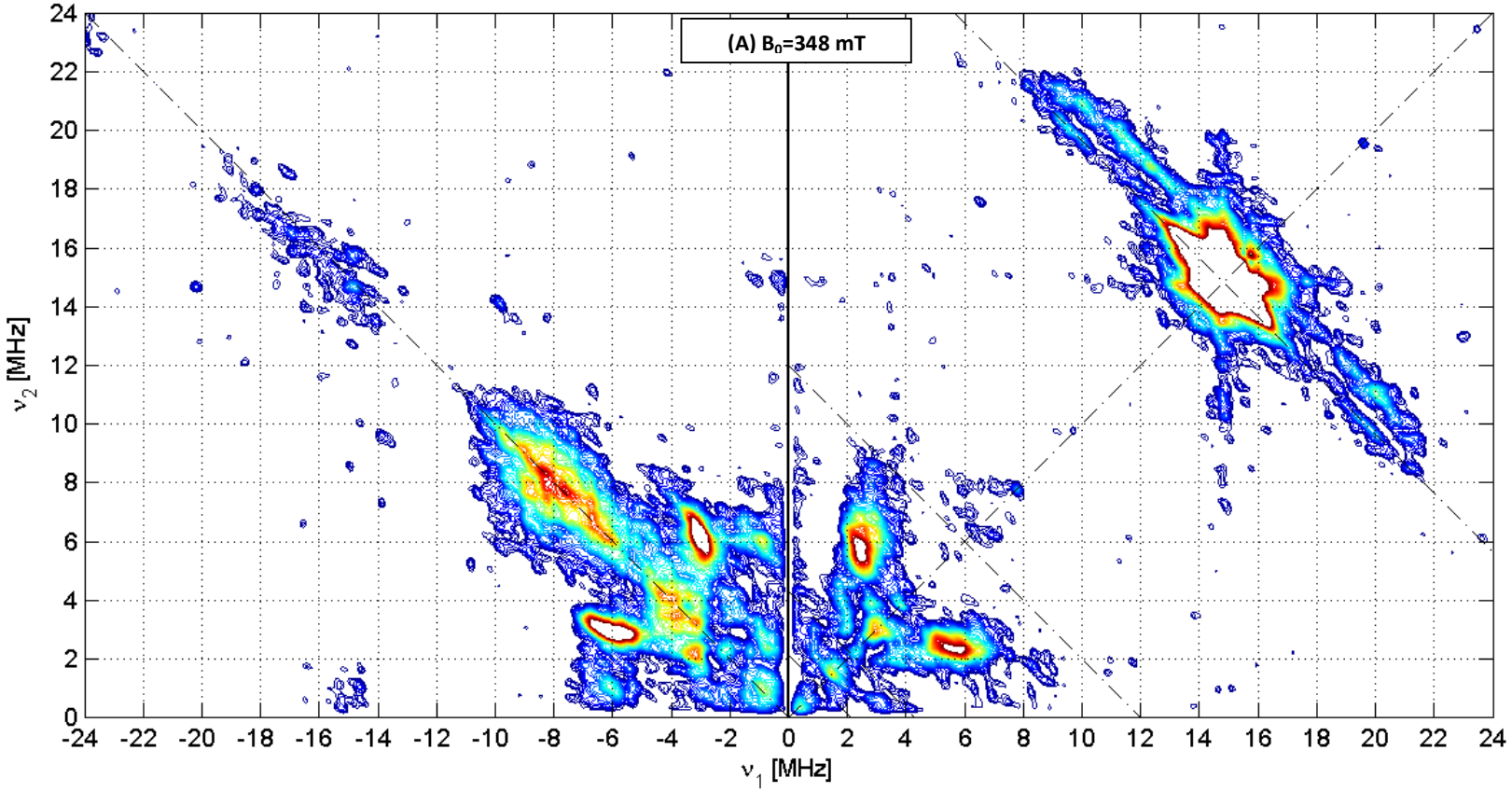


Fig. EPR3(A): HYSCORE spectrum of **3'** measured at B_0=348 mT.

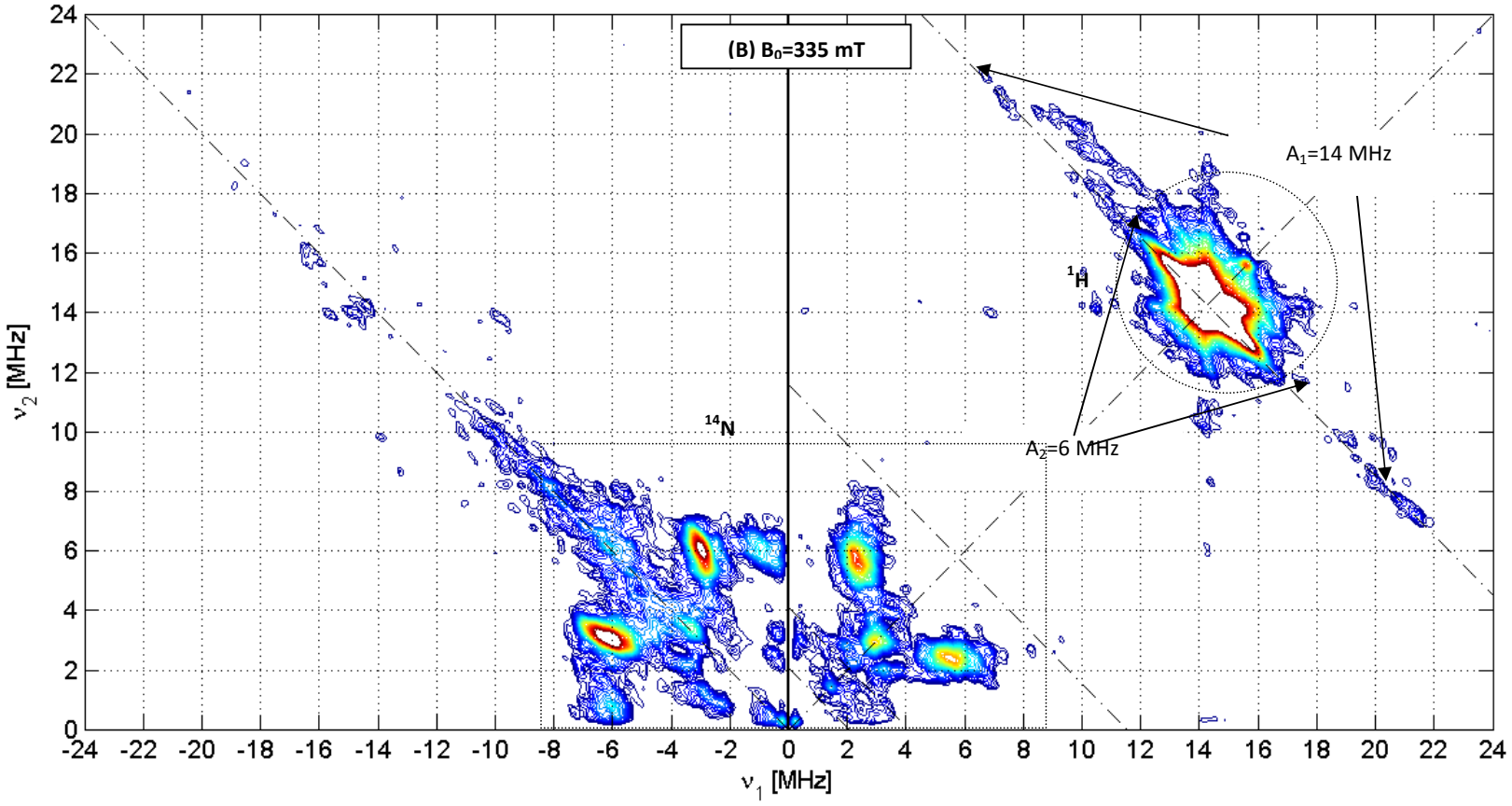


Fig. EPR3(B): HYSCORE spectrum of **3'** measured at B_0=335 mT.

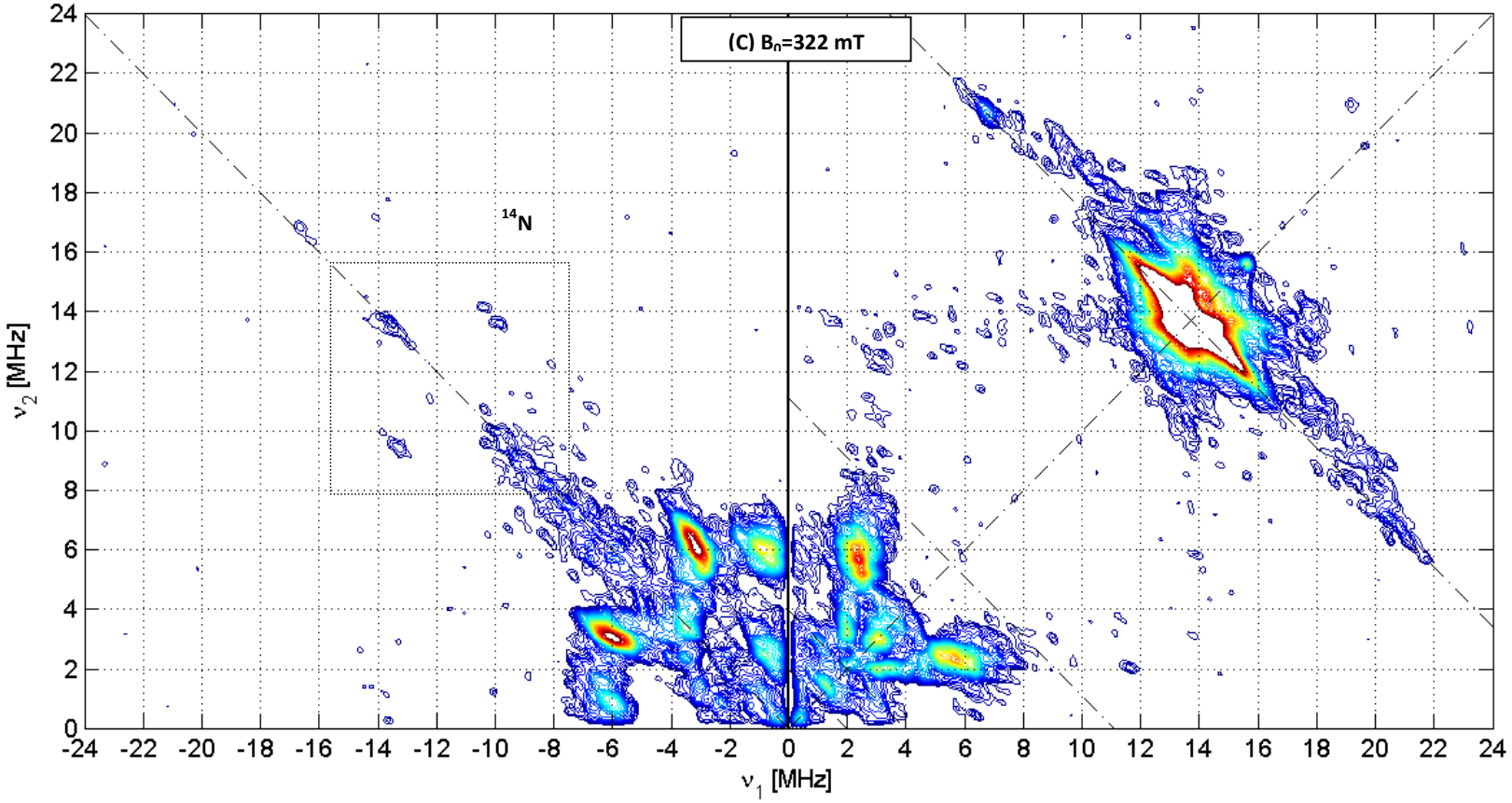


Fig. EPR3(C): HYSCORE spectrum of **3'** measured at B_0=322 mT.

Figures EPR3(A-C) show three HYSCORE spectra at different observer positions (same as ENDOR, see Figure **EPR2** upper part – field swept EPR). All spectra contain rich information and reveal proton and nitrogen couplings.

^{1}H-HYSCORE

The correlation ridges around the anti-diagonal at 15 MHz are assigned to weakly coupled protons. The hf couplings are in agreement with the ones observed in ENDOR spectra. For example, in Fig. **EPR3(b)** the two marked correlation peaks at (21,7) MHz and (7,21) MHz imply a proton coupling of A=21-7=14 MHz with a modest anisotropy. This coupling agrees with the coupling A_1 of ENDOR spectra (comparison with spectrum (d) Fig.**EPR2**). The stronger proton peaks appear close to diagonal and are marked by a circle (the contour plot cuts high intensity peaks in order to see better the low intensity peaks that are otherwise hidden in the baseline). The correlation peaks are spread up to 6 MHz and agree with the coupling A_2 of ENDOR spectra.

Finally, HYSCORE experiments revealed also a proton coupling with considerable anisotropy. The simulation of the spectrum at B_0=348 mT (position of correlation peaks, black arcs in figure **EPR4** below) give the principal values [A_x, A_y, A_z]=[-3.65,-3.65,14.8] MHz. Assuming an axial A tensor the anisotropic part is T=6.15 MHz which implies a dipole-dipole distance of r=2.34 Angstrom provided that the spin is 100% localized on Cu (this distance is reduced to 1.86 Angstrom if the spin density is 50% at Cu). The spectrum on the right-hand side of figure **EPR4** is the full HYSCORE simulation (in time domain, also including peak intensities) of this proton coupling.

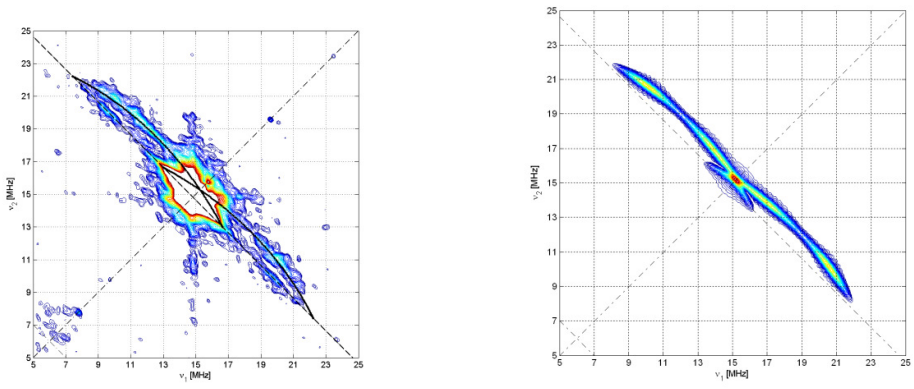


Fig. EPR4: ^{1}H-HYSCORE spectrum of **3'** measured at B_0=348 mT (left) and the corresponding simulation (right)

^{14}N-HYSCORE

In the (-,+) quadrant of all HYSCORE spectra there are two correlation peaks at (-9.9, 13.6) and (-13.3, 9.4) MHz, marked with a rectangular box in Fig. **EPR3(C)**. They are separated by approx. 3.9 MHz (= $4\nu_N$ = 3.96 MHz) and centred around 11.5 MHz. Therefore, these peaks are assigned to the double-quantum transitions of a strongly-coupled nitrogen with A=11.5 MHz. This value nicely agrees with the one observed in ENDOR, see ^{14}N of Fig. **EPR2**. In ENDOR spectrum we see the single-quantum transitions that contain information also about the nuclear quadrupole interaction (nqi). However, due to the limited resolution we cannot extract this interaction from ENDOR. Consequently, we cannot further identify this nitrogen.

Finally, in the area marked by a box in Fig. **EPR3(B)**, there are intense peaks in both quadrants (see Fig. **EPR5**). They are assigned to another nitrogen with A=4.0 MHz and a relatively strong nuclear quadrupole coupling.

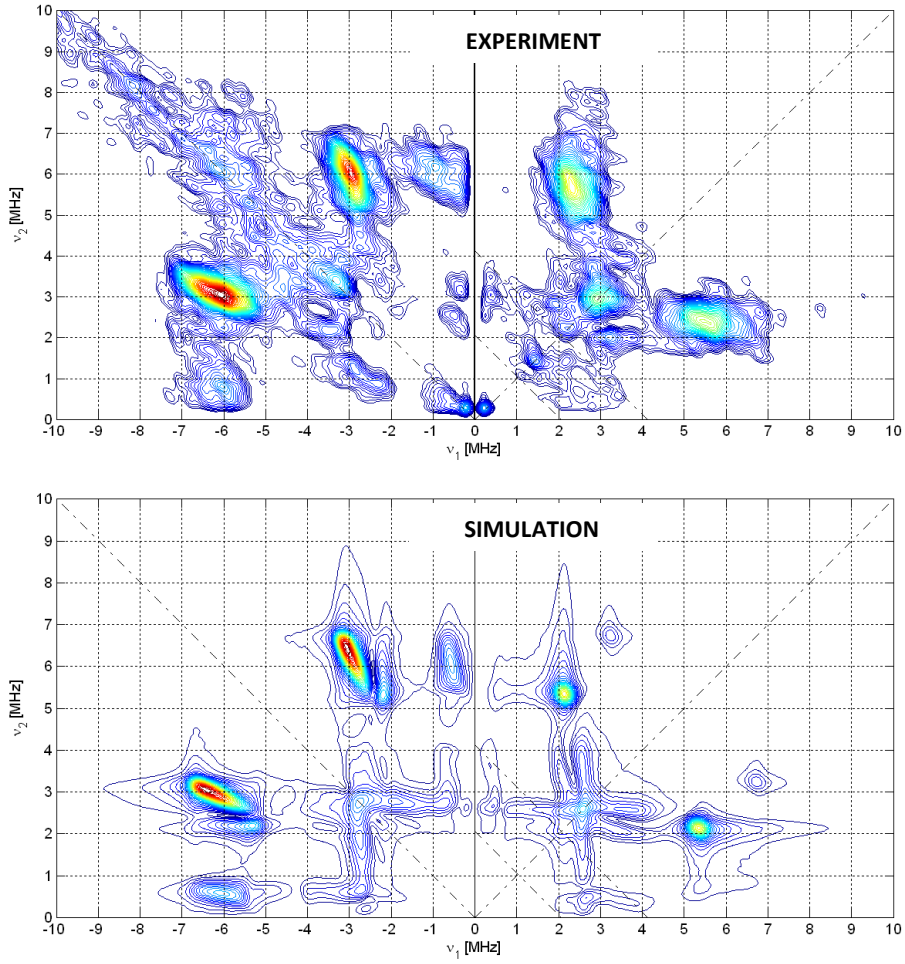


Fig. EPR5: ^{14}N-HYSCORE spectrum of **3'** measured at B_0=335 mT (top) and the corresponding simulation (bottom). The simulation parameters for the hf coupling are $[A_x, A_y, A_z]$=[2.7, 2.7, 4.2] MHz, whereas the nuclear quadrupole coupling constant is $\left|e^2qQ/h\right|$=3.0 MHz with asymmetry parameter η=0.2.

8. References

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6. Z. L. Madi, S. V. Doorslaer and A. Schweiger, *J. Magn. Reson.*, 2002, **154**, 181-191.