Electronic supplementary materials *Mendeleev Commun.*, 2020, **30**, 185–187

Regioselectivity of the Chan–Lam coupling of ambident nitropyrazoles with *trans*-styrylboronic acid

Dmitry V. Davydov, Petr K. Sazonov and Yurii F. Oprunenko

Table of Contents

All preparations were carried out in the reagent grade solvents. All other chemicals used in the syntheses were obtained from Aldrich and were used without further purification. The progress of all reactions was monitored on Merck silica gel plates (with fluorescence indicator UV-254) using benzene as solvent. Melting points (mp) were taken in open capillaries on a Stuart melting point apparatus SMP11 and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$, CD_3NO_2 or C_6D_6 solvents on a Bruker Avance 400 spectrometer (δ, ppm.). IR-spectra (cm^{-1}) were registered on Thermo Scientific Nicolet iS5 FT-IR spectrometer using iD3 Attenuated Total Reflectance (ATR) accessory. IR-bands in 2340-2365 cm^{-1} range belong to atmospheric CO_2. High resolution mass spectra (HRMS) were measured on a Bruker micrOTOF II instrument using electrospray ionization (ESI). The measurements were done in a positive ion mode (interface capillary voltage – 4500 V) or in a negative ion mode (3200 V); mass range from *m*/*z* 50 to *m*/*z* 3000; external or internal calibration was done with ESI Tuning Mix, Agilent. A syringe injection was used for solutions in CH_3OH and CH_3CN (flow rate 3 ml/min). Nitrogen was applied as a dry gas; temperature was set at 180°C.

General procedure for vinylation of nitroazoles (1a-d).

To a mixture of nitroazole (0.5 mmol), *trans*-styrylboronic acid (1 mmol) and base (1 mmol) in CH_2Cl_2 (25 ml), copper salt (0.05 mmol) was added after 15 min of stirring in a vessel flushed with oxygen. The resulting mixture was stirred in oxygen atmosphere (1 atm) from balloon at room temperature for 24 hours. The mixture was then treated with 10% aqueous NH_3 and extracted several times with CH_2Cl_2. The organic layer was dried with Mg_2SO_4 and purified from inorganic salts and tars by flash-chromatography through Merck silica gel 60 (eluent CH_2Cl_2). The resulting solution was evaporated, and the products were isolated by preparative chromatography on Merck silica gel plates (UV-254) using benzene as solvent. The difference in R_f between isomers was ~2-2.5. For NMR investigation and determination of melting points, the products were purified by double crystallization from heptane (CCl_4 with addition of $CHCl_3$ in the case of 1-*E*-styryl-3,4-dinitropyrazole **3c**).

Spectral characteristics of the products

3-Nitro-1-[(*E*)-2-phenylvinyl]-1*H*-pyrazole, (3a): Yield. 42 %, mp 140-142 ºC from heptane. ^{1}H NMR (400 MHz, C_6D_6, δ, ppm): 6.255 (d, 1H, J = 2.3 Hz, pyrazole ring); 6.395 (d, 1H, J = 2.3 Hz, pyrazole ring); 6.595 (d, 1H, J = 14.5 Hz, Vinyl); 6.92 (d, 1H, J = 14.5 Hz, Vinyl); 6.98-7.00 (m, 2H, Ph); 7.05-7.10 (m, 3H, Ph); ^{13}C NMR (100 MHz, CD_3NO_2, δ, ppm): 105.10, 122.61, 127.09, 128.15, 130.04, 130.37, 133.22, 135.39, 157.95. HRMS (m/z in MeCN): 216.0772, 238.0593, 254.0331; calculated for $C_{11}H_9N_3O_2$: $[M+H]^+$ 216.0768; for $[M+Na]^+$ 238.0587; for $[M+K]^+$ 254.0326.

5-Nitro-1-[(*E*)-2-phenylvinyl]-1*H*-pyrazole, (4a): Yield 51 %, 105-107 ºC from heptane. ^{1}H NMR (400 MHz, C_6D_6, δ, ppm): 6.415 (d, 1H, pyrazole ring); 6.935 (d, 1H, pyrazole ring); 7.01-7.072 (m, 3H, Ph); 7.116-7.18 (m, 2H, Ph); 7.425 (d, J=14.1 Hz, 1H, Vinyl); 8.045 (d, J=14.1 Hz, 1H, Vinyl). ^{13}C NMR (100 MHz, CD_3NO_2, δ, ppm): 109.14, 121.03, 124.78, 128.23, 130.02, 130.37, 135.82, 141.04, 146.66. HRMS (m/z in CH_3OH): 216.0774; calculated for $C_{11}H_9N_3O_2$ $[M+H]^+$ 216.0768.

5-Methyl-3-nitro-1-[(*E*)-2-phenylvinyl]-1*H*-pyrazole (**3b**): Yield. 38 %, Mp 139-141 ºC from heptane. ^{1}H NMR (400 MHz, C_6D_6, δ, ppm): 1.27 (s, 3H, CH_3); 6.14 (s, 1H, pyrazole ring); 7.08 (m, 5H, Ph); 6.60 (d, J = 14.1 Hz, 1H, vinyl); 7.39 (d, J = 14.1 Hz, 1H, vinyl). ^{13}C NMR (100 MHz, CD_3NO_2, δ, ppm): 11.42, 103,88, 123.26, 123.71, 129.92, 135.75, 144.69, 157.20. HRMS (m/z in CH_3OH): 230.0930, calculated for $C_{12}H_{11}N_3O_2$ $[M+H]^+$ 230.0924.

3-Methyl-5-nitro-1-[(*E*)-2-phenylvinyl]-1*H*-pyrazole (4b): Yield. 35 %, Mp 88-90 ºC from heptane. ^{1}H NMR (400 MHz, C_6D_6, δ, ppm): 1.28 (s, 3H, CH3); 6.14 (s., 1H, pyrazole ring); 6.605 (d, J = 14.1 Hz, 1H, vinyl); 7.08 (m, 5H, Ph); 7.385 (d, J = 14.1 Hz, 1H, vinyl). ^{13}C NMR (100 MHz, CD_3NO_2, δ, ppm): 13.96, 108,40, 123.26, 123.59, 125.02, 128.09, 129.80, 130.34, 136.06, 146.56, 151.15. HRMS (m/z in CH_3OH): 230.0931; calculated for $C_{12}H_{11}N_3O_2$ $[M+H]^+$ 230.0924.

3,4-Dinitro-1-[(*E*)-2-phenylvinyl]-1*H*-pyrazole (3c): Yield ~50 %, mp 199-201 ºC, with decomp. from CCl_4+ $CDCl_3$. ^{1}H NMR (400 MHz, C_6D_6, δ, ppm): 6.17 (d, 1H, J = 14.2,Vinyl), 6.46 (s, 1H, pyrazole ring), 6.65 (d, 1H, J = 14.2, Vinyl), 6.97-6.99 (m, 2H, Ph), 7.07-7.11 (m, 3H, Ph). ^{13}C NMR (100 MHz, CD_3NO_2, δ, ppm): 125.68; 125.75; 128.52; 128.99; 130.47;131.99; 134.43; 149.34. HRMS (m/z, in CH_3OH): 283.0444; calculated for $C_{11}H_8N_4O_4$ $[M+Na]^+$ 283.0438.

3,5-Dimethyl-4-nitro-[(*E*)-2-vinylphenyl]-1*H*-pyrazole (3d): Yield 70 %, mp 168-170 ºC with decomp. from heptane. ^{1}H NMR (400 MHz, C_6D_6, δ, ppm): 1.88 (s, 3H, CH_3); 2.50 (s, 3H, CH_3); 6.645 (d., J = 14.0 Hz, 1H, Vinyl); 7.05-7.15 (m, 5H, Ph); 7.445 (d, J = 14.0, 1H, Vinyl). ^{13}C NMR (100 MHz, CD_3NO_2, δ, ppm): 11.36, 14.56, 122.88, 123.14, 128.03, 129.69, 130.27, 136.06, 142.03, 148.95. HRMS (m/z, in CH_3OH): 244.1088; calculated for $C_{13}H_{13}N_3O_2$ $[M+H]^+$ 244.1081.

Experimental spectra

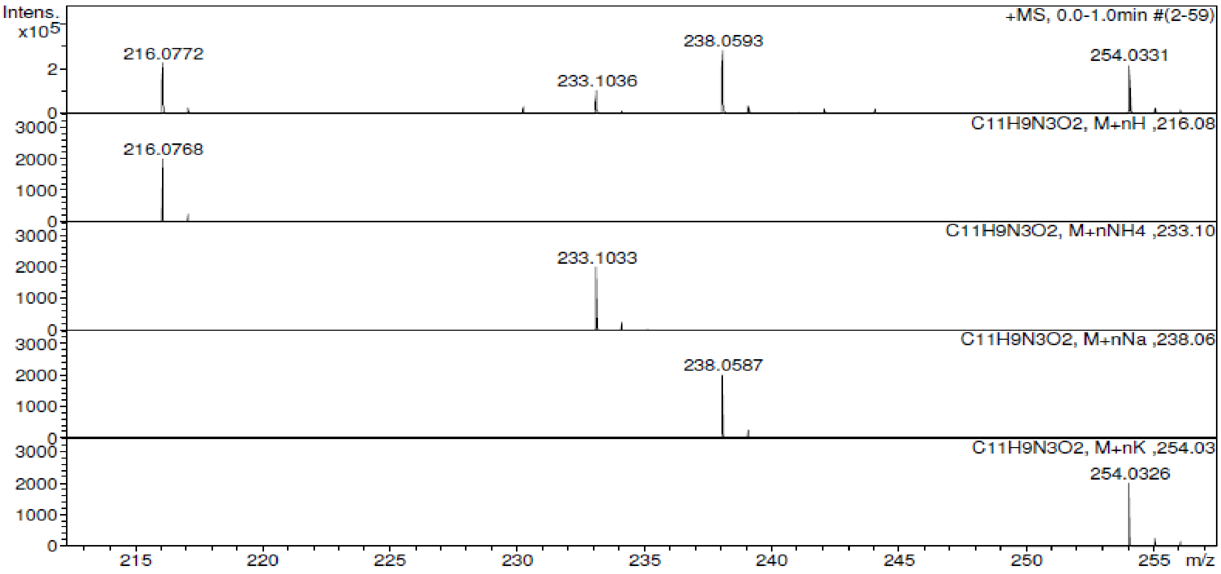


Figure S1 MS spectrum of 3-nitro-1-[(E)-2-phenylvinyl]-1H-pyrazole *3a*

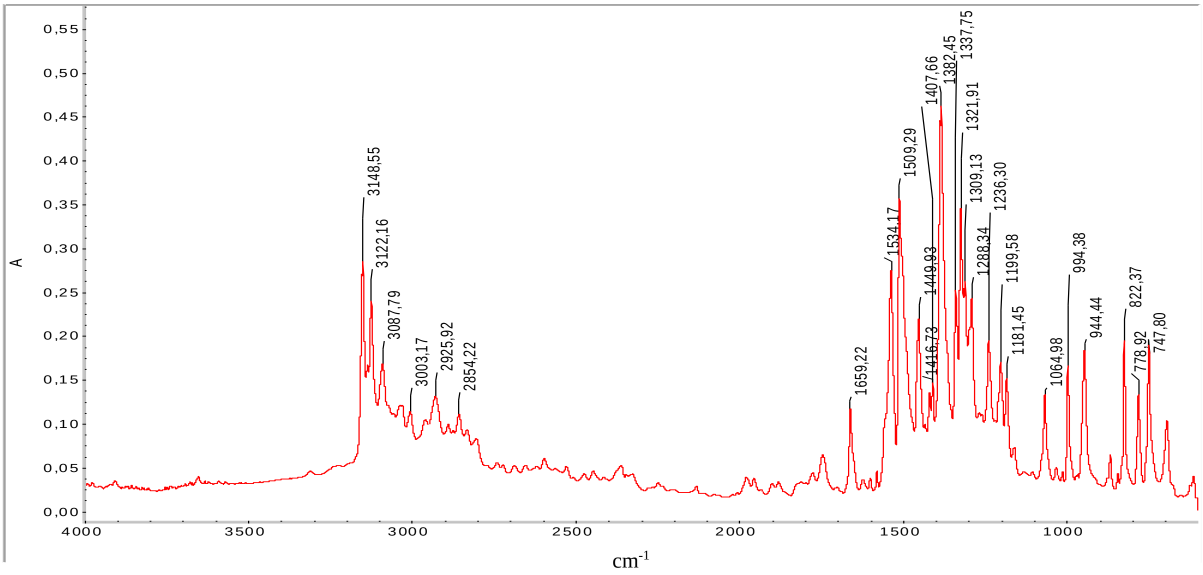


Figure S2 IR spectrum of 3-nitro-1-[(E)-2-phenylvinyl]-1H-pyrazole 3a

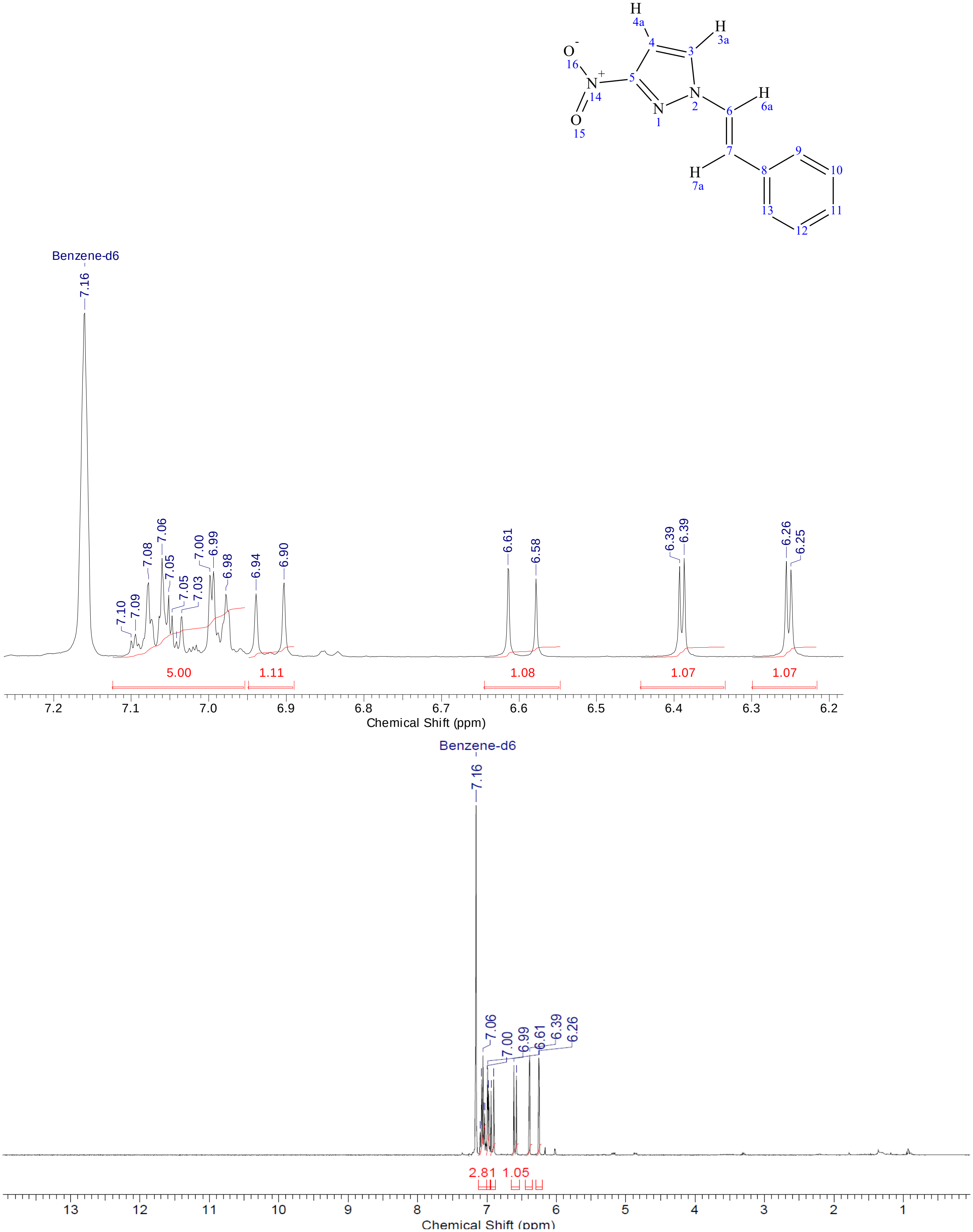


Figure S3 ^{1}H NMR spectrum (C_6D_6) of 3-nitro-1-[(E)-2-phenylvinyl]-1H-pyrazole **3a**

Acquisition Time (sec)	1.3107	***Date***	Apr 16 2019		
File Name	C:\Users\DIMA\vynylation sept 2018\dav1130dn-c_20190416_01\CARBON_01				
Frequency (MHz)	100.58	***Nucleus***	13C	***Number of Transients***	10000
Original Points Count	32768	***Points Count***	32768	***Pulse Sequence***	s2pul
Solvent	NITROMETHANE-D3			***Sweep Width (Hz)***	25000.00
Temperature (degree C)	22.000				

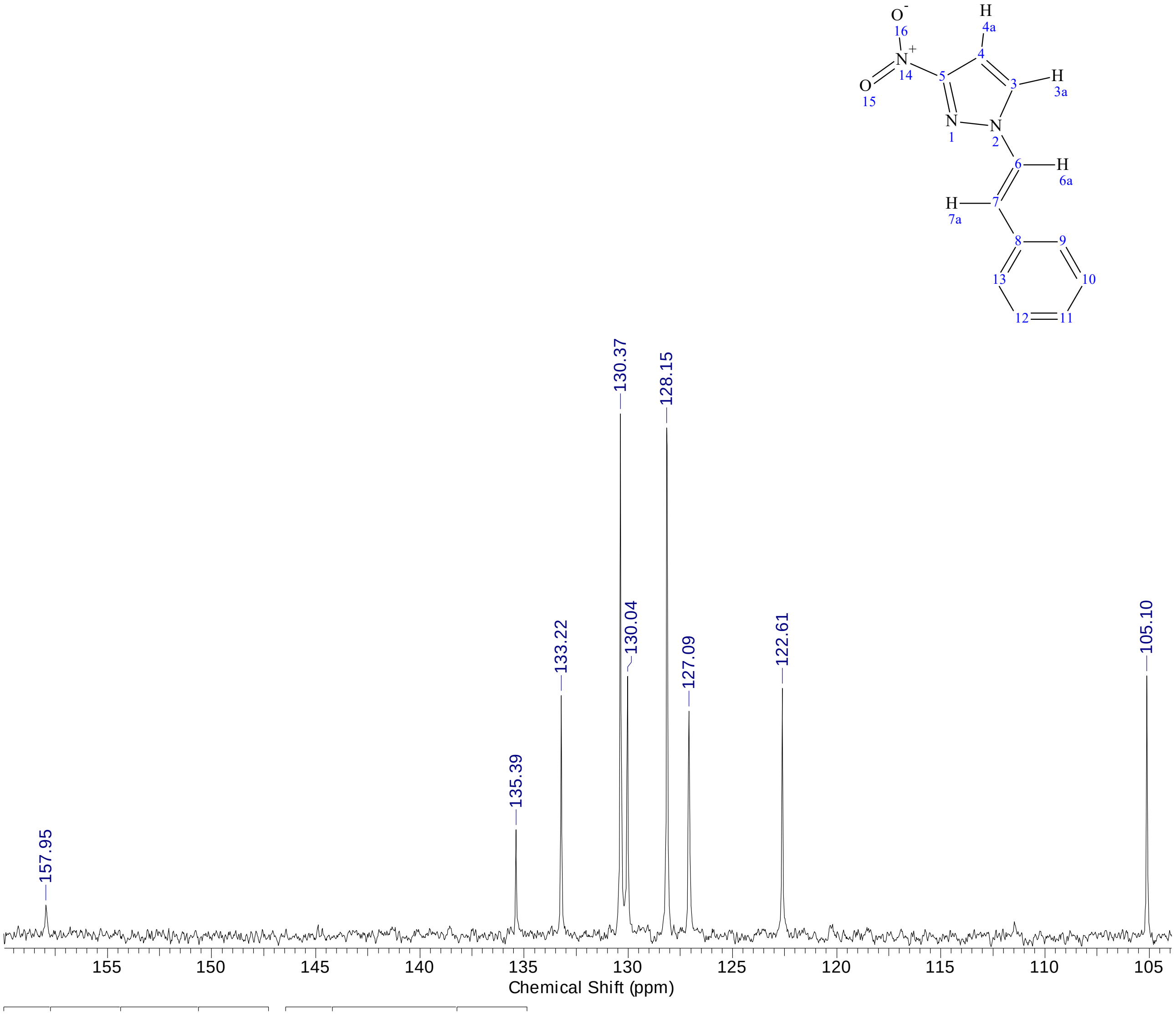


Figure S4 ^{13}C NMR spectrum (CD_3NO_2) of ***3-nitro-1-[(*E*)-2-phenylvinyl]-1H-pyrazole* 3a**

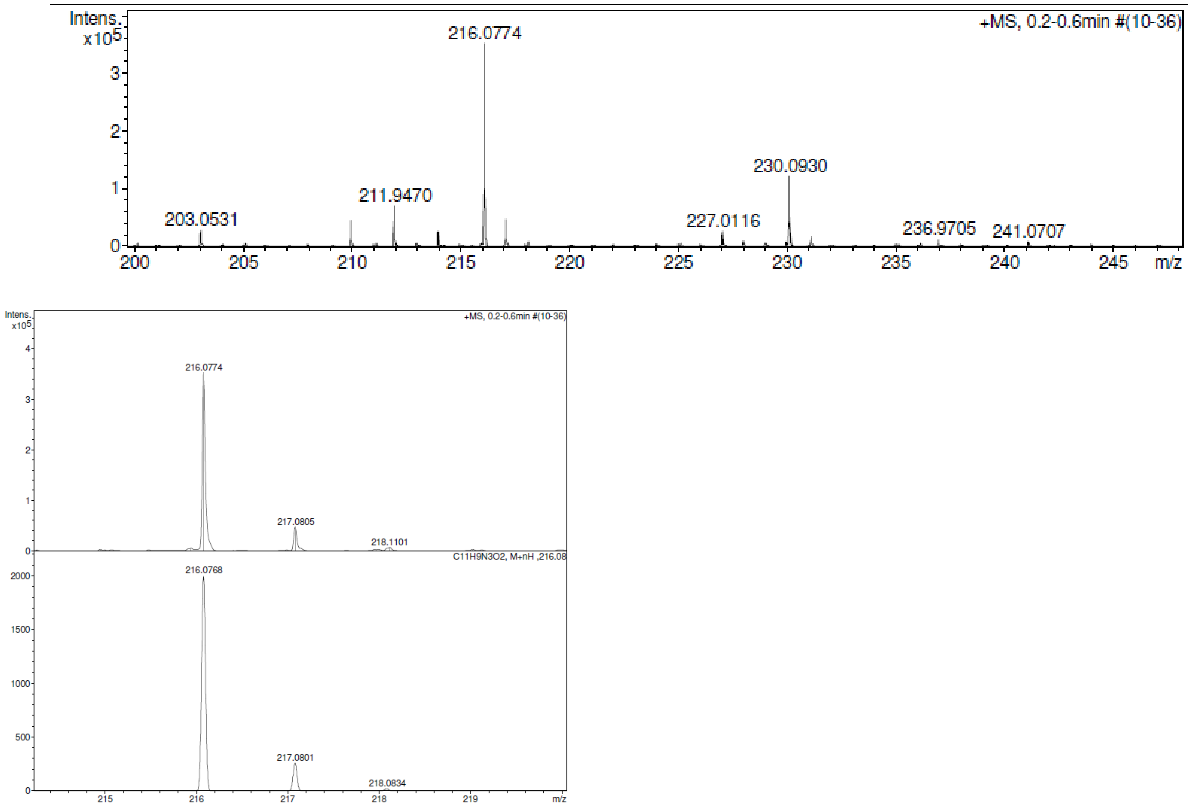


Figure S5 MS spectrum of ***5-nitro-1-[(*E*)-2-phenylvinyl]-1H-pyrazole* 4a**

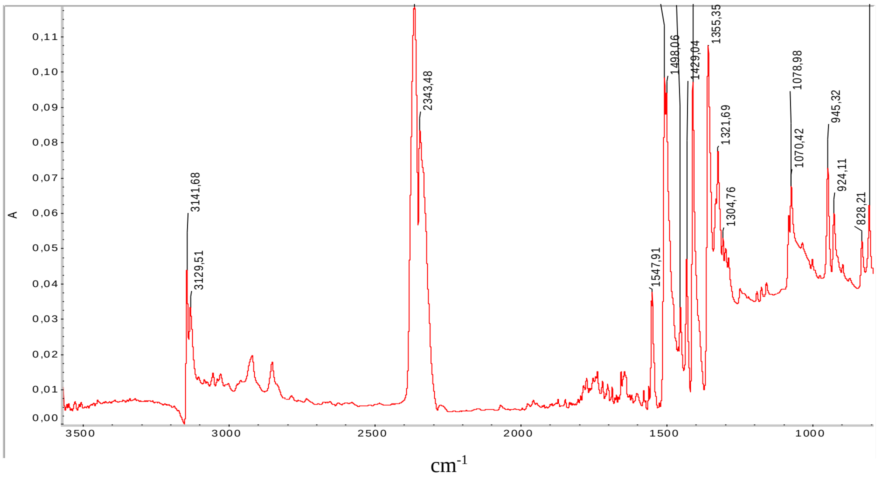


Figure S6 IR spectrum of ***5-nitro-1-[(*E*)-2-phenylvinyl]-1H-pyrazole* 4a**

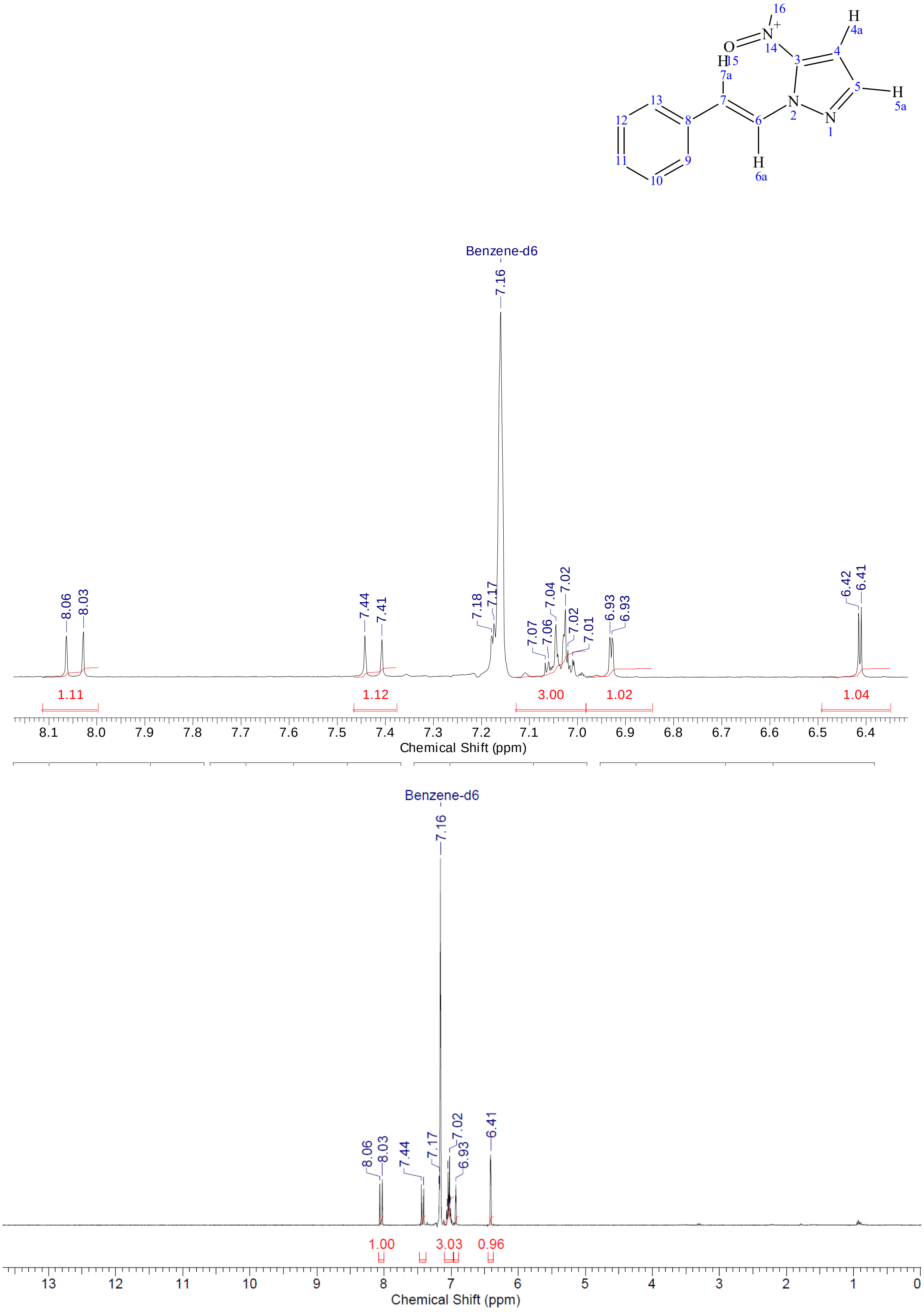
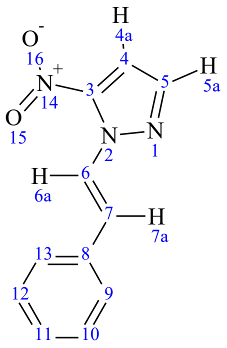


Figure S7 ^{1}H NMR spectrum (C_6D_6) of ***5-nitro-1-[(E)-2-phenylvinyl]-1H-pyrazole* 4a**

Formula $C_{11}H_9N_3O_2$	**FW** 215.2081

Acquisition Time (sec)	1.3107	**Date**	Mar 19 2019	**Date Stamp**	Mar 19 2019
File Name	C:\NMR\DAV1140UP-C_20190320_01\CARBON_01			**Frequency (MHz)**	100.58
Nucleus	13C	**Number of Transients**	9000	**Original Points Count**	32768
Points Count	32768	**Pulse Sequence**	s2pul	**Receiver Gain**	30.00
Solvent	NITROMETHANE-d3			**Spectrum Offset (Hz)**	11210.5615
Sweep Width (Hz)	25000.00	**Temperature (degree C)**	22.000		



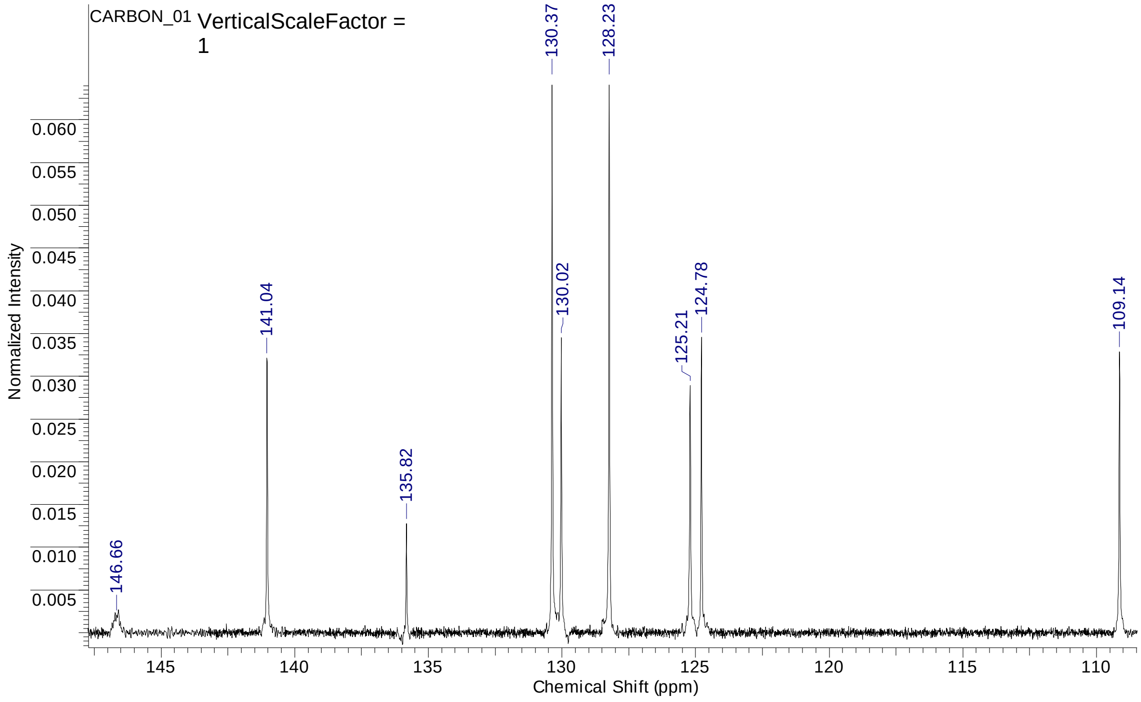


Figure S8 ^{13}C NMR spectrum (CD$_3$NO$_2$) of ***5-nitro-1-[(E)-2-phenylvinyl]-1H-pyrazole* 4a**

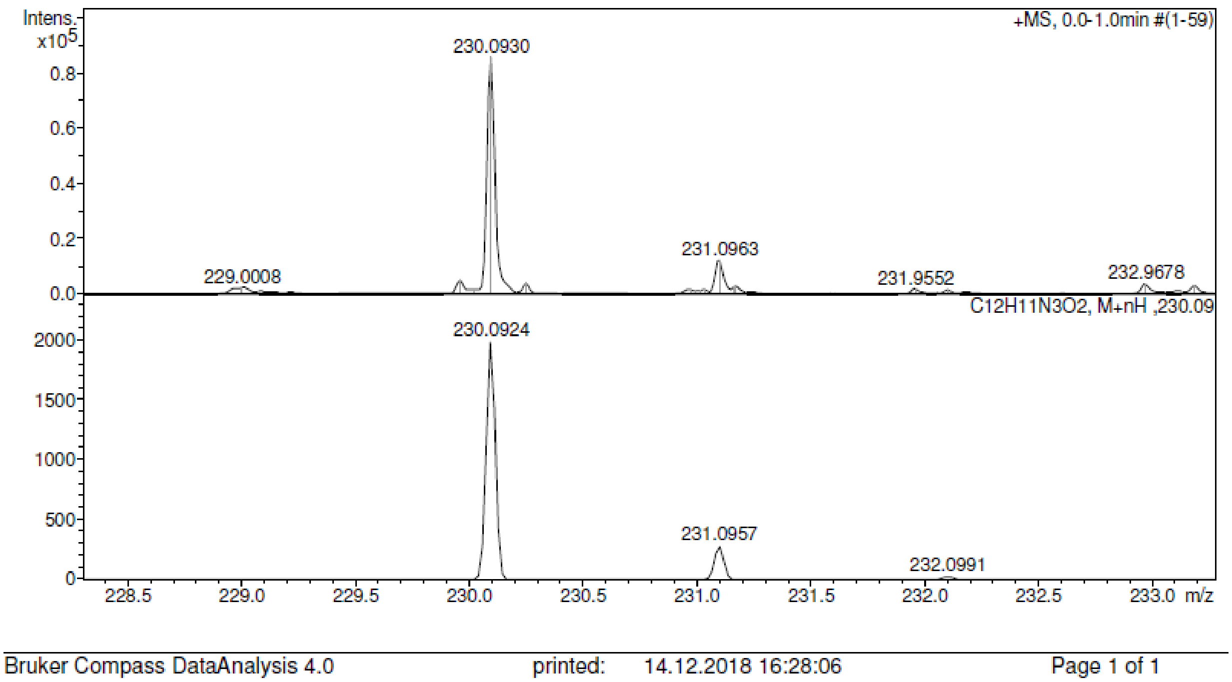


Figure S9 MS spectrum of 5-methyl-***3-nitro-1-[(*****E*****)-2-phenylvinyl]-1H-pyrazole*** **3b**

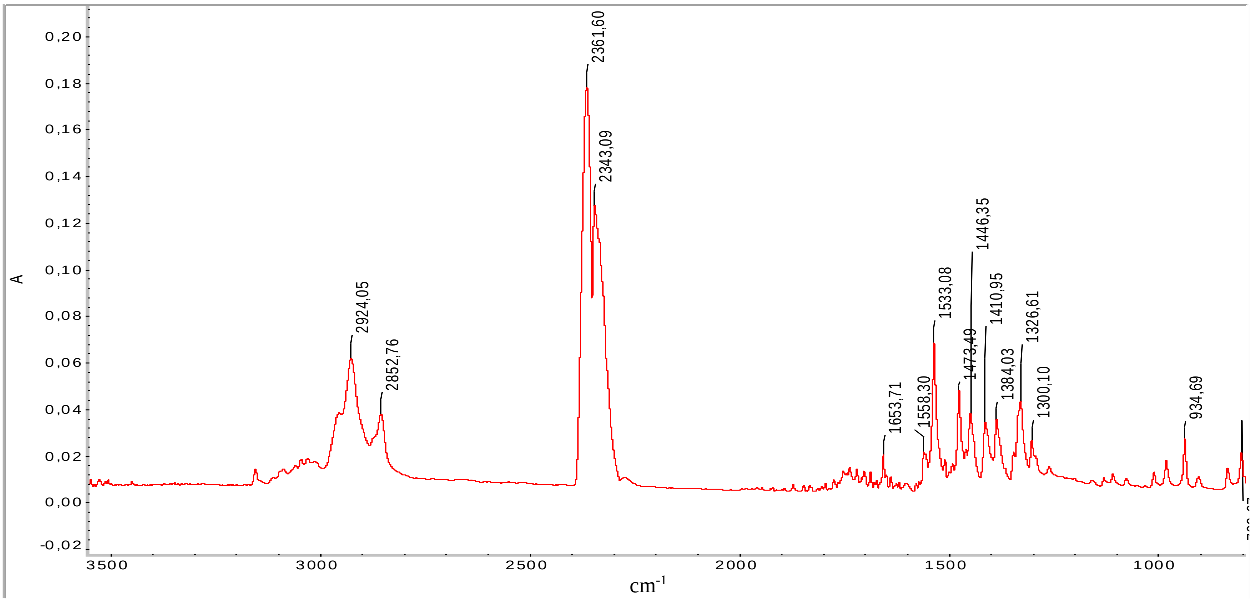


Figure S10 IR spectrum of 5-methyl-***3-nitro-1-[(*****E*****)-2-phenylvinyl]-1H-pyrazole*** **3b**

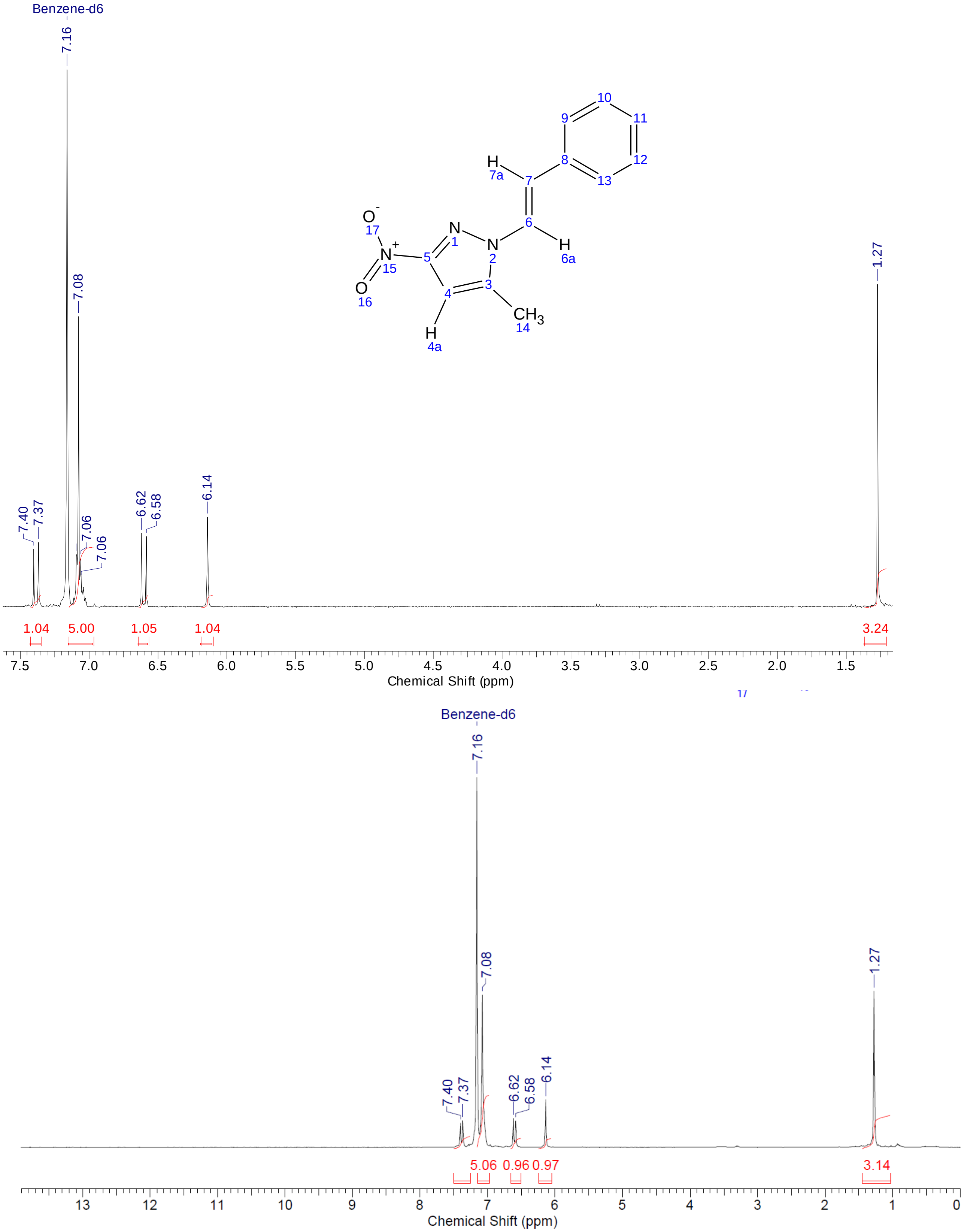


Figure S11 ^{1}H NMR spectrum (C_6D_6) of 5-methyl-**3-nitro-1-[(E)-2-phenylvinyl]-1H-pyrazole** 3b

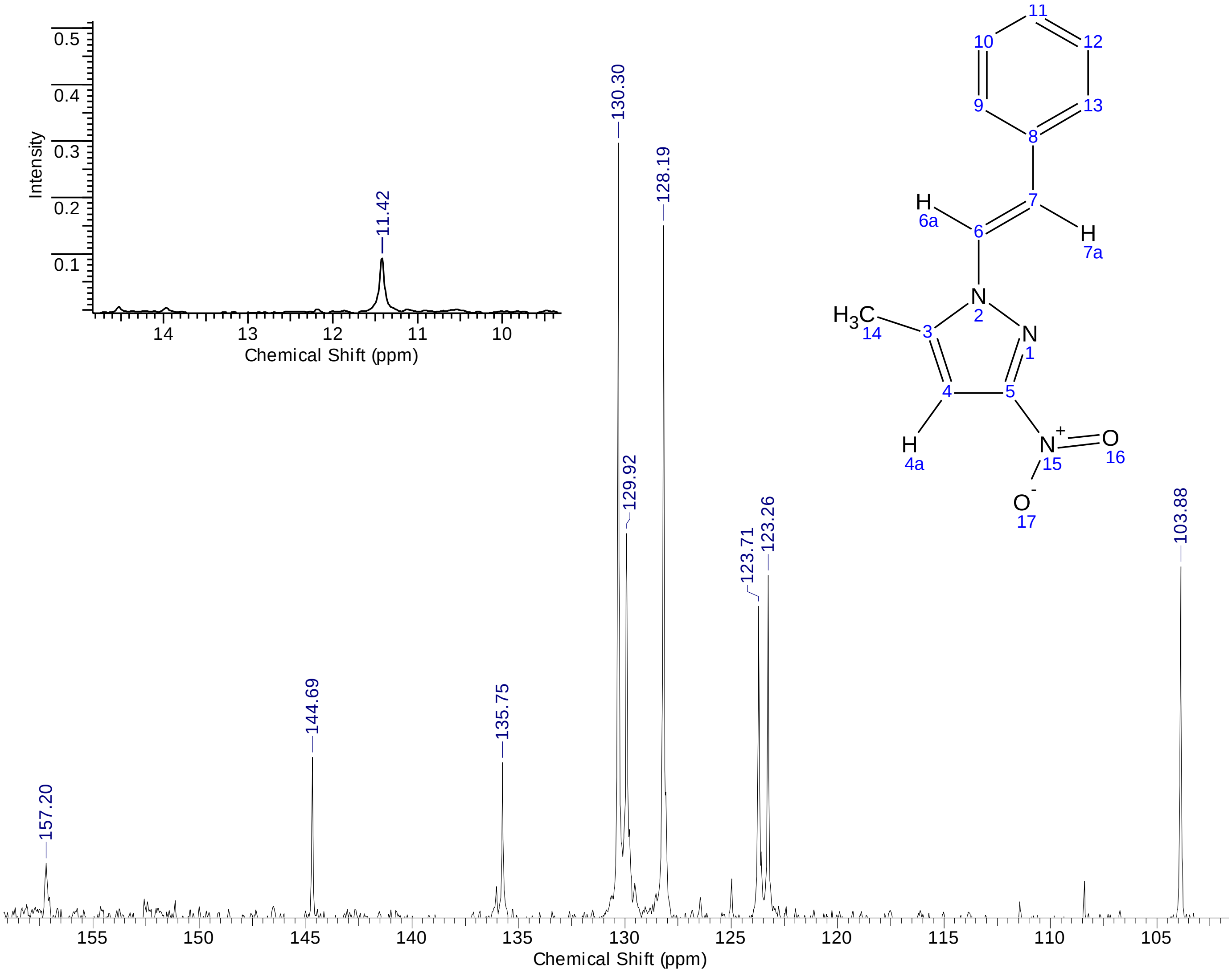


Figure S12 ^{13}C NMR spectrum (CD$_3$NO$_2$) of 5-methyl-***3-nitro-1-[(E)-2-phenylvinyl]-1H-pyrazole*** **3b**

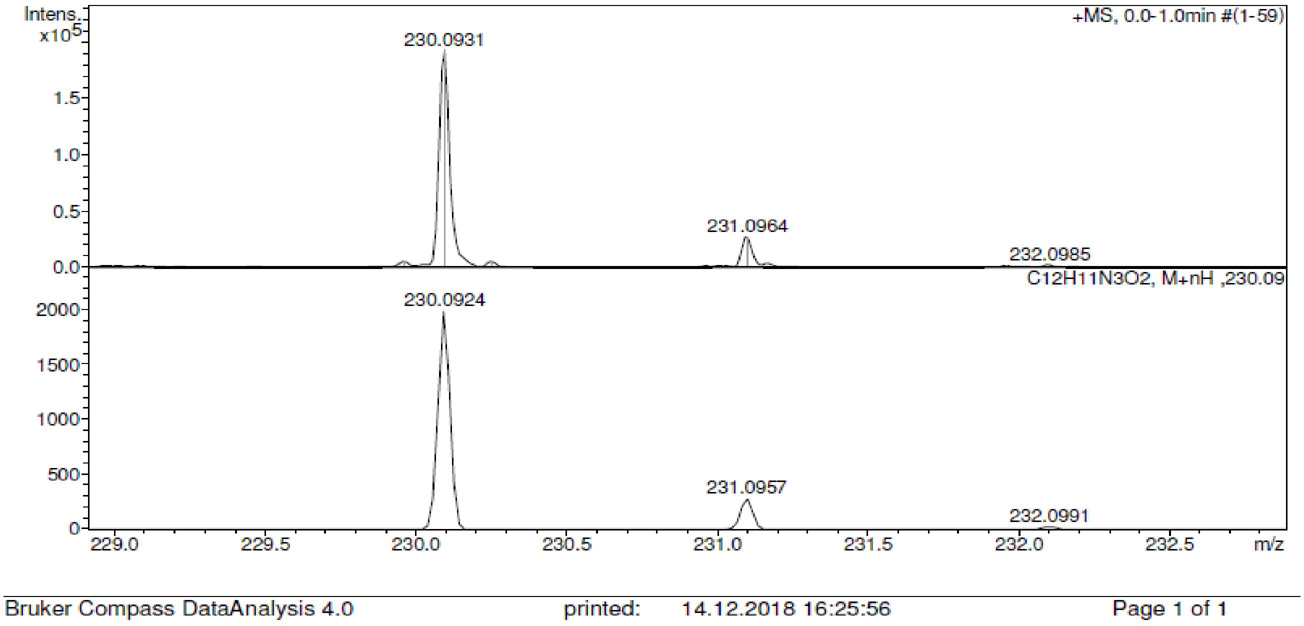


Figure S13 MS spectrum of 3-methyl-***5-nitro-1-[(*****E*****)-2-phenylvinyl]-1H-pyrazole* 4b**

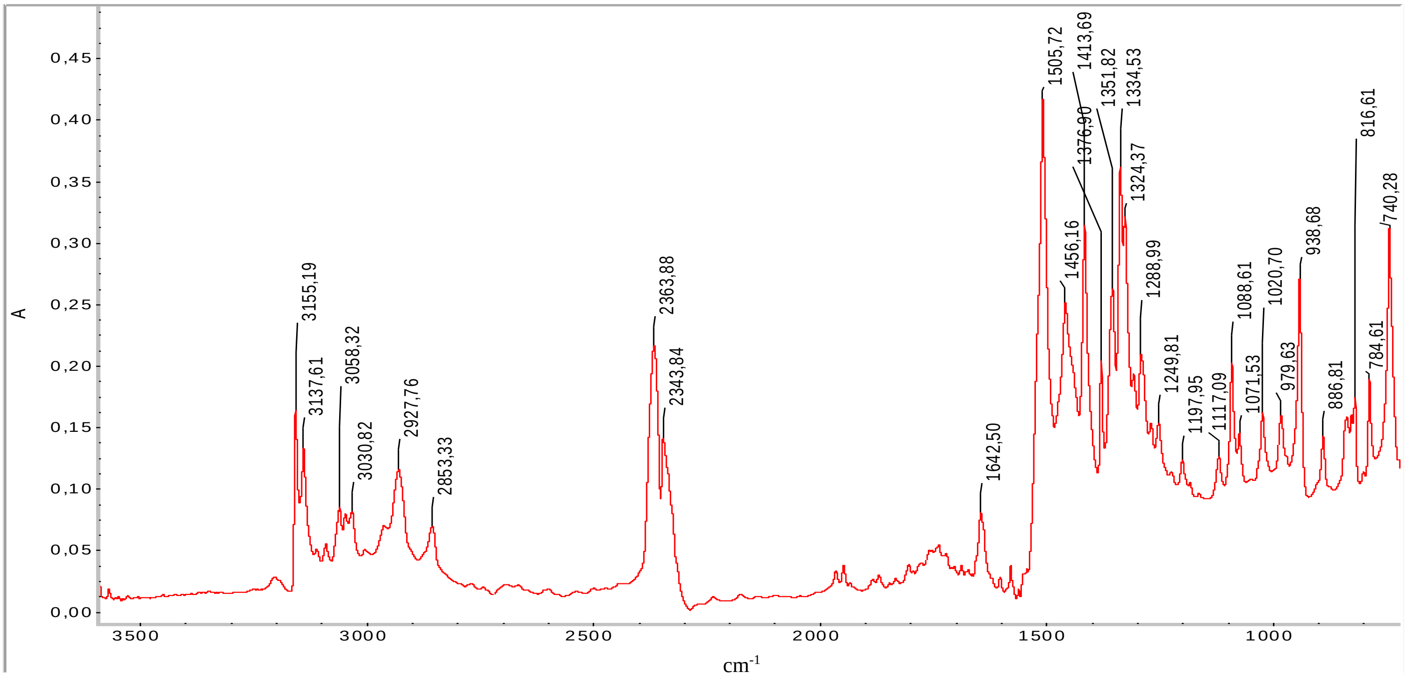


Figure S14 IR spectrum of 3-methyl-***5-nitro-1-[(*****E*****)-2-phenylvinyl]-1H-pyrazole* 4b**

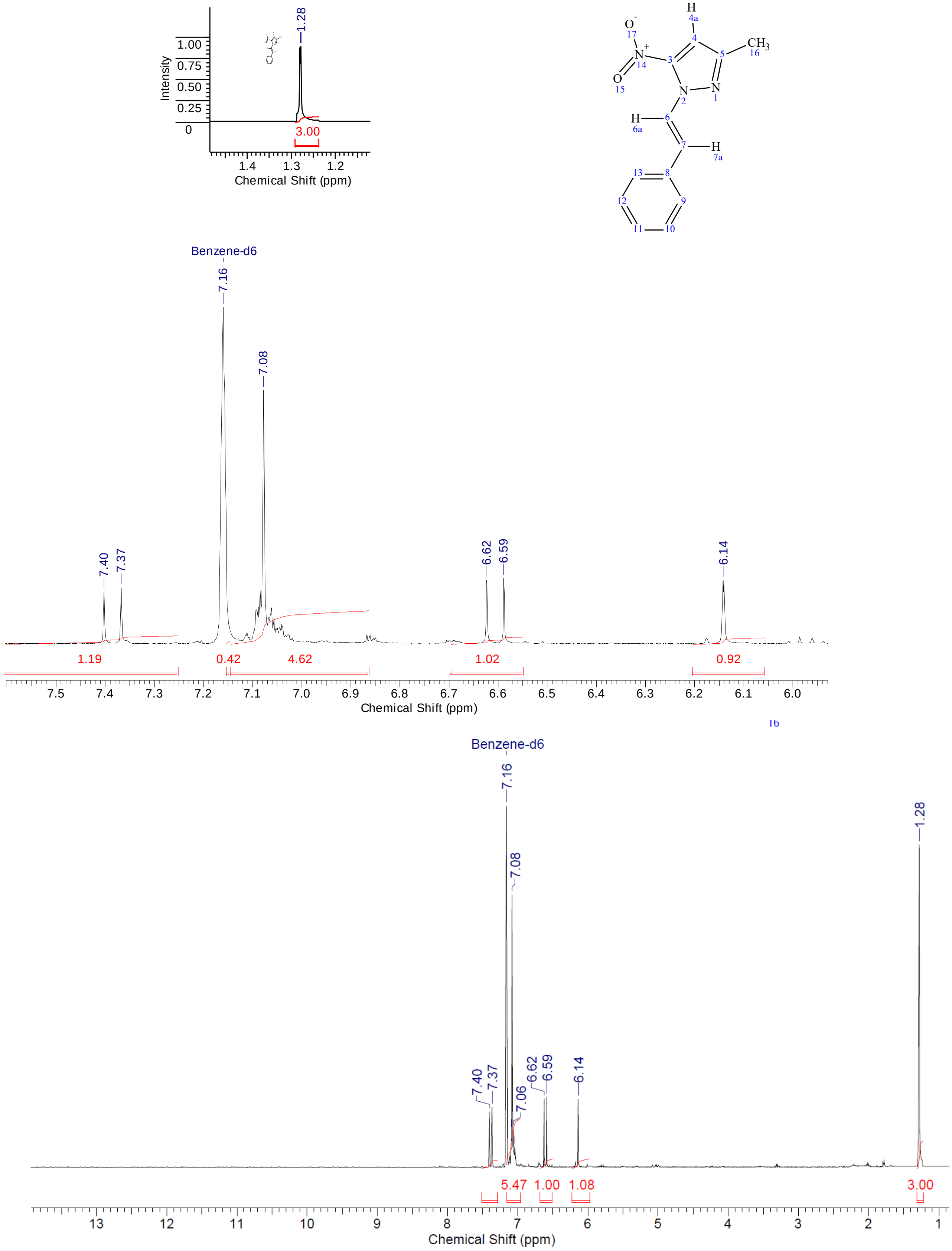


Figure S15 ^{1}H NMR spectrum (C_6D_6) of 3-methyl-***5-nitro-1-[(E)-2-phenylvinyl]-1H-pyrazole*** **4b**

Acquisition Time (sec)	1.3107	***Date***	Apr 9 2019	***Date Stamp***	Apr 9 2019
File Name	C:\NMR\dav1125-up-APT_20190410_01\APT_01			***Frequency (MHz)***	100.58
Nucleus	13C	***Number of Transients***	10000	***Original Points Count***	32768
Points Count	32768	***Pulse Sequence***	APT0	***Receiver Gain***	30.00
Solvent	NITROMETHANE-d3			***Spectrum Offset (Hz)***	11210.5615
Sweep Width (Hz)	25000.00	***Temperature (degree C)***	22.000		

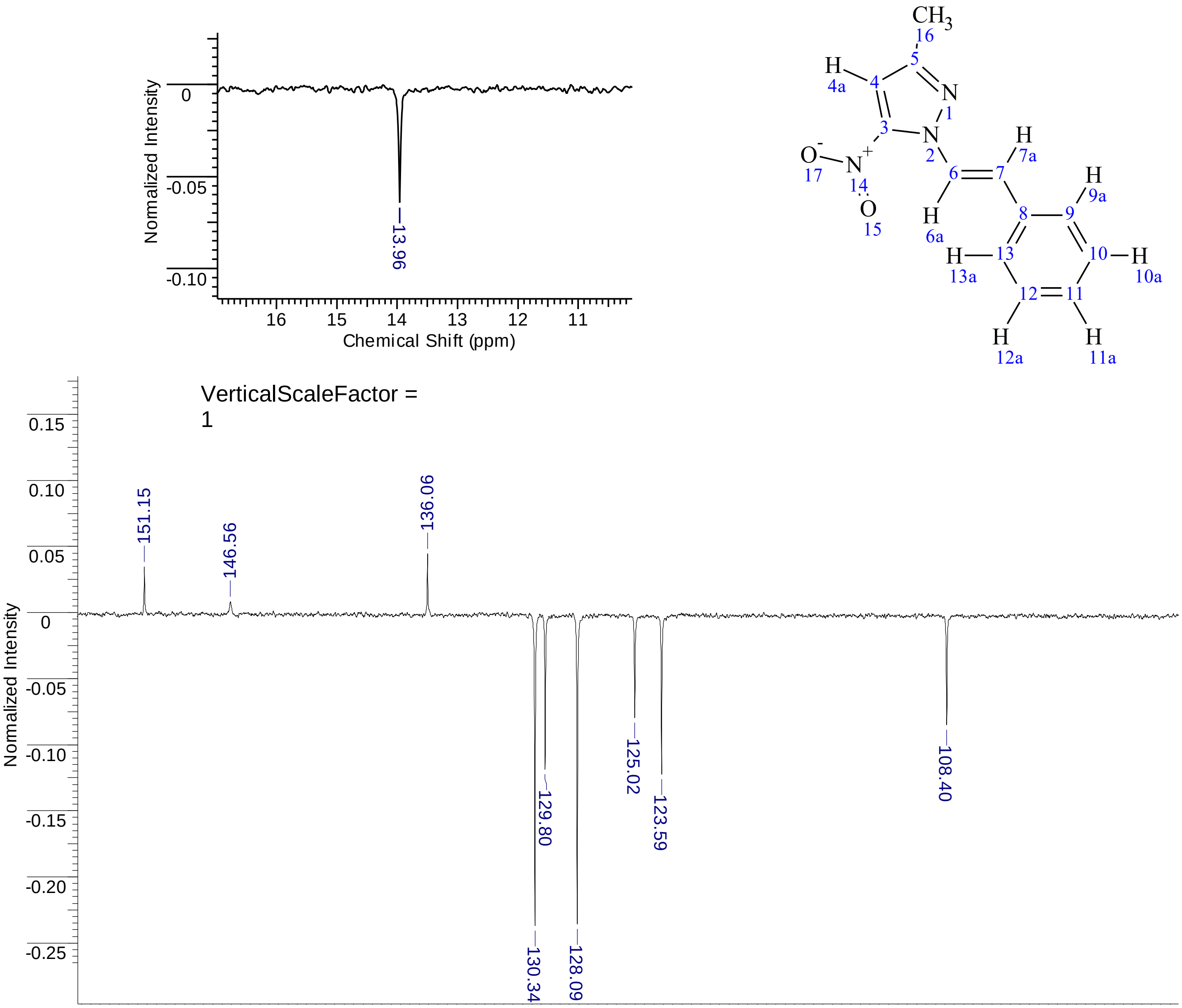


Figure S16 ^{13}C NMR APT spectrum (C_6D_6) of 3-methyl-***5-nitro-1-[(*****E*****)-2-phenylvinyl]-1H-pyrazole*** **4b**

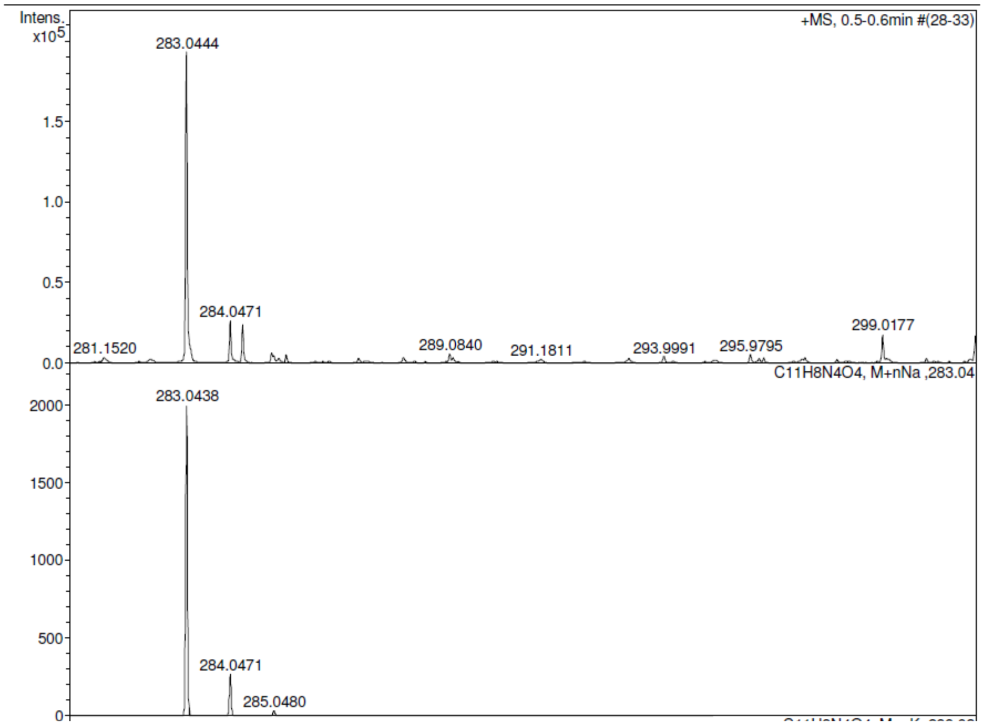


Figure S17 MS spectrum of 3***,4-dinitro-1-[(E)-2-phenylvinyl]-1H-pyrazole*** **3c**

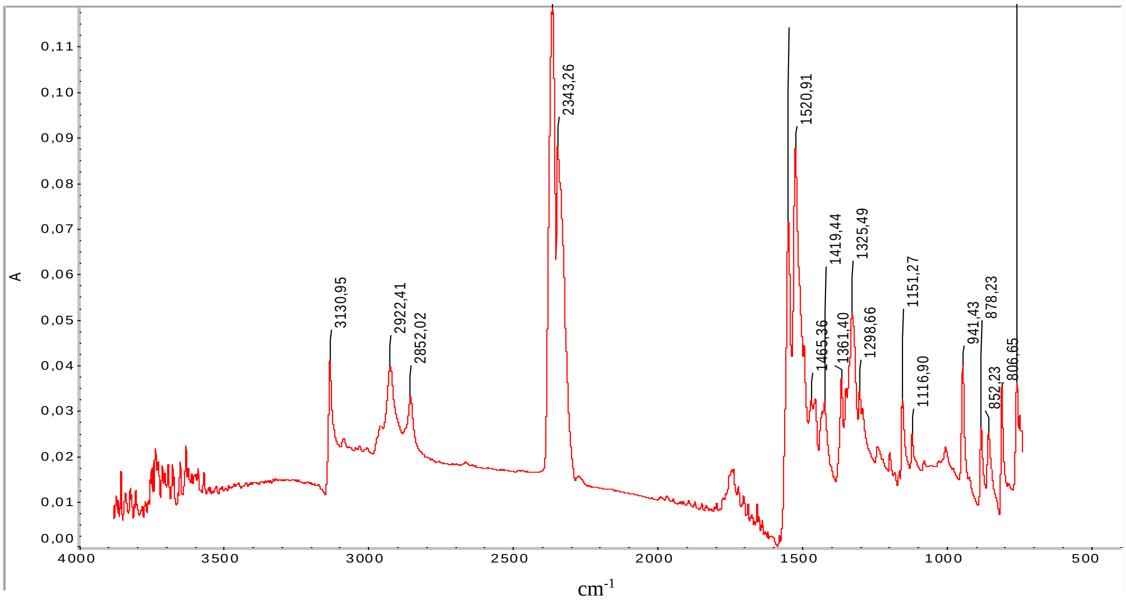
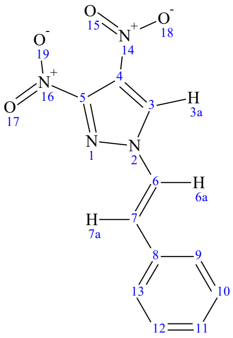


Figure S18 IR spectrum of 3***,4-dinitro-1-[(E)-2-phenylvinyl]-1H-pyrazole*** **3c**



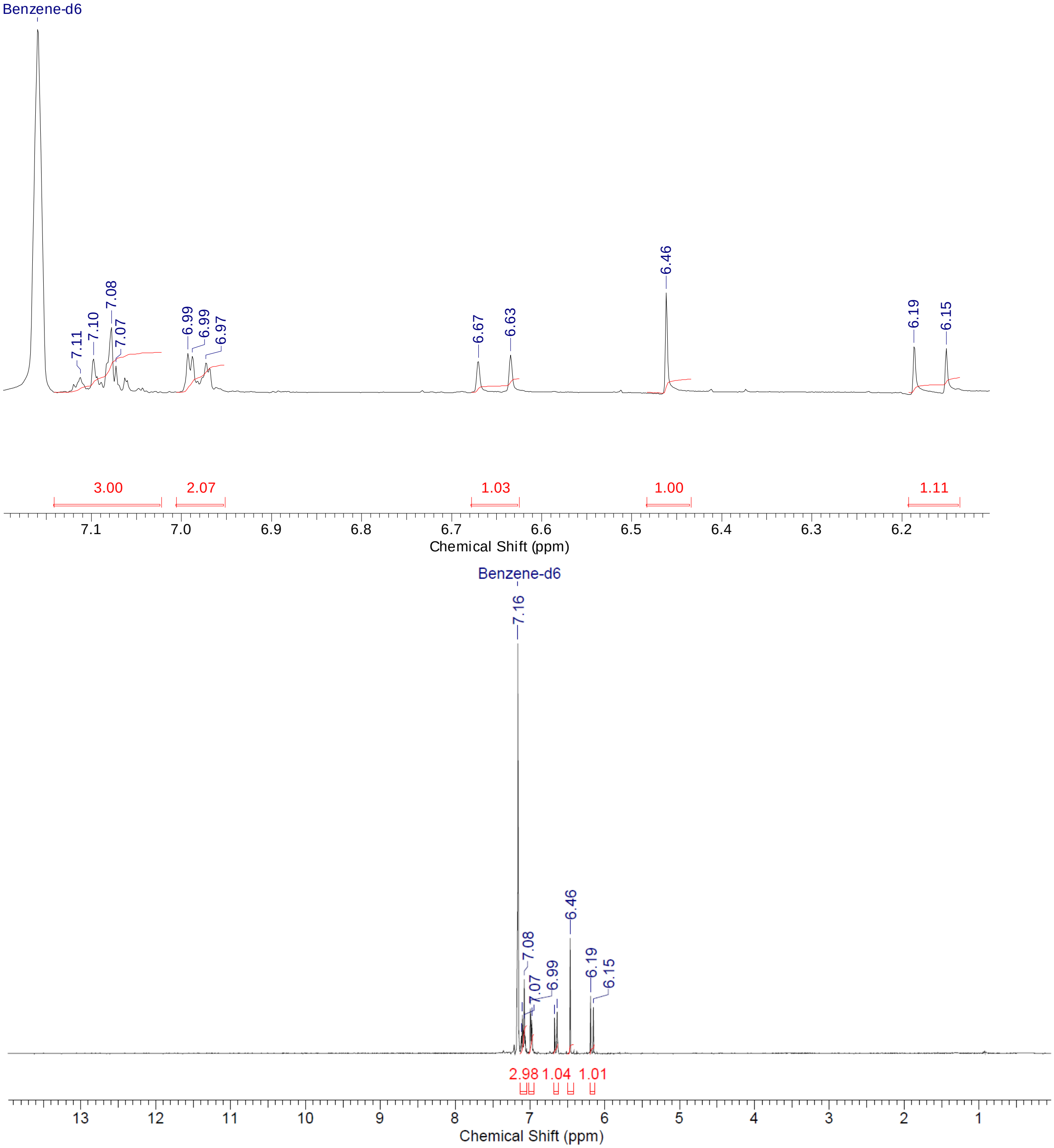


Figure S19 ^{1}H NMR spectrum (C_6D_6) of ***3,4-dinitro-1-[(E)-2-phenylvinyl]-1H-pyrazole* 3c**

Acquisition Time (sec)	1.3107	***Date***	Jan 29 2019		
File Name	C:\Users\DIMA\vynylation sept 2018\dav1131-c-apt_20190130_01\APT_01				
Frequency (MHz)	100.58	***Nucleus***	13C	***Number of Transients***	10000
Original Points Count	32768	***Points Count***	32768	***Pulse Sequence***	APT0
Solvent	NITROMETHANE-D3			***Sweep Width (Hz)***	25000.00
Temperature (degree C)	22.000				

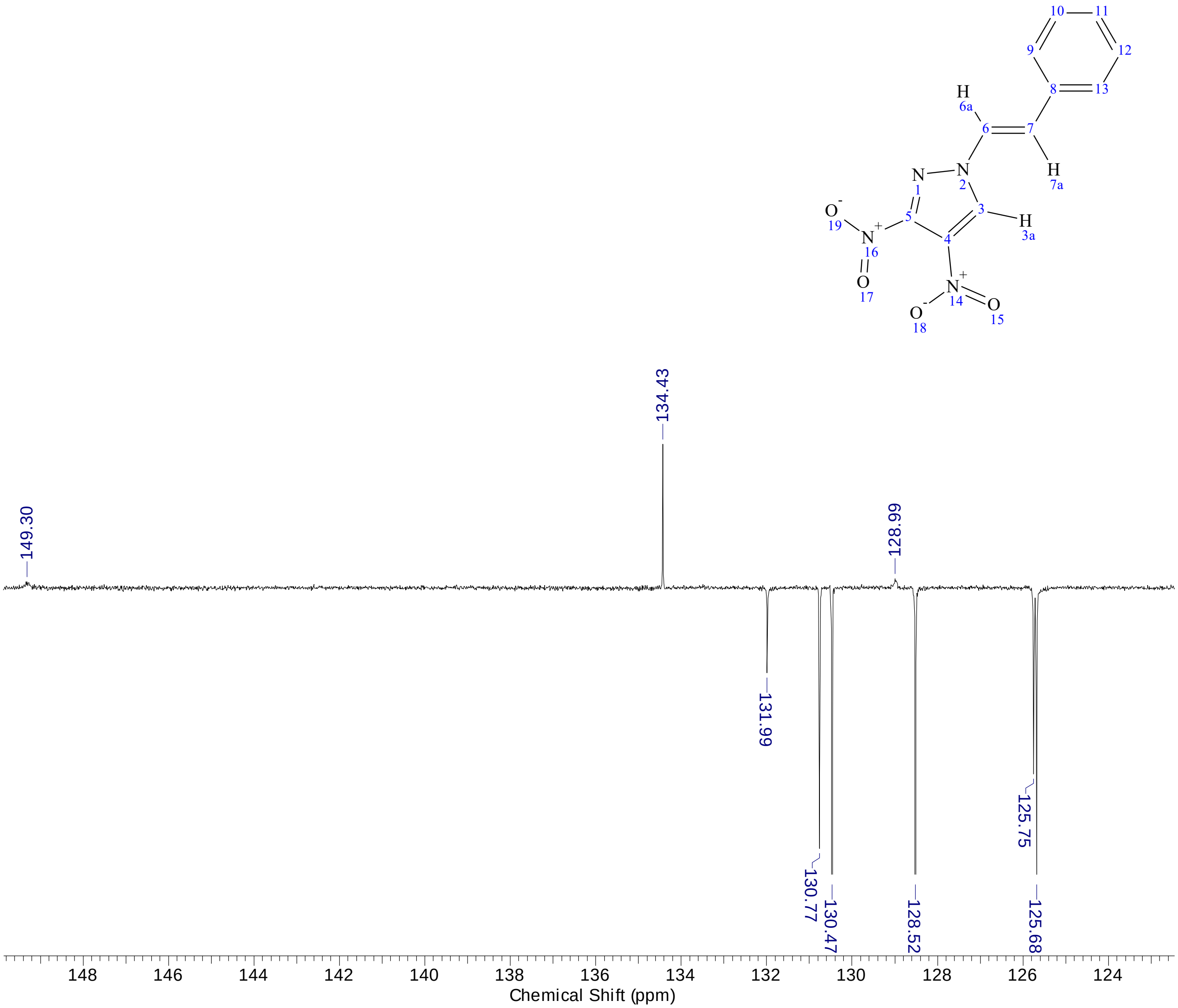


Figure S20 ^{13}C NMR APT spectrum (CD_3NO_2) of ***3,4-dinitro-1-[(E)-2-phenylvinyl]-1H-pyrazole* 3c**

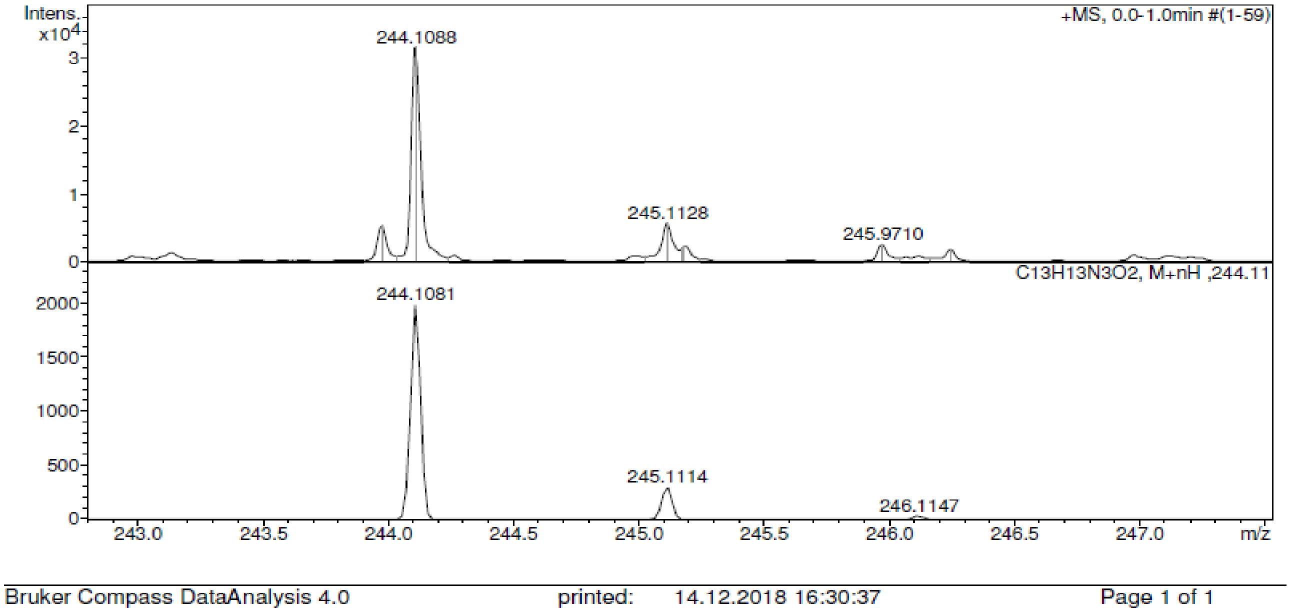


Figure S21 MS spectrum of ***3,5-dimethyl-4-nitro-1-[(E)-2-phenylvinyl]-1H-pyrazole* 3d**

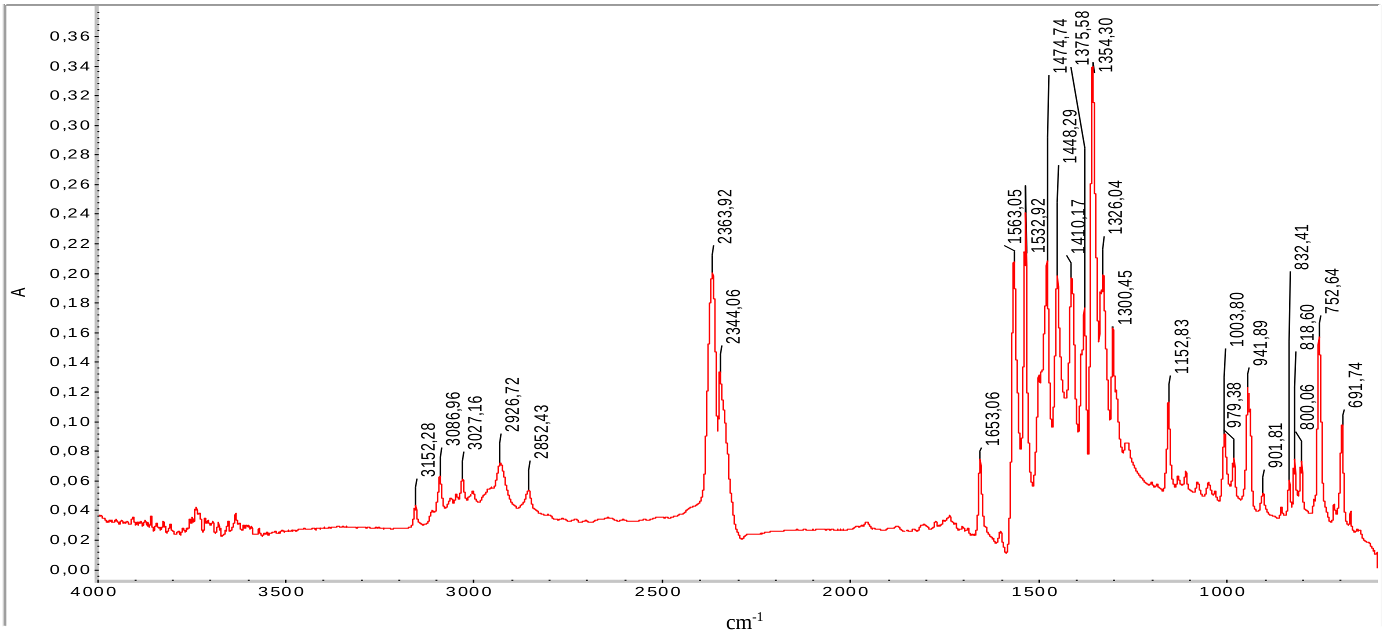


Figure S22 IR spectrum of ***3,5-dimethyl-4-nitro-1-[(E)-2-phenylvinyl]-1H-pyrazole* 3d**

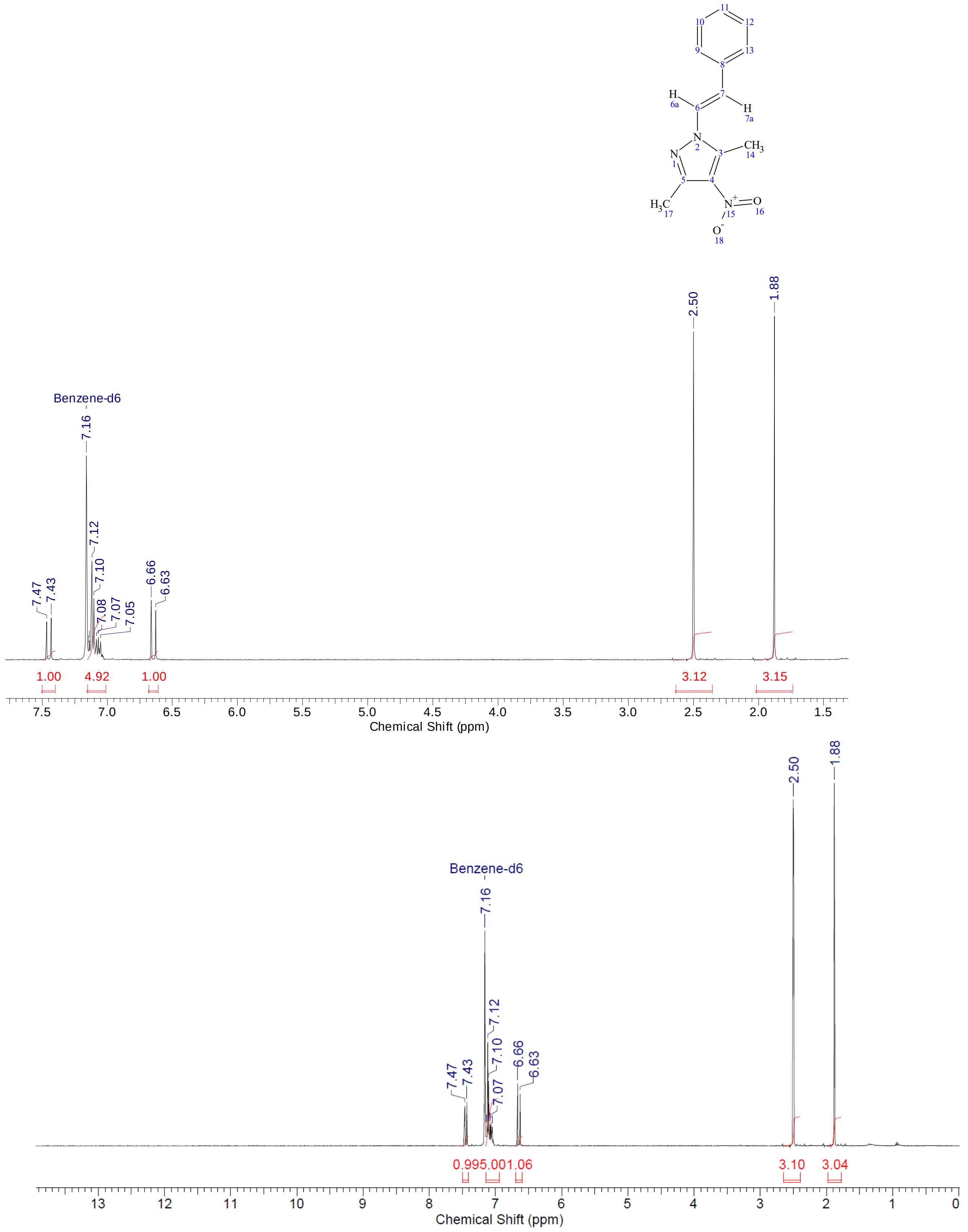


Figure S23 ^{1}H NMR spectrum (C_6D_6) of ***3,5-dimethyl-4-nitro-1-[(E)-2-phenylvinyl]-1H-pyrazole*** **3d**

Acquisition Time (sec)	0.2499	**Comment**	Imported from UXNMR.		
Date	13 Jul 2018 18:35:44				
File Name	C:\Users\DIMA\vynylation\16_07_2018\DAV-1117N-C13\DAV-1117N-C13_001000fid				
Frequency (MHz)	100.62	**Nucleus**	13C	**Number of Transients**	17733
Original Points Count	5994	**Points Count**	8192	**Pulse Sequence**	zgpg30
Solvent	CD3NO2	**Sweep Width (Hz)**	23980.81	**Temperature (degree C)**	27.000

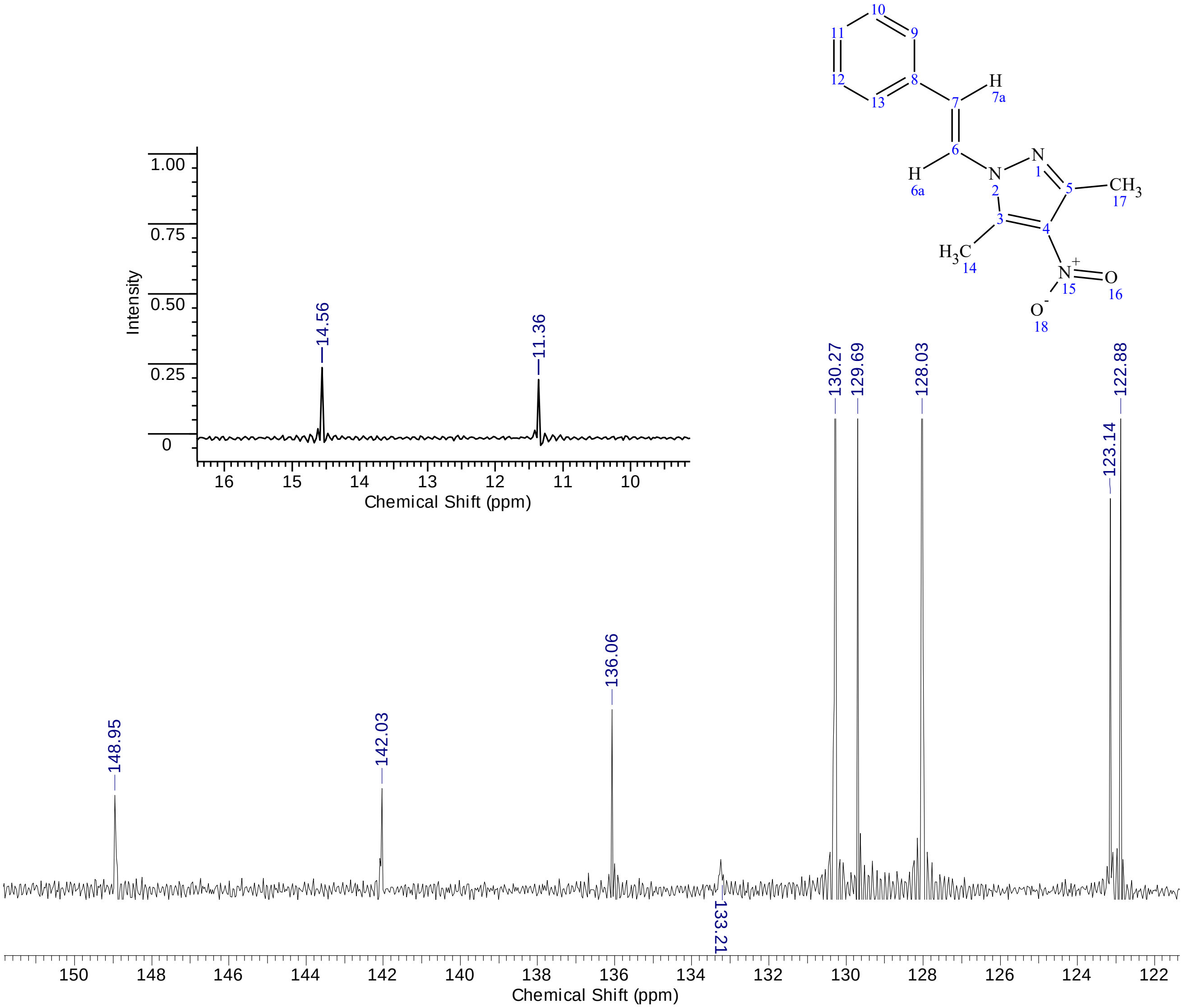


Figure S24 ^{13}C NMR spectrum of ***3,5-dimethyl-4-nitro-1-[(*E*)-2-phenylvinyl]-1H-pyrazole*** **3d**

Computational Details

All the quantum mechanical calculations were performed using ORCA 4.1.0 program package **S1**. Geometry optimization was performed at CPCM/B3LYP/Def2-TZVP level, and frequencies were calculated at the same level to confirm that the structures correspond to true minima. The CPCM/B3LYP/Def2-TZVP optimized geometries were next subjected to NMR calculations. The magnetic shielding constants (σ) were computed using GIAO (gauge including atomic orbitals) **S2** with the same Def2-TZVP basis set and mPW1PW91 functional **S3** (invoked by mPW1PW keyword in ORCA). The effect of the solvent was included using the conductor-like polarizable continuum model, CPCM, **S4** with the same solvent as used in the experimental NMR measurement.

The chemical shifts (δ_{calc}) were computed using benzene as reference standard according to $\delta_{calc} = \sigma_0 - \sigma_x + \delta_0$ where σ_0 isotropic shielding constant for benzene computed at the same level of theory, σ_x is the isotropic shielding constant of the nuclei x, δ_0 is the experimental NMR shift of benzene in the corresponding solvent **S5**.

For all compounds except **3a** and **3c** *s*-*cis*-rotamers were computed to be at least 2 kcal/mol more stable than *s*-*trans*-rotamers (Table S1), which means that only s-*cis*-rotamer is significantly populated, and only *s*-*cis*-rotamer was taken for the NMR calculation. For compounds **3a** and **3c** the Boltzmann averaging for *s*-*trans*- and *s*-*cis*-rotamers was done according to eq. 1:

$$\delta_{aver} = \frac{\delta_{calc}^{cis} \cdot e^{(\frac{-E_{cis}}{RT})} + \delta_{calc}^{trans} \cdot e^{(\frac{-E_{tras}}{RT})}}{e^{(\frac{-E_{cis}}{RT})} + e^{(\frac{-E_{tras}}{RT})}} \quad \text{(eq. 1)}$$

where δ_{calc}^{cis} and E_{cis} are the chemical shift of the corresponding nucleus and relative SCF energy of s-*cis*-rotamer and δ_{calc}^{trans} and E_{tras} are the same values for the s-*trans*-rotamer.

The experimental ^{13}C NMR shifts were assigned to the respective carbons based on line intensity – double for *ortho*-Ph and *meta*-Ph positions, single – for all other non-equivalent CH-groups and <<1 for quaternary carbon signals. Additionally, $\underline{C}$-NO$_2$ signals were identified by significant line broadening due to coupling with quadrupole ^{14}N nuclei. The experimental and computed chemical shifts were arranged for correlation in descending order.

The scaled chemical shifts were calculated $\delta_{scaled} = (\delta_{calc} - b)/a$ where *a* and *b* are the slope and intercept, respectively, obtained from a linear regression on a plot of δ_{calc} against $\delta_{\exp}$.

References

S1 F. Neese, *Wiley Interdiscip. Rev.: Comput. Mol. Sci.*, 2017, **8**, e1327.

S2 (*a*) T. A. Keith and R. F. W. Bader, *Chem. Phys. Lett.*, 1992, **194**, 1; (*b*) T. A. Keith and R. F. W. Bader, *Chem. Phys. Lett.*, 1993, **210**, 223.

S3 C. Adamo and V. Barone, *J. Chem. Phys.*, 1998, **108**, 664.

S4 V. Barone and M. Cossi, *J. Phys. Chem. A*, 1998, **102**, 1995.

S5 G. R. Fulmer, A. J. M. Miller, N. H. Sherden, H. E. Gottlieb, A. Nudelman, B. M. Stoltz, J. E. Bercaw and K. I. Goldberg, *Organometallics*, 2010, **29**, 2176.

Table S1 Computed energies of optimized structures of 1-styryl nitropyrazoles at CPCM/B3LYP/Def2-TZVP level.

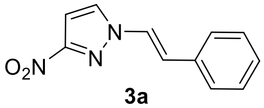
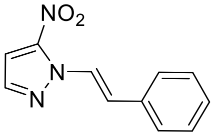
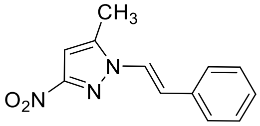
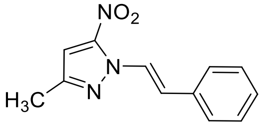
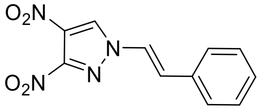
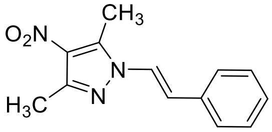
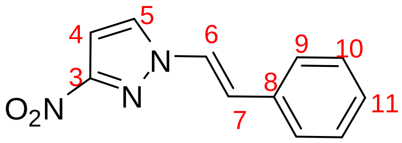
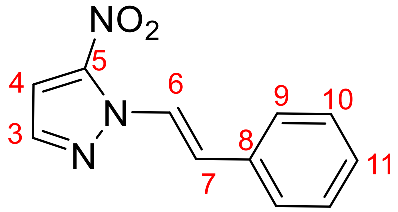
Structure	s-*cis*-rotamer		s-*trans*-rotamer	
	total, au	relative, kcal/mol	total, au	relative, kcal/mol
 **3a**	-739.04058	0.0	-739.03989	0.4
 **4a**	-739.03052	6.3	-739.0245	10.1
 **3b**	-778.47373	0.0	-778.47012	2.3
 **4b**	-778.47096	1.7	-778.46282	6.9
 **3c**	-943.53533	0.0	-943.53440	0.6
 **3d**	-817.800768	0.0	-817.79732	2.2

Table S2 Experimental ^{13}C NMR data and ^{13}C NMR shifts calculated at the CPCM/mPW1PW91/Def2-TZVP level for *s*-cis and *s*-trans rotamers of 3-nitro-1-[(*E*)-2-phenyl-vinyl]-1*H*-pyrazole, (**3a**), and the Boltzmann averaged values for the mixture of rotamers (in $CDCl_3$ solvent).



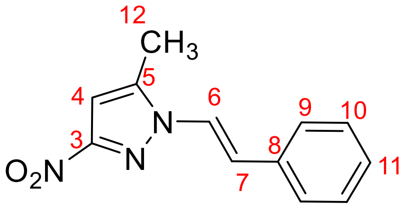
δ_{exp}	Nuclei	δ_{calc}(s-cis)	δ_{calc}(s-trans)	δ_{aver}	δ_{scaled}
156.43	C-3	158.41	157.86	158.24	155.84
104.13	C-4	104.89	106.53	105.39	105.16
122.19	C-7	122.49	120.78	121.97	121.06
133.25	C-8	134.51	134.35	134.46	133.04
129.04	C-9	127.57	127.28	127.48	126.34
128.9	C-10	129.27	129.37	129.30	128.09
128.9	C-11	129.65	129.7	129.67	128.44
125.02	C-6	124.11	126.97	124.98	123.94
130.27	C-5	133.21	126.99	131.33	130.03

Table S3 Experimental ^{13}C NMR data and ^{13}C NMR shifts calculated at the CPCM/mPW1PW91/Def2-TZVP level for 5-nitro-1-[(*E*)-2-phenyl-vinyl-1*H*-pyrazole, **4a** (in CD_3NO_2 solvent).



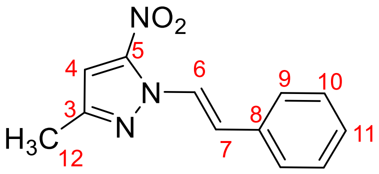
δ_{exp}	Nuclei	δ_{calc}	δ_{scaled}
146.65	C-5	151.58	149.45
109.14	C-4	111.91	111.41
125.2	C-7	125.67	124.61
135.82	C-8	136.71	135.20
130.37	C-9	129.93	128.69
128.23	C-10	131.16	129.87
130.02	C-11	131.66	130.35
124.78	C-6	124.52	123.51
141.03	C-3	142.86	141.09

Table S4 Experimental ^{13}C NMR data and ^{13}C NMR shifts calculated at the CPCM/mPW1PW91/Def2-TZVP level for 5-methyl-3-nitro-1-[(*E*)-2-phenylvinyl]-1*H*-pyrazole, **3b** (in CD_3NO_2 solvent).



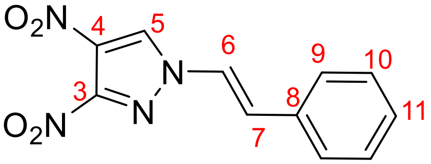
δ_{exp}	Nuclei	δ_{calc}	δ_{scaled}
157.2	C-3	160.77	158.26
103.88	C-4	105.98	105.73
123.26	C-7	123	122.05
135.75	C-8	136.40	134.90
128.19	C-9	129.11	127.91
130.3	C-10	130.81	129.53
130	C-11	131.08	129.79
123.71	C-6	123.53	122.55
144.69	C-5	148.09	146.10
11.42	C-12	7.36	11.17

Table S5 Experimental ^{13}C NMR data and ^{13}C NMR shifts calculated at the CPCM/mPW1PW91/Def2-TZVP level for 3-methyl-5-nitro-1-[(*E*)-2-phenylvinyl]-1*H*-pyrazole **4b** (in $CDCl_3$ solvent).



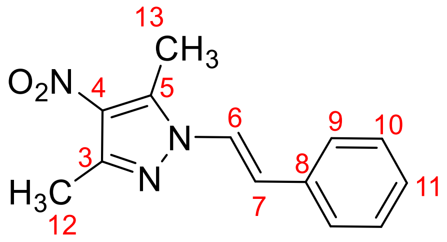
δ_{exp}	Nuclei	δ_{calc}	δ_{scaled}
144.83	C-5	148.65	146.64
107.19	C-4	109.92	109.50
123.07	C-7	123.19	122.23
134.35	C-8	136.52	135.01
128.9	C-9	128.49	127.31
128.6	C-10	130.15	128.90
126.8	C-11	130.16	128.91
123.28	C-6	124.32	123.31
149.07	C-3	153.53	151.32
13.96	C-12	10.33	14.02

Table S6 Experimental ^{13}C NMR data and ^{13}C NMR shifts calculated at the CPCM/mPW1PW91/Def2-TZVP level for *s*-cis and *s*-trans rotamers of 3.4-dinitro-1-[(*E*)-2-phenyl-vinyl]-1*H*-pyrazole, **3c**, and the Boltzmann averaged values for the mixture of rotamers (in CD_3NO_2 solvent).



δ_{exp}	Nuclei	δ_{calc}(s-cis)	δ_{calc}(s-trans)	δ_{calc}(aver)	δ_{scaled}
149.3	C-3	153.89	152.66	153.55	151.34
131.99	C-5	135.63	126.78	133.17	131.80
125.68	C-7	124.59	128.124	125.57	124.51
134.43	C-8	134.81	135.03	134.87	133.43
130.47	C-9	130.9	130.43	130.77	129.50
128.52	C-10	129.97	128.6	129.59	128.36
130.77	C-11	132.35	131.06	131.99	130.67
125.75	C-6	127.22	123.06	126.06	124.98
128.99	C-4	132.28	131.87	132.17	130.83

Table *S7* Experimental ^{13}C NMR data and ^{13}C NMR shifts calculated at the CPCM/mPW1PW91/Def2-TZVP level for 3,5-dimethyl-4-nitro-1-[(*E*)-2-phenylvinyl]-1*H*-pyrazole, **3d** (in CD_3NO_2 solvent).



δ_{exp}	Nuclei	δ_{calc}	δ_{scaled}
133.21	C-4	134.81	133.37
123.14	C-7	122.76	121.82
136.06	C-8	137.02	135.49
128.03	C-9	128.34	127.17
130.27	C-10	130.38	129.12
129.69	C-11	129.59	128.36
122.88	C-6	121.11	120.23
148.95	C-5	154.12	151.88
142.03	C-3	144.26	142.43
11.36	C-12	6.32	10.17
14.56	C-13	13.62	17.17

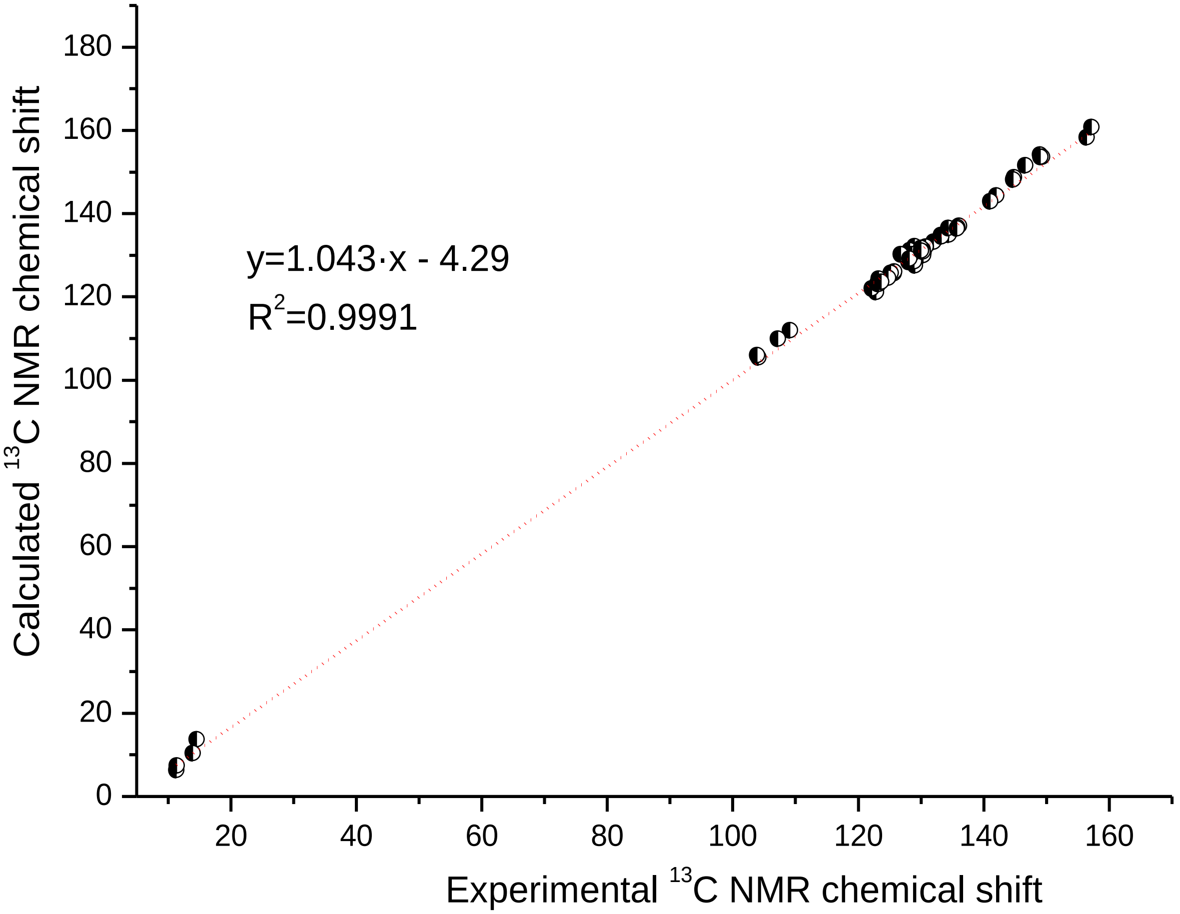


Figure S25 Correlation of experimental and calculated δ(13C) for the studied 1-[(E)-2-phenylvinyl]-1H-pyrazoles

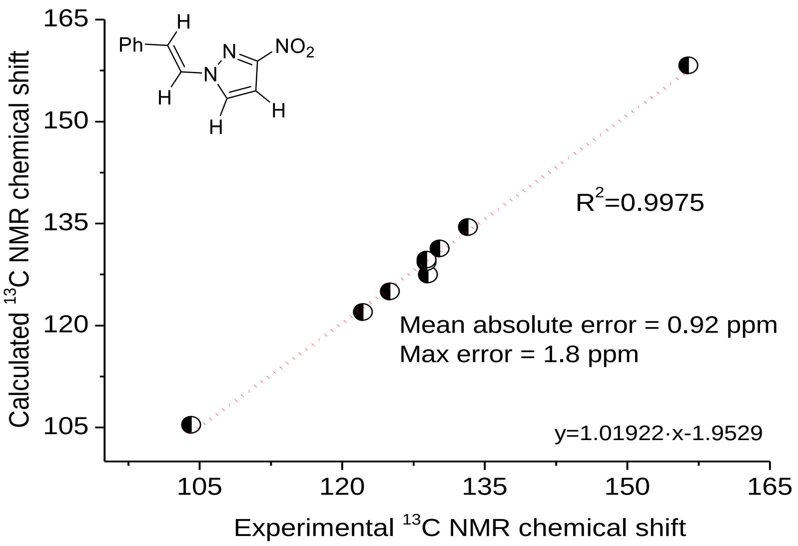


Figure S26. Correlation of experimental and calculated δ(13C) for 3-nitro-[(E)-2-phenylvinyl]-1H-pyrazole

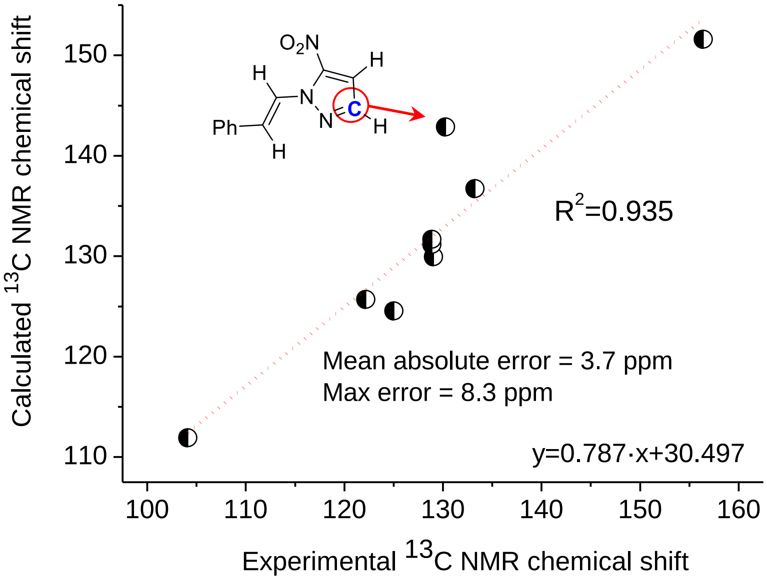


Figure S27. Experimental δ(13C) for 3-nitro-[(E)-2-phenylvinyl]-1H-pyrazole correlation with calculated δ(13C) for 5-nitro-1-[(E)-2-phenylvinyl]-1H-pyrazole