Electronic Supplementary Information

Nitrogen-Bound Diazeniumdiolated Amidines

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Experimental Section

General. All reactions were performed under an inert atmosphere. All chemicals were purchased from Sigma-Aldrich and used without further purification.

Ultraviolet (UV) spectra were recorded on an Agilent Model 8453 or a Hewlett-Packard model 8451A diode array spectrophotometer using 0.1 M NaOH solution, unless otherwise noted. Unless otherwise mentioned, nuclear magnetic resonance (NMR) spectra were collected with a 400-MHz Varian $^{\text{UNITY}}$ INOVA spectrometer using appropriate deuterated solvent with chemical shifts reported in parts per million (ppm) downfield from tetramethylsilane. Mass spectra were recorded on a Thermo Finn LCQ DECA ion trap mass spectrometer. Elemental analyses were performed by Midwest Microlab, LLC (Indianapolis, IN).

General Procedure for Diazeniumdiolation (NO) Reactions. The equipment used for conducting reactions with NO gas under anaerobic conditions has been described previously.[1] Nitric oxide was obtained in UHP grade from Matheson Tri-Gas (Montgomeryville, PA) and allowed to stand in a ballast tank at about five atmosphere pressure over potassium hydroxide pellets for a minimum of several hours before use. The indicated solvent was placed in a standard Parr thick-walled glass hydrogenation bottle and to this was added the material to be treated with NO. Argon gas was passed through the apparatus and bubbled through the solution for 5-10 min, the NO supply line was clamped into the bottle neck, and the headspace was further deoxygenated by 20-25 repeat cycles of argon pressurization to 5 atm followed by venting. Magnetic stirring was begun, and NO gas was admitted to a pressure of ca. 5 atm. After the reaction was over, excess NO was vented and argon was bubbled through the resulting slurry (unless noted!) for 5 min. The products were then isolated as described in the individual sections.

Reaction of Benzamidine with NO. Benzamidine (5.00 g, 41.7 mmol) was suspended in 300 mL of anhydrous diethyl ether and the solution was reacted with NO for 48 h at room temperature as reported.[1] The product was isolated by filtration, washed with ether, and recrystallized by dissolving in basified water (1-2 drops of 0.1M NaOH in 15 mL water) and precipitating by addition of acetone to yield 5.83 g (47% yield) of the benzamidinium salt of *N*-diazeniumdiolated benzamidine **2** (Found C, 55.59; H, 5.34; N, 27.45. $C_{14}H_{16}N_6O_2$ requires C, 55.99; H, 5.37; N, 27.98%); mp 99 - 101 ^{0}C (dec); ^{1}H NMR (D_2O with one drop of 40 wt% NaOD in D_2O, 400 MHz) δ 7.80 - 7.48 (m, 10H); ^{13}C NMR (D_2O with one drop of 40 wt% NaOD in D_2O, 100 MHz) δ 170.9, 165.6, 137.6, 134.6 (2C), 133.8, 131.9, 131.8, 131.5, 131.3, 130.1 (2C), 129.3, 129.1; λ_{max} (0.1 M NaOH)/nm 229 (ε/dm^3 mol^{-1} cm^{-1} 27 500). Benzamidinium salt **2** (5.00 g, 16.7 mmol) was added in one portion to a stirred solution of 25 wt% of sodium methoxide in methanol (3.61 g, 16.7 mmol) in 10 mL of anhydrous methanol at 0 ^{o}C. Initially, a clear solution was obtained and on stirring for 45 min at the same temperature, a pale white solid precipitated out. Filtration of the solid, followed by washing with ether and recrystallization from methanol – ethyl acetate afforded 3.00 g (89% yield) of the sodium salt of *N*-diazeniumdiolated benzamidine **3a**. The degree of hydration of this product varies from preparation to preparation because, as many free diazeniumdiolates do, it dissociates spontaneously under high vacuum and thus can not be completely dried. (Found C, 40.37; H, 3.93; N, 26.34. $C_{14}H_{16}N_6O_2$. 0.45 H_2O requires C, 39.99; H, 3.79; N, 26.65%); mp 275 - 277 ^{o}C (dec); ^{1}H NMR (methanol-*d*$_4$, 400 MHz) δ 7.85 - 7.82 (m, 2H), 7.53 - 7.42 (m, 3H); ^{13}C NMR (methanol-*d*$_4$, 100 MHz) δ 159.4, 133.4, 130.7, 128.1 (2C), 126.9 (2C); λ_{max} (0.1 M NaOH)/nm 233 (ε/dm^3 mol^{-1} cm^{-1} 16 500). This absorbance exhibits an extensive tail with the hint of a shoulder near 255 nm which is attributable to a diazeniumdiolate functionality. A separate peak is not observed due to overlap with the overwhelmingly more intense benzamidine absorbance.

***O*^{2}-Methylation of 3a to Produce 4.** Sodium *N*-diazeniumdiolated benzamidine **3a** (0.30 g, 1.5 mmol) was dissolved in a suspension of 0.31 g of finely powdered potassium carbonate in 5 mL of anhydrous methanol and cooled to 0 ^{o}C with constant stirring. To this mixture, a solution of dimethyl sulfate (0.22 g, 1.8 mmol) in 1 mL of anhydrous methanol was slowly added. The reaction mixture was then allowed to warm to room temperature and stirred for an additional 8 h. The reaction mixture was then filtered, the methanol was removed on a rotary evaporator, and the residue was extracted with ether (3x15 mL). The combined organic layers were washed with saturated brine solution and dried over anhydrous sodium sulfate. After concentration under reduced pressure, the crude product was purified on a silica gel column (hexanes:ethyl acetate:triethylamine 40:59.5:0.5) to afford 0.22 g (76% yield) of **4** (Found C, 49.33; H, 4.99; N, 28.79. $C_8H_{10}N_4O_2$ requires C, 49.48; H, 5.19; N, 28.82%); mp 104 - 106 ^oC; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.69 (br s, 1H), 7.79 - 7.76 (m, 2H), 7.54 - 7.44 (m, 3H), 5.84 (br s, 1H), 4.11 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.7, 132.2, 131.8, 128.6 (2C), 126.9 (2C), 60.7; λ_{max} (EtOH)/nm 236 ($\varepsilon/dm^3\ mol^{-1}\ cm^{-1}$ 14 300), and 280 (15 600).

***O^2*-Methoxymethylation of 3a to Produce 5.** Sodium *N*-diazeniumdiolated benzamidine **3a** (1.00 g, 5.0 mmol) was suspended in 15 mL of anhydrous dichloromethane containing 1 mL of anhydrous methanol and cooled to 0 ^oC with constant stirring. To this mixture, *N*,*N*-diisopropylethylamine (0.96 g, 7.4 mmol) was added, followed by the slow addition of a solution of chloromethyl methyl ether (0.48 g, 5.0 mmol) in 3 mL of dichloromethane. The reaction mixture was then allowed to warm to room temperature, stirred for an additional 10 h, and the solvent was removed on a rotary evaporator. The crude product was purified on a silica gel column (hexanes:ethyl acetate:triethylamine 70:29.5:0.5) to afford 0.68 g (61% yield) of **5** (Found C, 47.96; H, 5.27; N, 24.72. $C_9H_{12}N_4O_3$ requires C, 48.21; H, 5.39; N, 24.99%); mp 68 - 69 ^oC; ^1H NMR δ ($CDCl_3$) 7.78 - 7.76 (m, 2H), 7.59 - 7.41 (m, 3H), 5.30 (s, 2H), 3.52 (s, 3H); ^{13}C NMR δ ($CDCl_3$) 160.9, 132.6, 131.9, 128.7 (2C), 127.0 (2C), 98.0, 57.2; λ_{max} (EtOH)/nm 235 ($\varepsilon/dm^3\ mol^{-1}\ cm^{-1}$ 14 400), and 277 (15 800).

***O^2*-(2,4-Dinitrophenylation) of 3a to Produce 6.** Sodium *N*-diazeniumdiolated benzamidine **3a** (0.50 g, 2.5 mmol) was dissolved in a solution of 0.25 g of sodium bicarbonate in 7 mL of water which had been precooled to 0 ^oC and stirred for 10 min. To this mixture, a cold solution of 2,4-dinitro-1-fluorobenzene (0.55 g, 3.0 mmol) in 3 mL of *t*-butanol containing 1 mL of THF was added in one portion and stirring was continued for an additional 4 h at the same temperature. The reaction mixture was then filtered, the residue was washed with 20 mL of water, and then with 20 mL of ethanol. The crude product was purified on a silica gel column (dichloromethane:methanol:triethylamine 95:4.5:0.5) to afford 0.45 g (52% yield) of **6** (Found C, 44.97; H, 2.91; N, 24.16. $C_{13}H_{10}N_6O_6$ requires C, 45.09; H, 2.91; N, 24.27%); mp 107 - 109 ^oC; ^1H NMR (DMSO-d_6, 400 MHz) δ 8.88 (d, *J*=2.8 Hz, 1H), 8.65 (br s, 1H), 8.57 (dd, *J*=9.4 Hz, 2.8 Hz, 2H), 8.48 (br s, 1H), 7.88 (d, *J*=7.0 Hz, 3H), 7.64 – 7.61 (m, 1H), 7.55 – 7.53 (m, 2H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 162.6, 153.1, 142.1, 137.3, 132.2, 131.9, 130.2, 128.9 (2C), 128.0 (2C), 122.1, 118.4; λ_{max} (EtOH)/nm 275 (ε/dm^3 mol^{-1} cm^{-1} 21 700).

***O*^{2}-Glucosylation of 3a to Produce 7.** Sodium *N*-diazeniumdiolated benzamidine **3a** (0.20 g, 1.1 mmol) was dissolved in 4 mL of ice-cold 5% sodium bicarbonate in water, whereupon 0.45 g of acetobromo-α-D-glucose dissolved in 5 mL of acetone was slowly added to the reaction mixture with constant stirring. The reaction mixture was then allowed to warm to room temperature and stirred for an additional 12 h, following which it was extracted with ethyl acetate (3x10 mL). The combined organic layers were then washed with water and dried over anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the crude product was purified by recrystallization from methanol – ether to afford 0.34 g (61% yield) of **7** (Found C, 49.52; H, 5.23; N, 10.47. $C_{21}H_{26}N_4O_{11}$ requires C, 49.41; H, 5.13; N, 10.98%); mp 167 - 169 ^oC; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.72 (br s, 1H), 7.84 - 7.82 (m, 2H), 7.57 - 7.45 (m, 3H), 6.06 (br s, 1H), 5.33 - 5.28 (m, 3H), 5.17 - 5.12 (m, 1H), 4.29 - 4.14 (m, 2H), 3.85 - 3.80 (m, 1H), 2.07 (s, 3H), 2.05 (s, 3H), 2.03 (s, 3H), 2.02 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.6, 170.0, 169.5, 169.3, 161.3, 132.6, 132.0, 128.8 (2C), 127.1 (2C), 100.4, 72.7, 72.4, 69.4, 67.8, 61.5, 20.7, 20.6, 20.5 (2C); λ_{max} (EtOH)/nm 274 (ε/dm^3 mol^{-1} cm^{-1} 8 900).

***O*^{2}-Benzylation of 3a to Produce 8.** Sodium *N*-diazeniumdiolated benzamidine **3a** (0.50 g, 2.5 mmol) was dissolved in 5 mL of anhydrous dimethyl sulfoxide and cooled to 0 ^oC, whereupon a solution of benzyl bromide (0.51 g, 2.96 mmol) in 2 mL of THF was slowly added with stirring. The reaction mixture was then allowed to warm to room temperature and stirred for an additional 10 h, followed by extraction with ethyl acetate (3x15 mL). The combined organic layers were then washed with water and dried over anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the crude product was purified on a silica gel column (hexanes:ethyl acetate:triethylamine 40:59.5:0.5) to afford 0.39 g (58.5% yield) of **8**

(Found C, 62.19; H, 5.19; N, 20.53. $C_{14}H_{14}N_4O_2$ requires C, 62.21; H, 5.22; N, 20.73%); mp 72 – 74 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.59 (br s, 1H), 7.73 - 7.71 (m, 2H), 7.43 - 7.35 (m, 8H), 5.87 (br s, 1H), 5.30 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.7, 135.4, 132.6, 131.8, 128.8 (2C), 128.7 (2C), 128.6, 128.5 (2C), 127.0 (2C), 75.7; λ_{max} (EtOH)/nm 238 (ε/dm^3 mol^{-1} cm^{-1} 21 400), and 279 (29 600).

Methylation of 8 to Produce 9. Sodium hydride (0.04 g, 1.83 mmol) was suspended in 3 mL of anhydrous *N*,*N*-dimethylformamide, cooled to -10 °C, and stirred for 10 min. To this suspension, a solution of **8** (0.17 g, 0.61 mmol) in 5 mL of anhydrous *N*,*N*-dimethylformamide was added and stirring was continued for 2 h at the same temperature. Methyl iodide (0.22 g, 1.5 mmol) was slowly added to the reaction mixture and then it was allowed to warm to room temperature and stirred for an additional 10 h, following which the reaction mixture was quenched with saturated ammonium chloride solution at 0 °C and extracted with ethyl acetate (3x15 mL). The combined organic layers were then washed with water and dried over anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the crude product was purified on a silica gel column (hexanes:ethyl acetate:triethylamine (40:59.5:0.5) to afford 0.17 g (92% yield) of **9** (Found C, 64.51; H, 5.95; N, 18.88. $C_{16}H_{18}N_4O_2$ requires C, 64.41, H, 6.08; N, 18.78%); mp 65 - 67 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.36 - 7.14 9m, 10H), 5.30 (s, 2H), 3.15 (s, 3H), 2.73 (s, 3H); ^{13}C NMR δ ($CDCl_3$, 100 MHz) δ 169.2, 136.3, 130.0, 129.7, 128.3 (2C), 128.2 (2C), 128.1 (2C), 127.9, 127.3 (2C), 74.6, 40.1, 37.6; λ_{max} (EtOH)/nm 241 (ε/dm^3 mol^{-1} cm^{-1} 21 100), and 280 (8 400).

4-Nitrobenzoylation of 8 to Produce 10. Sodium hydride (0.08 g, 3.33 mmol) was suspended in 5 mL of anhydrous *N*,*N*-dimethylformamide, cooled to -10 °C, and stirred for 10 min. To this suspension, a solution of **8** (0.3 g, 1.11 mmol) in 5 mL of anhydrous *N*,*N*-dimethylformamide was added and stirring was continued for 2 h at the same temperature. 4-Nitrobenzoyl chloride (0.41 g, 2.22 mmol) dissolved in 5 mL of anhydrous *N*,*N*-dimethylformamide was slowly added to the reaction mixture and then it was allowed to warm to room temperature and stirred for an additional 10 h, following which the reaction mixture was quenched with saturated ammonium chloride solution at 0 ^{o}C and extracted with ethyl acetate (3x15 mL). The combined organic layers were then washed with water and dried over anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the crude product was purified by recrystallization from methanol - water to afford 0.11 g (42% yield) of **10** (Found C, 58.89; H, 3.96; N, 16.29. $C_{16}H_{18}N_4O_2$.0.5 H_2O requires C, 58.88, H, 4.24; N, 16.35%); mp 131 - 133 ^{o}C; ^{1}H NMR ($CDCl_{3,}$ 400 MHz) δ 12.71 (br s, 1H), 8.35 - 8.31 (m, 2H), 8.12 – 8.09 (m, 2H), 7.69 – 7.67 (m, 2H), 7.60 – 7.56 (m, 1H), 7.46 – 7.43 (m, 4H), 7.40 – 7.37 (m, 3H), 5.42 (s, 2H); ^{13}C NMR ($CDCl_{3,}$ 100 MHz) δ 161.7, 159.7, 150.7, 137.3, 134.3 (2C), 132.2, 130.9, 129.3 (2C), 129.1 (3C), 128.7 (4C), 128.4 (2C), 124.1 (2C), 77.3; λ_{max} (EtOH)/nm 265 (ε/dm^{3} mol^{-1} cm^{-1} 52 200).

Single-crystal X-ray Diffraction Analysis of 4 and 9. Single-crystal x-ray diffraction data on compounds **4** and **9** were collected using MoKα radiation and a Bruker APEX-2 CCD area detector. After data collection corrections were applied for Lorentz, polarization, and absorption effects. The structures were solved by direct methods and refined by full-matrix least squares on F^2 values using the programs found in the SHELXTL suite (Bruker, SHELXTL v6.14, 2000, Bruker AXS Inc., Madison, WI). Parameters refined included atomic coordinates and anisotropic thermal parameters for all non-hydrogen atoms. Hydrogen atoms on carbons were included using a riding model [coordinate shifts of C applied to H atoms] with C-H distance set at 0.96 Å.

For compound **4**, a 0.551 x 0.144 x 0.107 mm^3 crystal was prepared for data collection coating with high viscosity microscope oil (Paratone-N, Hampton Research). The oil-coated crystal was mounted on a MicroMesh mount (MiTeGen, Ithaca, NY), transferred to the diffractometer, and data were collected at room temperature (21 °C). The crystal was orthorhombic in space group *P*bca with unit cell dimensions *a* = 9.8141(5) Å,*b* = 11.4621(7) Å, *c* = 17.6029(9) Å. Data were 100% complete to 28.37° θ (approximately 0.75 Å) with an average redundancy of 7.45. The asymmetric unit contains a single molecule.

For compound **9**, a 0.488 x 0.337 x 0.275 mm^3 crystal was prepared for data collection coating with high viscosity microscope oil (Paratone-N, Hampton Research). The oil-coated crystal was mounted on a MicroMesh mount (MiTeGen, Ithaca, NY), transferred to the diffractometer, and data were collected at 100 °K. The crystal was orthorhombic in space group *P*bca with unit cell dimensions *a* = 9.9137(7) Å,*b* = 18.7220(10) Å, *c* = 22.4918(16) Å. Data were 100% complete to 29.17° θ (approximately 0.73 Å) with an average redundancy of 5.82. The asymmetric unit contains a single molecule.

Atomic coordinates for compounds **4** and **9** have been deposited with the Cambridge Crystallographic Data Centre (deposition numbers 761561 and 761562). Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK [fax: +44(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk]

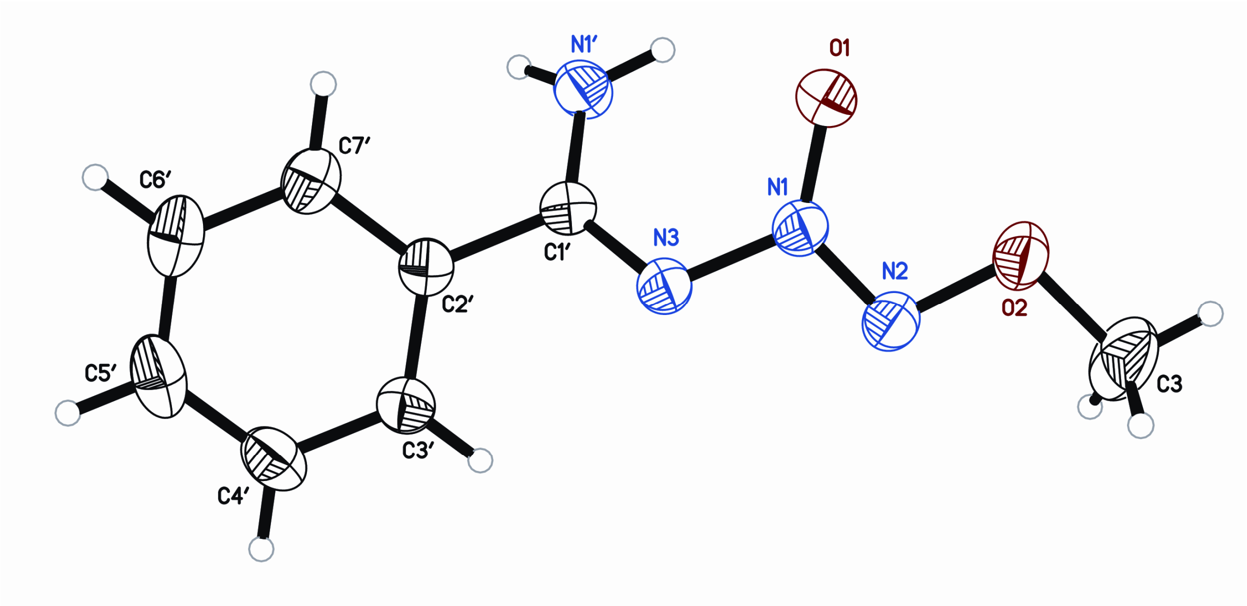

Figure S1. The molecular structure and numbering scheme for **4**.

Crystal data and structure refinement for **4**.

Empirical formula	$C_8H_{10}N_4O_2$	
Formula weight	194.20	
Temperature	294(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	Pbca	
Unit cell dimensions	a = 9.8141(5) Å	α= 90°
	b = 11.4621(7) Å	β= 90°
	c = 17.6029(9) Å	γ = 90°
Volume	1980.15(19) $Å^3$	
Z	8	
Density (calculated)	1.303 Mg/m^3	
Absorption coefficient	0.098 mm^{-1}	
F(000)	816	
Crystal size	0.551 x 0.144 x 0.107 mm^3	
Theta range for data collection	2.31 to 28.37°	
Index ranges	-13<=h<=11, -15<=k<=15, -23<=l<=23	
Reflections collected	19608	
Independent reflections	2462 [R(int) = 0.0195]	
Completeness to θ = 28.37°	99.5 %	

Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9896 and 0.9482
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2462 / 0 / 134
Goodness-of-fit on F^2	1.029
Final R indices [I>2σ(I)]	R1 = 0.0388, wR2 = 0.1086
R indices (all data)	R1 = 0.0503, wR2 = 0.1186
Largest diff. peak and hole	0.149 and -0.146 e.Å^{-3}

Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^2 x 10^3) for **4**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
N(1)	1641(1)	2484(1)	1186(1)	50(1)
O(1)	2376(1)	2950(1)	683(1)	71(1)
N(2)	2024(1)	1696(1)	1646(1)	59(1)
N(3)	307(1)	2862(1)	1340(1)	52(1)
O(2)	3372(1)	1448(1)	1481(1)	71(1)
C(3)	3848(2)	590(2)	2012(1)	101(1)
C(1')	-420(1)	3101(1)	738(1)	47(1)
N(1')	-63(1)	3017(1)	12(1)	63(1)
C(2')	-1818(1)	3529(1)	903(1)	49(1)
C(3')	-2594(1)	3022(1)	1474(1)	59(1)
C(4')	-3892(2)	3433(2)	1624(1)	71(1)
C(5')	-4408(2)	4356(2)	1215(1)	77(1)
C(6')	-3632(2)	4875(1)	654(1)	74(1)
C(7')	-2347(2)	4460(1)	493(1)	61(1)

Bond lengths [Å] and angles [°] for **4**.

N(1)-O(1)	1.2595(13)	N(1)-N(2)	1.2709(14)
N(1)-N(3)	1.4055(14)	N(2)-O(2)	1.3831(15)
N(3)-C(1')	1.3060(15)	O(2)-C(3)	1.4354(19)
C(3)-H(3A)	0.9600	C(3)-H(3B)	0.9600
C(3)-H(3C)	0.9600	C(1')-N(1')	1.3294(16)
C(1')-C(2')	1.4858(17)	N(1')-H(1'A)	0.88(2)
N(1')-H(2'B)	0.89(2)	C(2')-C(3')	1.3881(18)
C(2')-C(7')	1.3892(17)	C(3')-C(4')	1.3836(19)
C(3')-H(3'A)	0.9300	C(4')-C(5')	1.377(2)
C(4')-H(4'A)	0.9300	C(5')-C(6')	1.381(2)
C(5')-H(5'A)	0.9300	C(6')-C(7')	1.378(2)
C(6')-H(6'A)	0.9300	C(7')-H(7'A)	0.9300
O(1)-N(1)-N(2)	125.46(10)	O(1)-N(1)-N(3)	122.54(10)
N(2)-N(1)-N(3)	111.80(10)	N(1)-N(2)-O(2)	107.12(10)
C(1')-N(3)-N(1)	114.66(10)	N(2)-O(2)-C(3)	108.40(12)
O(2)-C(3)-H(3A)	109.5	O(2)-C(3)-H(3B)	109.5
H(3A)-C(3)-H(3B)	109.5	O(2)-C(3)-H(3C)	109.5
H(3A)-C(3)-H(3C)	109.5	H(3B)-C(3)-H(3C)	109.5
N(3)-C(1')-N(1')	128.37(12)	N(3)-C(1')-C(2')	114.51(10)
N(1')-C(1')-C(2')	117.12(11)	C(1')-N(1')-H(1'A)	118.5(13)
C(1')-N(1')-H(2'B)	116.9(12)	H(1'A)-N(1')-H(2'B)	123.0(18)
C(3')-C(2')-C(7')	119.52(12)	C(3')-C(2')-C(1')	120.66(11)
C(7')-C(2')-C(1')	119.81(11)	C(4')-C(3')-C(2')	120.07(13)
C(4')-C(3')-H(3'A)	120.0	C(2')-C(3')-H(3'A)	120.0
C(5')-C(4')-C(3')	120.02(15)	C(5')-C(4')-H(4'A)	120.0
C(3')-C(4')-H(4'A)	120.0	C(4')-C(5')-C(6')	120.13(14)
C(4')-C(5')-H(5'A)	119.9	C(6')-C(5')-H(5'A)	119.9
C(7')-C(6')-C(5')	120.25(14)	C(7')-C(6')-H(6'A)	119.9
C(5')-C(6')-H(6'A)	119.9	C(6')-C(7')-C(2')	119.98(14)
C(6')-C(7')-H(7'A)	120.0	C(2')-C(7')-H(7'A)	120.0

Anisotropic displacement parameters (Å^{2}x 10^3) for **4**. The anisotropic displacement factor exponent takes the form: $-2\pi^2$ [$h^2 a^{*2}U^{11}$ + ... + 2 h k a* b* U^{12}]

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
N(1)	50(1)	55(1)	44(1)	-1(1)	-2(1)	2(1)
O(1)	52(1)	91(1)	72(1)	25(1)	7(1)	2(1)
N(2)	62(1)	63(1)	53(1)	4(1)	-1(1)	11(1)
N(3)	49(1)	60(1)	46(1)	0(1)	0(1)	5(1)
O(2)	65(1)	84(1)	64(1)	5(1)	-4(1)	25(1)
C(3)	117(2)	90(1)	95(1)	8(1)	-11(1)	52(1)
C(1')	50(1)	45(1)	46(1)	-1(1)	0(1)	-4(1)
N(1')	52(1)	92(1)	45(1)	-2(1)	-2(1)	2(1)
C(2')	50(1)	49(1)	48(1)	-5(1)	-4(1)	1(1)
C(3')	59(1)	67(1)	51(1)	0(1)	3(1)	5(1)
C(4')	59(1)	92(1)	62(1)	-14(1)	9(1)	2(1)
C(5')	58(1)	88(1)	85(1)	-32(1)	-10(1)	21(1)
C(6')	74(1)	61(1)	86(1)	-9(1)	-19(1)	18(1)
C(7')	64(1)	52(1)	67(1)	2(1)	-8(1)	2(1)

Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^3) for **4**.

	x	y	z	U(eq)
H(3A)	4734	322	1860	151
H(3B)	3227	-57	2021	151
H(3C)	3902	930	2509	151
H(1'A)	780(20)	2831(17)	-98(11)	95
H(2'B)	-730(20)	2994(17)	-327(12)	95
H(3'A)	-2242	2405	1755	71
H(4'A)	-4417	3085	2001	85
H(5'A)	-5280	4632	1317	92
H(6'A)	-3979	5506	385	88
H(7'A)	-1834	4802	109	74

Torsion angles [°] for **4**.

O(1)-N(1)-N(2)-O(2)	-0.84(16)
N(3)-N(1)-N(2)-O(2)	-175.79(9)
O(1)-N(1)-N(3)-C(1')	41.94(15)
N(2)-N(1)-N(3)-C(1')	-142.94(11)
N(1)-N(2)-O(2)-C(3)	177.92(12)
N(1)-N(3)-C(1')-N(1')	0.89(18)
N(1)-N(3)-C(1')-C(2')	-178.47(9)
N(3)-C(1')-C(2')-C(3')	-41.56(16)
N(1')-C(1')-C(2')-C(3')	139.00(13)
N(3)-C(1')-C(2')-C(7')	137.40(12)
N(1')-C(1')-C(2')-C(7')	-42.04(16)
C(7')-C(2')-C(3')-C(4')	0.77(19)
C(1')-C(2')-C(3')-C(4')	179.73(12)
C(2')-C(3')-C(4')-C(5')	-0.9(2)
C(3')-C(4')-C(5')-C(6')	0.0(2)
C(4')-C(5')-C(6')-C(7')	1.0(2)
C(5')-C(6')-C(7')-C(2')	-1.1(2)
C(3')-C(2')-C(7')-C(6')	0.25(19)
C(1')-C(2')-C(7')-C(6')	-178.73(12)

Hydrogen bonds for **4** [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(1')-H(1'A)...O(1)	0.88(2)	2.09(2)	2.6703(17)	123.2(16)
N(1')-H(2'B)...O(1)#1	0.89(2)	2.24(2)	3.0075(17)	144.8(17)
N(1')-H(2'B)...O(2)#1	0.89(2)	2.30(2)	3.1051(16)	150.0(17)

Symmetry transformations used to generate equivalent atoms:
#1 x-1/2,-y+1/2,-z

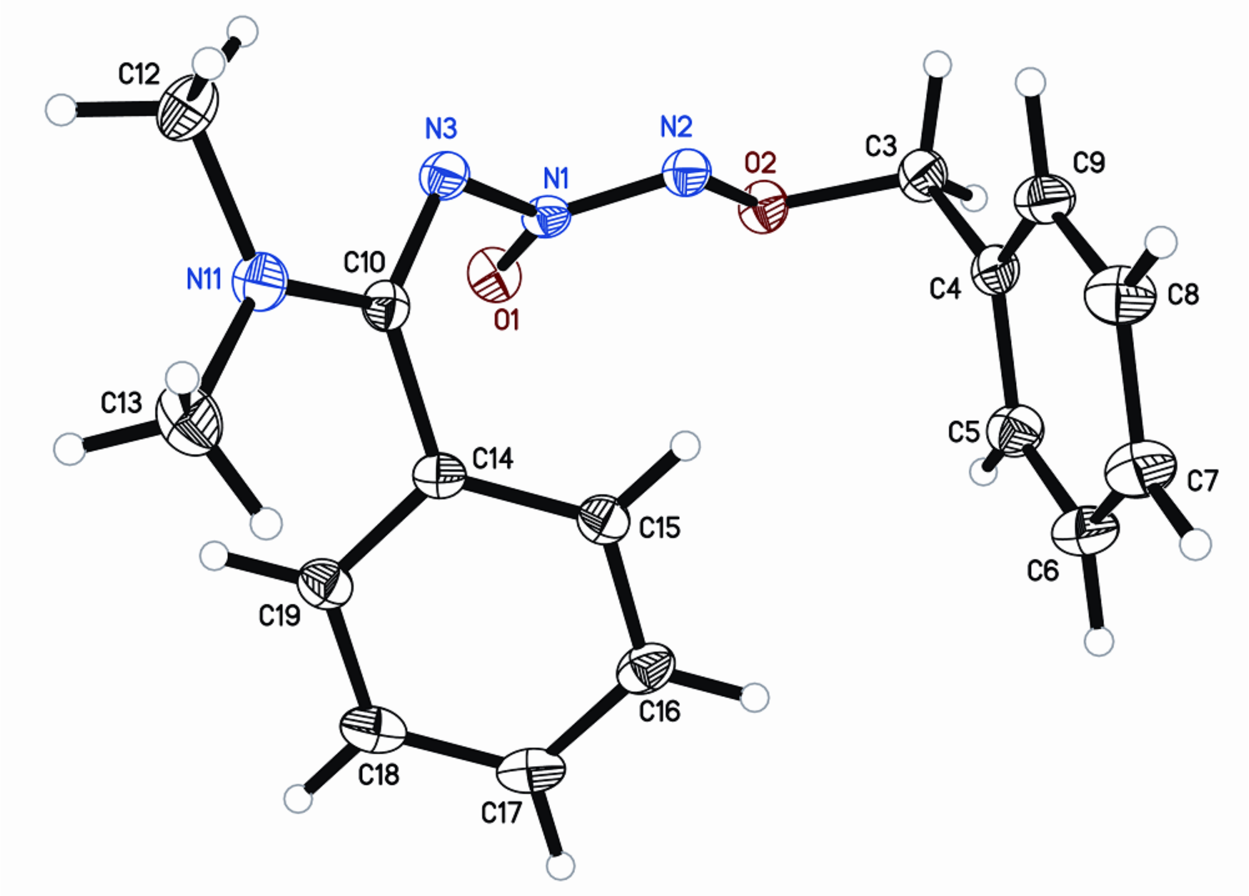

Figure S2. The molecular structure and numbering scheme for **9**.

Crystal data and structure refinement for **9**.

Empirical formula	$C_{16}H_{18}N_4O_2$	
Formula weight	298.34	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	Pbca	
Unit cell dimensions	a = 9.9137(7) Å	α= 90°
	b = 13.7220(10) Å	β= 90°
	c = 22.4918(16) Å	γ = 90°
Volume	3059.7(4) Å^3	
Z	8	

Density (calculated)	1.295 Mg/m^3
Absorption coefficient	0.089 mm^{-1}
F(000)	1264
Crystal size	0.488 x 0.337 x 0.275 mm^3
θ range for data collection	1.81 to 29.17°
Index ranges	-12<=h<=13, -18<=k<=18, -27<=l<=30
Reflections collected	25385
Independent reflections	4131 [R(int) = 0.0263]
Completeness to θ = 29.17°	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9761 and 0.9581
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4131 / 0 / 201
Goodness-of-fit on F^2	1.043
Final R indices [I>2σ(I)]	R1 = 0.0373, wR2 = 0.1032
R indices (all data)	R1 = 0.0444, wR2 = 0.1084
Largest diff. peak and hole	0.373 and -0.229 e.Å^{-3}

Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^2 x 10^3) for **9**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
N(1)	5314(1)	-969(1)	3645(1)	16(1)
O(1)	6332(1)	-930(1)	3977(1)	21(1)
N(2)	5297(1)	-1058(1)	3079(1)	17(1)
O(2)	6627(1)	-1087(1)	2883(1)	20(1)
N(3)	3999(1)	-999(1)	3886(1)	17(1)
C(3)	6580(1)	-1062(1)	2237(1)	22(1)
C(4)	5877(1)	-164(1)	2007(1)	19(1)
C(5)	6489(1)	751(1)	2055(1)	22(1)
C(6)	5828(1)	1582(1)	1851(1)	26(1)
C(7)	4548(1)	1508(1)	1601(1)	27(1)
C(8)	3931(1)	602(1)	1552(1)	25(1)
C(9)	4597(1)	-227(1)	1756(1)	22(1)
C(10)	3631(1)	-162(1)	4126(1)	16(1)
N(11)	2462(1)	-152(1)	4426(1)	20(1)
C(12)	1682(1)	-1044(1)	4510(1)	25(1)
C(13)	1798(1)	733(1)	4637(1)	26(1)
C(14)	4456(1)	750(1)	4098(1)	16(1)

C(15)	4897(1)	1126(1)	3553(1)	18(1)
C(16)	5742(1)	1938(1)	3545(1)	21(1)
C(17)	6139(1)	2379(1)	4073(1)	24(1)
C(18)	5681(1)	2013(1)	4612(1)	24(1)
C(19)	4842(1)	1202(1)	4628(1)	20(1)

Bond lengths [Å] and angles [°] for **9**.

N(1)-O(1)	1.2574(11)	N(1)-N(2)	1.2782(12)
N(1)-N(3)	1.4120(11)	N(2)-O(2)	1.3911(10)
O(2)-C(3)	1.4542(12)	N(3)-C(10)	1.3202(12)
C(3)-C(4)	1.5073(14)	C(3)-H(3B)	0.9900
C(3)-H(3A)	0.9900	C(4)-C(9)	1.3908(15)
C(4)-C(5)	1.3986(13)	C(5)-C(6)	1.3931(15)
C(5)-H(5)	0.9500	C(6)-C(7)	1.3919(16)
C(6)-H(6)	0.9500	C(7)-C(8)	1.3903(15)
C(7)-H(7)	0.9500	C(8)-C(9)	1.3931(15)
C(8)-H(8)	0.9500	C(9)-H(9)	0.9500
C(10)-N(11)	1.3414(12)	C(10)-C(14)	1.4967(13)
N(11)-C(12)	1.4603(13)	N(11)-C(13)	1.4602(13)
C(12)-H(12C)	0.9800	C(12)-H(12B)	0.9800
C(12)-H(12A)	0.9800	C(13)-H(13C)	0.9800
C(13)-H(13B)	0.9800	C(13)-H(13A)	0.9800
C(14)-C(19)	1.3970(13)	C(14)-C(15)	1.3999(14)
C(15)-C(16)	1.3935(13)	C(15)-H(15)	0.9500
C(16)-C(17)	1.3916(15)	C(16)-H(16)	0.9500
C(17)-C(18)	1.3879(16)	C(17)-H(17)	0.9500
C(18)-C(19)	1.3905(14)	C(18)-H(18)	0.9500
C(19)-H(19)	0.9500		
O(1)-N(1)-N(2)	127.37(8)	O(1)-N(1)-N(3)	120.91(8)
N(2)-N(1)-N(3)	111.53(8)	N(1)-N(2)-O(2)	107.76(7)
N(2)-O(2)-C(3)	106.56(7)	C(10)-N(3)-N(1)	112.76(8)
O(2)-C(3)-C(4)	112.24(8)	O(2)-C(3)-H(3B)	109.2
C(4)-C(3)-H(3B)	109.2	O(2)-C(3)-H(3A)	109.2
C(4)-C(3)-H(3A)	109.2	H(3B)-C(3)-H(3A)	107.9
C(9)-C(4)-C(5)	118.92(9)	C(9)-C(4)-C(3)	120.67(9)
C(5)-C(4)-C(3)	120.39(9)	C(6)-C(5)-C(4)	120.30(10)
C(6)-C(5)-H(5)	119.8	C(4)-C(5)-H(5)	119.8
C(7)-C(6)-C(5)	120.19(9)	C(7)-C(6)-H(6)	119.9
C(5)-C(6)-H(6)	119.9	C(8)-C(7)-C(6)	119.87(10)
C(8)-C(7)-H(7)	120.1	C(6)-C(7)-H(7)	120.1
C(7)-C(8)-C(9)	119.72(10)	C(7)-C(8)-H(8)	120.1

C(9)-C(8)-H(8)	120.1	C(4)-C(9)-C(8)	121.00(9)
C(4)-C(9)-H(9)	119.5	C(8)-C(9)-H(9)	119.5
N(3)-C(10)-N(11)	117.00(8)	N(3)-C(10)-C(14)	124.02(8)
N(11)-C(10)-C(14)	118.95(8)	C(10)-N(11)-C(12)	120.94(8)
C(10)-N(11)-C(13)	124.18(8)	C(12)-N(11)-C(13)	114.56(8)
N(11)-C(12)-H(12C)	109.5	N(11)-C(12)-H(12B)	109.5
H(12C)-C(12)-H(12B)	109.5	N(11)-C(12)-H(12A)	109.5
H(12C)-C(12)-H(12A)	109.5	H(12B)-C(12)-H(12A)	109.5
N(11)-C(13)-H(13C)	109.5	N(11)-C(13)-H(13B)	109.5
H(13C)-C(13)-H(13B)	109.5	N(11)-C(13)-H(13A)	109.5
H(13C)-C(13)-H(13A)	109.5	H(13B)-C(13)-H(13A)	109.5
C(19)-C(14)-C(15)	119.88(9)	C(19)-C(14)-C(10)	119.02(8)
C(15)-C(14)-C(10)	121.02(8)	C(16)-C(15)-C(14)	119.60(9)
C(16)-C(15)-H(15)	120.2	C(14)-C(15)-H(15)	120.2
C(15)-C(16)-C(17)	120.42(10)	C(15)-C(16)-H(16)	119.8
C(17)-C(16)-H(16)	119.8	C(18)-C(17)-C(16)	119.76(9)
C(18)-C(17)-H(17)	120.1	C(16)-C(17)-H(17)	120.1
C(17)-C(18)-C(19)	120.50(10)	C(17)-C(18)-H(18)	119.8
C(19)-C(18)-H(18)	119.8	C(18)-C(19)-C(14)	119.82(9)
C(18)-C(19)-H(19)	120.1	C(14)-C(19)-H(19)	120.1

Anisotropic displacement parameters ($Å^2 \times 10^3$) for **9**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
N(1)	15(1)	13(1)	19(1)	0(1)	1(1)	0(1)
O(1)	16(1)	26(1)	22(1)	-1(1)	-3(1)	2(1)
N(2)	15(1)	18(1)	20(1)	-1(1)	3(1)	0(1)
O(2)	15(1)	23(1)	22(1)	0(1)	5(1)	1(1)
N(3)	14(1)	18(1)	20(1)	-1(1)	3(1)	-2(1)
C(3)	23(1)	20(1)	21(1)	-1(1)	7(1)	3(1)
C(4)	21(1)	18(1)	18(1)	-1(1)	7(1)	1(1)
C(5)	19(1)	23(1)	25(1)	-1(1)	3(1)	-3(1)
C(6)	27(1)	19(1)	33(1)	-1(1)	1(1)	-5(1)
C(7)	27(1)	20(1)	34(1)	1(1)	1(1)	1(1)
C(8)	20(1)	23(1)	32(1)	-3(1)	0(1)	0(1)
C(9)	22(1)	18(1)	26(1)	-3(1)	6(1)	-3(1)
C(10)	14(1)	19(1)	14(1)	0(1)	-2(1)	0(1)
N(11)	16(1)	22(1)	22(1)	-2(1)	4(1)	0(1)
C(12)	18(1)	29(1)	28(1)	3(1)	5(1)	-4(1)

C(13)	19(1)	31(1)	28(1)	-6(1)	4(1)	6(1)
C(14)	13(1)	14(1)	20(1)	-1(1)	-1(1)	2(1)
C(15)	17(1)	16(1)	19(1)	-1(1)	0(1)	2(1)
C(16)	20(1)	17(1)	28(1)	3(1)	4(1)	2(1)
C(17)	20(1)	15(1)	36(1)	-1(1)	-2(1)	0(1)
C(18)	24(1)	18(1)	29(1)	-4(1)	-7(1)	1(1)
C(19)	21(1)	18(1)	20(1)	-1(1)	-3(1)	3(1)

Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$ x 10^3) for **9**.

	x	y	z	U(eq)
H(3B)	6102	-1648	2091	26
H(3A)	7512	-1079	2079	26
H(5)	7360	806	2229	27
H(6)	6251	2201	1883	31
H(7)	4097	2076	1463	32
H(8)	3058	548	1381	30
H(9)	4171	-845	1724	26
H(12C)	821	-988	4299	37
H(12B)	1511	-1143	4935	37
H(12A)	2189	-1600	4353	37
H(13C)	1833	755	5072	39
H(13B)	854	732	4506	39
H(13A)	2259	1304	4473	39
H(15)	4622	830	3191	21
H(16)	6048	2191	3176	26
H(17)	6721	2929	4066	29
H(18)	5942	2320	4973	28
H(19)	4533	954	4998	24

Torsion angles [°] for **9**.

O(1)-N(1)-N(2)-O(2)	-1.15(12)
N(3)-N(1)-N(2)-O(2)	-176.07(7)
N(1)-N(2)-O(2)-C(3)	-172.83(7)
O(1)-N(1)-N(3)-C(10)	71.02(11)
N(2)-N(1)-N(3)-C(10)	-113.68(9)
N(2)-O(2)-C(3)-C(4)	58.72(10)
O(2)-C(3)-C(4)-C(9)	-107.47(11)
O(2)-C(3)-C(4)-C(5)	70.84(12)
C(9)-C(4)-C(5)-C(6)	-0.56(15)
C(3)-C(4)-C(5)-C(6)	-178.89(10)
C(4)-C(5)-C(6)-C(7)	0.44(17)
C(5)-C(6)-C(7)-C(8)	-0.21(17)
C(6)-C(7)-C(8)-C(9)	0.11(17)
C(5)-C(4)-C(9)-C(8)	0.46(15)
C(3)-C(4)-C(9)-C(8)	178.78(9)
C(7)-C(8)-C(9)-C(4)	-0.23(16)
N(1)-N(3)-C(10)-N(11)	-172.48(8)
N(1)-N(3)-C(10)-C(14)	5.39(13)
N(3)-C(10)-N(11)-C(12)	3.41(14)
C(14)-C(10)-N(11)-C(12)	-174.58(9)
N(3)-C(10)-N(11)-C(13)	-169.76(9)
C(14)-C(10)-N(11)-C(13)	12.25(14)
N(3)-C(10)-C(14)-C(19)	-122.27(11)
N(11)-C(10)-C(14)-C(19)	55.57(12)
N(3)-C(10)-C(14)-C(15)	54.52(13)
N(11)-C(10)-C(14)-C(15)	-127.64(10)
C(19)-C(14)-C(15)-C(16)	1.26(14)
C(10)-C(14)-C(15)-C(16)	-175.50(9)
C(14)-C(15)-C(16)-C(17)	-0.51(14)
C(15)-C(16)-C(17)-C(18)	-0.53(15)
C(16)-C(17)-C(18)-C(19)	0.83(16)
C(17)-C(18)-C(19)-C(14)	-0.07(15)
C(15)-C(14)-C(19)-C(18)	-0.98(14)
C(10)-C(14)-C(19)-C(18)	175.85(9)

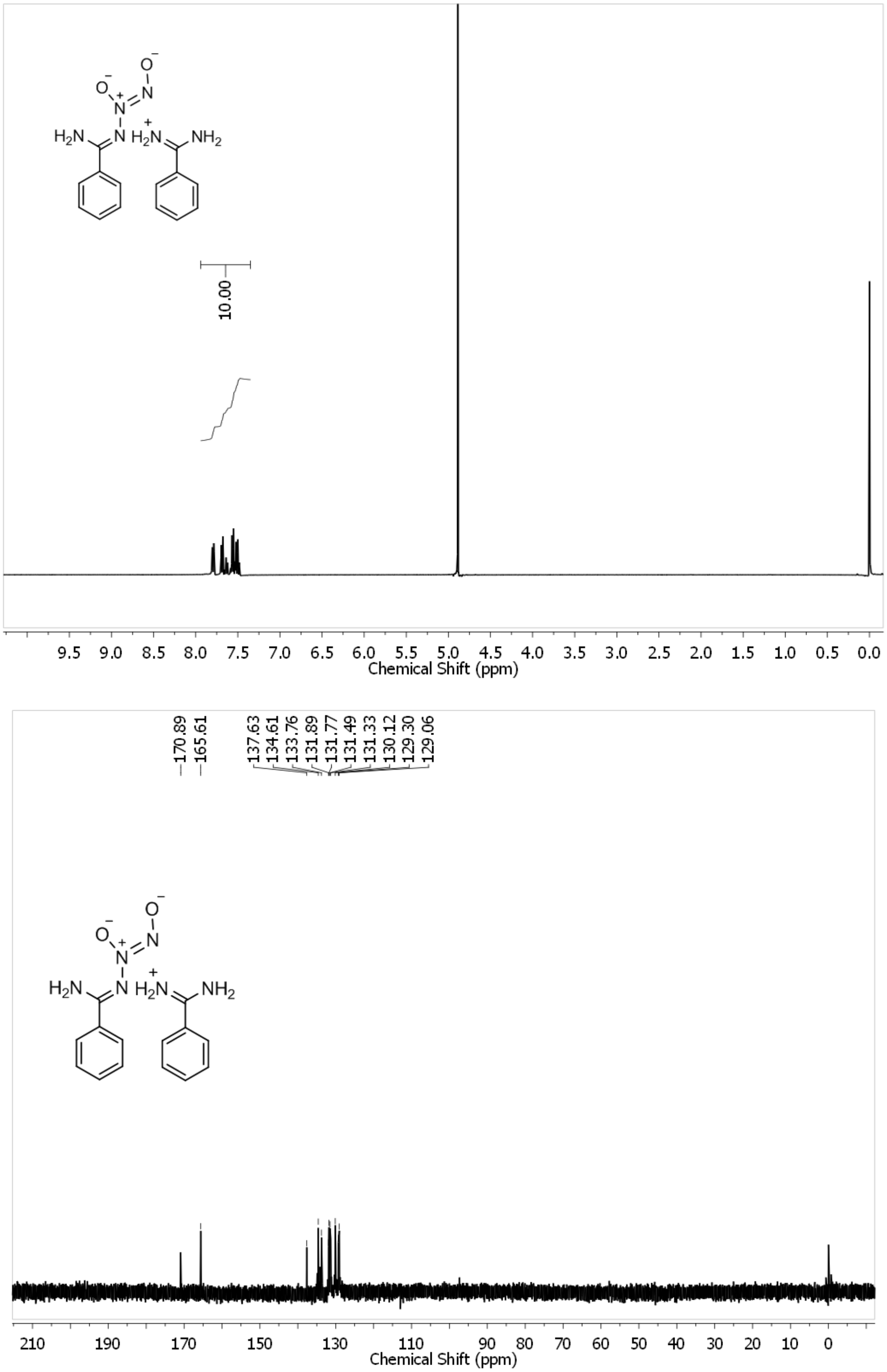

Figure S3. ^{1}H and ^{13}C NMR spectra of compound **2**.

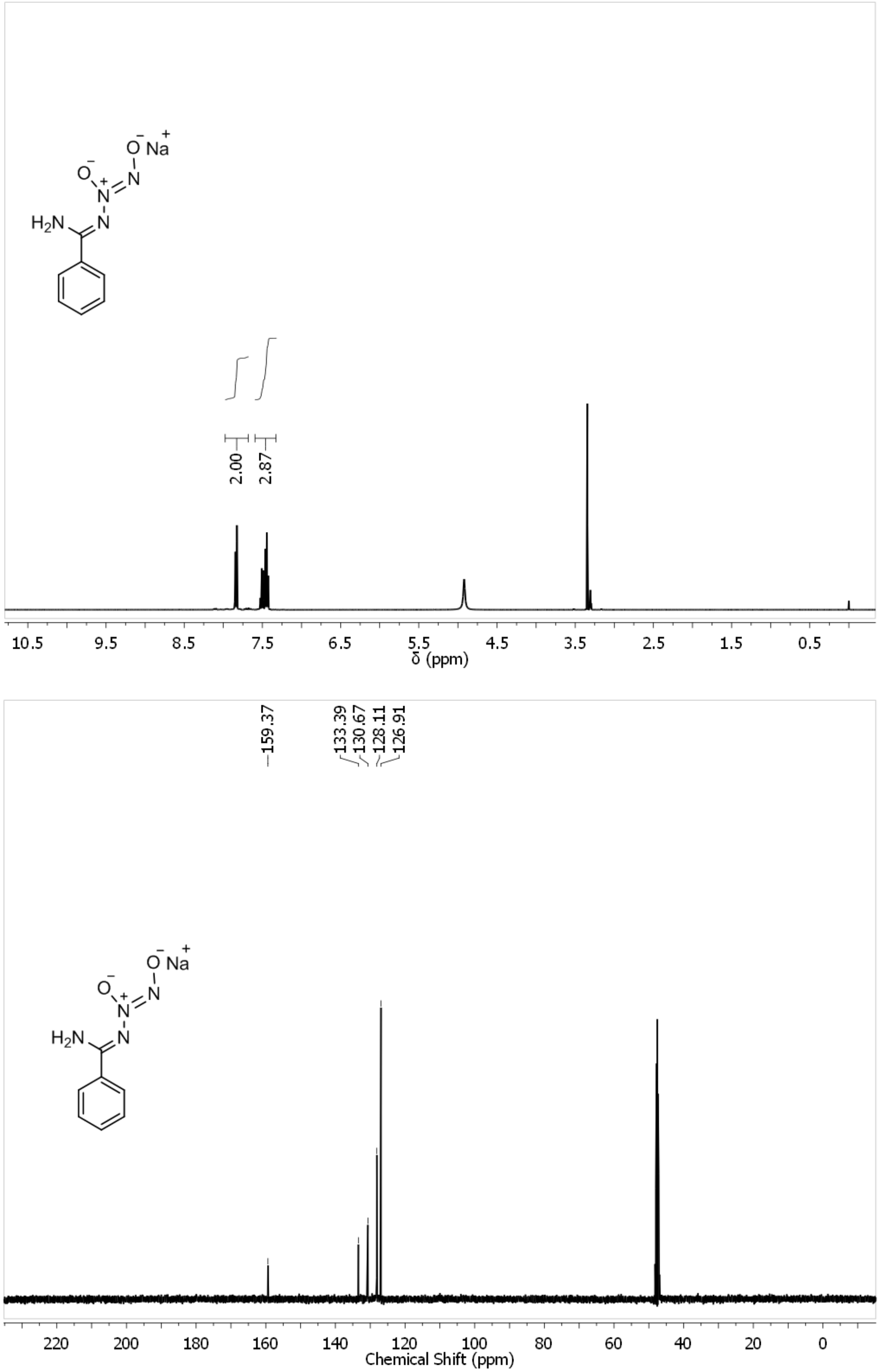

Figure S4. ^{1}H and ^{13}C NMR spectra of compound **3a**.

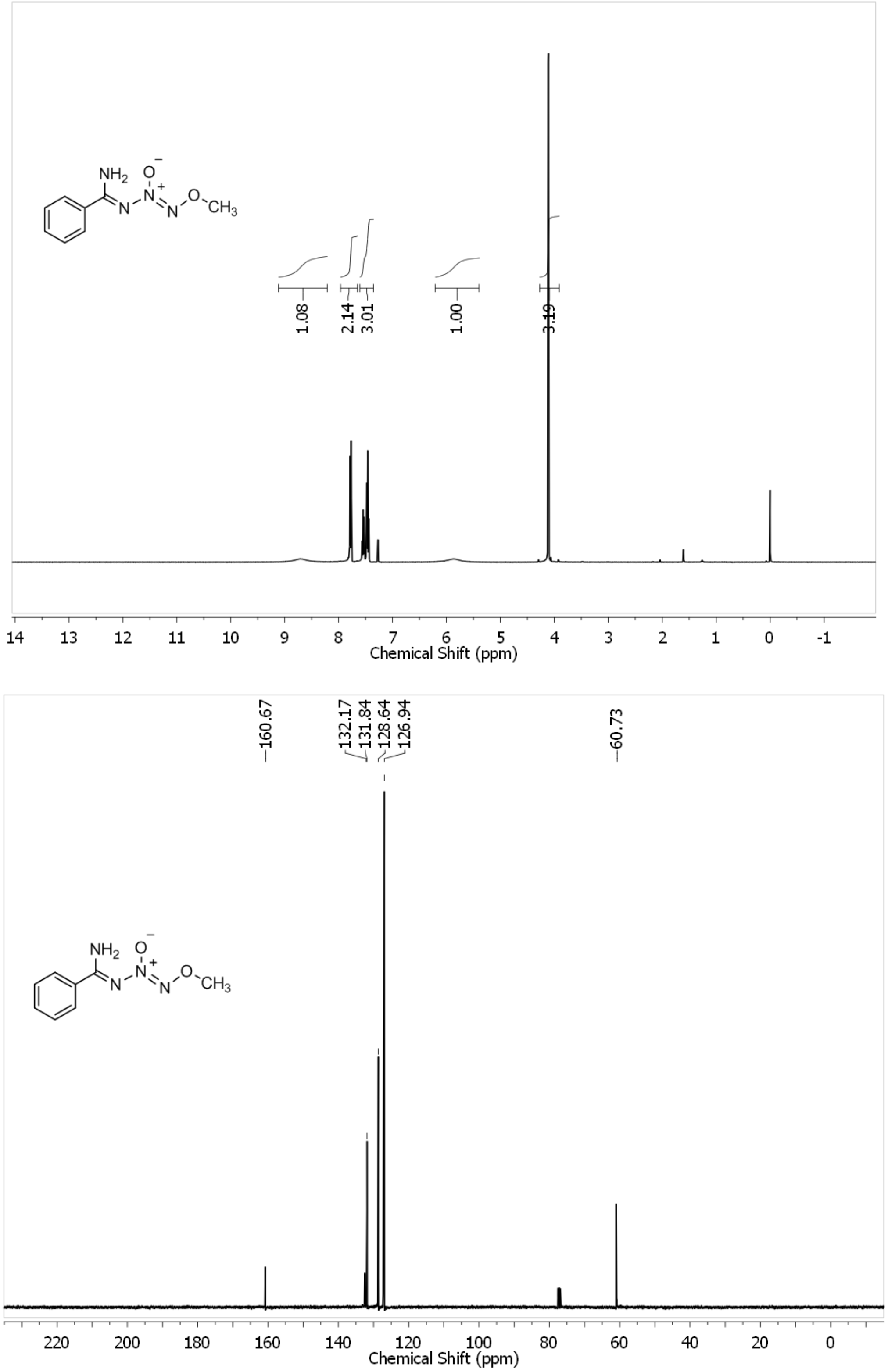

Figure S5. ^{1}H and ^{13}C NMR spectra of compound **4**.

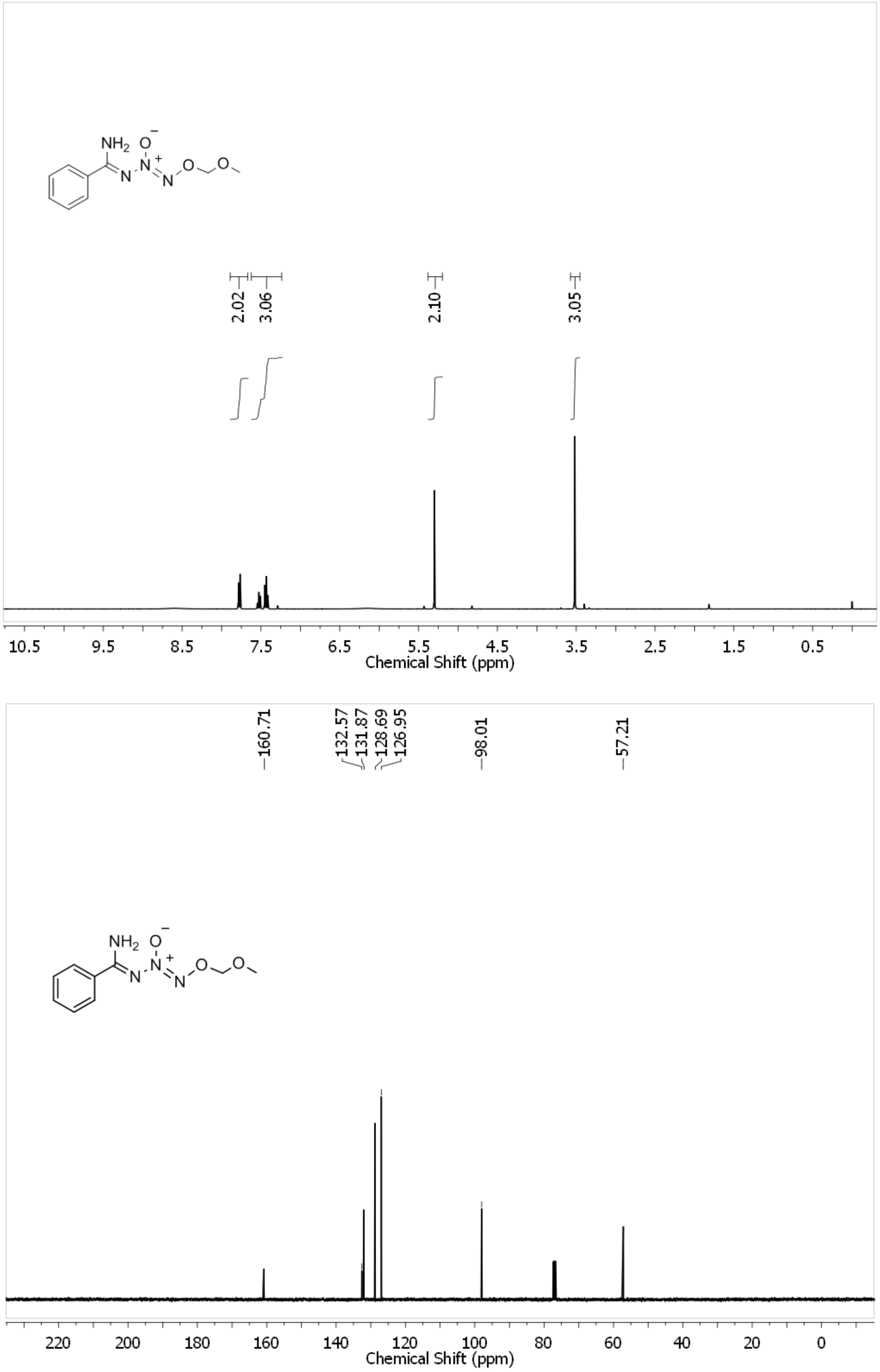

Figure S6. ^{1}H and ^{13}C NMR spectra of compound **5**.

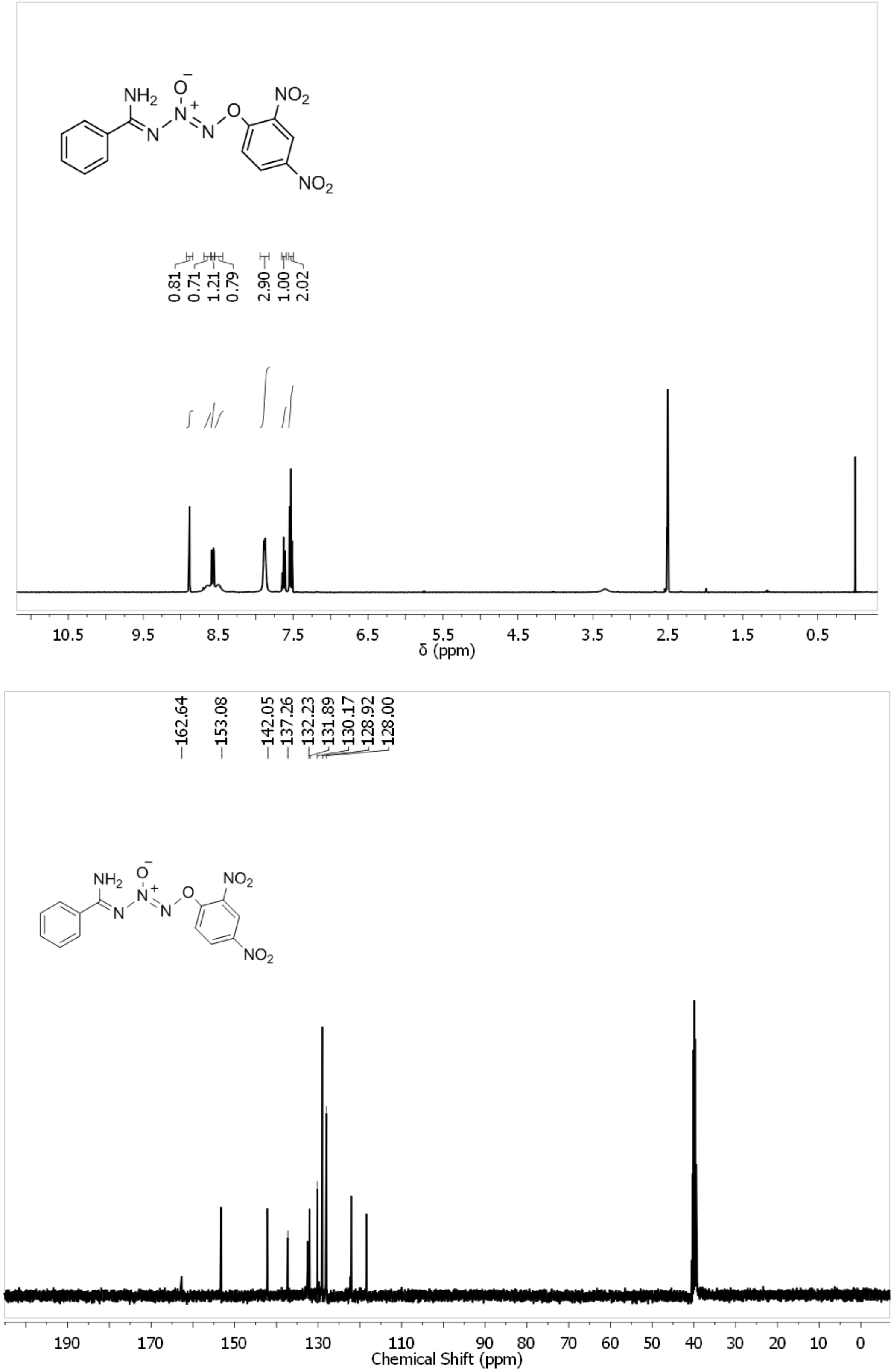

Figure S7. ^{1}H and ^{13}C NMR spectra of compound **6**.

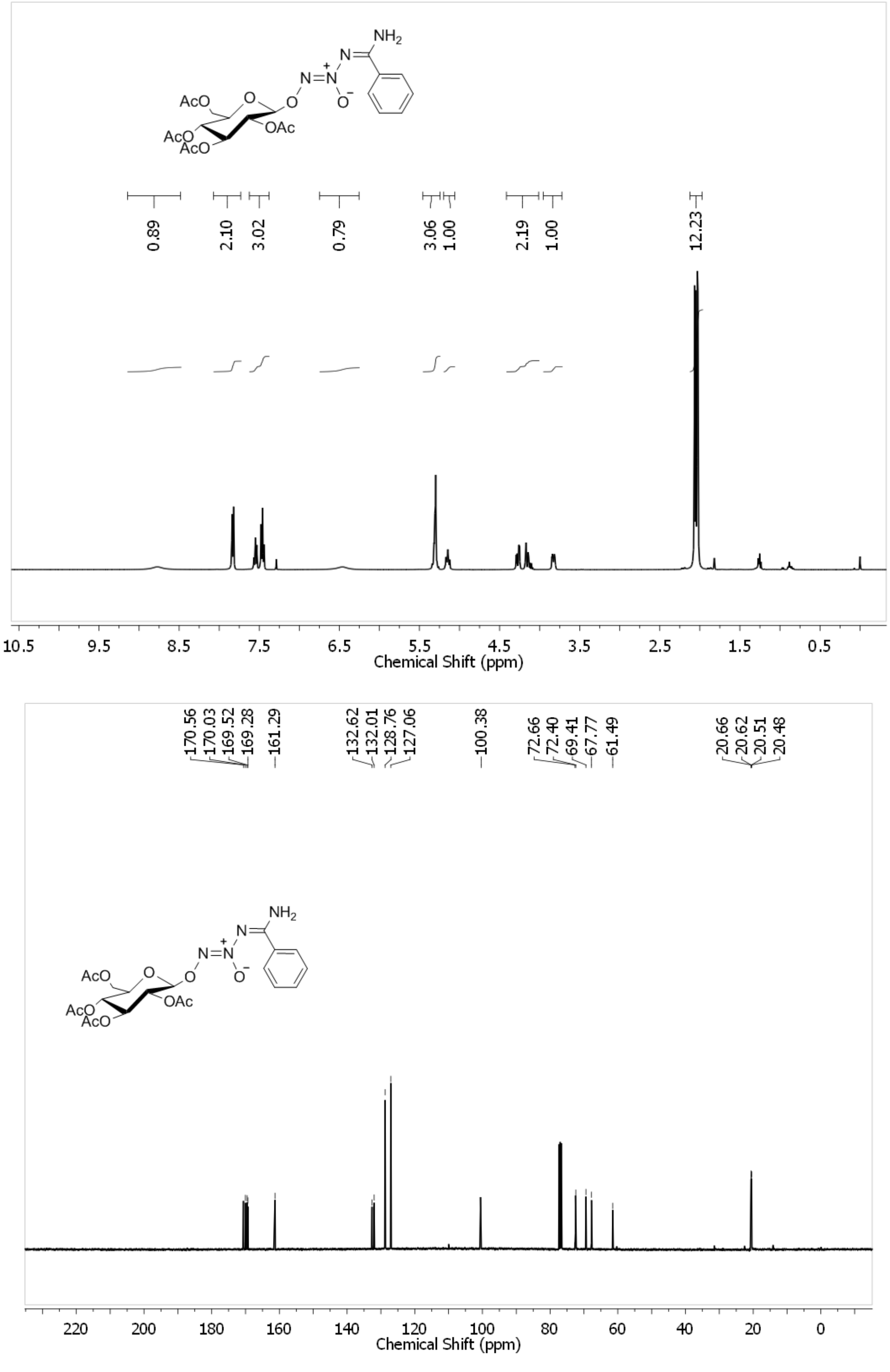

Figure S8. ^{1}H and ^{13}C NMR spectra of compound **7**.

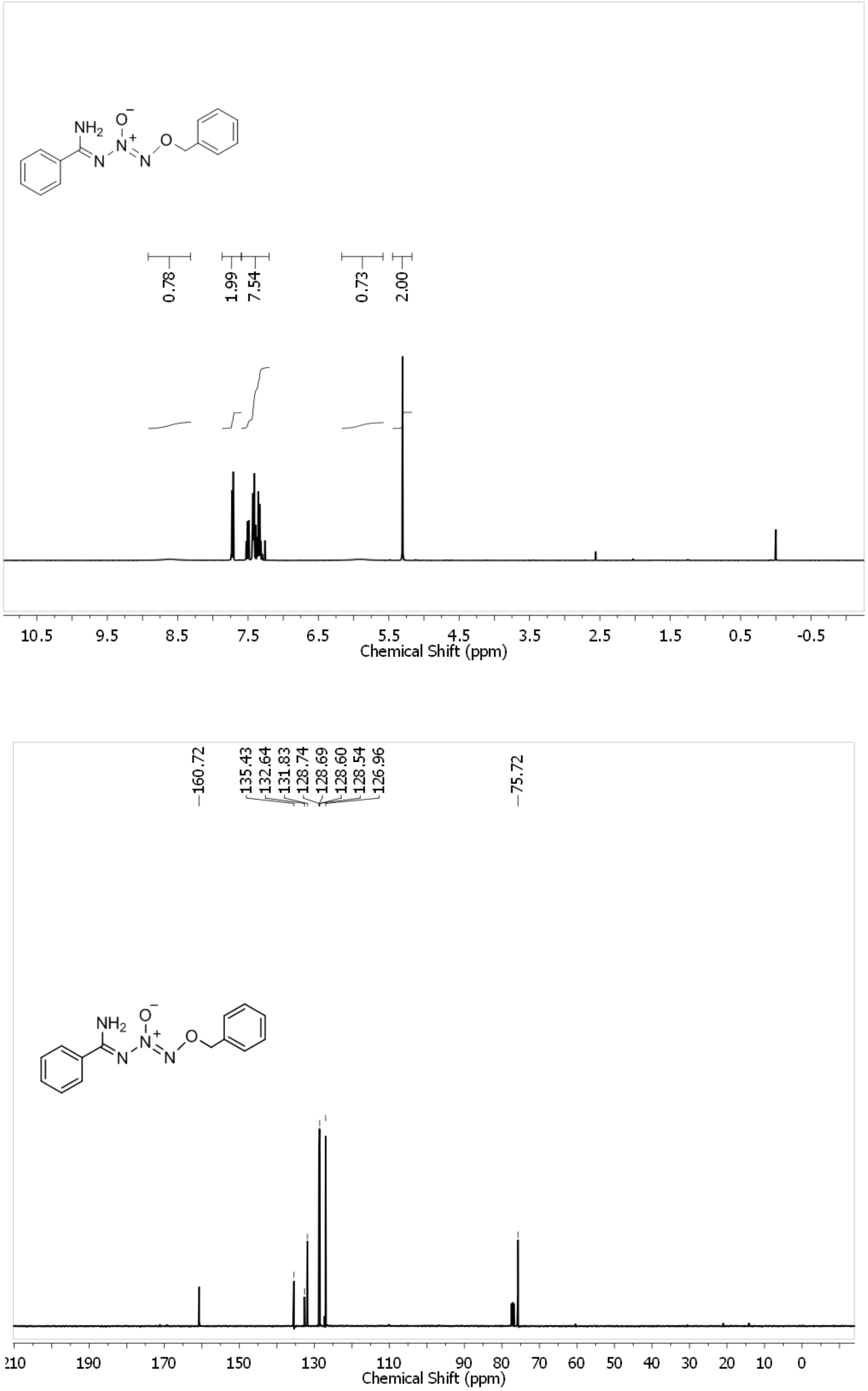

Figure S9. ^{1}H and ^{13}C NMR spectra of compound **8**.

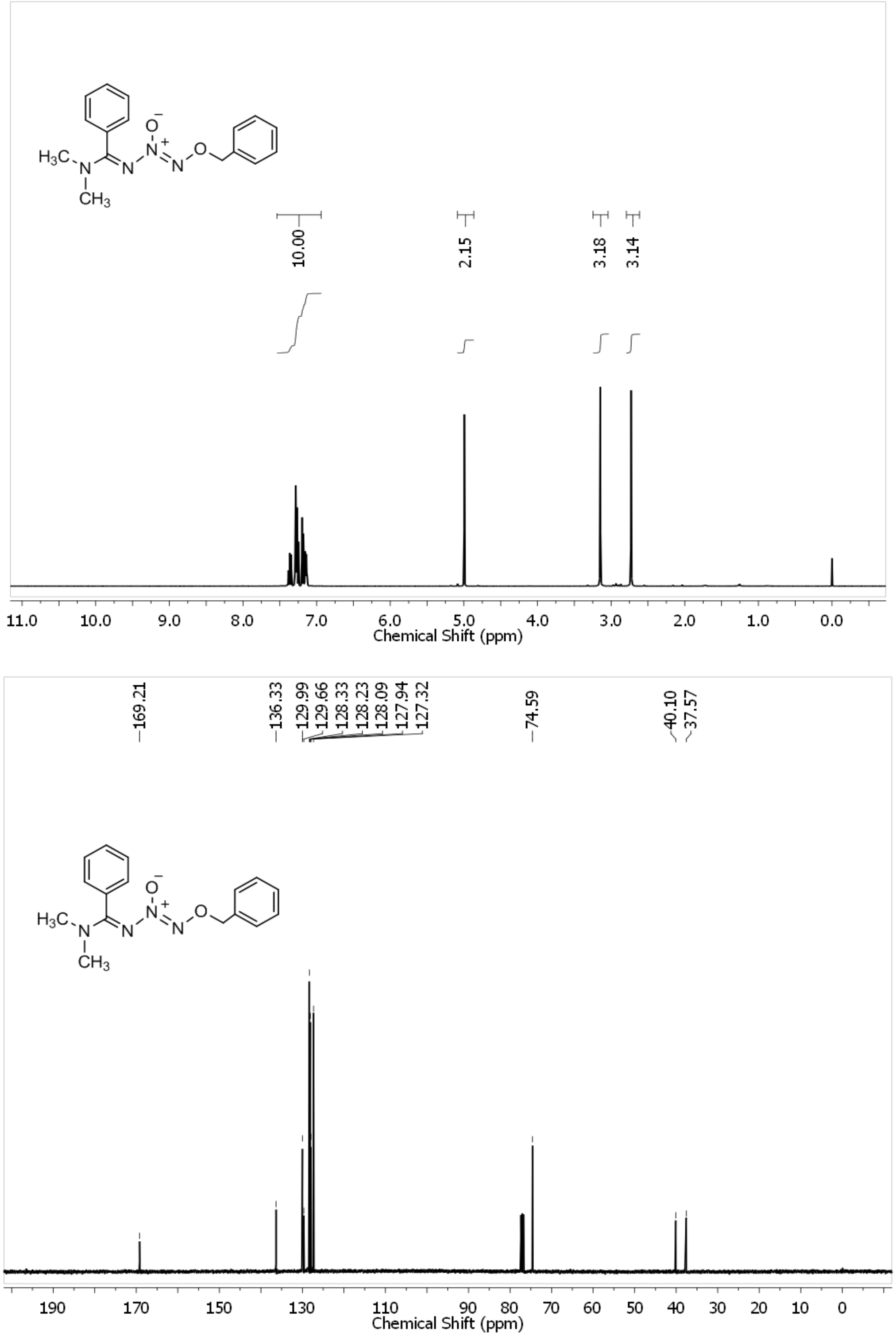

Figure S10. ^{1}H and ^{13}C NMR spectra of compound **9**.

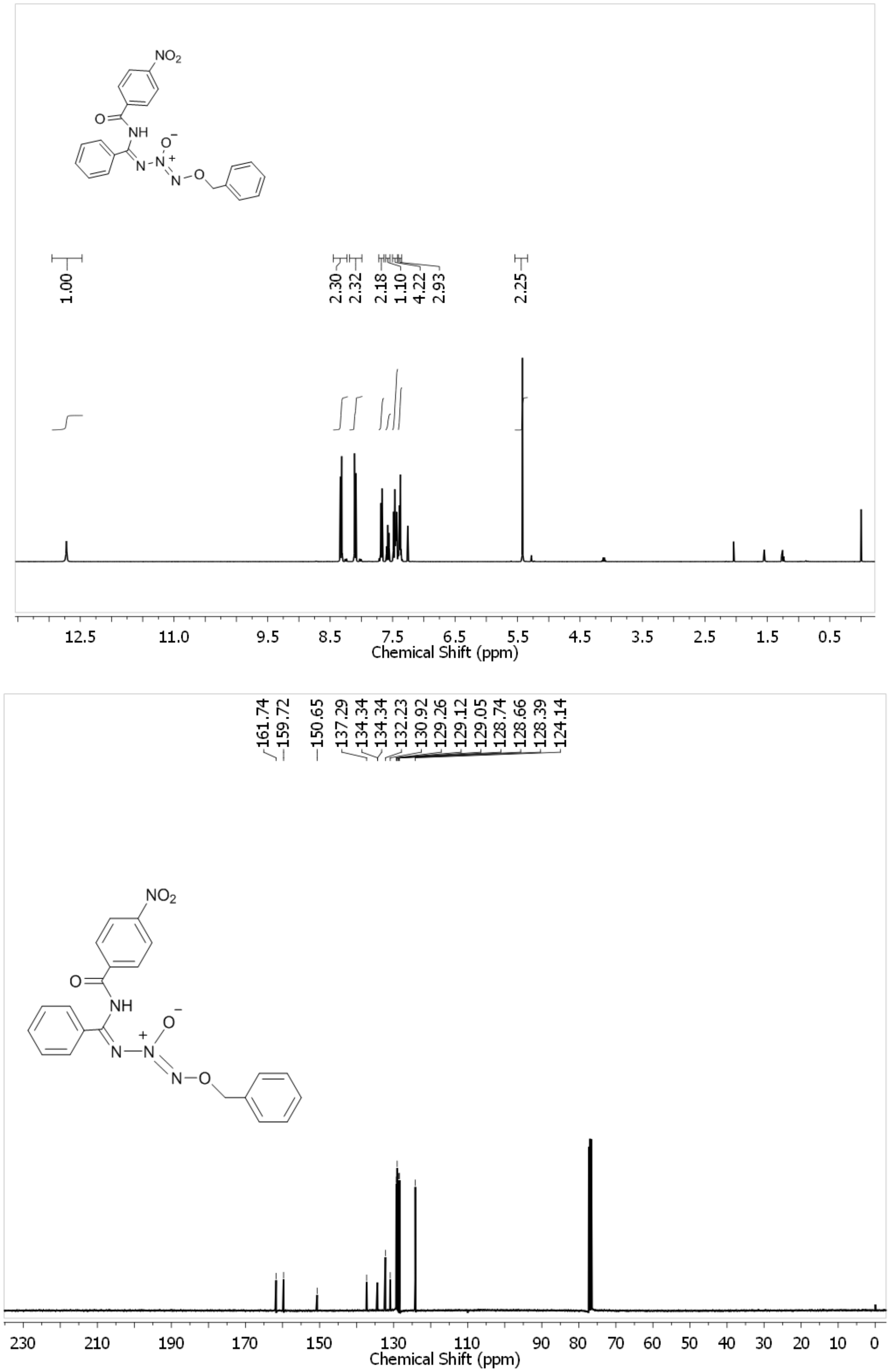

Figure S11. ^{1}H and ^{13}C NMR spectra of compound **10**.

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2. L. K. Keefer, R. W. Nims, K. M. Davies, D. A. Wink, *Methods Enzymol.* 1996, **268**, 281.