Highly Selective sp^3 C-N Bond Activation of Tertiary Anilines Modulated by Steric and Thermodynamic Factors

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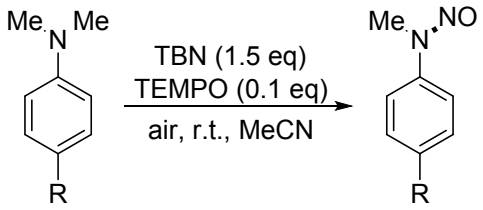
General:

All solvents are anhydrous. TBN and TEMPO were purchased from commercial source and used without further purification. Flash chromatography was carried out with silica gel (200-300 mesh). Analytical TLC was performed with silica gel GF254 plates, and the products were visualized by UV detection. ^{1}H NMR and ^{13}C NMR (400 MHz, 600MHz and 100 MHz, 150MHzrespectively) spectra were recorded in $CDCl_3$. Chemical shifts (δ) are reported in ppm using TMS as internal standard and spin-spin coupling constants (J) are given in Hz. The high resolution mass spectra (HRMS) were measured on an electrospray ionization (ESI) apparatus using time of flight (TOF) mass spectrometry.

General Experimental Procedure



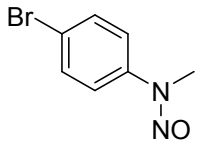
1 **2**

A solution of **1** (1 mmol) and TEMPO (10 mol %) in MeCN (10 mL) or 1,4-dioxane (10 mL) was mixed fully, then TBN (1.5 eq) was added dropwise under air atmosphere. The reaction solution was stirred under room temperature. After completion monitored by TLC (by UV visualization), the solvent was removed under reduced pressure. The products were separated by silica gel column chromatography eluted with petroleum ether/acetone (v/v 50:1) to afford the products.

Measurement of KIE

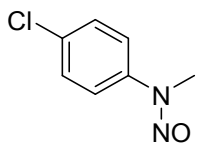
The deuterated substrate d_3-**1d** was synthesized by the nucleophilic substitution between N,4-dimethylaniline and CD_3I under basic condition. The reaction of d_3-**1d** was performed under the standard reaction conditions, and the KIE value was obtained by ^{1}H NMR of the products mixture.

Analytical data for compounds



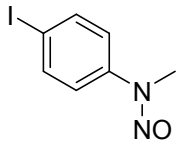
***N*-(4-Bromophenyl)-*N*-methylnitrous amide (2a)** [1]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, J = 9.0 Hz, 2H), 7.44 (d, J = 9.0 Hz, 2H), 3.43 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.3, 132.5, 120.6, 120.3, 31.1. HRMS (ESI): Calc'd for $C_7H_7BrN_2O$ + H^+, 214.9815; found, 214.9815.



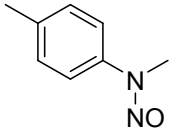
***N*-(4-Chlorophenyl)-*N*-methylnitrous amide (2b)** [1]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, J = 9.1 Hz, 2H), 7.43 (d, J = 9.1 Hz, 2H), 3.42 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.8, 132.9, 129.6, 120.1, 31.2. HRMS (ESI): Calc'd for $C_7H_7ClN_2O$ + H^+, 171.0320; found, 171.0321.



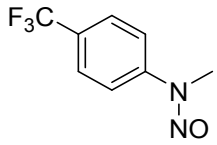
***N*-(4-Iodophenyl)-*N*-methylnitrous amide (2c)**

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, J = 9.0 Hz, 2H), 7.44 (d, J = 9.0 Hz, 2H), 3.43 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.0, 138.5, 120.5, 91.6, 31.0. HRMS (ESI): Calc'd for $C_7H_7IN_2O$ + H^+, 262.9676; found, 262.9665.



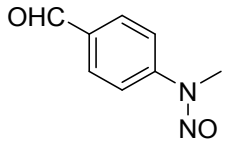
***N*-Methyl-*N*-(*p*-tolyl)nitrous amide (2d) [1]**

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, J = 8.5 Hz, 1H), 7.27 (d, J = 8.3 Hz, 1H), 3.44 (s, 1H), 2.40 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.9, 137.3, 129.9, 119.3, 31.7, 20.9. HRMS (ESI): Calc'd for $C_8H_{10}N_2O$ + H^+, 151.0866; found, 151.0871.



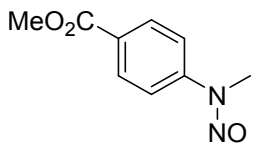
***N*-Methyl-*N*-(4-(trifluoromethyl)phenyl)nitrous amide (2e) [2]**

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, J = 8.7 Hz, 2H), 7.67 (d, J = 8.7 Hz, 2H), 3.44 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.9, 128.9 (q, $J_{C\text{-}F}$ = 33.0 Hz), 126.7 (q, $J_{C\text{-}F}$ = 3.8 Hz), 123.8 (q, $J_{C\text{-}F}$ = 271.9 Hz),118.4, 30.5. HRMS (ESI): Calc'd for $C_8H_7F_3N_2O$ + H^+, 205.0583; found, 205.0574.



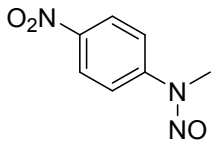
***N*-(4-Formylphenyl)-*N*-methylnitrous amide (2f)**

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.99 (s, 1H), 7.96 (d, J = 8.5 Hz, 2H), 7.72 (d, J = 8.4 Hz, 2H), 3.44 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 190.9, 146.7, 134.5, 131.1, 118.2, 30.3. HRMS (ESI): Calc'd for $C_8H_8N_2O_2$ + H^+, 165.0659; found, 165.0659.



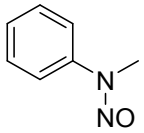
Methyl 4-(methyl(nitroso)amino)benzoate (2g)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, J = 6.7 Hz, 2H), 7.59 (d, J = 7.4 Hz, 2H), 3.89 (s, 3H), 3.41 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.1, 145.6, 131.0, 128.4, 117.8, 52.2, 30.4. HRMS (ESI): Calc'd for $C_9H_{10}N_2O_3$ + H^+, 195.0764; found, 195.0758.



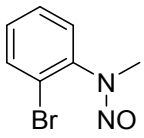
***N*-Methyl-*N*-(4-nitrophenyl)nitrous amide (2h)**

^{1}H NMR (400 MHz, CDC_3) δ 8.31 (d, *J* = 9.2 Hz, 2H), 7.74 (d, *J* = 9.1 Hz, 2H), 3.45 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 147.1, 145.9, 125.2, 117.9, 30.1; HRMS (ESI): Calc'd for $C_7H_7N_3O_3$ + H^+, 182.0560; found, 182.0557.



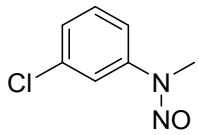
***N*-Methyl-*N*-phenylnitrous amide (2i)[1]**

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, *J* = 8.4 Hz, 2H), 7.46 (t, *J* = 7.9 Hz, 2H), 7.35 (t, *J* = 7.3 Hz, 1H), 3.45 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.3, 129.4, 127.3, 119.2, 31.4. HRMS (ESI):Calc'd for $C_7H_8N_2O$ + H^+, 137.0709; found, 137.0717.



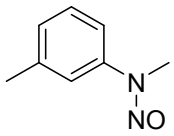
***N*-(2-Bromophenyl)-*N*-methylnitrous amide (2j)**

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, *J* = 8.5 Hz, 1H), 7.27 (d, *J* = 8.3 Hz, 1H), 3.44 (s, 1H), 2.40 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.6, 133.9, 130.8, 128.5, 128.3, 119.9, 35.4. HRMS (ESI): Calc'd for $C_7H_7BrN_2O$ + H^+, 214.9815; found, 214.9805.



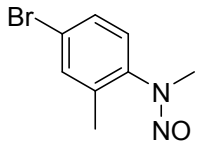
***N*-(3-Chlorophenyl)-*N*-methylnitrous amide (2k)[2]**

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (t, *J* = 1.8 Hz, 1H), 7.48 – 7.44 (m, 1H), 7.41 (t, *J* = 7.9 Hz, 1H), 7.36 – 7.31 (m, 1H), 3.43 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.3, 135.2, 130.5, 127.1, 119.0 , 116.8, 31.0. HRMS (ESI):Calc'd for $C_7H_7ClN_2O$ + H^+, 171.0320; found, 171.0316.



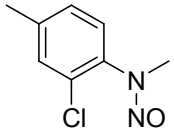
***N*-Methyl-*N*-(*m*-tolyl)nitrous amide (2l)[1]**

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.27 (m, 3H), 7.15 (d, *J* = 7.1 Hz, 1H), 3.42 (s, 3H), 2.40 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.2, 139.5, 129.2, 128.1, 119.9, 116.3, 31.6, 21.5. HRMS (ESI):Calc'd for $C_8H_{10}N_2O$ + H^+, 151.0866; found, 151.0867.



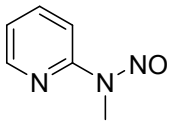
***N*-(4-Bromo-2-methylphenyl)-*N*-methylnitrous amide (2m)**

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 1.9 Hz, 1H), 7.44 (dd, *J* = 8.2, 2.0 Hz, 1H), 7.10 (d, *J* = 8.4 Hz, 1H), 3.35 (s, 3H), 2.22 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.5, 136.0, 134.4, 130.1, 127.1, 122.8, 35.1, 18.1. HRMS (ESI): Calc'd for $C_8H_9BrN_2O + H^+$, 228.9971; found, 228.9967.



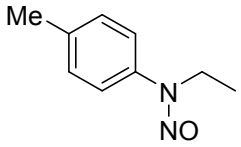
***N*-(2-Chloro-4-methylphenyl)-*N*-methylnitrous amide (2n)**

^{1}H NMR (400 MHz, $CDCl_3$) δ7.35 (s, 1H), 7.28 (d, *J* = 8.1 Hz, 1H), 7.18 (d, *J* = 8.0 Hz, 1H), 3.37 (s, 3H), 2.40 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.0, 137.5, 131.1, 129.7, 128.5, 127.6, 35.2, 20.9. HRMS (ESI):Calc'd for $C_8H_9ClN_2O + H^+$, 185.0476; found, 185.0468.



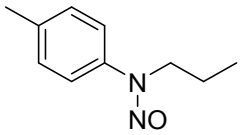
***N*-Methyl-*N*-(pyridin-2-yl)nitrous amide (2o)**

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (d, *J* = 4.3 Hz, 1H), 7.98 (d, *J* = 8.4 Hz, 1H), 7.77 (t, *J* = 7.8 Hz, 1H), 7.20 (dd, *J* = 7.2, 5.0 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 154.5, 147.9, 138.3, 121.6, 112.67, 28.2; ESI-MS m/z (relative intensity): 137 (40.1%), 107 (90.0%), 78 (100%).



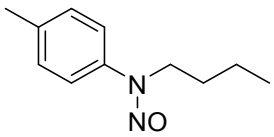
***N*-Ethyl-*N*-(*p*-tolyl)nitrous amide (2p)[3]**

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, *J* = 8.1 Hz, 2H), 7.26 (d, *J* = 7.9 Hz, 2H), 4.04 (q, *J* = 7.2 Hz, 2H), 2.38 (s, 3H), 1.15 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.0, 137.3, 130.0, 119.7, 39.4, 20.9, 11.7. HRMS (ESI): Calc'd for $C_9H_{12}N_2O + H^+$, 165.1022; found, 165.1019.



***N*-Propyl-*N*-(*p*-tolyl)nitrous amide (2q)**

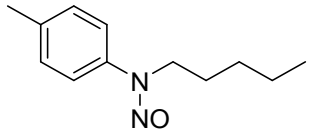
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, *J* = 8.2 Hz, 2H), 7.25 (d, *J* = 8.0 Hz, 2H), 4.00 – 3.93 (m, 2H), 2.38 (s, 3H), 1.62 – 1.50 (m, 2H), 0.87 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.2, 137.3, 130.0, 119.9, 45.5, 20.9, 19.9, 11.4. HRMS (ESI): Calc'd for $C_{10}H_{14}N_2O + H^+$, 179.1179; found, 179.1181.



***N*-Butyl-*N*-(*p*-tolyl)nitrous amide (2r)**

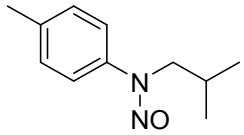
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, *J* = 8.1 Hz, 2H), 7.24 (d, *J* = 8.0 Hz, 2H), 4.03 – 3.95 (m, 2H), 2.38 (s, 3H), 1.56 – 1.45 (m, 2H), 1.34 – 1.23 (m, 2H), 0.88 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR

(101 MHz, $CDCl_3$) δ 139.2, 137.3, 130.0, 119.8, 43.8, 28.5, 20.9, 20.3, 13.6. HRMS (ESI):Calc'd for $C_{11}H_{16}N_2O + H^+$, 193.1335; found, 193.1335.



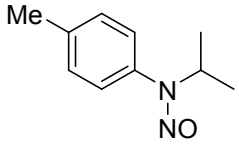
***N*-Pentyl-*N*-(*p*-tolyl)nitrous amide (2s)**

^1H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, *J* = 8.0 Hz, 2H), 7.25 (d, *J* = 8.0 Hz, 2H), 4.05 – 3.91 (m, 2H), 2.38 (s, 3H), 1.57 – 1.47 (m, 2H), 1.31 – 1.21 (m, 4H), 0.85 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.2, 137.2, 130.0, 119.8, 44.0, 29.1, 26.1, 22.2, 20.9, 13.8. HRMS (ESI):Calc'd for $C_{12}H_{18}N_2O + H^+$, 207.1492; found, 207.1483.



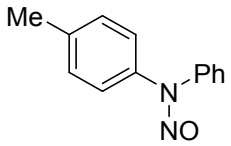
***N*-Isobutyl-*N*-(*p*-tolyl)nitrous amide (2t)**

^1H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, *J* = 8.0 Hz, 2H), 7.25 (d, *J* = 8.0 Hz, 2H), 3.89 (d, *J* = 7.5 Hz, 2H), 2.38 (s, 3H), 2.05 – 1.90 (m, 1H), 0.82 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.3, 130.0, 120.1, 50.1, 26.6, 20.9, 20.2, 19.8.HRMS (ESI):Calc'd for $C_{11}H_{16}N_2O + H^+$, 193.1335; found, 193.1328.



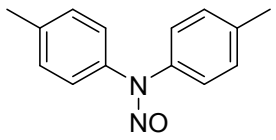
***N*-Isopropyl-*N*-(*p*-tolyl)nitrous amide (2u)**

Mixture of two isomers: ^1H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.16 (m, 6.6H), 6.83 (d, *J* = 7.8 Hz, 1.6H), 5.25 – 5.18 (m, 1.4H), 5.05 (m, 1H), 2.41 (s, 4H), 2.37 (s, 3H), 1.44 (d, *J* = 6.8 Hz, 6H), 1.16 (d, *J* = 6.9 Hz, 8H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.4, 138.9, 136.8, 133.6, 130.0, 129.7, 127.4, 126.0, 56.0, 46.1, 22.0, 21.2, 21.1, 19.7.HRMS (ESI):Calc'd for $C_{10}H_{14}N_2O + Na^+$, 201.1004; found, 201.0996.



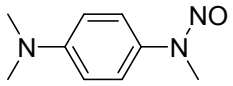
***N*-Phenyl-*N*-(*p*-tolyl)nitrous amide (2v)**

mixture of two isomers: ^1H NMR (400 MHz, $CDCl_3$) δ 7.51 (t, *J* = 7.5 Hz, 1H), 7.48 – 7.38 (m, 4H), 7.32 (d, *J* = 8.1 Hz, 4H), 7.27 – 7.20 (m, 2H), 7.10 (d, *J* = 7.8 Hz, 1H), 6.98 (d, *J* = 7.8 Hz, 2H), 2.43 (s, 3H), 2.40 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.7, 140.2, 139.7, 137.1, 134.1, 130.5, 129.9, 129.7, 129.4, 129.3, 127.3, 127.2, 126.9, 120.0, 119.6, 21.3, 21.0.HRMS (ESI):Calc'd for $C_{13}H_{12}N_2O + Na^+$, 235.0847; found, 235.0845.



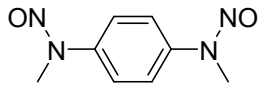
***N,N*-Di-*p*-tolylnitrous amide (2w)**

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (dd, *J* = 8.6, 2.1 Hz, 4H), 7.20 (d, *J* = 8.2 Hz, 2H), 6.96 (d, *J* = 8.3 Hz, 2H), 2.41 (s, 3H), 2.38 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.3, 139.5, 136.9, 134.4, 130.4, 129.9, 127.0, 119.8, 21.3, 21.0. HRMS (ESI): Calc'd for $C_{14}H_{14}N_2O$ + Na^+, 249.1004, found, 249.1001.



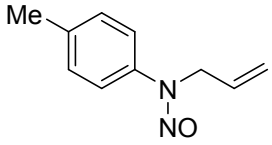
***N*-(4-(Dimethylamino)phenyl)-*N*-methylnitrous amide (5a)**

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, *J* = 8.9 Hz, 2H), 6.76 (d, *J* = 9.0 Hz, 2H), 3.42 (s, 3H), 2.99 (s, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 149.9, 132.1, 121.2, 112.6, 40.6, 32.6; HRMS (ESI): Calc'd for $C_9H_{13}N_3O$ + H^+, 180.1131; found, 180.1131.



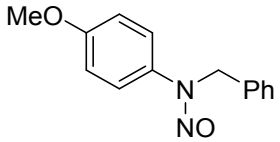
***N,N'*-(1,4-Phenylene)bis(*N*-methylnitrous amide) (5b)**

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (s, 4H), 3.46 (s, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 141.1, 119.81, 31.2; HRMS (ESI): Calc'd for $C_8H_{10}N_4O_2$ + Na^+, 217.0702; found, 217.0693.



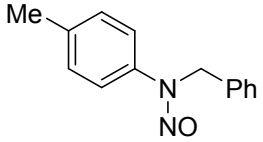
***N*-Allyl-*N*-(*p*-tolyl)nitrous amide (7a)**

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, *J* = 8.1 Hz, 2H), 7.24 (d, *J* = 8.0 Hz, 2H), 5.79 – 5.66 (m, 1H), 5.16 (d, *J* = 10.4 Hz, 1H), 5.07 (d, *J* = 17.3 Hz, 1H), 4.60 (d, *J* = 5.1 Hz, 2H), 2.38 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.4, 137.3, 130.0, 129.6, 119.5, 118.0, 46.8, 21.0. HRMS (ESI): Calc'd for $C_{10}H_{12}N_2O$ + H^+, 177.1022; found, 177.1015.



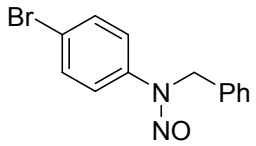
***N*-Benzyl-*N*-(4-methoxyphenyl)nitrous amide (7b)**

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, *J* = 9.1 Hz, 2H), 7.31 – 7.19 (m, 3H), 7.08 (d, *J* = 6.6 Hz, 2H), 6.93 (d, *J* = 9.1 Hz, 2H), 5.21 (s, 2H), 3.80 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 159.0, 135.0, 134.4, 128.8, 127.6, 127.3, 121.7, 114.6, 55.5, 47.9.HRMS (ESI): Calc'd for $C_{14}H_{14}N_2O_2$ + H^+, 243.1128; found, 243.1130.



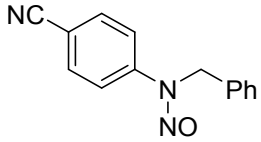
***N*-Benzyl-*N*-(*p*-tolyl)nitrous amide (7c)**

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, *J* = 8.4 Hz, 2H), 7.32 – 7.15 (m, 5H), 7.08 (d, *J* = 7.1 Hz, 2H), 5.23 (s, 2H), 2.37 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 139.4, 137.4, 134.4, 130.0, 128.8, 127.5, 127.1, 119.7, 47.4, 20.9.HRMS (ESI): Calc'd for $C_{14}H_{14}N_2O$ + H^+, 227.1179; found, 227.1175.



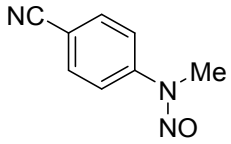
***N*-Benzyl-*N*-(4-bromophenyl)nitrous amide (7d)**

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, *J* = 8.9 Hz, 2H), 7.41 (d, *J* = 8.9 Hz, 2H), 7.34 – 7.20 (m, 3H), 7.05 (d, *J* = 6.7 Hz, 2H), 5.21 (s, 2H).^{13}C NMR (101 MHz, $CDCl_3$) δ 140.7, 133.9, 132.5, 128.9, 127.8, 126.9, 120.8, 120.7, 46.8.HRMS (ESI): Calc'd for $C_{13}H_{11}BrN_2O + H^+$, 291.0128; found, 291.0123.



***N*-Benzyl-*N*-(4-cyanophenyl)nitrous amide (7e)**

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (s, 4H), 7.34 – 7.20 (m, 3H), 7.02 (d, *J* = 6.6 Hz, 2H), 5.23 (s, 2H).^{13}C NMR (101 MHz, $CDCl_3$) δ 145.0, 133.6, 133.4, 129.1, 128.0, 126.6, 118.5, 118.1, 110.4, 45.9.HRMS (ESI): Calc'd for $C_{14}H_{11}N_3O + Na^+$, 260.0800; found, 260.0795.



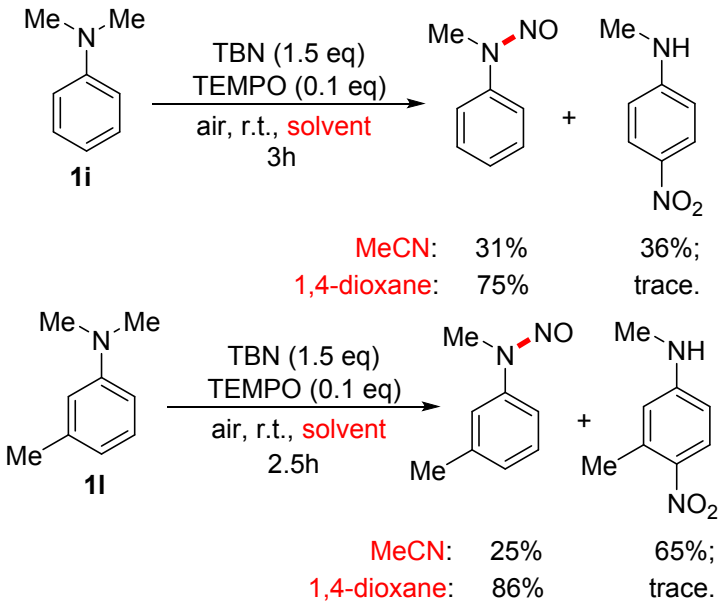
***N*-Methyl-*N*-(4-cyanophenyl)nitrous amide (7e')**

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 9.0 Hz, 2H), 7.69 (d, *J* = 8.9 Hz, 2H), 3.42 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 145.5, 133.6, 118.3, 118.1, 110.3, 30.0.HRMS (ESI): Calc'd for $C_8H_7N_3O + H^+$, 162.0662; found, 162.0658.

Solvent effect on the selected examples

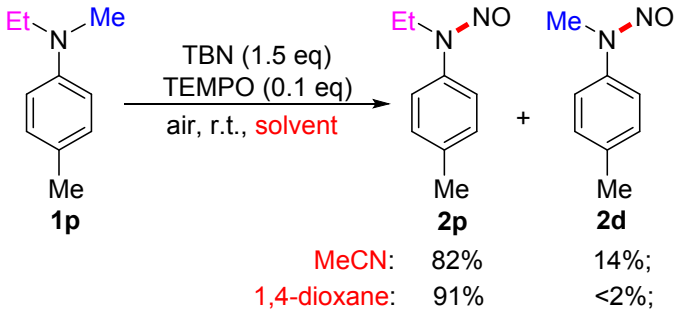
1. Solvent effect on 1i and 1l

For substrates **1i** and **1l**, when MeCN was employed as the solvent, *N*-nitrosoanilines were isolated in lower yields, and nitration on para-position occurred inevitably. While using 1,4-dioxane as the solvent, only trace amount of nitration products were detected.

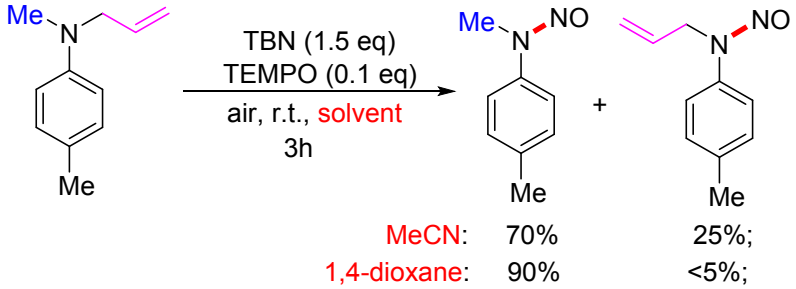


2. Solvent effect on reaction selectivity

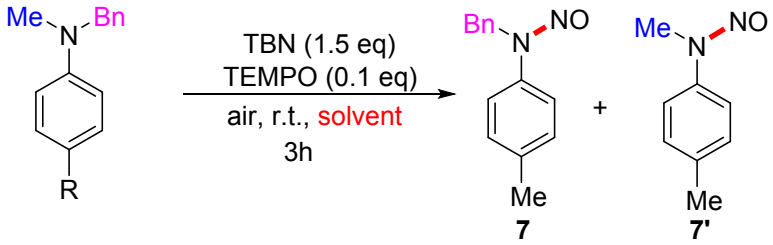
The selectivity was also affected by solvent effect. For unsymmetric substrate **1p**, when the reaction was performed in MeCN, a mixture of C-N cleavage products were isolated, in which demethylation was favored (ratio: 82:14). However, in 1,4-dioxane, only trace amount of the de-ethylation product was detected by GC-MS, and the desired product **2p** was obtained in 91% yield.



Similar results were also obtained for *N*-allylanilines. In MeCN, a mixture were afforded, and the C-N cleavage on *N*-allyl bond was preferred. In 1,4-dioxane, the N-Me cleavage was inhibited.



In the cases of N-benzyl-N-methylanilines, MeCN as the solvent gave higher site-selectivity, favoring N-Me cleavage. Furthermore, 1,4-dioxane as the solvent resulted in lower conversion of the substrates (about 80%) under air atmosphere (under O_2 balloon, full conversion could be realized). The exact reason of this solvent effect remains unknown at current stage.



R	Ratio of **7** : **7'**	
	MeCN	1,4-dioxane
OMe	**3.6 : 1**	0.29 : 1
Me	**6.1 : 1**	1 : 1
Br	**4.1 : 1**	1.3 : 1
CN	**1.8 : 1**	1.7 : 1

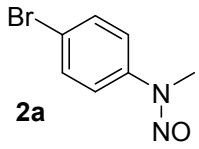
References

1. Sakai, N.; Sasaki, M.;Ogiwara Y. *Chem. Commun.*, 2015, **51**, 11638.

2. Kupper, R.; Hilton, B. D.; Kroeger-Koepke, M. B.;Koepke, S. R.; Michejda,C. J. *J. Org. Chem.*, 1984, **49**, 3781.

3. Masayuki, T.; Shoko, S. *Chem. Pharm. Bull.*1987, **35**, 1353.

^{1}H and ^{13}C spectra



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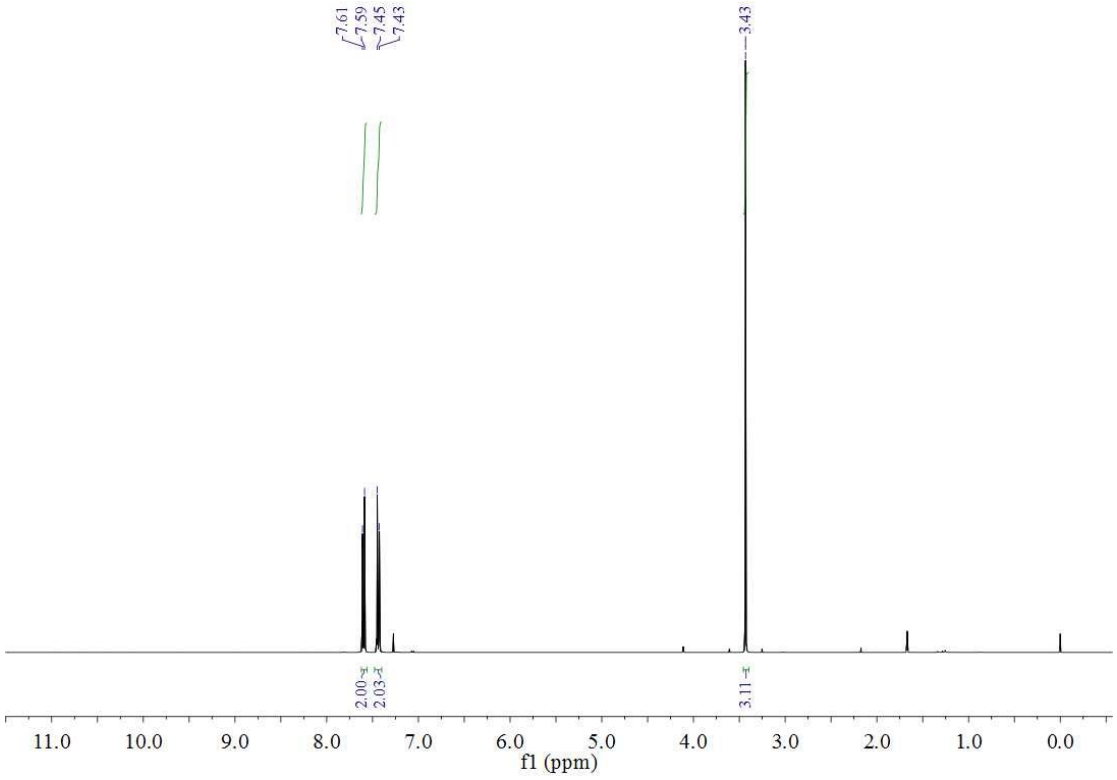

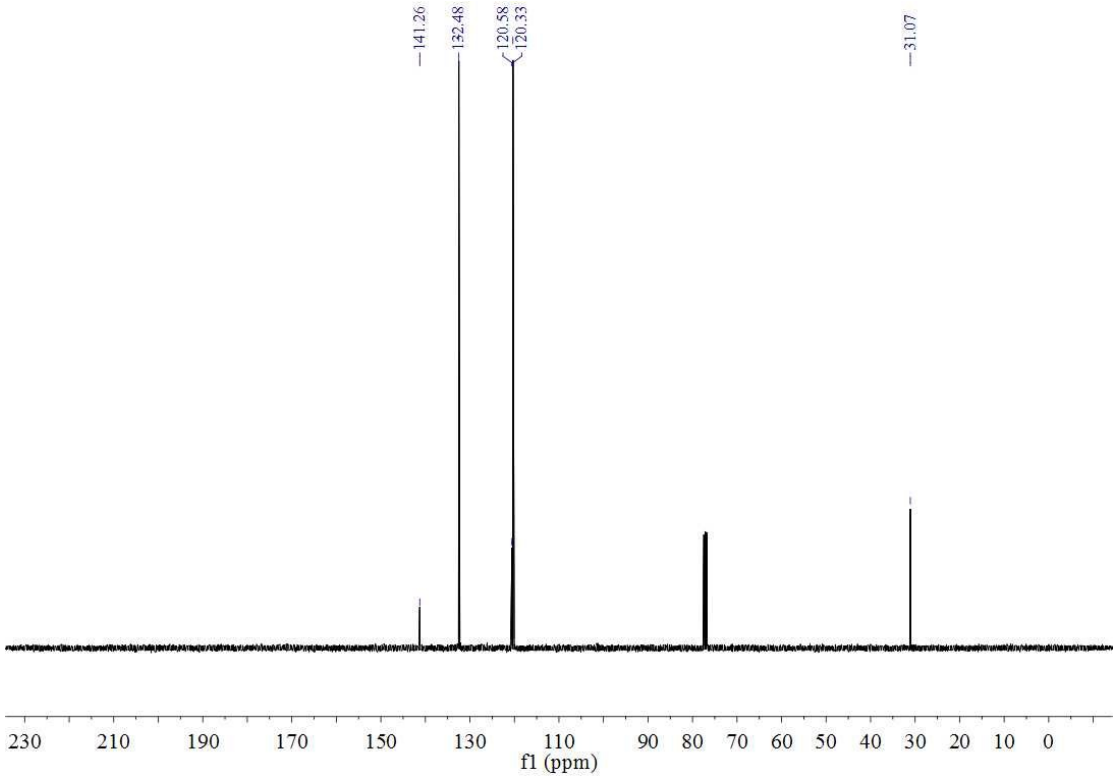

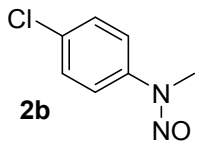
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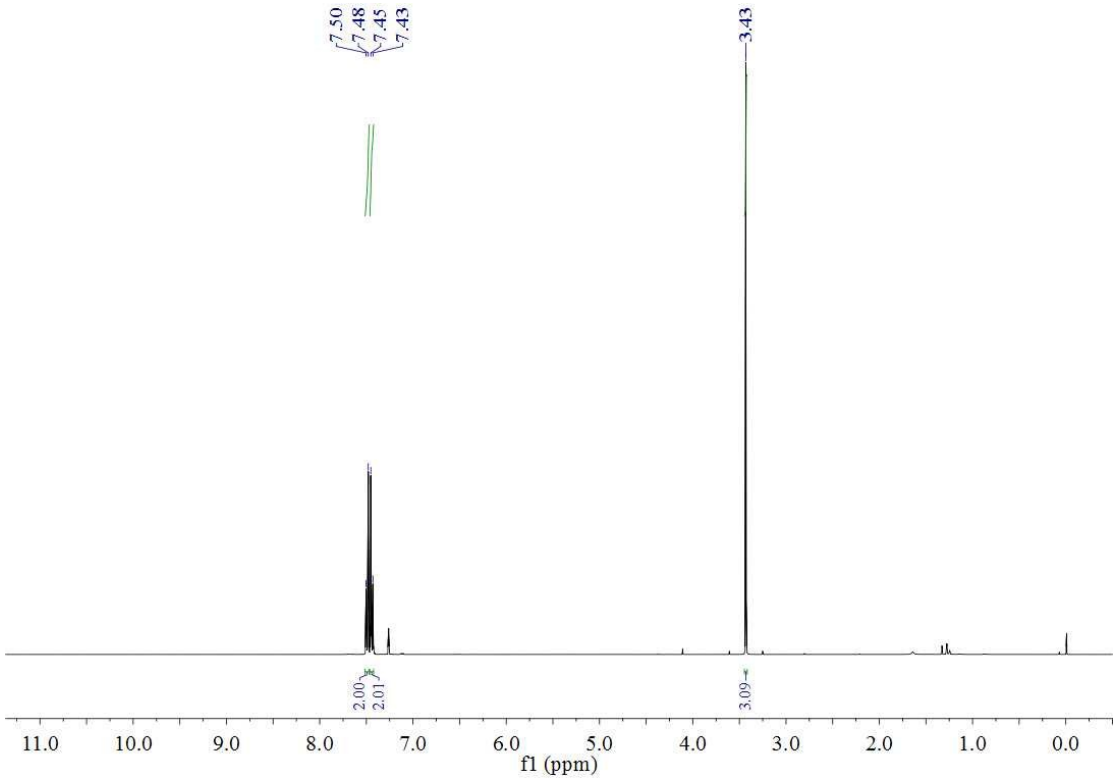
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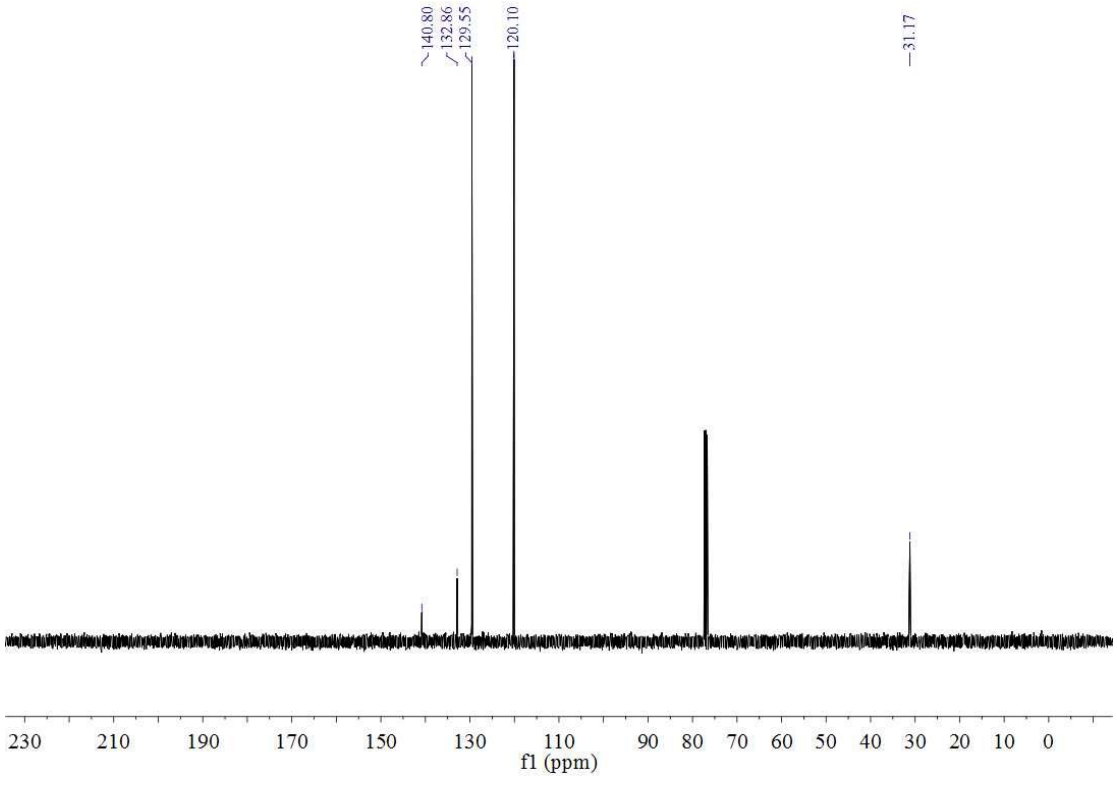
f1 (ppm)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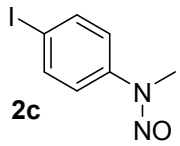
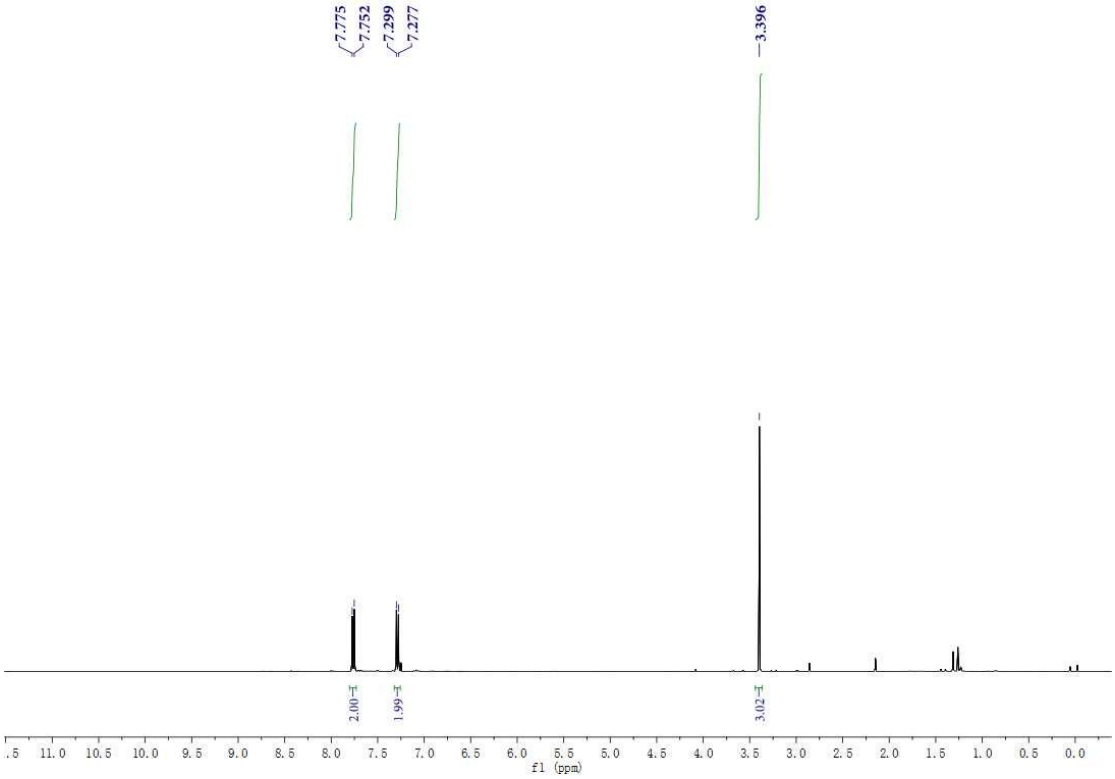
f1 (ppm)


I
N
NO

2c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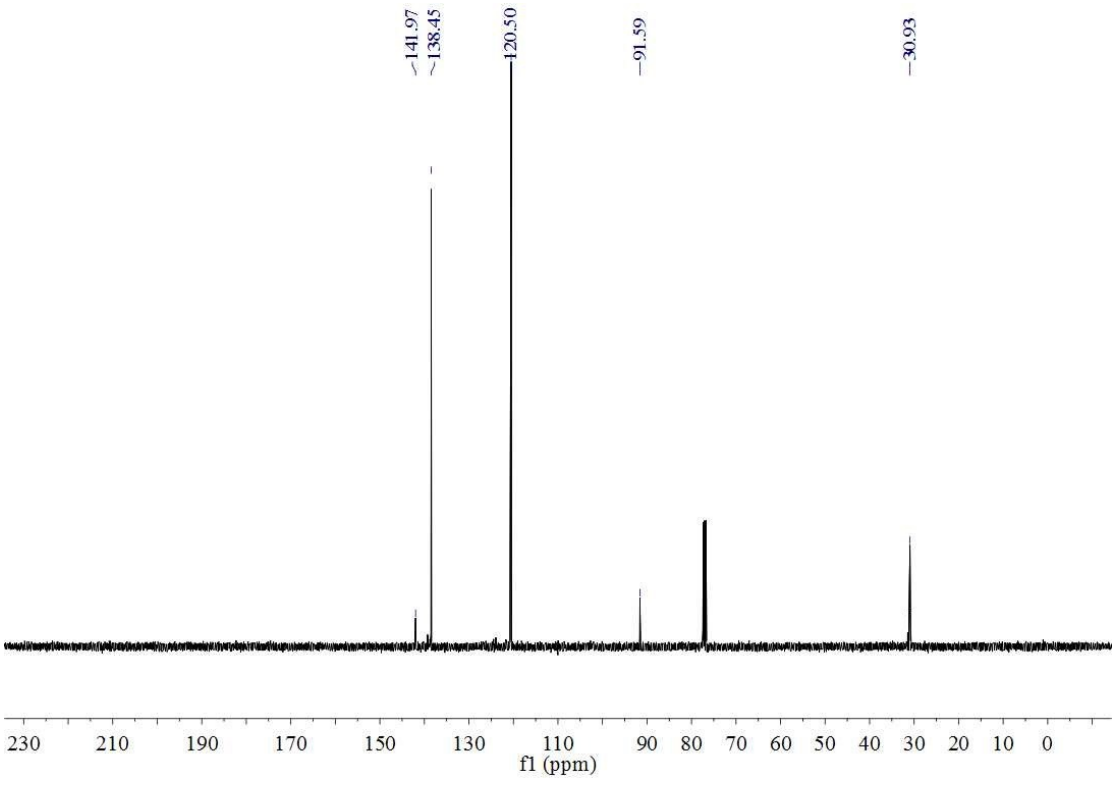
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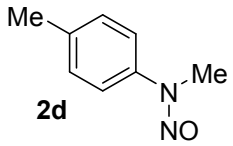
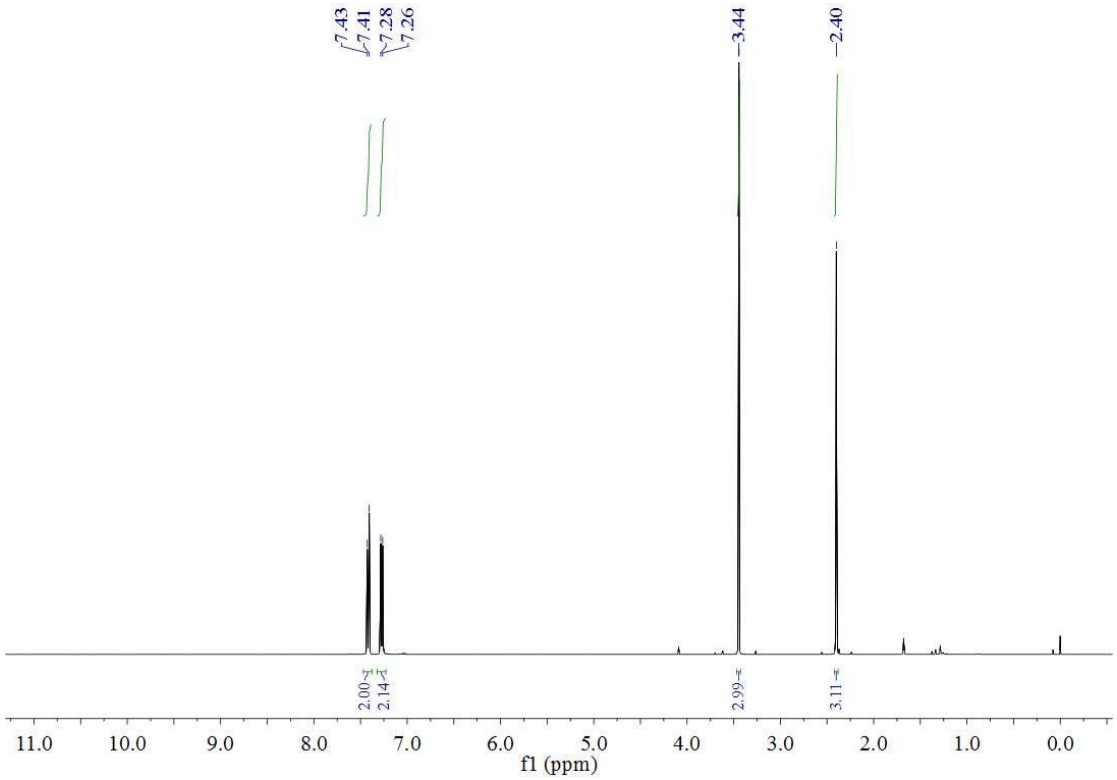

Me
Me
N
NO

2d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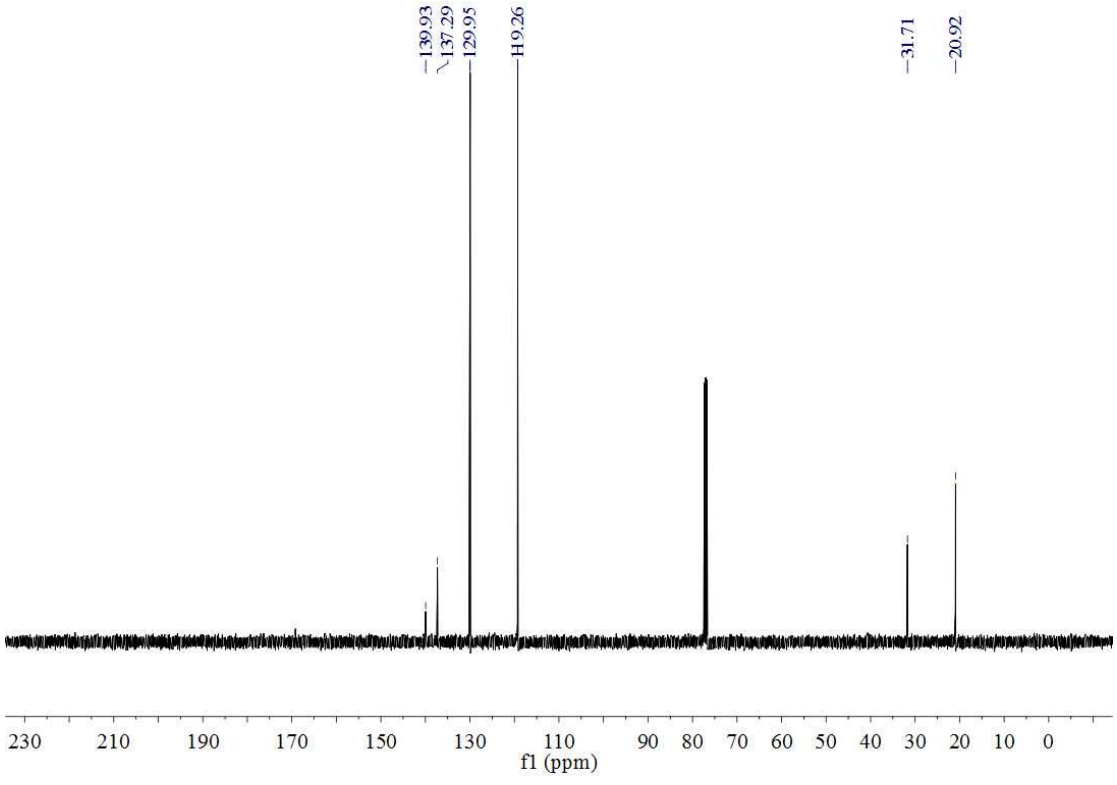
f1 (ppm)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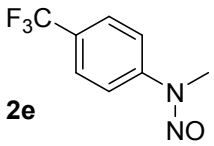

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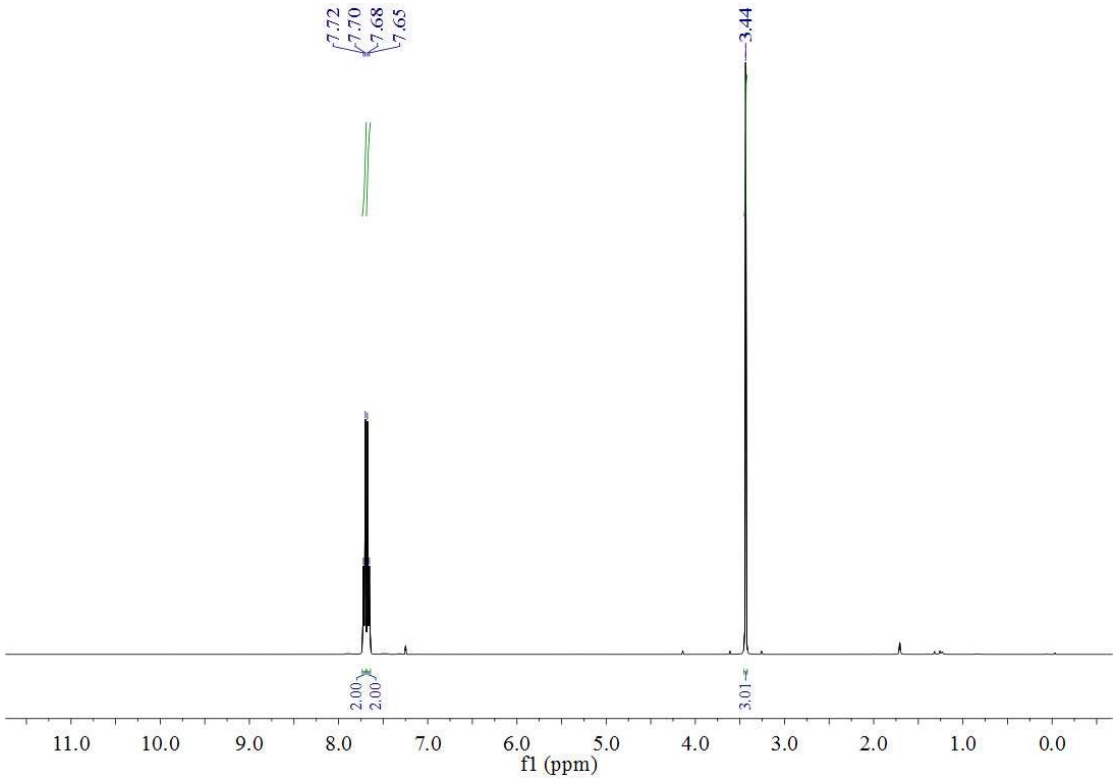
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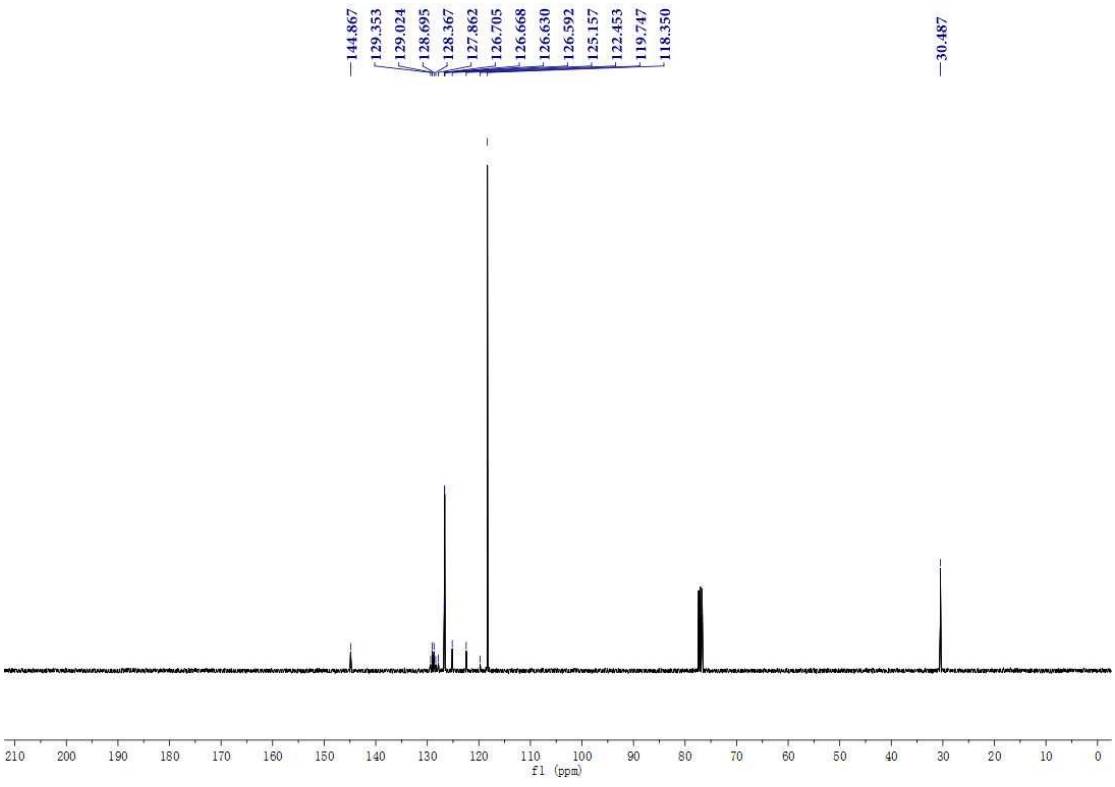
f1 (ppm)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30.487
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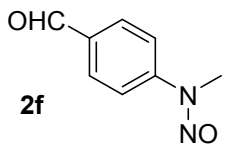
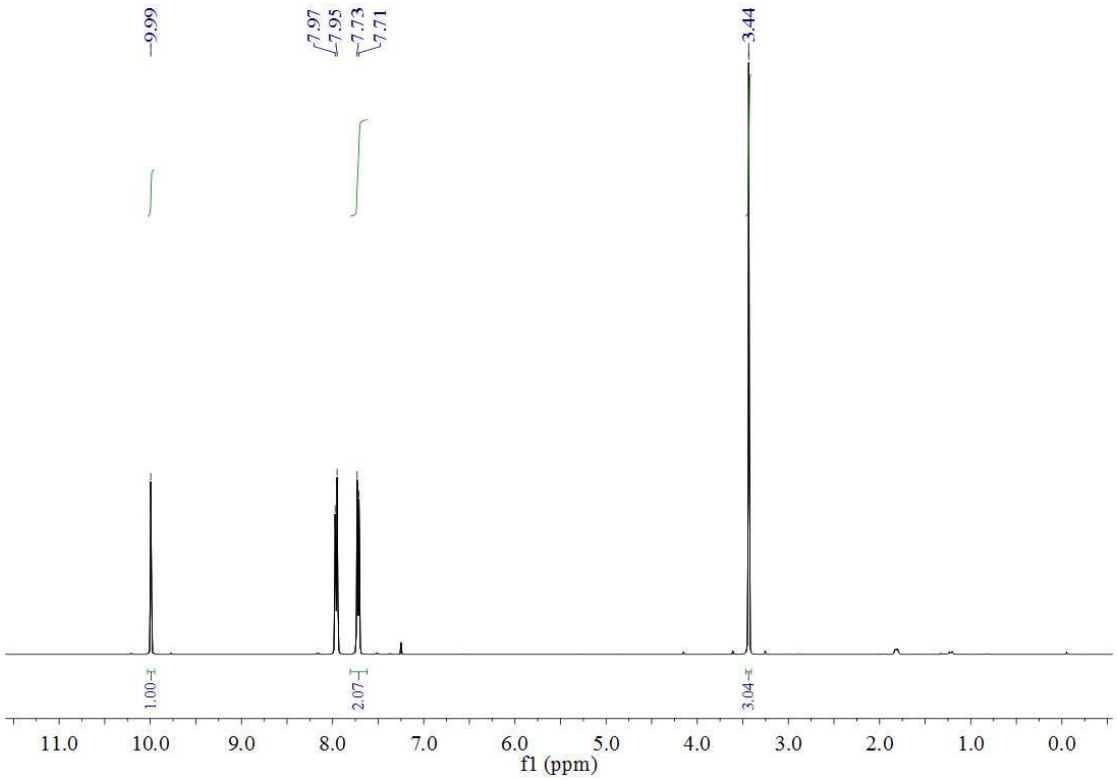
f1 (ppm)


OHC
N
NO

2f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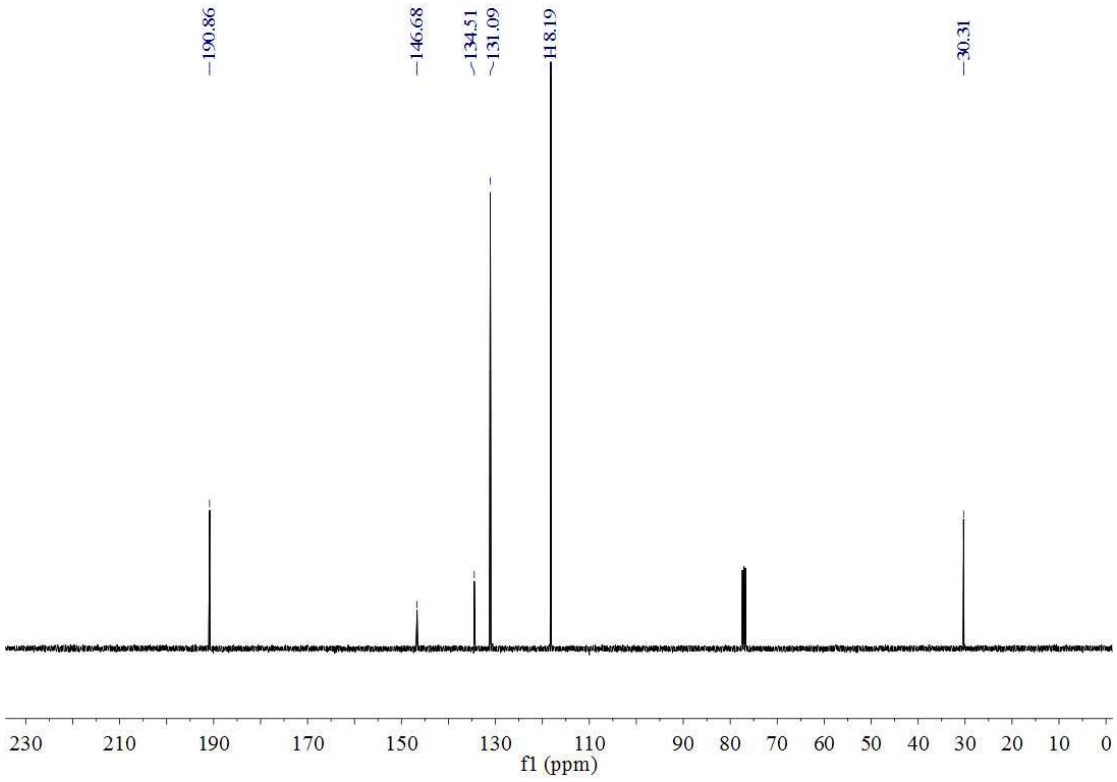
f1 (ppm)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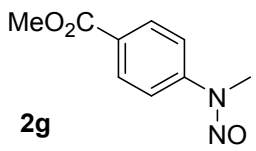
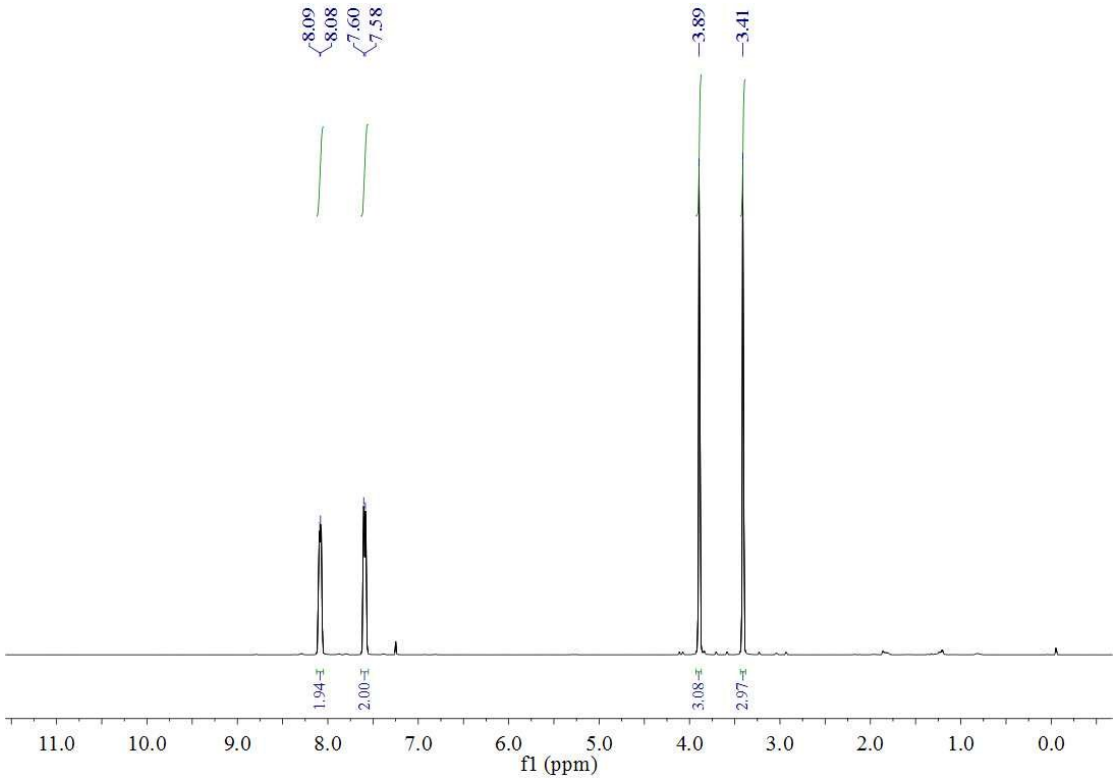
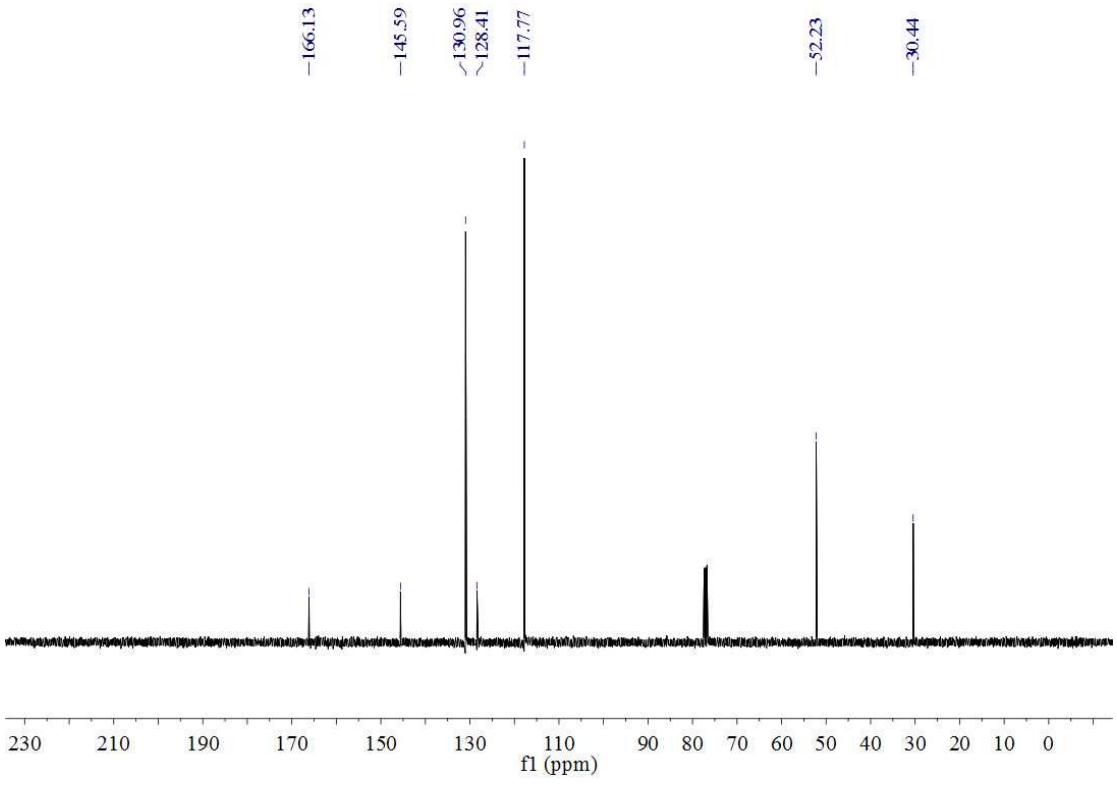
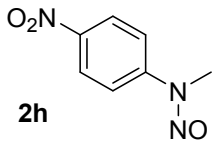
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


MeO2C
N
NO

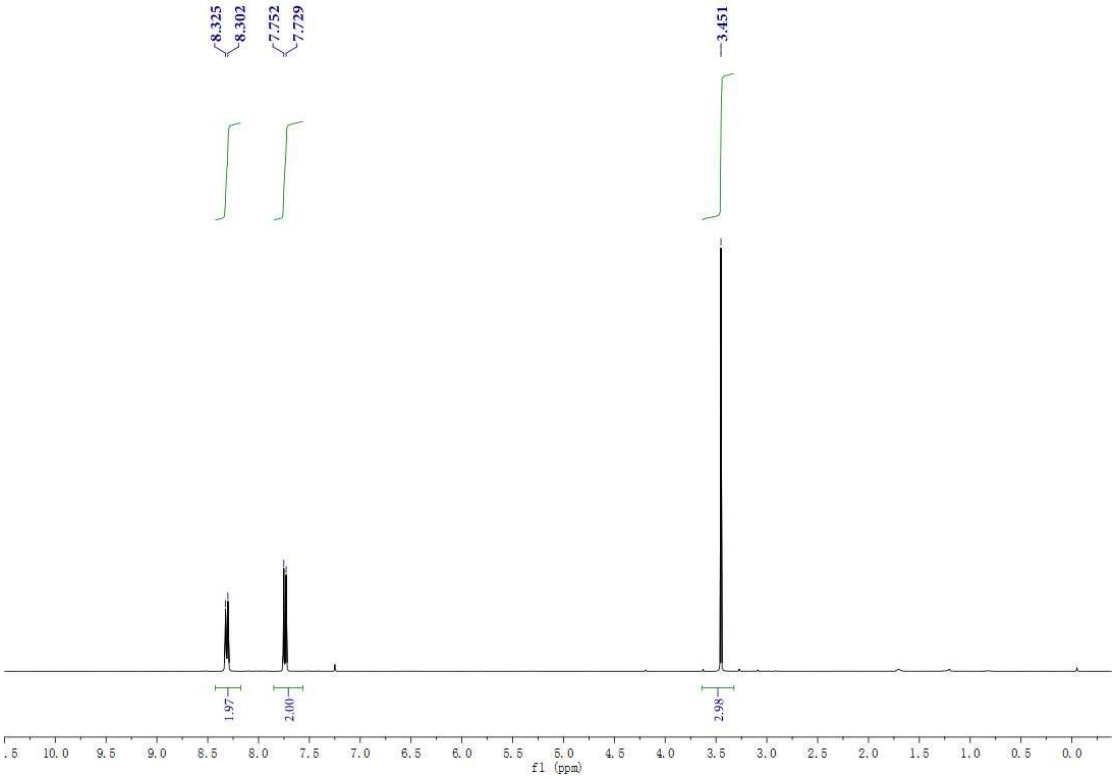
2g

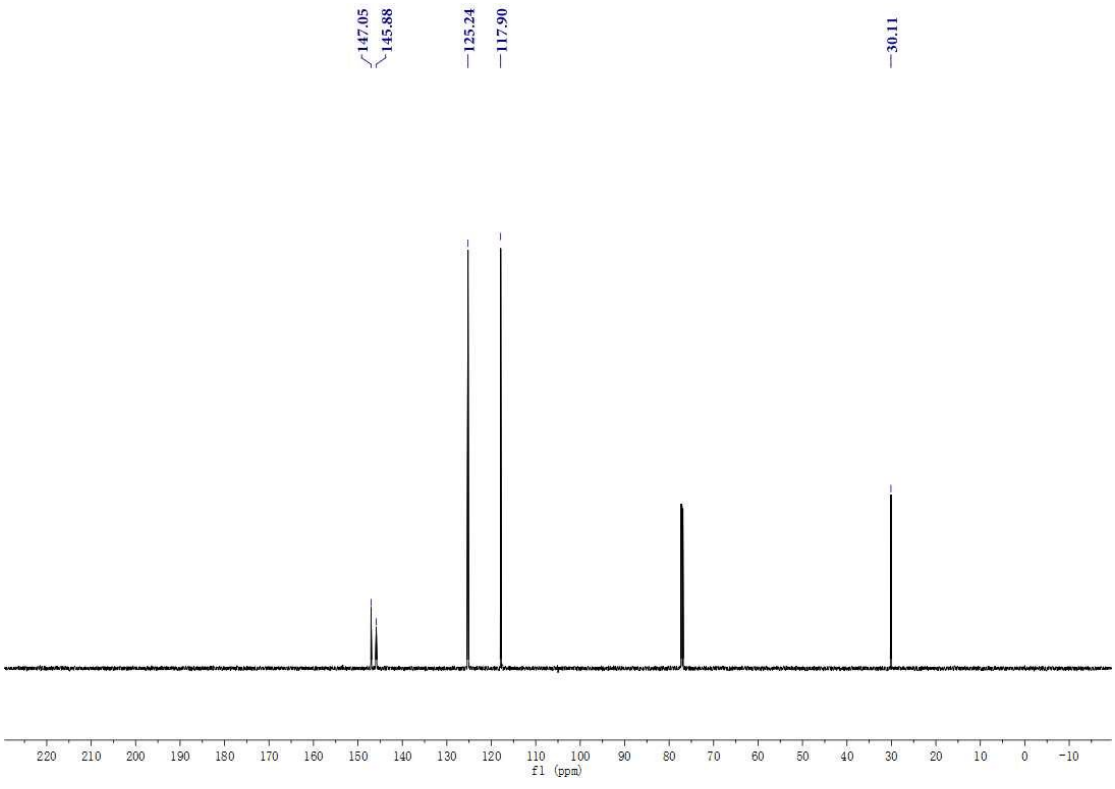

8.09
8.08
7.60
7.58
3.89
3.41
1.94
2.00
3.08
2.97
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

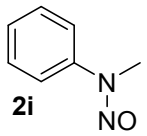

166.13
145.59
130.96
128.41
117.77
52.23
30.44
230
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


O2N
N
NO

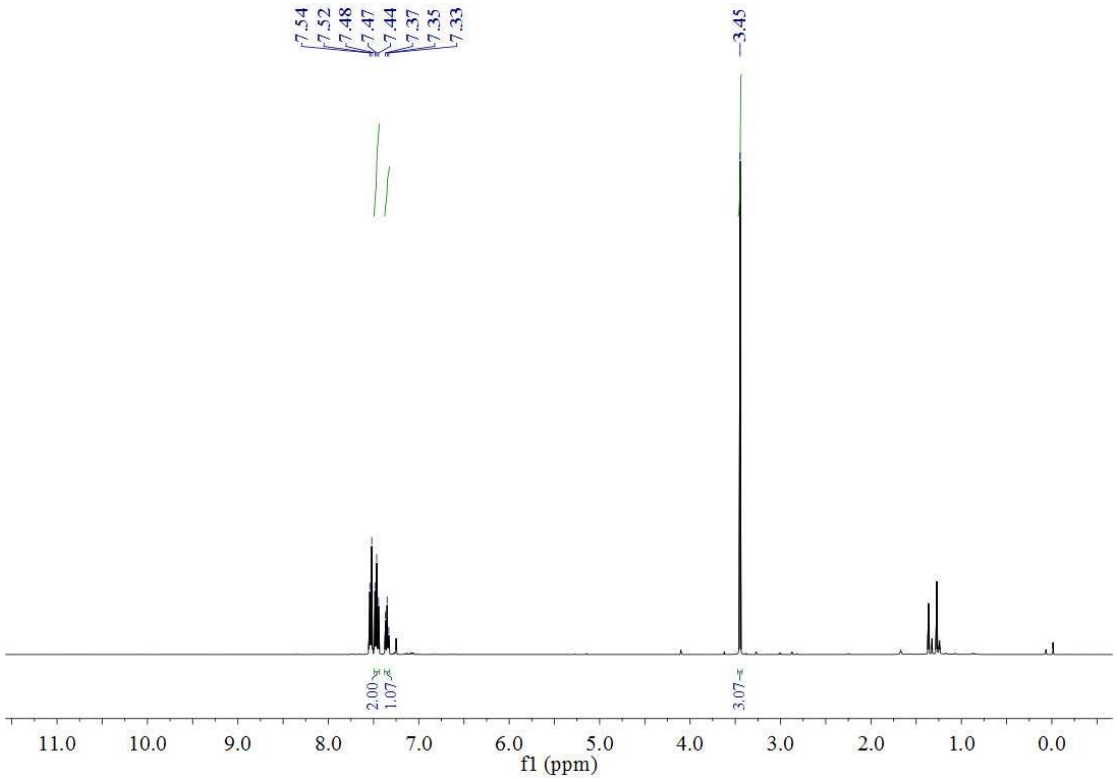
2h

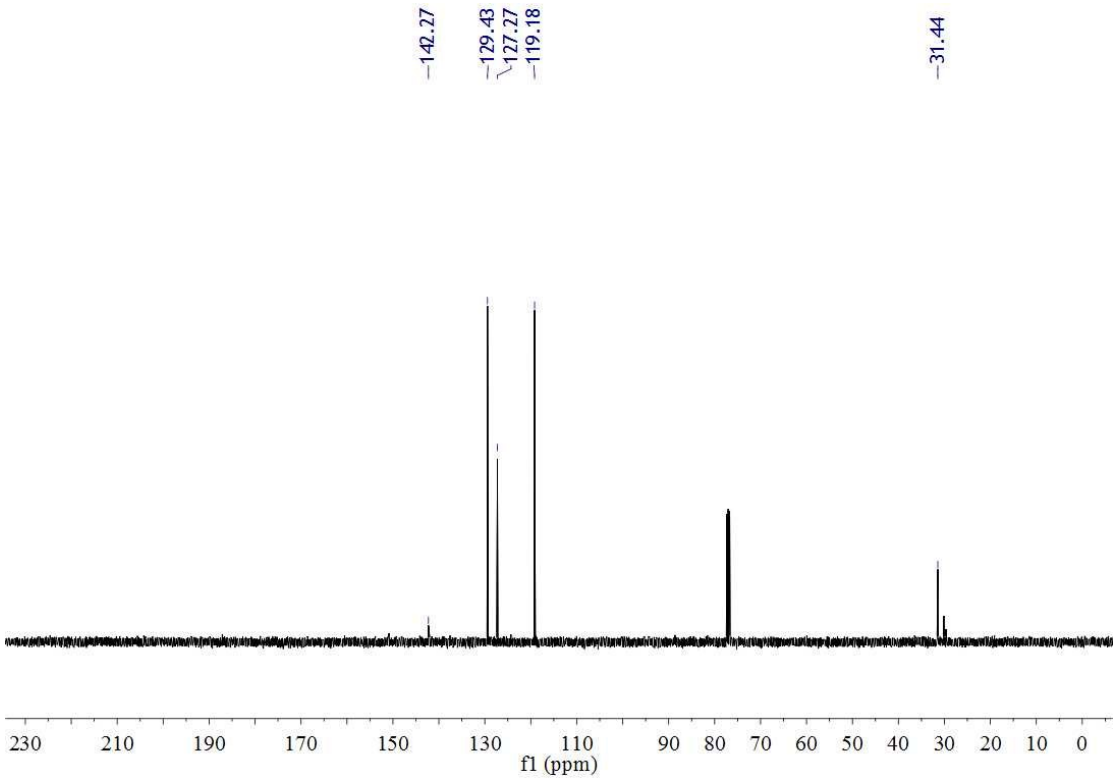

8.325
8.302
7.752
7.729
3.451
1.97
2.00
2.98
f1 (ppm)

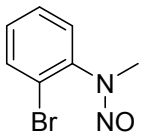

147.05
145.88
125.24
117.90
30.11
f1 (ppm)


N
NO

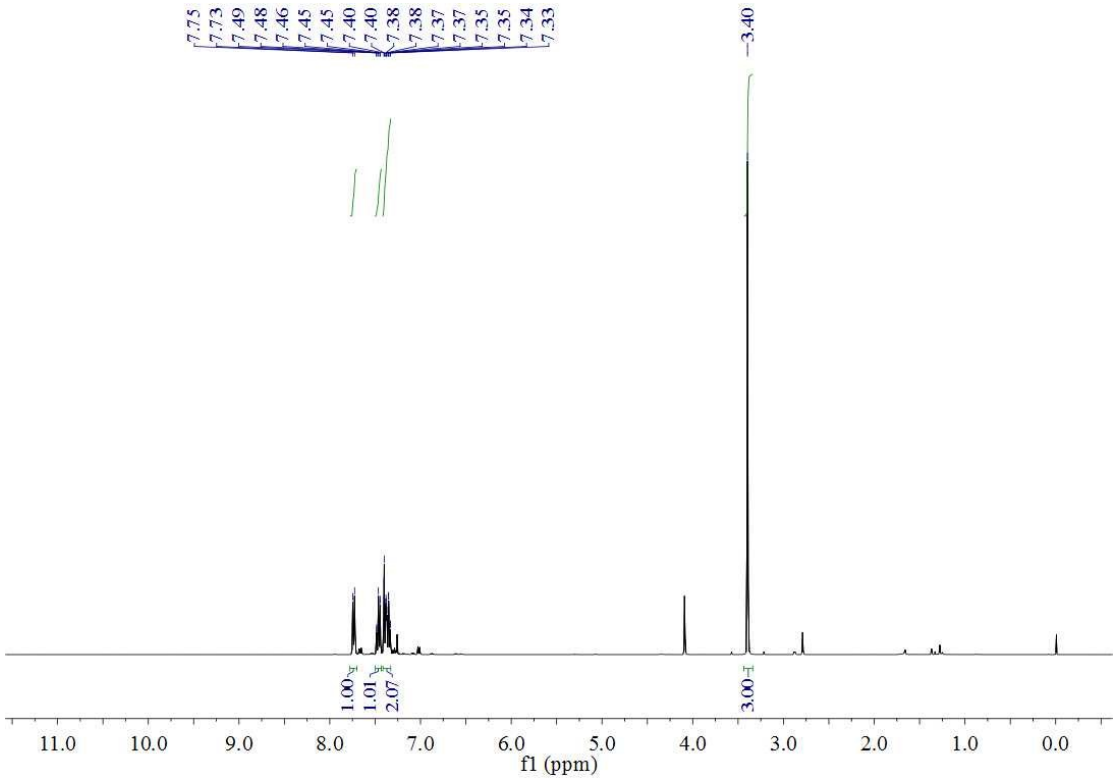
2i

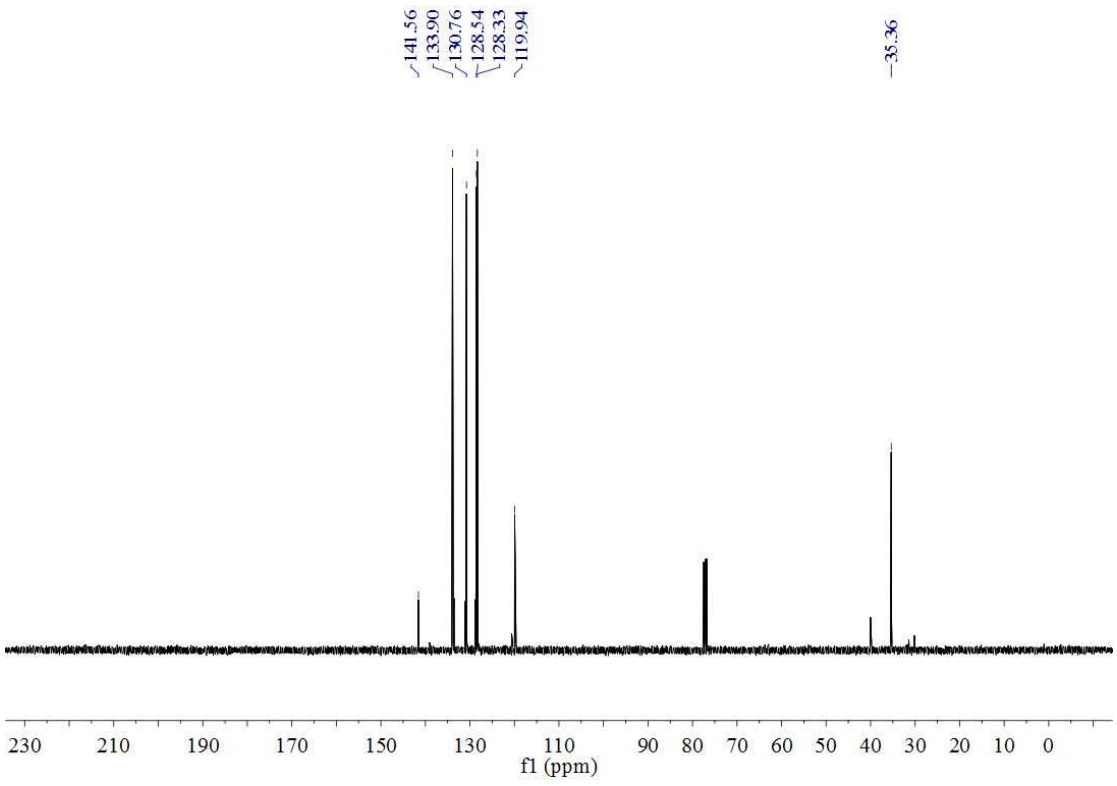

7.54
7.52
7.48
7.47
7.44
7.37
7.35
7.33
3.45
2.00
1.07
3.07
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

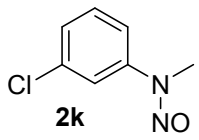

142.27
129.43
127.27
119.18
31.44
230
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


N
NO
Br

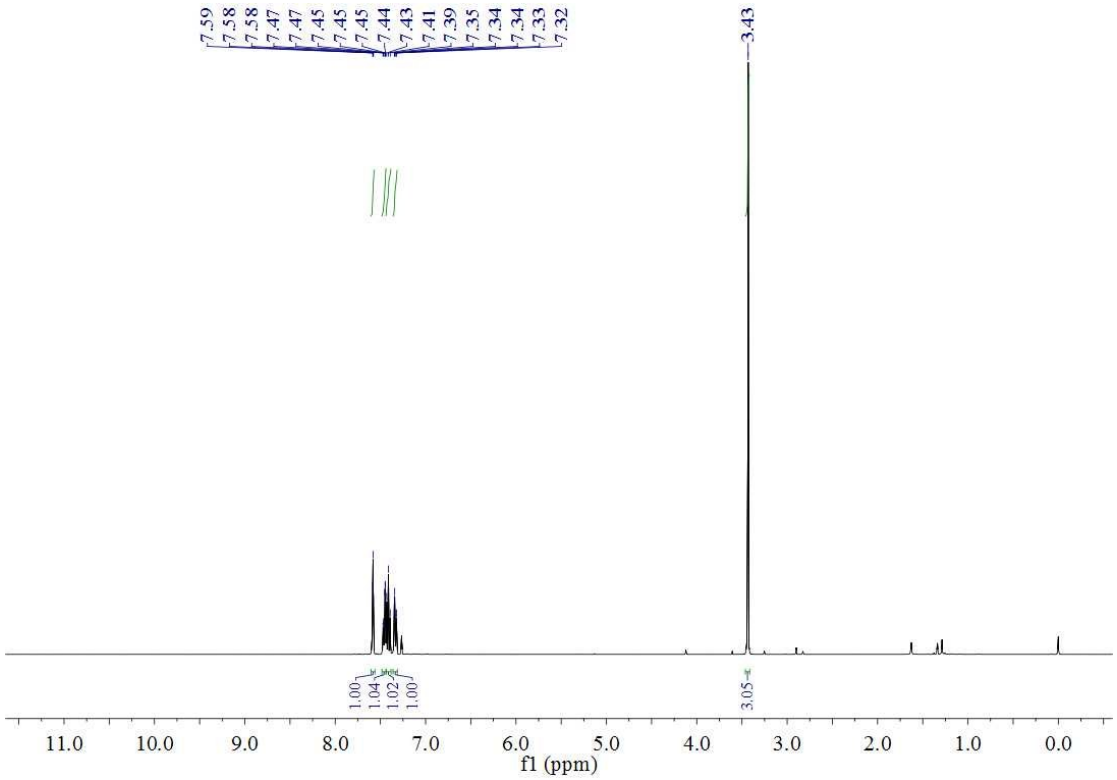
2j

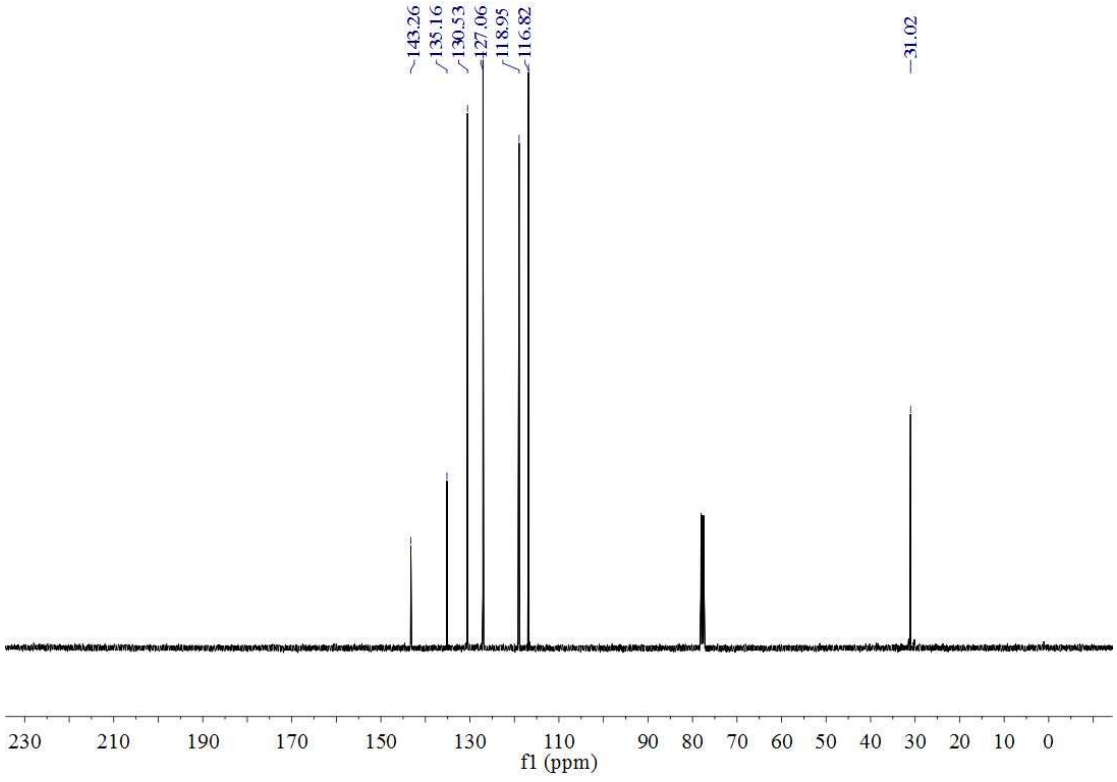

7.75
7.73
7.49
7.48
7.46
7.45
7.45
7.40
7.40
7.38
7.38
7.37
7.37
7.35
7.35
7.34
7.33
3.40
1.00
1.01
2.07
3.00
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

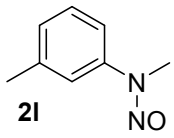

141.56
133.90
130.76
128.54
128.33
119.94
35.36
230
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


Cl
N
NO

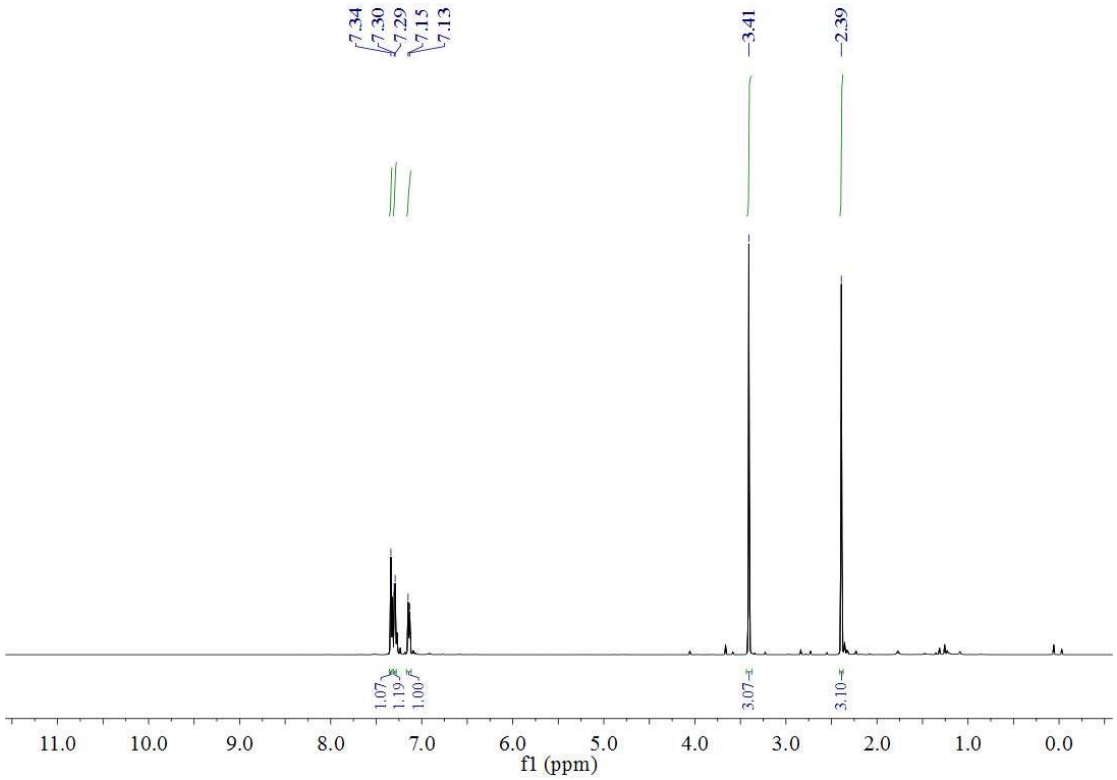
2k

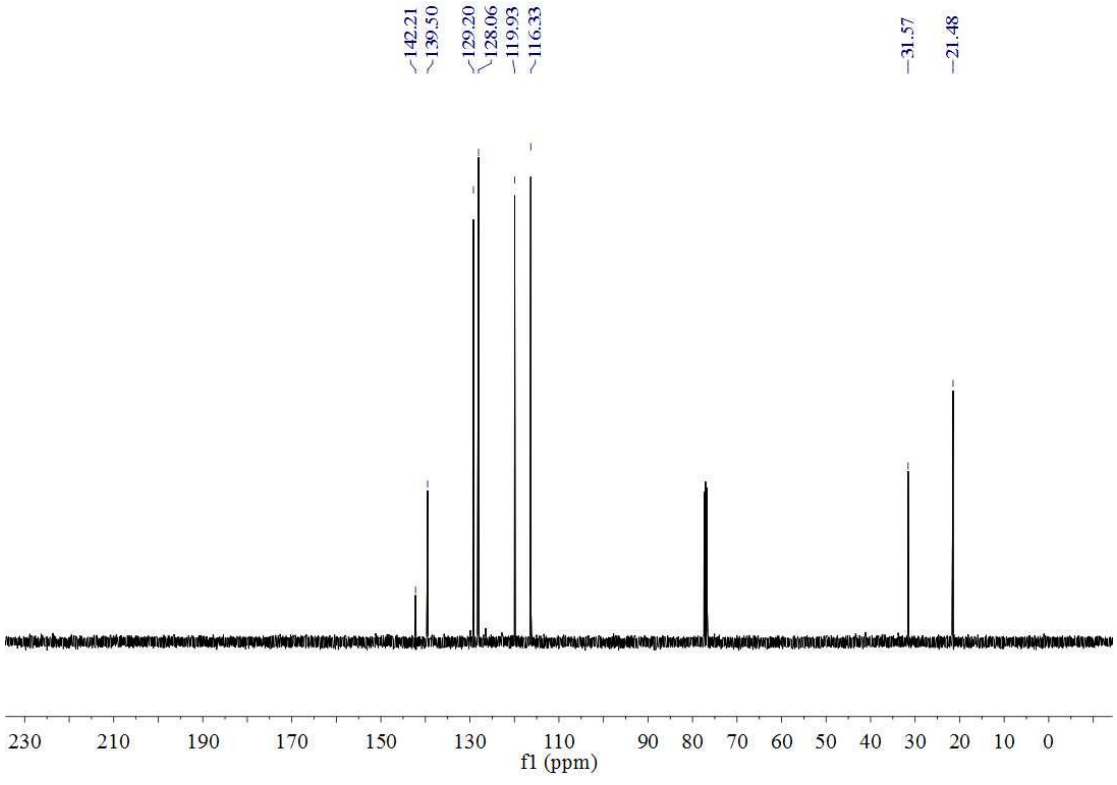

7.59
7.58
7.58
7.47
7.47
7.45
7.45
7.45
7.44
7.43
7.41
7.39
7.35
7.34
7.34
7.33
7.32
3.43
1.00
1.04
1.02
1.00
3.05
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

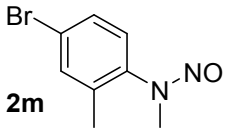

143.26
135.16
130.53
127.06
118.95
116.82
31.02
230
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


N
NO

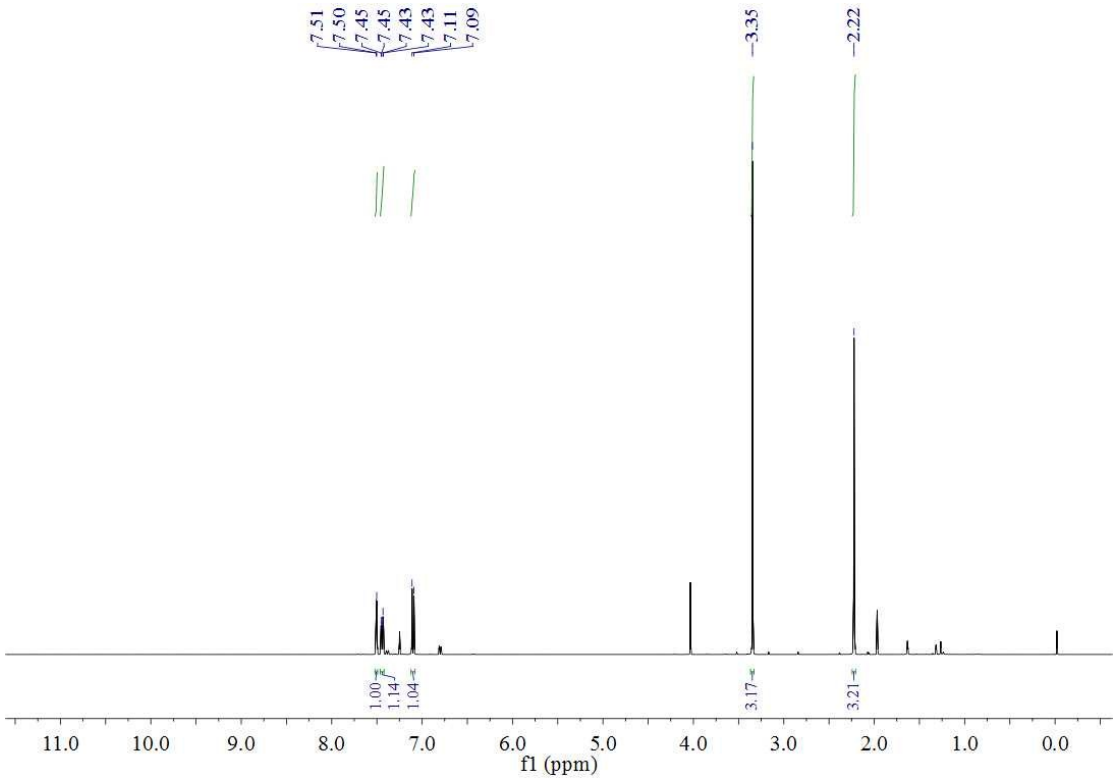
2l

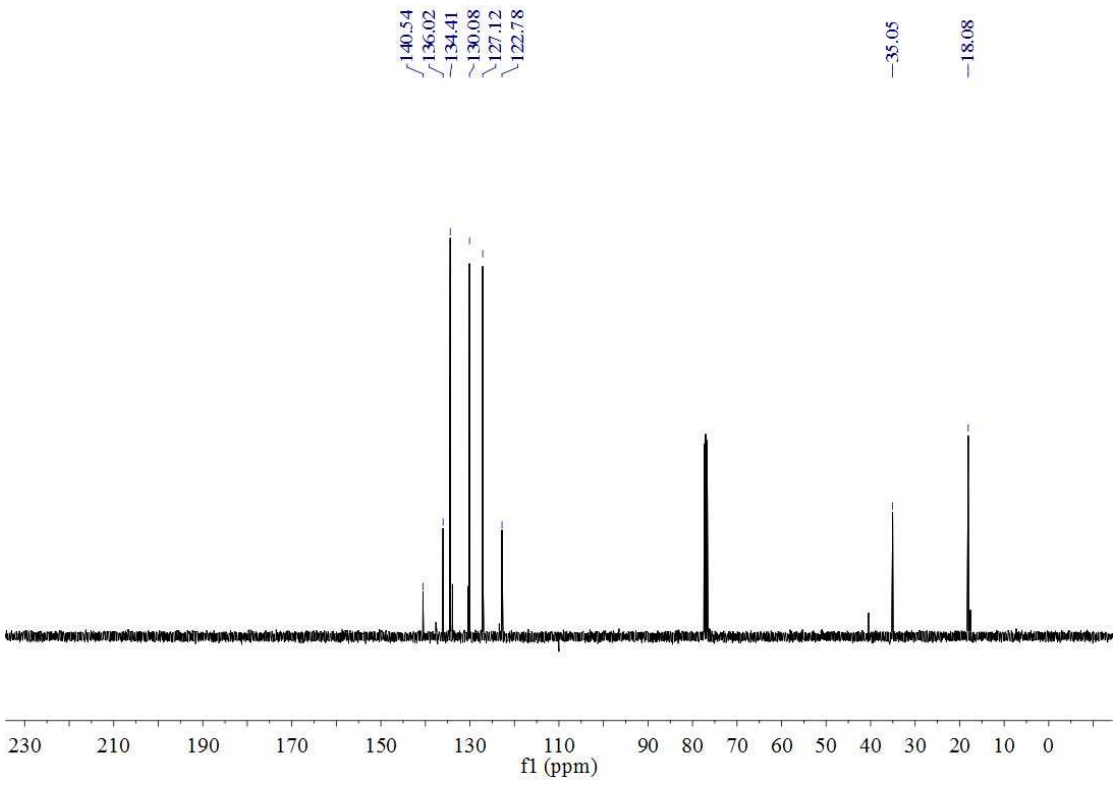

7.34
7.30
7.29
7.15
7.13
3.41
2.39
1.07
1.19
1.00
3.07
3.10
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

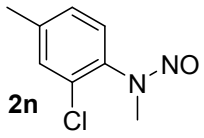

142.21
139.50
129.20
128.06
119.93
116.33
31.57
21.48
230
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


Br
N
NO

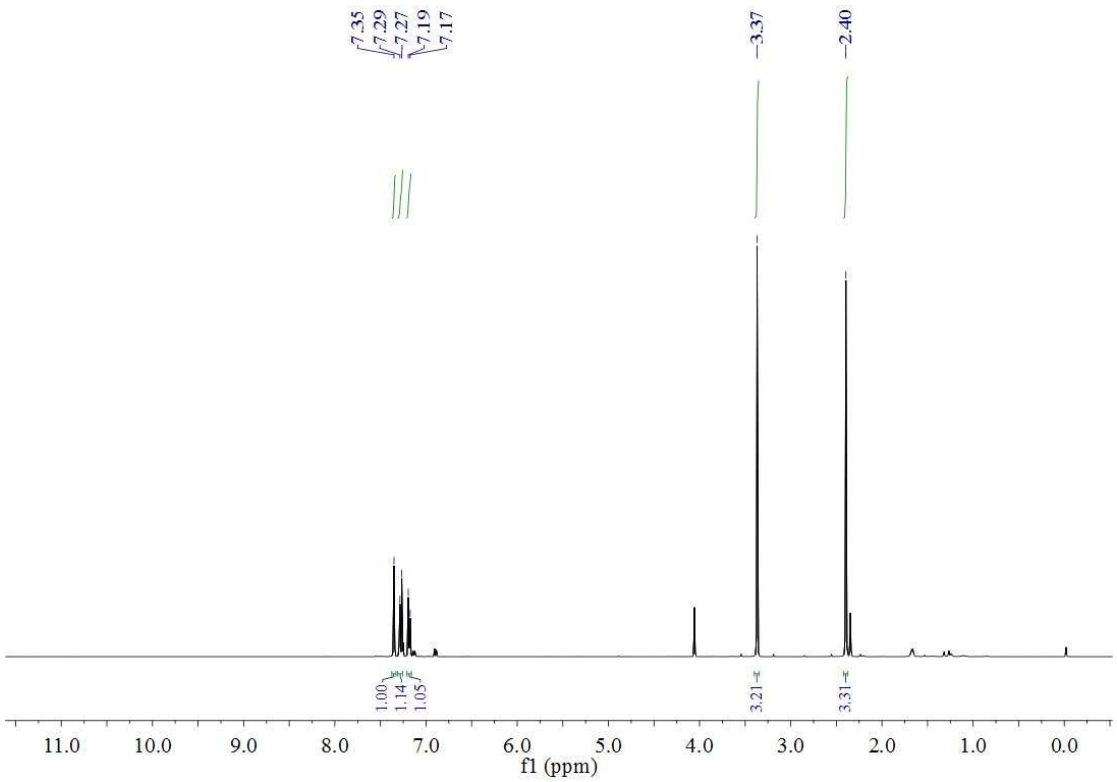
2m

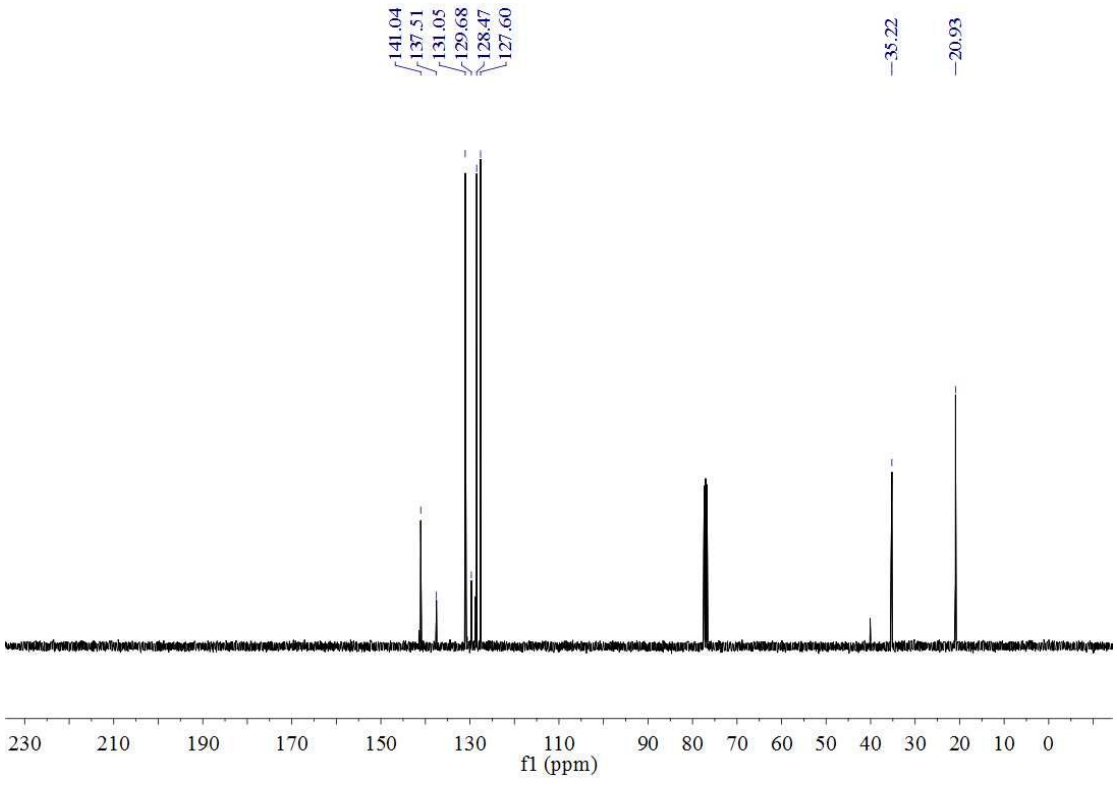

7.51
7.50
7.45
7.45
7.43
7.43
7.11
7.09
3.35
2.22
1.00
1.14
1.04
3.17
3.21
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

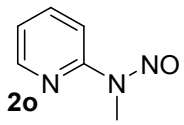

140.54
136.02
134.41
130.08
127.12
122.78
35.05
18.08
230
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


NO
N
Cl

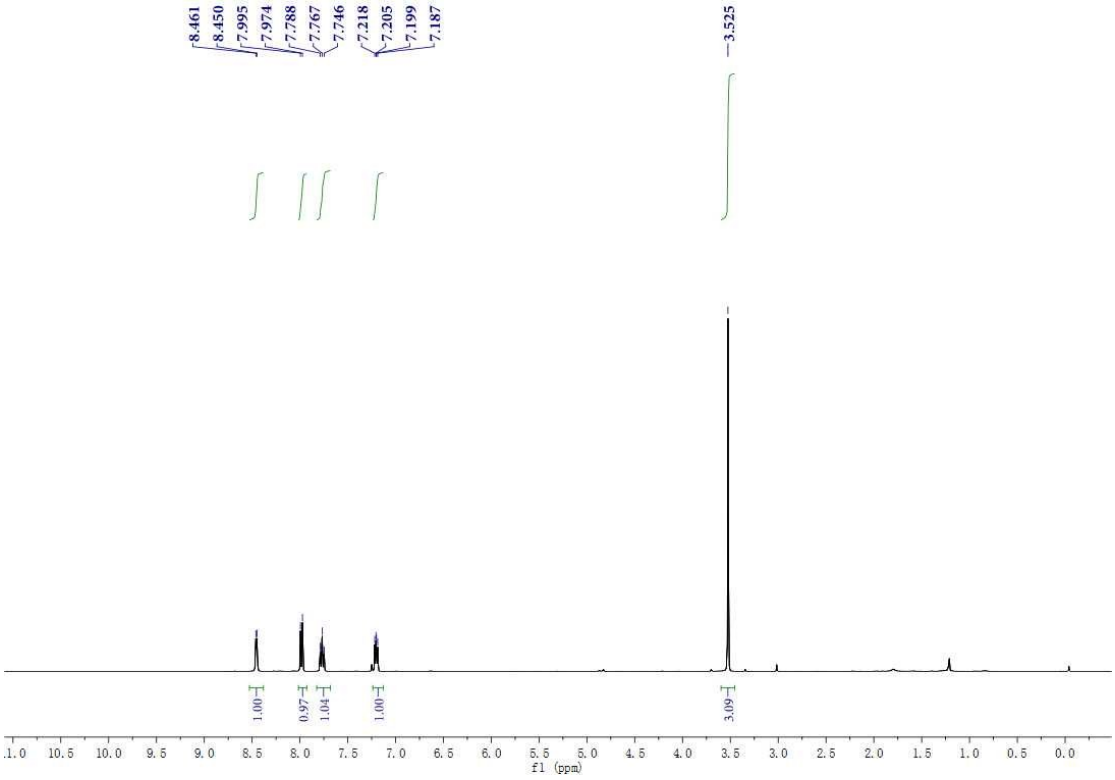
2n

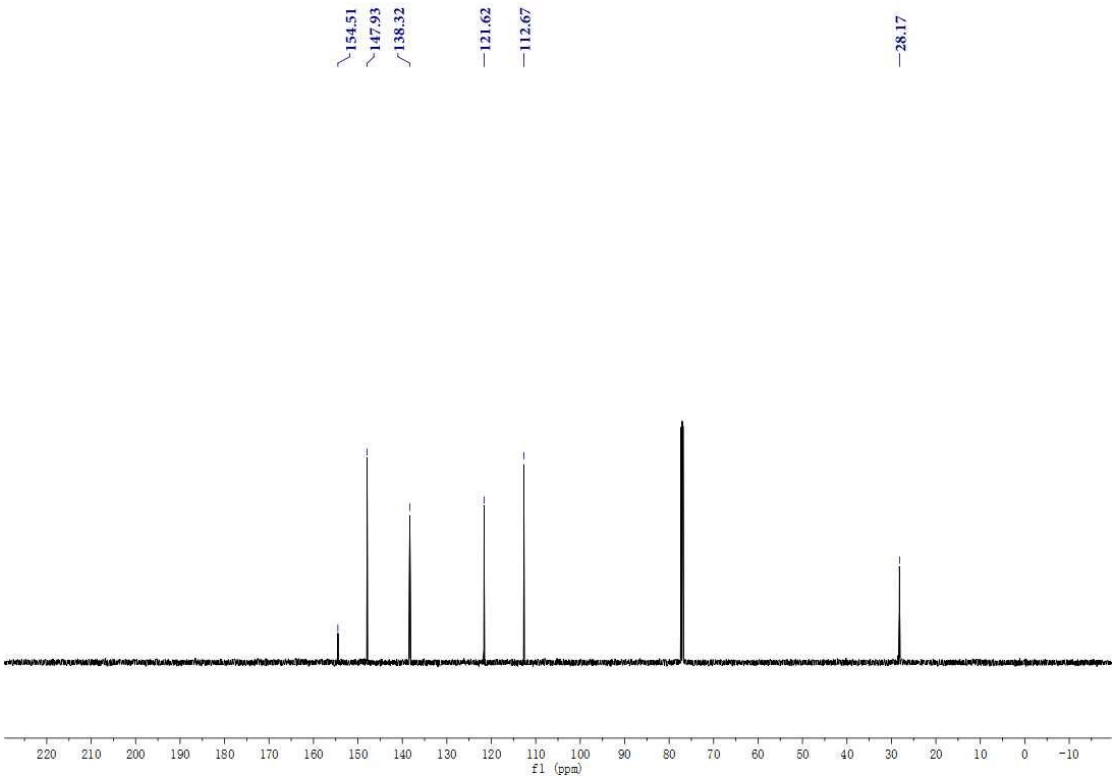

7.35
7.29
7.27
7.19
7.17
3.37
2.40
1.00
1.14
1.05
3.21
3.31
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

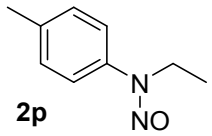

141.04
137.51
131.05
129.68
128.47
127.60
35.22
20.93
230
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


N
N
NO

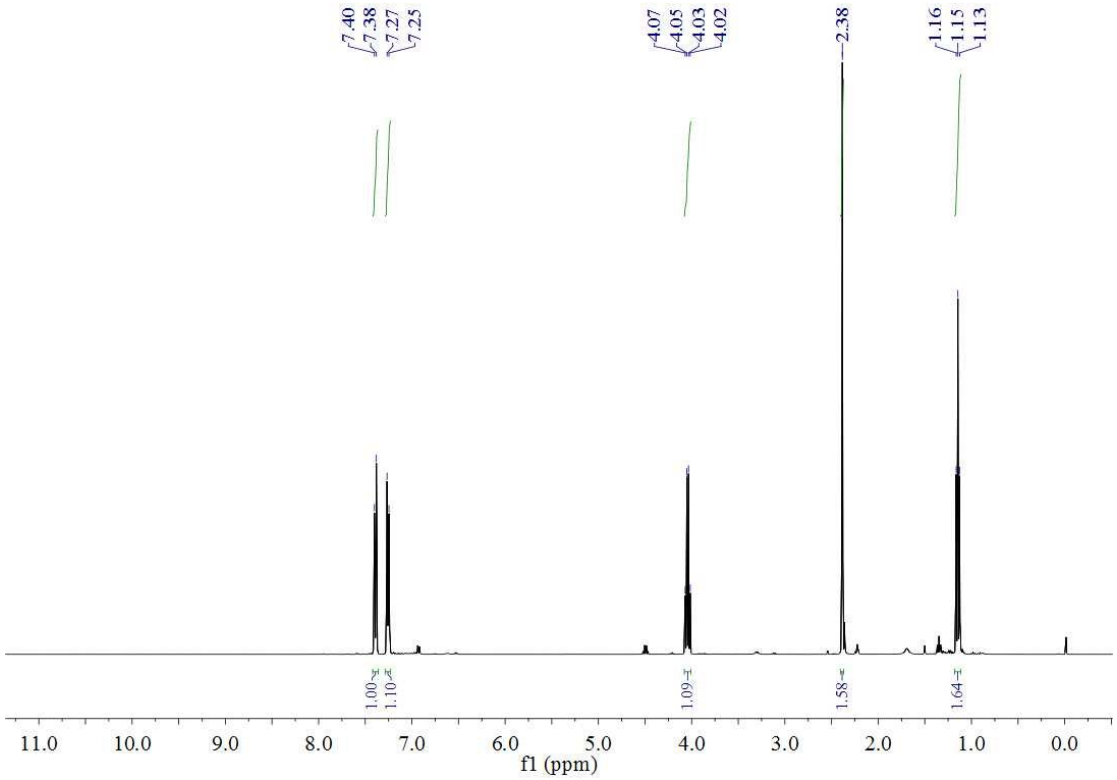
2o

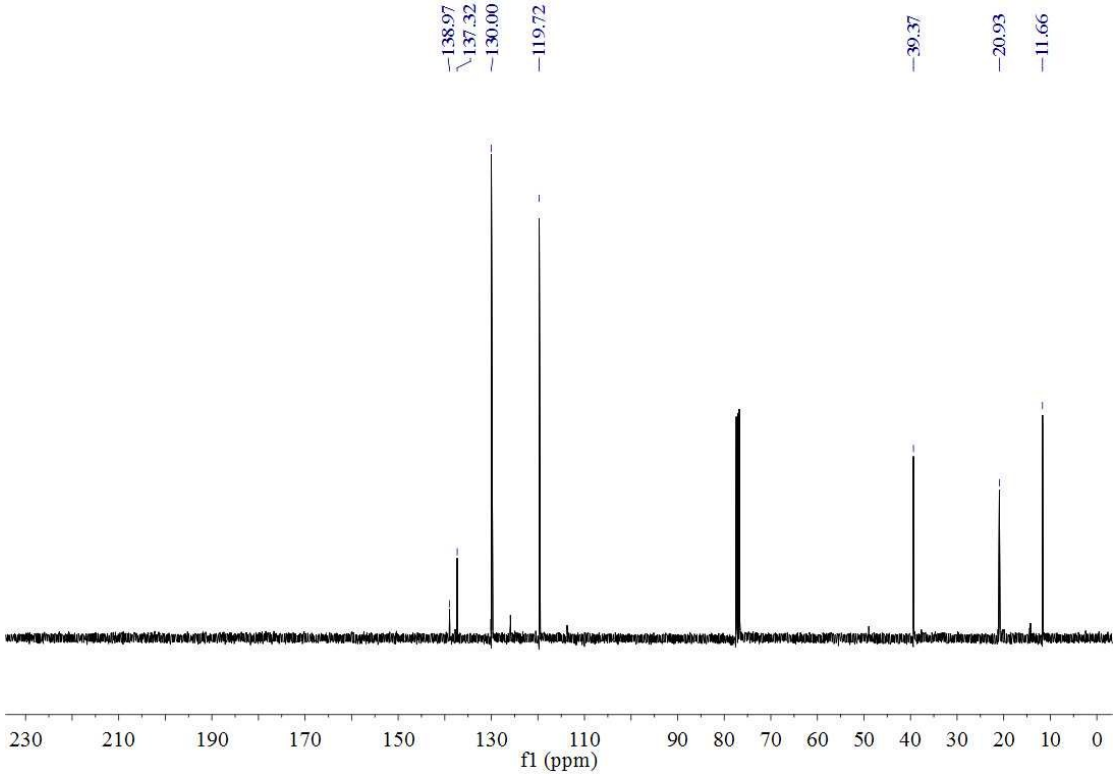

8.461
8.450
7.995
7.974
7.788
7.767
7.746
7.218
7.205
7.199
7.187
3.525
1.00
0.97
1.04
1.00
3.09
f1 (ppm)

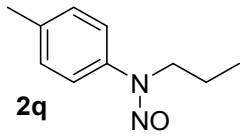

154.51
147.93
138.32
121.62
112.67
28.17
f1 (ppm)


N
NO

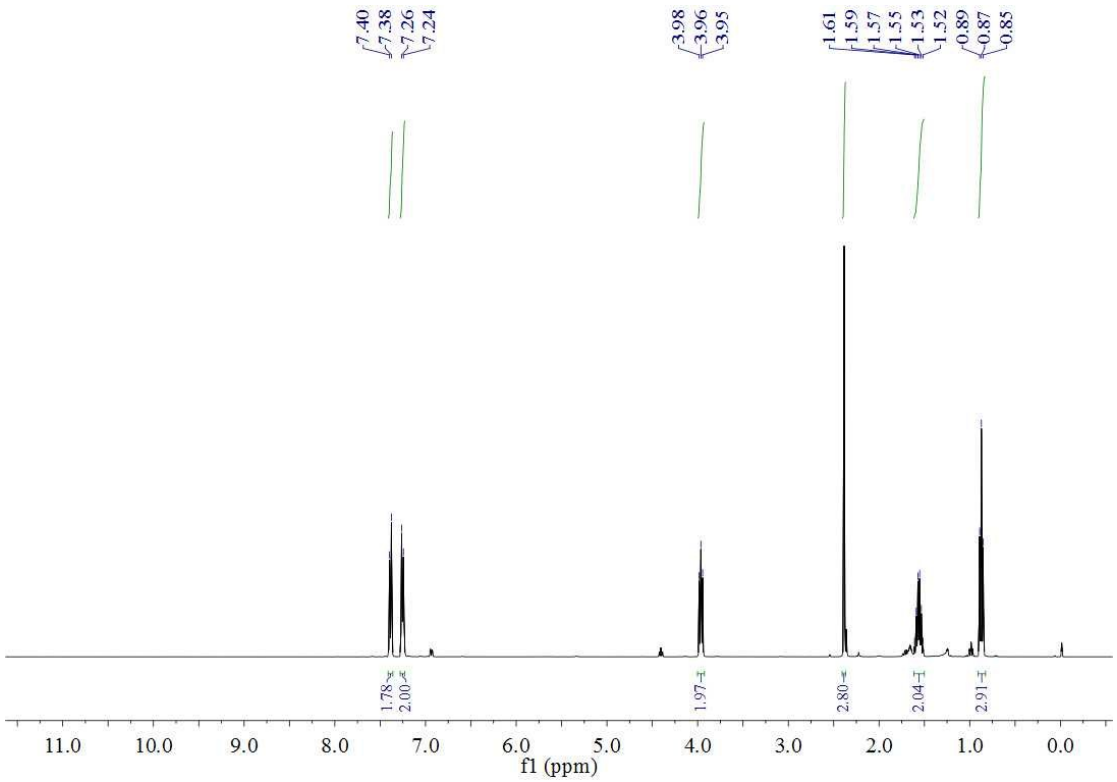
2p

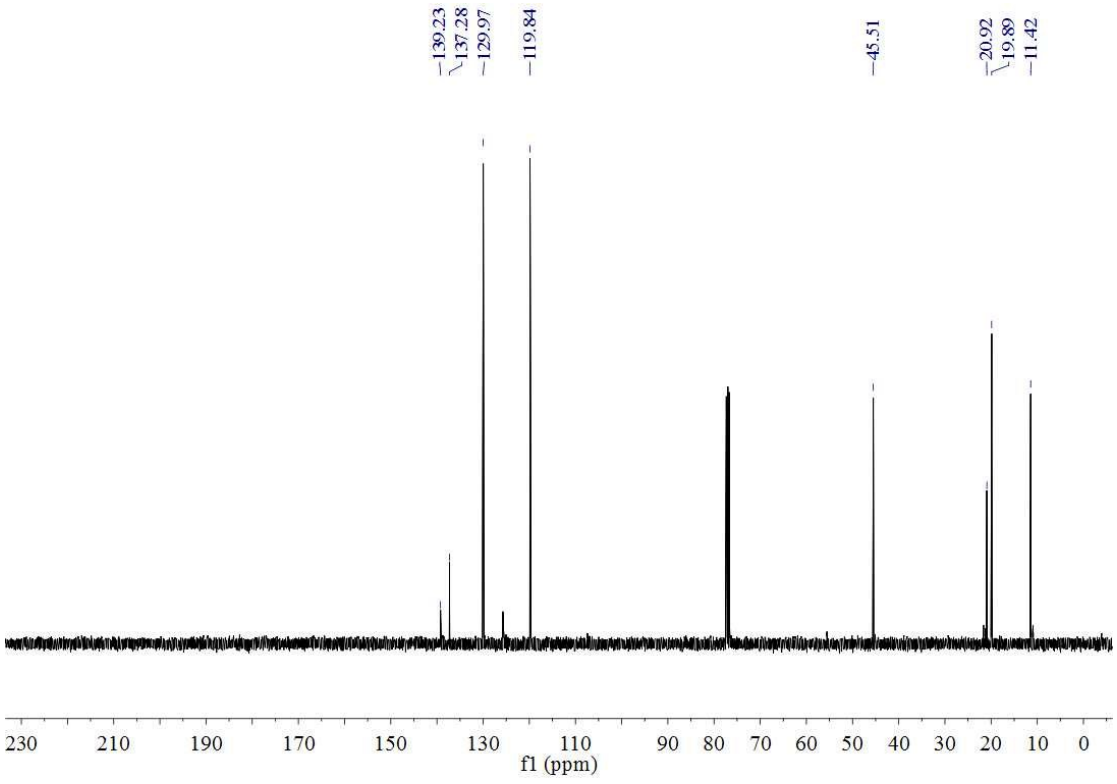

7.40
7.38
7.27
7.25
4.07
4.05
4.03
4.02
2.38
1.16
1.15
1.13
1.00
1.10
1.09
1.58
1.64
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

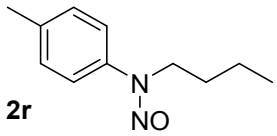

138.97
137.32
130.00
119.72
39.37
20.93
11.66
230
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


N
NO

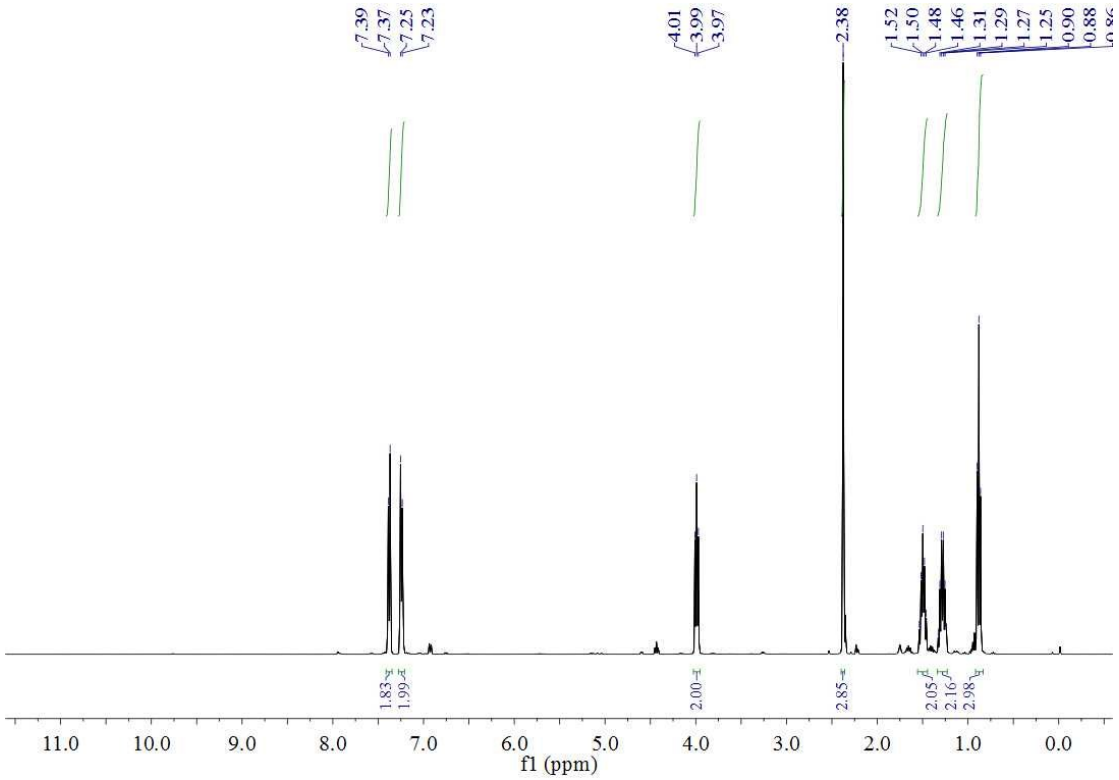
2q

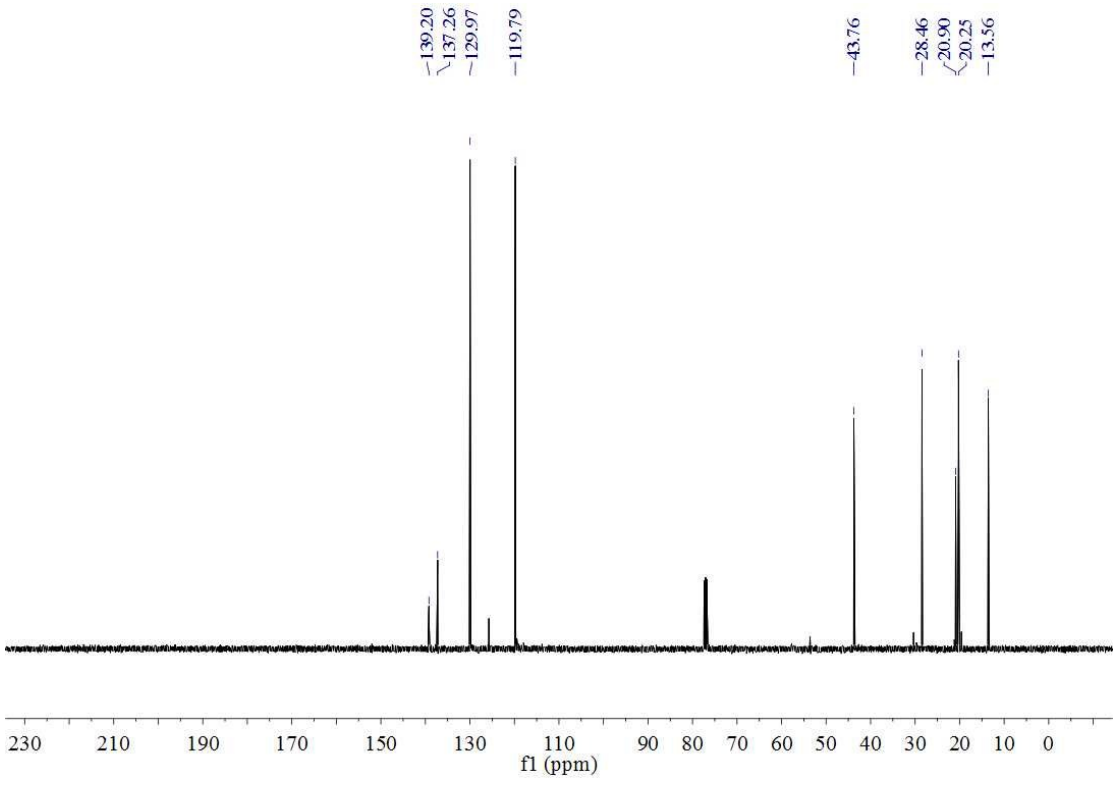

7.40
7.38
7.26
7.24
3.98
3.96
3.95
1.61
1.59
1.57
1.55
1.53
1.52
0.89
0.87
0.85
1.78
2.00
1.97
2.80
2.04
2.91
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

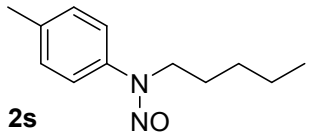

139.23
137.28
129.97
119.84
45.51
20.92
19.89
11.42
230
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


N
NO

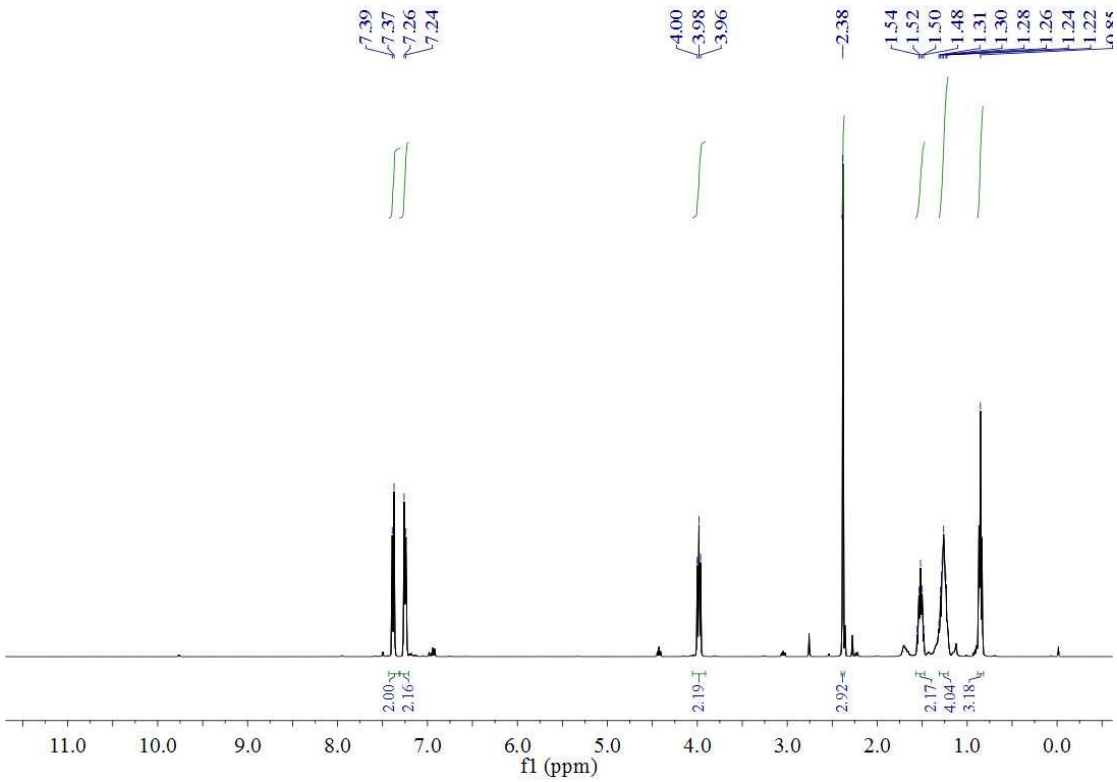
2r

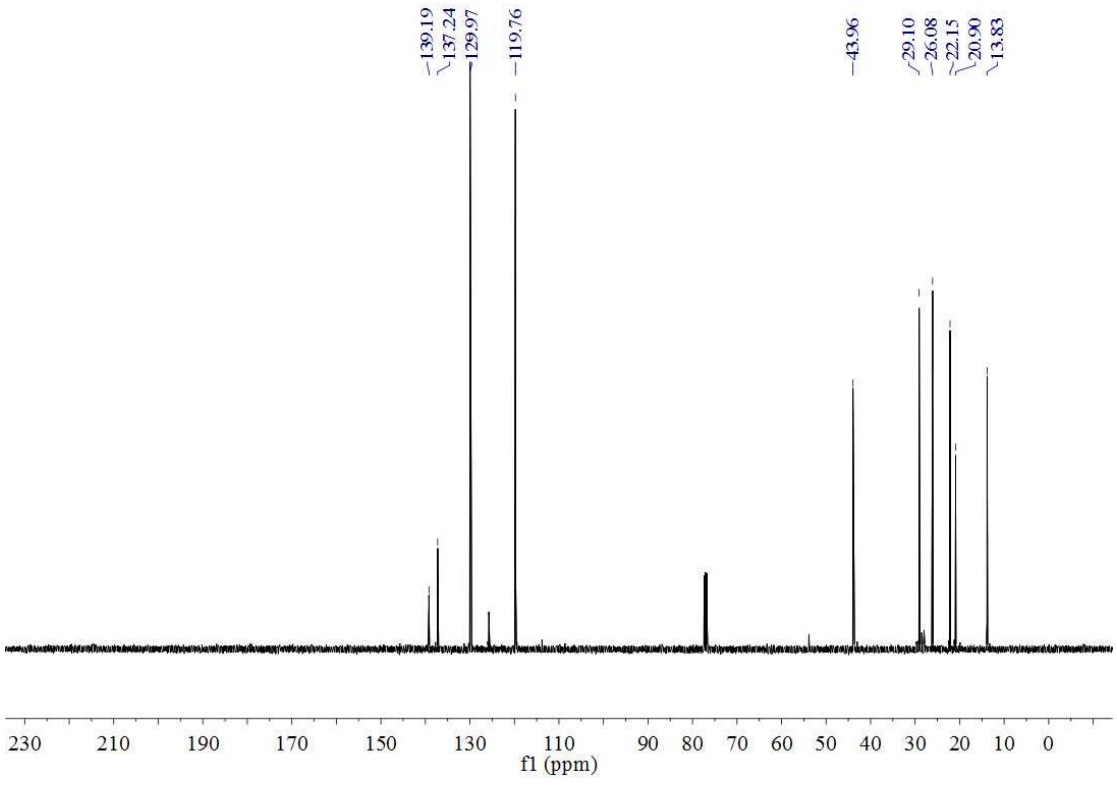

7.39
7.37
7.25
7.23
4.01
3.99
3.97
2.38
1.52
1.50
1.48
1.46
1.31
1.29
1.27
1.25
0.90
0.88
1.83
1.99
2.00
2.85
2.05
2.16
2.98
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)


139.20
137.26
129.97
119.79
43.76
28.46
20.90
20.25
13.56
230
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

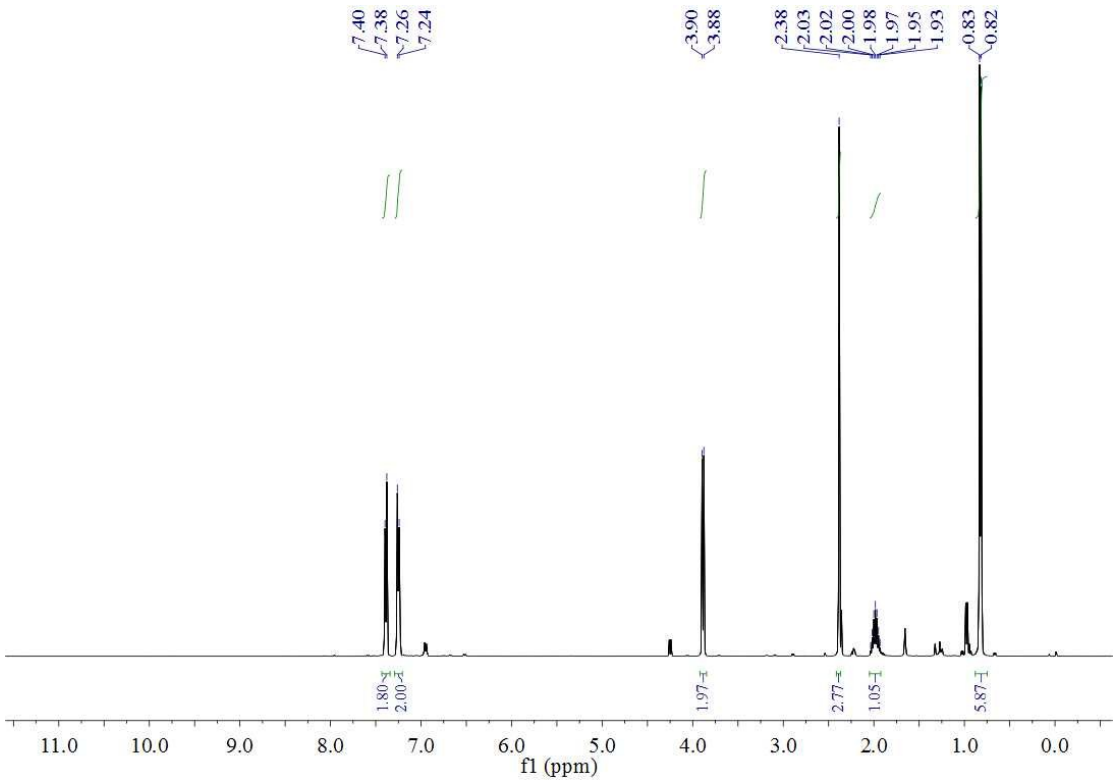

N
NO

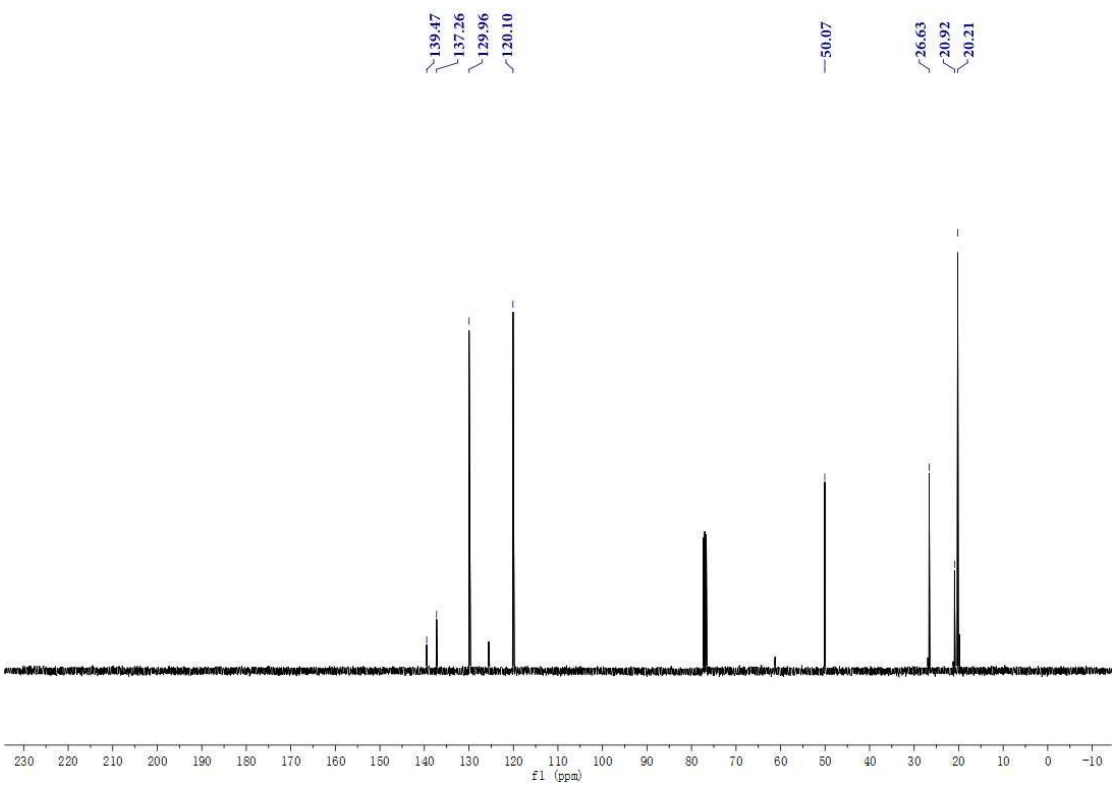
2s

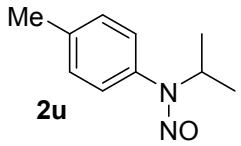

7.39
7.37
7.26
7.24
4.00
3.98
3.96
2.38
1.54
1.52
1.50
1.48
1.31
1.30
1.28
1.26
1.24
1.22
2.00
2.16
2.19
2.92
2.17
4.04
3.18
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)


139.19
137.24
129.97
119.76
43.96
29.10
26.08
22.15
20.90
13.83
230
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

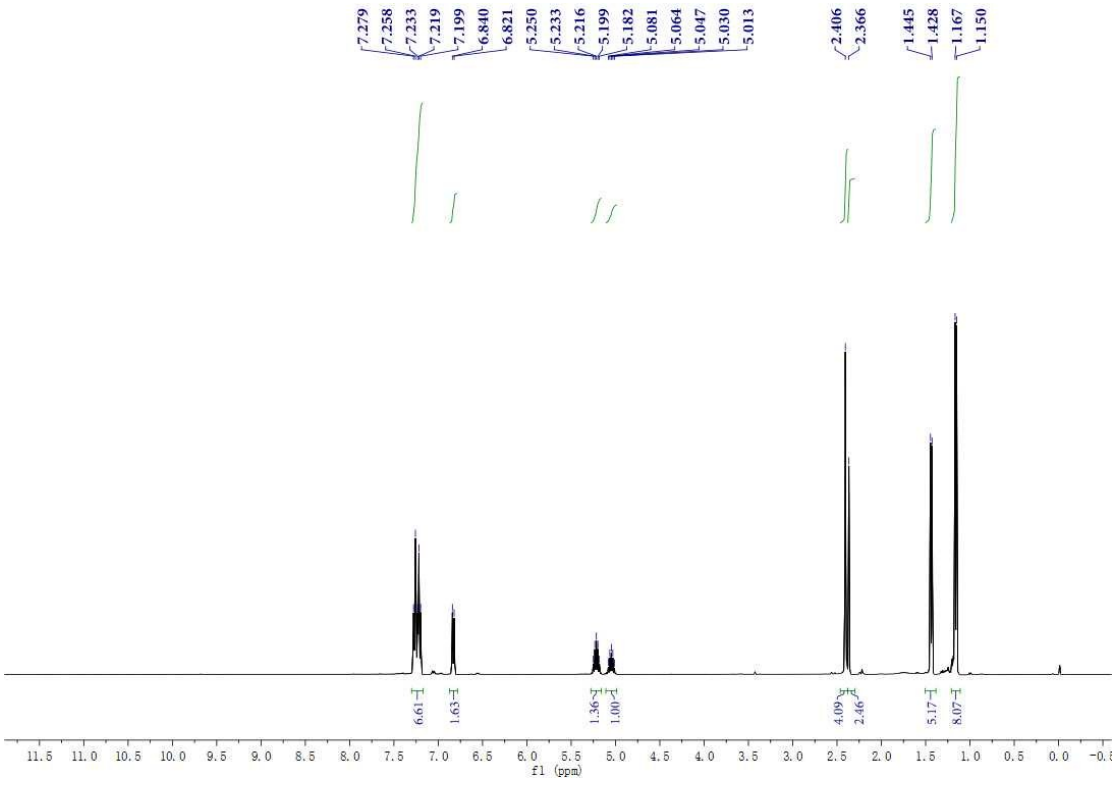
2t

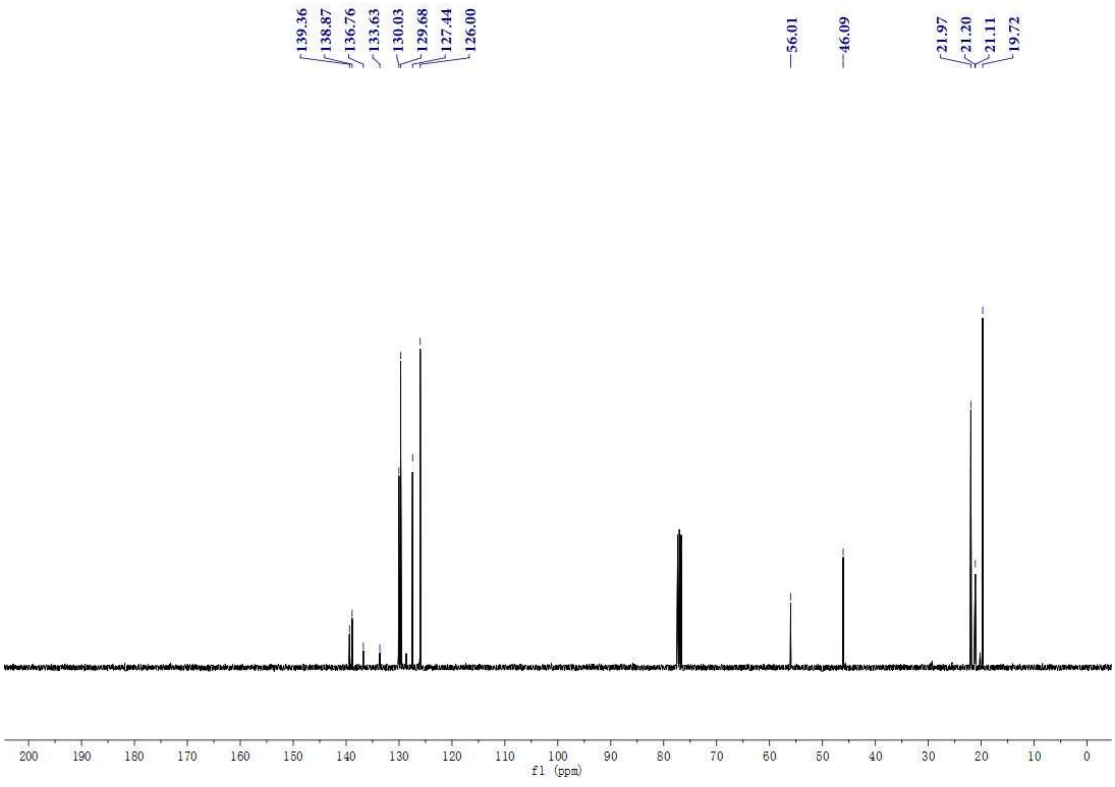

7.40
7.38
7.26
7.24
3.90
3.88
2.38
2.03
2.02
2.00
1.98
1.97
1.95
1.93
0.83
0.82
1.80
2.00
1.97
2.77
1.05
5.87
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

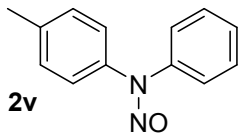

139.47
137.26
129.96
120.10
50.07
26.63
20.92
20.21
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

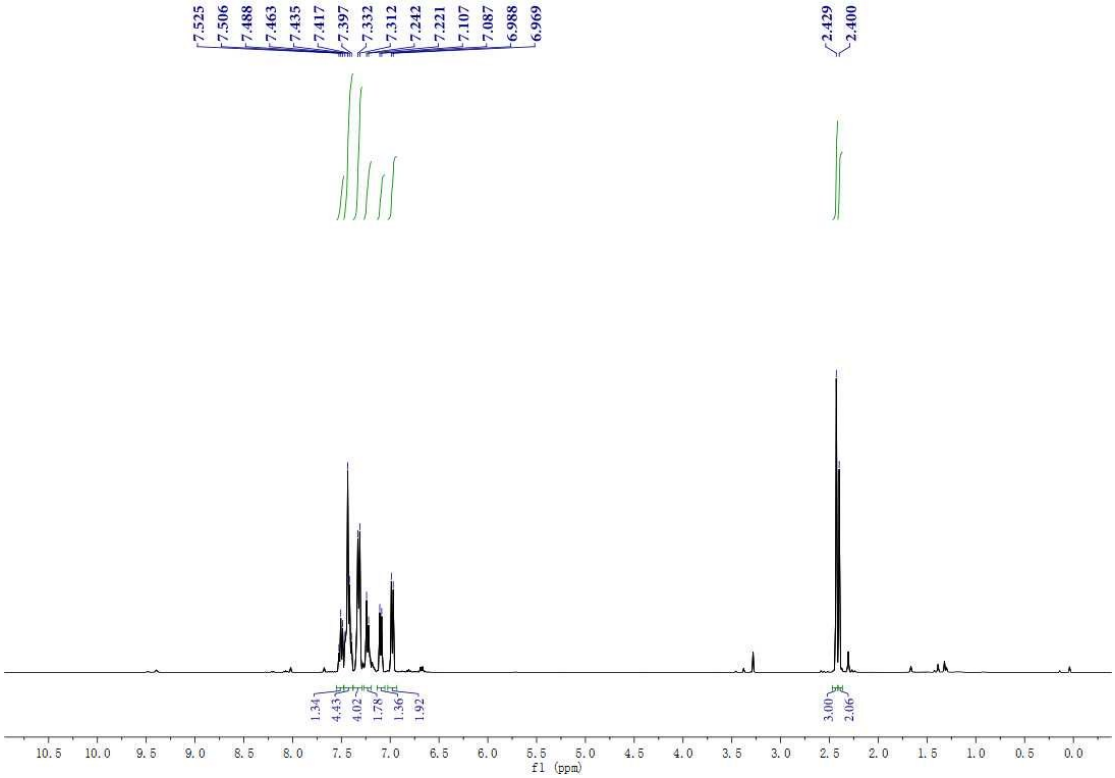

Me
N
NO

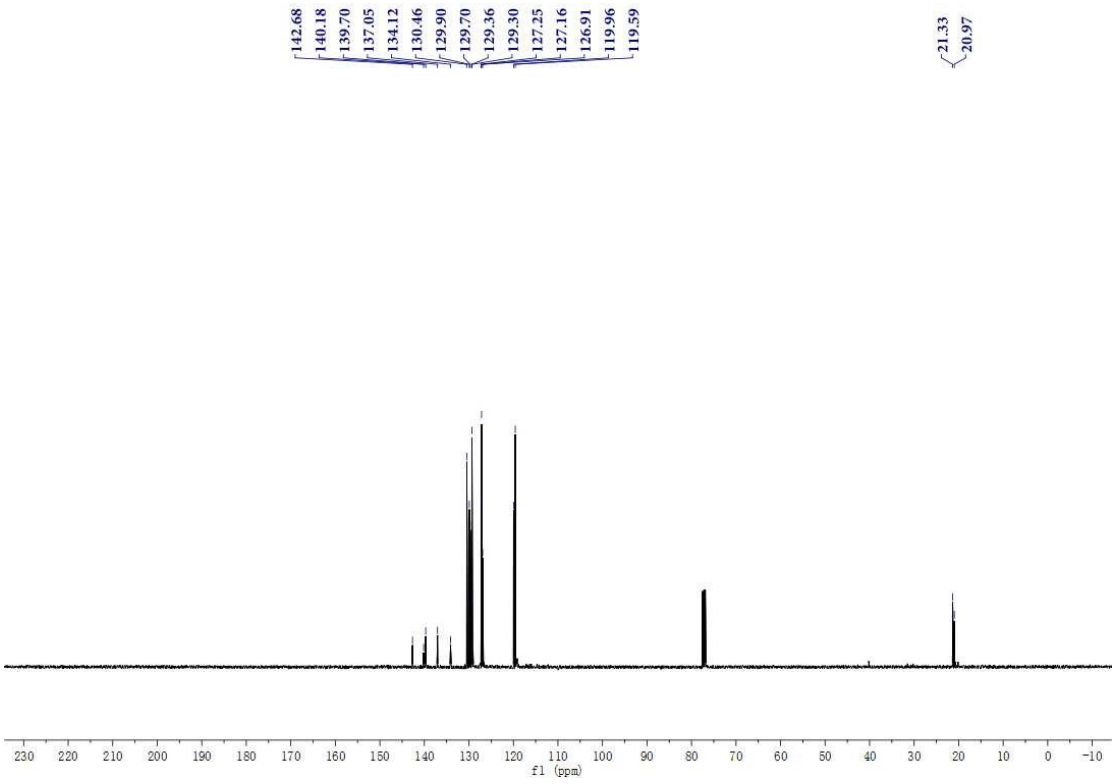
2u

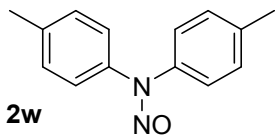

7.279
7.258
7.233
7.219
7.199
6.840
6.821
5.250
5.233
5.216
5.199
5.182
5.081
5.064
5.047
5.030
5.013
2.406
2.366
1.445
1.428
1.167
1.150
6.61
1.63
1.36
1.00
4.09
2.46
5.17
8.07
f1 (ppm)


139.36
138.87
136.76
133.63
130.03
129.68
127.44
126.00
56.01
46.09
21.97
21.20
21.11
19.72
f1 (ppm)

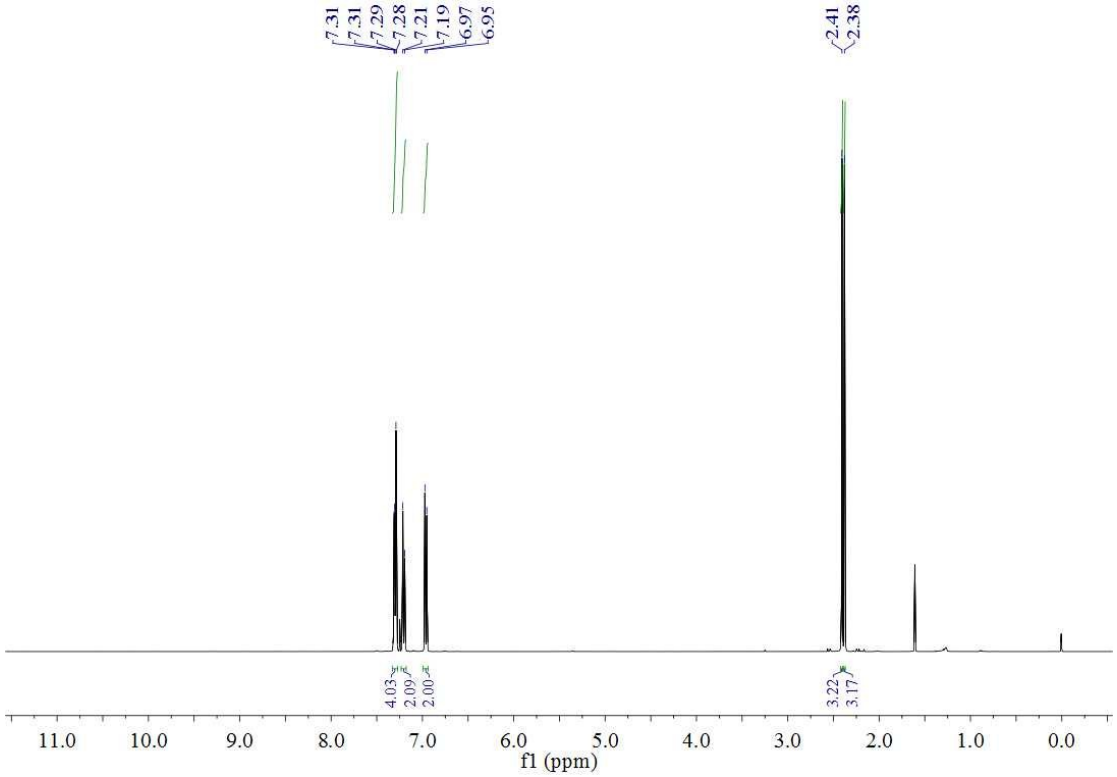

2v
N
NO

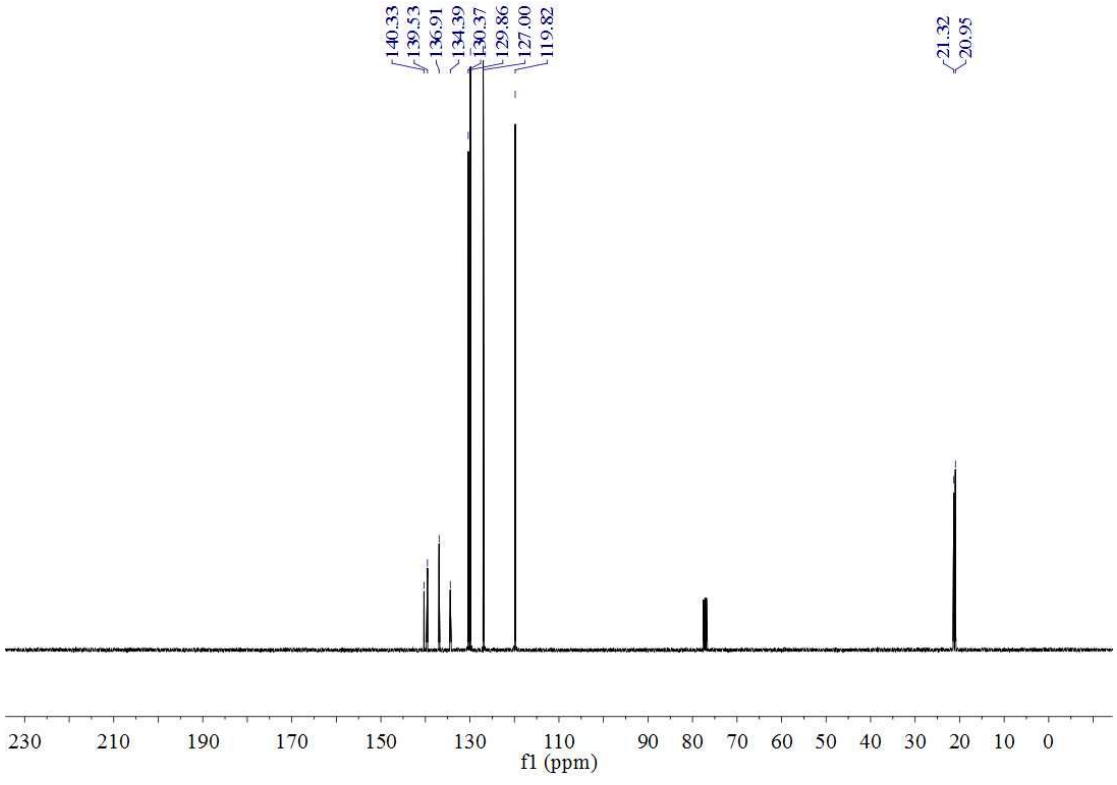

7.525
7.506
7.488
7.463
7.435
7.417
7.397
7.332
7.312
7.242
7.221
7.107
7.087
6.988
6.969
2.429
2.400
1.34
4.43
4.02
1.78
1.36
1.92
3.00
2.06
f1 (ppm)

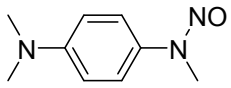

142.68
140.18
139.70
137.05
134.12
130.46
129.90
129.70
129.36
129.30
127.25
127.16
126.91
119.96
119.59
21.33
20.97
f1 (ppm)


N
NO

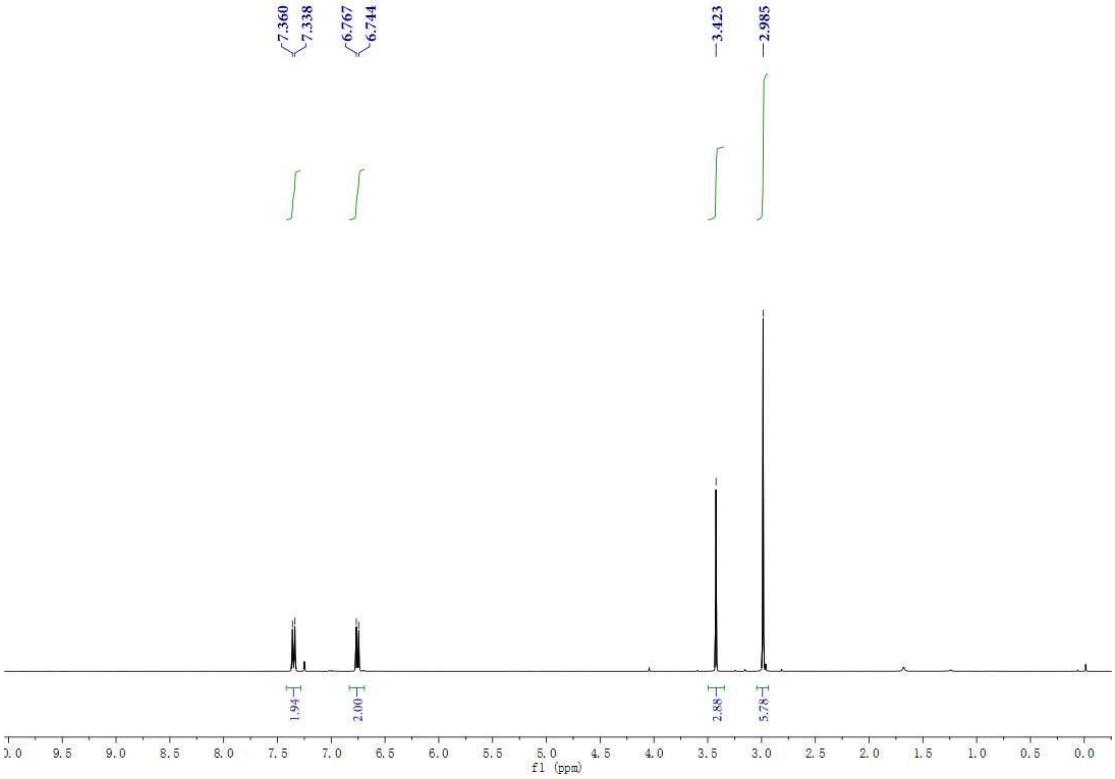
2w

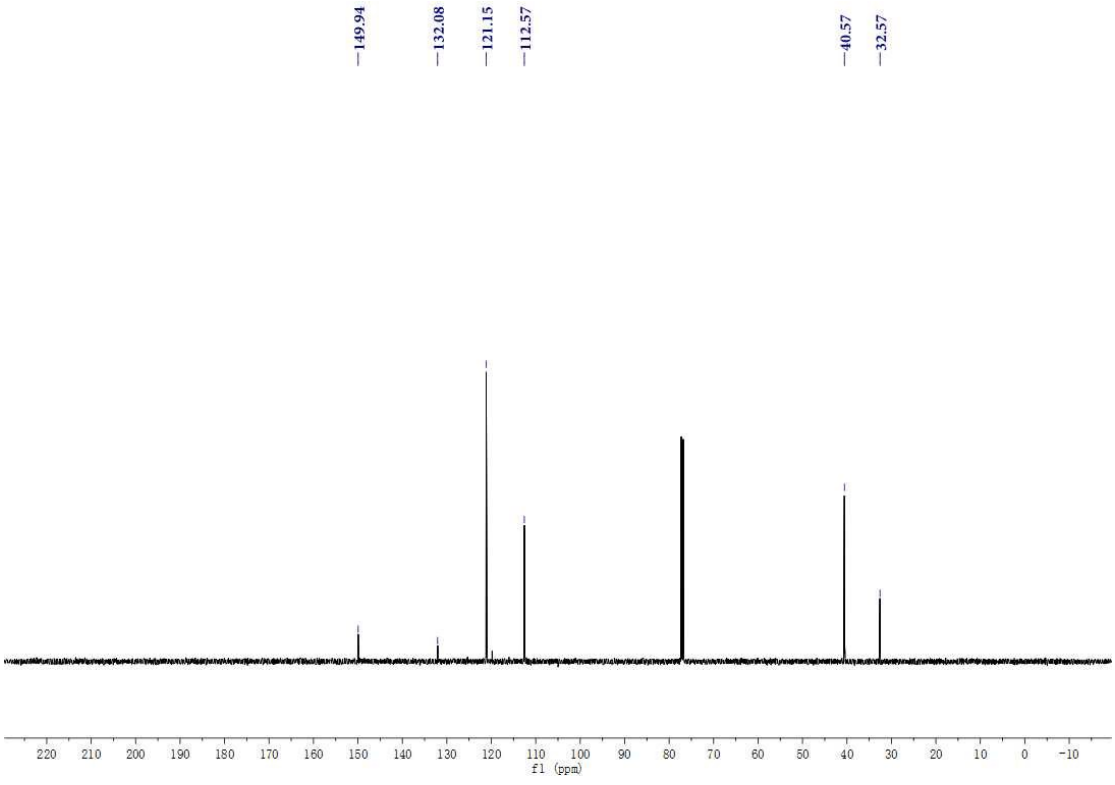

7.31
7.31
7.29
7.28
7.21
7.19
6.97
6.95
2.41
2.38
4.03
2.09
2.00
3.22
3.17
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

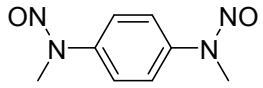

140.33
139.53
136.91
134.39
130.37
129.86
127.00
119.82
21.32
20.95
230
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


NO
N
N

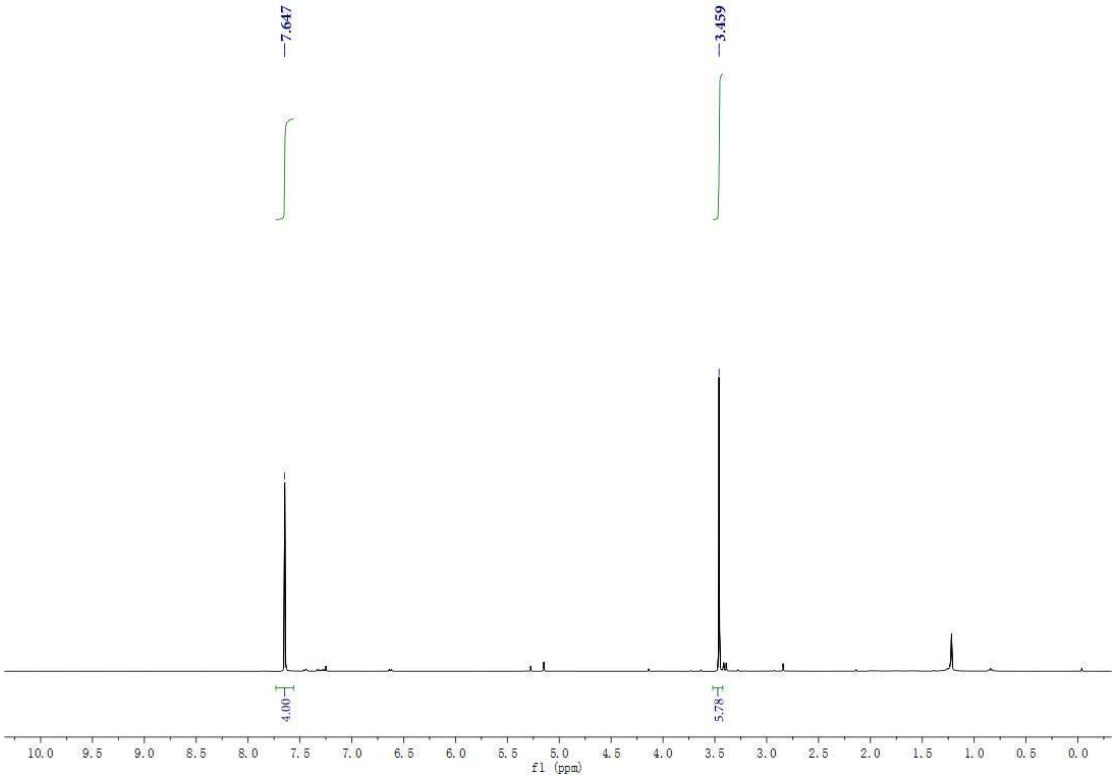
5a

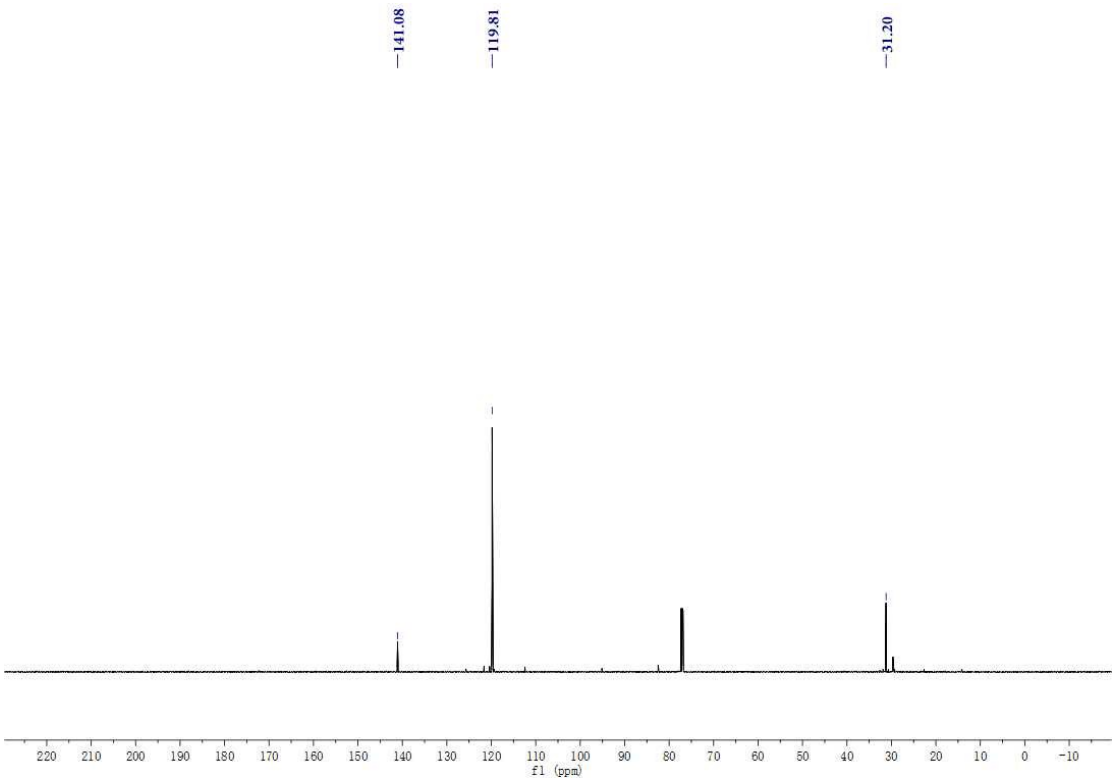

7.360
7.338
6.767
6.744
3.423
2.985
1.94
2.00
2.88
5.78
f1 (ppm)

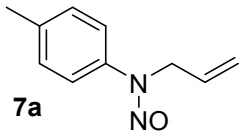

149.94
132.08
121.15
112.57
40.57
32.57
f1 (ppm)


ON
N
N
NO

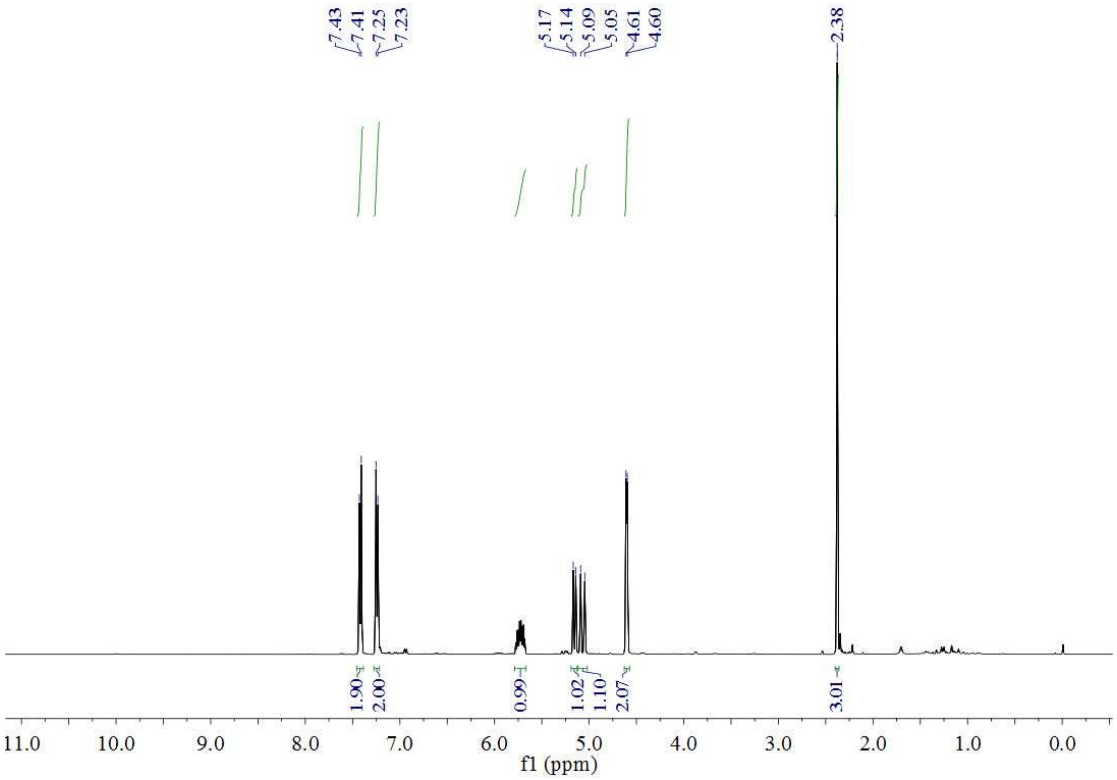
5b

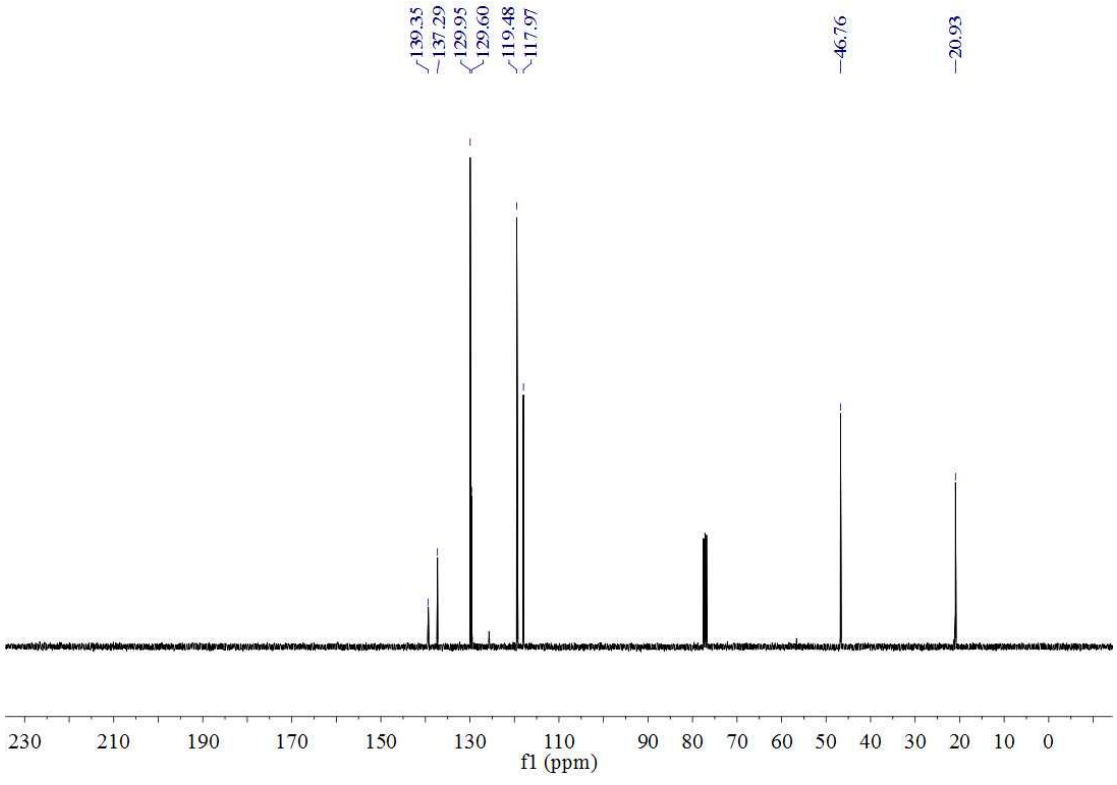

7.647
3.459
4.00
5.78
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

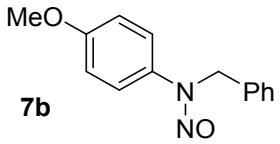

141.08
119.81
31.20
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


N
NO

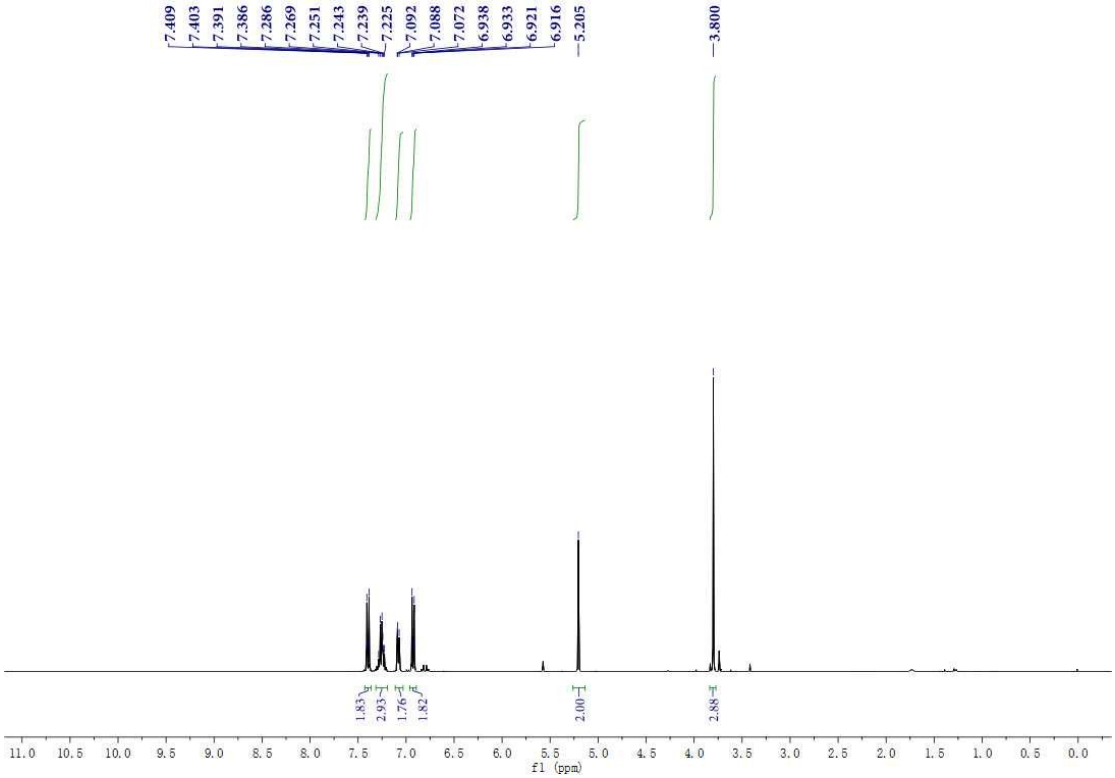
7a

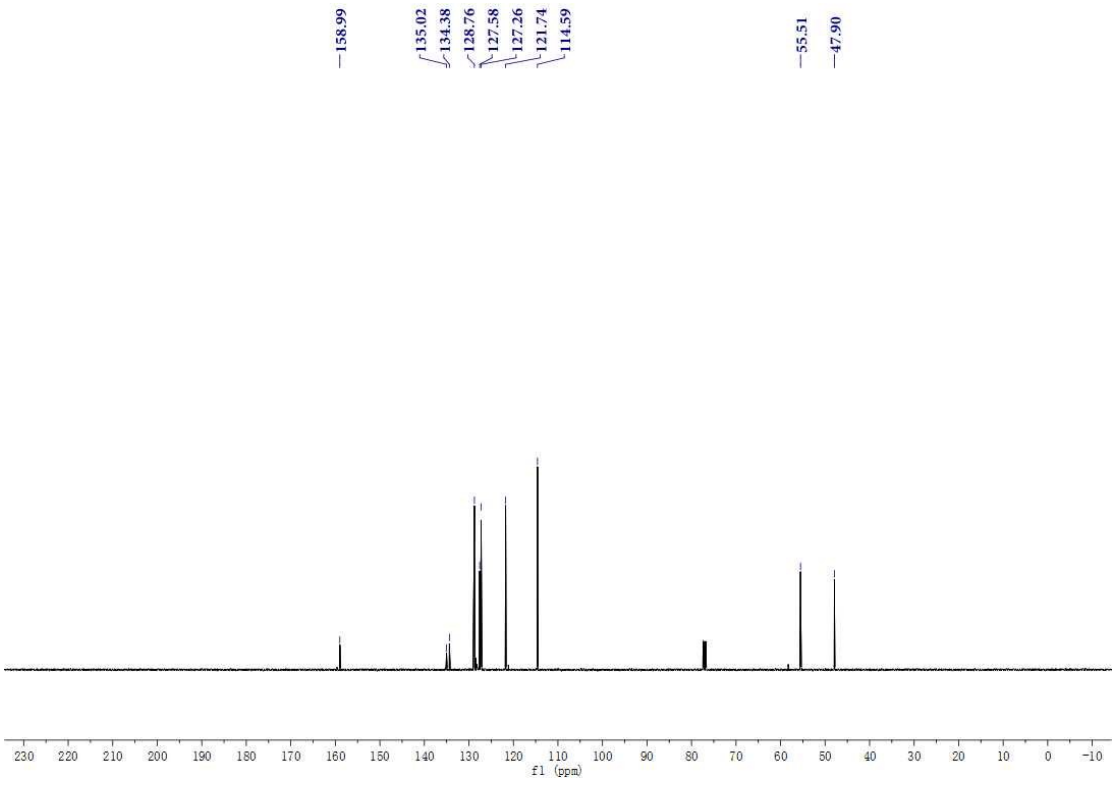

7.43
7.41
7.25
7.23
5.17
5.14
5.09
5.05
4.61
4.60
2.38
1.90
2.00
0.99
1.02
1.10
2.07
3.01
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

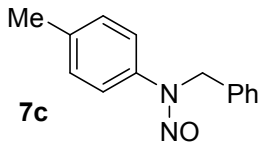

139.35
137.29
129.95
129.60
119.48
117.97
46.76
20.93
230
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


MeO
N
Ph
NO

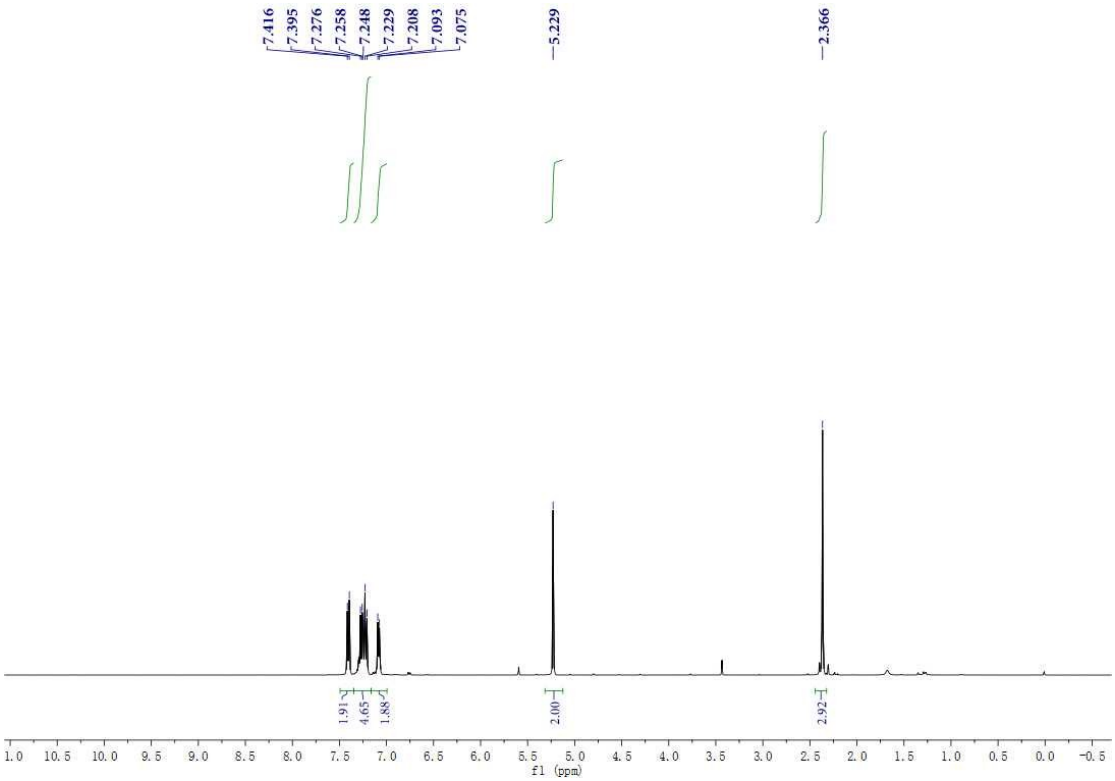
7b

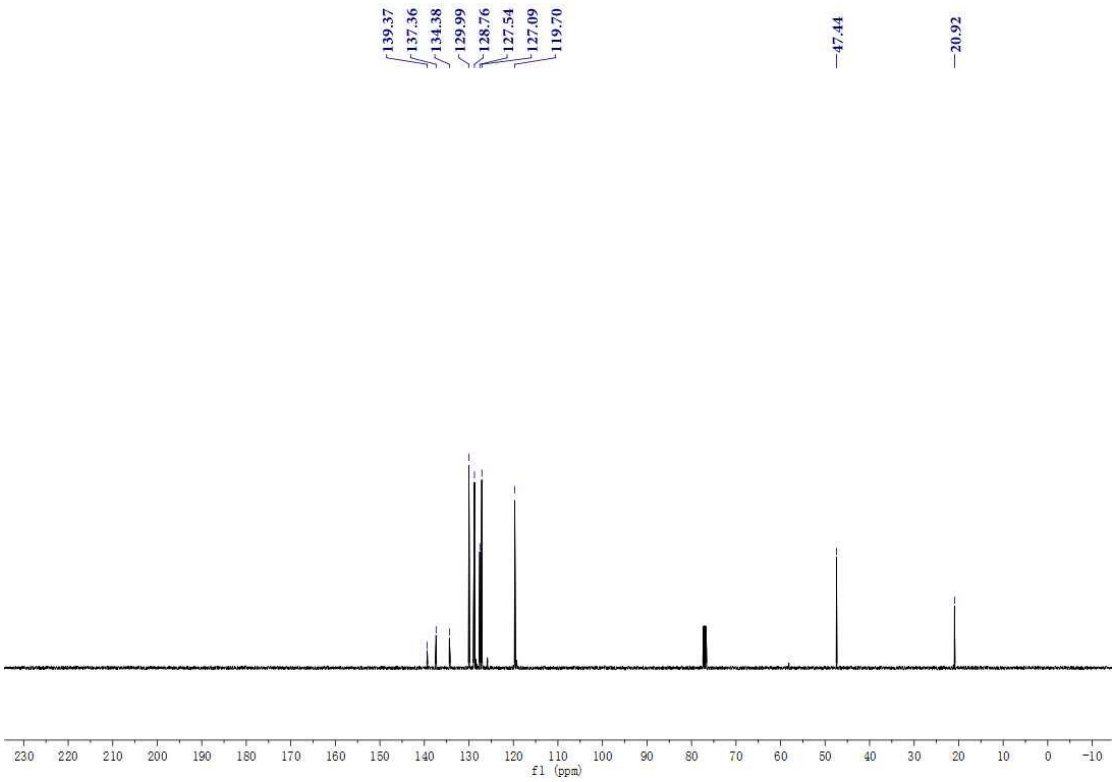

7.409
7.403
7.391
7.386
7.286
7.269
7.251
7.243
7.239
7.225
7.092
7.088
7.072
6.938
6.933
6.921
6.916
5.205
3.800
1.83
2.93
1.76
1.82
2.00
2.88
f1 (ppm)

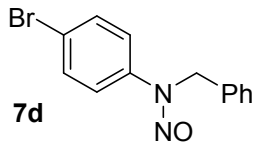

158.99
135.02
134.38
128.76
127.58
127.26
121.74
114.59
55.51
47.90
f1 (ppm)


Me
N
Ph
NO

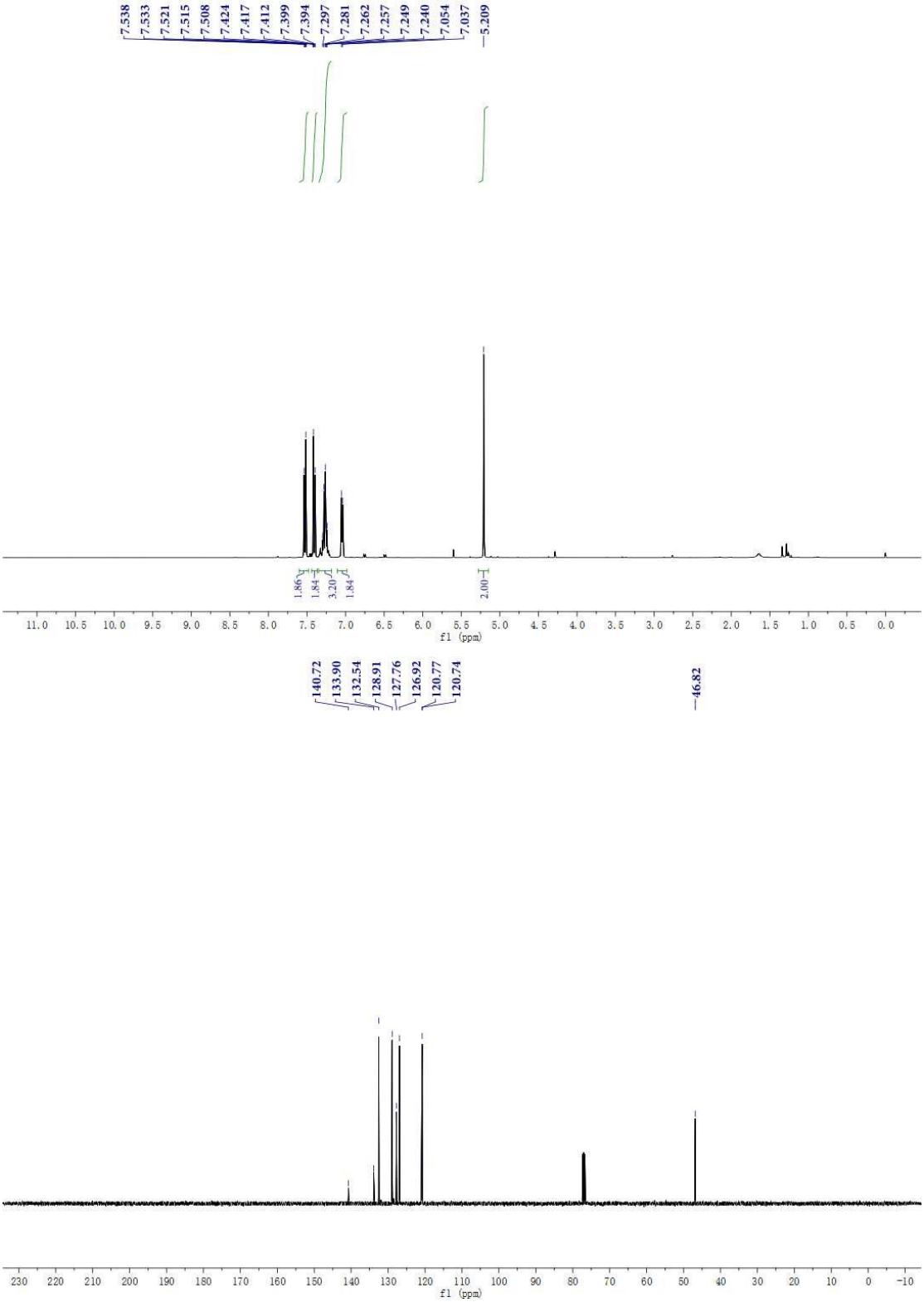
7c

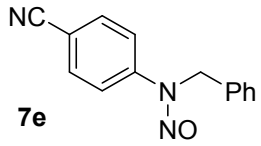

7.416
7.395
7.276
7.258
7.248
7.229
7.208
7.093
7.075
5.229
2.366
1.91
4.65
1.88
2.00
2.92
f1 (ppm)


139.37
137.36
134.38
129.99
128.76
127.54
127.09
119.70
47.44
20.92
f1 (ppm)

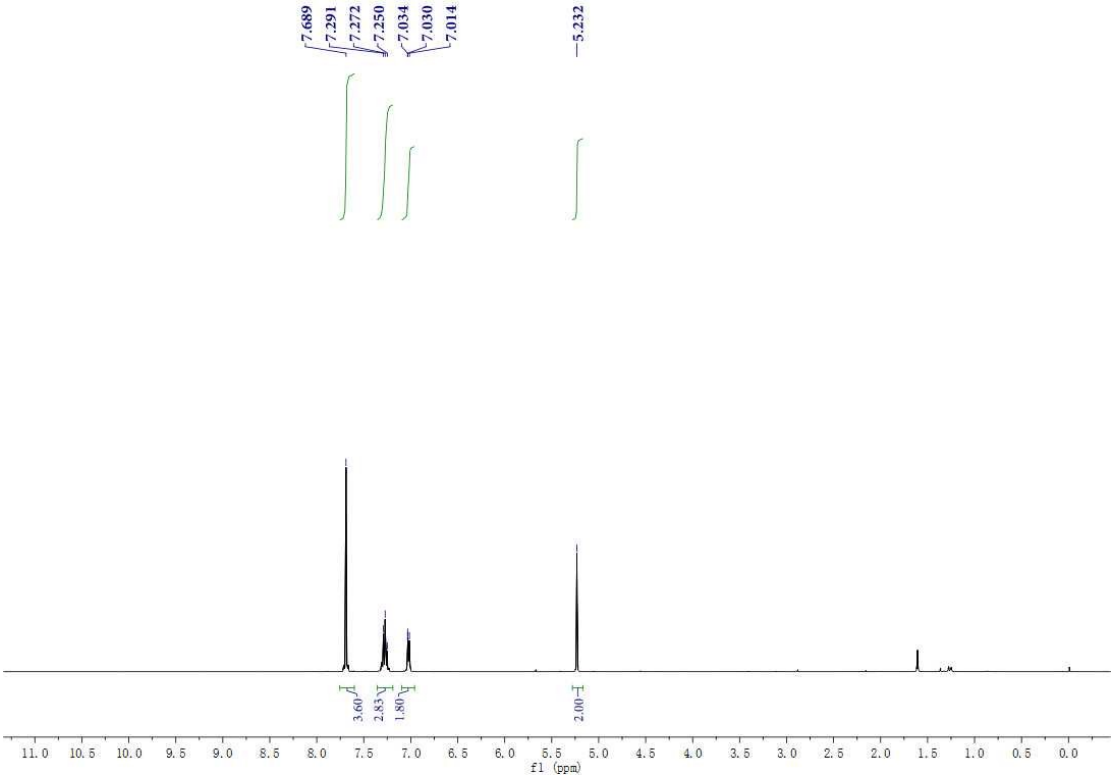

Br
N
Ph
NO

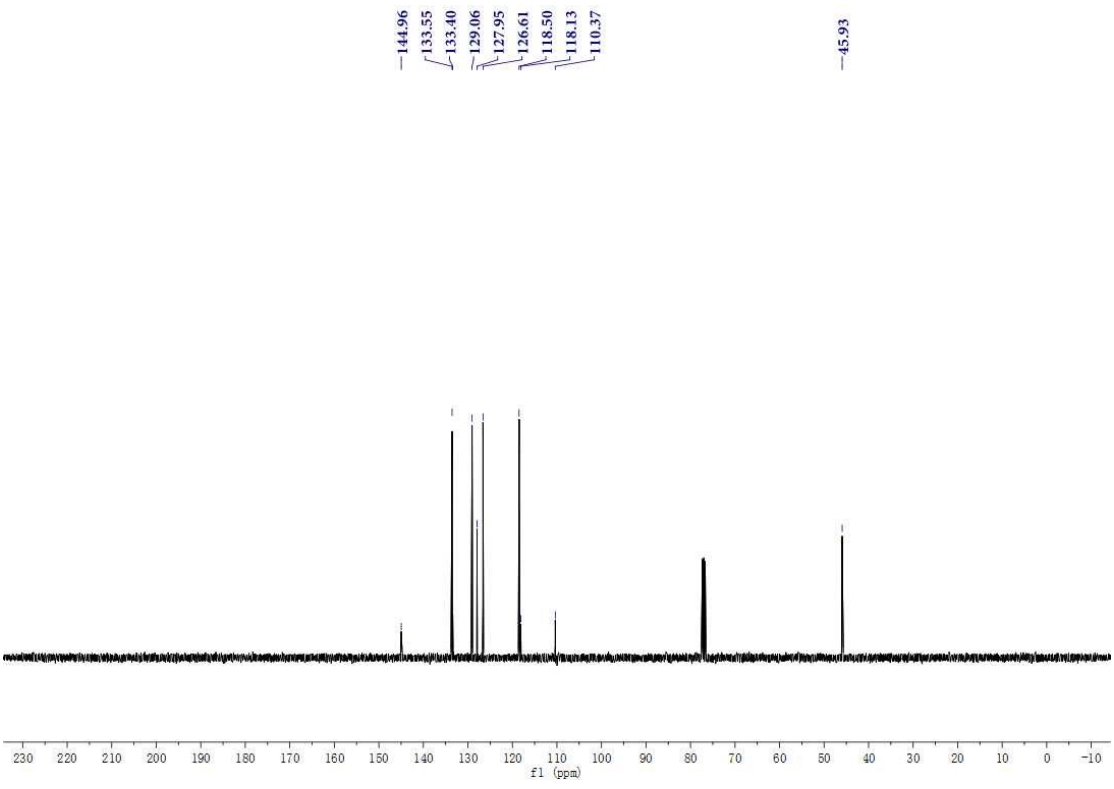
7d

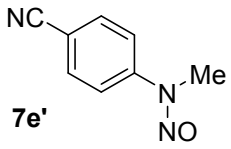

7.538
7.533
7.521
7.515
7.508
7.424
7.417
7.412
7.399
7.394
7.297
7.281
7.262
7.257
7.249
7.240
7.054
7.037
5.209
1.86
1.84
3.20
1.84
2.00
f1 (ppm)
140.72
133.90
132.54
128.91
127.76
126.92
120.77
120.74
46.82
f1 (ppm)


NC
N
Ph
NO

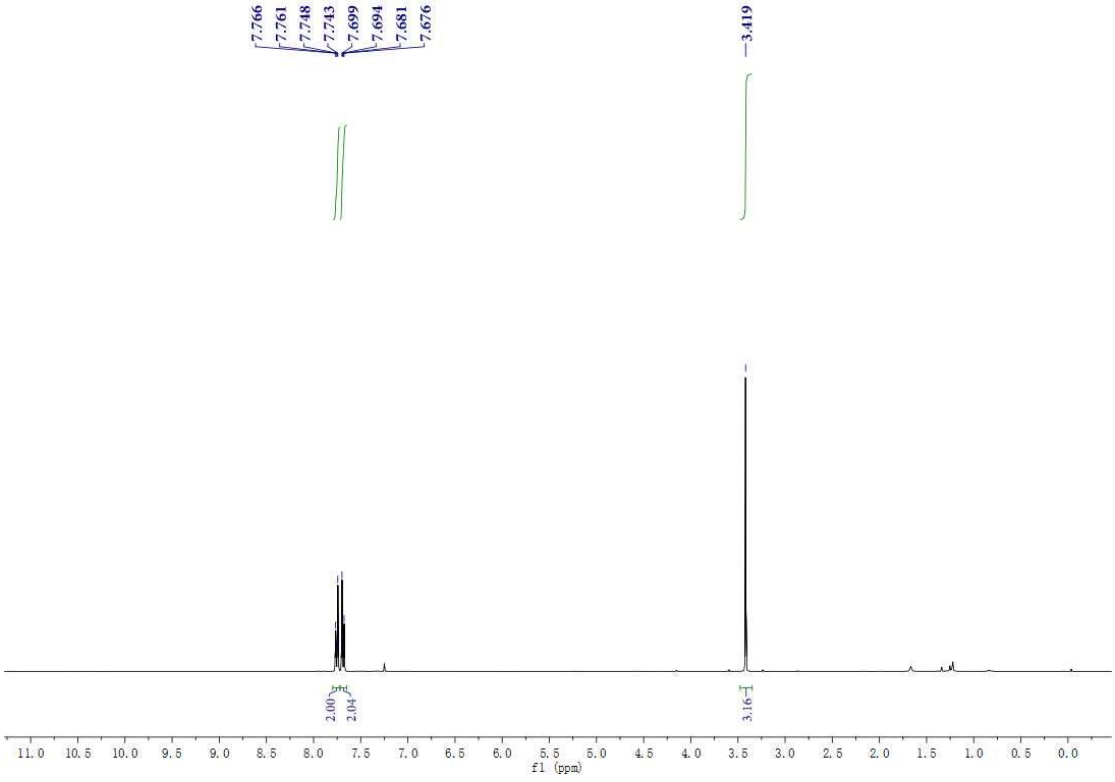
7e

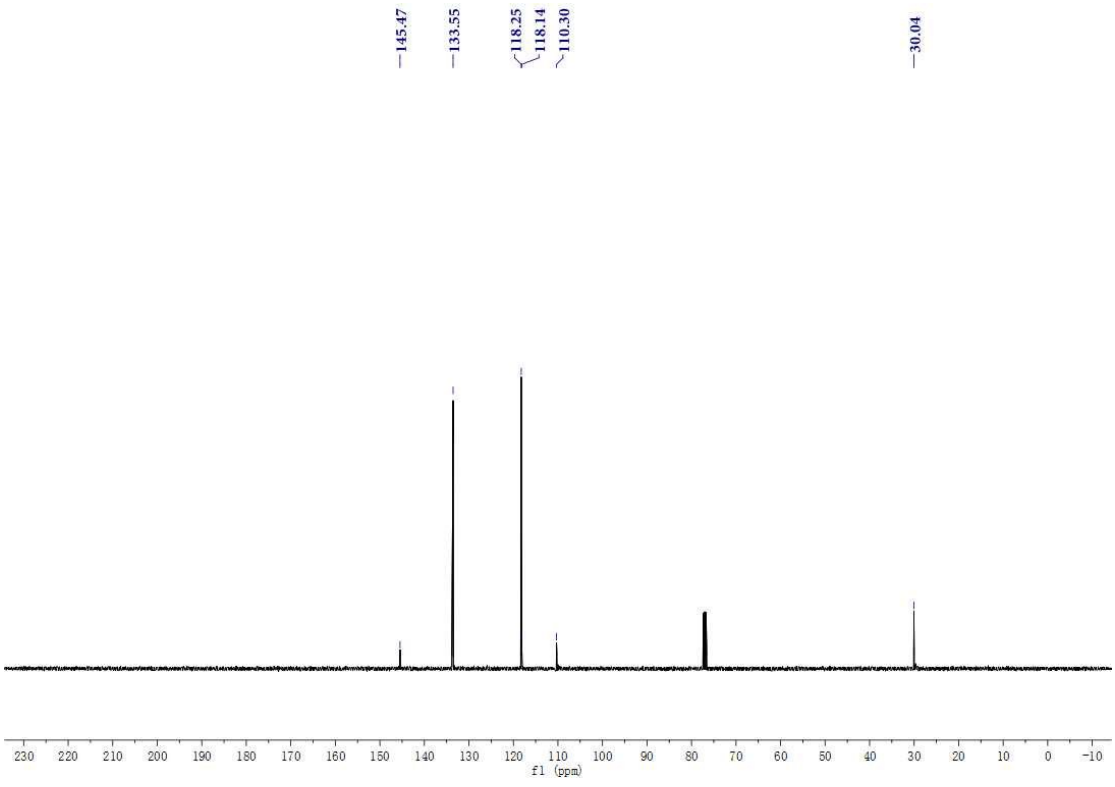

7.689
7.291
7.272
7.250
7.034
7.030
7.014
5.232
3.60
2.83
1.80
2.00
f1 (ppm)


144.96
133.55
133.40
129.06
127.95
126.61
118.50
118.13
110.37
45.93
f1 (ppm)


NC
Me
N
NO

7e'


7.766
7.761
7.748
7.743
7.699
7.694
7.681
7.676
3.419
2.00
2.04
3.16
f1 (ppm)


145.47
133.55
118.25
118.14
110.30
30.04
f1 (ppm)