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Synthesis of 1,2,3-triazole derivative at 3rd position of coumarin via copper(I) catalyzed click chemistry using ternary solvent system (DMF + t-BuOH + water)

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ABSTRACT

Coumarin-based triazoles were synthesized from 2-azido-N-phenylacetamide and terminal acetylenic compound by click chemistry. Whereas the $CuSO_4$ used catalyts and sodium ascorbate used as a reducant affords only the favourable 1,4-regioisomer of triazole. Here DMF + t-BuOH + water used as a solvent.

***Keywords*:** Triazole, Coumarin, Click Chemistry, heterocyclic hybrids

1. INTRODUCTION

The discovery of pharmaceutical lead candidate is very complex and challenging process, there is several methodologies involve in drug discovery or lead development but main disadvantage is that it take at least 12 to 15 year, despite the among all approach “hybrid molecules” concept reduce the time domain of lead expansion and increase the success rate of lead discovery, this strategy provide a wide variety of biologically active chemical space and

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diverse compounds library1. In recent day, a combination of different Heterocycles drags our attention due to its structural diversity and easy to synthesize. This strategy leads to the design of novel hybrid building blocks, which possess an individual therapeutics or possibility of new biologically activity. Various linkers like ester, amide, carbamate, sulfonamide etc. generally used for a combination of Heterocycles. Figure 1 example of drugs contains a heterocyclic hybrid core.

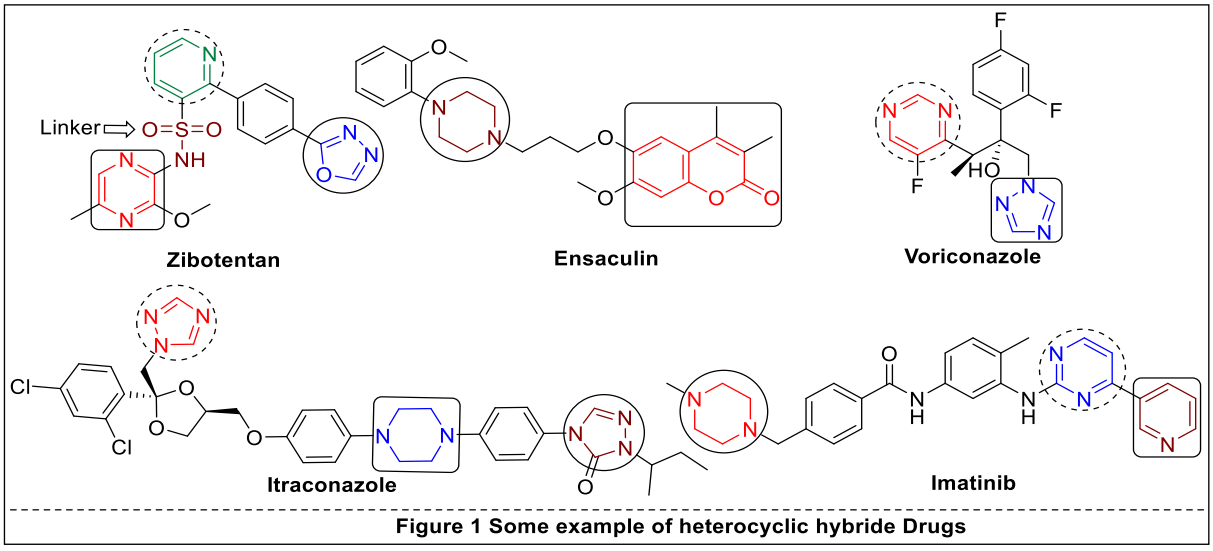
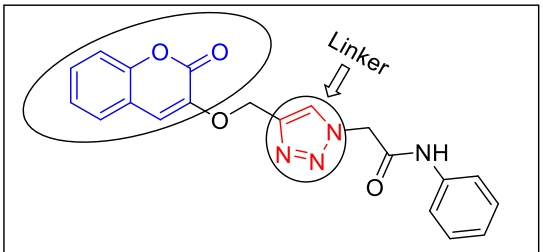


Figure 1 Some example of heterocyclic hybride Drugs

After the discovery of click chemistry, it become an efficient and rapid tool for regioselective synthesis of 1,2,3-triazole. Copper catalyzed click chemistry provided a high yield product within short duration[2,3]. Click chemistry is continuing growing. This methodology has shown by various applications in scientific area like synthesis of poly substituted1,2,3-trizole based bioconjugate[4], peptide, macromolecules like polymer and dendrimer[5,6], self-assembly, fluorescence probe[7], radio-chemistry[8] etc.

Click chemistry is powerful template for synthesis of biologically active small triazole-heterocyclic hybrids. Among the all Heterocycles 1,2,3-triazole-coumarin adduct generate a great interest because 1,2,3-triazole-coumarin hybrid endowed with various pharmacological assets like antitumor, pancreatic lipase[9], antitubercular, antioxidant[10], antimicrobial, antibacterial, antifungal, anti-inflammatory[11] etc. various triazole-coumarin hybrids also used as flurophore[12]. Various click chemistry based methodology of 1,2,3-triazole-coumarin analogous reported. Here triazole plays a dual roll like linker[13] and heterocycles itself.



Triazole play dual roll itself heterocycle and linker

Figure 2

Optical activity of Coumarin-triazole hybrids

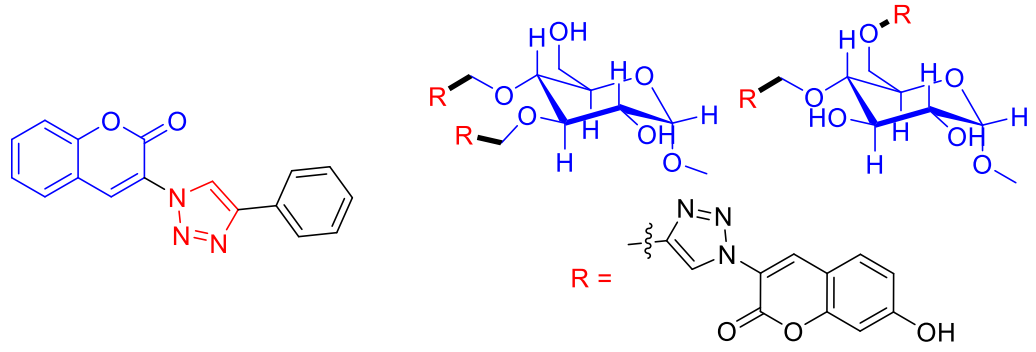


Figure 3 Some selected flurophore coumarin-triazole hybrids

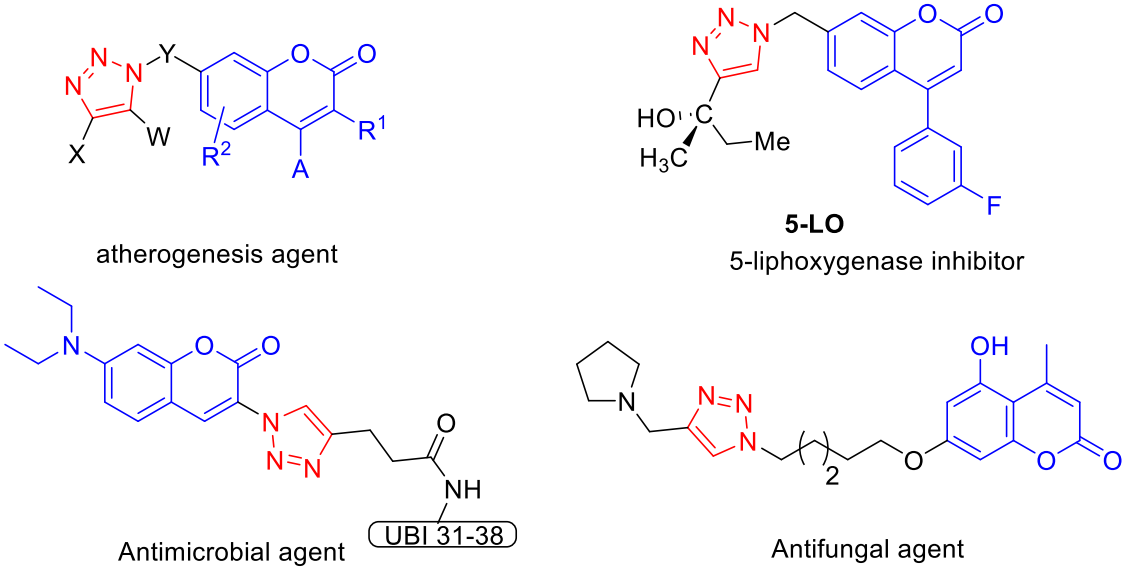


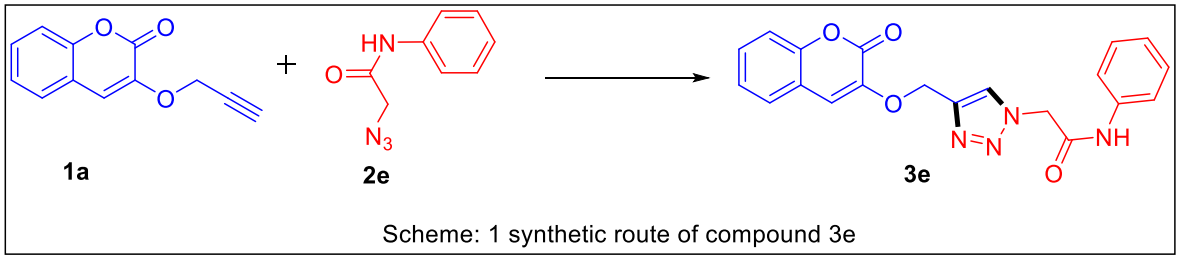
Figure 4 Some selected biologically active coumarin-triazole hybrids

3-substituted coumarin derivative less explored. So our ongoing interest to construct a 1,2,3-triazole at 3rd position at coumarin by click transformation. We successfully synthesize a 1,2,3-triazole derivatives by using a copper sulphate as a catalyst and sodium ascorbate as a reductant in ternary solvent system (DMF + t-BuOH + water).

2. RESULT AND DISCUSSION

The synthesis of 2-(4-(((2-oxo-2*H*-chromen-3-yl)oxy)methyl)-1*H*-1,2,3-triazol-1-yl)-N-phenylacetamide by reaction between 2-azido-N-phenylacetamide and 3-(prop-2-yn-1-yloxy)-2*H*-chromen-2-one. We optimized this reaction (Scheme 1), in this report $CuSO_4$ is best catalyst along with sodium ascorbate. Sodium ascorbate play a dual role, it act as a ligand and reducing agent. We observed that without the use of reducing agent reaction is not progressed. (Table 1,

entry 1). We also optimization solvent selection, DMF + t-BuOH + water with (2:1:2) ratio gets a highest yield (Table 1, entry 2). Firstly we synthesize 3-hydroxy coumarin according to related literature[14,15]. 2-azido-N-substituted phenylacetamide synthesis by reaction between 2-chloro-N-substituted phenylacetamide and sodium azide in DMF.



Scheme: 1 synthetic route of compound 3e

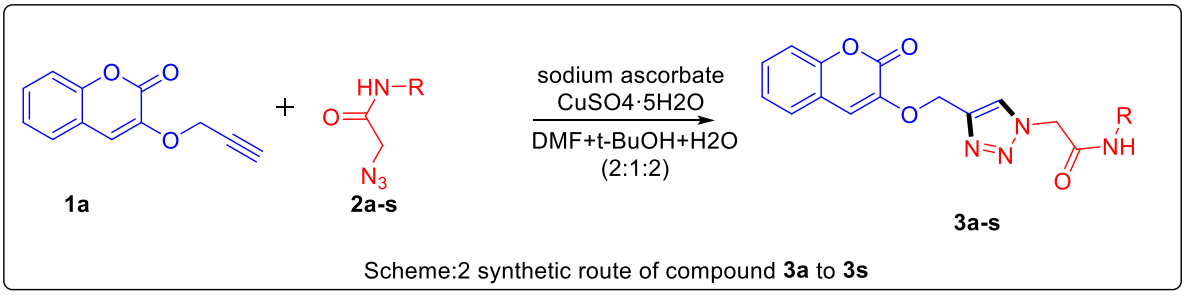
Table 1. Optimization of Cu catalyzed click chemistry.

Entry	Solvent	Catalyst	Reducing agent	Yield
1.	DMF + t-BuOH + water (2:1:2)	$CuSO_4 \cdot 5H_2O$	-	Traces
2.	DMF + t-BuOH + water (2:1:2)	$CuSO_4 \cdot 5H_2O$	Sodium Ascorbate	93%
3.	DMF + t-BuOH + water (2:1:2)	CuI-DIPEA	-	87%
4.	DMF + t-BuOH + water (2:1:2)	CuBr-DIPEA	-	85%
5.	DMF + t-BuOH + water (2:1:2)	$Cu(OAc)_2$	Sodium Ascorbate	86%
6.	DMF + t-BuOH + water (2:1:2)	$Cu(OAc)_2$	-	Traces
7.	DMF + t-BuOH + water (1:1:1)	$CuSO_4 \cdot 5H_2O$	Sodium Ascorbate	82%
8.	t-BuOH	$CuSO_4 \cdot 5H_2O$	Sodium Ascorbate	42%
9.	DMF	$CuSO_4 \cdot 5H_2O$	Sodium Ascorbate	86%
10.	THF	$CuSO_4 \cdot 5H_2O$	Sodium Ascorbate	52%

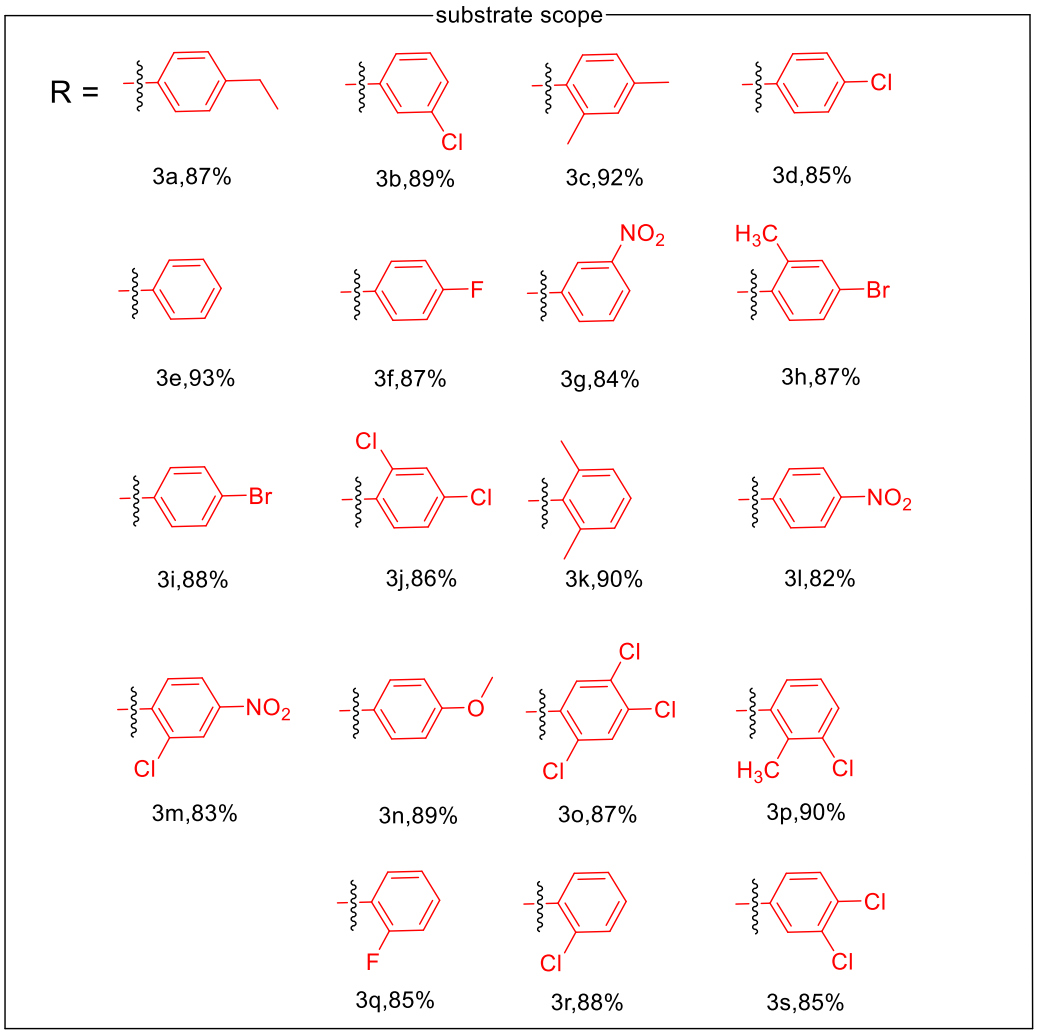
2. 1. Reaction condition

Starting materials 3-(prop-2-yn-1-yloxy)-2*H*-chromen-2-one (1 mmol), **2e** (1 mmol), 0.2 equiv. of appropriate Cu-Sources, reducing agent and solvent.

For further investigation, we checked followed reaction methodology against various amine substrate scopes; reaction is successfully carried out without the any problem. All subtracts are sufficient pure and having a moderate yield (Scheme 2).



Scheme:2 synthetic route of compound **3a** to **3s**



All 1,2,3-triazol-coumarin hybrids (**3a-3s**) is well characterize by ^{1}H and ^{13}C NMR spectra, in compound (**3e**) ^{1}H spectra, one NH signal was observed at 10-11 δ ppm, in ^{13}C NMR amide and cyclic ester observed at 164.66 and 156.50 δ ppm respectively. With more analytical analysis, all compounds showed a proposed mass in their Mass-ESI data. IR-spectroscopy shows broad band NH stretching at 3200-3300 cm^{-1}, and C=O stretching at 1710-1650 range. All compounds are sufficient pure and confirmed by thin layer chromatography.

2. 2. Proposed reaction mechanism for formation of triazole

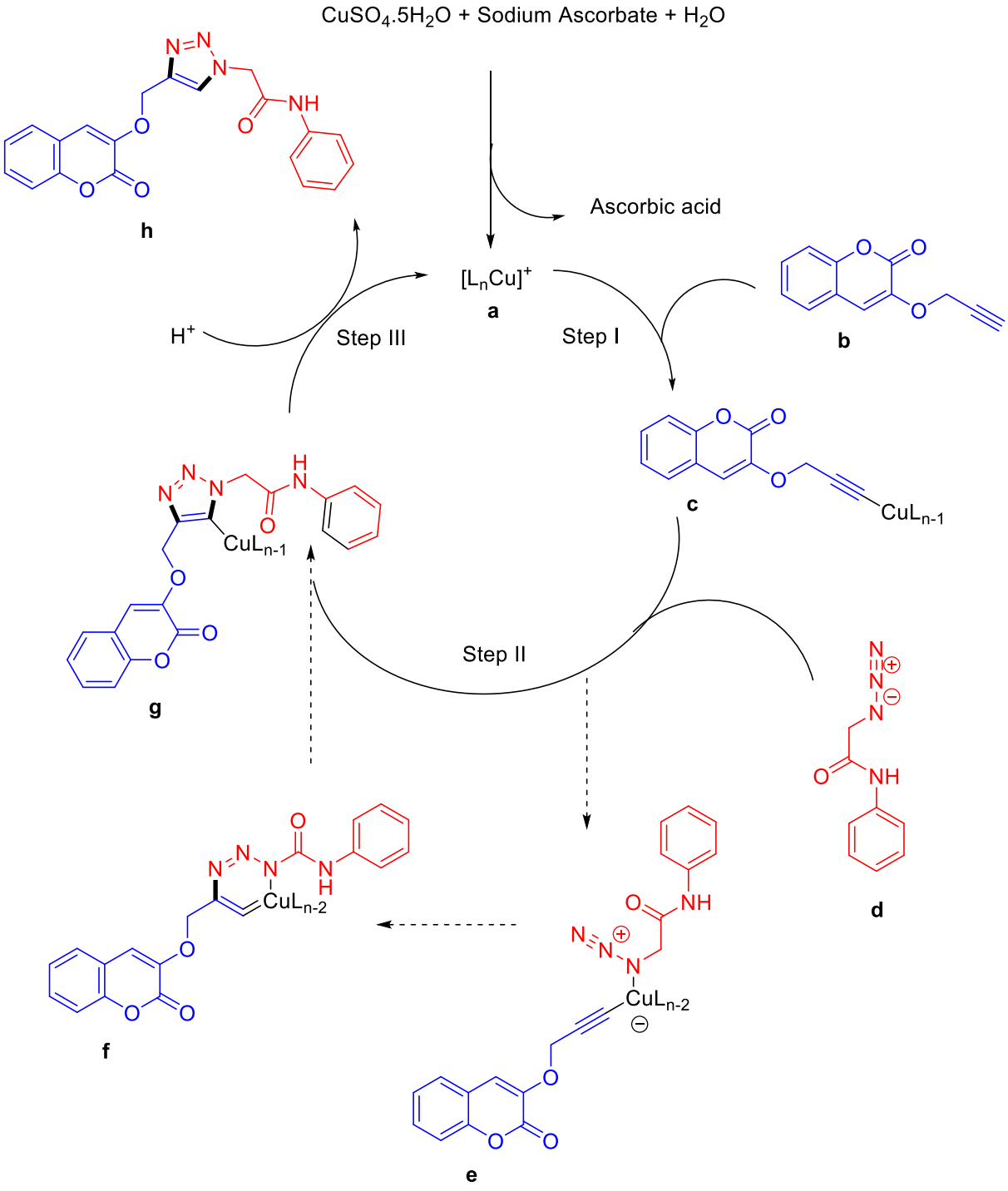


Figure 5

Based upon literature analysis and DFT calculation[16] proposed reaction mechanism shown **Figure 5**, **a** mentioned that copper (II) convert into copper (I) reduction by sodium

ascorbate, it also work as a ligand and made adduct with **b** convert into **c**, intermediate **c** spontaneous react with **d** to form intermediate **e,** intermolecular [3+2] cycloaddition take place convert into **h** via g and f, finally ligand and Cu (I) eliminated and goes to next cycles.

3. EXPERIMENTAL

3. 1. General Information

Solvent and reagents were obtained from spectrochem and most of used without further purification; aliphatic amine used after simple distillation due to colour impurities. TLC for reaction monitoring using silica gel GF254 (Merck) plates. Melting points measure by open glass capillary method. IR spectra recorded on a bruker IR spectrophotometer via KBr pallet method, proton, carbon spectrum were recorded on a Bruker AVANCE-III 400 MHz spectrometer with 5 mm BBO probe head, TMS as internal reference. Mass (EI) spectra were recorded on a SHIMADZU QP-2010 mass spectrometer.

3. 2. Synthesis of 3-(prop-2-yn-1-yloxy)-2H-chromen-2-one (1a)

In single-necked flat-bottomed flask was equipped with a Teflon-coated magnetic stir bar, 3-(prop-2-yn-1-yloxy)-2*H*-chromen-2-one (1.2 mmol) in DMF, add $CsCO_3$ (1.2 mmol) and 80% propargyl bromide in toluene (1.2 mmol) drop wise and stir the resulting mixture for 2 h at room temperature. Progress of the reaction was monitored by TLC. After completions of reaction into crushed ice, desired solid product precipitated out. Filter it, pale yellow solid, 85% yield.

3. 3. General procedure for the synthesis

In 50 ml single-necked flat-bottomed flask was equipped with a Teflon-coated magnetic stir bar, added substituted azide (1 mmol) (**2a** to **2s**) and 3-(prop-2-yn-1-yloxy)-2*H*-chromen-2-one (1 mmol) were charged in DMF + t-BuOH + H_2O (2:1:2, v/v, 5 mL) and stirred. After 5minute stirring sequential addition of sodium ascorbate (1 mmol) and $CuSO_4 \cdot 5H_2O$ (0.2 equiv.) in resulting mixture was stirred for 10-12 h at room temperature. Progress of the reaction was monitored by TLC. After completion of reaction pour the reaction into crushed ice, off white coloured desired solid product precipitated out. Filter the product by vacuum filtration and washed well with saturated NH_4Cl solution.

N-(4-ethylphenyl)-2-(4-(((2-oxo-2*H*-chromen-3-yl)oxy)methyl)-1*H*-1,2,3-triazol-1-yl)acetamide (3a): Off White solid, Yield (351 mg, 87%) M.P. = 200 °C, $\mathbf{R_f}$ = 0.60, (10:90; MeOH:$CHCl_3$), **^{1}H NMR** (400 MHz, DMSO-d_6) δ 10.42 (s, 1H), 8.35 (s, 1H), 7.80-7.25(m,7H), 7.23-7.02 (m, 2H), 5.36 (s, 2H), 5.26 (s, 2H), 2.63 – 2.52 (m, 2H), 1.15 (t, *J* = 7.9 Hz, 3H). **^{13}C NMR** (100 MHz, DMSO) δ 163.88, 156.49, 149.18, 142.55, 141.22, 139.20, 136.09, 128.59, 128.11, 127.02, 126.95, 124.78, 119.68, 119.30, 115.74, 114.93, 62.02, 52.24, 27.60, 15.65. **Mass (EI)** calcd for $C_{22}H_{20}N_4O_4$ $[M+H]^+$ 404 found 404. **(IR cm^{-1}):** 3252, 1728, 1718, 1678, 1626, 1552, 1456, 1411, 1367, 1298, 1261, 1230, 1160, 1111, 1053, 976, 883, 750, 667.

N-(3-chlorophenyl)-2-(4-(((2-oxo-2*H*-chromen-3-yl)oxy)methyl)-1*H*-1,2,3-triazol-1-yl) acetamide (3b): Off White solid, Yield (364 mg, 89%) Off White solid, M.P = 208 °C, $\mathbf{R_f}$ = 0.57, (10:90; MeOH:$CHCl_3$), ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.68 (s, 1H), 8.35 (s, 1H),

7.77 (s, 1H), 7.66 – 7.56 (m, 2H), 7.52-7.40 (m, 2H), 7.40 – 7.29 (m, 3H), 7.15 (d, *J* = 7.9 Hz, 1H), 5.40 (s, 2H), 5.27 (s, 2H). **^{13}C NMR** (100 MHz, DMSO) δ 164.66, 156.50, 149.20, 142.55, 141.28, 139.83, 133.22, 130.69, 128.61, 127.03, 126.98, 124.80, 123.55, 119.69, 118.74, 117.65, 115.76, 114.96, 62.02, 52.26. **Mass (EI)** calcd for $C_{20}H_{15}ClN_4O_4$ $[M+2]^+$ 412 found 412. **(IR cm^{-1}):**3230, 1853, 1708, 1678, 1602, 1548, 1489, 1404, 1294, 1224, 1195, 1149, 1112, 1091, 1055, 985, 887, 827, 752, 682.

N-(2,4-dimethylphenyl)-2-(4-(((2-oxo-2*H*-chromen-3-yl)oxy)methyl)-1*H*-1,2,3-triazol-1-yl)acetamide (3c): Off White solid, Yield (371 mg, 92%), M.P = 224 °C, **R_f =** 0.71, (10:90; MeOH:$CHCl_3$), **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.76 (s, 1H), 8.35 (s, 1H), 7.68 – 7.55 (m, 2H), 7.49-7.41 (m, 1H), 7.41-7.31 (m, 2H), 7.28 (d, *J* = 8.1 Hz, 1H), 7.03 (s, 1H), 6.97 (d, *J* = 8.1 Hz, 1H), 5.41 (s, 2H), 5.25 (s, 2H), 2.24 (s, 3H), 2.19 (s, 3H). **^{13}C NMR** (100 MHz, DMSO) δ 164.28, 156.49, 149.19, 142.55, 141.20, 134.70, 132.91, 131.55, 130.96, 128.60, 127.03, 126.93, 126.59, 124.80, 119.70, 115.76, 114.91, 62.02, 51.95, 20.50, 17.76. **Mass (EI)** calcd for $C_{22}H_{20}N_4O_4$ $[M+H]^+$ 405 found 405. **(IR cm^{-1}):** 3242, 3055, 1743, 1660, 1628, 1541, 1452, 1415, 1377, 1302, 1227, 1148, 976, 902, 821, 752.

N-(4-chlorophenyl)-2-(4-(((2-oxo-2*H*-chromen-3-yl)oxy)methyl)-1*H*-1,2,3-triazol-1-yl) acetamide (3d): White solid, Yield (348 mg, 85%), M.P = 242 °C, **R_f =** 0.60, (10:90; MeOH:$CHCl_3$), **^{1}H NMR** (400 MHz, DMSO-d_6) δ 10.63 (s, 1H), 8.36 (s, 1H), 7.71 – 7.52 (m, 4H), 7.50-7.24 (m, 5H), 5.40 (s, 2H), 5.26 (s, 2H). **^{13}C NMR** (100 MHz, DMSO) δ 164.39, 156.51, 149.18, 142.55, 141.28, 137.38, 128.87, 128.59, 127.40, 127.02, 126.98, 124.78, 120.79, 119.69, 115.75, 114.91, 62.03, 52.27. **Mass (EI)** calcd for $C_{20}H_{15}ClN_4O_4$ $[M+2]^+$ 412 found 412. **(IR cm^{-1}):** 3330, 3136, 3082, 1715, 1686, 1607, 1547, 1493, 1402, 1298, 1253, 1160, 1055, 986, 891, 829, 754.

2-(4-(((2-oxo-2*H*-chromen-3-yl)oxy)methyl)-1*H*-1,2,3-triazol-1-yl)-N-phenylacetamide (3e): Off White solid, Yield (349 mg, 93%), M.P = 184 °C, **R_f =** 0.61, (10:90; MeOH:$CHCl_3$), **^{1}H NMR** (400 MHz, DMSO-d6) δ 10.51 (s, 1H), 8.37 (s, 1H), 7.67-7.52 (m, 4H), 7.50 – 7.39 (m, 1H), 7.40-7.28 (m, 4H), 7.13-7.04 (3, 1H), 5.39 (s, 2H), 5.26 (s, 2H). **^{13}C NMR** (100 MHz, DMSO) δ 164.17, 156.51, 149.19, 142.56, 141.25, 138.43, 128.95, 128.60, 127.03, 126.99, 124.79, 123.80, 119.69, 119.22, 115.75, 114.91, 62.03, 52.28. **Mass (EI)** calcd for $C_{20}H_{16}N_4O_4$ $[M+H]^+$ 377 found 377. **(IR cm^{-1}):** 3306, 3130, 3080, 1703, 1678, 1601, 1550, 1485, 1444, 1396, 1294, 1147, 1114, 1058, 985, 875, 854, 756, 684.

N-(4-fluorophenyl)-2-(4-(((2-oxo-2*H*-chromen-3-yl)oxy)methyl)-1*H*-1,2,3-triazol-1-yl) acetamide (3f): Off White solid, Yield (342 mg, 87%), M.P = 224 °C, **R_f =** 0.57, (10:90; MeOH:$CHCl_3$), **^{1}H NMR** (400 MHz, DMSO-d_6) δ 10.55 (s, 1H), 8.36 (s, 1H), 7.82 – 7.51 (m, 4H), 7.48-7.40 (m, 1H), 7.40 – 7.28 (m, 2H), 7.25-7.11 (m, 2H), 5.38 (s, 2H), 5.26 (s, 2H).**^{13}C NMR** (100 MHz, DMSO) δ 164.14, 156.51, 149.20, 142.56, 134.84, 128.61, 127.04, 126.99, 124.80, 121.08, 121.00, 119.70, 115.76, 115.68, 115.46, 114.91, 62.03, 52.21. **Mass (EI)** calcd for $C_{20}H_{15}FN_4O_4$ $[M+H]^+$ 395 found 395. **(IR cm^{-1}):** 3330, 3140, 3085, 1708, 1678, 1608, 1550, 1510, 1481, 1408, 1296, 1261, 1217, 1149, 1053, 985, 831, 752, 682.

N-(3-nitrophenyl)-2-(4-(((2-oxo-2*H*-chromen-3-yl)oxy)methyl)-1*H*-1,2,3-triazol-1-yl) acetamide (3g): Off White solid, Yield (353 mg, 84%), M.P = 236 °C, **R_f =** 0.50, (10:90;

MeOH:$CHCl_3$), **^{1}H NMR** (400 MHz, DMSO-d_6) δ 11.02 (s, 1H), 8.59 (s, 1H), 8.38 (s, 1H), 7.99 – 7.93 (m, 1H), 7.93-7.7.87 (m, 1H), 7.69 – 7.56 (m, 3H), 7.47 – 7.30 (m, 3H), 5.46 (s, 2H), 5.27 (s, 2H). **^{13}C NMR** (100 MHz, DMSO) δ 165.10, 156.50, 149.20, 148.00, 142.55, 141.34, 139.50, 130.48, 128.61, 127.03, 125.23, 124.80, 119.69, 118.37, 115.80, 115.76, 114.97, 113.39, 62.03, 52.29. **Mass (EI)** calcd for $C_{20}H_{15}N_5O_6$ $[M+H]^+$ 422 found 422. **(IR cm^{-1}):** 3315, 3112, 3095, 1703, 1624, 1554, 1529, 1458, 1352, 1265, 1159, 1051, 977, 889, 842, 804.

N-(4-bromo-2-methylphenyl)-2-(4-(((2-oxo-2*H*-chromen-3-yl)oxy)methyl)-1*H*-1,2,3-triazol-1-yl)acetamide (3h) Off White solid, Yield (407 mg, 87%), M.P = 226 °C, **R_f =** 0.65, (10:90; MeOH:$CHCl_3$), **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.88 (s, 1H), 8.36 (s, 1H), 7.68 – 7.55 (m, 2H), 7.44 (d, *J* = 11.0 Hz, 3H), 7.40-7.29(m,3H), 5.45 (s, 2H), 5.25 (s, 2H), 2.24 (s, 3H). **^{13}C NMR** (100 MHz, DMSO) δ 164.57, 156.51, 149.19, 142.56, 141.27, 135.02, 134.17, 132.89, 128.61, 127.03, 126.99, 126.41, 124.81, 119.70, 117.60, 115.81, 115.76, 115.70, 114.89, 62.02, 52.01. **Mass (EI)** calcd for $C_{21}H_{17}BrN_4O_4$ $[M+2]^+$ 470 found 470. **(IR cm^{-1}):** 3330, 3130, 3080, 1710, 1676, 1600, 1533, 1481, 1390, 1296, 1224, 1197, 1147, 1111, 1053, 981, 885, 817, 852, 678.

N-(4-bromophenyl)-2-(4-(((2-oxo-2*H*-chromen-3-yl)oxy)methyl)-1*H*-1,2,3-triazol-1-yl) acetamide (3i): Off White solid, Yield (399 mg, 88%), M.P = 244 °C, **R_f =** 0.59, (10:90; MeOH:$CHCl_3$), **^{1}H NMR** (400 MHz, DMSO-d_6) δ 10.66 (s, 1H), 8.38 (s, 1H), 7.77-7.49 (m, 6H), 7.49-7.41 (m, 1H), 7.42 – 7.31 (m, 2H), 5.41 (s, 2H), 5.28 (s, 2H). **^{13}C NMR** (100 MHz, DMSO) δ 164.41, 156.50, 149.18, 142.54, 141.28, 137.79, 131.77, 128.58, 127.02, 126.98, 124.78, 121.15, 119.68, 115.74, 115.44, 114.90, 62.02, 52.29. **Mass (EI)** calcd for $C_{20}H_{15}BrN_4O_4$ $[M+2]^+$ 456 found 456. **(IR cm^{-1}):** 3310, 3130, 3022, 1710, 1678, 1546, 1485, 1456, 1394, 1298, 1255, 1232, 1199, 1149, 1114, 1053, 1010, 977, 889, 815, 752, 680.

N-(2,4-dichlorophenyl)-2-(4-(((2-oxo-2*H*-chromen-3-yl)oxy)methyl)-1*H*-1,2,3-triazol-1-yl)acetamide (3j): Off White solid, Yield (381 mg, 86%), M.P = 182 °C, **R_f** = 0.74, (10:90; MeOH:$CHCl_3$), **^{1}H NMR** (400 MHz, DMSO-d_6) δ 10.15 (s, 1H), 8.34 (s, 1H), 7.79 (d, *J* = 8.8 Hz, 1H), 7.72 – 7.58 (m, 3H), 7.43 (dd, *J* = 10.5, 5.3 Hz, 2H), 7.36 (dd, *J* = 14.4, 5.9 Hz, 2H), 5.49 (s, 2H), 5.26 (s, 2H). **^{13}C NMR** (100 MHz, DMSO) δ 165.07, 156.50, 149.19, 142.54, 141.28, 129.80, 129.11, 128.91, 128.62, 127.74, 127.14, 127.03, 126.84, 119.69, 115.76, 115.72, 114.93, 79.63, 62.01, 52.00. **Mass (EI)** calcd for $C_{20}H_{14}Cl_2N_4O_4$ $[M+2]^+$ 446 found 466. **(IR cm^{-1}):** 3329, 3138, 3082, 2129, 1708, 1678, 1600, 1548, 1481, 1444, 1390, 1292, 1224, 1197, 1143, 1112, 1053, 754, 680.

N-(2,6-dimethylphenyl)-2-(4-(((2-oxo-2*H*-chromen-3-yl)oxy)methyl)-1*H*-1,2,3-triazol-1-yl)acetamide (3k): Off White solid, Yield (363 mg, 90%), M.P = 232 °C, **R_f =** 0.70, (10:90; MeOH:$CHCl_3$), **^{1}H NMR** (400 MHz, DMSO-d_6) δ 10.11 (s, 1H), 8.69 (s, 1H), 7.95 (d, *J* = 11.9 Hz, 2H), 7.78 (d, J = 7.9 Hz, 1H), 7.74 – 7.57 (m, 2H), 7.41 (s, 3H), 5.76 (s, 2H), 5.60 (s, 2H), 2.50 (s, 6H). **^{13}C NMR** (100 MHz, DMSO) δ 164.02, 156.50, 149.19, 142.55, 141.22, 135.10, 134.21, 128.60, 127.79, 127.03, 126.90, 126.79, 124.80, 119.70, 115.75, 114.90, 62.02, 51.69, 18.07. **Mass (EI)** calcd for $C_{22}H_{20}N_4O_4$ $[M+H]^+$ 405 found 405. **(IR cm^{-1}):** 3330, 3132, 3080, 1919, 1907, 1870, 1826, 1770, 1716, 1683, 1622, 1510, 1458, 1357, 1300, 1153, 1078, 1055, 877, 750, 670.

N-(4-nitrophenyl)-2-(4-(((2-oxo-2*H*-chromen-3-yl)oxy)methyl)-1*H*-1,2,3-triazol-1-yl) acetamide (3l): Off White solid, Yield (345 mg, 82%), M.P = 230 °C, **R_f =** 0.60, (10:90; MeOH:$CHCl_3$), **^{1}H NMR** (400 MHz, DMSO-d_6) δ 11.11 (s, 1H), 8.37 (s, 1H), 8.24 (d, *J* = 8.8 Hz, 2H), 7.82 (d, *J* = 8.9 Hz, 2H), 7.69 – 7.55 (m, 2H), 7.50 – 7.25 (m, 3H), 5.48 (s, 2H), 5.27 (s, 2H). **^{13}C NMR** (100 MHz, DMSO) δ 165.34, 156.50, 149.18, 144.51, 142.59, 141.34, 128.60, 127.02, 125.14, 124.79, 119.68, 119.04, 115.79, 115.75, 115.71, 114.94, 62.03, 52.40. **Mass (EI)** calcd for $C_{20}H_{15}N_5O_6$ $[M+H]^+$ 422 found 422. **(IR cm^{-1}):** 3310, 3125, 3085, 1700, 1624, 1554, 1532, 1460, 1350, 1260, 1160, 1050, 980, 890, 845, 805.

N-(2-chloro-4-nitrophenyl)-2-(4-(((2-oxo-2*H*-chromen-3-yl)oxy)methyl)-1*H*-1,2,3-triazol-1-yl)acetamide (3m): Off White solid, Yield (377 mg, 83%), M.P = 204°C, **R_f =** 0.53, (10:90; MeOH:$CHCl_3$), **^{1}H NMR** (400 MHz, DMSO-d_6) δ 10.45 (s, 1H), 8.38 (d, *J* = 4.2 Hz, 1H), 8.22 (s, 1H), 7.72 – 7.52 (m, 2H), 7.43 (d, *J* = 10.2 Hz, 2H), 7.40 – 7.24 (m, 3H), 5.61 (s, 2H), 5.27 (s, 2H). **^{13}C NMR** (100 MHz, DMSO) δ 165.82, 156.49, 156.36, 149.29, 149.18, 143.60, 142.54, 128.89, 128.60, 127.12, 125.09, 124.85, 124.80, 123.84, 123.25, 115.80, 115.75, 114.94, 62.02, 52.34. **Mass (EI)** calcd for $C_{20}H_{14}ClN_5O_6$ $[M+2]^+$ 457 found 457. **(IR cm^{-1}):** 3316, 3130, 3096, 1919, 1843, 1793, 1718, 1681, 1620, 1554, 1519, 1456, 1417, 1340, 1301, 1186, 1151, 1055, 894, 752, 670.

N-(4-methoxyphenyl)-2-(4-(((2-oxo-2*H*-chromen-3-yl)oxy)methyl)-1*H*-1,2,3-triazol-1-yl) acetamide (3n): Off White solid, Yield (361 mg, 89%), M.P = 222 °C, **R_f =** 0.60, (10:90; MeOH:$CHCl_3$), **^{1}H NMR** (400 MHz, DMSO-d_6) δ 10.37 (s, 1H), 8.35 (s, 1H), 7.77 – 7.56 (m, 2H), 7.52-7.42 (m,3H),7.40-7.30 (m, 2H),6.90(d, J = 8.7Hz 2H), 5.35 (s, 2H), 5.25 (s, 2H), 3.72 (s, 3H). **^{13}C NMR** (100 MHz, DMSO) δ 163.62, 156.50, 155.54, 149.19, 142.56, 141.21, 131.52, 128.60, 127.03, 126.95, 124.80, 120.77, 119.70, 115.76, 114.92, 114.03, 62.03, 55.17, 52.19. **Mass (EI)** calcd for $C_{21}H_{18}N_4O_5$ $[M+H]^+$ 407 found 407. **(IR cm^{-1}):** 3310, 3125, 3089, 1919, 1716, 1685, 1622, 1554, 1512, 1458, 1415, 1359, 1298, 1147, 1078, 1055, 983, 877, 752, 670.

2-(4-(((2-oxo-2*H*-chromen-3-yl)oxy)methyl)-1*H*-1,2,3-triazol-1-yl)-N-(2,4,5-trichlorophenyl)acetamide (3o): Off White solid, Yield (415 mg, 87%), M.P = 242 °C, **R_f =** 0.65, (10:90; MeOH:$CHCl_3$), **^{1}H NMR** (400 MHz, DMSO-d_6) δ 10.26 (s, 1H), 8.35 (s, 1H), 8.11 (s, 1H), 7.91 (s, 1H), 7.69 – 7.52 (m, 2H), 7.49-7.40 (m, 1H), 7.33 (dd, *J* = 15.3, 7.8 Hz, 2H), 5.52 (s, 2H), 5.27 (s, 2H). ^{13}C NMR (100 MHz, DMSO) δ 165.47, 156.49, 149.19, 142.54, 141.34, 134.39, 130.70, 129.95, 128.60, 127.67, 127.02, 125.84, 125.01, 124.79, 119.68, 115.74, 114.96, 62.01, 52.08. **Mass (EI)** calcd for $C_{20}H_{13}Cl_3N_4O_4$ $[M+2]^+$ 479 found 479. **(IR cm^{-1}):** 3257, 3136, 3093, 1718, 1685, 1640, 1626, 1585, 1525, 1494, 1460, 1365, 1327, 1303, 1155, 976, 754.

N-(3-chloro-2-methylphenyl)-2-(4-(((2-oxo-2*H*-chromen-3-yl)oxy)methyl)-1*H*-1,2,3-triazol-1-yl)acetamide (3p): Off White solid, Yield (381 mg, 90%), M.P = 226 °C, **R_f =** 0.72, (10:90; MeOH:$CHCl_3$), **^{1}H NMR** (400 MHz, DMSO-d_6) δ 10.11 (s, 1H), 8.37 (s, 1H), 7.69 – 7.54 (m, 2H), 7.48-7.41 (m, 1H), 7.40 – 7.25 (m, 4H), 7.25-7.16 (m, 1H), 5.46 (s, 2H), 5.26 (s, 2H), 2.26 (s, 3H). **^{13}C NMR** (100 MHz, DMSO) δ 164.69, 156.50, 149.18, 142.54, 141.27, 137.02, 133.90, 130.40, 128.60, 127.02, 126.99, 126.95, 126.45, 124.79, 124.34, 119.69,

115.75, 114.91, 62.02, 51.93, 15.13. **Mass (EI)** calcd for $C_{21}H_{17}ClN_4O_4$ $[M+2]^+$ 426 found 426. **(IR cm^{-1}):** 3270, 3226, 3080, 2806, 1914, 1867, 1793, 1716, 1680, 1618, 1541, 1508, 1458, 1359, 1301, 1134, 1065, 933, 875, 752, 682.

N-(2-fluorophenyl)-2-(4-(((2-oxo-2*H*-chromen-3-yl)oxy)methyl)-1*H*-1,2,3-triazol-1-yl) acetamide (3q): Off White solid, Yield (334 mg, 85%), M.P = 188 °C, **R_f =** 0.69, (10:90; MeOH:$CHCl_3$), **^{1}H NMR** (400 MHz, DMSO-d_6) δ 10.36 (s, 1H), 8.37 (s, 1H), 7.93 (d, *J* = 9.4 Hz, 1H), 7.71 – 7.53 (m, 2H), 7.49 – 7.26 (m, 4H), 7.23 – 7.09 (m, 2H), 5.49 (s, 2H), 5.26 (s, 2H). **^{13}C NMR** (100 MHz, DMSO) δ 164.81, 156.50, 152.23, 149.19, 142.55, 141.29, 128.60, 125.66, 125.54, 125.43, 124.79, 124.56, 124.52, 123.75, 119.69, 115.75, 115.54, 114.92, 62.02, 52.08. **Mass (EI)** calcd for $C_{20}H_{15}FN_4O_4$ $[M+H]^+$ 395 found 395. **(IR cm^{-1}):** 3250, 3132, 3090, 2814, 1919, 1869, 1793, 1716, 1680, 1620, 1541, 1519, 1458, 1433, 1357, 1300, 1151, 1055, 991, 875, 752, 670.

N-(2-chlorophenyl)-2-(4-(((2-oxo-2*H*-chromen-3-yl)oxy)methyl)-1*H*-1,2,3-triazol-1-yl) acetamide (3r): Off White solid, Yield (360 mg, 88%), M.P = 188 °C, **R_f =** 0.65, (10:90; MeOH:$CHCl_3$), **^{1}H NMR** (400 MHz, DMSO-d_6) δ 10.12 (s, 1H), 8.36 (s, 1H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.66 – 7.58 (m, 2H), 7.53 (d, *J* = 8.0 Hz, 1H), 7.48-7.41 (m, 1H), 7.40 – 7.30 (m, 3H), 7.26-7.17 (m, 1H), 5.50 (s, 2H), 5.26 (s, 2H). **^{13}C NMR** (100 MHz, DMSO) δ 164.88, 156.49, 149.19, 142.55, 141.26, 134.16, 129.66, 128.61, 127.60, 127.03, 126.99, 126.76, 126.28, 125.92, 124.80, 119.69, 115.76, 114.93, 62.01, 51.99. **Mass (EI)** calcd for $C_{20}H_{15}ClN_4O_4$ $[M+2]^+$ 412 found 412. **(IR cm^{-1}):** 3232, 3132, 3040, 2798, 1716, 1683, 1622, 1523, 1473, 1458, 1417, 1359, 1300, 1230, 1201, 1153, 1116, 1078, 1055, 989, 877, 750, 667.

N-(3,4-dichlorophenyl)-2-(4-(((2-oxo-2H-chromen-3-yl)oxy)methyl)-1H-1,2,3-triazol-1-yl)acetamide (3s): Off White solid, Yield (378 mg, 85%), M.P = 188 °C, **R_f =** 0.65, (10:90; MeOH:$CHCl_3$), **^{1}H NMR** (400 MHz, DMSO) δ 9.81 (s, 1H), 7.60 (d, J = 1.5 Hz, 1H), 7.58 – 7.53 (m, 2H), 7.43 – 7.36 (m, 1H), 7.32 (d, J = 7.4 Hz, 1H), 7.23 – 7.14 (m, 3H), 6.81 (s, 1H), 5.20 (s, 2H), 4.79 (s, 1H), 4.75 (s, 1H). **^{13}C NMR** (100 MHz, DMSO) δ 167.06, 156.84, 152.08, 143.47, 138.41, 136.95, 133.00, 131.54, 131.35, 128.40, 127.48, 125.47, 123.08, 121.59, 121.45, 121.35, 120.97, 118.38, 54.81, 49.45. **Mass (EI)** calcd for $C_{20}H_{14}Cl_2N_4O_4$ $[M+2]^+$ 444 found 444.

4. CONCLUSION

3-hydroxy coumarin is less explored over the decade in this summery we synthesized 3-hydroxy coumarin variant and its triazole derivative by click chemistry in this methodology we used ternary solvent system like t-butanol: DMF: water along the side with copper sulphate and sodium ascorbate gave an excellent yield and purity.

Acknowledgment

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References

[1] Meunier B. Hybrid Molecules with a Dual Mode of Action : Dream or Reality ? *Acc Chem Res.* 2008 Jan; 41(1): 69-77

[2] Himo F, Lovell T, Hilgraf R, et al. Copper(I)-catalyzed synthesis of azoles. DFT study predicts unprecedented reactivity and intermediates. *Journal of the American Chemical Society*. 2005; 127(1): 210-216. doi:10.1021/ja0471525

[3] Garner AL. cat-ELCCA: catalyzing drug discovery through click chemistry. *Chemical Communications*. 2018; 54(50): 6531-6539. doi:10.1039/C8CC02332H

[4] Thirumurugan P, Matosiuk D, Jozwiak K. Click chemistry for drug development and diverse chemical-biology applications. *Chemical Reviews*. 2013; 113(7): 4905-4979. doi:10.1021/cr200409f

[5] Huo J, Hu H, Zhang M, et al. A mini review of the synthesis of poly-1,2,3-triazole-based functional materials. *RSC Advances*. 2017; 7(4): 2281-2287. doi:10.1039/c6ra27012c

[6] Pasini D. The click reaction as an efficient tool for the construction of macrocyclic structures. *Molecules*. 2013;18(8):9512-9530. doi:10.3390/molecules18089512.

[7] Hu MH, Chen X, Chen S Bin, et al. A new application of click chemistry in situ: Development of fluorescent probe for specific G-quadruplex topology. *Scientific Reports*. 2015; 5(October): 1-9. doi:10.1038/srep17202

[8] Meyer JP, Adumeau P, Lewis JS, Zeglis BM. Click Chemistry and Radiochemistry: The First 10 Years. *Bioconjugate Chemistry*. 2016; 27(12): 2791-2807. doi:10.1021/acs.bioconjchem.6b00561

[9] Kahveci B, Yılmaz F, Menteşe E, Ülker S. Design, Synthesis, and Biological Evaluation of Coumarin–Triazole Hybrid Molecules as Potential Antitumor and Pancreatic Lipase Agents. *Archiv der Pharmazie*. 2017; 350(8): 1-9. doi:10.1002/ardp.201600369

[10] Shaikh MH, Subhedar DD, Khan FAK, Sangshetti JN, Shingate BB. 1,2,3-Triazole incorporated coumarin derivatives as potential antifungal and antioxidant agents. *Chinese Chemical Letters*. 2016; 27(2): 295-301. doi:10.1016/j.cclet.2015.11.003

[11] Shaabani S, Shaabani A, Ng SW. One-pot synthesis of coumarin-3-carboxamides containing a triazole ring via an isocyanide-based six-component reaction. *ACS Combinatorial Science*. 2014; 16(4): 176-183. doi:10.1021/co4001259

[12] Key JA, Koh S, Timerghazin QK, Brown A, Cairo CW. Photophysical characterization of triazole-substituted coumarin fluorophores. *Dyes and Pigments*. 2009; 82(2): 196-203. doi:10.1016/j.dyepig.2009.01.001

[13] De Miguel G, Wielopolski M, Schuster DI, et al. Triazole bridges as versatile linkers in electron donor-acceptor conjugates. *Journal of the American Chemical Society*. 2011; 133(33): 13036-13054. doi:10.1021/ja202485s

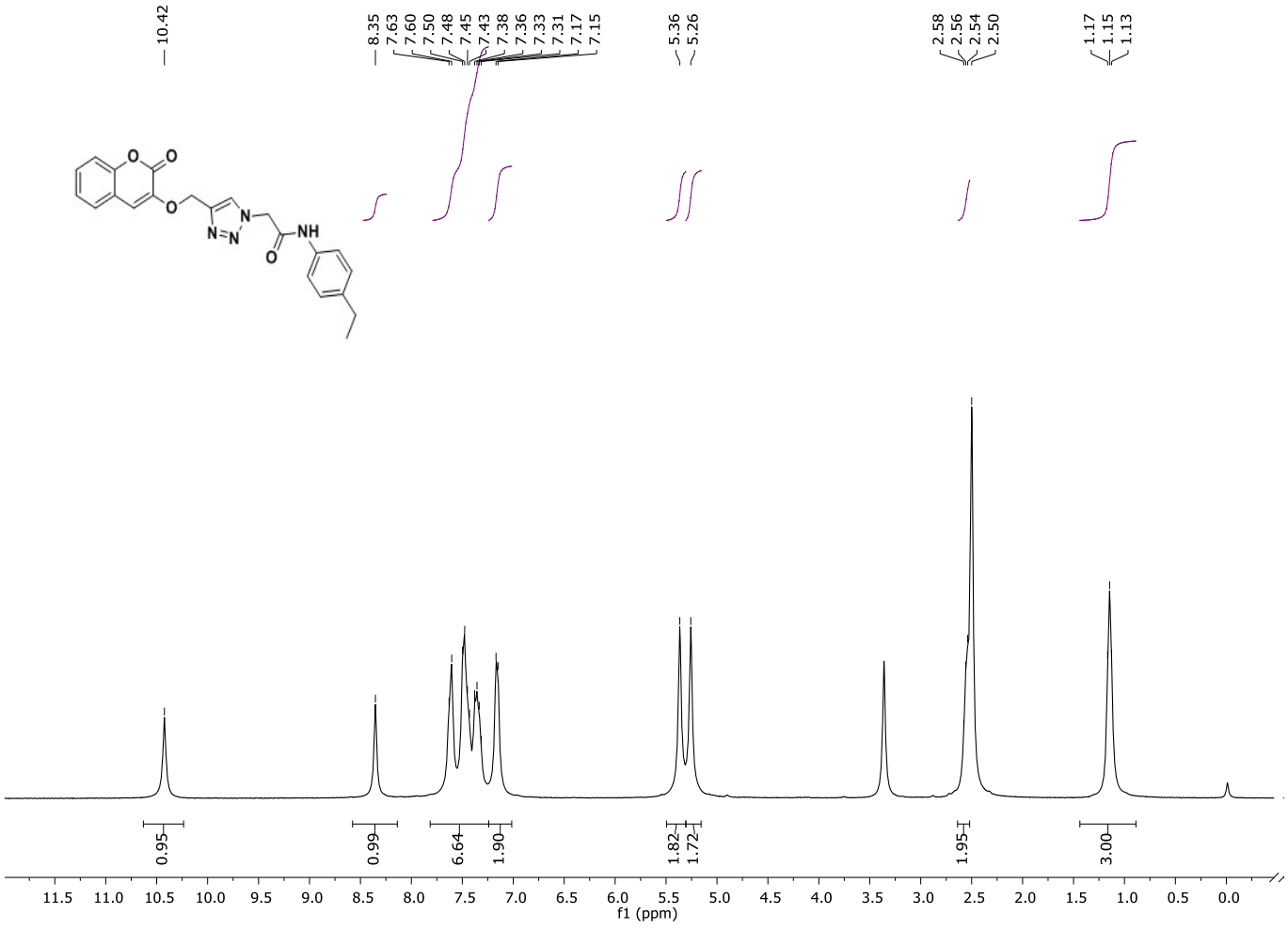
[14] Das DK, Sarkar S, Khan M, Belal M, Khan AT. A mild and efficient method for large scale synthesis of 3-aminocoumarins and its further application for the preparation of 4-

bromo-3-aminocoumarins. *Tetrahedron Letters*. 2014; 55(35): 4869-4874. doi:10.1016/j.tetlet.2014.07.035

[15] Kokotos G, Tzougraki C. Synthesis and study of substituted coumarins. A facile preparation of D,L-o-tyrosine. *Journal of Heterocyclic Chemistry*. 1986; 23(1): 87-92. doi:10.1002/jhet.5570230118

[16] Özkllç Y, Tüzün NS. A DFT Study on the Binuclear CuAAC Reaction: Mechanism in Light of New Experiments. *Organometallics*. 2016; 35(16): 2589-2599. doi:10.1021/acs.organomet.6b00279

Supplementary data



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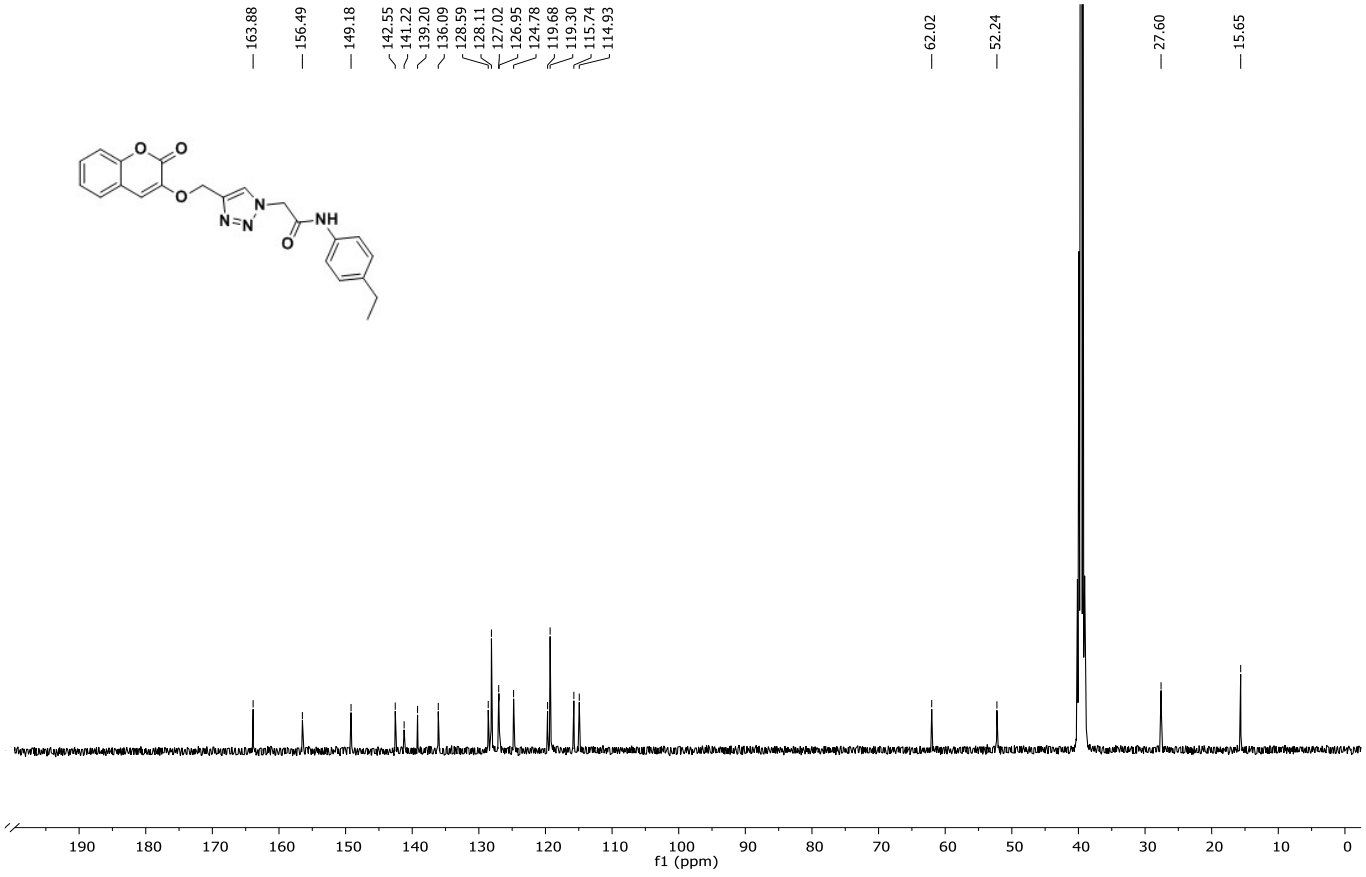
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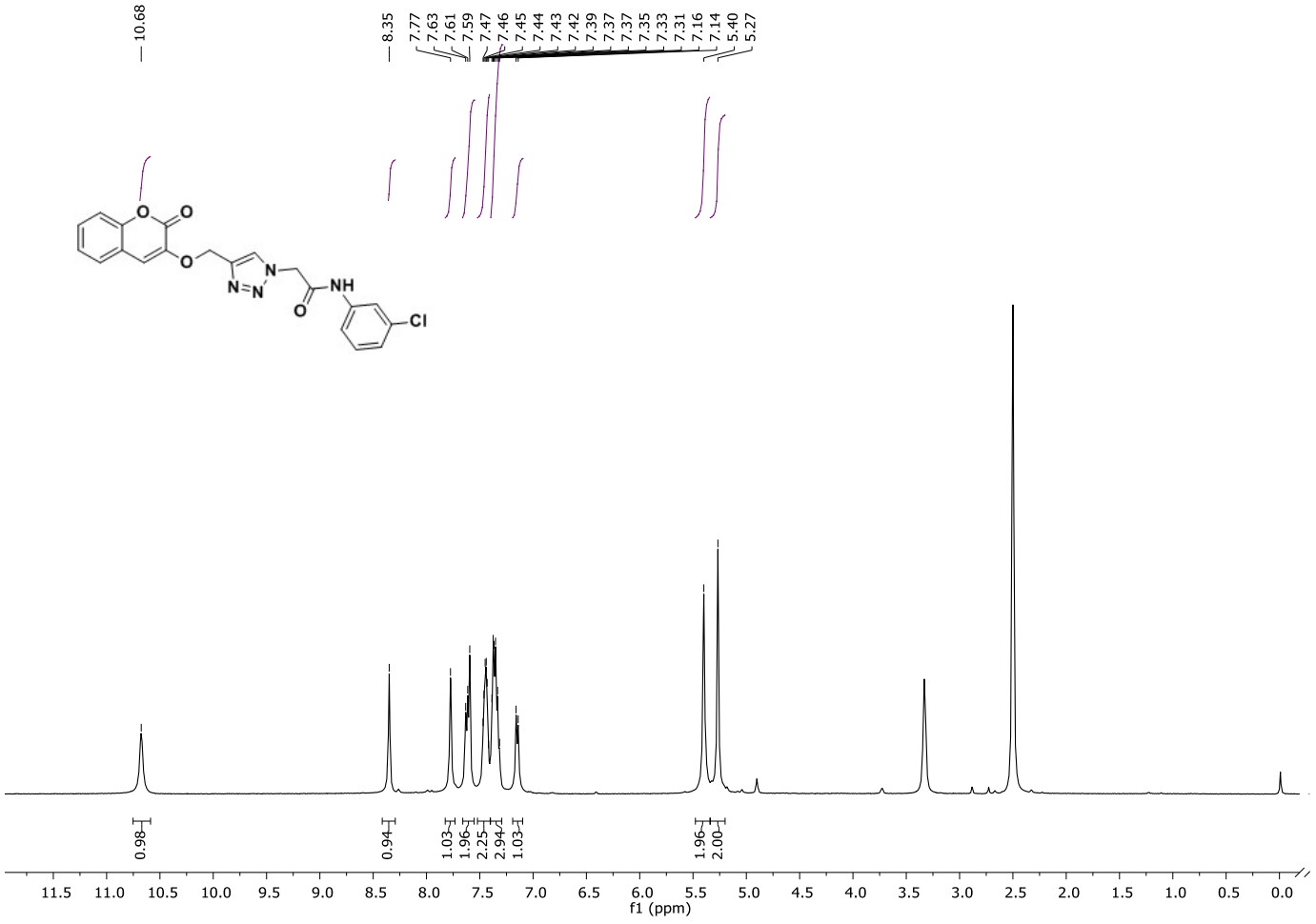
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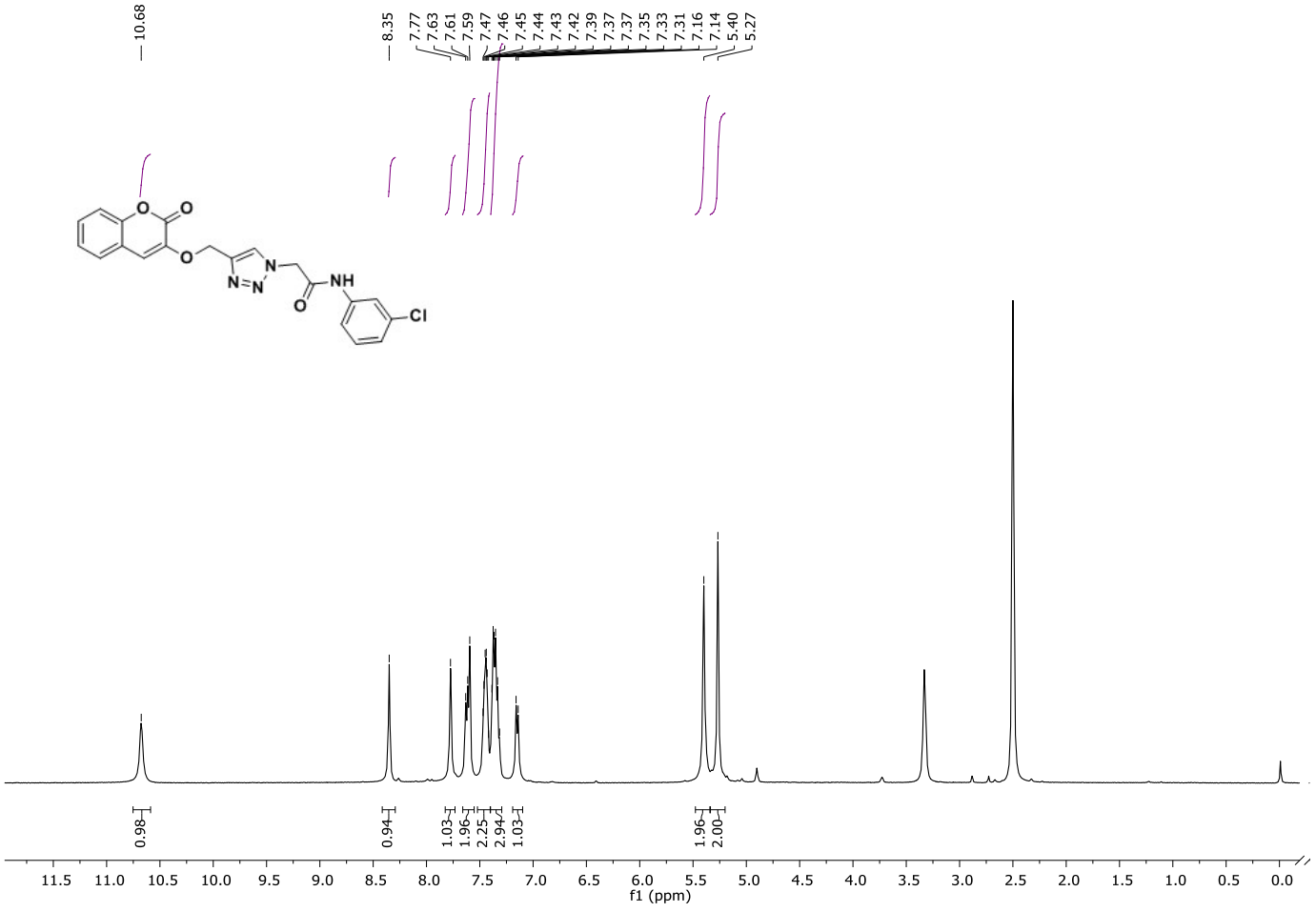
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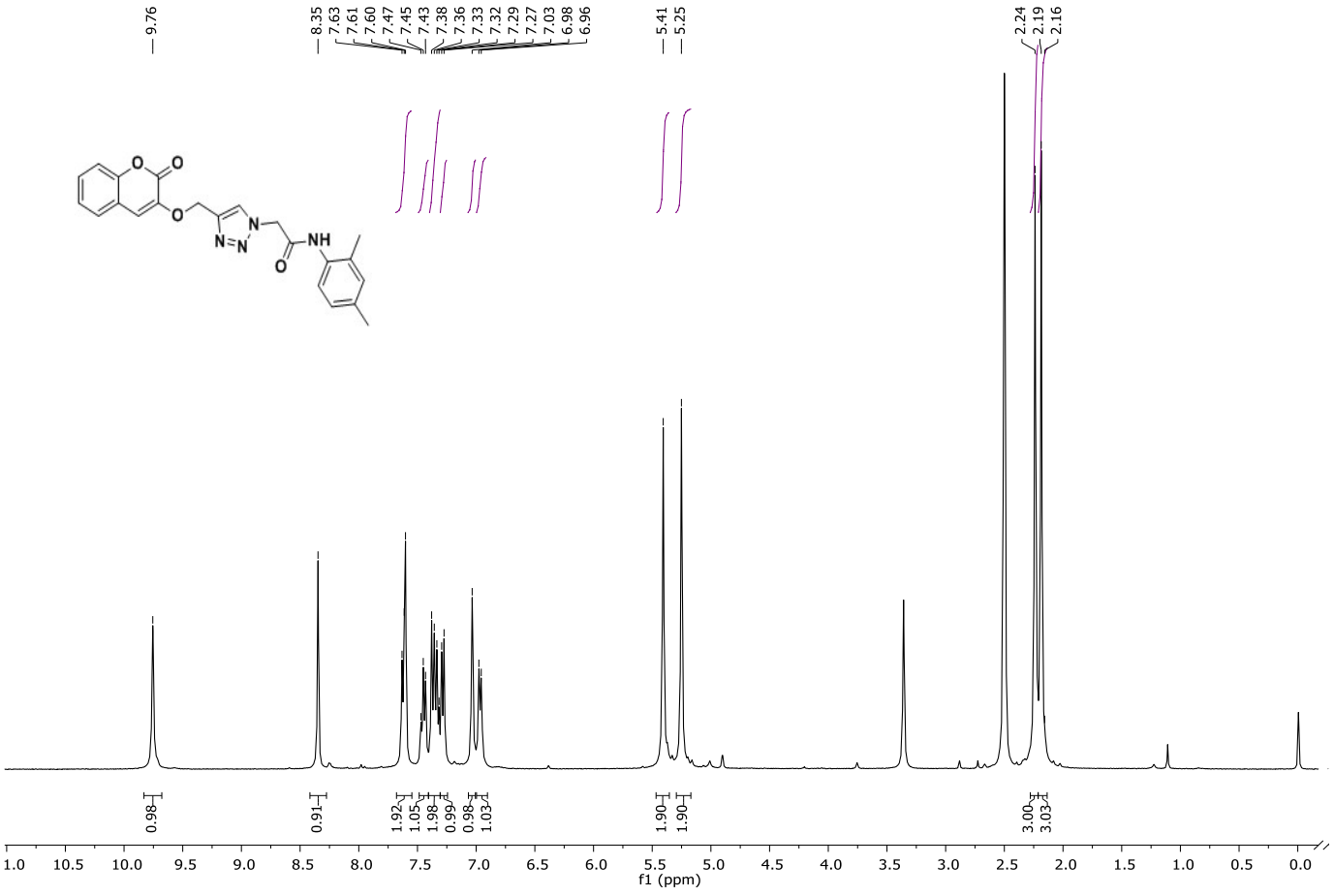
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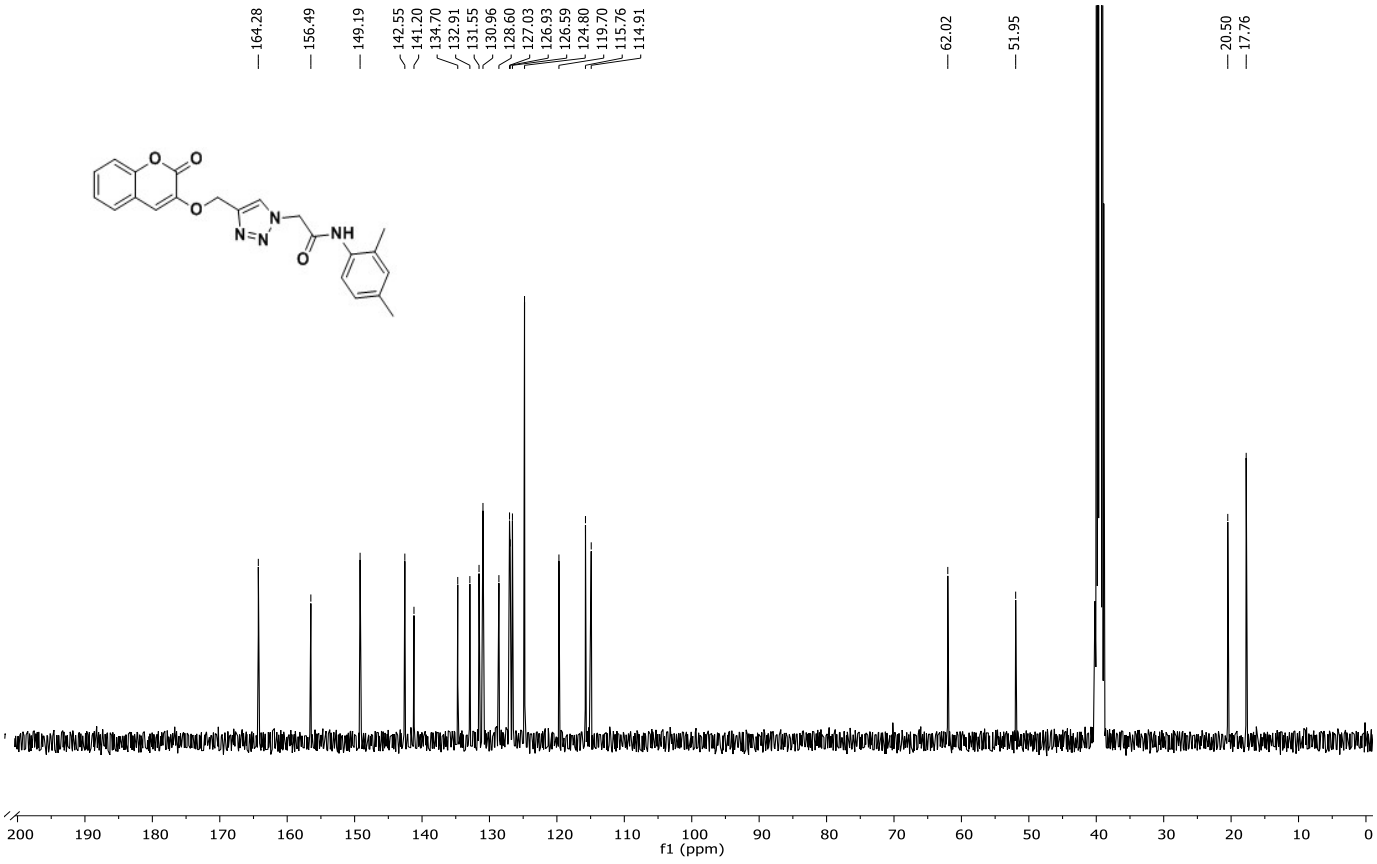
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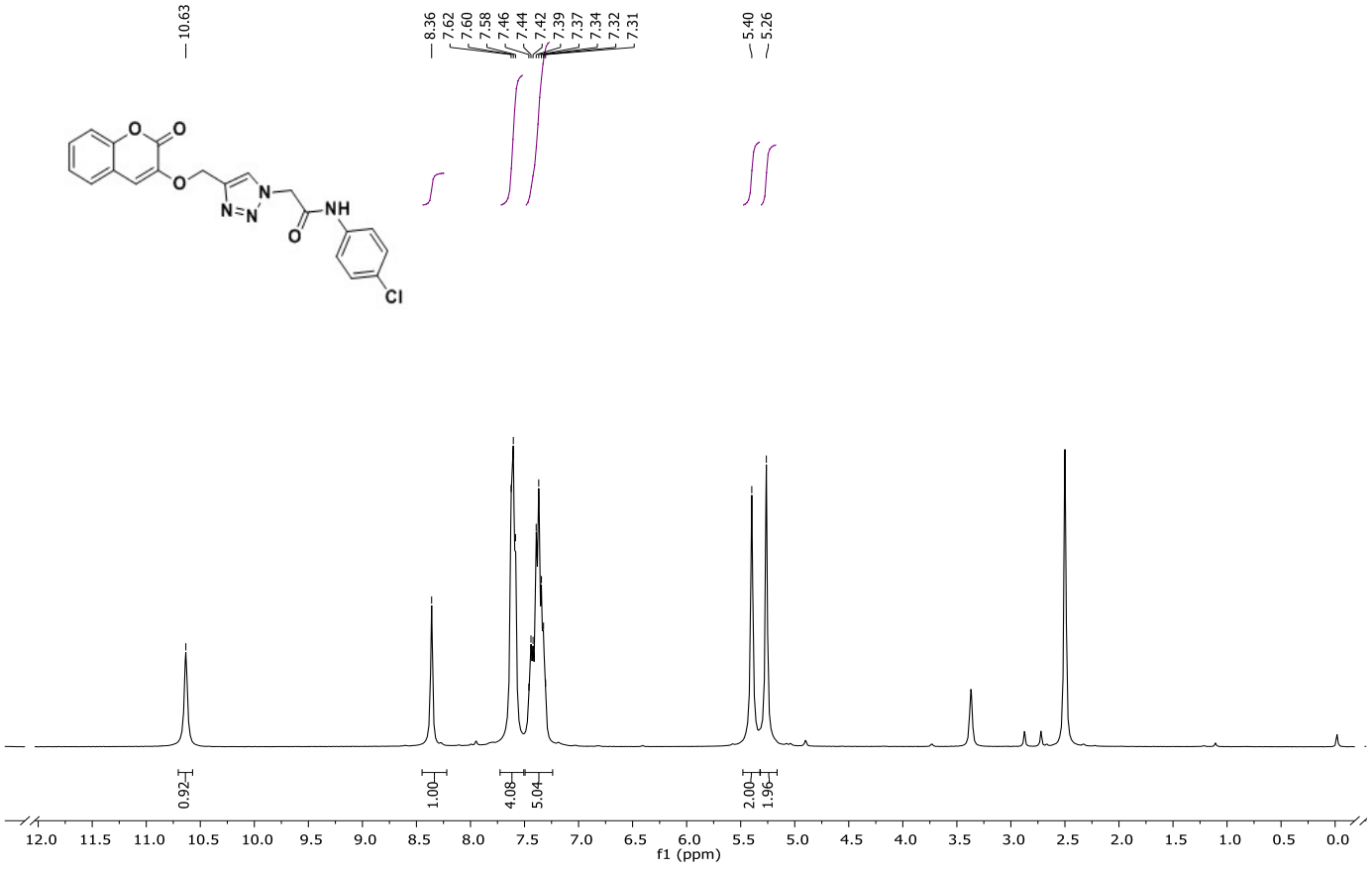
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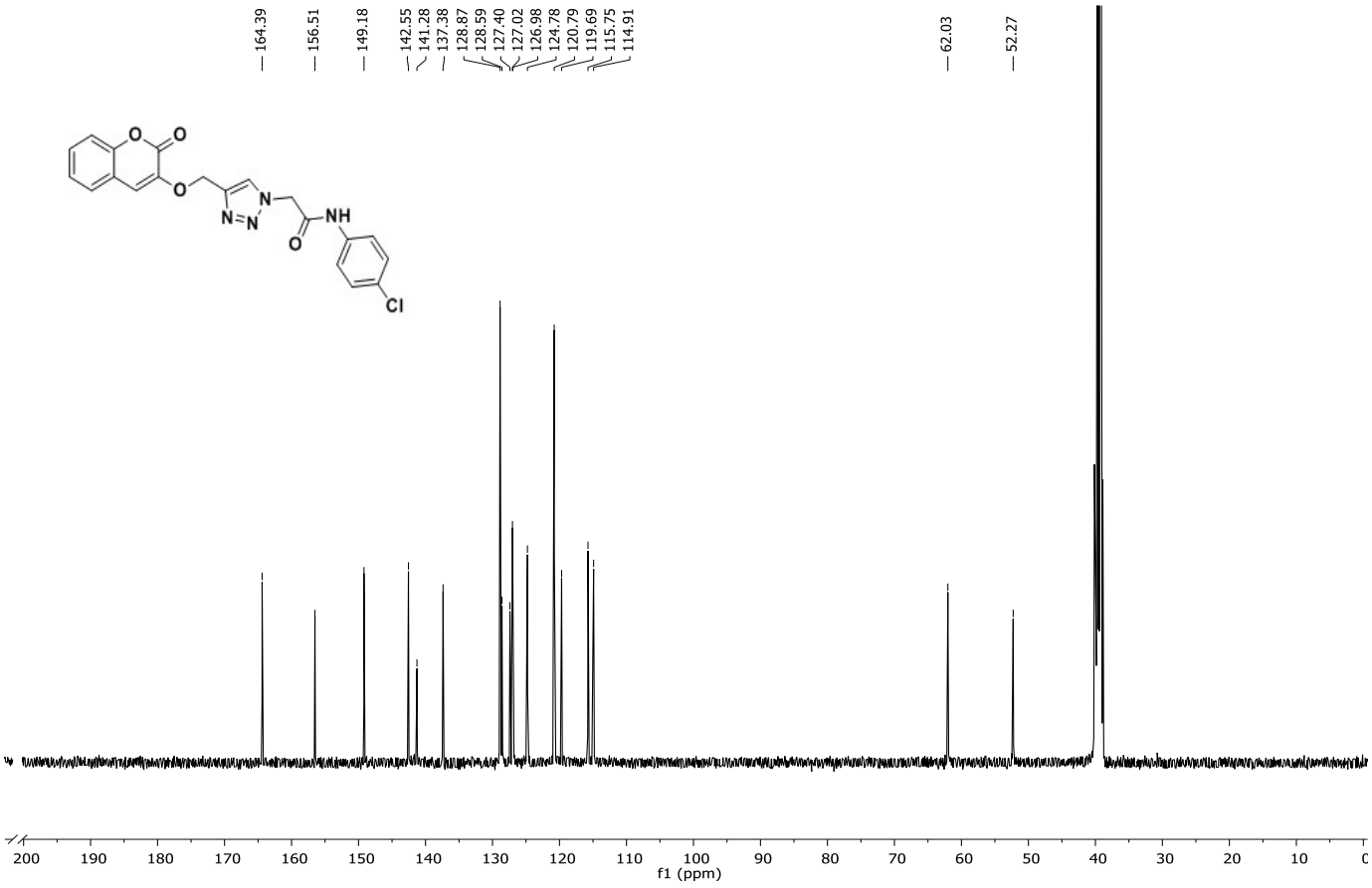
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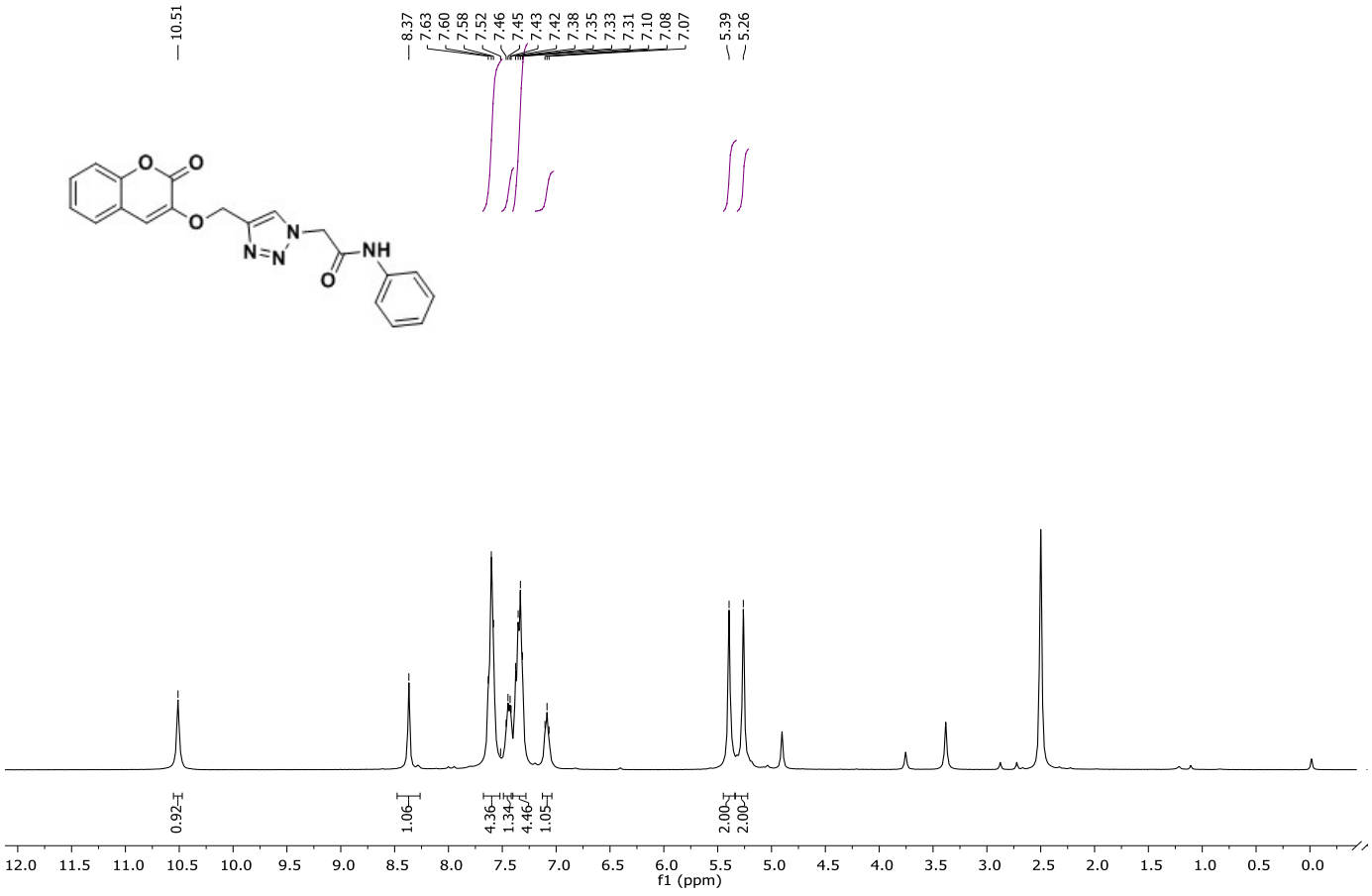
f1 (ppm)

^{13}C NMR of 3d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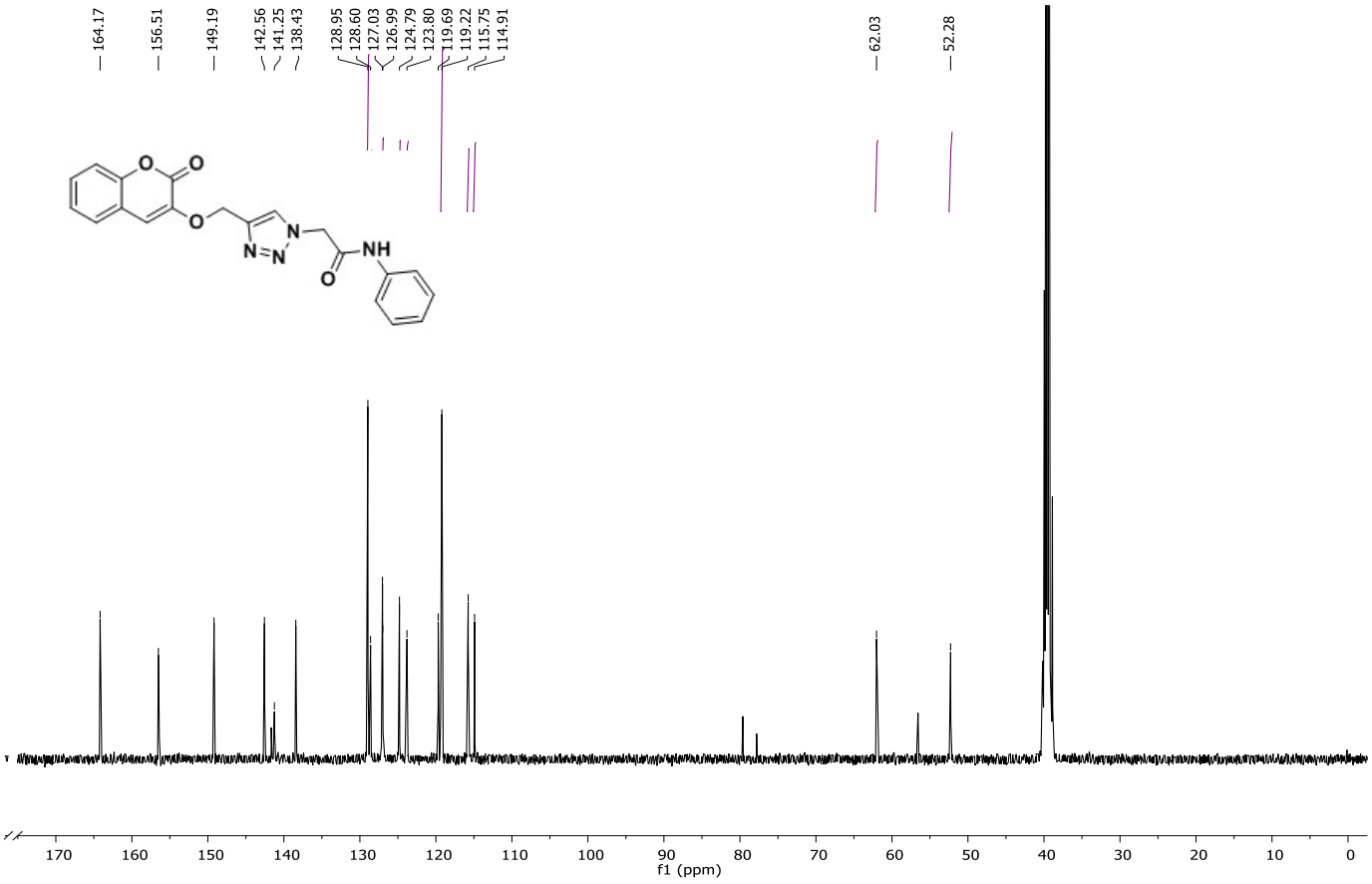
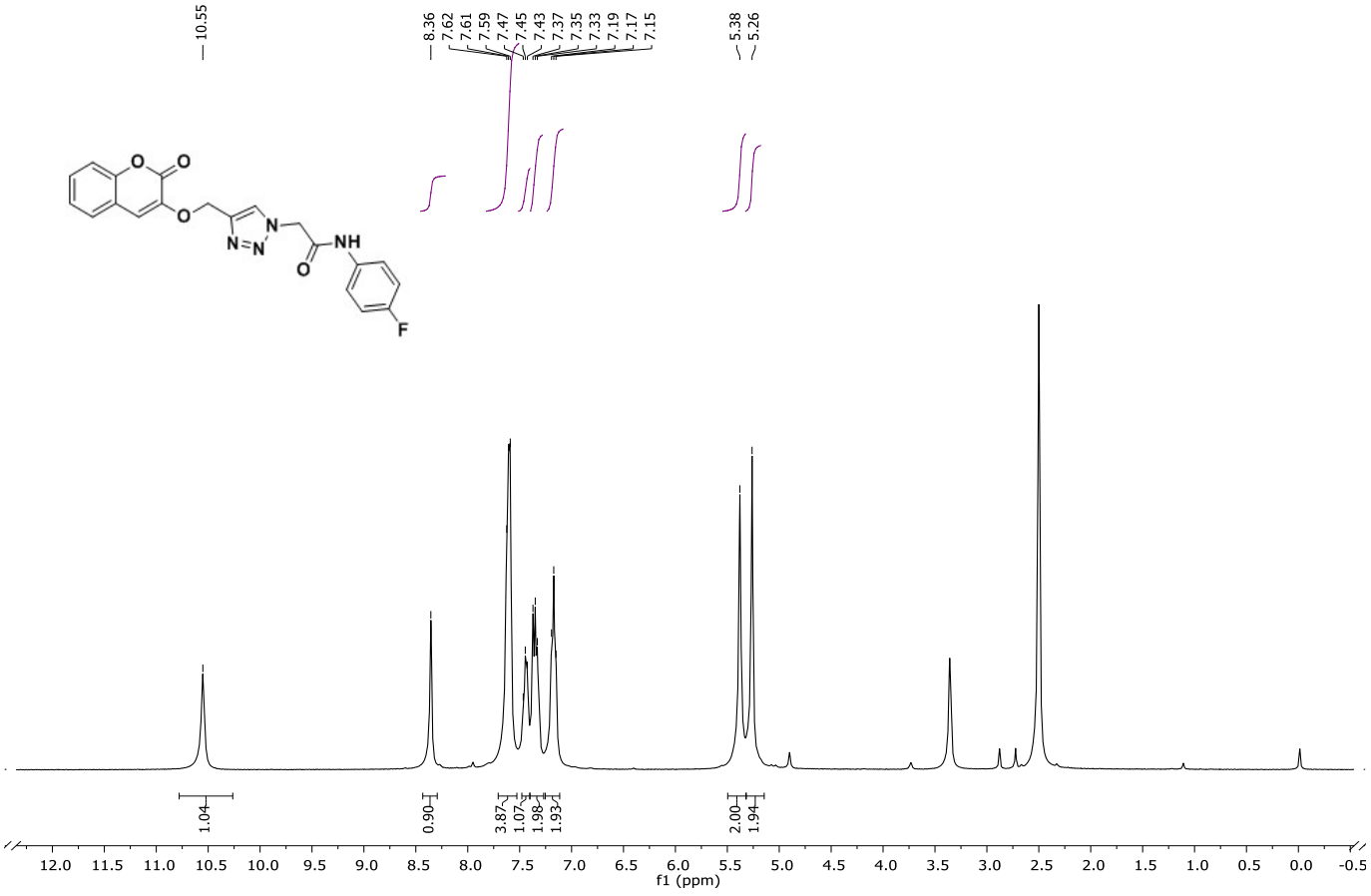
8.37
7.63
7.60
7.58
7.52
7.46
7.45
7.43
7.42
7.38
7.35
7.33
7.31
7.10
7.08
7.07
5.39
5.26
O
O
O
N
N=N
NH
O
0.92
1.06
4.36
1.34
4.46
1.05
2.00
2.00
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

^{1}H NMR of 3e


164.17
156.51
149.19
142.56
141.25
138.43
128.95
128.60
127.03
126.99
124.79
123.80
119.69
119.22
115.75
114.91
62.03
52.28
O
O
O
N
N
N
NH
O
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

^{13}C NMR of 3e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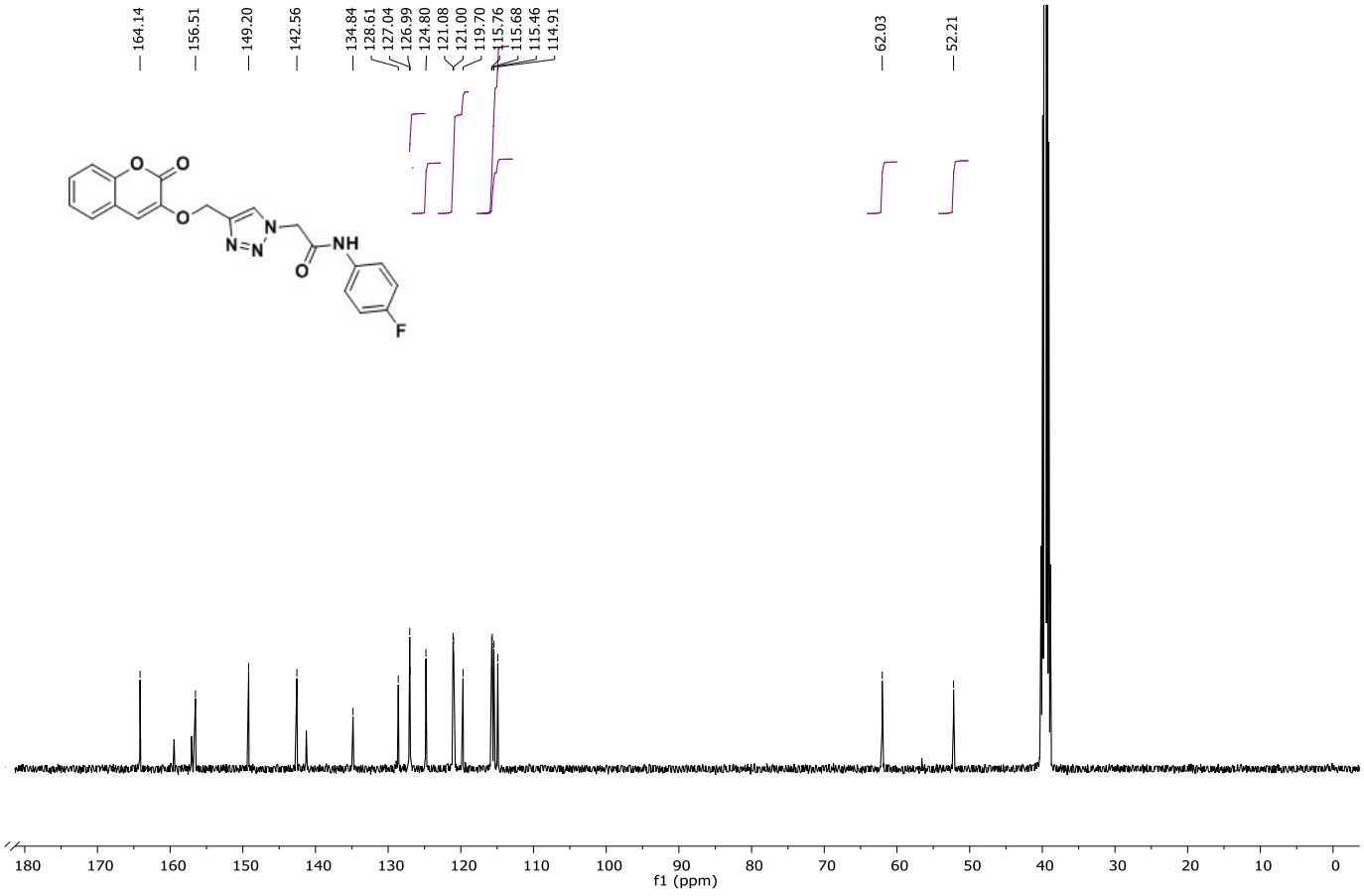
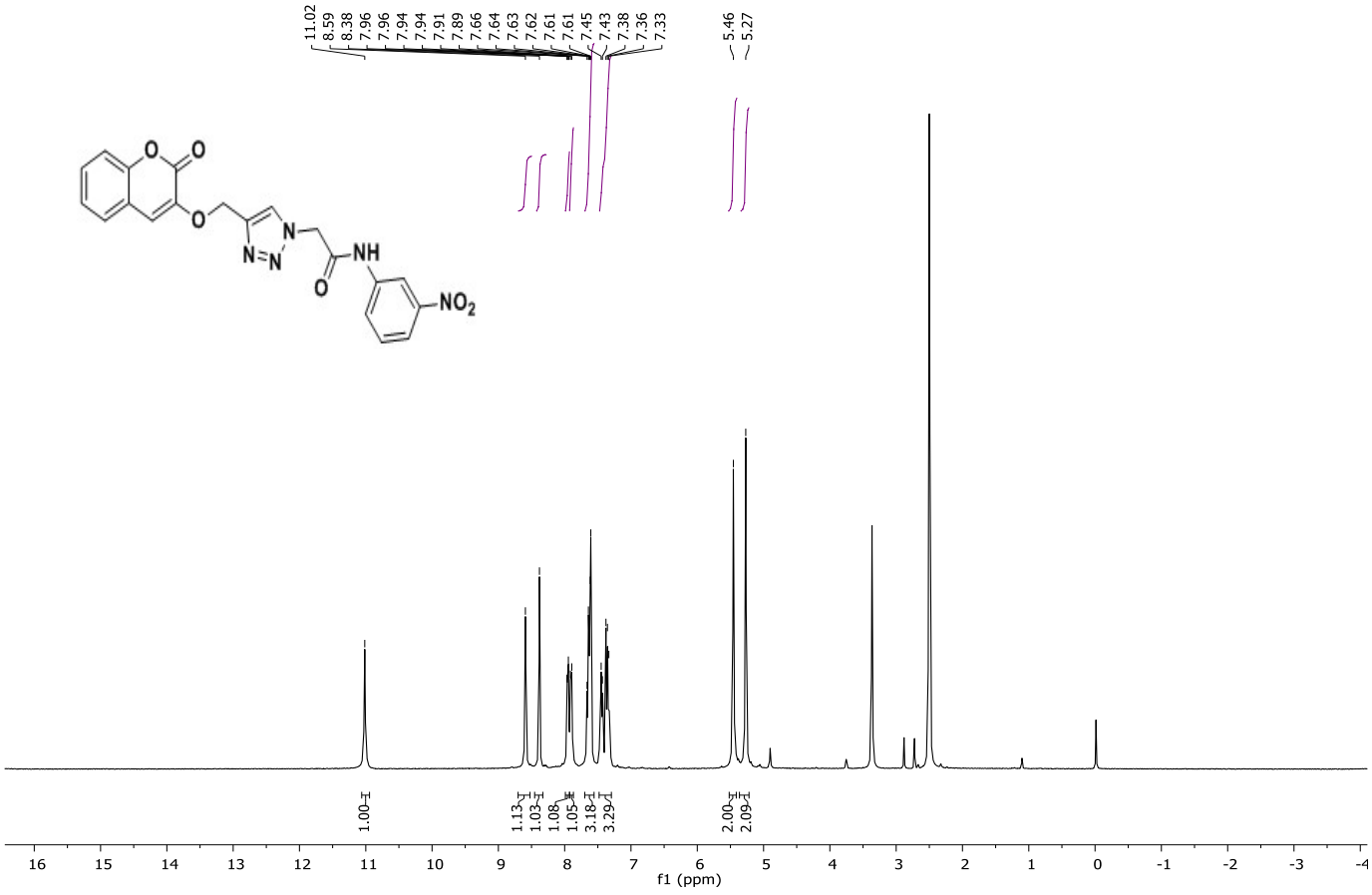
8.36
7.62
7.61
7.59
7.47
7.45
7.43
7.37
7.35
7.33
7.19
7.17
7.15
5.38
5.26
O
O
O
N
N
N
NH
O
F
1.04
0.90
3.87
1.07
1.98
1.93
2.00
1.94
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

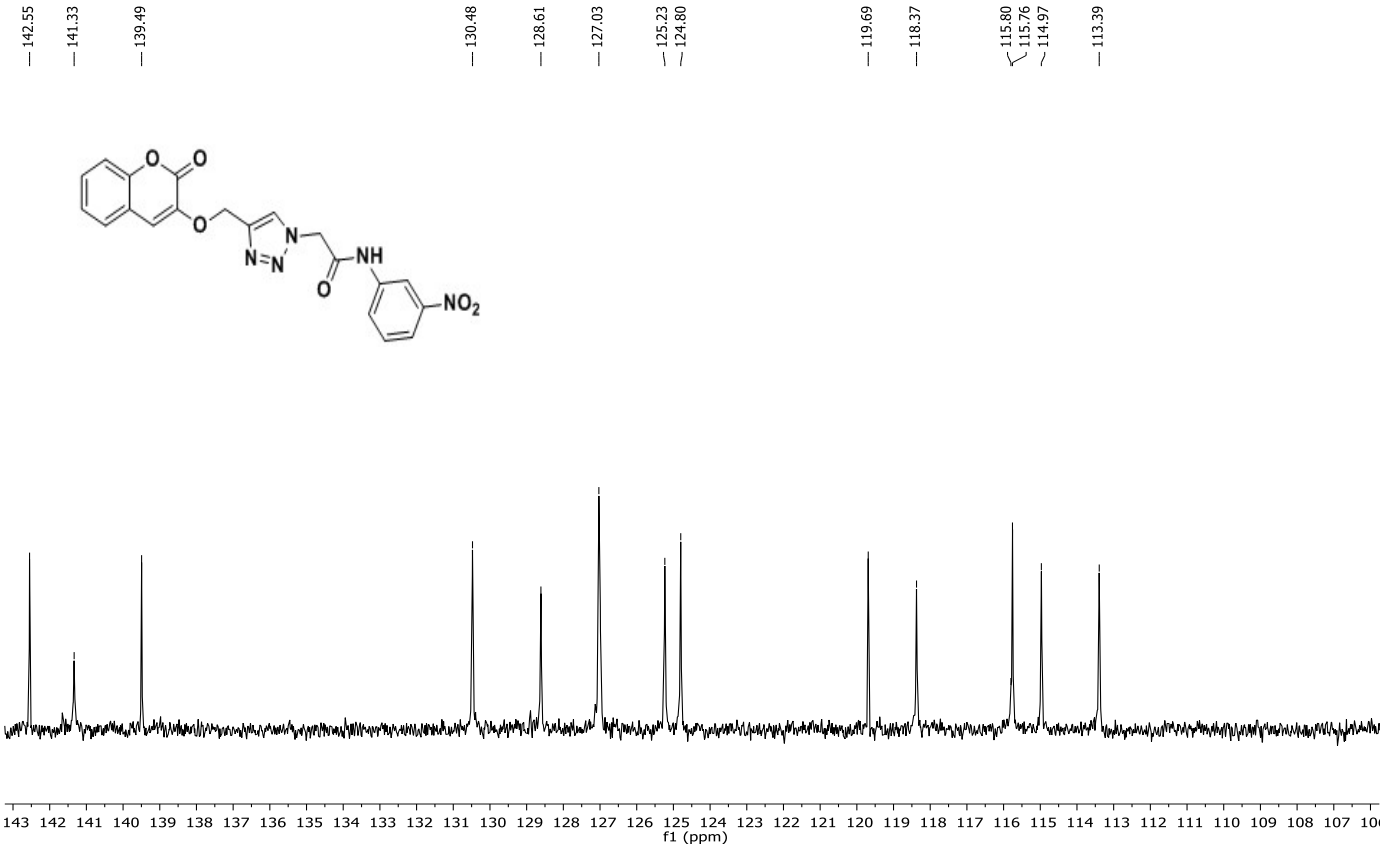
^{1}H NMR of 3f


164.14
156.51
149.20
142.56
134.84
128.61
127.04
126.99
124.80
121.08
121.00
119.70
115.76
115.68
115.46
114.91
62.03
52.21
O
O
O
N
N=N
NH
O
F
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

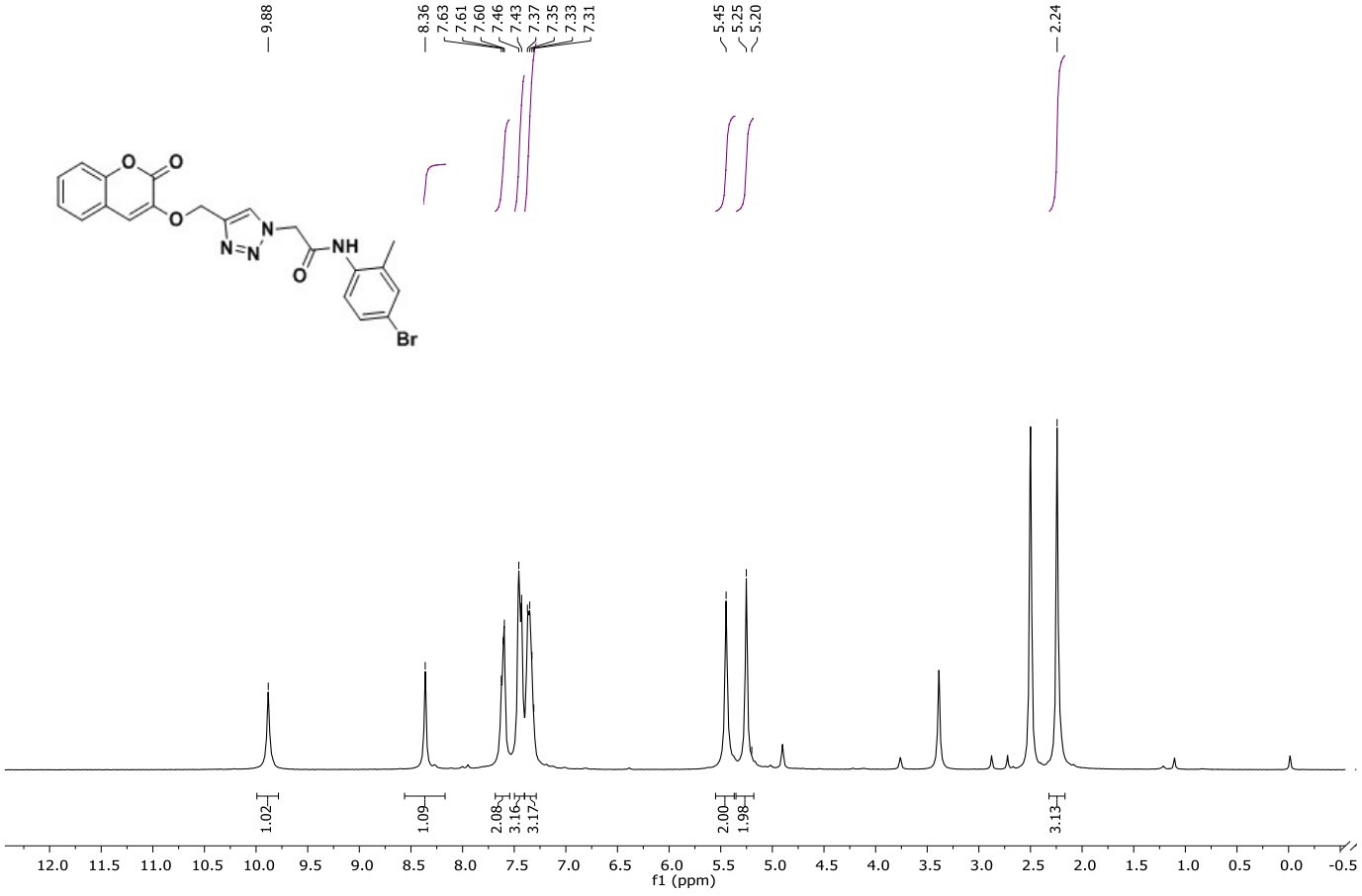
^{13}C NMR of 3f


11.02
8.59
8.38
7.96
7.96
7.94
7.94
7.91
7.89
7.66
7.64
7.63
7.62
7.61
7.61
7.45
7.43
7.38
7.36
7.33
5.46
5.27
O
O
O
N
N=N
O
NH
NO2
1.00
1.13
1.03
1.08
1.05
3.18
3.29
2.00
2.09
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)

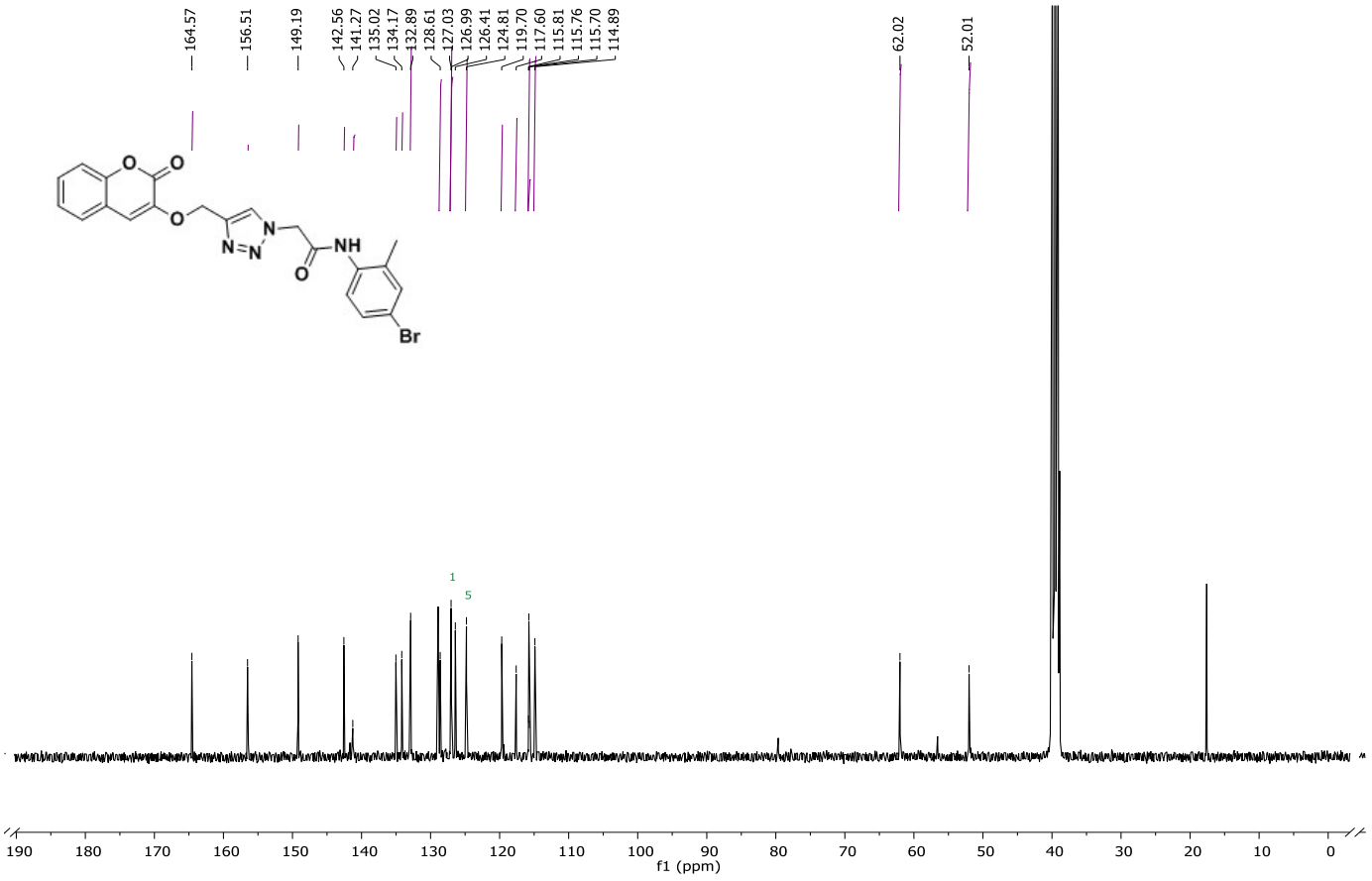
^{1}H NMR of 3g


142.55
141.33
139.49
130.48
128.61
127.03
125.23
124.80
119.69
118.37
115.80
115.76
114.97
113.39
O
O
O
N
N=N
NH
O
NO2
143 142 141 140 139 138 137 136 135 134 133 132 131 130 129 128 127 126 125 124 123 122 121 120 119 118 117 116 115 114 113 112 111 110 109 108 107
f1 (ppm)

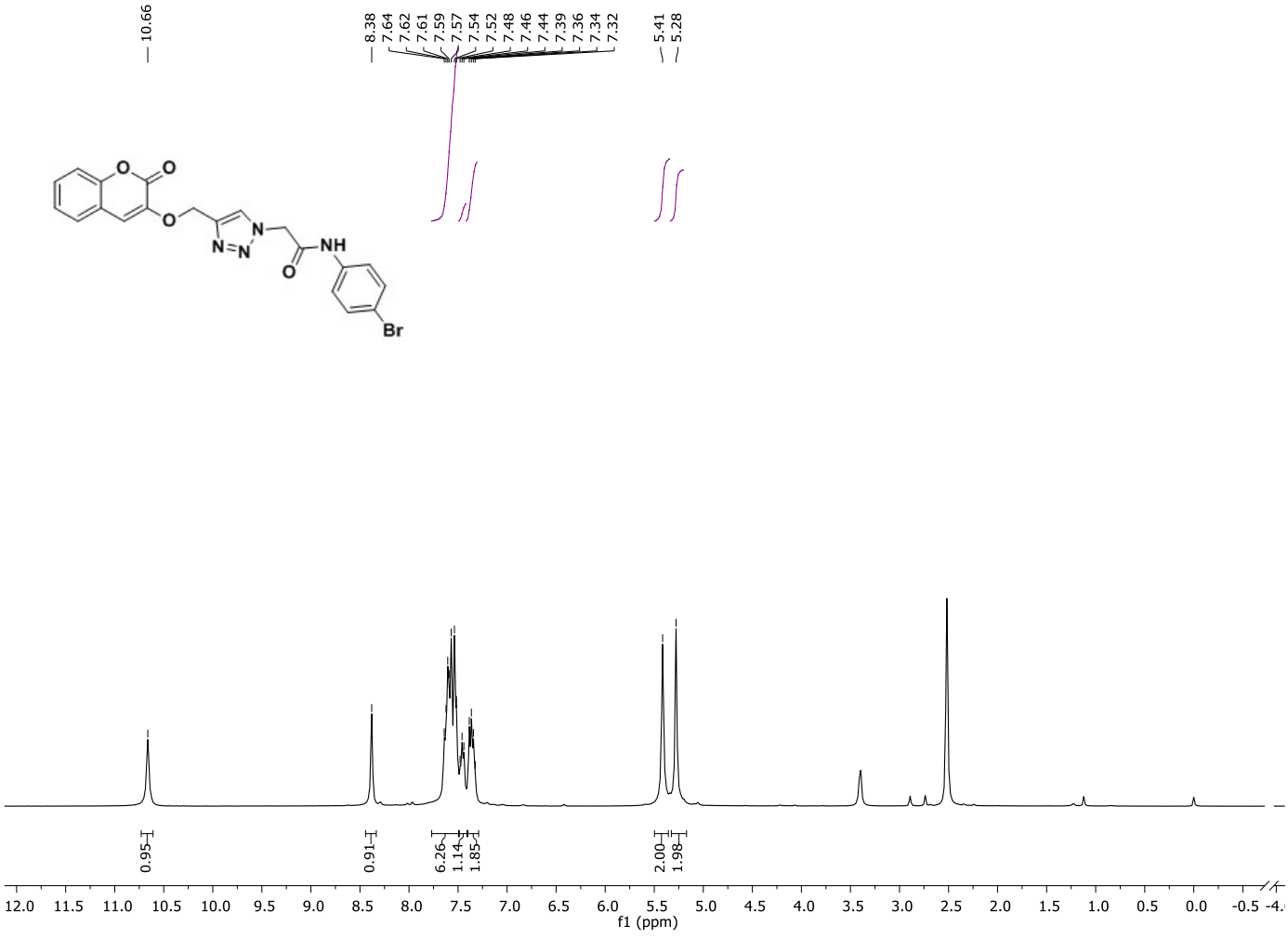
^{13}C NMR of 3g


9.88
8.36
7.63
7.61
7.60
7.46
7.43
7.37
7.35
7.33
7.31
5.45
5.25
5.20
2.24
O
O
O
N
N=N
O
NH
Br
1.02
1.09
2.08
3.16
3.17
2.00
1.98
3.13
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

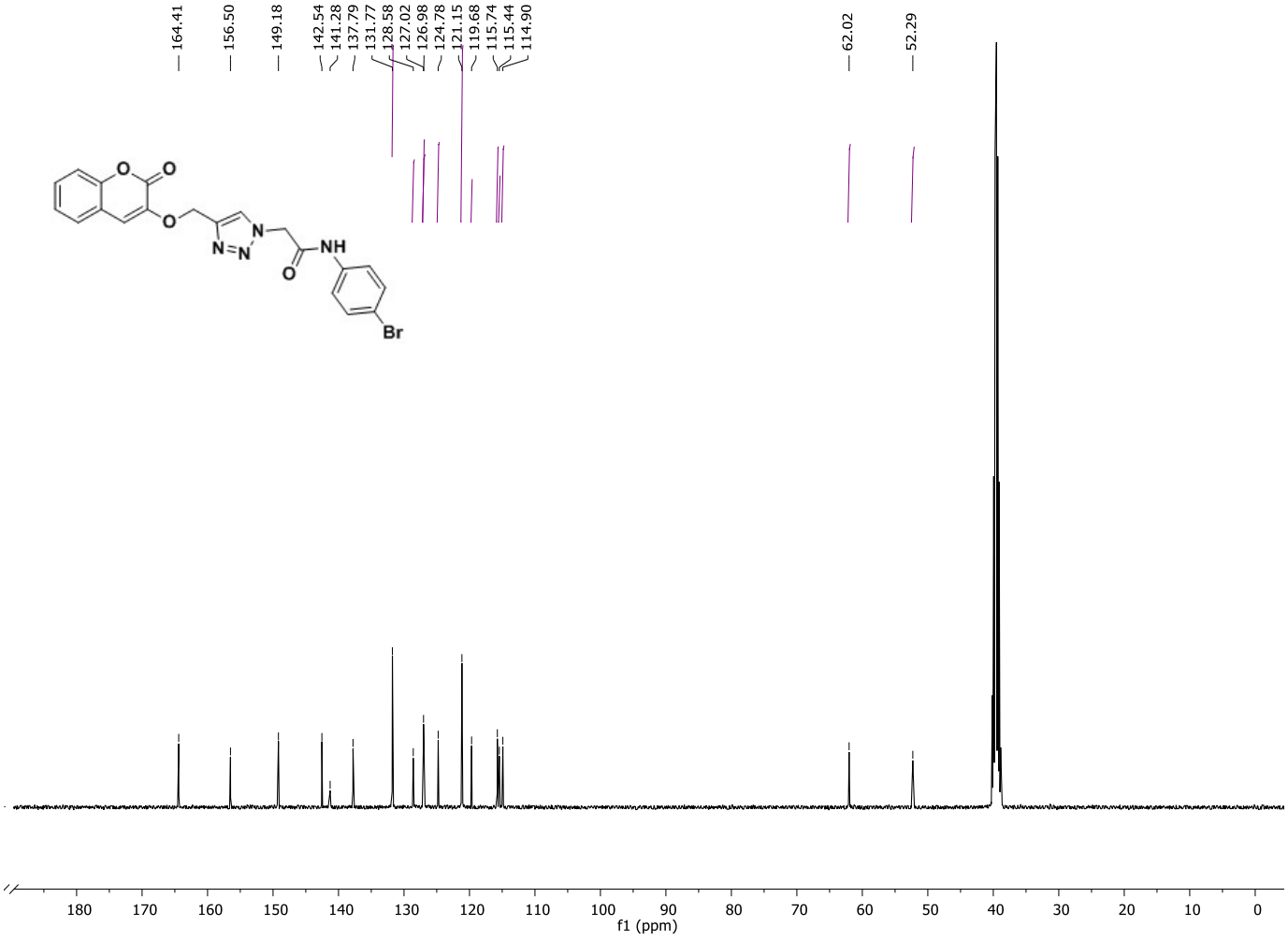
^{1}H NMR of 3h


164.57
156.51
149.19
142.56
141.27
135.02
134.17
132.89
128.61
127.03
126.99
126.41
124.81
119.70
117.60
115.81
115.76
115.70
114.89
62.02
52.01
O
O
O
N
N=N
NH
O
Br
1
5
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

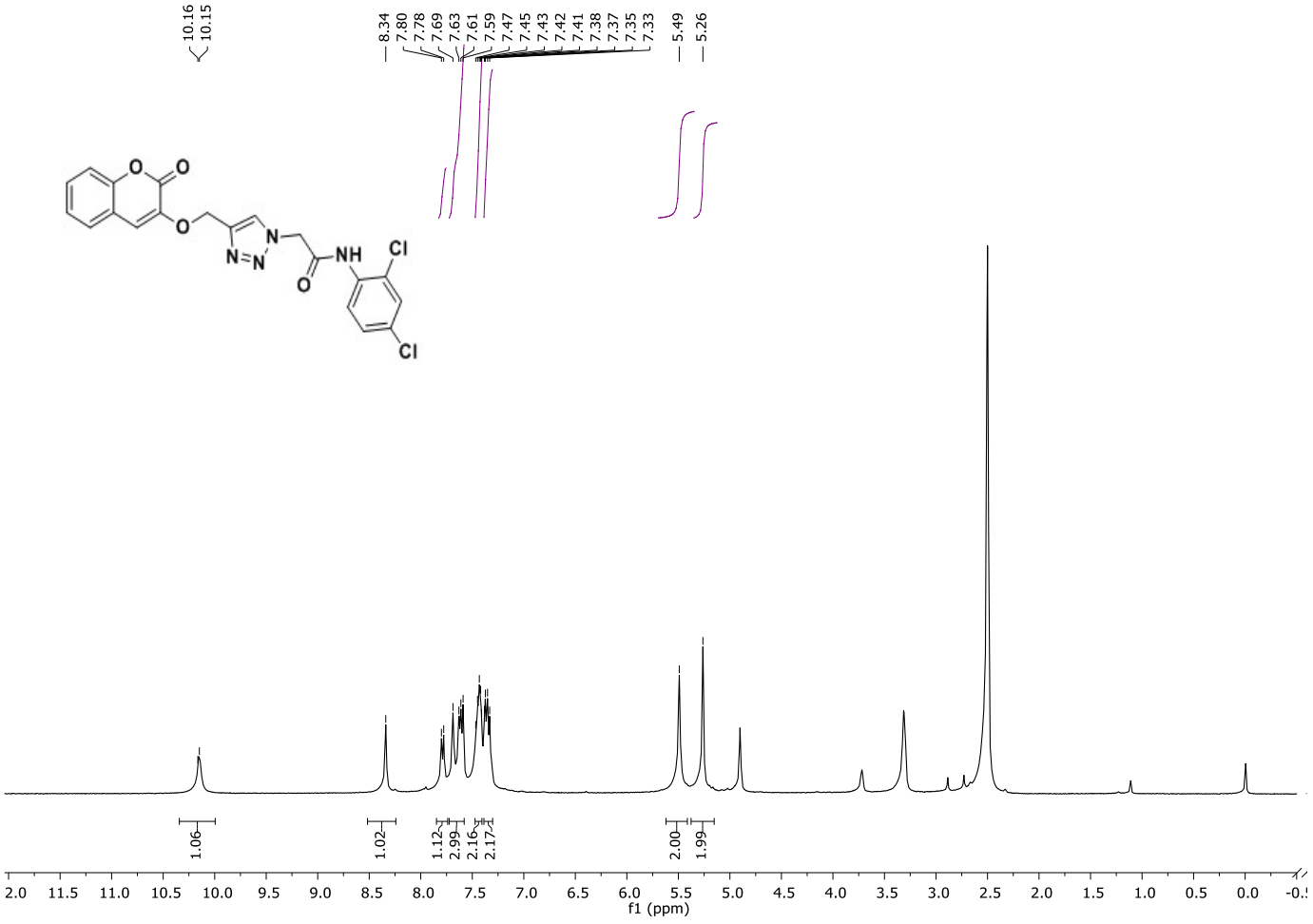
^{13}C NMR of 3h


10.66
8.38
7.64
7.62
7.61
7.59
7.57
7.54
7.52
7.48
7.46
7.44
7.39
7.36
7.34
7.32
5.41
5.28
O
O
O
N
N=N
NH
O
Br
0.95
0.91
6.26
1.14
1.85
2.00
1.98
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

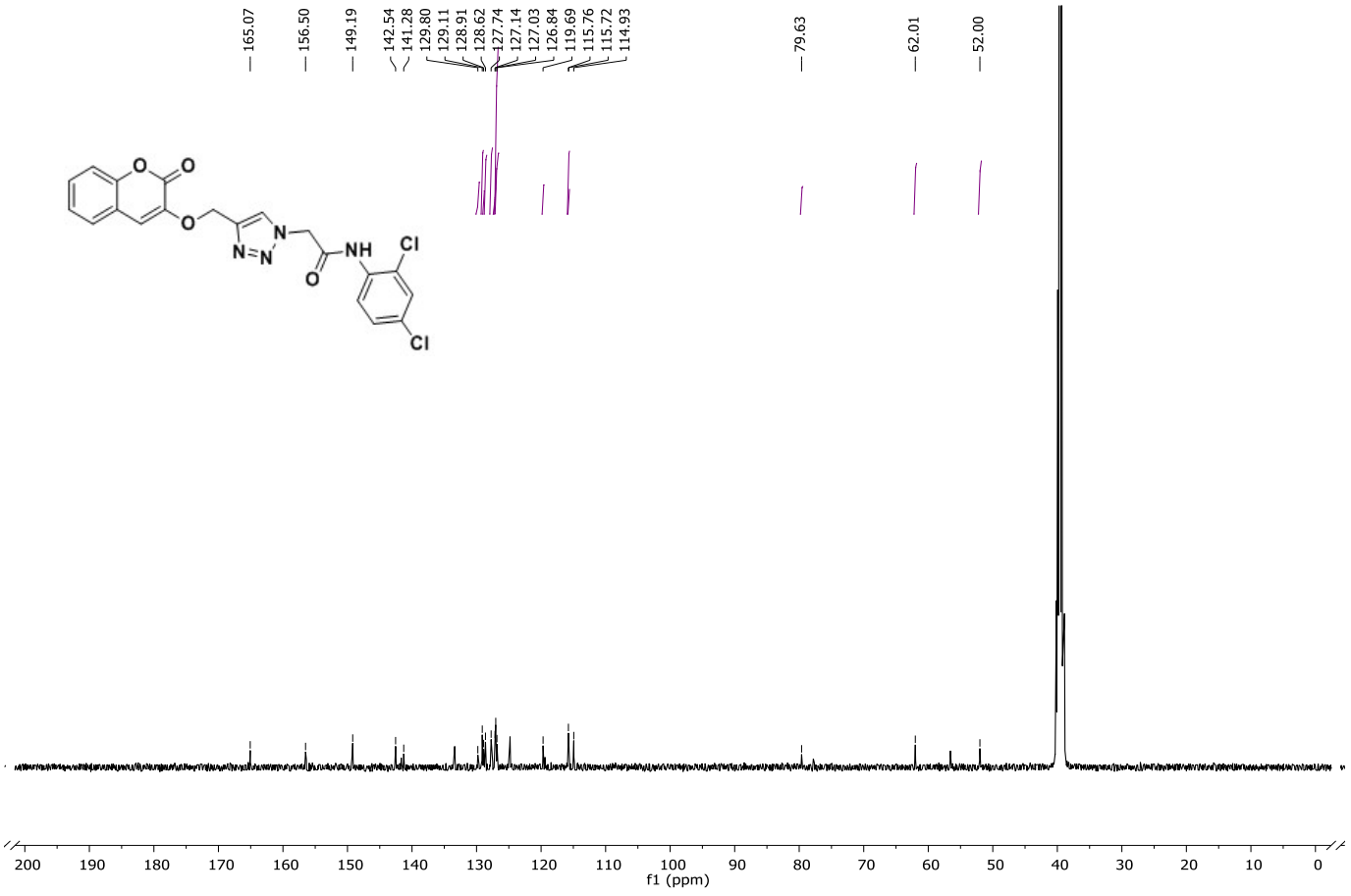
^{1}H NMR of 3i


164.41
156.50
149.18
142.54
141.28
137.79
131.77
128.58
127.02
126.98
124.78
121.15
119.68
115.74
115.44
114.90
62.02
52.29
O
O
O
N
N=N
O
NH
Br
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

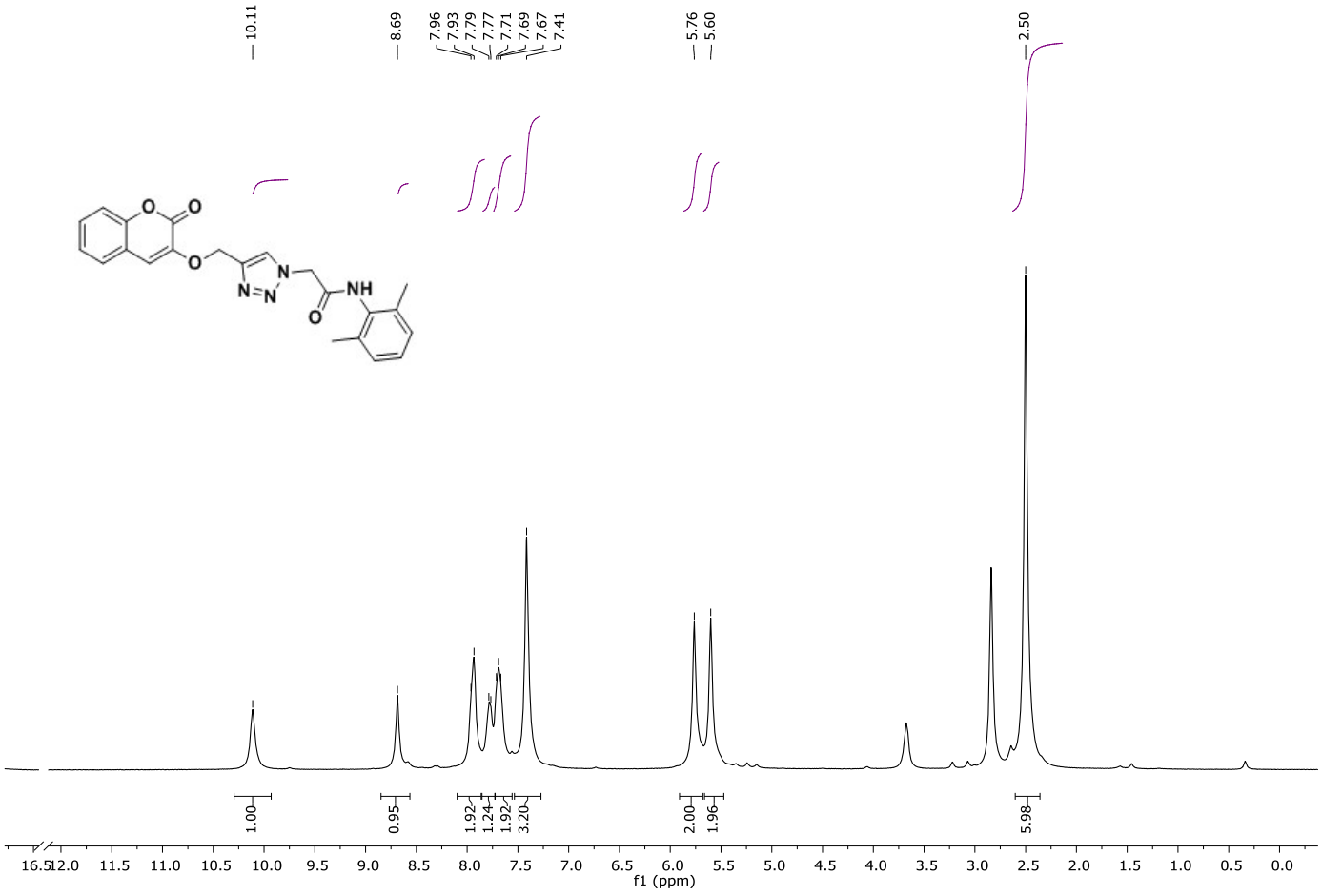
^{13}C NMR of 3i


10.16
10.15
8.34
7.80
7.78
7.69
7.63
7.61
7.59
7.47
7.45
7.43
7.42
7.41
7.38
7.37
7.35
7.33
5.49
5.26
O
O
O
N
N=N
NH
O
Cl
Cl
1.06
1.02
1.12
2.99
2.16
2.17
2.00
1.99
2.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

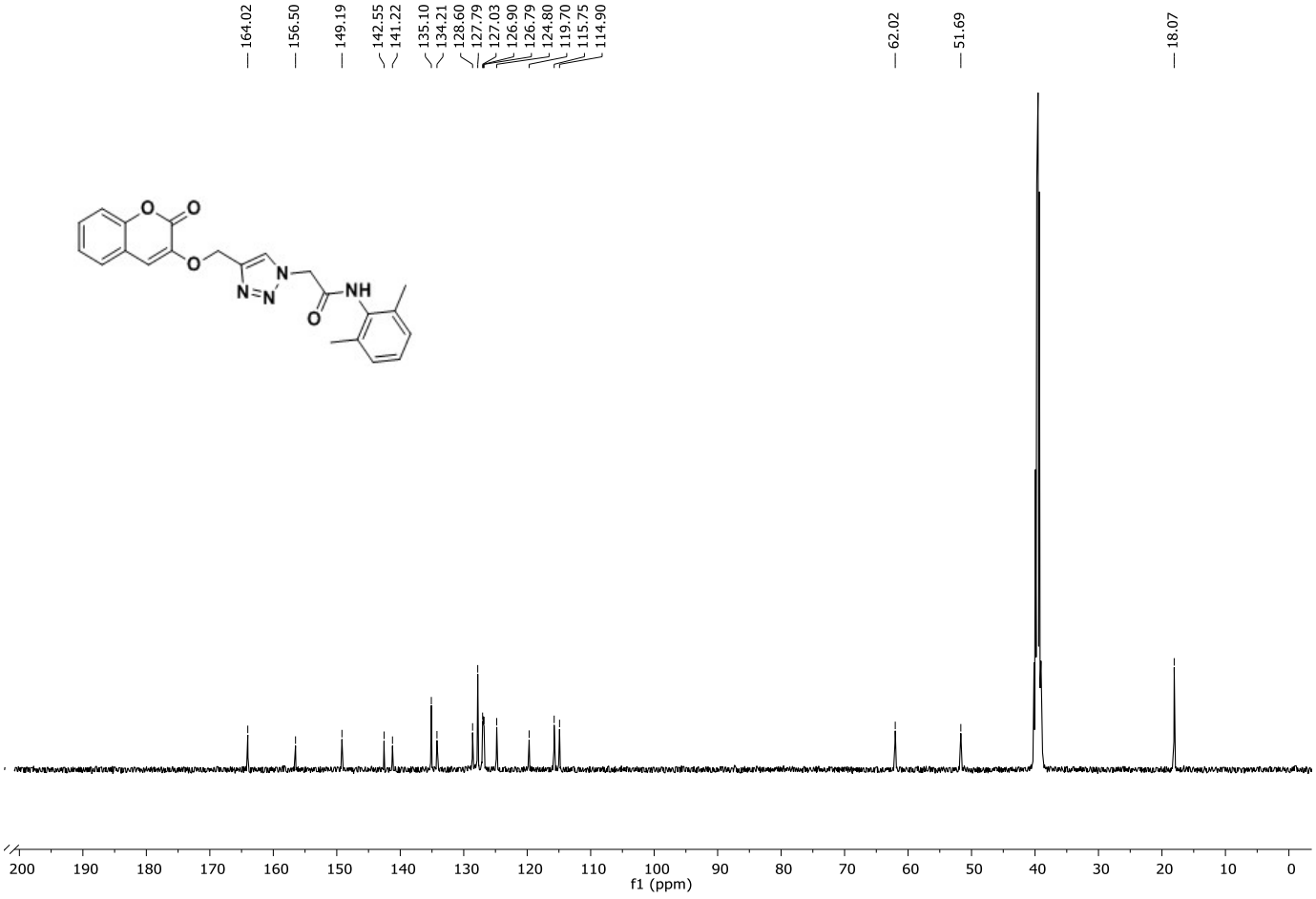
^{1}H NMR of 3j


165.07
156.50
149.19
142.54
141.28
129.80
129.11
128.91
128.62
127.74
127.14
127.03
126.84
119.69
115.76
115.72
114.93
79.63
62.01
52.00
O
O
O
N
N=N
NH
O
Cl
Cl
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

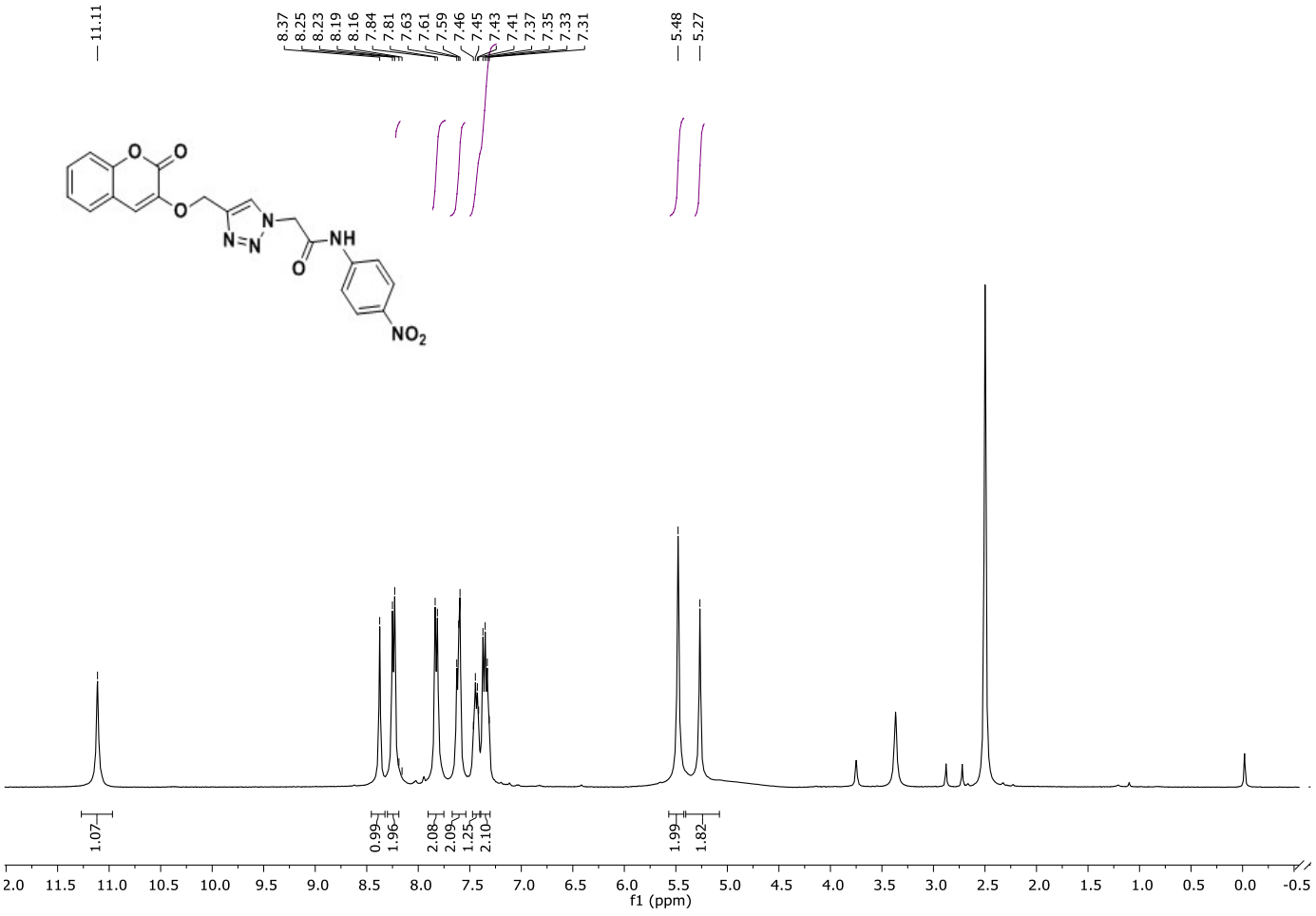
^{13}C NMR of 3j


10.11
8.69
7.96
7.93
7.79
7.77
7.71
7.69
7.67
7.41
5.76
5.60
2.50
O
O
O
N
N=N
O
NH
1.00
0.95
1.92
1.24
1.92
3.20
2.00
1.96
5.98
16.5
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

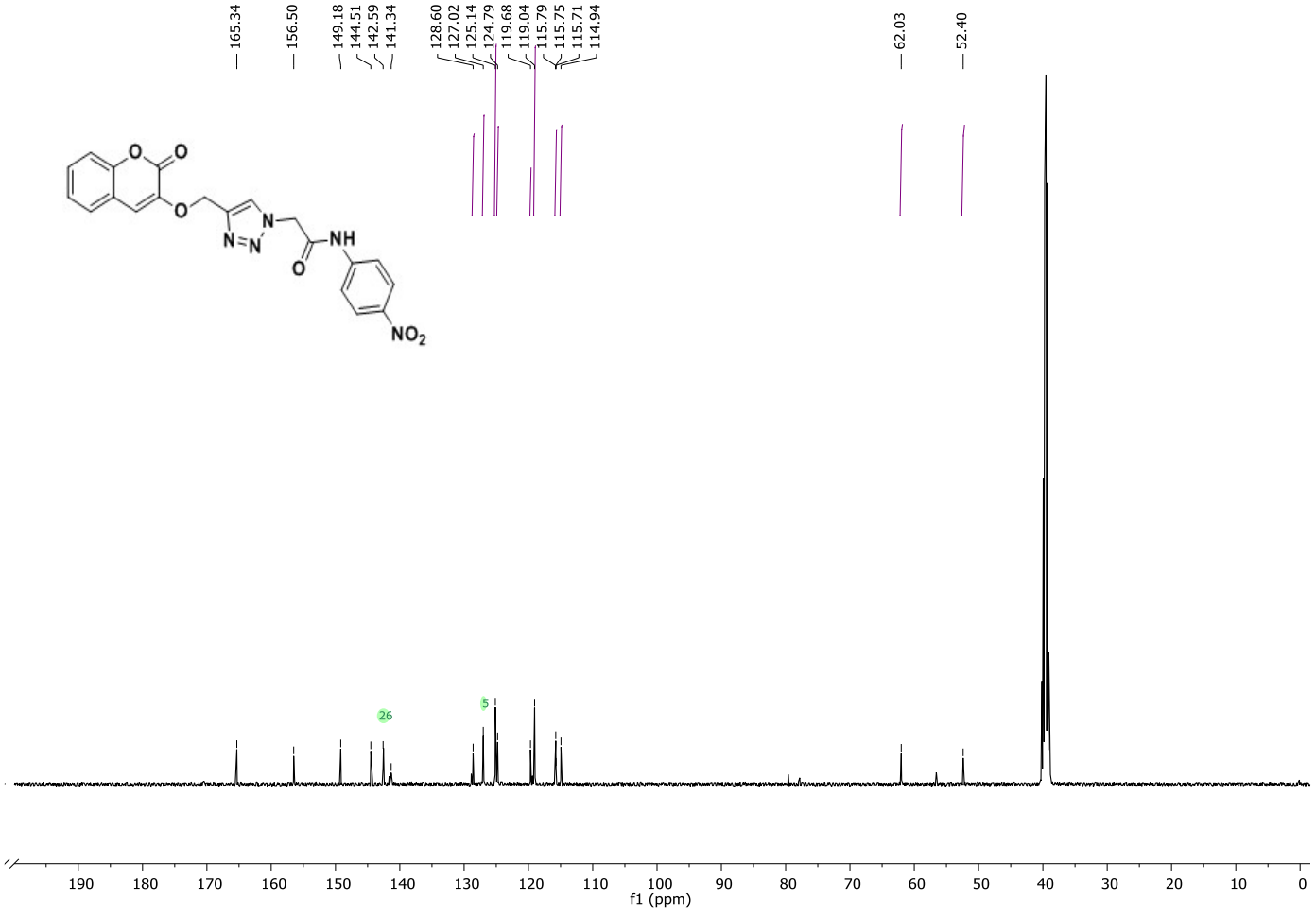
^{1}H NMR of 3k


164.02
156.50
149.19
142.55
141.22
135.10
134.21
128.60
127.79
127.03
126.90
126.79
124.80
119.70
115.75
114.90
62.02
51.69
18.07
O
O
O
N
N=N
NH
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

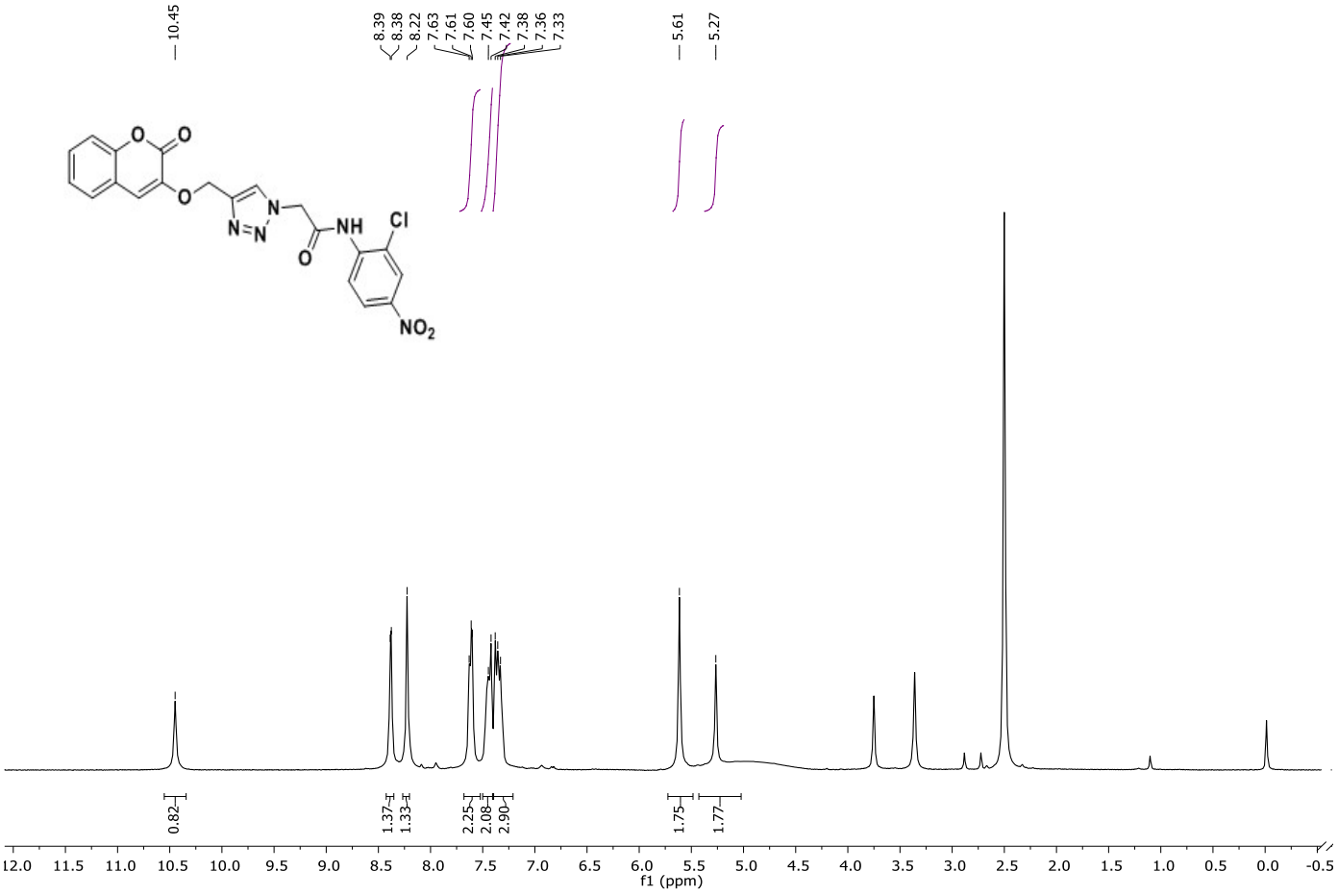
^{13}C NMR of 3k


11.11
8.37
8.25
8.23
8.19
8.16
7.84
7.81
7.63
7.61
7.59
7.46
7.45
7.43
7.41
7.37
7.35
7.33
7.31
5.48
5.27
O
O
O
N
N
N
NH
O
NO2
1.07
0.99
1.96
2.08
2.09
1.25
2.10
1.99
1.82
2.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

^{1}H NMR of 3l

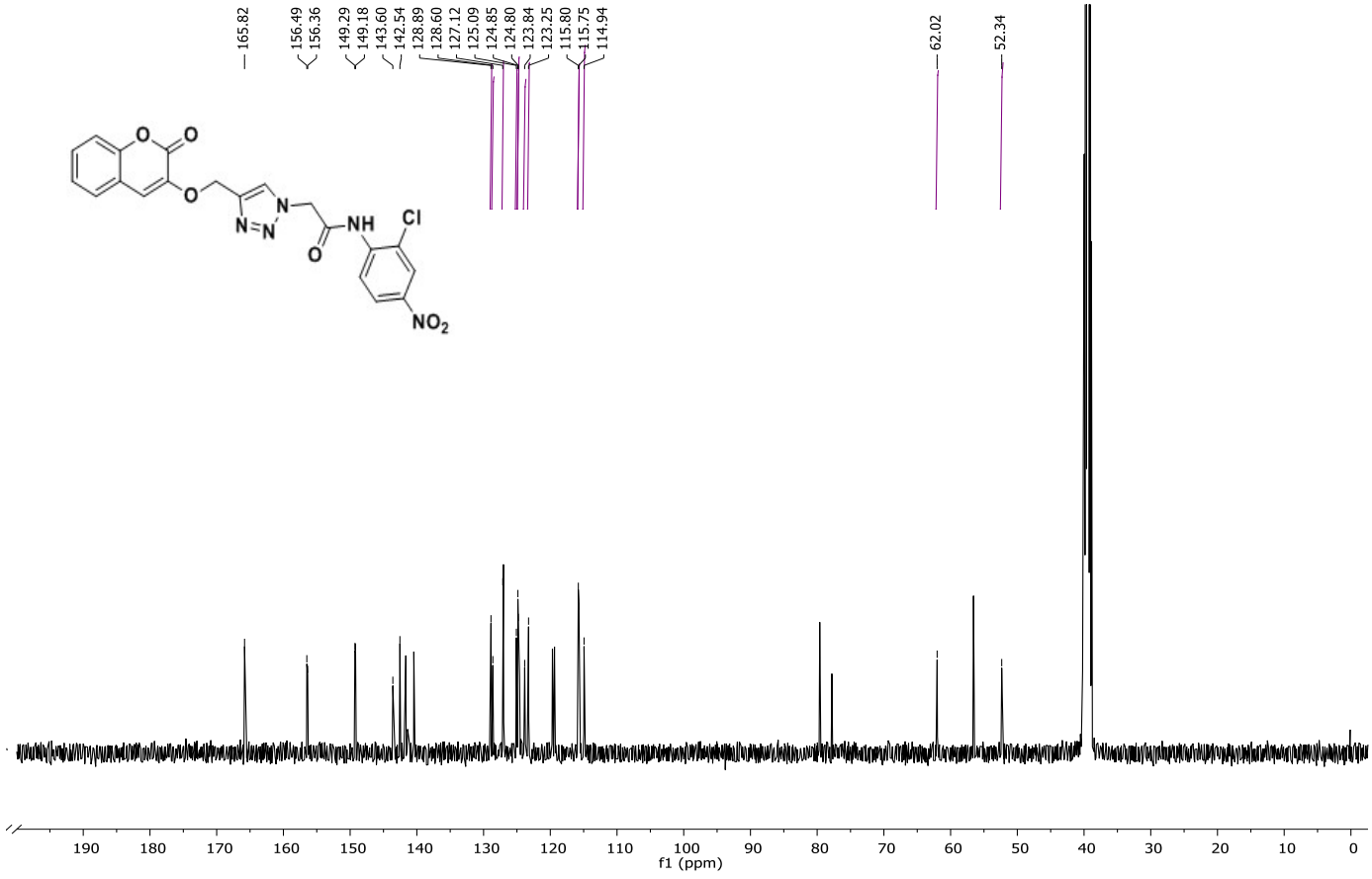

165.34
156.50
149.18
144.51
142.59
141.34
128.60
127.02
125.14
124.79
119.68
119.04
115.79
115.75
115.71
114.94
62.03
52.40
O
O
O
N
N=N
NH
O
NO2
26
5
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

^{13}C NMR of 3l

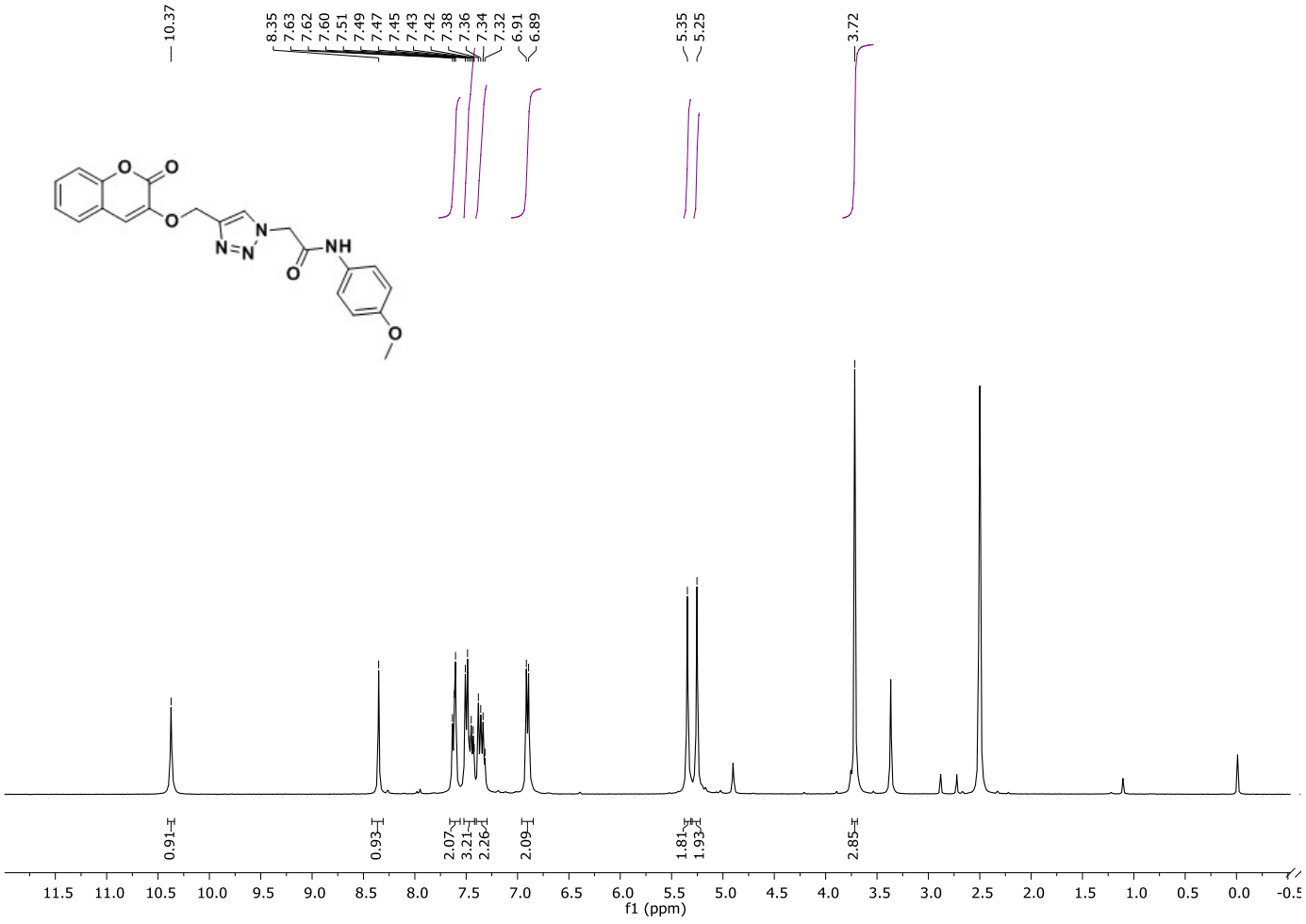

10.45
8.39
8.38
8.22
7.63
7.61
7.60
7.45
7.42
7.38
7.36
7.33
5.61
5.27
O
O
O
N
N=N
NH
O
Cl
NO2
0.82
1.37
1.33
2.25
2.08
2.90
1.75
1.77
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

^{1}H NMR of 3m

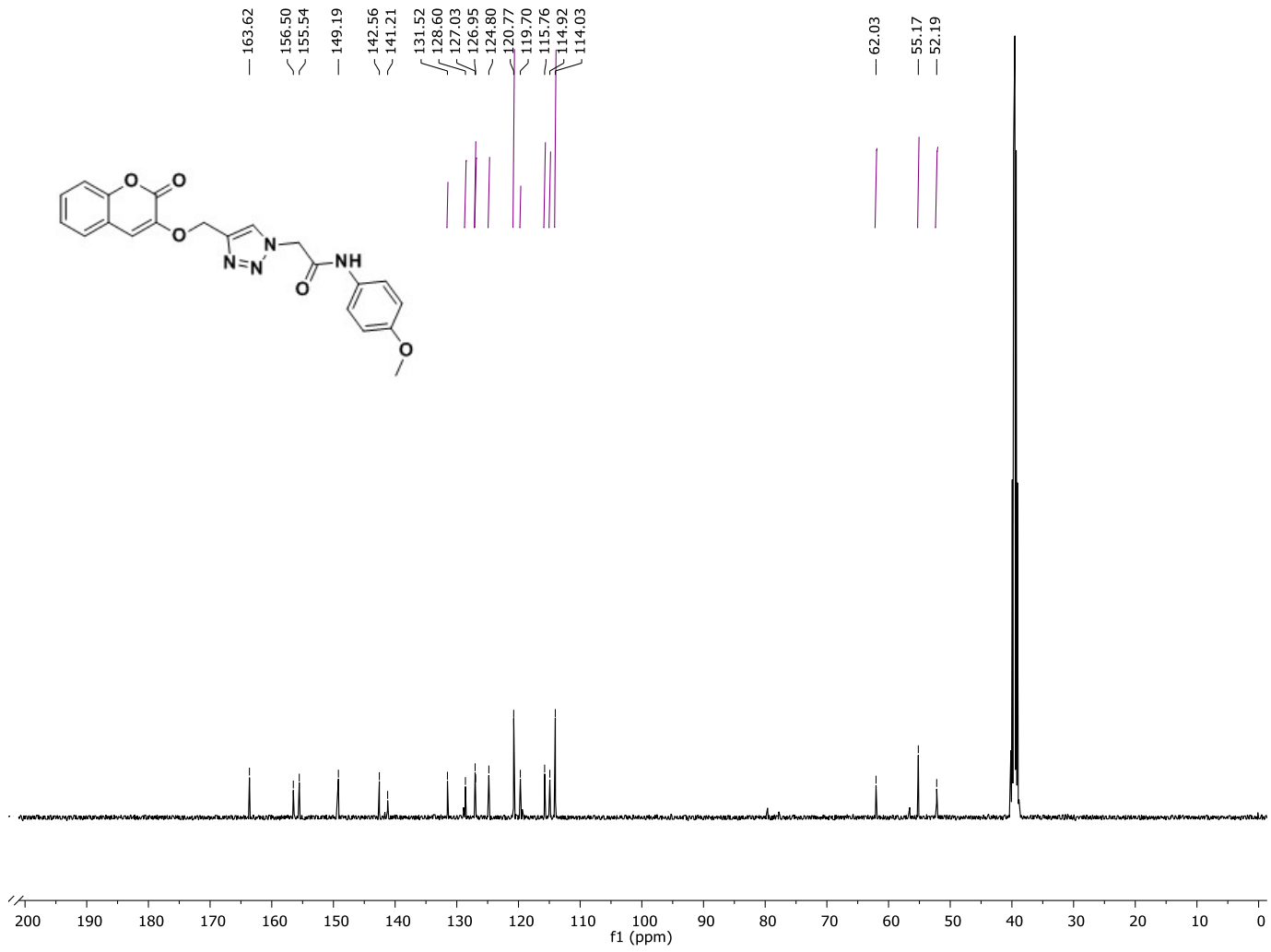
^{13}C NMR of 3m



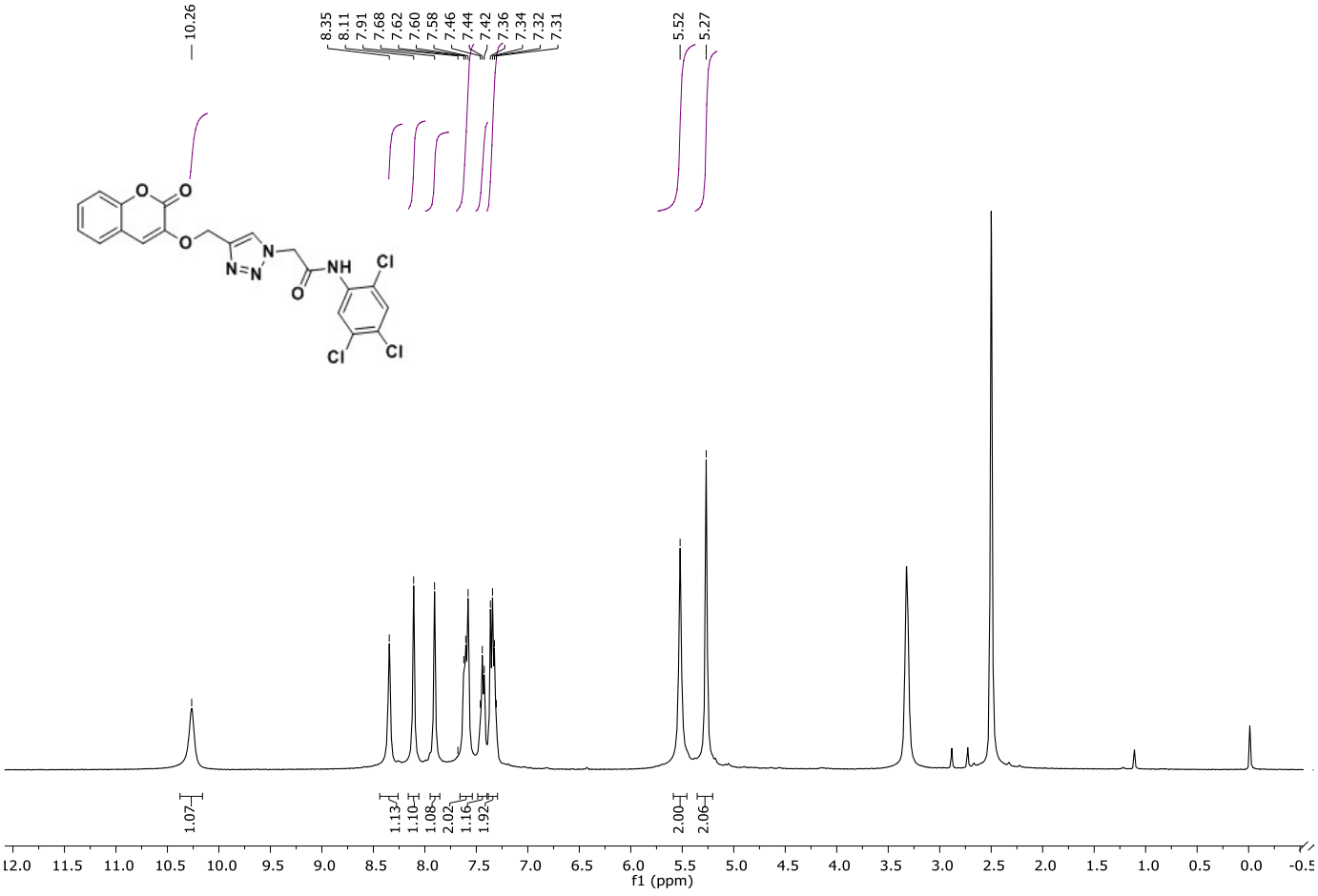
^{13}C NMR of 3m


10.37
8.35
7.63
7.62
7.60
7.51
7.49
7.47
7.45
7.43
7.42
7.38
7.36
7.34
7.32
6.91
6.89
5.35
5.25
3.72
O
O
O
N
N=N
NH
O
O
0.91
0.93
2.07
3.21
2.26
2.09
1.81
1.93
2.85
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

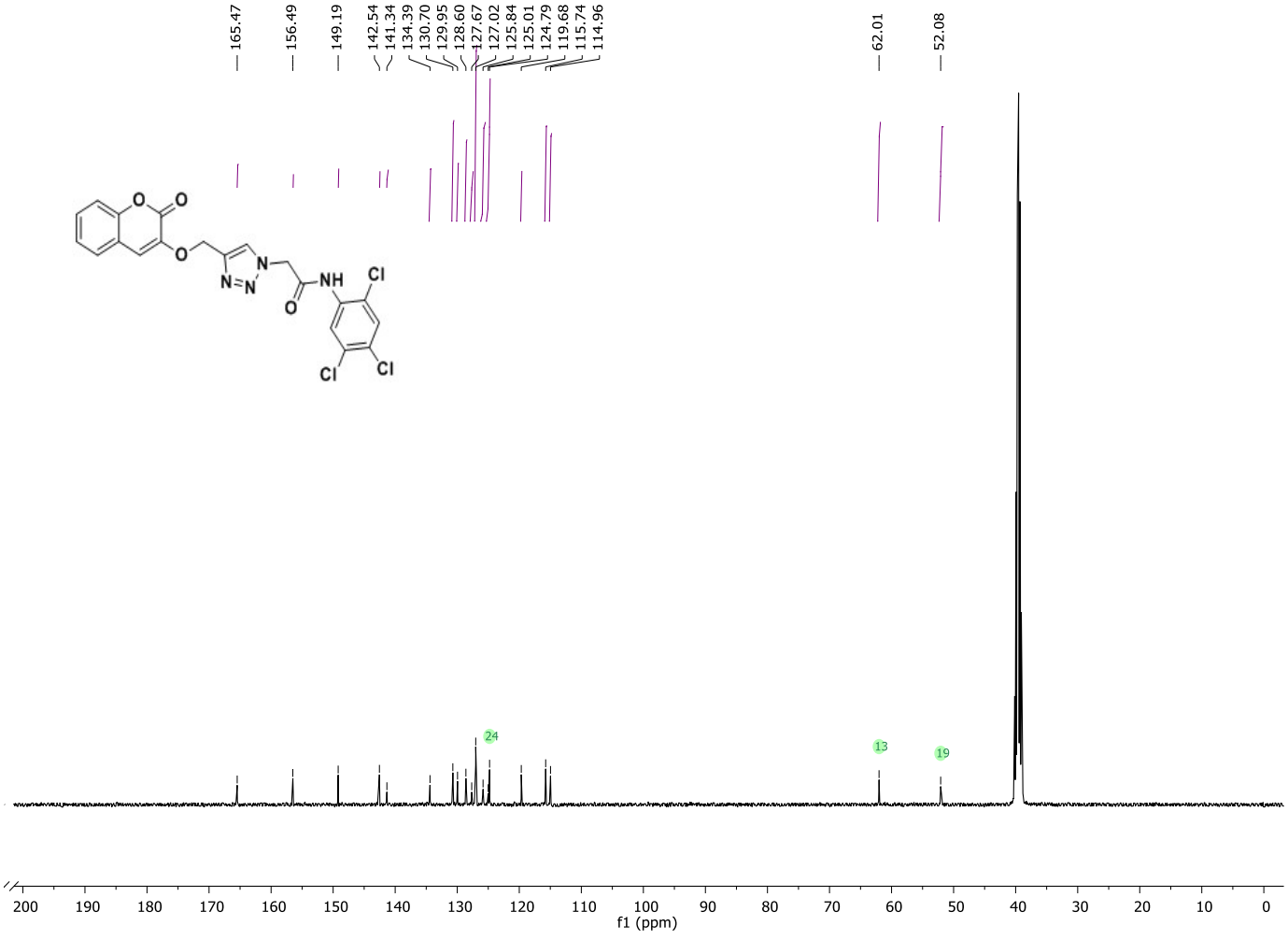
^{1}H NMR of 3n


163.62
156.50
155.54
149.19
142.56
141.21
131.52
128.60
127.03
126.95
124.80
120.77
119.70
115.76
114.92
114.03
62.03
55.17
52.19
O
O
O
N
N=N
NH
O
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

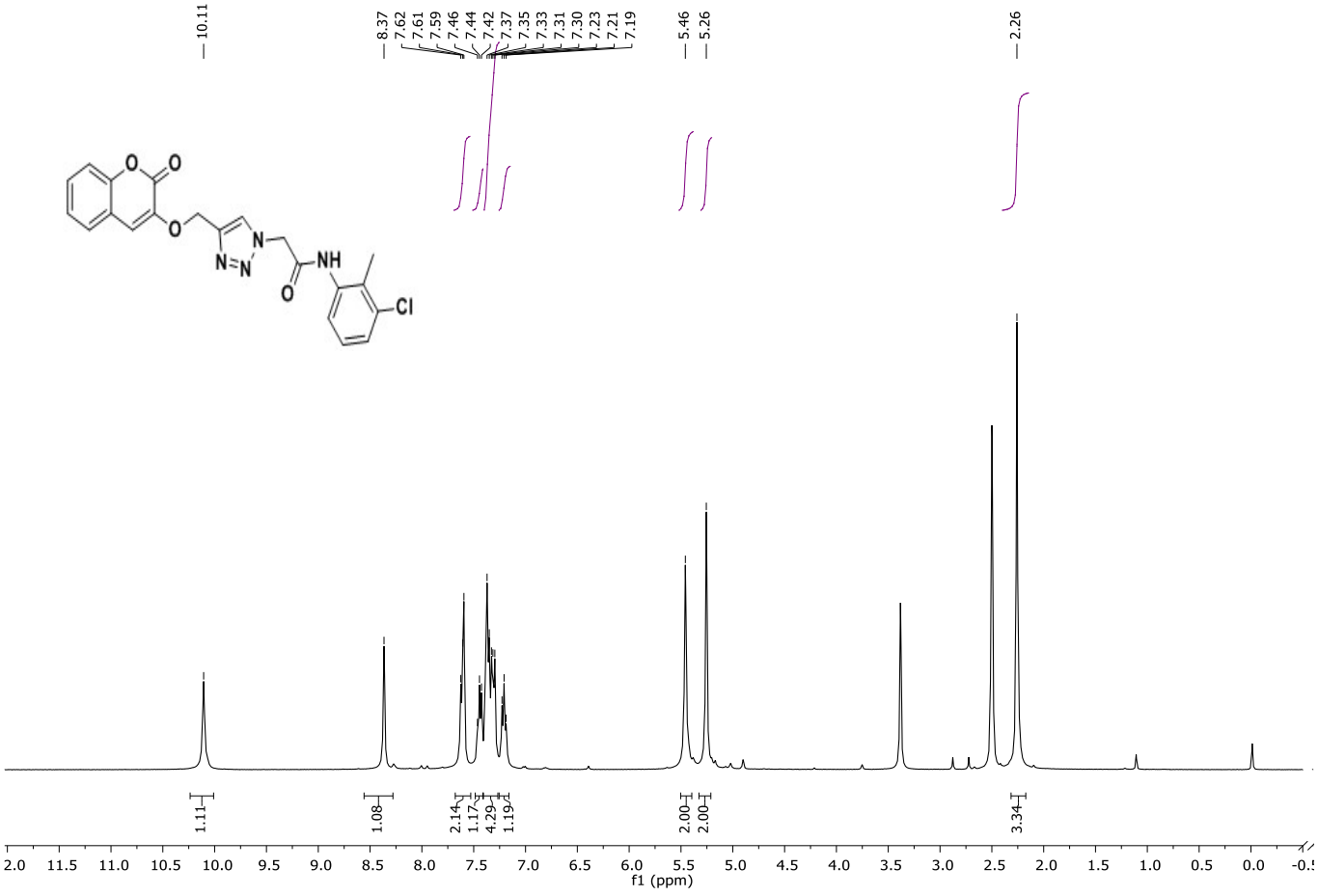
^{13}C NMR of 3n


10.26
8.35
8.11
7.91
7.68
7.62
7.60
7.58
7.46
7.44
7.42
7.36
7.34
7.32
7.31
5.52
5.27
O
O
O
N
N=N
NH
O
Cl
Cl
Cl
1.07
1.13
1.10
1.08
2.02
1.16
1.92
2.00
2.06
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

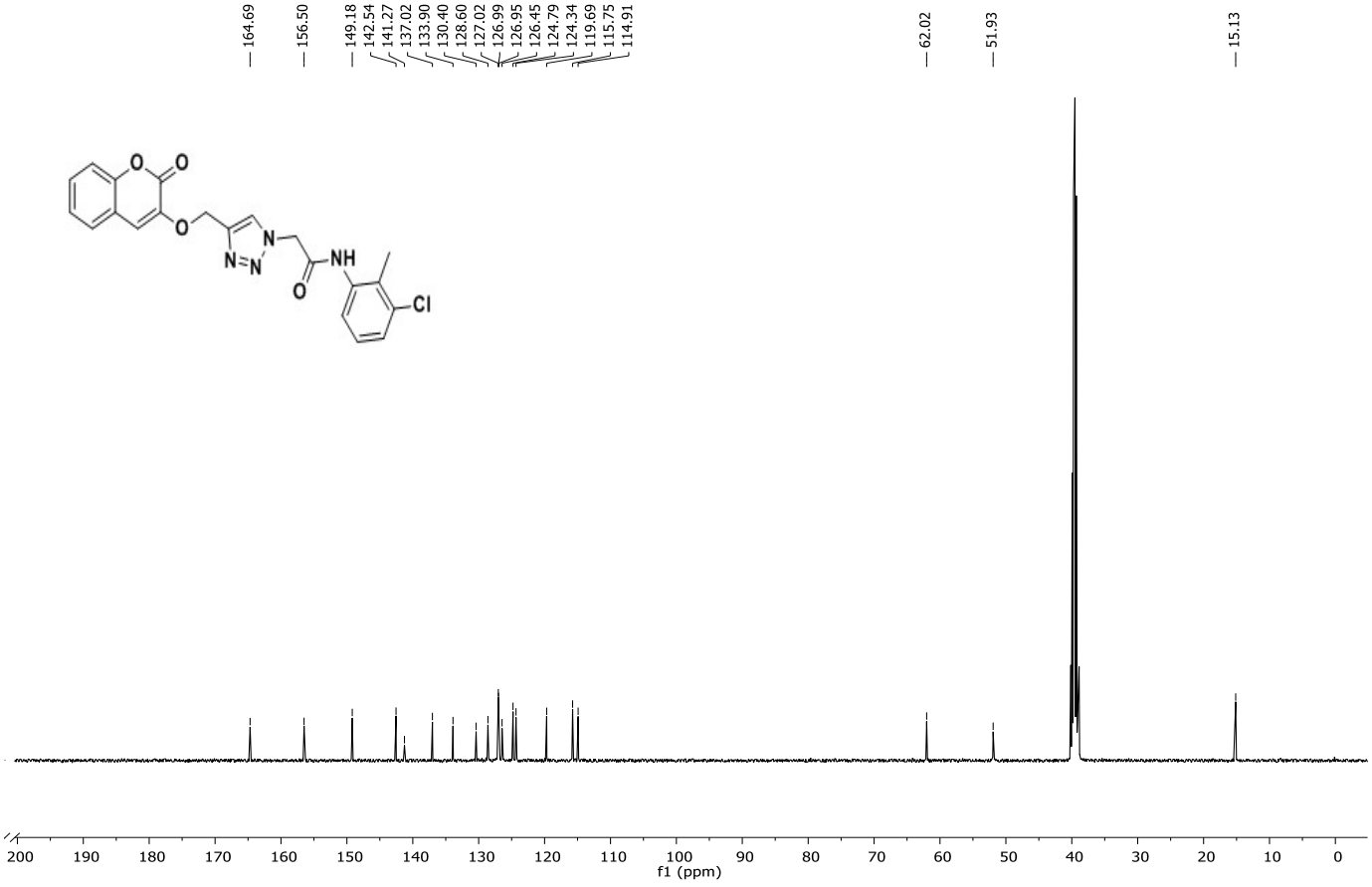
^{1}H NMR of 3o


165.47
156.49
149.19
142.54
141.34
134.39
130.70
129.95
128.60
127.67
127.02
125.84
125.01
124.79
119.68
115.74
114.96
62.01
52.08
O
O
O
N
N=N
NH
O
Cl
Cl
Cl
24
13
19
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

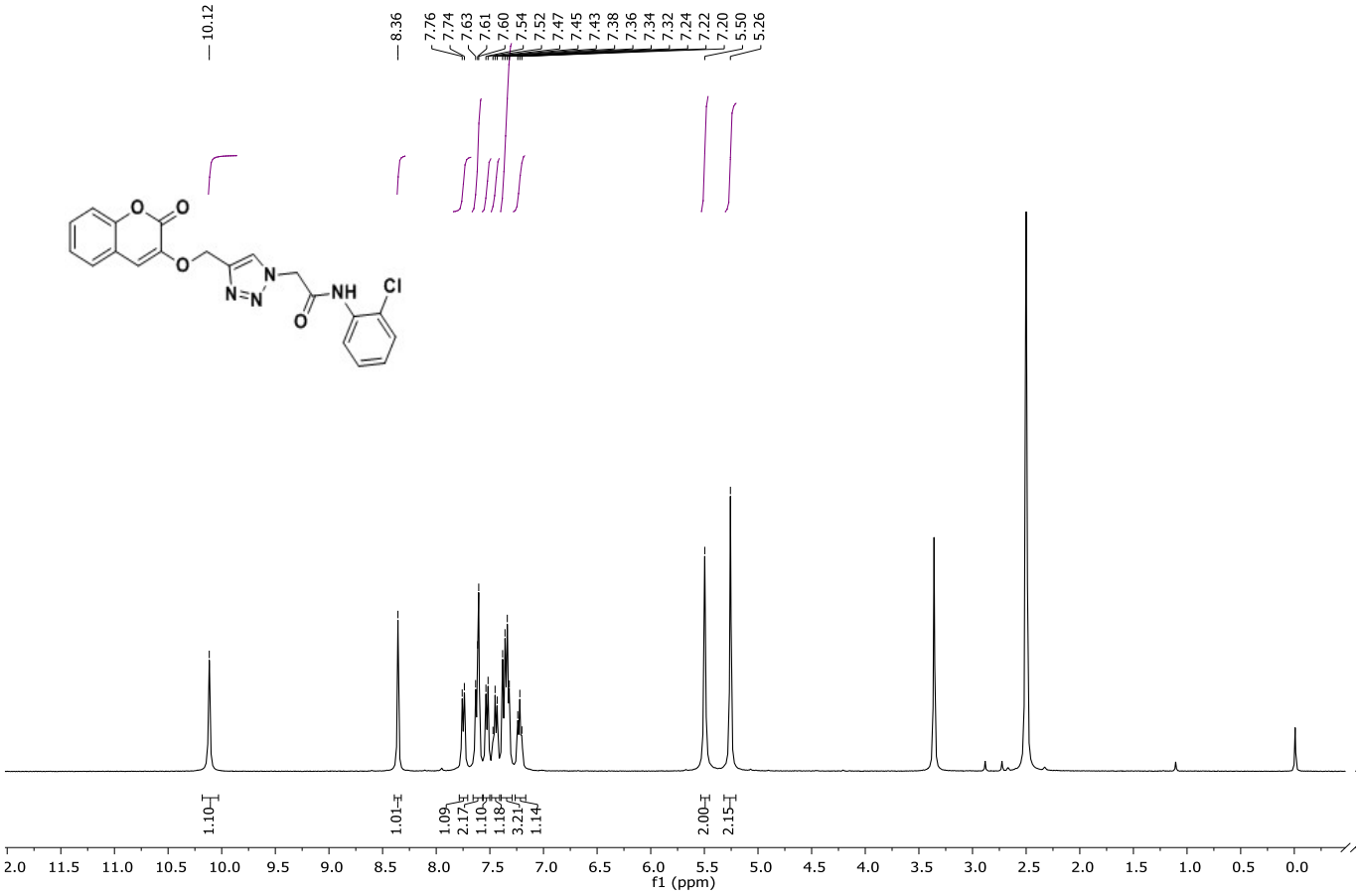
^{13}C NMR of 3o


10.11
8.37
7.62
7.61
7.59
7.46
7.44
7.42
7.37
7.35
7.33
7.31
7.30
7.23
7.21
7.19
5.46
5.26
2.26
O
O
O
N
N=N
NH
O
Cl
1.11
1.08
2.14
1.17
4.29
1.19
2.00
2.00
3.34
2.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

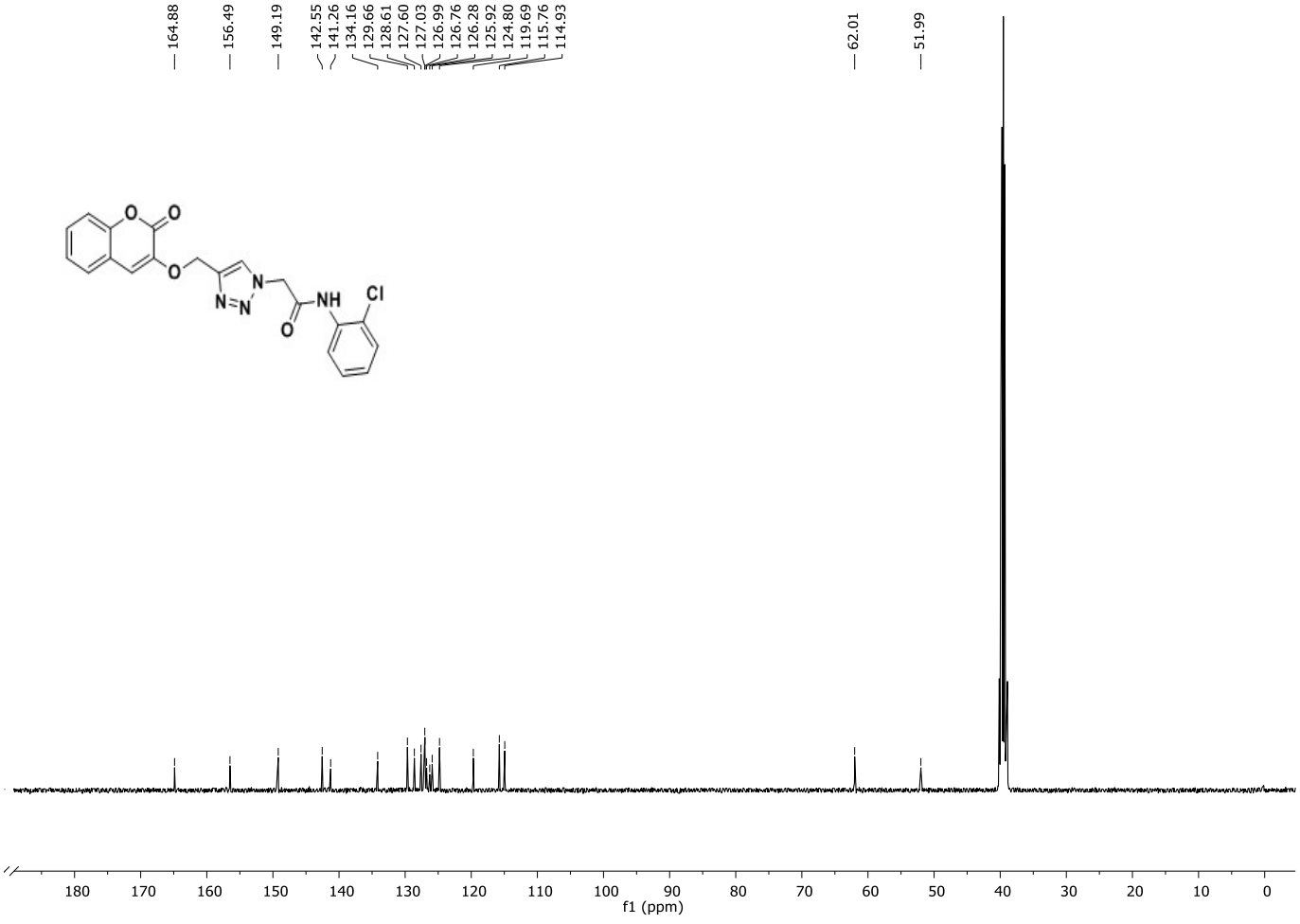
^{1}H NMR of 3p


164.69
156.50
149.18
142.54
141.27
137.02
133.90
130.40
128.60
127.02
126.99
126.95
126.45
124.79
124.34
119.69
115.75
114.91
62.02
51.93
15.13
O
O
O
N
N=N
NH
O
Cl
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

^{13}H NMR of 3p


10.12
8.36
7.76
7.74
7.63
7.61
7.60
7.54
7.52
7.47
7.45
7.43
7.38
7.36
7.34
7.32
7.24
7.22
7.20
5.50
5.26
O
O
O
N
N=N
NH
O
Cl
1.10
1.01
1.09
2.17
1.10
1.18
3.21
1.14
2.00
2.15
2.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

^{1}H NMR of 3r


164.88
156.49
149.19
142.55
141.26
134.16
129.66
128.61
127.60
127.03
126.99
126.76
126.28
125.92
124.80
119.69
115.76
114.93
62.01
51.99
O
O
O
N
N=N
NH
O
Cl
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

^{13}C NMR of 3r