

## Supplementary Materials

# Hybrids of 1,4-quinone with quinoline derivatives: synthesis, biological activity and molecular docking with DT-diaphorase

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Table S1: The NQO1 activity of hybrids **11-14** and **ST** monitored at the absorbance of A340 nm.

Compound	NQO1 activity [μmol NADPH/μmol NQO1/min]
<b>11a</b>	1399 ± 26
<b>12a</b>	1505 ± 54
<b>13a</b>	1210 ± 23
<b>14a</b>	1282 ± 29
<b>11b</b>	1294 ± 51
<b>12b</b>	1437 ± 42
<b>13b</b>	1143 ± 36
<b>14b</b>	1260 ± 15
<b>11c</b>	1100 ± 35
<b>12c</b>	470 ± 22
<b>13c</b>	318 ± 19
<b>14c</b>	550 ± 62
<b>11d</b>	800 ± 64
<b>12d</b>	890 ± 21
<b>13d</b>	633 ± 32
<b>14d</b>	1001 ± 43
<b>11e</b>	1082 ± 51
<b>12e</b>	600 ± 35
<b>13e</b>	214 ± 21
<b>14e</b>	354 ± 22
<b>11f</b>	113 ± 19
<b>12f</b>	210 ± 20
<b>13f</b>	143 ± 26
<b>14f</b>	87 ± 15
<b>ST</b>	725 ± 84

Table S2: The selectivity index (SI) value for compounds **11-14** and doxorubicin.

Compound	SI ( $\text{IC}_{50}$ HFF-1/ $\text{IC}_{50}$ cancer line)					
	Colo-829	SK-OV-3	MDA-MB-231	T47D	MCF-7	A549
<b>11a</b>	0.55	6.59	0.89	0.55	0.53	6.08
<b>11b</b>	13.56	15.40	15.87	10.76	12.34	14.62
<b>11c</b>	0.90	5.91	0.73	0.47	0.57	7.26
<b>11d</b>	9.48	8.81	6.77	6.54	6.51	8.04
<b>11e</b>	0.76	6.66	5.81	0.55	5.64	0.94
<b>11f</b>	1.83	2.35	1.86	1.38	1.58	2.03
<b>12a</b>	11.41	346.80	8.80	10.91	8.30	20.40
<b>12b</b>	6.01	6.81	6.46	5.34	5.70	7.10
<b>12c</b>	1.23	8.28	0.85	0.77	0.94	5.70
<b>12d</b>	0.78	0.67	0.66	0.64	0.59	7.04
<b>12e</b>	11.48	16.72	11.71	1.01	9.29	1.16
<b>12f</b>	1.49	1.48	1.95	1.15	1.41	1.72
<b>13a</b>	162.88	60.20	27.15	307.67	23.87	923.00
<b>13b</b>	66.77	53.14	236.73	20.19	42.69	45.68
<b>13c</b>	38.97	41.41	17.67	25.48	14.89	10.04
<b>13d</b>	5.66	0.65	6.64	-	6.34	184.83
<b>13e</b>	0.79	0.98	0.93	-	0.92	1.11
<b>13f</b>	8.76	14.95	141.46	8.55	17.85	15.07
<b>14a</b>	0.84	7.54	0.84	-	0.91	19.71
<b>14b</b>	0.74	0.66	0.58	0.50	0.68	5.30
<b>14c</b>	-	71.84	0.71	11.09	-	43.80
<b>14d</b>	0.80	1.01	6.99	-	1.23	1.76
<b>14e</b>	0.85	1.17	2.43	-	0.78	0.84
<b>14f</b>	1.98	1.59	9.58	-	1.29	1.61
<b>Doxorubicin</b>	2.40	0.80	0.19	3.00	1.00	6.00

Table S3: Interaction of selected hybrids with active site of NQO1 protein.

Ligand	H-bonding residues and length (Å)	$\pi$ -interaction residues and length (Å)
<b>11b</b>	TYR128 (2.143) GLY149 (2.902; 2.870)	TYR128 (3.746; 4.729; 5.497) PHE178 (4.802; 5.482) TRP105 (5.420; 4.795) MET154 (4.574) HIS161 (3.937) FAD (4.050; 3.530; 3.934; 4.444; 5.139; 5.051)
<b>12b</b>	TYR128 (2.095)	TYR128 (3.726; 4.686; 5.419) TYR126 (4.296) PHE178 (5.532; 4.918) TRP105 (3.873; 3.832) MET154 (4.410) HIS161 (3.860) FAD (3.856; 3.603; 3.942; 4.555; 3.840; 5.081; 5.278; 4.202)
<b>13b</b>	TYR128 (2.117) GLY149 (2.918; 2.857)	TYR128 (3.744; 4.717; 5.505) PHE178 (5.473; 4.800) TRP105 (5.423; 4.796) MET154 (4.580) HIS161 (3.898) FAD (3.528; 4.060; 4.443; 3.940; 5.141; 5.026)
<b>14b</b>	TYR128 (2.061)	TYR128 (4.344; 3.572; 5.104; 4.488) TYR126 (4.675) PHE178 (5.807; 5.126) PHE236 (4.688) TRP105 (5.800; 5.245) MET154 (4.468; 5.251) HIS161 (4.340) FAD (3.780; 4.016; 4.602; 3.818; 4.992)

Figure S1. Visualization of hydrogen bond (green) and hydrophobic interactions (violet) between NQO1 enzyme and hybrid: (a) 11b; (b) 12b; (c) 13b; (d) 14b.

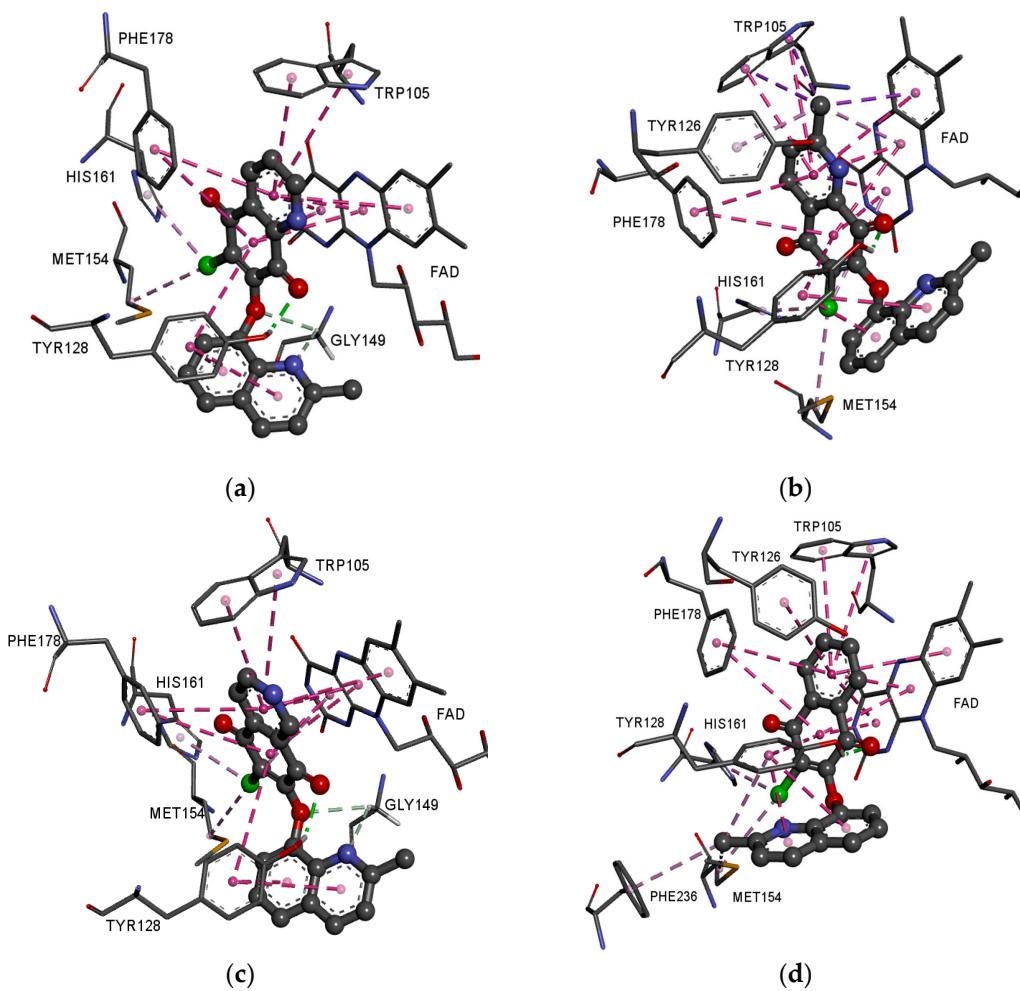


Figure S2: Spectra of 6-chloro-7-(quinolin-8-yloxy)quinoline-5,8-dione (**11a**).

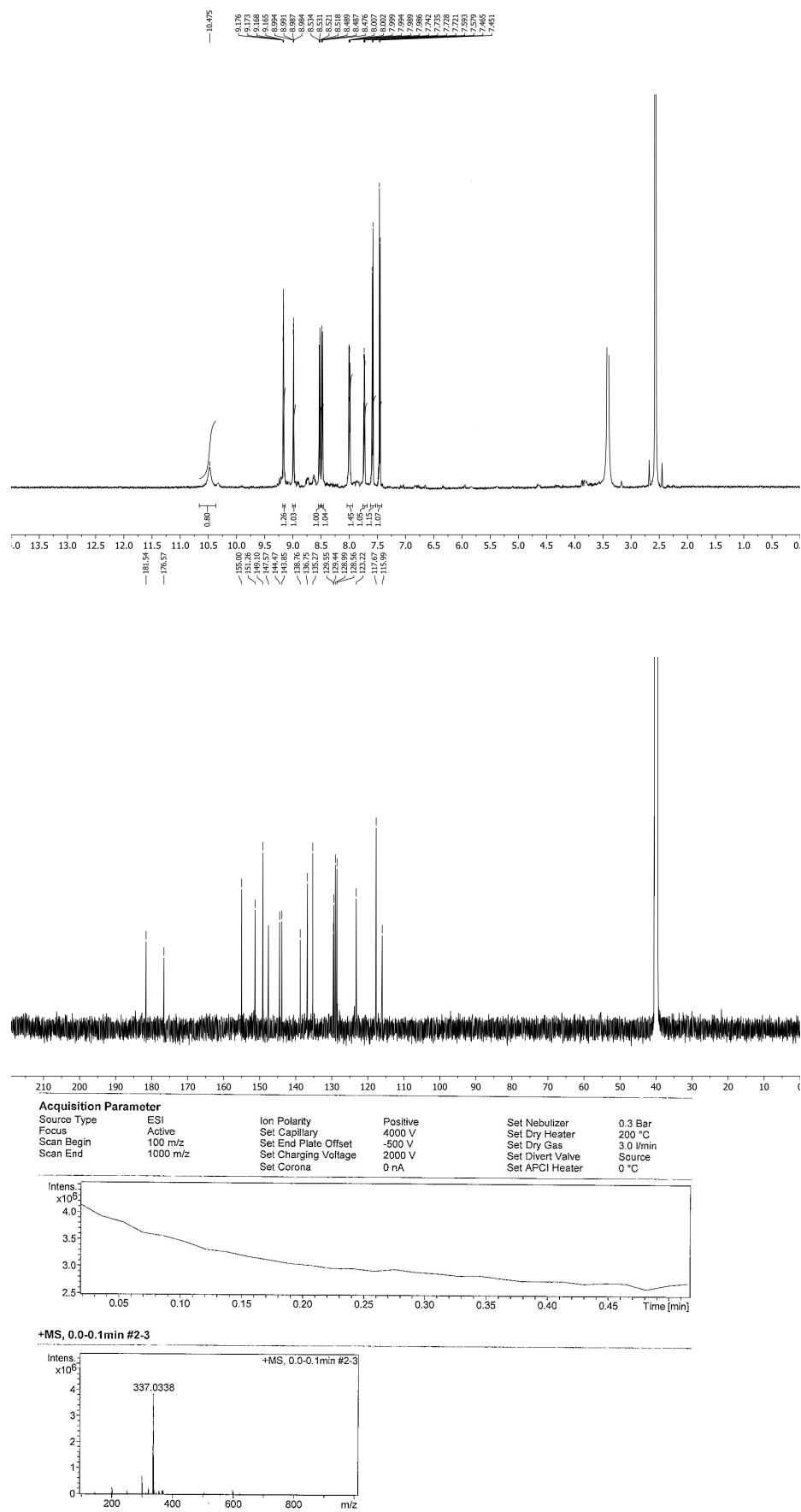


Figure S3: Spectra of 6-chloro-7-[(2-methylquinolin-8-yl)oxy]quinoline-5,8-dione (**11b**)

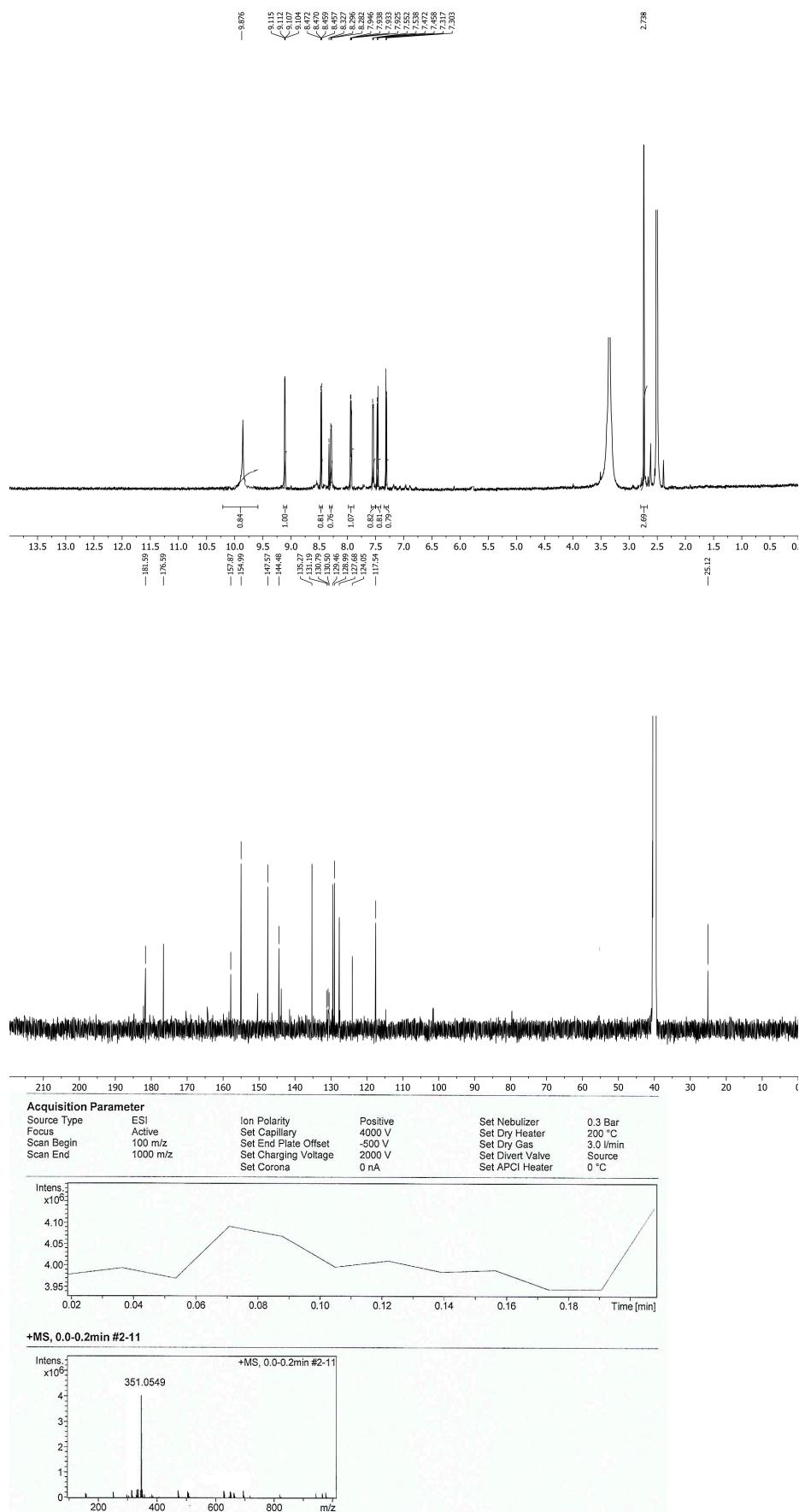


Figure S4: Spectra of 8-[(6-chloro-5,8-dioxo-5,8-dihydroquinolin-7-yl)oxy]quinoline-2-carbaldehyde (**11c**).

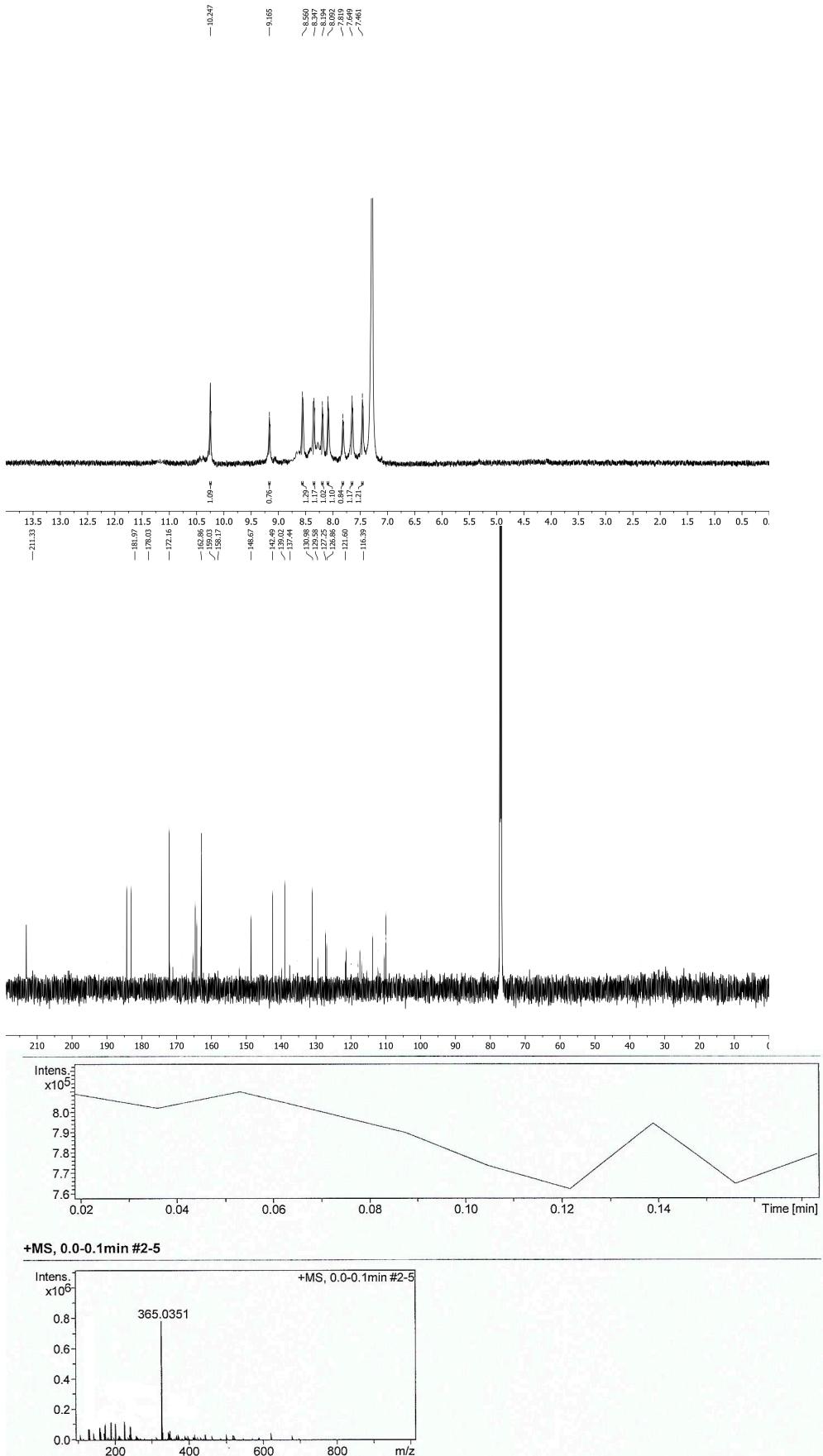


Figure S5: Spectra of 6-chloro-7-[(2-chloroquinolin-8-yl)oxy]quinoline-5,8-dione (**11d**).

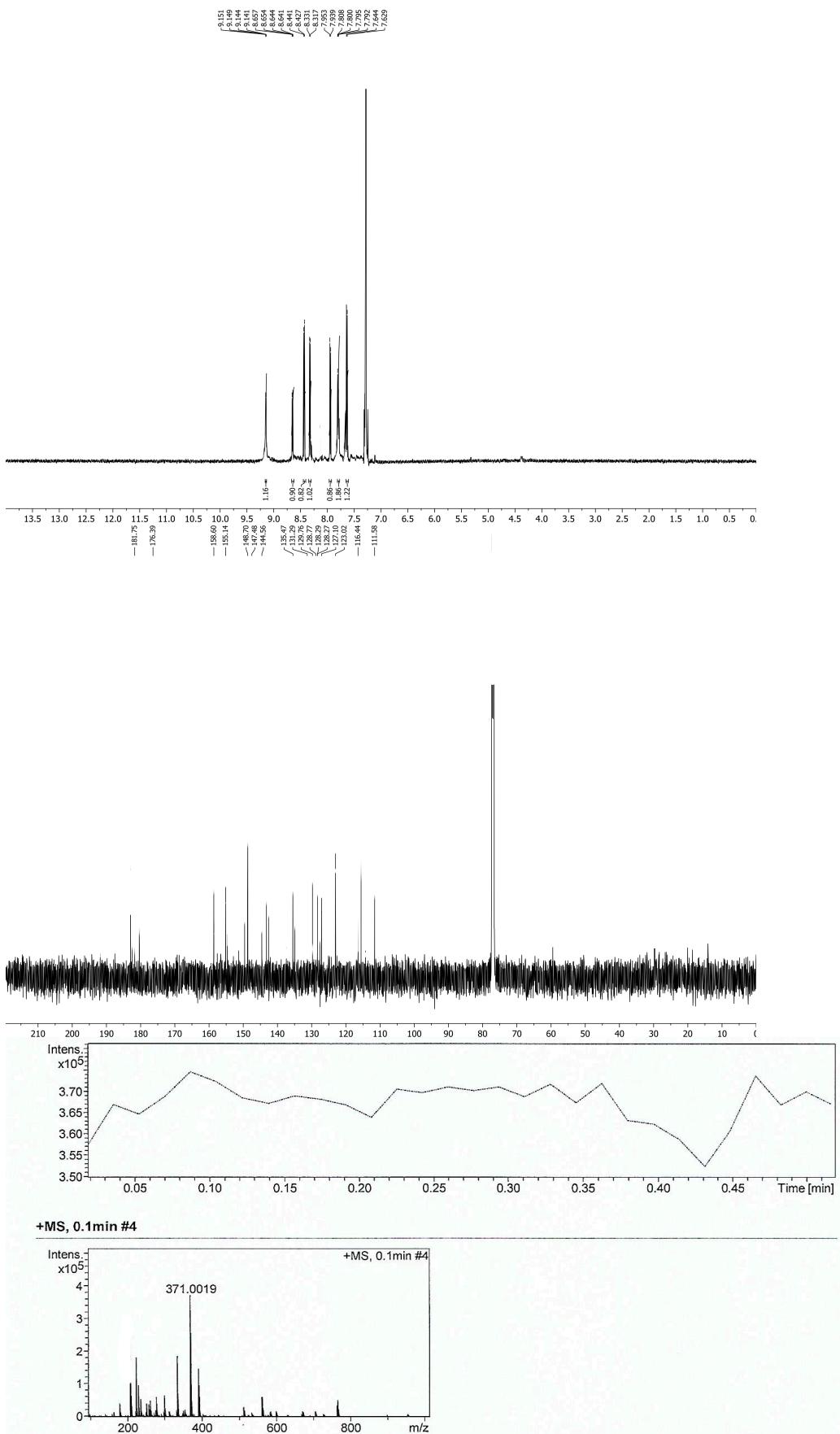


Figure S6: Spectrum of 6-chloro-7-[{2-(pyrrolidin-1-yl)quinolin-8-yl]oxy}quinoline-5,8-dione (**11e**).

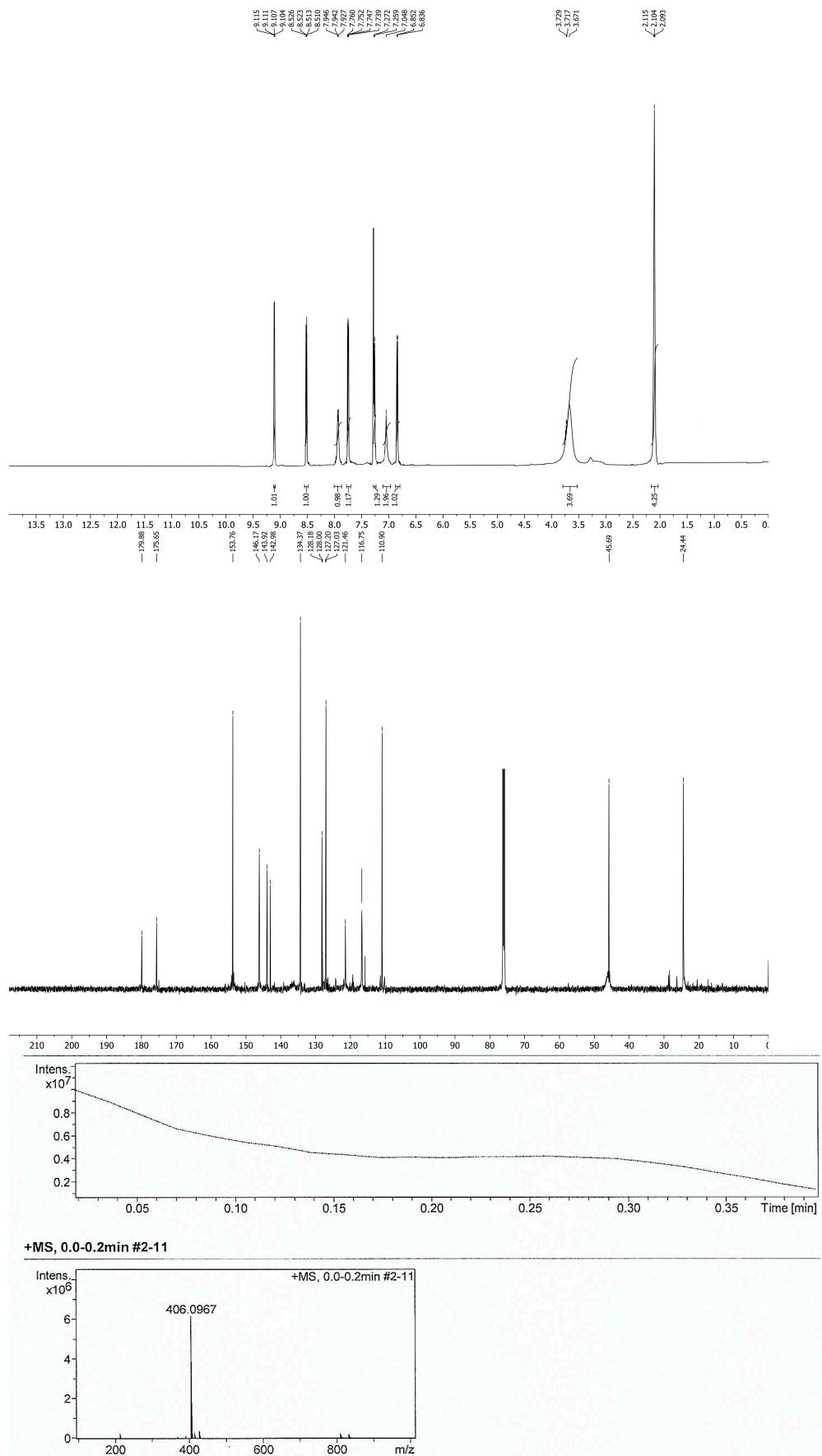


Figure S7: Spectra of 6-chloro-7-[{2-(morpholin-4-yl)quinolin-8-yl]oxy}quinoline-5,8-dione (**11f**).

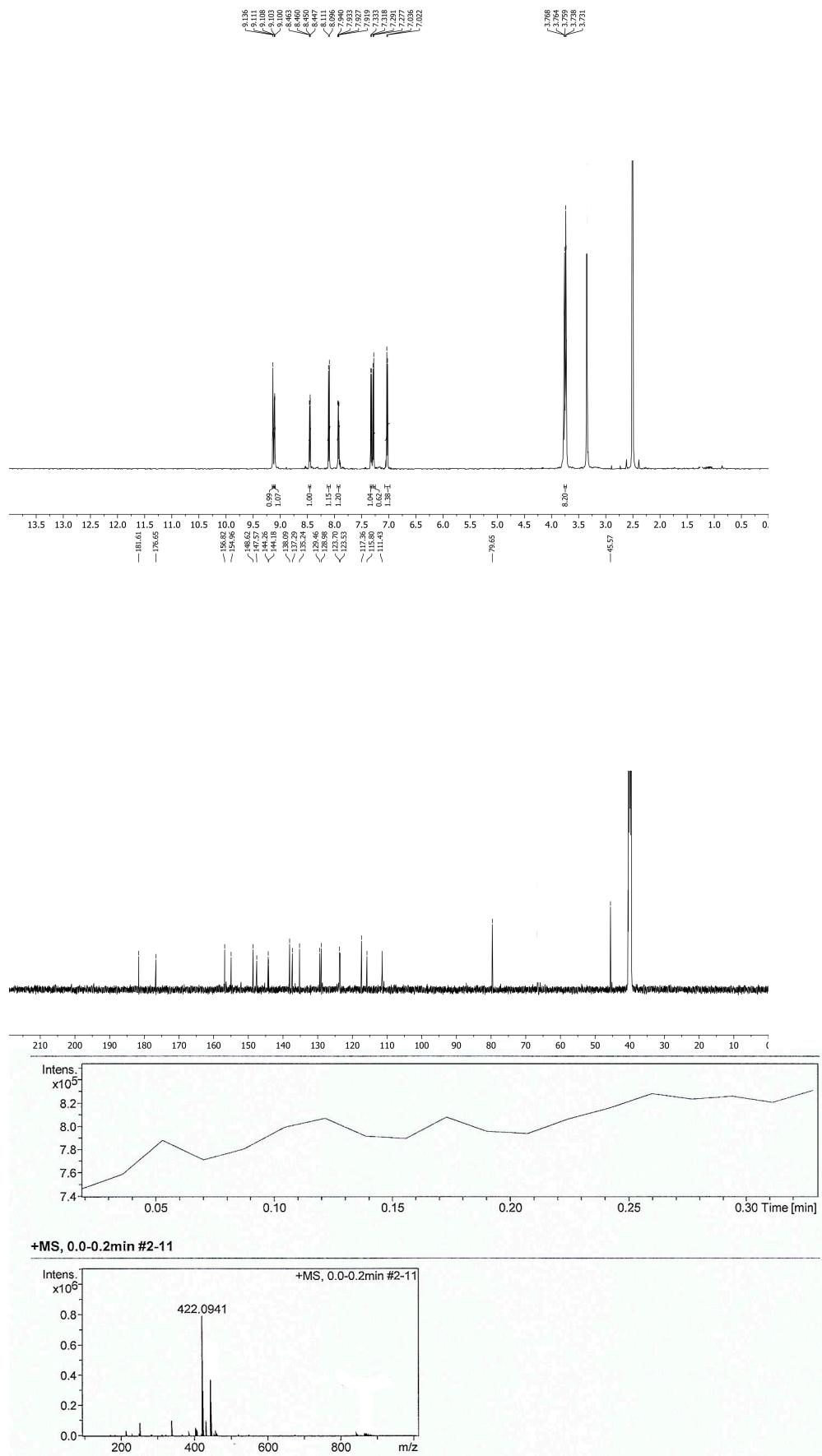


Figure S8: Spectra of 6-chloro-2-methyl-7-(quinolin-8-yloxy)quinoline-5,8-dione (**12a**).

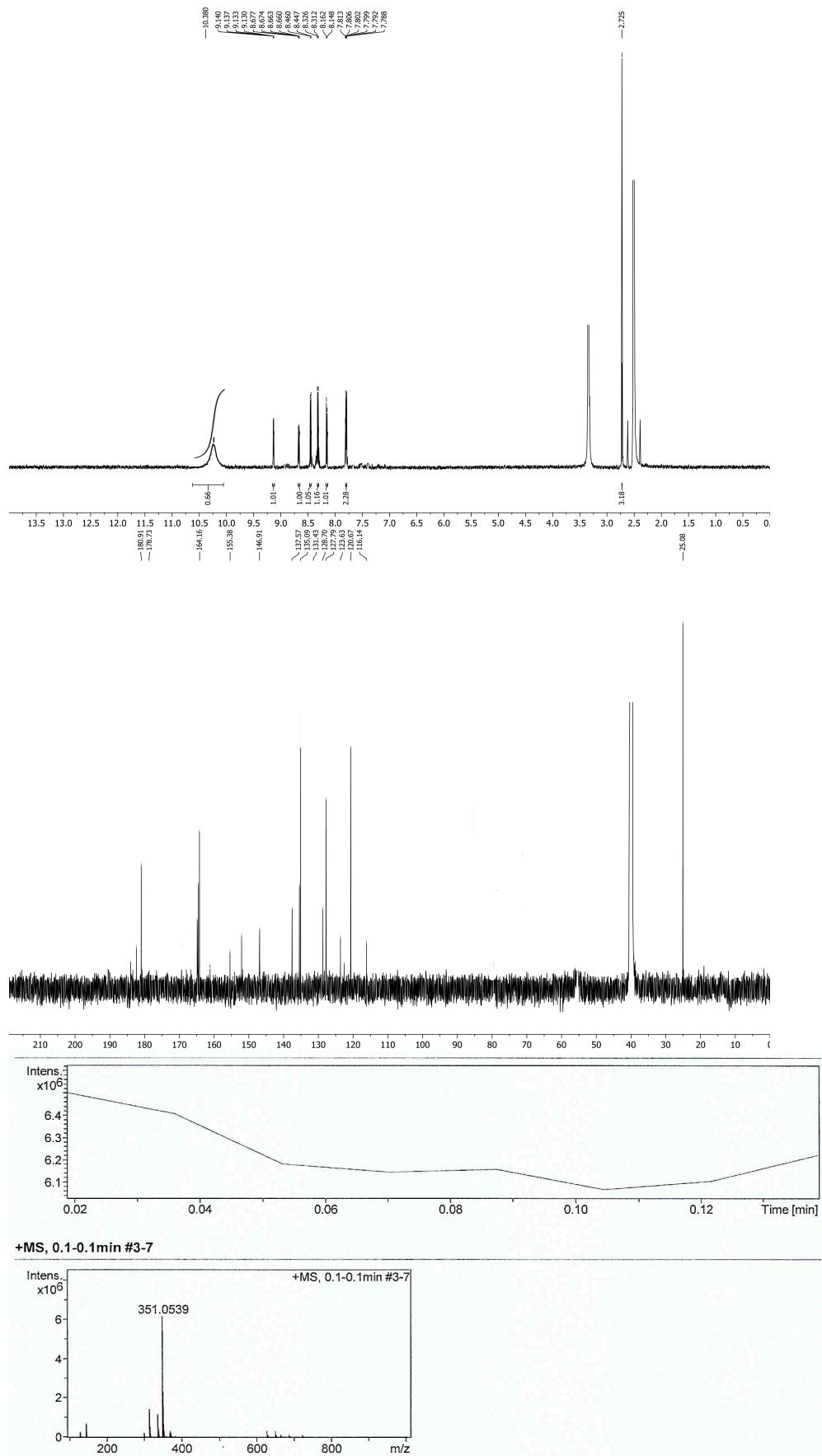


Figure S9: Spectra of 6-chloro-2-methyl-7-[(2-methylquinolin-8-yl)oxy]quinoline-5,8-dione (**12b**)

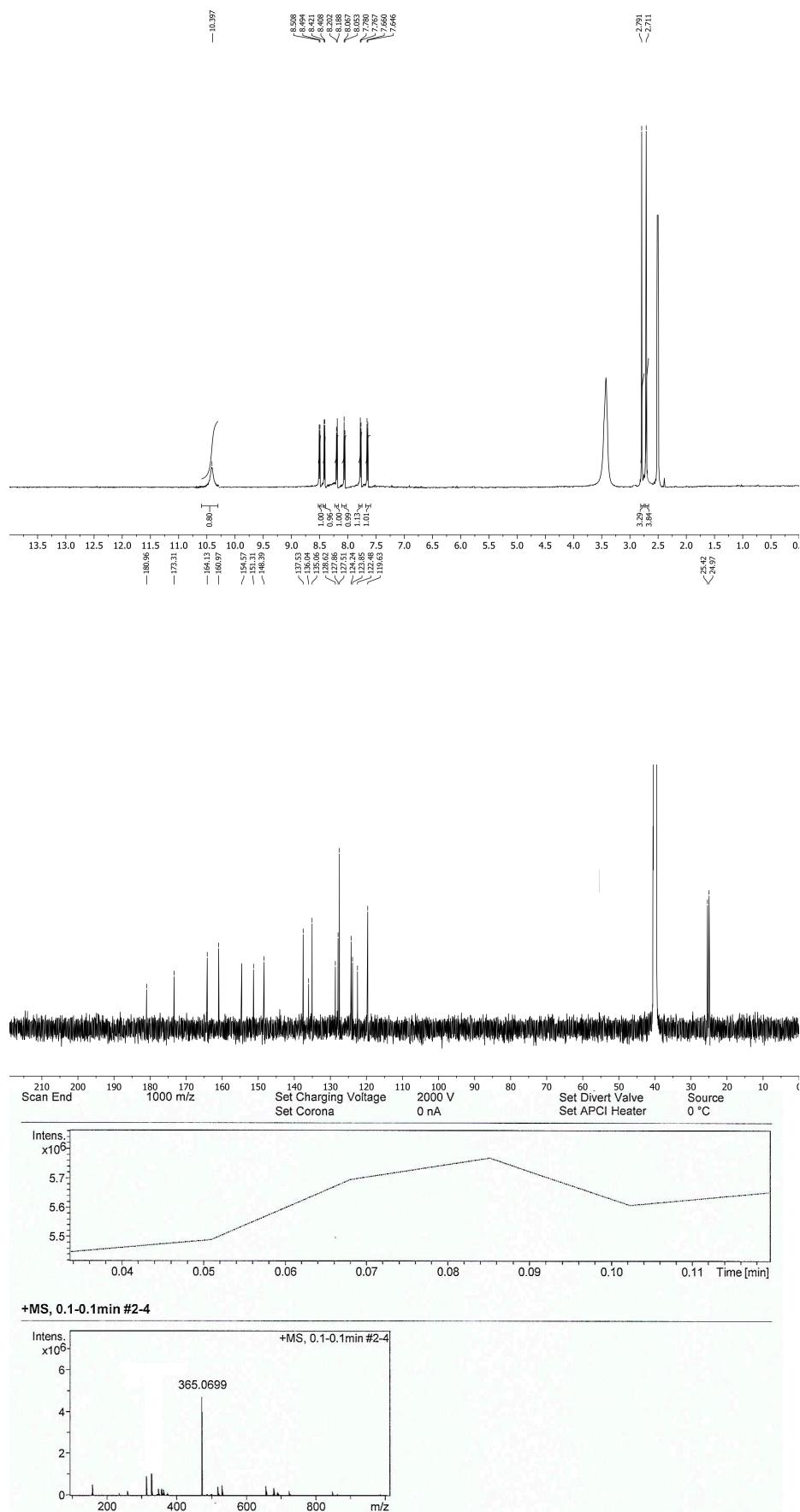


Figure S10: Spectra of 8-[(6-chloro-2-methyl-5,8-dioxo-5,8-dihydroquinolin-7-yl)oxy]quinoline-2-carbaldehyde (**12c**).

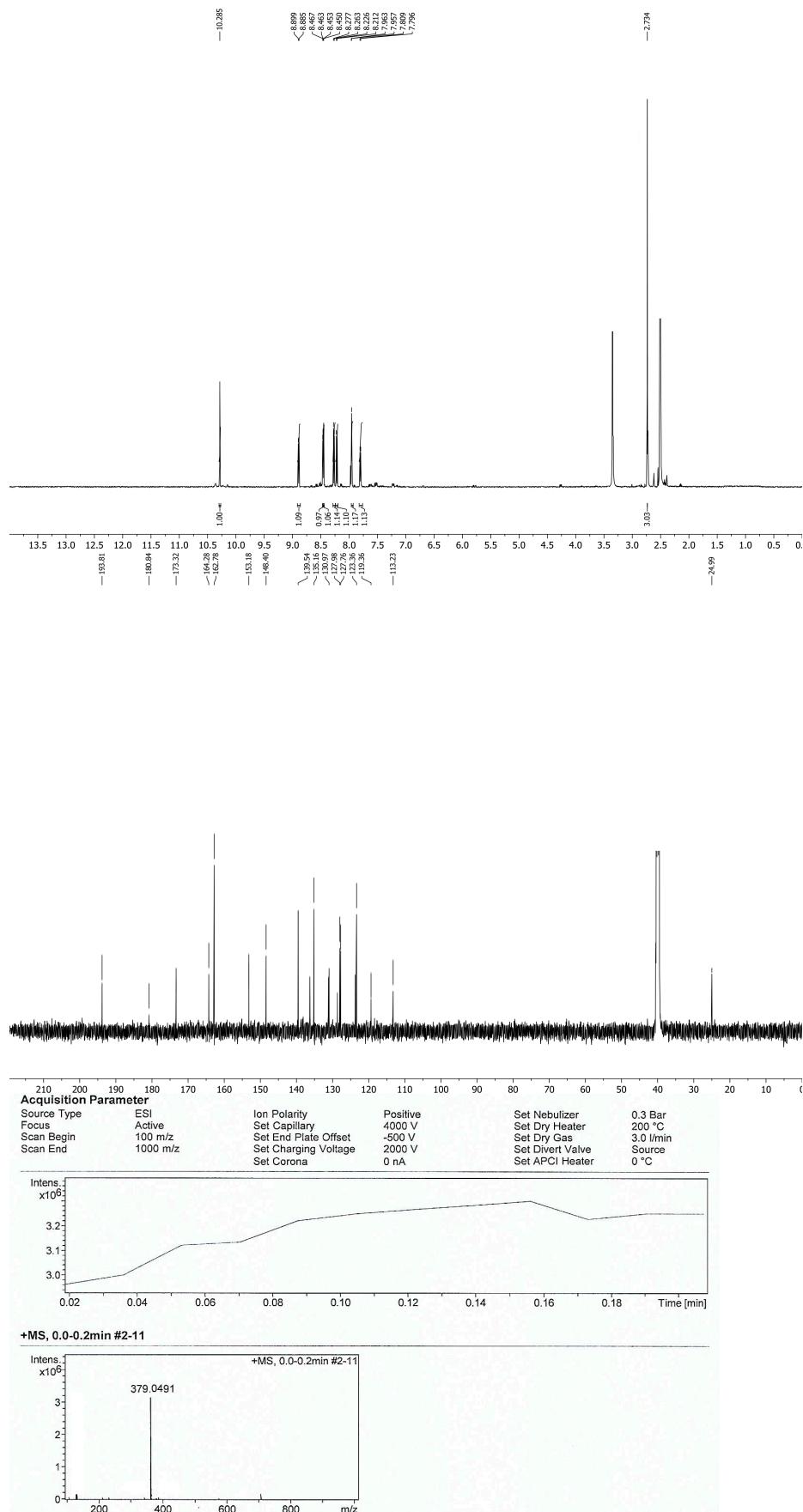


Figure S11: Spectra of 6-chloro-2-methyl-7-[(2-chloroquinolin-8-yl)oxy]quinoline-5,8-dione (**12d**).

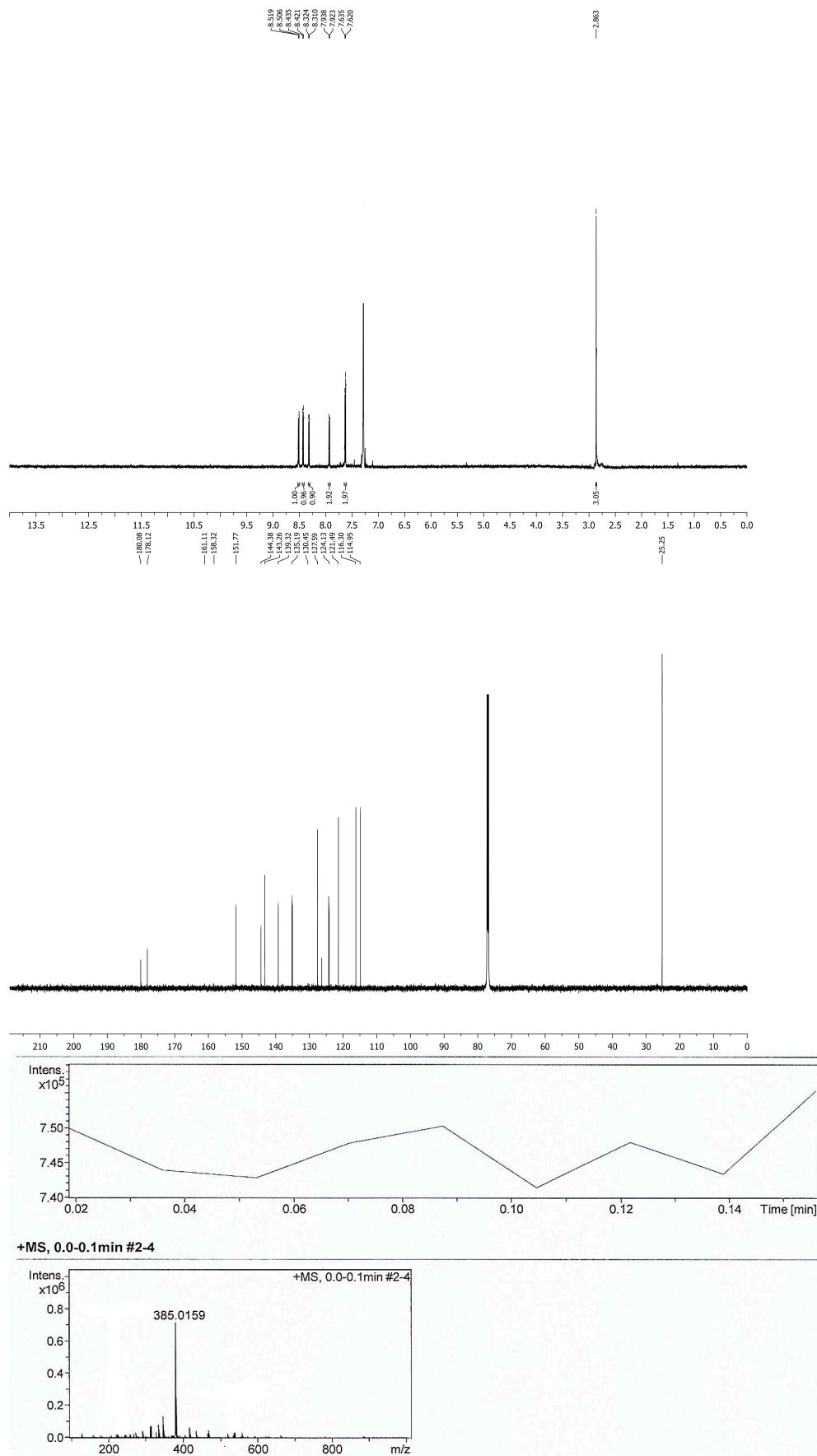


Figure S12: Spectra of 6-chloro-2-methyl-7-[(2-(pyrrolidin-1-yl)quinolin-8-yl]oxy}quinoline-5,8-dione (**12e**).

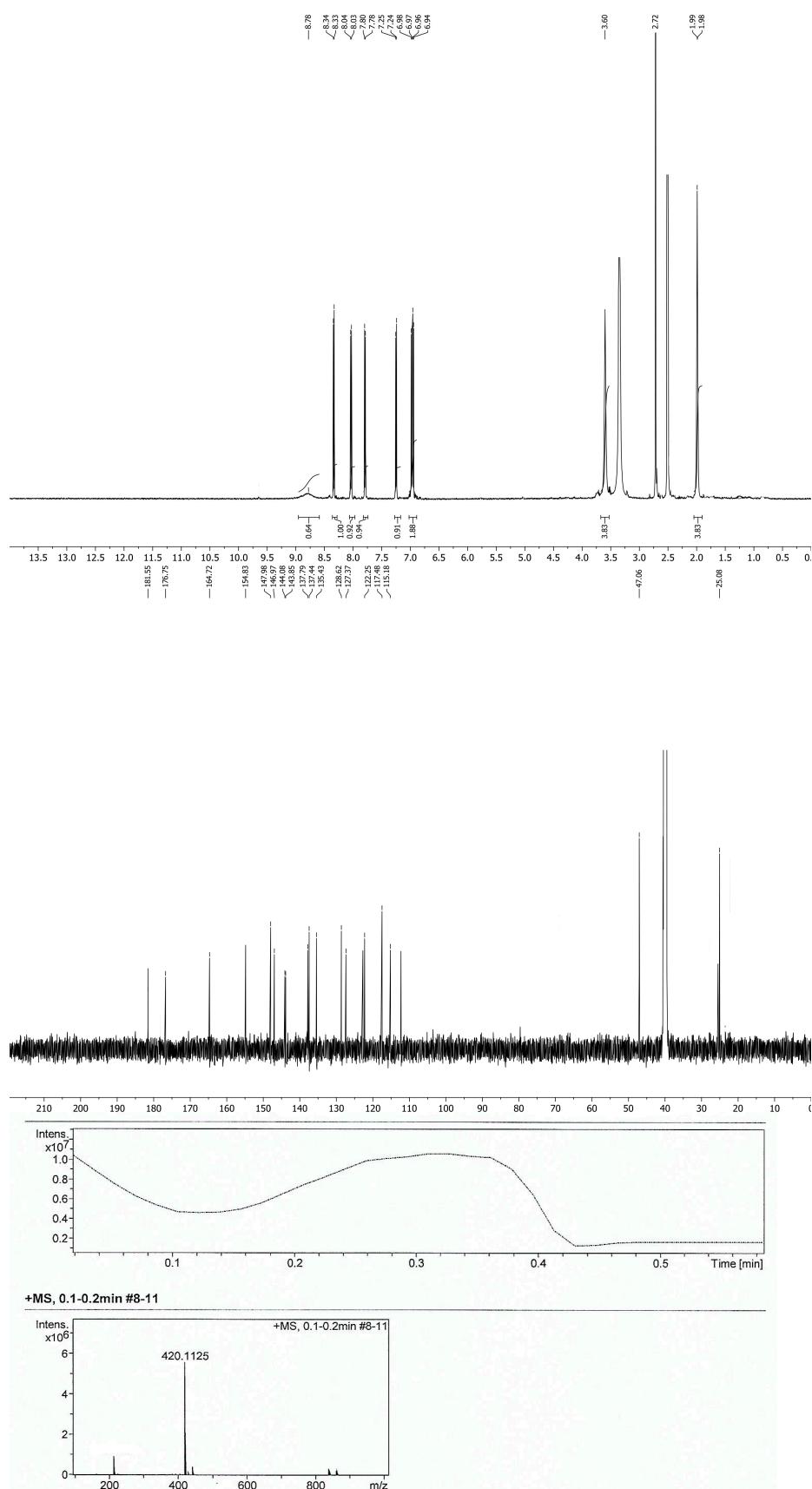


Figure S13: Spectra of 6-chloro-2-methyl-7-[(2-(morpholin-4-yl)quinolin-8-yl)oxy]quinoline-5,8-dione (**12f**).

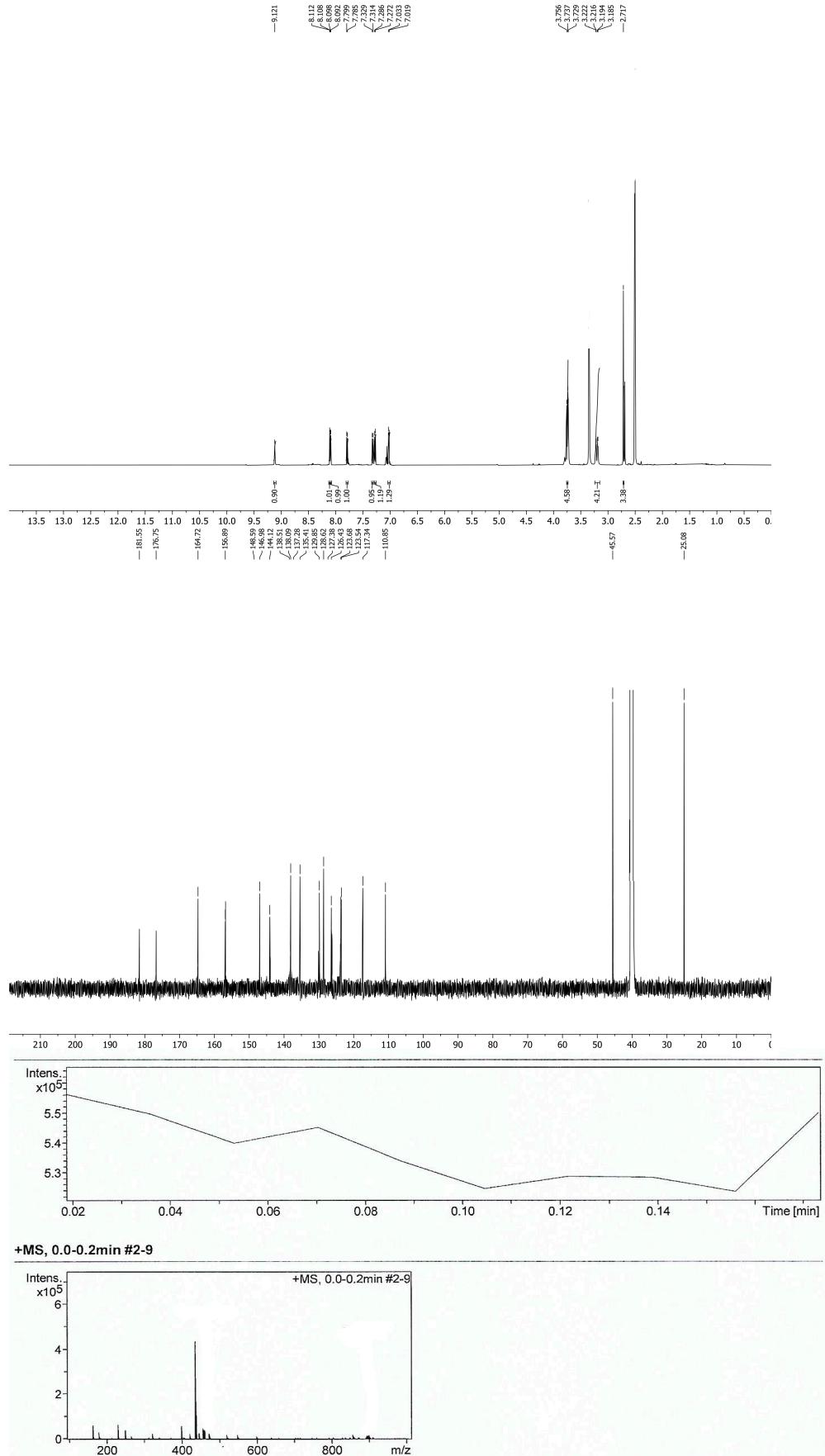


Figure S14: Spectra of 6-chloro-7-(quinolin-8-yloxy)isoquinoline-5,8-dione (**13a**).

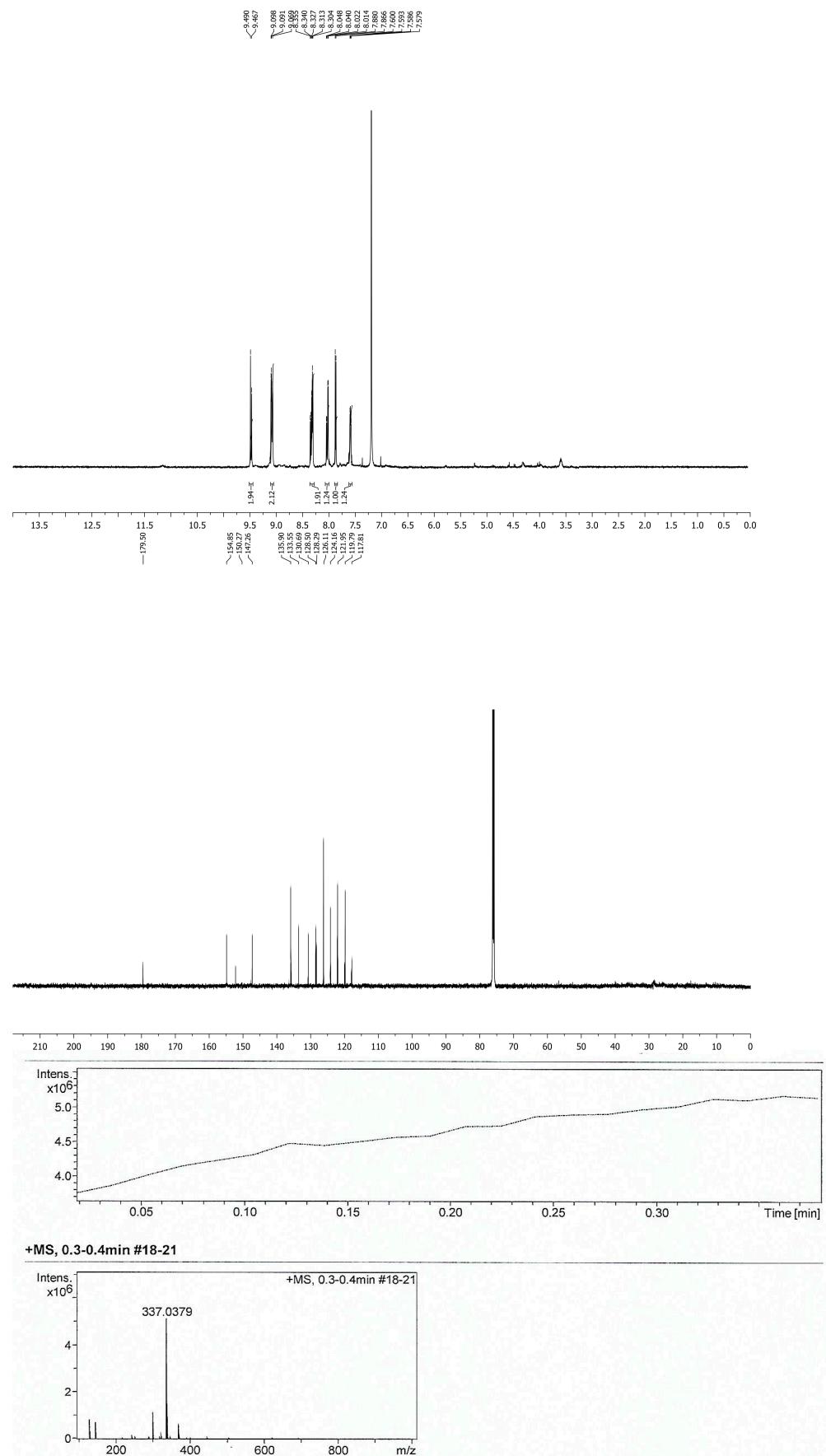


Figure S15: Spectra of 6-chloro-7-[(2-methylquinolin-8-yl)oxy]isoquinoline-5,8-dione (**13b**)

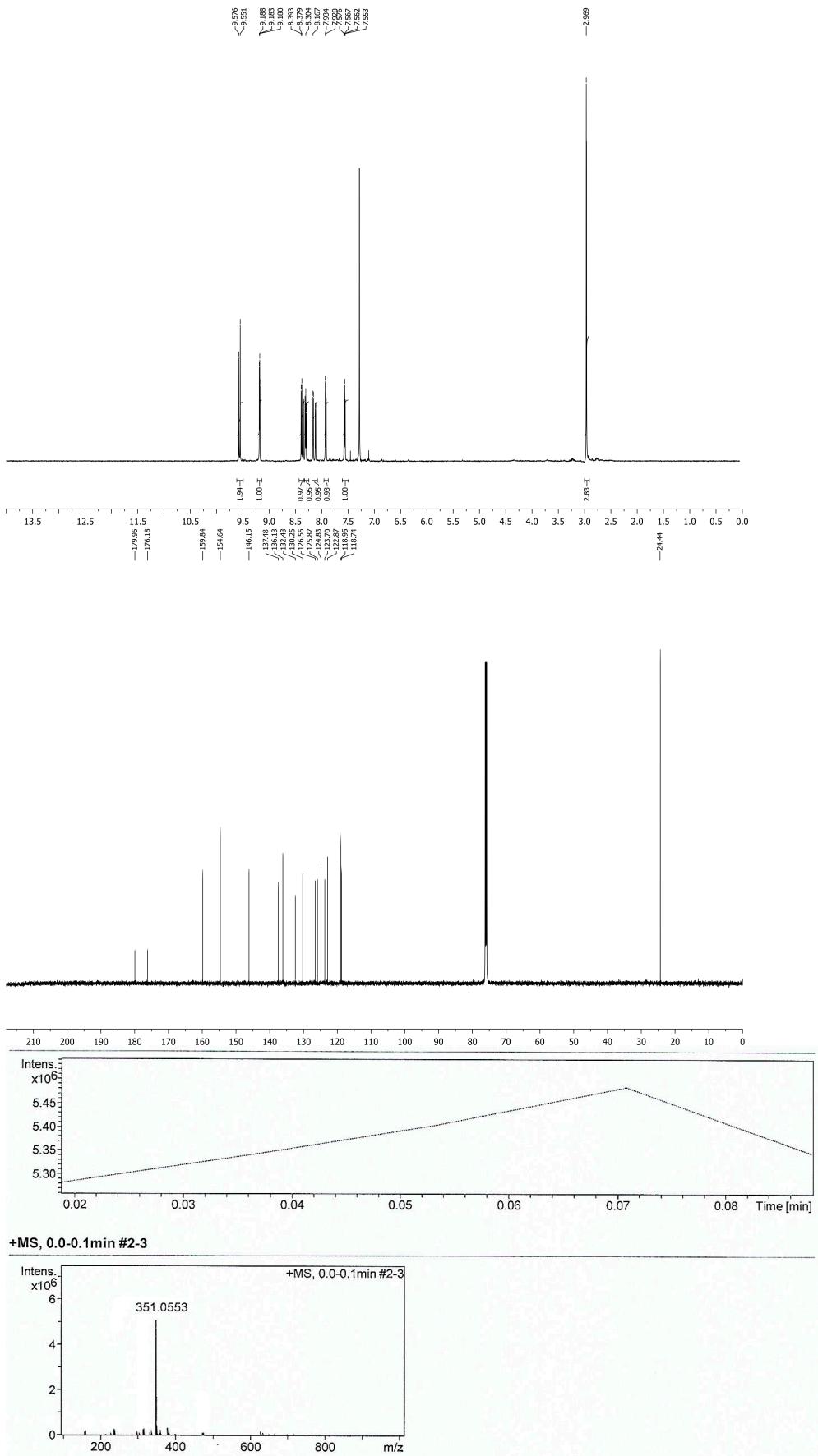


Figure S16: Spectra of 8-[(6-chloro-5,8-dioxo-5,8-dihydroquinolin-7-yl)oxy]isoquinoline-2-carbaldehyde (**13c**).

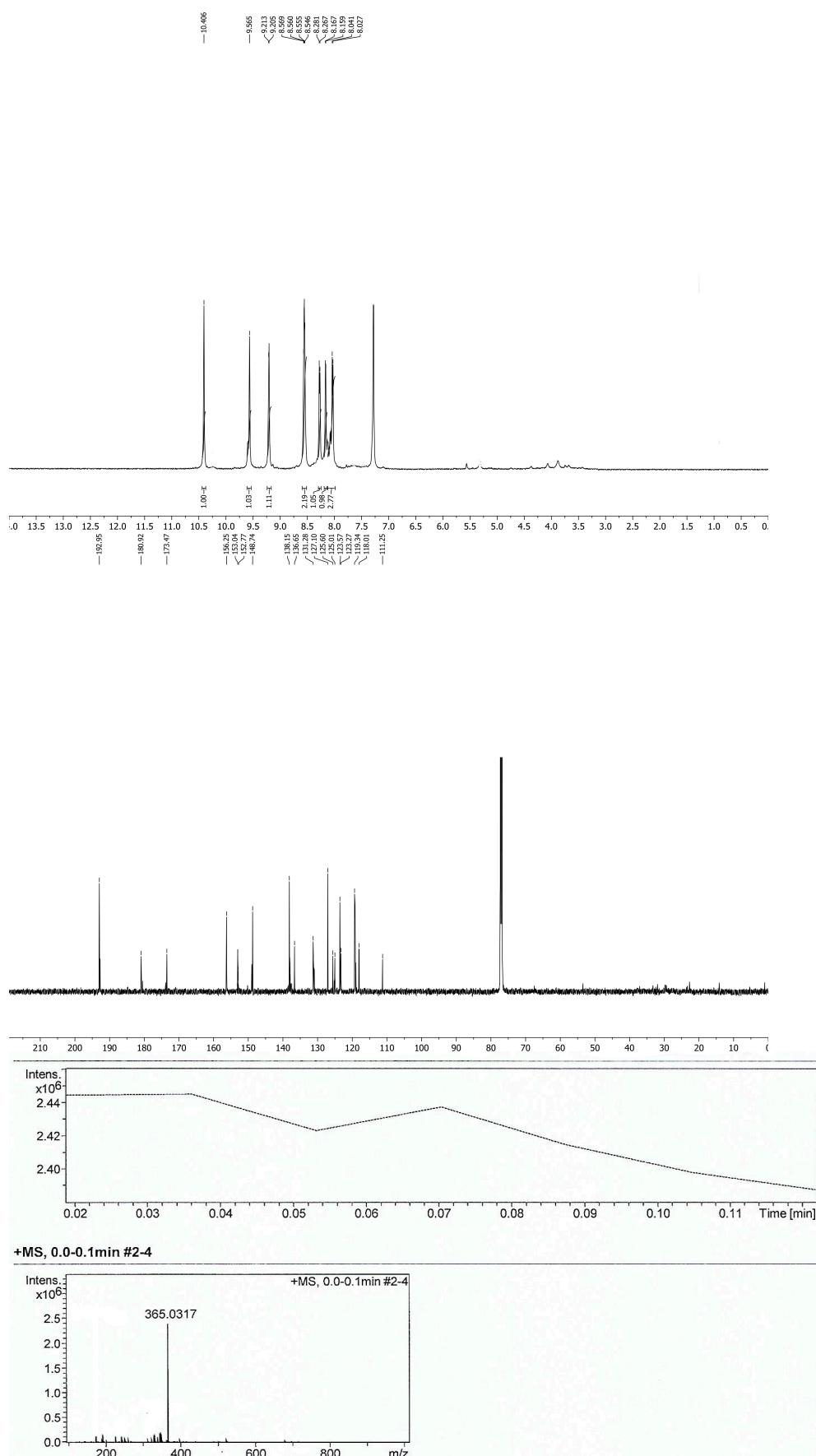


Figure S17: Spectra of 6-chloro-7-[(2-chloroquinolin-8-yl)oxy]isoquinoline-5,8-dione (**13d**).

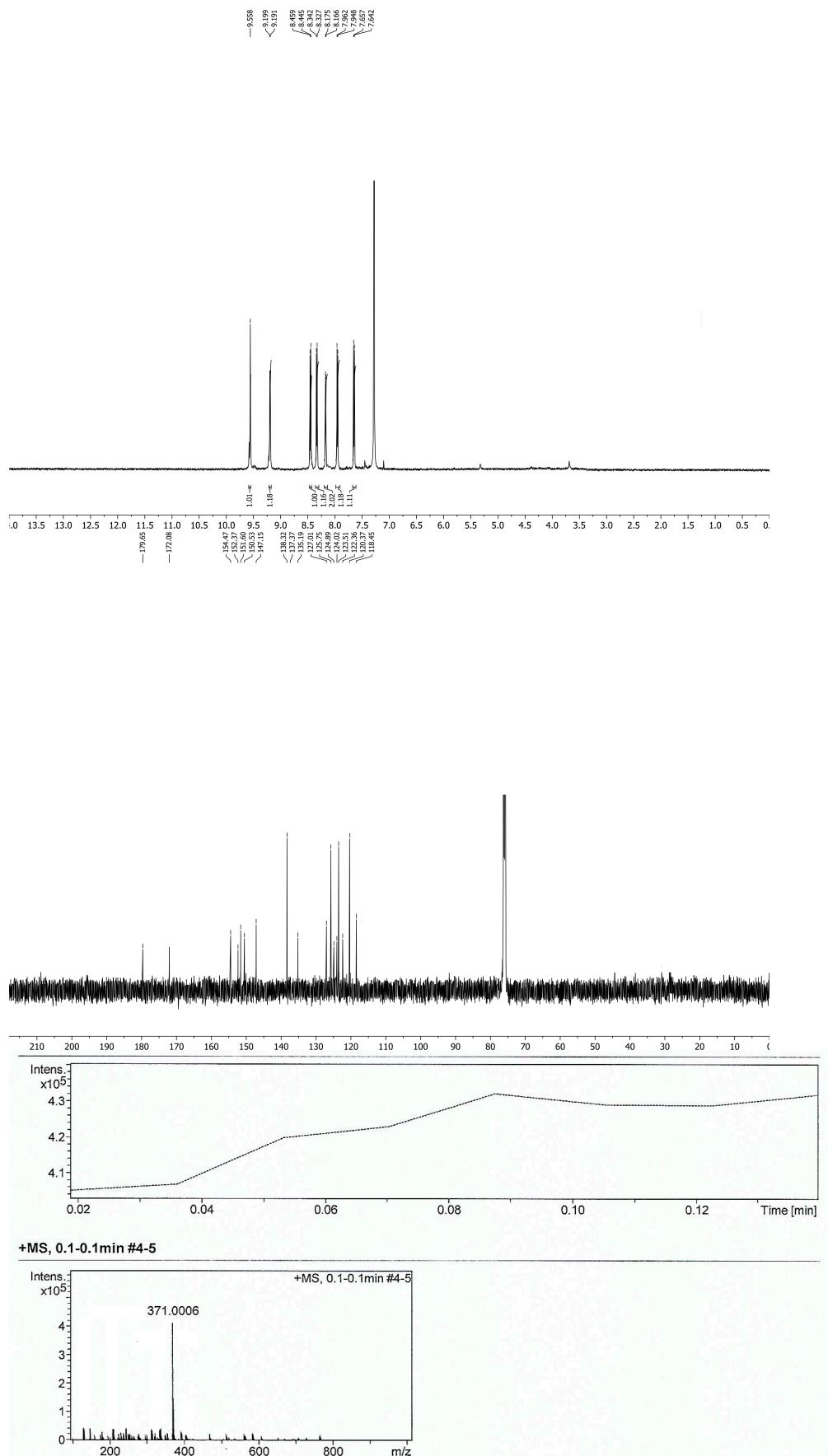


Figure S18: Spectra of 6-chloro-7-[2-(pyrrolidin-1-yl)quinolin-8-yl]oxy]isoquinoline-5,8-dione (**13e**).

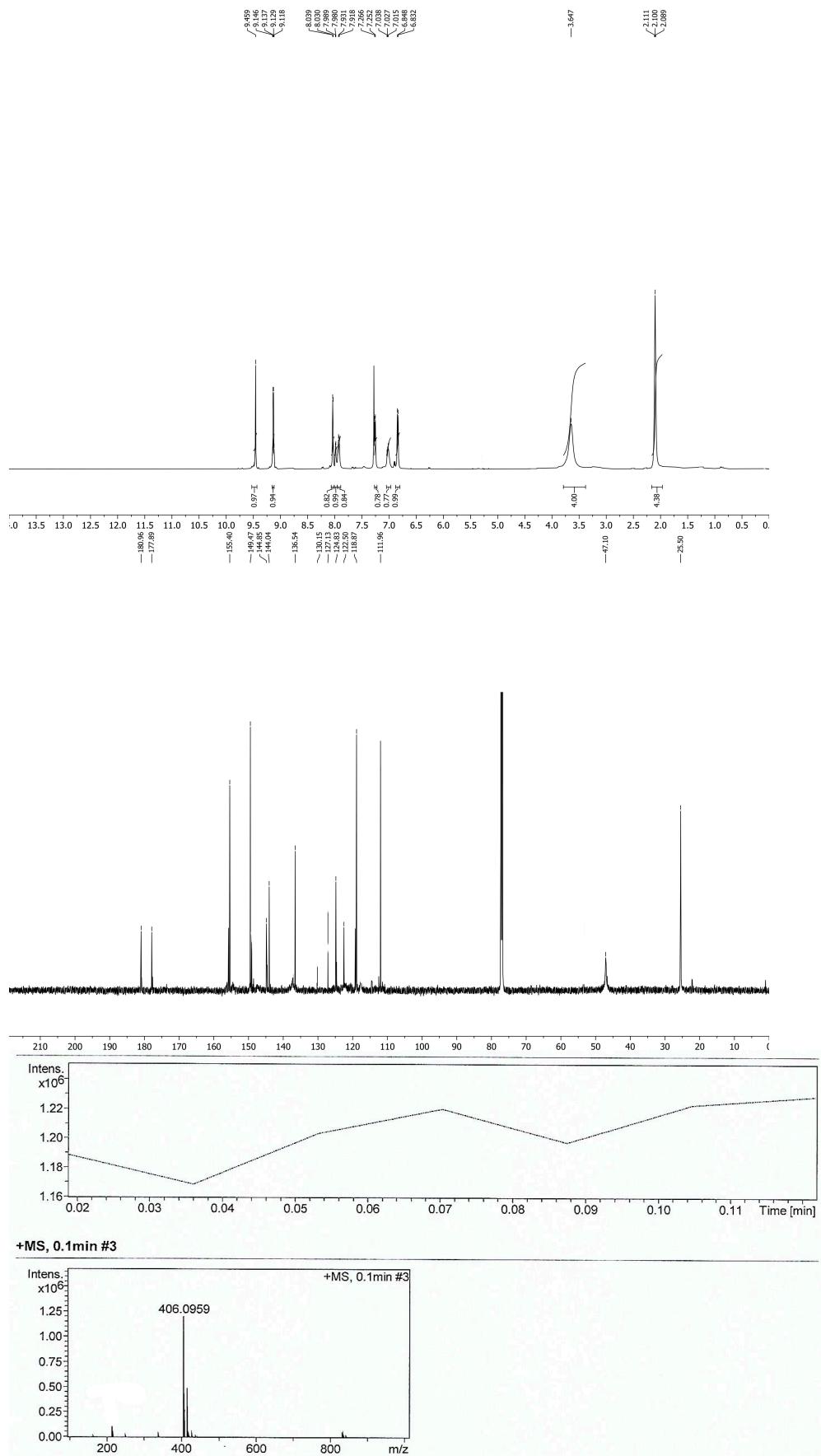


Figure S19: Spectra of 6-chloro-7-[2-(morpholin-4-yl)quinolin-8-yl]oxy)isoquinoline-5,8-dione (**13f**).

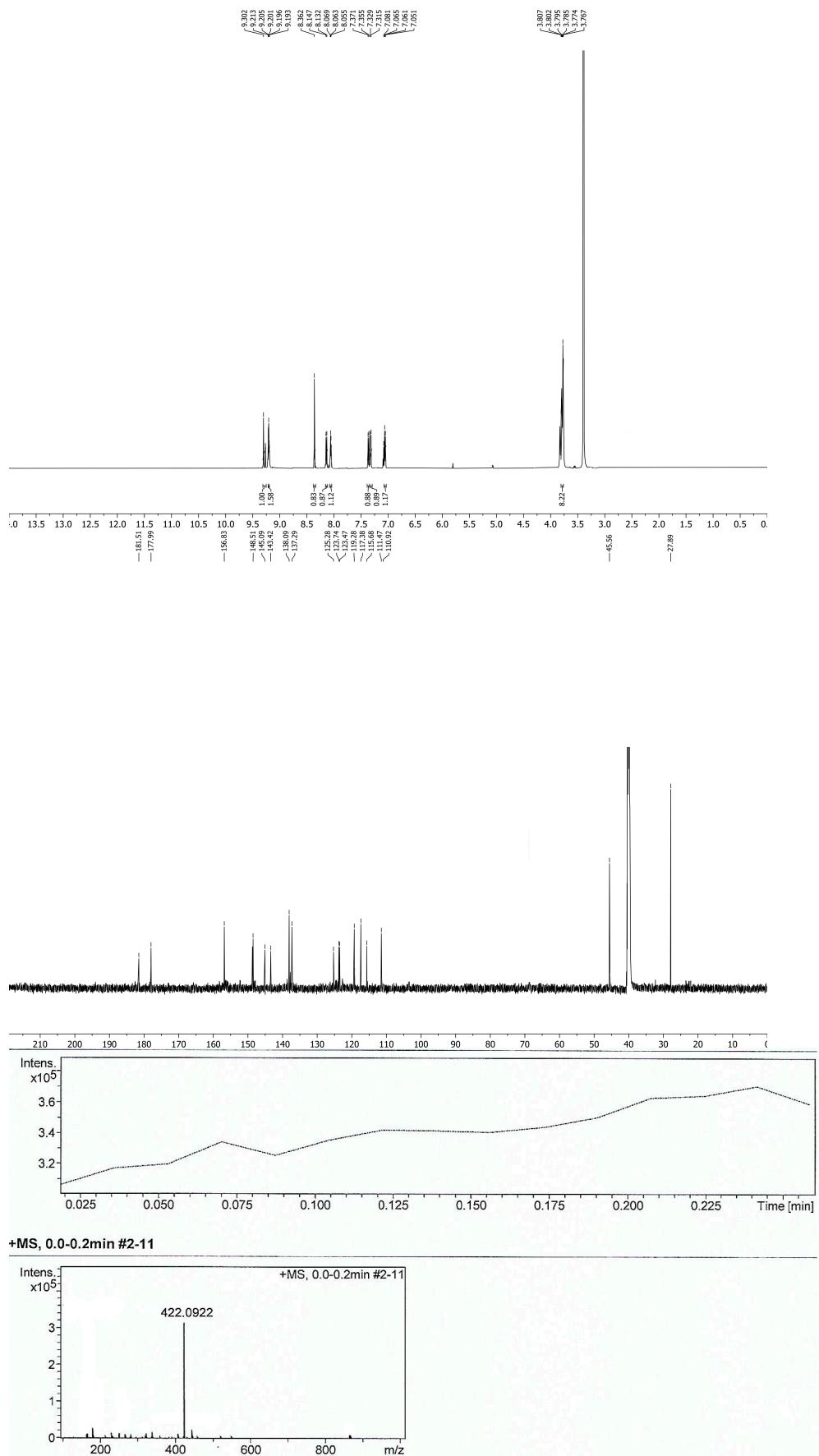


Figure S20: Spectra of 2-chloro-3-[(quinolin-8-yl)oxy]naphthalene-1,4-dione (**14a**).

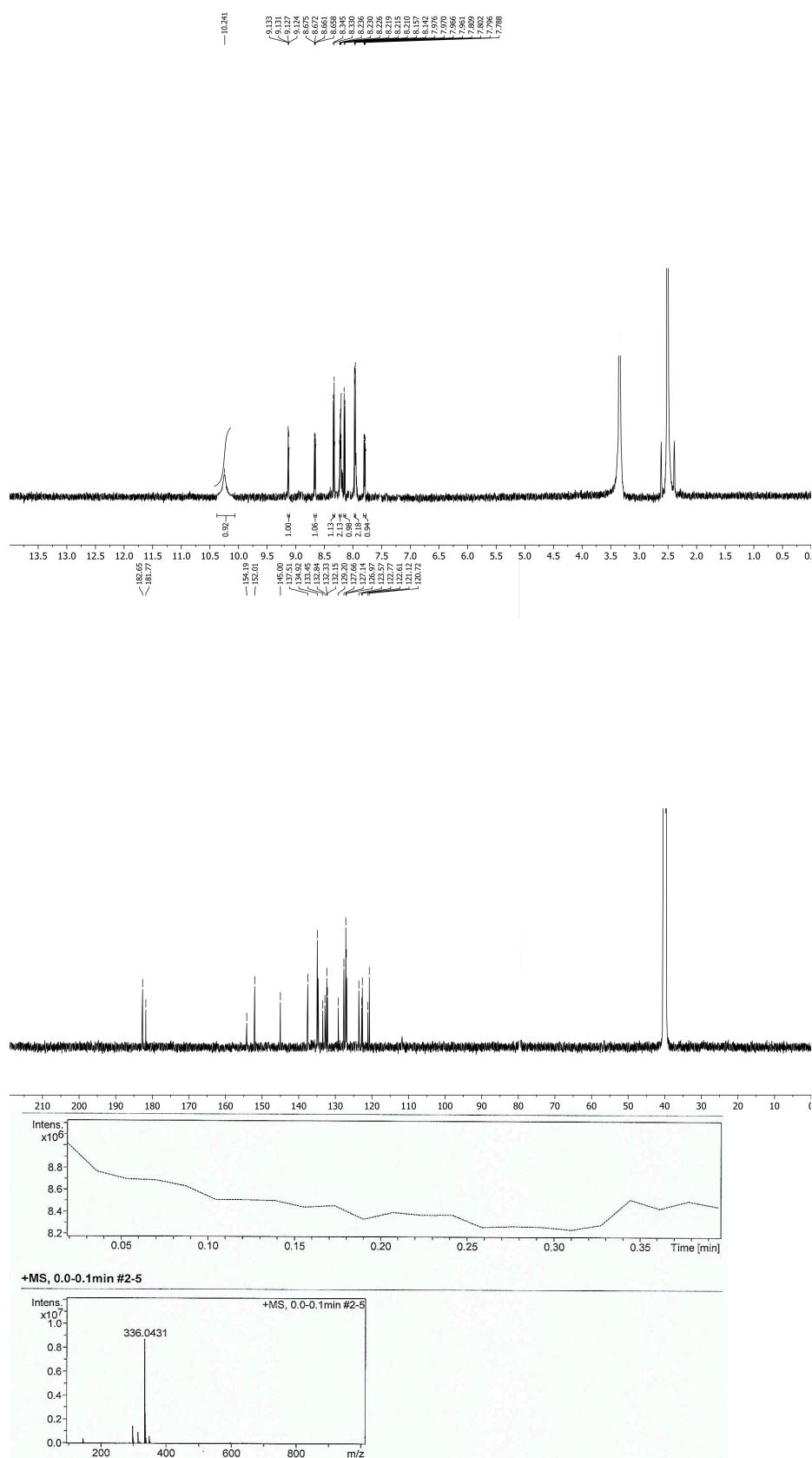


Figure S21: Spectra of 2-chloro-3-[(2-methylquinolin-8-yl)oxy]naphthalene-1,4-dione (**14b**).

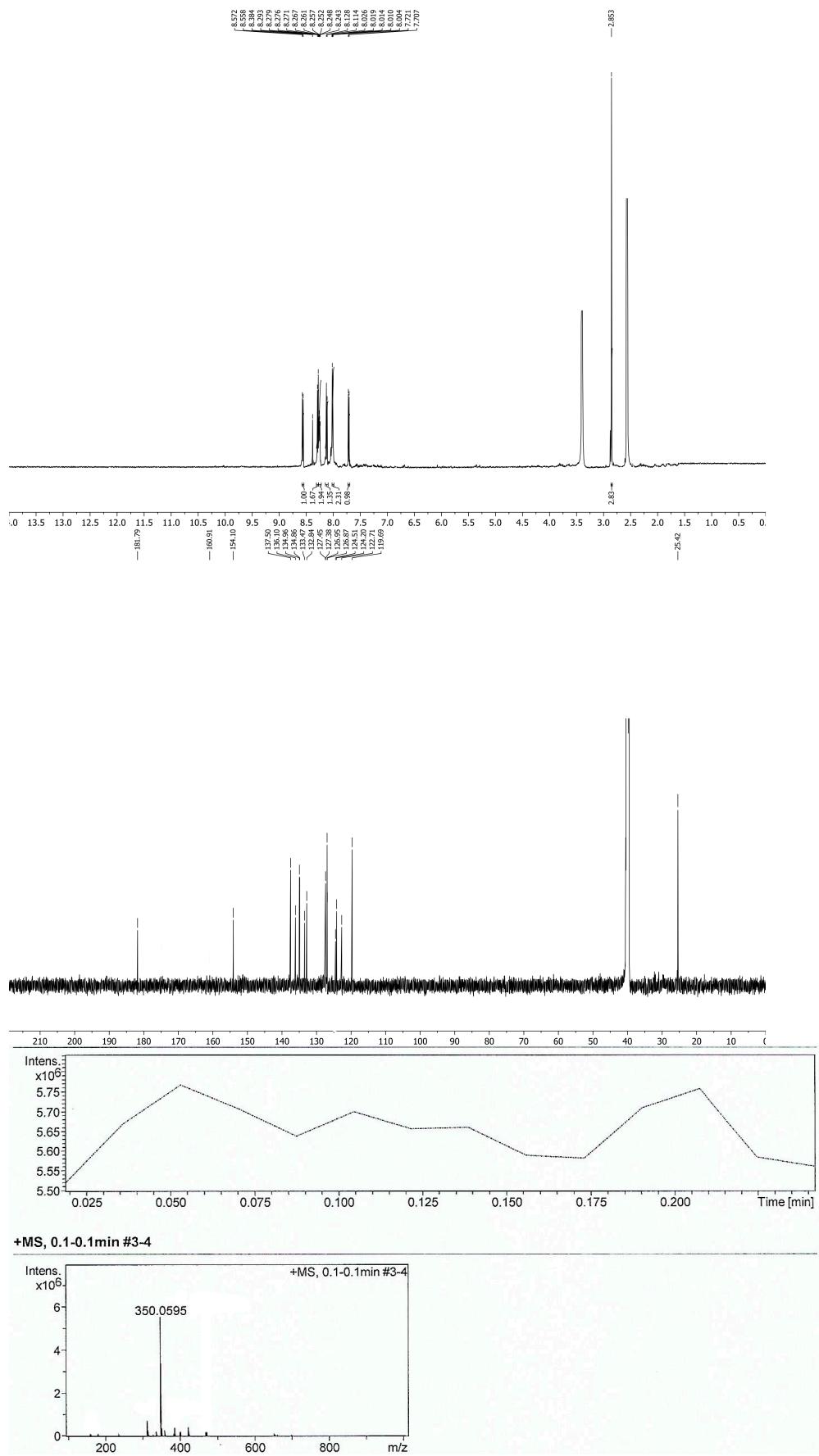


Figure S22: Spectra of 8-[(3-chloro-1,4-dioxo-1,4-dihydronaphthalen-2-yl)oxy]quinoline-2-carbaldehyde (**14c**).

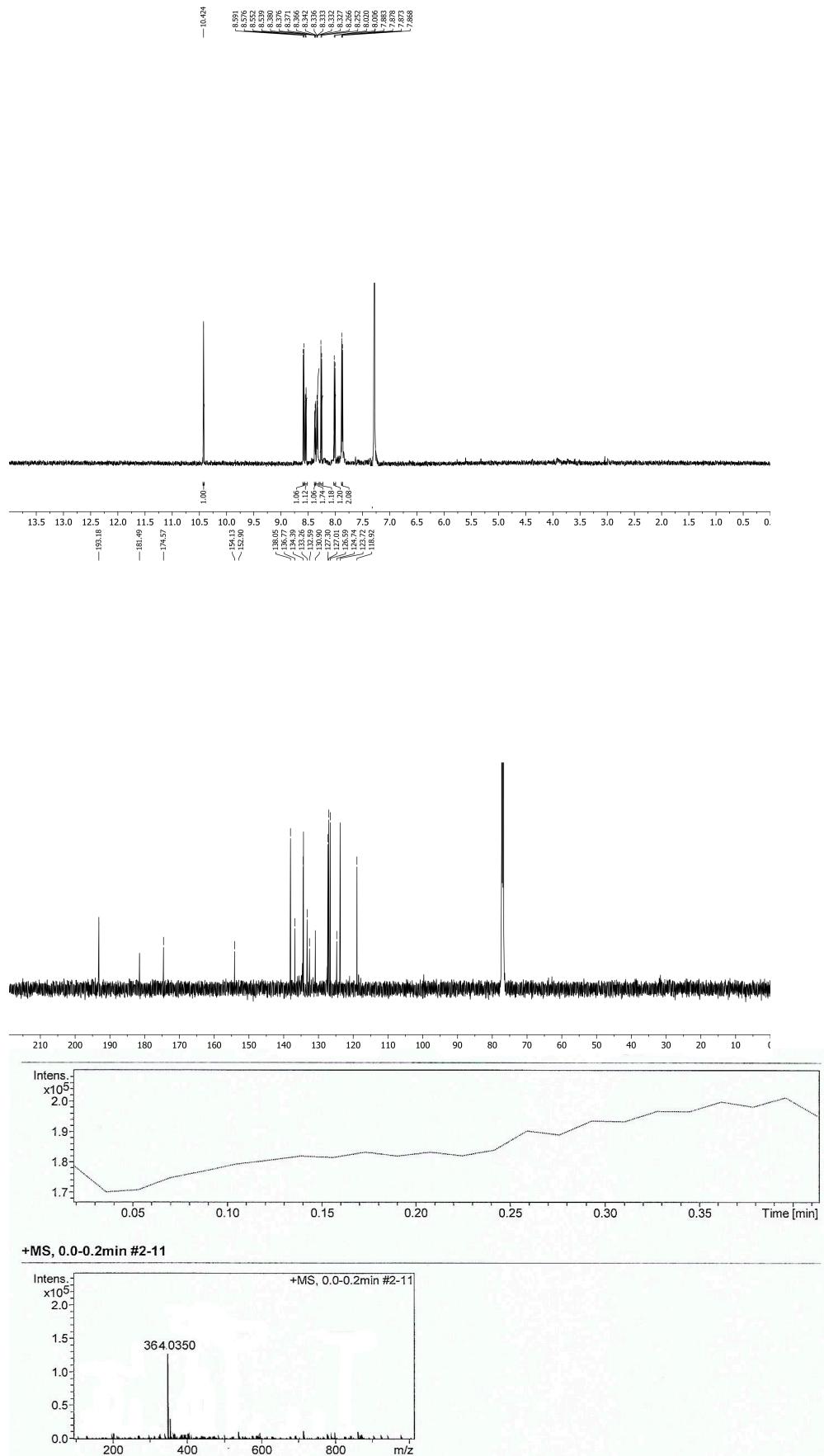


Figure S23: Spectra of 2-chloro-3-[(2-chloroquinolin-8-yl)oxy]naphthalene-1,4-dione (**14d**).

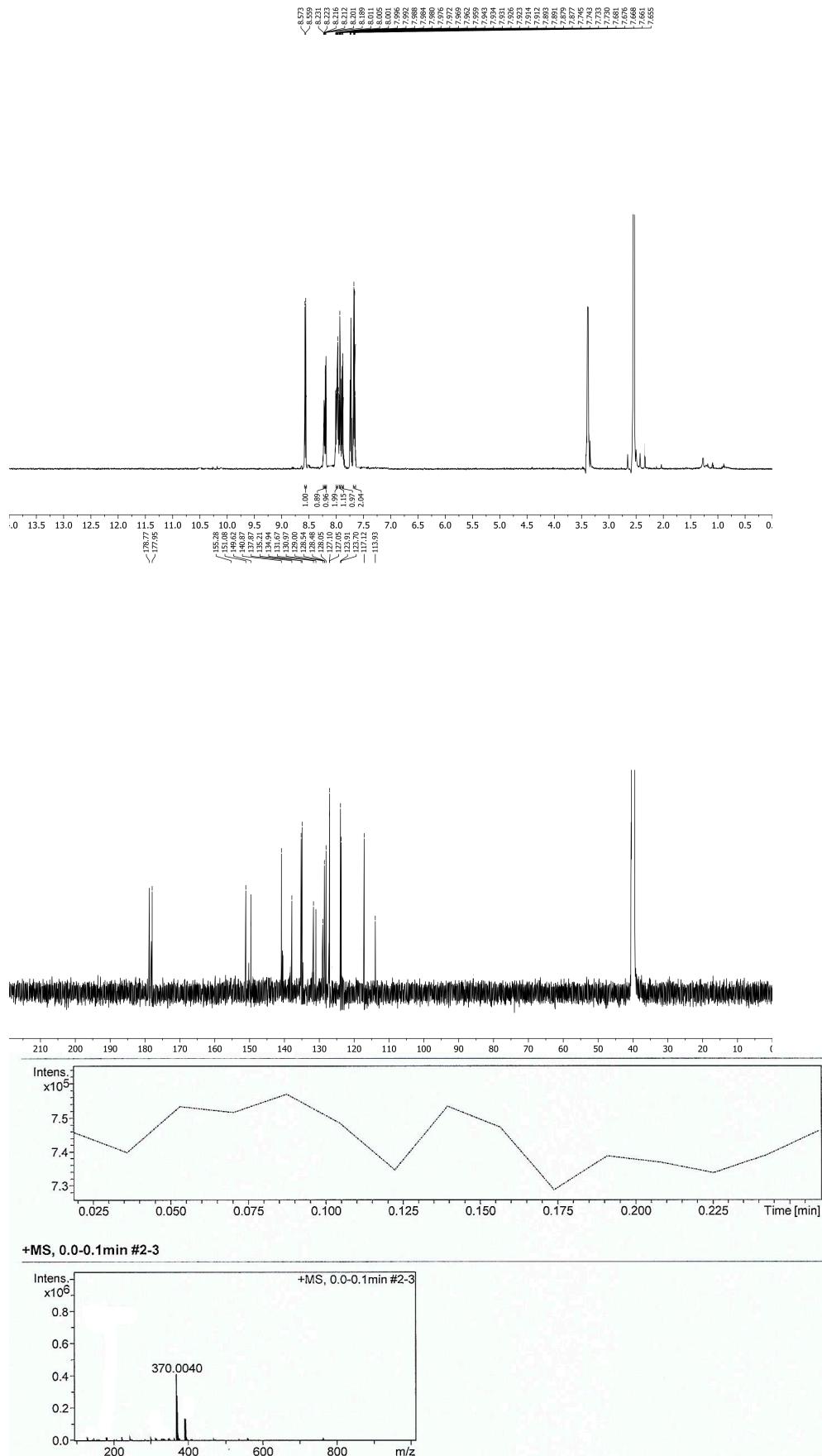


Figure S24: Spectra of 2-chloro-3-[2-(pyrrolidin-1-yl)quinolin-8-yl]oxy)naphthalene-1,4-dione (**14e**).

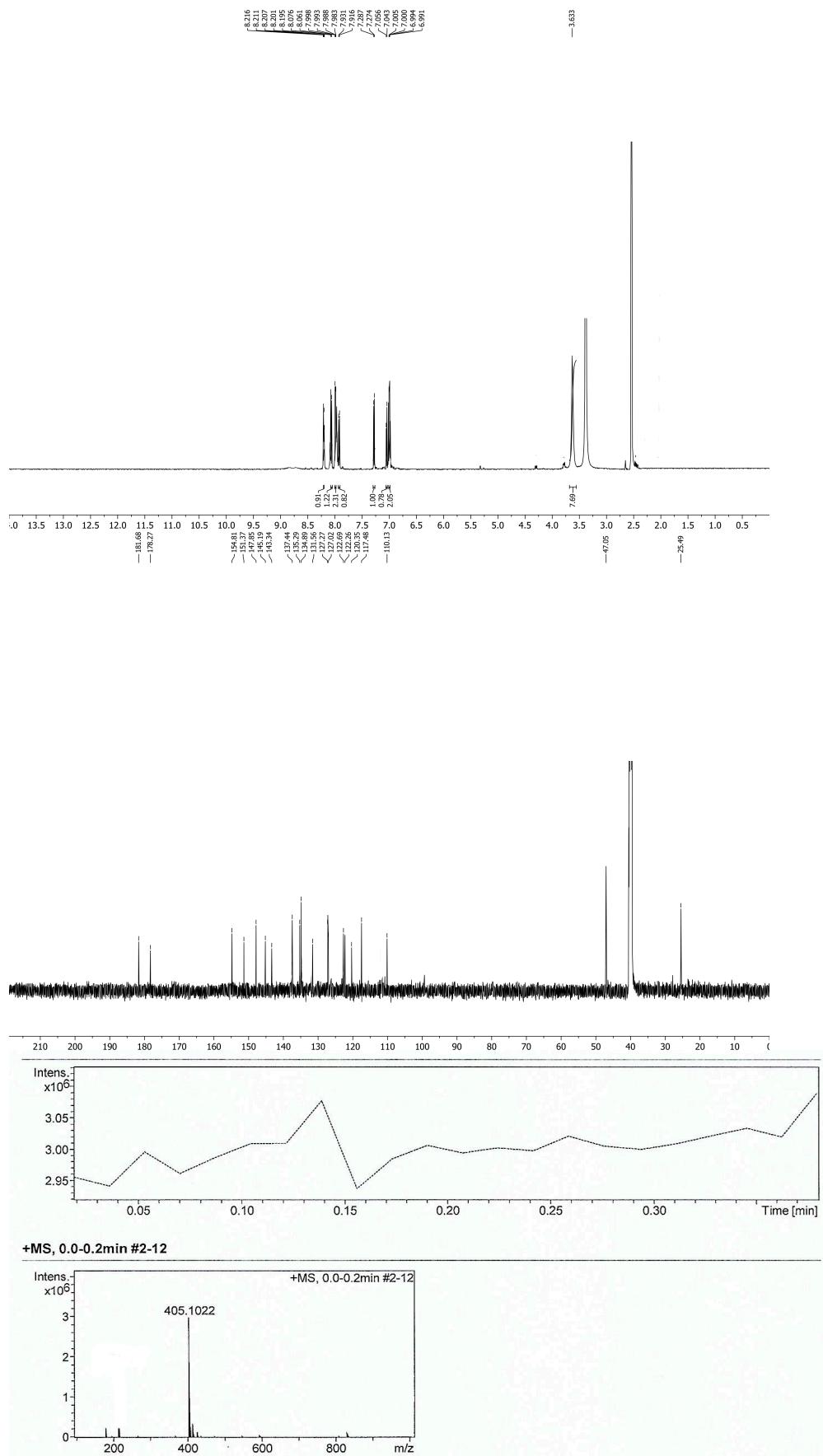


Figure S25: Spectra of 2-chloro-3-{{[2-(morpholin-4-yl)quinolin-8-yl]oxy}naphthalene-1,4-dione (**14f**).

