Supporting Information

Catalyst-controlled Regioselective Sonogashira Coupling of 9-Substituted-6-chloro-2,8-diiodopurines

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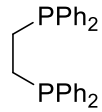
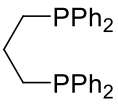
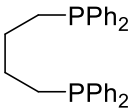
Fig. S1. The chemical structures ligands and their abbreviations



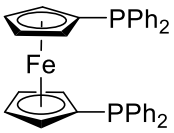
1,2-Bis(diphenylphosphino) ethane (**dppe**)



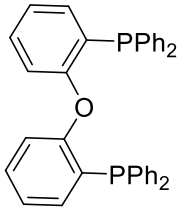
1,2-Bis(diphenylphosphino) propane (**dppp**)



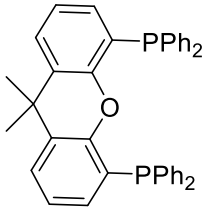
1,2-Bis(diphenylphosphino) butane (**dppb**)



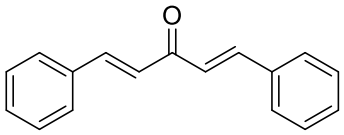
1,1 -Bis(diphenylphosphino) ferrocene (**dppf**)



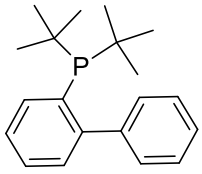
Bis[(2-diphenylphosphino) phenyl]ether (**DPEphos**)



4,5-Bis(diphenylphosphino)-9,9-dimethylxanthene (**Xantphos**)

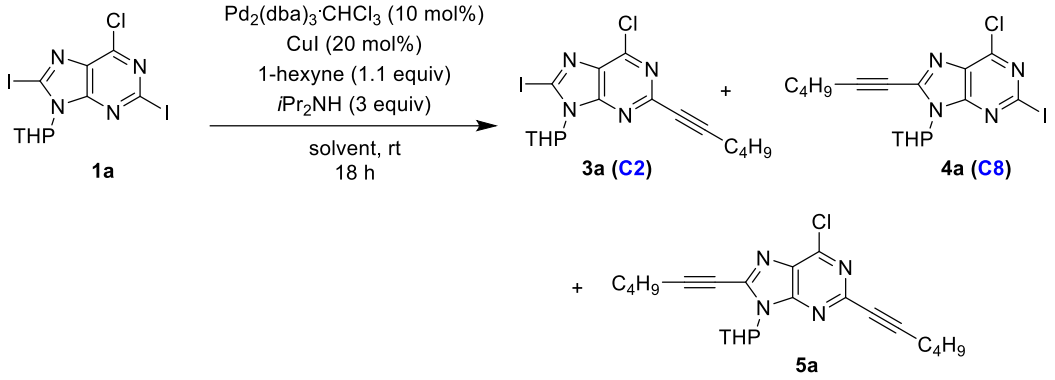


Dibenzylideneacetone (**dba**)



2-Biphenyl)di-tert-butylphosphine (**JohnPhos**)

Table S1. Solvent Screening of regioselective Sonogashira coupling reaction[a]



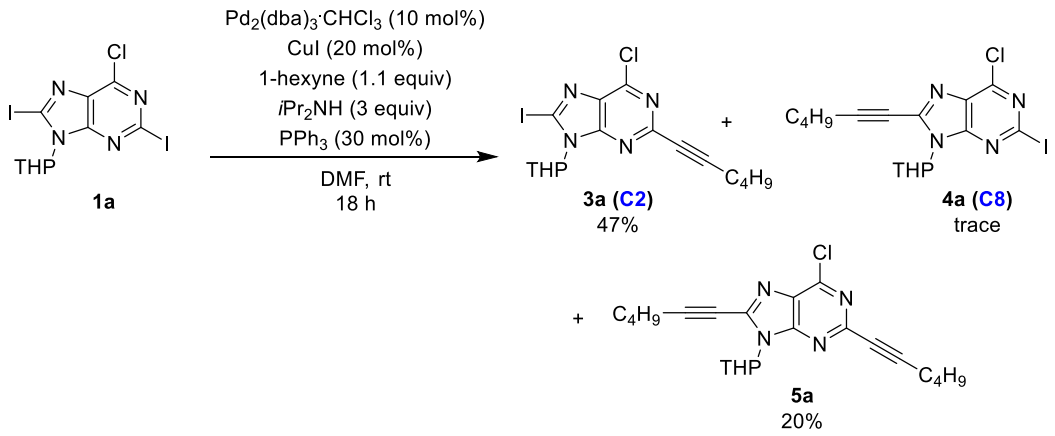
entry	solvent	yield (%)[b]		
		3a	**4a**	**5a**
1	DMF	4	69	9
2	Toluene	7	42	15
3	dichloromethane	11	38	13
4	THF	3	49	11
5	1,4-dioxane	3	49	5
6[c]	Acetonitrile	trace	20	9
7	DMF/Toluene (1:1)	trace	59	9

[a]Unless otherwise noted, all the reactions were performed with **1a** (0.2 mmol, 1 equiv), CuI (0.04 mmol, 0.2 equiv), $Pd_2(dba)_3{\cdot}CHCl_3$ (0.02 mmol, 0.1 equiv), 1-hexyne (0.22 mmol, 1.1 equiv), and iPr$_2$NH (0.6 mmol, 3 equiv) in 5.0 mL of solvent for 18 h under nitrogen atmosphere. [b]Isolated yield after silica gel column chromatography. [c]45% of **1a** was recovered.

In an attempt to improve the yield of the reaction, we briefly investigated the effect of solvent on the Sonogashira cross-coupling of **1a** with 1-hexyne. Examination of solvent effects revealed that aprotic polar solvents such as DMF, dioxane, and THF showed good results (Table S1). Among them, the use of DMF solvent showed an enhancement in the yield of the reaction as well as the regioisomeric ratio (entry 1). The use of non-polar solvents toluene and dichloromethane resulted in a greatly diminished yield of C8-alkynylated product **4a** to 42 and 38%, respectively, and also regioisomeric ratio was decreased (entries 2 and 3). When the reaction was performed in a polar solvent such as THF and 1,4-dioxane, the yield of C8-alkynylated product was increased in comparison to non-polar solvents, and only a trace amount of the C2-alkynylated product was observed (entries 4 and 5). The use of acetonitrile gave a low yield of **4a**, but 45% of **1a** was recovered (entry 6). It implies acetonitrile made the

reaction sluggish. When a mixture of DMF and toluene (1:1) was used as solvent, no improvement in the yield of **4a** was observed (entry 7).

Scheme S1. Investigation of the effect of the mixed ligands for selectivity



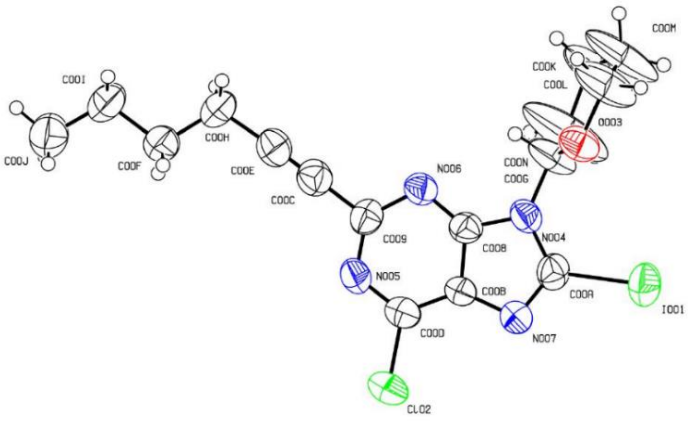
To investigate how does mixed ligand affect the regioselectivity, we also performed experiment of the Sonogashira reaction of **1a** with 1-hexyne using $Pd_2(dba)_3{\cdot}CHCl_3$-PPh_3 combination to explore the selectivity. Under this condition, C2-selective coupling product (**3a**) was obtained in 47% of isolated yield without being formation of C8-coupling product (**4a**). It demonstrated that Pd catalyst enters catalytic cycle as $Pd(PPh_3)_2$ species. Although $Pd(dba)(PPh_3)_2$ was preliminarily formed as resting state, it was converted to $Pd(PPh_3)_n$ as active species.[1]

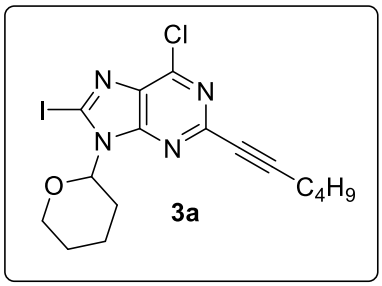
2. Single-Crystal X-ray crystallography data of compounds 3a and 4a

Sample preparation: Compound **3a** or **4a** (~5 mg) was dissolved in dichloromethane and n-hexane (0.6 mL, 1:5) in a glass vial. After slow evaporation at room temperature, the single crystals of **3a** or **4a** suitable for X-ray analysis were obtained.

Crystal structure determination: X-ray diffraction data of **3a** (CCDC: 2164196) and **4a** (CCDC: 2164194) were collected on a SuperNova, Dual, Cu at zero, AtlasS2 diffractometer. The crystal was kept at 294.1(2) K (for **3a**) and 291.7(6) K (for **4a**) during data collection. Using Olex2 [2], the structure was solved with the ShelXT [3] structure solution program using Intrinsic Phasing and refined with the ShelXL[4] refinement package using Least Squares minimization

2.1 Single-Crystal X-ray crystallography data of compound 3a





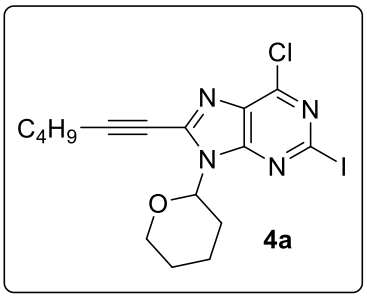
CCDC No: 2164196

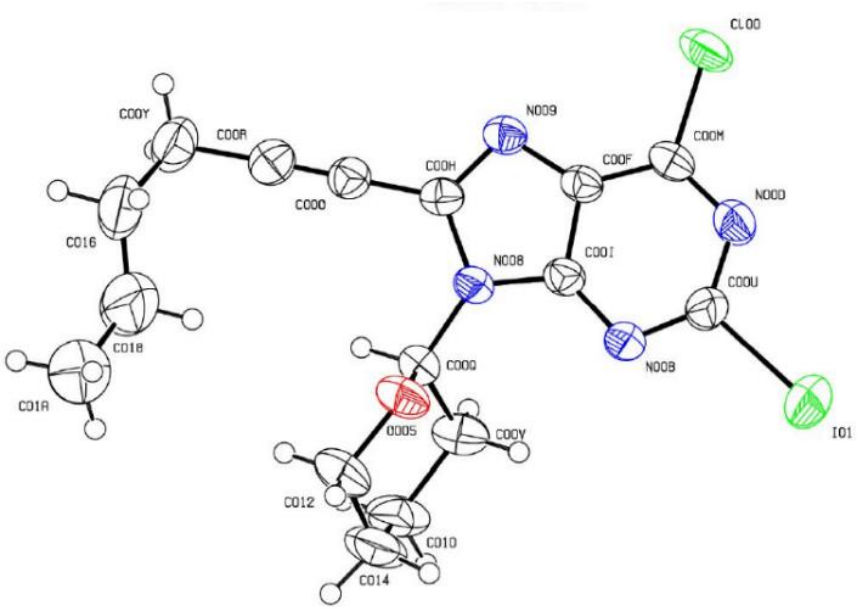
Fig S2. ORTEP diagram of compound **3a** showing thermal ellipsoid at 50% probability.

Table S2. Crystal data and structure refinement for 3a

Empirical formula	$C_{16}H_{18}ClIN_4O$
Formula weight	443.68
Temperature/K	294.1(2)
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	10.3449(9)
b/Å	15.2749(15)
c/Å	11.5805(13)
α/°	90
β/°	98.234(10)
γ/°	90
Volume/Å^3	1811.1(3)
Z	4
ρ_{calc}g/cm^3	1.627
μ/mm^{-1}	1.925
F(000)	876.0
Crystal size/mm^3	0.5 × 0.3 × 0.1
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.444 to 59.278
Index ranges	$-12 \leq h \leq 14$, $-16 \leq k \leq 20$, $-12 \leq l \leq 14$
Reflections collected	8344
Independent reflections	4171 [R_{int} = 0.0644, R_{sigma} = 0.0744]
Data/restraints/parameters	4171/0/210
Goodness-of-fit on F^2	1.032
Final R indexes [I>=2σ (I)]	R_1 = 0.0726, wR_2 = 0.1998
Final R indexes [all data]	R_1 = 0.1110, wR_2 = 0.2446
Largest diff. peak/hole / e Å^{-3}	1.03/-0.85

2.2 Single-Crystal X-ray crystallography data of compound 4a





CCDC No: 2164194

Fig S3. ORTEP diagram of compound **4a** showing thermal ellipsoid at 50% probability.

Table S3. Crystal data and structure refinement for 4a

Empirical formula	$C_{16}H_{18}ClIN_4O$
Formula weight	444.69
Temperature/K	291.7(6)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	11.7366(6)
b/Å	17.1589(6)
c/Å	9.5008(6)
α/°	90
β/°	108.684(6)
γ/°	90
Volume/Å^3	1812.51(17)
Z	4
ρ_{calc}g/cm^3	1.630
μ/mm^{-1}	1.923
F(000)	880.0
Crystal size/mm^3	0.325 × 0.268 × 0.162
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.366 to 59.382
Index ranges	$-14 \leq h \leq 15$, $-23 \leq k \leq 22$, $-13 \leq l \leq 11$
Reflections collected	16669
Independent reflections	4552 [R_{int} = 0.0326, R_{sigma} = 0.0331]
Data/restraints/parameters	4552/0/209
Goodness-of-fit on F^2	1.049
Final R indexes [I>=2σ (I)]	R_1 = 0.0579, wR_2 = 0.1218
Final R indexes [all data]	R_1 = 0.0842, wR_2 = 0.1348
Largest diff. peak/hole / e Å^{-3}	1.12/-0.84

Computational details

The B3LYP density functional method[5] was used for the geometry optimization, natural bond orbital (NBO) analysis in implicit solvent using the conductor-like polarizable continuum model (CPCM)[6] to consider the effect of toluene. The vibrational frequency analysis was performed to calculate the zero-point energy and thermal correction at 298.15 K, 1 atm. The basis sets of 6-31+G(d)[7] and Lanl2dz[8] (Pd, I) were employed depending on the substrate and analysis. The bonding dissociation energy was calculated by sum of enthalpy for cleaved molecules and substrate **1a**. All of these calculations were carried out by Gaussian 09.[9]

Cartesian Coordinates and Energies

1a

	Center Number	Atomic Number	Atomic Type		
1	7	0	2.641960	-1.440055	0.017372
2	6	0	2.580792	-0.172890	-0.021335
3	7	0	1.500970	0.491414	-0.052565
4	6	0	0.413810	-0.149309	-0.045187
5	6	0	0.405494	-1.490864	-0.005164
6	6	0	1.581592	-2.133687	0.027343
7	7	0	-0.820399	0.130293	-0.066402
8	6	0	-1.544600	-0.910309	-0.041041
9	7	0	-0.784030	-1.924534	-0.000988
10	17	0	1.656960	-3.858293	0.080661
11	53	0	4.440785	0.933358	-0.031983
12	53	0	-3.685634	-1.115994	0.012320
13	6	0	-1.296825	1.527678	-0.123822
14	8	0	-2.310189	1.707101	-1.090258
15	6	0	-2.688919	3.051395	-1.244934
16	6	0	-3.253619	3.606320	0.059655
17	6	0	-2.211948	3.477832	1.176549
18	6	0	-1.747078	2.018791	1.253339
19	1	0	-0.433539	2.157882	-0.449833
20	1	0	-3.466324	3.085633	-2.043446
21	1	0	-1.817422	3.646639	-1.600753
22	1	0	-3.546730	4.675028	-0.071561
23	1	0	-4.174567	3.040378	0.338682
24	1	0	-2.639430	3.806552	2.153311
25	1	0	-1.340677	4.138966	0.953944
26	1	0	-2.583011	1.387510	1.633028

27	1	0	-0.909740	1.925702	1.985242

Zero-point correction= 0.190229 (Hartree/Particle)
Thermal correction to Energy= 0.206410
Thermal correction to Enthalpy= 0.207354
Thermal correction to Gibbs Free Energy= 0.142104
Sum of electronic and zero-point Energies= -1163.488250
Sum of electronic and thermal Energies= -1163.472068
Sum of electronic and thermal Enthalpies= -1163.471124
Sum of electronic and thermal Free Energies= -1163.536374

C8-I fragment (fragment of purine)

	Center Number	Atomic Number	Atomic Type		
1	7	0	2.211823	1.045746	0.061577
2	6	0	1.613107	-0.143016	-0.035524
3	7	0	0.312340	-0.403669	-0.123697
4	6	0	-0.425329	0.701354	-0.105806
5	6	0	0.063394	2.025771	-0.008744
6	6	0	1.448687	2.134917	0.074489
7	7	0	-1.807925	0.819213	-0.194534
8	6	0	-2.032511	2.173133	-0.122092
9	7	0	-1.004556	2.923004	-0.024502
10	17	0	2.230971	3.680380	0.196814
11	53	0	2.912636	-1.833671	-0.053582
12	6	0	-2.785943	-0.257562	-0.207438
13	8	0	-3.228683	-0.417948	1.132374
14	6	0	-4.154382	-1.510660	1.276104
15	6	0	-5.399976	-1.299329	0.417143
16	6	0	-5.003315	-1.075190	-1.050239
17	6	0	-3.946342	0.036986	-1.159816
18	1	0	-2.240528	-1.156951	-0.525986
19	1	0	-4.390513	-1.545319	2.342287
20	1	0	-3.645454	-2.449193	1.003232
21	1	0	-6.059631	-2.171007	0.513008
22	1	0	-5.951269	-0.427731	0.794226
23	1	0	-5.879461	-0.815464	-1.655151
24	1	0	-4.595623	-2.007181	-1.467820
25	1	0	-4.386410	1.005149	-0.885304
26	1	0	-3.563954	0.120883	-2.183844

Zero-point correction= 0.188181 (Hartree/Particle)
Thermal correction to Energy= 0.202623
Thermal correction to Enthalpy= 0.203567
Thermal correction to Gibbs Free Energy= 0.142167

Sum of electronic and zero-point Energies= -1152.028524
Sum of electronic and thermal Energies= -1152.014082
Sum of electronic and thermal Enthalpies= -1152.013138
Sum of electronic and thermal Free Energies= -1152.074538

C2-I fragment (fragment of purine)

	Center Number	Atomic Number	Atomic Type		
1	7	0	3.806459	1.656455	-0.043029
2	6	0	2.949574	2.591469	-0.092471
3	7	0	1.694295	2.412208	-0.113195
4	6	0	1.267391	1.225048	-0.083173
5	6	0	2.118360	0.188451	-0.030658
6	6	0	3.433985	0.445753	-0.010338
7	7	0	0.139195	0.651418	-0.087959
8	6	0	0.247095	-0.611197	-0.041858
9	7	0	1.480405	-0.904877	-0.004170
10	17	0	4.594141	-0.831819	0.057712
11	53	0	-1.268190	-2.136096	0.046356
12	6	0	-1.120441	1.421038	-0.150918
13	8	0	-2.020371	0.895409	-1.103251
14	6	0	-3.171513	1.684947	-1.264466
15	6	0	-3.952692	1.773197	0.043491
16	6	0	-3.062633	2.358634	1.145352
17	6	0	-1.772378	1.534532	1.228425
18	1	0	-0.860930	2.451713	-0.495979
19	1	0	-3.796170	1.201200	-2.051195
20	1	0	-2.883527	2.693471	-1.639134
21	1	0	-4.861757	2.405833	-0.093044
22	1	0	-4.297896	0.754328	0.341871
23	1	0	-3.595684	2.354977	2.125508
24	1	0	-2.816126	3.419953	0.903273
25	1	0	-2.009839	0.521410	1.626743
26	1	0	-1.064414	2.010165	1.948176

Zero-point correction= 0.188733 (Hartree/Particle)
Thermal correction to Energy= 0.202999
Thermal correction to Enthalpy= 0.203943
Thermal correction to Gibbs Free Energy= 0.144388
Sum of electronic and zero-point Energies= -1152.031122
Sum of electronic and thermal Energies= -1152.016856
Sum of electronic and thermal Enthalpies= -1152.015912
Sum of electronic and thermal Free Energies= -1152.075467

Iodine

Zero-point correction=	0.000000 (Hartree/Particle)
Thermal correction to Energy=	0.001416
Thermal correction to Enthalpy=	0.002360
Thermal correction to Gibbs Free Energy=	-0.017503
Sum of electronic and zero-point Energies=	-11.363637
Sum of electronic and thermal Energies=	-11.362221
Sum of electronic and thermal Enthalpies=	-11.361277
Sum of electronic and thermal Free Energies=	-11.381140

Molecular Orbital Coefficients of Substrate(1a), LUMO = 59

				59	60	61	62	63
				O	O	O	O	O
		Eigenvalues --		-0.29066	-0.28658	-0.27362	-0.27099	-0.25943
1	1	N	1S	0.00371	-0.00140	0.03079	-0.02154	-0.00017
2			2S	-0.00966	0.00330	-0.07024	0.04824	0.00037
3			3S	-0.00142	0.00241	-0.11299	0.07791	0.00016
4			4PX	0.01027	-0.00912	0.17594	-0.13763	-0.00086
5			4PY	0.04281	-0.00170	-0.06792	0.07532	0.00108
6			4PZ	-0.07623	-0.02729	0.02809	0.03260	-0.09753
7			5PX	0.01212	-0.00329	0.05676	-0.03413	0.00007
8			5PY	0.02543	-0.00173	-0.04113	0.05320	0.00156
9			5PZ	-0.04071	-0.01577	0.01448	0.01731	-0.04736
10	2	C	1S	-0.00544	0.00085	-0.00197	-0.00155	-0.00006
11			2S	0.01249	-0.00163	0.00477	0.00392	0.00010
12			3S	0.03573	-0.00669	0.01765	0.01310	0.00171
13			4PX	0.00904	0.00093	-0.02694	0.03077	0.00225
14			4PY	-0.02426	0.00064	0.04504	-0.04582	-0.00119
15			4PZ	0.02962	0.04420	0.00636	0.01217	-0.21157
16			5PX	-0.02253	-0.00097	0.02441	-0.02764	0.00098
17			5PY	0.01860	0.00002	-0.02052	0.04103	0.00178
18			5PZ	0.01829	0.03636	0.00128	0.00224	-0.07776
19	3	N	1S	0.00771	-0.00012	-0.02271	0.02605	0.00046
20			2S	-0.02054	0.00110	0.05218	-0.05941	-0.00100
21			3S	0.01868	-0.00824	0.06333	-0.08183	-0.00219
22			4PX	0.01683	-0.00559	-0.00352	0.00278	0.00133
23			4PY	0.11578	-0.01163	-0.16083	0.18511	0.00273
24			4PZ	0.02783	-0.12956	-0.00756	-0.00838	-0.14584
25			5PX	0.02955	-0.00627	0.02726	-0.01202	0.00077
26			5PY	0.05472	-0.00712	-0.06245	0.06859	0.00027
27			5PZ	0.01433	-0.06814	-0.00530	-0.00703	-0.07542

28	4	C	1S	0.00811	-0.00116	0.00989	-0.00088	0.00079
29			2S	-0.01179	0.00188	-0.02619	0.00397	-0.00262
30			3S	-0.17672	0.02490	-0.07911	-0.04725	-0.00509
31			4PX	-0.02039	0.00106	0.03191	-0.06919	-0.00635
32			4PY	-0.07734	0.01215	0.06923	-0.04561	0.00259
33			4PZ	-0.02979	-0.08159	-0.00471	-0.00734	0.19051
34			5PX	0.00505	-0.00737	-0.00072	-0.02281	-0.00123
35			5PY	0.03278	-0.00912	-0.06422	-0.00553	-0.00236
36			5PZ	-0.01844	-0.04780	0.00387	0.00505	0.07220
37	5	C	1S	-0.00959	0.00125	0.00368	-0.00691	-0.00016
38			2S	0.02879	-0.00424	-0.01189	0.01458	-0.00017
39			3S	0.00181	0.00688	0.01297	0.06915	0.00484
40			4PX	0.07686	-0.01455	0.03095	-0.00032	-0.00102
41			4PY	0.09202	-0.01538	-0.08577	0.07625	0.00074
42			4PZ	0.02974	-0.02718	-0.03222	-0.04426	0.21998
43			5PX	-0.06959	0.00784	0.03506	-0.06000	-0.00023
44			5PY	-0.07393	0.01053	-0.05998	0.00594	-0.00114
45			5PZ	0.01722	0.00551	-0.01595	-0.02294	0.08813
46	6	C	1S	-0.00532	0.00108	-0.00614	0.00585	0.00023
47			2S	0.01902	-0.00329	0.01446	-0.01171	-0.00072
48			3S	-0.01957	-0.00185	0.05685	-0.08768	-0.00166
49			4PX	0.00249	0.00180	-0.07651	0.04587	-0.00163
50			4PY	-0.01019	0.00231	-0.03332	0.02918	0.00086
51			4PZ	-0.05361	-0.06475	-0.00161	-0.00537	0.17362
52			5PX	0.02798	-0.00634	0.03402	-0.01777	0.00054
53			5PY	0.07690	-0.00899	-0.03759	0.05718	0.00061
54			5PZ	-0.01921	-0.03250	0.00144	0.00018	0.05575
55	7	N	1S	0.00217	-0.00100	-0.00283	-0.00469	-0.00093
56			2S	-0.01015	0.00312	0.00593	0.00923	0.00197
57			3S	0.01298	0.00022	0.02186	0.03505	0.00664
58			4PX	-0.01835	-0.00022	0.05084	-0.00628	0.00424
59			4PY	0.01552	-0.01253	0.01084	0.00086	0.00181
60			4PZ	-0.07282	0.12862	0.03430	0.04064	0.02948
61			5PX	-0.05413	0.00347	0.01371	-0.05851	-0.00146
62			5PY	0.06215	-0.02233	0.00126	0.00194	0.00373
63			5PZ	-0.03641	0.09563	0.01576	0.01825	0.02084
64	8	C	1S	-0.01187	0.00085	0.00789	-0.00870	0.00043
65			2S	0.02849	-0.00312	-0.01975	0.02194	0.00001
66			3S	0.03585	0.01181	-0.01476	0.06137	-0.00636
67			4PX	-0.00761	0.00246	0.01173	-0.02918	-0.00264
68			4PY	0.02725	-0.00217	-0.03630	0.00430	-0.00398
69			4PZ	0.01374	0.06712	0.02424	0.03320	-0.23180
70			5PX	0.00587	-0.01046	-0.00747	-0.01560	0.00343

71			5PY	0.03922	-0.01419	0.03060	0.00235	0.00081
72			5PZ	0.00171	0.00789	0.01201	0.01630	-0.10108
73	9	N	1S	0.04082	-0.00679	-0.00979	0.01772	0.00004
74			2S	-0.09420	0.01607	0.02199	-0.03946	-0.00018
75			3S	-0.13117	0.02111	0.02024	-0.06681	0.00051
76			4PX	-0.11969	0.02100	0.00235	-0.04052	0.00030
77			4PY	-0.15218	0.01938	0.07512	-0.06932	-0.00025
78			4PZ	0.09782	0.10256	-0.01641	-0.01650	-0.22527
79			5PX	-0.07532	0.01272	0.00123	-0.02087	0.00124
80			5PY	-0.05422	0.00935	0.03796	-0.02434	-0.00048
81			5PZ	0.04820	0.05397	-0.00796	-0.00763	-0.11661
82	10	Cl	1S	-0.00278	0.00022	0.00833	-0.00738	-0.00002
83			2S	-0.03328	0.00392	0.02801	-0.02890	0.00004
84			3PX	0.00787	0.00044	0.00440	0.00426	0.00100
85			3PY	0.03597	-0.00386	-0.04747	0.04222	0.00009
86			3PZ	0.04571	0.05328	0.00193	0.00483	-0.09719
87			4PX	0.00446	0.00110	0.00718	0.00289	0.00109
88			4PY	0.05021	-0.00561	-0.06066	0.05385	-0.00005
89			4PZ	0.05237	0.06426	0.00191	0.00513	-0.11511
90	11	I	1S	-0.00021	-0.00016	0.00095	-0.00012	-0.00001
91			2S	-0.00583	-0.00011	0.00395	-0.00136	0.00041
92			3PX	-0.01909	-0.00305	-0.20863	0.15753	-0.00123
93			3PY	0.09457	-0.01095	0.35203	-0.23221	0.00005
94			3PZ	0.12191	0.37049	-0.03021	-0.03611	0.33870
95			4PX	-0.02135	-0.00197	-0.18042	0.13684	-0.00096
96			4PY	0.07510	-0.00890	0.30376	-0.20375	0.00007
97			4PZ	0.10461	0.32271	-0.02700	-0.03262	0.31970
98	12	I	1S	0.00189	0.00104	-0.00286	-0.00243	-0.00121
99			2S	-0.00307	0.00492	-0.00173	-0.00212	-0.00276
100			3PX	-0.08881	0.01588	-0.00630	-0.02274	-0.00075
101			3PY	0.43149	-0.11348	0.13824	0.19163	0.02380
102			3PZ	-0.06773	-0.36692	-0.00324	-0.00380	0.26695
103			4PX	-0.06314	0.01223	-0.00616	-0.01569	-0.00068
104			4PY	0.35470	-0.09126	0.11328	0.15488	0.01831
105			4PZ	-0.06093	-0.31844	-0.00732	-0.00991	0.25607
106	13	C	1S	-0.00673	0.00295	0.00540	0.00305	0.00101
107			2S	0.01064	-0.00561	-0.01337	-0.01332	-0.00334
108			3S	0.08472	-0.02378	-0.03160	0.02402	0.00338
109			4PX	0.01917	-0.01357	-0.06005	-0.10492	-0.01283
110			4PY	0.00392	0.00152	0.00356	-0.01999	-0.00101
111			4PZ	0.08771	-0.05723	-0.06776	-0.08532	-0.00571
112			5PX	-0.03915	0.01196	0.08041	0.07240	0.00258
113			5PY	0.03421	-0.00973	0.02598	0.02053	0.00025

114		5PZ	-0.01431	-0.01789	0.02082	0.02490	0.00831
115	14 O	1S	-0.01188	0.00646	-0.00048	-0.00346	-0.00274
116		2S	0.02935	-0.01500	0.00045	0.00693	0.00565
117		3S	0.02643	-0.01965	0.00553	0.01771	0.01337
118		4PX	-0.10026	0.00635	0.27028	0.36934	0.03842
119		4PY	0.04804	-0.03510	0.05120	0.09000	0.01656
120		4PZ	-0.17382	0.08222	0.20698	0.26863	0.02966
121		5PX	-0.05079	0.00558	0.14062	0.19672	0.01941
122		5PY	0.03263	-0.02234	0.02537	0.04658	0.01126
123		5PZ	-0.08982	0.04204	0.10540	0.13627	0.01790
124	15 C	1S	-0.00173	0.00131	0.00410	0.00623	0.00092
125		2S	0.00281	-0.00144	-0.01079	-0.01664	-0.00300
126		3S	0.01754	-0.01792	-0.01557	-0.01884	0.00307
127		4PX	0.03287	-0.00374	-0.06982	-0.08884	-0.00648
128		4PY	-0.03932	0.01963	-0.00200	-0.01671	-0.00613
129		4PZ	0.07463	-0.03463	-0.06952	-0.08796	-0.01035
130		5PX	-0.01538	0.00624	0.01616	0.02988	0.00185
131		5PY	0.00869	-0.00588	-0.01292	-0.01912	-0.00317
132		5PZ	0.01442	-0.00561	-0.00881	-0.01320	-0.00274
133	16 C	1S	-0.00532	0.00225	0.00948	0.01272	0.00104
134		2S	0.01072	-0.00408	-0.02110	-0.02836	-0.00245
135		3S	0.03831	-0.01838	-0.06965	-0.09326	-0.00878
136		4PX	-0.01342	0.00764	0.05135	0.06606	0.00499
137		4PY	0.06225	-0.02179	-0.04483	-0.05284	-0.00532
138		4PZ	-0.09356	0.03562	0.09524	0.12194	0.01253
139		5PX	-0.00406	0.00486	0.00876	0.00984	0.00113
140		5PY	0.00499	0.00290	0.01117	0.01760	0.00207
141		5PZ	-0.03849	0.01038	0.04760	0.06823	0.00784
142	17 C	1S	0.00370	-0.00158	0.00074	0.00218	-0.00074
143		2S	-0.00886	0.00392	-0.00064	-0.00326	0.00141
144		3S	-0.00937	0.00292	-0.02972	-0.04828	0.00324
145		4PX	-0.00249	-0.01272	-0.02161	-0.02431	-0.00166
146		4PY	-0.05753	0.01494	0.02020	0.01406	0.01027
147		4PZ	0.05065	-0.02928	-0.04053	-0.05027	-0.00502
148		5PX	0.00992	-0.00281	-0.01009	-0.02165	-0.00373
149		5PY	-0.01452	-0.00035	0.00732	0.00443	0.00586
150		5PZ	0.02014	-0.01620	-0.04304	-0.05974	-0.00545
151	18 C	1S	-0.01221	0.00370	0.00885	0.01126	0.00374
152		2S	0.02295	-0.00742	-0.01917	-0.02493	-0.00673
153		3S	0.09266	-0.01473	-0.07263	-0.09297	-0.03256
154		4PX	0.01654	0.03470	0.05848	0.07853	0.00118
155		4PY	0.09936	-0.01999	-0.04105	-0.04024	-0.01825
156		4PZ	-0.09240	0.05733	0.10032	0.12923	0.01469

157		5PX	-0.00470	0.01101	0.00644	0.02692	0.00124
158		5PY	0.03599	-0.01382	-0.04336	-0.04975	-0.00693
159		5PZ	-0.02123	0.02012	0.04999	0.06612	0.00777
160	19 H	1S	-0.02086	0.01040	0.05773	0.08102	0.00899
161		2S	-0.05674	0.01977	0.14533	0.15277	0.01436
162	20 H	1S	-0.02907	0.01855	0.00474	0.00434	0.00127
163		2S	-0.02907	0.02258	0.00359	-0.00112	-0.00057
164	21 H	1S	-0.01357	-0.00160	0.05741	0.07925	0.00839
165		2S	-0.02589	0.00281	0.09462	0.13359	0.01186
166	22 H	1S	-0.02925	0.01020	0.01861	0.01988	0.00200
167		2S	-0.04369	0.01666	0.04900	0.06154	0.00716
168	23 H	1S	0.00939	-0.00151	0.01450	0.02054	0.00118
169		2S	0.00281	-0.00165	0.02225	0.03191	0.00188
170	24 H	1S	0.03594	-0.02322	-0.04034	-0.04905	-0.00524
171		2S	0.03706	-0.02382	-0.02680	-0.02623	-0.00363
172	25 H	1S	0.01568	0.00580	0.01181	0.01736	-0.00138
173		2S	0.02722	0.00392	0.02223	0.02899	-0.00154
174	26 H	1S	0.02545	0.00786	0.01613	0.02826	-0.00147
175		2S	0.00036	0.00839	0.03352	0.04281	0.00900
176	27 H	1S	-0.03808	0.01024	0.01670	0.01957	0.00290
177		2S	-0.06165	0.01617	0.02325	0.03118	0.00668

Experimental Section

^{1}H NMR and ^{13}C NMR were measured by Jeol JNM-ECZ 400s (400 MHz / 100MHz) and Bruker AV800 (800MHz/200MHz) spectrometer in $CDCl_3$, DMSO-d_6, and chemical shifts were reported as ppm (δ) unit relative to the solvent peaks. The ^{1}H NMR data were reported as peak multiplicities: s for singlet; d for doublet; dd for doublet of doublets; t for triplet; td for triplet of doublet; q for quartet; quin for quintet; bs for broad singlet and m for multiplet. Coupling constants were reported in Hertz. All reactions were routinely carried out under an inert atmosphere of dry nitrogen. Reactions were checked by thin –layer chromatography (Kieselgel 60 F254, Merck). Spots were detected by viewing under a UV light, and by colorizing with charring after dipping in a *p*-anisaldehyde solution. High Resolution Mass Spectra (HRMS) were obtained using Electrospray Ionization (ESI), Fast atom bombardment (FAB), and Electron Ionization (EI). Flash column chromatograph was performed on silica gel (Kieselgel 60, 230). All materials were purchased from TCI, Alfa Aesar, Sigma Aldrich, and other commercial suppliers and were used without further purification.

General Procedure for C2-Selective Sonogashira Coupling (A)

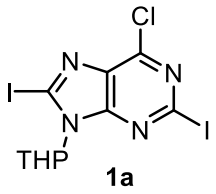
To a solution of **1** (0.2 mmol, 1 equiv) in DMF (5.0 mL) were added $Pd(PPh_3)_4$ (0.02 mmol, 0.1 equiv), CuI (0.04 mmol, 0.2 equiv), *i*Pr_2NH (0.6 mmol, 3 equiv), and followed by appropriate alkyne (0.22 mmol, 1.1 equiv) dropwise. After being stirred at room temperature under N_2, the reaction mixture was quenched by H_2O and extracted by Et_2O. The combined organic layers were dried with $MgSO_4$, filtered, and evaporated. Then, the residue was purified by flash silica gel chromatography.

General Procedure for C8-Selective Sonogashira Coupling (B)

To a solution of **1** (0.2 mmol, 1 equiv) in DMF (5.0 mL) were added $Pd_2(dba)_3{\cdot}CHCl_3$ (0.02 mmol, 0.1 equiv), CuI (0.04 mmol, 0.2 equiv), *i*Pr_2NH (0.6 mmol, 3 equiv), and followed by appropriate alkyne (0.22 mmol, 1.1 equiv) dropwise. After being stirred at room temperature under N_2, the reaction mixture was quenched by H_2O and extracted by Et_2O. The combined organic layers were dried with $MgSO_4$, filtered, and evaporated. Then, the residue was purified by flash silica gel chromatography.

General Procedure for Screening of Phosphine Ligand (C)

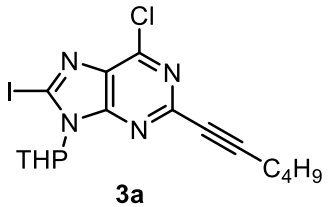
To a solution of **1a** (0.2 mmol, 1 equiv) in DMF (5.0 mL) were added $Pd(OAc)_2$ (0.02 mmol, 0.1 equiv), CuI (0.04 mmol, 0.2 equiv), *i*Pr_2NH (0.6 mmol, 3 equiv), and appropriate phosphine ligand (0.02 mmol, 0.1 equiv for bidentate ligand or 0.04 mmol, 0.2 equiv for monodentate ligand), then stirred for 30 min at room temperature under N_2. To the reaction mixture was dropwise added 1-hexyne (0.22 mmol, 1.1 equiv) and stirred for 18 h at room temperature under N_2. The reaction mixture was quenched by H_2O and extracted by Et_2O. The combined organic layers were dried with $MgSO_4$, filtered, and evaporated. Then, the residue was purified by flash silica gel chromatography.



1a

6-Chloro-2,8-diiodo-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine (1a)[10]

Compound **1a** was prepared by following the reported procedure. [10] ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.66 (dd, *J* = 11.3, 2.5 Hz, 1H), 4.21-4.17 (m, 1H), 3.74 (td, *J* = 11.8, 2.5 Hz, 1H), 3.04 (qd, *J* = 12.3, 4.1 Hz, 1H), 2.18-2.15 (m, 1H), 1.91-1.63 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 153.00, 146.82, 133.45, 117.94, 113.02, 86.38, 68.24, 27.96, 24.39, 22.44; HRMS (ESI) found 490.8637 [calcd for $C_{10}H_{10}ClI_2N_4O^+(M+H)^+$ 490.8627].

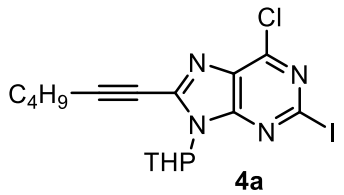


3a

6-Chloro-2-(hex-1-yn-1-yl)-8-iodo-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine (3a)

Compound **3a** was prepared from **1a** (100 mg, 0.20 mmol) as a white solid (52 mg, 57%) by following general procedure **(A)** using 1-hexyne (0.025 mL, 0.22 mmol). (Reaction time: 18

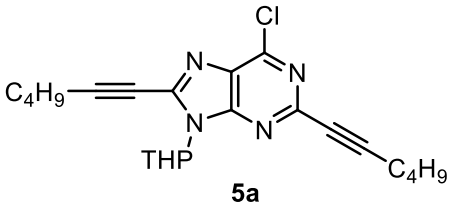
h). R_f = 0.55 (silica gel, hexane/EtOAc, 2/1); ^{1}H NMR (400 MHz, DMSO-d_6) δ 5.64 (dd, J = 11.0, 1.8 Hz, 1H), 4.08 (d, J = 11.0 Hz, 1H), 3.71 (td, J = 11.1, 2.6 Hz, 1H), 2.93 (qd, J = 12.2, 3.6 Hz, 1H), 2.51 (t, J = 6.8 Hz, 2H), 2.02 (d, J = 11.9 Hz, 1H), 1.91 (d, J = 12.4 Hz, 1H), 1.76-1.40 (m, 7H), 0.92 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 152.32, 147.23, 144.00, 132.56, 113.25, 90.21, 86.28, 79.72, 68.25, 29.60, 28.07, 24.38, 22.46, 21.51, 17.99, 13.43; HRMS (FAB) found 445.0288 [calcd for $C_{16}H_{19}ClIN_4O^+(M+H)^+$ 445.0292].



4a

6-Chloro-8-(hex-1-yn-1-yl)-2-iodo-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine (4a)

Compound **4a** was prepared from **1a** (100 mg, 0.20 mmol) as a white solid (63 mg, 69%) by following general procedure **(B)** using 1-hexyne (0.025 mL, 0.22 mmol). (Reaction time: 18 h). R_f = 0.70 (silica gel, hexane/EtOAc, 2/1); H NMR (400 MHz, DMSO-d_6) δ 5.72 (dd, J = 11.0, 1.8 Hz, 1H), 4.07 (d, J = 11.5 Hz, 1H), 3.71-3.65 (m, 1H), 2.73 (qd, J = 12.4, 3.6 Hz, 1H), 2.66 (t, J = 6.9 Hz, 2H), 2.00 (d, J = 12.9 Hz, 1H), 1.91 (d, J = 12.9 Hz, 1H), 1.75-1.44 (m, 7H), 0.94 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 151.87, 148.19, 138.64, 130.55, 118.89, 101.76, 83.37, 70.24, 68.26, 29.18, 28.32, 24.42, 22.41, 21.45, 18.40, 13.40; HRMS (ESI) found 445.0299 [calcd for $C_{16}H_{19}ClIN_4O^+(M+H)^+$ 445.0287].

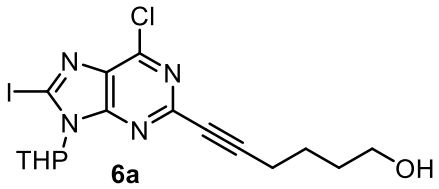


5a

6-Chloro-2,8-di(hex-1-yn-1-yl)-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine (5a)

Compound **5a** was prepared from **1a** (100 mg, 0.20 mmol) as a white solid (7 mg, 9%) by general procedure **(B)** using 1-hexyne (0.025 mL, 0.22 mmol). (Reaction time: 18 h). R_f = 0.68

(silica gel, hexane/EtOAc, 1/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.84 (dd, *J* = 11.2, 2.5 Hz, 1H), 4.18 (d, *J* = 11.4 Hz, 1H), 3.71 (td, *J* = 12.0, 2.4 Hz, 1H), 2.90 (qd, *J* = 12.2, 4.1 Hz, 1H), 2.57 (t, *J* = 7.1 Hz, 2H), 2.48 (t, *J* = 7.3 Hz, 2H), 2.10 (d, *J* = 11.0 Hz, 1H), 1.86-1.44 (m, 12H), 0.97 (t, *J* = 7.2 Hz, 3H), 0.94 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.33, 150.11, 146.31, 139.61, 130.22, 101.59, 91.17, 83.46, 79.78, 70.91, 69.29, 30.21, 29.84, 29.42, 24.87, 23.30, 22.30, 22.18, 19.51, 19.29, 13.75, 13.65; HRMS (ESI) found 399.1955 [calcd for $C_{22}H_{28}ClN_4O^+(M+H)^+$ 339.1946].



6a

6-(6-Chloro-8-iodo-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purin-2-yl)hex-5-yn-1-ol (6a)

Compound **6a** was prepared from **1a** (100 mg, 0.20 mmol) as a white solid (54 mg, 59%) by following general procedure **(A)** using 5-hexynol (0.024 mL, 0.22 mmol). (Reaction time: 4 h). R_f = 0.26 (silica gel, hexane/EtOAc, 1/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.76 (dd, *J* = 11.6, 2.4 Hz, 1H), 4.22-4.18 (m, 1H), 3.74 (td, *J* = 11.6 Hz, 1H), 3.72 (t, *J* = 5.6 Hz, 2H), 3.05 (qd, *J* = 12.4, 4.3 Hz, 1H), 2.56-2.52 (m, 2H), 2.17-2.13 (m, 1H), 1.89-1.72 (m, 7H), 1.63 (d, *J* = 14.7 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 152.34, 147.25, 144.01, 132.58, 113.34, 90.29, 86.29, 79.77, 68.27, 60.11, 31.72, 28.10, 24.40, 24.29, 22.47, 18.17; HRMS (FAB) found 461.0231 [calcd for $C_{16}H_{19}ClIN_4O_2^+(M+H)^+$ 461.0241].

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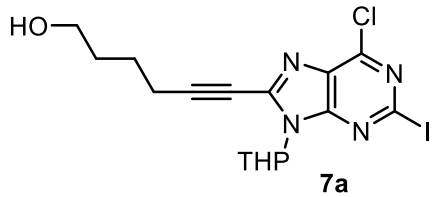
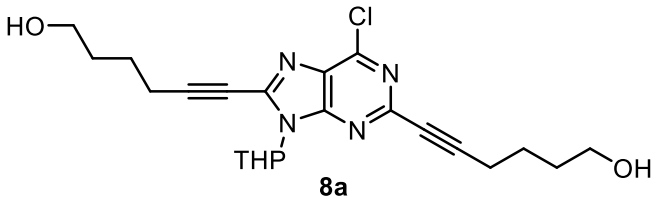


7a

6-(6-Chloro-2-iodo-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purin-8-yl)hex-5-yn-1-ol (7a)

Compound **7a** was prepared from **1a** (100 mg, 0.20 mmol) as a white solid (47 mg, 51%) by

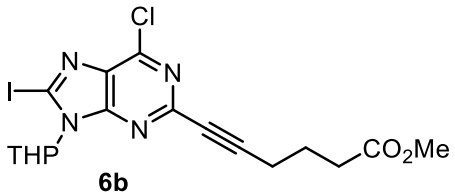
following general procedure **(B)** using 5-hexynol (0.024 mL, 0.22 mmol). (Reaction time: 4 h). R_f = 0.25 (silica gel, hexane/EtOAc, 1/3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.77 (dd, *J* = 11.4, 2.4 Hz, 1H), 4.20-4.16 (m, 1H), 3.73 (t, *J* = 6.0 Hz, 2H), 3.72 (td, *J* = 11.6, 2.4 Hz, 1H), 2.89 (qd, *J* = 12.3, 4.2 Hz, 1H), 2.63 (t, *J* = 6.8 Hz, 2H), 2.14-2.10 (m, 1H), 1.88-1.59 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.89, 149.79, 139.13, 131.28, 117.00, 101.30, 83.90, 70.75, 69.31, 62.20, 31.87, 29.24, 24.85, 24.27, 23.24, 19.65; HRMS (ESI) found 461.0221 [calcd for $C_{16}H_{19}ClIN_4O_2^+(M+H)^+$ 461.0236].



8a

6,6'-(6-Chloro-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine-2,8-diyl)bis(hex-5-yn-1-ol) (8a)

Compound **8a** was prepared from **1a** (100 mg, 0.20 mmol) as a white solid (14 mg, 16%) by following general procedure **(A)** using 5-hexynol (0.024 mL, 0.22 mmol). (Reaction time: 4 h). R_f = 0.07 (silica gel, hexane/EtOAc, 1/3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.84 (dd, *J* = 11.4, 2.3 Hz, 1H), 4.20-4.17 (m, 1H), 3.75-3.69 (m, 5H), 2.89 (qd, *J* = 12.2, 4.1 Hz, 1H), 2.62 (t, *J* = 6.6 Hz, 2H), 2.54 (t, *J* = 6.6 Hz, 2H), 2.12-2.09 (m, 1H), 1.86-1.61 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.32, 150.18, 146.22, 139.55, 130.28, 101.15, 90.63, 83.54, 80.13, 71.17, 69.32, 62.44, 62.20, 32.06, 31.89, 29.46, 24.89, 24.44, 24.28, 23.28, 19.65, 19.37; HRMS (ESI) found 431.1843 [calcd for $C_{22}H_{28}ClN_4O_3^+(M+H)^+$ 431.1844].

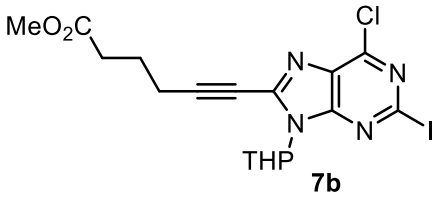


6b

Methyl 6-(6-chloro-8-iodo-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purin-2-yl)hex-5-ynoate (6b)

Compound **6b** was prepared from **1a** (100 mg, 0.20 mmol) as a white solid (51 mg, 52%) by

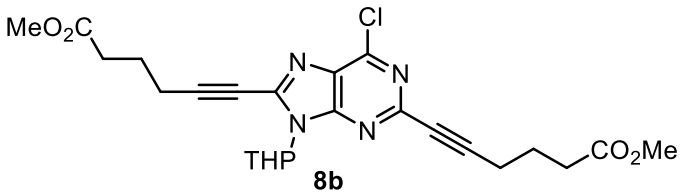
following general procedure **(A)** using methyl 5-hexynoate (0.029 mL, 0.22 mmol). (Reaction time: 15 h). R_f = 0.26 (silica gel, hexane/EtOAc, 2/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.76 (dd, *J* = 11.0, 2.5 Hz, 1H), 4.23-4.19 (m, 1H), 3.74 (td, *J* = 12.1, 2.2 Hz, 1H), 3.70 (s, 3H), 3.06 (qd, *J* = 12.5, 4.3 Hz, 1H), 2.57 (t, *J* = 7.6 Hz, 2H), 2.54 (t, *J* = 7.6 Hz, 2H), 2.17-2.13 (m, 1H), 2.04-1.97 (m, 2H), 1.89-1.73 (m, 3H), 1.64 (d, *J* = 12.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.51, 152.57, 149.20, 145.40, 133.22, 105.87, 89.54, 86.40, 80.34, 69.38, 51.82, 33.01, 29.09, 24.68, 23.31, 23.25, 18.99; HRMS (FAB) found 489.0187 [calcd for $C_{17}H_{19}ClIN_4O_3^+$(M+H)$^+$ 489.0190].



7b

Methyl 6-(6-chloro-2-iodo-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purin-8-yl)hex-5-ynoate (7b)

Compound **7b** was prepared from **1a** (100 mg, 0.20 mmol) as a white solid (52 mg, 53%) by following general procedure **(B)** using methyl 5-hexynoate (0.029 mL, 0.22 mmol). (Reaction time: 15 h). R_f = 0.27 (silica gel, hexane/EtOAc, 1/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.77 (dd, *J* = 11.5, 2.5 Hz, 1H), 4.20-4.17 (m, 1H), 3.73 (td, *J* = 11.6, 2.0 Hz, 1H), 3.70 (s, 3H), 2.87 (qd, *J* = 8.8, 4.0 Hz, 1H), 2.66 (t, *J* = 7.0 Hz, 2H), 2.55 (t, *J* = 7.2 Hz, 2H), 2.14-2.11 (m, 1H), 2.07-1.99 (m, 2H), 1.89-1.85 (m, 1H), 1.78-1.72 (m, 2H), 1.66-1.63 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.17, 151.86, 149.89, 138.89, 131.25, 117.09, 100.11, 83.88, 71.19, 69.31, 51.91, 32.76, 29.32, 24.84, 23.21, 23.07, 19.20; HRMS (ESI) found 489.0168 [calcd for $C_{17}H_{19}ClIN_4O_3^+$(M+H)$^+$ 489.0185].

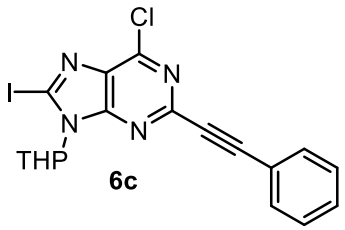


8b

Dimethyl 6,6'-(6-chloro-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine-2,8-diyl)bis(hex-5-ynoate) (8b)

Compound **8b** was prepared from **1a** (100 mg, 0.20 mmol) as a white solid (18 mg, 18%) by

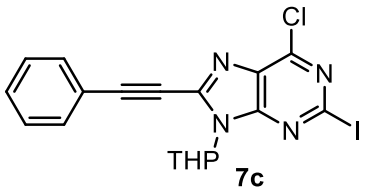
general procedure **(A)** using methyl 5-hexynoate (0.029 mL, 0.22 mmol). (Reaction time: 15 h). R_f = 0.10 (silica gel, hexane/EtOAc, 2/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.84 (dd, *J* = 11.3, 2.5 Hz, 1H), 4.19 (dd, *J* = 13.7, 2.2 Hz, 1H), 3.75 (td, *J* = 11.6, 2.4 Hz, 1H), 3.70 (s, 3H), 3.70 (s, 3H), 2.88 (qd, *J* = 12.3, 4.1 Hz, 1H), 2.67 (t, *J* = 6.9 Hz, 2H), 2.58 (t, *J* = 6.8 Hz, 3H), 2.54 (t, *J* = 6.8 Hz, 3H) 2.13-2.10 (m, 1H), 2.06-1.97 (m, 4H), 1.88-1.68 (m, 3H), 1.64 (d, *J* = 10.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.50, 173.21, 151.28, 150.29, 146.12, 139.37, 130.33, 99.98, 89.50, 83.54, 80.48, 71.60, 69.32, 51.89, 51.81, 33.00, 32.77, 29.54, 24.88, 23.31, 23.25, 23.09, 19.21, 19.01; HRMS (ESI) found 487.1738 [calcd for $C_{24}H_{28}ClN_4O_5^+$(M+H)$^+$ 487.1743].



6c

6-Chloro-8-iodo-2-(phenylethynyl)-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine (6c) [4]

Compound **6c** was prepared from **1a** (100 mg, 0.20 mmol) as a white solid (51 mg, 55%) by following general procedure **(A)** using phenylacetylene (0.024 mL, 0.22 mmol). (Reaction time: 18 h). R_f = 0.27 (silica gel, hexane/EtOAc, 3/1), and the ^{1}H NMR data of **6c** was identical to those reported before.[4] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70-7.67 (m, 2H), 7.43-7.36 (m, 3H), 5.77 (dd, *J* = 11.1, 2.3 Hz, 1H), 4.25-4.21 (m, 1H), 3.76 (td, *J* = 12.1, 2.2 Hz, 1H), 3.12 (qd, *J* = 12.4, 4.1 Hz, 1H), 2.19-2.16 (m, 1H), 1.93-1.64 (m, 4H).

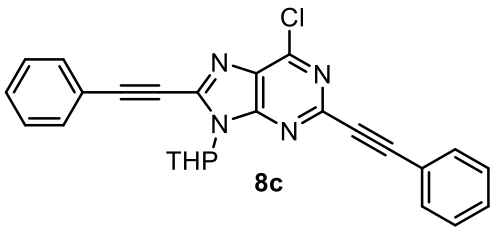


7c

6-Chloro-2-iodo-8-(phenylethynyl)-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine (7c)

Compound **7c** was prepared from **1a** (100 mg, 0.20 mmol) as a white solid (56 mg, 60%) by

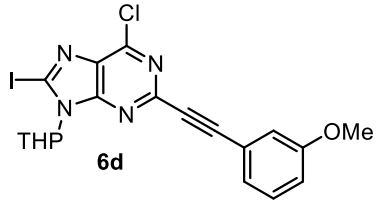
following general procedure **(B)** using phenylacetylene (0.024 mL, 0.22 mmol). (Reaction time: 18 h). R_f = 0.43 (silica gel, hexane/EtOAc, 3/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (s, 1H), 7.65 (s, 1H), 7.52-7.42 (m, 3H), 5.88 (dd, *J* = 11.3, 2.1 Hz, 1H), 4.25-4.22 (m, 1H), 3.77 (td, *J* = 12.0, 4.0 Hz, 1H), 2.92 (qd, *J* = 12.2, 4.1 Hz, 1H), 2.17-2.14 (m, 1H), 1.94 (d, *J* = 12.2 Hz, 1H), 1.89-1.72 (m, 2H), 1.68 (d, *J* = 11.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.93, 150.00, 138.89, 132.43, 131.48, 130.89, 128.95, 120.34, 117.24, 98.43, 83.84, 78.58, 69.39, 29.55, 24.99, 23.25; HRMS (FAB) found 464.9969 [calcd for $C_{18}H_{15}ClIN_4O^+(M+H)^+$ 464.9979].



8c

6-Chloro-2,8-bis(phenylethynyl)-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine (8c)[4]

Compound **8c** was prepared from **1a** (100 mg, 0.20 mmol) as a white solid (18 mg, 21%) by general procedure **(A)** using phenylacetylene (0.024 mL, 0.22 mmol). (Reaction time: 18 h). R_f = 0.37 (silica gel, hexane/EtOAc, 3/1). The ^{1}H and ^{13}C NMR data of **8c** was in agreement with literature.[4] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70-7.67 (m, 4H), 7.52-7.37 (m, 6H), 5.98 (dd, *J* = 11.0, 1.8 Hz, 1H), 4.26 (d, *J* = 11.6 Hz, 1H), 3.80 (t, *J* = 11.3 Hz, 1H), 2.98 (qd, *J* = 12.1, 3.7 Hz, 1H), 2.18-2.15 (m, 1H), 1.98-1.68 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.46, 150.54, 146.38, 139.56, 132.77, 132.41, 130.79, 130.65, 129.88, 128.94, 128.57, 121.41, 120.51, 98.53, 88.59, 87.97, 83.69, 69.44, 29.74, 25.05, 23.32.

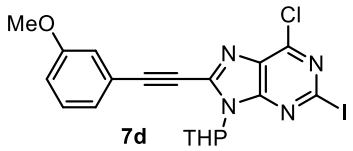


6d

6-Chloro-8-iodo-2-((3-methoxyphenyl)ethynyl)-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine (6d)

Compound **6d** was prepared from **1a** (100 mg, 0.20 mmol) as a white solid (57 mg, 58%) by

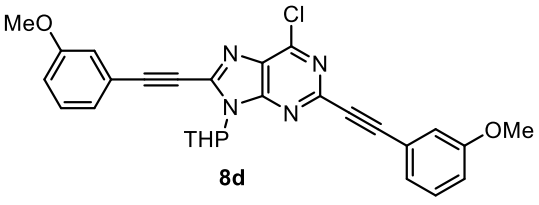
following general procedure **(A)** using 3-methoxyphenylacetylene (0.028 mL, 0.22 mmol). (Reaction time: 1.5 h). R_f = 0.21 (silica gel, hexane/EtOAc, 2/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30-7.28 (m, 2H), 7.21 (d, *J* = 1.8 Hz, 1H), 6.99-6.96 (m, 1H), 5.77 (dd, *J* = 11.3, 2.5 Hz, 1H), 4.25-4.21 (m, 1H), 3.83 (s, 3H), 3.76 (td, *J* = 12.1, 2.1 Hz, 1H), 3.12 (qd, *J* = 12.3, 4.0 Hz, 1H), 2.19-2.15 (m, 1H), 1.93-1.71 (m, 3H), 1.65 (d, *J* = 13.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.46, 152.67, 149.35, 145.56, 133.30, 129.68, 125.33, 122.34, 117.21, 116.88, 106.35, 88.34, 87.58, 86.66, 69.44, 55.54, 29.09, 24.71, 23.37; HRMS (FAB) found 495.0073 [calcd for $C_{19}H_{17}ClIN_4O_2^+(M+H)^+$ 495.0085].



7d

6-Chloro-2-iodo-8-((3-methoxyphenyl)ethynyl)-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine (7d)

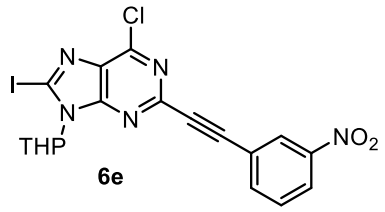
Compound **7d** was prepared from **1a** (100 mg, 0.20 mmol) as a white solid (55 mg, 56%) by following general procedure **(B)** using 3-methoxyphenylacetylene (0.028 mL, 0.22 mmol). (Reaction time: 1.5 h). R_f = 0.51 (silica gel, hexane/EtOAc, 2/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (t, *J* = 7.9 Hz, 1H), 7.25 (d, *J* = 10.2 Hz, 1H), 7.17 (s, 1H), 7.05 (dd, *J* = 8.6, 2.4 Hz, 1H), 5.87 (dd, *J* = 11.0, 2.4 Hz, 1H), 4.25-4.22 (m, 1H), 3.85 (s, 3H), 3.77 (td, *J* = 11.6, 2.4 Hz, 1H), 2.91 (qd, *J* = 12.1, 4.0 Hz, 1H), 2.17-2.14 (m, 1H), 1.94 (d, *J* = 12.2 Hz, 1H), 1.86-1.72 (m, 2H), 1.68 (d, *J* = 11.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.62, 151.92, 150.01, 138.84, 131.48, 130.07, 124.85, 121.26, 117.37, 117.26, 98.36, 83.82, 78.31, 69.38, 55.57, 29.57, 24.99, 23.24; HRMS (FAB) found 495.0091 [calcd for $C_{19}H_{17}ClIN_4O_2^+(M+H)^+$ 495.0085].



8d

6-Chloro-2,8-bis((3-methoxyphenyl)ethynyl)-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine (8d)

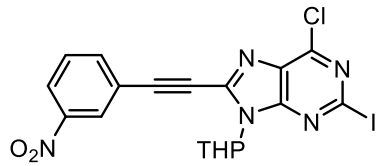
Compound **8d** was prepared from **1a** (100 mg, 0.20 mmol) as a white solid (9 mg, 9%) by following general procedure **(A)** using 3-methoxyphenylacetylene (0.028 mL, 0.22 mmol). (Reaction time: 1.5 h). R_f = 0.40 (silica gel, hexane/EtOAc, 1/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (t, *J* = 8.3 Hz, 1H), 7.31-7.27 (m, 3H), 7.23-7.22 (m, 1H), 7.20-7.19 (m, 1H), 7.05 (dd, *J* = 7.9, 2.4 Hz, 1H), 7.00-6.97 (m, 1H), 5.98 (dd, *J* = 11.0, 2.4 Hz, 1H), 4.26 (d, *J* = 12.2 Hz, 1H), 3.86 (s, 3H), 3.84 (s, 3H), 3.80 (t, *J* = 11.9 Hz, 1H), 2.98 (qd, *J* = 12.2, 4.1 Hz, 1H), 2.17 (d, *J* = 11.0 Hz, 1H), 1.96 (d, *J* = 12.8 Hz, 1H), 1.90-1.74 (m, 2H), 1.70 (d, *J* = 11.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.62, 159.42, 151.45, 150.56, 146.33, 139.53, 130.67, 130.05, 129.67, 125.34, 124.83, 122.34, 121.43, 117.31, 117.22, 117.17, 116.90, 98.48, 88.55, 87.69, 83.66, 78.72, 69.44, 55.57, 55.53, 29.76, 25.05, 23.32; HRMS (FAB) found 499.1530 [calcd for $C_{28}H_{24}ClN_4O_3^+$(M+H)$^+$ 499.1537].



6e

6-Chloro-8-iodo-2-((3-nitrophenyl)ethynyl)-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine (6e)

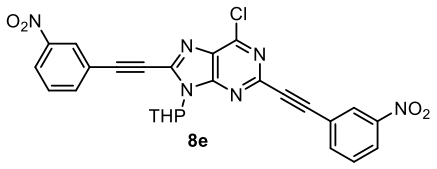
Compound **6e** was prepared from **1a** (100 mg, 0.20 mmol) as a white solid (47 mg, 46%) by following general procedure **(A)** using 3-nitrophenylacetylene (0.027 mL, 0.22 mmol). (Reaction time: 3.5 h). R_f = 0.38 (silica gel, hexane/EtOAc, 2/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (t, *J* = 1.8 Hz, 1H), 8.29-8.26 (m, 1H), 7.98 (dd, *J* = 6.1, 1.2 Hz, 1H), 7.60 (t, *J* = 8.0 Hz, 1H), 5.76 (dd, *J* = 11.7, 2.5 Hz, 1H), 4.26-4.22 (m, 1H), 3.77 (td, *J* = 12.0, 2.2 Hz, 1H), 3.14 (qd, *J* = 12.3, 4.1 Hz, 1H), 2.19 (d, *J* = 12.3 Hz, 1H), 1.95-1.72 (m, 3H), 1.67 (d, *J* = 13.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.60, 149.49, 148.20, 144.69, 138.19, 133.71, 129.79, 127.55, 124.51, 123.34, 107.31, 89.66, 86.98, 84.90, 69.49, 29.05, 24.69, 23.37; HRMS (EI) found 424.9173 [calcd for $C_{13}H_5ClIN_5O_2^+$ (M-THP)$^+$ 424.9177].



7e

6-Chloro-2-iodo-8-((3-nitrophenyl)ethynyl)-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine (7e)

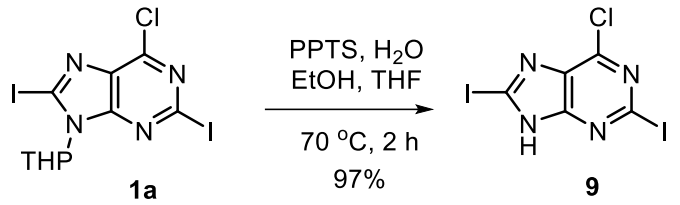
Compound **7e** was prepared from **1a** (100 mg, 0.20 mmol) as a white solid (63 mg, 62%) by following general procedure **(B)** using 3-nitrophenylacetylene (0.027 mL, 0.22 mmol). (Reaction time: 3.5 h). R_f = 0.24 (silica gel, hexane/EtOAc, 2/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (t, *J* = 1.8 Hz, 1H), 8.35 (dd, *J* = 7.9, 1.8 Hz, 1H), 7.97 (d, *J* = 7.9 Hz, 1H), 7.67 (t, *J* = 7.9 Hz, 1H), 5.90 (dd, *J* = 11.6, 2.4 Hz, 1H), 4.28-4.24 (m, 1H), 3.80 (td, *J* = 11.6, 2.4 Hz, 1H), 2.83 (qd, *J* = 12.0, 4.1 Hz, 1H), 2.19-2.16 (m, 1H), 1.98 (d, *J* = 12.8 Hz, 1H), 1.84-1.71 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.74, 150.54, 148.36, 137.86, 137.70, 131.39, 130.24, 127.11, 125.35, 122.21, 117.84, 94.78, 83.81, 80.56, 69.45, 29.93, 25.00, 23.14; HRMS (FAB) found 509.9838 [calcd for $C_{18}H_{14}ClIN_5O_3^+$(M+H)$^+$ 509.9830].



8e

6-Chloro-2,8-bis((3-nitrophenyl)ethynyl)-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine (8e)

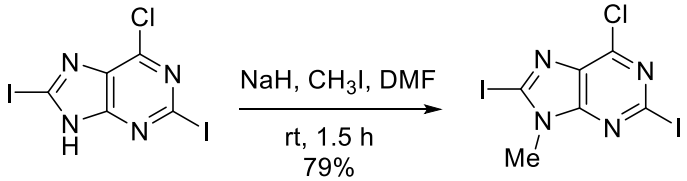
Compound **8e** was prepared from **1a** (100 mg, 0.20 mmol) as a white solid (11 mg, 10%) by following general procedure **(A)** using 3-nitrophenylacetylene (0.027 mL, 0.22 mmol). (Reaction time: 3.5 h). R_f = 0.14 (silica gel, hexane/EtOAc, 2/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (t, *J* = 1.8 Hz, 1H), 8.52 (t, *J* = 1.8 Hz, 1H), 8.38-8.35 (m, 1H), 8.30-8.28 (m, 1H), 8.01-7.98 (m, 2H), 7.68 (t, *J* = 8.0 Hz, 1H), 7.61 (t, *J* = 8.0 Hz, 1H), 6.00 (dd, *J* = 11.3, 2.1 Hz, 1H), 4.32-4.28 (m, 1H), 3.83 (td, *J* = 11.7, 2.2 Hz, 1H), 2.92 (qd, *J* = 12.3, 4.1 Hz, 1H), 2.22-2.17 (m, 1H), 2.05-2.00 (m, 2H), 1.89-1.73 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.30, 151.25, 148.39, 148.28, 145.88, 138.86, 138.19, 137.88, 131.03, 130.27, 129.82, 127.59, 127.15, 125.38, 124.58, 123.24, 122.27, 95.24, 89.66, 85.42, 83.91, 80.77, 69.58, 30.07, 25.05, 23.24; HRMS (FAB) found 445.0451 [calcd for $C_{21}H_{10}ClN_6O_4^+$(M-THP+H)$^+$ 445.0452].



1a **9**

6-Chloro-2,8-diiodo-9*H*-purine (9)

To a solution of **1a** (4.1 g, 8.36 mmol, 1 equiv) in EtOH (25 mL) and THF (25 mL) was added Pyridinium *p*-toluenesulfonate (260 mg, 1.03 mmol, 0.12 equiv) in H_2O (5 mL) at room temperature. After being stirred for 2 h at 70 °C, the reaction mixture was cooled to room temperature, and the solvent was evaporated. Then, the residue was purified by flash silica gel chromatography (silica gel, hexanc/THF, 3/1) to give **9** (3.30 g, 97%) as white solid. R_f = 0.25 (silica gel, hexane/EtOAc, 2/1); ^{13}C NMR (200 MHz, DMSO-d_6) δ 155.98, 145.59, 133.00, 117.62, 108.17; HRMS (ESI) found 406.8054 [calcd for $C_5H_2ClI_2N_4^+(M+H)^+$ 406.8052].

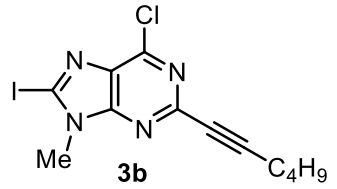


9 **1b**

6-Chloro-2,8-diiodo-9-methyl-9*H*-purine (1b)

To a solution of **9** (1.0 g, 2.46 mmol, 1 equiv) in DMF (15 mL) was added NaH (60% dispersion in paraffin oil, 108 mg, 2.71 mmol, 1.1 equiv) and stirred for 5 min at room temperature under N_2. To the above reaction mixture was added CH_3I (0.17 mL, 2.71 mmol, 1.1 equiv) and stirred for 1.5 h at room temperature under N_2, then the reaction mixture was cooled to 0 °C, and quenched slowly by saturated NH_4Cl. The aqueous layer was extracted by EtOAc, then the combined organic layers were dried over $MgSO_4$, filtered and evaporated. The residue was purified by flash silica gel chromatography. (silica gel, hexane/EtOAc, 2/1) to give **1b** (821 mg, 79%) as white solid. R_f = 0.50 (silica gel, hexane/EtOAc, 1/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.82 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 153.89, 146.12, 132.91, 117.92, 115.41, 32.94;

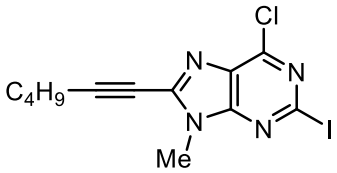
HRMS (FAB) found 420.8226 [calcd for $C_6H_4ClI_2N_4^+(M+H)^+$ 420.8214].



3b

6-Chloro-2-(hex-1-yn-1-yl)-8-iodo-9-methyl-9*H*-purine (3b)

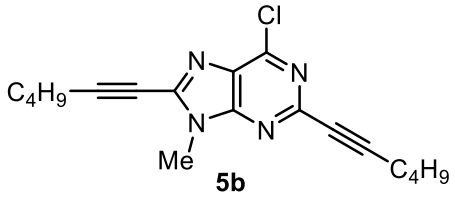
3b was prepared from **1b** (84 mg, 0.20 mmol) as a white solid (30 mg, 40%) by following general procedure **(A)** using 1-hexyne (0.025 mL, 0.22 mmol). (Reaction time: 0.5 h). R_f = 0.42 (silica gel, hexane/EtOAc, 2/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.83 (s, 3H), 2.49 (t, *J* = 7.4 Hz, 2H), 1.70-1.62 (m, 2H), 1.52-1.45 (m, 2H), 0.95 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 153.05, 146.57, 144.18, 132.08, 115.76, 89.89, 79.66, 32.78, 29.62, 21.49, 17.94, 13.44; HRMS (ESI) found 374.9871 [calcd for $C_{12}H_{13}ClIN_4^+(M+H)^+$ 374.9868].



4b

6-Chloro-8-(hex-1-yn-1-yl)-2-iodo-9-methyl-9*H*-purine (4b)

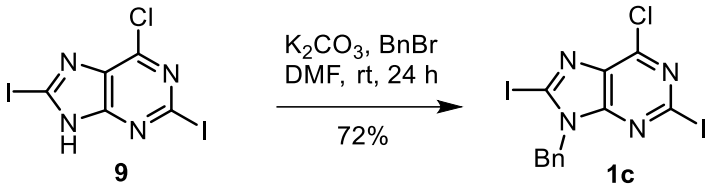
3b was prepared from **1b** (84 mg, 0.20 mmol) as a white solid (24 mg, 32%) by following general procedure **(B)** using 1-hexyne (0.025 mL, 0.22 mmol). (Reaction time: 0.5 h). R_f = 0.28 (silica gel, hexane/EtOAc, 8/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.85 (s, 3H), 2.57 (t, *J* = 7.0 Hz, 2H), 1.72-1.64 (m, 2H), 1.55-1.47 (m, 2H), 0.97 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 152.84, 147.62, 140.16, 130.47, 118.45, 101.90, 69.56, 30.20, 29.30, 21.45, 18.37, 13.42; HRMS (ESI) found 374.9867 [calcd for $C_{12}H_{13}ClIN_4^+(M+H)^+$ 374.9868].



5b

6-Chloro-2,8-di(hex-1-yn-1-yl)-9-methyl-9*H*-purine (5b)

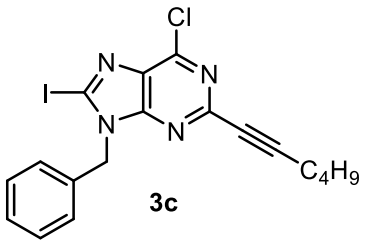
5b was prepared from **1b** (84 mg, 0.20 mmol) as a white solid (20 mg, 31%) by following general procedure **(A)** using 1-hexyne (0.025 mL, 0.22 mmol). (Reaction time: 0.5 h). R_f = 0.21 (silica gel, hexane/EtOAc, 8/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.87 (s, 3H), 2.56 (t, *J* = 7.1 Hz, 2H), 2.49 (t, *J* = 7.1 Hz, 2H), 1.71-1.62 (m, 4H), 1.56-1.45 (m, 4H), 0.97 (t, *J* = 7.2 Hz, 3H), 0.94 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 151.95, 147.96, 144.83, 140.78, 129.64, 101.89, 90.07, 79.75, 69.72, 30.02, 29.64, 29.33, 21.49, 21.45, 18.38, 17.96, 13.43, 13.41; HRMS (ESI) found 329.1526 [calcd for $C_{18}H_{22}ClN_4^+(M+H)^+$ 329.1528].



9 **1c**

9-Benzyl-6-chloro-2,8-diiodo-9*H*-purine (1c)

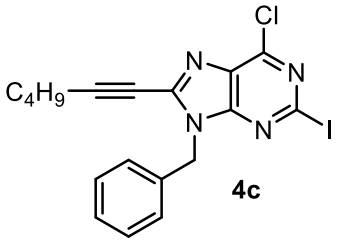
To a solution of **9** (987 mg, 2.42 mmol, 1 equiv) in DMF (10 mL) were added K_2CO_3 (369 mg, 2.67 mmol, 1.1 equiv) and BnBr (0.31 mL, 2.67 mmol, 1.1 equiv) at room temperature under N_2. After being stirred for 24 h at room temperature under N_2, the reaction mixture was quenched by H_2O, extracted by CH_2Cl_2. The combined organic layers were dried with $MgSO_4$, filtered and evaporated. The residue was purified by flash silica gel chromatography (silica gel, hexane/EtOAc, 1/1) to give **1c** (868 mg, 72%) as a white solid. R_f = 0.30 (silica gel, hexane/EtOAc, 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.30 (m, 5H), 5.42 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.76, 148.70, 134.05, 133.83, 129.19, 128.88, 128.11, 117.04, 108.21, 49.87; HRMS (ESI) found 496.8529 [calcd for $C_{12}H_8ClI_2N_4^+(M+H)^+$ 496.8521].



3c

9-Benzyl-6-chloro-2-(hex-1-yn-1-yl)-8-iodo-9*H*-purine (3c)

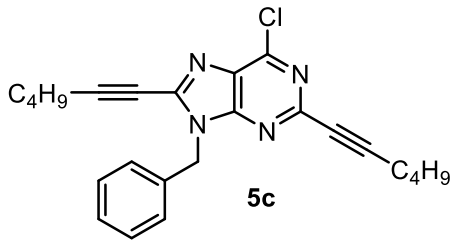
3c was prepared from **1c** (100 mg, 0.20 mmol) as a white solid (32 mg, 35%) by following general procedure **(A)** using 1-hexyne (0.025 mL, 0.22 mmol). (Reaction time: 4 h). R_f = 0.20 (silica gel, hexane/EtOAc, 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33-7.27 (m, 5H), 5.45 (s, 2H), 2.49 (t, *J* = 7.1 Hz, 2H), 1.69-1.61 (m, 2H), 1.54-1.45 (m, 2H), 0.94 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.20, 149.23, 146.24, 134.38, 132.81, 129.09, 128.66, 127.92, 108.50, 91.52, 79.53, 49.54, 30.17, 22.29, 19.27, 13.73; HRMS (ESI) found 451.0180 [calcd for $C_{16}H_{19}ClIN_4O^+(M+H)^+$ 451.0181].



4c

9-Benzyl-6-chloro-8-(hex-1-yn-1-yl)-2-iodo-9*H*-purine (4c)

4c was prepared from **1c** (100 mg, 0.20 mmol) as a white solid (32 mg, 35%) by following general procedure **(B)** using 1-hexyne (0.025 mL, 0.22 mmol). (Reaction time: 4 h). R_f = 0.53 (silica gel, hexane/EtOAc, 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.33 (m, 5H), 5.44 (s, 2H), 2.53 (t, *J* = 7.0 Hz, 2H), 1.66-1.59 (m, 2H), 1.49-1.40 (m, 2H), 0.93 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.44, 149.76, 140.03, 134.82, 131.29, 129.09, 128.73, 128.20, 117.09, 102.39, 70.05, 47.72, 29.83, 22.15, 19.43, 13.63; HRMS (ESI) found 451.0180 [calcd for $C_{18}H_{17}ClIN_4^+(M+H)^+$ 451.0181].



5c

9-Benzyl-6-chloro-2,8-di(hex-1-yn-1-yl)-9*H*-purine (5c)

5c was prepared from **1c** (100 mg, 0.20 mmol) as a white solid (31 mg, 38%) by following general procedure **(A)** using 1-hexyne (0.025 mL, 0.22 mmol). (Reaction time: 4 h). R_f = 0.47 (silica gel, hexane/EtOAc, 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.30 (m, 5H), 5.48 (s, 2H), 2.51 (t, *J* = 7.0 Hz, 2H), 2.49 (t, *J* = 7.3 Hz, 2H), 1.70-1.57 (m, 4H), 1.54-1.38 (m, 4H), 0.94 (t, *J* = 7.6 Hz, 3H), 0.92 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.78, 150.12, 146.51, 140.63, 135.15, 130.29, 128.95, 128.49, 128.00, 102.16, 91.17, 79.75, 70.27, 47.38, 30.21, 29.82, 22.30, 22.10, 19.39, 19.28, 13.74, 13.62; HRMS (ESI) found 405.1834 [calcd for $C_{24}H_{25}ClN_4^+(M+H)^+$ 405.1841].

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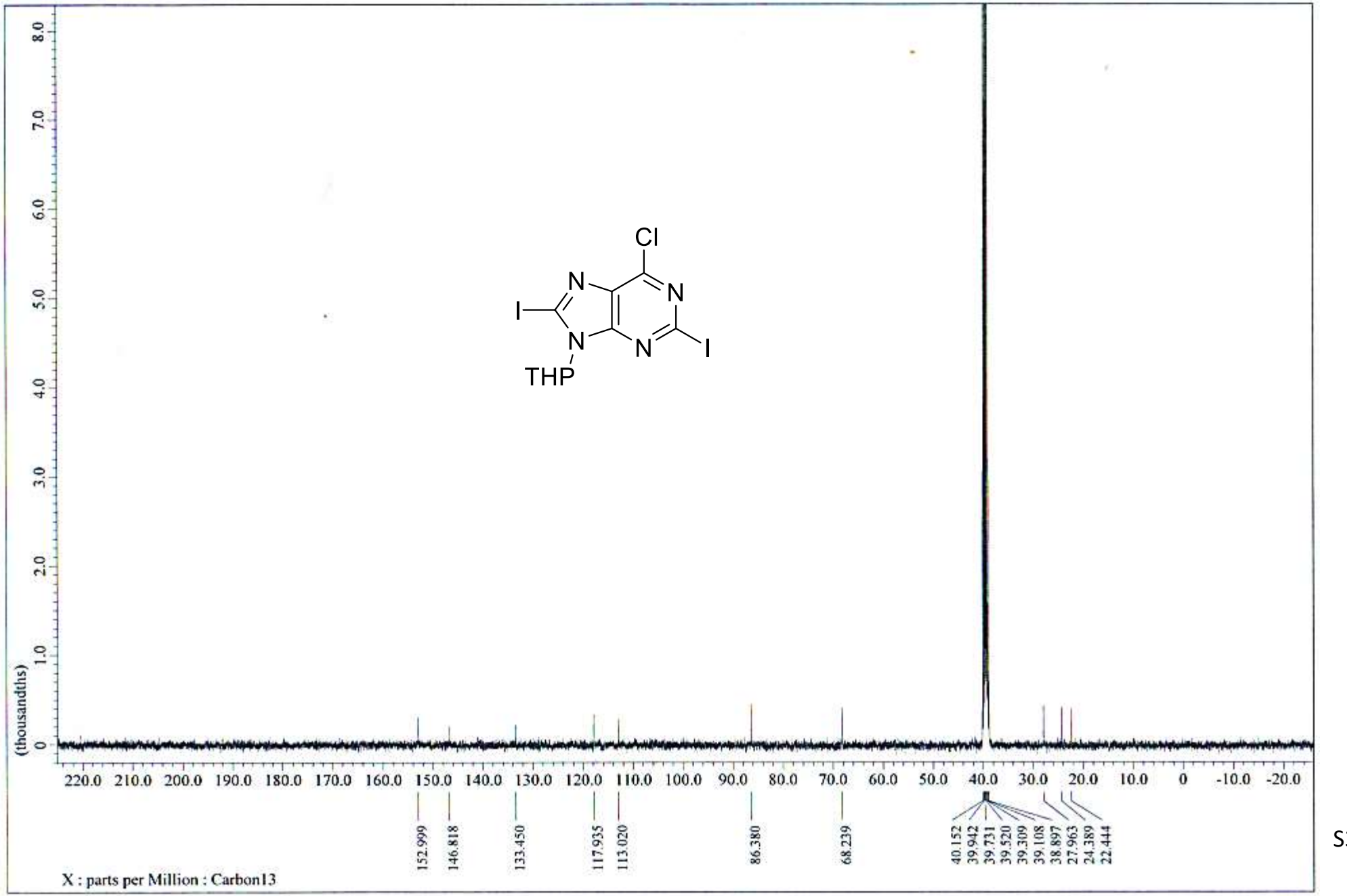
^{13}C NMR (100 MHz, DMSO-d_6) of **1a**



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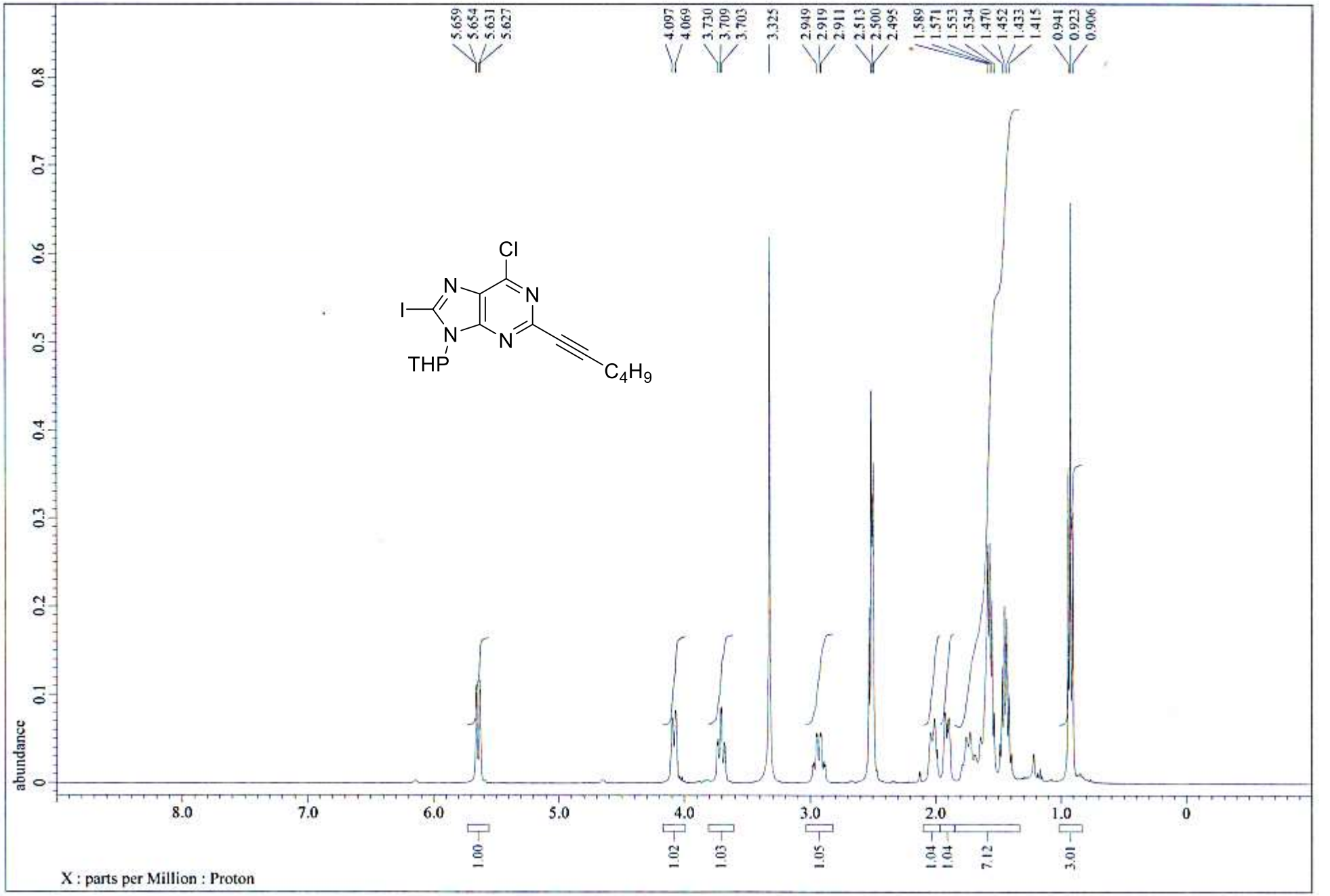
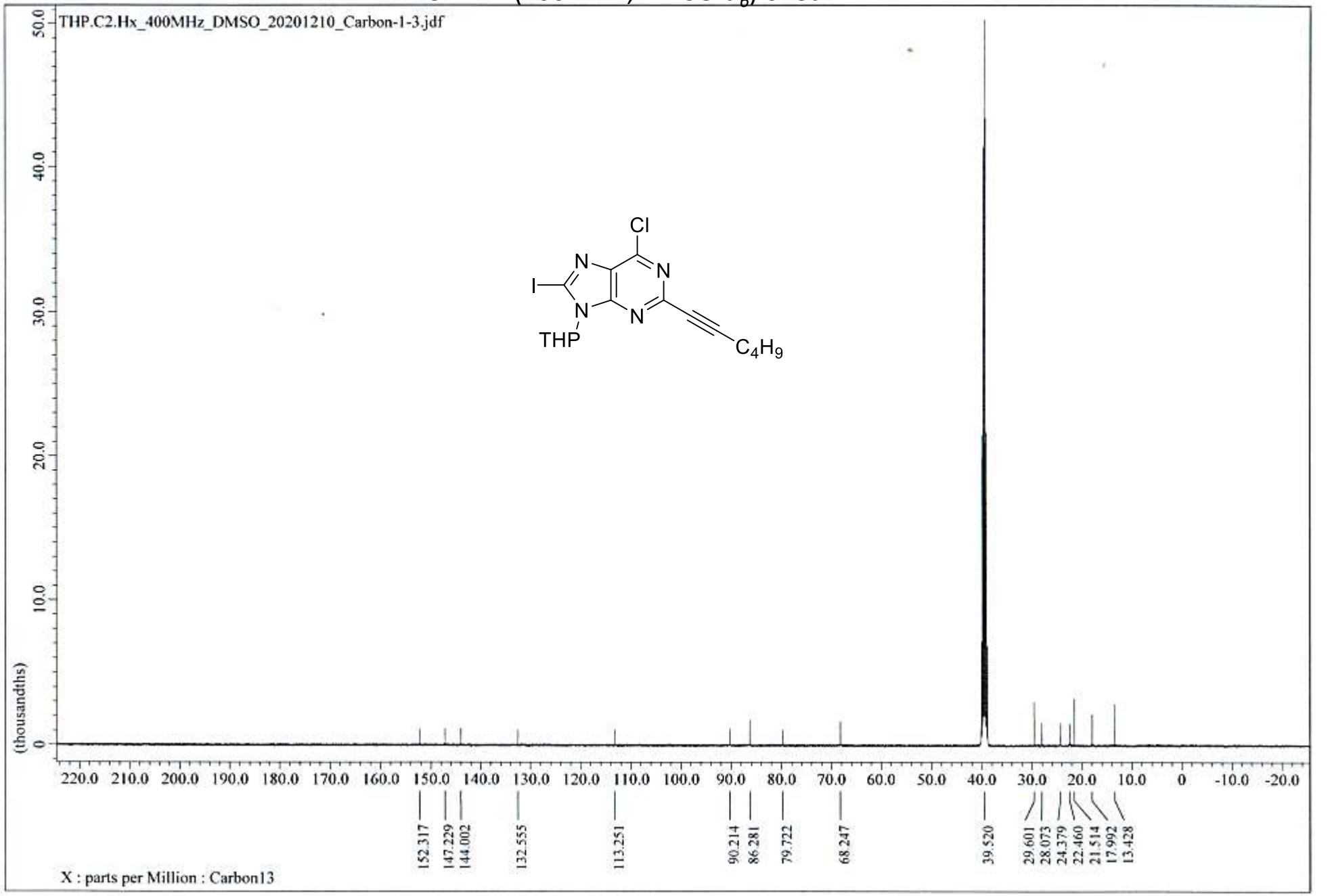


^{13}C NMR (100 MHz, DMSO-d_6) of **3a**



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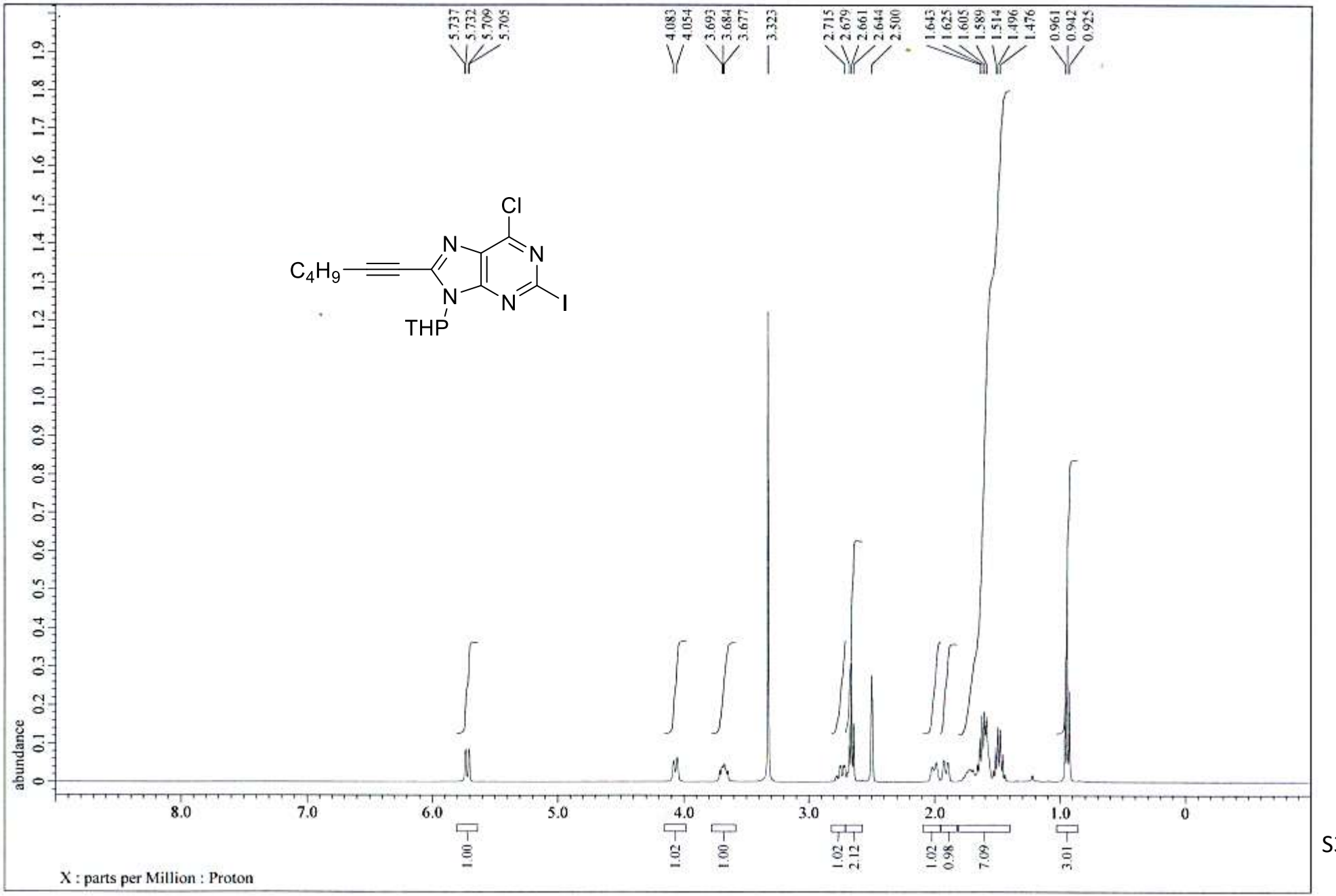

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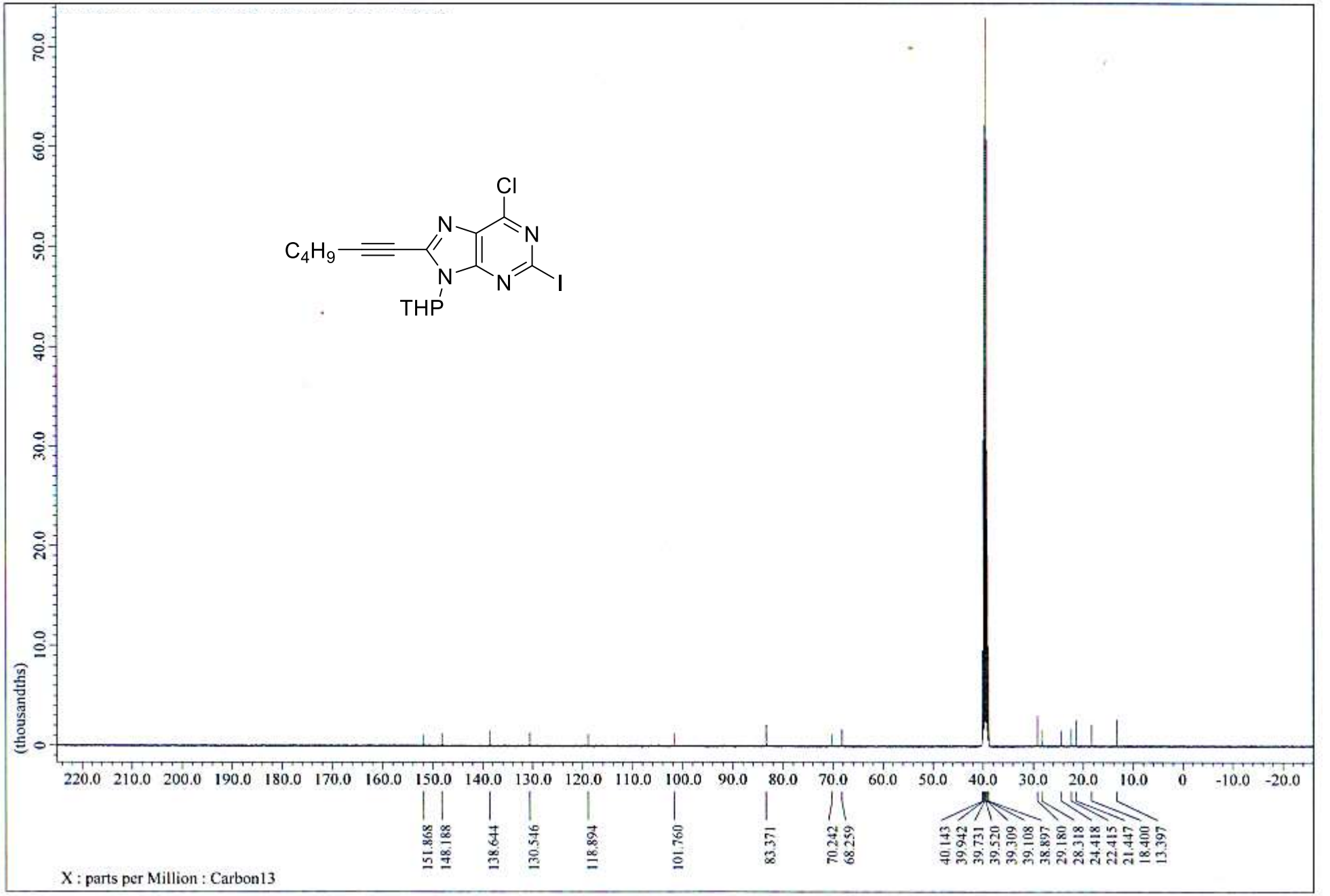

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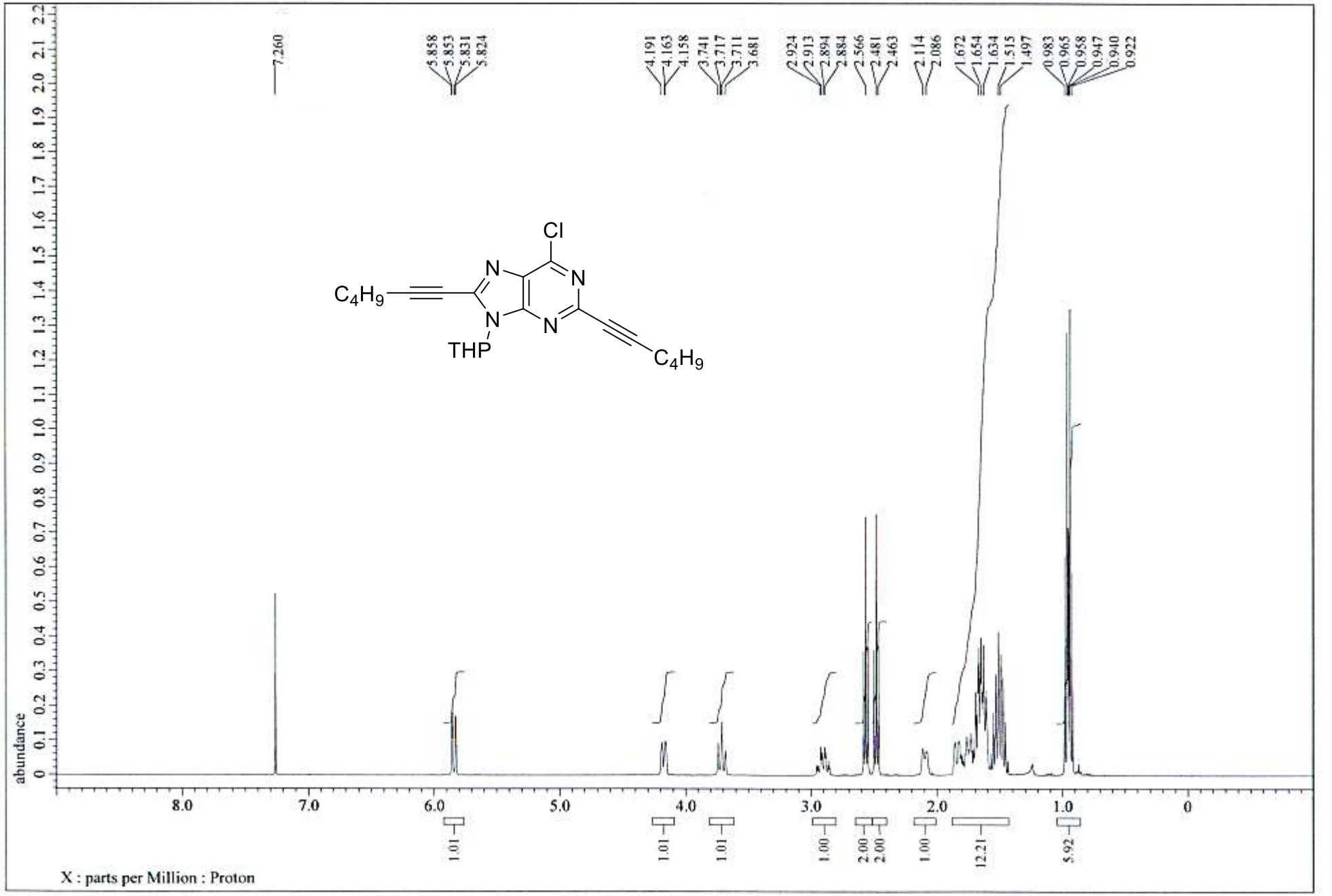

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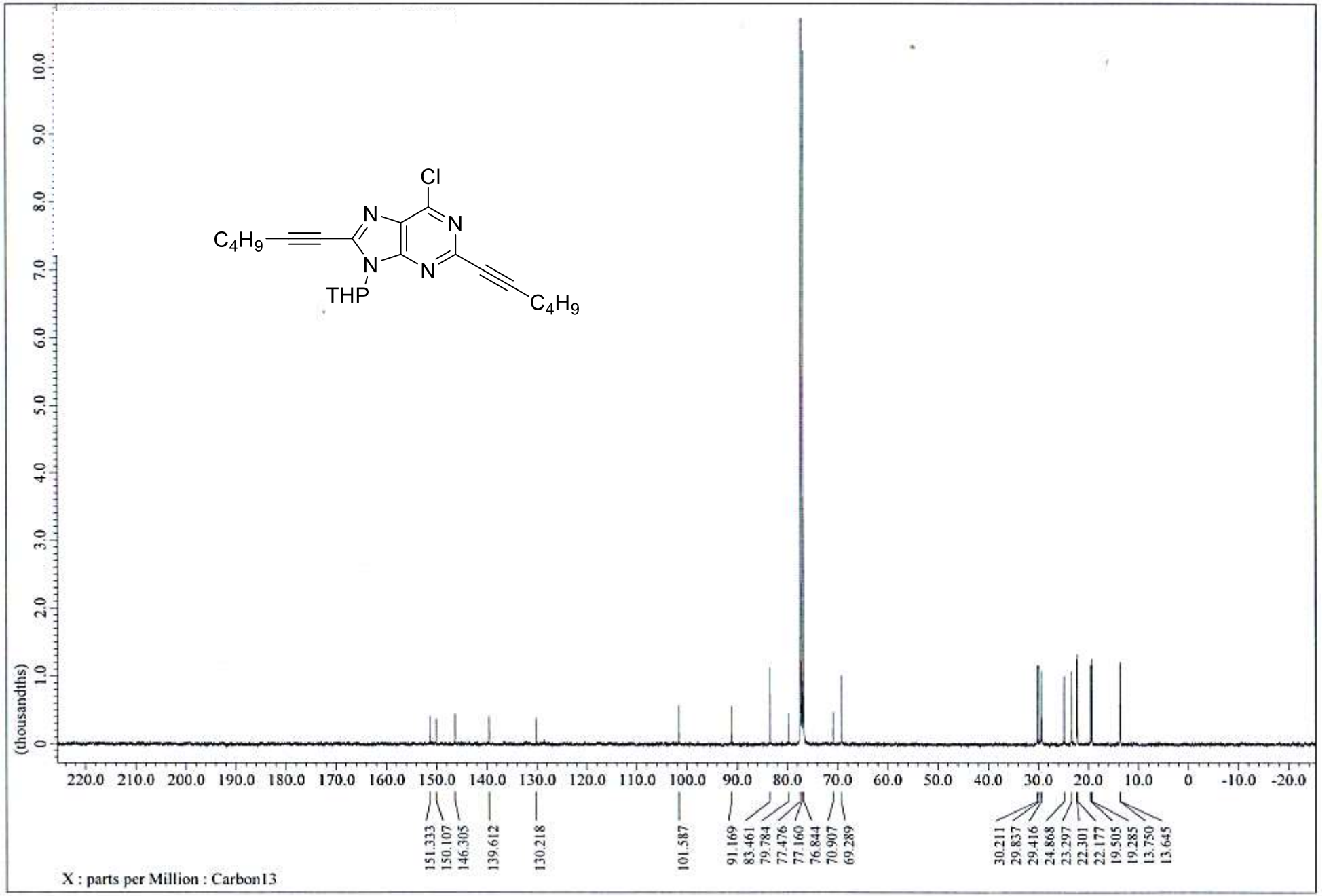
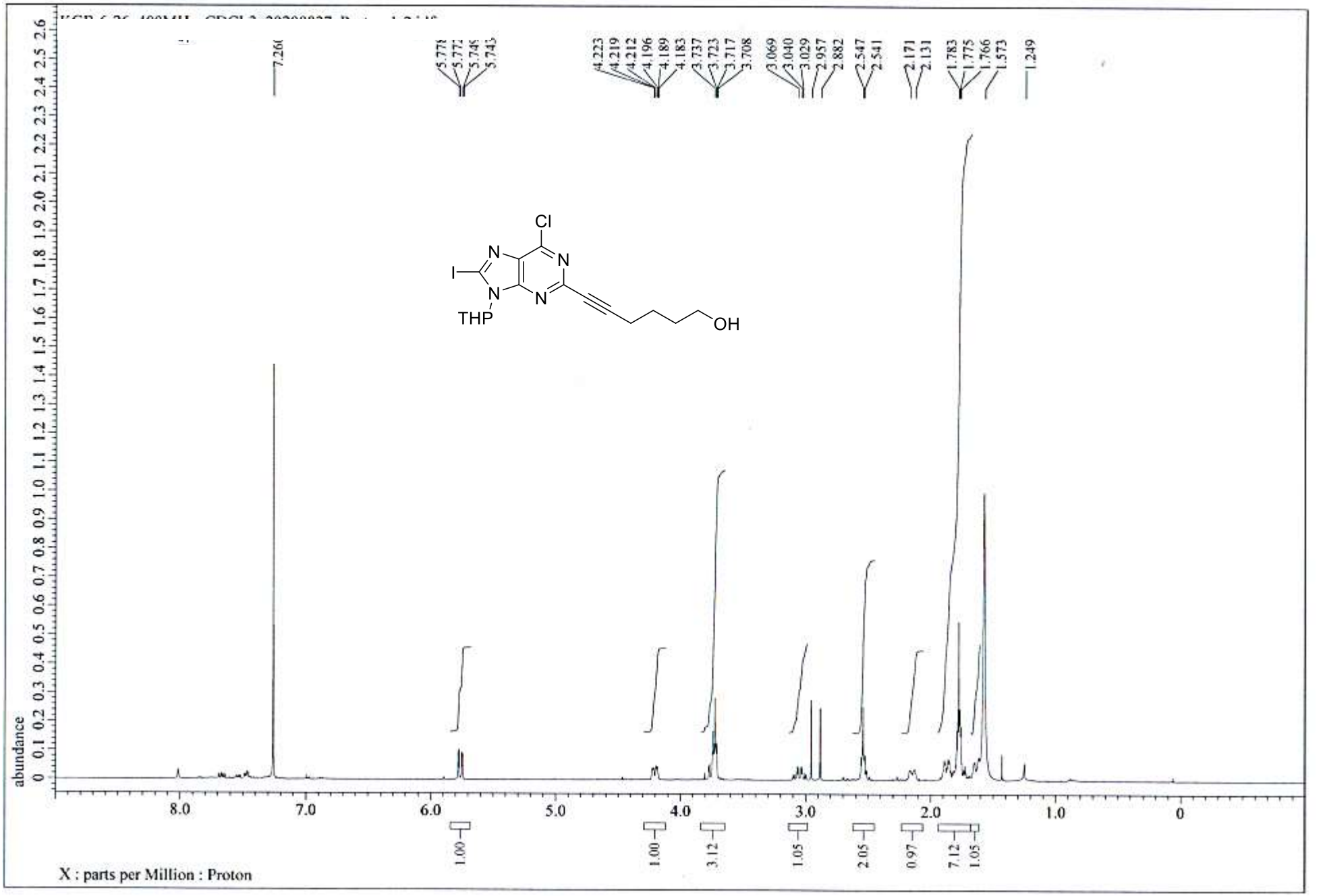
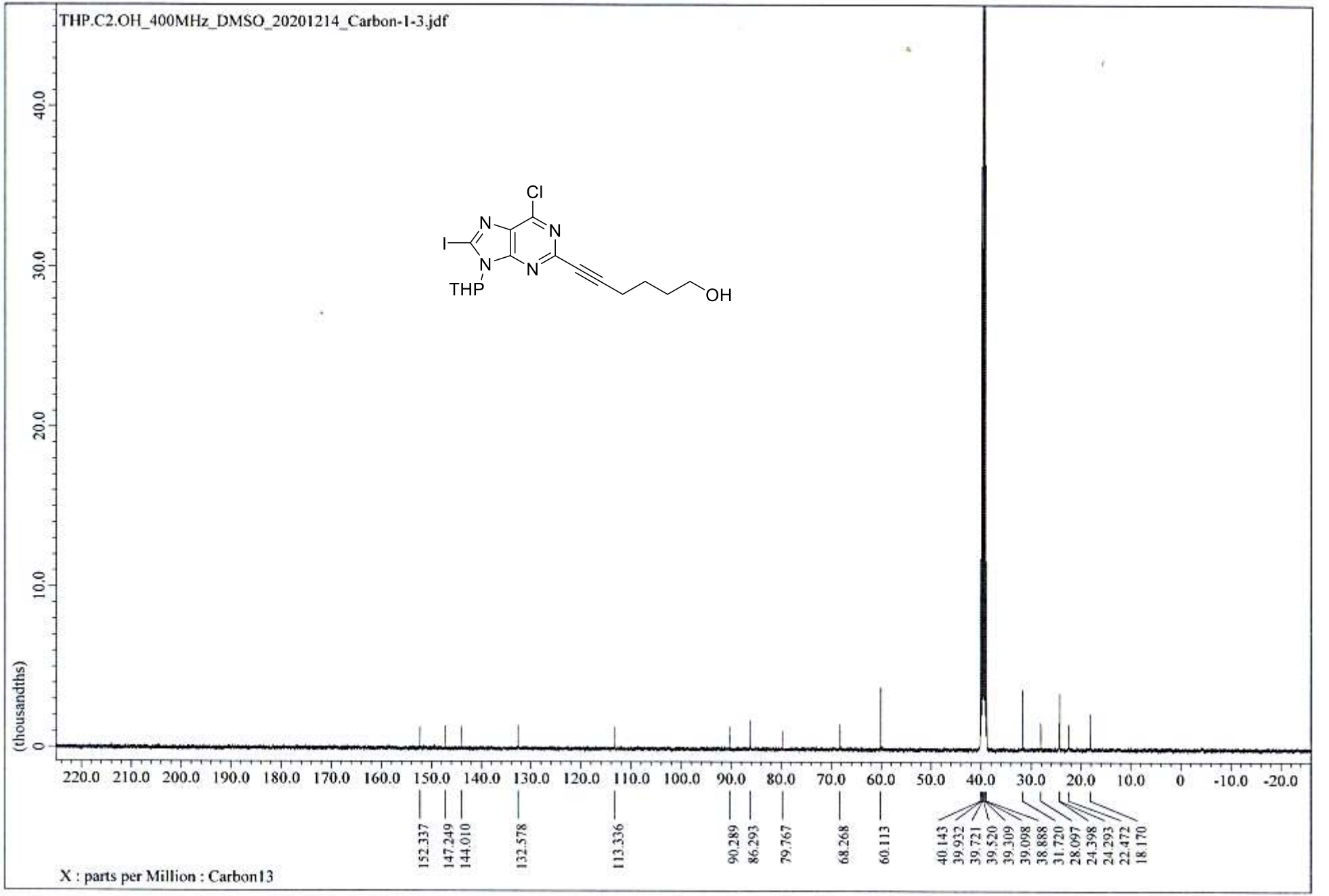


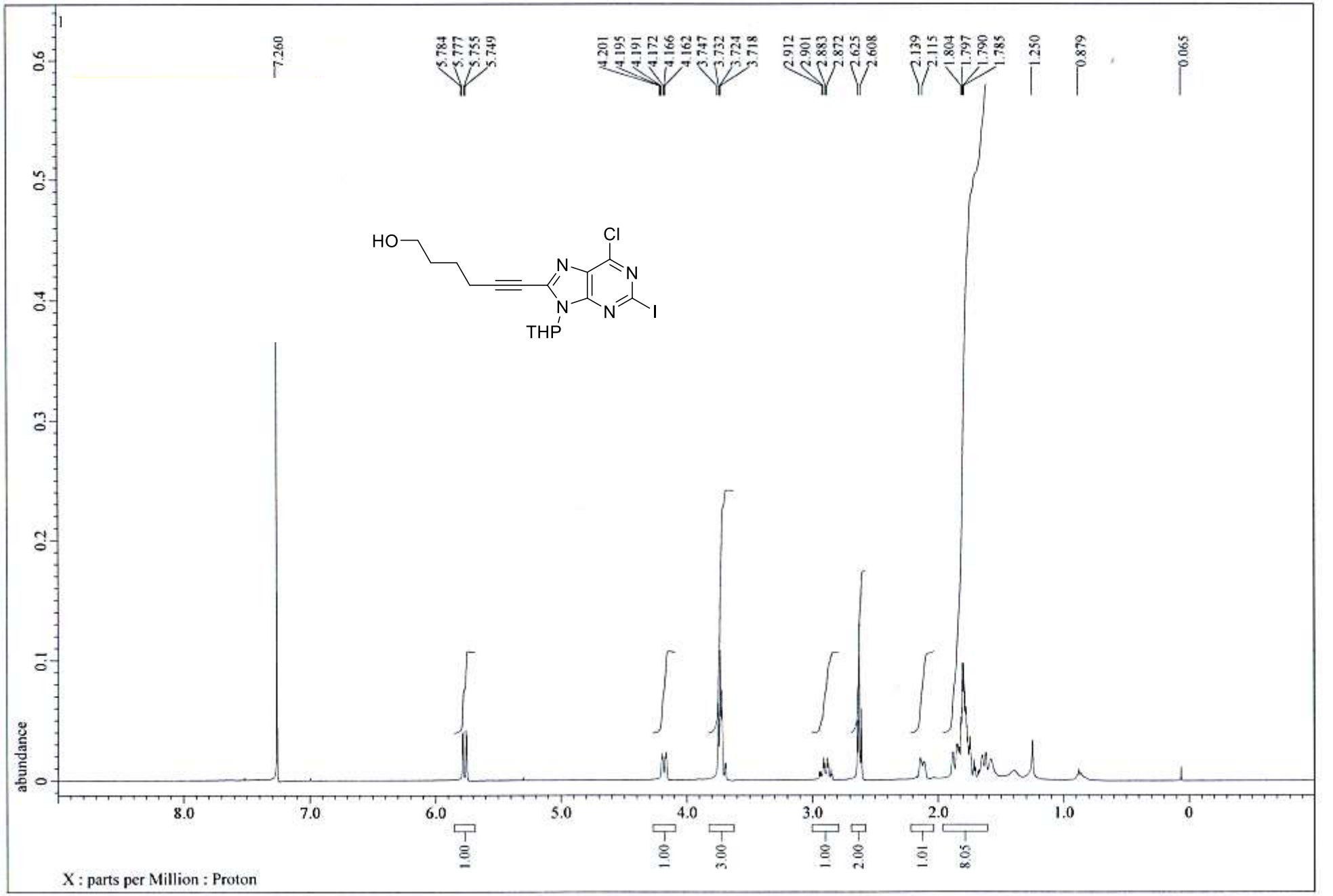
^{1}H NMR (400 MHz, $CDCl_3$) of **6a**



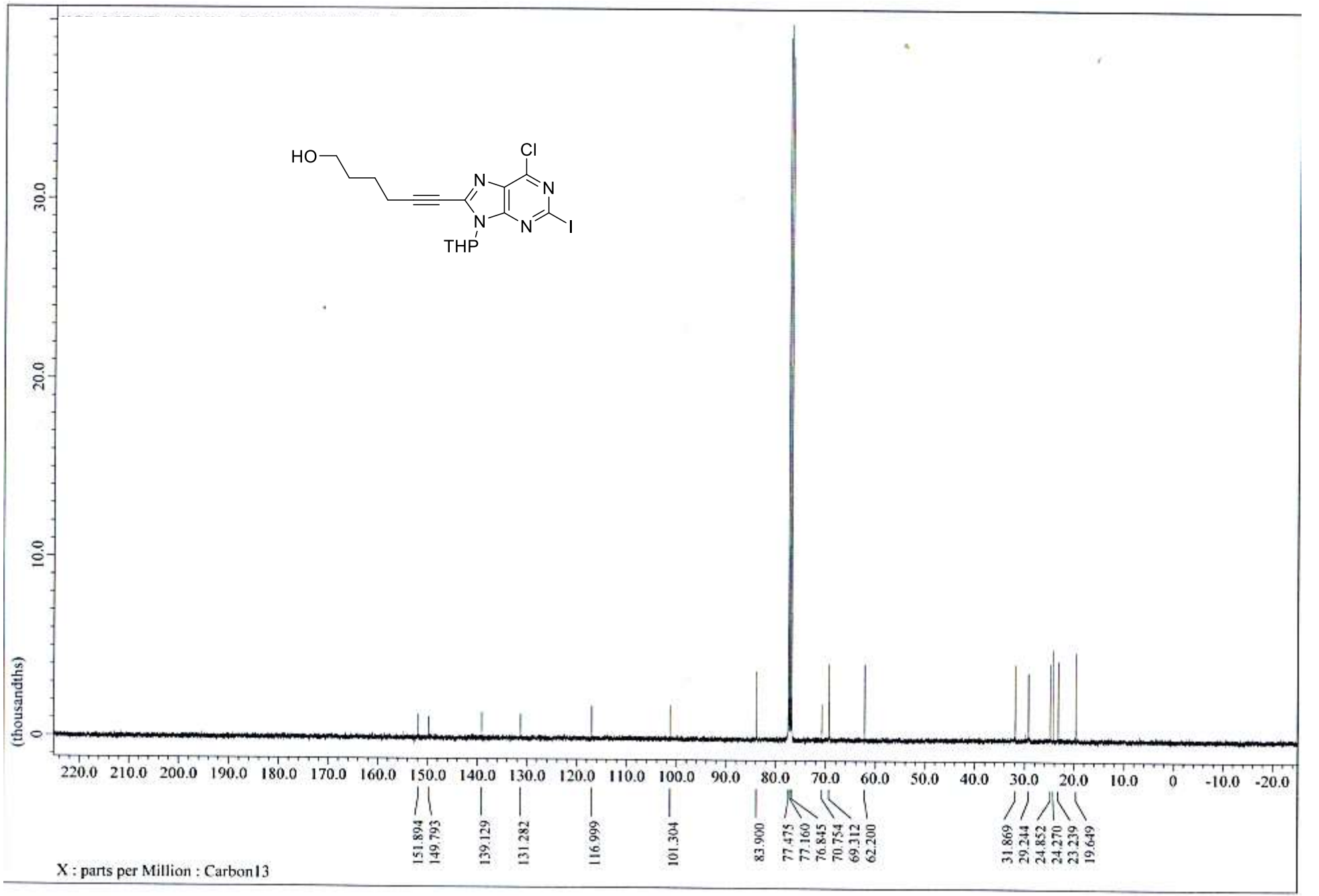
^{13}C NMR (100 MHz, $CDCl_3$) of **6a**



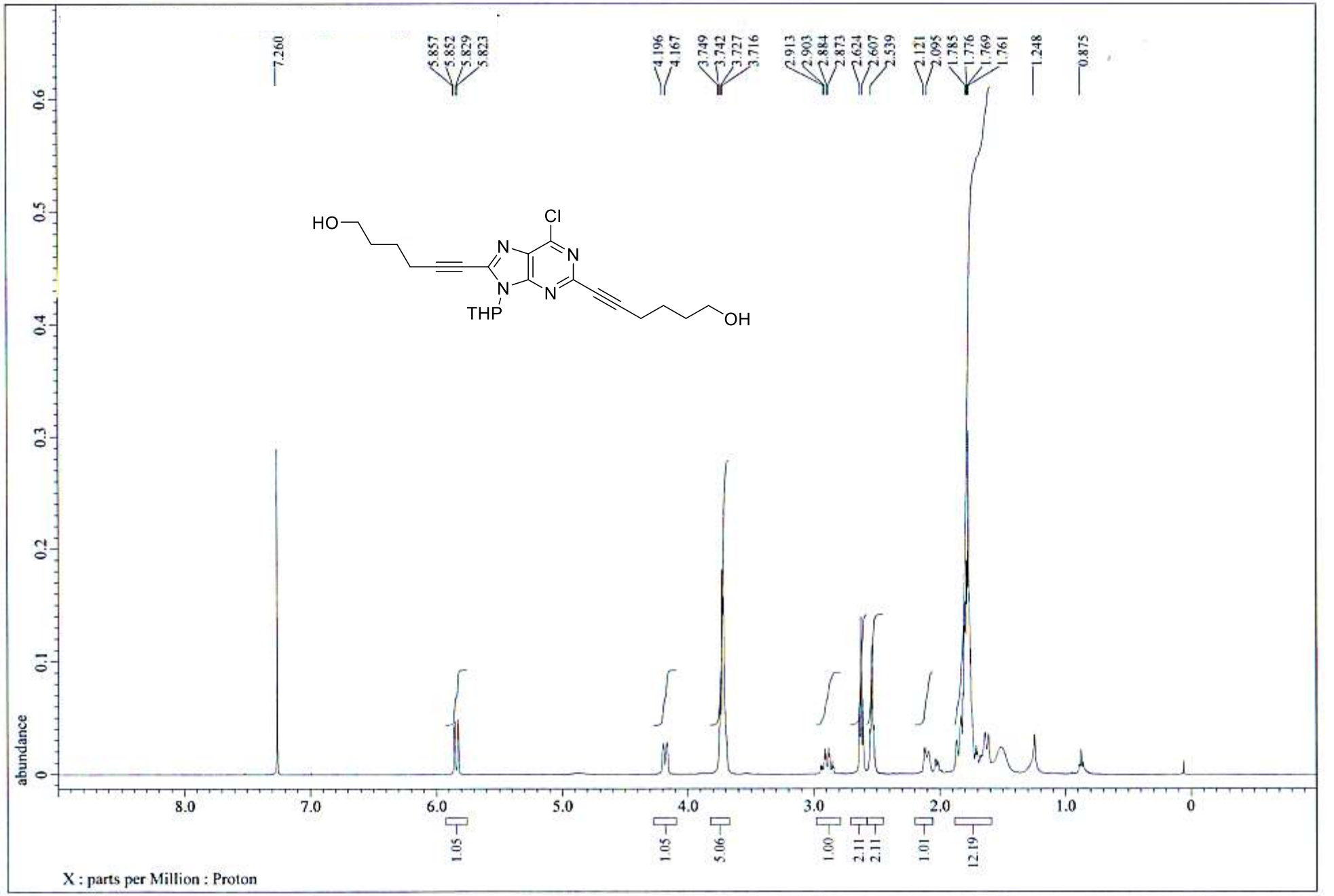
^{1}H NMR (400 MHz, $CDCl_3$) of **7a**



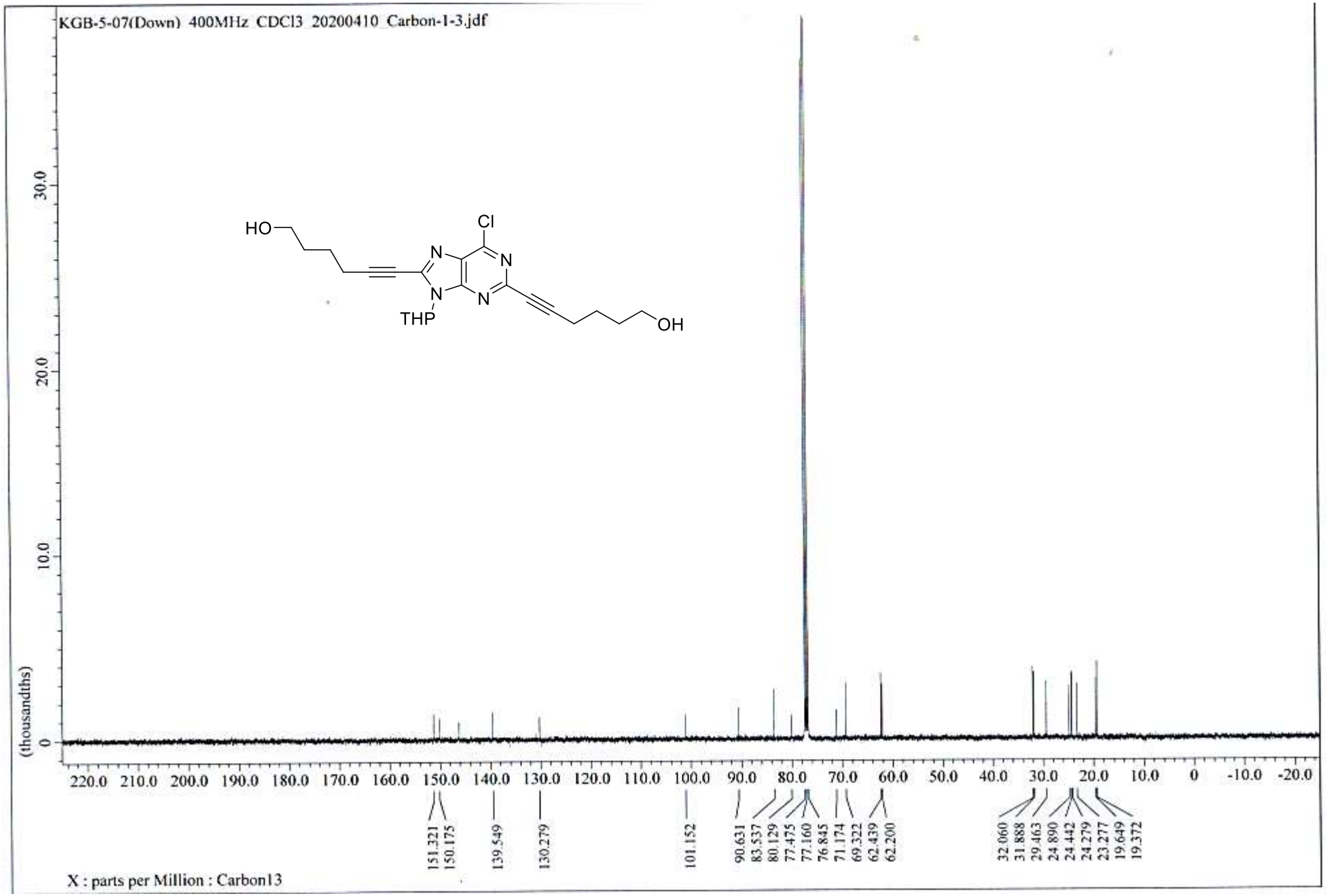
^{13}C NMR (100 MHz, $CDCl_3$) of **7a**



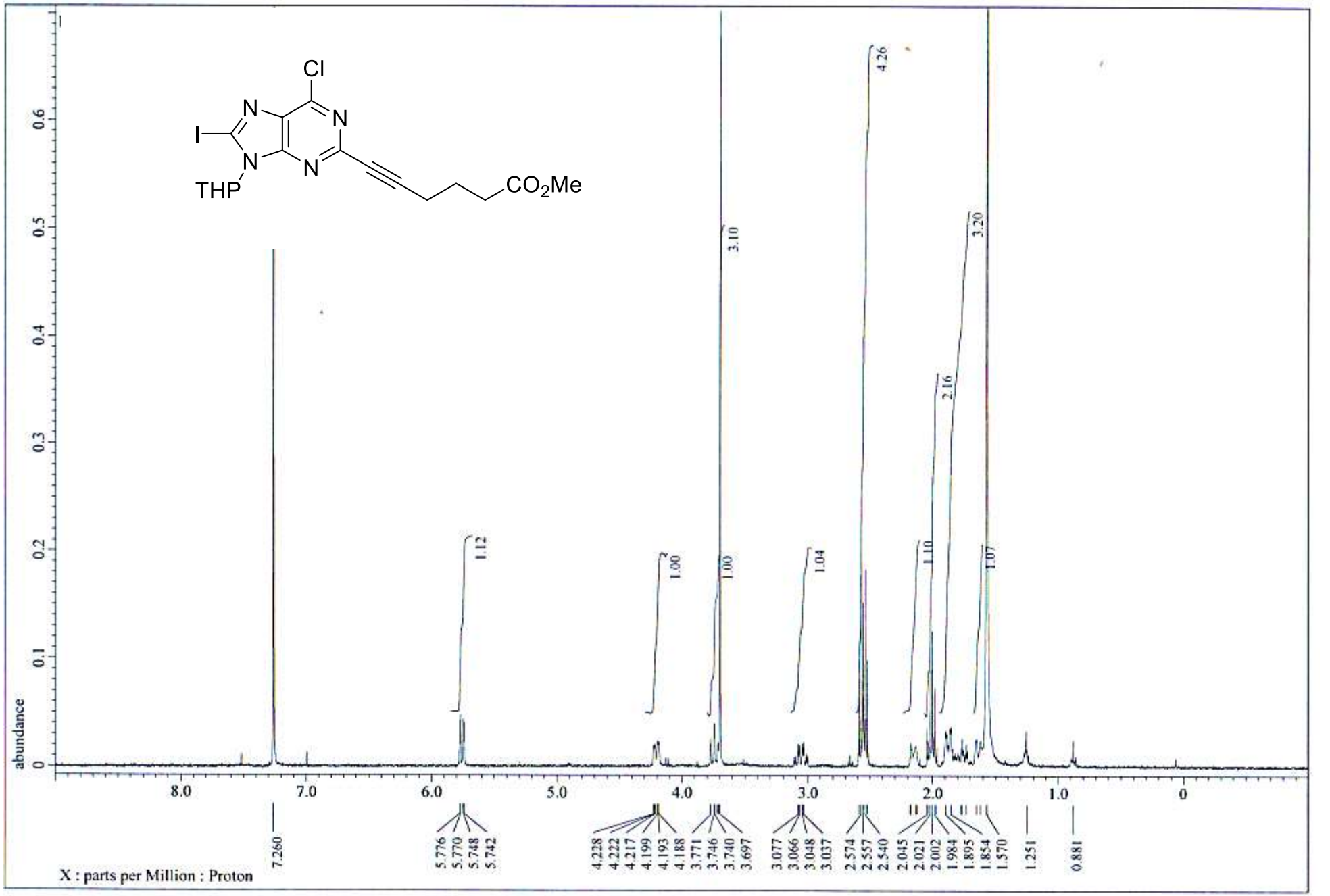
^{1}H NMR (400 MHz, $CDCl_3$) of **8a**



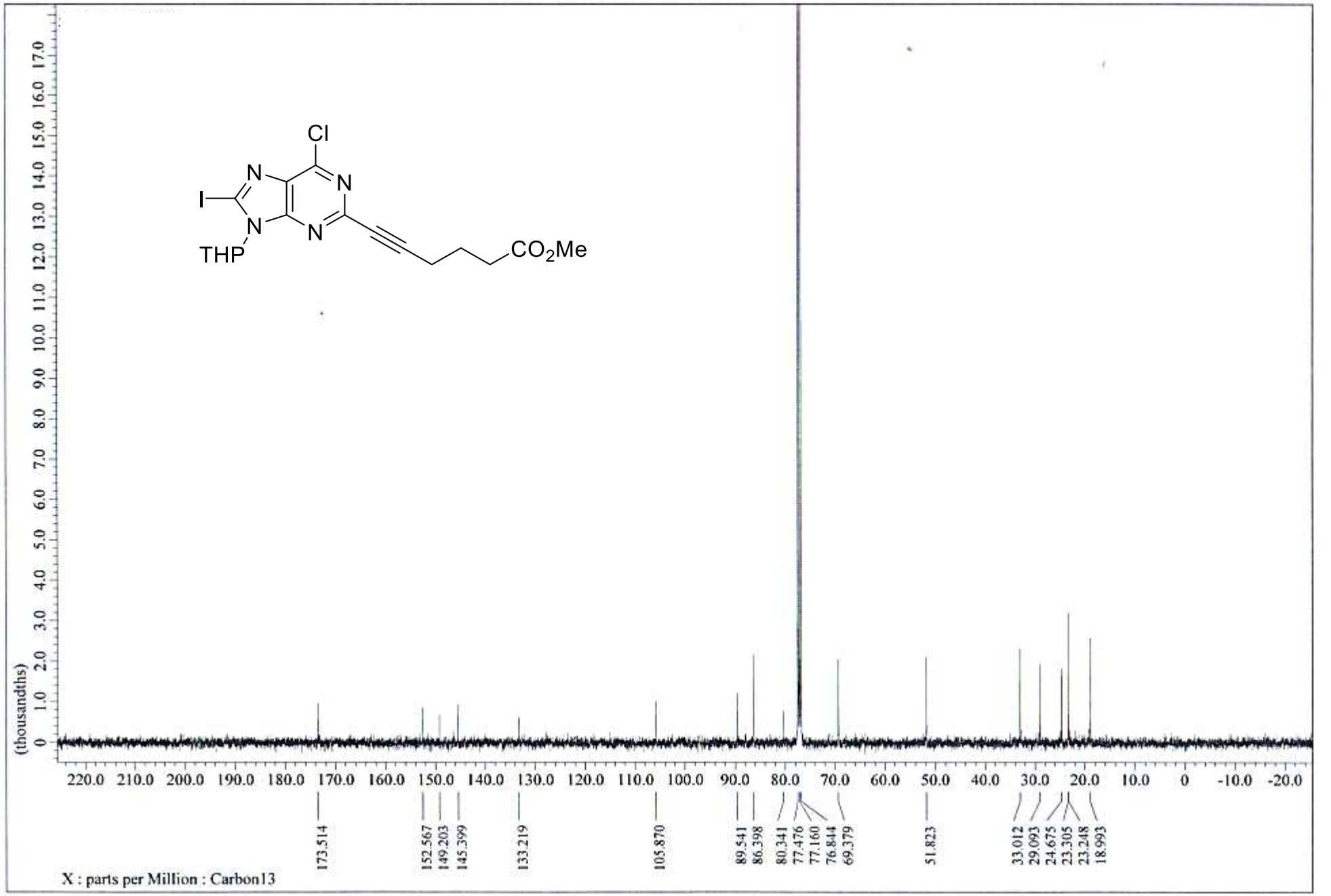
^{13}C NMR (100 MHz, $CDCl_3$) of **8a**



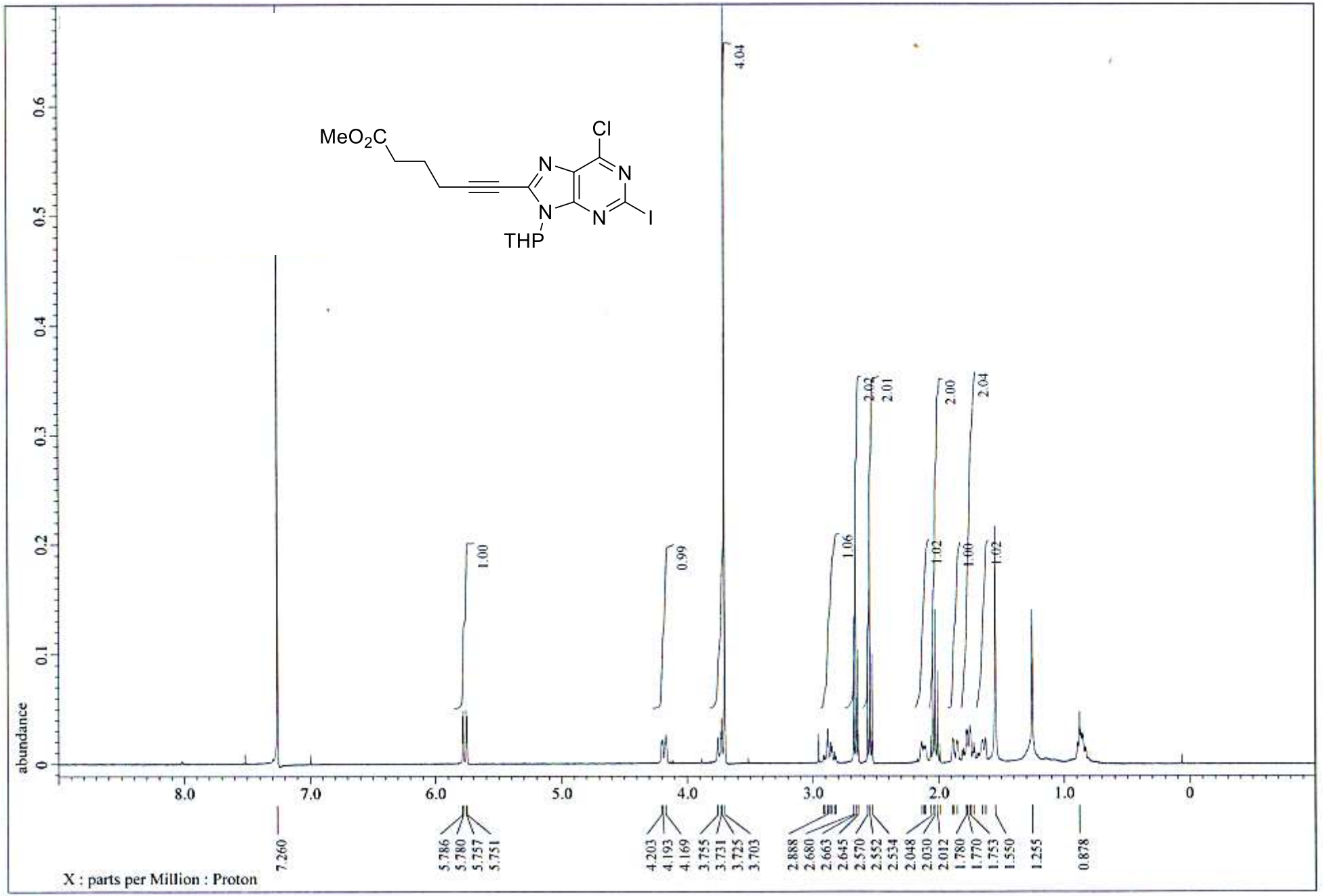
^{1}H NMR (400 MHz, $CDCl_3$) of **6b**



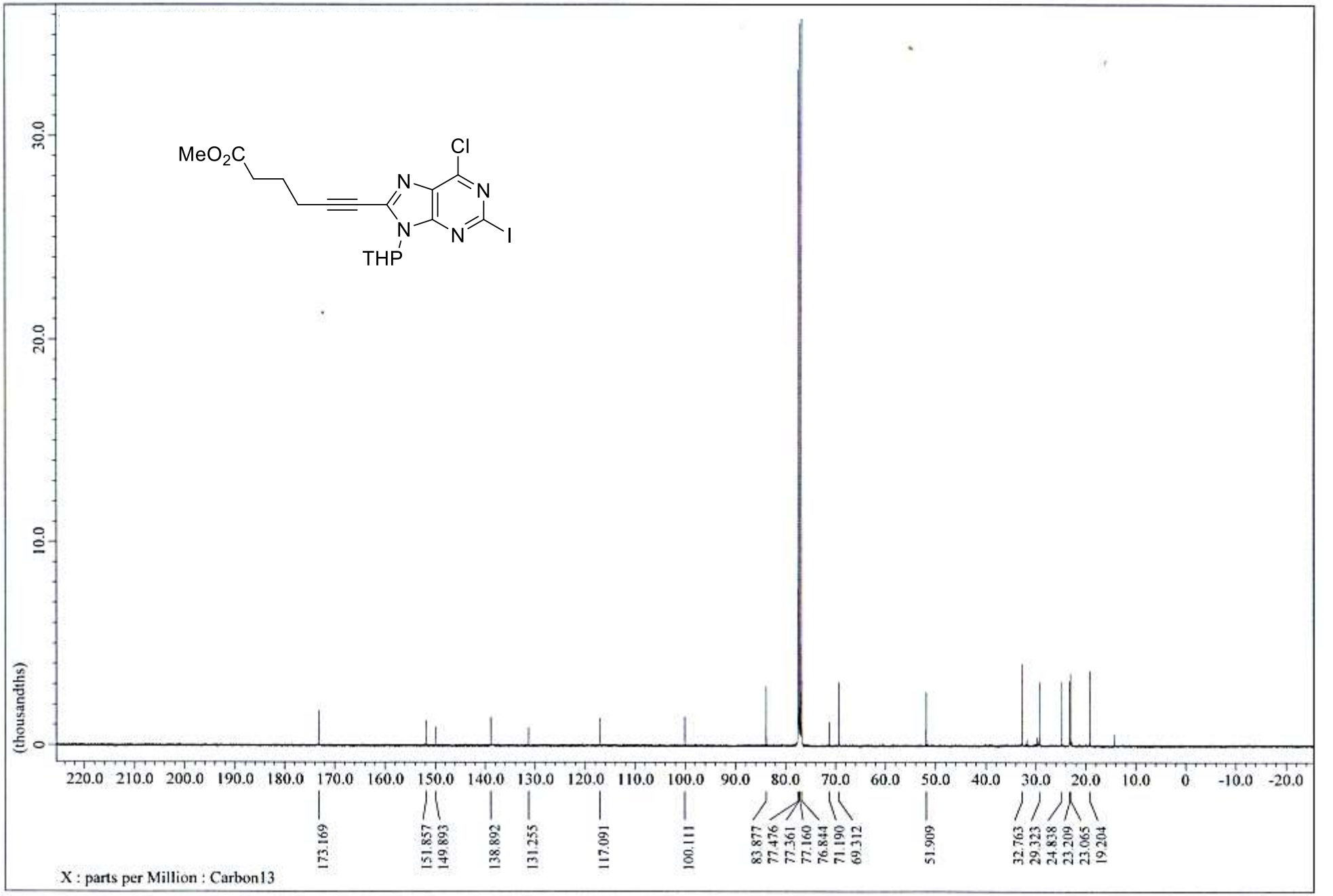
^{13}C NMR (100 MHz, $CDCl_3$) of **6b**



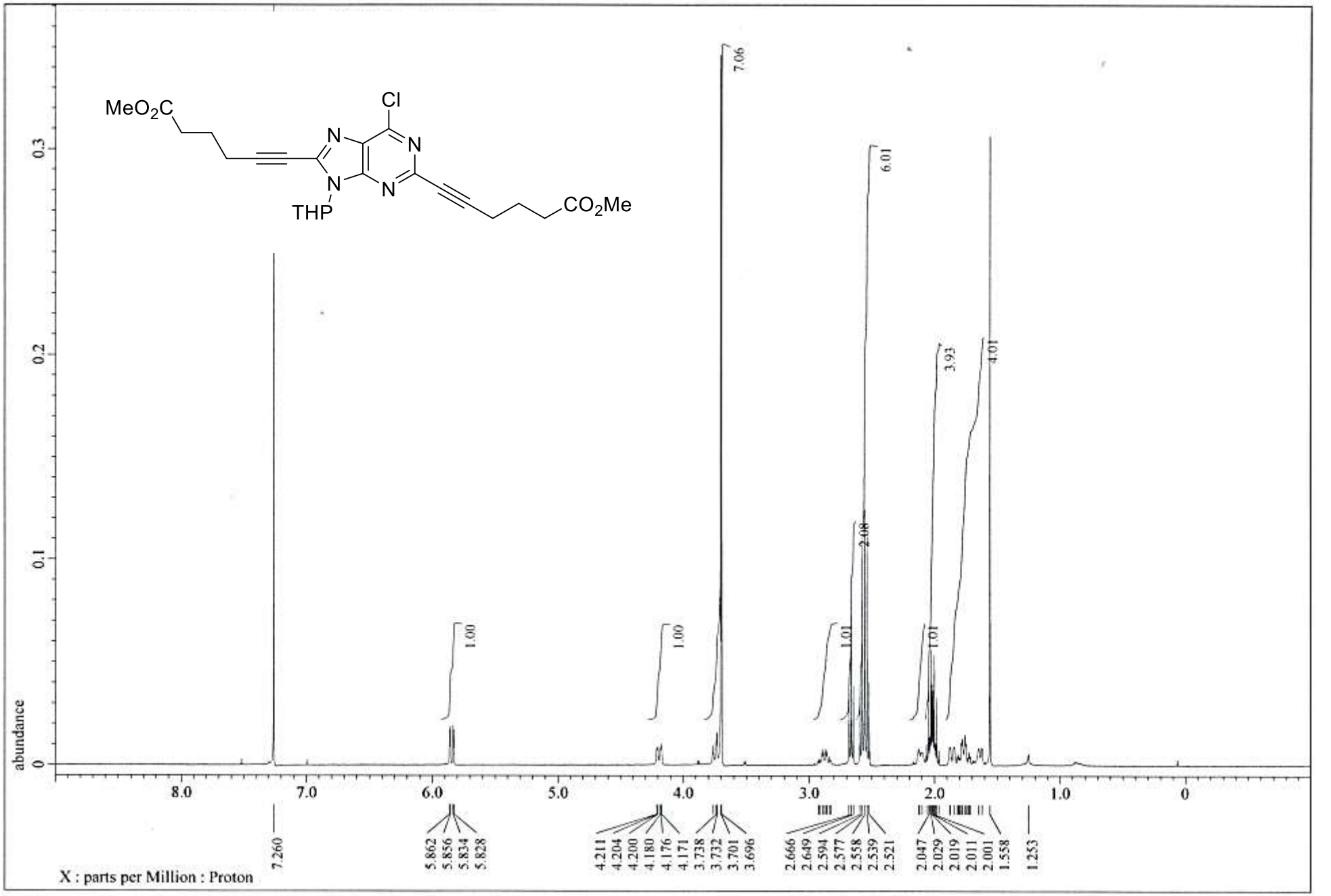
^{1}H NMR (400 MHz, $CDCl_3$) of **7b**



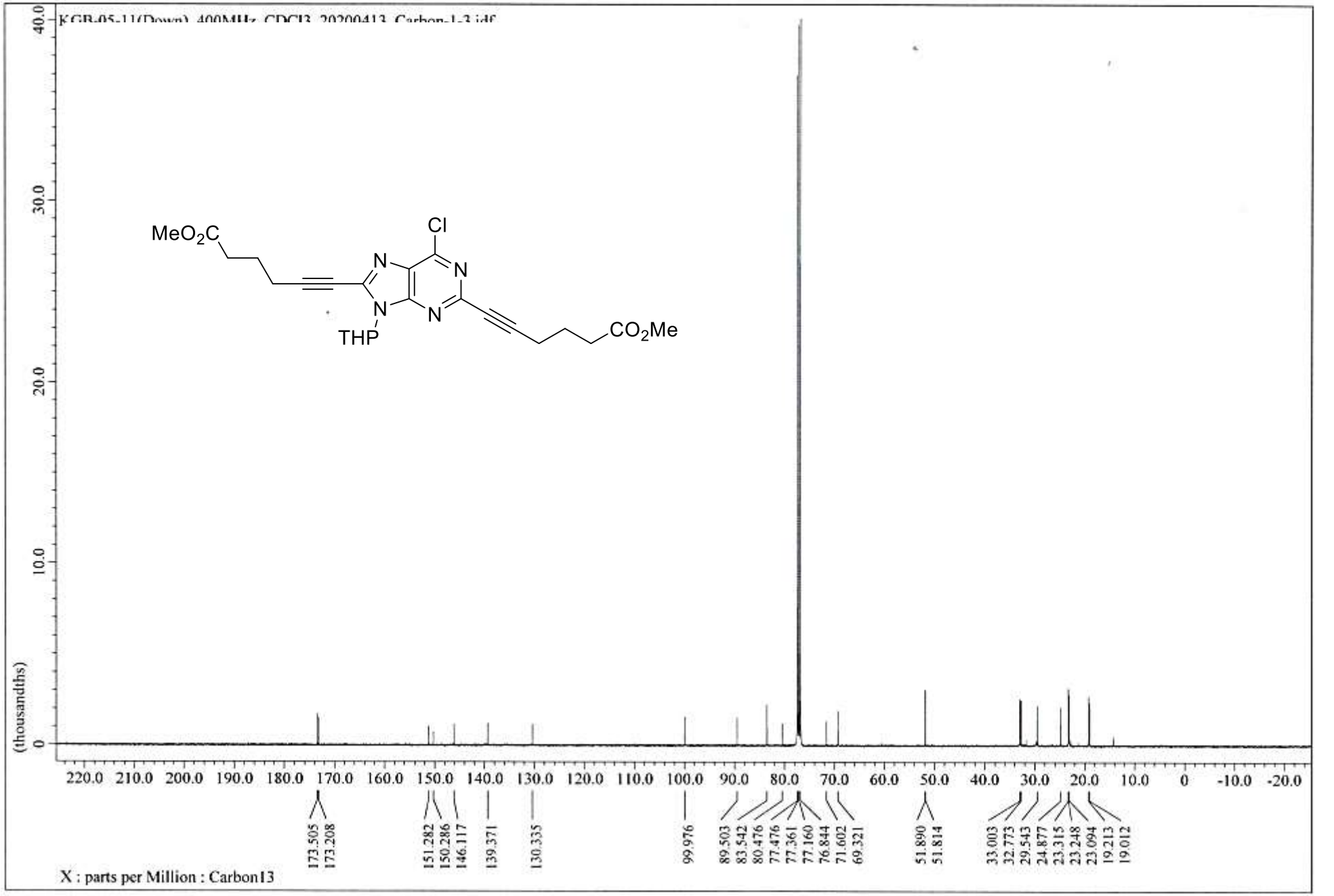
^{13}C NMR (100 MHz, $CDCl_3$) of **7b**



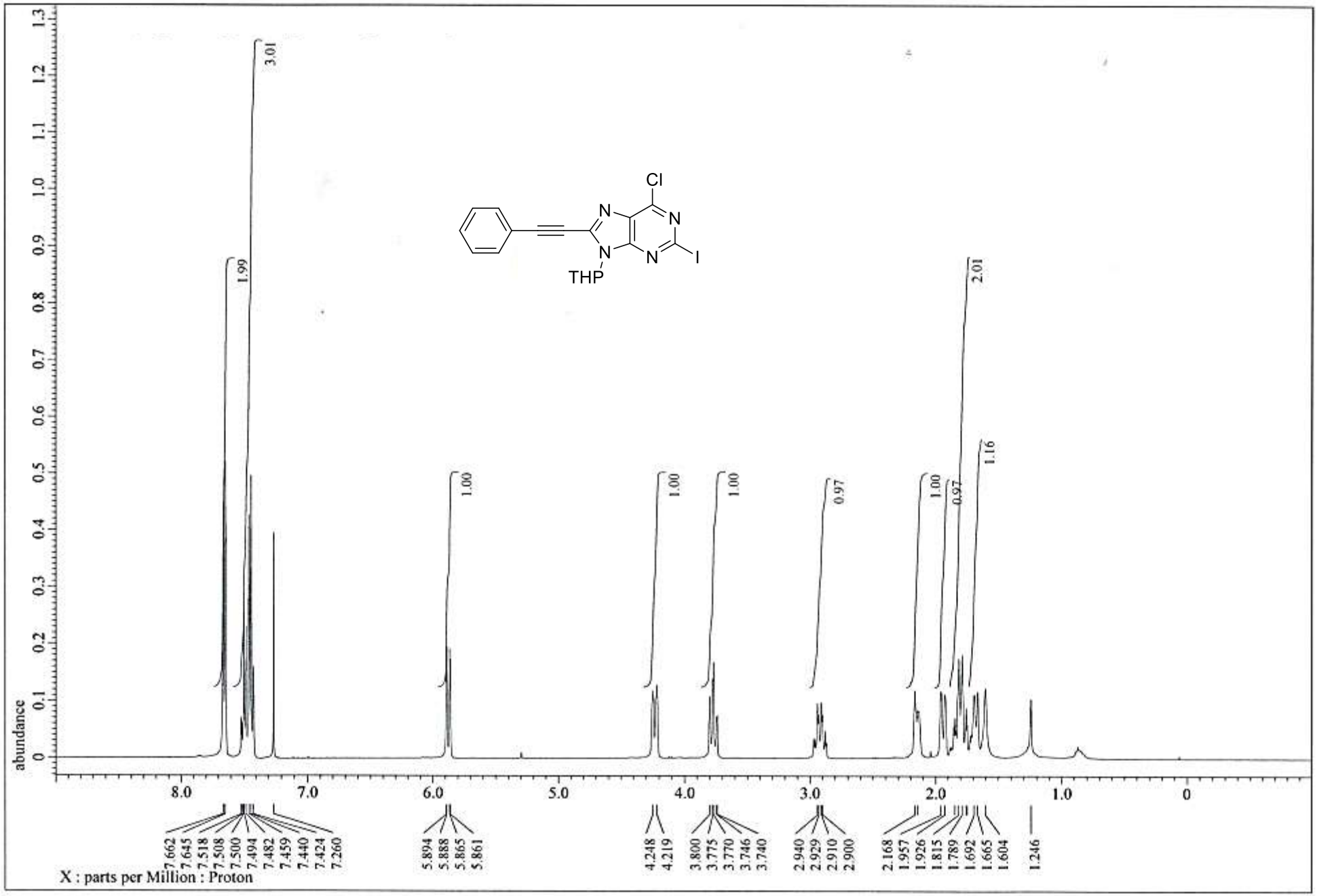
^{1}H NMR (400 MHz, $CDCl_3$) of **8b**



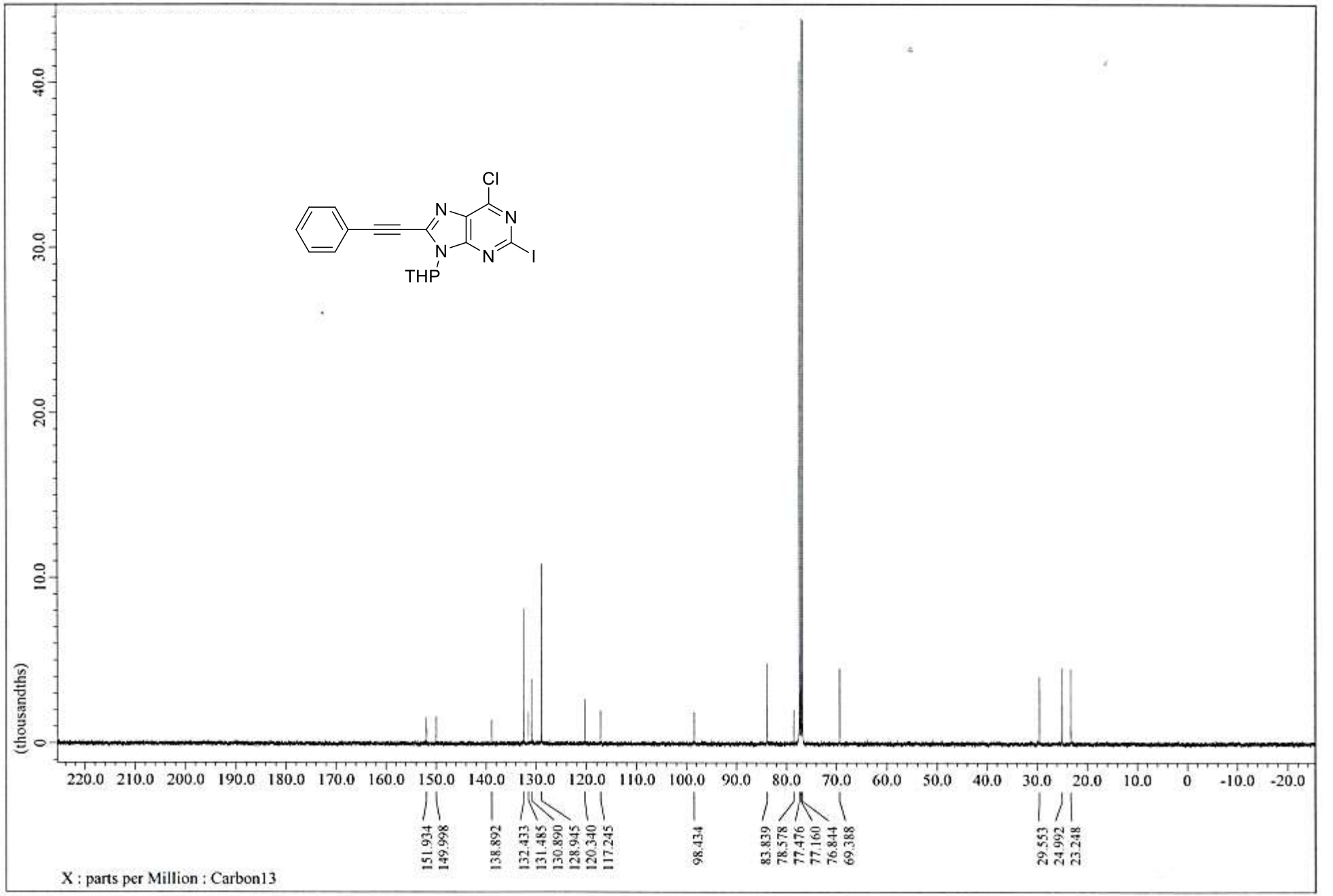
^{13}C NMR (100 MHz, $CDCl_3$) of **8b**



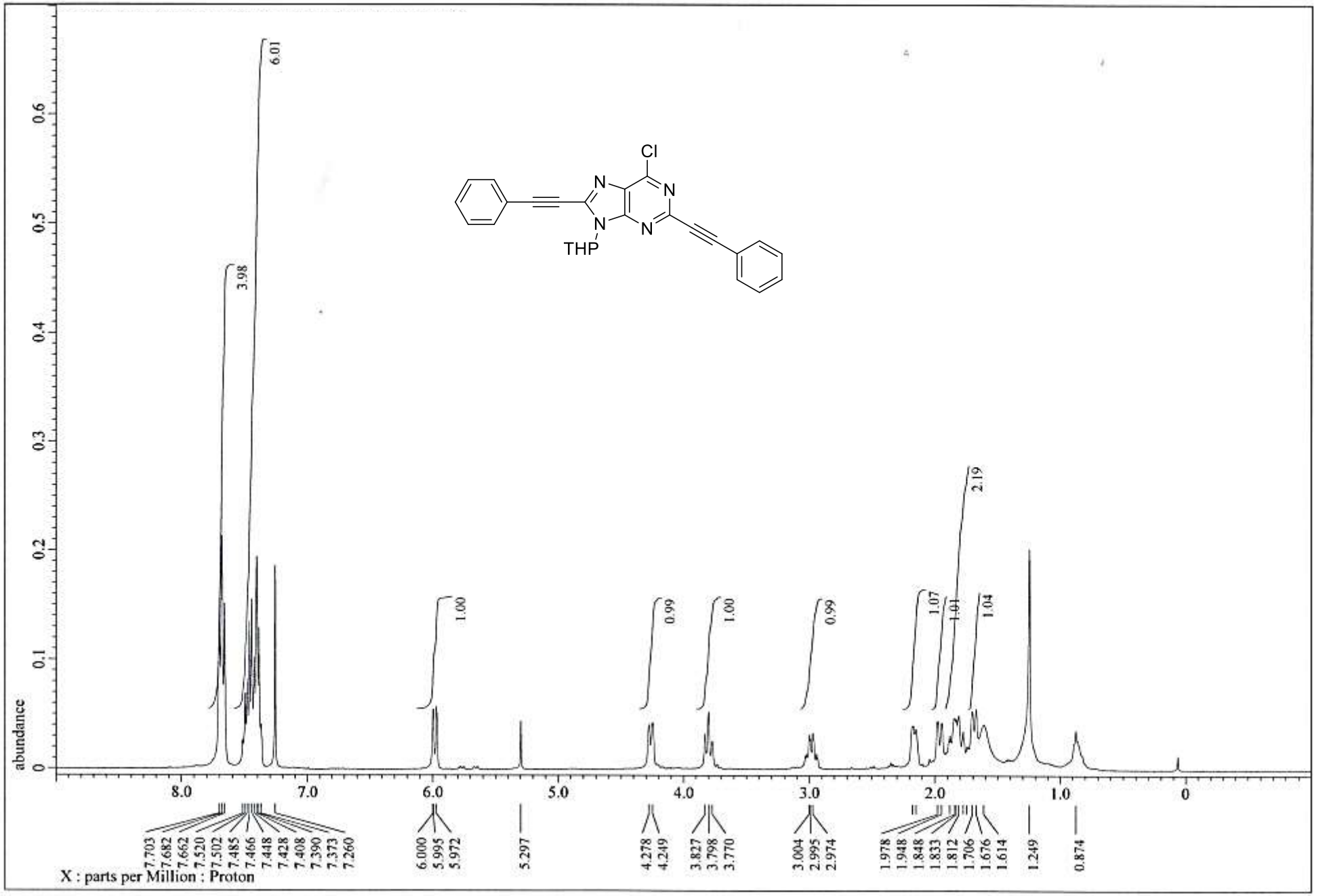
^{1}H NMR (400 MHz, $CDCl_3$) of **7c**



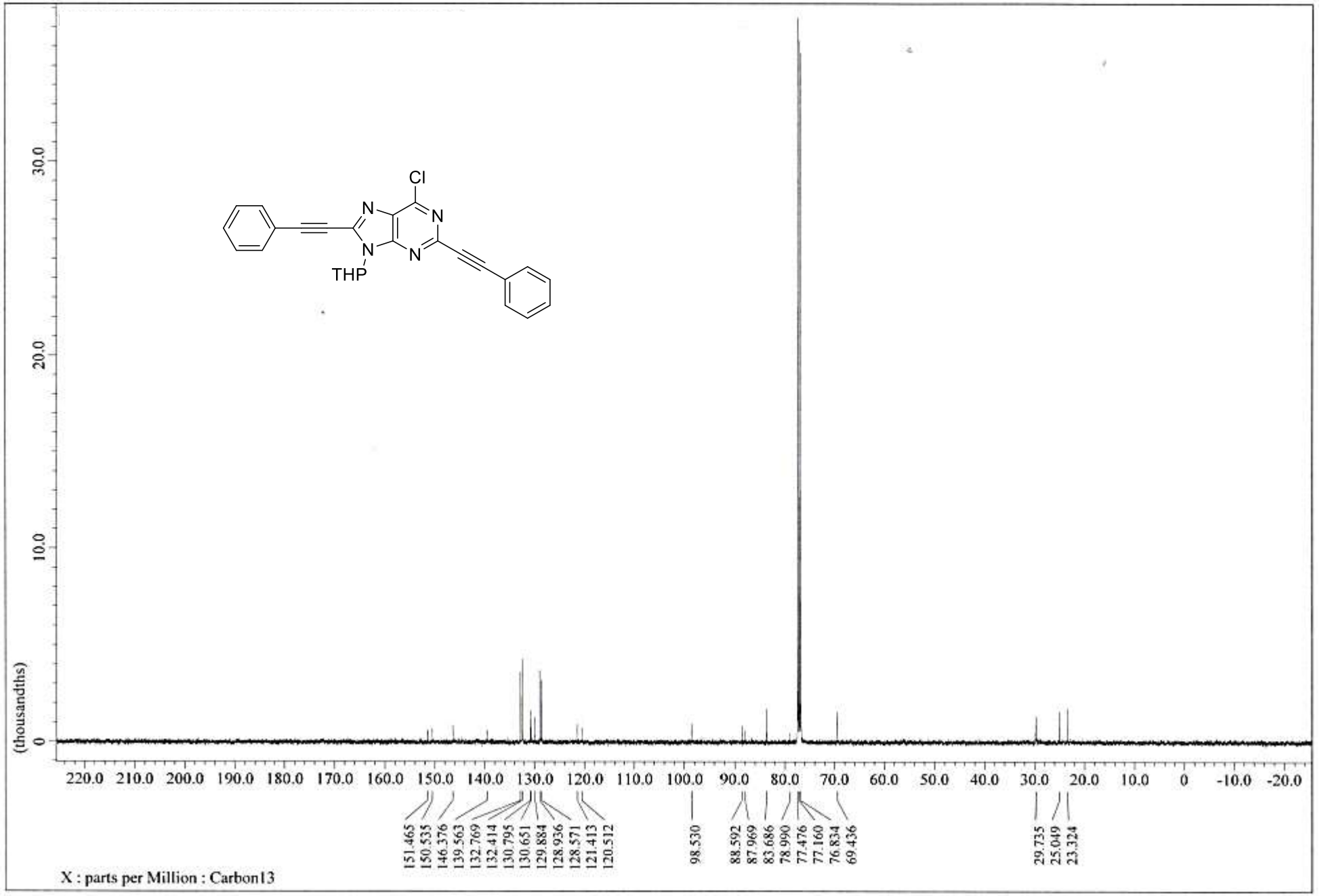
^{13}C NMR (100 MHz, $CDCl_3$) of **7c**



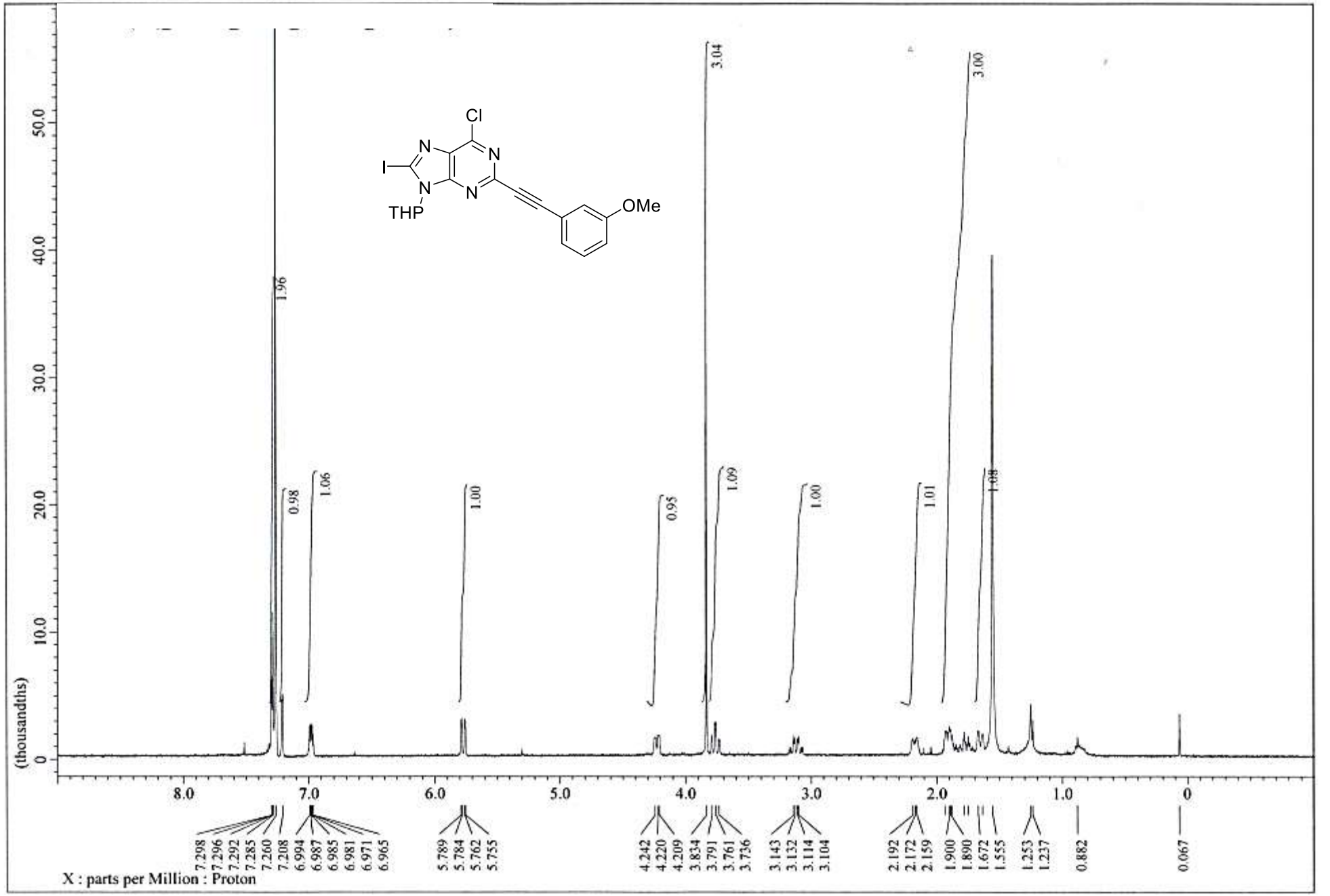
^{1}H NMR (400 MHz, $CDCl_3$) of **8c**



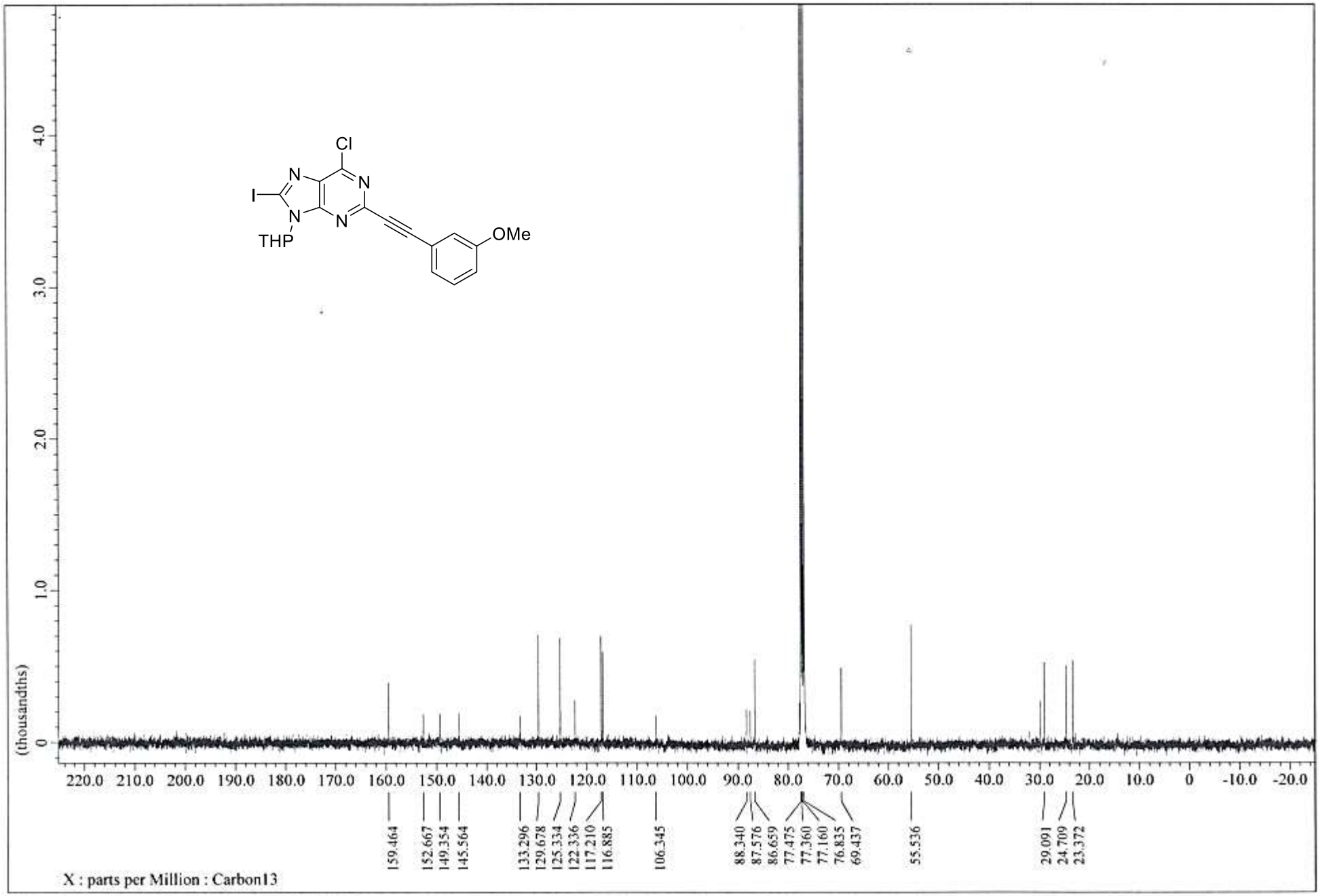
^{13}C NMR (100 MHz, $CDCl_3$) of **8c**



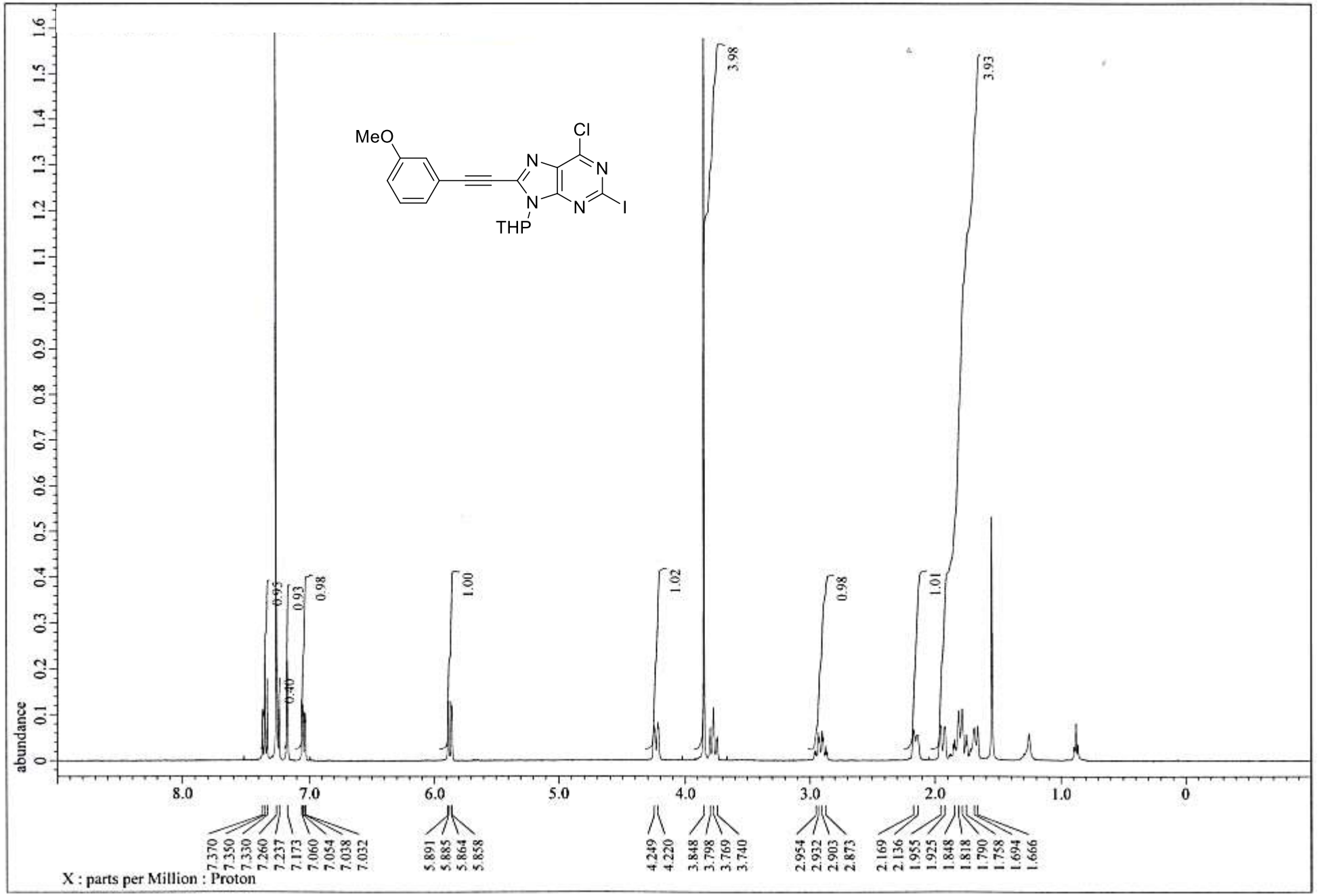
^{1}H NMR (400 MHz, $CDCl_3$) of **6d**



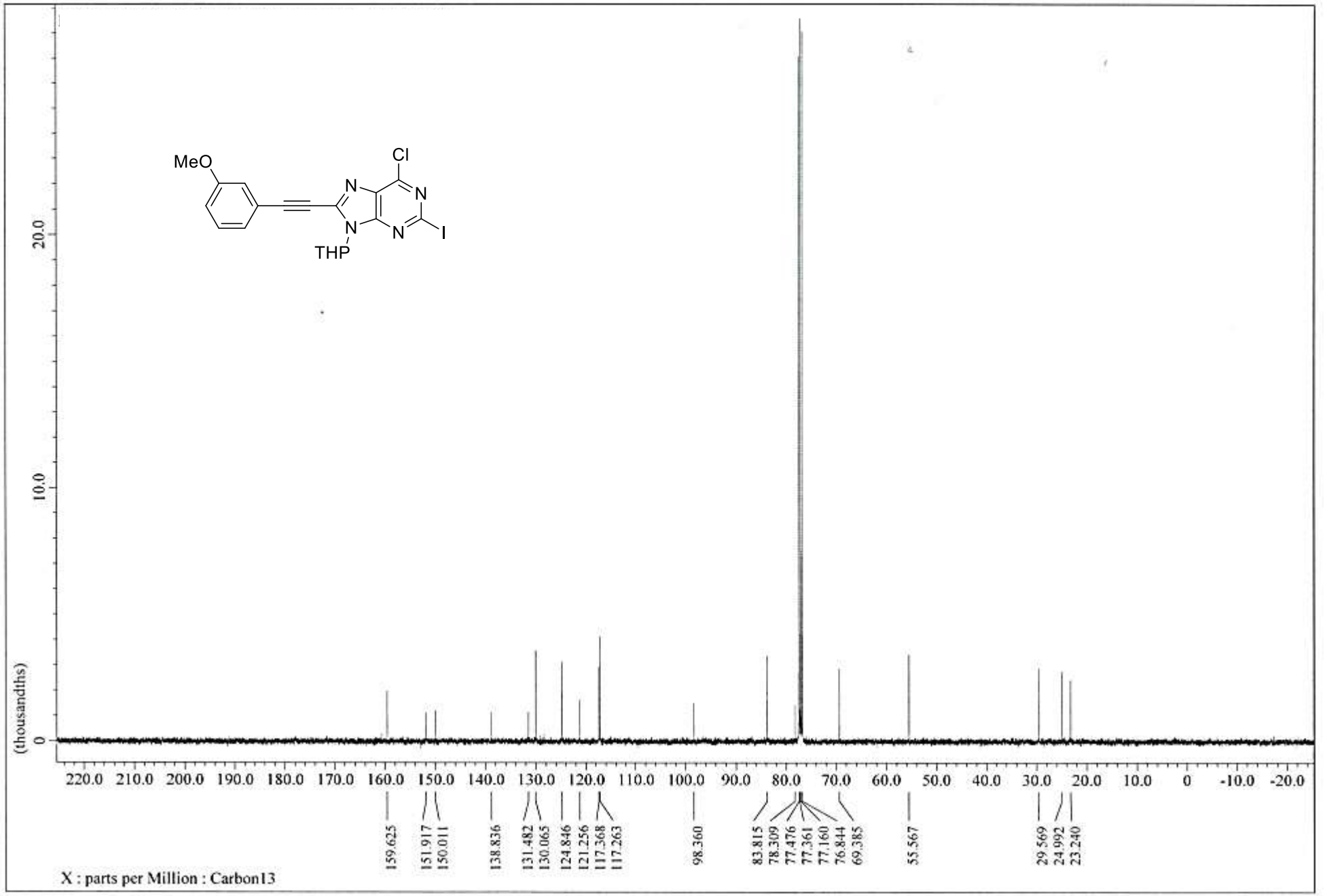
^{13}C NMR (100 MHz, $CDCl_3$) of **6d**



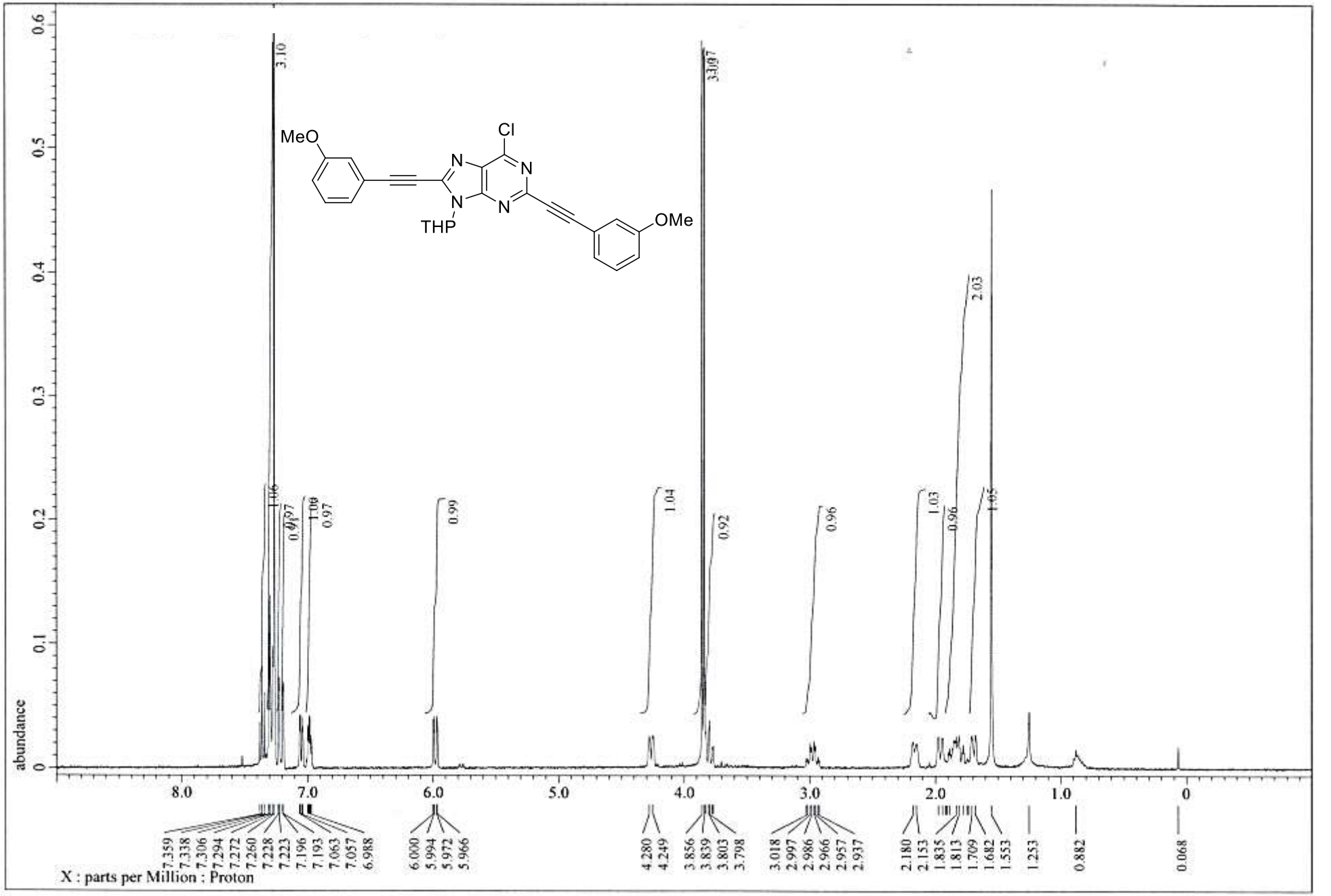
^{1}H NMR (400 MHz, $CDCl_3$) of **7d**



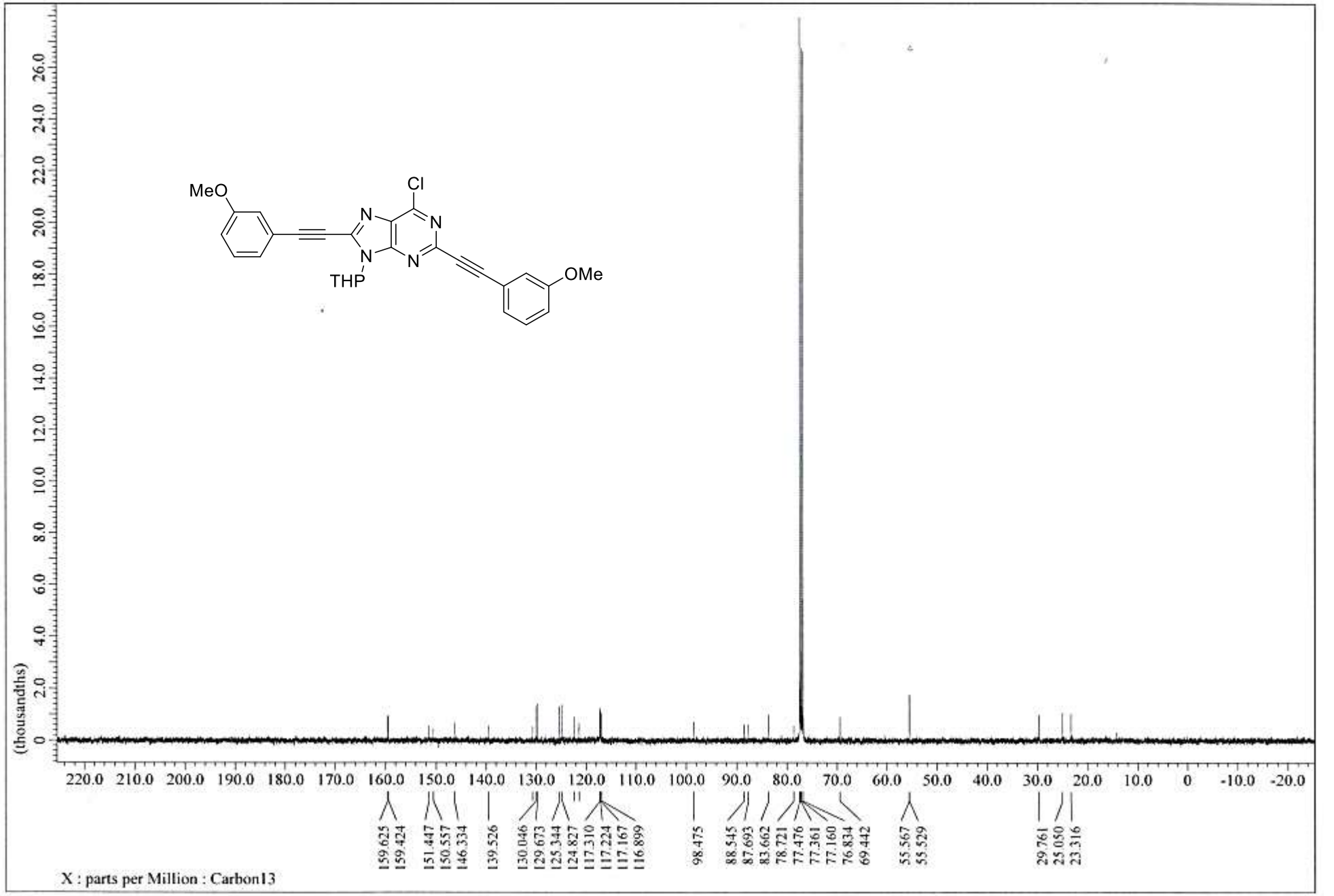
^{13}C NMR (100 MHz, $CDCl_3$) of **7d**



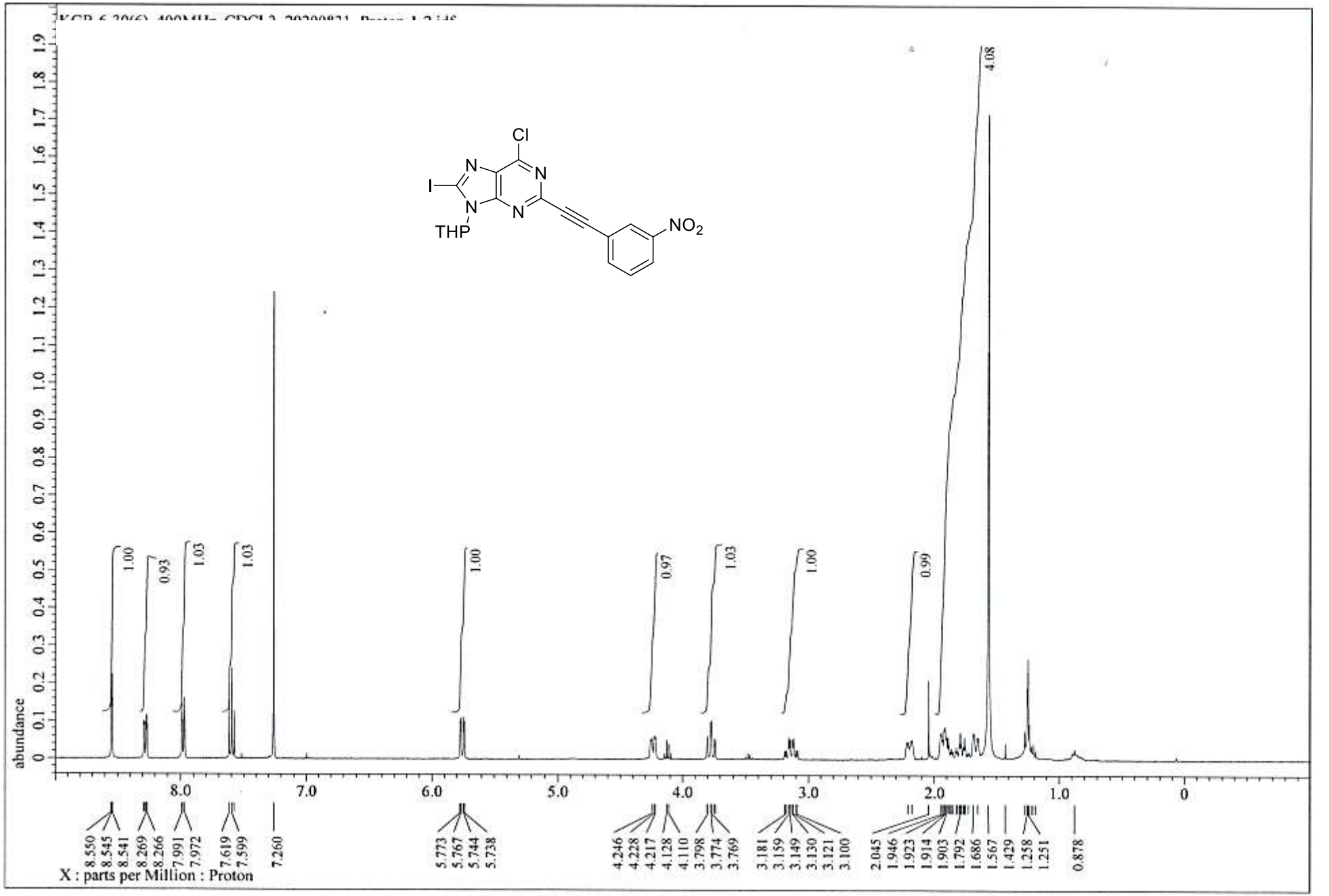
^{1}H NMR (400 MHz, $CDCl_3$) of **8d**



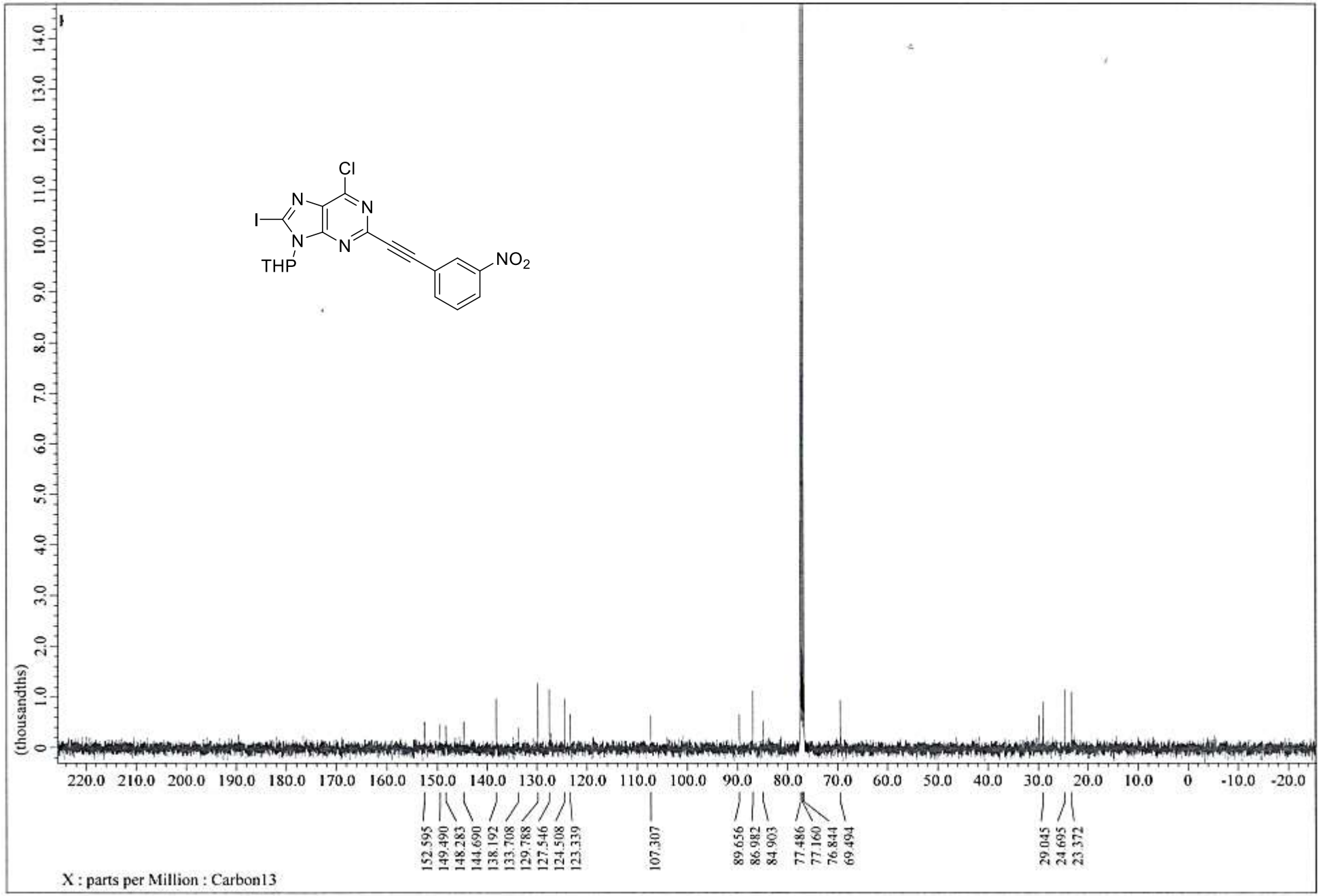
^{13}C NMR (100 MHz, $CDCl_3$) of **8d**



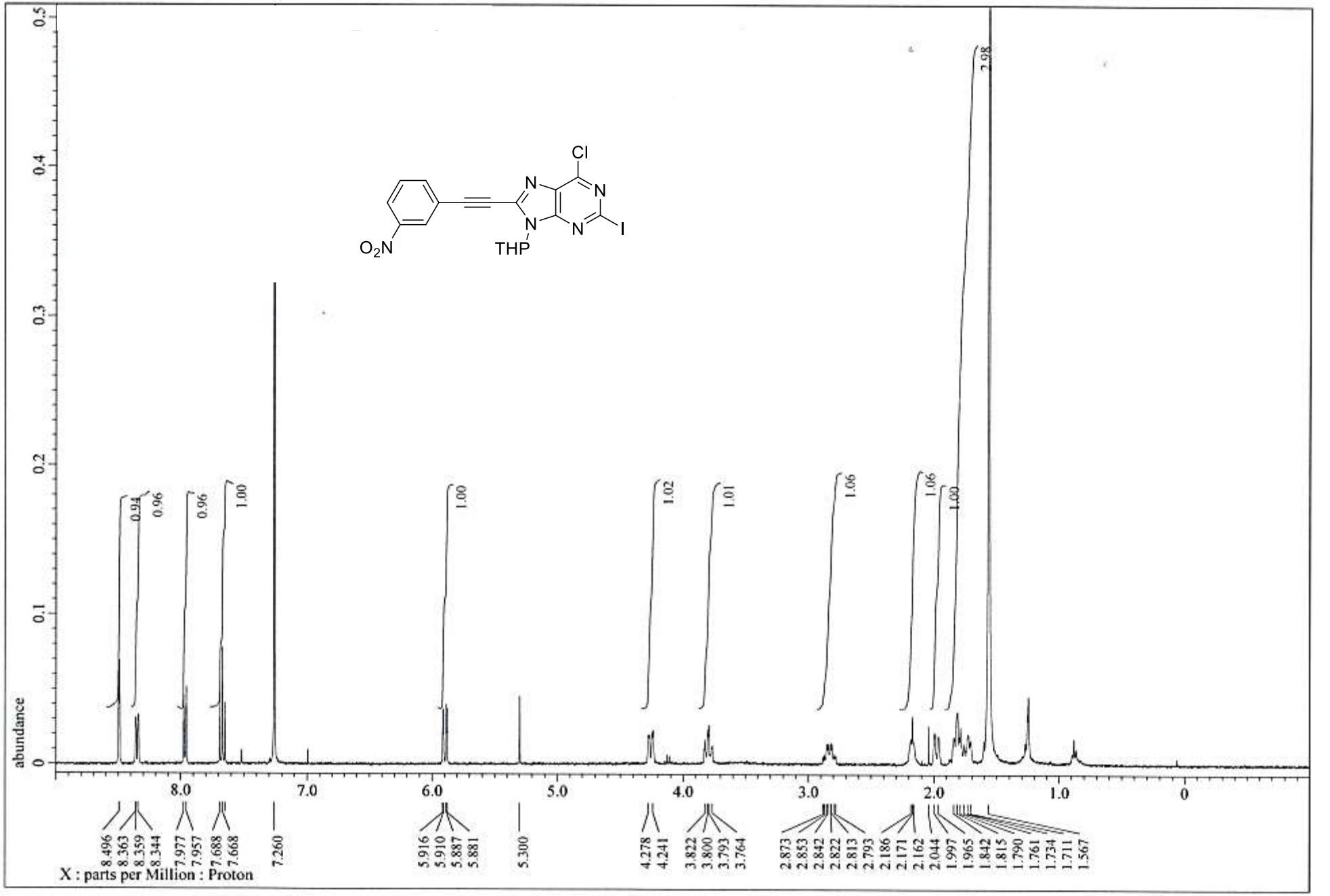
^{1}H NMR (400 MHz, $CDCl_3$) of **6e**



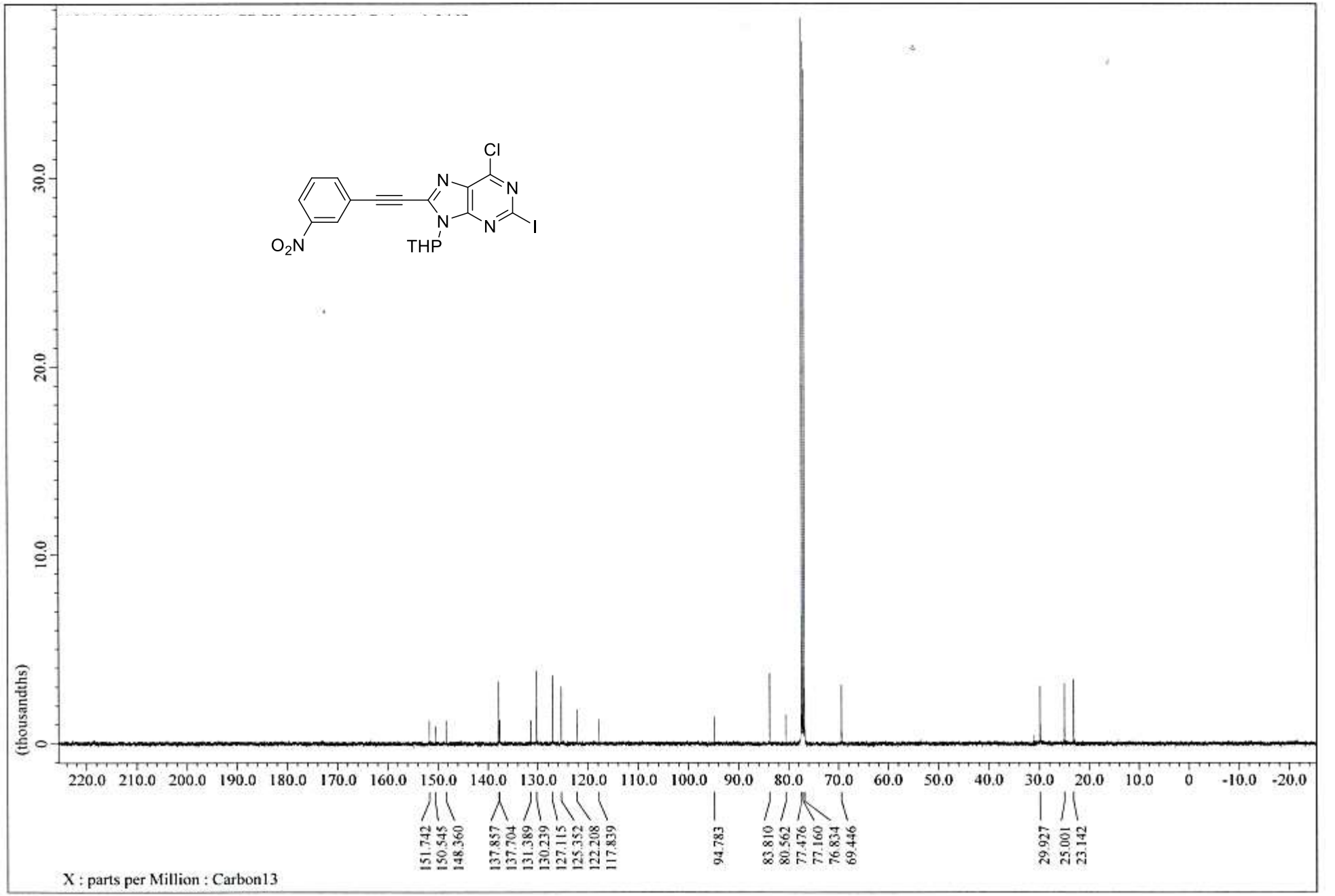
^{13}C NMR (100 MHz, $CDCl_3$) of **6e**



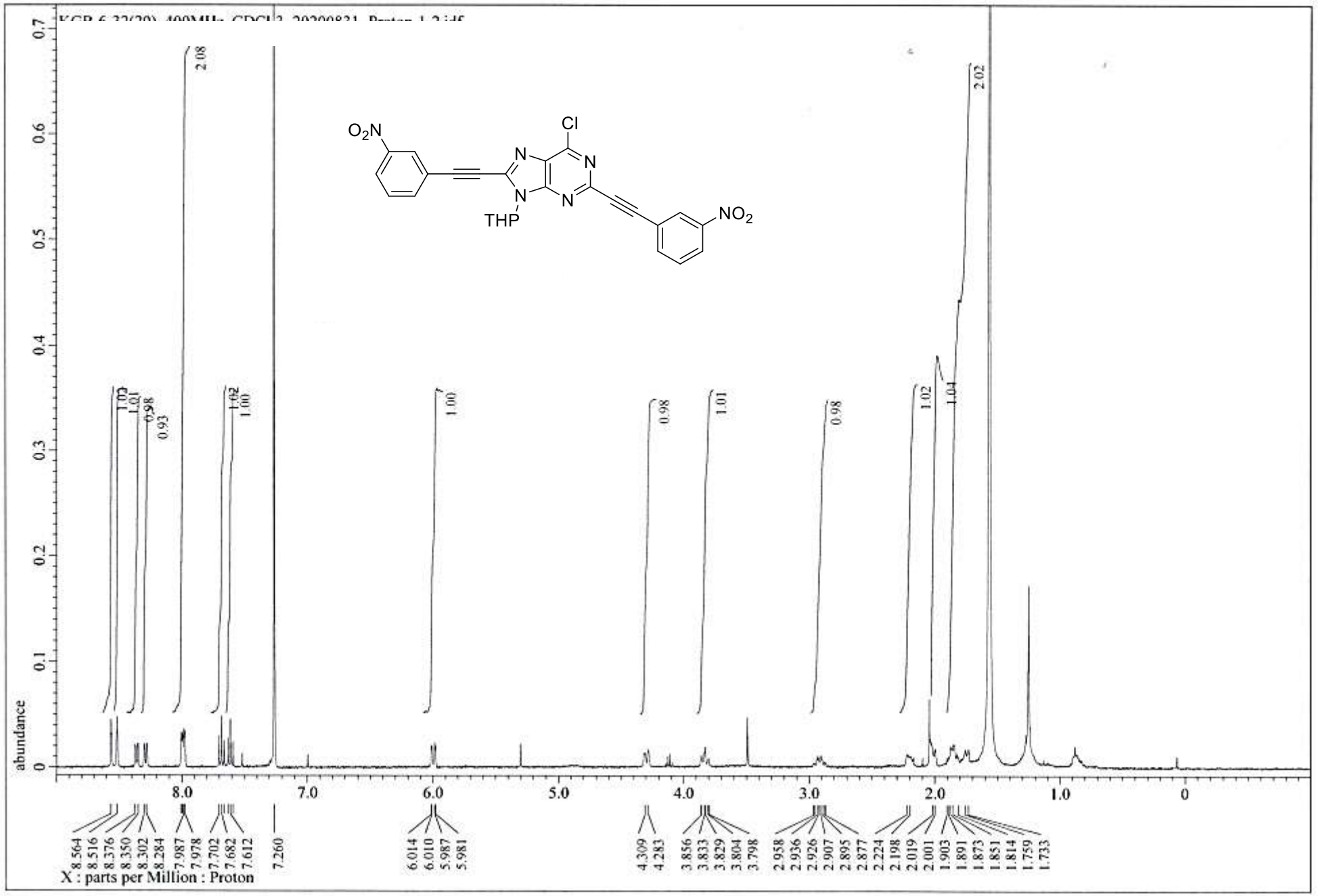
^{1}H NMR (400 MHz, $CDCl_3$) of **7e**



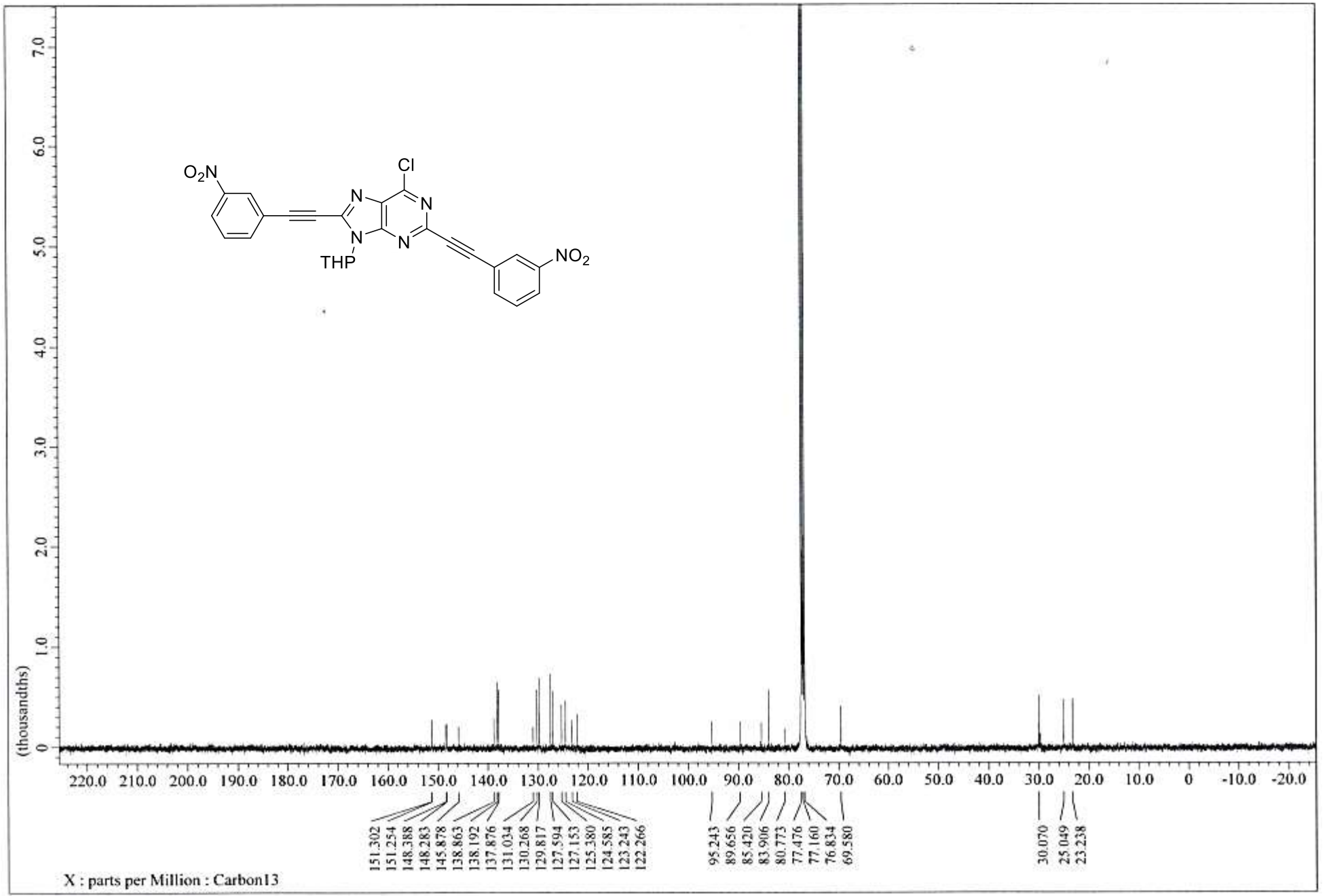
^{13}C NMR (100 MHz, $CDCl_3$) of **7e**



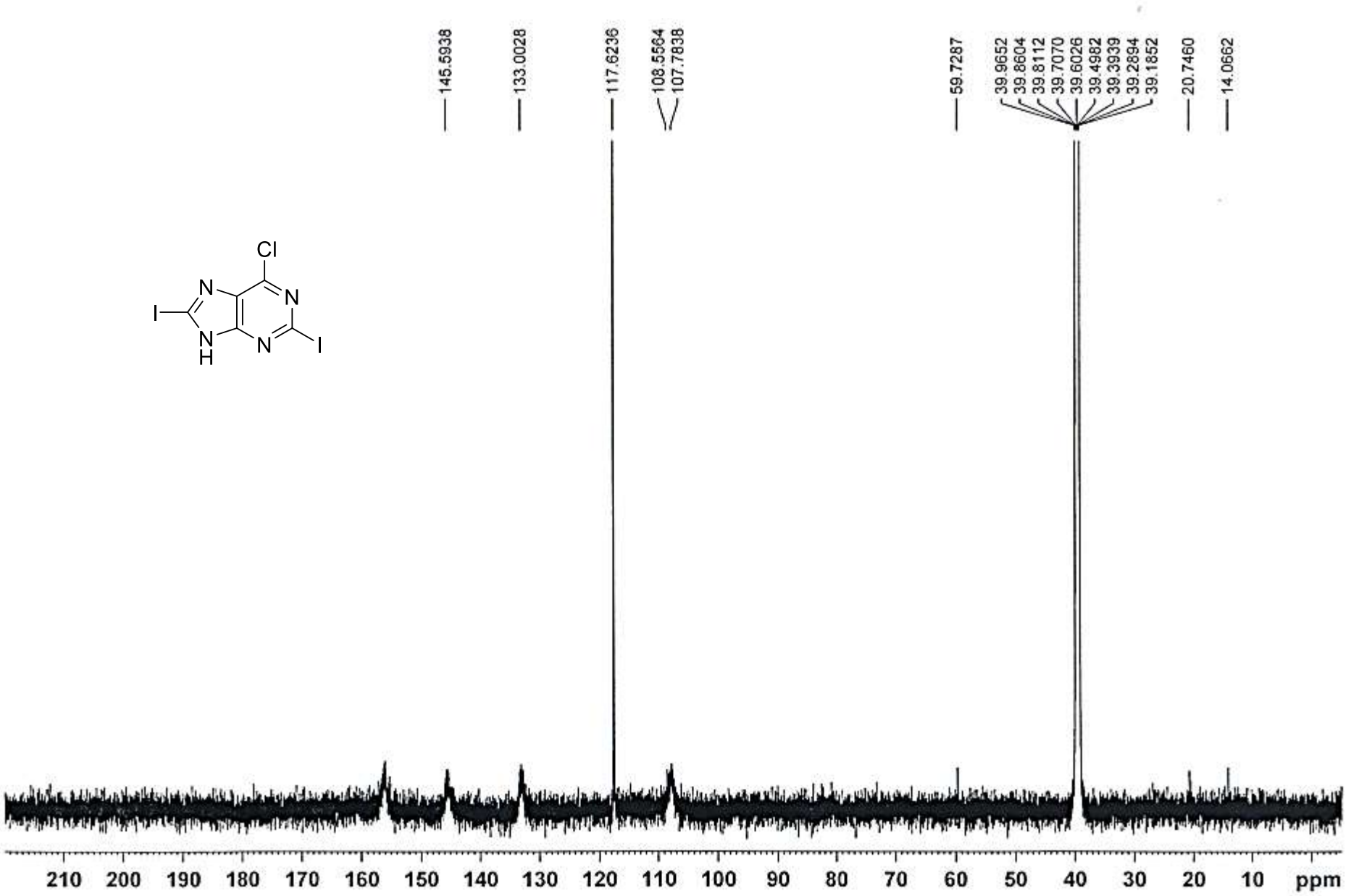
^{1}H NMR (400 MHz, $CDCl_3$) of **8e**



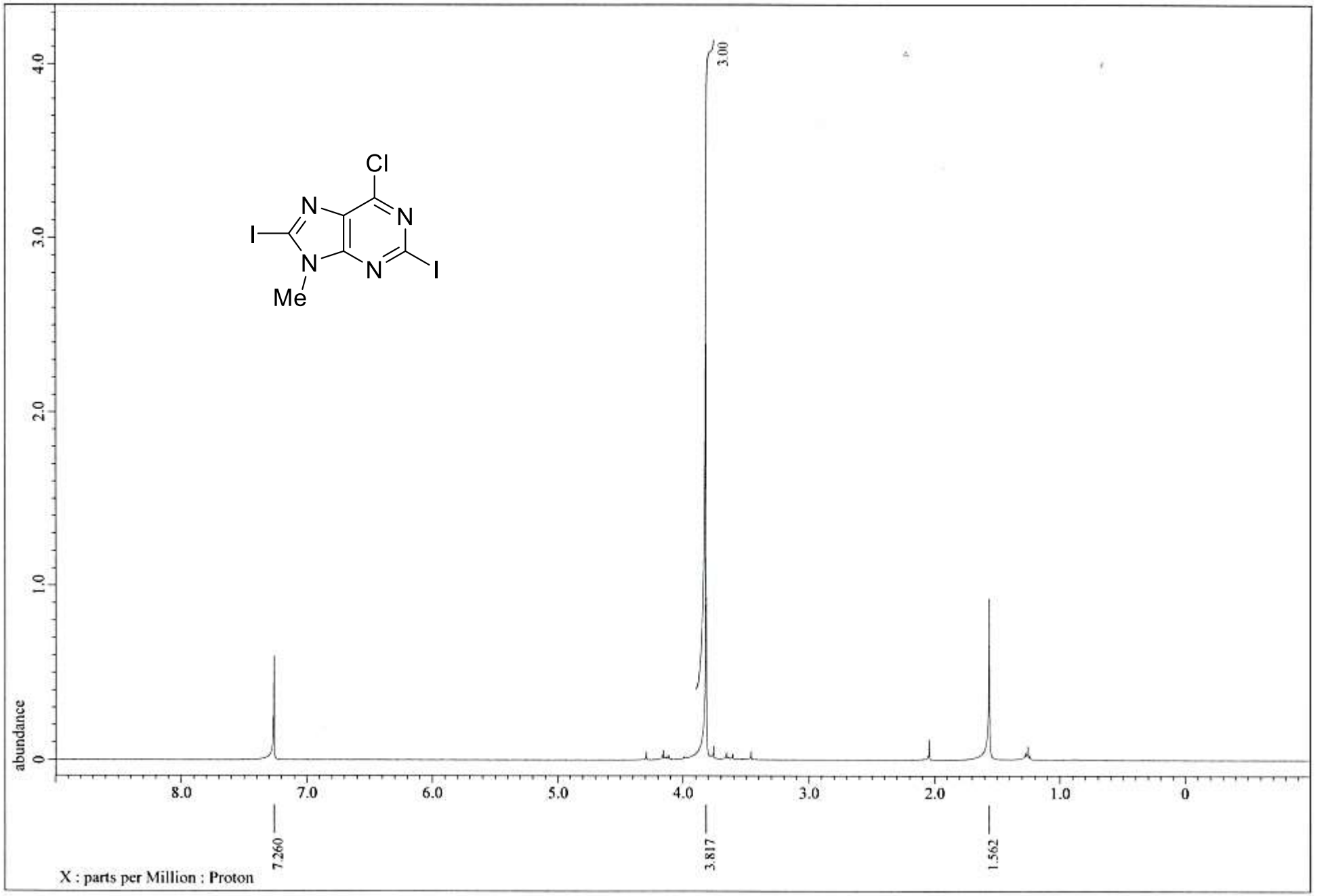
^{13}C NMR (100 MHz, $CDCl_3$) of **8e**



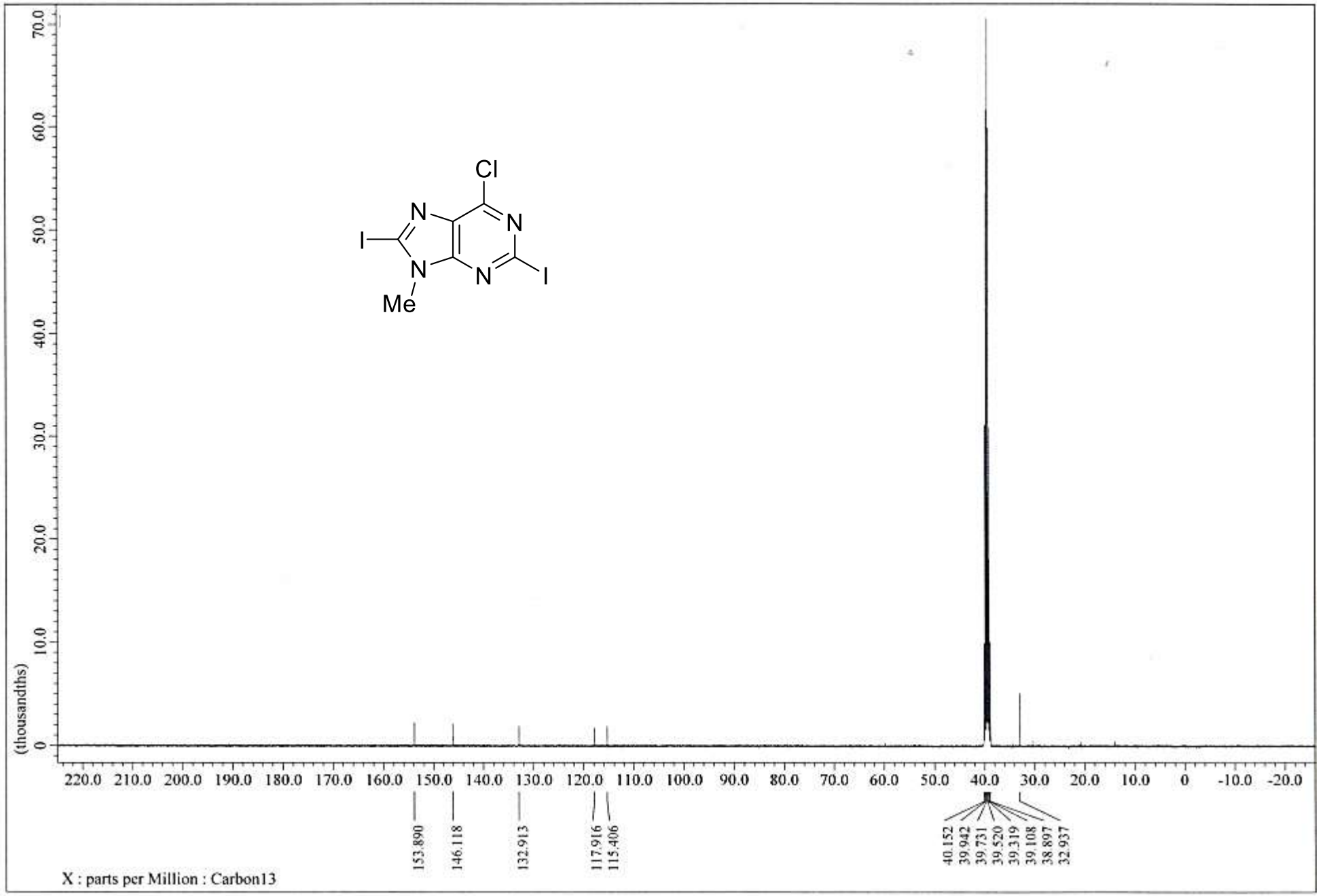
^{13}C NMR (200 MHz, DMSO-d_6) of **9**



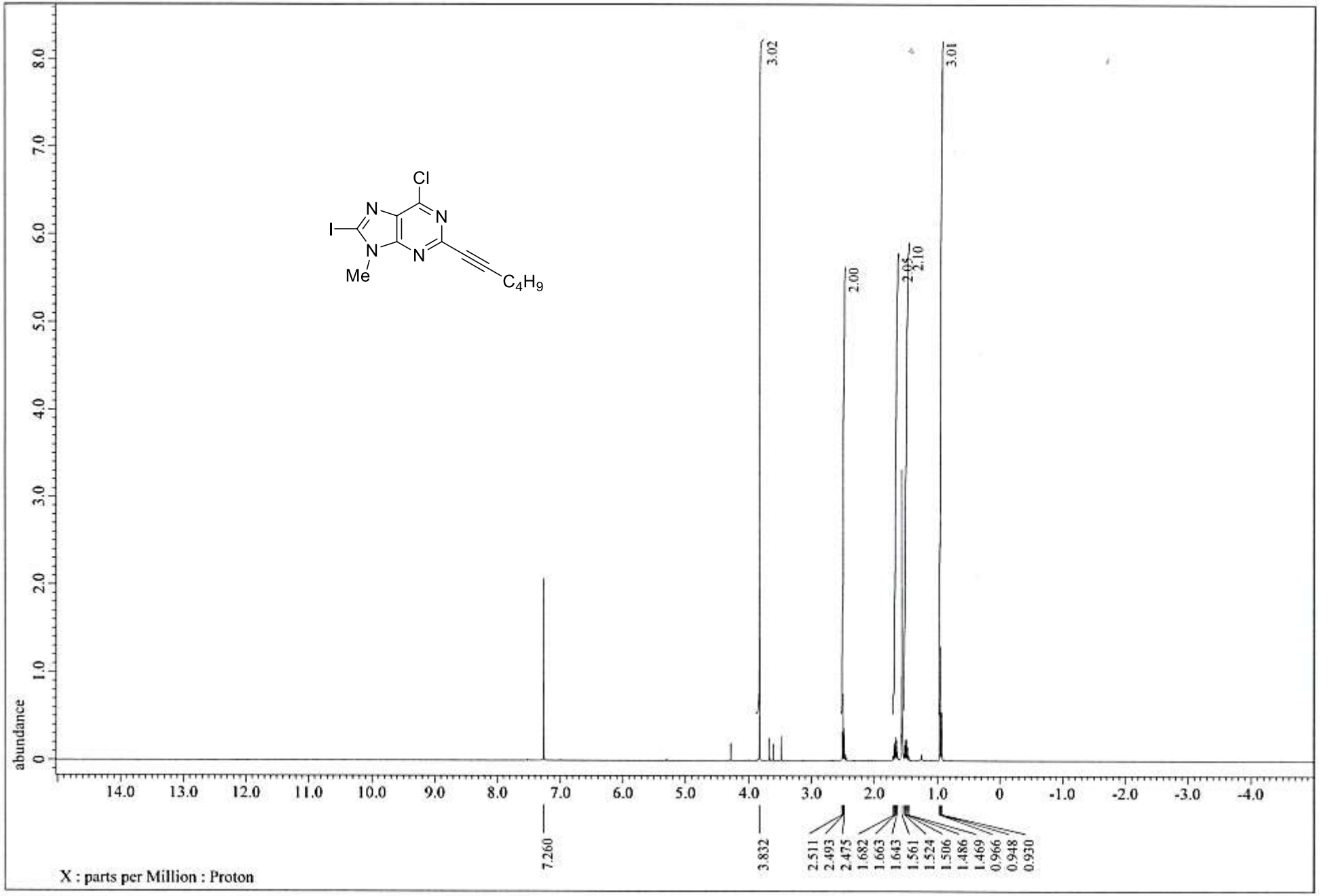
^{1}H NMR (400 MHz, $CDCl_3$) of **1b**



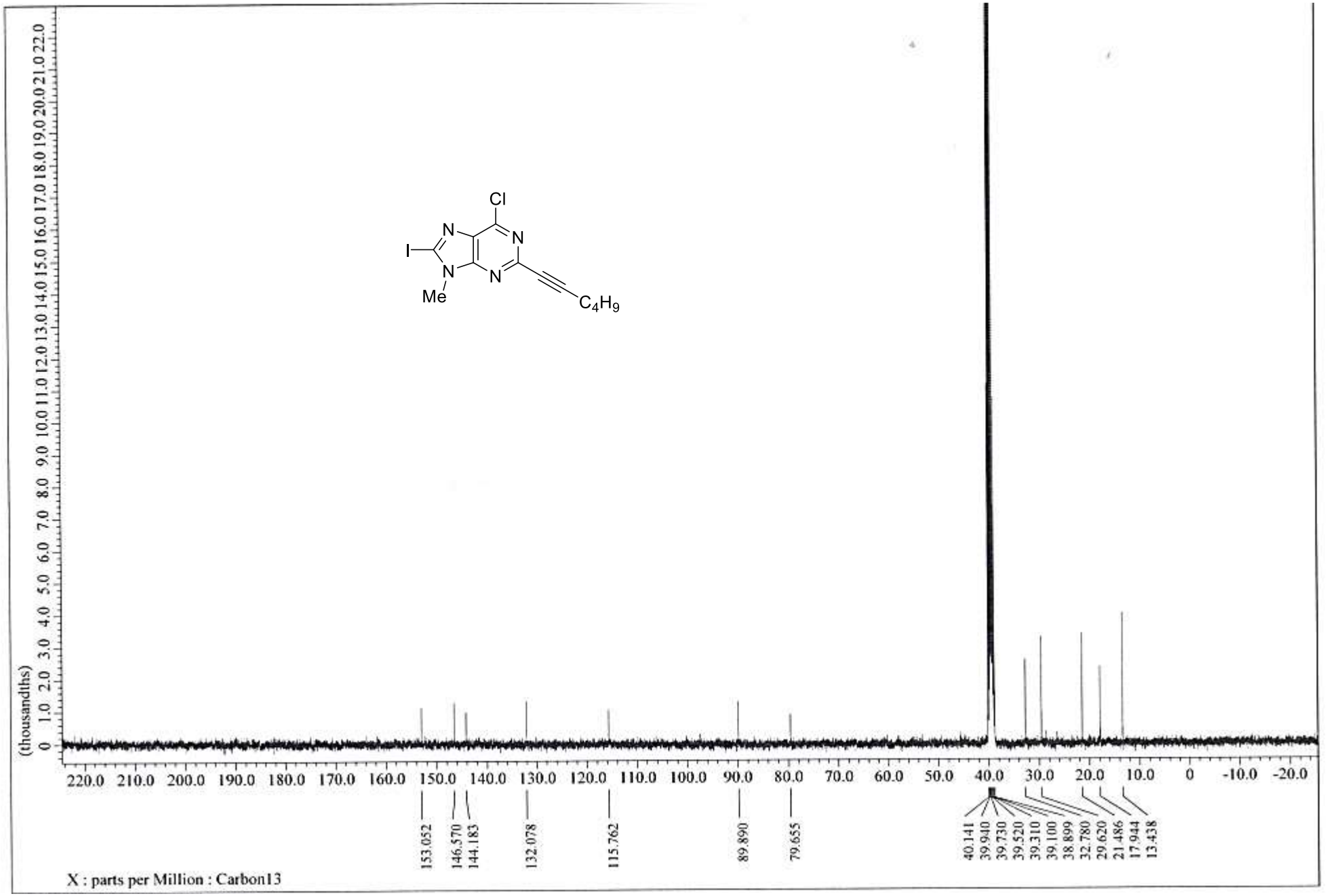
^{13}C NMR (100 MHz, $CDCl_3$) of **1b**



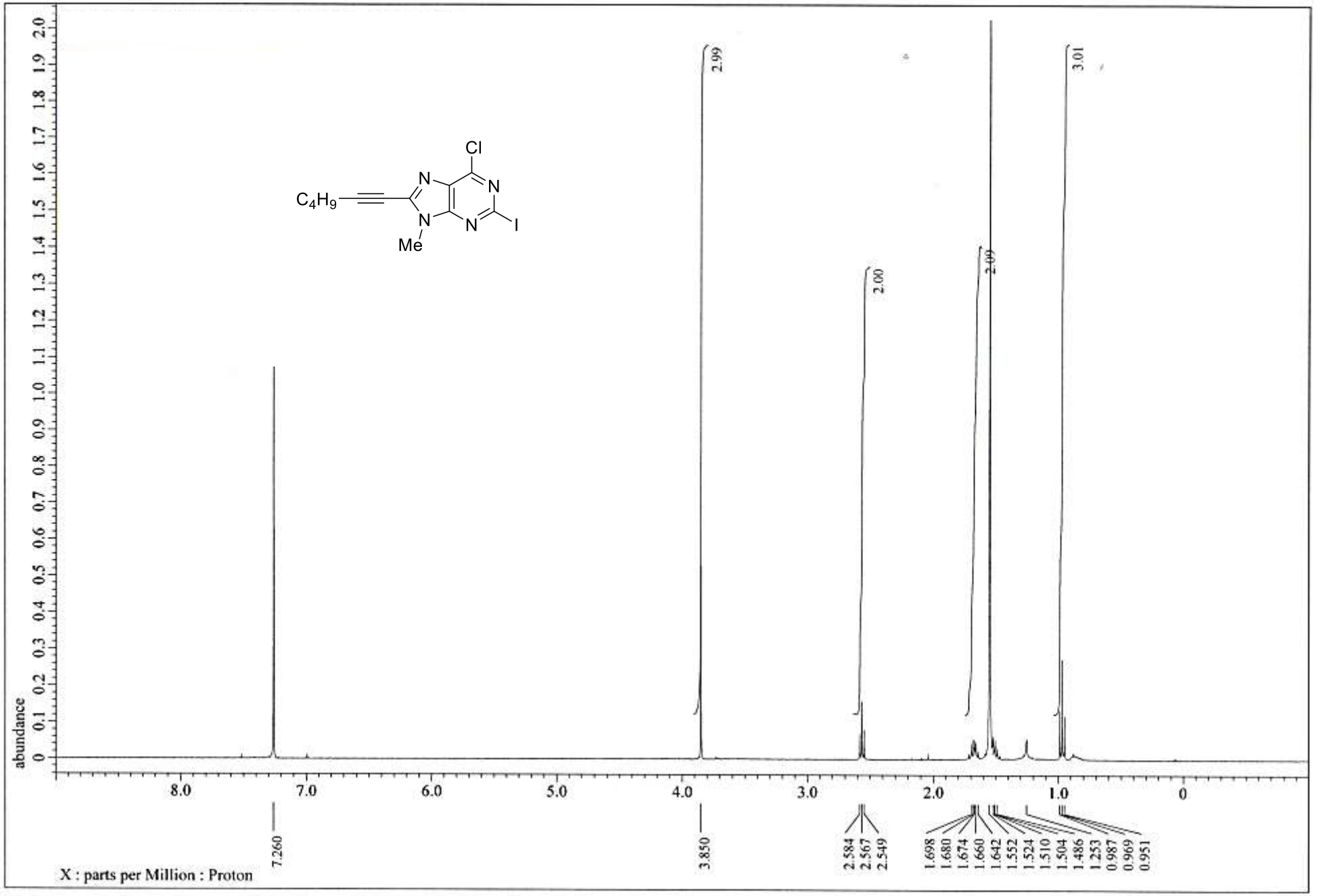
^{1}H NMR (400 MHz, $CDCl_3$) of **3b**



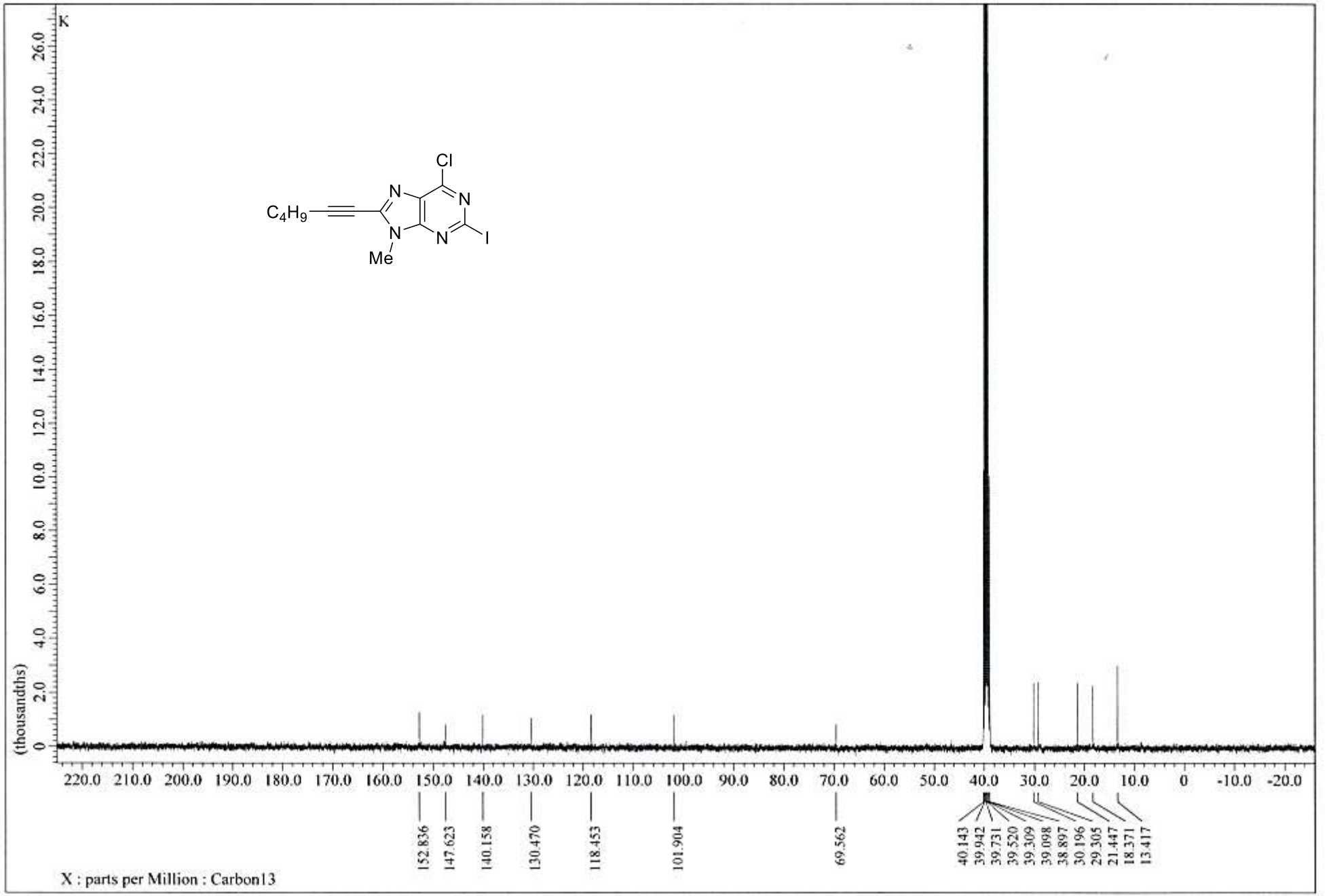
^{13}C NMR (100 MHz, $CDCl_3$) of **3b**



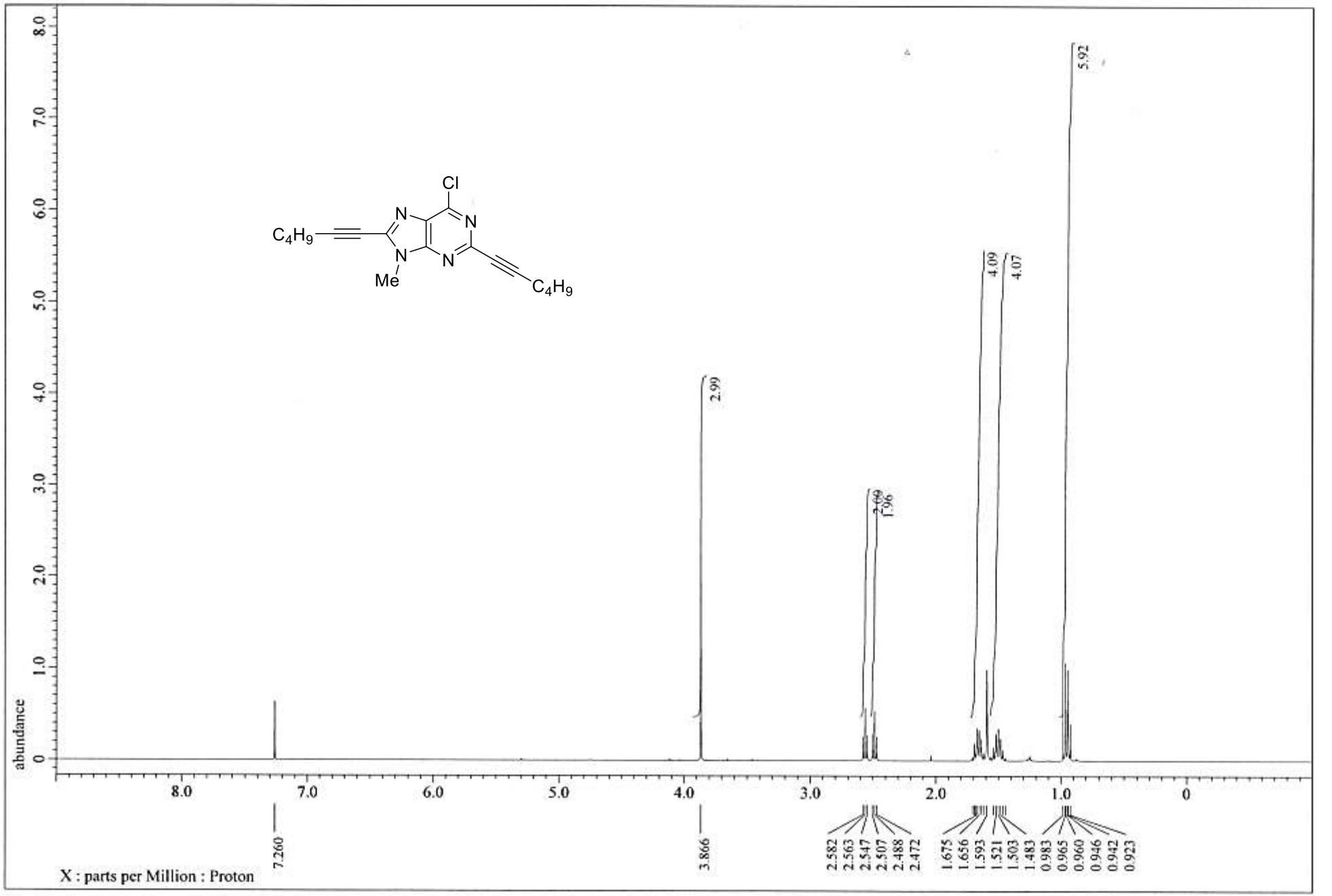
^{1}H NMR (400 MHz, $CDCl_3$) of **4b**



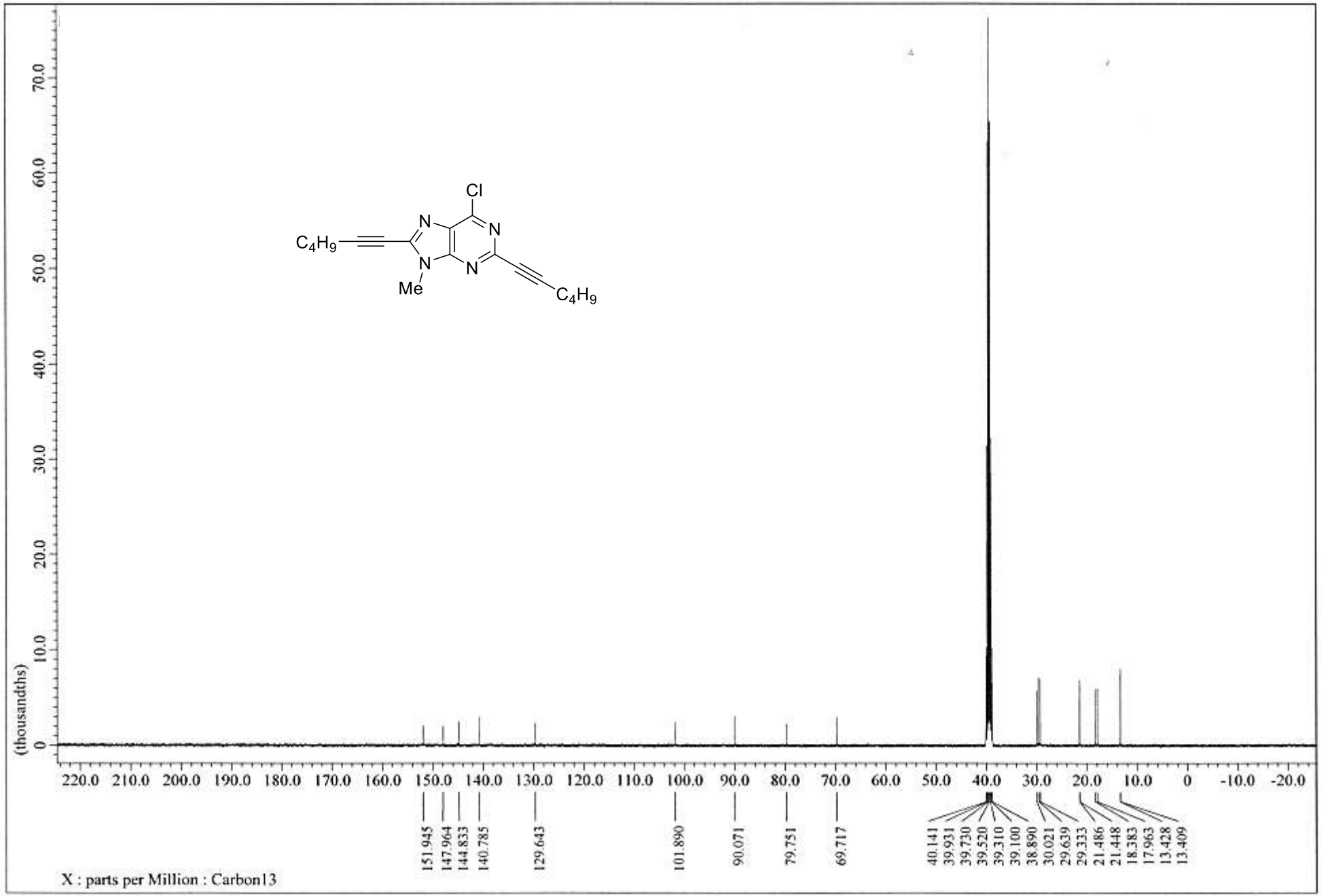
^{13}C NMR (100 MHz, $CDCl_3$) of **4b**



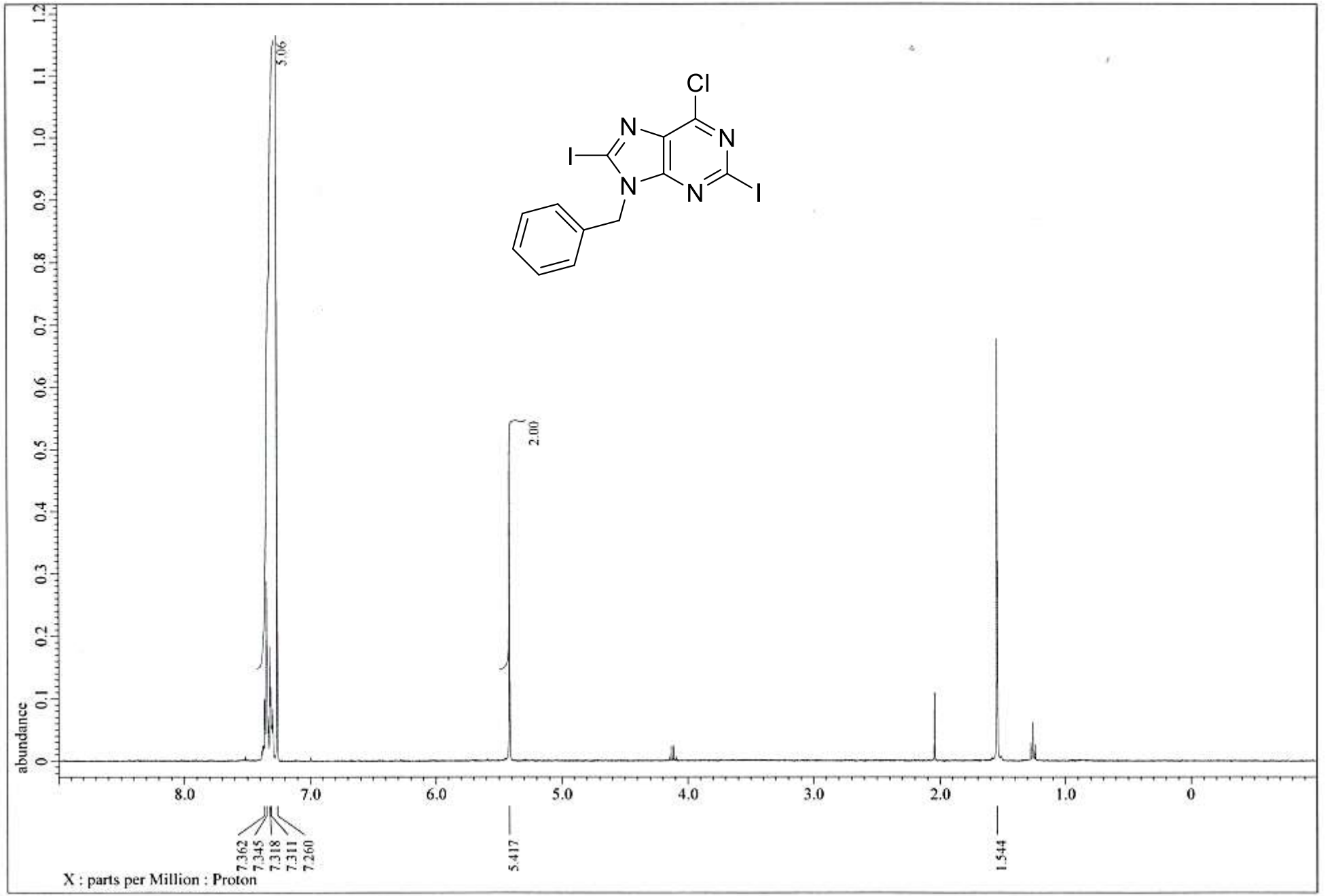
^{1}H NMR (400 MHz, $CDCl_3$) of **5b**



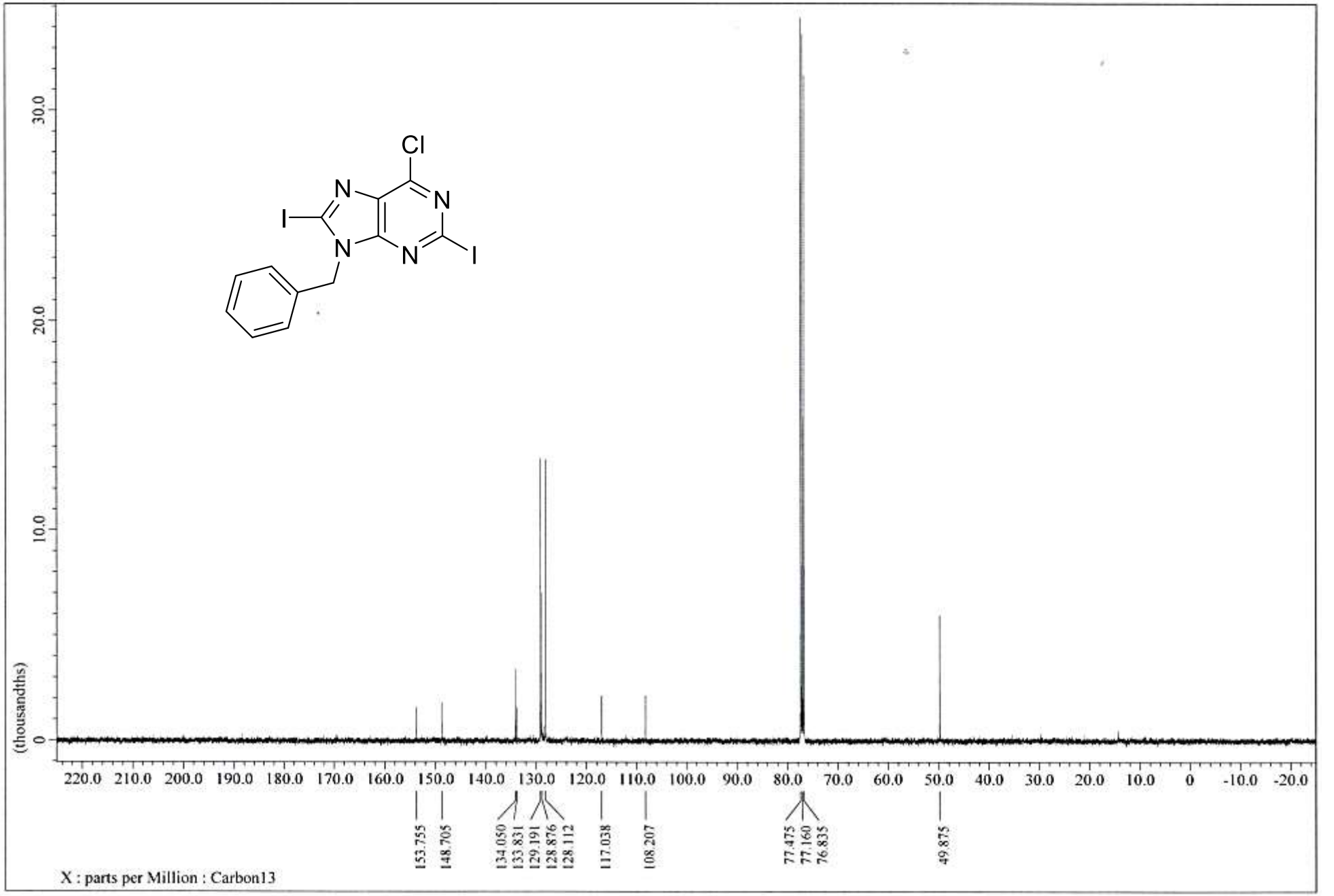
^{13}C NMR (100 MHz, $CDCl_3$) of **5b**



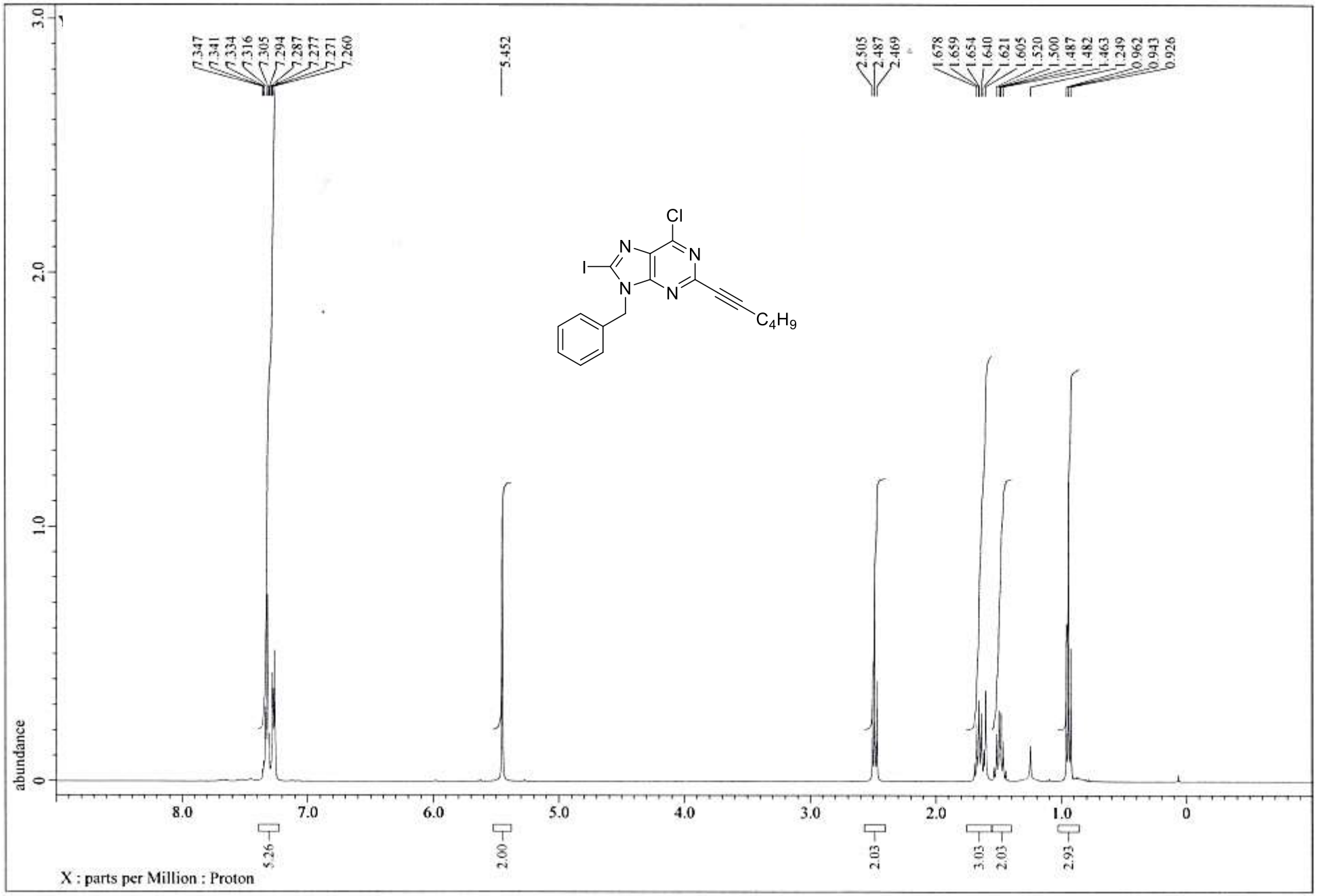
^{1}H NMR (400 MHz, $CDCl_3$) of **1c**



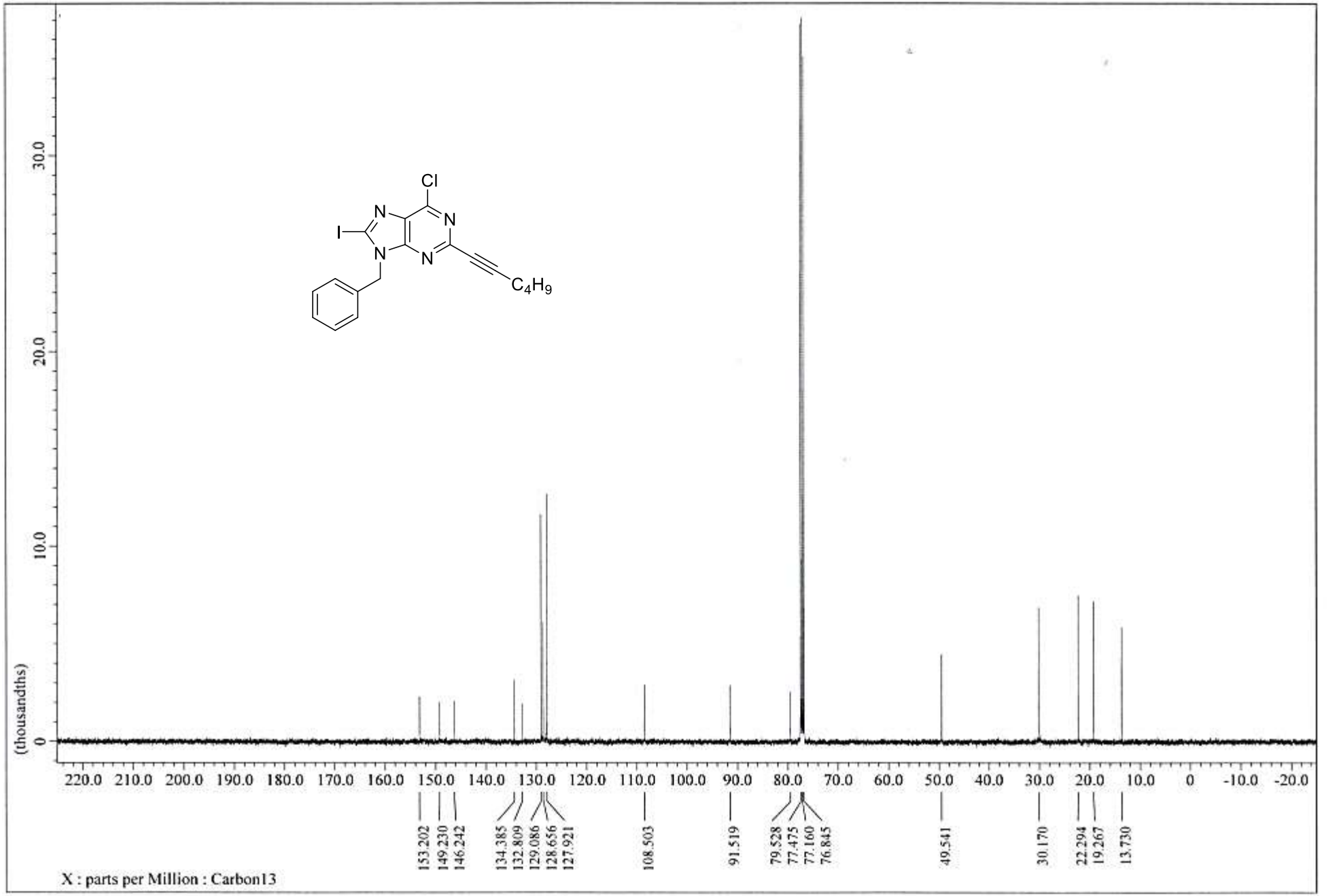
^{13}C NMR (100 MHz, $CDCl_3$) of **1c**



^{1}H NMR (400 MHz, $CDCl_3$) of **3c**



^{13}C NMR (100 MHz, $CDCl_3$) of **3c**



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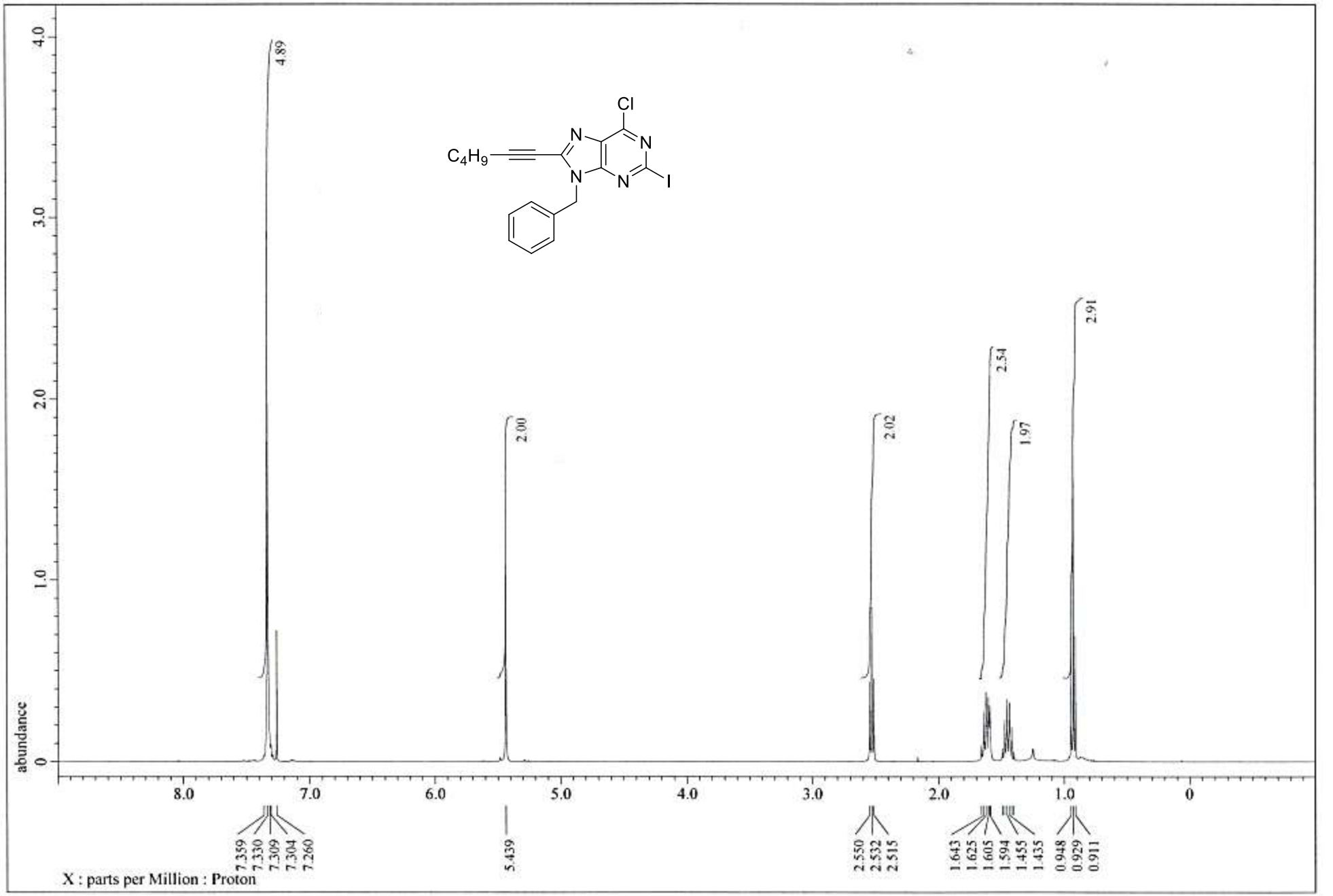
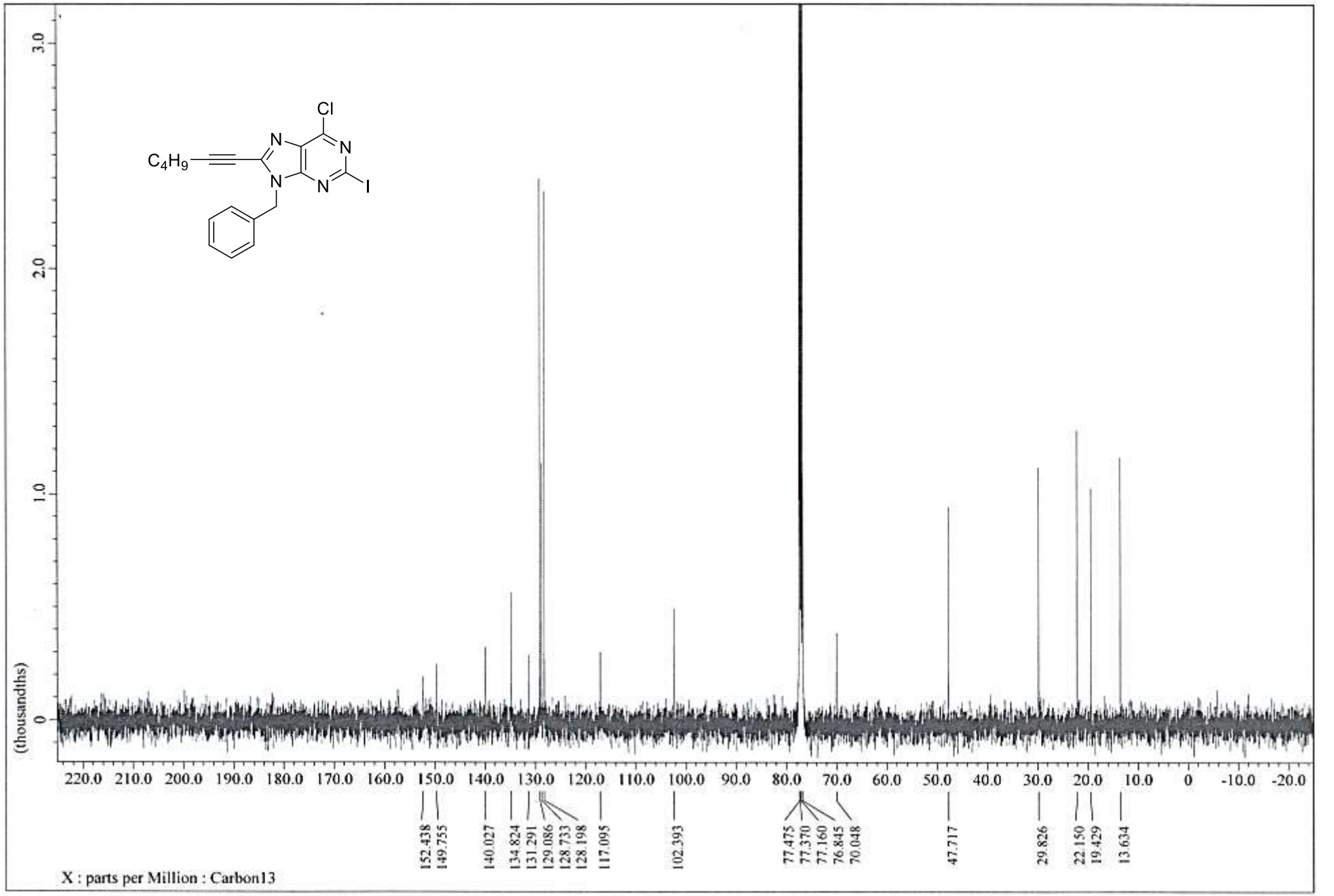
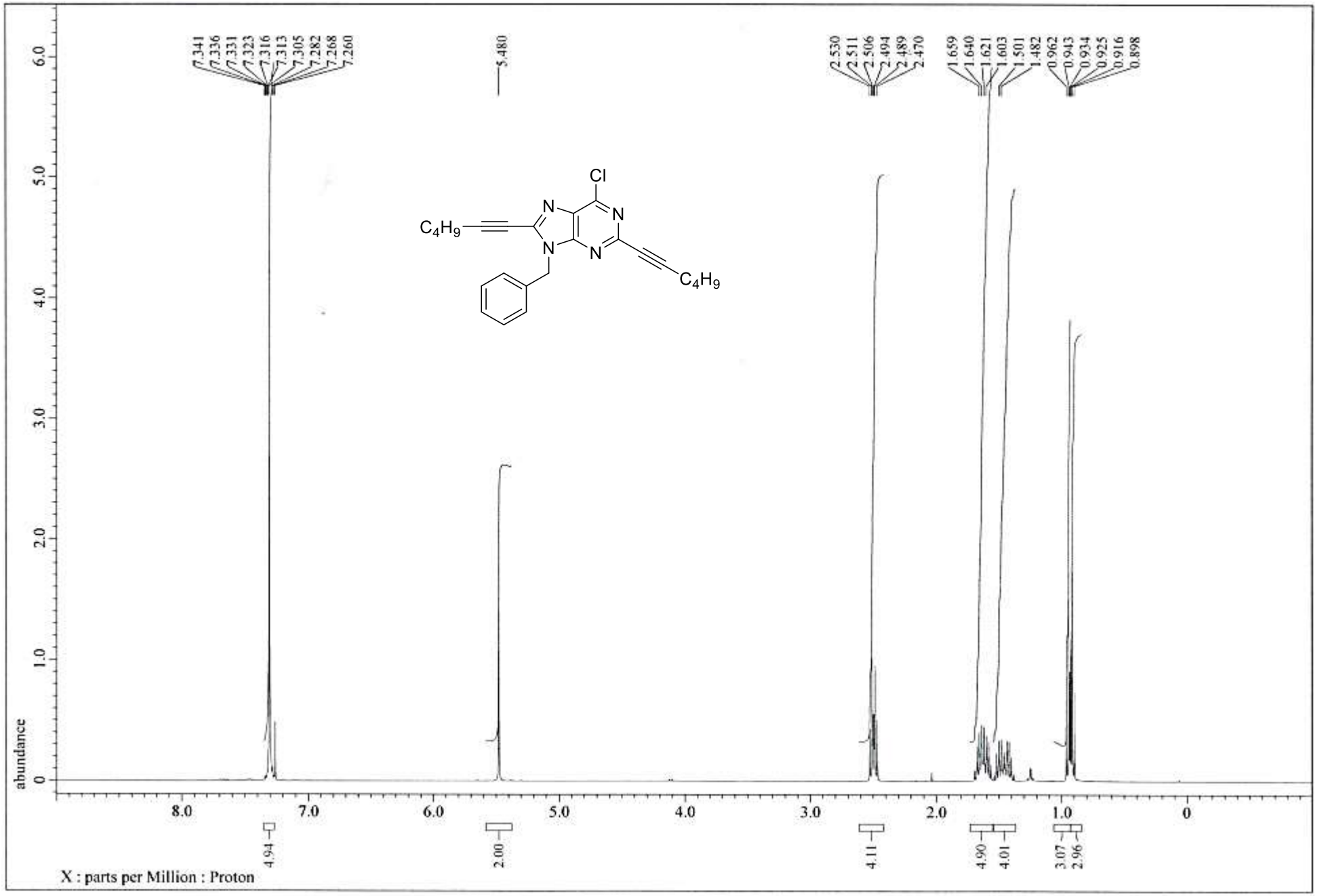


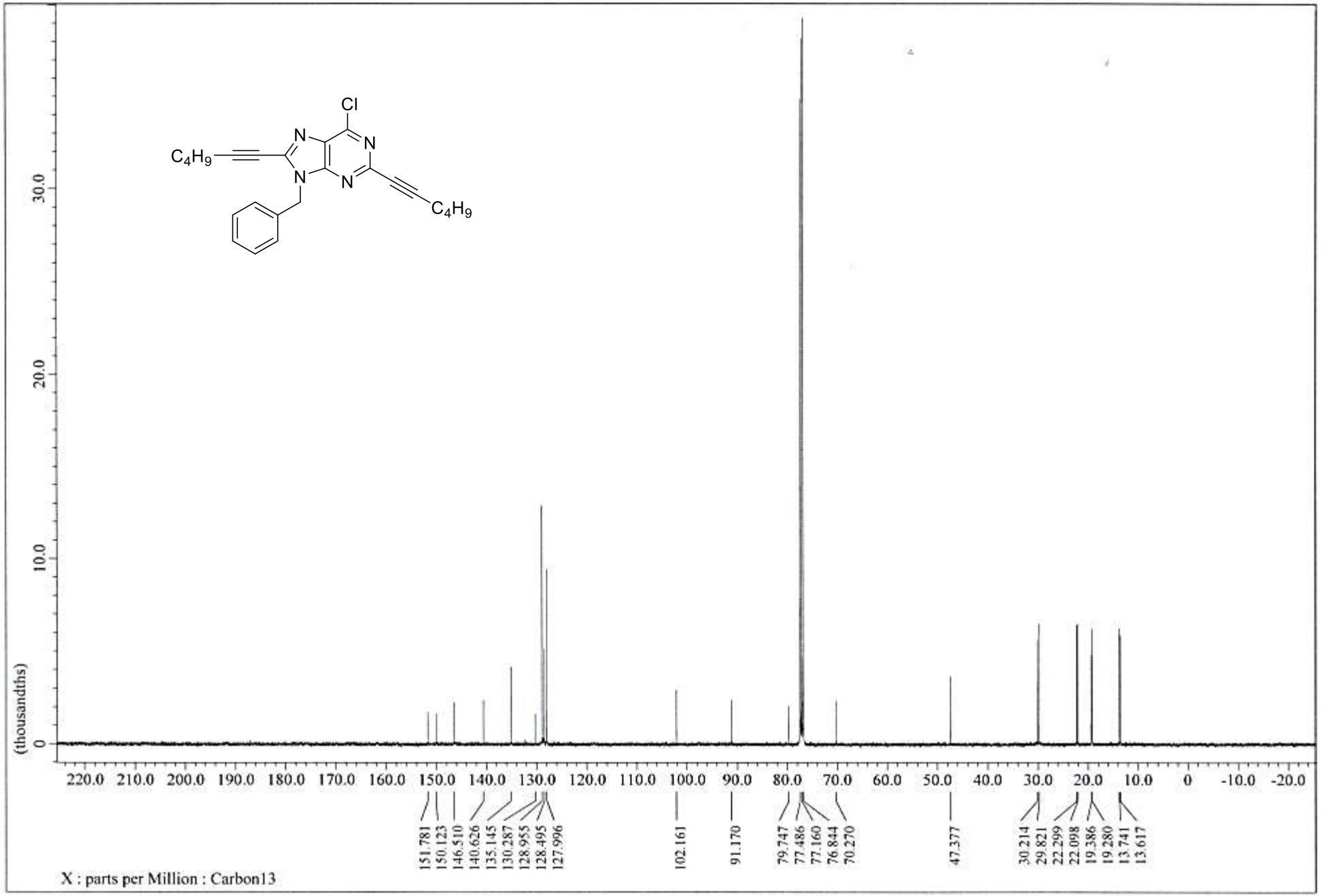
^{13}C NMR (100 MHz, $CDCl_3$) of **4c**

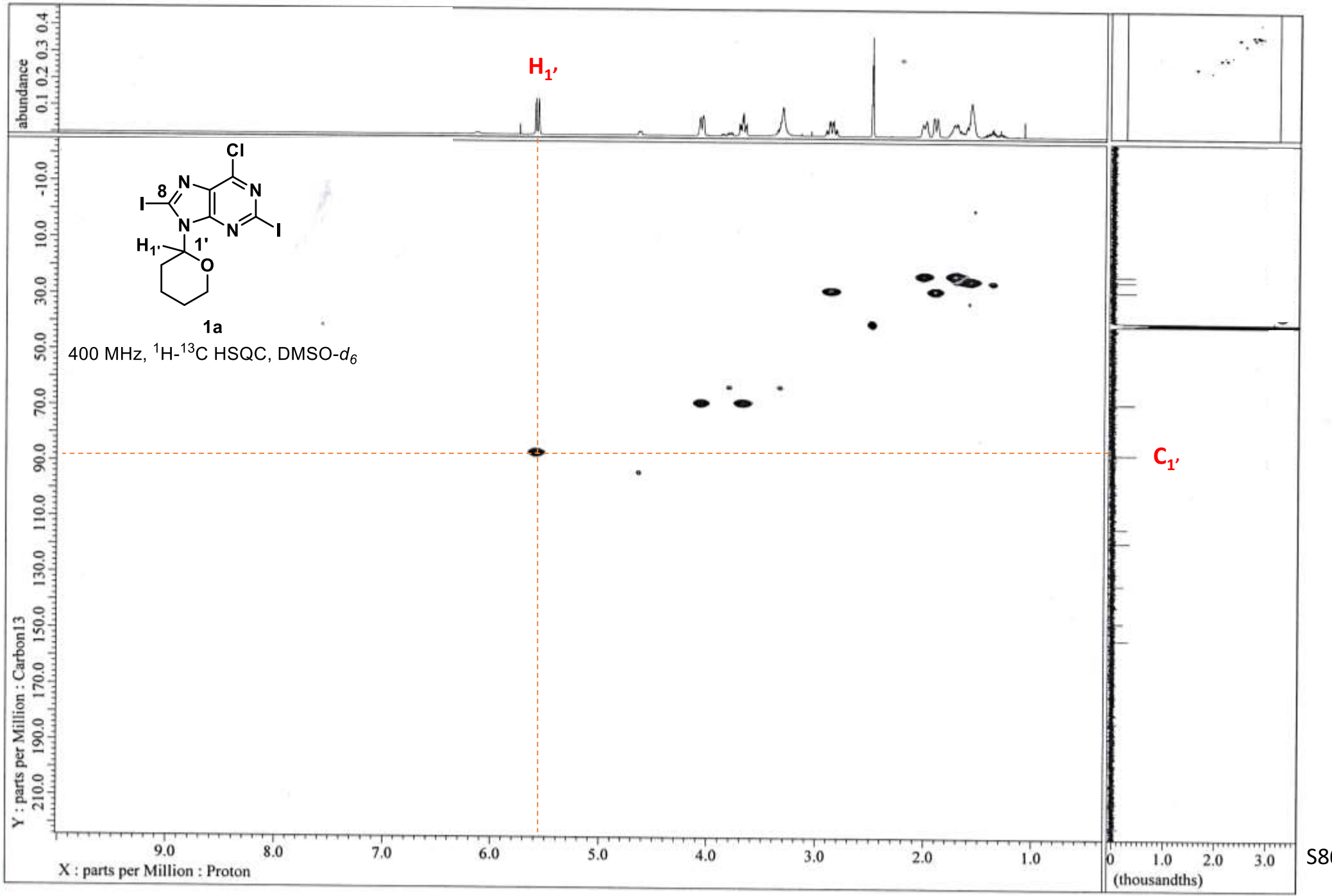


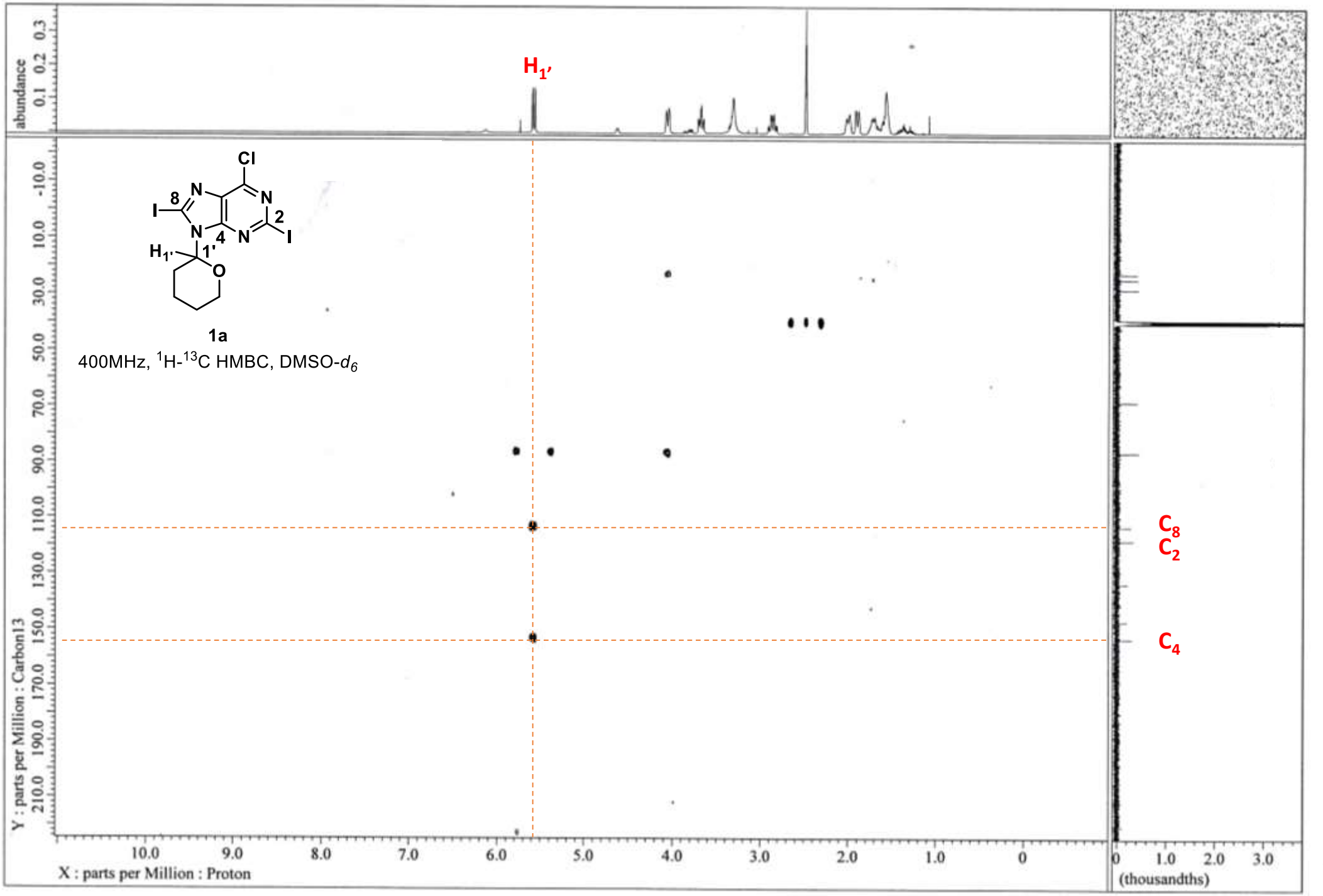
^{1}H NMR (400 MHz, $CDCl_3$) of **5c**

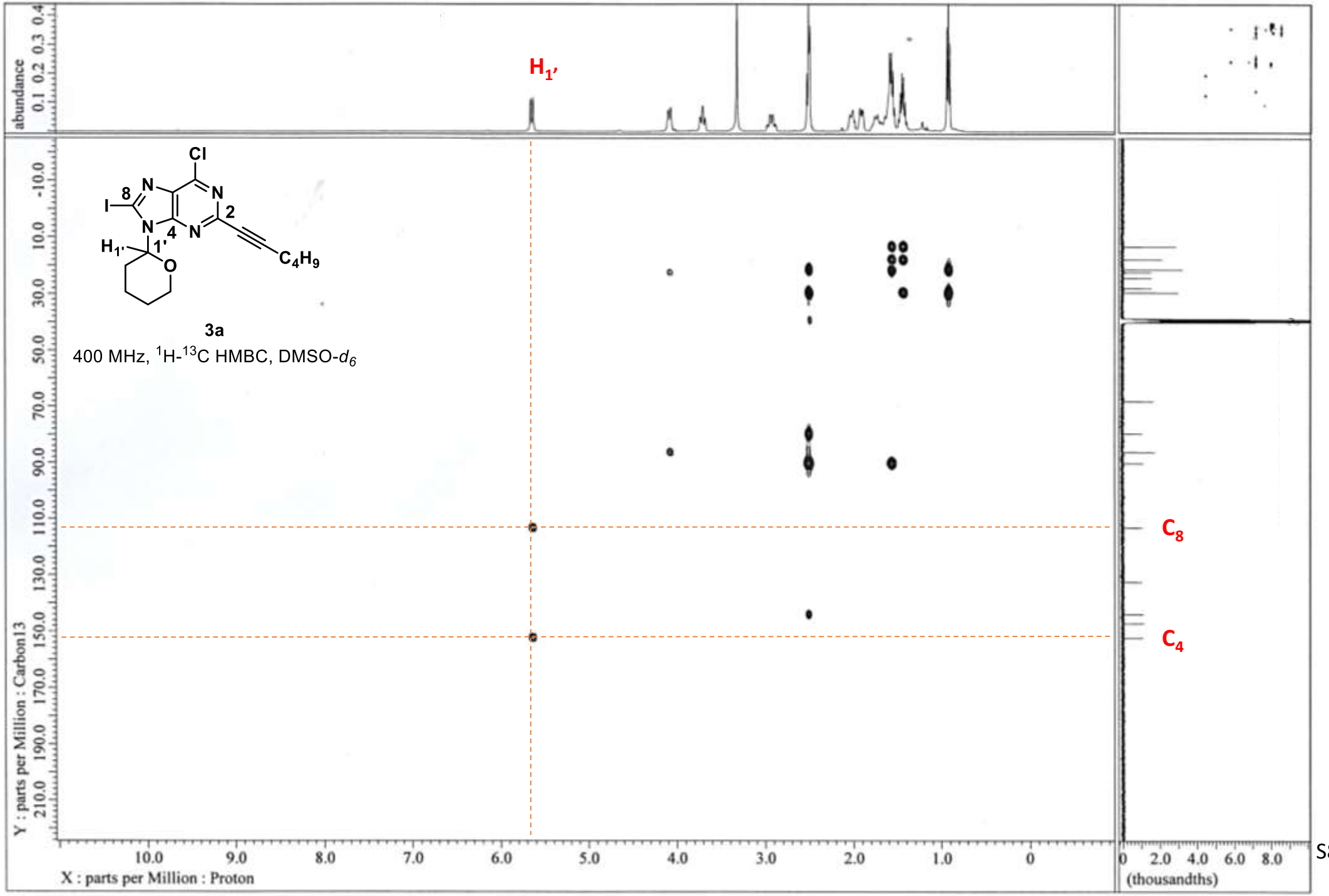


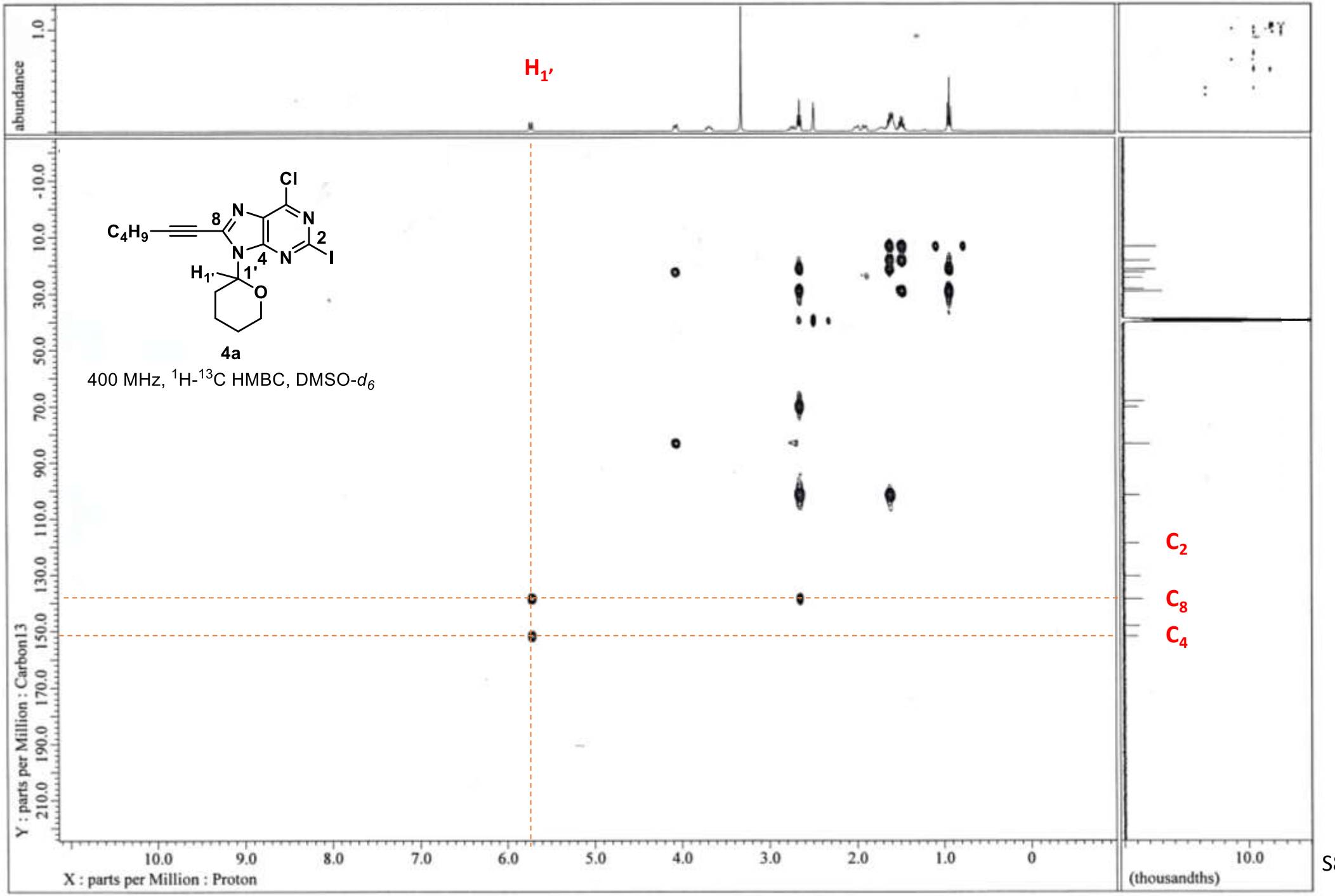
^{13}C NMR (100 MHz, $CDCl_3$) of **5c**




abundance
0.1 0.2 0.3 0.4
H1'
Cl
N
8
I
N
N
I
H1'
1'
O
1a
400 MHz, 1H-13C HSQC, DMSO-d6
C1'
-10.0 10.0 30.0 50.0 70.0 90.0 110.0 130.0 150.0 170.0 190.0 210.0
Y : parts per Million : Carbon13
9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0
X : parts per Million : Proton
0 1.0 2.0 3.0
(thousandths)

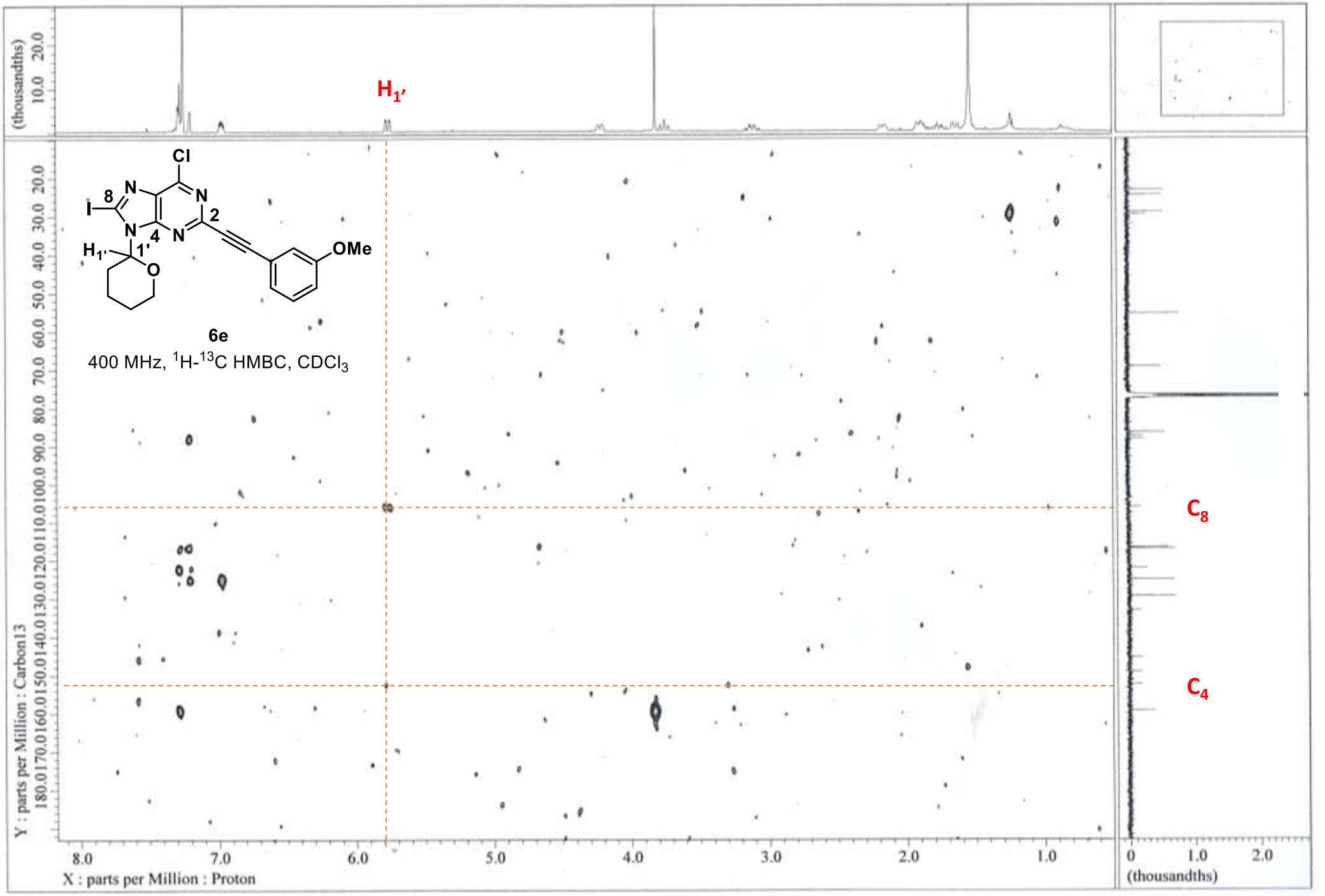

abundance
0.1 0.2 0.3
$H_{1'}$
Cl
N
8
I
N
2
I
N
4
N
$H_{1'}$
1'
O
1a
400MHz, ^{1}H-^{13}C HMBC, DMSO-d_6
-10.0 10.0 30.0 50.0 70.0 90.0 110.0 130.0 150.0 170.0 190.0 210.0
Y : parts per Million : Carbon13
10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
X : parts per Million : Proton
C_8
C_2
C_4
0 1.0 2.0 3.0
(thousandths)

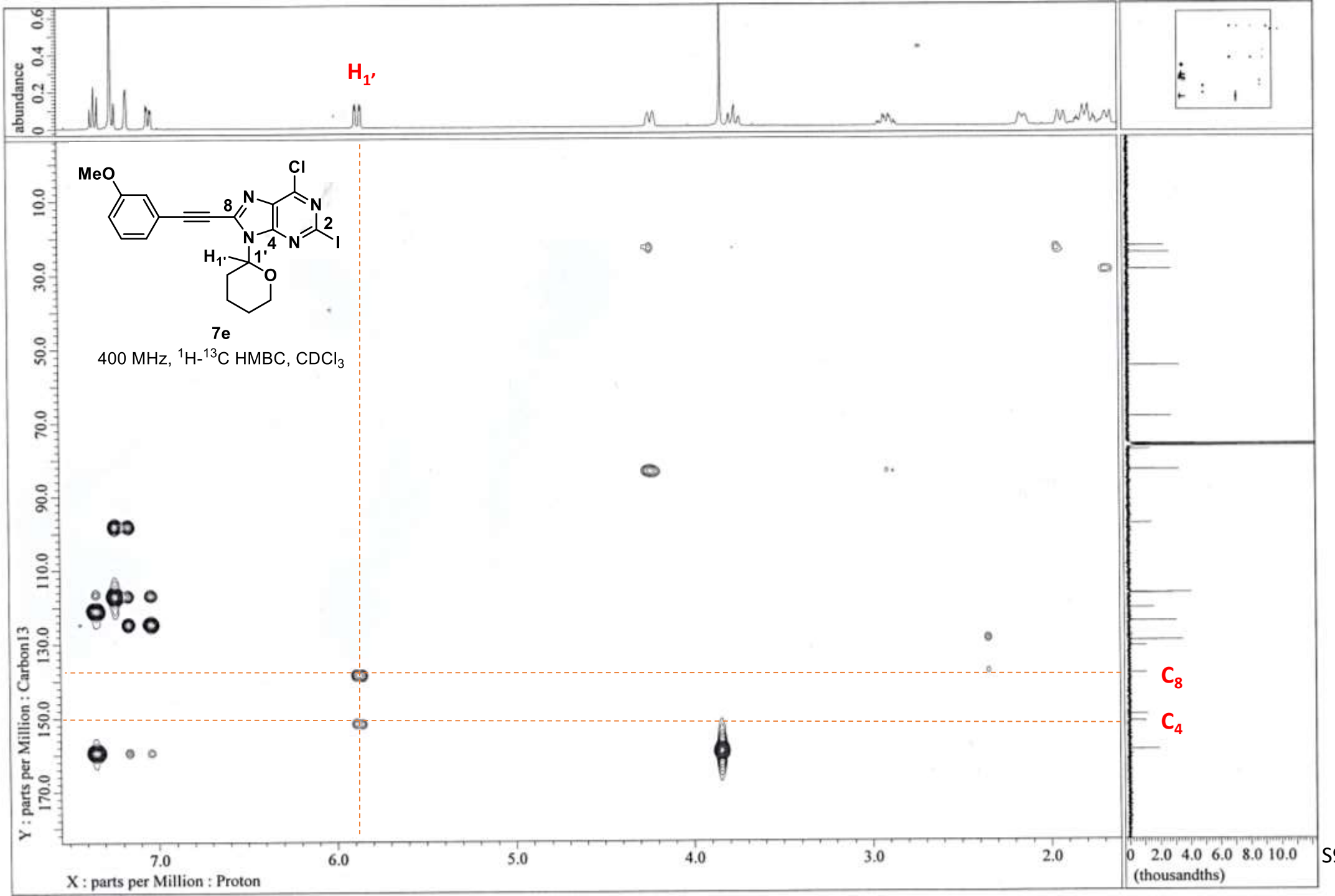

abundance
0.1 0.2 0.3 0.4
H1'
Cl
I
8
N
N
2
N
4
N
H1'
1'
O
C4H9
3a
400 MHz, 1H-13C HMBC, DMSO-d6
-10.0 10.0 30.0 50.0 70.0 90.0 110.0 130.0 150.0 170.0 190.0 210.0
Y : parts per Million : Carbon13
10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
X : parts per Million : Proton
C8
C4
0 2.0 4.0 6.0 8.0
(thousandths)

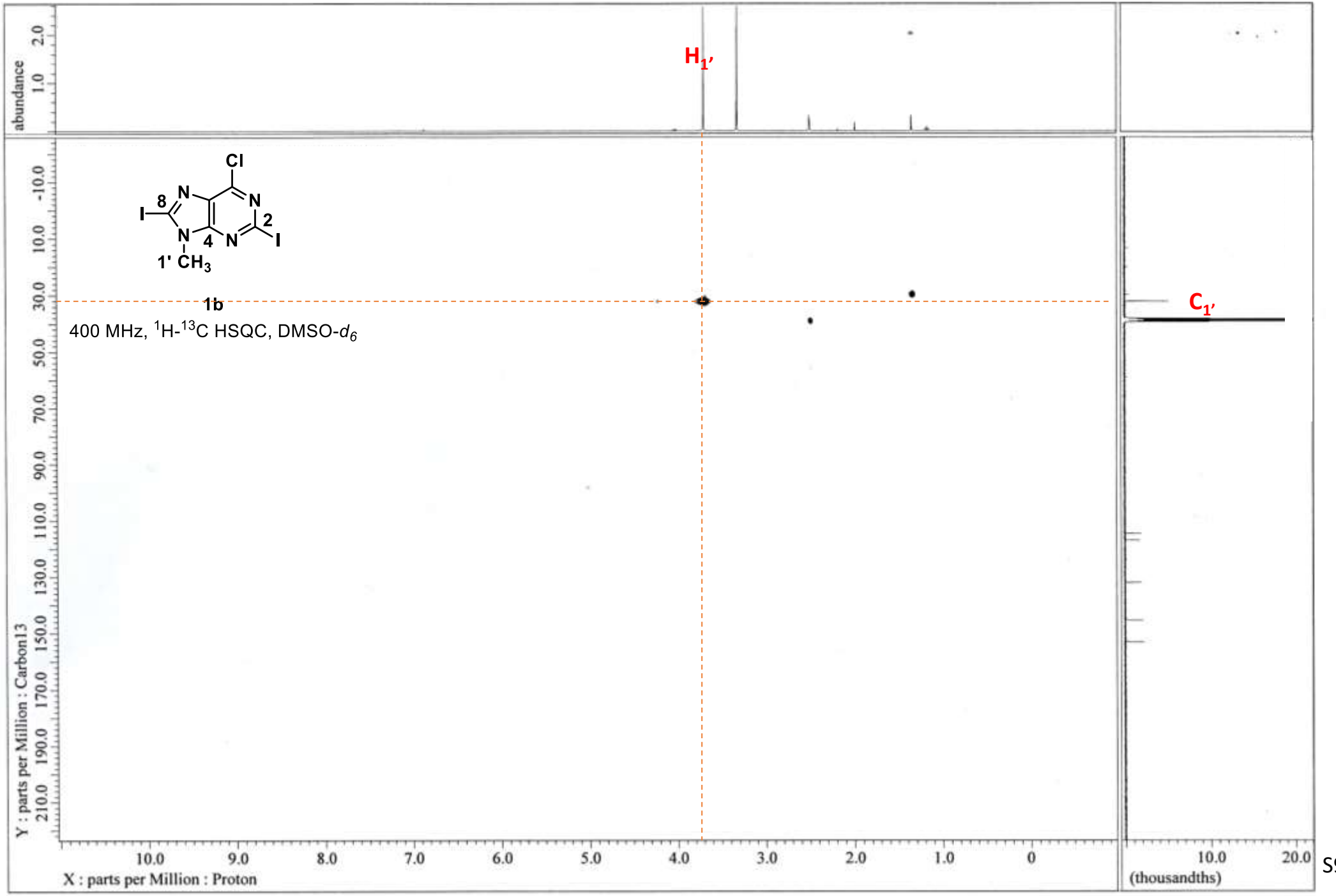


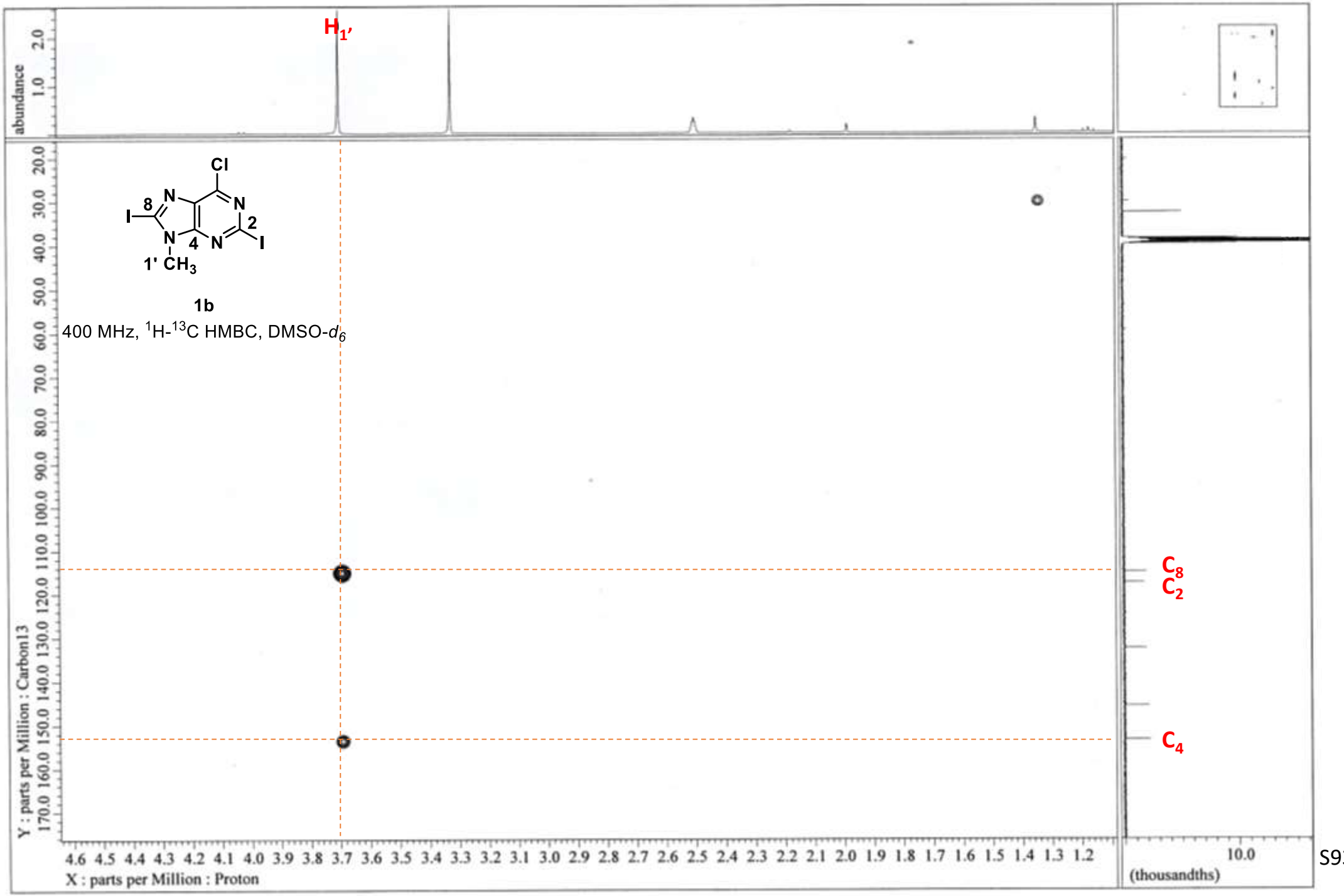
4a

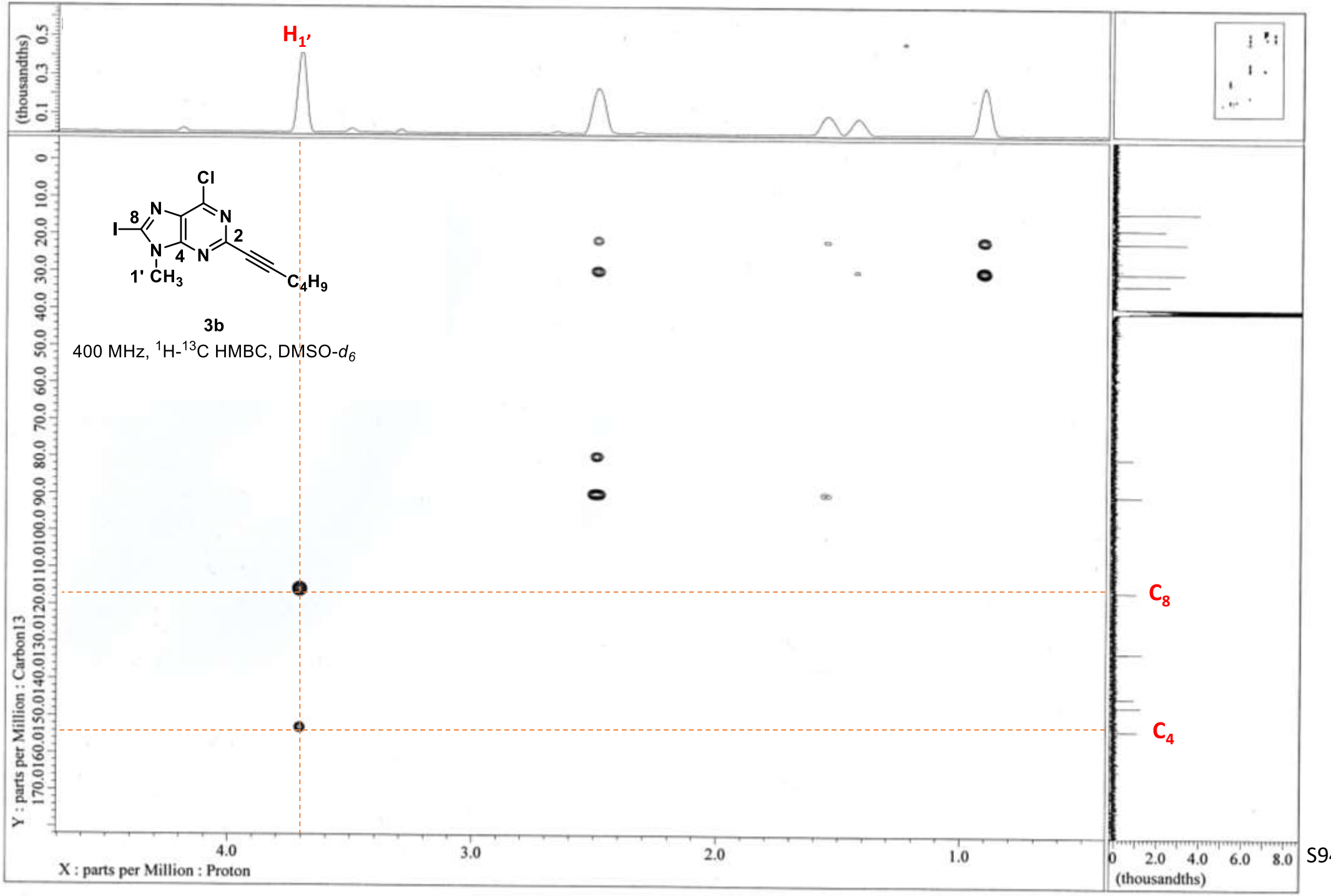
400 MHz, ^{1}H-^{13}C HMBC, DMSO-d_6

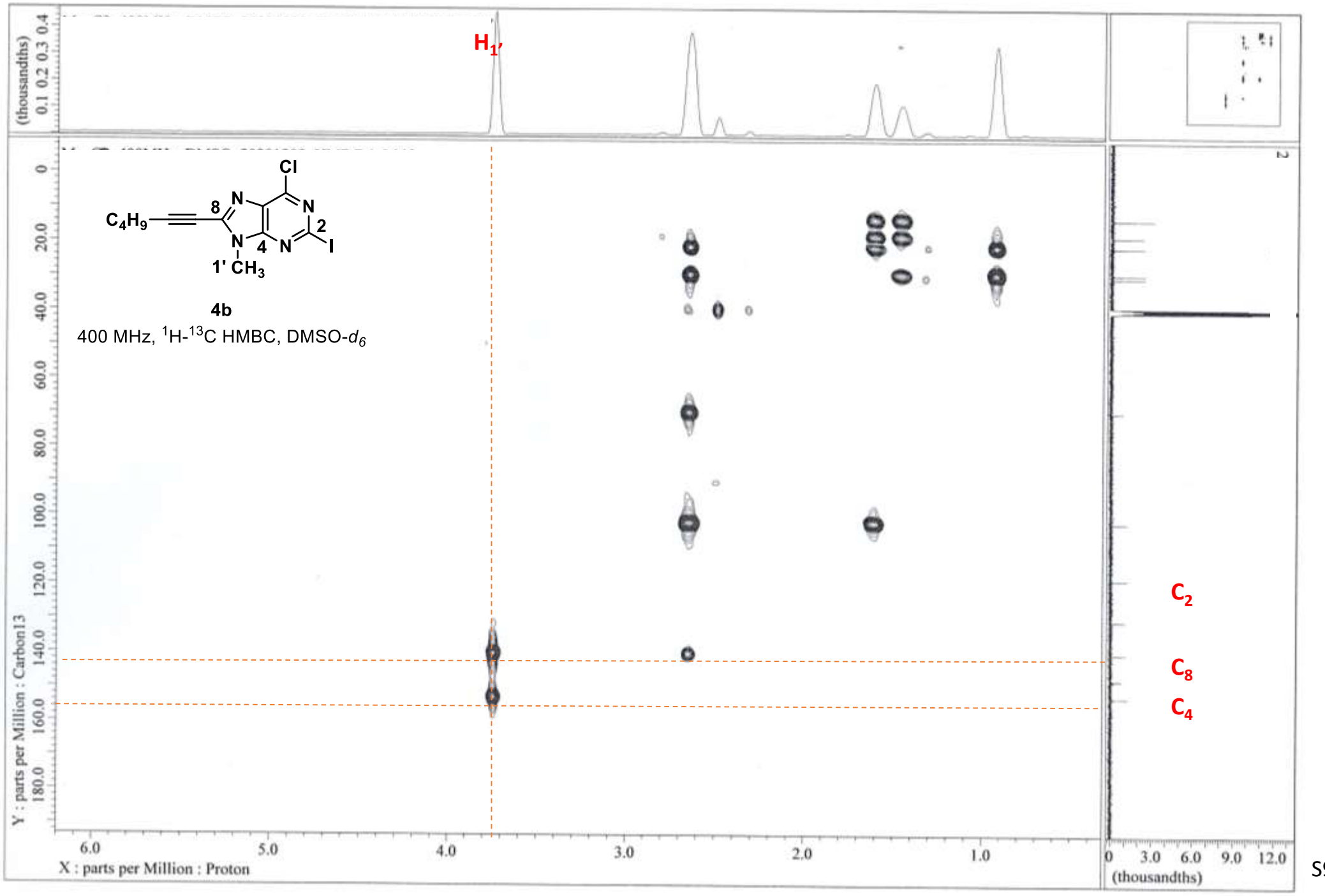

H1'
C8
C4
6e
400 MHz, 1H-13C HMBC, CDCl3
X : parts per Million : Proton
Y : parts per Million : Carbon13
(thousandths)

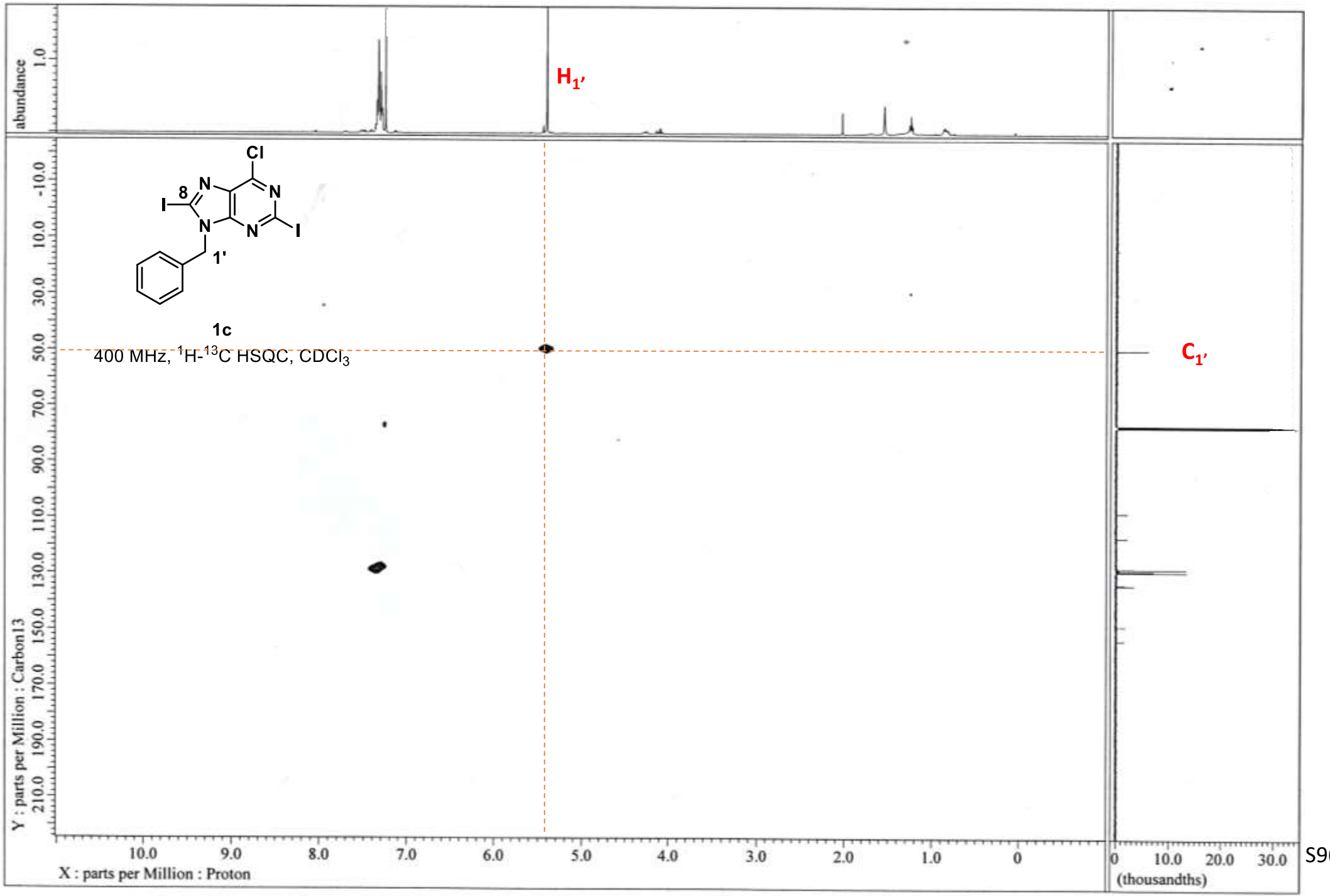

abundance
H1'
MeO
Cl
8
N
N
2
I
N
4
N
H1'
1'
O
7e
400 MHz, 1H-13C HMBC, CDCl3
C8
C4
Y : parts per Million : Carbon13
X : parts per Million : Proton
(thousandths)

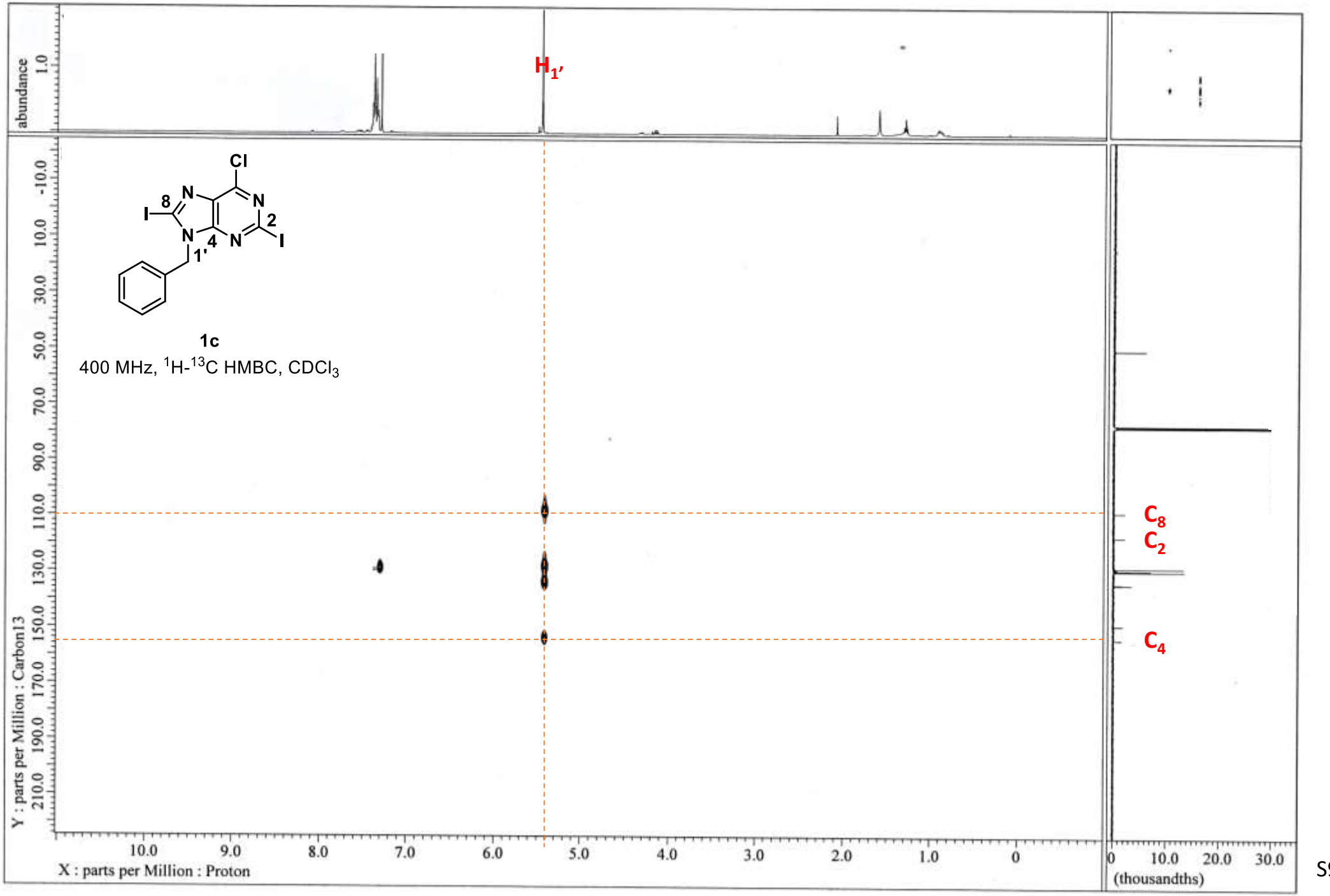

abundance
2.0
1.0
H1'
C1'
Cl
8
N
I
N
2
I
N
4
N
1' CH3
1b
400 MHz, 1H-13C HSQC, DMSO-d6
-10.0
10.0
30.0
50.0
70.0
90.0
110.0
130.0
150.0
170.0
190.0
210.0
Y : parts per Million : Carbon13
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
X : parts per Million : Proton
10.0
20.0
(thousandths)

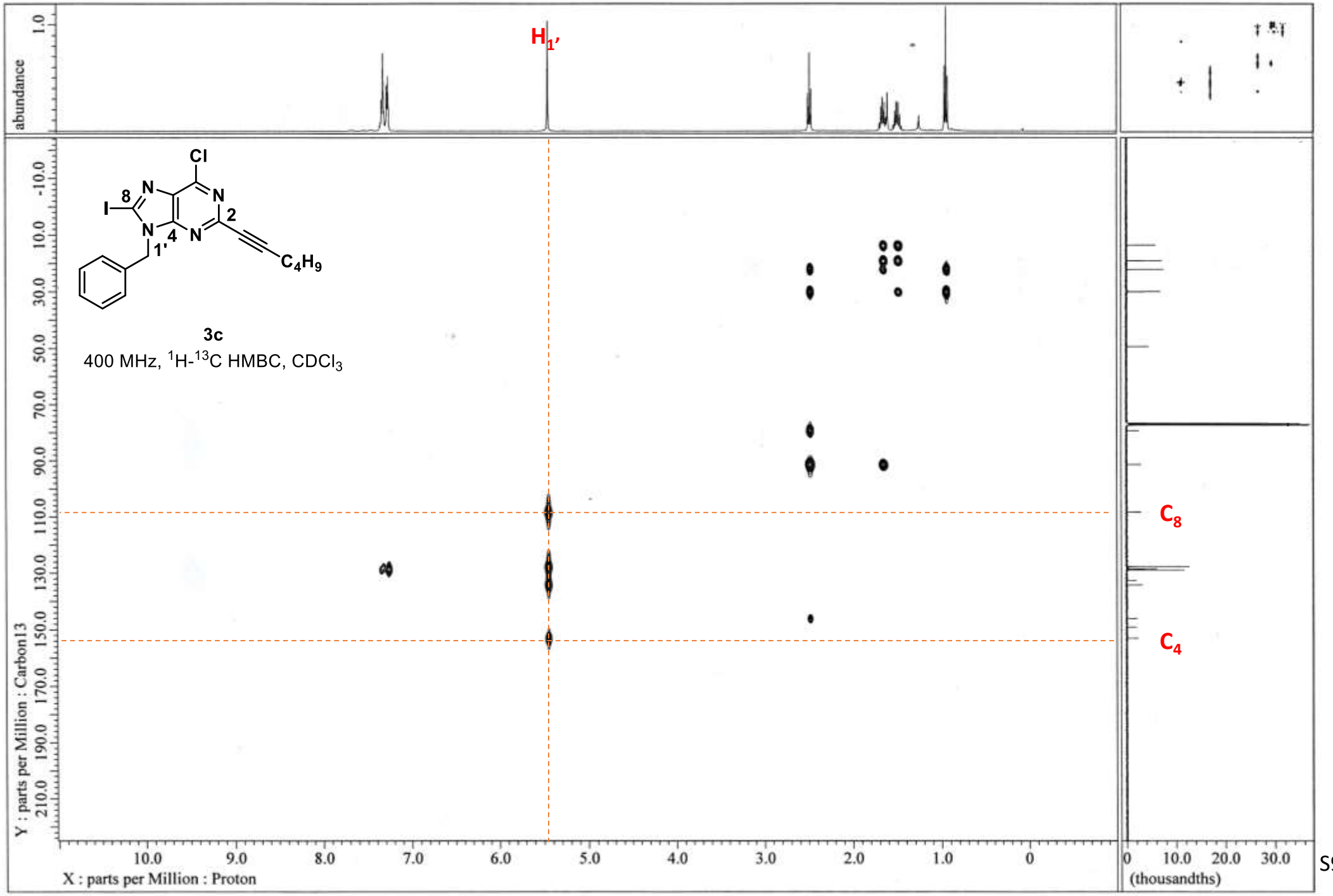

H1'
abundance
Cl
8
N
I
N
2
I
N
4
N
1' CH3
1b
400 MHz, 1H-13C HMBC, DMSO-d6
C8
C2
C4
Y : parts per Million : Carbon13
X : parts per Million : Proton
(thousandths)


H1'
Cl
I
8
N
N
2
N
4
N
1' CH3
C4H9
3b
400 MHz, 1H-13C HMBC, DMSO-d6
C8
C4
Y : parts per Million : Carbon13
X : parts per Million : Proton
(thousandths)


H1'
Cl
C4H9
8
N
N
2
I
N
4
N
1' CH3
4b
400 MHz, 1H-13C HMBC, DMSO-d6
C2
C8
C4
Y : parts per Million : Carbon13
X : parts per Million : Proton
(thousandths)


abundance
1.0
H1'
Cl
8
I
N
N
N
N
I
1'
1c
400 MHz, 1H-13C HSQC, CDCl3
C1'
-10.0
10.0
30.0
50.0
70.0
90.0
110.0
130.0
150.0
170.0
190.0
210.0
Y : parts per Million : Carbon13
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
X : parts per Million : Proton
0
10.0
20.0
30.0
(thousandths)


abundance
1.0
$H_{1'}$
Cl
8
N
N
I
2
N
4
N
I
1'
1c
400 MHz, ^{1}H-^{13}C HMBC, $CDCl_3$
C_8
C_2
C_4
Y : parts per Million : Carbon13
-10.0
10.0
30.0
50.0
70.0
90.0
110.0
130.0
150.0
170.0
190.0
210.0
X : parts per Million : Proton
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
0
10.0
20.0
30.0
(thousandths)


H1'
abundance
1.0
Cl
I
8
N
N
2
N
4
N
1'
C4H9
3c
400 MHz, 1H-13C HMBC, CDCl3
C8
C4
Y : parts per Million : Carbon13
-10.0
10.0
30.0
50.0
70.0
90.0
110.0
130.0
150.0
170.0
190.0
210.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
X : parts per Million : Proton
0
10.0
20.0
30.0
(thousandths)


abundance
H1'
Cl
C4H9
8
N
N
2
I
N
4
N
1'
4c
400 MHz, 1H-13C HMBC, CDCl3
C2
C8
C4
Y : parts per Million : Carbon13
X : parts per Million : Proton
(thousandths)