Deuteration and Tautomeric Reactivity of the 1-Methyl Functionality of Free-base Dipyrrins

Brandon R. Groves, T.Stanley Cameron and Alison Thompson*

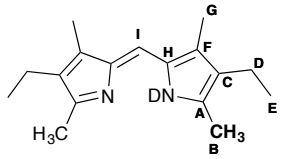
Department of Chemistry, Dalhousie University, P.O. Box 15000, Halifax, NS, B3H 4R2, Canada
Alison.Thompson@dal.ca

Supporting Information

Table of contents

Structural assignment

Table 1. Structural assignment of free-base dipyrrin 7



Proton Label	Shift (ppm)	Carbon Label	Shift (ppm)
---	---	A	151.2
B	2.31[a]	B	14.3[a]
---	---	C	130.0
D	2.37	D	17.9
E	1.06	E	15.0
---	---	F	133.3
G	2.13	G	9.6
---	---	H	136.8
I	6.40	I	115.39

[a]Signal significantly suppressed in spectrum of deuterated compound

The proton signals correlating to H^D, H^E and H^I of **7** were assigned using a 1D ^{1}H-NMR spectrum, due to their diagnostic chemical shifts and splitting pattern (ethyl and *meso*-hydrogen). Carbon atoms C^D, C^E and C^I were assigned through C–H correlation in the HSQC spectrum. Analysis of the HMBC spectrum revealed the signal at 130.0 ppm in the ^{13}C-NMR spectrum to correspond to C^C, through correlation to H^E (Figure 1). The methyl signal at 2.13 ppm in the ^{1}H-NMR spectrum showed HMBC correlation to all pyrrolic C atoms (C^A, C^C, C^F and C^H), but correlated weakly with the signal at 151.2 ppm. The methyl signal at 2.31 ppm correlated to two of the pyrrolic carbon signals (130.0 and 151.2 ppm) but not to the signals at 133.3 and 136.8 ppm. As the *meso*-H correlated to only these two carbon signals in the HMBC spectrum (133.3 and 136.8 ppm), these signals must be C^F and C^H. Of these two, only C^F should correlate to the ethyl signal, and indeed, only the signal at 133.3 ppm showed this correlation. Thus, C^F was assigned at 133.3 ppm, and C^H at 136.8 ppm. Only the 3-methyl of **7** is expected to correlate to C_H via HMBC. Thus, it was unequivocally concluded that H^B and H^G were represented by the signals at 2.31 and 2.13 ppm, respectively, and that the reactive, and deuterium exchanging, methyl groups are indeed the 1,9-dimethyl groups.

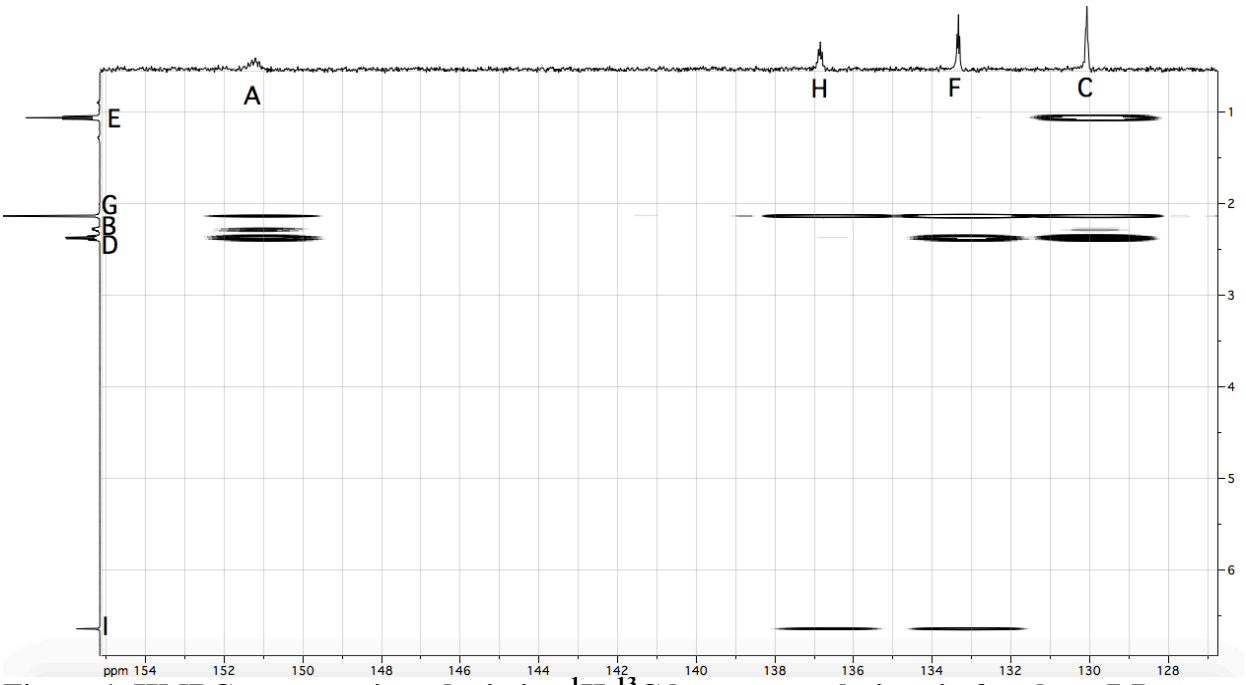
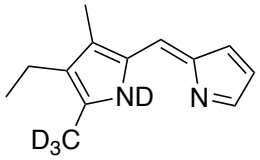


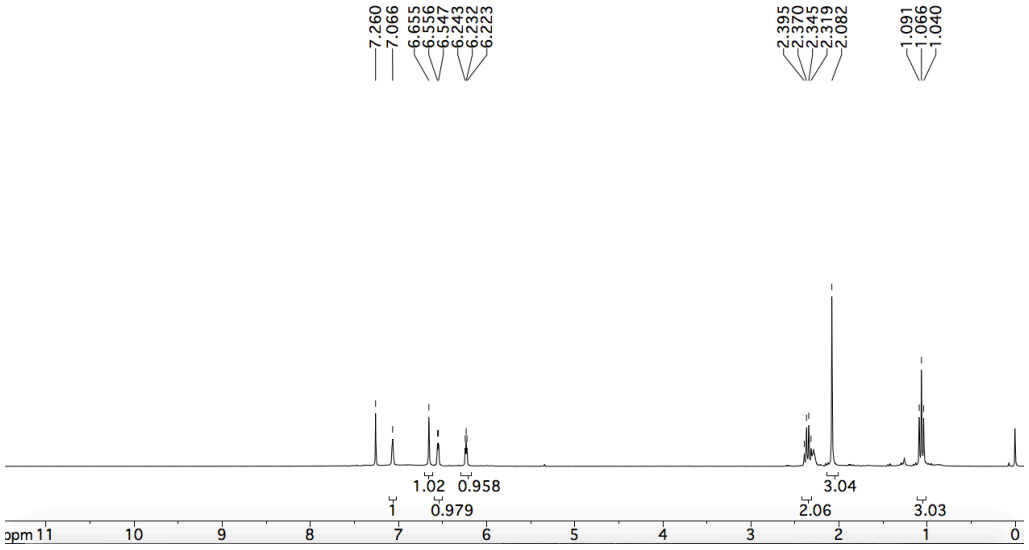
Figure 1. HMBC cross-sections depicting ^{1}H-^{13}C hetero-correlations in free-base 7-D_7

NMR spectra

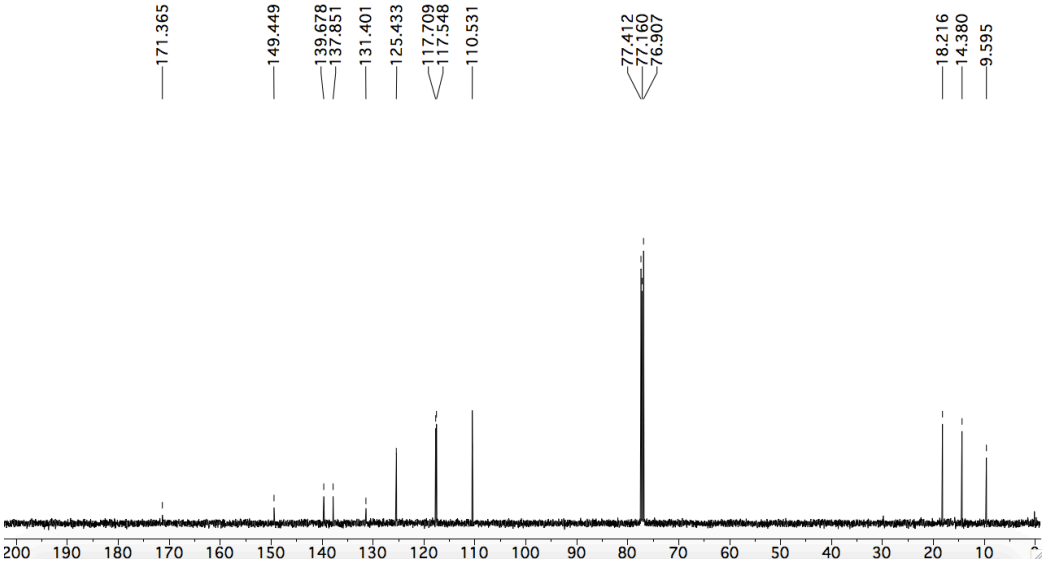
(Z)-2-((2H-Pyrrol-2-ylidene)methyl)-4-ethyl-3,5(2H3)-dimethyl-12H-pyrrole (1-D_4)



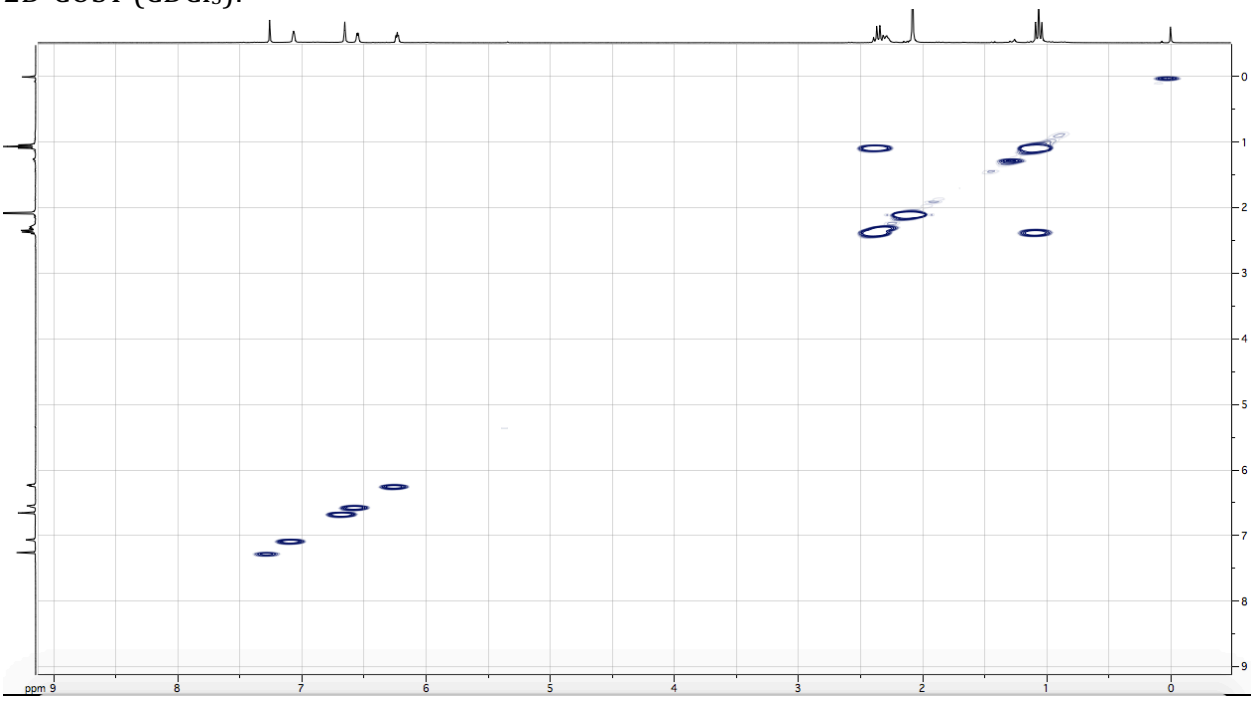
^{1}H-NMR ($CDCl_3$, 300 MHz):



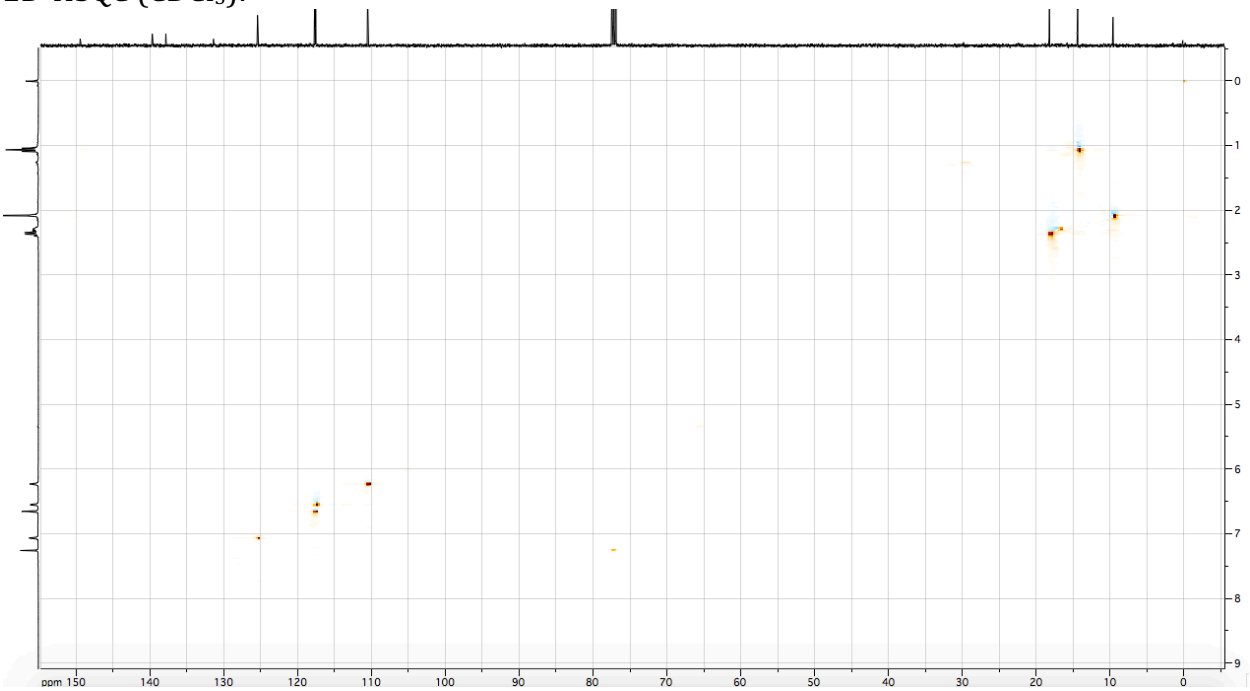
^{13}C UDEFT NMR ($CDCl_3$, 125 MHz):



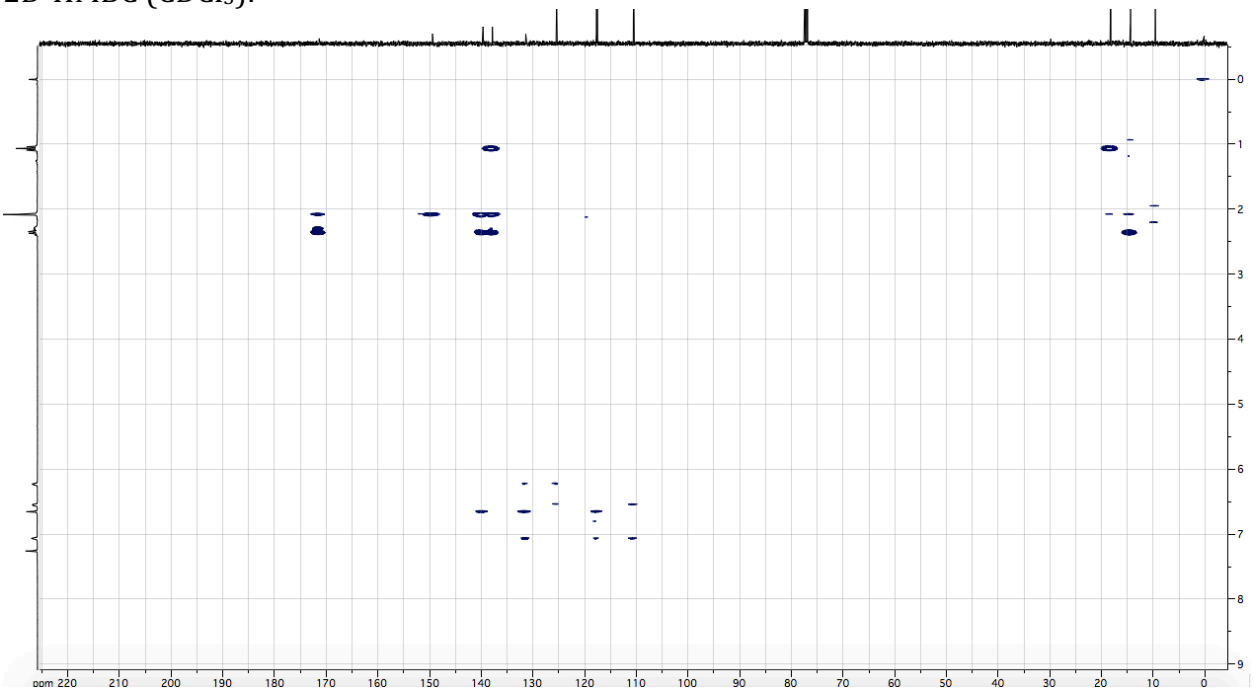
2D-COSY ($CDCl_3$):



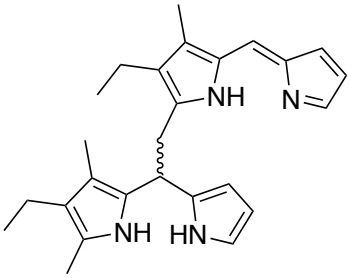
2D-HSQC ($CDCl_3$):



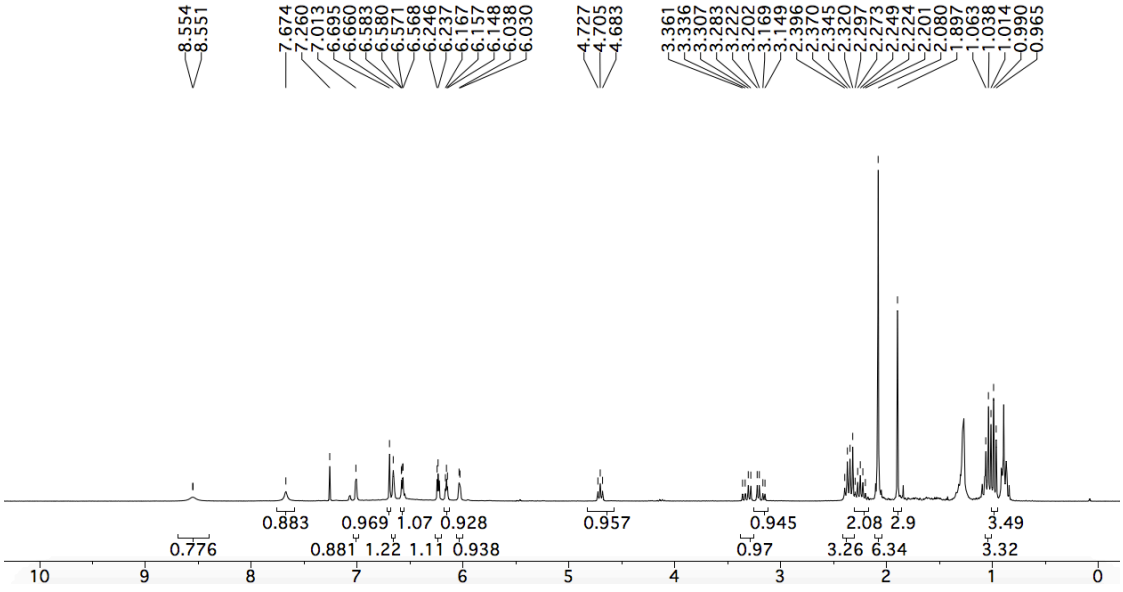
2D-HMBC ($CDCl_3$):



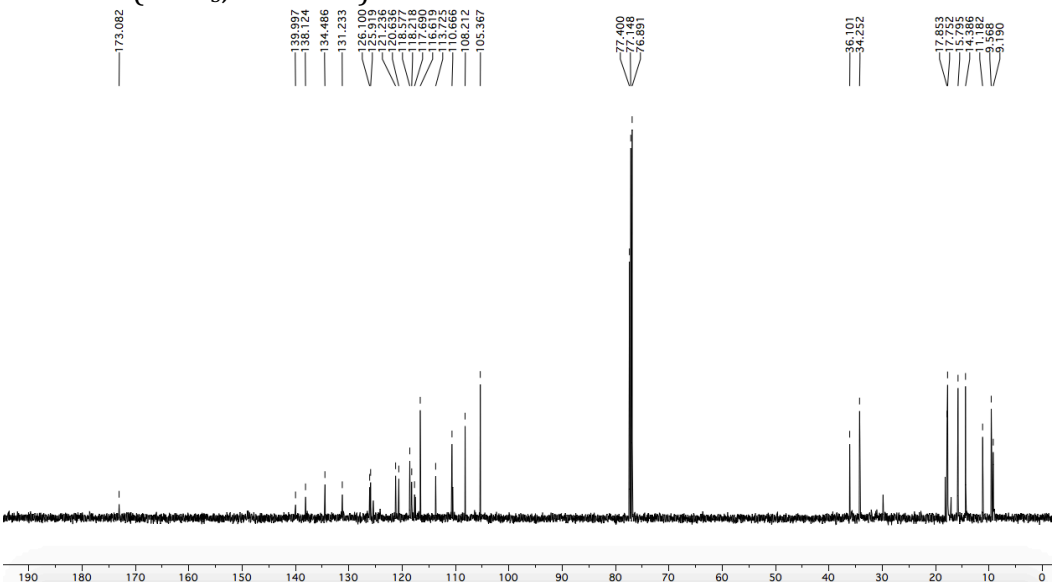
(*Z*)-2-((2*H*-Pyrrol-2-ylidene)methyl)-4-ethyl-5-(2-(4-ethyl-3,5-dimethyl-1*H*-pyrrol-2-yl)-2-(1*H*-pyrrol-2-yl)ethyl)-3-methyl-1*H*-pyrrole (2)



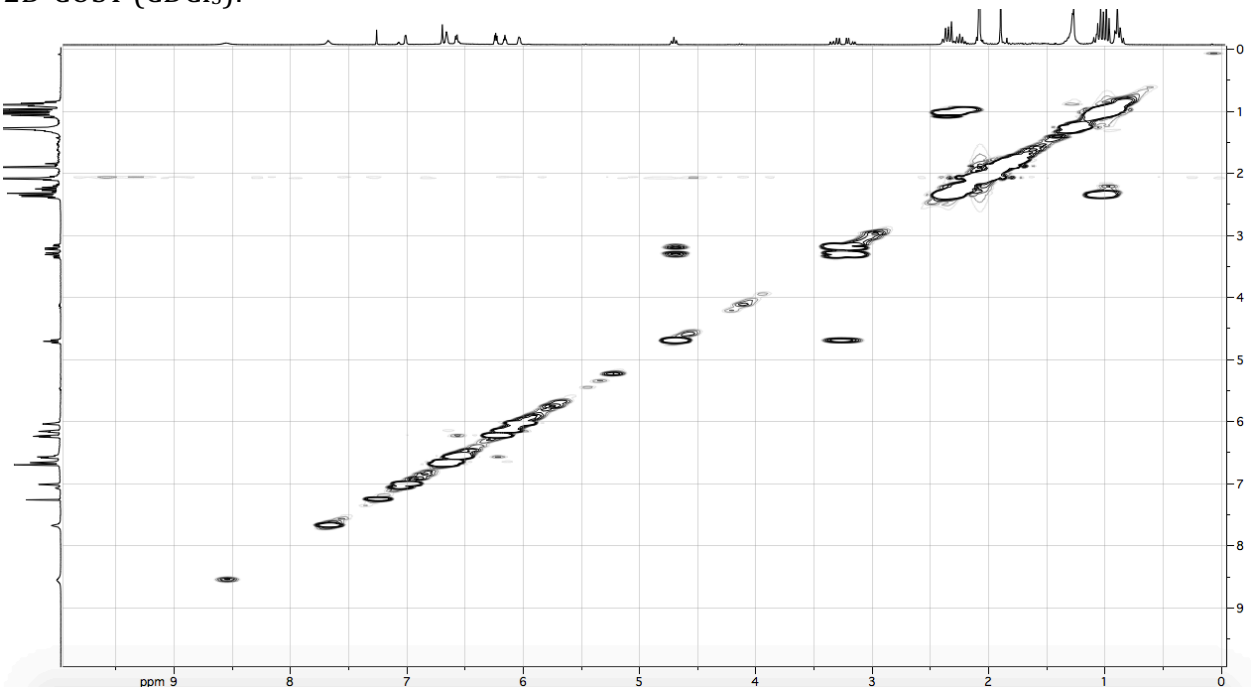
^{1}H-NMR ($CDCl_3$, 300 MHz):



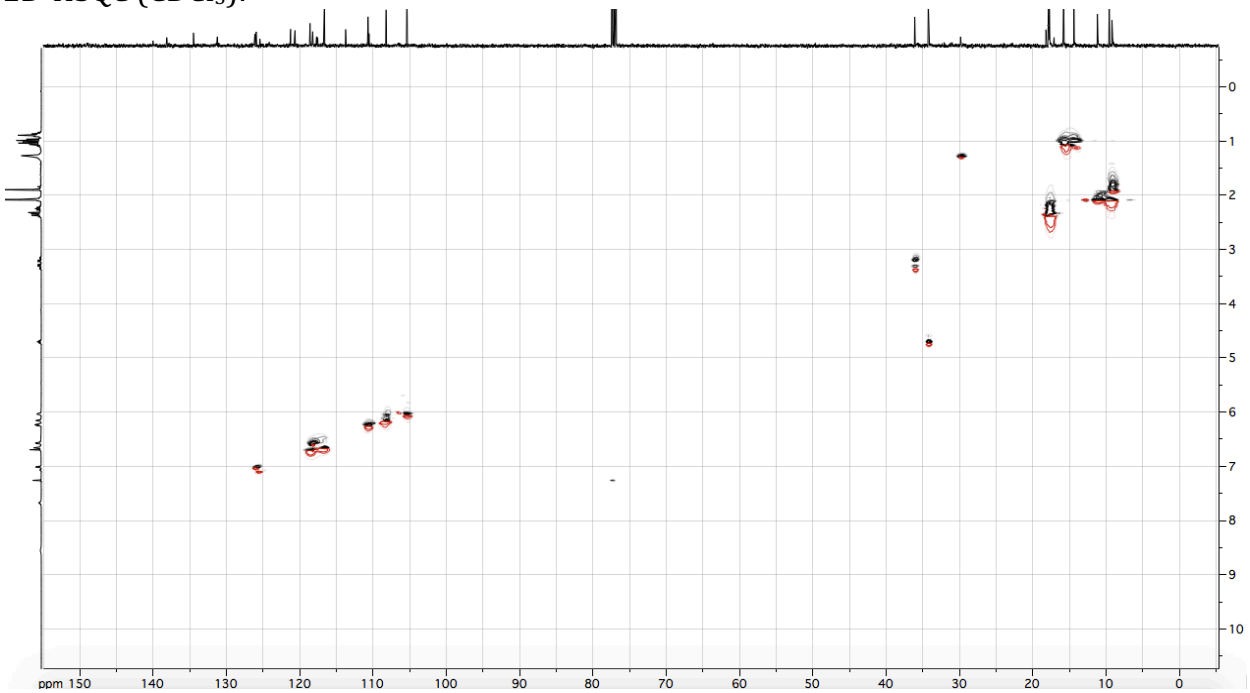
^{13}C UDEFT NMR ($CDCl_3$, 125 MHz):



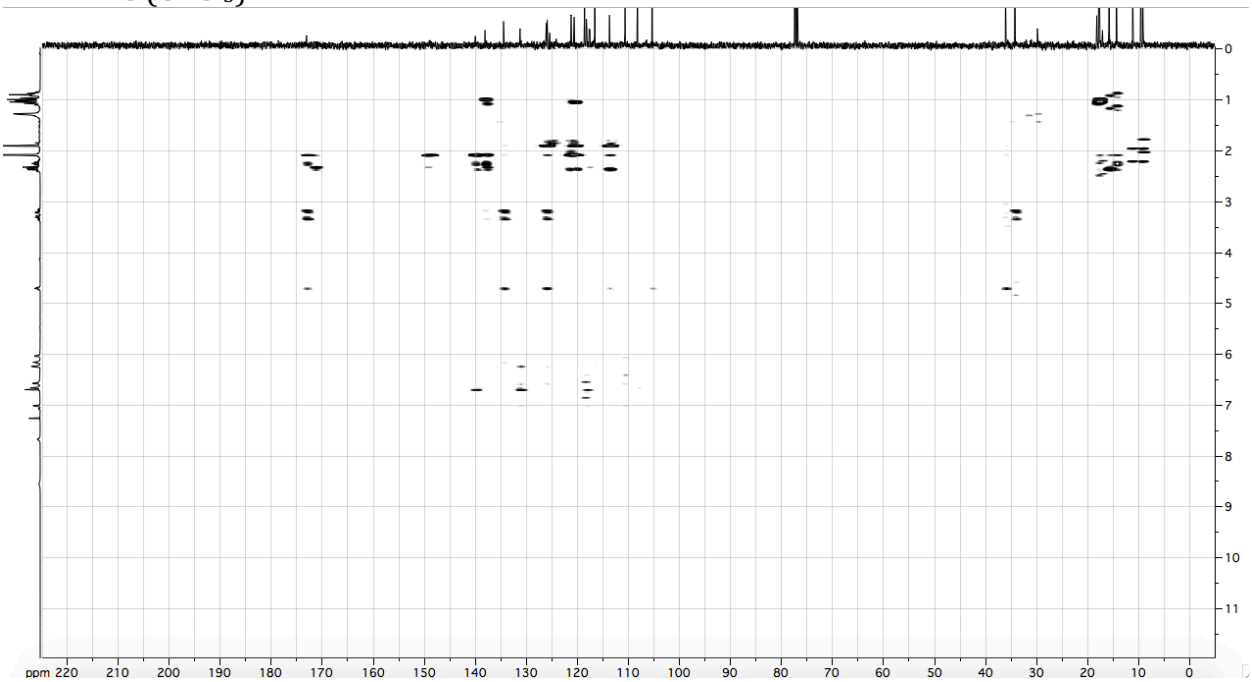
2D-COSY ($CDCl_3$):



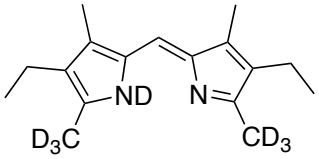
2D-HSQC ($CDCl_3$):



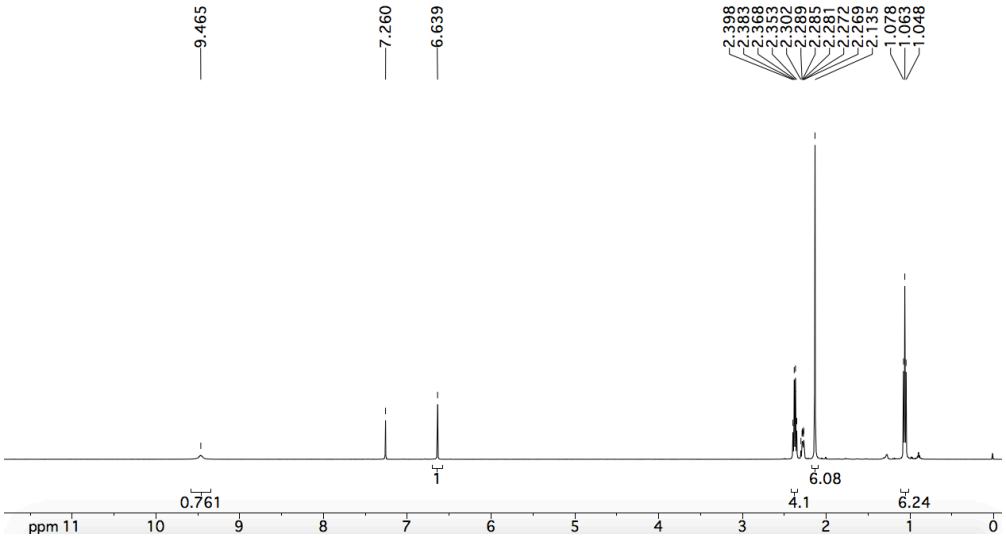
2D-HMBC ($CDCl_3$):



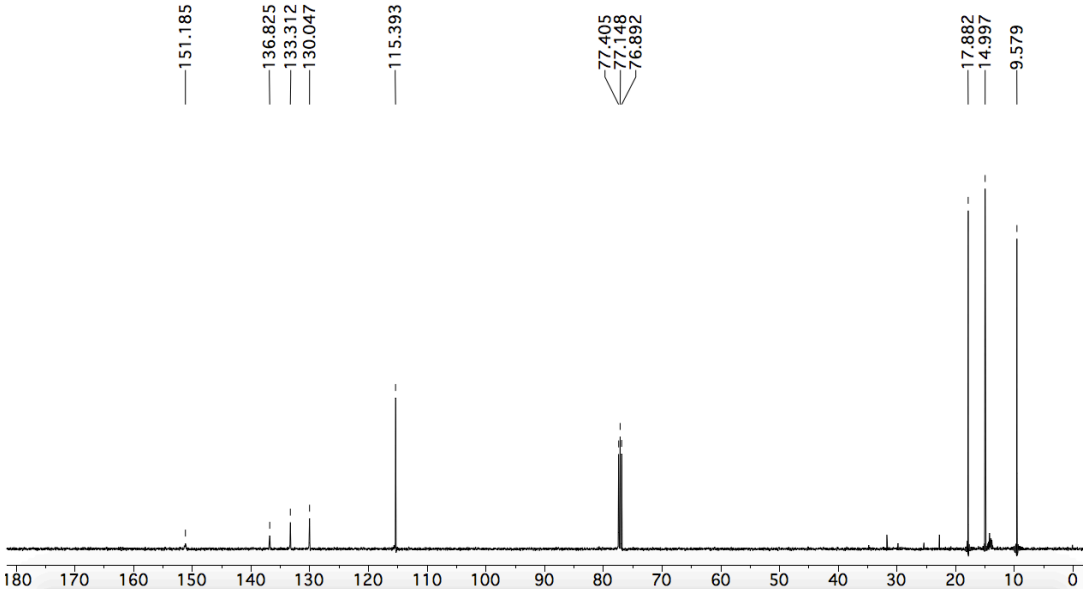
(*Z*)-3-Ethyl-5-((4-ethyl-3,5($^2H_3$)-dimethyl-2*H*-pyrrol-2-ylidene)methyl)-2,4($^2H_3$)-dimethyl-1^2*H*-pyrrole (7-D_7)



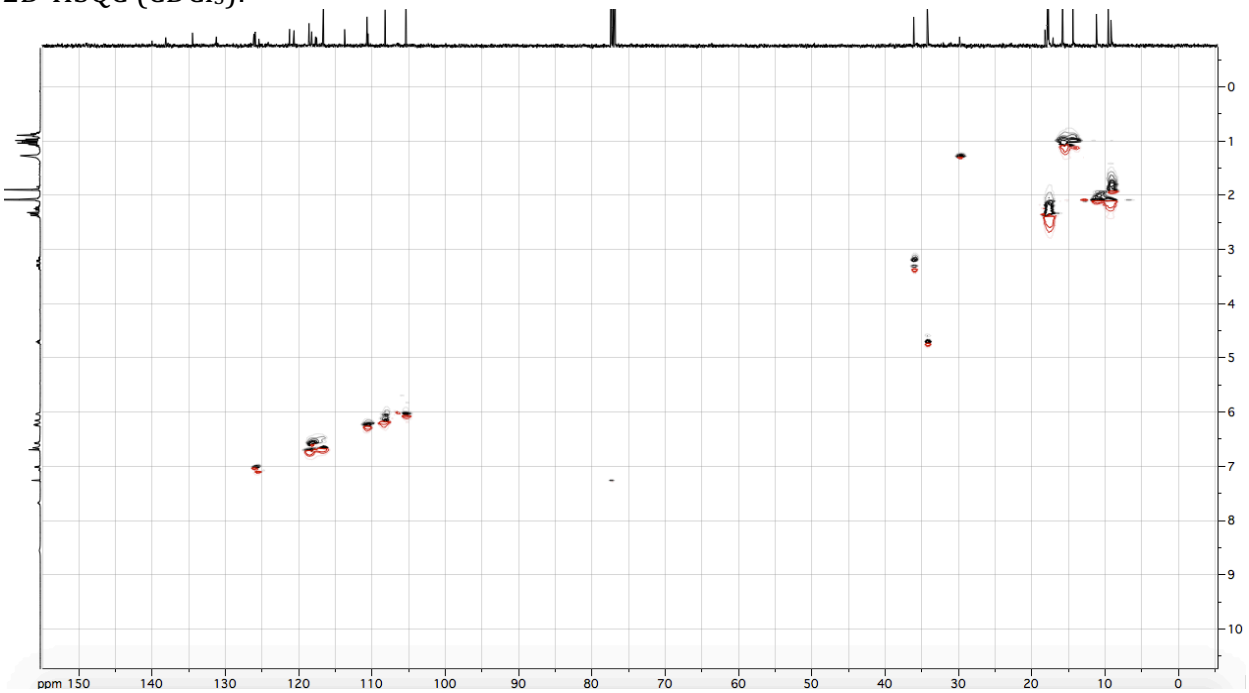
^{1}H-NMR ($CDCl_3$, 500 MHz):



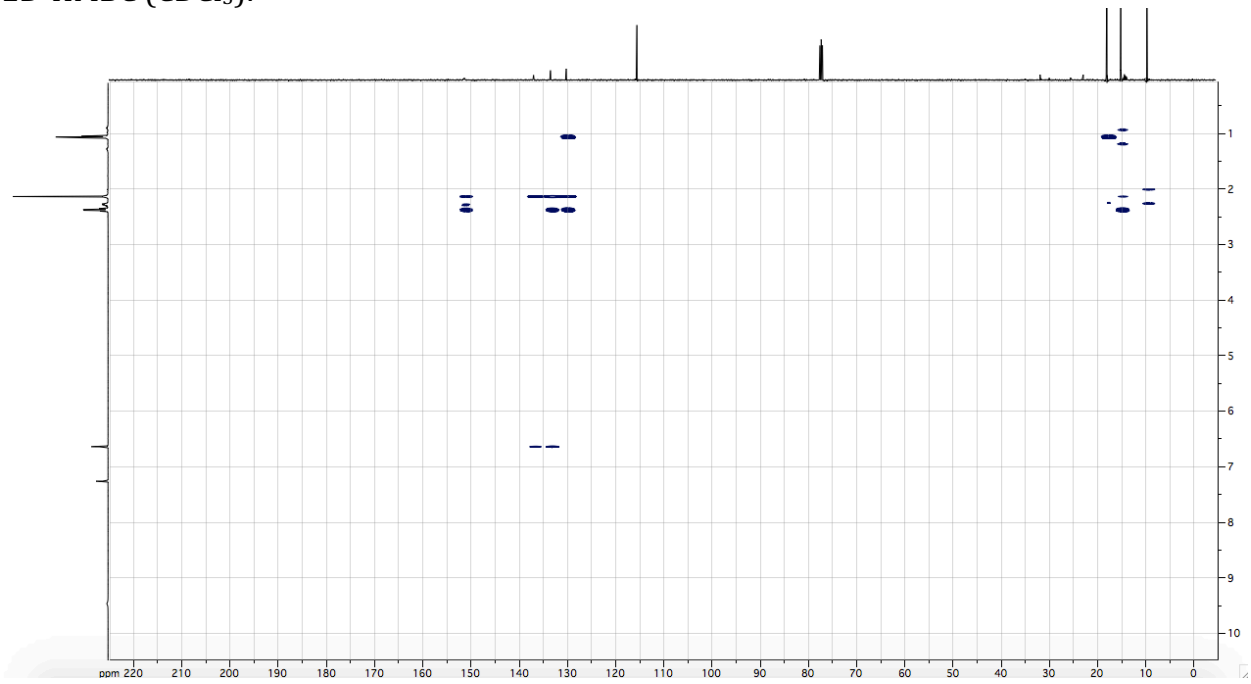
^{13}C UDEFT NMR ($CDCl_3$, 125 MHz):



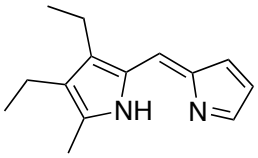
2D-HSQC ($CDCl_3$):



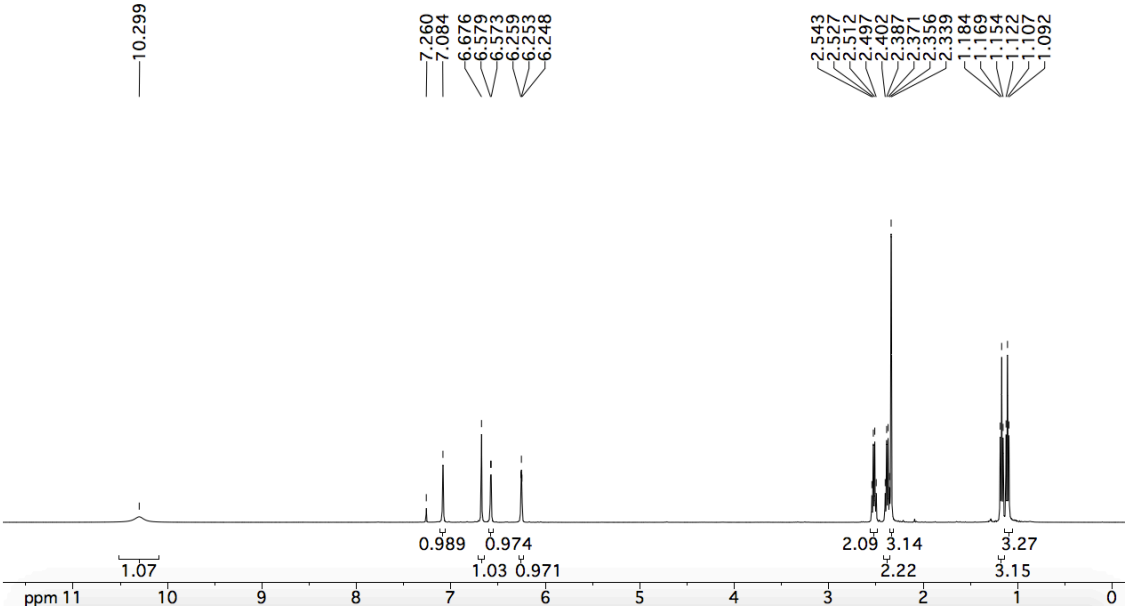
2D-HMBC ($CDCl_3$):



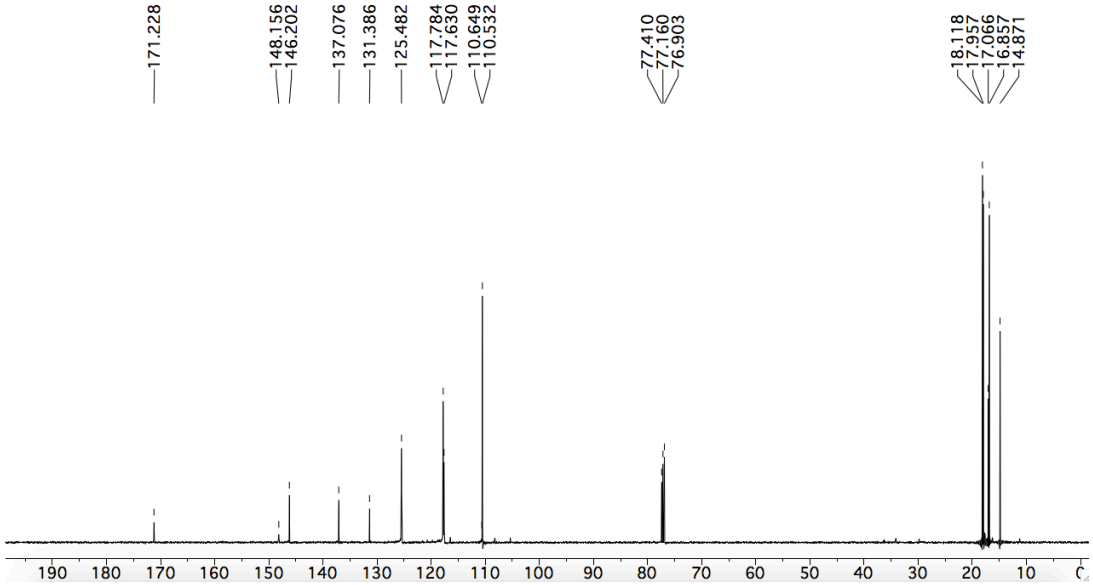
(*Z*)-2-((2*H*-Pyrrol-2-ylidene)methyl)-3,4-diethyl-5-methyl-1*H*-pyrrole (8)



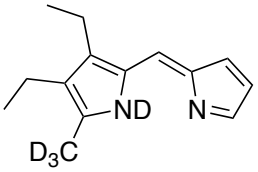
^{1}H-NMR ($CDCl_3$, 500 MHz):



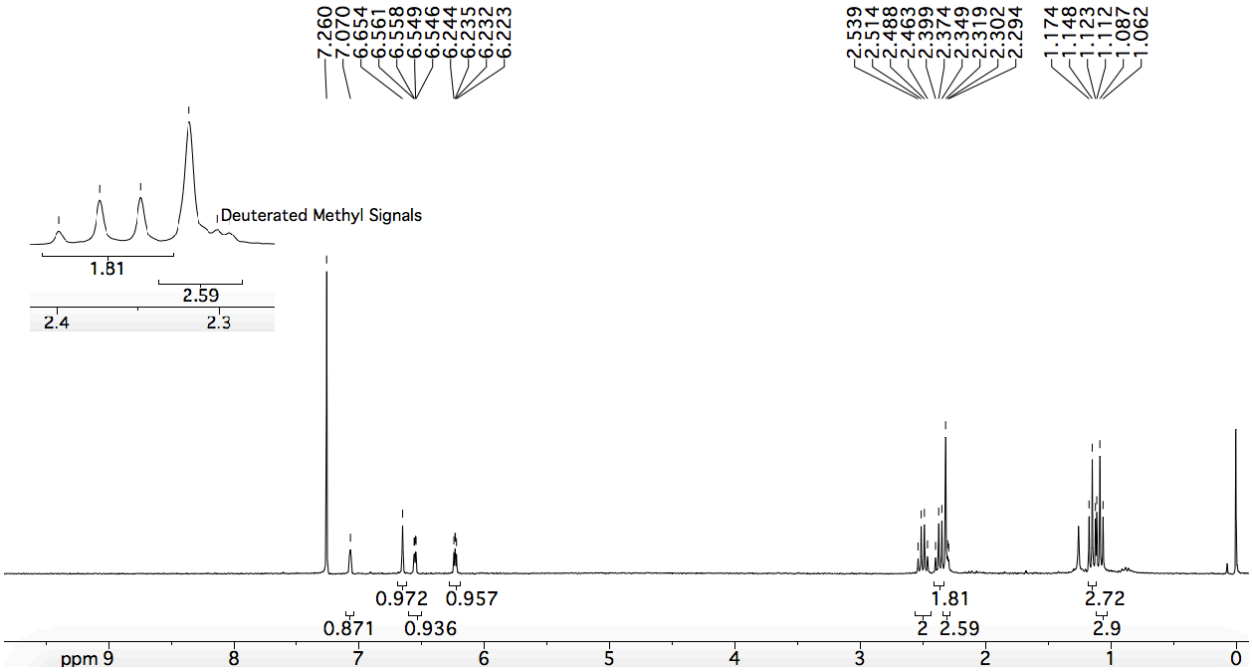
^{13}C UDEFT NMR ($CDCl_3$, 125 MHz)



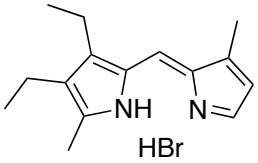
(*Z*)-2-((2*H*-Pyrrol-2-ylidene)methyl)-3,4-diethyl-5($^2H_3$)-methyl-1^2*H*-pyrrole (8-D_4)



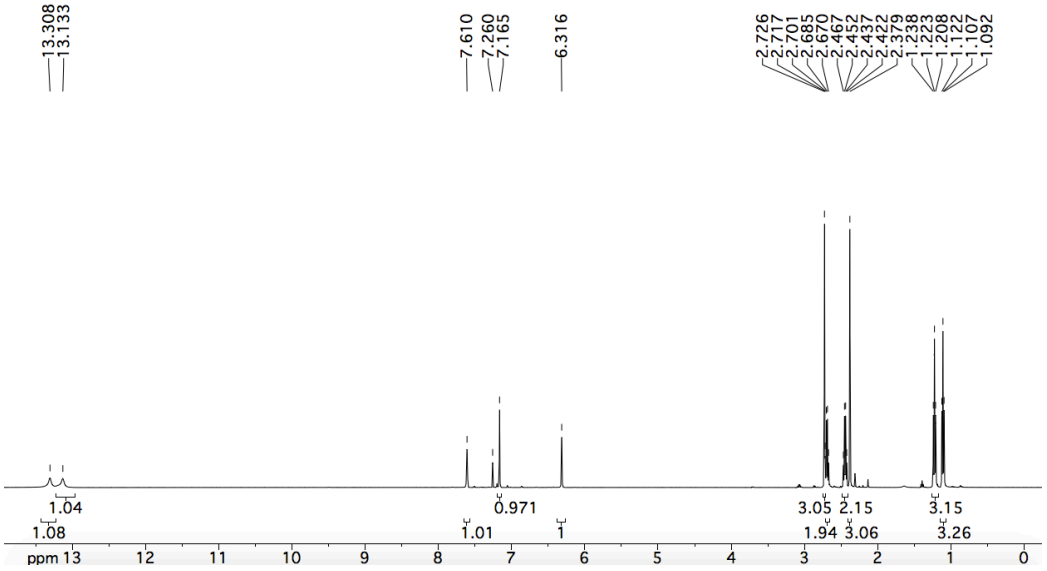
^{1}H-NMR ($CDCl_3$, 300 MHz):



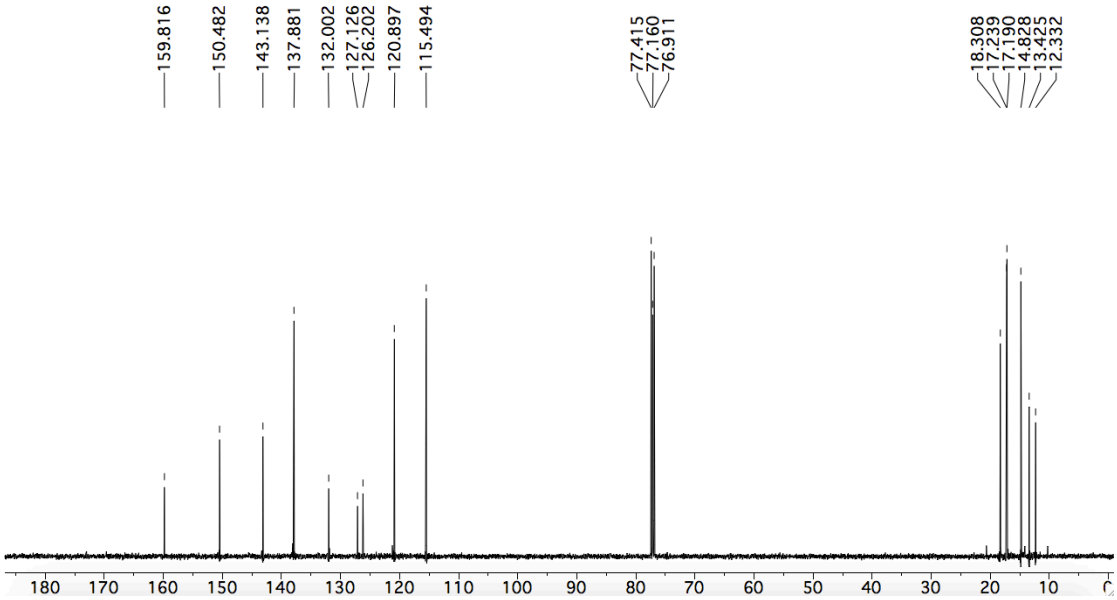
(*Z*)-3,4-Diethyl-2-methyl-5-((3-methyl-2*H*-pyrrol-2-ylidene)methyl)-1*H*-pyrrole hydrobromide (9•HBr)



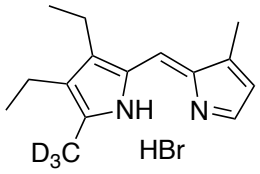
^{1}H-NMR ($CDCl_3$, 500 MHz):



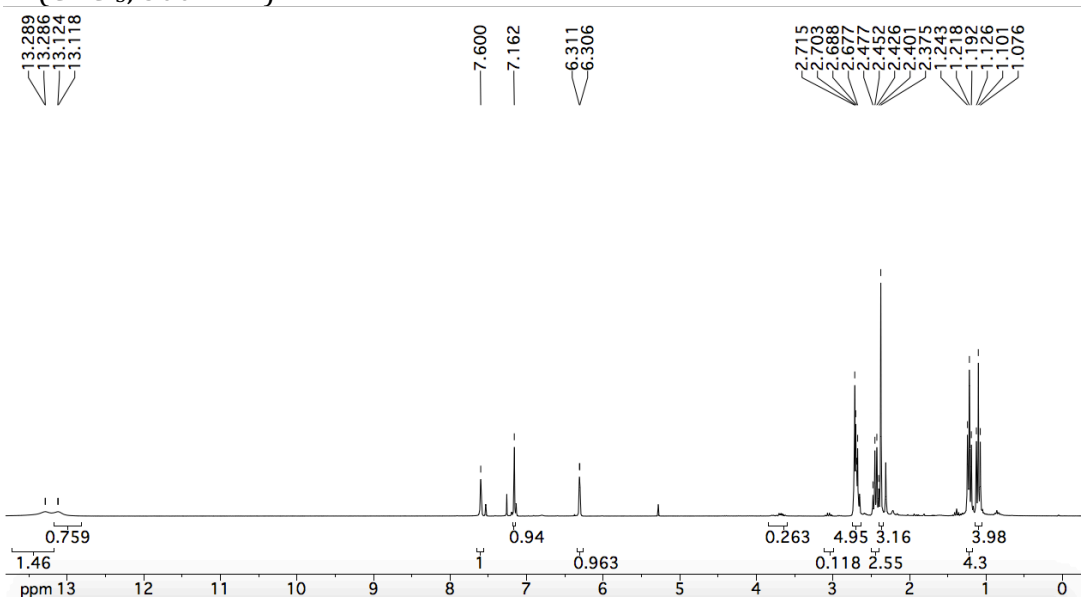
^{13}C UDEFT NMR ($CDCl_3$, 125 MHz)



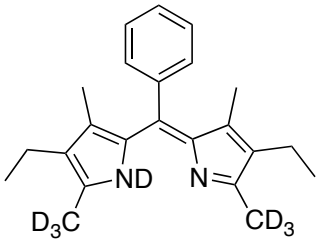
(*Z*)-3,4-Diethyl-2($^2H_3$)-methyl-5-((3-methyl-2*H*-pyrrol-2-ylidene)methyl)-1*H*-pyrrole hydrobromide (9-D_3•HBr)



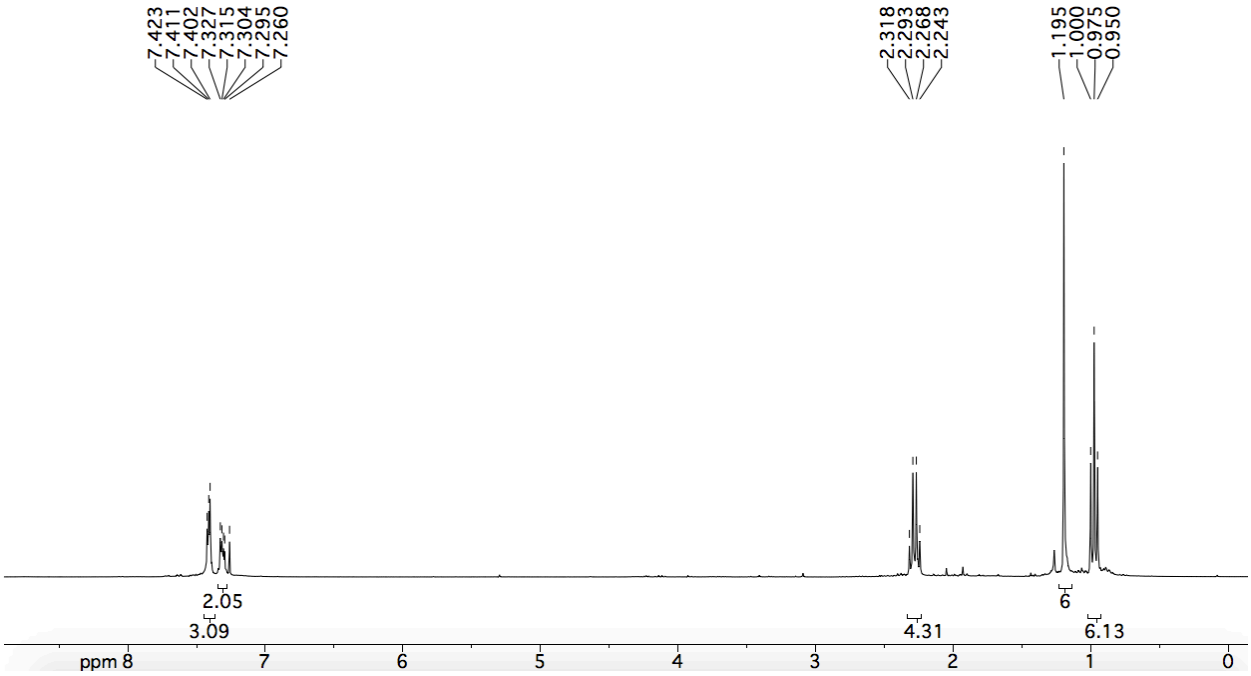
^{1}H-NMR ($CDCl_3$, 300 MHz):



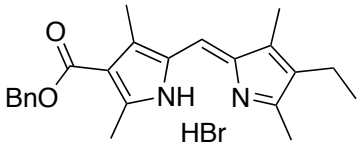
(*Z*)-3-Ethyl-5-((4-ethyl-3($^2H_3$),5-dimethyl-2*H*-pyrrol-2-ylidene)(phenyl)methyl)-2($^2H_3$),4-dimethyl-1^2*H*-pyrrole (11-D_7)



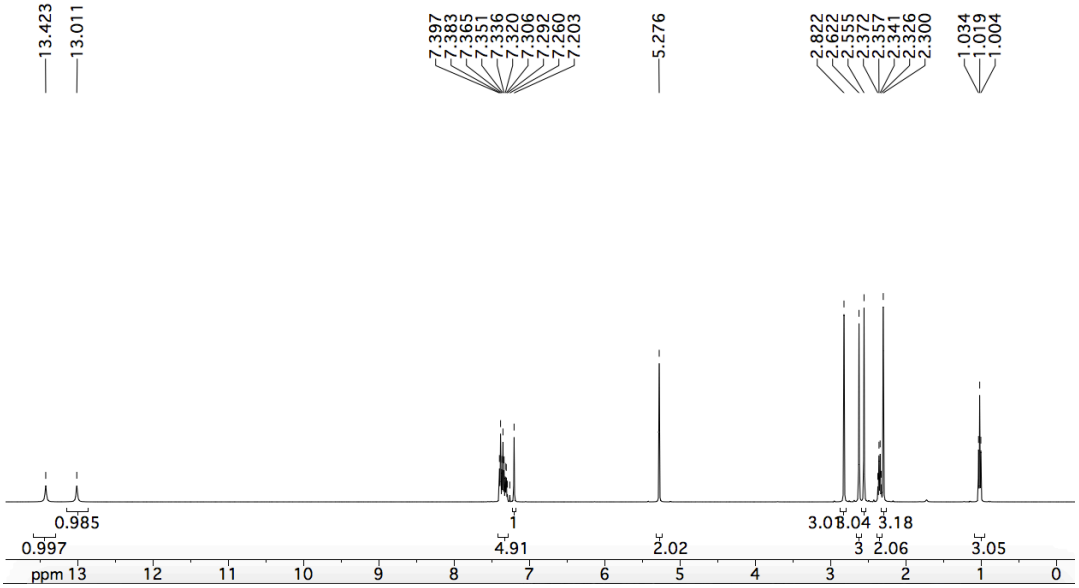
^{1}H-NMR ($CDCl_3$, 300 MHz):



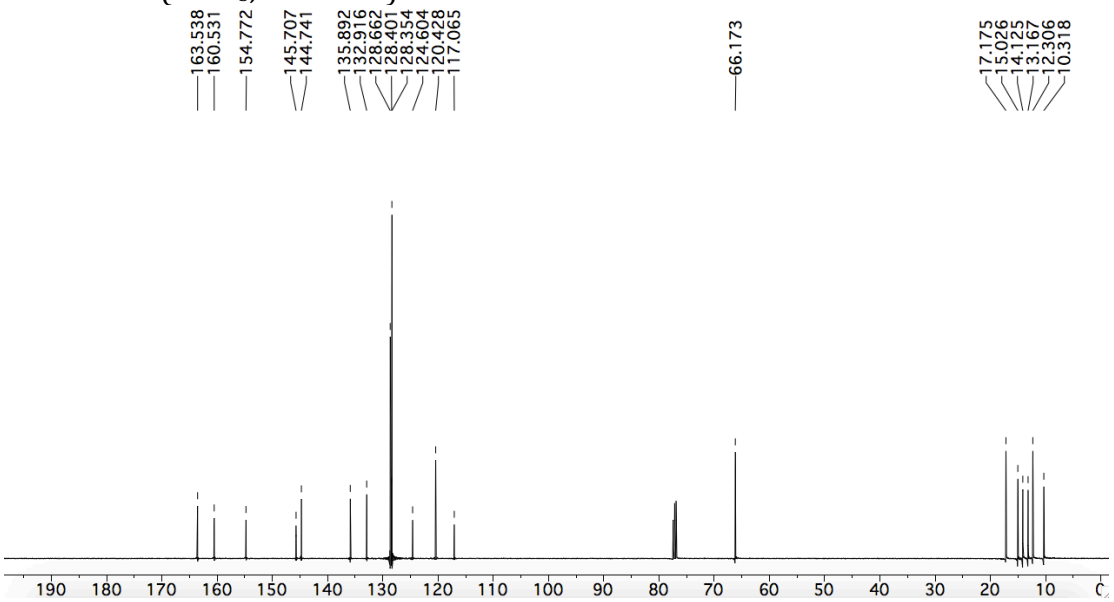
(*Z*)-Benzyl 5-((4-ethyl-3,5-dimethyl-2*H*-pyrrol-2-ylidene)methyl)-2,4-dimethyl-1*H*-pyrrole-3-carboxylate hydrobromide (12•HBr)



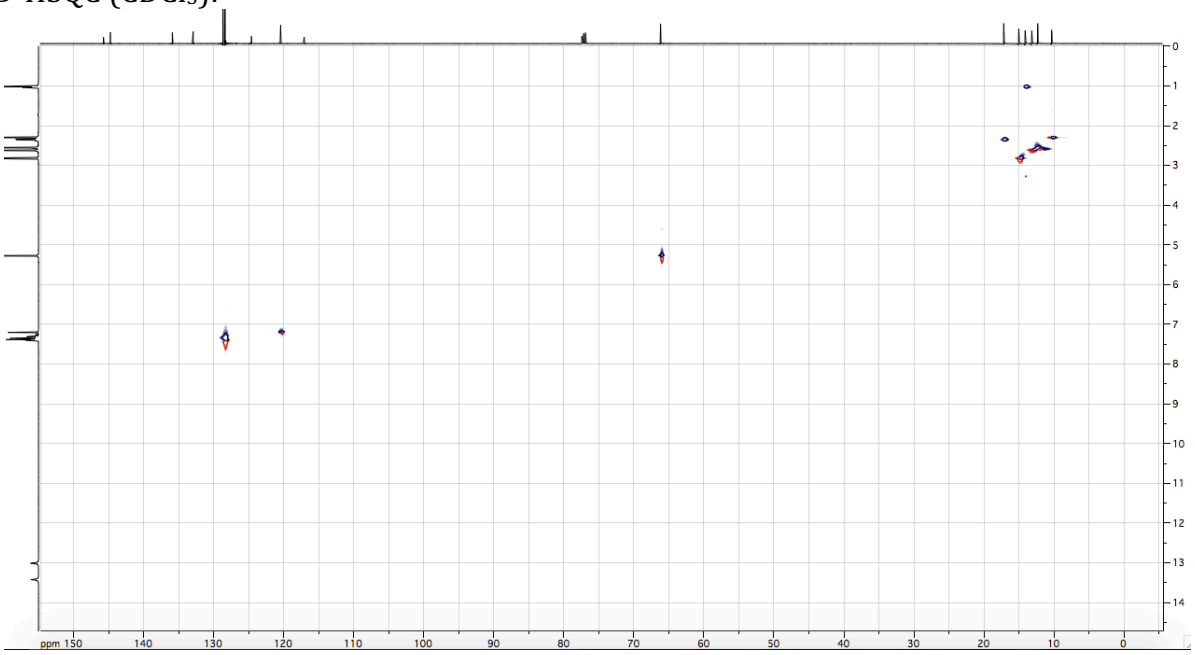
^{1}H-NMR ($CDCl_3$, 500 MHz):



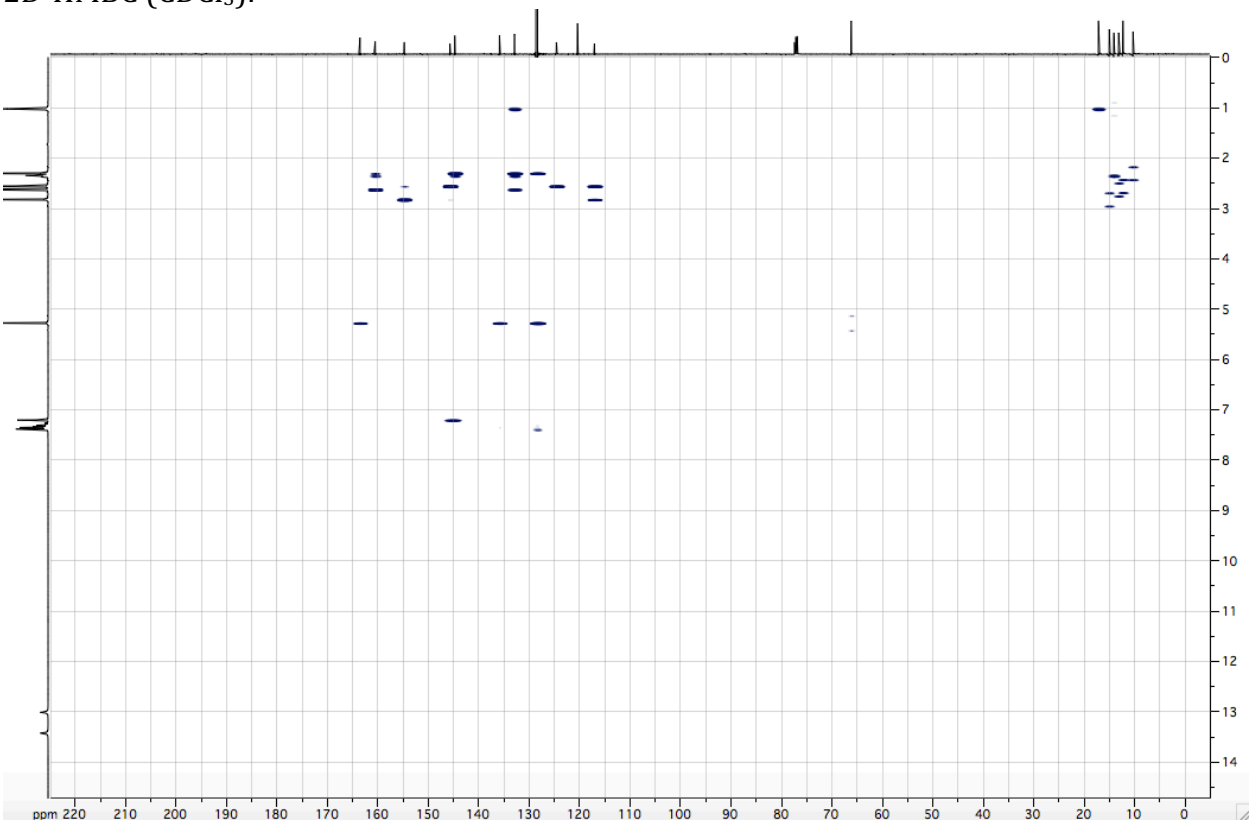
^{13}C UDEFT NMR ($CDCl_3$, 125 MHz):



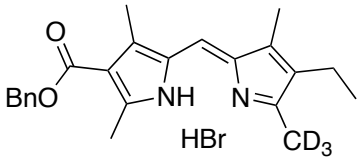
2D-HSQC ($CDCl_3$):



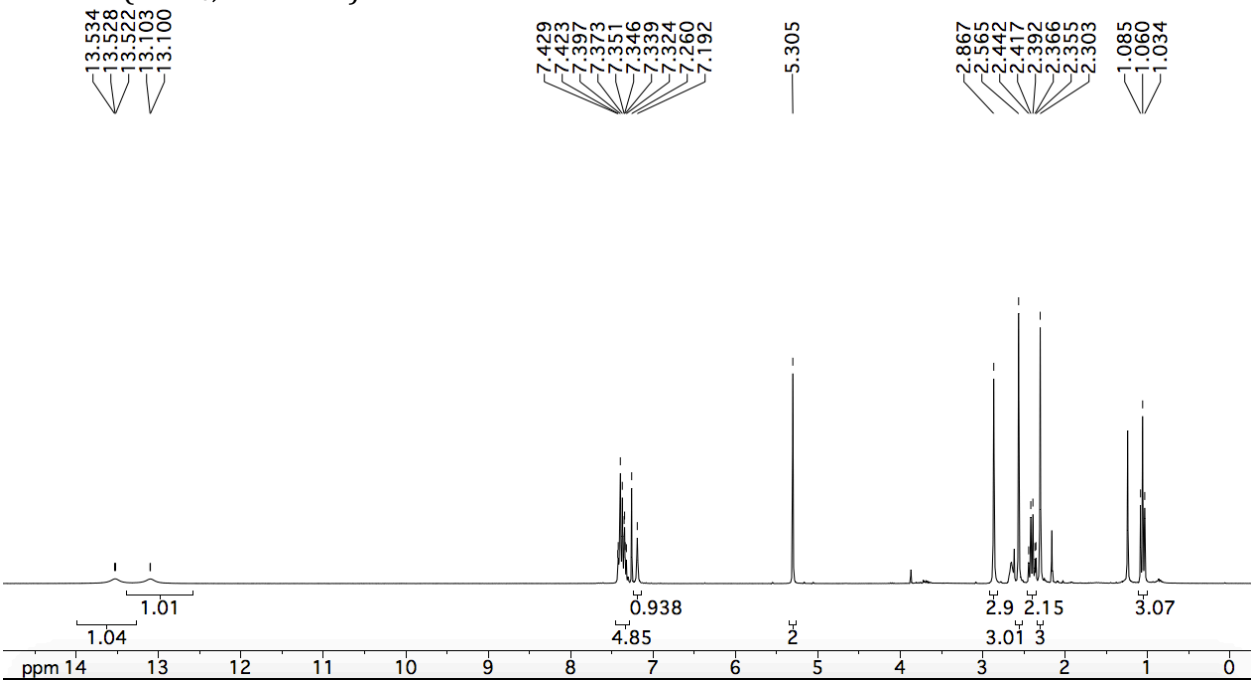
2D-HMBC ($CDCl_3$):



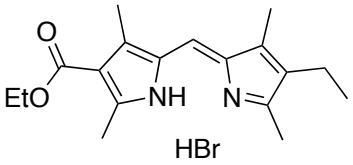
(*Z*)-Benzyl 5-((4-ethyl-3,5 -dimethyl-2*H*-pyrrol-2-ylidene)methyl)-2,4-dimethyl-1*H*-pyrrole-3-carboxylate hydrobromide (12-D_3•HBr)



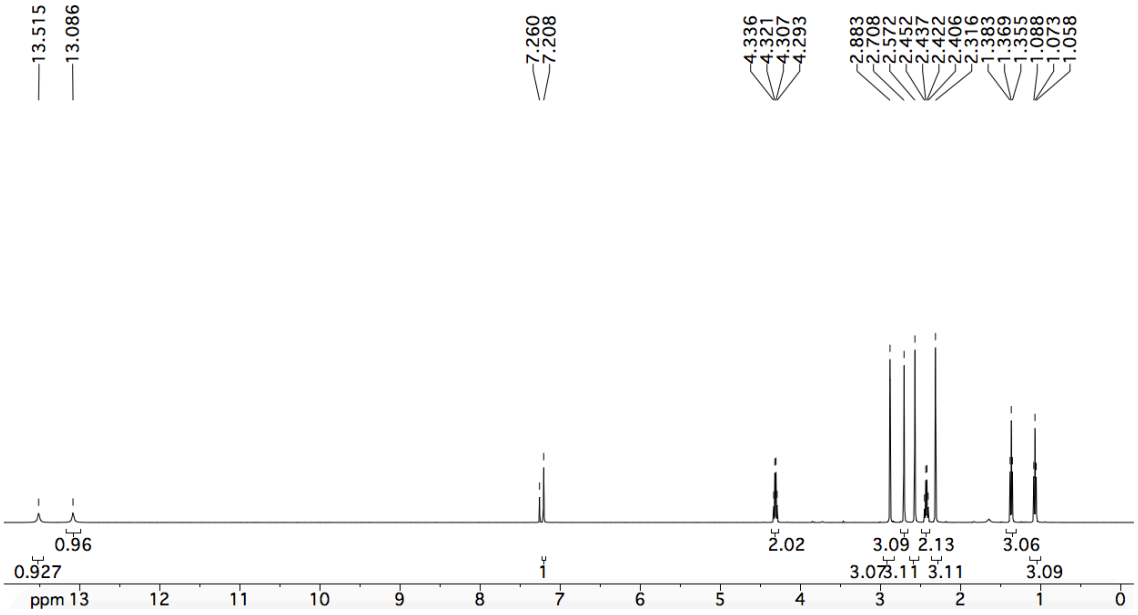
^{1}H-NMR ($CDCl_3$, 300 MHz):



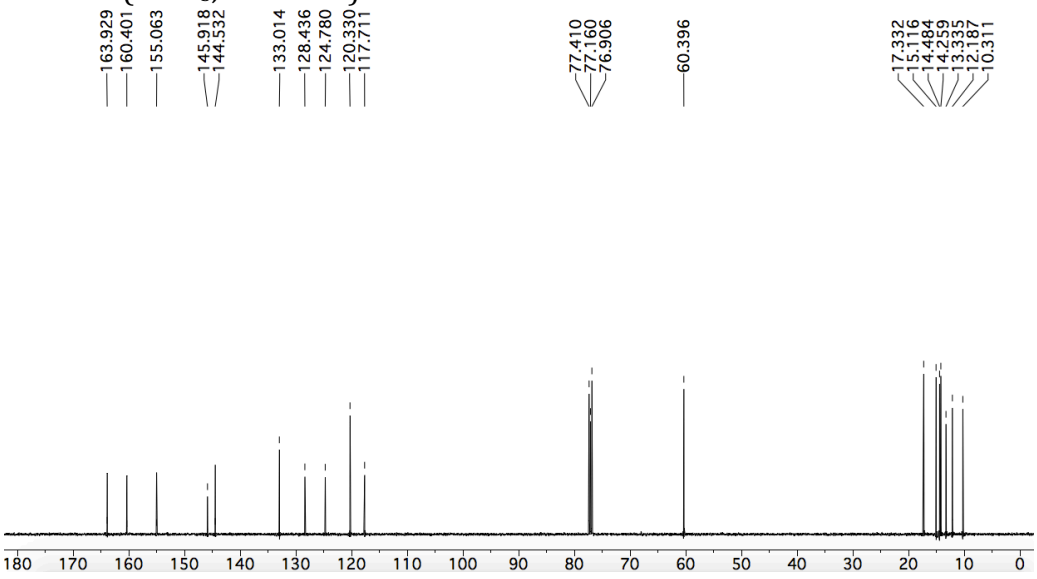
(*Z*)-Ethyl 5-((4-ethyl-3,5-dimethyl-2*H*-pyrrol-2-ylidene)methyl)-2,4-dimethyl-1*H*-pyrrole-3-carboxylate hydrobromide (13•HBr)



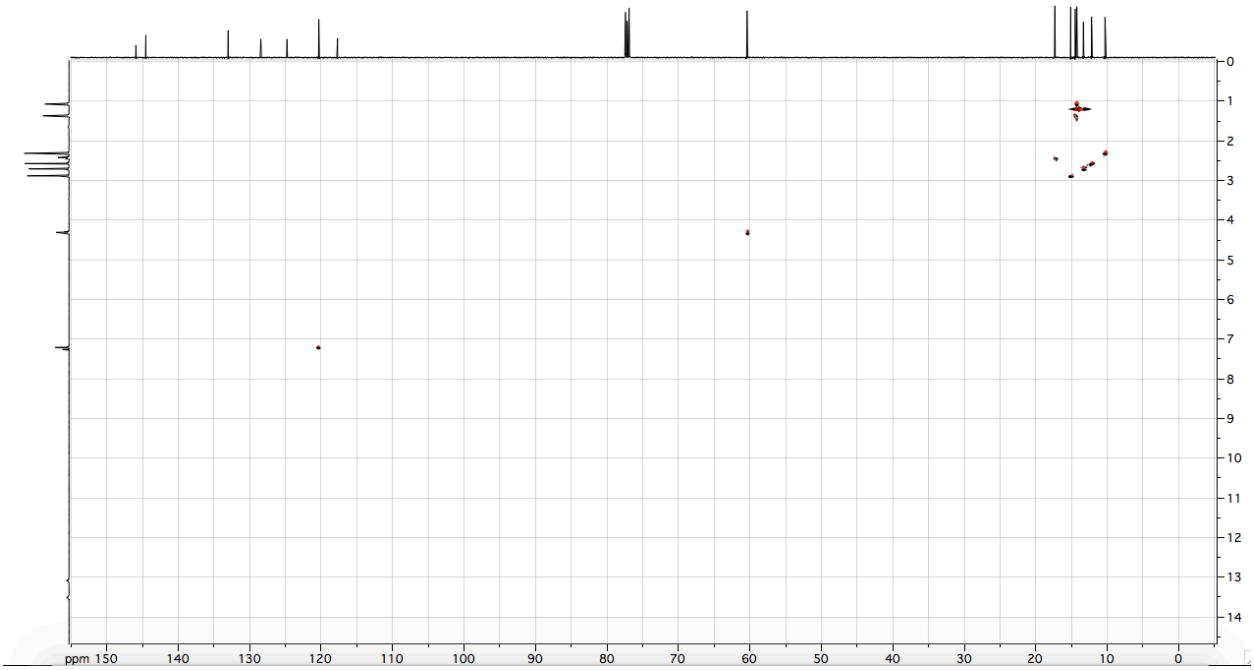
^{1}H-NMR ($CDCl_3$, 500 MHz):



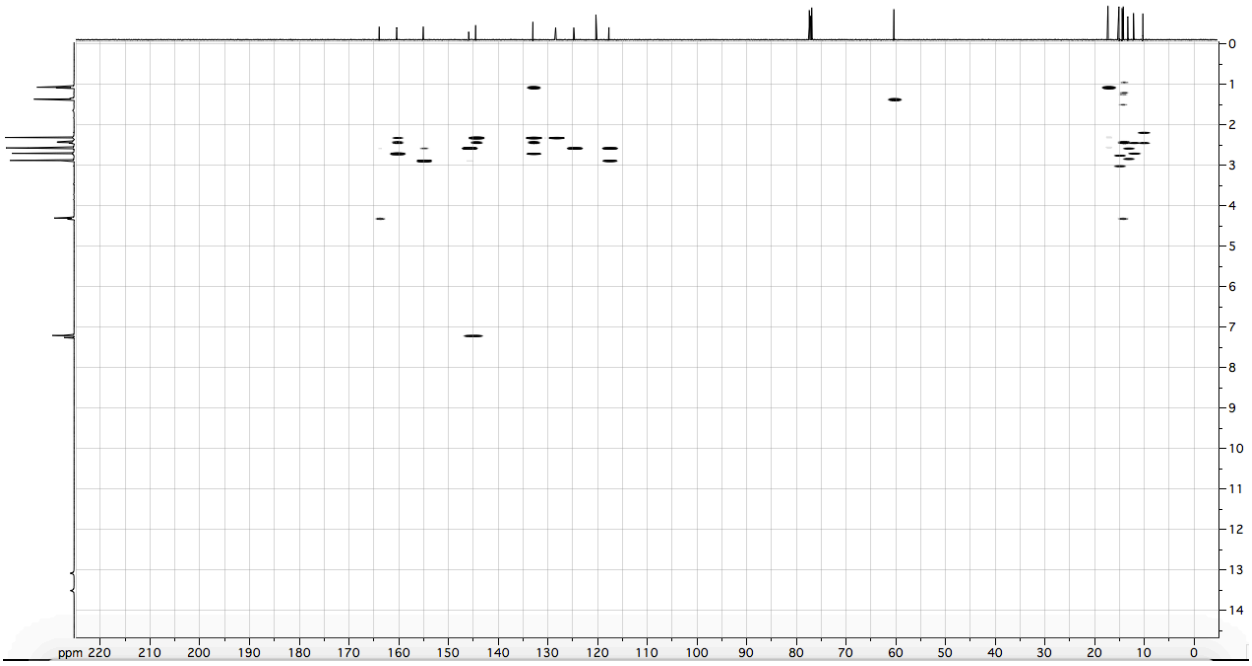
^{13}C UDEFT NMR ($CDCl_3$, 125 MHz):



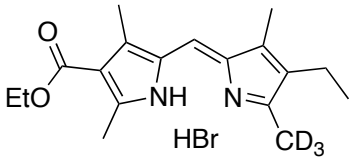
2D-HSQC ($CDCl_3$):



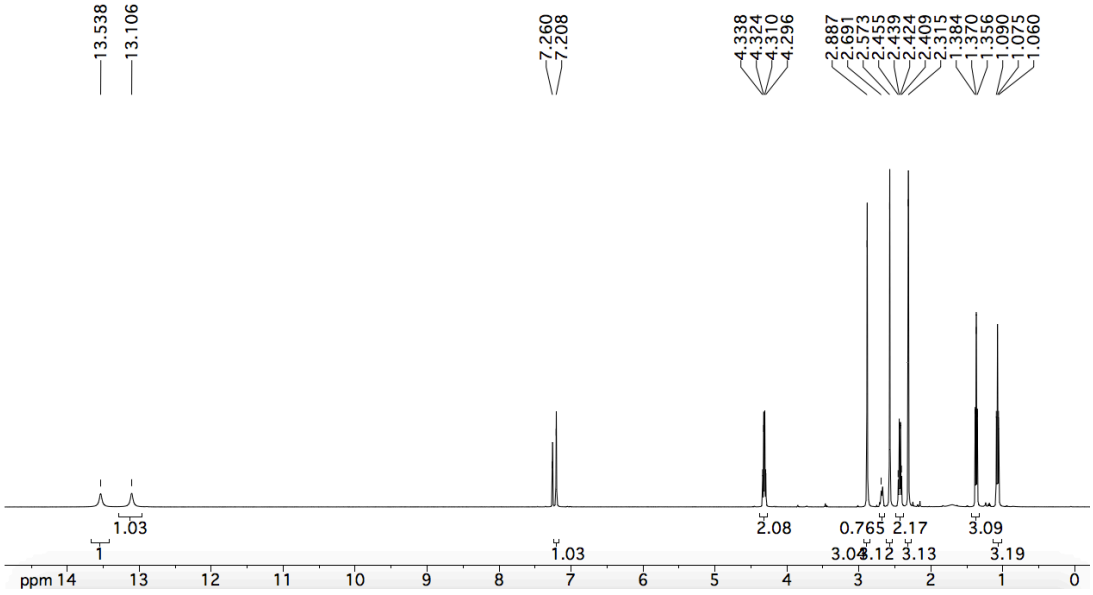
2D-HMBC ($CDCl_3$):



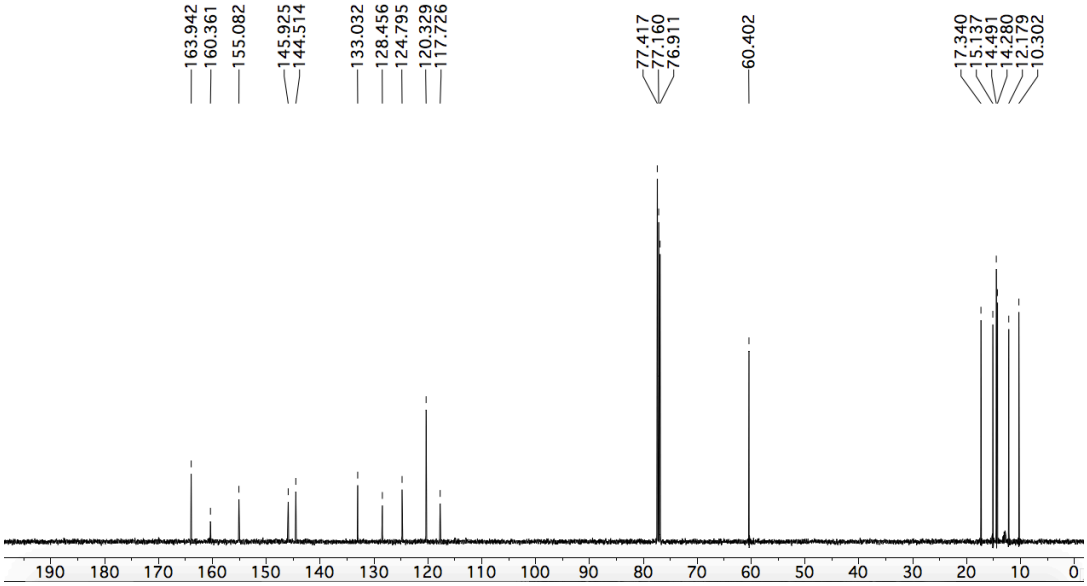
(*Z*)-Ethyl 5-((4-ethyl-3,5($^2H_3$)-dimethyl-2*H*-pyrrol-2-ylidene)methyl)-2($^2H_3$),4-dimethyl-1*H*-pyrrole-3-carboxylate hydrobromide (13-D_3•HBr)



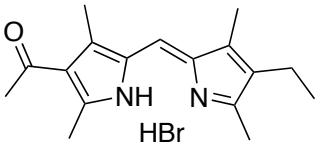
. ^{1}H-NMR ($CDCl_3$, 500 MHz):



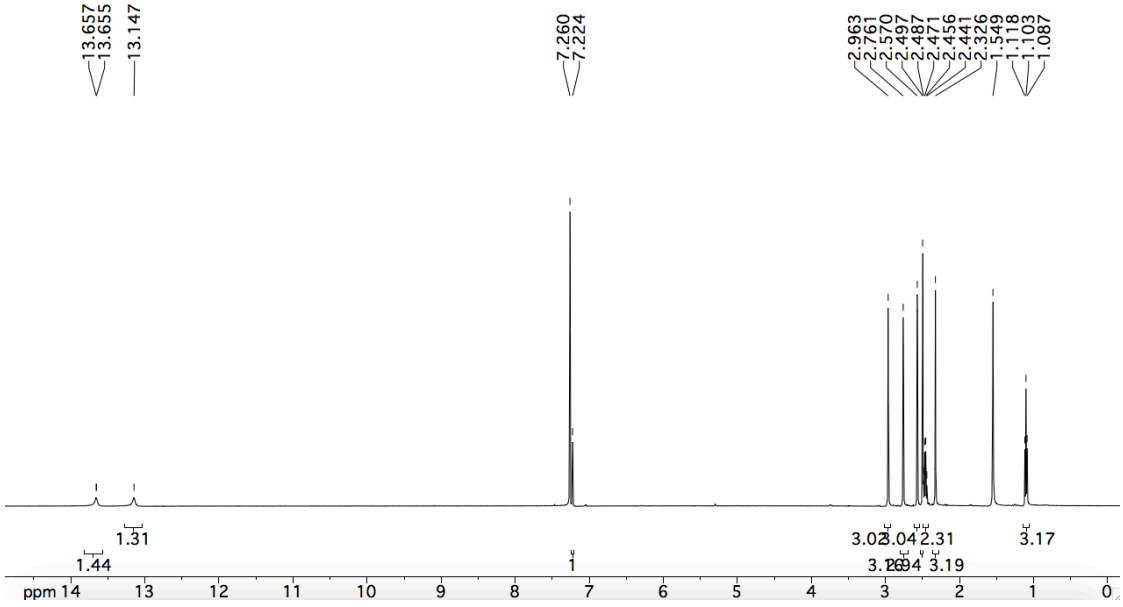
^{13}C UDEFT NMR ($CDCl_3$, 125 MHz):



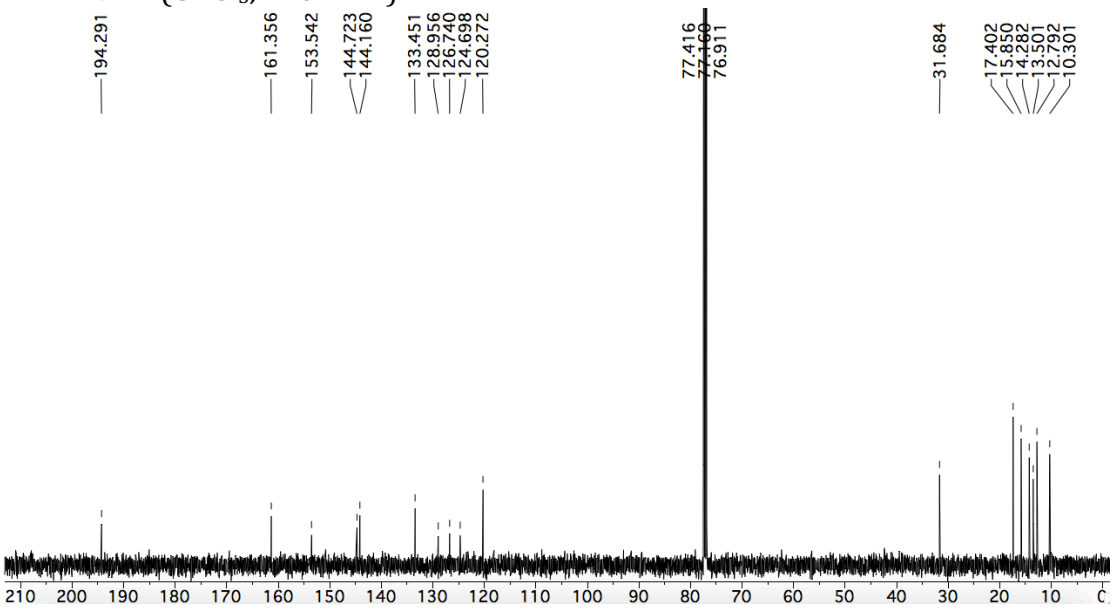
(*Z*)-1-(5-((4-Ethyl-3,5-dimethyl-2*H*-pyrrol-2-ylidene)methyl)-2,4-dimethyl-1*H*-pyrrol-3-yl)ethanone hydrobromide (14•HBr)



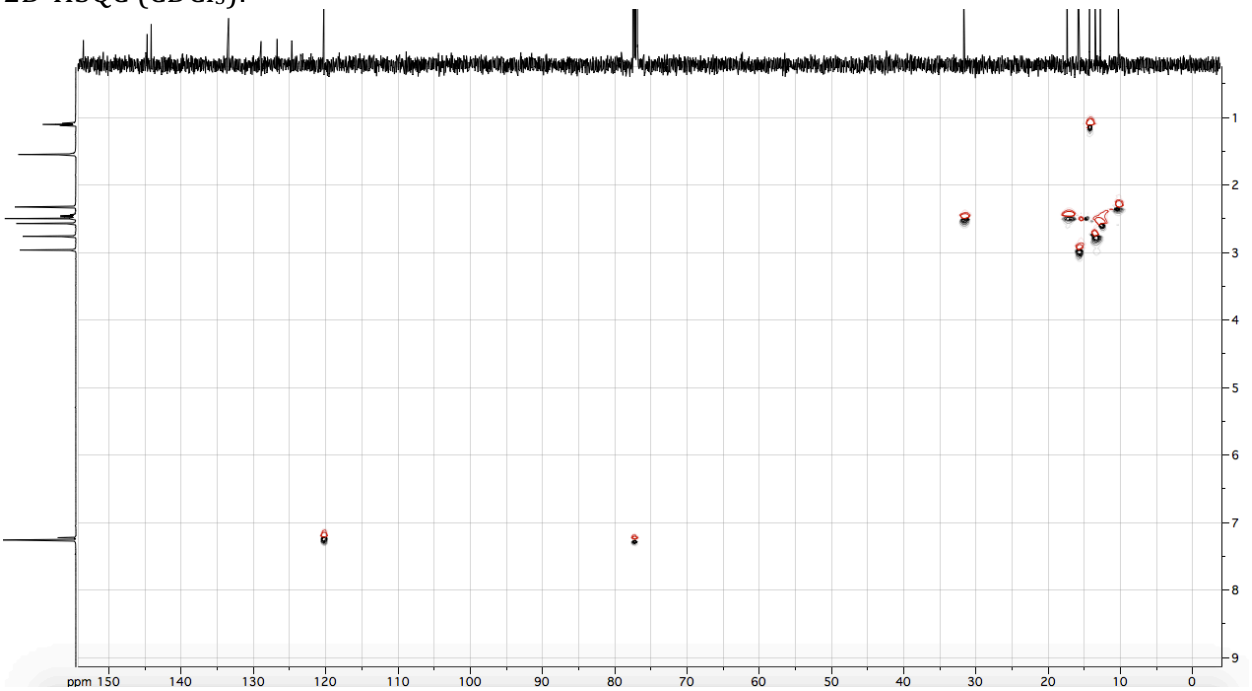
^{1}H-NMR ($CDCl_3$, 500 MHz):



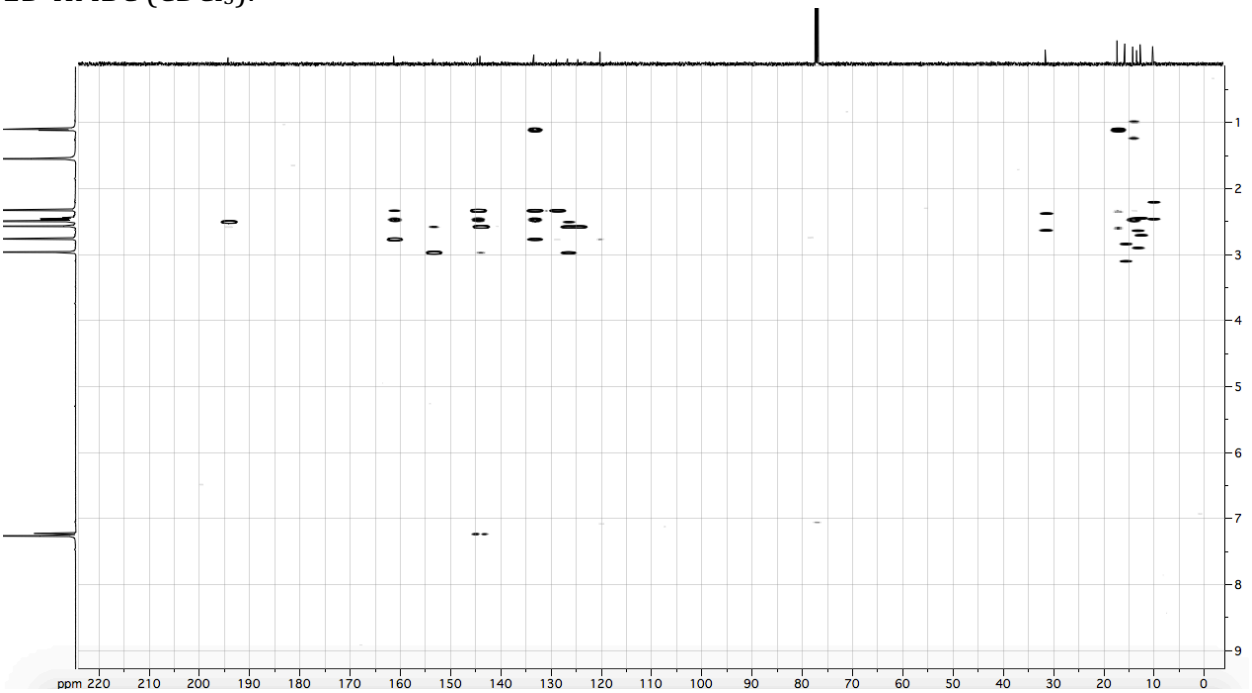
^{13}C UDEFT NMR ($CDCl_3$, 125 MHz):



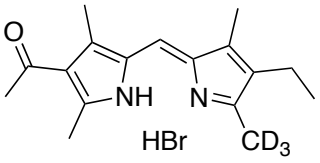
2D-HSQC ($CDCl_3$):



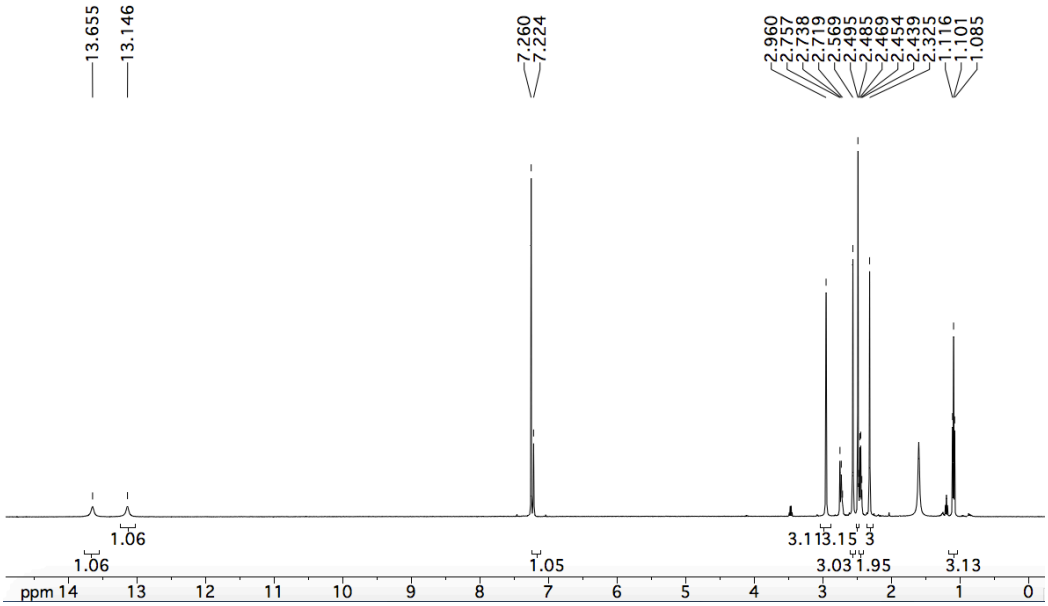
2D-HMBC ($CDCl_3$):



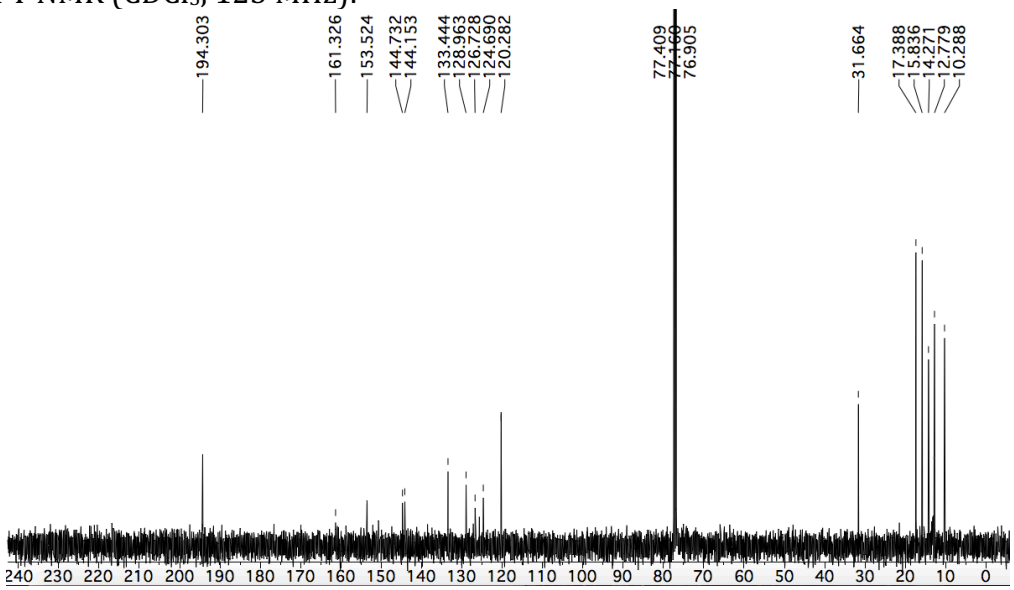
(*Z*)-1-(5-((4-Ethyl-3,5($^2H_3$)-dimethyl-2*H*-pyrrol-2-ylidene)methyl)-2,4-dimethyl-1*H*-pyrrol-3-yl)ethanone hydrobromide (14-D_3•HBr)



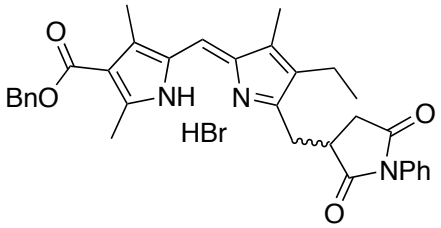
^{1}H-NMR ($CDCl_3$, 500 MHz):



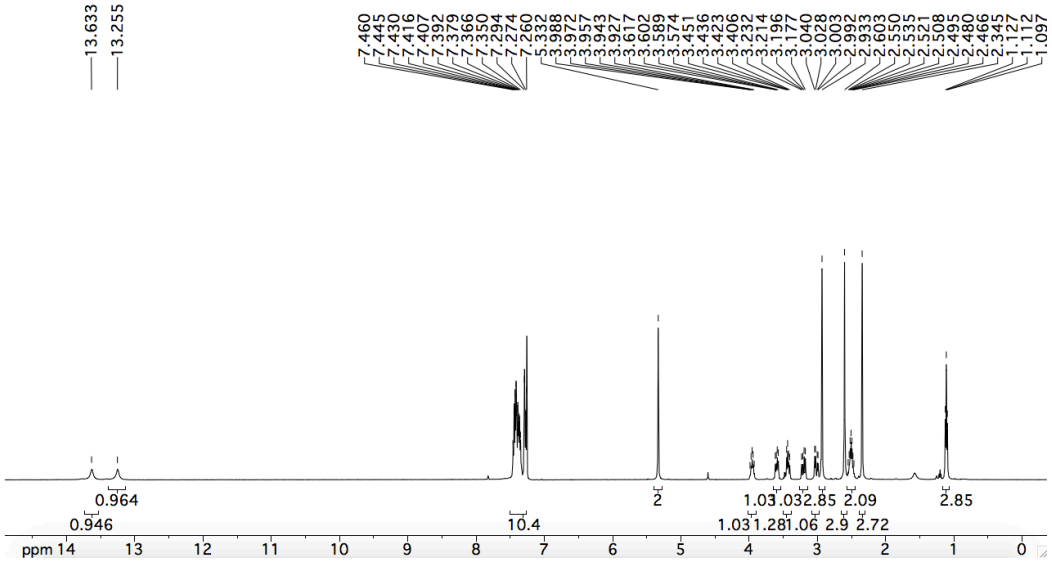
^{13}C UDEFT NMR ($CDCl_3$, 125 MHz):



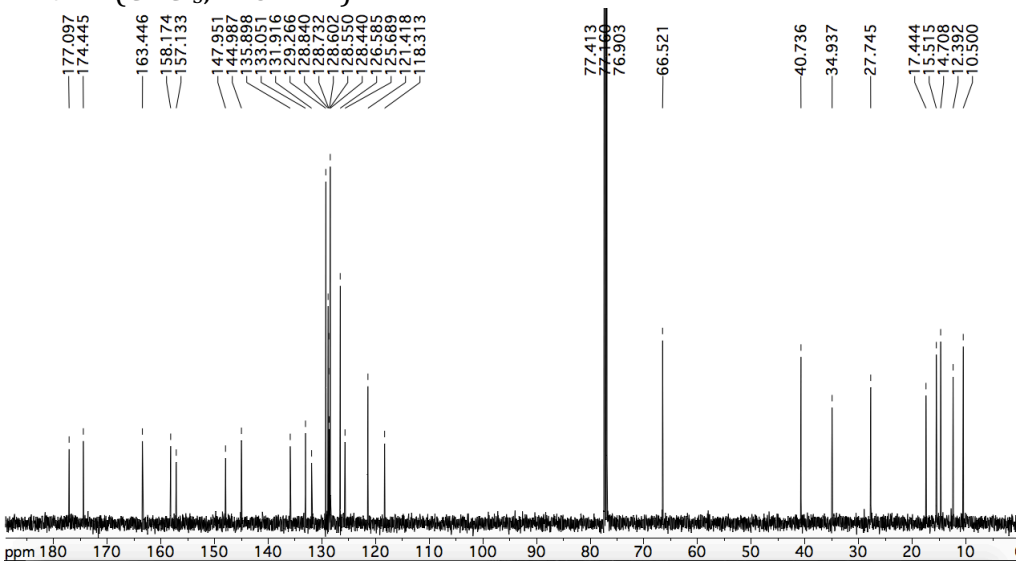
(*Z*)-Benzyl 5-((5-((2,5-dioxo-1-phenylpyrrolidin-3-yl)methyl)-4-ethyl-3-methyl-2*H*-pyrrol-2-ylidene)methyl)-2,4-dimethyl-1*H*-pyrrole-3-carboxylate hydrobromide (16•HBr)



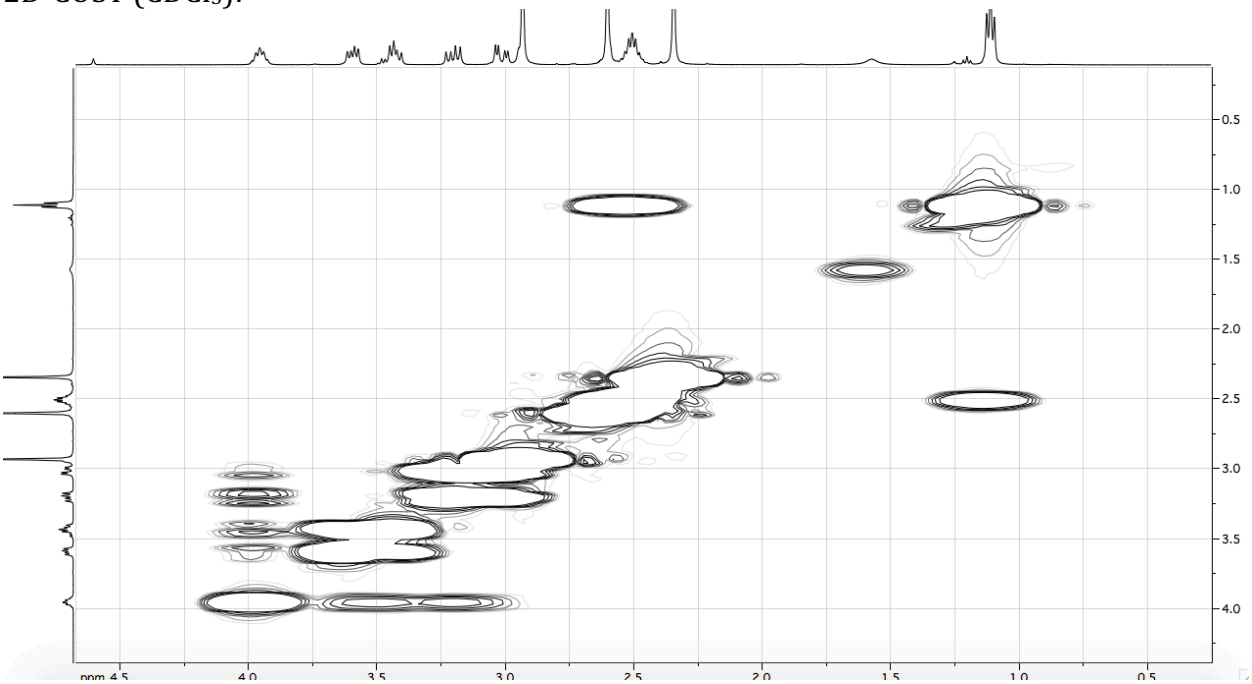
^{1}H-NMR ($CDCl_3$, 500 MHz):



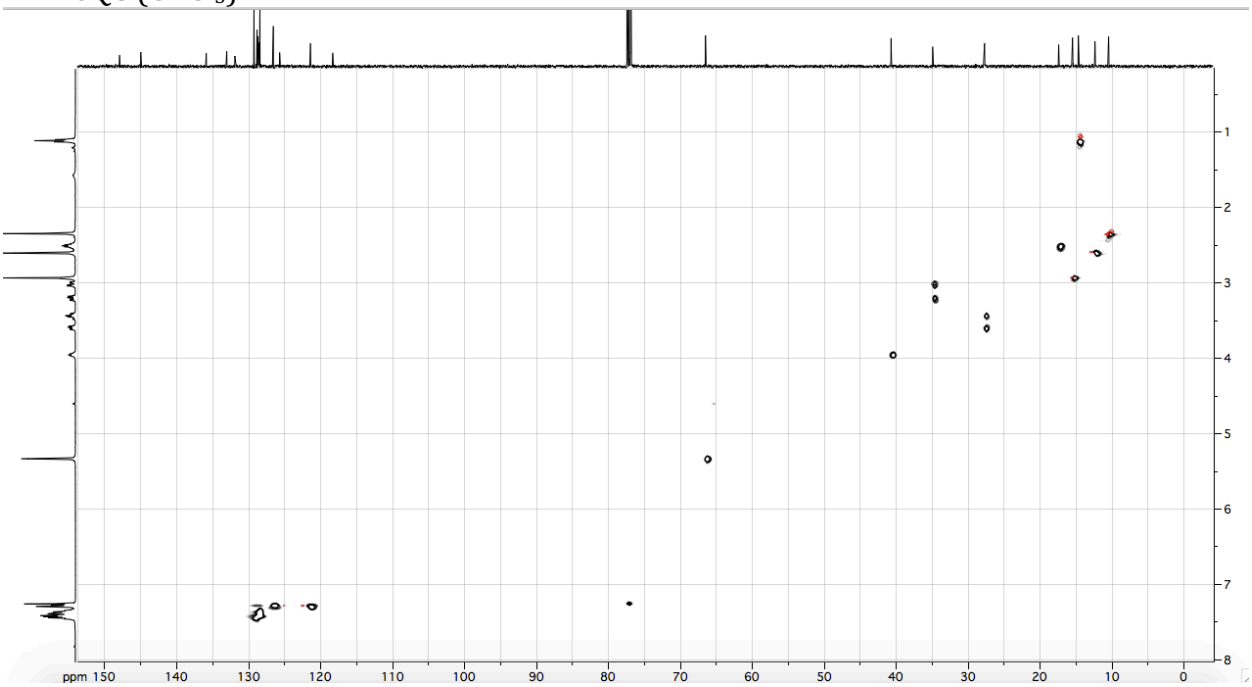
^{13}C UDEFT NMR ($CDCl_3$, 125 MHz):



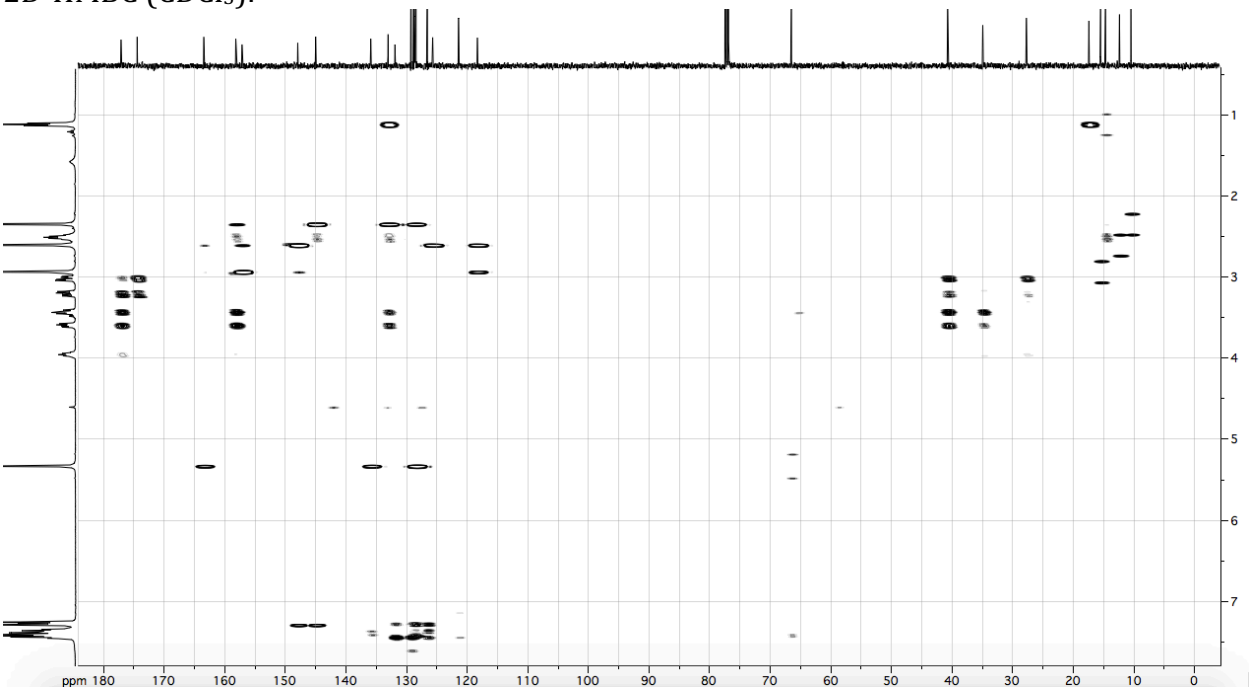
2D-COSY ($CDCl_3$):



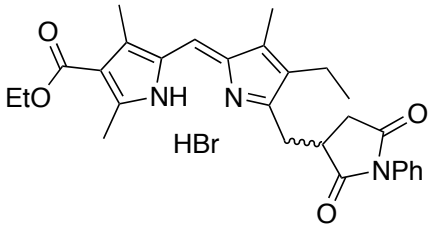
2D-HSQC ($CDCl_3$):



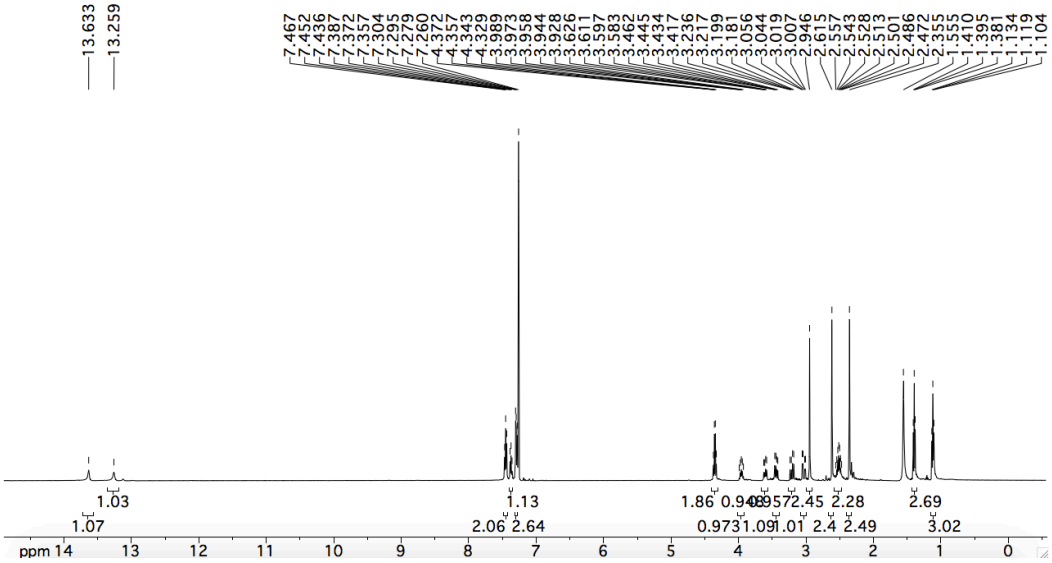
2D-HMBC ($CDCl_3$):



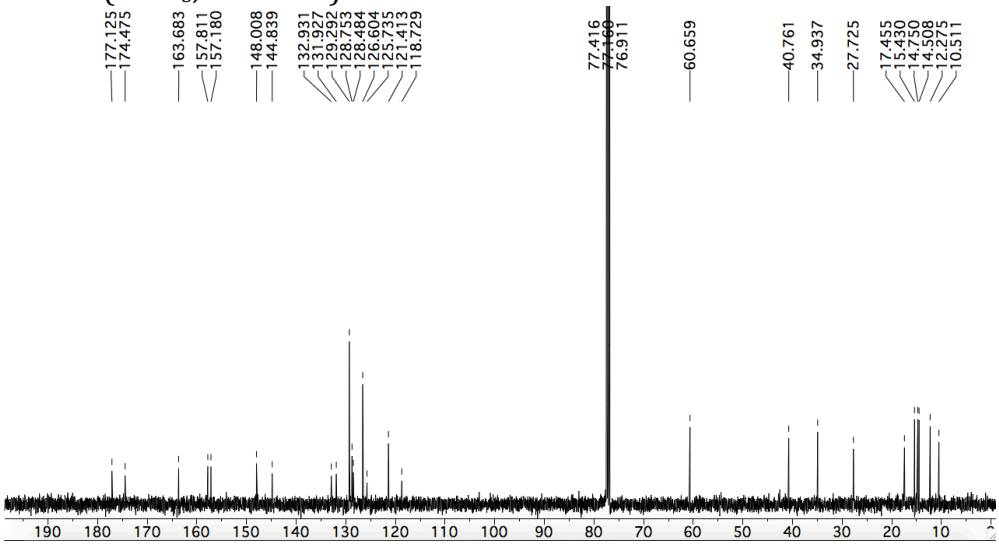
(*Z*)-Ethyl 5-((5-((2,5-dioxo-1-phenylpyrrolidin-3-yl)methyl)-4-ethyl-3-methyl-2*H*-pyrrol-2-ylidene)methyl)-2,4-dimethyl-1*H*-pyrrole-3-carboxylate hydrobromide (17•HBr)



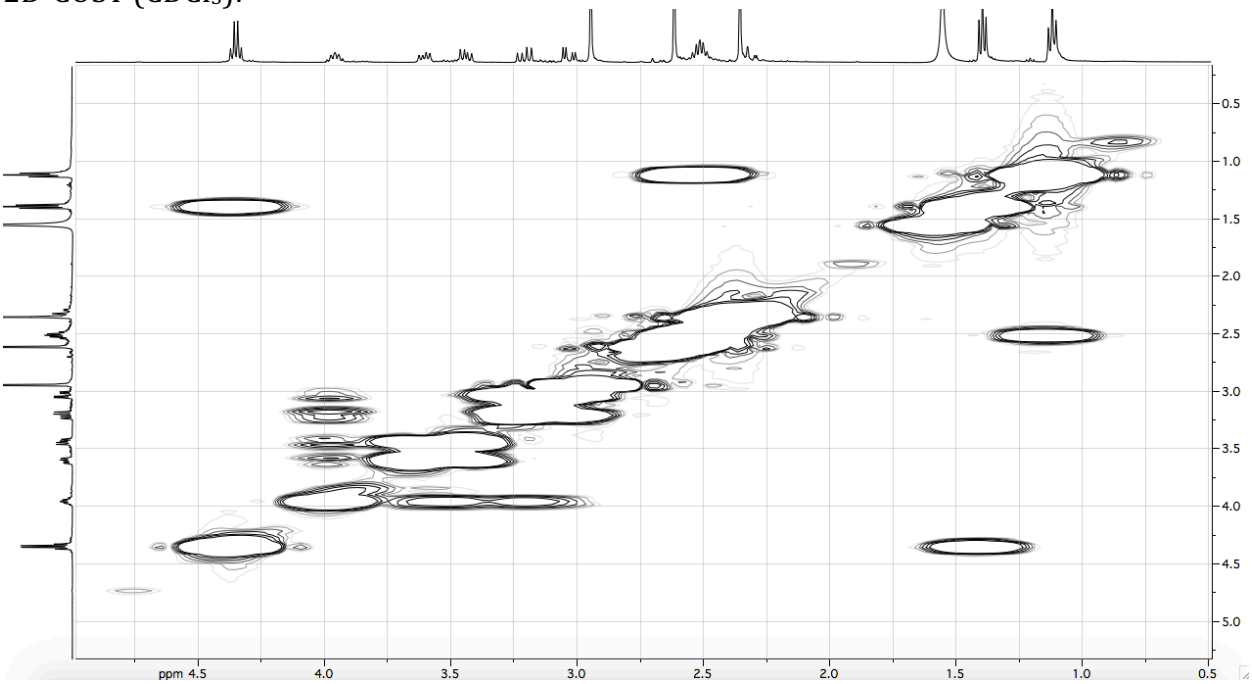
^{1}H-NMR ($CDCl_3$, 500 MHz):



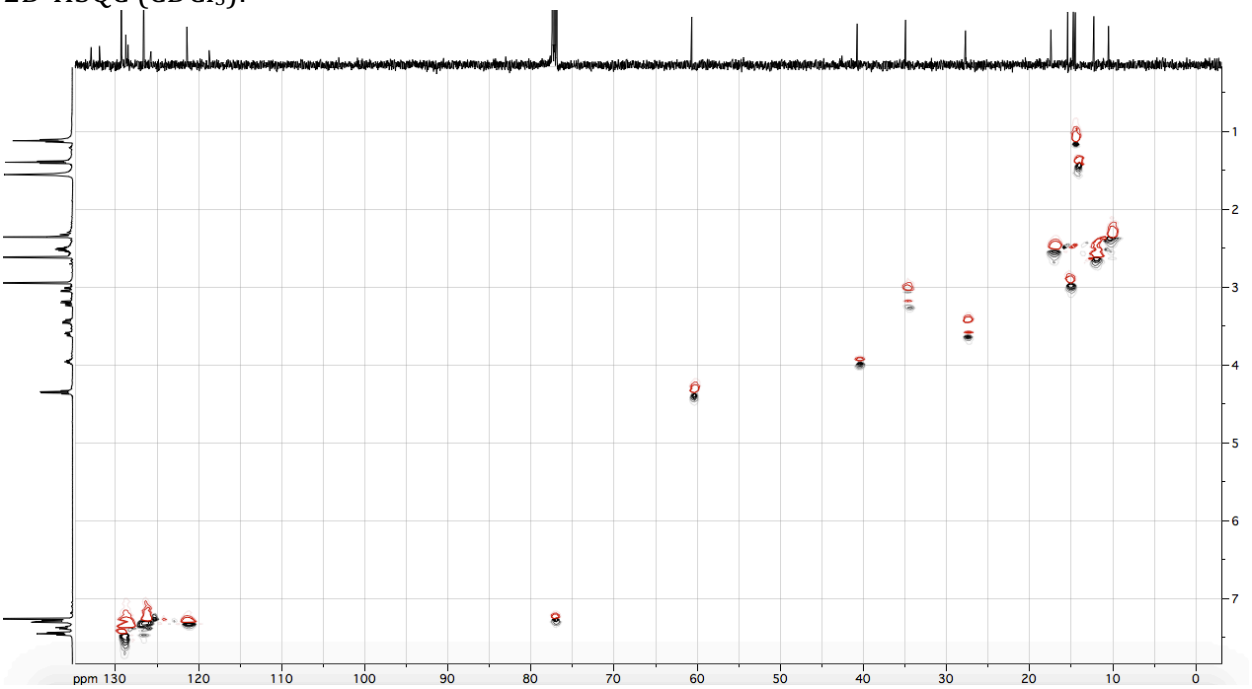
^{13}C UDEFT NMR ($CDCl_3$, 125 MHz):



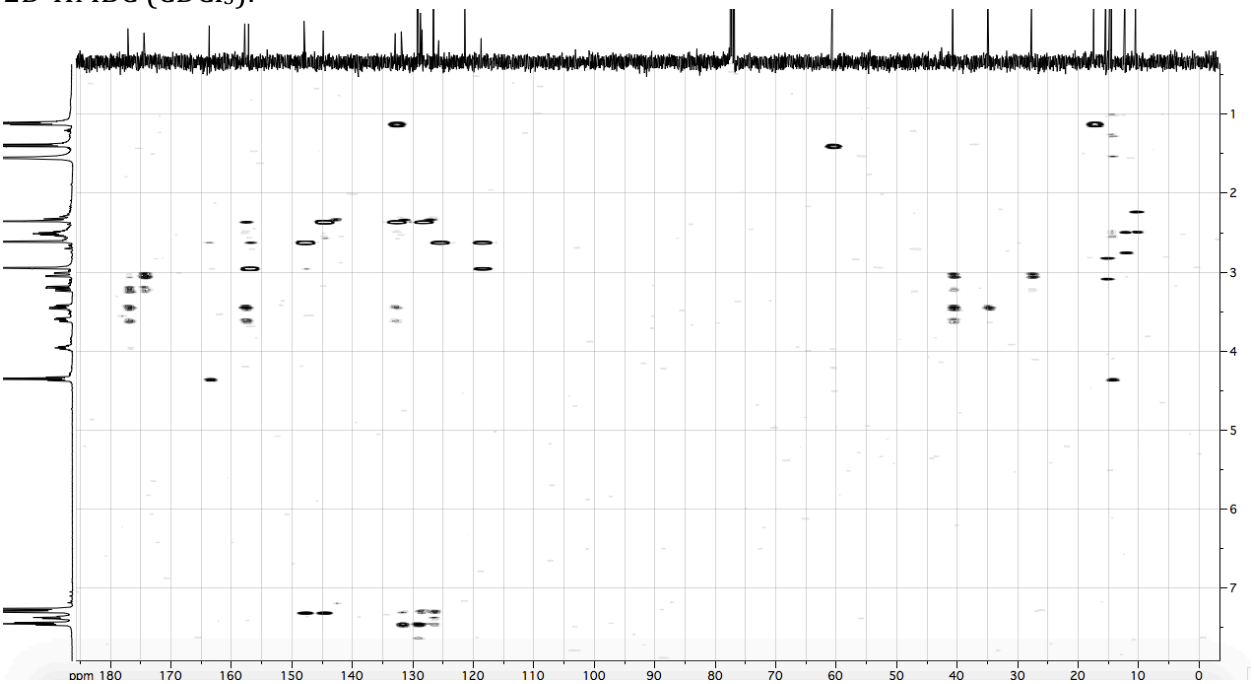
2D-COSY ($CDCl_3$):



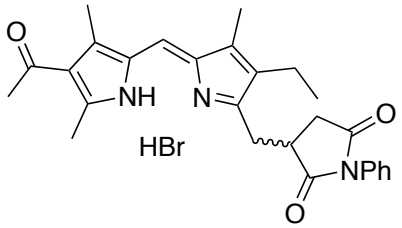
2D-HSQC ($CDCl_3$):



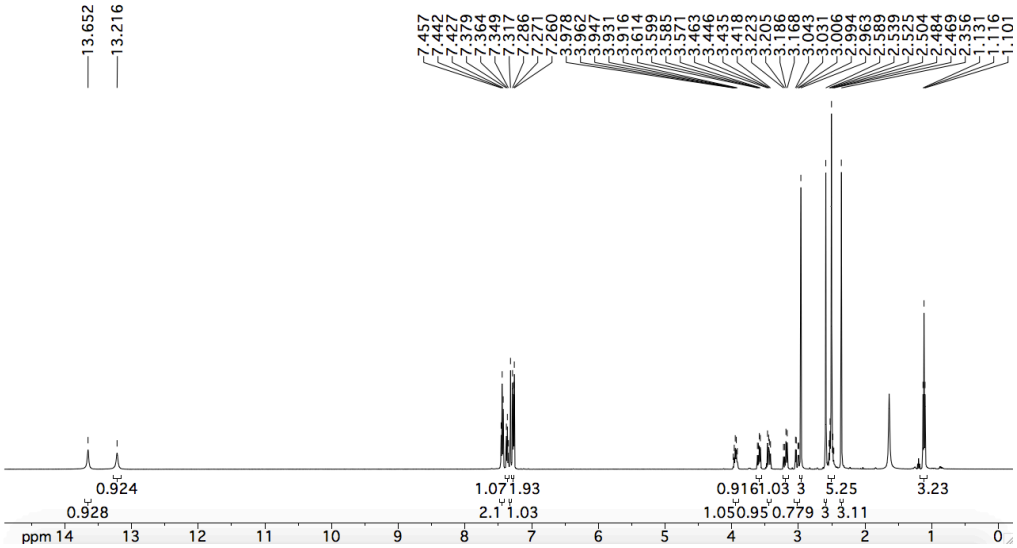
2D-HMBC ($CDCl_3$):



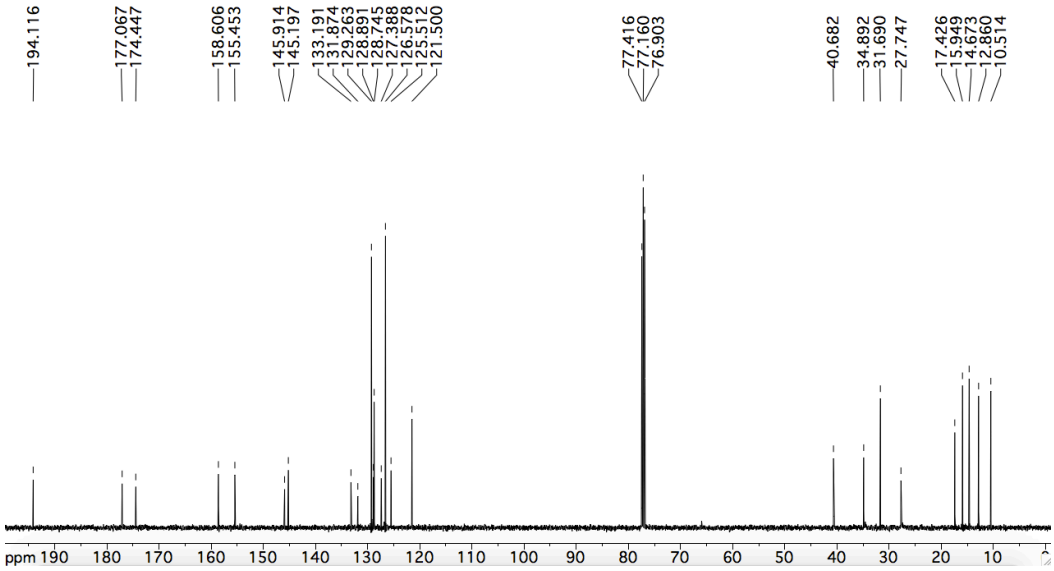
(*Z*)-3-((2-((4-Acetyl-3,5-dimethyl-1*H*-pyrrol-2-yl)methylene)-4-ethyl-3-methyl-2*H*-pyrrol-5-yl)methyl)-1-phenylpyrrolidine-2,5-dione hydrobromide (18•HBr)



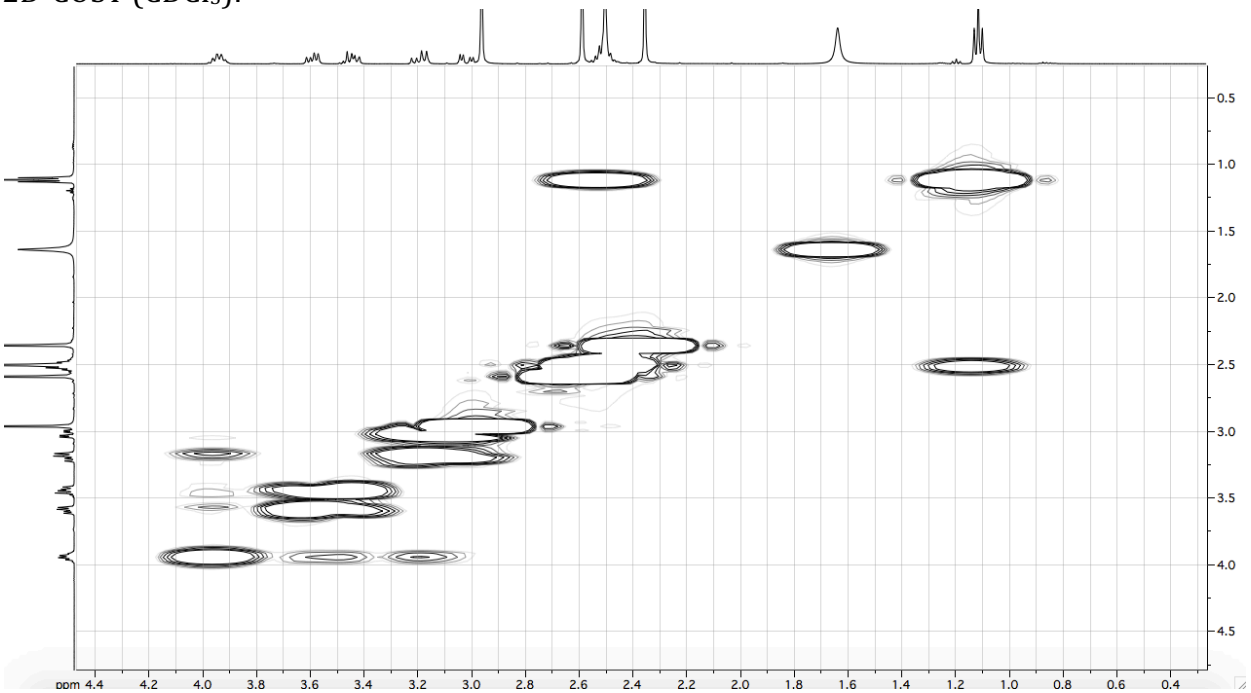
^{1}H-NMR ($CDCl_3$, 500 MHz):



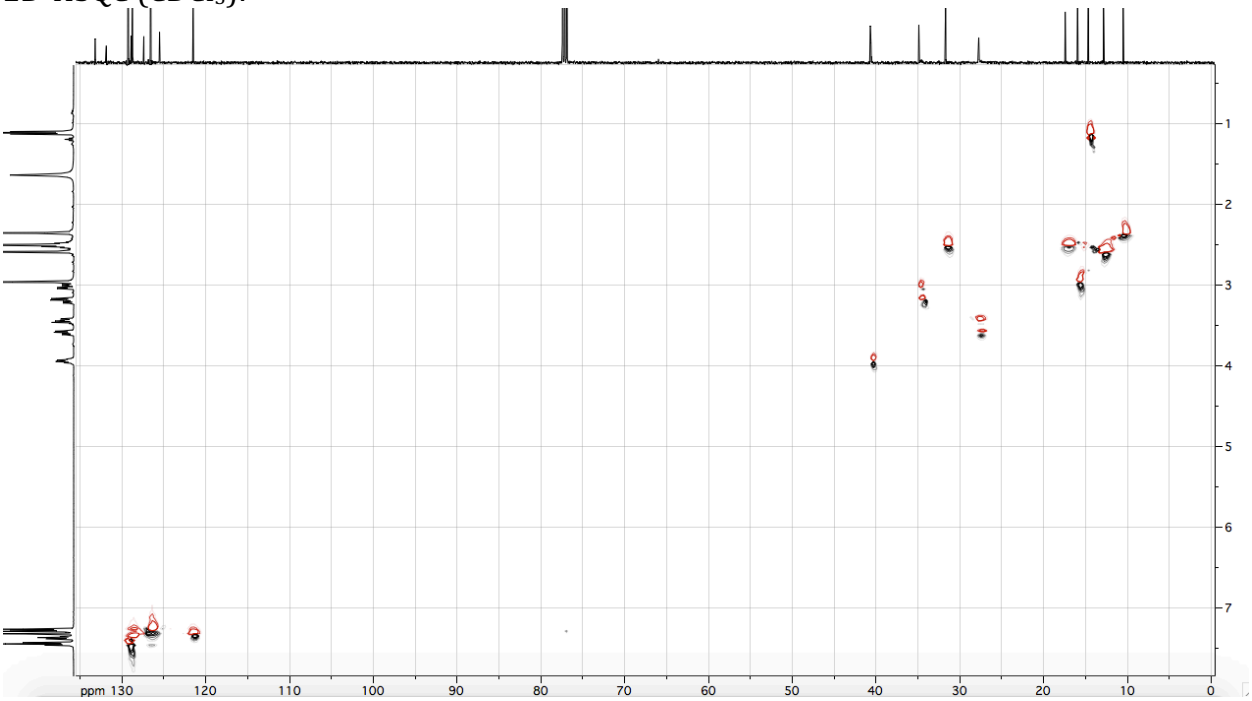
^{13}C UDEFT NMR ($CDCl_3$, 125 MHz):



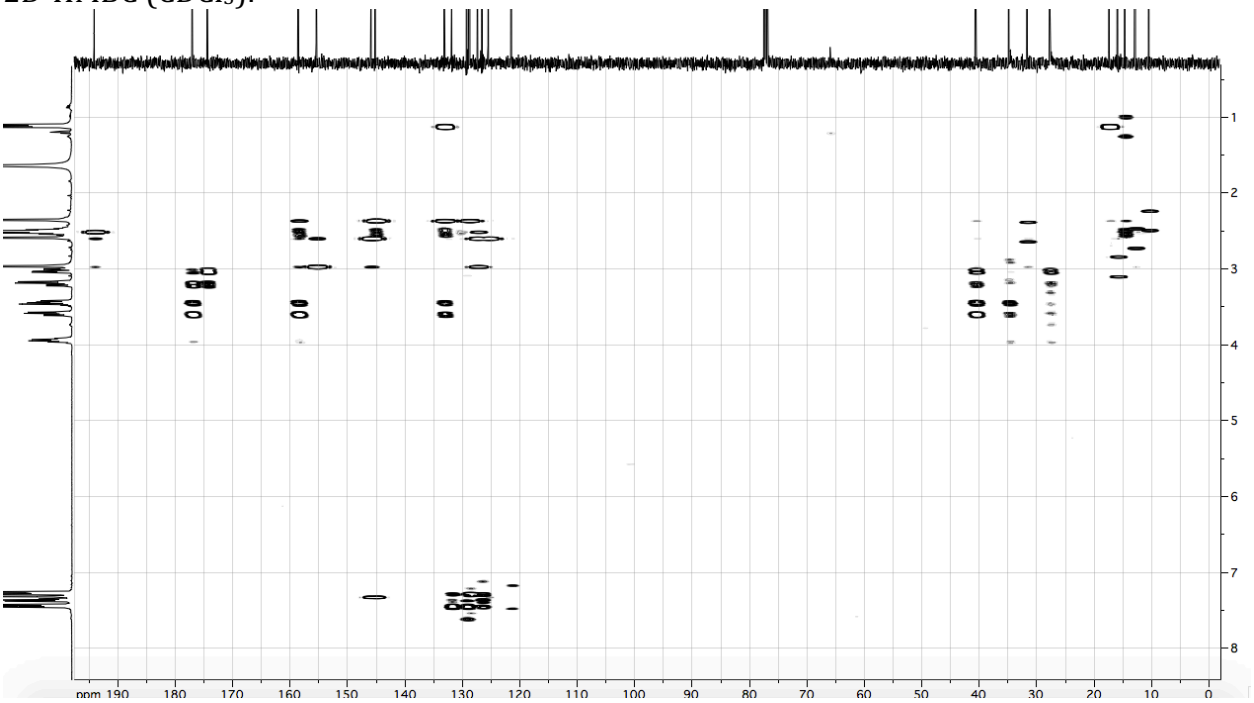
2D-COSY ($CDCl_3$):



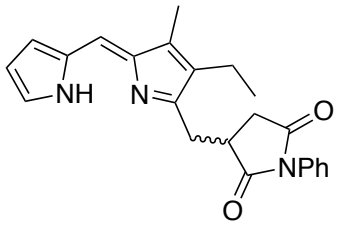
2D-HSQC ($CDCl_3$):



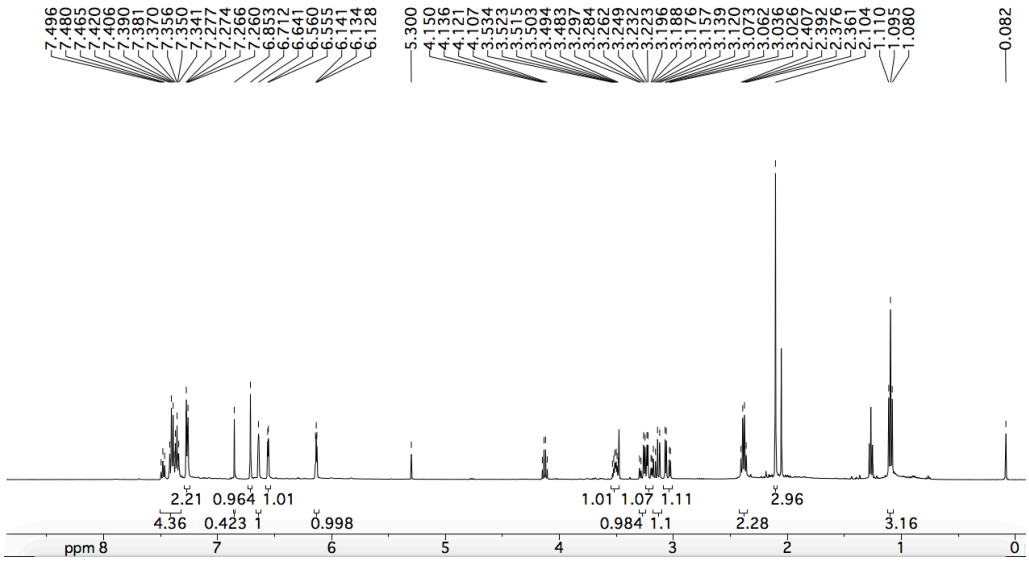
2D-HMBC ($CDCl_3$):



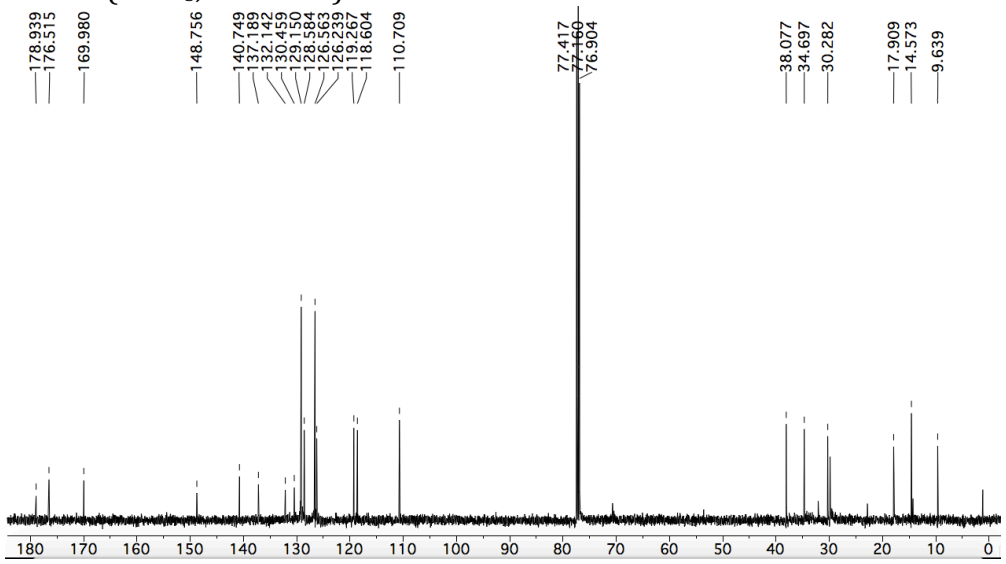
(*Z*)-3-((2-((1*H*-Pyrrol-2-yl)methylene)-4-ethyl-3-methyl-2*H*-pyrrol-5-yl)methyl)-1-phenylpyrrolidine-2,5-dione (19)



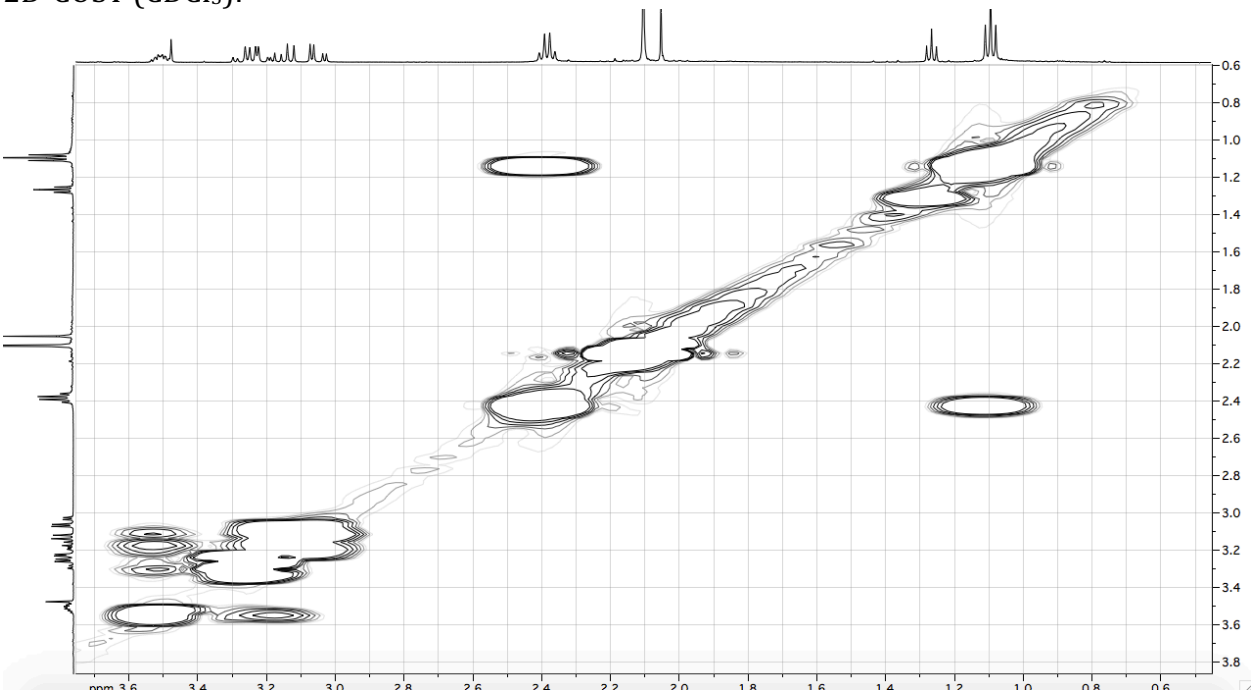
^{1}H-NMR ($CDCl_3$, 500 MHz):



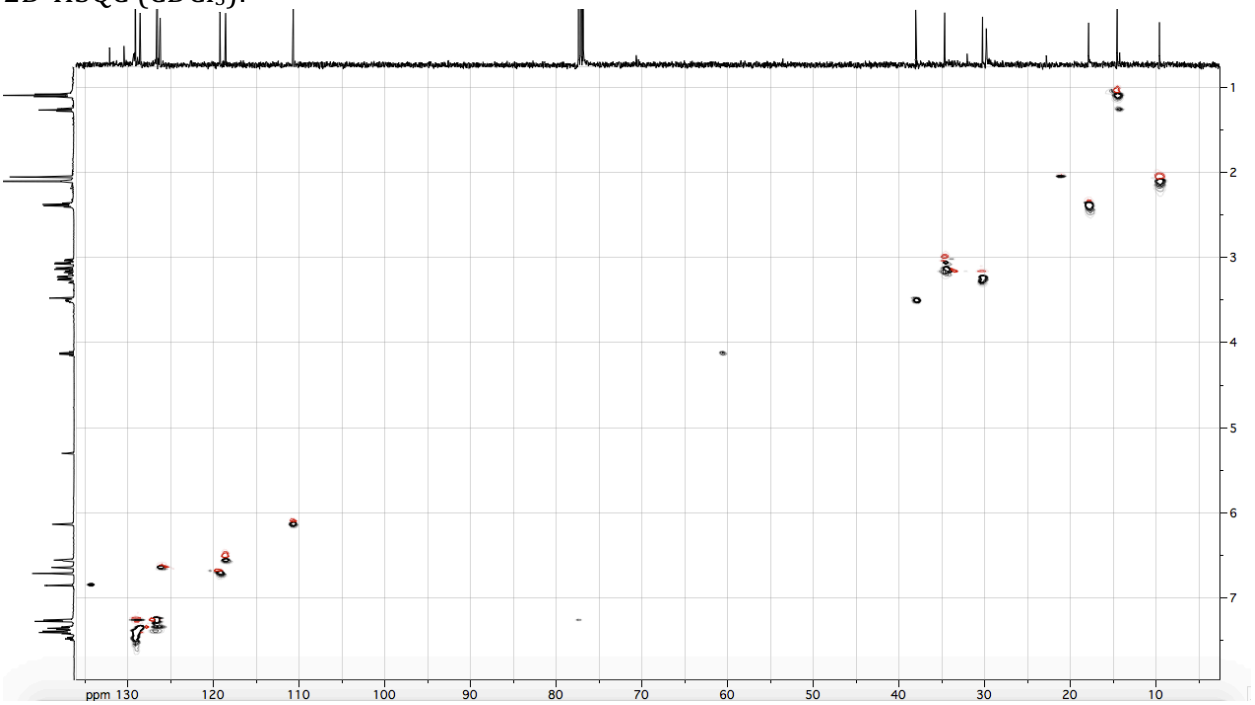
^{13}C UDEFT NMR ($CDCl_3$, 125 MHz):



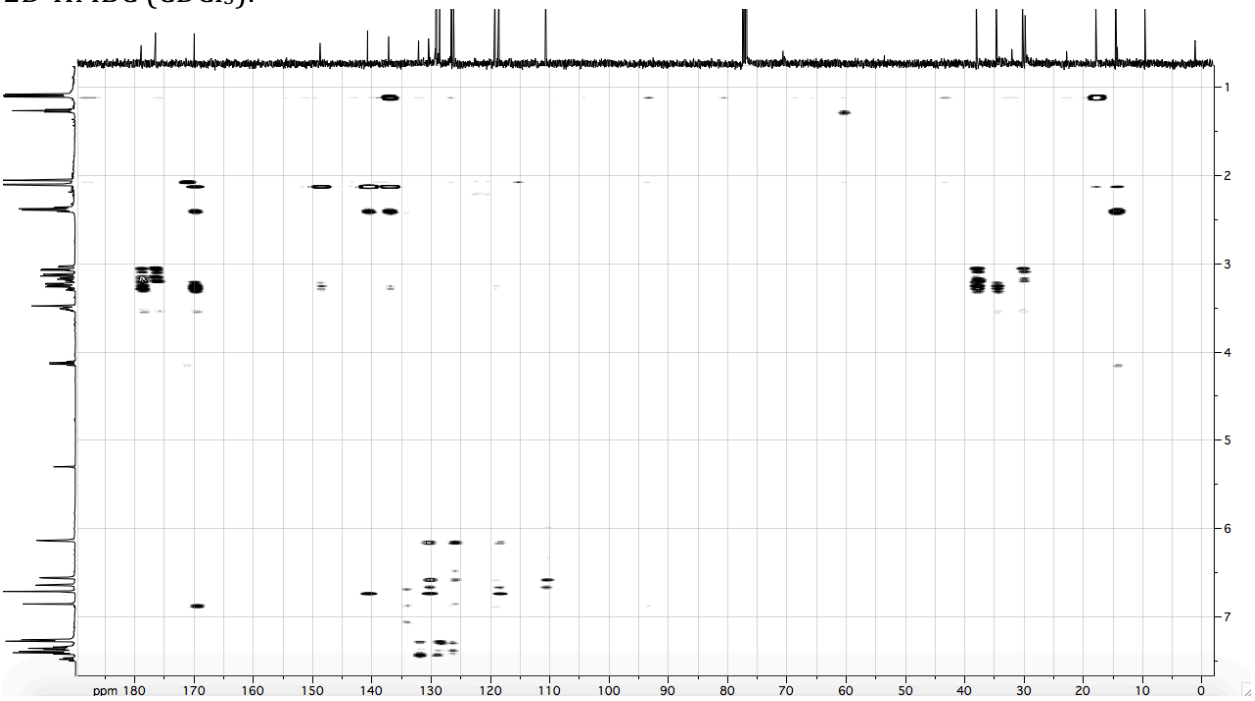
2D-COSY ($CDCl_3$):



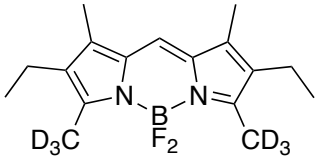
2D-HSQC ($CDCl_3$):



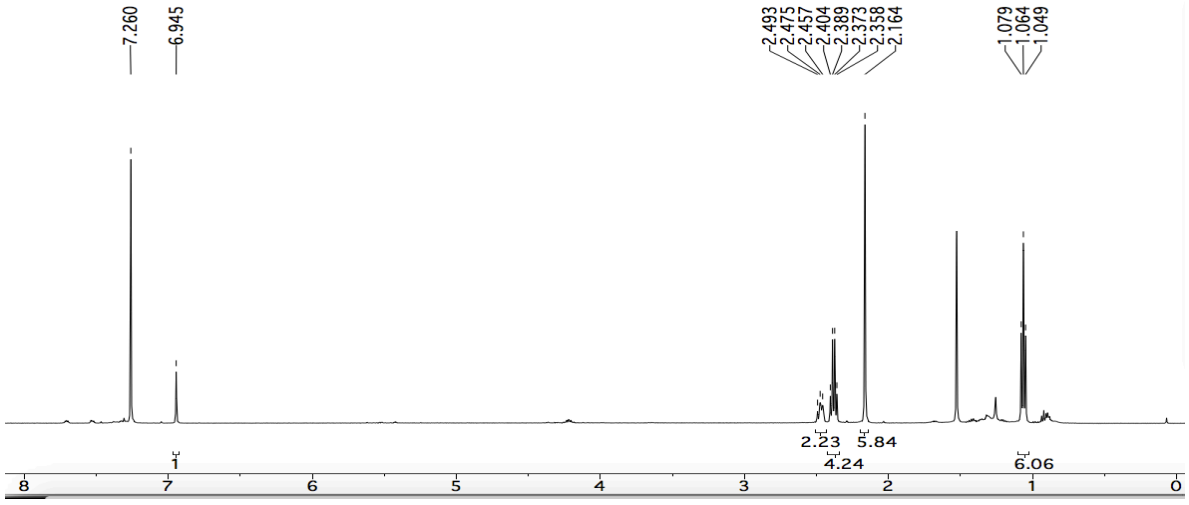
2D-HMBC ($CDCl_3$):



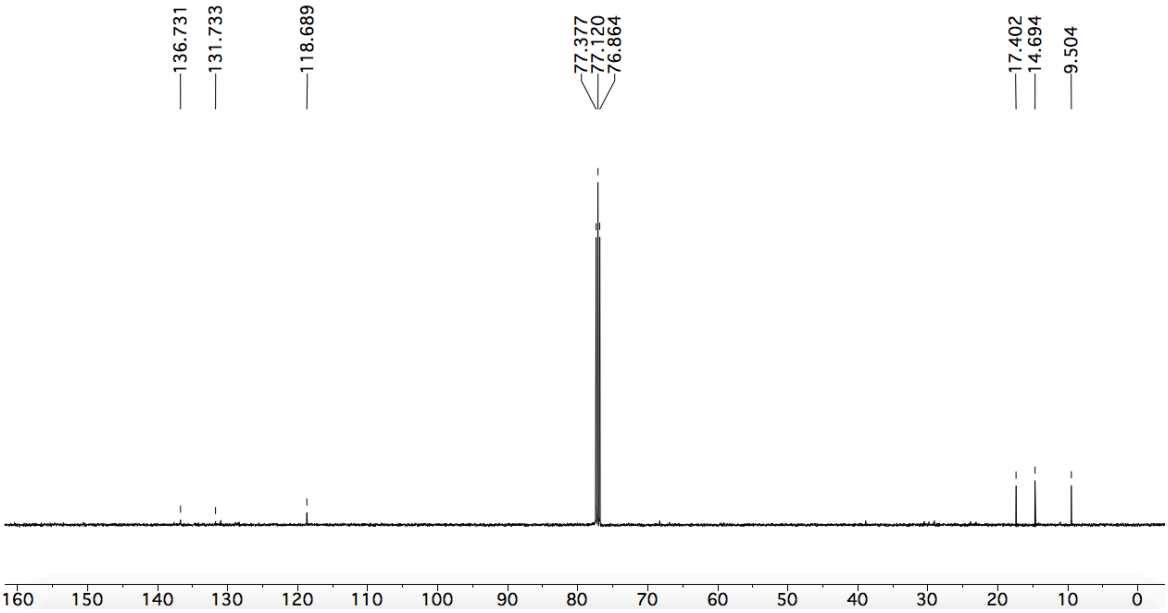
4,4-Difluoro-1,3($^2H_3$),5($^2H_3$),7-tetramethyl-2,6-diethyl-8-*H*-4-bora-3a,4a-diaza-*s*-indacene (20-D_6)



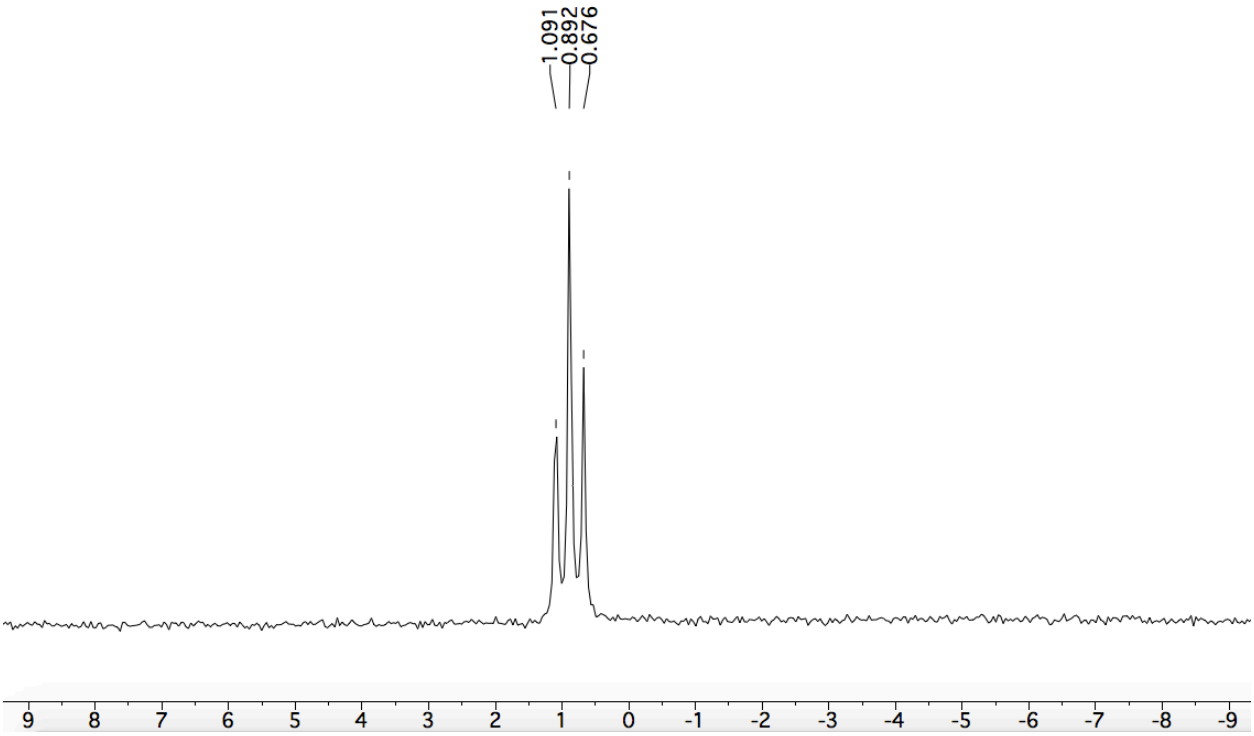
^{1}H NMR ($CDCl_3$, 500 MHz):



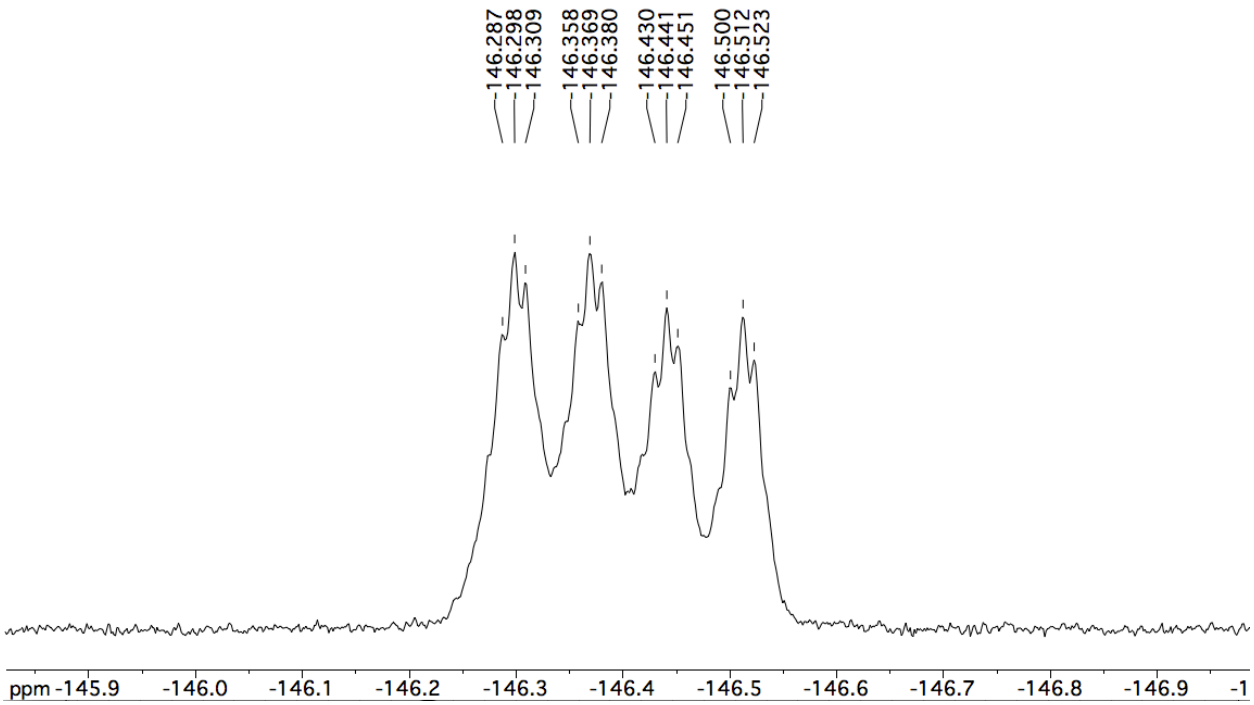
^{13}C UDEFT NMR ($CDCl_3$, 125 MHz):



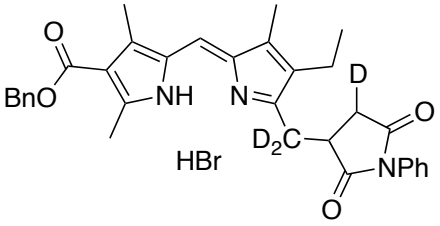
^{11}B NMR ($CDCl_3$, 160 MHz):



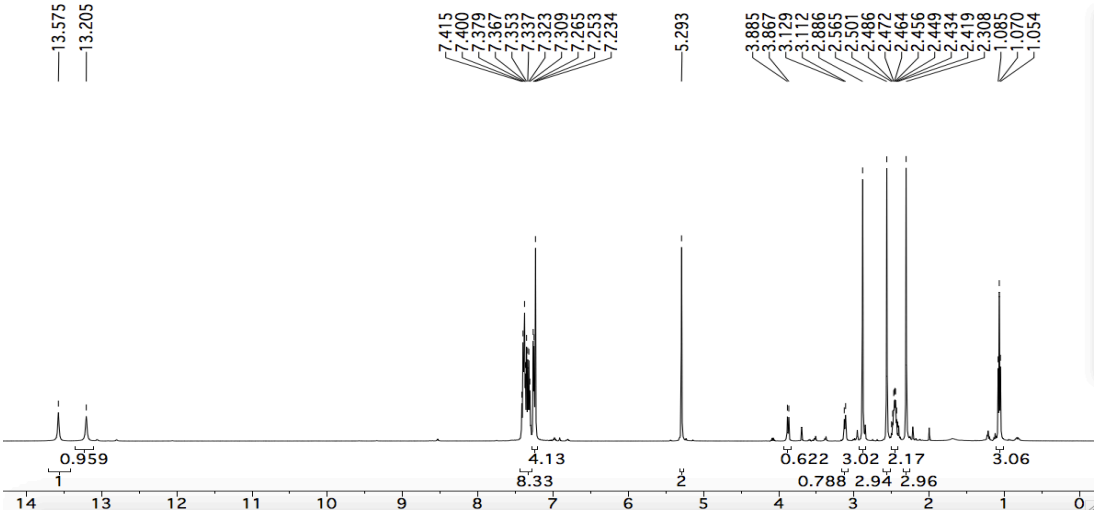
^{19}F NMR ($CDCl_3$, 470 MHz):



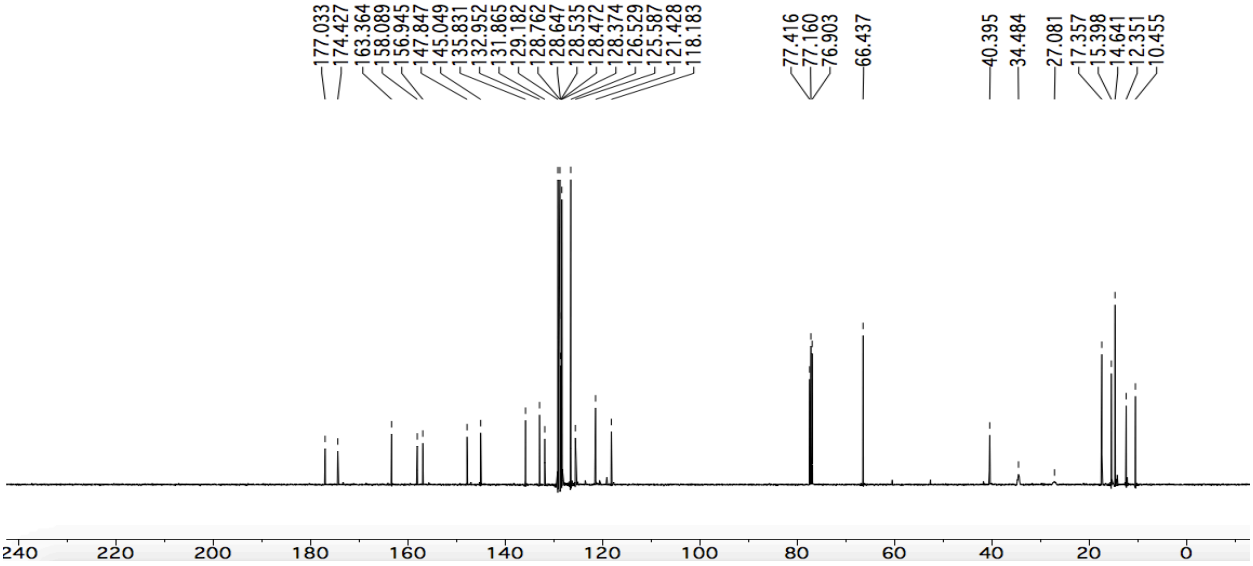
(*Z*)-Benzyl 5-((5($^2H_2$)-((2,5-dioxo-1-phenylpyrrolidin-4(^{2}H)-3-yl)methyl)-4-ethyl-3-methyl-2*H*-pyrrol-2-ylidene)methyl)-2,4-dimethyl-1*H*-pyrrole-3-carboxylate hydrobromide (21-D_3•HBr)



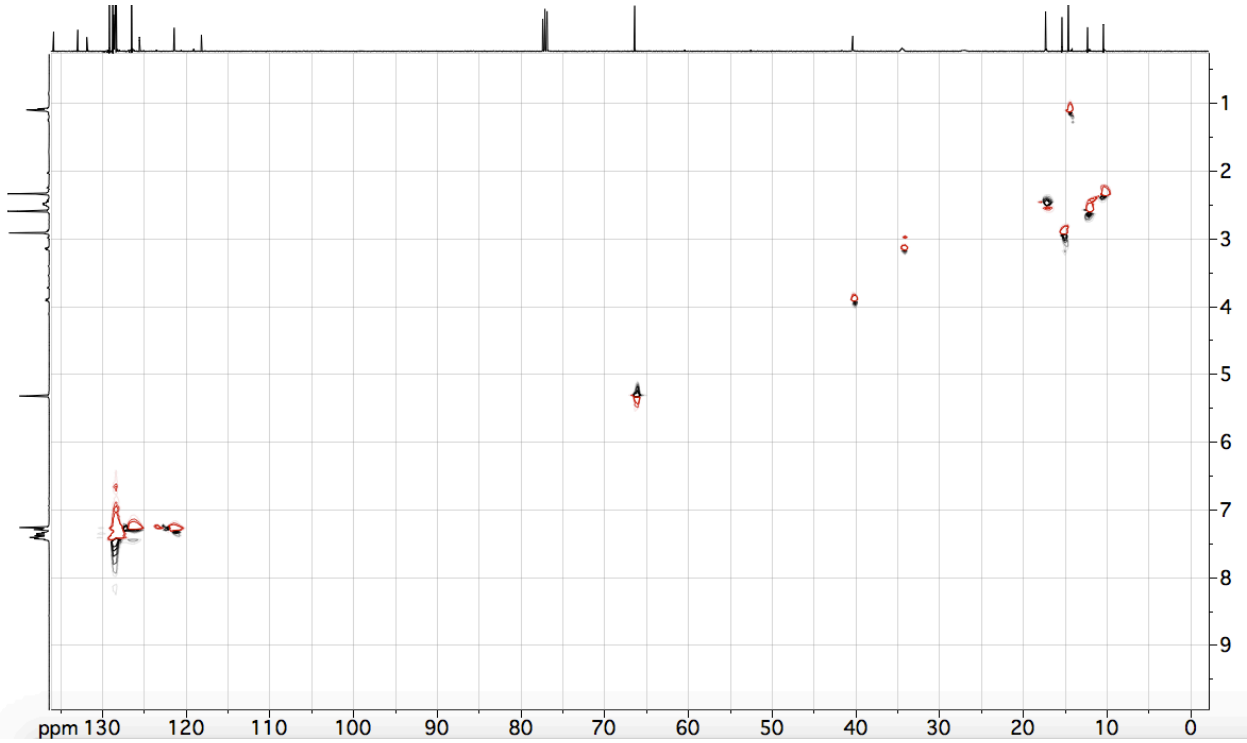
^{1}H NMR ($CDCl_3$, 500 MHz):



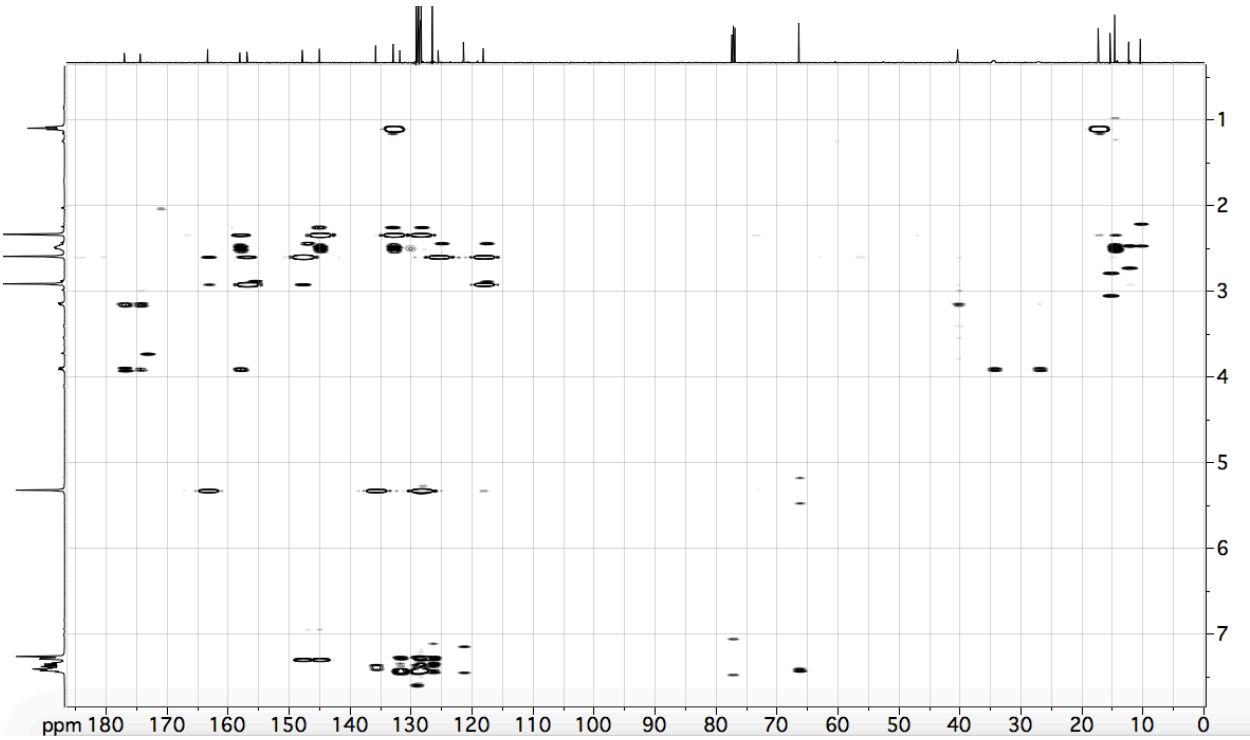
^{13}C UDEFT NMR ($CDCl_3$, 125 MHz):



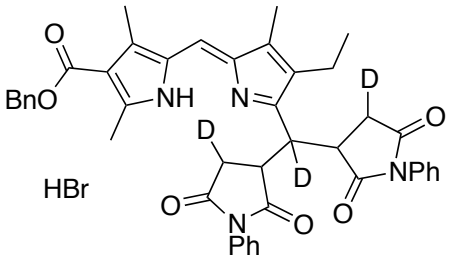
2D HSQC ($CDCl_3$):



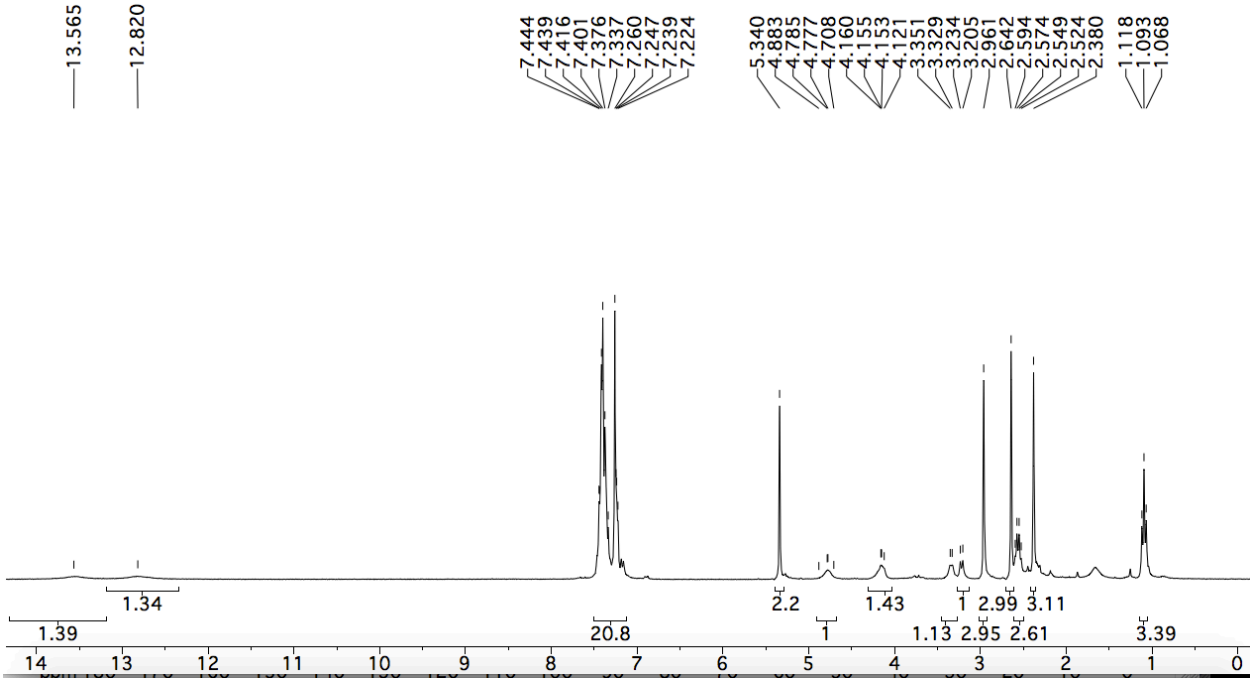
2D HMBC ($CDCl_3$):



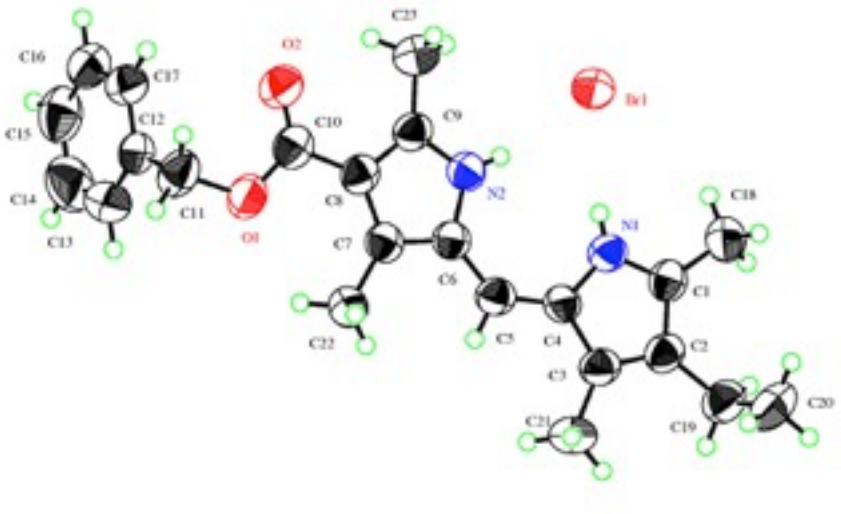
(*Z*)-benzyl 5-((5-(bis(2,5-dioxo-1-phenylpyrrolidin-3-yl)methyl)-4-ethyl-3-methyl-2*H*-pyrrol-2-ylidene)methyl)-2,4-dimethyl-1*H*-pyrrole-3-carboxylate hydrobromide (22-D_3•HBr)



^{1}H NMR ($CDCl_3$, 300 MHz):



X-Ray Crystal Structure of 12•HBr



$C_{23}H_{23}N_2O_2Br$ MM = 443.38 g/mol. Orange needle-plate crystal, dimensions 0.38 x 0.21 x 0.16 mm; monoclinic space group, C2/c (#15); a = 24.5150(15) Å, b = 8.3180(4), c = 22.0494(15) Å, β = 100.632(3) °, V = 4419.0(5) Å^3; d = 1.333 g/cm^3, μ(Mo-Kα) = 18.555 cm^{-1}, 64426 reflections (5254 unique, R_{int} = 0.068), R = 0.0395, R_w = 0.0502, GOF = 1.070. CCDC deposition number: 1548887.