

Supporting Information

A Combined Experimental and DFT Mechanistic Study for the Unexpected Nitrosolysis of *N*-hydroxymethyldialkylamines in Fuming Nitric Acid

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1. Experimental section

General information

100% HNO₃ was prepared by reported procedure,¹ other chemical reagents and solvents were obtained from commercial sources and used without further purification. ¹H-NMR and ¹³C-NMR spectra were recorded on a Bruker Avance-III DRX spectrometer operating at 500 MHz and 125 MHz respectively, using CDCl₃ as solvent. MS/MS (ESI) mass spectra were recorded on a Finnigan TSQ Quantum ultra-AM mass spectrometer (Thermo Fisher Scientific, Waltham, MA USA). GC analyses were performed with a GC-9860 gas chromatograph.

General procedure for the synthesis of *N*-hydroxymethylmorpholine. paraformaldehyde (0.1 mol) and morpholine (0.1 mol) were mixed in a 100 mL flask and stirred at room temperature for 1 h. Then the mixture was heated to 65°C and stirred for another 12 h. After being cooled to room temperature, CH₂Cl₂ was added and stirred for a while. The product was obtained by filtration and concentration as the mixture of *N*-hydroxymethylmorpholine and dimorpholinomethane. According to the ¹H-NMR spectrum, the molar ratio of *N*-hydroxymethylmorpholine to dimorpholinomethane was 1:1.1.

***N*-hydroxymethylmorpholine.** ¹H-NMR (500 MHz, CDCl₃) δ= 4.13 (s, 2 H), 3.74-3.69 (m, 4 H), 2.72-2.67 (m, 4 H), 2.04 (br, 1H) ppm. ¹³C-NMR (125 MHz, CDCl₃) δ= 87.3, 67.0, 49.8 ppm.

General procedure for the synthesis of *N*-hydroxymethyldibutylamine and *N*-hydroxymethylpiperidine. Formaline (0.1 mol) and dibutylamine (0.1 mol) or piperidine (0.1 mol) were mixed in a 100 mL flask and stirred at room temperature for 1 h. Then the mixture was heated to 65°C and stirred for another 2.5 h. After being cooled to room temperature, NaCl was added and stirred. The organic layer was obtained by funnel separation and dried with Na₂SO₄. The product was achieved after filtration and concentration as the mixture of dibutylamine and *N*-hydroxymethyldibutylamine (1:1.17) or *N*-hydroxymethylpiperidine and dipiperidinomethane (1:1.25).

***N*-hydroxymethylpiperidine.** ¹H-NMR (500 MHz, CDCl₃) δ= 4.14 (s, 2 H), 2.64 (t, 4H, *J*=5.0 Hz), 1.58-1.52 (m, 4 H), 1.46-1.42 (m, 2 H) ppm. ¹³C-NMR (125 MHz, CDCl₃) δ= 88.5, 53.1, 26.1, 25.0 ppm.

Dipiperidinomethane. ¹H-NMR (500 MHz, CDCl₃) δ= 2.84 (s, 2 H), 2.4 (s, 8 H), 1.58-1.52 (m, 8 H), 1.46-1.42 (m, 8 H) ppm. ¹³C-NMR (125 MHz, CDCl₃) δ= 82.9, 50.7, 26.0, 24.3 ppm.

***N*-hydroxymethyldibutylamine.** ¹H-NMR (500 MHz, CDCl₃) δ= 4.18 (s, 2 H), 2.66-2.62 (m, 2 H), 2.47-2.43 (m, 2 H), 1.29-1.28 (m, 8H), 0.93-0.90 (m, 6 H) ppm. ¹³C-NMR (125 MHz, CDCl₃) δ= 83.5, 51.9, 29.4, 14.1 ppm.

General procedure for the nitrosolysis of the mixture of *N*-hydroxymethyldialkamines in fuming nitric acid. the mixture of *N*-hydroxymethyldialkamines (5 mmol) was added in portions into fuming nitric acid (200 mmol) under vigorous stirred at 0°C, the reaction mixture was then

warmed to certain temperature. The reaction was quenched by being poured into ice water (20 mL). The result mixture was extracted with dichloromethane (3 x 30 mL). The combined organic layer was washed with the saturated NaHCO₃ and dried with Na₂SO₄. After filtration, the mixture was concentrated under reduced pressure to afford the crude product, and the desire product was obtained by column chromatograph.

The same procedure described above for the nitrosolysis of dimorpholinomethane.

N-nitrosomorpholine. ¹H-NMR (500 MHz, CDCl₃) δ= 4.31(t, 2 H, *J*=5.0 Hz), 3.90 (t, 2 H, *J*=5.0 Hz), 3.87(t, 2 H, *J*=5.0 Hz), 3.67(t, 2 H, *J*=5.0 Hz) ppm. ¹³C-NMR (125 MHz, CDCl₃) δ= 67.3, 66.0, 50.0, 40.4 ppm. ESI-MS: *m/z* [(M+H)⁺]=117.10.

N-nitromorpholine. ¹H-NMR (500 MHz, CDCl₃) δ= 3.83 (s, 8H) ppm. ¹³C-NMR (125 MHz, CDCl₃) δ= 65.5, 49.0 ppm. ESI-MS: *m/z* [(M+H)⁺]=133.01.

N-nitrosopiperidine. ¹H-NMR (500 MHz, CDCl₃) δ= 4.19 (t, 2 H, *J*=5.0 Hz), 3.78 (t, 2 H, *J*=5.0 Hz), 1.81-1.74 (m, 4 H), 1.58-1.54 (m, 4 H) ppm. ¹³C-NMR (125 MHz, CDCl₃) δ= 50.9, 39.8, 26.4, 24.8, 24.1 ppm. ESI-MS: *m/z* [(M+H)⁺]=115.09.

N-nitrosodibutylamine. ¹H-NMR (500 MHz, CDCl₃) δ= 4.08 (t, 2 H, *J*=7.5 Hz), 3.54 (t, 2 H, *J*=7.5 Hz), 1.76-1.70 (m, 2 H), 1.50-1.44 (m, 2 H), 1.43-1.35 (m, 2 H), 1.33-1.26 (m, 2H), 0.97 (t, 3H, *J*=7.4 Hz), 0.92 (t, 3H, *J*=7.4 Hz) ppm. ¹³C-NMR (125 MHz, CDCl₃) δ= 52.0, 43.4, 30.3, 28.1, 20.4, 19.7, 13.6, 13.5 ppm. ESI-MS: *m/z* [(M+H)⁺]=159.21.

N-nitrodibutylamine. ¹H-NMR (500 MHz, CDCl₃) δ= 3.72 (t, 4 H, *J*=7.5 Hz), 1.70-1.64 (m, 4 H), 1.40-1.33 (m, 4 H), 0.96 (t, 6 H, 7.4 Hz) ppm. ¹³C-NMR (125 MHz, CDCl₃) δ= 51.9, 28.9, 20.3, 13.9 ppm. ESI-MS: *m/z* [(M+H)⁺]=175.97.

General procedure for the nitrosation of secondary amines in fuming nitric acid. paraformaldehyde (5 mmol) was dissolved in fuming nitric acid (200 mmol) at 0°C, secondary amine (5 mmol) was added in portions under vigorous stirred, the mixture was then warmed to 25°C. After 1 hour, the reaction was quenched by pouring into ice water (20 mL). The workup procedure was the same as mentioned above.

1. Z.Y. He, J. Luo, C. X. Lv, *Chin. J. Explos. Propellants.*, 2010, **33**, 1-4.

2. Computational detail

All computations were carried out using the Gaussian 09 software package.² We used the B3LYP exchange-correlation functional combined with 6-31G (d, p) basis set for geometry optimizations of the reactants, transition states, and products. The vibrational frequency calculations were performed on fully optimized geometries to ensure that the reactants and products have no negative frequencies. The multicoordinate driven method³ was applied to find the approximate transition states, which were further optimized to the true transition states. Vibrational analysis was performed to confirm that there is only one negative frequency. These computations also provided the Gibbs free energy profiles of the two reactions models. Intrinsic

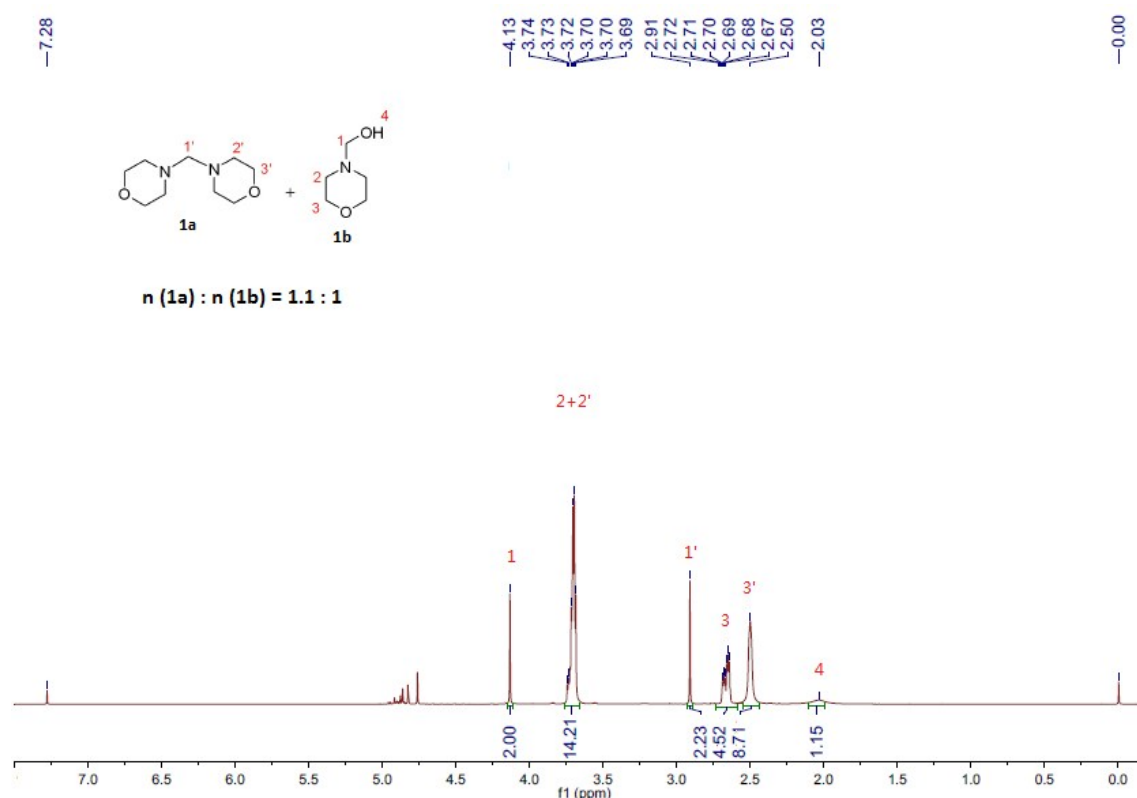
Reaction Coordinate calculations were conducted to generate the variations of the four chemical bonds along the reaction coordinate.

2. M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, T. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, D. J. Fox, Gaussian 09, Revision E.01, Gaussian, Inc., Wallingford CT, 2013.

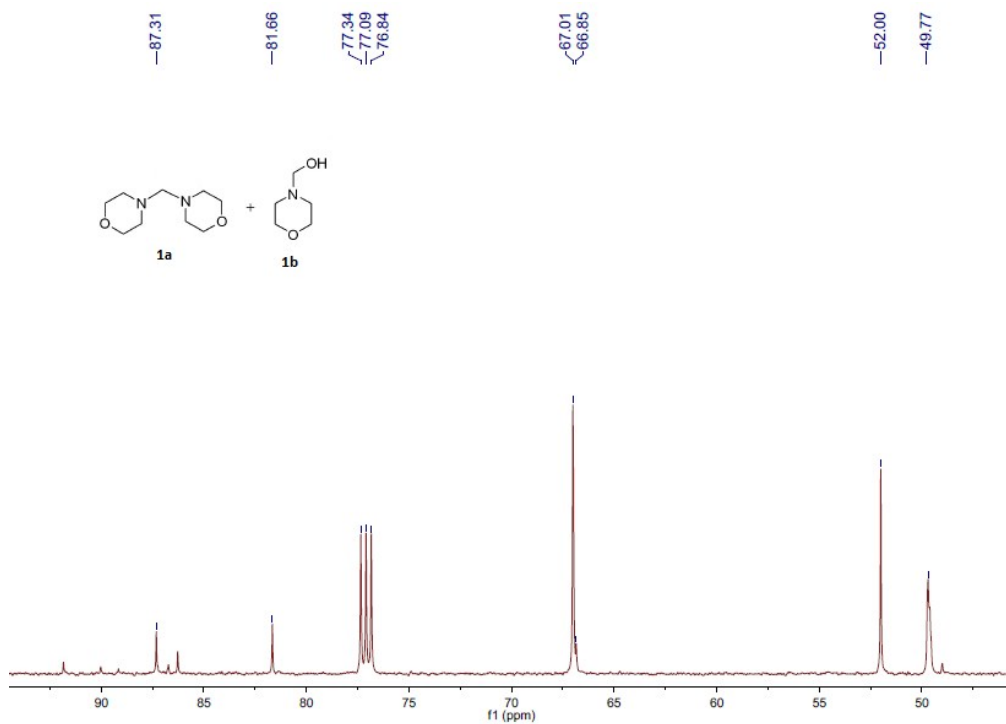
3. I. Berente, G. Naray-Szabo, *J. Phys. Chem. A* 2006, **110**, 772-778.

3. Copies of identification spectra

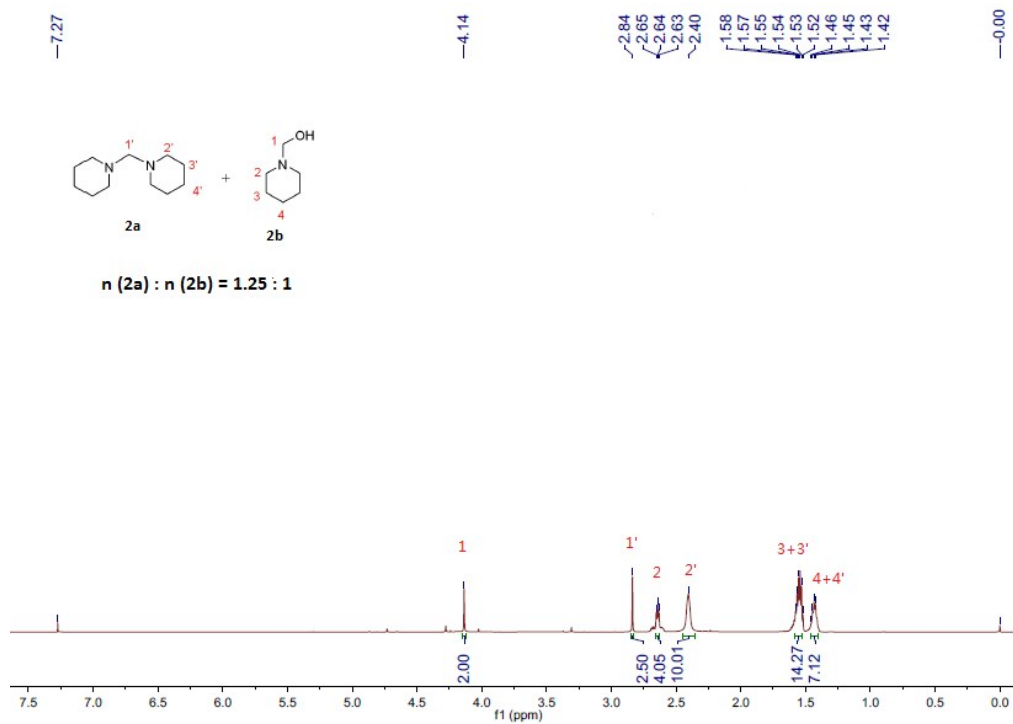
¹H NMR spectrum of the mixture of N-hydroxymethylmorpholine and dimorpholinomethane (CDCl₃, 500 MHz)



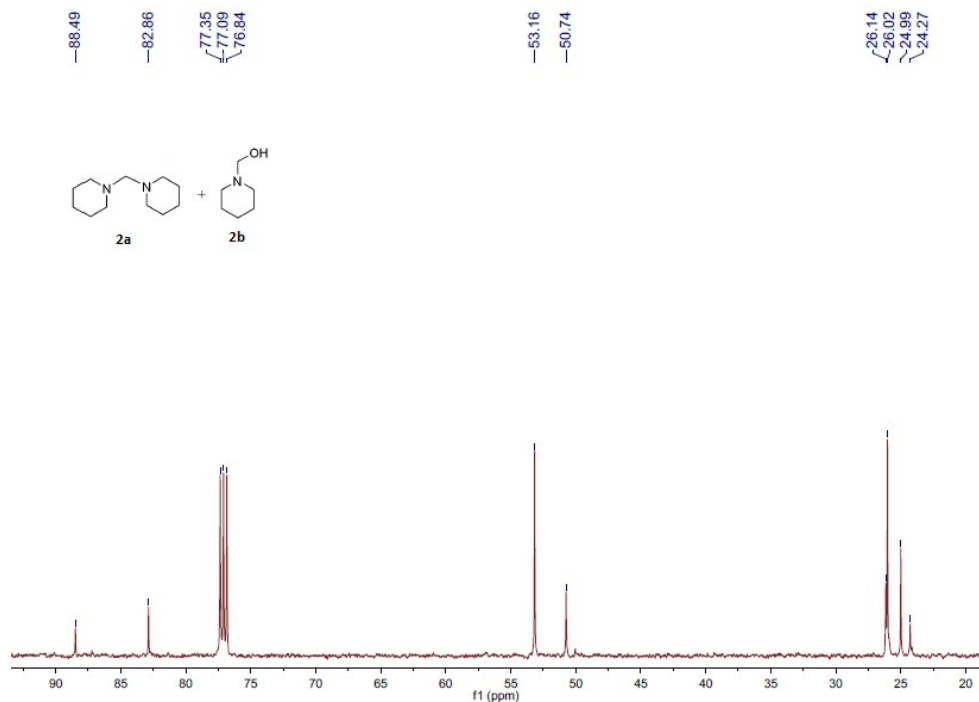
^{13}C NMR spectrum of the mixture of N-hydroxymethylmorpholine and dimorpholinomethane (CDCl_3 , 126 MHz)



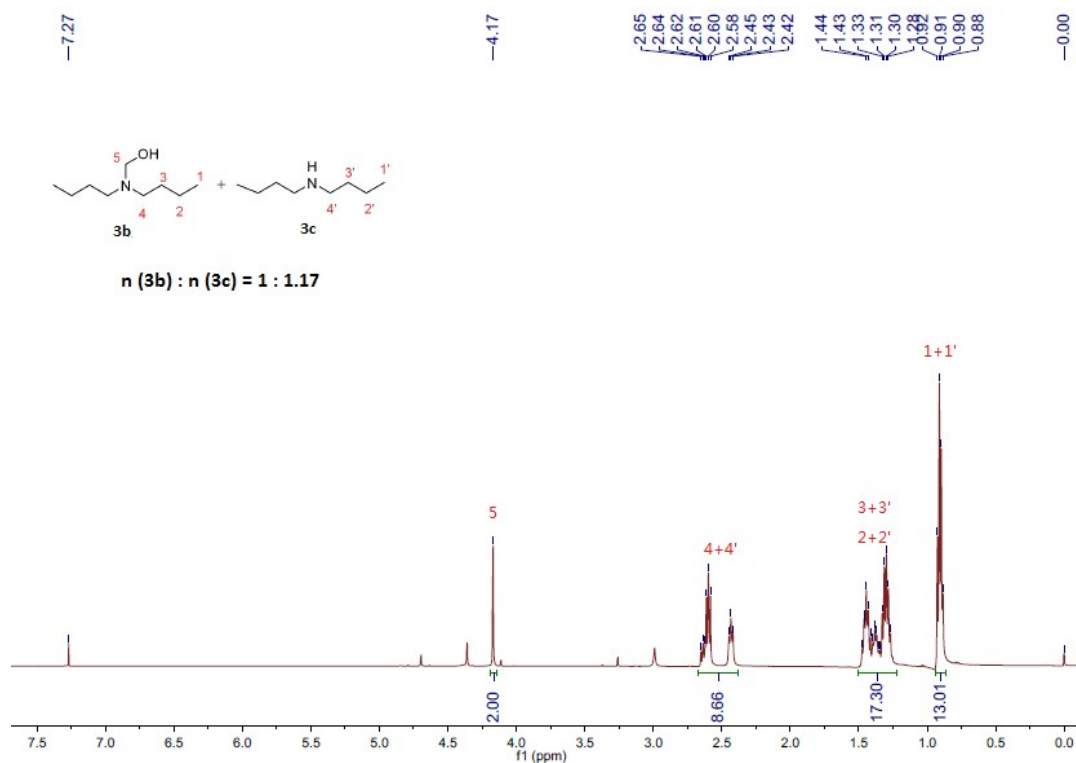
^1H NMR spectrum of the mixture of N-hydroxymethylpiperidine and dipiperidinomethane (CDCl_3 , 500 MHz)



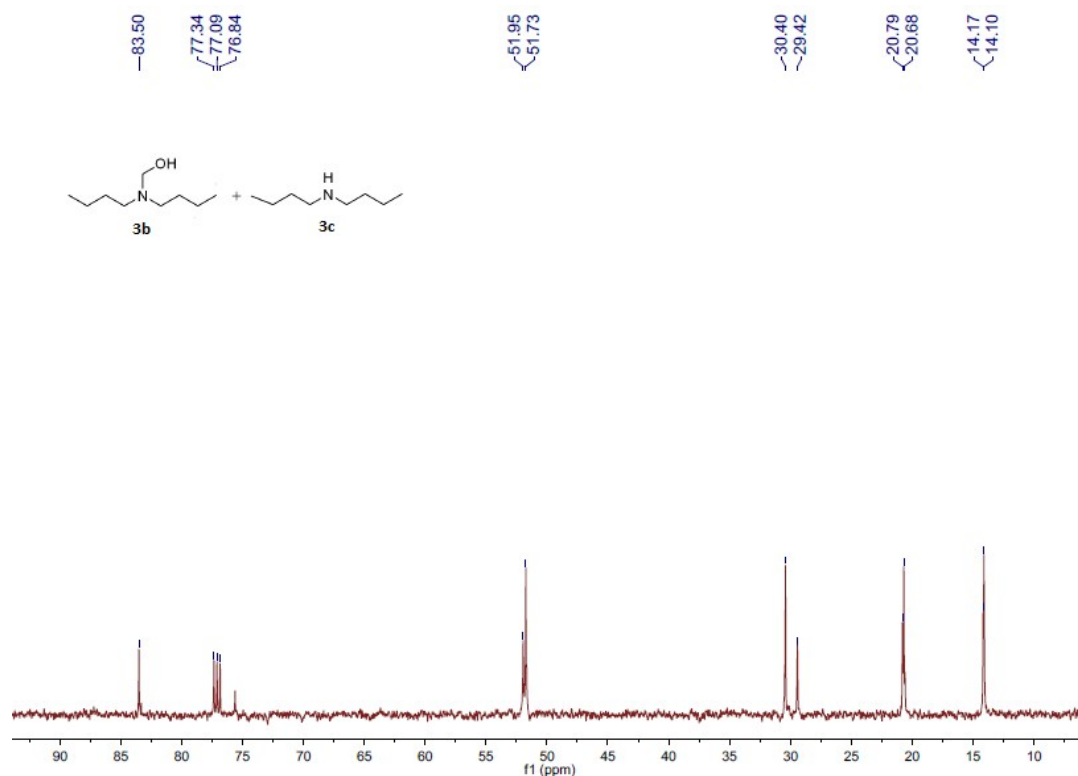
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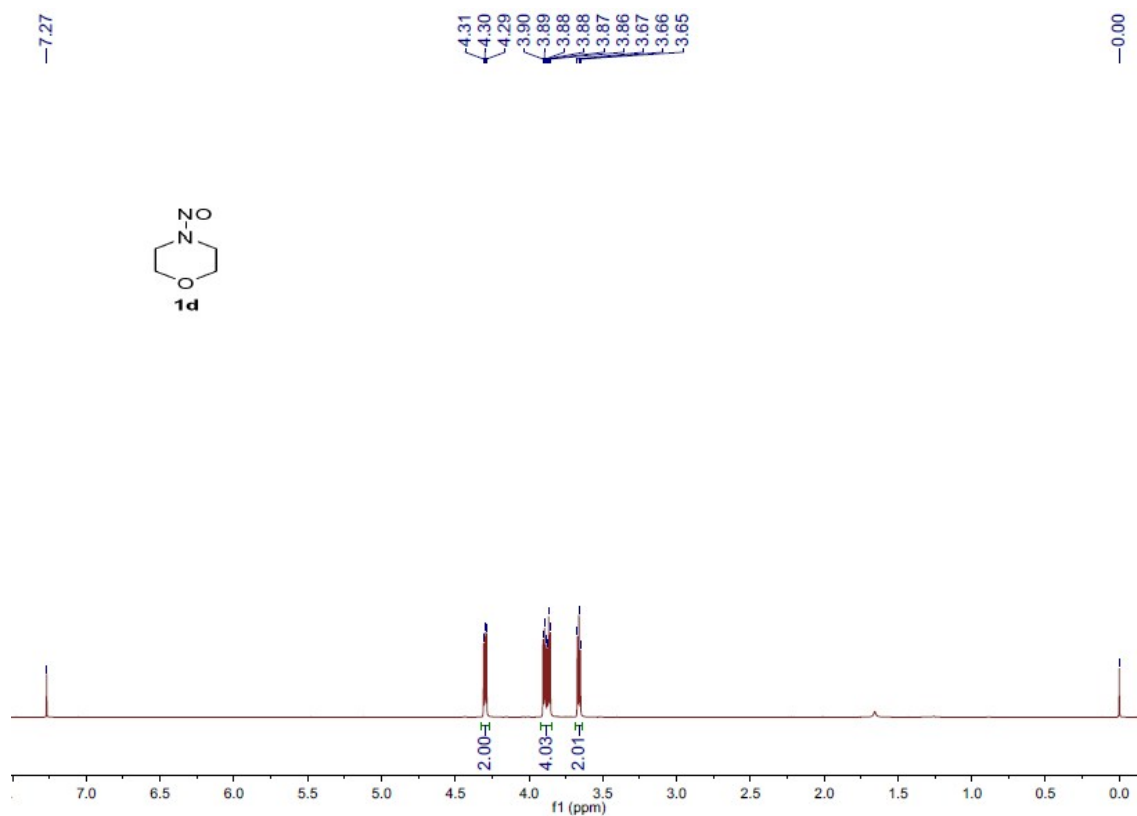
^1H NMR spectrum of the mixture of N-hydroxymethyldibutylamine and dibutylamine (CDCl_3 , 500 MHz)



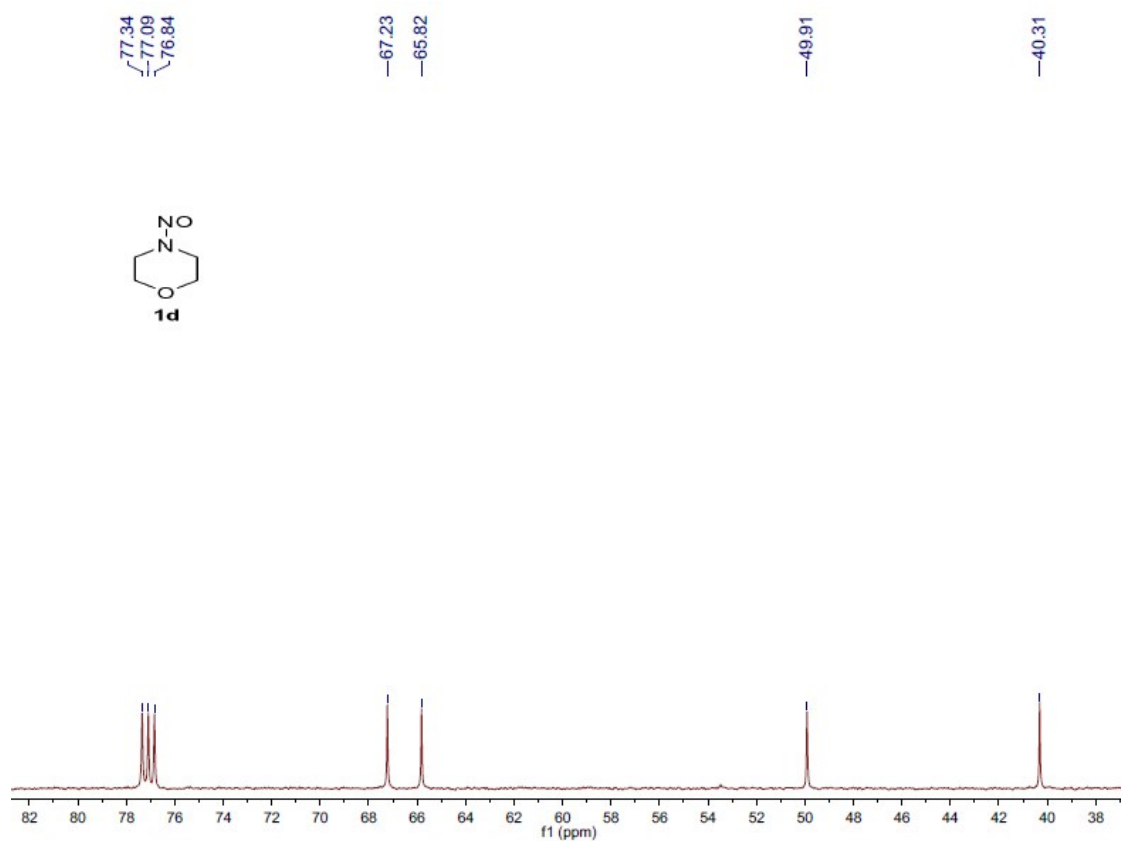
¹³C NMR spectrum of the mixture of N-hydroxymethyldibutylamine and dibutylamine (CDCl₃, 126 MHz)



¹H NMR spectrum of N-nitrosomorpholine (CDCl₃, 500 MHz)

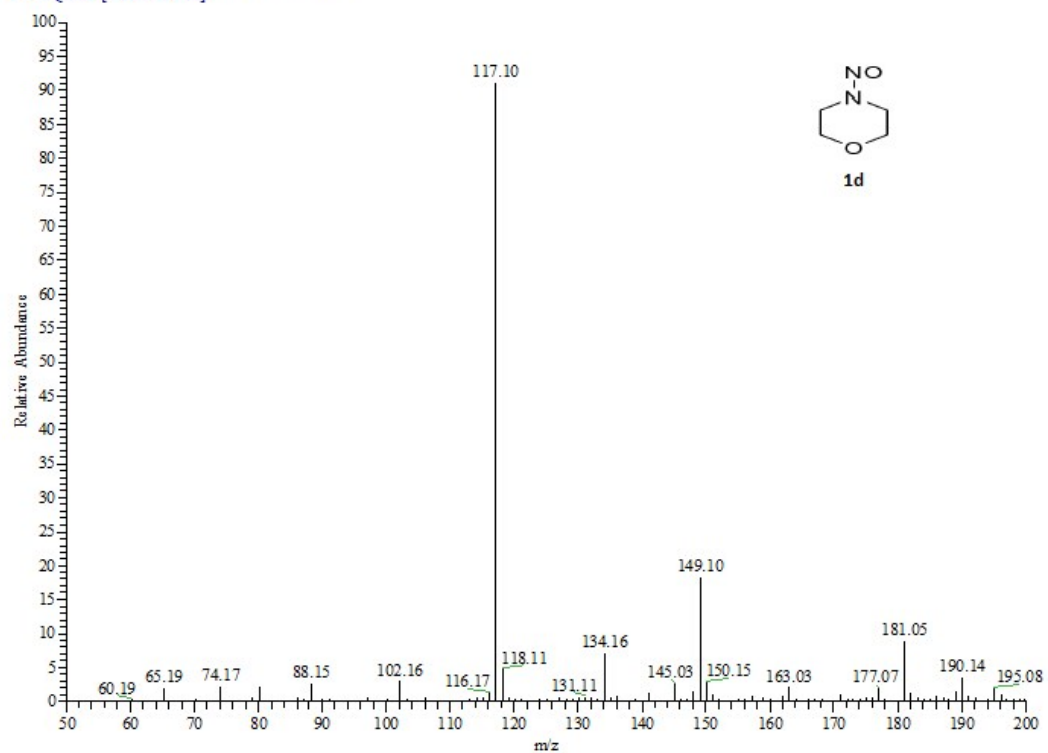


¹³C NMR spectrum of N-nitrosomorpholine (CDCl₃, 126 MHz)

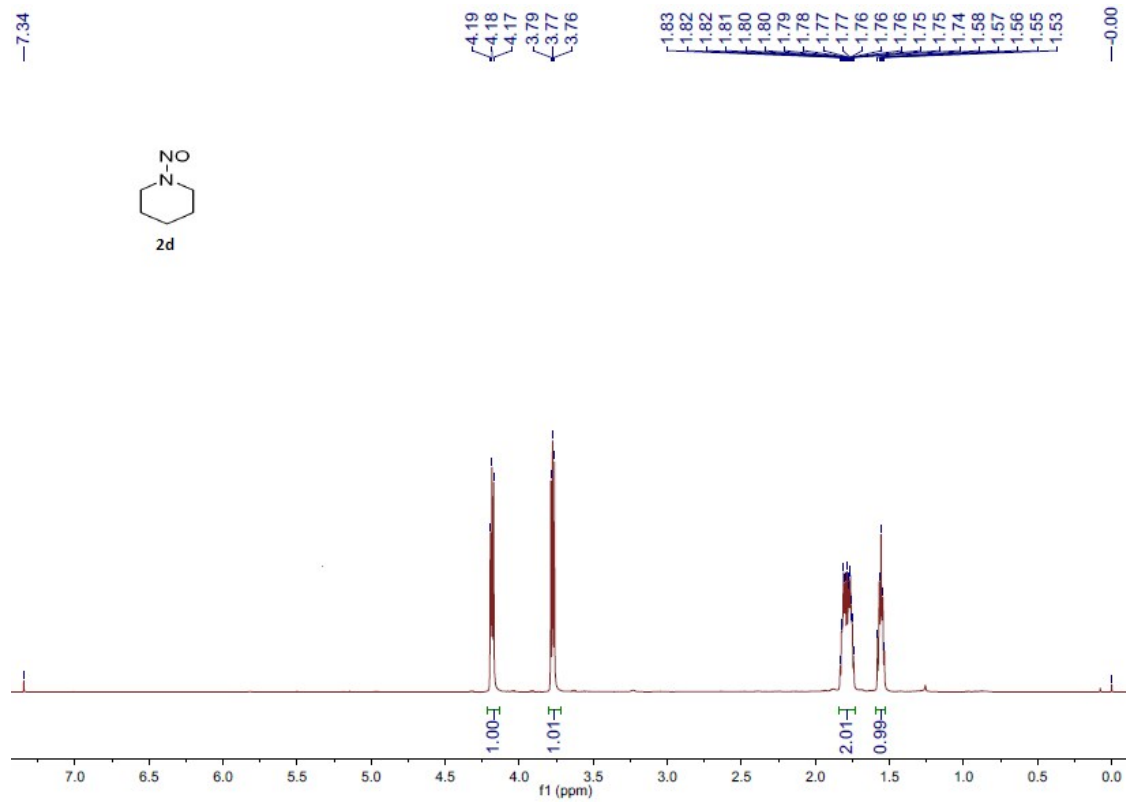


Electrospray Ionization (ESI) Mass Spectrometry of N-nitrosomorpholine (m/z of 117.10)

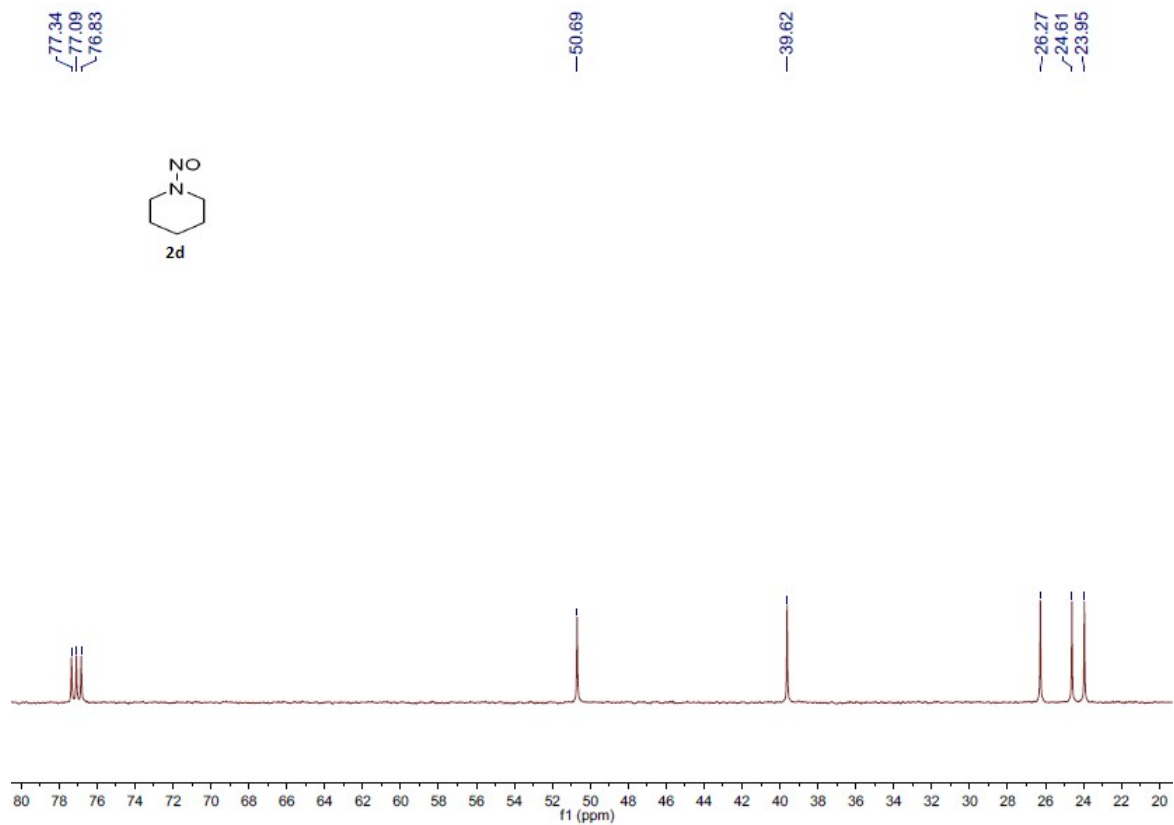
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¹H NMR spectrum of N-nitrosopiperidine (CDCl₃, 500 MHz)

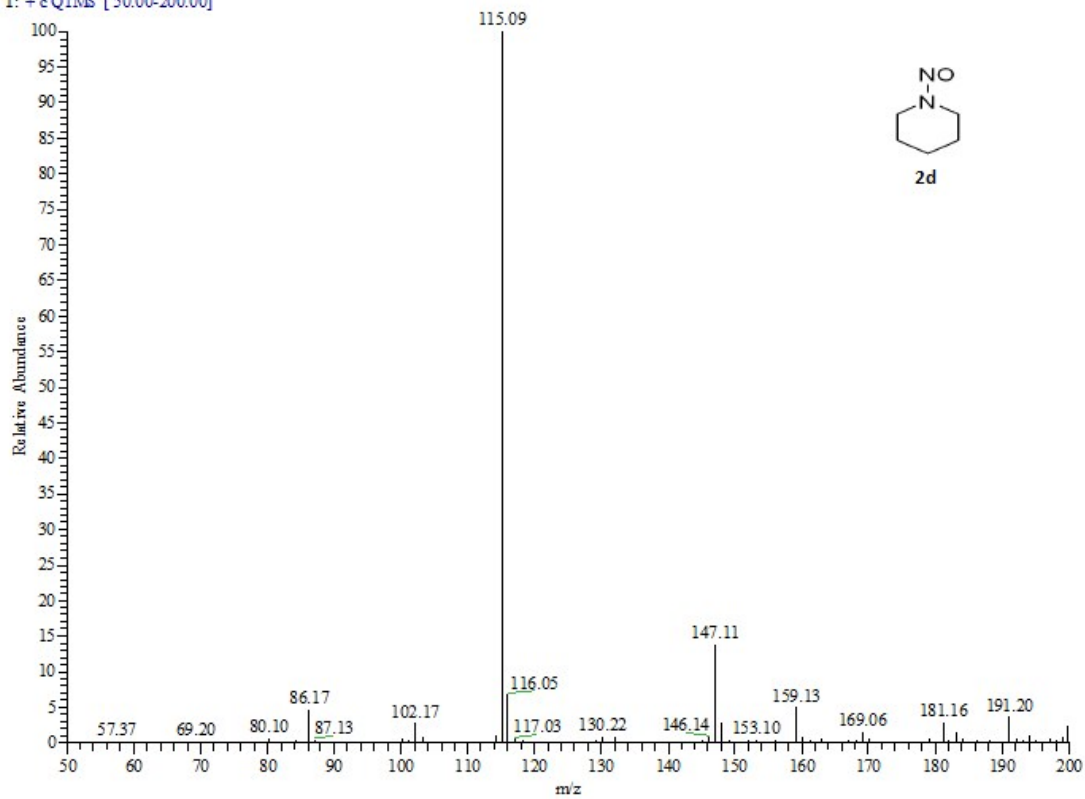


¹³C NMR spectrum of N-nitrosopiperidine (CDCl₃, 126 MHz)

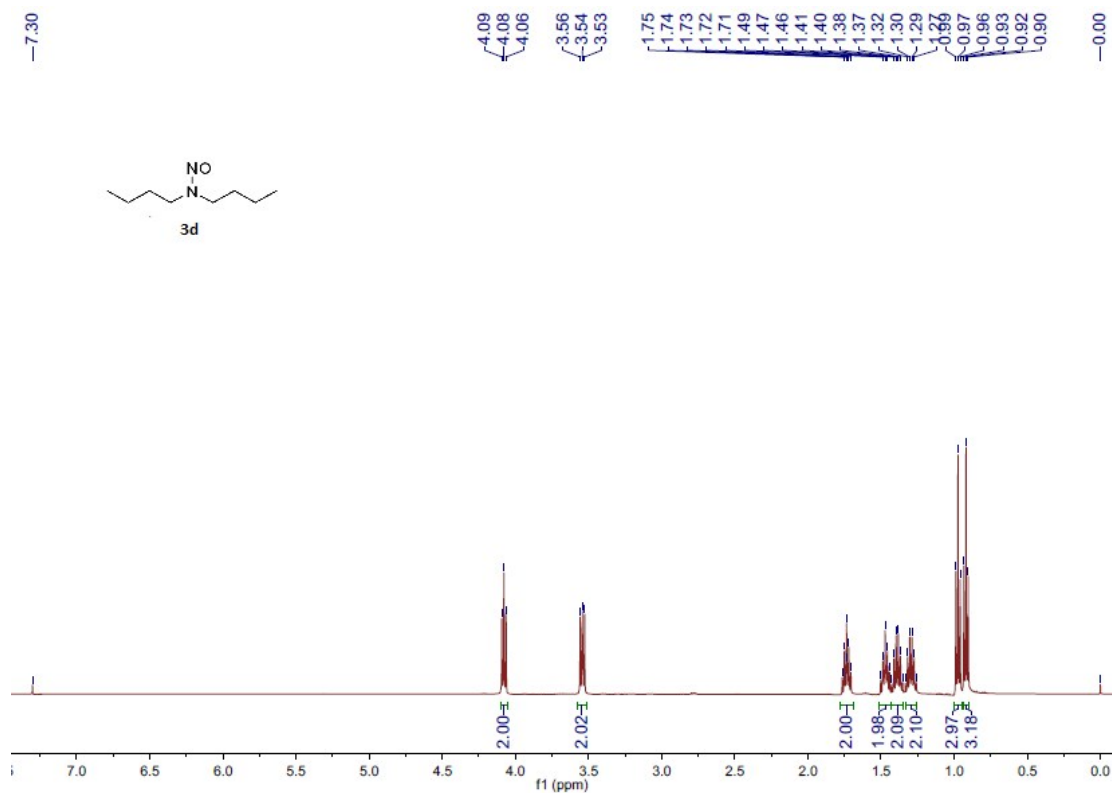


Electrospray Ionization (ESI) Mass Spectrometry of N-nitrosopiperidine (m/z of 115.09)

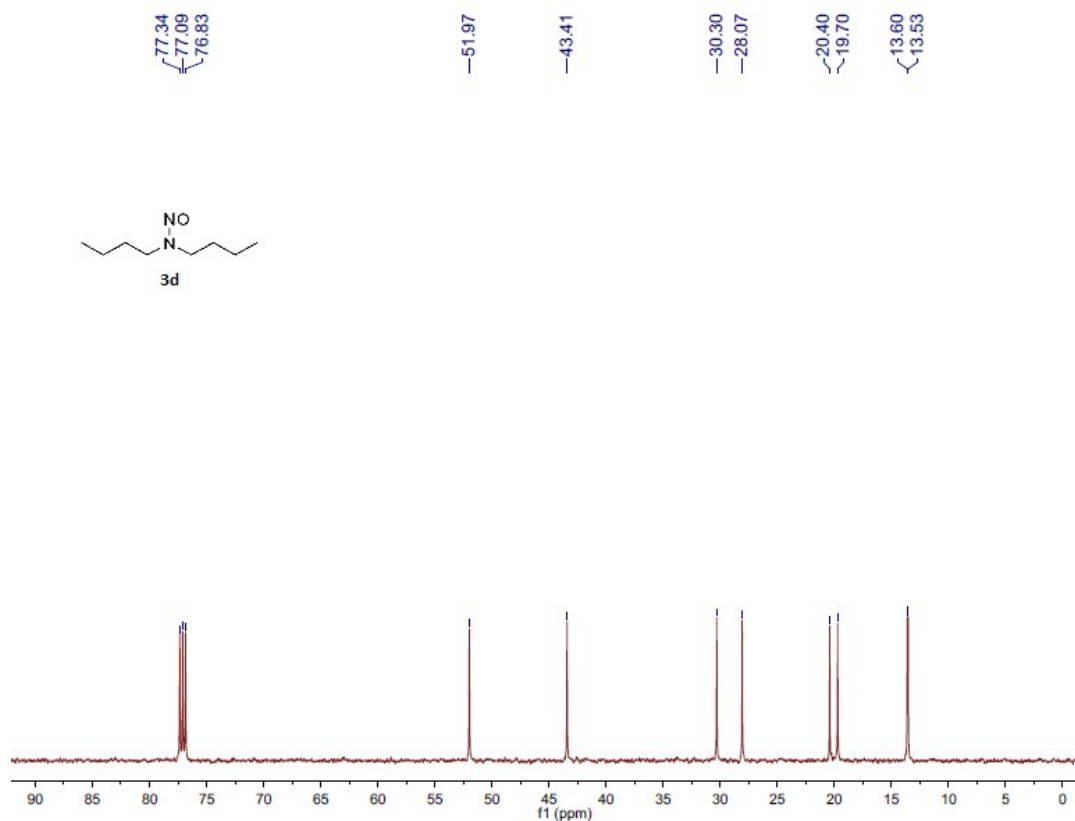
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¹H NMR spectrum of N-nitrosodibutylamine (CDCl₃, 500 MHz)

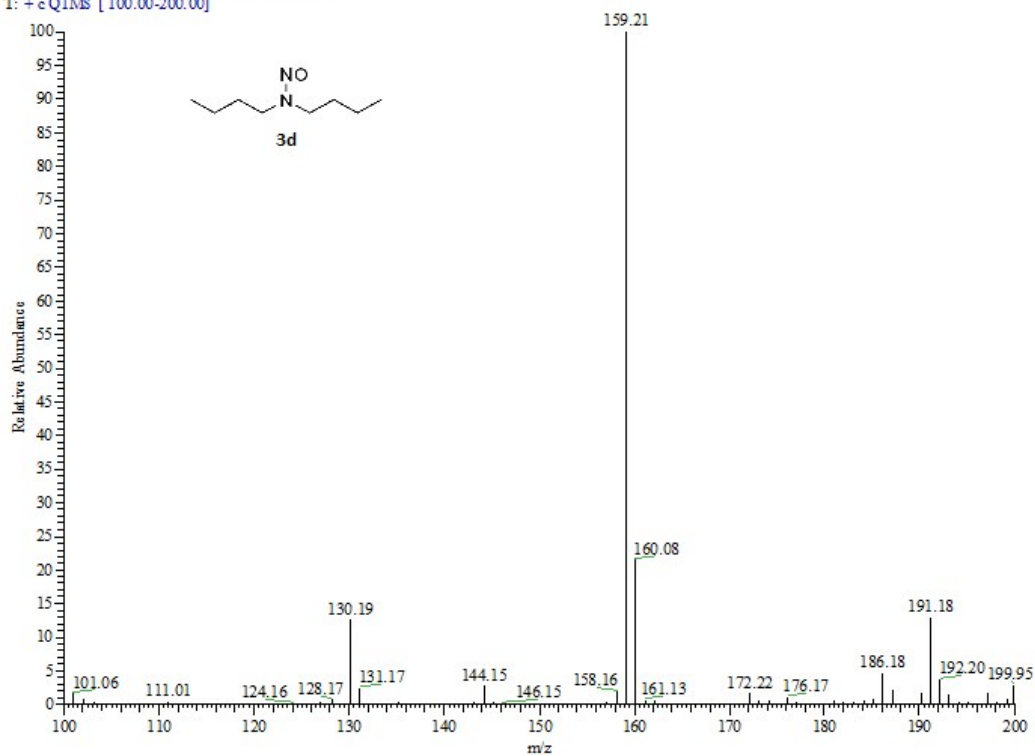


¹³C NMR spectrum of N-nitrosodibutylamine (CDCl₃, 126 MHz)

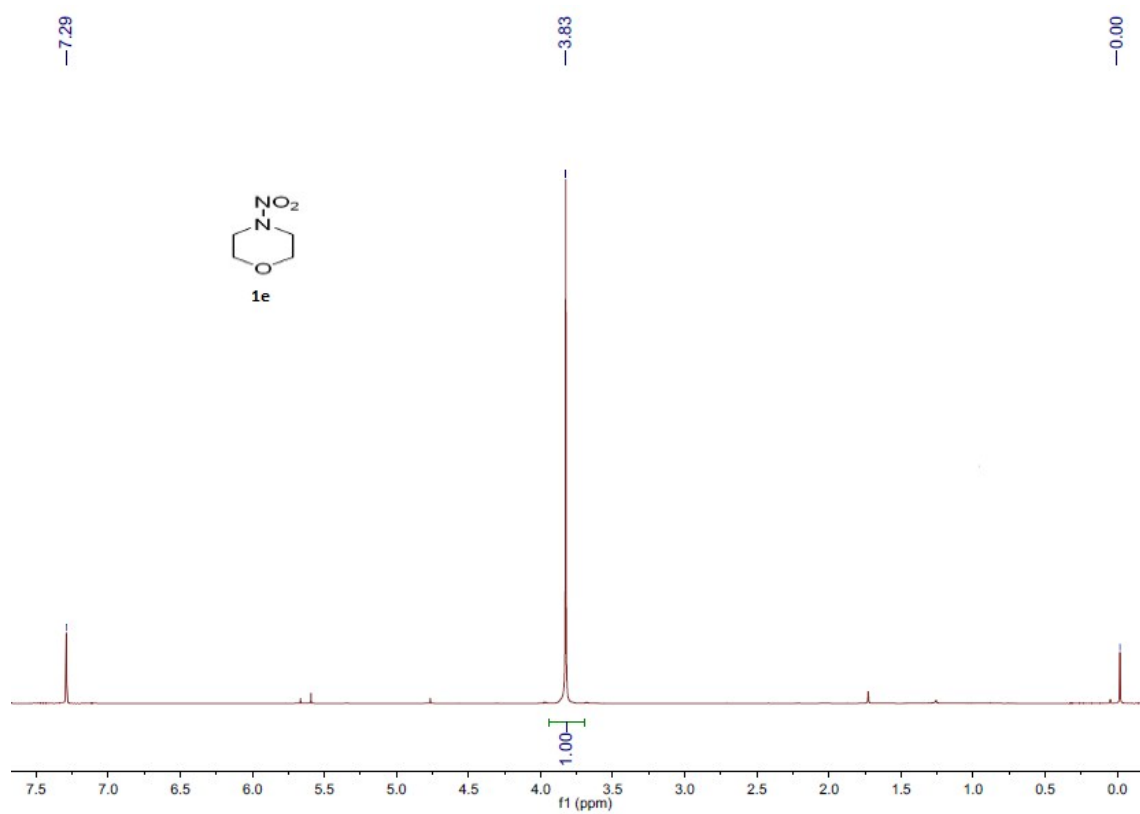


Electrospray Ionization (ESI) Mass Spectrometry of N-nitrosodibutylamine (m/z of 159.21)

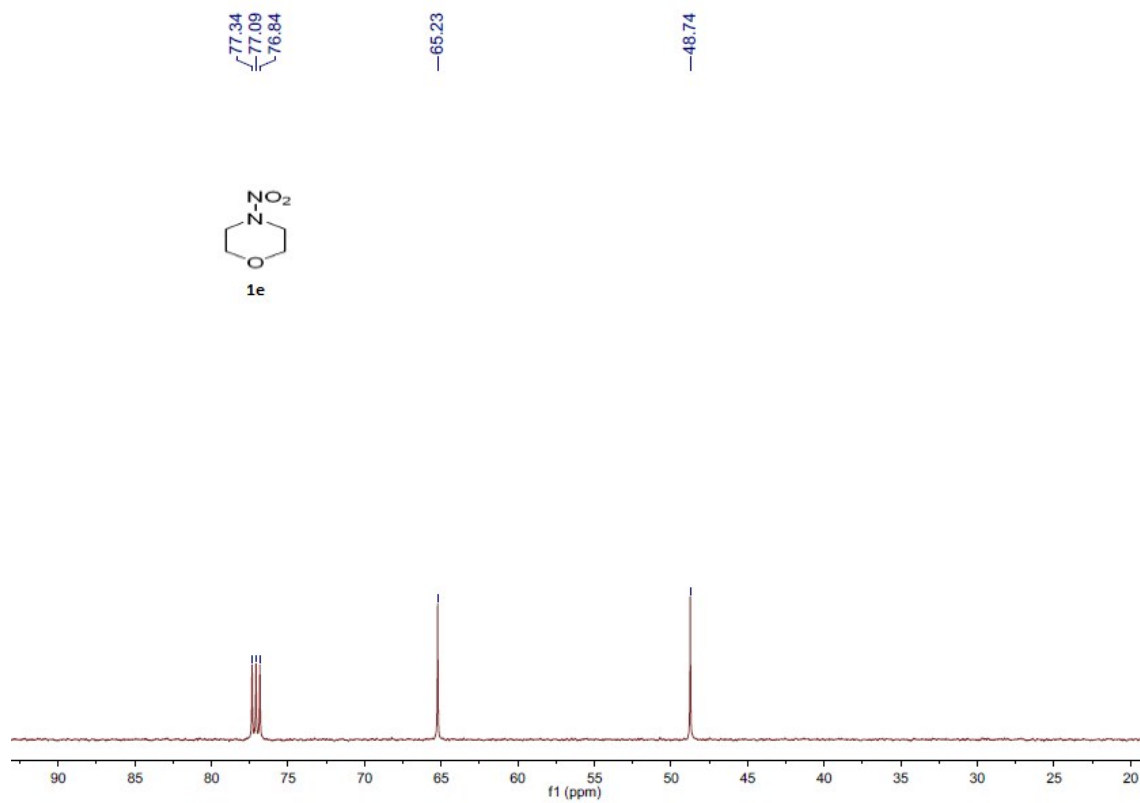
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¹H NMR spectrum of N-nitromorpholine (CDCl₃, 500 MHz)

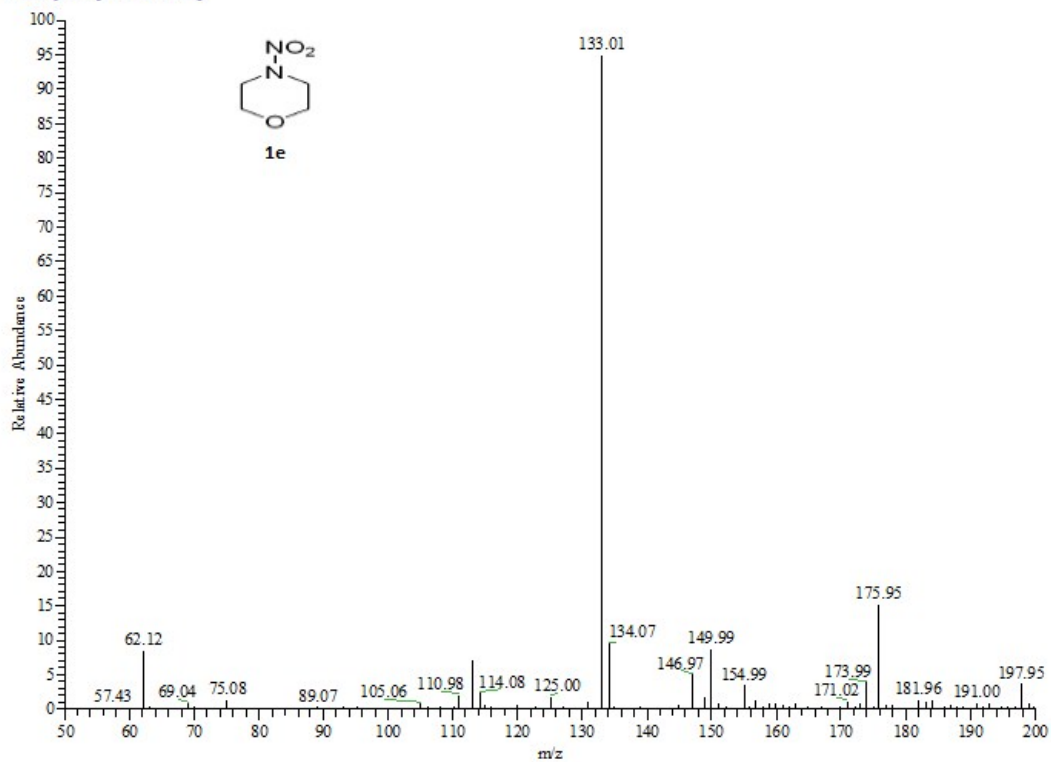


¹³C NMR spectrum of N-nitromorpholine (CDCl₃, 126 MHz)

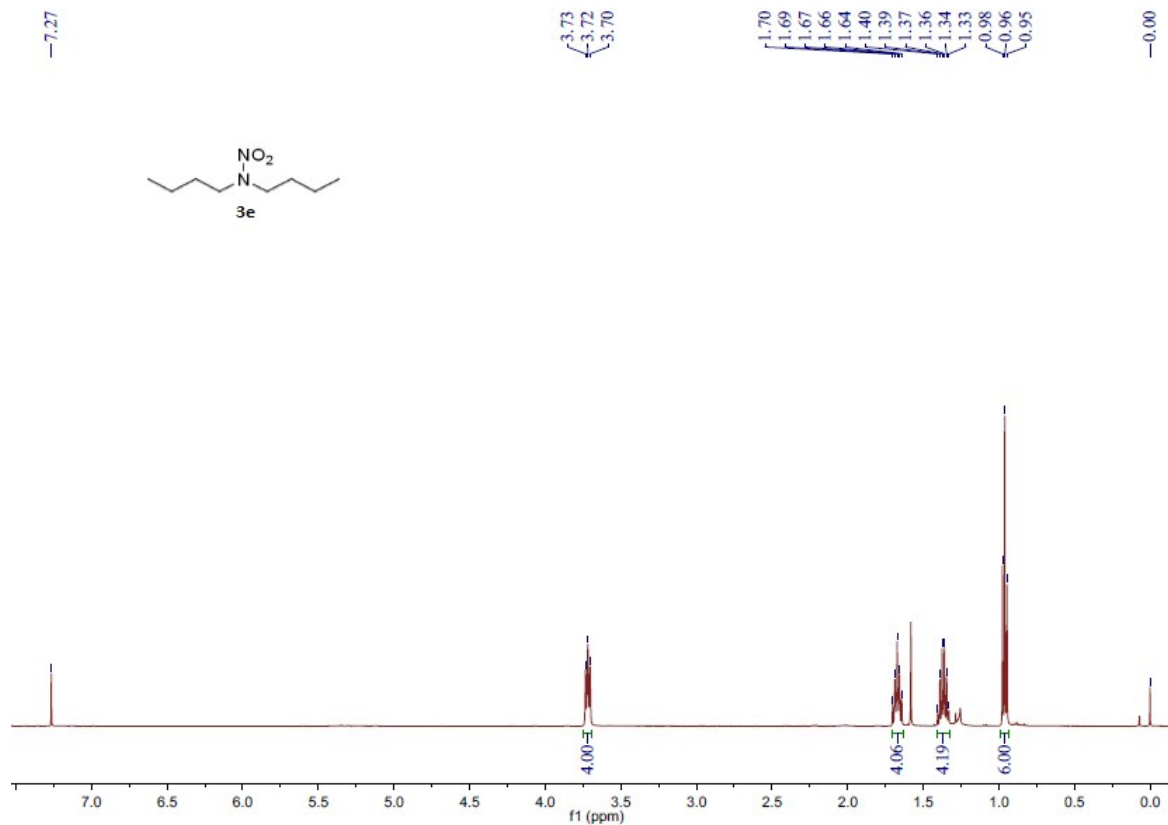


Electrospray Ionization (ESI) Mass Spectrometry of N-nitromorpholine (m/z of 133.01)

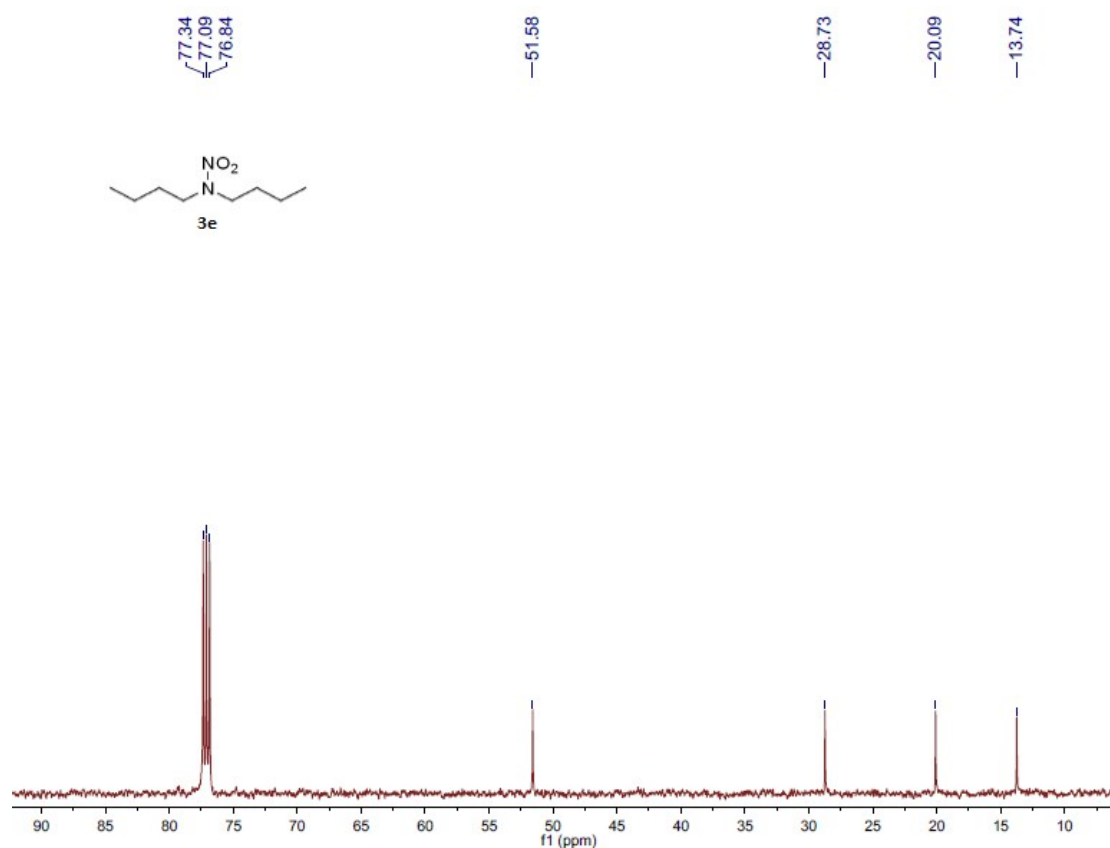
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¹H NMR spectrum of N-nitrodibutylamine (CDCl₃, 500 MHz)

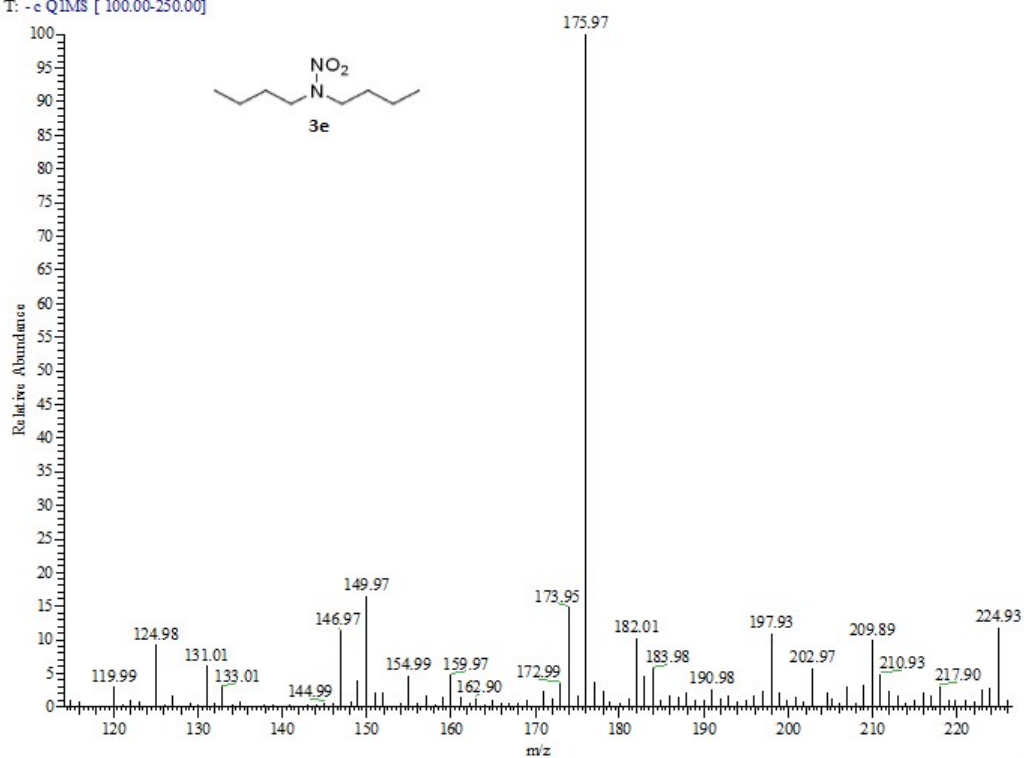


¹³C NMR spectrum of N-nitrodibutylamine (CDCl₃, 126 MHz)

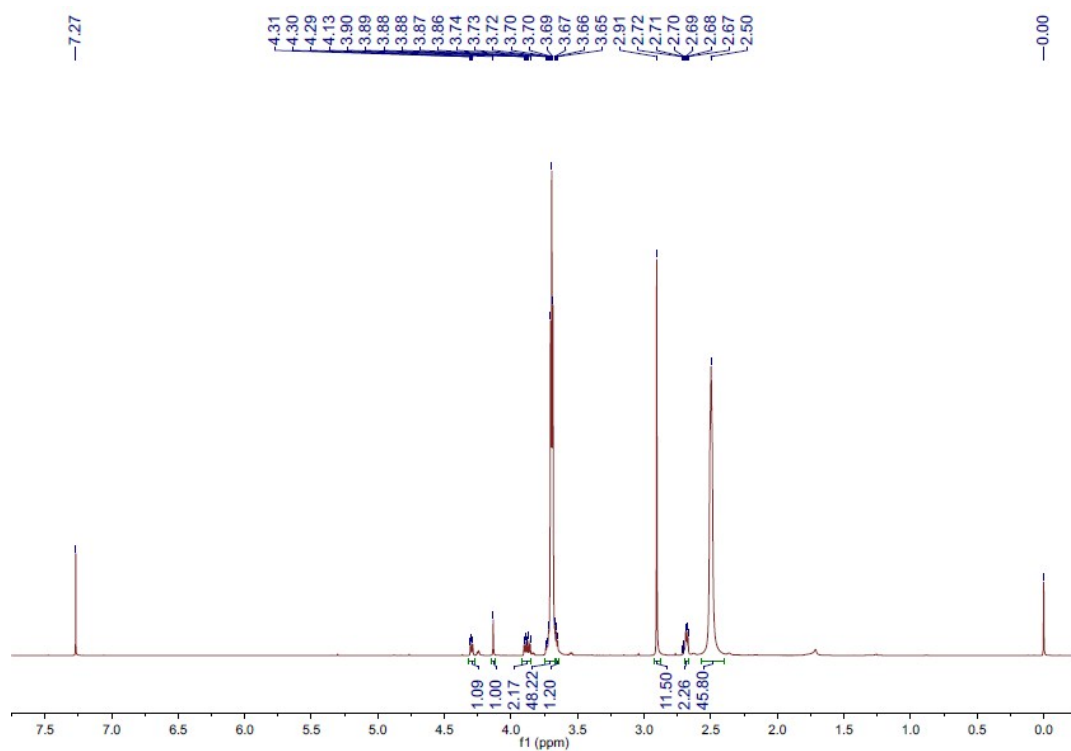


Electrospray Ionization (ESI) Mass Spectrometry of N-nitromorpholine (m/z of 175.97)

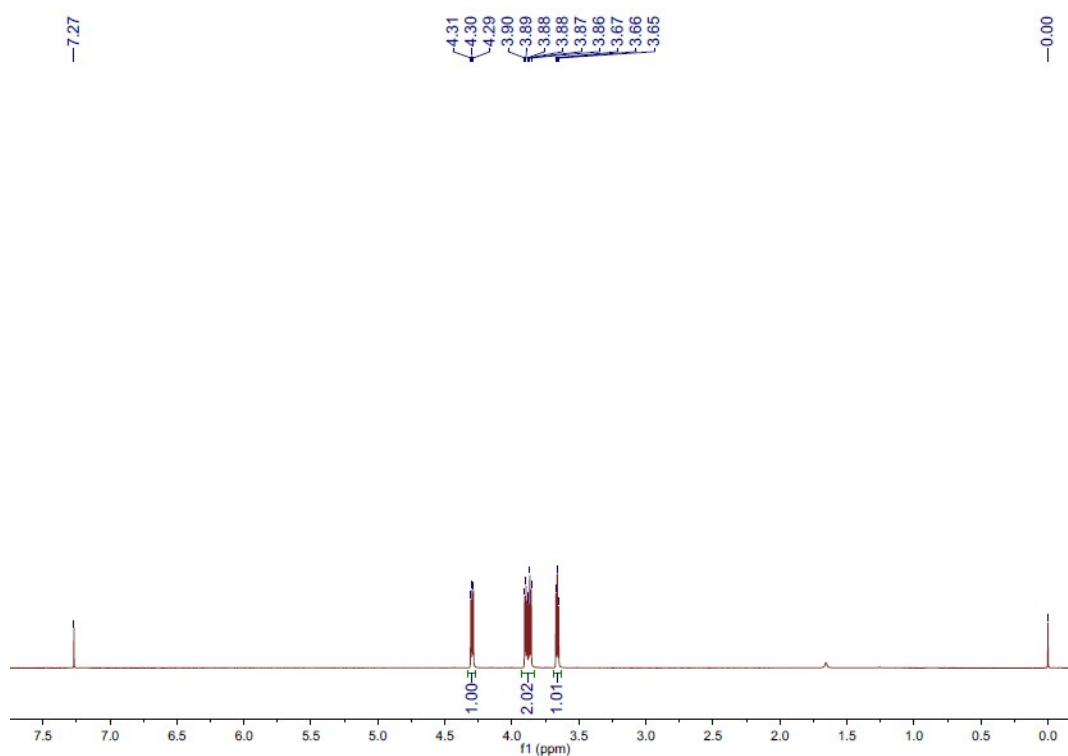
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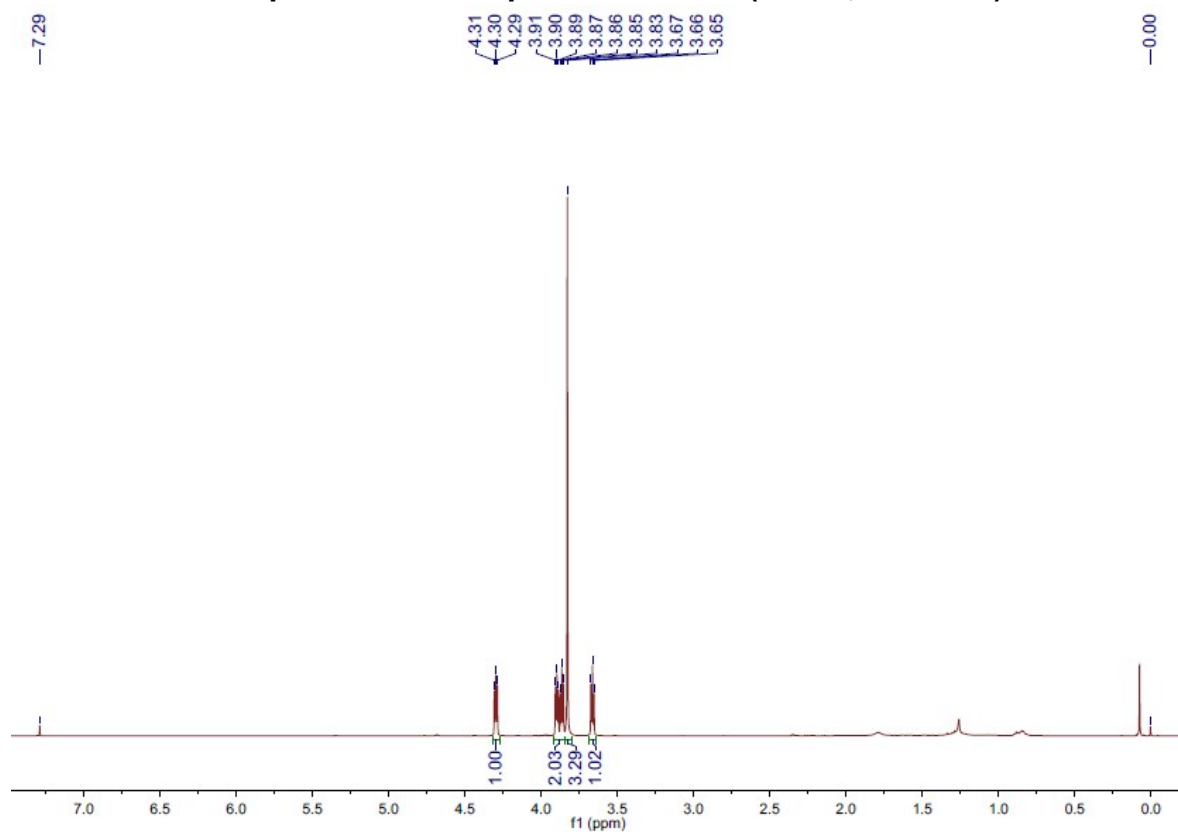
^1H NMR spectrum for the product of the reaction of dimorpholinomethane in fuming HNO_3 at low reaction temperature (CDCl_3 , 500 MHz)



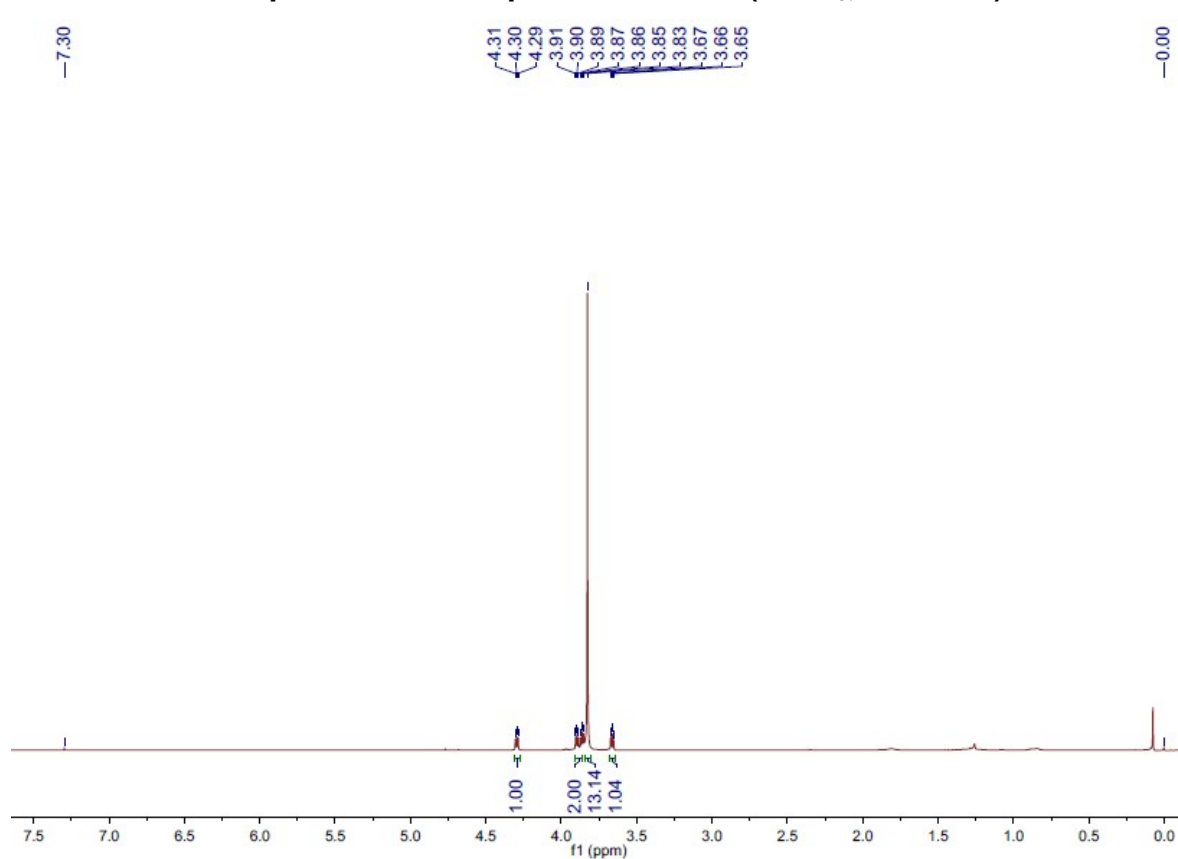
^1H NMR spectrum of sample taken at the end of feeding course (CDCl_3 , 500 MHz)



^1H NMR spectrum of sample taken at 2 h (CDCl_3 , 500 MHz)



^1H NMR spectrum of sample taken at 4 h (CDCl_3 , 500 MHz)



¹H NMR spectrum of sample taken at 6 h (CDCl₃, 500 MHz)

