

Supplementary Materials

Design, Synthesis, and Cytotoxicity and Topoisomerase I/II α Inhibition Activity of Pyrazolo[4,3-*f*]quinoline Derivatives

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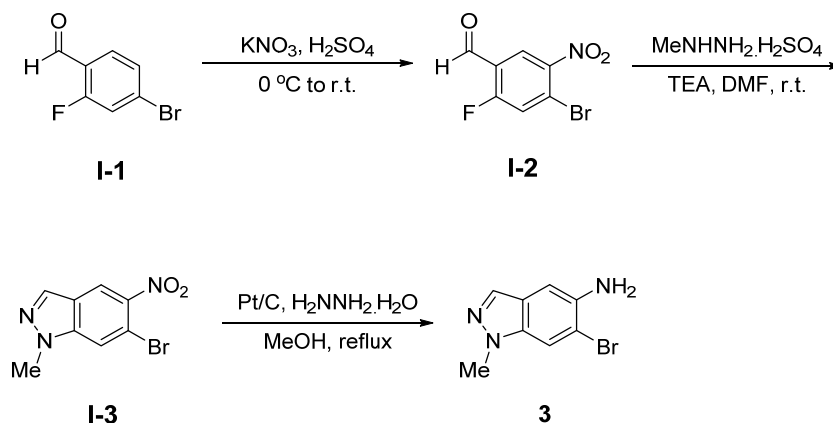
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† These authors contributed equally to this work.

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1. Synthesis



Scheme S1. Synthesis of starting precursor **3**.

4-Bromo-2-fluoro-5-nitrobenzaldehyde (**I-2**)[31]

As shown in Scheme S1, KNO₃ (1.1 g, 10.84 mmol) in the round bottom flask was added H₂SO₄ (8.2 ml, 153.66 mmol) dropwise at 0 °C under nitrogen atmosphere. To the solution, 4-bromo-2-fluorobenzaldehyde (**I-1**) (2.0 g, 9.85 mmol) was added and stirred at room temperature for 3 h. The reaction mixture was quenched by dropwise addition of ice water. Then, the resulting solid precipitate was filtered, dried, and obtained as a product **I-2**. White solid; 93% yield; ¹H NMR (400 MHz, CDCl₃) δ 10.13 (s, 1H), 8.49 (d, J = 6.4 Hz, 1H), 8.22 (d, J = 10.4 Hz, 1H).

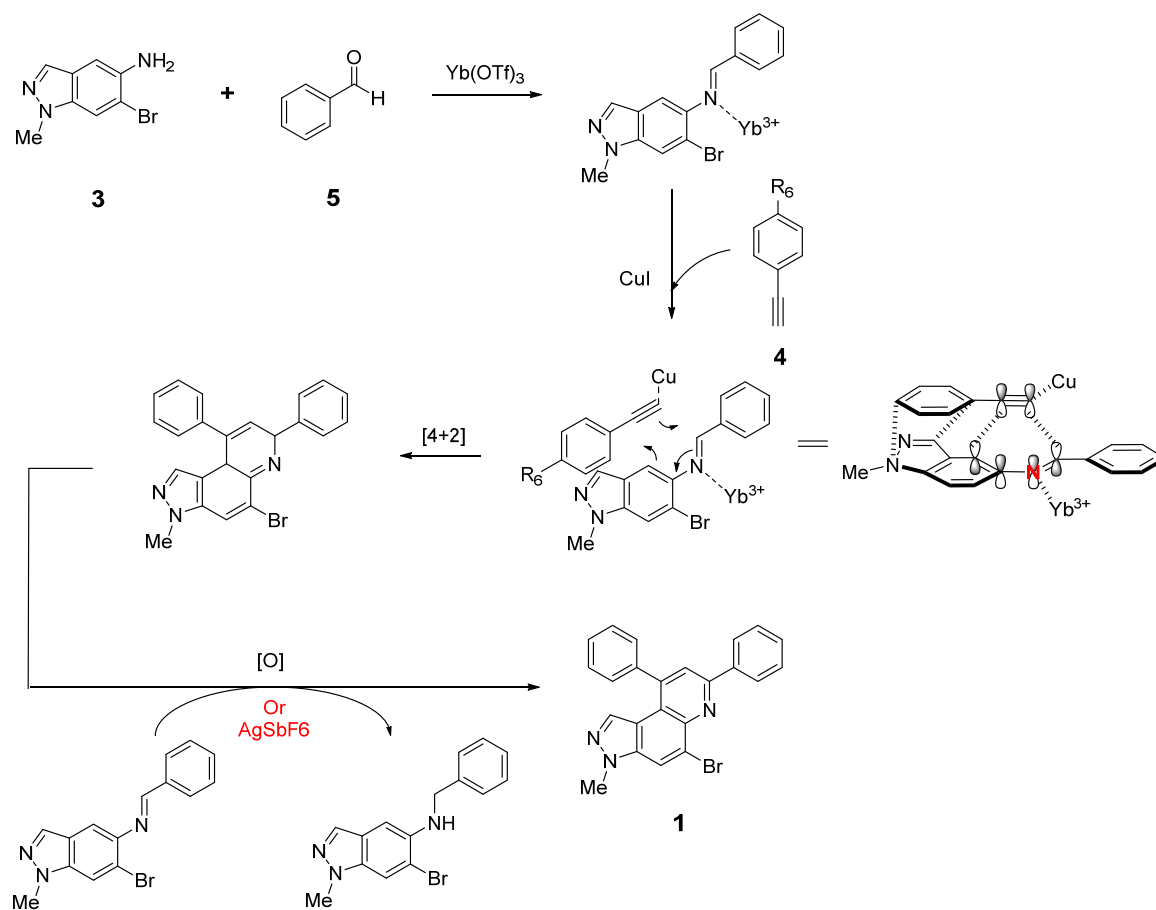
6-Bromo-5-nitro-1H-indazole (**I-3**)[33]

To a methylhydrazine sulfate (0.9 g, 6.05 mmol) in DMF (10 ml) was added TEA (1.69 mL, 12.090 mmol) dropwise under nitrogen exchange. The mixture was stirred at room temperature for 1 h. then added **I-2** (1 g, 4.03 mmol) and stirring continued for an additional 1 h. After completion, the reaction was terminated by the addition of water. The mixture was further stirred, and the resulting precipitate was collected by filtration and water washing. The obtained solid was washed again with EtOAc to afford **I-3**. Yellow solid; 93% yield; ¹H NMR (400 MHz, CDCl₃): δ 8.38 (s, 1H), 8.13 (s, 1H), 7.77 (s, 1H), 4.11 (s, 3H).

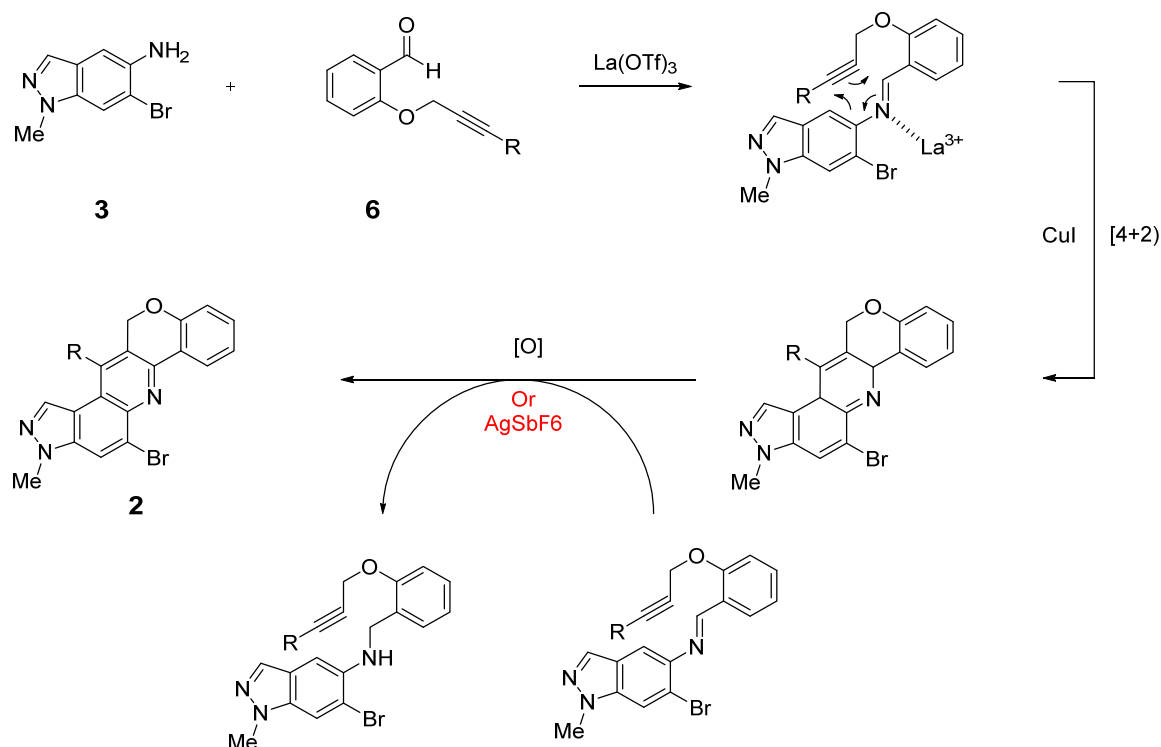
6-Bromo-1-methyl-1H-indazol-5-amine (**3**)[34,35]

To intermediate **I-3** (0.5 g, 1.95 mmol) and platinum on carbon (0.03 g, 0.13 mmol) in MeOH (25 ml) was added hydrazine monohydrate (1 ml, 19.50 mmol) dropwise and refluxed under nitrogen atmosphere for 12 h. The reaction mixture was filtered through a pad of celite. The

filtrate was concentrated and purified by silica gel column chromatography Hex:EtOAc = 3:1) to afford **3** as a starting precursor. Yellow solid; 93% yield; ^1H NMR (400 MHz, DMSO- d_6): δ 7.84 (s, 1H), 7.76 (s, 1H), 7.03 (s, 1H), 4.94 (s, 2H), 3.93 (s, 3H).

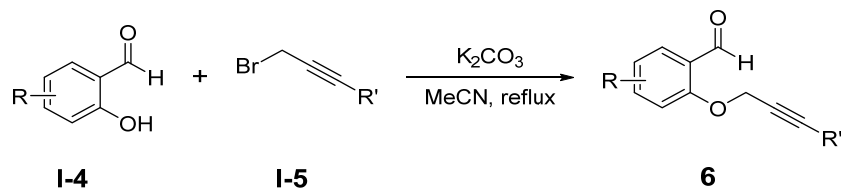


Scheme S2. A plausible mechanism of intermolecular Diels-Alder reaction.



Scheme S3. A plausible mechanism of intramolecular Diels-Alder reaction

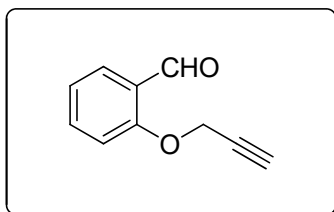
General procedure for the synthesis of intermediates[30,32]



Scheme S4. Representative synthetic method of compounds **6**.

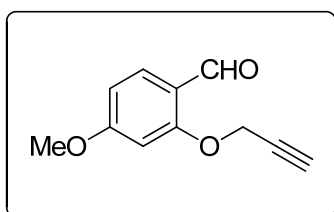
The substituted salicylaldehydes **I-4** (500 mg, 1 eq) and K_2CO_3 (5 eq) in MeCN (10 ml) was added stirred at room temperature for 15 min under nitrogen atmosphere. Then, the substituted propargyl bromides **I-5** (1 eq) was added dropwise. The resulting mixture was reflux for 4 h. After completion, the reaction mixture was filtered off, and the filtrate was concentrated for further purification in silica gel column chromatography (Hex:EtOAc = 5:1) to afford intermediates **6**.

2-(Prop-2-yn-1-yloxy)benzaldehyde (6A) [CAS RN: 29978-83-4]



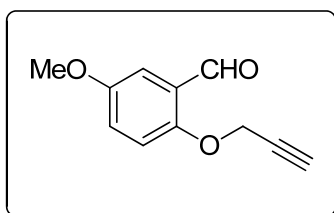
Orange solid; 97% yield; ^1H NMR (400 MHz, CDCl_3): δ 10.48 (s, 1H), 7.86 (dd, $J = 7.6, 1.6$ Hz, 1H), 7.57 (ddd, $J = 7.6, 7.6, 1.6$ Hz, 1H), 7.12 (d, $J = 8.8$ Hz, 1H), 7.08 (td, $J = 8.8, 7.6$ Hz, 1H), 4.83 (d, $J = 2.4$ Hz, 2H), 2.57 (t, $J = 2.4$ Hz, 1H).

4-Methoxy-2-(prop-2-yn-1-yloxy)benzaldehyde (6B) [CAS RN: 236390-57-1]



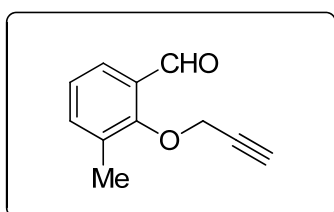
Orange solid; 94% yield; ^1H NMR (400 MHz, CDCl_3): δ 10.31 (s, 1H), 7.85 (dd, $J = 8.0, 2.0$ Hz, 1H), 6.62 – 6.60 (m, 2H), 4.81 (d, $J = 2.4$ Hz, 2H), 2.58 (t, $J = 2.4$ Hz, 1H).

5-Methoxy-2-(prop-2-yn-1-yloxy)benzaldehyde (6C) [CAS RN: 224317-65-1]



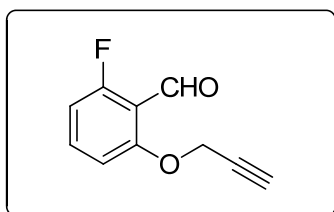
Brown solid; 98% yield; ^1H NMR (400 MHz, CDCl_3): δ 10.45 (s, 1H), 7.35 (d, $J = 3.2$ Hz, 1H), 7.14 (dd, $J = 9.2, 3.2$ Hz, 1H), 7.08 (d, $J = 9.2$ Hz, 1H), 4.79 (d, $J = 2.4$ Hz, 2H), 3.81 (s, 3H), 2.55 (t, $J = 2.4$ Hz, 1H).

3-Methyl-2-(prop-2-yn-1-yloxy)benzaldehyde (6D) [CAS RN: 1006030-20-1]



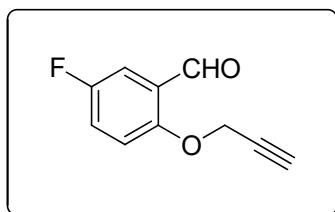
Yellow liquid; 90% yield; ^1H NMR (400 MHz, CDCl_3): δ 10.42 (s, 1H), 7.71 (d, $J = 7.6$ Hz, 1H), 7.46 (d, $J = 7.6$ Hz, 1H), 7.18 (t, $J = 7.6$ Hz, 1H), 4.68 (d, $J = 2.0$ Hz, 2H), 2.53 (t, $J = 2.0$ Hz, 1H), 2.36 (s, 3H).

6-Fluoro-2-(prop-2-yn-1-yloxy)benzaldehyde (6E) [CAS RN: 1692480-05-9]



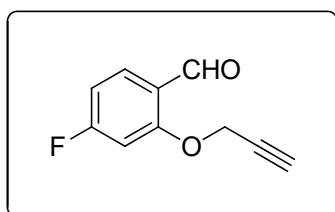
Orange solid; 73% yield; ^1H NMR (400 MHz, CDCl_3): δ 10.44 (s, 1H), 7.51 (dt, $J = 8.4, 6.4$ Hz, 1H), 6.92 (d, $J = 8.4$ Hz, 1H), 6.80 (dd, $J = 10.0, 8.4$ Hz, 1H), 4.84 (d, $J = 2.4$ Hz, 2H), 2.58 (t, $J = 2.4$ Hz, 1H).

5-Fluoro-2-(prop-2-yn-1-yloxy)benzaldehyde (6F) [CAS RN: 1096333-23-1]



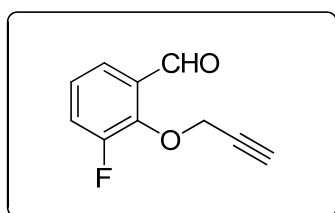
Yellow solid; 96% yield; ^1H NMR (400 MHz, CDCl_3): δ 10.43 (d, $J = 3.2$ Hz, 1H), 7.54 (dd, $J = 8.4, 3.2$ Hz, 1H), 7.30 – 7.25 (m, 1H), 7.11 (dd, $J = 9.2, 4.0$ Hz, 1H), 4.82 (d, $J = 2.4$ Hz, 2H), 2.58 (t, $J = 2.8$ Hz, 1H).

4-Fluoro-2-(prop-2-yn-1-yloxy)benzaldehyde (6G) [CAS RN: 1279702-70-3]



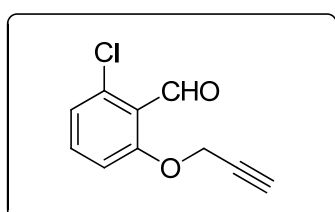
Pale yellow solid; 87% yield; ^1H NMR (400 MHz, CDCl_3): δ 10.37 (s, 1H), 7.88 (dd, $J = 8.4, 6.8$ Hz, 1H), 6.84 (dd, $J = 10.4, 2.4$ Hz, 1H), 6.78 (dd, $J = 8.4, 2.4$ Hz, 1H), 4.82 (d, $J = 2.4$ Hz, 2H), 2.61 (t, $J = 2.8$ Hz, 1H).

3-Fluoro-2-(prop-2-yn-1-yloxy)benzaldehyde (6H) [CAS RN: 1271773-10-4]



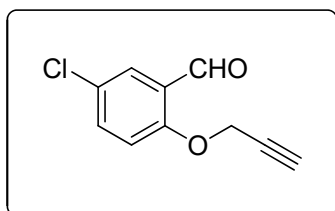
Orange liquid; 92% yield; ^1H NMR (400 MHz, CDCl_3): δ 10.44 (s, 1H), 7.65 (dt, $J = 8.0$ Hz, 1H), 7.36 (ddd, $J = 11.2, 8.0, 1.6$ Hz, 1H), 7.18 (dt, $J = 8.0, 4.4$ Hz, 1H), 4.91 (d, $J = 2.4$ Hz, 2H), 2.52 (t, $J = 2.4$ Hz, 1H).

6-Chloro-2-(prop-2-yn-1-yloxy)benzaldehyde (6I) [CAS RN: 1092306-71-2]



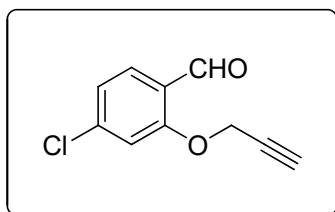
Pale yellow solid; 93% yield; ^1H NMR (400 MHz, CDCl_3): δ 10.46 (s, 1H), 7.81 (dd, $J = 8.0, 1.6$ Hz, 1H), 7.65 (d, $J = 8.0, 1.6$ Hz, 1H), 7.24 (t, $J = 8.0$ Hz, 1H), 4.90 (d, $J = 2.4$ Hz, 2H), 2.54 (t, $J = 2.4$ Hz, 1H).

5-Chloro-2-(prop-2-yn-1-yloxy)benzaldehyde (6J) [CAS RN: 224317-64-0]



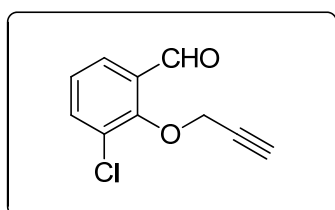
Pale yellow solid; 90% yield; ^1H NMR (400 MHz, CDCl_3): δ 10.40 (s, 1H), 7.80 (d, $J = 2.8$ Hz, 1H), 7.51 (dd, $J = 8.4, 2.8$ Hz, 1H), 7.09 (d, $J = 8.4$ Hz, 1H), 4.83 (d, $J = 2.8$ Hz, 2H), 2.59 (t, $J = 2.8$ Hz, 1H).

4-Chloro-2-(prop-2-yn-1-yloxy)benzaldehyde (6K) [CAS RN: 1595918-82-3]



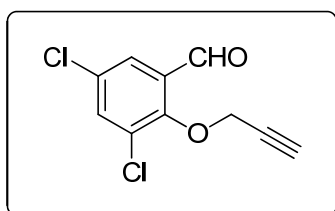
Pale yellow solid; 96% yield; ^1H NMR (400 MHz, CDCl_3): δ 10.39 (s, 1H), 7.79 (d, $J = 8.0$ Hz, 1H), 7.12 (d, $J = 1.2$ Hz, 1H), 7.08 – 7.05 (m 1H), 4.82 (d, $J = 2.4$ Hz, 2H), 2.62 (t, $J = 2.4$ Hz, 1H).

3-Chloro-2-(prop-2-yn-1-yloxy)benzaldehyde (6L) [CAS RN: 1271773-06-8]



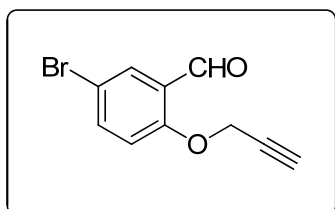
Pale yellow solid; 93% yield; ^1H NMR (400 MHz, CDCl_3): δ 10.51 (s, 1H), 7.43 (t, $J = 8.4$ Hz, 1H), 7.10 (d, $J = 8.4$ Hz, 1H), 7.06 (d, $J = 8.4$ Hz, 1H), 4.82 (d, $J = 2.4$ Hz, 2H), 2.56 (t, $J = 2.4$ Hz, 1H).

3,5-Dichloro-2-(prop-2-yn-1-yloxy)benzaldehyde (6M) [CAS RN: 1126527-53-4]



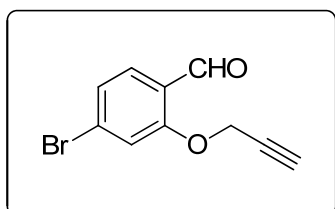
Pale yellow solid; 94% yield; ^1H NMR (400 MHz, CDCl_3): δ 10.39 (s, 1H), 7.75 (d, $J = 2.8$ Hz, 1H), 7.64 (d, $J = 2.8$ Hz, 1H), 4.89 (d, $J = 2.4$ Hz, 2H), 2.55 (t, $J = 2.4$ Hz, 1H).

5-Bromo-2-(prop-2-yn-1-yloxy)benzaldehyde (6N) [CAS RN: 122835-14-7]



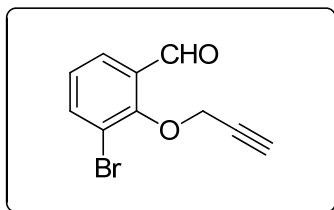
Pale yellow solid; 94% yield; ^1H NMR (400 MHz, CDCl_3): δ 10.39 (s, 1H), 7.95 (d, $J = 2.4$ Hz, 1H), 7.65 (dd, $J = 9.2, 2.4$ Hz, 1H), 7.03 (d, $J = 9.2$ Hz, 1H), 4.82 (d, $J = 2.4$ Hz, 2H), 2.59 (t, $J = 2.4$ Hz, 1H).

4-Bromo-2-(prop-2-yn-1-yloxy)benzaldehyde (6O) [CAS RN: 1099609-05-8]



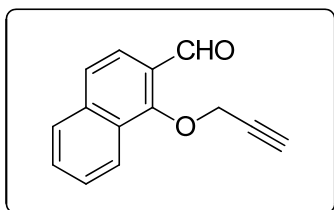
Pale yellow solid; 93% yield; ^1H NMR (400 MHz, CDCl_3): δ 10.41 (s, 1H), 7.72 (d, $J = 8.8$ Hz, 1H), 7.29 (d, $J = 1.2$ Hz, 1H), 7.26 – 7.23 (m, 1H), 4.83 (d, $J = 2.0$ Hz, 2H), 2.62 (t, $J = 2.0$ Hz, 1H).

3-Bromo-2-(prop-2-yn-1-yloxy)benzaldehyde (6P) [CAS RN: 1271773-00-2]



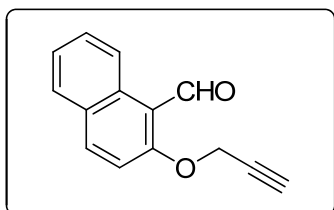
Pale yellow solid; 75% yield; ^1H NMR (400 MHz, CDCl_3): δ 10.45 (s, 1H), 7.85 (dd, $J = 8.0, 1.6$ Hz, 1H), 7.82 (dd, $J = 8.0, 1.6$ Hz, 1H), 7.18 (t, $J = 8.0$ Hz, 1H), 4.89 (d, $J = 2.4$ Hz, 2H), 2.55 (t, $J = 2.4$ Hz, 1H).

1-(Prop-2-yn-1-yloxy)-2-naphthaldehyde (6Q) [CAS RN: 1271773-34-2]



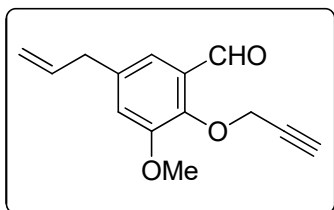
Orange solid; 82% yield; ^1H NMR (400 MHz, CDCl_3): δ 10.66 (s, 1H), 8.23 (d, $J = 8.4$ Hz, 1H), 7.90 (d, $J = 8.0$ Hz, 1H), 7.89 (d, $J = 8.0$ Hz, 1H), 7.71 (d, $J = 8.4$ Hz, 1H), 7.65 (td, $J = 8.0, 1.6$ Hz, 1H), 7.60 (td, $J = 8.0, 1.6$ Hz, 1H), 4.94 (d, $J = 2.4$ Hz, 2H), 2.61 (t, $J = 2.4$ Hz, 1H).

2-(Prop-2-yn-1-yloxy)-1-naphthaldehyde (6R) [CAS RN: 58758-48-8]



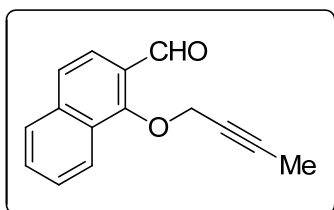
Brown solid; 87% yield; ^1H NMR (400 MHz, CDCl_3): δ 10.90 (s, 1H), 9.28 (d, $J = 9.2$ Hz, 1H), 8.06 (d, $J = 8.8$ Hz, 1H), 7.78 (d, $J = 8.0$ Hz, 1H), 7.63 (ddd, $J = 8.8, 6.8, 1.2$ Hz, 1H), 7.45 (ddd, $J = 8.0, 6.8, 1.2$ Hz, 1H), 7.37 (d, $J = 9.2$ Hz, 1H), 4.93 (d, $J = 2.4$ Hz, 2H), 2.58 (t, $J = 2.4$ Hz, 1H).

5-Allyl-3-methoxy-2-(prop-2-yn-1-yloxy)benzaldehyde (6S)

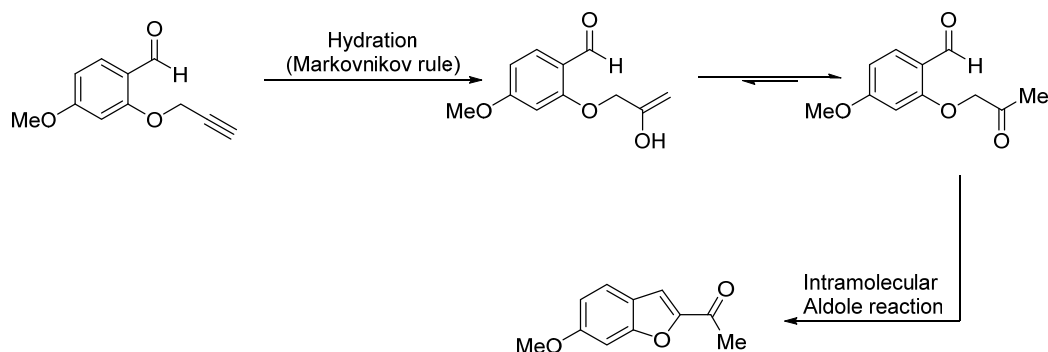


Brown liquid; 99% yield; ^1H NMR (400 MHz, CDCl_3): δ 10.47 (s, 1H), 7.29 (d, $J = 2.4$ Hz, 1H), 6.98 (d, $J = 2.4$ Hz, 1H), 5.99 – 5.89 (m, 1H), 5.14 – 5.08 (m, 2H), 4.85 (d, $J = 2.4$ Hz, 2H), 3.90 (s, 3H), 3.39 (d, $J = 6.4$ Hz, 1H), 2.47 (t, $J = 2.4$ Hz, 1H).

2-(But-2-yn-1-yloxy)-1-naphthaldehyde (6T)

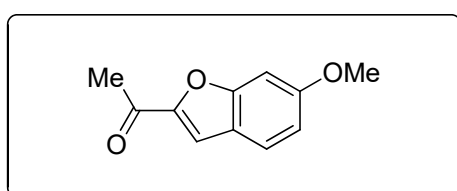


Brown solid; 87% yield; ^1H NMR (400 MHz, CDCl_3): δ 10.90 (s, 1H), 9.29 (d, $J = 8.4$ Hz, 1H), 8.06 (d, $J = 9.2$ Hz, 1H), 7.79 (d, $J = 7.2$ Hz, 1H), 7.63 (ddd, $J = 8.4, 8.0, 1.2$ Hz, 1H), 7.44 (ddd, $J = 8.0, 7.2, 1.2$ Hz, 1H), 7.39 (d, $J = 9.2$ Hz, 1H), 4.90 (q, $J = 2.4$ Hz, 2H), 1.85 (t, $J = 2.4$ Hz, 3H).



Scheme S5. A plausible mechanism of benzofuran formation.

1-(6-Methoxybenzofuran-2-yl)ethenone [CAS RN: 52814-92-3]



Brown solid; 27% yield; ^1H NMR (CDCl_3 , 400 MHz): δ 7.56 (d, $J = 8.8$ Hz, 1H), 7.45 (s, 1H), 7.05 (d, $J = 2.4$ Hz, 1H), 6.95 (dd, $J = 8.8, 2.4$ Hz, 1H), 3.88 (s, 3H), 2.56 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 188.04, 161.27, 157.44, 152.46, 123.73, 120.48, 114.55, 113.90, 95.73, 55.87, 26.34.

2. Biology

In vitro cytotoxicity assay[38]

The cytotoxicity was performed using sulforhodamine B (SRB) assay. Six human cancer cell lines, including ACHN (ATCC, CRL-1611), HCT-15 (ATCC, CCL-225), MDA-MB-231 (ATCC, HTB-26), NCI-H23 (ATCC, CRL-5800), NUGC-3 (JCRB Cell Bank, JCRB0822), and PC-3 (ATCC, CRL-1435, 5×10^3 cells/well), were seeded in 96-well plates (5×10^3 cells/well), incubated overnight and treated with different concentrations of compounds for 48 h. Cells were fixed using 50% trichloroacetic acid for 1 hr at 4°C and stained with 0.4% SRB solution for 30 min. The unbound dye was removed by rinsing with 1% acetic acid, the stain was extracted using 10 mM Tris and the absorbance at 540 nm was measured using Versamax microplate reader (Molecular Devices, San Jose, CA, USA). GI_{50} values were calculated using GraphPad Prism (GraphPad Software Inc., San Diego, CA, USA).

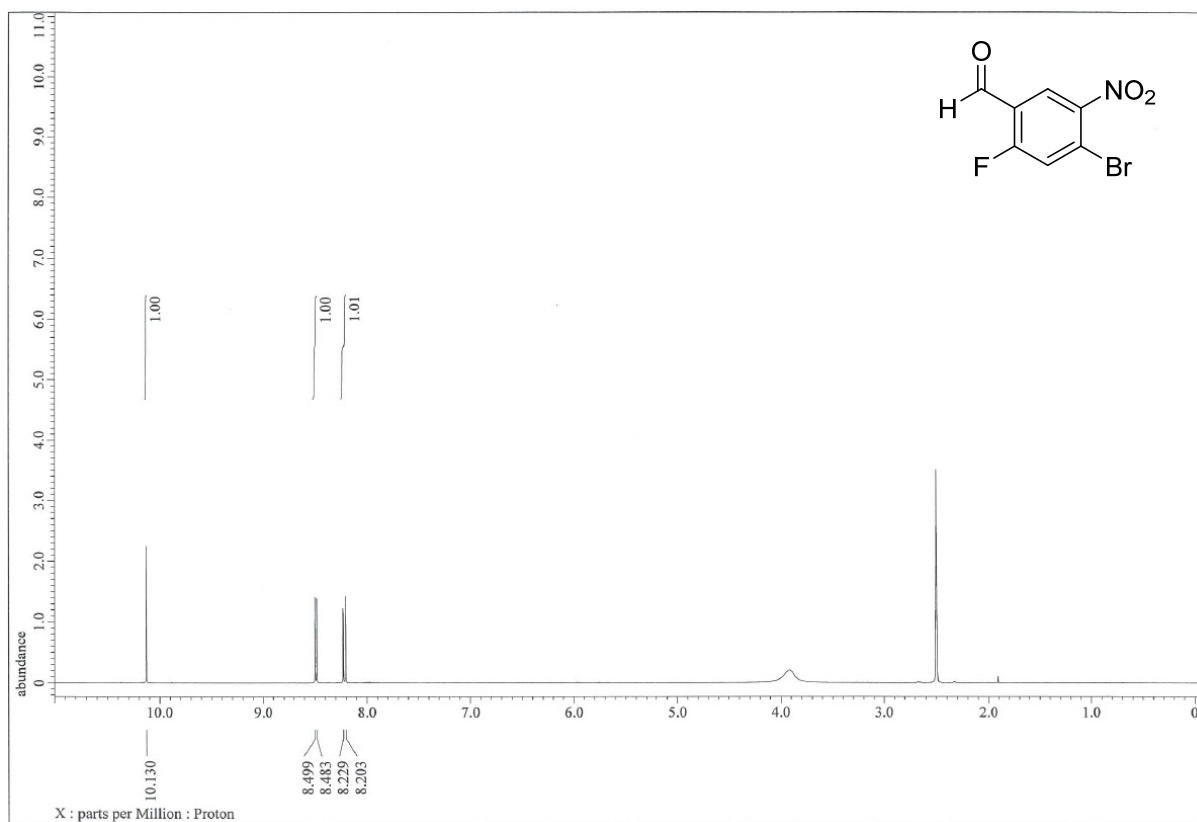
In vitro DNA topoisomerase I or II α relaxation assay[39]

A mixture comprising of 100 ng supercoiled pBR322 plasmid DNA (Thermo Scientific, USA) and 0.2~1 unit of recombinant human DNA topo I (TopoGEN INC., USA) or topo II α (USB Corp., USA) was incubated with or without the prepared compounds in the assay buffer (For

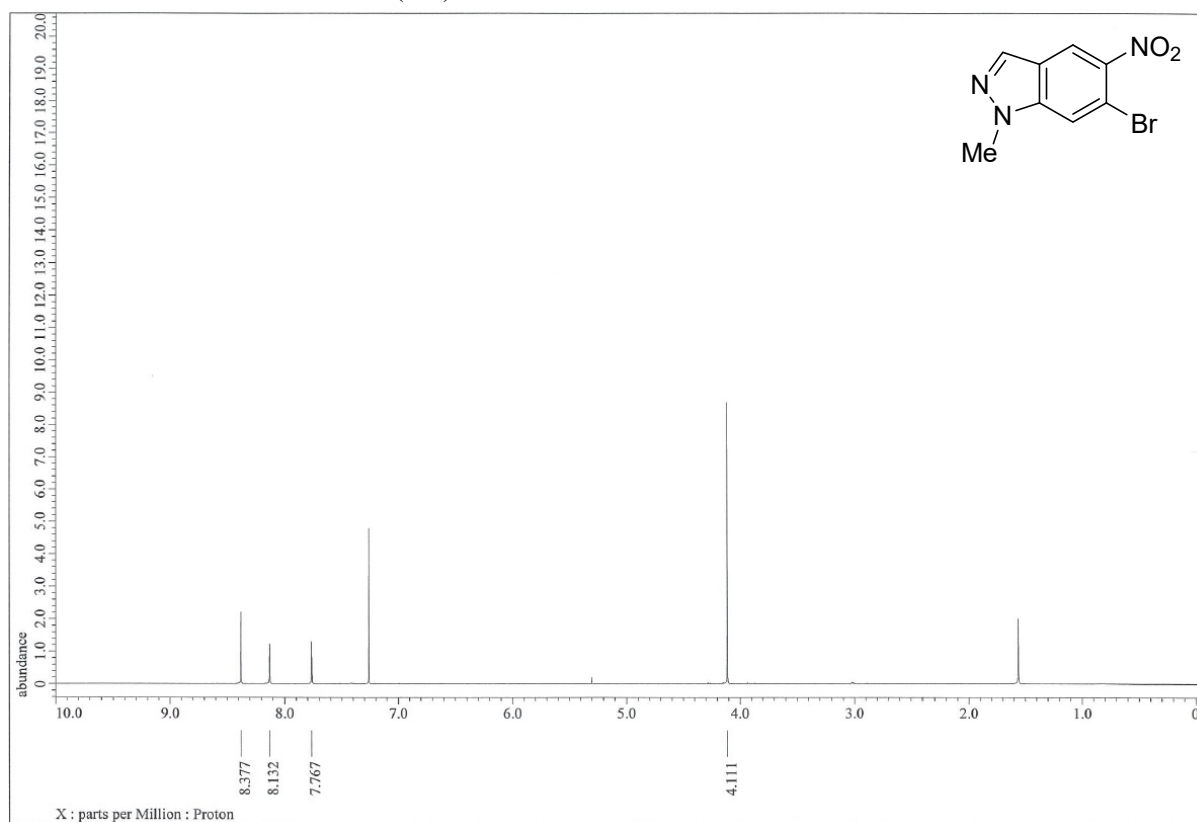
topo I, 10 mM Tris-HCl (pH 7.9), 150 mM NaCl and 0.1% BSA, 0.1 mM spermidine and 5% glycerol; for topo II, 10 mM Tris-HCl (pH 7.9), 50 mM NaCl, 50 mM KCl, 5 mM MgCl₂, 1 mM EDTA, 1 mM ATP and 15 mg/mL BSA) for 30 min at 37 °C. The reaction with a final volume of 10 µL was stopped by adding the topo stop buffer (For topo I, 10% SDS solution containing 0.2% bromophenol blue, 0.2% xylene cyanol and 30% glycerol; for topo II, 7 mM EDTA). The reaction products were electrophoresed on 0.8% agarose gel at 50 V for 1 h with TAE electrophoresis buffer. The gels were stained in an EtBr solution (0.5 mg/mL) and visualized by transillumination with UV light and were quantitated using Alpha Tech ImagerTM (Alpha Innotech Corp., USA).

4. NMR and HRMS spectra

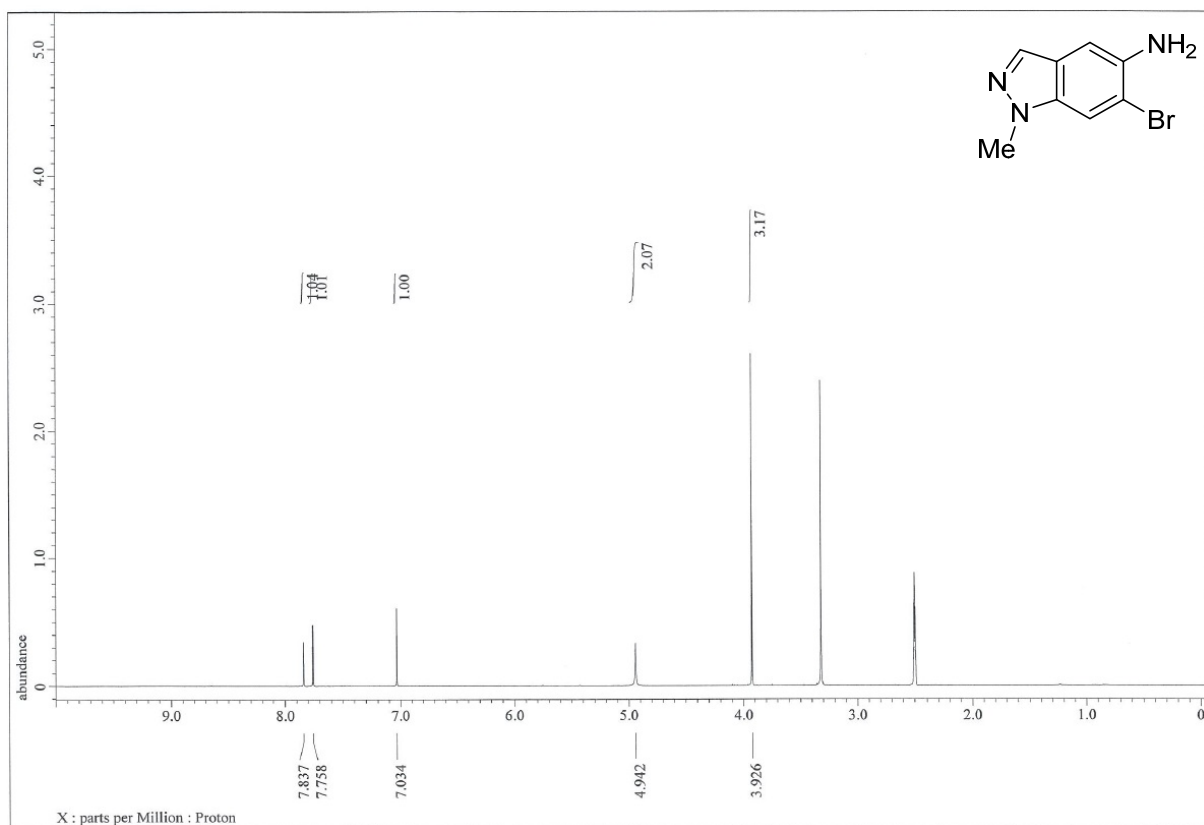
4-Bromo-2-fluoro-5-nitrobenzaldehyde (**I-2**)



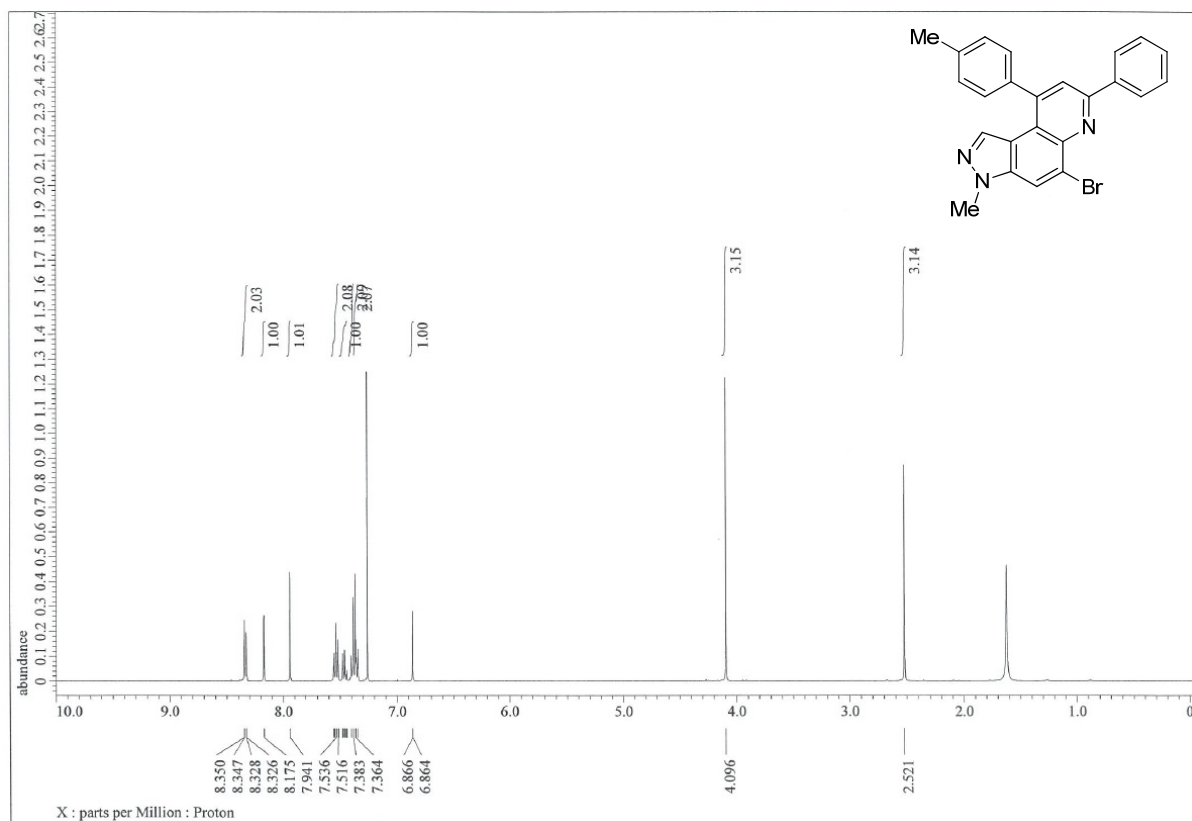
6-Bromo-5-nitro-1*H*-indazole (**I-3**)

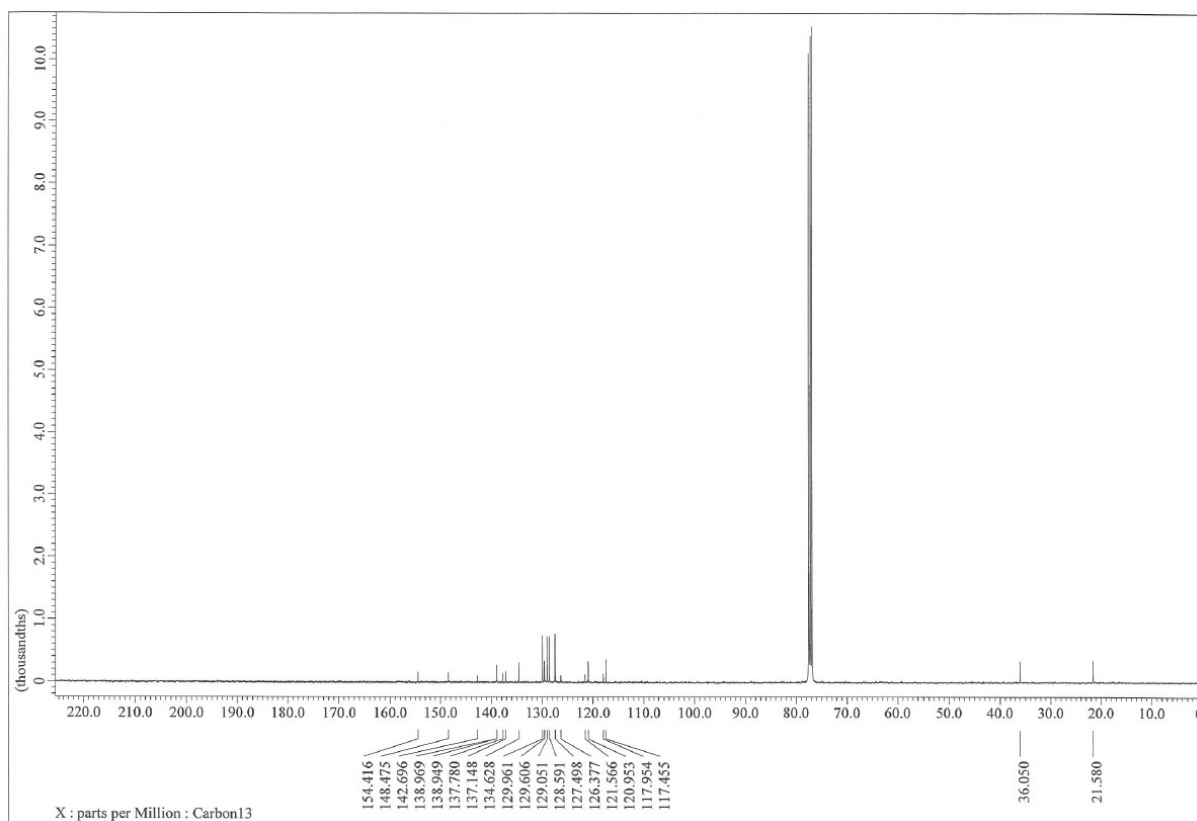


6-Bromo-1-methyl-1*H*-indazol-5-amine (**3**)

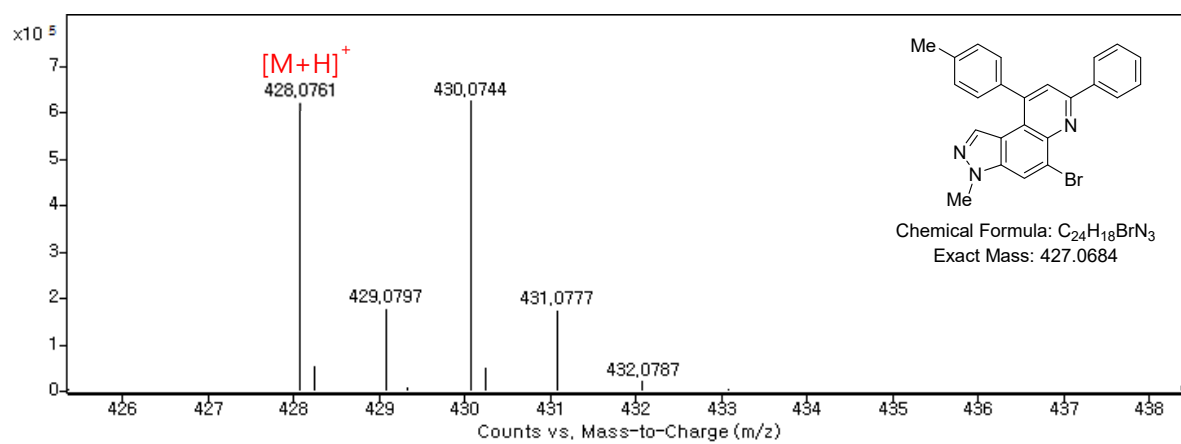


5-Bromo-3-methyl-7-phenyl-9-(*p*-tolyl)-3*H*-pyrazolo[4,3-*f*]quinoline (**1A**)

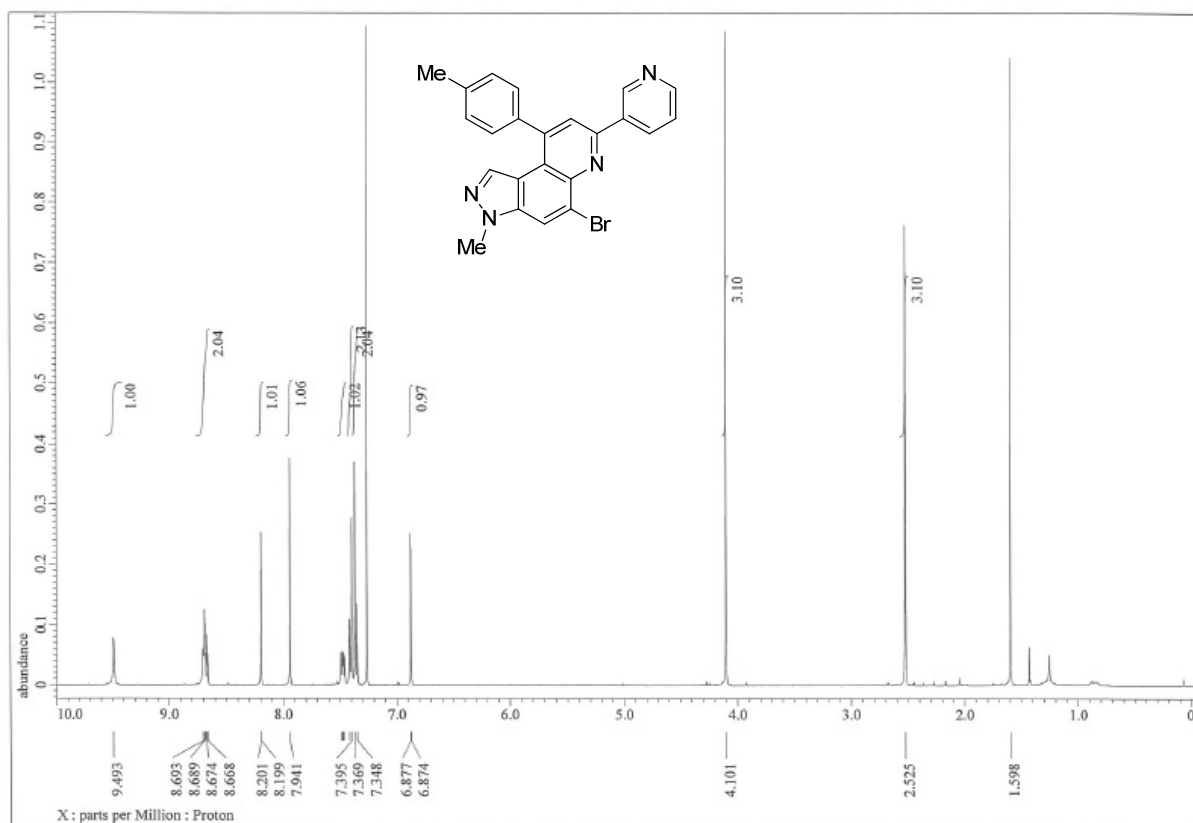


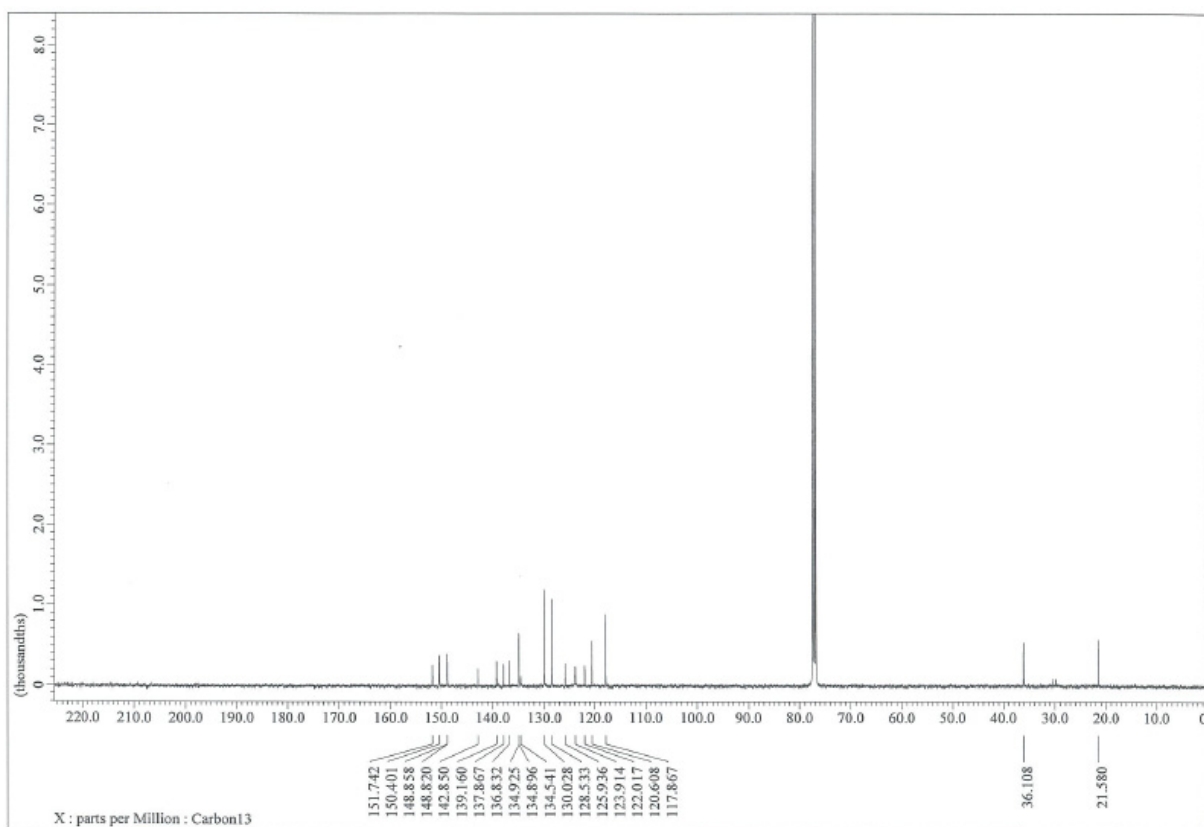


S15

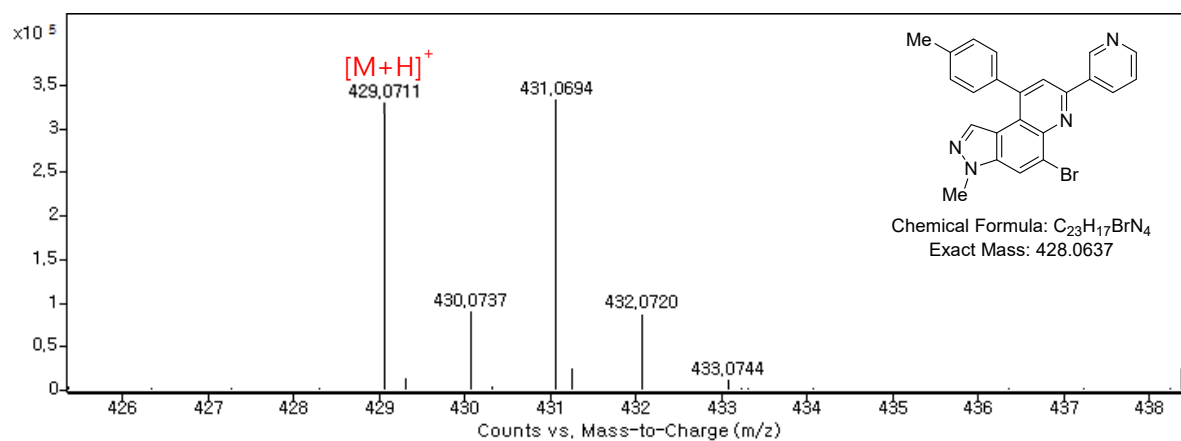


5-Bromo-3-methyl-7-(pyridin-3-yl)-9-(*p*-tolyl)-3*H*-pyrazolo[4,3-*f*]quinoline (**1B**)

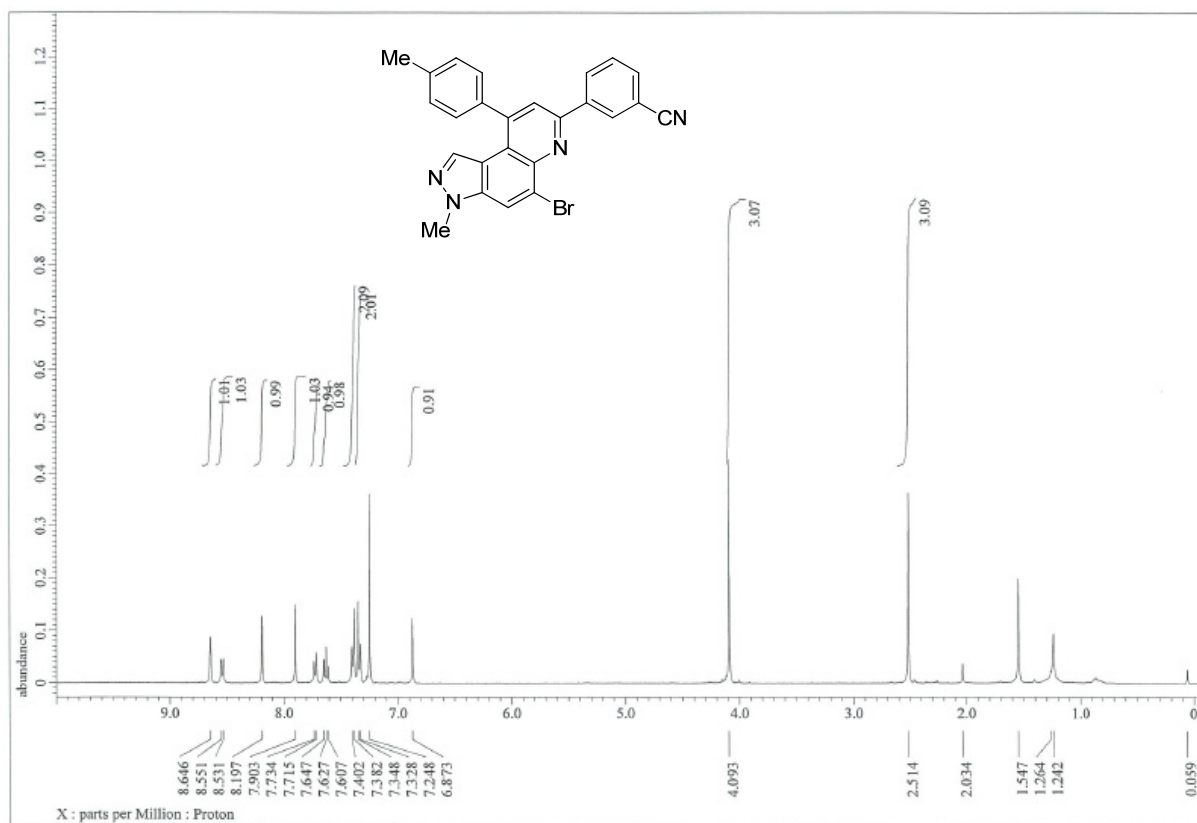


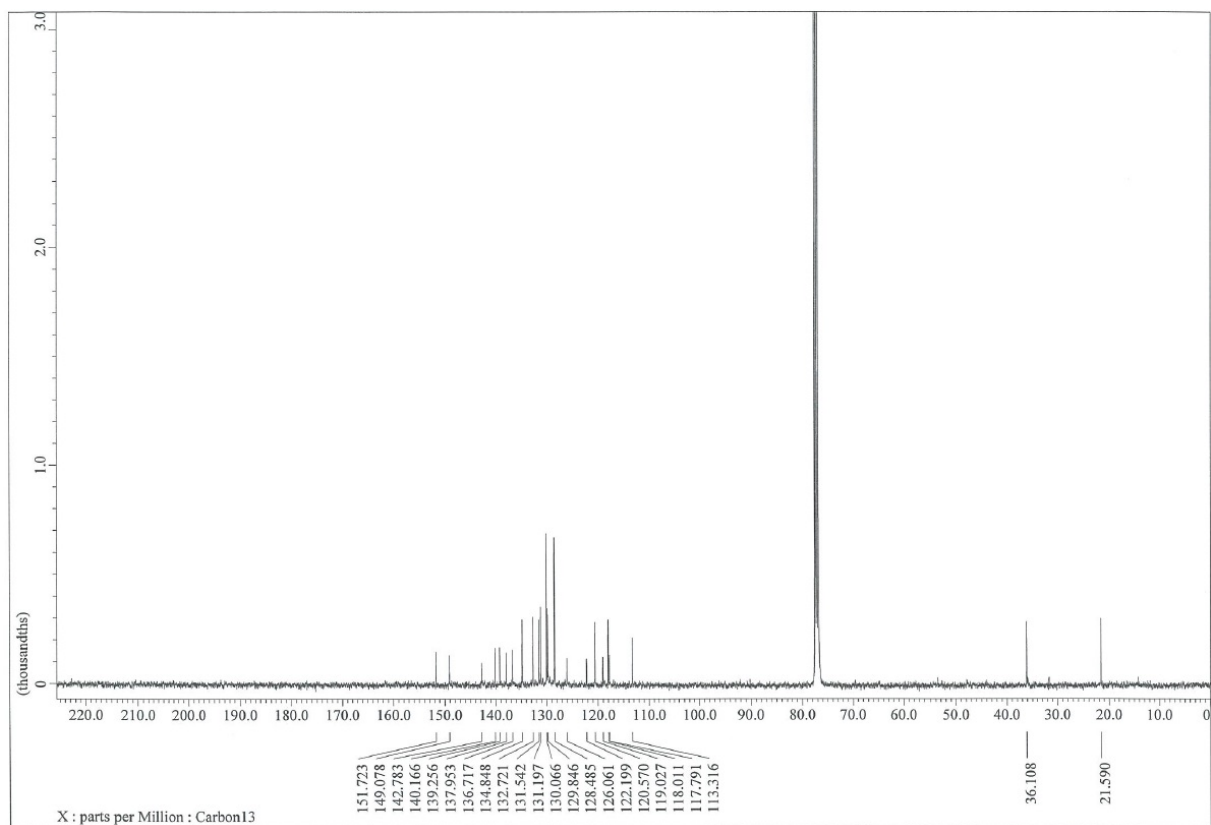


S18

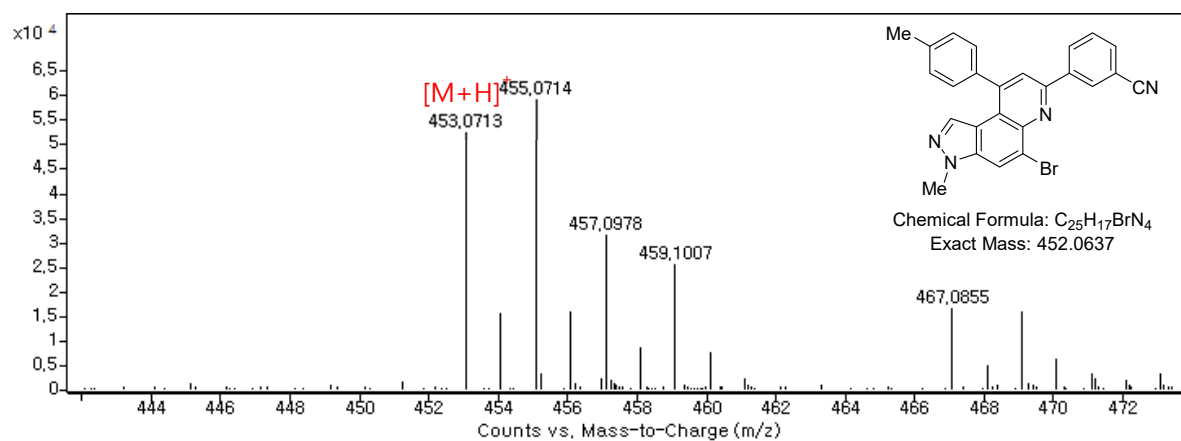


3-(5-Bromo-3-methyl-9-(*p*-tolyl)-3*H*-pyrazolo[4,3-*f*]quinolin-7-yl)benzonitrile (**1C**)

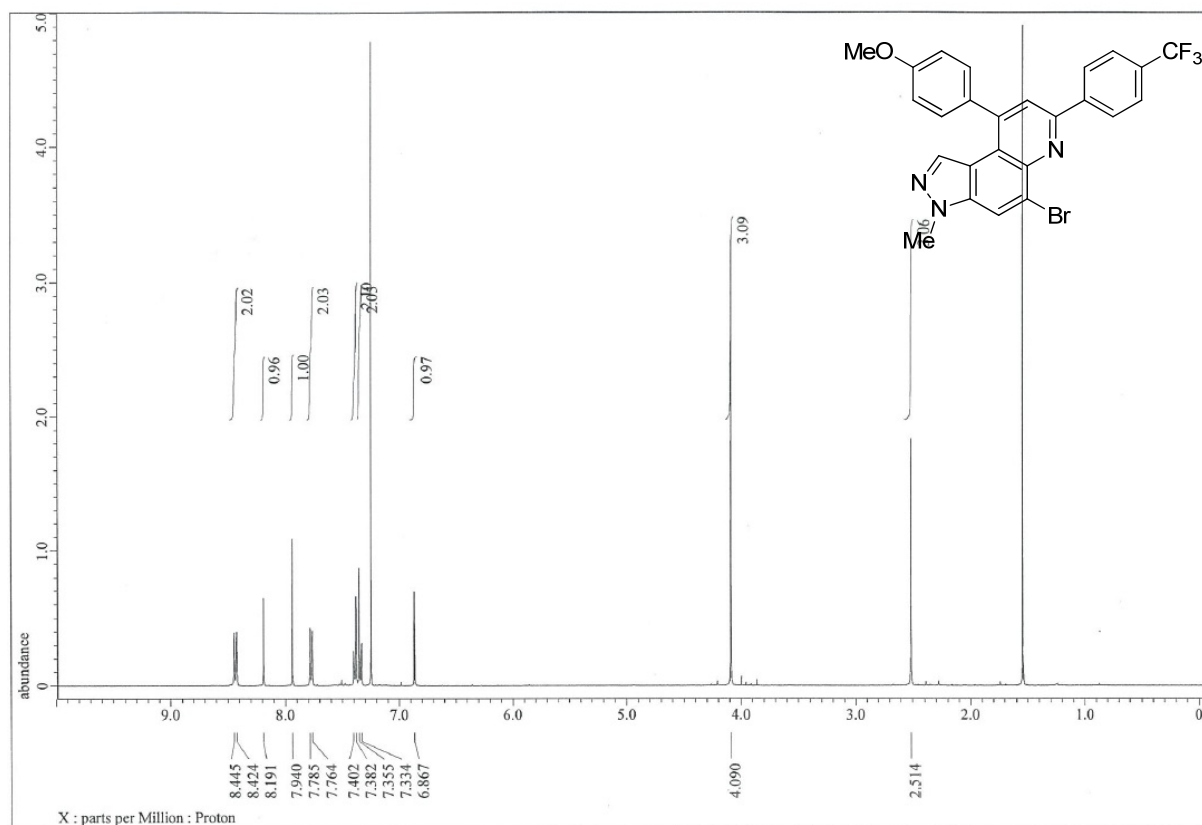


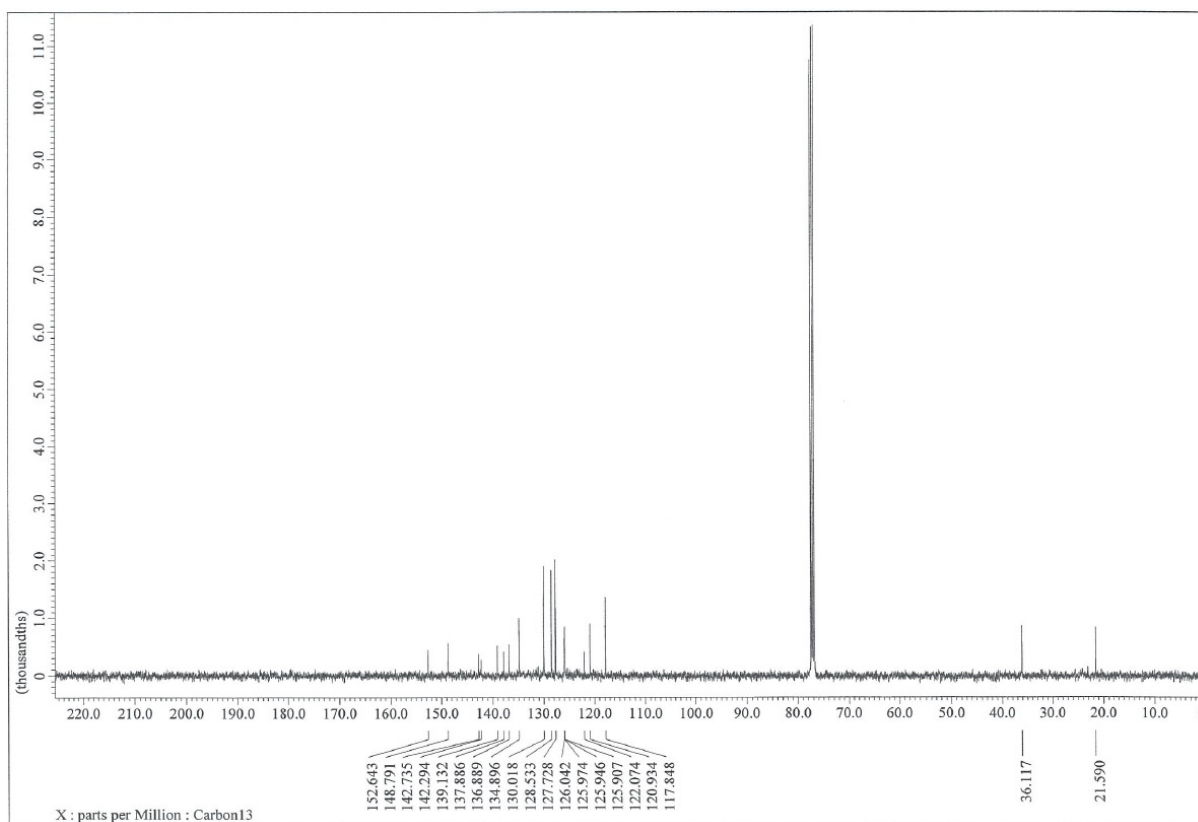


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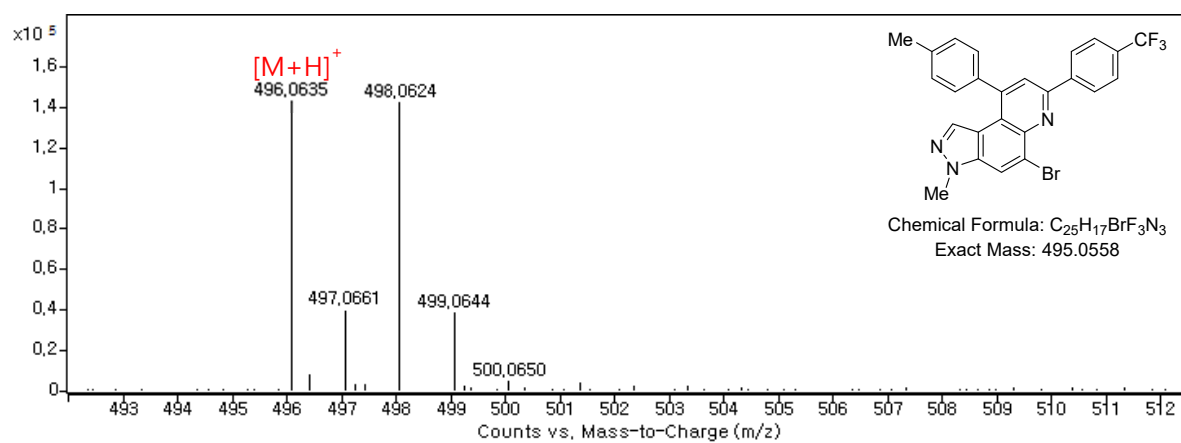


5-Bromo-3-methyl-9-(*p*-tolyl)-7-(4-(trifluoromethyl)phenyl)-3*H*-pyrazolo[4,3-*f*]quinoline (**1D**)

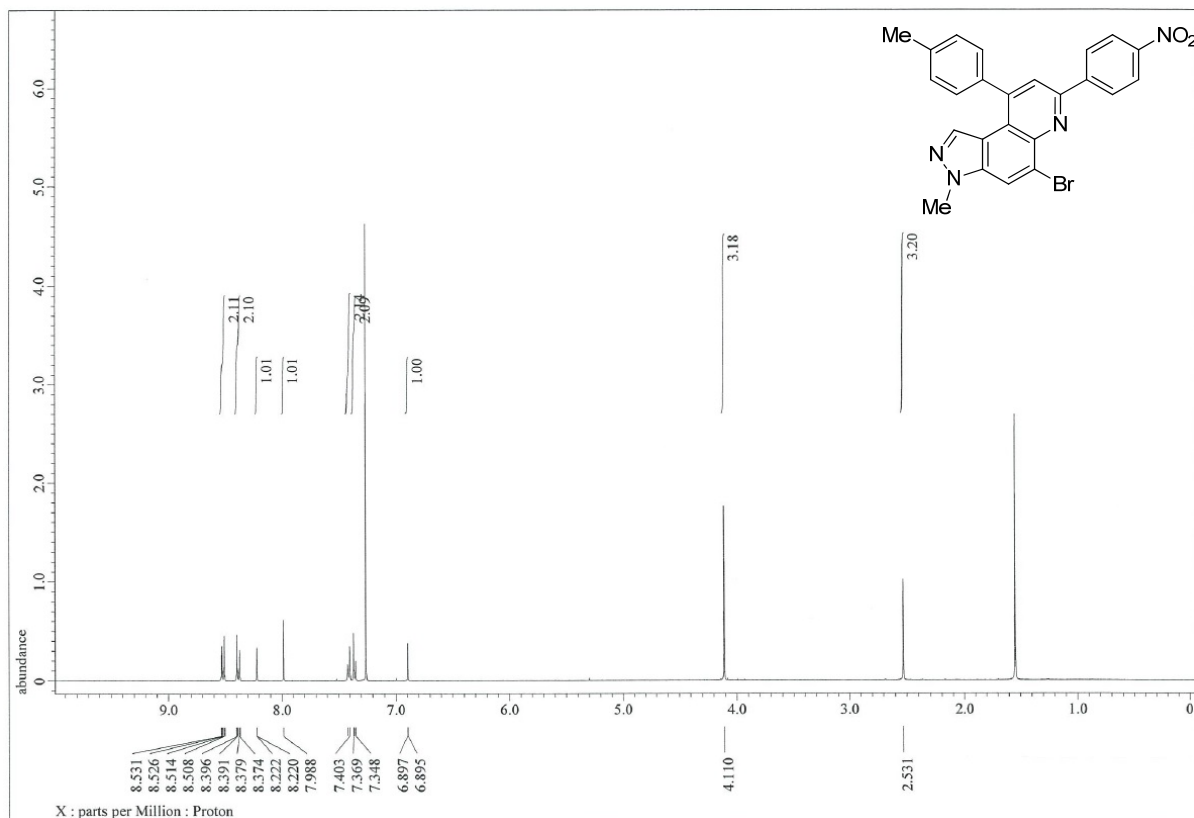


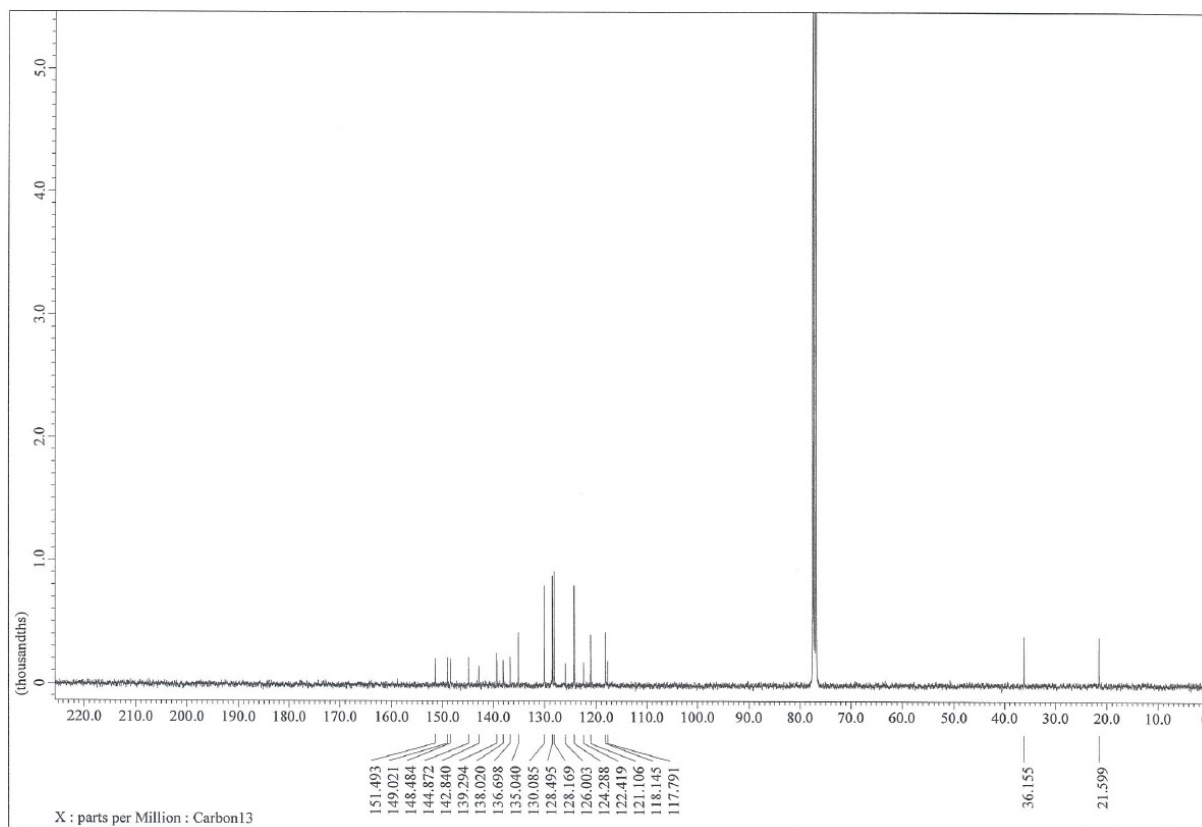


S24

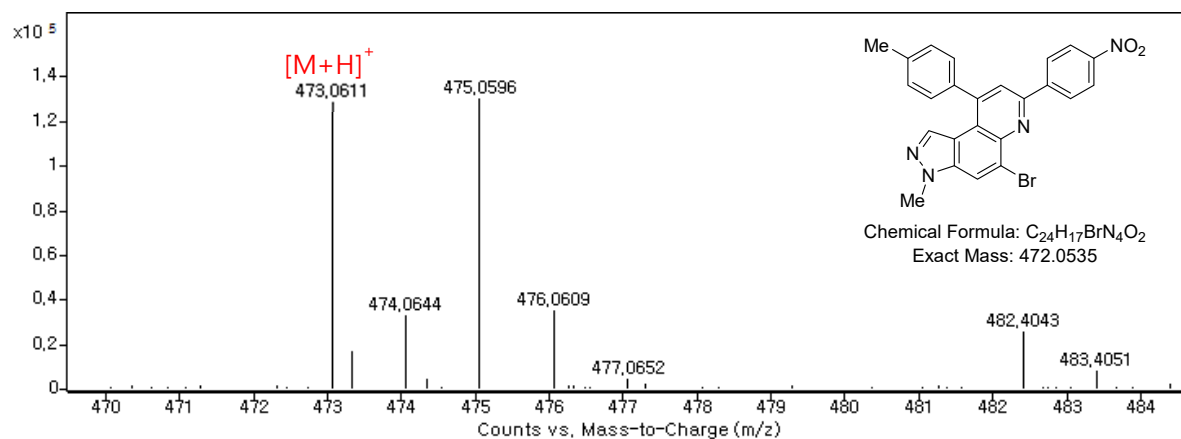


5-Bromo-3-methyl-7-(4-nitrophenyl)-9-(*p*-tolyl)-3*H*-pyrazolo[4,3-*f*]quinoline (**1E**)

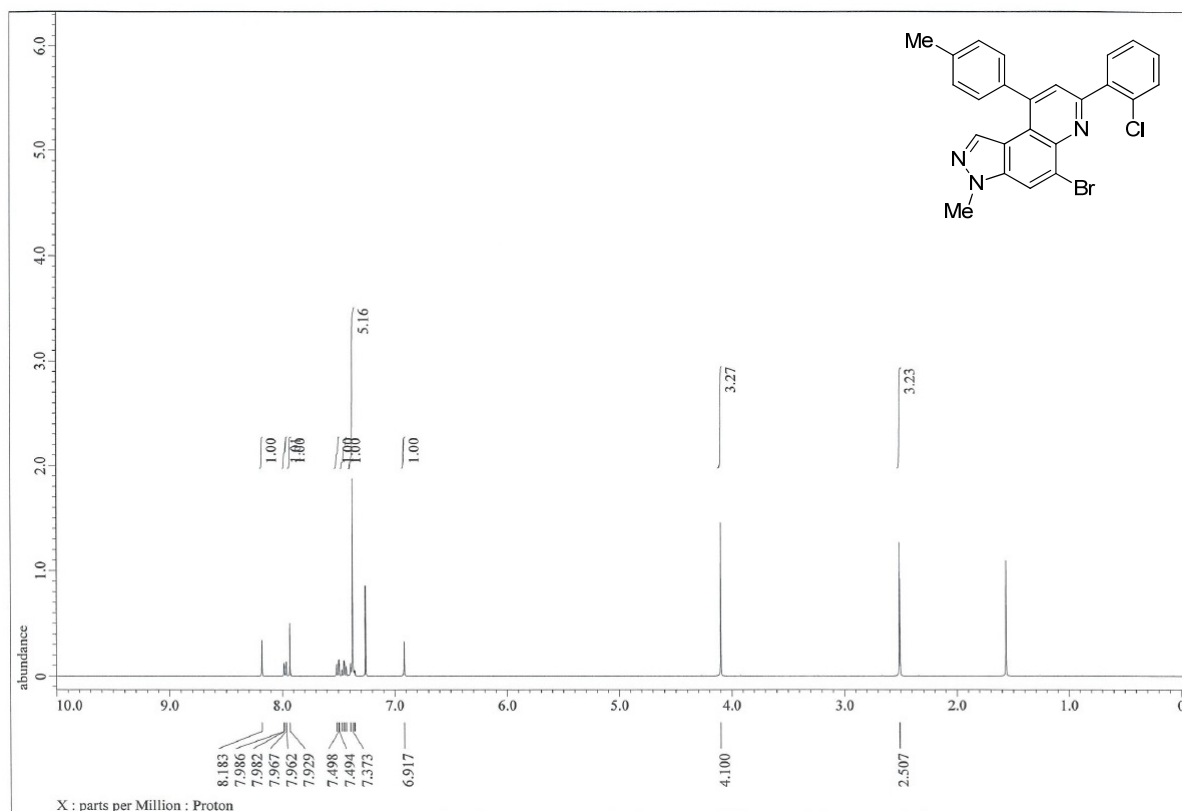


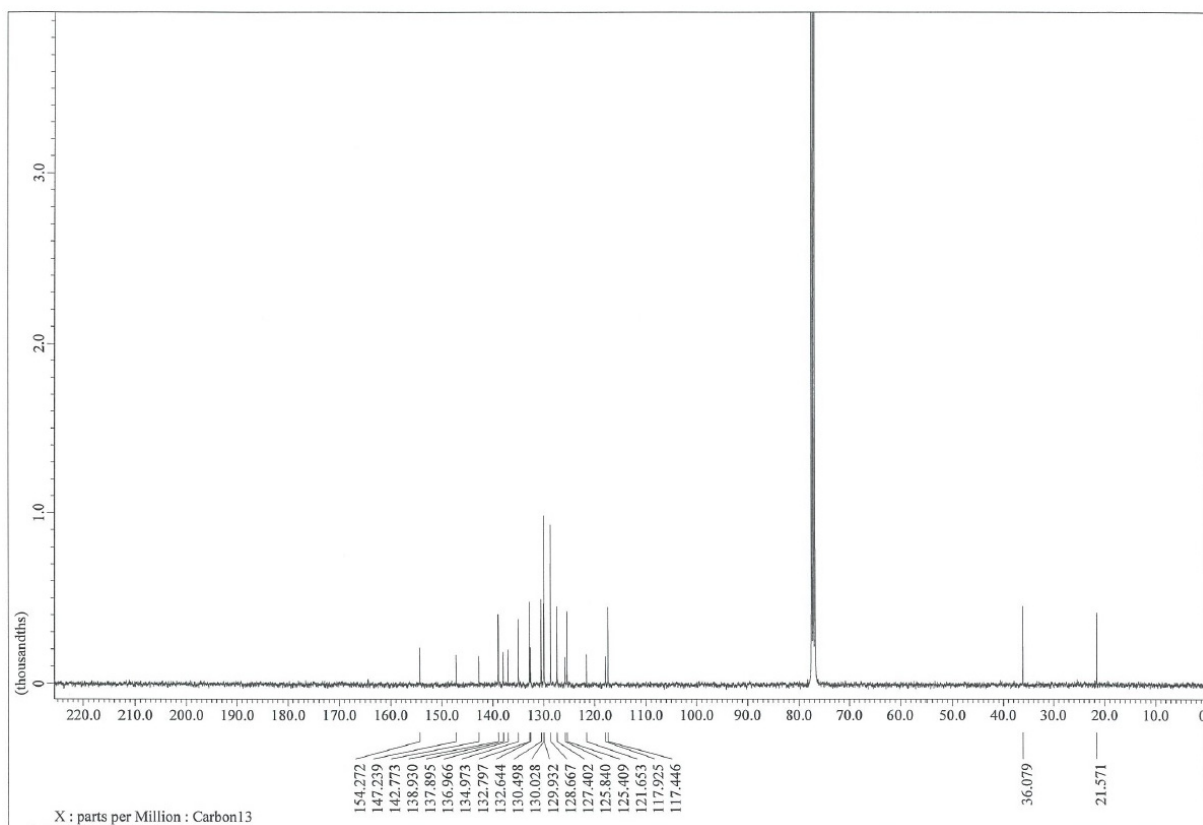


S27

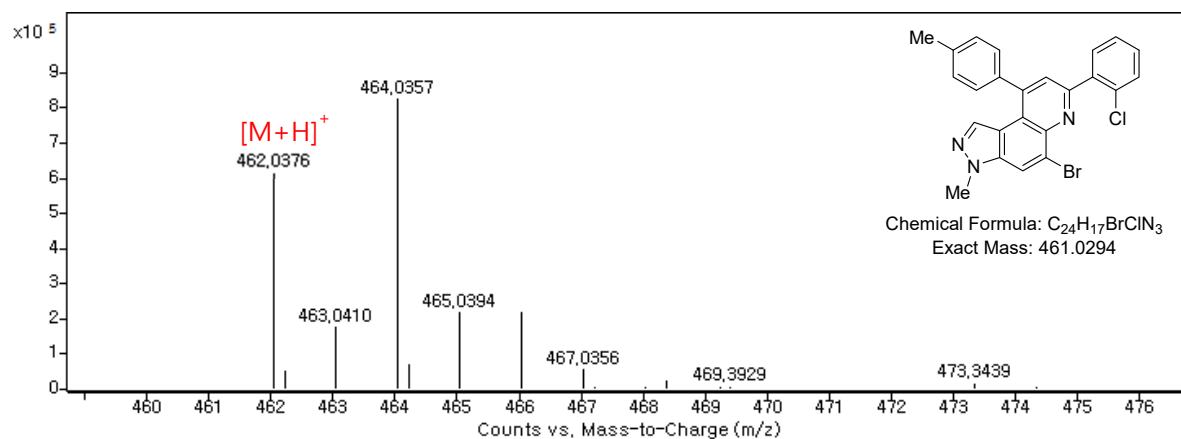


5-Bromo-7-(2-chlorophenyl)-3-methyl-9-(*p*-tolyl)-3H-pyrazolo[4,3-*f*]quinoline (**1F**)

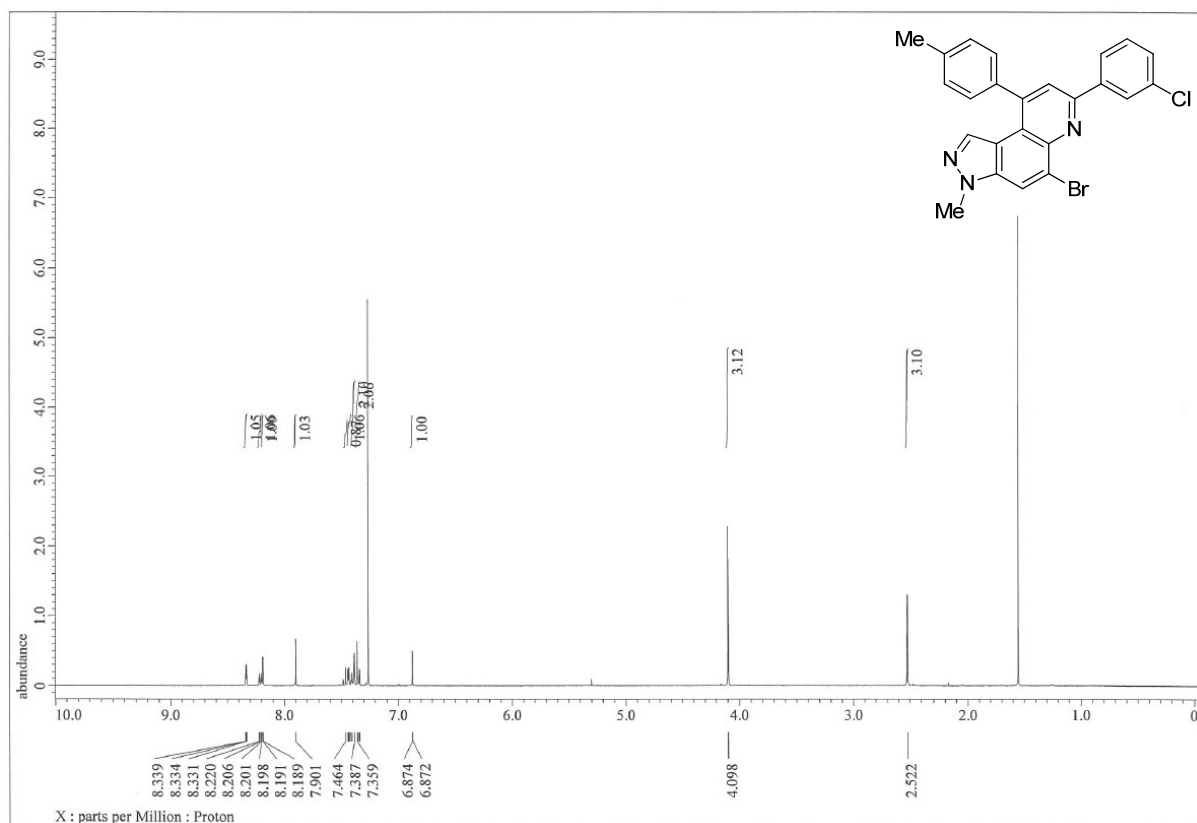


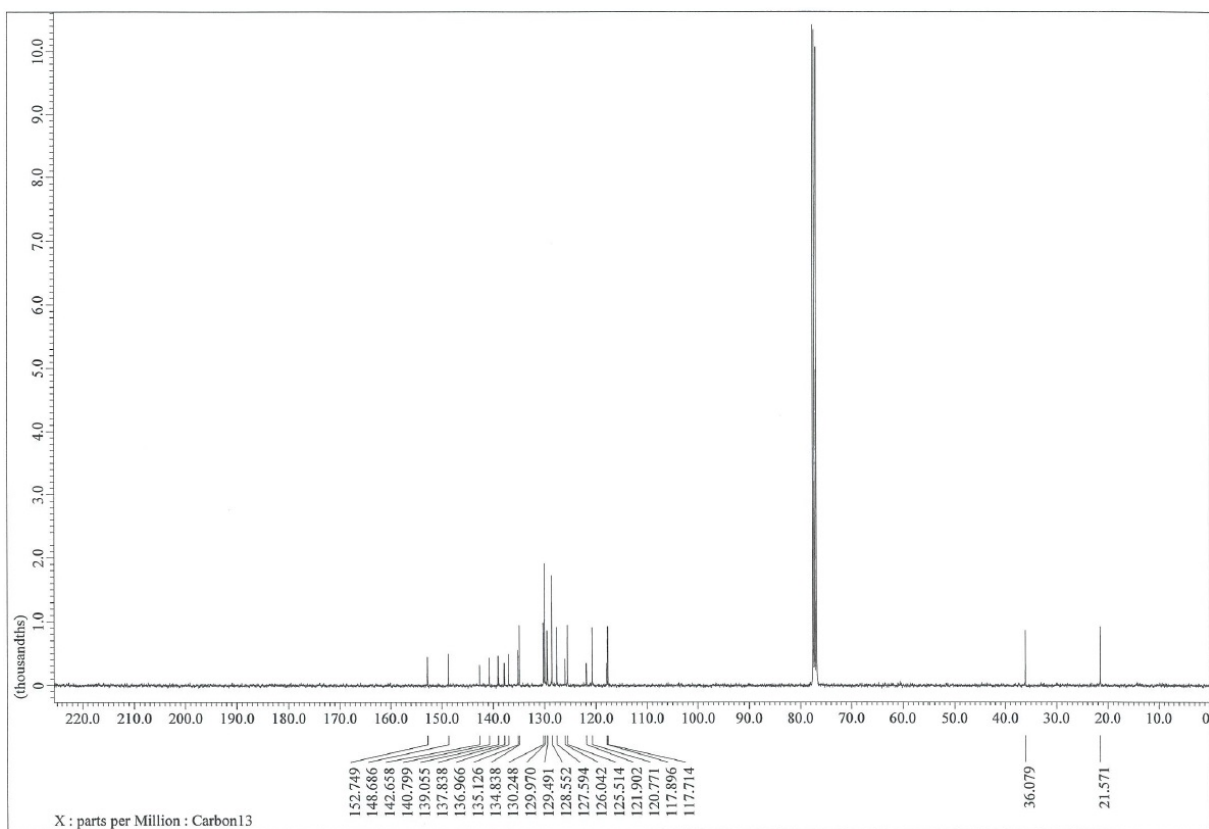


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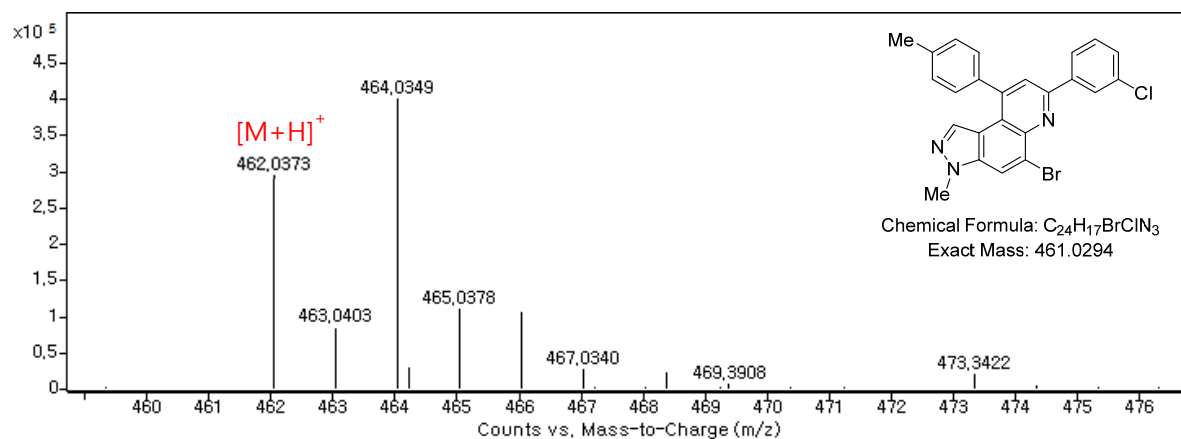


5-Bromo-7-(3-chlorophenyl)-3-methyl-9-(p-tolyl)-3H-pyrazolo[4,3-f]quinoline (1G)

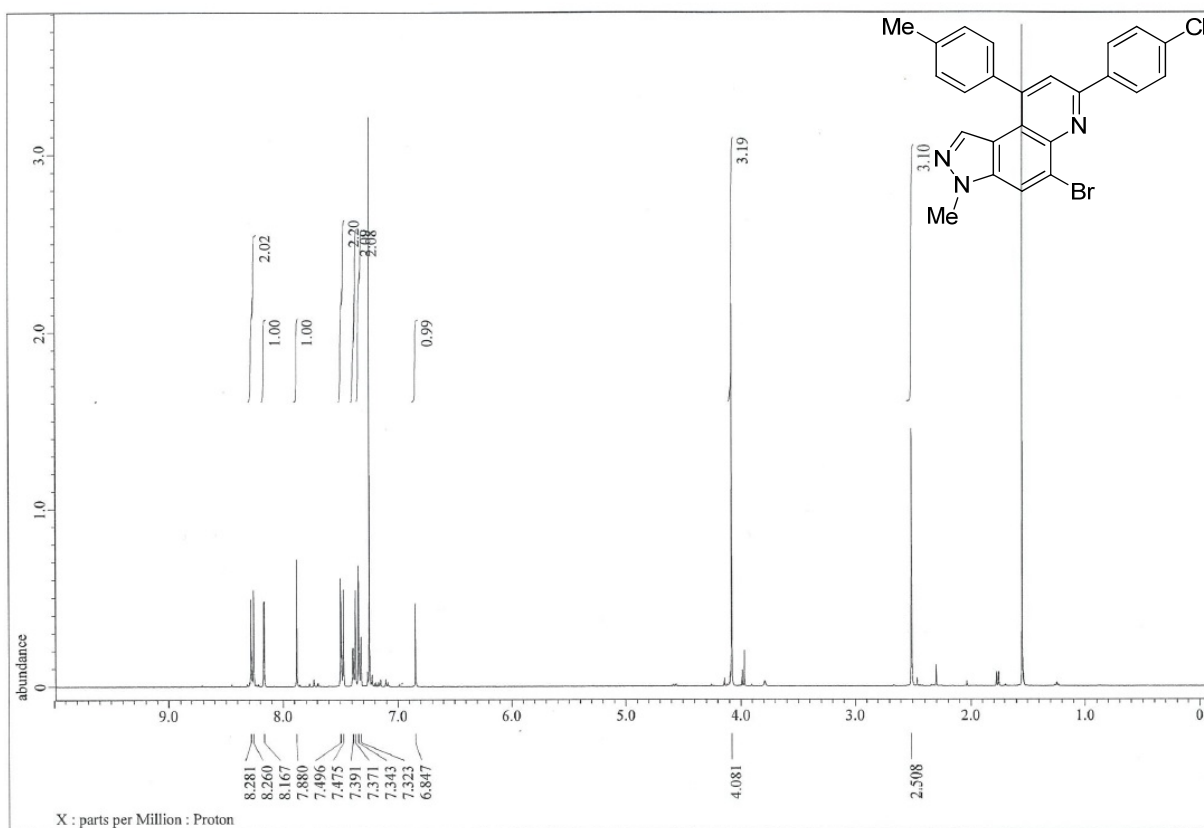


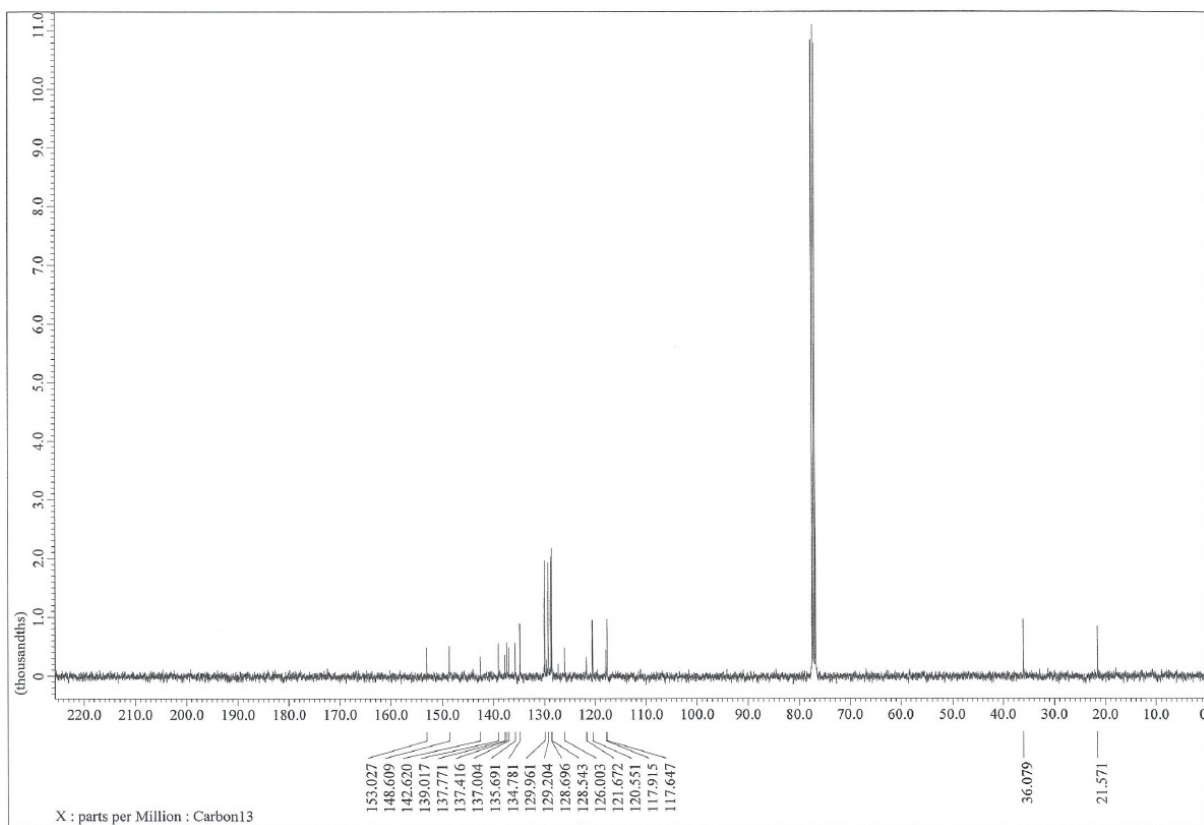


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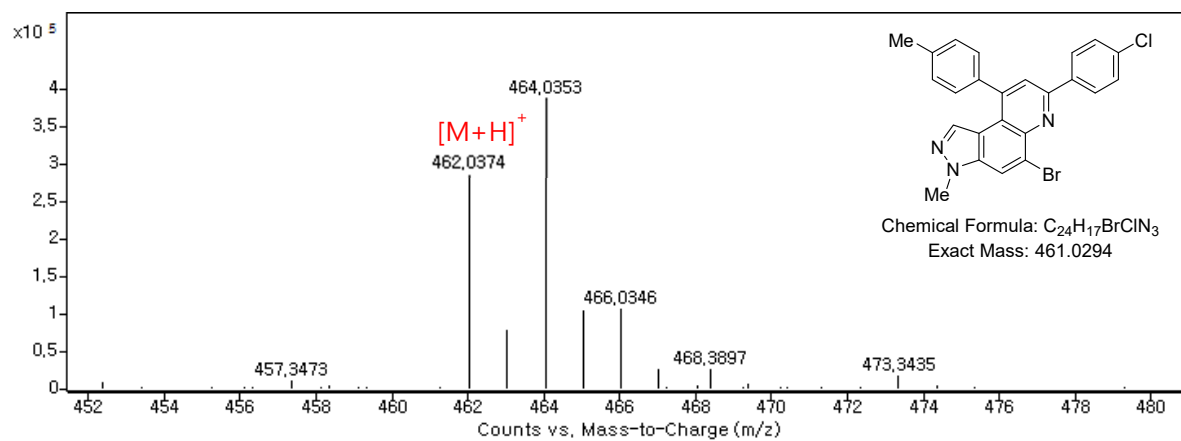


5-Bromo-7-(4-chlorophenyl)-3-methyl-9-(p-tolyl)-3H-pyrazolo[4,3-f]quinoline (1H)

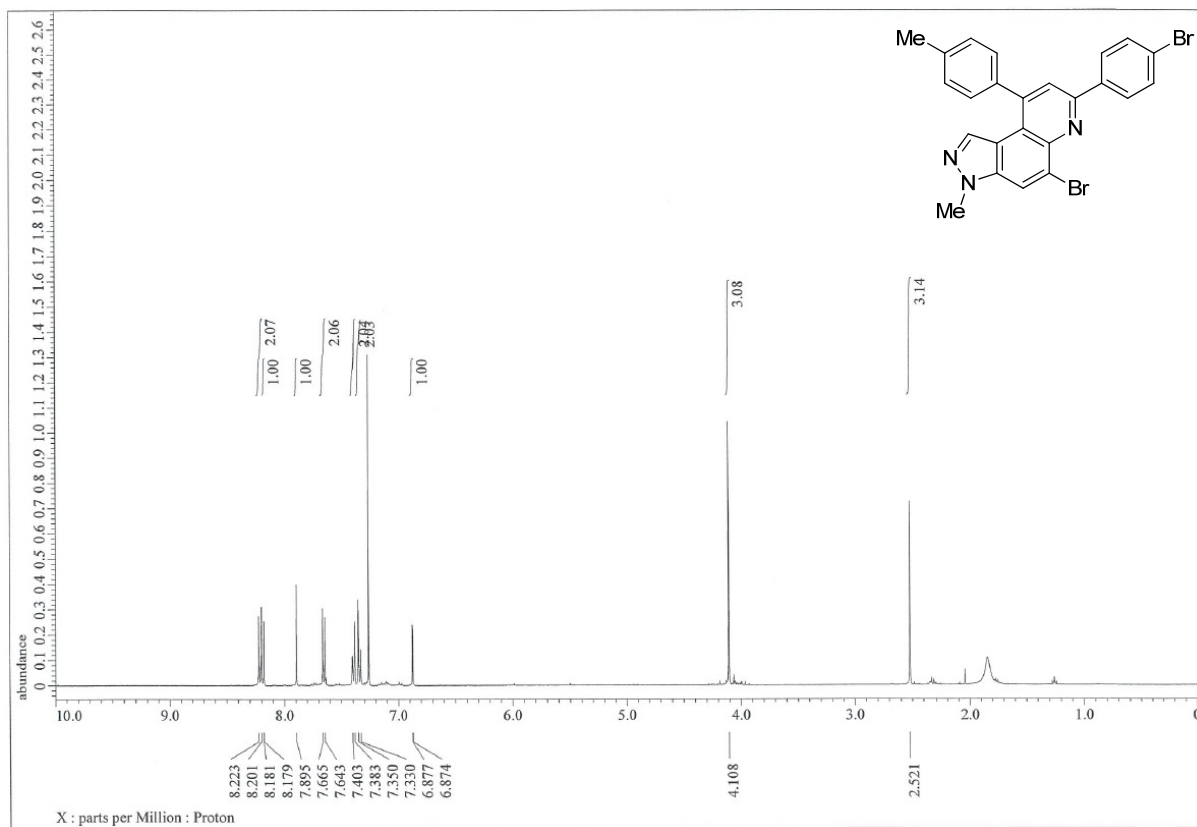


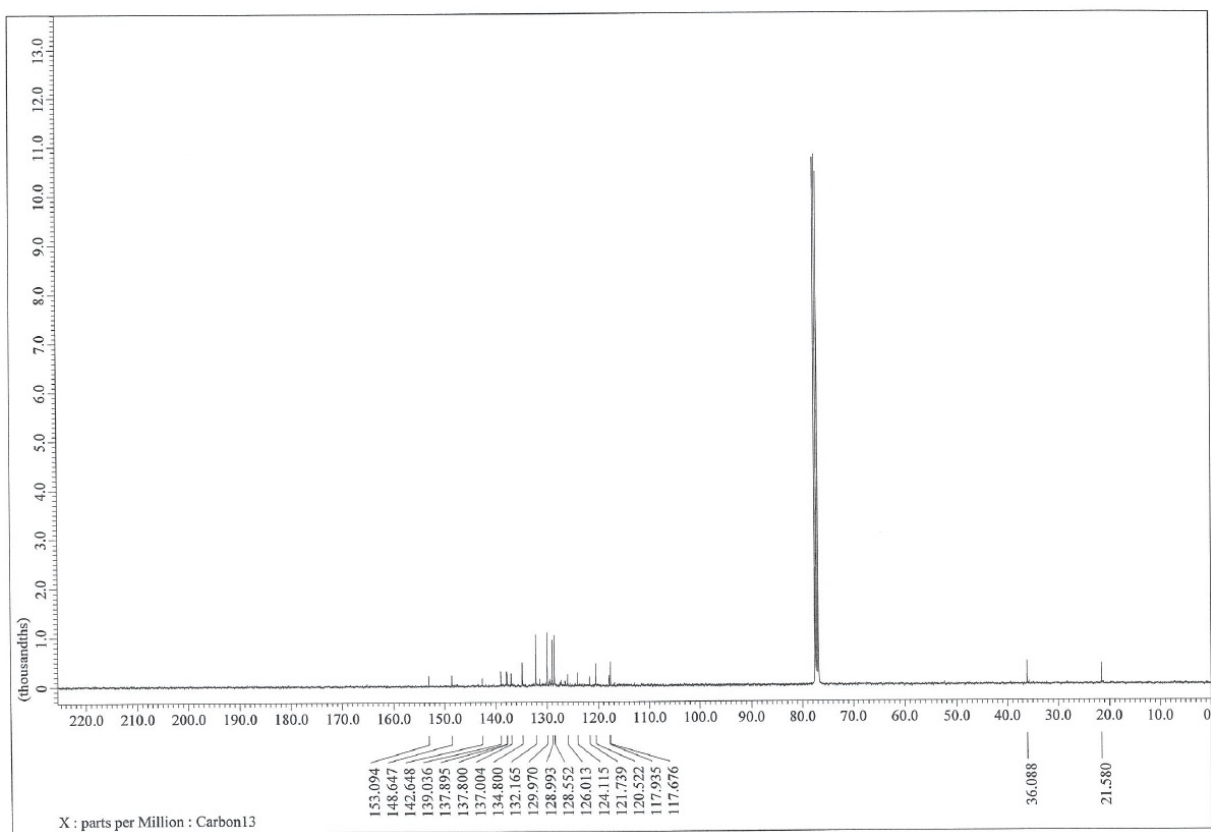


S36

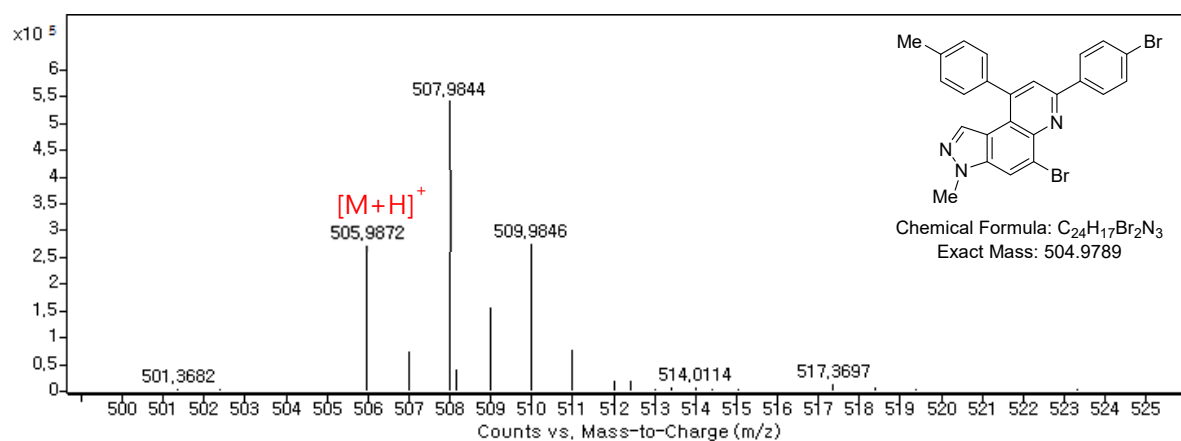


5-Bromo-7-(4-bromophenyl)-3-methyl-9-(p-tolyl)-3H-pyrazolo[4,3-f]quinoline (11)

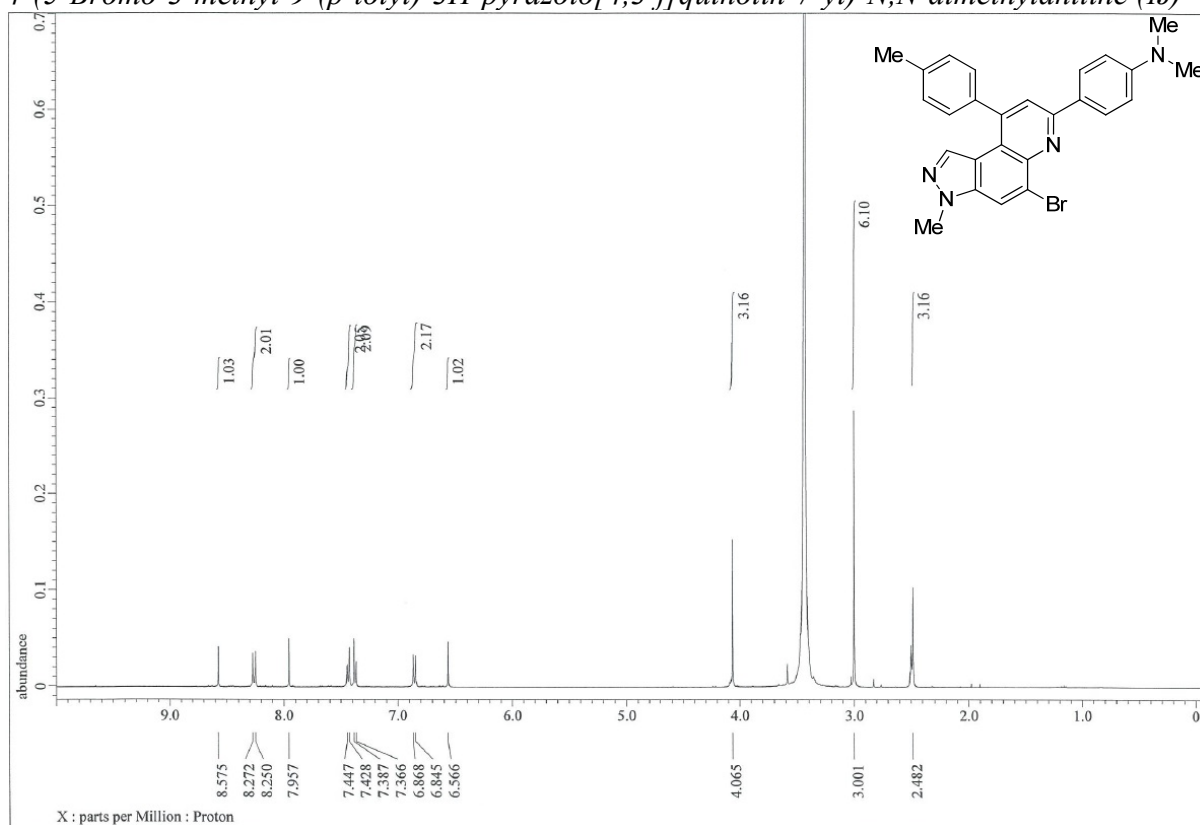


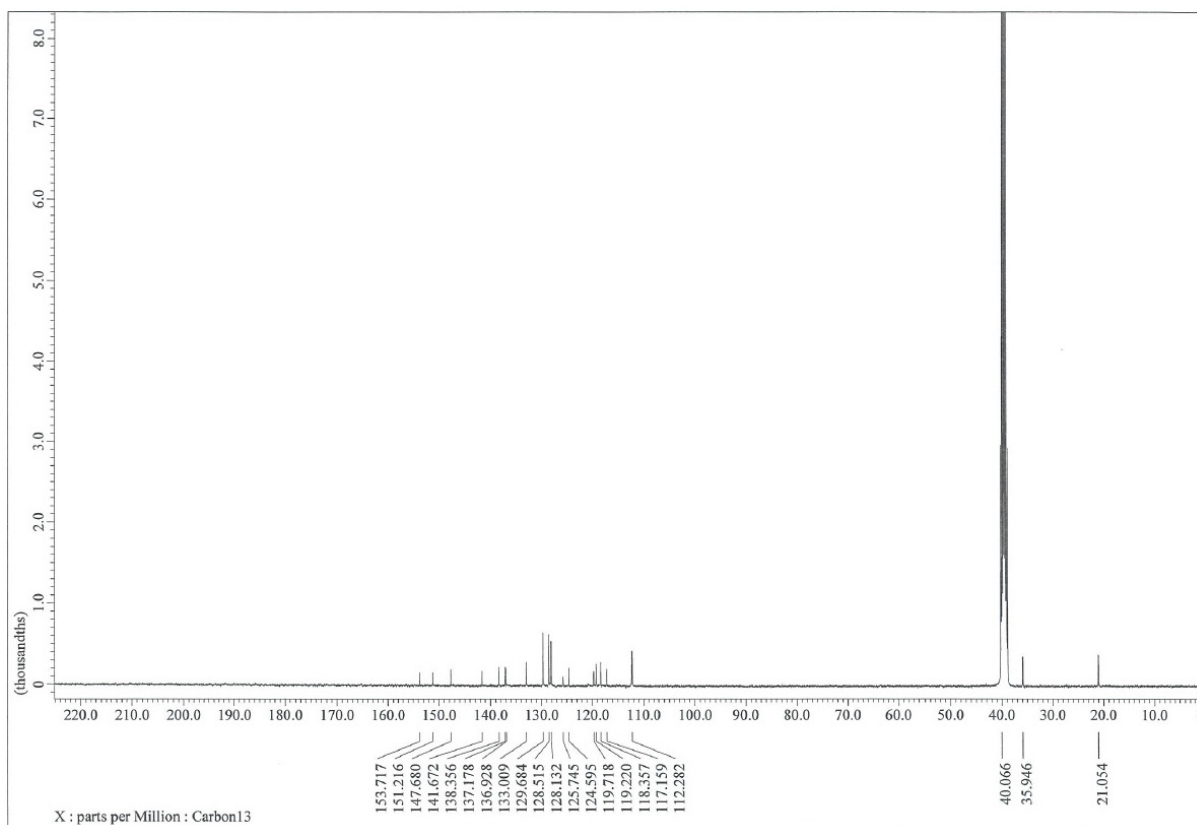


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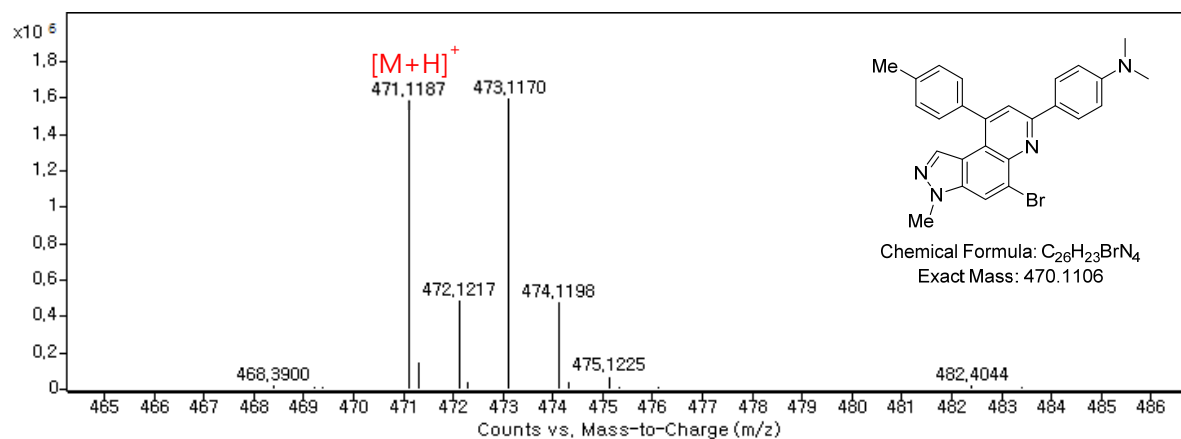


4-(5-Bromo-3-methyl-9-(*p*-tolyl)-3*H*-pyrazolo[4,3-*f*]quinolin-7-yl)-*N,N*-dimethylaniline (1J)

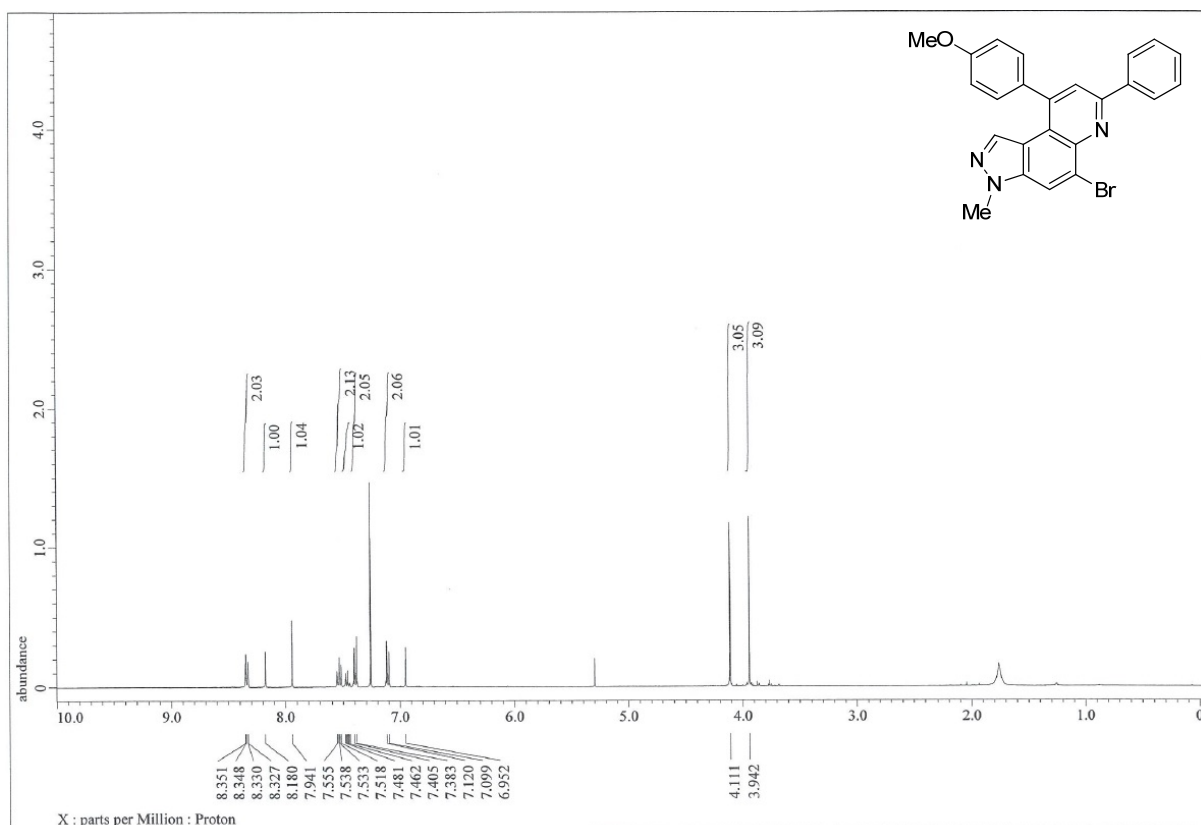


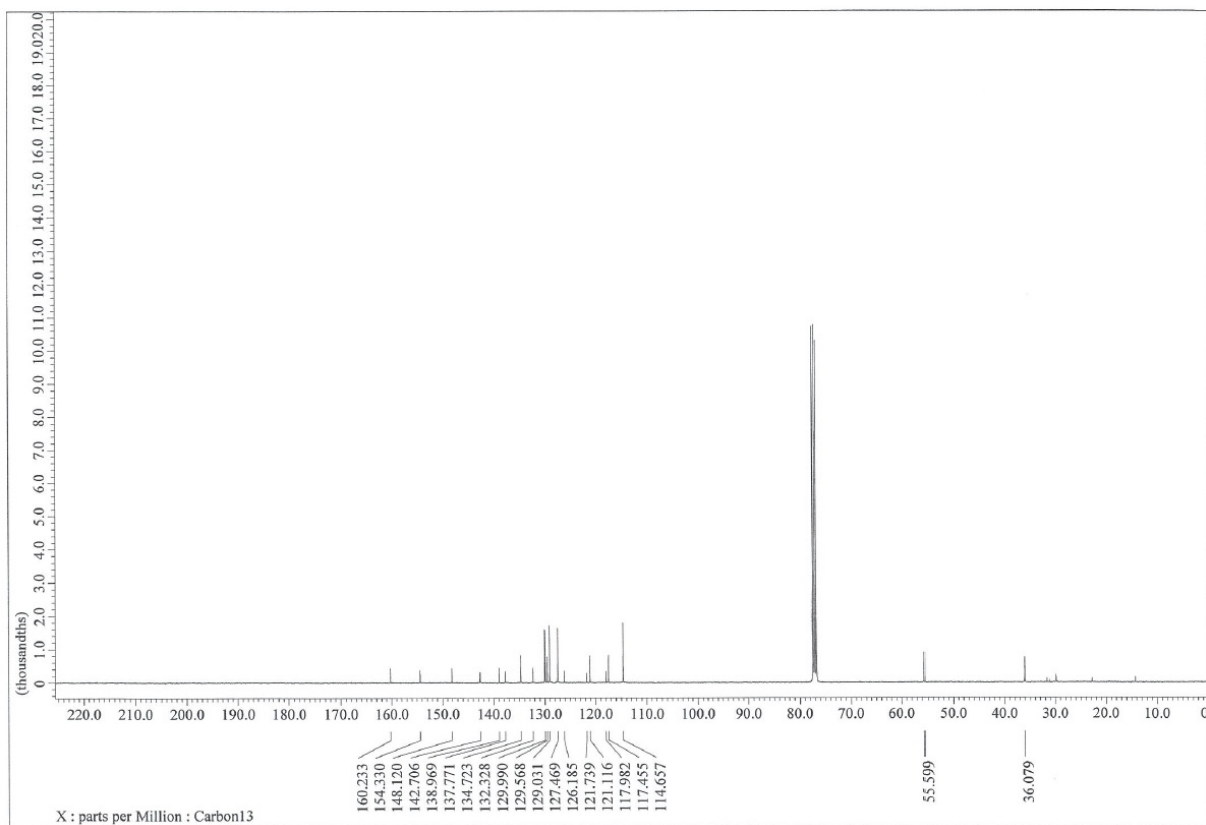


S42

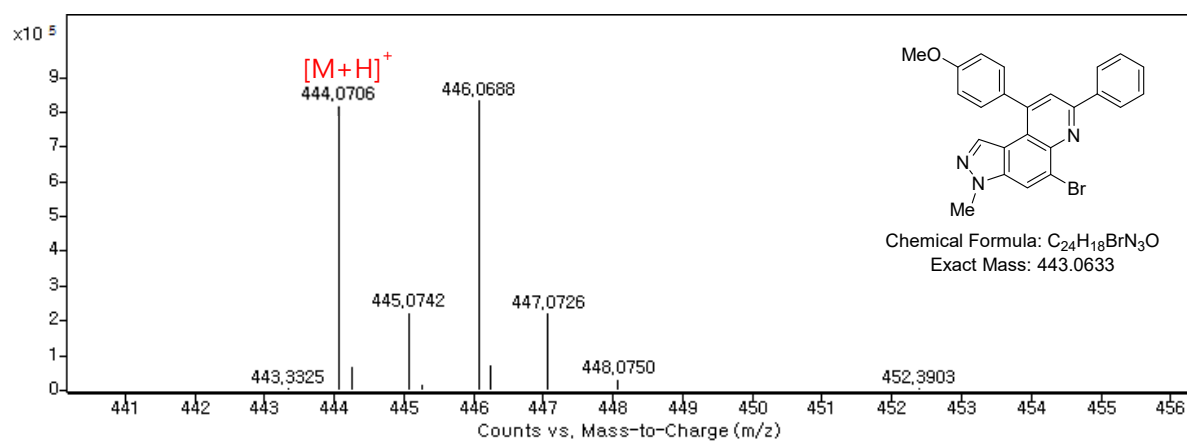


5-Bromo-9-(4-methoxyphenyl)-3-methyl-7-phenyl-3H-pyrazolo[4,3-f]quinoline (1K)

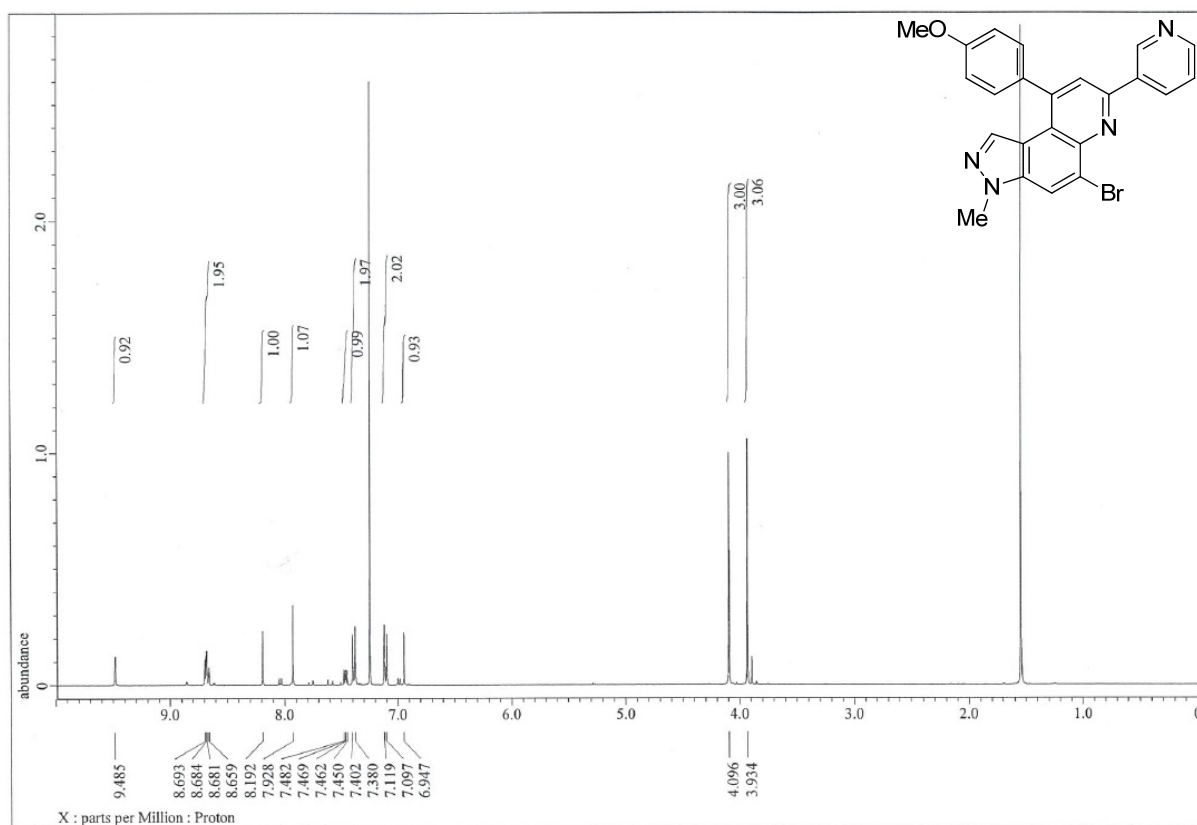


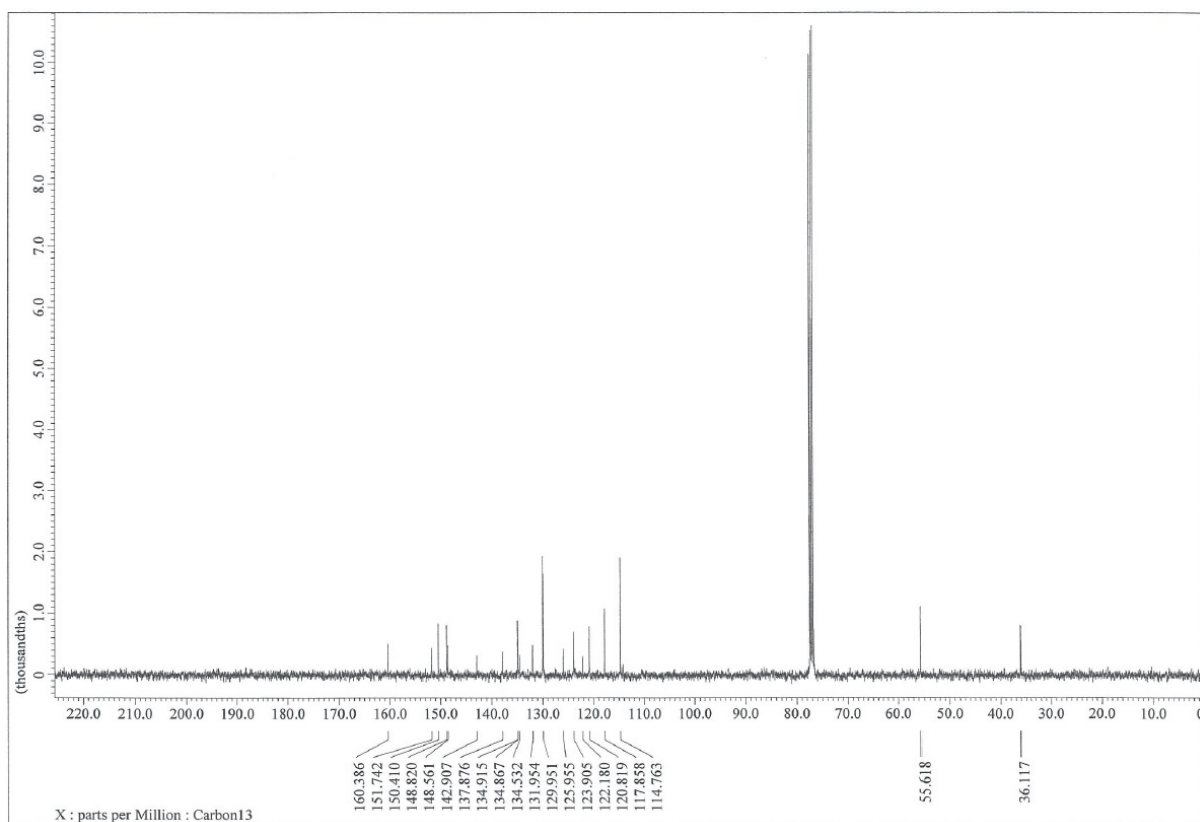


S45

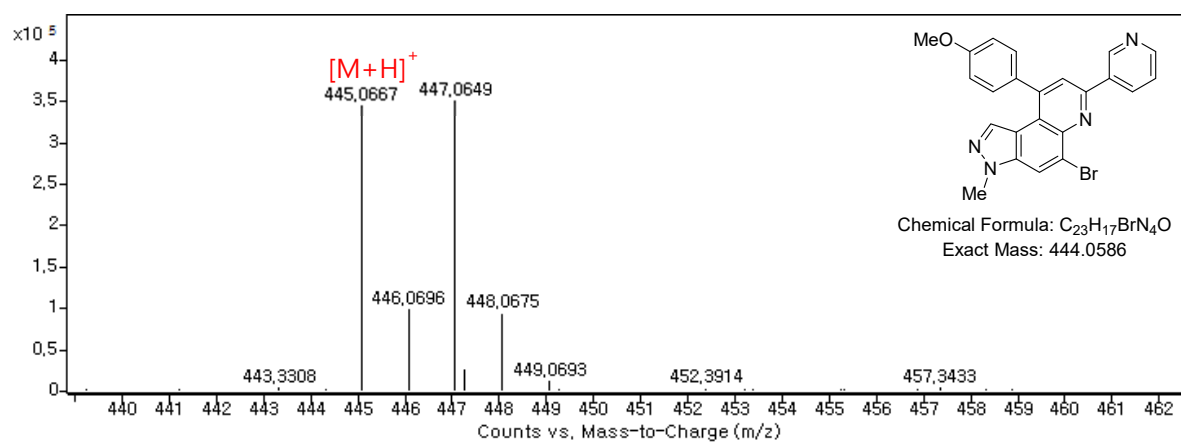


5-Bromo-9-(4-methoxyphenyl)-3-methyl-7-(pyridin-3-yl)-3H-pyrazolo[4,3-f]quinoline (1L)

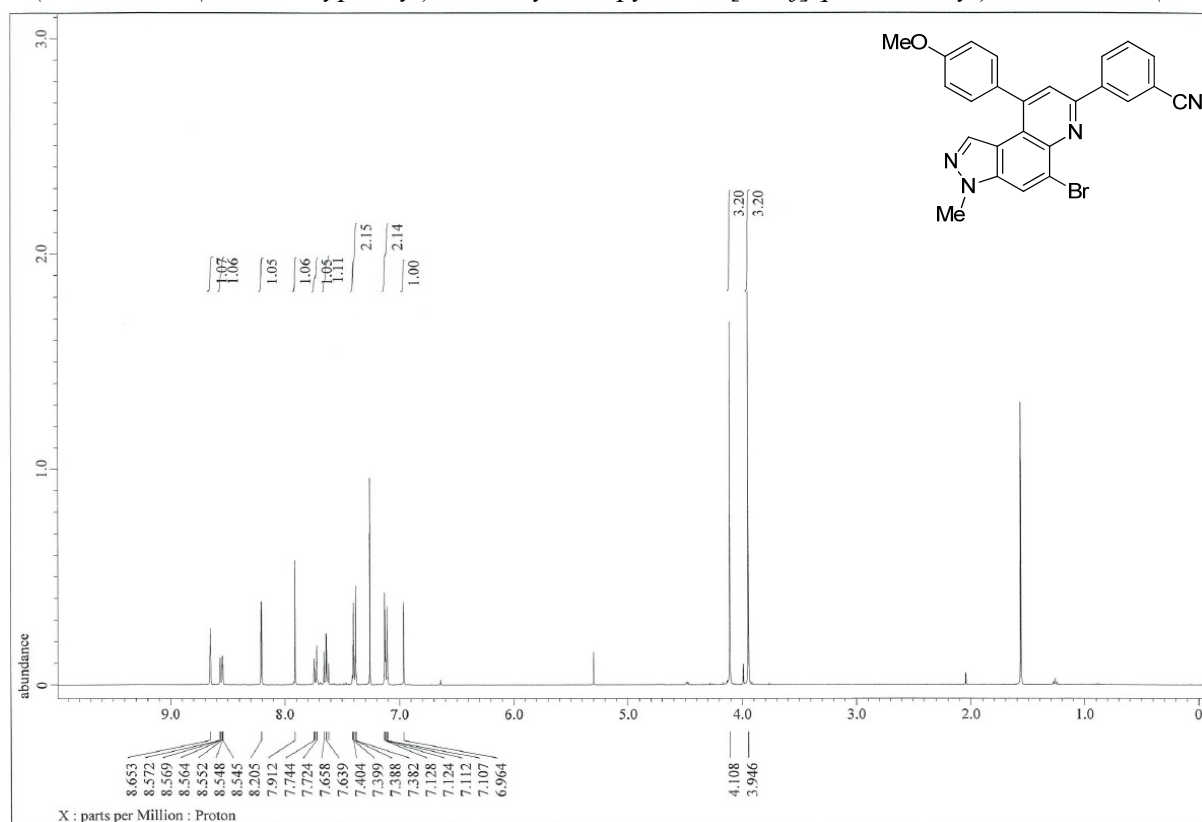


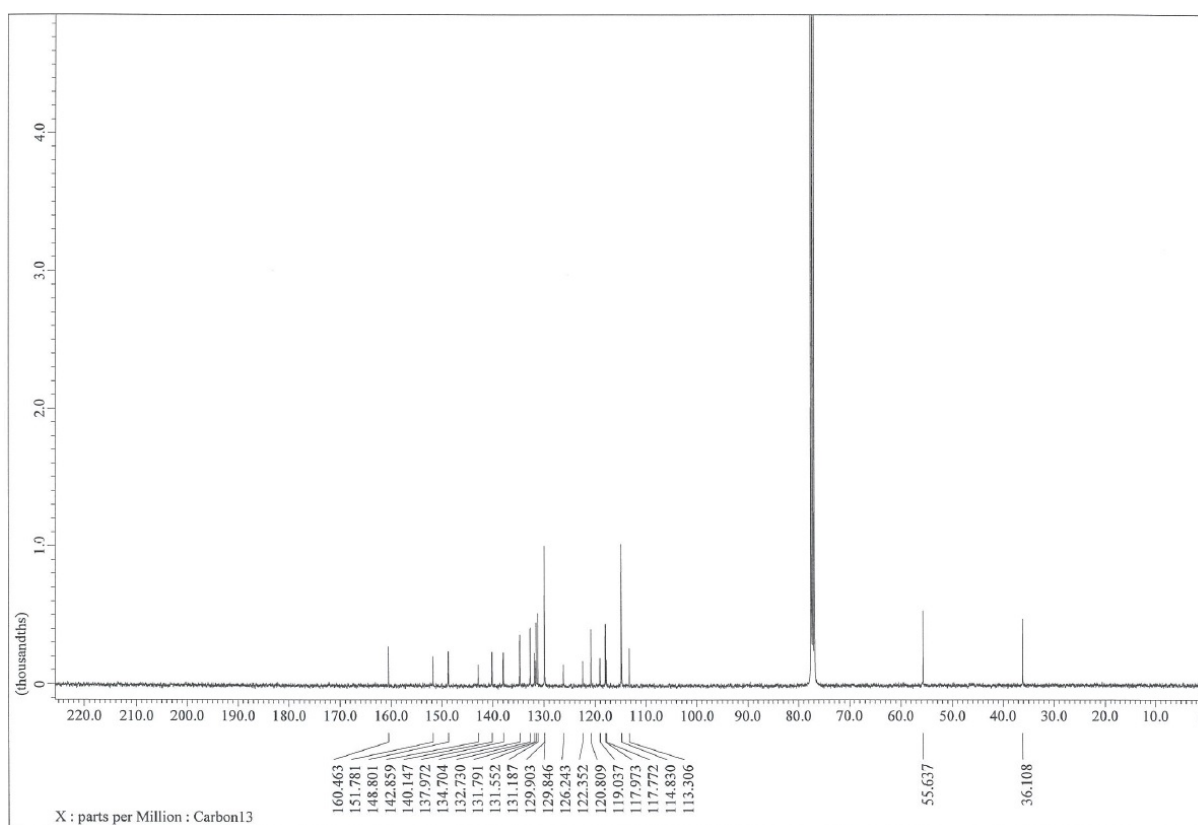


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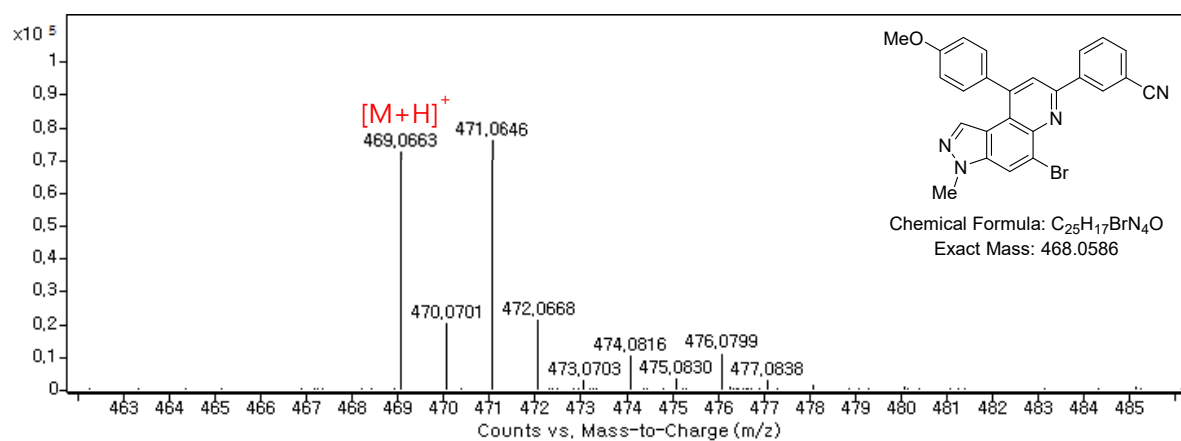


3-(5-Bromo-9-(4-methoxyphenyl)-3-methyl-3H-pyrazolo[4,3-f]quinolin-7-yl)benzonitrile (1M)

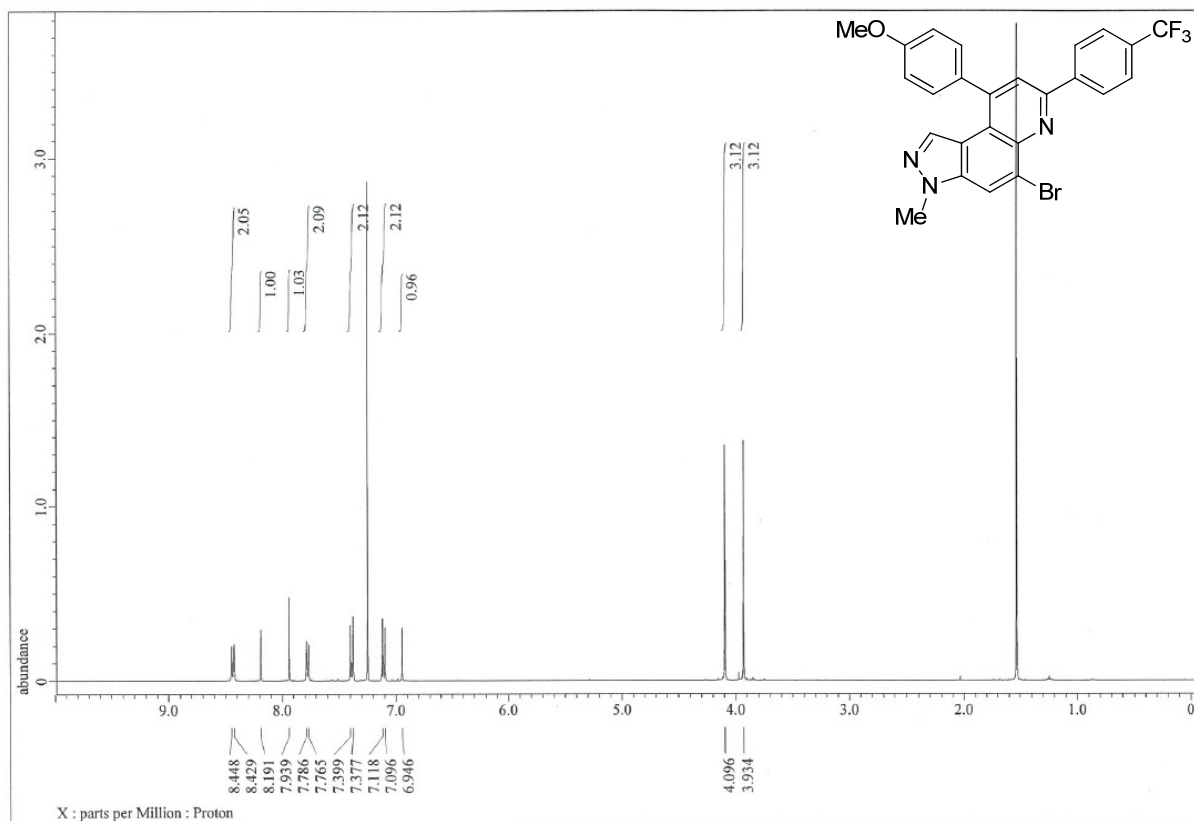


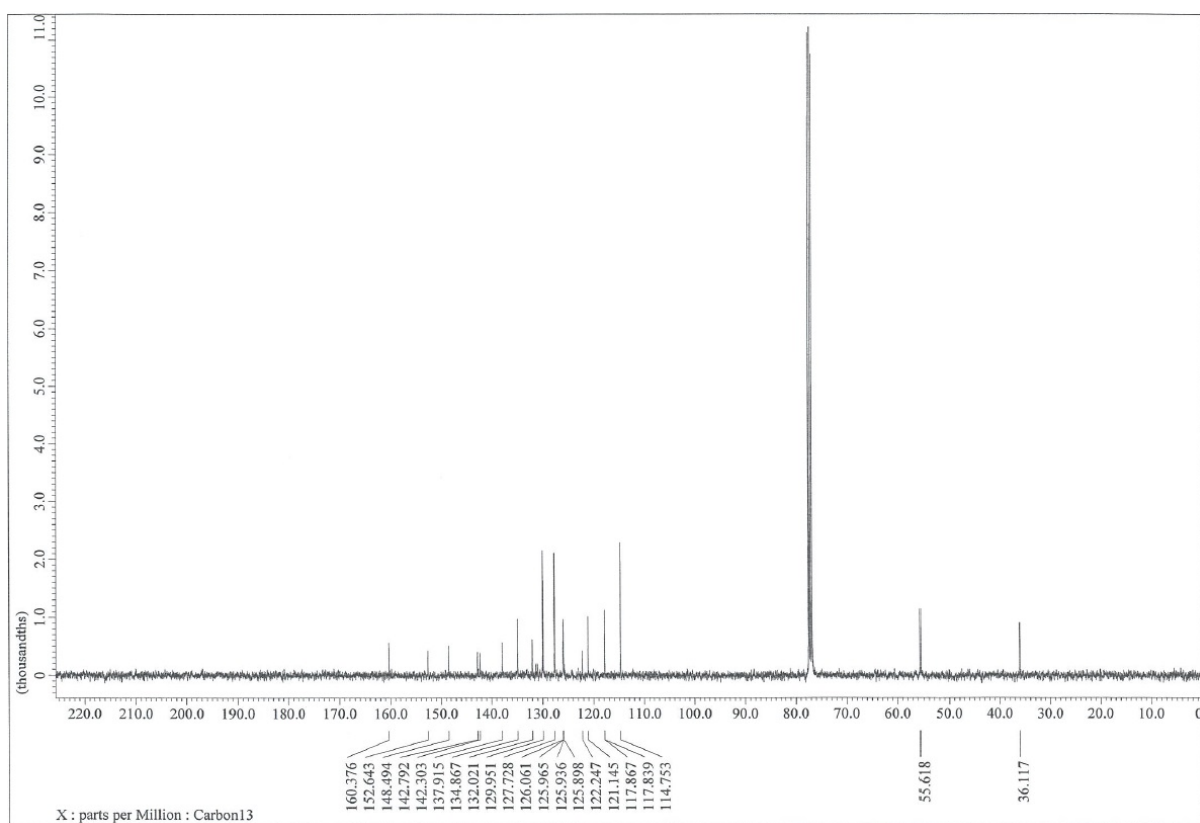


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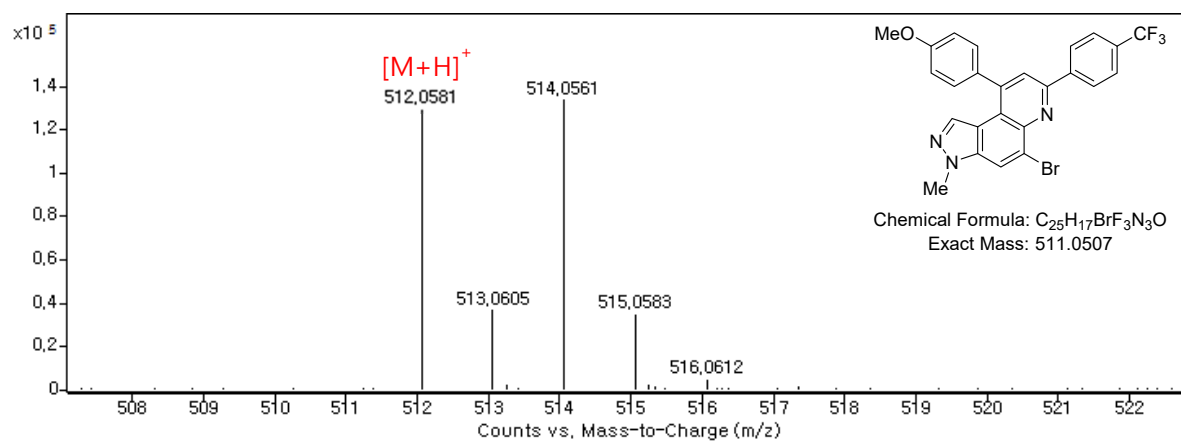


*5-Bromo-9-(4-methoxyphenyl)-3-methyl-7-(4-(trifluoromethyl)phenyl)-3H-pyrazolo[4,3-*f*]quinoline (1N)*

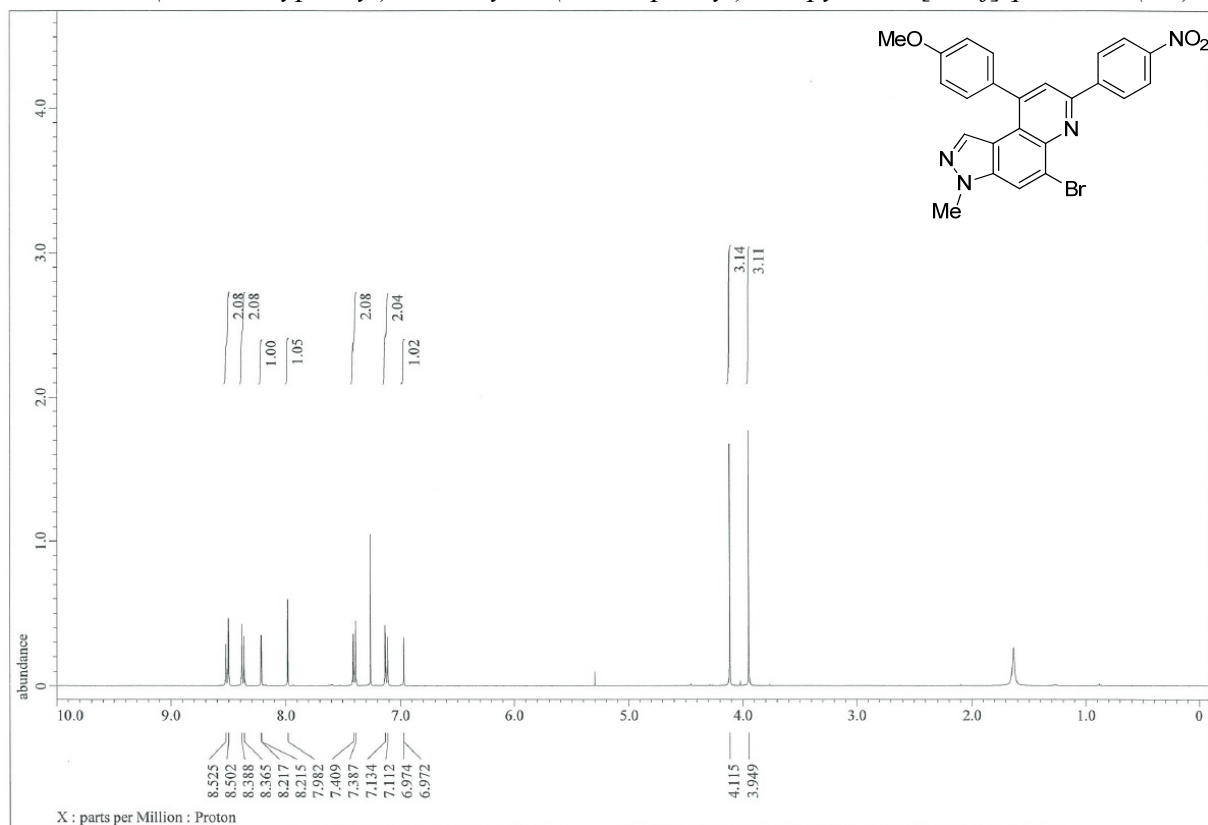


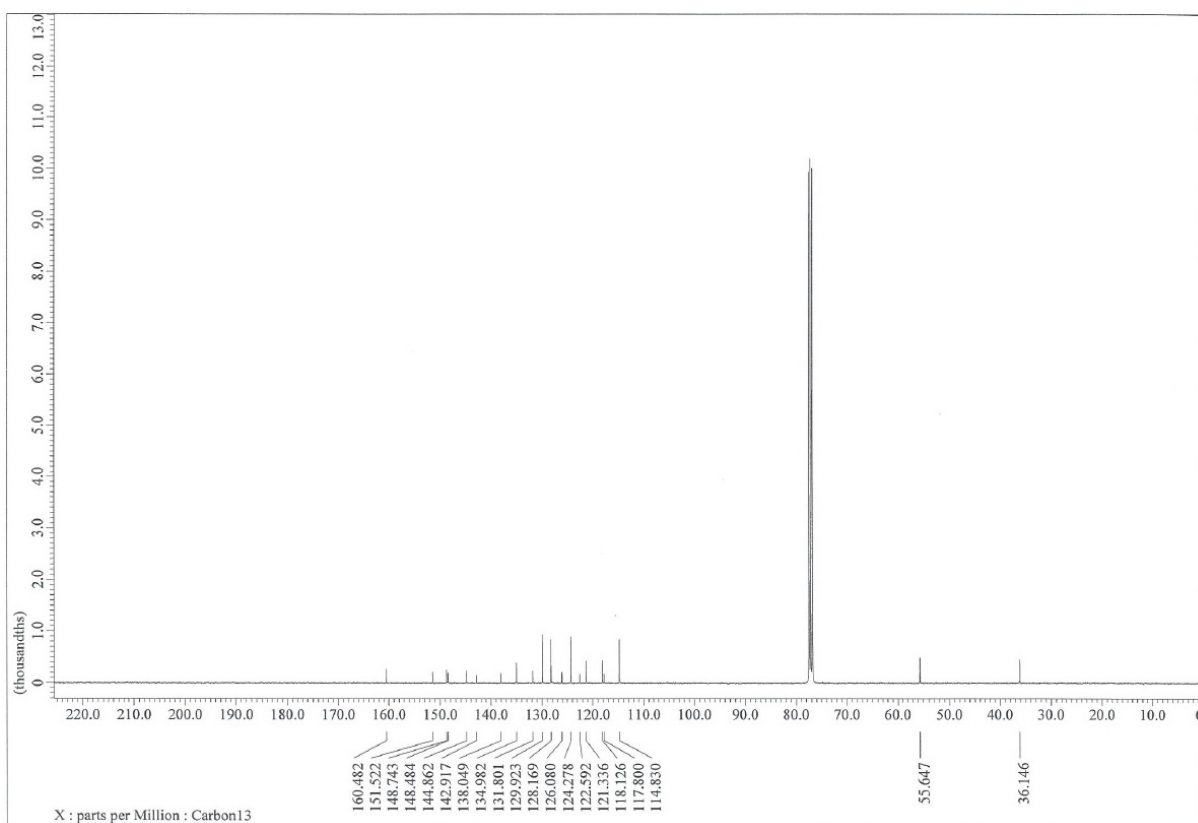


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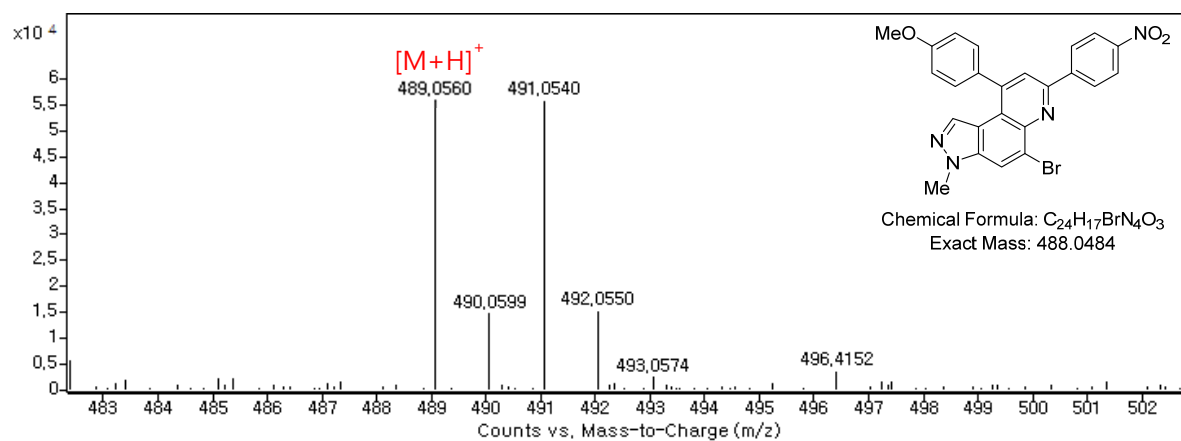


5-Bromo-9-(4-methoxyphenyl)-3-methyl-7-(4-nitrophenyl)-3H-pyrazolo[4,3-f]quinoline (10)

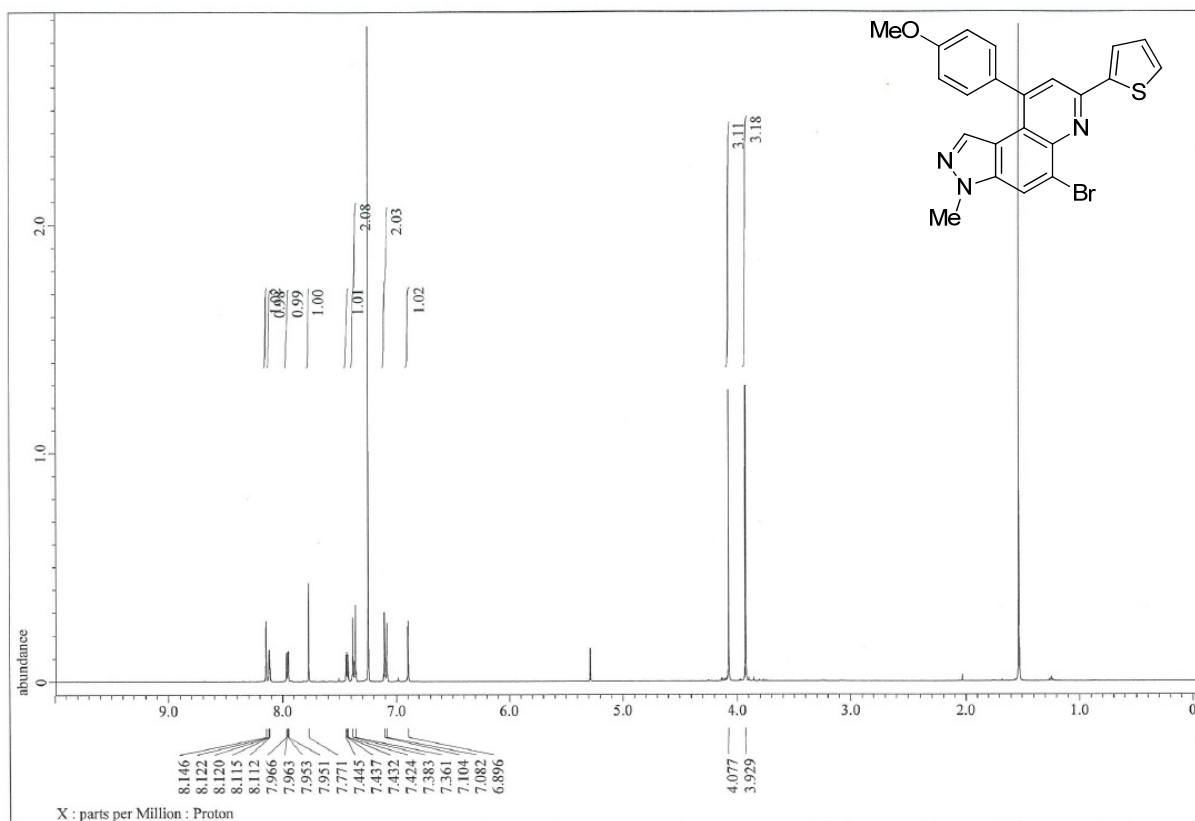


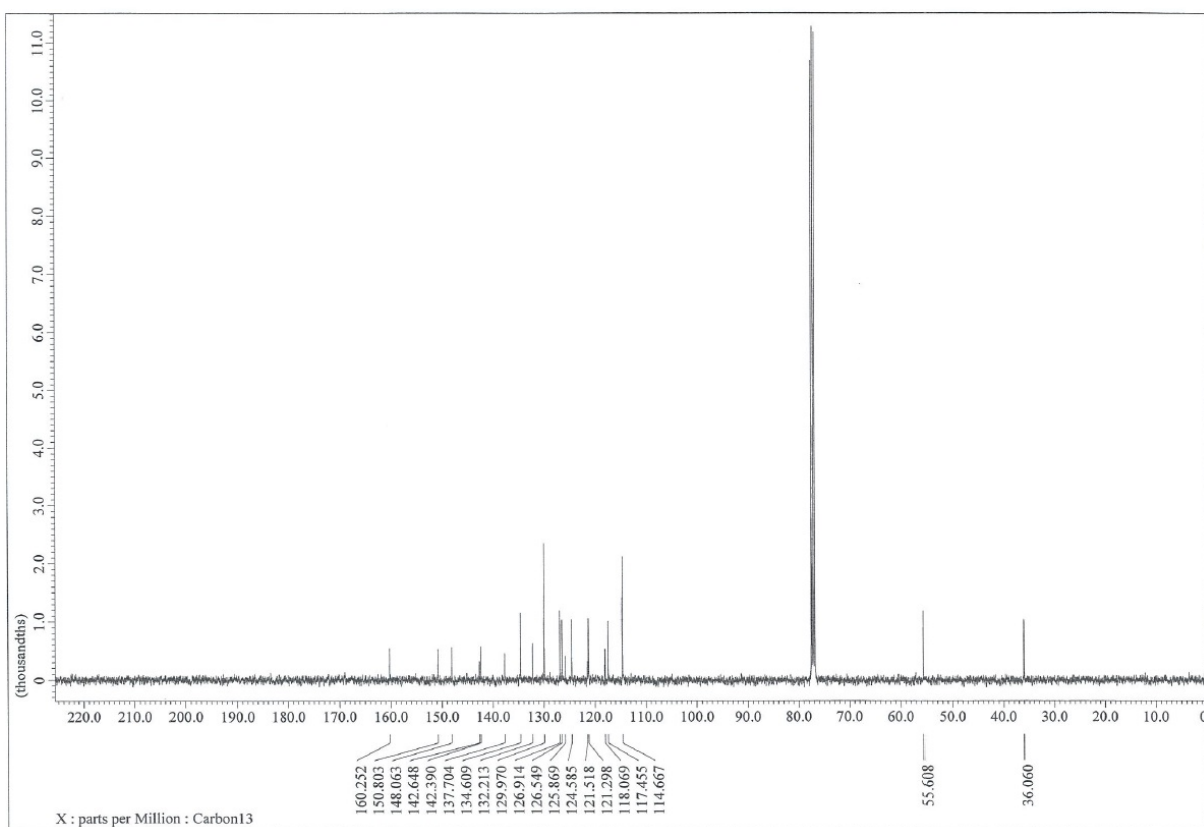


S57

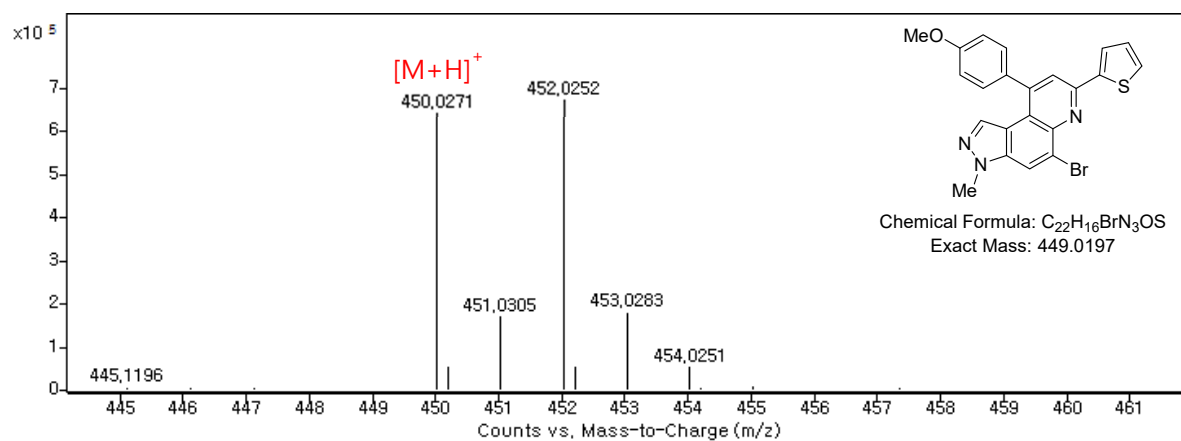


5-Bromo-9-(4-methoxyphenyl)-3-methyl-7-(thiophen-2-yl)-3H-pyrazolo[4,3-f]quinoline (1P)

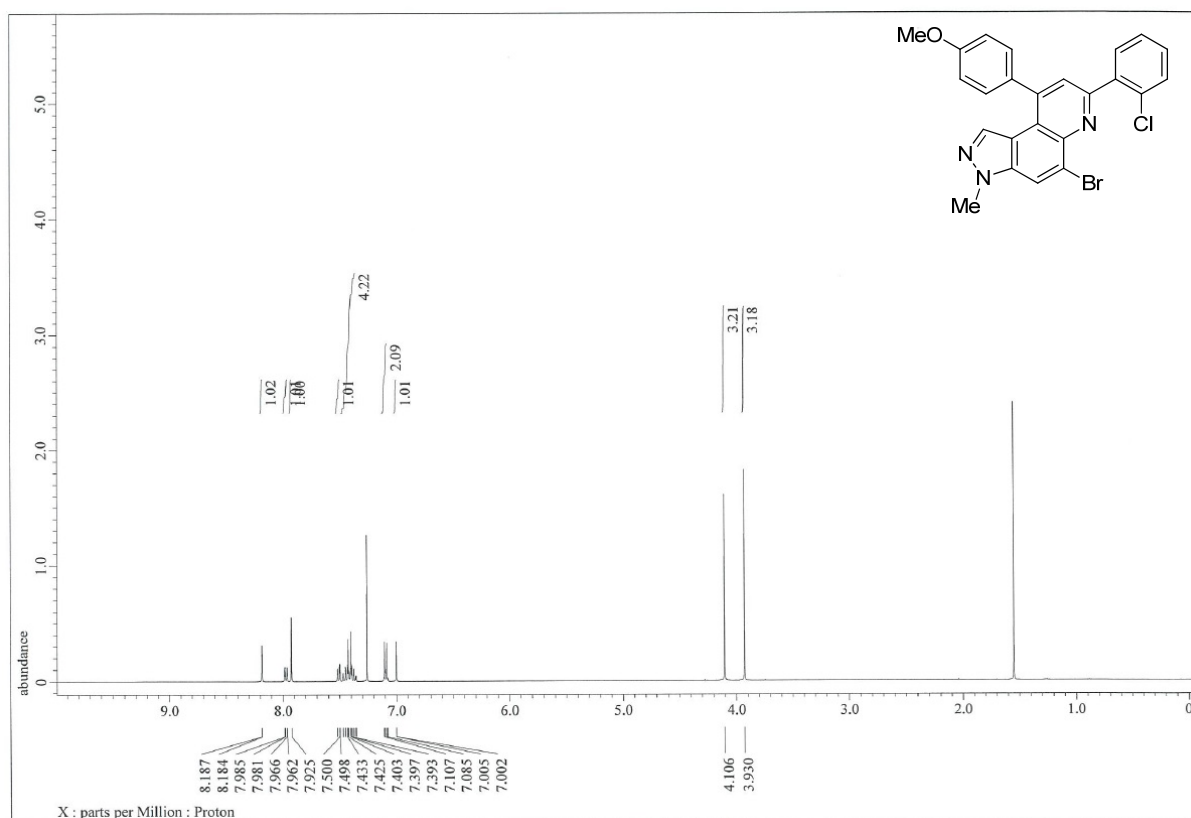


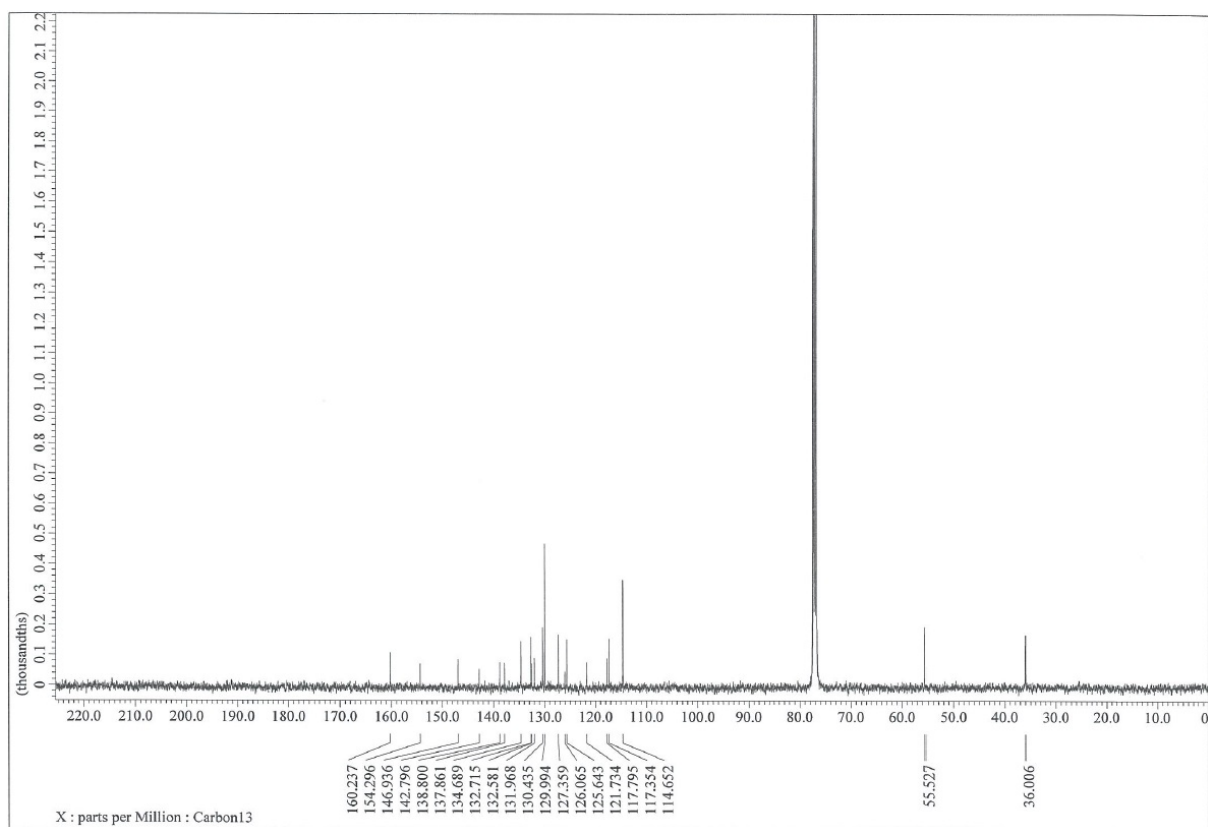


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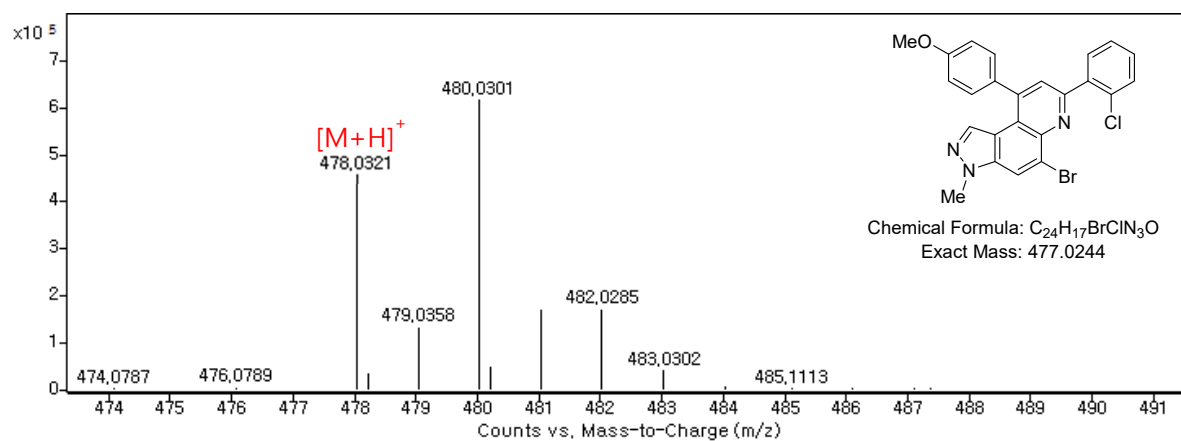


5-Bromo-7-(2-chlorophenyl)-9-(4-methoxyphenyl)-3-methyl-3H-pyrazolo[4,3-f]quinoline (1Q)

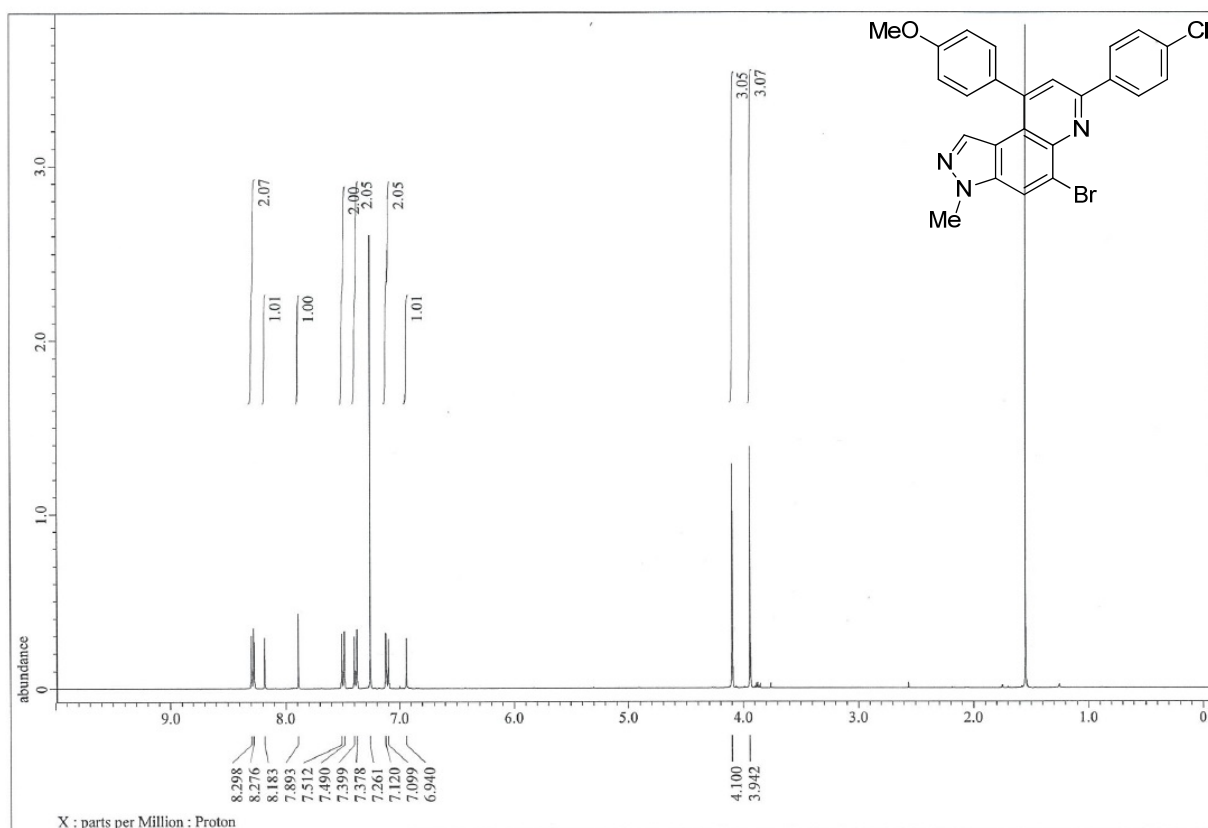


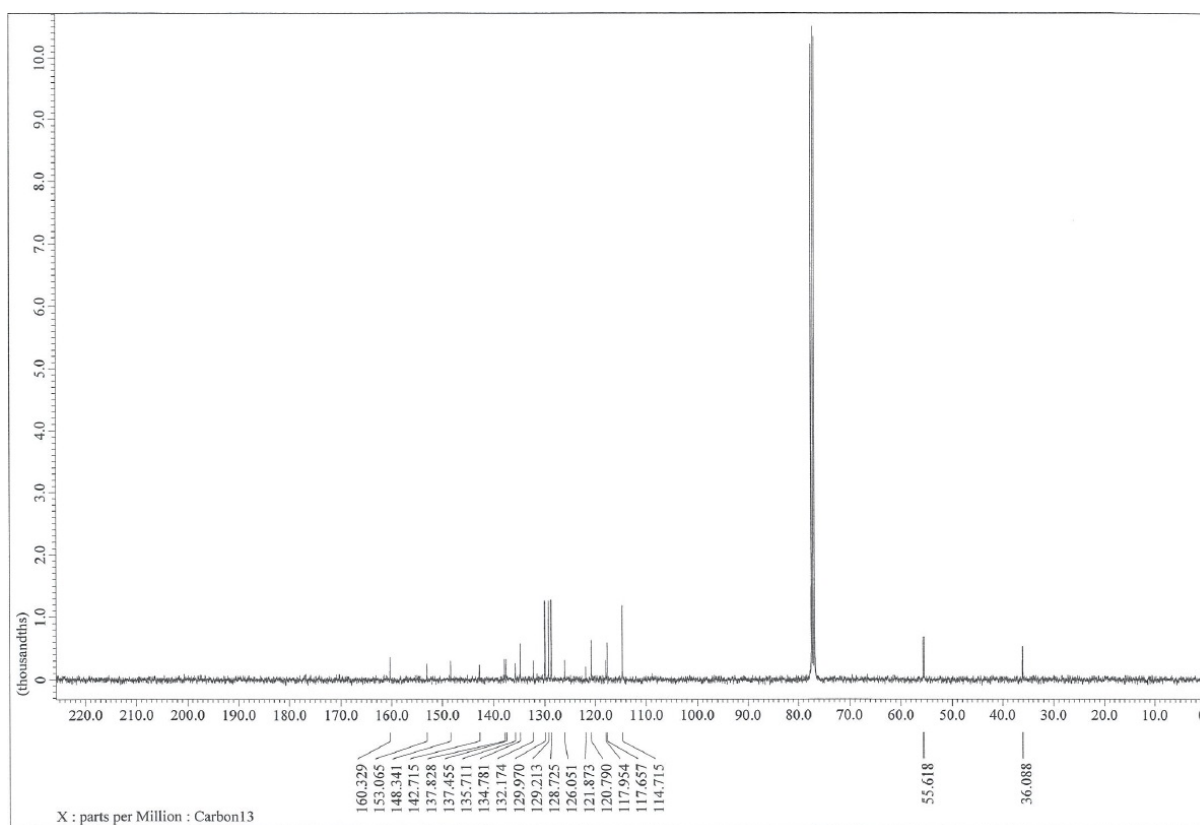


S63

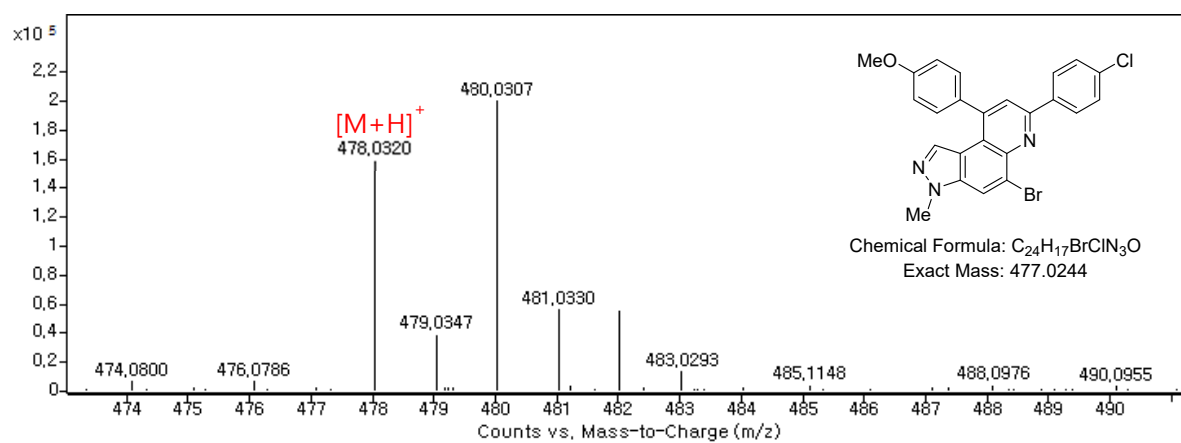


5-Bromo-7-(4-chlorophenyl)-9-(4-methoxyphenyl)-3-methyl-3H-pyrazolo[4,3-f]quinoline (1R)

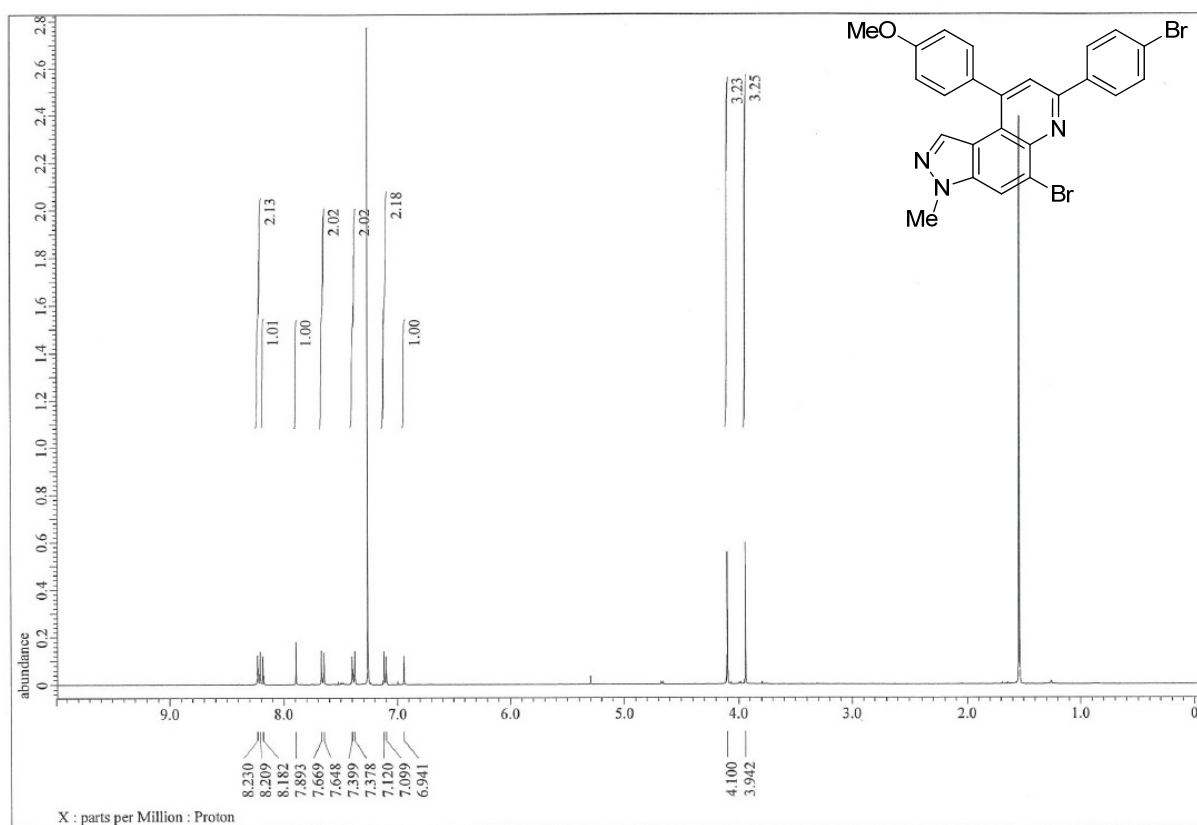


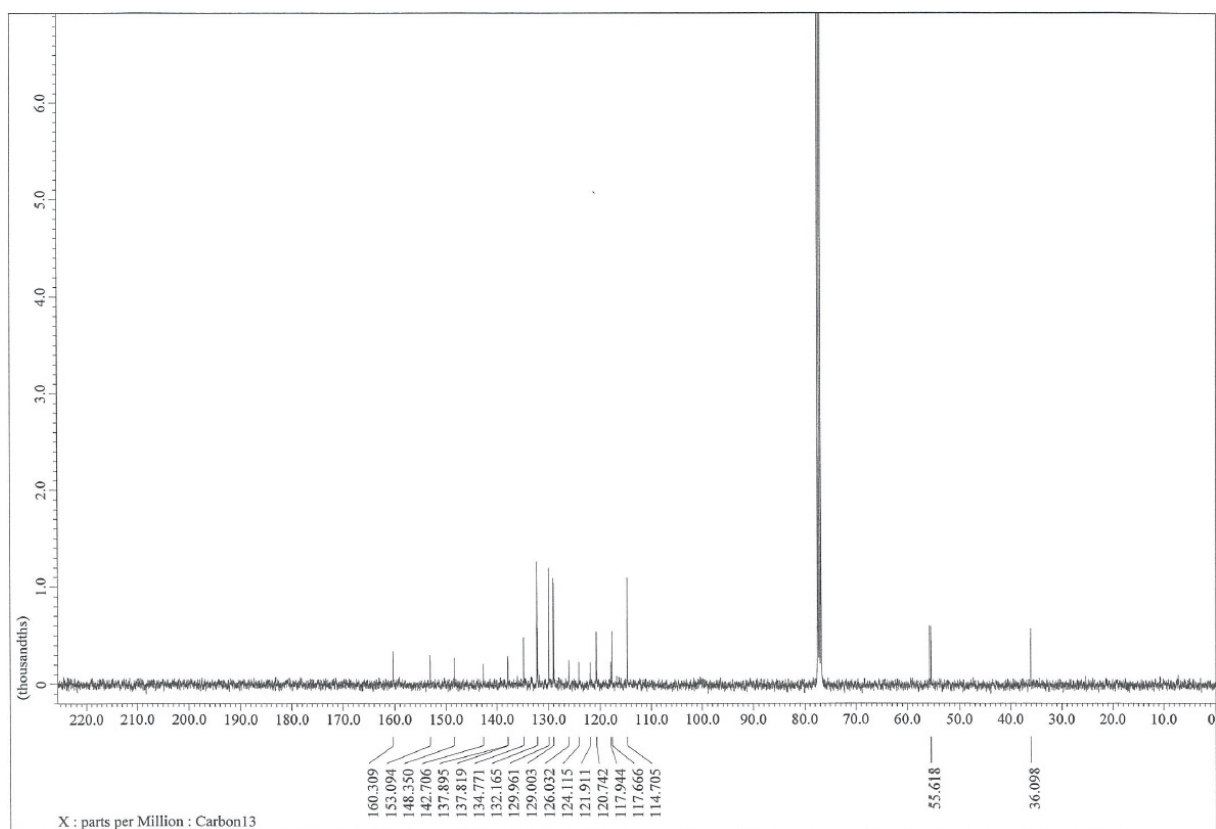


S66

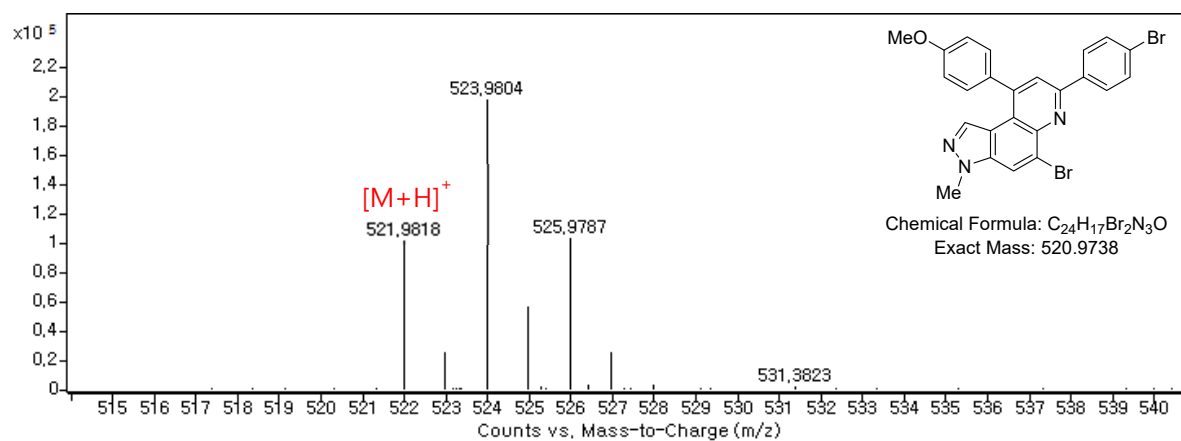


5-Bromo-7-(4-bromophenyl)-9-(4-methoxyphenyl)-3-methyl-3H-pyrazolo[4,3-f]quinoline (1S)

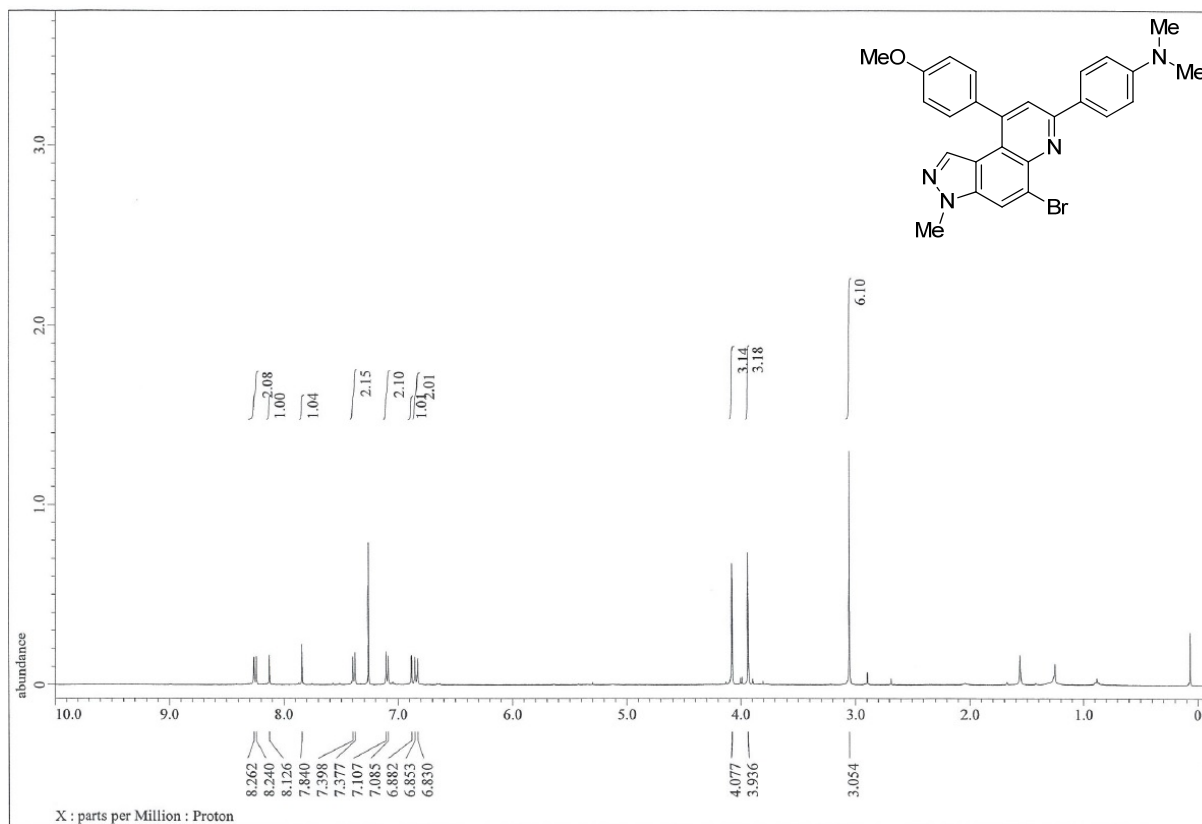


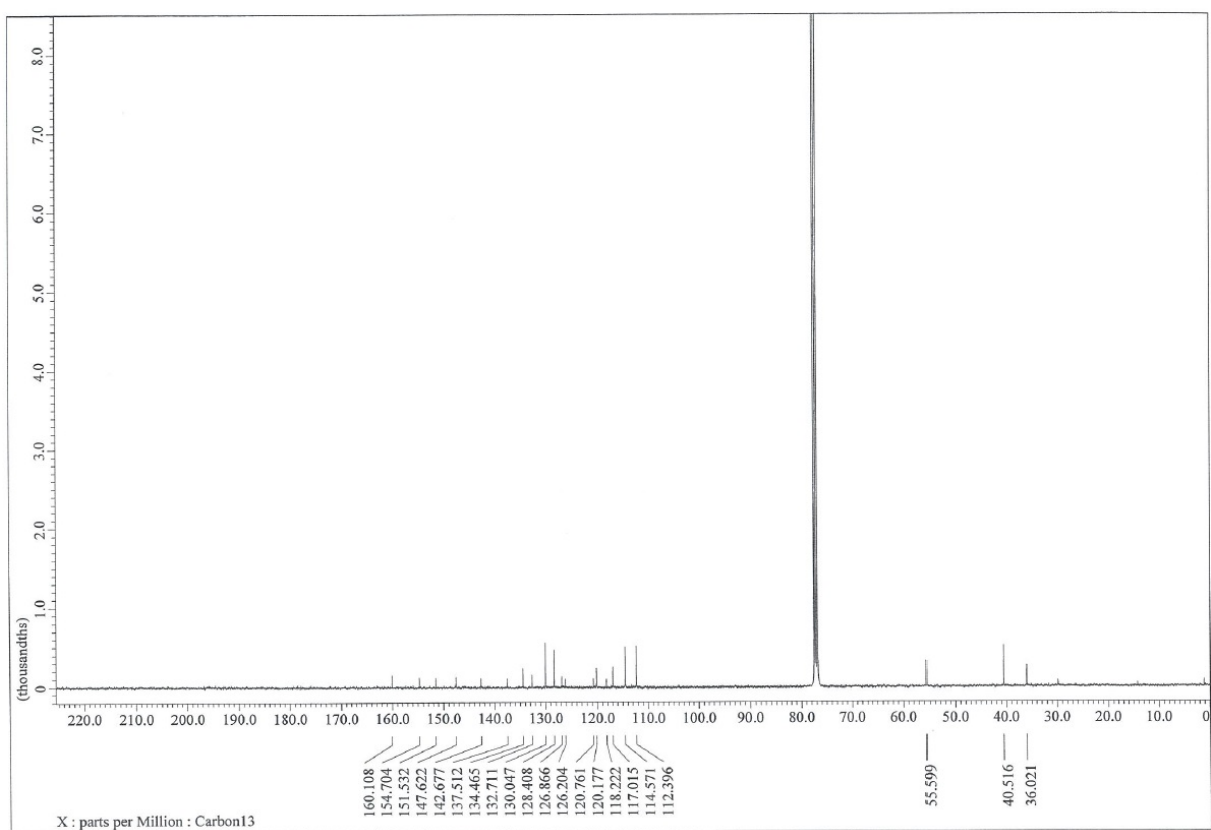


S69

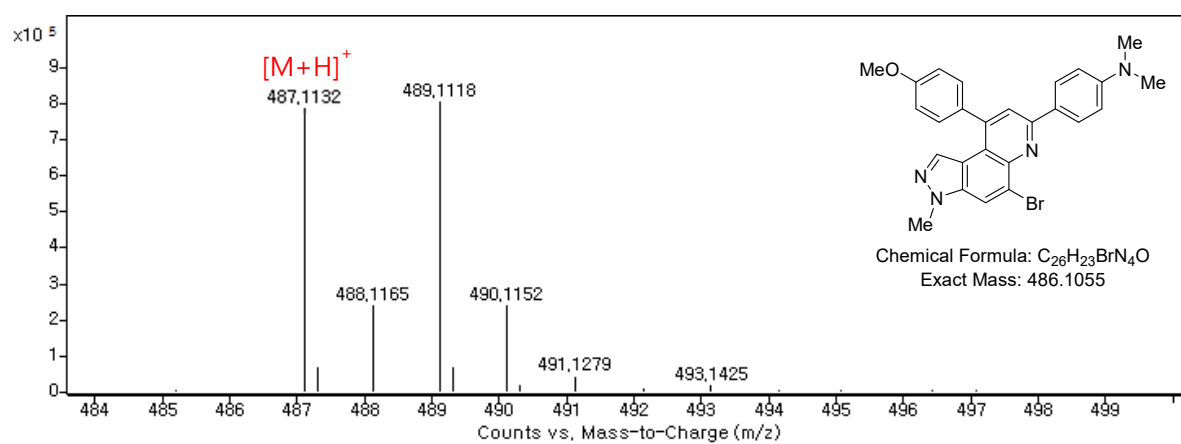


4-(5-Bromo-9-(4-methoxyphenyl)-3-methyl-3H-pyrazolo[4,3-f]quinolin-7-yl)-N,N-dimethylaniline (1T)

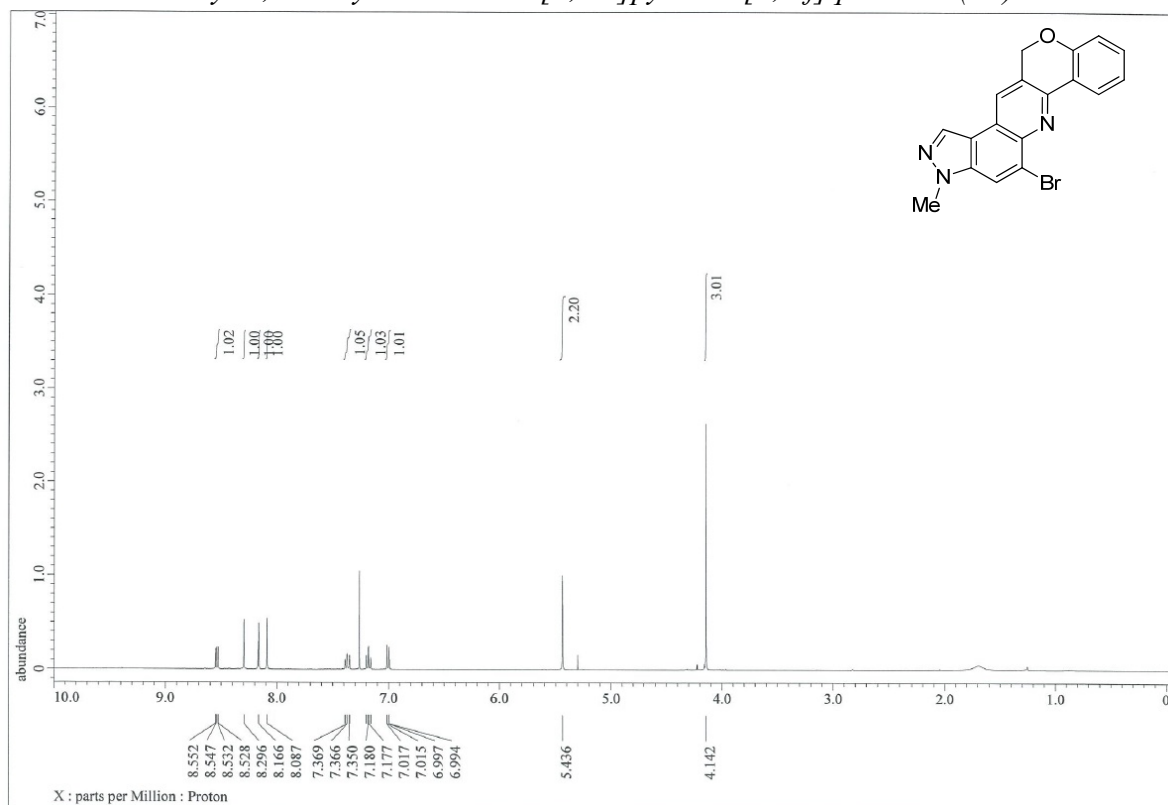


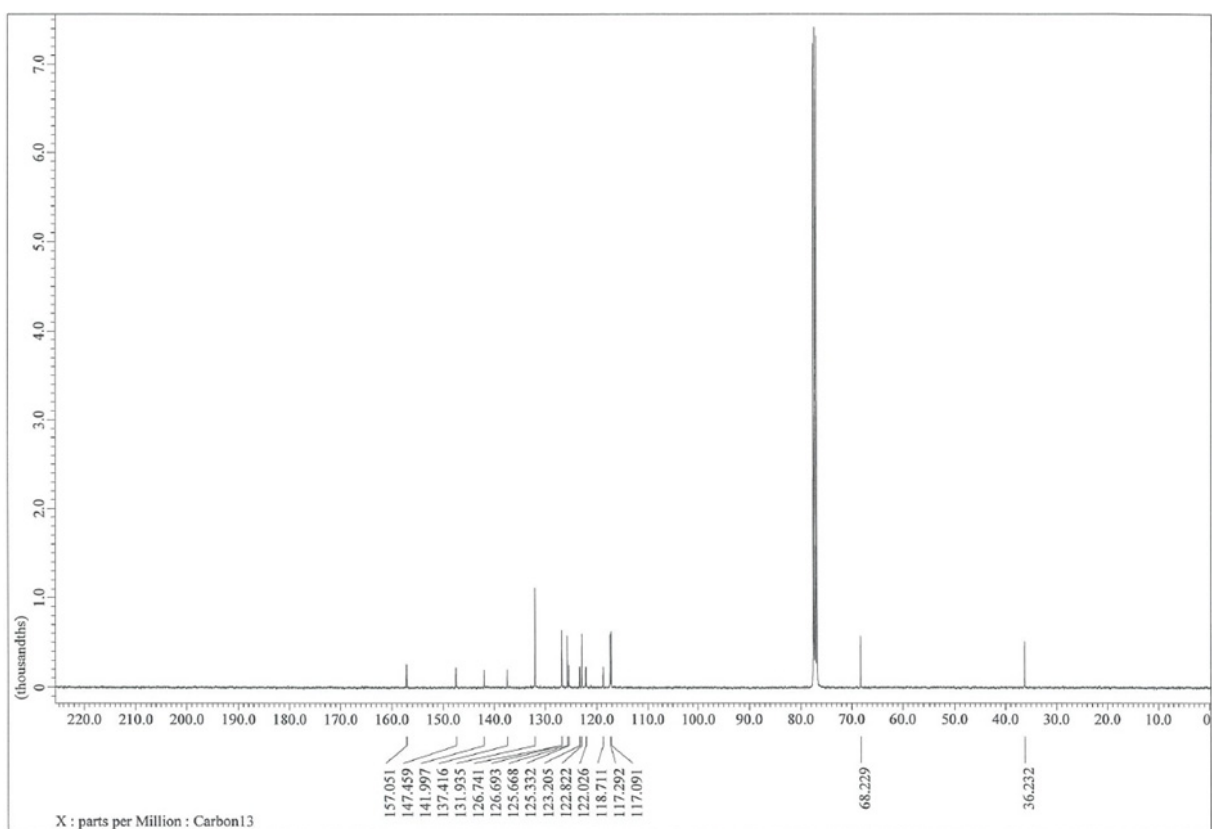


S72

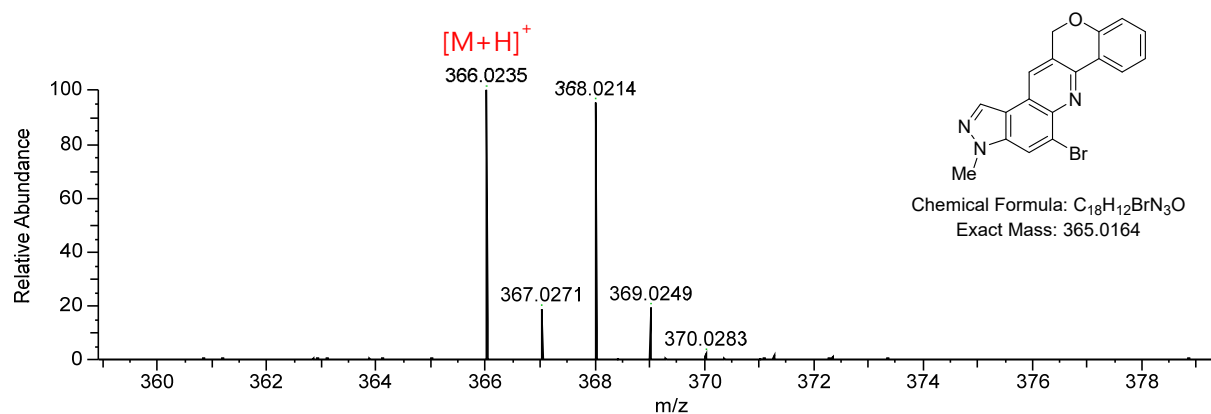


5-Bromo-3-methyl-3,12-dihydrochromeno[4,3-b]pyrazolo[4,3-f]quinoline (2A)

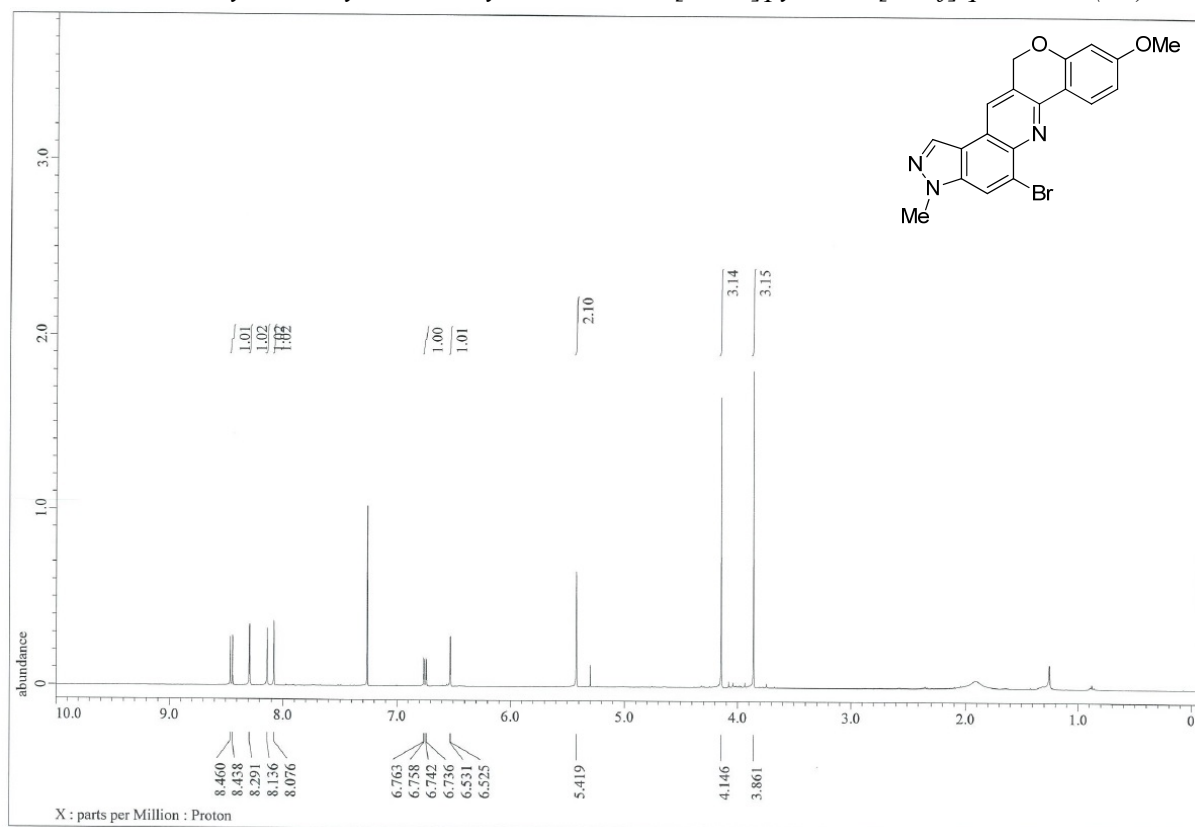


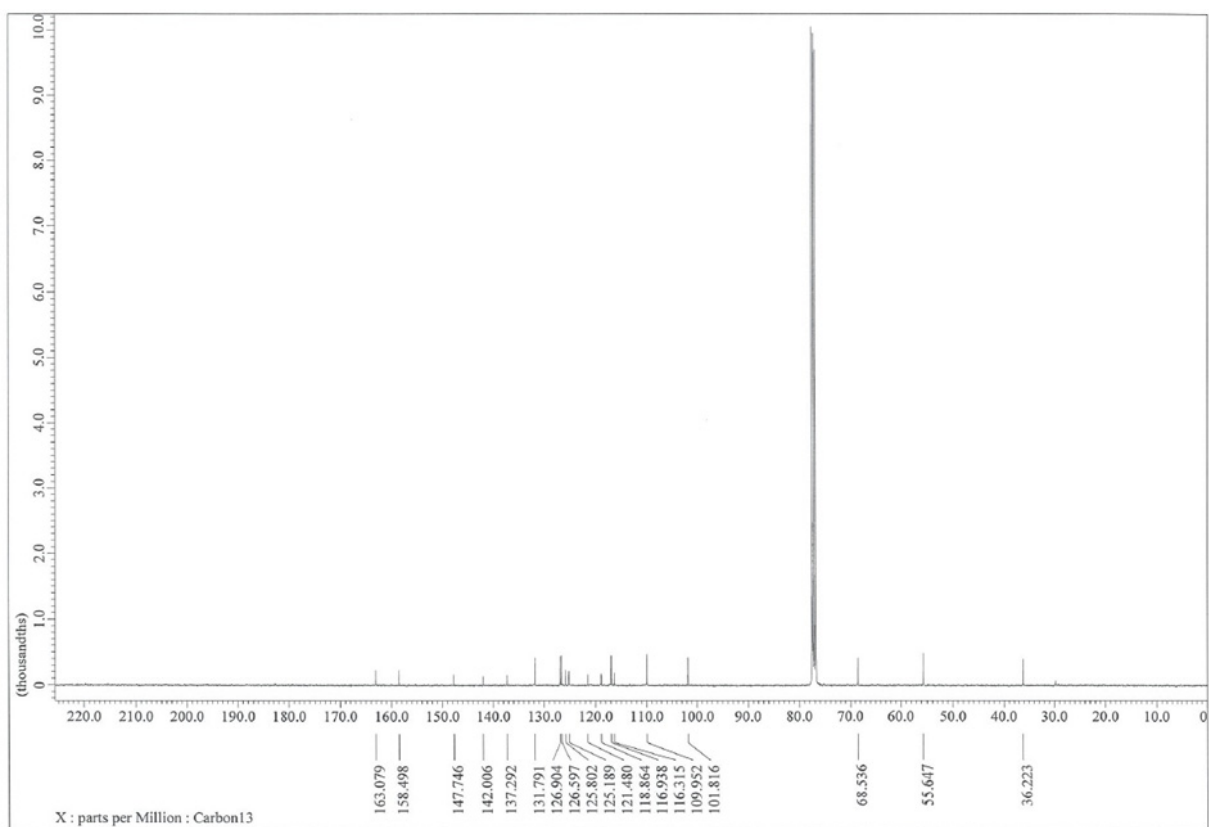


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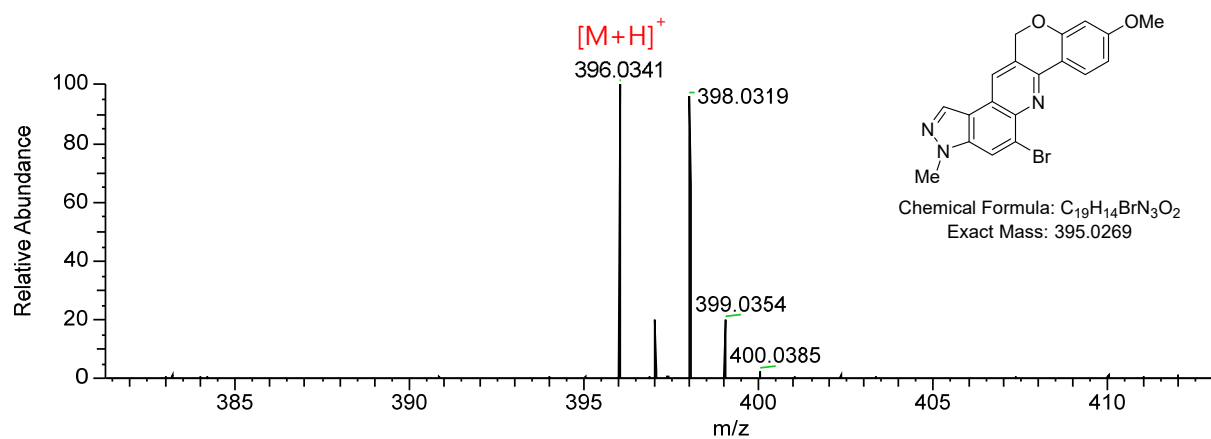


5-Bromo-9-methoxy-3-methyl-3,12-dihydrochromeno[4,3-b]pyrazolo[4,3-f]quinoline (2B)

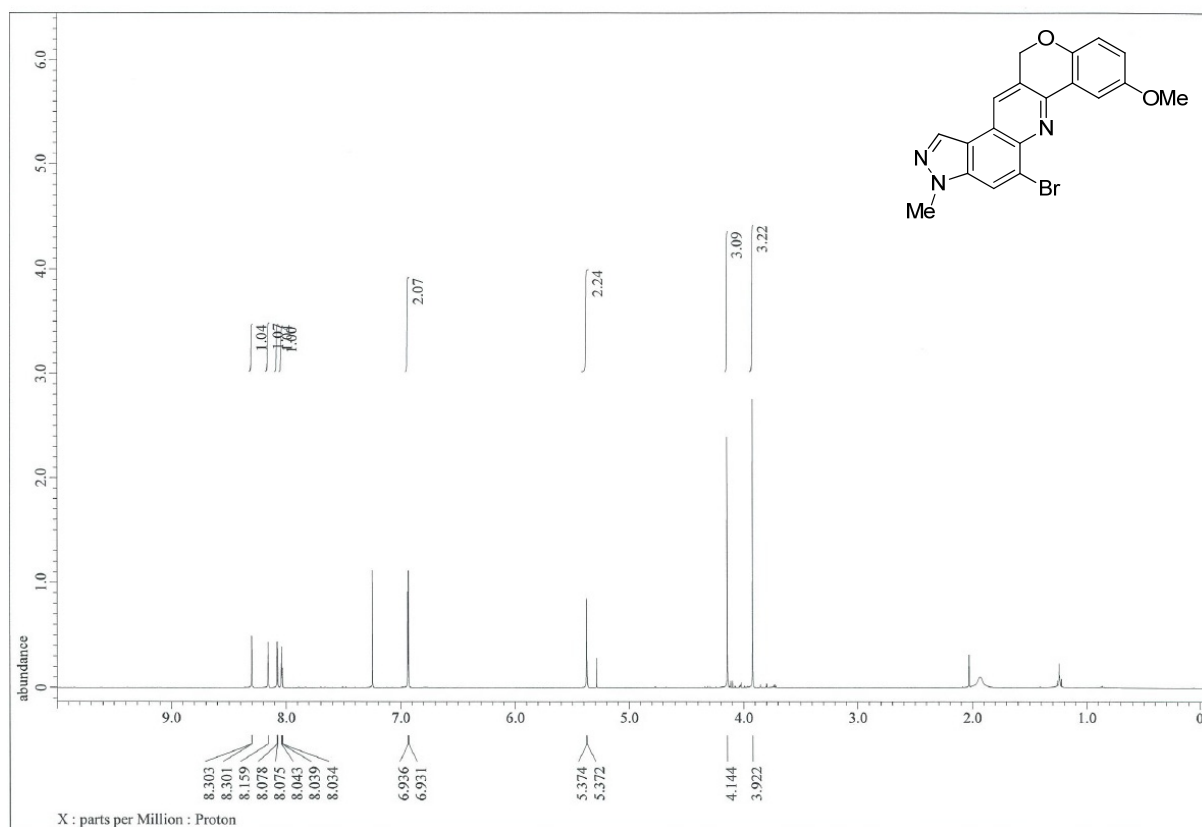


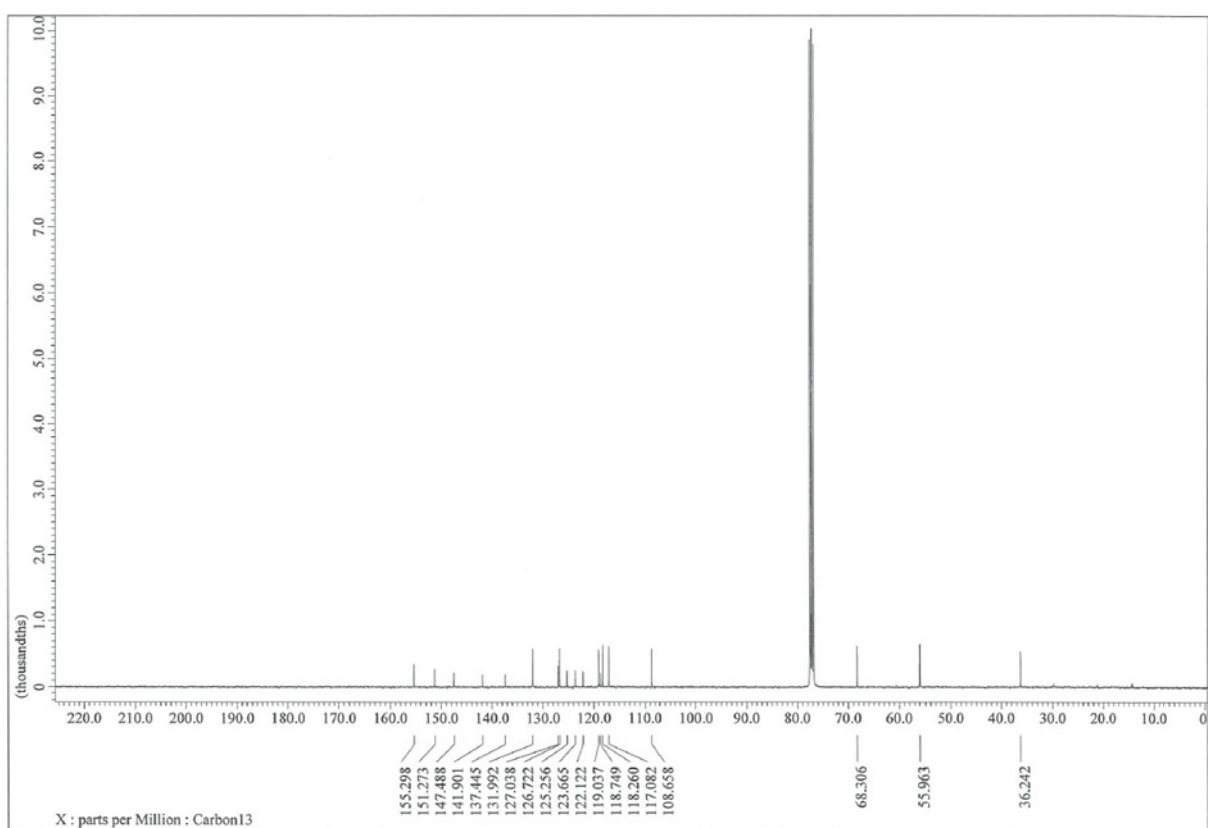


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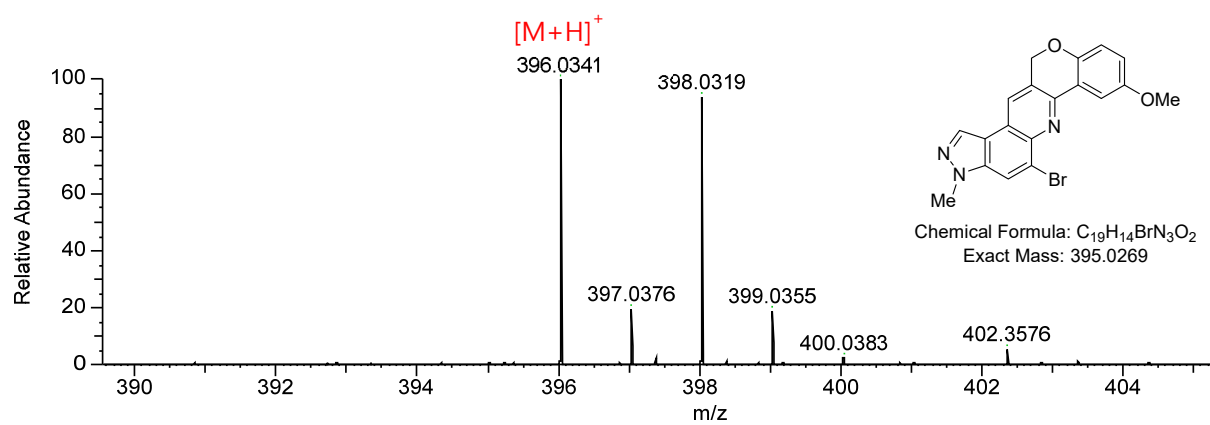


5-Bromo-8-methoxy-3-methyl-3,12-dihydrochromeno[4,3-b]pyrazolo[4,3-f]quinoline (2C)

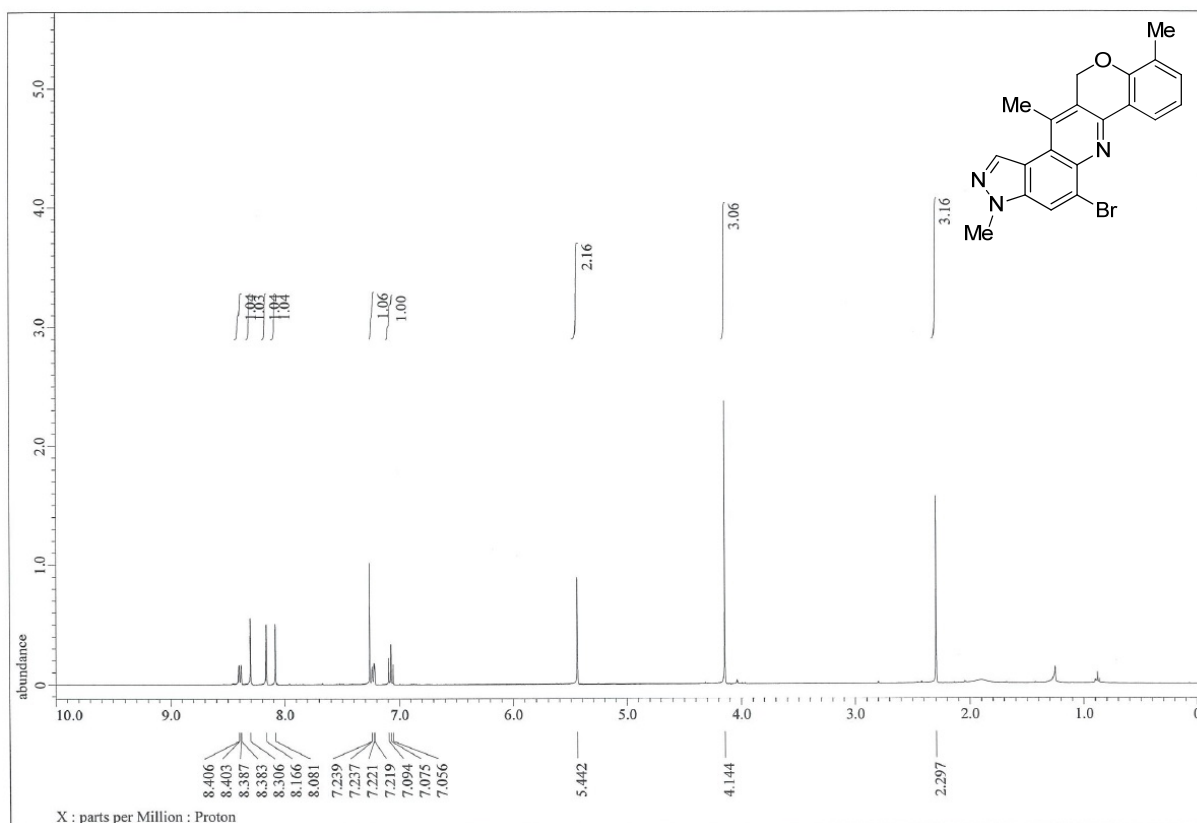


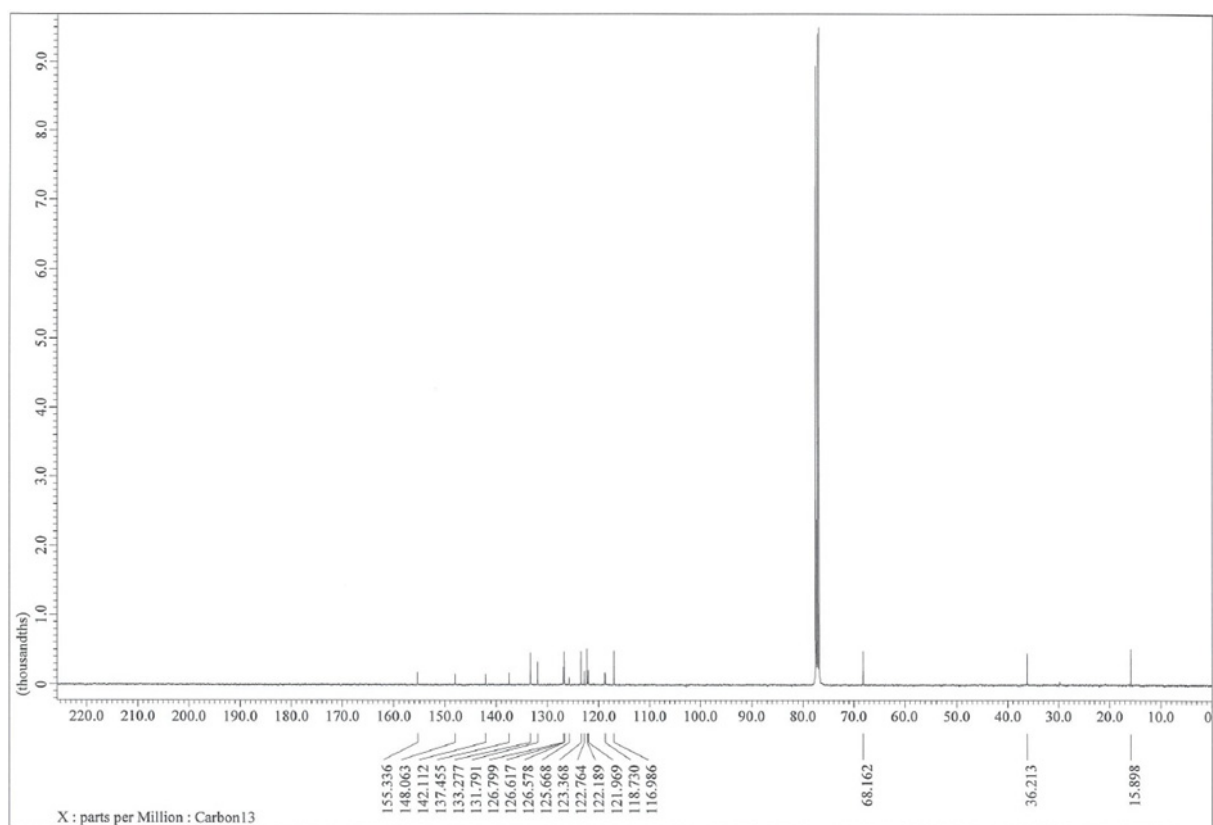


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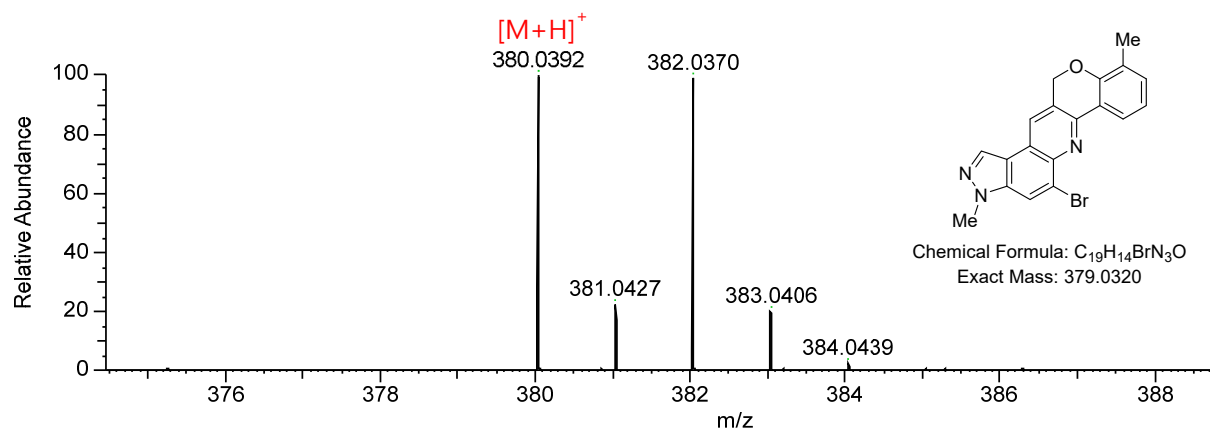


5-Bromo-3,10-dimethyl-3,12-dihydrochromeno[4,3-b]pyrazolo[4,3-f]quinoline (2D)

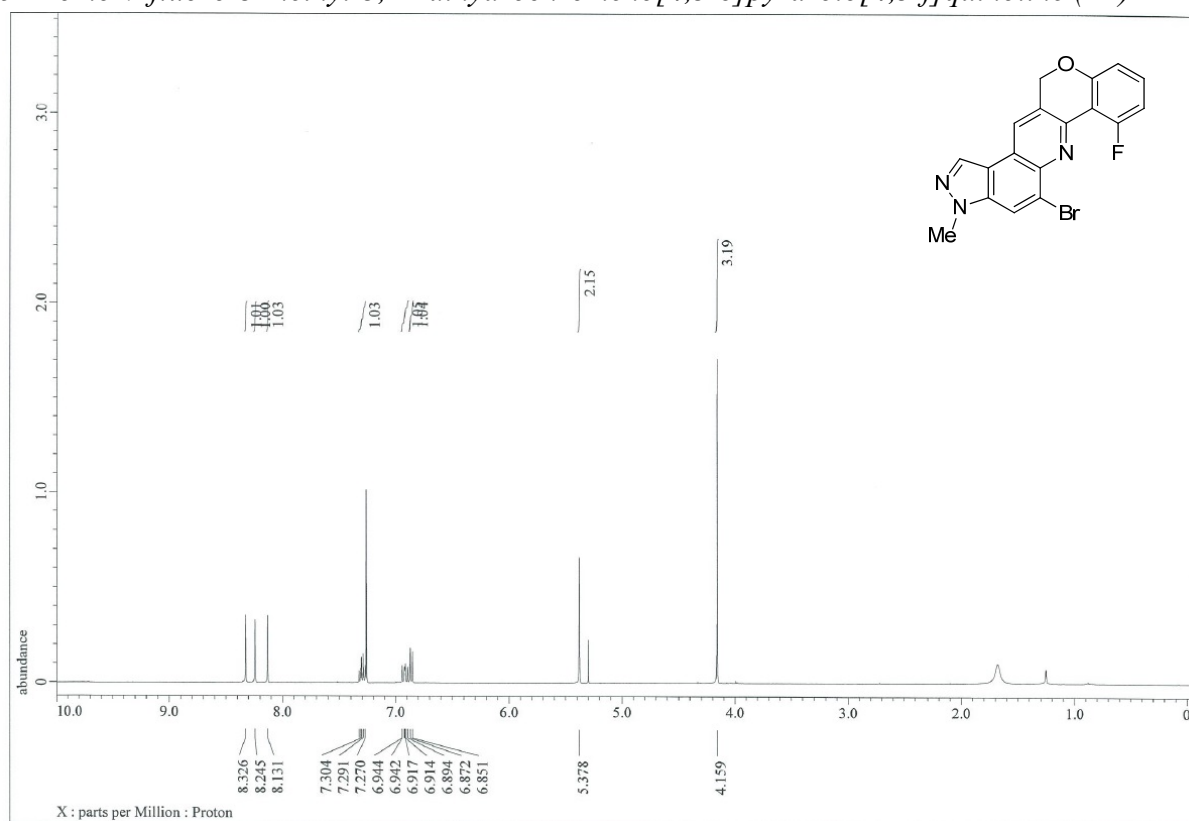


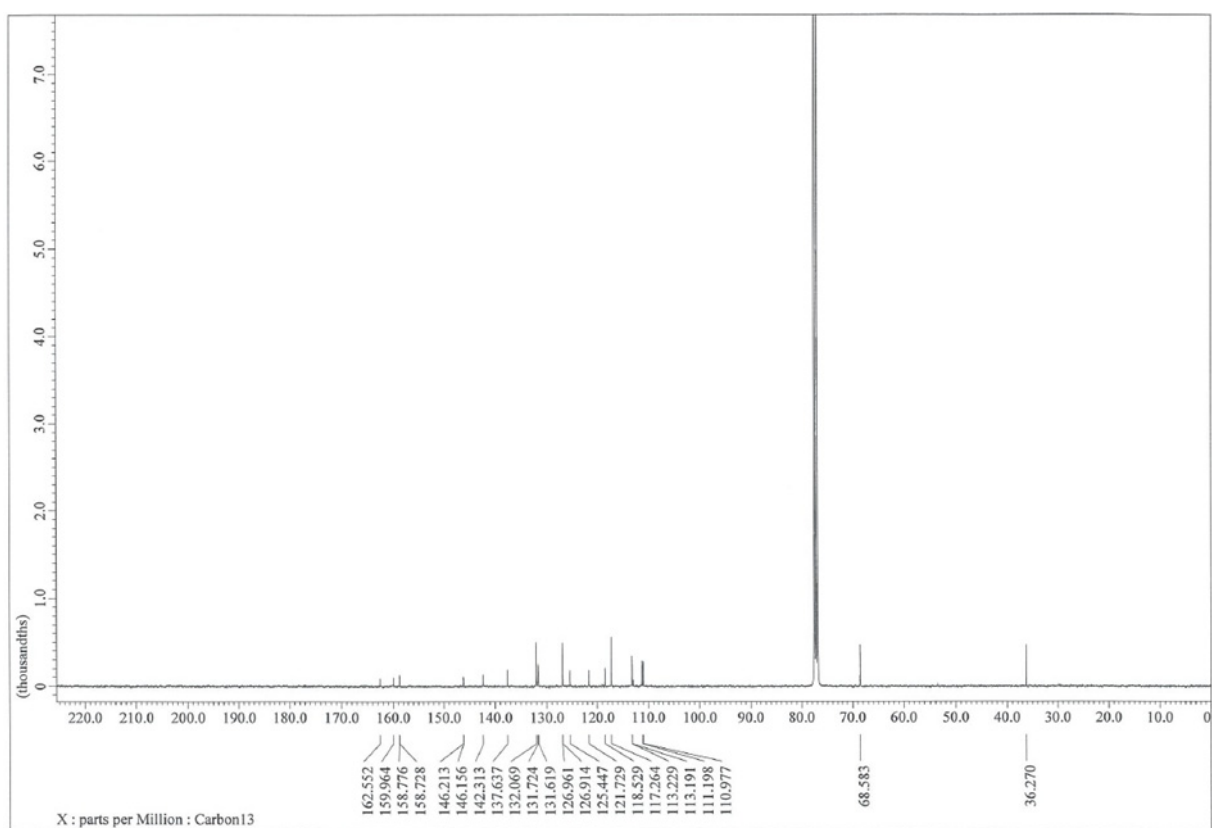


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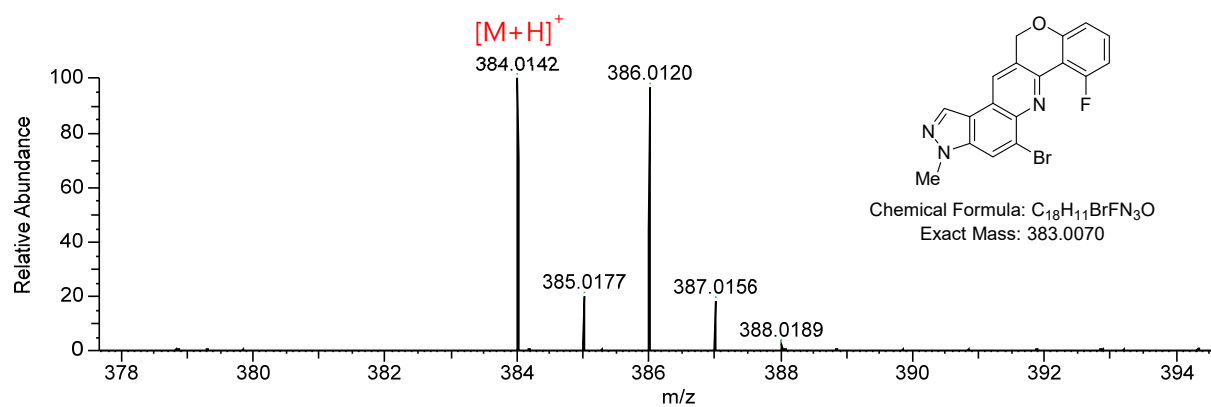


5-Bromo-7-fluoro-3-methyl-3,12-dihydrochromeno[4,3-b]pyrazolo[4,3-f]quinoline (2E)

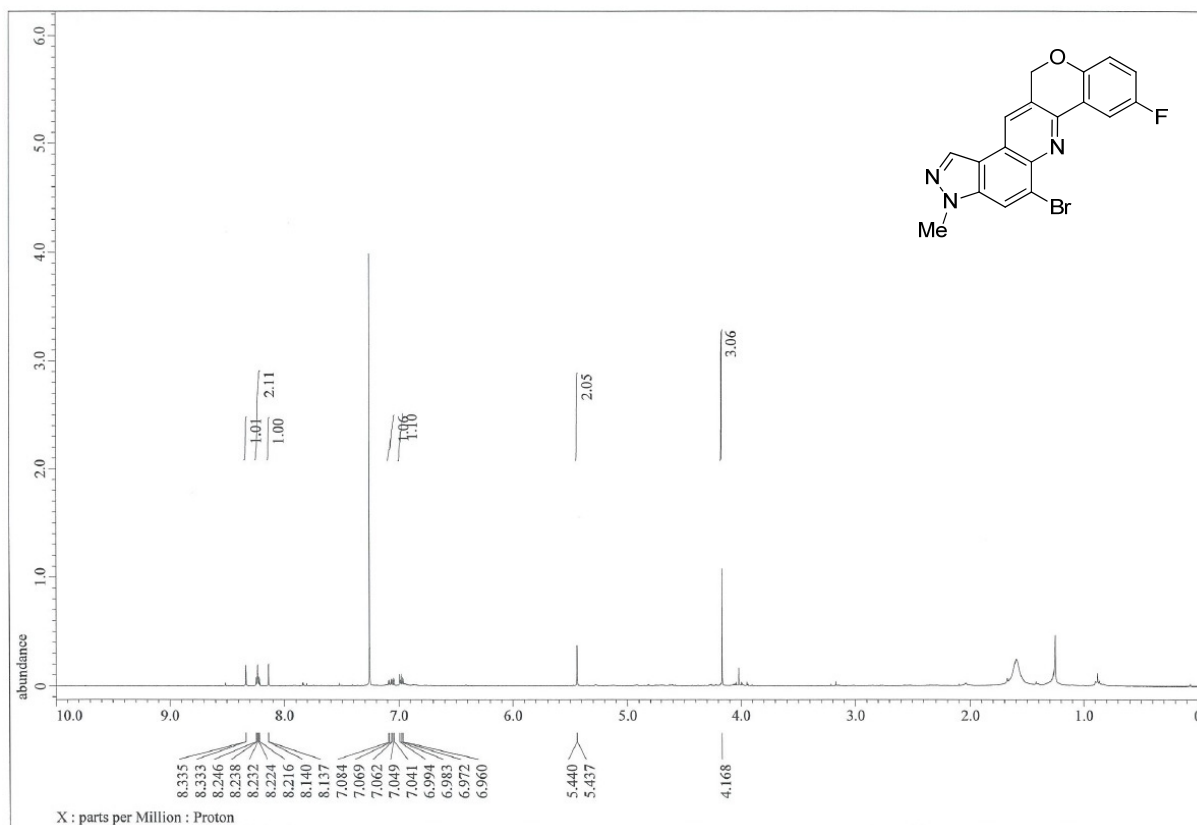


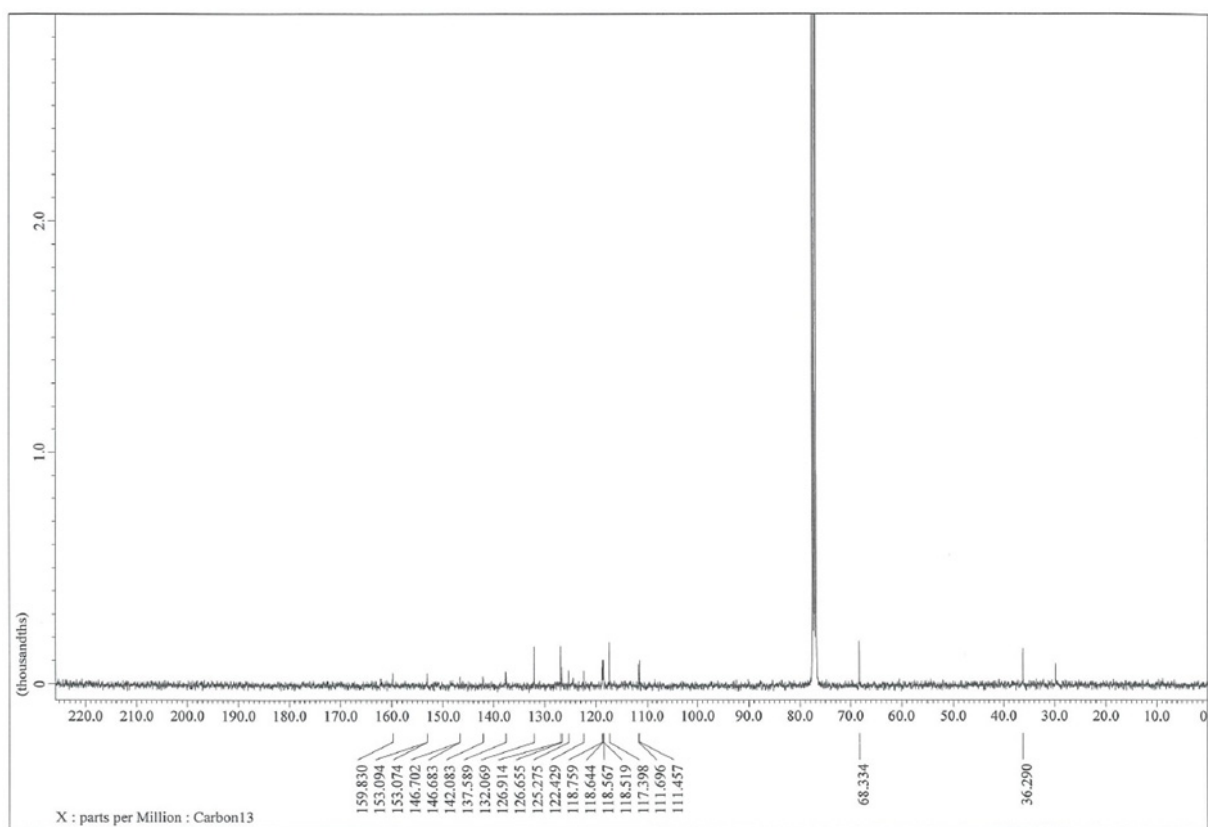


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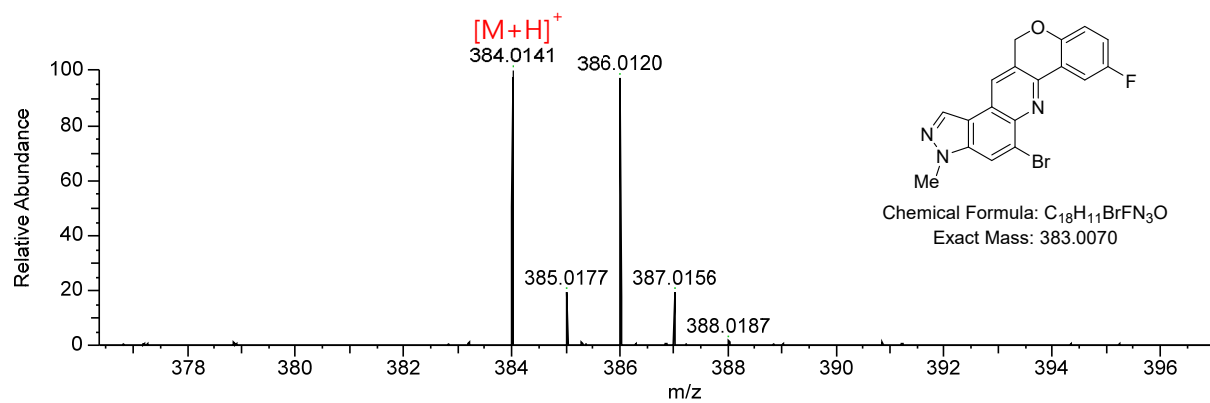


5-Bromo-8-fluoro-3-methyl-3,12-dihydrochromeno[4,3-b]pyrazolo[4,3-f]quinoline (2F)

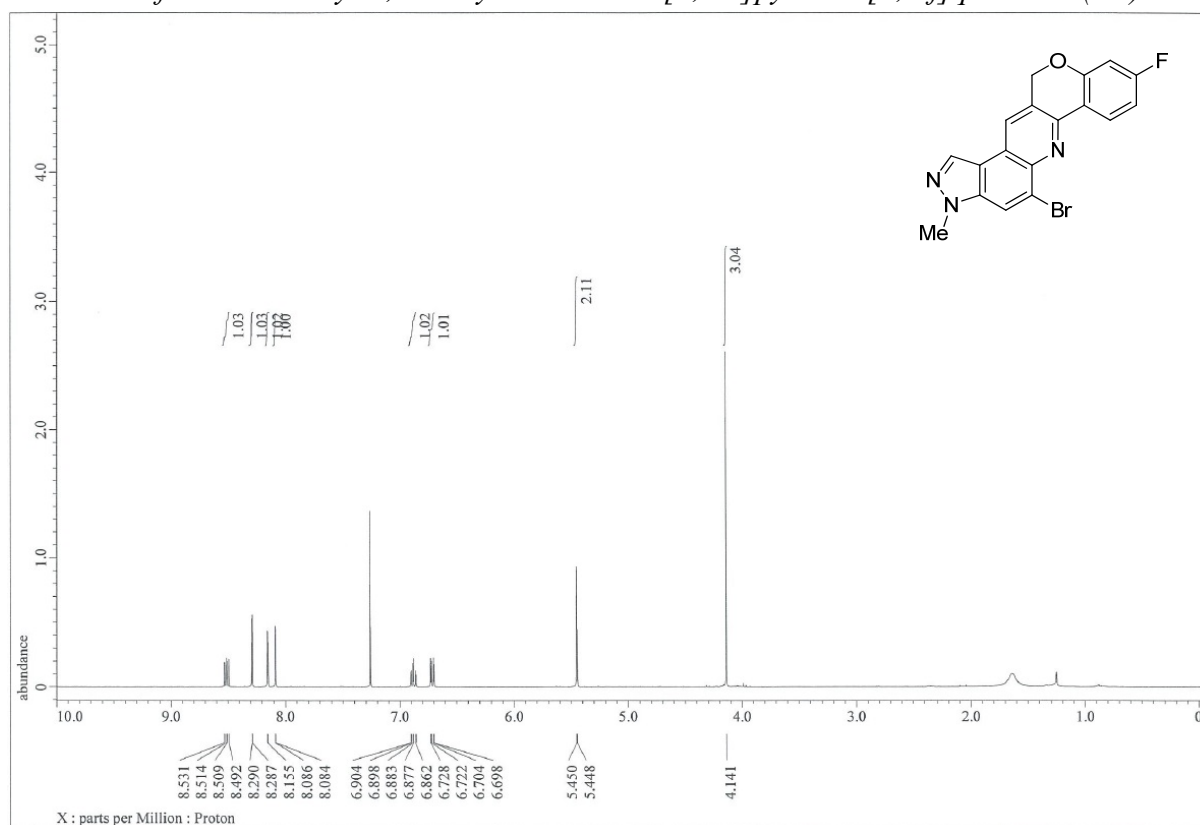


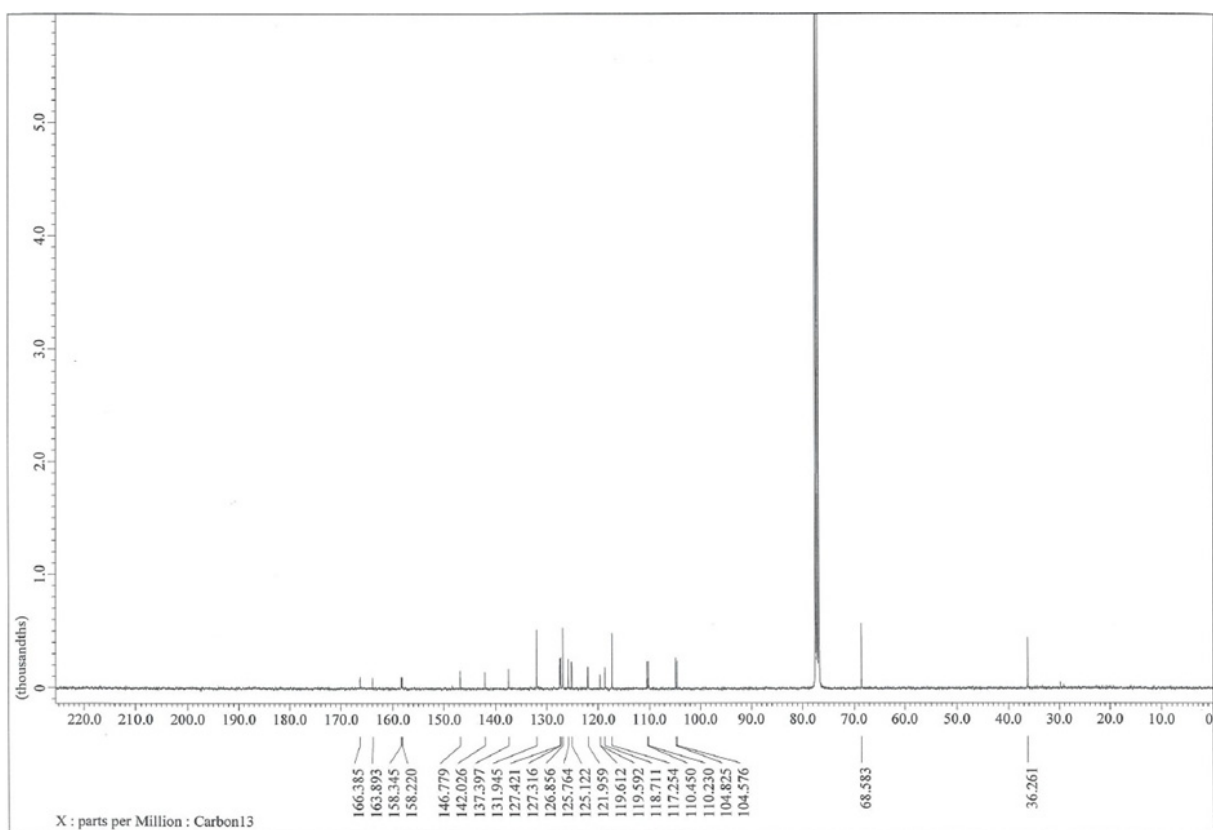


S90

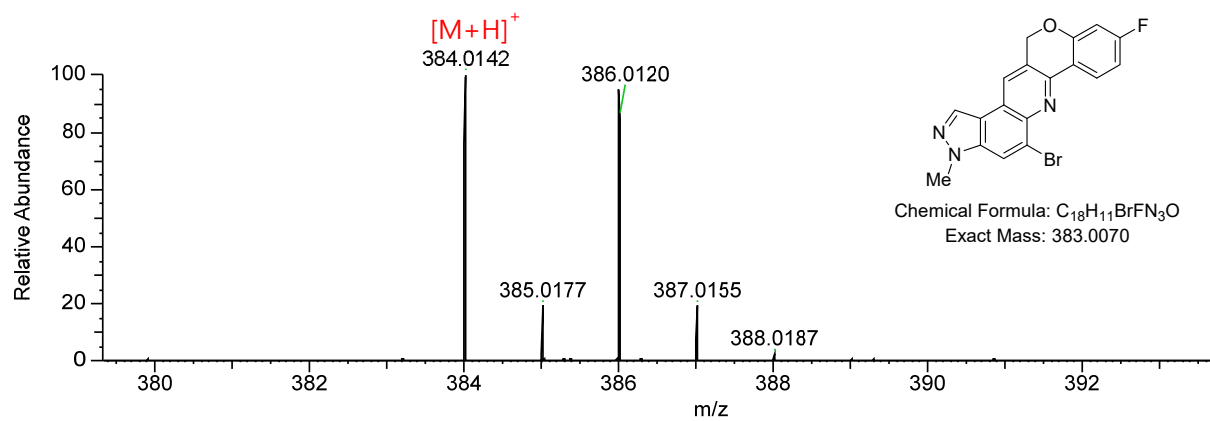


5-Bromo-9-fluoro-3-methyl-3,12-dihydrochromeno[4,3-b]pyrazolo[4,3-f]quinoline (2G)

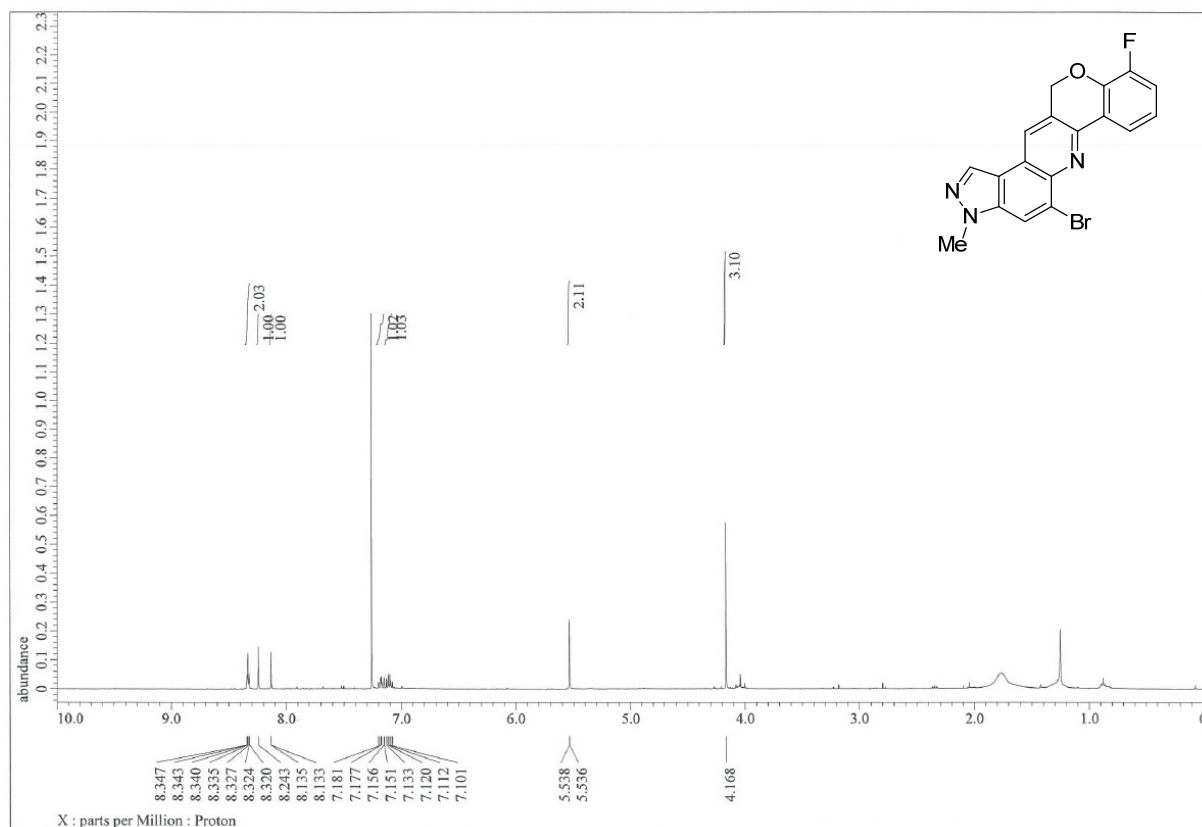


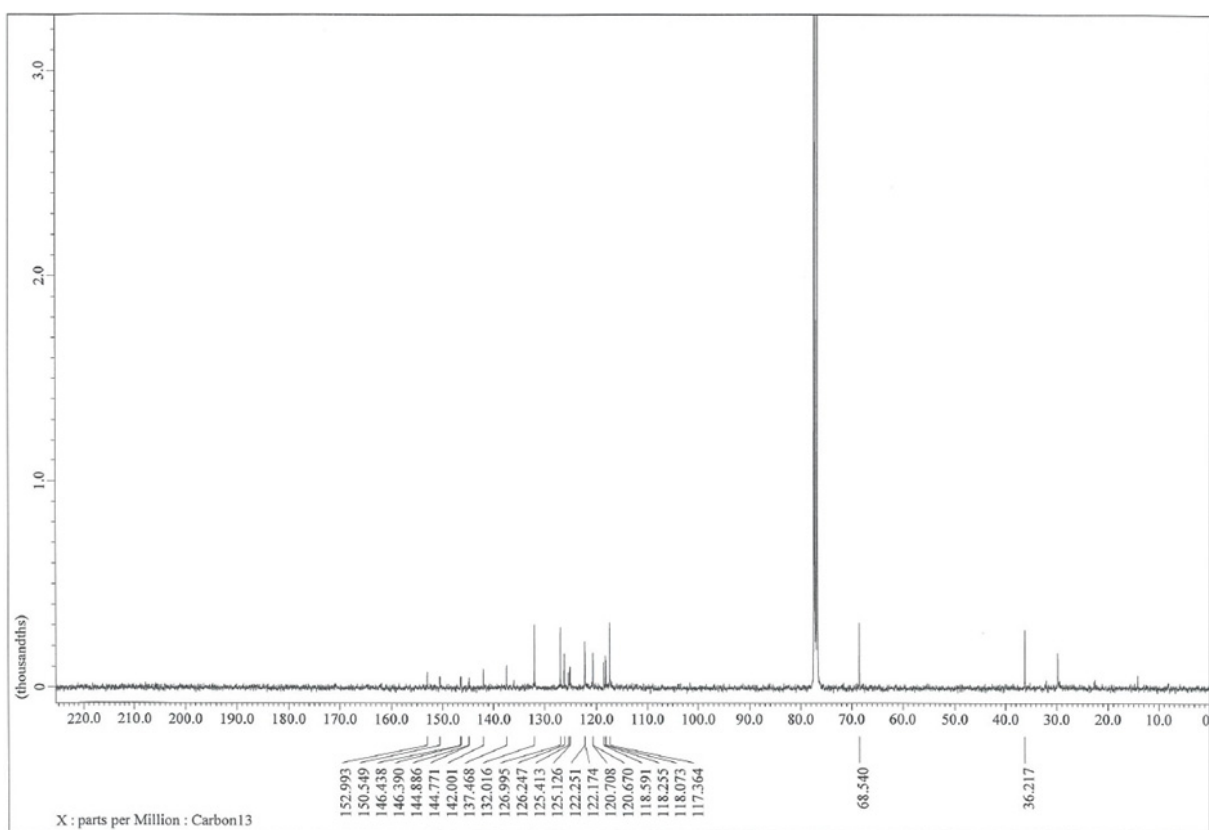


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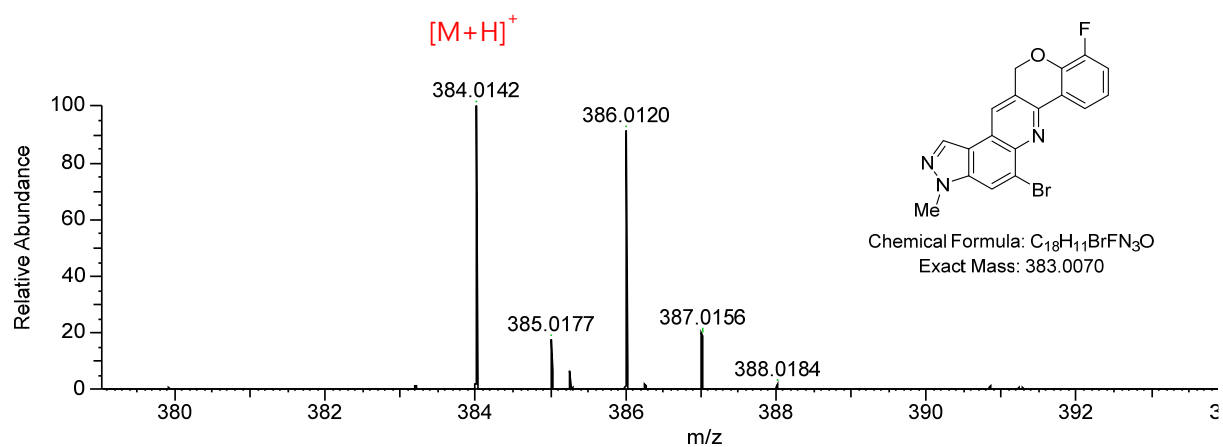


5-Bromo-10-fluoro-3-methyl-3,12-dihydrochromeno[4,3-b]pyrazolo[4,3-f]quinoline (2H)

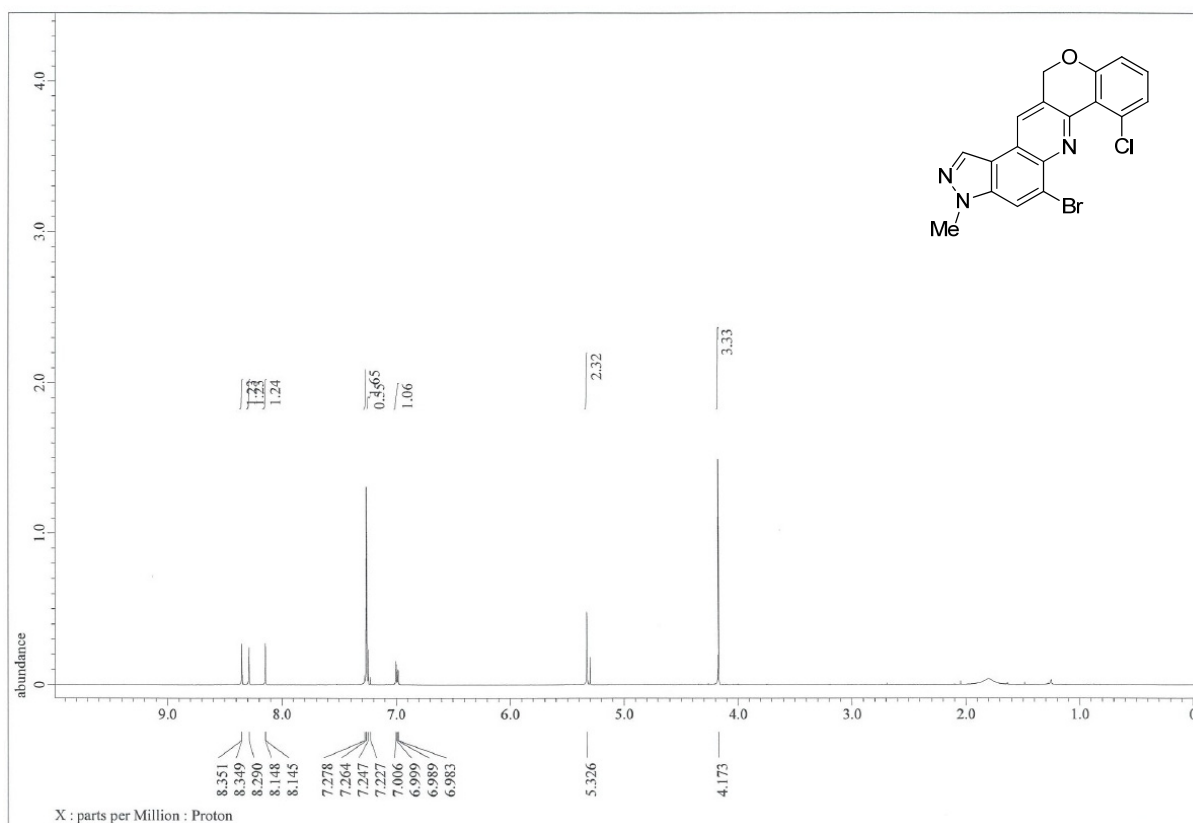


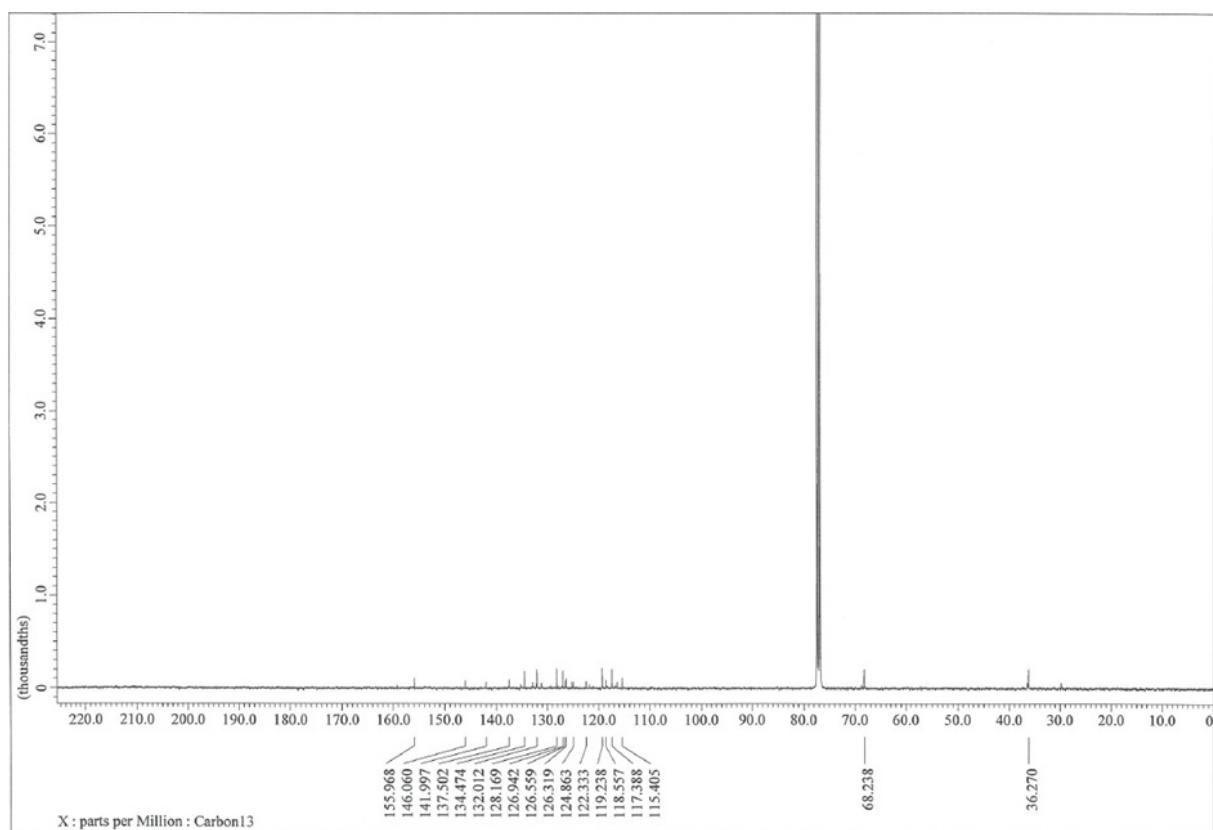


S96

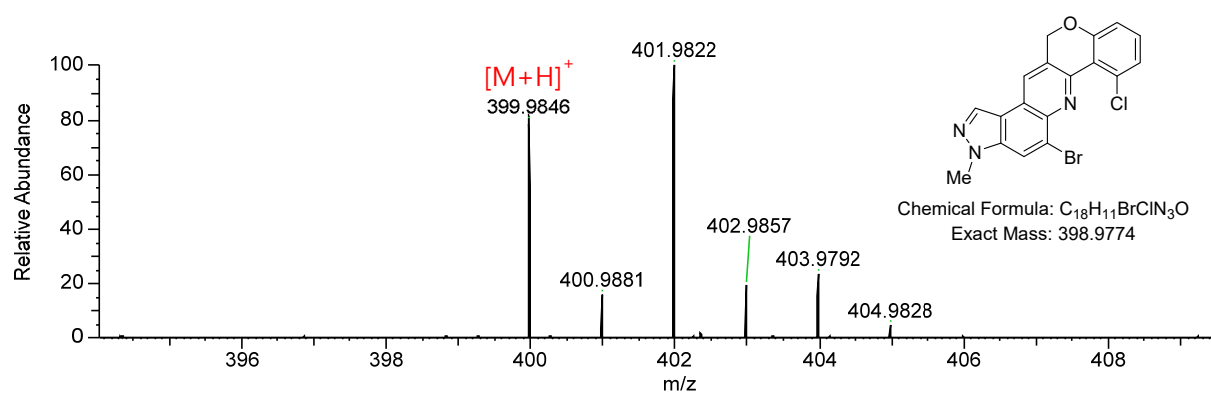


5-Bromo-7-chloro-3-methyl-3,12-dihydrochromeno[4,3-b]pyrazolo[4,3-f]quinoline (2I)



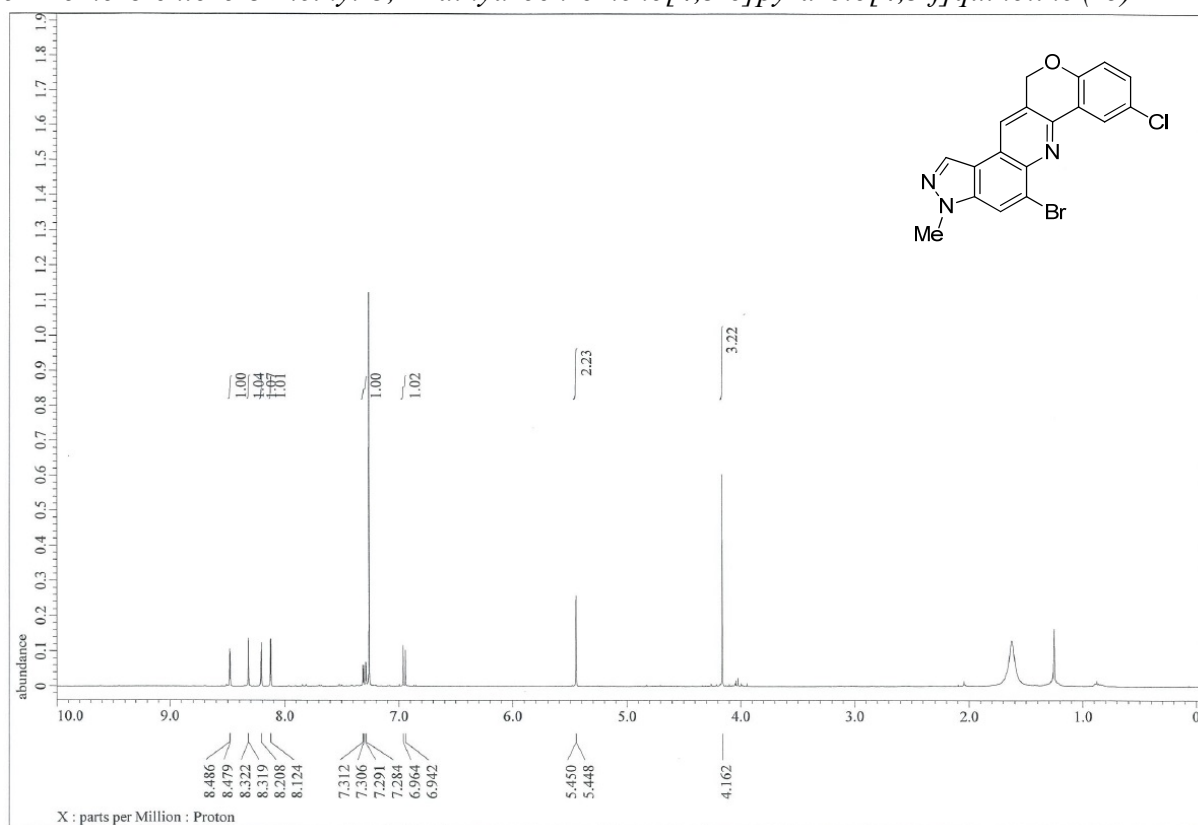


S99

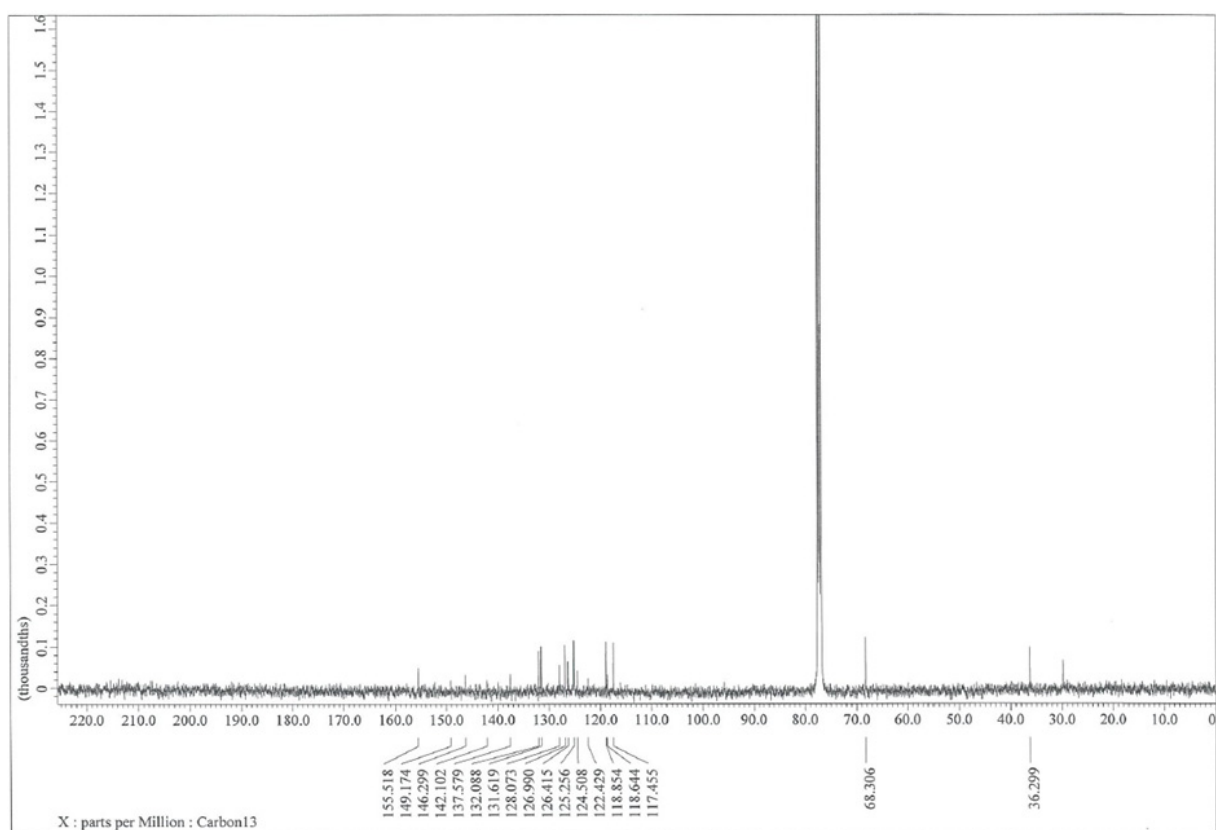


S100

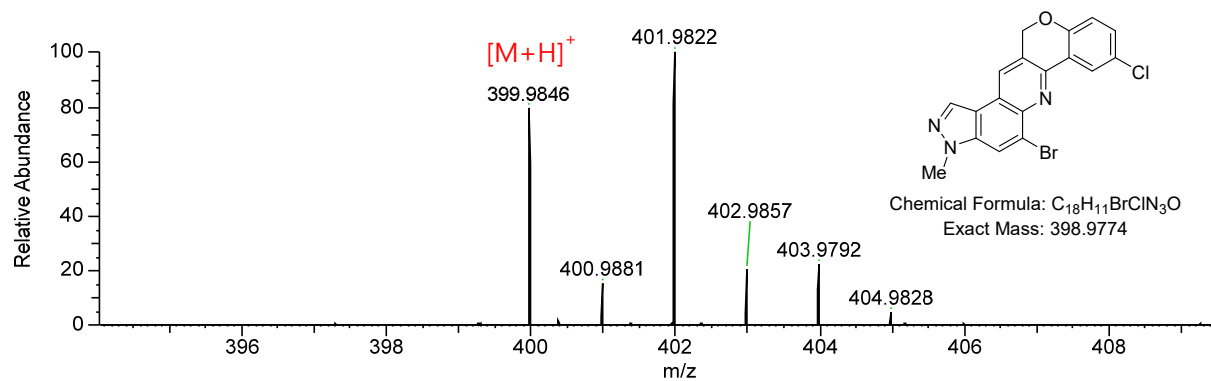
5-Bromo-8-chloro-3-methyl-3,12-dihydrochromeno[4,3-b]pyrazolo[4,3-f]quinoline (2J)



S101

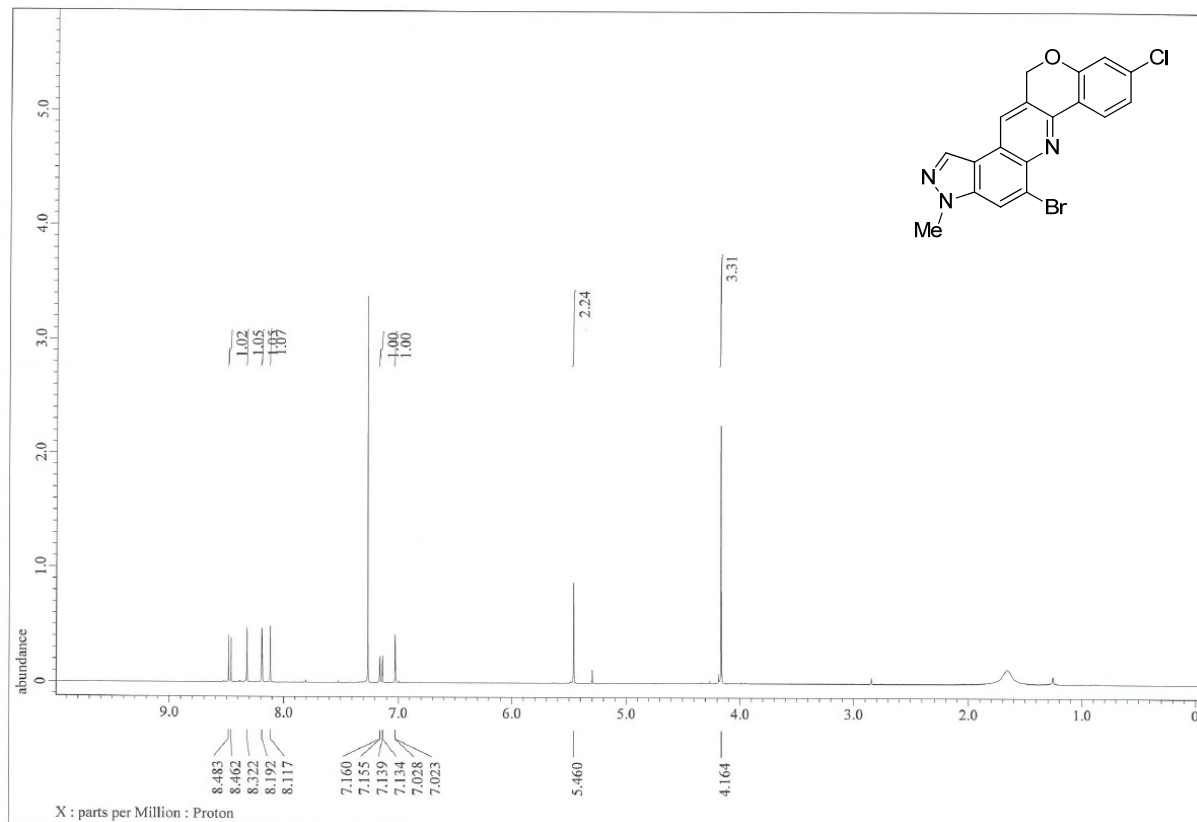


S102

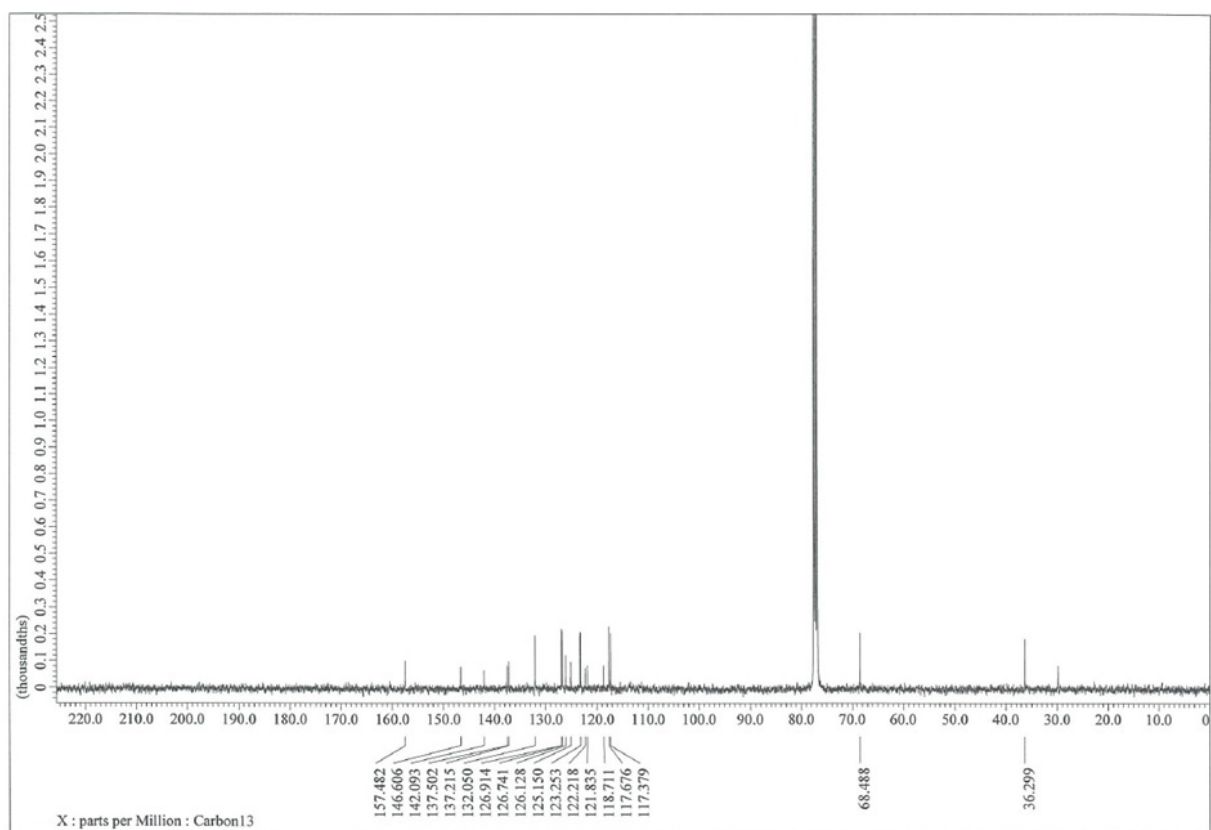


S103

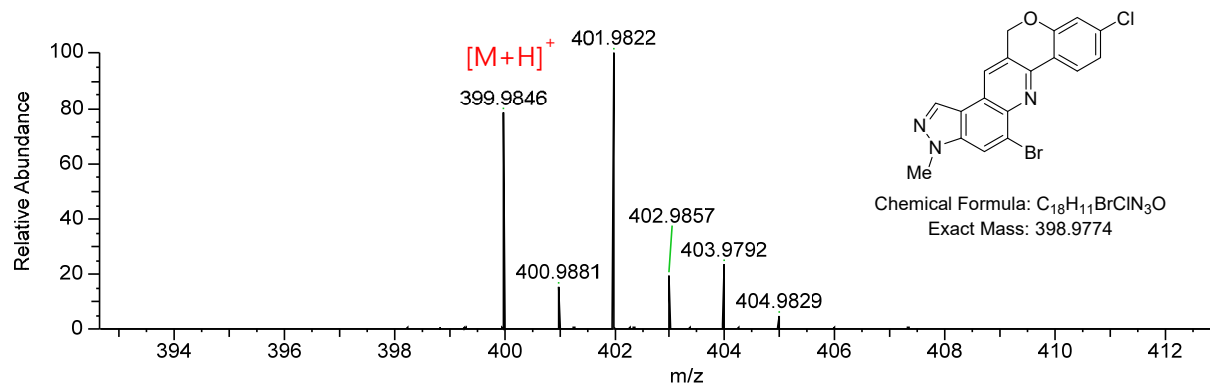
5-Bromo-9-chloro-3-methyl-3,12-dihydrochromeno[4,3-b]pyrazolo[4,3-f]quinoline (2K)



S104

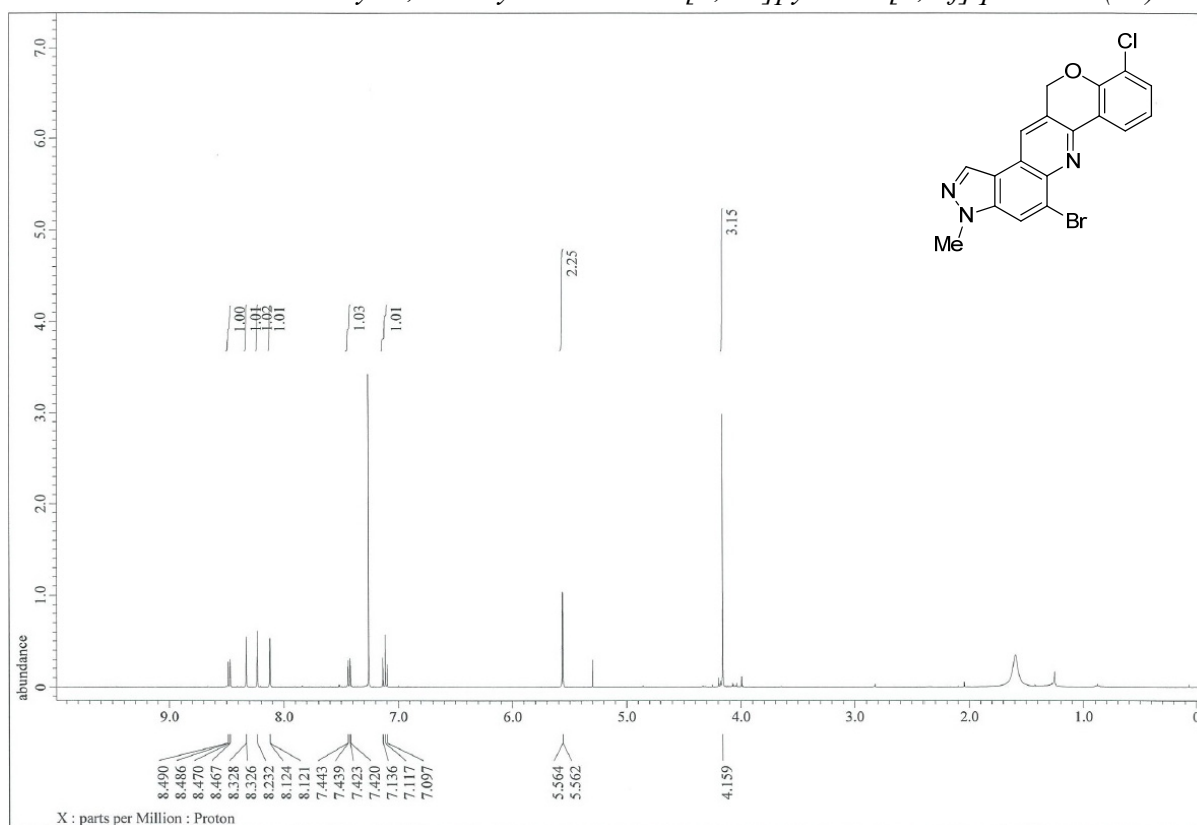


S105

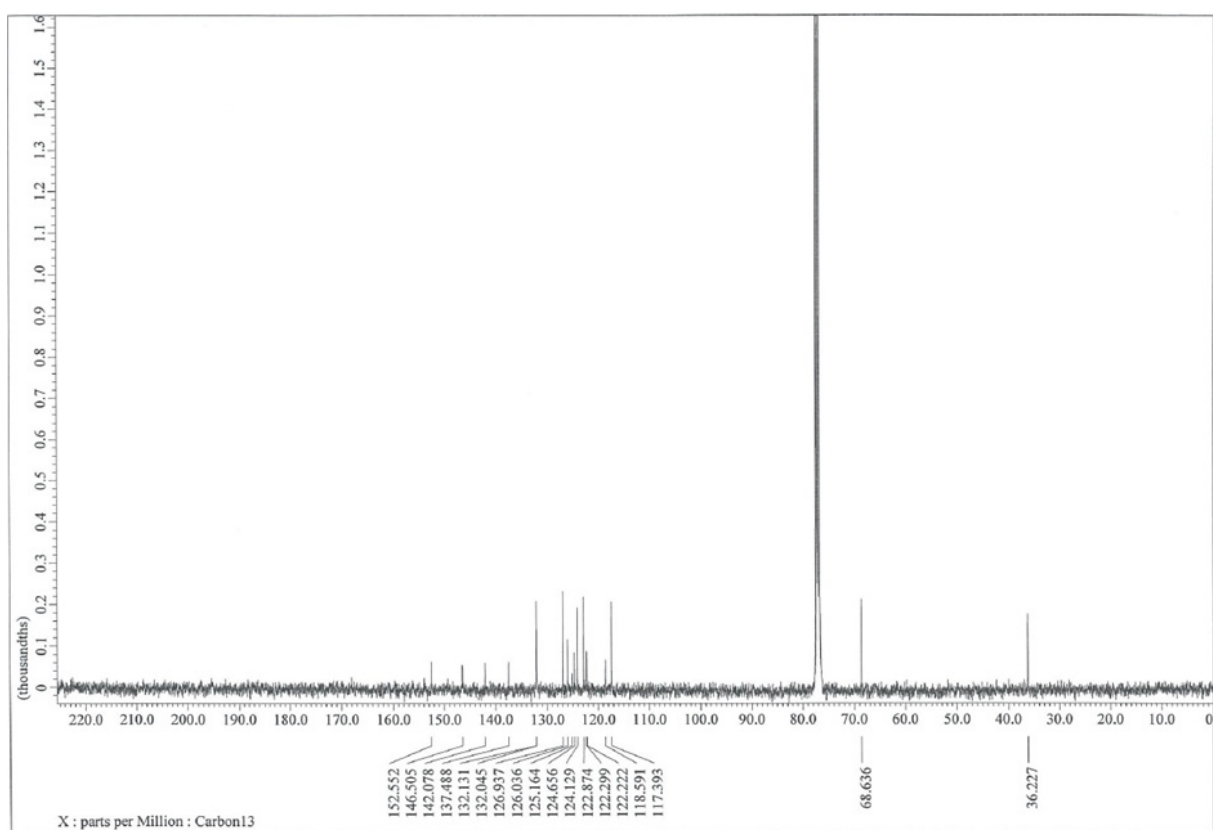


S106

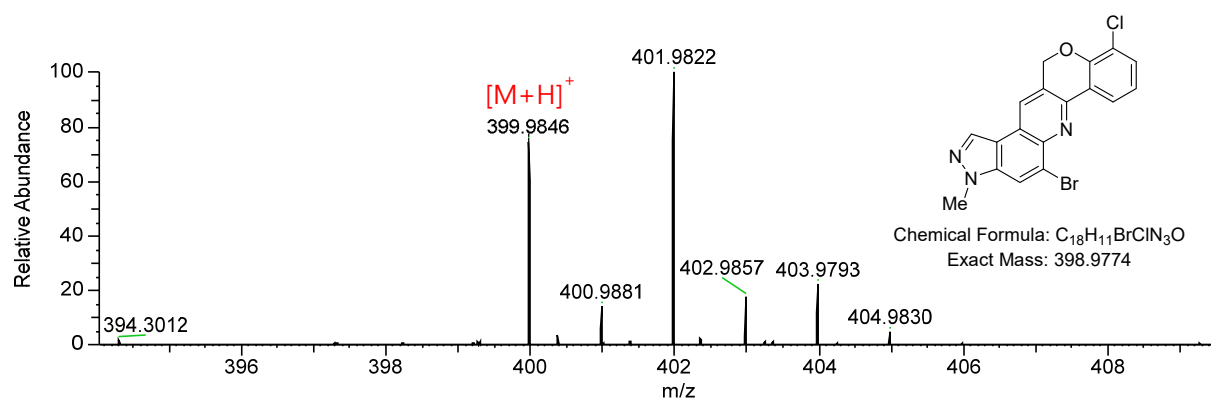
5-Bromo-10-chloro-3-methyl-3,12-dihydrochromeno[4,3-b]pyrazolo[4,3-f]quinoline (2L)



S107

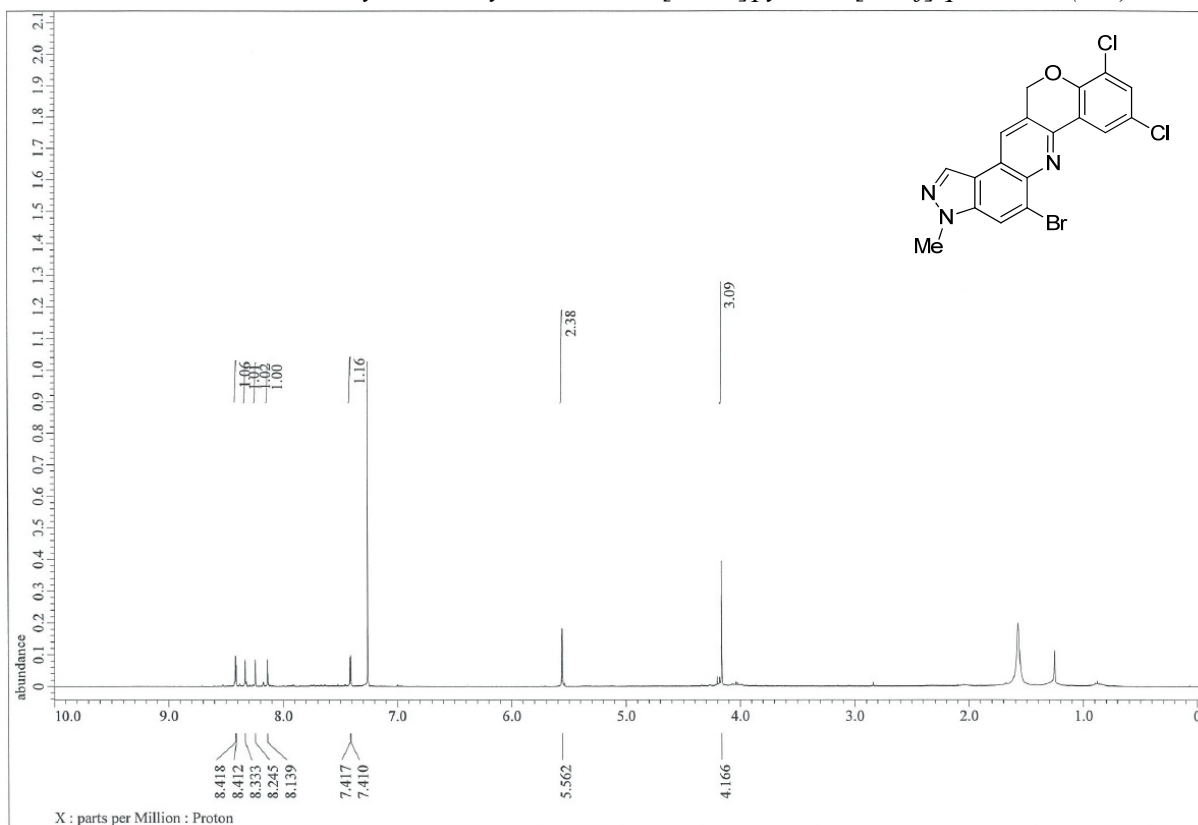


S108

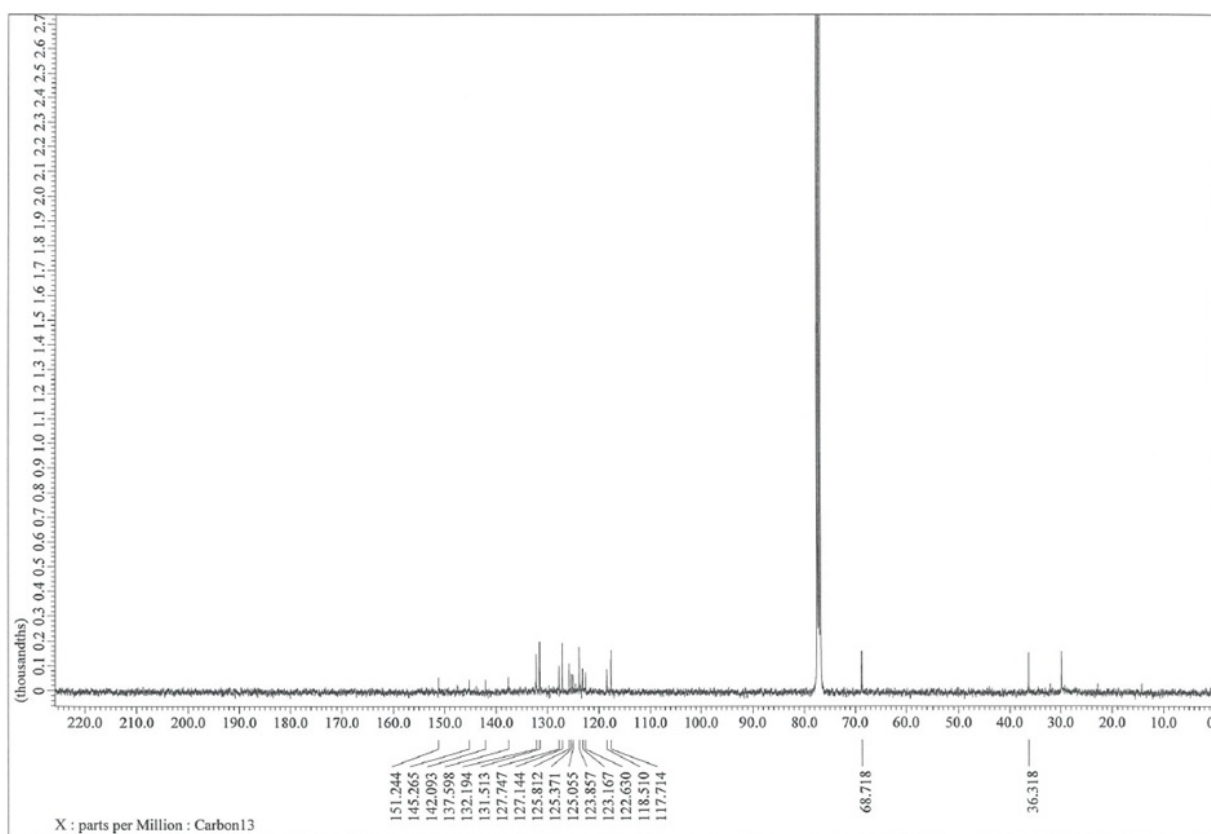


S109

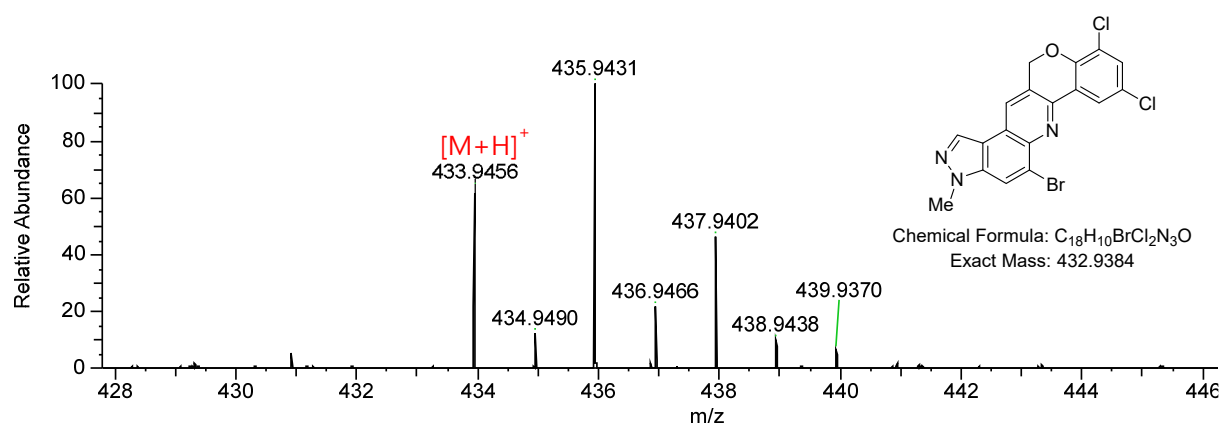
5-Bromo-8,10-dichloro-3-methyl-3,12-dihydrochromeno[4,3-b]pyrazolo[4,3-f]quinoline (2M)



S110

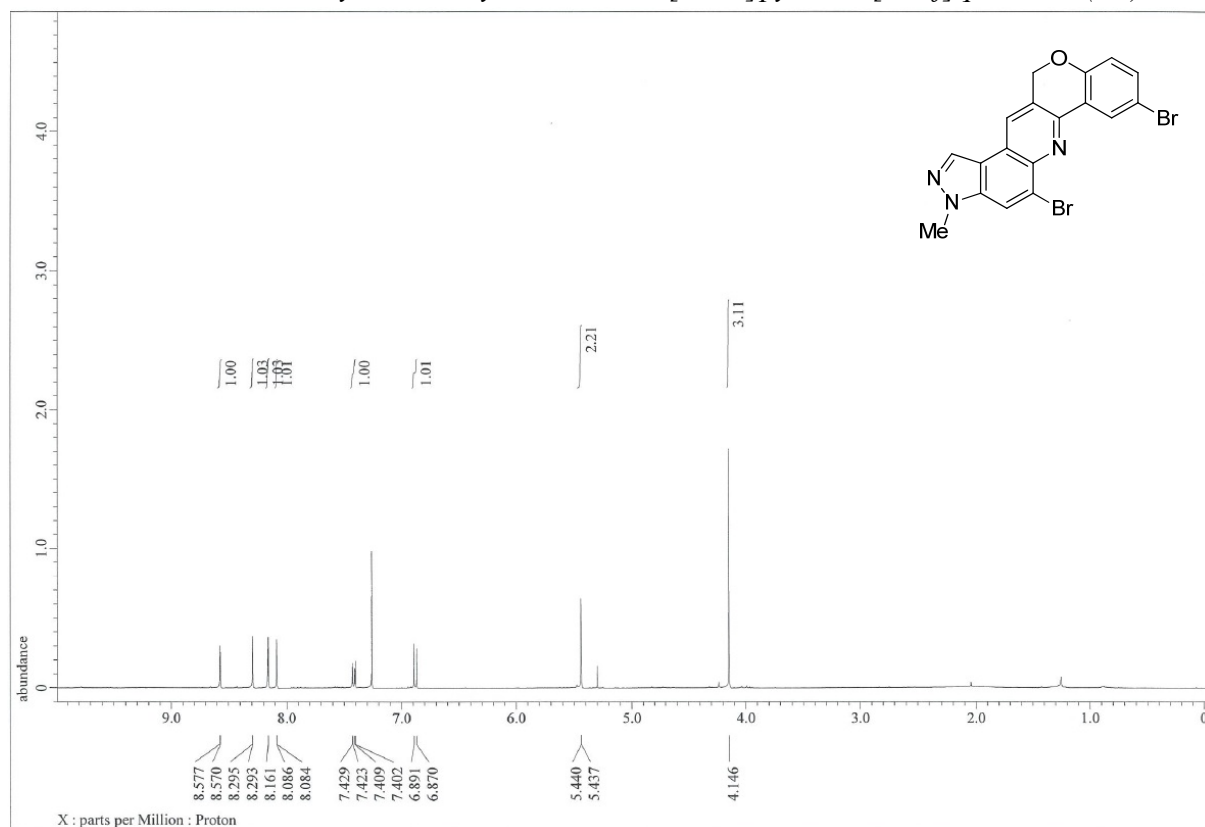


S111

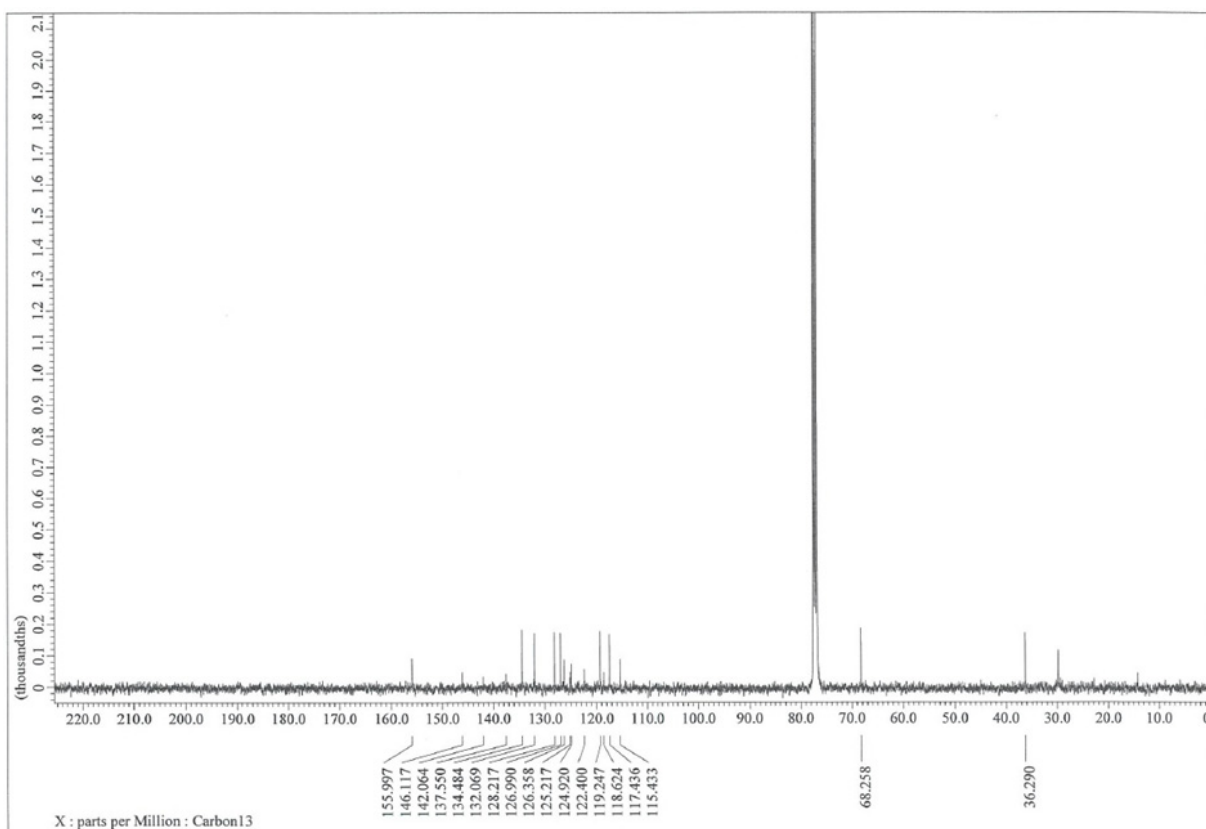


S112

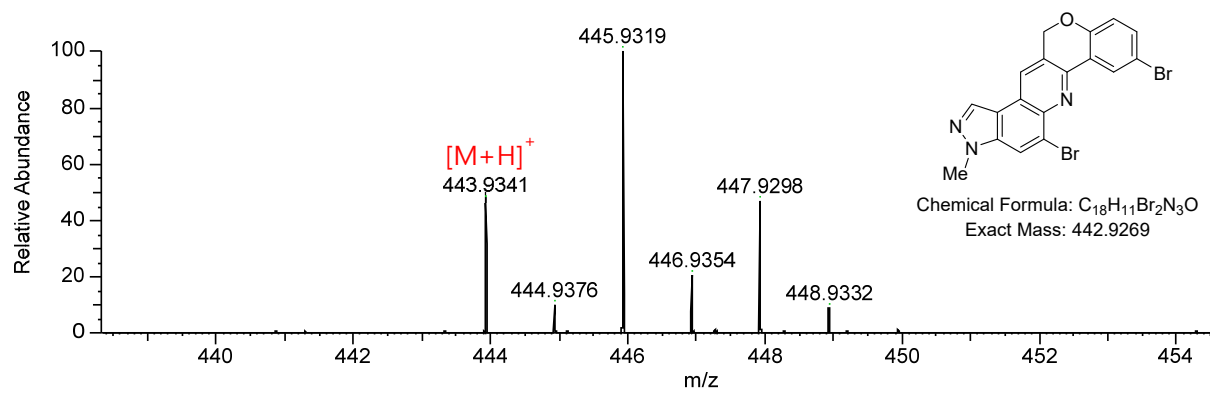
5-Bromo-8-bromo-3-methyl-3,12-dihydrochromeno[4,3-b]pyrazolo[4,3-f]quinoline (2N)



S113



S114

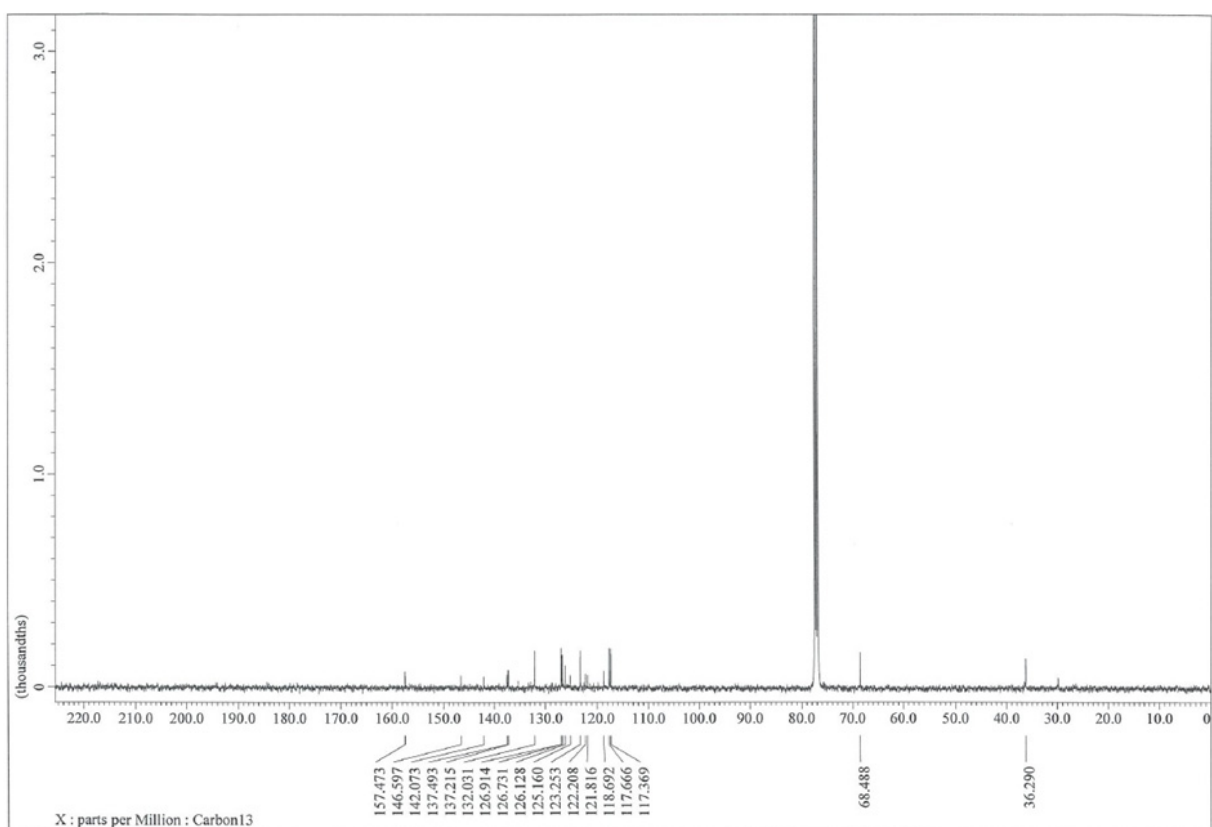


S115

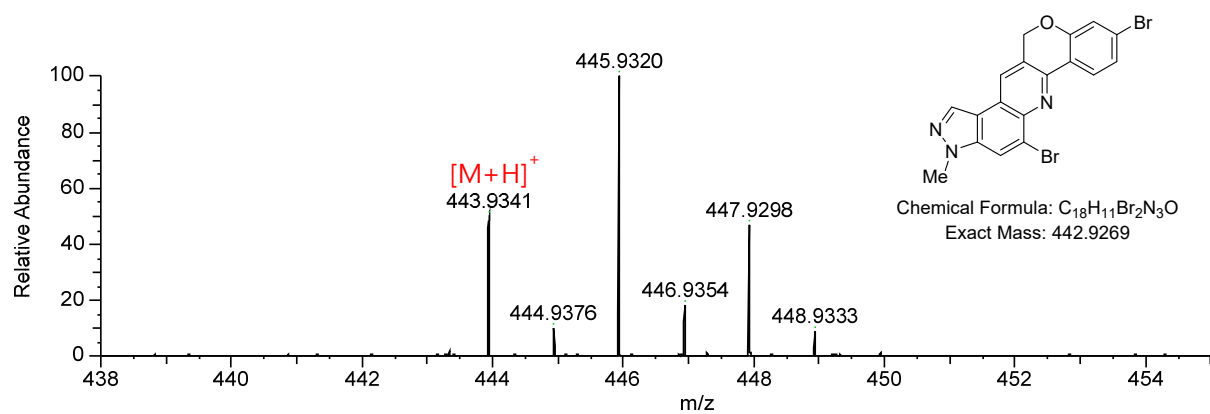
5-Bromo-9-bromo-3-methyl-3,12-dihydrochromeno[4,3-b]pyrazolo[4,3-f]quinoline (20)



S116

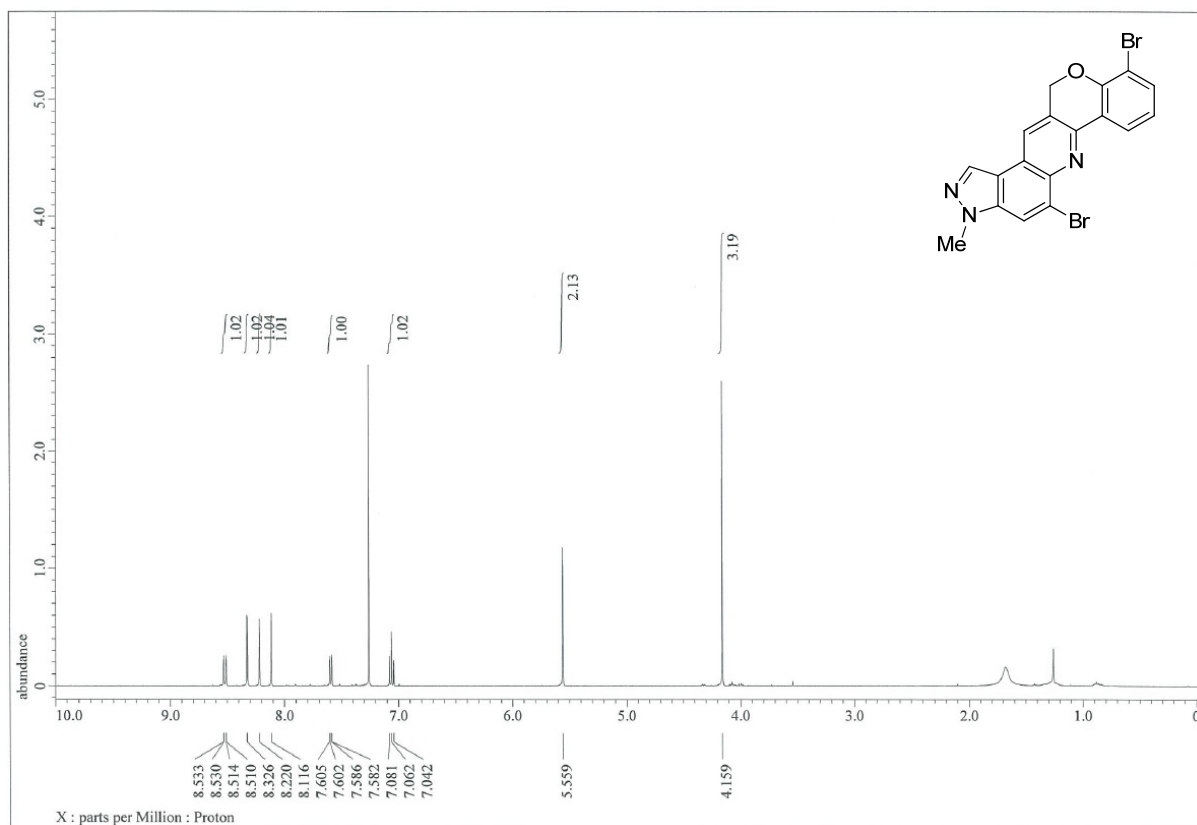


S117

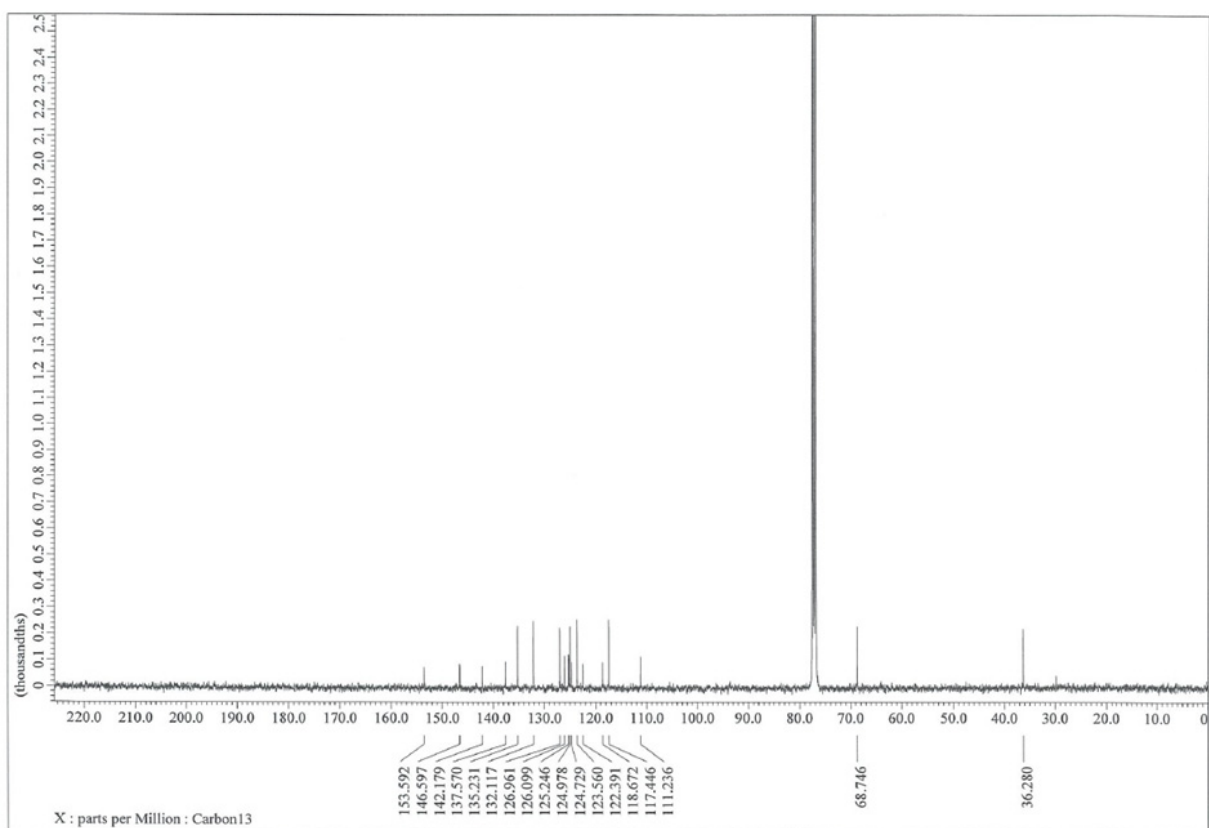


S118

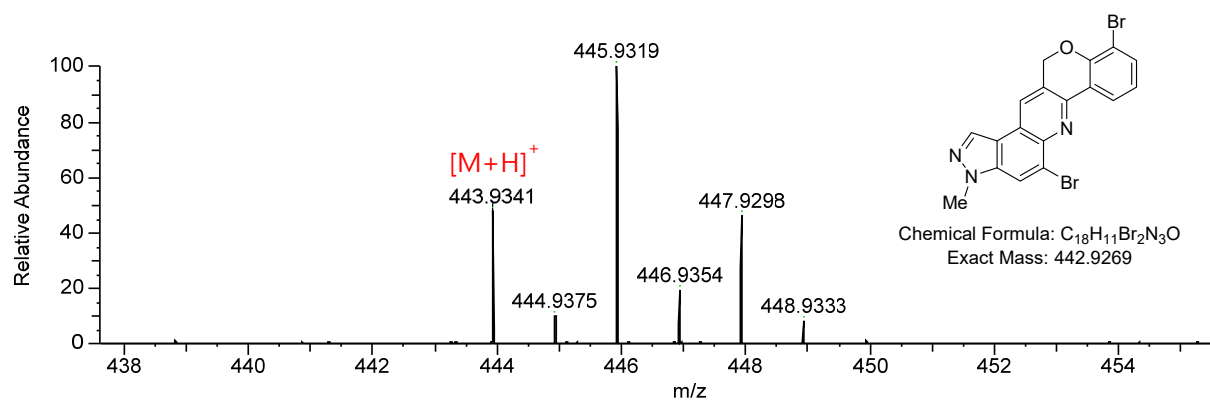
5-Bromo-10-bromo-3-methyl-3,12-dihydrochromeno[4,3-b]pyrazolo[4,3-f]quinoline (2P)



S119

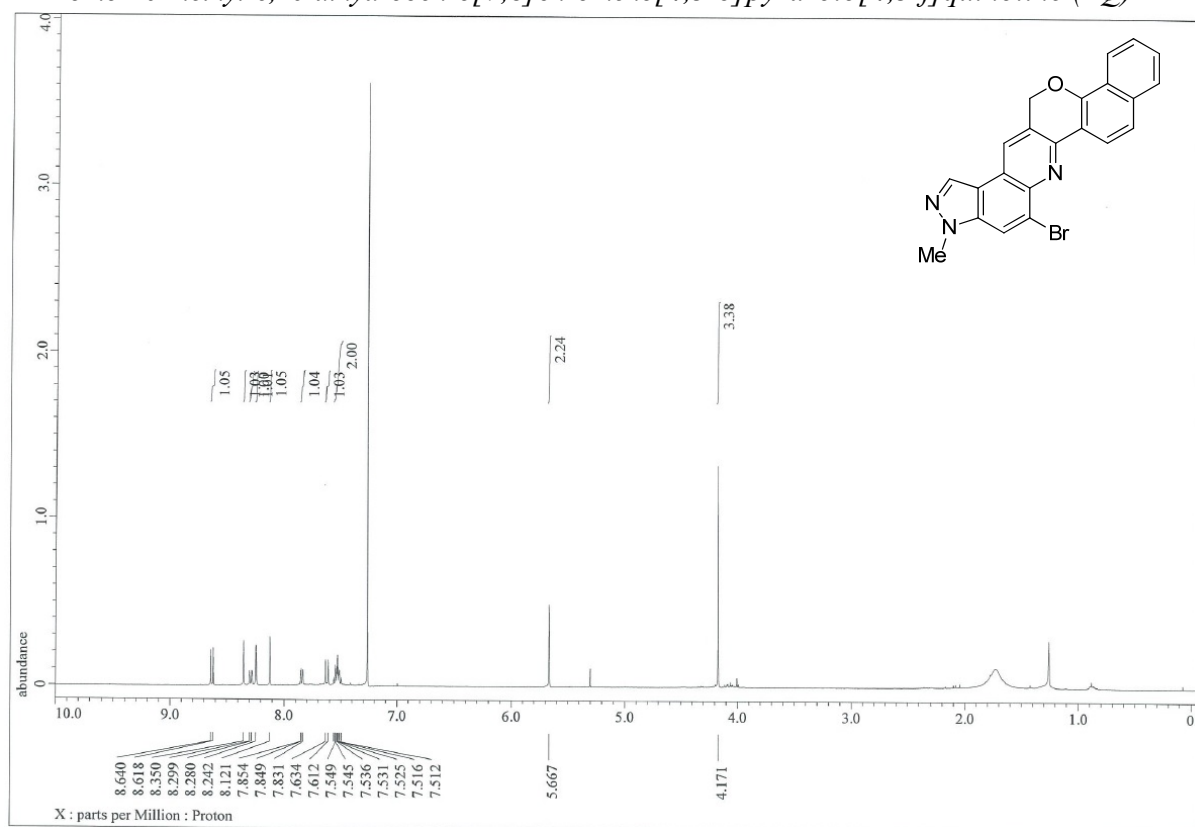


S120

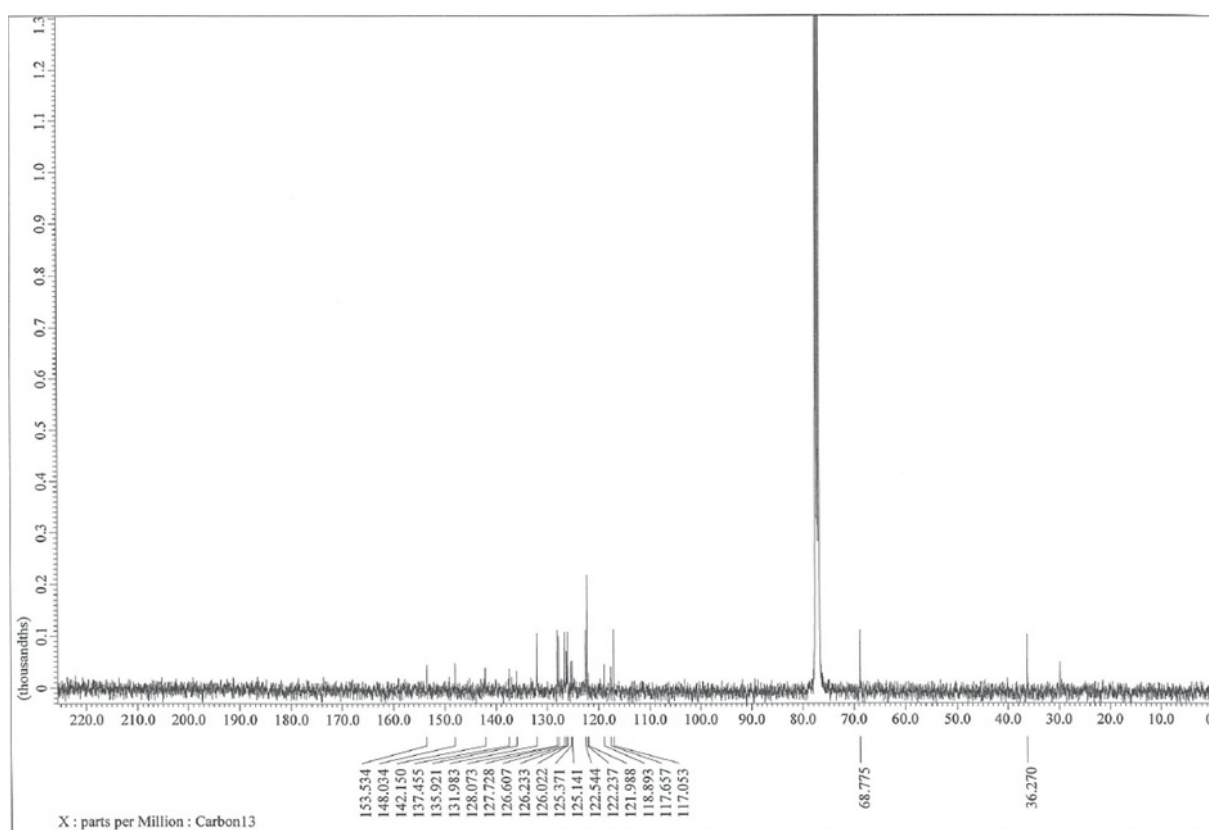


S121

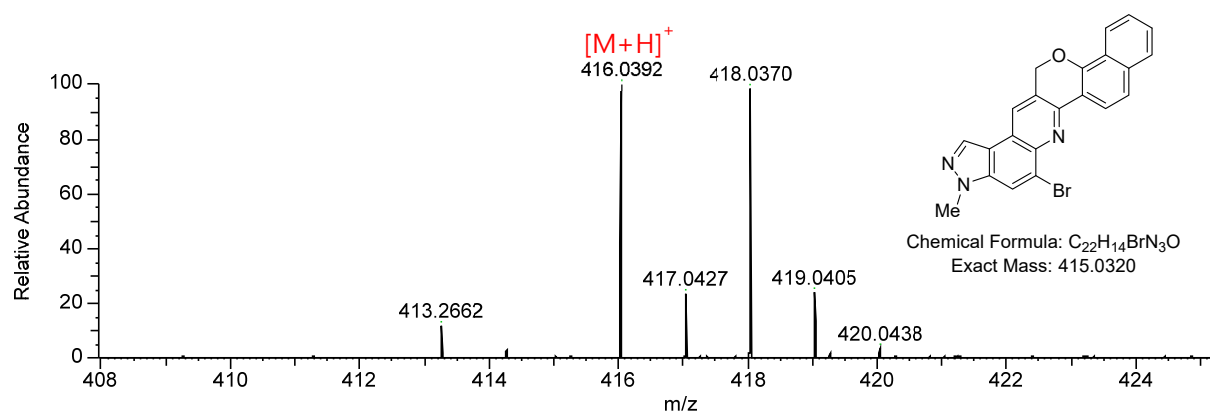
12-Bromo-10-methyl-6,10-dihydrobenzo[7,8]chromeno[4,3-b]pyrazolo[4,3-f]quinoline (2Q)



S122

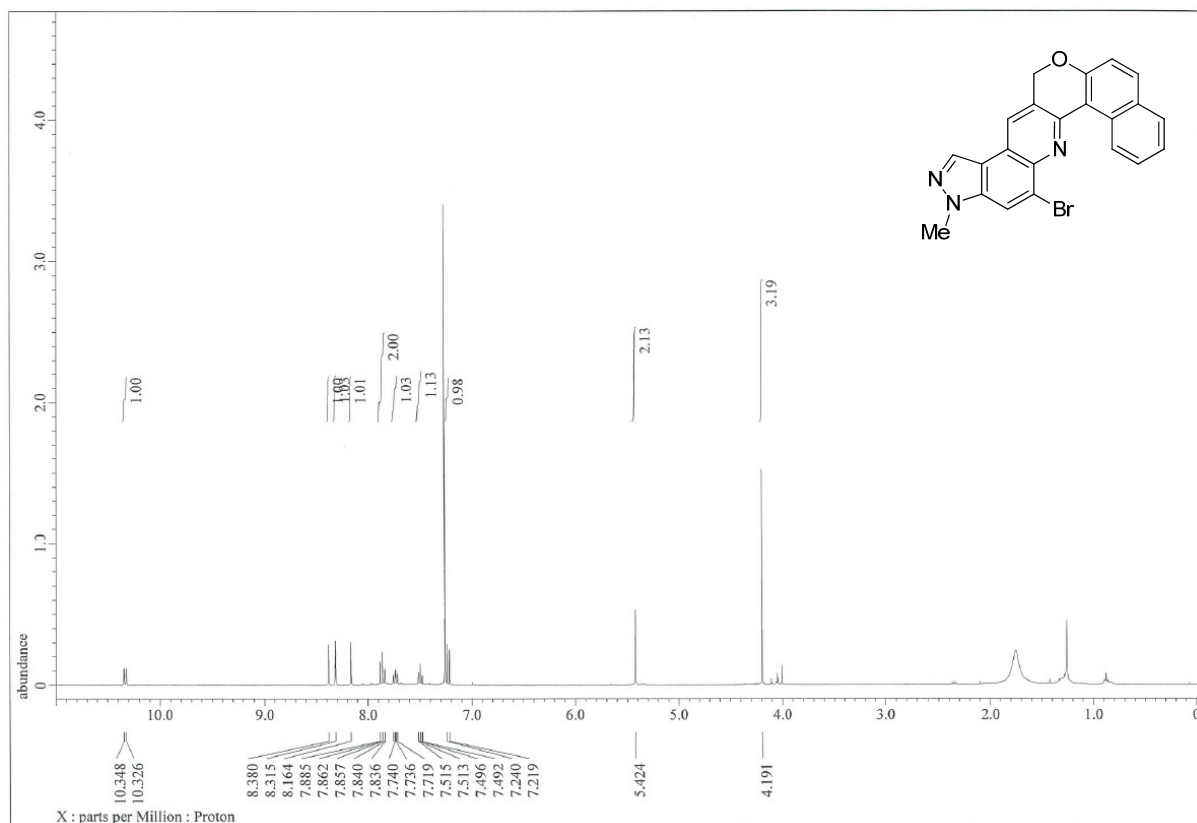


S123

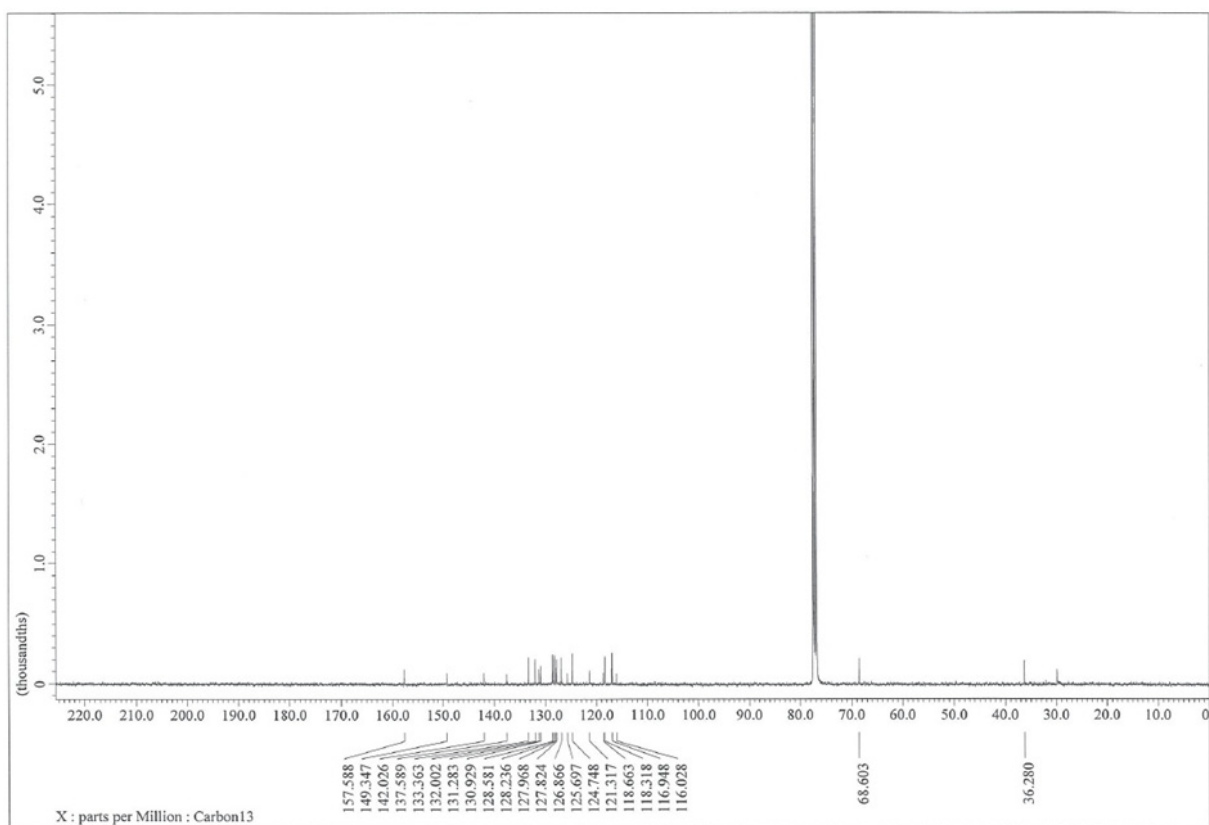


S124

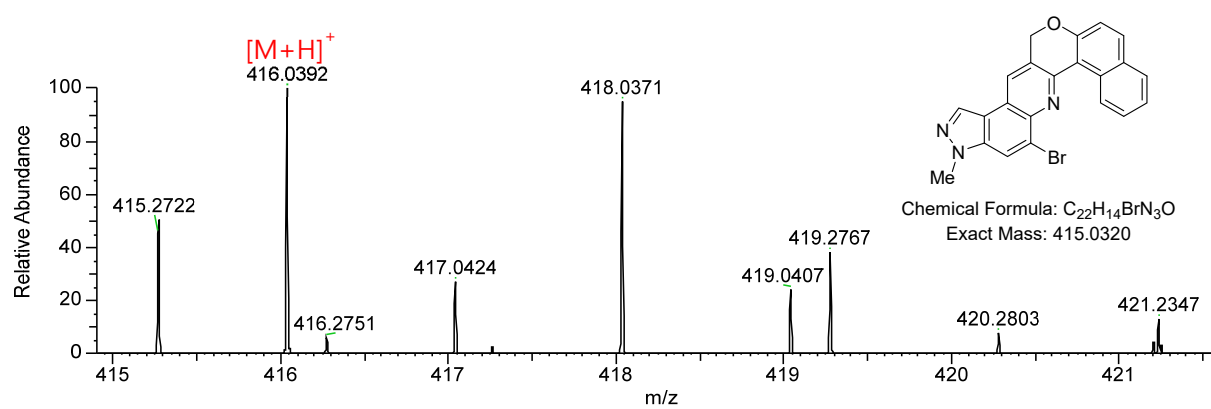
14-Bromo-12-methyl-8,12-dihydrobenzo[5,6]chromeno[4,3-b]pyrazolo[4,3-f]quinoline (2R)



S125

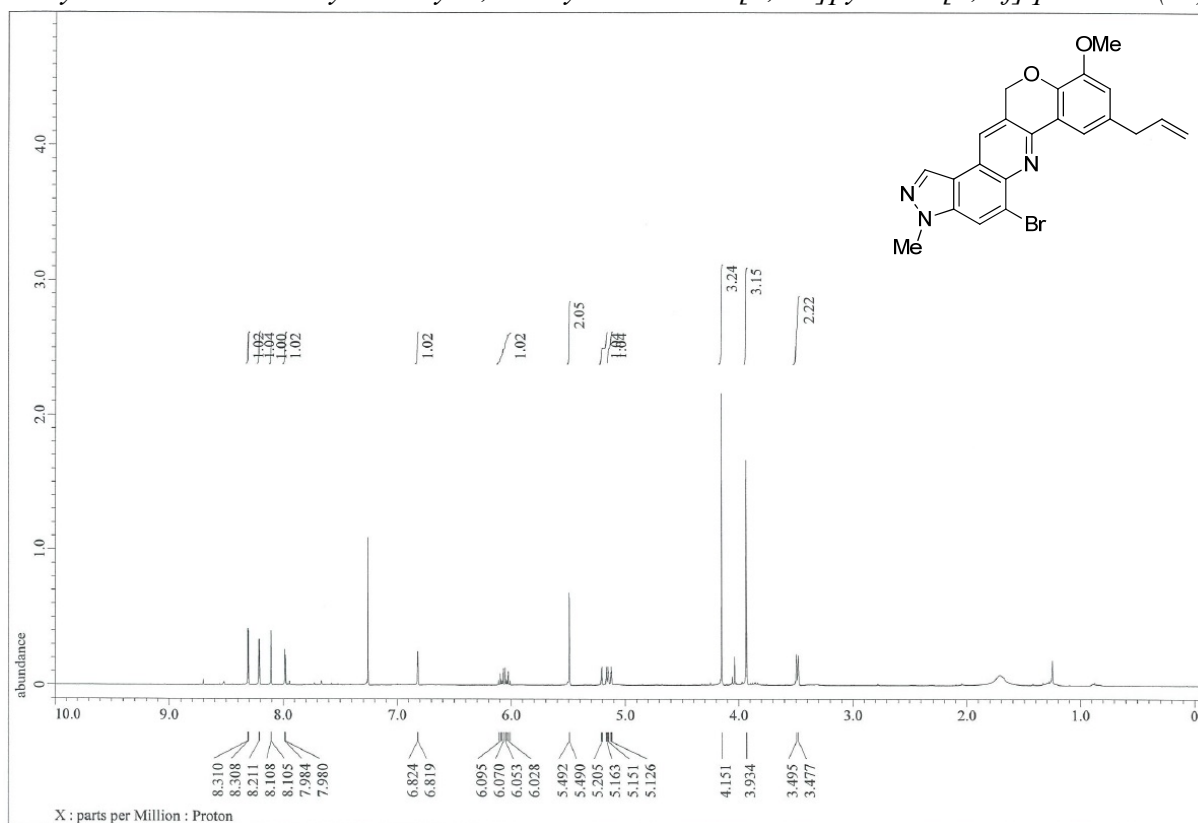


S126

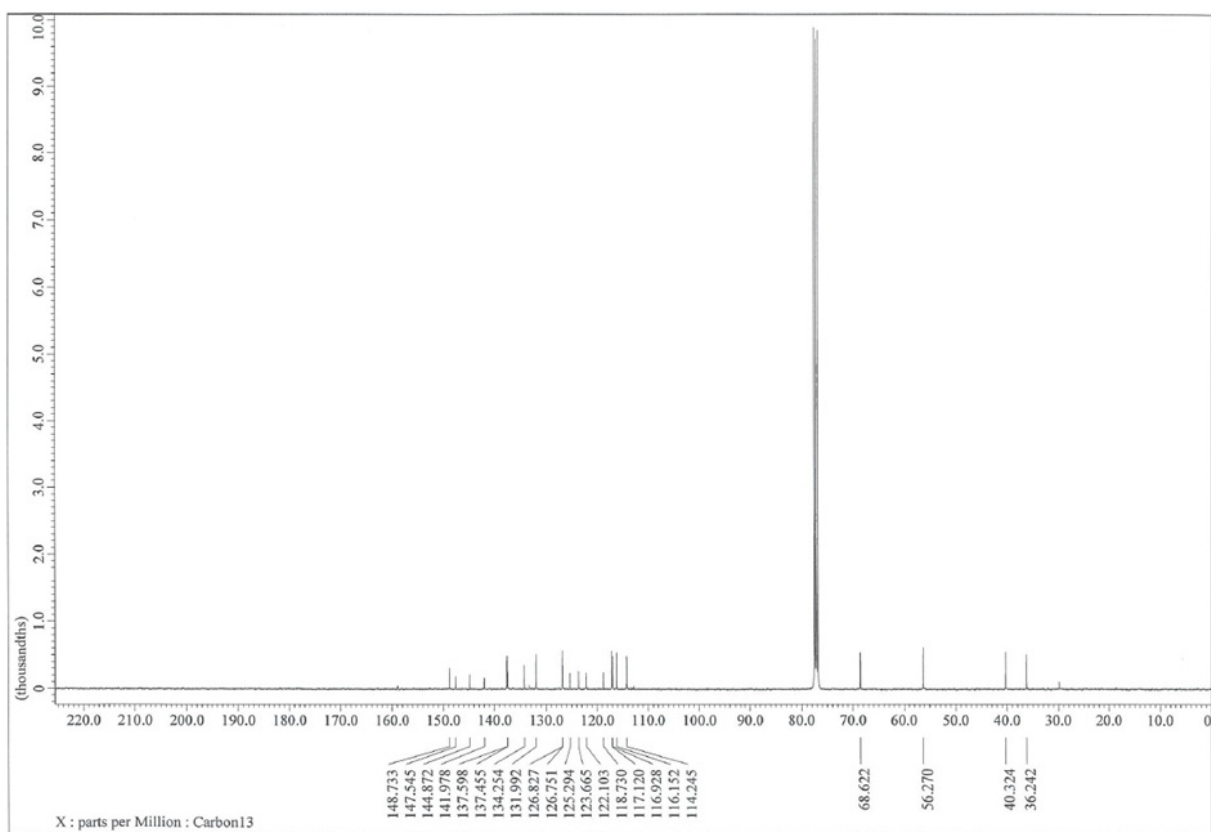


S127

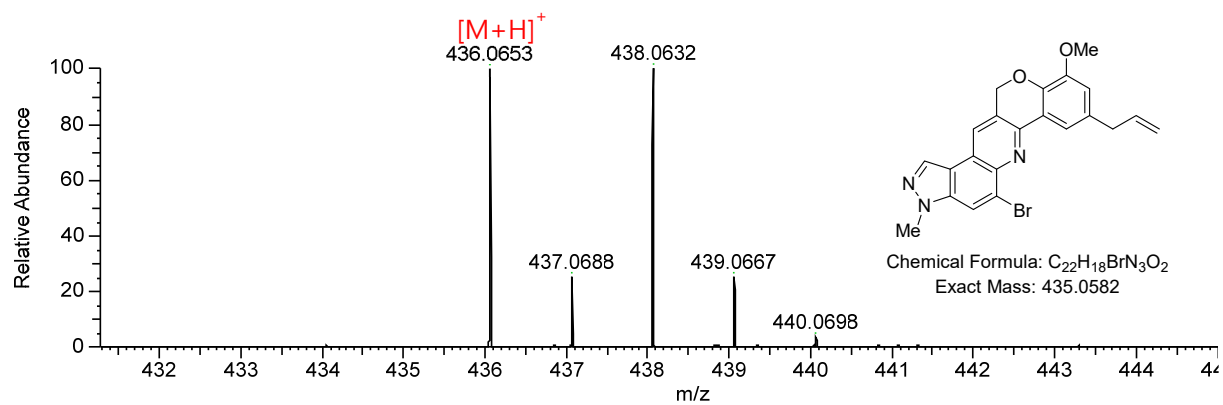
8-Allyl-5-bromo-10-methoxy-3-methyl-3,12-dihydrochromeno[4,3-b]pyrazolo[4,3-f]quinoline (2S)



S128

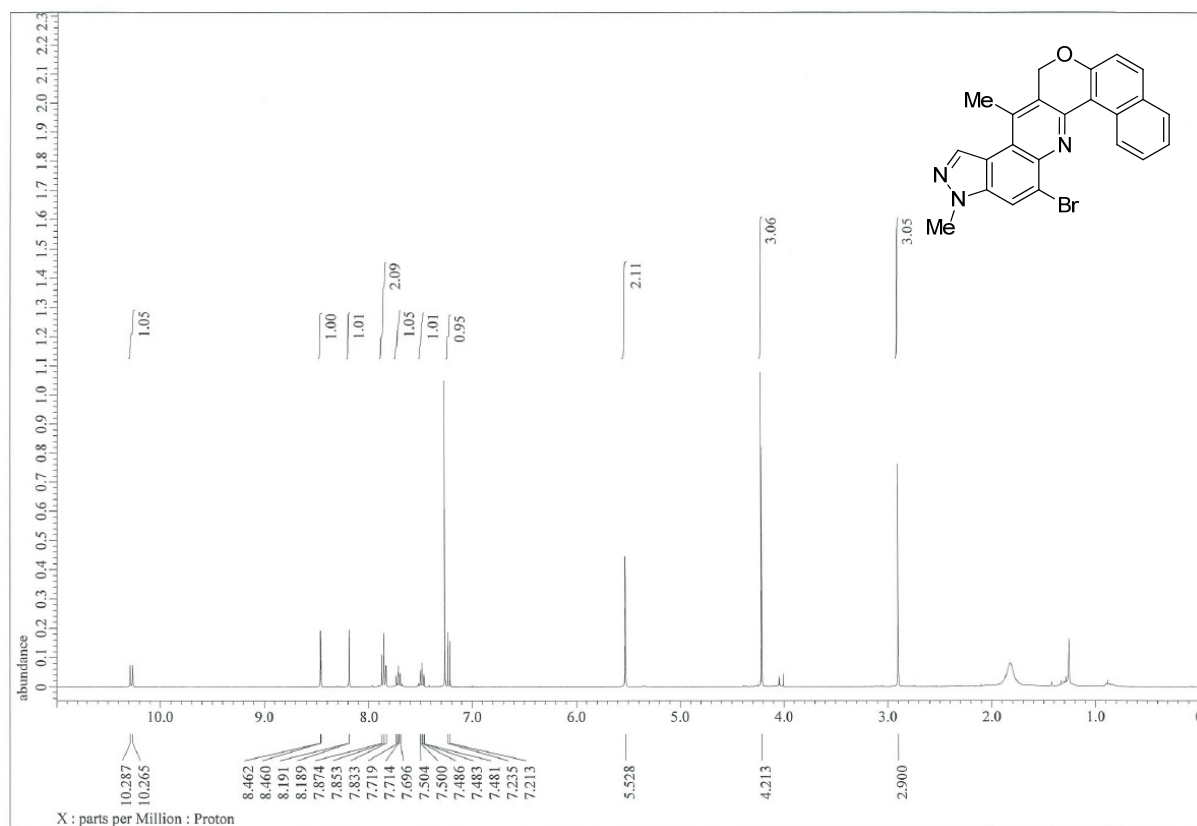


S129

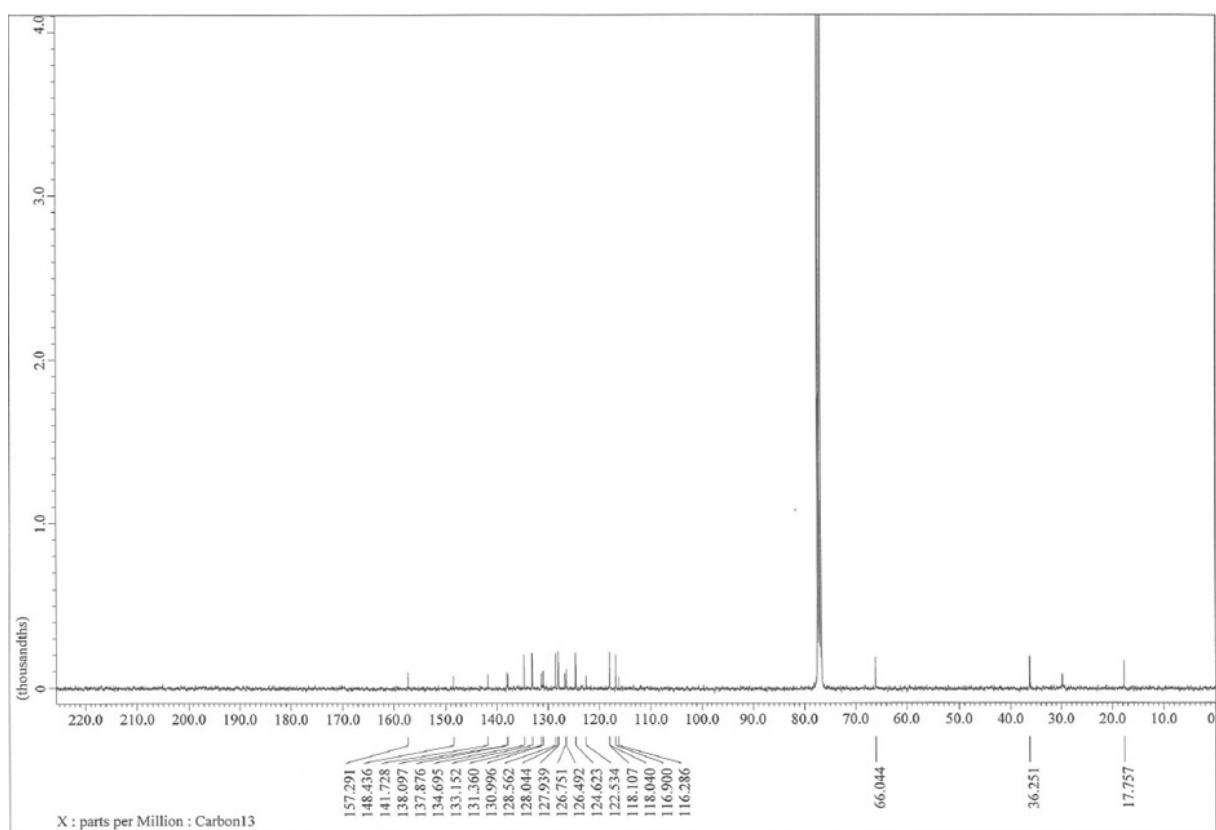


S130

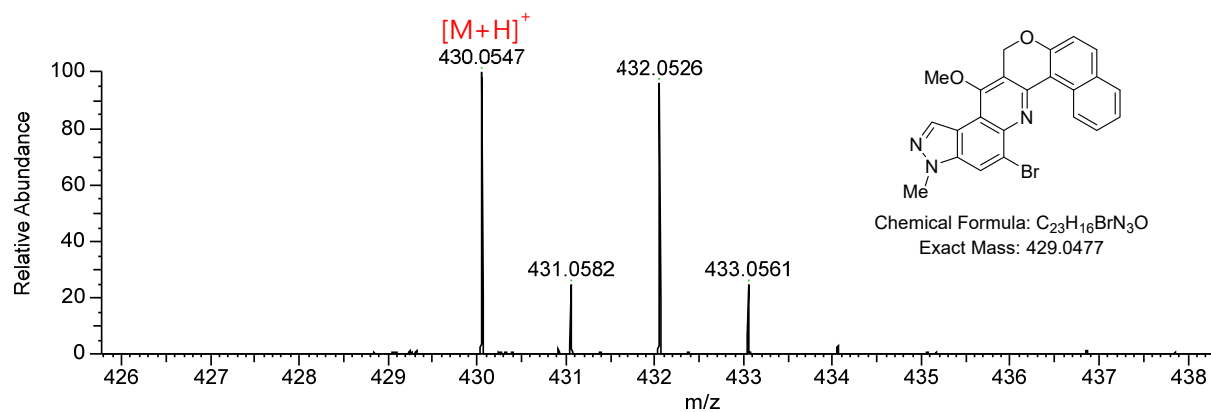
14-Bromo-9,12-dimethyl-8,12-dihydrobenzo[5,6]chromeno[4,3-b]pyrazolo[4,3-f]quinoline (2T)



S131

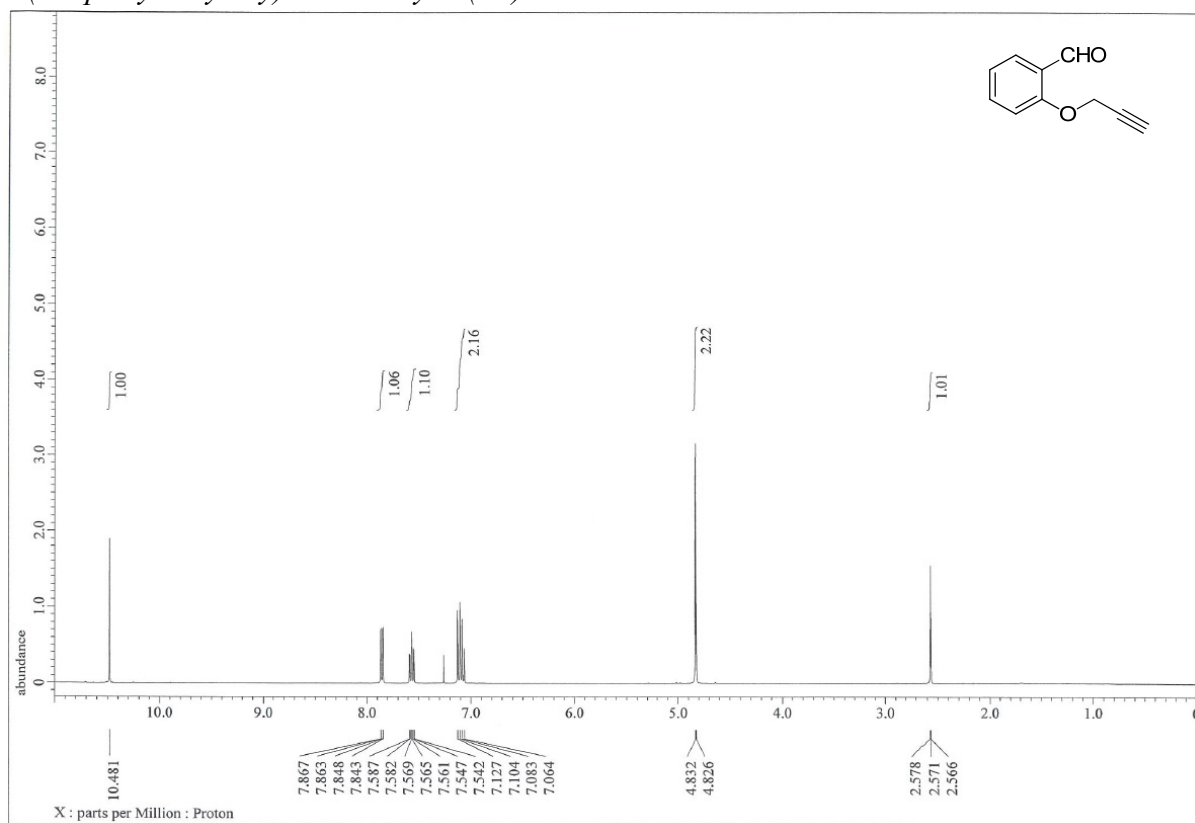


S132



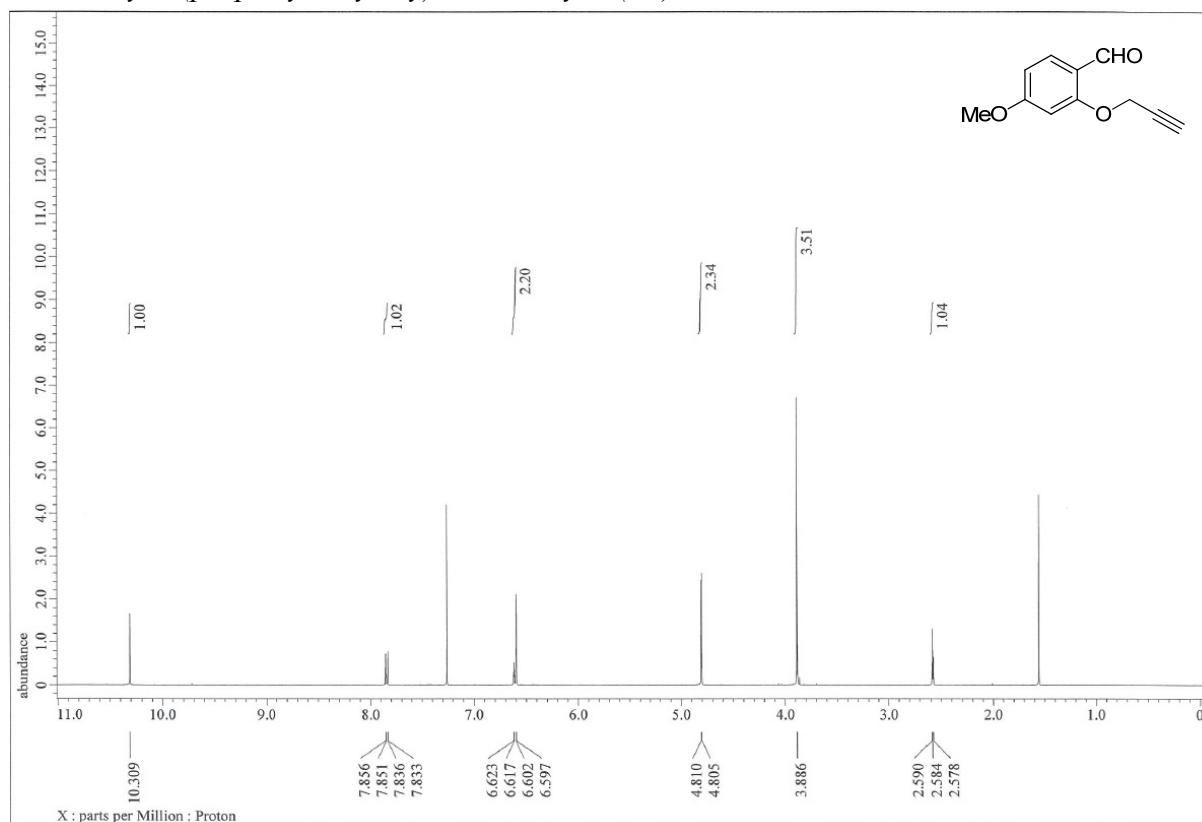
S133

2-(Prop-2-yn-1-yloxy)benzaldehyde (6A)



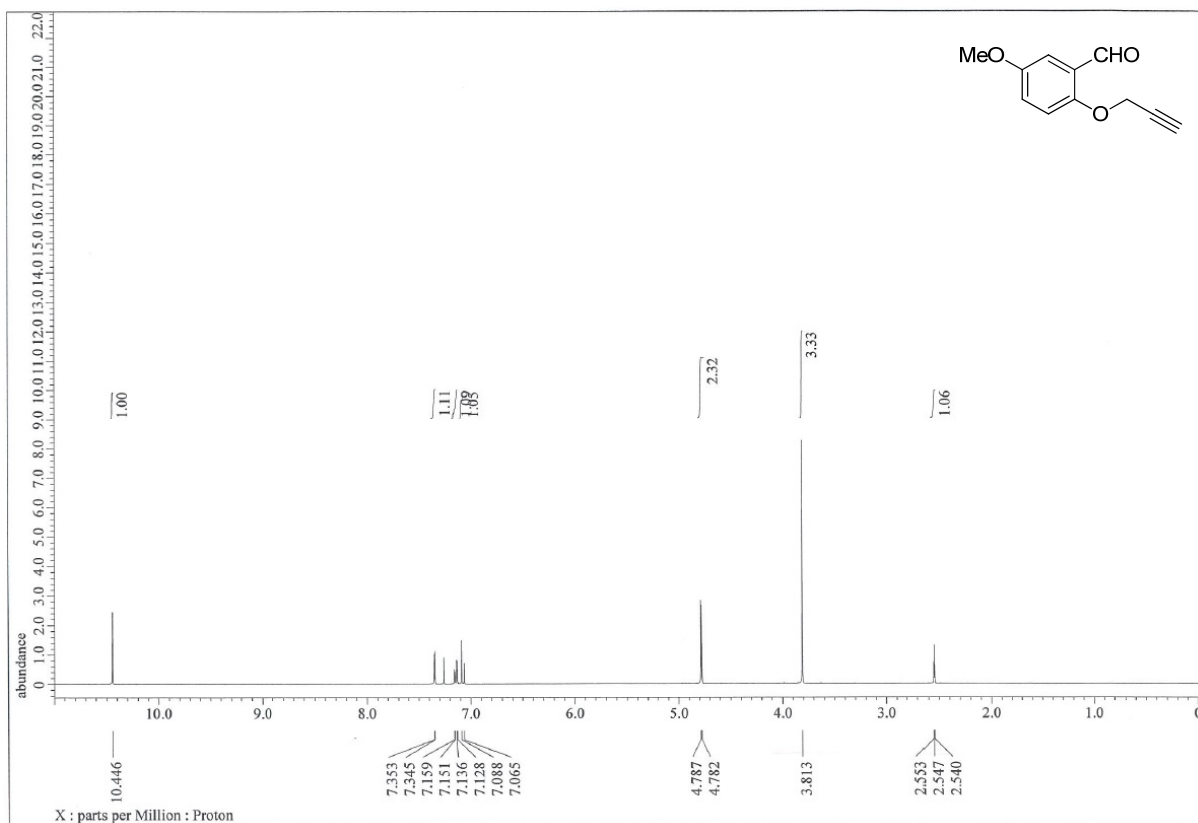
S134

4-Methoxy-2-(prop-2-yn-1-yloxy)benzaldehyde (6B)



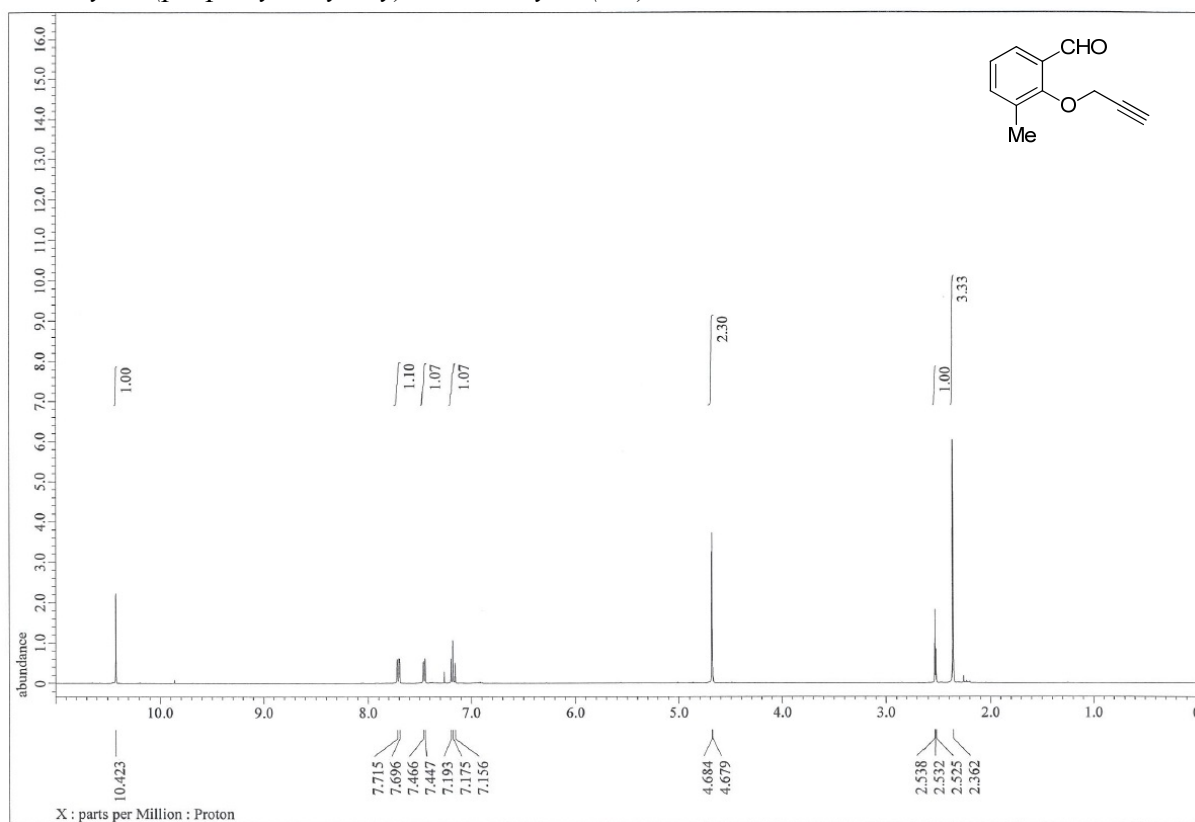
S135

5-Methoxy-2-(prop-2-yn-1-yloxy)benzaldehyde (6C)



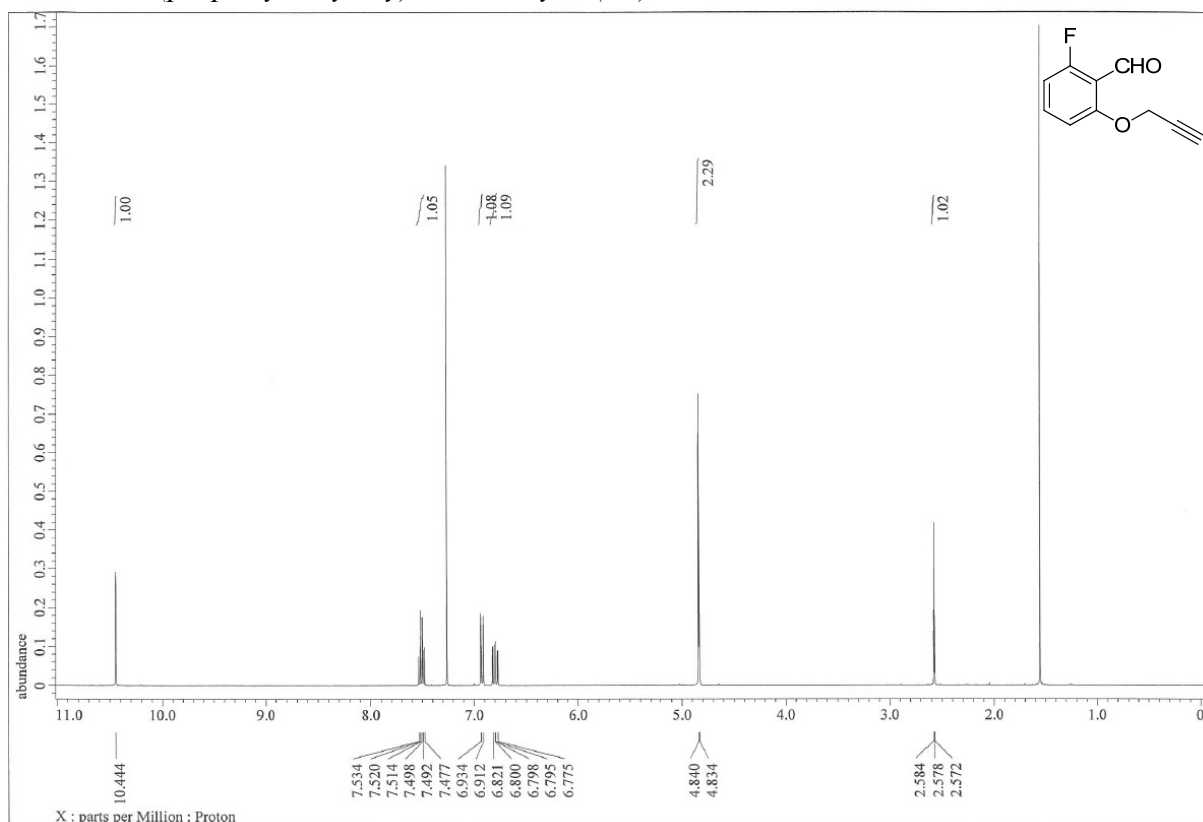
S136

3-Methyl-2-(prop-2-yn-1-yloxy)benzaldehyde (6D)



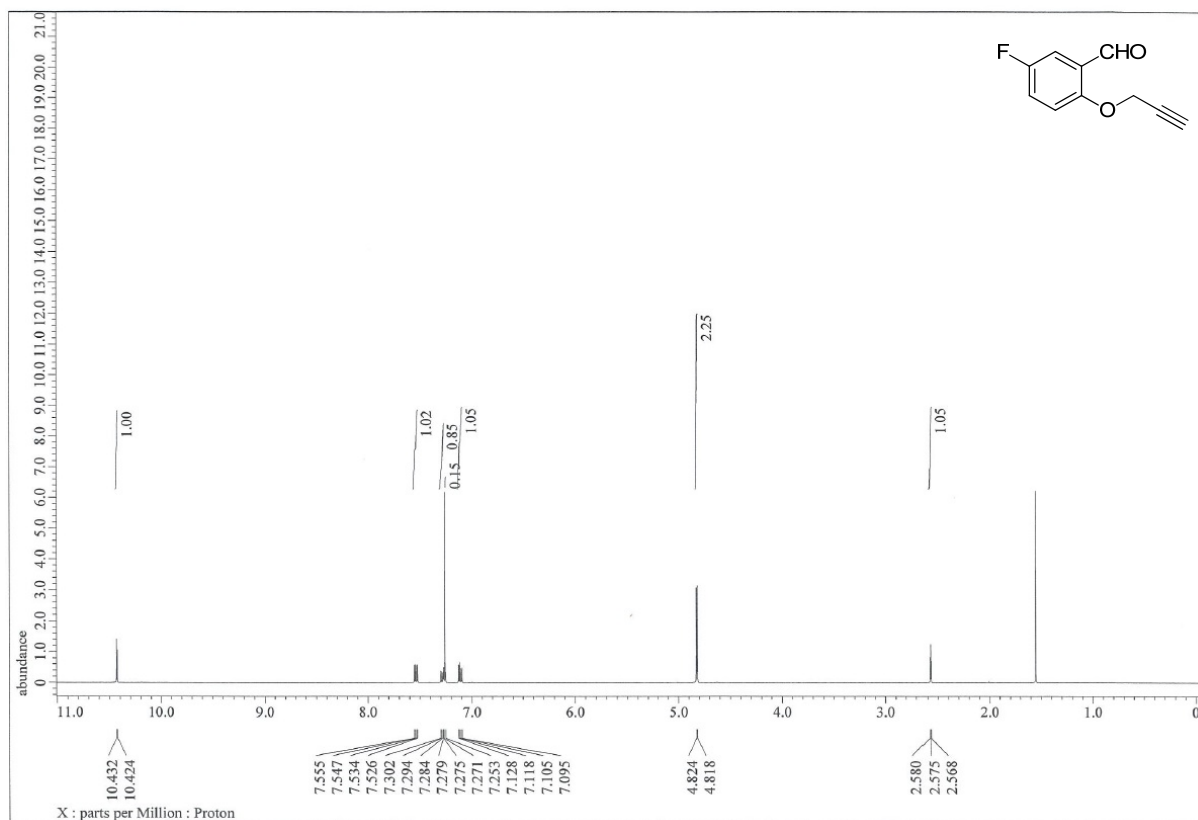
S137

6-Fluoro-2-(prop-2-yn-1-yloxy)benzaldehyde (6E)



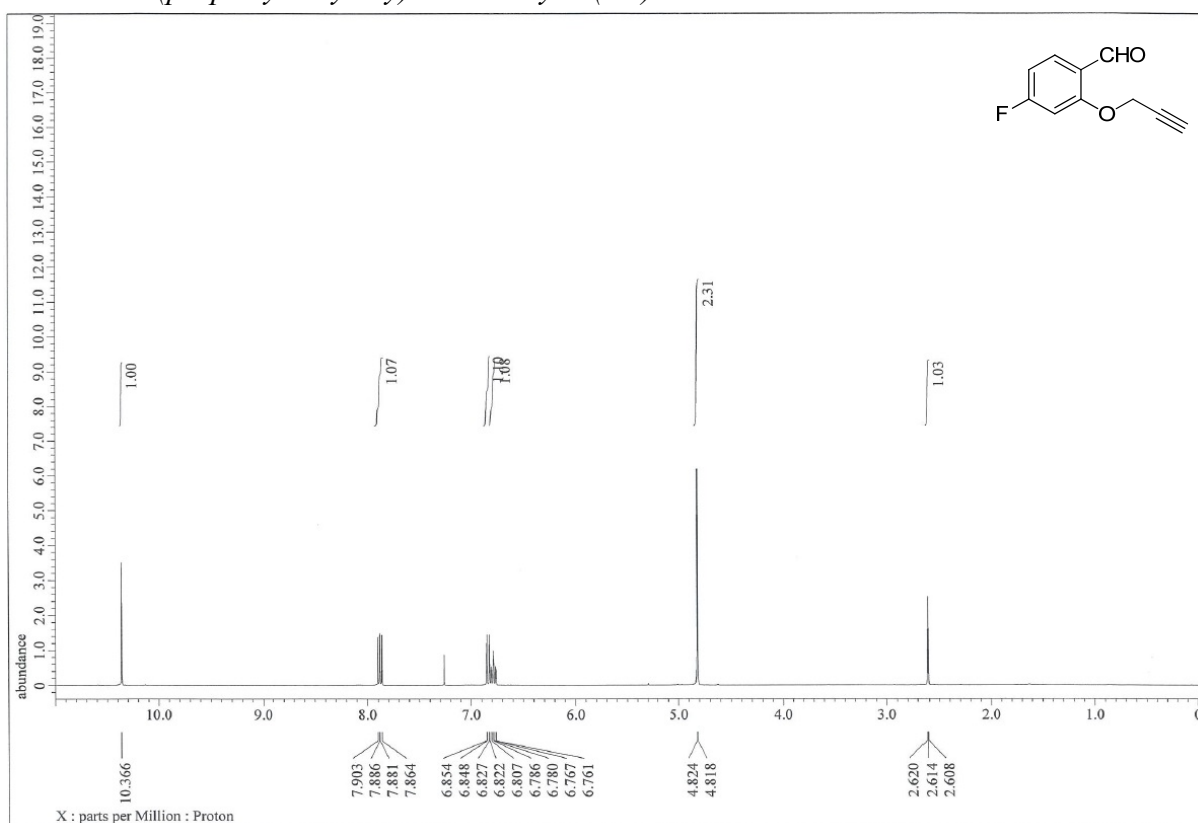
S138

5-Fluoro-2-(prop-2-yn-1-yloxy)benzaldehyde (6F)



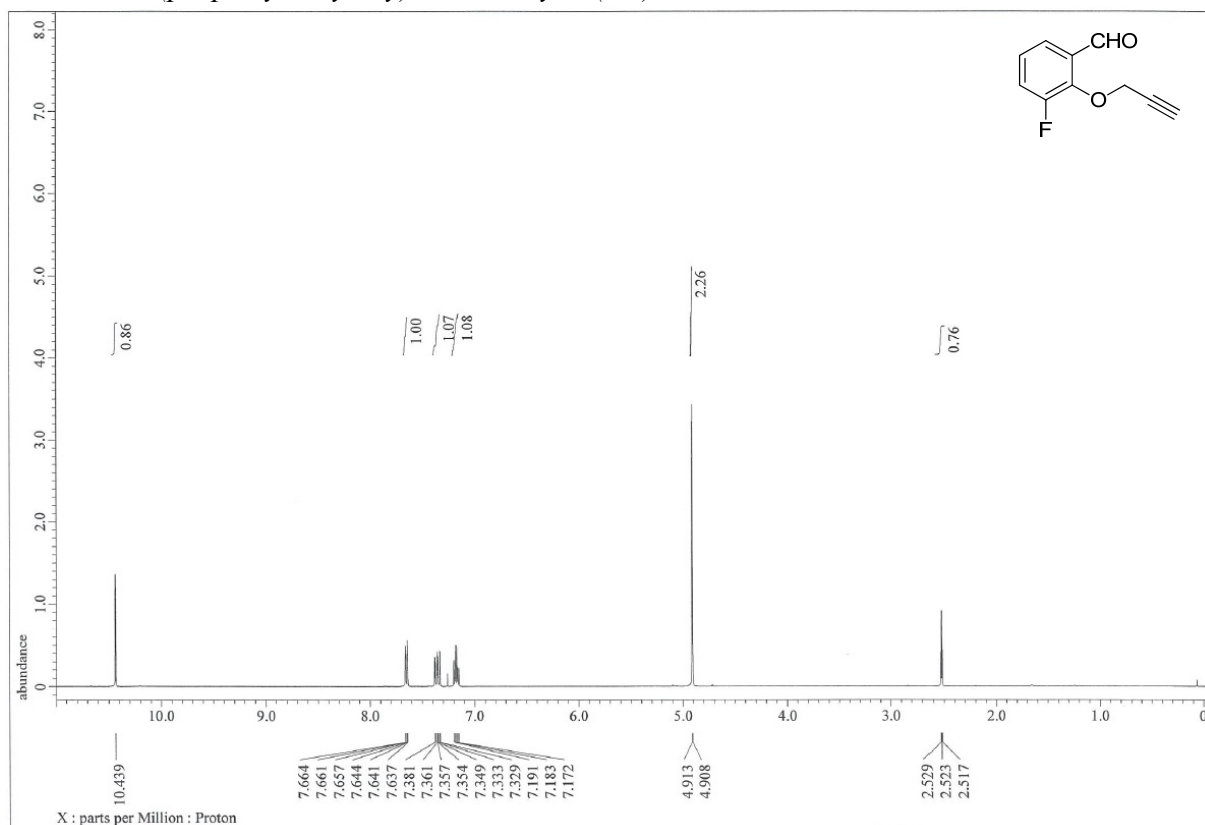
S139

4-Fluoro-2-(prop-2-yn-1-yloxy)benzaldehyde (6G)



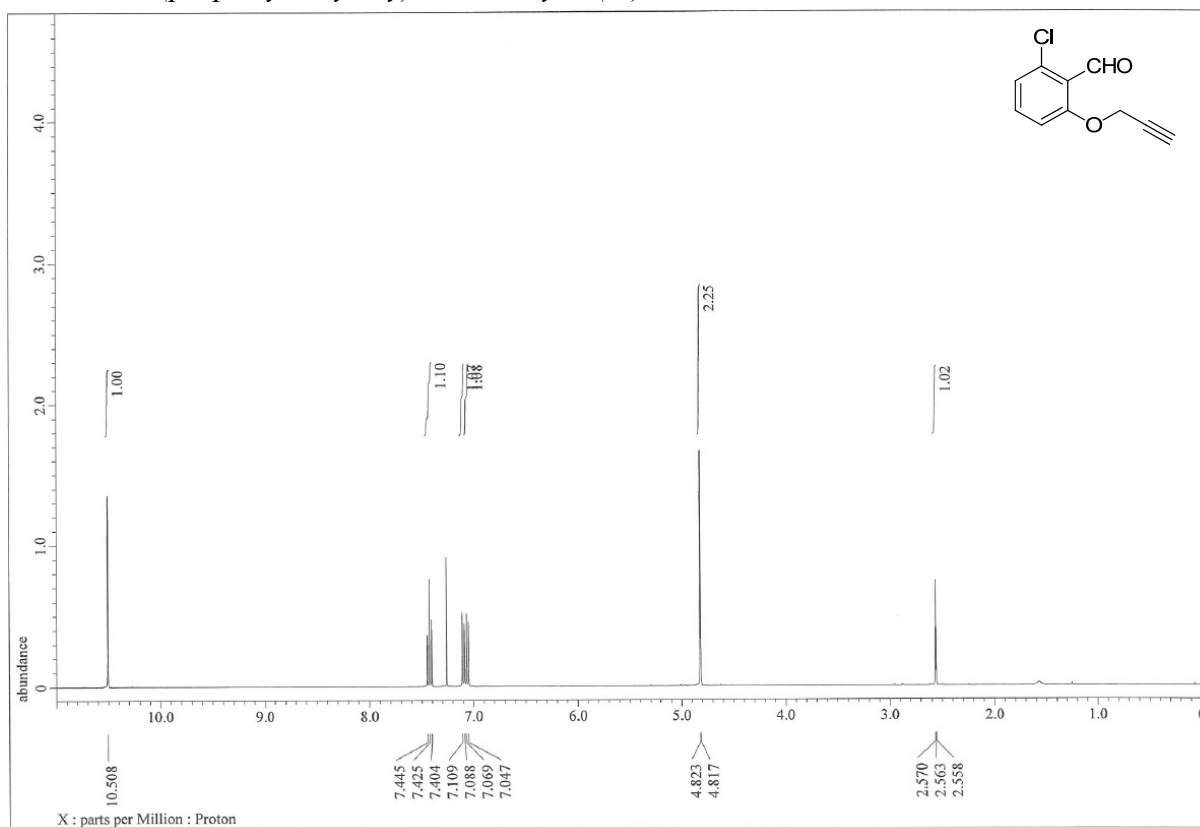
S140

3-Fluoro-2-(prop-2-yn-1-yloxy)benzaldehyde (6H)



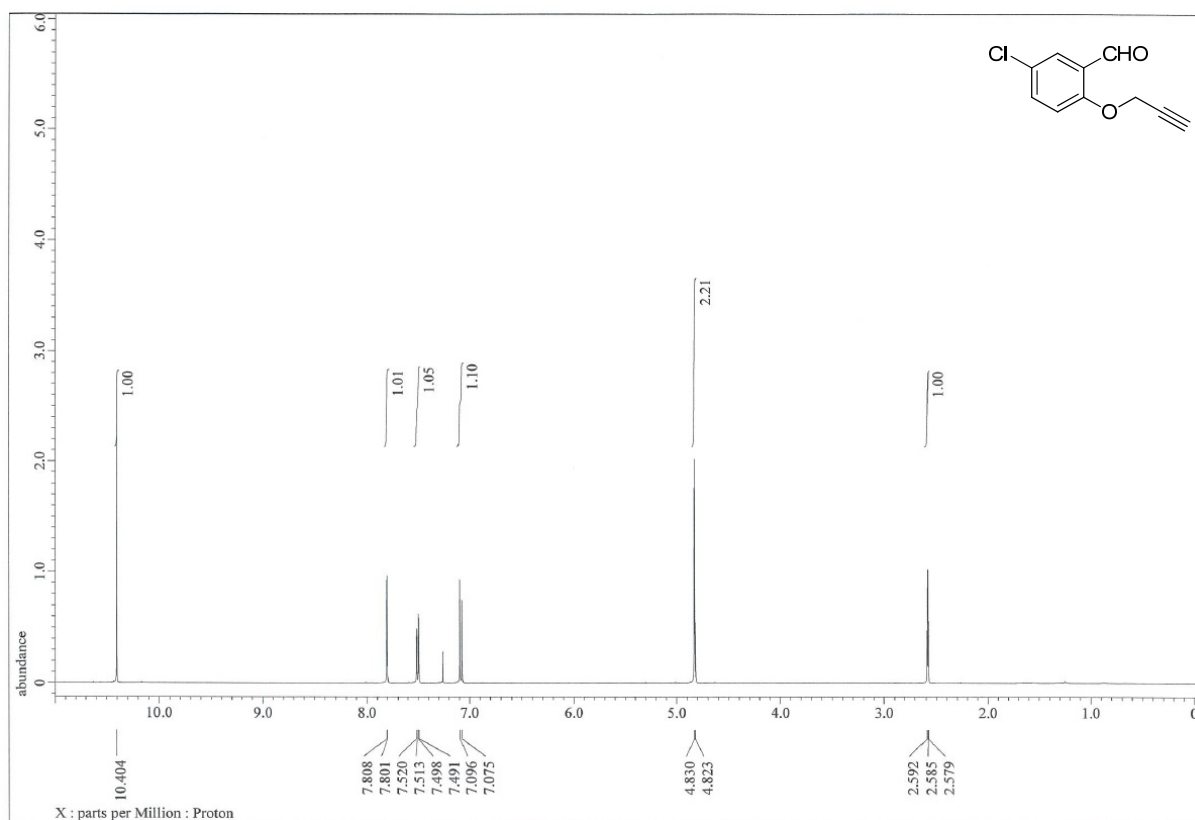
S141

6-Chloro-2-(prop-2-yn-1-yloxy)benzaldehyde (6I)



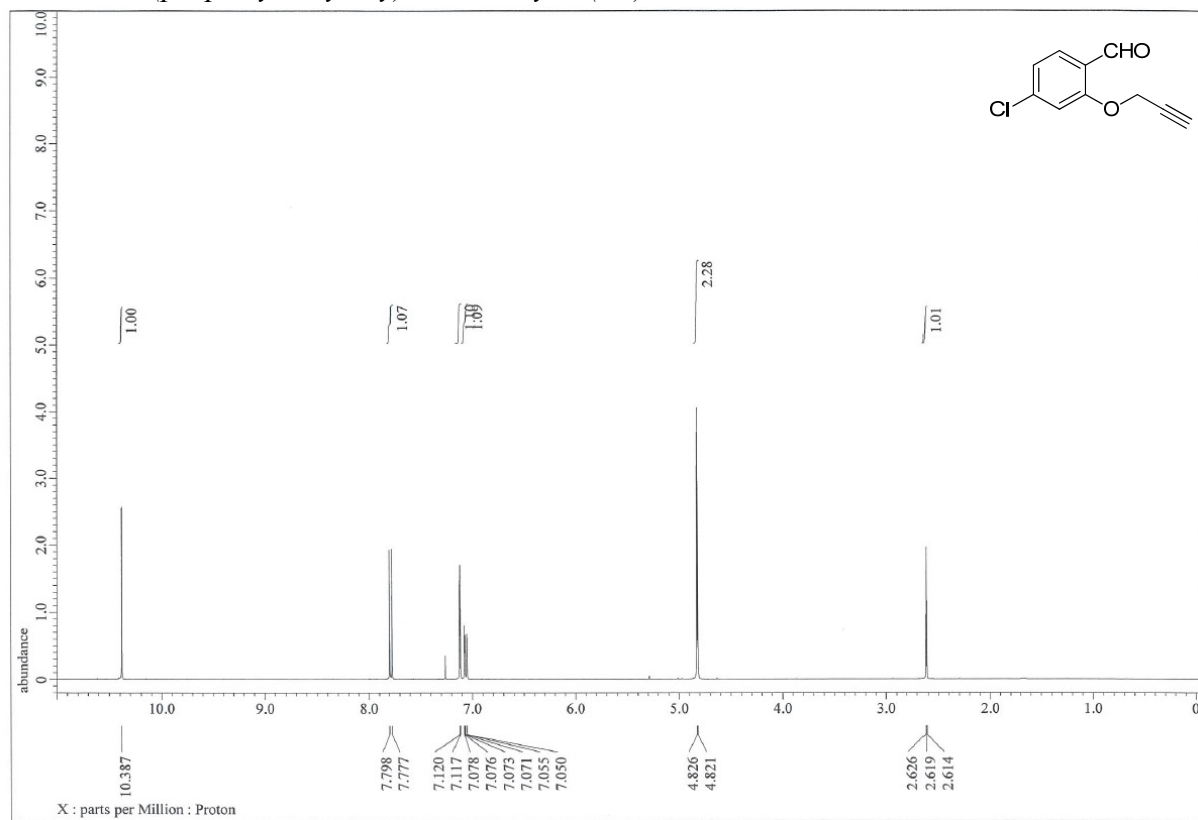
S142

5-Chloro-2-(prop-2-yn-1-yloxy)benzaldehyde (6J)



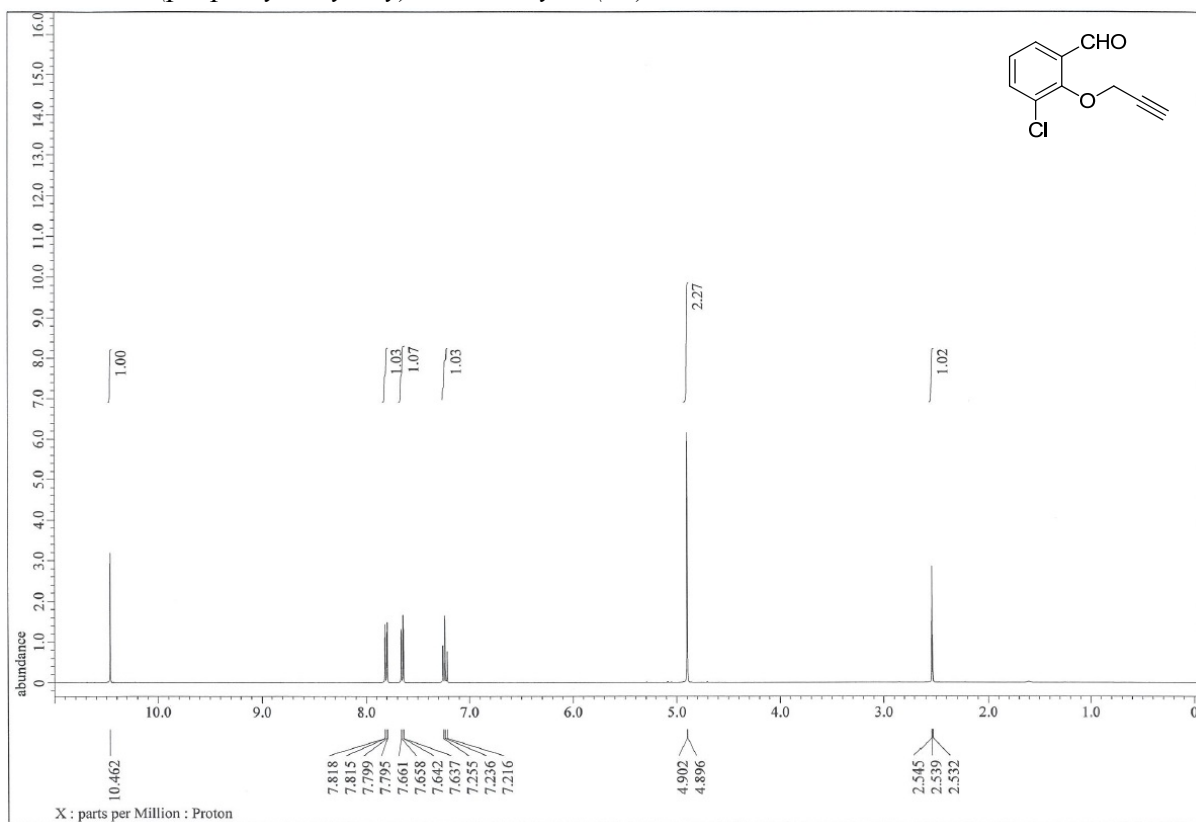
S143

4-Chloro-2-(prop-2-yn-1-yloxy)benzaldehyde (6K)



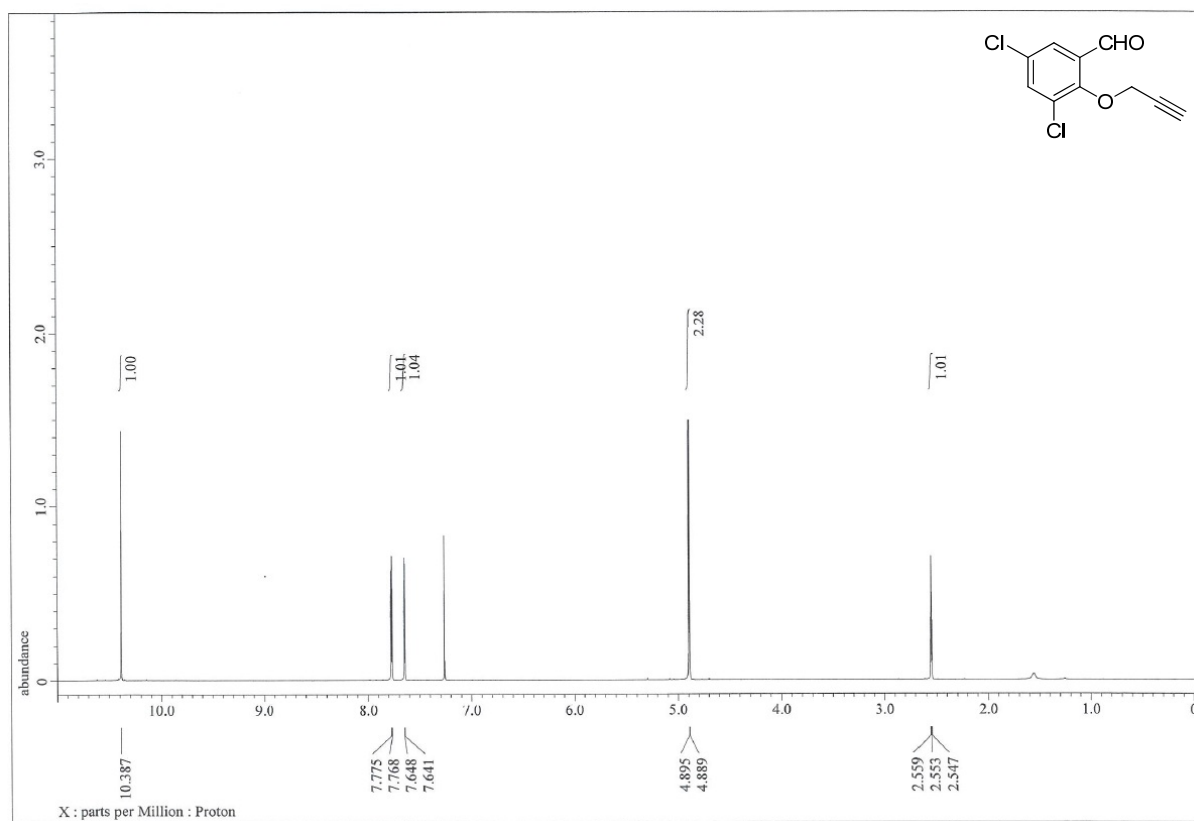
S144

3-Chloro-2-(prop-2-yn-1-yloxy)benzaldehyde (6L)



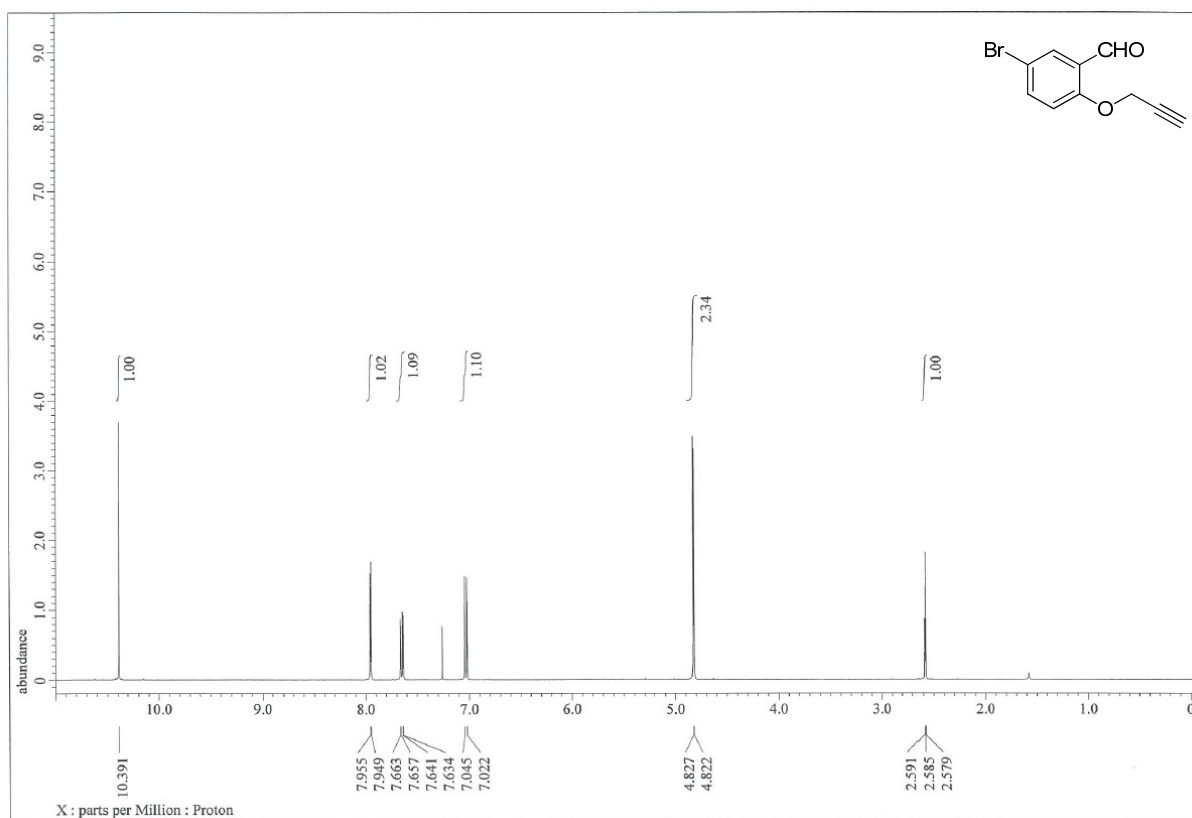
S145

3,5-Dichloro-2-(prop-2-yn-1-yloxy)benzaldehyde (6M)



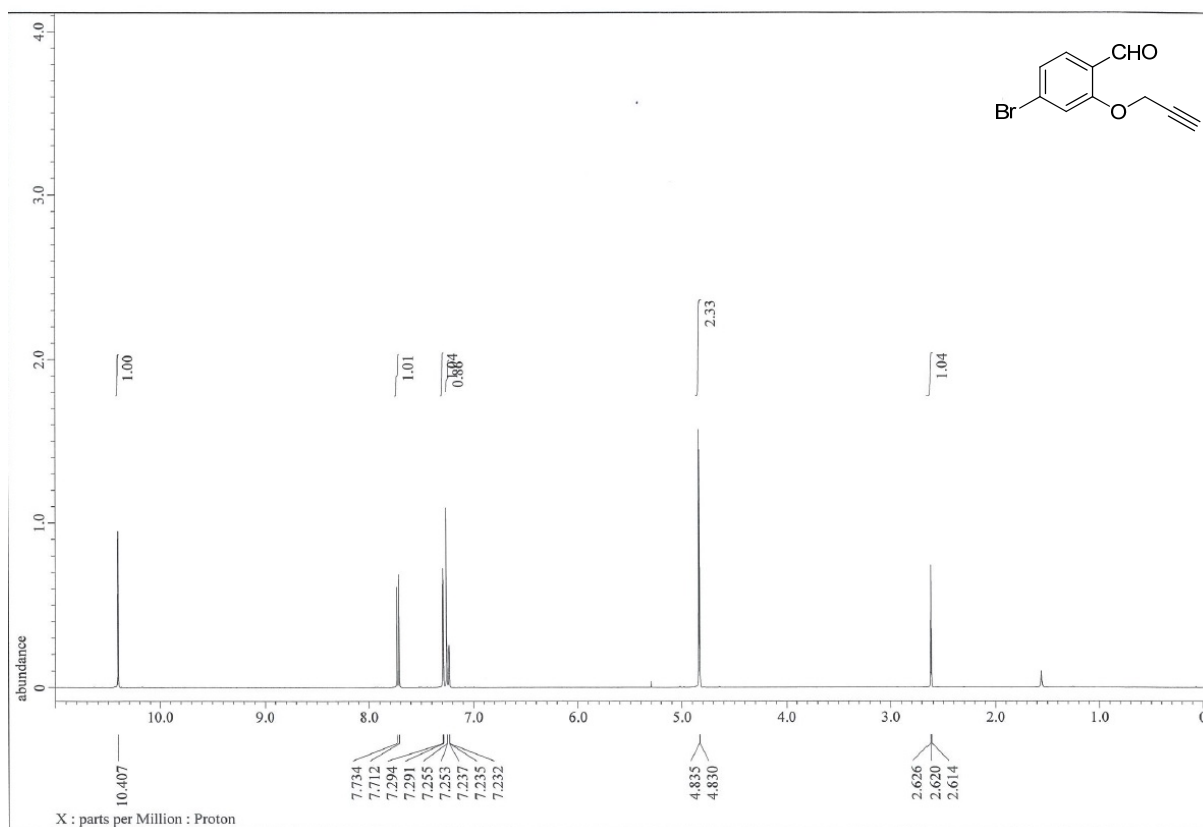
S146

5-Bromo-2-(prop-2-yn-1-yloxy)benzaldehyde (6N)



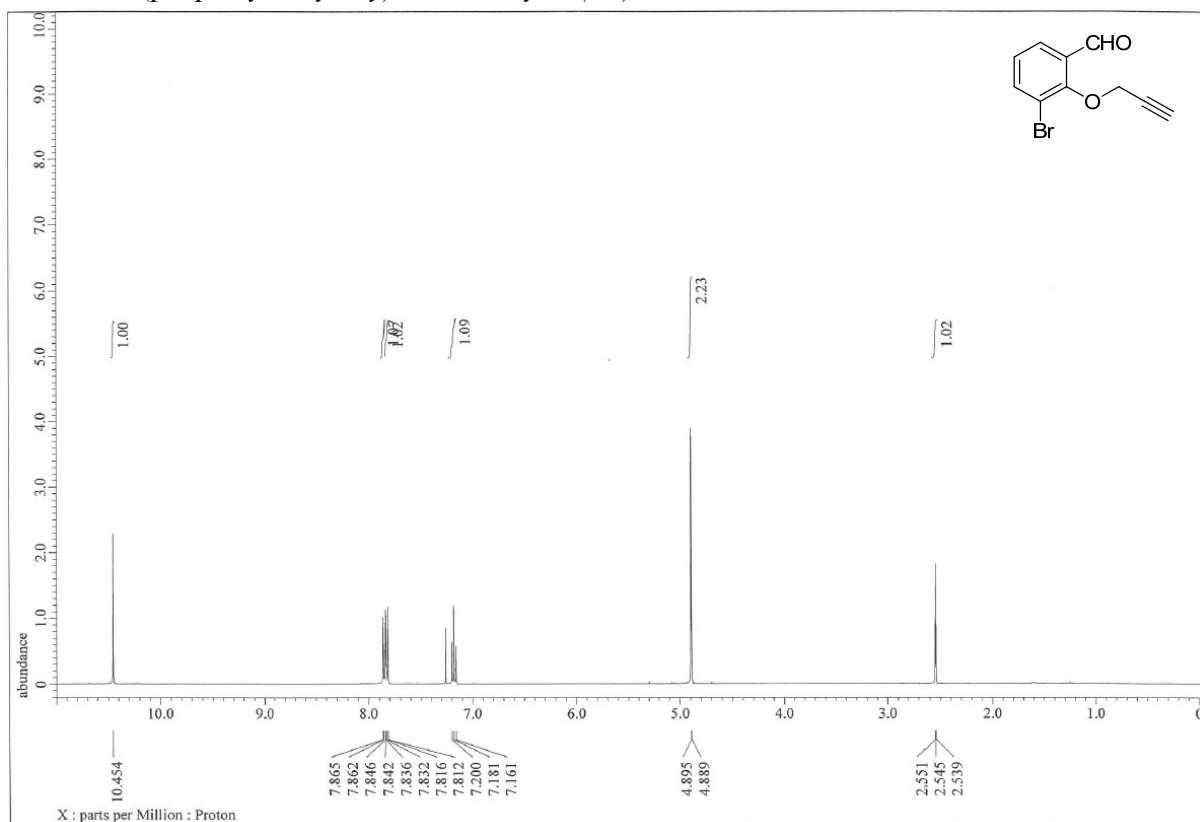
S147

4-Bromo-2-(prop-2-yn-1-yloxy)benzaldehyde (6O)



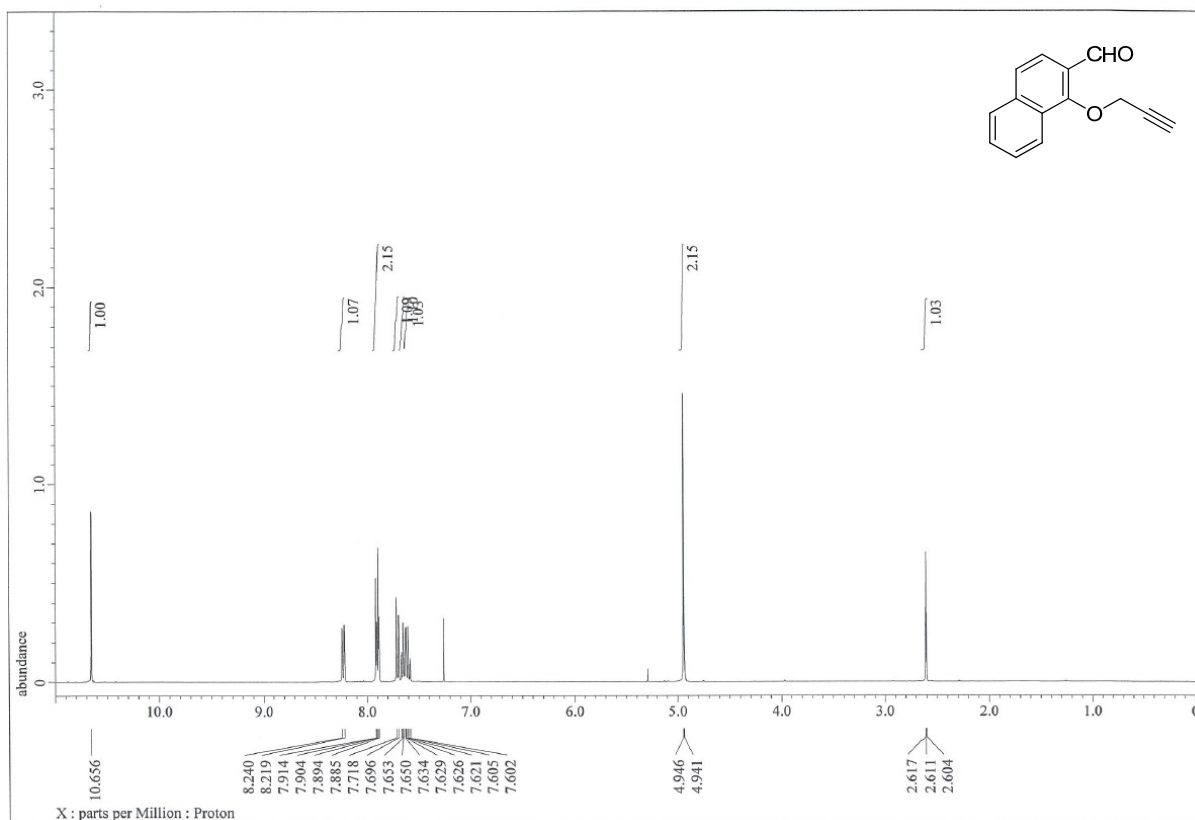
S148

3-Bromo-2-(prop-2-yn-1-yloxy)benzaldehyde (6P)



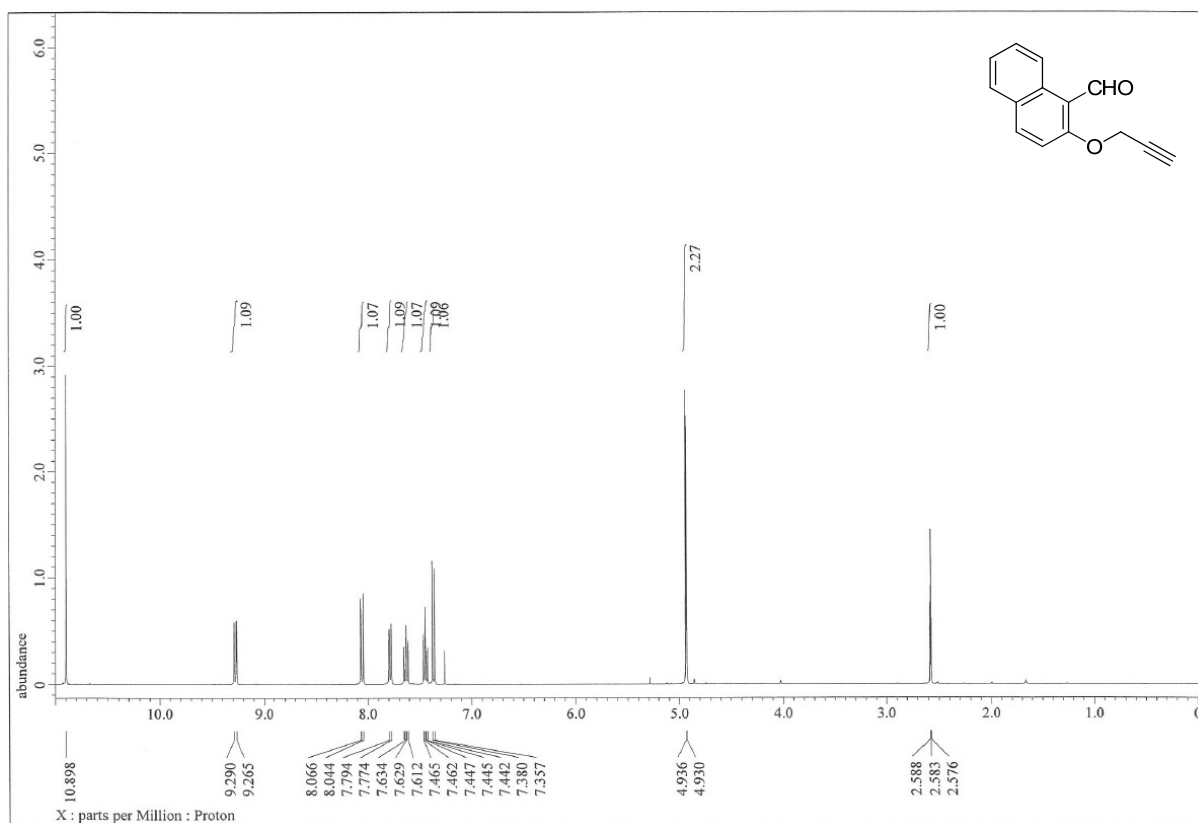
S149

1-(Prop-2-yn-1-yloxy)-2-naphthaldehyde (6Q)



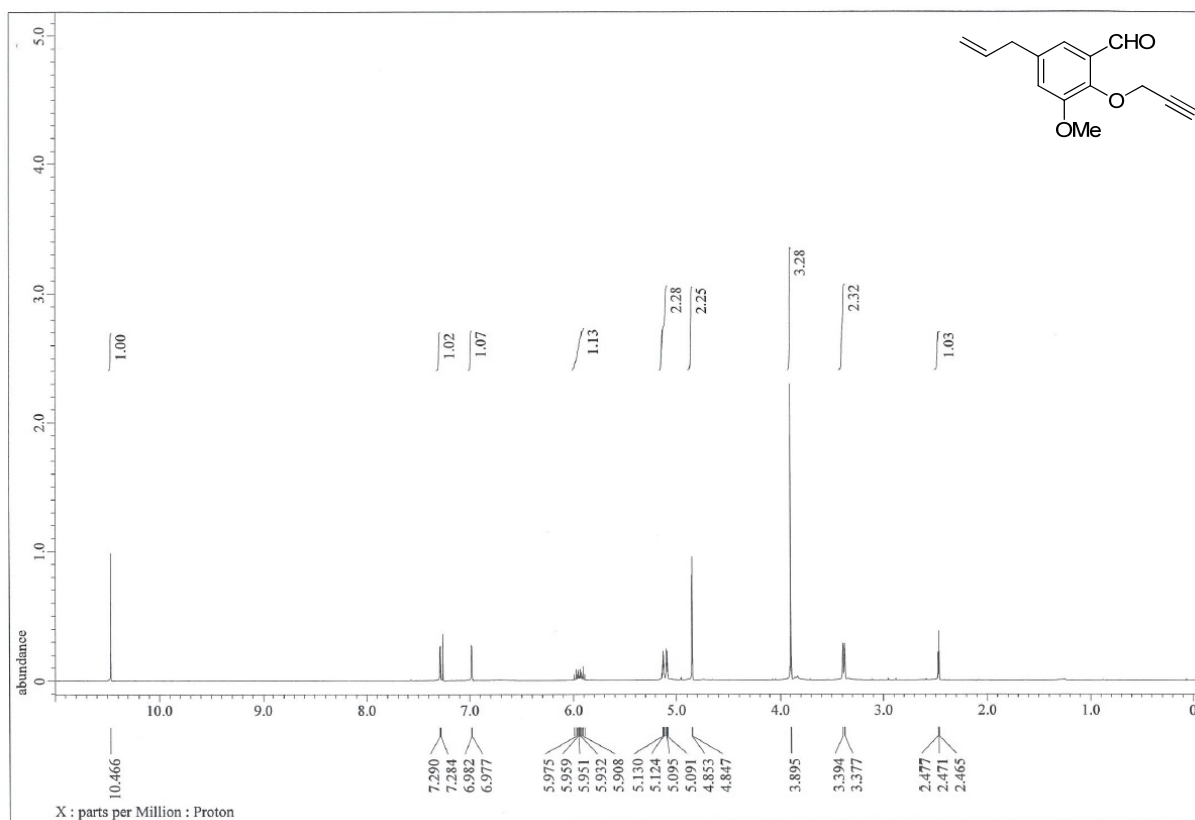
S150

2-(Prop-2-yn-1-yloxy)-1-naphthaldehyde (6R)



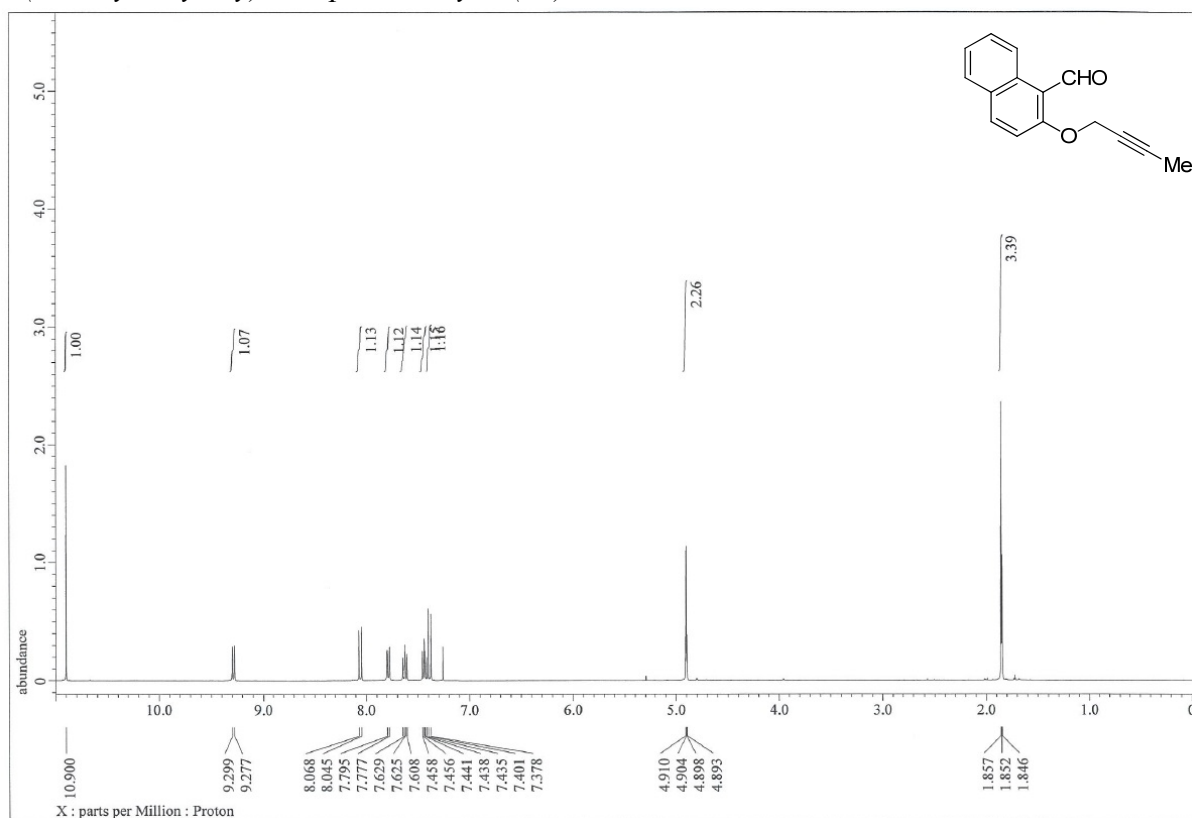
S151

5-Allyl-3-methoxy-2-(prop-2-yn-1-yloxy)benzaldehyde (6S)



S152

2-(But-2-yn-1-yloxy)-1-naphthaldehyde (6T)



THE END