Electronic Supplementary Material (ESI) for RSC Advances.

Supporting Information

Intramolecular Hydrogen Bond Directed Stable Conformations of Benzoyl Phenyl Oxalamides: Unambiguous Evidence by Extensive NMR Studies and DFT Based Computations

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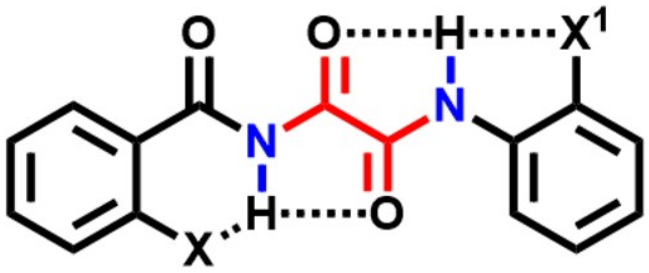
S41: 800 MHz proton decoupled 2D ^{15}N-^{1}H HSQC spectrum of molecule **5** in the solvent DMSO-d_6.



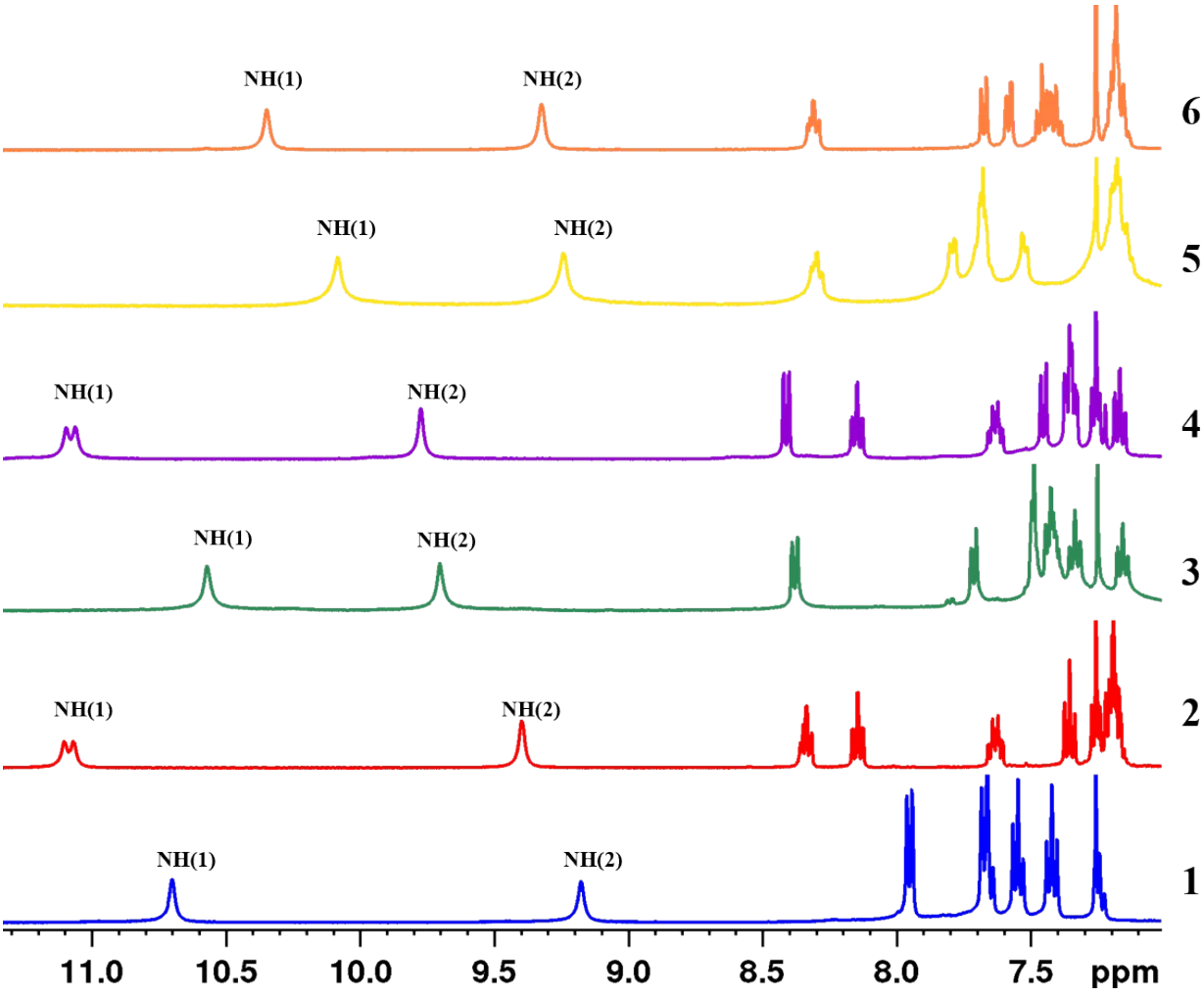
(1) X = X¹ = H **(4) X = F ; X¹ = Cl**

(2) X = X¹ = F **(5) X = CF_3 ; X¹ = F**

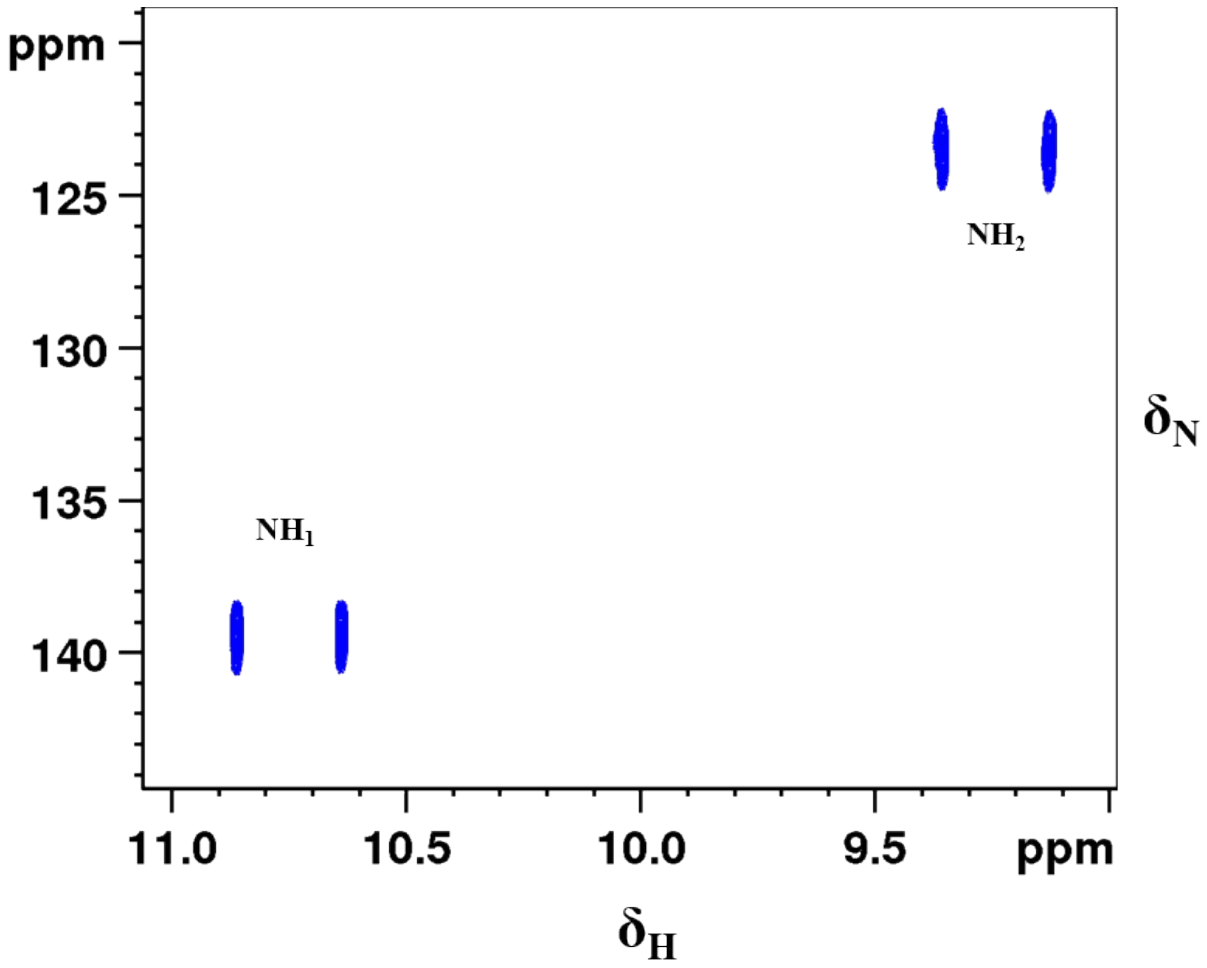
(3) X = X¹ = Cl **(6) X = Br ; X¹ = F**

The chemical structures of N^1-benzoyl-N^2-phenyl oxalamide and its derivatives. The molecules **1-6** differ in their substituents, X and X^1 as mentioned in the scheme.

S1

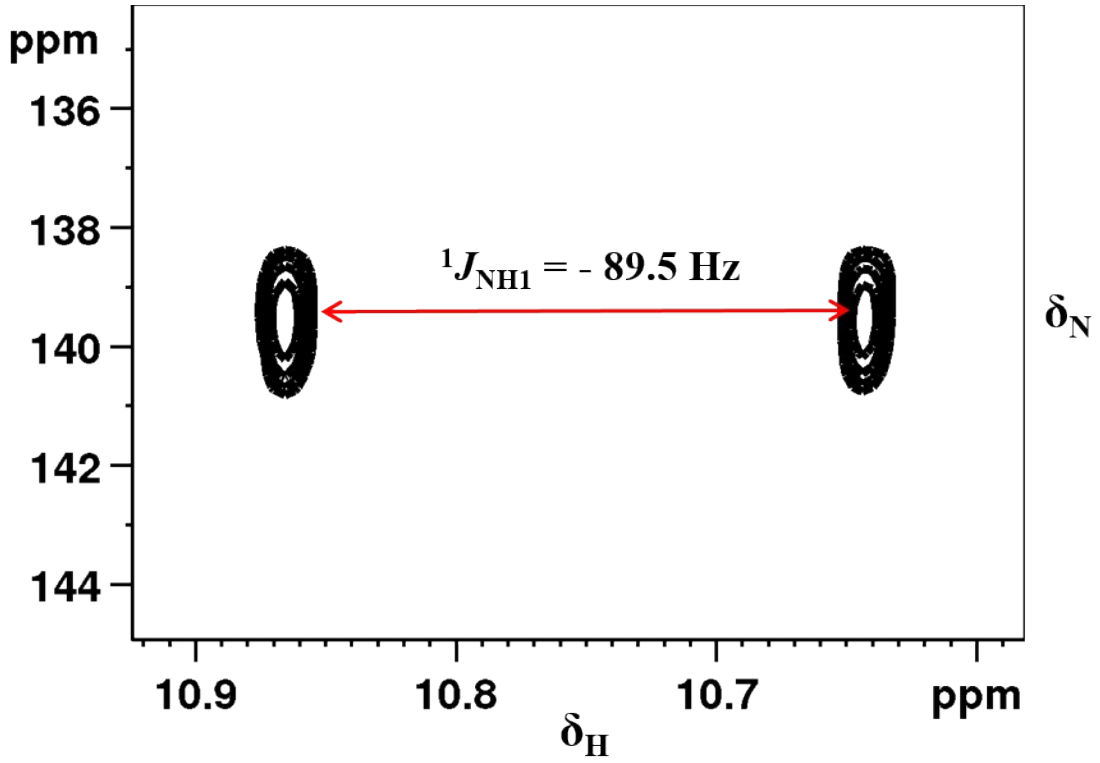


Selected regions of the 400 MHz ^{1}H-NMR spectra of molecules **1–6** (from bottom trace to top trace), recorded in the solvent $CDCl_3$ at 298 K and the spectra were referenced to internal tetramethylsilane.

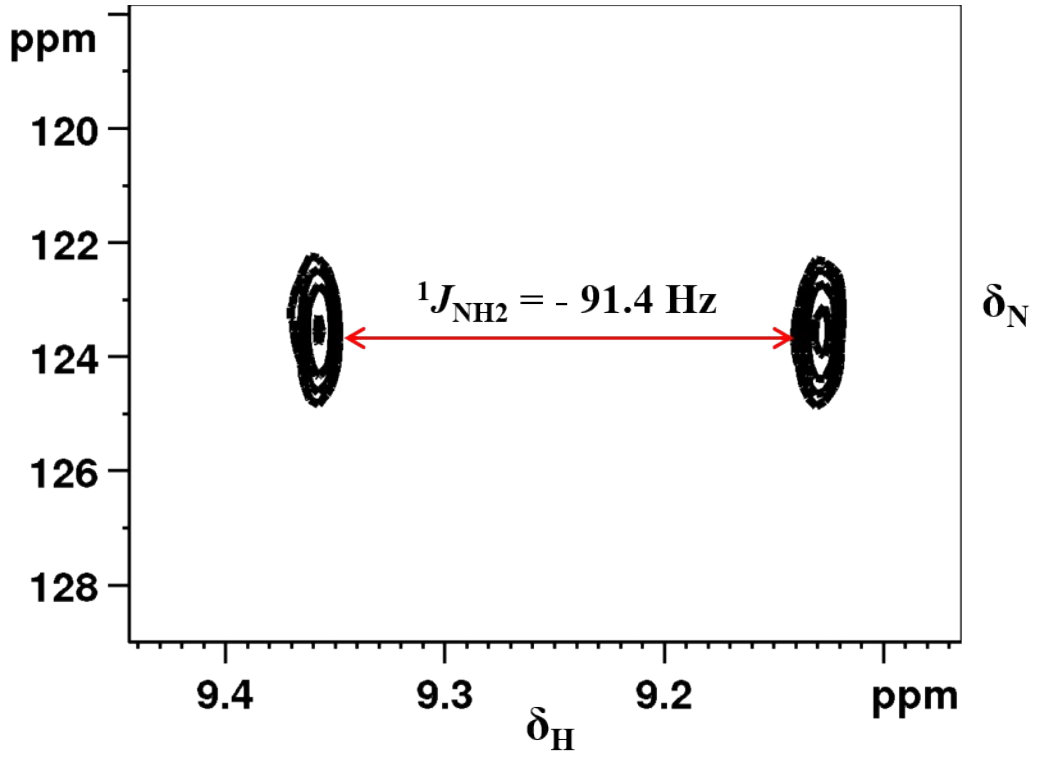


400 MHz 2D ^{15}N-^{1}H coupled HSQC spectrum of molecule **1** in the solvent $CDCl_3$.

S3

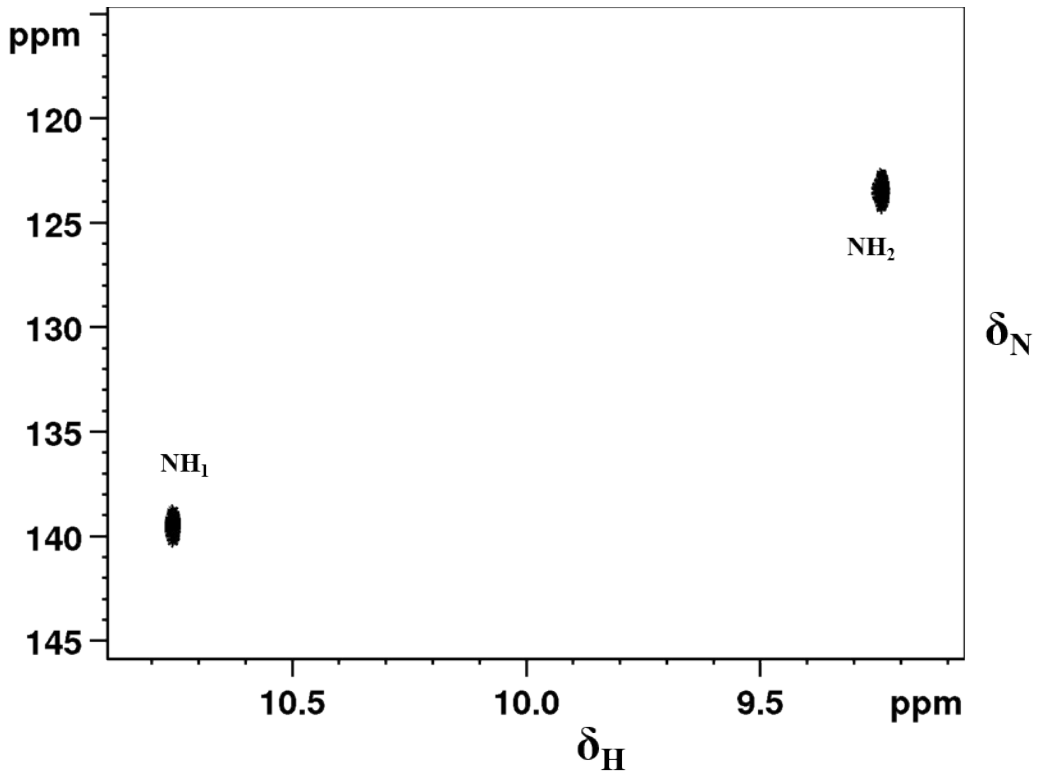


Expanded region of HSQC spectrum of molecule 1 **(Fig. S3)** pertaining to NH(1) region, showing the scalar coupling $^1J_{NH}$.

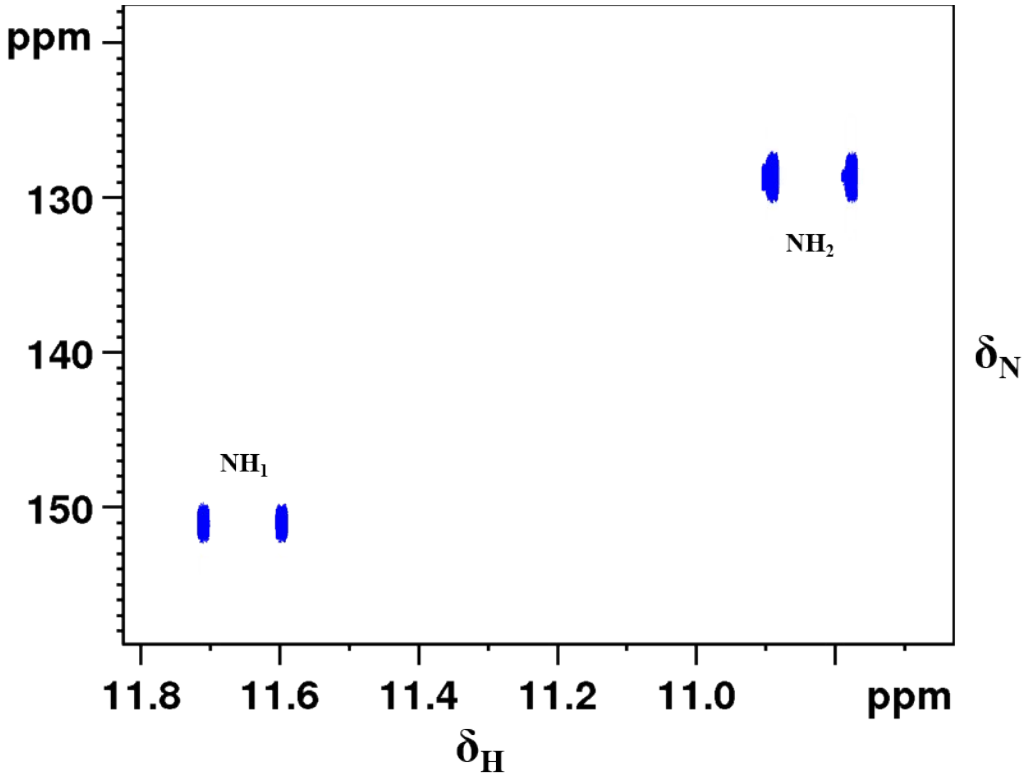


Expanded region of HSQC spectrum of molecule 1 **(Fig. S3)** pertaining to NH(2) region, showing the scalar coupling $^1J_{NH}$.

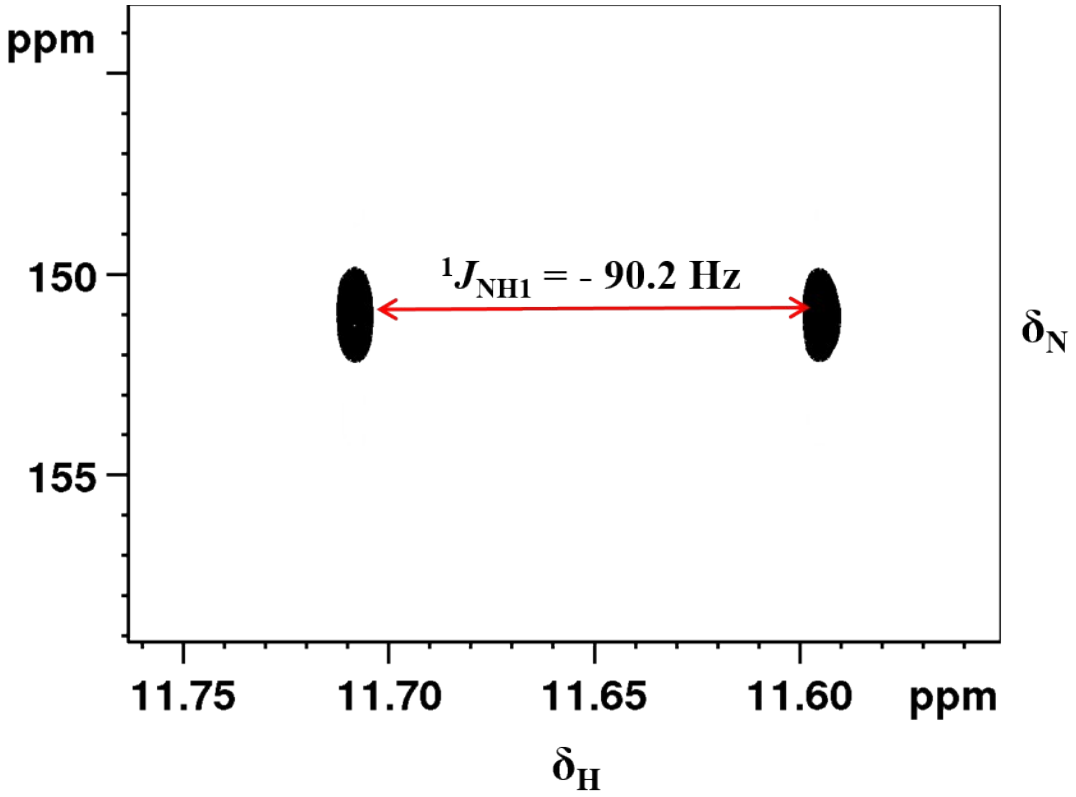
S5



400 MHz proton decoupled 2D ^{15}N-^{1}H HSQC spectrum of molecule **1** in the solvent $CDCl_3$.

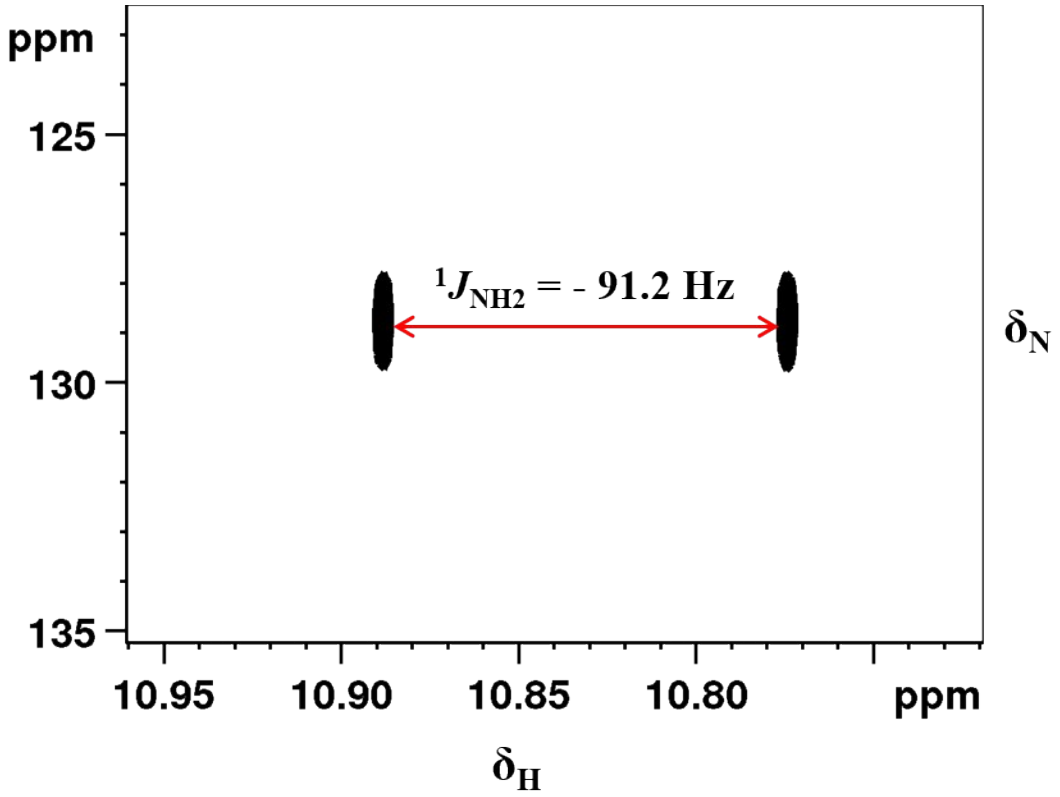


800 MHz 2D ^{15}N-^{1}H coupled HSQC spectrum of molecule **1** in the solvent DMSO-d_6.

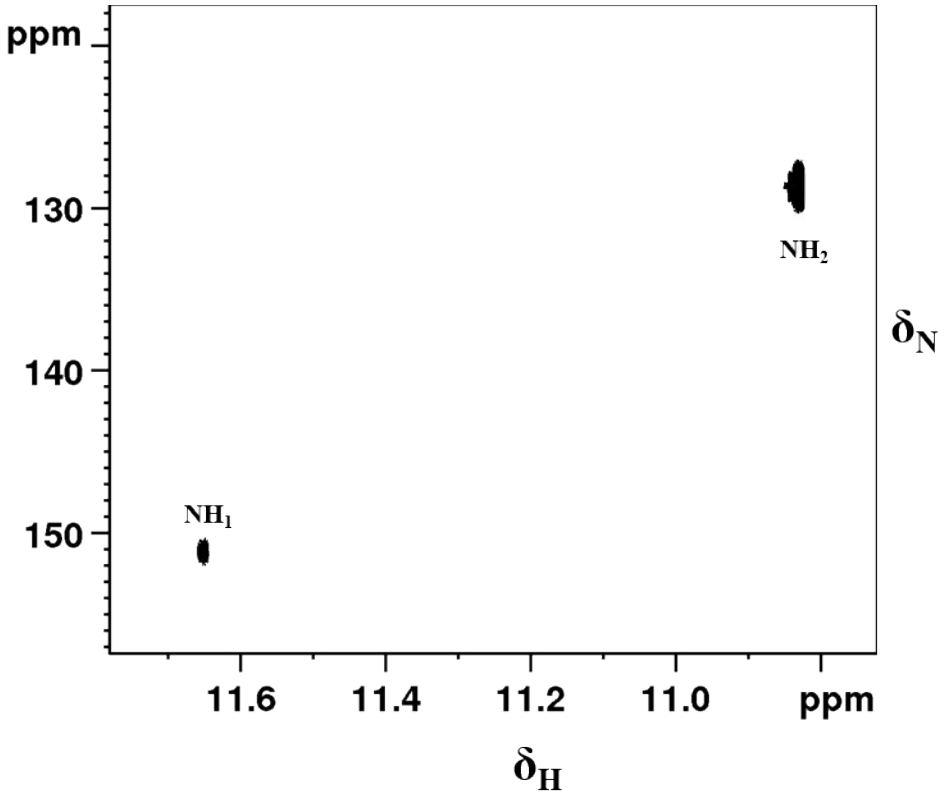


Expanded region of HSQC spectrum of molecule **1 (Fig. S7)** pertaining to NH(1) proton, showing the scalar coupling $^1J_{NH}$.

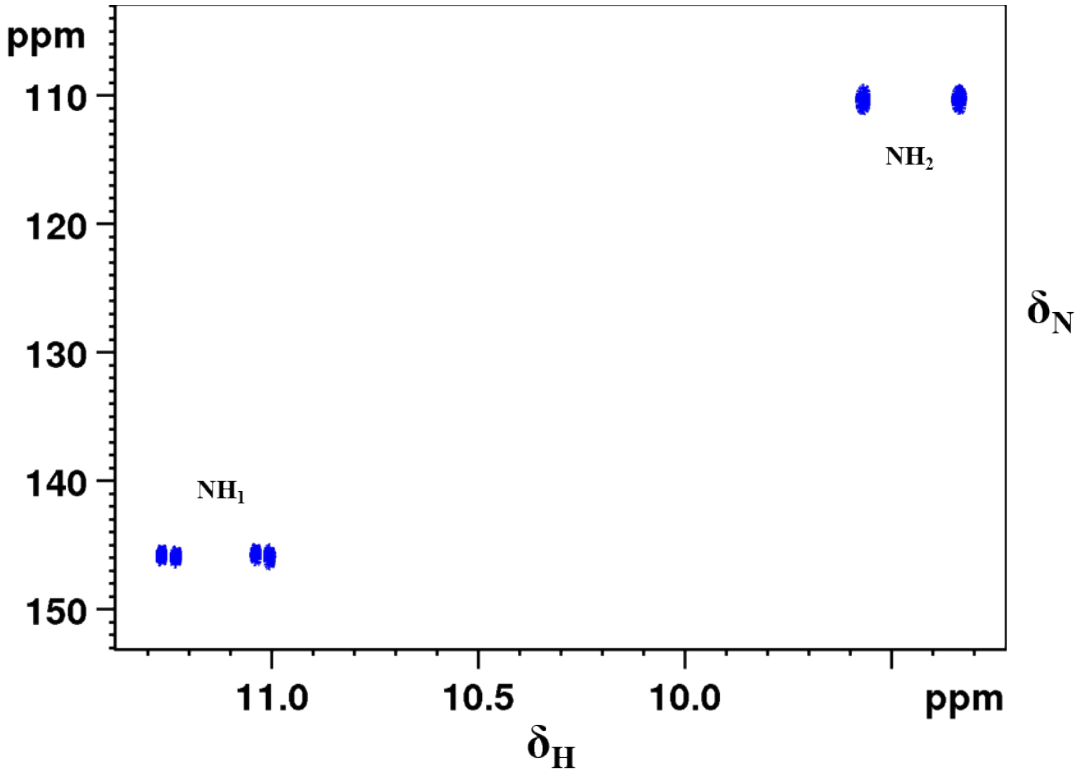
S8



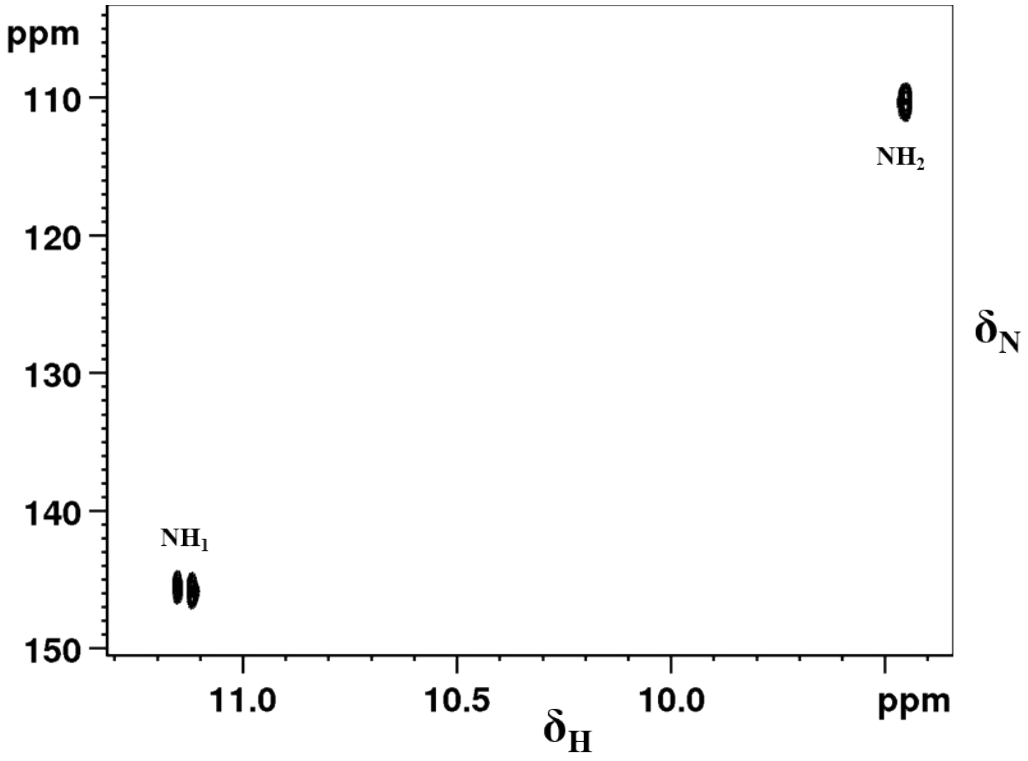
Expanded region of HSQC spectrum of molecule **1 (Fig. S7)** pertaining to NH(2) proton, showing the scalar coupling $^1J_{NH}$.



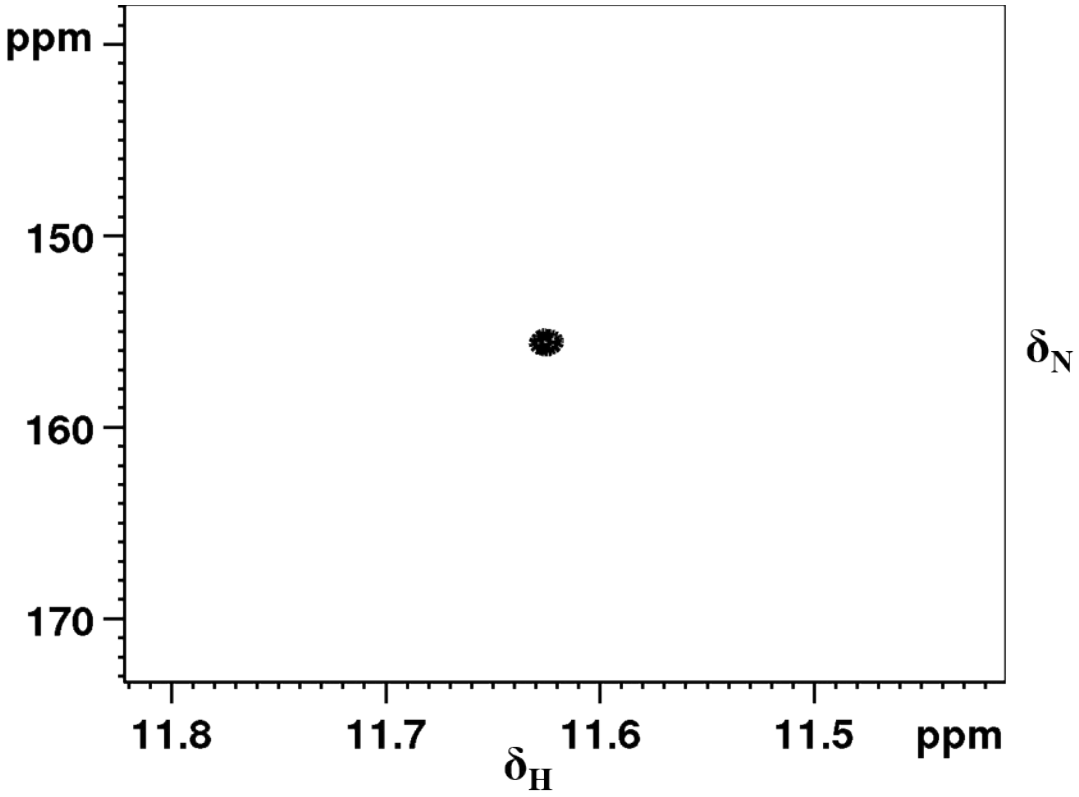
800 MHz proton decoupled 2D ^{15}N-^{1}H HSQC spectrum of molecule **1** in the solvent DMSO-d_6.



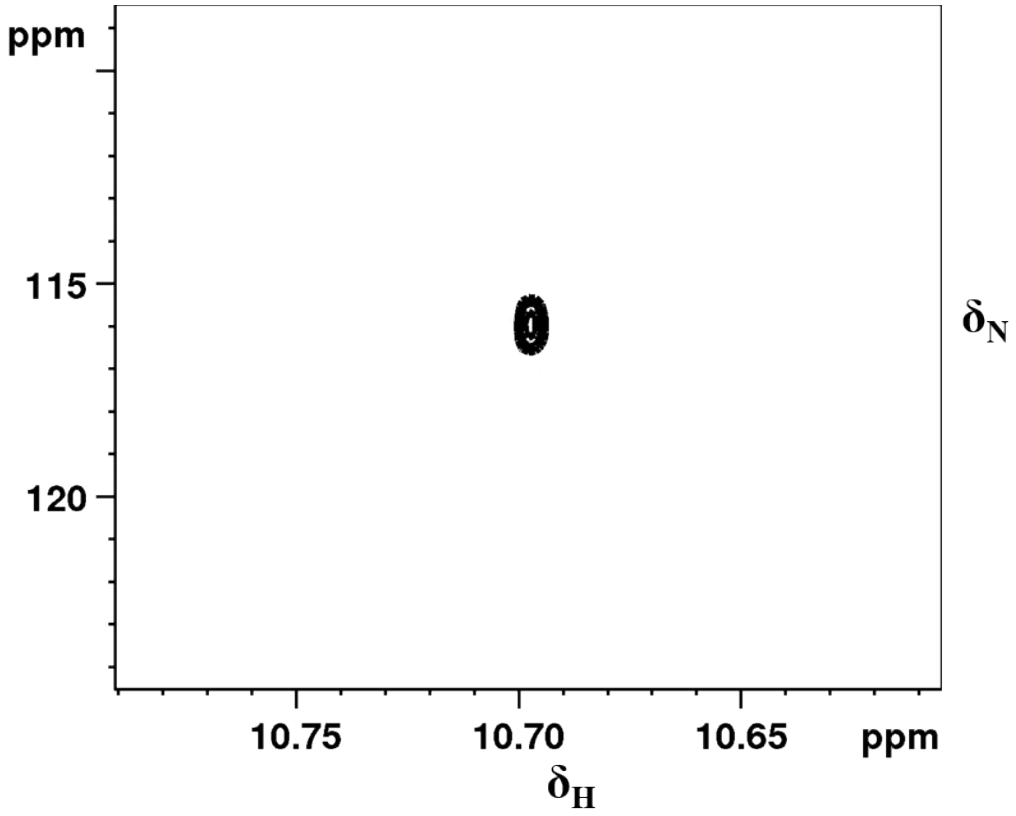
400 MHz 2D ^{15}N-^{1}H coupled HSQC spectrum of molecule **2** in the solvent $CDCl_3$.



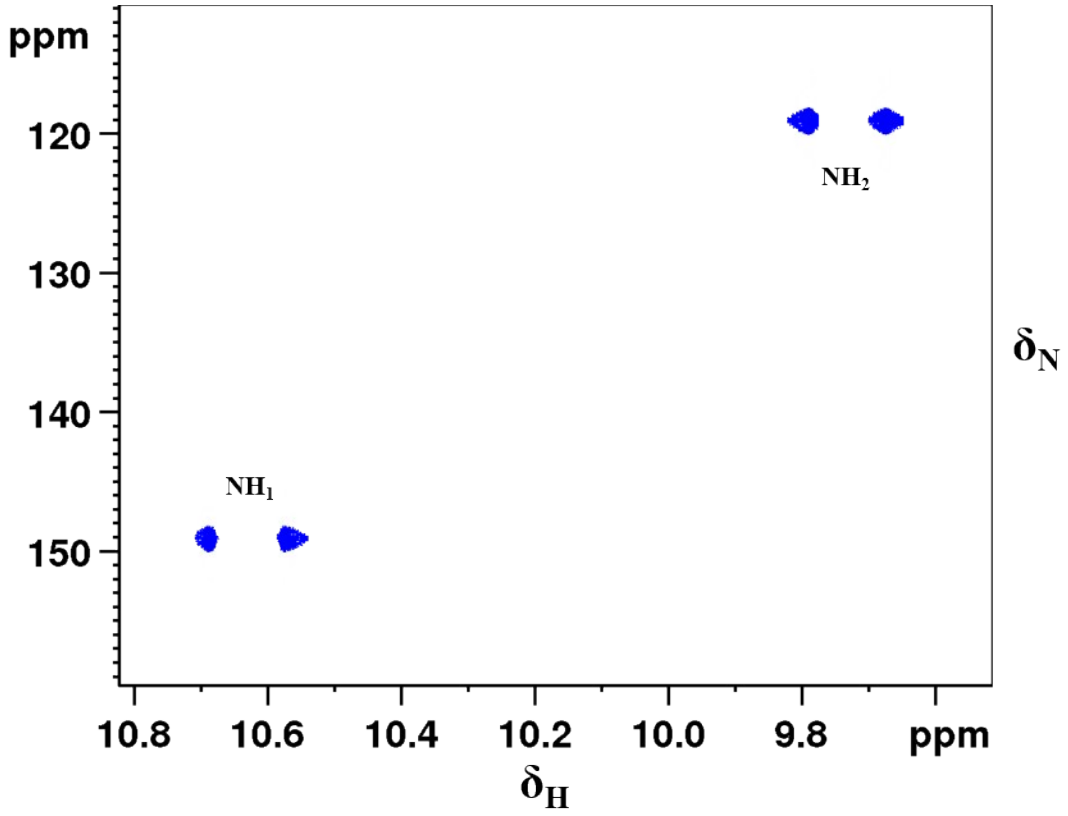
400 MHz proton decoupled 2D ^{15}N-^{1}H HSQC spectrum of molecule **2** in the solvent $CDCl_3$.



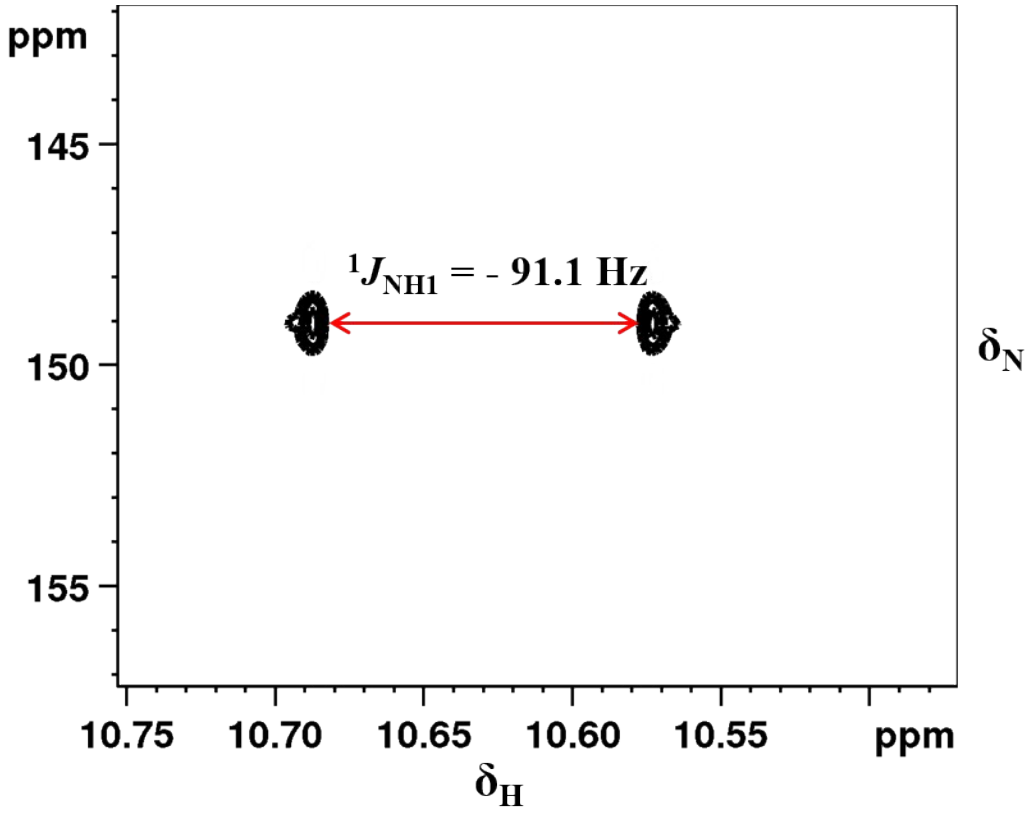
800 MHz proton decoupled 2D ^{15}N-^{1}H HSQC spectrum of molecule **2** in the solvent DMSO-d_6 showing the NH(1) region.



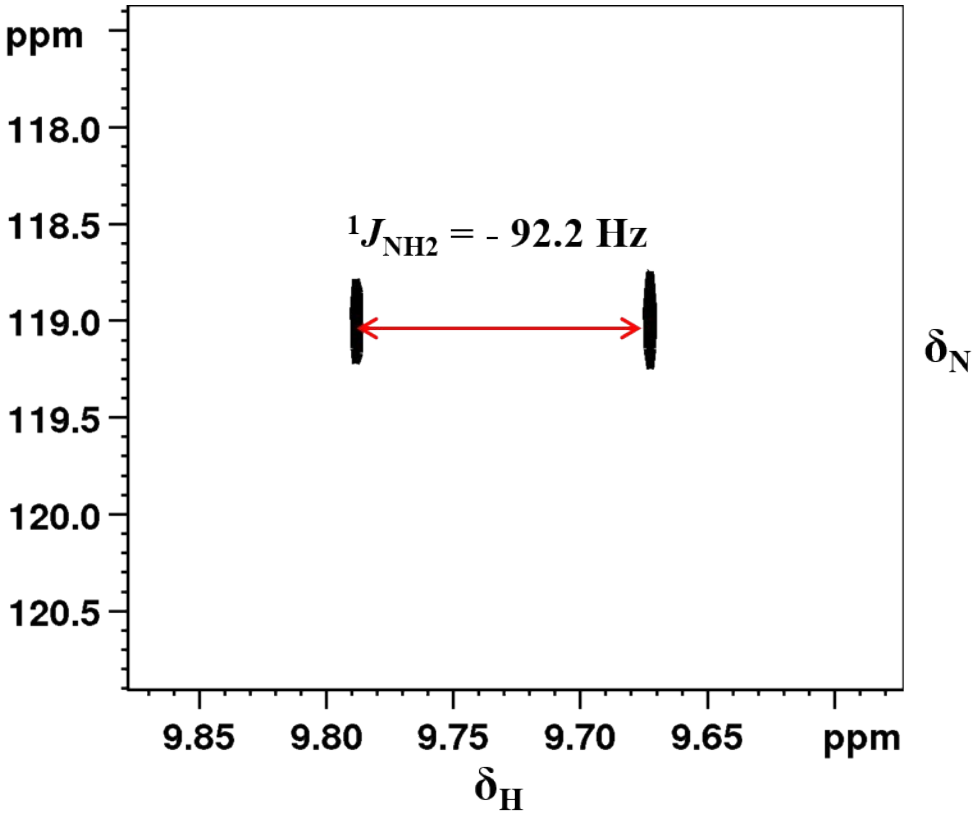
800 MHz proton decoupled 2D ^{15}N-^{1}H HSQC spectrum of molecule **2** in the solvent DMSO-d_6 showing the NH(2) region.



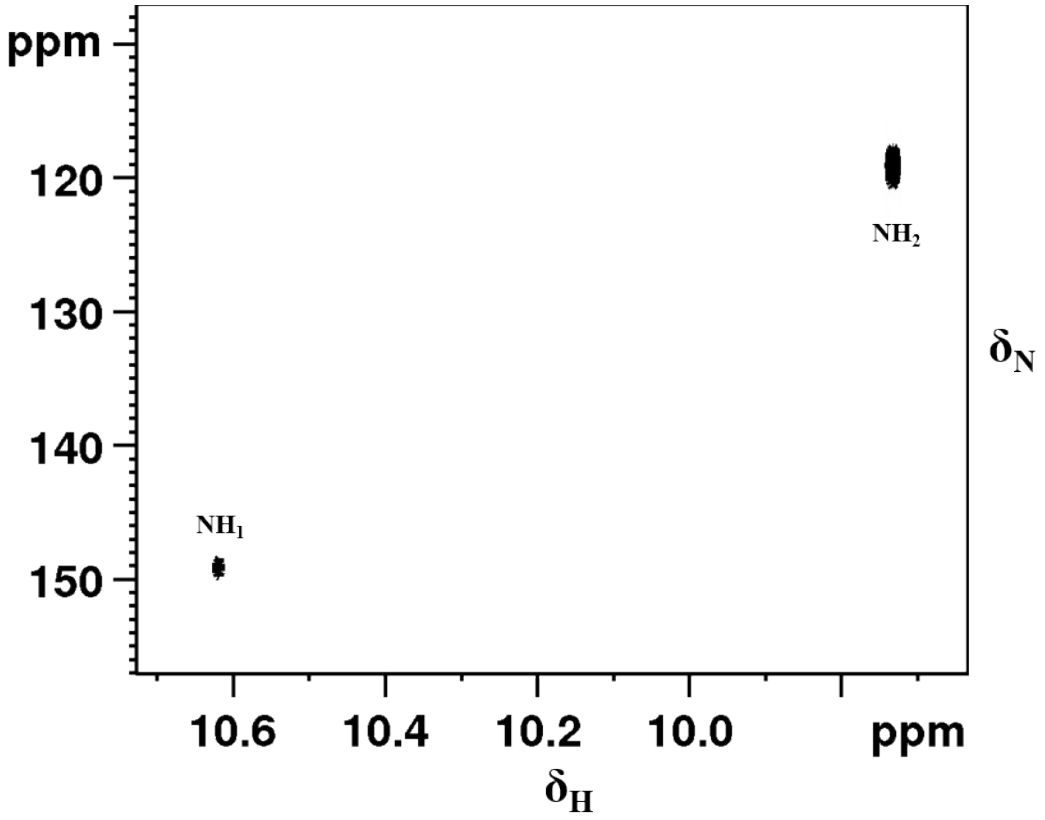
800 MHz 2D ^{15}N-^{1}H coupled HSQC spectrum of molecule **3** in the solvent $CDCl_3$.



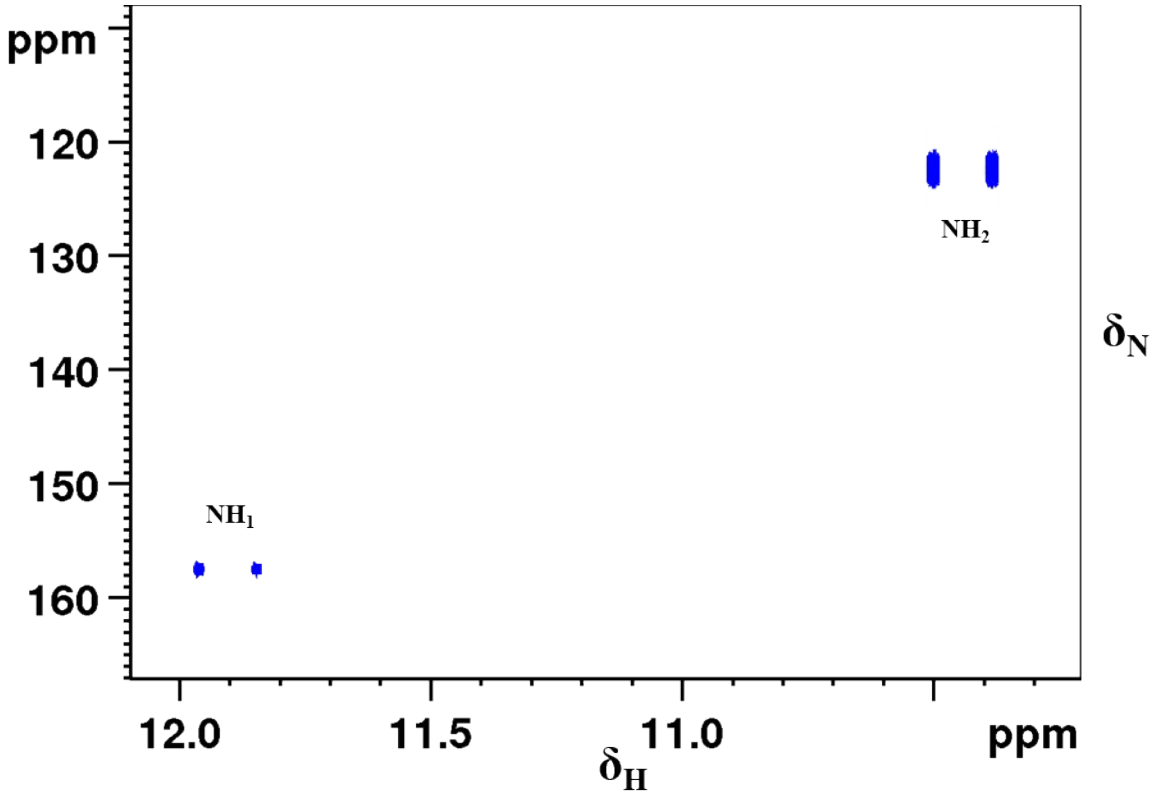
Expanded region of 2D ^{15}N-^{1}H coupled HSQC spectrum of molecule **3 (Fig. S15)** pertaining to NH(1) region showing scalar coupling $^1J_{NH}$.



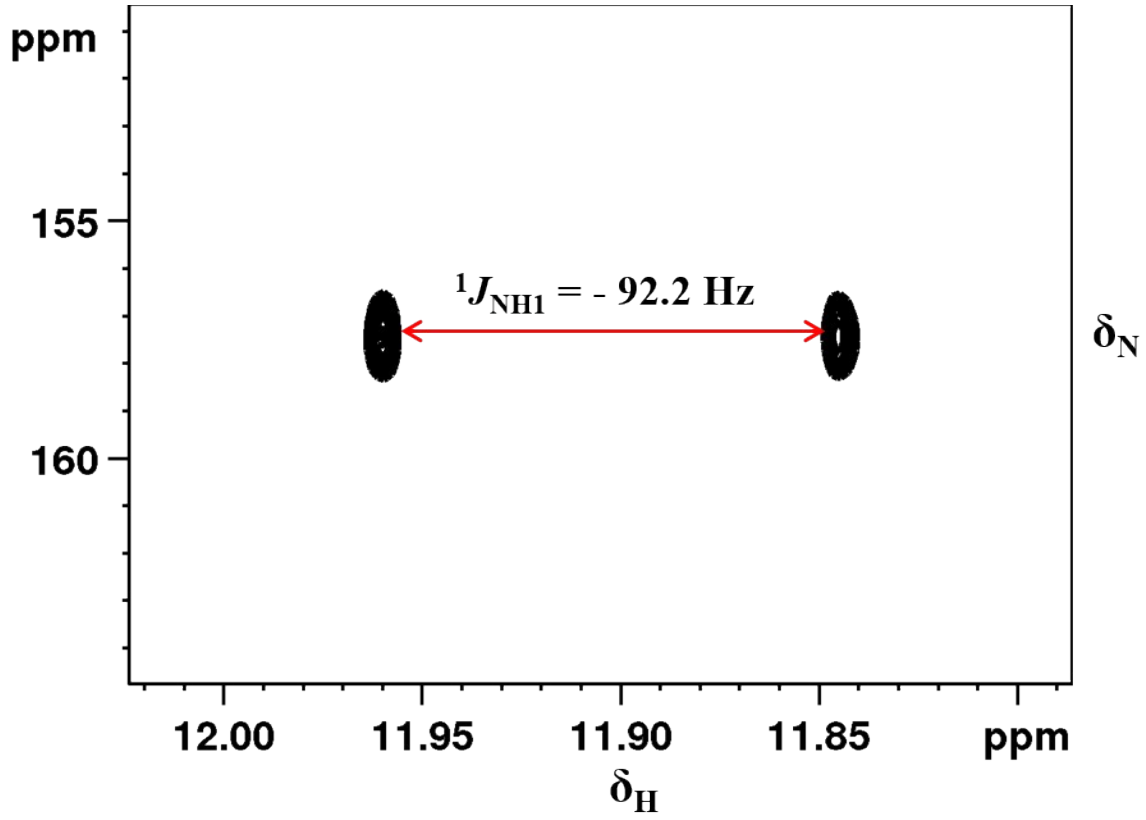
Expanded region of 2D ^{15}N-^{1}H coupled HSQC spectrum of molecule **3 (Fig. S15)** pertaining to NH(2) region showing scalar coupling $^1J_{NH}$.



800 MHz proton decoupled 2D ^{15}N-^{1}H HSQC spectrum of molecule **3** in the solvent $CDCl_3$.

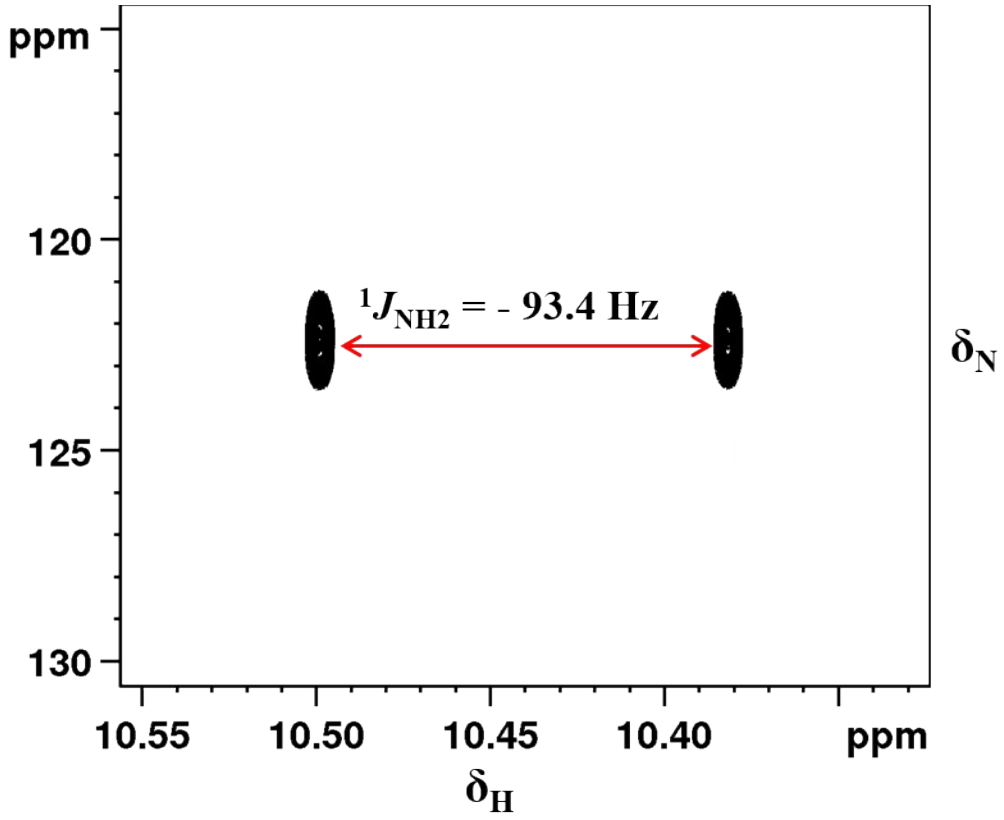


800 MHz 2D ^{15}N-^{1}H coupled HSQC spectrum of molecule **3** in the solvent DMSO-d_6.

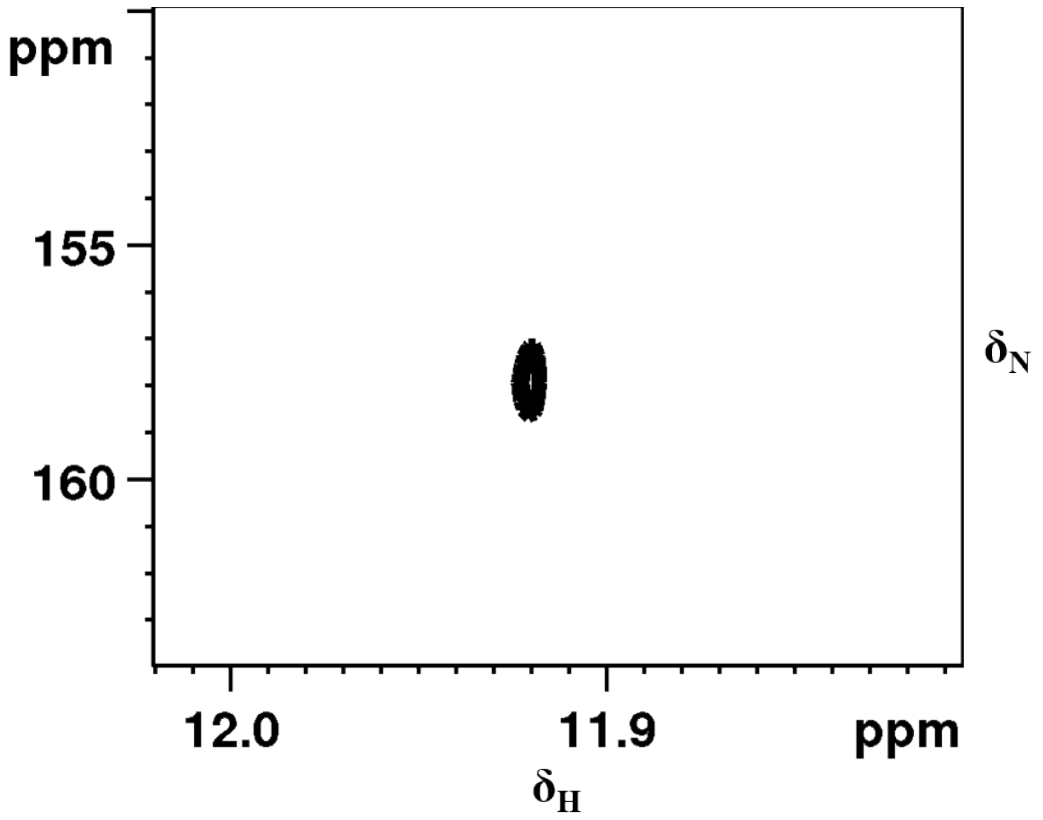


Expanded region pertaining to NH(1) of 2D ^{15}N-^{1}H HSQC spectrum of molecule **3 (Fig. S19)** showing scalar coupling $^1J_{NH}$.

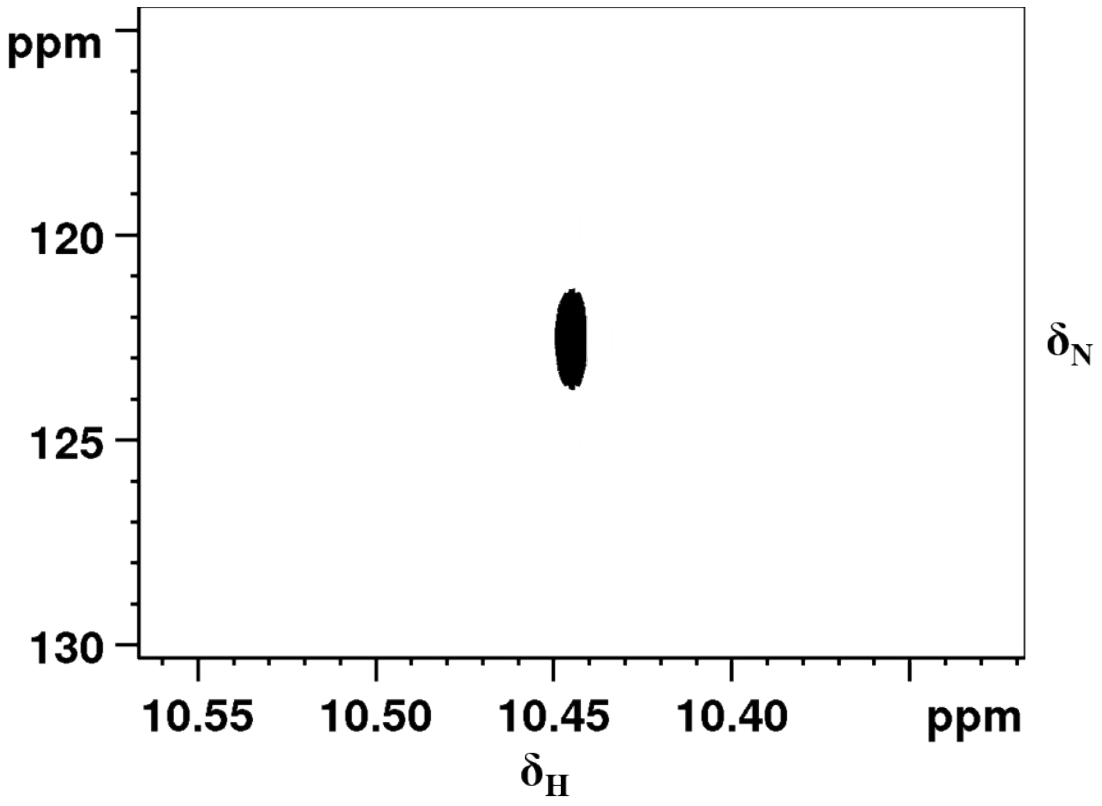
S20



Expanded region pertaining to NH(2) of 2D ^{15}N-^{1}H HSQC spectrum of molecule **3 (Fig. S19)** showing scalar coupling $^1J_{NH}$.

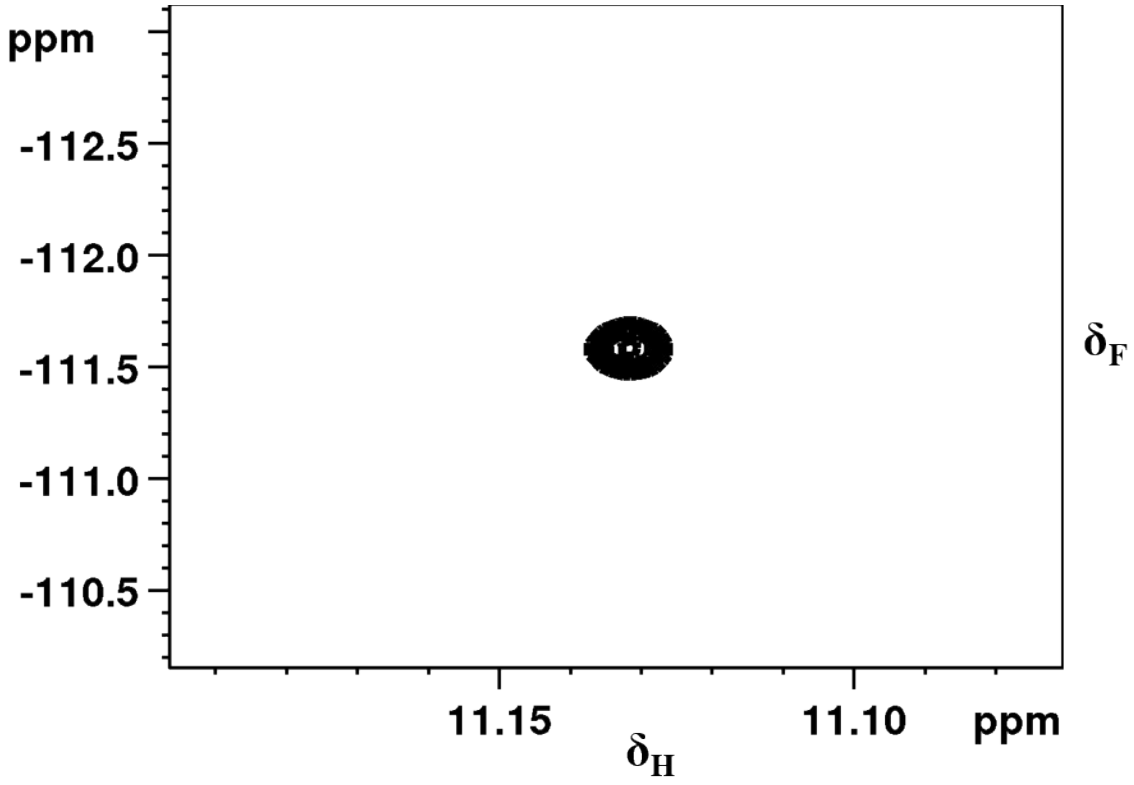


800 MHz proton decoupled 2D ^{15}N-^{1}H HSQC spectrum of molecule **3** in the solvent DMSO-d_6 showing region pertaining to NH(1).



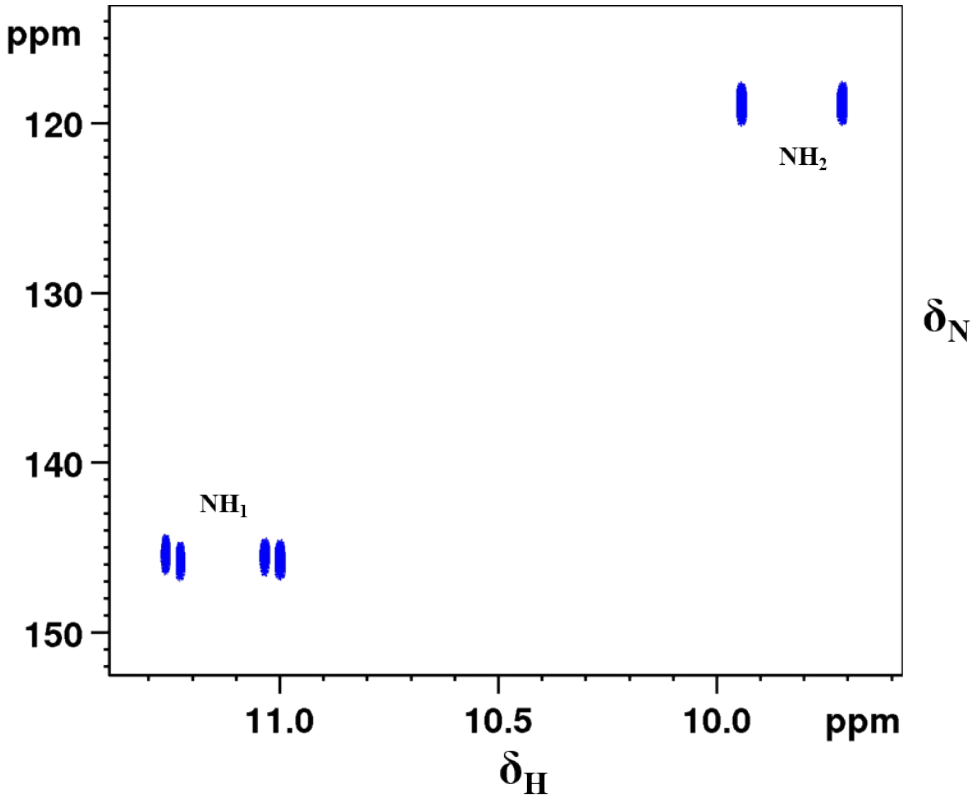
800 MHz proton decoupled 2D ^{15}N-^{1}H HSQC spectrum of molecule **3** in the solvent DMSO-d_6 showing region pertaining to NH(2).

S23

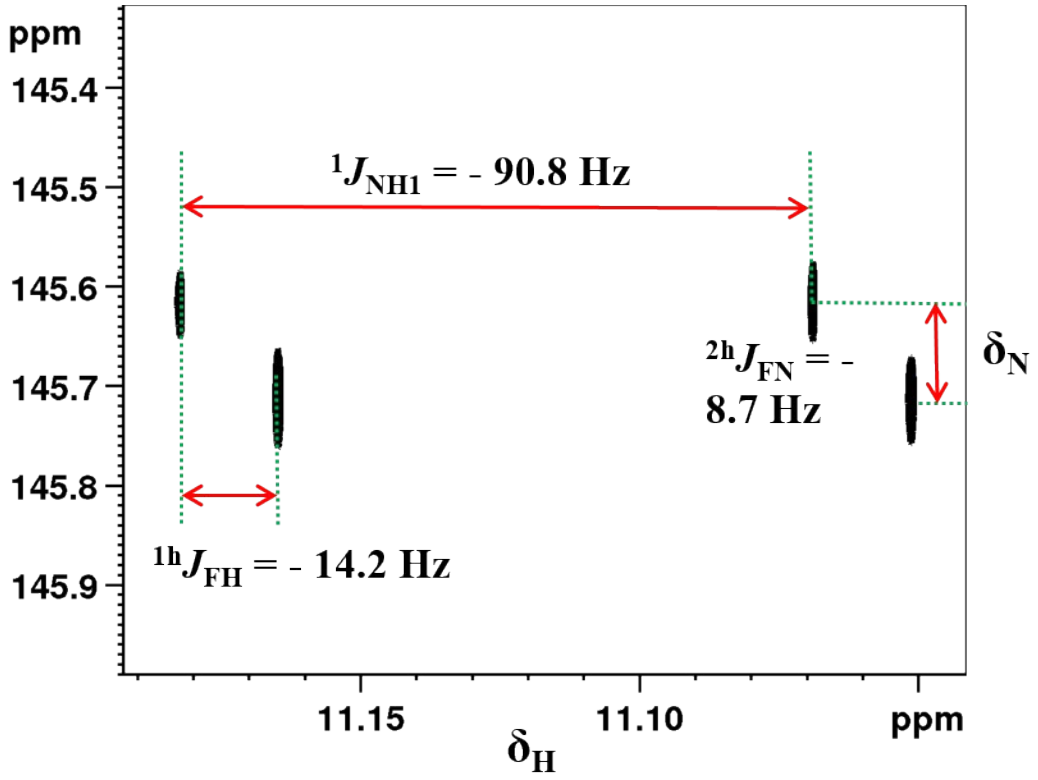


400 MHz 2D ^{19}F-^{1}H HOESY spectrum of molecule **4** in the solvent $CDCl_3$ showing strong correlation between F and NH proton.

S24

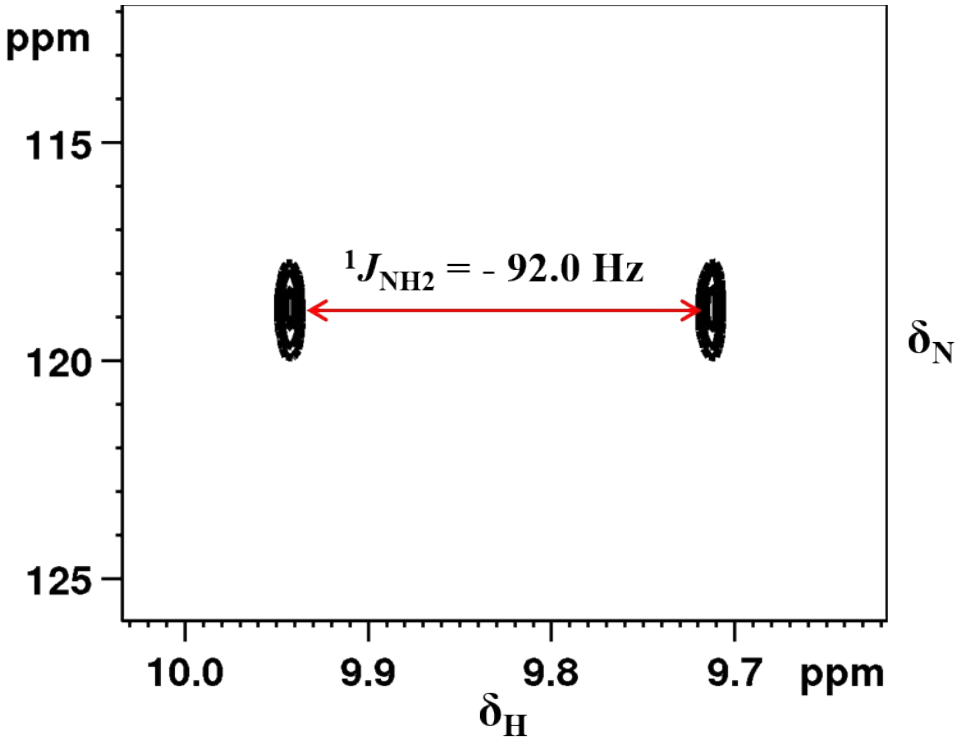


400 MHz 2D ^{15}N-^{1}H coupled HSQC spectrum of molecule **4** in the solvent $CDCl_3$.

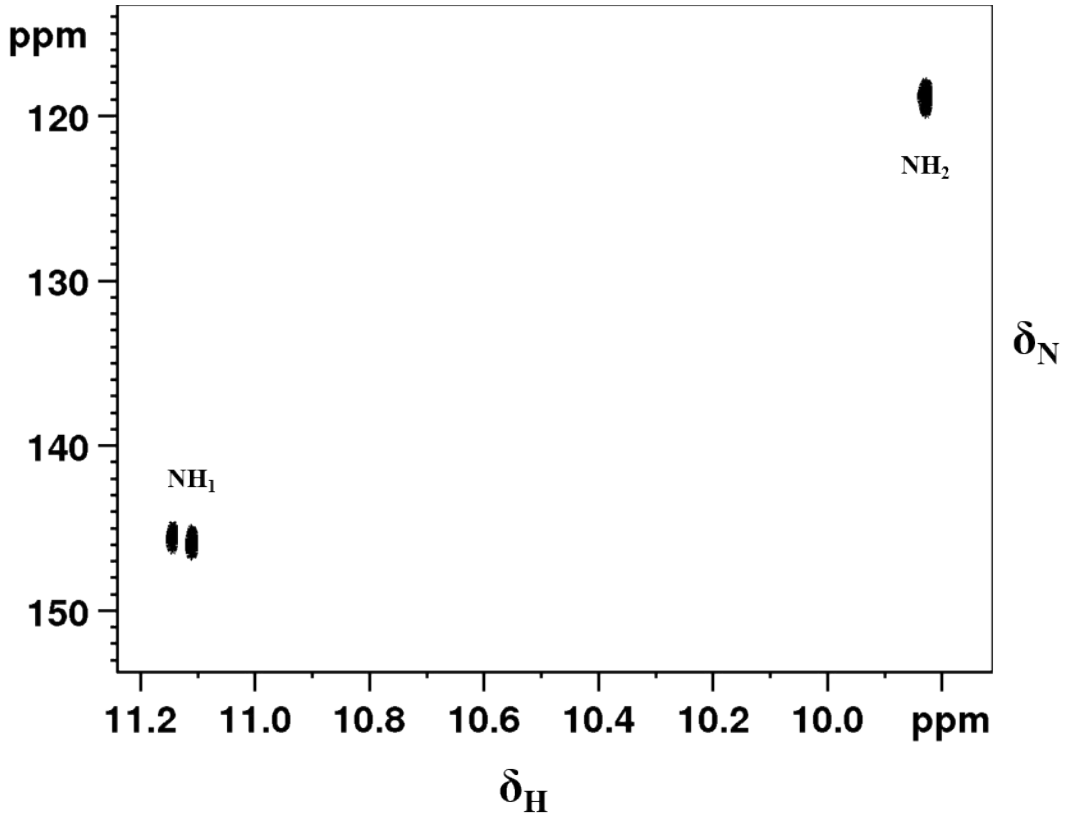


Expanded region of **(Fig. S25)** pertaining to NH(1) showing scalar couplings $^{1}J_{NH,}$ $^{1h}J_{FH}$ and $^{2h}J_{NF.}$

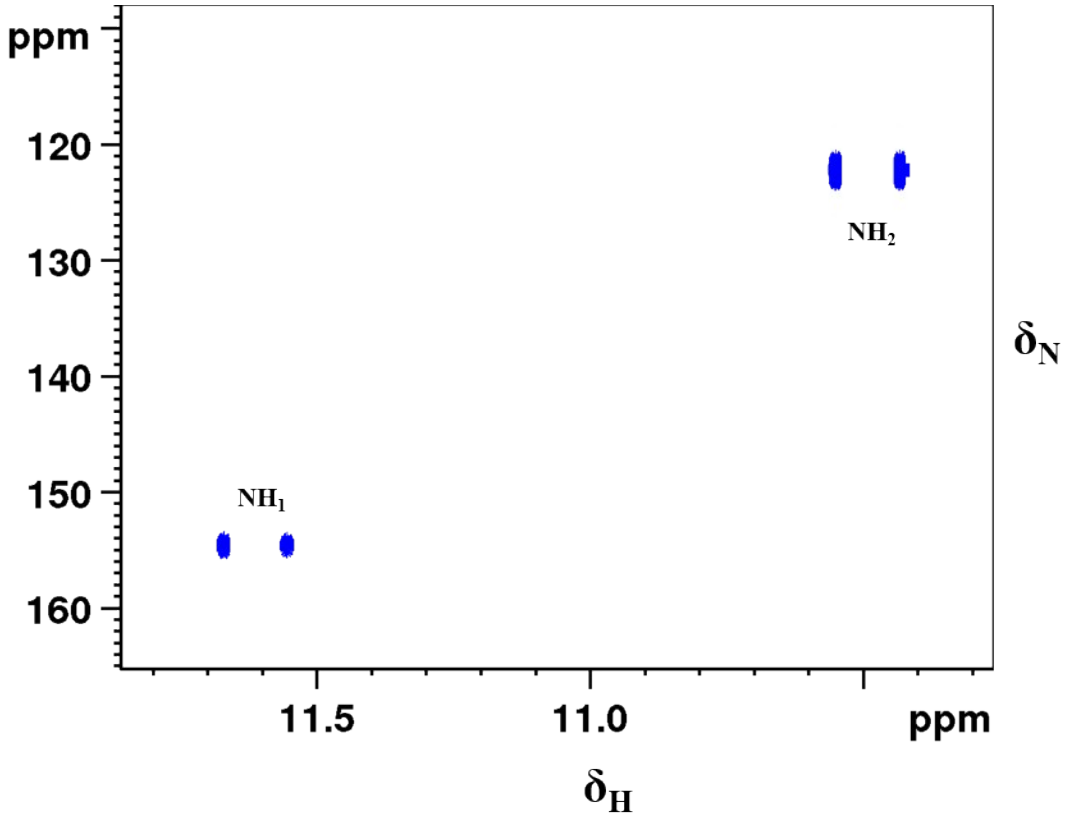
S26



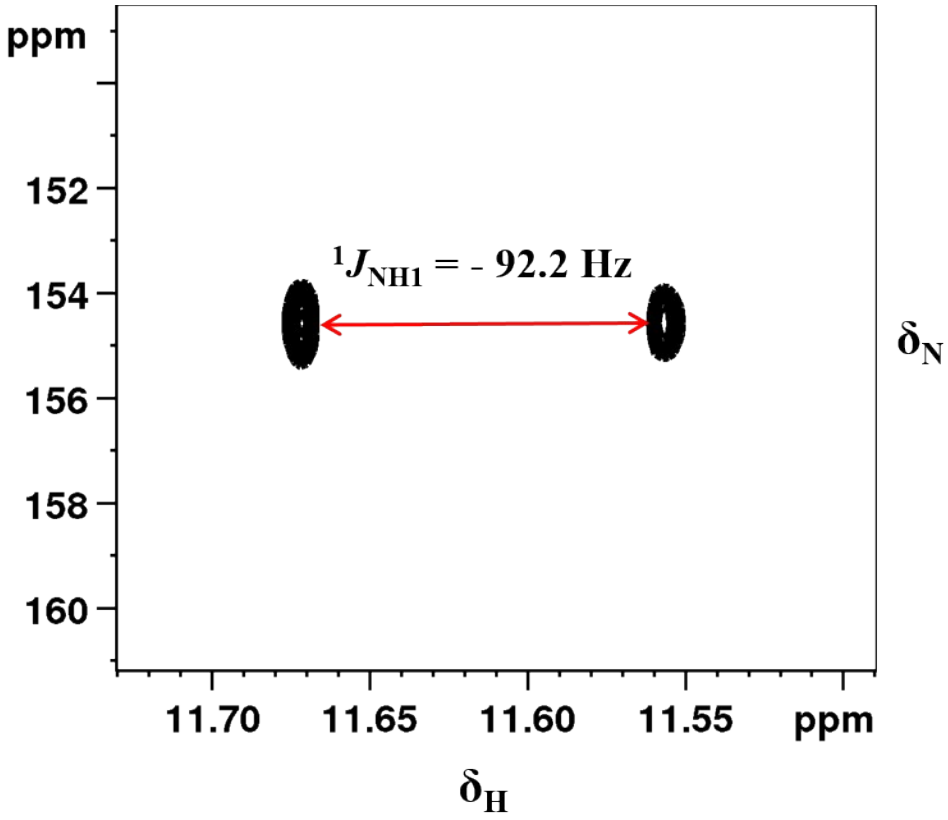
Expanded region of **(Fig. S25)** pertaining to NH(2) showing scalar coupling $^1J_{NH.}$



400 MHz proton decoupled 2D ^{15}N-^{1}H HSQC spectrum of molecule **4** in the solvent $CDCl_3$.

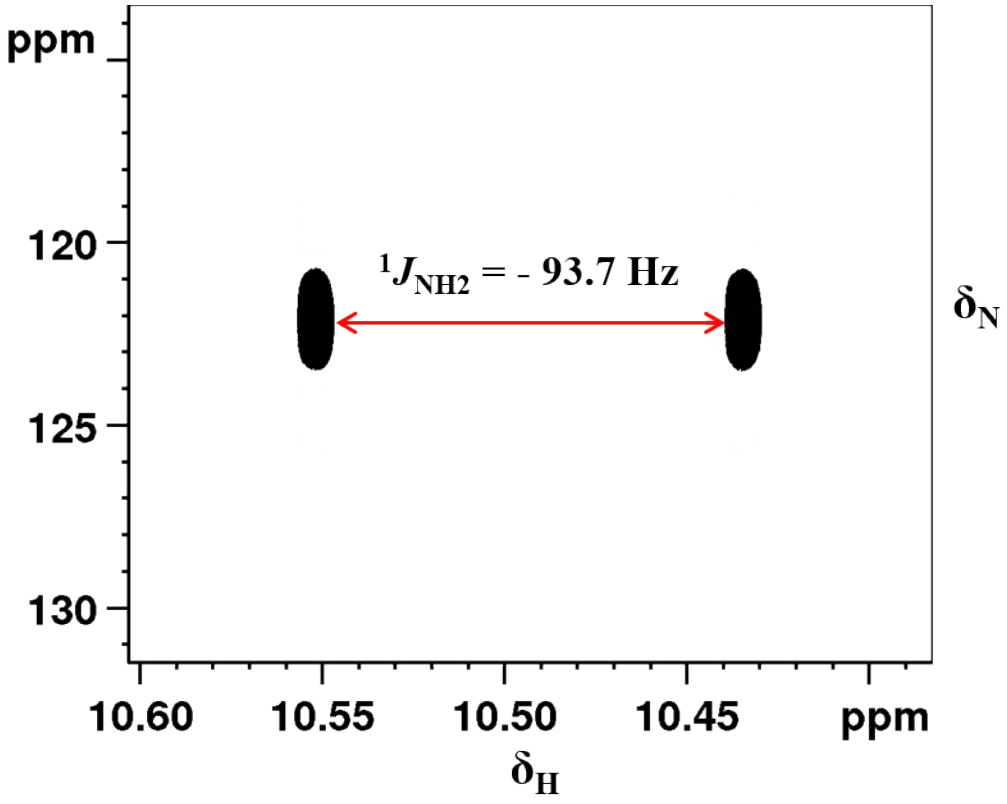


800 MHz 2D ^{15}N-^{1}H coupled HSQC spectrum of molecule **4** in the solvent DMSO-d_6.

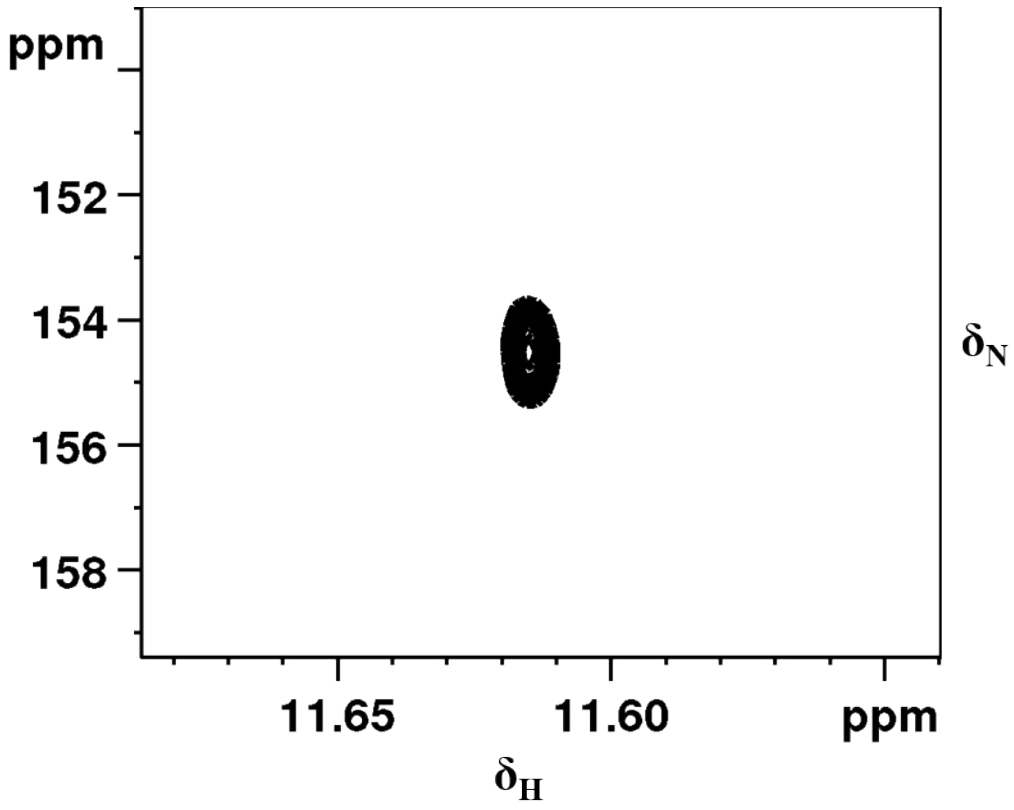


Expansion of **(Fig.S29)** pertaining to NH(1) region showing scalar coupling $^1J_{NH.}$

S30

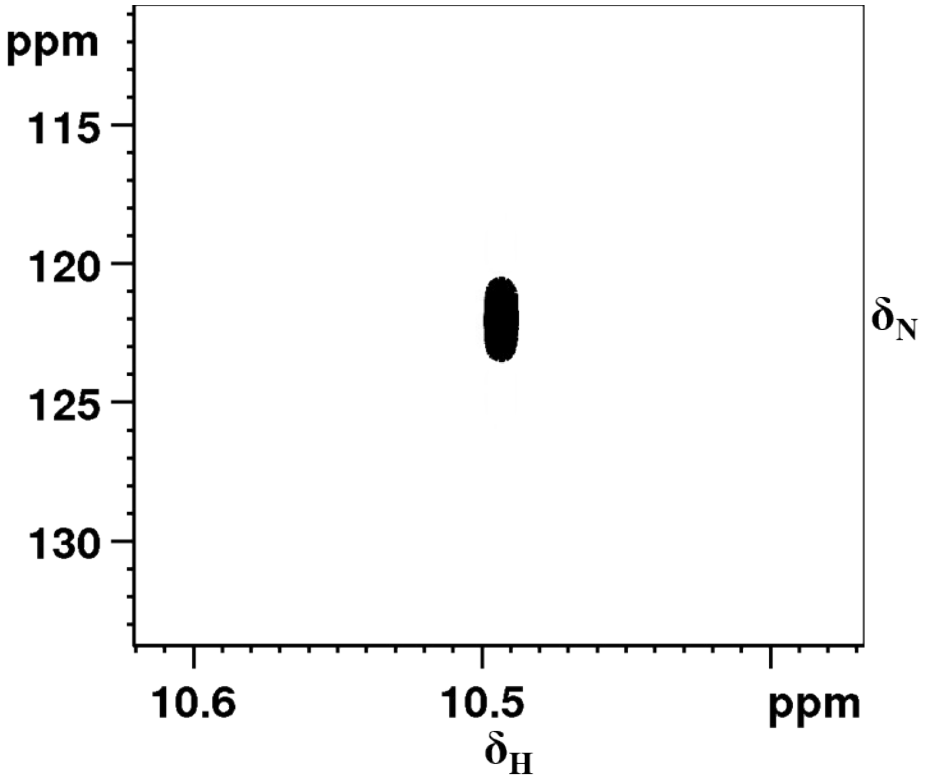


Expansion of **(Fig.S29)** pertaining to NH(2) region showing scalar coupling $^1J_{NH.}$

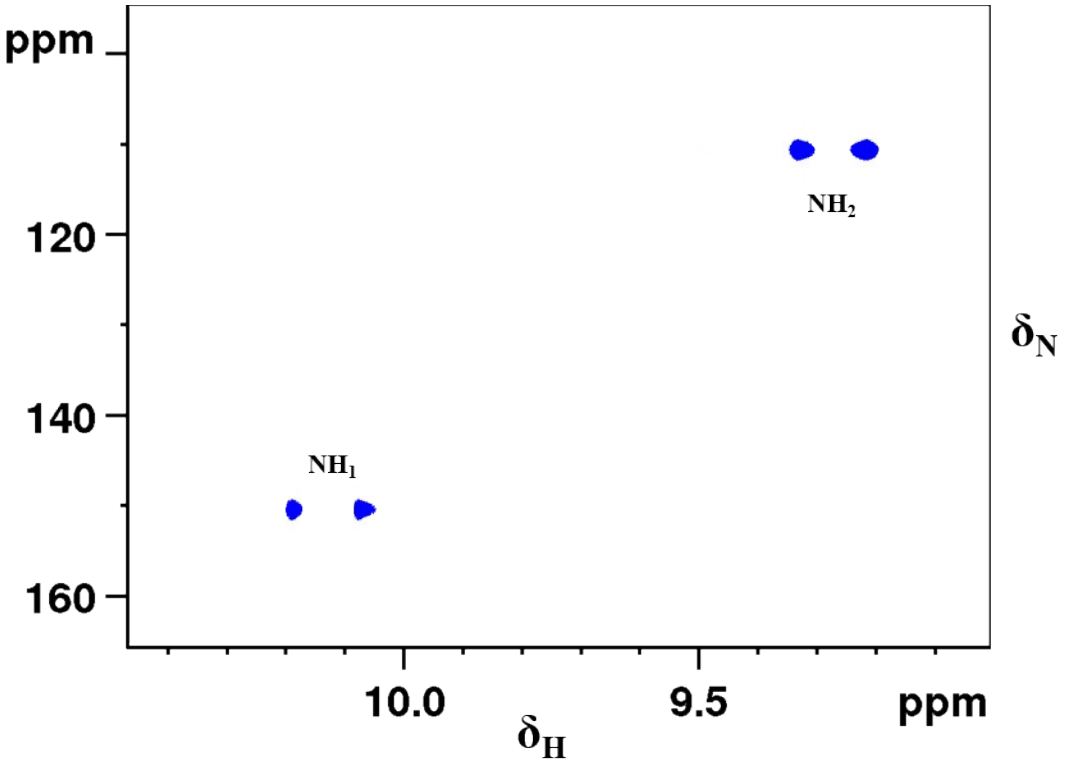


800 MHz proton decoupled 2D ^{15}N-^{1}H HSQC spectrum of molecule **4** in the solvent DMSO-d_6 showing the region pertaining to NH(1).

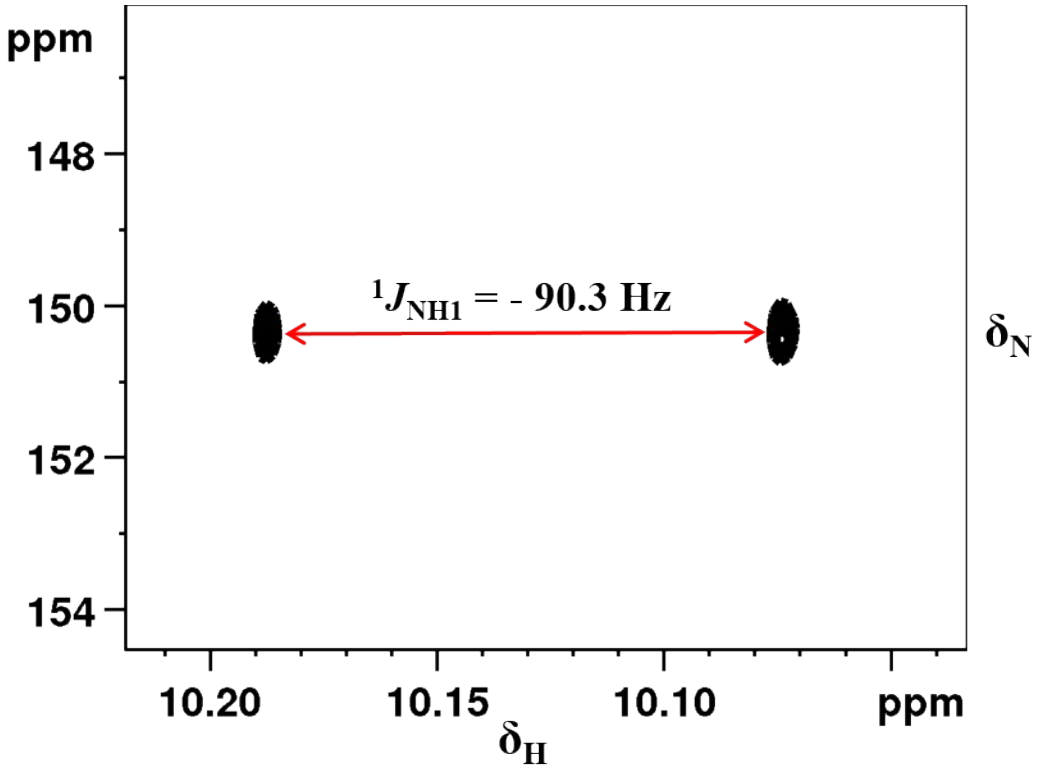
S32



800 MHz proton decoupled 2D ^{15}N-^{1}H HSQC spectrum of molecule **4** in the solvent DMSO-d_6 showing the region pertaining to NH(2).

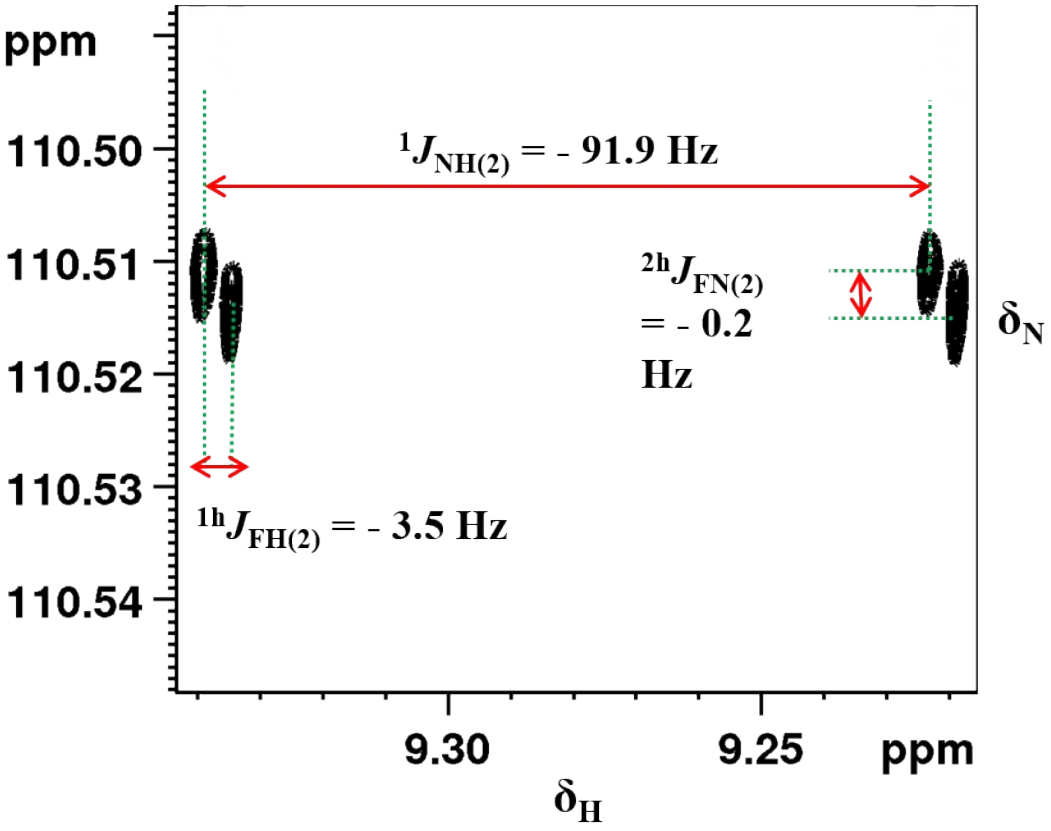


800 MHz 2D ^{15}N-^{1}H coupled HSQC spectrum of molecule **5** in the solvent $CDCl_3$.

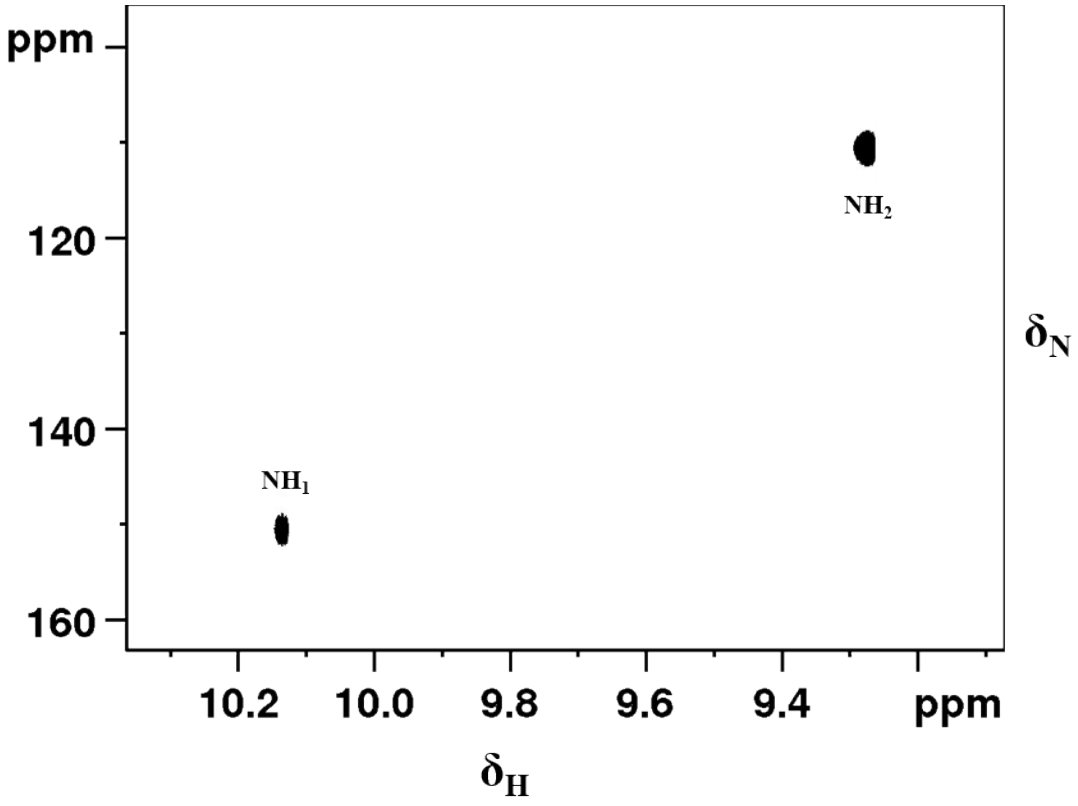


Expansion of **(Fig. S34)** pertaining to NH(1) region showing the scalar coupling $^1J_{NH.}$

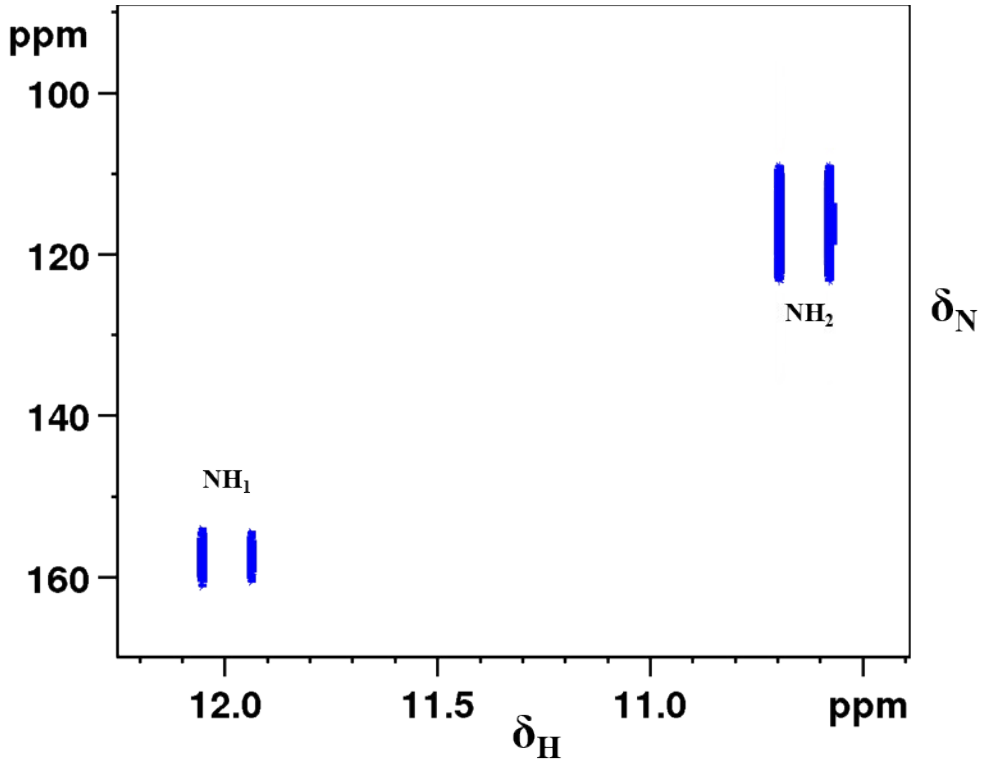
S35



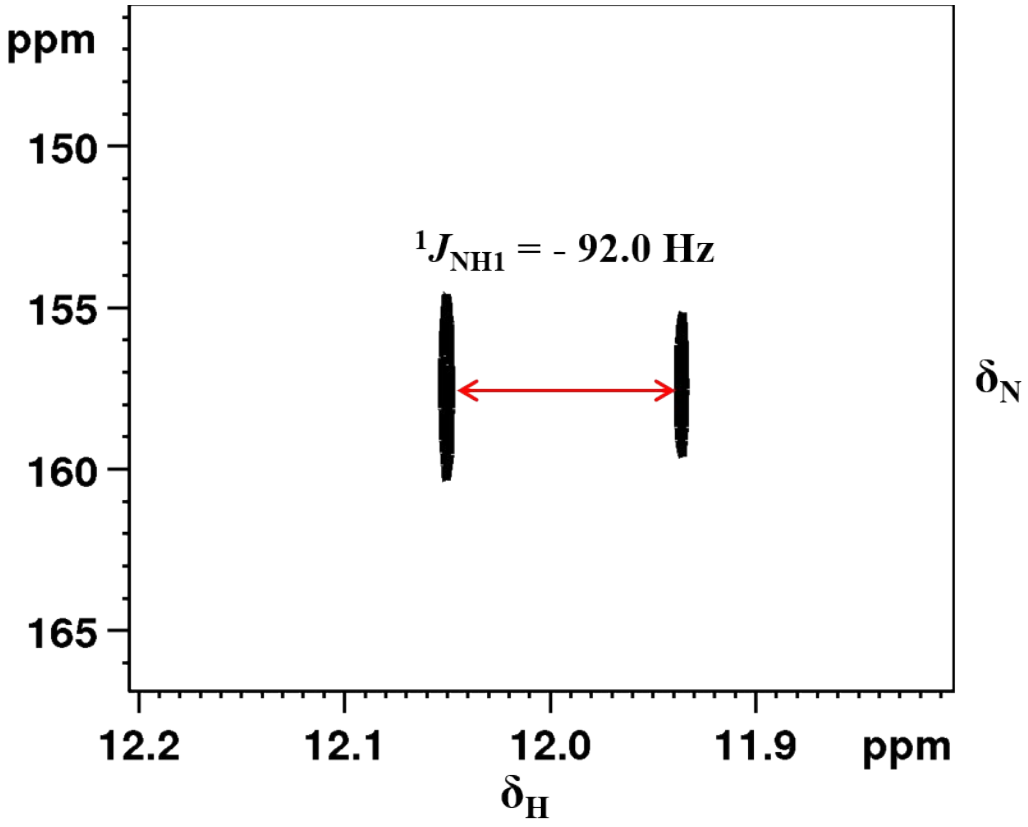
Expansion of **(Fig. S34)** pertaining to NH(2) region showing all the scalar couplings.



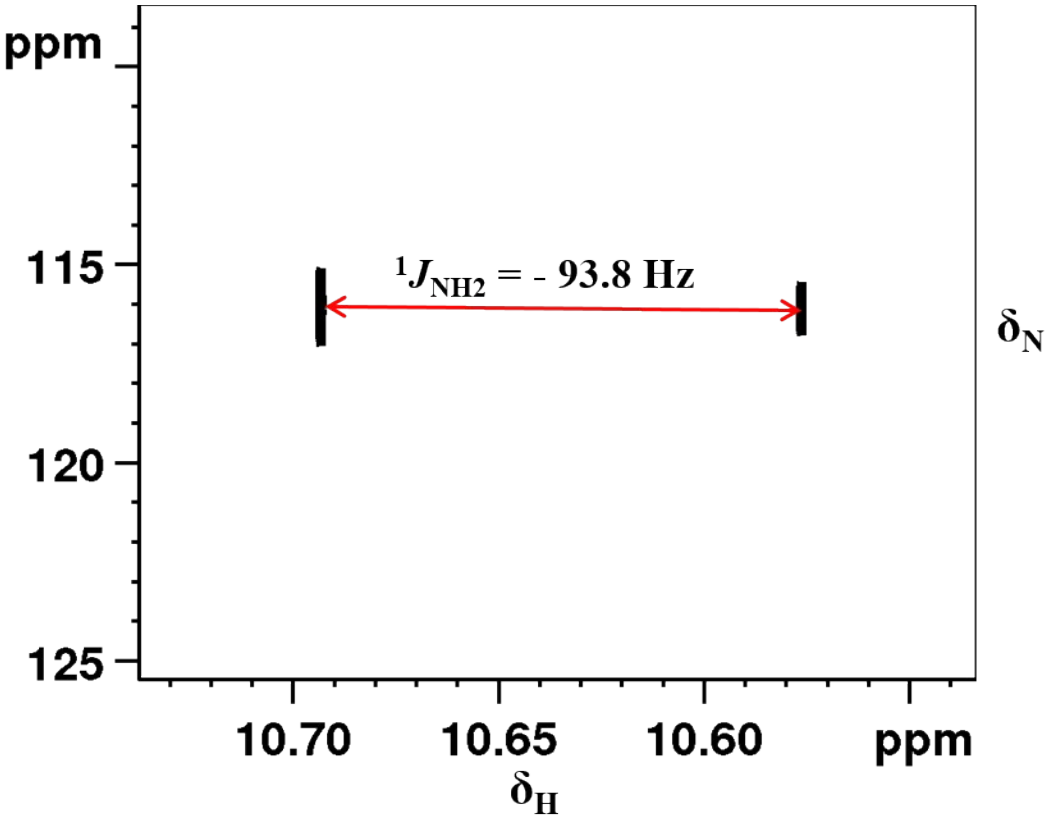
800 MHz proton decoupled 2D ^{15}N-^{1}H HSQC spectrum of molecule **5** in the solvent $CDCl_3$.



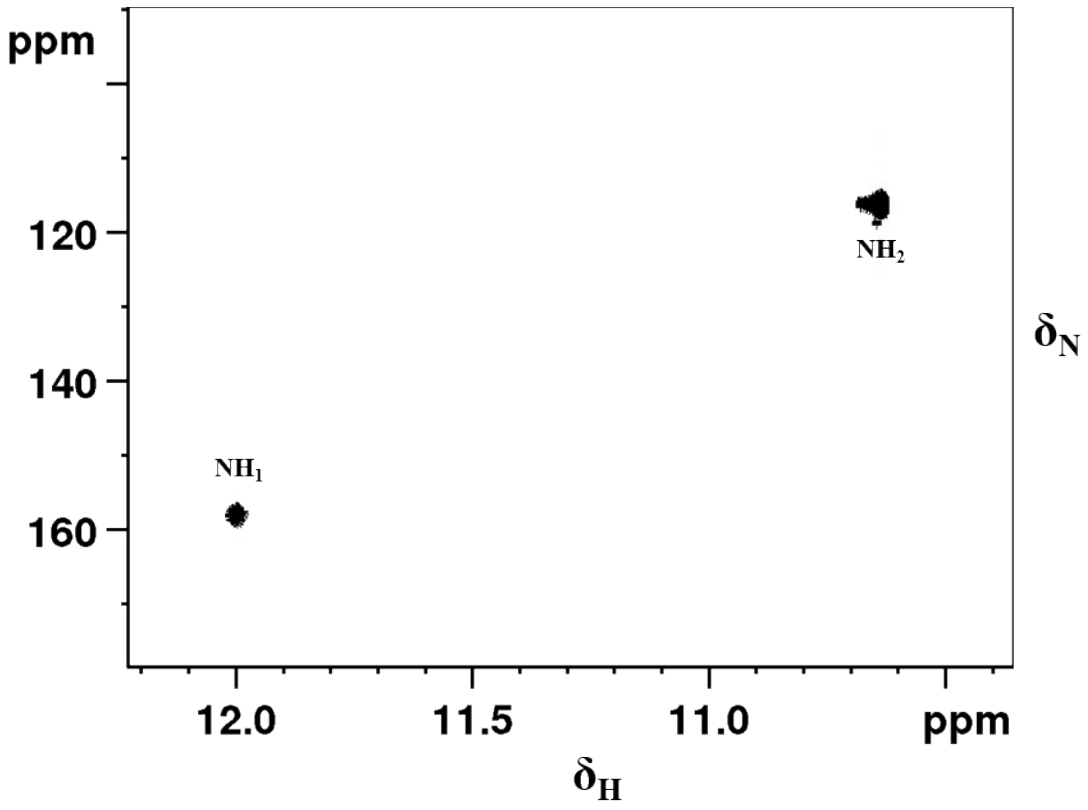
800 MHz 2D ^{15}N-^{1}H coupled HSQC spectrum of molecule **5** in the solvent DMSO-d_6.



800 MHz 2D ^{15}N-^{1}H coupled HSQC spectrum of molecule **5** in the solvent DMSO-d_6 pertaining to NH(1) region showing scalar coupling $^1J_{NH.}$

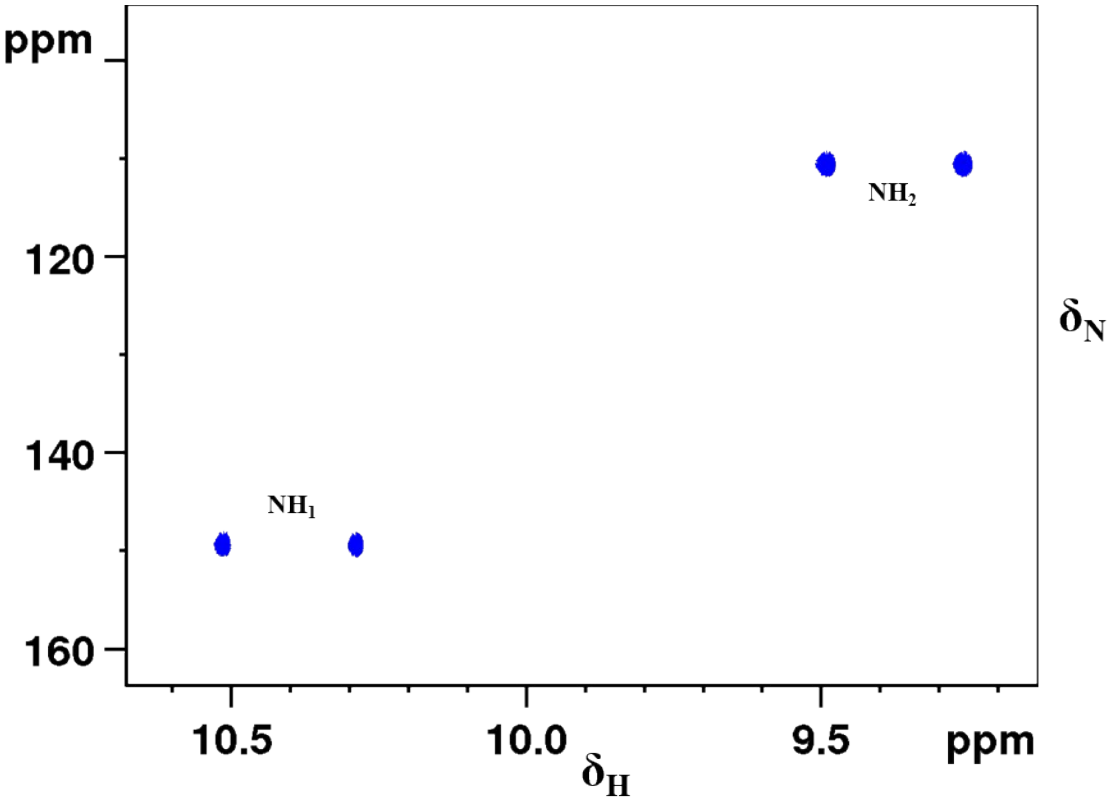


800 MHz 2D ^{15}N-^{1}H coupled HSQC spectrum of molecule **5** in the solvent DMSO-d_6 pertaining to NH(2) region showing scalar coupling $^1J_{NH.}$

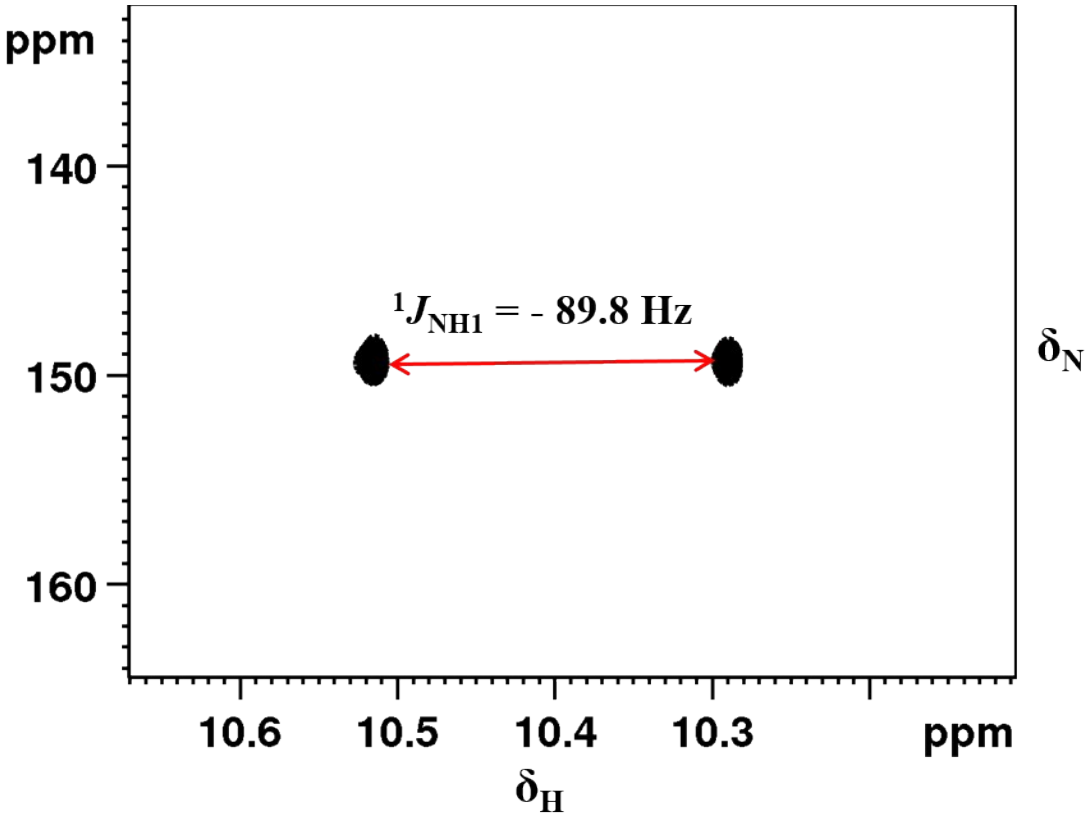


800 MHz proton decoupled 2D ^{15}N-^{1}H HSQC spectrum of molecule **5** in the solvent DMSO-d_6.

S41

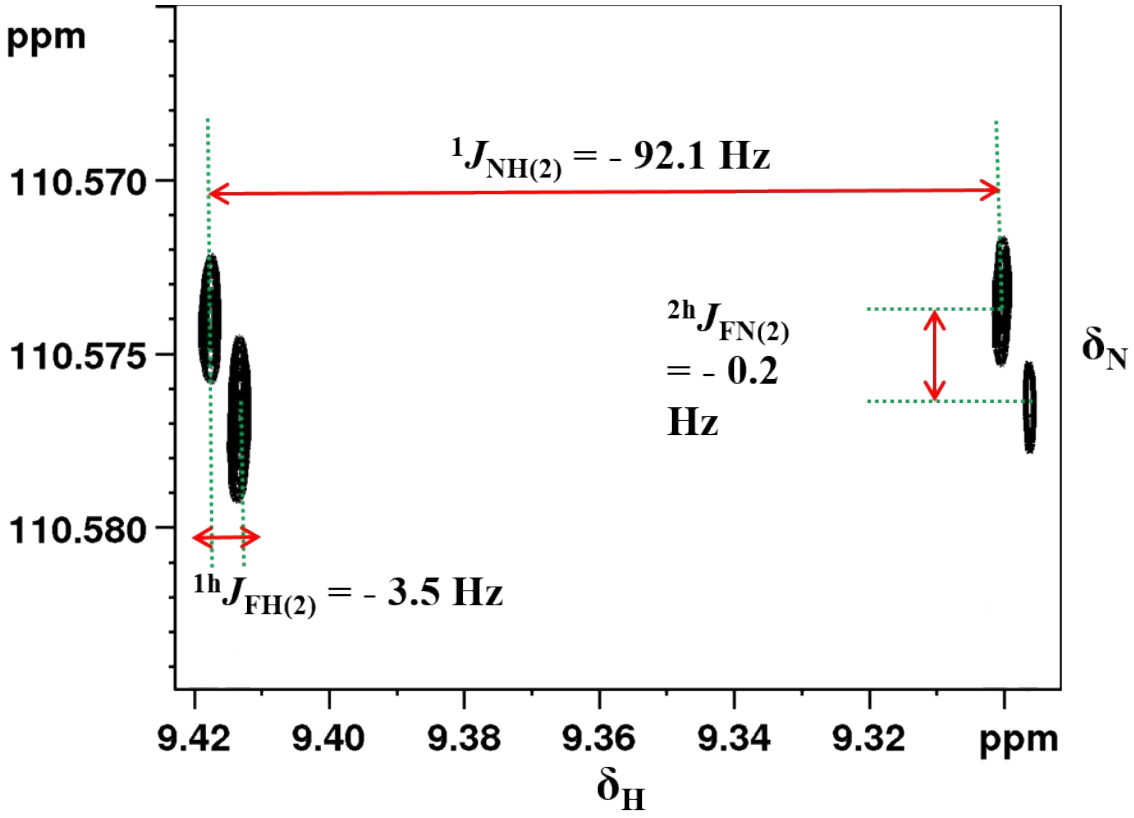


400 MHz 2D ^{15}N-^{1}H coupled HSQC spectrum of molecule **6** in the solvent $CDCl_3$.

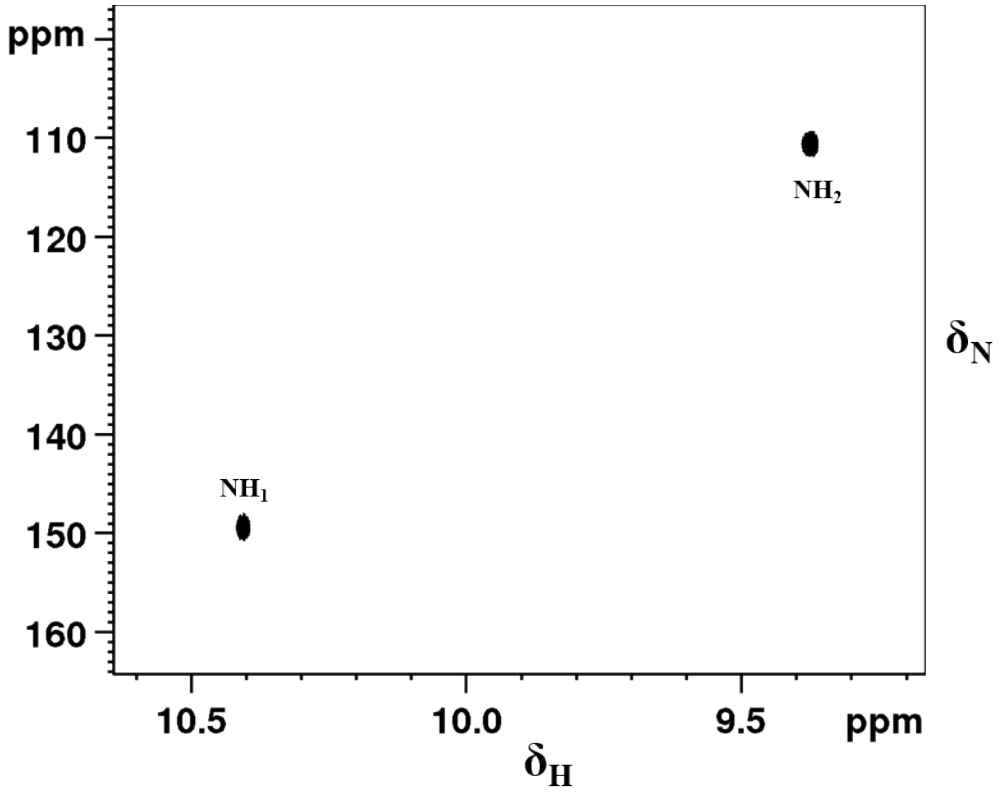


Expansion of **(Fig. S42)** pertaining to NH(1) region showing scalar coupling $^1J_{NH}$

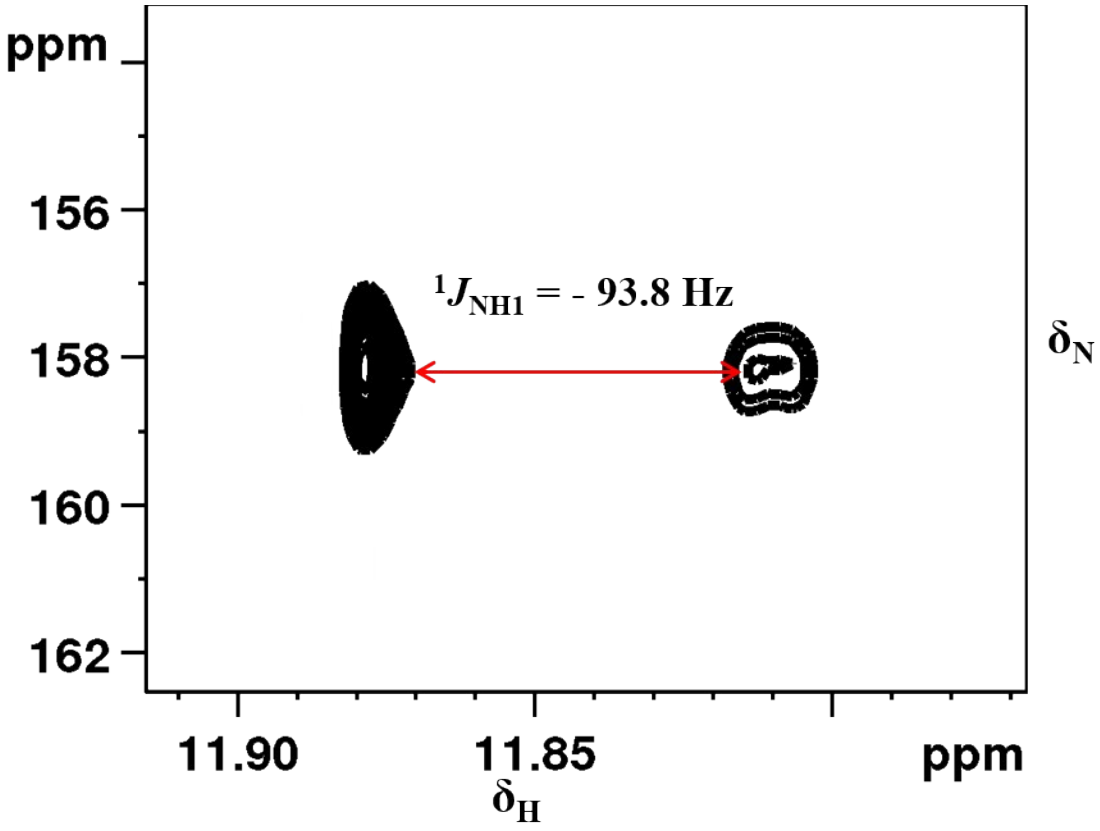
S43



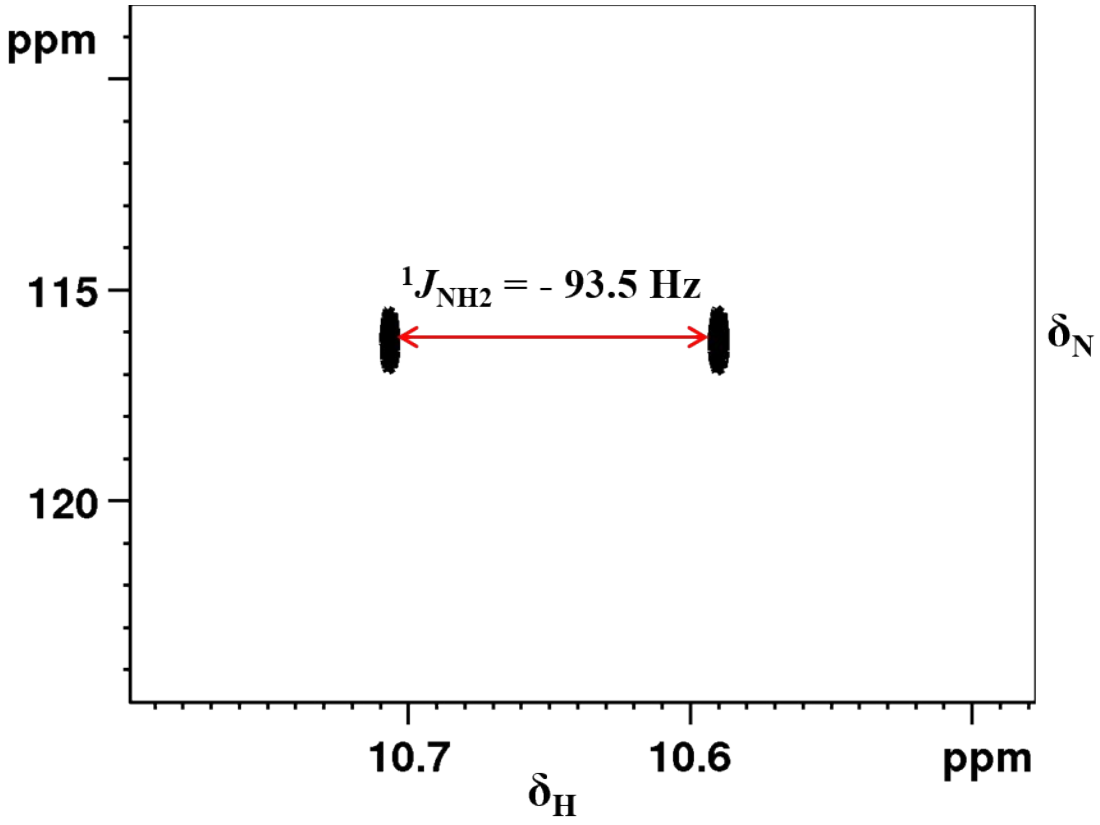
Expansion of **(Fig. S42)** pertaining to NH(2) region showing all the scalar couplings.



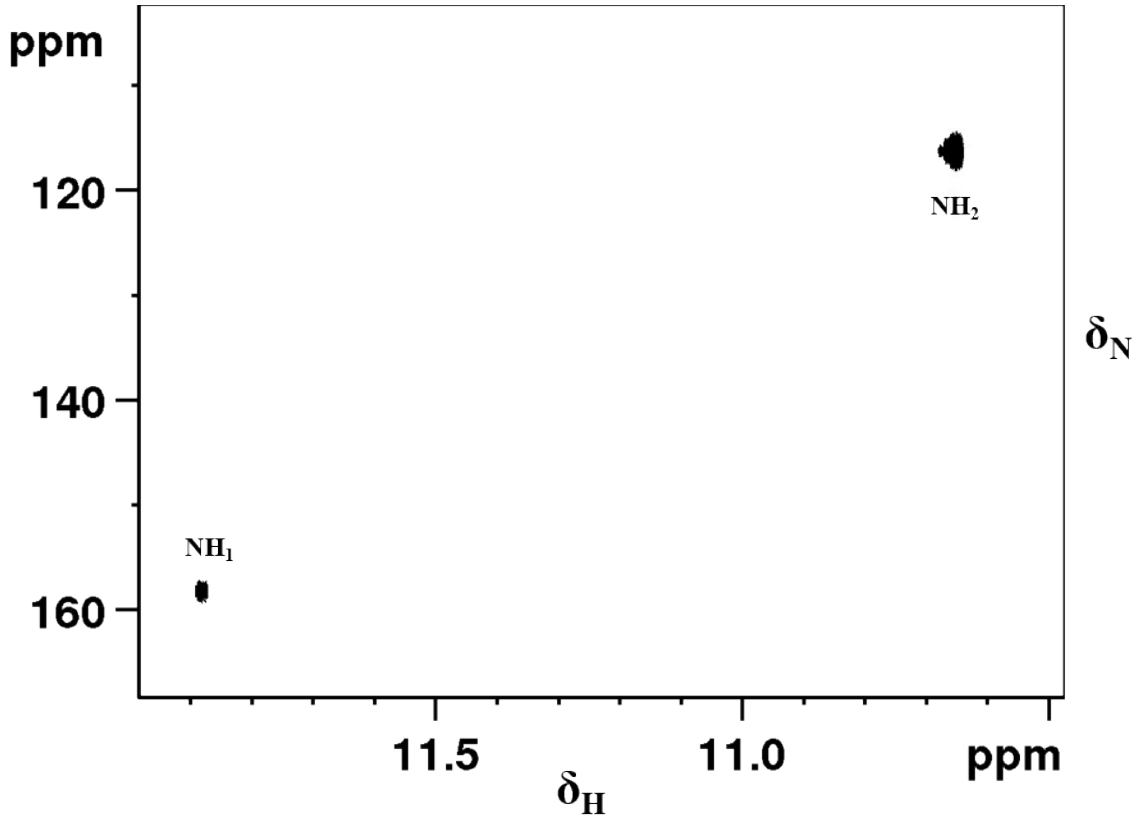
400 MHz proton decoupled 2D ^{15}N-^{1}H HSQC spectrum of molecule **6** in the solvent $CDCl_3$.



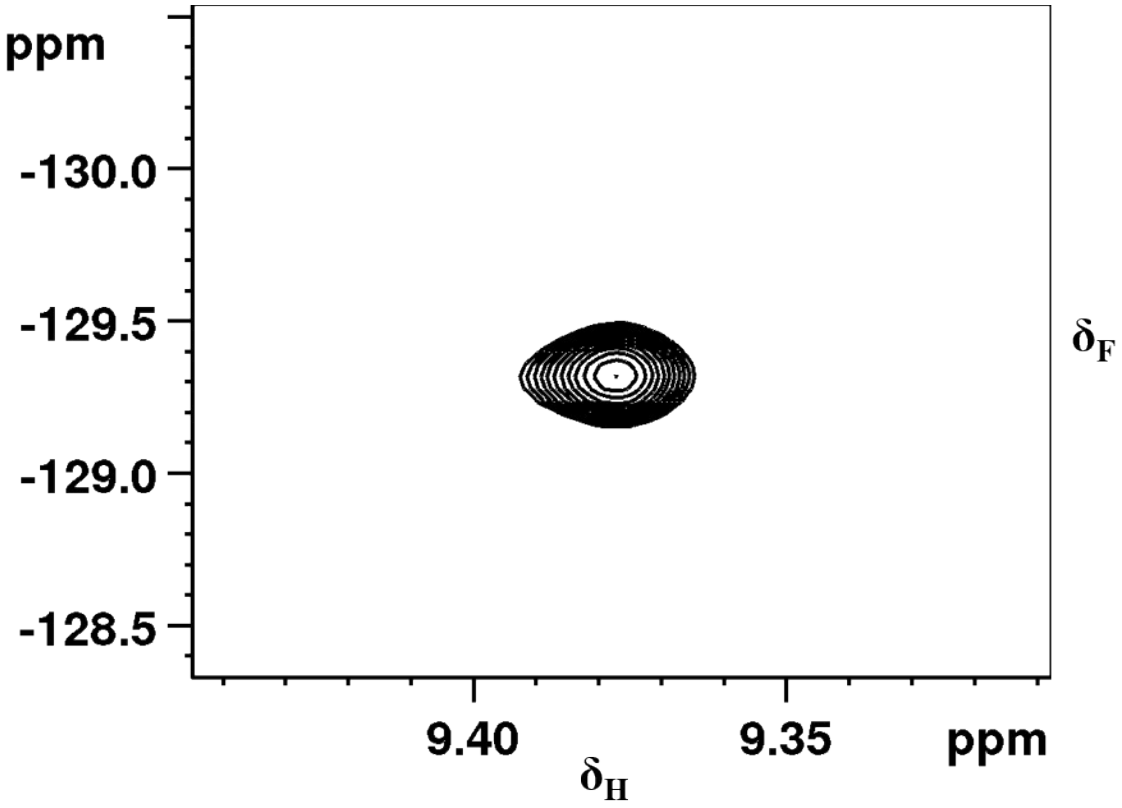
800 MHz 2D ^{15}N-^{1}H coupled HSQC spectrum of molecule **6** in the solvent DMSO-d_6 pertaining to NH(1) region showing scalar coupling $^1J_{NH.}$



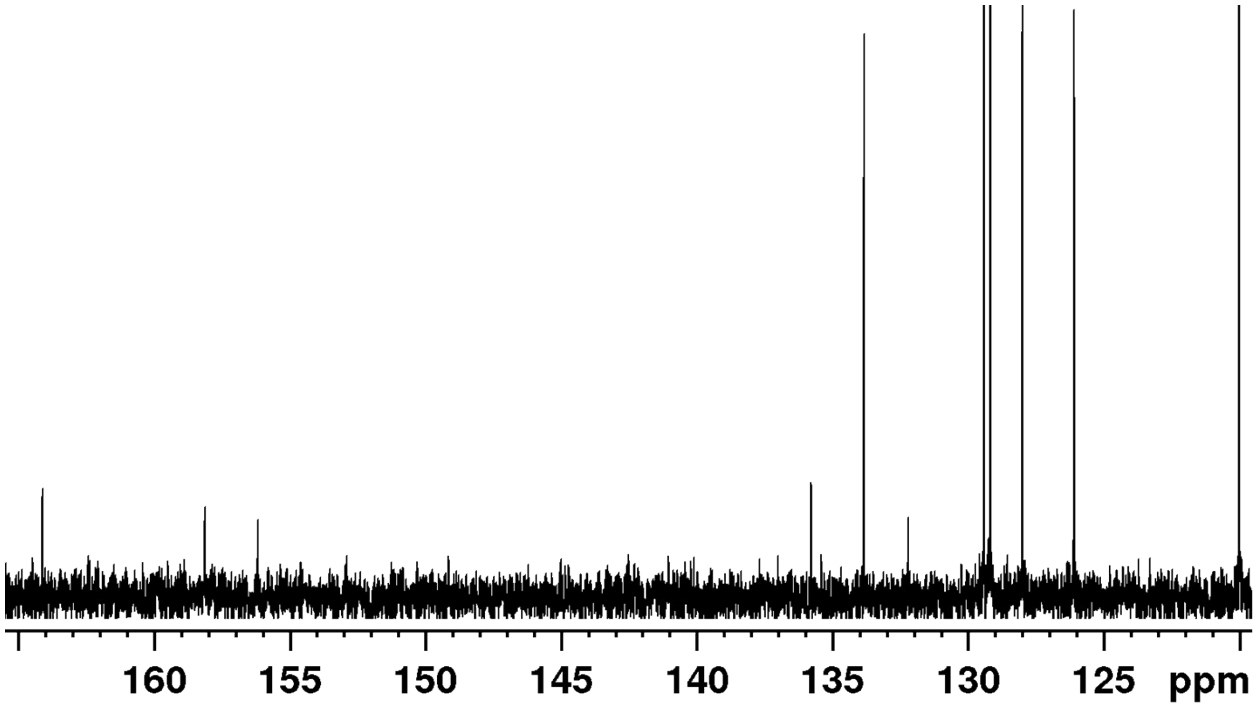
800 MHz 2D ^{15}N-^{1}H coupled HSQC spectrum of molecule **6** in the solvent DMSO-d_6 pertaining to NH(2) region showing scalar coupling $^1J_{NH.}$



800 MHz proton decoupled 2D ^{15}N-^{1}H HSQC spectrum of molecule **6** in the solvent DMSO-d_6.

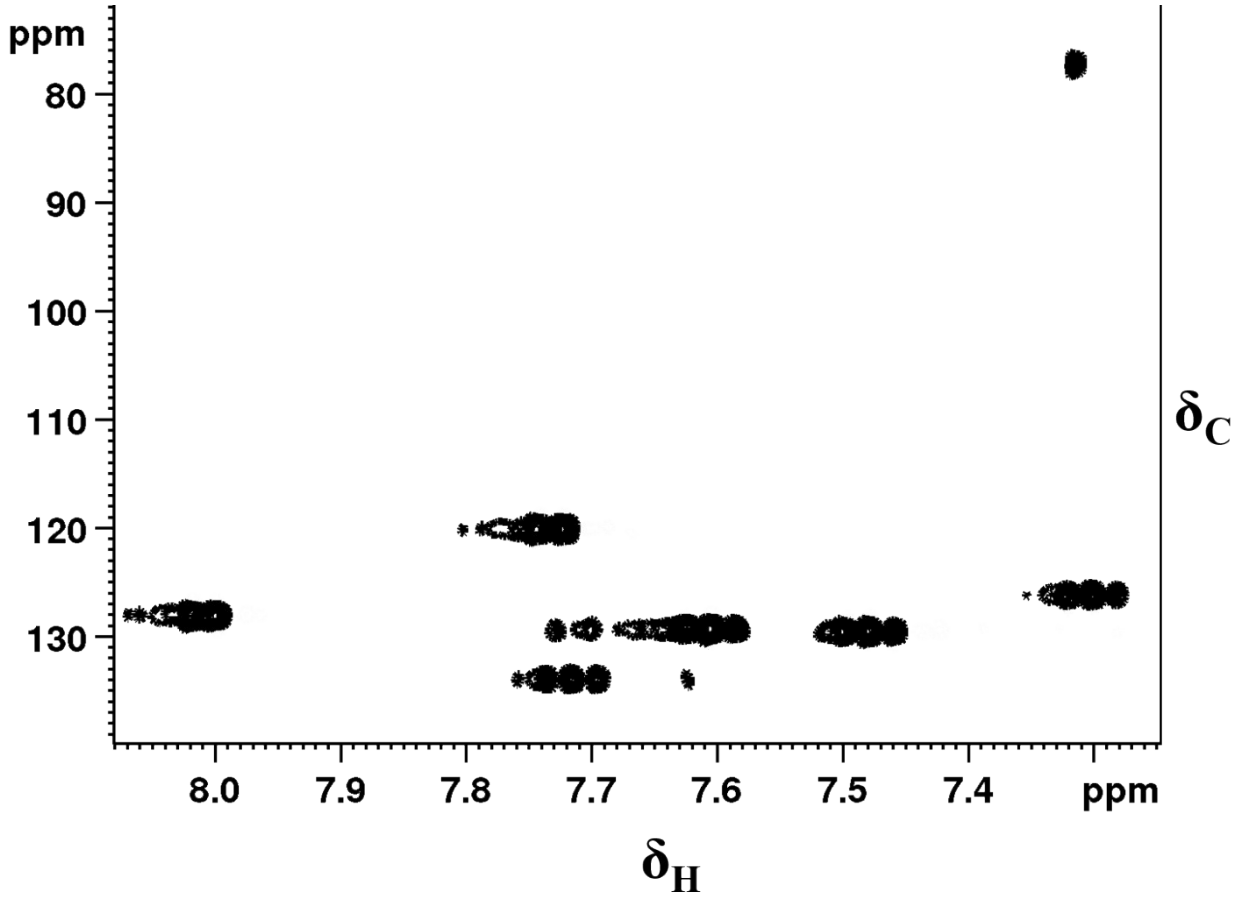


400 MHz 2D ^{19}F-^{1}H HOESY spectrum of molecule **6** in the solvent $CDCl_3$ showing strong correlation between F and NH proton.

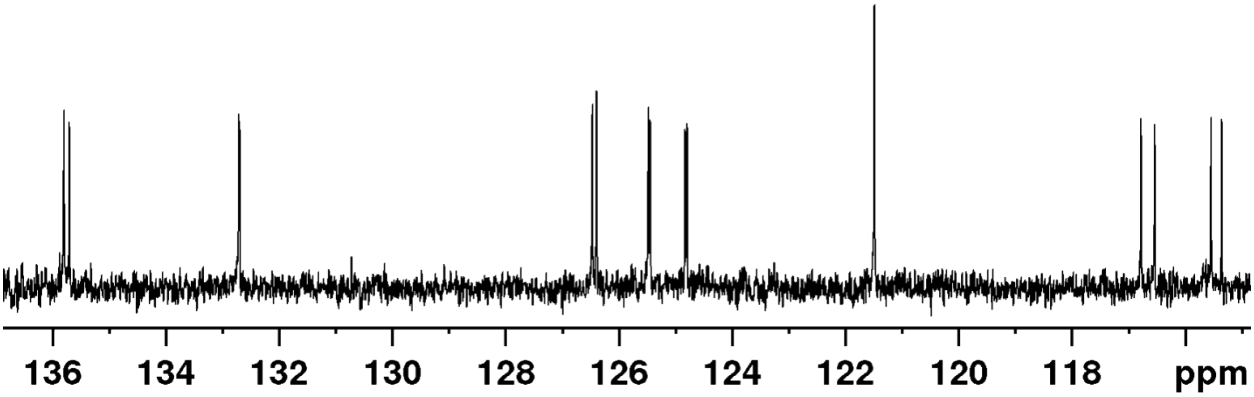


400 MHz ^{1}H-NMR spectra of molecules **1** in the solvent $CDCl_3$.

S50

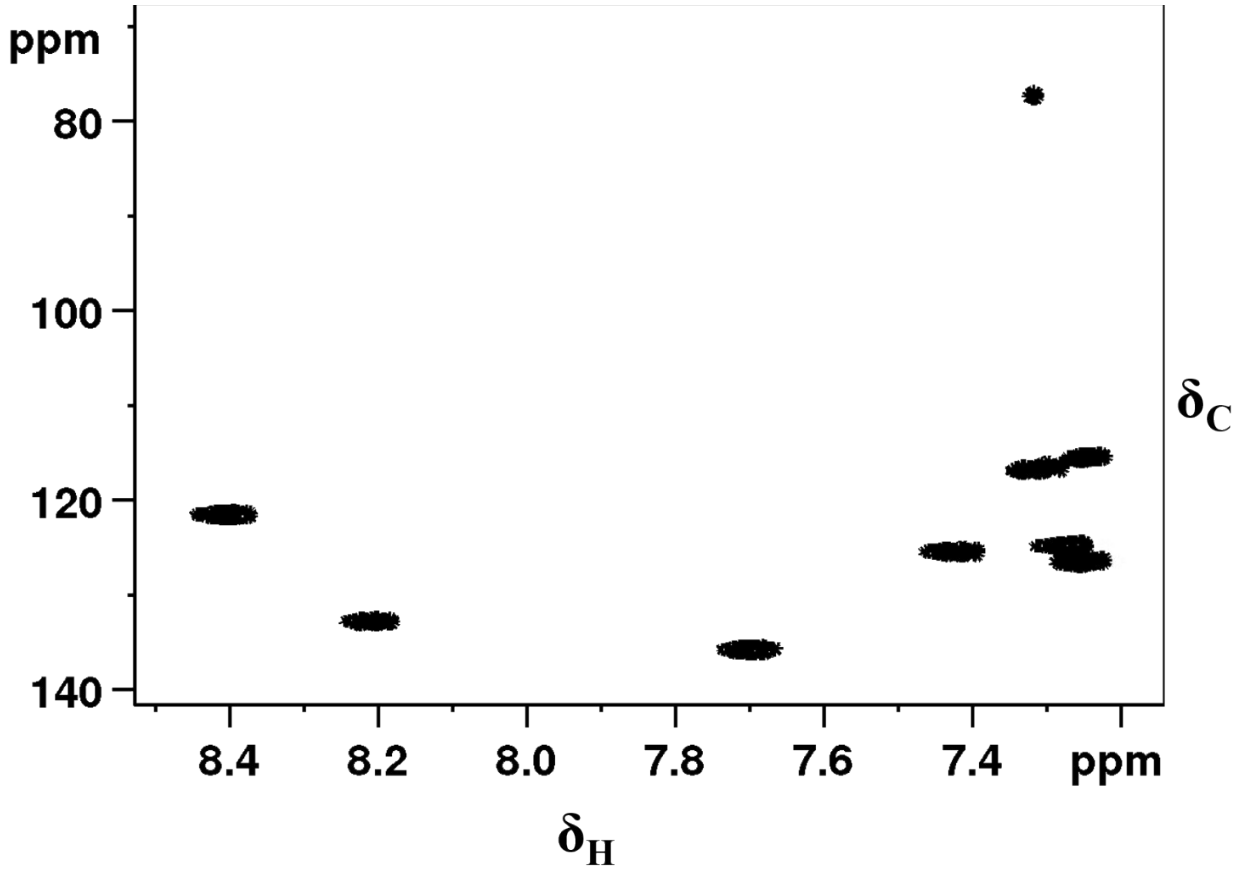


400 MHz 2D ^{13}C-^{1}H HSQC spectrum of molecule **1** in the solvent $CDCl_3$.



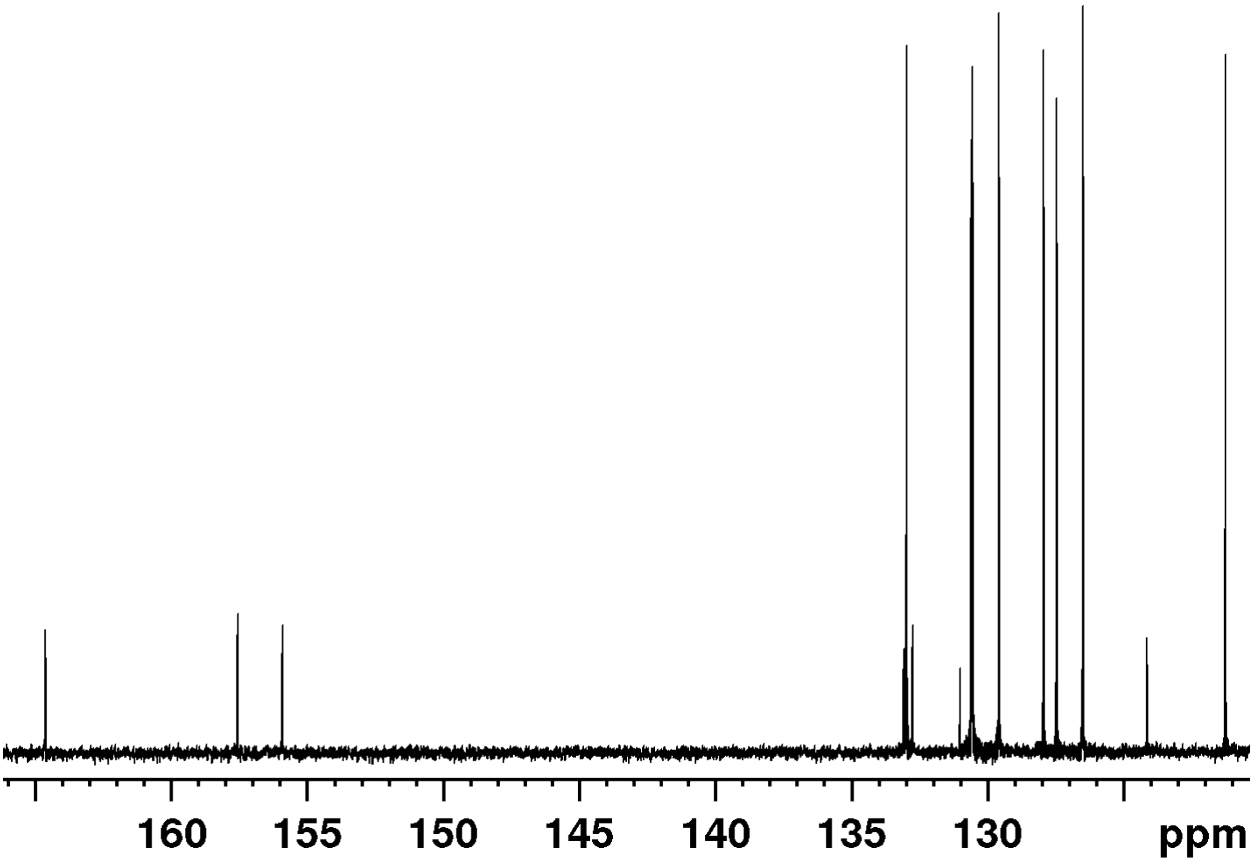
400 MHz ^{1}H-NMR spectra of molecules **2** in the solvent $CDCl_3$.

S52



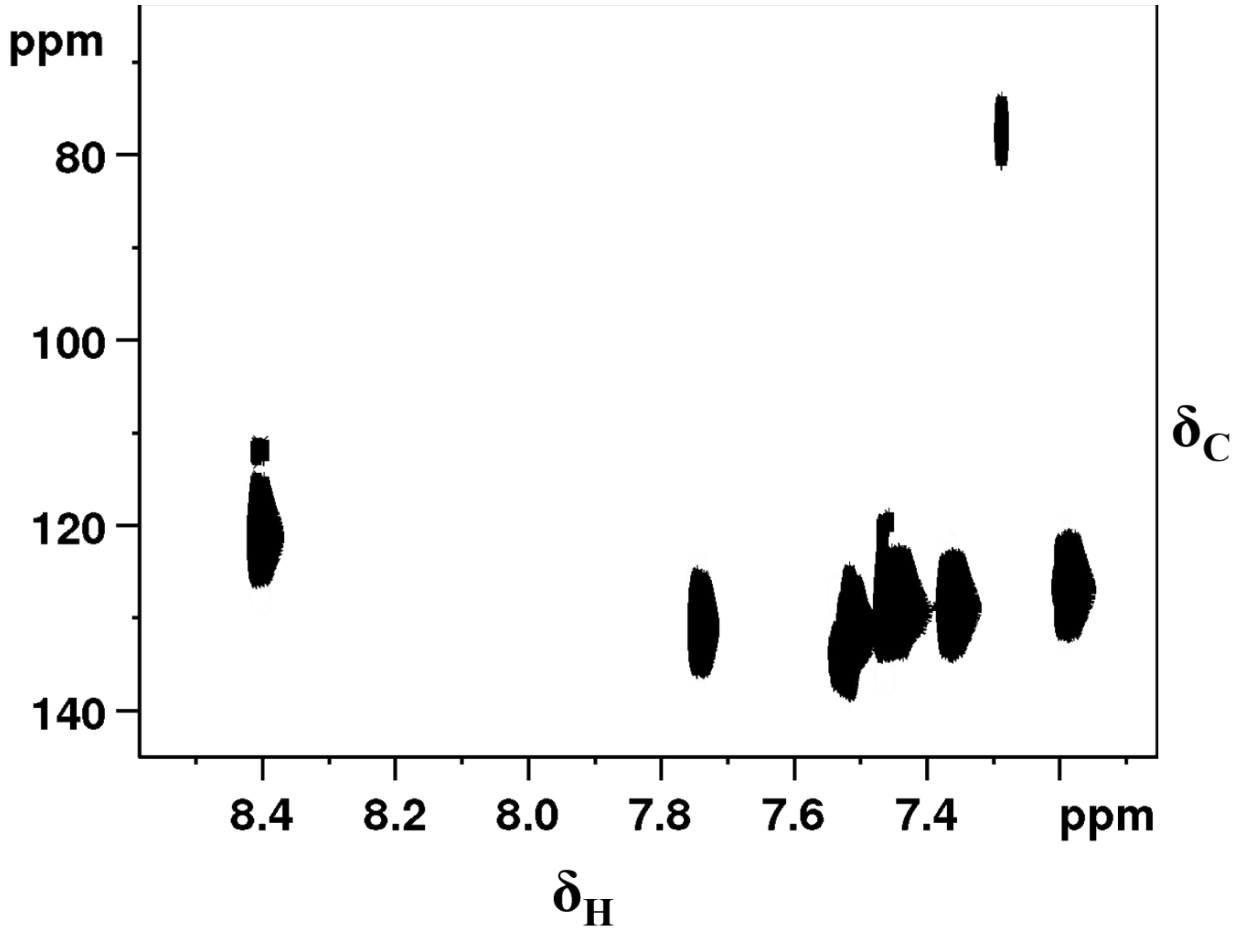
400 MHz 2D ^{13}C-^{1}H HSQC spectrum of molecule **2** in the solvent $CDCl_3$.

S53



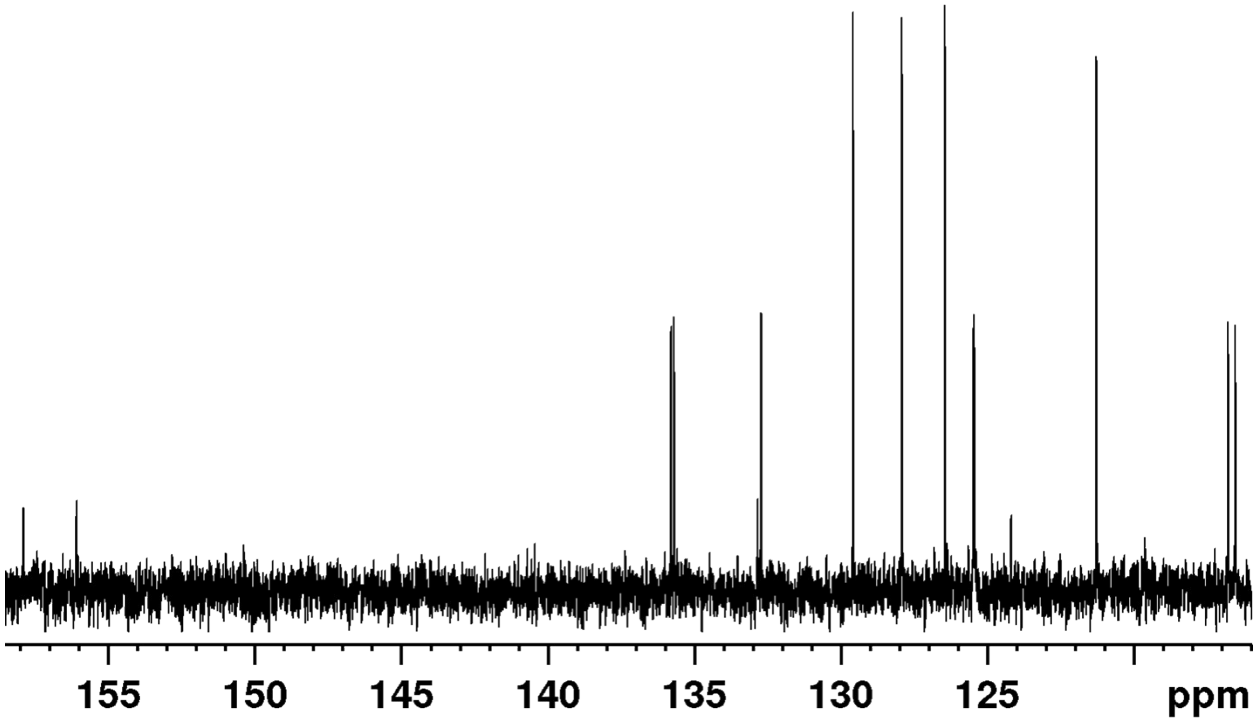
400 MHz ^{1}H-NMR spectra of molecules **3** in the solvent $CDCl_3$.

S54



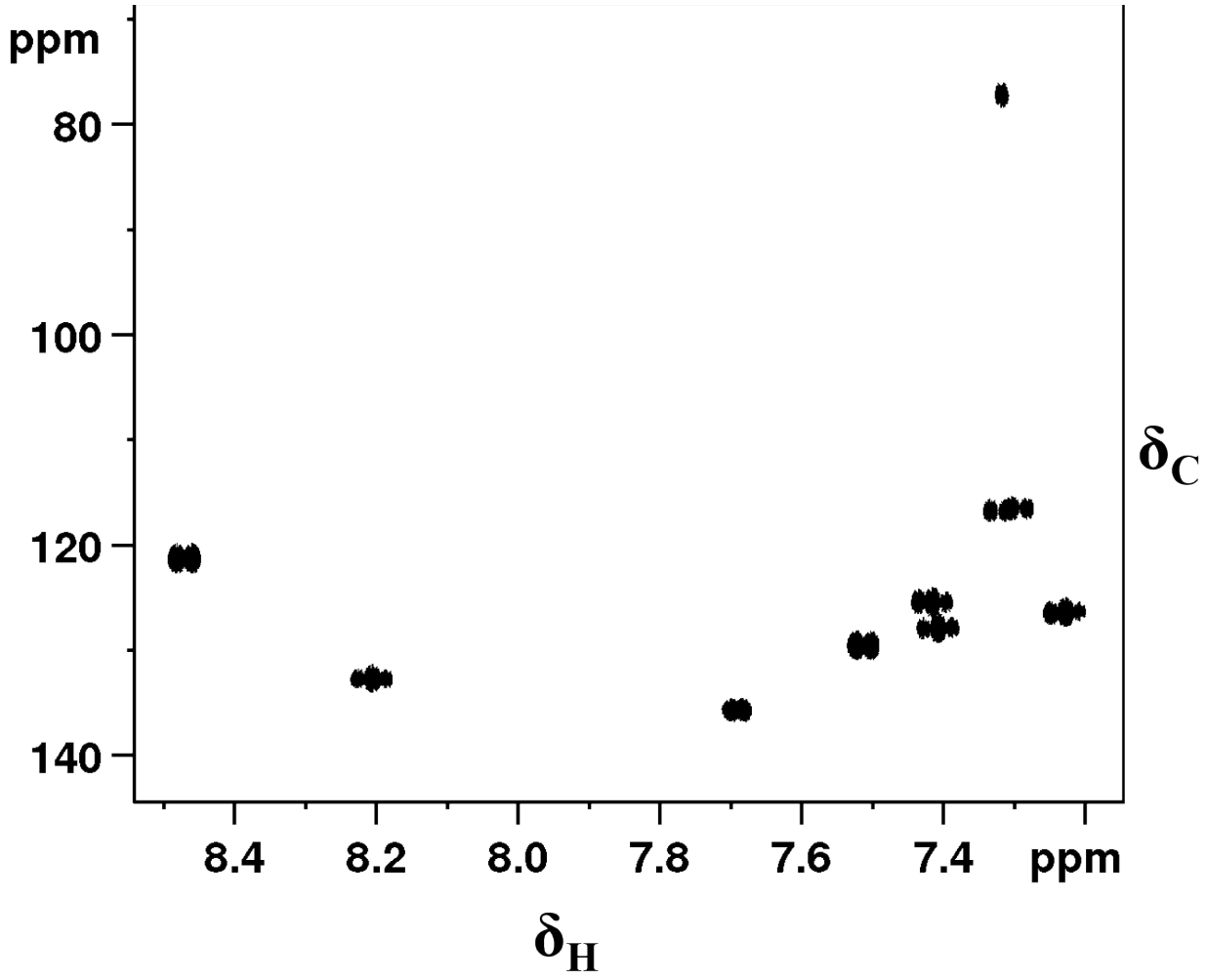
800 MHz 2D ^{13}C-^{1}H HSQC spectrum of molecule **3** in the solvent $CDCl_3$.

S55



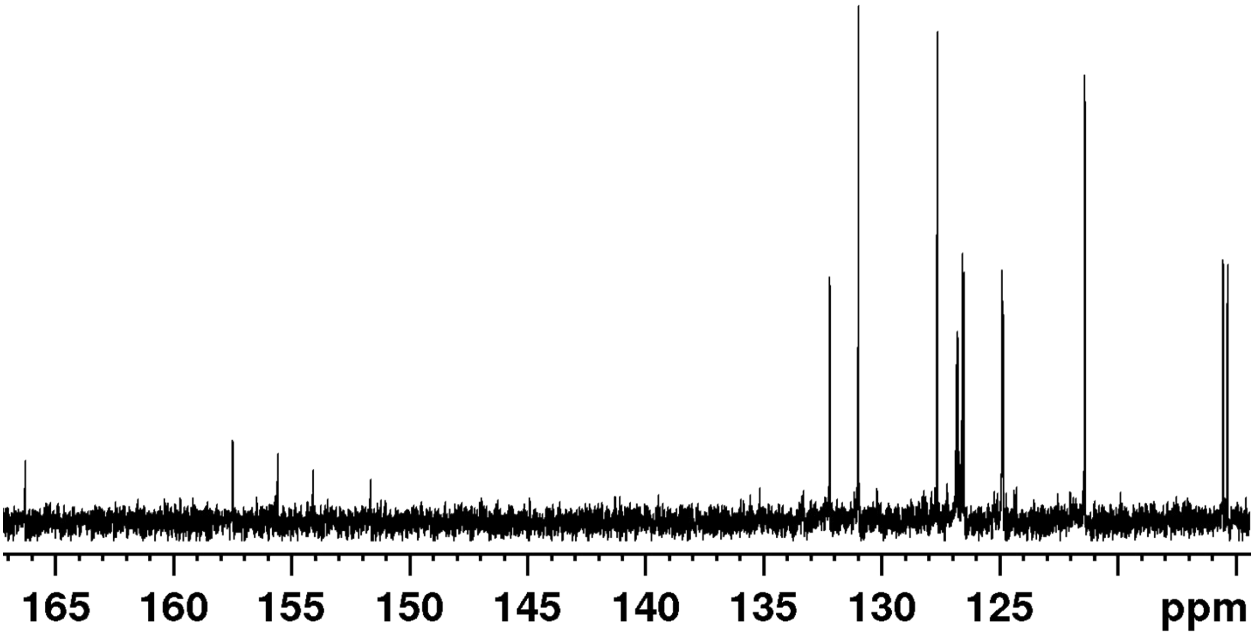
400 MHz ^{1}H-NMR spectra of molecules **4** in the solvent $CDCl_3$.

S56



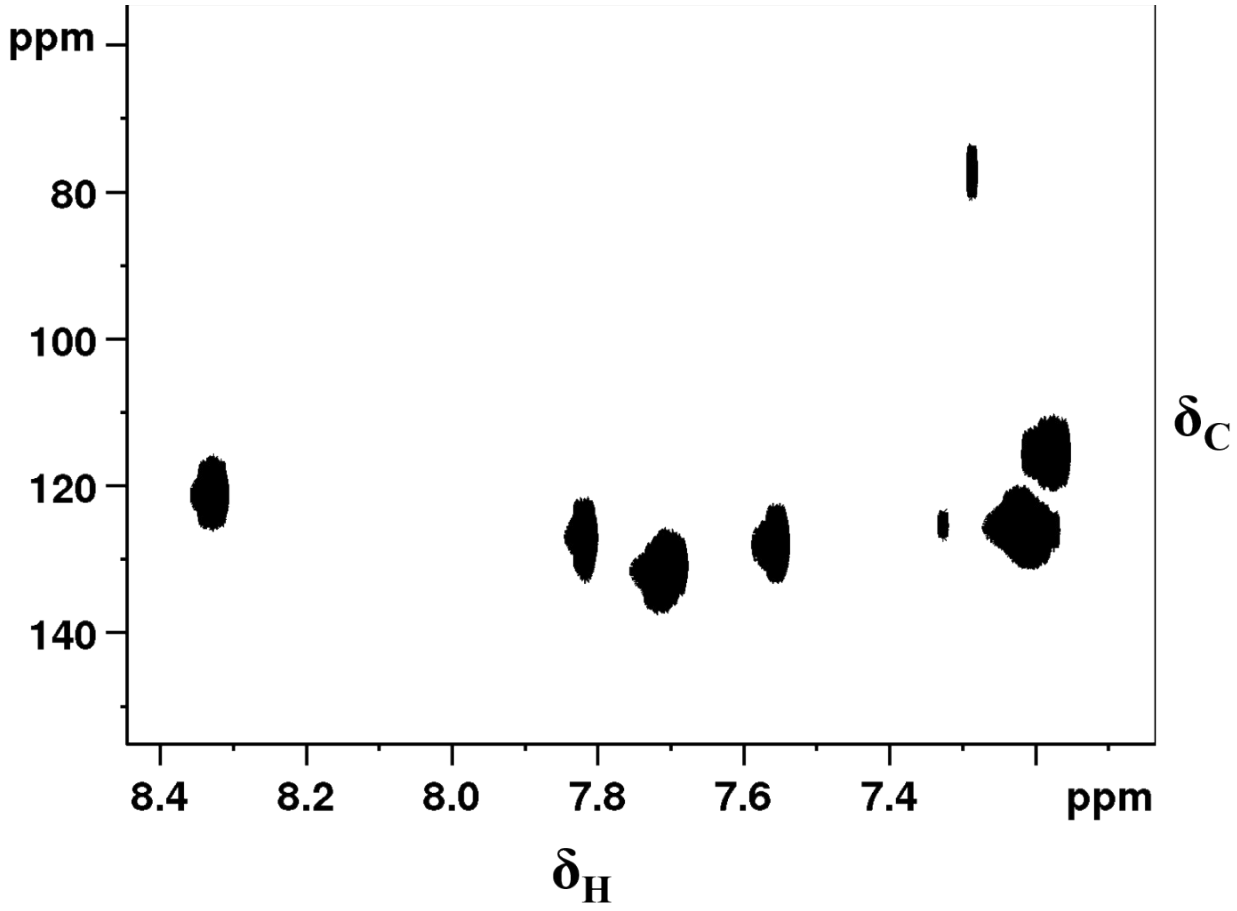
400 MHz 2D ^{13}C-^{1}H HSQC spectrum of molecule **4** in the solvent $CDCl_3$.

S57

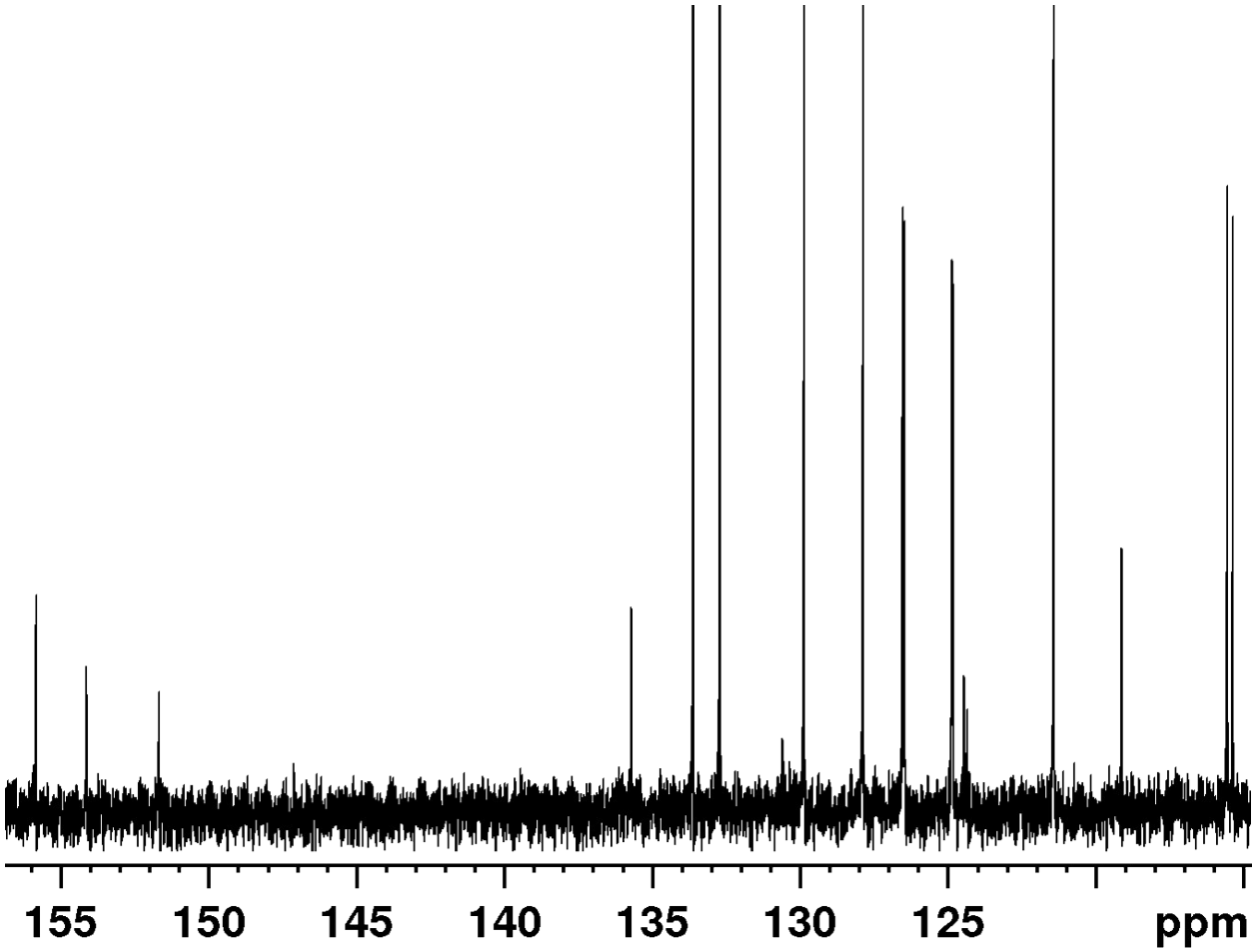


400 MHz ^{1}H-NMR spectra of molecules **5** in the solvent $CDCl_3$.

S58

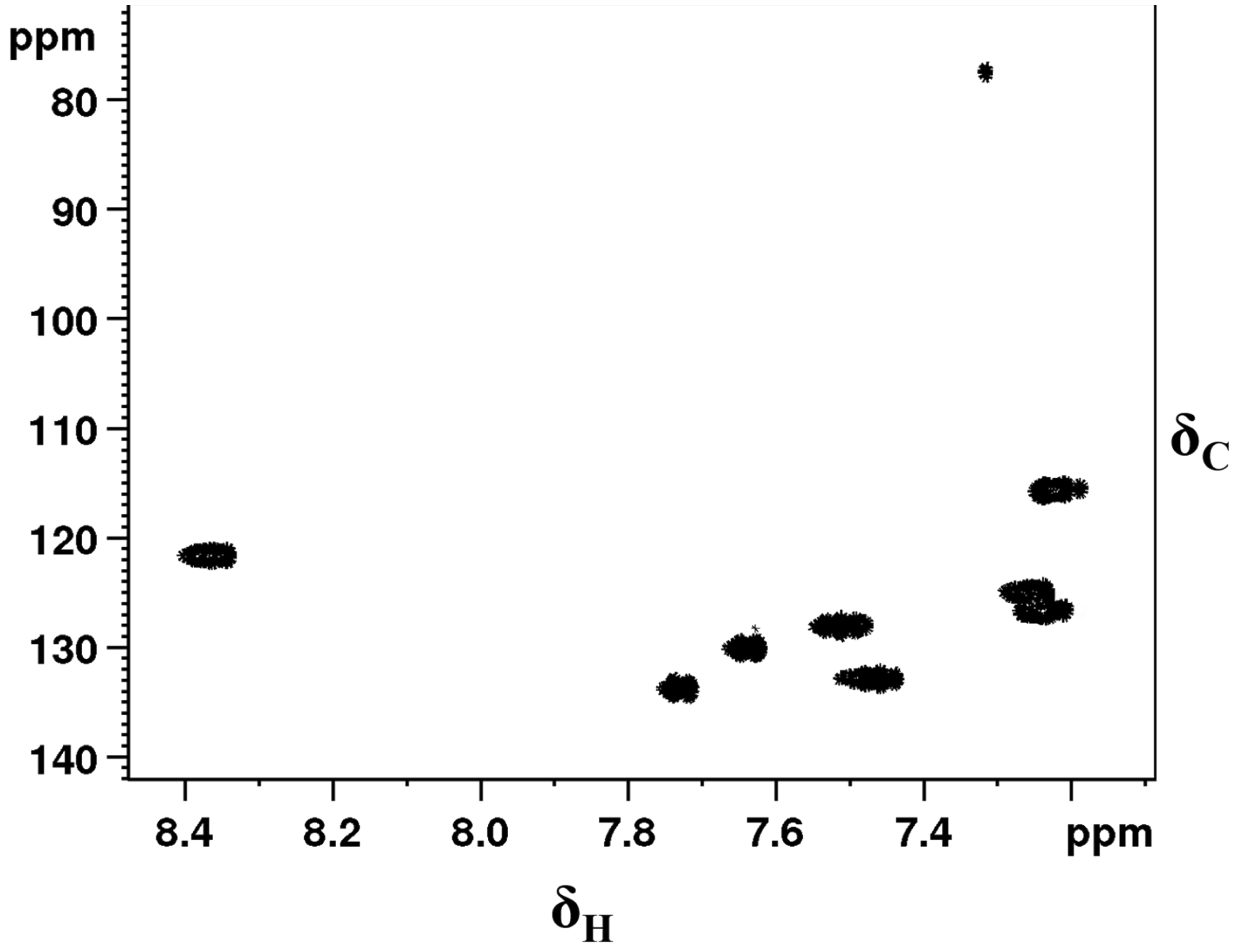


800 MHz 2D ^{13}C-^{1}H HSQC spectrum of molecule **5** in the solvent $CDCl_3$.



400 MHz ^{1}H-NMR spectra of molecules **6** in the solvent $CDCl_3$.

S60



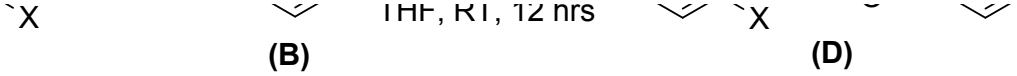
400 MHz 2D ^{13}C-^{1}H HSQC spectrum of molecule **6** in the solvent $CDCl_3$.

Materials

Benzamide, 2-Fluorobenzamide, 2-Chlorobenzamide, 2-Bromobenzamide, 2-trifluoromethylbenzamide, Aniline, 2-Fluoroaniline, 2-Chloroaniline, Oxalylchloride, Tetrahydrofuran.

Synthesis of Benzoyl Phenyl Oxalamides

Commercially available reactants of high purity were purchased and used without any further purification. The AR grade solvent THF was used in the synthesis. All the reactants were taken in 1:1:1 ratio. The calculated amount of oxalyl chloride (C) dissolved in tetrahydrofuran (THF) was taken in a round bottom flask. The calculated amounts of benzamide (A) and aniline (B) derivatives were also separately dissolved in THF. Firstly, the solution (A) was added to solution (C), followed by the solution (B). The RBF was fitted with a $CaCl_2$ guard tube to vent the HCl gas. The reaction was monitored by TLC on regular intervals. The reaction was carried out under dilute conditions in order to minimize the reaction between two amides or anilines. The product was purified by column chromatography using ethyl acetate/hexane solvent system with polarity gradient. The elaborate details of the synthesis of six benzoyl phenyl oxalamides given in the supporting information. To the best of our knowledge this method of synthesis of benzoyl phenyl oxalamides has not been reported in literature.



(B) **(D)**

Synthesis of N^1-benzoyl-N^2-phenyloxalamide (1):

A solution of benzamide (500 mg, 4.12 mmol) in 10 mL of THF and aniline (376 µL, 4.12 mmol) in 10 mL of THF were prepared separately. The benzamide solution was added to a solution of oxalyl chloride (353 µL, 4.12 mmol) in 10 mL THF, followed by aniline solution. The reaction was stirred under ambient conditions for 12 hours, monitored by TLC at regular intervals. The reaction mixture was concentrated in vacuo to obtain a colorless solid and chromatographed on silica gel using ethyl acetate/hexane eluent (30% v/v). The product (91 % yield) is confirmed by nmr and mass spectrometry (m/z: 268.267).

Synthesis of N^1-(2-fluorobenzoyl)-N^2-(2-fluorophenyl)oxalamide (2):

A pre-weighed amount of 2-fluorobenzamide (500 mg, 3.59 mmol) in 10 mL THF and 2-fluoroaniline (346 µL, 3.59 mmol) in 10 mL of THF were added to oxalyl chloride solution (308 µL, 3.59 mmol in 10 mL THF) in a sequence respectively. The mixture was stirred overnight at room temperature. The solvent was evaporated, and the fluffy solid was subjected to column chromatography on silica gel with 30 % v/v EtOAc in Hexane. The purified product (82% yield) was confirmed by nmr and mass spectrometry (m/z: 304.248).

Synthesis of N^1-(2-chlorobenzoyl)-N^2-(2-chlorophenyl)oxalamide (3):

The solution of 2-chlorobenzamide (500 mg, 3.21 mmol in 10 mL of THF) was added to oxalyl chloride solution (275 µL, 3.21 mmol in 10 mL THF) which is followed by the immediate addition of already made 2-chloroaniline solution (338 µL, 3.21 mmol in 10 mL THF). The reaction was stirred under ambient conditions for 12 hrs, then concentrated in vacuo to obtain a white solid. The latter was flash chromatographed on silica gel with 30 % v/v EtOAc in Hexane. The product (78%

yield) was characterized by nmr and mass spectrometry (m/z: 337.15).

Synthesis of N^1-(2-fluorobenzoyl)-N^2-(2-chlorophenyl)oxalamide (4):

To a solution of oxalyl chloride (308 µL, 3.59 mmol in 10 mL THF), a solution of 2-fluorobenzamide (500 mg, 3.59 mmol in 10 mL THF) and 2-chloroaniline (378 µL, 3.59 mmol in 10 mL THF) were added in consecutive steps and stirred for 12 hrs. The solvent was evaporated in vacuum, and the residue was chromatographed on silica gel with 30% v/v EtOAc in Hexane. The product (yield 78%) was confirmed by nmr and mass spectrometry (m/z: 320.036).

Synthesis of N^1-(2-fluorophenyl)-N^2-(2-(trifluoromethyl)benzoyl)oxalamide (5):

The 2-(trifluoromethyl)benzamide solution (100 mg, 0.53 mmol in 5 mL THF) was added to oxalyl chloride (45 µL, 0.53 mmol) in 10 mL THF, followed by the addition of 2-fluoroaniline (51 µL, 0.53 mmol in 5 mL THF). The mixture was stirred for 12 hrs, concentrated in vacuo and purified by column chromatography on silica gel with 30% EtOAc in hexane eluent. The yield of the product was determined to be 72% and confirmed by nmr and mass spectrometry (m/z: 354.260).

Synthesis of N^1-(2-bromobenzoyl)-N^2-(2-fluorophenyl)oxalamide (6):

2-bromobenzamide (500 mg, 2.45 mmol in 10 mL THF) and 2-fluoroaniline (241 µL, 2.45 mmol in 10 mL THF) were added one after the other respectively to oxalyl chloride solution (214 µL, 2.45 mmol in 10 mL THF). It was stirred overnight, THF solvent was evaporated using rota-evaporator and the residue was chromatographed on silica gel with 30% v/v EtOAc/Hexane solution. The product (yield 88%) was confirmed by mass spectrometry (m/z: 365.154) and nmr.

S64