

Improved HDAC Inhibition, Stronger Cytotoxic Effect and Higher Selectivity against Leukemias and Lymphomas of Novel, Tricyclic Vorinostat Analogues

Bartosz Bieszczad,^{1,†} Damian Garbicz,^{1,†} Marta Świtalska,² Marta K. Dudek,³
Dawid Warszzycki,⁴ Joanna Wietrzyk,² Elżbieta Grzesiuk ^{1,*} and Adam Mieczkowski ^{1,*}

1 Institute of Biochemistry and Biophysics, Polish Academy of Sciences, 02-106 Warsaw, Poland; b.bieszczad@ibb.waw.pl (B.B.)

2 Hirszfeld Institute of Immunology and Experimental Therapy, Polish Academy of Sciences, 53-114 Wrocław, Poland; marta.switalska@hirszfeld.pl (M.Ś), joanna.wietrzyk@hirszfeld.pl (J.W.)

3 Centre of Molecular and Macromolecular Studies, Polish Academy of Sciences, 90-363 Lodz, Poland; mdudek@cbmm.lodz.pl

4 Maj Institute of Pharmacology, Polish Academy of Sciences, 31-343 Cracow, Poland; warszyc@if-pan.krakow.pl

* Correspondence: elag@ibb.waw.pl (E.G.); amiecz@ibb.waw.pl (A.M.); Tel.: +48-22-592-3506 (A.M.)

† These authors contributed equally to this work.

1. Materials and Methods

1.1. *In silico* modelling

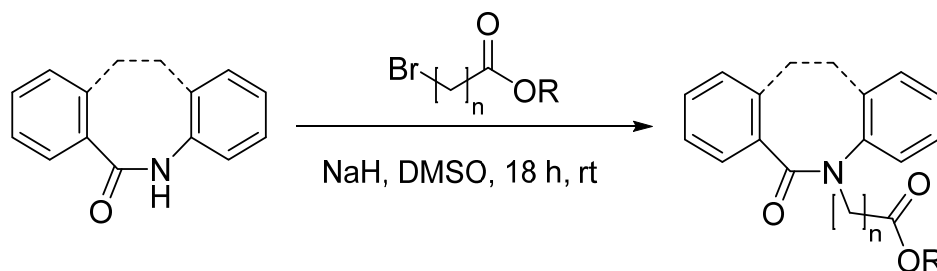
Table S1. Glide Score for the best scored pose (the lower the better) for every compound in seven different HDAC crystals (PDBids given in parenthesis).

Compound	HDAC1 (5ICN)	HDAC2 (4LXZ)	HDAC3 (4A69)	HDAC4 (2VQM)	HDAC6 (5EDU)	HDAC7 (3C0Z)	HDAC8 (1T69)
7a	-2.752	not docked	not docked	-2.938	not docked	-2.412	-3.697
7b	-5.643	-2.555	not docked	-4.142	-5.169	-4.862	-3.737
7c	-6.712	-4.997	not docked	-4.210	-8.164	-5.751	-7.762
7d	-7.615	-7.028	not docked	-5.237	-8.593	-6.613	-8.860
7e	-8.642	-7.826	not docked	-6.567	-8.517	-7.324	-9.251
7f	-8.477	-6.260	not docked	-5.816	-8.277	-6.883	-8.472
7g	-2.994	-1.488	not docked	-3.413	-3.831	-4.057	-4.118
7h	-6.009	-3.531	not docked	-3.817	-7.035	-6.403	-4.786
7i	-6.173	-4.353	not docked	-4.429	-8.649	-6.583	-8.015
7j	-8.655	-7.077	not docked	-5.092	-8.490	-7.329	-8.232
7k	-8.363	-8.129	not docked	-6.245	-8.368	-7.152	-8.839
7l	-8.161	-7.568	not docked	-5.701	-7.988	-7.074	-8.634
7m	-8.585	-6.634	not docked	-5.843	-8.663	-6.930	-8.532
7n	-8.470	-6.525	not docked	-5.582	-8.442	-6.800	-8.754
7o	-7.927	-7.892	not docked	-5.789	-8.430	-7.425	-8.423

7p	-8.653	-7.679	not docked	-6.143	-8.607	-7.134	-8.038
7r	-7.790	-7.353	not docked	-6.138	-8.533	-6.909	-8.374
7s	-9.187	-7.644	not docked	-6.446	-8.183	-7.354	-8.675
7t	-8.411	-7.450	not docked	-6.690	-9.083	-6.775	-9.070
Vorinostat	-5.259	-5.777	-3.798	-3.625	-6.043	-3.961	-5.736

2. Synthetic procedures and physicochemical data

2.1 General procedure for alkylation of 8-membered lactams



To a solution of appropriate heterocyclic amide (1.0 equiv.) in anhydrous DMSO (5 mL/mmol), 60% sodium hydride in mineral oil (1.5 equiv.) was added and the resulting mixture was stirred for 30 min. After the addition of alkyl halide (1.5 equiv.) the reaction mixture was stirred for 18 hrs at room temperature, then was poured into water and the crude product was extracted with ethyl acetate (3 x 50 mL). The organic phase was washed with brine (1 x 50 mL) and dried over anhydrous magnesium sulfate. The crude product was purified by column chromatography (hexane:ethyl acetate; gradient).

ethyl 2-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[b,f][1,5]diazocin-5(6H)-yl)acetate (10a): Yield: 78 %, white crystals, mp 125.0-126.0 °C, Rf = 0.33 (hexane:ethyl acetate 1:1). ¹H NMR (500 MHz, CDCl₃) δ 7.31 – 7.12 (m, 7H, H_{Ar}), 7.04 (d, J = 8.0 Hz, 1H, H_{Ar}), 4.56 (d, J = 17.1 Hz, 1H, H_{CH}), 4.32 (d, J = 17.1 Hz, 1H, H_{CH}), 4.29 – 4.16 (m, 2H, H_{CH2}), 3.41 (s, 3H, H_{CH3}), 1.26 (t, J = 7.2 Hz, 3H, H_{CH3}); ¹³C NMR (126 MHz, CDCl₃) δ 168.6, 168.4, 168.1, 140.5, 139.5, 134.8, 133.8, 131.0, 131.0, 128.7, 128.4, 128.0, 128.0, 125.3, 125.2, 61.8, 51.6, 36.9, 14.3; HRMS (ESI): m/z [M+H]⁺ calcd for C₁₉H₁₉N₂O₄: 339.13393, found: 339.13334.

ethyl 3-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[b,f][1,5]diazocin-5(6H)-yl)propanoate (10b): Yield 85 %, white crystals, mp 124.0-125.0 °C, Rf = 0.35 (hexane:ethyl acetate 1:1). ¹H NMR (500 MHz, CDCl₃) δ 7.32 – 7.23 (m, 4H, H_{Ar}), 7.23 – 7.15 (m, 2H, H_{Ar}), 7.07 (dd, J = 17.2, 8.0 Hz, 2H, H_{Ar}), 4.75 (ddd, J = 13.6, 9.8, 6.1 Hz, 1H, H_{CH}), 4.09 (q, J = 7.1 Hz, 2H, H_{CH2}), 3.62 (ddd, J = 13.6, 9.8, 5.4 Hz, 1H, H_{CH}), 3.42 (s, 3H, H_{CH3}), 2.70 (ddd, J = 16.1, 9.7, 6.1 Hz, 1H, H_{CH}), 2.53 (ddd, J = 16.4, 9.8, 5.4 Hz, 1H, H_{CH}), 1.20 (t, J = 7.2 Hz, 3H, H_{CH3}); ¹³C NMR (126 MHz, CDCl₃) δ 171.1, 168.2, 167.8, 140.4, 138.7, 135.5, 134.6, 131.0, 130.8, 128.7, 128.4, 127.6, 127.6, 125.9, 125.3, 60.7, 45.0, 36.7, 32.4, 14.2; HRMS (ESI): m/z [M+H]⁺ calcd for C₂₀H₂₁N₂O₄: 339.13393, found: 339.13333.

ethyl 4-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[b,f][1,5]diazocin-5(6H)-yl)butanoate (10c): Yield: 83 %, white crystals, mp 89.0-90.0 °C, Rf = 0.28 (hexane:ethyl acetate 1:1). ¹H NMR (500 MHz, CDCl₃) δ 7.31 – 7.22 (m, 4H, H_{Ar}), 7.18 (qd, J = 7.6, 1.2 Hz, 2H, H_{Ar}), 7.09 – 7.03 (m, 2H, H_{Ar}), 4.48 (ddd, J = 13.4, 8.4, 7.3 Hz, 1H, H_{CH}), 4.09 (qd, J = 7.1, 1.4 Hz, 2H, H_{CH2}), 3.51 – 3.37 (m, 4H, H_{CH}+H_{CH3}), 2.34 (t, J = 7.2 Hz, 2H, H_{CH2}), 1.94 – 1.76 (m, 2H, H_{CH2}), 1.21 (t, J = 7.2 Hz, 3H, H_{CH3}); ¹³C NMR (126 MHz, CDCl₃) δ 172.8, 168.3, 168.0, 140.3, 138.9, 135.5, 134.8, 130.9, 130.7, 128.5, 128.4, 127.7, 127.5, 125.8, 125.2, 60.5, 48.3, 36.7, 31.4, 23.2, 14.3; **HRMS (ESI)**: m/z [M+H]⁺ calcd for C₂₁H₂₃N₂O₄: 367.16523, found: 367.16461.

methyl 5-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[b,f][1,5]diazocin-5(6H)-yl)pentanoate (10d): Yield: 80 %, white crystals, mp 107.0-108.0 °C, Rf = 0.25 (hexane:ethyl acetate 1:1). ¹H NMR (500 MHz, CDCl₃) δ 7.34 – 7.22 (m, 4H, H_{Ar}), 7.22 – 7.14 (m, 2H, H_{Ar}), 7.06 (t, J = 7.6 Hz, 2H, H_{Ar}), 4.51 (dt, J = 13.4, 7.7 Hz, 1H, H_{CH}), 3.62 (s, 3H, H_{CH3}), 3.43 (s, 3H, H_{CH3}), 3.32 (ddd, J = 13.1, 7.8, 5.2 Hz, 1H, H_{CH}), 2.44 – 2.24 (m, 2H, H_{CH2}), 1.75 – 1.44 (m, 4H, 2xH_{CH2}); ¹³C NMR (126 MHz, CDCl₃) δ 173.9, 168.4, 167.8, 140.4, 139.0, 135.6, 134.9, 130.9, 130.7, 128.5, 128.4, 127.7, 127.6, 125.9, 125.2, 51.6, 48.7, 36.7, 33.6, 27.3, 22.3; **HRMS (ESI)**: m/z [M+H]⁺ calcd for C₂₁H₂₃N₂O₄: 367.16523, found: 367.16457.

methyl 6-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[b,f][1,5]diazocin-5(6H)-yl)hexanoate (10e): Yield: 76 %, white crystals, mp 95.0-96.0 °C, Rf = 0.27 (hexane:ethyl acetate 1:1). ¹H NMR (500 MHz, CDCl₃) δ 7.32 – 7.21 (m, 4H, H_{Ar}), 7.18 (qd, J = 7.5, 1.2 Hz, 2H, H_{Ar}), 7.05 (dd, J = 7.9, 4.6 Hz, 2H, H_{Ar}), 4.49 (ddd, J = 13.4, 9.0, 7.1 Hz, 1H, H_{CH}), 3.62 (s, 3H, H_{CH3}), 3.42 (s, 3H, H_{CH3}), 3.29 (ddd, J = 13.7, 8.9, 5.0 Hz, 1H, H_{CH}), 2.27 (t, J = 7.5 Hz, 2H, H_{CH2}), 1.69 – 1.44 (m, 4H, 2xH_{CH2}), 1.39 – 1.26 (m, 2H, H_{CH2}); ¹³C NMR (126 MHz, CDCl₃) δ 174.1, 168.3, 167.7, 140.3, 139.1, 135.6, 134.9, 130.8, 130.6, 128.4, 128.3, 127.6, 127.6, 125.9, 125.2, 51.5, 49.0, 36.7, 34.0, 27.5, 26.4, 24.5; **HRMS (ESI)**: m/z [M+H]⁺ calcd for C₂₂H₂₅N₂O₄: 381.18088, found: 381.18028.

ethyl 7-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[b,f][1,5]diazocin-5(6H)-yl)heptanoate (10f): Yield: 83%, pale oil, Rf = 0.41 (hexane:ethyl acetate 1:1). ¹H NMR (500 MHz, CDCl₃) δ 7.32 – 7.22 (m, 4H, H_{Ar}), 7.18 (qd, J = 7.6, 1.2 Hz, 2H, H_{Ar}), 7.05 (t, J = 7.0 Hz, 2H, H_{Ar}), 4.48 (ddd, J = 13.3, 9.1, 7.1 Hz, 1H, H_{CH}), 4.09 (q, J = 7.1 Hz, 2H, H_{CH2}), 3.43 (s, 3H, H_{CH3}), 3.28 (ddd, J = 13.6, 9.1, 5.0 Hz, 1H, H_{CH}), 2.25 (t, J = 7.6 Hz, 2H, H_{CH2}), 1.63 – 1.43 (m, 4H, 2xH_{CH2}), 1.37 – 1.27 (m, 4H, 2xH_{CH2}), 1.22 (t, J = 7.1 Hz, 3H, H_{CH3}); ¹³C NMR (126 MHz, CDCl₃) δ 173.9, 168.4, 167.8, 140.4, 139.2, 135.6, 135.0, 130.9, 130.7, 128.4, 128.4, 127.7, 127.6, 125.9, 125.2, 60.3, 49.2, 36.7, 34.4, 28.9, 27.7, 26.7, 25.1, 14.4; **HRMS (ESI)**: m/z [M+H]⁺ calcd for C₂₄H₂₉N₂O₄: 409.21218, found: 409.21156.

ethyl 2-(6-oxodibenzo[b,f]azocin-5(6H)-yl)acetate (10g): Yield: 90 %, white crystals, mp 86.0-87.0 °C, Rf = 0.78 (hexane:ethyl acetate 1:1). ¹H NMR (500 MHz, CDCl₃) δ 7.45 – 7.33 (m, 2H,

H_{CH=CH}), 7.26 – 7.11 (m, 4H, H_{Ar}), 7.11 – 7.04 (m, 1H, H_{Ar}), 7.03 – 6.93 (m, 2H, H_{Ar}), 6.89 (d, *J* = 11.5 Hz, 1H, H_{Ar}), 4.57 (d, *J* = 17.0 Hz, 1H, H_{CH}), 4.34 – 4.18 (m, 3H, H_{CH}+H_{CH₂}), 1.30 (t, *J* = 7.2 Hz, 3H, H_{CH₃});

¹³C NMR (126 MHz, CDCl₃) δ 171.5, 169.0, 141.7, 136.4, 135.4, 133.6, 132.8, 129.9, 129.0, 128.8, 128.7, 127.6, 127.6, 127.5, 127.3, 126.1, 61.4, 52.5, 14.3;

HRMS (ESI): *m/z* [M+H]⁺ calcd for C₁₉H₁₈NO₃: 308.12812, found: 308.12810.

methyl 3-(6-oxodibenzo[b,f]azocin-5(6H)-yl)propanoate (10h): Yield: 90 %, white crystals, mp 89.0-90.0 °C, R_f = 0.57 (hexane:ethyl acetate 1:1). ¹H NMR (500 MHz, CDCl₃) δ 7.39 – 7.31 (m, 1H, H_{Ar}), 7.25 – 7.12 (m, 5H, H_{Ar}), 7.07 (d, *J* = 7.7 Hz, 1H, H_{Ar}), 7.00 – 6.90 (m, 2H, H_{Ar}), 6.82 (d, *J* = 11.5 Hz, 1H, H_{Ar}), 4.74 (ddd, *J* = 13.5, 8.7, 5.9 Hz, 1H, H_{CH}), 3.64 – 3.50 (m, 4H, H_{CH}+H_{CH₃}), 2.67 (ddd, *J* = 16.2, 8.6, 5.9 Hz, 1H, H_{CH}), 2.51 (ddd, *J* = 16.2, 8.7, 6.4 Hz, 1H, H_{CH}); ¹³C NMR (126 MHz, CDCl₃) δ 171.8, 171.0, 140.9, 137.0, 136.1, 133.5, 133.3, 129.5, 128.9, 128.8, 128.6, 127.7, 127.6, 127.3, 127.2, 127.0, 51.8, 46.5, 32.8; **HRMS (ESI):** *m/z* [M+H]⁺ calcd for C₁₉H₁₈NO₃: 308.12812, found: 308.12808.

ethyl 4-(6-oxodibenzo[b,f]azocin-5(6H)-yl)butanoate (10i): Yield: 77 %, white crystals, mp 90.0-91.0 °C, R_f = 0.68 (hexane:ethyl acetate 1:1). ¹H NMR (500 MHz, CDCl₃) δ 7.39 – 7.31 (m, 1H, H_{Ar}), 7.23 – 7.10 (m, 5H, H_{Ar}), 7.07 (d, *J* = 7.6 Hz, 1H, H_{Ar}), 7.01 – 6.92 (m, 2H, H_{Ar}), 6.87 (d, *J* = 11.5 Hz, 1H, H_{Ar}), 4.49 (dt, *J* = 13.3, 7.7 Hz, 1H, H_{CH}), 4.08 (q, *J* = 7.1 Hz, 2H, H_{CH₂}), 3.31 (ddd, *J* = 13.4, 7.7, 5.9 Hz, 1H, H_{CH}), 2.47 – 2.24 (m, 2H, H_{CH₂}), 1.91 – 1.69 (m, 2H, H_{CH₂}), 1.20 (t, *J* = 7.1 Hz, 3H, H_{CH₃}); ¹³C NMR (126 MHz, CDCl₃) δ 173.1, 171.1, 141.1, 137.3, 136.1, 133.4, 133.4, 129.6, 128.7, 128.7, 128.6, 127.6, 127.6, 127.2, 127.1, 126.8, 60.4, 49.7, 31.8, 23.2, 14.3; **HRMS (ESI):** *m/z* [M+H]⁺ calcd for C₂₁H₂₂NO₃: 336.15942, found: 336.15944.

methyl 5-(6-oxodibenzo[b,f]azocin-5(6H)-yl)pentanoate (10j): Yield: 91 %, white crystals, m.p 99.0-100.0 °C, R_f = 0.60 (hexane:ethyl acetate 1:1). ¹H NMR (500 MHz, CDCl₃) δ 7.39 – 7.31 (m, 1H, H_{Ar}), 7.25 – 7.10 (m, 5H, H_{Ar}), 7.08 (d, *J* = 7.6 Hz, 1H, H_{Ar}), 7.01 – 6.91 (m, 2H, H_{Ar}), 6.86 (d, *J* = 11.4 Hz, 1H, H_{Ar}), 4.47 (ddd, *J* = 13.3, 8.5, 6.8 Hz, 1H, H_{CH}), 3.63 (s, 3H, H_{CH₃}), 3.26 (ddd, *J* = 13.5, 8.4, 5.3 Hz, 1H, H_{CH}), 2.29 (td, *J* = 7.5, 1.4 Hz, 2H, H_{CH₂}), 1.73 – 1.56 (m, 2H, H_{CH₂}), 1.56 – 1.39 (m, 2H, H_{CH₂}); ¹³C NMR (126 MHz, CDCl₃) δ 173.9, 171.0, 141.2, 137.4, 136.2, 133.5, 133.3, 129.6, 128.7, 128.6, 128.6, 127.6, 127.6, 127.2, 127.0, 126.9, 51.6, 50.1, 33.8, 27.3, 22.4; **HRMS (ESI):** *m/z* [M+H]⁺ calcd for C₂₁H₂₂NO₃: 336.15942, found: 336.15931.

methyl 6-(6-oxodibenzo[b,f]azocin-5(6H)-yl)hexanoate (10k): Yield: 82 %, pale oil, R_f = 0.64 (hexane:ethyl acetate 1:1). ¹H NMR (500 MHz, CDCl₃) δ 7.38 – 7.31 (m, 1H, H_{Ar}), 7.23 – 7.10 (m, 5H, H_{Ar}), 7.07 (d, *J* = 7.6 Hz, 1H, H_{Ar}), 7.01 – 6.90 (m, 2H, H_{Ar}), 6.84 (d, *J* = 11.4 Hz, 1H, H_{Ar}), 4.45 (ddd, *J* = 13.3, 8.7, 6.7 Hz, 1H, H_{CH}), 3.63 (s, 3H, H_{CH₃}), 3.22 (ddd, *J* = 13.6, 9.0, 4.8 Hz, 1H, H_{CH}), 2.26 (t, *J* = 7.5 Hz, 2H, H_{CH₂}), 1.69 – 1.54 (m, 2H, H_{CH₂}), 1.54 – 1.45 (m, 1H, H_{CH}), 1.45 – 1.32 (m, 2H, H_{CH₂}), 1.31 – 1.21 (m, 1H, H_{CH}); ¹³C NMR (126 MHz, CDCl₃) δ 174.1, 170.9,

141.2, 137.4, 136.2, 133.4, 133.2, 129.6, 128.6, 128.6, 128.5, 127.6, 127.5, 127.2, 127.0, 126.9, 51.6, 50.4, 34.0, 27.6, 26.6, 24.7; **HRMS (ESI):** m/z $[M+H]^+$ calcd for $C_{22}H_{24}NO_3$: 350.17507, found: 350.17502.

ethyl 7-(6-oxodibenzo[b,f]azocin-5(6H)-yl)heptanoate (10l): Yield: 90 %, pale oil, R_f = 0.78 (hexane:ethyl acetate 1:1). **1H NMR** (500 MHz, $CDCl_3$) δ 7.40 – 7.30 (m, 1H, H_{Ar}), 7.24 – 7.10 (m, 5H, H_{Ar}), 7.07 (d, J = 7.6 Hz, 1H, H_{Ar}), 7.01 – 6.91 (m, 2H, H_{Ar}), 6.84 (d, J = 11.4 Hz, 1H, H_{Ar}), 4.45 (ddd, J = 13.2, 8.8, 6.6 Hz, 1H, H_{CH}), 4.10 (q, J = 7.1 Hz, 2H, H_{CH_2}), 3.22 (ddd, J = 13.6, 9.1, 4.8 Hz, 1H, H_{CH_2}), 2.25 (t, J = 7.5 Hz, 2H, H_{CH_2}), 1.57 (p, J = 7.4 Hz, 2H, H_{CH_2}), 1.53 – 1.44 (m, 1H, H_{CH}), 1.44 – 1.32 (m, 2H, H_{CH_2}), 1.31 – 1.21 (m, 6H, $H_{CH}+H_{CH_2}+H_{CH_3}$); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 173.9, 170.9, 141.3, 137.5, 136.2, 133.4, 133.3, 129.6, 128.6, 128.6, 128.5, 127.6, 127.6, 127.2, 127.0, 126.9, 60.3, 50.5, 34.3, 29.0, 27.8, 26.7, 25.0, 14.4; **HRMS (ESI):** m/z $[M+H]^+$ calcd for $C_{24}H_{28}N_3O$: 378.20637, found: 378.20618.

methyl 6-(12-methyl-6,11-dioxo-11,12-dihydrodibenzo[b,f][1,4]diazocin-5(6H)-yl)hexanoate (10m): Yield: 88 %, white crystals, mp 169.0-170.0 °C, R_f = 0.29 (hexane:ethyl acetate 1:1). **1H NMR** (500 MHz, $CDCl_3$) δ 7.26 – 7.21 (m, 4H, H_{Ar}), 7.19 – 7.13 (m, 4H, H_{Ar}), 4.46 (ddd, J = 13.4, 9.5, 6.4 Hz, 1H, H_{CH}), 3.60 (s, 3H, H_{CH_3}), 3.39 (s, 3H, H_{CH_3}), 3.29 (ddd, J = 13.4, 9.8, 4.6 Hz, 1H, H_{CH}), 2.26 (t, J = 7.4 Hz, 2H, H_{CH_2}), 1.69 – 1.49 (m, 3H, $H_{CH_2}+H_{CH}$), 1.48 – 1.25 (m, 3H, $H_{CH_2}+H_{CH}$); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 173.9, 169.7, 169.1, 141.8, 139.5, 133.2, 132.6, 130.2, 130.0, 128.9, 128.8, 127.4, 126.7, 126.5, 126.5, 51.5, 48.9, 36.8, 33.9, 28.1, 26.3, 24.6; **HRMS (ESI):** m/z $[M+H]^+$ calcd for $C_{22}H_{25}N_2O_4$: 381.18088, found: 381.18032.

methyl 6-(8,9-dichloro-12-methyl-6,11-dioxo-11,12-dihydrodibenzo[b,f][1,4]diazocin-5(6H)-yl)hexanoate (10n): Yield: 83 %, white crystals, mp 158.0-159.0 °C, R_f = 0.55 (hexane:ethyl acetate 1:1). **1H NMR** (500 MHz, $CDCl_3$) δ 7.35 (d, J = 6.2 Hz, 2H, H_{Ar}), 7.29 – 7.17 (m, 4H, H_{Ar}), 4.43 (ddd, J = 13.5, 9.6, 6.3 Hz, 1H, H_{CH}), 3.62 (s, 3H, H_{CH_3}), 3.39 (s, 3H, H_{CH_3}), 3.30 (ddd, J = 14.1, 9.8, 4.6 Hz, 1H, H_{CH}), 2.27 (t, J = 7.4 Hz, 2H, H_{CH_2}), 1.68 – 1.48 (m, 3H, $H_{CH_2}+H_{CH}$), 1.48 – 1.25 (m, 3H, $H_{CH_2}+H_{CH}$); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 173.9, 167.5, 166.9, 141.3, 139.0, 134.7, 134.5, 132.8, 132.3, 129.4, 129.4, 129.0, 128.7, 127.6, 126.8, 51.6, 49.1, 37.0, 33.9, 28.0, 26.3, 24.6; **HRMS (ESI):** m/z $[M+H]^+$ calcd for $C_{22}H_{23}Cl_2N_2O_4$: 449.10294, 451.09999, found: 449.10243, 451.09958.

methyl 6-(12-benzyl-6,11-dioxo-11,12-dihydrodibenzo[b,f][1,4]diazocin-5(6H)-yl)hexanoate (10o): Yield: 78 %, white crystals, mp 148.0-149.0 °C, R_f = 0.48 (hexane:ethyl acetate 1:1). **1H NMR** (500 MHz, $CDCl_3$) δ 7.35 – 7.20 (m, 9H, H_{Ar}), 7.18 – 7.04 (m, 4H, H_{Ar}), 5.21 (d, J = 14.3 Hz, 1H, H_{Bn}), 4.88 (d, J = 14.3 Hz, 1H, H_{Bn}), 3.65 (s, 3H, H_{CH_3}), 3.38 (ddd, J = 13.5, 10.7, 5.2 Hz, 1H, H_{CH}), 2.87 (ddd, J = 13.6, 10.7, 5.5 Hz, 1H, H_{CH}), 2.29 (t, J = 7.5 Hz, 2H, H_{CH_2}), 1.65 – 1.52 (m, 3H, $H_{CH_2}+H_{CH}$), 1.49 – 1.35 (m, 1H, H_{CH}), 1.32 – 1.14 (m, 2H, H_{CH_2}); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 174.0, 169.5, 169.1, 140.8, 140.0, 137.1, 133.3, 132.7, 130.2, 130.0, 129.14 (2xC), 128.9, 128.9

(2xC), 128.7, 128.0, 127.6, 127.4, 126.5, 126.5, 52.7, 51.6, 49.0, 34.0, 28.1, 26.5, 24.6; **HRMS (ESI)**: m/z [M+H]⁺ calcd for C₂₈H₂₉N₂O₄: 457.21218, found: 457.21159.

methyl 6-(6-oxo-11,12-dihydrodibenzo[b,f]azocin-5(6H)-yl)hexanoate (10p): Yield: 85 %, white crystals, mp 77.0-78.0 °C, Rf = 0.75 (hexane:ethyl acetate 1:1). **¹H NMR** (500 MHz, CDCl₃) δ 7.15 (dd, J = 7.2, 1.7 Hz, 1H, H_{Ar}), 7.08 – 6.98 (m, 6H, H_{Ar}), 6.87 (d, J = 7.1 Hz, 1H, H_{Ar}), 4.17 (ddd, J = 13.2, 10.4, 5.6 Hz, 1H, H_{CH}), 3.63 (s, 3H, H_{CH3}), 3.52 (ddd, J = 13.2, 10.3, 5.3 Hz, 1H, H_{CH}), 3.43 – 3.34 (m, 1H, H_{CH}), 3.31 – 3.22 (m, 1H, H_{CH}), 2.95 – 2.83 (m, 2H, H_{CH2}), 2.29 (t, J = 7.5 Hz, 2H, H_{CH2}), 1.78 – 1.68 (m, 1H, H_{CH}), 1.64 (p, J = 7.6 Hz, 2H, H_{CH2}), 1.61 – 1.52 (m, 1H, H_{CH}), 1.45 – 1.31 (m, 2H, H_{CH2}); **¹³C NMR** (126 MHz, CDCl₃) δ 174.0, 172.1, 142.2, 138.2, 137.8, 135.4, 130.3, 129.1, 129.0, 127.9, 127.5, 127.0, 126.7, 126.3, 51.5, 49.2, 34.0, 33.0, 30.8, 27.6, 26.7, 24.7; **HRMS (ESI)**: m/z [M+H]⁺ calcd for C₂₂H₂₆NO₃: 352.19072, found: 352.19024.

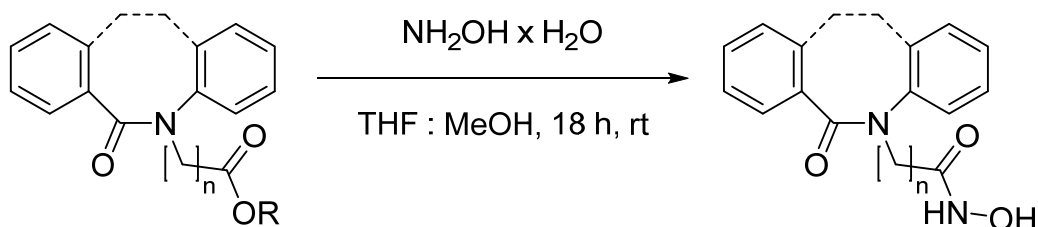
methyl 6-(2-bromo-11-methyl-6,12-dioxo-11,12-dihydrodibenzo[b,f][1,5]diazocin-5(6H)-yl)hexanoate (10r): Yield: 87 %, pale oil, Rf = 0.42 (hexane:ethyl acetate 1:1). **¹H NMR** (500 MHz, CDCl₃) δ 7.43 (d, J = 2.3 Hz, 1H, H_{Ar}), 7.39 (dd, J = 8.5, 2.3 Hz, 1H, H_{Ar}), 7.35 – 7.18 (m, 3H, H_{Ar}), 7.08 (d, J = 8.0 Hz, 1H, H_{Ar}), 6.95 (d, J = 8.5 Hz, 1H, H_{Ar}), 4.49 (ddd, J = 13.4, 9.0, 7.1 Hz, 1H, H_{CH}), 3.64 (s, 3H, H_{CH3}), 3.42 (s, 3H, H_{CH3}), 3.25 (ddd, J = 13.7, 8.9, 5.0 Hz, 1H, H_{CH}), 2.29 (t, J = 7.5 Hz, 2H, H_{CH2}), 1.69 – 1.59 (m, 2H, H_{CH2}), 1.59 – 1.45 (m, 2H, H_{CH2}), 1.38 – 1.28 (m, 2H, H_{CH2}); **¹³C NMR** (126 MHz, CDCl₃) δ 174.1, 167.5, 166.8, 140.0, 138.2, 137.3, 134.7, 134.0, 131.0, 130.7, 128.7, 127.7, 127.6, 125.4, 122.0, 51.6, 49.1, 36.8, 34.1, 27.5, 26.4, 24.6; **HRMS (ESI)**: m/z [M+H]⁺ calcd for C₂₂H₂₄BrN₂O₄: 459.09140, 461.08935, found: 459.09106, 461.08887.

methyl 6-(2,3-dimethoxy-11-methyl-6,12-dioxo-11,12-dihydrodibenzo[b,f][1,5]diazocin-5(6H)-yl)hexanoate (10s): Yield: 74 %, white crystals, mp 115.0-116.0 °C, Rf = 0.15 (hexane:ethyl acetate 1:1). **¹H NMR** (500 MHz, CDCl₃) δ 7.31 – 7.21 (m, 2H, H_{Ar}), 7.18 (td, J = 7.5, 1.2 Hz, 1H, H_{Ar}), 7.02 (d, J = 8.0 Hz, 1H, H_{Ar}), 6.72 (s, 1H, H_{Ar}), 6.45 (s, 1H, H_{Ar}), 4.48 (ddd, J = 13.3, 8.8, 7.2 Hz, 1H, H_{CH}), 3.76 (d, J = 2.4 Hz, 6H, H_{OCH3}), 3.60 (s, 3H, H_{CH3}), 3.38 (s, 3H, H_{CH3}), 3.17 (ddd, J = 13.5, 8.8, 4.9 Hz, 1H, H_{CH}), 2.26 (t, J = 7.5 Hz, 2H, H_{CH2}), 1.66 – 1.56 (m, 2H, H_{CH2}), 1.55 – 1.41 (m, 2H, H_{CH2}), 1.36 – 1.25 (m, 2H, H_{CH2}); **¹³C NMR** (126 MHz, CDCl₃) δ 174.1, 168.3, 167.9, 150.5, 148.6, 140.6, 134.8, 132.1, 130.6, 128.2, 127.6, 127.5, 125.1, 109.3, 108.4, 56.2, 56.0, 51.5, 48.9, 36.8, 34.0, 27.4, 26.4, 24.6; **HRMS (ESI)**: m/z [M+H]⁺ calcd for C₂₄H₂₉N₂O₆: 441.20201, found: 441.20158.

methyl 6-(5-methyl-6,14-dioxo-5,14-dihydrobenzonaphtho[2,3-f][1,5]diazocin-13(6H)-yl)hexanoate (10t): Yield: 69 %, white crystals, mp 198.0-199.0 °C, Rf = 0.43 (hexane:ethyl acetate 1:1). **¹H NMR** (500 MHz, CDCl₃) δ 7.84 (s, 1H, H_{Ar}), 7.82 – 7.70 (m, 2H, H_{Ar}), 7.57 (s, 1H, H_{Ar}), 7.50 (pd, J = 6.9, 1.4 Hz, 2H, H_{Ar}), 7.27 (d, J = 2.4 Hz, 1H, H_{Ar}), 7.16 (dd, J = 8.6, 2.4 Hz, 1H, H_{Ar}), 7.01 (d, J = 8.6 Hz, 1H, H_{Ar}), 4.53 (ddd, J = 13.3, 9.1, 6.9 Hz, 1H, H_{CH}), 3.63 (s, 3H, H_{CH3}), 3.50 – 3.40 (m, 4H, H_{CH3}+H_{CH}), 2.28 (t, J = 7.5 Hz, 2H, H_{CH2}), 1.67 – 1.49 (m, 4H, 2xH_{CH2}), 1.42 – 1.28 (m, 2H,

H_{CH_2}); ^{13}C NMR (126 MHz, CDCl_3) δ 174.1, 168.3, 166.6, 138.6, 136.9, 136.5, 134.2, 133.8, 133.7, 132.2, 130.9, 128.3, 128.1, 128.0, 127.8, 127.6, 127.5, 126.9, 125.2, 51.6, 50.1, 36.9, 34.1, 27.6, 26.5, 24.6; **HRMS (ESI)**: m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{26}\text{H}_{26}\text{ClN}_2\text{O}_4$: 465.15756, 467.15461 found: 465.15716, 467.15450.

2.2 General procedure for synthesis of hydroxamic acids



Ester from previous step was dissolved in mixture of THF (2 mL/mmol) and methanol (1 mL/mmol), then aqueous hydroxylamine solution (50% wt.; 2 ml/mmol) was added, reaction mixture was stirred for 18 hrs at room temperature. Volatiles were evaporated and resulting solid was dissolved in small amount of methanol, then small amount of chromatographic gel was added. Volatiles were evaporated, resulting solid was placed on top of chromatographic column and eluted with mixture of chloroform and methanol (1% to 10% of CH_3OH in CHCl_3).

N-hydroxy-2-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)acetamide (**7a**): Yield: 38 %, white crystals, mp 233.0-234.0 °C, R_f = 0.35 (methanol:chloroform 1:9). ^1H NMR (500 MHz, CD_3OD) δ 7.41 – 7.25 (m, 8H, H_{Ar}), 4.57 (d, J = 15.7 Hz, 1H, H_{CH}), 4.16 (d, J = 15.7 Hz, 1H, H_{CH}), 3.44 (s, 3H, H_{CH_3}); ^{13}C NMR (126 MHz, CD_3OD) δ 170.5, 170.3, 167.3, 141.5, 140.8, 135.7, 134.9, 132.4, 132.3, 129.8, 129.6, 128.7, 128.6, 127.1, 126.6, 51.1, 37.0; **HRMS (ESI)**: m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{17}\text{H}_{16}\text{N}_3\text{O}_4$: 326.11353, found: 326.11332.

N-hydroxy-3-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)propanamide (**7b**): Yield: 55 %, white crystals, mp 105.0-106.0 °C, R_f = 0.54 (methanol:chloroform 1:9). ^1H NMR (500 MHz, CD_3OD) δ 7.42 – 7.34 (m, 2H, H_{Ar}), 7.32 – 7.25 (m, 6H, H_{Ar}), 4.70 (ddd, J = 13.6, 9.5, 6.0 Hz, 1H, H_{CH}), 3.71 (ddd, J = 13.5, 9.4, 5.8 Hz, 1H, H_{CH}), 3.43 (s, 3H, H_{CH_3}), 2.45 (ddd, J = 14.2, 9.4, 6.0 Hz, 1H, H_{CH}), 2.32 (ddd, J = 14.2, 9.5, 5.9 Hz, 1H, H_{CH}); ^{13}C NMR (126 MHz, CD_3OD) δ 170.5, 169.9, 169.6, 141.4, 139.8, 136.3, 135.5, 132.4, 132.2, 129.9, 129.7, 128.4, 128.3, 127.3, 126.6, 46.8, 37.0, 32.1; **HRMS (ESI)**: m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{18}\text{H}_{18}\text{N}_3\text{O}_4$: 340.12918, found: 340.12909.

N-hydroxy-4-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)butanamide (**7c**): Yield: 52 %, white crystals, mp 190.0-191.0 °C, R_f = 0.42 (methanol:chloroform 1:9). ^1H NMR (500 MHz, CD_3OD) δ 7.41 – 7.33 (m, 2H, H_{Ar}), 7.31 – 7.25 (m, 6H, H_{Ar}), 4.54 – 4.40 (m,

1H, H_{CH}), 3.50 (ddd, *J* = 13.6, 8.2, 5.4 Hz, 1H, H_{CH}), 3.45 (s, 3H, H_{CH3}), 2.13 (t, *J* = 7.5 Hz, 2H, H_{CH2}), 1.94 – 1.84 (m, 1H, H_{CH}), 1.83 – 1.74 (m, 1H, H_{CH}); ¹³C NMR (126 MHz, CD₃OD) δ 171.9, 170.5, 170.2, 141.4, 140.0, 136.4, 135.7, 132.4, 132.2, 129.8, 129.7, 128.4, 128.3, 127.2, 126.6, 49.6, 36.9, 31.1, 25.1; **HRMS (ESI):** *m/z* [M+H]⁺ calcd for C₁₉H₂₀N₃O₄: 354.14483, found: 354.14478.

N-hydroxy-5-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)pentanamide (**7d**): Yield: 60 %, white crystals, mp 217.0-218.0 °C, *R*_f = 0.42 (methanol:chloroform 1:9). ¹H NMR (500 MHz, CD₃OD) δ 7.43 – 7.33 (m, 2H, H_{Ar}), 7.32 – 7.22 (m, 6H, H_{Ar}), 4.53 (dt, *J* = 13.5, 7.7 Hz, 1H, H_{CH}), 3.46 – 3.39 (m, 4H, H_{CH} + H_{CH3}), 2.10 (hept, *J* = 7.2 Hz, 2H, H_{CH2}), 1.64 (p, *J* = 7.5 Hz, 2H, H_{CH2}), 1.57 – 1.47 (m, 2H, H_{CH2}); ¹³C NMR (126 MHz, DMSO) δ 168.9, 167.3, 166.8, 140.0, 138.5, 135.3, 134.6, 130.8, 130.6, 128.2, 128.1, 127.2, 127.0, 126.1, 125.5, 47.7, 36.0, 31.8, 26.9, 22.4; **HRMS (ESI):** *m/z* [M+H]⁺ calcd for C₂₀H₂₂N₃O₄: 368.16048, found: 368.16052.

N-hydroxy-6-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)hexanamide (**7e**): Yield: 57 %, white crystals, mp 155.0-156.0 °C, *R*_f = 0.43 (methanol:chloroform 1:9). ¹H NMR (500 MHz, CD₃OD) δ 7.41 – 7.33 (m, 2H, H_{Ar}), 7.31 – 7.24 (m, 6H, H_{Ar}), 4.53 (dt, *J* = 13.5, 7.8 Hz, 1H, H_{CH}), 3.44 (s, 3H, H_{CH3}), 3.39 (ddd, *J* = 13.2, 7.2, 5.7 Hz, 1H, H_{CH}), 2.08 (t, *J* = 7.4 Hz, 2H, H_{CH2}), 1.71 – 1.58 (m, 2H, H_{CH2}), 1.57 – 1.47 (m, 2H, H_{CH2}), 1.43 – 1.28 (m, 2H, H_{CH2}); ¹³C NMR (126 MHz, CD₃OD) δ 172.8, 170.4, 170.0, 141.4, 140.1, 136.4, 135.7, 132.4, 132.1, 129.7, 129.6, 128.4, 128.3, 127.2, 126.6, 50.0, 36.9, 33.6, 28.5, 27.4, 26.3; **HRMS (ESI):** *m/z* [M+H]⁺ calcd for C₂₁H₂₄N₃O₄: 382.17613, found: 382.17611.

N-hydroxy-7-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)heptanamide (**7f**): Yield: 31 %, white crystals, mp 145.0-146.0 °C, *R*_f = 0.45 (methanol:chloroform 1:9). ¹H NMR (500 MHz, CD₃OD) δ 7.41 – 7.33 (m, 2H, H_{Ar}), 7.31 – 7.24 (m, 6H, H_{Ar}), 4.54 (dt, *J* = 13.5, 7.8 Hz, 1H, H_{CH}), 3.43 (s, 3H, H_{CH3}), 3.39 (dt, *J* = 13.2, 6.4 Hz, 1H, H_{CH}), 2.08 (t, *J* = 7.4 Hz, 2H, H_{CH2}), 1.66 – 1.56 (m, 2H, H_{CH2}), 1.54 – 1.45 (m, 2H, H_{CH2}), 1.40 – 1.29 (m, 4H, 2xH_{CH2}); ¹³C NMR (126 MHz, CD₃OD) δ 172.9, 170.4, 170.0, 141.4, 140.1, 136.5, 135.8, 132.3, 132.1, 129.6, 129.6, 128.5, 128.3, 127.2, 126.6, 50.1, 36.9, 33.7, 29.7, 28.7, 27.6, 26.7; **HRMS (ESI):** *m/z* [M+H]⁺ calcd for C₂₂H₂₆N₃O₄: 396.19178, found: 396.19180.

N-hydroxy-2-(6-oxodibenzo[*b,f*]azocin-5(6*H*)-yl)acetamide (**7g**): Yield: 69 %, white crystals, mp 119.0-120.0 °C, *R*_f = 0.47 (methanol:chloroform 1:9). ¹H NMR (500 MHz, CD₃OD) δ 7.33 – 6.90 (m, 10H, H_{Ar} + H_{CH=CH}), 4.45 (d, *J* = 15.5 Hz, 1H, H_{CH}), 4.12 (d, *J* = 15.5 Hz, 1H, H_{CH}); ¹³C NMR (126 MHz, CD₃OD) δ 173.8, 167.6, 142.7, 137.5, 136.6, 135.1, 133.6, 131.4, 130.3, 129.8, 129.7, 128.6, 128.6, 128.6, 128.1, 127.6, 52.1; **HRMS (ESI):** *m/z* [M+H]⁺ calcd for C₁₇H₁₅N₂O₃: 295.10772, found: 295.10774.

N-hydroxy-3-(6-oxodibenzo[*b,f*]azocin-5(6*H*)-yl)propanamide (**7h**): Yield: 66 %, white crystals, mp 173.0-174.0 °C, *R*_f = 0.47 (methanol:chloroform 1:9). ¹H NMR (500 MHz, CD₃OD) δ 7.37 – 6.91

(m, 10H, H_{Ar} + $H_{CH=CH}$), 4.57 (ddd, J = 13.8, 8.4, 5.8 Hz, 1H, H_{CH}), 3.65 (ddd, J = 14.0, 8.2, 6.5 Hz, 1H, H_{CH}), 2.39 (qdd, J = 14.6, 8.3, 6.3 Hz, 2H, H_{CH_2}); ^{13}C NMR (126 MHz, CD_3OD) δ 173.4, 169.8, 142.2, 138.0, 137.2, 135.1, 133.8, 131.3, 130.1, 129.9, 129.7, 128.7, 128.6, 128.5, 127.8 (2x), 48.4, 32.1; **HRMS (ESI)**: m/z $[M+H]^+$ calcd for $C_{18}H_{17}N_2O_3$: 309.12337, found: 309.12329.

N-hydroxy-4-(6-oxodibenzo[*b,f*]azocin-5(6*H*)-yl)butanamide (**7i**): Yield: 71 %, white crystals, mp 172.0-173.0 °C, R_f = 0.48 (methanol:chloroform 1:9). 1H NMR (500 MHz, CD_3OD) δ 7.33 – 6.96 (m, 10H, H_{Ar} + $H_{CH=CH}$), 4.40 (dt, J = 13.4, 7.8 Hz, 1H, H_{CH}), 3.39 (dt, J = 13.5, 6.8 Hz, 1H, H_{CH}), 2.14 (qt, J = 14.6, 7.6 Hz, 2H, H_{CH_2}), 1.77 (p, J = 7.4 Hz, 2H, H_{CH_2}); ^{13}C NMR (126 MHz, CD_3OD) δ 173.5, 172.0, 141.9, 138.2, 137.4, 135.0, 134.0, 131.3, 130.1, 129.9, 129.7, 128.7, 128.6, 128.5, 127.8, 127.7, 51.0, 31.3, 24.9; **HRMS (ESI)**: m/z $[M+H]^+$ calcd for $C_{19}H_{19}N_2O_3$: 323.13902, found: 323.13893.

N-hydroxy-5-(6-oxodibenzo[*b,f*]azocin-5(6*H*)-yl)pentanamide (**7j**): Yield: 59 %, white crystals, mp 175.0-176.0 °C, R_f = 0.48 (methanol:chloroform 1:9). 1H NMR (500 MHz, CD_3OD) δ 7.35 – 6.90 (m, 10H, H_{Ar} + $H_{CH=CH}$), 4.43 (dt, J = 13.4, 7.6 Hz, 1H, H_{CH}), 3.35 (ddd, J = 13.5, 7.5, 5.9 Hz, 1H, H_{CH}), 2.08 (td, J = 7.2, 2.9 Hz, 2H, H_{CH_2}), 1.75 – 1.55 (m, 2H, H_{CH_2}), 1.53 – 1.43 (m, 2H, H_{CH_2}); ^{13}C NMR (126 MHz, CD_3OD) δ 173.4, 172.5, 142.1, 138.3, 137.4, 135.0, 133.9, 131.4, 130.0, 129.9, 129.7, 128.7, 128.6, 128.4, 127.8, 127.7, 51.2, 33.4, 28.3, 24.3; **HRMS (ESI)**: m/z $[M+H]^+$ calcd for $C_{20}H_{21}N_2O_3$: 337.15467, found: 337.15448.

N-hydroxy-6-(6-oxodibenzo[*b,f*]azocin-5(6*H*)-yl)hexanamide (**7k**): Yield: 63 %, white crystals, mp 180.0-181.0 °C, R_f = 0.47 (methanol:chloroform 1:9). 1H NMR (500 MHz, CD_3OD) δ 7.32 – 6.95 (m, 10H, H_{Ar} + $H_{CH=CH}$), 4.43 (dt, J = 13.4, 7.6 Hz, 1H, H_{CH}), 3.40 – 3.32 (m, 1H, H_{CH}), 2.06 (td, J = 7.3, 1.3 Hz, 2H, H_{CH_2}), 1.66 – 1.52 (m, 2H, H_{CH_2}), 1.52 – 1.42 (m, 2H, H_{CH_2}), 1.42 – 1.26 (m, 2H, H_{CH_2}); ^{13}C NMR (126 MHz, CD_3OD) δ 173.4, 172.8, 142.1, 138.4, 137.4, 135.0, 134.0, 131.4, 130.0, 129.8, 129.7, 128.7, 128.6, 128.4, 127.8, 127.8, 51.5, 33.6, 28.5, 27.6, 26.5; **HRMS (ESI)**: m/z $[M+H]^+$ calcd for $C_{21}H_{23}N_2O_3$: 351.17032, found: 351.17046.

N-hydroxy-7-(6-oxodibenzo[*b,f*]azocin-5(6*H*)-yl)heptanamide (**7l**): Yield: 54 %, white crystals, mp 151.0-152.0 °C, R_f = 0.47 (methanol: chloroform 1 : 9). 1H NMR (500 MHz, CD_3OD) δ 7.32 – 6.92 (m, 10H, H_{Ar} + $H_{CH=CH}$), 4.42 (dt, J = 13.3, 7.6 Hz, 1H, H_{CH}), 3.34 – 3.31 (m, 1H, H_{CH}), 2.06 (t, J = 7.4 Hz, 2H, H_{CH_2}), 1.57 (p, J = 7.4 Hz, 2H, H_{CH_2}), 1.50 – 1.41 (m, 2H, H_{CH_2}), 1.40 – 1.25 (m, 4H, 2x H_{CH_2}); ^{13}C NMR (126 MHz, CD_3OD) δ 173.3, 172.9, 142.2, 138.4, 137.4, 135.0, 133.9, 131.3, 130.0, 129.8, 129.6, 128.7, 128.6, 128.4, 127.8, 127.8, 51.5, 33.6, 29.8, 28.6, 27.7, 26.6; **HRMS (ESI)**: m/z $[M+H]^+$ calcd for $C_{22}H_{25}N_2O_3$: 365.18597, found: 365.18616.

N-hydroxy-6-(12-methyl-6,11-dioxo-11,12-dihydrodibenzo[*b,f*][1,4]diazocin-5(6*H*)-yl)hexanamide (**7m**): Yield: 58 %, white crystals, mp 95.0-96.0 °C, R_f = 0.47 (methanol:chloroform 1:9). 1H NMR (500 MHz, CD_3OD) δ 7.42 – 7.33 (m, 4H, H_{Ar}), 7.33 – 7.22 (m, 4H, H_{Ar}), 4.49 (ddd, J =

13.4, 8.6, 7.2 Hz, 1H, H_{CH}), 3.53 – 3.39 (m, 4H, H_{CH} + H_{CH3}), 2.10 (t, *J* = 7.4 Hz, 2H, H_{CH2}), 1.73 – 1.60 (m, 2H, H_{CH2}), 1.60 – 1.47 (m, 2H, H_{CH2}), 1.45 – 1.32 (m, 2H, H_{CH2}); ¹³C NMR (126 MHz, CD₃OD) δ 172.7, 171.7, 171.3, 142.8, 140.4, 134.3, 133.9, 131.5, 131.4, 130.4, 130.4, 128.7, 127.8, 127.5, 127.2, 50.11, 37.3, 33.6, 29.0, 27.4, 26.4; **HRMS (ESI):** *m/z* [M+H]⁺ calcd for C₂₁H₂₄N₃O₄: 382.17613, found: 382.17558.

N-hydroxy-6-(8,9-dichloro-12-methyl-6,11-dioxo-11,12-dihydrodibenzo[*b,f*][1,4]diazocin-5(6*H*)-yl)hexanamide (**7n**): Yield: 64 %, white crystals, mp 104-105.0 °C, *R*_f = 0.48 (methanol:chloroform 1:9). ¹H NMR (500 MHz, CD₃OD) δ 7.46 (d, *J* = 4.0 Hz, 2H, H_{Ar}), 7.45 – 7.33 (m, 4H, H_{Ar}), 4.46 (ddd, *J* = 13.5, 8.6, 7.3 Hz, 1H, H_{CH}), 3.52 – 3.39 (m, 4H, H_{CH} + H_{CH3}), 2.09 (t, *J* = 7.4 Hz, 2H, H_{CH2}), 1.74 – 1.60 (m, 2H, H_{CH2}), 1.59 – 1.46 (m, 2H, H_{CH2}), 1.46 – 1.31 (m, 2H, H_{CH2}); ¹³C NMR (126 MHz, CD₃OD) δ 172.7, 169.2, 168.8, 142.4, 140.0, 135.6, 135.5, 134.4, 134.0, 130.8, 130.8, 129.7, 129.5, 128.9, 128.1, 50.3, 37.4, 33.6, 29.0, 27.4, 26.3; **HRMS (ESI):** *m/z* [M+H]⁺ calcd for C₂₁H₂₂Cl₂N₃O₄: 450.09819, 452.09524, found: 450.09780, 452.09489.

N-hydroxy-6-(12-benzyl-6,11-dioxo-11,12-dihydrodibenzo[*b,f*][1,4]diazocin-5(6*H*)-yl)hexanamide (**7o**): Yield: 52 %, white crystals, mp 172.0-173.0 °C, *R*_f = 0.49 (methanol:chloroform 1:9). ¹H NMR (500 MHz, CD₃OD) δ 7.41 – 7.18 (m, 13H, H_{Ar}), 5.49 (d, *J* = 14.3 Hz, 1H, H_{Bn}), 4.77 (d, *J* = 14.3 Hz, 1H, H_{Bn}), 3.37 (ddd, *J* = 13.6, 10.6, 5.3 Hz, 1H, H_{CH}), 2.55 (ddd, *J* = 13.5, 10.5, 5.5 Hz, 1H, H_{CH}), 2.08 (t, *J* = 7.4 Hz, 2H, H_{CH2}), 1.67 – 1.50 (m, 3H, H_{CH2} + H_{CH}), 1.49 – 1.36 (m, 1H, H_{CH}), 1.31 – 1.12 (m, 2H, H_{CH2}); ¹³C NMR (126 MHz, CD₃OD) δ 172.7, 171.4, 171.2, 141.8, 140.7, 138.4, 134.4, 133.9, 131.5, 131.4, 130.4, 130.3, 130.3 (2xC), 130.0 (2xC), 129.3, 128.9, 128.6, 127.2, 127.2, 53.6, 50.3, 33.6, 28.8, 27.5, 26.2; **HRMS (ESI):** *m/z* [M+H]⁺ calcd for C₂₇H₂₈N₃O₄: 458.20743, found: 458.20681.

N-hydroxy-6-(6-oxo-11,12-dihydrodibenzo[*b,f*]azocin-5(6*H*)-yl)hexanamide (**7p**): Yield: 49 %, white crystals, mp 164.0-165.0 °C, *R*_f = 0.47 (methanol:chloroform 1:9). ¹H NMR (500 MHz, CD₃OD) δ 7.09 (qd, *J* = 7.7, 6.0 Hz, 7H, H_{Ar}), 6.97 (d, *J* = 7.5 Hz, 1H, H_{Ar}), 4.15 (ddd, *J* = 13.3, 9.8, 5.9 Hz, 1H, H_{CH}), 3.60 (ddd, *J* = 11.8, 9.7, 5.5 Hz, 1H, H_{CH}), 3.41 – 3.31 (m, 2H, H_{CH2-CH2}), 3.10 – 2.90 (m, 2H, H_{CH2-CH2}), 2.10 (t, *J* = 7.4 Hz, 2H, H_{CH2}), 1.83 – 1.71 (m, 1H, H_{CH}), 1.71 – 1.53 (m, 3H, H_{CH2} + H_{CH}), 1.52 – 1.34 (m, 2H, H_{CH2}); ¹³C NMR (126 MHz, CD₃OD) δ 174.6, 172.7, 143.2, 139.4, 138.8, 137.1, 131.6, 130.5, 130.3, 129.3, 128.7, 128.0, 127.4, 127.3, 50.5, 33.7, 33.6, 31.6, 28.6, 27.7, 26.5; **HRMS (ESI):** *m/z* [M+H]⁺ calcd for C₂₁H₂₅N₂O₃: 353.18597, found: 353.18549.

N-hydroxy-6-(2-bromo-11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)hexanamide (**7r**): Yield: 56 %, white crystals, mp 76.0-77.0 °C, *R*_f = 0.55 (methanol:chloroform 1:9). ¹H NMR (500 MHz, CD₃OD) δ 7.52 (dd, *J* = 8.6, 2.3 Hz, 1H, H_{Ar}), 7.46 (d, *J* = 2.3 Hz, 1H, H_{Ar}), 7.44 – 7.37 (m, 1H, H_{Ar}), 7.34 – 7.25 (m, 3H, H_{Ar}), 7.22 (d, *J* = 8.6 Hz, 1H, H_{Ar}), 4.52 (dt, *J* = 13.5, 7.8 Hz, 1H, H_{CH}), 3.43 (s, 3H, H_{CH3}), 3.37 (dt, *J* = 13.3, 6.4 Hz, 1H, H_{CH}), 2.08 (t, *J* = 7.4 Hz, 2H, H_{CH2}), 1.70 – 1.57 (m, 2H, H_{CH2}), 1.56 – 1.46 (m, 2H, H_{CH2}), 1.41

– 1.27 (m, 2H, H_{CH2}); ¹³C NMR (126 MHz, CD₃OD) δ 172.8, 169.8, 168.6, 141.1, 139.3, 138.3, 135.5, 135.3, 132.3, 131.3, 129.9, 129.2, 128.4, 126.7, 122.8, 49.9, 37.0, 33.6, 28.5, 27.4, 26.3; **HRMS (ESI):** *m/z* [M+H]⁺ calcd for C₂₁H₂₃BrN₃O₄: 460.08665, 462.08460, found: 460.08622, 462.08401.

N-hydroxy-6-(2,3-dimethoxy-11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)hexanamide (**7s**): Yield: 50 %, white crystals, mp 82.0-83.0 °C, R_f = 0.49 (methanol:chloroform 1:9). ¹H NMR (500 MHz, CD₃OD) δ 7.42 – 7.34 (m, 1H, H_{Ar}), 7.34 – 7.22 (m, 3H, H_{Ar}), 6.81 (d, *J* = 11.5 Hz, 2H, H_{Ar}), 4.54 (dt, *J* = 13.5, 7.8 Hz, 1H, H_{CH}), 3.76 (d, *J* = 5.1 Hz, 6H, HOCH₃), 3.42 (s, 3H, H_{CH3}), 3.38 – 3.32 (m, 1H, H_{CH}), 2.09 (t, *J* = 7.4 Hz, 2H, H_{CH2}), 1.74 – 1.56 (m, 2H, H_{CH2}), 1.57 – 1.44 (m, 2H, H_{CH2}), 1.44 – 1.27 (m, 2H, H_{CH2}); ¹³C NMR (126 MHz, CD₃OD) δ 172.8, 170.5, 170.2, 152.4, 150.3, 141.7, 135.8, 133.2, 132.0, 129.5, 128.3, 128.2, 126.5, 110.4, 110.0, 56.6, 56.5, 49.8, 37.1, 33.6, 28.4, 27.4, 26.4; **HRMS (ESI):** *m/z* [M+H]⁺ calcd for C₂₃H₂₈N₃O₆: 442.19726, found: 442.19664.

N-hydroxy-6-(5-methyl-6,14-dioxo-5,14-dihydrobenzonaphtho[2,3-*f*][1,5]diazocin-13(6*H*)-yl)hexanamide (**7t**): Yield: 50 %, white crystals, mp 161.0-162.0 °C, R_f = 0.41 (methanol:chloroform 1:9). ¹H NMR (500 MHz, DMSO-*d*₆) δ 7.91 (dd, *J* = 24.5, 8.4 Hz, 4H, H_{Ar}), 7.56 (pd, *J* = 6.8, 1.5 Hz, 2H, H_{Ar}), 7.44 – 7.30 (m, 3H, H_{Ar}), 4.42 (dt, *J* = 13.3, 7.8 Hz, 1H, H_{CH}), 3.53 – 3.40 (m, 4H, H_{CH} + H_{CH3}), 1.91 (t, *J* = 7.4 Hz, 2H, H_{CH2}), 1.57 – 1.30 (m, 4H, 2xH_{CH2}), 1.30 – 1.18 (m, 2H, H_{CH2}); ¹³C NMR (126 MHz, DMSO) δ 168.9, 167.2, 165.5, 138.5, 136.7, 136.0, 133.7, 133.2, 132.4, 131.5, 130.7, 128.0, 127.9, 127.9, 127.8, 127.4, 127.2, 126.7, 125.1, 48.9, 36.1, 32.2, 27.2, 26.0, 24.8; **HRMS (ESI):** *m/z* [M+H]⁺ calcd for C₂₅H₂₅ClN₃O₄: 466.15281, 468.14986, found: 466.15250, 468.14997.

3. Spectra

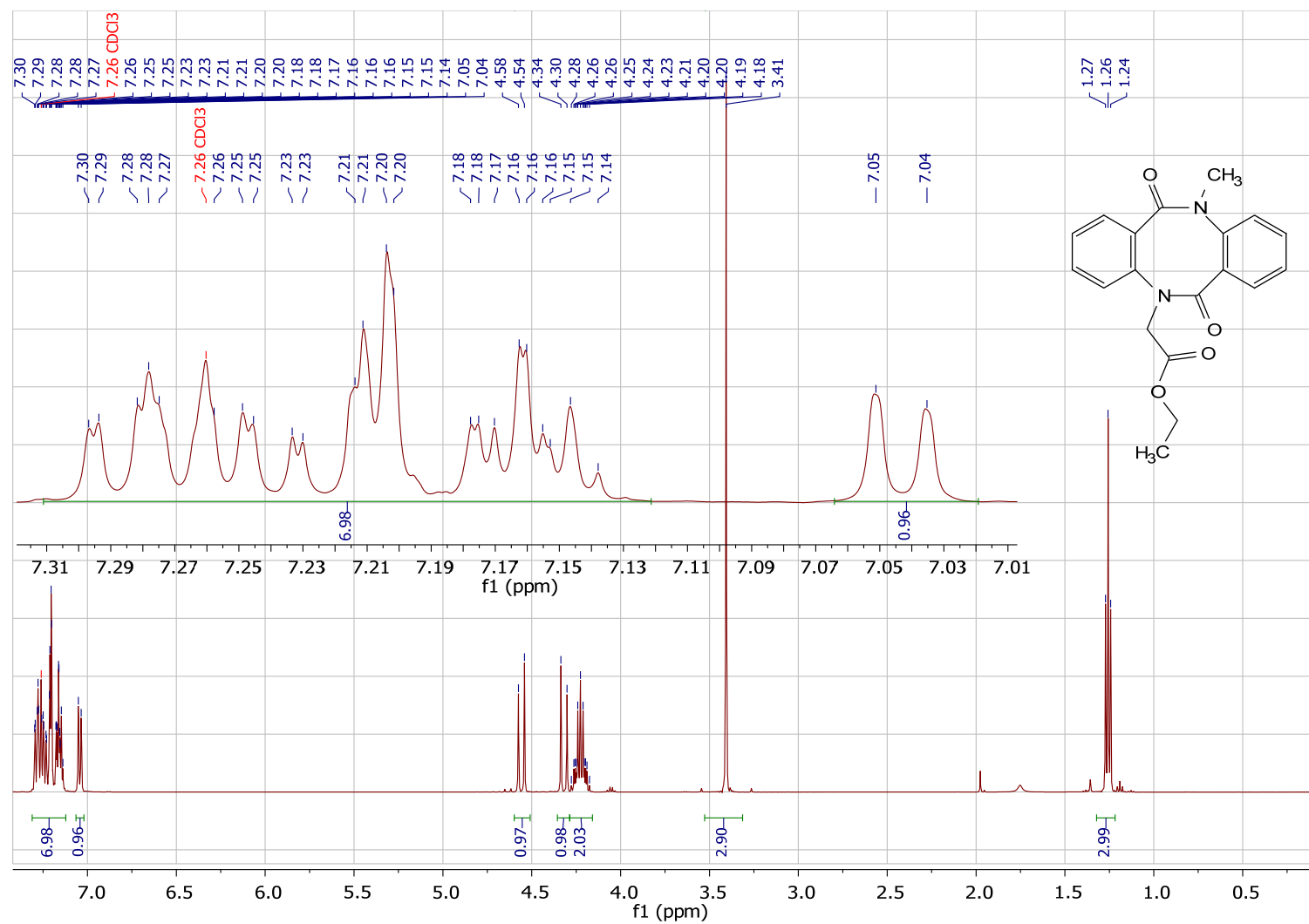


Figure S1. ^1H NMR spectrum of ethyl 2-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)acetate (**10a**).

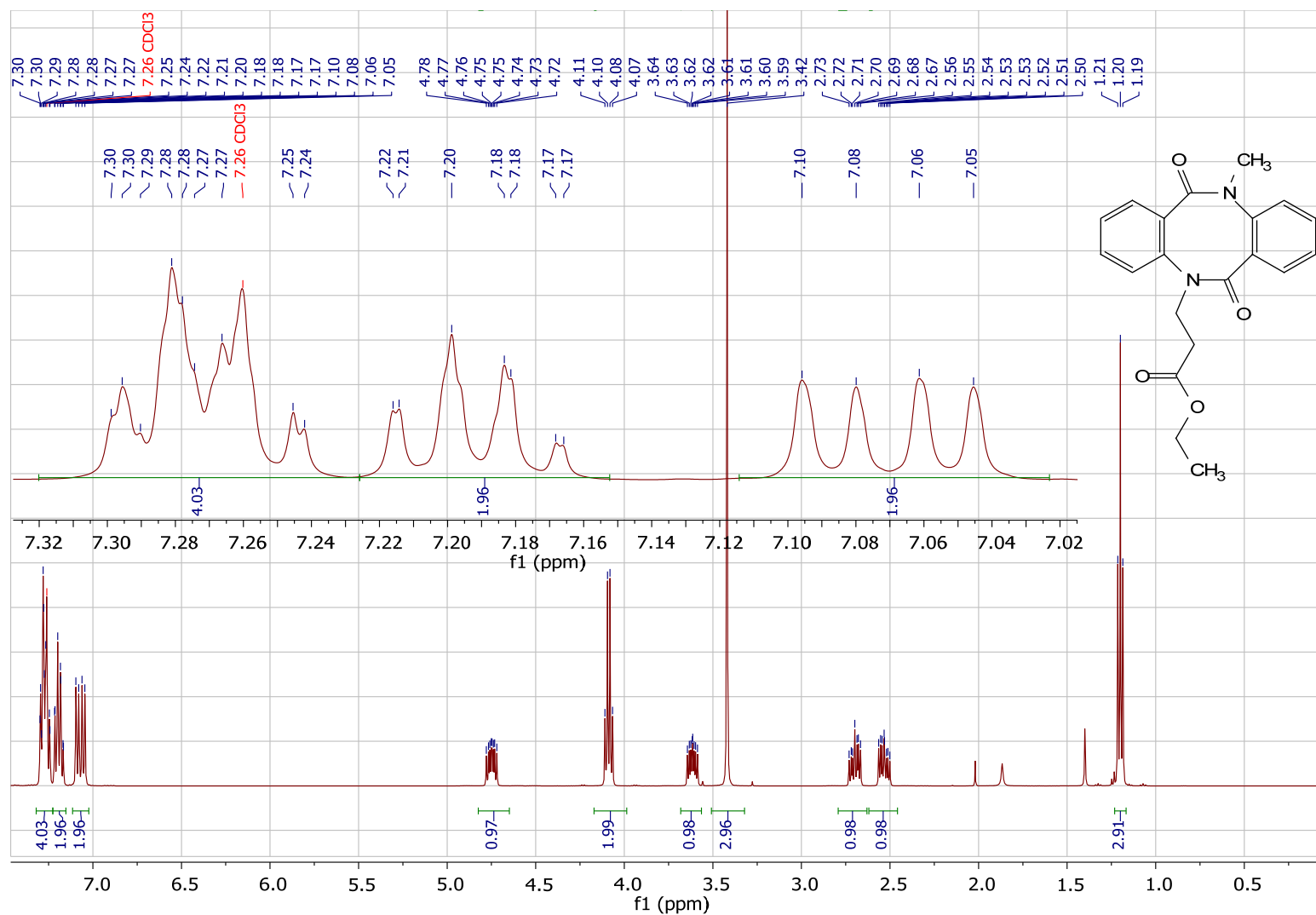


Figure S2. ¹H NMR spectrum of ethyl 3-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[b,f][1,5]diazocin-5(6H)-yl)propanoate (10b).

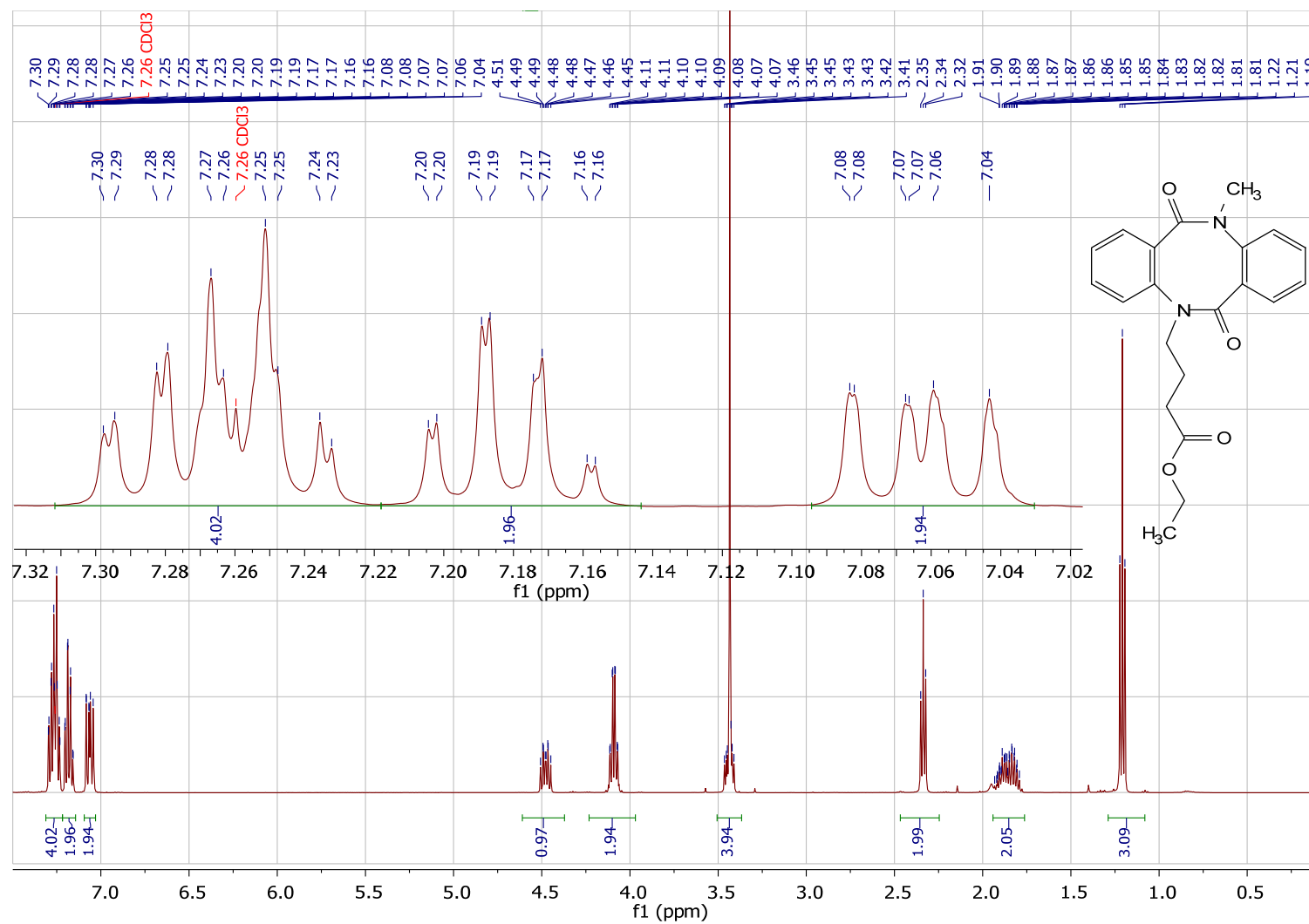


Figure S3. ^1H NMR spectrum of ethyl 4-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)butanoate (**10c**).

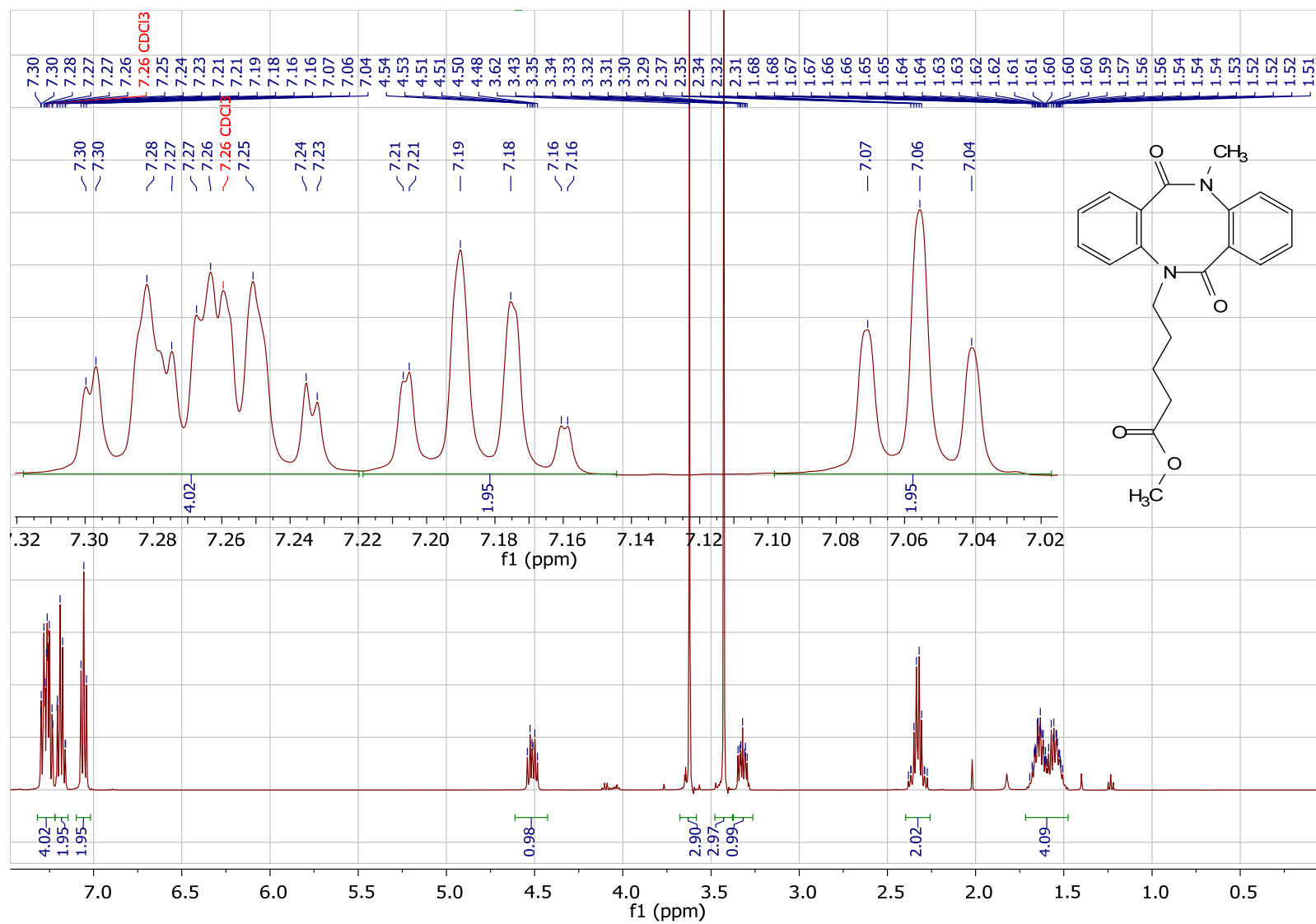


Figure S4. ^1H NMR spectrum of methyl 5-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)pentanoate (**10d**).

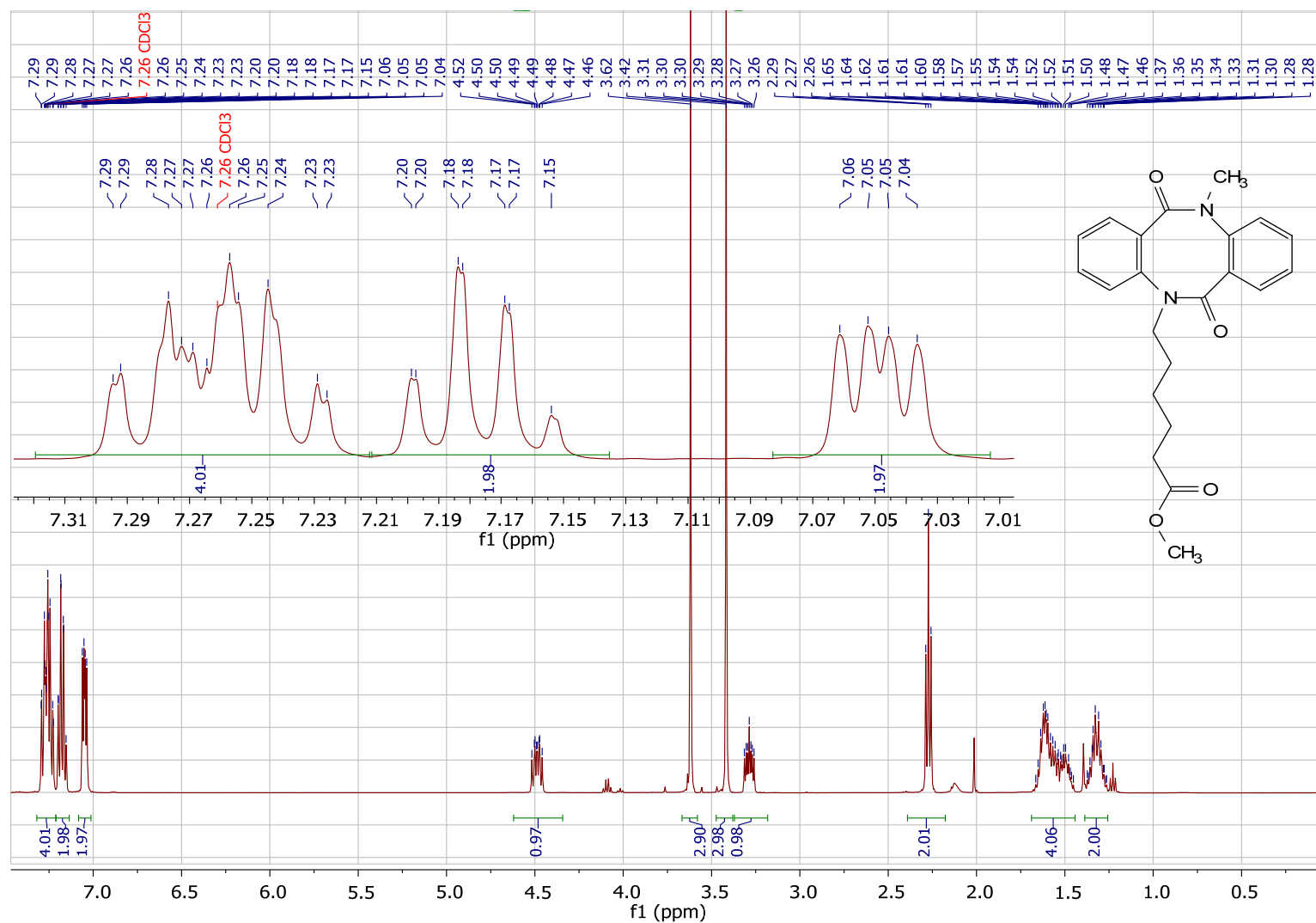


Figure S5. ^1H NMR spectrum of methyl 6-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)hexanoate (**10e**).

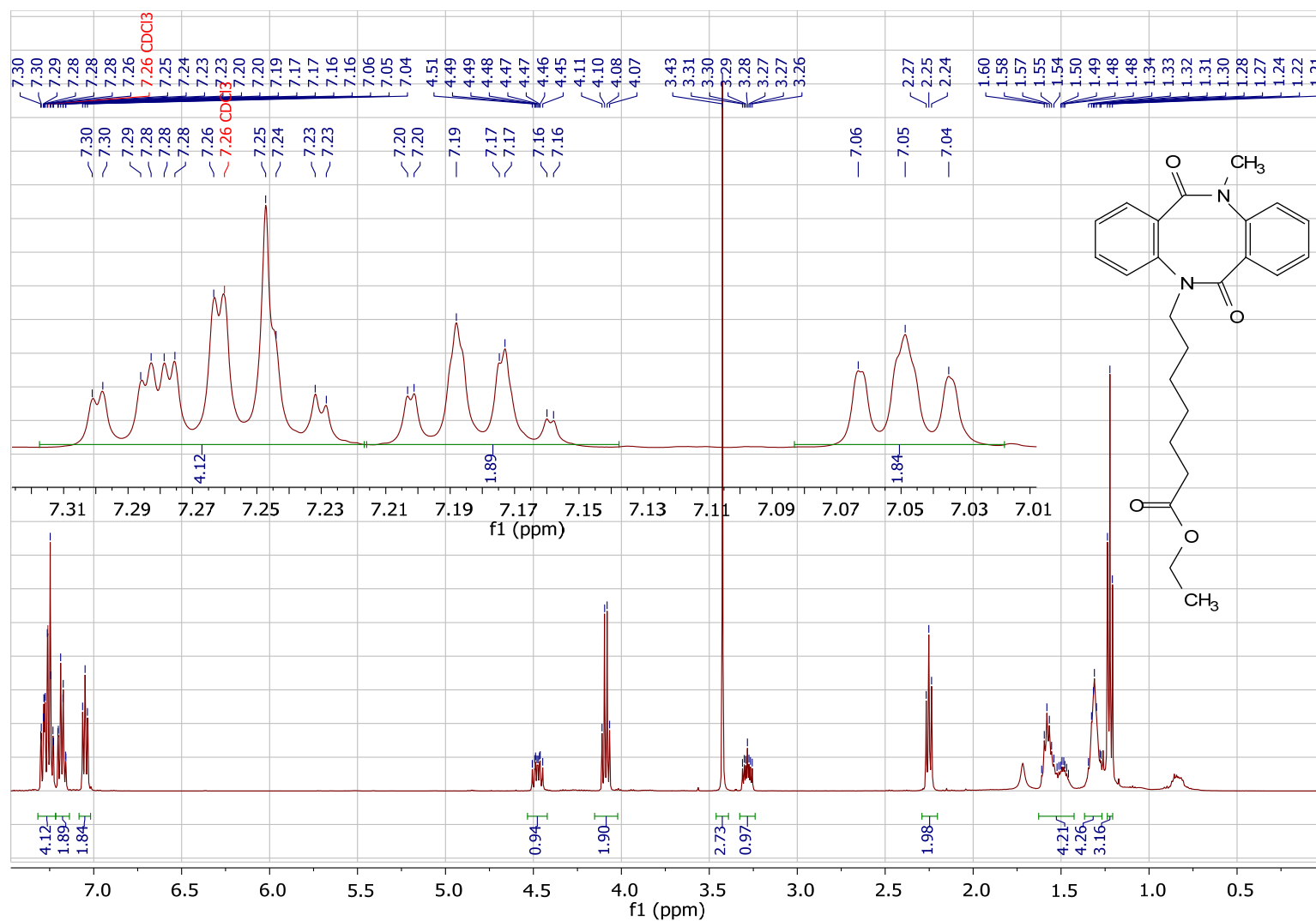


Figure S6. ^1H NMR spectrum of ethyl 7-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)heptanoate (**10f**).

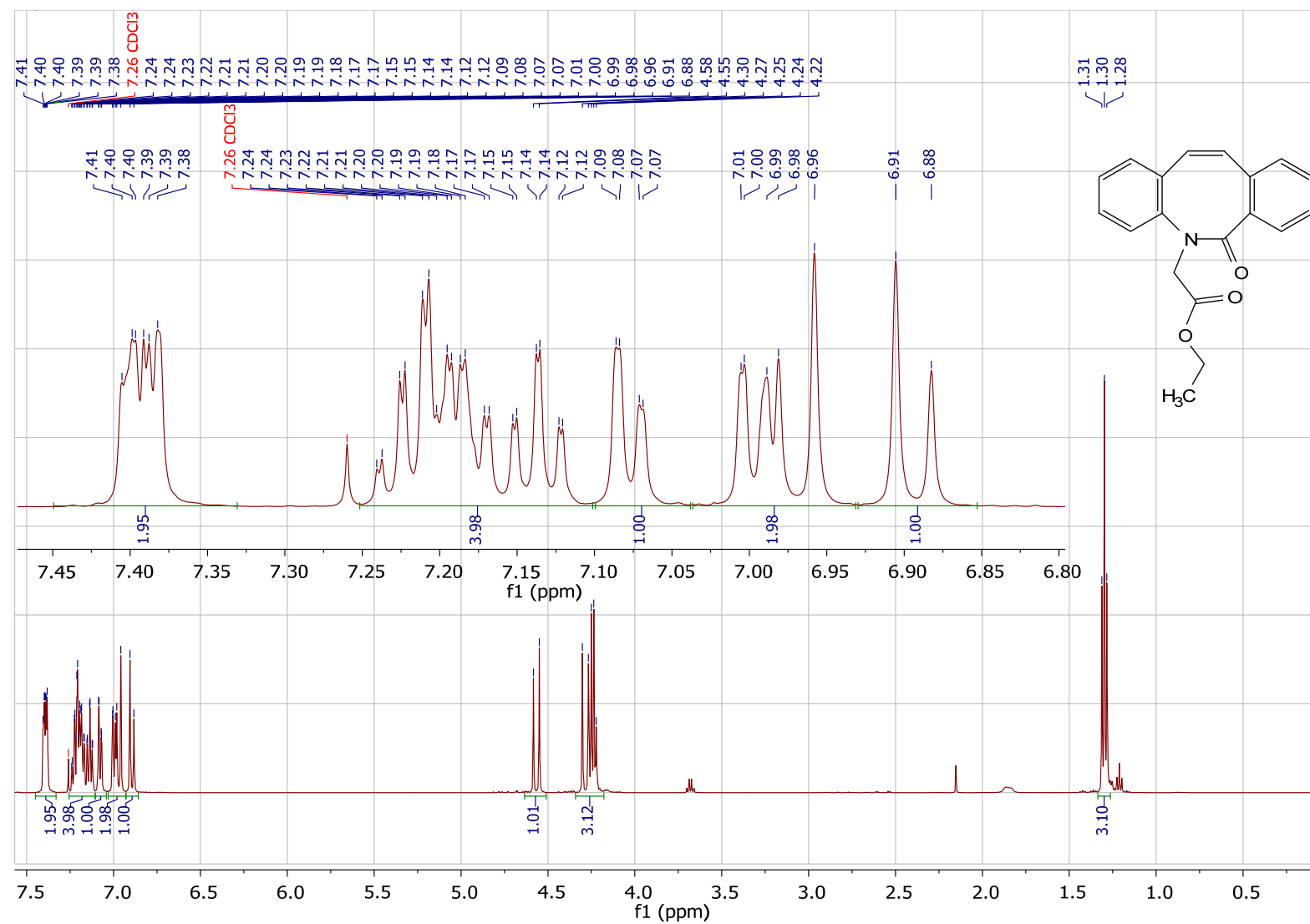


Figure S7. ¹H NMR spectrum of ethyl 2-(6-oxodibenzo[*b,f*]azocin-5(6*H*)-yl)acetate (**10g**).

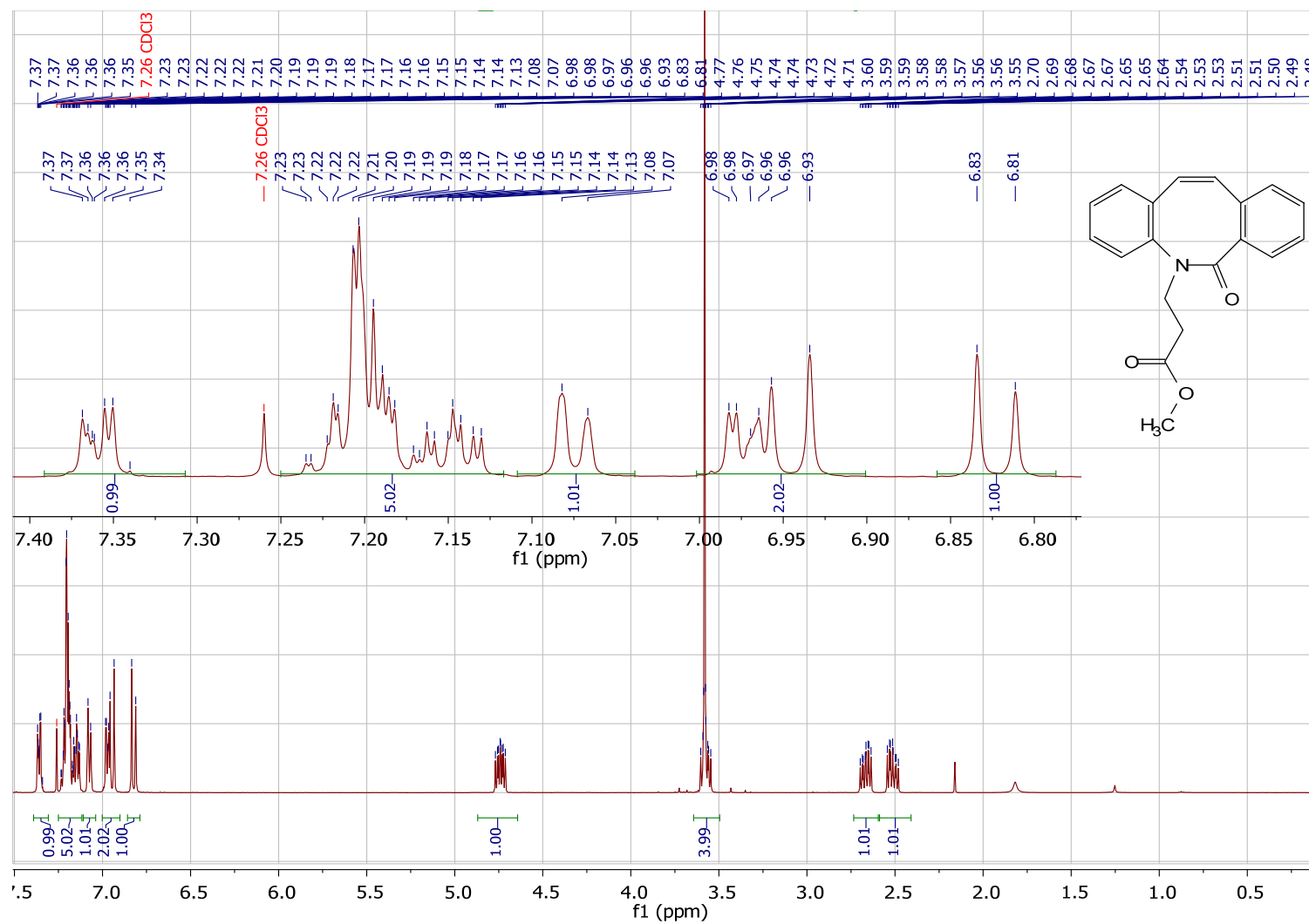


Figure S8. ^1H NMR spectrum of methyl 3-(6-oxodibenzo[*b,f*]azocin-5(6*H*)-yl)propanoate (**10h**).

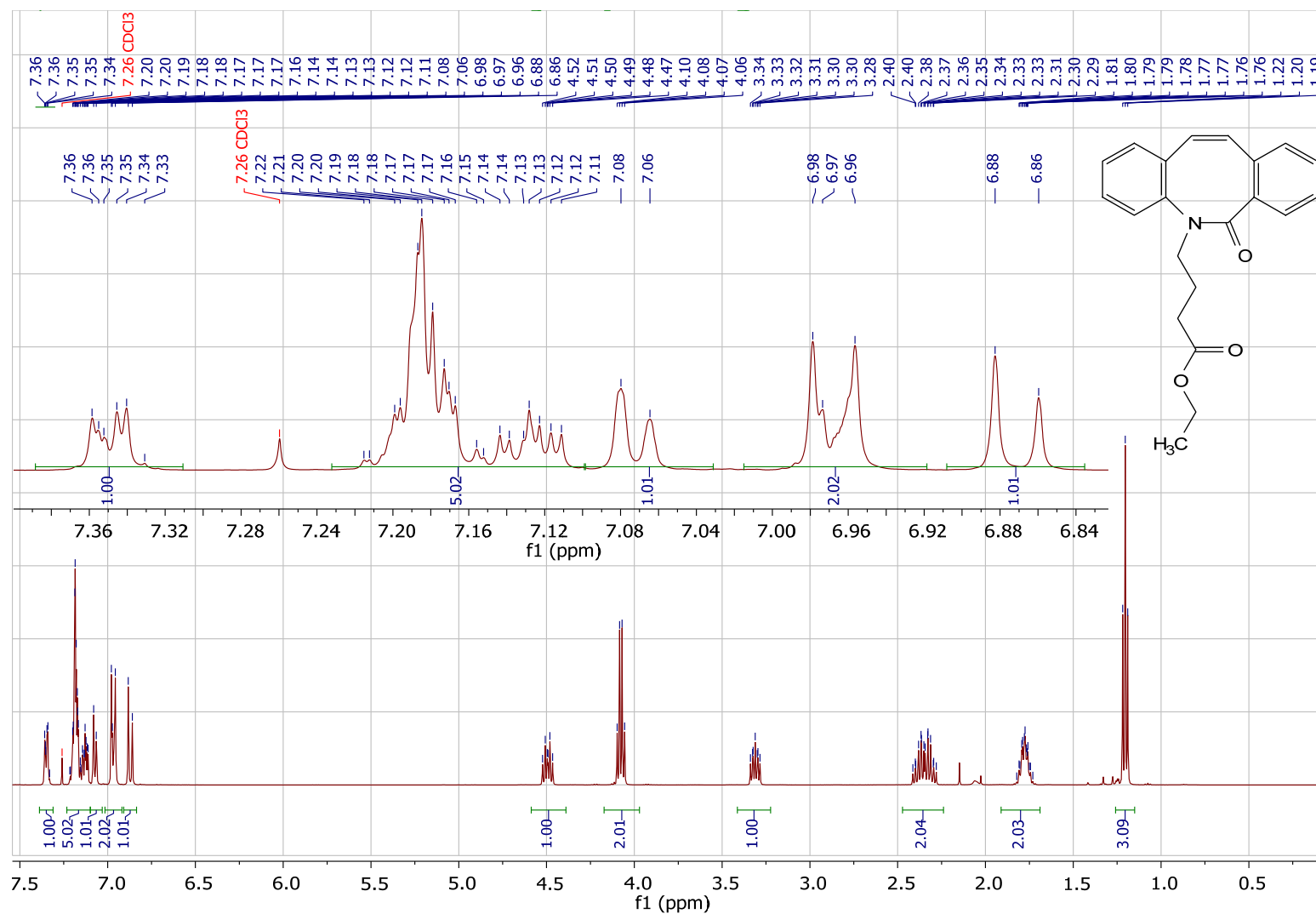


Figure S9. ^1H NMR spectrum of ethyl 4-(6-oxodibenzo[*b,f*]azocin-5(6*H*)-yl)butanoate (**10i**).

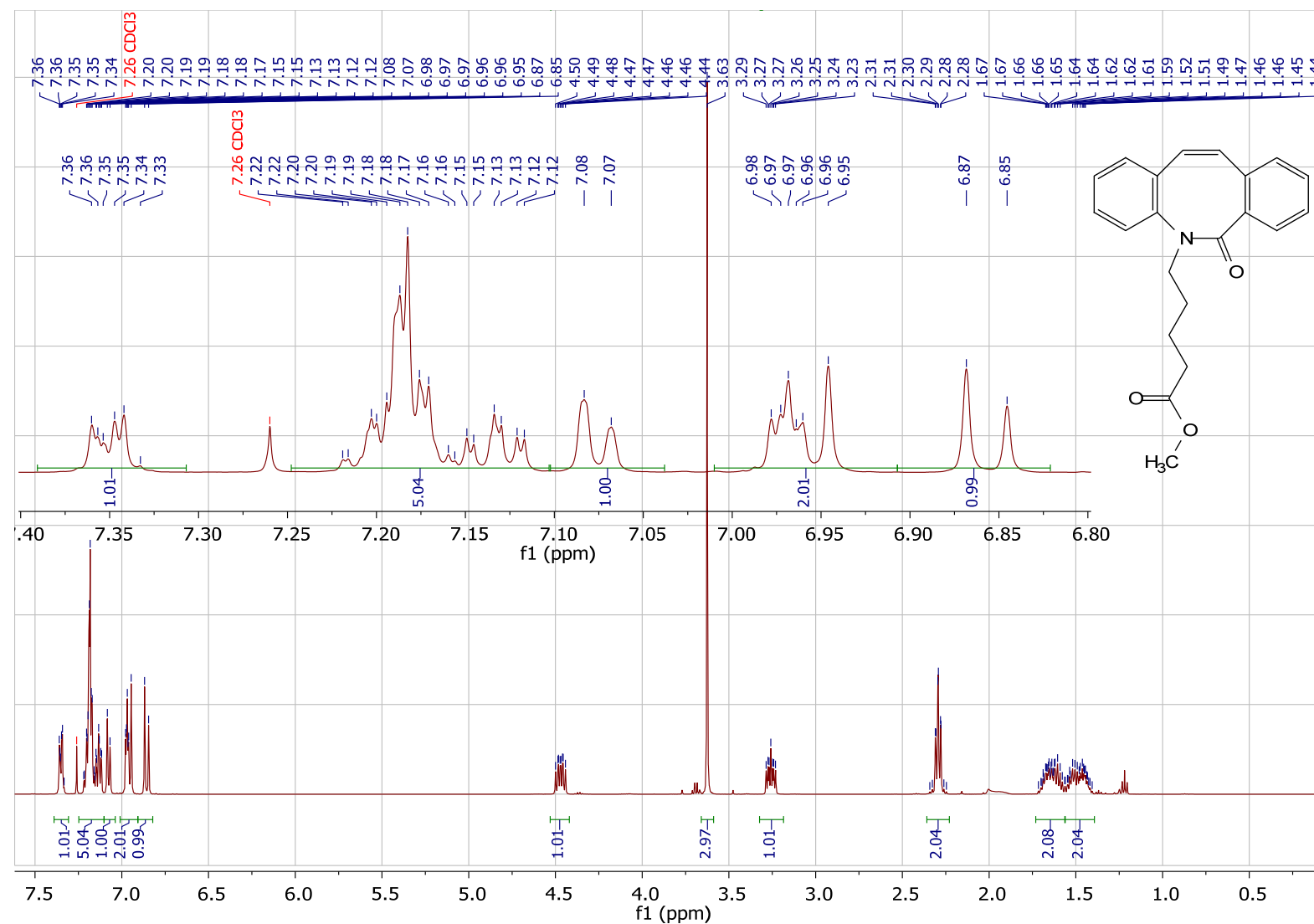


Figure S10. ^1H NMR spectrum of methyl 5-(6-oxodibenzo[*b,f*]azocin-5(6*H*)-yl)pentanoate (10j).

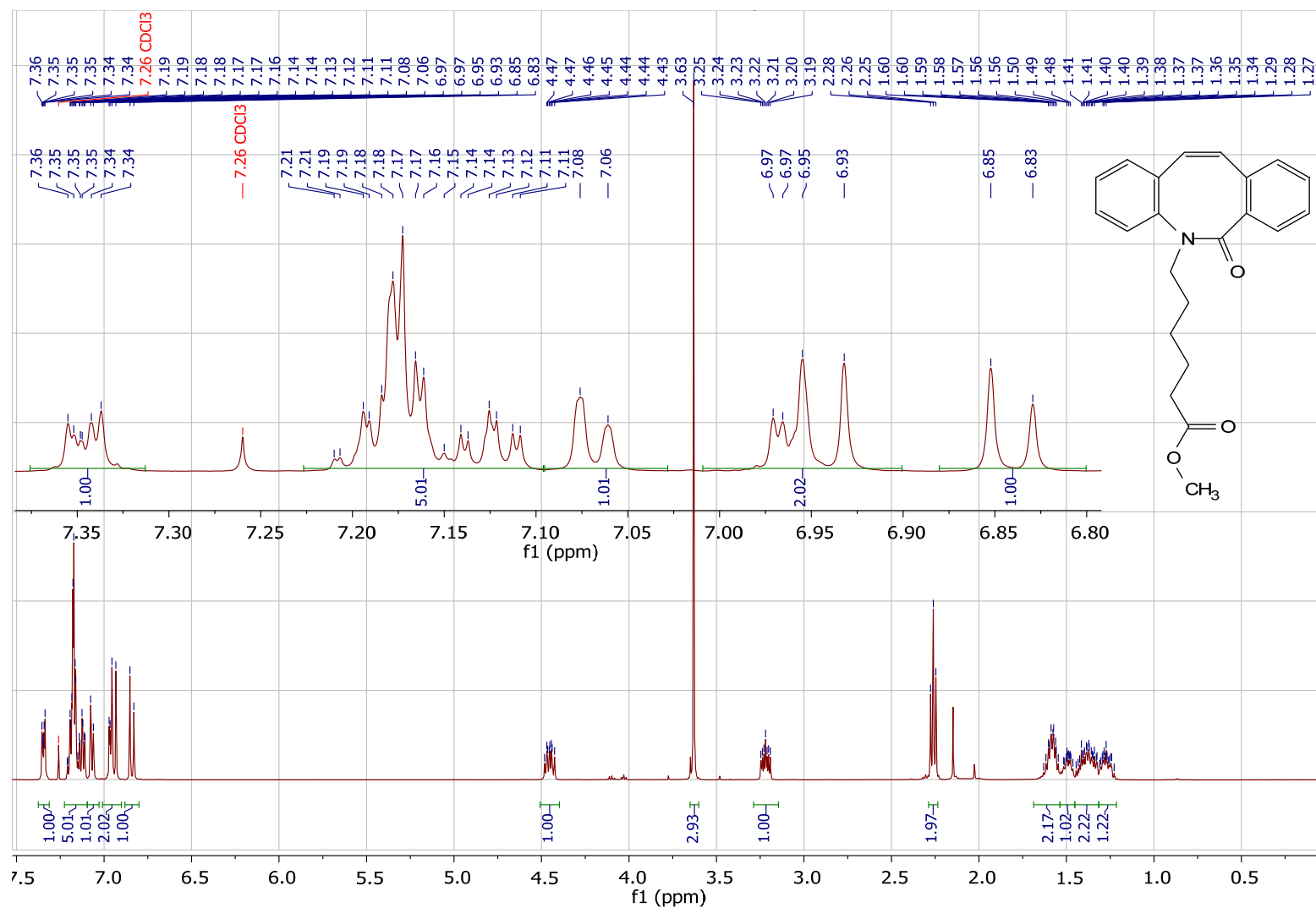


Figure S11. ^1H NMR spectrum of methyl 6-(6-oxodibenzo[*b,f*]azocin-5(6*H*)-yl)hexanoate (**10k**).

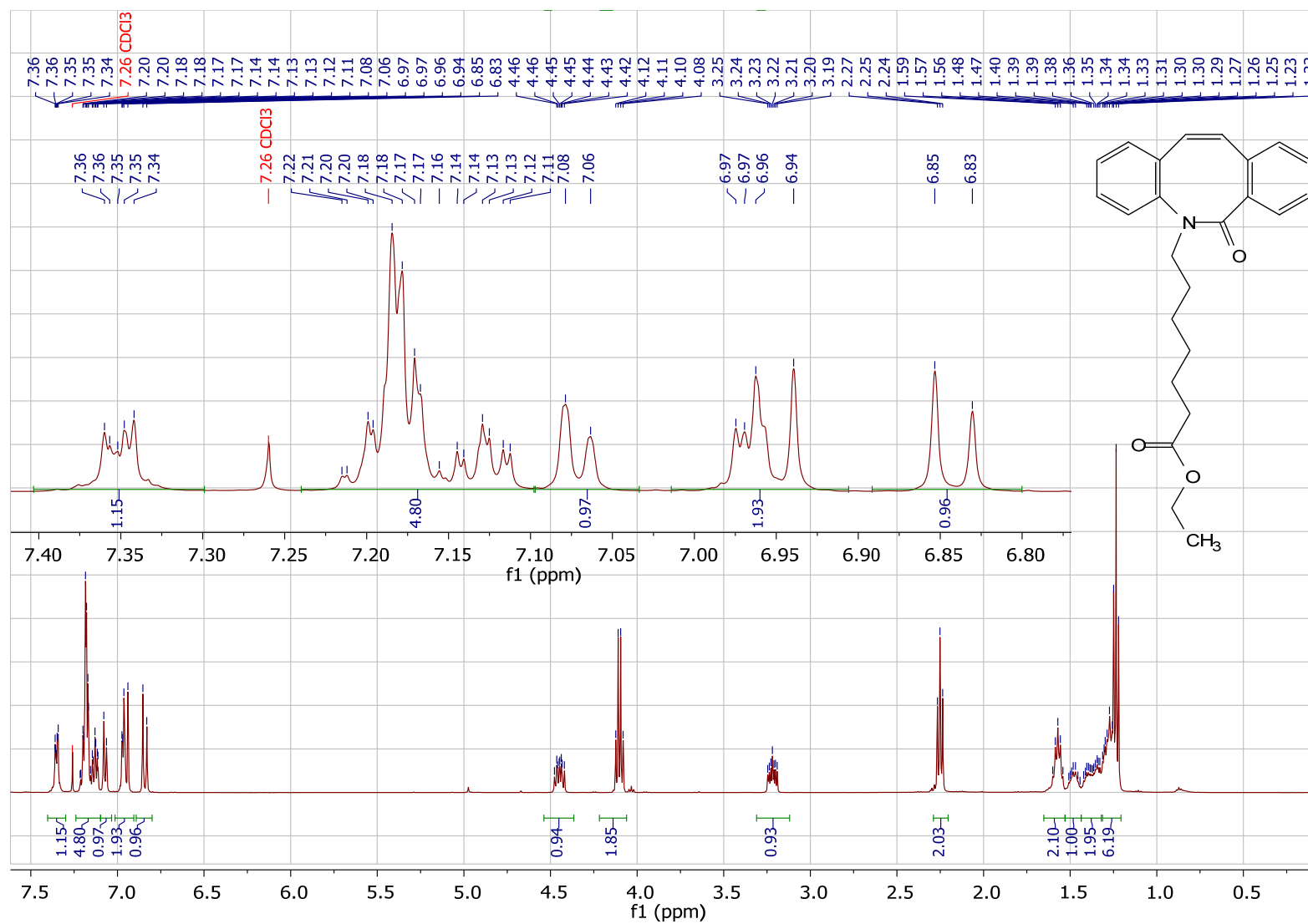


Figure S12. ^1H NMR spectrum of ethyl 7-(6-oxodibenzo[*b,f*]azocin-5(6*H*)-yl)heptanoate (**101**).

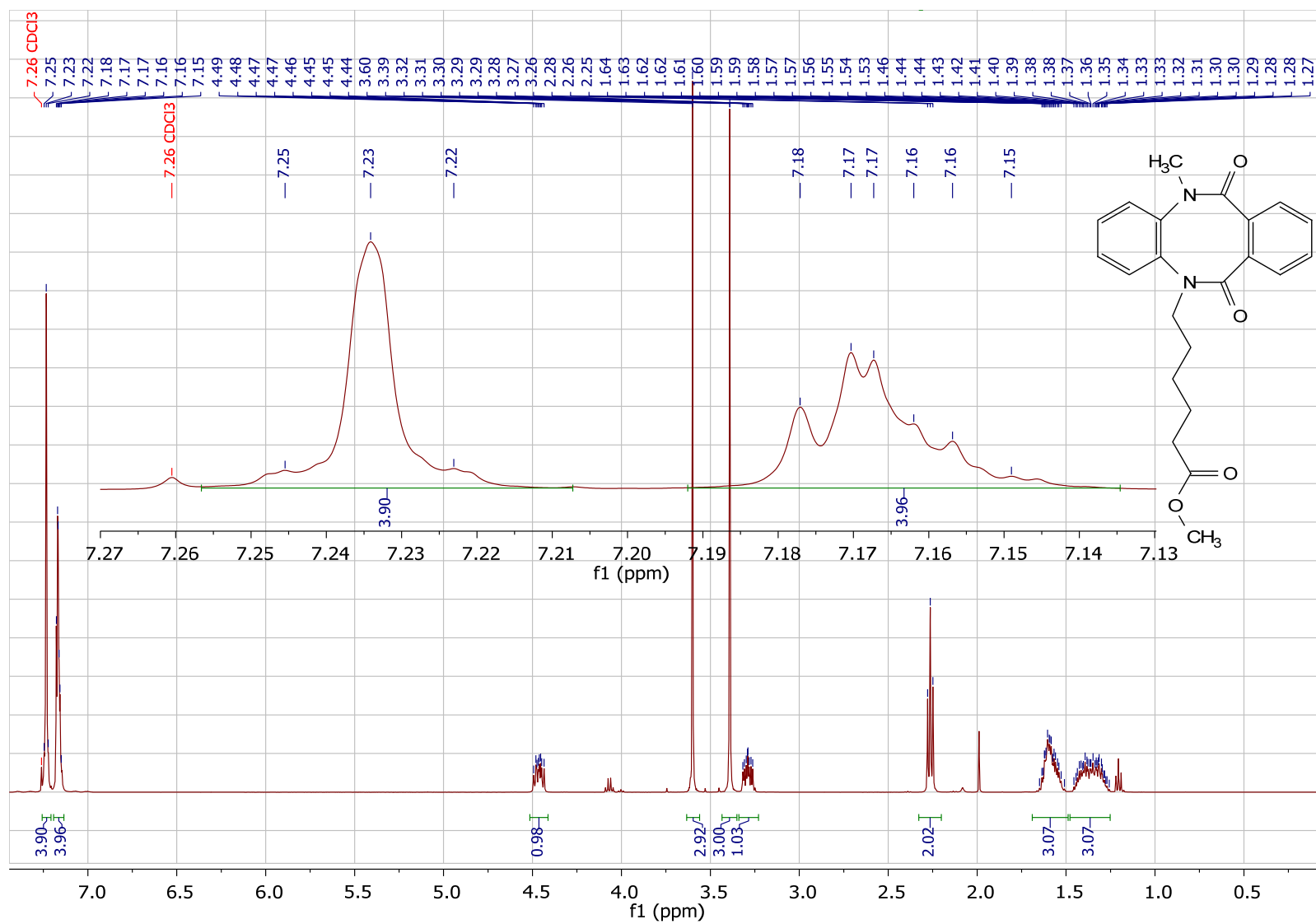


Figure S13. ¹H NMR spectrum of methyl 6-(12-methyl-6,11-dioxo-11,12-dihydrodibenzo[*b,f*][1,4]diazocin-5(6*H*)-yl)hexanoate (**10m**).

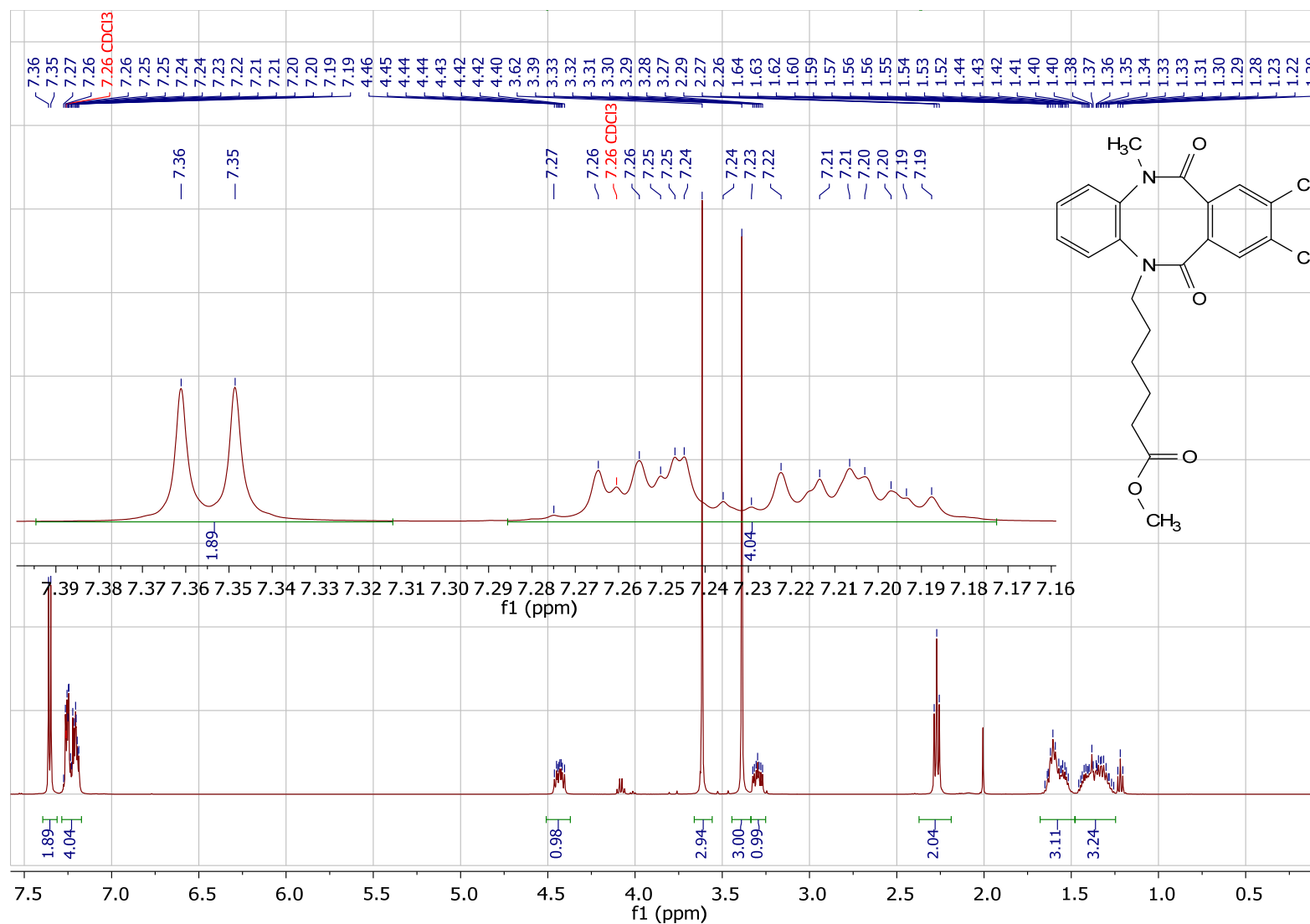


Figure S14. ^1H NMR spectrum of methyl 6-(8,9-dichloro-12-methyl-6,11-dioxo-11,12-dihydrodibenzo[*b,f*][1,4]diazocin-5(6*H*)-yl) hexanoate (**10n**).

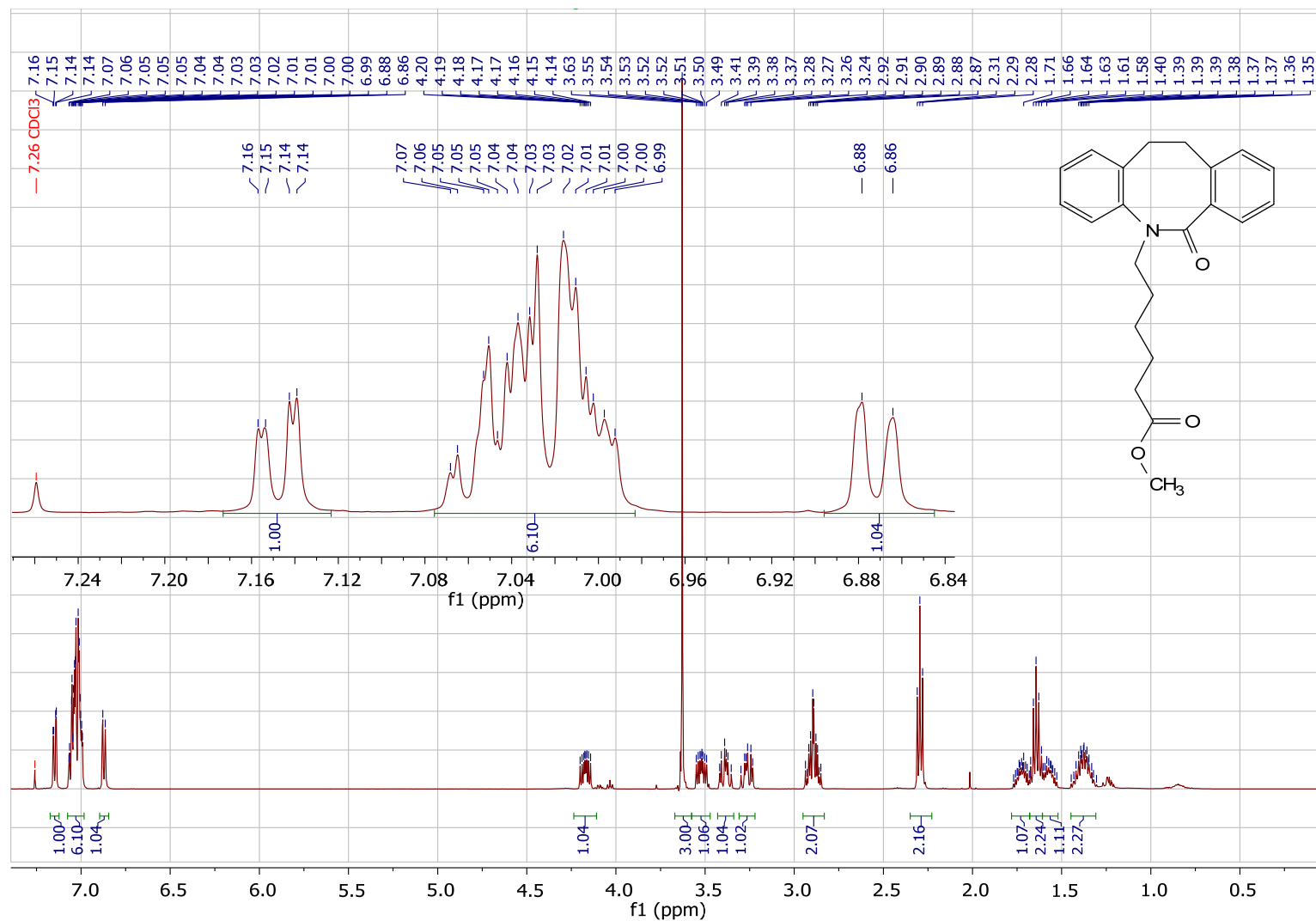


Figure S16. ¹H NMR spectrum of methyl 6-(6-oxo-11,12-dihydrodibenzo[b,f]azocin-5(6H)-yl)hexanoate (10p).

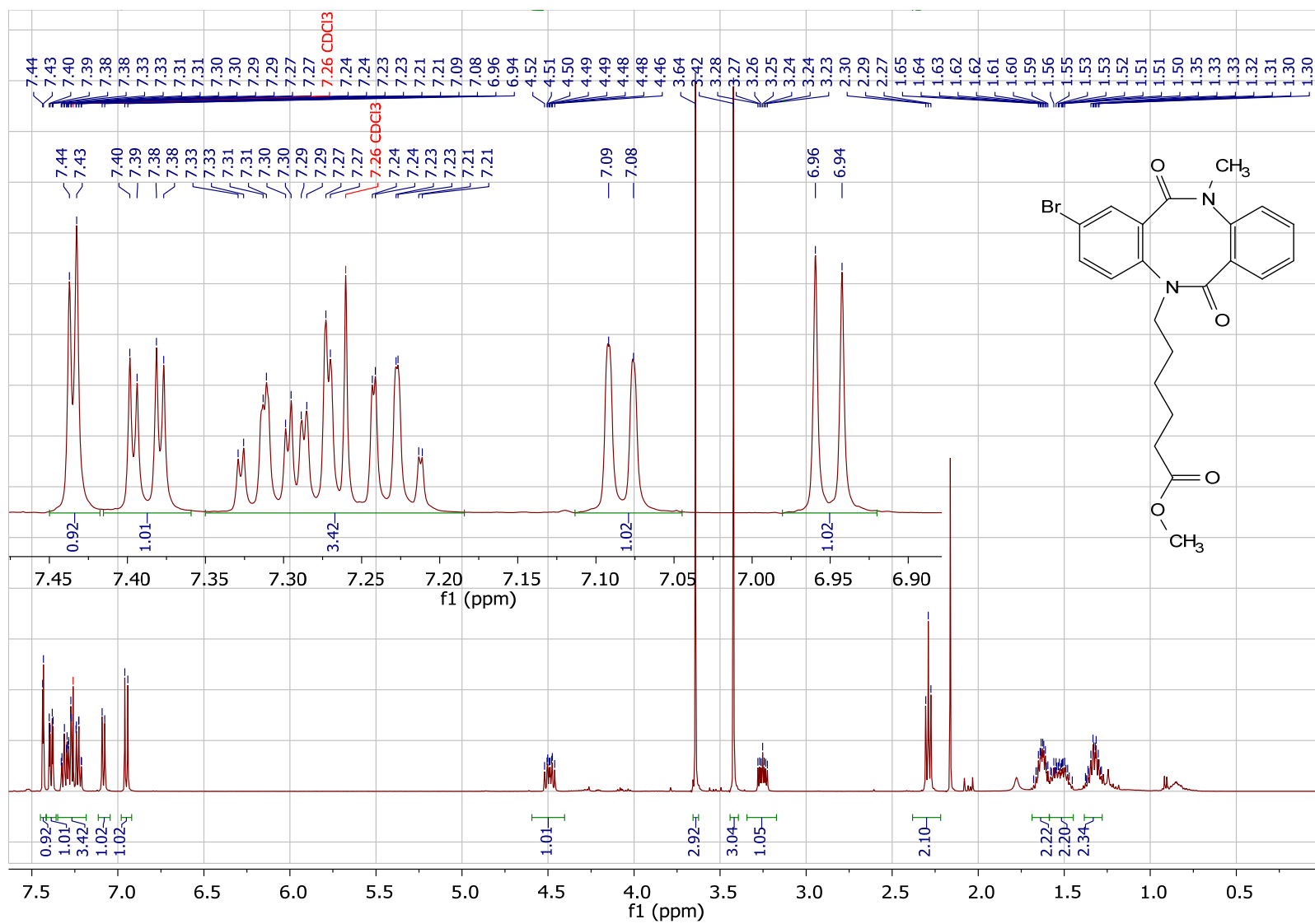


Figure S17. ^1H NMR spectrum of methyl 6-(2-bromo-11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)hexanoate (**10r**).

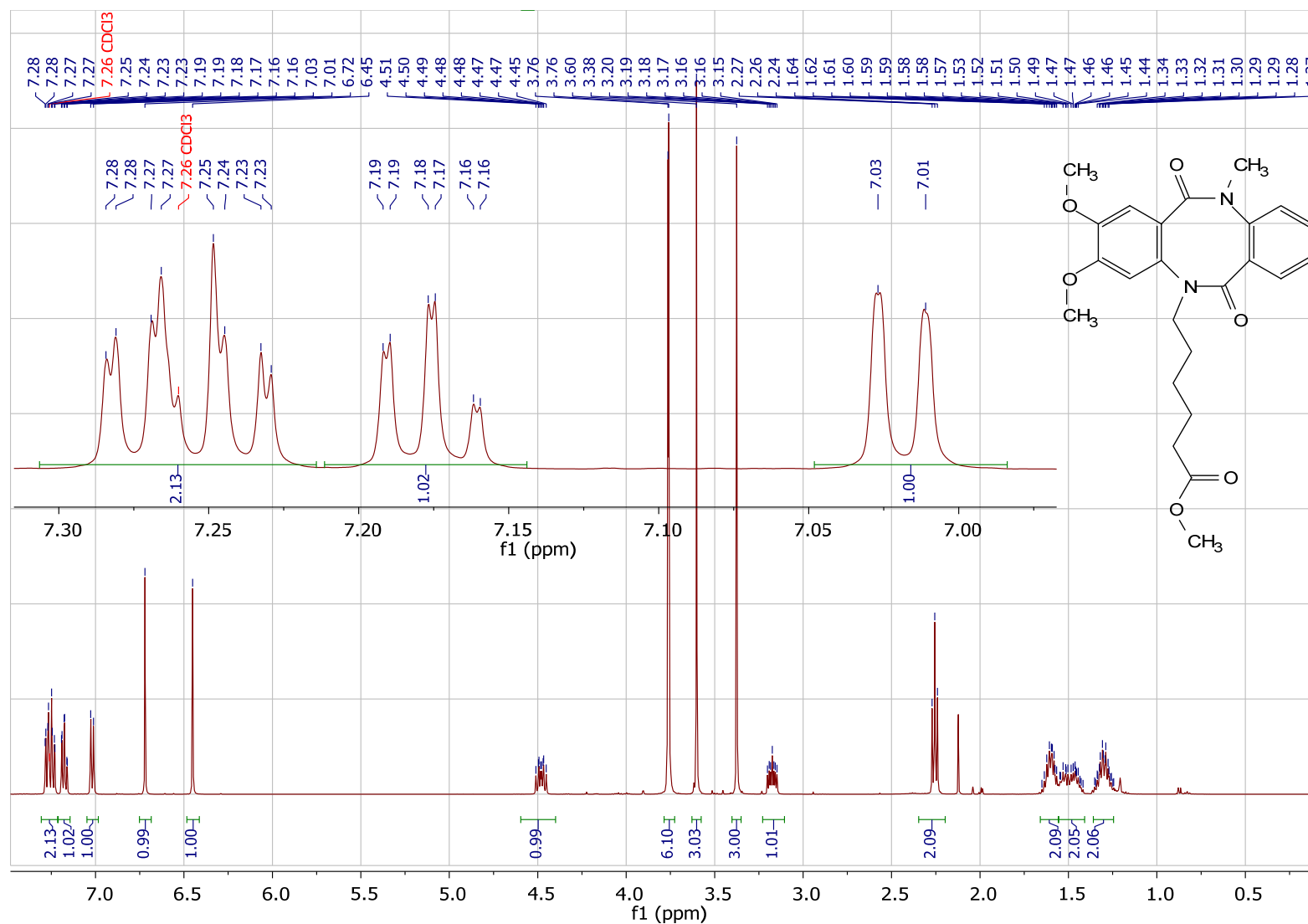


Figure S18. ¹H NMR spectrum of methyl 6-(2,3-dimethoxy-11-methyl-6,12-dioxo-11,12-dihydrodibenzo[b,f][1,5]diazocin-5(6H)-yl)hexanoate (10s).

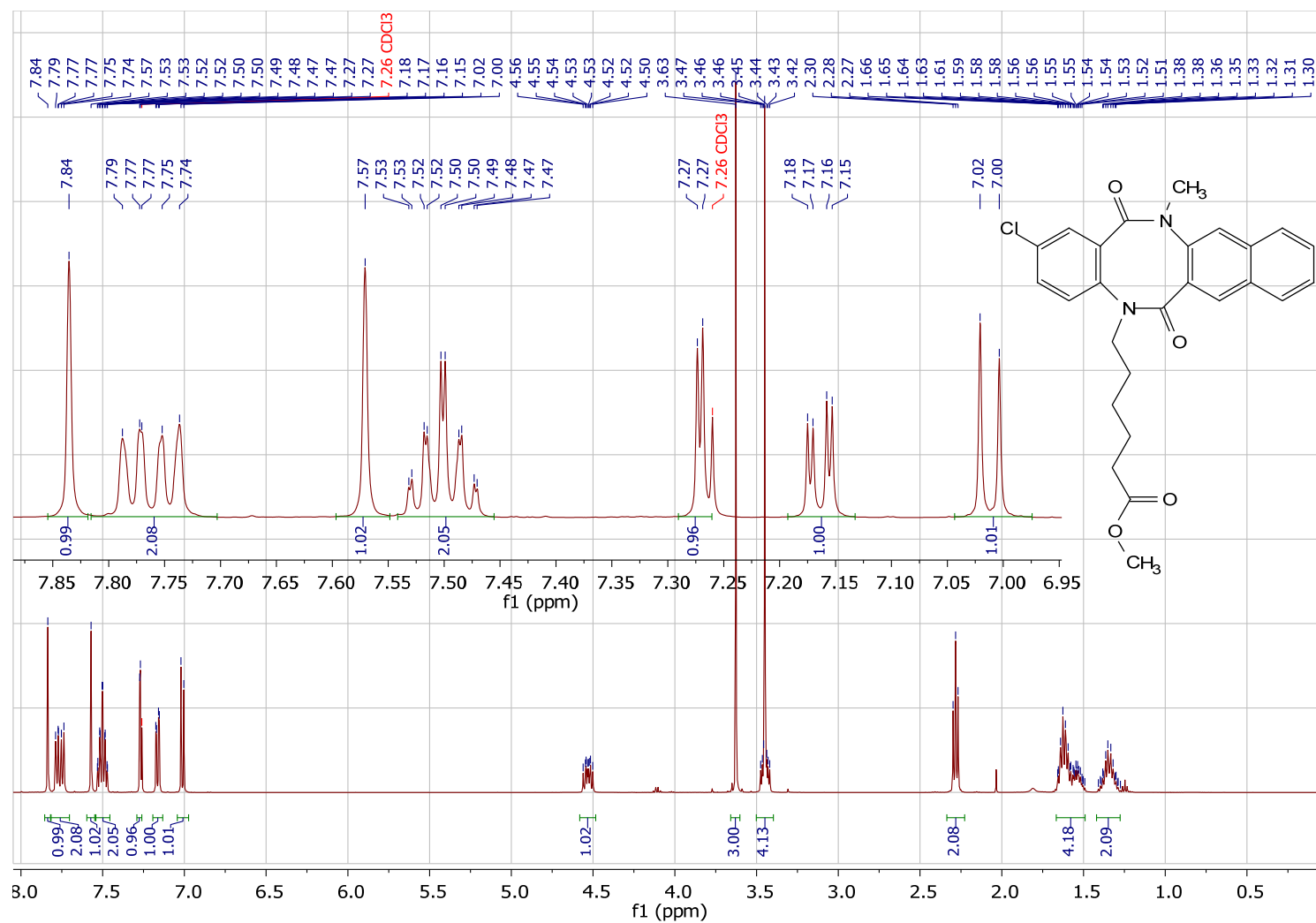


Figure S19. ^1H NMR spectrum of methyl 6-(5-methyl-6,14-dioxo-5,14-dihydrobenzonaphtho[2,3-f][1,5]diazocin-13(6H)-yl)hexanoate (**10t**).

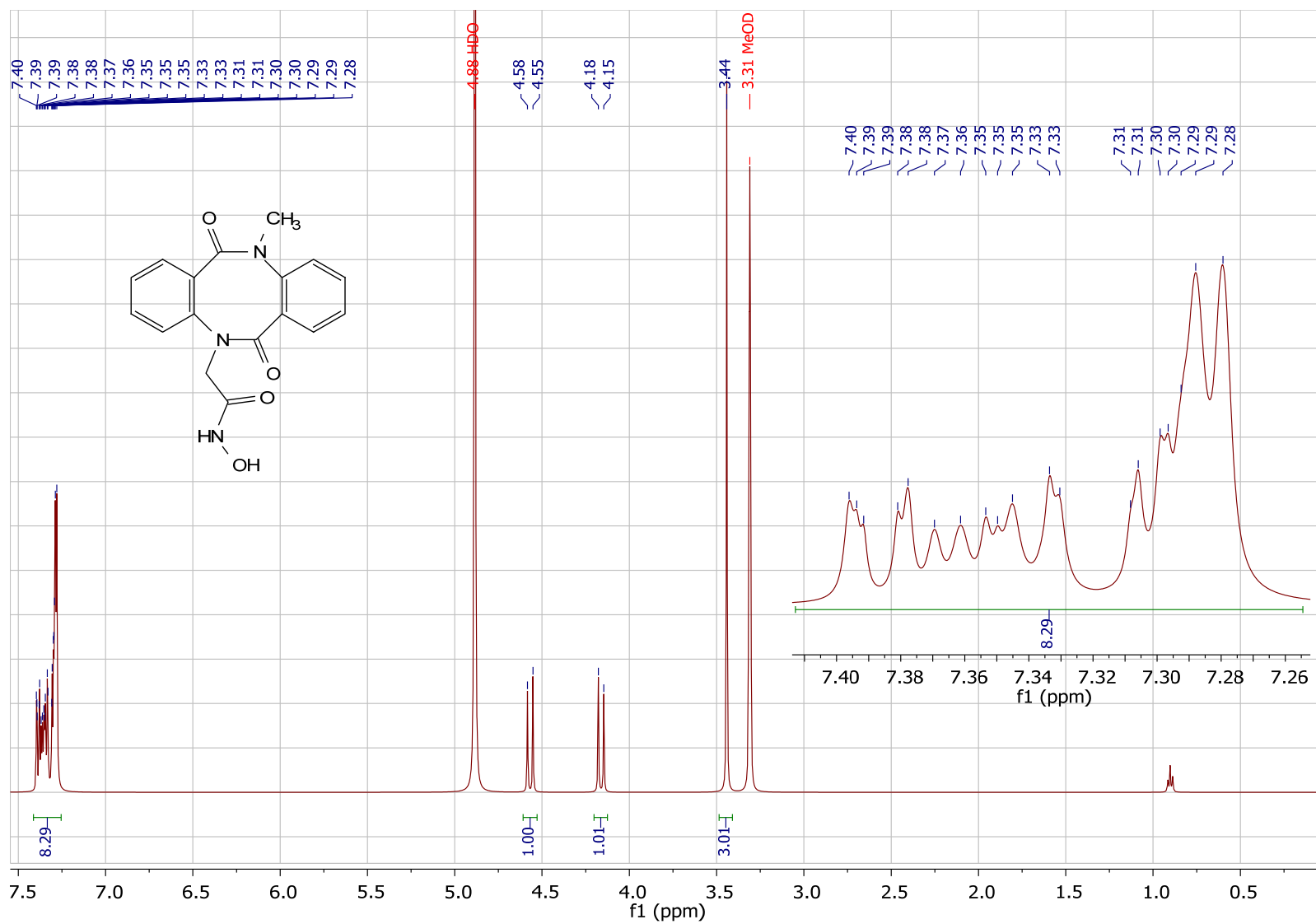


Figure S20. ¹H NMR spectrum of *N*-hydroxy-2-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)acetamide (**7a**).

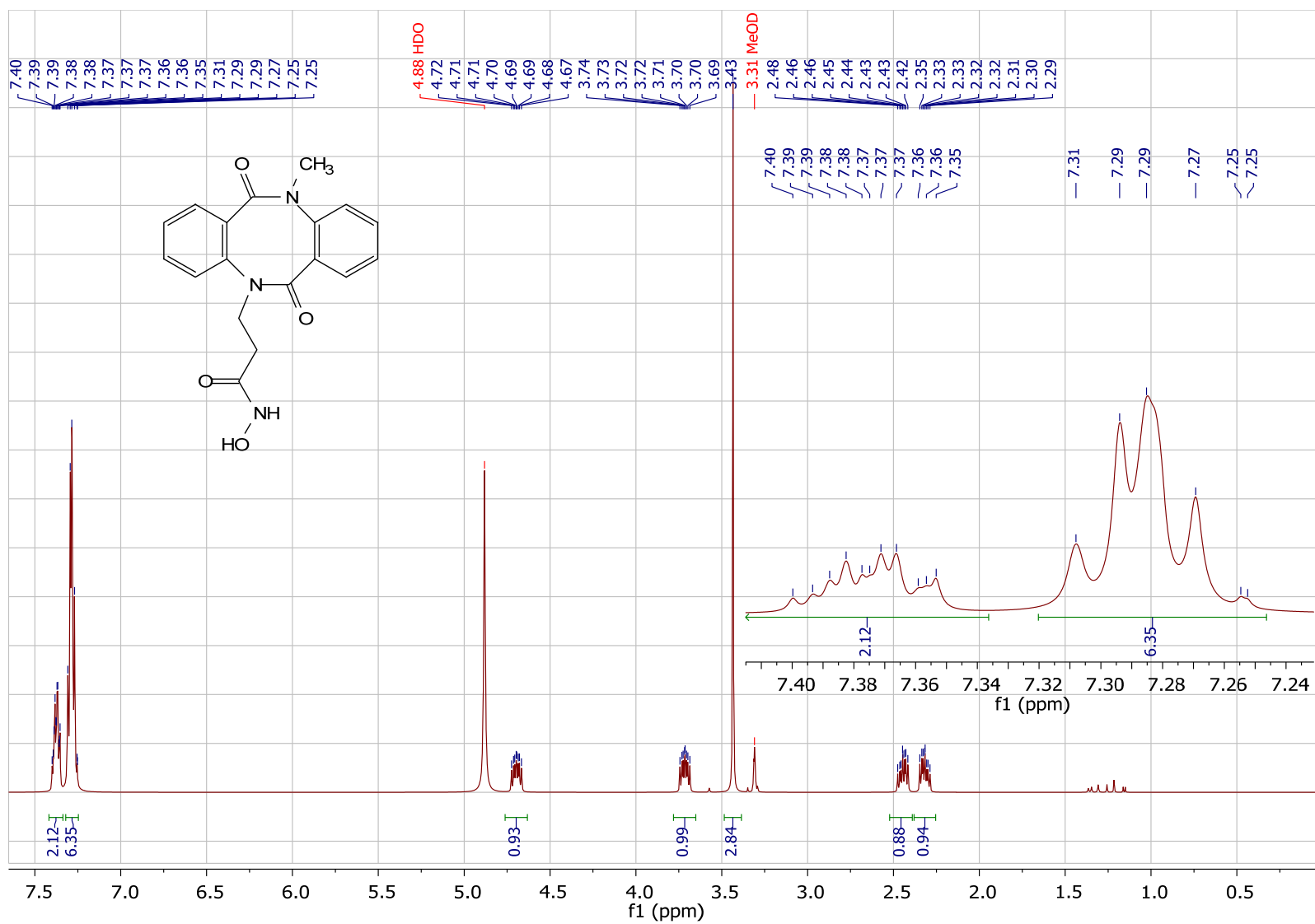


Figure S21. ¹H NMR spectrum of *N*-hydroxy-3-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)propanamide (**7b**).

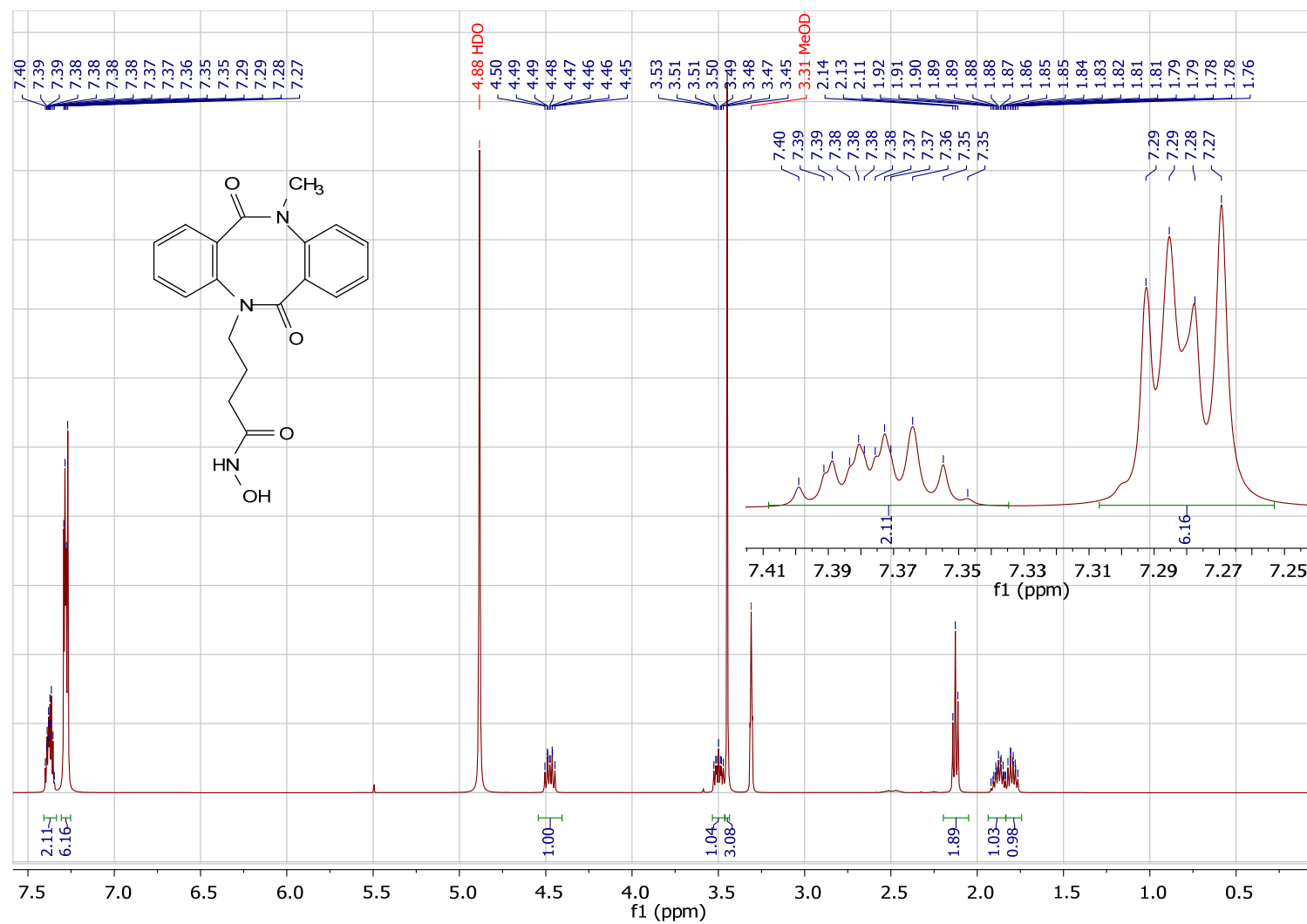


Figure S22. ¹H NMR spectrum of *N*-hydroxy-4-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)butanamide (7c).

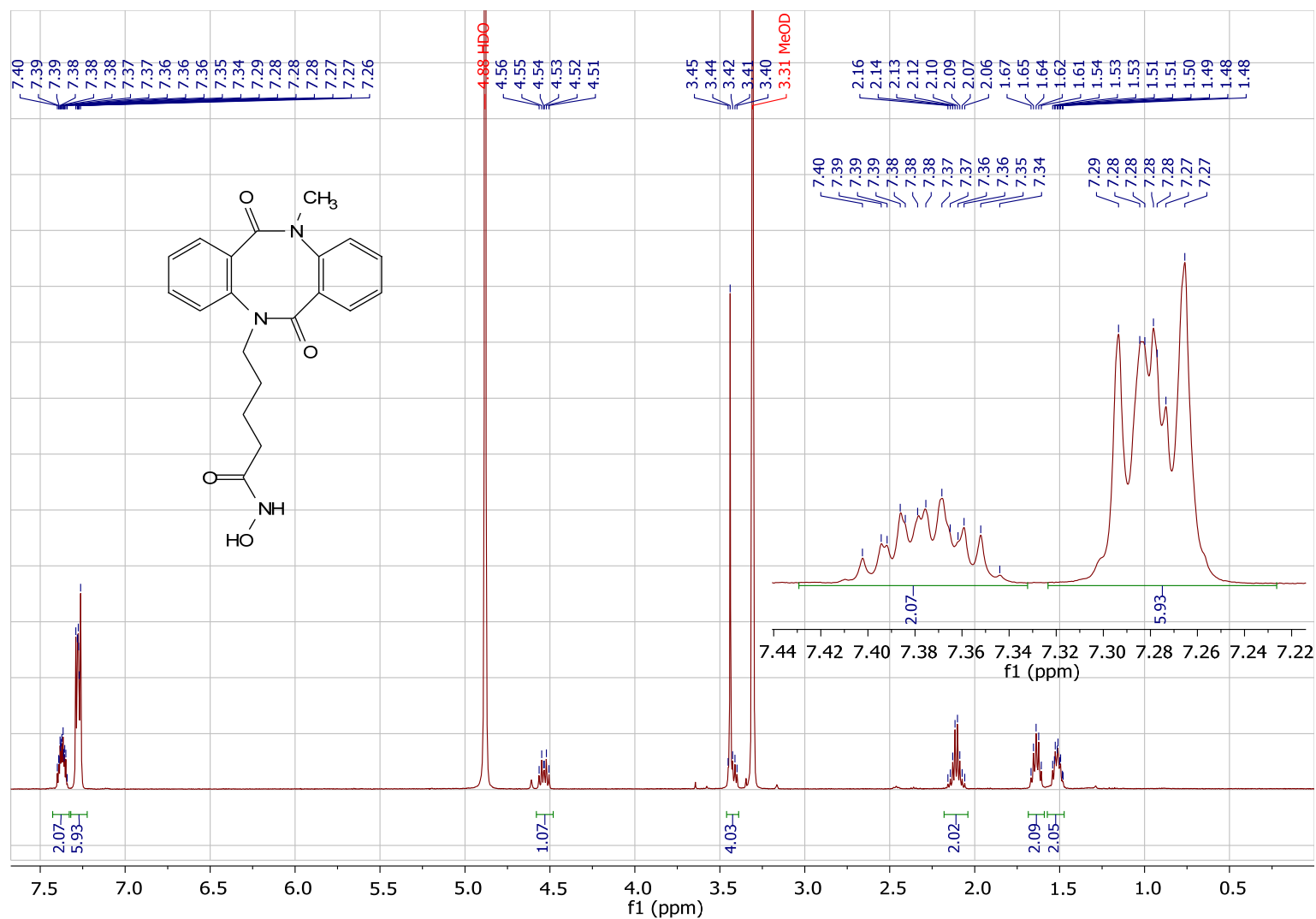


Figure S23. ¹H NMR spectrum of *N*-hydroxy-5-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)pentanamide (7d).

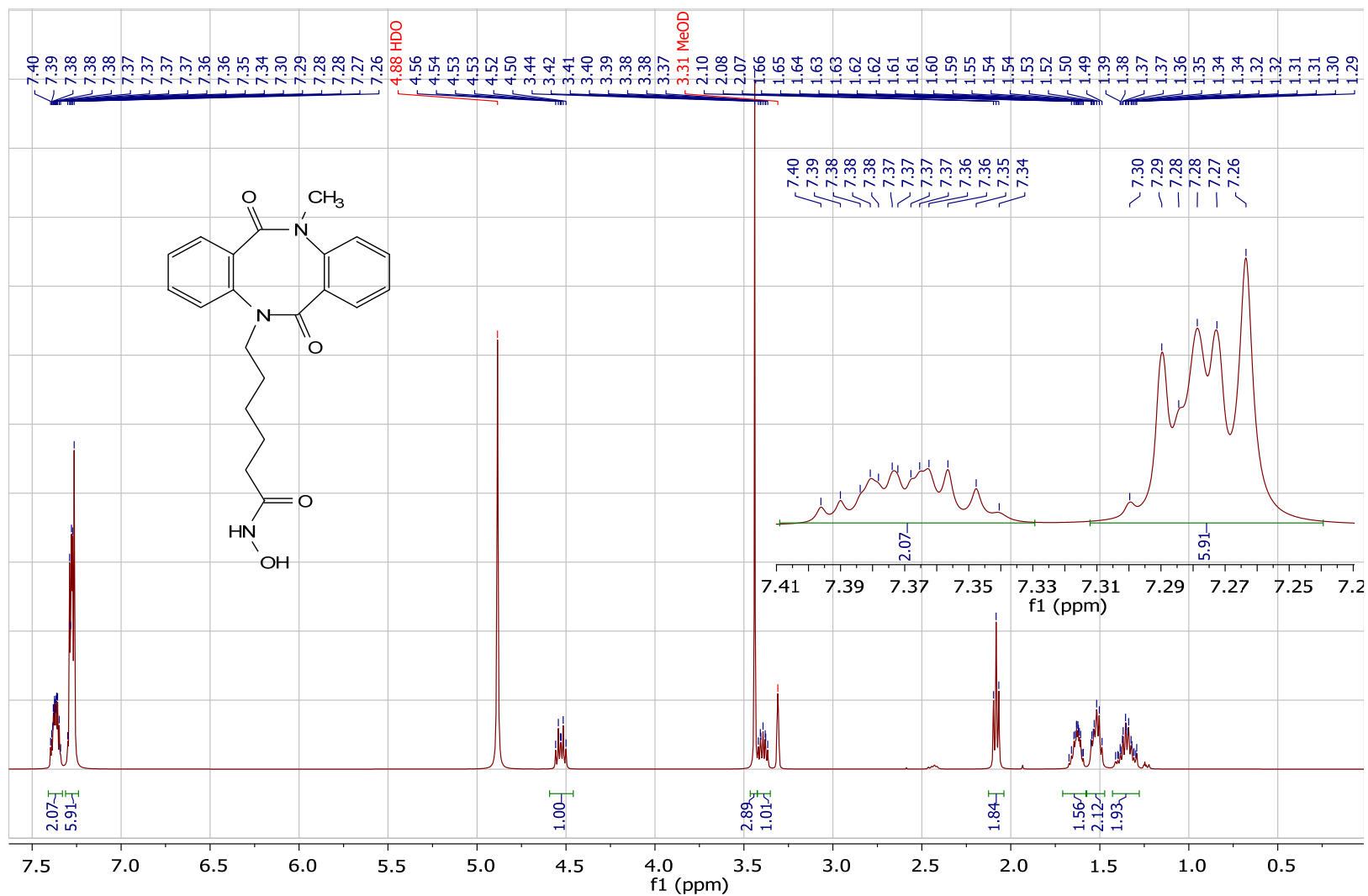


Figure S24. ¹H NMR spectrum of *N*-hydroxy-6-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)hexanamide (**7e**).

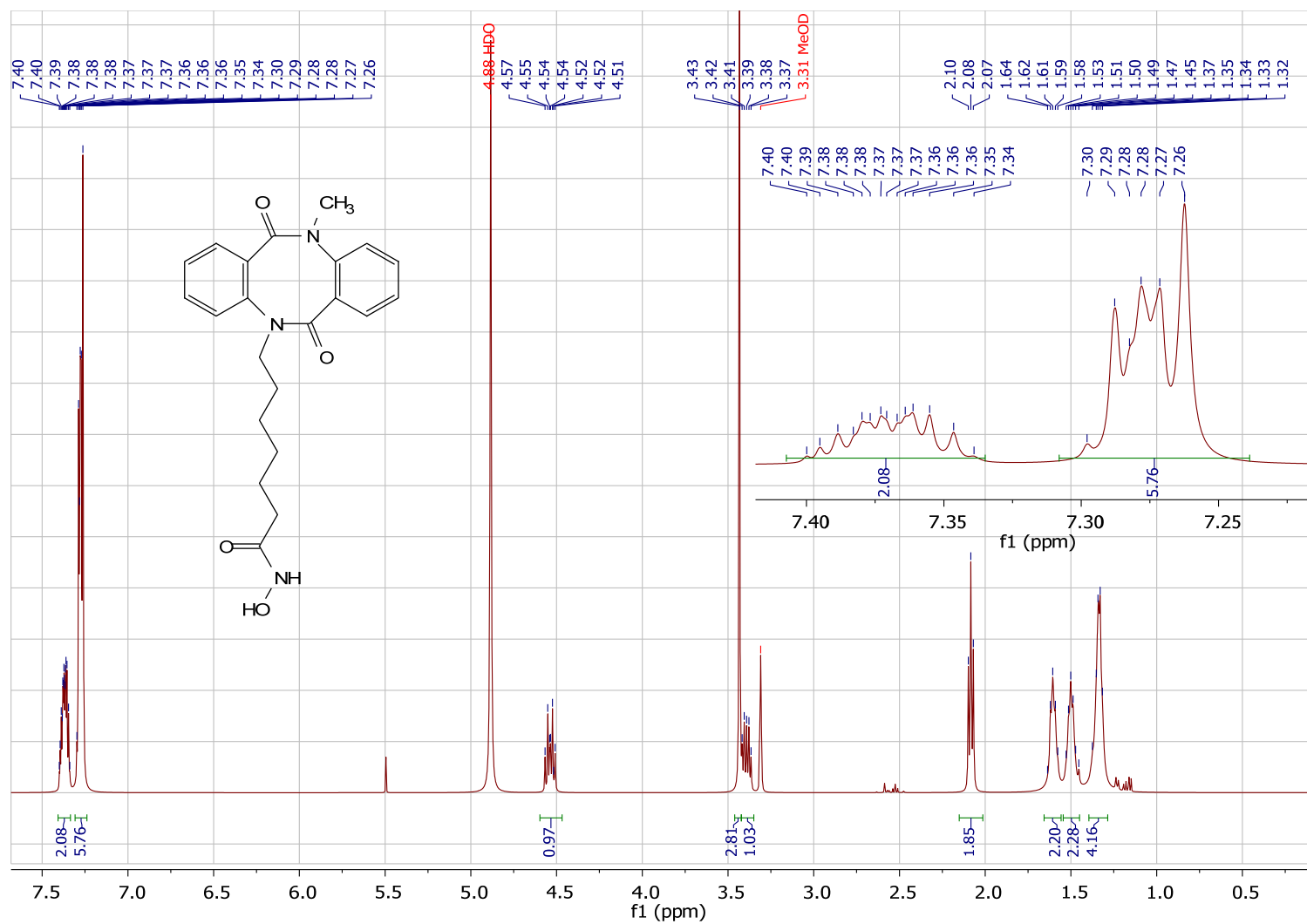


Figure S25. ¹H NMR spectrum of *N*-hydroxy-7-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)heptanamide (**7f**).

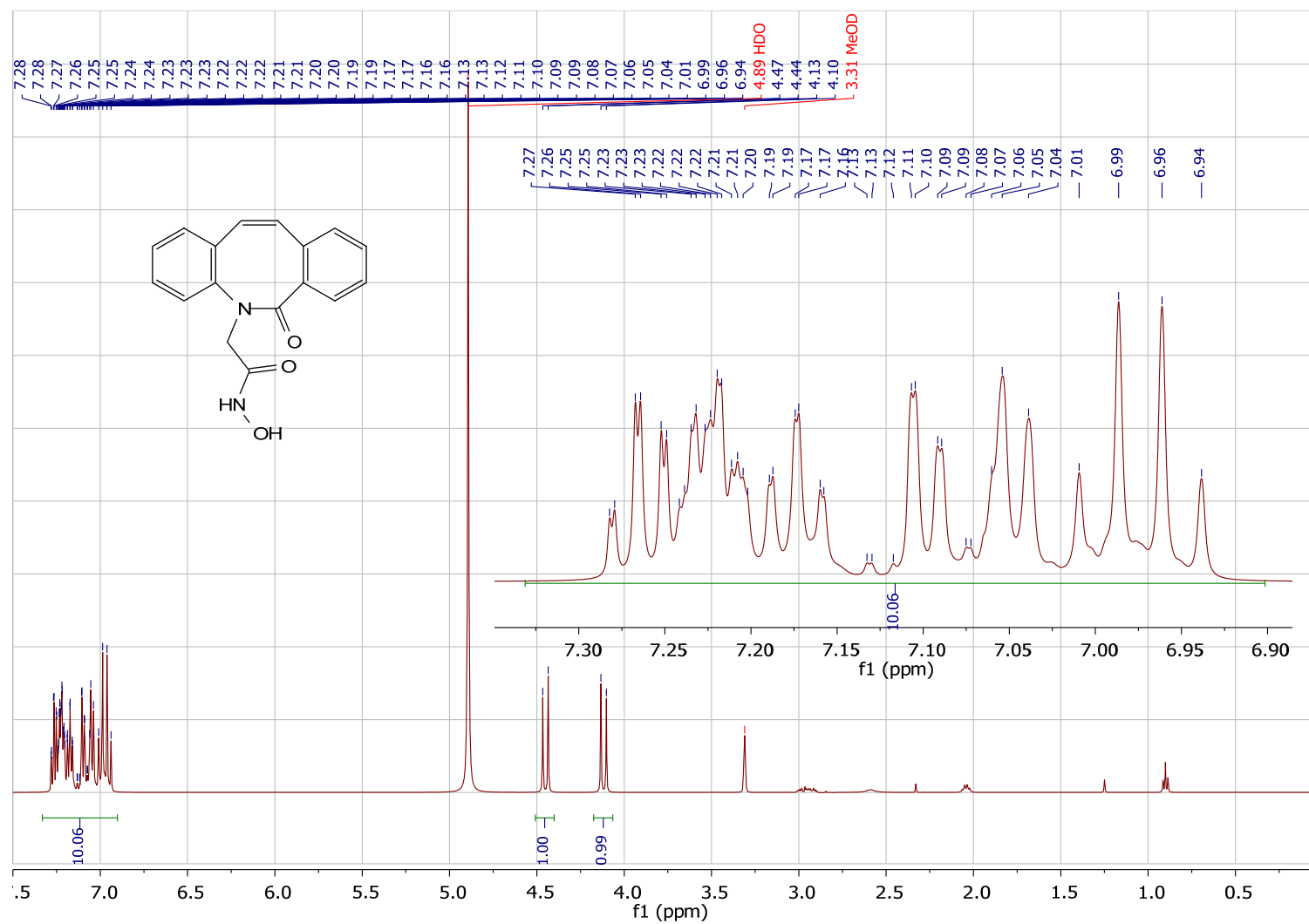


Figure S26. ¹H NMR spectrum of *N*-hydroxy-2-(6-oxodibenzo[*b,f*]azocin-5(6*H*)-yl)acetamide (7g).

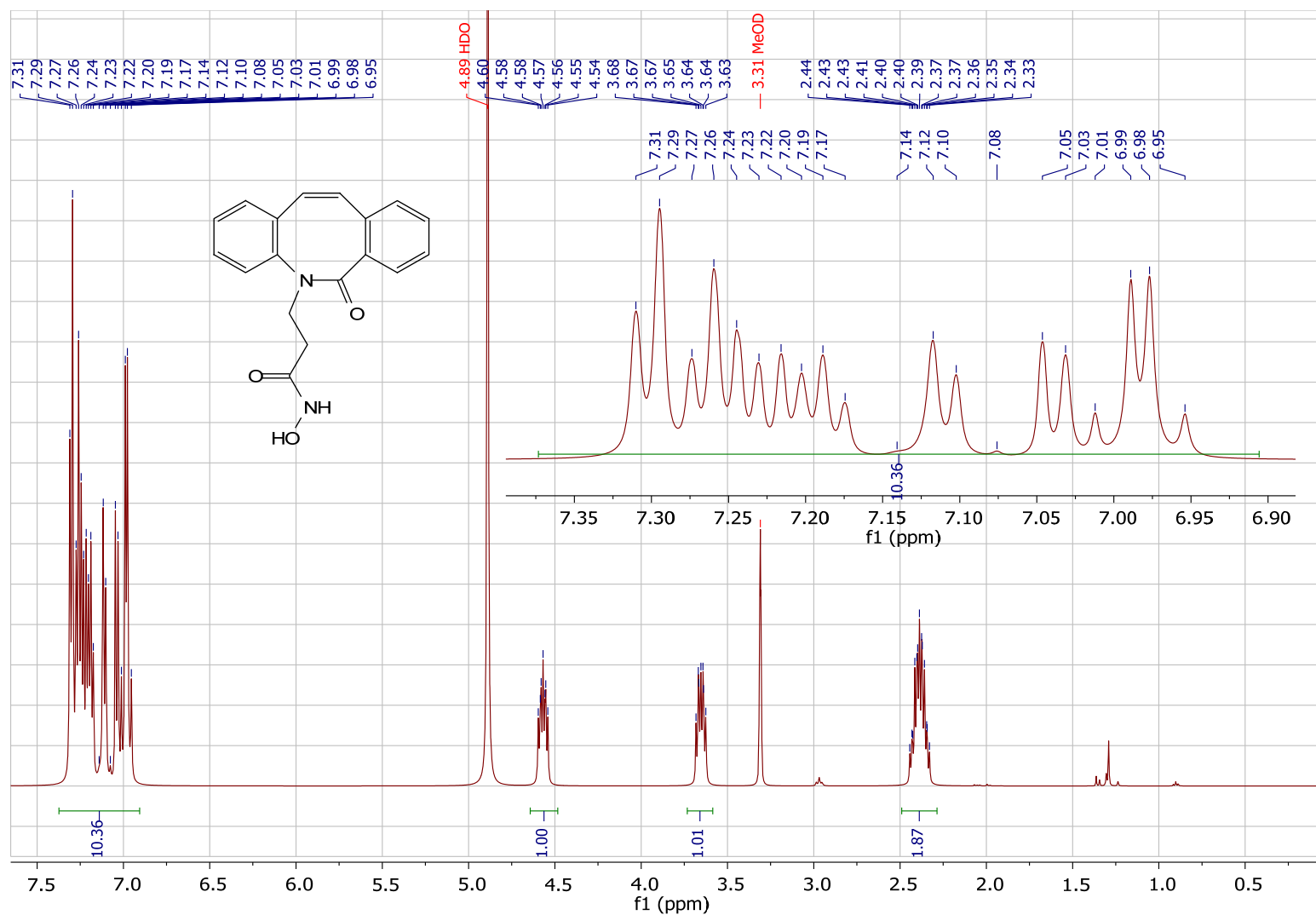


Figure S27. ¹H NMR spectrum of *N*-hydroxy-3-(6-oxodibenzo[*b,f*]azocin-5(6*H*)-yl)propanamide (7h).

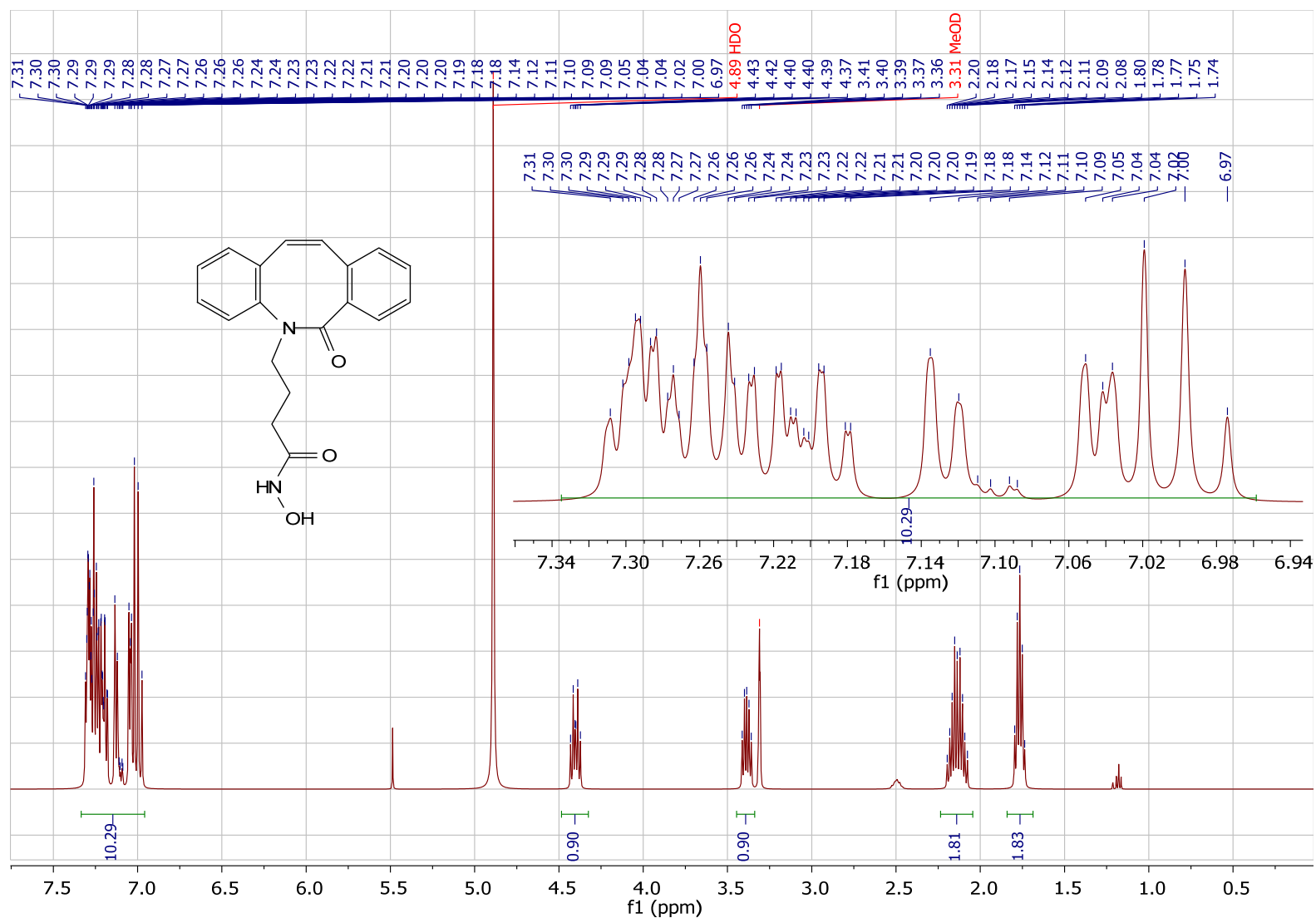


Figure S28. ¹H NMR spectrum of *N*-hydroxy-4-(6-oxodibenzo[*b,f*]azocin-5(6*H*)-yl)butanamide (7i).

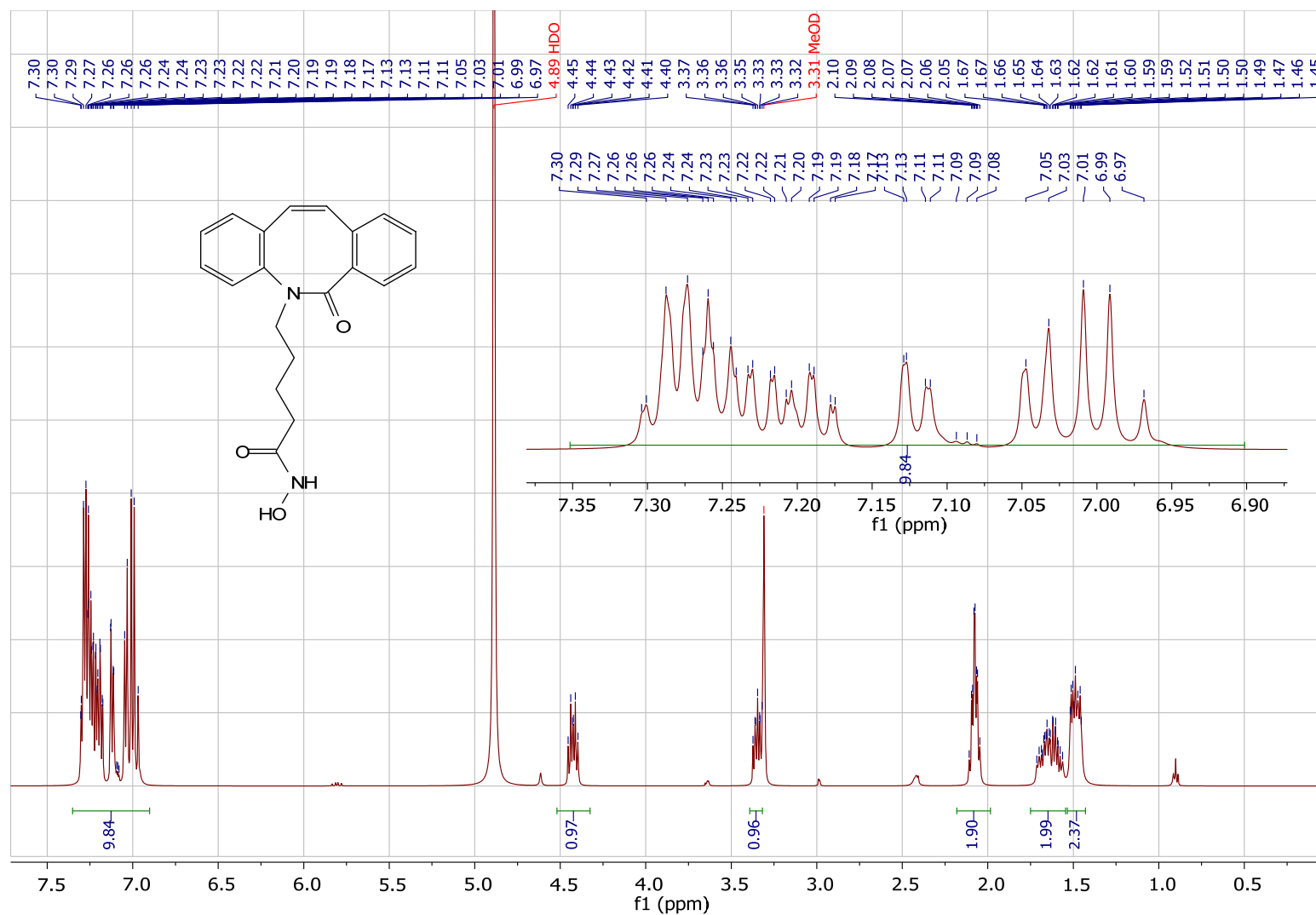


Figure S29. ¹H NMR spectrum of *N*-hydroxy-5-(6-oxodibenzo[*b,f*]azocin-5(6*H*)-yl)pentanamide (7j).

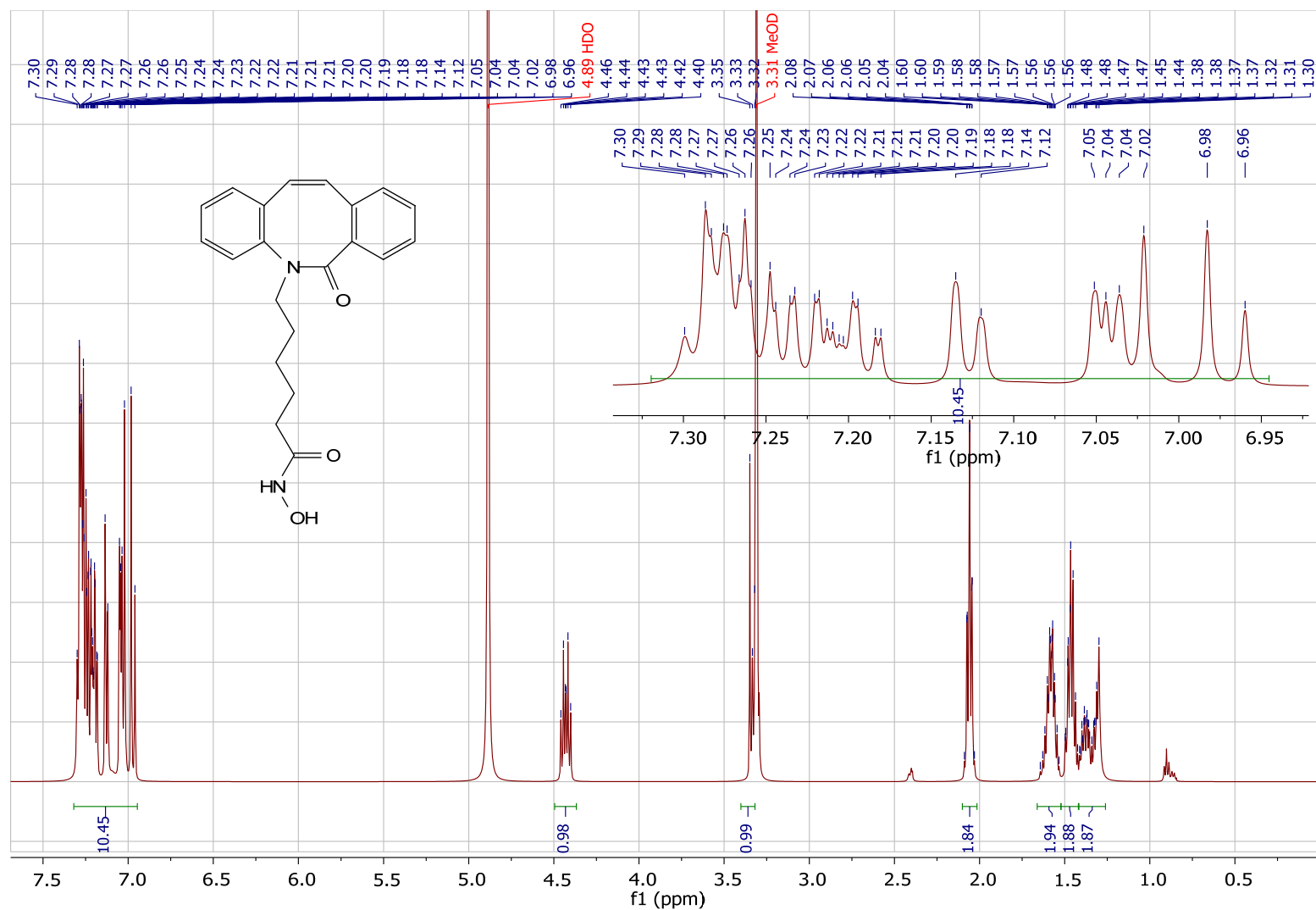


Figure S30. ¹H NMR spectrum of *N*-hydroxy-6-(6-oxodibenzo[*b,f*]azocin-5(6*H*)-yl)hexanamide (7k).

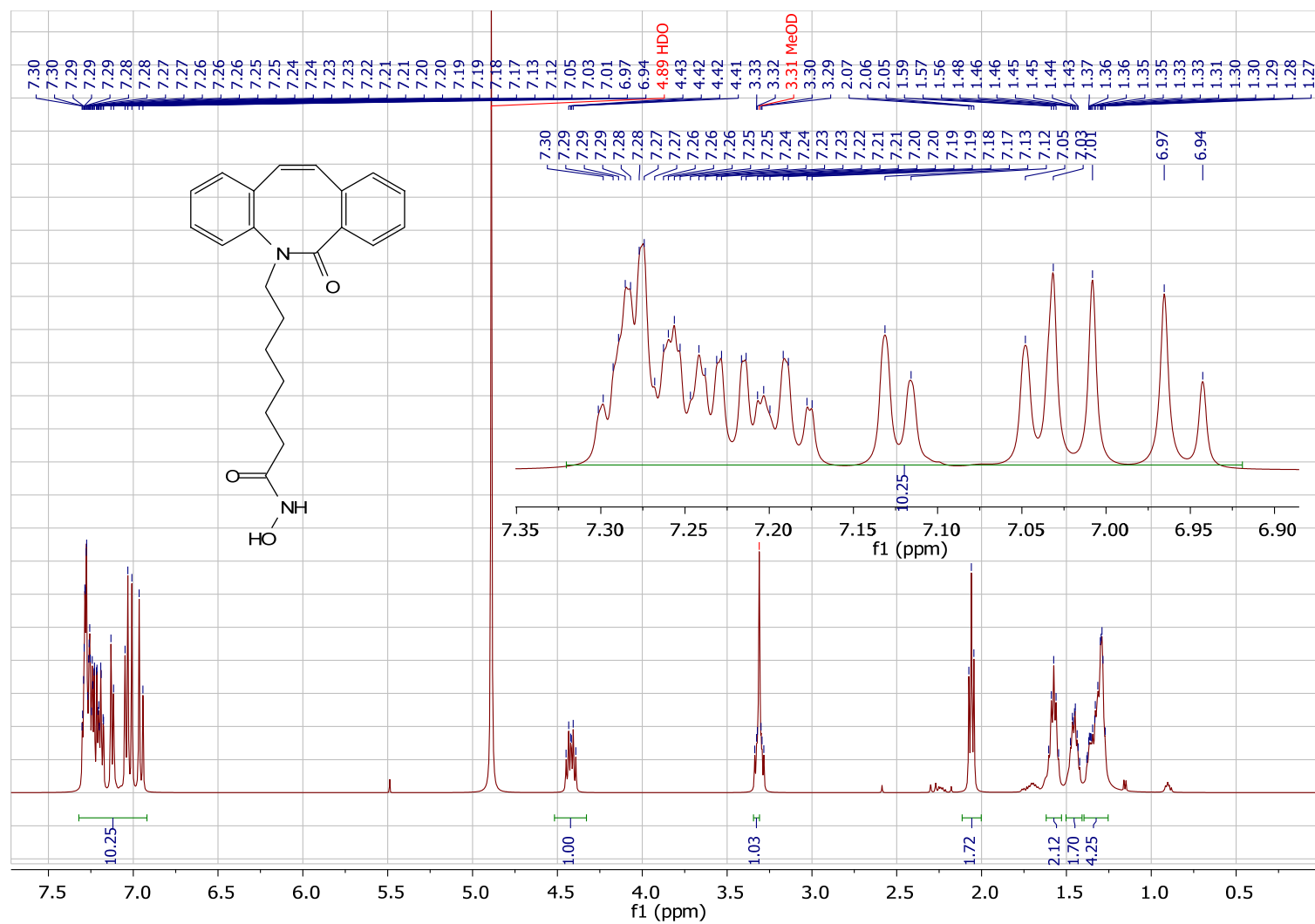


Figure S31. ¹H NMR spectrum of *N*-hydroxy-7-(6-oxodibenzo[*b,f*]azocin-5(6*H*)-yl)heptanamide (71).

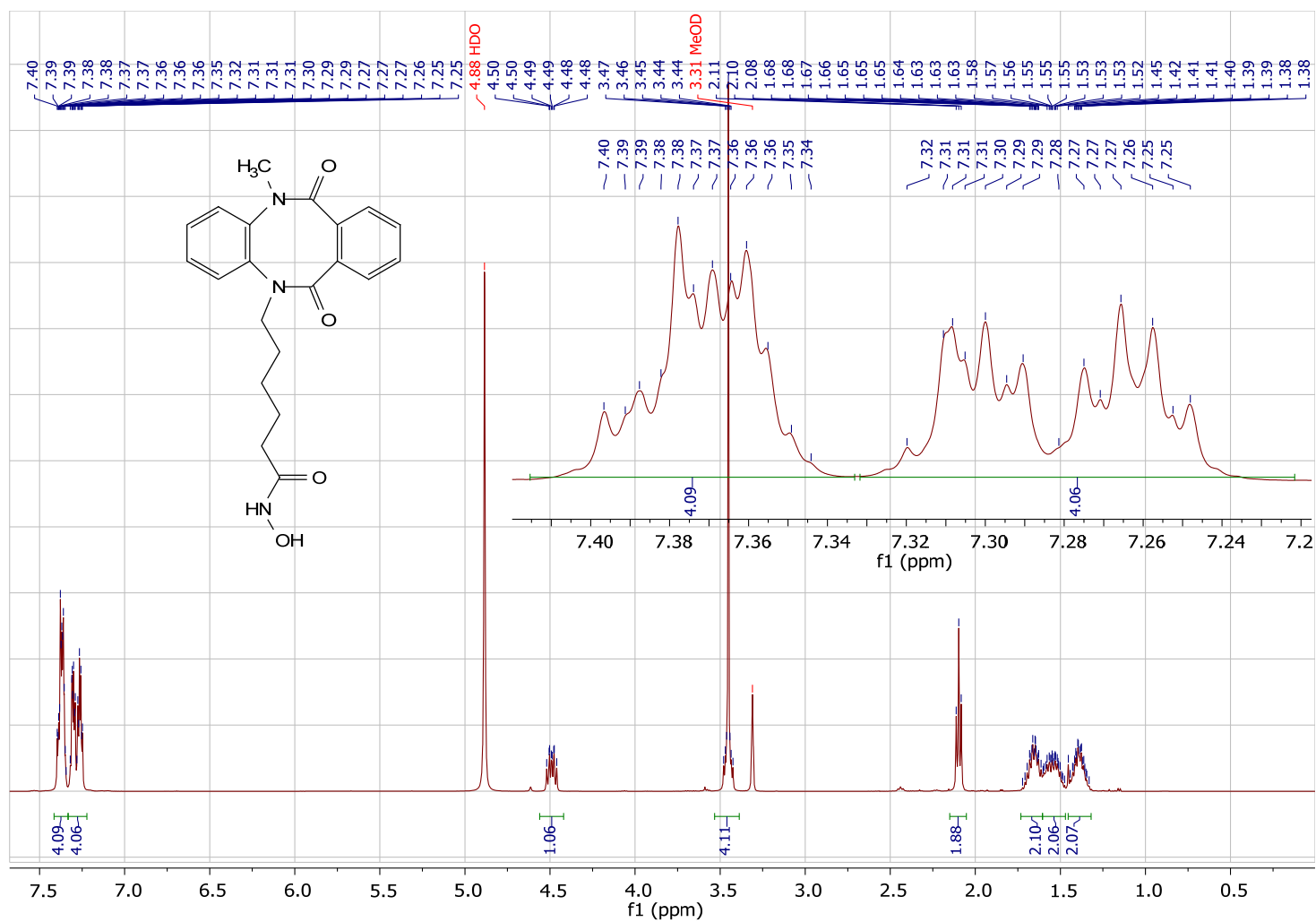


Figure S32. ¹H NMR spectrum of *N*-hydroxy-6-(12-methyl-6,11-dioxo-11,12-dihydrodibenzo[*b,f*][1,4]diazocin-5(6*H*)-yl)hexanamide (**7m**).

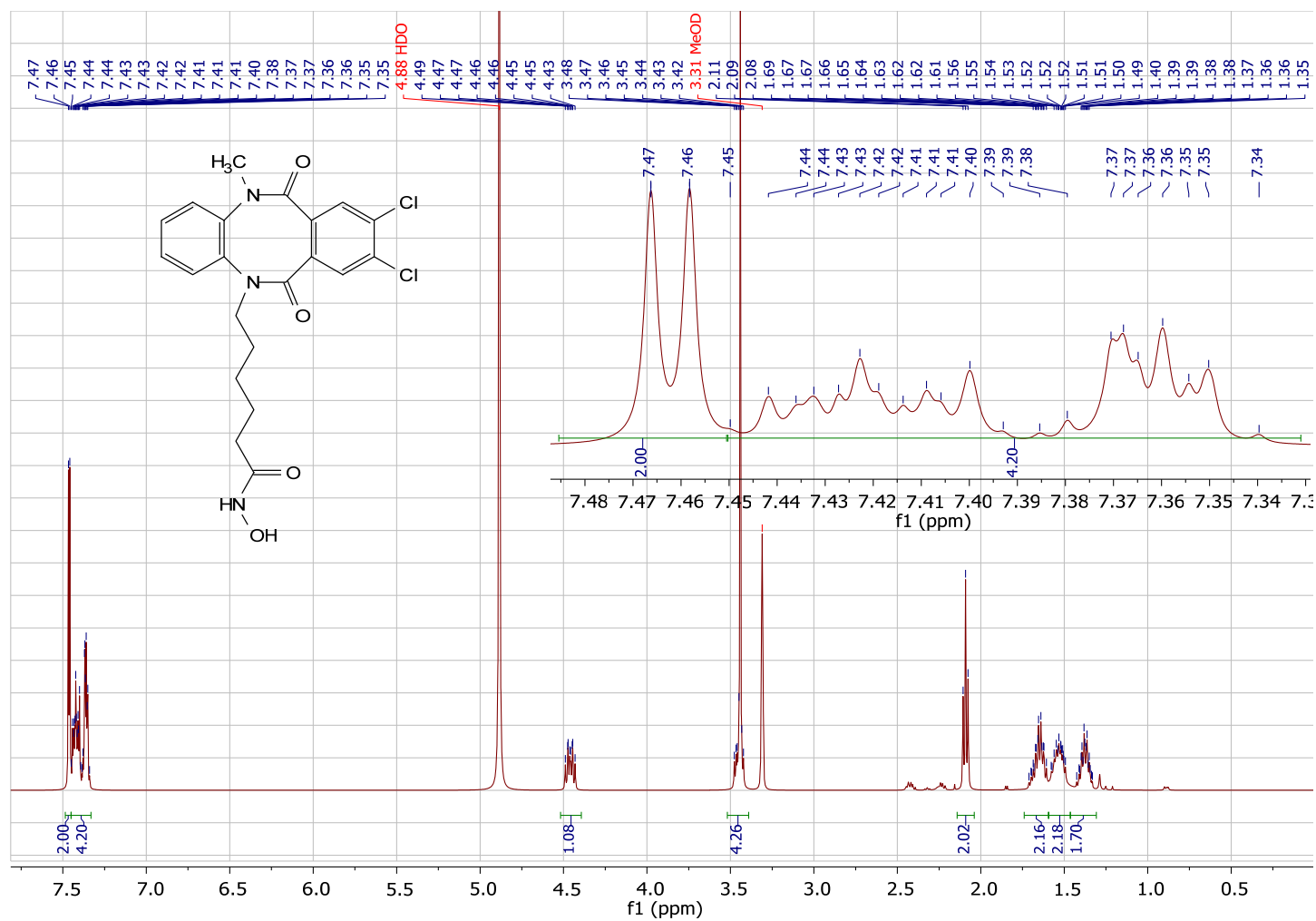


Figure S33. ¹H NMR spectrum of *N*-hydroxy-6-(8,9-dichloro-12-methyl-6,11-dioxo-11,12-dihydrodibenzo[*b,f*][1,4]diazocin-5(6*H*)-yl)hexanamide (**7n**).

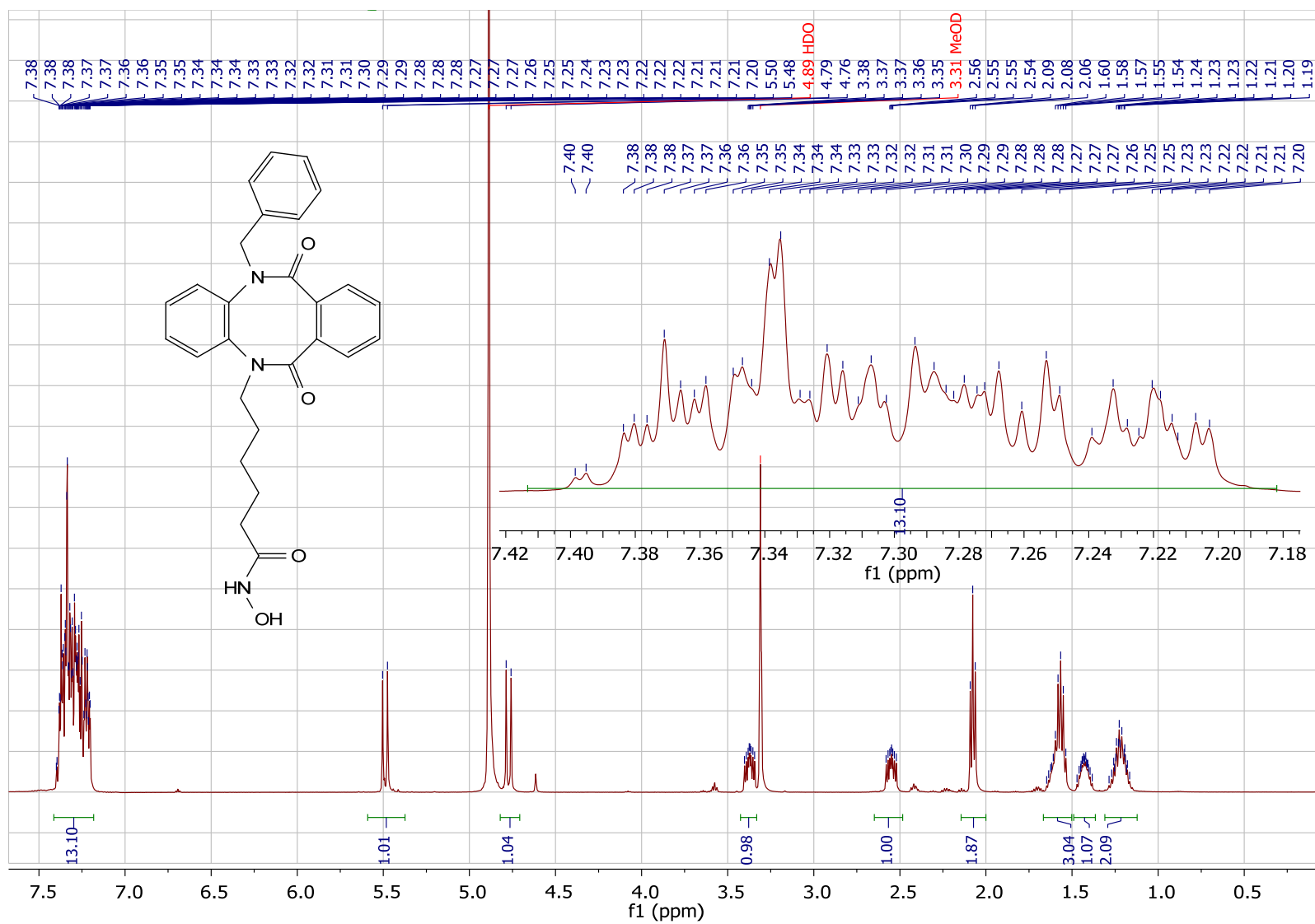


Figure S34. ¹H NMR spectrum of *N*-hydroxy-6-(12-benzyl-6,11-dioxo-11,12-dihydrodibenzo[*b,f*][1,4]diazocin-5(6*H*)-yl)hexanamide (**7o**).

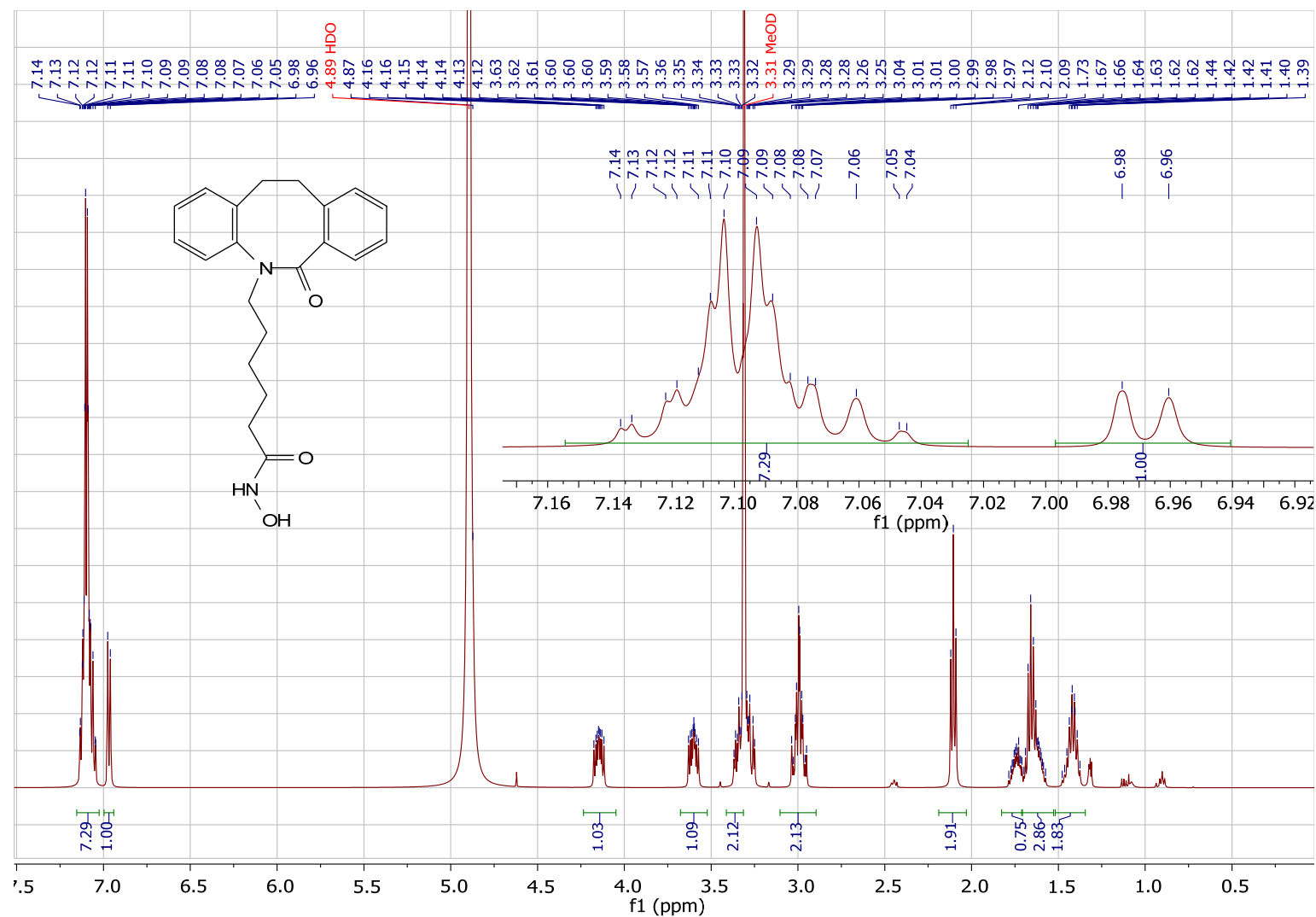


Figure S35. ¹H NMR spectrum of *N*-hydroxy-6-(6-oxo-11,12-dihydrodibenzo[*b,f*]azocin-5(6*H*)-yl)hexanamide (7p).

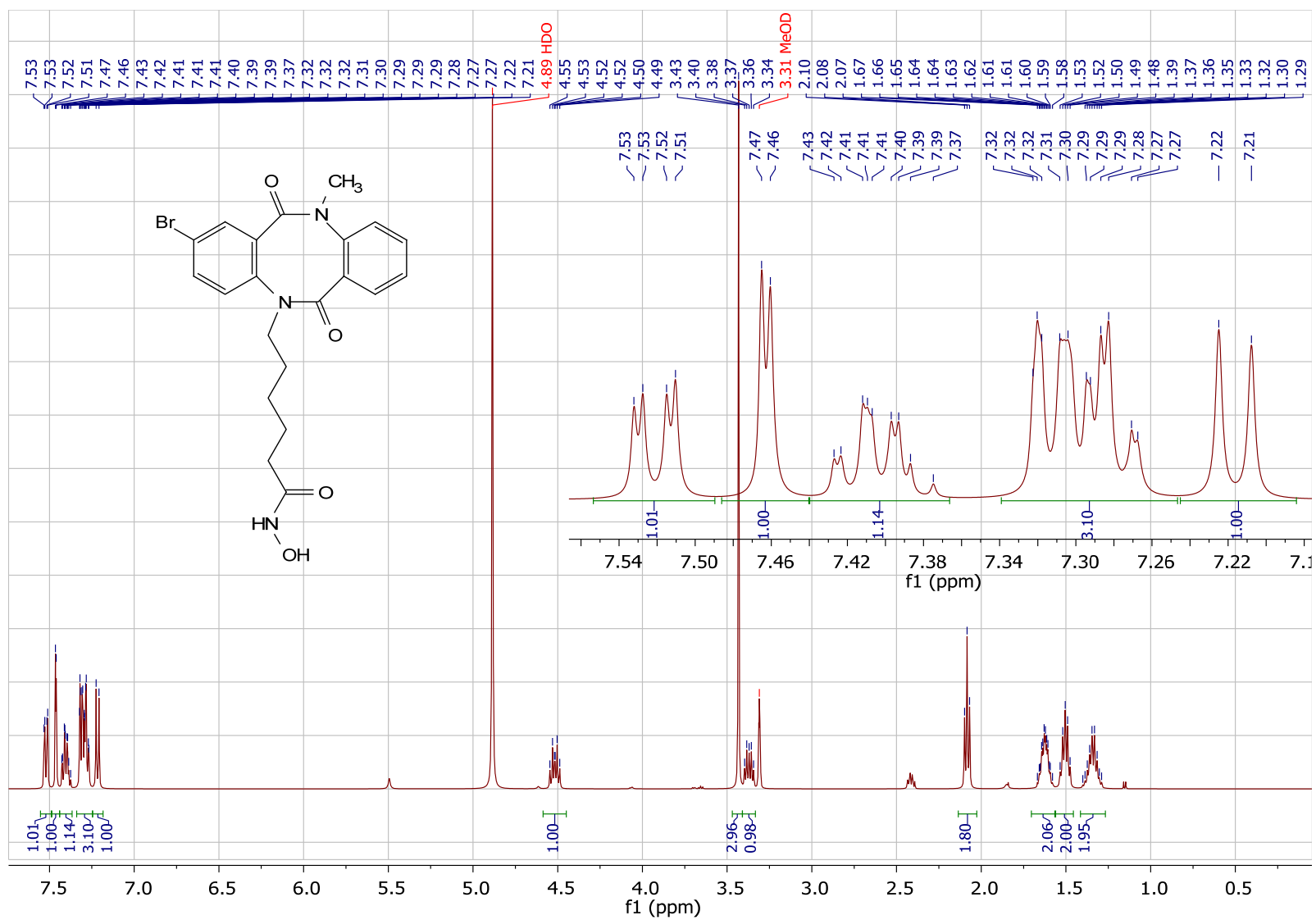
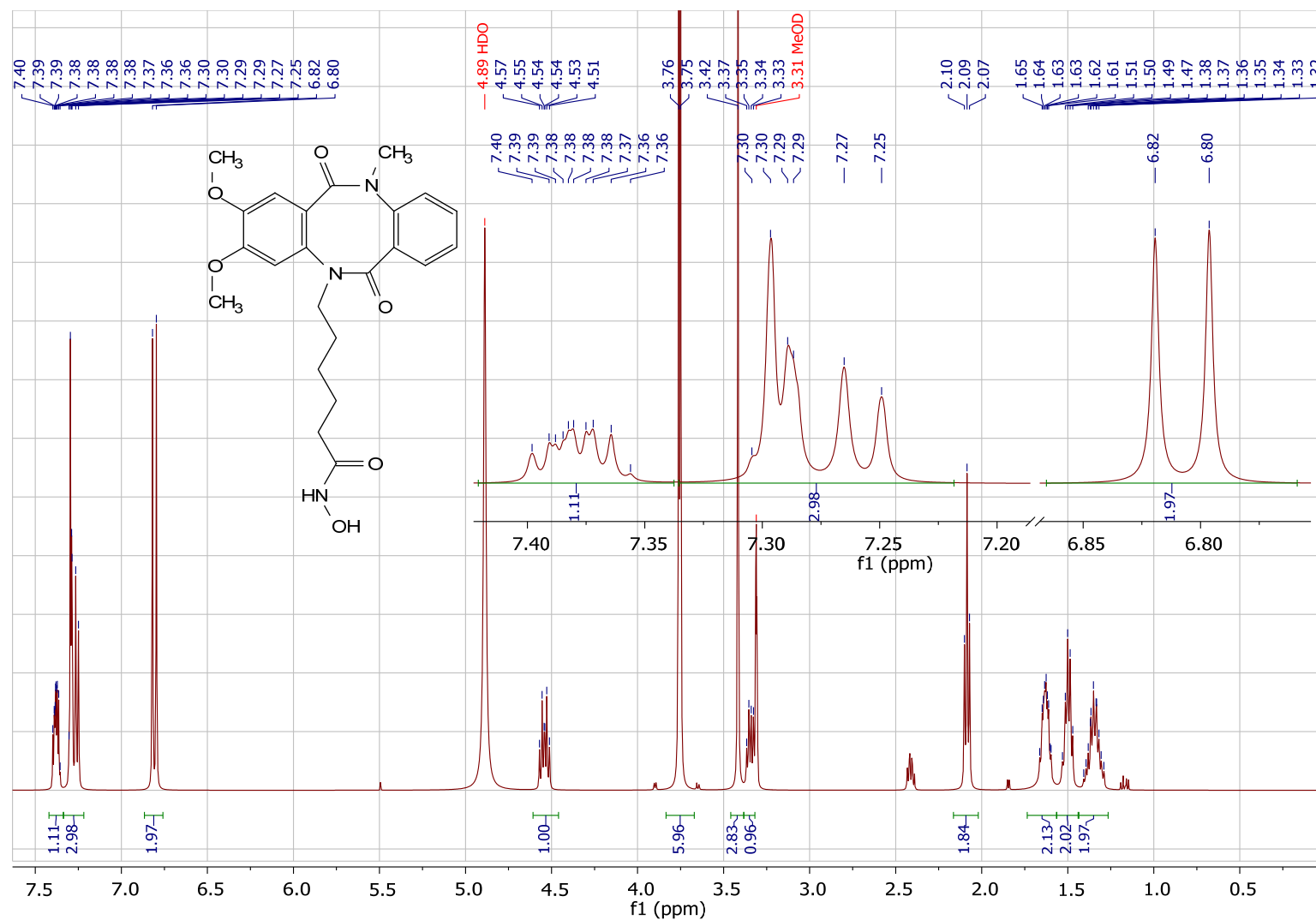


Figure S36. ¹H NMR spectrum of *N*-hydroxy-6-(2-bromo-11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)hexanamide (**7r**).



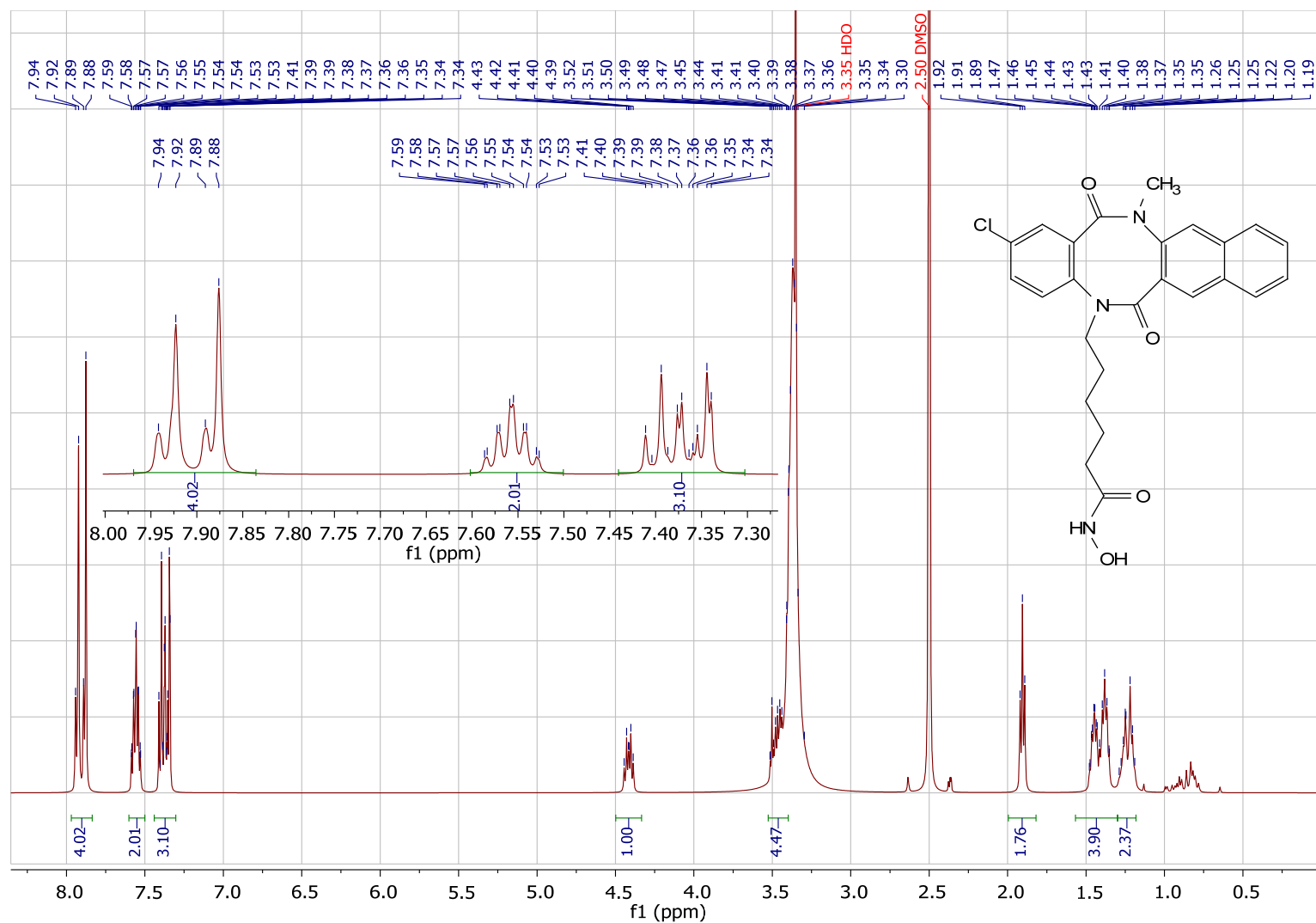


Figure S38. ^1H NMR spectrum of *N*-hydroxy-6-(5-methyl-6,14-dioxo-5,14-dihydrobenzonaphtho[2,3-*f*][1,5]diazocin-13(6*H*)-yl)hexanamide (**7t**).

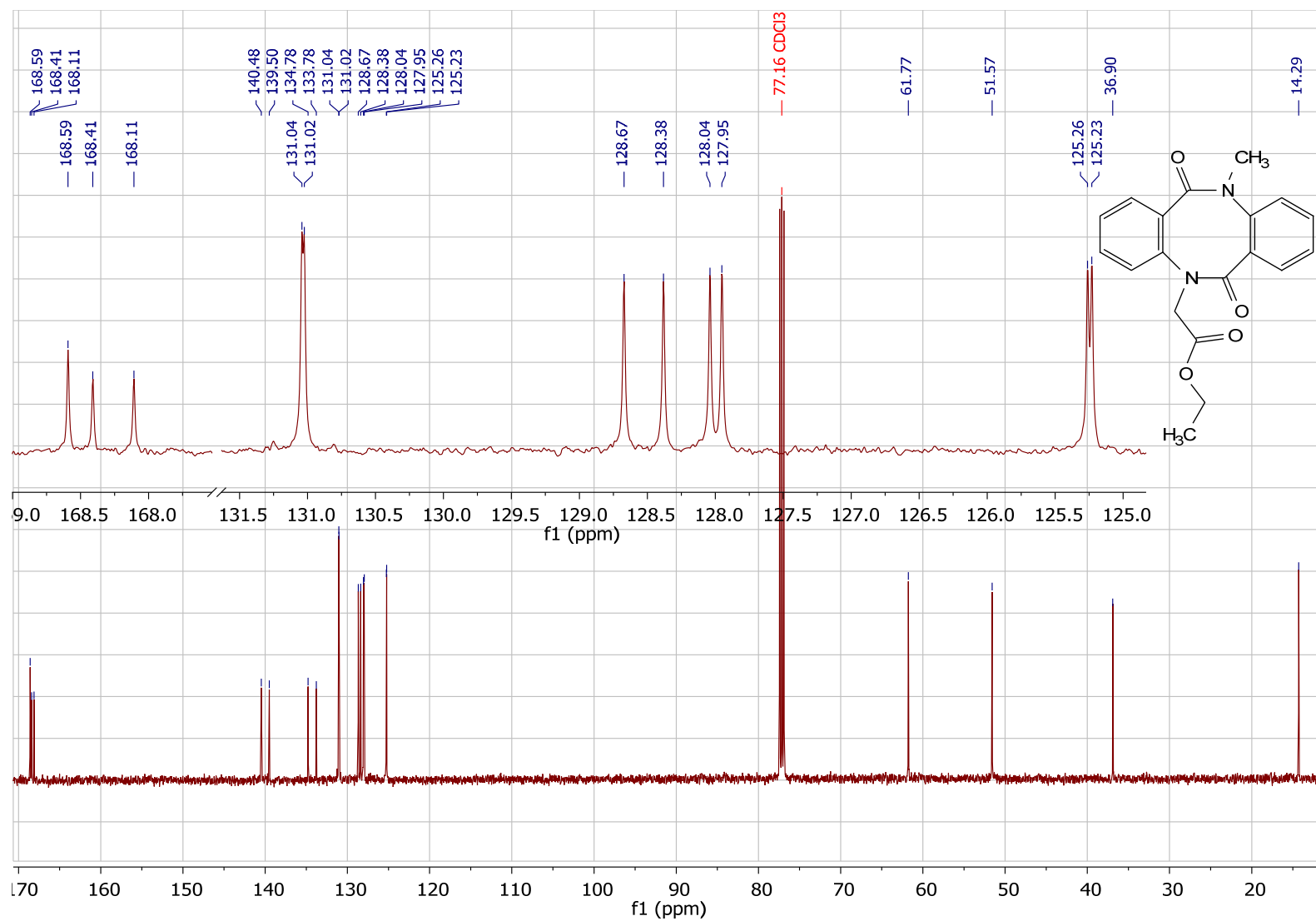


Figure S39. ¹³C NMR spectrum of ethyl 2-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)acetate (10a).

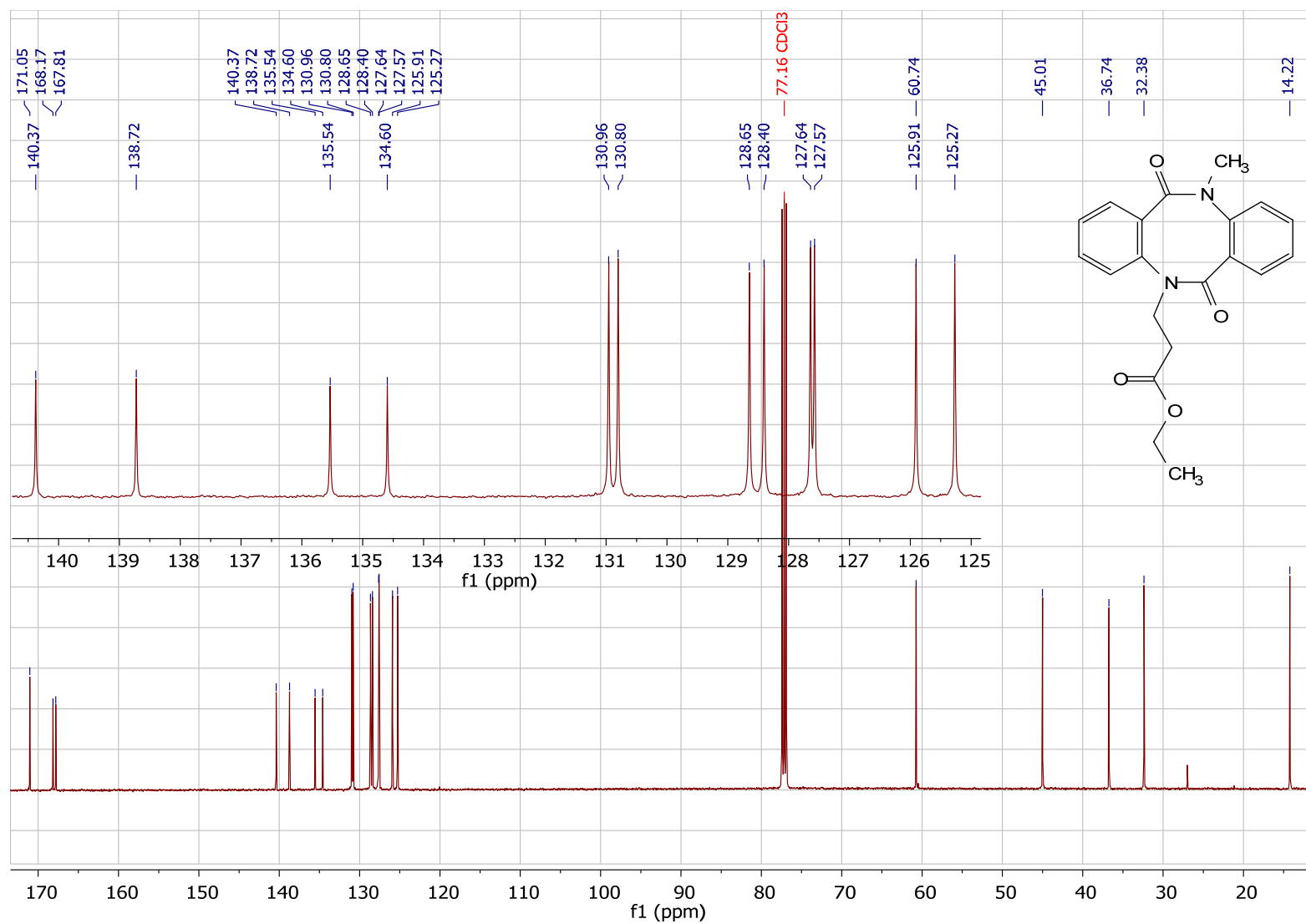


Figure S40. ¹³C NMR spectrum of ethyl 3-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)propanoate (**10b**).

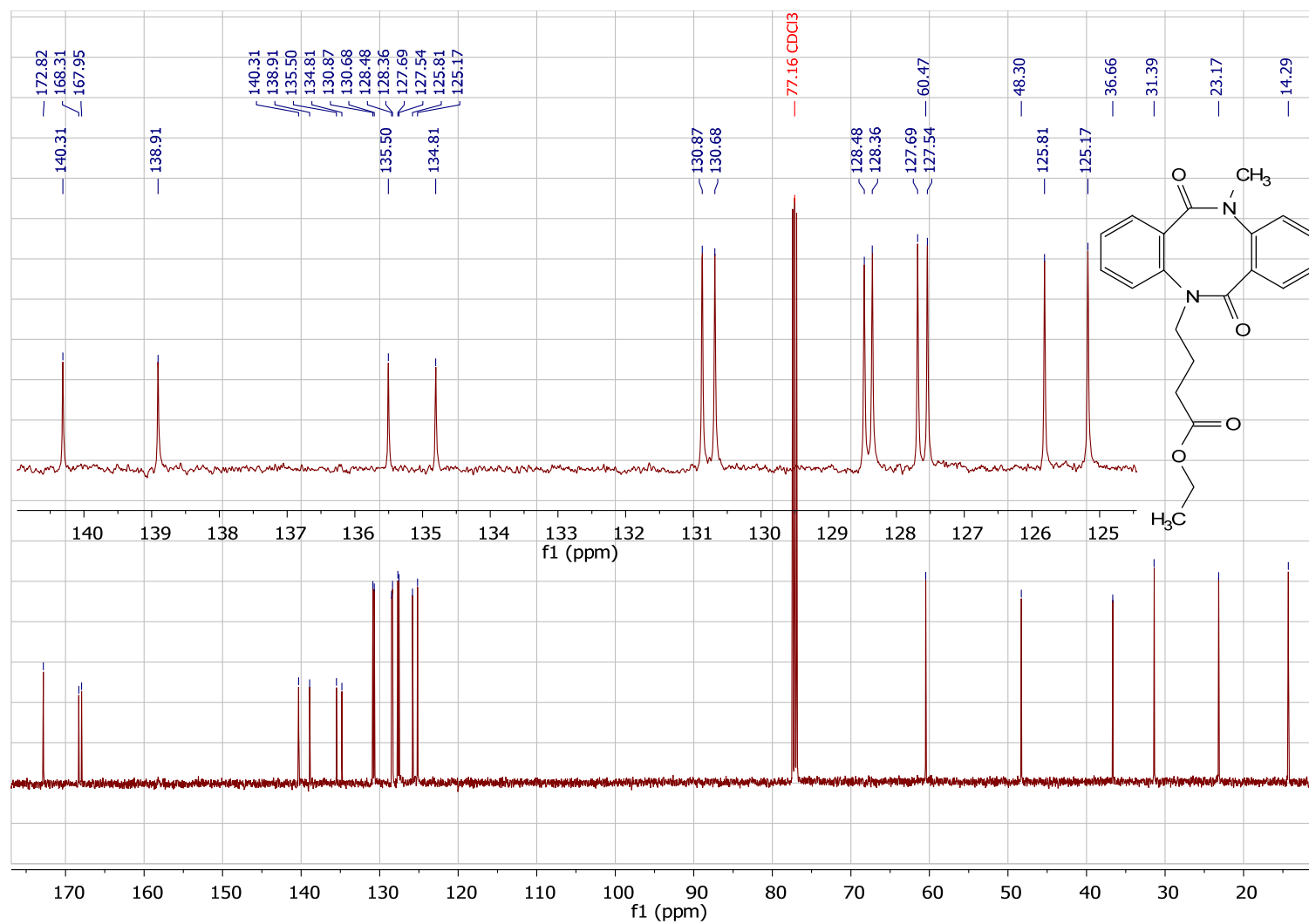


Figure S41. ¹³C NMR spectrum of ethyl 4-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)butanoate (**10c**).

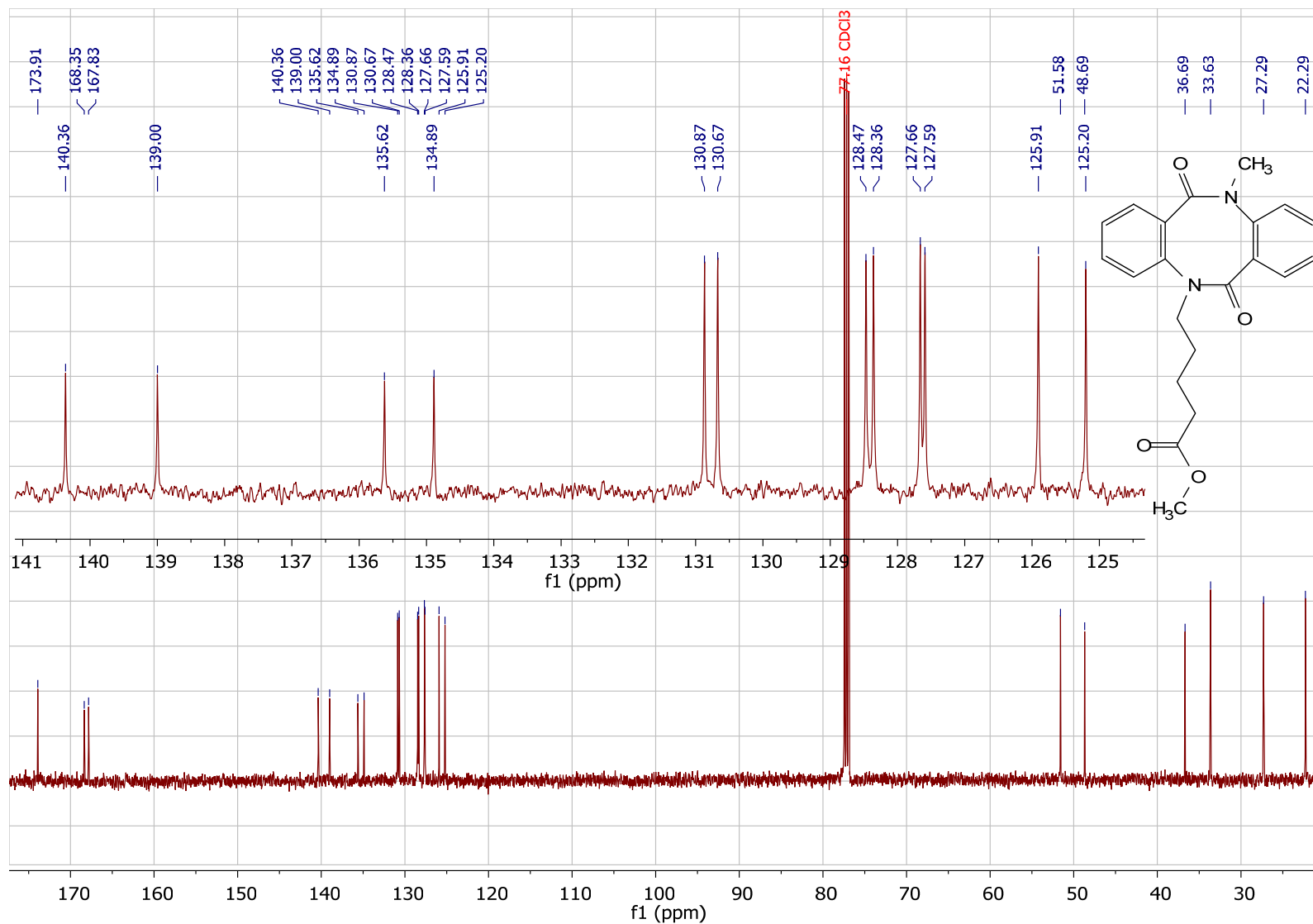


Figure S42. ^{13}C NMR spectrum of methyl 5-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)pentanoate (10d).

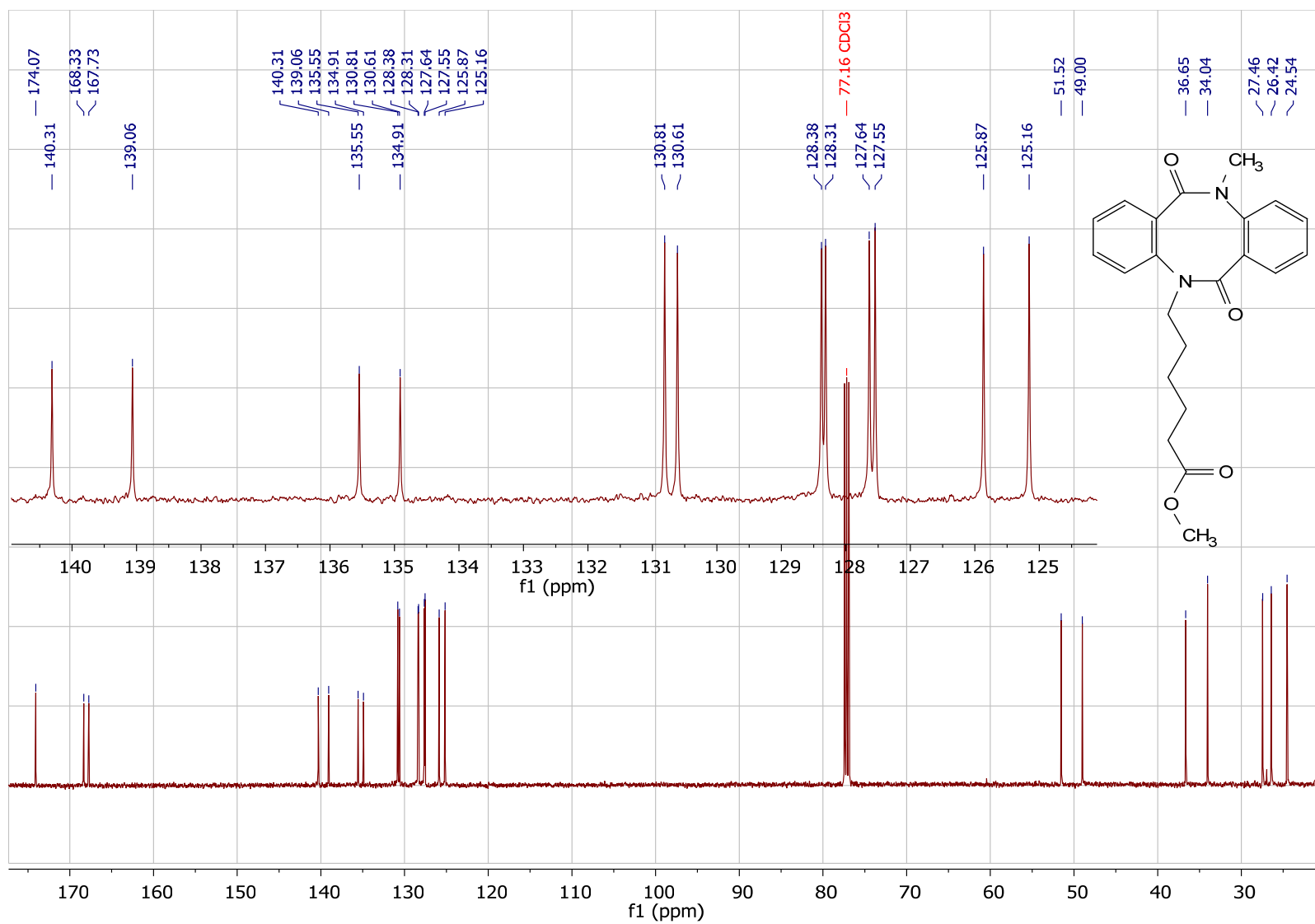


Figure S43. ¹³C NMR spectrum of methyl 6-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)hexanoate (10e).

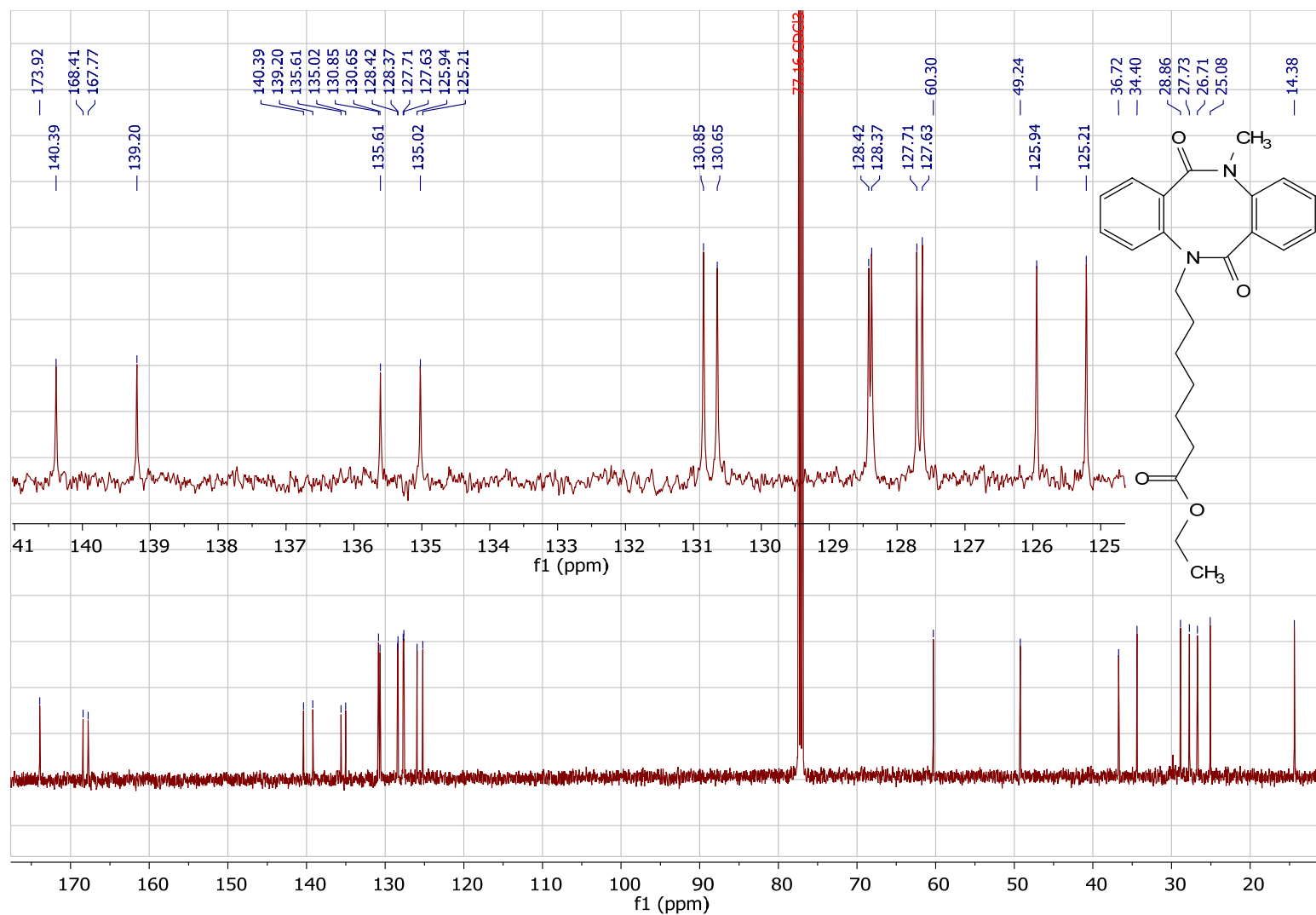


Figure S44. ¹³C NMR spectrum of ethyl 7-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)heptanoate (**10f**).

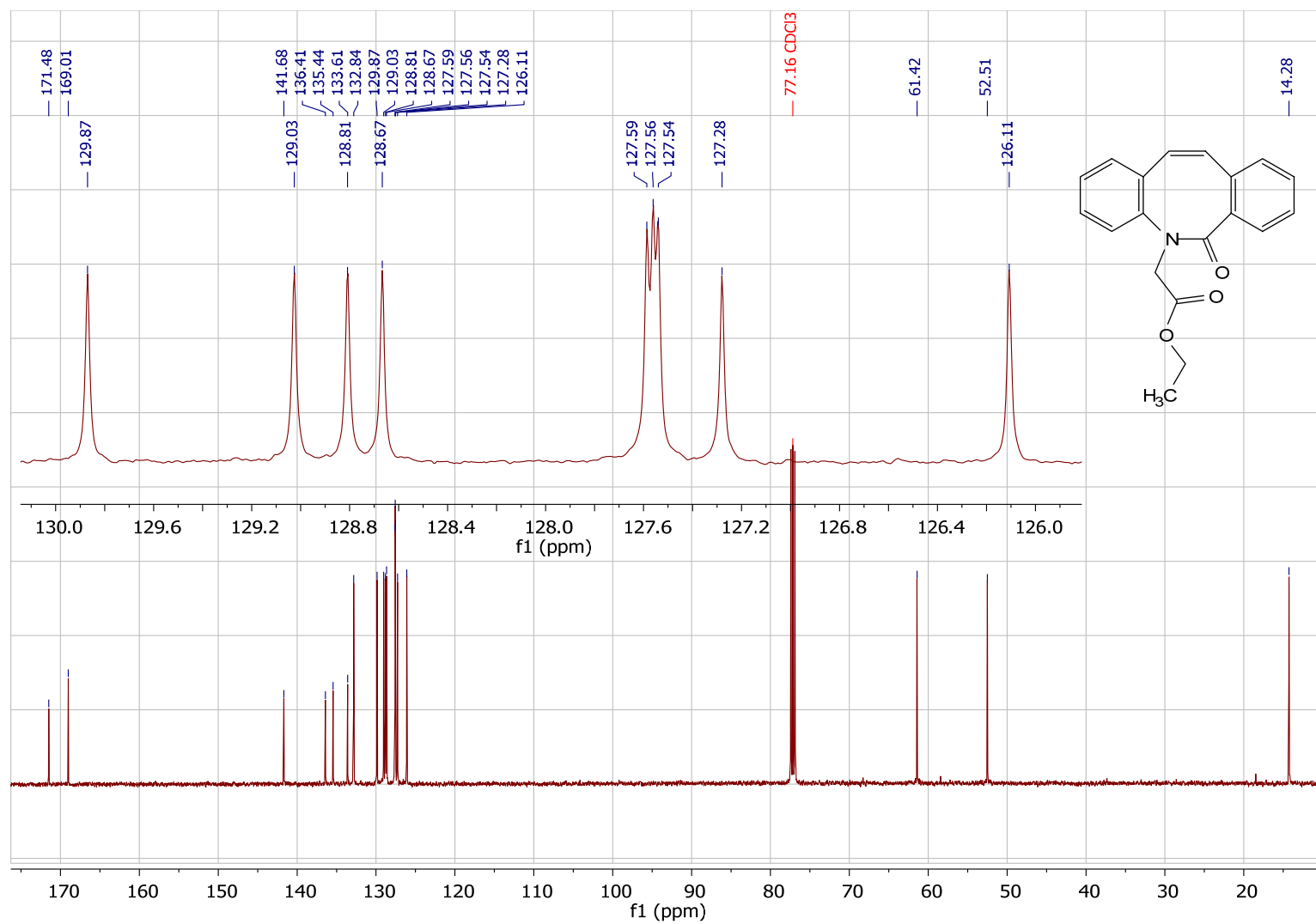


Figure S45. ^{13}C NMR spectrum of ethyl 2-(6-oxodibenzo[*b,f*]azocin-5(6*H*)-yl)acetate (10g).

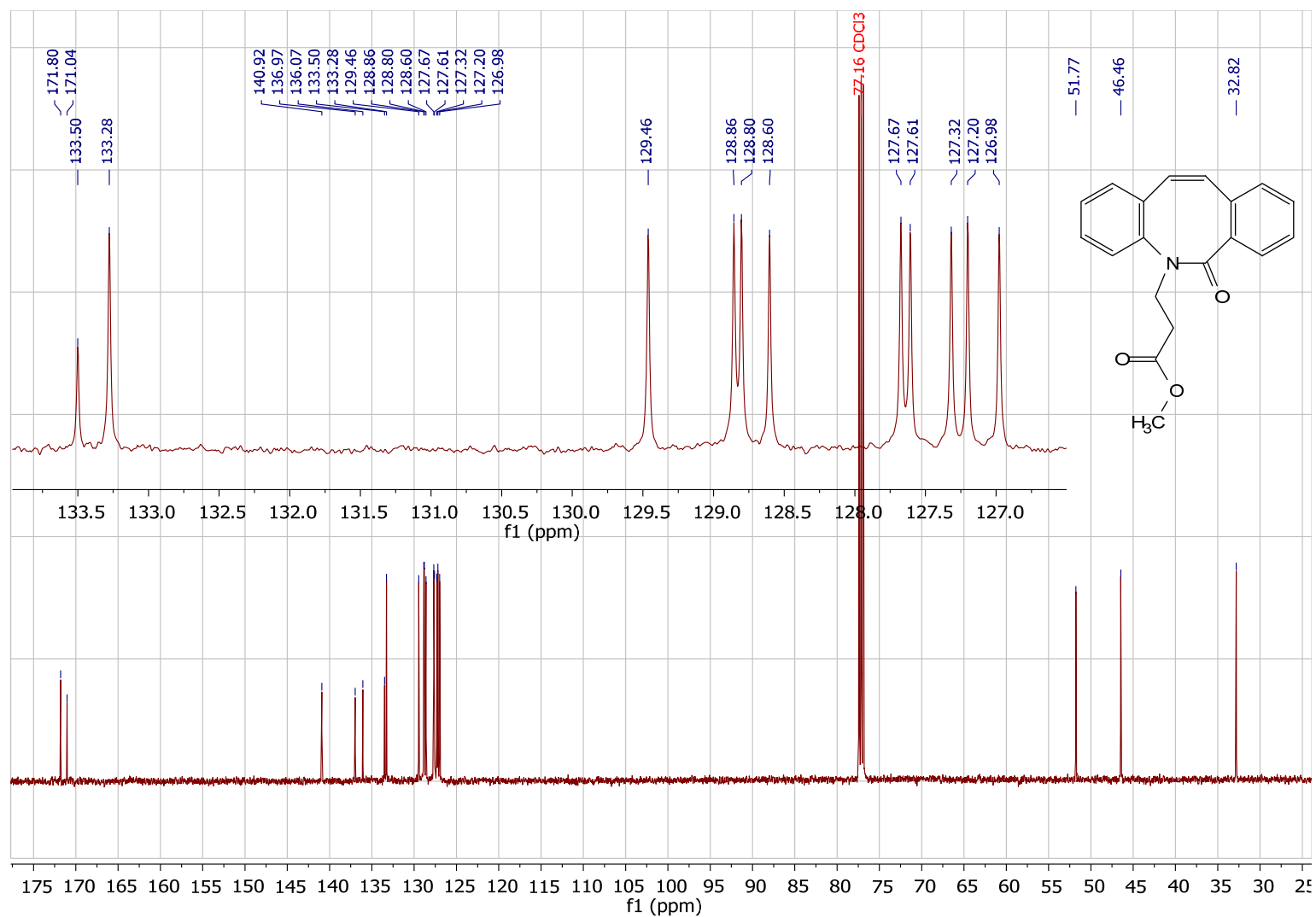


Figure S46. ^{13}C NMR spectrum of methyl 3-(6-oxodibenzo[*b,f*]azocin-5(6*H*)-yl)propanoate (**10h**).

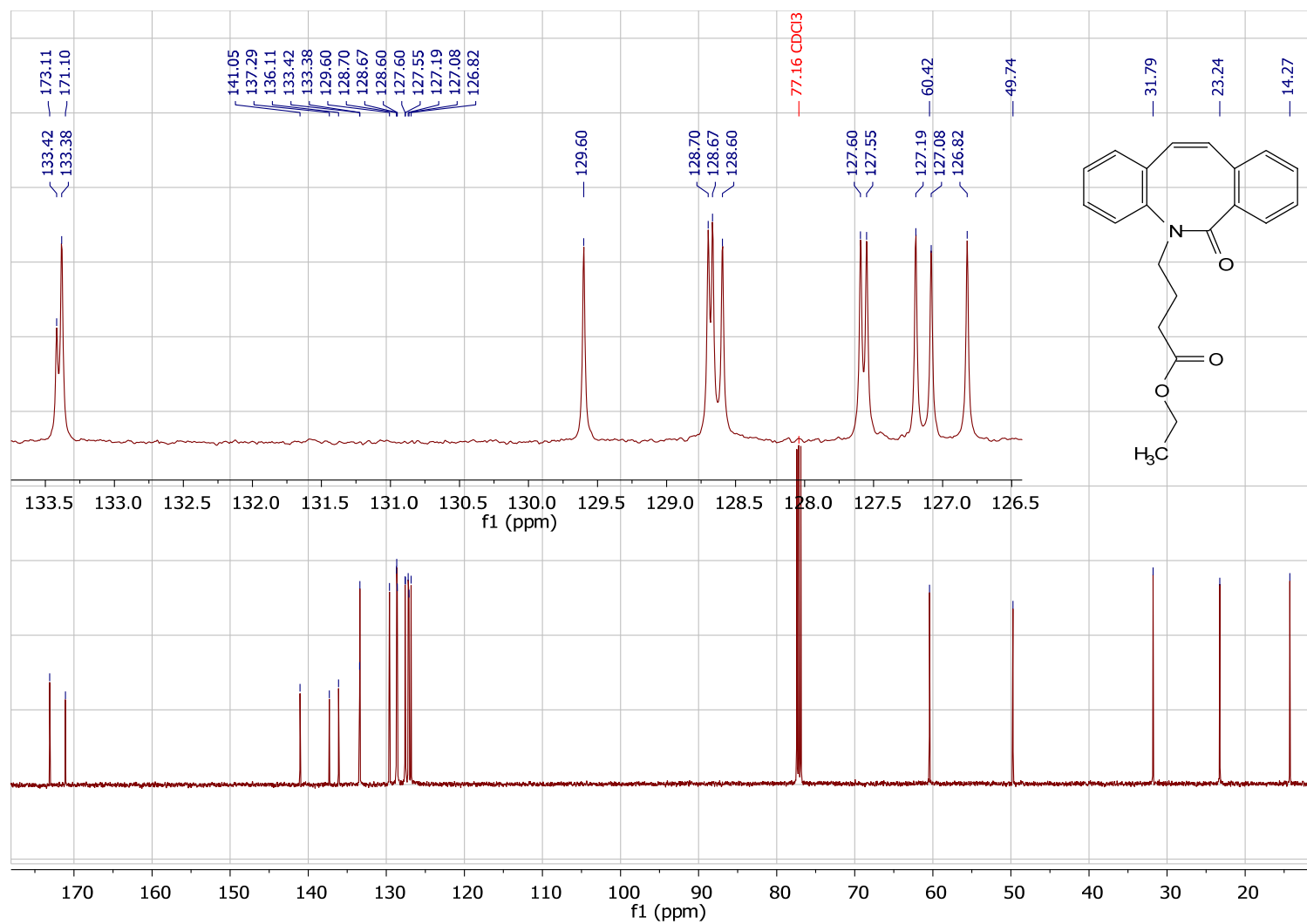


Figure S47. ^{13}C NMR spectrum of ethyl 4-(6-oxodibenzo[*b,f*]azocin-5(6*H*)-yl)butanoate (**10i**).

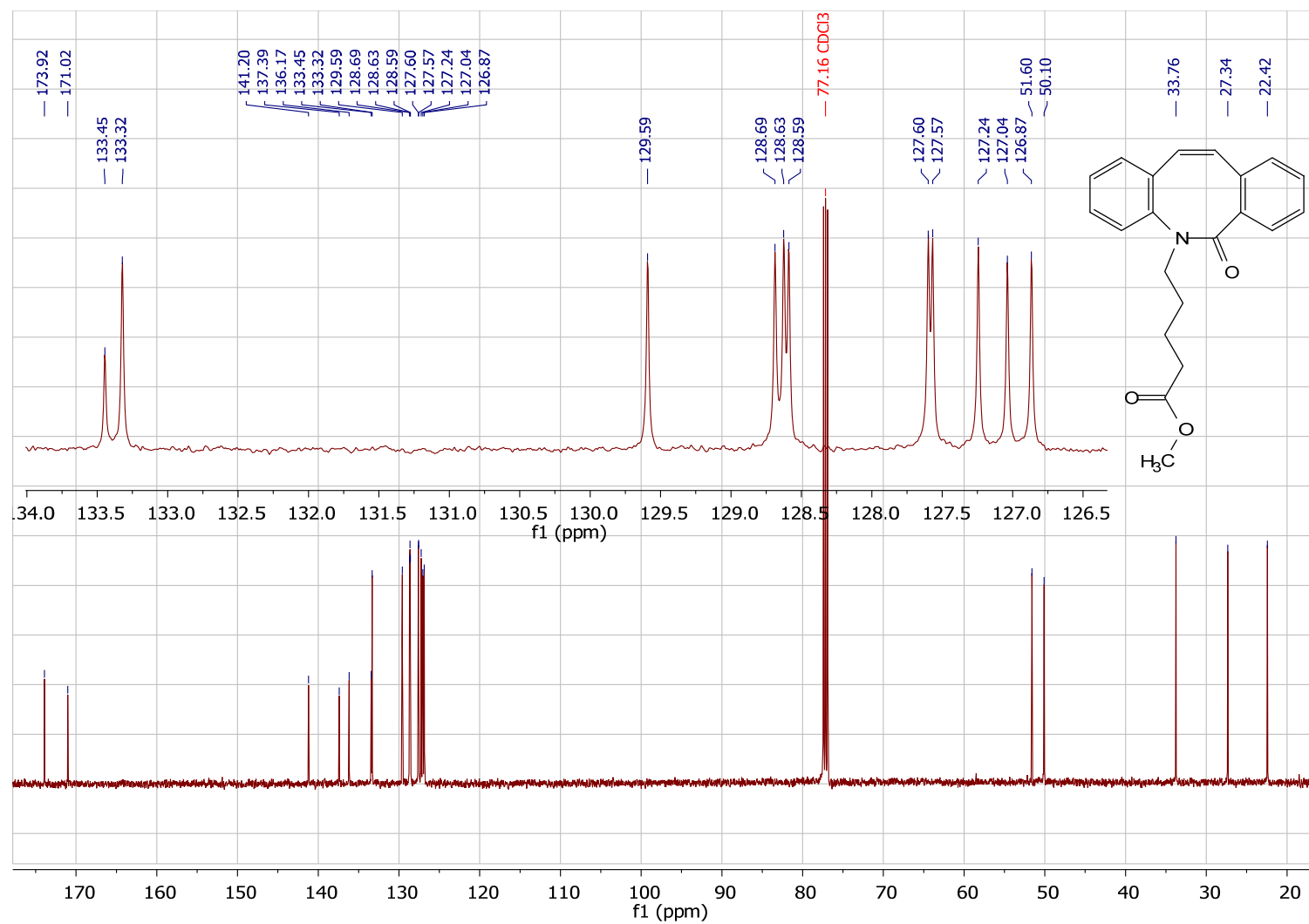


Figure S48. ¹³C NMR spectrum of methyl 5-(6-oxodibenzo[*b,f*]azocin-5(6*H*)-yl)pentanoate (**10j**).

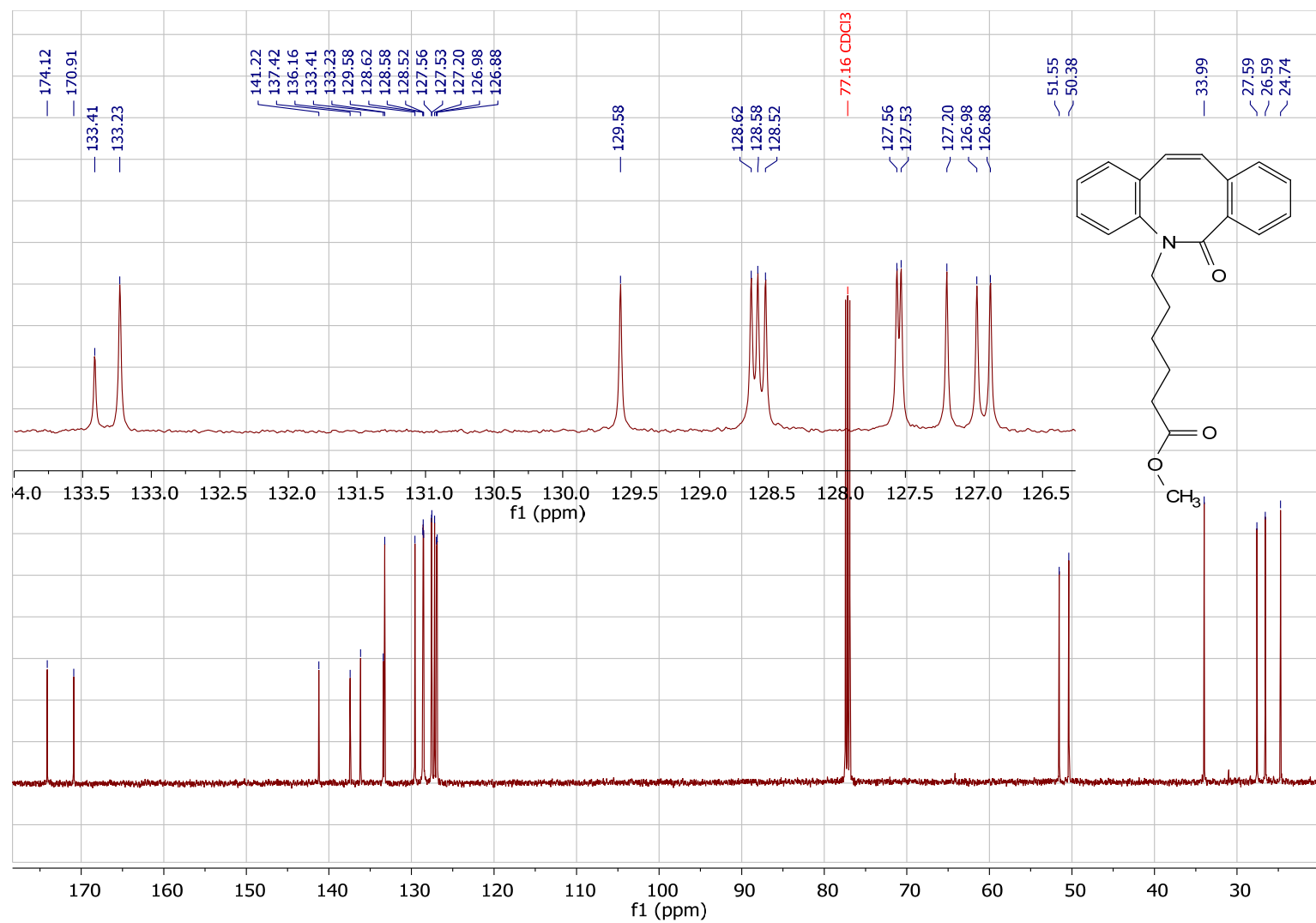


Figure S49. ¹³C NMR spectrum of methyl 6-(6-oxodibenzo[*b,f*]azocin-5(6*H*)-yl)hexanoate (10k).

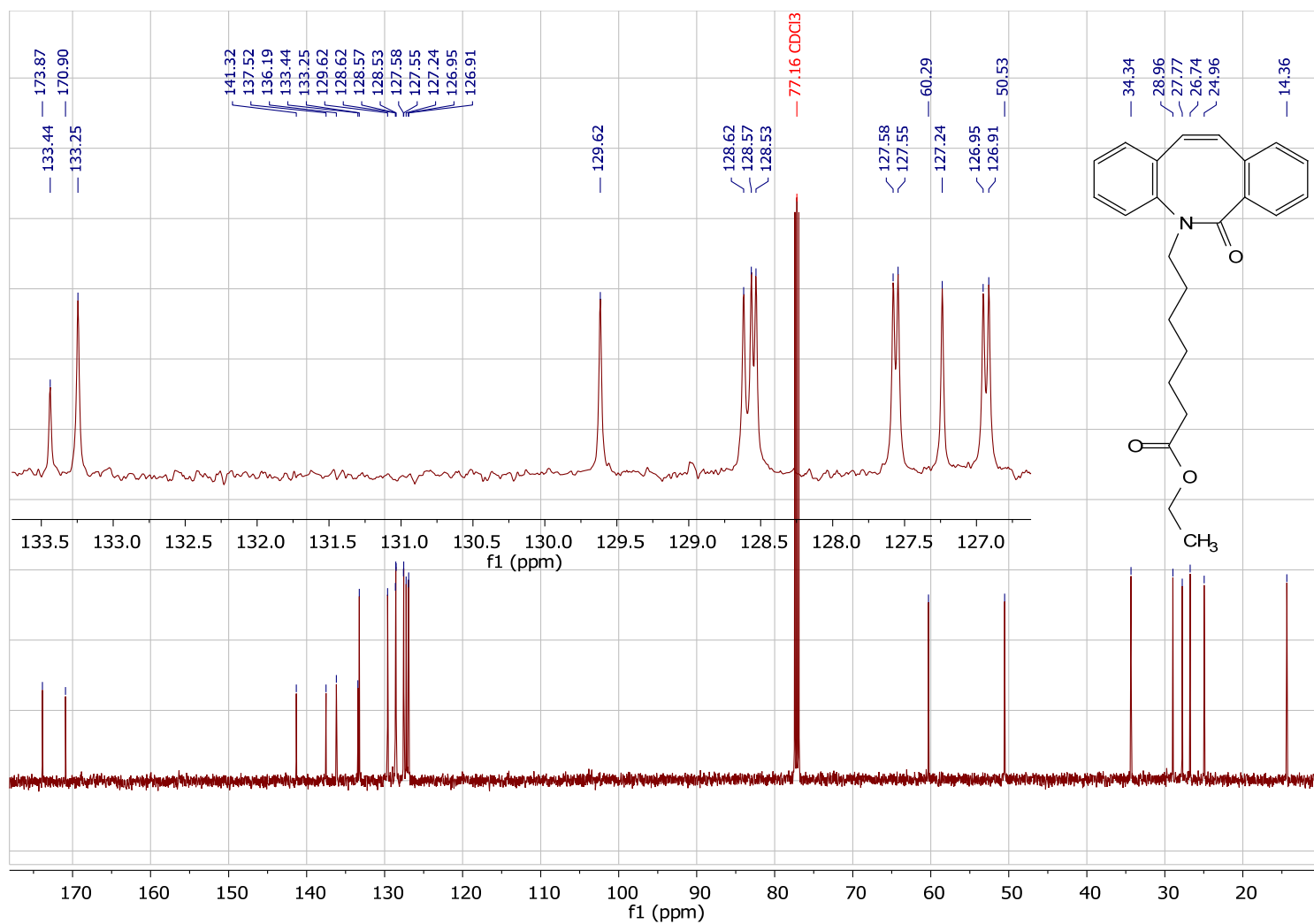


Figure S50. ^{13}C NMR spectrum of ethyl 7-(6-oxodibenzo[*b,f*]azocin-5(6*H*)-yl)heptanoate (101).

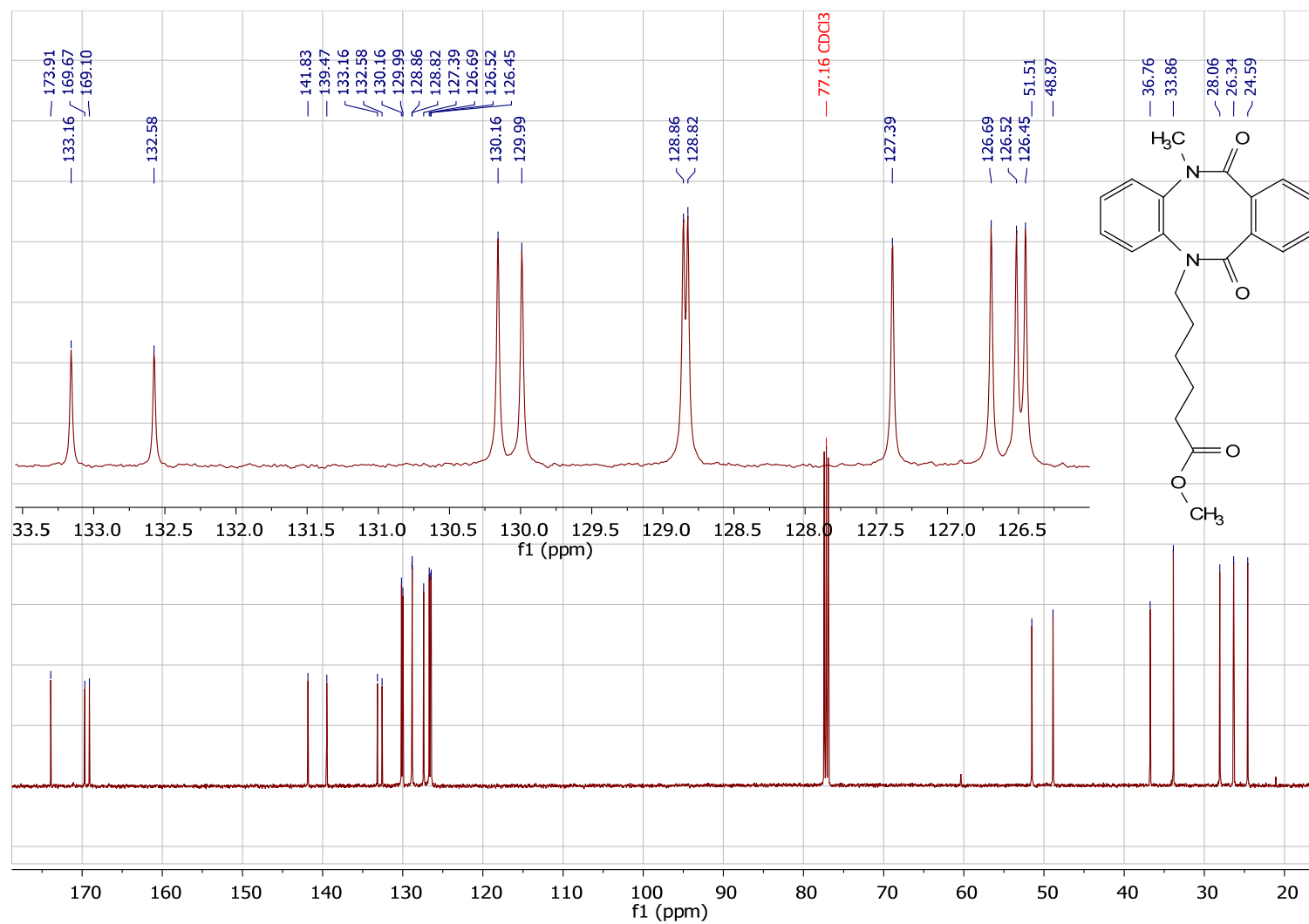


Figure S51. ¹³C NMR spectrum of methyl 6-(12-methyl-6,11-dioxo-11,12-dihydrodibenzo[*b,f*][1,4]diazocin-5(6*H*)-yl)hexanoate (**10m**).

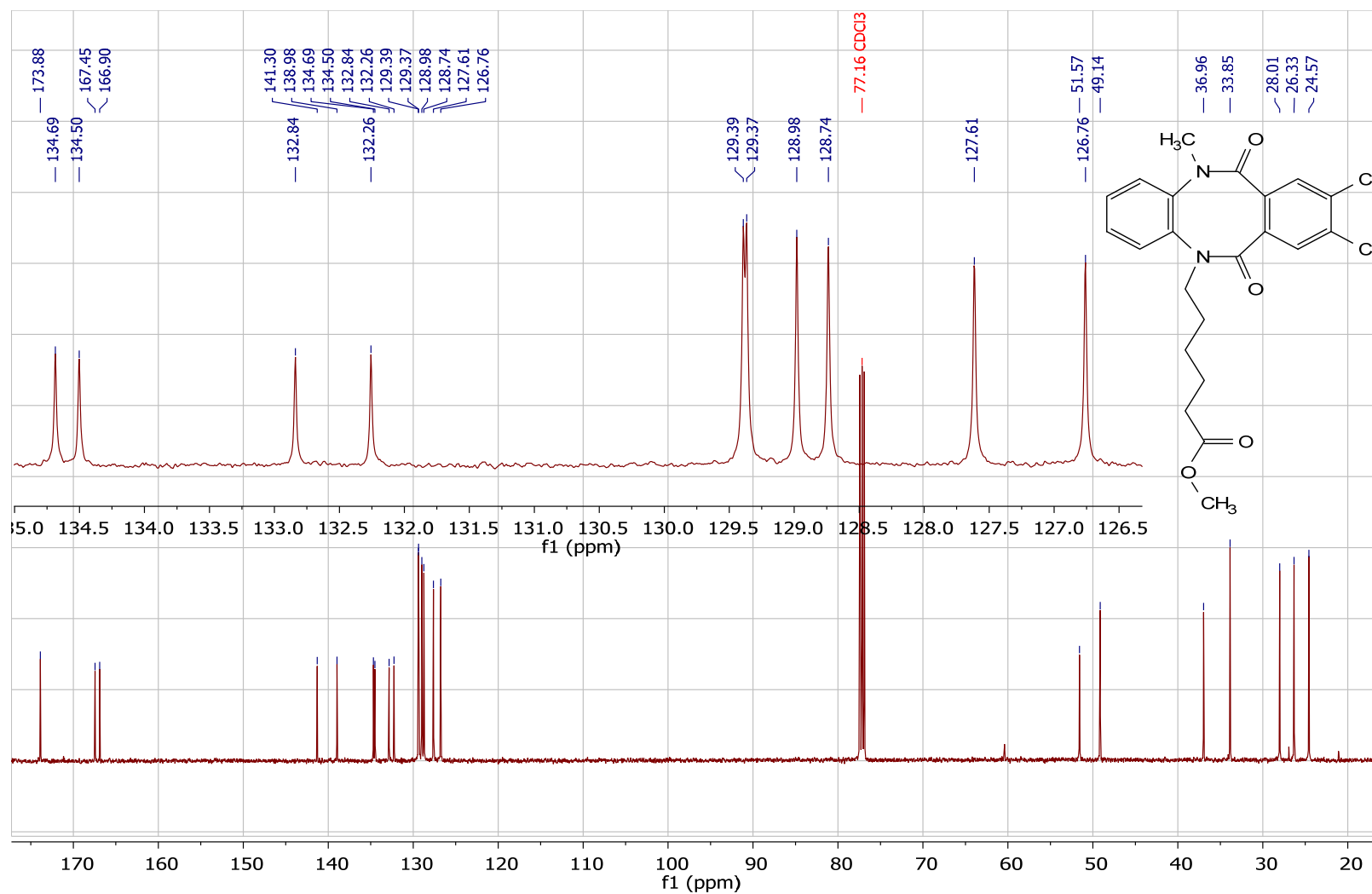


Figure S52. ^{13}C NMR spectrum of methyl 6-(8,9-dichloro-12-methyl-6,11-dioxo-11,12-dihydrodibenzo[*b,f*][1,4]diazocin-5(6*H*)-yl) hexanoate (**10n**).

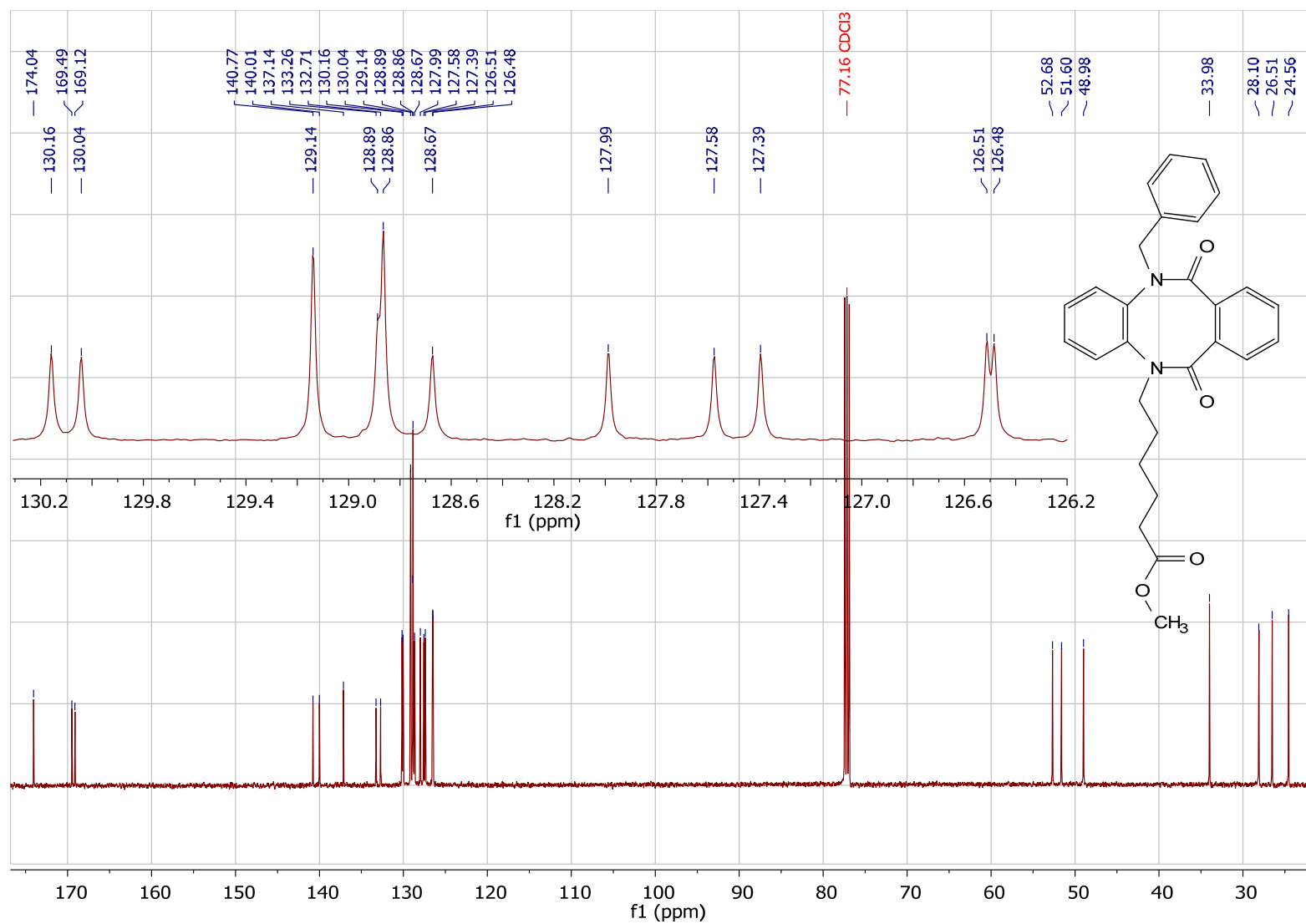


Figure S53. ¹³C NMR spectrum of methyl 6-(12-benzyl-6,11-dioxo-11,12-dihydrodibenzo[*b,f*][1,4]diazocin-5(6*H*)-yl)hexanoate (**10o**).

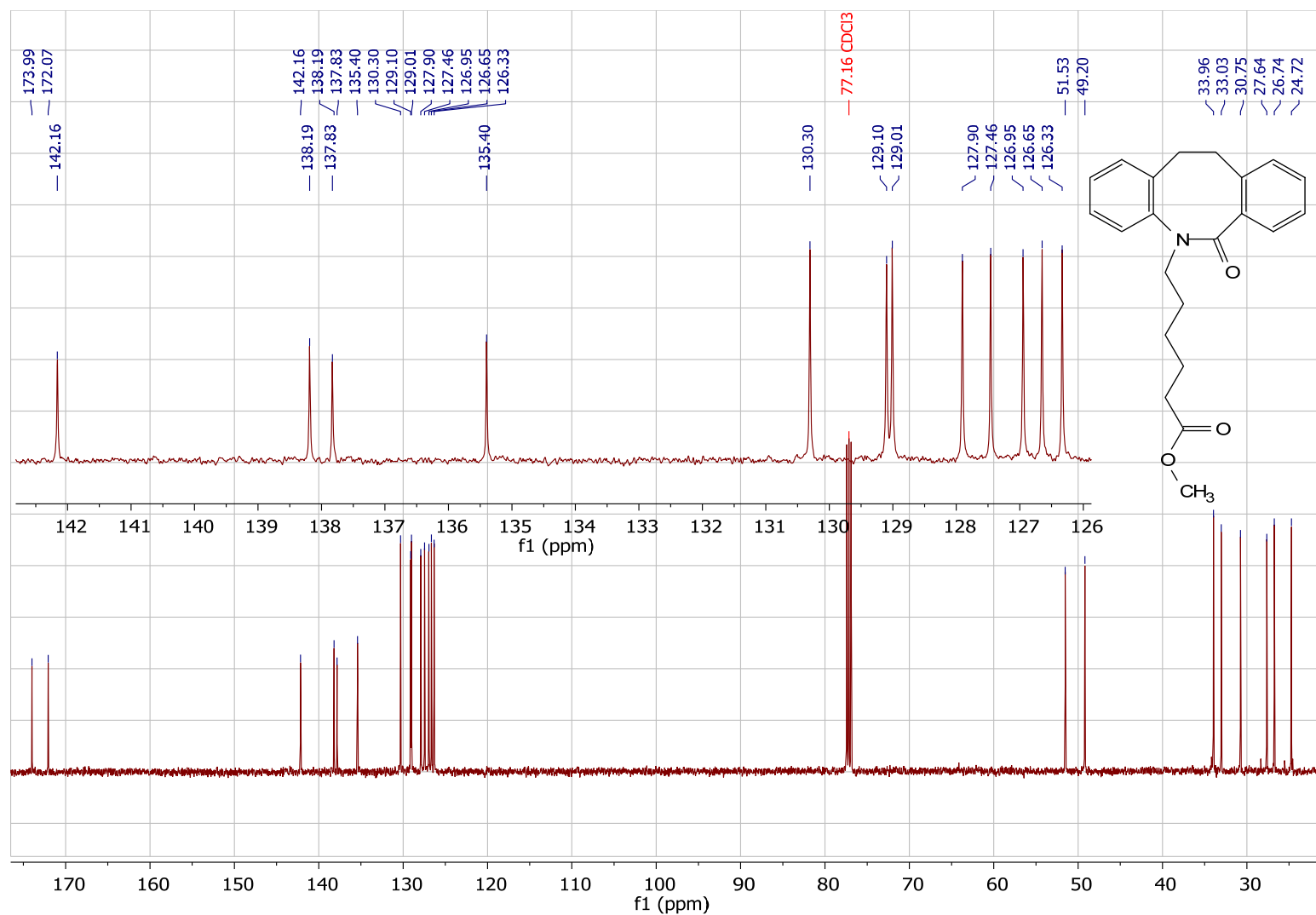


Figure S54. ¹³C NMR spectrum of methyl 6-(6-oxo-11,12-dihydrodibenzo[*b,f*]azocin-5(6*H*)-yl)hexanoate (10p).

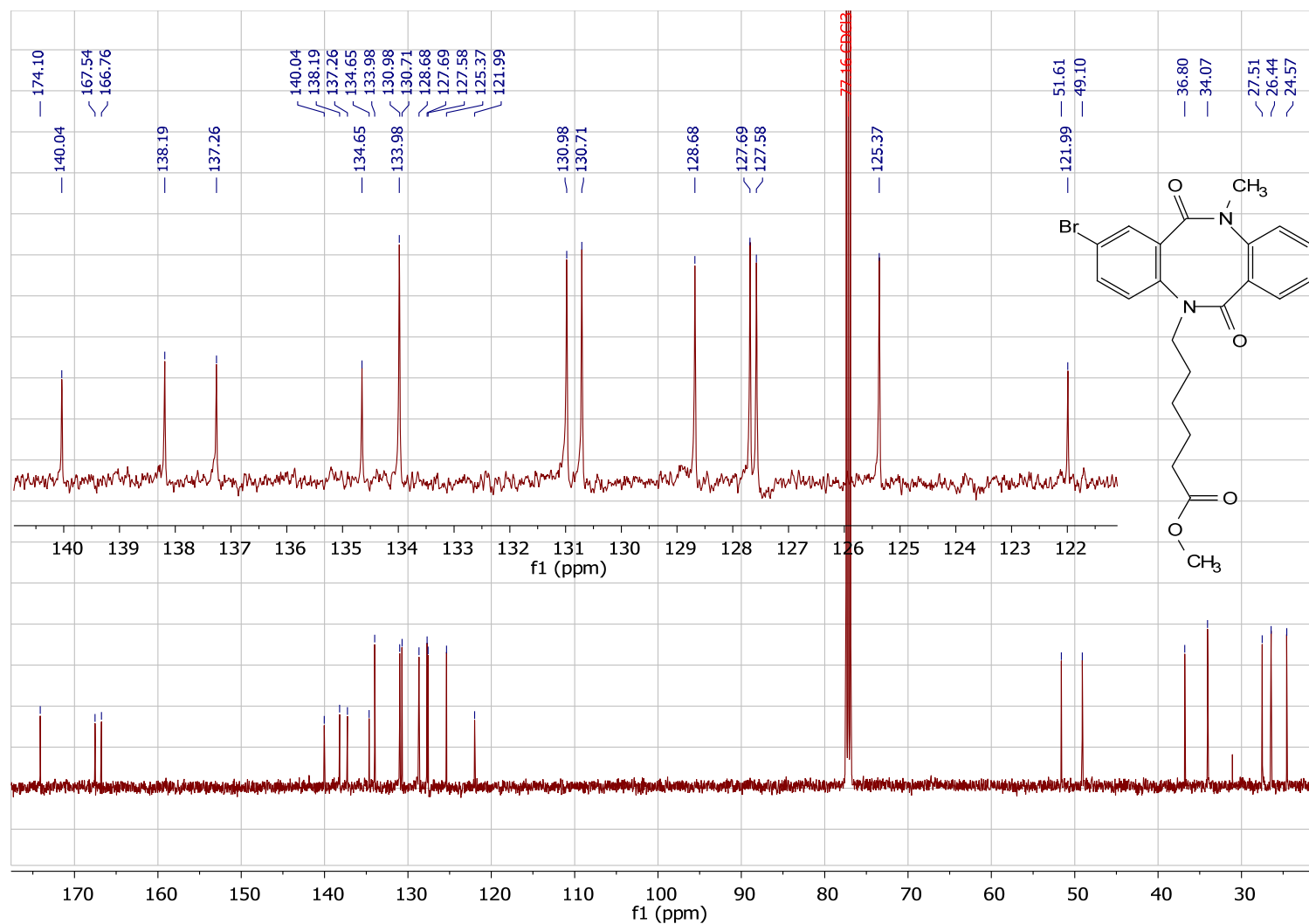


Figure S55. ¹³C NMR spectrum of methyl 6-(2-bromo-11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)hexanoate (**10r**).

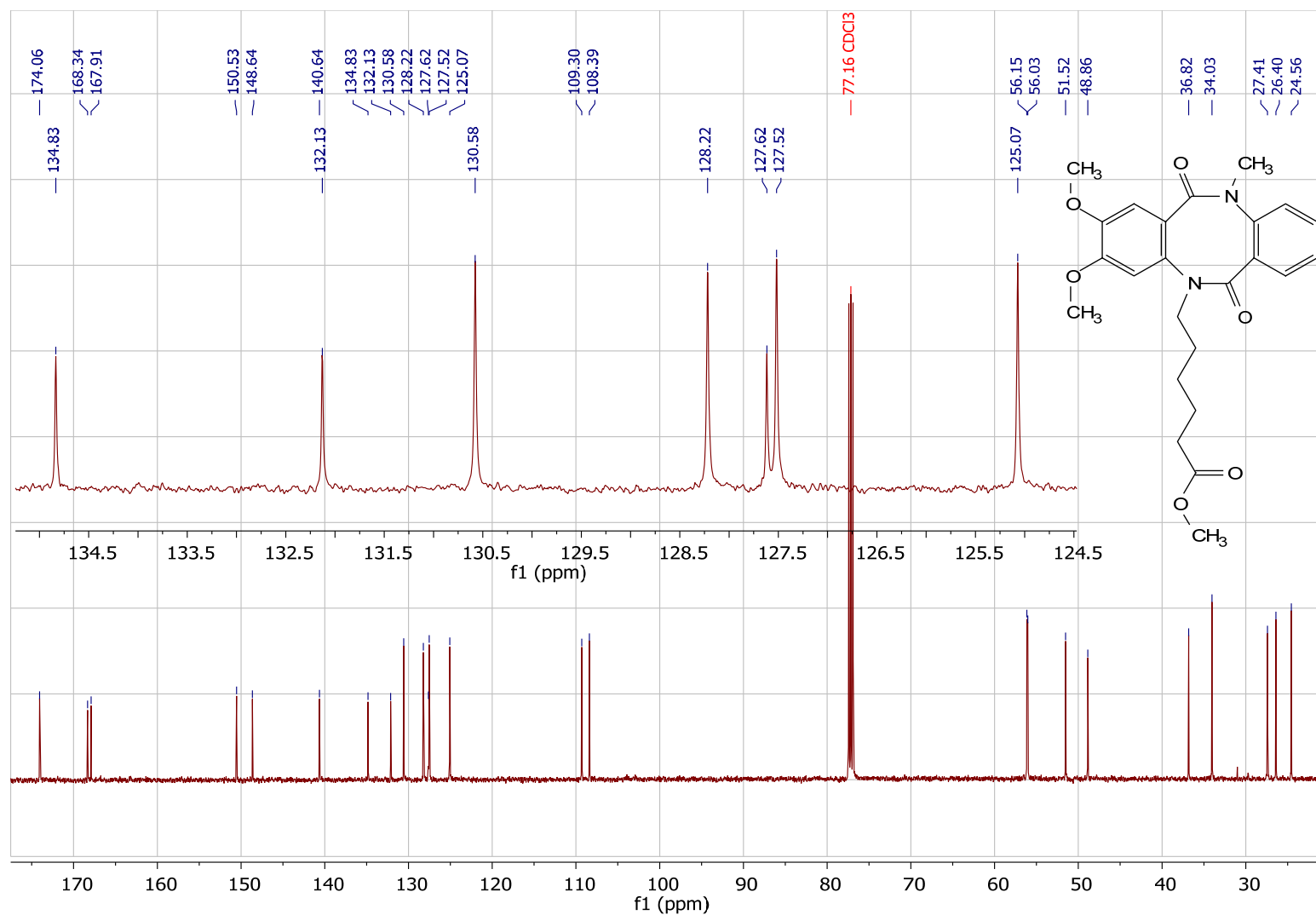


Figure S56. ¹³C NMR spectrum of methyl 6-(2,3-dimethoxy-11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)hexanoate (**10s**).

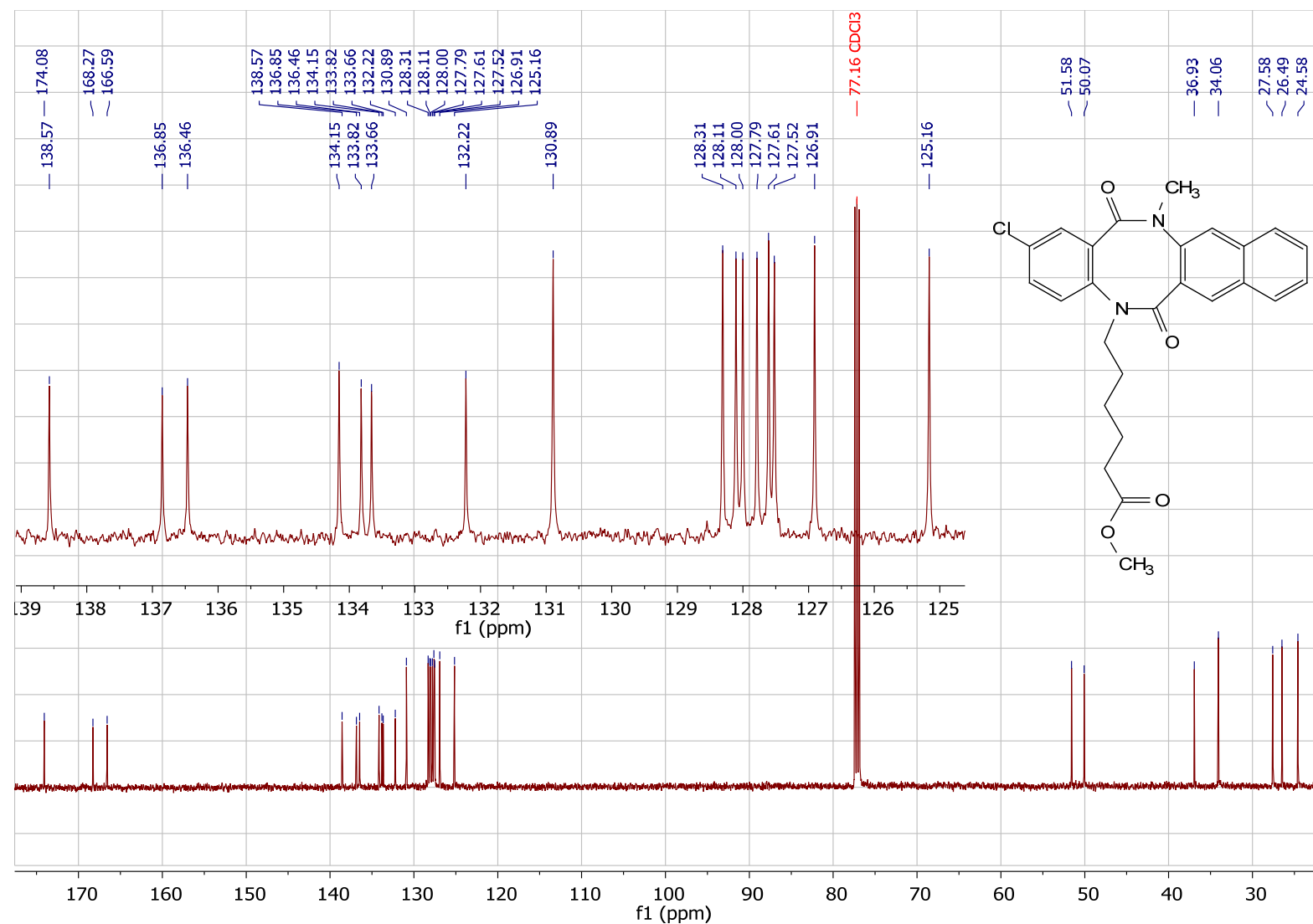


Figure S57. ^{13}C NMR spectrum of methyl 6-(5-methyl-6,14-dioxo-5,14-dihydrobenzonaphtho[2,3-f][1,5]diazocin-13(6H)-yl)hexanoate (10t).

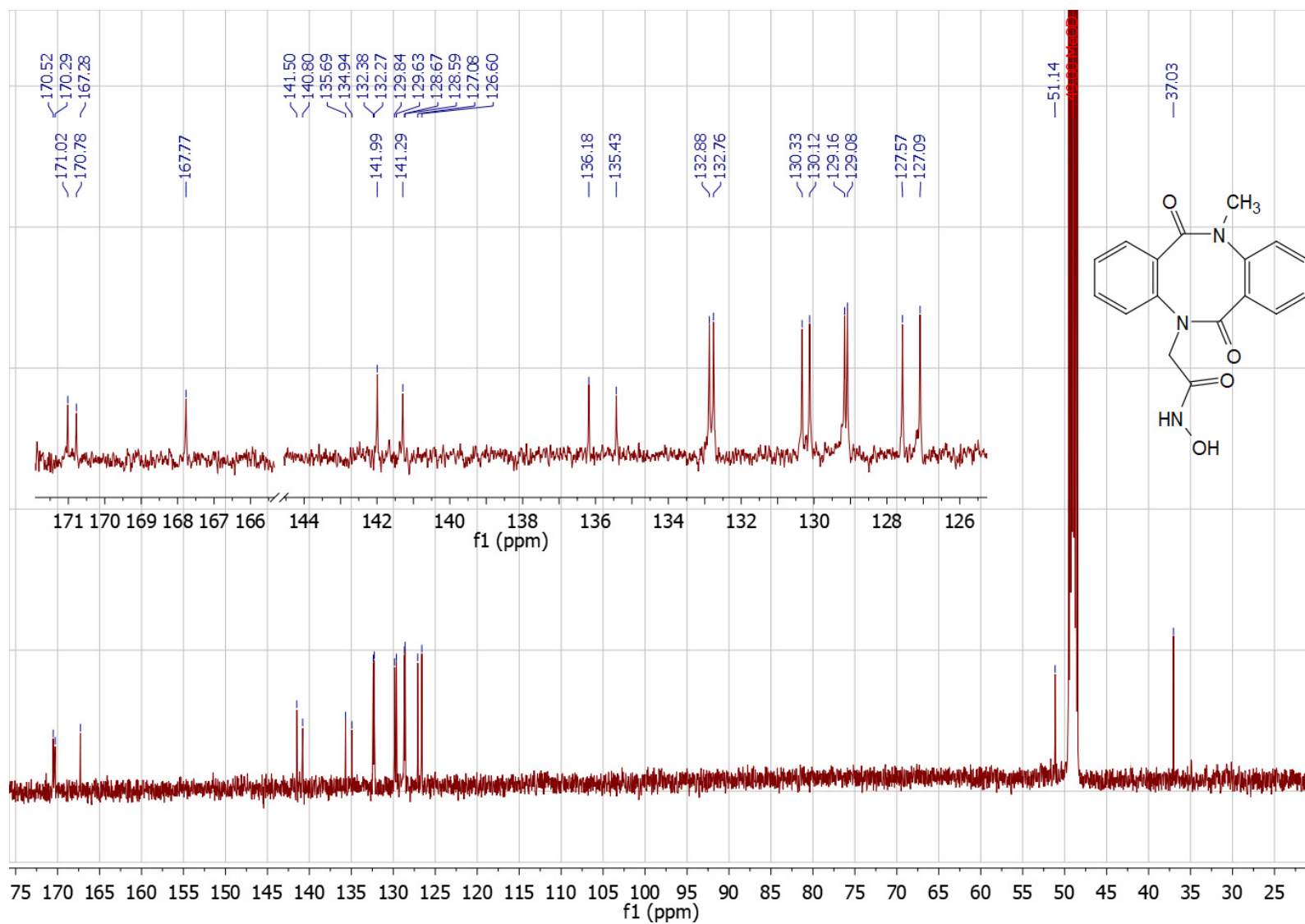


Figure S58. ¹³C NMR spectrum of *N*-hydroxy-2-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)acetamide (7a).

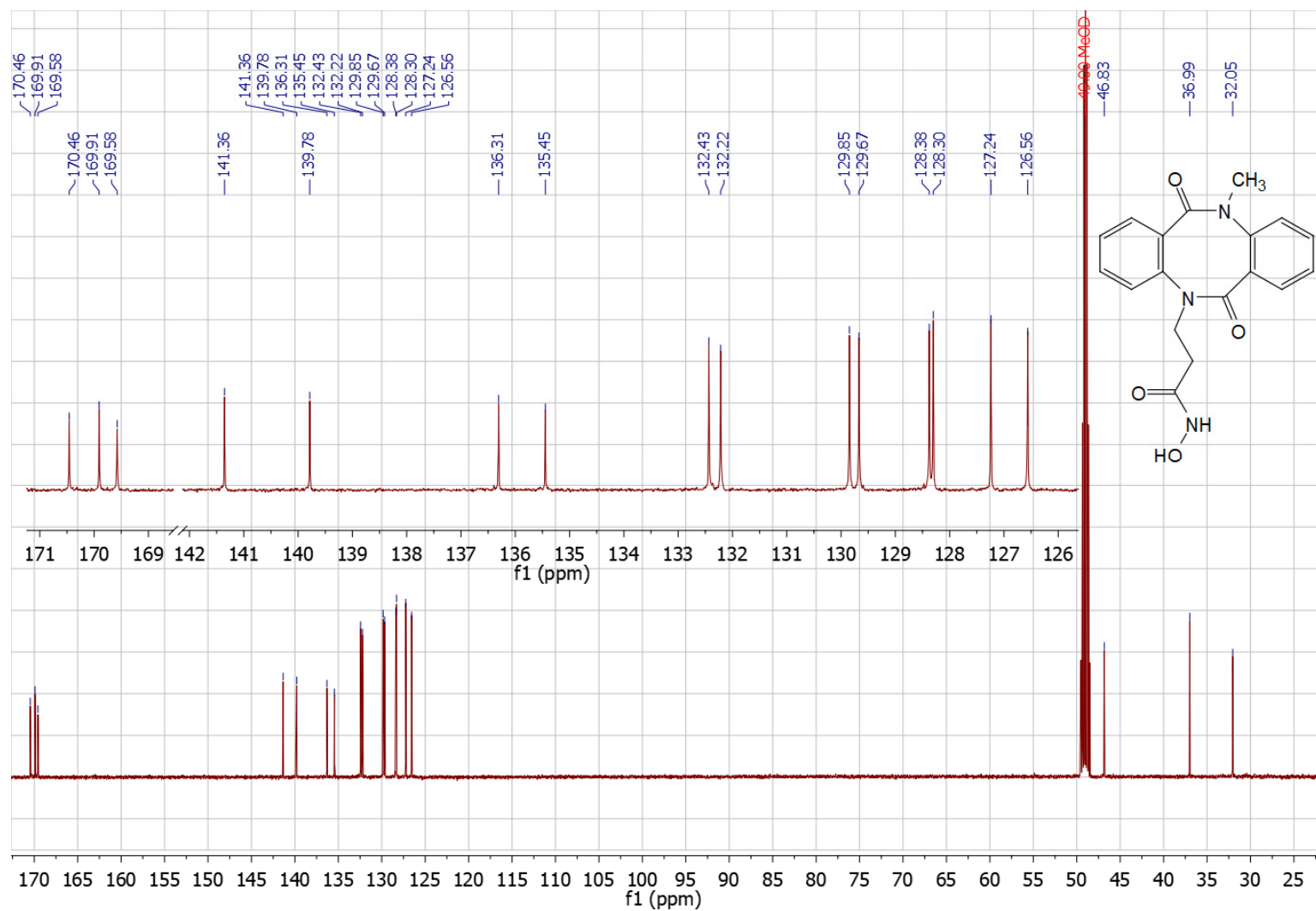


Figure S59. ¹³C NMR spectrum of *N*-hydroxy-3-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)propanamide (**7b**).

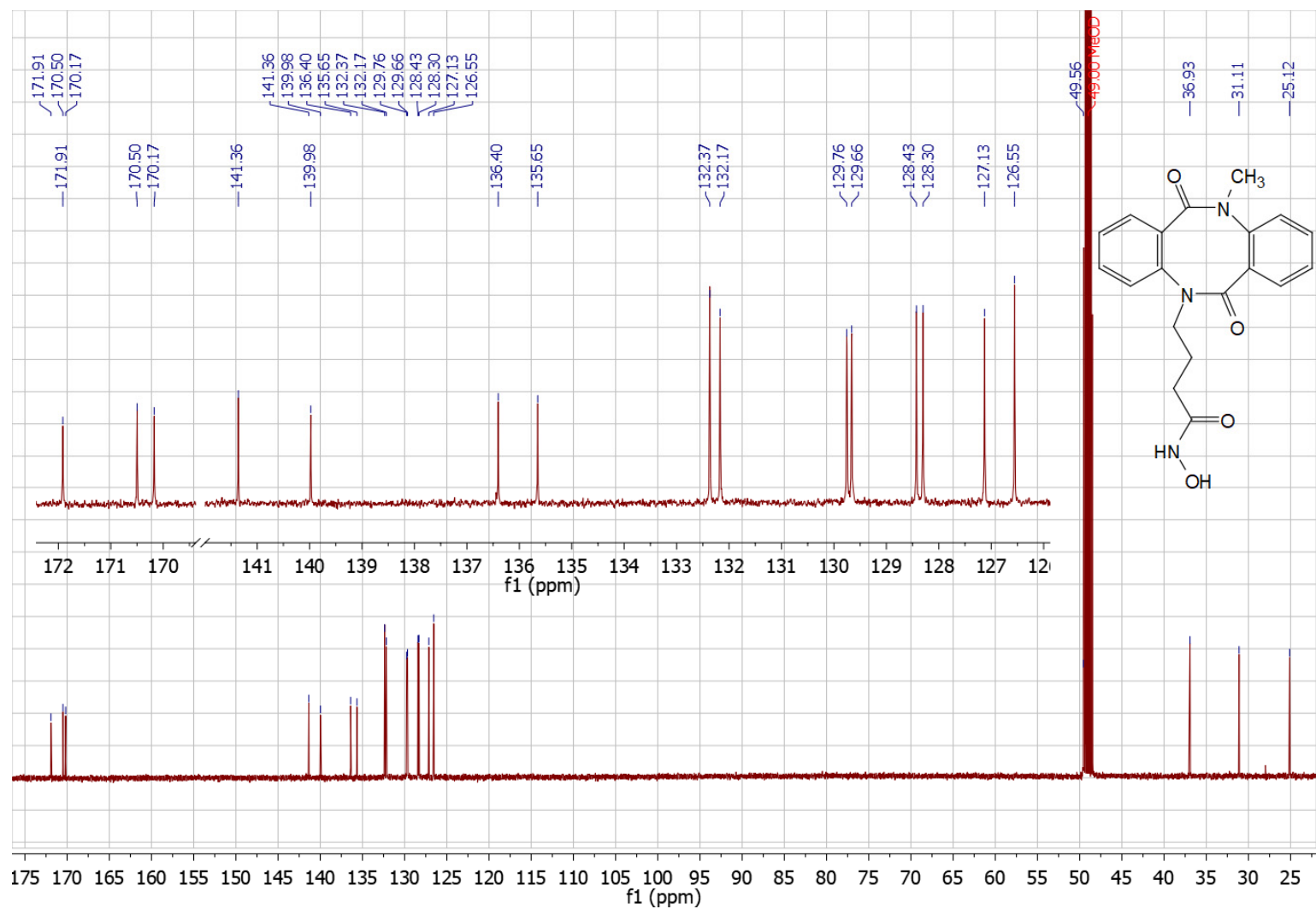


Figure S60. ^{13}C NMR spectrum of *N*-hydroxy-4-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)butanamide (**7c**).

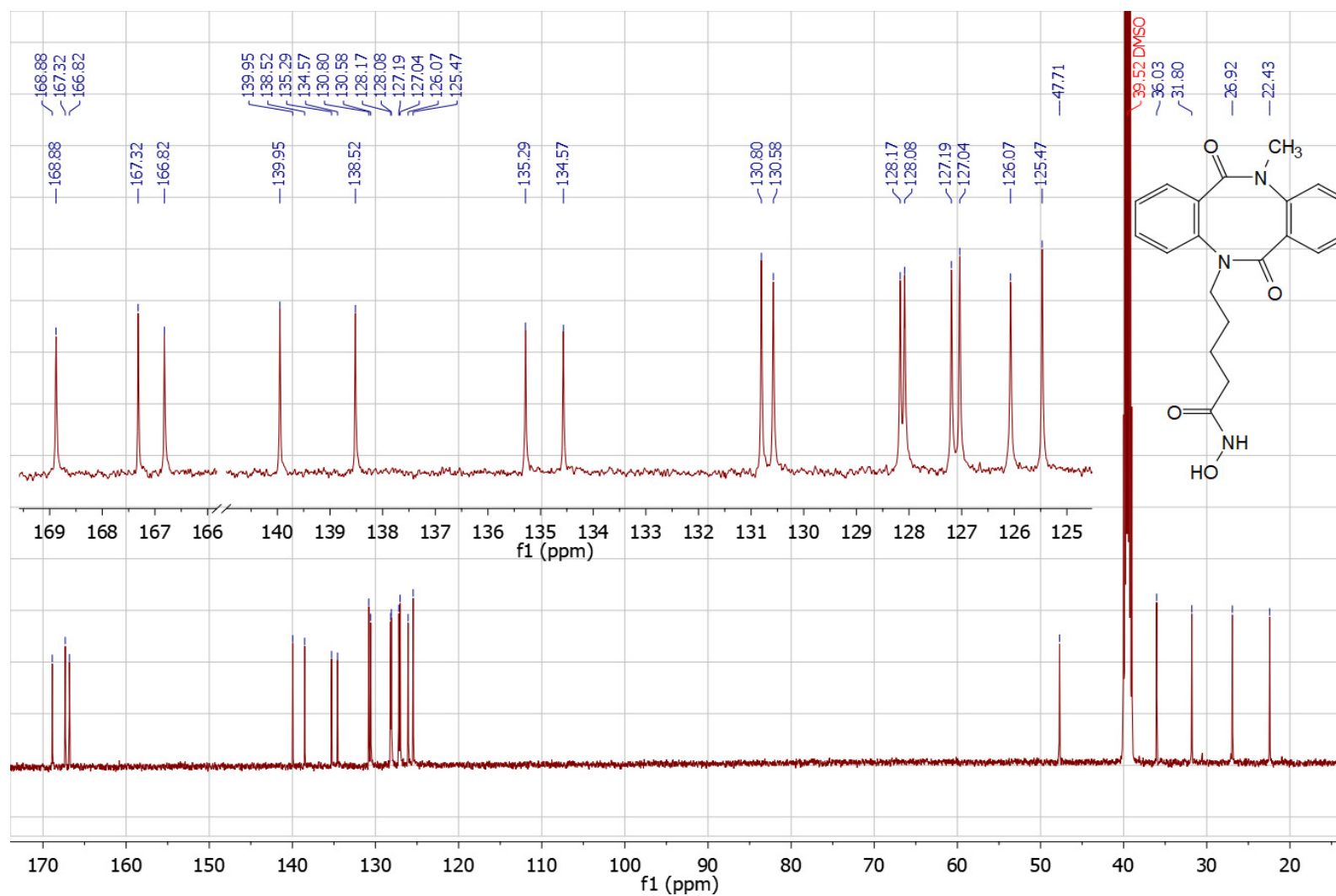


Figure S61. ¹³C NMR spectrum of *N*-hydroxy-5-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)pentanamide (7d).

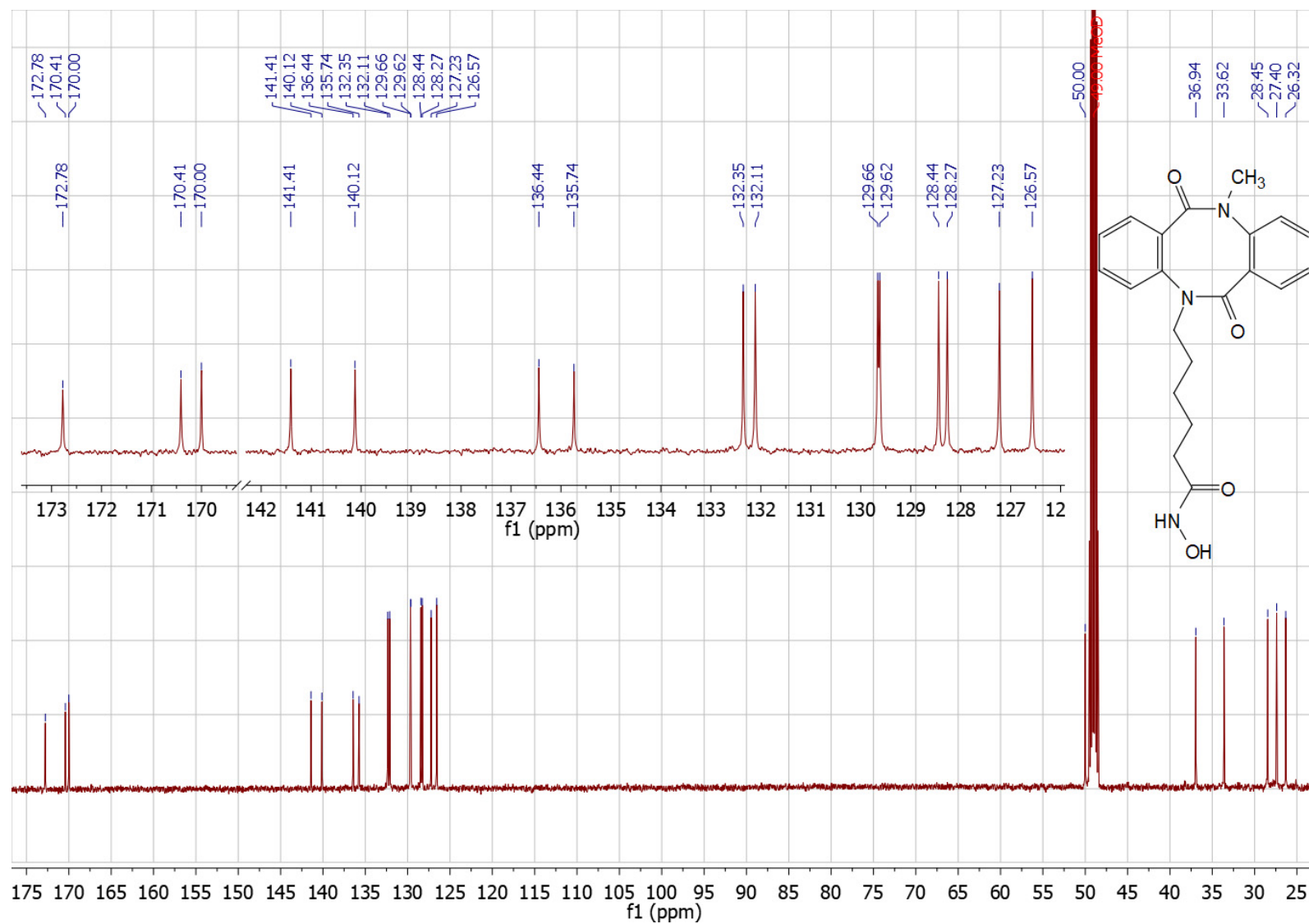


Figure S62. ¹³C NMR spectrum of *N*-hydroxy-6-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)hexanamide (7e).

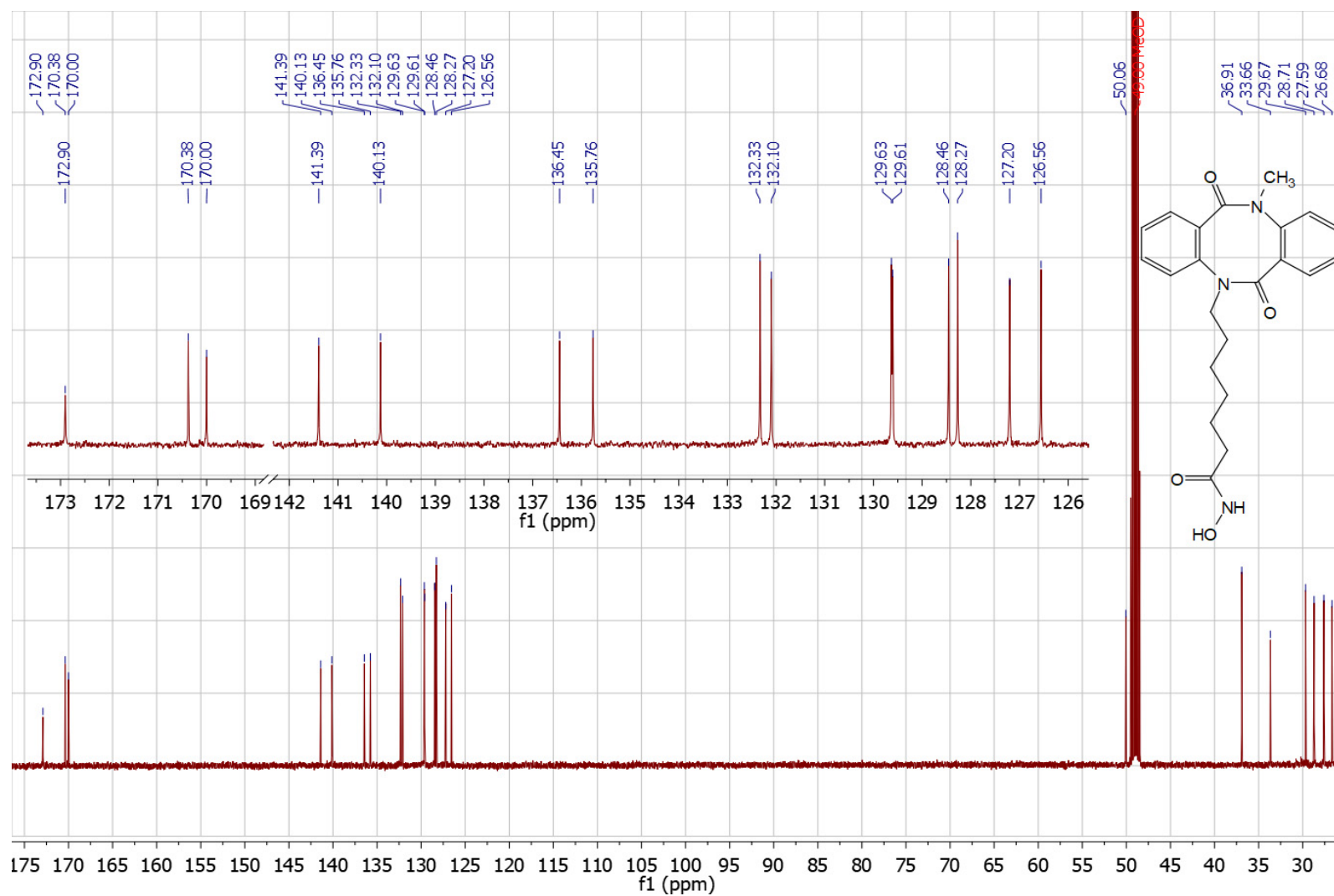


Figure S63. ^{13}C NMR spectrum of *N*-hydroxy-7-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)heptanamide (7f).

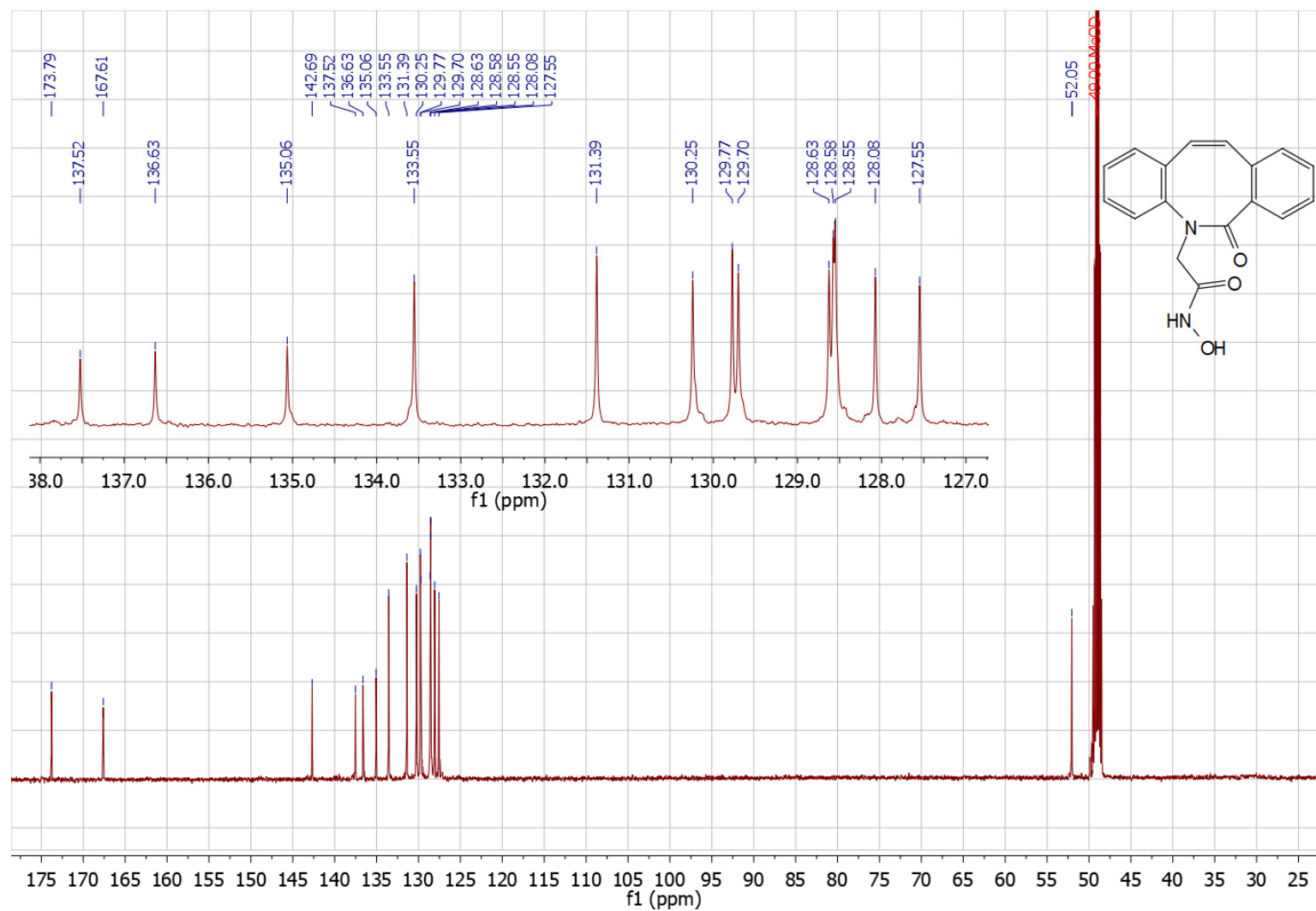


Figure S64. ^{13}C NMR spectrum of *N*-hydroxy-2-(6-oxodibenzo[*b,f*]azocin-5(6*H*)-yl)acetamide (7g).

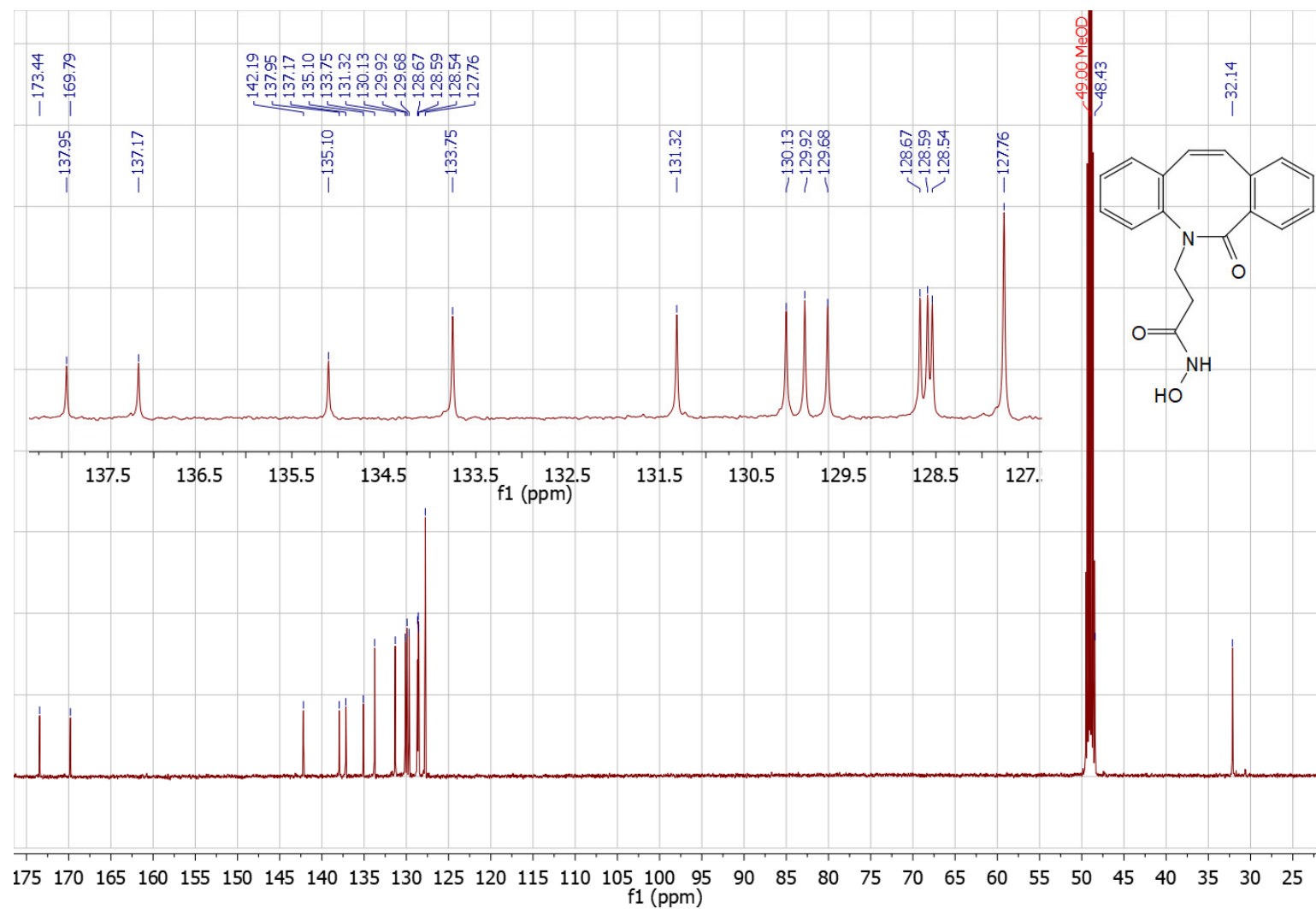


Figure S65. ^{13}C NMR spectrum of *N*-hydroxy-3-(6-oxodibenzo[*b,f*]azocin-5(6*H*)-yl)propanamide (**7h**).

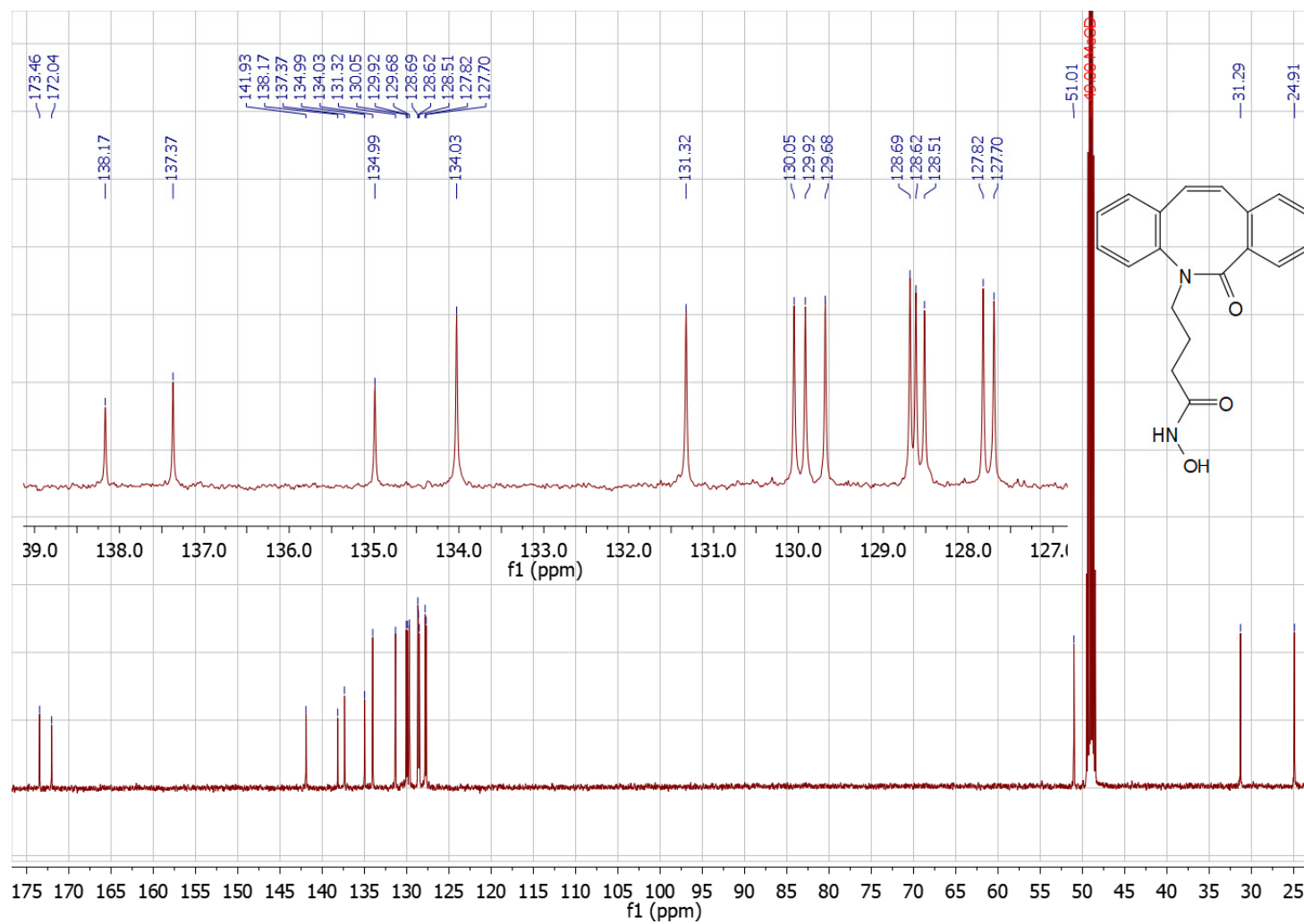


Figure S66. ¹³C NMR spectrum of *N*-hydroxy-4-(6-oxodibenzo[*b,f*]azocin-5(6*H*)-yl)butanamide (7i).

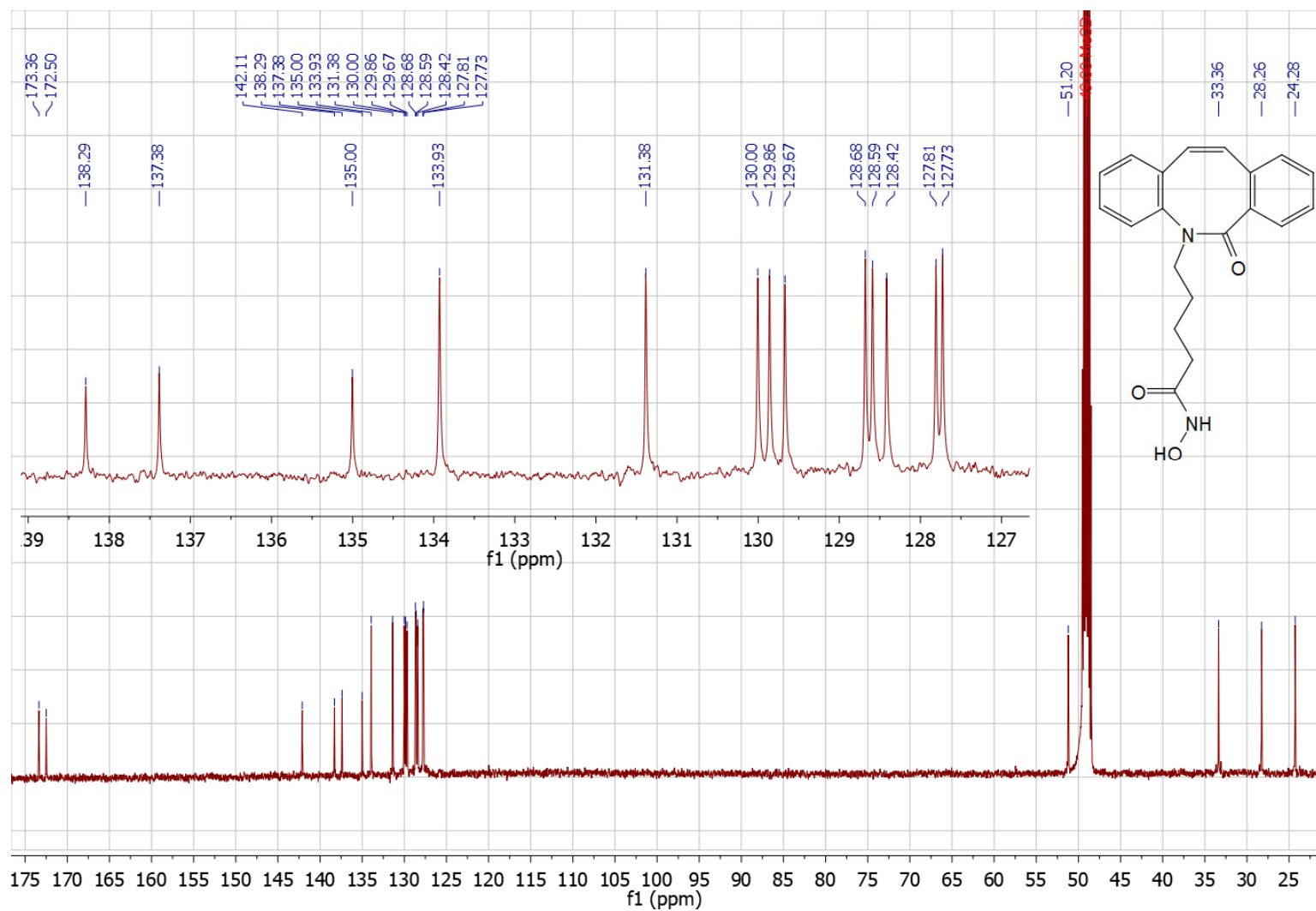


Figure S67. ^{13}C NMR spectrum of *N*-hydroxy-5-(6-oxodibenzo[*b,f*]azocin-5(6*H*)-yl)pentanamide (**7j**).

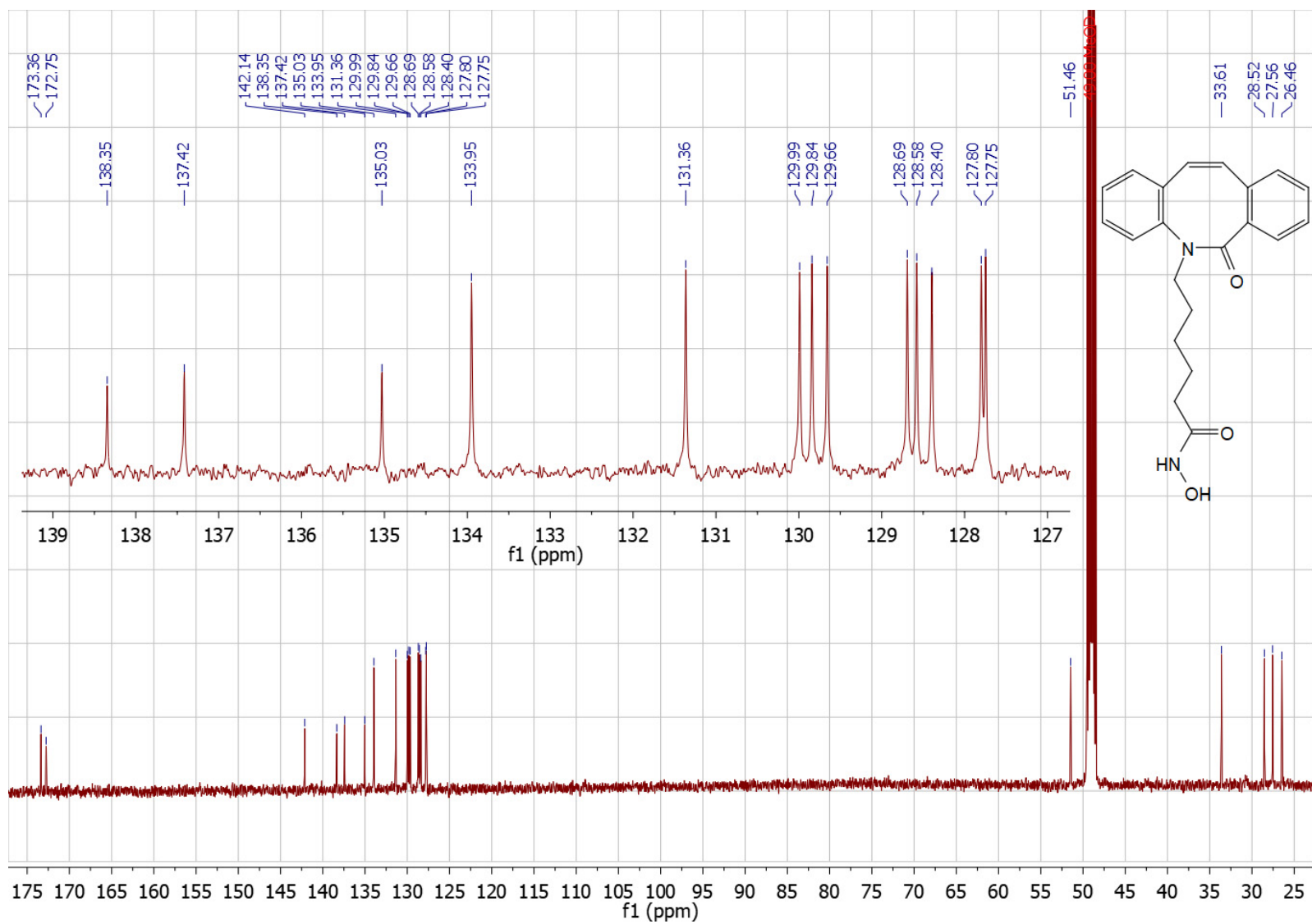


Figure S68. ¹³C NMR spectrum of N-hydroxy-6-(6-oxodibenzo[*b,f*]azocin-5(6*H*)-yl)hexanamide (7k).

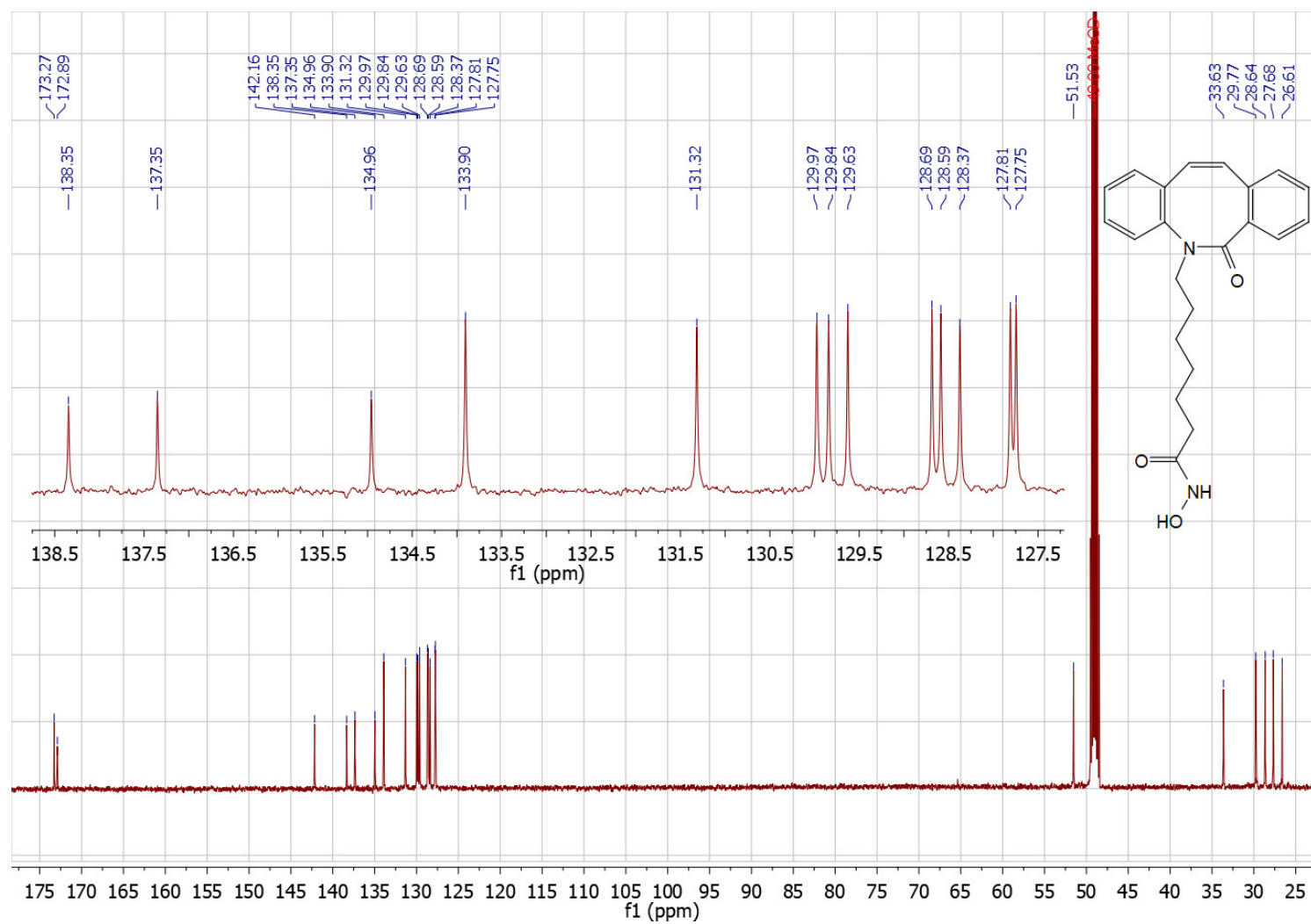


Figure S69. ¹³C NMR spectrum of *N*-hydroxy-7-(6-oxodibenzo[*b,f*]azocin-5(6*H*)-yl)heptanamide (71).

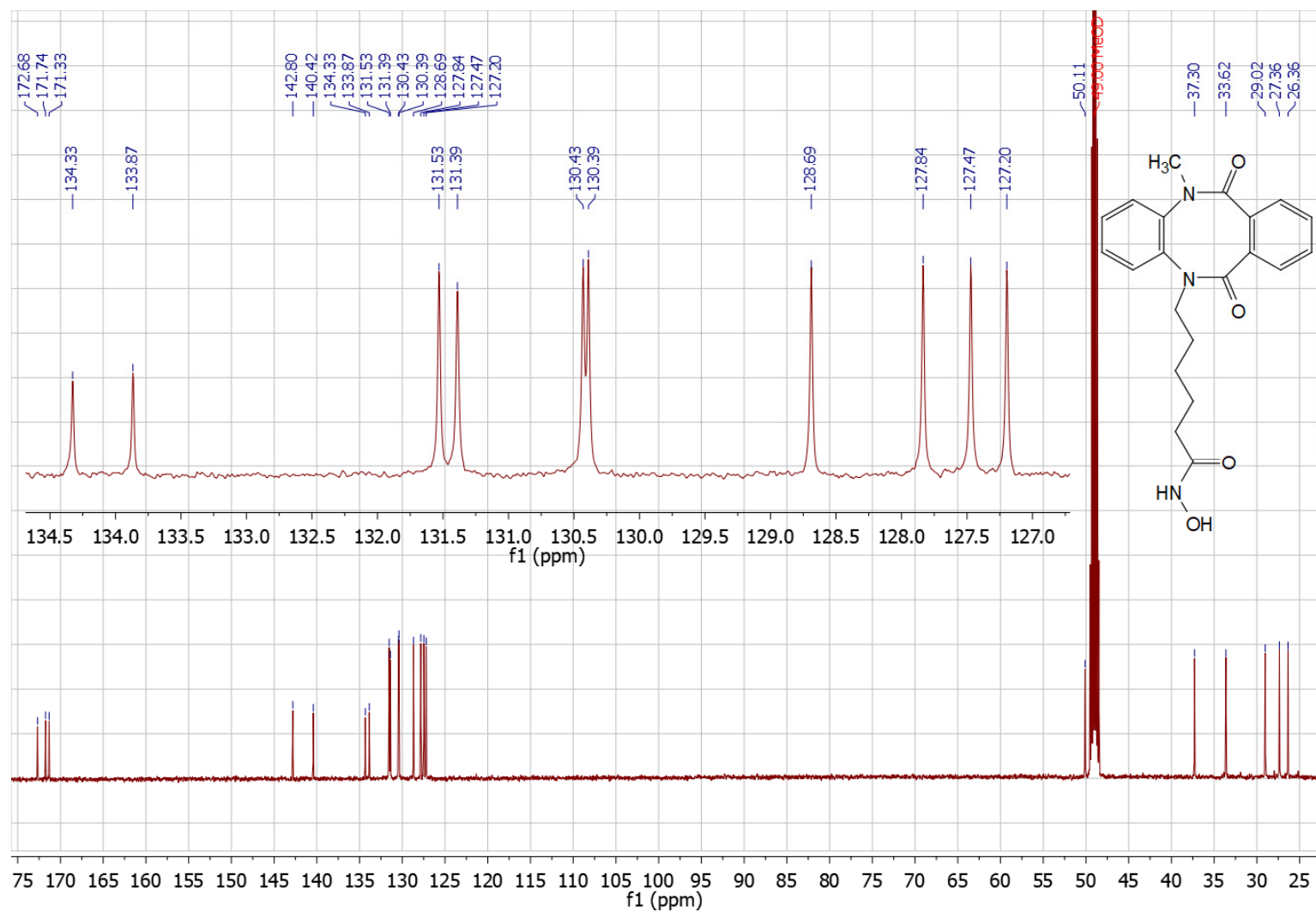


Figure S70. ^{13}C NMR spectrum of *N*-hydroxy-6-(12-methyl-6,11-dioxo-11,12-dihydrodibenzo[*b,f*][1,4]diazocin-5(6*H*)-yl)hexanamide (**7m**).

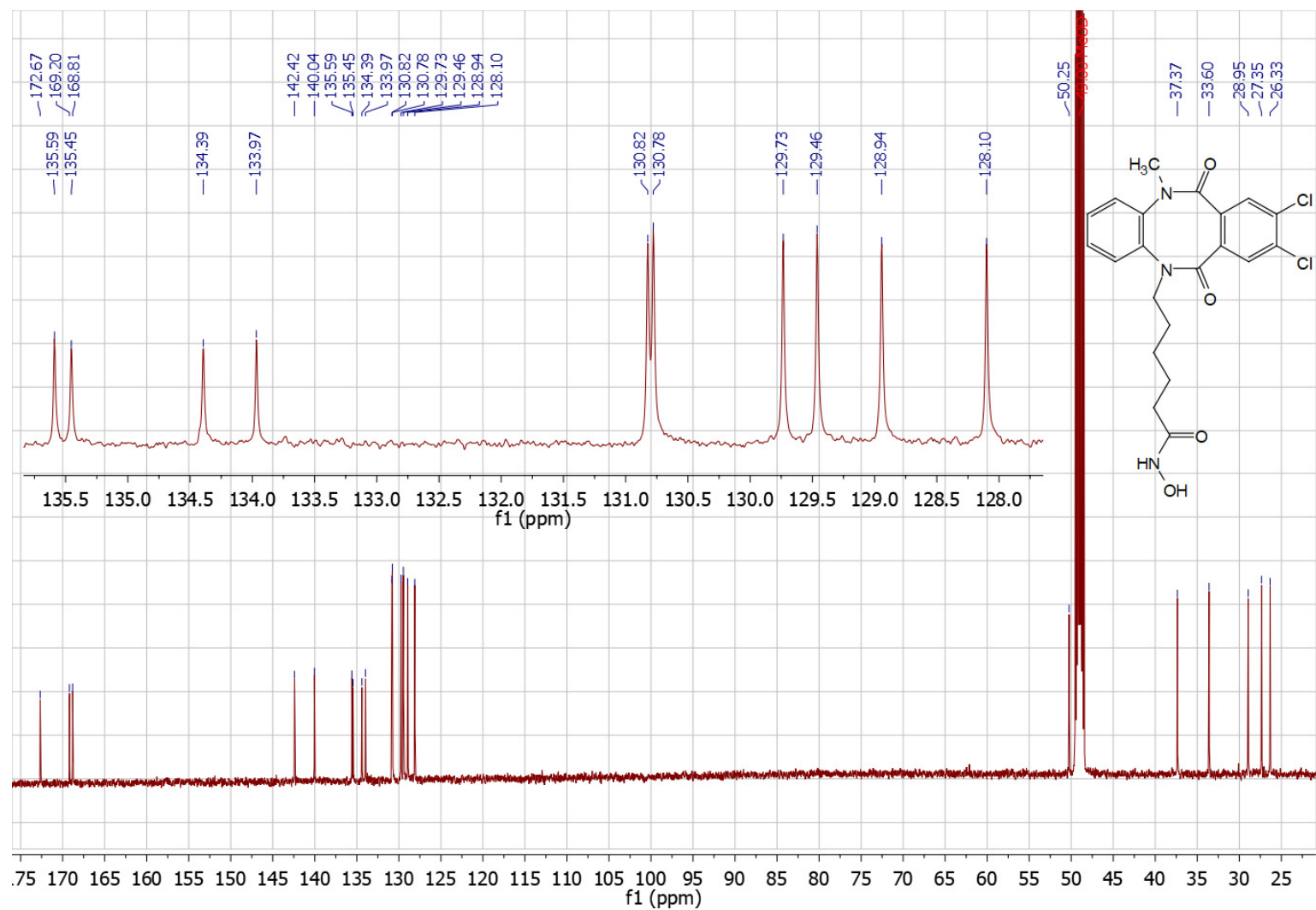


Figure S71. ^{13}C NMR spectrum of *N*-hydroxy-6-(8,9-dichloro-12-methyl-6,11-dioxo-11,12-dihydrodibenzo[*b,f*][1,4]diazocin-5(6*H*)-yl)hexanamide (**7n**).

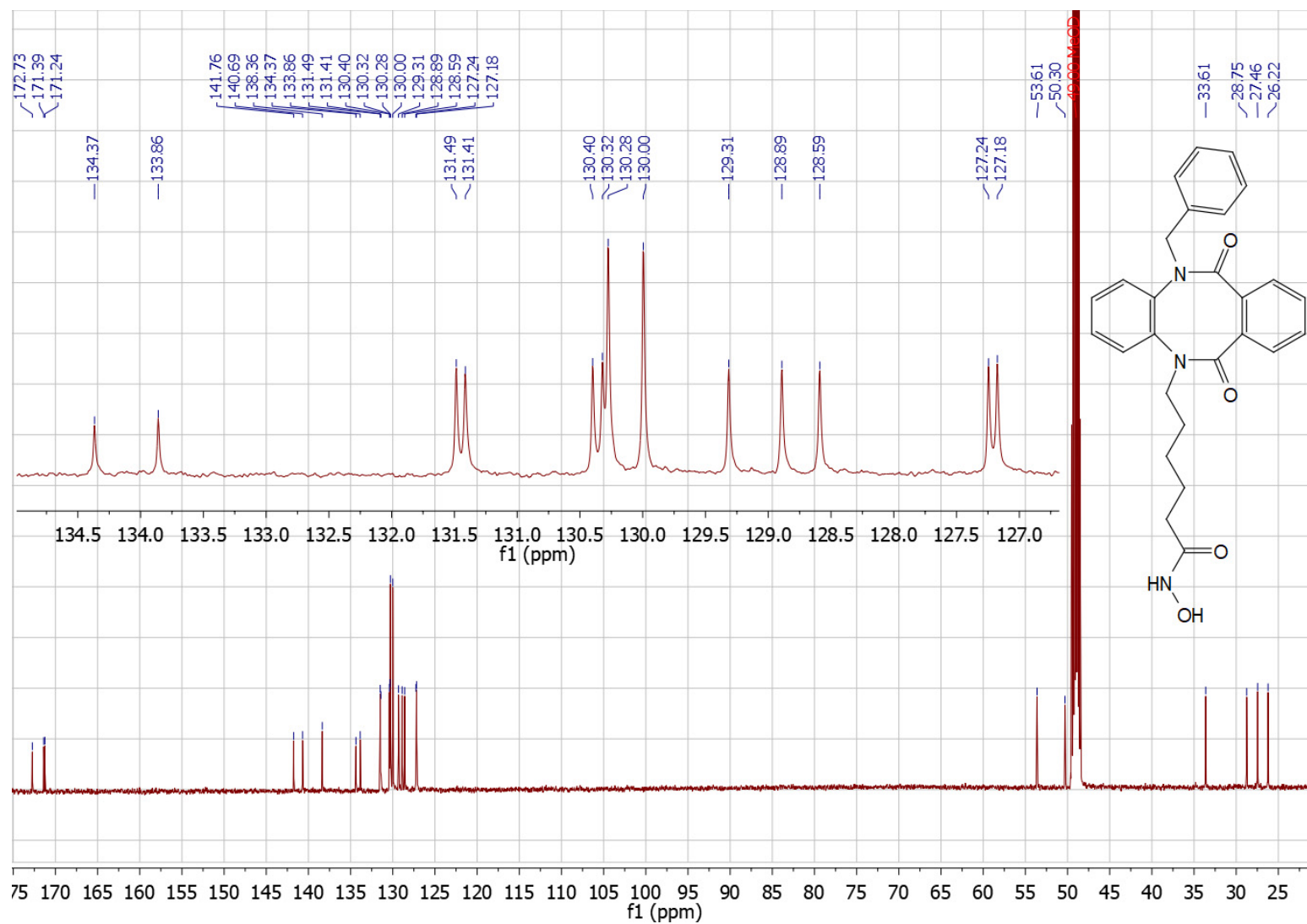


Figure S72. ¹³C NMR spectrum of *N*-hydroxy-6-(12-benzyl-6,11-dioxo-11,12-dihydrodibenzo[*b,f*][1,4]diazocin-5(6*H*)-yl)hexanamide (**7o**).

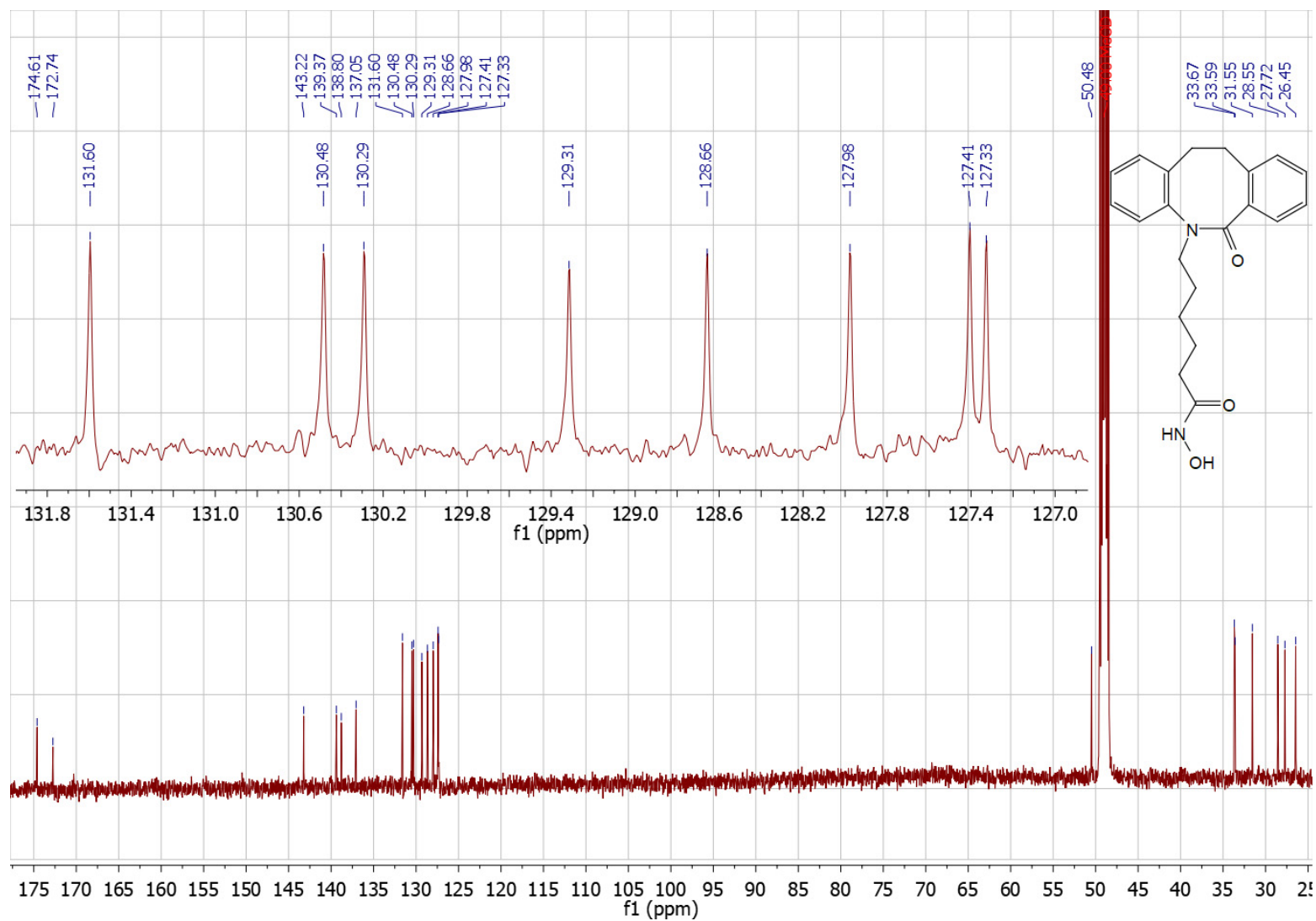


Figure S73. ^{13}C NMR spectrum of *N*-hydroxy-6-(6-oxo-11,12-dihydrodibenzo[*b,f*]azocin-5(6*H*)-yl)hexanamide (7p).

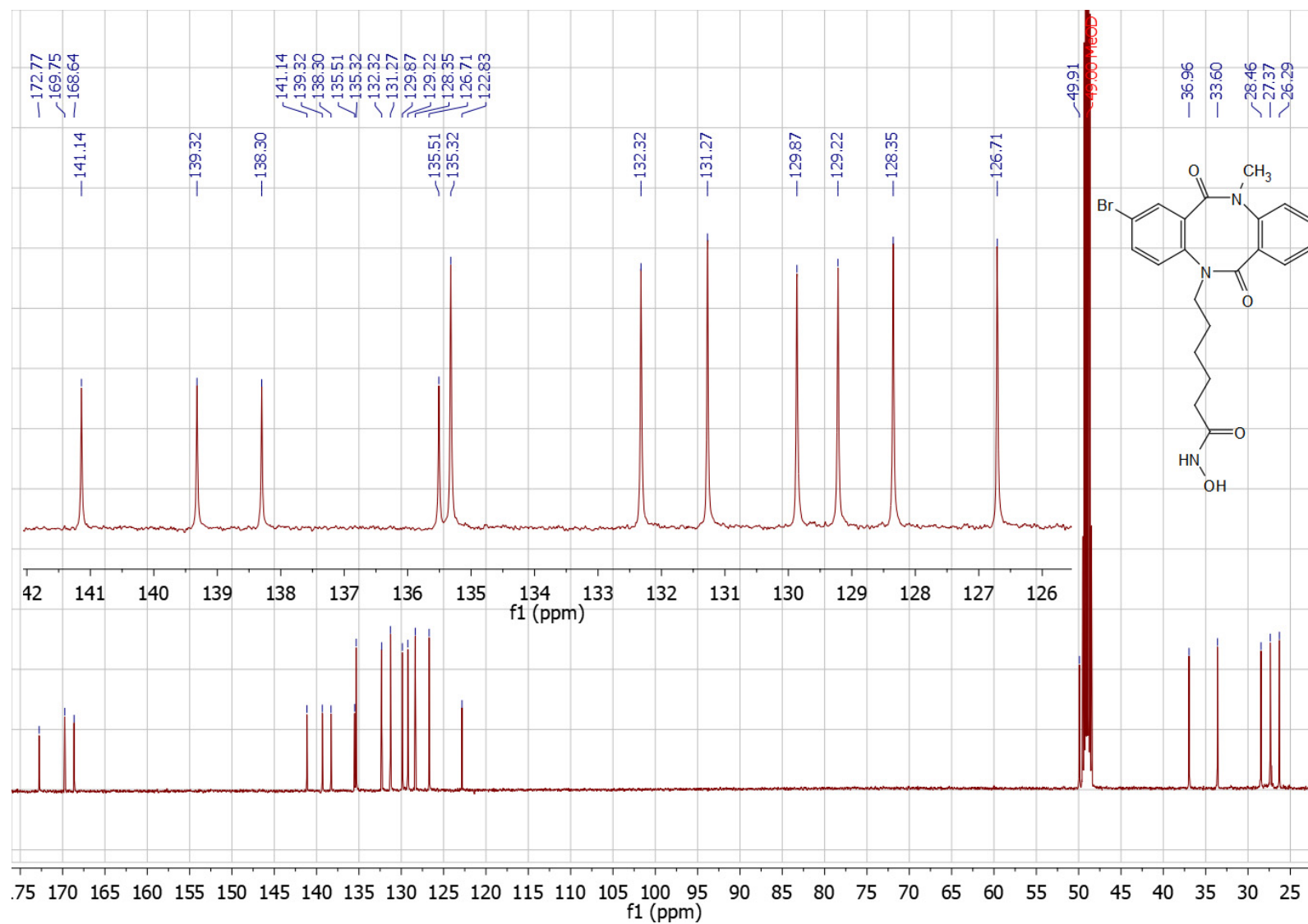


Figure S74. ^{13}C NMR spectrum of *N*-hydroxy-6-(2-bromo-11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)hexanamide (**7r**).

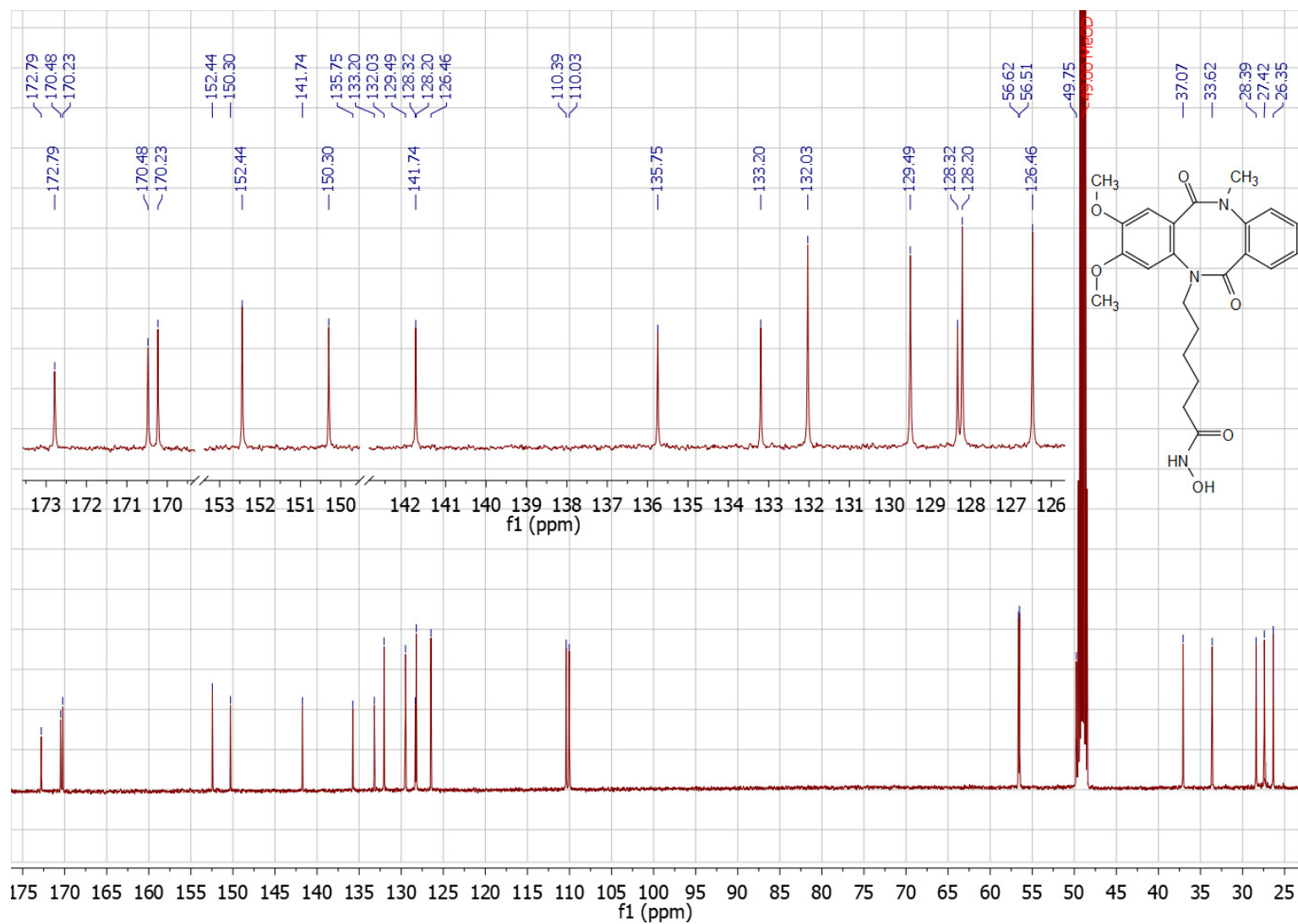


Figure S75. ¹³C NMR spectrum of *N*-hydroxy-6-(2,3-dimethoxy-11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)hexanamide (**7s**).

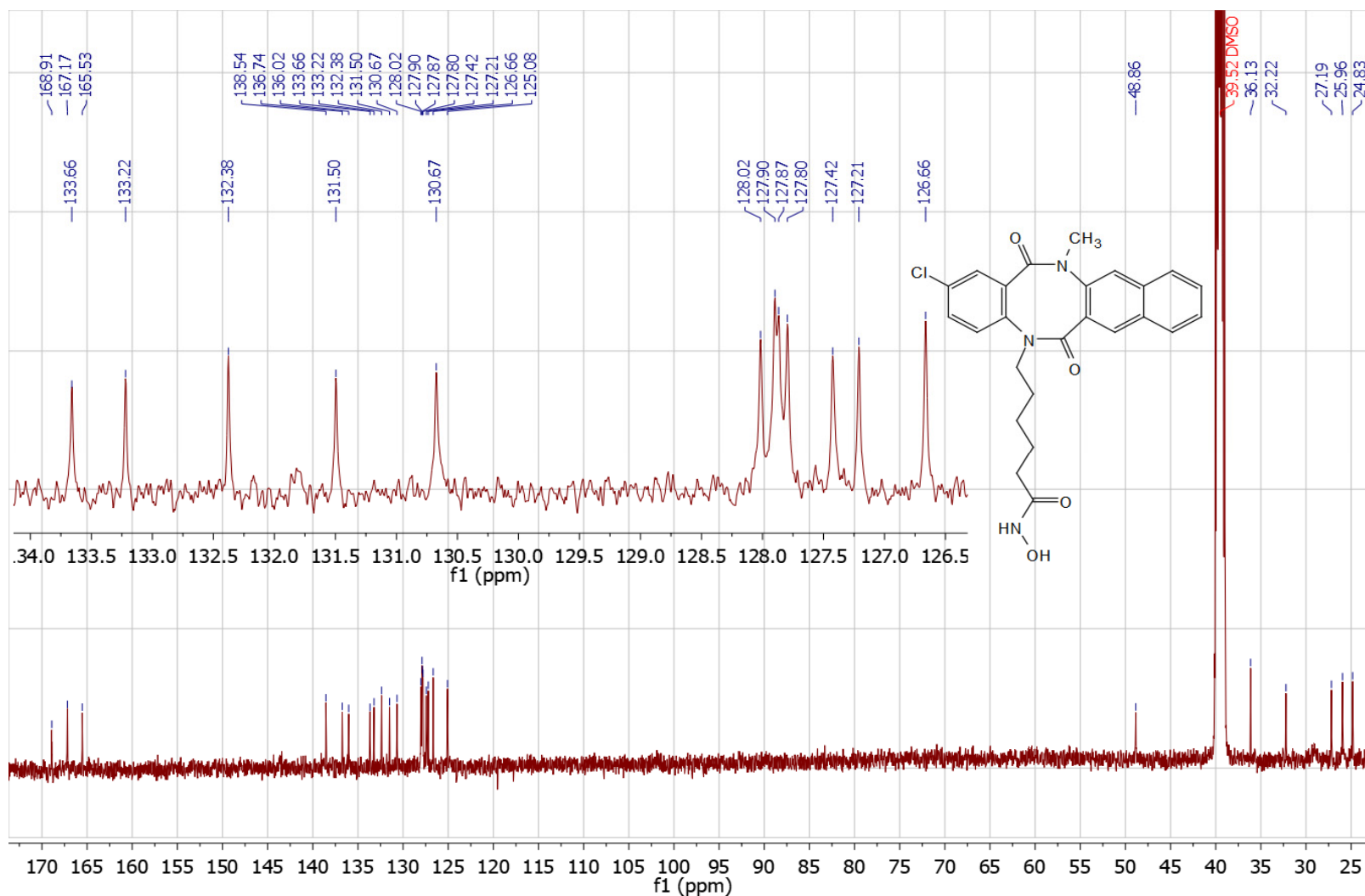


Figure S76. ¹³C NMR spectrum of *N*-hydroxy-6-(5-methyl-6,14-dioxo-5,14-dihydrobenzonaphtho[2,3-*f*][1,5]diazocin-13(6*H*)-yl)hexanamide (**7t**).

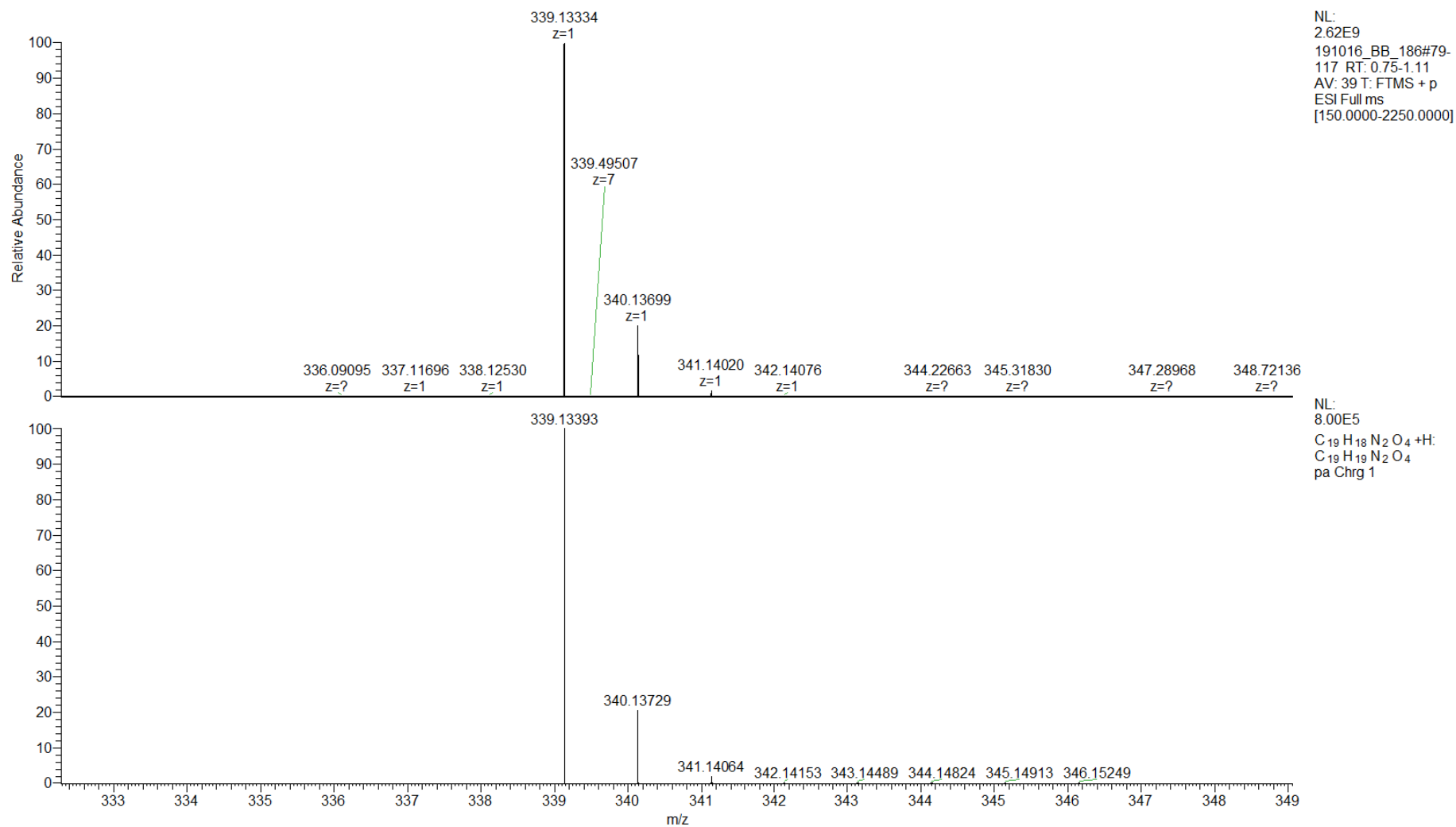


Figure S77. ESI HRMS spectrum of ethyl 2-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)acetate (**10a**).

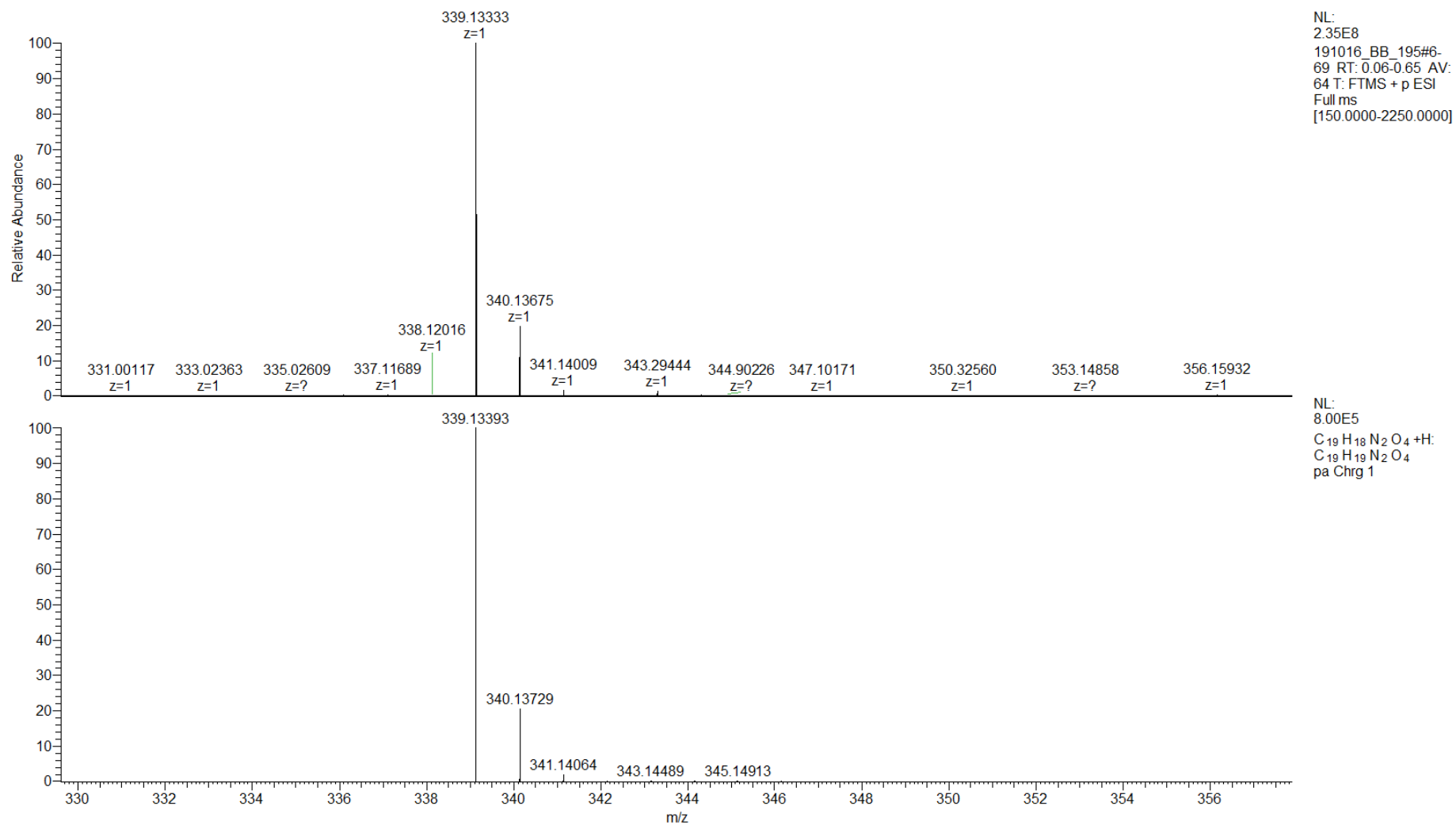


Figure S78. ESI HRMS spectrum of ethyl 3-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)propanoate (**10b**).

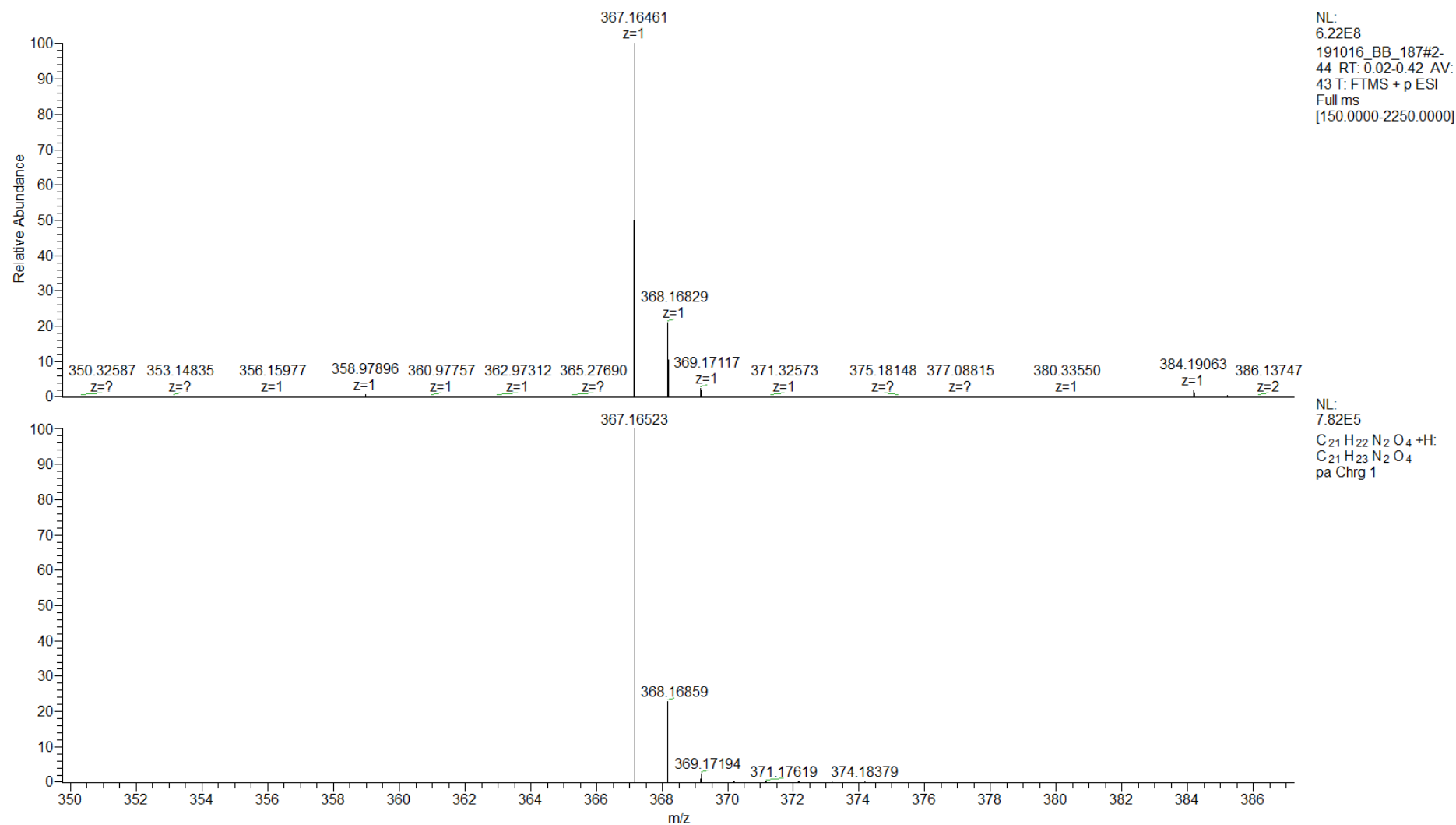


Figure S79. ESI HRMS spectrum of ethyl 4-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)butanoate (**10c**).

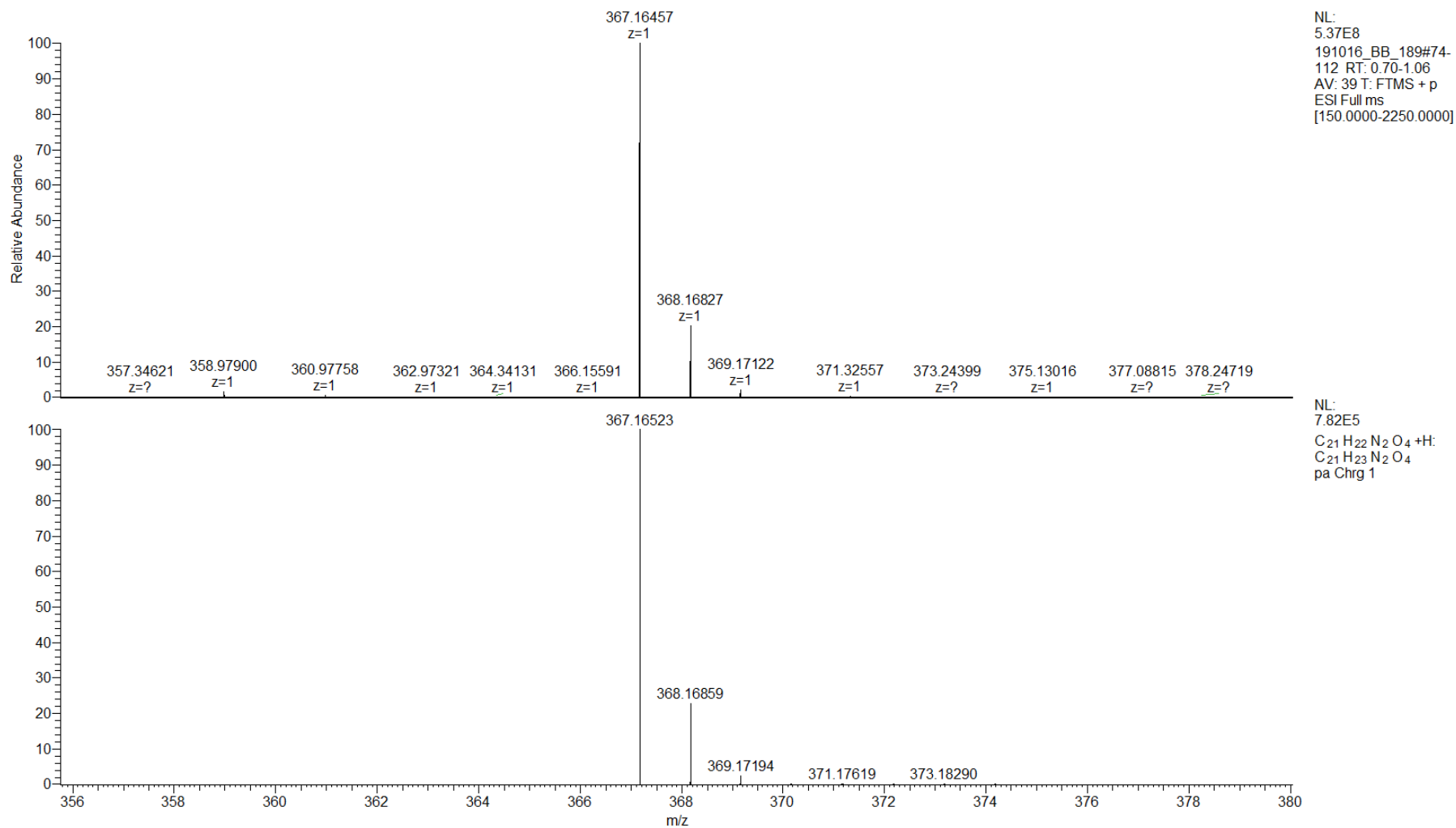


Figure S80. ESI HRMS spectrum of methyl 5-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)pentanoate (**10d**).

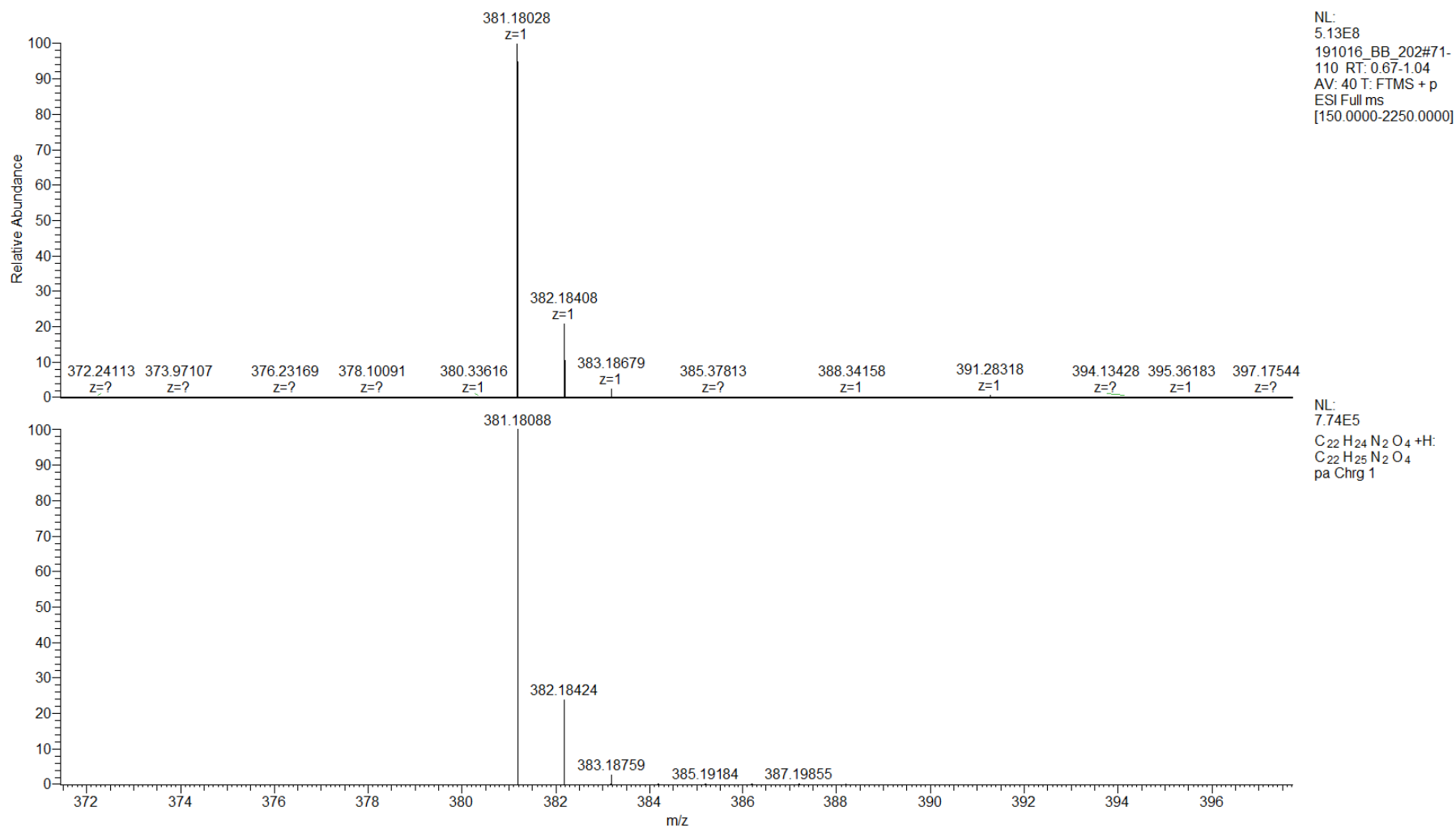


Figure S81. ESI HRMS spectrum of methyl 6-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)hexanoate (**10e**).

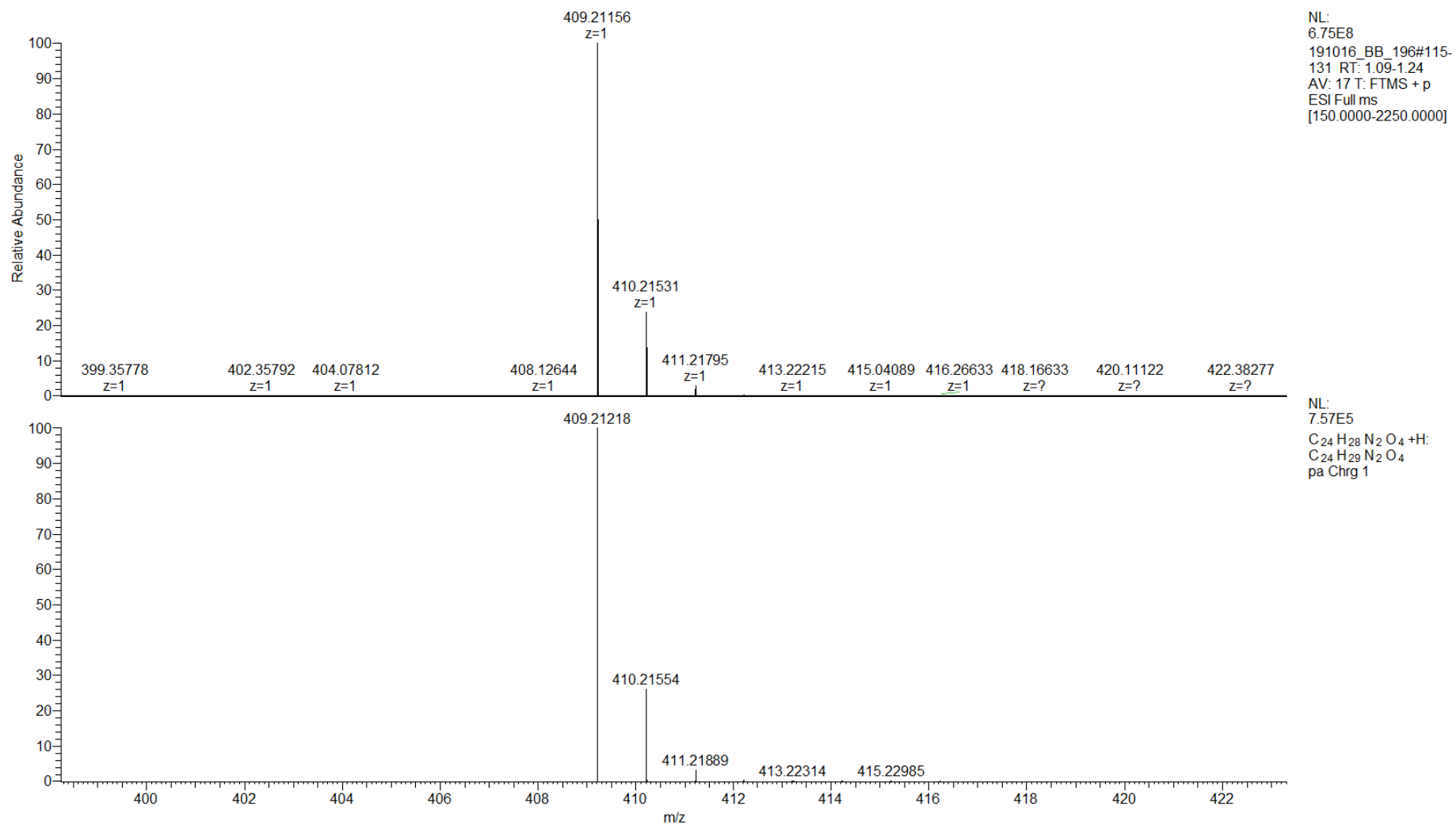


Figure S82. ESI HRMS spectrum of ethyl 7-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)heptanoate (**10f**).

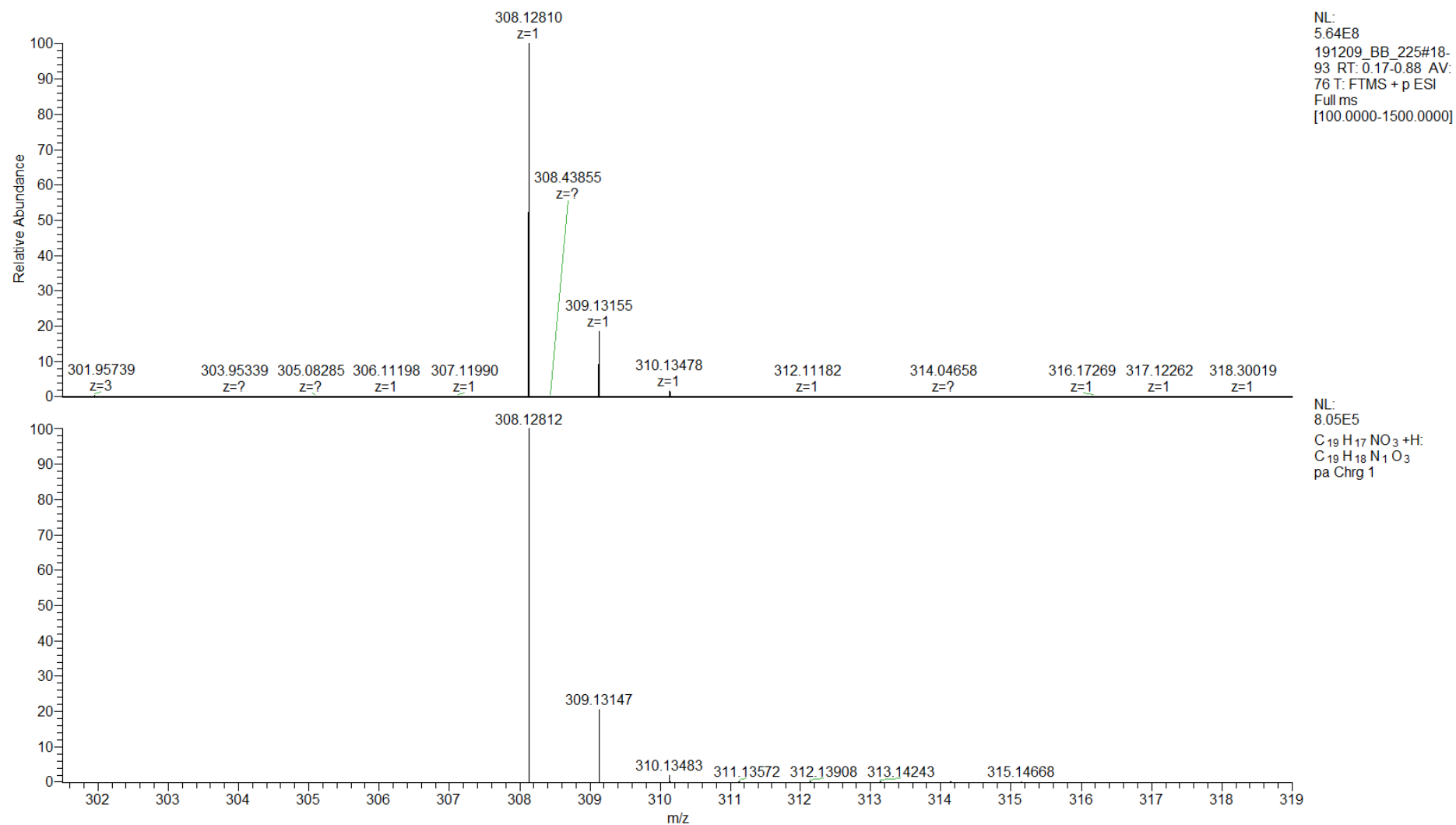


Figure S83. ESI HRMS spectrum of ethyl 2-(6-oxodibenzo[*b,f*]azocin-5(6*H*)-yl)acetate (**10g**).

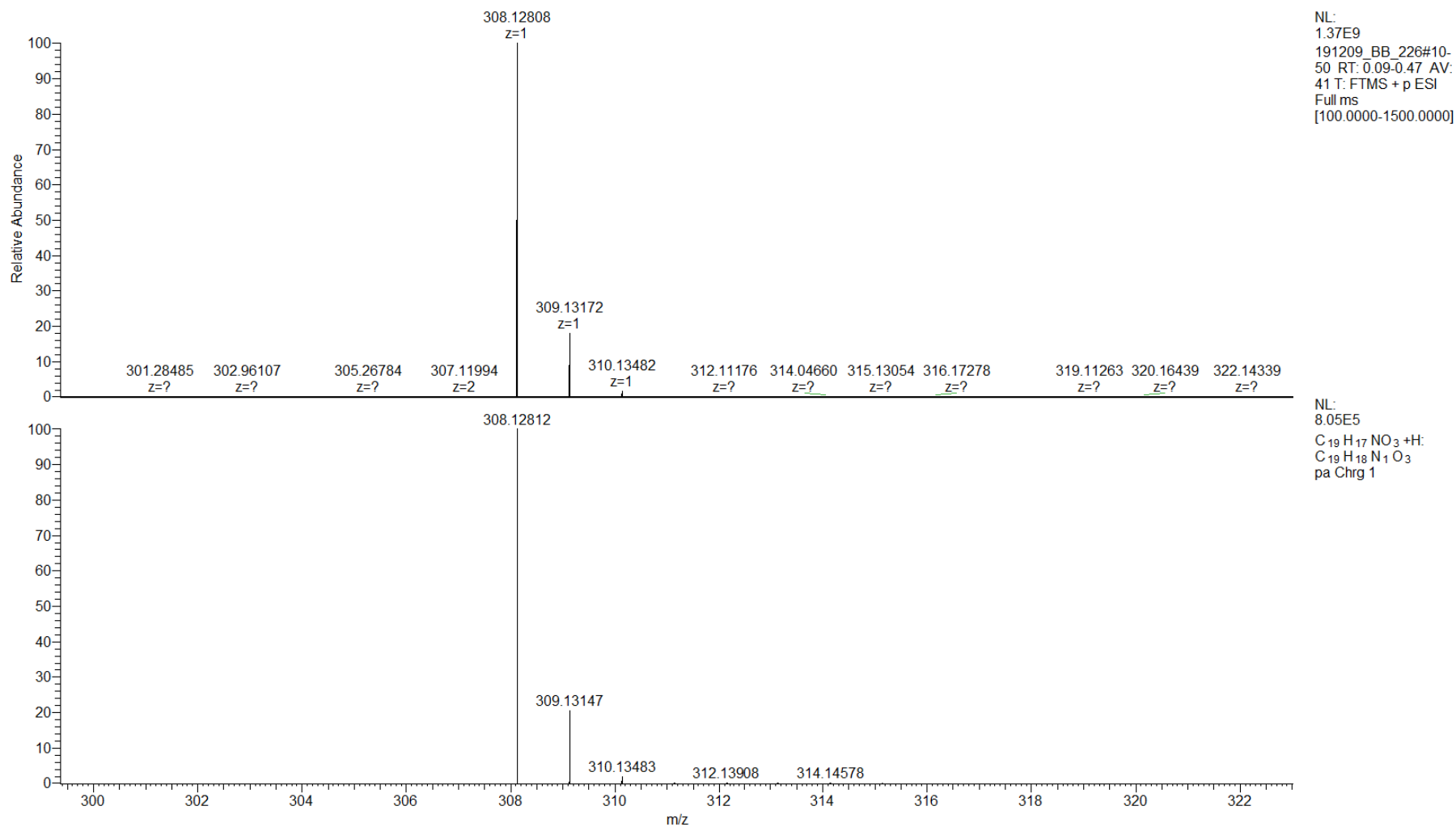


Figure S84. ESI HRMS spectrum of methyl 3-(6-oxodibenzo[*b,f*]azocin-5(6*H*)-yl)propanoate (**10h**).

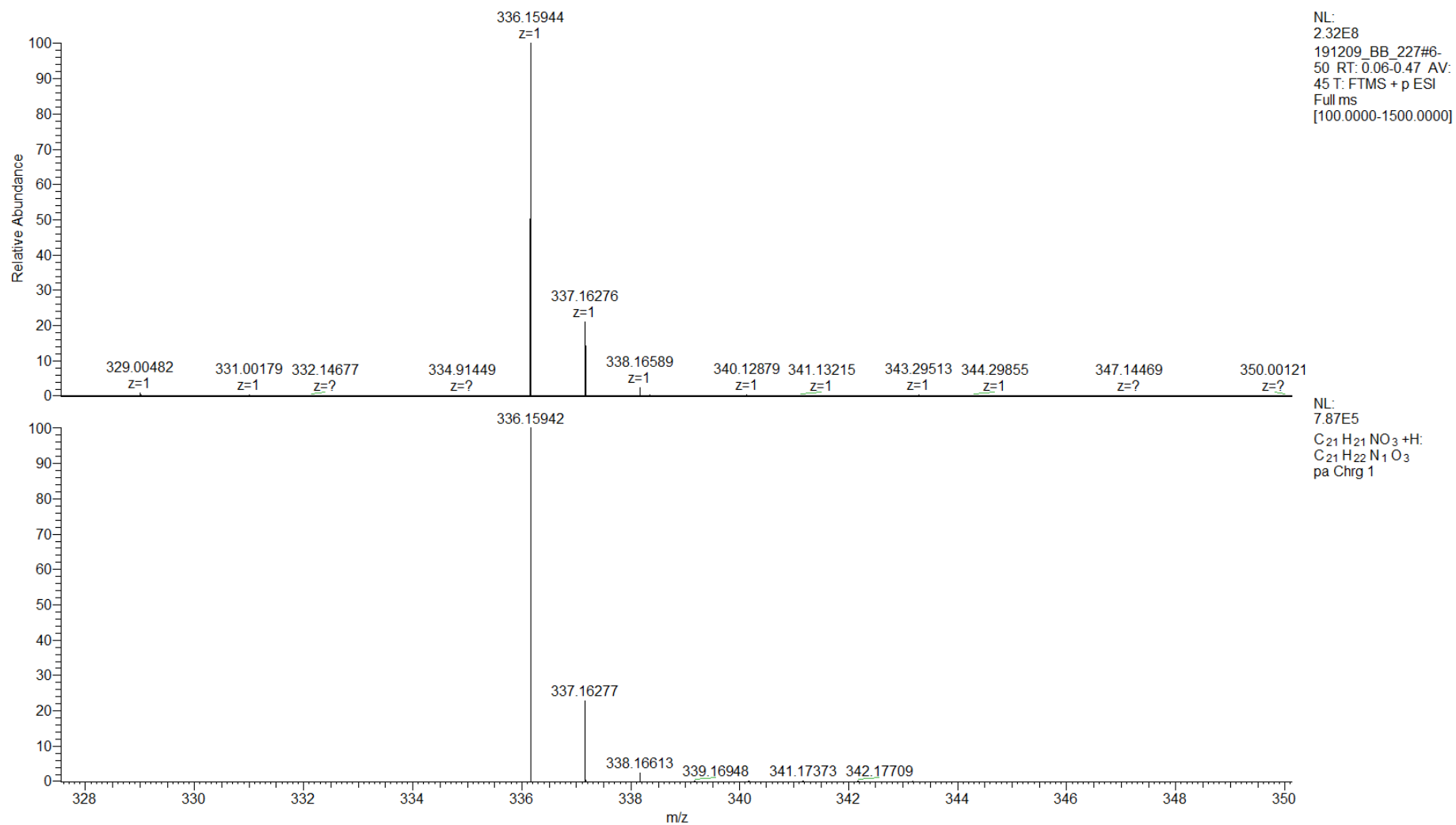


Figure S85. ESI HRMS spectrum of ethyl 4-(6-oxodibenzo[*b,f*]azocin-5(6*H*)-yl)butanoate (**10i**).

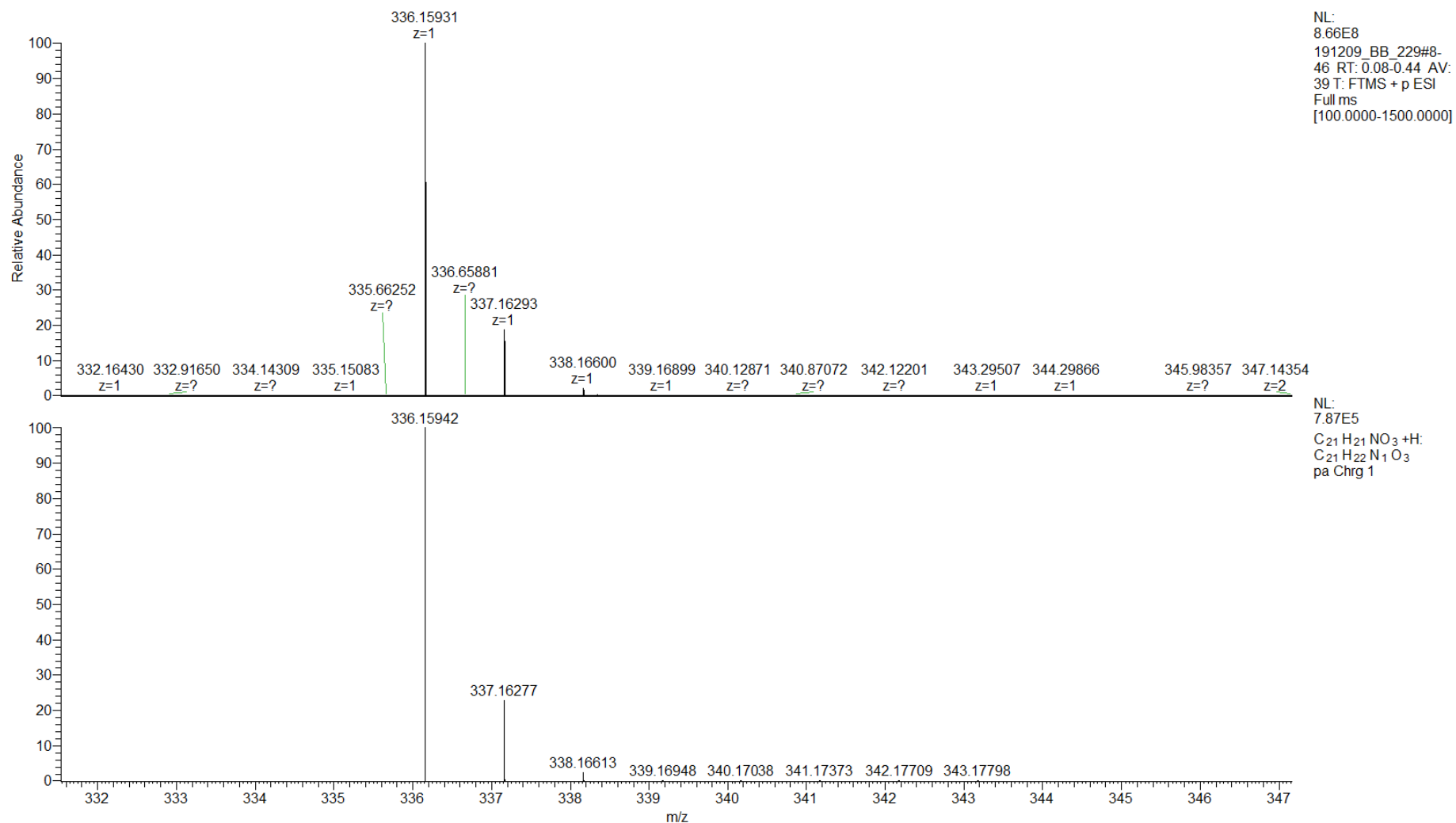


Figure S86. ESI HRMS spectrum of methyl 5-(6-oxodibenzo[*b,f*]azocin-5(6*H*)-yl)pentanoate (**10j**).

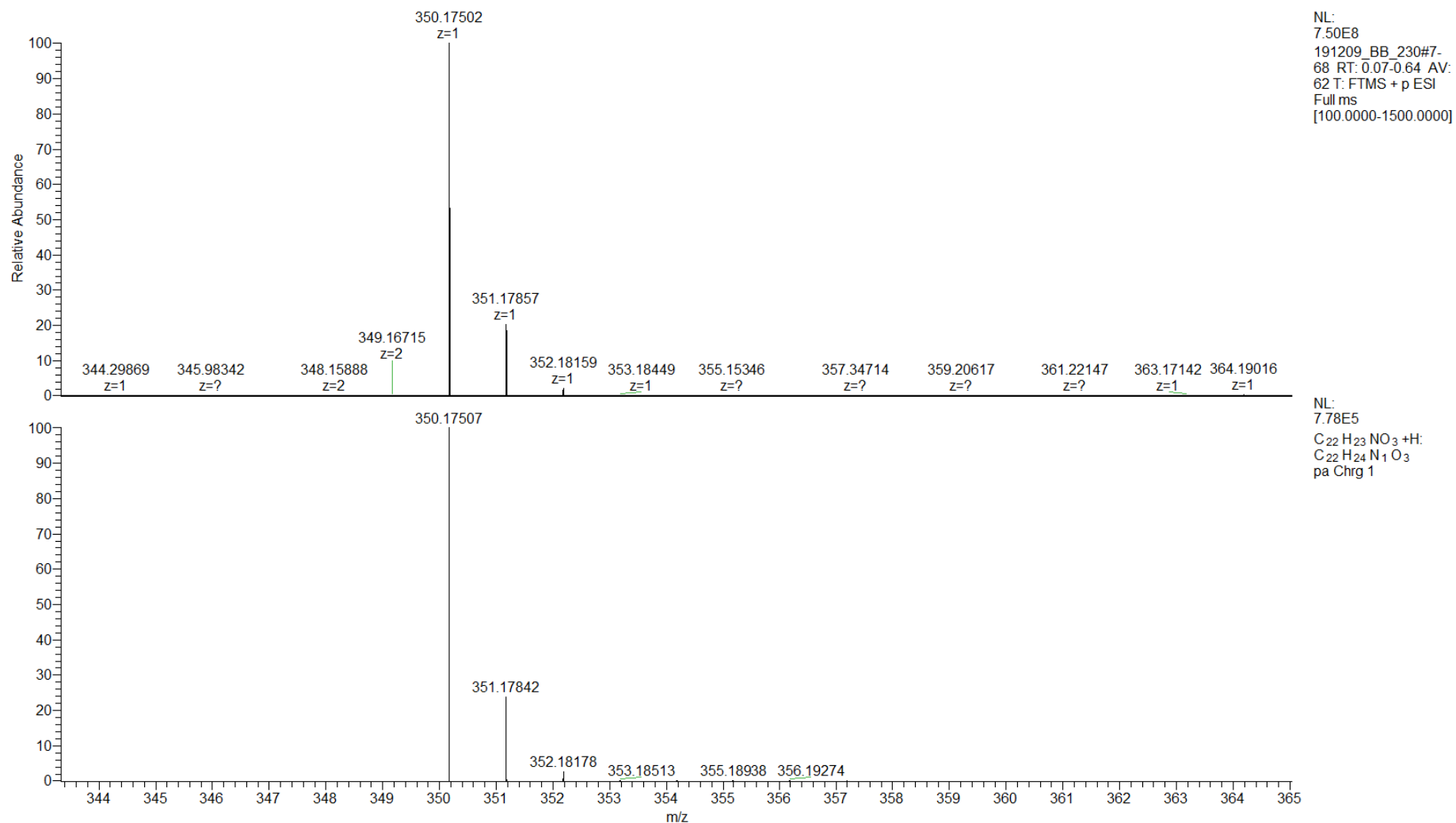


Figure S87. ESI HRMS spectrum of methyl 6-(6-oxodibenzo[*b,f*]azocin-5(6*H*)-yl)hexanoate (**10k**).

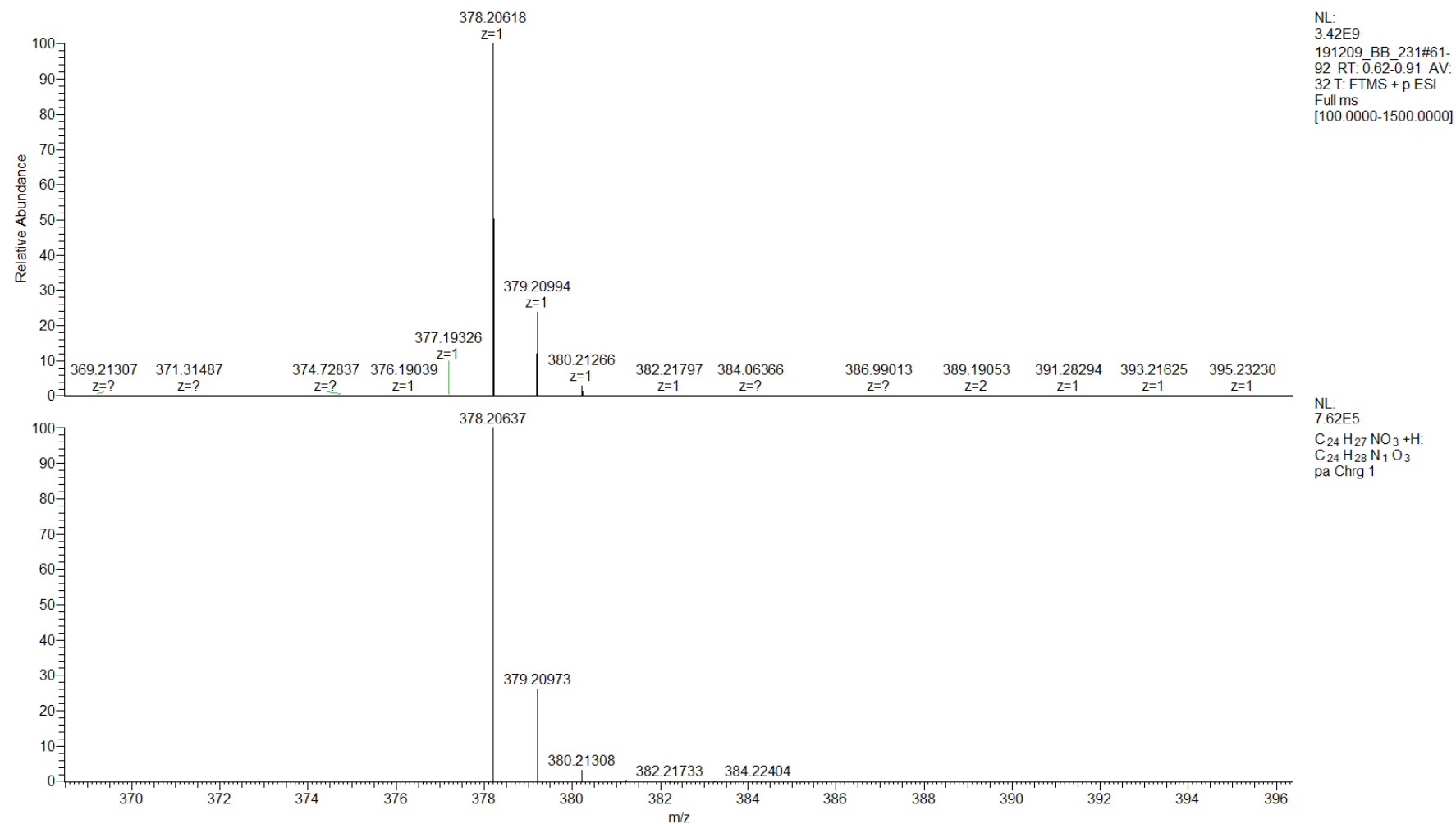


Figure S88. ESI HRMS spectrum of ethyl 7-(6-oxodibenzo[*b,f*]azocin-5(6*H*)-yl)heptanoate (**101**).

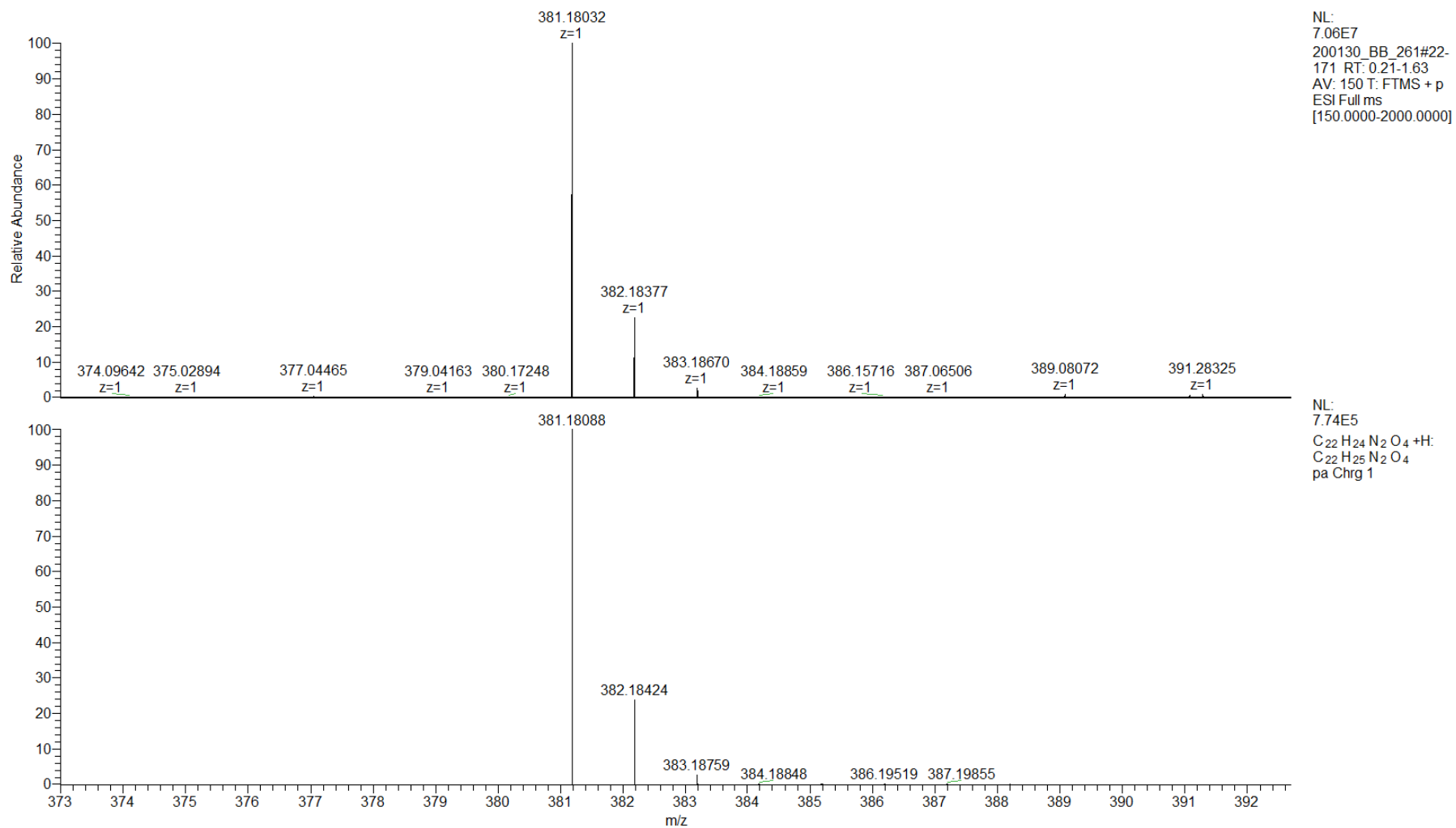


Figure S89. ESI HRMS spectrum of methyl 6-(12-methyl-6,11-dioxo-11,12-dihydrodibenzo[*b,f*][1,4]diazocin-5(6*H*)-yl)hexanoate (**10m**).

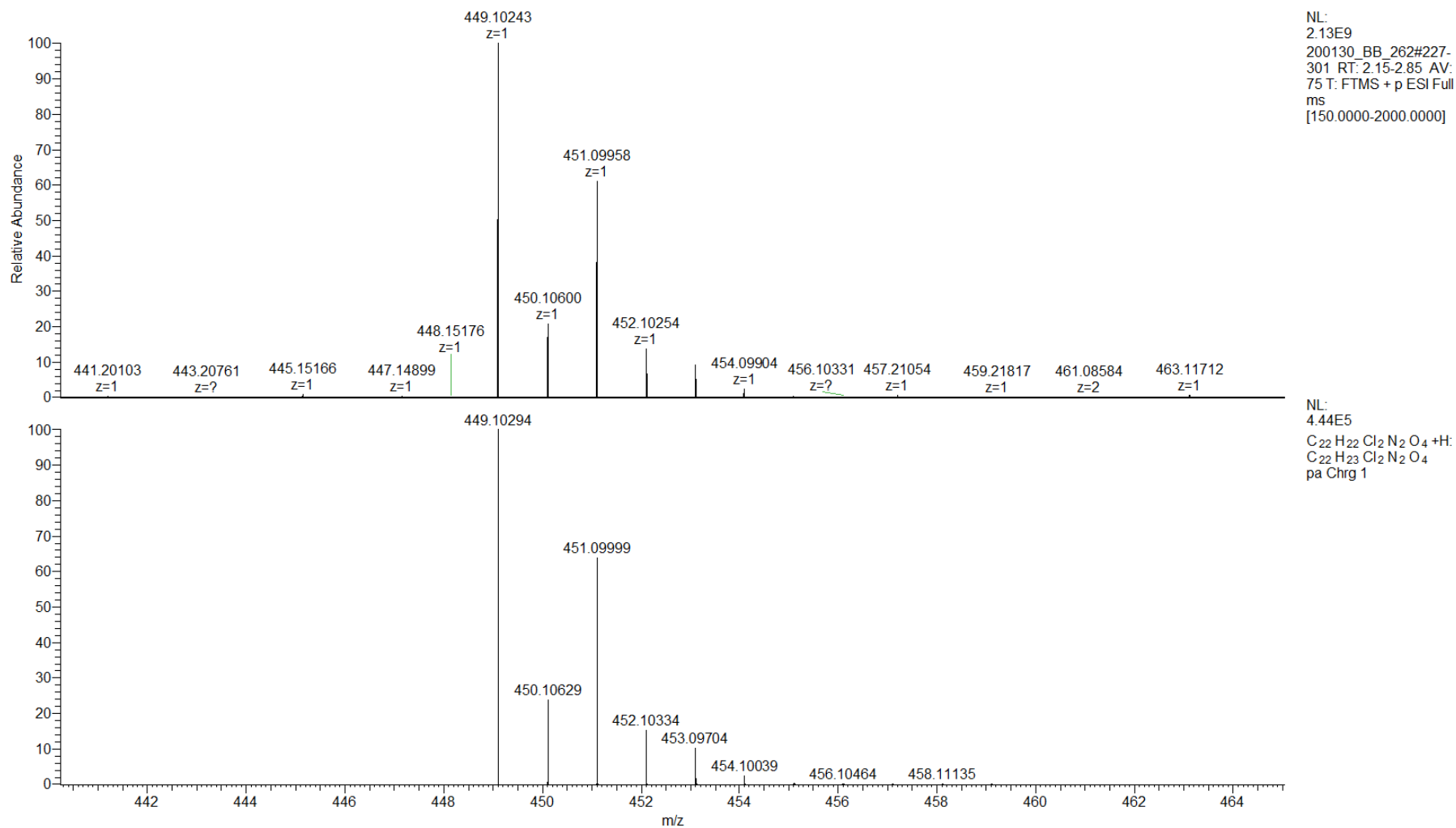


Figure S90. ESI HRMS spectrum of methyl 6-(8,9-dichloro-12-methyl-6,11-dioxo-11,12-dihydrodibenzo[*b,f*][1,4]diazocin-5(6*H*)-yl) hexanoate (**10n**).

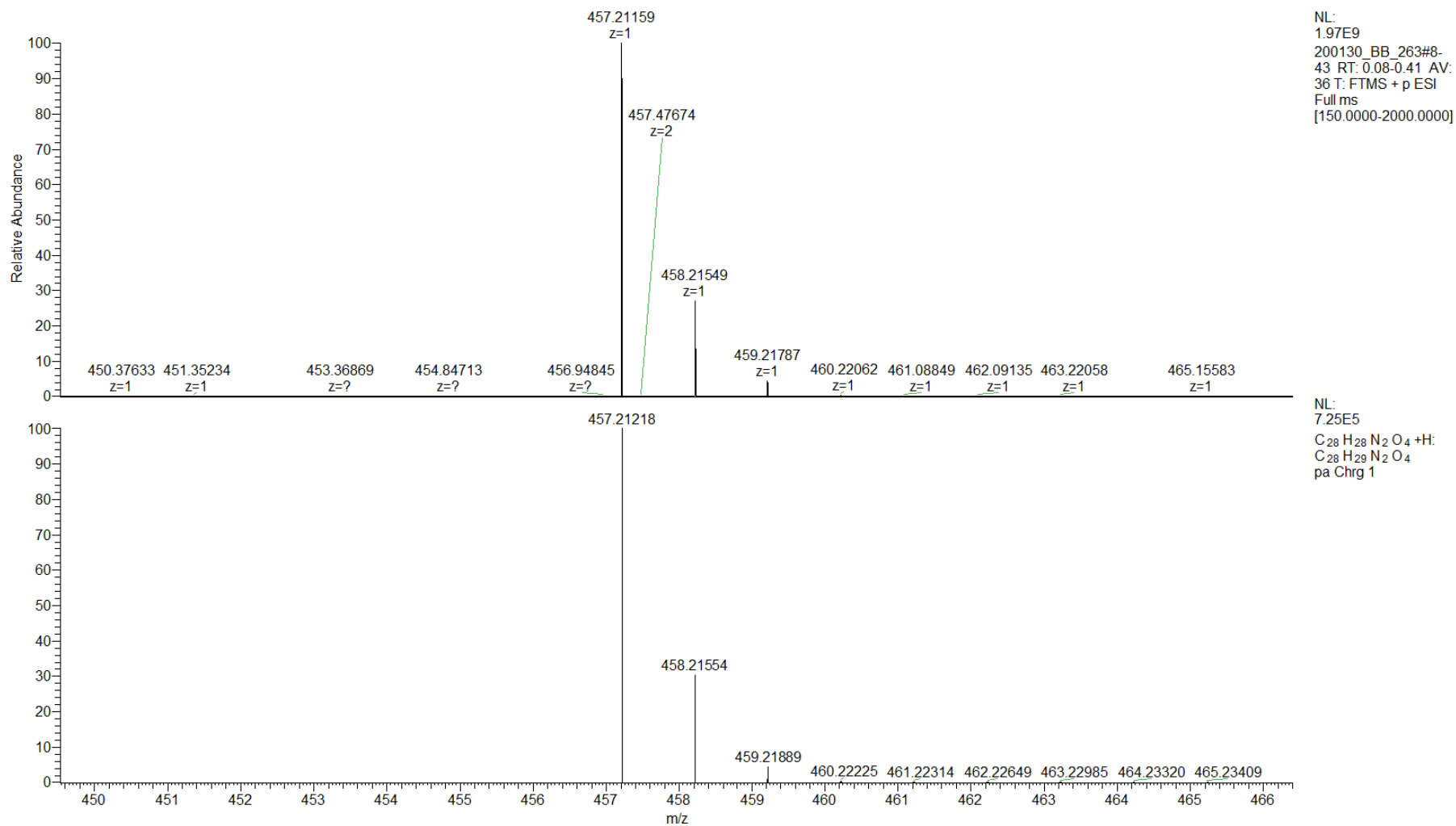


Figure S91. ESI HRMS spectrum of methyl 6-(12-benzyl-6,11-dioxo-11,12-dihydrodibenzo[*b,f*][1,4]diazocin-5(6*H*)-yl)hexanoate (**10o**).

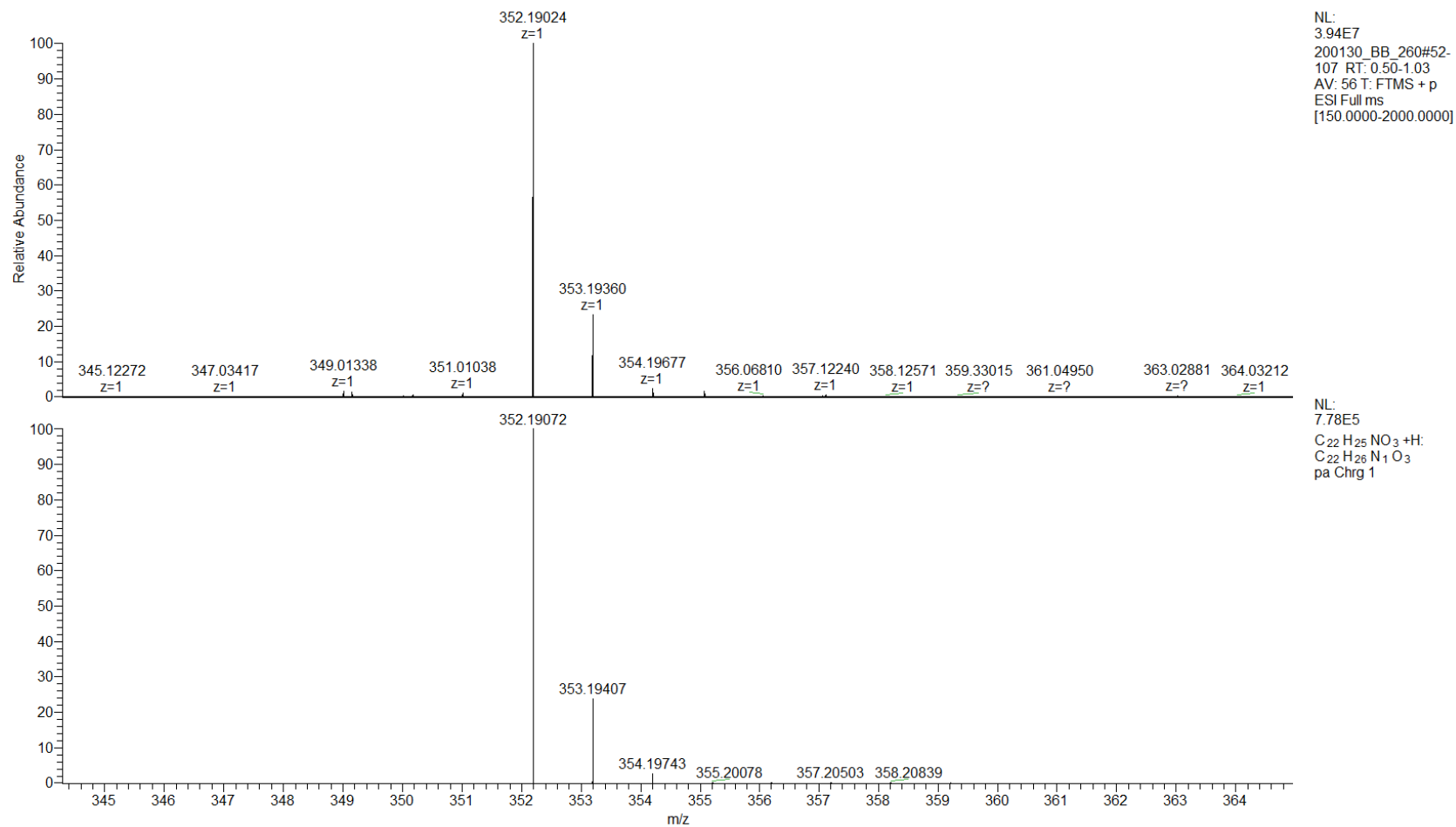


Figure S92. ESI HRMS spectrum of methyl 6-(6-oxo-11,12-dihydrodibenzo[*b,f*]azocin-5(6*H*)-yl)hexanoate (**10p**).

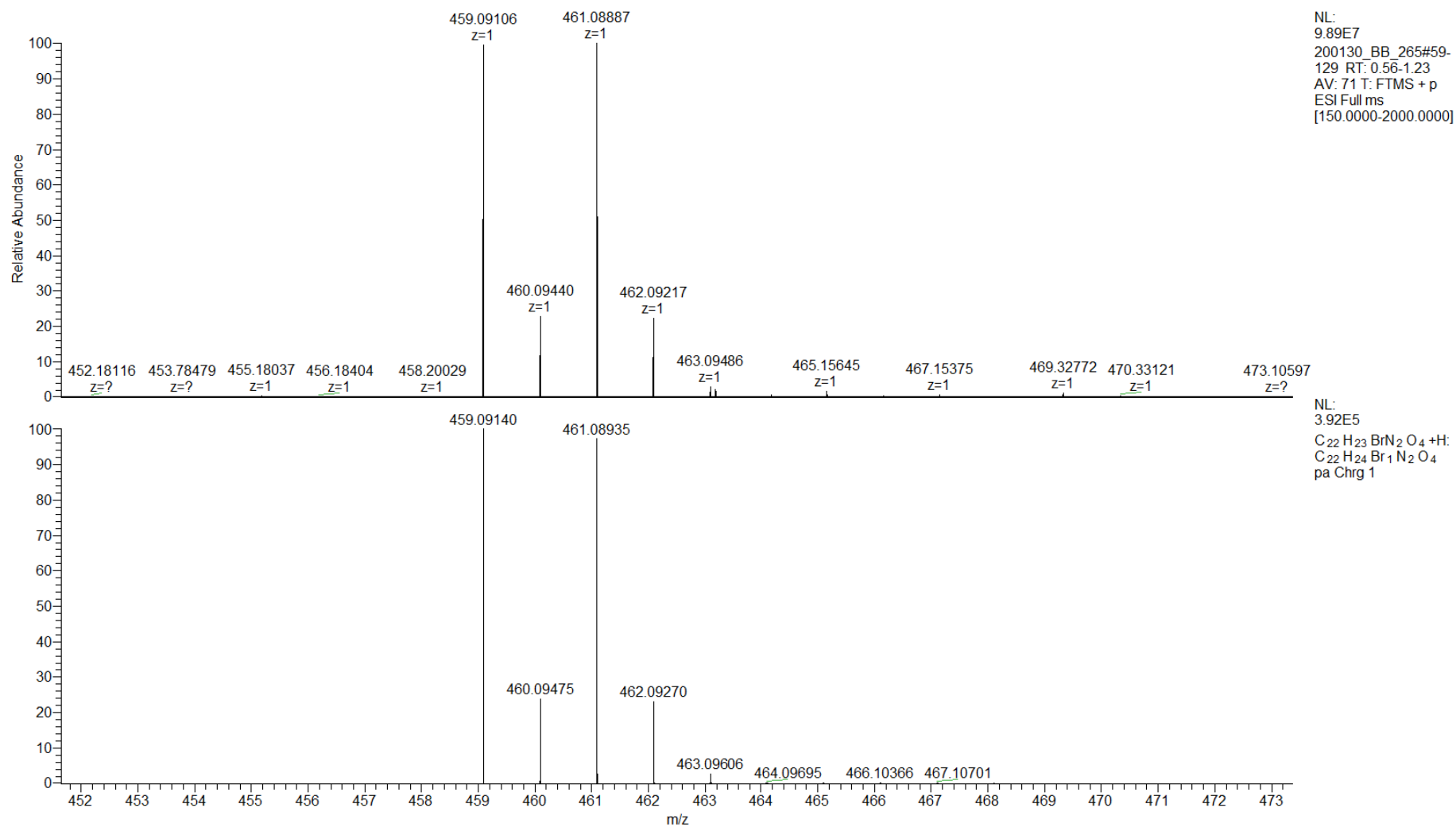


Figure S93. ESI HRMS spectrum of methyl 6-(2-bromo-11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)hexanoate (**10r**).

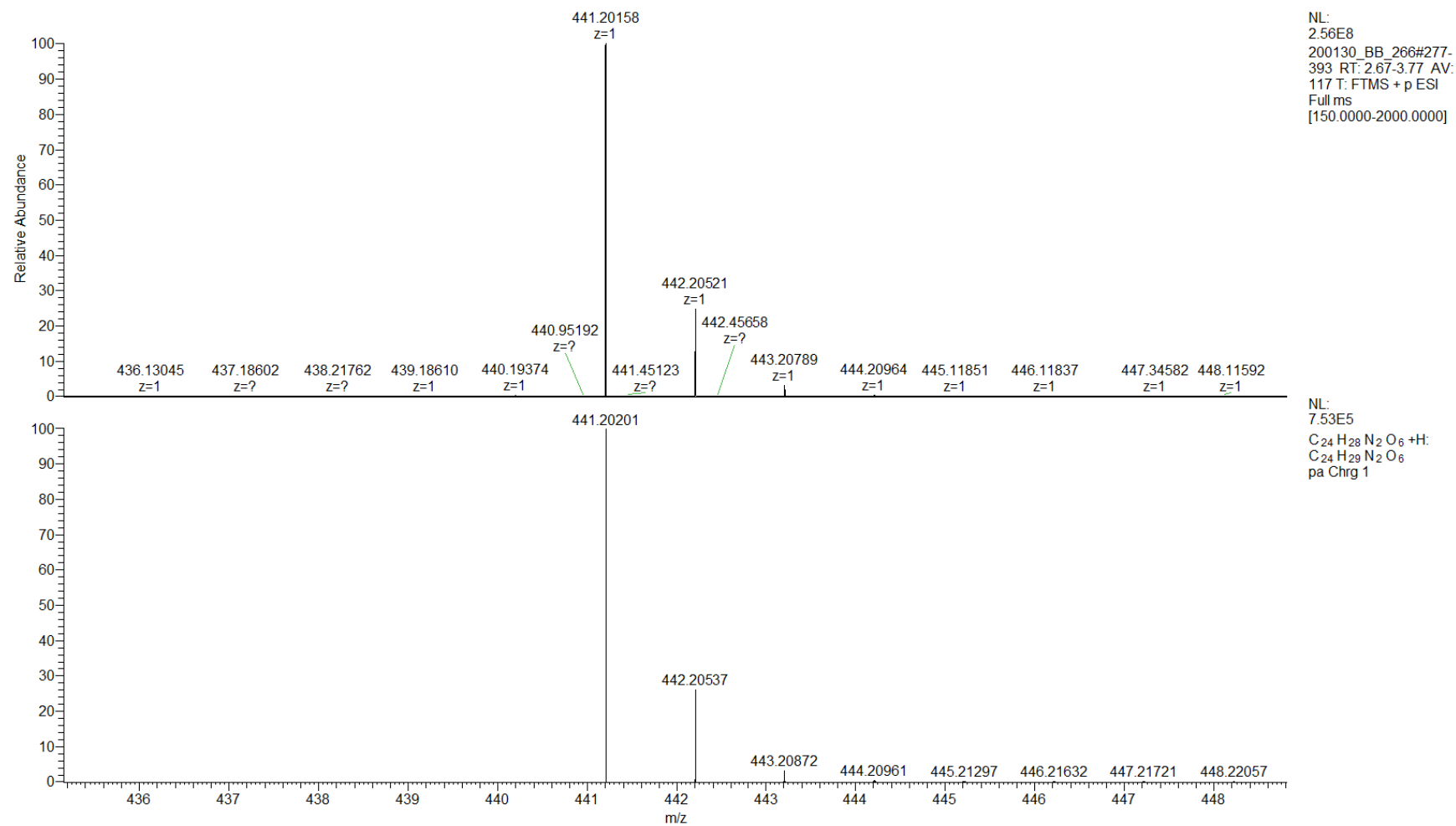


Figure S94. ESI HRMS spectrum of methyl 6-(2,3-dimethoxy-11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)hexanoate (**10s**).

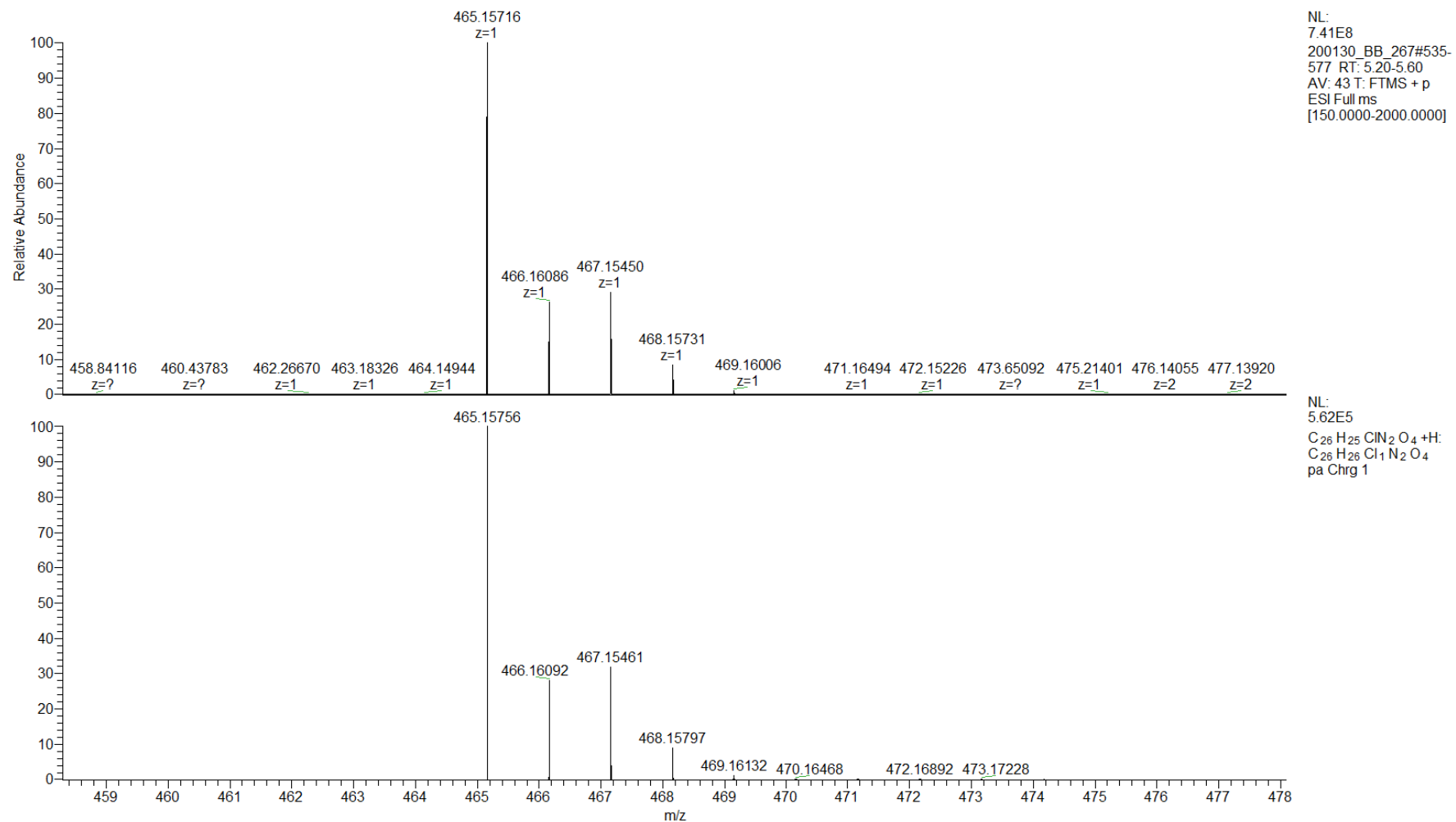


Figure S95. ESI HRMS spectrum of methyl 6-(5-methyl-6,14-dioxo-5,14-dihydrobenzonaphtho[2,3-*f*][1,5]diazocin-13(6*H*)-yl)hexanoate (**10t**).

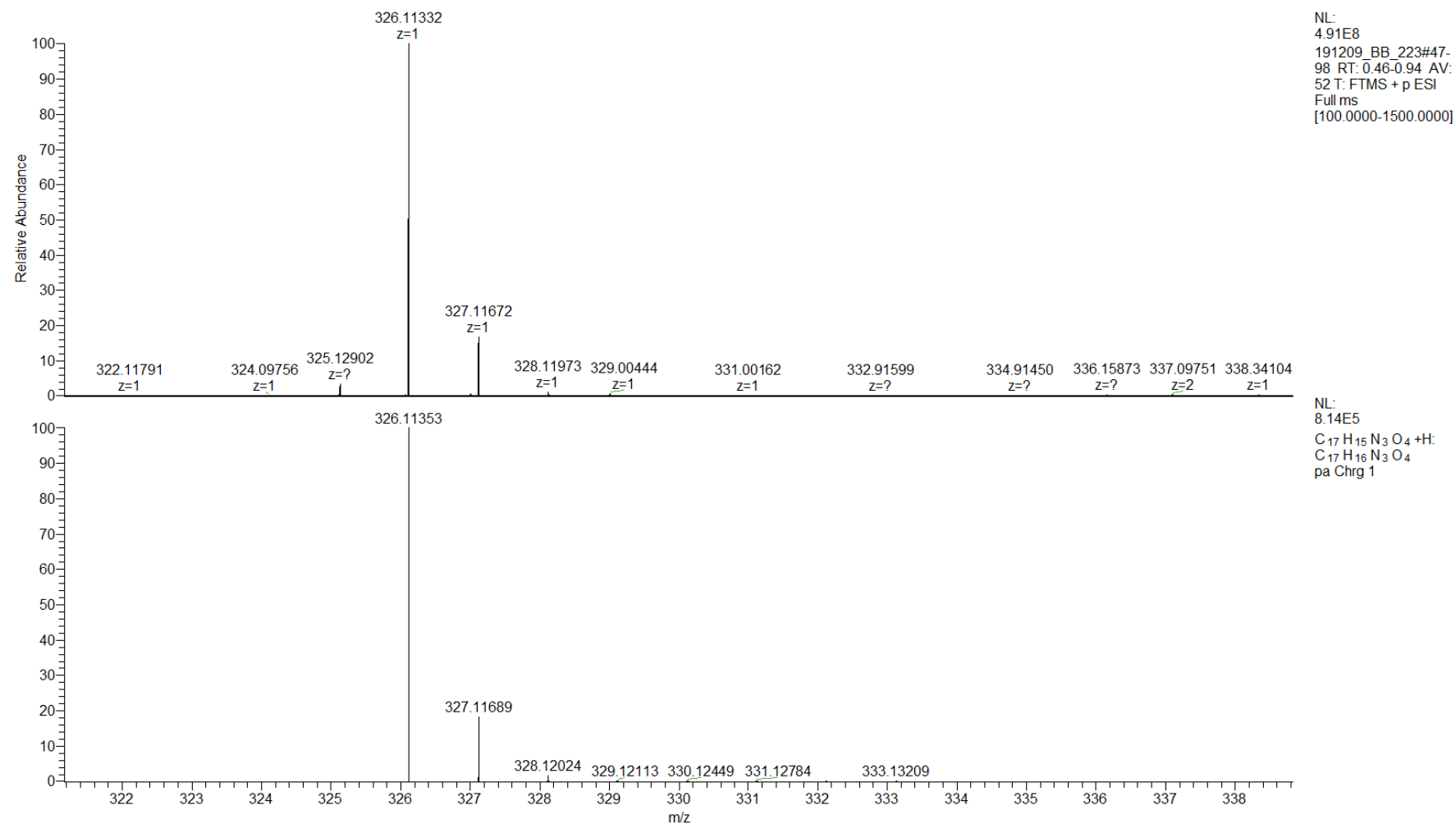


Figure S96. ESI HRMS spectrum of *N*-hydroxy-2-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)acetamide (**7a**).

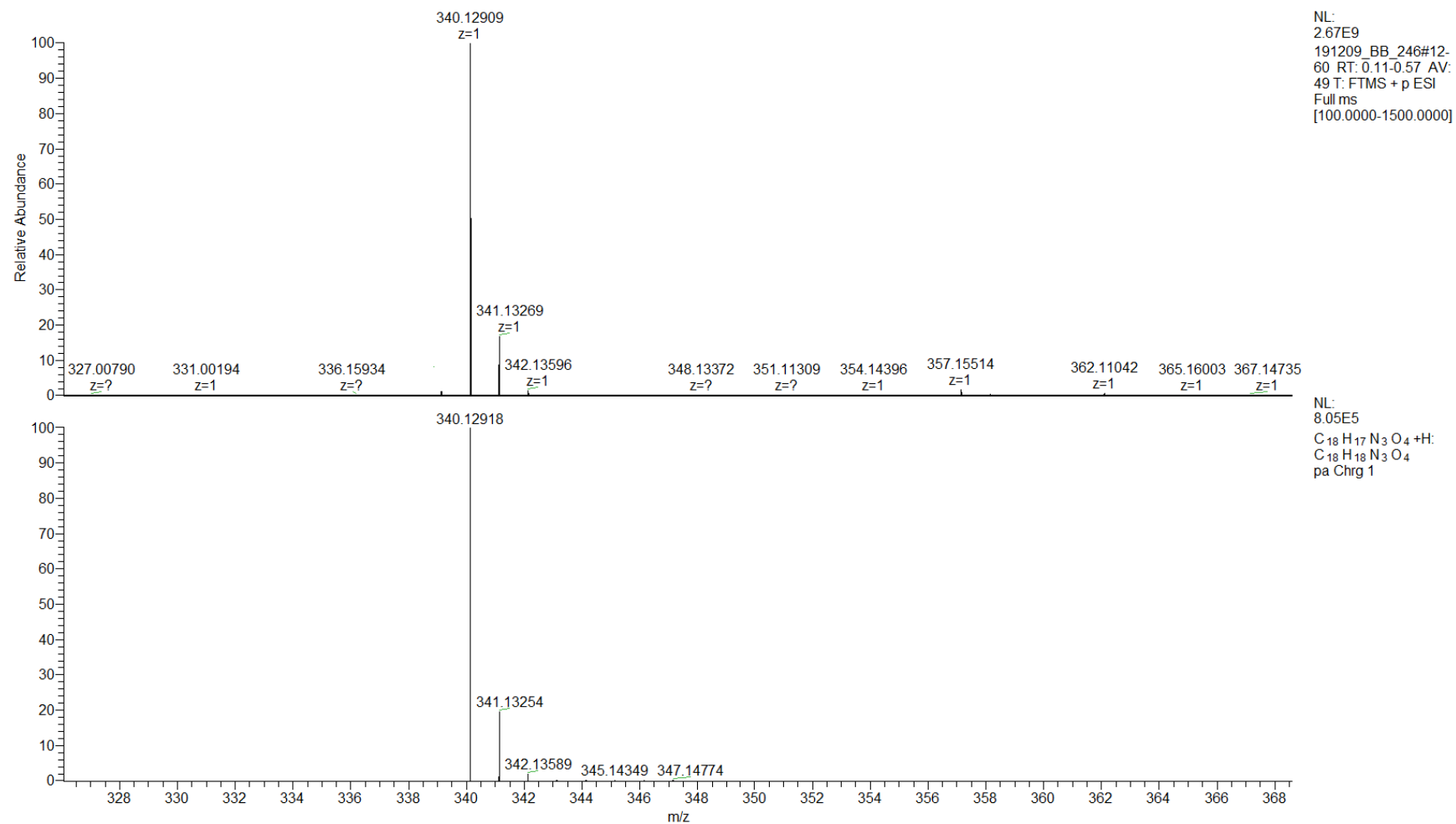


Figure S97. ESI HRMS spectrum of *N*-hydroxy-3-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)propanamide (**7b**).

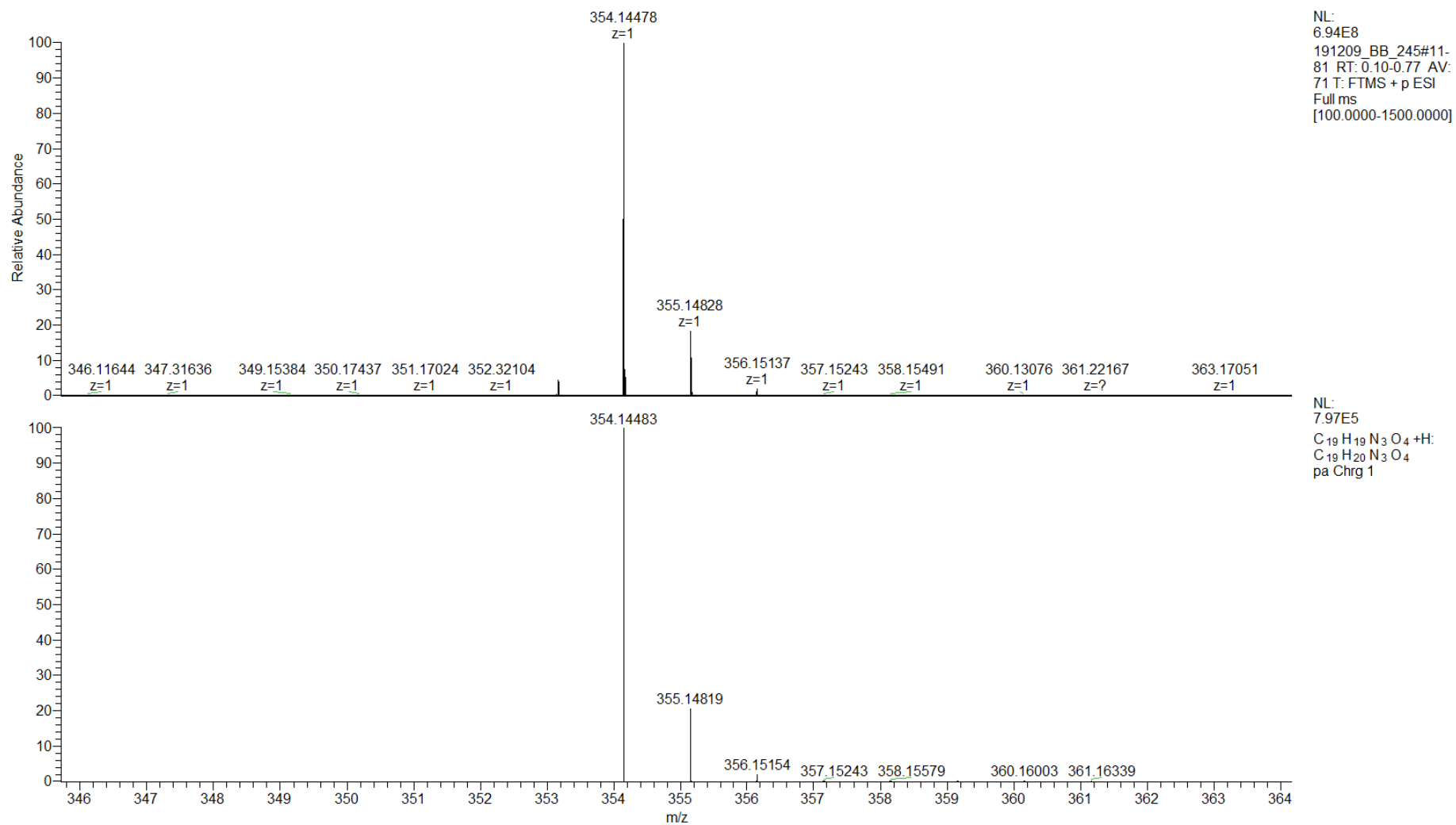


Figure S98. ESI HRMS spectrum of *N*-hydroxy-4-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)butanamide (**7c**).

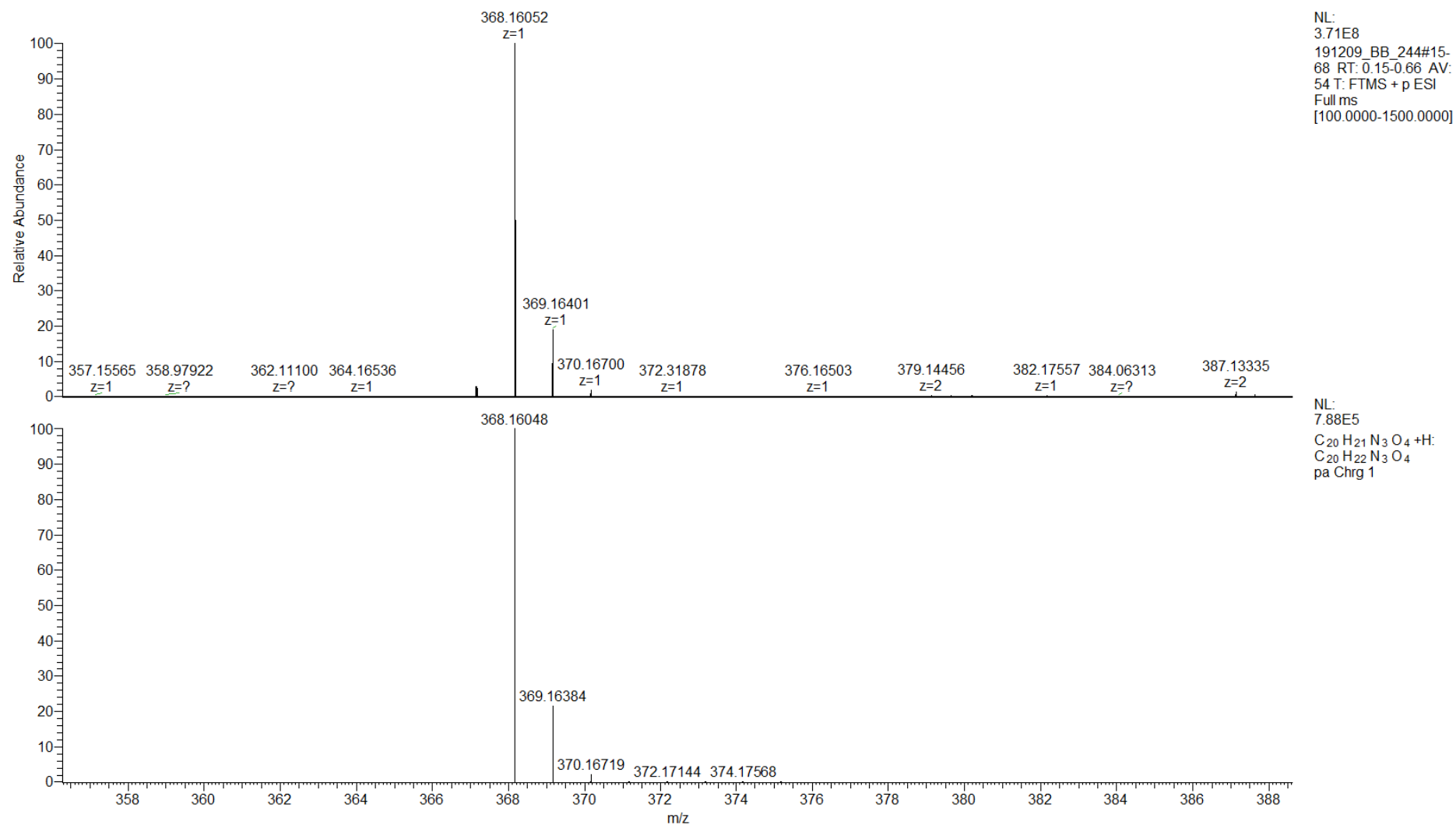


Figure S99. ESI HRMS spectrum of *N*-hydroxy-5-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)pentanamide (**7d**).

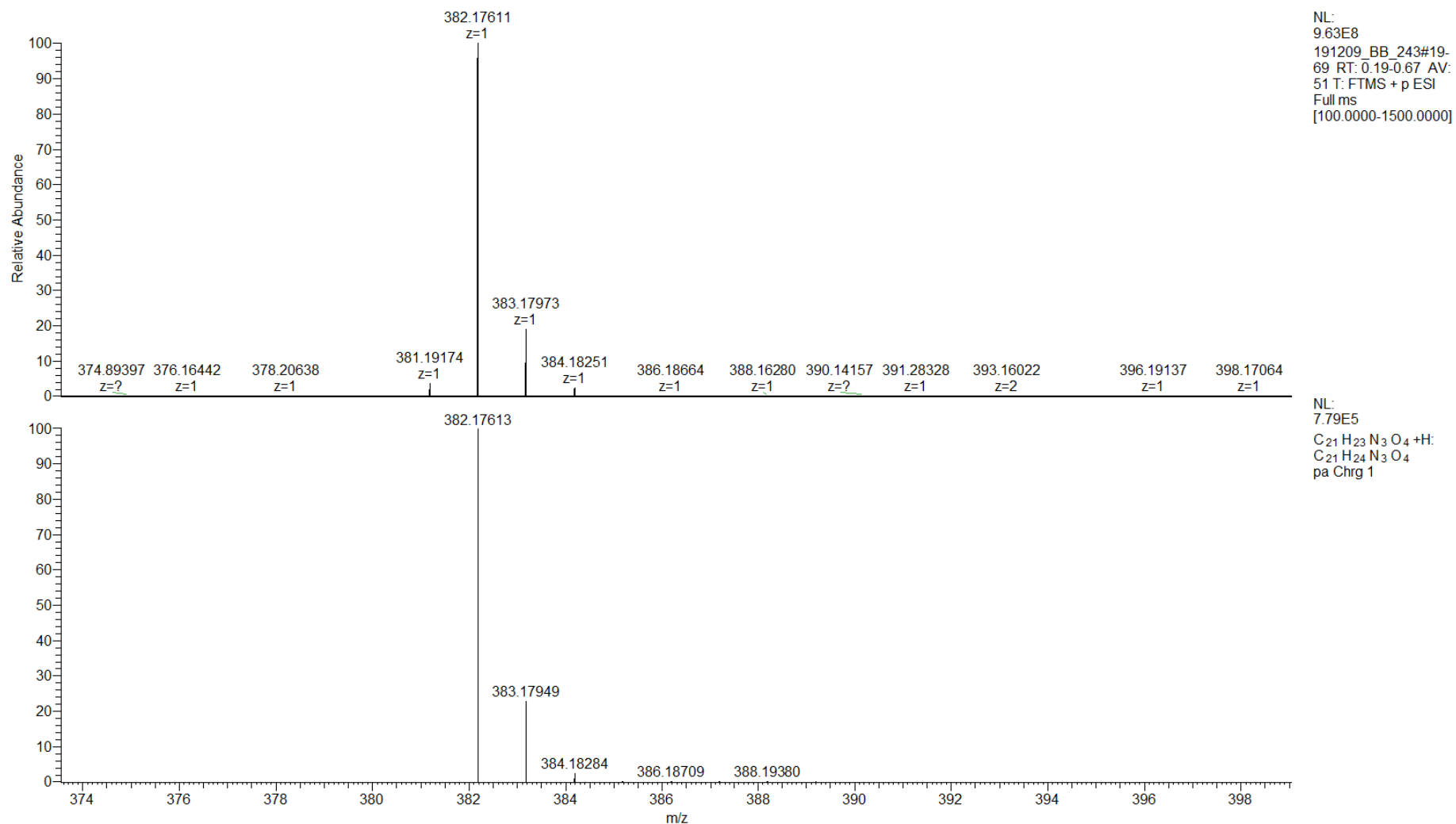


Figure S100. ESI HRMS spectrum of *N*-hydroxy-6-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)hexanamide (**7e**).

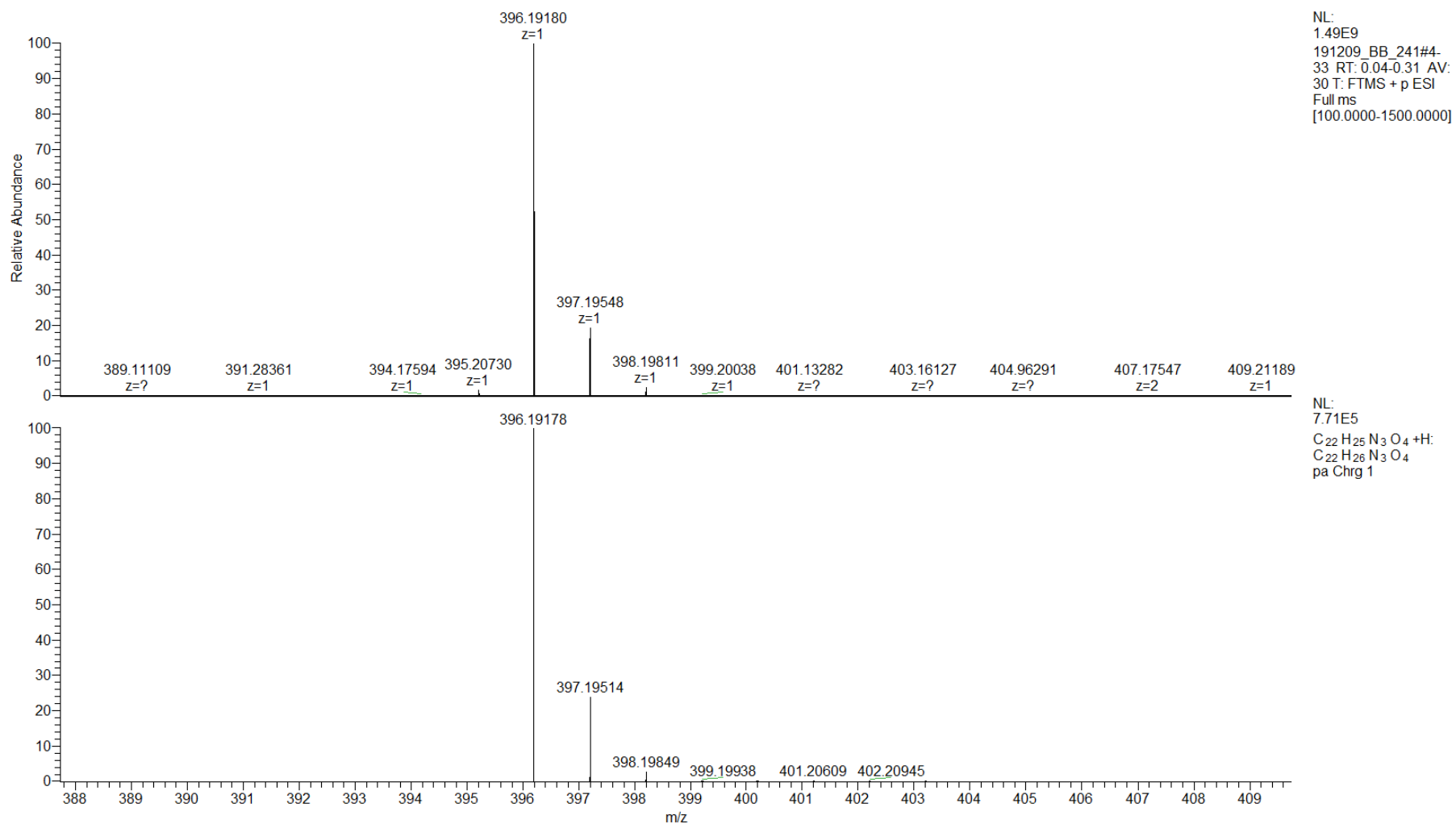


Figure S101. ESI HRMS spectrum of *N*-hydroxy-7-(11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)heptanamide (**7f**).

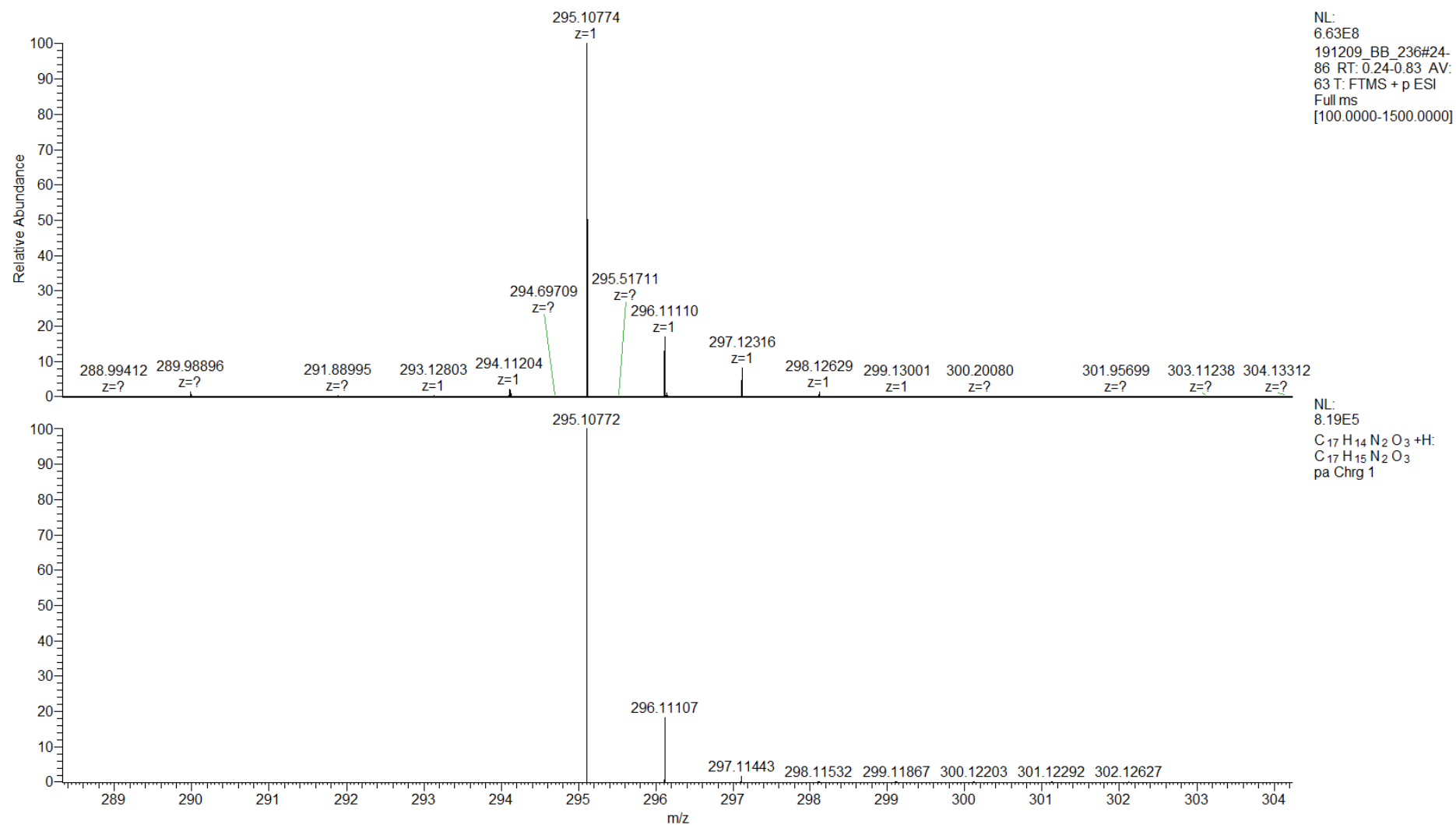


Figure S102. ESI HRMS spectrum of *N*-hydroxy-2-(6-oxodibenzo[*b,f*]azocin-5(6H)-yl)acetamide (**7g**).

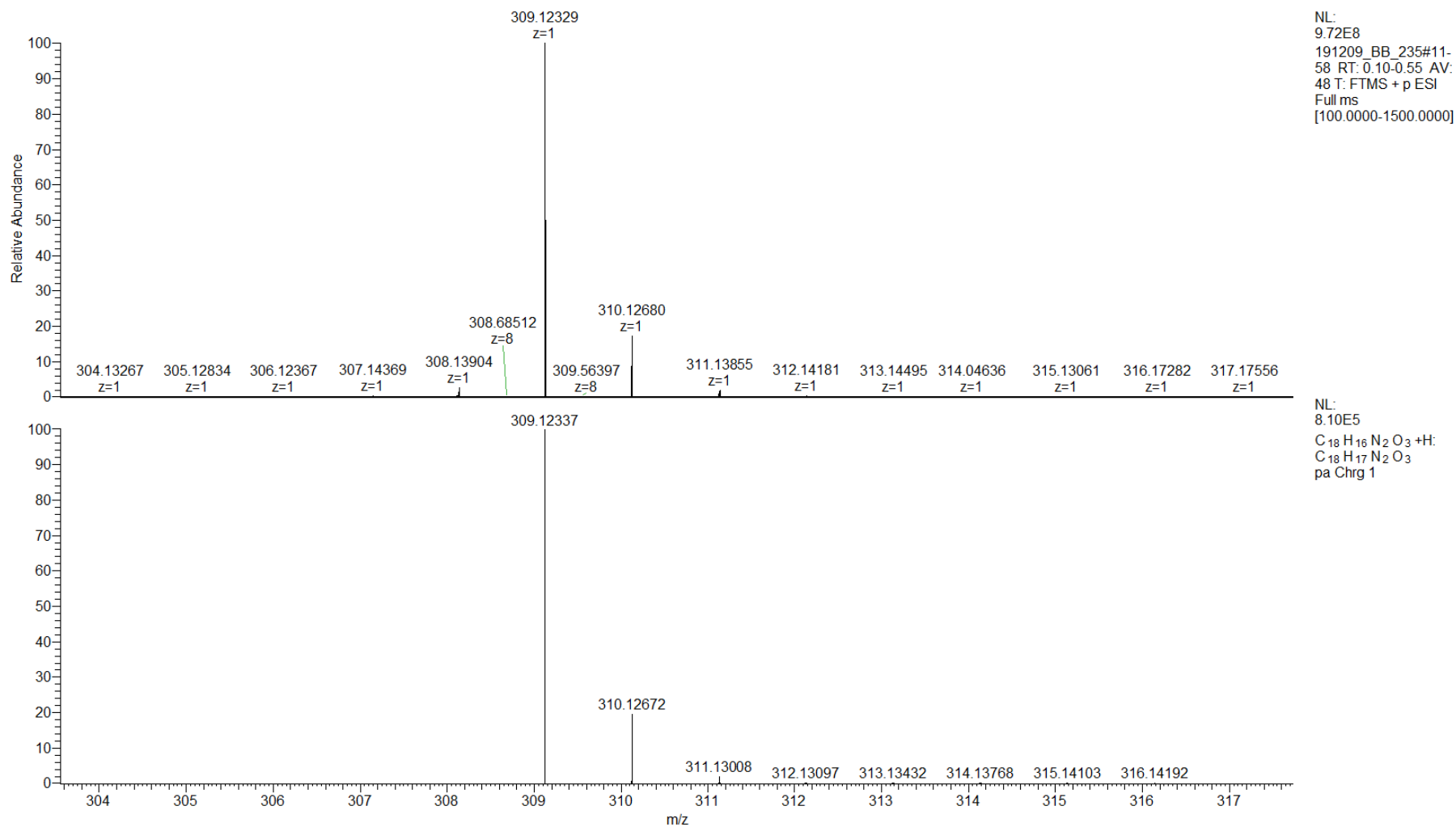


Figure S103. ESI HRMS spectrum of *N*-hydroxy-3-(6-oxodibenzo[*b,f*]azocin-5(6*H*)-yl)propanamide (**7h**).

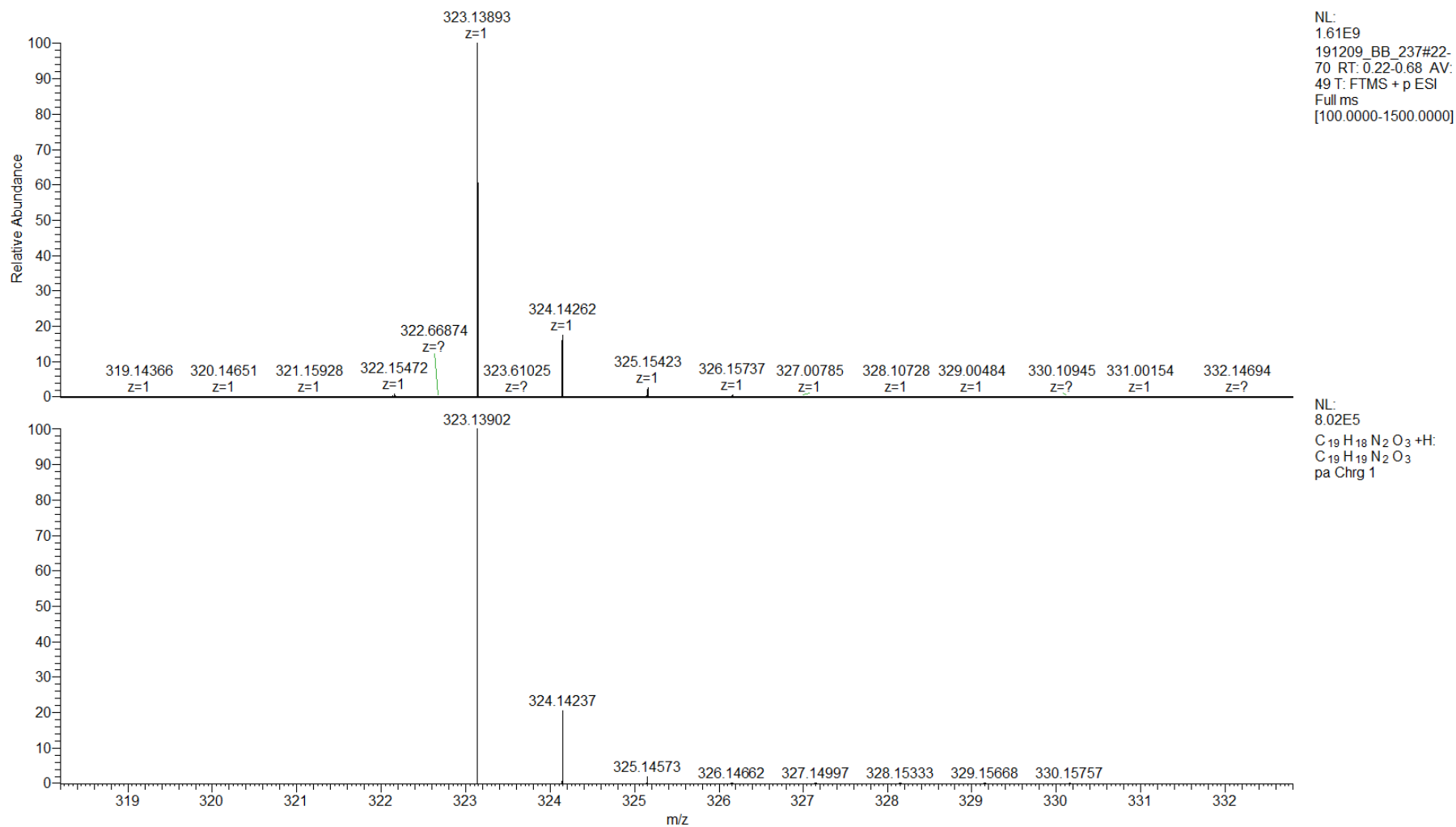


Figure S104. ESI HRMS spectrum of *N*-hydroxy-4-(6-oxodibenzo[*b,f*]azocin-5(6*H*)-yl)butanamide (**7i**).

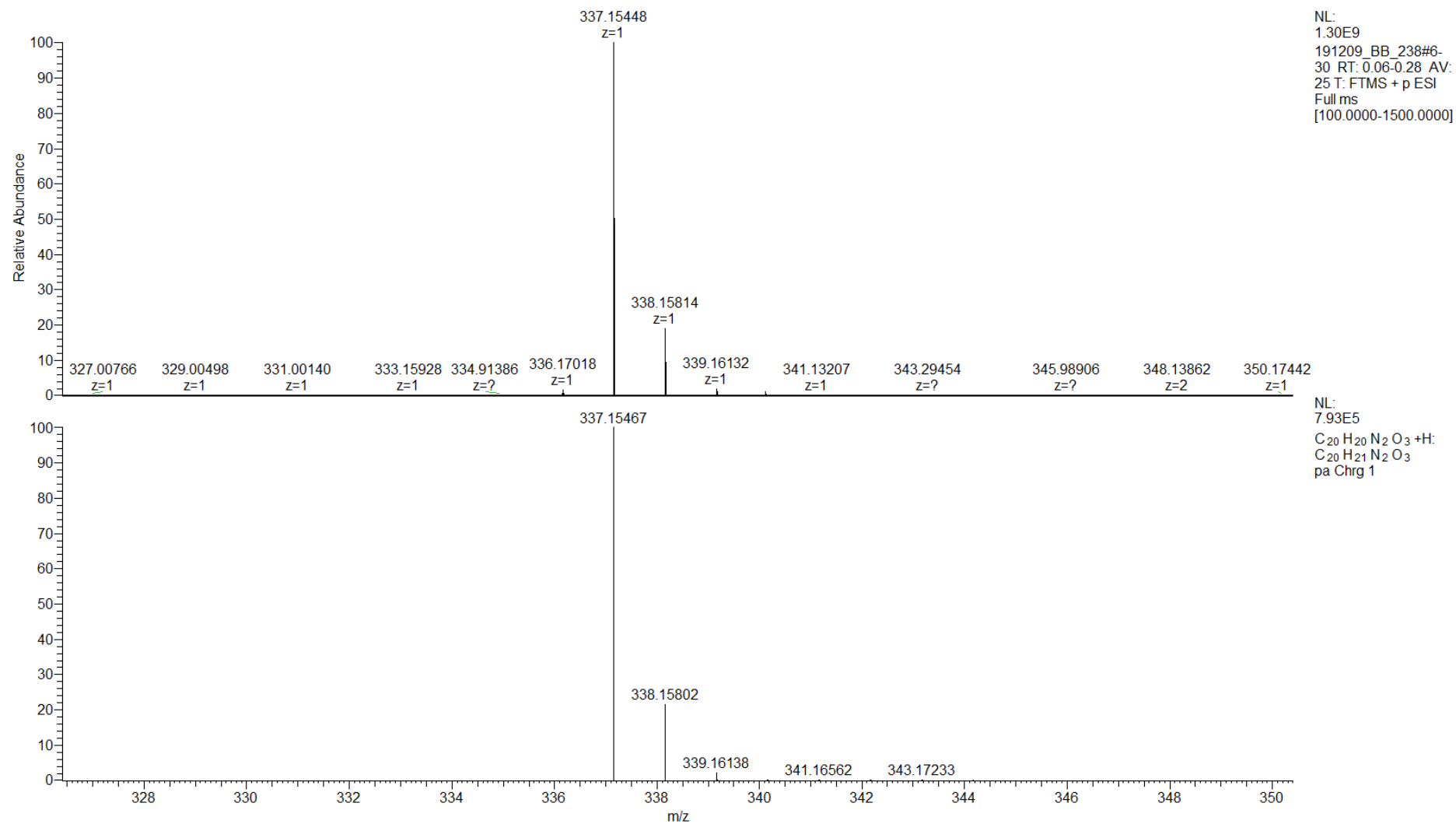


Figure S105. ESI HRMS spectrum of *N*-hydroxy-5-(6-oxodibenzo[*b,f*]azocin-5(6*H*)-yl)pentanamide (**7j**).

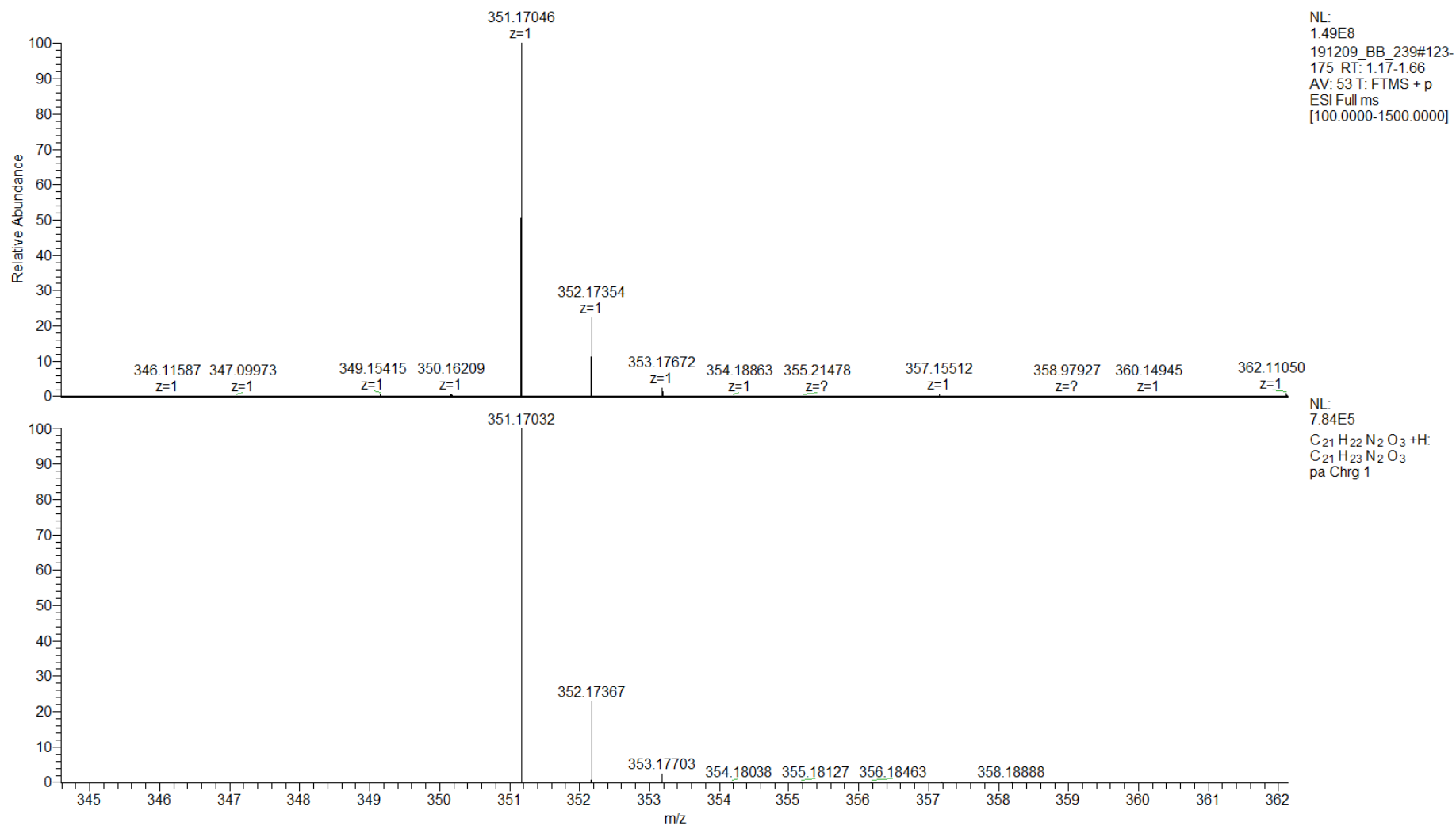


Figure S106. ESI HRMS spectrum of *N*-hydroxy-6-(6-oxodibenzo[*b,f*]azocin-5(6*H*)-yl)hexanamide (**7k**).

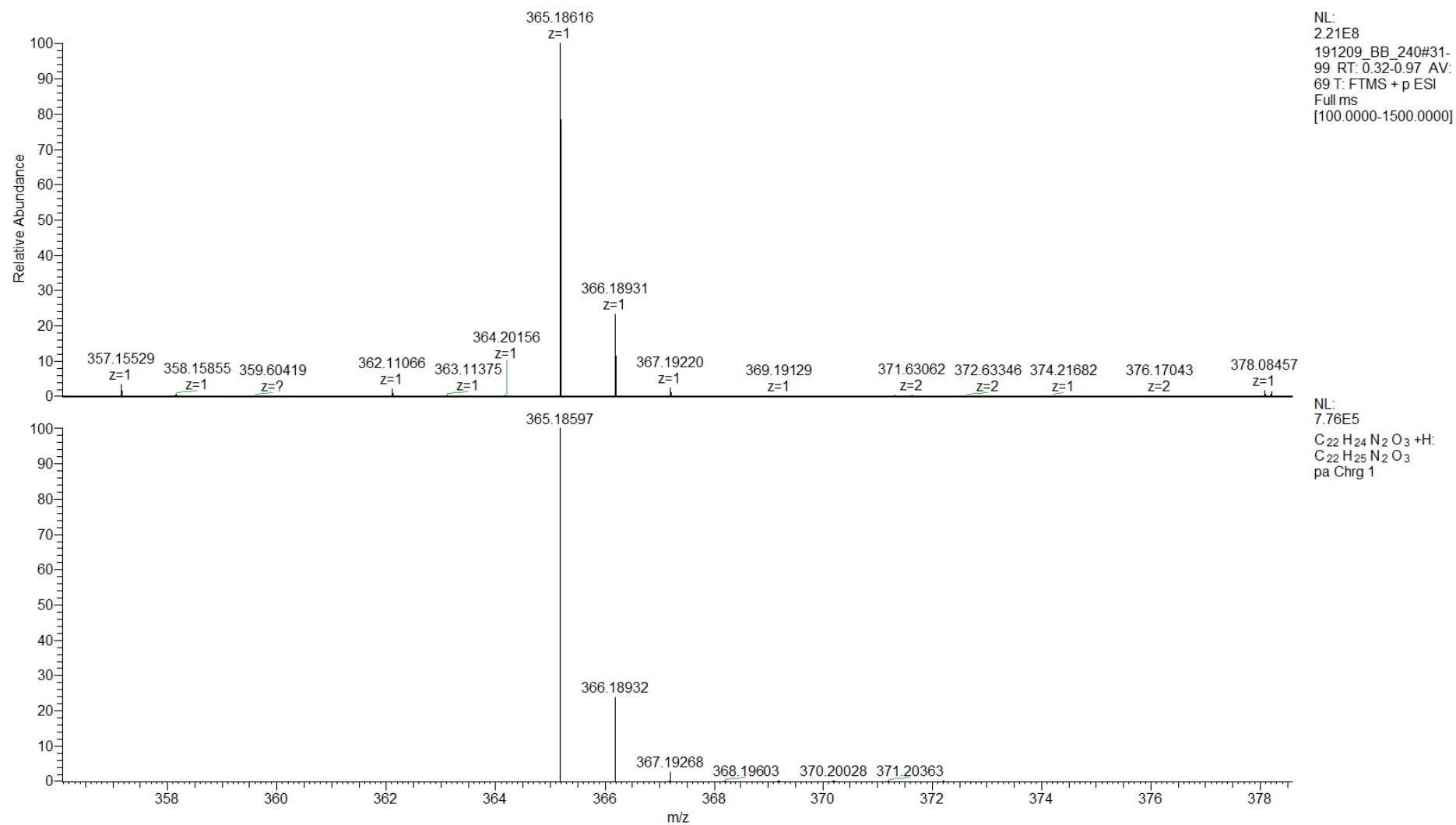


Figure S107. ESI HRMS spectrum of *N*-hydroxy-7-(6-oxodibenzo[*b,f*]azocin-5(6*H*)-yl)heptanamide (**71**).

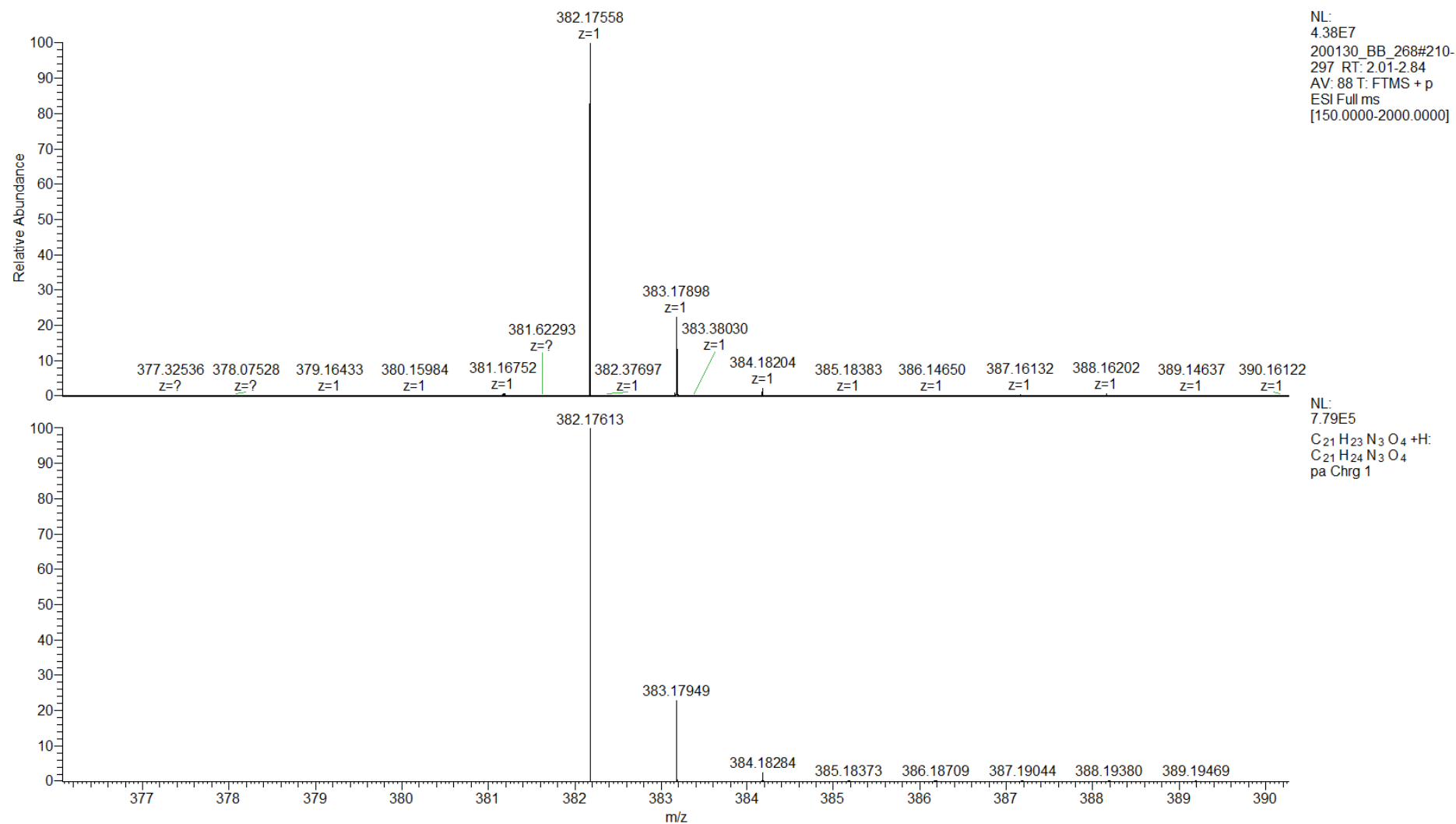


Figure S108. ESI HRMS spectrum of *N*-hydroxy-6-(12-methyl-6,11-dioxo-11,12-dihydrodibenzo[*b,f*][1,4]diazocin-5(6*H*)-yl)hexanamide (**7m**).

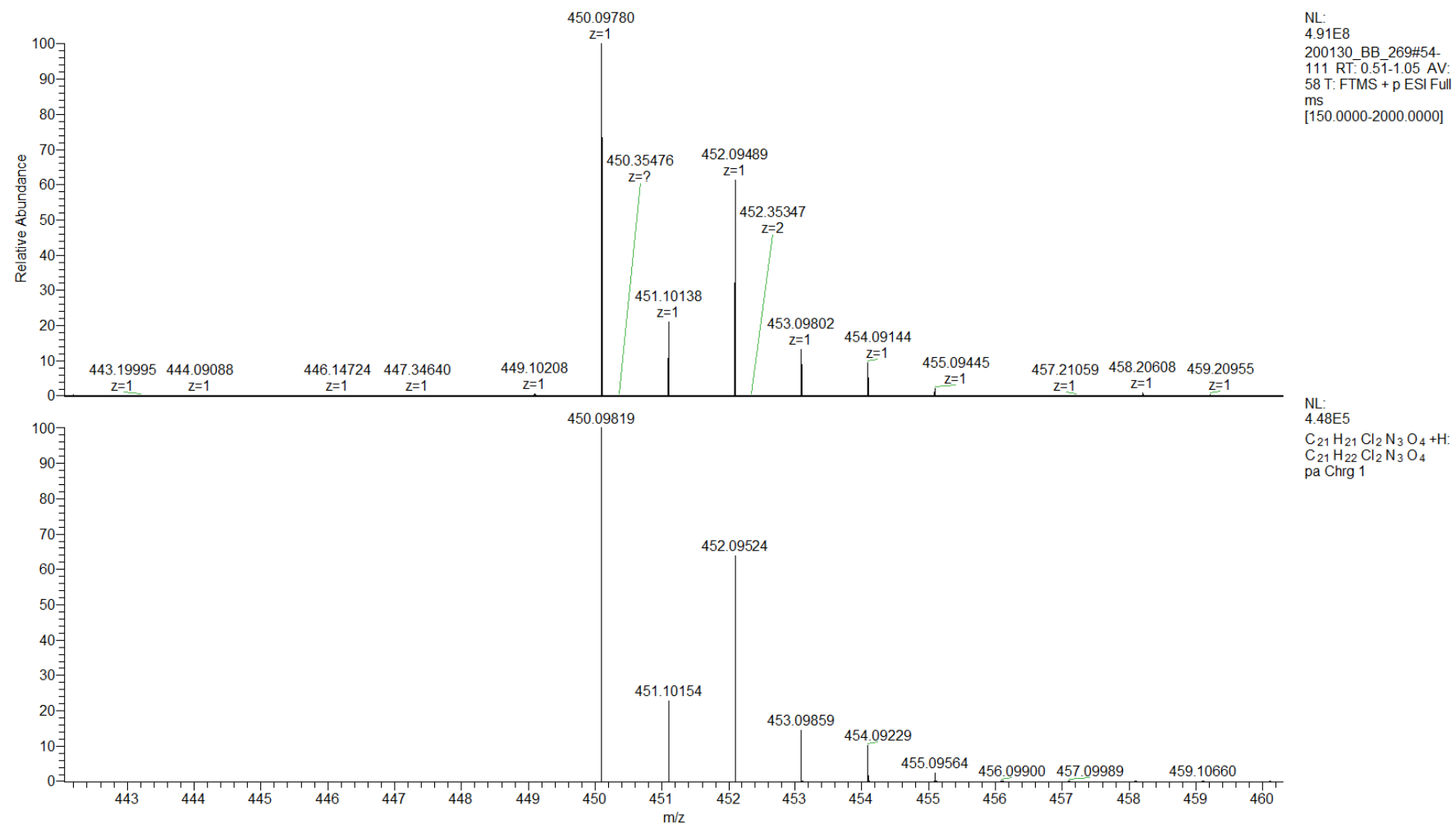


Figure S109. ESI HRMS spectrum of *N*-hydroxy-6-(8,9-dichloro-12-methyl-6,11-dioxo-11,12-dihydrodibenzo[*b,f*][1,4]diazocin-5(6*H*)-yl)hexanamide (**7n**).

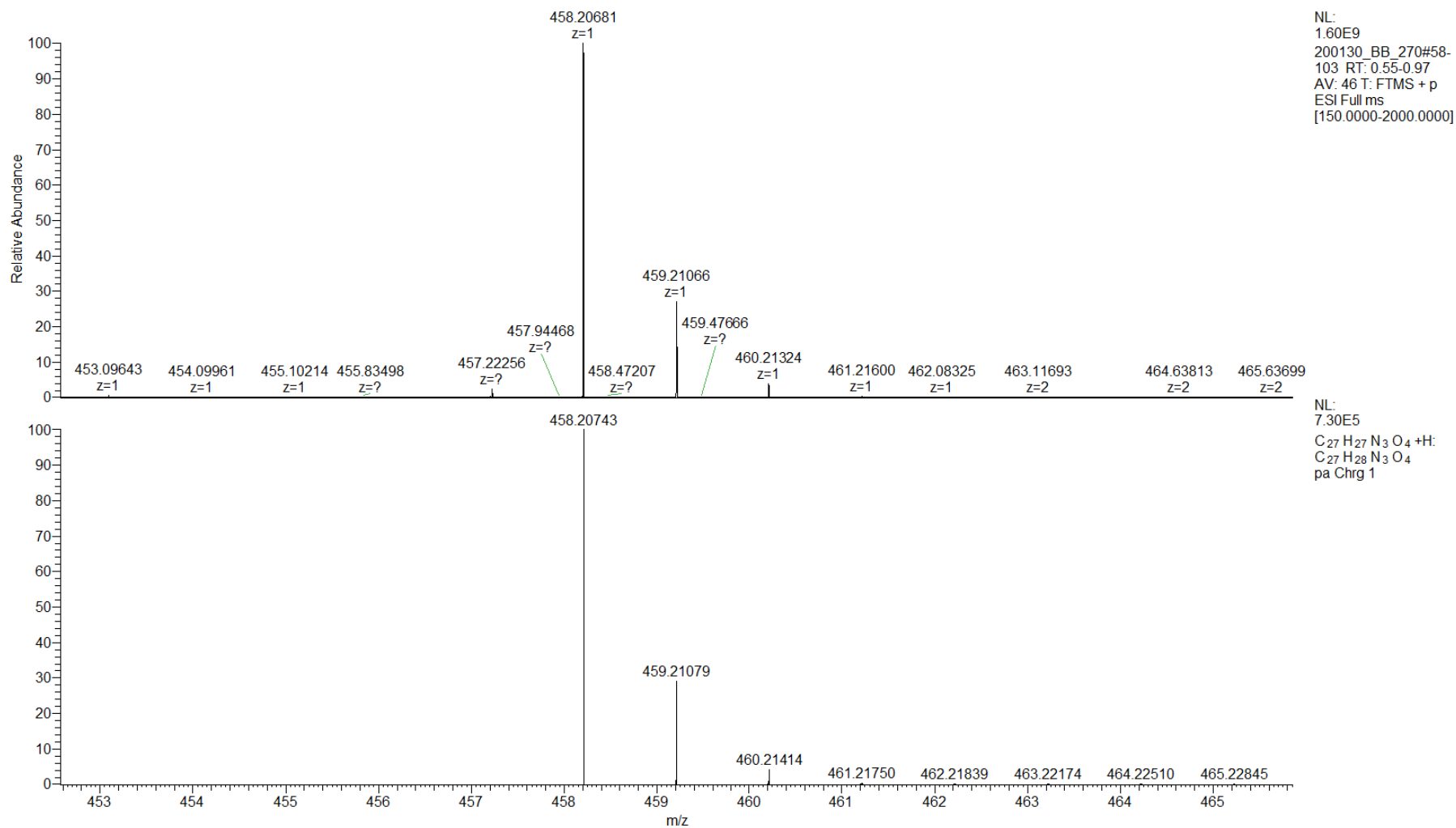


Figure S110. ESI HRMS spectrum of *N*-hydroxy-6-(12-benzyl-6,11-dioxo-11,12-dihydrodibenzo[*b,f*][1,4]diazocin-5(6*H*)-yl)hexanamide (**7o**).

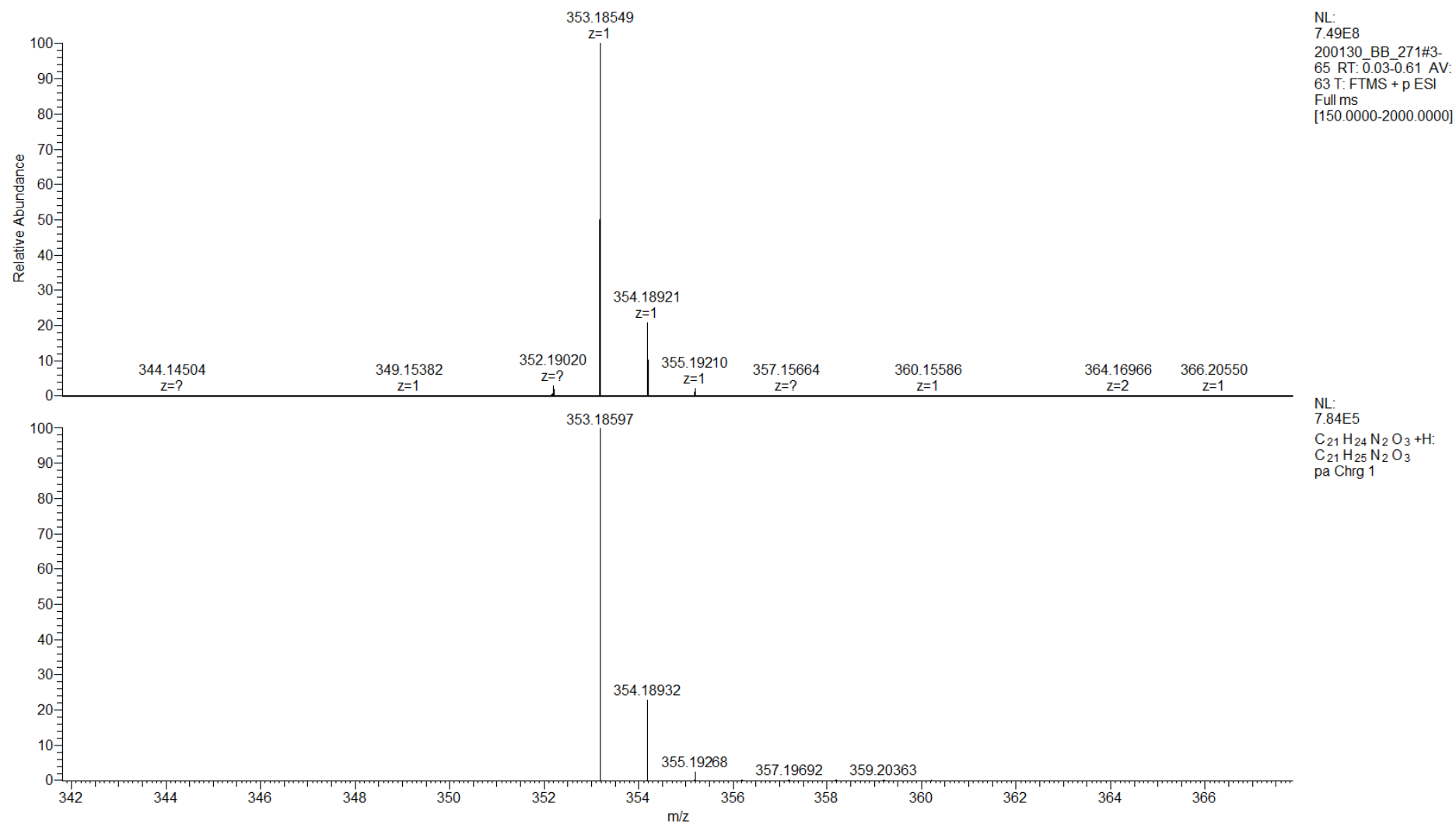


Figure S111. ESI HRMS spectrum of *N*-hydroxy-6-(6-oxo-11,12-dihydrodibenzo[*b,f*]azocin-5(6*H*)-yl)hexanamide (**7p**).

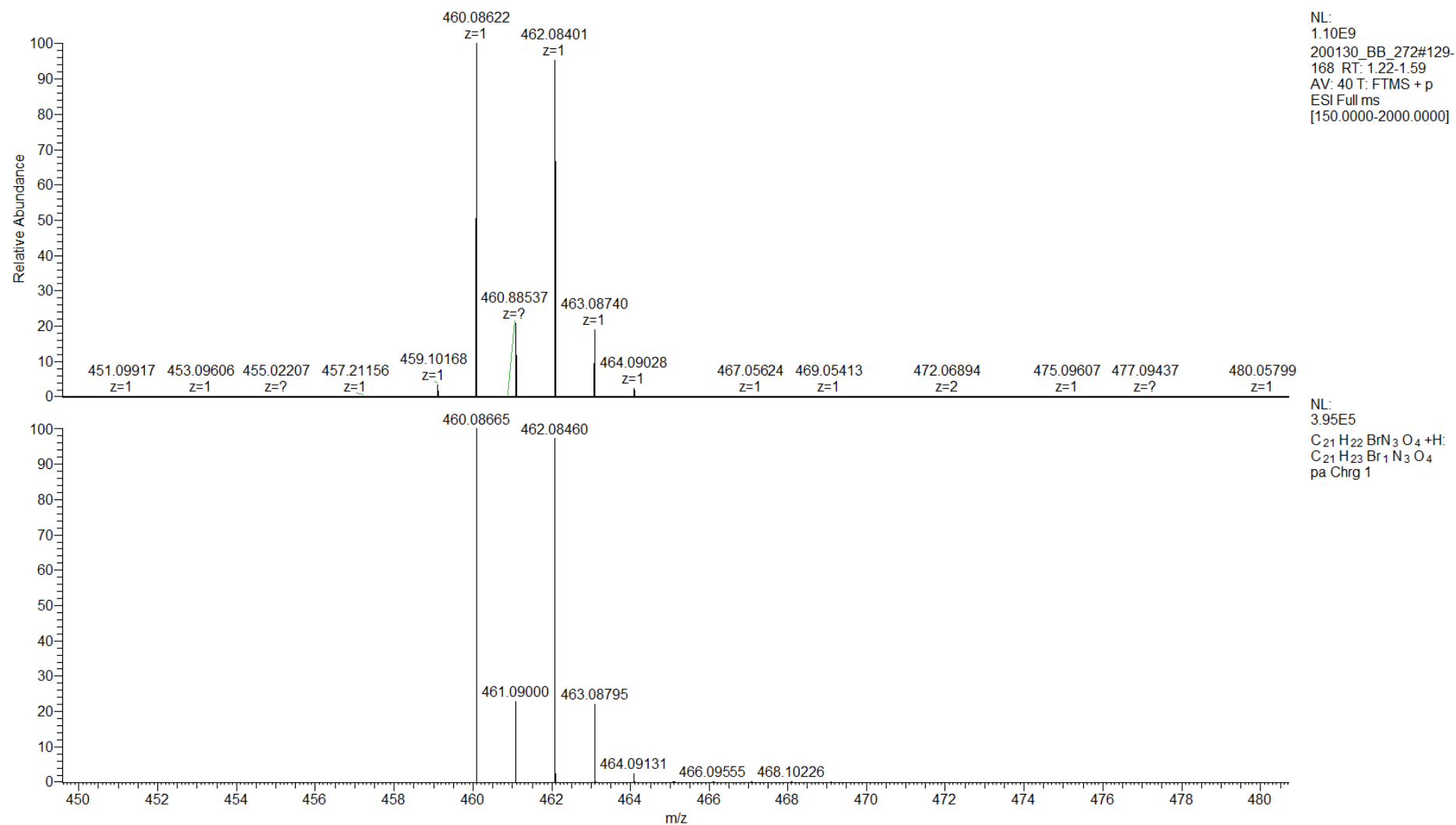


Figure S112. ESI HRMS spectrum of *N*-hydroxy-6-(2-bromo-11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)hexanamide (**7r**).

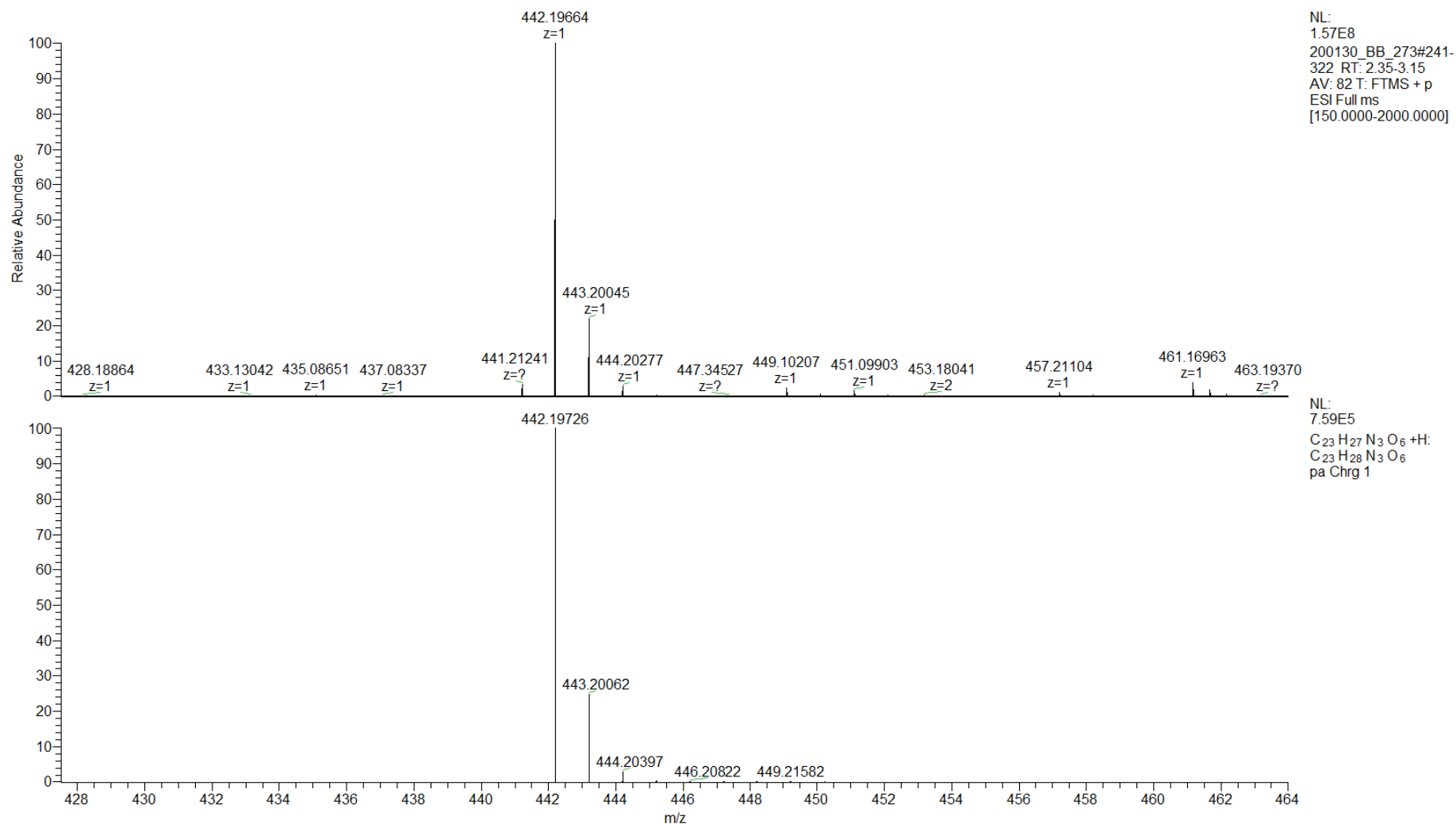


Figure S113. ESI HRMS spectrum of *N*-hydroxy-6-(2,3-dimethoxy-11-methyl-6,12-dioxo-11,12-dihydrodibenzo[*b,f*][1,5]diazocin-5(6*H*)-yl)hexanamide (**7s**).

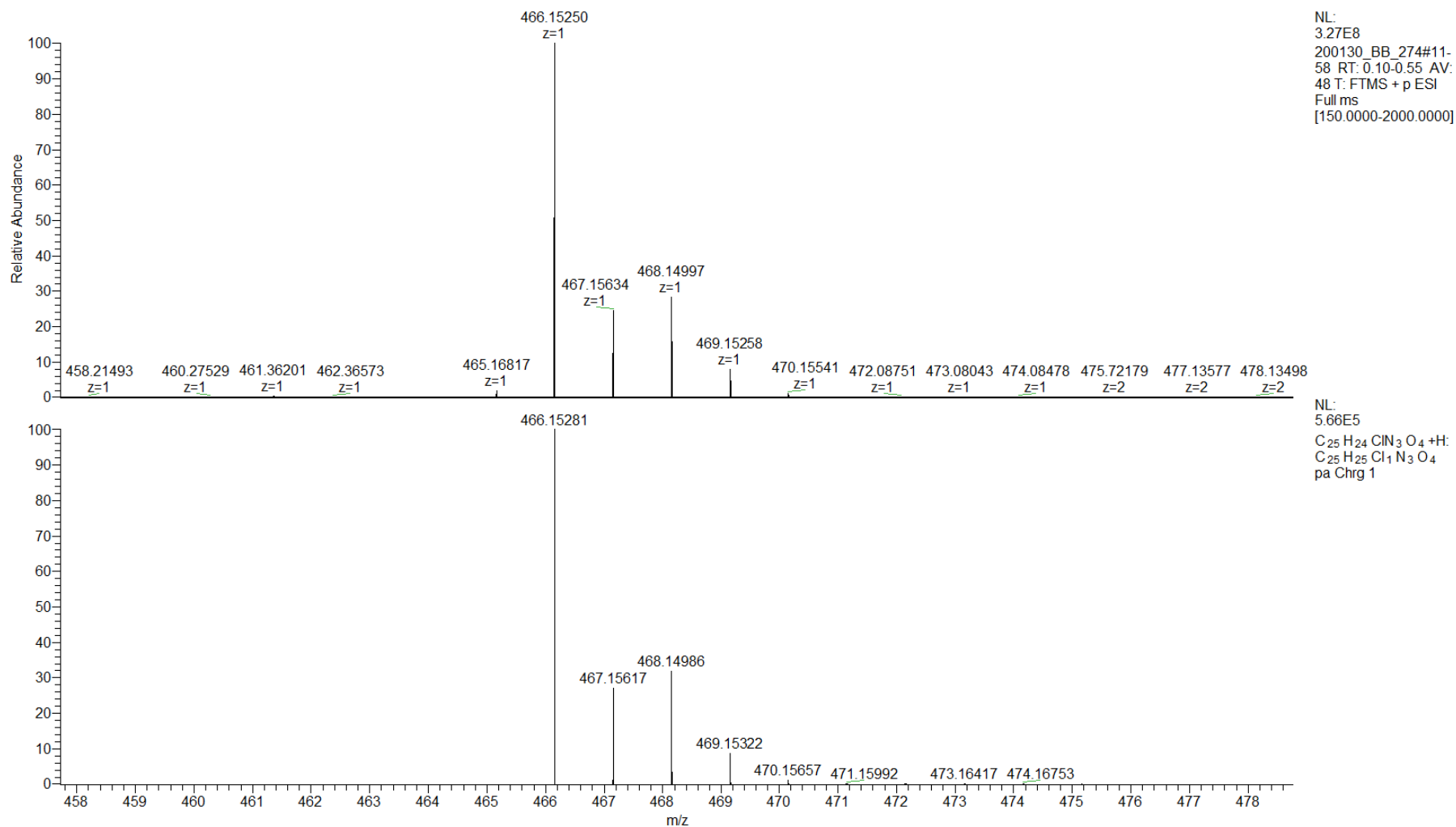


Figure S114. ESI HRMS spectrum of *N*-hydroxy-6-(5-methyl-6,14-dioxo-5,14-dihydrobenzonaphtho[2,3-*f*][1,5]diazocin-13(6*H*)-yl)hexanamide (**7t**).