Supplementary Information

Base-Mediated Diastereoselective [4+3] Annulation of in situ Generated *ortho*-Quinone Methides with *C*,*N*-Cyclic Azomethine Imines

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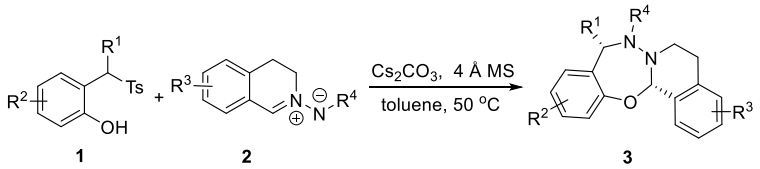
Table of Contents

General Information

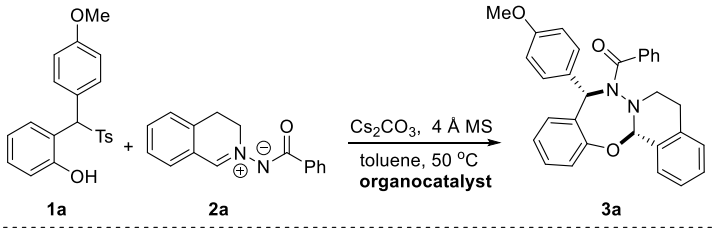
Commercially available materials purchased from Energy-Chemical were used as received. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded on a Bruker AV 400 (400 MHz) spectrometer. Chemical shifts were recorded in parts per million (ppm, δ) relative to tetramethylsilane (δ 0.00) or chloroform (δ = 7.26, singlet). ^{1}H NMR splitting patterns are designated as singlet (s), doublet (d), triplet (t), quartet (q), dd (doublet of doublets); m (multiplets), and etc. All first-order splitting patterns were assigned on the basis of the appearance of the multiplet. Splitting patterns that could not be easily interpreted are designated as multiplet (m) or broad (br). Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on a Bruker AV 400 (100 MHz) spectrometer. High resolution mass spectral analysis (HRMS) was performed on Waters Xevo G2-S QTof mass spectrometer. X-ray crystallography analysis was performed on Bruker X8 APEX Xray diffractionmeter. Analytical thin-layer chromatography (TLC) was carried out on with GF 254 silica gel coated plates. Visualization was performed using a UV lamp. Flash column chromatography was carried out using 200-300 mesh silica gel. Melting points are uncorrected. 2-(1-Tosylalkyl)phenols **1** were prepared following the literatures procedures.[1] C,N-Cyclic azomethine imines **2** were synthesized according to reported method.[2]

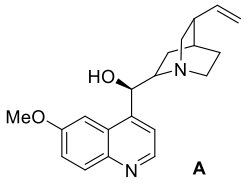
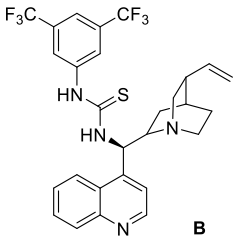
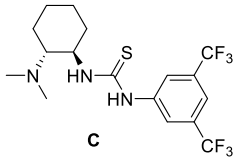
General procedure for the [4+3] annulation reaction:



To a dry 10 mL Schlenk tube equipped with a magnetic stirring bar, were added 2-(1-tosylalkyl)phenol **1** (0.2 mmol), C,N-cyclic azomethine imine **2** or N,N-cyclic azomethine imine **4** (0.24 mmol), 4 Å MS (200 mg), Cs_2CO_3 (0.24 mmol), and toluene (2 mL). The tube was sealed with a septum and the reaction mixture was stirred at 50 °C (or 80 °C) until the full consumption of the phenol **1**. Then the reaction mixture was cooled to room temperature and toluene was removed under reduced pressure. The residue was subjected to column chromatography using petroleum ether/EtOAc = 8/1 as eluent to afford the desired product **3** or **5**.

Catalytic asymmetric synthesis of 3a:



organocatalyst (20 mol%)	ee of **3a** (%)
none	0
 **A**	-2
 **B**	4
 **C**	0

We have tried to develop a catalytic asymmetric version of this reaction, but unfortunately, all of the three organocatalysts (20 mol%) that have been investigated under the optimal reaction conditions afforded **3a** with almost no enantioselectivities.

References cited in the SI:

[1] M.-W. Chen, L.-L. Cao, Z.-S. Ye, G.-F. Jiang, Y.-G. Zhou, *Chem. Commun.* **2013**, *49*, 1660-1662.

[2] a) T. Hashimoto, Y. Maeda, M. Omote, H. Nakatsu, K. Maruoka, *J. Am. Chem. Soc.* **2010**, *132*, 4076–4077. b) B.-S. Li, Y. Wang, Z. Jin, Y. R. Chi, *Chem. Sci.* **2015**, *6*, 6008-6012.

X-ray structure of product 3c

Relative configurations of the products **3** were assigned based on the crystal X-ray structures of **3c**. CCDC 1553421 (**3c**, obtained as colorless needles *via* evaporation of a petroleum ether/EtOAc solution) contains the supplementary X-ray crystallographic data. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

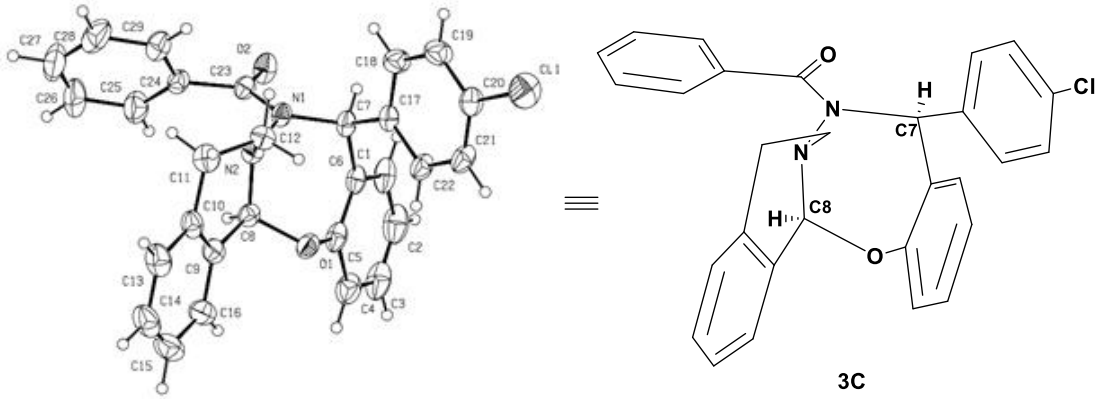
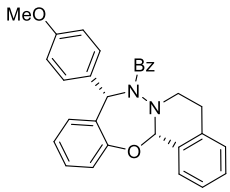


Table S1. Crystal data and structure refinement for 3c.

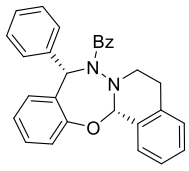
Empirical formula	$C_{29}H_{23}ClN_2O_2$
Formula weight	466.94
Temperature	293 K
Wavelength	0.71073 Å
Crystal system, Space group	triclinic, P -1
Unit cell dimensions	a= 8.8691(9) Å α= 92.638(7) °
	b= 11.1836(9) Å β= 99.870(8) °
	c= 12.6245(12) Å γ= 105.055(8) °
Volume	1185.9(2) $Å^3$
Z	2
Density (calculated)	1.308 Mg/m^3
Absorption coefficient	0.191 mm^{-1}
F(000)	488.0
Crystal size	0.43*0.32*0.16 mm^3
Theta range for data collection	3.291 to 25.349 °.
Index ranges	-10<=h<=8, -12<=k<=13, -15<=l<=15
Reflections collected	7390
Independent reflections	4314 [*R*(int)= 0.0378]
Completeness to theta= 25.242 °	99.4%
Absorption correction	Multi-scan from equivalents
Max. and min. transmission	1.000 and 0.806
Refinement method	Full-matrix squares on F2
Data/restraints/parameters	4314/0/307
Goodness-of-fit on F2	1.070
Final R indices [I>2sigma(I)]	*R1*= 0.0588, *wR2*= 0.1557
R indices(all data)	*R1*= 0.0866, *wR2*= 0.1817
Extinction coefficient	n/a
Largest diff. peak and hole	0.195 and -0.470 e.$Å^{-3}$

Characterization of products:



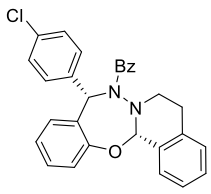
3a

(9-(4-Methoxyphenyl)-5,14*a*-dihydro-6*H*-benzo[6,7][1,3,4]oxadiazepino[2,3-*a*]isoquinolin-8(9*H*)-yl)(phenyl)methanone (3a): 86.9 mg, 94% yield, white solid; mp 169-171 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44-7.33 (m, 6H), 7.31-7.27 (m, 4H), 7.24-7.16 (m, 5H), 6.88 (d, *J* = 7.6 Hz, 1H), 6.80 (d, *J* = 8.8 Hz, 2H), 5.63 (s, 1H), 3.76 (s, 3H), 3.06-2.99 (m, 1H), 2.51-2.47 (m, 1H), 2.23-2.19 (m, 1H), 2.14-2.05 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.1, 159.4, 159.1, 136.8, 134.2, 132.9, 131.3, 131.1, 130.8, 130.3, 129.5, 129.2, 128.8, 128.6, 128.2, 127.6, 126.4, 126.1, 124.6, 122.2, 113.7, 92.8, 62.1, 55.2, 48.0, 29.6; HRMS (ESI, m/z): calcd. for $C_{30}H_{26}N_2O_3H^+$ 463.2022, found 463.2025.



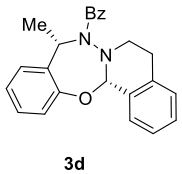
3b

Phenyl(9-phenyl-5,14*a*-dihydro-6*H*-benzo[6,7][1,3,4]oxadiazepino[2,3-*a*]isoquinolin-8(9*H*)-yl)methanone (3b): 50.0 mg, 58% yield; white solid, mp 79-81 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (s, 1H), 7.43-7.32 (m, 8H), 7.29-7.27 (m, 2H), 7.25-7.15 (m, 7H), 6.88 (d, *J* = 7.6 Hz, 1H), 5.64 (s, 1H), 3.01-2.94 (m, 1H), 2.52-2.48 (m, 1H), 2.21-2.18 (m, 1H), 2.14-2.06 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.2, 159.5, 139.1, 136.7, 134.2, 132.9, 131.4, 130.4, 129.6, 129.2, 129.1, 128.8, 128.6, 128.4, 128.2, 127.7, 127.6, 126.4, 126.1, 124.6, 122.2, 92.8, 62.5, 47.9, 29.6; HRMS (ESI, m/z): calcd. for $C_{29}H_{24}N_2O_2H^+$ 433.1916, found 433.1910.



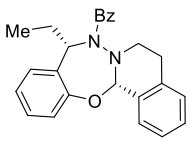
3c

(9-(4-Chlorophenyl)-5,14*a*-dihydro-6*H* benzo[6,7][1,3,4]oxadiazepino[2,3-*a*]isoquinolin-8(9*H*)-yl)(phenyl)methanone (3c): 83.9 mg, 90% yield, white solid; mp 156-158 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (s, 1H), 7.42-7.39 (m, 5H), 7.34-7.28 (m, 3H), 7.25-7.15 (m, 8H), 6.89 (d, *J* = 7.6 Hz, 1H), 5.65 (s, 1H), 3.05-2.98 (m, 1H), 2.51-2.46 (m, 1H), 2.25-2.22 (m, 1H), 2.15-2.06 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.2, 159.4, 137.8, 136.4, 134.1, 133.7, 132.7, 131.3, 130.5, 130.0, 129.8, 129.4, 128.8, 128.7, 128.6, 128.3, 127.7, 126.5, 126.2, 124.8, 122.3, 92.8, 61.9, 48.2, 29.5; HRMS (ESI, m/z): calcd. for $C_{29}H_{23}ClN_2O_2H^+$ 467.1526, found 467.1520.



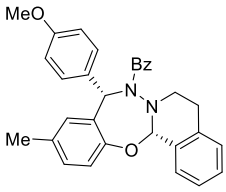
3d

(9-Methyl-5,14*a*-dihydro-6*H*-benzo[6,7][1,3,4]oxadiazepino[2,3-*a*]isoquinolin-8(9*H*)-yl)(phenyl)methanone (3d): 47.4 mg, 64% yield, white solid; mp 117-119 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, *J* = 7.6 Hz, 1H), 7.35 (d, *J* = 6.4 Hz, 3H), 7.28-7.19 (m, 7H), 7.12 (t, *J* = 7.2 Hz, 1H), 7.00 (d, *J* = 7.2 Hz, 1H), 6.20-6.19 (m, 1H), 5.54 (s, 1H), 4.15-4.09 (m, 1H), 3.18-3.16 (m, 1H), 2.50-2.46 (m, 1H), 2.26-2.24 (m, 1H), 1.76 (d, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.8, 158.8, 137.0, 134.5, 134.3, 133.1, 129.6, 129.1, 129.0, 128.8, 128.6, 128.3, 127.6, 126.3, 126.2, 124.2, 122.0, 92.9, 57.4, 49.3, 29.9, 21.4; HRMS (ESI, m/z): calcd. for $C_{24}H_{22}N_2O_2H^+$ 371.1760, found 371.1764.



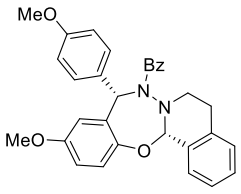
3e

(9-Ethyl-5,14*a*-dihydro-*6H*-benzo[6,7][1,3,4]oxadiazepino[2,3-*a*] isoquinolin-8(*9H*)-yl)(phenyl)methanone (3e): 20.0 mg, 26% yield, colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47-7.41 (m, 1H), 7.34-7.27 (m, 5H), 7.25-7.19 (m, 5H), 7.11 (t, *J* = 7.2 Hz, 1H), 6.99 (d, *J* = 7.2 Hz, 1H), 5.88 (s, 1H), 5.54 (s, 1H), 4.09-4.04 (m, 1H), 3.20 (s, 1H), 2.46 (d, *J* = 15.6 Hz, 1H), 2.28-2.10 (m, 3H), 0.92 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.1, 159.0, 137.2, 134.3, 133.1, 132.6, 131.1, 129.0, 129.0, 128.8, 128.6, 128.3, 127.6, 126.3, 126.2, 123.8, 121.9, 93.0, 63.9, 49.0, 29.8, 27.5, 12.1; HRMS (ESI, m/z): calcd. for $C_{25}H_{24}N_2O_2H^+$ 385.1916, found 385.1919.



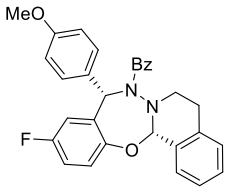
3f

(9-(4-Methoxyphenyl)-11-methyl-5,14*a*-dihydro-6*H*-benzo[6,7] [1,3,4]oxadiazepino[2,3-*a*]isoquinolin-8(9*H*)-yl)(phenyl)methanone (3f): 64.7 mg, 68% yield, white solid; mp 177-179 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.38 (m, 4H), 7.30 (d, *J* = 8.4 Hz, 2H), 7.26-7.13 (m, 8H), 6.87 (d, *J* = 7.6 Hz, 1H), 6.80 (d, *J* = 8.4 Hz, 2H), 5.59 (s, 1H), 3.76 (s, 3H), 3.06-2.99 (m, 1H), 2.50-2.47 (m, 1H), 2.34 (s, 3H), 2.22-2.18 (m, 1H), 2.13-2.05 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.1, 159.1, 157.1, 136.9, 134.2, 134.1, 133.0, 131.7, 131.2, 130.4, 130.3, 129.9, 129.1, 128.8, 128.5, 128.2, 127.6, 126.4, 126.1, 121.9, 113.7, 92.8, 62.0, 55.2, 48.0, 29.6, 20.6; HRMS (ESI, m/z): calcd. for $C_{31}H_{28}N_2O_3H^+$ 477.2178, found 477.2173.



3g

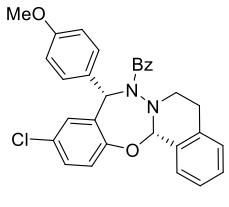
(11-Methoxy-9-(4-methoxyphenyl)-5,14*a*-dihydro-6*H*-benzo [6,7][1,3,4]oxadiazepino[2,3-*a*]isoquinolin-8(9*H*)-yl)(phenyl) methanone (3g): 64.9 mg, 66% yield, white solid; mp 98-100 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.37 (m, 4H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.26-7.20 (m, 5H), 7.15 (t, *J* = 7.2 Hz, 1H), 6.92-6.86 (m, 3H), 6.81 (d, *J* = 8.4 Hz, 2H), 5.78 (s, 1H), 3.79 (s, 3H), 3.76 (s, 3H), 3.04-2.98 (m, 1H), 2.50-2.45 (m, 1H), 2.22-2.18 (m, 1H), 2.13-2.04 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.2, 159.1, 156.2, 153.0, 136.8, 134.2, 133.0, 131.6, 130.9, 130.4, 129.2, 128.8, 128.5, 128.2, 127.6, 126.4, 126.1, 122.9, 115.3, 115.0, 113.7, 92.8, 62.0, 55.6, 55.2, 48.0, 29.6; HRMS (ESI, m/z): calcd. for $C_{31}H_{28}N_2O_4H^+$ 493.2127, found 493.2123.



3h

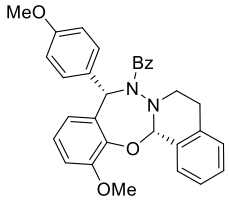
(11-Fluoro-9-(4-methoxyphenyl)-5,14*a*-dihydro-6*H*-benzo[6,7] [1,3,4]oxadiazepino[2,3-*a*]isoquinolin-8(9*H*)-yl)(phenyl)methanone (3h): 71.0 mg, 74% yield, white solid; mp 121-123 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41-7.35 (m, 4H), 7.30-7.16 (m, 7H), 7.14-7.11 (m, 2H), 7.07-7.02 (m, 1H), 6.88 (d, *J* = 7.2 Hz, 2H), 6.81 (d, *J* = 8.8 Hz, 2H), 5.59 (s, 1H), 3.76 (s, 3H), 3.04-2.97 (m, 1H), 2.53-2.50 (m, 1H), 2.24-2.20 (m, 1H), 2.16-2.09 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.2, 159.2, 159.1 (d, $J_{C\text{-}F}$ = 242 Hz), 155.3, 136.5 134.2, 132.6, 132.5 (d, $J_{C\text{-}F}$ = 7.0 Hz), 130.3, 130.2, 129.3, 128.7 (d, $J_{C\text{-}F}$ = 11 Hz), 128.2, 127.6, 126.4, 126.1, 123.4 (d, $J_{C\text{-}F}$ = 9 Hz), 117.6 (d, $J_{C\text{-}F}$ = 23 Hz), 115.8 (d, $J_{C\text{-}F}$ = 23 Hz), 113.8,

92.9, 61.5, 55.2, 48.0, 29.5; HRMS (ESI, m/z): calcd. for $C_{30}H_{25}FN_2O_3H^+$ 481.1927, found 481.1927.



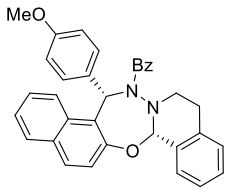
3i

(11-Chloro-9-(4-methoxyphenyl)-5,14*a*-dihydro-6*H*-benzo[6,7][1,3,4]oxadiazepino[2,3-*a*]isoquinolin-8(9*H*)-yl)(phenyl)methanone (3i): 79.4 mg, 80% yield, white solid; mp 192-194 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.36 (m, 5H), 7.33-7.20 (m, 8H), 7.16 (t, *J* = 7.2 Hz, 1H), 6.88 (d, *J* = 7.6 Hz, 1H), 6.81 (d, *J* = 7.6 Hz, 2H), 5.59 (s, 1H), 3.76 (s, 3H), 3.04-2.98 (m, 1H), 2.51-2.49 (m, 1H), 2.24-2.20 (m, 1H), 2.16-2.09 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.3, 159.4, 158.0, 136.5, 134.3, 132.6, 132.6, 131.1, 130.3, 129.5, 129.4, 129.4, 128.9, 128.8, 128.3, 127.7, 126.5, 126.2, 123.7, 113.9, 93.2, 61.7, 55.3, 48.1, 29.6; HRMS (ESI, m/z): calcd. for $C_{30}H_{25}ClN_2O_3H^+$ 497.1632, found 497.1620.



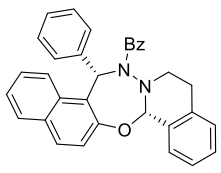
3j

(13-Methoxy-9-(4-methoxyphenyl)-5,14*a*-dihydro-6*H*-benzo[6,7][1,3,4]oxadiazepino[2,3-*a*]isoquinolin-8(9*H*)-yl)(phenyl)methanone (3j): 64.9 mg, 66% yield, white solid; mp 189-191 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 7.6 Hz, 1H), 7.42-7.34 (m, 5H), 7.26-7.21 (m, 4H), 7.17-7.12 (m, 2H), 7.01 (d, *J* = 8.4 Hz, 2H), 6.86 (d, *J* = 7.2 Hz, 1H), 6.79 (d, *J* = 8.4 Hz, 2H), 5.58 (s, 1H), 3.99 (s, 3H), 3.76 (s, 3H), 3.02-2.95 (m, 1H), 2.50-2.46 (m, 1H), 2.20-2.16 (m, 1H), 2.12-2.04 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.2, 159.1, 152.5, 148.4, 136.9, 134.4, 132.9, 132.6, 130.5, 130.5, 129.3, 129.1, 128.4, 128.0, 127.6, 126.4, 126.2, 124.8, 122.4, 113.6, 111.7, 93.2, 61.9, 56.0, 55.2, 48.2, 29.7; HRMS (ESI, m/z): calcd. for $C_{31}H_{28}N_2O_4H^+$ 493.2127, found 493.2126.



3k

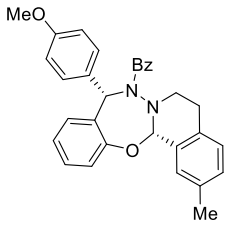
(9-(4-Methoxyphenyl)-5,16*a*-dihydro-6*H*-naphtho[1',2':6,7][1,3,4]oxadiazepino[2,3-*a*]isoquinolin-8(9*H*)-yl)(phenyl)methanone (3k): 60.4 mg, 59% yield, yellow solid, mp 130-132 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (s, 1H), 8.27 (d, *J* = 8.4 Hz, 1H), 7.89 (t, *J* = 8.0 Hz, 2H), 7.56-7.31 (m, 9H), 7.25-7.17 (m, 4H), 6.92 (d, *J* = 7.2 Hz, 1H), 6.78 (d, *J* = 8.4 Hz, 2H), 5.73 (s, 1H), 3.74 (s, 3H), 3.17-3.10 (m, 1H), 2.62-2.58 (m, 1H), 2.29-2.15 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.4, 159.3, 157.7, 136.9, 134.4, 133.0, 132.3, 131.3, 130.5, 130.3, 130.3, 129.2, 129.0, 128.7, 128.6, 128.3, 127.6, 127.5, 126.5, 126.2, 125.0, 124.6, 123.1, 122.4, 113.8, 92.5, 55.6, 55.2, 48.1, 29.6; HRMS (ESI, m/z): calcd. for $C_{34}H_{28}N_2O_3H^+$ 513.2178, found 513.2188.



3l

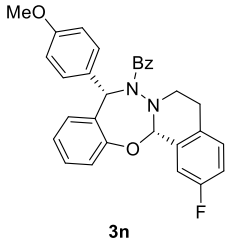
Phenyl(9-phenyl-5,16*a*-dihydro-6*H*-naphtho[1',2':6,7][1,3,4]oxadiazepino[2,3-*a*]isoquinolin-8(9*H*)-yl)methanone (3l): 64.6 mg, 67% yield, yellow solid, mp 169-171 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.28 (d, *J* = 8.4 Hz, 1H), 7.89 (t, *J* = 9.2 Hz, 2H), 7.53-7.40 (m, 8H), 7.23-7.15 (m, 8H), 6.90 (d, *J* = 7.2 Hz, 1H), 5.73 (s, 1H), 3.10-3.04 (m, 1H), 2.61-2.59 (m, 1H), 2.26-2.16 (m, 2H); ^{13}C NMR

(100 MHz, $CDCl_3$) δ 173.5, 157.9, 138.3, 136.7, 134.3, 132.9, 132.4, 131.3, 130.4, 129.3, 129.2, 128.9, 128.7, 128.6, 128.5, 128.3, 127.9, 127.6, 127.5, 126.4, 126.2, 125.0, 124.1, 123.0, 122.3, 92.5, 56.0, 47.9, 29.6; HRMS (ESI, m/z): calcd. for $C_{33}H_{26}N_2O_2H^+$ 483.2073, found 483.2072.



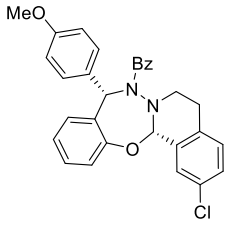
3m

(9-(4-Methoxyphenyl)-2-methyl-5,14*a*-dihydro-6*H*-benzo[6,7][1,3,4]oxadiazepino[2,3-*a*]isoquinolin-8(9*H*)-yl)(phenyl)methanone (3m): 68.5 mg, 72% yield, white solid; mp 165-167 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43-7.33 (m, 6H), 7.30-7.15 (m, 7H), 6.97 (d, J = 7.6 Hz, 1H), 6.80-6.76 (m, 3H), 5.59 (s, 1H), 3.75 (s, 3H), 3.03-2.97 (m, 1H), 2.48-2.45 (m, 1H), 2.33 (s, 3H), 2.17-2.14 (m, 1H), 2.07-2.01 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.1, 159.4, 159.1, 136.8, 135.7, 132.7, 131.3, 131.2, 131.1, 130.8, 130.3, 129.6, 129.4, 129.1, 128.1, 127.6, 126.4, 124.6, 122.2, 113.7, 92.9, 62.0, 55.2, 48.2, 29.2, 21.0; HRMS (ESI, m/z): calcd. for $C_{31}H_{28}N_2O_3H^+$ 477.2178, found 477.2178.



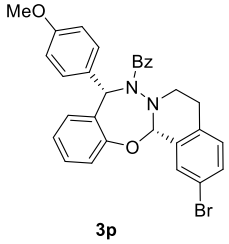
3n

(2-Fluoro-9-(4-methoxyphenyl)-5,14*a*-dihydro-6*H*-benzo[6,7][1,3,4]oxadiazepino[2,3-*a*]isoquinolin-8(9*H*)-yl)(phenyl)methanone (3n): 76.8 mg, 80% yield, white solid; mp 158-160 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44-7.37 (m, 5H), 7.32-7.19 (m, 7H), 7.09 (dd, J_1 = 9.2 Hz, J_2 = 2.0 Hz, 1H), 6.88-6.79 (m, 4H), 5.58 (s, 1H), 3.75 (s, 3H), 3.02-2.95 (m, 1H), 2.50-2.46 (m, 1H), 2.19-2.15 (m, 1H), 2.04-1.99 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.1, 161.0 (d, $J_{C\text{-}F}$ = 240 Hz), 159.1 (d, $J_{C\text{-}F}$ = 5 Hz), 136.7, 134.4 (d, $J_{C\text{-}F}$ = 7.0 Hz), 131.4, 130.9, 130.7, 130.2, 129.9, 129.7(d, $J_{C\text{-}F}$ = 8 Hz), 129.6, 129.2, 127.6, 126.3, 124.8, 122.1, 116.0 (d, $J_{C\text{-}F}$ = 21 Hz), 115.2 (d, $J_{C\text{-}F}$ = 21 Hz), 113.7, 92.1, 62.1, 55.2, 47.9, 28.9; HRMS (ESI, m/z): calcd. for $C_{30}H_{25}FN_2O_3H^+$ 481.1927, found 481.1928.



3o

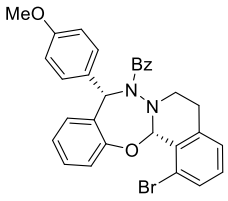
(2-Chloro-9-(4-methoxyphenyl)-5,14*a*-dihydro-6*H*-benzo[6,7][1,3,4]oxadiazepino[2,3-*a*]isoquinolin-8(9*H*)-yl)(phenyl)methanone (3o): 70.4 mg, 71% yield, white solid; mp 131-133 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43-7.33 (m, 7H), 7.28-7.18 (m, 6H), 7.13 (d, J = 8 Hz, 1H), 6.81 (t, J = 6.8 Hz, 3H), 5.57 (s, 1H), 3.75 (s, 3H), 3.00-2.94 (m, 1H), 2.49-2.45 (m, 1H), 2.19-2.15 (m, 1H), 2.04-1.96 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.1, 159.1, 159.0, 136.7, 134.4, 132.7, 131.7, 131.3, 130.9, 130.6, 130.2, 129.7, 129.6, 129.2, 128.8, 128.7, 127.6, 126.3, 124.8, 122.1, 113.7, 91.9, 62.0, 55.2, 47.7, 29.1; HRMS (ESI, m/z): calcd. for $C_{30}H_{25}ClN_2O_3H^+$ 497.1632, found 497.1628.



3p

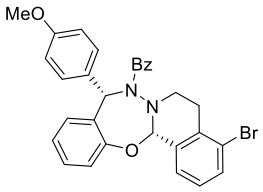
(2-Bromo-9-(4-methoxyphenyl)-5,14*a*-dihydro-6*H*-benzo[6,7][1,3,4]oxadiazepino[2,3-*a*]isoquinolin-8(9*H*)-yl)(phenyl)methanone (3p): 72.4 mg, 67% yield, white solid; mp 108-110 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (s, 1H), 7.52-7.34 (m, 6H), 7.29-7.18 (m, 7H), 6.80 (d, J = 8.4 Hz, 2H), 6.76 (d, J = 8.4 Hz, 1H),

5.57 (s, 1H), 3.76 (s, 3H), 3.00-2.93 (m, 1H), 2.49-2.45 (m, 1H), 2.18-2.14 (m, 1H), 2.03-1.94 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.1, 159.1, 159.0, 136.6, 134.8, 133.3, 131.7, 131.7, 131.3, 130.9, 130.6, 130.3, 130.0, 129.6, 129.3, 127.7, 126.3, 124.9, 122.2, 119.6, 113.7, 91.8, 62.0, 55.2, 47.7, 29.1; HRMS (ESI, m/z): calcd. for $C_{30}H_{25}BrN_2O_3H^+$ 541.1127, found 541.1120.



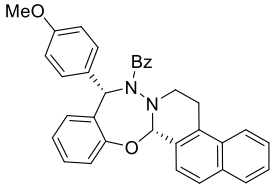
3q

(1-Bromo-9-(4-methoxyphenyl)-5,14*a*-dihydro-6*H*-benzo[6,7][1,3,4]oxadiazepino[2,3-*a*]isoquinolin-8(9*H*)-yl)(phenyl)methanone (3q): 95.0 mg, 88% yield, white solid; mp 150-152 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43-7.34 (m, 6H), 7.30-7.16 (m, 8H), 7.04 (s, 1H), 6.80 (d, *J* = 8.4 Hz, 2H), 5.57 (s, 1H), 3.75 (s, 3H), 3.02-2.95 (m,1H), 2.48-2.44 (m, 1H), 2.19-2.15 (m, 1H), 2.08-2.02 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.1, 159.1, 159.1, 136.7, 136.4, 131.9, 131.4, 131.0, 130.9, 130.6, 130.4, 130.2, 129.5, 129.4, 129.2, 127.6, 126.2, 124.8, 122.5, 122.1, 113.7, 92.1, 62.0, 55.2, 47.5, 29.4; HRMS (ESI, m/z): calcd. for $C_{30}H_{25}BrN_2O_3H^+$ 541.1127, found 541.1127.



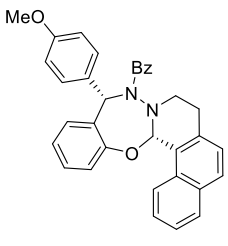
3r

(4-Bromo-9-(4-methoxyphenyl)-5,14*a*-dihydro-6*H*-benzo[6,7][1,3,4]oxadiazepino[2,3-*a*]isoquinolin-8(9*H*)-yl)(phenyl)methanone (3r): 82.1 mg, 76% yield, white solid; mp 117-120 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45-7.33 (m, 7H), 7.31-7.17 (m, 7H), 7.10 (t, *J* = 7.6 Hz, 1H), 6.80 (d, *J* = 8.4 Hz, 2H), 5.58 (s, 1H), 3.76 (s, 3H), 3.06-2.99 (m, 1H), 2.58-2.53 (m, 1H), 2.48-2.44 (m, 1H), 1.99-1.90 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.2, 159.3, 159.2, 136.6, 135.2, 134.2, 132.7, 131.5, 131.1, 130.7, 130.3, 129.6, 129.5, 128.2, 127.8, 127.6, 126.4, 124.9, 124.4, 122.1, 113.8, 92.2, 62.0, 55.3, 47.6, 30.6; HRMS (ESI, m/z): calcd. for $C_{30}H_{25}BrN_2O_3H^+$ 541.1127, found 541.1121.



3s

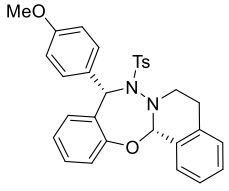
(9-(4-Methoxyphenyl)-5,14*a*-dihydro-6*H*-benzo[*f*]benzo[6,7][1,3,4]oxadiazepino[2,3-*a*]isoquinolin-8(9*H*)-yl)(phenyl)methanone (3s): 97.3 mg, 95% yield, white solid; mp 192-194 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 7.2 Hz, 1H), 7.73 (d, *J* = 8.8 Hz, 1H), 7.69 (d, *J* = 8 Hz, 1H), 7.49-7.37 (m, 9H), 7.32 (d, *J* = 8 Hz, 2H), 7.25-7.18 (m, 4H), 6.81 (d, *J* = 8.4 Hz, 2H), 5.72 (s, 1H), 3.75 (s, 3H), 3.19-3.13 (m, 1H), 2.82-2.78 (m, 1H), 2.72-2.67 (m, 1H), 2.35-2.26 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.2, 159.5, 159.2, 136.7, 133.3, 131.4, 131.2, 131.2, 130.9, 130.5, 130.3, 129.9, 129.6, 129.2, 128.4, 127.6, 126.8, 126.5, 126.3, 126.3, 126.0, 124.7, 123.3, 122.2, 113.8, 93.0, 62.0, 55.2, 47.6, 26.3; HRMS (ESI, m/z): calcd. for $C_{34}H_{28}N_2O_3H^+$ 513.2178, found 513.2175.



3t

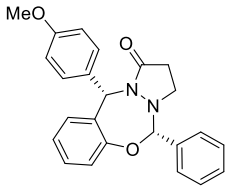
(11-(4-Methoxyphenyl)-7,16*a*-dihydro-8*H*-benzo[*h*]benzo[6,7][1,3,4]oxadiazepino[2,3-*a*]isoquinolin-10(11*H*)-yl)(phenyl)methanone (3t): 76.8 mg, 75% yield, white solid; mp 171-173 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.4 Hz, 1H), 7.81 (d, *J*

= 8 Hz, 1H), 7.67 (d, *J* = 8.4 Hz, 1H), 7.60 (t, *J* = 7.2 Hz, 1H), 7.55 (s, 1H), 7.50-7.40 (m, 5H), 7.34-7.26 (m, 4H), 7.24-7.15 (m, 3H), 6.99 (d, *J* = 8.4 Hz, 1H), 6.80 (d, *J* = 8.8 Hz, 1H), 6.17 (s, 1H), 3.75 (s, 3H), 3.29-3.22 (m, 1H), 2.59-2.56 (m, 1H), 2.36-2.32 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.1, 159.1, 159.0, 136.7, 132.6, 132.4, 131.6, 130.9, 130.8, 130.2, 129.6, 129.3, 129.2, 128.7, 127.5, 127.4, 126.6, 126.6, 125.2, 124.7, 123.4, 122.1, 113.7, 91.0, 61.9, 55.2, 47.7, 30.3; HRMS (ESI, m/z): calcd. for $C_{34}H_{28}N_2O_3H^+$ 513.2178, found 513.2177.



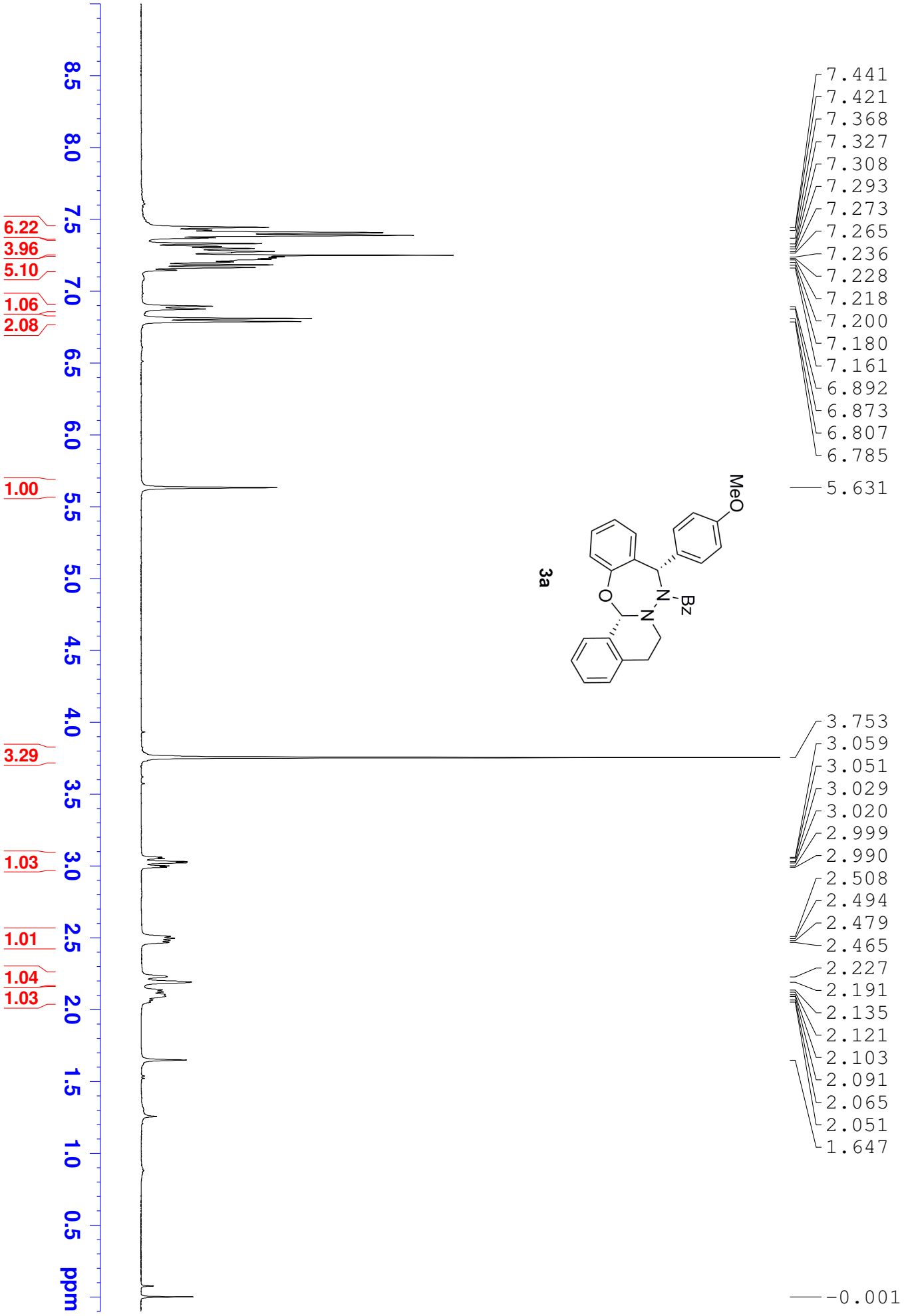
3u

9-(4-Methoxyphenyl)-8-tosyl-5,8,9,14*a*-tetrahydro-6*H*-benzo [6,7][1,3,4]oxadiazepino[2,3-*a*]isoquinoline (3u): 41.0 mg, 40% yield, yellow solid; mp 79-81 °C;^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.0 Hz, 2H), 7.35 (t, *J* = 6.0 Hz, 2H), 7.28-7.18 (m, 6H), 7.15 (d, *J* = 8.4 Hz, 3H), 6.99 (t, *J* = 4.8 Hz, 1H), 6.79 (m, 3H), 5.36 (s, 1H), 3.74 (s, 3H), 2.87-2.80 (m, 1H), 2.63-2.55(m, 1H), 2.43-2.39 (m, 1H), 2.36 (s, 3H), 2.33-2.29 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4, 159.1, 143.5, 136.4, 134.3, 133.4, 131.1, 130.4, 130.4, 129.7, 129.3, 129.0, 128.7, 128.4, 128.2, 126.2, 124.8, 122.2, 113.6, 91.1, 64.7, 55.2, 47.7, 30.3, 21.6; HRMS (ESI, m/z): calcd. for $C_{30}H_{28}N_2O_4SH^+$ 513.1848, found 513.1852.



5

11-(4-Methoxyphenyl)-5-phenyl-2,3-dihydro-1*H*,5*H*,11*H*-benzo[*f*]pyrazolo[1,2-*c*][1,3,4]oxadiazepin-1-one: 71.8 mg, 93% yield, white solid; mp 191-193 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33-7.31 (m, 5H), 7.27-7.20 (m, 4H), 7.15 (d, *J* = 8.4 Hz, 1H), 7.09 (t, *J* = 7.2 Hz, 1H), 6.93 (s, 1H), 6.89 (d, *J* = 8.4 Hz, 2H), 6.02 (s, 1H), 3.82 (s, 3H), 3.24-3.17 (m, 1H), 2.81 (t, *J* = 8.4 Hz, 1H), 2.69-2.60 (m, 1H), 2.55-2.49 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.1, 159.0, 157.2, 134.3, 131.6, 131.2, 128.6, 128.6, 128.3, 126.5, 125.4, 122.6, 120.4, 113.9, 91.8, 56.1, 55.3, 42.6, 30.8; HRMS (ESI, m/z): calcd. for $C_{24}H_{22}N_2O_3H^+$ 387.1709, found 387.1707.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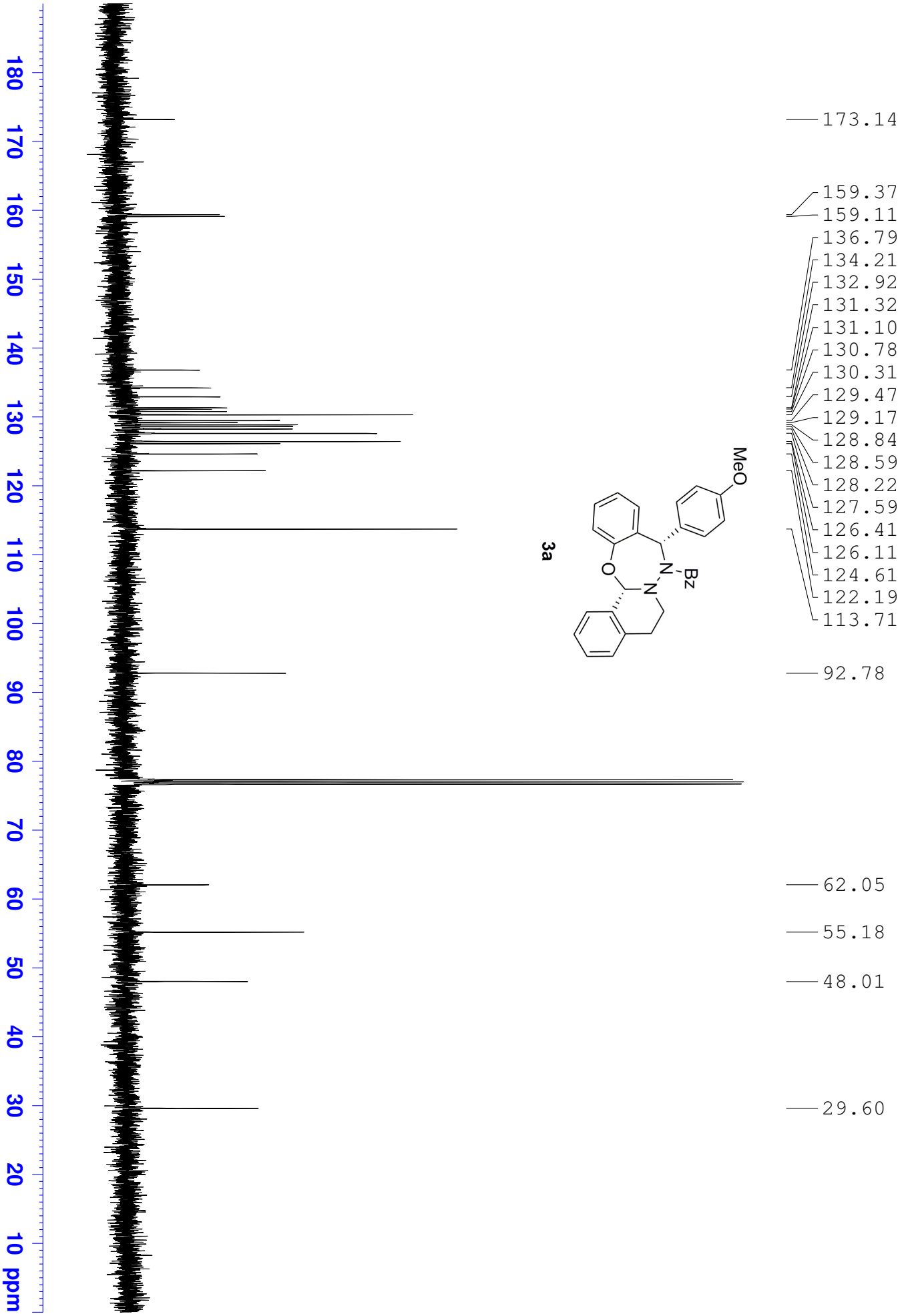
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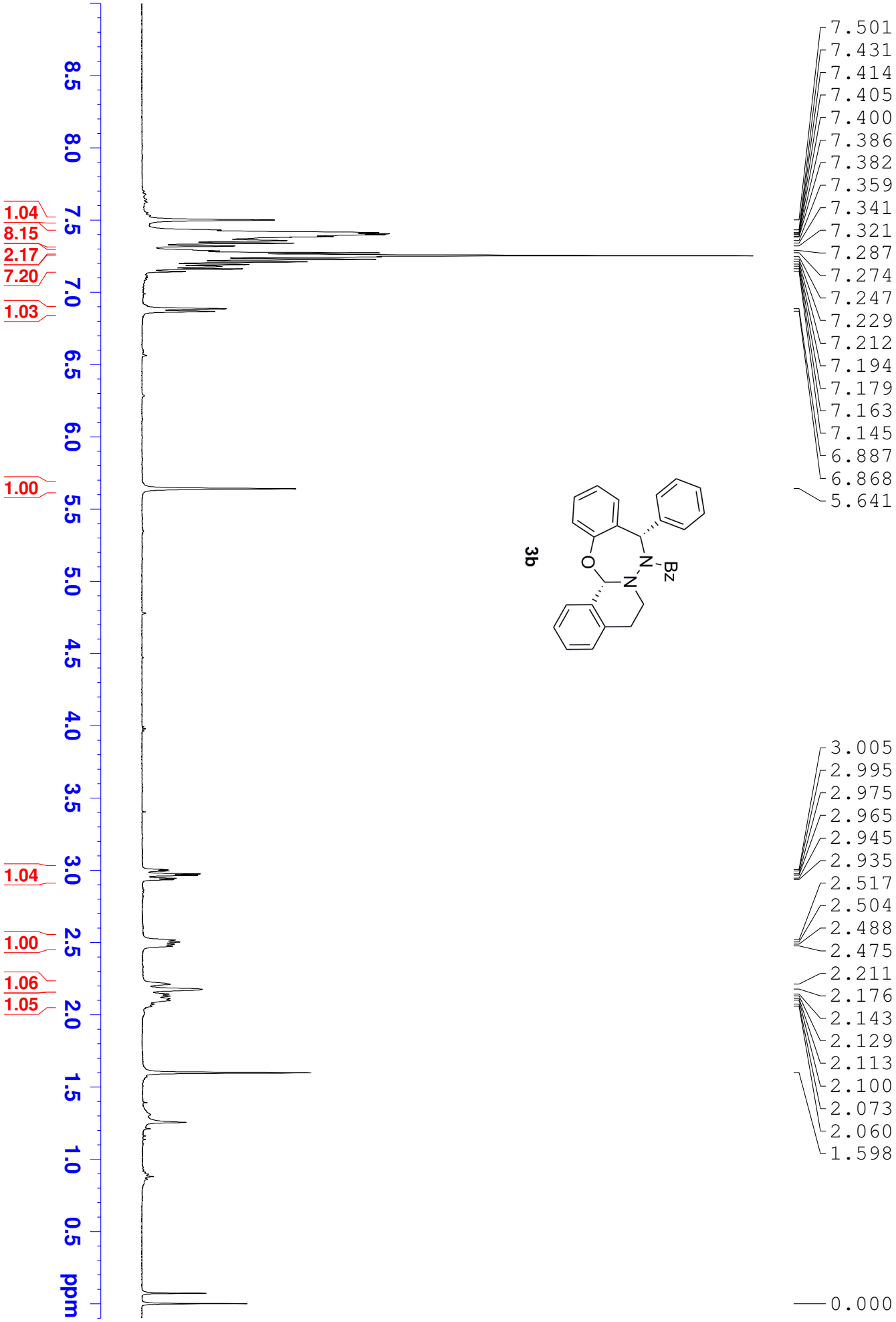
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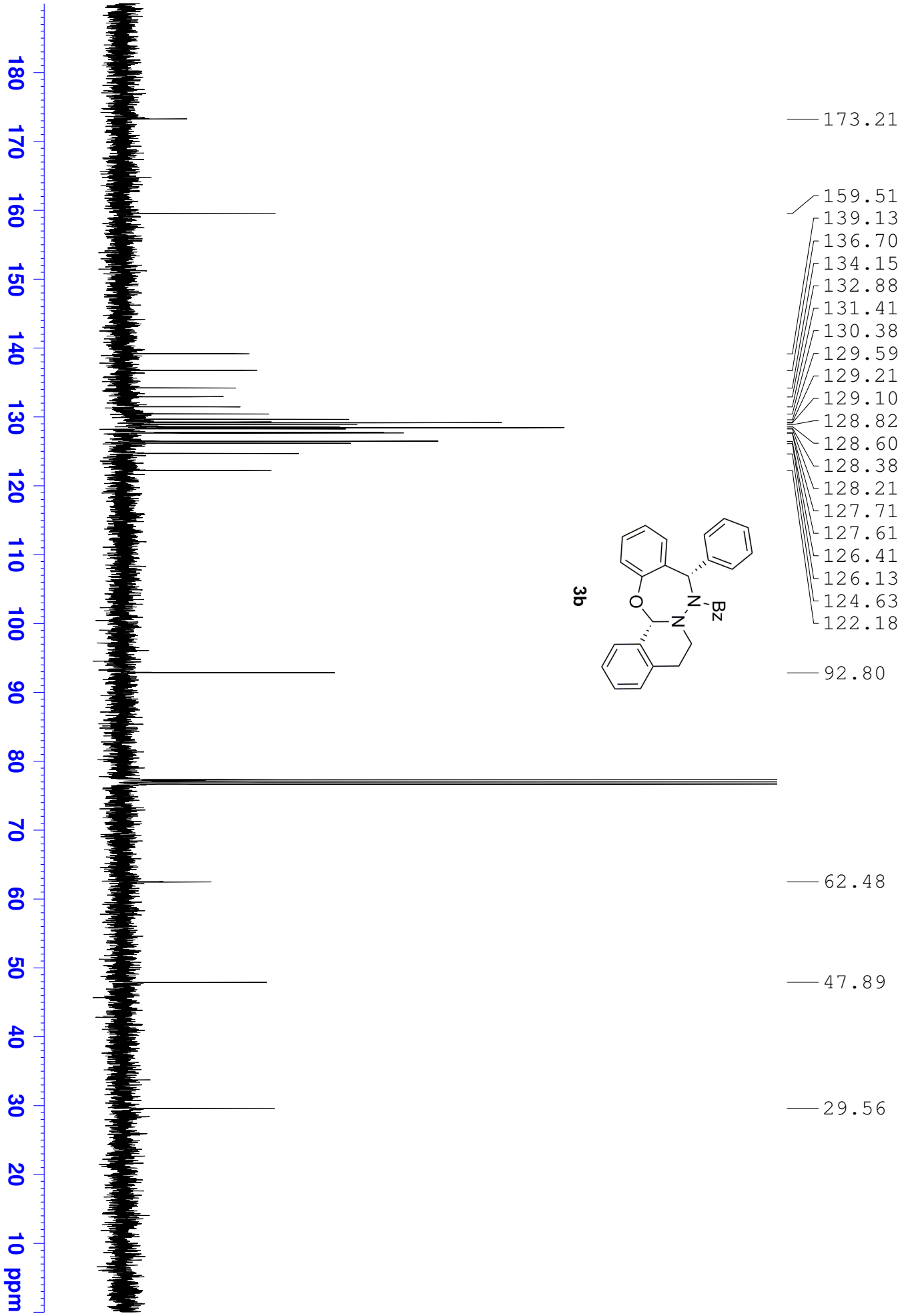
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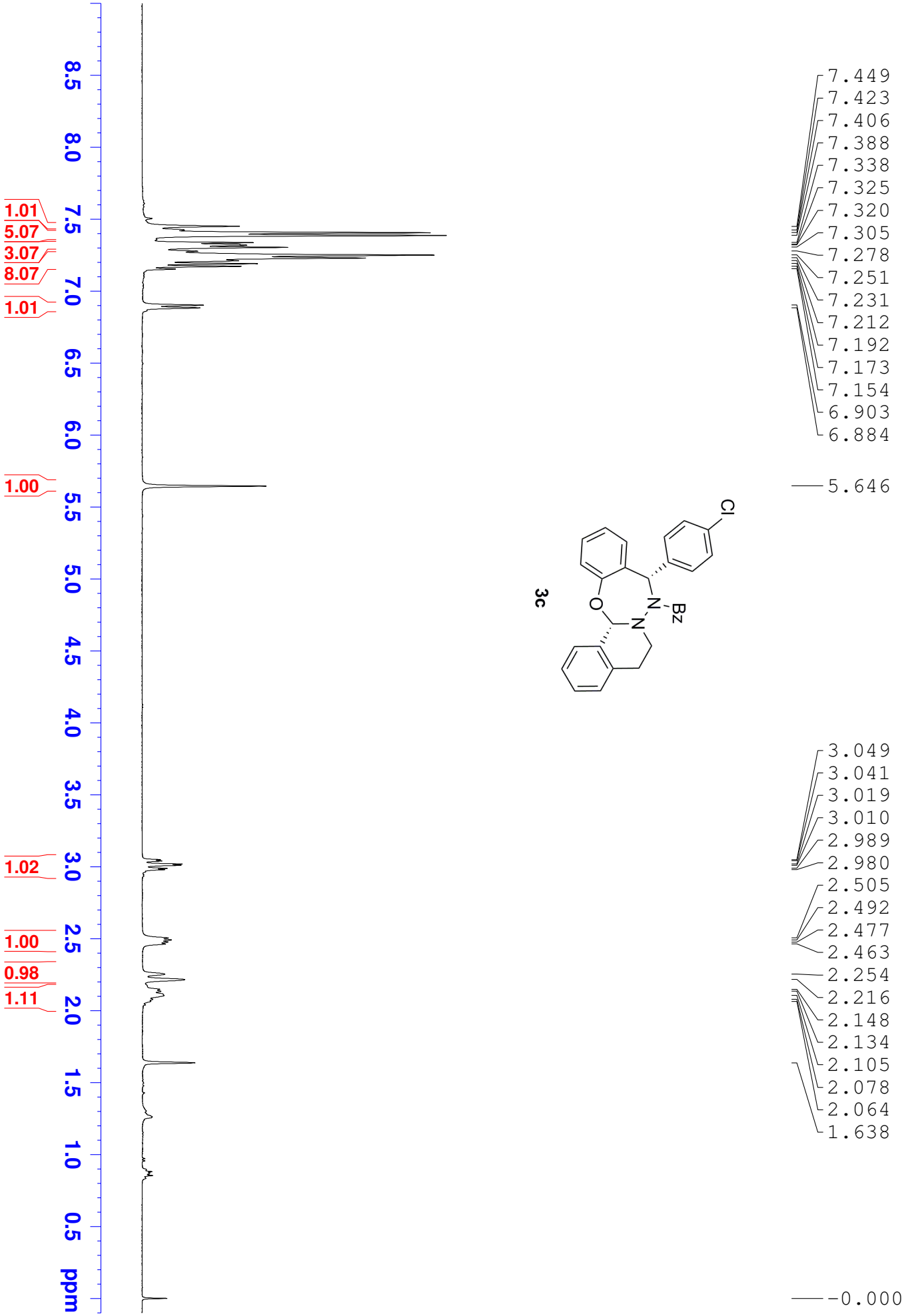
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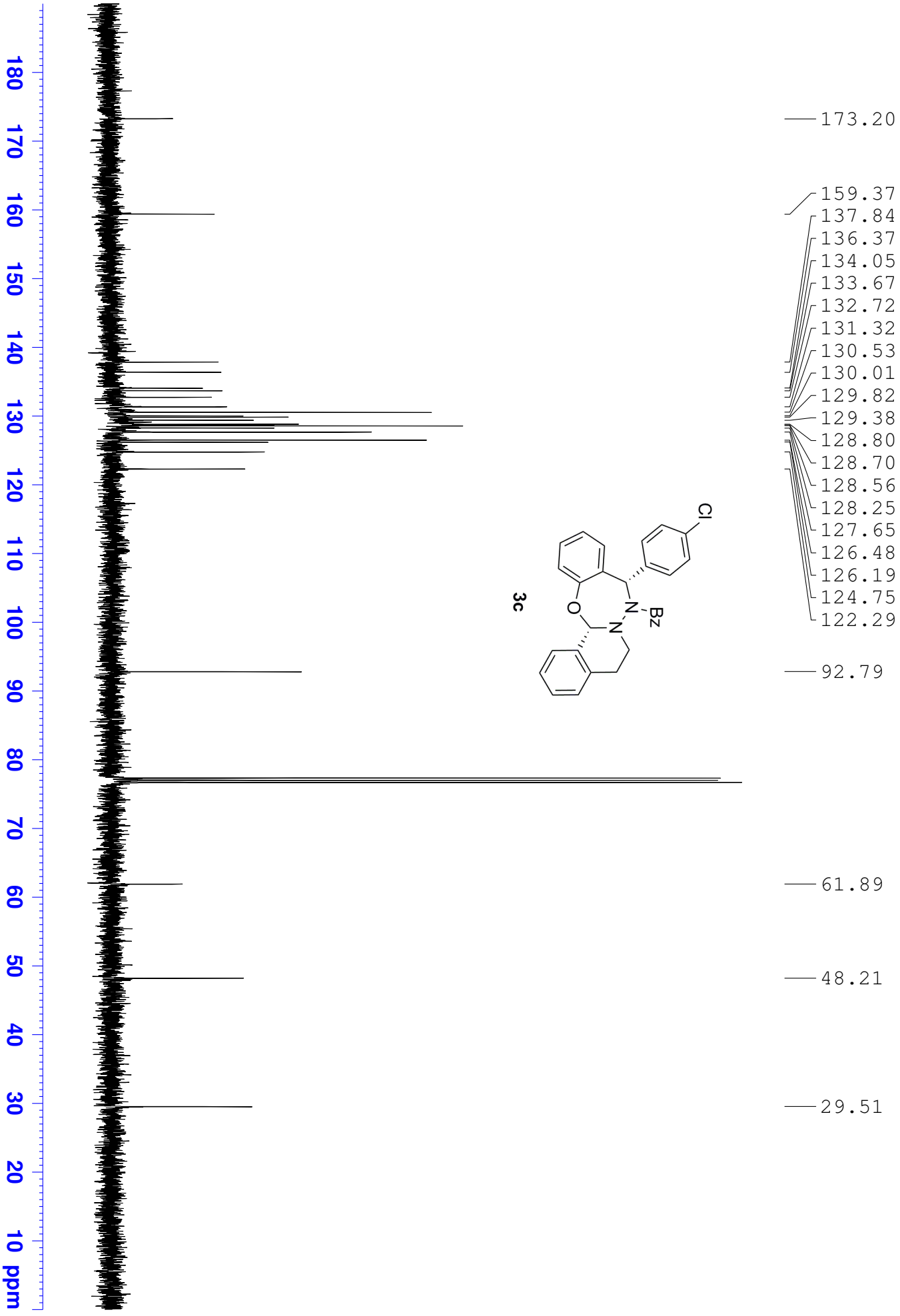
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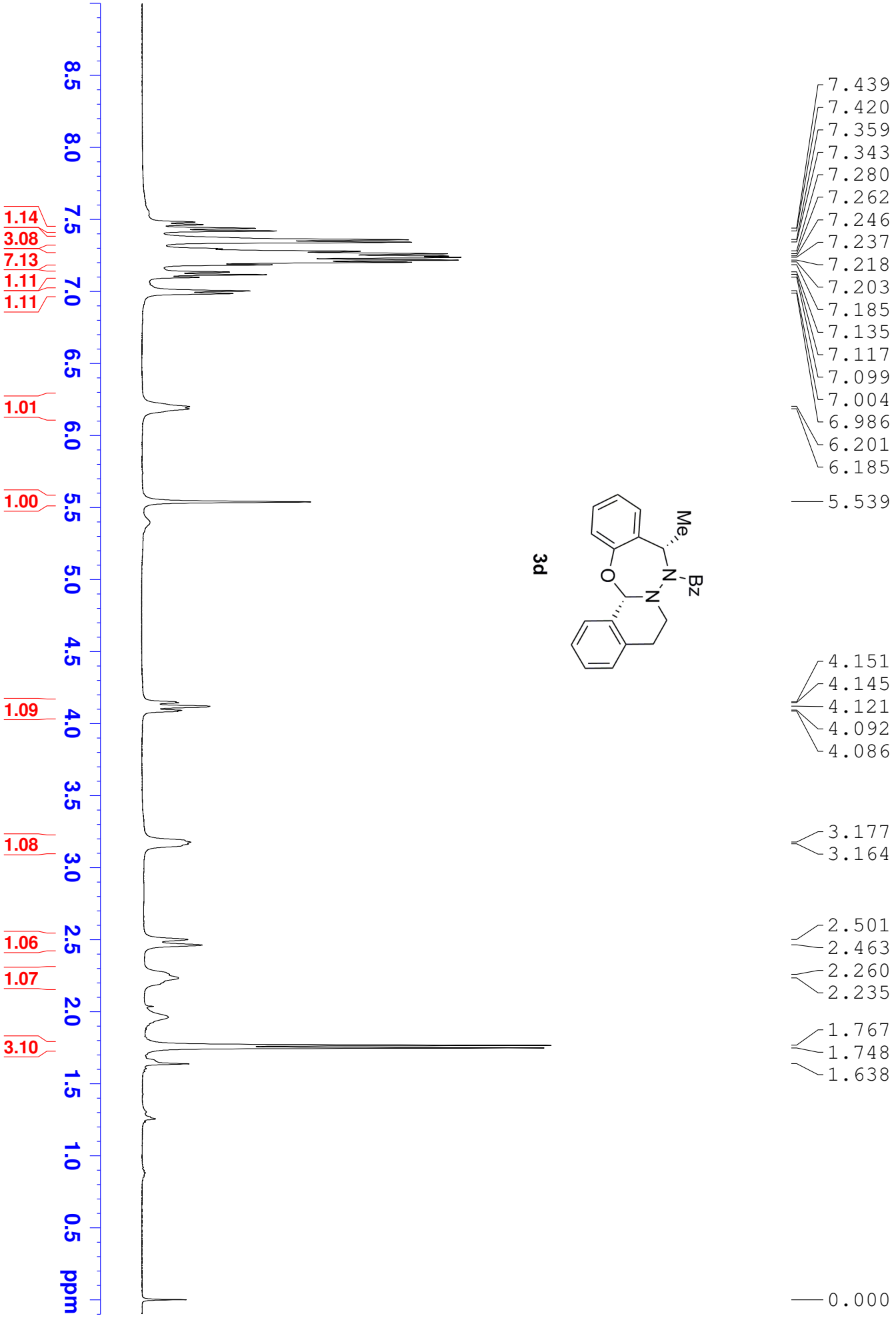
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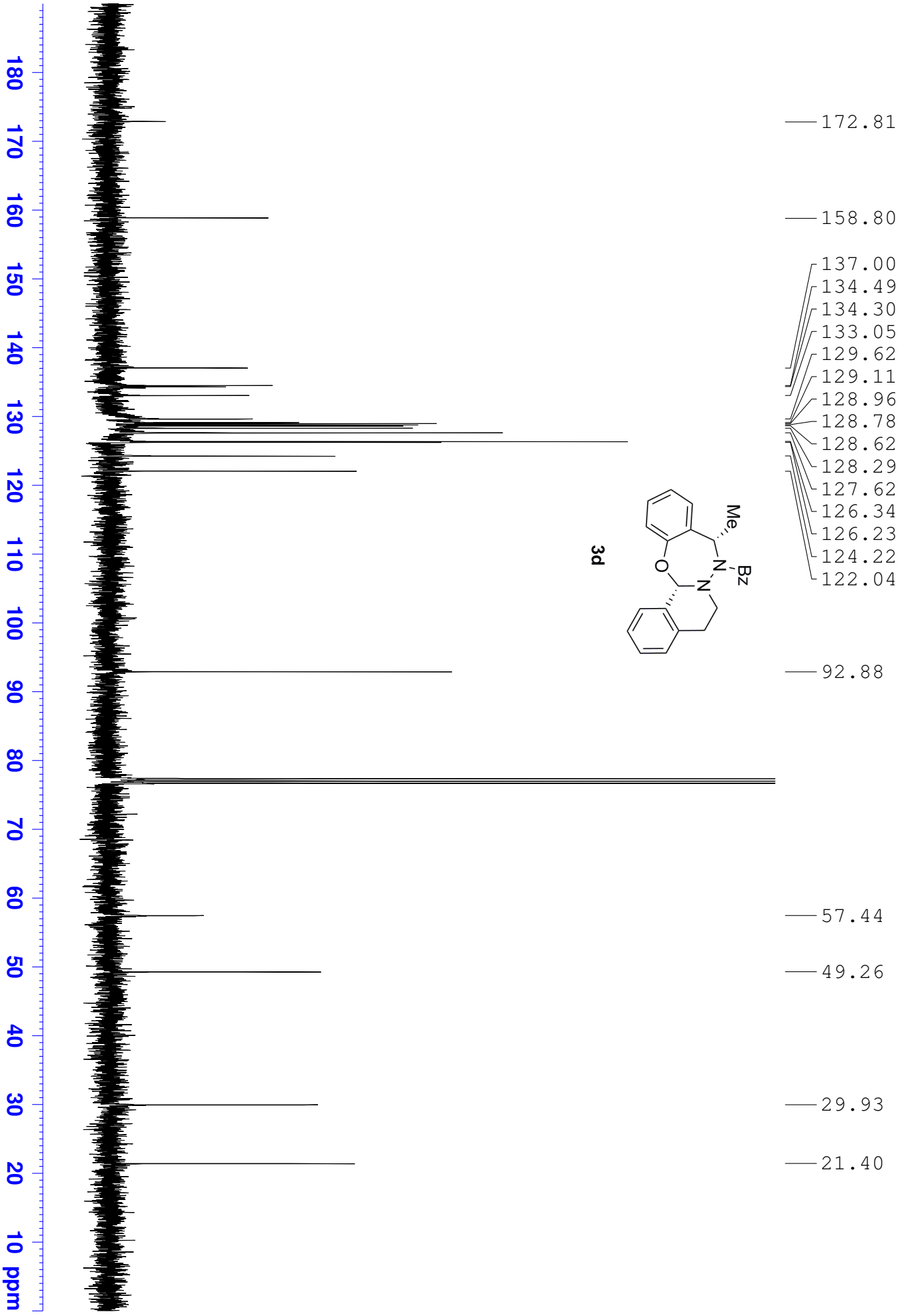
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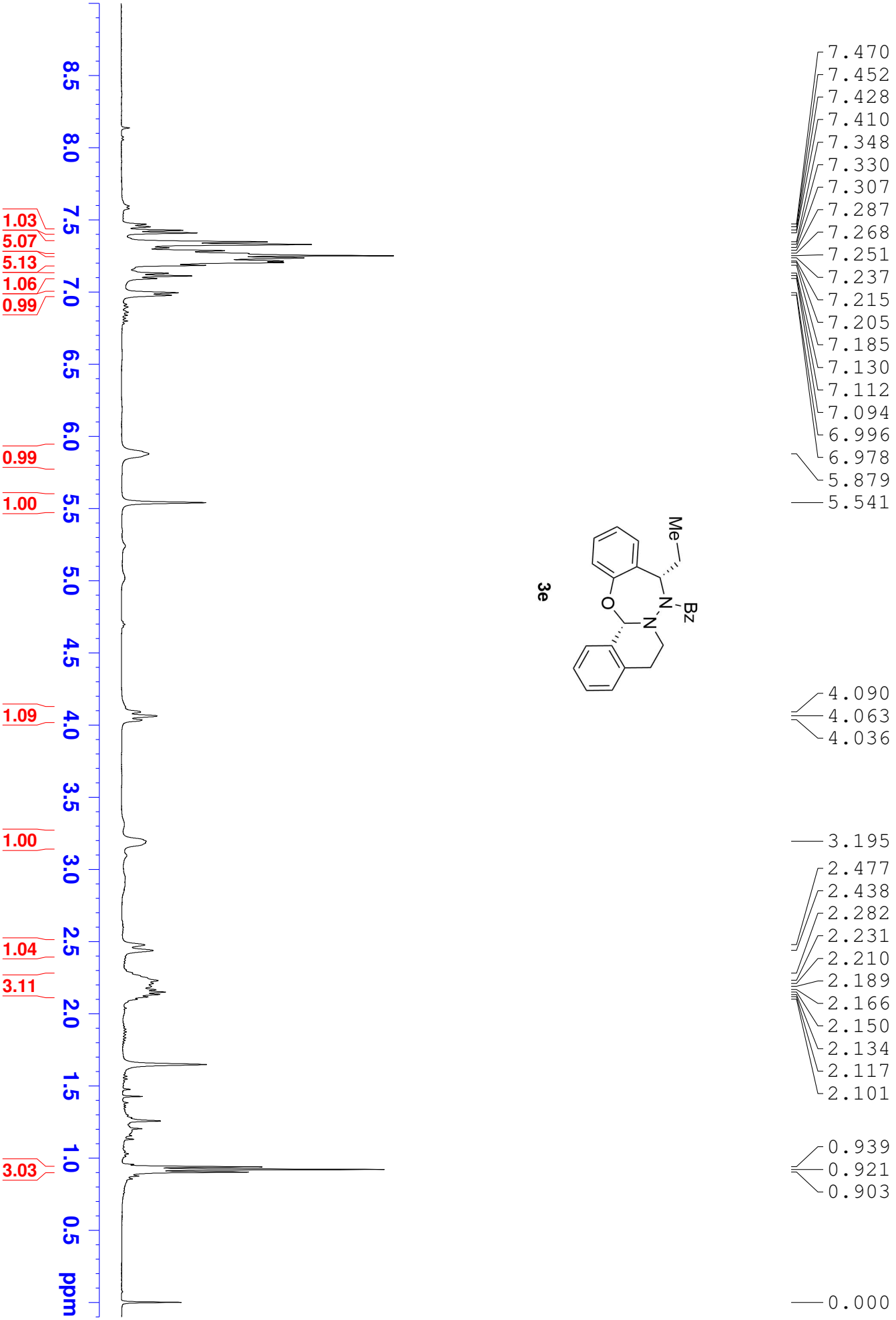
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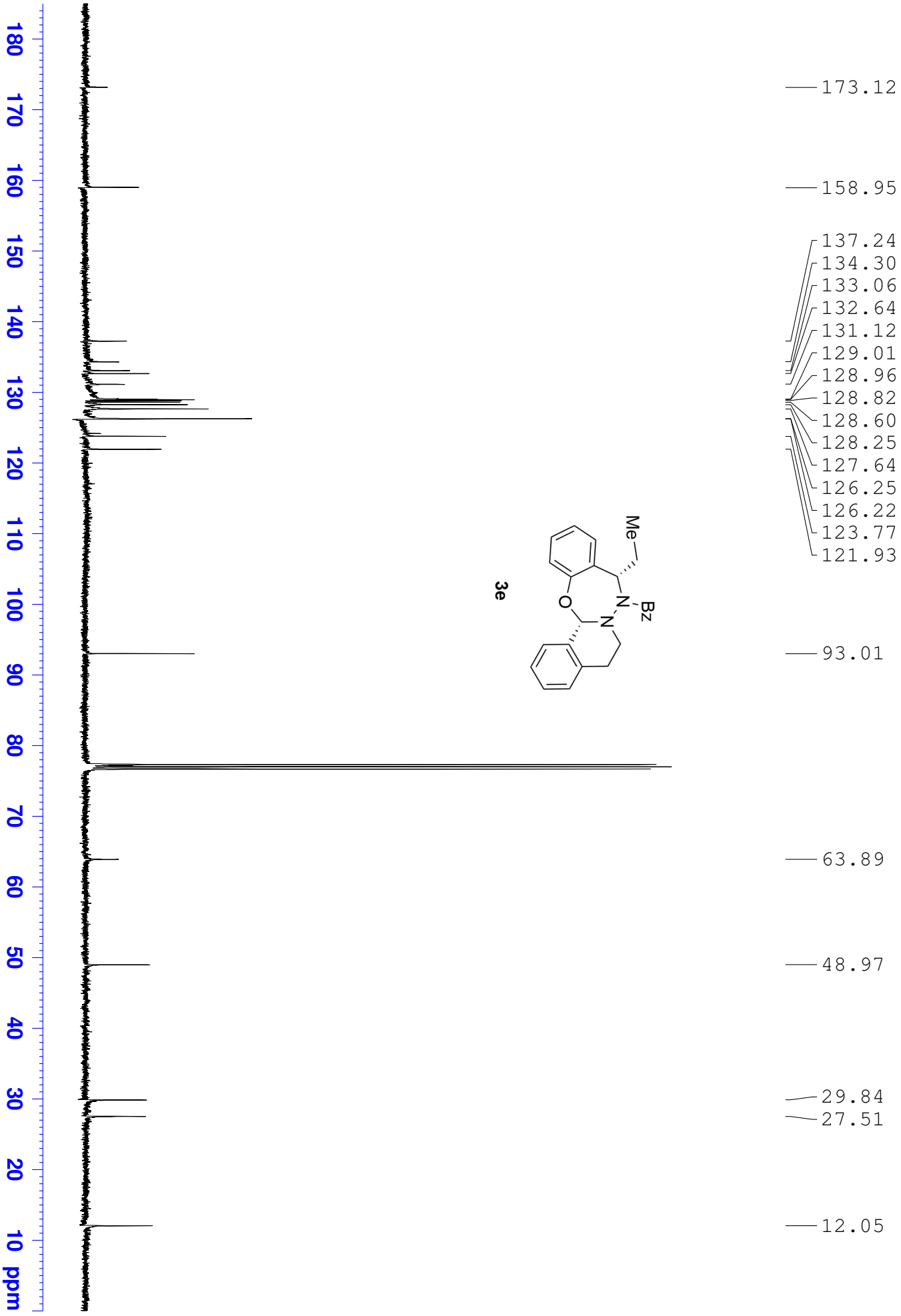
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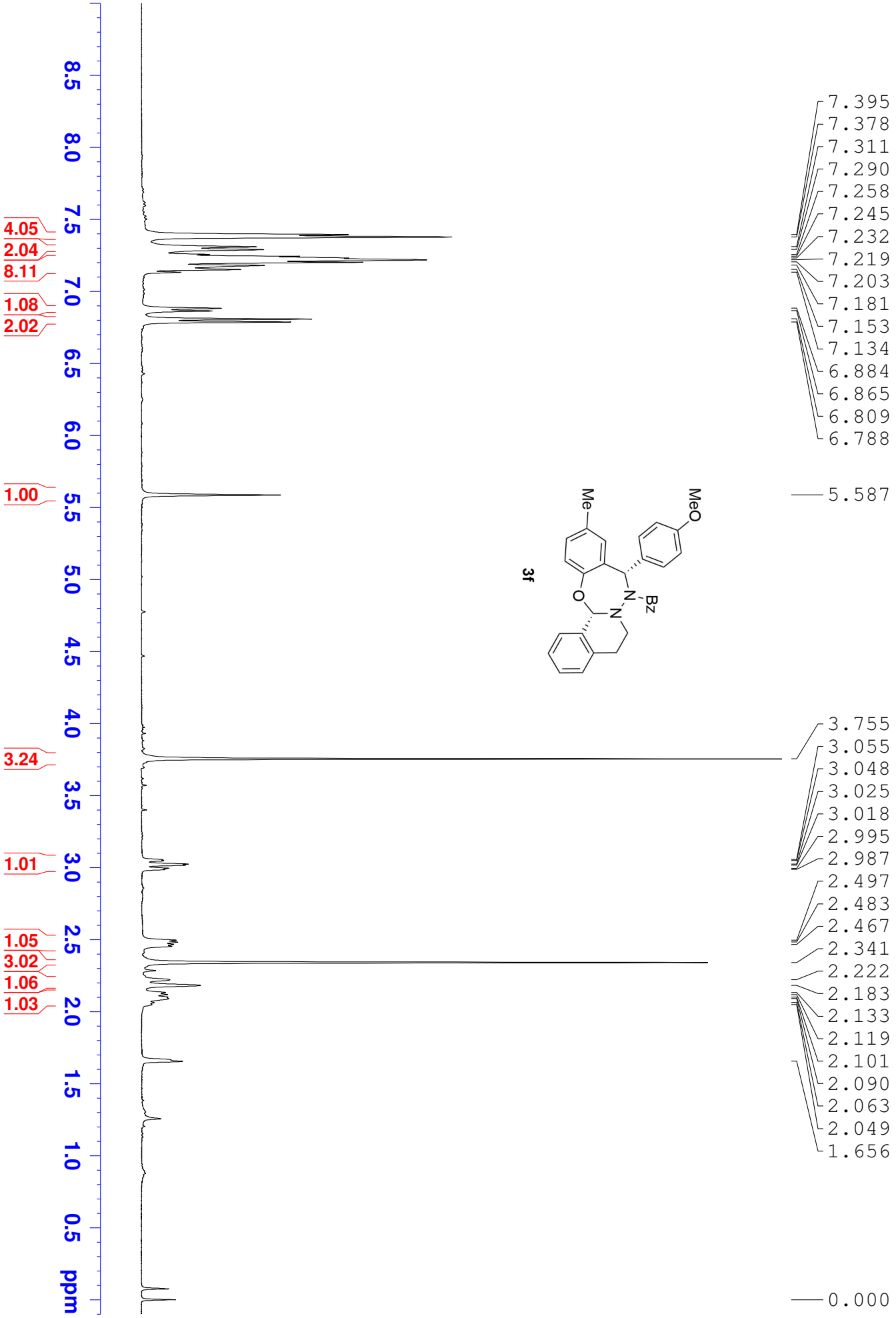
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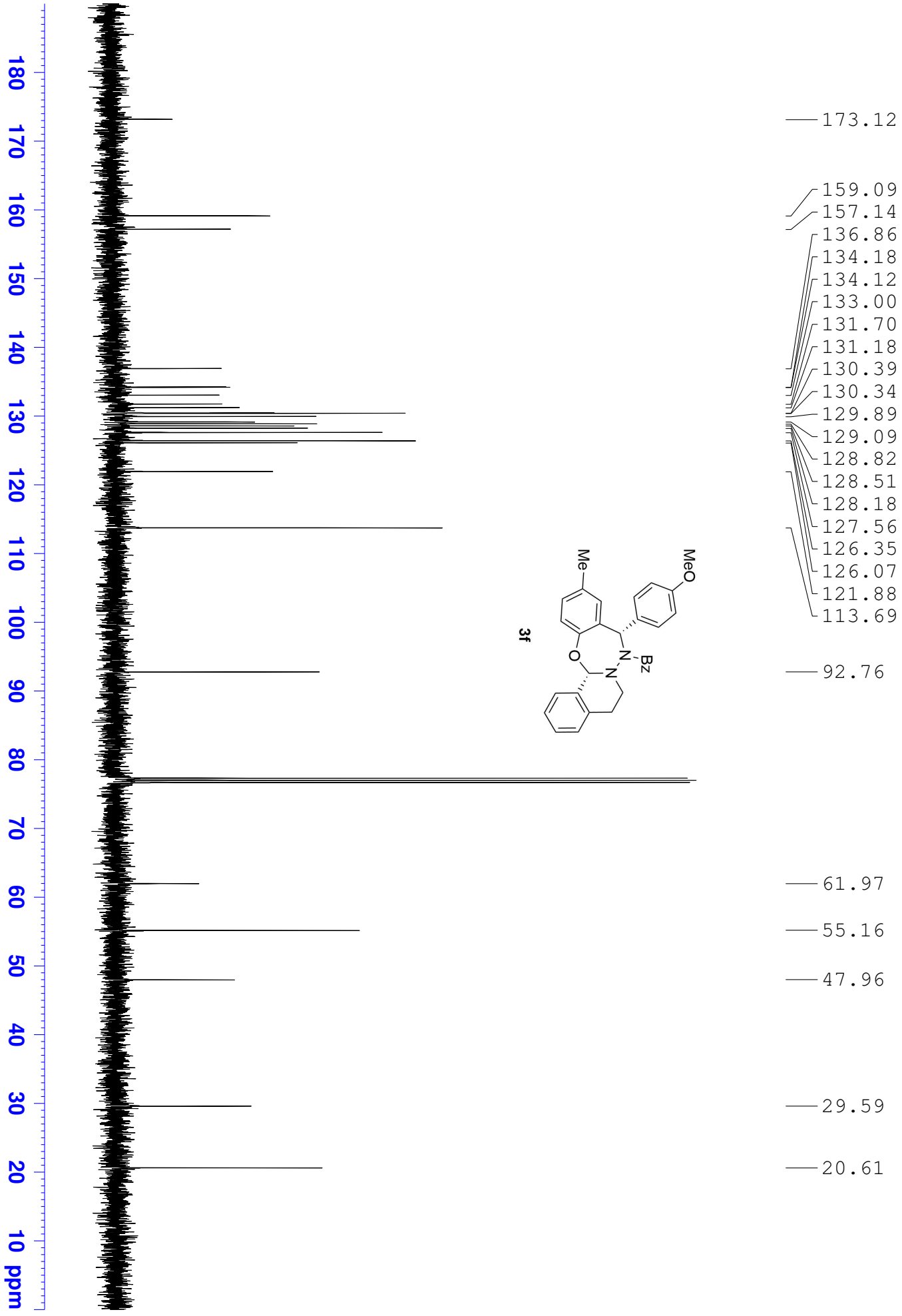
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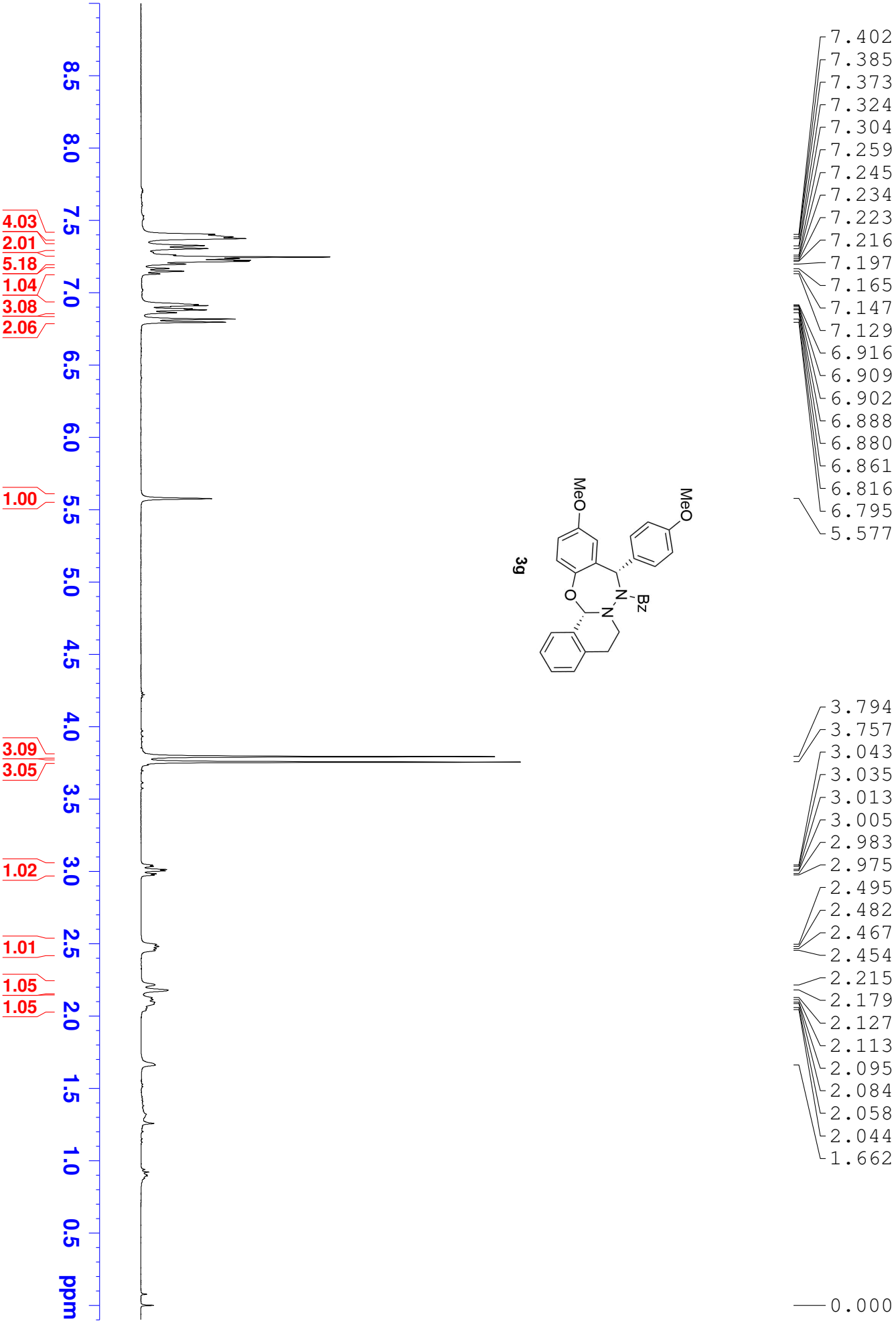
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Bz
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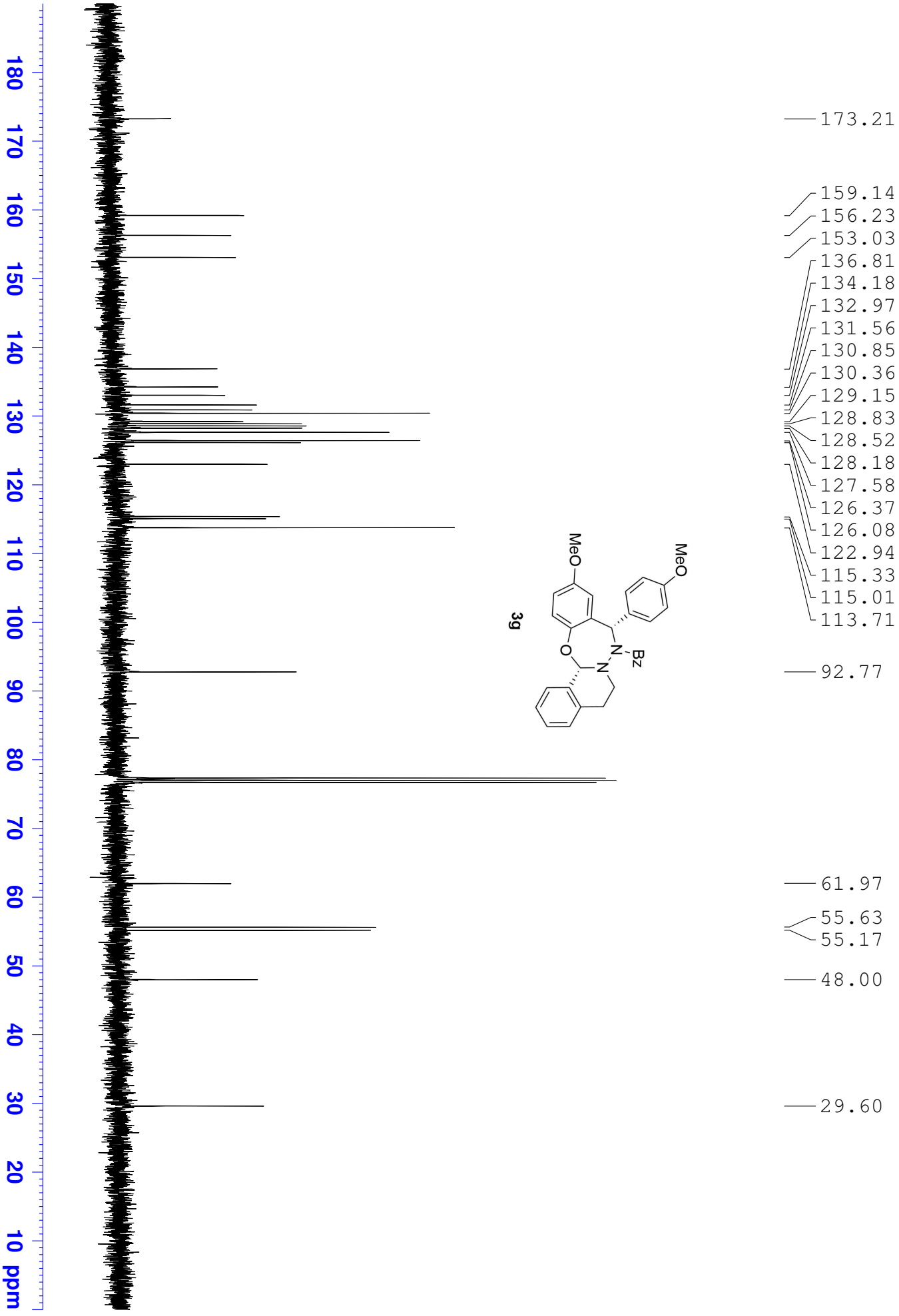
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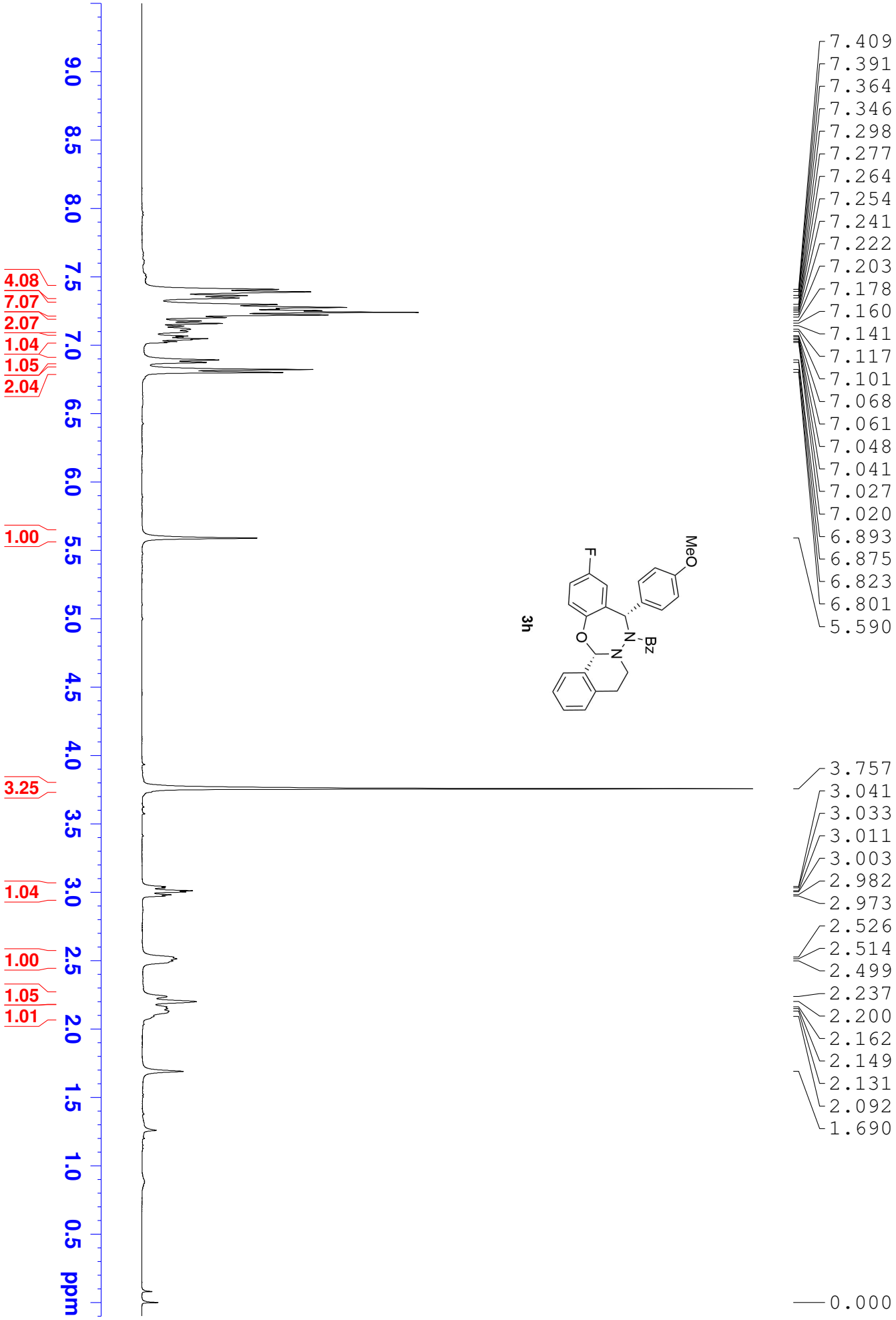
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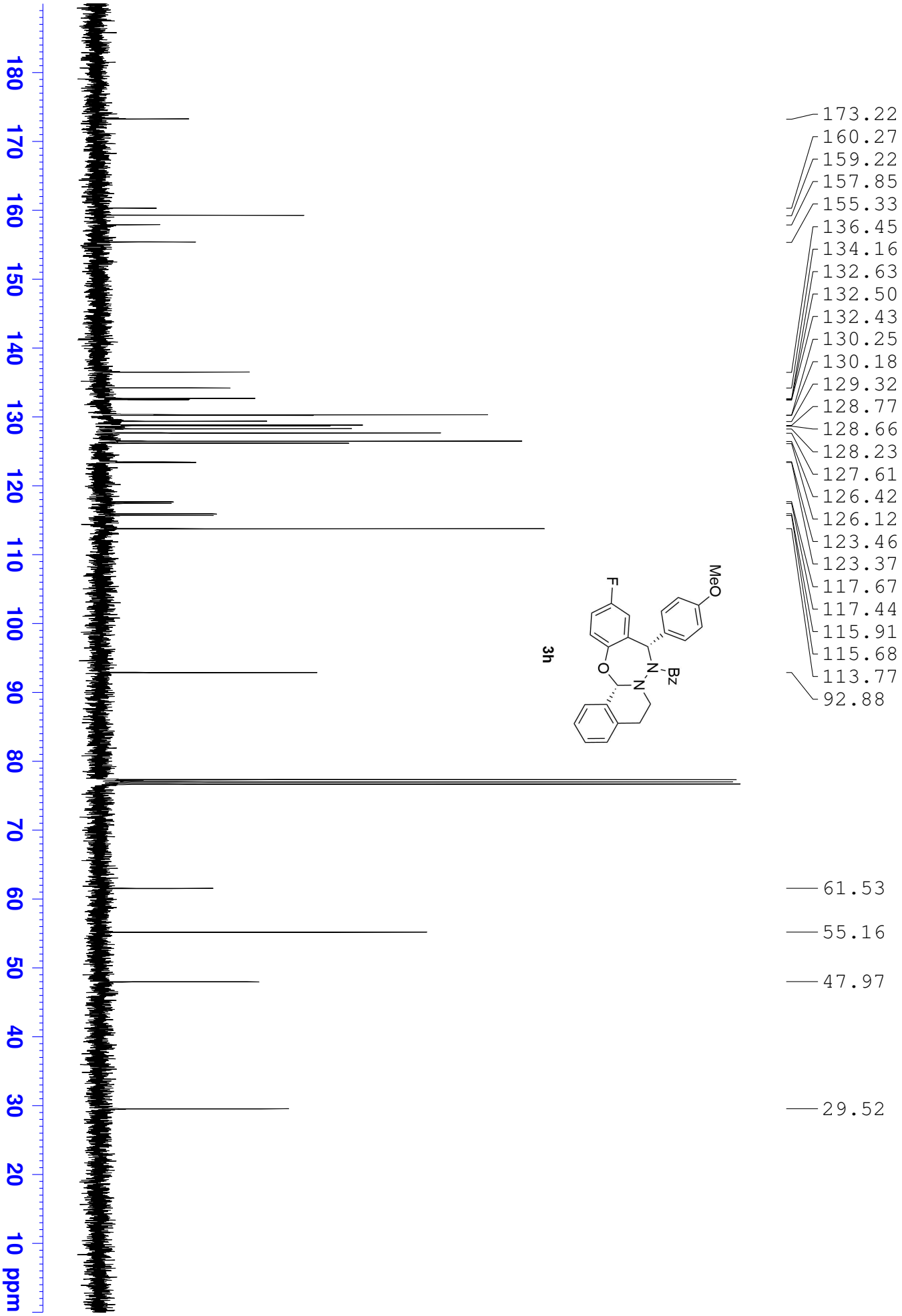
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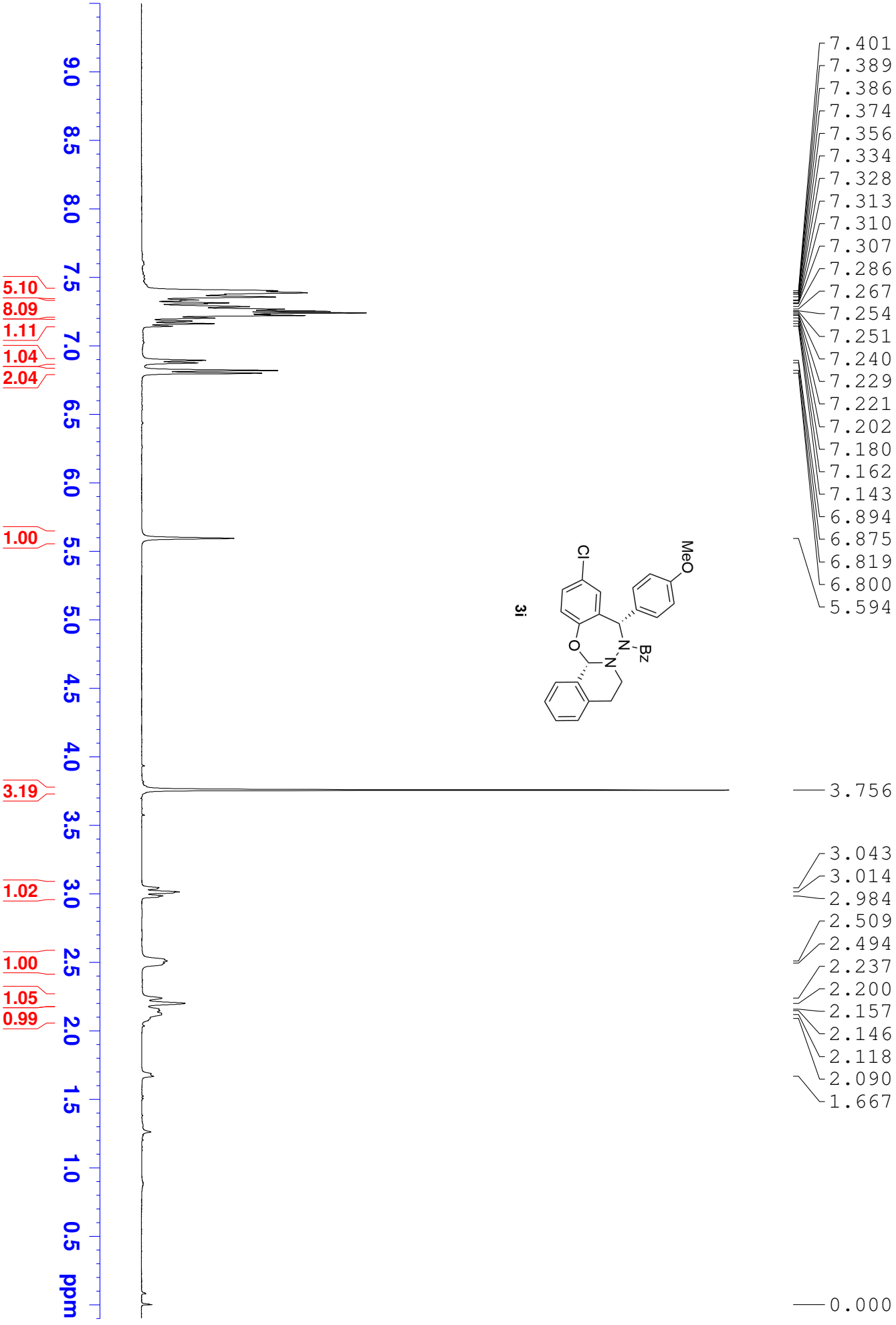
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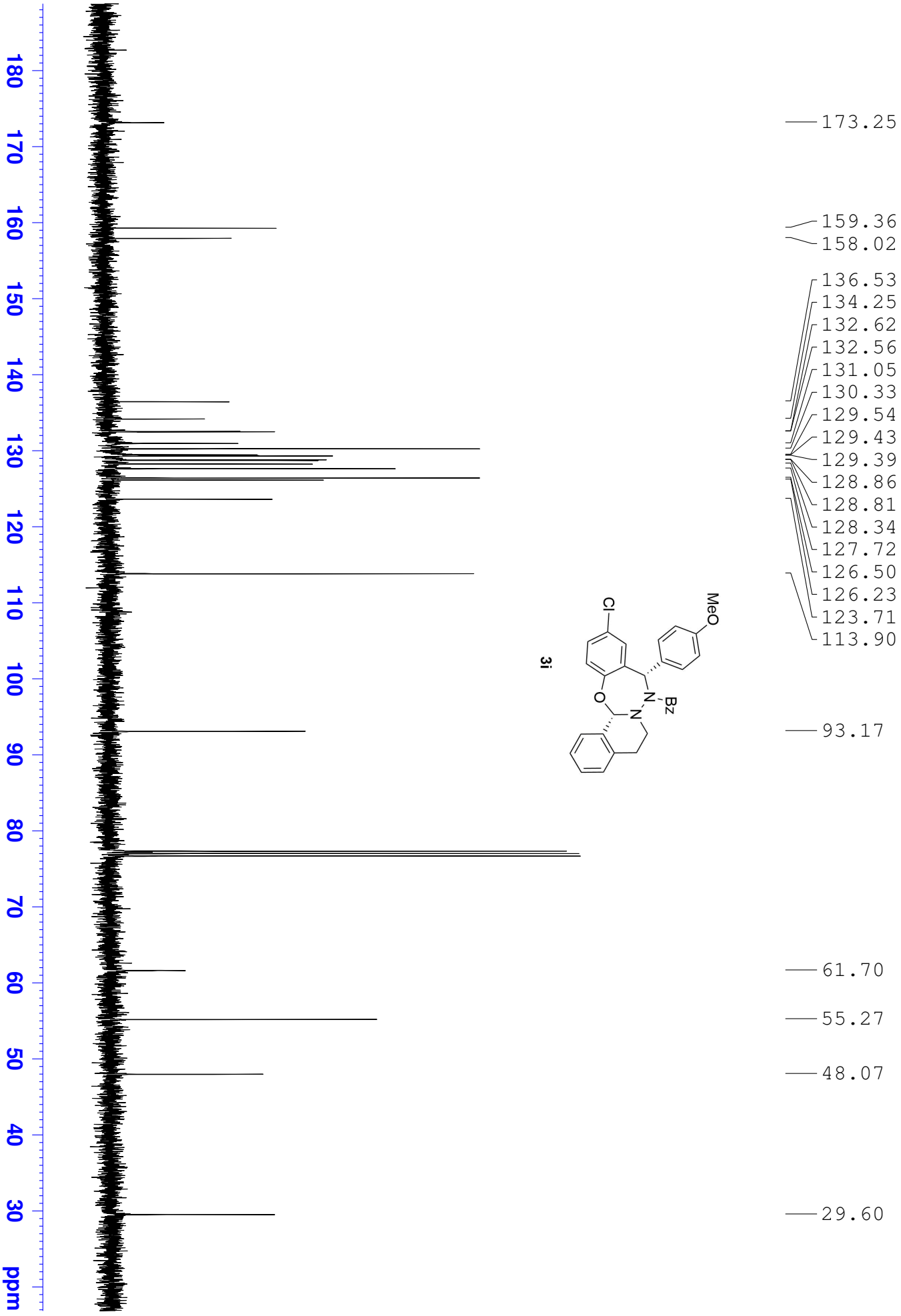
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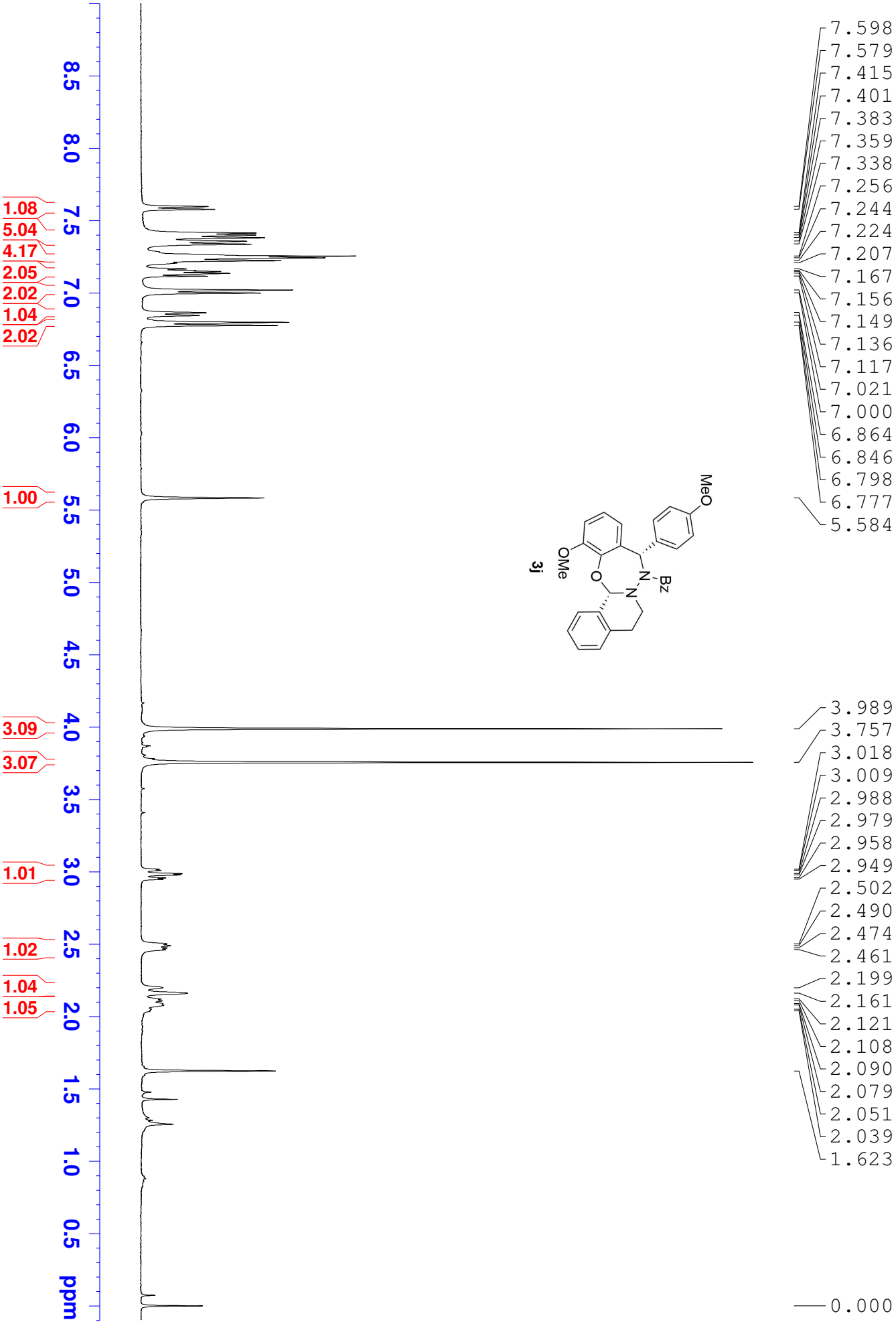
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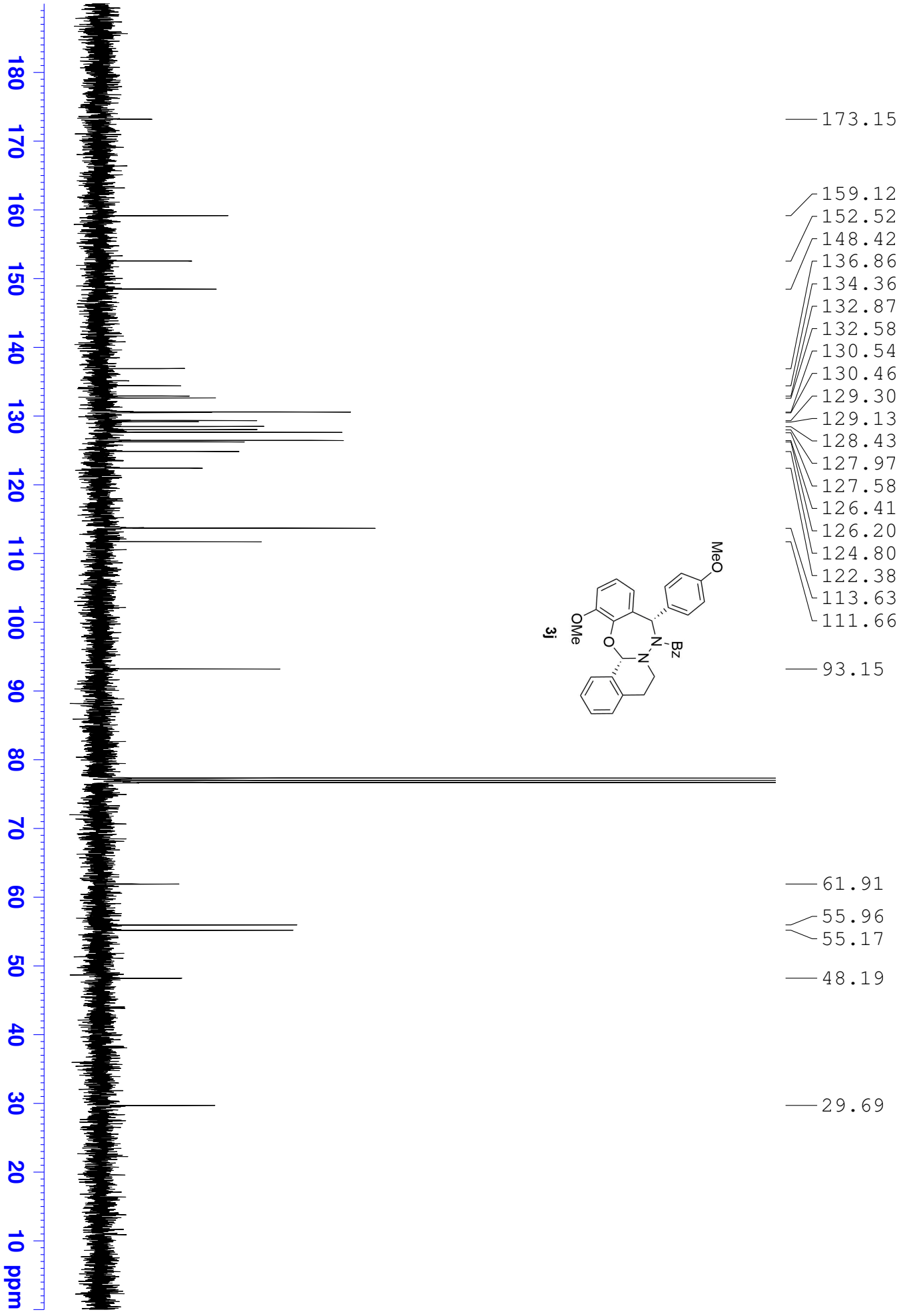
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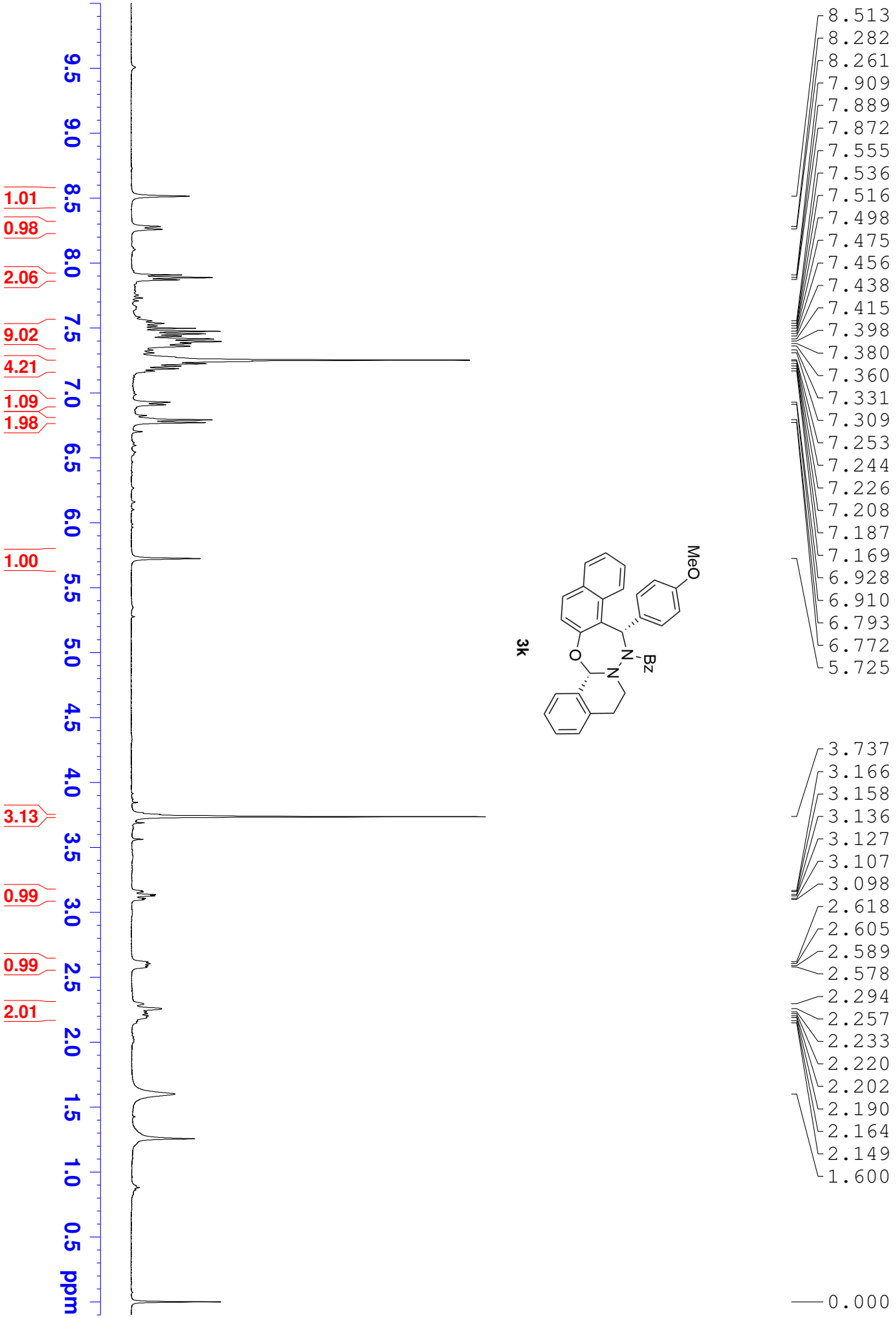
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O
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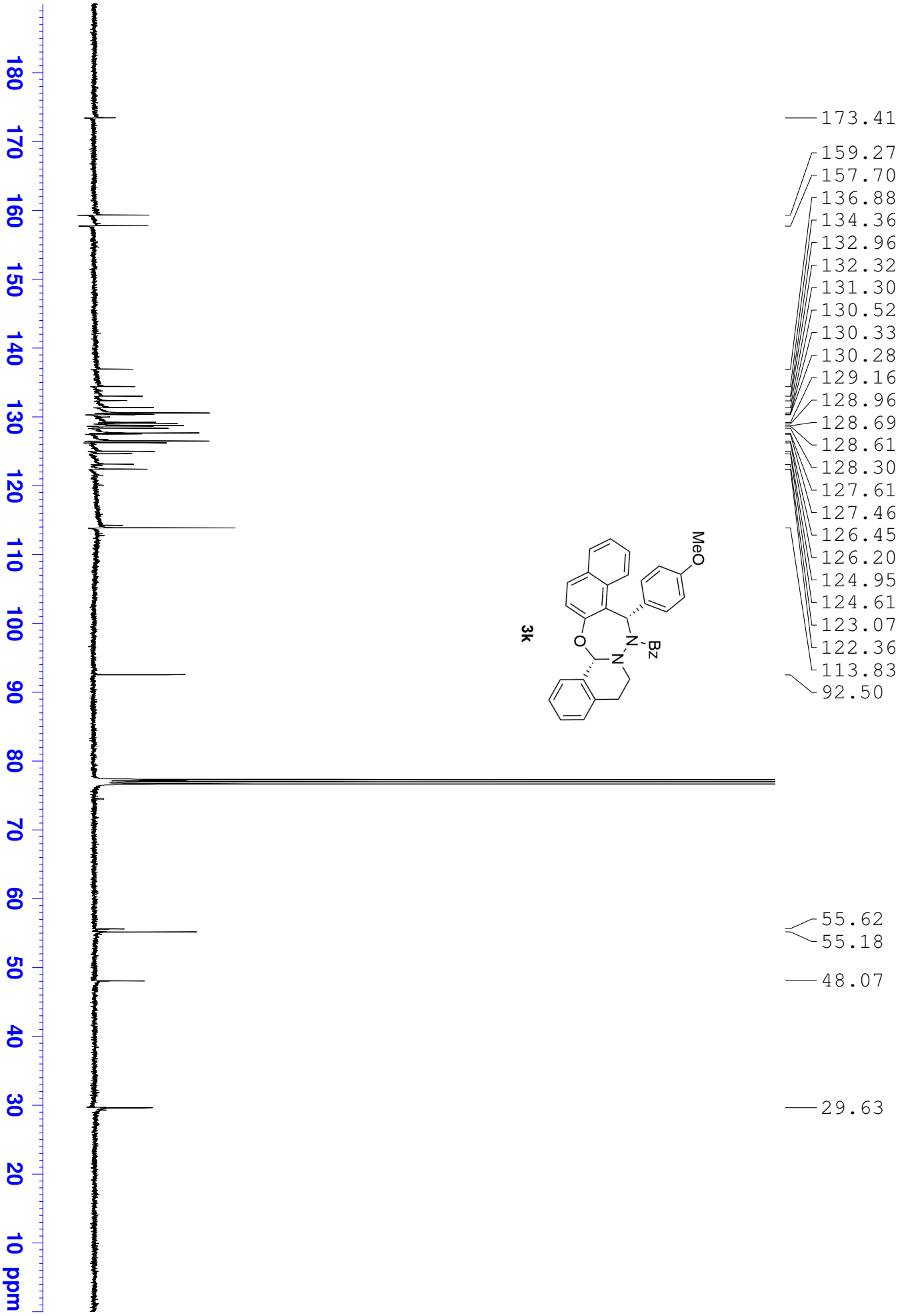
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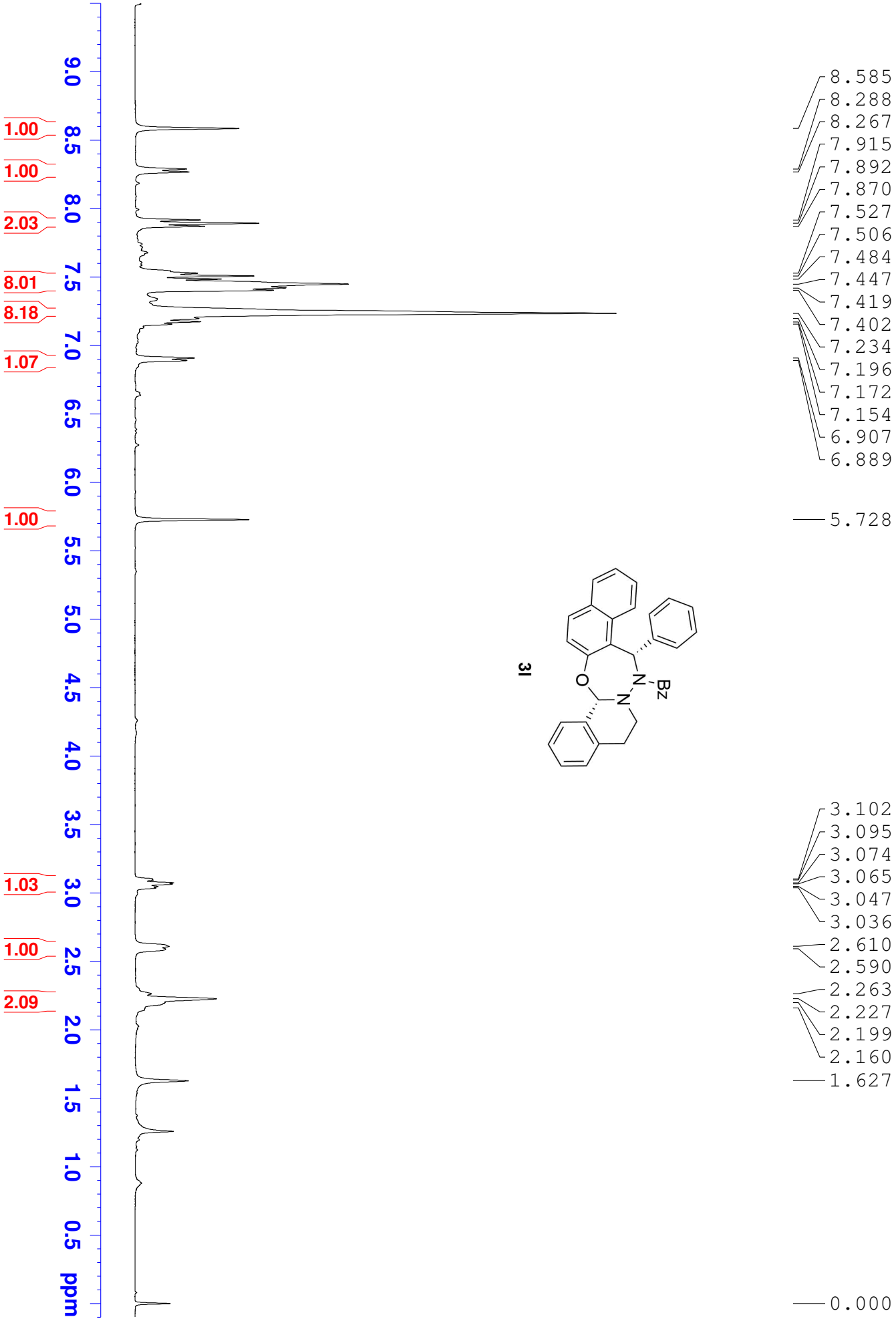
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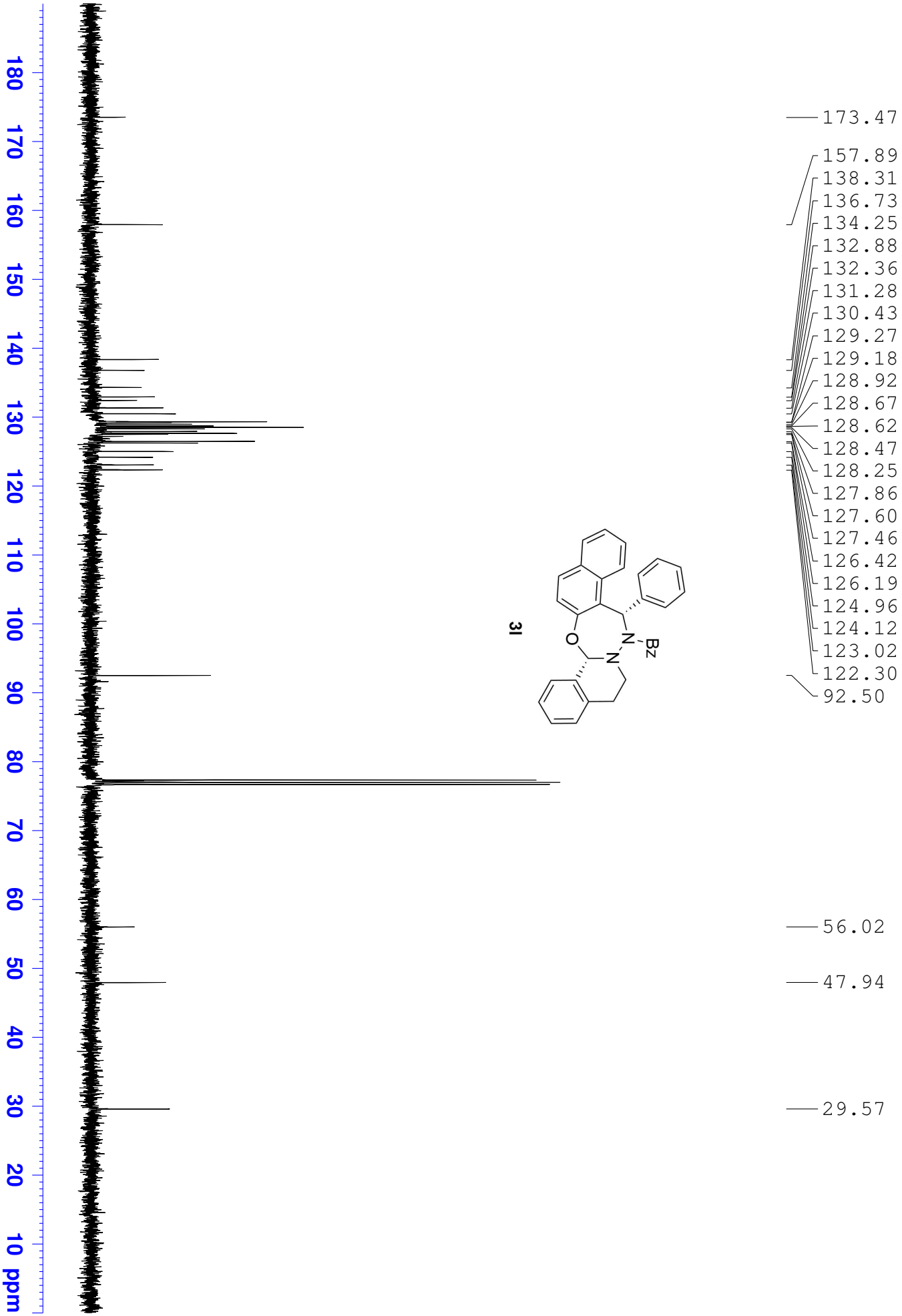
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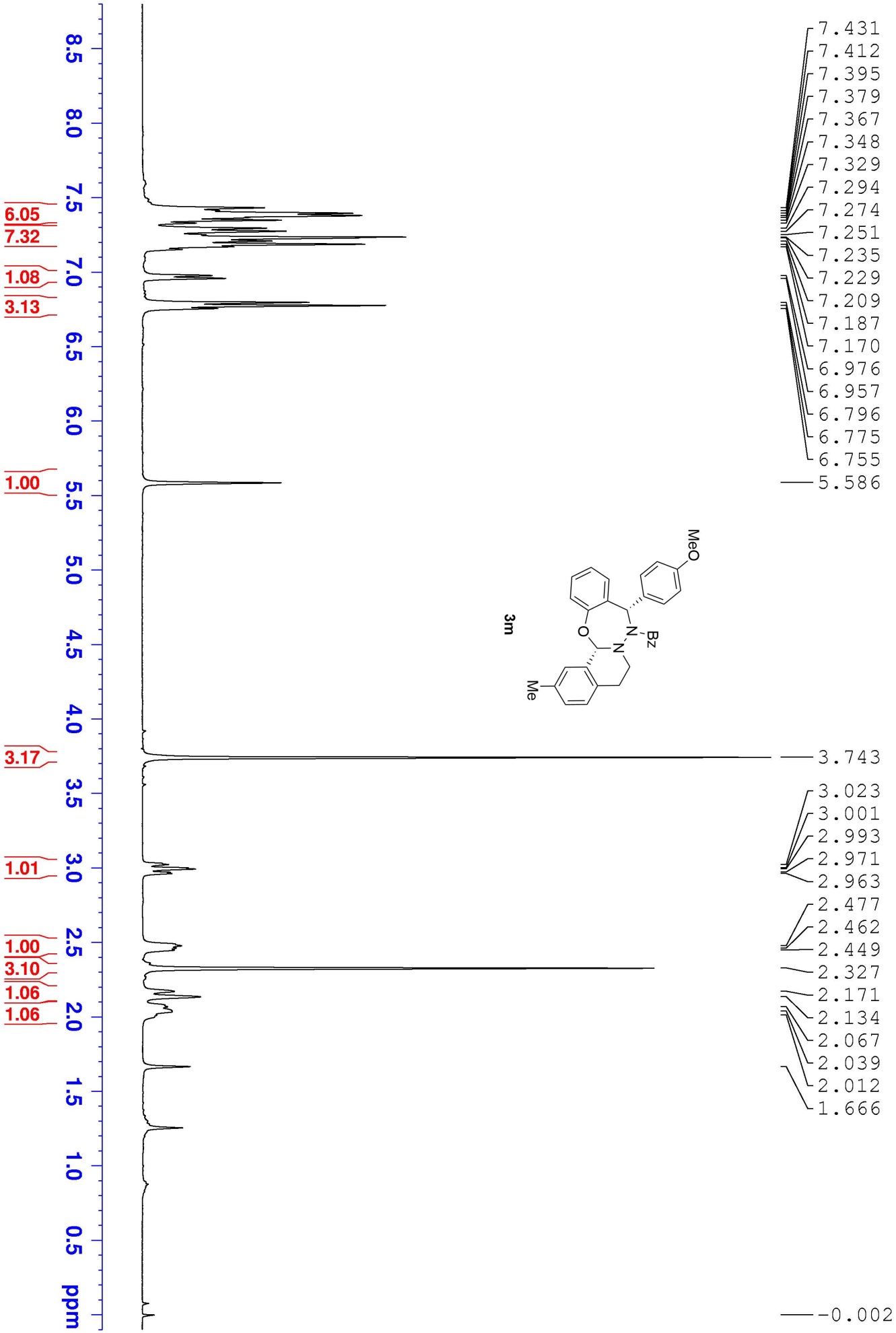
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1.00
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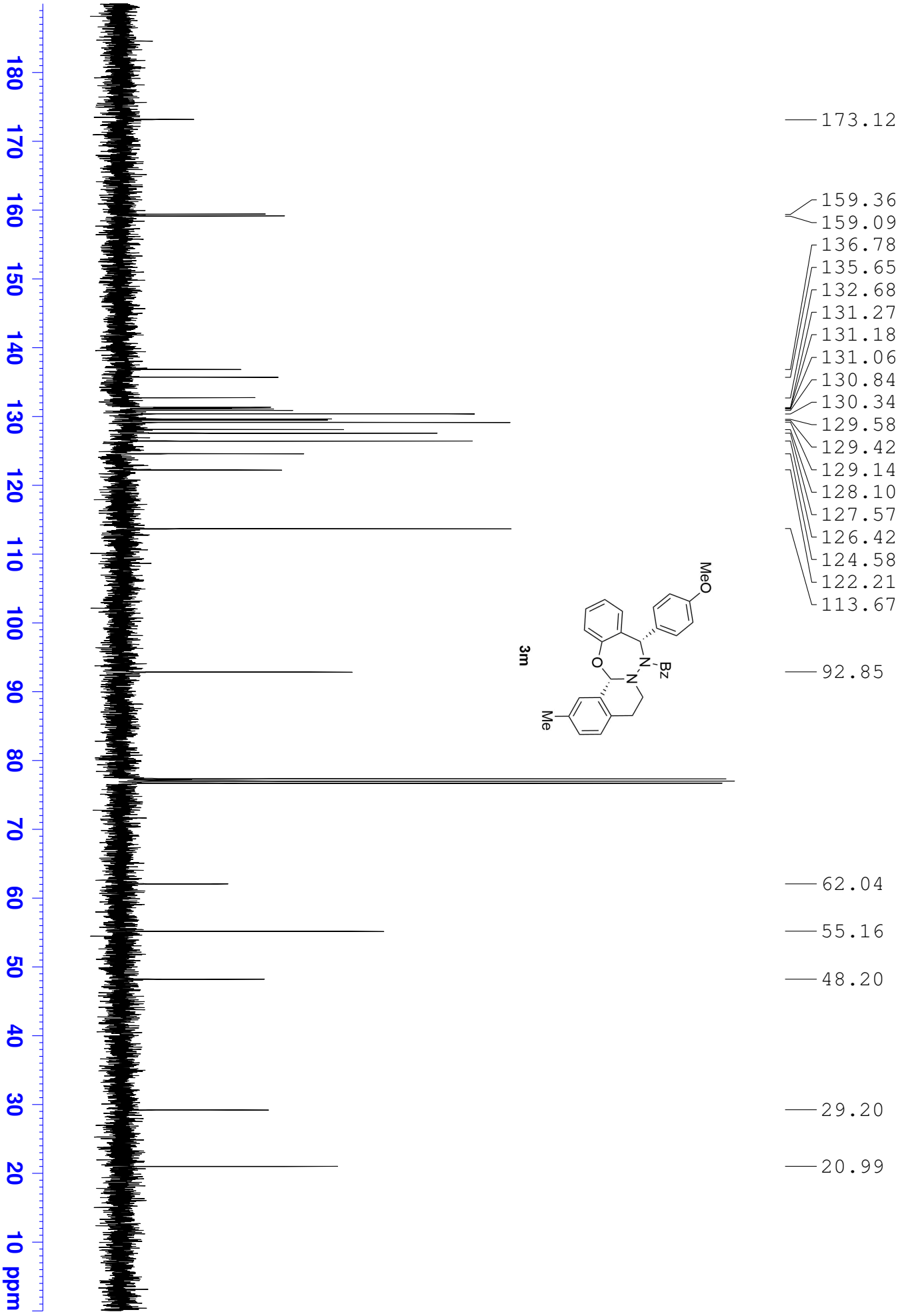
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Bz
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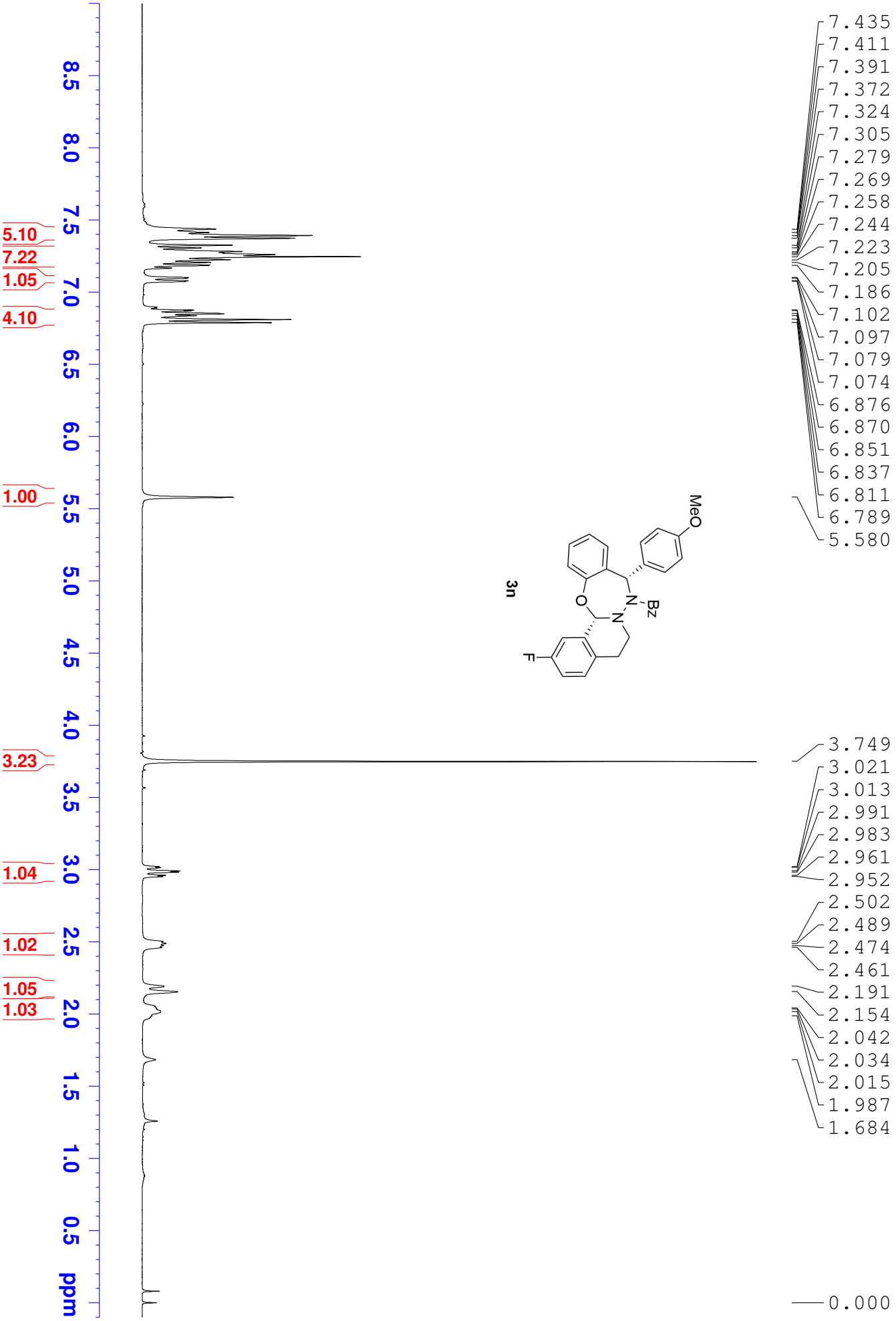
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7.079
7.074
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1.05
1.03
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Bz
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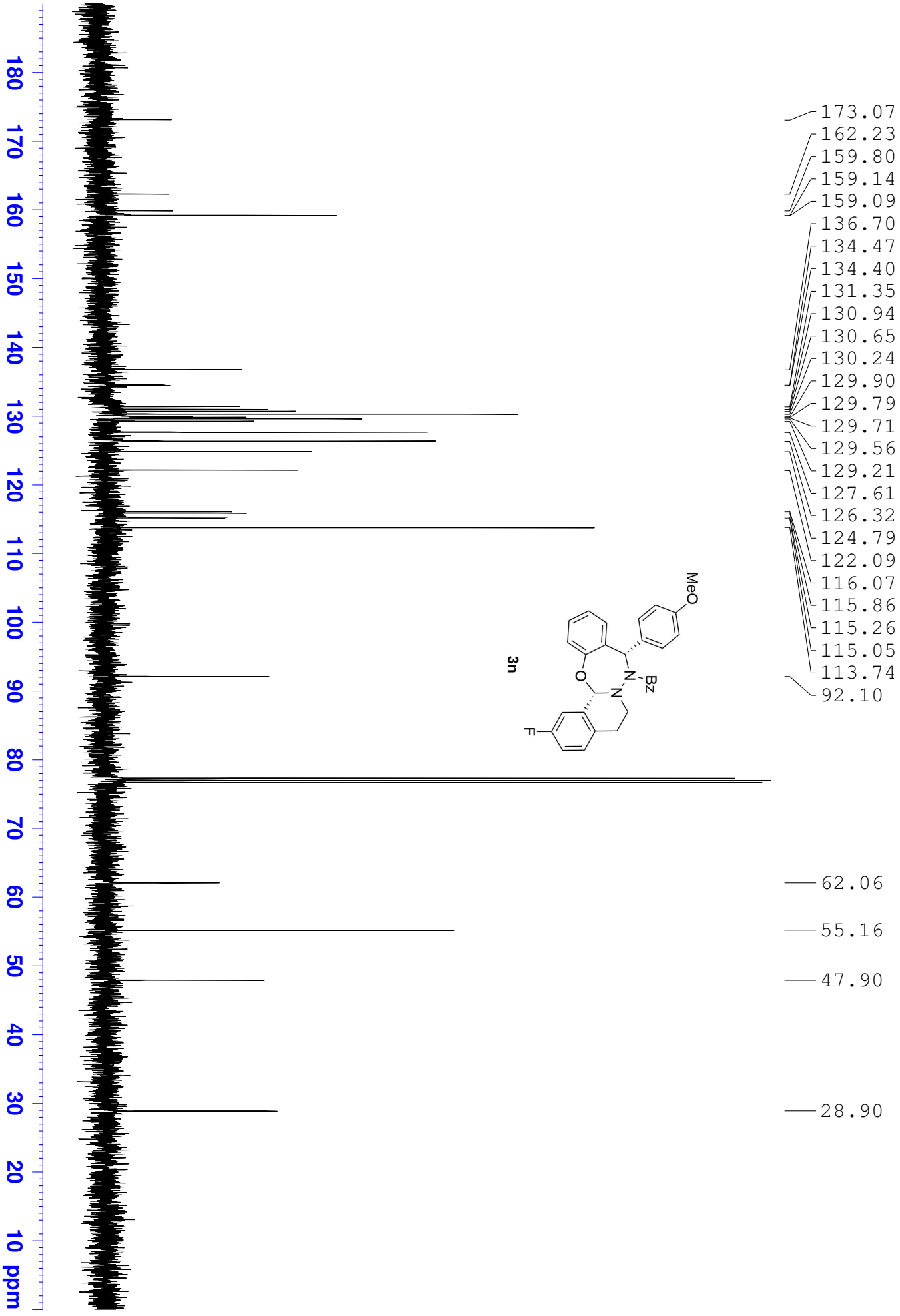
N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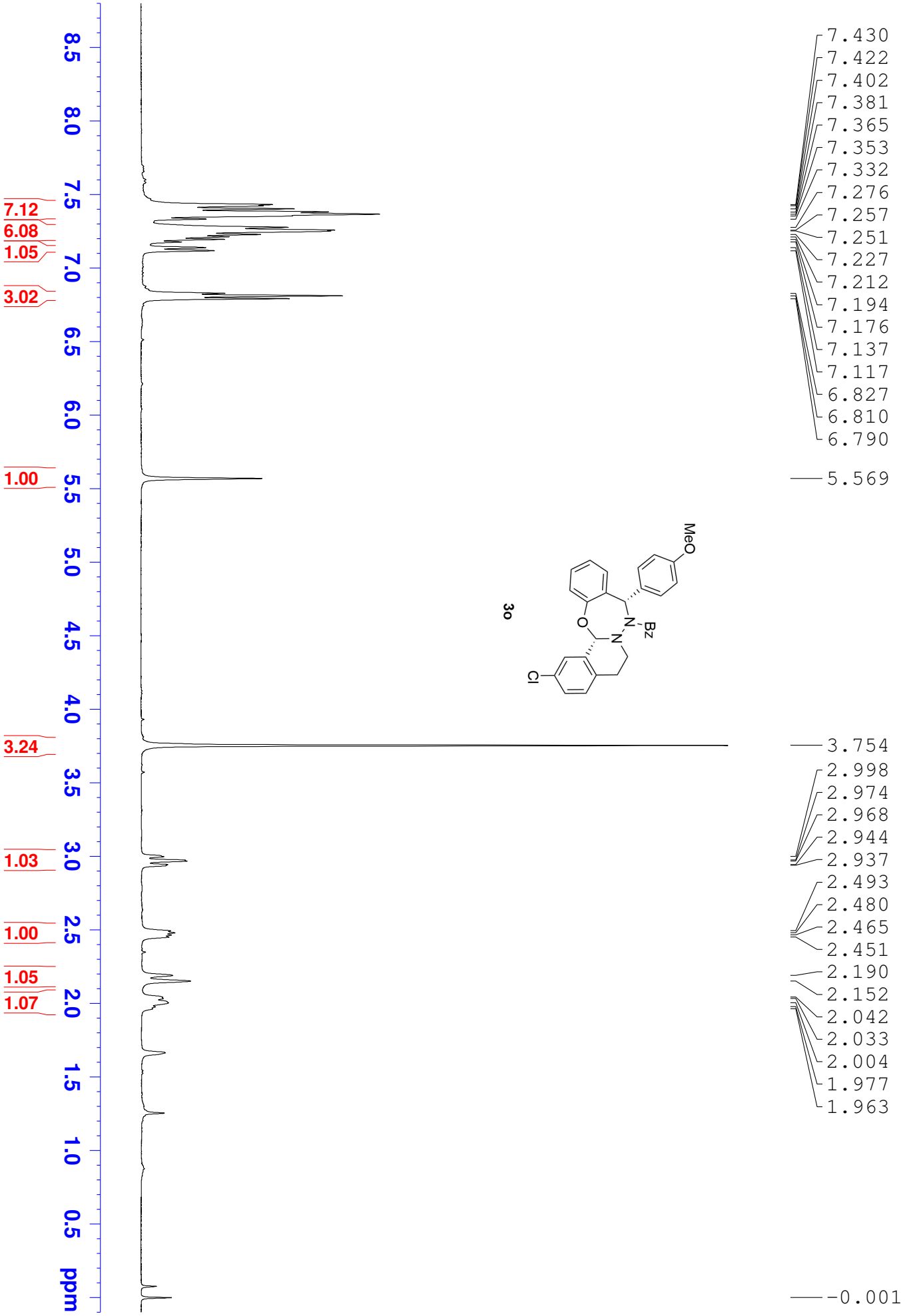
Bz
N
N
O
F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7.176
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7.117
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6.790
5.569
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2.968
2.944
2.937
2.493
2.480
2.465
2.451
2.190
2.152
2.042
2.033
2.004
1.977
1.963
-0.001
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6.08
1.05
3.02
1.00
3.24
1.03
1.00
1.05
1.07
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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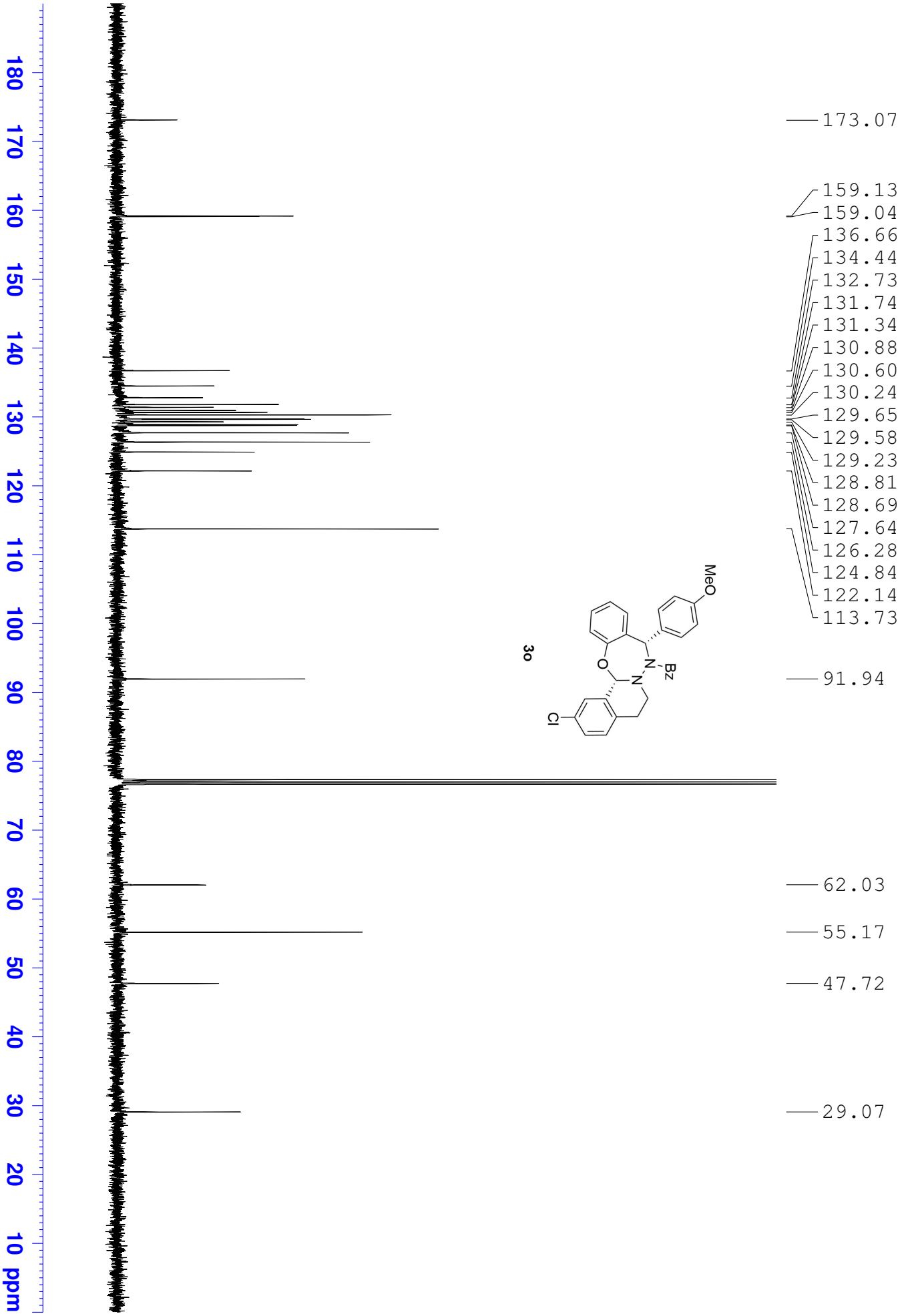
N
O
Cl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127.64
126.28
124.84
122.14
113.73
91.94
62.03
55.17
47.72
29.07
3o
MeO
Bz
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30
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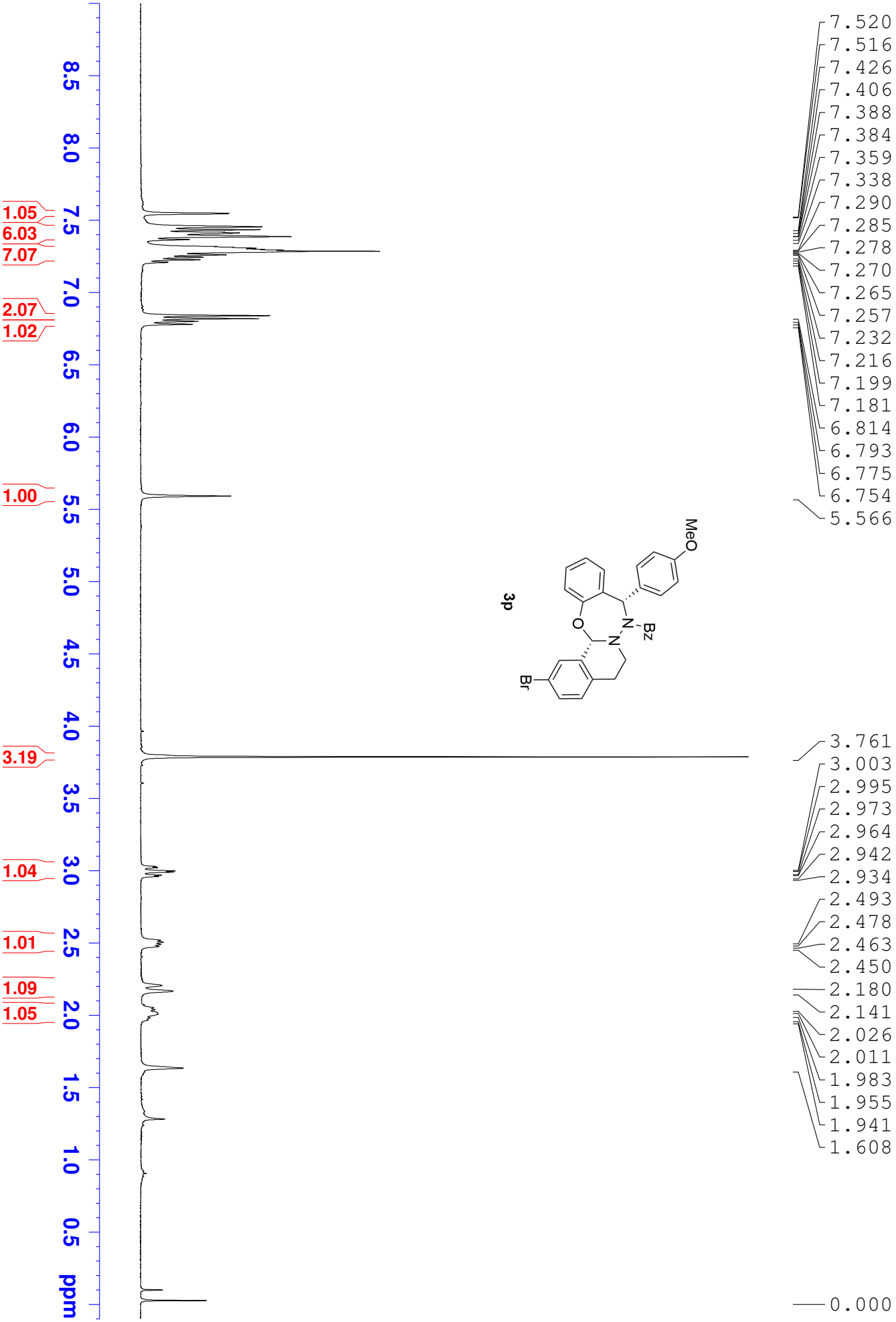
10
ppm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7.265
7.257
7.232
7.216
7.199
7.181
6.814
6.793
6.775
6.754
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3.761
3.003
2.995
2.973
2.964
2.942
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2.478
2.463
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1.955
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0.000
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2.07
1.02
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1.04
1.01
1.09
1.05
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6.0
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5.0
4.5
4.0
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3p
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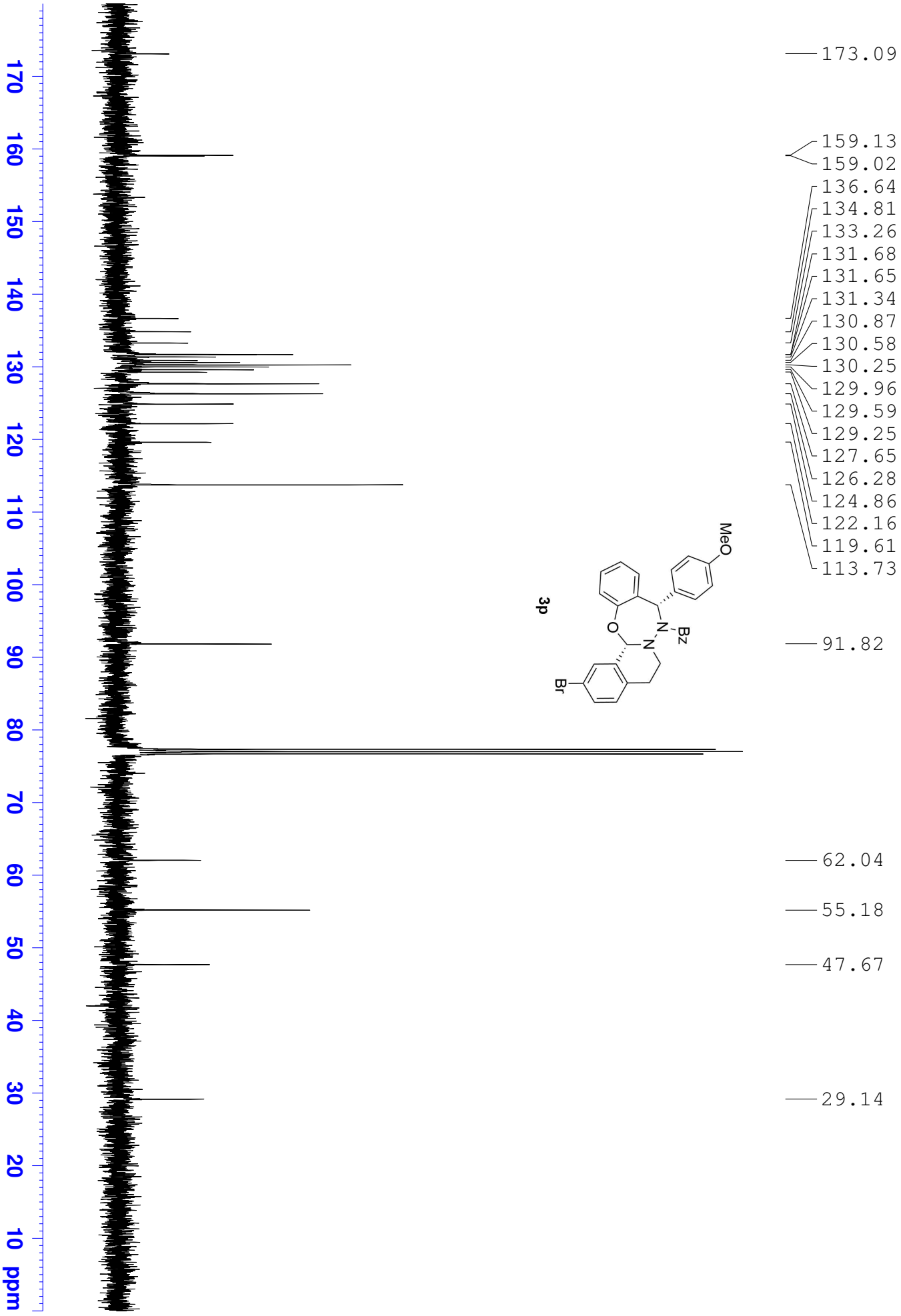
Bz
N
N
O
Br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91.82
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3p
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Bz
N
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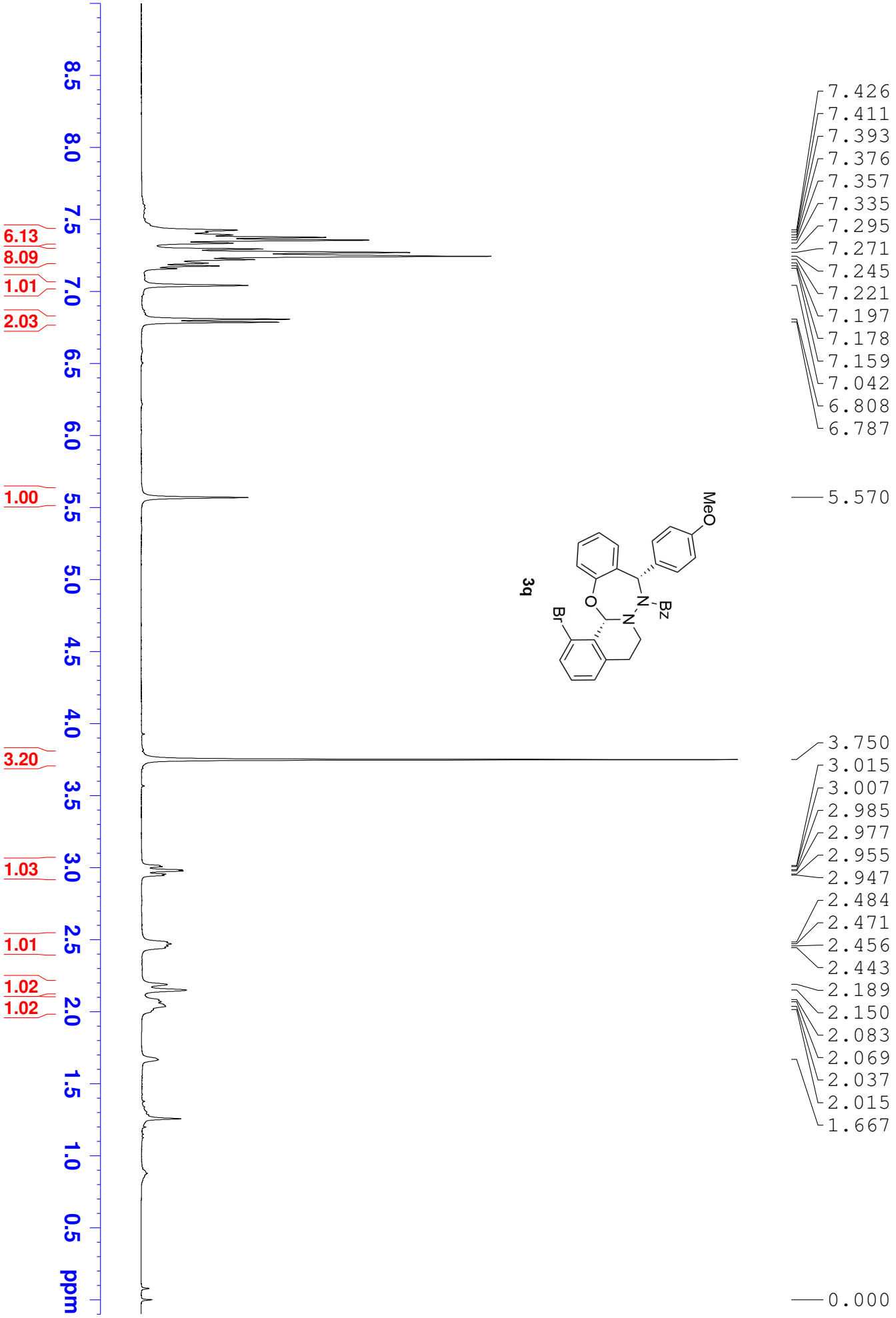
ppm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1.5
1.0
0.5
ppm
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1.01
1.02
1.02
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O
Br
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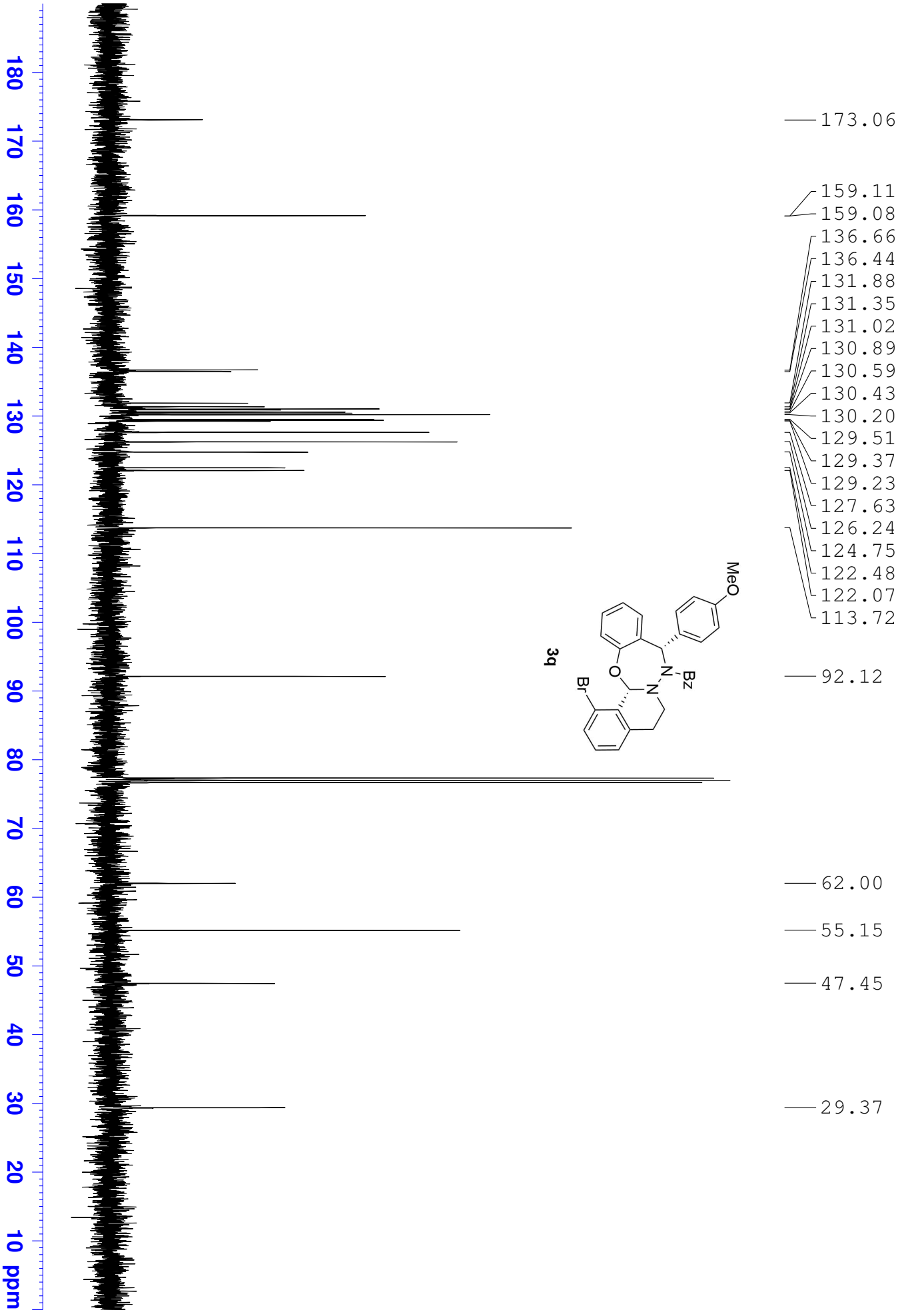
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129.23
127.63
126.24
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122.48
122.07
113.72
92.12
62.00
55.15
47.45
29.37
MeO
Bz
N
N
O
Br
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20
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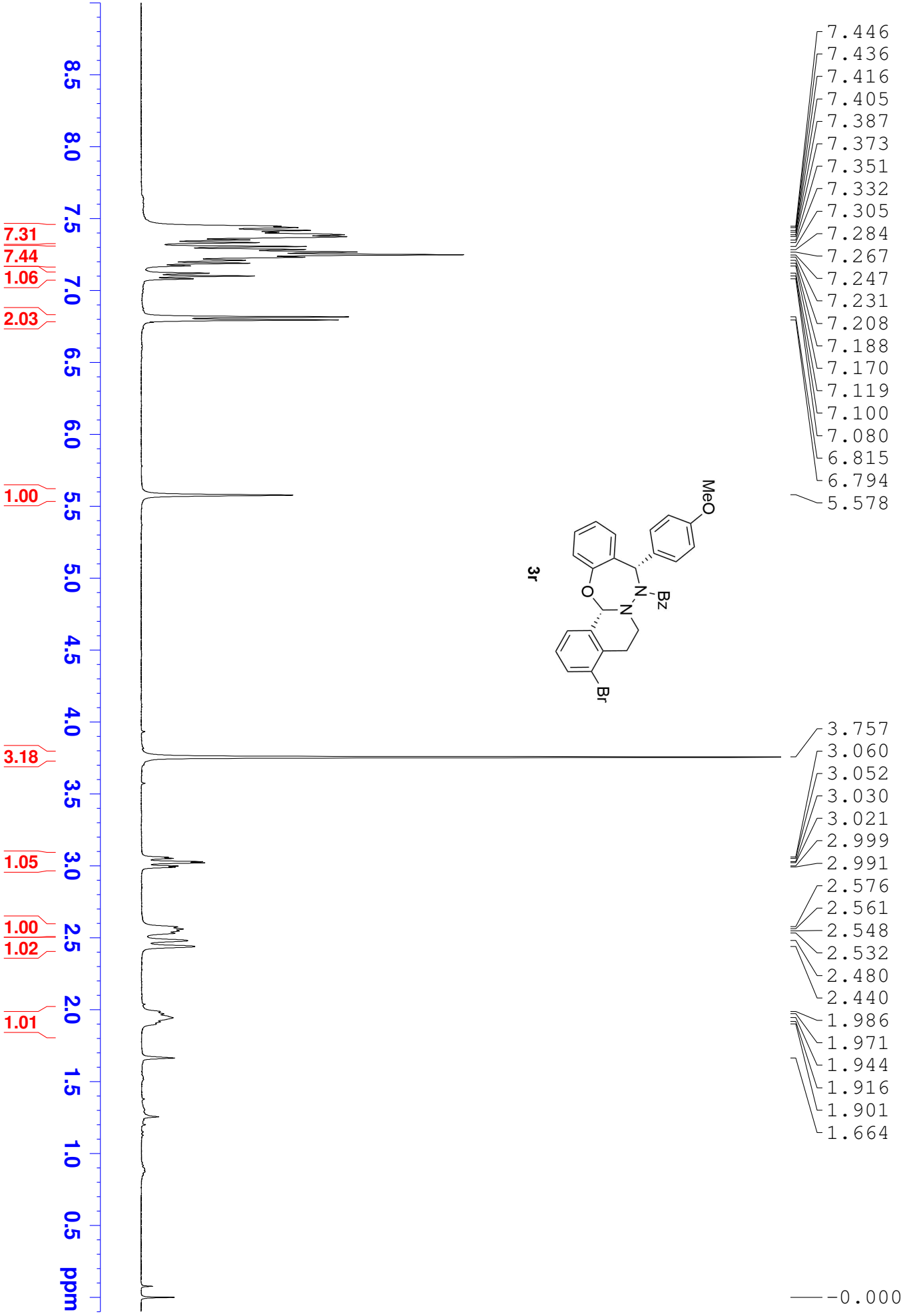
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6.794
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3.030
3.021
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1.00
1.02
1.01
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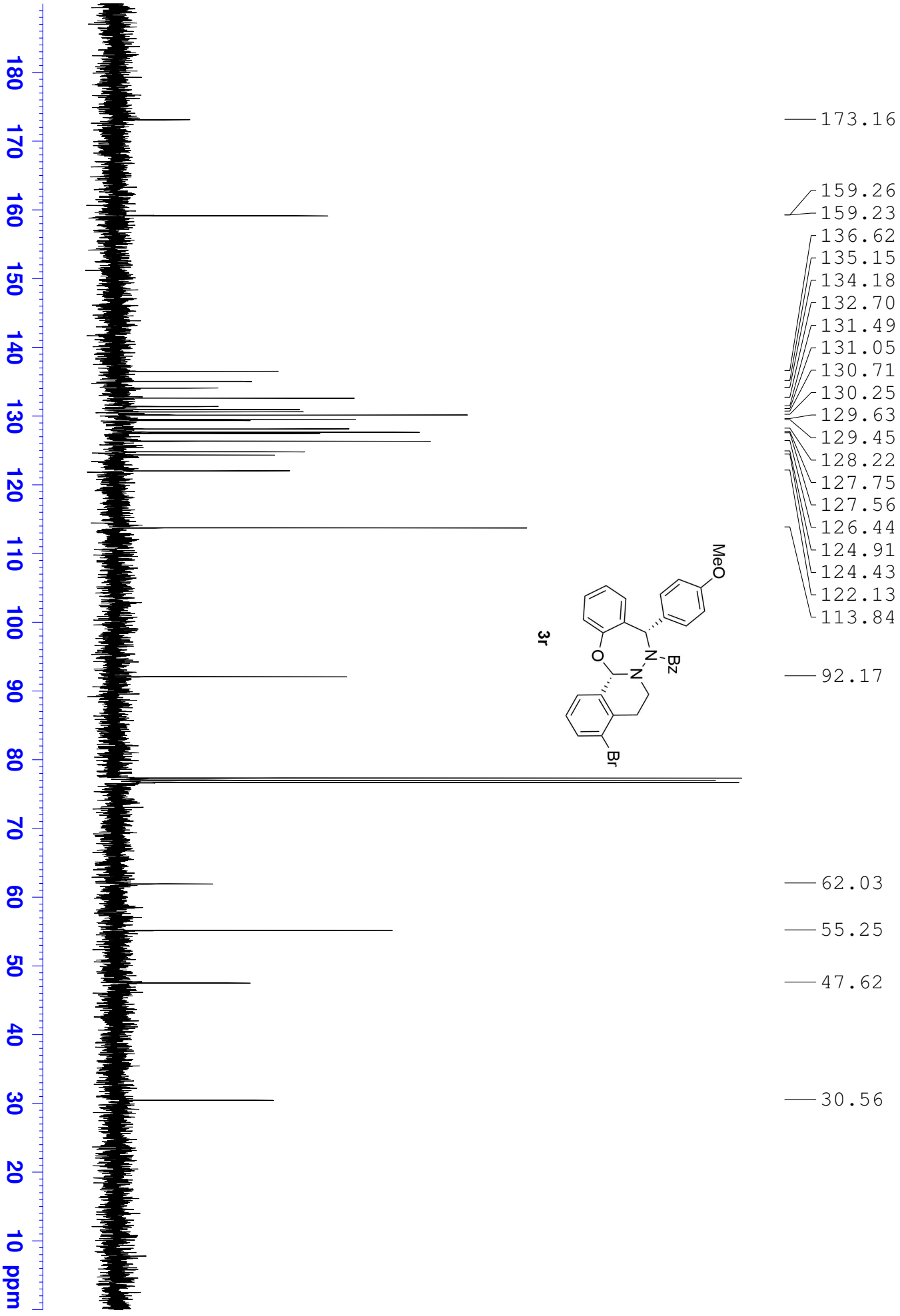
O
Br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122.13
113.84
92.17
62.03
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47.62
30.56
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Bz
N
N
O
Br
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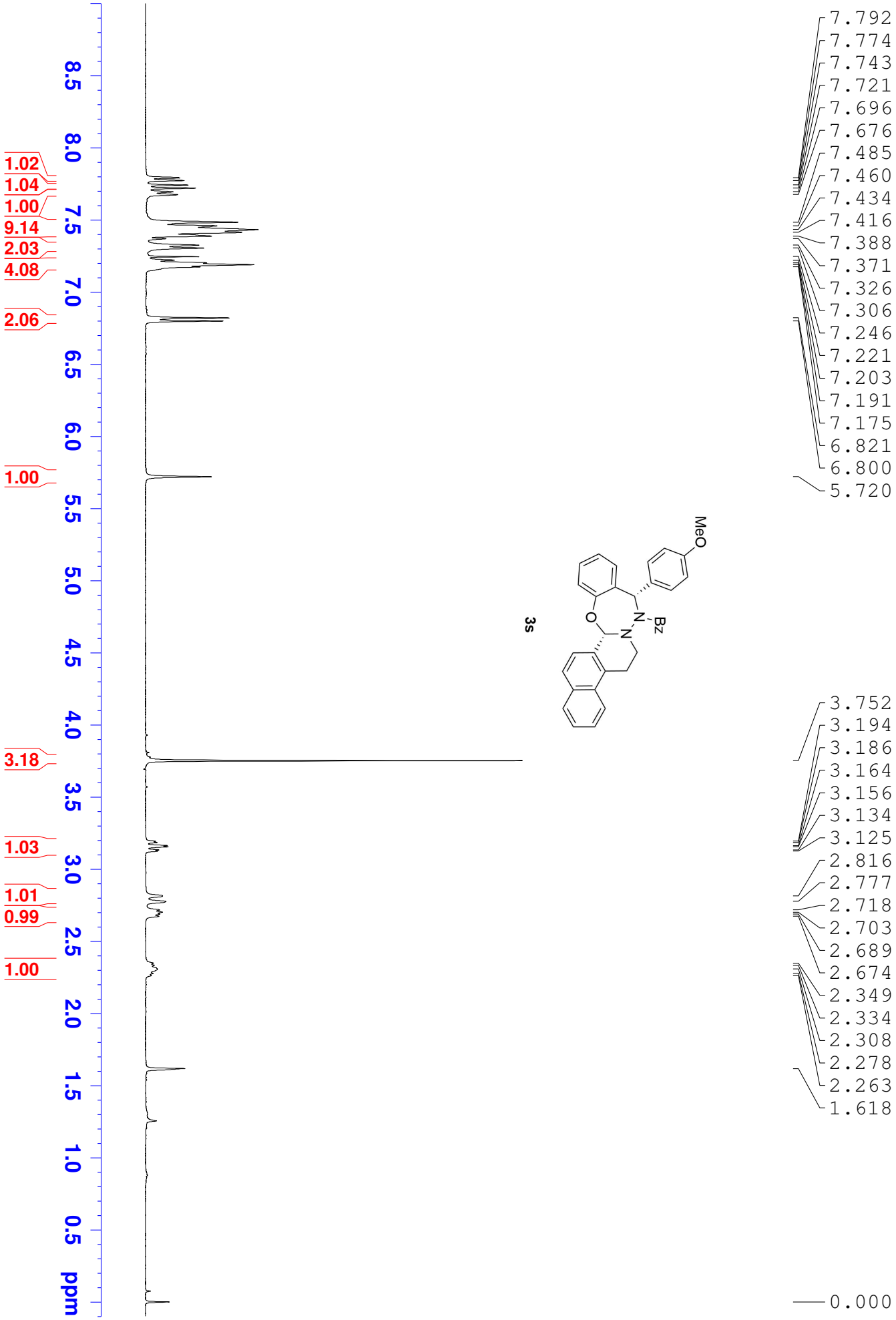
ppm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3.186
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1.04
1.00
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MeO
Bz
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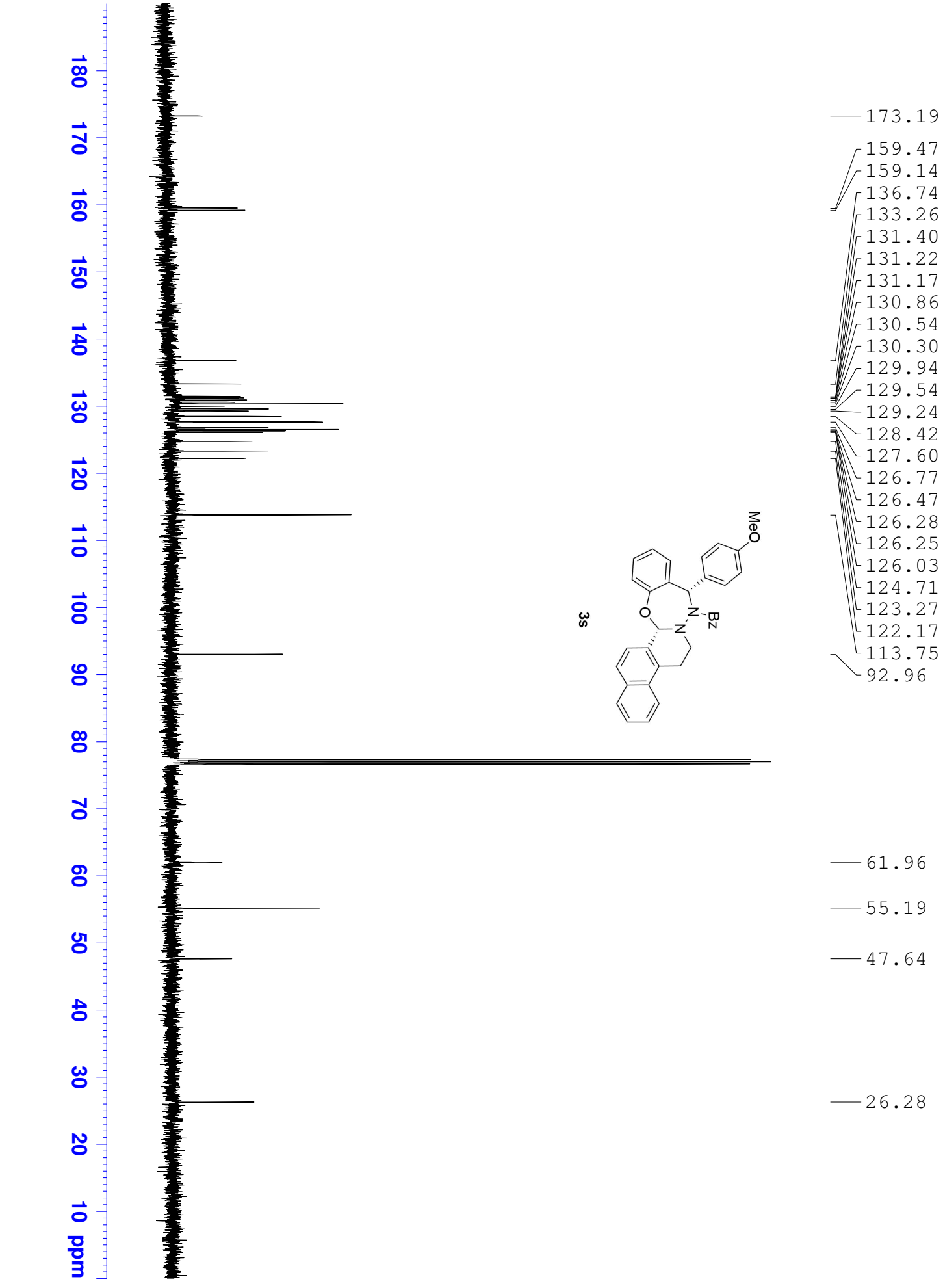
N
O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140
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Bz
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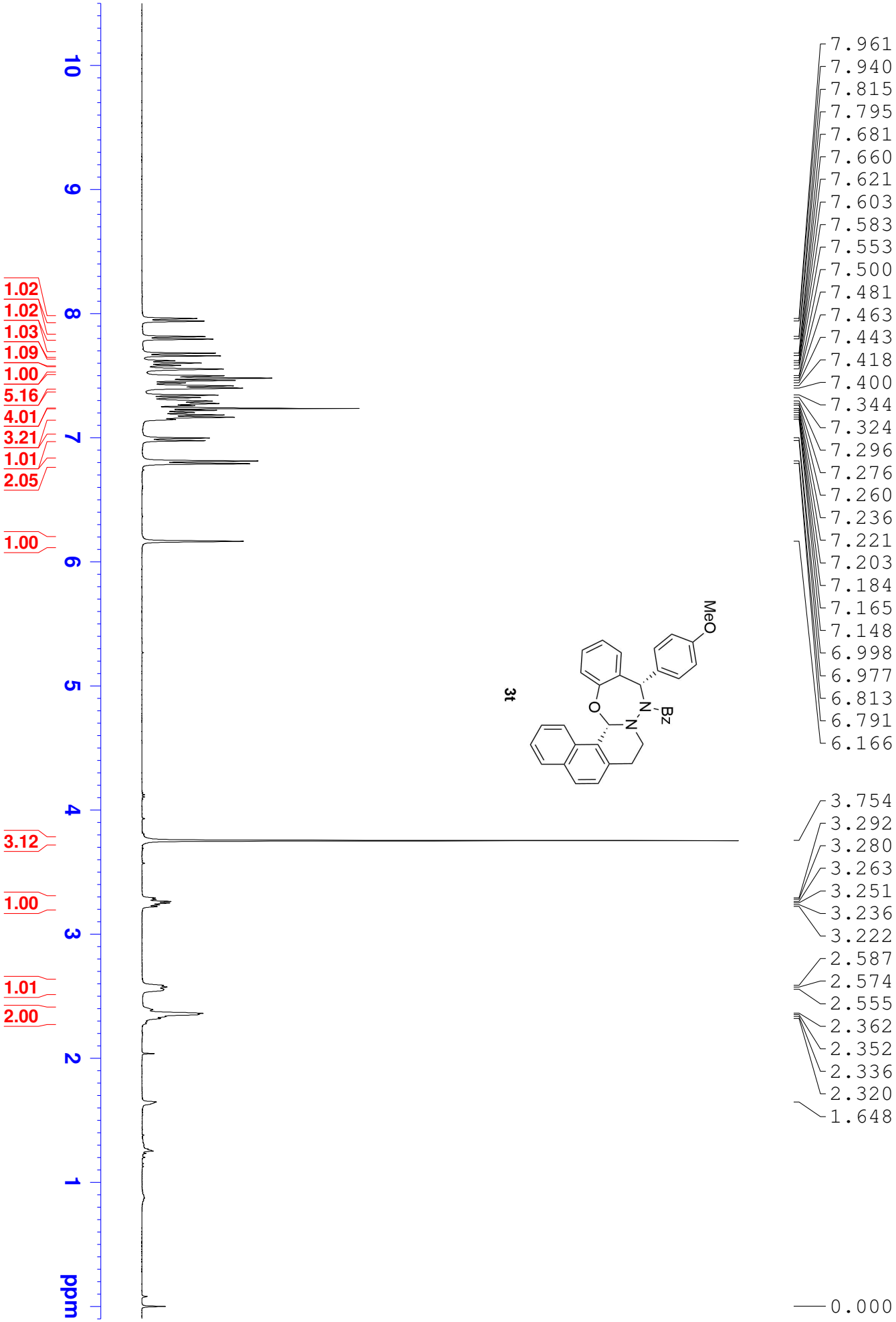
N
O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1.03
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1.01
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1.00
3.12
1.00
1.01
2.00
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6.998
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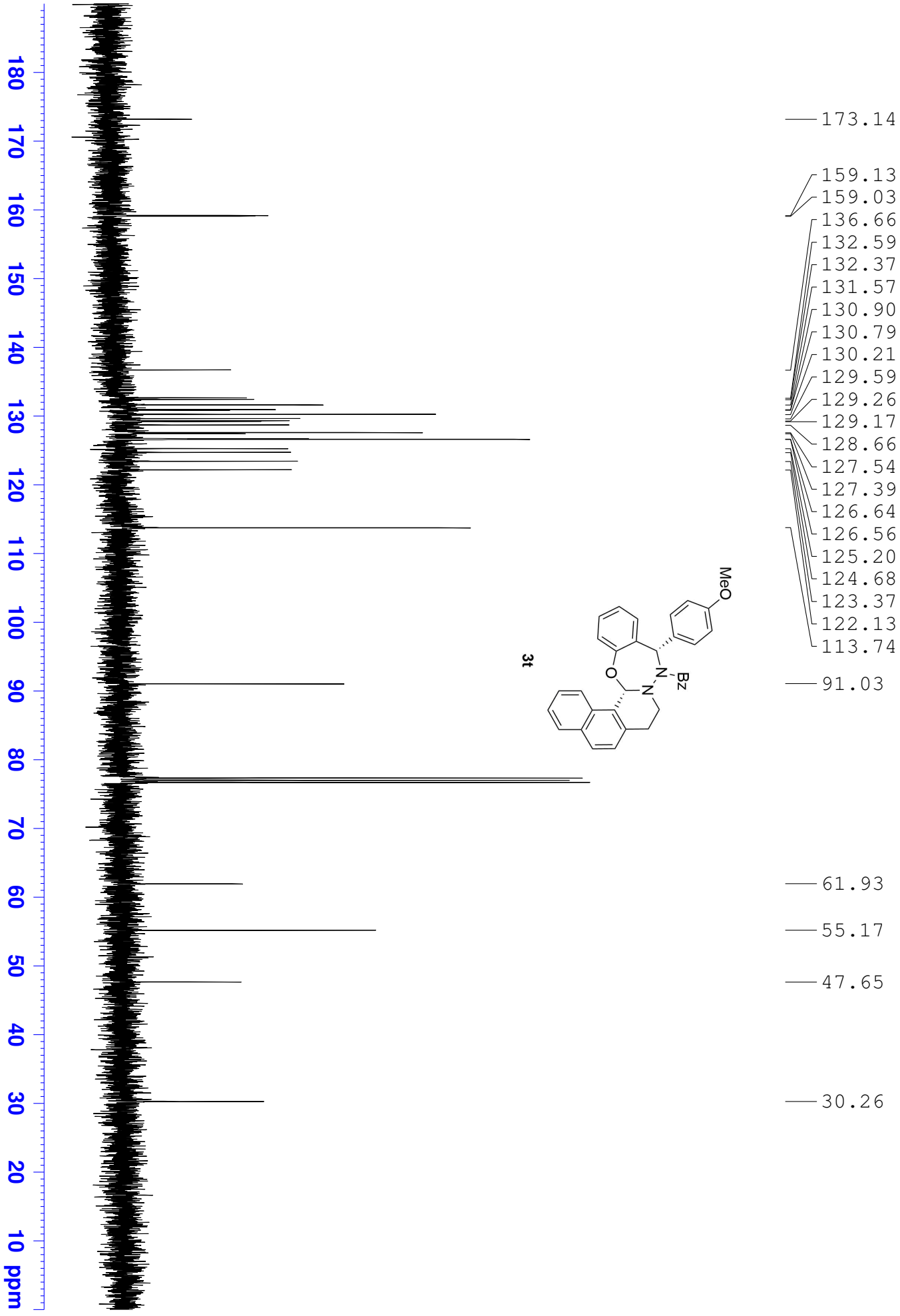
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127.54
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126.64
126.56
125.20
124.68
123.37
122.13
113.74
91.03
61.93
55.17
47.65
30.26
3t
MeO
Bz
N
N
O
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140
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120
110
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70
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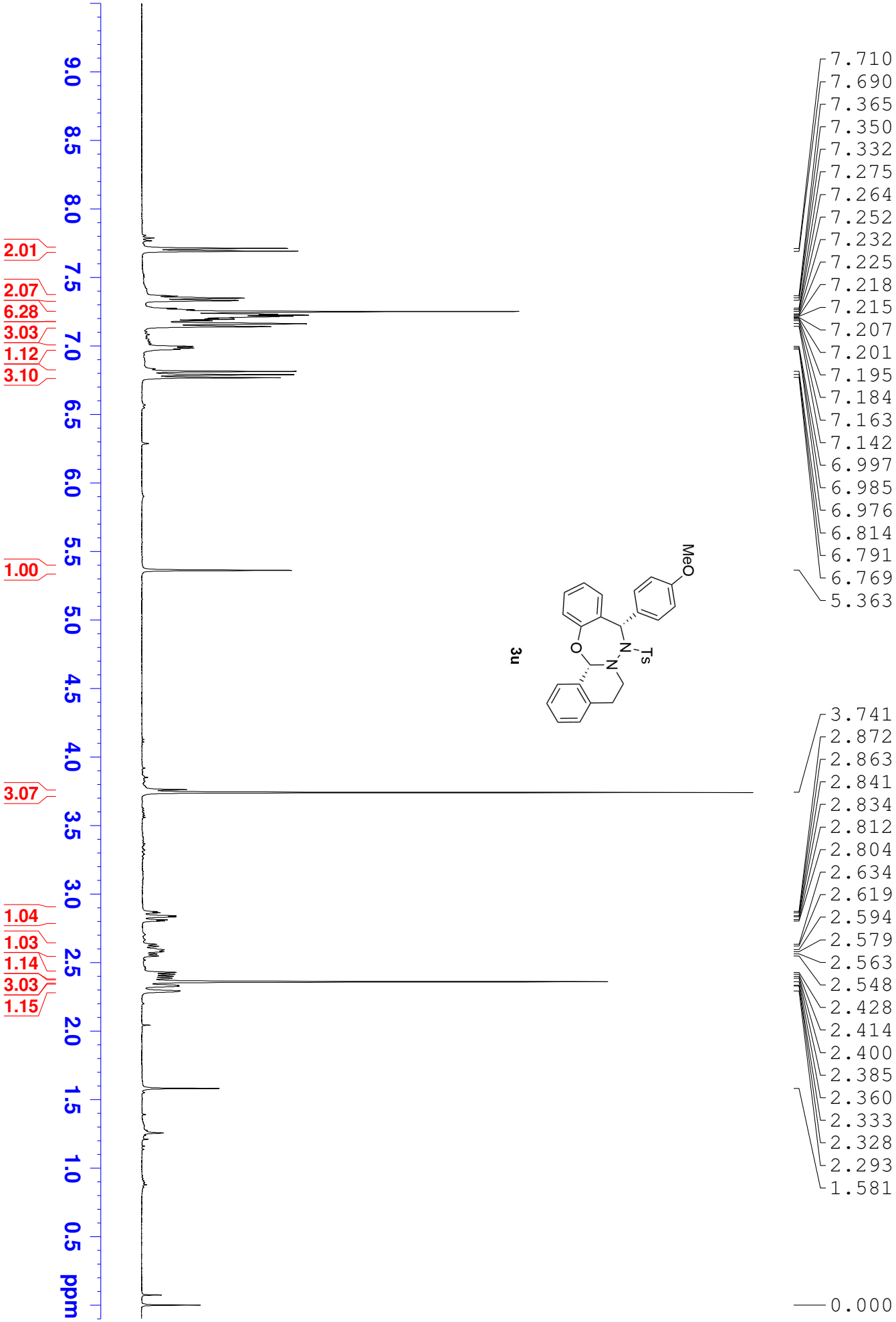
30
20
10
ppm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2.5
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1.5
1.0
0.5
ppm
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2.07
6.28
3.03
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1.04
1.03
1.14
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1.15
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Ts
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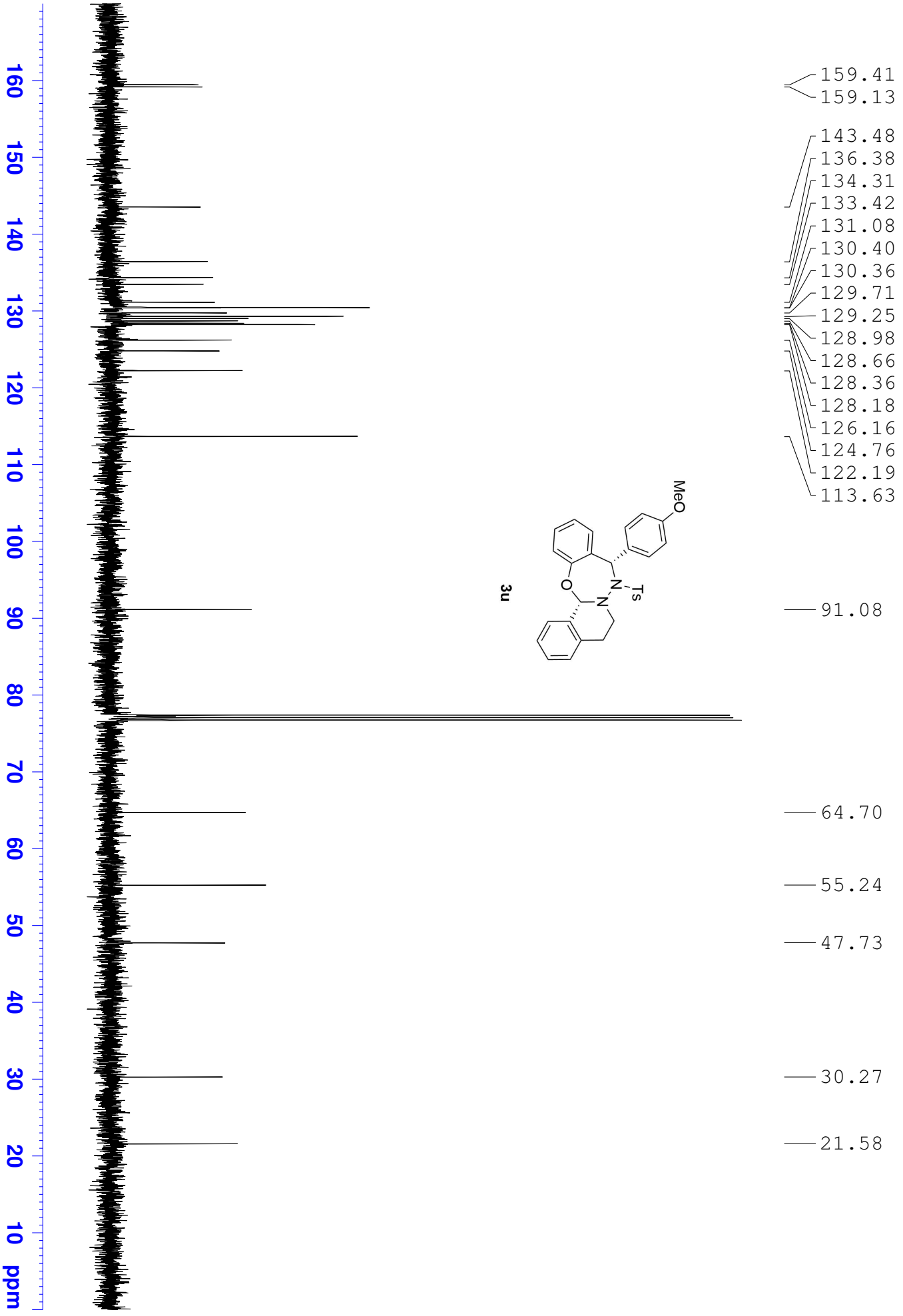
N
O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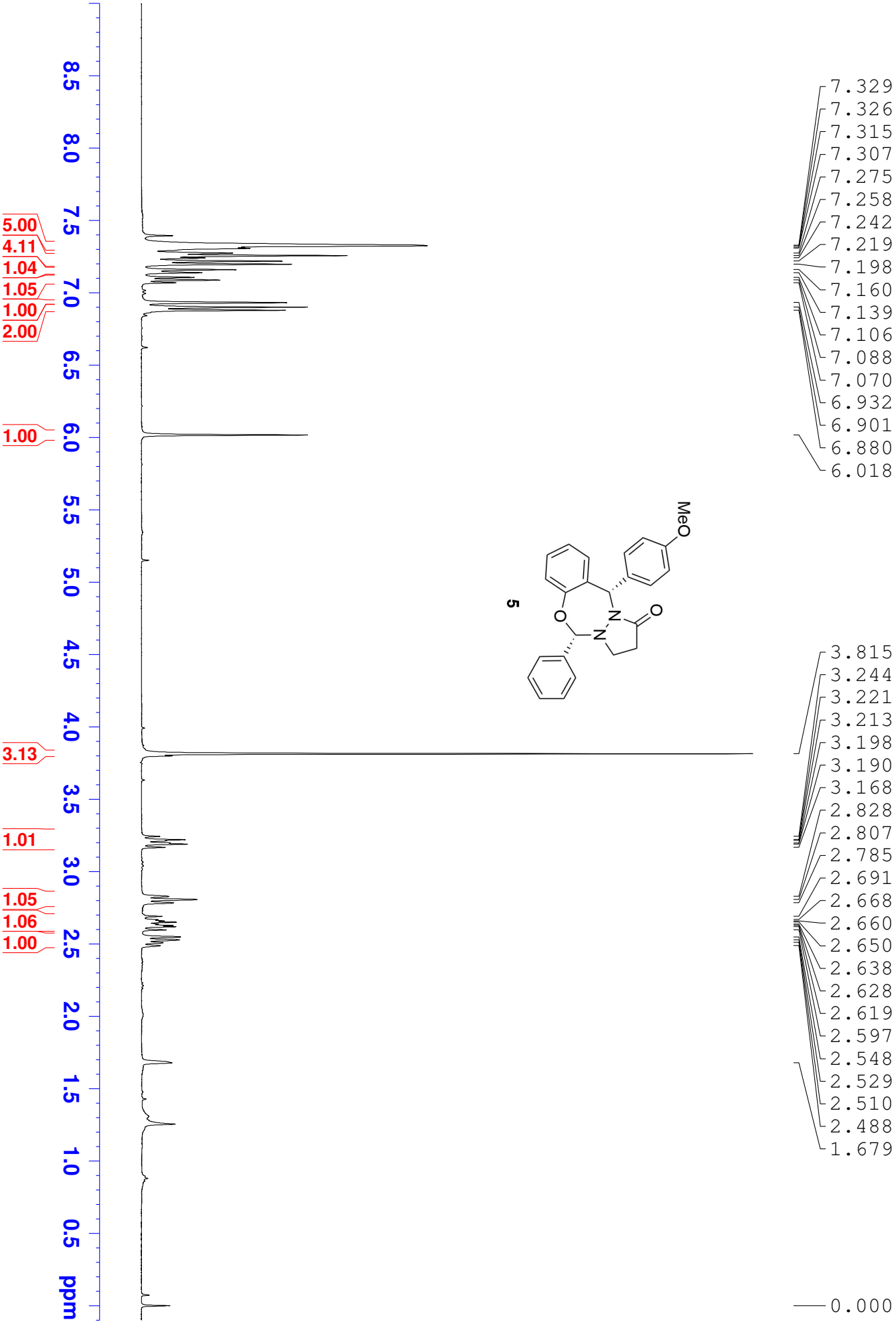
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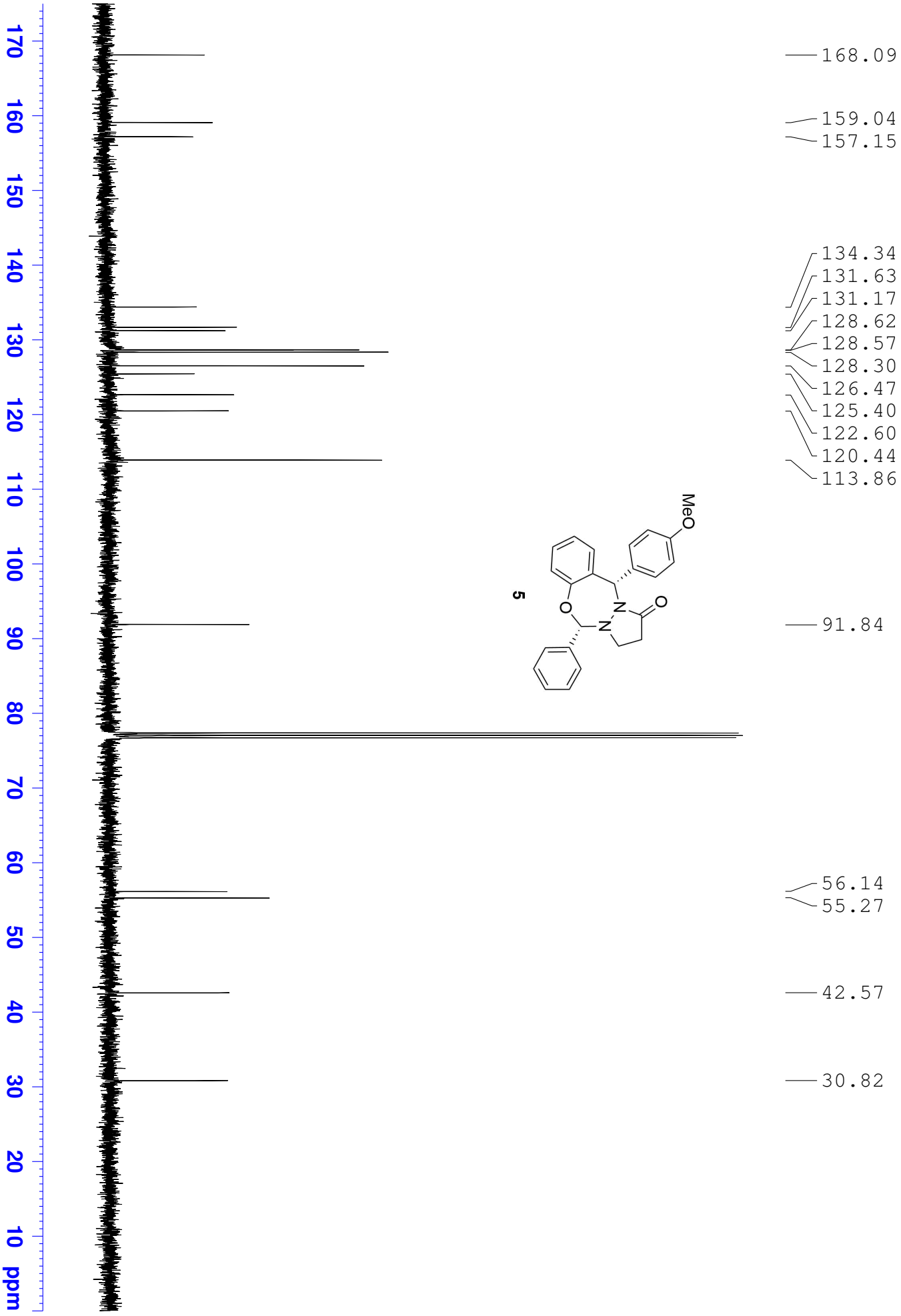
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