ELECTRONIC SUPPLEMENTARY INFORMATION

for

Synthesis of 6-substituted 6-nitroperhydro-1,4-diazepines *via* novel *tandem* retro-Henry and Mannich/Michael reactions

Jonathan Martinelli, Giuseppe Gugliotta, and Lorenzo Tei*

Dipartimento di Scienze e Innovazione Tecnologica, Università del Piemonte Orientale "A. Avogadro"

Viale T. Michel 11, 15121, Alessandria, Italy

lorenzo.tei@mfn.unipmn.it

Table of contents

1. Materials and Instrumentation

All chemicals were purchased from Sigma-Aldrich Co., Alfa Aesar Co. and Bachem Co. and were used without purification unless otherwise stated. "H_2O" refers to high purity water with conductivity of 0.04 μS cm^{-1}, obtained from a "MILLI-Q" purification system. "Petroleum ether" (PetEt) refers to petroleum ether with boiling point in the range 40-60 °C. 6-hydroxymethyl-6-nitroperhydro-1,4-diazepine **1** was synthesized according to the procedure referred to in the text. Thin-layer chromatography (TLC) was carried out on silica plates (silica gel 60 F_{254}, Merck 5554) and visualized by UV lamp (254 nm) or stained in $KMnO_4$ solution. Preparative column chromatography was carried out using silica gel (Merck Silica Gel 60, 230 ± 400 mesh) pre-soaked in the starting eluent. ^{1}H and ^{13}C NMR spectra were recorded on a JEOL Eclipse Plus 400 and on a Bruker AvanceIII spectrometers operating at 9.4 and 11.7 T, respectively. Chemical shifts are reported relative to TMS and were referenced using the residual proton solvent resonances. Chemical shifts are reported in ppm and coupling constants in Hz. Splitting patterns are described as singlet (s), broad singlet (br s), doublet (d), double doublet (dd), triplet (t), quartet (q), or multiplet (m). Electrospray ionization mass spectra (ESI MS) were recorded on a SQD 3100 Mass Detector (Waters), operating in positive or negative ion mode, with 1% v/v HCOOH in methanol as the carrier solvent. Infrared (IR) spectra were recorded in the range 4000–400 cm^{-1} at 4 cm^{-1} resolution using a Bruker Equinox 55 spectrometer. Elemental analysis were performed on a EuroVector EA 3000 instrument.

2. Experimental Part

Potassium 1,4-dibenzylperhydro-1,4-diazepine-6-carbonitrate (2)

Hydroxymethyl diazepine **1** (504 mg, 1.42 mmol) was dissolved in dry THF (3 ml). *t*-BuOK (191 mg, 1.71 mmol) was added, and the mixture was stirred at room temperature for 15 minutes. The suspension was filtered and the filtrate was evaporated to dryness yielding **2** as a yellow colored wax (499 mg, 97% yield).

ESI^- MS, m/z: 324 ($[M-K]^-$). IR (KBr disk), cm^{-1}: 3341, 2935, 2814, 1658, 1597, 1565, 1452, 1348, 1167, 1137, 1094, 1053, 1028, 736, 698. ^1H NMR (400 MHz, 25 °C, CD_3OD), δ (ppm): 7.4-7.1 (m, 10H, Ph), 3.74 (s, 4H, $PhCH_2$), 3.69 (s, 4H, $CH_2C{=}N$), 2.57 (s, 4H, NCH_2CH_2N). ^{13}C NMR (100 MHz, 25 °C, CD_3OD), δ (ppm): 138.6 (C^i), 128.7 (C^m), 127.8 (C^o), 126.6 (C^p), 121.7 (C=N), 61.7 (CH_2Ph), 55.9 ($\underline{C}H_2C{=}N$), 55.3 (NCH_2CH_2N).

1-Adamantanemethyl acrylate

Acryloyl chloride (0.37 ml, 4.51 mmol) was dissolved in dry THF (5 ml) and left stirring on an ice bath. A solution of 1-adamantanemethanol (0.50 g, 3.01 mmol) and dry Et_3N (0.63 ml, 4.51 mmol) in dry THF (5 ml) was added dropwise in 30 min. The mixture was left stirring at room temperature for 15 hours, then it was evaporated under reduced pressure and the residue was suspended in H_2O (50 ml) and extracted with DCM (4x25 ml). The organic phase was dried over anhydrous Na_2SO_4 and evaporated to yield a yellow oil that was purified by column chromatography (SiO_2, PetEt/EtOAc 95:5). The product was obtained as a white solid in 78% yield (550 mg, 2.35 mmol).

TLC (PetEt/EtOAc 95:5): R_f 0.45. ESI^+ MS, m/z: 267 ($[M+Na]^+$). IR (KBr disk), cm^{-1}: 2938, 2860, 1723, 1684, 1638, 1468, 1406, 1370, 1361, 1298, 1054, 1017, 985, 962, 811. ^1H NMR (400 MHz, 25 °C, $CDCl_3$), δ (ppm): 6.39 (dd, $^2J_{HH}$ = 1.5 Hz, $^3J_{HH}$ = 17.2 Hz, 1H, $CH\underline{H}^{cis}{=}CH$), 6.13 (dd, $^3J_{HH}$ = 17.2 Hz, $^3J_{HH}$ = 10.3 Hz, 1H, $CH_2{=}\underline{C}H$), 5.80 (dd, $^2J_{HH}$ = 1.5 Hz, $^3J_{HH}$ = 10.3 Hz, 1H, $CH\underline{H}^{trans}{=}CH$), 3.75 (s, 2H, $AdCH_2$), 2.0-1.5 (m, 15H, Ad). ^{13}C NMR (100 MHz, 25 °C, $CDCl_3$), δ (ppm): 166.6 (C=O), 130.4 ($\underline{C}H_2{=}CH$), 128.8 ($CH_2{=}\underline{C}H$), 74.2 ($AdCH_2$), 39.3, 37.0, 33.4, 28.1 (Ad). Elemental analysis: calculated C 76.33%, H 9.15%; found C 76.25%, H 9.12%.

***N*-(1-adamantyl)acrylammide**

Acryloyl chloride (5 ml) was dissolved in dry THF (10 ml) and stirred for 10 min on an ice bath. DIPEA (2.78 ml, 15.99 mmol) was added, followed by 1-adamantylamine (1.00 g, 5.33 mmol) portionwise. After addition, the mixture was left stirring at room temperature for 15 hours, then it was evaporated under reduced pressure and the residue was dissolved in EtOAc (50 ml) and washed with 0.1 M HCl (50 ml) and brine (2x25 ml). The organic phase was dried over anhydrous Na_2SO_4 and evaporated to yield an orange oil that was purified by column chromatography (SiO_2, PetEt/EtOAc 7:3). The product was obtained as a white solid in 55% yield (603 mg, 2.94 mmol).

TLC (PetEt/EtOAc 7:3): R_f 0.38. ESI^+ MS, m/z: 228 ($[M+Na]^+$). IR (KBr disk), cm^{-1}: 3290, 2933, 2855, 1668, 1624, 1562, 1446, 1409, 1250, 1234, 1098, 974, 710. ^1H NMR (400 MHz, 25 °C, $CDCl_3$), δ (ppm): 6.50 (dd, $^2J_{HH}$ = 1.3 Hz, $^3J_{HH}$ = 17.5 Hz, 1H, $CH\underline{H}^{cis}{=}CH$), 6.17 (dd, $^3J_{HH}$ = 17.5 Hz, $^3J_{HH}$ = 11.1 Hz, 1H, $CH_2{=}\underline{C}H$), 6.03 (br s, 1H, NH), 5.51 (dd, $^2J_{HH}$ = 1.3 Hz, $^3J_{HH}$ = 11.1 Hz, 1H, $CH\underline{H}^{trans}{=}CH$), 2.2-1.0 (m, 15H, Ad). ^{13}C NMR (100 MHz, 25 °C, $CDCl_3$), δ (ppm): 164.8 (C=O), 132.2 ($\underline{C}H_2{=}CH$), 125.7 ($CH_2{=}\underline{C}H$), 52.2, 41.5, 36.4, 29.4 (Ad). Elemental analysis: calculated C 76.06%, H 9.33%, N 6.82%; found C 76.01%, H 9.41%, N 6.66%.

General procedure for the synthesis of 6-substituted 1,4-dibenzyl-6-nitroperhydro-1,4-diazepines *via tandem* retro-Henry and Michael reactions.

Hydroxymethyl diazepine **1** (1 equivalent) was dissolved in dry THF (2 ml/mmol). The acrylic derivative (2 equivalents) was added, and the mixture was stirred at room temperature for 5 minutes. *t*-BuOK (1.2 equivalents) was added to the solution, and stirring was continued at room temperature for 3 hours. After removal of the solvent under reduced pressure, the residue was taken up in EtOAc and washed with brine (3x). The organic phase was dried over anhydrous Na_2SO_4 and evaporated to dryness to give the crude product.

6-methoxycarbonylethyl-6-nitro-1,4-dibenzylperhydro-1,4-diazepine (3)

Purified by column chromatography (SiO_2, PetEt/EtOAc 9:1). Yield (oil): 92%.
TLC (PetEt/EtOAc 9:1): R_f 0.34. ESI^+ MS, m/z: 412 ($[M+H]^+$). IR (KBr disk), cm^{-1}: 3026, 2928, 2823, 1721, 1538, 1454, 1357, 1155, 1127, 1054, 952, 837, 738, 697. ^1H NMR (400 MHz, 25 °C, $CDCl_3$), δ (ppm): 7.4-7.1 (m, 10H, Ph), 3.72 (d, $^2J_{HH}$ = 13.2 Hz, 2H, PhC<u>H</u>H'), 3.60 (s, 3H, CH_3), 3.57 (d, $^2J_{HH}$ = 13.2 Hz, 2H, PhCH<u>H</u>'), 3.51 (d, $^2J_{HH}$ = 14.3 Hz, 2H, NC<u>H</u>H'CNO_2), 2.96 (d, $^2J_{HH}$ = 14.3 Hz, 2H, NCH<u>H</u>'CNO_2), 2.58 (m, 4H, NCH_2CH_2N), 1.95 (m, 2H, CH_2C=O), 1.76 (m, 2H, C<u>H</u>$_2CH_2C$=O). ^{13}C NMR (100 MHz, 25 °C, $CDCl_3$), δ (ppm): 172.3 (C=O), 139.0 (C^i), 129.2 (C^m), 128.4 (C^o), 127.4 (C^p), 94.0 (CNO_2), 64.0 (CH_2Ph), 61.4 (N<u>C</u>H_2CNO_2), 58.8 (NCH_2CH_2N), 51.8 (CH_3), 31.3 (<u>C</u>H_2C=O), 27.7 (<u>C</u>H_2CH_2C=O). Elemental analysis: calculated C 67.13%, H 7.10%, N 10.21%; found C 66.98%, H 7.21%, N 10.18%.

6-(2-methoxycarbonyl)propyl-6-nitro-1,4-dibenzylperhydro-1,4-diazepine (4)

Purified by column chromatography (SiO_2, PetEt/EtOAc 9:1). Yield (oil): 92%.
TLC (PetEt/EtOAc 9:1): R_f 0.25. ESI^+ MS, m/z: 426 ($[M+H]^+$). IR (KBr disk), cm^{-1}: 3029, 2926, 2824, 1725, 1536, 1452, 1361, 1176, 1124, 1055, 951, 841, 732, 696. ^1H NMR (400 MHz, 25 °C, $CDCl_3$), δ (ppm): 7.4-7.2 (m, 10H, Ph+Ph'), 3.77 (d, $^2J_{HH}$ = 13.2 Hz, 1H, PhC<u>H</u>H'), 3.76 (d, $^2J_{HH}$ = 13.2 Hz, 1H, Ph'C<u>H</u>''H'''), 3.63 (d, $^2J_{HH}$ = 14.3 Hz, 1H, NC<u>H</u>H'CNO_2), 3.62 (s, 3H, OCH_3), 3.58 (d, $^2J_{HH}$ = 13.2 Hz, 1H, PhCH<u>H</u>'), 3.57 (d, $^2J_{HH}$ = 13.2 Hz, 1H, Ph'CH''<u>H</u>'''), 3.54 (d, $^2J_{HH}$ = 13.9 Hz, 1H, N'C<u>H</u>''H'''CNO_2), 3.02 (d, $^2J_{HH}$ = 13.9 Hz, 1H, N'CH''<u>H</u>'''CNO_2), 2.96 (d, $^2J_{HH}$ = 14.3 Hz, 1H, NCH<u>H</u>'CNO_2), 2.54 (m, 4H, NCH_2CH_2N), 2.33 (m, 2H, C<u>H</u>$_2CH$), 1.69 (m, 1H, CH), 0.99 (d, $^3J_{HH}$ = 7.0 Hz, 3H, C<u>H</u>$_3CH$). ^{13}C NMR (100 MHz, 25 °C, $CDCl_3$), δ (ppm): 175.9 (C=O), 139.2 (d, C^i), 129.1 (d, C^m), 128.4 (d, C^o), 127.2 (d, C^p), 94.0 (CNO_2), 64.0 (d, CH_2Ph), 62.4 (N<u>C</u>H_2CNO_2), 58.3 (d, NCH_2CH_2N), 51.9 (OCH_3), 40.4 (CH), 34.8 (<u>C</u>H_2CH), 19.2 (<u>C</u>H_3CH). Elemental analysis: calculated C 67.74%, H 7.34%, N 9.87%; found C 67.82%, H 7.29%, N 10.00%.

6-*t*-butoxycarbonylethyl-6-nitro-1,4-dibenzylperhydro-1,4-diazepine (5)

Purified by column chromatography (SiO_2, PetEt/EtOAc 8:2). Yield (oil): 52%.
TLC (PetEt/EtOAc 8:2): R_f 0.38. ESI^+ MS, m/z: 454 ($[M+H]^+$). IR (KBr disk), cm^{-1}: 3026, 2975, 2927, 2821, 1729, 1536, 1453, 1366, 1150, 1056, 950, 842, 741, 699. ^1H NMR (400 MHz, 25 °C, $CDCl_3$), δ (ppm): 7.4-7.2 (m, 10H, Ph), 3.74 (d, $^2J_{HH}$ = 12.8 Hz, 2H, PhC<u>H</u>H'), 3.59 (d, $^2J_{HH}$ = 12.8 Hz, 2H, PhCH<u>H</u>'), 3.53 (d, $^2J_{HH}$ = 14.3 Hz, 2H, NC<u>H</u>H'CNO_2), 2.97 (d, $^2J_{HH}$ = 14.3 Hz, 2H, NCH<u>H</u>'CNO_2), 2.61 (m, 4H, NCH_2CH_2N), 1.95 (m, 2H, CH_2C=O), 1.74 (m, 2H, C<u>H</u>$_2CH_2C$=O), 1.42 (s, 9H, CH_3). ^{13}C NMR (100 MHz, 25 °C, $CDCl_3$), δ (ppm): 171.1 (C=O), 139.0 (C^i), 129.0 (C^m), 128.2 (C^o), 127.2 (C^p), 93.9 (CNO_2), 80.7 ($C_q^{t\text{-}Bu}$), 64.0 (CH_2Ph), 61.8 (N<u>C</u>H_2CNO_2), 58.8 (NCH_2CH_2N), 32.2 (<u>C</u>H_2C=O), 29.7 (<u>C</u>H_2CH_2C=O), 28.6 (CH_3). Elemental analysis: calculated C 68.85%, H 7.78%, N 9.26%; found C 68.78%, H 7.64%, N 9.21%.

6-(1-adamantane)methoxycarbonylethyl-6-nitro-1,4-dibenzylperhydro-1,4-diazepine (6)

Purified by column chromatography (SiO_2, PetEt/EtOAc 9:1). Yield (oil): 44%.
TLC (PetEt/EtOAc 9:1): R_f 0.41. ESI^+ MS, m/z: 546 ($[M+H]^+$). IR (KBr disk), cm^{-1}: 3027, 2924, 2825, 1724, 1534, 1451, 1358, 1164, 1125, 1053, 953, 849, 736, 698. ^1H NMR (400 MHz, 25 °C, $CDCl_3$), δ (ppm): 7.4-7.2 (m, 10H, Ph), 3.72 (d, $^2J_{HH}$ = 12.8 Hz, 2H, PhC<u>H</u>H'), 3.60 (s, 2H, $AdCH_2O$), 3.58 (d, $^2J_{HH}$ = 12.8 Hz, 2H, PhCH<u>H</u>'), 3.53 (d, $^2J_{HH}$ = 14.3 Hz, 2H, NC<u>H</u>H'CNO_2), 2.97 (d, $^2J_{HH}$ = 14.3 Hz, 2H, NCH<u>H</u>'CNO_2), 2.61 (m, 4H, NCH_2CH_2N), 2.1-1.4 (m, 15H, Ad). ^{13}C NMR (100 MHz, 25 °C, $CDCl_3$), δ (ppm): 172.4 (C=O), 140.3 (C^i), 131.0 (C^m), 130.5 (C^o), 129.4 (C^p), 94.9

(CNO_2), 74.2 (CH_2O), 64.0 (CH_2Ph), 61.4 ($N\underline{C}H_2CNO_2$), 59.0 (NCH_2CH_2N), 39.0, 36.5, 33.0 (Ad). Elemental analysis: calculated C 72.63%, H 7.94%, N 7.70%; found C 72.61%, H 7.79%, N 7.81%.

6-carbamoylethyl-6-nitro-1,4-dibenzylperhydro-1,4-diazepine (7)

Purified by column chromatography (SiO_2, DCM/MeOH 97:3). Yield (oil): 77%.
TLC (DCM/MeOH 97:3): R_f 0.33. ESI^+ MS, m/z: 397 ($[M+H]^+$). IR (KBr disk), cm^{-1}: 3415, 3363, 3303, 3199, 2822, 1675, 1634, 1534, 1450, 1409, 1352, 1323, 1122, 1055, 950, 729, 697. ^1H NMR (400 MHz, 25 °C, $CDCl_3$), δ (ppm): 7.4-7.2 (m, 10H, Ph), 5.84 (br s, 1H, N<u>H</u>H'), 5.37 (br s, 1H, NH<u>H</u>'), 3.72 (d, $^2J_{HH}$ = 13.0 Hz, 2H, PhC<u>H</u>H'), 3.57 (d, $^2J_{HH}$ = 13.0 Hz, 2H, PhCH<u>H</u>'), 3.51 (d, $^2J_{HH}$ = 14.3 Hz, 2H, NC<u>H</u>H'CNO_2), 2.95 (d, $^2J_{HH}$ = 14.3 Hz, 2H, NCH<u>H</u>'CNO_2), 2.58 (m, 4H, NCH_2CH_2N), 1.97 (m, 2H, CH_2C=O), 1.62 (m, 2H, C<u>H</u>$_2CH_2C$=O). ^{13}C NMR (100 MHz, 25 °C, $CDCl_3$), δ (ppm): 173.6 (C=O), 139.1 (C^i), 129.2 (C^m), 128.4 (C^o), 127.4 (C^p), 94.4 (CNO_2), 64.0 (CH_2Ph), 61.5 ($N\underline{C}H_2CNO_2$), 58.7 (NCH_2CH_2N), 31.8 ($\underline{C}H_2C$=O), 29.2 ($\underline{C}H_2CH_2C$=O). Elemental analysis: calculated C 66.64%, H 7.12%, N 14.13%; found C 66.74%, H 7.06%, N 14.16%.

6-cyanoethyl-6-nitro-1,4-dibenzylperhydro-1,4-diazepine (8)

Purified by column chromatography (SiO_2, PetEt/EtOAc 9:1). Yield (oil): 81%.
TLC (PetEt/EtOAc 9:1): R_f 0.37. ESI^+ MS, m/z: 379 ($[M+H]^+$). IR (KBr disk), cm^{-1}: 3553, 3119, 3027, 2927, 2820, 1667, 1649, 1539, 1456, 1356, 1288, 1123, 1057, 952, 839, 735, 696. ^1H NMR (400 MHz, 25 °C, $CDCl_3$), δ (ppm): 7.4-7.2 (m, 10H, Ph), 3.73 (d, $^2J_{HH}$ = 12.8 Hz, 2H, PhC<u>H</u>H'), 3.56 (d, $^2J_{HH}$ = 12.8 Hz, 2H, PhCH<u>H</u>'), 3.46 (d, $^2J_{HH}$ = 14.3 Hz, 2H, NC<u>H</u>H'CNO_2), 2.87 (d, $^2J_{HH}$ = 14.3 Hz, 2H, NCH<u>H</u>'CNO_2), 2.68 (m, 4H, NCH_2CH_2N), 1.89 (m, 2H, CH_2C=O), 1.50 (m, 2H, C<u>H</u>$_2CH_2C$=O). ^{13}C NMR (100 MHz, 25 °C, $CDCl_3$), δ (ppm): 138.7 (C^i), 129.3 (C^m), 128.7 (C^o), 127.8 (C^p), 118.2 (C≡N), 93.3 (CNO_2), 63.9 (CH_2Ph), 60.5 ($N\underline{C}H_2CNO_2$), 59.3 (NCH_2CH_2N), 31.7 ($\underline{C}H_2C$=O), 11.5 ($\underline{C}H_2CH_2C$=O). Elemental analysis: calculated C 69.82%, H 6.92%, N 14.80%; found C 69.75%, H 7.07%, N 14.86%.

6-(1-adamantyl)carbamoylethyl-6-nitro-1,4-dibenzylperhydro-1,4-diazepine (9)

Purified by column chromatography (SiO_2, PetEt/EtOAc 7:3). Yield (oil): 31%.
TLC (PetEt/EtOAc 7:3): R_f 0.64. ESI^+ MS, m/z: 531 ($[M+H]^+$). IR (KBr disk), cm^{-1}: 3031, 2926, 2822, 1672, 1614, 1535, 1452, 1439, 1362, 1259, 1127, 1052, 954, 829, 733, 698. ^1H NMR (400 MHz, 25 °C, $CDCl_3$), δ (ppm): 7.4-7.2 (m, 10H, Ph), 4.98 (br s, 1H, NH), 3.72 (d, $^2J_{HH}$ = 13.0 Hz, 2H, PhC<u>H</u>H'), 3.59 (d, $^2J_{HH}$ = 13.0 Hz, 2H, PhCH<u>H</u>'), 3.54 (d, $^2J_{HH}$ = 14.3 Hz, 2H, NC<u>H</u>H'CNO_2), 2.98 (d, $^2J_{HH}$ = 14.3 Hz, 2H, NCH<u>H</u>'CNO_2), 2.56 (m, 4H, NCH_2CH_2N), 2.05, 1.93, 1.66 (m, 15H, Ad), 2.00 (m, 2H, CH_2C=O), 1.56 (m, 2H, C<u>H</u>$_2CH_2C$=O). ^{13}C NMR (100 MHz, 25 °C, $CDCl_3$), δ (ppm): 169.9 (C=O), 139.1 (C^i), 129.2 (C^m), 128.4 (C^o), 127.4 (C^p), 94.7 (CNO_2), 63.9 (CH_2Ph), 61.7 ($N\underline{C}H_2CNO_2$), 58.3 (NCH_2CH_2N), 52.0, 41.6, 36.4, 29.5 (Ad), 32.4 ($\underline{C}H_2C$=O), 31.0 ($\underline{C}H_2CH_2C$=O). Elemental analysis: calculated C 72.42%, H 7.98%, N 10.56%; found C 72.37%, H 7.82%, N 10.64%.

General procedure for the synthesis of 6-substituted 1,4-dibenzyl-6-nitroperhydro-1,4-diazepines *via tandem* retro-Henry and Mannich reactions.

Hydroxymethyl diazepine **1** (1 equivalent) was dissolved in dry THF (2 ml/mmol). *t*-BuOK (1.2 equivalents), the amine (1.2 equivalents) and paraformaldehyde (1.2 equivalents) were added. The suspension was stirred at 50 °C for 15 hours. After removal of the solvent under reduced pressure, the residue was taken up in EtOAc and washed with brine (3x). The organic phase was dried over anhydrous Na_2SO_4 and evaporated to dryness to give the crude product.

6-*N*-dodecylaminomethyl-6-nitro-1,4-dibenzylperhydro-1,4-diazepine (10)

Purified by column chromatography (SiO_2, PetEt/EtOAc 8:2). Yield (oil): 68%.
TLC (PetEt/EtOAc 8:2): R_f 0.40. ESI^+ MS, m/z: 412 ($[M+H]^+$). IR (KBr disk), cm^{-1}: 3087, 3063, 3030, 2925, 2853, 1538, 1495, 1455, 1352, 1129, 1066, 1029, 954, 852, 742, 699. ^1H NMR (400 MHz, 25 °C, $CDCl_3$), δ (ppm): 7.4-7.2 (m, 10H, Ph), 3.70 (d, $^2J_{HH}$ = 12.8 Hz, 2H, PhCHH'), 3.59 (d, $^2J_{HH}$ = 12.8 Hz, 2H, PhCHH'), 3.47 (d, $^2J_{HH}$ = 14.3 Hz, 2H, NCHH'CNO_2), 3.00 (d, $^2J_{HH}$ = 14.3 Hz, 2H, NCHH'CNO_2), 2.72 (s, 2H, NHC$H_2$$CNO_2$), 2.7-2.5 (m, 5H, NCH_2CH_2N + NH), 2.24 (m, 2H, CH_2CH_2NH), 1.4-1.1 (m, 20H, $CH_3(CH_2)_{10}$), 0.88 (t, $^3J_{HH}$ = 7.1 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, 25 °C, $CDCl_3$), δ (ppm): 139.3 (C^i), 129.2 (C^m), 128.4 (C^o), 127.3 (C^p), 95.3 (CNO_2), 64.0 (CH_2Ph), 60.3 (N$CH_2$$CNO_2$), 59.1 ($NCH_2CH_2N$), 54.3 (NH$CH_2$$CNO_2$), 50.3 ($CH_2CH_2NH$), 32-22 ($(CH_2)_{10}$), 14.2 ($CH_3$). Elemental analysis: calculated C 73.52%, H 9.64%, N 10.72%; found C 73.56%, H 9.80%, N 10.67%.

6-*N*-(ethoxycarbonylmethyl)aminomethyl-6-nitro-1,4-dibenzylperhydro-1,4-diazepine (11)

Purified by column chromatography (SiO_2, PetEt/EtOAc 8:2). Yield (oil): 73%.
TLC (PetEt/EtOAc 8:2): R_f 0.48. ESI^+ MS, m/z: 441 ($[M+H]^+$). IR (KBr disk), cm^{-1}: 3025, 2923, 2825, 1728, 1537, 1493, 1451, 1359, 1125, 1064, 1026, 957, 822, 740, 698. ^1H NMR (400 MHz, 25 °C, $CDCl_3$), δ (ppm): 7.4-7.2 (m, 10H, Ph), 4.13 (q, $^3J_{HH}$ = 7.0 Hz, 2H, CH_3CH_2), 3.71 (d, $^2J_{HH}$ = 13.2 Hz, 2H, PhCHH'), 3.60 (d, $^2J_{HH}$ = 13.2 Hz, 2H, PhCHH'), 3.48 (d, $^2J_{HH}$ = 14.3 Hz, 2H, NCHH'CNO_2), 3.02 (s, 1H, NH), 2.99 (d, $^2J_{HH}$ = 14.3 Hz, 2H, NCHH'CNO_2), 2.81 (s, 2H, $COCH_2NH$), 2.64 (m, 4H, NCH_2CH_2N), 1.25 (t, $^3J_{HH}$ = 7.0 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, 25 °C, $CDCl_3$), δ (ppm): 172.3 (CO), 139.2 (C^i), 129.2 (C^m), 128.4 (C^o), 127.4 (C^p), 95.3 (CNO_2), 64.0 (CH_2Ph), 60.8 (CH_3CH_2), 60.2 (N$CH_2$$CNO_2$), 59.1 ($NCH_2CH_2N$), 54.0 ($COCH_2NH$), 51.3 (NH$CH_2$$CNO_2$), 14.3 ($CH_3$). Elemental analysis: calculated C 65.43%, H 7.32%, N 12.72%; found C 65.39%, H 7.44%, N 12.78%.

6-*N*-(*N'*-(*t*-butoxycarbonyl)aminoethyl)aminomethyl-6-nitro-1,4-dibenzylperhydro-1,4-diazepine (12)

Purified by column chromatography (SiO_2, PetEt/EtOAc 8:2). Yield (oil): 42%.
TLC (PetEt/EtOAc 8:2): R_f 0.15. ESI^+ MS, m/z: 498 ($[M+H]^+$). IR (KBr disk), cm^{-1}: 3421, 3339, 3026, 2967, 2929, 2820, 1708, 1538, 1496, 1453, 1365, 1257, 1170, 1126, 1063, 1027, 800, 737, 699. ^1H NMR (400 MHz, 25 °C, $CDCl_3$), δ (ppm): 7.4-7.2 (m, 10H, Ph), 4.63 (br s, 1H, CONH), 3.72 (d, $^2J_{HH}$ = 13.0 Hz, 2H, PhCHH'), 3.59 (d, $^2J_{HH}$ = 13.0 Hz, 2H, PhCHH'), 3.47 (d, $^2J_{HH}$ = 14.3 Hz, 2H, NCHH'CNO_2), 2.96 (d, $^2J_{HH}$ = 14.3 Hz, 2H, NCHH'CNO_2), 2.94 (t, $^3J_{HH}$ = 5.8 Hz, 2H, $CONHCH_2$), 2.70 (s, 2H, $NHCH_2C$), 2.67 (m, 4H, NCH_2CH_2N), 2.32 (t, $^3J_{HH}$ = 5.8 Hz, 2H, $CONHCH_2CH_2$), 1.46 (s, 9H, Bu^t), 1.12, (t, $^3J_{HH}$ = 7.2 Hz, 1H, NH). ^{13}C NMR (100 MHz, 25 °C, $CDCl_3$), δ (ppm): 156.0 (CO), 139.1 (C^i), 129.2 (C^m), 128.3 (C^o), 127.4 (C^p), 95.0 (CNO_2), 79.1 ($C^{t\text{-}Bu}$), 63.9 (CH_2Ph), 59.7 (N$CH_2$$CNO_2$), 59.3 ($NCH_2CH_2N$), 53.3 ($NHCH_2C$), 49.3 ($CONHCH_2CH_2$), 40.0 ($CONHCH_2$), 28.4 ($CH_3$). Elemental analysis: calculated C 65.17%, H 7.90%, N 14.07%; found C 65.12%, H 7.98%, N 14.15%.

6-benzylaminomethyl-6-nitro-1,4-dibenzylperhydro-1,4-diazepine (13)

Method a

Diazepine **13a** was synthesized according to the general procedure described above *via* combined retro-Henry and Mannich reactions, and purified by column chromatography (SiO_2, PetEt/EtOAc 95:5). Yield (oil): 29%.

TLC (PetEt/EtOAc 95:5): R_f 0.21. ESI^+ MS, m/z: 445 ($[M+H]^+$). IR (KBr disk), cm^{-1}: 3086, 3062, 3028, 2924, 2880, 2825, 1679, 1537, 1495, 1453, 1353, 1125, 1065, 1028, 956, 920, 851, 742, 699. ^1H NMR (400 MHz, 25 °C, $CDCl_3$), δ

(ppm): 7.4-7.2 (m, 10H, Ph), 3.81 (d, $^2J_{HH}$ = 13.1 Hz, 2H, PhC<u>H</u>H'), 3.59 (d, $^2J_{HH}$ = 13.1 Hz, 2H, PhCH<u>H</u>'), 3.53 (d, $^2J_{HH}$ = 14.2 Hz, 2H, NC<u>H</u>H'CNO_2), 3.49 (s, 2H, PhC<u>H</u>$_2$NH), 3.03 (d, $^2J_{HH}$ = 14.2 Hz, 2H, NCH<u>H</u>'CNO_2), 2.78 (s, 2H, NHC<u>H</u>$_2CNO_2$), 2.64 (m, 4H, NCH_2CH_2N). ^{13}C NMR (100 MHz, 25 °C, $CDCl_3$), δ (ppm): 139.9 (C^i-$NHCH_2Ph$), 139.1 (C^i-NCH_2Ph), 129.1 (C^m-$NHCH_2Ph$), 128.32 (C^m-NCH_2Ph), 128.31 (C^o-$NHCH_2Ph$), 128.0 (C^o-NCH_2Ph), 127.3 (C^p-NCH_2Ph), 127.0 (C^p-$NHCH_2Ph$), 95.3 (CNO_2), 63.9 (NCH_2Ph), 60.2 (N<u>C</u>H$_2CNO_2$), 59.0 (NCH_2CH_2N), 53.8 ($NHCH_2Ph$), 53.2 (NH<u>C</u>H$_2$C). Elemental analysis: calculated C 72.94%, H 7.26%, N 12.60%; found C 72.92%, H 7.21%, N 12.62%.

Method b

Hydroxymethyl diazepine **1** (264 mg, 0.74 mmol) was dissolved in dry THF (3 ml). Benzylamine (0.32 ml, 2.96 mmol) was added, followed by paraformaldehyde (27 mg, 0.89 mmol). The mixture was stirred at 50 °C for 15 hours. After filtration and removal of the solvent under reduced pressure, the residue was purified by column chromatography (SiO_2, PetEt/EtOAc 95:5). Yield (oil): 16%.

See above for characterization.

Method c

Hydroxymethyl diazepine **1** (284 mg, 0.80 mmol) was dissolved in benzylamine (3 ml). The mixture was stirred at 50 °C for 15 hours. After removal of most benzylamine under high vacuum overnight, the residue was purified by column chromatography (SiO_2, PetEt/EtOAc 95:5). Yield (oil): 27%.

See above for characterization.

6-(1-piperidyl)methyl-6-nitro-1,4-dibenzylperhydro-1,4-diazepine (14)

Purified by column chromatography (SiO_2, PetEt/EtOAc 8:2). Yield (oil): 73%.
TLC (PetEt/EtOAc 8:2): R_f 0.41. ESI$^+$ MS, m/z: 423 ([M+H]$^+$). IR (KBr disk), cm^{-1}: 3029, 2933, 2926, 2823, 2806, 1534, 1494, 1454, 1443, 1360, 1318, 1147, 1128, 1066, 1025, 957, 860, 853, 741, 697. ^{1}H NMR (400 MHz, 25 °C, $CDCl_3$), δ (ppm): 7.4-7.2 (m, 10H, Ph), 3.76 (d, $^2J_{HH}$ = 13.4 Hz, 2H, PhC<u>H</u>H'), 3.64 (d, $^2J_{HH}$ = 13.4 Hz, 2H, PhCH<u>H</u>'), 3.54 (d, $^2J_{HH}$ = 14.3 Hz, 2H, N_{Diaz}C<u>H</u>H'CNO_2), 3.06 (d, $^2J_{HH}$ = 14.3 Hz, 2H, N_{Diaz}CH<u>H</u>'CNO_2), 2.65 (s, 2H, $N_{Pi}CH_2CNO_2$), 2.53 (m, 4H, NCH_2CH_2N), 2.22 (m, 4H, CH_2C<u>H</u>$_2N_{Pi}$), 1.44 (m, 4H, C<u>H</u>$_2CH_2N_{Pi}$), 1.32 (m, 2H, C<u>H</u>$_2CH_2CH_2N_{Pi}$). ^{13}C NMR (100 MHz, 25 °C, $CDCl_3$), δ (ppm): 139.4 (C^i), 129.0 (C^m), 128.4 (C^o), 127.3 (C^p), 95.3 (CNO_2), 64.2 (N_{Pi}<u>C</u>H$_2CNO_2$), 64.1 (CH_2Ph), 61.2 (N_{Diaz}<u>C</u>H$_2CNO_2$), 58.4 (NCH_2CH_2N), 56.2 (CH_2<u>C</u>H$_2N_{Pi}$), 26.3 (<u>C</u>H$_2CH_2N_{Pi}$), 24.0 (<u>C</u>H$_2CH_2CH_2N_{Pi}$). Elemental analysis: calculated C 71.06%, H 8.11%, N 13.26%; found C 71.14%, H 8.22%, N 13.31%.

6-(4-morpholino)methyl-6-nitro-1,4-dibenzylperhydro-1,4-diazepine (15)

Purified by column chromatography (SiO_2, PetEt/EtOAc 8:2). Yield (oil): 71%.
TLC (PetEt/EtOAc 8:2): R_f 0.37. ESI$^+$ MS, m/z: 425 ([M+H]$^+$). IR (KBr disk), cm^{-1}: 3027, 2949, 2927, 2851, 2822, 1534, 1494, 1463, 1455, 1361, 1318, 1142, 1128, 1097, 1027, 955, 851, 835, 743, 698. ^{1}H NMR (400 MHz, 25 °C, $CDCl_3$), δ (ppm): 7.4-7.2 (m, 10H, Ph), 3.75 (d, $^2J_{HH}$ = 13.4 Hz, 2H, PhC<u>H</u>H'), 3.61 (d, $^2J_{HH}$ = 13.4 Hz, 2H, PhCH<u>H</u>'), 3.52 (d, $^2J_{HH}$ = 13.9 Hz, 2H, N_{Diaz}C<u>H</u>H'CNO_2), 3.50 (t, J = 4.6 Hz, 4H, OC<u>H</u>$_2CH_2N$), 3.03 (d, $^2J_{HH}$ = 13.9 Hz, 2H, N_{Diaz}CH<u>H</u>'CNO_2), 2.61 (s, 2H, $N_{Mor}CH_2CNO_2$), 2.57 (m, 4H, NCH_2CH_2N), 2.18 (t, J = 4.6 Hz, 4H, OCH_2C<u>H</u>$_2N$). ^{13}C NMR (100 MHz, 25 °C, $CDCl_3$), δ (ppm): 139.3 (C^i), 129.1 (C^m), 128.4 (C^o), 127.3 (C^p), 94.8 (CNO_2), 67.1

(O<u>C</u>$H_2$$CH_2$N), 64.2 ($CH_2$Ph), 63.6 ($N_{Mor}$<u>C</u>$H_2$$CNO_2$), 60.9 ($N_{Diaz}$<u>C</u>$H_2$$CNO_2$), 54.9 (O$CH_2$<u>C</u>$H_2$N). Elemental analysis: calculated C 67.90%, H 7.60%, N 13.20%; found C 67.67%, H 7.67%, N 13.26%.

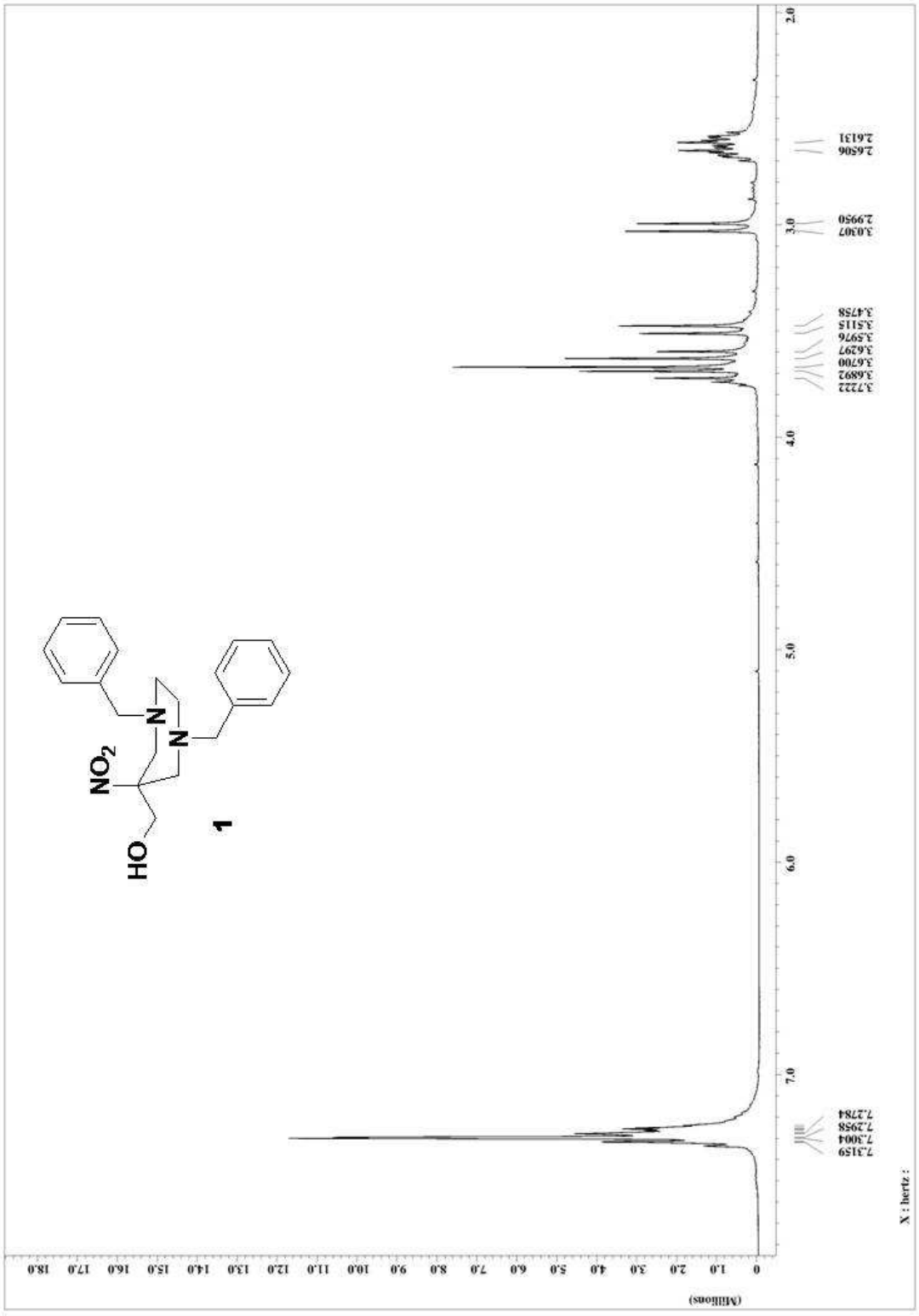
6-amino-6-*t*-butoxycarbonylethyl-1,4-dibenzylperhydro-1,4-diazepine (16)

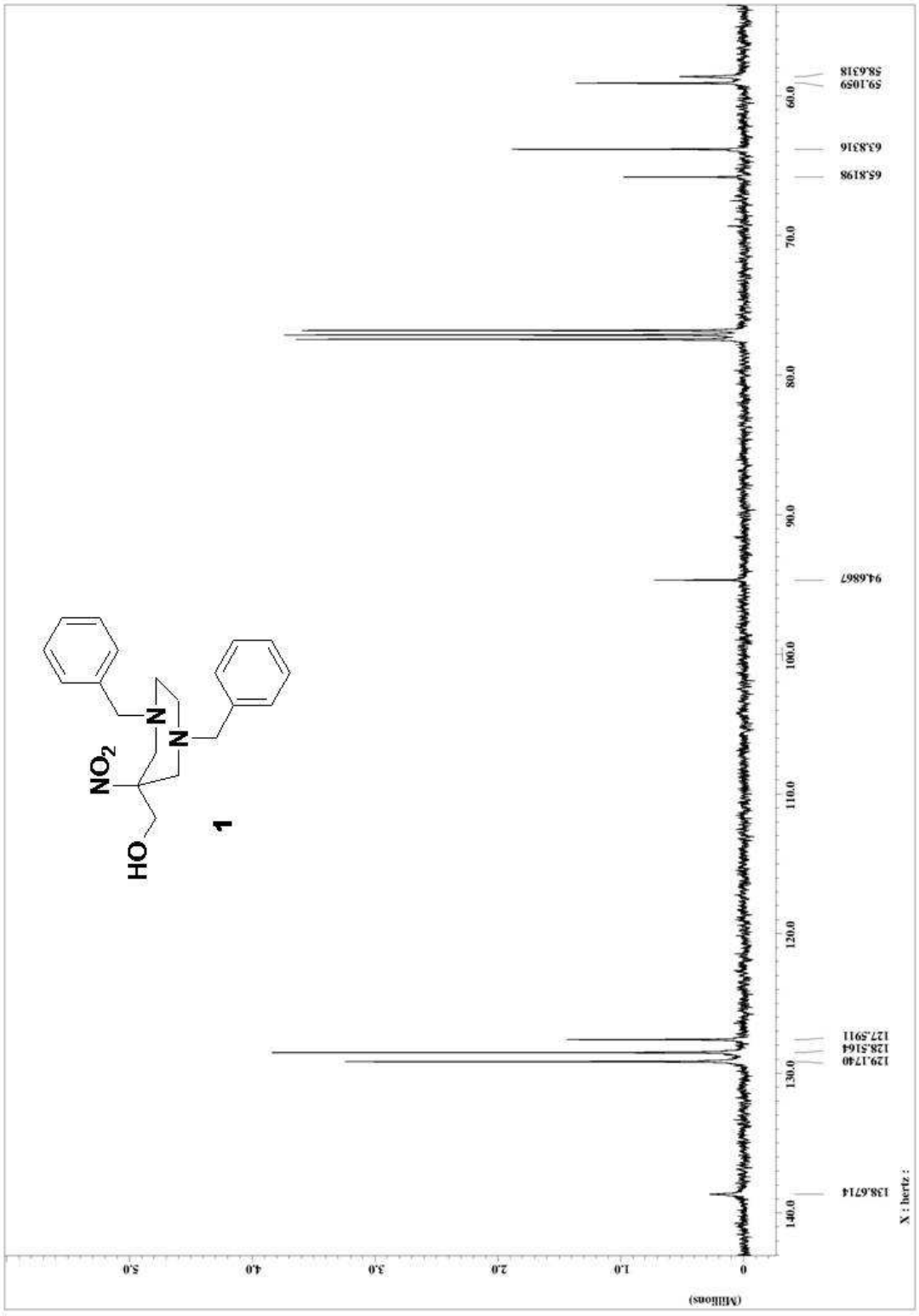
Nitrodiazepine **5** (104 mg, 0.23 mmol) was dissolved in EtOH (5 ml). Nickel-Raney (21 mg in 1 ml H_2O) was added and the suspension was stirred at room temperature for 15 hours. After filtration through Celite, the residue was dried under vacuum, suspended in Et_2O (2 ml) and filtered. The filtrate was evaporated under reduced pressure, leading to the desired product as a yellow colored wax (42 mg) that was characterized without further purification.
ESI^+ MS, m/z: 423 (M^+). IR (KBr disk), cm^{-1}: 3445, 3277, 2978, 2934, 2891, 1727, 1575, 1454, 1415, 1393, 1367, 1257, 1152, 1027, 848, 758, 704. ^{1}H NMR (400 MHz, 25 °C, $CDCl_3$), δ (ppm): 7.4-7.2 (m, 10H, Ph), 3.69 (d, $^2J_{HH}$ = 13.0 Hz, 2H, PhC<u>H</u>H'), 3.59 (d, $^2J_{HH}$ = 13.0 Hz, 2H, PhCH<u>H</u>'), 3.38 (d, $^2J_{HH}$ = 14.1 Hz, 2H, NC<u>H</u>H'CNH_2), 2.71 (d, $^2J_{HH}$ = 14.1 Hz, 2H, NCH<u>H</u>'CNH_2), 2.35 (m, 4H, NCH_2CH_2N), 2.24 (br s, 2H, NH_2), 1.54 (m, 2H, CH_2C=O), 1.44 (s, 9H, CH_3), 1.27 (m, 2H, C<u>H</u>$_2$$CH_2C$=O). ^{13}C NMR (100 MHz, 25 °C, $CDCl_3$), δ (ppm): 172.8 (C=O), 139.7 (C^i), 129.1 (C^m), 128.2 (C^o), 127.1 (C^p), 80.2 ($C_q^{t\text{-}Bu}$), 64.5 (N<u>C</u>$H_2$$CNH_2$), 60.4 ($CH_2$Ph), 59.2 ($NCH_2CH_2N$), 43.2 ($CNH_2$), 30.4 ($CH_3$), 21.2 (<u>C</u>$H_2C$=O), 17.1 (<u>C</u>$H_2CH_2C$=O).

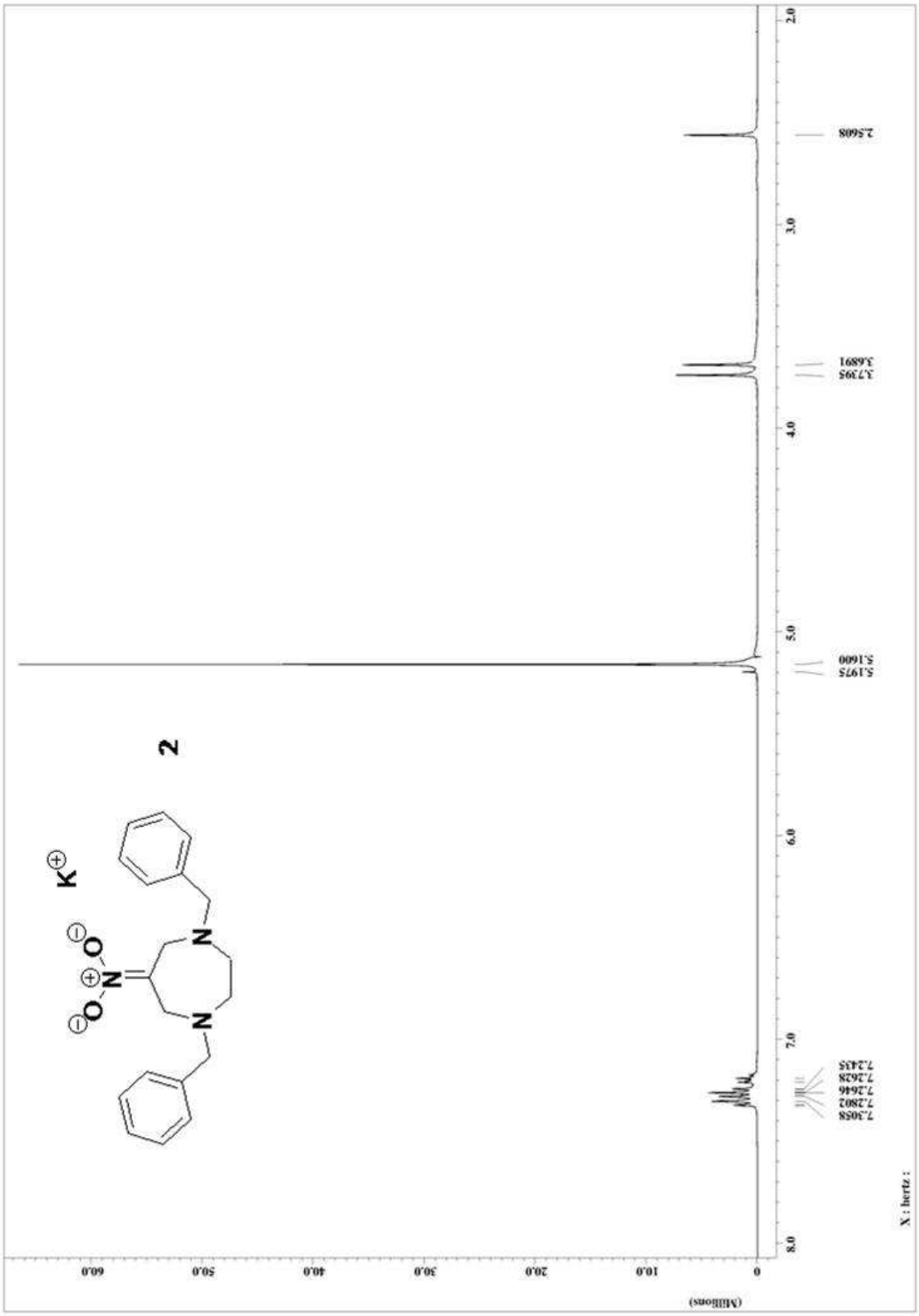
6-amino-6-*t*-butoxycarbonylethylperhydro-1,4-diazepine (17)

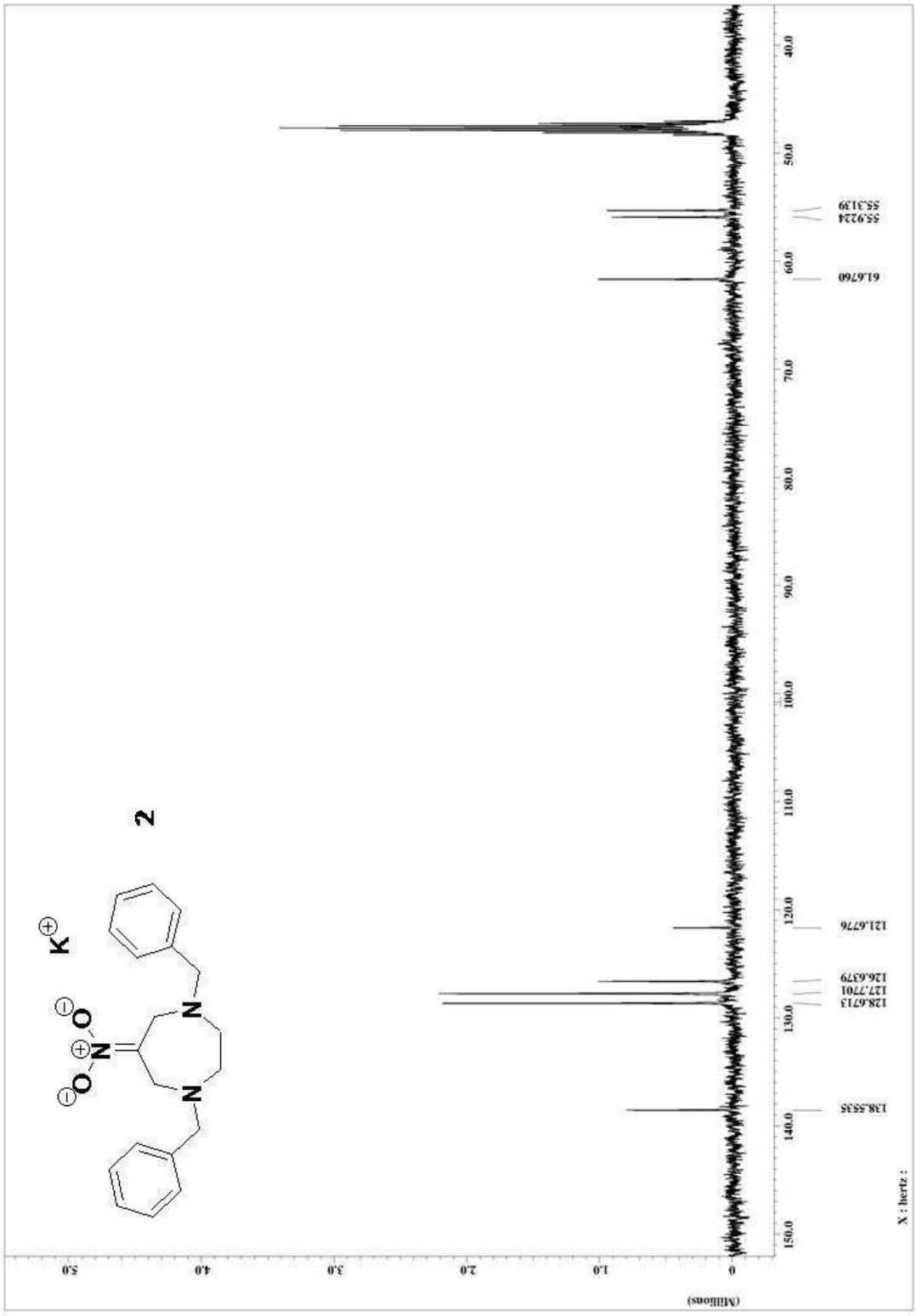
Nitrodiazepine **5** (206 mg, 0.45 mmol) was dissolved in MeOH (30 ml), in a flask equipped with a mechanical stirrer and connected to a H_2 cylinder. 10 w% Pd/C (21 mg) and AcOH (78 µl, 1.35 mmol) were added, and the flask underwent 3 times a vacuum-H_2 cycle. The suspension was stirred (2000 rpm) at room temperature for 4 hours. After filtration through Celite, the filtrate was evaporated under reduced pressure, leading to the desired crude product as a yellow colored wax (78 mg) that was characterized without further purification.
ESI^+ MS, m/z: 244 ($[M+H]^+$). ^{1}H NMR (400 MHz, 25 °C, CD_3OD), δ (ppm):, 3.0-2.8 (m, 4H, NCH_2CH_2N), 2.92 (d, $^2J_{HH}$ = 14.2 Hz, 2H, NC<u>H</u>H'CNH_2), 2.77 (d, $^2J_{HH}$ = 14.1 Hz, 2H, NCH<u>H</u>'CNH_2), 1.69 (m, 2H, CH_2C=O), 1.55 (s, 9H, CH_3), 1.39 (m, 2H, C<u>H</u>$_2$$CH_2C$=O). ^{13}C NMR (100 MHz, 25 °C, CD_3OD), δ (ppm): 173.1 (C=O), 81.4 ($C_q^{t\text{-}Bu}$), 54-47 (N<u>C</u>$H_2$$CNH_2$ + NCH_2CH_2N), 49.6 (CNH_2), 32.1 (CH_3), 23.9 (<u>C</u>H_2C=O), 21.9 (<u>C</u>H_2CH_2C=O).

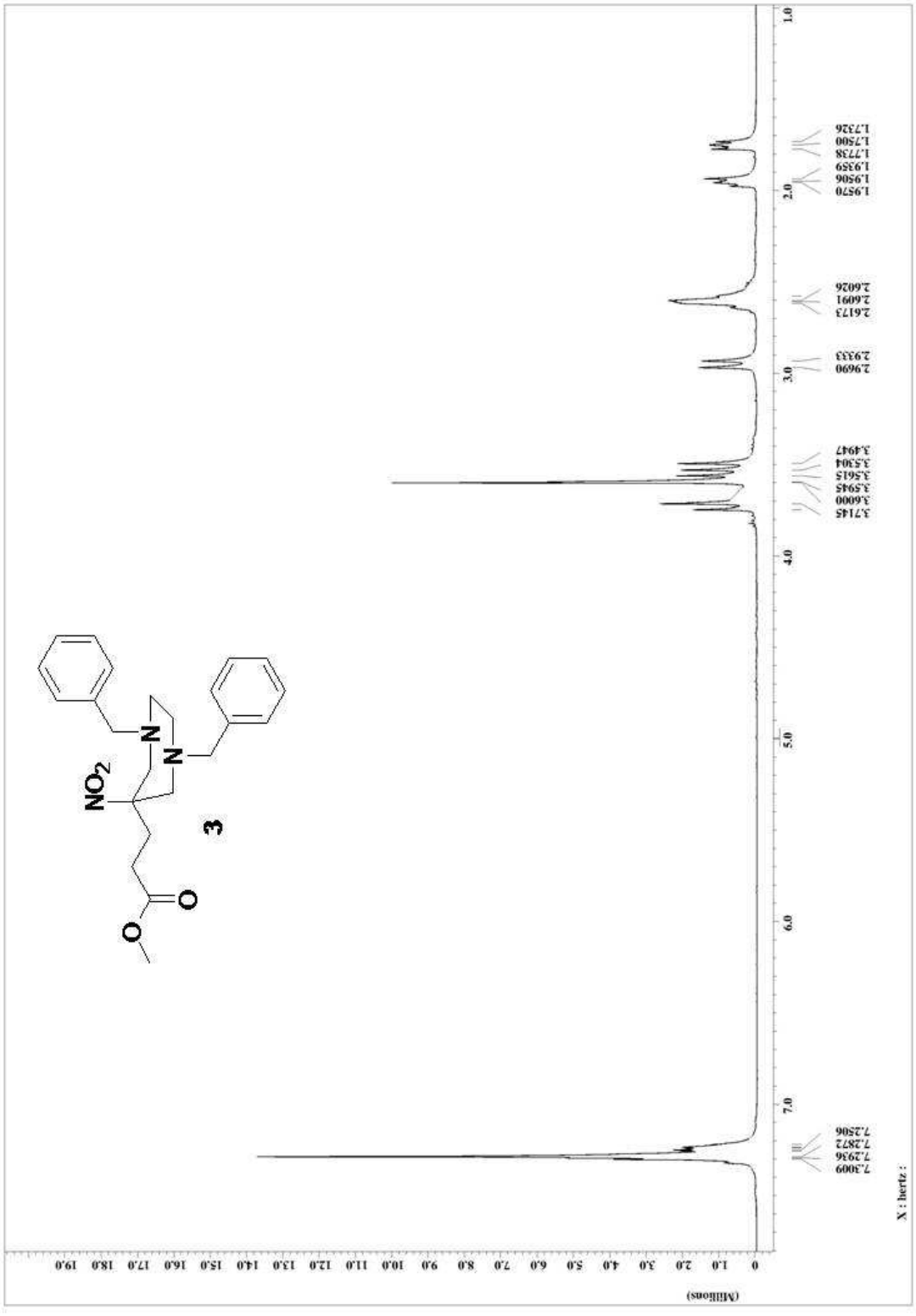
3. ^{1}H and ^{13}C NMR Spectra

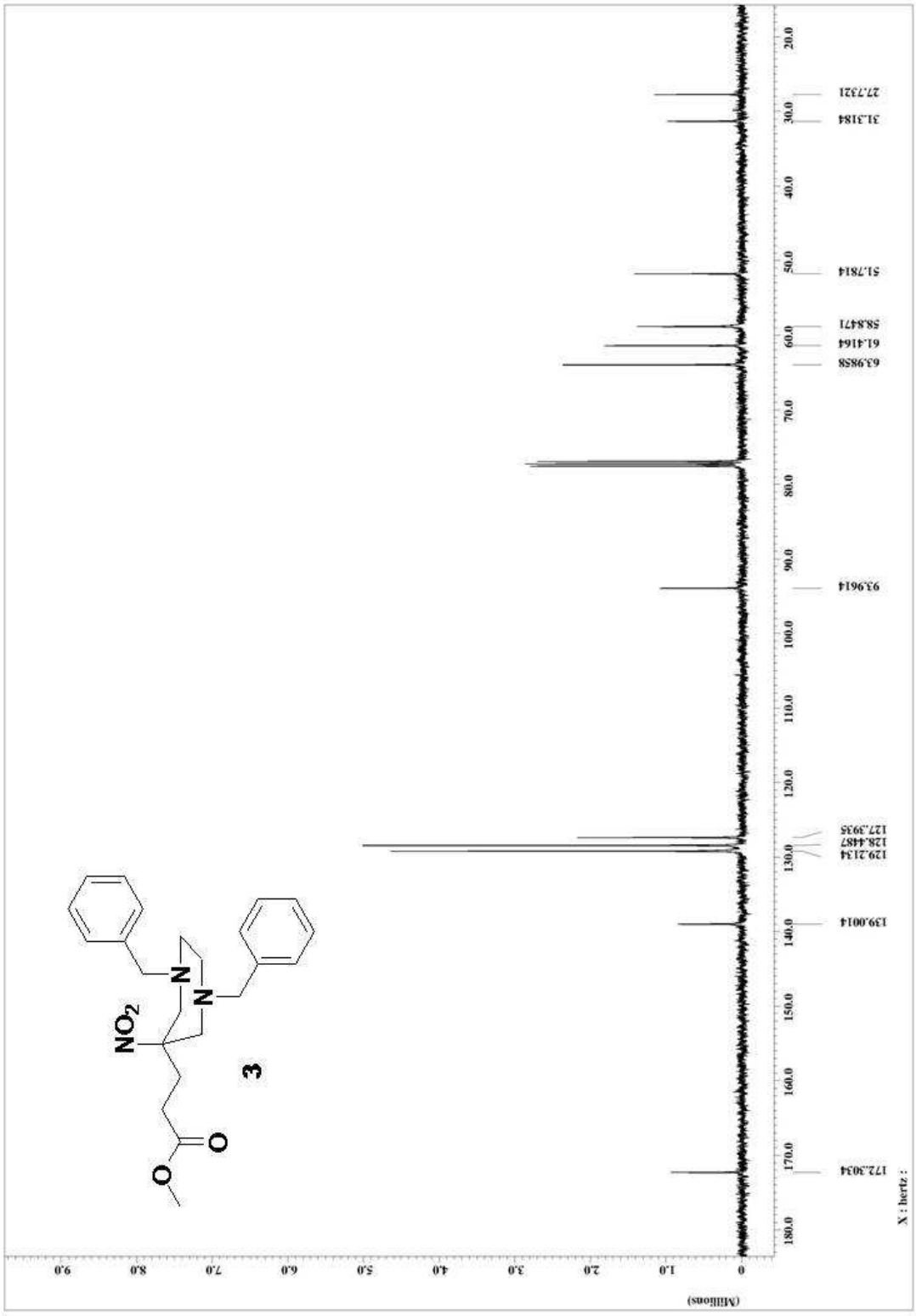


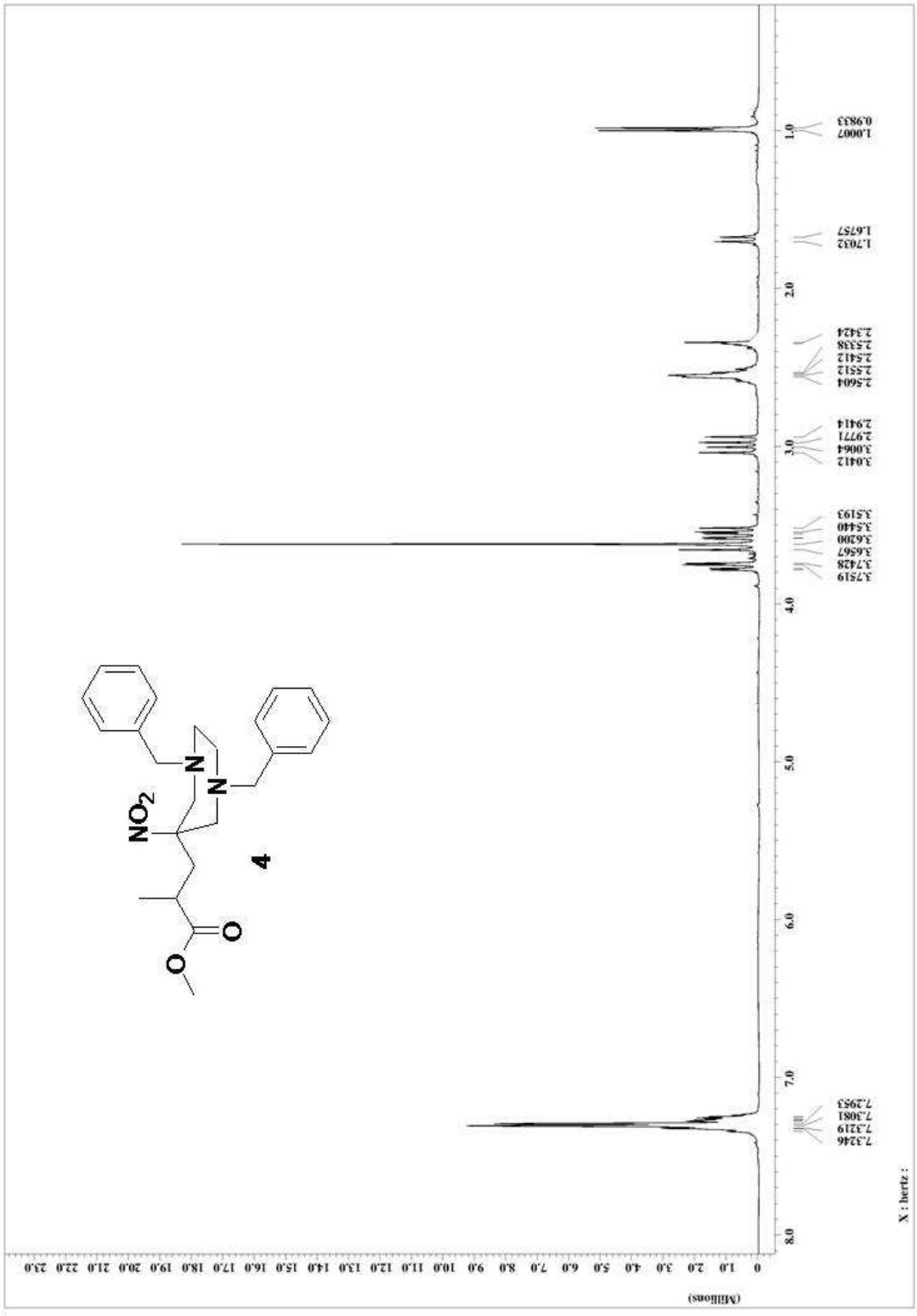

1
HO
NO2
N
N
(Millions)
0
1.0
2.0
3.0
4.0
5.0
X : hertz :
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
138.6714
129.1740
128.5164
127.5911
94.6867
65.8198
63.8316
59.1059
58.6318

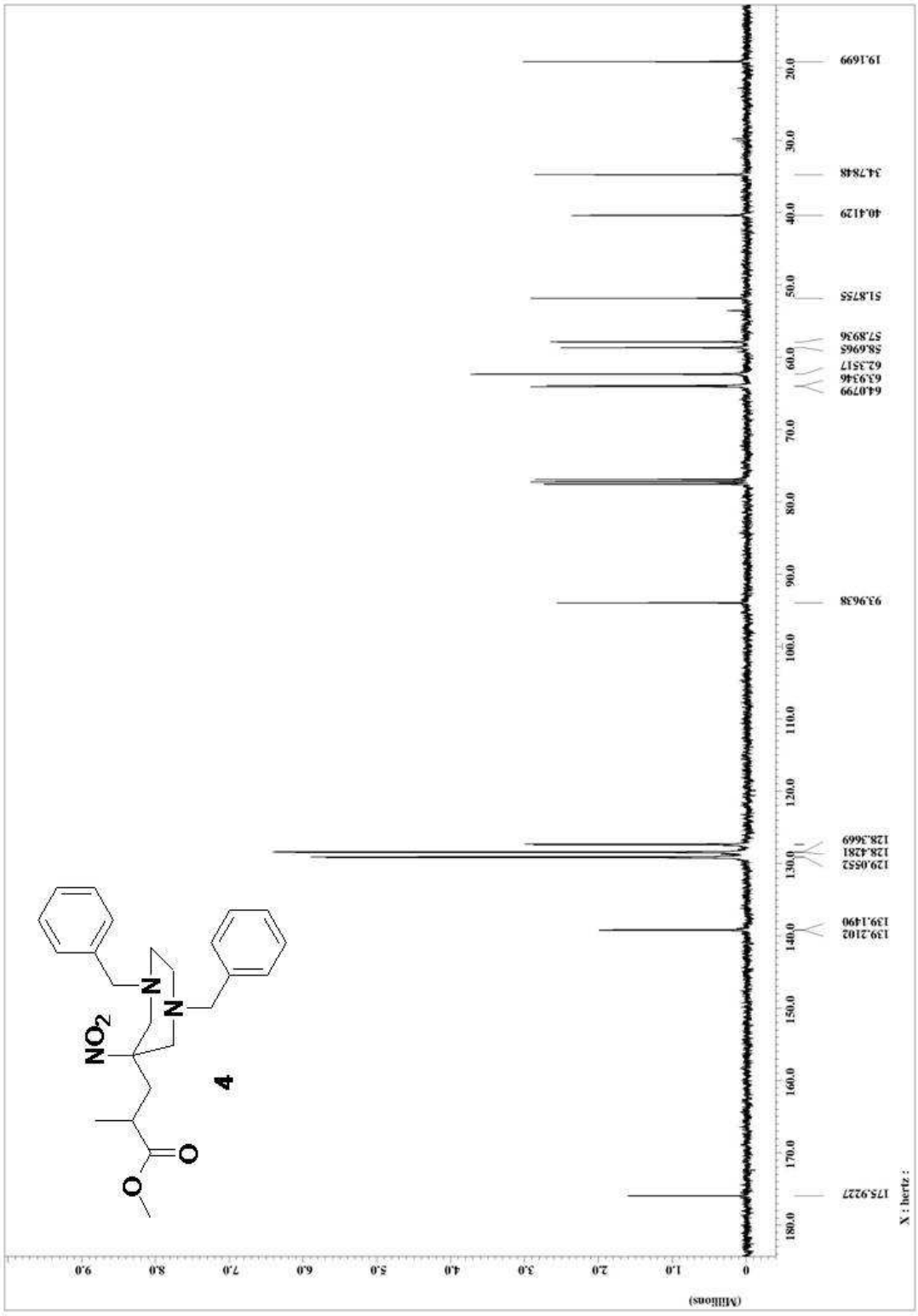

2
K
N
N
O
O
N
(Millions)
0
10.0
20.0
30.0
40.0
50.0
60.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
2.5608
3.7395
3.6891
5.1975
5.1600
7.3058
7.2802
7.2646
7.2628
7.2435
X : hertz :

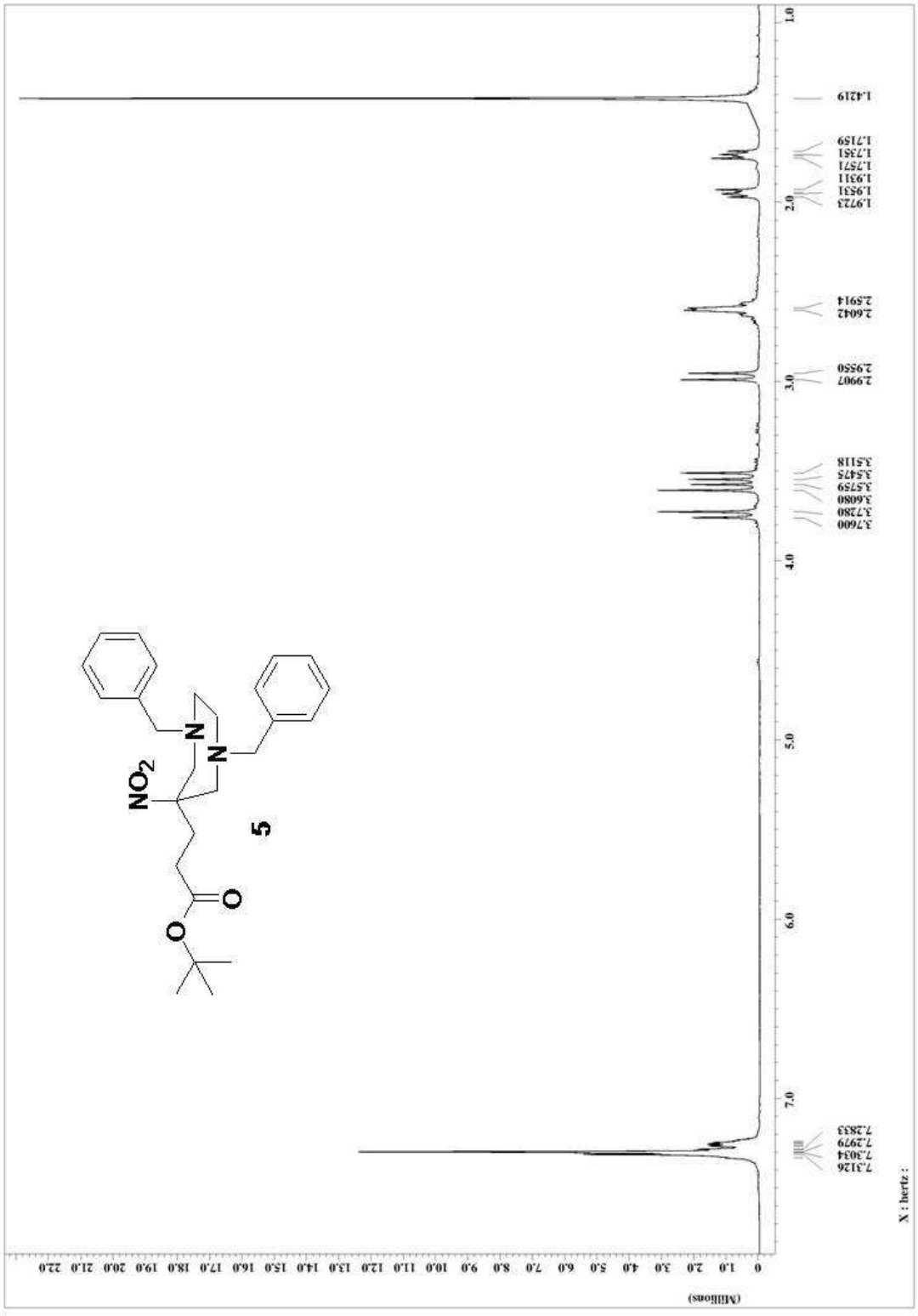

2
K
(Millions)
X : hertz :
138.5535
128.6713
127.7701
126.6379
121.6776
61.6760
55.9224
55.3139

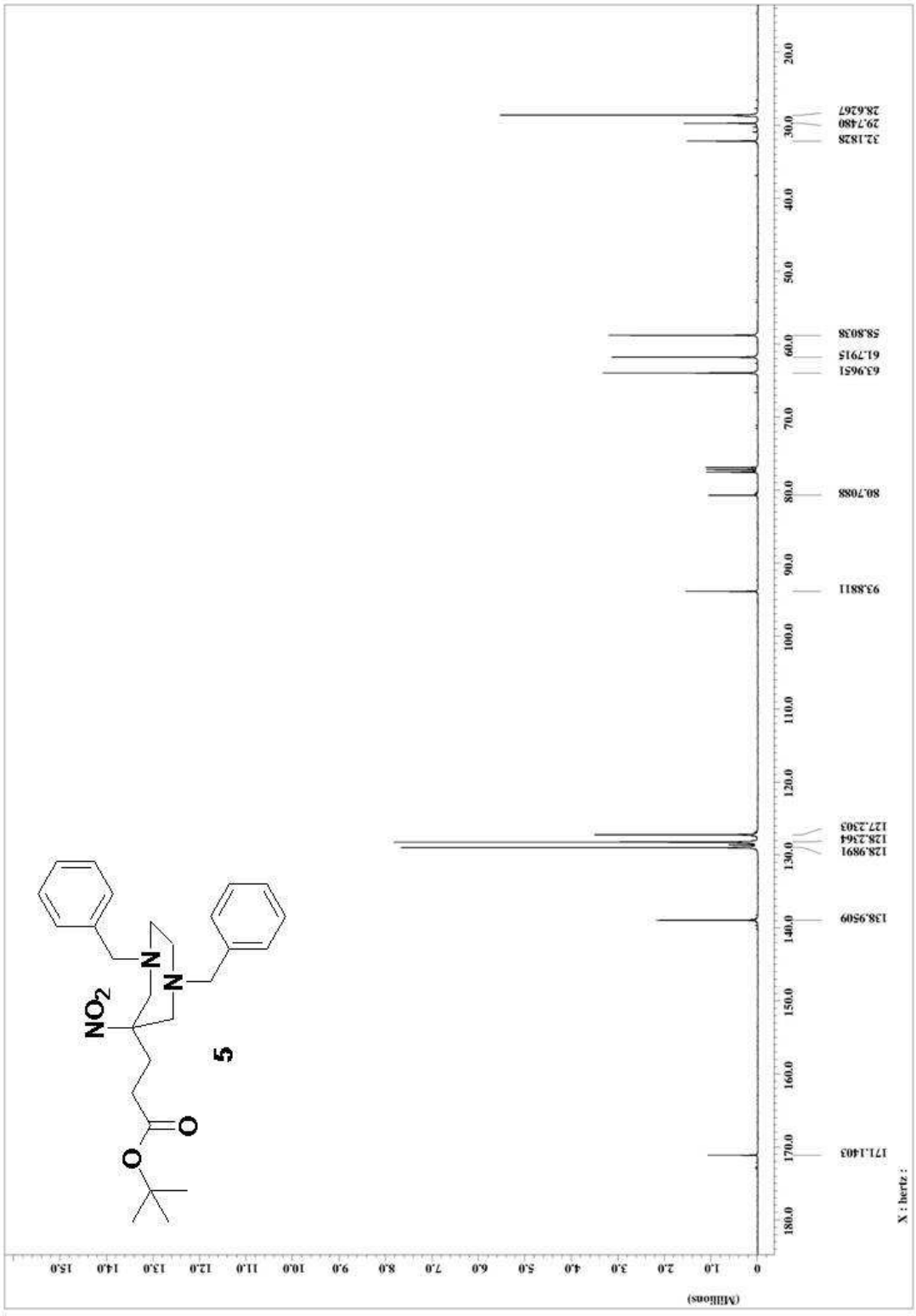

NO2
N
N
O
O
3
X : hertz :
7.3009
7.2936
7.2872
7.2506
3.7145
3.6000
3.5945
3.5615
3.5304
3.4947
2.9690
2.9333
2.6173
2.6091
2.6026
1.9570
1.9506
1.9359
1.7738
1.7500
1.7326

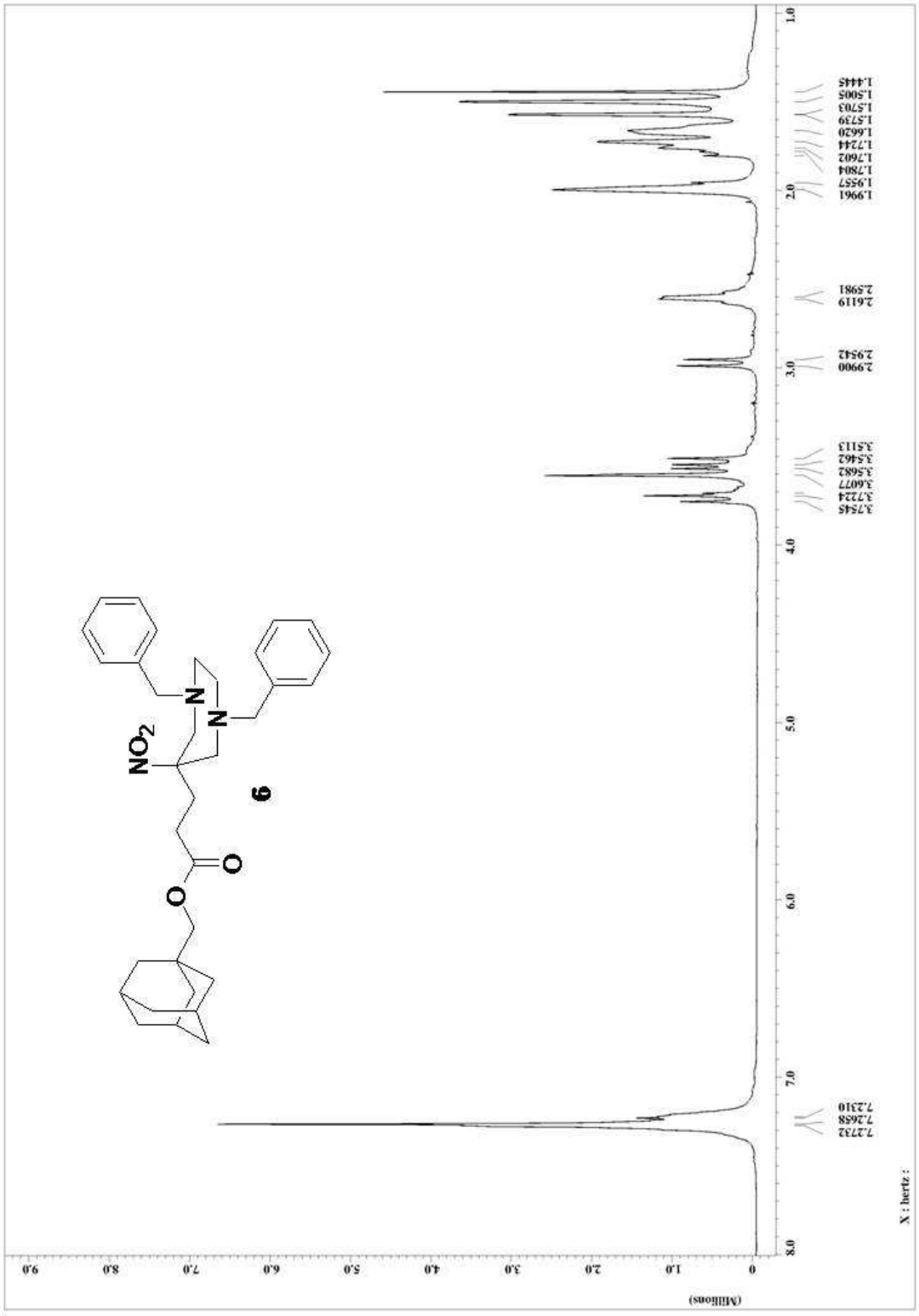

27.7321
31.3184
51.7814
58.8471
61.4164
63.9858
93.9614
129.2134
128.4487
127.3935
139.0014
172.3034
X : hertz :
(Millions)
3
NO2
N
N
O
O

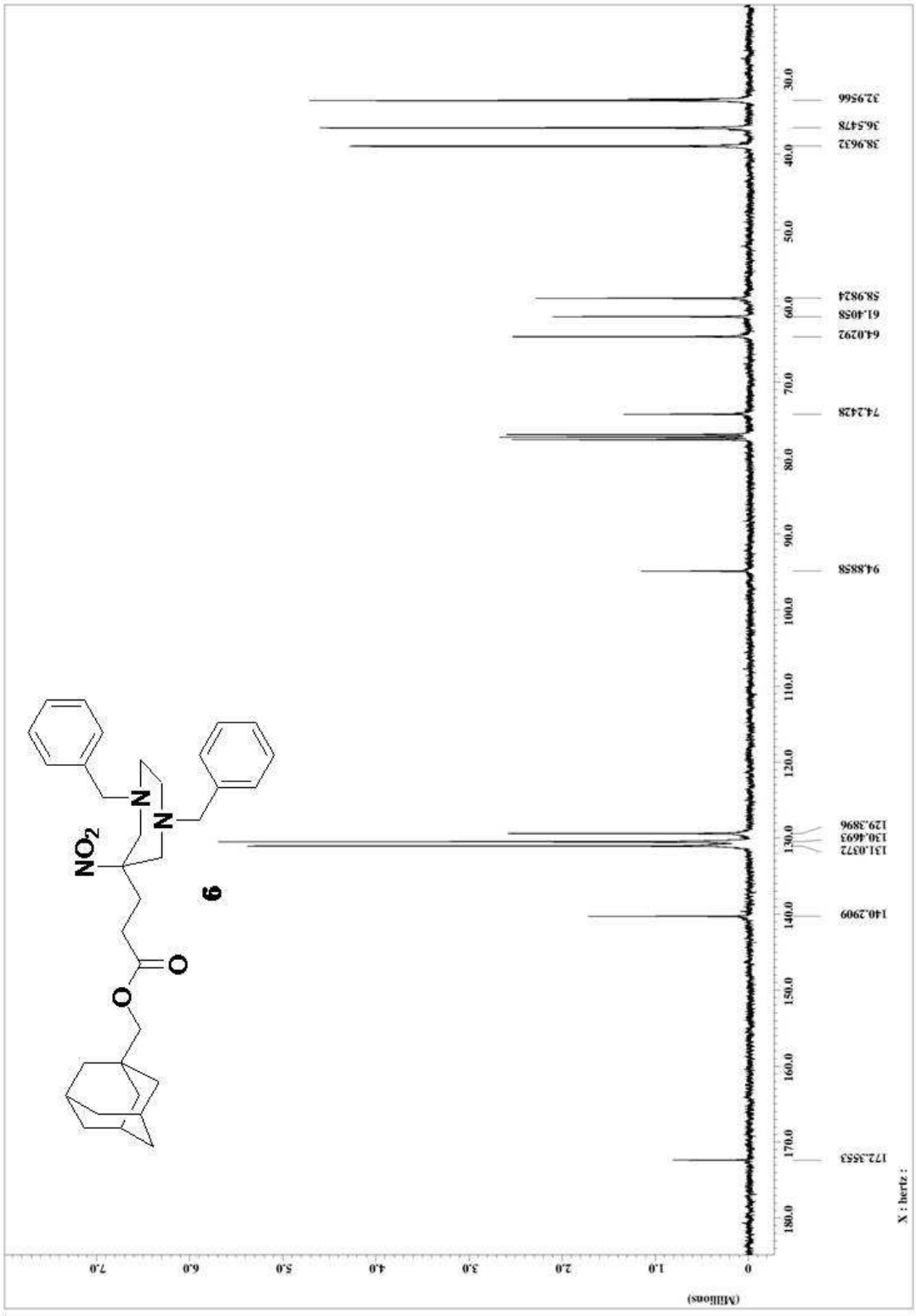

4
NO2
N
N
O
O
(Millions)
X : hertz :
7.3246
7.3219
7.3081
7.2953
3.7519
3.7428
3.6567
3.6200
3.5440
3.5193
3.0412
3.0064
2.9771
2.9414
2.5604
2.5512
2.5412
2.5338
2.3424
1.7032
1.6757
1.0007
0.9833

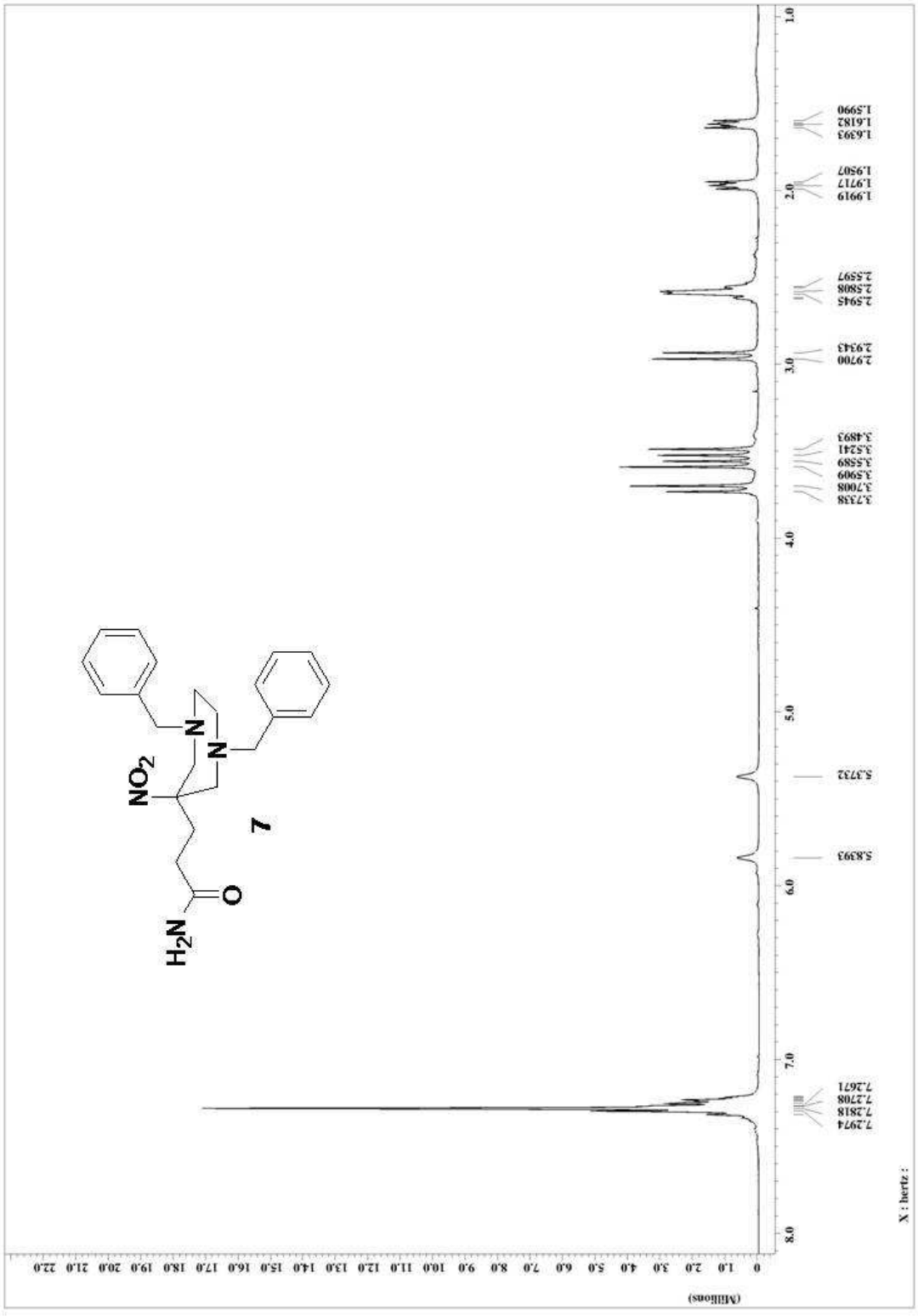

4
NO2
N
N
O
O
19.1699
34.7848
40.4129
51.8755
57.8936
58.6965
62.3517
63.9346
64.0799
93.9638
128.3669
128.4281
129.0552
139.1490
139.2102
175.9227
X : hertz :
(Millions)

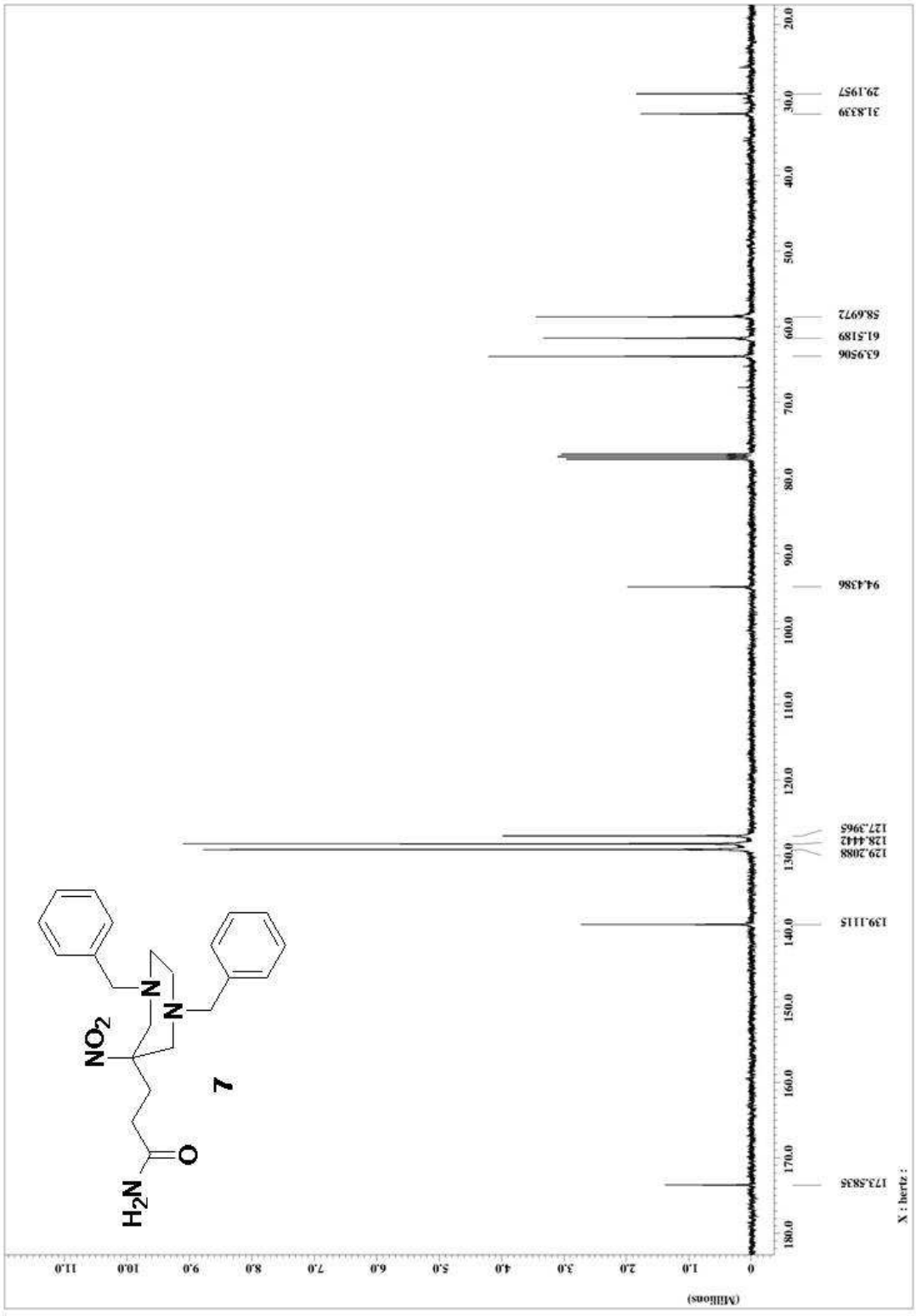

7.3126
7.3034
7.2979
7.2833
1.4219
1.9723
1.9531
1.9311
1.7571
1.7351
1.7159
2.6042
2.5914
2.9907
2.9550
3.7600
3.7280
3.6080
3.5759
3.5475
3.5118
X : hertz :
(Millions)
5

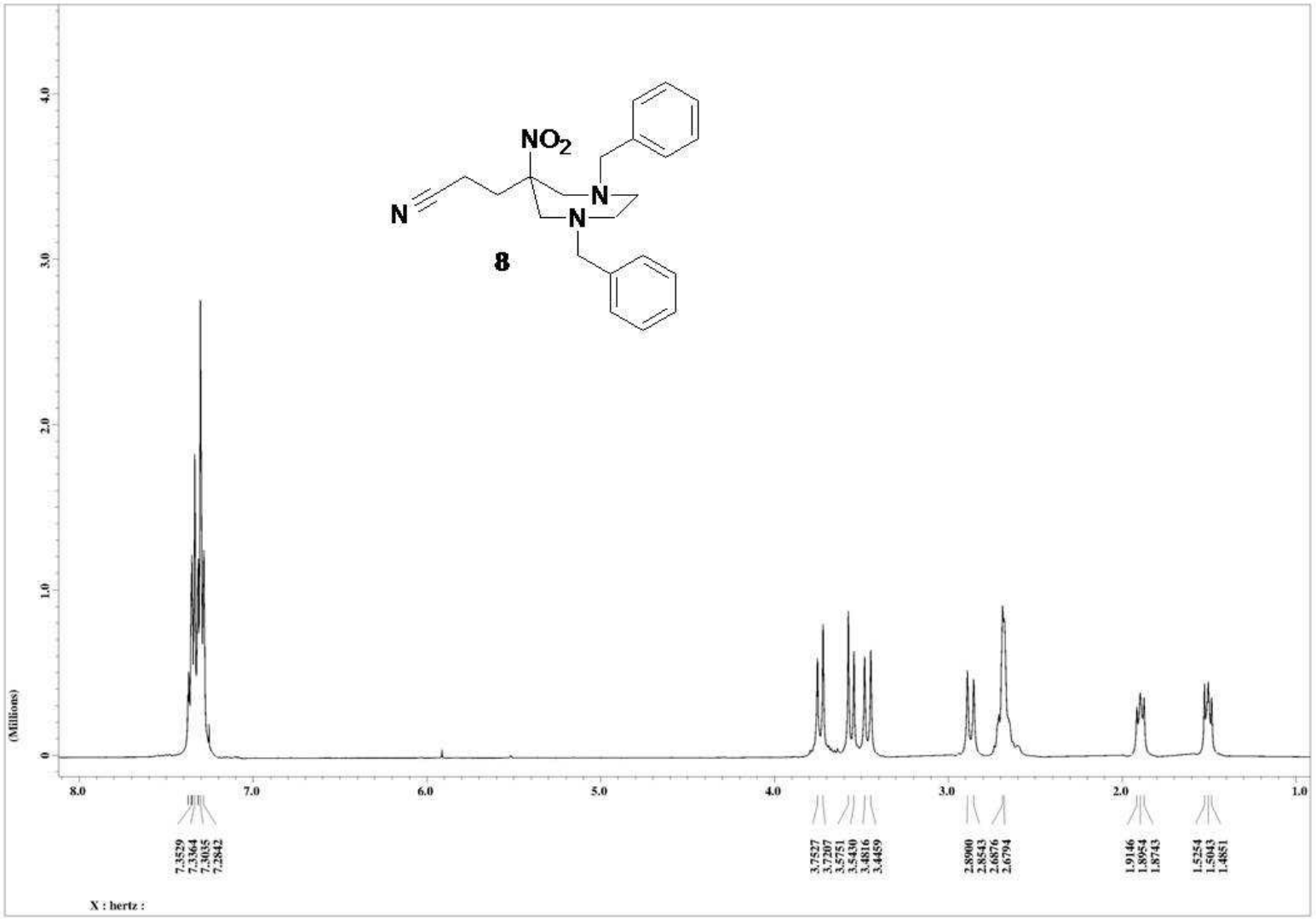

5
NO2
N
N
O
O
28.6267
29.7480
32.1828
58.8038
61.7915
63.9651
80.7088
93.8811
127.2303
128.2364
128.9891
138.9509
171.1403
X : hertz :
(Millions)

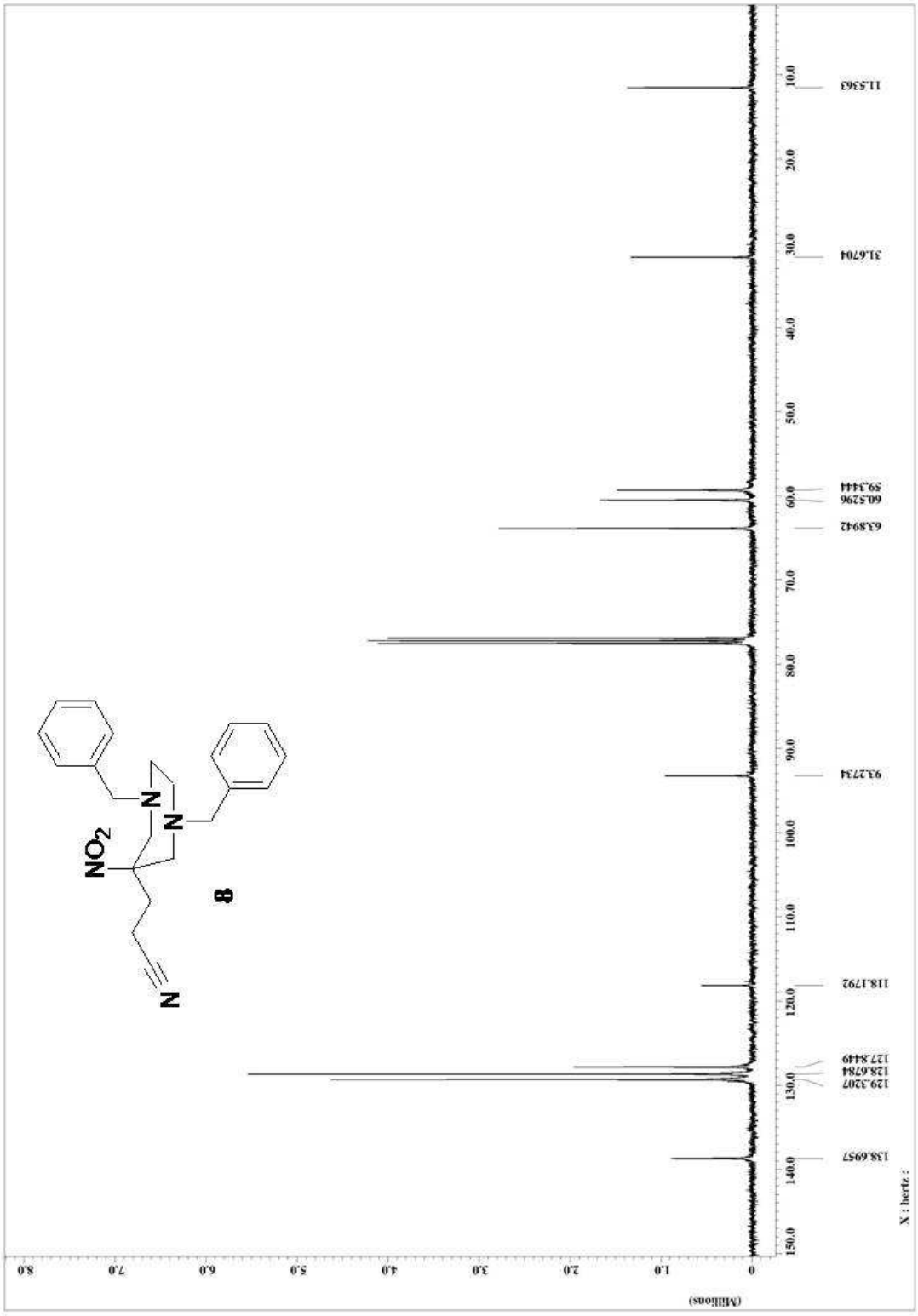

6
NO2
N
N
O
O
X : hertz :
7.2732
7.2658
7.2310
3.7545
3.7224
3.6077
3.5682
3.5462
3.5113
2.9900
2.9542
2.6119
2.5981
1.9961
1.9557
1.7804
1.7602
1.7244
1.6620
1.5739
1.5703
1.5005
1.4445

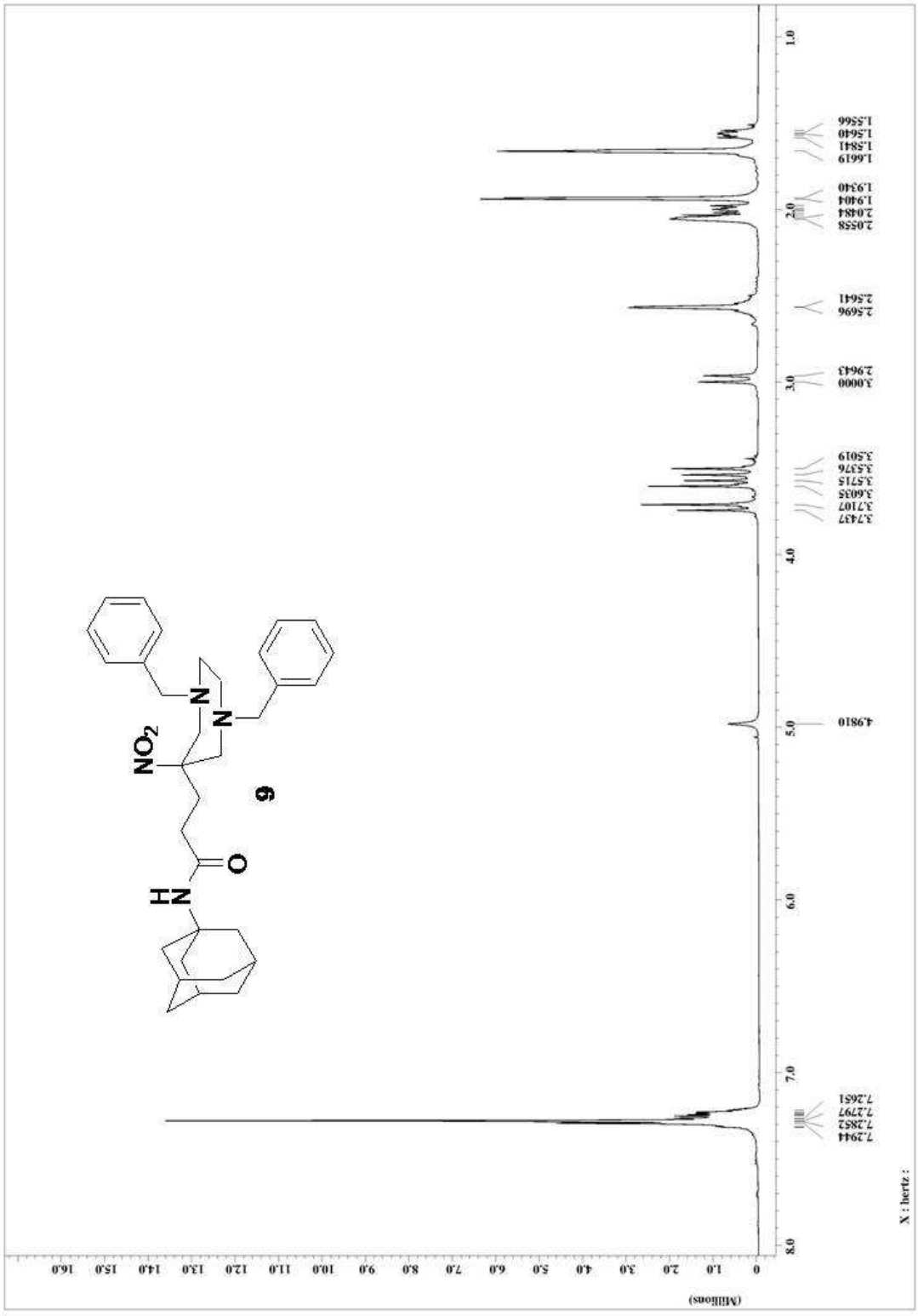

6
NO2
N
N
O
O
(Millions)
0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
X : hertz :
172.3553
140.2909
131.0372
130.4693
129.3896
94.8858
74.2428
64.0292
61.4058
58.9824
38.9632
36.5478
32.9566

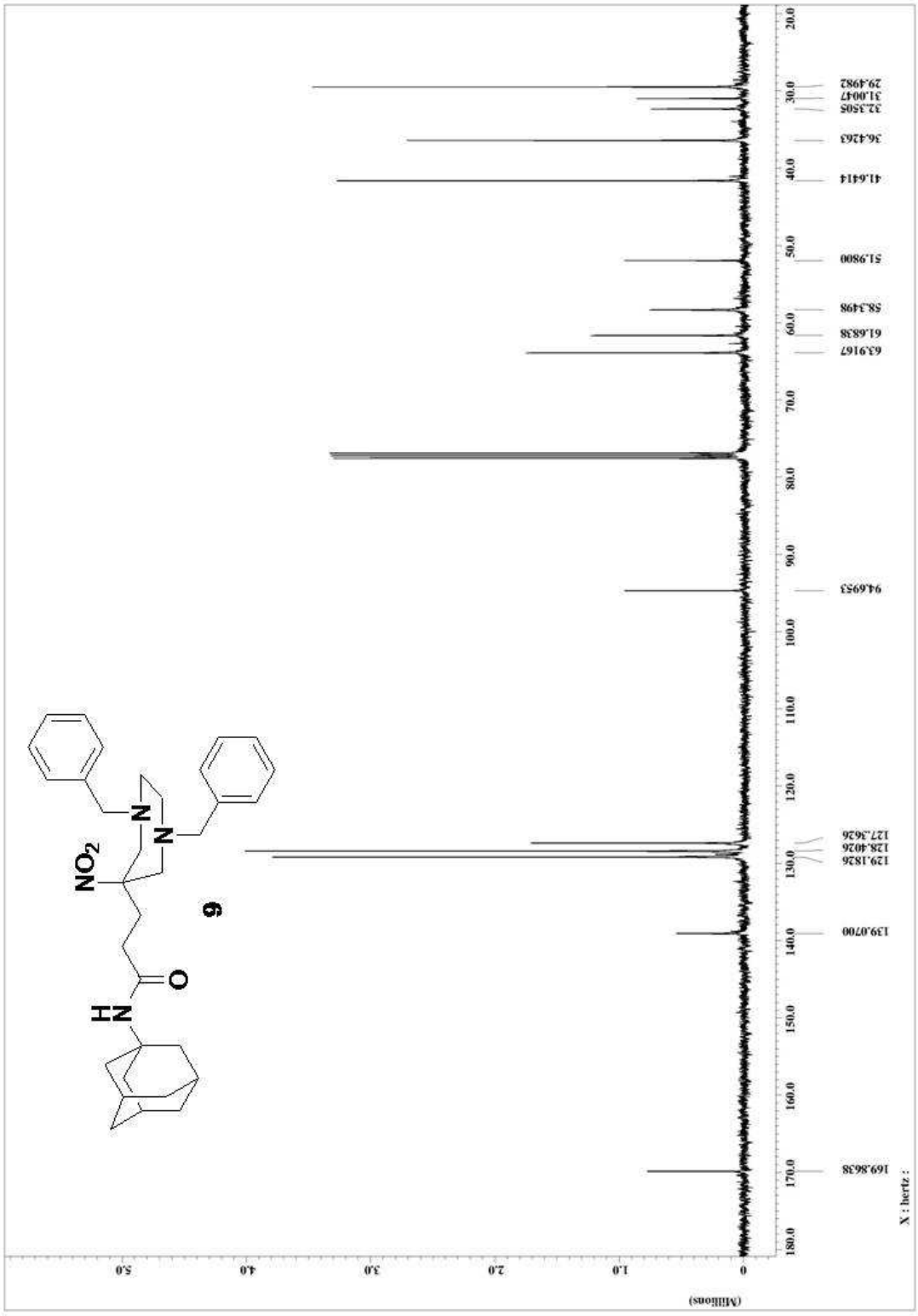

7
NO2
H2N
O
N
N
X : hertz :
7.2974
7.2818
7.2708
7.2671
5.8393
5.3732
3.7338
3.7008
3.5909
3.5589
3.5241
3.4893
2.9700
2.9443
2.5945
2.5808
2.5597
1.9919
1.9717
1.9507
1.6393
1.6182
1.5990

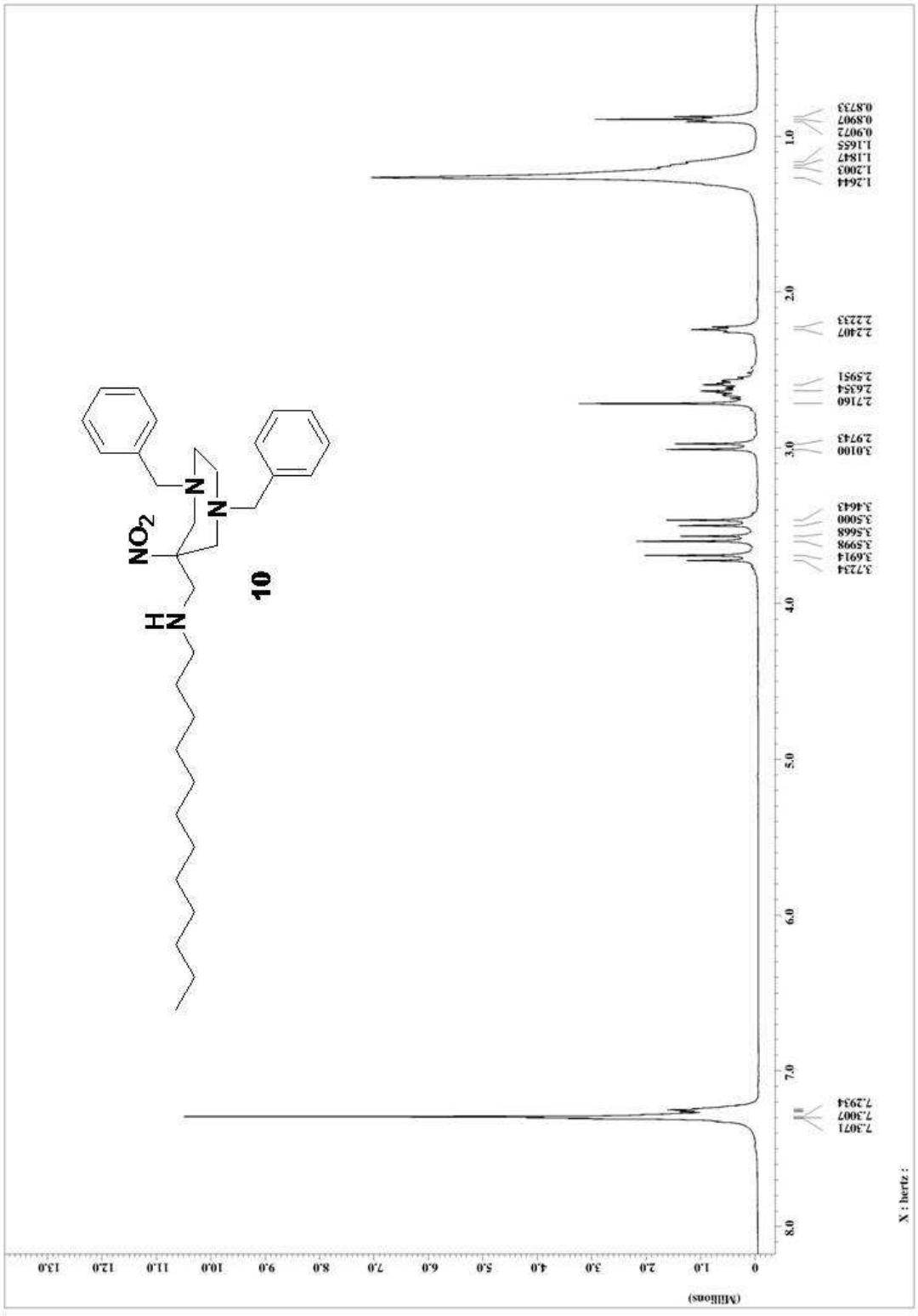

7
NO_2
H_2N
O
N
N
(Millions)
X : hertz :
173.5835
139.1115
129.2088
128.4442
127.3965
94.4386
63.9506
61.5189
58.6972
31.8339
29.1957

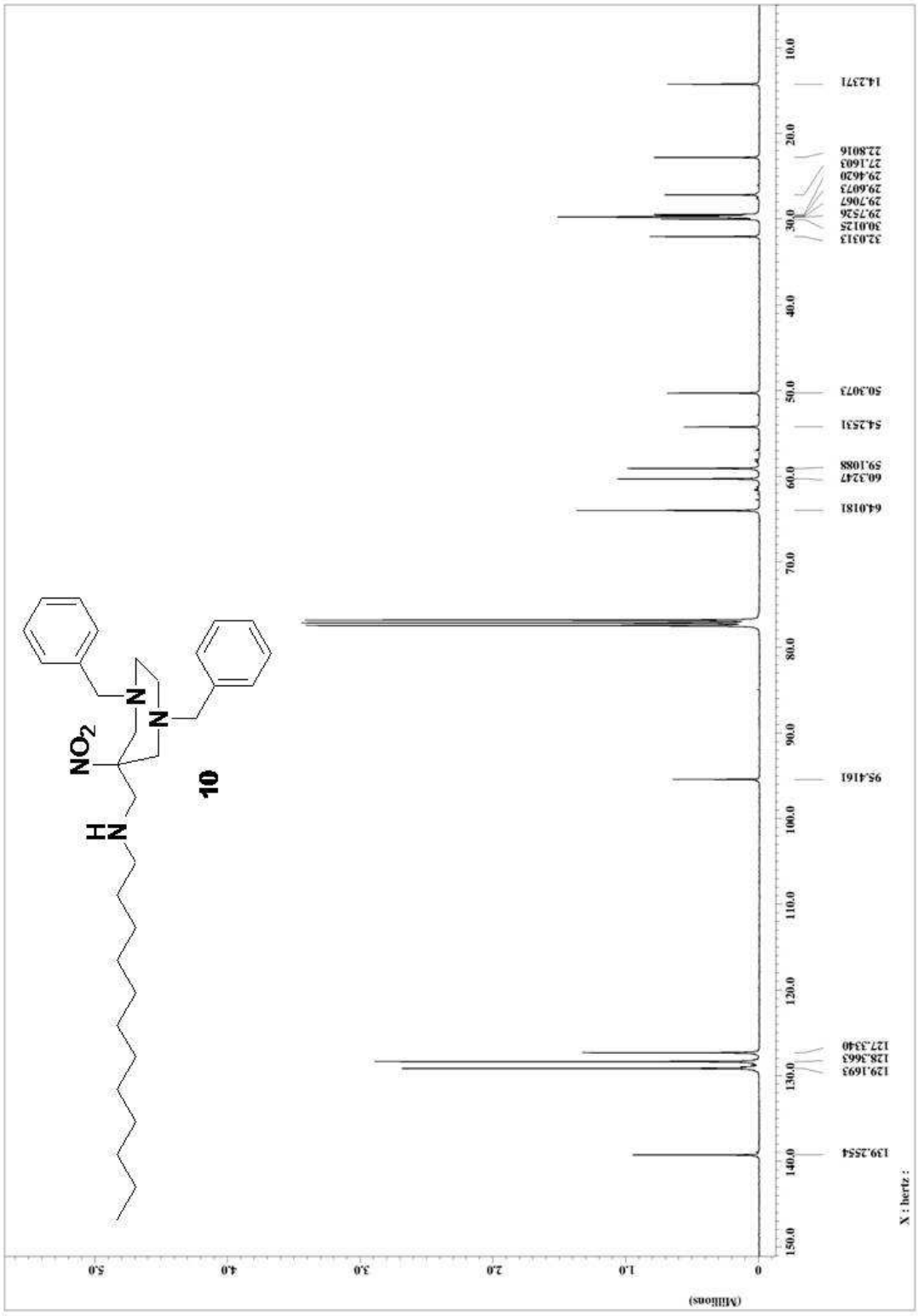

NO2
N
N
N
8
(Millions)
4.0
3.0
2.0
1.0
0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
7.3529
7.3364
7.3035
7.2842
3.7527
3.7307
3.5751
3.5430
3.4816
3.4459
2.8900
2.8543
2.6876
2.6794
1.9146
1.8954
1.8743
1.5254
1.5043
1.4851
X : hertz :

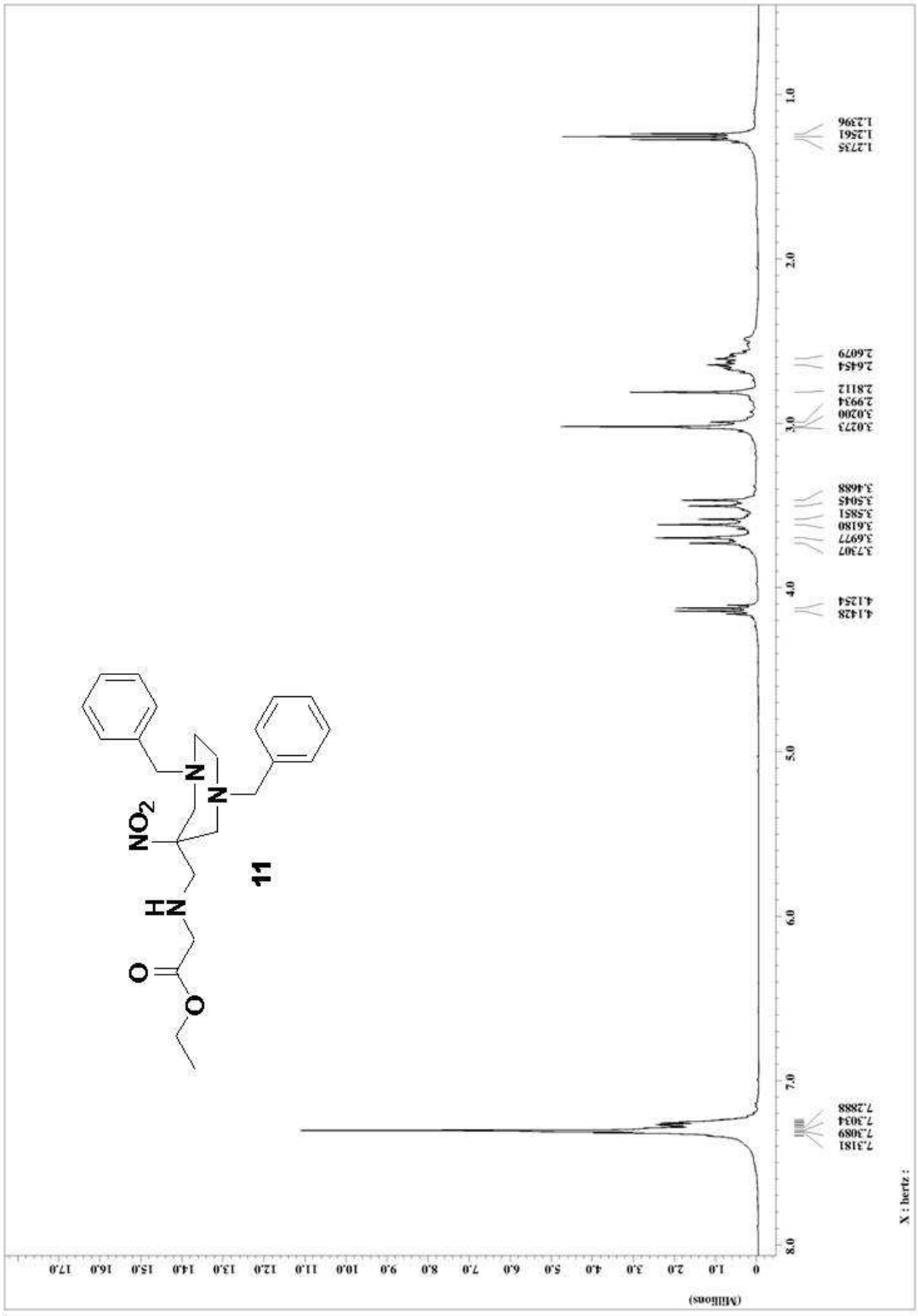

11.5363
31.6704
59.3444
60.5296
63.8942
93.2734
118.1792
127.3449
128.6784
129.3207
138.6957
X : hertz :
(Millions)
8
NO2
N
N
N

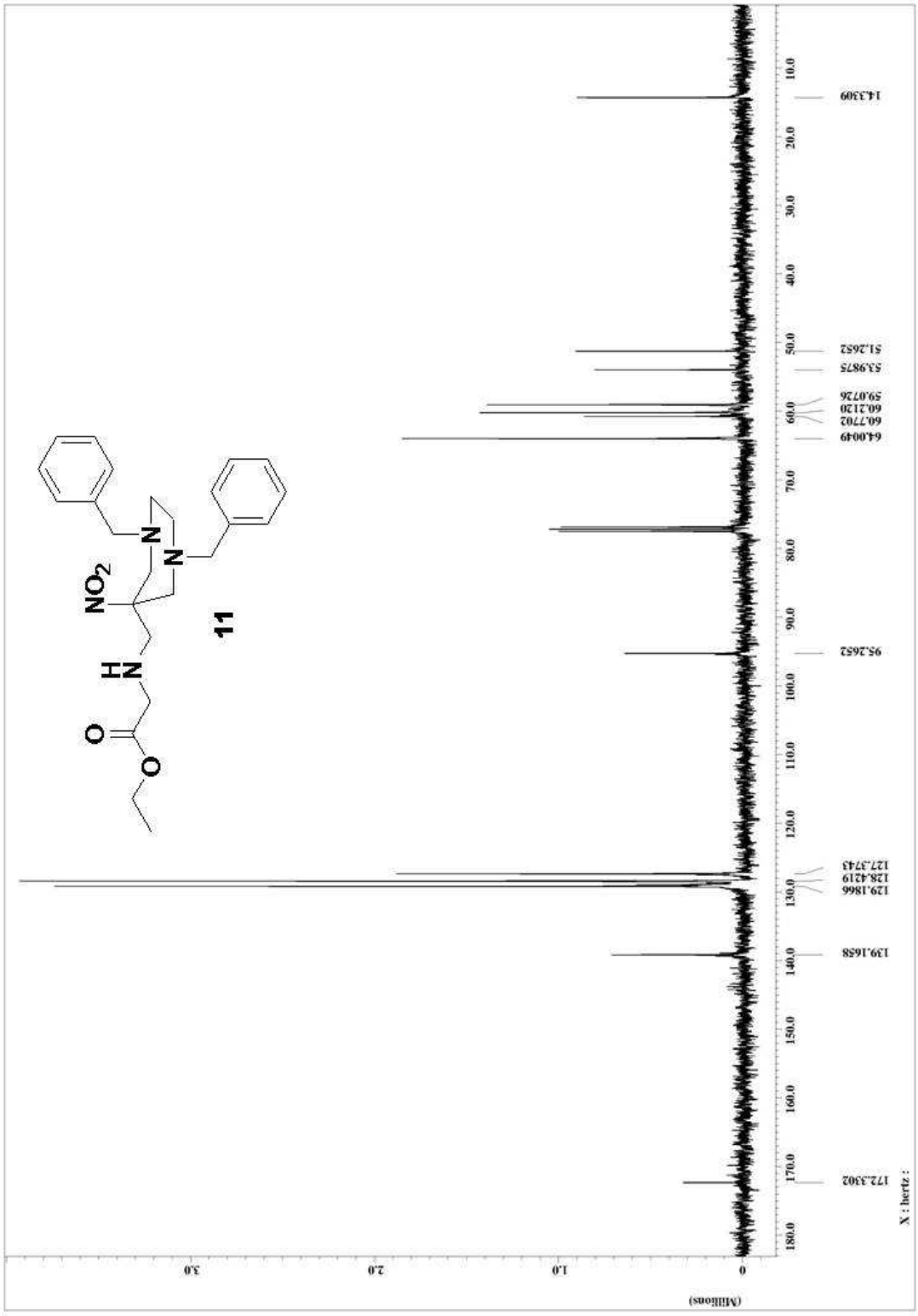

NO2
N
N
H
N
O
9
X : hertz :
7.2944
7.2852
7.2797
7.2651
4.9810
3.7437
3.7107
3.6035
3.5715
3.5376
3.5019
3.0000
2.9643
2.5696
2.5641
2.0558
2.0384
1.9404
1.9340
1.6619
1.5841
1.5640
1.5566

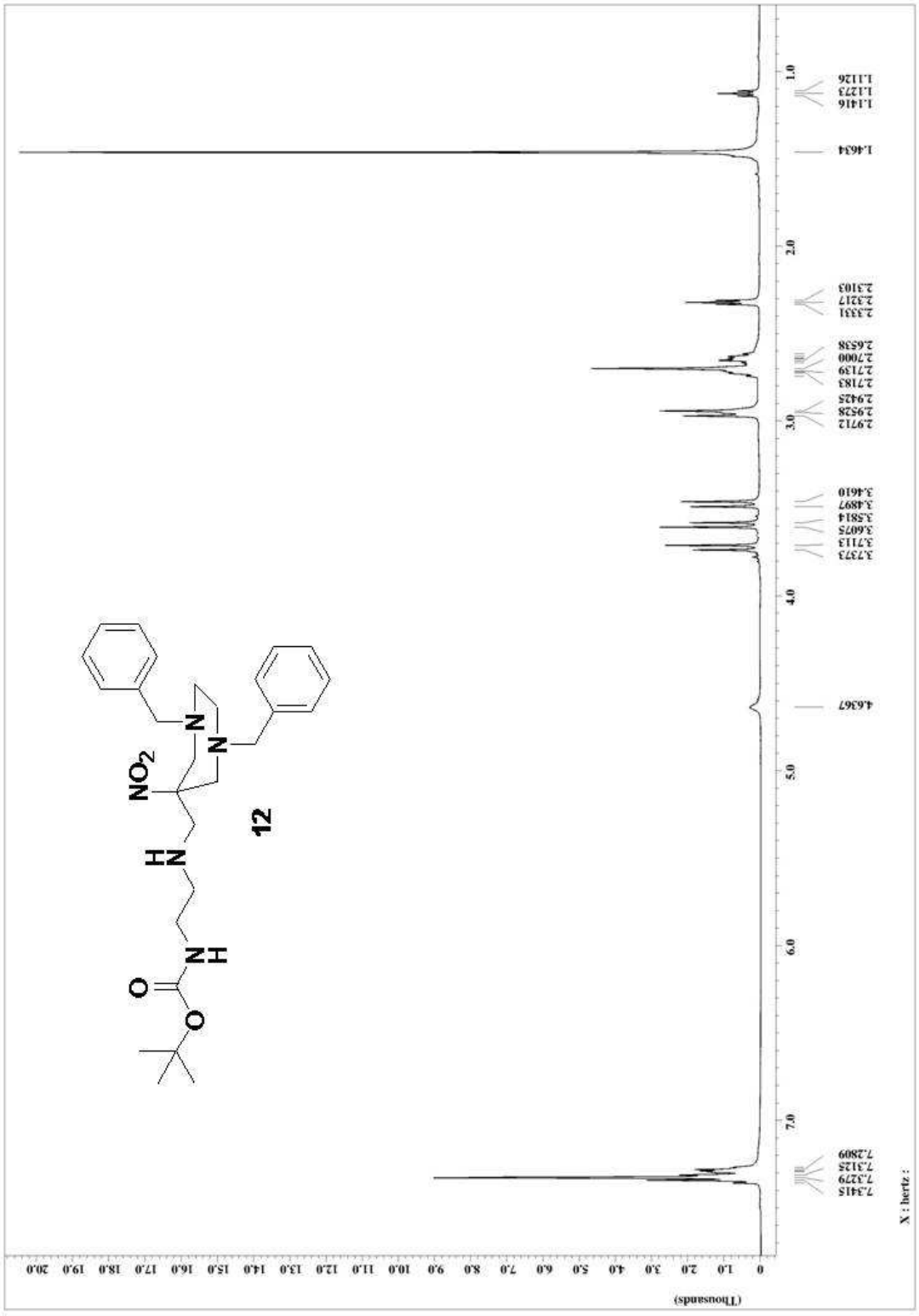

29.4982
31.0037
32.3505
36.4263
41.6414
51.9800
58.3498
61.6838
63.9167
94.6953
127.3626
128.4026
129.1826
139.0700
169.8638
X : hertz :
(Millions)
9
NO2
O
HN
N

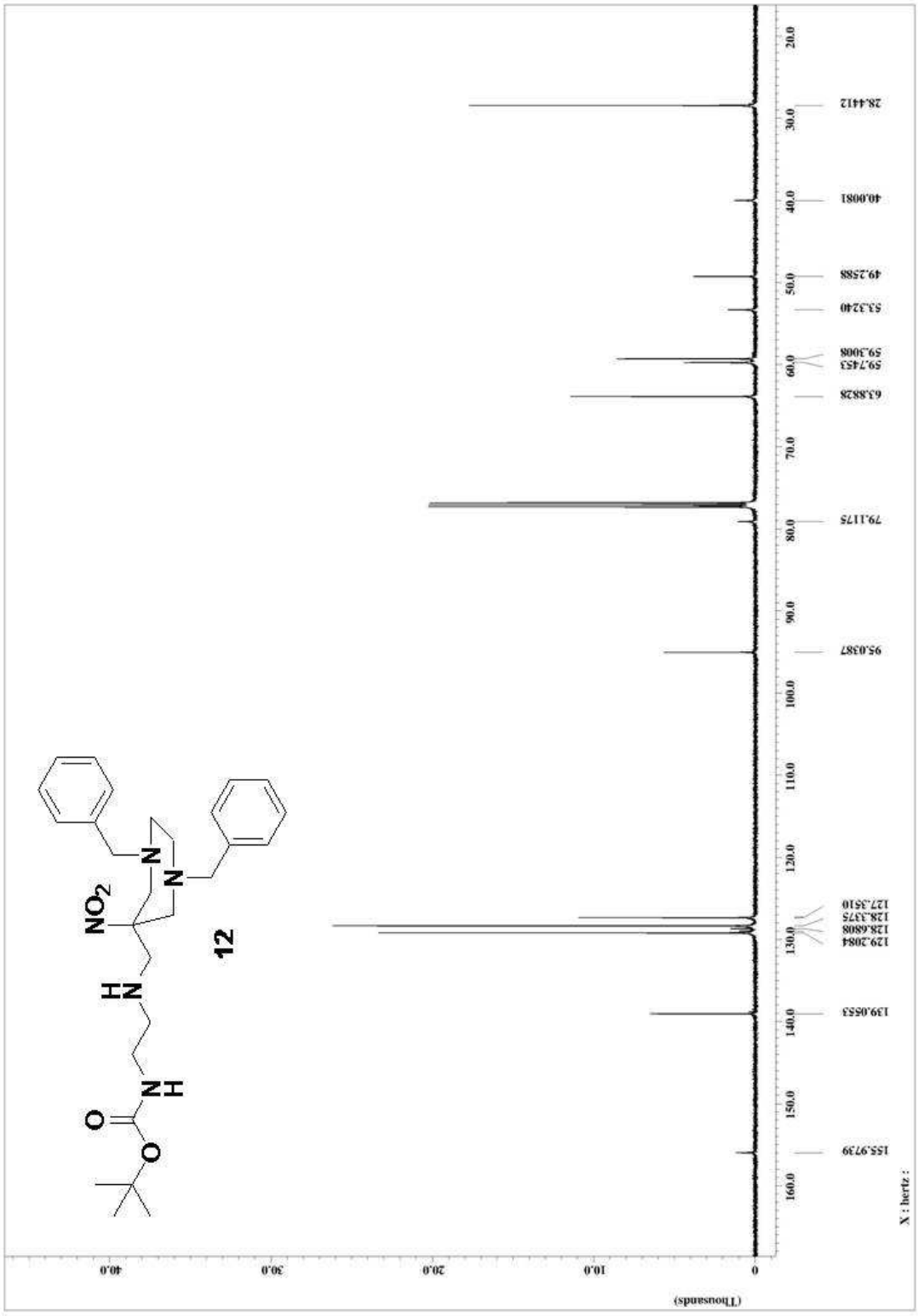

10
X : hertz :

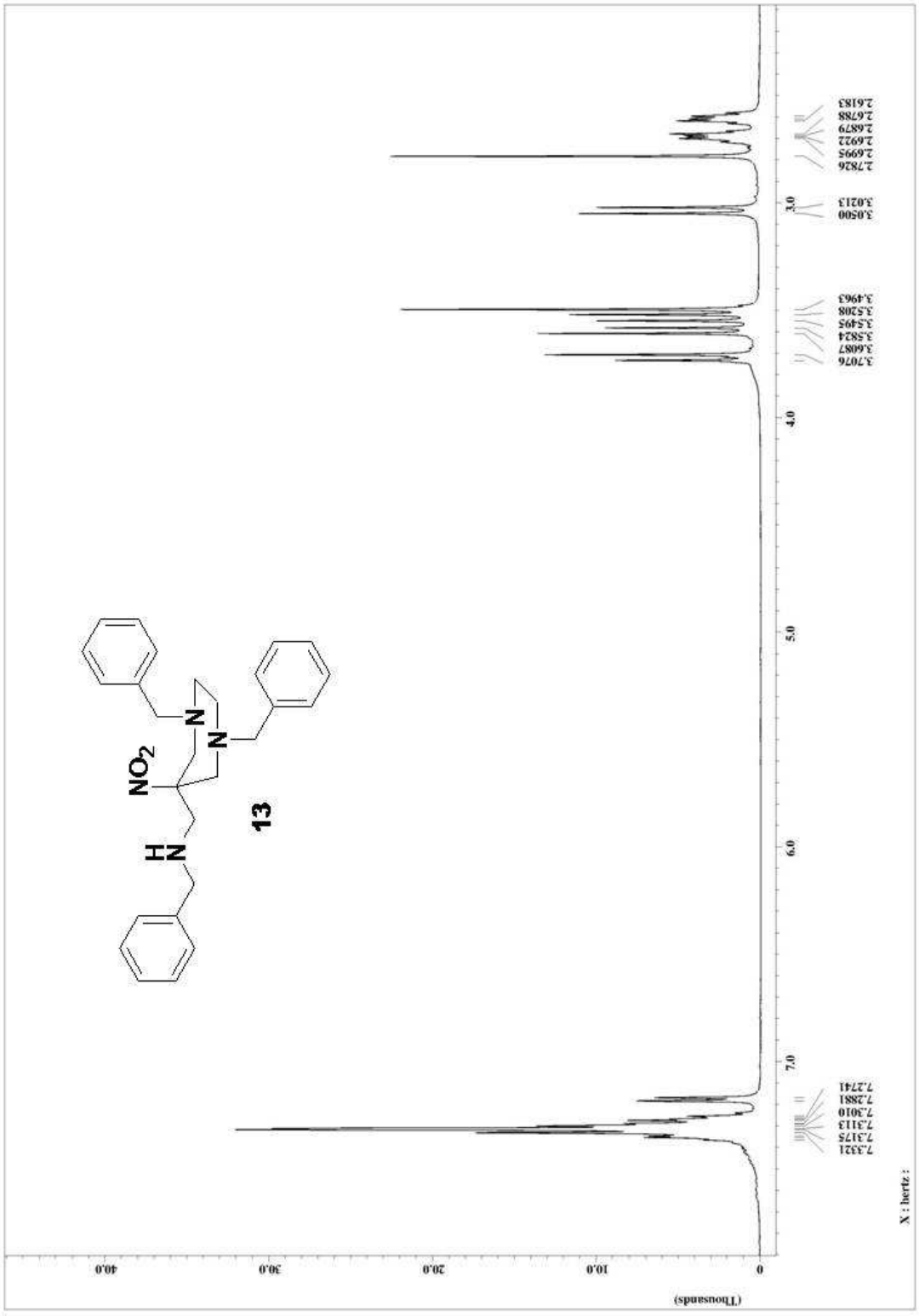

10
NO2
H
N
N
N
14.2371
22.8016
27.1603
29.4620
29.6073
29.7067
29.7536
30.0125
32.0313
50.3073
54.2531
59.1088
60.3247
64.0181
95.4161
127.3340
128.3663
129.1693
139.2554
X : hertz :
(Millions)

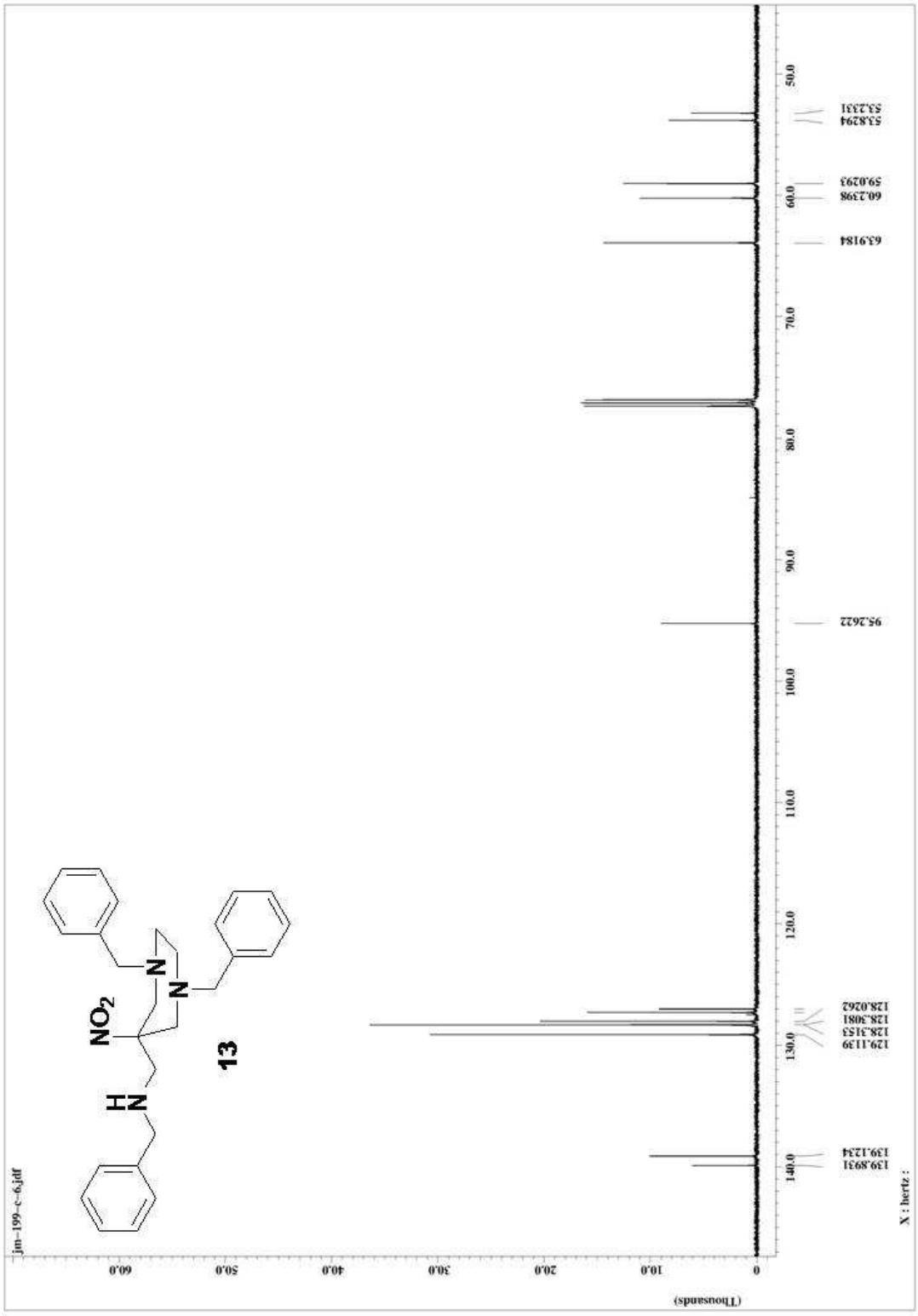

11
X : hertz :
7.3181
7.3089
7.3034
7.2888
4.1428
4.1254
3.7307
3.6977
3.6180
3.5851
3.5045
3.4688
3.0273
3.0200
2.9934
2.8112
2.6454
2.6079
1.2735
1.2561
1.2396

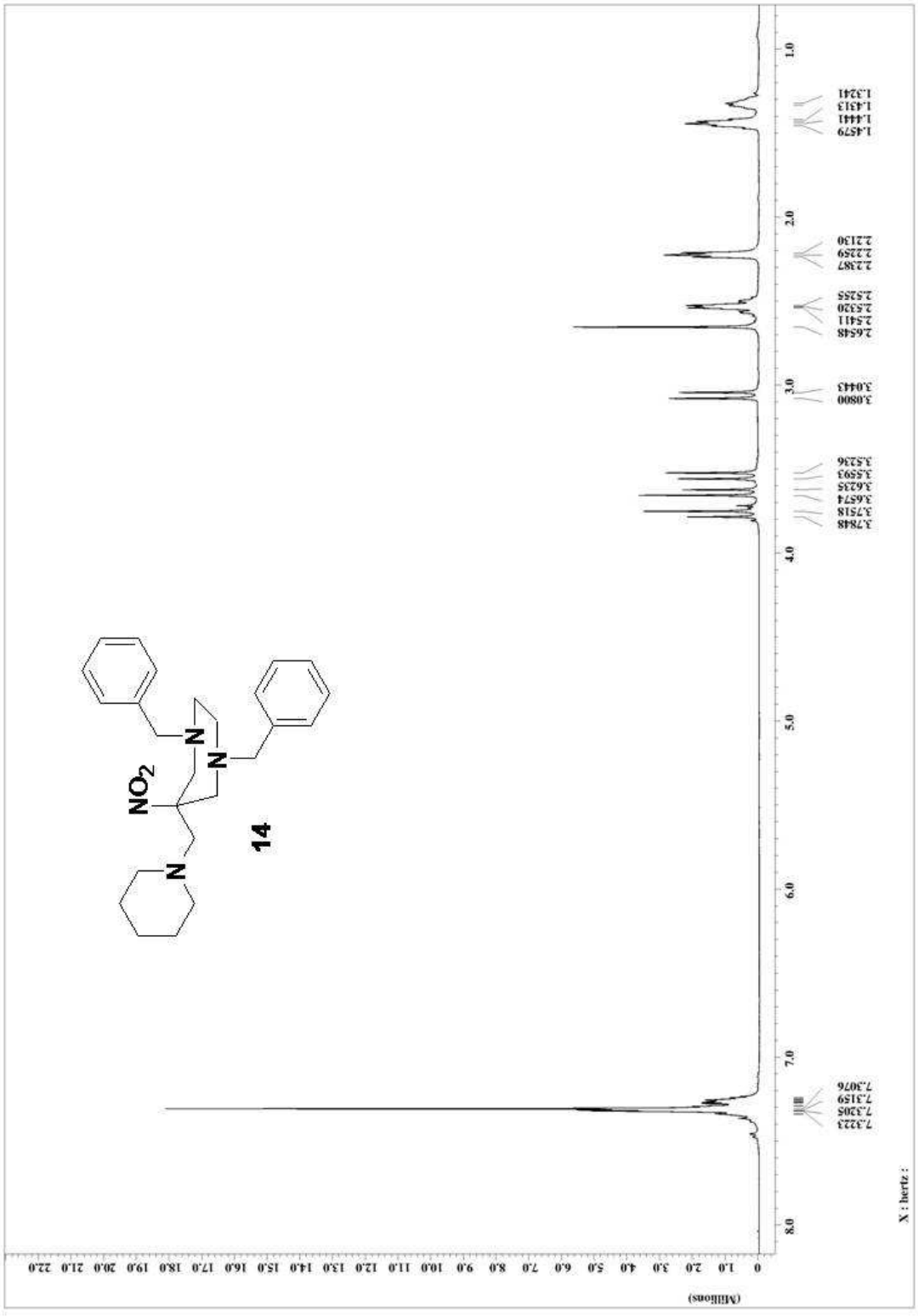

11
NO2
N
N
H
N
O
O
O
14.3309
51.2652
53.9875
59.0726
60.2120
60.7702
64.0049
95.2652
127.3743
128.4219
129.1866
139.1658
172.3302
X : hertz :
(Millions)

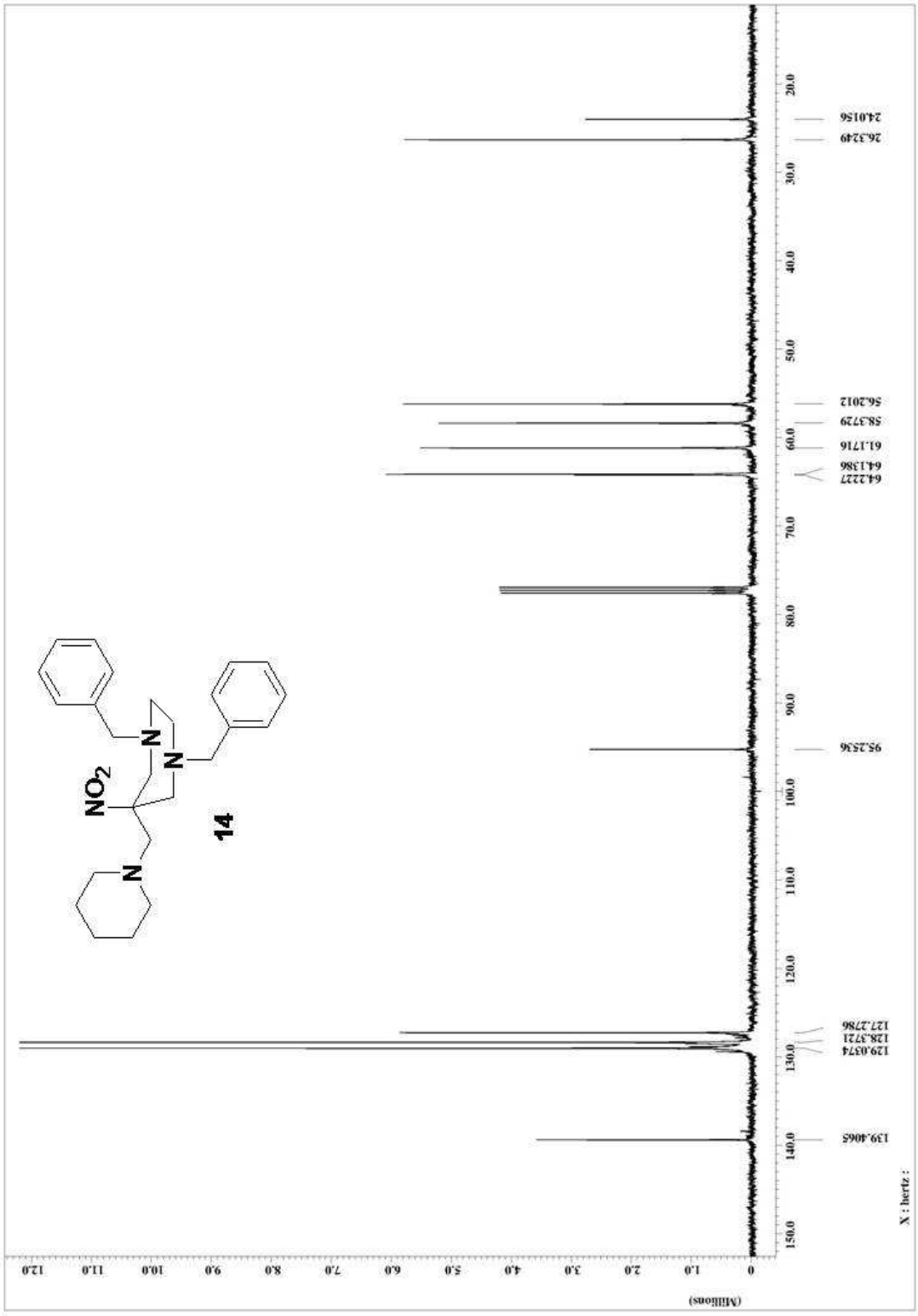

12
X : hertz :

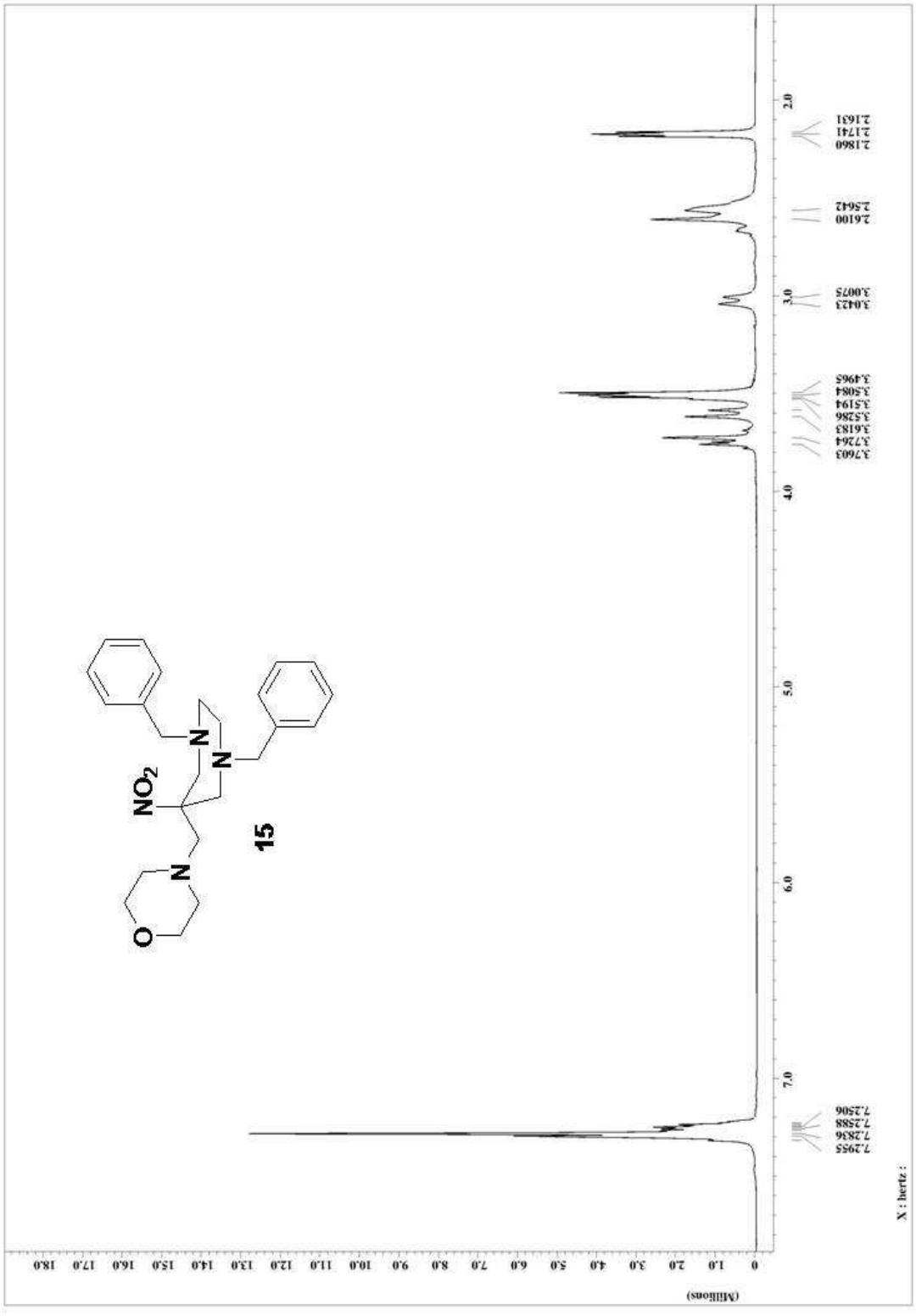

12
28.4412
40.0081
49.2588
53.3240
59.3008
59.7453
63.8828
79.1175
95.0387
127.3510
128.3375
128.6808
129.2084
139.0553
155.9739
X : hertz :
(Thousands)

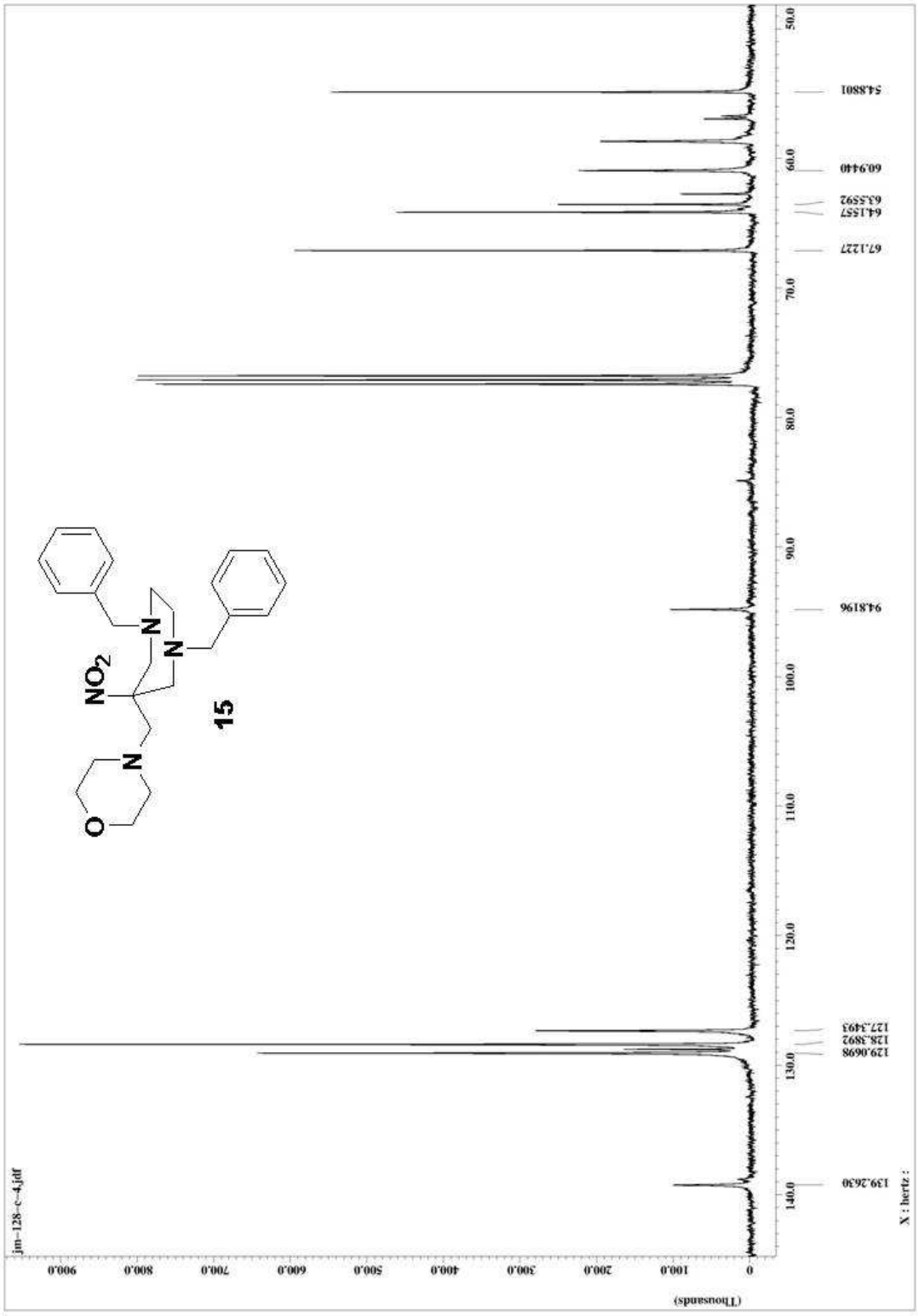

13
NO2
N
N
H
N
(Thousands)
0
10.0
20.0
30.0
40.0
3.0
4.0
5.0
6.0
7.0
X : hertz :
7.3321
7.3175
7.3113
7.3010
7.2881
7.2741
3.7076
3.6087
3.5824
3.5495
3.5208
3.4963
3.0500
3.0213
2.7826
2.6995
2.6922
2.6879
2.6788
2.6183


jm-199-c-6.jdf
13
NO2
N
N
H
N
(Thousands)
0
10.0
20.0
30.0
40.0
50.0
60.0
50.0
60.0
70.0
80.0
90.0
100.0
110.0
120.0
130.0
140.0
53.2331
53.8294
59.0293
60.2398
63.9184
95.2622
128.0262
128.3081
128.3153
129.1139
139.8931
139.1234
X : hertz :


14
X : hertz :
7.3223
7.3205
7.3159
7.3076
3.7848
3.7518
3.6574
3.6235
3.5593
3.5236
3.0800
3.0443
2.6548
2.5411
2.5320
2.5285
2.2387
2.2259
2.2130
1.4579
1.4441
1.4313
1.3241


14
NO2
N
N
N
(Millions)
X : hertz :
24.0156
26.3249
56.2012
58.3729
61.1716
64.1386
64.2227
95.2536
127.2786
128.3721
129.0374
139.4065


15
X : hertz :
7.2955
7.2836
7.2588
7.2506
3.7603
3.7264
3.6183
3.5286
3.5194
3.5084
3.4965
3.0423
3.0075
2.6100
2.5642
2.1860
2.1741
2.1631


jm-128-c-4.jdf
(Thousands)
X : hertz :
139.2630
129.0698
128.3892
127.3493
94.8196
67.1227
64.1557
63.5592
60.9440
54.8801
NO2
15