Supporting Information

It takes two to tango: synthesis of cytotoxic quinones containing two redox active centers with potential antitumor activity

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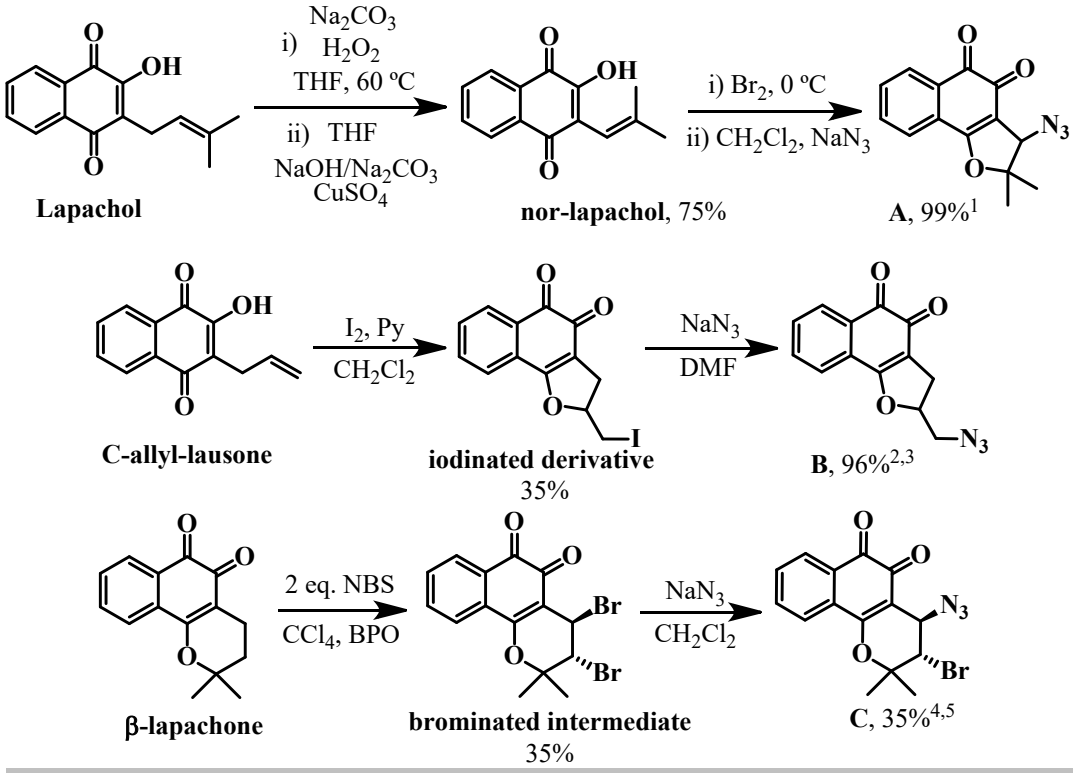
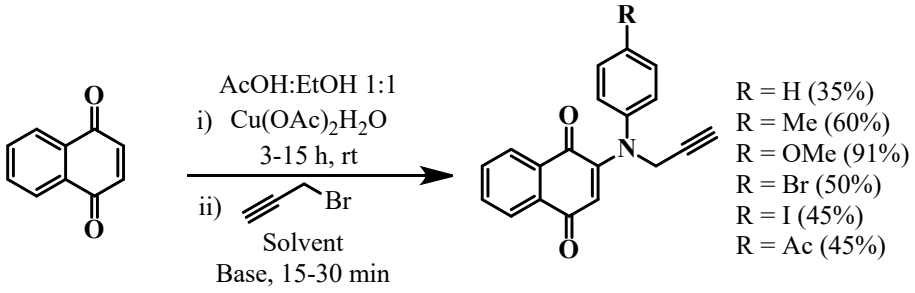
(A) Synthesis of the clickable azide precursors:



(B) Synthesis of the clickable alkyne quinone derivatives[6]:



Scheme S1. BPO = Benzoyl peroxide. Note: compounds were obtained in a racemic form, but the *trans* relative configuration was confirmed by X-ray crystallography as a part of previous studie.[5]

Table S1. Crystal data collection and structure refinement for the compounds **20**, **21** and **35**.

Compound	**20**	**21**	**35**
Chemical formula	$C_{16}H_{15}N_3O_3$	$C_{25}H_{23}N_3O_3Se$	$C_{25}H_{23}N_3O_3Se$
M (g mol^{-1})	297.31	492.42	492.42
Crystal system	Triclinic	Triclinic	Triclinic
Space group	P-1	P-1	P-1
Unit cell a (Å)	7.890(4)	9.364(2)	7.573(2)
b (Å)	9.750(5)	10.472(2)	11.910(3)
c (Å)	9.847(5)	12.443(3)	15.396(4)
α	99.739(6)	72.327(5)	69.978(4)
β	103.567(6)	75.582(5)	81.094(4)
γ	91.493(6)	80.655(5)	78.524(4)
V (Å^3)	730.2(6)	1120.15(5)	1272.9(5)
Z	2	2	2
D_c /g cm^{-3}	1.352	1.460	1.285
Index ranges	$-9 \le h \le 9$	$-11 \le h \le 11$	$-9 \le h \le 9$
	$-11 \le k \le 11$	$-12 \le k \le 12$	$-14 \le k \le 14$
	$-11 \le l \le 11$	$-15 \le l \le 15$	$-18 \le l \le 18$
Absorption coefficient /mm^{-1}	0.096	1.709	1.503
Absorption correction	multi-scan	multi-scan	multi-scan
Max/min transmission	0.7452 / 0.4097	0.7452 / 0.5965	0.7452 / 0.5965
Measured reflections	11855	26279	29902
Independent reflections / R_{int}	2686 / 0.0773	4155 / 0.0951	4729 / 0.1064
Refined parameters	202	289	294
R1 (F) / wR2 (F^2) ($I > 2\sigma(I)$)	0.0514 / 0.1213	0.0539 / 0.1106	0.0552 / 0.1199
GooF	1.015	1.006	0.910
Largest diff. peak and hole (eÅ^{-3})	0.167 and -0.149	0.820 and -0.586	0.259 and -0.139

Experimental section

General Procedures: Starting materials obtained from commercial suppliers were employed as received unless otherwise stated. For reagents requiring purification, standard laboratory techniques based on methods published by Perrin, Armarego and Perrin were employed.[7] Flash column chromatography (FCC) was performed using silica gel (Aldrich 40-63 μm, 230-400 mesh). Thin layer chromatography (TLC) was performed on aluminum-backed 60 F254 silica plates. Visualization was achieved by UV fluorescence. Proton nuclear magnetic resonance (NMR) spectra were recorded using a Bruker DRX 400 or a Bruker AVANCE 400 spectrometer. ^{13}C NMR spectra were recorded at 100 MHz as stated. Chemical shifts (δ) are given in parts per million (ppm). Peaks are described as singlets (s), doublets (d), doublet of doublets (dd), doublet of triplets (dt), triplets (t), triplet of doublets (td), quartets (q), quintets and multiplets (m). The ^{1}H and ^{13}C NMR spectra were referenced to the appropriate residual solvent peak or TMS peak. Coupling constants (*J*) were quoted to the nearest 0.5 Hz. Mass spectra were recorded using a Brüker Daltonics micrOTOF-Q II ($APPI^+$ and ESI^+ mode). Infrared spectra were recorded on a Perkin Elmer Spectrum One FTIR spectrometer as thin films or solids compressed on a diamond plate. IR bands are described by the wavenumber ($\bar{\nu}$, cm^{-1}). Elemental analysis of selected compounds was performed with a Perkin-Elmer 2400-II CHN analyzer. Melting points were determined on the Stuart SMP30 melting point apparatus and are uncorrected.

Synthesis of substrates: Diselenides were synthesized via the Grignard reaction followed by transmetalation with Se powder (200 mesh).[8] Substituted propargyl selenides were synthesized by reaction of the corresponding diselenides with $NaBH_4$ in THF/EtOH (2:1) under argon atmosphere, followed by slow addition of propargyl bromide[9] Lapachol (2-hydroxy-3-(3'-methyl-2'-butenyl)-1,4-naphthoquinone) was extracted from the heartwood of *Tabebuia sp.* (Tecoma) and purified by a series of recrystallizations in an appropriate solvent. From this quinone, nor-lapachol (2-hydroxy-3-(2'-methyl-propenyl)-1,4-naphthoquinone) was obtained by the Hooker oxidation method.[10] From lawsone, C-allyl-lawsone was synthesized following the procedure described by Fieser.[11] Hydroxylated lapachones **19** and **29** were synthesized via acidic cyclisation of lapachol and nor-lapachol with paraformaldehyde in formic acid under

reflux.[12] Clickable quinone-alkyne derivatives, and quinonoid azide compounds **A**, **B** and **C** were synthesized by following a previously reported procedure by our research group.[3,4,5]

General procedure for Cu(I) catalyzed "Click" cycloadditions

A 5 mL resealable tube was charged with the corresponding quinone-azide (0.200 mmol), the corresponding quinone-alkynes or selenated alkynes (0.220 mmol), $CuSO_4.5H_2O$ (1.0 mg, 0.0020 mmol, 1 mol%) and sodium ascorbate (4.0 mg, 0.010 mmol, 5 mol%). Then, 4 mL of a mixture of CH_2Cl_2/H_2O (1:1) was added to the vessel. The reaction was submitted to vigorous stirring at room temperature for 24 h, and TLC analysis showed complete consumption of the quinone-azides. The mixture was extracted with CH_2Cl_2 (3 × 5 mL) and the organic phase was washed with brine (3 × 5 mL). The organic phase was dried, and the crude product was purified by FCC, utilizing *n*-hexane and ethyl acetate as eluent.

3-(4-(((1,4-dioxo-1,4-dihydronaphthalen-2-yl)(phenyl)amino)methyl)-1*H*-1,2,3-triazol-1-yl)-2,2-dimethyl-2,3-dihydronaphtho[1,2-*b*]furan-4,5-dione (1): Purification by column chromatography (*n*-hexane/EtOAc) led to product **1** (44.5 mg, 0.080 mmol, 40% yield) obtained as a brown solid; m.p: 146–148 (ºC); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.11 (dd, J = 7.5, 1.0 Hz, 1H), 7.92 (dd, J = 7.5, 1.0 Hz, 1H), 7.84 (dd, J = 7.5, 1.0 Hz, 1H), 7.76–7.66 (m, 3H), 7.63 (td, J = 7.5, 1.5 Hz, 1H), 7.56 (td, J = 7.5, 1.5 Hz, 1H), 7.51 (s, 1H), 7.35 (t, J = 7.5 Hz, 2H), 7.22 (t, J = 7.5 Hz, 1H), 7.11 (m, 2H), 6.06 (s, 1H), 5.91 (s, 1H), 5.14 (s, 2H), 1.71 (s, 3H), 1.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 183.7, 183.1, 180.1, 174.6, 171.2, 151.6, 145.5, 143.6, 134.9, 134.0, 133.4, 132.5, 132.5, 132.4, 130.0, 130.0, 127.1, 126.7, 126.7, 126.4, 125.7, 125.6, 122.7, 113.0, 111.2, 95.9, 67.1, 50.0, 27.8, 21.1; IR (solid, cm^{-1}) ν: 3130, 2852, 1621, 1591, 1565, 1406, 1297, 1260, 777; HRMS (ESI$^+$): 557.1819 $[M+H]^+$. Calculated for $[C_{33}H_{25}N_4O_5]^+$: 557.1823.

3-(4-(((1,4-dioxo-1,4-dihydronaphthalen-2-yl)(p-tolyl)amino)methyl)-1*H*-1,2,3-triazol-1-yl)-2,2-dimethyl-2,3-dihydronaphtho[1,2-*b*]furan-4,5-dione (2): Purification by column chromatography (*n*-hexane/EtOAc) led to product **2** (74.2 mg, 0.130 mmol, 65% yield) obtained as a red solid; m.p: 156–158 (ºC); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.12 (d, J = 7.5 Hz, 1H), 7.92 (d, J = 7.5 Hz, 1H), 7.84 (d, J = 7.5 Hz, 1H), 7.75–7.60 (m, 4H), 7.57–7.49 (m, 2H),

7.14 (d, *J* = 7.5 Hz, 2H), 6.98 (d, *J* = 7.5 Hz, 2H), 6.00 (s, 1H), 5.91 (s, 1H), 5.30 (s, 1H), 5.12 (s, 2H), 5.04 (s, 1H), 2.31 (s, 3H), 1.72 (s, 3H), 1.07 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 183.5, 183.2, 180.1, 174.6, 171.2, 151.7, 143.7, 142.8, 137.0, 134.9, 134.0, 133.4, 132.6, 132.5, 132.4, 131.6, 130.6, 130.0, 126.8, 126.6, 126.3, 125.7, 125.5, 122.7, 112.4, 111.2, 95.9, 67.1, 53.6, 50.1, 27.8, 21.2; IR (solid, cm^{-1}) ν: 3125, 2922, 1659, 1623, 1556, 1591, 1412, 1261, 776, 722; HRMS (ESI^+): 571.1976 $[M+H]^+$. Calculated for $[C_{34}H_{27}N_4O_5]^+$ 571.1980.

3-(4-(((1,4-dioxo-1,4-dihydronaphthalen-2-yl)(4-methoxyphenyl)amino)methyl)-1*H*-1,2,3-triazol-1-yl)-2,2-dimethyl-2,3-dihydronaphtho[1,2-*b*]furan-4,5-dione (3): Purification by column chromatography (*n*-hexane/EtOAc) led to product **3** (105.5 mg, 0.180 mmol, 90% yield) obtained as a red solid; m.p: 155–157 (ºC); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.08 (d, *J* = 7.5 Hz, 1H), 7.88 (d, *J* = 7.5 Hz, 1H), 7.82 (d, *J* = 7.5 Hz, 1H), 7.75–7.56 (m, 6H), 7.53 (dd, *J* = 7.5, 7.5 Hz, 1H), 7.01 (d, *J* = 8.0 Hz, 2H), 6.85 (d, *J* = 8.0 Hz, 2H), 5.91 (d, *J* = 8.0 Hz, 2H), 5.11 (s, 2H), 3.78 (s, 3H), 1.72 (s, 3H), 1.08 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 183.3, 183.0, 180.0, 174.5, 171.0, 158.4, 151.6, 143.6, 137.9, 134.7, 133.7, 133.1, 132.4, 132.3, 132.2, 131.5, 129.7, 127.9, 126.7, 126.4, 125.5, 125.2, 123.0, 115.1, 111.3, 111.1, 95.8, 67.0, 60.4, 55.5, 50.2, 27.7, 21.1, 14.2; IR (solid, cm^{-1}) ν: 3132, 2932, 1655, 1623, 1588, 1509, 1414, 1248, 780, 725; HRMS (ESI^+): 587.2073 $[M+H]^+$. Calculated for $[C_{34}H_{27}N_4O_6]^+$: 587.1931; Anal. Calcd for $C_{34}H_{26}N_4O_6$: C, 69.62; H, 4.47; N, 9.55. Found: C, 69.54; H, 4.93; N, 9.05**.**

3-(4-(((4-bromophenyl)(1,4-dioxo-1,4-dihydronaphthalen-2-yl)amino)methyl)-1*H*-1,2,3-triazol-1-yl)-2,2-dimethyl-2,3-dihydronaphtho[1,2-*b*]furan-4,5-dione (4): Purification by column chromatography (*n*-hexane/EtOAc) led to product **4** (63.5 mg, 0.100 mmol, 50% yield) obtained as a red solid; m.p: 235–237 (ºC); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.08 (d, *J* = 7.5 Hz, 1H), 7.90 (d, *J* = 7.5 Hz, 1H), 7.81 (d, *J* = 7.5 Hz, 1H), 7.74 (t, *J* = 6.5 Hz, 1H), 7.71–7.60 (m, 3H), 7.58–7.53 (m, 2H), 7.44 (d, *J* = 8.5 Hz, 2H), 7.00 (d, *J* = 8.5 Hz, 2H), 6.12 (s, 1H), 5.90 (s, 1H), 5.06 (s, 2H), 1.71 (s, 3H), 1.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 183.6, 182.7, 180.0, 174. 6, 171.2, 151.1, 144.8, 143.1, 134.9, 134.1, 133.4, 133.0, 132.7, 132.7, 132.4, 132.3, 131.6, 130.0, 128.1, 126.7, 126.7, 125.7, 125.6, 122.8, 120.4, 113.8, 111.1, 95.8, 67.2, 49.8, 27.8, 21.2; IR (solid, cm^{-1}) ν: 3137, 1654, 1591, 1560, 1488, 1407, 1295, 1258, 1224, 1114,

1046, 777, 719; HRMS (ESI$^+$): 635.1196 [M+H]$^+$. Calculated for [$C_{33}H_{24}BrN_4O_5$]$^+$: 635.0930; Anal. Calcd for $C_{33}H_{23}BrN_4O_5$: C, 62.37; H, 3.65; N, 8.82. Found: C, 60.49; H, 3.49; N, 8.49.

3-(4-(((1,4-dioxo-1,4-dihydronaphthalen-2-yl)(4-iodophenyl)amino)methyl)-1*H*-1,2,3-triazol-1-yl)-2,2-dimethyl-2,3-dihydronaphtho[1,2-*b*]furan-4,5-dione (5): Purification by column chromatography (*n*-hexane/EtOAc) led to product **5** (61.4 mg, 0.090 mmol, 45% yield) obtained as a red solid; m.p: 159–161 (ºC); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.11 (dd, *J* = 7.5, 1.0 Hz, 1H), 7.93 (dd, *J* = 7.5, 1.0 Hz, 1H), 7.83 (dd, *J* = 7.5, 1.0 Hz, 1H), 7.75 (td, *J* = 6.5, 5.5, 1.5 Hz, 1H), 7.69 (ddd, *J* = 11.0, 7.5, 1.5 Hz, 2H), 7.63 (dd, *J* = 8.0, 6.0 Hz, 3H), 7.56 (td, *J* = 7.5, 1.5 Hz, 1H), 6.87 (d, *J* = 8.5 Hz, 2H), 6.15 (s, 1H), 5.90 (s, 1H), 5.06 (s, 2H), 1.71 (s, 3H), 1.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 183.7, 182.7, 180.0, , 174.6, 171.2, 151.1, 145.6, 143.1, 139.0, 134.9, 134.1, 133.4, 132.7, 132.4, 132.3, 131.7, 130.1, 128.2, 126.8, 126.7, 125.7, 122.7, 114.1, 111.1, 95.8, 91.5, 67.2, 49.8, 27.9, 21.2; IR (solid, cm^{-1}) ν: 3130, 1656, 1622, 1558, 1482, 1407, 1297, 1258, 1115, 1084, 1047, 776, 723; HRMS (ESI$^+$): 683.0831 [M+H]$^+$. Calculated for [$C_{33}H_{24}IN_4O_5$]$^+$: 683.0791.

3-(4-(((4-acetylphenyl)(1,4-dioxo-1,4-dihydronaphthalen-2-yl)amino)methyl)-1*H*-1,2,3-triazol-1-yl)-2,2-dimethyl-2,3-dihydronaphtho[1,2-*b*]furan-4,5-dione (6): Purification by column chromatography (*n*-hexane/EtOAc) led to product **6** (53.9 mg, 0.090 mmol, 45% yield) obtained as a red solid; m.p: 223–225 (ºC); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.10 (d, *J* = 7.0 Hz, 1H), 7.96 (d, *J* = 7.5 Hz, 1H), 7.90 (d, *J* = 8.5 Hz, 2H), 7.84 (d, *J* = 7.5 Hz, 1H), 7.76–7.64 (m, 5H), 7.59 (t, *J* = 7.5 Hz, 1H), 7.47 (s, 1H), 7.16 (d, *J* = 8.5 Hz, 2H), 6.42 (s, 1H), 5.89 (s, 1H), 5.10 (s, 2H), 2.56 (s, 3H), 1.70 (s, 3H), 1.01 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 196.9, 183.9, 182.4, 180.0, 174.6, 171.3, 151.0, 150.1, 142.9, 134.9, 134.4, 134.2, 133.5, 133.0, 132.4, 132.3, 131.6, 130.1, 126.9, 126.7, 125.9, 125.7, 124.9, 122.6, 116.8, 111.1, 95.8, 67.2, 49.5, 27.8, 26.6, 21.2; IR (solid, cm^{-1}) ν: 3126, 2926, 1655, 1591, 1570, 1408, 1261, 1225, 1115, 780; HRMS (ESI$^+$): 599.1925 [M+H]$^+$. Calculated for [$C_{35}H_{27}N_4O_6$]$^+$: 599.1927.

2-((4-(((1,4-dioxo-1,4-dihydronaphthalen-2-yl)(phenyl)amino)methyl)-1*H*-1,2,3-triazol-1-yl)methyl)-2,3-dihydronaphtho[1,2-*b*]furan-4,5-dione (7): Purification by column chromatography (*n*-hexane/EtOAc) led to product **7** (32.5 mg, 0.060 mmol, 30% yield) obtained as a red solid; m.p: 141–142 (ºC); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.04 (t, *J* = 7.5 Hz,

1H), 7.93 (d, *J* = 7.5 Hz, 1H), 7.73–7.70 (m, 2H), 7.66 (t, *J* = 8.0 Hz, 1H), 7.58-7.52 (m, 3H), 7.37 (t, *J* = 7.5 Hz, 2H), 7.12 (d, *J* = 7.5 Hz, 2H), 6.10 (s, 1H), 5.50–5.48 (m, 1H), 5.23–5.12 (m, 2H), 4.80 (dd, *J* = 14.0, 3.5 Hz, 1H), 4.68 (dd, *J* = 14.5, 7.5 Hz, 1H), 3.33 (dd, *J* = 15.5, 10.5 Hz, 1H), 2.94 (dd, *J* = 16.0, 7.0 Hz, 1H), 1.28 (2H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 183.6, 183.0, 182.2, 180.5, 175.3, 168.8, 151.5, 145.7, 135.1, 134.9, 134.2, 132.7, 132.6, 132.4, 130.7, 130.0, 129.9, 127.0, 126.9, 126.3, 125.9, 122.8, 114.9, 113.3, 103.6, 84.5, 53.6, 50.1, 32.1, 29.8; IR (solid, cm^{-1}) ν: 2922, 1618, 1592, 1574, 1558; HRMS (ESI^+): 543.1663 $[M+H]^+$. Calculated for $[C_{33}H_{23}N_4O_5]^+$: 543.1665.

2-((4-(((1,4-dioxo-1,4-dihydronaphthalen-2-yl)(p-tolyl)amino)methyl)-1*H*-1,2,3-triazol-1-yl)methyl)-2,3-dihydronaphtho[1,2-*b*]furan-4,5-dione (8): Purification by column chromatography (*n*-hexane/EtOAc) led to product **8** (50.1 mg, 0.090 mmol, 45% yield) obtained as a red solid; m.p: 213–215 (ºC); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.04–7.99 (m, 2H), 7.91 (d, *J* = 7.5 Hz, 1H), 7.74–7.70 (m, 2H), , 7.64 (t, *J* = 7.5 Hz, 1H), 7.55–7.47 (m, 3H), 7.16 (d, *J* = 7.5 Hz, 2H), 6.97 (d, *J* = 7.5 Hz, 2H), 5.99 (s, 1H), 5.50–5.48 (m, 1H), 5.23–5.10(m, 2H), 4,80 (dd, *J* = 15.0, 3.0 Hz, 1H), 4.68 (dd, *J* = 15.0, 7.0 Hz, 1H), 3.33 (dd, *J* = 16.0, 10.5 Hz, 1H), 2.94 (dd, *J* = 16.0, 7.5 Hz, 1H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 183.5, 183.2, 180.5, 175.3, 168.7, 151.6, 144.7, 143.0, 137.2, 134.9, 134.2, 132.6, 132.6, 132.4, 130.7, 130.7, 129.9, 126.9, 126.7, 125.9, 125.7, 124.5, 123.8, 114.9, 112.6, 84.4, 53.5, 50.3, 29.6, 21.2; IR (solid, cm^{-1}) ν: 3125, 1620, 1595, 1553, 1403; HRMS (ESI^+): 557.1925 $[M+H]^+$. Calculated for $[C_{33}H_{25}N_4O_5]^+$: 557.1825.

2-((4-(((1,4-dioxo-1,4-dihydronaphthalen-2-yl)(4-methoxyphenyl)amino)methyl)-1*H*-1,2,3-triazol-1-yl)methyl)-2,3-dihydronaphtho[1,2-*b*]furan-4,5-dione (9): Purification by column chromatography (*n*-hexane/EtOAc) led to product **9** (69.8 mg, 0.122 mmol, 61% yield) obtained as a red solid; m.p: 202–204 (ºC); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.99 (dd, *J* = 15.0, 7.5 Hz, 2H), 7.90 (d, *J* = 7.5 Hz, 1H), 7.75 (s, 1H), 7.70 (t, *J* = 7.0 Hz, 1H), 7.62 (t, *J* = 7.5 Hz, 1H), 7.55–7.45 (m, 3H), 7.00 (d, *J* = 9.0 Hz, 2H), 6.86 (d, *J* = 9.0 Hz, 2H), 5.91 (s, 1H), 5.48 (dtd, *J* = 10.5, 7.0, 3.5 Hz, 2H), 5.22–5.08 (m, 2H), 4.80 (dd, *J* = 14.5, 3.5 Hz, 1H), 4.69 (dd, *J* = 14.5, 7.0 Hz, 1H), 3.80 (s, 3H), 3.31 (dd, *J* = 16.0, 10.5 Hz, 1H), 2.93 (dd, *J* = 15.5, 7.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 183.5, 183.4, 180.5, 175.3, 168.8, 158.6, 151.7, 144.7, 138.1, 134.9, 134.2, 132.6, 132.6, 132.4, 130.6, 1290.9, 127.5, 126.9, 126.7, 125.7, 124.5,

124.0, 115.3, 114.9, 111.9, 84.5, 55.6, 53.4, 50.5, 29.6; IR (solid, cm^{-1}) ν: 3117, 1619, 1591, 1560, 1507, 1246, 774; HRMS (ESI^+): 573.1724 $[M+H]^+$. Calculated for $[C_{33}H_{25}N_4O_6]^+$: 573.1774.

2-((4-(((4-bromophenyl)(1,4-dioxo-1,4-dihydronaphthalen-2-yl)amino)methyl)-1*H*-1,2,3-triazol-1-yl)methyl)-2,3-dihydronaphtho[1,2-*b*]furan-4,5-dione (10): Purification by column chromatography (*n*-hexane/EtOAc) led to product **10** (49.7 mg, 0.080 mmol, 40% yield) obtained as a red solid; m.p: 193–195 (ºC); ^1H NMR (400 MHz, $CDCl_3$) δ: 8.02 (td, *J* = 7.5, 1.0 Hz, 2H), 7.89 (dd, *J* = 7.5, 1.0 Hz, 1H), 7.734–7.73 (dd, *J* = 7.5, 1.0 Hz, 1H), 7.70 (s, 1H), 7.65 (dd, *J* = 7.5, 1.0 Hz, 1H), 7.62 (dd, *J* = 5.0, 1.0 Hz, 1H), 7.58 (dd, *J* = 7.5 1.0 Hz, 1H), 7.53 (dd, *J* = 7.5, 1.0 Hz, 1H) 7.51-7.46 (m, 3H), 7.02 (d, *J* = 8.5 Hz, 2H), 6.16 (s, 1H), 5.48 (dtd, *J* = 10.5, 7.0, 3.5 Hz, 1H), 5.17-5.06 (m, 2H), 4.79 (dd, *J* = 14.5, 3.5 Hz, 1H), 4.66 (dd, *J* = 14.5, 7.5 Hz, 1H), 3.33 (dd, *J* = 16.0, 10.5 Hz, 1H), 2.93 (dd, *J* = 16.0, 7.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 183.6, 182.7, 180.4, 175.3, 168.7, 151.0, 145.0, 144.0, 135.0, 134.4, 133.1, 132.9, 132.5, 132.4, 130.7, 129.9, 127.4, 126.9, 126.8, 125.8, 124.5, 123.7, 120.3, 114.8, 114.3, 84.4, 53.5, 50.0, 29.7; IR (solid, cm^{-1}) ν: 3132, 2944, 1620, 1591, 1556, 1489, 773; HRMS (ESI^+): 621.0768 $[M+H]^+$. Calculated for $[C_{32}H_{22}BrN_4O_5]^+$: 621.0761.

2-((4-(((1,4-dioxo-1,4-dihydronaphthalen-2-yl)(4-iodophenyl)amino)methyl)-1*H*-1,2,3-triazol-1-yl)methyl)-2,3-dihydronaphtho[1,2-*b*]furan-4,5-dione (11): Purification by column chromatography (*n*-hexane/EtOAc) led to product **11** (66.8 mg, 0.100 mmol, 50% yield) obtained as a red solid; m.p: 208–210 (ºC); ^1H NMR (400 MHz, $CDCl_3$) δ: 8.02 (t, *J* = 7.0 Hz, 2H), 7.90 (d, *J* = 7.5 Hz, 1H), 7.745-7.64 (m, 5H), 7.59 (d, *J* = 7.5 Hz, 1H), 7.55–7.48 (m, 2H), 6.90 (d, *J* = 8.5 Hz, 2H), 6.18 (s, 1H), 5.47 (dtd, *J* = 10.5, 7.5, 3.5 Hz, 1H), 5.15 (d, *J* = 16.0 Hz, 1H), 5.08 (d, *J* = 16.0 Hz, 1H), 4.79 (dd, *J* = 15.0, 3.5 Hz, 1H), 4.66 (dd, *J* = 15.0, 7.5 Hz, 1H), 3.33 (dd, *J* = 16.0, 10.5 Hz, 1H), 2.93 (dd, *J* = 16.0, 7.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 183.6, 182.6, 180.4, 175.3, 168.8, 151.0, 145.8, 143.9, 139.0, 134.9, 134.3, 132.9, 132.4, 132.4, 132.4, 132.4, 130.6, 129.8, 127.6, 126.9, 126.8, 124.5, 123.9, 114.9, 114.4, 91.2, 84.5, 53.5, 49.9, 29.6; IR (solid, cm^{-1}) ν: 3120, 2923, 1625, 1556, 1486, 1408, 1296, 1259, 776; HRMS (ESI^+): 669.0645 $[M+H]^+$. Calculated for $[C_{32}H_{22}IN_4O_5]^+$: 669.0635; Anal. Calcd for $C_{32}H_{21}IN_4O_5$: C, 57.50; H, 3.17; N, 8.38. Found: C, 57.55; H, 3.54; N, 8.15.

2-((4-(((4-acetylphenyl)(1,4-dioxo-1,4-dihydronaphthalen-2-yl)amino)methyl)-1*H*-1,2,3-triazol-1-yl)methyl)-2,3-dihydronaphtho[1,2-*b*]furan-4,5-dione (12): Purification by column chromatography (*n*-hexane/EtOAc) led to product **12** (78.3 mg, 0.134 mmol, 67% yield) obtained as a red solid; m.p: 231–233 (ºC); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.04 (d, *J* = 8.0 Hz, 1H), 7.93 (dt, *J* = 17.0, 8.0 Hz, 4H), 7.77–7.56 (m, 4H), 7.59–7.44 (m, 2H), 7.17 (d, *J* = 8.5 Hz, 2H), 6.44 (s, 1H), 5.50–5.42 (m, 1H), 5.24–5.09 (m, 2H), 4.78 (dd, *J* = 14.5, 3.0 Hz, 1H), 4.67 (dd, *J* = 14.5, 7.0 Hz, 1H), 3.29 (dd, *J* = 16.0, 10.0 Hz, 1H), 2.90 dd, *J* = 16.0, 7.0 Hz, 1H), 2.58 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 196.8, 183.8, 182.3, 180.4, 175.3, 168.8, 151.0, 150.2, 135.0, 134.4, 134.2, 133.2, 132.5, 132.4, 132.3, 130.6, 130.1, 129.9, 127.0, 126.8, 126.0, 124.5, 124.0, 117.5, 114.8, 84.4, 77.4, 53.5, 49.6, 29.6, 26.6; IR (solid, cm^{-1}) ν: 3125, 2923, 1677, 1623, 1590, 1551, 1405, 1261, 1184, 1125, 778; HRMS (ESI^+): 585.1759 $[M+H]^+$. Calculated for $[C_{34}H_{25}N_4O_6]^+$: 585.1774.

3-bromo-4-(4-(((1,4-dioxo-1,4-dihydronaphthalen-2-yl)(phenyl)amino)methyl)-1*H*-1,2,3-triazol-1-yl)-2,2-dimethyl-3,4-dihydro-2*H*-benzo[*h*]chromene-5,6-dione (13): Purification by column chromatography (*n*-hexane/EtOAc) led to product **13** (97.4 mg, 0.150 mmol, 75% yield) obtained as an orange solid; m.p: 153–155 (ºC); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.09 (d, *J* = 7.5 Hz, 1H), 8.00 (d, *J* = 7.5 Hz, 1H), 7.91 (dd, *J* = 18.0, 7.5 Hz, 2H), 7.79 (s, 1H), 7.73 (t, *J* = 7.5 Hz, 1H), 7.69-7.57 (m, 3H), 7.39 (t, *J* = 7.5 Hz, 2H), 7.27 (t, *J* = 7.5 Hz, 1H), 7.17 (d, *J* = 7.5 Hz, 2H), 6.13 (s, 1H), 5.58 (d, *J* = 9.0 Hz, 1H), 5.20 (s, 2H), 4.88 (d, *J* = 9.0 Hz, 1H), 1.72 (s, 3H), 1.62 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 183.7, 183.1, 177.9, 176.5, 162.8, 151.7, 145.6, 142.7, 135.3, 133.9, 132.6, 132.5, 132.5, 132.4, 130.7, 130.7, 130.0, 129.3, 127.1, 126.8, 126.6, 126.2, 125.6, 125.4, 113.0, 110.4, 83.5, 59.1, 54.7, 50.0, 27.6, 20.7; IR (solid, cm^{-1}) ν: 2956, 1669, 1590, 1554, 1490, 1370, 1324, 1293, 1119, 775, 722, 698; HRMS (ESI^+): 649.1081 $[M+H]^+$. Calculated for $[C_{34}H_{26}BrN_4O_5]^+$: 649.1072.

3-bromo-4-(4-(((1,4-dioxo-1,4-dihydronaphthalen-2-yl)(p-tolyl)amino)methyl)-1*H*-1,2,3-triazol-1-yl)-2,2-dimethyl-3,4-dihydro-2*H*-benzo[*h*]chromene-5,6-dione (14): Purification by column chromatography (*n*-hexane/EtOAc) led to product **14** (79.6 mg, 0.120 mmol, 60% yield) obtained as a red solid; m.p: 155–157 (ºC); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.09 (d, *J* = 7.5 Hz, 1H), 8.00 (d, *J* = 7.0 Hz, 1H), 7.91 (dd, *J* = 17.5, 7.5 Hz, 2H), 7.81 (s, 1H), 7.78–7.70 (m, 1H), 7.70–7.55 (m, 3H), 7.18 (d, *J* = 7.5 Hz, 2H), 7.04 (d, *J* = 7.5 Hz, 2H), 6.08 (s, 1H),

5.59 (d, *J* = 9.0 Hz, 1H), 5.18 (s, 2H), 4.88 (d, *J* = 9.0 Hz, 1H), 2.35 (s, 3H), 1.72 (s, 3H), 1.62 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 183.7, 183.3, 177.9, 176.5, 162.8, 151.8, 142.9, 142.8, 137.0, 135.3, 134.0, 132.7, 132.6, 132.5, 130.7, 130.7, 129.4, 126.8, 126.5, 126.2, 125.6, 125.4, 112.5, 110.5, 83.6, 59.1, 54.7, 50.2, 27.6, 21.2, 20.6; IR (solid, cm^{-1}) ν: 2952, 1668, 1591, 1508, 1480, 1369, 1324, 1293, 1260, 1245, 1118, 1044, 777, 720, 688; HRMS (ESI$^+$): 663.1238 $[M+H]^+$. Calculated for $[C_{35}H_{28}BrN_4O_5]^+$: 663.1218.

3-bromo-4-(4-(((1,4-dioxo-1,4-dihydronaphthalen-2-yl)(4-methoxyphenyl)amino)methyl)-1*H*-1,2,3-triazol-1-yl)-2,2-dimethyl-3,4-dihydro-2*H*-benzo[*h*]chromene-5,6-dione (15): Purification by column chromatography (*n*-hexane/EtOAc) led to product **15** (80.2 mg, 0.118 mmol, 59% yield) obtained as a purple solid; m.p: 165–167 (ºC); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.08 (d, *J* = 7.5 Hz, 1H), 8.00–7.98 (m, 1H), 7.94 (d, *J* = 7.5 Hz, 1H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.84 (s, 1H), 7.72 (td, *J* = 7.5, 1.0 Hz, 1H), 7.69–7.56 (m, 3H), 7.07 (d, *J* = 9.0 Hz, 2H), 6.90 (d, *J* = 9.0 Hz, 2H), 6.00 (s, 1H), 5.60 (d, *J* = 9.0 Hz, 1H), 5.18 (d, *J* = 2.5 Hz, 2H), 4.90 (d, *J* = 9.0 Hz, 1H), 3.81 (s, 3H), 1.73 (s, 3H), 1.63 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 183.6, 183.4, 177.9, 176.5, 162.8, 158.6, 152.1, 142.9, 138.0, 135.3, 133.9, 132.7, 132.6, 132.4, 132.4, 130.7, 130.7, 129.3, 128.1, 126.7, 126.3, 125.5, 125.4, 115.2, 111.9, 110.5, 83.6, 59.1, 55.6, 54.7, 50.3, 27.6, 20.6; IR (solid, cm^{-1}) ν: 2937, 2298, 1668, 1591, 1553, 1506, 1454, 1370, 1324, 1290, 1243, 1118, 778, 720, 682; HRMS (ESI$^+$): 679.1187 $[M+H]^+$. Calculated for $[C_{35}H_{28}BrN_4O_6]^+$: 679.1178.

3-bromo-4-(4-(((4-bromophenyl)(1,4-dioxo-1,4-dihydronaphthalen-2-yl)amino)methyl)-1*H*-1,2,3-triazol-1-yl)-2,2-dimethyl-3,4-dihydro-2*H*-benzo[*h*]chromene-5,6-dione (16): Purification by column chromatography (*n*-hexane/EtOAc) led to product **16** (80.1 mg, 0.110 mmol, 55% yield) obtained as an orange solid; m.p: 161–163 (ºC); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.07 (d, *J* = 7.5 Hz, 1H), 8.00 (d, *J* = 7.5 Hz, 1H), 7.89 (dd, *J* = 14.5 7.5 Hz, 2H), 7.79 (s, 1H), 7.77–7.65 (m, 2H), 7.65–7.59 (m, 2H), 7.49 (d, *J* = 8.5 Hz, 2H), 7.04 (d, *J* = 8.5 Hz, 2H), 6.20 (s, 1H), 5.57 (d, *J* = 9.5 Hz, 1H), 5.12 (s, 2H), 4.87 (d, *J* = 9.5 Hz, 1H), 1.73 (s, 3H), 1.62 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 183.7, 182.8, 177.9, 176.5, 162.8, 151.3, 144.8, 142.1, 135.3, 134.1, 133.1, 132.7, 132.5, 132.5, 132.4, 130.7, 129.4, 128.3, 126.8, 126.3, 125.7, 125.4, 120.5, 113.9, 110.4, 83.6, 59.2, 54.7, 49.9, 27.7, 20.5; IR (solid, cm^{-1}) ν: 2959, 2297 1655, 1591, 1559, 1486, 1370, 1324, 1294, 1259, 1119, 777, 722, 688; HRMS (ESI$^+$): 727.0186 $[M+H]^+$.

Calculated for $[C_{34}H_{25}Br_2N_4O_5]^+$: 727.0181; Anal. Calcd for $C_{34}H_{24}Br_2N_4O_5$: C, 56.06; H, 3.32; N, 7.69. Found: C, 55.70; H, 3.76; N, 7.21**.**

3-bromo-4-(4-(((1,4-dioxo-1,4-dihydronaphthalen-2-yl)(4-iodophenyl)amino)methyl)-1*H*-1,2,3-triazol-1-yl)-2,2-dimethyl-3,4-dihydro-2*H*-benzo[*h*]chromene-5,6-dione (17): Purification by column chromatography (*n*-hexane/EtOAc) led to product **17** (74.4 mg, 0.096 mmol, 48% yield) obtained as an orange solid; m.p: 159–161 (ºC); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.10 (dd, *J* = 7.5, 1.0 Hz, 1H), 8.02 (dd, *J* = 7.5, 1.0 Hz, 1H), 7.95–7.87 (m, 2H), 7.78 (s, 1H), 7.74 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.72–7.66 (m, 3H), 7.62 (tdd, *J* = 7.5, 4.0, 1.0 Hz, 2H), 6.92 (d, *J* = 8.5 Hz, 2H), 6.24 (s, 1H), 5.57 (d, *J* = 9.5 Hz, 1H), 5.13 (s, 2H), 4.87 (d, *J* = 9.5 Hz, 1H), 1.74 (s, 3H), 1.63 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 183.8, 182.8, 177.9, 176.5, 162.8, 151.2, 145.5, 142.1, 139.1, 135.3, 134.1, 132.7, 132.5, 132.5, 132.4, 130.7, 129.4, 128.4, 126.9, 126.3, 125.7, 125.4, 114.1, 110.5, 91.7, 83.7, 59.2, 54.7, 49.7, 27.7, 20.5; IR (solid, cm^{-1}) ν: 2951, 1591, 1557, 1483, 1454, 1371, 1324, 1294, 1259, 1118, 777, 723, 688; HRMS (ESI^+): 775.0048 $[M+H]^+$. Calculated for $[C_{34}H_{25}BrIN_4O_5]^+$: 775.0040.

4-(4-(((4-acetylphenyl)(1,4-dioxo-1,4-dihydronaphthalen-2-yl)amino)methyl)-1*H*-1,2,3-triazol-1-yl)-3-bromo-2,2-dimethyl-3,4-dihydro-2*H*-benzo[*h*]chromene-5,6-dione (18): Purification by column chromatography (*n*-hexane/EtOAc) led to product **18** (68.15 mg, 0.10 mmol, 50% yield) obtained as an orange solid; m.p: 161–163 (ºC); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.05 (dd, *J* = 17.0, 7.5 Hz, 2H), 7.96 (d, *J* = 8.5 Hz, 2H), 7.92–7.87 (m, 2H), 7.76 (s, 1H), 7.74–7.67 (m, 2H), 7.63 (dd, *J* = 12.5, 7.0 Hz, 2H), 7.22 (d, *J* = 8.5 Hz, 2H), 6.49 (s, 1H), 5.56 (d, *J* = 9.0 Hz, 1H), 5.17 (s, 2H), 4.85 (d, *J* = 9.5 Hz, 1H), 2.60 (s, 3H), 1.72 (s, 3H), 1.61 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 197.2, 184.0, 182.4, 178.0, 176.6, 163.0, 151.1, 150.3, 142.0, 135.4, 134.4, 134.3, 133.1, 132.6, 132.5, 132.4, 130.8, 130.7, 130.2, 129.5, 127.0, 126.2, 125.9, 125.5, 125.3, 116.8, 110.4, 83.7, 59.3, 54.8, 49.7, 27.7, 26.8, 20.6; IR (solid, cm^{-1}) ν: 2958, 1673, 1590, 1558, 1454, 1370, 1324, 1294, 1183, 1118, 1087, 778, 723, 688; HRMS (ESI^+): 691.1187 $[M+H]^+$. Calculated for $[C_{36}H_{28}BrN_4O_6]^+$: 691.1179.

Procedure for the synthesis of azide compounds 20 and 30[13]

3-(azidomethyl)-2,2-dimethyl-3,4-dihydro-2*H*-benzo[*h*]chromene-5,6-dione (20): Purification by column chromatography (*n*-hexane/EtOAc) led to product **20** (276.5 mg, 0.930 mmol, 93% yield) obtained as an orange crystals; m.p: 168–169 (°C); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.06 (dd, *J* = 7.5, 1.0 Hz, 1H), 7.79 (d, *J* = 7.5 Hz, 1H), 7.65 (td, *J* = 7.5, 1.5 Hz, 1H), 7.52 (dd, *J* = 7.5, 1.0 Hz, 1H), 3.58 (dd, *J* = 12.5, 5.0 Hz, 1H), 3.26 (dd, *J* = 12.5, 8.0 Hz, 1H), 2.82 (dd, *J* = 18.0, 5.5 Hz, 1H), 2.34 (dd, *J* = 18.0, 9.5 Hz, 1H), 2.12–2.01 (m, 1H), 1.59 (s, 3H), 1.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 179.5, 178.4, 161.3, 134.9, 132.1, 130.9, 130.2, 128.8, 124.1, 112.0, 80.8, 52.2, 40.0, 27.3, 22.0, 20.7; IR (solid, cm^{-1}) ν: 2995, 2100, 1610, 1280, 820; HRMS (APPI$^+$): 298.1173 $[M+H]^+$. Calculated for $[C_{16}H_{16}N_3O_3]^+$: 298.1186.

3-(azidomethyl)-2,2-dimethyl-2,3-dihydronaphtho[1,2-*b*]furan-4,5-dione (30): Purification by column chromatography (*n*-hexane/EtOAc) led to product **30** (257.7 mg, 0.910 mmol, 91% yield) obtained as an deep red crystals; m.p: 157–158 (°C); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.07 (d, *J* = 7.5 Hz, 1H), 7.70–7.65 (m, 2H), 7.65–7.55 (m, 1H), 4.03 (dd, *J* = 13.0, 3.0 Hz, 1H), 3.56 (dd, *J* = 13.0, 9.0 Hz, 1H), 3.34 (dd, *J* = 9.0, 3.0 Hz, 1H), 1.63 (s, 3H), 1.60 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 180.9, 175.5, 169.2, 134.5, 132.2, 131.0, 129.3, 127.4, 124.8, 114.3, 95.0, 48.8, 48.7, 29.7, 22.2; IR (solid, cm^{-1}) ν: 3011, 2097, 1656, 1471, 1218; HRMS (APPI$^+$): 284.1011 $[M+H]^+$. Calculated for $[C_{15}H_{14}N_3O_3]^+$: 284.1030.

2,2-dimethyl-3-((4-((phenylselanyl)methyl)-1*H*-1,2,3-triazol-1-yl)methyl)-3,4-dihydro-2*H*-benzo[*h*]chromene-5,6-dione (21): Purification by column chromatography (*n*-hexane/EtOAc) led to product **21** (88.6 mg, 0.180 mmol, 90% yield) obtained as an orange solid; m.p: 173–174 (°C); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.06 (d, *J* = 7.5 Hz, 1H), 7.79 (d, *J* = 7.5 Hz, 1H), 7.67 (t, *J* = 8.5 Hz, 1H), 7.53 (t, *J* = 7.5 Hz, 1H), 7.48 (dd, *J* = 7.5, 1.5 Hz, 2H), 7.34–7.17 (m, 4H), 4.56 (dd, *J* = 14.0, 4.5 Hz, 1H), 4.16 (s, 2H), 4.09 (dd, *J* = 14.0, 9.0 Hz, 1H), 2.49 (dt, *J* = 13.5, 5.5 Hz, 2H), 2.19 (dd, *J* = 19.0, 10.0 Hz, 1H), 1.55 (s, 3H), 1.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 179.4, 178.3, 161.4, 134.9, 146.2, 135.0, 133.5, 131.9, 131.2, 130.2, 129.7, 129.3, 128.9, 127.7, 124.3, 111.4, 80.6, 50.9, 40.9, 27.1, 22.0, 20.6; IR (solid, cm^{-1}) ν: 3004, 1612, 1463, 764; HRMS (APPI$^+$): 494.0979 $[M+H]^+$. Calculated for

$[C_{25}H_{24}N_3O_3Se]^+$: 494.0982; Anal. Calcd for $C_{25}H_{23}N_3O_3Se$: C, 60.98; H, 4.71; N, 8.53. Found: C, 60.90; H, 4.57; N, 8.48.

3-((4-(((4-methoxyphenyl)selanyl)methyl)-1*H*-1,2,3-triazol-1-yl)methyl)-2,2-dimethyl-3,4-dihydro-2*H*-benzo[*h*]chromene-5,6-dione (22) Purification by column chromatography (*n*-hexane/EtOAc) led to product **22** (98.2 mg, 0.188 mmol, 94% yield) obtained as an orange solid; m.p: 92–93 (°C); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.07 (dd, *J* = 7.5, 1.0 Hz, 1H), 7.80 (d, *J* = 7.0 Hz, 1H), 7.67 (td, *J* = 7.5, 1.5 Hz, 1H), 7.54 (td, *J* = 7.5, 1.0 Hz, 1H), 7.41 (d, *J* = 9.0 Hz, 2H), 7.15 (s, 1H), 6.81 (d, *J* = 9.0 Hz, 2H), 4.57 (dd, *J* = 14.0, 4.5 Hz, 1H), 4.10–4.04 (m, 3H), 3.75 (s, 3H), 2.52–2.45 (m, 2H), 2.21–2.14 (m, 1H), 1.57 (s, 3H), 1.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 179.3, 178.2, 161.3, 159.7, 146.2, 136.4, 135.0, 131.8, 131.1, 130.1, 128.8, 124.2, 122.4, 119.4, 114.9, 111.3, 80.5, 55.3, 50.8, 40.9, 27.0, 21.9, 21.3, 20.4; IR (solid, cm^{-1}) ν: 3437, 1607, 1242, 821; HRMS (APPI$^+$): 524.1085 $[M+H]^+$. Calculated for $[C_{26}H_{26}N_3O_4Se]^+$: 524.1088; Anal. Calcd for $C_{26}H_{25}N_3O_4Se$: C, 59.77; H, 4.82; N, 8.04. Found: C, 59.61; H, 4.82; N, 8.26**.**

3-((4-(((4-chlorophenyl)selanyl)methyl)-1*H*-1,2,3-triazol-1-yl)methyl)-2,2-dimethyl-3,4-dihydro-2*H*-benzo[*h*]chromene-5,6-dione (23): Purification by column chromatography (*n*-hexane/EtOAc) led to product **23** (101.0 mg, 0.192 mmol, 96% yield) obtained as an orange solid; m.p: 165–166 (°C); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.06 (d, *J* = 8.5 Hz, 1H), 7.80 (d, *J* = 7.5 Hz, 1H), 7.67 (td, *J* = 7.5, 1.5 Hz, 1H), 7.54 (t, *J* = 7.5 Hz, 1H), 7.41 (d, *J* = 8.5 Hz, 2H), 7.28 (s, 1H), 7.23 (d, *J* = 8.5 Hz, 2H), 4.58 (dd, *J* = 14.0, 4.5 Hz, 1H), 4.17–4.07 (m, 3H), 2.55–2.45 (m, 2H), 2.17 (dd, *J* = 19.0, 10.0 Hz, 1H), 1.56 (s, 3H), 1.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 179.4, 178.3, 161.5, 145.9, 135.1, 135.0, 133.9, 131.9, 131.2, 130.2, 129.5, 129.0, 127.8, 124.3, 122.7, 111.3, 80.5, 50.9, 40.9, 27.1, 22.1, 20.8, 20.5; IR (solid, cm^{-1}) ν: 3118, 1607, 1391, 814; Anal. Calcd for $C_{25}H_{22}ClN_3O_3Se$: C, 56.99; H, 4.21; N, 7.98. Found: C, 56.71; H, 4.13; N, 7.96**.**

3-((4-(((4-fluorophenyl)selanyl)methyl)-1*H*-1,2,3-triazol-1-yl)methyl)-2,2-dimethyl-3,4-dihydro-2*H*-benzo[*h*]chromene-5,6-dione (24): Purification by column chromatography (*n*-hexane/EtOAc) led to product **24** (90.8 mg, 0.178 mmol, 89% yield) obtained as an orange solid; m.p: 172–173 (°C); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.07 (d, *J* = 7.5 Hz, 1H), 7.80 (d, *J* =

7.5 Hz, 1H), 7.67 (t, *J* = 7.5 Hz, 1H), 7.54 (t, *J* = 7.5 Hz, 1H), 7.54–7.41 (m, 2H), 7.24 (s, 1H), 6.98 (t, *J* = 8.5 Hz, 2H), 4.59 (dd, *J* = 14.0, 4.5 Hz, 1H), 4.22–4.03 (m, 3H), 2.61–2.40 (m, 2H), 2.17 (q, *J* = 9.5, 8.5 Hz, 1H), 1.57 (s, 3H), 1.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 179.4, 178.3, 163.8 (d, J_{C-F} = 247.5 Hz), 161.5, 146.0, 136.4 (d, J_{C-F} = 8.0 Hz), 135.1, 131.9, 131.2, 130.2, 129.0, 124.3, 124.0(d, J_{C-F} = 3.5 Hz), 122.6, 122.5, 116.5 (d, J_{C-F} = 21.5 Hz), 111.3, 80.5, 50.9, 40.9, 27.1, 22.1, 21.3, 20.4; IR (solid, cm^{-1}) ν: 3437, 1610, 1387, 1221; HRMS (APPI$^+$): 512.0885 $[M+H]^+$. Calculated for $[C_{25}H_{23}FN_3O_3Se]^+$: 512.0887; Anal. Calcd for $C_{25}H_{22}FN_3O_3Se$: C, 58.83; H, 4.34; N, 8.23. Found: C, 58.58; H, 4.25; N, 8.19.

2,2-dimethyl-3-((4-((p-tolylselanyl)methyl)-1*H*-1,2,3-triazol-1-yl)methyl)-3,4-dihydro-2*H*-benzo[*h*]chromene-5,6-dione (25): Purification by column chromatography (n-hexane/EtOAc) led to product **25** (82.0 mg, 0.162 mmol, 81% yield) obtained as an orange solid; m.p: 146–147 (°C); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.06 (d, *J* = 7.5 Hz, 1H), 7.80 (d, *J* = 7.5 Hz, 1H), 7.67 (t, *J* = 7.6 Hz, 1H), 7.53 (t, *J* = 7.5 Hz, 1H), 7.37 (d, *J* = 8.0 Hz, 2H), 7.24 (s, 1H), 7.07 (d, *J* = 8.0 Hz, 2H), 4.56 (dd, *J* = 14.0, 4.5 Hz, 1H), 4.13–4.07 (m, 3H), 2.54–2.45 (m, 2H), 2.29 (s, 3H), 2.25–2.16 (m, 1H), 1.55 (s, 3H), 1.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 179.4, 178.3, 161.4, 146.3, 137.7, 135.0, 133.9, 131.9, 131.2, 130.2, 130.1, 128.9, 125.9, 124.3, 122.6, 111.4, 80.6, 50.9, 40.9, 27.1, 22.0, 21.2, 20.9, 20.5; IR (solid, cm^{-1}) ν: 3132, 1610, 1384, 782; HRMS (APPI$^+$): 508.1135 $[M+H]^+$. Calculated for $[C_{26}H_{26}N_3O_3Se]^+$: 508.1133; Anal. Calcd for $C_{26}H_{25}N_3O_3Se$: C, 61.66; H, 4.98; N, 8.30. Found: C, 61.46; H, 4.74; N, 8.14**.**

2,2-dimethyl-3-((4-((naphthalen-1-ylselanyl)methyl)-1*H*-1,2,3-triazol-1-yl)methyl)-3,4-dihydro-2*H*-benzo[*h*]chromene-5,6-dione (26): Purification by column chromatography (n-hexane/EtOAc) led to product **26** (99.8 mg, 0.184 mmol, 92% yield) obtained as an orange solid; m.p: 110–111 (°C); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.33 (d, *J* = 8.5 Hz, 1H), 8.06 (d, *J* = 8.5 Hz, 1H), 7.80–7.76 (m, 4H), 7.67 (t, *J* = 7.5 Hz, 1H), 7.53 (t, *J* = 8.0 Hz, 2H), 7.47 (t, *J* = 7.5 Hz, 1H), 7.38 (t, *J* = 15.5 Hz, 1H), 6.95 (s, 1H), 4.44 (dd, *J* = 14.0, 4.5 Hz, 1H), 4.18 (s, 2H), 3.97 (dd, *J* = 14.0, 9.0 Hz, 1H), 2.43 (dd, *J* = 17.5, 5.5 Hz, 1H), 2.31 (quintet, *J* = 9.5 Hz, 1H), 2.11 (dd, *J* = 17.5, 9.0 Hz, 1H), 1.50 (s, 3H), 1.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 179.4, 178.3, 161.4, 145.9, 135.1, 134.5, 134.0, 133.9, 131.9, 131.2, 130.2, 129.1, 128.9, 128.9, 128.7, 127.7, 126.9, 126.3, 126.0, 124.2, 122.5, 111.4, 80.5, 50.8, 40.9, 27.0, 21.9, 20.7,

20.6; IR (solid, cm^{-1}) ν: 3447, 1607, 1387, 771; HRMS ($APPI^+$): 544.1136 $[M+H]^+$. Calculated for $[C_{29}H_{26}N_3O_3Se]^+$: 544.1137; Anal. Calcd for $C_{29}H_{25}N_3O_3Se$: C, 64.21; H, 4.65; N, 7.75. Found: C, 63.72; H, 4.62; N, 8.84**.**

2,2-dimethyl-3-((4-(((3-(trifluoromethyl)phenyl)selanyl)methyl)-1*H*-1,2,3-triazol-1-yl)methyl)-3,4-dihydro-2*H*-benzo[*h*]chromene-5,6-dione (27): Purification by column chromatography (*n*-hexane/EtOAc) led to product **27** (80.7 mg, 0.144 mmol, 72% yield) obtained as an orange solid; m.p: 92–93 (°C); ^1H NMR (400 MHz, $CDCl_3$) δ: 8.06 (d, *J* = 7.5 Hz, 1H), 7.80 (d, *J* = 7.5 Hz, 1H), 7.77–7.59 (m, 3H), 7.61–7.45 (m, 2H), 7.42 (t, *J* = 8.0 Hz, 1H), 7.32 (s, 1H), 4.59 (dd, *J* = 14.0, 4.5 Hz, 1H), 4.21 (s, 2H), 4.10 (dd, *J* = 14.0, 9.0 Hz, 1H), 2.50 (dt, *J* = 14.5, 5.5 Hz, 2H), 2.18 (dd, *J* = 19.0, 10.0 Hz, 1H), 1.54 (s, 3H), 1.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 179.4, 178.3, 161.5, 145.6, 136.5, 135.1, 131.9, 131.2, 130.9, 130.2, 128.8(d, $J_{C\text{-}F}$ = 3.5 Hz), 129.7, 129.9, 124.3, 124.3, 124.3, 122.7, 111.2, 80.6, 50.9, 40.8, 27.1, 22.1, 20.7, 20.5; IR (solid, cm^{-1}) ν: 2987, 1610, 1320, 1125; HRMS ($APPI^+$): 562.0853 $[M+H]^+$. Calculated for $[C_{26}H_{23}F_3N_3O_3Se]^+$: 562.0852.

2,2-dimethyl-3-((4-((thiophen-2-ylselanyl)methyl)-1*H*-1,2,3-triazol-1-yl)methyl)-3,4-dihydro-2*H*-benzo[*h*]chromene-5,6-dione (28): Purification by column chromatography (*n*-hexane/EtOAc) led to product **28** (99.6 mg, 0.20 mmol, 99% yield) obtained as an orange solid; m.p: 174–175 (°C); ^1H NMR (400 MHz, $CDCl_3$) δ: 8.07 (*d*, J = 8.5 Hz, 1H), 7.81 (d, *J* = 7.5 Hz, 1H), 7.68 (t, *J* = 8.0 Hz, 1H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.42 (d, *J* = 6.0 Hz, 1H), 7.22–7.05 (m, 2H), 6.98 (dd, *J* = 5.5, 3.5 Hz, 1H), 4.60 (dd, *J* = 14.0, 4.5 Hz, 1H), 4.20–3.98 (m, 3H), 2.67–2.40 (m, 2H), 2.20 (dd, *J* = 10.5, 8.5 Hz, 1H), 1.60 (s, 3H), 1.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 179.4, 178.3, 161.5, 145.6, 136.8, 135.1, 132.0, 131.9, 131.2, 130.2, 129.0, 128.4, 124.3, 123.0, 122.7, 111.4, 80.5, 50.9, 41.0, 27.2, 23.9, 22.1, 20.6; IR (solid, cm^{-1}) ν: 2987, 1607, 1391, 697; HRMS ($APPI^+$): 500.0542 $[M+H]^+$. Calculated for $[C_{23}H_{22}N_3O_3SSe]^+$: 500.0549; Anal. Calcd for $C_{23}H_{21}N_3O_3SSe$: C, 55.42; H, 4.25; N, 8.43. Found: C, 55.27; H, 4.10; N, 8.26.

2,2-dimethyl-3-((4-((phenylselanyl)methyl)-1*H*-1,2,3-triazol-1-yl)methyl)-2,3-dihydronaphtho[1,2-*b*]furan-4,5-dione (31): Purification by column chromatography (*n*-hexane/EtOAc) led to product **31** (73.6 mg, 0.154 mmol, 77% yield) obtained as an deep orange

solid; m.p: 116–118 (°C); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.09 (d, *J* = 7.5 Hz, 1H), 7.77–7.60 (m, 3H), 7.55–7.42 (m, 2H), 7.36 (s, 1H), 7.34–7.15 (m, 3H), 5.01 (dd, *J* = 14.5, 3.0 Hz, 1H), 4.50 (dd, *J* = 14.5, 10.5 Hz, 1H), 4.18 (s, 2H), 3.78 (dd, *J* = 10.5, 3.0 Hz, 1H), 1.54 (s, 3H), 1.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 180.9, 175.8, 169.5, 146.1, 134.8, 133.2, 132.6, 132.1, 129.8, 129.6, 129.3, 127.5, 127.3, 125.1, 122.5, 113.9, 95.8, 49.9, 47.6, 29.4, 22.7, 20.5; IR (solid, cm^{-1}) ν: 3122, 1621, 1405, 736; HRMS (APPI$^+$): 480.0822 $[M+H]^+$. Calculated for $[C_{24}H_{22}N_3O_3Se]^+$: 480.0819.

3-((4-(((4-methoxyphenyl)selanyl)methyl)-1*H*-1,2,3-triazol-1-yl)methyl)-2,2-dimethyl-2,3-dihydronaphtho[1,2-*b*]furan-4,5-dione (32): Purification by column chromatography (*n*-hexane/EtOAc) led to product **32** (84.4 mg, 0.166 mmol, 83% yield) obtained as an orange solid; m.p: 159–160 (°C); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.09 (d, *J* = 7.5 Hz, 1H), 7.71–7.60 (m, 3H), 7.40 (d, *J* = 8.5 Hz, 2H), 7.31 (s, 1H), 6.79 (d, *J* = 8.5 Hz, 2H), 5.01 (dd, *J* = 14.5, 3.0 Hz, 1H), 4.50 (dd, *J* = 14.5, 10.5 Hz, 1H), 4.08 (s, 2H), 3.81–3.79 (m, 4H), 1.55 (s, 3H), 1.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 180.8, 175.7, 169.4, 159.6, 146.1, 136.1, 134.7, 132.5, 131.0, 129.5, 127.2, 125.0, 122.2, 119.5, 114.8, 113.9, 95.7, 55.3, 49.8, 47.5, 29.3, 22.7, 21.3; IR (solid, cm^{-1}) ν: 3122, 1617, 1235, 821; HRMS (APPI$^+$): 510.0928 $[M+H]^+$. Calculated for $[C_{25}H_{24}N_3O_4Se]^+$: 510.0936; Anal. Calcd for $C_{25}H_{23}N_3O_4Se$: C, 59.06; H, 4.56; N, 8.26. Found: C, 58.75; H, 4.49; N, 8.20.

3-((4-(((4-chlorophenyl)selanyl)methyl)-1*H*-1,2,3-triazol-1-yl)methyl)-2,2-dimethyl-2,3-dihydronaphtho[1,2-*b*]furan-4,5-dione (33) Purification by column chromatography (*n*-hexane/EtOAc) led to product **33** (98.4 mg, 0.192 mmol, 96% yield) obtained as an red crystals; m.p: 132–133 (°C); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.08 (d, *J* = 7.5 Hz, 1H), 7.75-7.57 (m, 3H), 7.46 (s, 1H), 7.39 (d, *J* = 8.5 Hz, 2H), 7.20 (d, *J* = 8.5 Hz, 2H), 5.02 (dd, *J* = 14.5, 3.0 Hz, 1H), 4.52 (dd, *J* = 14.5, 10.5 Hz, 1H), 4.16 (s, 2H), 3.79 (dd, *J* = 10.5, 3.0 Hz, 1H), 1.55 (s, 3H), 1.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 180.8, 175.7, 169.5, 145.7, 134.8, 134.5, 133.7, 132.6, 131.0, 129.4, 129.4, 127.9, 127.3, 125.1, 122.6, 113.9, 95.7, 49.8, 47.7, 29.4, 22.7, 20.7; IR (solid, cm^{-1}) ν: 2973, 1614, 1090, 807; HRMS (APPI$^+$): 514.0430 $[M+H]^+$. Calculated for $[C_{24}H_{21}ClN_3O_3Se]^+$: 514.0432; Anal. Calcd for $C_{24}H_{20}ClN_3O_3Se$: C, 56.21; H, 3.93; N, 8.19. Found: C, 56.56; H, 3.98; N, 8.22.

3-((4-(((4-fluorophenyl)selanyl)methyl)-1*H*-1,2,3-triazol-1-yl)methyl)-2,2-dimethyl-2,3-dihydronaphtho[1,2-*b*]furan-4,5-dione (34): Purification by column chromatography (*n*-hexane/EtOAc) led to product **34** (90.3 mg, 0.182 mmol, 81% yield) obtained as an deep orange solid; m.p: 110–111 (°C); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.09 (d, *J* = 7.5 Hz, 1H), 7.72–7.59 (m, 3H), 7.45 (dd, *J* = 9.0, 5.5 Hz, 2H), 7.41 (s, 1H), 6.95 (t, *J* = 9.0 Hz, 2H), 5.01 (dd, *J* = 14.5, 3.0 Hz, 1H), 4.52 (dd, *J* = 14.5, 10.5 Hz, 1H), 4.14 (s, 2H), 3.79 (dd, *J* = 10.5, 3.0 Hz, 1H), 33.72 (q, *J* = 7.0 Hz, 1H), 1.56 (s, 3H), 1.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 180.9, 175.8, 169.5, 162.5 (d, J_{C-F} = 248.0 Hz), 145.9, 135.9 (d, J_{C-F} = 8.0 Hz), 134.8, 132.7, 131.1, 129.6, 127.3, 125.2, 124.1 (d, J_{C-F} = 3.5 Hz) 122.5, 116.4 (d, J_{C-F} = 21.5 Hz), 114.0, 95.7, 49.9, 47.7, 29.4, 22.8, 21.2; IR (solid, cm^{-1}) ν: 3433, 1621, 1224, 824; HRMS (APPI^{+}): 498.0728 $[M+H]^{+}$. Calculated for $[C_{24}H_{21}FN_3O_3Se]^{+}$: 498.0720; Anal. Calcd for $C_{24}H_{20}FN_3O_3Se$: C, 58.07; H, 4.06; N, 8.47. Found: C, 57.98; H, 3.98; N, 8.42.

2,2-dimethyl-3-((4-((p-tolylselanyl)methyl)-1*H*-1,2,3-triazol-1-yl)methyl)-2,3-dihydronaphtho[1,2-*b*]furan-4,5-dione (35): Purification by column chromatography (*n*-hexane/EtOAc) led to product **35** (89.6 mg, 0.182 mmol, 91% yield) obtained as an orange crystals; m.p: 112–113 (°C); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.09 (d, *J* = 7.5 Hz, 1H), 7.72–7.60 (m, 3H), 7.34–7.36 (m, 3H), 7.06 (d, *J* = 8.0 Hz, 2H), 5.01 (dd, *J* = 14.5, 3.0 Hz, 1H), 4.49 (dd, *J* = 15.5, 10.5 Hz, 1H), 4.12 (s, 2H), 3.79 (dd, *J* = 10.5, 3.0 Hz, 1H), 2.31 (s, 3H), 1.53 (s, 3H), 1.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 180.9, 175.7, 169.4, 146.2, 137.7, 134.7, 133.7, 132.6, 131.1, 130.1, 129.6, 127.3, 125.9, 125.1, 122.4, 113.9, 95.8, 49.8, 47.6, 29.3, 22.7, 21.2, 20.8; IR (solid, cm^{-1}) ν: 3125, 1617, 1331, 797; HRMS (APPI^{+}): 494.0983 $[M+H]^{+}$. Calculated for $[C_{25}H_{24}N_3O_3Se]^{+}$: 494.0982; Anal. Calcd for $C_{25}H_{23}N_3O_3Se$: C, 60.98; H, 4.71; N, 8.53. Found: C, 59.31; H, 4.64; N, 8.05.

2,2-dimethyl-3-((4-((naphthalen-1-ylselanyl)methyl)-1*H*-1,2,3-triazol-1-yl)methyl)-2,3-dihydronaphtho[1,2-*b*]furan-4,5-dione (36): Purification by column chromatography (*n*-hexane/EtOAc) led to product **36** (101.4 mg, 0.192 mmol, 96% yield) obtained as an red solid; m.p: 97–98 (°C); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.32 (d, *J* = 8.0 Hz, 1H), 8.08 (d, *J* = 7.5 Hz, 1H), 7.86–7.71 (m, 4H), 7.67–7.59 (m, 2H), 7.56-7.49 (m, 1H), 7.35 (t, *J* = 8.0 Hz, 1H), 7.09 (s, 1H), 4.89 (dd, *J* = 14.5, 3.0 Hz, 1H), 4.39 (dd, *J* = 14.5, 10.5 Hz, 1H), 4.19 (s, 2H), 3.68 (dd, *J* = 10.5, 3.0 Hz, 1H), 1.46 (s, 3H), 1.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 180.9, 175.7,

169.4, 145.7, 134.7, 134.5, 134.0, 133.5, 132.6, 131.0, 129.6, 129.1, 128.8, 127.6, 127.3, 126.9, 126.4, 125.9, 125.1, 122.4, 113.9, 95.7, 49.7, 47.5, 29.3, 22.7, 20.7; IR (solid, cm^{-1}) ν: 3447, 1614, 1401, 771; HRMS ($APPI^+$): 530.0979 $[M+H]^+$. Calculated for $[C_{28}H_{24}N_3O_3Se]^+$: 530.0980; Anal. Calcd for $C_{28}H_{23}N_3O_3Se$: C, 63.64; H, 4.39; N, 7.95. Found: C, 63.09; H, 4.40; N, 7.72.

2,2-dimethyl-3-((4-(((3-(trifluoromethyl)phenyl)selanyl)methyl)-1*H*-1,2,3-triazol-1-yl)methyl)-2,3-dihydronaphtho[1,2-*b*]furan-4,5-dione (37): Purification by column chromatography (*n*-hexane/EtOAc) led to product **37** (104.9 mg, 0.192 mmol, 96% yield) obtained as an red solid; m.p: 129–130 (°C); ^1H NMR (400 MHz, $CDCl_3$) δ: 8.09 (d, *J* = 7.5 Hz, 1H), 7.71–7.60 (m, 5H), 7.55–7.44 (m, 2H), 7.39 (t, *J* = 8.0 Hz, 1H), 5.03 (dd, *J* = 14.5, 3.0 Hz, 1H), 4.53 (dd, *J* = 14.5, 10.5 Hz, 1H), 4.23 (s, 2H), 3.80 (dd, *J* = 10.0, 3.0 Hz, 1H), 1.55 (s, 3H), 1.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 180.7, 175.7, 169.4, 145.4, 136.0, 134.7, 132.6, 131.5, 131.0, 129.5, 129.3, 127.2, 125.0, 124.1, 122.5, 113.8, 95.6, 49.8, 47.6, 29.2, 22.6, 20.5; IR (solid, cm^{-1}) ν: 2991, 1617, 1323, 1122; HRMS ($APPI^+$): 548.0696 $[M+H]^+$. Calculated for $[C_{25}H_{21}F_3N_3O_3Se]^+$: 548.0697; Anal. Calcd for $C_{25}H_{20}N_3O_3Se$: C, 54.95; H, 3.69; N, 7.69. Found: C, 55.12; H, 3.69; N, 7.69.

2,2-dimethyl-3-((4-((thiophen-2-ylselanyl)methyl)-1*H*-1,2,3-triazol-1-yl)methyl)-2,3-dihydronaphtho[1,2-*b*]furan-4,5-dione (38): Purification by column chromatography (*n*-hexane/EtOAc) led to product **38** (95.9 mg, 0.196 mmol, 98% yield) obtained as an red solid; m.p: 153–154 (°C); ^1H NMR (400 MHz, $CDCl_3$) δ: 8.10 (d, *J* = 7.5 Hz, 1H), 7.72–7.60 (m, 3H), 7.37 (d, *J* = 6.5 Hz, 1H), 7.27 (s, 1H), 7.09 (d, *J* = 4.5 Hz, 1H), 6.96 (dd, *J* = 5.5, 3.5 Hz, 1H), 5.02 (dd, *J* = 14.5, 3.0 Hz, 1H), 4.53 (dd, *J* = 14.5, 10.5 Hz, 1H), 4.06 (s, 2H), 3.81 (dd, *J* = 10.5, 3.0 Hz, 1H), 1.60 (s, 3H), 1.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 180.9, 175.8, 169.5, 145.5, 136.5, 134.8, 132.7, 131.6, 131.1, 129.6, 128.3, 127.3, 125.2, 123.3, 122.4, 114.0, 95.8, 50.0, 47.6, 29.5, 24.1, 22.9; IR (solid, cm^{-1}) ν: 3111, 1621, 1401, 732; HRMS ($APPI^+$): 486.0386 $[M+H]^+$. Calculated for $[C_{22}H_{20}N_3O_3SSe]^+$: 486.0392; Anal. Calcd for $C_{22}H_{19}N_3O_3SSe$: C, 54.55; H, 3.95; N, 8.67. Found: C, 54.33; H, 3.89; N, 8.58.

3-(4-(((4-methoxyphenyl)selanyl)methyl)-1*H*-1,2,3-triazol-1-yl)-2,2-dimethyl-2,3-dihydronaphtho[1,2-*b*]furan-4,5-dione (39): Purification by column chromatography (*n*-

hexane/EtOAc) led to product **39** (70.7 mg, 0.146 mmol, 73% yield) obtained as an orange solid; m.p: 98–100 (ºC); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.18 (dd, *J* = 1.7 and 6.8 Hz, 1H), 7.79-7.70 (m, 3H), 7.32 (d, *J* = 8.7 Hz, 2H), 6.97 (s, 1H), 6.73 (d, *J* = 8.7 Hz, 2H), 5.88 (s, 1H), 4,00 (s, 2H), 3.72 (s, 3H), 1.71 (s, 3H), 1.09 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 180.2, 174.6, 171.3, 160.0, 145.8, 137.1, 135.1, 133.6, 131.7, 130.1, 126.8, 125.8, 121.4, 119.3, 115.0, 111.4, 96.1, 67.0, 55.4, 27.8, 21.6, 21.3. IR (solid, cm^{-1}) ν: 3124, 1652, 1614 1405, 738; HRMS (ESI^+): 518.0578 $[M+Na]^+$. Calculated for $[C_{24}H_{21}N_3O_4SeNa]^+$: 518.0595.

2,2-dimethyl-3-(4-((p-tolylselanyl)methyl)-1*H*-1,2,3-triazol-1-yl)-2,3-dihydronaphtho[1,2-*b*]furan-4,5-dione (40): Purification by column chromatography (*n*-hexane/EtOAc) led to product **40** (53.3 mg, 0.110 mmol, 55% yield) obtained as an orange solid; m.p: 177–179 (ºC); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.17 (d, *J* = 7.0 Hz, 1H), 7.79-7.70 (m, 3H), 7.28 (d, *J* = 8.0 Hz, 2H), 7.03 (s, 1H), 6.98 (d, *J* = 8.0 Hz, 2H), 5.88 (s, 1H), 4.05 (s, 2H), 2.21 (s, 3H), 1.71 (s, 3H), 1.06 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 180.0, 174.4, 171.0, 145.6, 137.8, 134.9, 134.5, 133.4, 131.5, 129.9, 126.6, 125.5, 125.4, 121.3, 111.2, 95.9, 66.8, 27.6, 21.0, 20.8. IR (solid, cm^{-1}) ν: 3129, 1652, 1619, 1348, 785; HRMS (ESI^+): 502.0621 $[M+Na]^+$. Calculated for $[C_{24}H_{21}N_3O_3SeNa]^+$: 502.0645.

3-(4-(((4-fluorophenyl)selanyl)methyl)-1*H*-1,2,3-triazol-1-yl)-2,2-dimethyl-2,3-dihydronaphtho[1,2-*b*]furan-4,5-dione (41): Purification by column chromatography (*n*-hexane/EtOAc) led to product **41** (83.8 mg, 0.170 mmol, 85% yield) obtained as an orange solid; m.p: 121–123 (ºC); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.08 (d, *J* = 7.0 Hz, 1H), 7.72-7.62 (m, 3H), 7.32-7.28 (m, 2H), 7.05 (s, 1H), 6.83-6.79 (m, 2H), 5.81 (s, 1H), 3.97 (s, 2H), 1.64 (s, 3H), 0.99 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 180.2, 174.7, 171.4, 164.1, 161.7, 137.0, 136.9, 135.1, 133.6, 131.7, 130.2, 126.8, 125.8, 123.8, 116.6, 116.4, 111.4, 96.1, 67.0, 27.8, 21.4, 21.2. IR (solid, cm^{-1}) ν: 2970, 1695, 1649, 1614, 1589, 1571, 1410, 1214, 773; HRMS (ESI^+): 484.0567 $[M+H]^+$. Calculated for $[C_{23}H_{19}FN_3O_3Se]^+$: 484.0575.

3-(4-(((4-chlorophenyl)selanyl)methyl)-1*H*-1,2,3-triazol-1-yl)-2,2-dimethyl-2,3-dihydronaphtho[1,2-*b*]furan-4,5-dione (42): Purification by column chromatography (*n*-hexane/EtOAc) led to product **42** (45.1 mg, 0.088 mmol, 44% yield) obtained as an orange solid; m.p: 182–184 (ºC); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.26 (d, *J* = 5.8 Hz, 1H), 7.89-7.80

(m, 3H), 7.42 (d, *J* = 6.7 Hz, 2H), 7.26-7.23 (m, 3H), 5.98 (s, 1H), 4.17 (s, 2H), 1.81 (s, 3H), 1.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 180.2, 174.6, 171.3, 145.4, 135.6, 135.0, 134.1, 133.6, 131.6, 130.1, 129.4, 127.5, 126.7, 125.8, 121.5, 111.3, 96.0, 66.9, 27.8, 21.1. IR (solid, cm^{-1}) ν: 2980, 1707, 1653, 1621, 1588, 1572, 1408, 1085, 778; HRMS (ESI^+): 500.0278 $[M+H]^+$. Calculated for $[C_{23}H_{19}ClN_3O_3Se]^+$: 500.0280.

3-(4-(((4-bromophenyl)selanyl)methyl)-1*H*-1,2,3-triazol-1-yl)-2,2-dimethyl-2,3-dihydronaphtho[1,2-*b*]furan-4,5-dione (43): Purification by column chromatography (*n*-hexane/EtOAc) led to product **43** (74.5 mg, 0.140 mmol, 70% yield) obtained as an orange solid; m.p: 130–131 (ºC); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.10 (dd, *J* = 0.76 and 5.8 Hz, 1H), 7.73-7.63 (m, 3H), 7.23 (d, *J* = 6.8 Hz, 2H), 7.18 (d, *J* = 6.8 Hz, 2H), 7.07 (s, 1H), 5.82 (s, 1H), 4.01 (m, 2H), 1.65 (s, 3H), 0.98 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 180.2, 174.6, 171.3, 145.4, 135.8, 135.1, 133.6, 132.4, 131.6, 130.2, 128.2, 126.7, 125.8, 122.2, 121.5, 111.3, 96.0, 67.0, 27.8, 21.0. IR (solid, cm^{-1}) ν: 2981, 1707, 1658, 1627, 1598, 1408, 787; HRMS (ESI^+): 543.9761 $[M+H]^+$. Calculated for $[C_{23}H_{19}BrN_3O_3Se]^+$: 543.9775.

2,2-dimethyl-3-(4-(((4-nitrophenyl)selanyl)methyl)-1*H*-1,2,3-triazol-1-yl)-2,3-dihydronaphtho[1,2-*b*]furan-4,5-dione (44): Purification by column chromatography (*n*-hexane/EtOAc) led to product **44** (73.2 mg, 0.144 mmol, 72% yield) obtained as an orange solid; m.p: 141–143 (ºC); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.16-8.15 (m, 1H), 8.02 (d, *J* = 7.2 Hz, 2H), 7.76-7.68 (m, 3H), 7.52 (d, *J* = 7.2 Hz, 2H), 7.31 (s, 1H), 5.88 (s, 1H), 4.26-4.18 (m, 2H), 1.70 (s, 3H), 1.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 180.1, 174.7, 171.4, 146.8, 144.8, 140.5, 135.1, 133.7, 131.8, 131.7, 130.3, 126.7, 125.8, 124.1, 121.8, 111.2, 96.0, 27.9, 21.2, 20.2. IR (solid, cm^{-1}) ν: 2982, 1668, 1624, 1556, 1512, 1412, 778; HRMS (ESI^+): 533.0315 $[M+Na]^+$. Calculated for $[C_{23}H_{18}N_4O_5SeNa]^+$: 533.0340.

3-(4-((benzylselanyl)methyl)-1*H*-1,2,3-triazol-1-yl)-2,2-dimethyl-2,3-dihydronaphtho[1,2-*b*]furan-4,5-dione (45): Purification by column chromatography (*n*-hexane/EtOAc) led to product **45** (79.5 mg, 0.166 mmol, 83% yield) obtained as an orange solid; m.p: 197–199 (ºC); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.11 (dd, *J* = 1.1 and 8.6 Hz, 1H), 7.75-7.63 (m, 3H), 7.21-7.12 (m, 4H), 7.09 (s, 1H), 7.03-7.00 (m, 1H), 5.84 (s, 1H), 3.71 (s, 2H), 3.69-3.59 (m, 2H), 1.66 (s, 3H), 1.09 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 180.3, 174.7,

171.3, 146.9, 139.3, 135.1, 133.6, 131,8, 130.2, 129.3, 128.7, 126.9, 125.8, 121.5, 111.5, 96.2, 67.1, 28.1, 27.9, 21.3, 16.0. IR (solid, cm^{-1}) ν: 2925, 1693, 1651, 1611, 1587, 1567, 1407, 1220, 776.

2,2-dimethyl-3-(4-(((thiophen-2-yl)selanyl)methyl)-1*H*-1,2,3-triazol-1-yl)-2,3-dihydronaphtho[1,2-*b*]furan-4,5-dione (46): Purification by column chromatography (*n*-hexane/EtOAc) led to product **46** (82.5 mg, 0.176 mmol, 88% yield) obtained as a yellow solid; m.p: 159–161 (ºC); . ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.21 (dd, *J* = 1.5 and 6.8 Hz, 1H), 7.82-7.73 (m, 3H), 7.28 (s, 1H), 7.01 (d, *J* = 2.6 Hz, 1H), 6.98 (s, 1H), 6.88 (dd, *J* = 3,6 and 5.2 Hz, 1H), 5.91 (s, 1H), 4.02 (s, 2H), 1.74 (s, 3H), 1.64 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 180.0, 174.4, 171.1, 137.1, 134.9, 133.4, 131.5, 130.0, 128.3, 126.6, 125.6, 122.7, 111.2, 95.9, 66.9, 27.6, 23.6, 21.2. IR (solid, cm-1) ν: 2978, 1703, 1651, 1618, 1410, 1219, 779. IR (solid, cm-1) ν: 2978, 1703, 1651, 1618, 1410, 1219, 779; HRMS (ESI+): 472.0238 $[M+H]^+$. Calculated for $[C_{21}H_{18}N_3O_3SSe]^+$: 472.0234.

3-(4-((butylselanyl)methyl)-1*H*-1,2,3-triazol-1-yl)-2,2-dimethyl-2,3-dihydronaphtho[1,2-*b*]furan-4,5-dione (47): Purification by column chromatography (*n*-hexane/EtOAc) led to product **47** (44.0 mg, 0.100 mmol, 50% yield) obtained as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.17 (d, *J* = 6.4 Hz, 1H), 7.81-7.72 (m, 3H), 7.44 (s, 1H), 5.94 (s, 1H), 3.83-3.74 (m, 2H), 2.55 (t, *J* = 6.9 Hz, 2H), 1.75 (s, 3H), 1.59 (qt, *J* = 7.0 Hz, 2H), 1.35 (qt, *J* = 7.4 Hz, 2H), 1.20 (s, 3H), 0.86 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 180.3, 174.7, 171.4, 147.0, 135.1, 133.6, 131.7, 130.2, 126.9, 125.8, 121.7, 111.4, 96.1, 67.2, 32.5, 28.0, 24.6, 23.1, 21.4, 15.4, 13.7. IR (solid, cm^{-1}) ν: 3132, 1629, 1401, 767.

Procedure for the synthesis of azide compound D[5]

2-((4-((phenylselanyl)methyl)-1*H*-1,2,3-triazol-1-yl)methyl)-2,3-dihydronaphtho[2,3-*b*]furan-4,9-dione (48): Purification by column chromatography (*n*-hexane/EtOAc) led to product **48** (80.1 mg, 0.178 mmol, 89% yield) obtained as an orange solid; m.p: 157–159 (ºC); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.00-7,95 (m, 2H), 7.60-7.67 (m, 2H), 7.35-7.33 (m, 3H), 7.16-7.11 (m, 3H), 5.31-5.35 (m, 1H), 4.64 (dd, *J* = 3.2 and 11.8 Hz, 1H), 4.57 (dd, *J* = 4.5 and 11.8 Hz, 1H), 4.05 (s, 2H), 3.25 (dd, *J* = 8.5 and 14.0 Hz, 1H), 2.94 (dd, *J* = 6.5 and 14,0 Hz, 1H);

^{13}C NMR (100 MHz, $CDCl_3$) δ: 180.6, 176.2, 158.0, 133.4, 132.2, 132.0, 131.7, 130.3, 128.7, 128.1, 126.4, 125.4, 125.2, 123.1, 122.0, 82.0, 51.8, 29.1, 19.3. IR (solid, cm^{-1}) ν: 2957, 1682, 1599, 1574, 1552. IR (solid, cm^{-1}) ν: 2957, 1682, 1599, 1574, 1552; HRMS (ESI+): 452.0512 $[M+H]^+$. Calculated for $[C_{22}H_{18}N_3O_3Se]^+$: 452.0517.

2-((4-(((4-fluorophenyl)selanyl)methyl)-1*H*-1,2,3-triazol-1-yl)methyl)-2,3-dihydronaphtho[2,3-*b*]furan-4,9-dione (49): Purification by column chromatography (*n*-hexane/EtOAc) led to product **49** (75.8 mg, 0.162 mmol, 81% yield) obtained as a yellow solid; m.p: 190–192 (ºC); ^{1}H NMR (400 MHz, DMSO-d_6) δ: 7.96-7.93 (m, 3H), 7.85-7.78 (m, 2H), 6.85-6.81 (m, 2H), 6.57-6.54 (m, 2H), 5.49-5.43 (m, 1H), 4.76 (d, *J* = 4,4 Hz, 2H), 4.23 (dd, *J* = 1.8 and 4.6 Hz, 2H), 3.26 (dd, *J* = 8.5 and 13.7 Hz, 1H), 2.91 (dd, *J* = 5.6 and 13.7 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 181.5, 176.9, 159.1, 145.8, 145.0, 134.4, 133.4, 132.3, 131.1, 125.8, 125.4, 123.9, 123.6, 115.2, 115.0, 113.0, 83.3, 54.9, 52.3, 29.7. IR (solid, cm^{-1}) ν: 2958, 1730, 1676, 1593, 1571, 1510. IR (solid, cm^{-1}) ν: 2958, 1730, 1676, 1593, 1571, 1510.

2-((4-((benzylselanyl)methyl)-1*H*-1,2,3-triazol-1-yl)methyl)-2,3-dihydronaphtho[2,3-*b*]furan-4,9-dione (50): Purification by column chromatography (*n*-hexane/EtOAc) led to product **50** (27.8 mg, 0.060 mmol, 30% yield) obtained as an orange solid; m.p: 149–151 (ºC); ^{1}H NMR (400 MHz, DMSO-d_6) δ: 7.97 (s, 1H), 7.95-7.91 (m, 2H), 7.83-7.76 (m, 2H), 7.29-7.24 (m, 4H), 7.21-7.17 (m, 1H), 5.52-5.47 (m, 1H), 4.77-4.76 (m, 2H), 3.69-3.68 (m, 4H), 3.30 (dd, *J* = 8.5 and 13.7 Hz, 1H), 2.98 (dd, *J* = 5.3 and 13.7 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 181.4, 176.8, 159.1, 145.4, 139.4, 134.4, 133.4, 132.3, 131.1, 128.8, 128.3, 126.5, 125.8, 125.4, 123.9, 123.6, 83.1, 52.4, 29.7, 26.6, 15.3. IR (solid, cm^{-1}) ν: 2956, 1682, 1655, 1599, 1574, 1550. IR (solid, cm^{-1}) ν: 2956, 1682, 1655, 1599, 1574, 1550; HRMS (ESI^+): 466.0672 $[M+H]^+$. Calculated for $[C_{23}H_{20}N_3O_3Se]^+$: 466.0669.

2-((4-((decylselanyl)methyl)-1*H*-1,2,3-triazol-1-yl)methyl)-2,3-dihydronaphtho[2,3-*b*]furan-4,9-dione (51): Purification by column chromatography (*n*-hexane/EtOAc) led to product **51** (15.4 mg, 0.030 mmol, 15% yield) obtained as an orange solid; m.p: 144–146 (ºC); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.01-7.97 (m, 2H), 7.68-7.61 (m, 2H), 7.55 (s, 1H), 5.37-5.31 (m, 1H), 4.71 (dd, *J* = 3.0 and 11.8 Hz, 1H), 4.62 (dd, *J* = 4.4 and 11.8 Hz, 1H), 3.72-3.65 (m, 2H), 3.30 (dd, *J* = 8.5 and 14.0 Hz, 1H), 3.02 (dd, *J* = 6.2 and 14.0 Hz, 1H), 2.44-2.35 (m, 2H),

1.54-1.48 (m, 4H), 1.22-1.17 (m, 12H), 0.81 (t, J = 5.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 181.8, 177.4, 159.3, 147.9, 134.6, 133.5, 133.0, 131.6, 126.6, 126.5, 124.4, 123.0, 83.2, 53.2, 32.2, 30.3, 30.1, 29.9, 29.9, 29.8, 29.6, 29.4, 24.9, 22.9, 15.3, 14.4. IR (solid, cm^{-1}) ν: 2953, 1682, 1656, 1599, 1575, 1548. IR (solid, cm^{-1}) ν: 2953, 1682, 1656, 1599, 1575, 1548.

4.2. Crystallographic data

Single-crystal X-ray diffraction measurements of three compounds were performed on a Bruker CCD SMART APEX II single-crystal diffractometer with Mo Kα radiation (0.71073 Å) at 296 K. Data were processed with SAINT[14] and corrected for absorption by SADABS.[15] The structure was solved by direct methods employing SHELXS-97 and refined by full-matrix least-squares on F^2 by SHELXL-97.[16] All non-hydrogen atoms were refined successfully by anisotropic displacement parameters. Molecular graphics were generated by the ORTEP-3[17] program. Squeeze program was employed to modulate the disorder of solvent molecules in **35**. Crystallographic data for the structures were deposited with the Cambridge Crystallographic Data Centre, with numbers CCDC 1984588, 1984589 and 1984590.

4.3. Biological assays

Antitumor activity of compounds was evaluated in cell culture *in vitro* using several human cancer cell lines obtained from the National Cancer Institute, NCI (Bethesda, MD, USA). The L929 cells (mouse fibroblast L cells NCTC clone 929) employed in this study as a control cell line, were obtained from the American Type Culture Collection (Manassas, VA, USA). Cancer cell lines were maintained in RPMI 1640 medium and L929 cells were cultivated under standard conditions in DMEM with Earle's salts. Culture media were supplemented with 10% (cancer and L929 cells) fetal bovine serum, 2 mM L-glutamine, 100 IU/mL penicillin, 100 µg/mL streptomycin at 37 ^{o}C with 5% CO_2. Compounds tested were dissolved in DMSO. The final concentration of DMSO in the culture medium was kept constant (0.1%, v/v). Doxorubicin (0.001–1.10 µM) served as positive control, and negative control groups received the same amount of vehicle (DMSO). Cell viability was determined by reduction of the yellow dye 3-(4,5-dimethyl-2-thiazol)-2,5-diphenyl-2H-tetrazolium bromide (MTT) to a purple formazan product as described by Mosmann.[18] After completion of the incubation at 72 h, plates were

centrifuged, and the medium was replaced by fresh medium (200 µL) containing 0.5 mg/mL MTT. For the mechanism assays, IC_{50} was stablished in a 24 hours incubation period. After 3 h, the MTT formazan product was dissolved in DMSO (150 µL), and the absorbance was measured in a multiplate reader (Spectra Count, Packard, ON, Canada). Influences of the compound on cell proliferation and survival were quantified as the percentage of control absorbance of the reduced dye at 550 nm. Cell treatments were performed with three replicates and cells were mycoplasma-free.

Cell membrane integrity and viability

Cell viability and cell membrane integrity analysis were performed by the exclusion of propidium iodide (PI, 5 µg/mL, Sigma Aldrich Co., St. Louis, MO, USA) using flow cytometry. Briefly, after 24 h of treatment with compound **42** (0.85 µM, 1.7 µM and 3.5 µM), 400 µL of treated and untreated cells were incubated with PI, in the dark. After 10 min of incubation, fluorescence was measured by flow cytometry in a BD FACSCalibur™, and cell morphology, granularity and membrane integrity were analyzed. For comparative purposes, Nor-β-lapachone (NBL, 4 µM) was used as positive control. Data are expressed as mean ± SEM from three independent experiments.

Phosphatidylserine (PS) externalization

PS externalization, an apoptotic related event, was analyzed by flow cytometry using the Guava Nexin Assay kit (Annexin V/7-AAD staining). Annexin V is a phospholipid- binding protein that has a high affinity for PS. 7-AAD is a fluorescent intercalator of DNA impermeant to the cell, indicating membrane integrity. Double staining is used to distinguish between viable, early apoptotic, and late apoptotic/ necrotic cells. Briefly, after 24 h of treatment with compound **42** (0.85 µM, 1.7 µM and 3.5 µM), 50 µL of treated and untreated HCT-116 cells were incubated, in the dark, with Guava Nexin solution (Guava Technologies) for 20 min. Fluorescence (Annexin V-PE at 583 nm and 7-AAD at 680 nm) was measured with BD FACSCalibur™. The percentages of viable, early, and late apoptotic/ necrotic cells were then calculated. For comparative purposes, Nor-β-lapachone (NBL, 4 µM) was used as positive control. Data are expressed as mean ± SEM from three independent experiments.

Mitochondrial transmembrane potential

Mitochondrial depolarization was evaluated after incorporation of Rhodamine 123 (Sigma Aldrich Co., St. Louis, MO, USA). Briefly, after 24h of treatment with compound **42** (0.85 μM, 1.7 μM and 3.5 μM), 800 μl of treated and untreated cells was resuspended in 250 μl of a solution containing 1μg/mL of Rhodamine 123. After 15 min of incubation at 37°C and 5% CO_2, cells were centrifuged and resuspended in 400 μl of PBS and kept at room temperature (RT), in the dark, for 30 min before being analyzed by flow cytometry. Fluorescence was measured with BD FACSCalibur™ and the percentage of mitochondrial depolarization was analyzed. For comparative purposes, Nor-β-lapachone (NBL, 4 μM) was used as positive control. Data are expressed as mean ± SEM from three independent experiments.

Measurement of intracellular reactive oxygen species levels

Intracellular reactive oxygen species (ROS) accumulation was monitored using 5-(6)-chloromethyl-2′,7′-dichlorodihydrofluorescein diacetate (CM-H_2DCFDA), which is converted to the highly fluorescent dichlorofluorescein (DCF) in the presence of intracellular ROS. HCT-116 cells (colon carcinoma) were pre-loaded with 10 μM CM-H_2DCFDA and incubated for 45 min, in the dark, at 37 ºC / 5% CO_2. After that time, cells were centrifuged, the medium containing CM-H_2DCFDA was removed, and cells were washed twice with PBS buffer. From this stage, cells were always protected from light. Fresh medium containing compound **42** was added (1.7 μM and 3.5 μM), and cells were incubated at the times of interest (1, 3 and 5 hours). Nor-β-lapachone (NBL, 4 μM) was used as positive control. After the incubation time, cells were centrifuged, washed, and re-suspended in PBS containing propidium iodide (PI) to a final concentration of 1 μg/mL. Tubes were placed on ice and immediately analyzed by flow cytometry (BD FACSVerse™). Living cells, which are PI negative, were selected by gating. In those living cells, the DCF fluorescence was recorded using excitation and emission wavelengths of 490 and 525 nm, respectively. A total of 10.000 events were analyzed per sample. Data are expressed as mean ± SEM from three independent experiments.

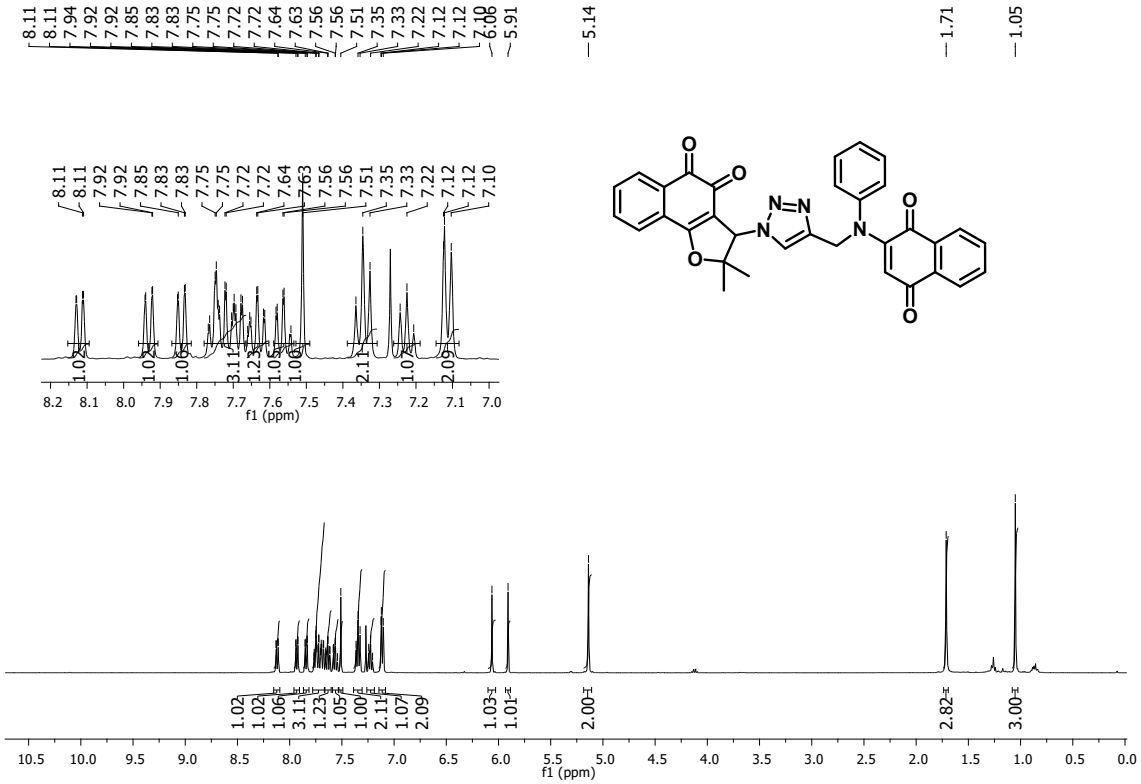


Figure S1. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **1**

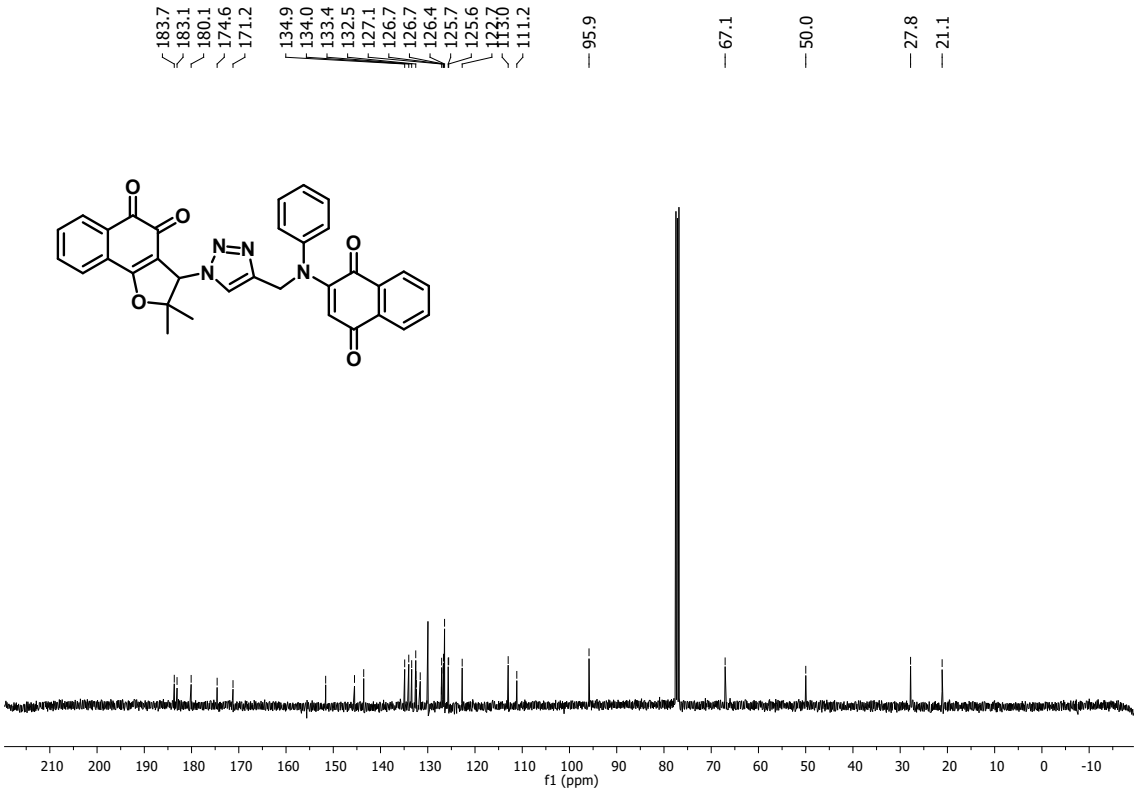


Figure S2. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **1**

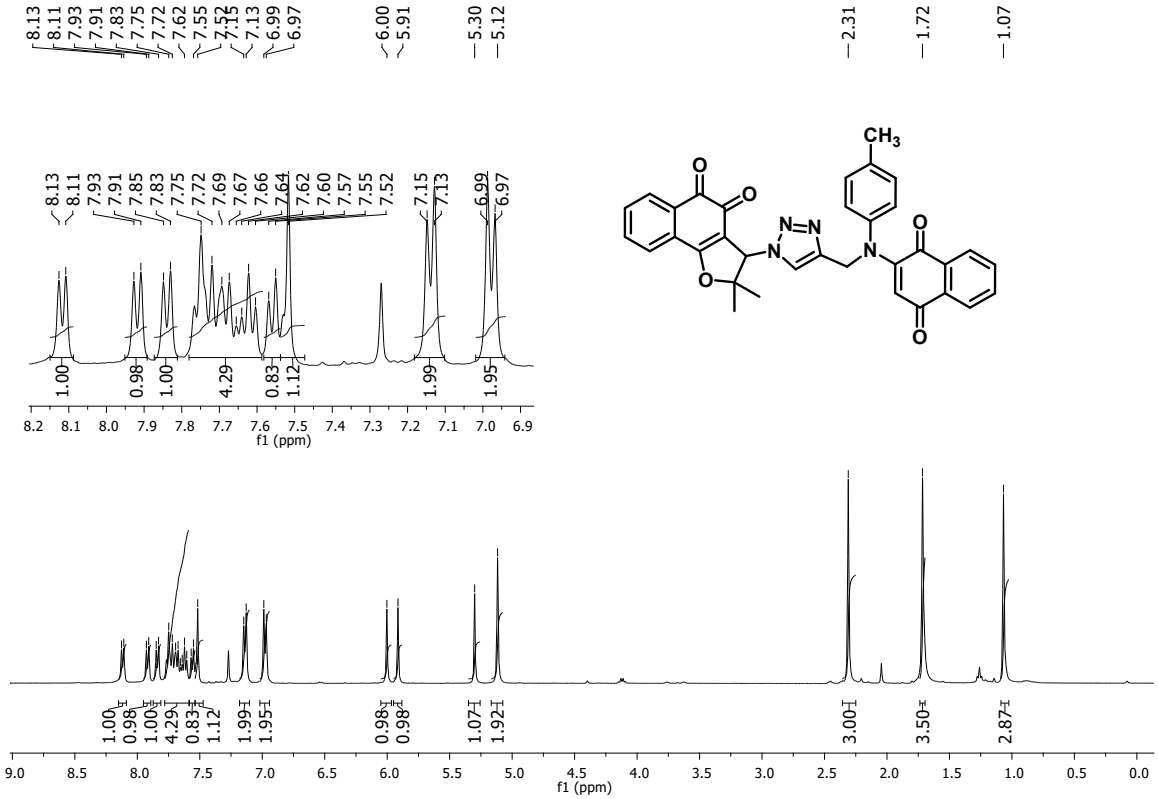


Figure S3. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **2**

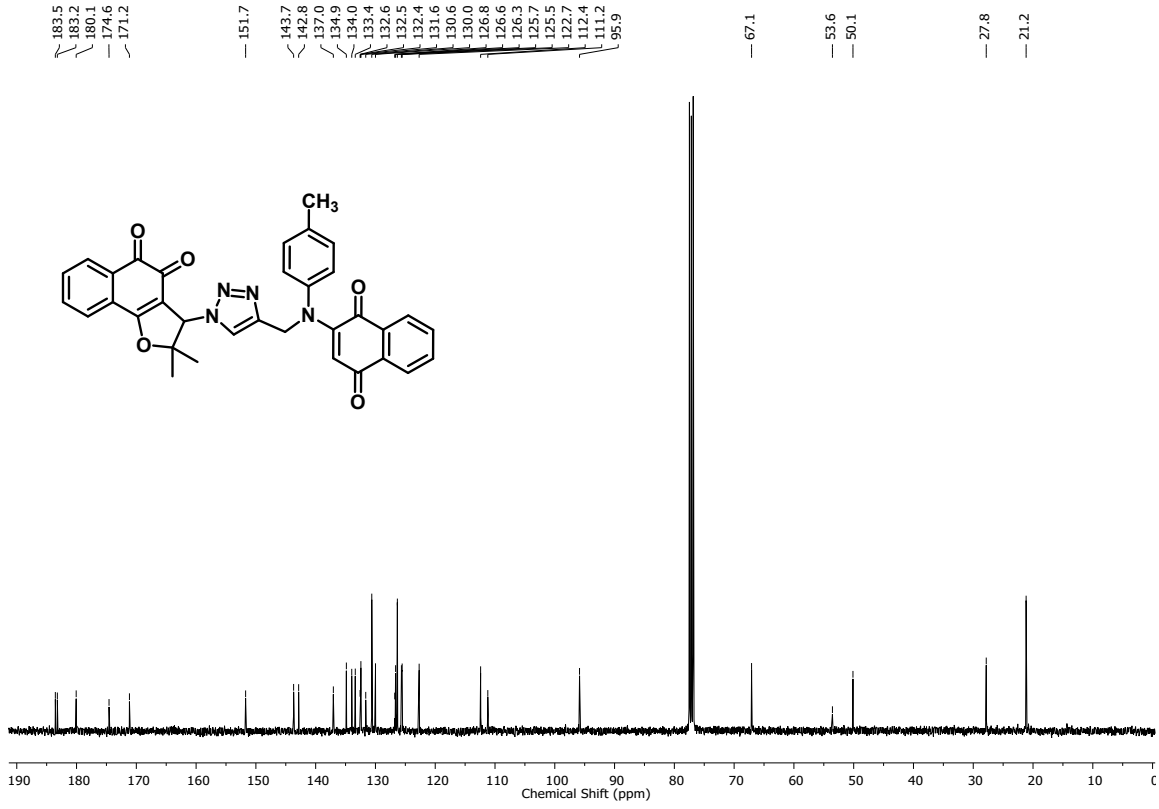


Figure S4. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **2**

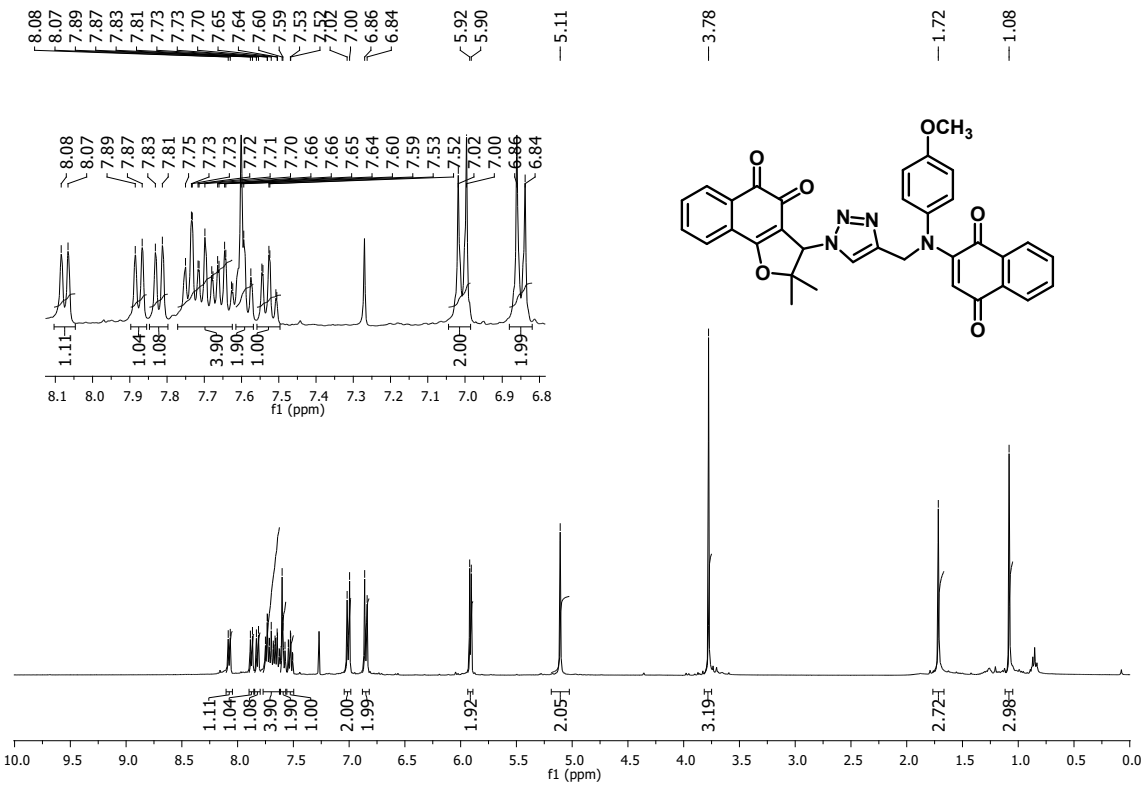


Figure S5. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **3**

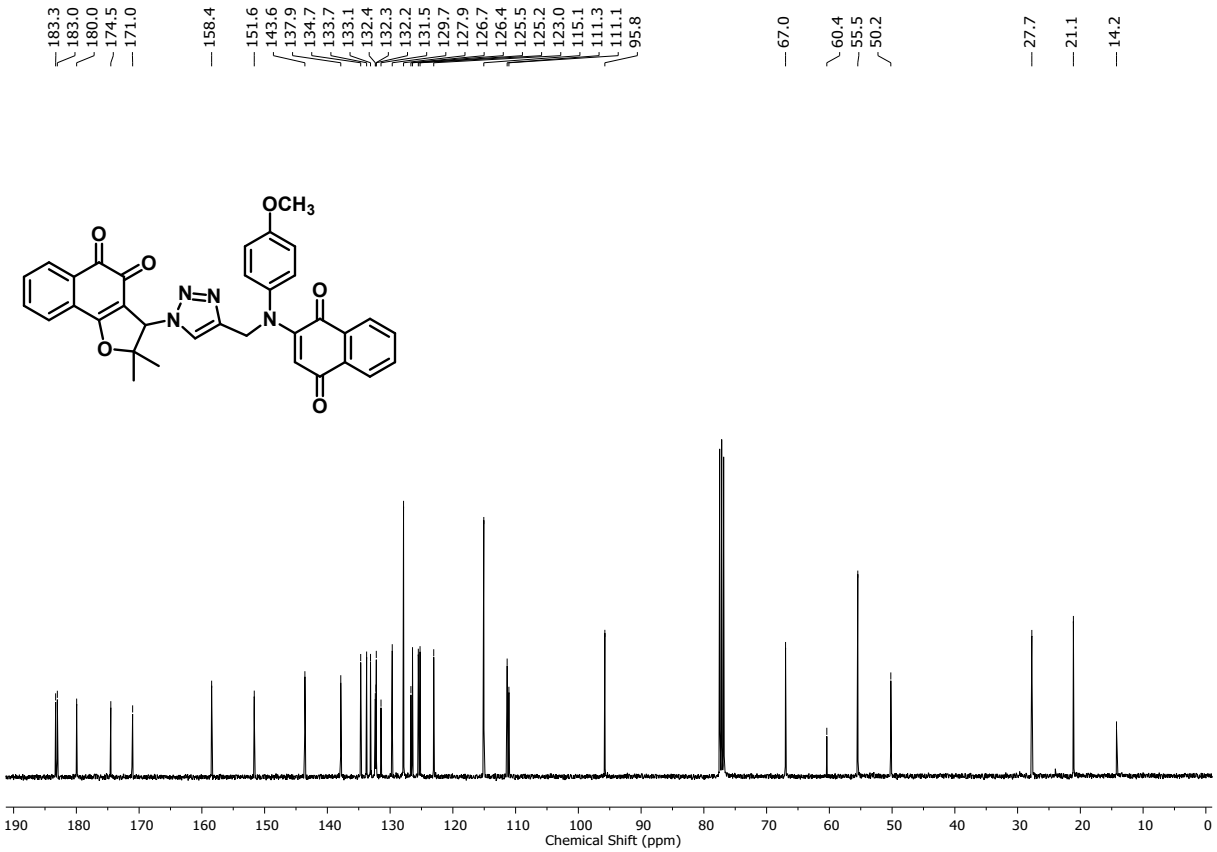


Figure S6. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **3**

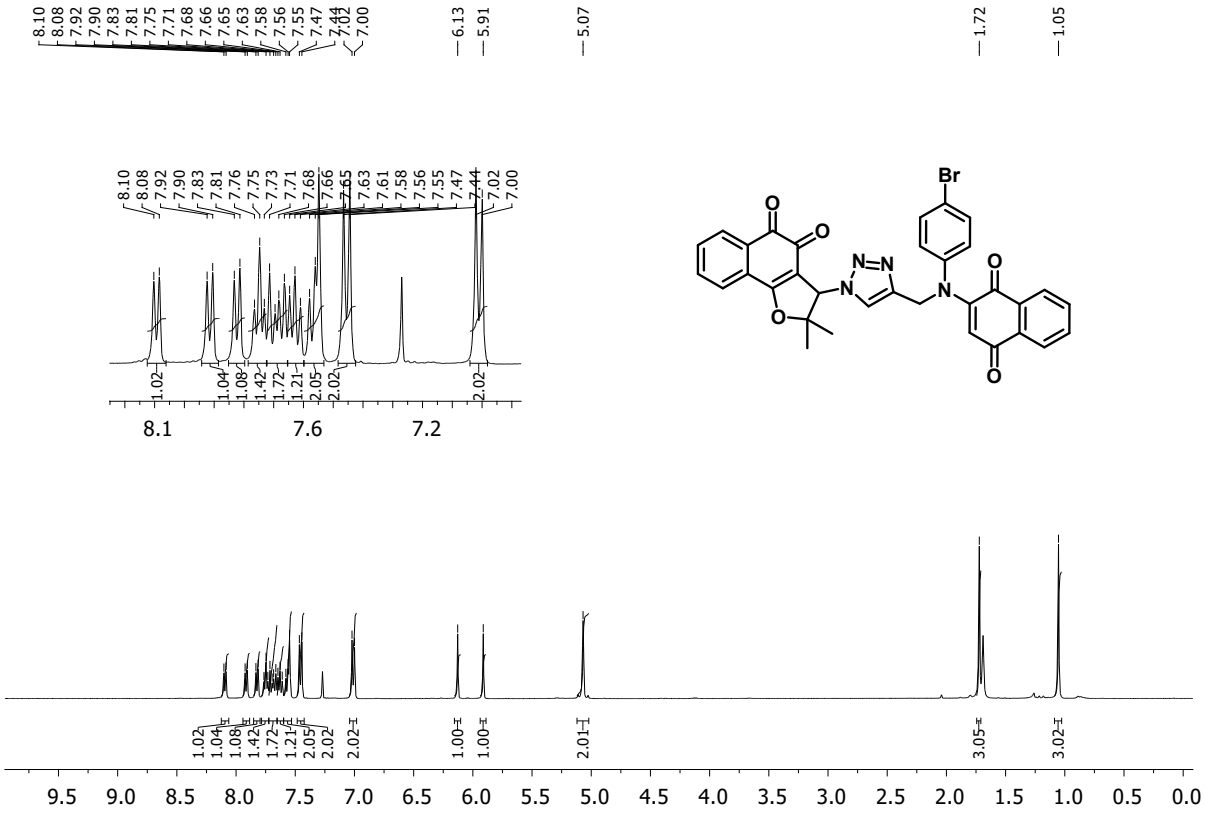


Figure S7. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **4**

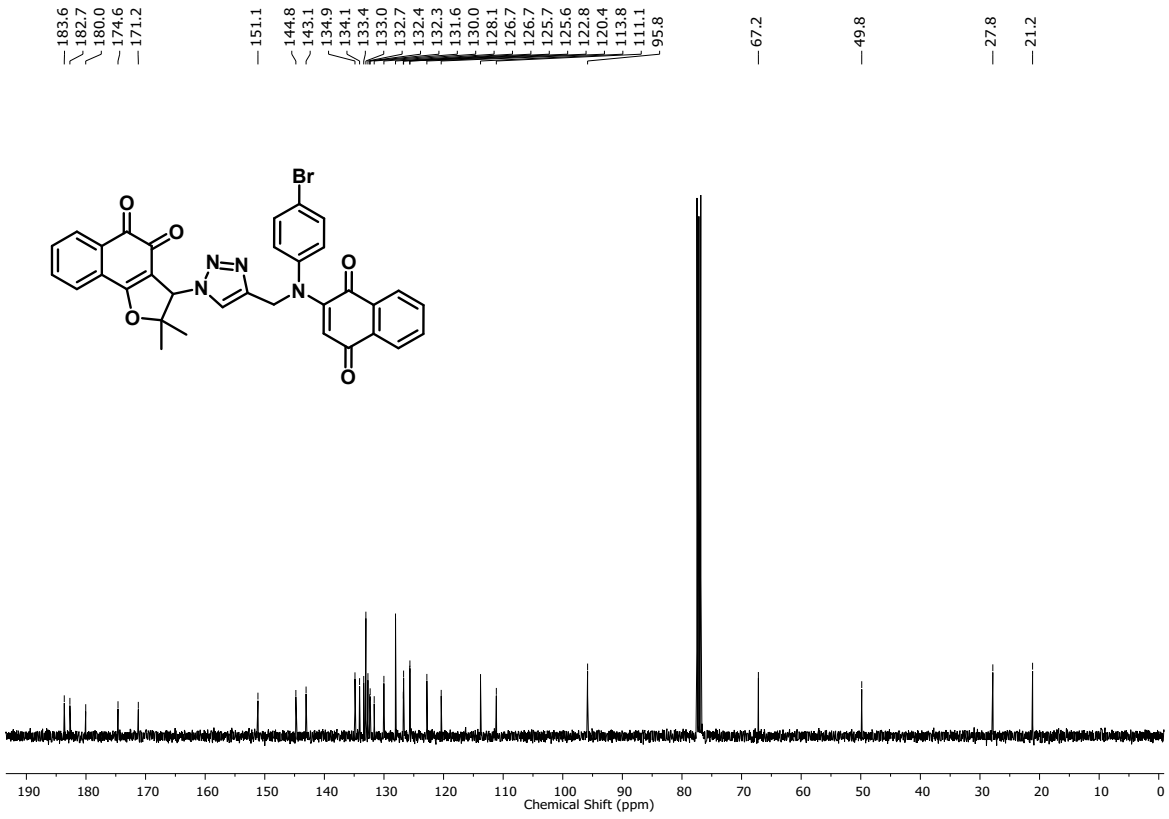


Figure S8. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **4**

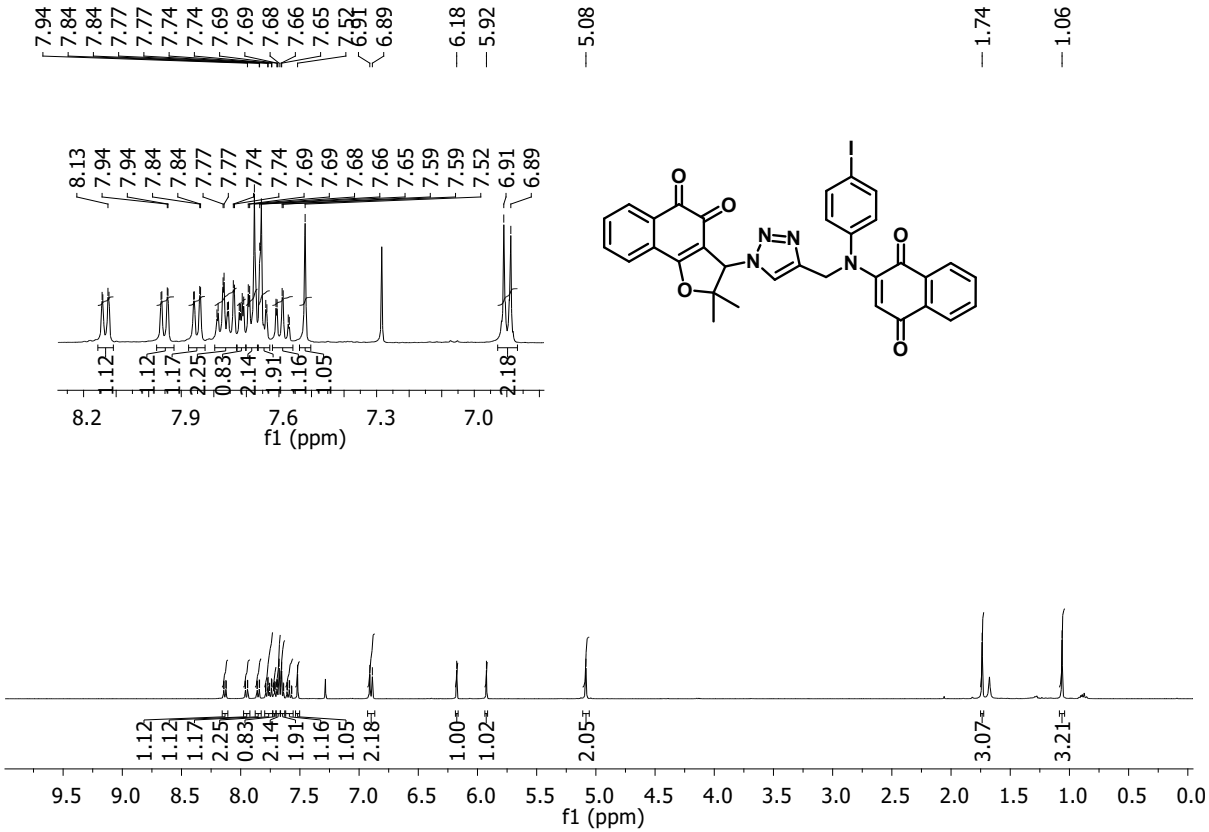


Figure S9. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **5**

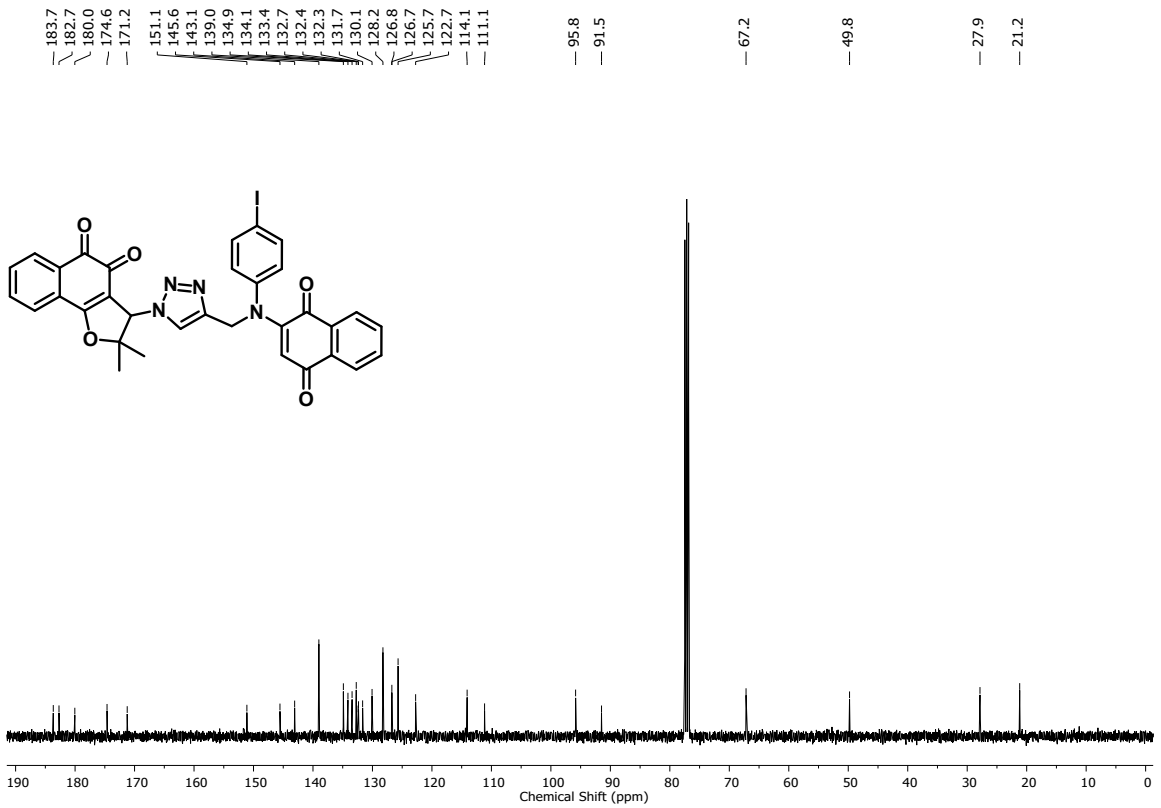


Figure S10. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **5**

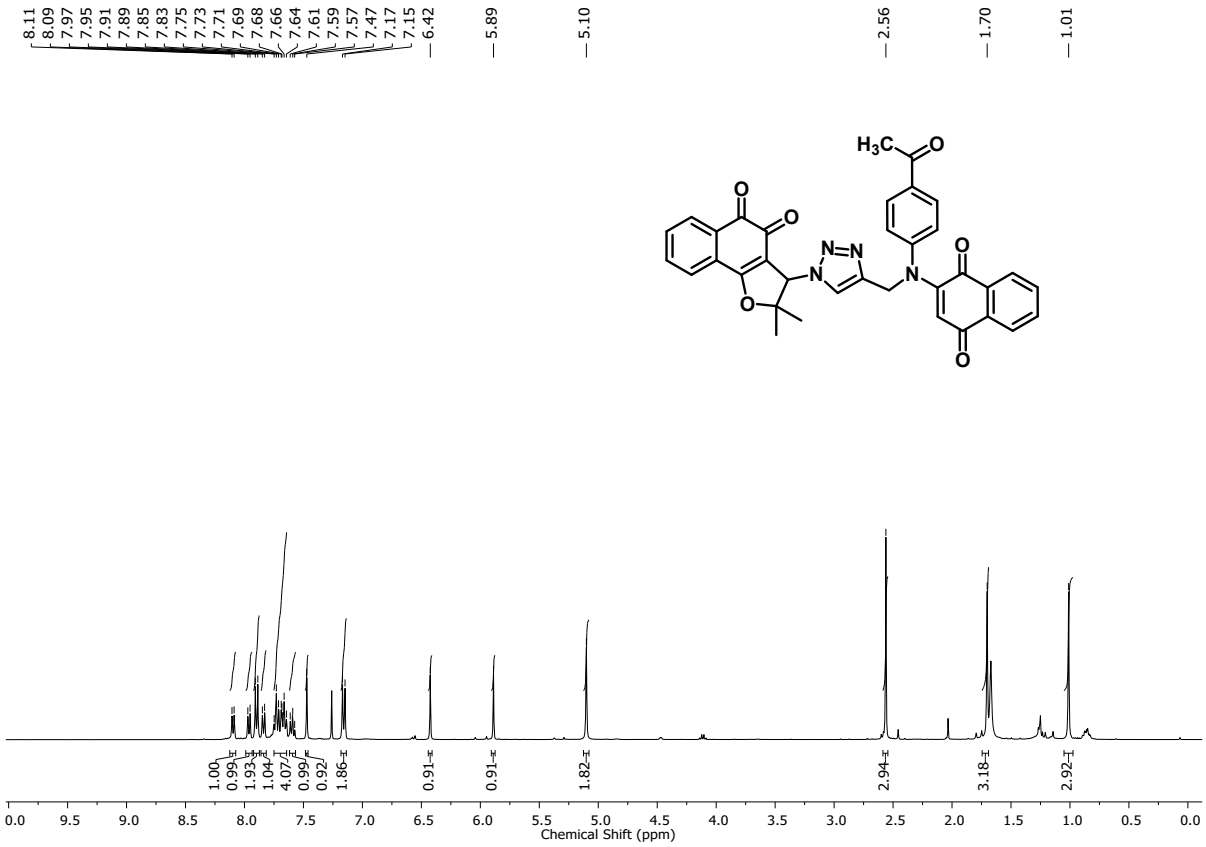


Figure S11. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **6**

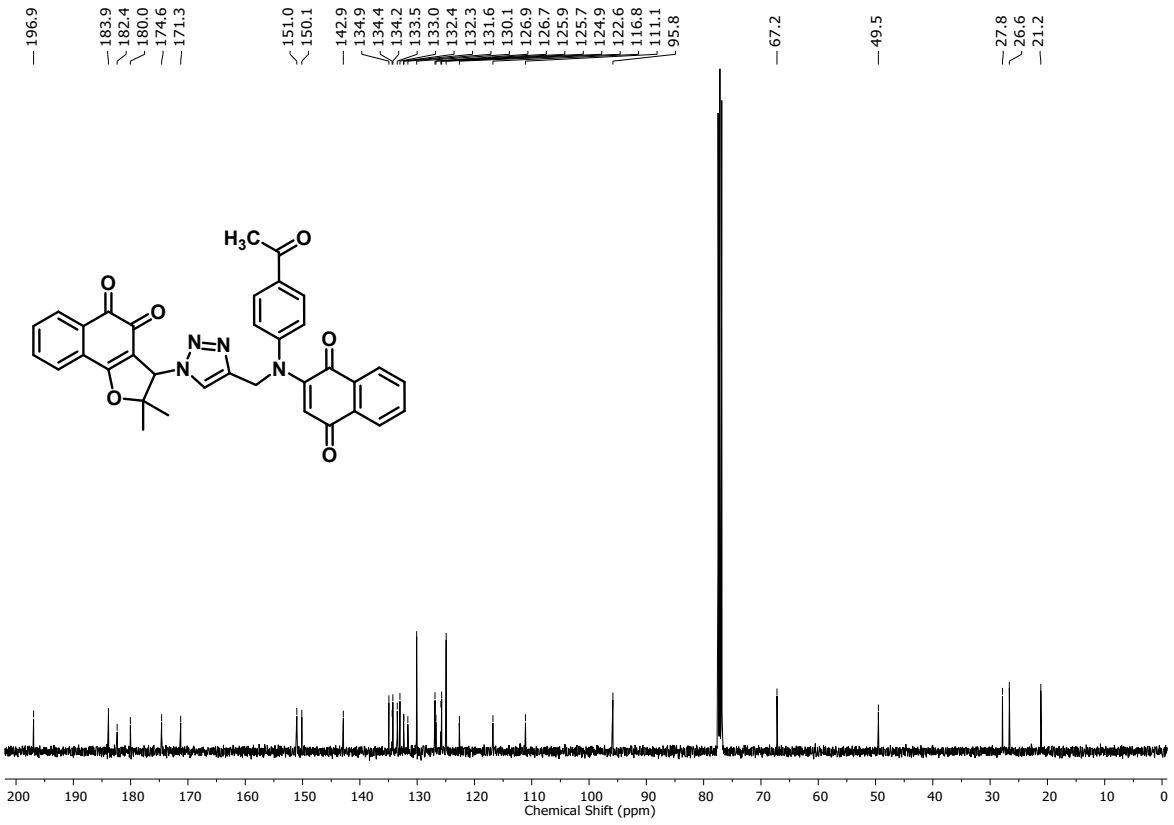


Figure S12. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **6**

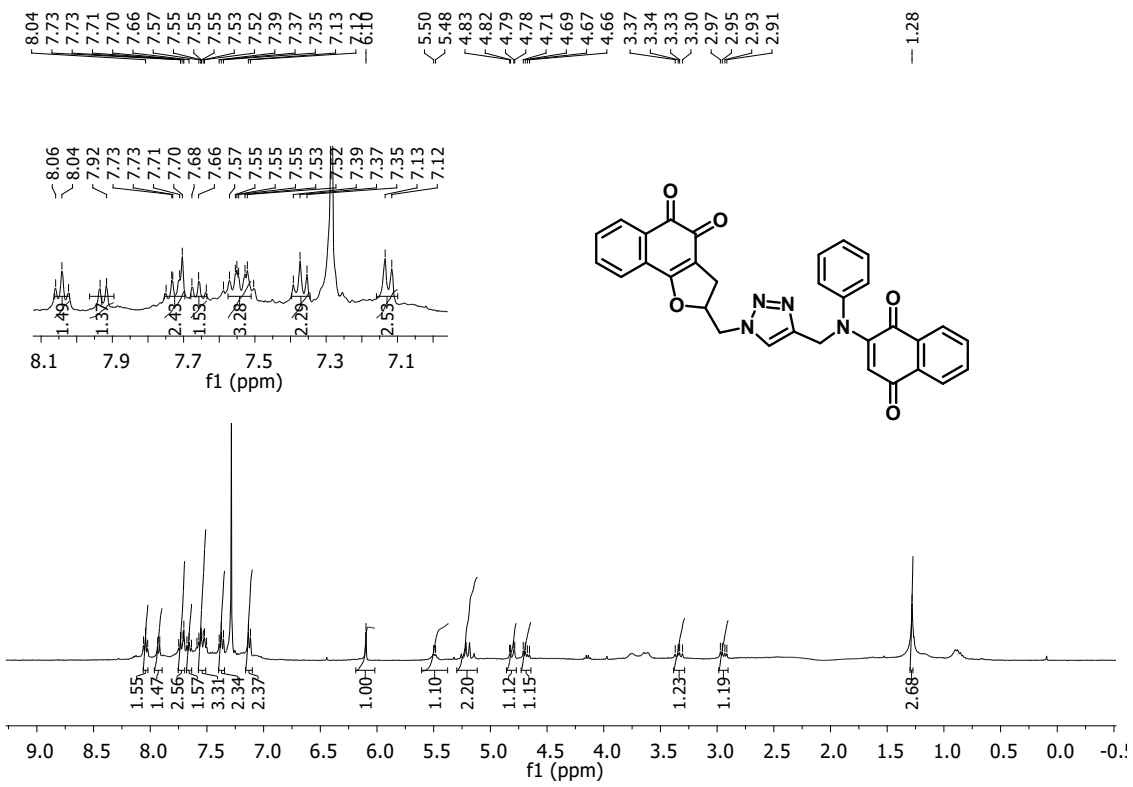


Figure S13. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **7**

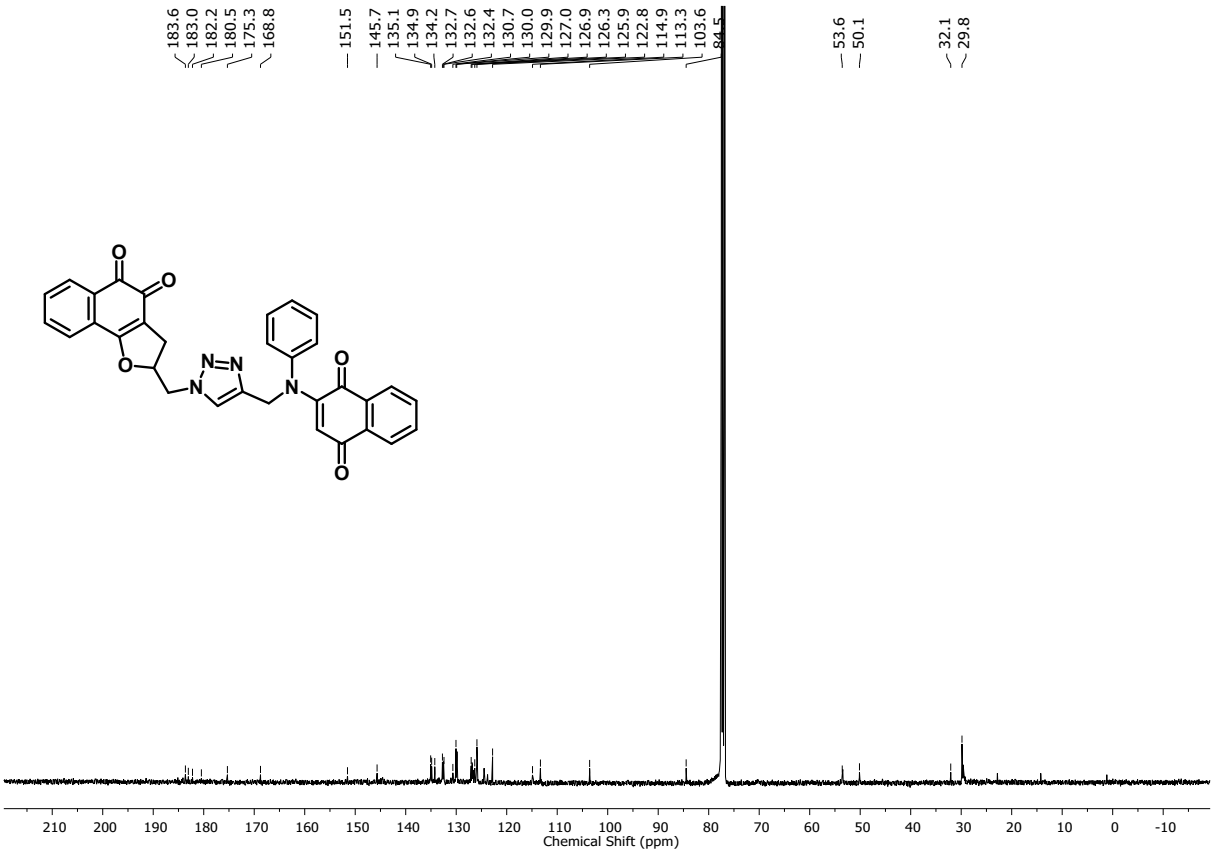


Figure S14. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **7**

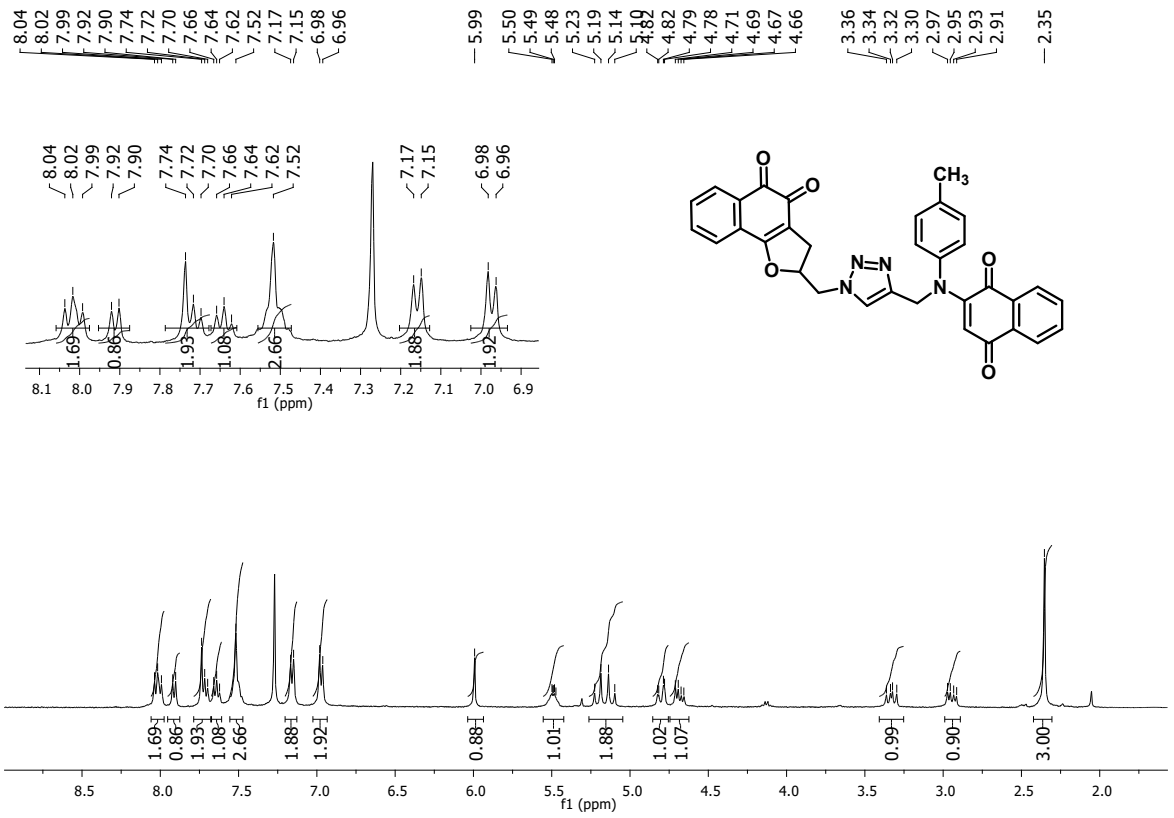


Figure S15. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **8**

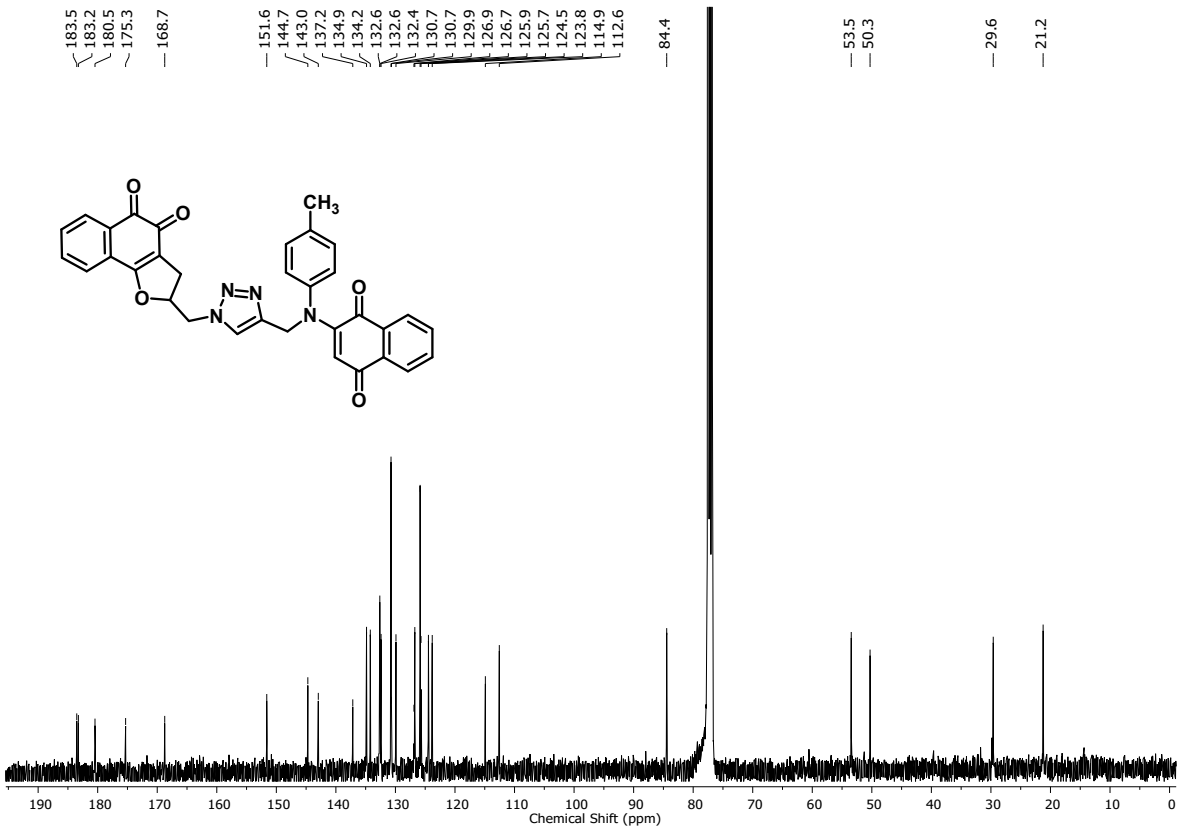


Figure S16. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **8**

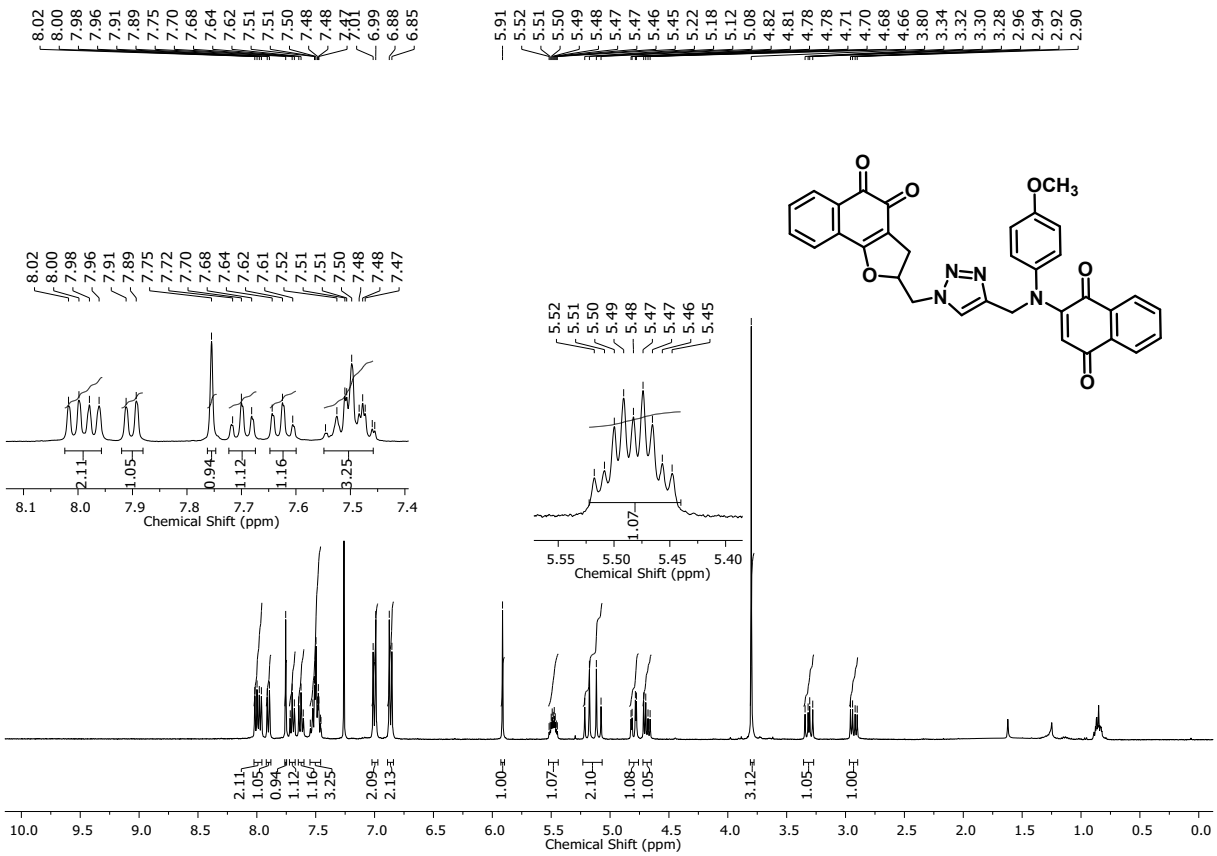


Figure S17. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **9**

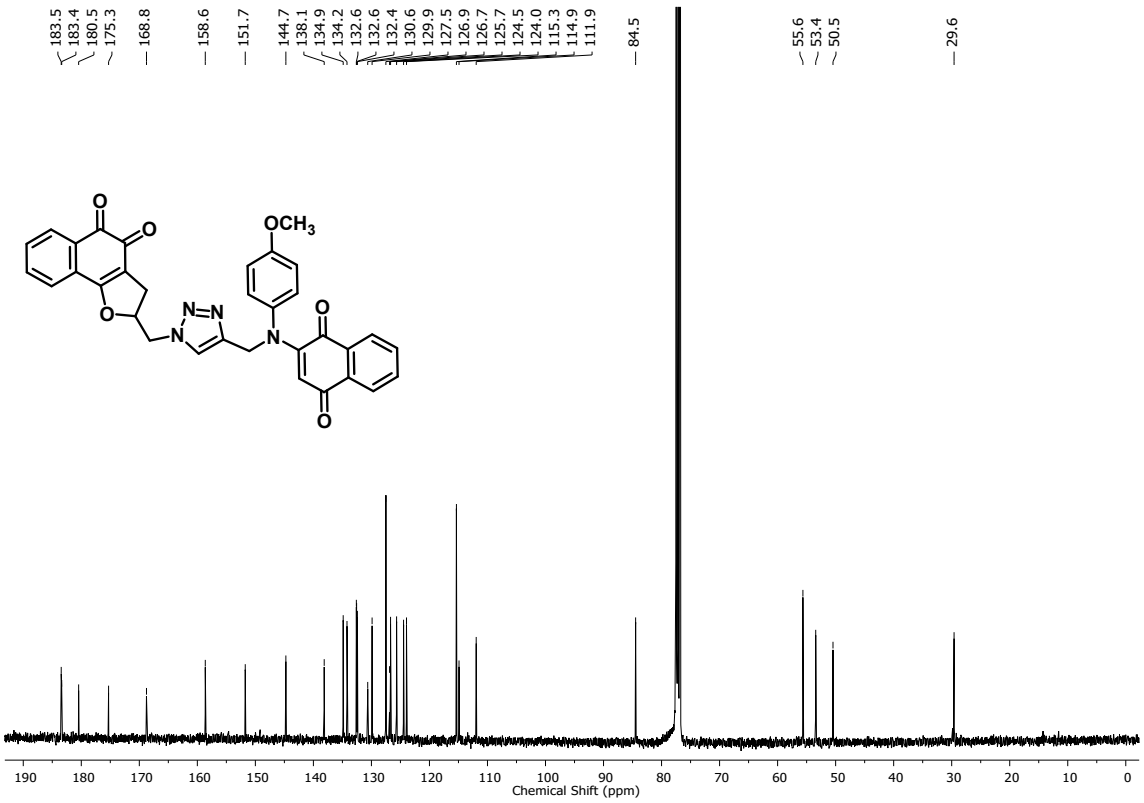


Figure S18. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **9**

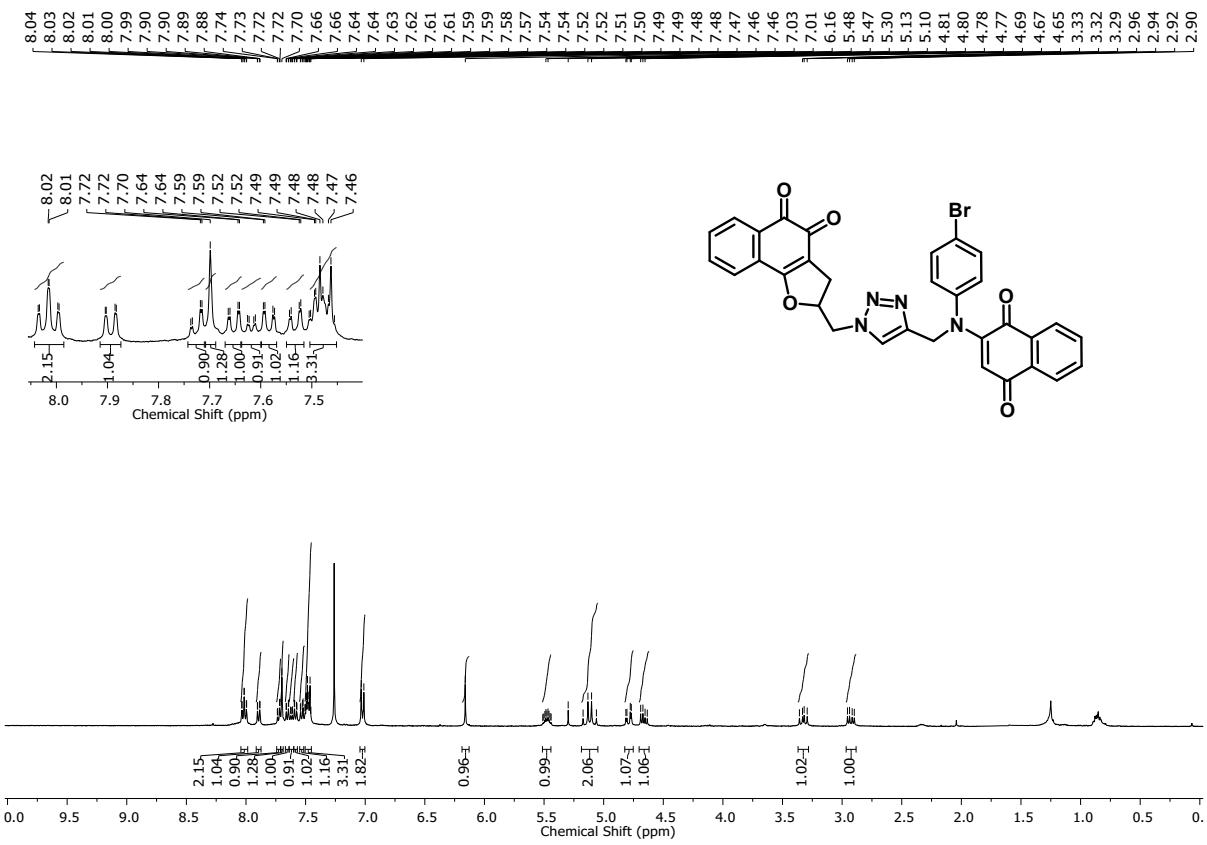


Figure S19. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **10**

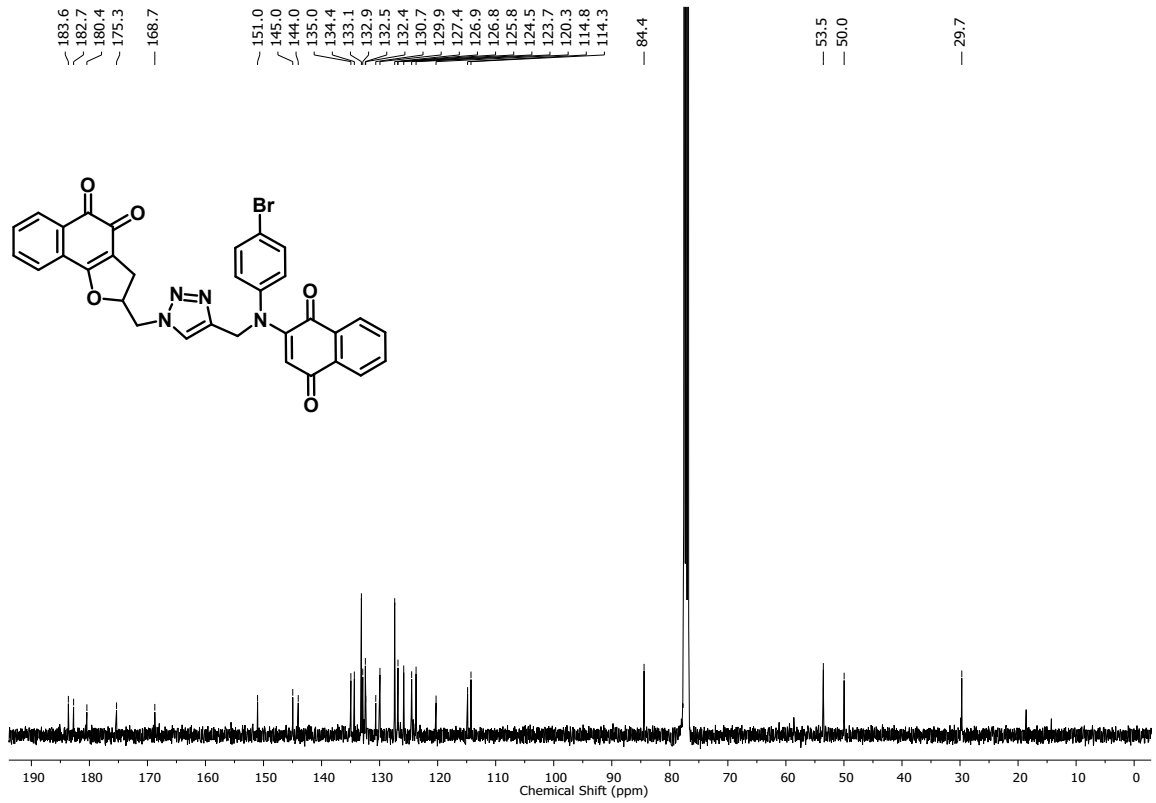


Figure S20. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **10**

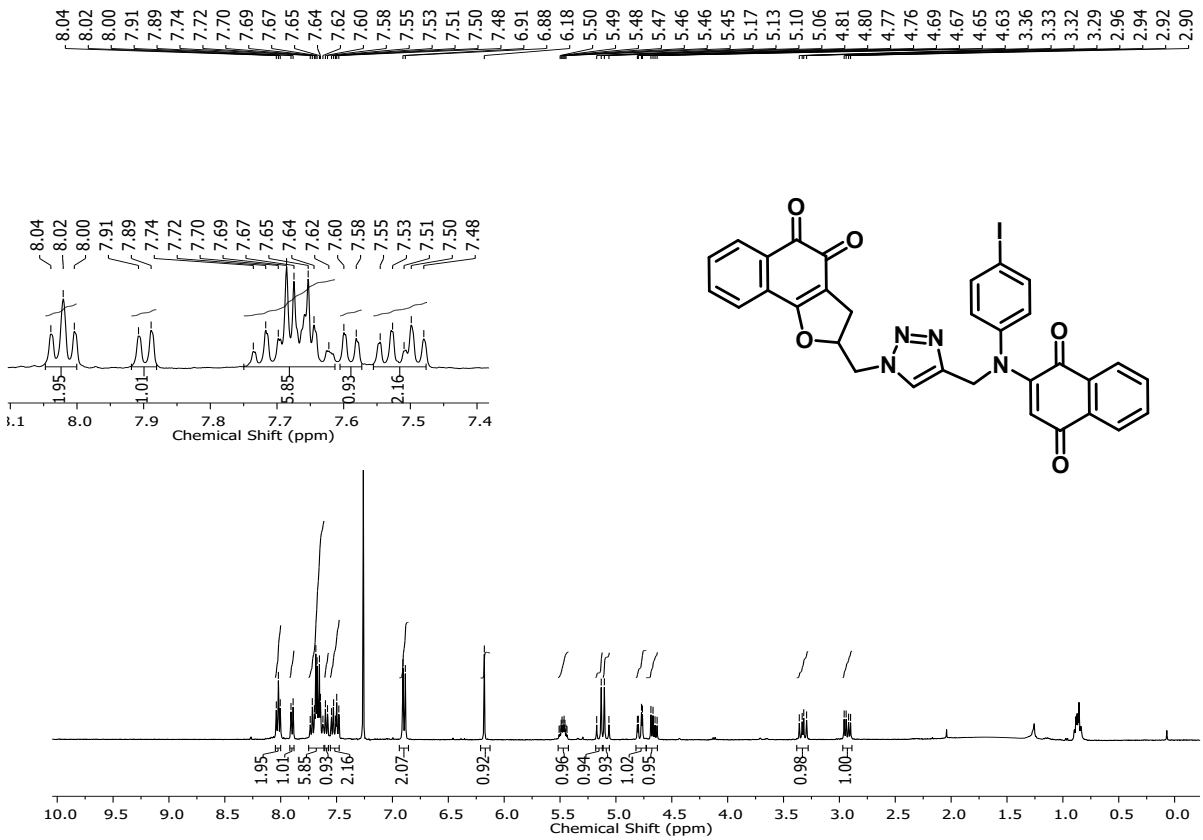


Figure S21. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **11**

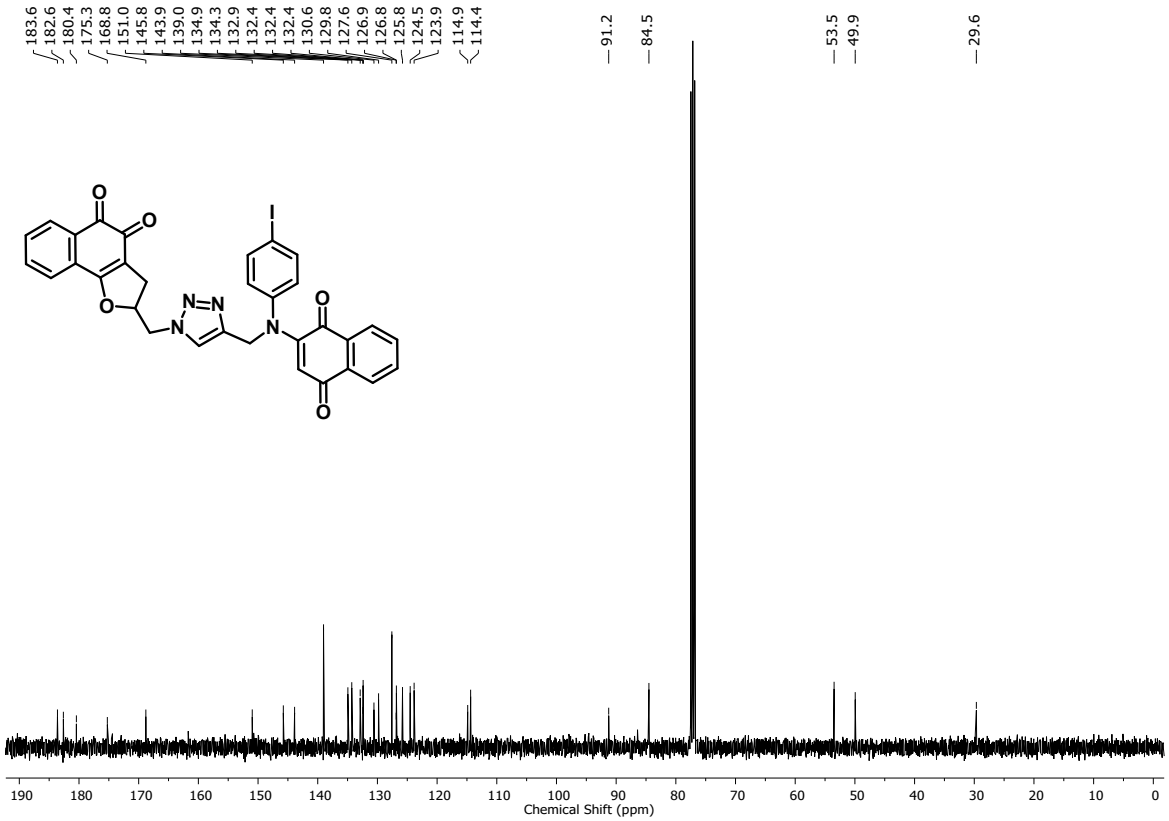


Figure S22. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **11**

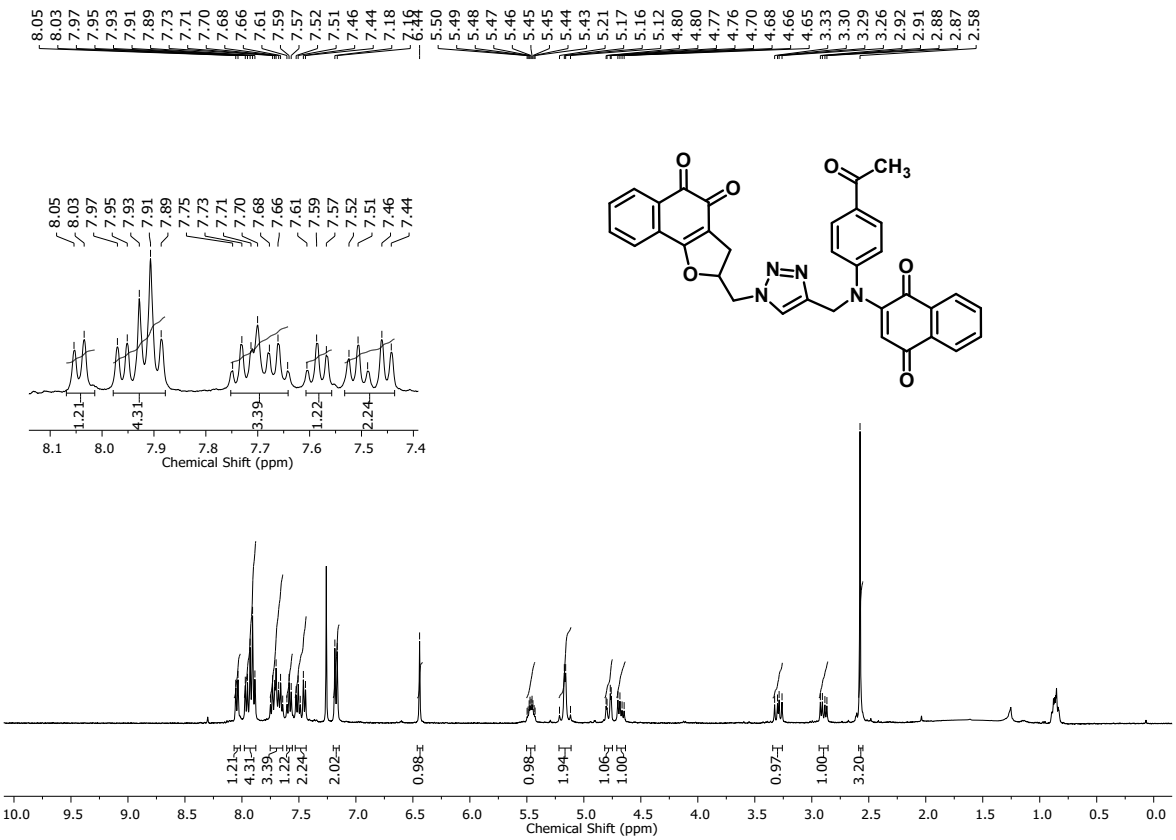


Figure S23. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **12**

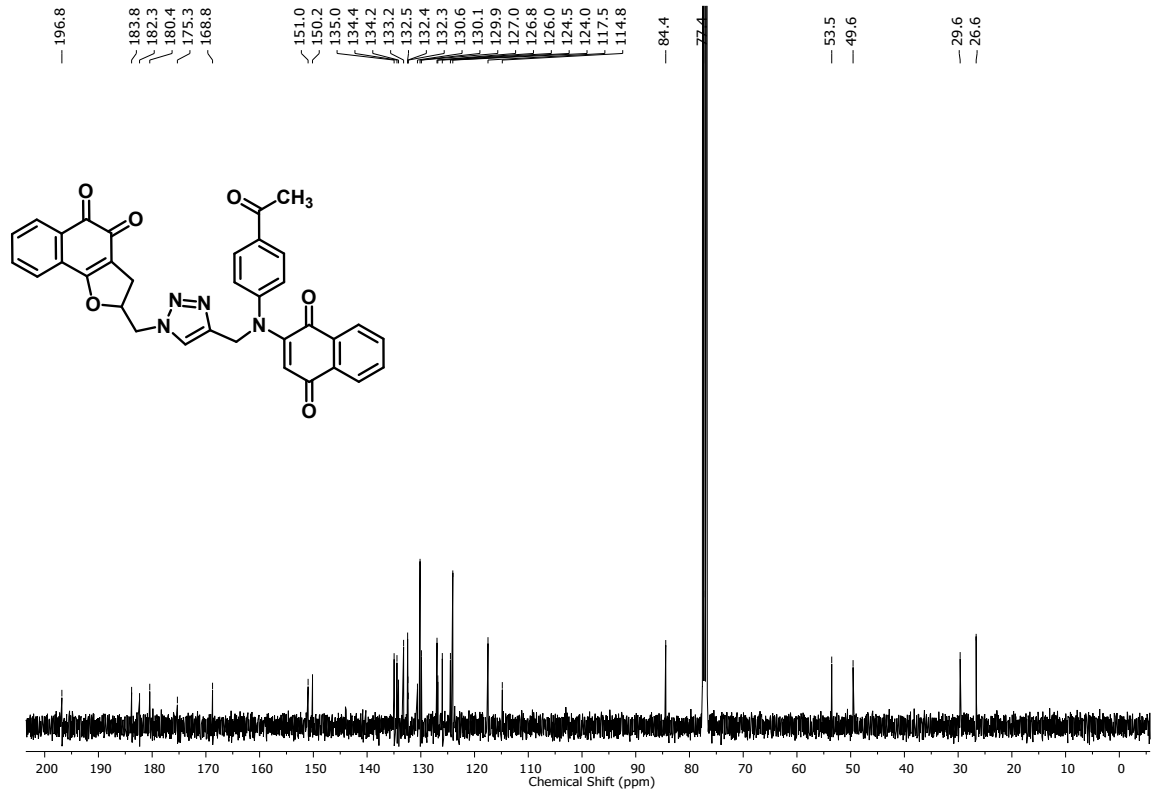


Figure S24. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **12**

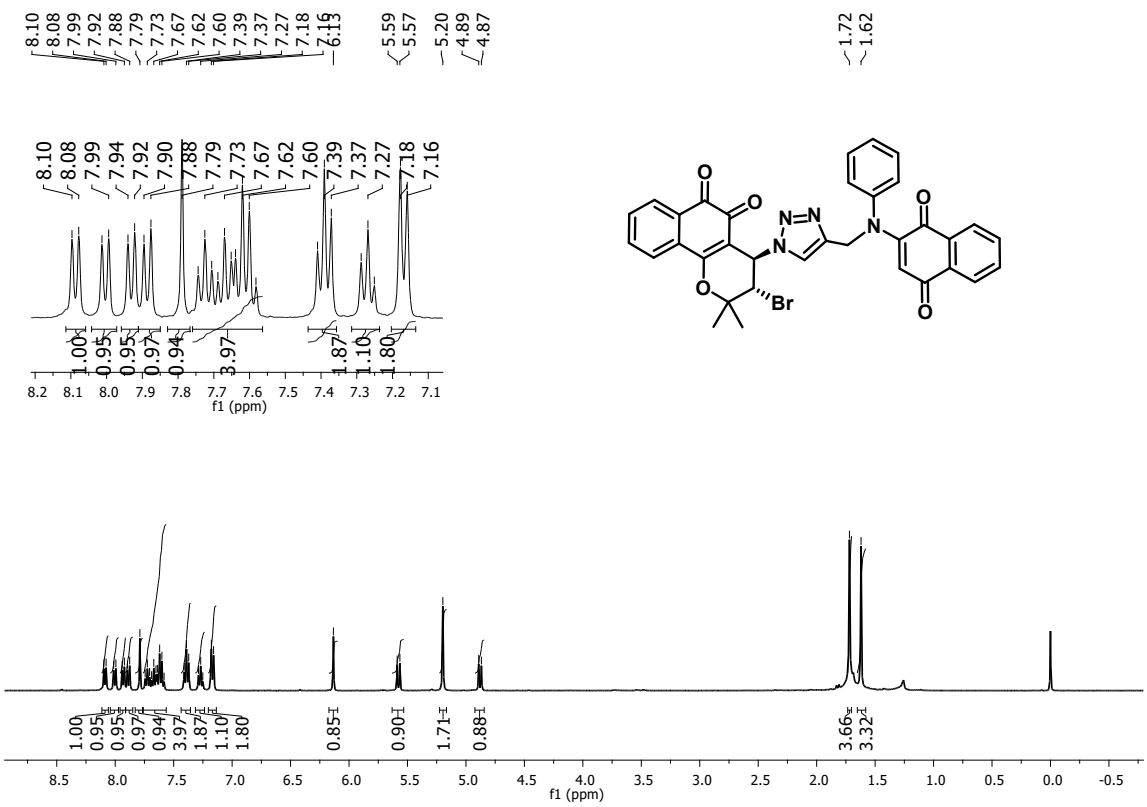


Figure S25. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **13**

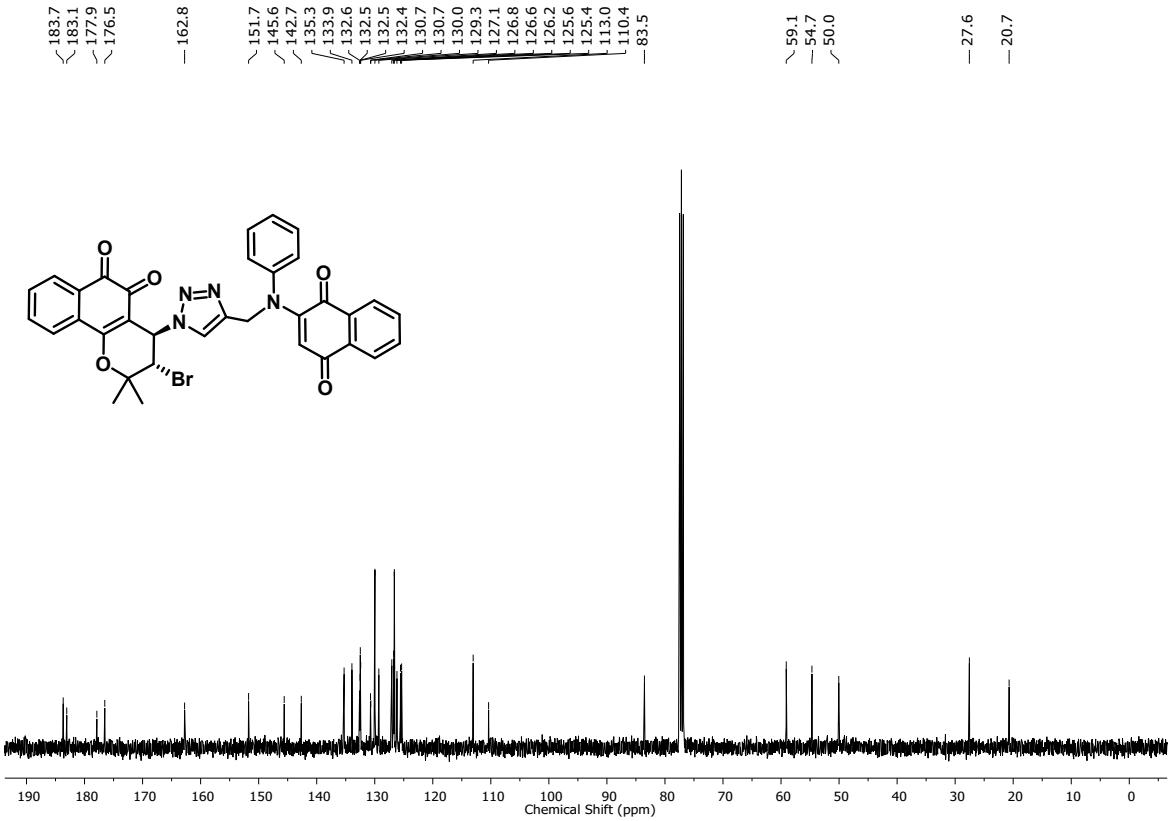


Figure S26. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **13**

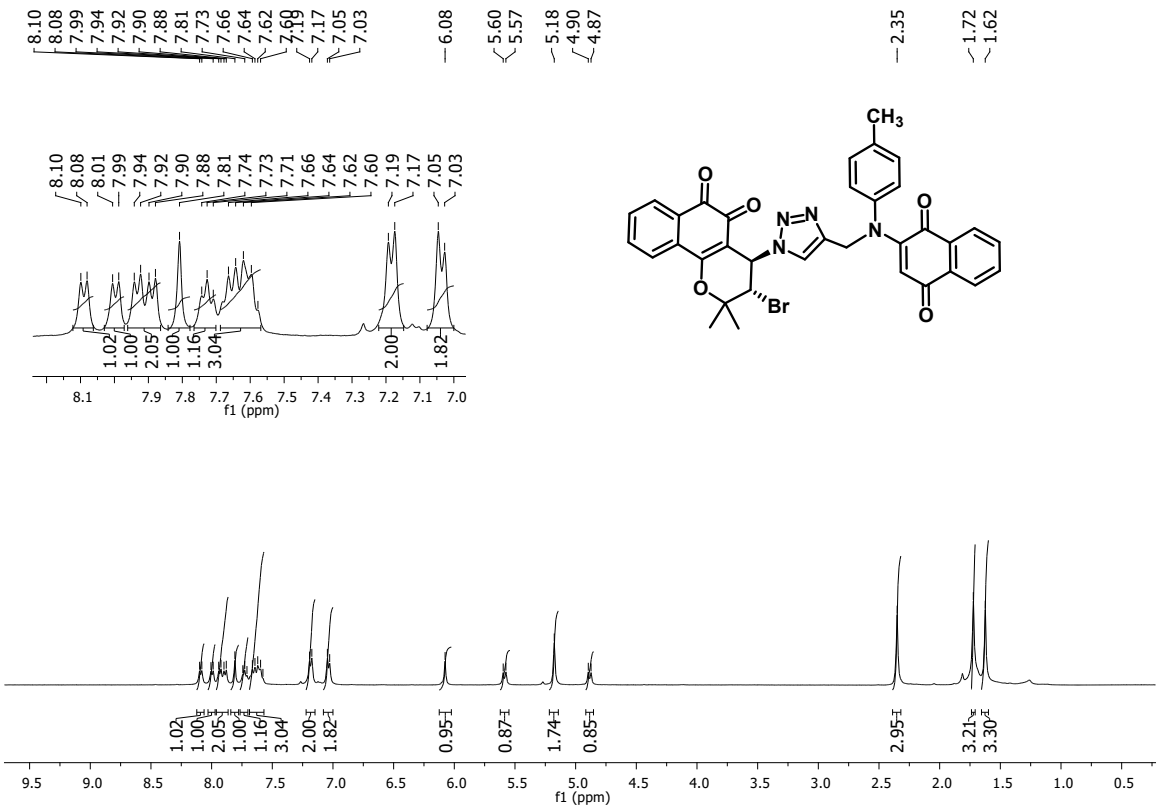


Figure S27. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **14**

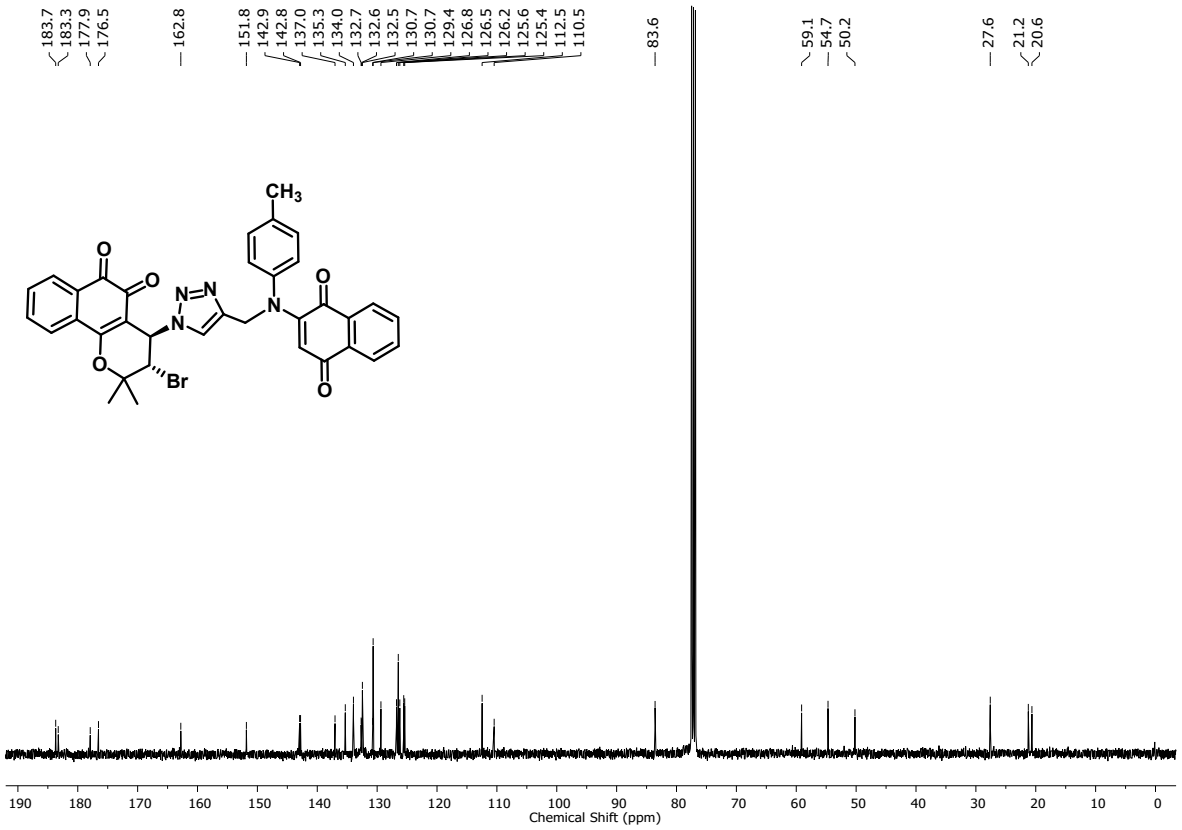


Figure S28. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **14**

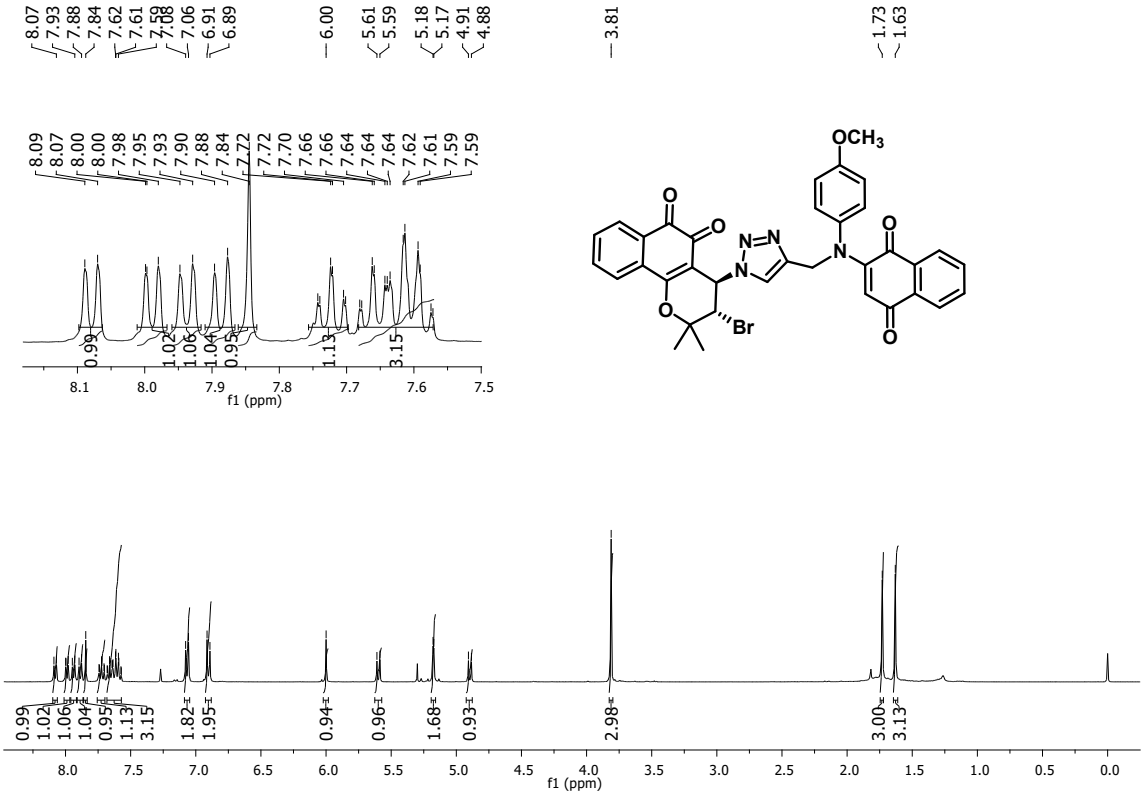


Figure S29. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **15**

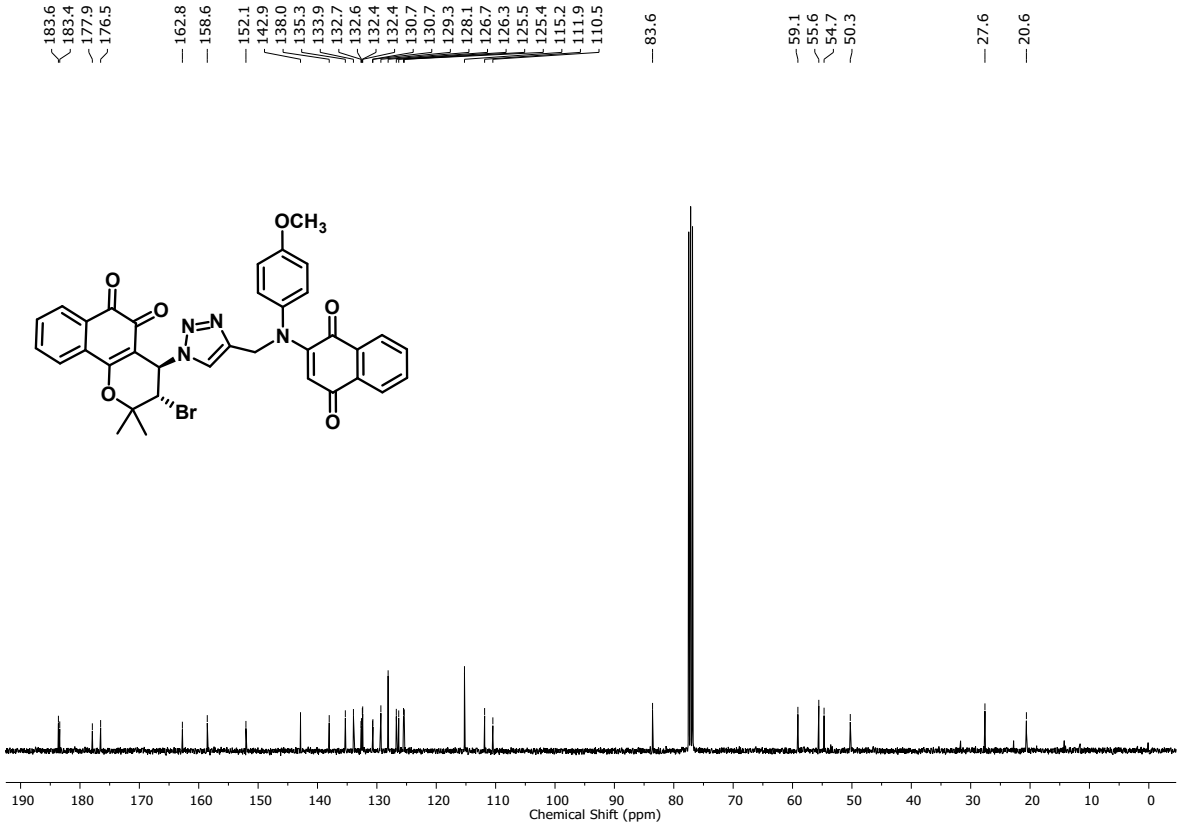


Figure S30. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **15**

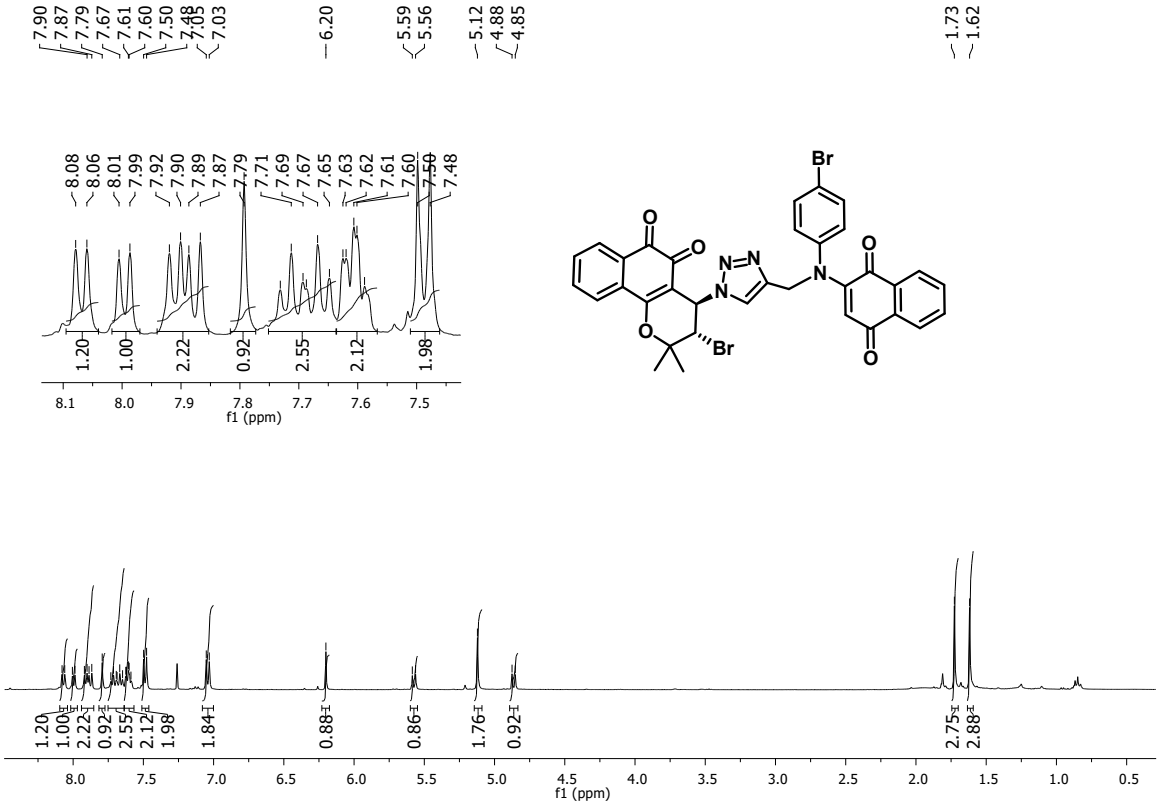


Figure S31. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **16**

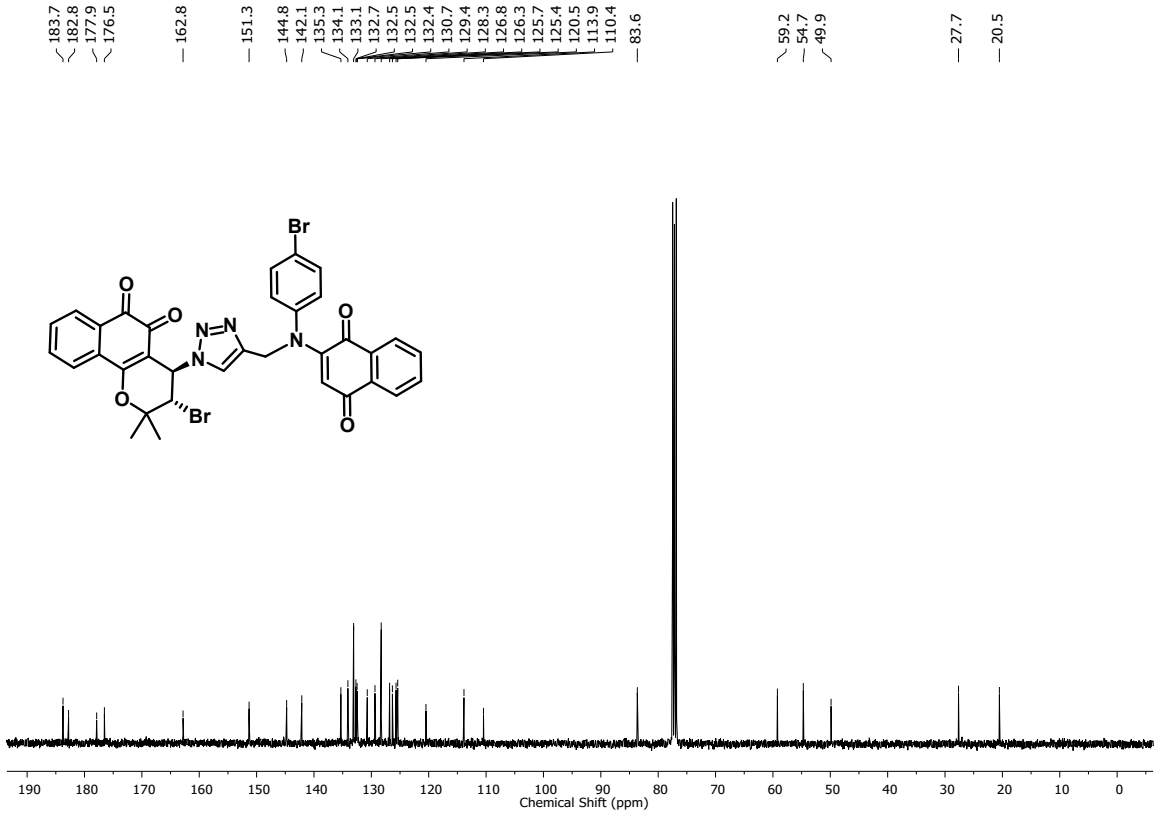


Figure S32. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **16**

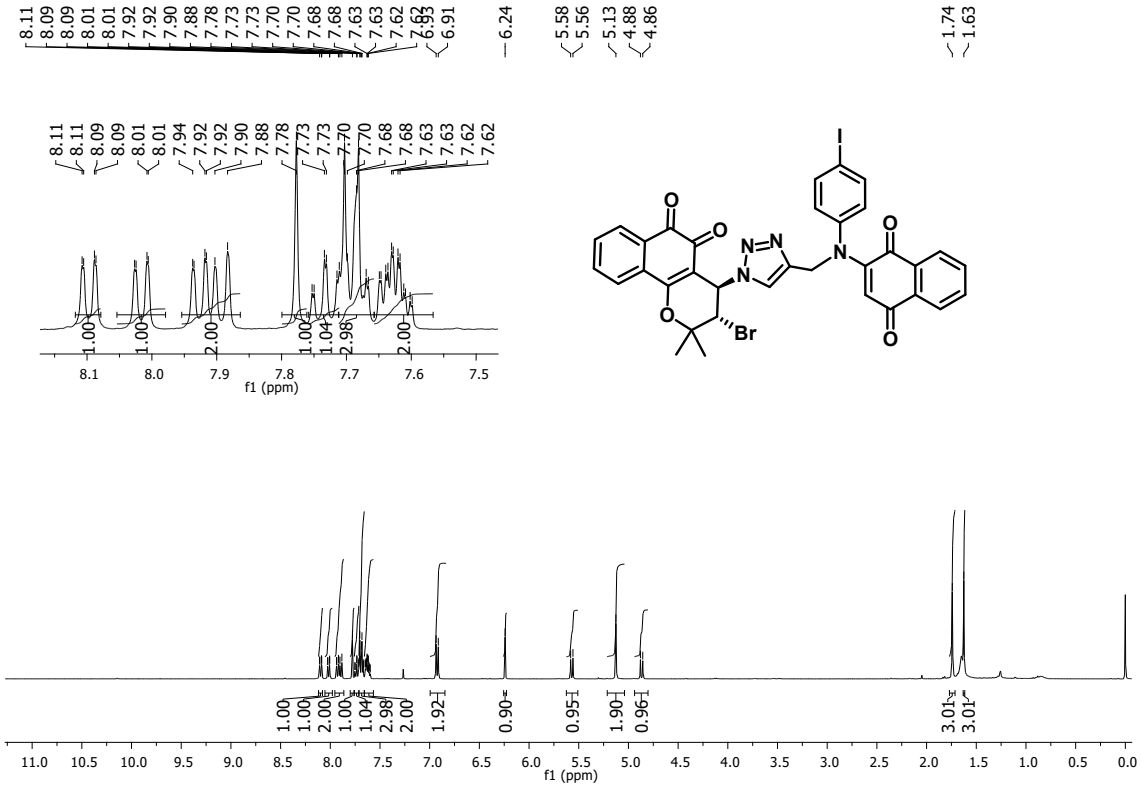


Figure S33. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **17**

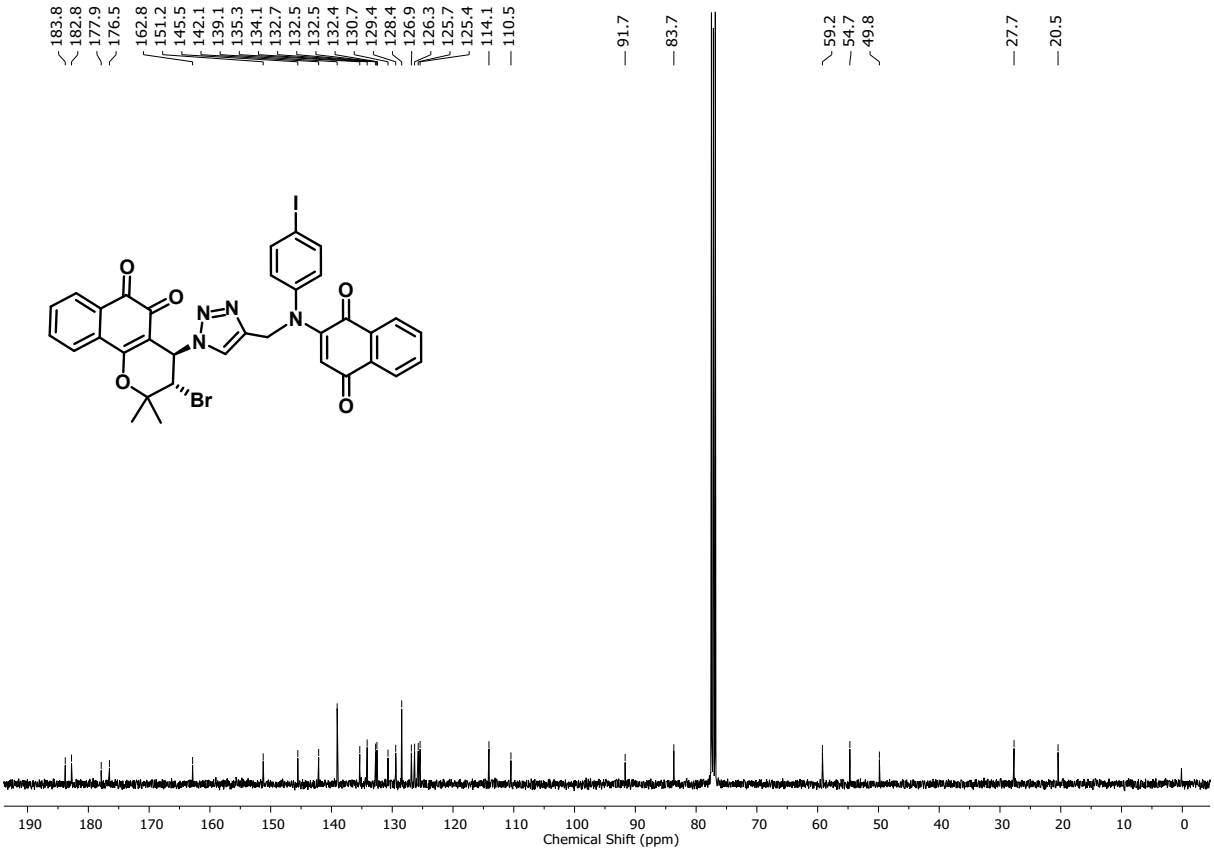


Figure S34. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **17**

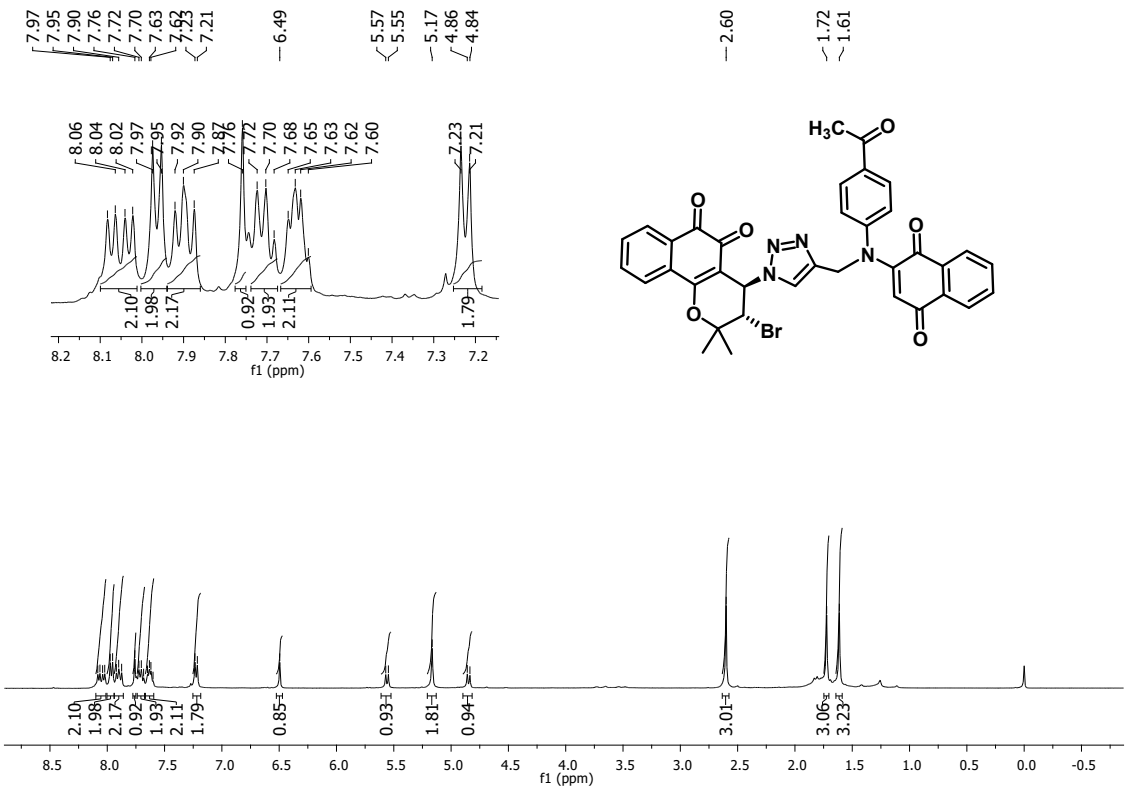


Figure S35. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **18**

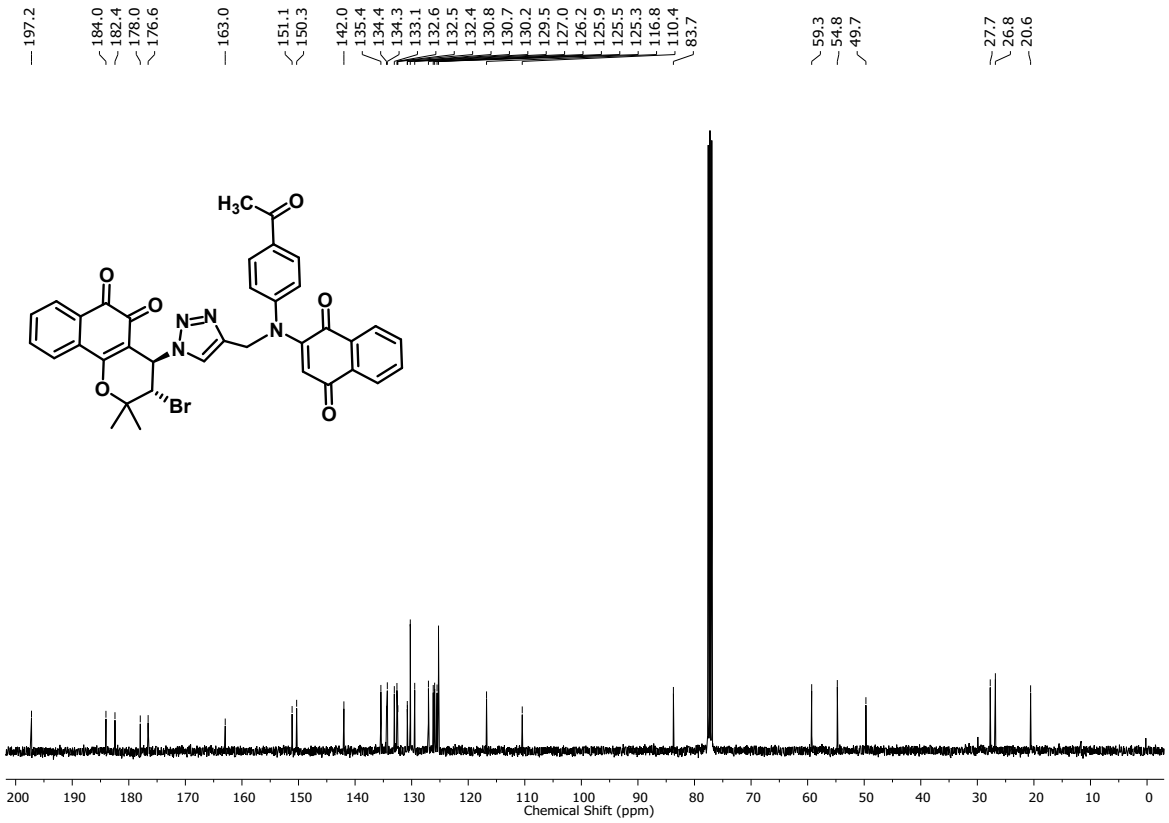


Figure S36. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **18**

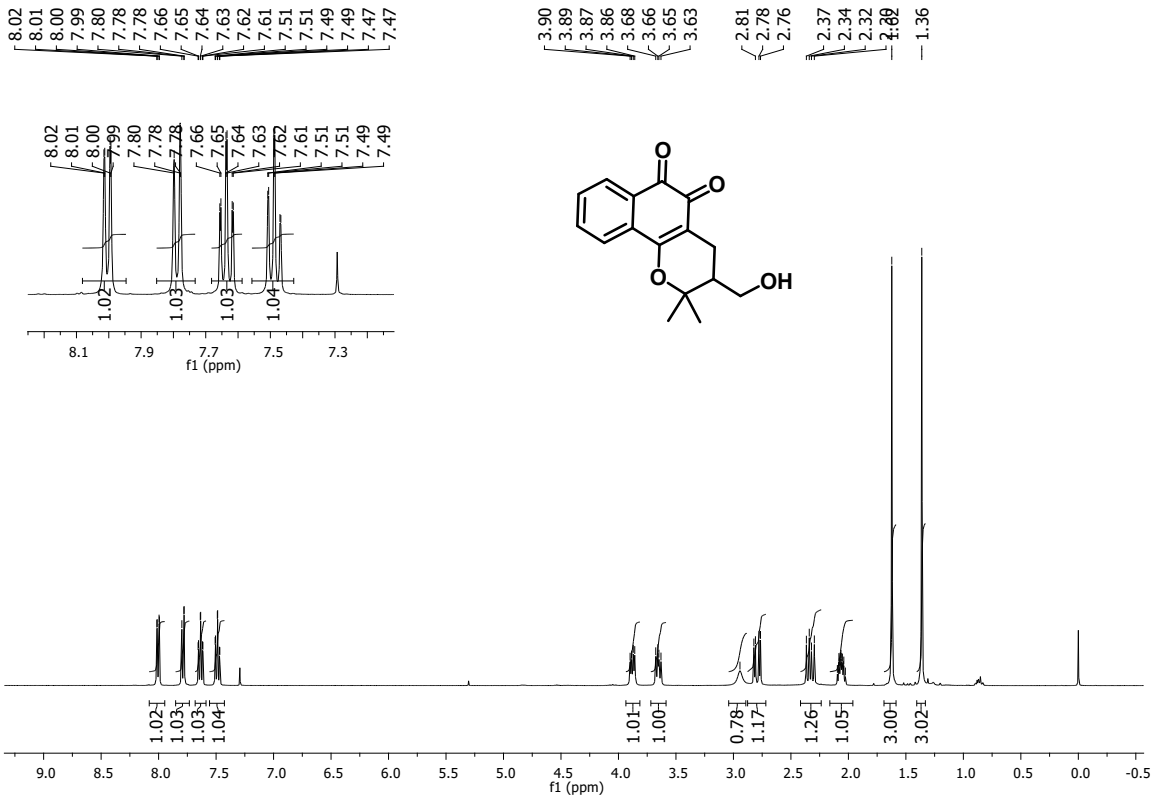


Figure S37. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **19**

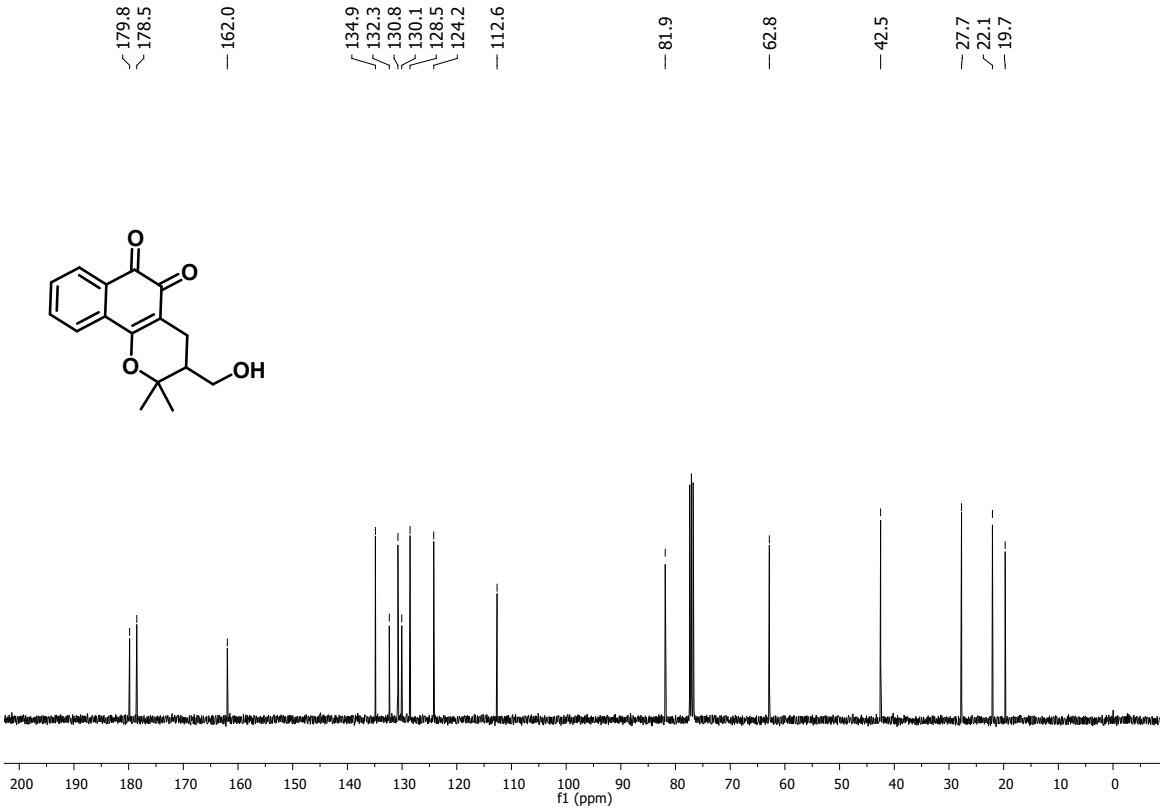


Figure S38. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **19**

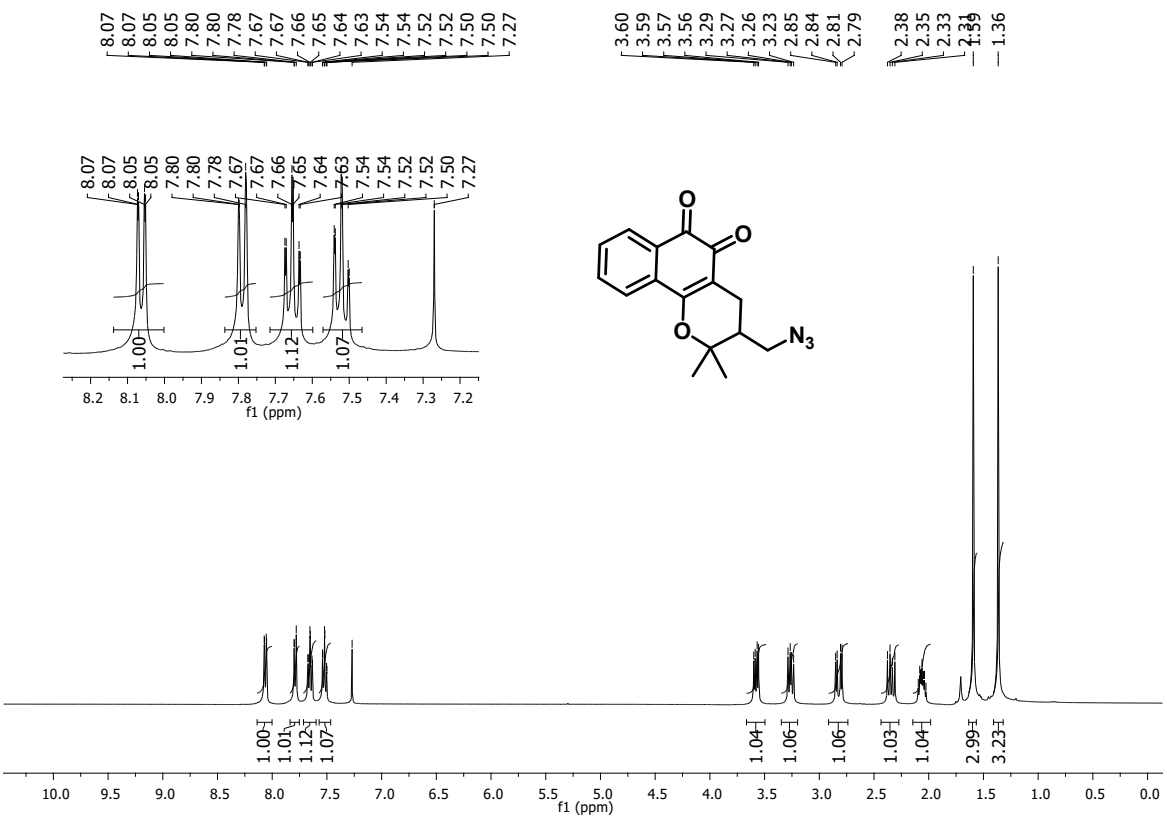


Figure S39. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **20**

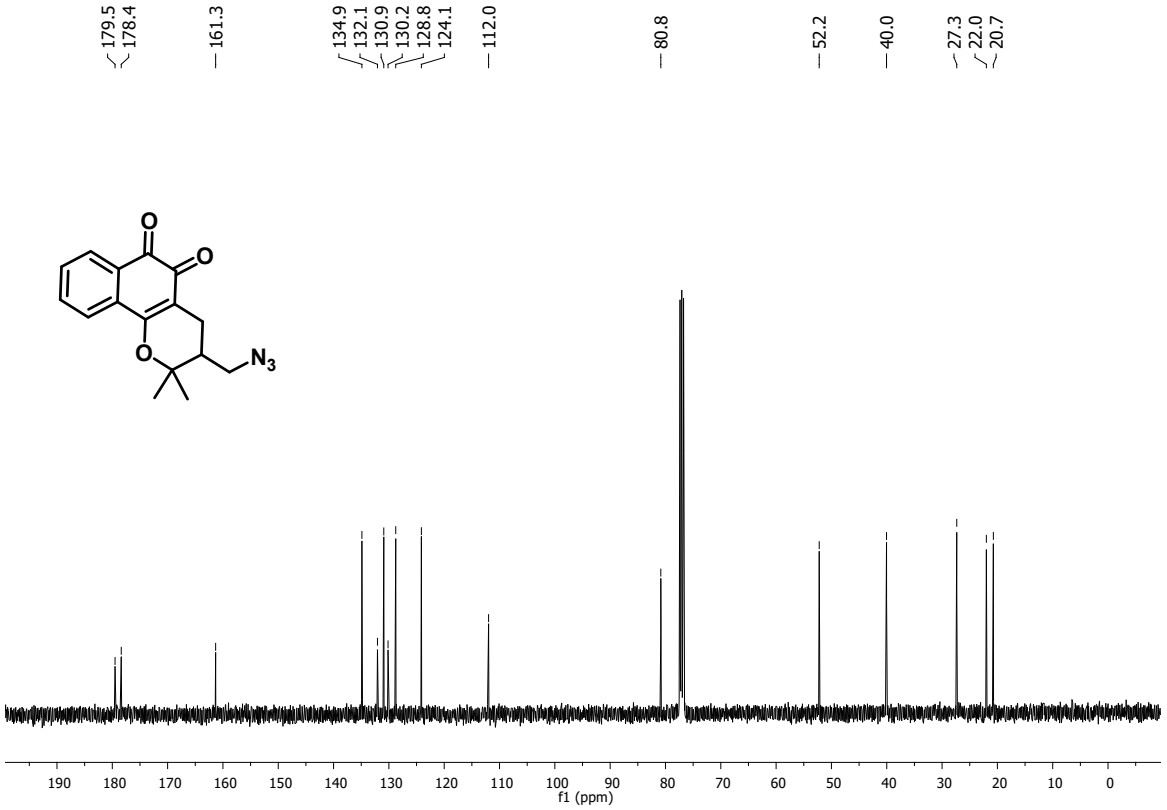


Figure S40. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **20**

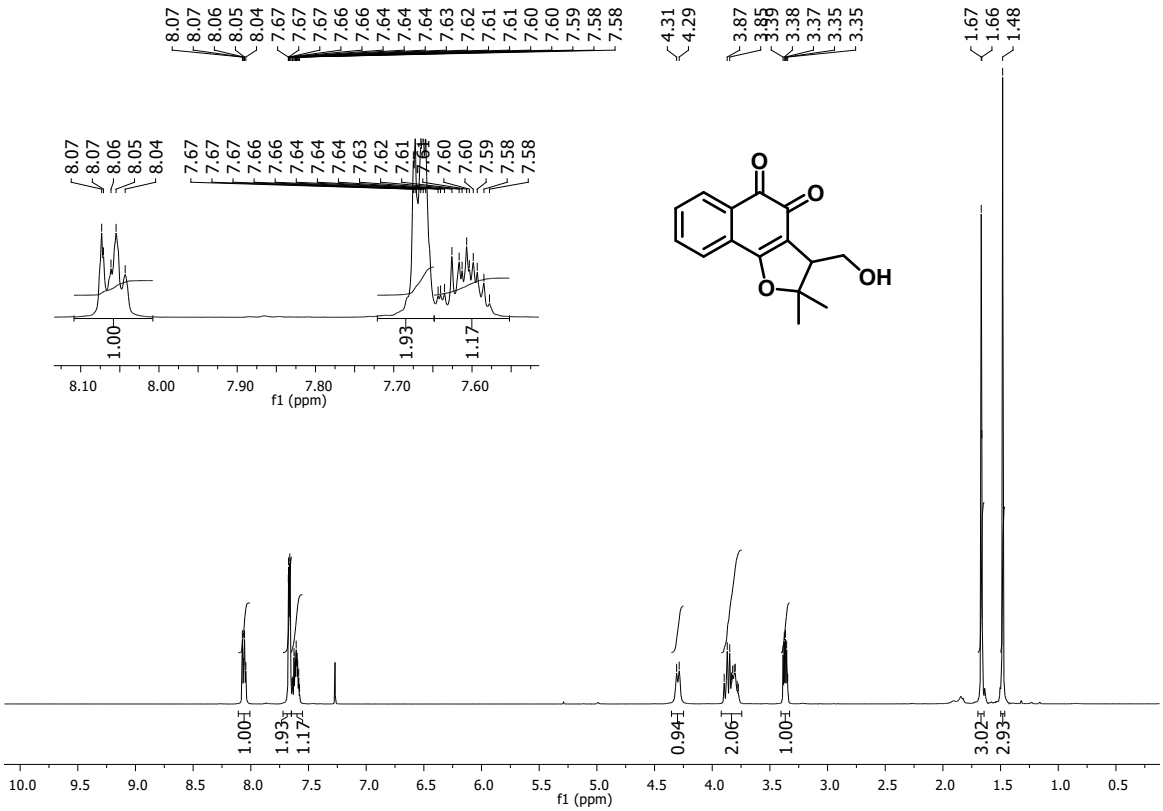


Figure S41. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **29**

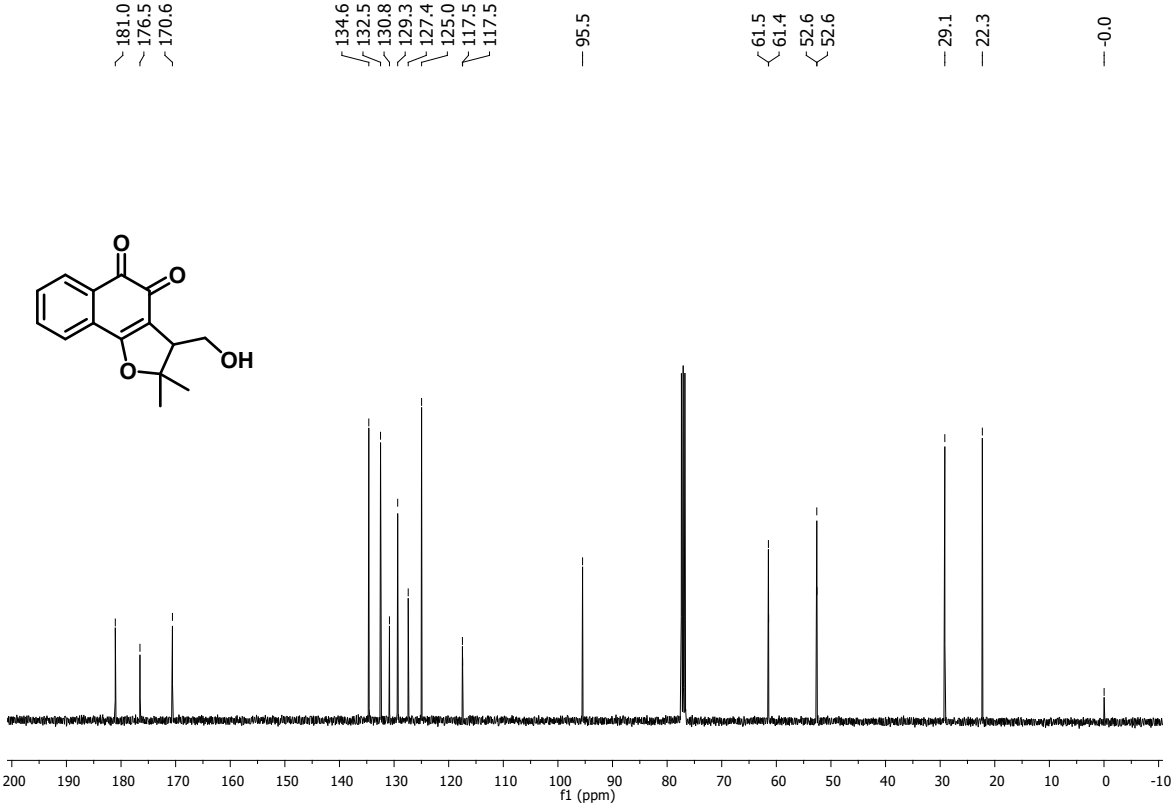


Figure S42. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **29**

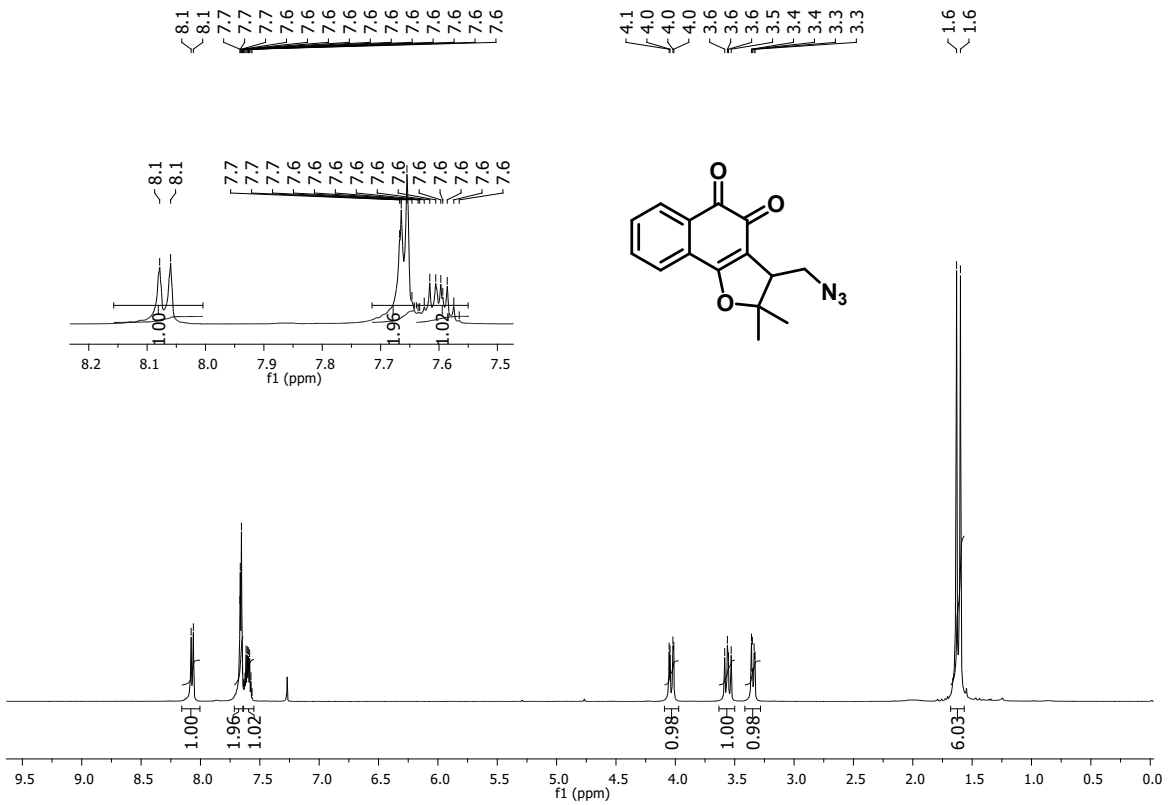


Figure S43. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **30**

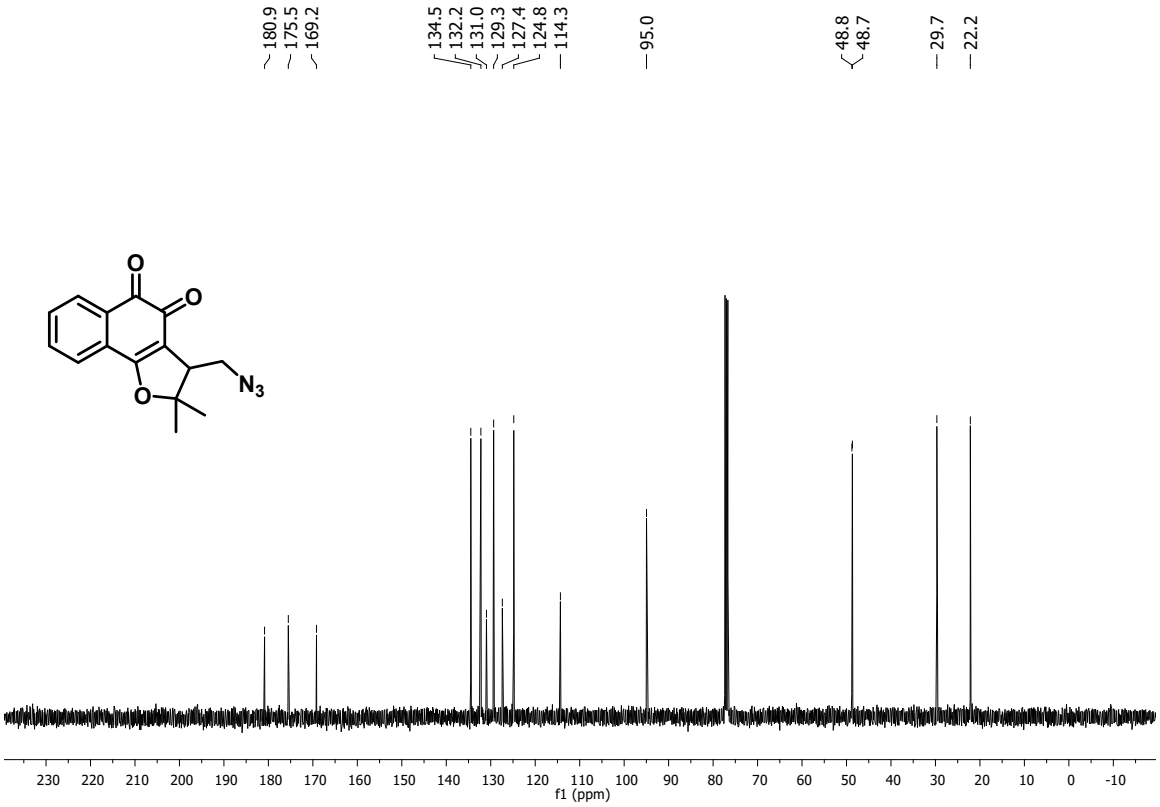


Figure S44. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **30**

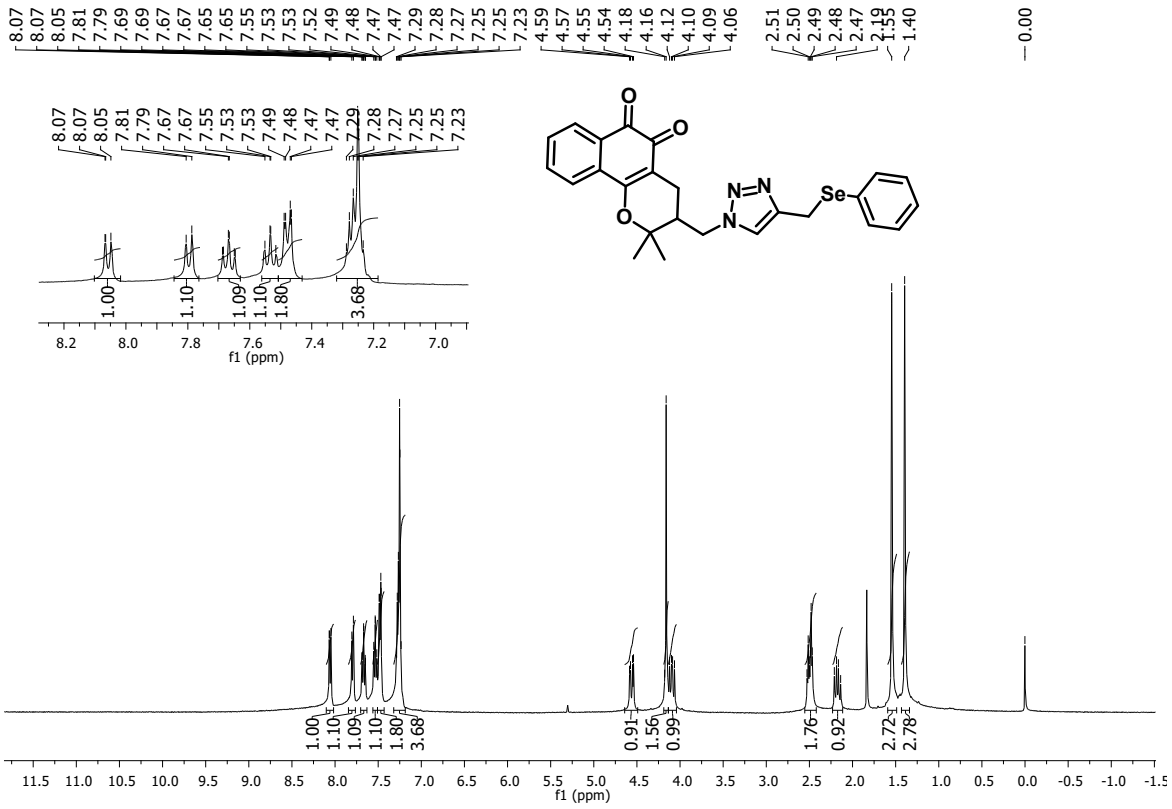


Figure S45. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **21**

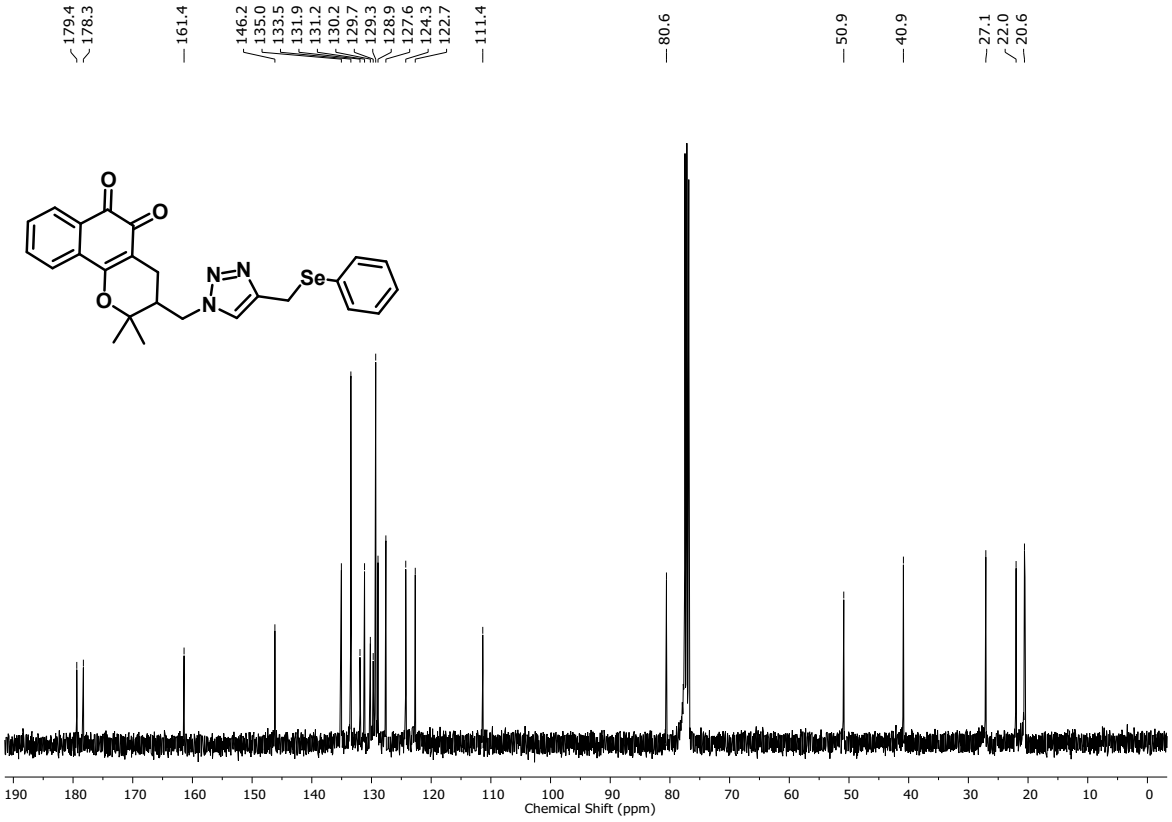


Figure S46. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **21**

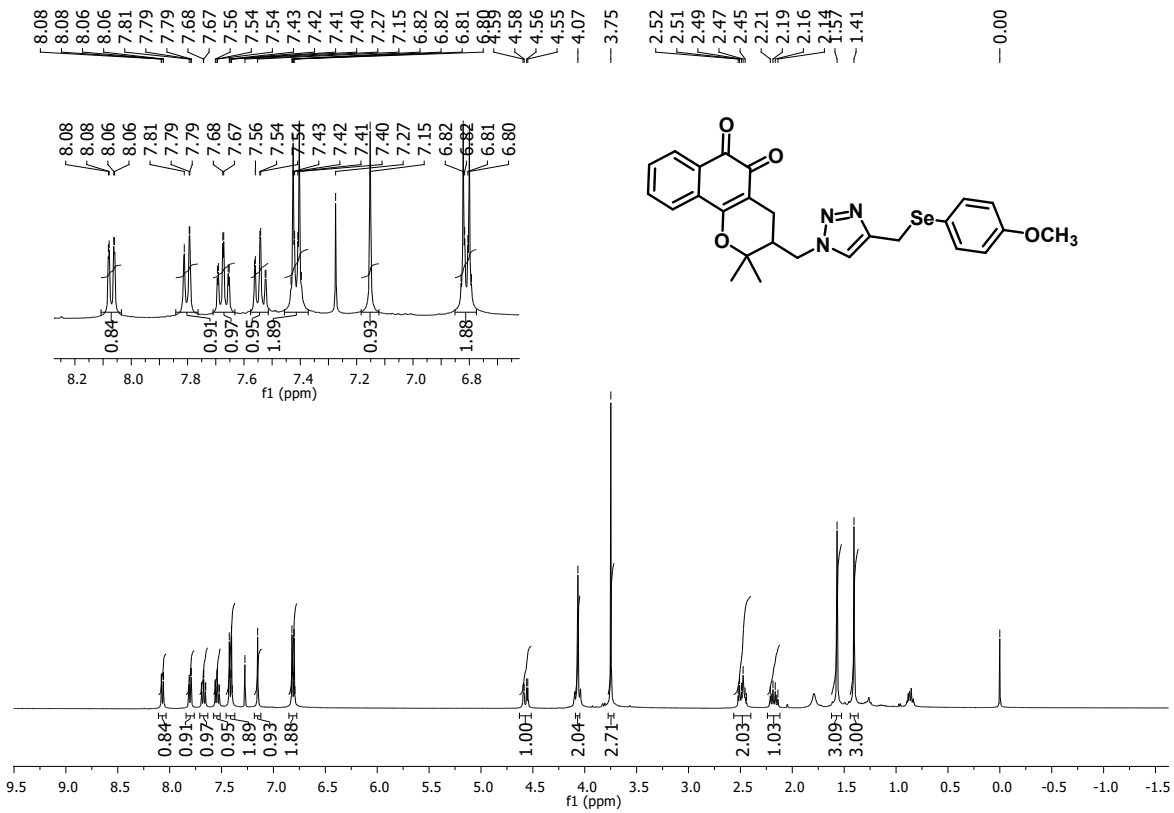


Figure S47. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **22**

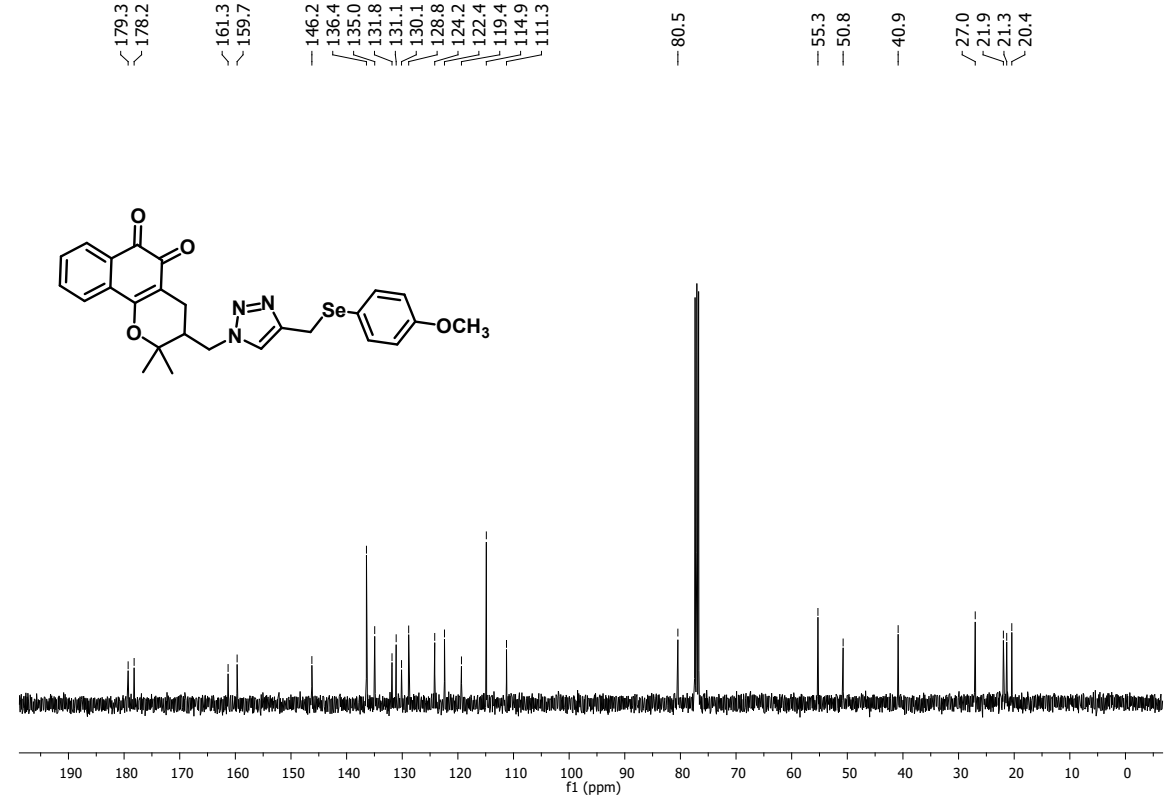


Figure S48. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **22**

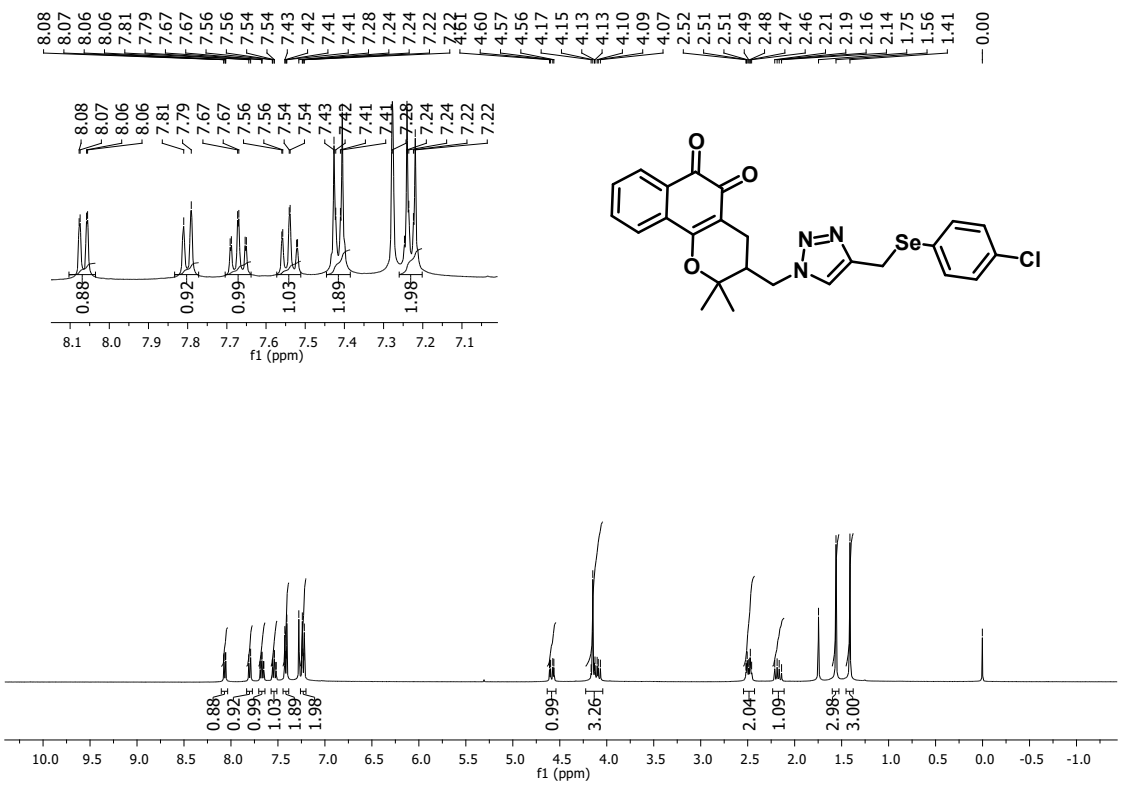


Figure S49. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **23**

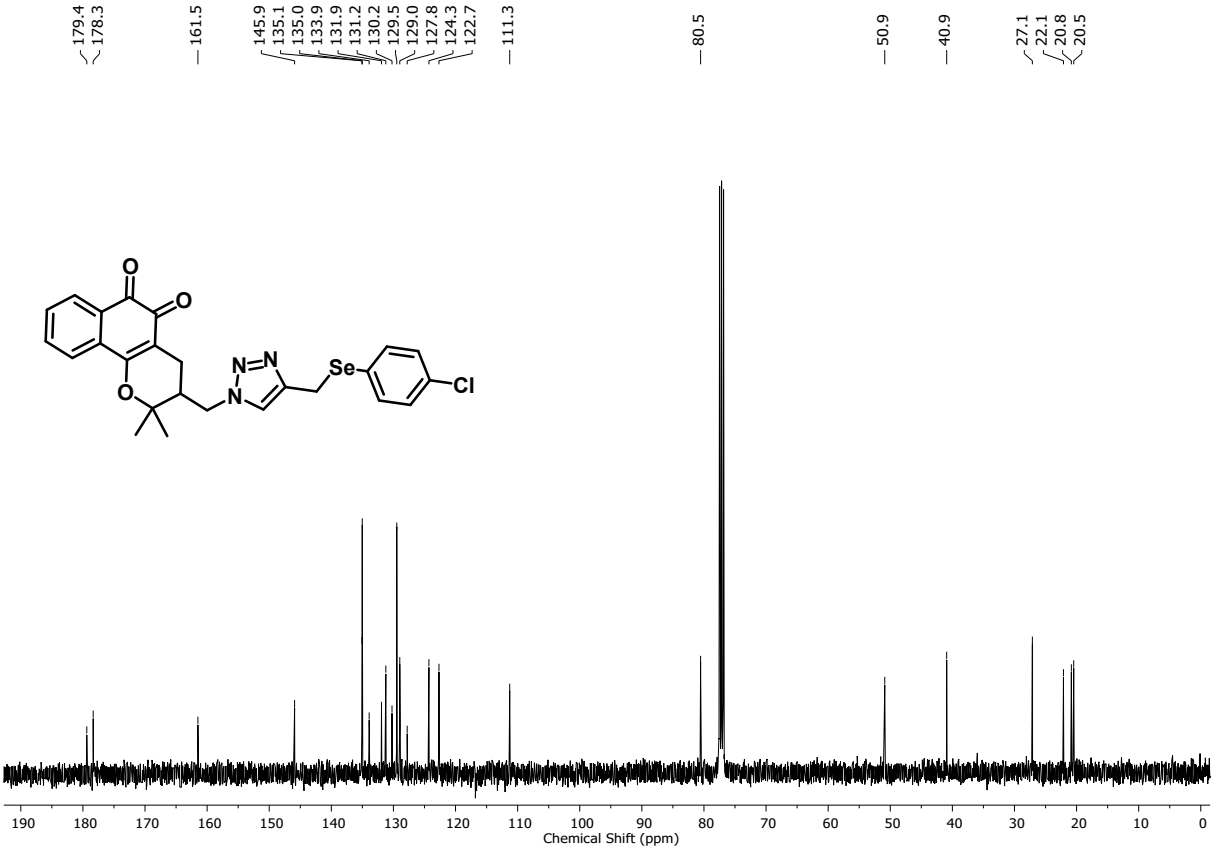


Figure S50. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **23**

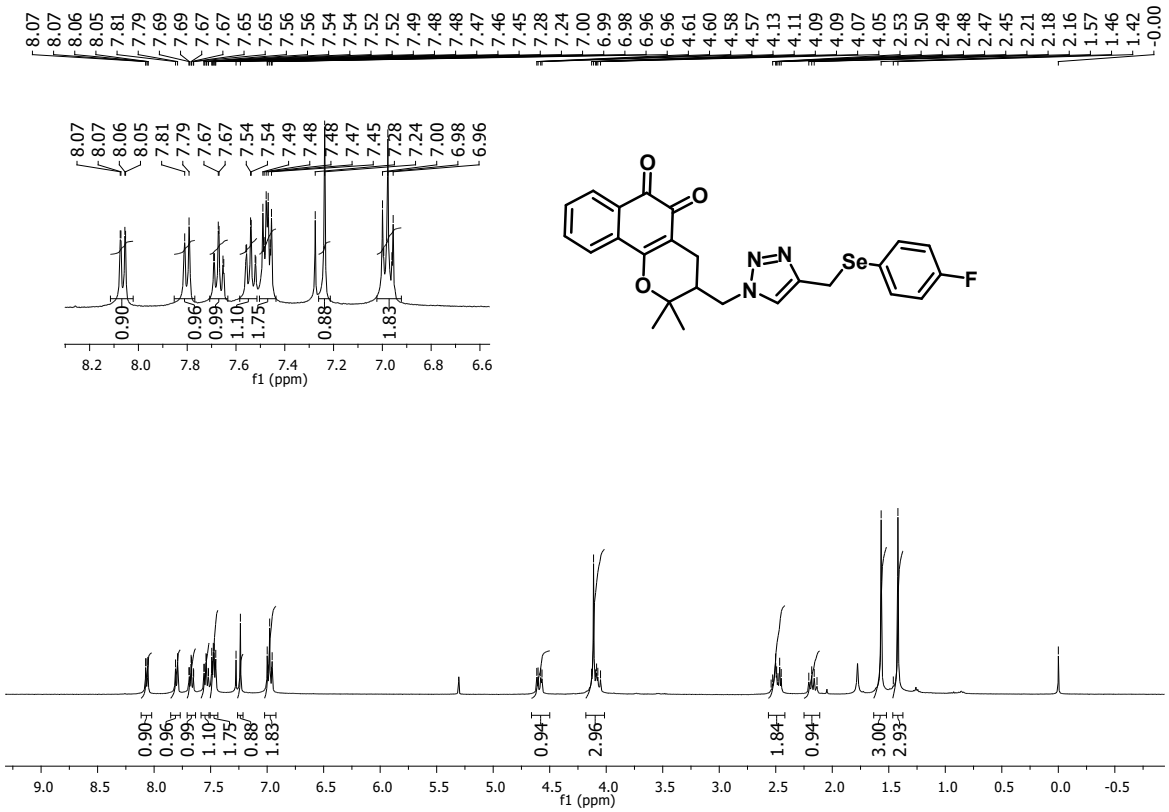


Figure S51. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **24**

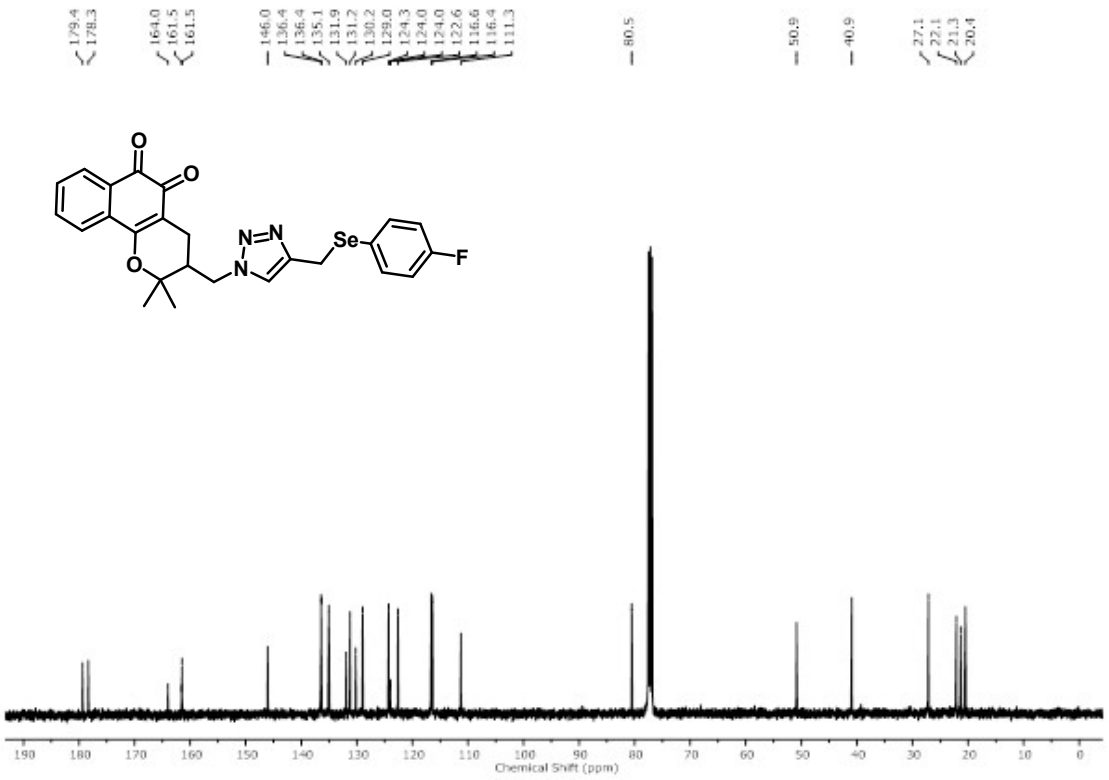


Figure S52. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **24**

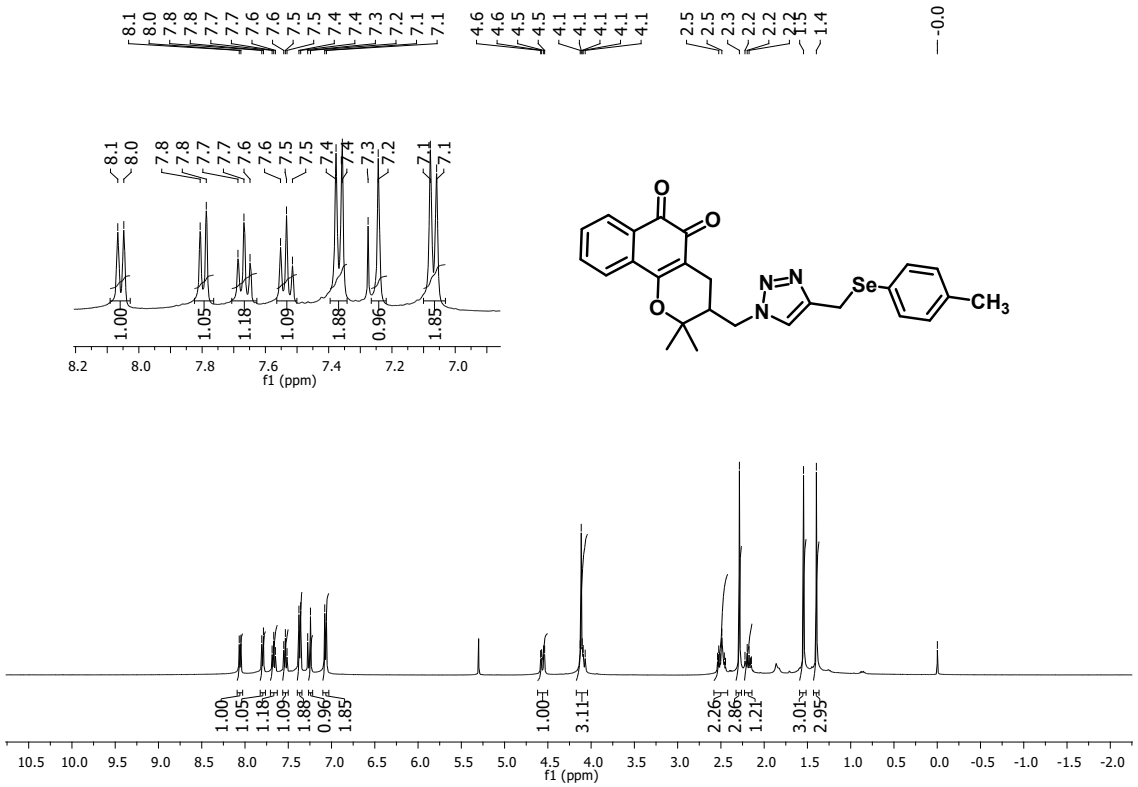


Figure S53. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **25**

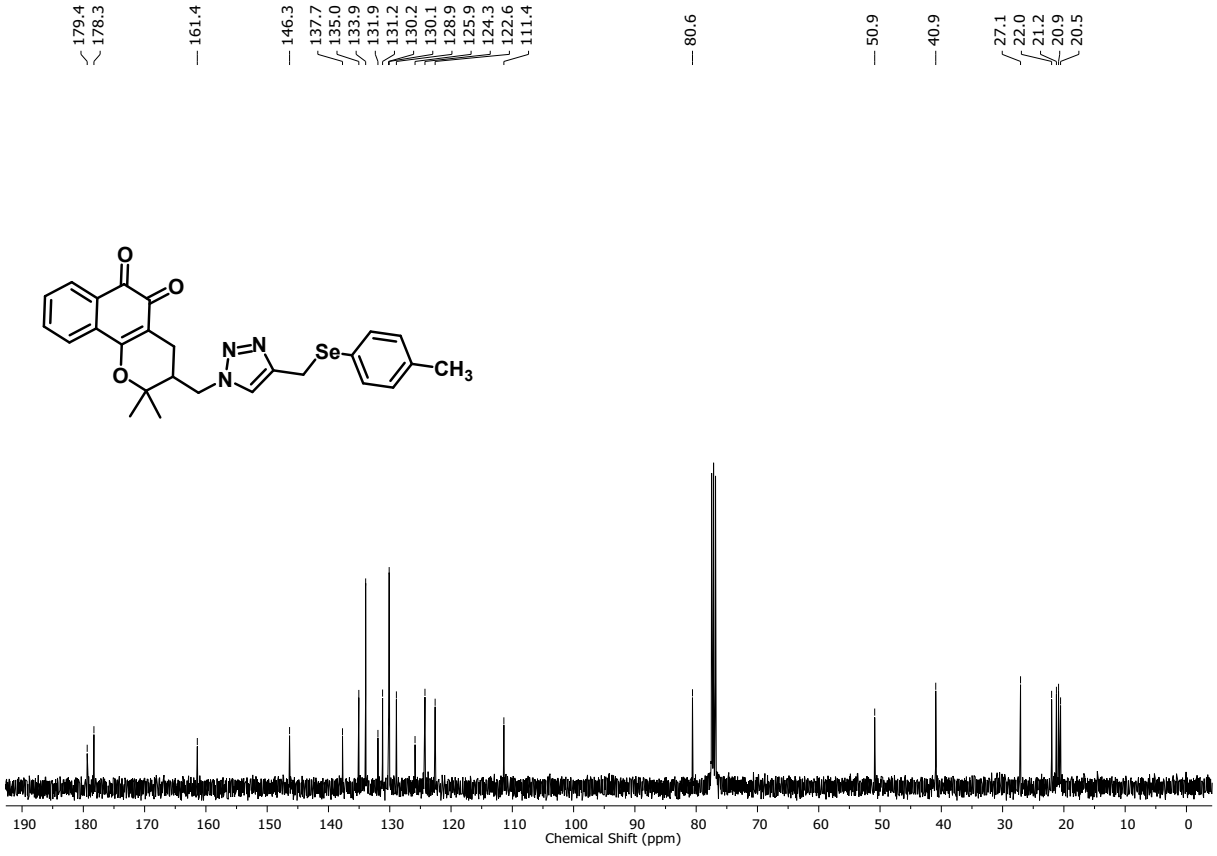


Figure S54. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **25**

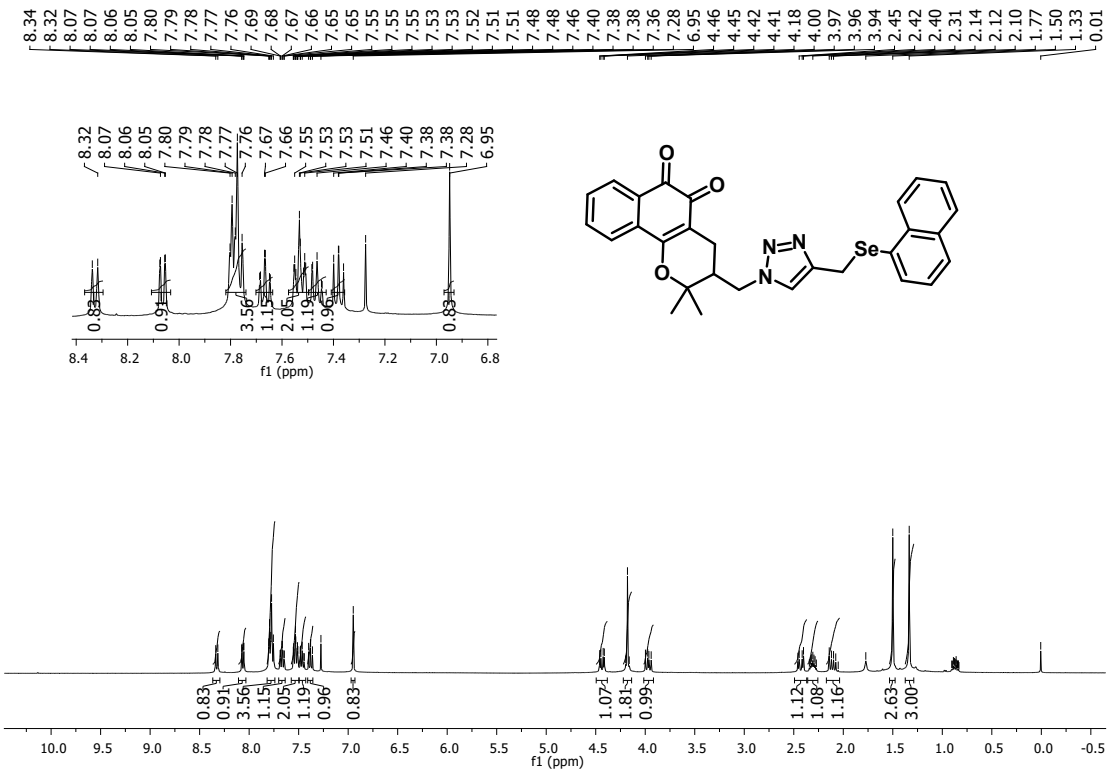


Figure S55. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **26**

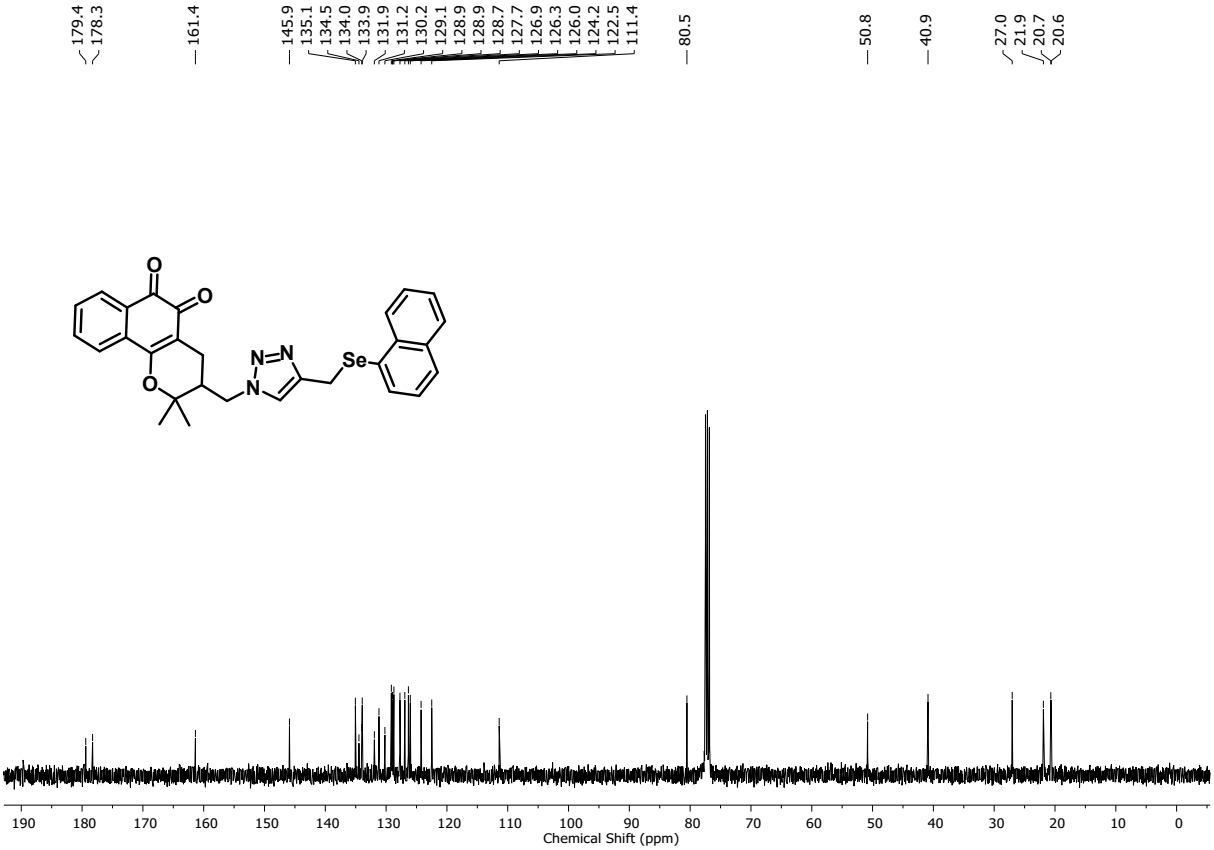


Figure S56. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **26**

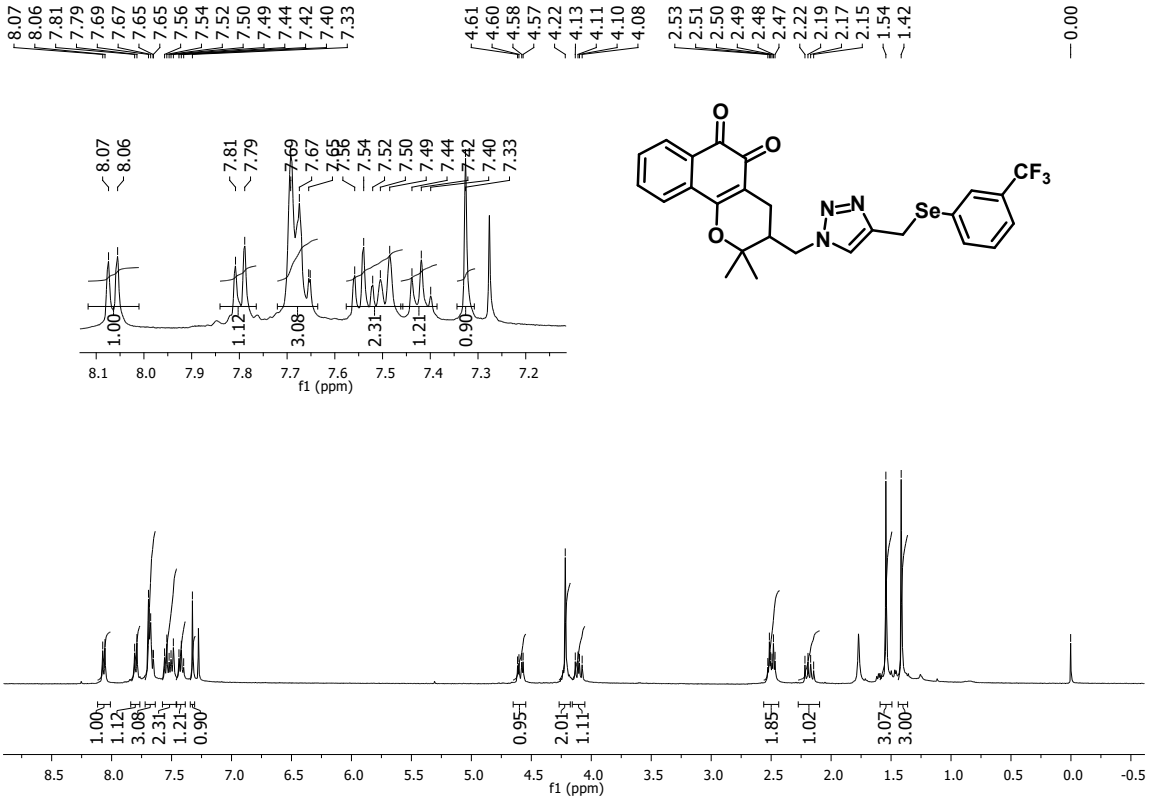


Figure S57. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **27**

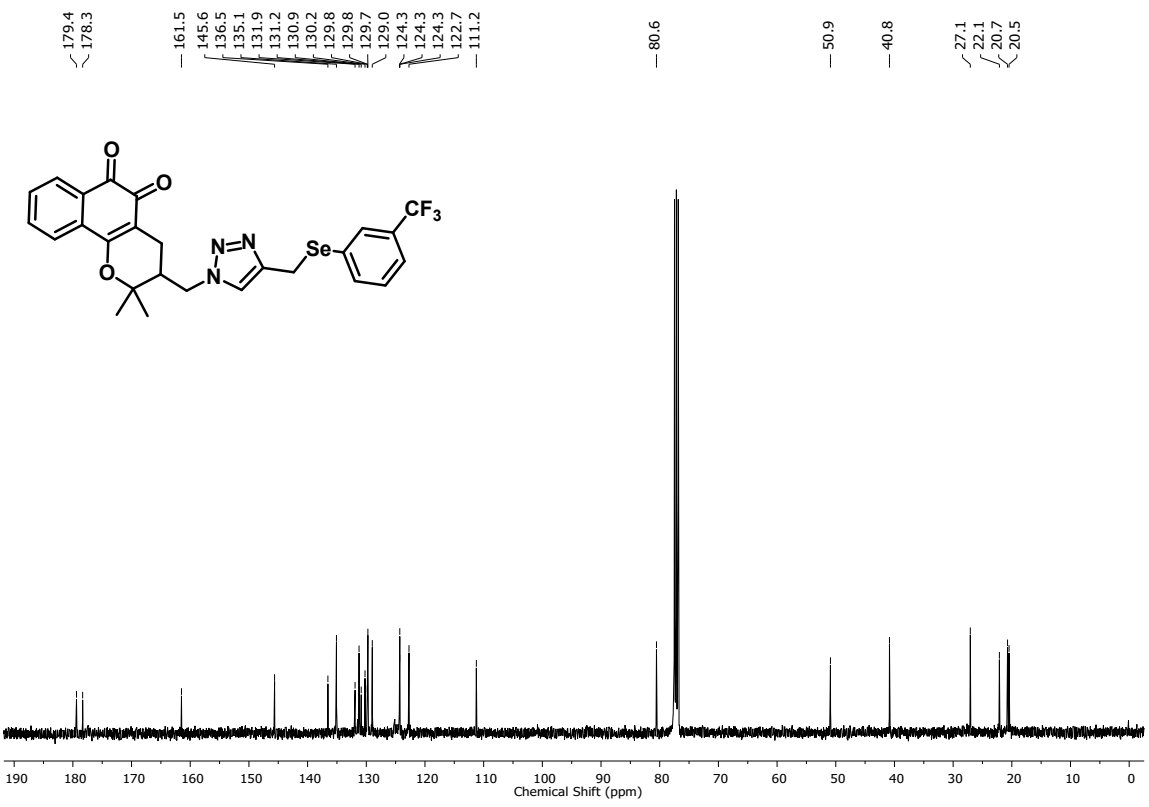


Figure S58. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **27**

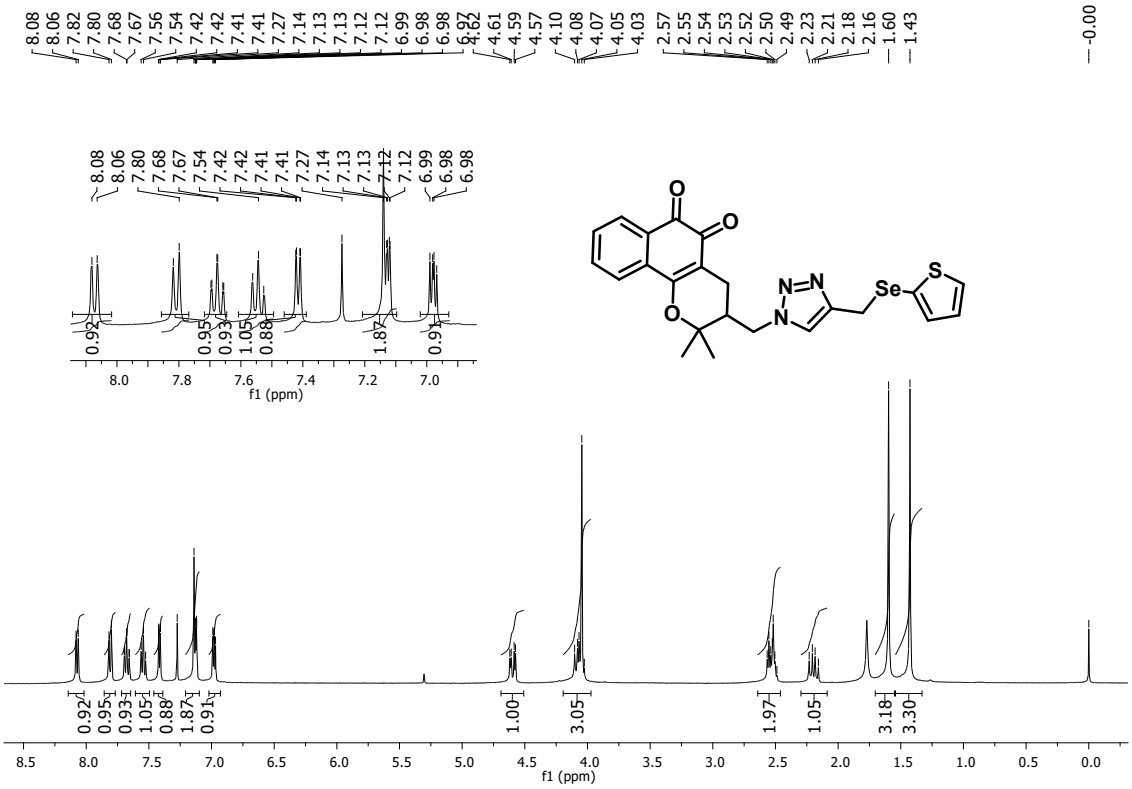


Figure S59. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **28**

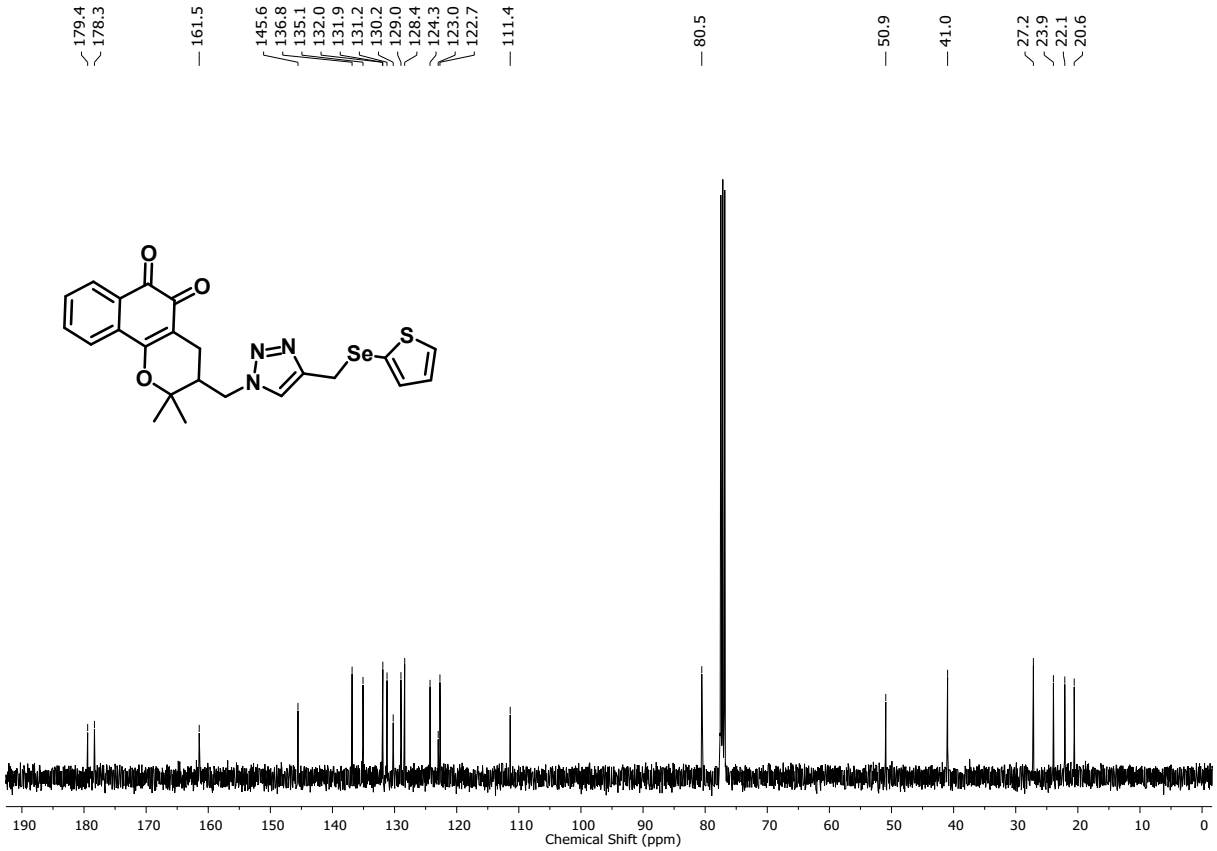


Figure S60. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **28**

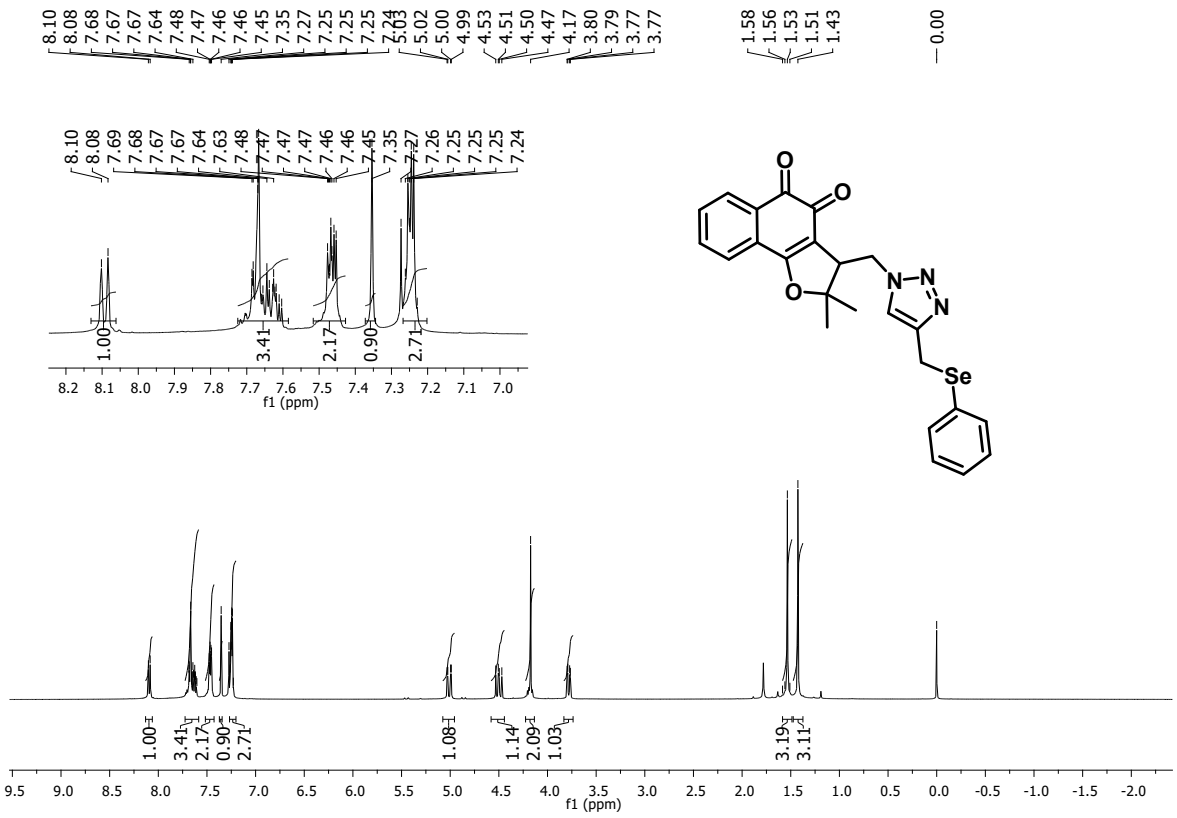


Figure S61. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **31**

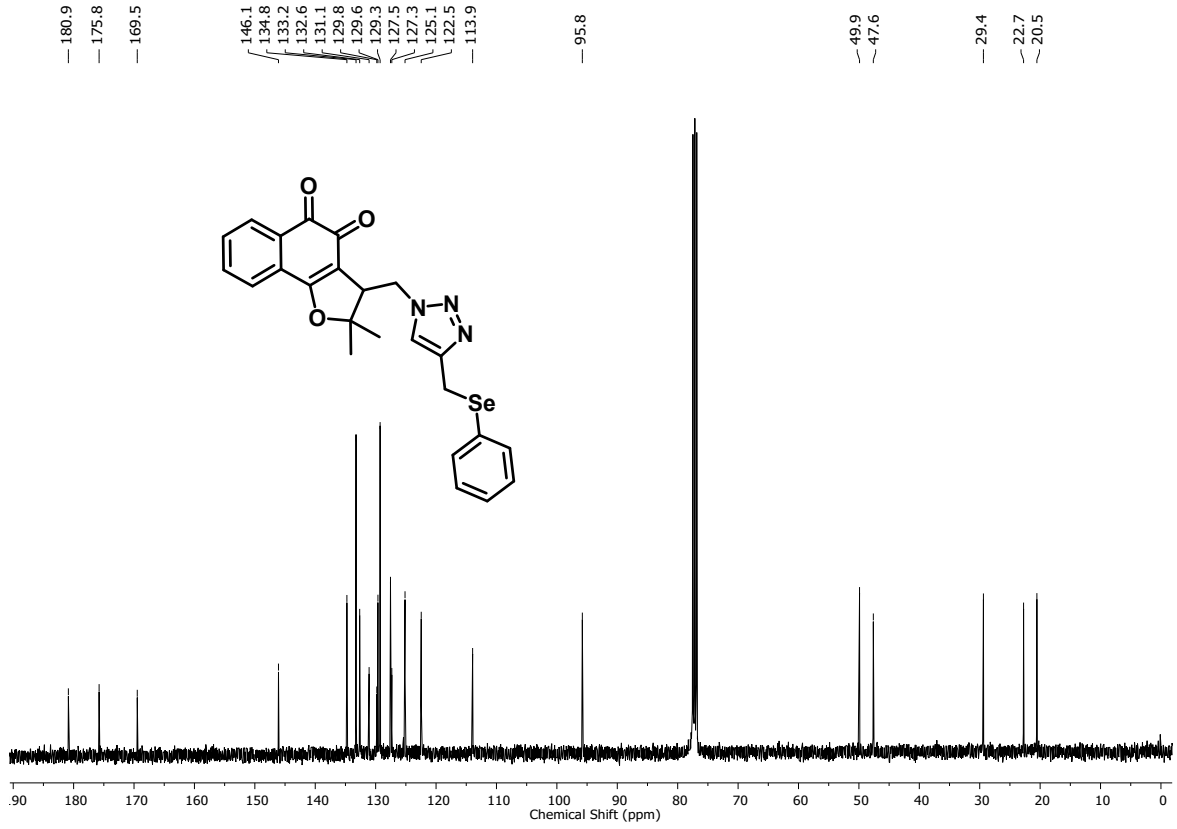


Figure S62. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **31**

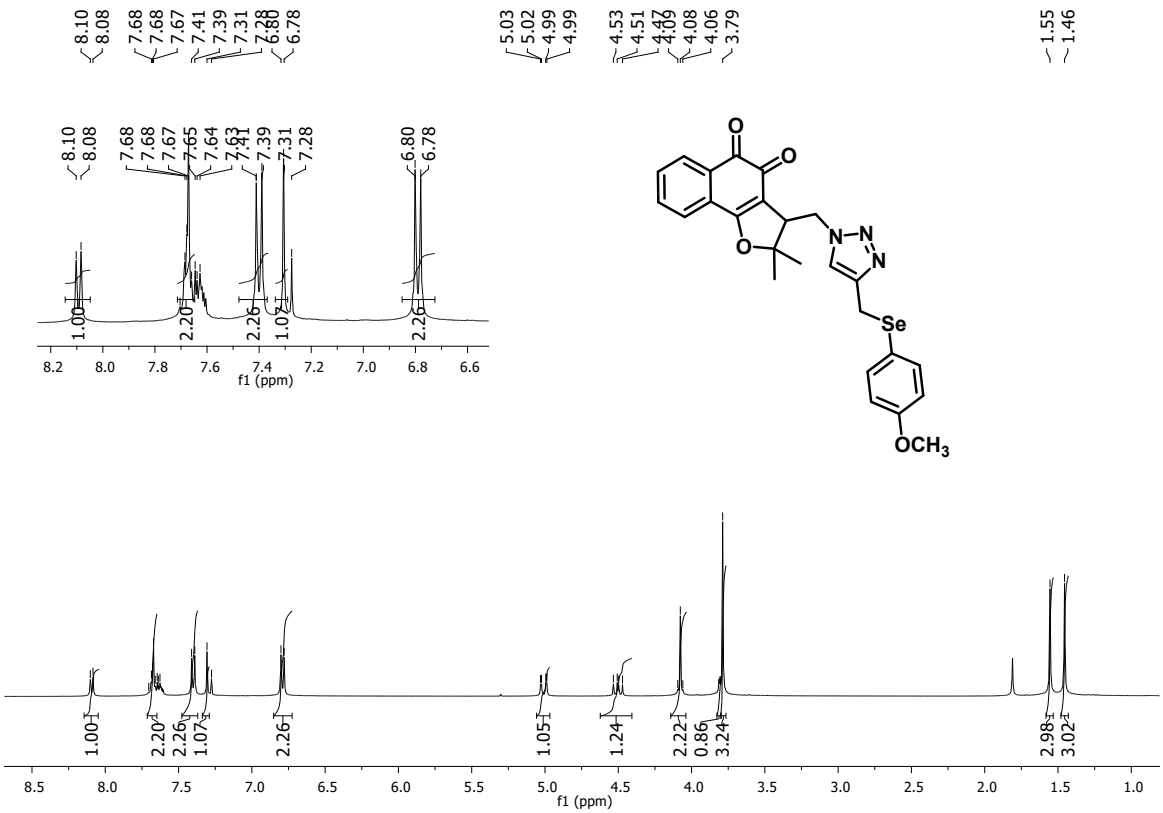


Figure S63. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **32**

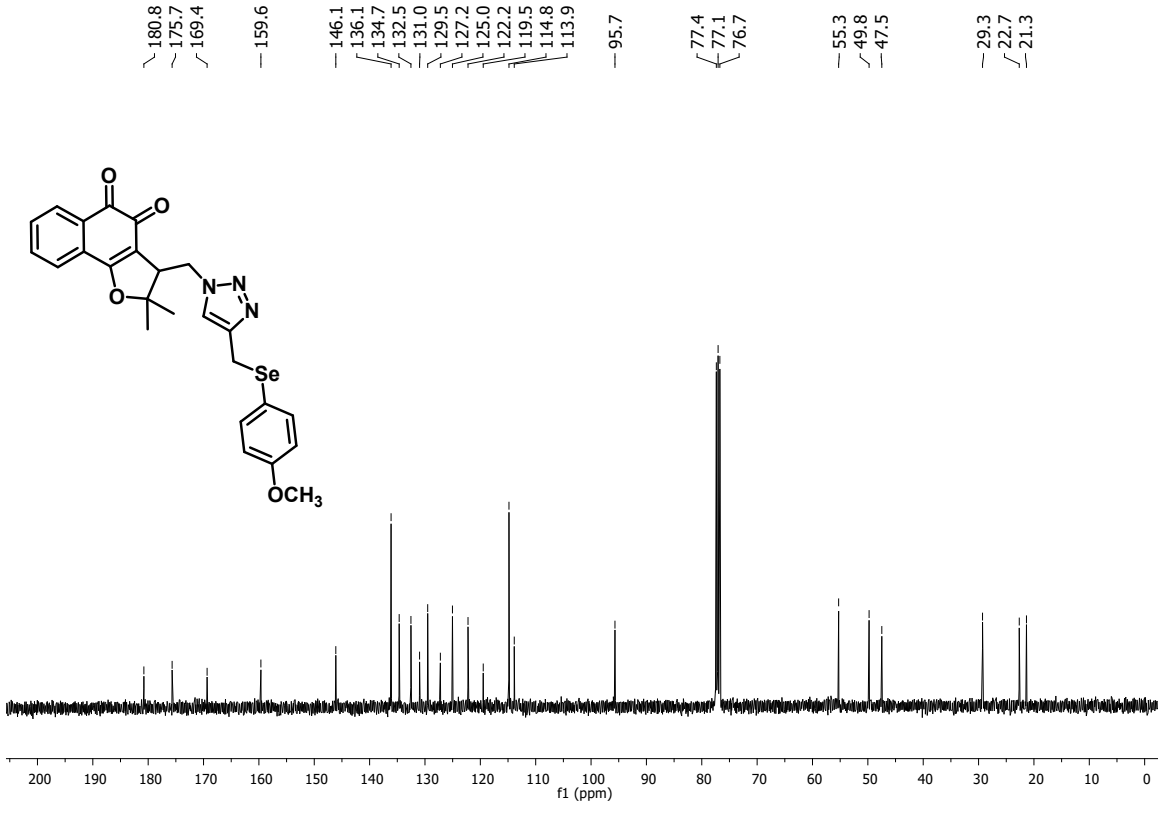


Figure S64. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **32**

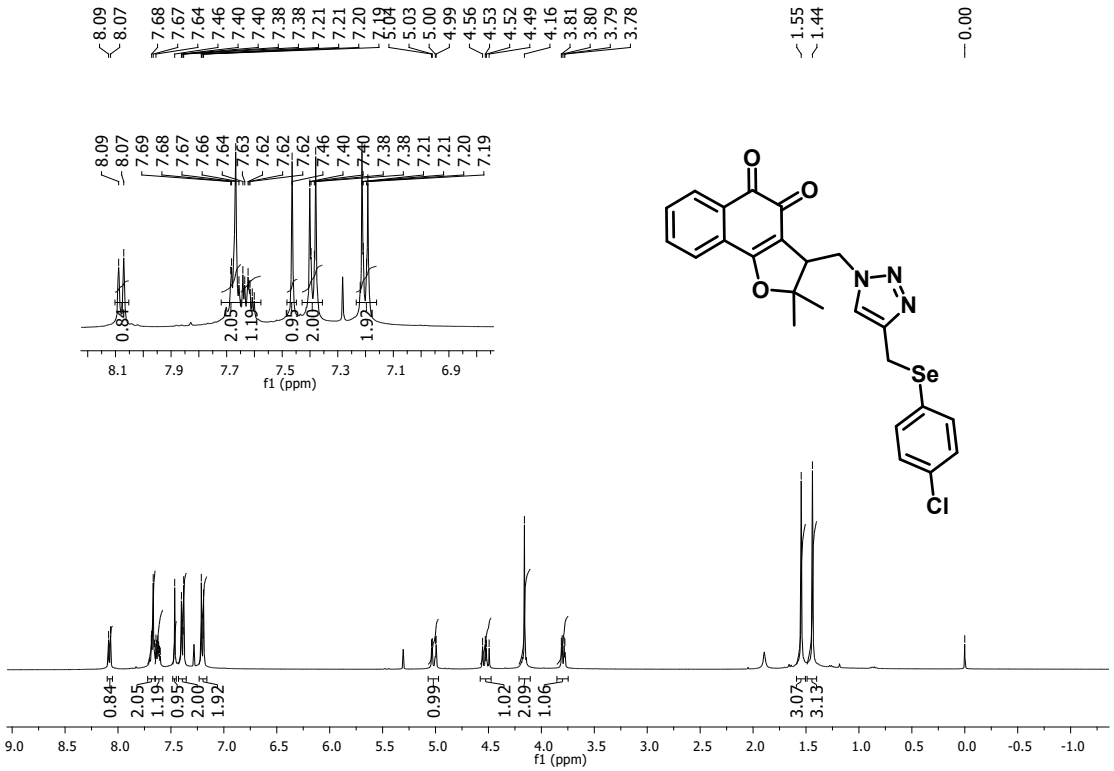


Figure S65. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **33**

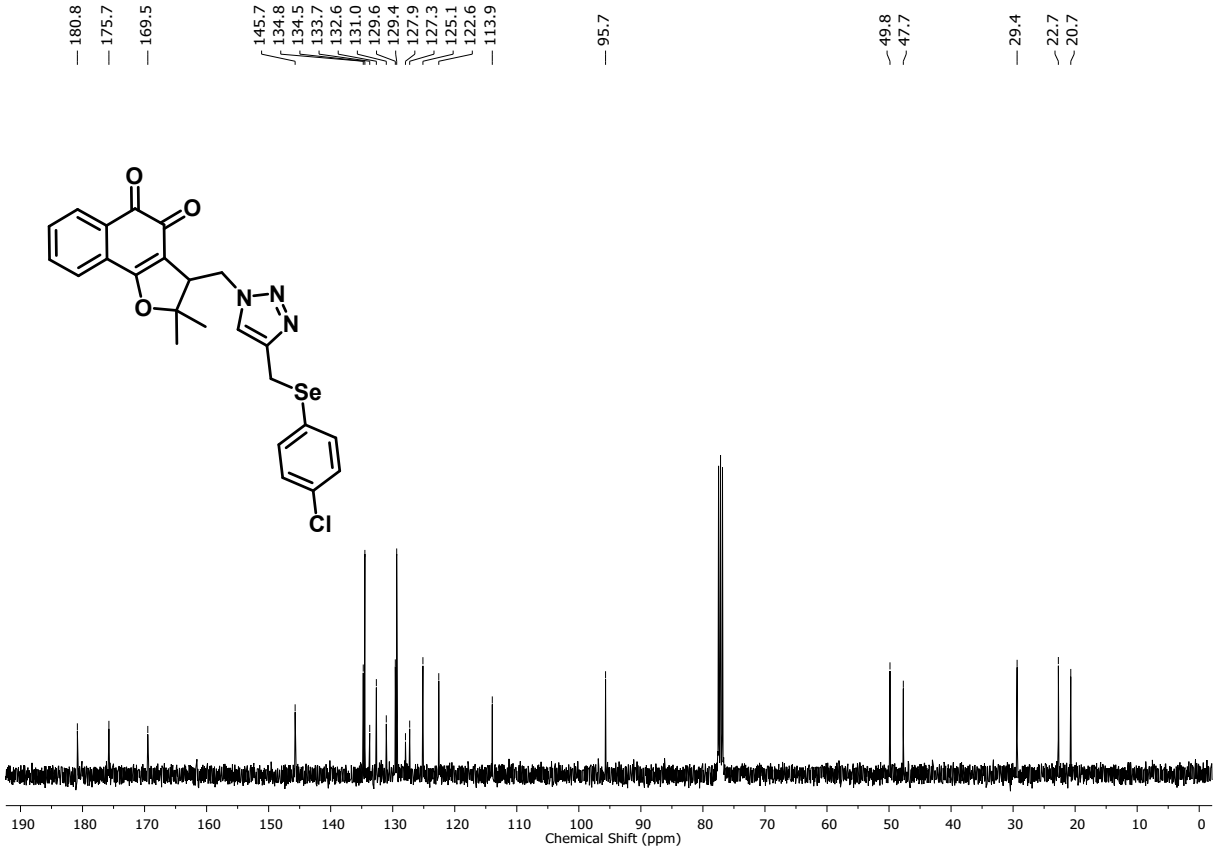


Figure S66. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **33**

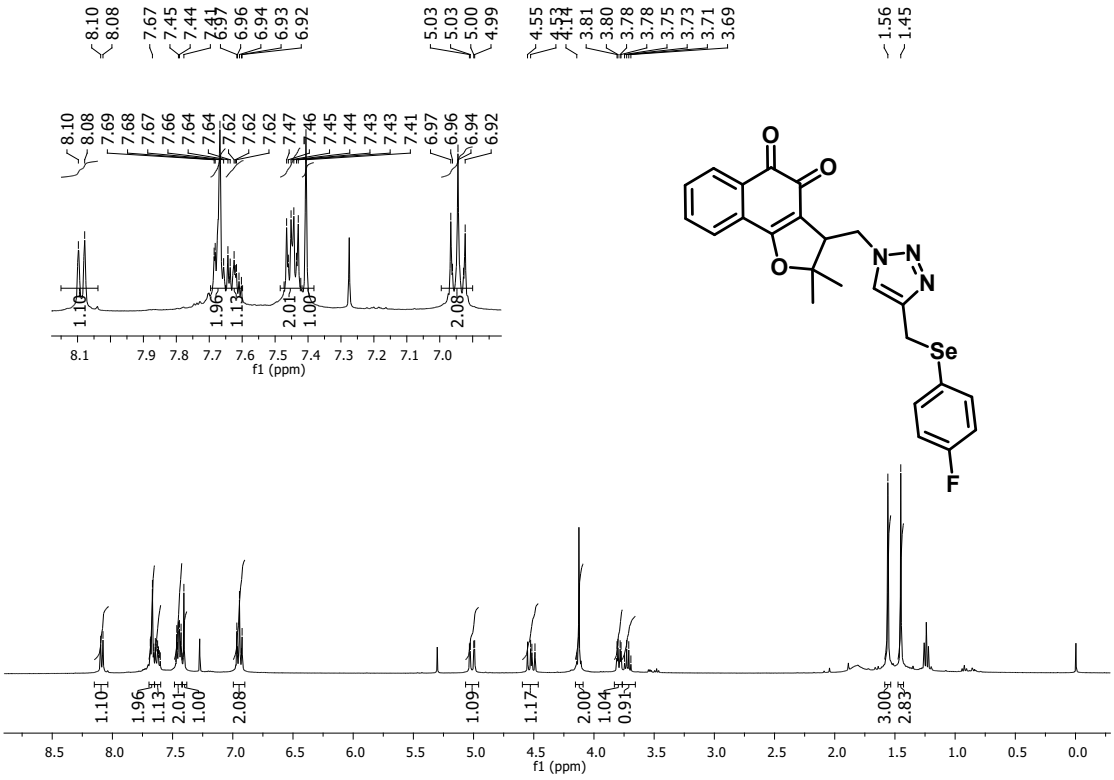


Figure S67. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **34**

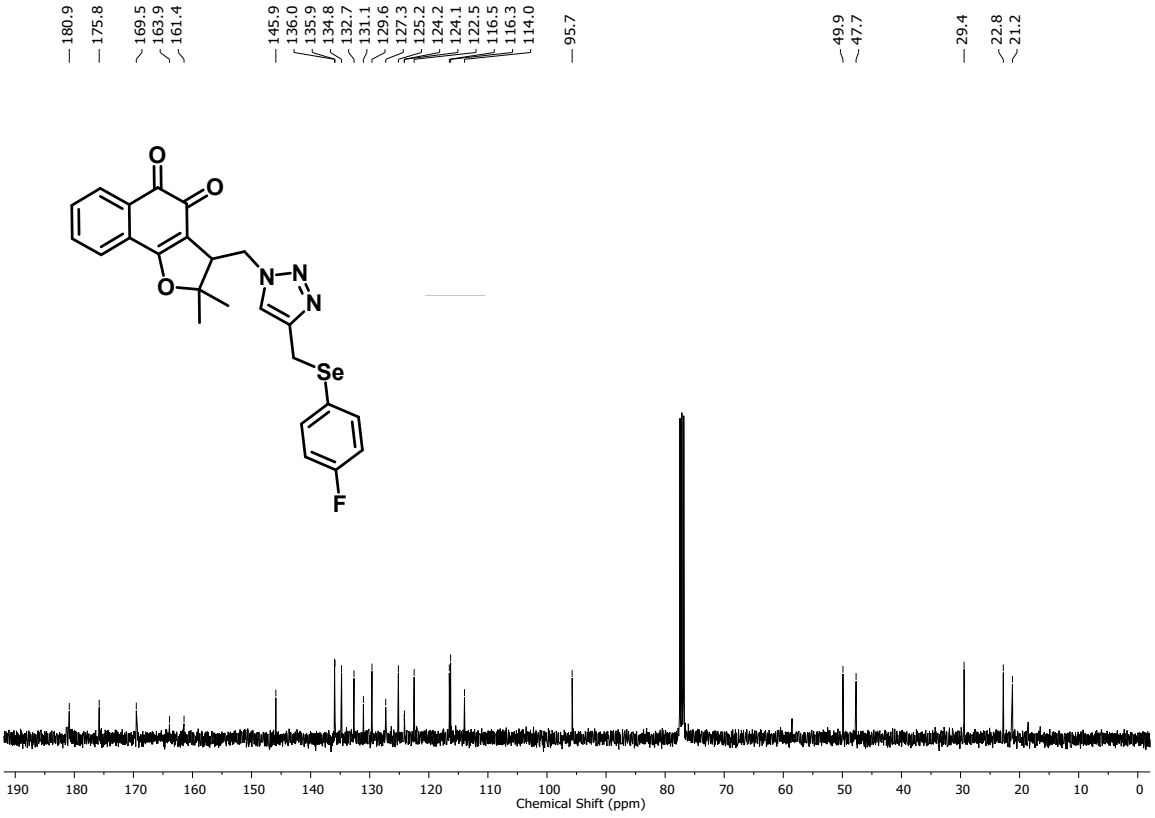


Figure S68. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **34**

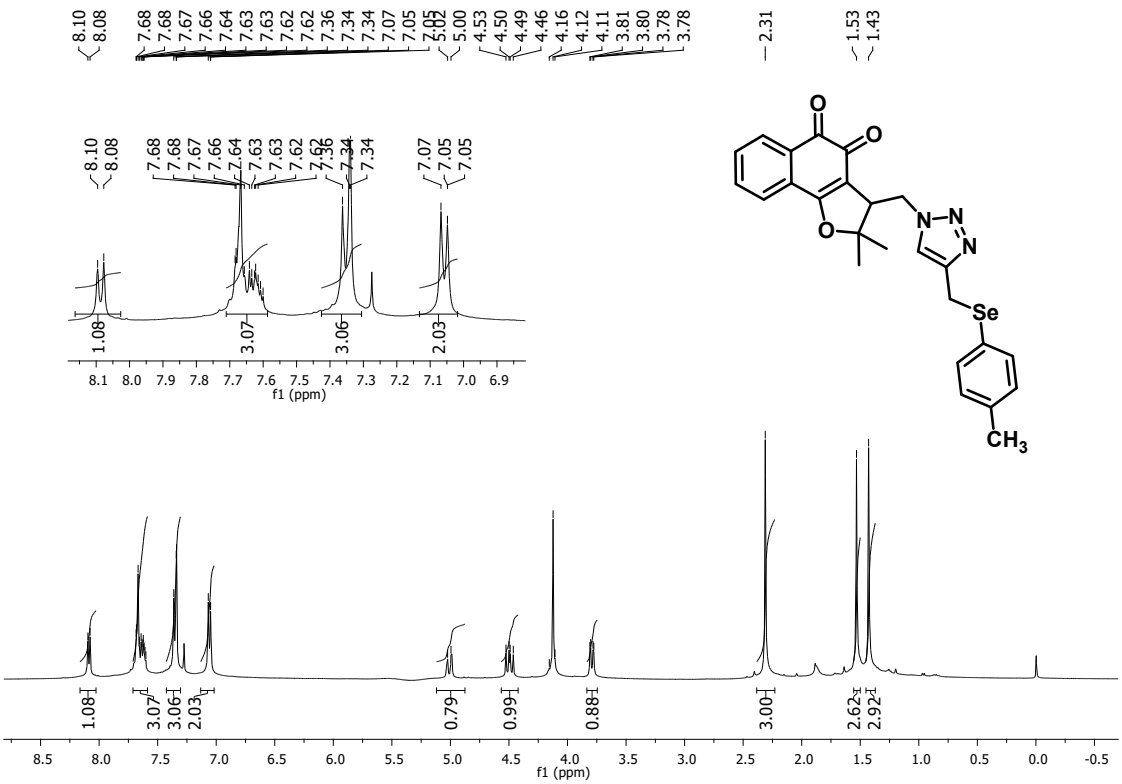


Figure S69. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **35**

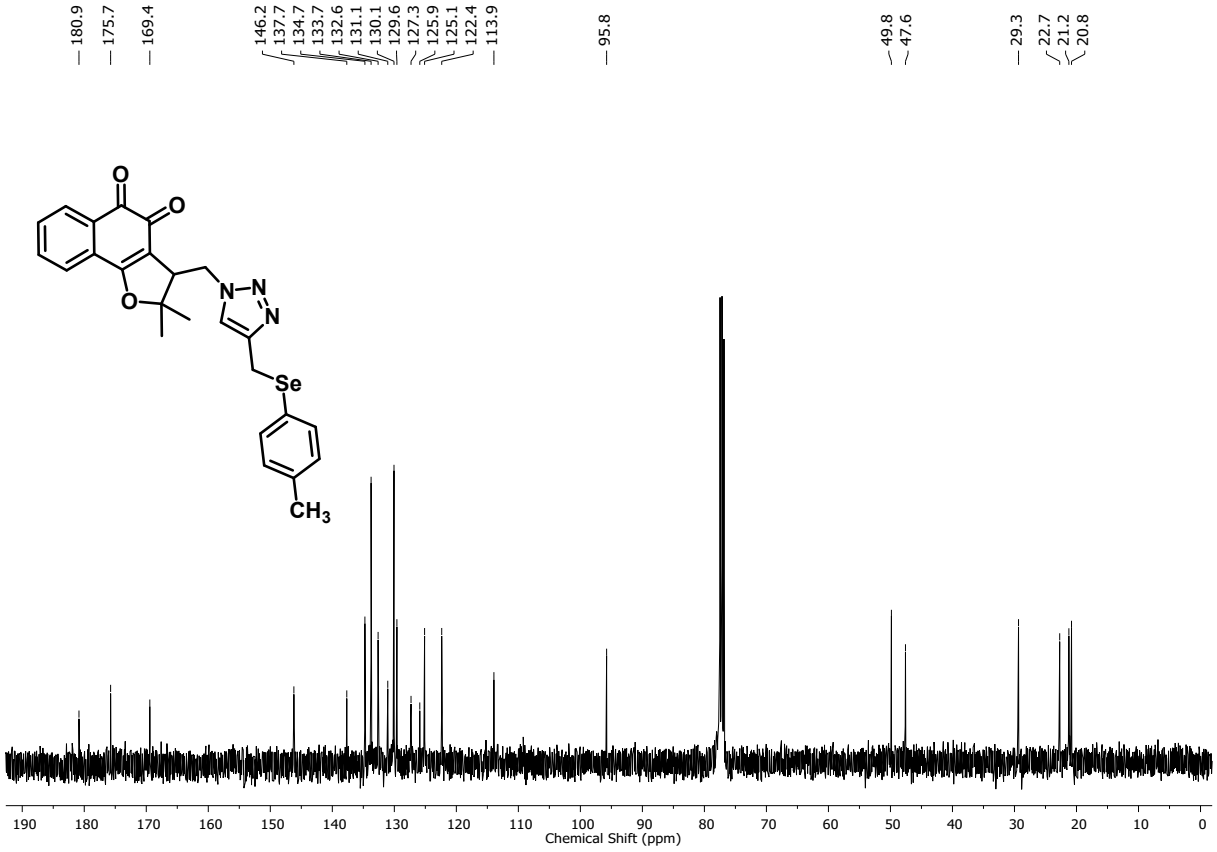


Figure S70. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **35**

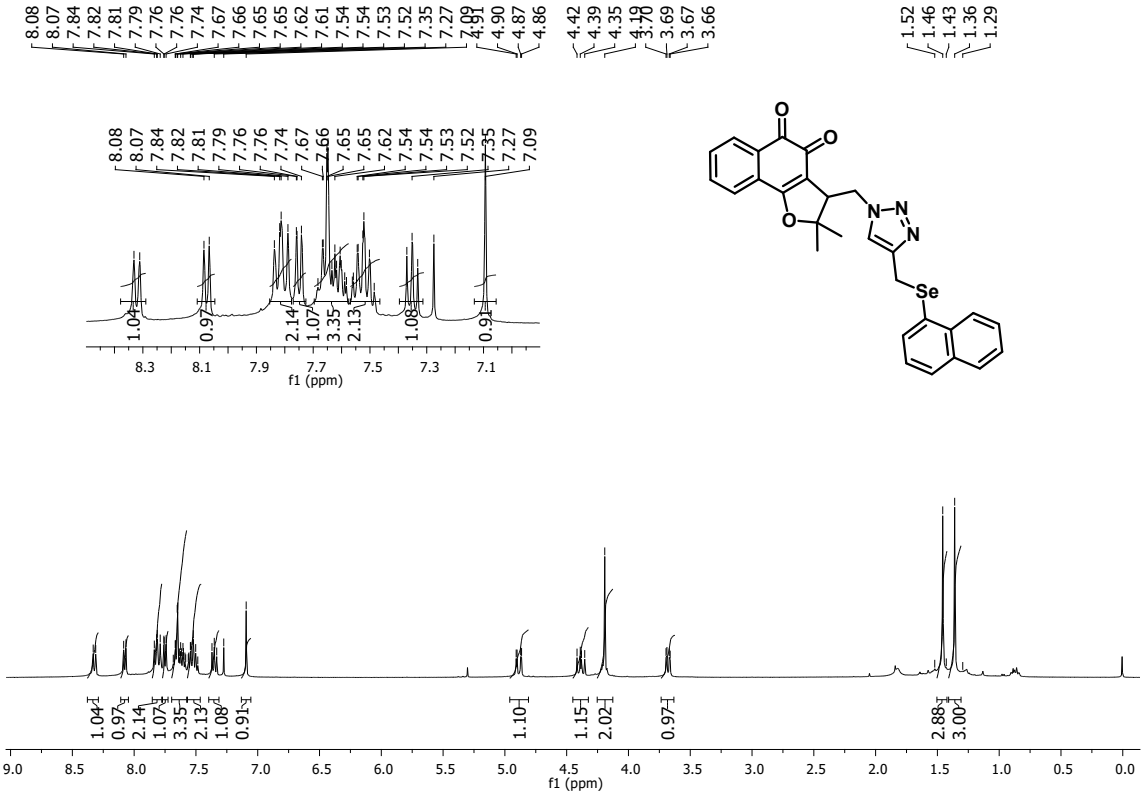


Figure S71. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **36**

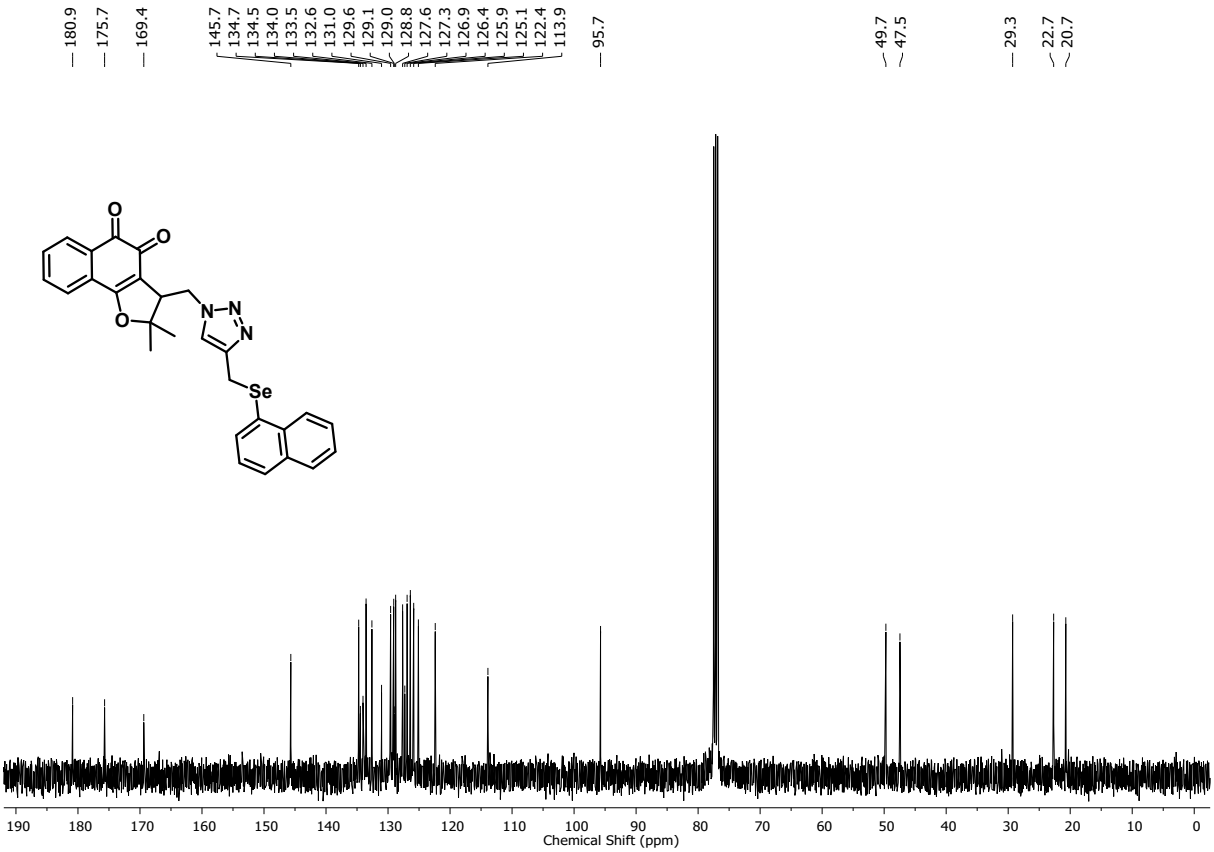


Figure S72. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **36**

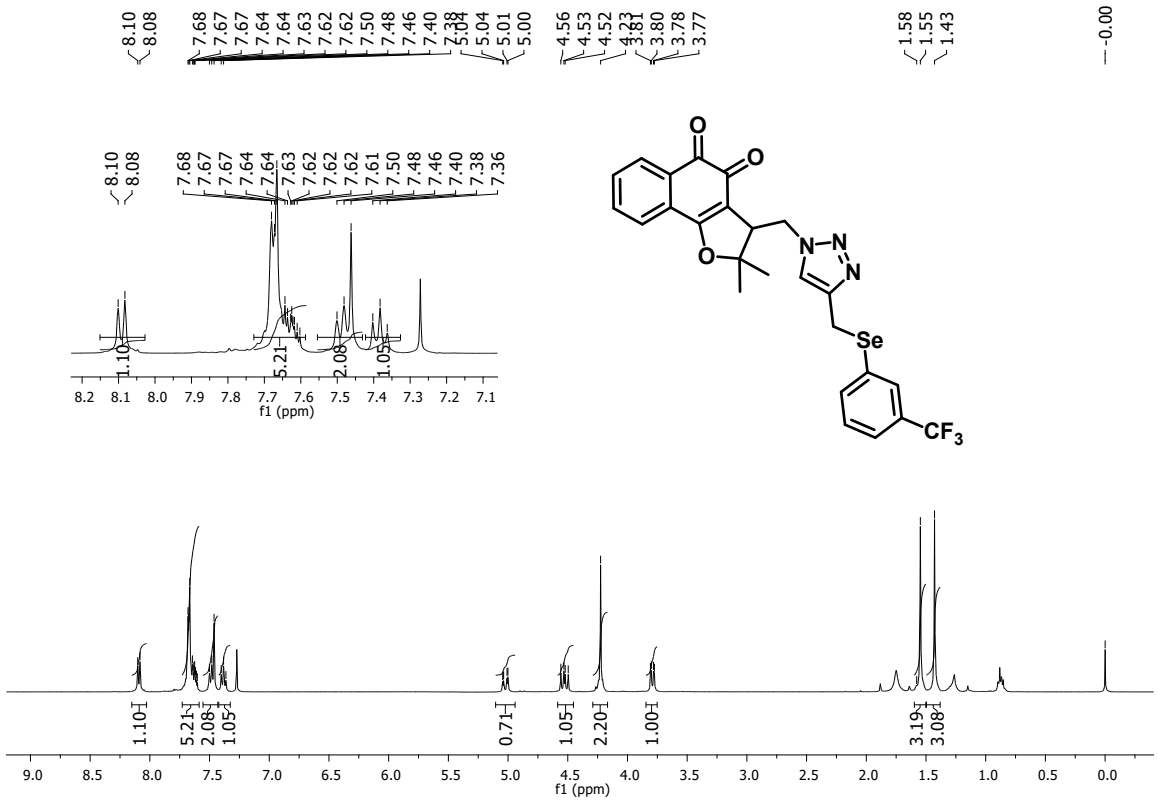


Figure S73. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **37**

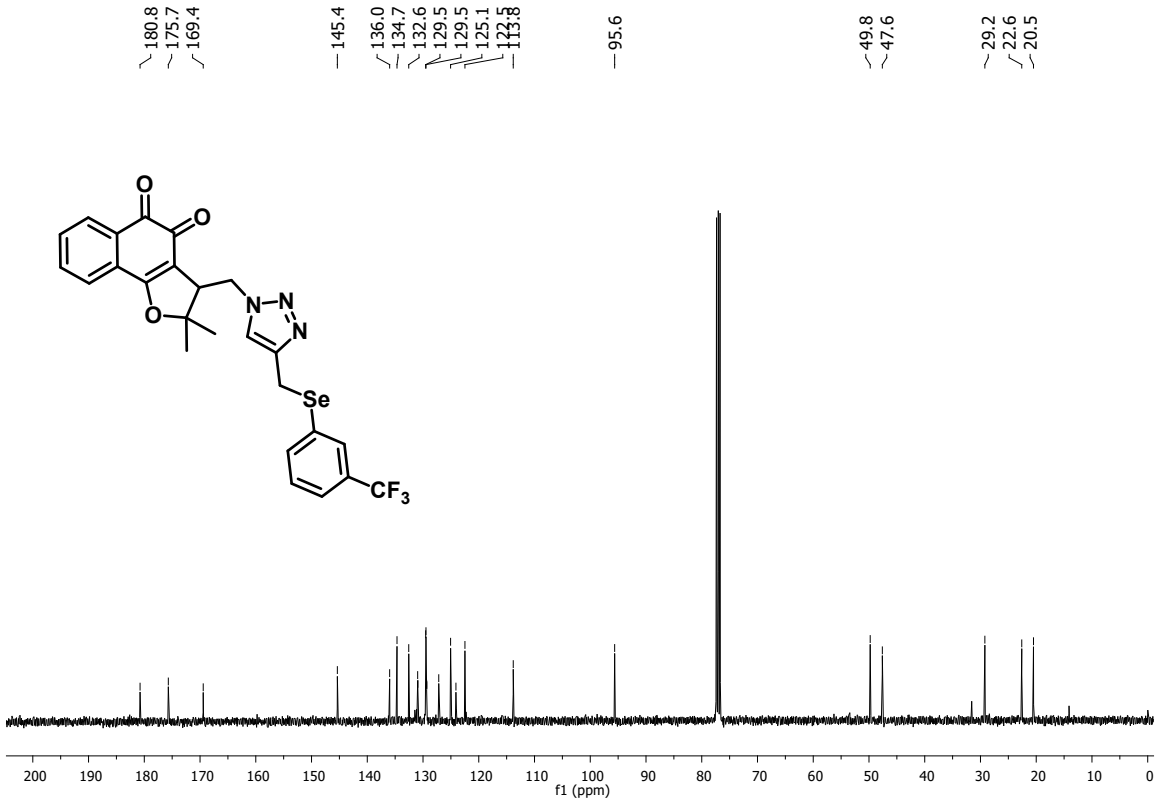


Figure S74. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **37**

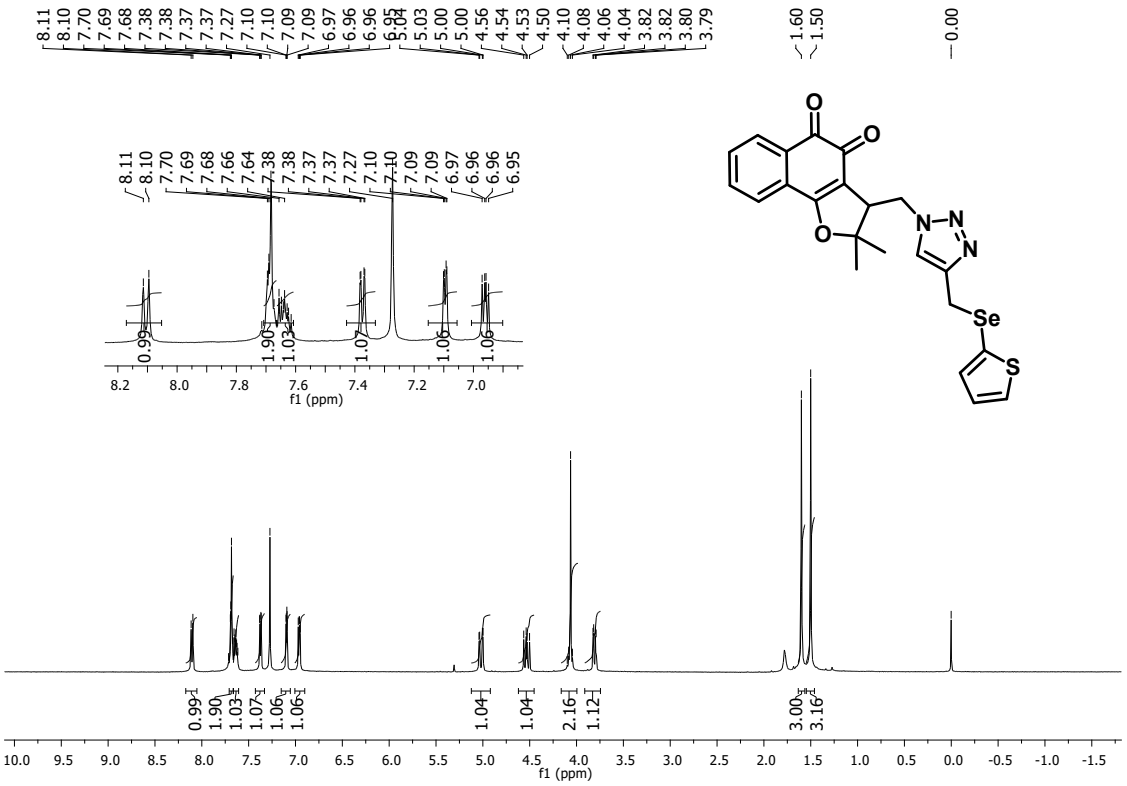


Figure S75. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **38**

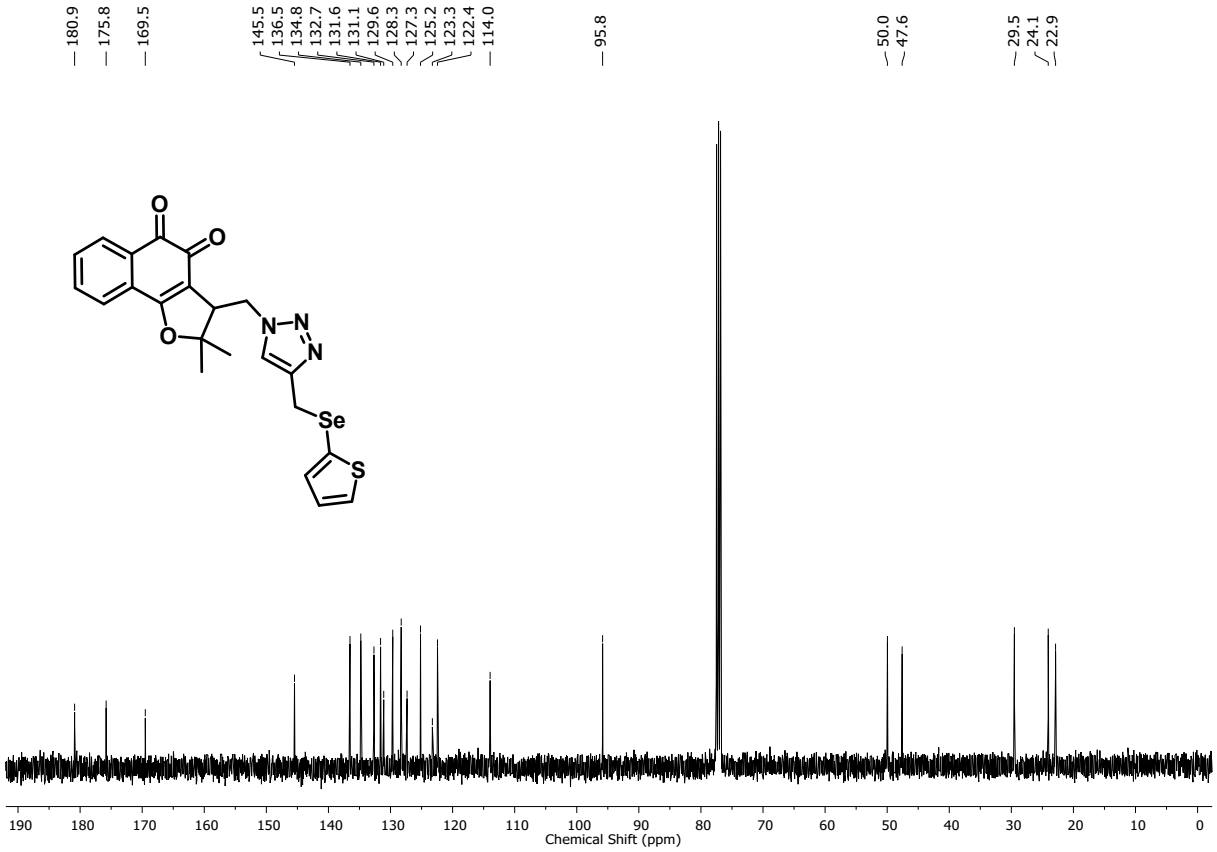


Figure S76. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **38**

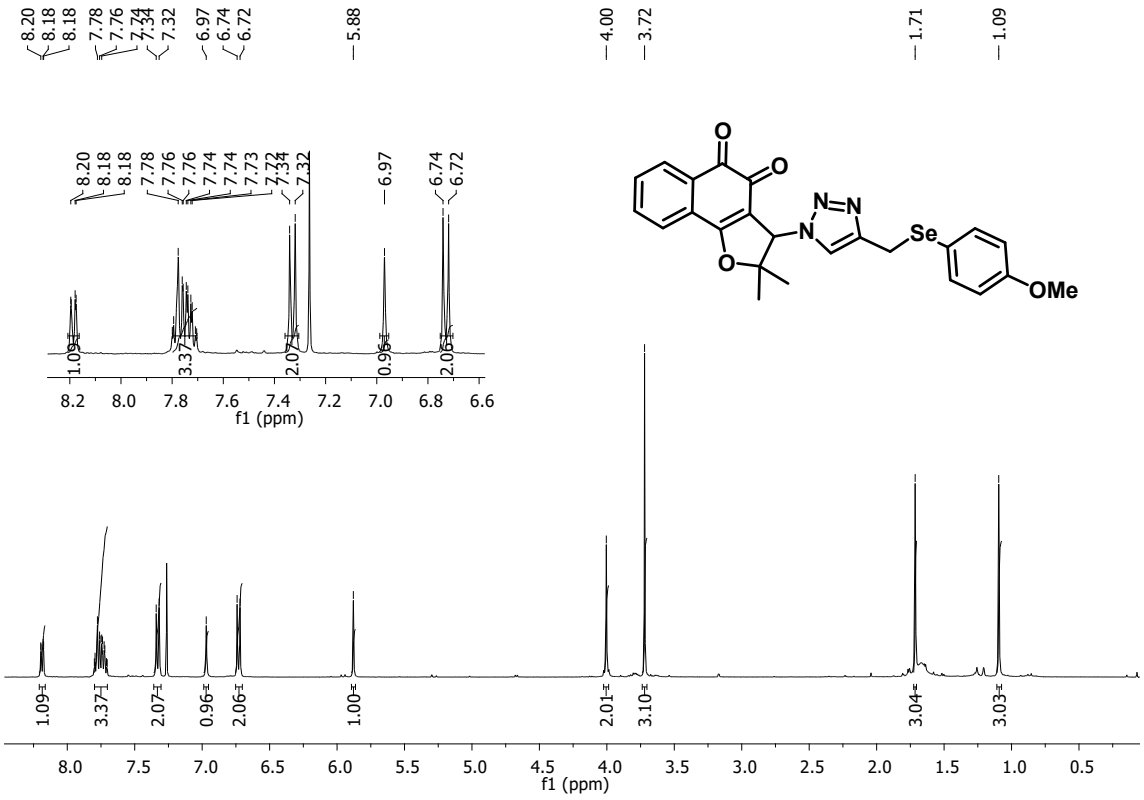


Figure S77. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **39**

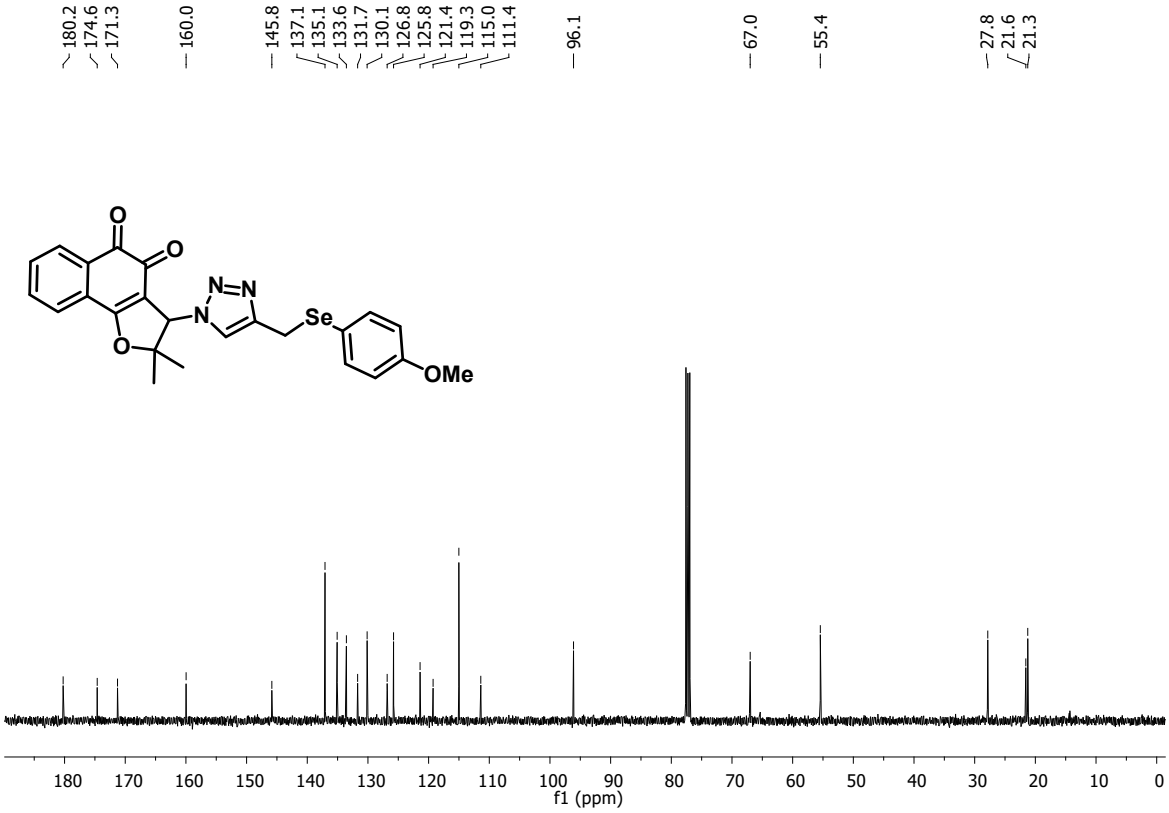


Figure S78. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **39**

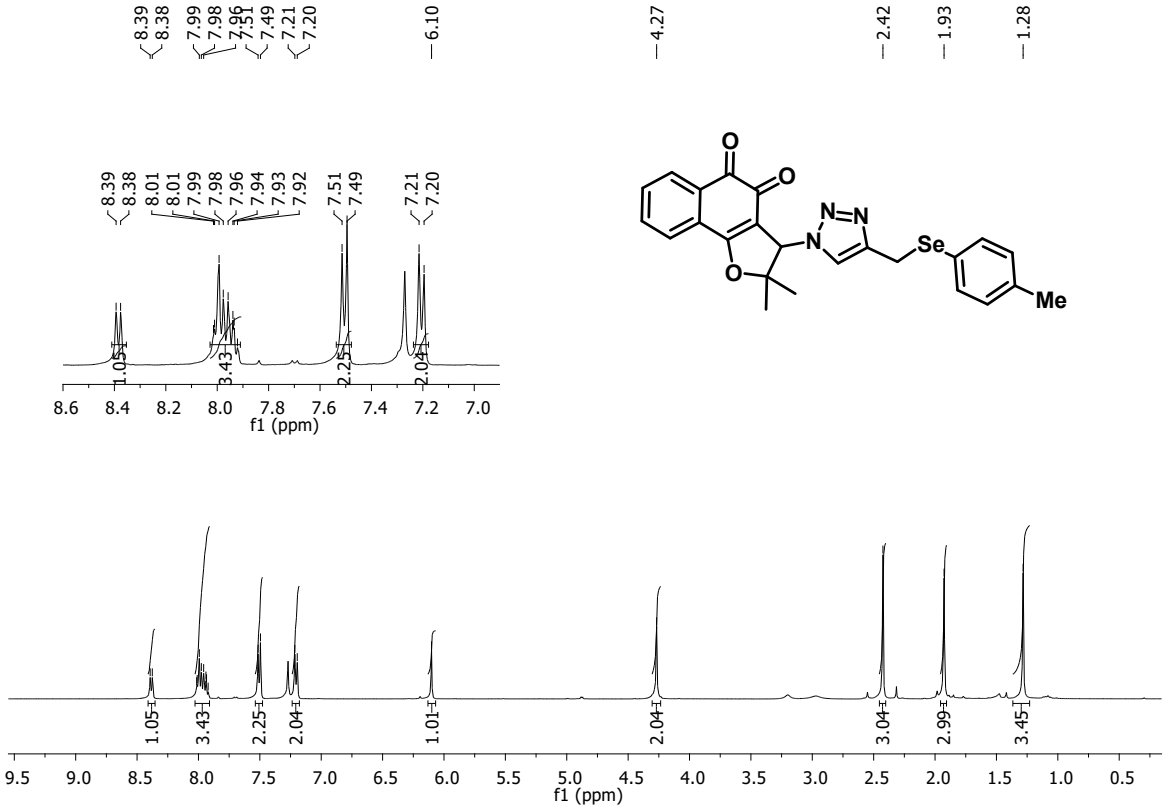


Figure S79. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **40**

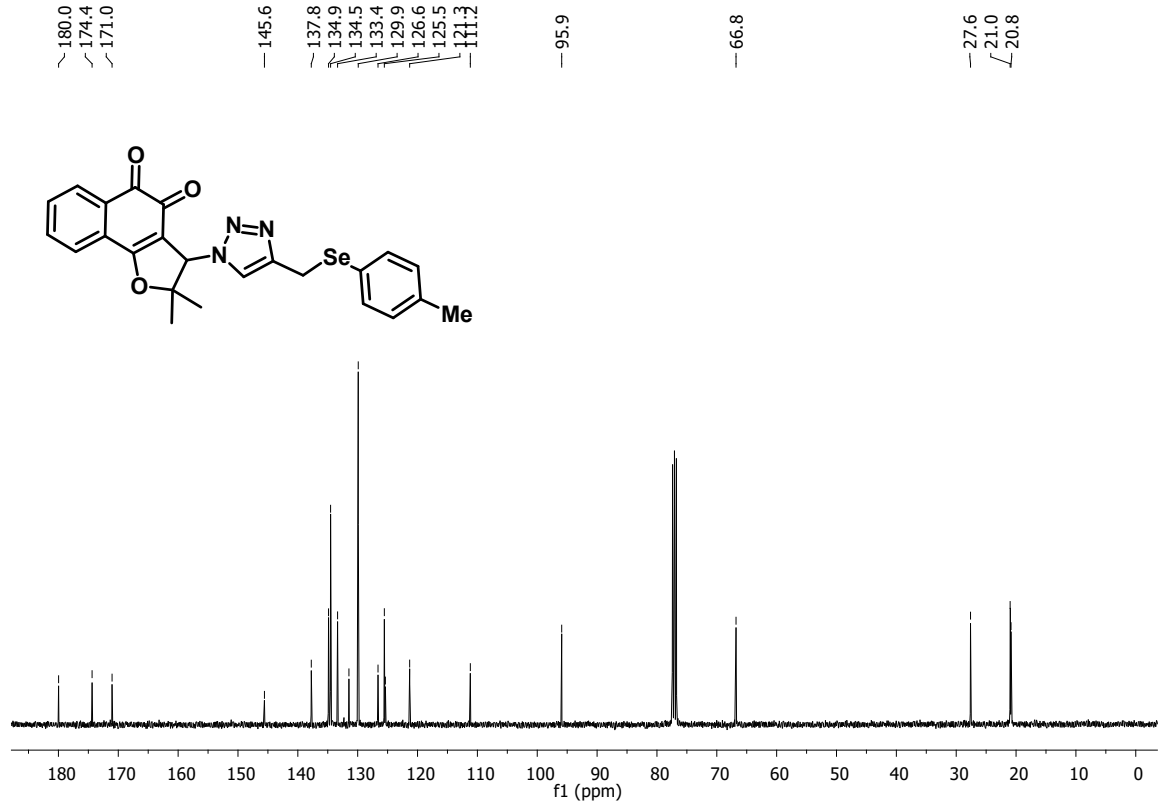


Figure S80. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **40**

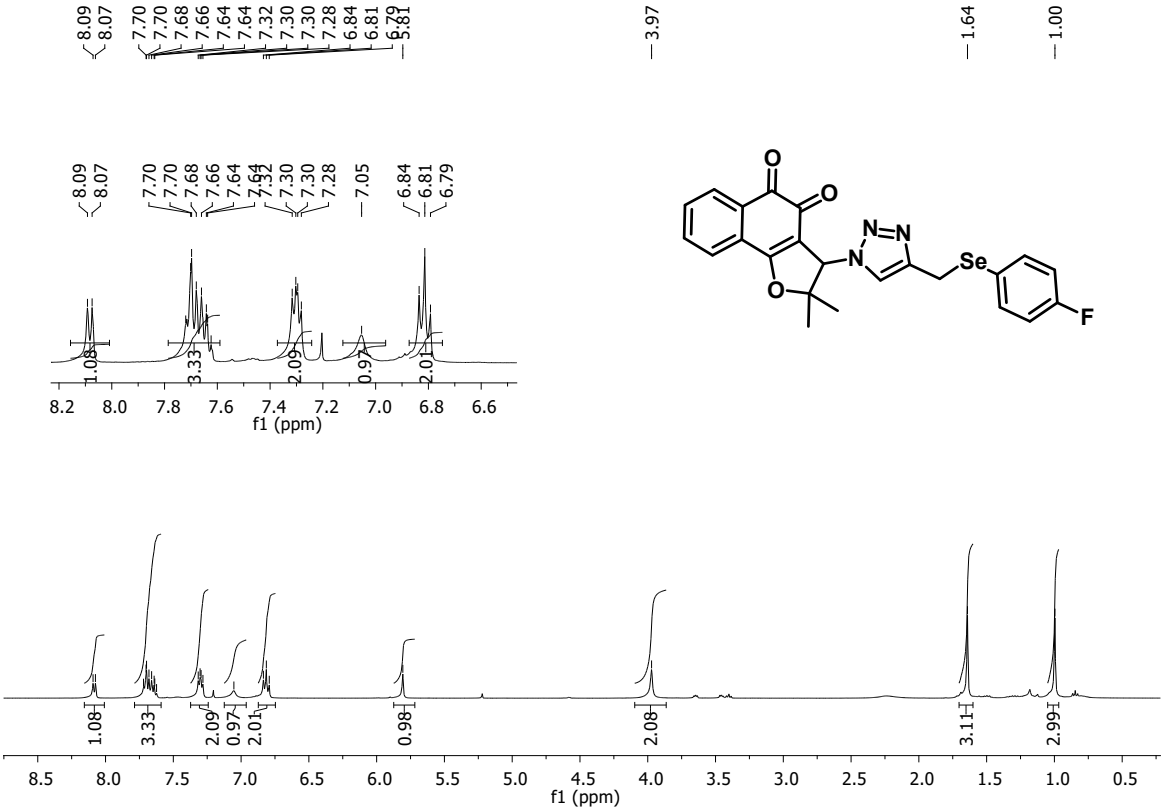


Figure S81. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **41**

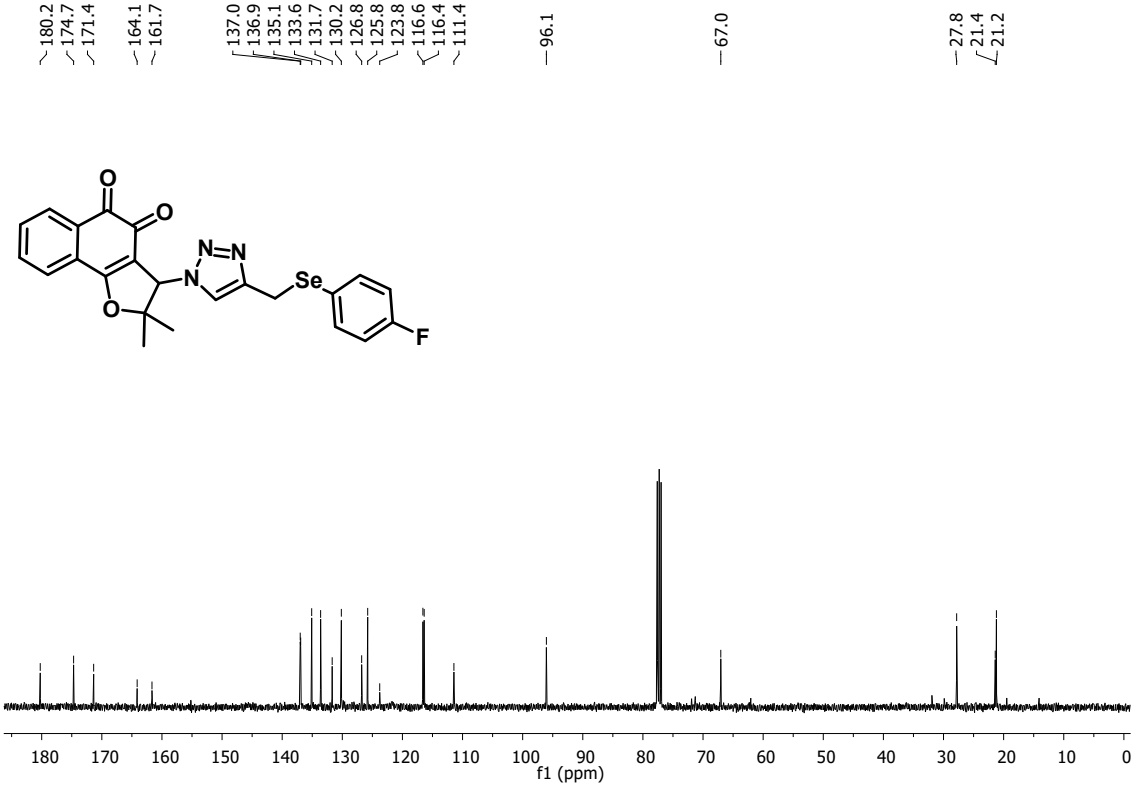


Figure S82. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **41**

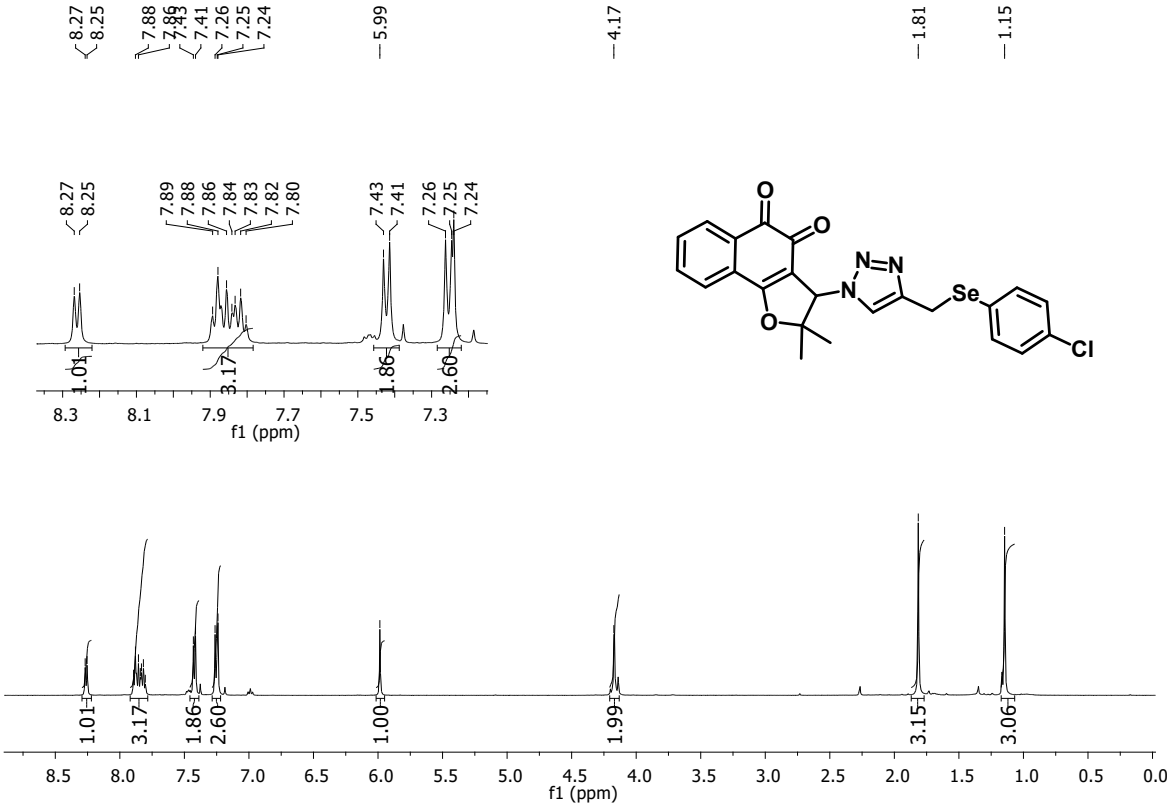


Figure S83. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **42**

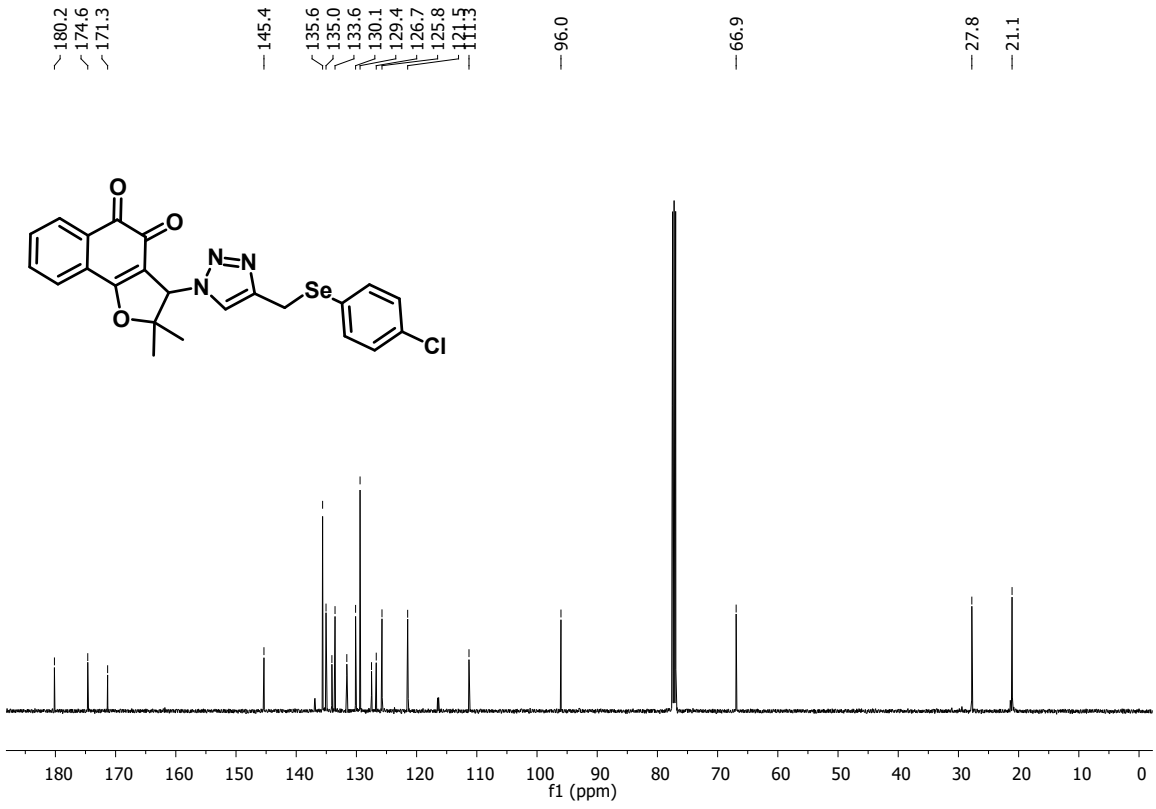


Figure S84. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **42**

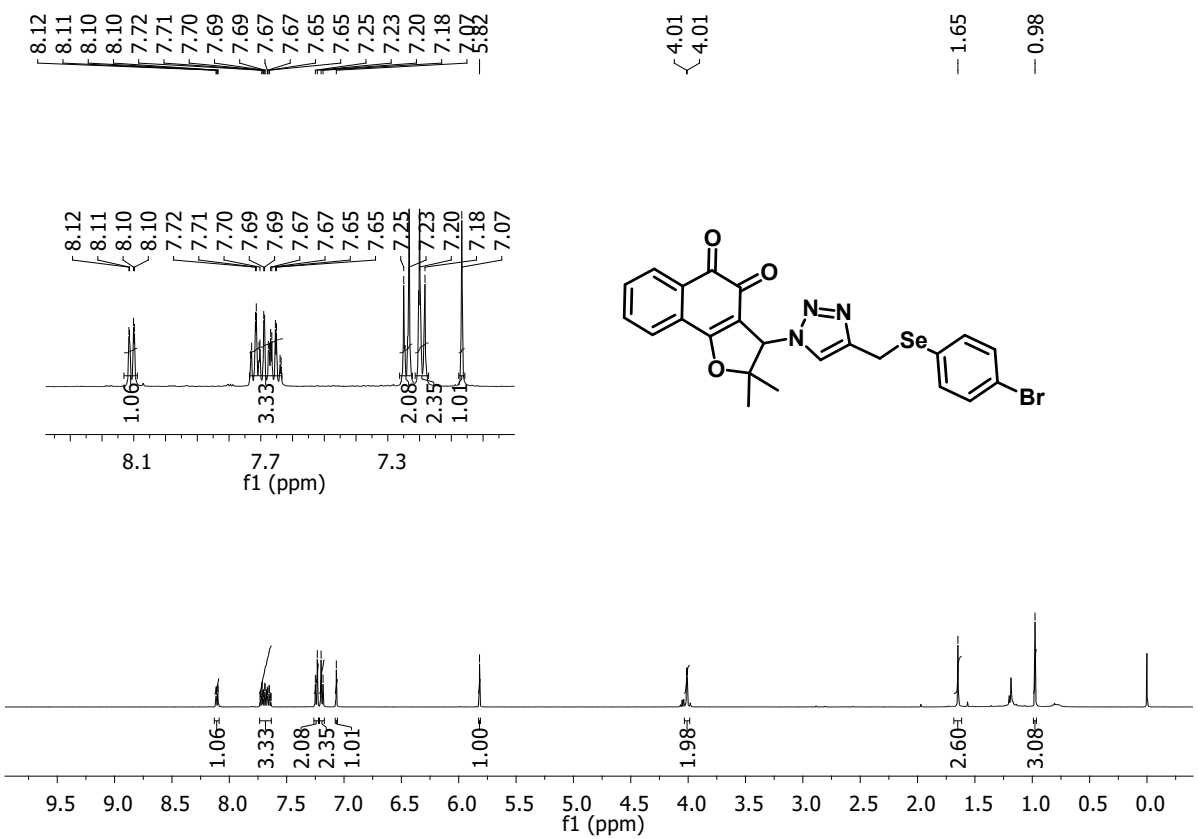


Figure S85. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **43**

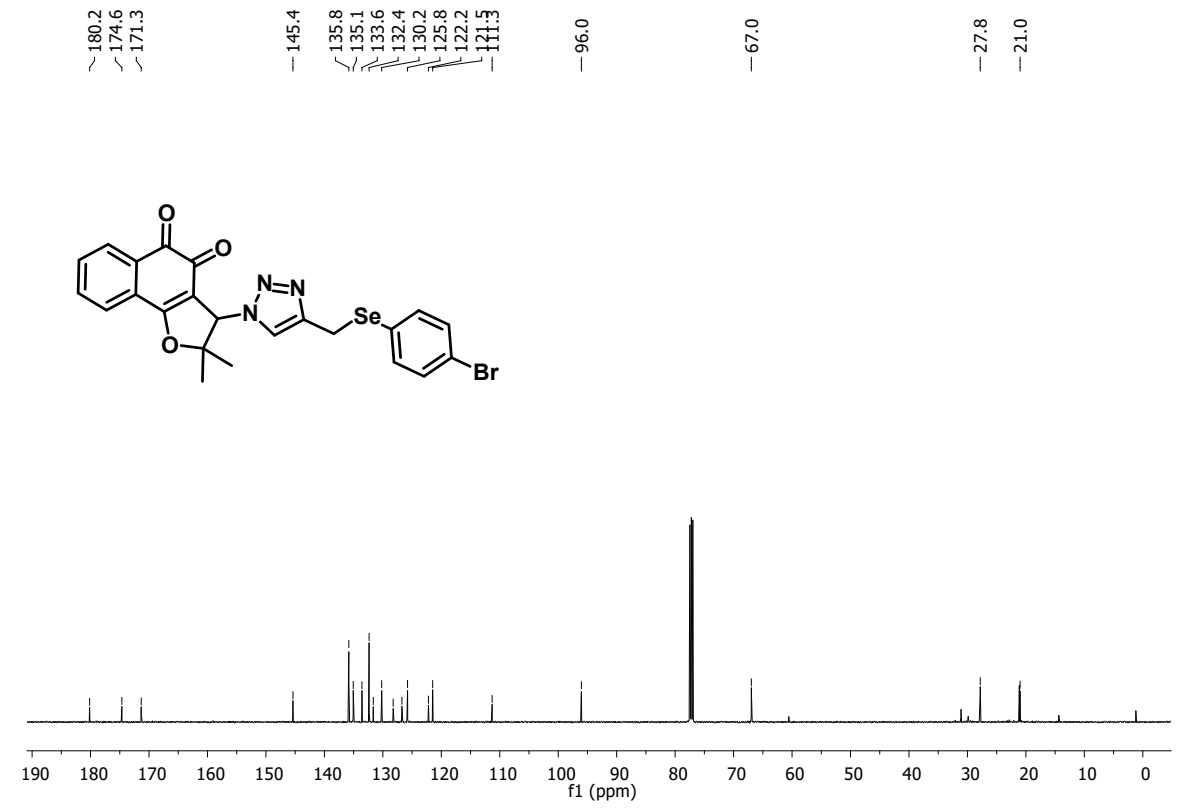


Figure S86. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **43**

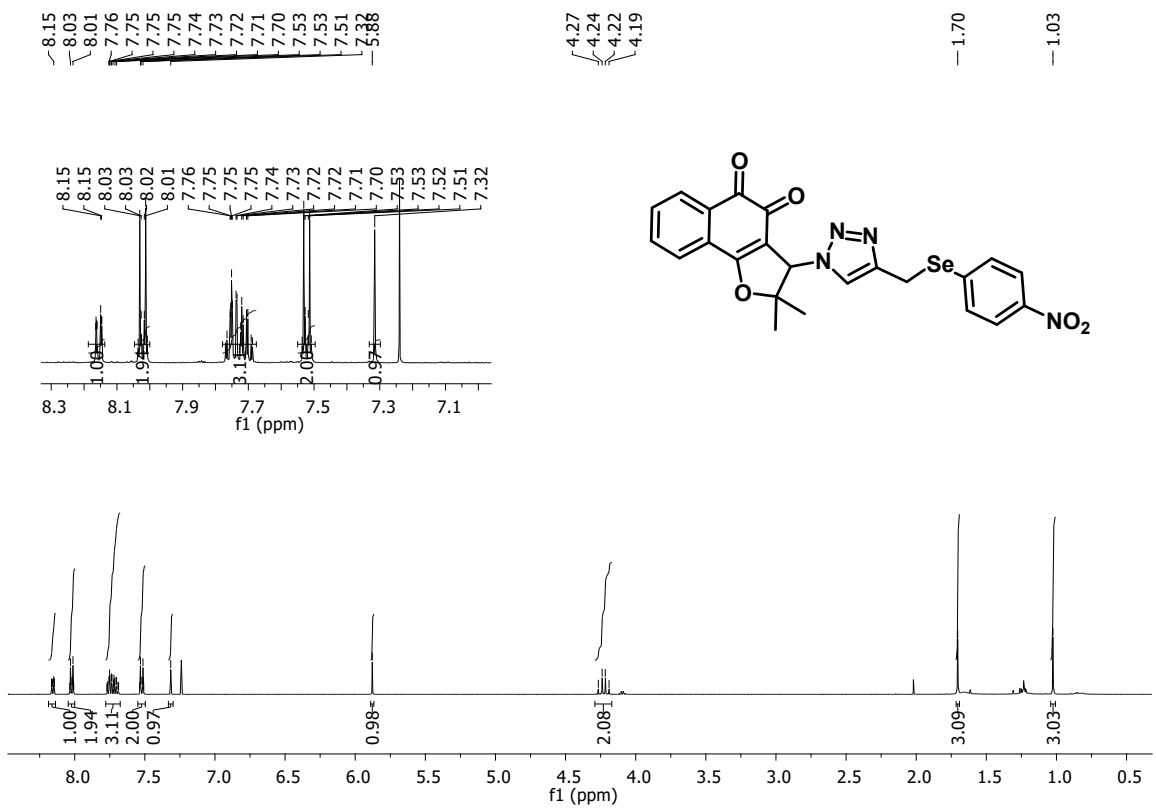


Figure S87. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **44**

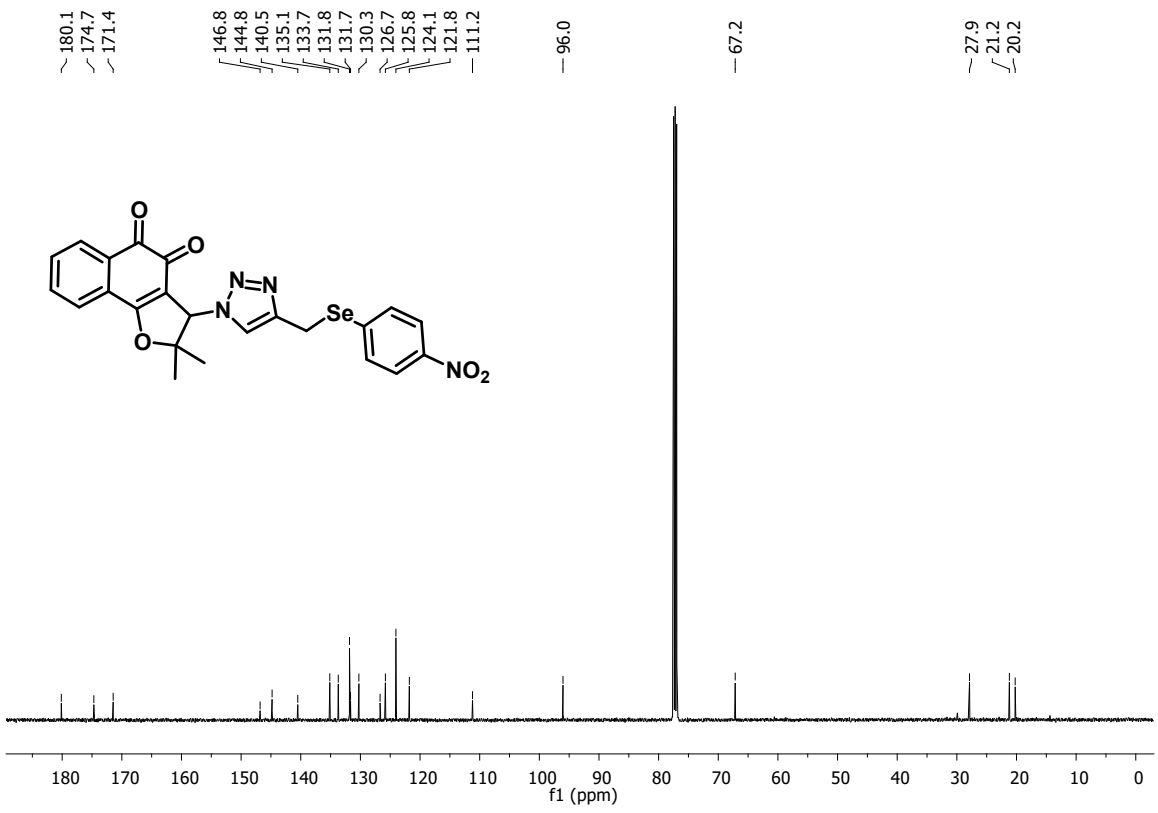


Figure S88. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **44**

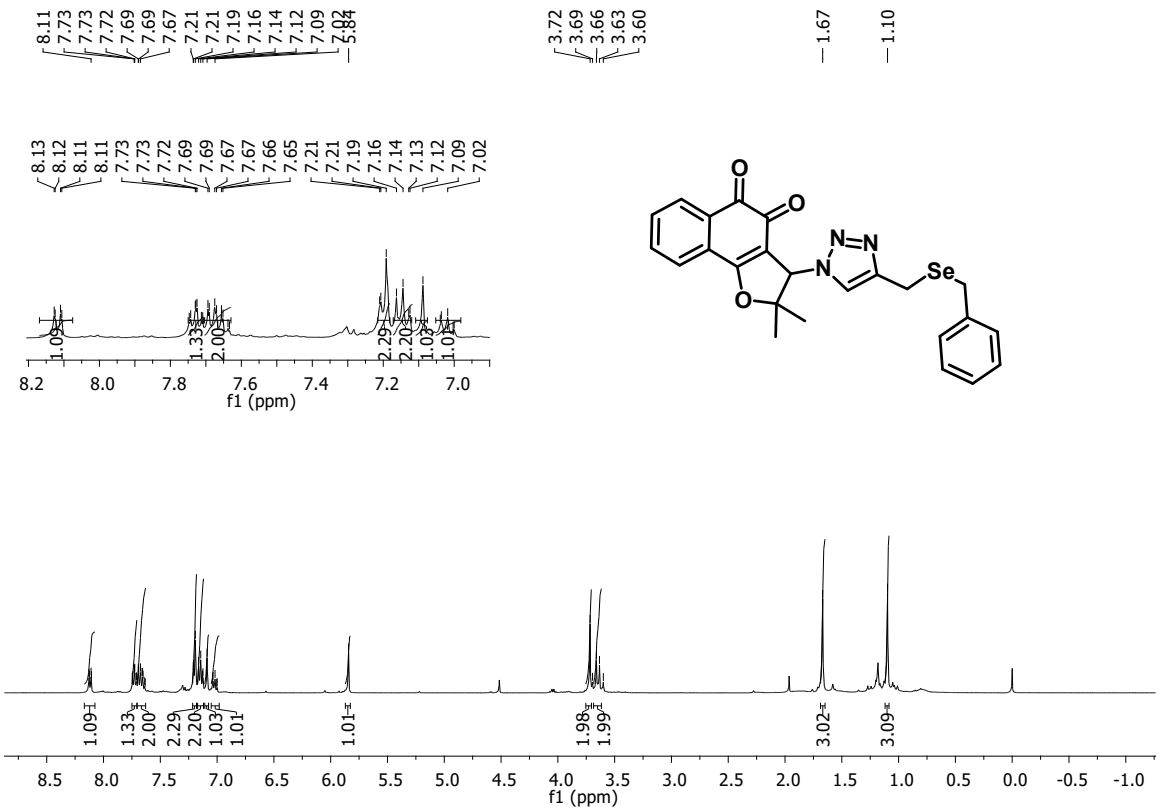


Figure S89. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **45**

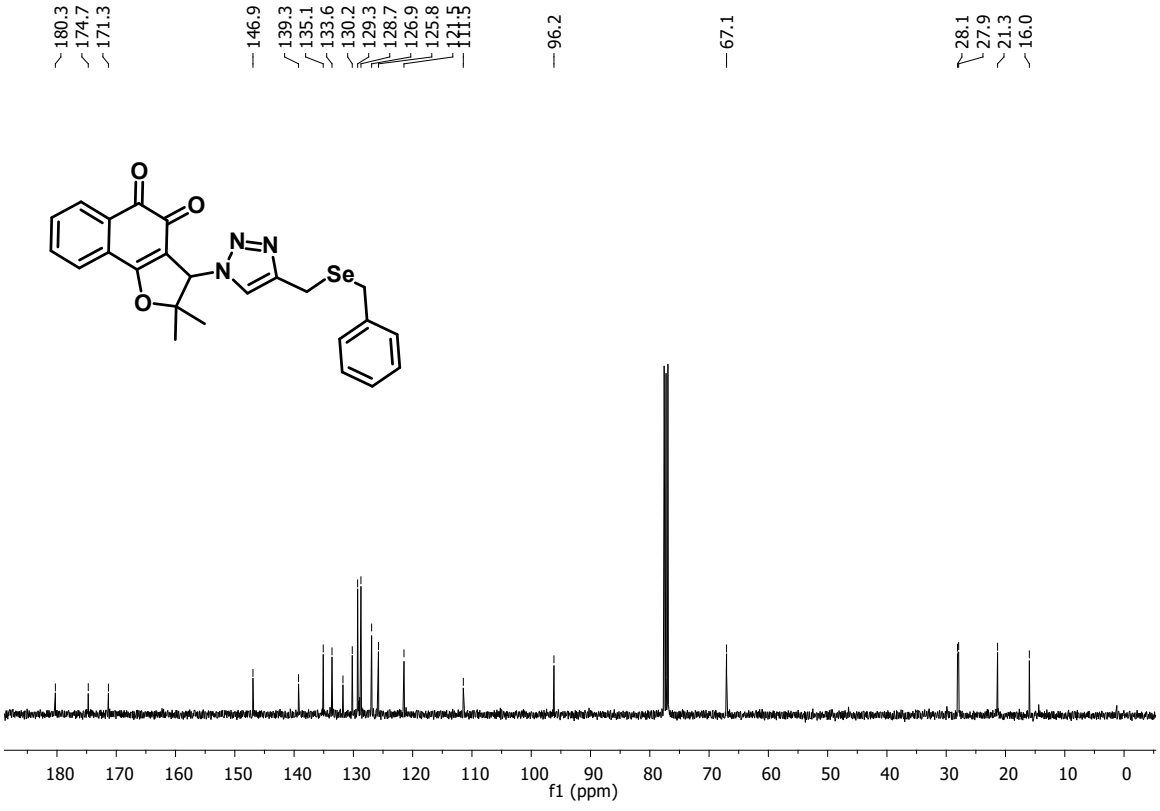


Figure S90. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **45**

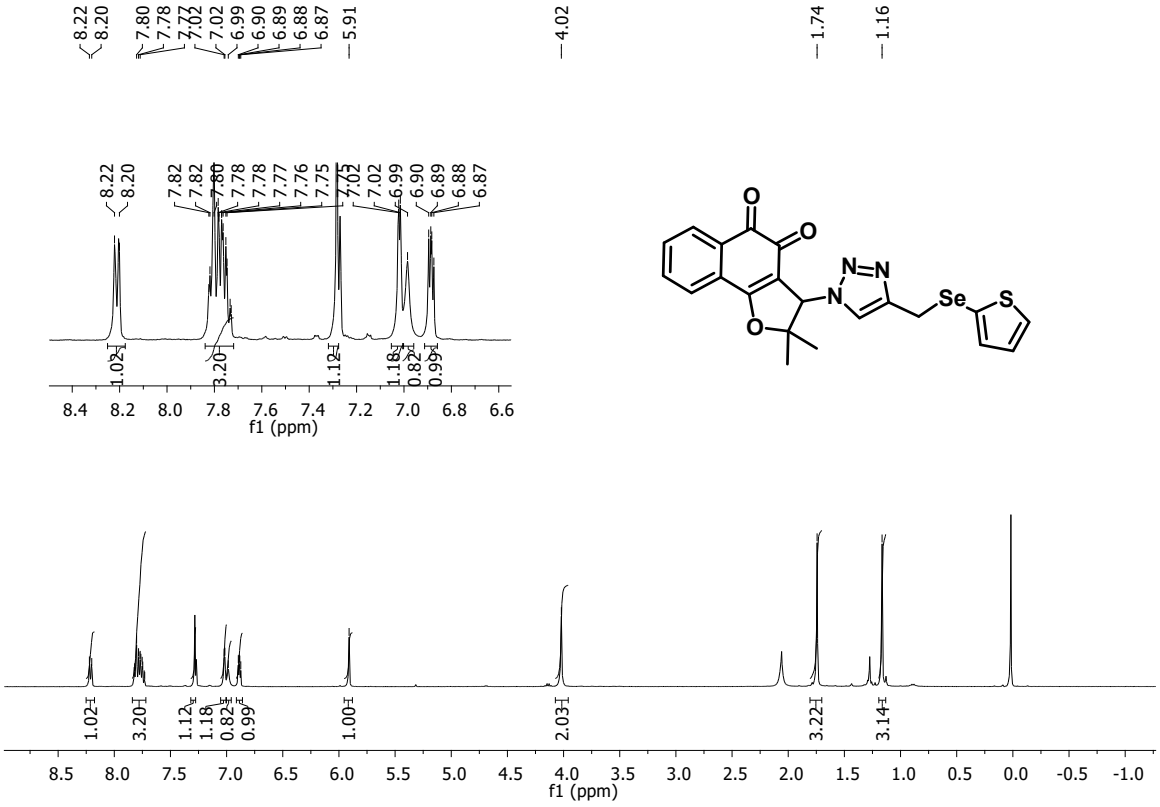


Figure S91. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **46**

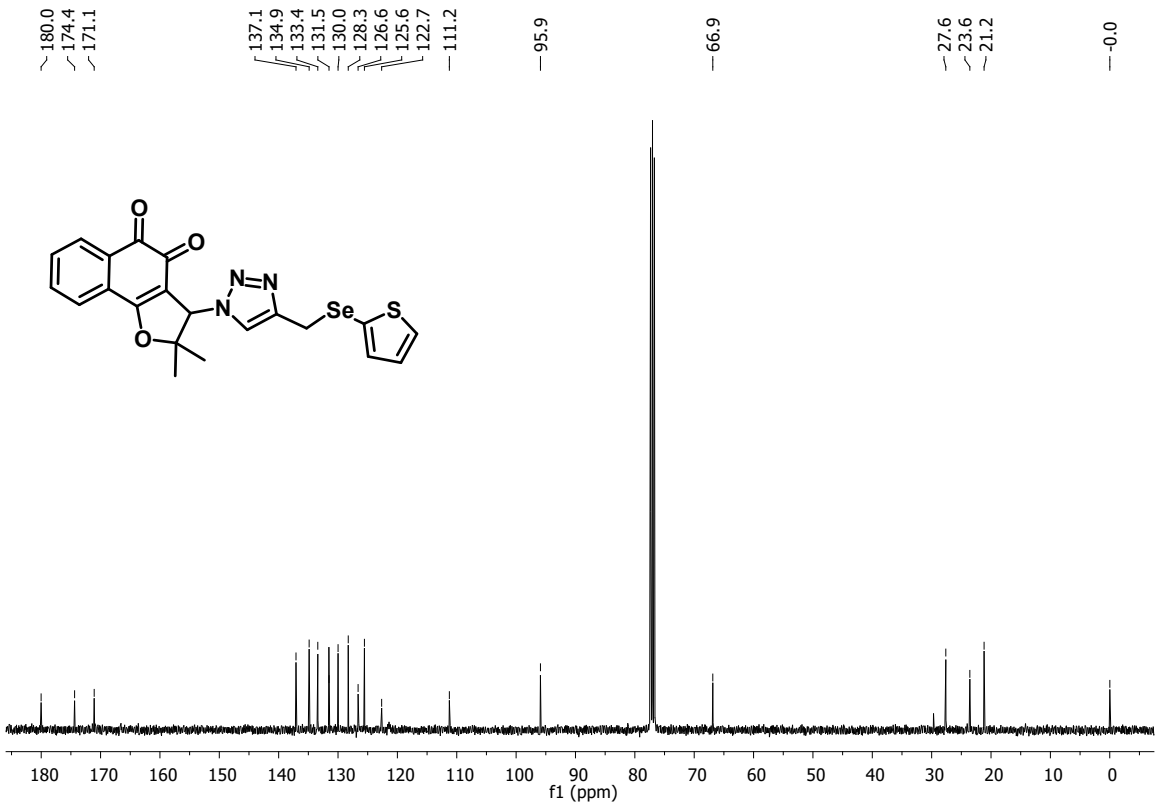


Figure S92. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **46**

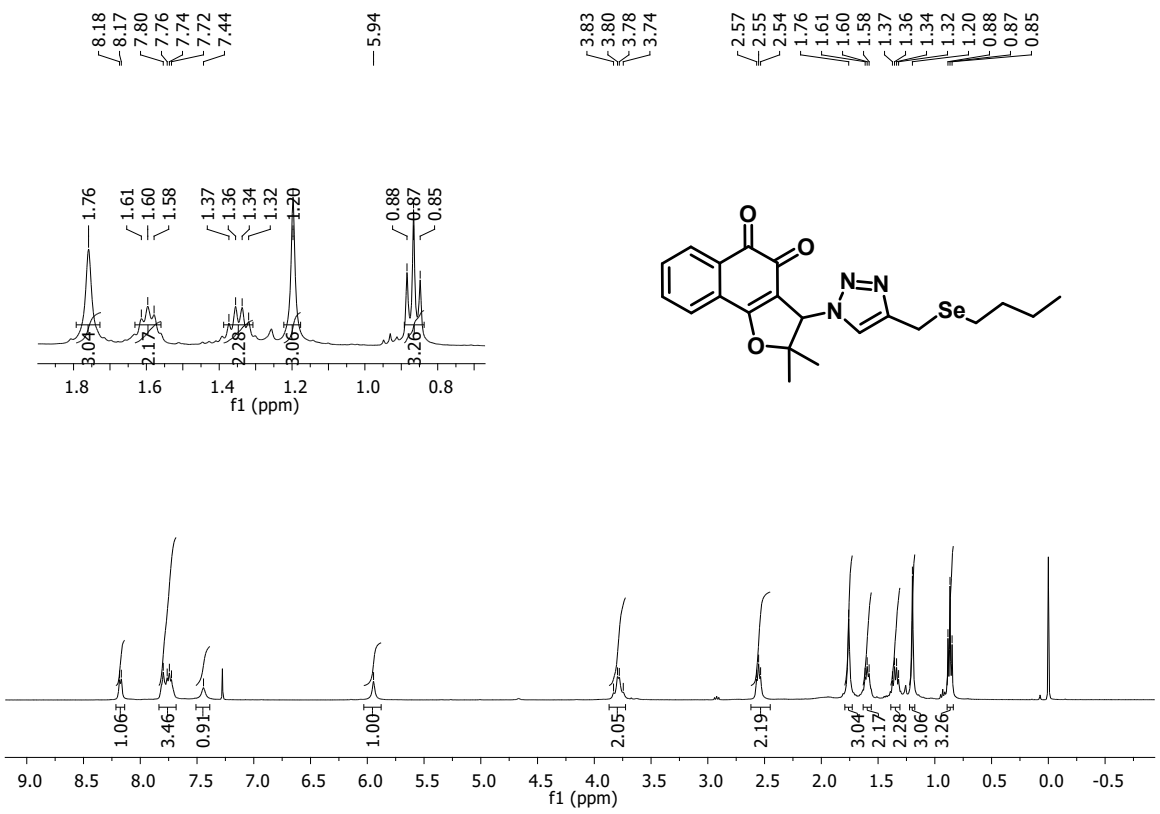


Figure S93. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **47**

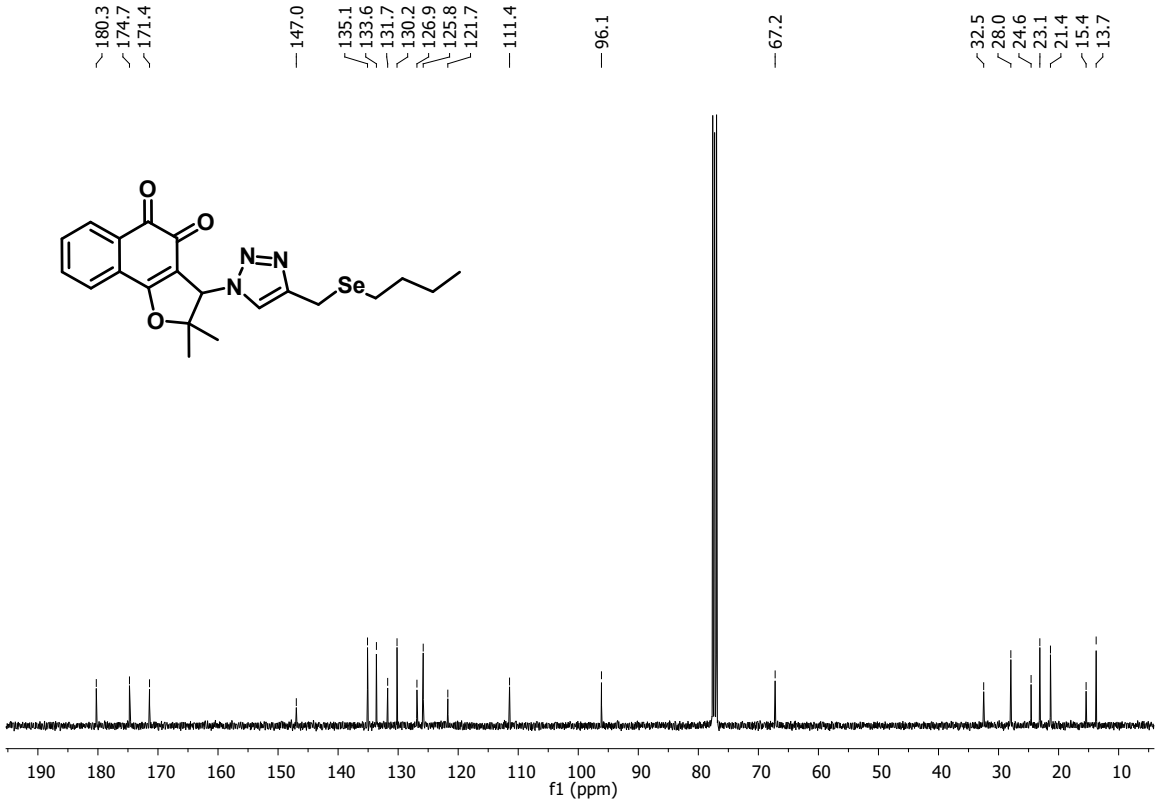


Figure S94. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **47**

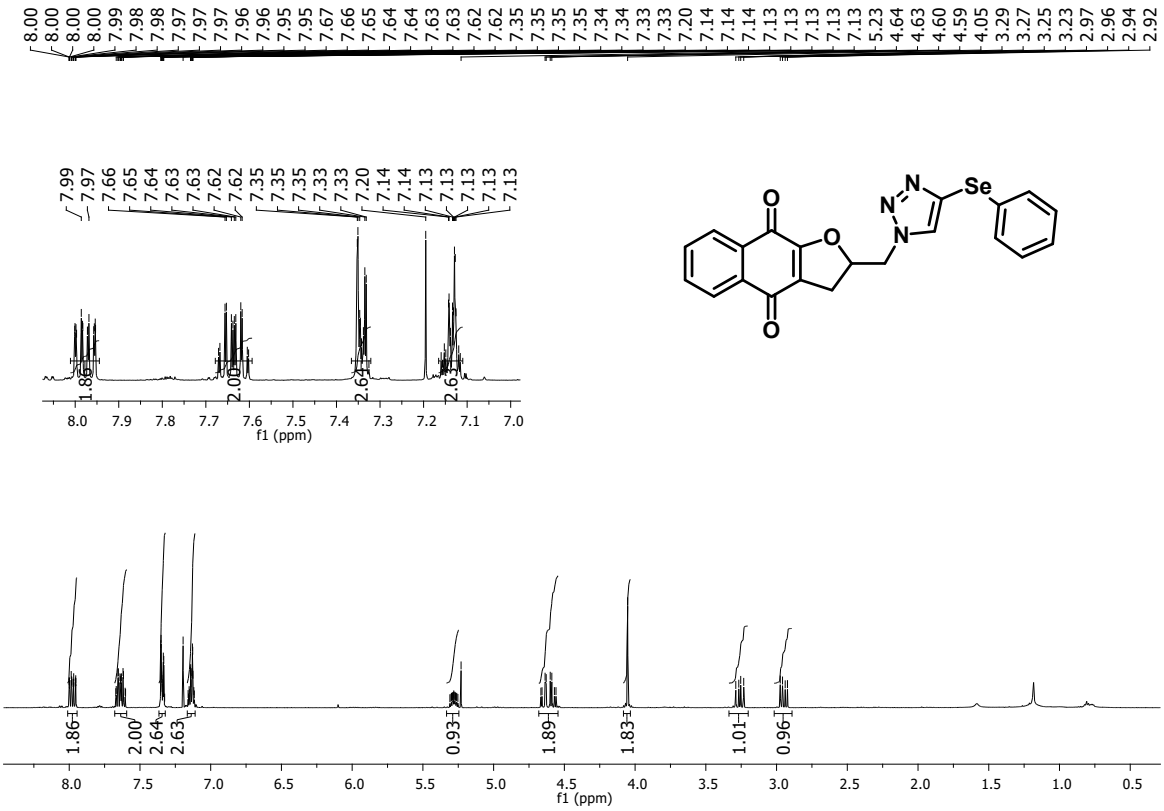


Figure S95. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **48**

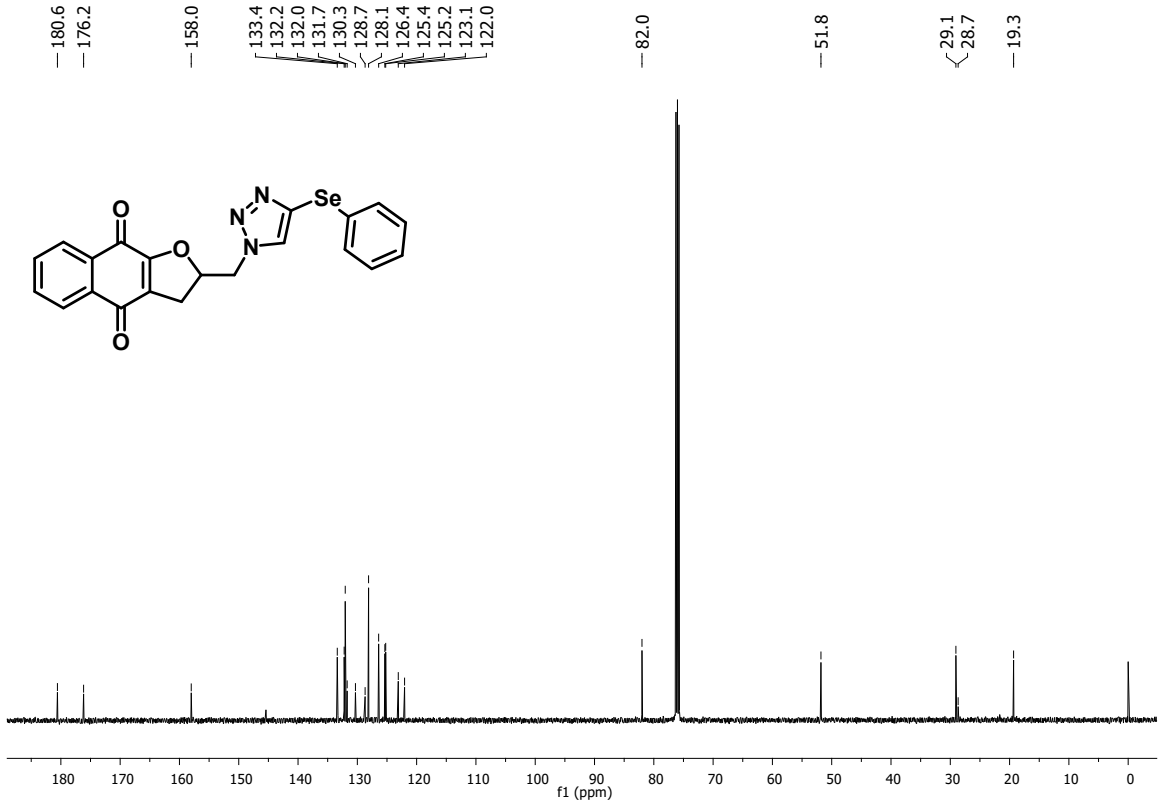


Figure S96. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **48**

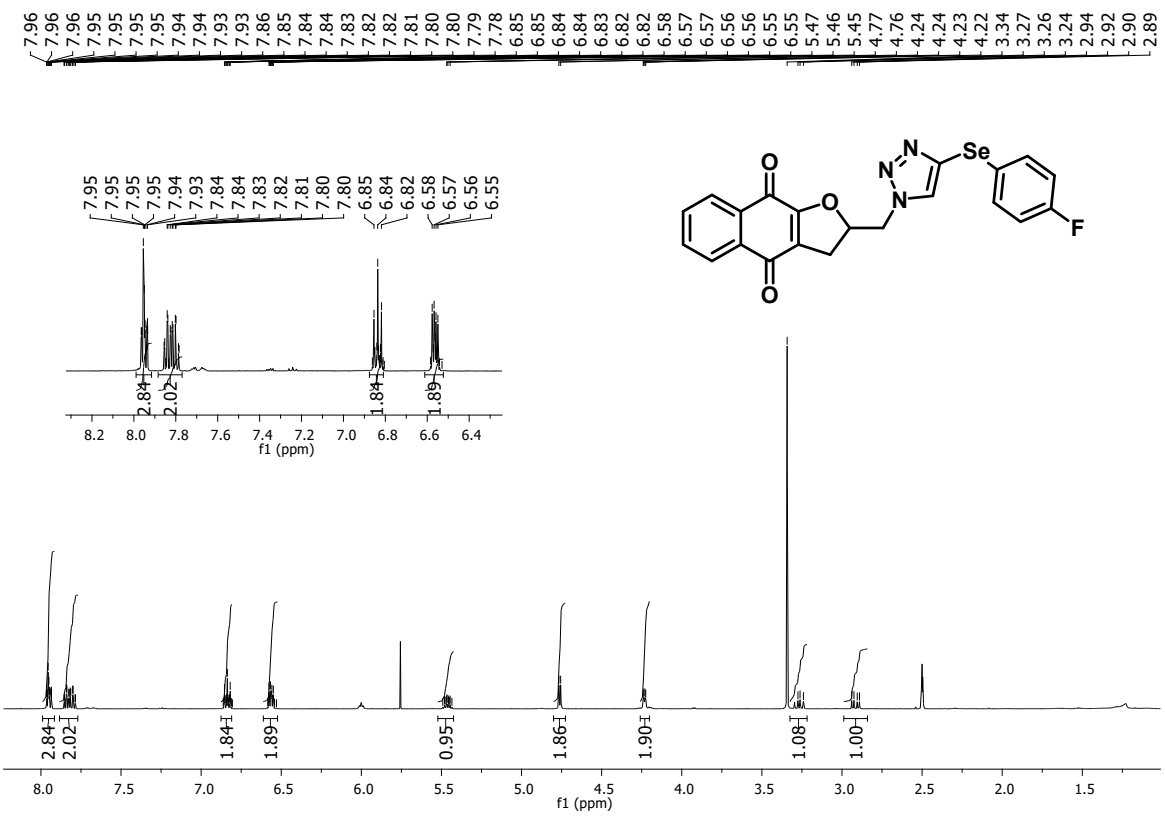


Figure S97. ^{1}H NMR Spectrum (400 MHz, DMSO-d_6) of **49**

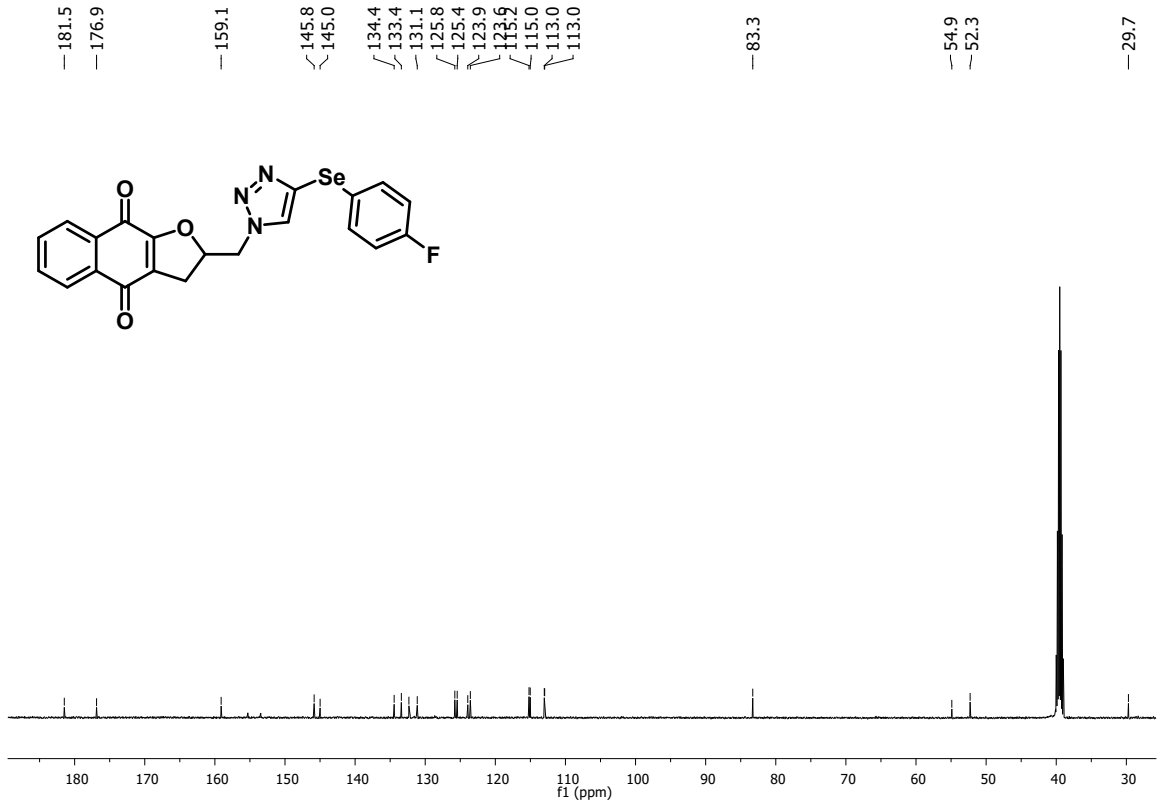


Figure S98. ^{13}C NMR Spectrum (100 MHz, DMSO-d_6) of **49**

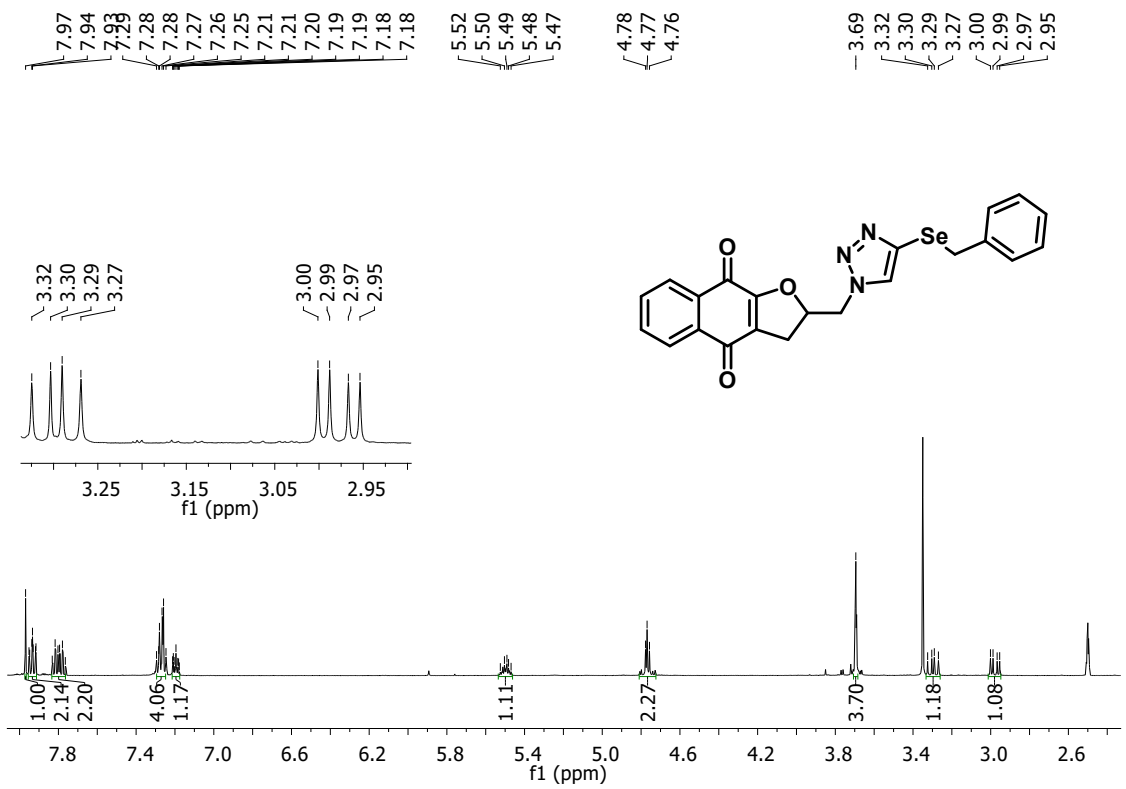


Figure S99. [1]H NMR Spectrum (400 MHz, DMSO-d_6) of **50**

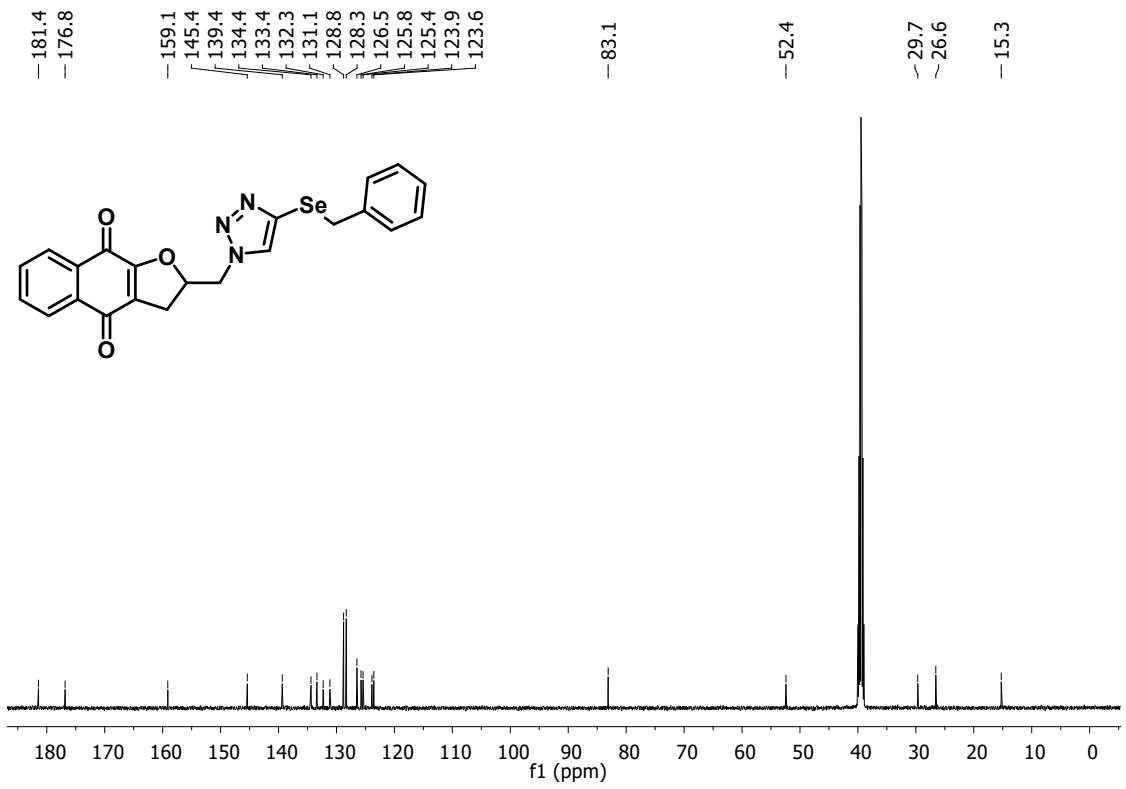


Figure S100. [13]C NMR Spectrum (100 MHz, DMSO-d_6) of **50**

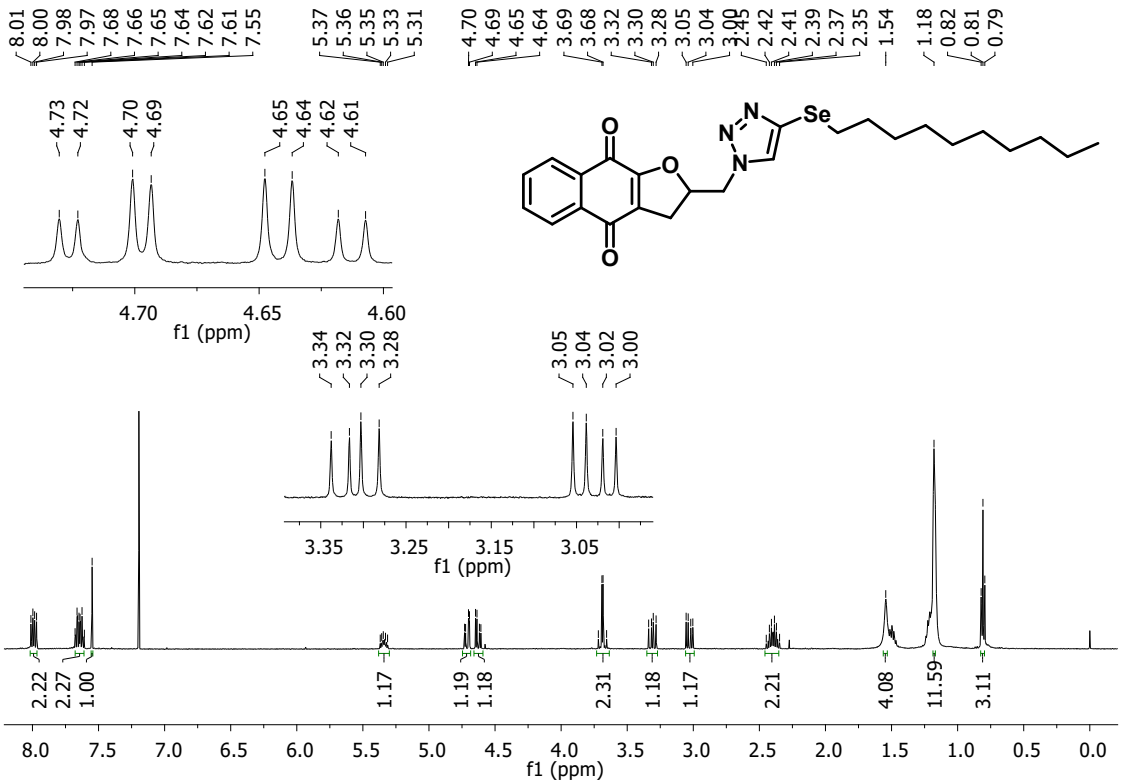


Figure S101. ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of **51**

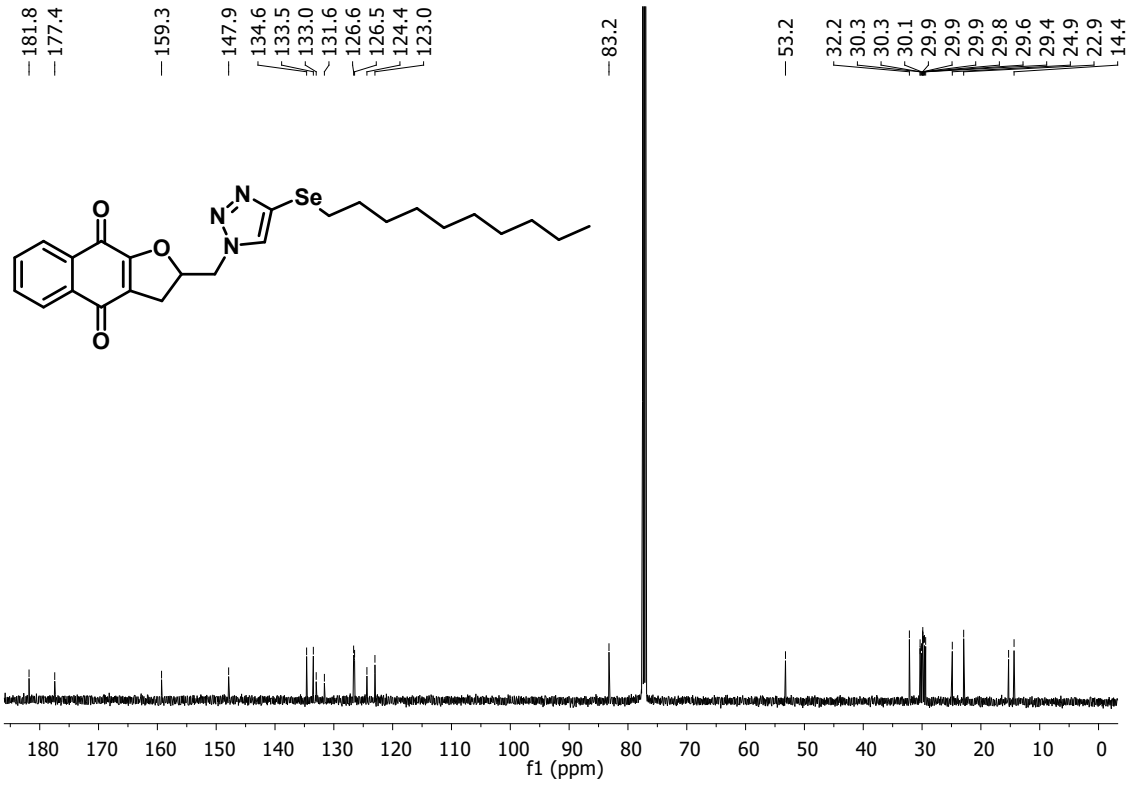


Figure S102. ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) of **51**

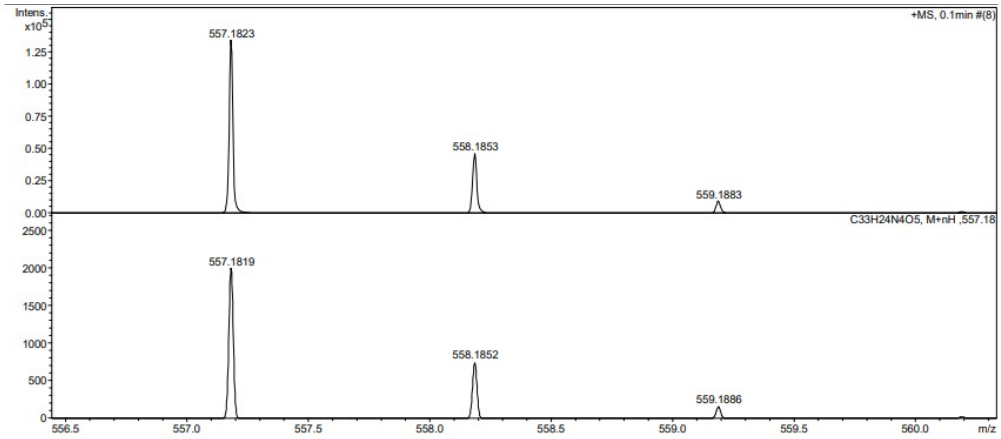


Figure S103. HRMS (ESI+) of **1**

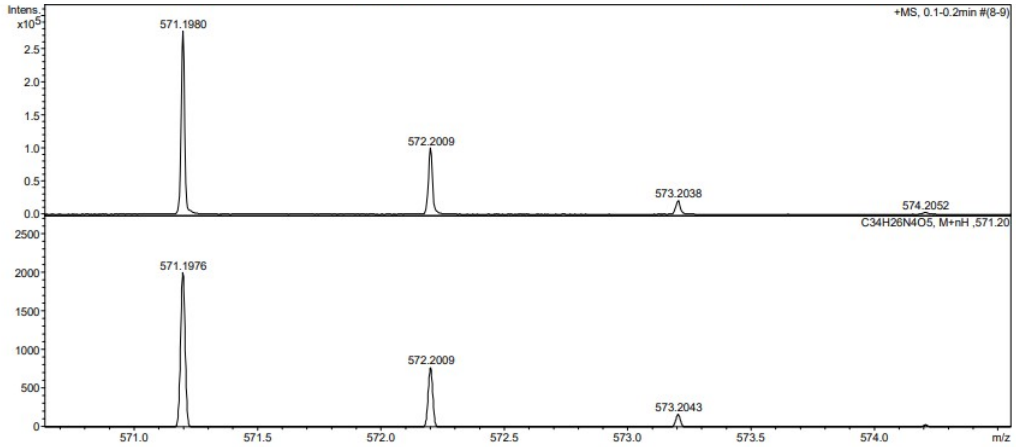


Figure S104. HRMS (ESI+) of **2**

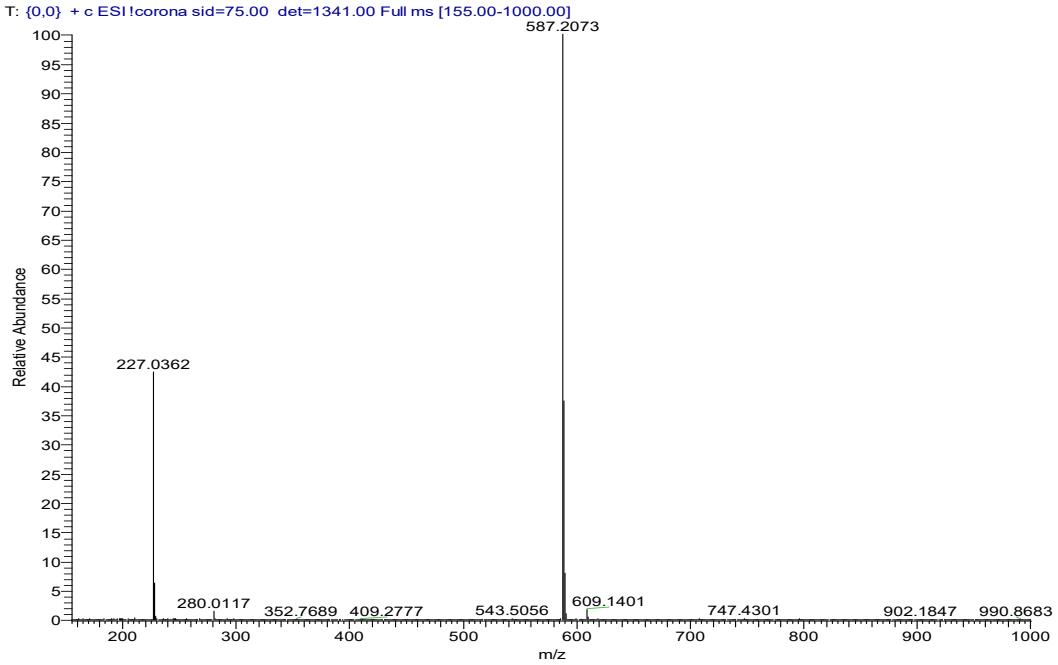


Figure S105. HRMS (ESI+) of **3**

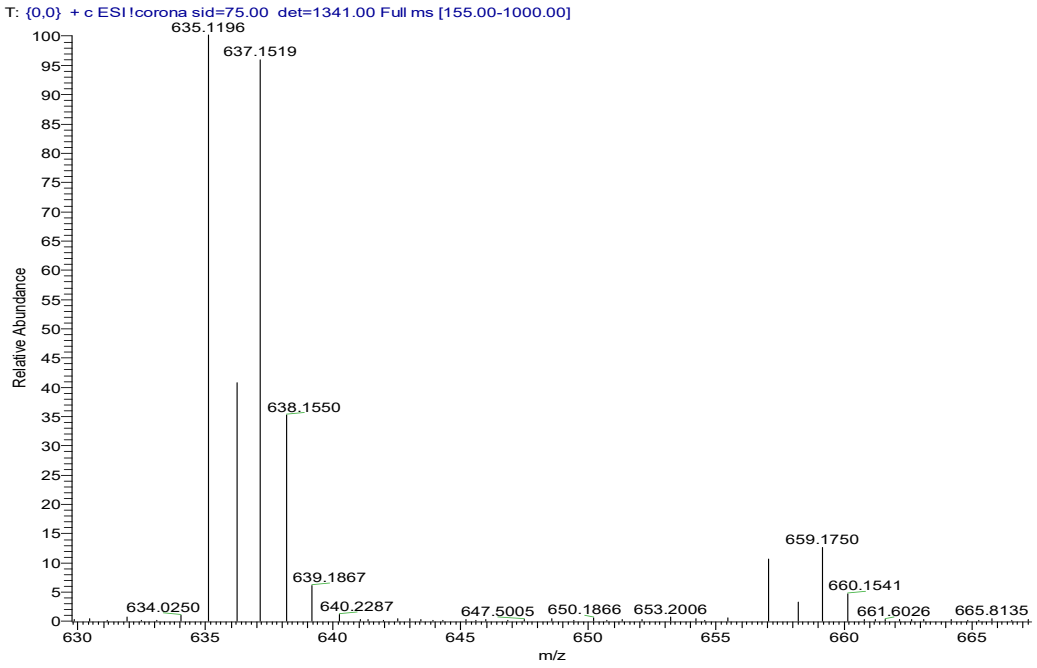


Figure S106. HRMS (ESI+) of **4**

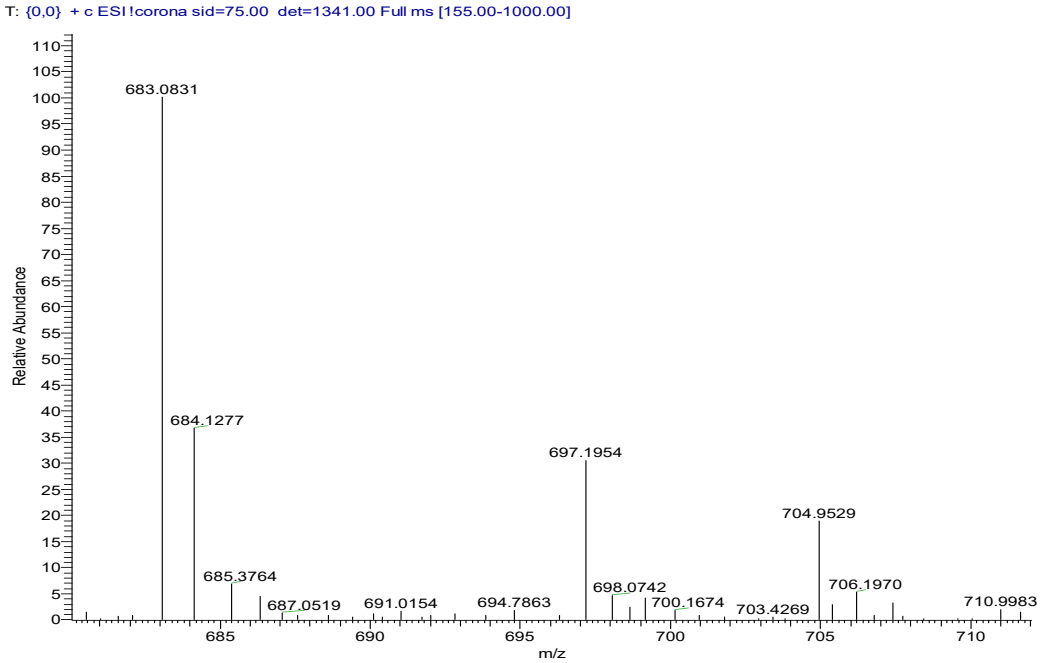


Figure S107. HRMS (ESI+) of **5**

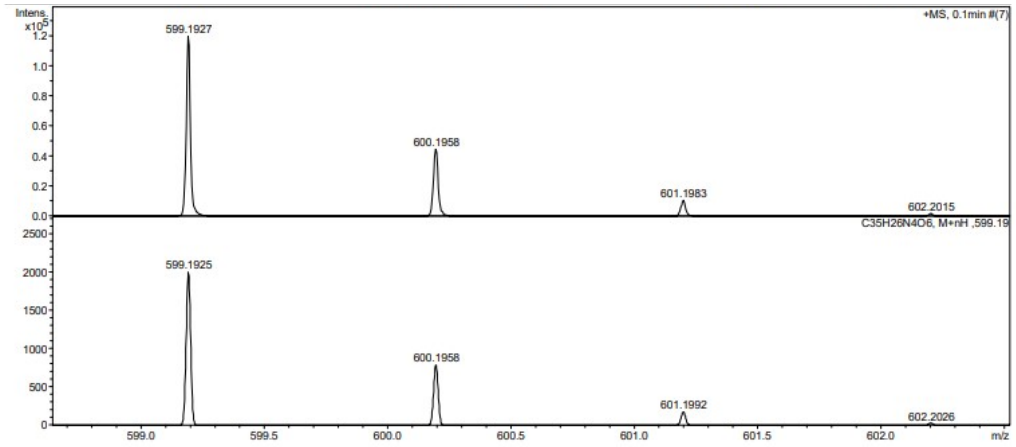


Figure S108. HRMS (ESI+) of **6**

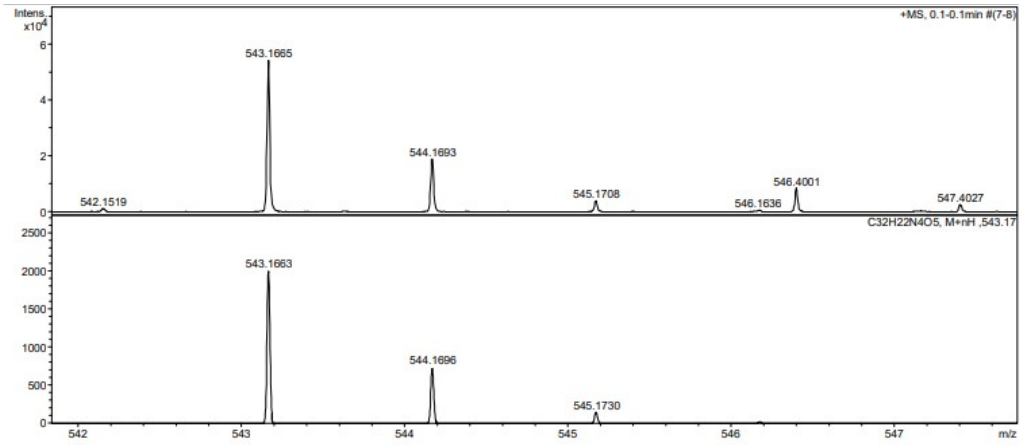


Figure S109. HRMS (ESI+) of **7**

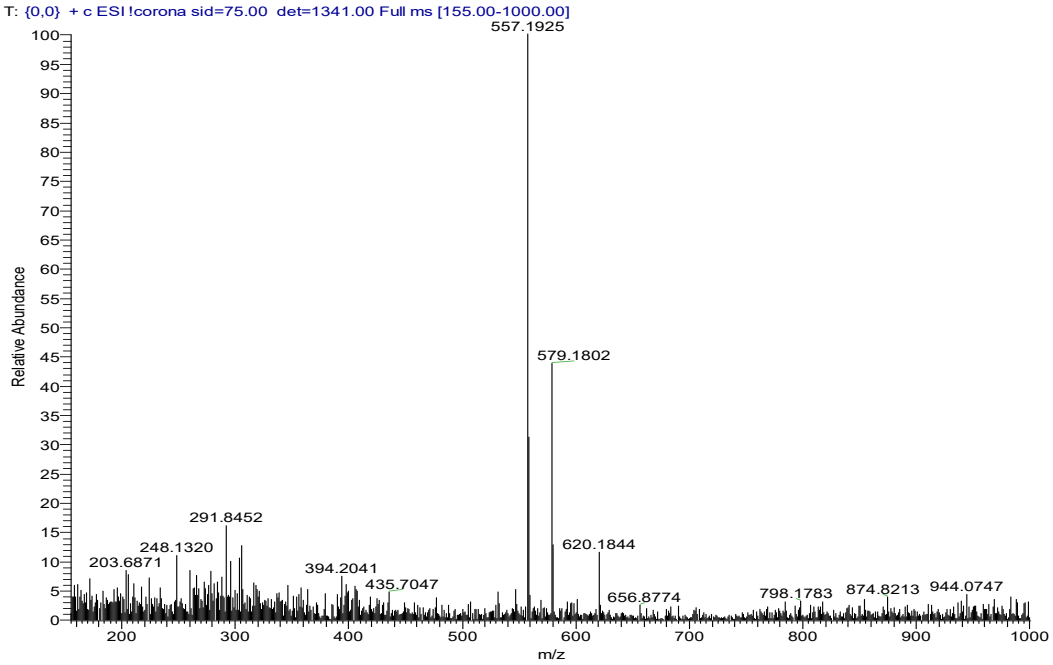


Figure S110. HRMS (ESI+) of **8**

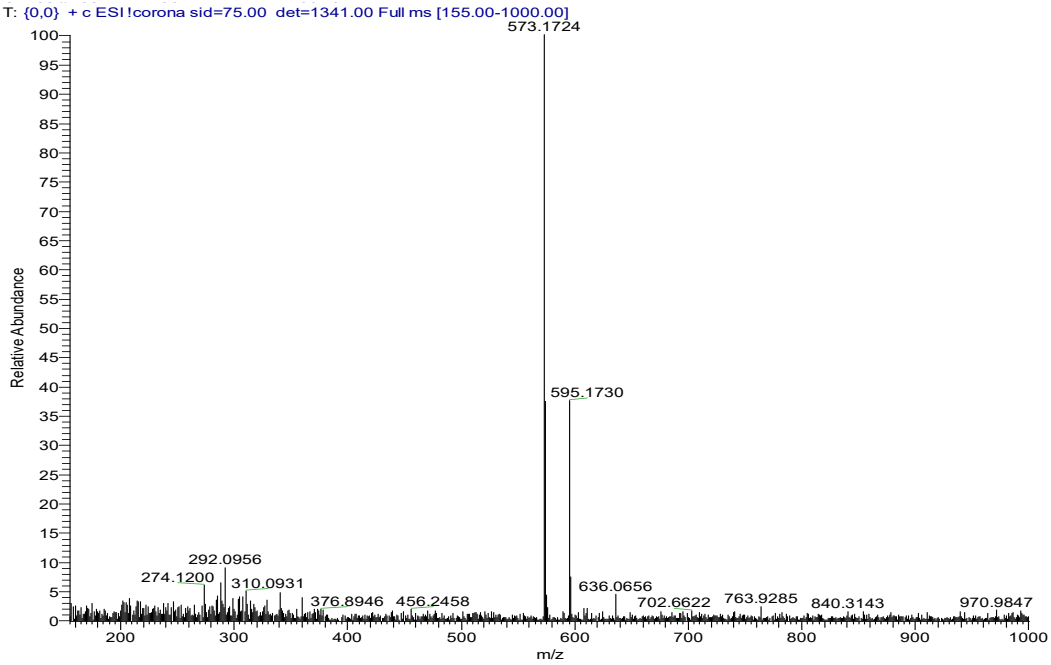


Figure S111. HRMS (ESI+) of **9**

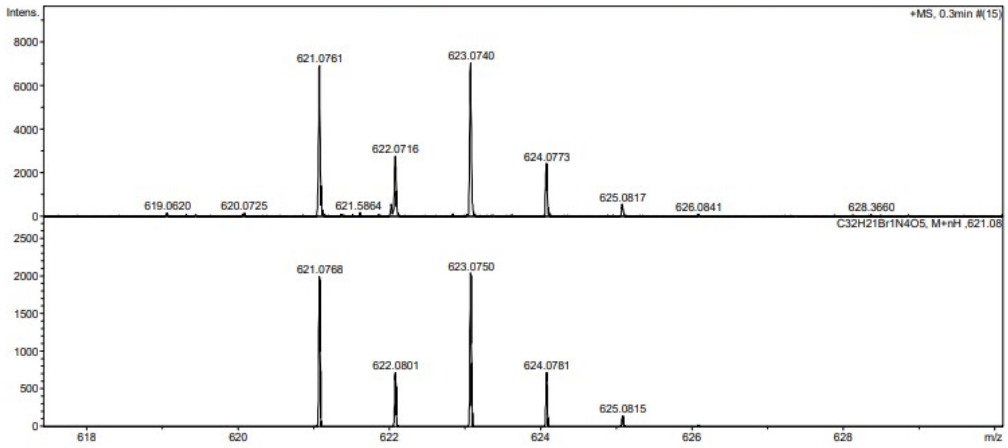


Figure S112. HRMS (ESI+) of **10**

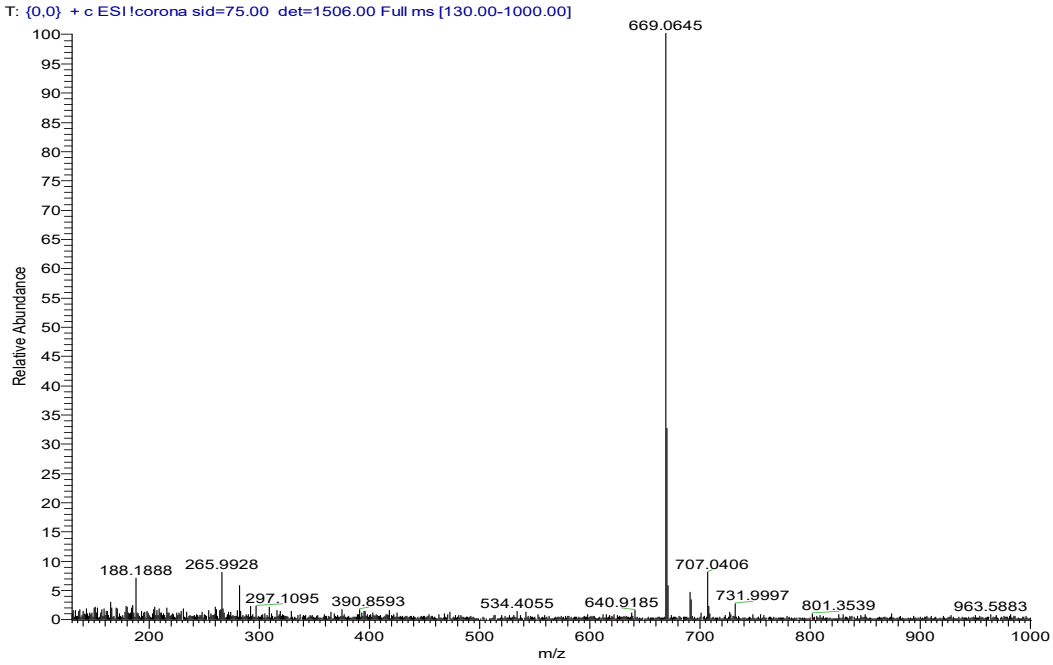


Figure S113. HRMS (ESI+) of **11**

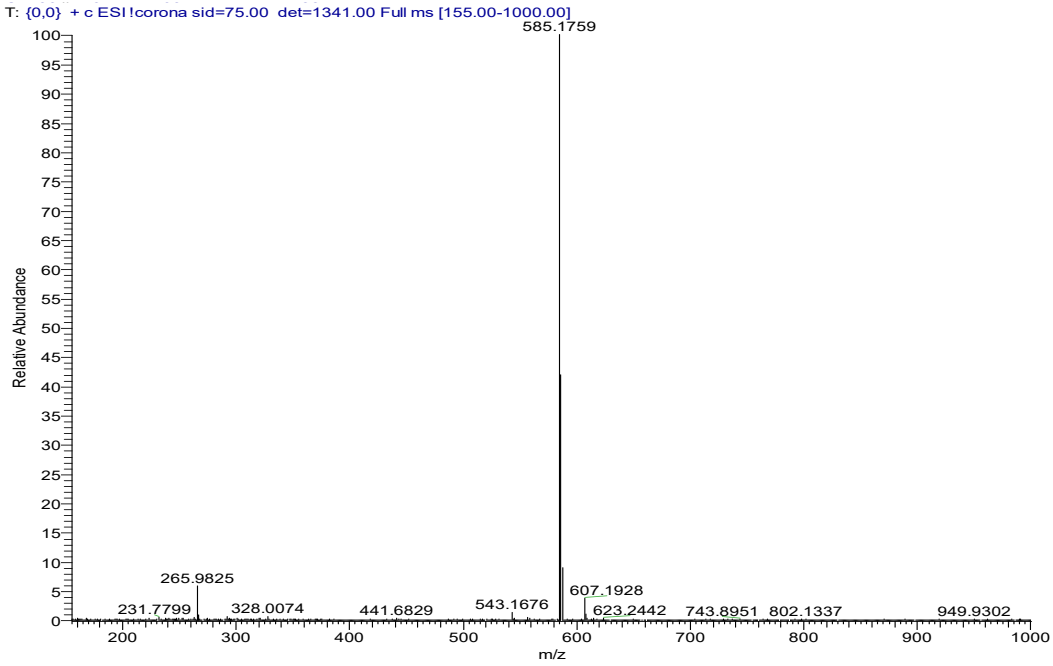


Figure S114. HRMS (ESI+) of **12**

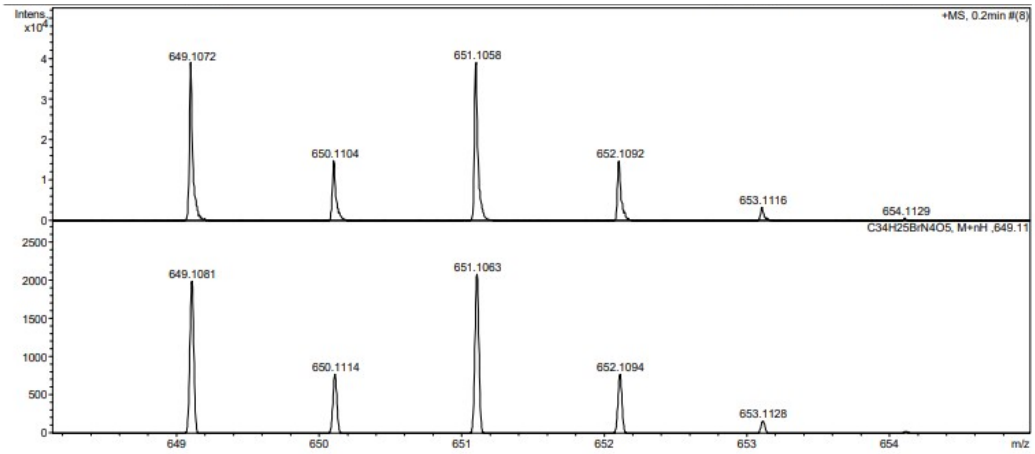


Figure S115. HRMS (ESI+) of **13**

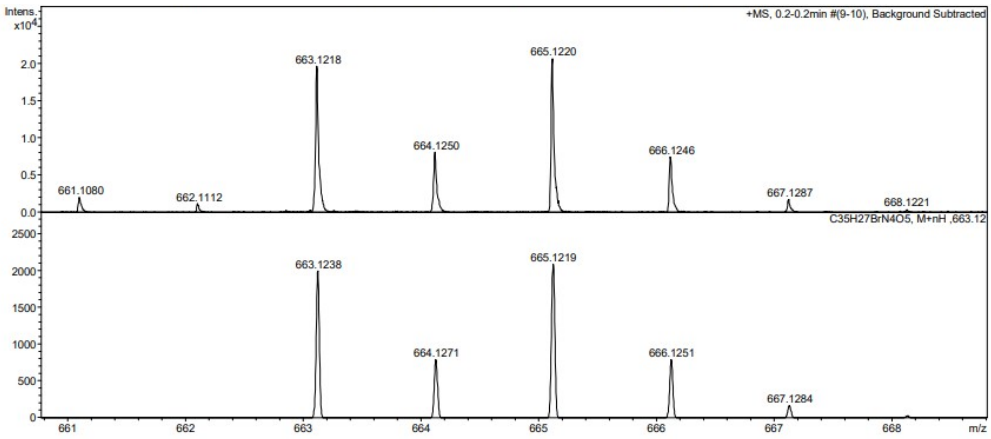


Figure S116. HRMS (ESI+) of **14**

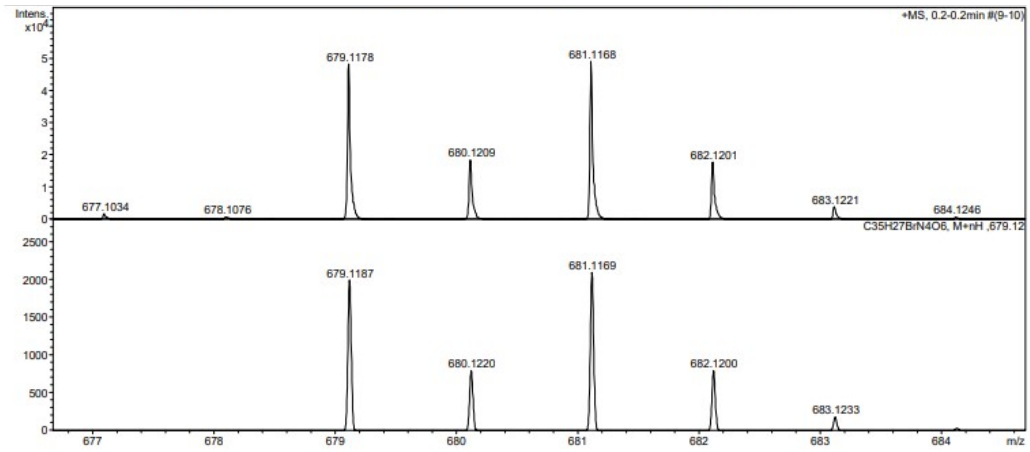


Figure S117. HRMS (ESI+) of **15**

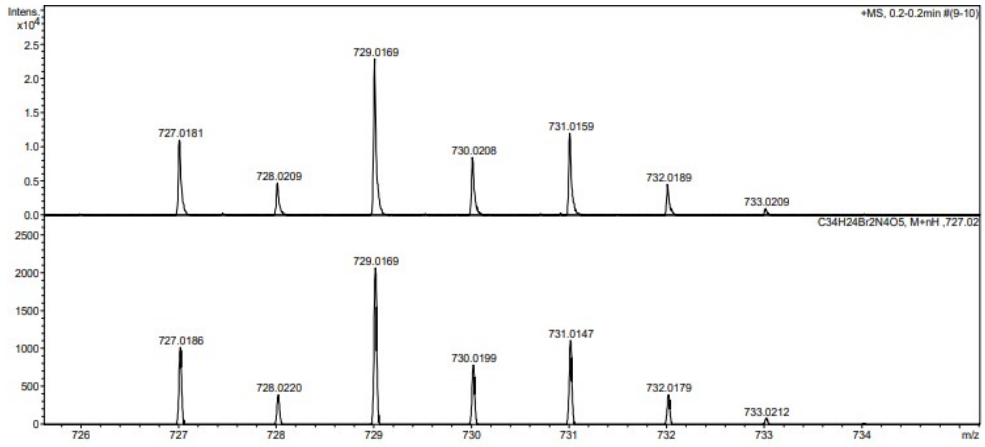


Figure S118. HRMS (ESI+) of **16**

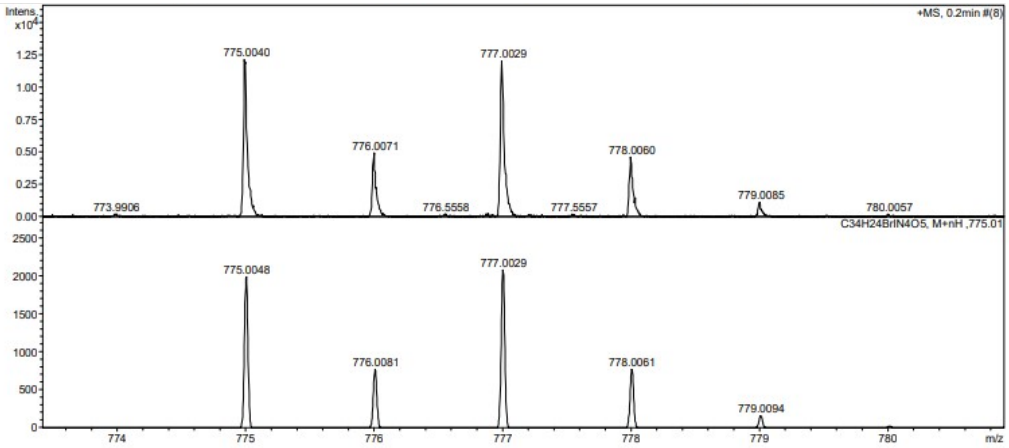


Figure S119. HRMS (ESI+) of **17**

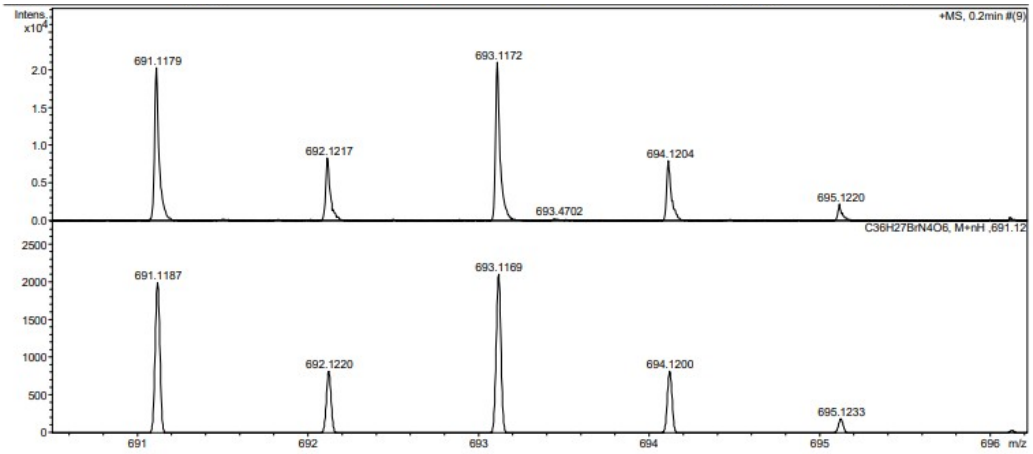


Figure S120. HRMS (ESI+) of **18**

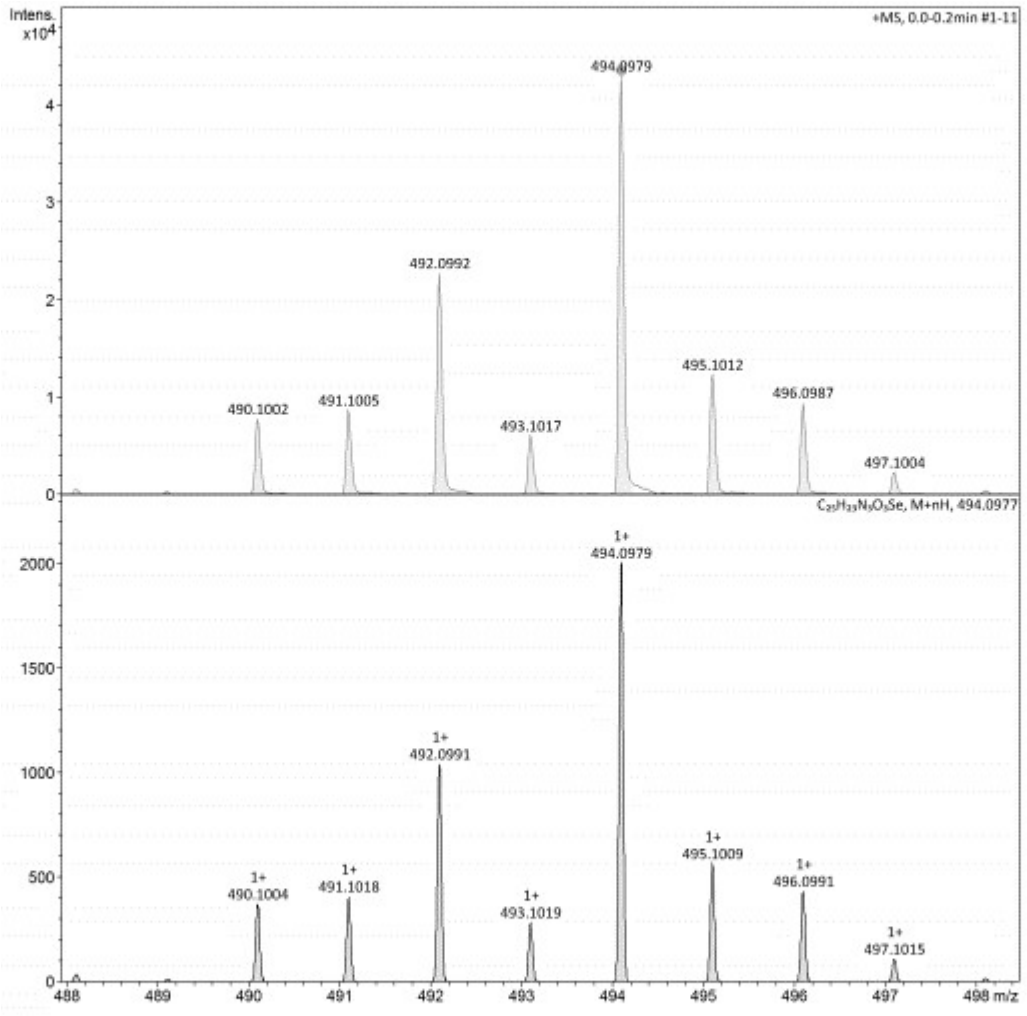


Figure S121. HRMS (APPI$^+$) of **21**

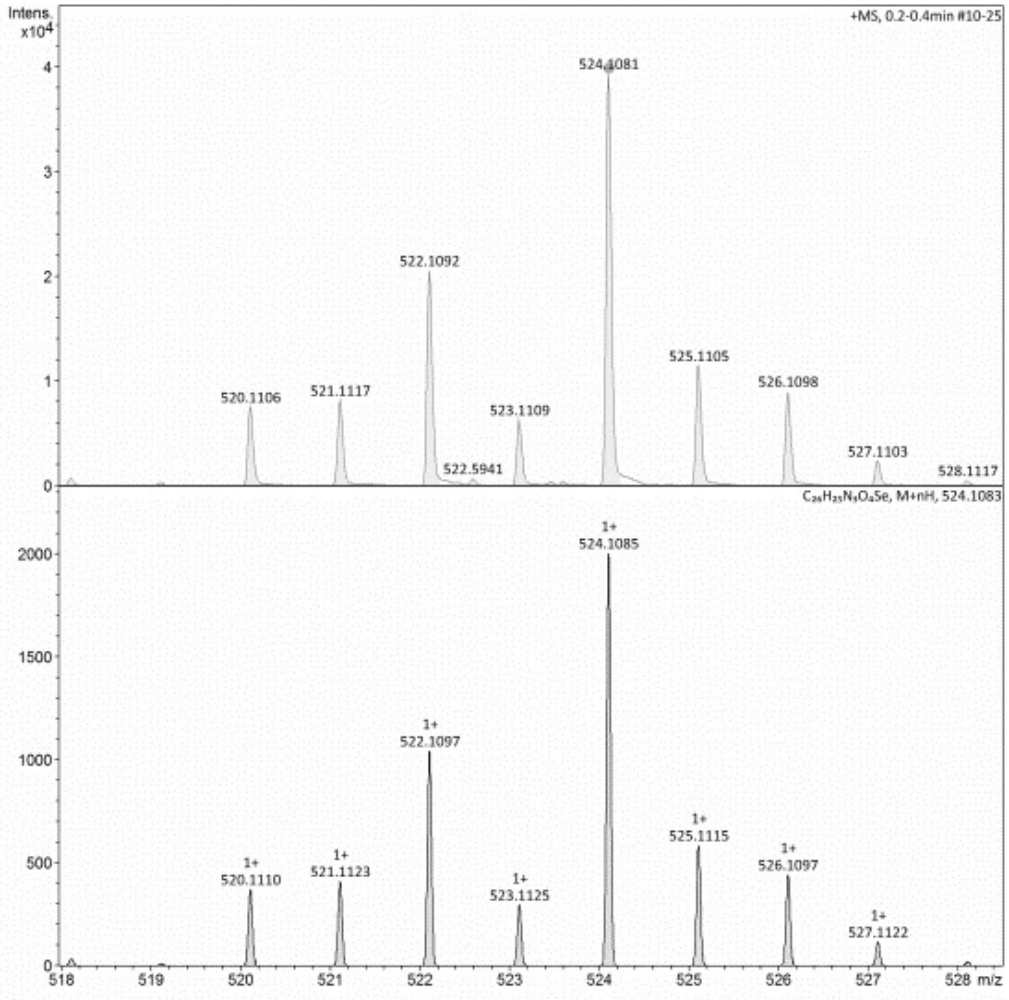


Figure S122. HRMS (APPI$^+$) of **22**

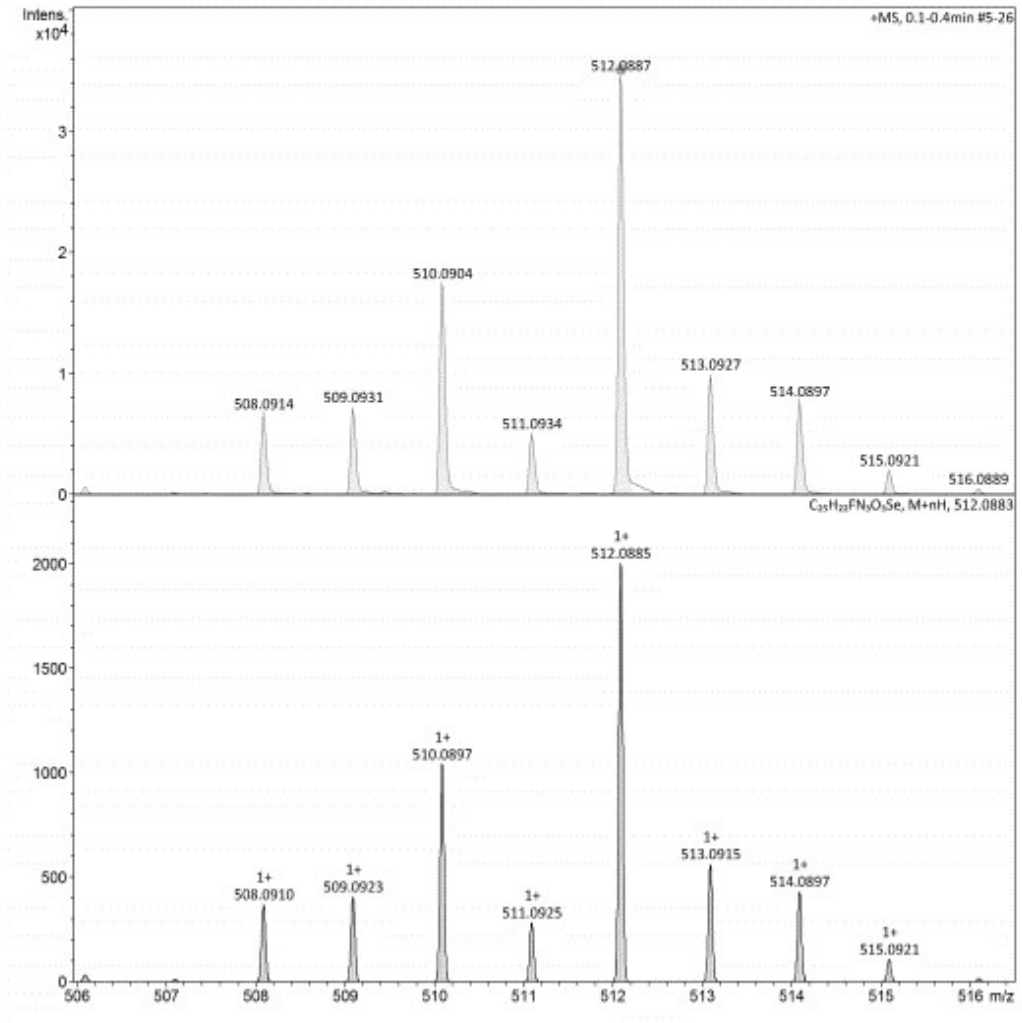


Figure S123. HRMS (APPI$^+$) of **24**

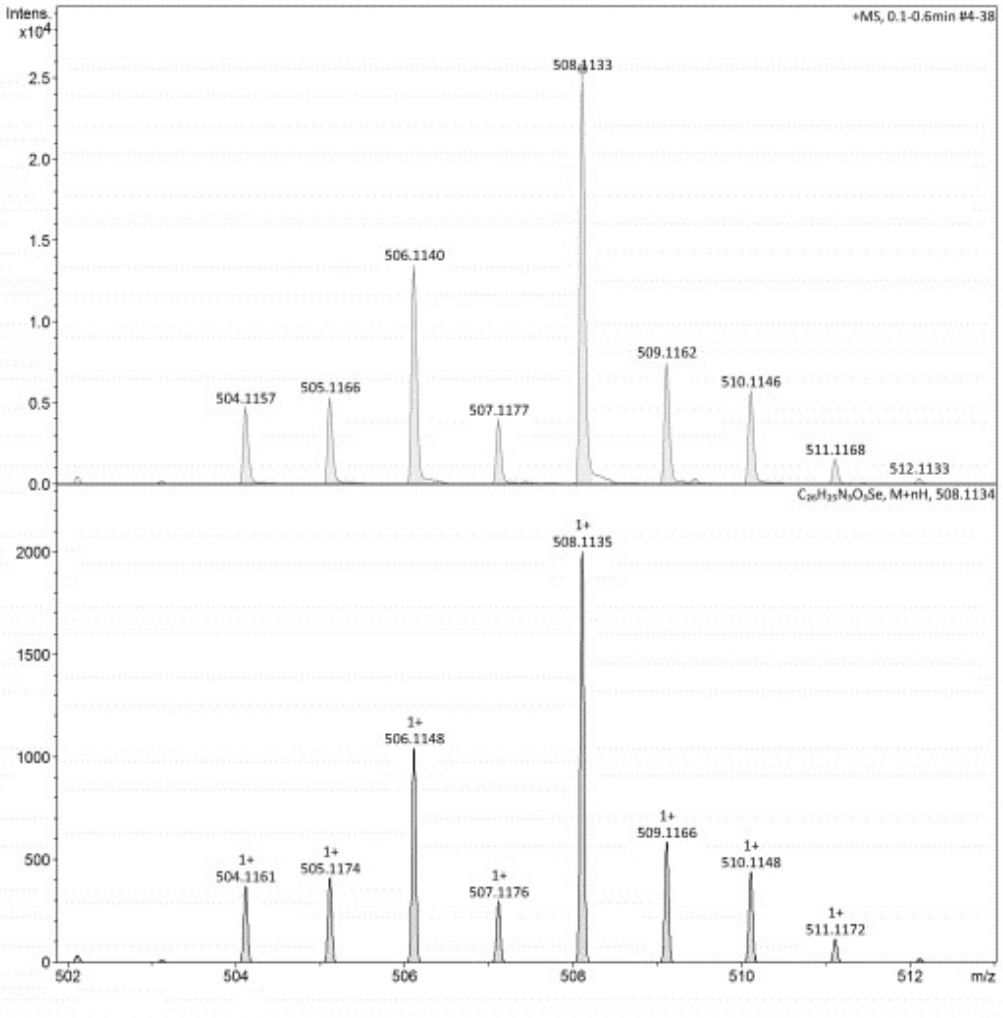


Figure S124. HRMS (APPI$^+$) of **25**

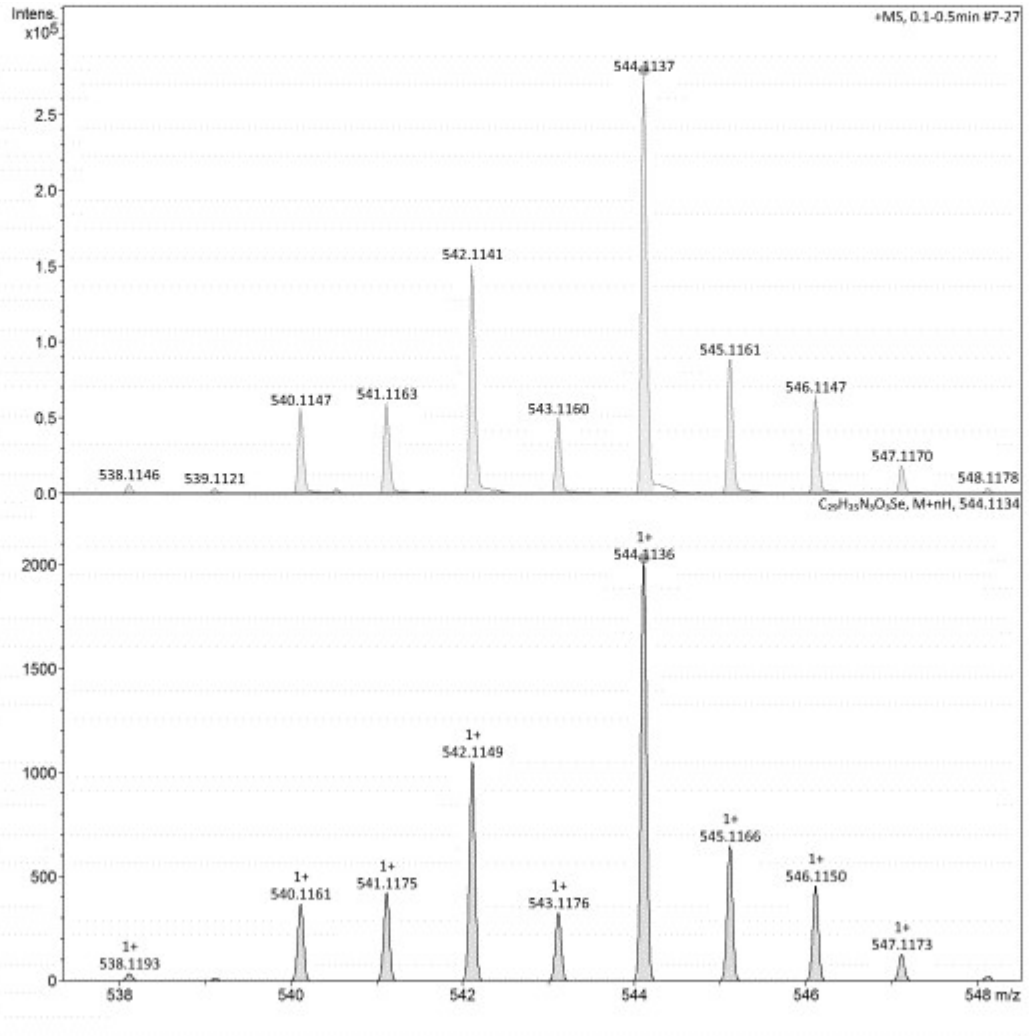


Figure S125. HRMS (APPI$^+$) of **26**

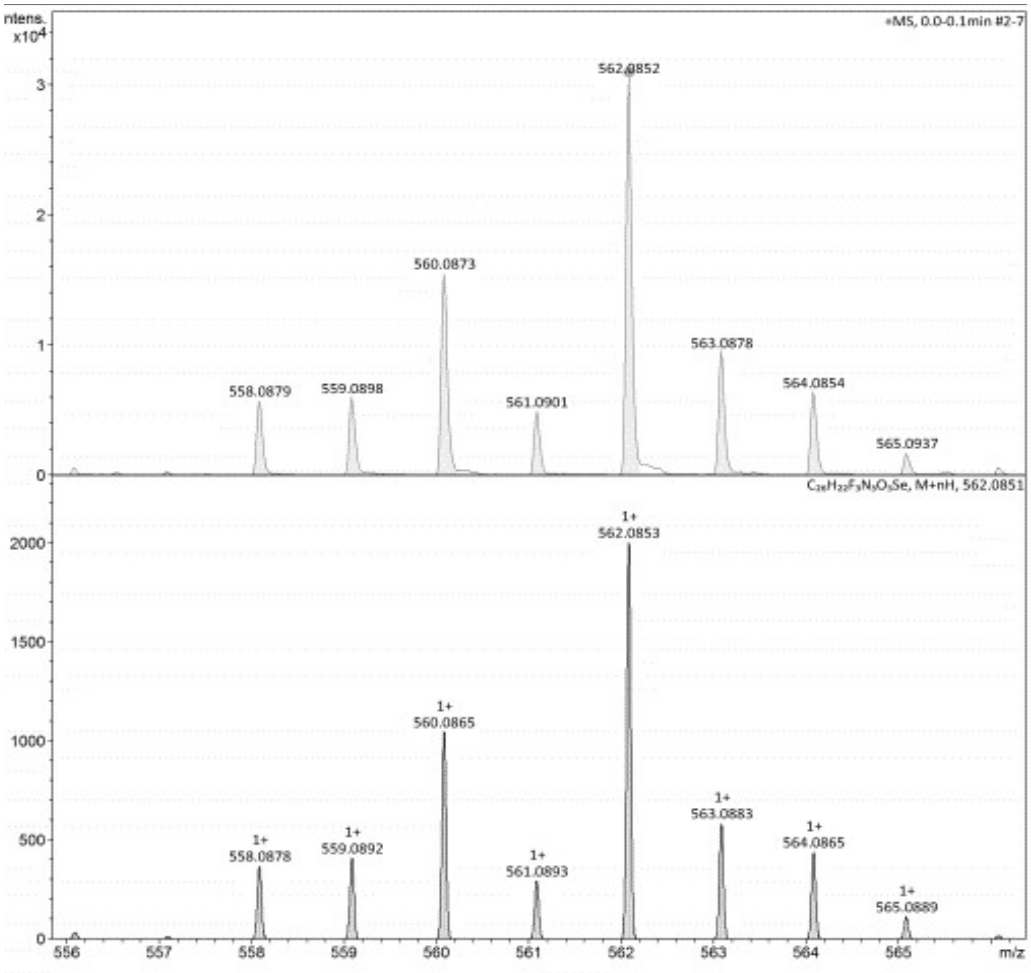


Figure S126. HRMS (APPI$^+$) of **27**

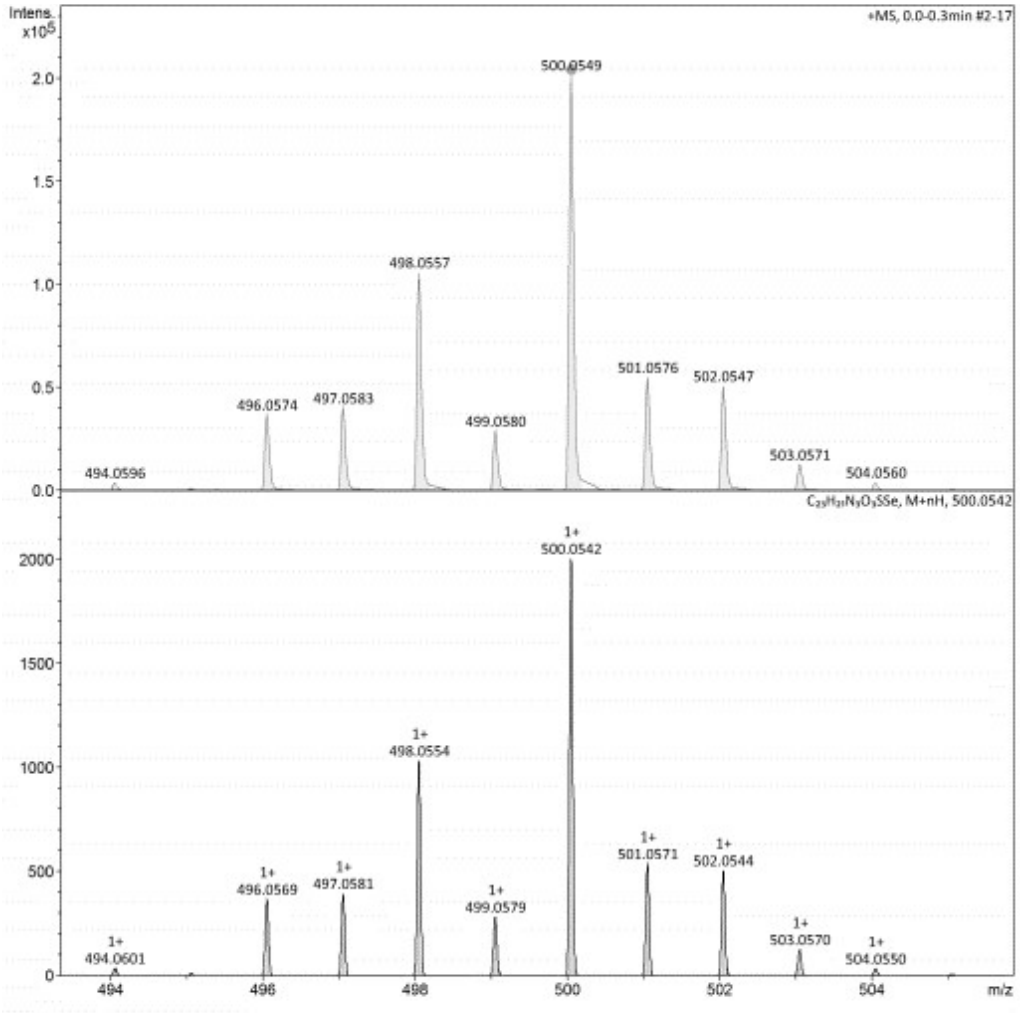


Figure S127. HRMS (APPI$^+$) of **28**

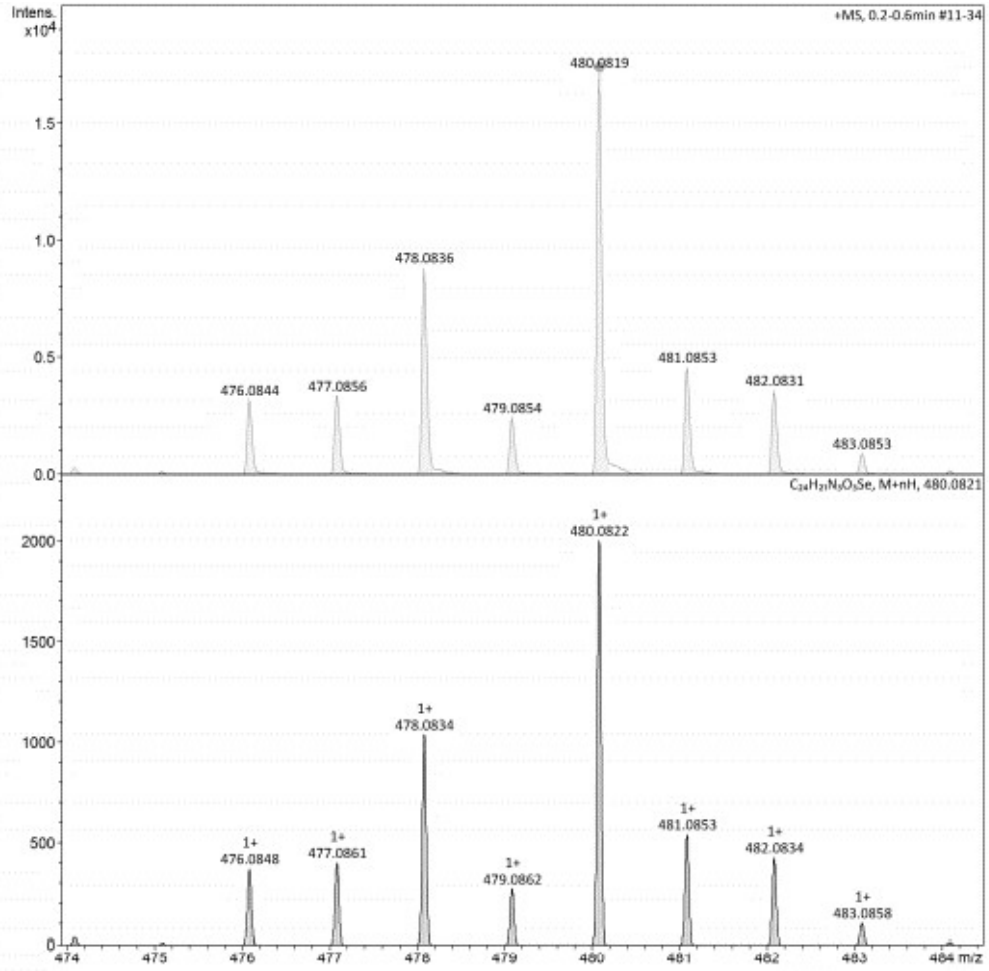


Figure S128. HRMS (APPI$^+$) of **31**

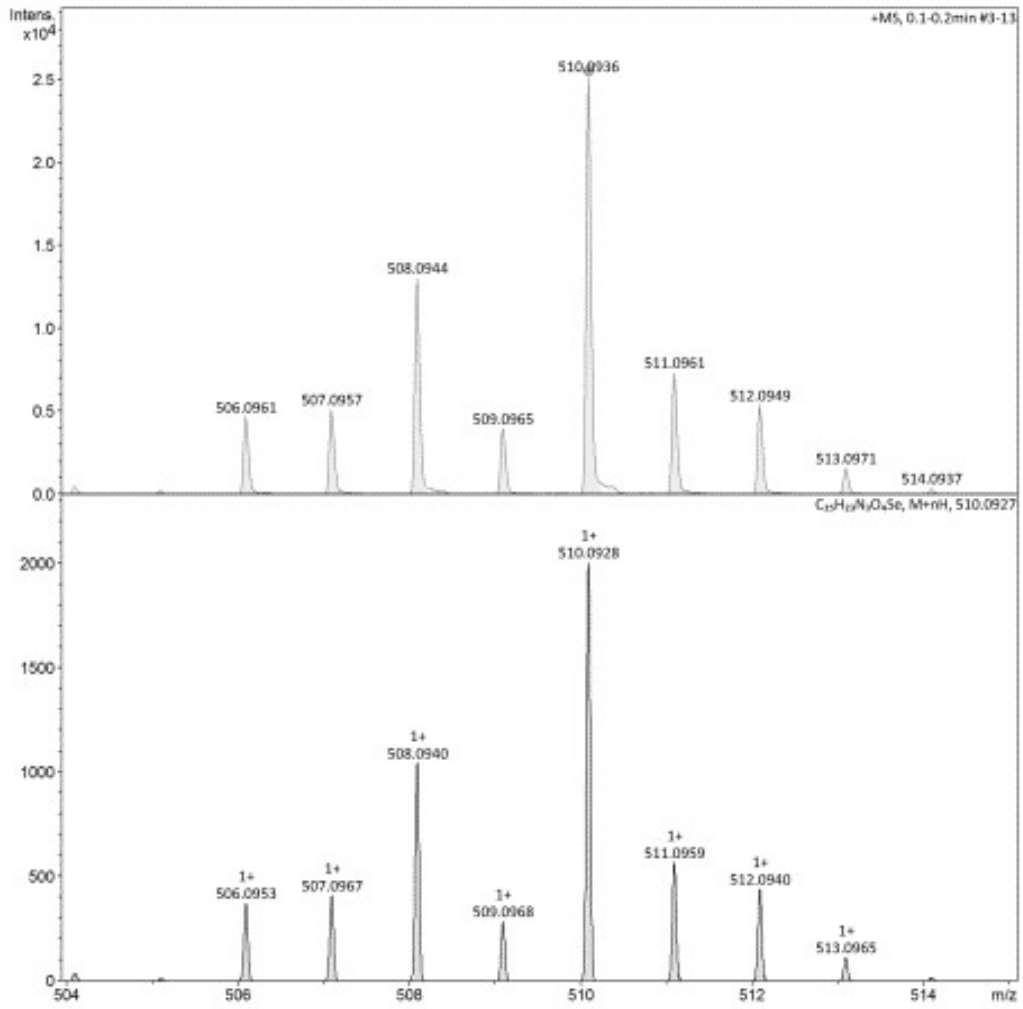


Figure S129. HRMS (APPI$^+$) of **32**

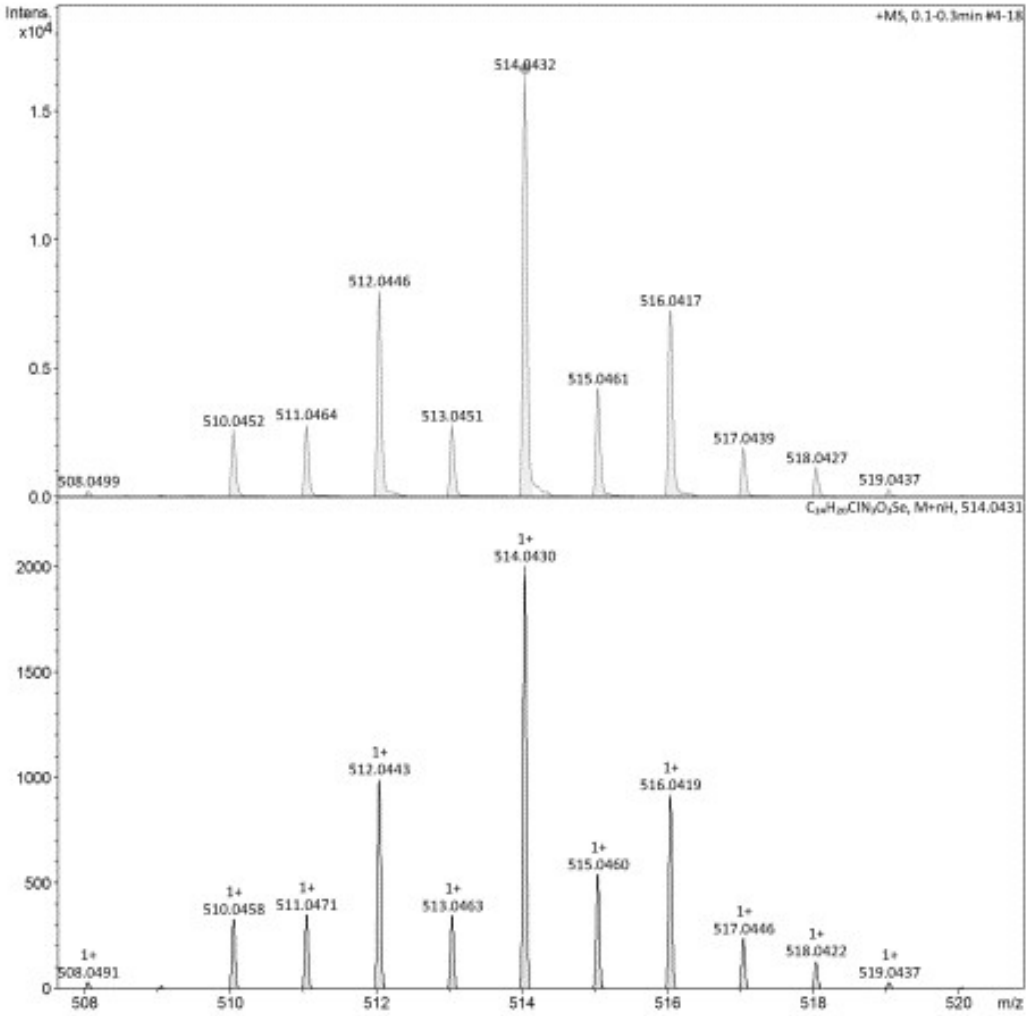


Figure S130. HRMS (APPI$^+$) of **33**

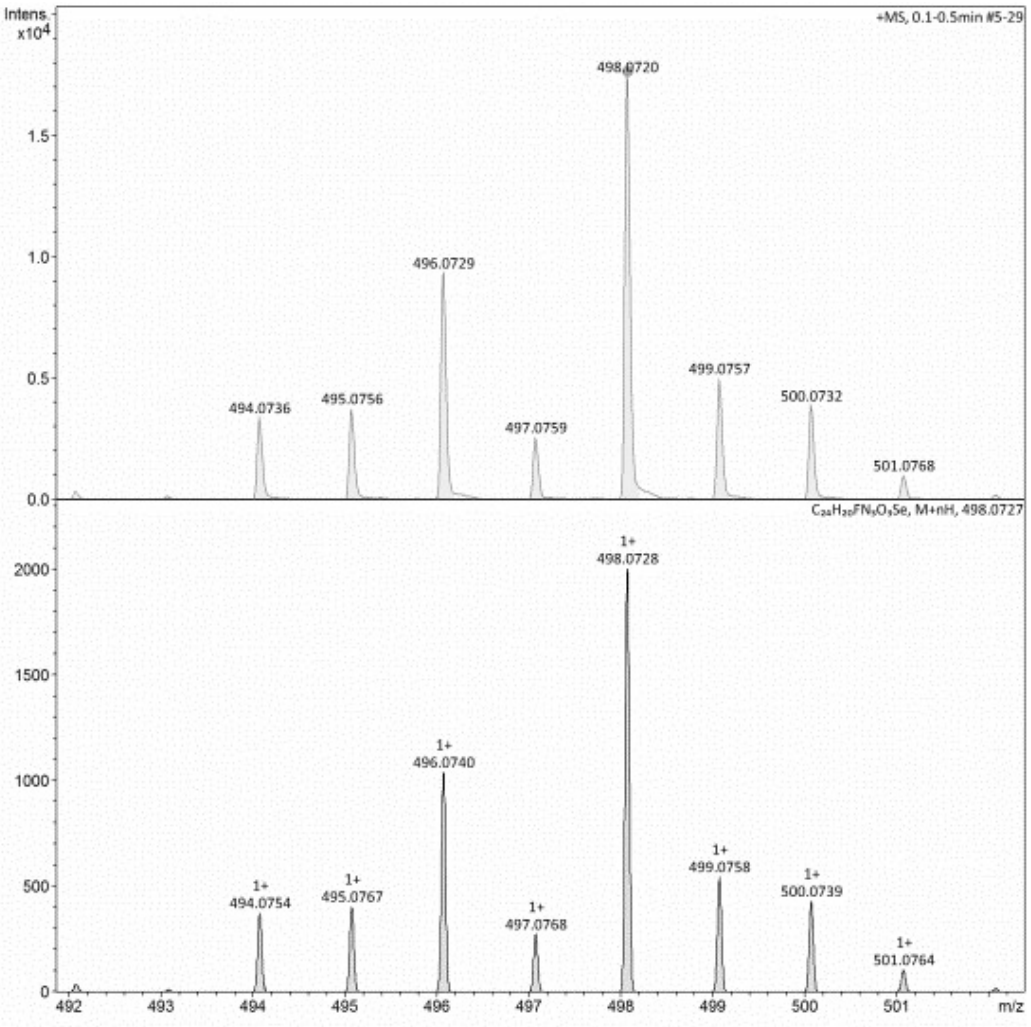


Figure S131. HRMS (APPI$^+$) of **34**

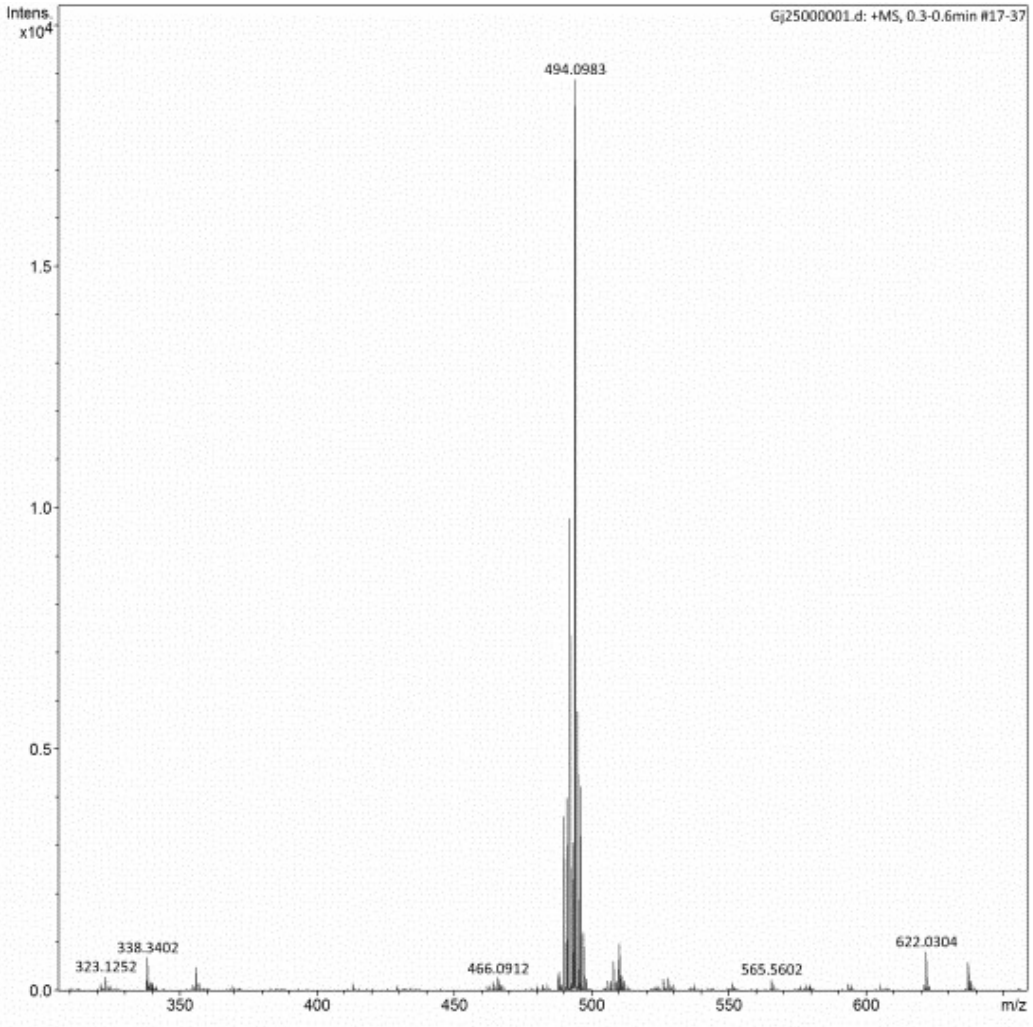


Figure S132. HRMS (APPI$^+$) of **35**

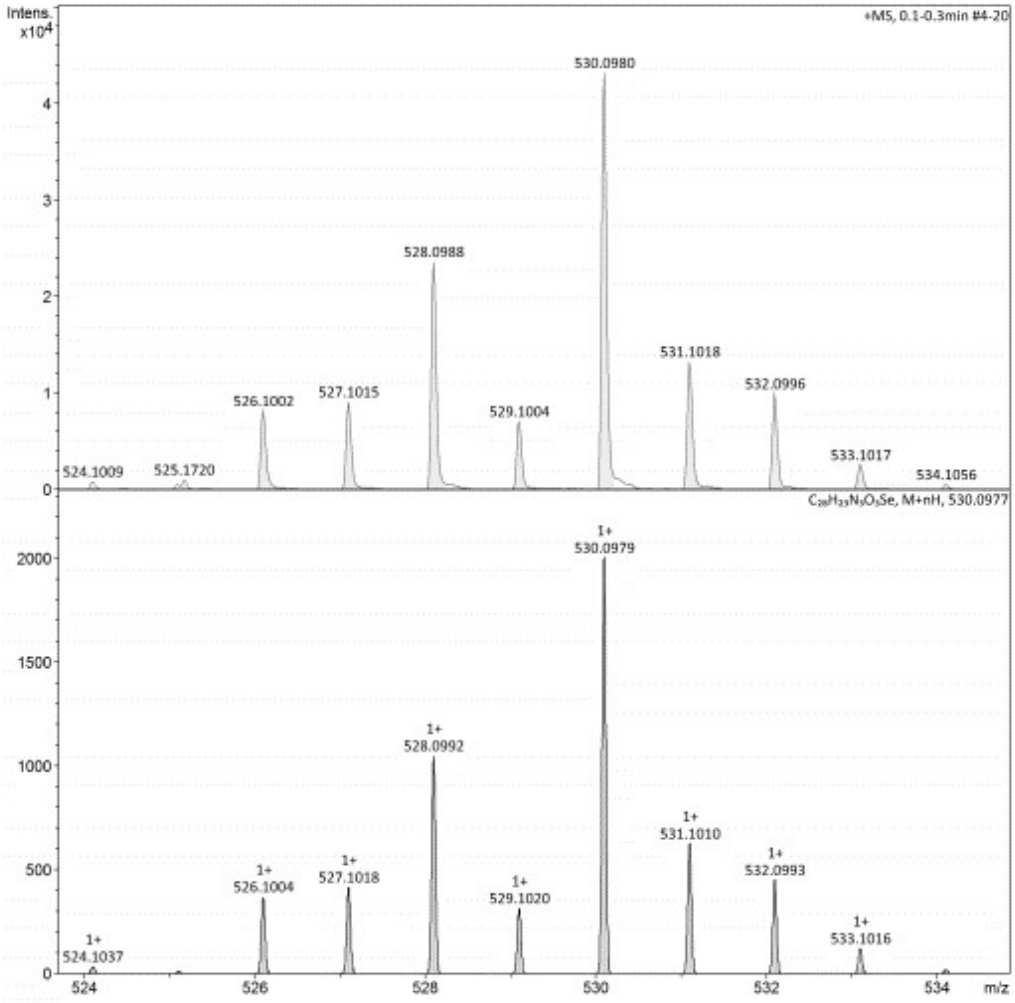


Figure S133. HRMS (APPI$^+$) of **36**

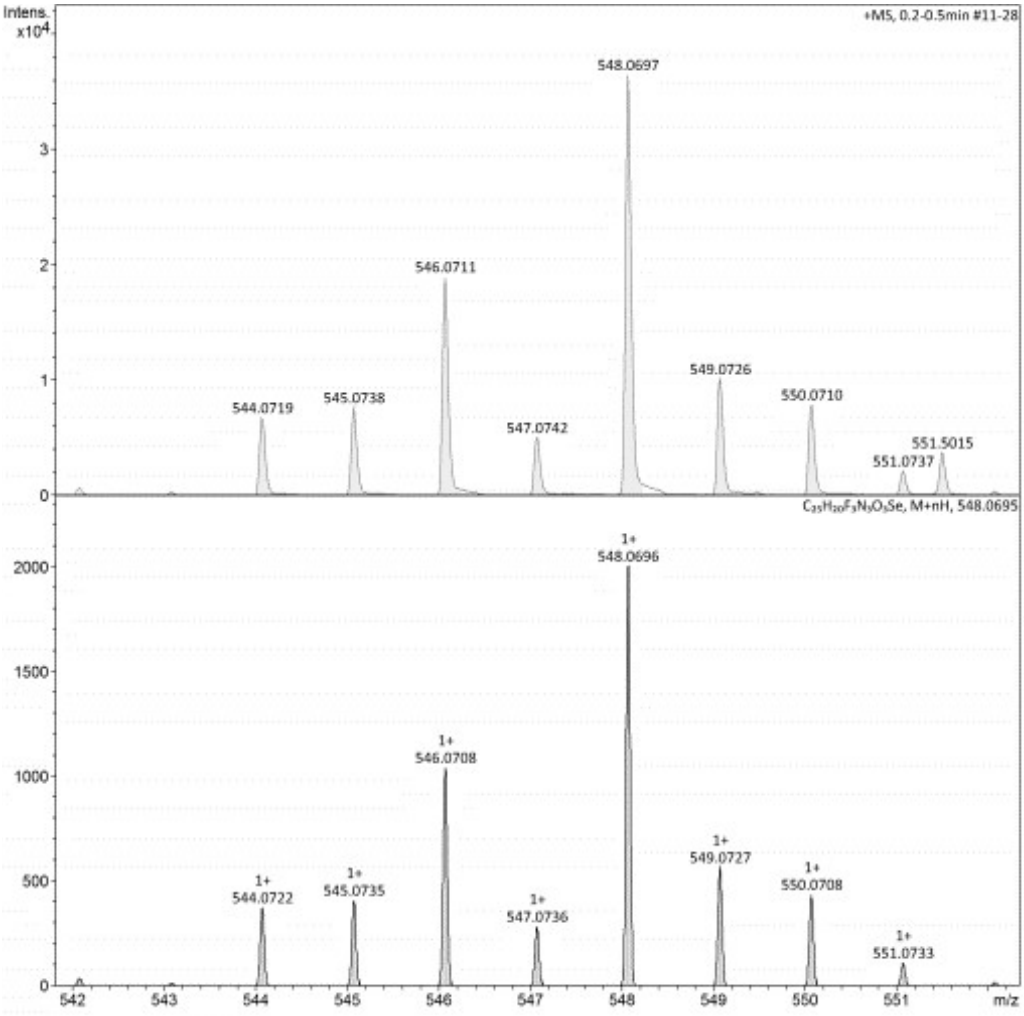


Figure S134. HRMS (APPI$^+$) of **37**

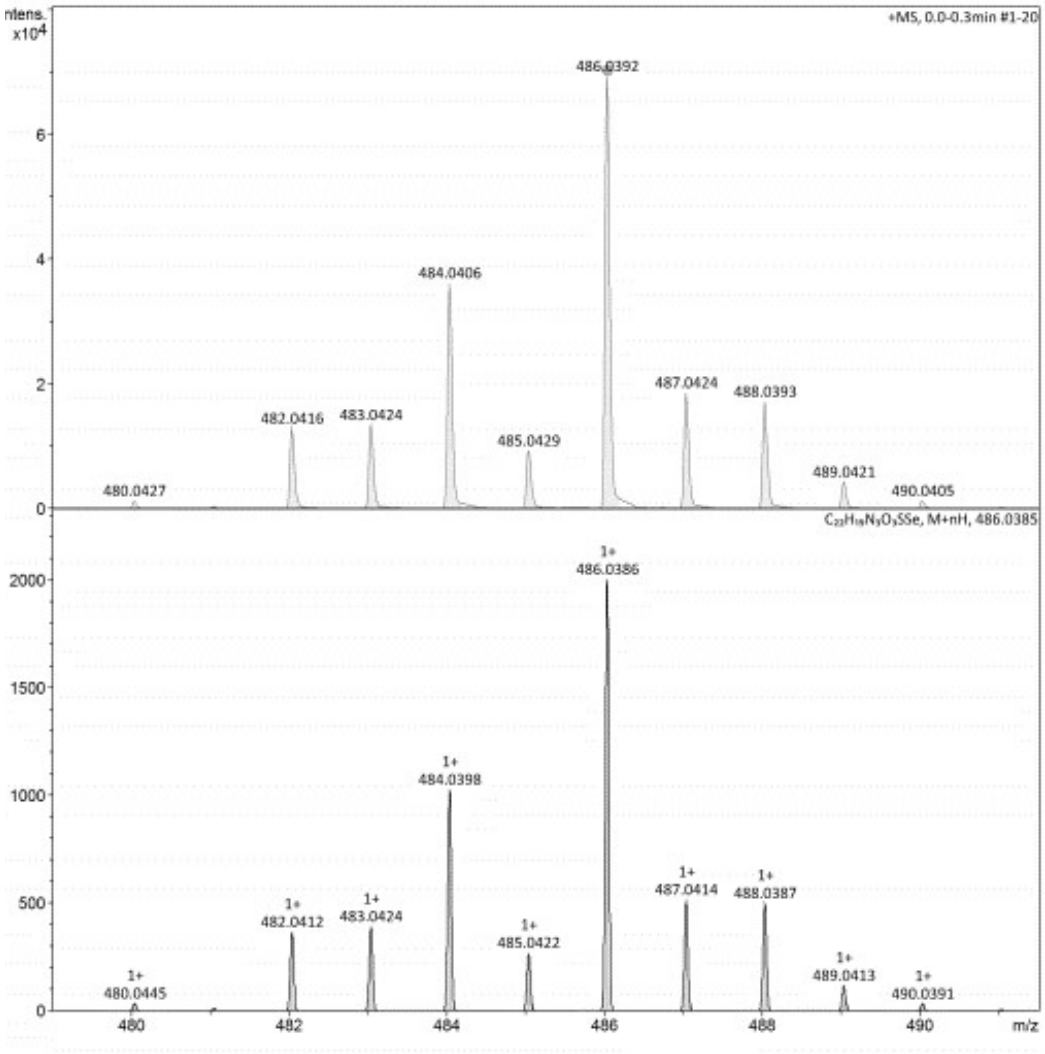


Figure S135. HRMS (APPI$^+$) of **38**

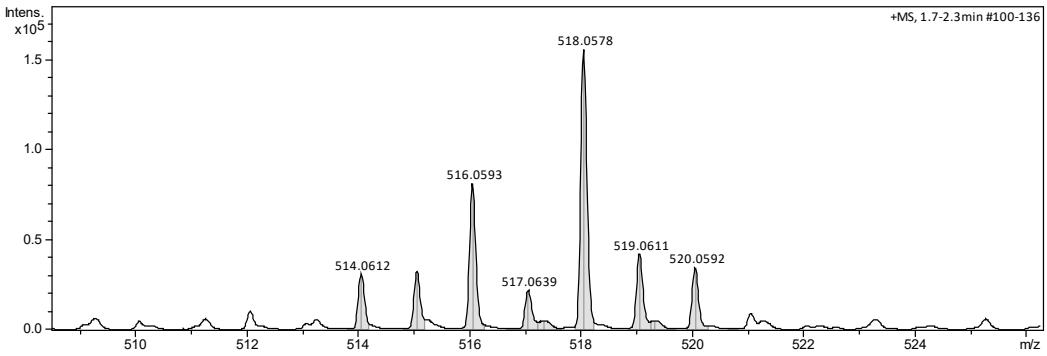


Figure S136. HRMS (ESI+) of **39**

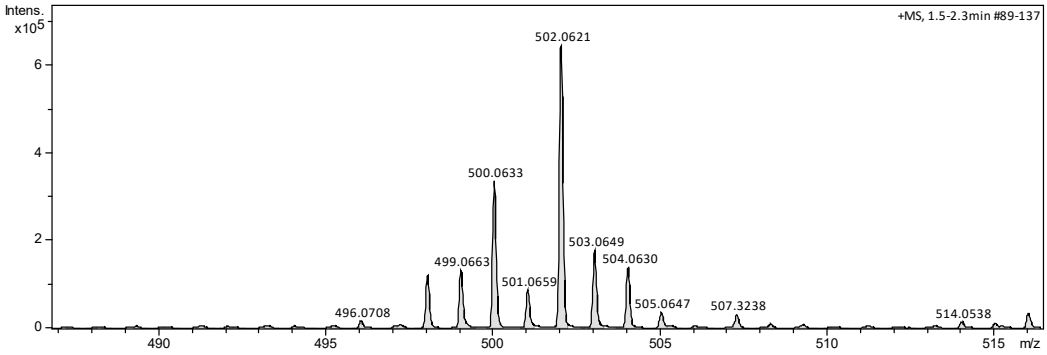


Figure S137. HRMS (ESI+) of **40**

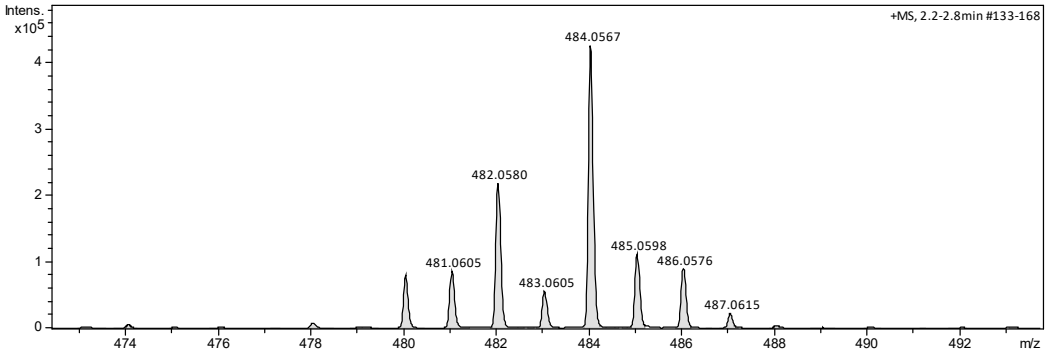


Figure S138. HRMS (ESI+) of **41**

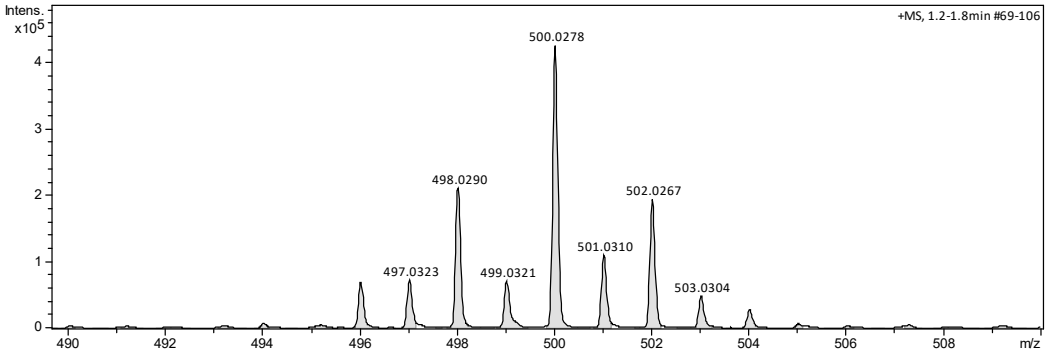


Figure S139. HRMS (ESI+) of **42**

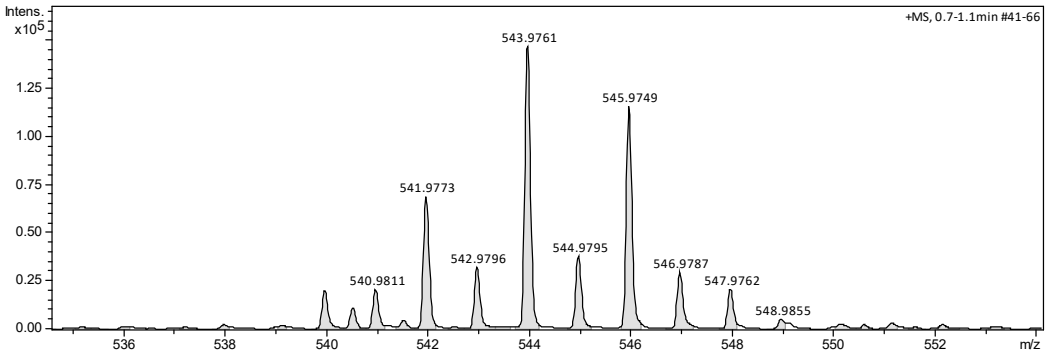


Figure S140. HRMS (ESI+) of **43**

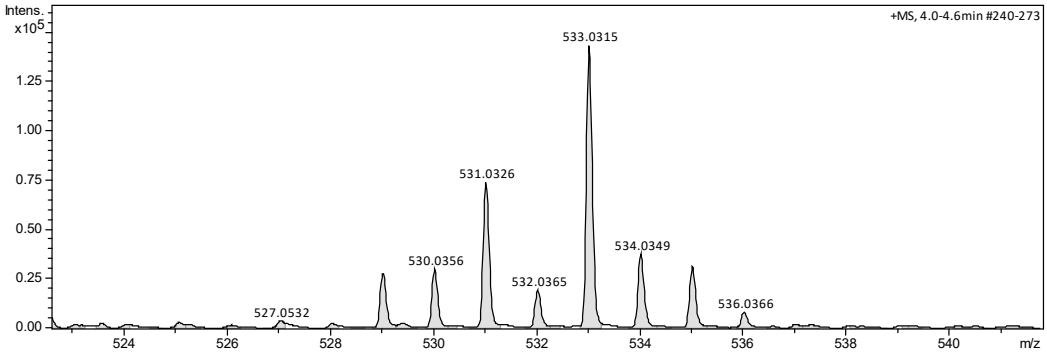


Figure S141. HRMS (ESI+) of **44**

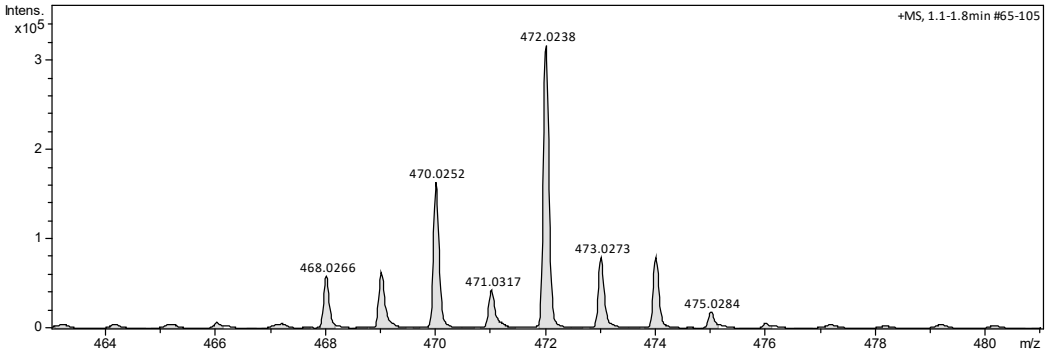


Figure S142. HRMS (ESI+) of **46**

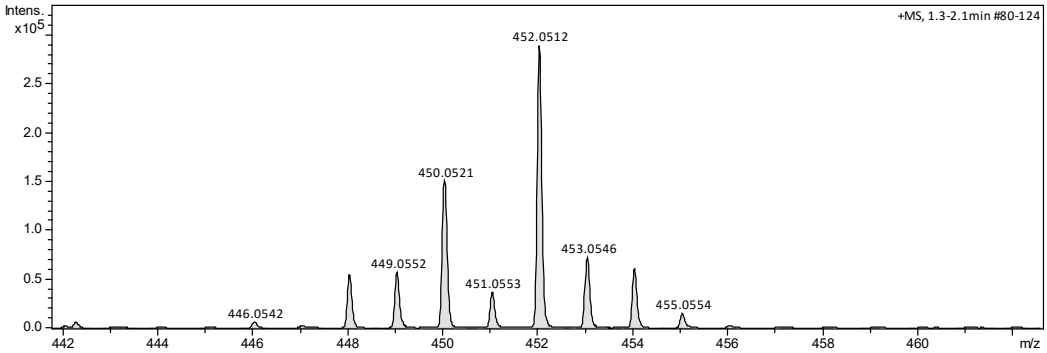


Figure S143. HRMS (ESI+) of **48**

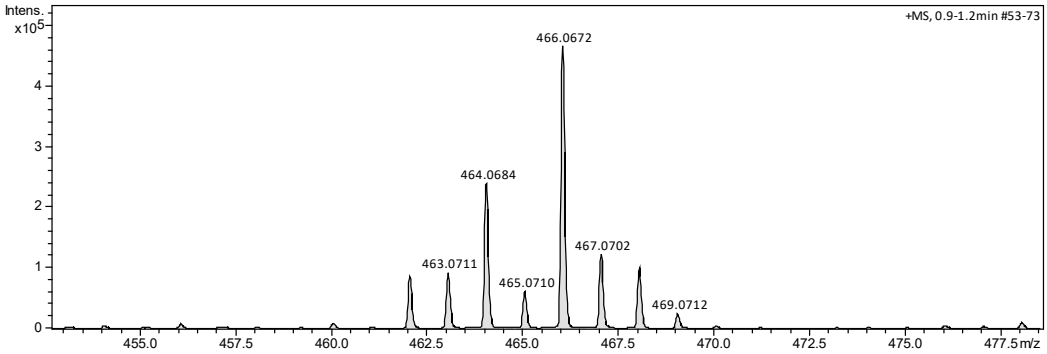


Figure S144. HRMS (ESI+) of **50**

1. (a) M. C. F. R. Pinto, A. V. Pinto and C. G. T. Oliveira, *An. Acad. Brasil. Ciências.,* 1980, **52**, 481; (b) L. F. Fieser and M. Fieser, *J. Am. Chem. Soc.,* 1948, **70**, 3215; (c) E. N. da Silva Júnior, M. C. B. V. Souza, A. V. Pinto, M. C. F. R. Pinto, V. F. Ferreira, R. F. S. Menna-Barreto, R. S. F. Silva, D. V. Teixeira, C. A. de Simone, S. L. de Castro, *Eur. J. Med. Chem.* 2008, **43**, 1774.

2. R. S. F. Silva, E. M. Costa, U. L. T. Trindade, D. V. Teixeira, M. C. F. R. Pinto, G. L. Santos, V. R. S. Malta, C. A. de Simone and A. V. Pinto and S. L. de Castro, *Eur. J. Med. Chem.,* 2006, **41**, 526.

3. G. A. M. Jardim, E. H. G. Cruz, W. O. Valença, J. M. Resende, B. L. Rodrigues, D. F. Ramos, R. N. Oliveira, P. E. A. Silva and E. N. da Silva Júnior, *J. Braz. Chem. Soc.,* 2015, **26**, 1013.

4. S. L. Castro, F. S. Emery and E. N. da Silva Júnior. *Eur. J. Med. Chem.,* 2013, **69**, 678.

5. E. N. da Silva Júnior, T. T. Guimarães, R. F. S. Menna-Barreto, M. C. Pinto, C. A. Simone, C. Pessoa, B. C. Cavalcanti, J. R. Sabino, C. K. Andrade, M. O. F. Goulart, S. L. Castro and A. V. Pinto, *Bioorg. Med. Chem.,* 2010, **18**, 3224.

6. (a) C. S. Lisboa, V. G. Santos, B. G. Vaz, N. C. de Lucas, M. N. Eberlin and S. J. Garden, *J. Org. Chem.*, 2011, **76**, 5264; (b) B. D. Bala, S. Muthusaravanan, T. S. Choon, M. A. Ali and S. Perumal, *Eur. J. Med. Chem.,* 2014, **85**, 737; (c) B. D. Bala, S. Muthusaravanan and S. Perumal, *Tetrahedron Lett.* 2013, **54**, 3735.

7. D. D. Perrin, W. L. F. Armarego and D. R. Perrin, Purification of Laboratory Chemicals, second ed., Pergamon, Oxford, 1980.

8. H. J Reich, J. M. Renga and L. Reich, *J. Am. Chem. Soc.,* 1975, **97**, 5434.

9. H. J. Reich, S. K. Shah, P. M. Gold and R. E. Olson, *J. Am. Chem. Soc.*, 1981, **103**, 3112.

10. F. L. Ansari, S. Umbreen, L. Hussain, T. Makhmoor, S. A. Nawaz, M. A. Lodhi, S. N. Khan, F. Shaheen, M. I. Choudhary and A. Rahman, *Chem. Biodiversity.* 2005, **2**, 487-496.

11. F. F. Fieser, *J. Am. Chem. Soc.,* 1926, **11**, 2922.

12. W. O. Valença, T. V. Baiju, F. G. Brito, M. H. Araujo, C. Pessoa, B. C. Cavalcanti, C. A. de Simone, C. Jacob, I. N. N. Namboothiri and E. N. da Silva Júnior, *ChemistrySelect*., 2017, **2**, 4301.

13. T. F. Borgati, R. B. Alves, R. R. Teixeira, R. P. Freitas, T. G. Perdigão, S. F. Silva, A. A. dos Santos and A. J. O. Bastidas, *J. Braz. Chem. Soc.,* 2013, **24**, 953.

14. Bruker, SMART and SAINT, Area Detector Control Integration Softhware, Bruker Analytical X-ray Instruments, *Inc., Madison.,* WI, USA, 1999.
15. G. M. Sheldrick, SADABS, *Program for Empirical Absorption Correction of Area Detector Data*, University of Göttingen, Germany, 1997.
16. G. M. Sheldric, *Acta Crystallogr*., 2008, **A64**; 112.
17. L. J. Farrugia, *J. Appl. Cryst.,* 2012, **45**, 849.
18. T. Mosmann, *J. Immunol. Methods.,* 1983, **16**, 55.