Supplementary Information

Visible light-mediated photocatalytic coupling between tetrazoles and carboxylic acids for biomolecule labelling

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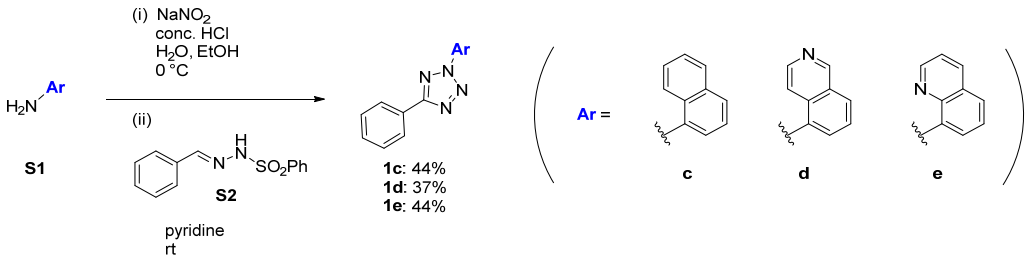
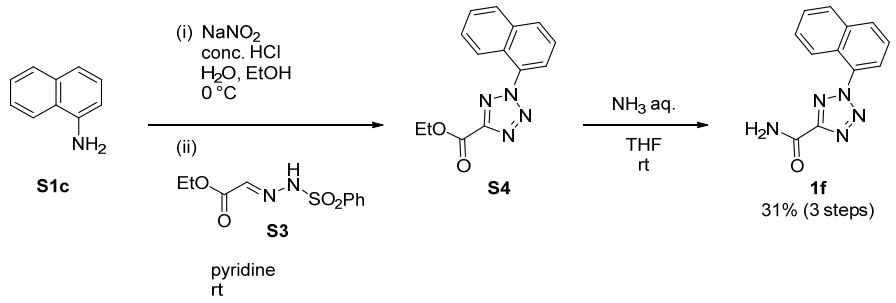
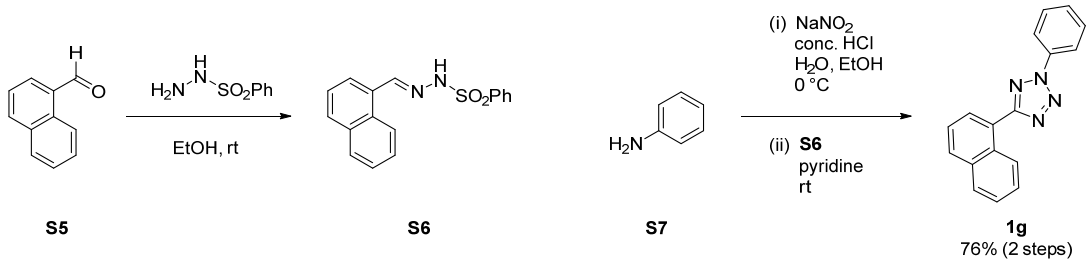
I. Synthetic Schemes



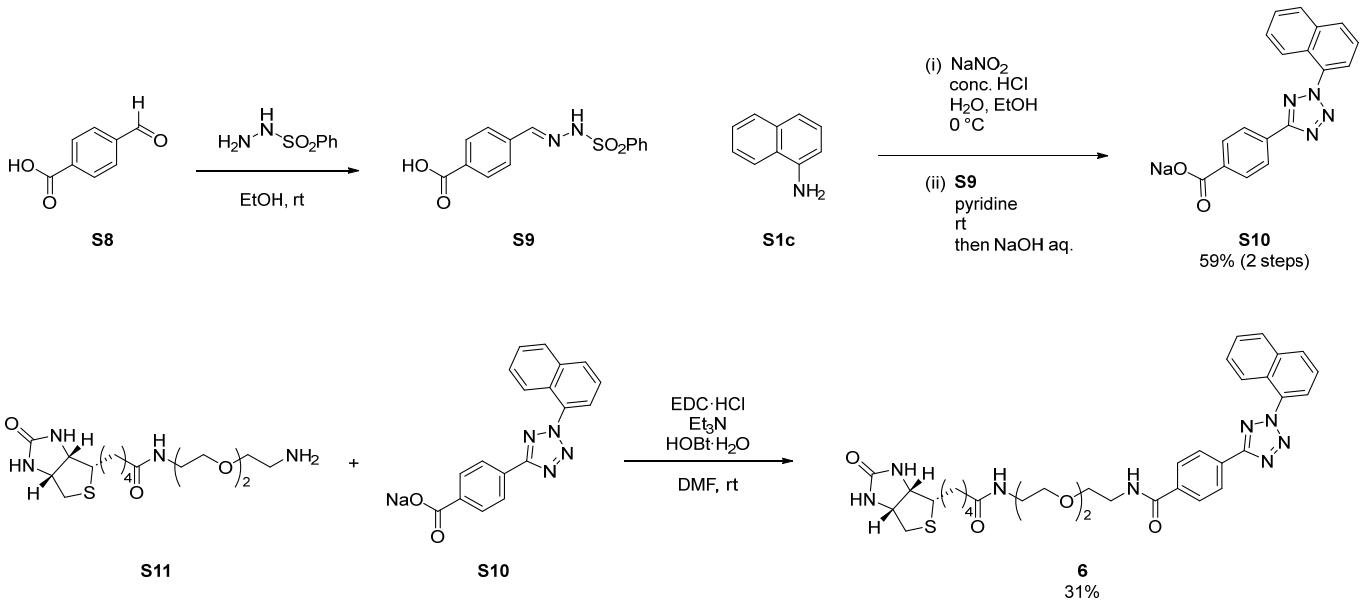
Scheme S1. Synthesis of **1c**–**e**.



Scheme S2. Synthesis of **1f**.



Scheme S3. Synthesis of **1g**.



Scheme S4. Synthesis of **6**.

II. Supplementary Data

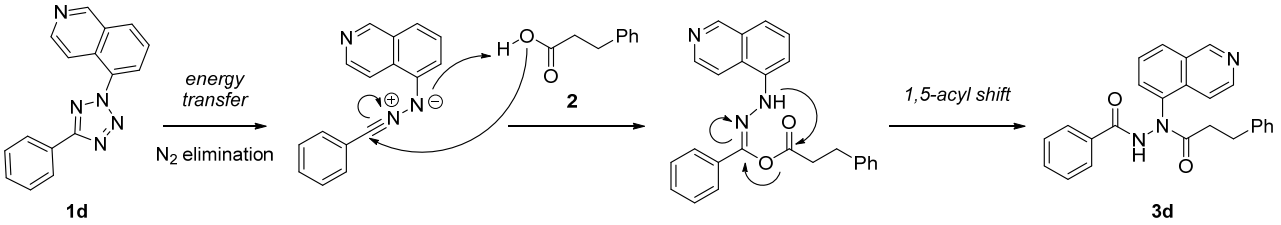
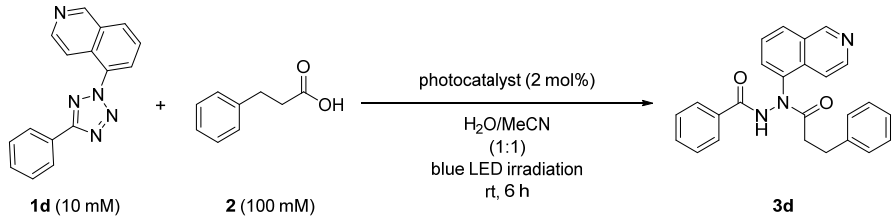
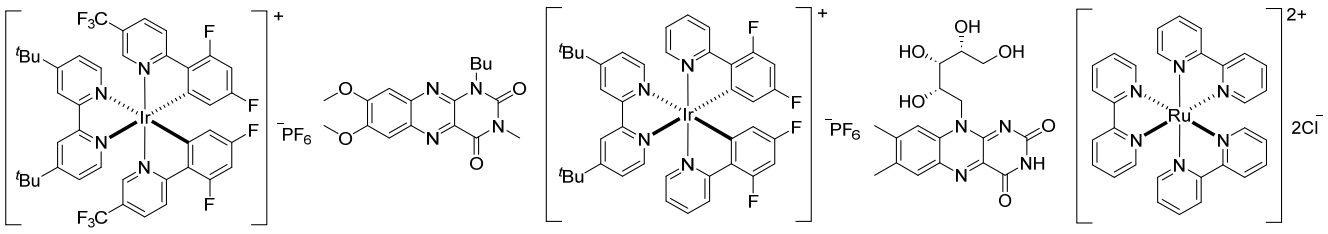


Fig. S1 Plausible reaction mechanism from **1d**.

Table S1 Investigation of optimal condition for the photocatalytic coupling between tetrazole and carboxylic acid.



entry[a]	photocatalyst[b]	E_T (kcal/mol)	yield (%)
1	$Ir[dF(CF_3)ppy]_2(dtbpy)PF_6$	60.1	73
2	1-butyl-7,8-dimethoxy-3-methylalloxazine	65.1	trace[c]
3	$Ir(dFppy)_2(dtbpy)PF_6$	55.4	60
4	riboflavin	50.0	trace
5	$Ru(bpy)_3Cl_2$	46.0	ND



[a] Reaction conditions: The solution of substrate (0.200 mmol), 3-phenylpropionic acid (2.00 mmol) and photocatalyst (2 mol%) in 20.0 mL H_2O/MeCN (1:1) was irradiated with two 40 W blue LED lights for 6 h. [b] The photocatalysts used were dissolved in the reaction solvent (H_2O/MeCN = 1:1). [c] The cause of the reaction not proceeding with 1-butyl-7,8-dimethoxy-3-methylalloxazine, which has high triplet excitation energy, is currently under investigation. ND = Not detected; ppy = 2-phenylpyridine; dtbpy = 4,4'-di-*tert*-butyl-2,2'-bipyridyl; bpy = 2,2'-bipyridine.

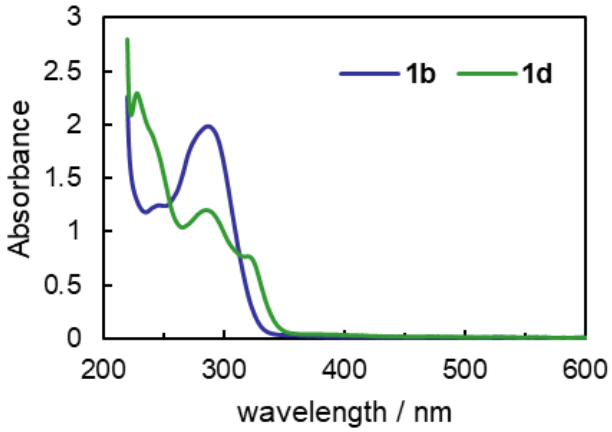


Fig. S2 UV/Vis absorption spectra of **1b** and **1d**. Solutions of tetrazole **1b** (0.1 mM) and **1d** (0.1 mM) in H_2O/MeCN = 1:1 were prepared and measured in 10.0 mm quartz cuvettes.

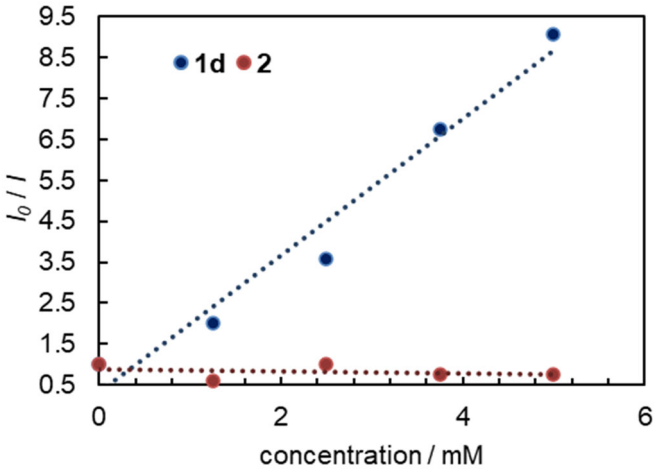


Fig. S3 Stern–Volmer plot for the quenching of 0.1 mM Ir[dF(CF_3)ppy]$_2$(dtbpy)]PF_6. All stock solutions and samples were prepared in a nitrogen-filled glovebox. MeCN was degassed by sparging with N_2 prior to use. The samples were measured in 10.0 mm cuvettes equipped with screw caps. Fluorescent spectra were obtained from 300–600 nm (excitation slit width: 3.0 nm; emission slit width: 3.0 nm). I_0: emission intensity in the absence of a quencher, I: fluorescent intensity in the presence of a quencher). Stock solutions of Ir[dF(CF_3)ppy]$_2$(dtbpy)]PF_6 (1 mM in MeCN), tetrazole **1d** (10 mM in MeCN), and carboxylic acid **2** (10 mM in MeCN) were added to each cuvette and diluted with MeCN to total volume of 2.0 mL. The samples were irradiated at 400 nm and the emission intensity was measured at 463 nm.

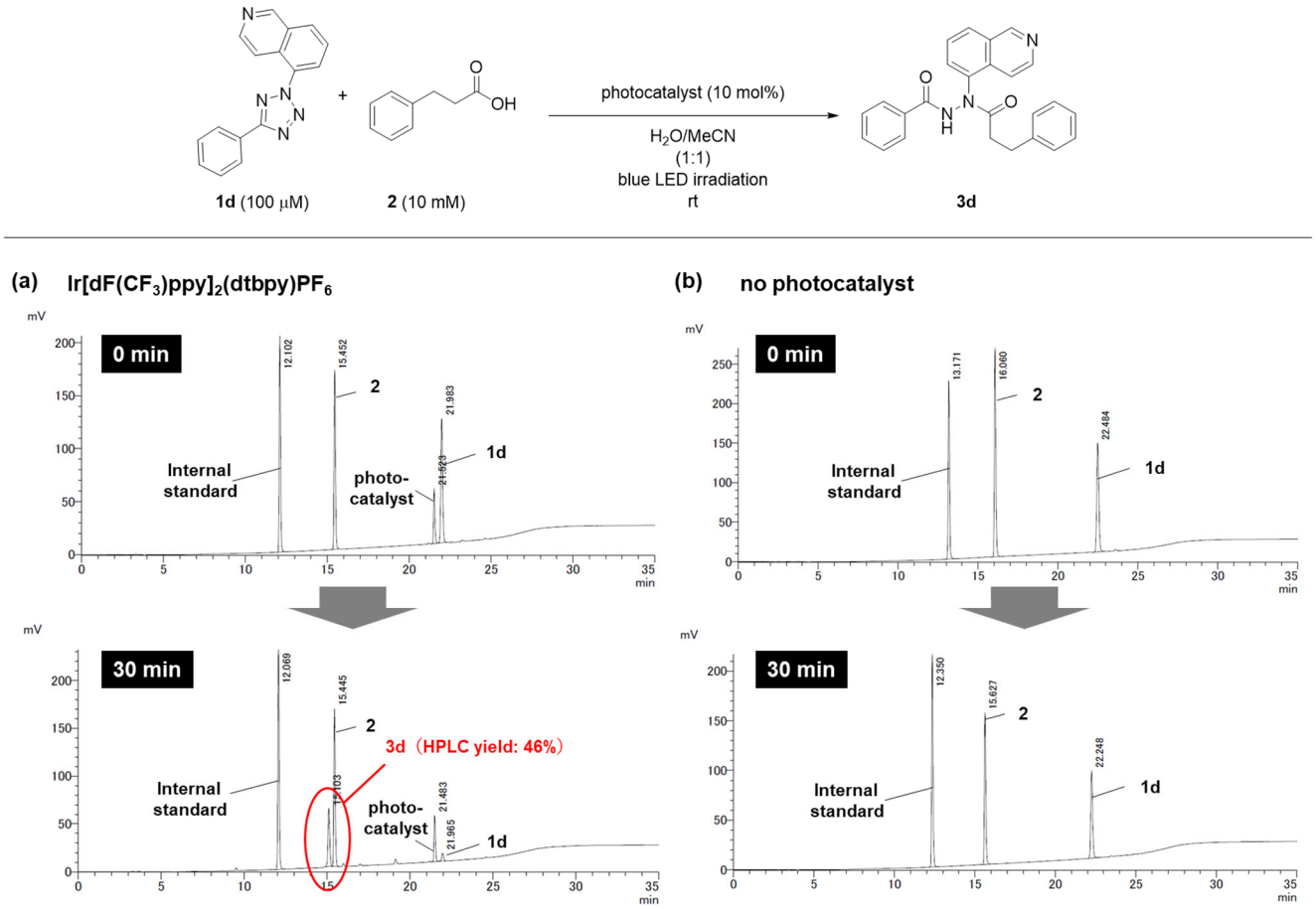
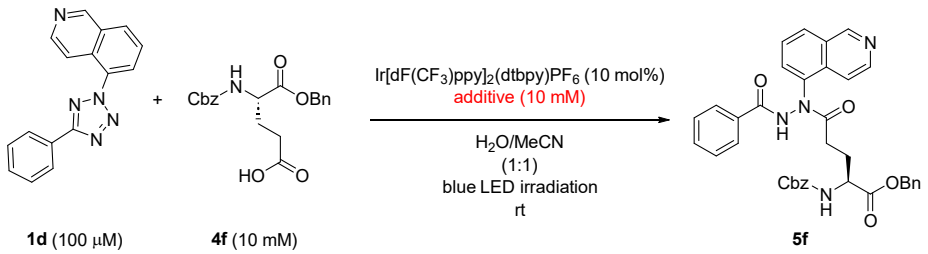


Fig. S4 Photocatalyst-dependent labelling of carboxylic acid in the diluted aqueous solution. Internal standard: *p*-toluamide.

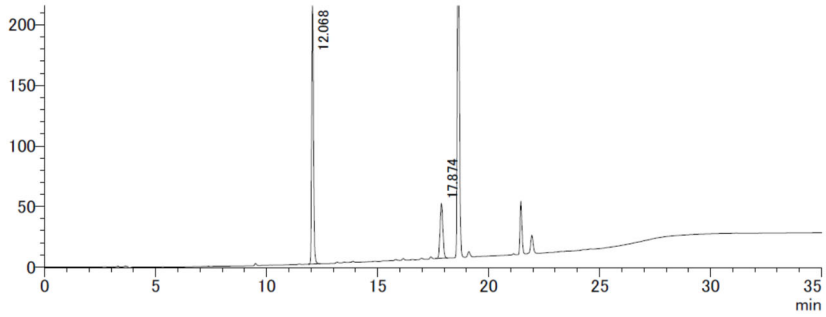
Table S2 Investigation of tolerance against various proteinogenic amino acids. The progress of the photoreaction was evaluated by HPLC in the presence of the same amount of each amino acid derivative as glutamic acid **4f**.



entry	additive	HPLC yield of **5f** (%)
1	-	quant.
2	*N*-Ac-Trp methyl ester	0
3	*N*-Boc-Ser methyl ester	quant.
4	*N*-Boc-Asn methyl ester	quant.
5	*N*-Benzoyl-Arg ethyl ester hydrochloride salt	63
6	*N*-Boc-Cys methyl ester	69
7	*N*-Boc-His methyl ester	86
8	*N*-Boc-Tyr methyl ester	43
9	*Nα*-Boc-Lys methyl ester acetate salt	70

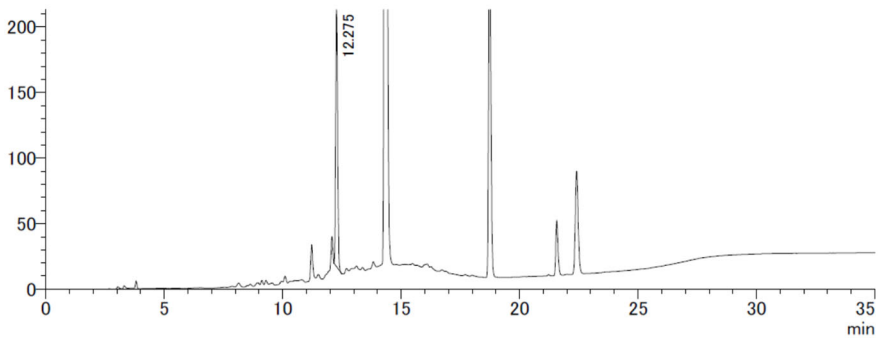
In the below HPLC chromatograms, the peak at 12 min shows the internal standard (*p*-toluamide) and the peak at 18 min shows the desired product **5f**.

entry 1



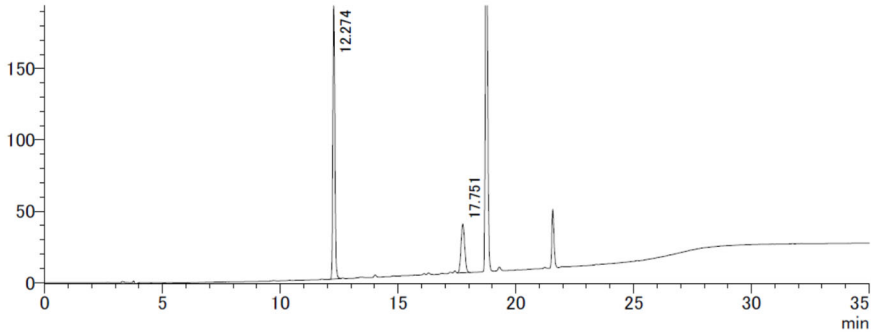
Retention time	Peak area
12.068	1216312
17.874	400409

entry 2



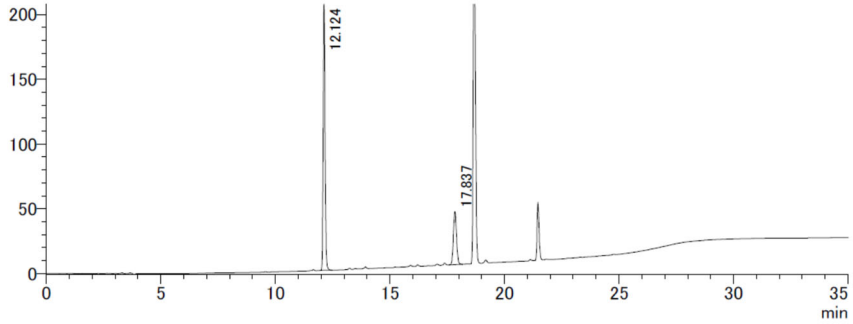
Retention time	Peak area
12.275	1122334

entry 3



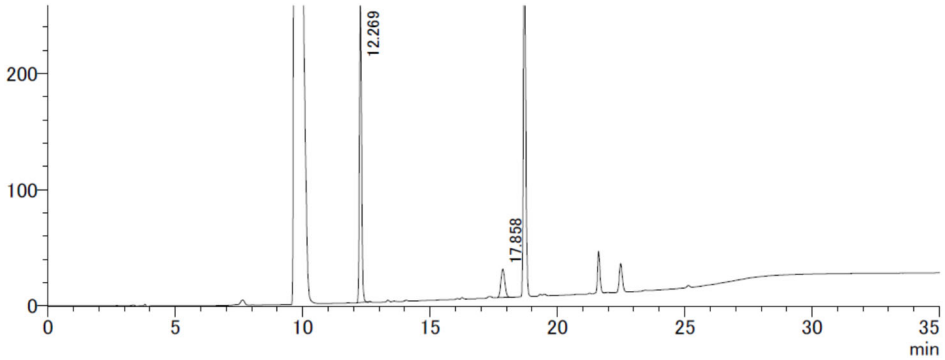
Retention time	Peak area
12.274	1134894
17.751	366172

entry 4



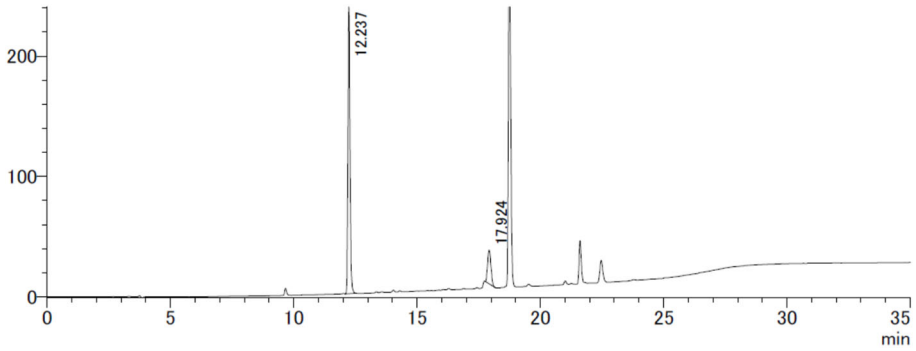
Retention time	Peak area
12.124	1180453
17.837	386947

entry 5



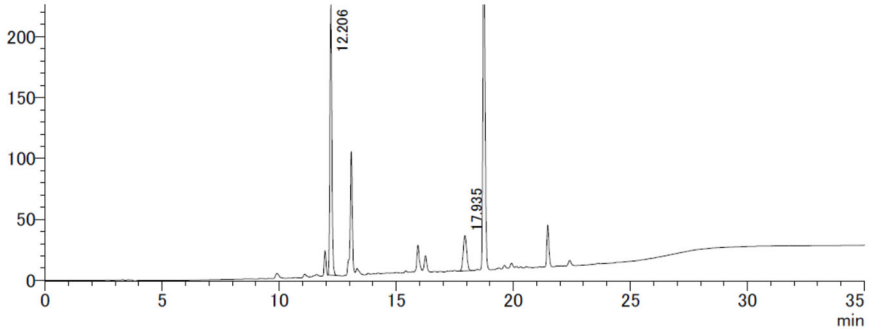
Retention time	Peak area
12.269	1493539
17.858	259803

entry 6



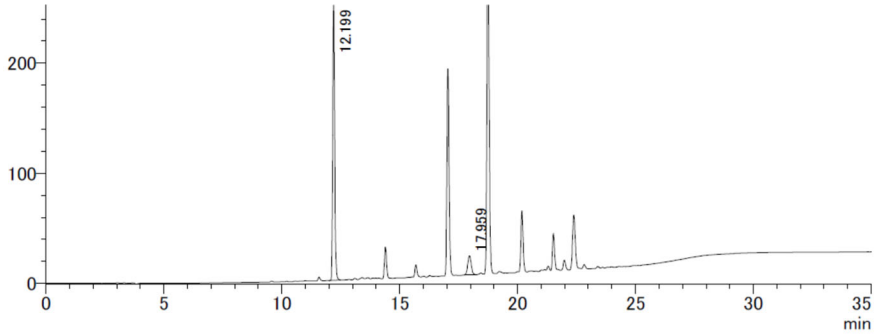
Retention time	Peak area
12.237	1399329
17.924	264715

entry 7



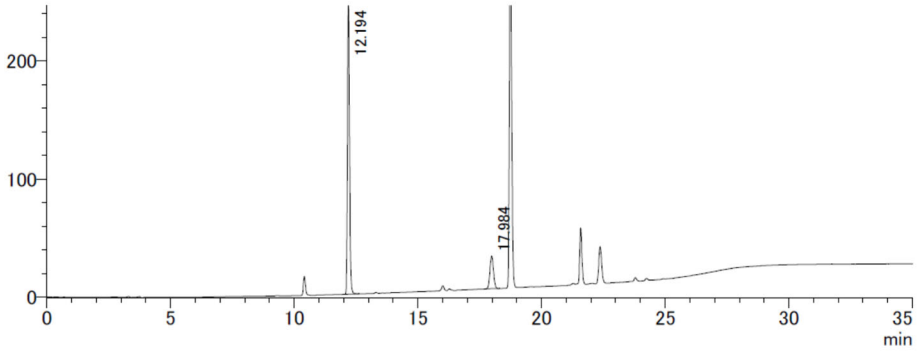
Retention time	Peak area
12.206	1285899
17.935	303082

entry 8



Retention time	Peak area
12.199	1453548
17.959	174581

entry 9



Retention time	Peak area
12.194	1422550
17.984	274463

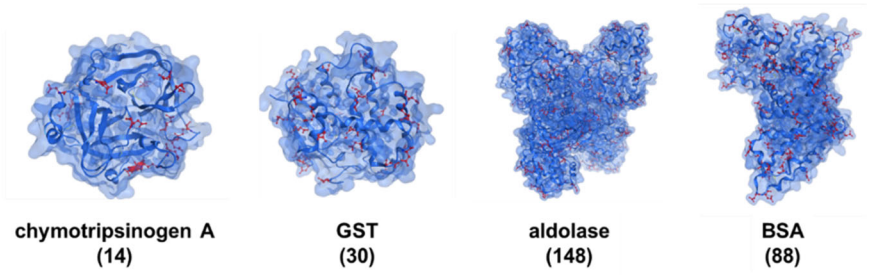
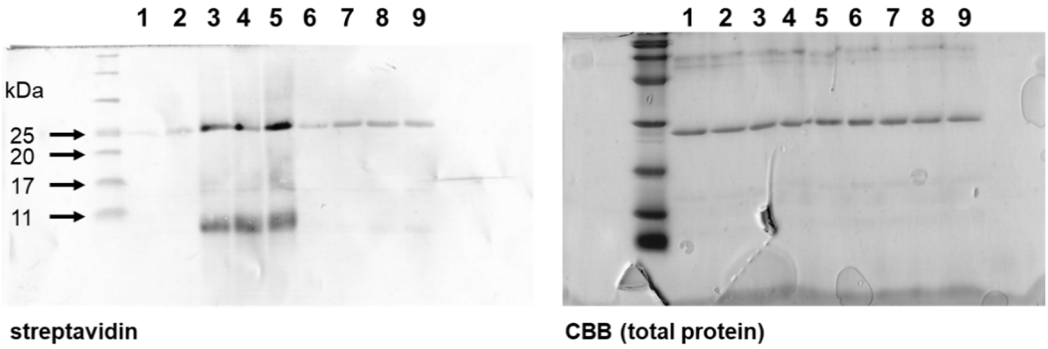
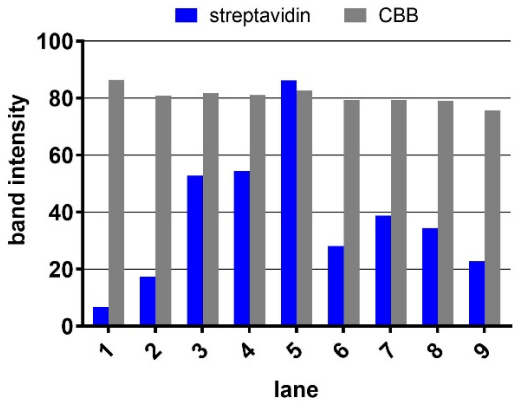


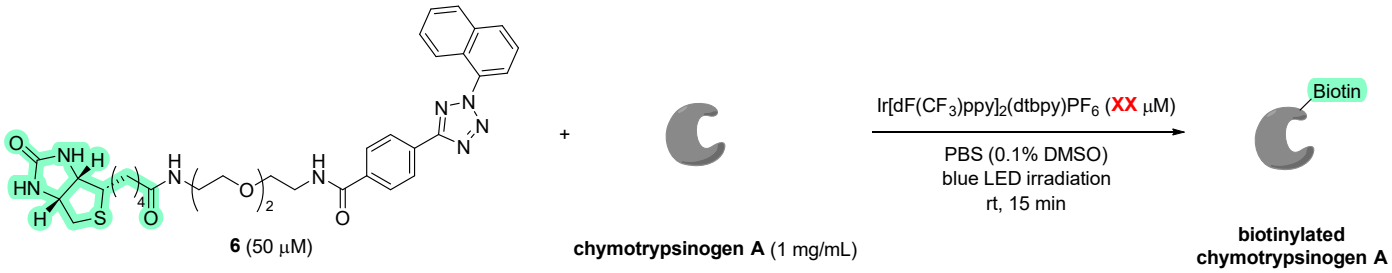
Fig. S5 Structures of chymotrypsinogen A (PDB ID: 1EX3), GST (PDB ID: 1M99), aldolase (PDB ID: 7KA4) and BSA (PDB ID: 4F5S). The number of acidic amino acid is shown in parentheses.

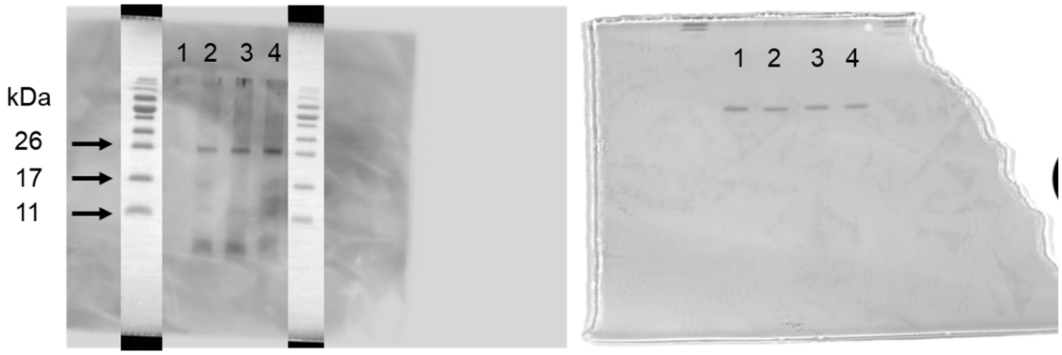




lane	tetrazole	photocatalyst	blue LED irradiation time (min)
1	−	−	−
2	+	+	0
3	+	+	5
4	+	+	10
5	+	+	15
6	+	−	0
7	+	−	5
8	+	−	10
9	+	−	15

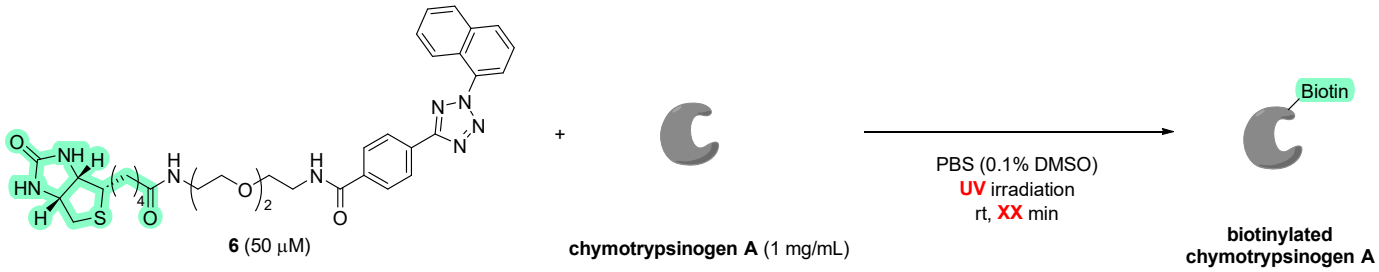
Fig. S6 Raw data of photocatalytic labelling of chymotrypsinogen A. Western blot analysis of biotinylation and coomassie brilliant blue (CBB)-staining for detection of total protein.

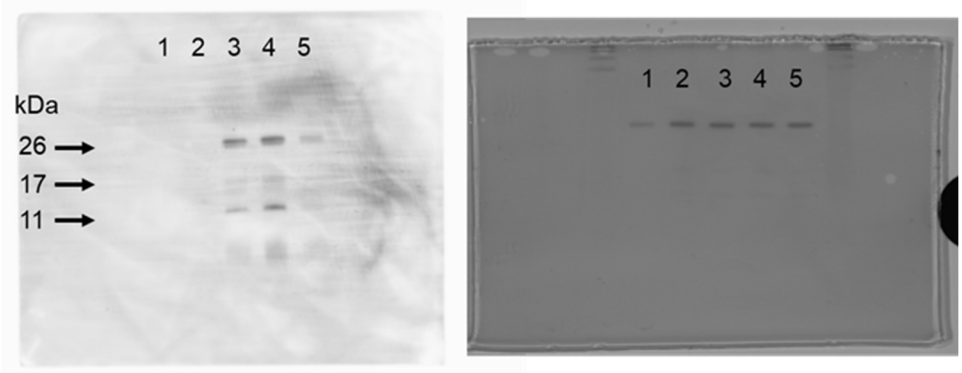




lane	tetrazole	photocatalyst	Concentration of photocatalyst (μM)
1	−	−	−
2	+	+	5
3	+	+	10
4	+	+	20

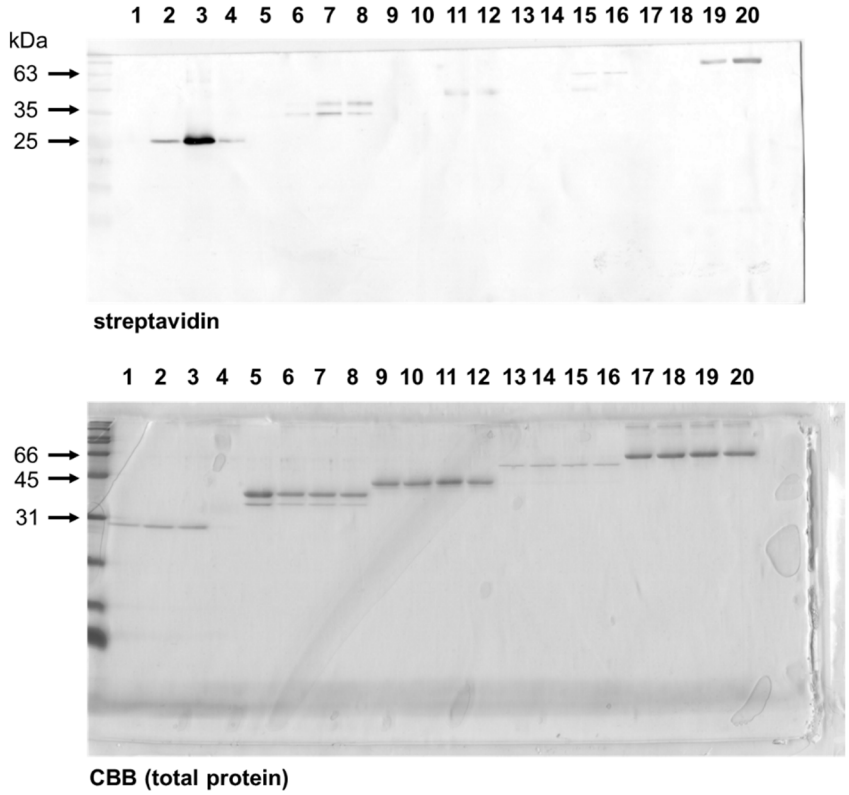
Fig. S7 Concentration dependency of photocatalyst in the photocatalytic labelling of chymotrypsinogen A. Western blot analysis of biotinylation (left) and coomassie brilliant blue (CBB)-staining (right) for detection of total protein. These results suggest that the 10 μM of photocatalyst is optimal.





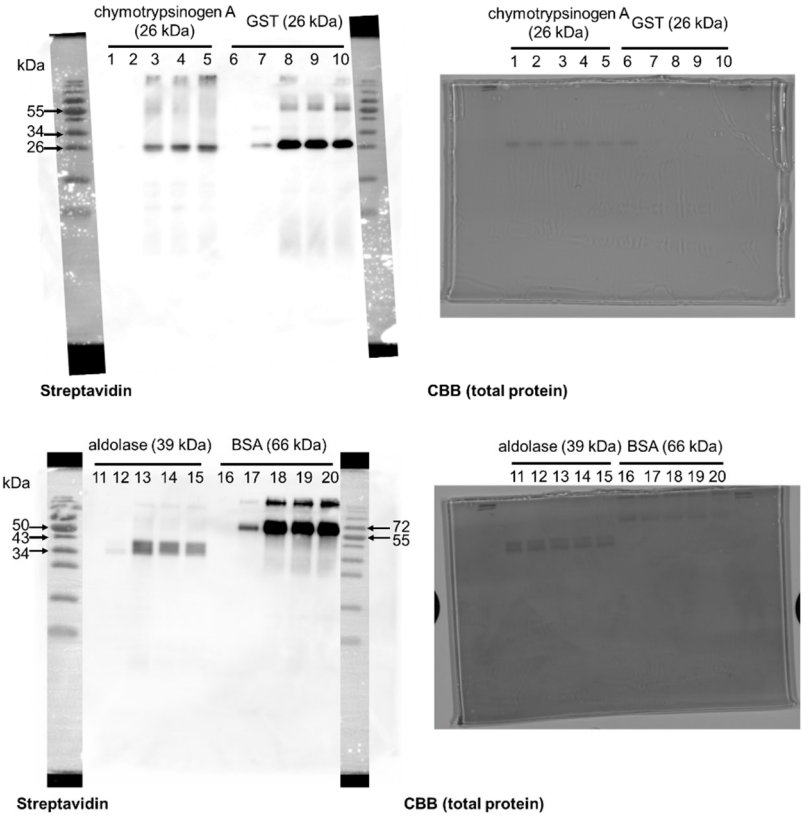
lane	tetrazole	photocatalyst	UV irradiation time (min)
1	−	−	−
2	+	−	0
3	+	−	15
4	+	−	30
5	+	−	60

Fig. S8 Protein labelling under UV irradiation instead of blue light and photocatalysts. Western blot analysis of biotinylation (left) and coomassie brilliant blue (CBB)-staining (right) for detection of total protein. The protein labelling was observed under UV irradiation without photocatalysis.



lane	protein	tetrazole	photocatalyst	blue LED irradiation time (min)
1	GST (26 kDa)	−	−	−
2	GST	+	+	0
3	GST	+	+	5
4	GST	+	+	15
5	aldolase (39 kDa)	−	−	−
6	aldolase	+	+	0
7	aldolase	+	+	5
8	aldolase	+	+	15
9	ovalbumin (45 kDa)	−	−	−
10	ovalbumin	+	+	0
11	ovalbumin	+	+	5
12	ovalbumin	+	+	15
13	catalase (60 kDa)	−	−	−
14	catalase	+	+	0
15	catalase	+	+	5
16	catalase	+	+	15
17	BSA (66 kDa)	−	−	−
18	BSA	+	+	0
19	BSA	+	+	5
20	BSA	+	+	15

Fig. S9 Raw data of photocatalytic labelling of GST, aldolase, ovalbumin, catalase and BSA. Western blot analysis of biotinylation and coomassie brilliant blue (CBB)-staining for detection of total protein.



lane	protein	tetrazole	photocatalyst	blue LED irradiation time (min)
1	Chymotrypsinogen A	−	−	−
2	Chymotrypsinogen A	+	+	0
3	Chymotrypsinogen A	+	+	15
4	Chymotrypsinogen A	+	+	30
5	Chymotrypsinogen A	+	+	60
6	GST	−	−	−
7	GST	+	+	0
8	GST	+	+	15
9	GST	+	+	30
10	GST	+	+	60
11	aldolase	−	−	−
12	aldolase	+	+	0
13	aldolase	+	+	15
14	aldolase	+	+	30
15	aldolase	+	+	60
16	BSA	−	−	−
17	BSA	+	+	0
18	BSA	+	+	15
19	BSA	+	+	30
20	BSA	+	+	60

Fig. S10 Photocatalytic labelling of proteins for 15, 30 or 60 min. Western blot analysis of biotinylation and coomassie brilliant blue (CBB)-staining for detection of total protein. These results suggest that the labelling reaches near saturation within 15 min.

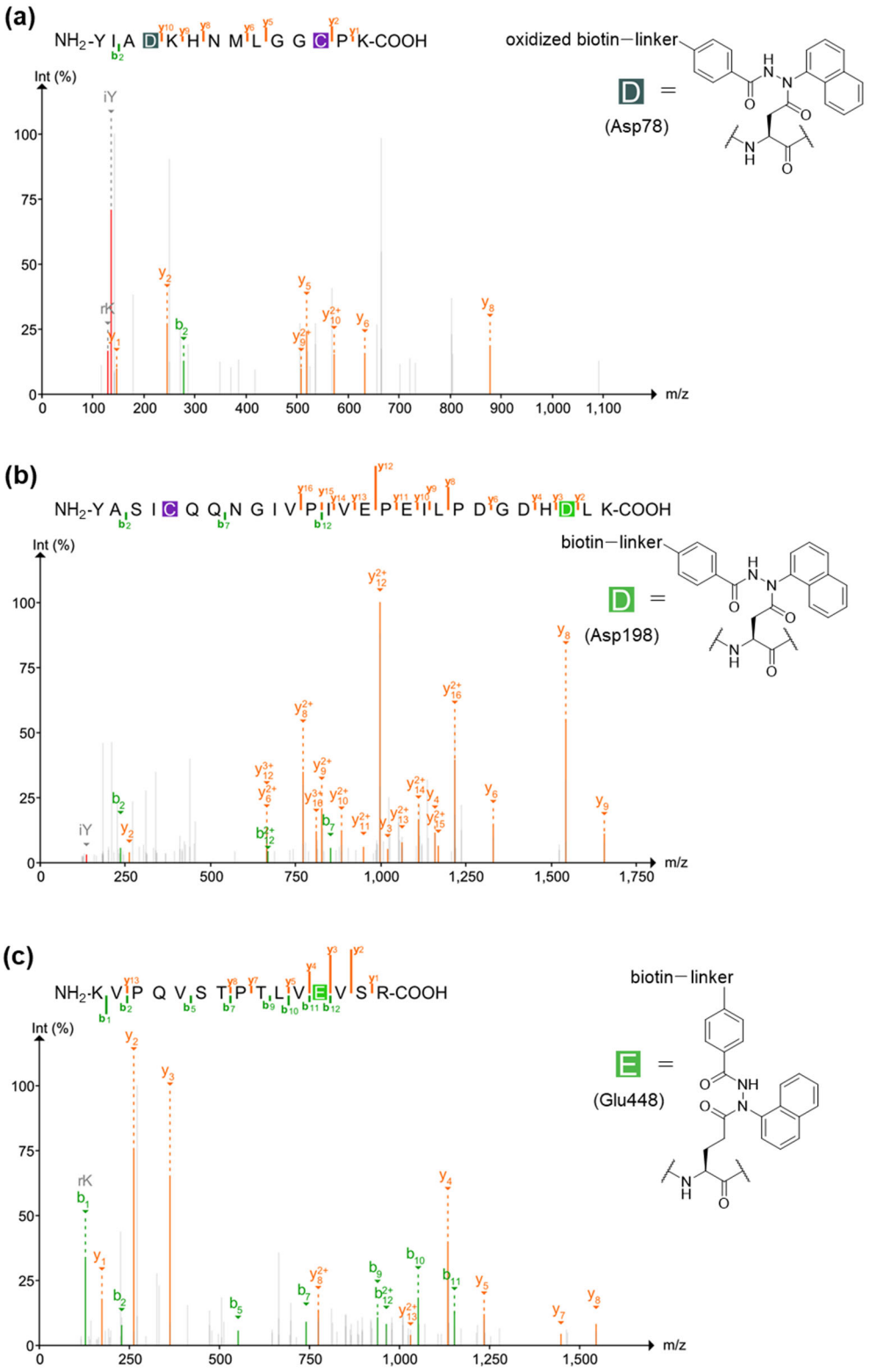


Fig. S11 The MS/MS spectra of the labelled peptides identified from the tryptic digests of labelled proteins. (a) GST, (b) aldolase, (c) BSA. The cysteine residues (purple highlight) were detected as modifications by iodoacetamide used for sample preparation.

(a) chymotrypsinogen A

Red: identified sequence
Blue highlight: labelled D or E

>sp|P00766|CTRA_BOVIN
CGVPAIQPVLSGLSRIVNGEEAVPGSWPWQVSLQDKTGFHFCGGSLINENWVVTAAHCGV
TTSDVVVAGEFDQGSSSEKIQKLKIAKVFKNSKYNSLTINNDITLLKLSTAASFSQTVSA
VCLPSASDDFAAGTTCVTTGWGLTRYTNANTPDRLQQASLPLLSNTNCKKYWGTKIKDAM
ICAGASGVSSCMGDSGGPLVCKKNGAWTLVGIVSWGSSTCSTSTPGVYARVTALVNWVQQ
TLAAN

(b) GST

>sp|P08515|GST26_SCHJ
MSPILGYWKIKGLVQPTRLLLEYLEEKYEEHLYERDEGDKWRNKKFELGLEFPNLPYYID
GDVKLTQSMAIIRYIADKHNMLGGCPKERAEISMLEGAVLDIRYGVSRIAYSKDFETLKV
DFLSKLPEMLKMFEDRLCHKTYLNGDHVTHPDFMLYDALDVVLYMDPMCLDAFPKLVCFK
KRIEAIPQIDKYLKSSKYIAWPLQGWQATFGGGDHPPK

(c) aldolase

>sp|P00883|ALDOA_RABIT
MPHSHPALTPEQKKELSDIAHRIVAPGKGILAADESTGSIAKRLQSIGTENTEENRRFYR
QLLLTADDRVNPCIGGVILFHETLYQKADDGRPFPQVIKSKGGVVGIKVDKGVVPLAGTN
GETTTQGLDGLSERCAQYKKDGADFAKWRCVLKIGEHTPSALAIMENANVLARYASICQQ
NGIVPIVEPEILPDGDHDLKRCQYVTEKVLAAVYKALSDHHIYLEGTLLKPNMVTPGHAC
TQKYSHEEIAMATVTALRRTVPPAVTGVTFLSGGQSEEEASINLNAINKCPLLKPWALTF
SYGRALQASALKAWGGKKENLKAAQEEYVKRALANSLACQGKYTPSGQAGAAASESLFIS
NHAY

(d) BSA

>sp|P02769|ALBU_BOVIN
MKWVTFISLLLLFSSAYSRGVFRRDTHKSEIAHRFKDLGEEHFKGLVLIAFSQYLQQCPF
DEHVKLVNELTEFAKTCVADESHAGCEKSLHTLFGDELCKVASLRETYGDMADCCEKQEP
ERNECFLSHKDDSPDLPKLKPDPNTLCDEFKADEKKFWGKYLYEIARRHPYFYAPELLYY
ANKYNGVFQECCQAEDKGACLLPKIETMREKVLASSARQRLRCASIQKFGERALKAWSVA
RLSQKFPKAEFVEVTKLVTDLTKVHKECCHGDLLECADDRADLAKYICDNQDTISSKLKE
CCDKPLLEKSHCIAEVEKDAIPENLPPLTADFAEDKDVCKNYQEAKDAFLGSFLYEYSRR
HPEYAVSVLLRLAKEYEATLEECCAKDDPHACYSTVFDKLKHLVDEPQNLIKQNCDQFEK
LGEYGFQNALIVRYTRKVPQVSTPTLVEVSRSLGKVGTRCCTKPESERMPCTEDYLSLIL
NRLCVLHEKTPVSEKVTKCCTESLVNRRPCFSALTPDETYVPKAFDEKLFTFHADICTLP
DTEKQIKKQTALVELLKHKPKATEEQLKTVMENFVAFVDKCCAADDKEACFAVEGPKLVV
STQTALA

Fig. S12 Sequence coverage map. Map of sequence coverage in LC-MS/MS analyses of (a) chymotrypsinogen A, (b) GST, (c) aldolase, (d) BSA. The red letters show identified sequences. The blue highlight shows labelled Asp and Glu residues.

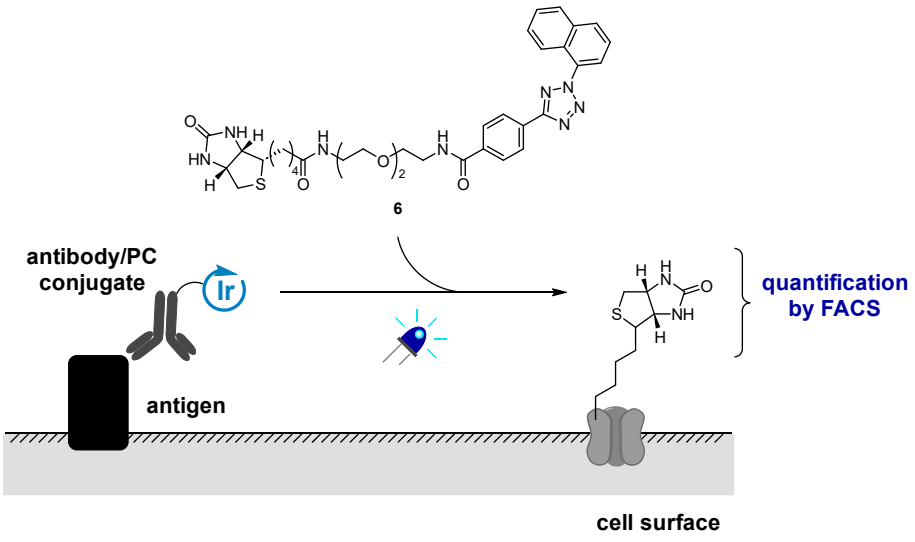


Fig. S13 Outline of photocatalytic cell labelling using antibody-photocatalyst conjugates and biotin-linked tetrazole **6**.

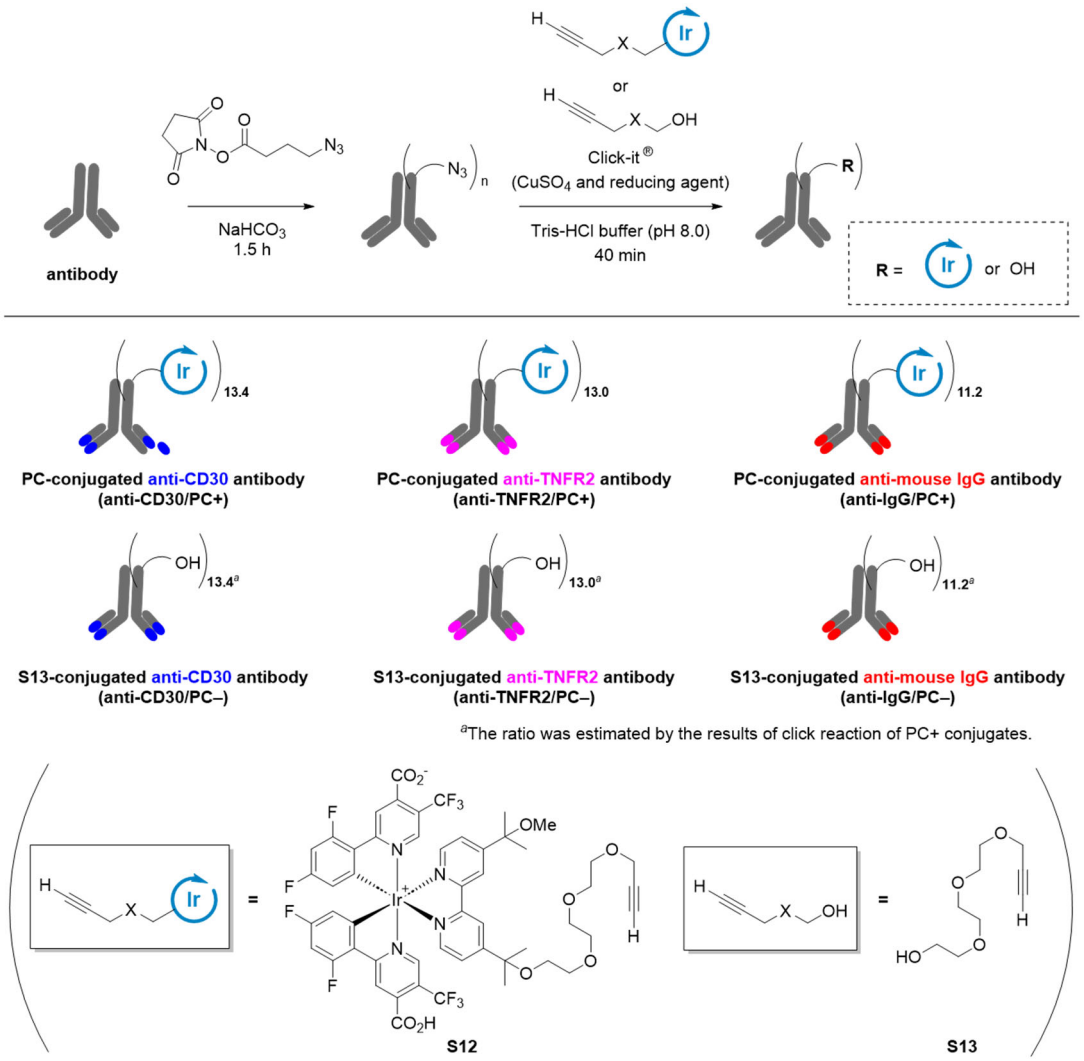


Fig. S14 Preparation of photocatalyst/antibody conjugates. Each antibody-photocatalyst conjugate was obtained by the reaction of an antibody with azidobutyric acid NHS ester under basic conditions followed by a click reaction with a photocatalyst having a terminal alkyne.

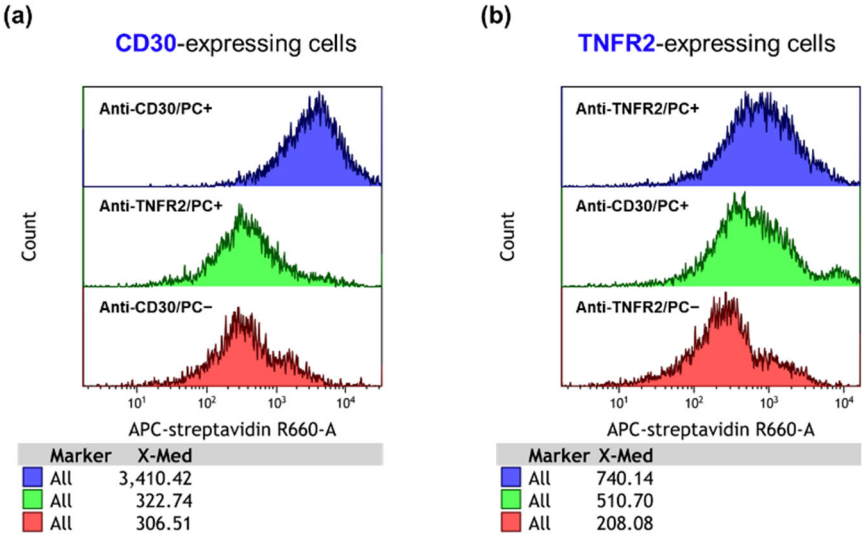
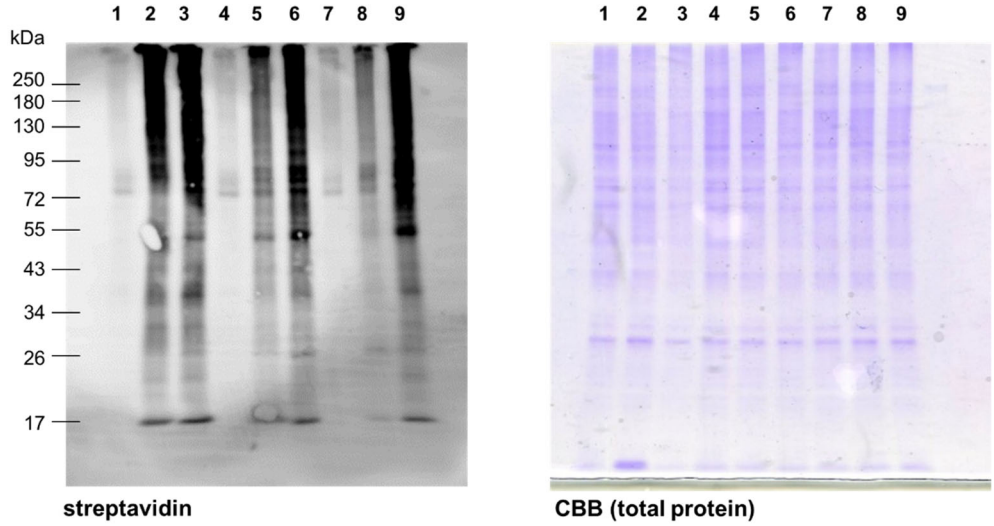


Fig. S15 Raw data of photocatalytic labelling of RB cells. (a) Labelling of RB.CD30 cells with biotin-tetrazole **6**. The cell surface levels of biotin on RB.CD30 cells treated with anti-CD30/PC+, anti-TNFR2/PC+ or anti-CD30/PC− were analyzed by flow cytometry. (b) Labelling of RB.TNFR2 cells with **6**. The cell surface levels of biotin on RB.TNFR2 cells treated with anti-TNFR2/PC+, anti-CD30/PC+ or anti-TNFR2/PC− were analyzed by flow cytometry.



lane	conjugate	irradiation time (min)
1	anti-CD30 antibody/PC+	0
2	anti-CD30 antibody/PC+	30
3	anti-CD30 antibody/PC+	60
4	anti-TNFR2 antibody/PC+	0
5	anti-TNFR2 antibody/PC+	30
6	anti-TNFR2 antibody/PC+	60
7	anti-CD30 antibody/PC−	0
8	anti-CD30 antibody/PC−	30
9	anti-CD30 antibody/PC−	60

Fig. S16 Western blotting analysis of photocatalytically biotin-labeled RB.CD30 cell lysates. The biotinylated proteins on RB.CD30 cells treated with anti-CD30/PC+, anti-TNFR2/PC+ or anti-CD30/PC− were analyzed by western blotting after the photoreaction for 0–60 min in the presence of biotin-tetrazole **6**, followed by labeling with an HRP-conjugated streptavidin.

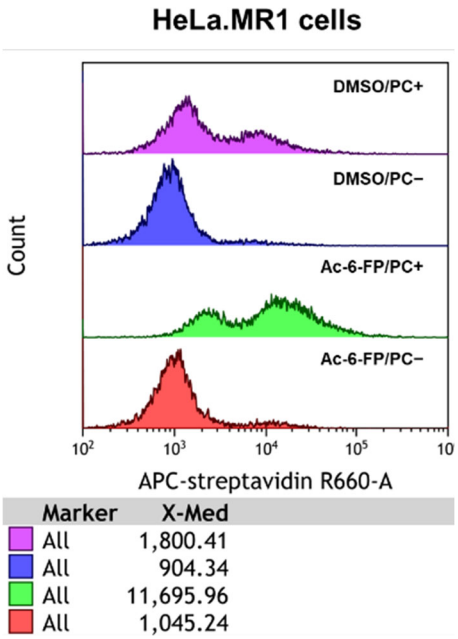


Fig. S17 Raw data of photocatalytic labelling of HeLa.MR1 cells with **6**. The cell surface levels of biotin on HeLa.MR1 cells treated with anti-MR1 antibody, and anti-IgG/PC+ or anti-IgG/PC− were analyzed by flow cytometry.

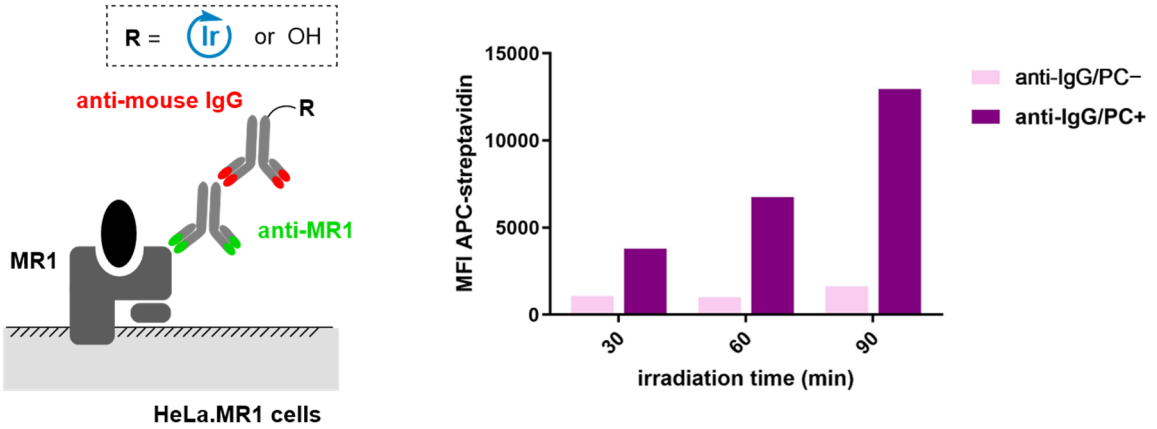


Fig. S18 Investigation of irradiation time dependence. The cell surface levels of biotin on HeLa.MR1 cells treated with anti-MR1 antibody, and with anti-IgG/PC+ or anti-IgG/PC− were analyzed by flow cytometry after the photoreaction for 30–90 min in the presence of biotin-tetrazole **6**, followed by labelling with an APC-conjugated streptavidin. The results shown are representative of at least two independent experiments.

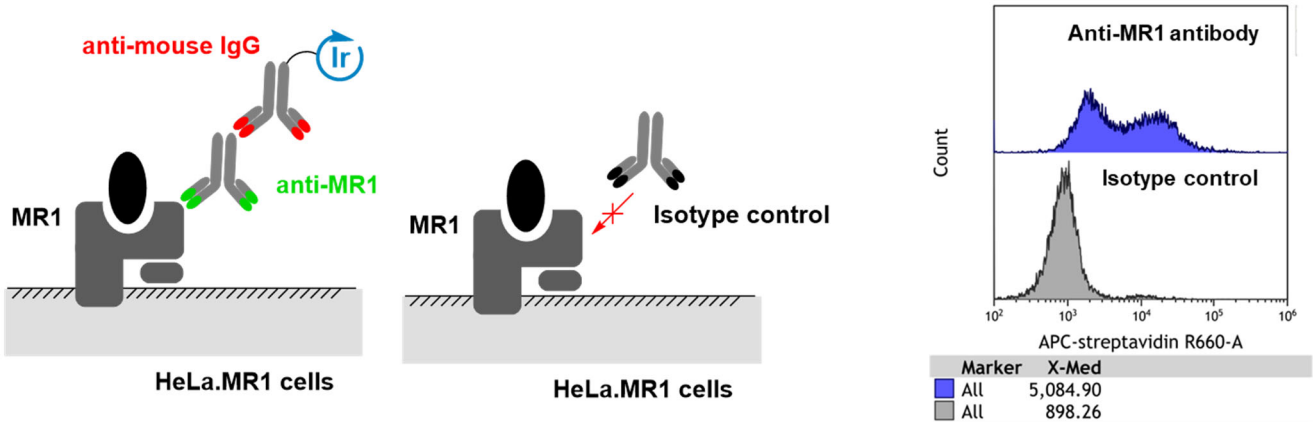


Fig. S19 Control experiment of primary antibody. The cell surface levels of biotin on HeLa.MR1 cells treated with anti-MR1 antibody or its isotype control, and with anti-IgG/PC+ were analyzed by flow cytometry after the photoreaction for 1 h in the presence of biotin-tetrazole **6**, followed by labelling with an APC-conjugated streptavidin.

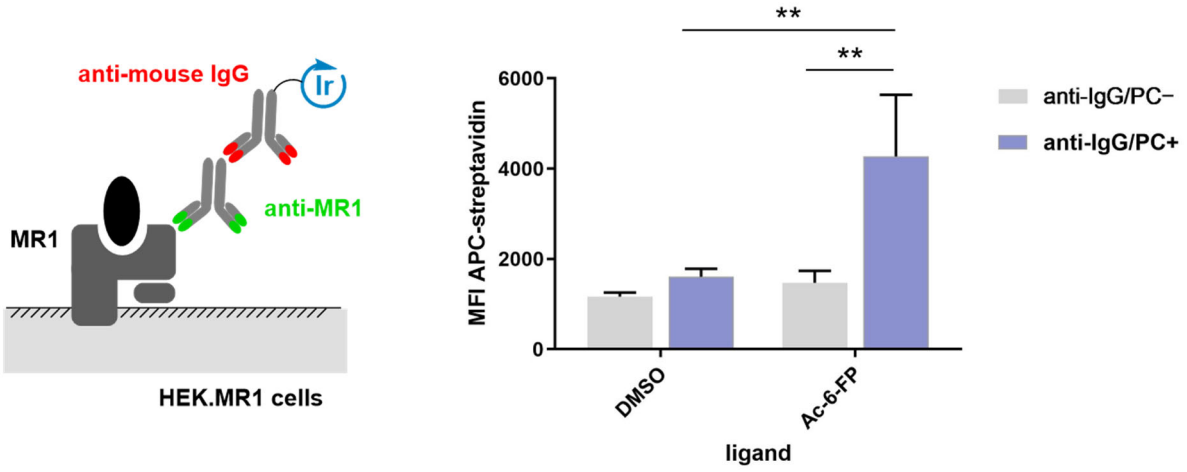


Fig. S20 Photocatalytic cell labelling using photocatalyst (PC)/antibody conjugates. Labeling of HEK.MR1 cells with **6**. The cell surface levels of biotin on HEK.MR1 cells treated with anti-MR1 antibody, and anti-IgG/PC+ or anti-IgG/PC− were analyzed by flow cytometry. The graphs show the mean ± SD of triplicate measurements. Statistical analysis was performed using one-way ANOVA and Tukey multiple comparison test. *$P < 0.05$; **$P < 0.01$; ***$P < 0.001$; ****$P < 0.0001$.

III. Experimental Procedure

General information

^{1}H NMR spectra were recorded using a JEOL ECA-500 or JEOL ECZ600R spectrometer. Chemical shifts are reported in δ (ppm) relative to Me_4Si (in $CDCl_3$, CD_3OD or DMSO-d_6) or residual H_2O (in D_2O) as internal standard. ^{13}C NMR spectra were recorded using a JEOL ECA-500 or JEOL ECZ600R and referenced to the residual $CHCl_3$ signal (in $CDCl_3$), the residual CH_3OH signal (in CD_3OD) and the residual DMSO signal (in DMSO-d_6). Exact mass (HRMS) spectra were recorded on a Shimadzu LC-ESI-IT-TOF-MS equipment (ESI). IR spectra were obtained on a JASCO FT/IR-4100 spectrometer. Optical rotations were measured with a JASCO P-1020 polarimeter. Column chromatography was performed using flash chromatography on a Wakogel C-300E (Wako) or Biotage Isolera flash purification system on Sfär Silica D (Biotage). For photocatalysis in batch manner, A160WE Tuna Blue (40W, Kessil) was utilized. Synthetic method for compounds **1a**[1], **1b**[2], **S2**[2], **S3**[3], **S11**[4], **S12**[5], **S13**[6] are reported. Compounds **S1**, **S5** and **S8** are commercially available.

2-(Naphthalen-1-yl)-5-phenyl-2*H*-tetrazole (1c)

To a stirred solution of aniline **S1c** (1.31 g, 9.15 mmol) and conc. HCl (3.37 mL) in H_2O (6.77 mL) and EtOH (8.41 mL) was added $NaNO_2$ (636 mg, 9.22 mmol) in H_2O (2.52 mL) dropwise at 0 °C. After being stirred for 30 min at this temperature, the suspension was added to the stirred solution of **S2** (2.52 g, 9.68 mmol) in pyridine (50.6 mL) at −10 °C. Then the solution was stirred for 3 h at room temperature, and the mixture was concentrated *in vacuo*. The whole was extracted with CH_2Cl_2, washed with 1 M HCl and brine and dried over $MgSO_4$. After concentration *in vacuo,* the residue was purified by flash chromatography over silica gel with *n*-hexane–EtOAc (40:1) to give **1c** (1.11 g, 44% yield): brown solid; mp 75–77 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.51−7.58 (m, 3H), 7.61−7.67 (m, 3H), 7.92 (dd, J = 7.4, 1.1 Hz, 1H), 7.99−8.02 (m, 1H), 8.08−8.10 (m, 2H), 8.30−8.33 (m, 2H); ^{13}C{^{1}H} NMR (125 MHz, CD_3OD): δ 123.4, 124.7, 126.1, 128.0 (2C), 128.3, 128.4, 128.5, 129.3, 129.6, 130.2 (2C), 131.9, 132.5, 134.7, 135.8, 166.5; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{17}H_{13}N_4$, 273.1135; found, 273.1136.

5-(5-Phenyl-2*H*-tetrazol-2-yl)isoquinoline (1d)

By a procedure identical with that described for synthesis of **1c** from **S1c**, the aniline **S1d** (453 mg, 3.14 mmol) was converted into **1d** (321 mg, 37% yield). Column chromatography: silica gel (gradient 10% to 60% EtOAc in *n*-hexane): yellow solid; mp 121–123 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.52–7.60 (m, 3H), 7.82 (t, J = 8.0 Hz, 1H), 8.21–8.24 (m, 2H), 8.27–8.34 (m, 3H), 8.70 (d, J = 5.7 Hz, 1H), 9.43 (d, J = 1.1 Hz, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 115.9, 126.5, 126.6, 126.8, 127.1 (2C), 129.0 (2C), 129.1, 129.2, 130.6, 130.8, 132.4, 145.1, 152.8, 165.4; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{16}H_{12}N_5$, 274.1087; found, 274.1083.

8-(5-Phenyl-2*H*-tetrazol-2-yl)quinoline (1e)

By a procedure identical with that described for synthesis of **1c** from **S1c**, the aniline **S1e** (444 mg, 3.07 mmol) was converted into **1e** (370 mg, 44% yield). Column chromatography: silica gel (gradient 6% to 40% EtOAc in *n*-hexane), followed by silica gel (toluene:EtOAc = 15:1): pale pink solid; mp 144–145 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.48–7.57 (m, 4H), 7.75 (t, J = 7.4 Hz, 1H), 8.05 (dd, J = 7.4, 1.7 Hz, 1H), 8.10 (dd, J = 7.4, 1.7 Hz, 1H), 8.29–8.32 (m, 3H), 9.01 (dd, J = 4.0, 1.7 Hz, 1H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 122.5, 125.7, 127.2 (2C), 127.3, 127.4, 128.9 (2C), 129.2, 130.4, 131.2, 134.5, 136.1, 142.5, 152.3, 165.3; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{16}H_{12}N_5$, 274.1087; found, 274.1085.

2-(Naphthalen-1-yl)-2*H*-tetrazole-5-carboxamide (1f)

To a stirred solution of aniline **S1c** (439 mg, 3.06 mmol) and conc. HCl (1.12 mL) in H_2O (2.26 mL) and EtOH (2.80 mL) was added $NaNO_2$ (210 mg, 3.04 mmol) in H_2O (840 μL) dropwise at 0 °C. After being stirred for 20 min at this temperature, the suspension was added to the stirred solution of **S3** (842 mg, 3.29 mmol) in pyridine (16.9 mL) at −10 °C. Then the solution was stirred for 3 h at room temperature, and the mixture was diluted with CH_2Cl_2 and H_2O. The whole was extracted with CH_2Cl_2, washed with 1 M HCl and brine and dried over $MgSO_4$. After concentration *in vacuo,* the residue was purified by flash chromatography over silica gel with a gradient of 6% to 35% EtOAc in *n*-hexane, followed by silica gel with *n*-hexane–EtOAc (7:1) to give **S4** (353 mg), which was used without further purification. Then, to a stirred solution of **S4** (261 mg) in THF (10.0 mL) was added NH_3 aq. (28% in H_2O; 5.04 mL) at room temperature. After being stirred for 19 h at this temperature, the mixture was concentrated *in vacuo*. The residue was purified by flash chromatography over silica gel with *n*-hexane–EtOAc (1:1) to give **1f** (169 mg, 31% yield, 3 steps): pale orange solid; mp 174–175 °C; IR (neat cm^{-1}): 1721 (C=O); ^1H NMR (500 MHz, DMSO-d_6): δ 7.69–7.80 (m, 4H), 8.03 (d, J = 6.8 Hz, 1H), 8.13–8.18 (m, 1H), 8.19 (d, J = 8.6 Hz, 1H), 8.33 (d, J = 8.6 Hz, 1H), 8.52–8.57 (m, 1H); $^{13}C\{^1H\}$ NMR (150 MHz, DMSO-d_6): δ 121.9, 124.5, 125.4, 126.6, 127.5, 128.5, 128.6, 131.9, 132.4, 133.6, 157.9, 160.1; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{12}H_9N_5NaO$, 262.0699; found, 262.0698.

5-(Naphthalen-1-yl)-2-phenyl-2*H*-tetrazole (1g)

To a stirred solution of benzenesulfonyl hydrazide (1.74 g, 10.1 mmol) in EtOH (20.0 mL) was added **S5** (1.36 mL, 10.0 mmol) at room temperature. After being stirred for 4 h at this temperature, the mixture was diluted with H_2O. Then, the suspension was filtered through Kiriyama funnel to afford **S6**, which was used without further purification. Then, to a stirred solution of aniline **S7** (273 μL, 3.00 mmol) and conc. HCl (1.12 mL) in H_2O (2.26 mL) and EtOH (2.80 mL) was added $NaNO_2$ (217 mg, 3.14 mmol) in H_2O (840 μL) dropwise at 0 °C. After being stirred for 30 min at this temperature, the suspension was added to the stirred solution of **S6** (999 mg, 3.22 mmol) in pyridine (16.9 mL) at −10 °C. Then the solution was stirred for 3 h at room temperature, and the mixture was concentrated *in vacuo*. The residue was suspended in H_2O/MeOH (1:1), followed by filtration with Kiriyama funnel to give **1g** (622 mg, 76% yield, 2 steps): white solid; mp 75–77 °C; ^1H NMR (500 MHz, CD_3OD): δ 7.54–7.69 (m, 6H), 7.98 (d, J = 8.0 Hz, 1H), 8.06 (d, J = 8.0 Hz, 1H), 8.24 (d, J = 7.4 Hz, 2H), 8.29 (d, J = 6.9 Hz, 1H), 8.92 (d, J = 8.6 Hz, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, CD_3OD): δ 121.0 (2C), 125.0, 126.3, 126.7, 127.5, 128.5, 129.6, 129.8, 131.0 (2C), 131.1, 131.8, 132.4, 135.5, 138.3, 166.5; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{17}H_{13}N_4$, 273.1135; found, 273.1136.

***N*'-(4-Methoxyphenyl)-*N*'-(3-phenylpropanoyl)benzohydrazide (3b)**

The solution of **1b** (50.2 mg, 0.199 mmol), 3-phenylpropionic acid (300 mg, 2.00 mmol) and $Ir[dF(CF_3)ppy]_2(dtbpy)PF_6$ (4.39 mg, 3.91×10^{-3} mmol) in H_2O (10.0 mL) and MeCN (10.0 mL) was stirred under Ar and irradiated with two blue LED lamps (Kessil) 4 cm away from the reaction vessel at room temperature. After being stirred for 6 h at this temperature, the mixture was concentrated *in vacuo* to remove MeCN. Then, the whole was extracted with EtOAc, washed with saturated aqueous solution of $NaHCO_3$ and brine, and dried over $MgSO_4$. After concentration *in vacuo,* the residue was purified by flash chromatography over silica gel with $CHCl_3$–MeOH (10:1), followed by silica gel with a gradient of 12% to 60% EtOAc in *n*-hexane to give **3b** (27.9 mg, 37% yield): orange oil; IR (neat cm^{-1}): 1739 (C=O), 1686 (C=O); ^1H NMR (500 MHz, DMSO-d_6, 140 °C): δ 2.52–3.08 (m, 4H), 3.75 (s, 3H), 6.92 (d, J = 8.0 Hz, 2H), 7.13–7.25 (m, 5H), 7.38 (d, J = 8.6 Hz, 2H), 7.48 (dd, J = 7.4, 7.4 Hz, 2H), 7.56–7.58 (m, 1H), 7.86 (d, J = 7.4 Hz, 2H), 11.18 (s, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, DMSO-d_6): δ 29.9, 30.4, 34.2, 35.2, 55.17, 55.25, 113.6, 114.4, 125.8, 127.4, 128.1–

128.4, 128.7, 129.0, 131.6, 131.9, 132.1, 132.4, 134.6, 134.9, 140.8, 141.1, 157.3, 158.8, 164.8, 165.5, 170.0, 172.5 (rotamer mixture); HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{23}H_{22}N_2NaO_3$, 397.1523; found, 397.1525.

_N_'-(Naphthalen-1-yl)-_N_'-(3-phenylpropanoyl)benzohydrazide (3c)

By a procedure identical with that described for synthesis of **3b** from **1b**, the aniline **1c** (55.2 mg, 0.203 mmol) was converted into **3c** (56.4 mg, 70% yield). Column chromatography: silica gel (gradient 12% to 60% EtOAc in *n*-hexane): orange oil; IR (neat cm^{-1}): 1739 (C=O), 1656 (C=O); ^1H NMR (500 MHz, DMSO-d_6, 140 °C): δ 2.78–3.12 (m, 4H), 6.95–7.29 (m, 5H), 7.44 (dd, J = 7.7, 7.7 Hz, 2H), 7.48–7.55 (m, 4H), 7.75–7.80 (m, 1H), 7.83 (d, J = 7.4 Hz, 2H), 7.86–7.95 (m, 2H), 8.05–8.23 (m, 1H), 10.97 (s, 1H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 31.2, 35.5, 122.2, 125.7, 126.1, 126.6, 127.5 (2C), 127.6, 127.8, 128.26 (2C), 128.30 (2C), 128.4 (2C), 128.6, 129.8, 130.2, 131.4, 131.9, 134.5, 137.1, 140.4, 166.5, 173.2; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{26}H_{23}N_2O_2$, 395.1754; found, 395.1756.

_N_'-(Isoquinolin-5-yl)-_N_'-(3-phenylpropanoyl)benzohydrazide (3d)

By a procedure identical with that described for synthesis of **3b** from **1b**, the aniline **1d** (55.1 mg, 0.202 mmol) was converted into **3d** (58.2 mg, 73% yield). Column chromatography: silica gel (gradient 5% to 80% EtOAc in *n*-hexane): yellow oil; IR (neat cm^{-1}): 1686 (C=O); ^1H NMR (600 MHz, DMSO-d_6, 140 °C): δ 2.75–2.82 (m, 2H), 2.88–2.97 (m, 2H), 7.10–7.18 (m, 2H), 7.19–7.25 (m, 2H), 7.42–7.47 (m, 2H), 7.51–7.55 (m, 1H), 7.68 (t, J = 7.2 Hz, 1H), 7.83 (d, J = 7.6 Hz, 2H), 7.98 (d, J = 6.9 Hz, 2H), 8.05–8.12 (m, 2H), 8.50 (d, J = 6.9 Hz, 1H), 9.30 (s, 1H), 11.01 (s, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, DMSO-d_6, 140 °C): δ 29.6, 33.4, 115.7, 125.2 126.5, 126.8, 127.4–127.7, 128.4, 131.3, 131.8, 132.0, 137.4, 140.3, 142.5, 151.7, 165.6; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{25}H_{22}N_3O_2$, 396.1707; found, 396.1706.

2-[2-(Naphthalen-1-yl)-2-(3-phenylpropanoyl)hydrazineyl]-2-oxoacetamide (3f)

By a procedure identical with that described for synthesis of **3b** from **1b**, the aniline **1f** (47.6 mg, 0.199 mmol) was converted into **3f** containing inseparable impurities (18.8 mg, 26% yield). Column chromatography: silica gel with a gradient of 1% to 10% MeOH in $CHCl_3$, followed by silica gel with $CHCl_3$–MeOH (10:1): yellow oil; IR (neat cm^{-1}): 1662 (C=O); ^1H NMR (500 MHz, $CDCl_3$): δ 2.29–2.36 (m, 1H), 2.43–2.52 (m, 1H), 2.88–3.00 (m, 2H), 5.91 (s, 0.8H), 5.99 (s, 0.2H), 6.97 (d, J = 6.9 Hz, 2H), 7.10–7.25 (m, 3H), 7.27–7.33 (m, 1H), 7.44 (t, J = 8.0 Hz, 1H), 7.52–7.56 (m, 2H), 7.63 (d, J = 6.9 Hz, 1H), 7.80–7.91 (m, 2H), 8.01–8.02 (m, 1H), 9.72 (s, 0.8H), 9.96 (s, 0.2H) (rotamer mixture); $^{13}C\{^1H\}$ NMR (125 MHz, DMSO-d_6): δ 29.8, 30.5, 33.7, 34.8, 123.3, 125.7, 125.8, 126.0–126.2, 126.7, 127.2, 127.4, 128.1–128.5, 129.6, 129.7, 130.0, 133.7, 134.0, 137.3, 140.6, 141.1, 159.4, 161.1, 161.3, 169.9, 173.0 (rotamer mixture); HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{21}H_{19}N_3NaO_3$, 384.1319; found, 384.1317.

_N_'-Decanoyl-_N_'-(isoquinolin-5-yl)benzohydrazide (5a)

By a procedure identical with that described for synthesis of **3b** from **1b** and 3-phenylpropionic acid, the aniline **1d** (55.6 mg, 0.203 mmol) and decanoic acid (346 mg, 2.01 mmol) was converted into **5a** (62.2 mg, 73% yield). Column chromatography: silica gel with a gradient of 1% to 10% MeOH in $CHCl_3$: orange oil; IR (neat cm^{-1}): 1739 (C=O), 1687 (C=O); ^1H NMR (500 MHz, DMSO-d_6, 140 °C): δ 0.76 (t, J = 6.9 Hz, 3H), 0.95–1.31 (m, 12H), 1.38–1.54 (m, 2H), 2.10 (t, J = 7.4 Hz, 0.5H), 2.83 (m, 1.5H), 7.38 (dd, J = 6.9, 6.9 Hz, 2H), 7.42–7.50 (m, 1H), 7.63 (t, J = 7.7 Hz, 1H), 7.72–7.81 (m, 2H), 7.85–8.03 (m, 3H), 8.48 (d, J = 4.6 Hz, 1H), 9.25 (s, 1H), 11.0 (s, 1H) (rotamer mixture); $^{13}C\{^1H\}$ NMR (150 MHz, DMSO-d_6): δ 13.88, 13.90, 22.0, 22.1, 24.1, 24.5, 24.6, 28.1, 28.50, 28.54, 28.65, 28.77, 28.84, 31.16, 31.24, 31.8, 32.8, 33.7, 115.7, 127.4–127.7, 128.5, 128.7, 128.8, 129.0, 129.1, 131.6, 131.7, 132.0, 132.1,

132.2, 132.5, 132.7, 136.9, 138.2, 142.9, 144.0, 152.5, 152.7, 165.9, 171.1, 174.3, 174.5 (rotamer mixture); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{26}H_{32}N_3O_2$, 418.2489; found, 418.2488.

_N_'-(Isoquinolin-5-yl)-_N_'-pivaloylbenzohydrazide (5b)

By a procedure identical with that described for synthesis of **3b** from **1b** and 3-phenylpropionic acid, the aniline **1d** (55.4 mg, 0.203 mmol) and pivalic acid (204 mg, 2.00 mmol) was converted into **5b** (26.8 mg, 38% yield). Column chromatography: silica gel with a gradient of 1% to 10% MeOH in $CHCl_3$: dark red oil; IR (neat cm^{-1}): 1739 (C=O), 1684 (C=O); ^1H NMR (500 MHz, DMSO-d_6, 140 °C): δ 1.29 (s, 9H), 7.47 (dd, J = 7.2, 7.2 Hz, 2H), 7.52–7.58 (m, 1H), 7.68 (t, J = 8.0 Hz, 1H), 7.80–7.85 (m, 2H), 8.00–8.16 (m, 3H), 8.55 (d, J = 5.2 Hz, 1H), 9.31 (s, 1H), 10.99 (s, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, DMSO-d_6): δ 26.4, 27.0, 27.8, 29.9, 110.7, 114.1, 127.4–128.7, 131.2, 132.5, 134.3, 152.5, 152.6, 167.9 (rotamer mixture); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{21}H_{22}N_3O_2$, 348.1707; found, 348.1710.

_N_'-Benzoyl-_N_-(isoquinolin-5-yl)-4-methylbenzohydrazide (5c)

By a procedure identical with that described for synthesis of **3b** from **1b** and 3-phenylpropionic acid, the aniline **1d** (54.7 mg, 0.200 mmol) and *p*-toluic acid (279 mg, 2.05 mmol) was converted into **5c** (44.9 mg, 59% yield). Column chromatography: silica gel with a gradient of 12% to 80% EtOAc in *n*-hexane: orange oil; IR (neat cm^{-1}): 1738 (C=O), 1682 (C=O); ^1H NMR (500 MHz, $CDCl_3$): δ 2.21 (s, 3H), 6.83–6.94 (m, 2H), 7.08–7.25 (m, 4H), 7.32–7.40 (m, 2H), 7.74–7.87 (m, 4H), 8.00–8.11 (m, 1H), 8.28–8.40 (m, 1H), 9.17 (s, 1H), 10.40 (s, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, DMSO-d_6): δ 21.4, 115.7, 127.0, 127.5, 128.3–128.8, 129.2, 130.4, 131.6, 132.2, 132.5, 132.7, 137.8, 141.8, 144.1, 152.7, 166.9, 171.5; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{24}H_{20}N_3O_2$, 382.1550; found, 382.1548.

_N_'-Benzoyl-_N_-(isoquinolin-5-yl)-4-methoxybenzohydrazide (5d)

By a procedure identical with that described for synthesis of **3b** from **1b** and 3-phenylpropionic acid, the aniline **1d** (55.5 mg, 0.203 mmol) and 4-methoxybenzoic acid (311 mg, 2.04 mmol) was converted into **5d** (19.8 mg, 25% yield). Column chromatography: silica gel with a gradient of 12% to 80% EtOAc in *n*-hexane: orange oil; IR (neat cm^{-1}): 1739 (C=O), 1684 (C=O); ^1H NMR (500 MHz, DMSO-d_6, 140 °C): δ 3.65 (s, 3H), 6.76 (d, J = 8.0 Hz, 2H), 7.35 (dd, J = 7.7, 7.7 Hz, 2H), 7.43–7.52 (m, 3H), 7.57 (t, J = 7.7 Hz, 1H), 7.66 (d, J = 7.4 Hz, 2H), 7.81 (d, J = 6.9 Hz, 1H), 7.98 (d, J = 8.0 Hz, 1H), 8.03–8.08 (m, 1H), 8.48 (d, J = 6.3 Hz, 1H), 9.24 (s, 1H), 11.14 (s, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, DMSO-d_6): δ 55.21, 55.33, 113.5, 115.7, 126.0, 126.3, 127.1–128.1, 128.7, 129.9, 130.0, 131.6, 131.8, 132.0, 132.3, 138.4, 138.5, 143.2, 144.0, 152.6, 153.0, 161.0, 161.5, 165.6, 166.0, 168.6, 170.7 (rotamer mixture); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{24}H_{20}N_3O_3$, 398.1499; found, 398.1501.

_N_'-Benzoyl-_N_-(isoquinolin-5-yl)nicotinohydrazide (5e)

By a procedure identical with that described for synthesis of **3b** from **1b** and 3-phenylpropionic acid, the aniline **1d** (54.3 mg, 0.199 mmol) and nicotinic acid (251 mg, 2.04 mmol) was converted into **5e** (18.8 mg, 26% yield). Column chromatography: silica gel with a gradient of 2% to 10% MeOH in $CHCl_3$: orange oil; IR (neat cm^{-1}): 1739 (C=O), 1686 (C=O); ^1H NMR (500 MHz, DMSO-d_6, 140 °C): δ 7.35 (s, 1H), 7.40–7.48 (m, 2H), 7.50–7.55 (m, 1H), 7.62–7.75 (m, 3H), 7.95–8.03 (m, 1H), 8.12 (d, J = 6.9 Hz, 1H), 8.15–8.20 (m, 2H), 8.55 (s, 1H), 8.61 (d, J = 5.7 Hz, 1H), 8.83 (s, 1H), 9.35 (s, 1H), 11.41 (s, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, DMSO-d_6): δ 115.5, 116.4, 123.2, 123.3, 127.2, 127.6, 128.3, 128.7–128.8, 130.6, 131.2, 131.7, 131.8, 132.0, 132.3, 132.4, 132.5, 135.1, 135.2, 137.1, 137.5, 143.4, 144.2, 147.8, 147.9, 151.3, 151.5, 152.7, 152.9, 165.7, 165.8, 167.0, 169.6 (rotamer mixture); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{22}H_{17}N_4O_2$, 369.1346; found, 369.1345.

Benzyl N^5-benzamido-N^2-[(benzyloxy)carbonyl]-N^5-(isoquinolin-5-yl)-L-glutaminate (5f)

By a procedure identical with that described for synthesis of **3b** from **1b** and 3-phenylpropionic acid, the aniline **1d** (55.2 mg, 0.202 mmol) and 1-benzyl *N*-benzyloxycarbonyl-L-glutamate (743 mg, 2.00 mmol) was converted into **5f** (78.6 mg, 63% yield). Column chromatography: silica gel with a gradient of 2% to 10% MeOH in $CHCl_3$, followed by silica gel with a gradient of 0% to 5% MeOH in $CHCl_3$: orange oil; $[\alpha]^{25}_D$ −7.9 (*c* 0.57, $CHCl_3$); IR (neat cm^{-1}): 1739 (C=O), 1725 (C=O); ^1H NMR (500 MHz, DMSO-d_6, 140 °C): δ 1.89–2.11 (m, 1.5H), 2.12–2.26 (m, 1H), 2.28–2.39 (m, 0.5H), 4.11–4.34 (m, 1H), 4.97–5.18 (m, 4H), 7.25–7.38 (m, 12H), 7.45–7.50 (m, 2H), 7.52–7.60 (m, 1H), 7.68–7.72 (m, 1H), 7.85 (d, *J* = 7.4 Hz, 2H), 7.95–8.15 (m, 2H), 8.55 (s, 1H), 9.35 (s, 1H), 11.26 (s, 1H) (rotamer mixture); $^{13}C\{^1H\}$ NMR (125 MHz, DMSO-d_6): δ 25.8, 26.0, 26.2, 28.4, 29.3, 29.9, 53.3, 53.4, 65.6, 66.0, 115.7, 115.8, 127.6–128.8, 129.2, 131.7, 131.8, 132.0, 132.1, 132.2, 132.5, 132.7, 135.8, 135.9, 136.0, 136.5, 136.6, 136.7, 136.79, 136.84, 136.9, 138.0, 143.0, 144.1, 152.5, 152.7, 152.8, 156.0, 156.1, 156.2, 156.3, 165.9, 166.0, 170.3, 170.4, 172.0, 172.1, 173.6, 173.7 (rotamer mixture); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{36}H_{33}N_4O_6$, 617.2395; found, 617.2392.

Benzyl N^4-benzamido-N^2-(*tert*-butoxycarbonyl)-N^4-(isoquinolin-5-yl)-L-asparaginate (5g)

By a procedure identical with that described for synthesis of **3b** from **1b** and 3-phenylpropionic acid, the aniline **1d** (55.2 mg, 0.202 mmol) and 1-benzyl *N*-(*tert*-butoxycarbonyl)-L-aspartate (658 mg, 2.03 mmol) was converted into **5g** (122 mg, quant). Column chromatography: silica gel with a gradient of 1% to 10% MeOH in $CHCl_3$: orange oil; $[\alpha]^{25}_D$ +17.3 (*c* 0.56, $CHCl_3$); IR (neat cm^{-1}): 1739 (C=O), 1686 (C=O); ^1H NMR (500 MHz, DMSO-d_6, 140 °C): δ 1.39 (m, 9H), 2.63–2.80 (m, 1.2H), 3.00–3.40 (m, 0.8H), 4.46 (dd, *J* = 13.7, 7.4 Hz, 0.4H), 4.50–4.75 (m, 0.6H), 5.14 (s, 2H), 6.69 (s, 1H), 7.30–7.35 (m, 6H), 7.45–7.56 (m, 2H), 7.70 (t, *J* = 7.4 Hz, 1H), 7.79–8.21 (m, 4H), 8.51 (s, 1H), 9.33 (s, 1H), 11.34 (s, 1H) (rotamer mixture); $^{13}C\{^1H\}$ NMR (150 MHz, DMSO-d_6): δ 27.5, 27.6, 28.00, 28.05, 35.8, 50.3, 66.0, 78.4, 78.5, 79.1, 115.7, 115.9, 116.9, 127.3–129.2, 131.5, 131.9, 132.0, 132.1, 132.5, 135.7, 135.8, 135.9, 137.6, 142.9, 143.9, 144.0, 152.4, 152.5, 155.16, 155.19, 165.8, 168.5, 168.7, 171.0, 171.2, 171.3, 171.4, 171.6 (rotamer mixture); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{32}H_{33}N_4O_6$, 569.2395; found, 569.2394.

Sodium 4-[2-(naphthalen-1-yl)-2*H*-tetrazol-5-yl]benzoate (S10)

To a stirred solution of **S8** (1.51 g, 10.1 mmol) in EtOH (100 mL) was added benzenesulfonyl hydrazide (1.74 g, 10.1 mmol) at room temperature. After being stirred for 1 h at this temperature, the mixture was diluted with H_2O. Then, the suspension was filtered through Kiriyama funnel to afford **S9** (2.83 g), which was used without further purification. Then, to a stirred solution of aniline **S1c** (434 mg, 3.03 mmol) and conc. HCl (1.12 mL) in H_2O (2.26 mL) and EtOH (2.80 mL) was added $NaNO_2$ (206 mg, 2.99 mmol) in H_2O (840 μL) dropwise at 0 °C. After being stirred for 30 min at this temperature, the suspension was added to the stirred solution of **S9** (997 mg) in pyridine (16.9 mL) at −10 °C. Then the solution was stirred for 3.5 h at room temperature, the mixture was diluted with CH_2Cl_2 and H_2O. The whole was extracted with CH_2Cl_2, washed with H_2O and brine and dried over $MgSO_4$. After concentration *in vacuo,* the residue was purified by flash chromatography over silica gel with a gradient of 10% to 70% EtOAc in *n*-hexane. Then, to the suspension of that purified residue in CH_2Cl_2 was added 1 M NaOH, followed by filtration through Kiriyama funnel to give **S10** (602 mg, 59% yield, 2 steps): brown solid; mp >300 °C; ^1H NMR (500 MHz, D_2O): δ 7.50–7.59 (m, 3H), 7.71 (d, *J* = 8.0 Hz, 2H), 7.88–7.95 (m, 5H), 8.04 (d, *J* = 8.0 Hz, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, CD_3OD): δ 123.5, 124.8, 126.2, 127.4 (2C), 128.4, 128.6, 129.4, 129.6, 129.8, 131.0 (2C), 132.5, 134.8, 135.8, 141.7, 166.4, 174.4; HRMS (FAB) *m/z*: $[M - Na]^-$ calcd for $C_{18}H_{11}N_4O_2$, 315.0887; found, 315.0888.

4-[2-(Naphthalen-1-yl)-2*H*-tetrazol-5-yl]-*N*-{2-[2-(2-{5-[(3a*S*,4*S*,6a*R*)-2-oxohexahydro-1*H*-thieno[3,4-*d*]imidazol-4-yl]pentanamido}ethoxy)ethoxy]ethyl}benzamide (6)

To a stirred solution of aniline **S10** (93.6 mg, 0.277 mmol) and Et_3N (78.0 μL, 0.56 mmol) in DMF (1.57 mL) were added EDC·HCl (116 mg, 0.605 mmol) and HOBt·H_2O (94.9 mg, 0.620 mmol) successively at room temperature. The suspension was stirred for 30 min at this temperature, followed by the addition of freshly prepared **S11** (0.617 mmol) in DMF (1.57 mL). After being stirred for 16 h at this temperature, the mixture was concentrated *in vacuo*. The whole was extracted with EtOAc, washed with saturated aqueous solution of $NaHCO_3$ and dried over $MgSO_4$. After concentration *in vacuo,* the residue was purified by flash chromatography over silica gel with a gradient of 2% to 10% MeOH in $CHCl_3$, followed by silica gel with a gradient of 2% to 10% MeOH in $CHCl_3$ to give **6** (58.5 mg, 31%): brown amorphous; $[\alpha]^{25}_D$ +25.9 (*c* 0.085, $CHCl_3$); IR (neat cm^{-1}): 1739 (C=O), 1702 (C=O), 1651 (C=O); ^1H NMR (500 MHz, $CDCl_3$): δ 1.35–1.43 (m, 2H), 1.57–1.72 (m, 4H), 2.18 (t, *J* = 7.4 Hz, 2H), 2.69 (d, *J* = 12.6 Hz, 1H), 2.82 (dd, *J* = 12.6, 4.9 Hz, 1H), 3.05–3.08 (m, 1H), 3.34–3.46 (m, 2H), 3.55 (t, *J* = 5.2 Hz, 2H), 3.61–3.71 (m, 8H), 4.24 (dd, *J* = 7.4, 5.2 Hz, 1H), 4.44 (dd, *J* = 7.7, 4.9 Hz, 1H), 5.89 (s, 1H), 6.75–6.80 (m, 1H), 6.86 (s, 1H), 7.49–7.55 (m, 1H), 7.59–7.67 (m, 3H), 7.91 (d, *J* = 7.2 Hz, 1H), 7.97–8.00 (m, 1H), 8.03 (d, *J* = 8.6 Hz, 2H), 8.05–8.09 (m, 2H), 8.33 (d, *J* = 7.2 Hz, 2H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 25.5, 28.0, 28.1, 35.9, 39.0, 39.9, 40.3, 55.6, 60.2, 61.7, 69.67, 69.81, 69.9, 70.0, 122.6, 123.3, 124.8, 126.9, 127.0 (2C), 127.1, 127.9 (2C), 128.2, 128.4, 129.7, 131.3, 133.3, 134.2, 136.2, 164.3, 164.4, 166.9, 173.5; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{34}H_{40}N_8NaO_5S$, 695.2735; found, 695.2735.

Condition of HPLC analysis

HPLC analysis in the photoreaction under the diluted condition was performed using the following method.

- Column: $5C_{18}$ AR-II (COSMOSIL)
- Flow rate: 1 mL/min
- Column temperature: room temperature
- UV detection: 254 nm
- Gradient condition:

Time (min)	Solvent A (%)[a]	Solvent B (%)[b]
0	90	10
20	10	90
20.1	0	100
35	0	100

[a]Solvent A: H_2O containing 0.1% formic acid

[b]Solvent B: MeCN containing 0.1% formic acid

Photocatalytic labeling of proteins

Protein solutions were prepared in PBS to a final concentration of 1 mg/mL (only GST: 0.275 mg/mL) followed by addition of biotinylated tetrazole **6** to give a final concentration of 50 μM. $Ir[dF(CF_3)ppy]_2(dtbpy)PF_6$ was added to this mixture to a final concentration of 10 μM with 200 μL total solution volume. The solution was irradiated with blue LED lamp (Kessil) for the indicated time points (0–15 min). After visible light irradiation, 10 μL of each sample was mixed with 90 μL of loading buffer and boiled at 95 °C for 5 min. The samples were then analyzed by western blotting according to the general western blotting procedure described below.

Western blotting for biotinylated proteins

Samples were loaded onto 15% acrylamide gels and subjected to gel electrophoresis. The proteins were then blotted onto PVDF membranes using the transfer device (Bio-rad). Membranes were blocked in PBST with 3% BSA followed by incubation with Streptavidin alkaline phosphatase (Promega) at a 1:5,000 dilution for 0.5–1 h. After being washed with PBST, the membrane was incubated with alkaline phosphatase substrate (Promega).

Coomasie brilliant blue staining of gels

After the protein electrophoresis was completed, the gel was carefully placed in coomassie brilliant blue stain (nacalai). After 2 h, the gel was washed with milliQ and imaged for total protein concentration.

Sample preparation for LC/MS/MS analysis

Chymotrypsinogen A, aldolase and BSA were purchased from Cytiva. Recombinant GST was expressed in *E.coli*. BL21 cells harboring pGEX6P1 at 15 °C for 24 h by induction with 0.2 mM isopropyl β-D-thiogalactopyranoside and purified using glutathione-sepharose (Cytiva). Chymotrypsinogen A, GST, aldolase and BSA were dissolved in a 50 mM ammonium bicarbonate buffer containing 8 M urea. The protein was reduced with 10 mM dithiothreitol (Fujifilm Wako) for 30 minutes. It was then alkylated with 50 mM iodoacetamide (Fujifilm Wako) for 30 minutes in the dark. The resulting mixture was diluted 4-fold with a 50 mM ammonium bicarbonate buffer. Next, trypsin was added to the mixture and incubated overnight to digest the protein. The digestion was stopped by adding trifluoroacetic acid (TFA) (Fujifilm Wako) to a final concentration of 0.5%. The peptide mixture solution was desalted using SDB-XC StageTips.[7] The peptides were dried, reconstituted in a solution of 4% ACN with 0.5% TFA, and finally analyzed by LC/MS/MS.

LC/MS/MS analysis

LC/MS/MS analyses were performed using an Orbitrap Fusion Lumos (Thermo Fisher Scientific) connected to an Ultimate 3000 pump (Thermo Fisher Scientific) and an HTC-PAL autosampler (CTC analytics). The peptides were separated using a self-pulled needle column (150 mm length, 100 µm ID, 6 µm needle opening) packed with Reprosil-Pur 120 C18-AQ 1.9 µm reversed-phase material (Dr. Maisch GmbH). A 30-minute gradient of 5–40% B (mobile phase A: 0.5% acetic acid, mobile phase B: 0.5% acetic acid / 80% acetonitrile) was used at a flow rate of 500 nL/min. The applied ESI voltage was 2.4 kV. The following parameters were used: MS scan range of 300–1500, MS1 orbitrap resolution of 120,000, quadrupole isolation window of 1.6, HCD collision energy of 30%, MS2 orbitrap resolution of 15,000, and MS2 AGC target value of 50,000.

Database Searching and Data Processing

The acquired data files were processed using FragPipe v20.0 (MSFragger v3.8)[8] for peptide identification. Peptides and proteins were identified by conducting an automated database search against the sequence of chymotrypsinogen A, GST, aldolase and BSA (Swiss-Prot accessed on 2025/01/09). The database also included common contaminants/decoys added by FragPipe. The search settings included strict trypsin specificity (C-terminal of K and R) and allowed for up to 2 missed cleavages. Carbamidomethylation of cysteine (C, +57.02146) was considered as a fixed modification, while oxidation of methionine (M, +15.9949), acetylation of protein N-terminus (Protein N-term, +42.0106), and modification with probe 6 and oxidized probe 6 (D, E, and protein C-term, +644.2731 and +660.273, respectively) were treated as variable modifications. The peptide mapping was based on the peptide.tsv files from FragPipe outputs. The peptide spectrum match was then visualized using PDV v2.1.0.[9]

Data availability

The raw MS data and analysis files have been deposited in the ProteomeXchange Consortium (http://proteomecentral.proteomexchange.org) via the jPOST partner repository[10] (https://jpostdb.org) and can be accessed using the dataset identifier PXD054950.

Preparation of photocatalyst/antibody conjugate

The preparation of photocatalyst/antibody conjugate was carried out based on the modified method reported by MacMillan et al.[5] The solution of 1.0 M $NaHCO_3$ (15 μL) and 10 mM stock of azidobutyric acid NHS ester (10 μL, TCI, D5873) in DMSO were added to the solution of antibody (required volumes are listed in the table below). The mixture was incubated at room temperature for 1.5 h. After this time, the reaction mixture was passed through a desalting column (Cytiva, PDminitrap G-25) which had been equilibrated with Tris-HCl (pH 8.0, 50 mM). The Tris-HCl solution was concentrated to 200 μL using an ultrafiltration spin-column (Merck, Amicon Ultra-4, 30K). After dividing the resulting solution (*ca*. 100 μL) into two tubes, each antibody solution was then treated with 4 μL of a 5.0 mM solution of **S12** or **S13** in DMSO, then the components of the Click-It kit (Thermo Fisher Scientific, C10276) were added: reaction buffer A (25 μL), $CuSO_4$, (10 μL) and additive 1 (10 μL). The mixture was incubated for 5 min, then additive 2 (20 μL) was added and the mixture allowed to incubate in the dark for 1 h. The reaction mixture was then passed through a desalting column (Cytiva, PDminitrap G-25) to afford *ca*. 670 μL of Ir-antibody or control antibody solution, which was concentrated to *ca.* 120 μL using an ultrafiltration spin-column (Merck, Amicon Ultra-4, 30K). The Ir-antibody conjugate was analyzed by BCA protein assay kit (Thermo Fisher) for total protein concentration and A350 for Ir concentration against serial dilutions of BSA and **S12** as authentic standards, respectively.

antibody	photocatalyst	final concentration (mg/mL)	Ir/Ab ratio
anti-CD30 antibody (4.4 mg/mL, 69 μL)	**S12**	1.03	13.4
anti-CD30 antibody (4.4 mg/mL, 69 μL)	**S13**	0.531	–
anti-TNFR2 antibody (2.9 mg/mL, 100 μL)	**S12**	1.04	13.0
anti-TNFR2 antibody (2.9 mg/mL, 100 μL)	**S13**	0.856	–
anti-mouse IgG polyclonal antibody (2.0 mg/mL, 150 μL, Millipore, AP124)	**S12**	0.581	11.2
anti-mouse IgG polyclonal antibody (2.0 mg/mL, 150 μL, Millipore, AP124)	**S13**	0.699	–

Photocatalytic cell labeling

Targeted labeling of CD30 on CD30-expressing Ramos Blue cells for flow cytometry analysis and Western blot analysis

To initiate the labeling reaction, cells were removed from culture, washed twice in cold PBS and resuspended in PBS at 1×10^6 cells/mL. The cells were pelleted, the supernatant removed, and then resuspended in 100 μL of PBS. Fc-Block (5 μL, Biolegend, 422301) was added and the resulting cell suspension was incubated at room temperature for 10 min. The cells were pelleted to remove the supernatant, washed twice with 1 mL of PBS and treated with 5 μg of photocatalyst (**S12**)-conjugated anti-CD30 antibody, 5 μg of photocatalyst (**S12**)-conjugated anti-TNFR2 antibody or 5 μg of **S13**-conjugated anti-CD30 antibody. After incubation at 4 °C for 1 h, the cells were pelleted to remove the supernatant, washed twice with 1 mL PBS and resuspended in 50 μM of biotin-tetrazole **6** in PBS (1 mL). The labelling reactions were carried out at room temperature for 1 h with irradiation from a 40 W blue LED light using an EvoluChem™ PhotoRedOx Box. After irradiation, the cells were then pelleted to remove the supernatant.

For flow cytometry analysis, the cell pellets were subsequently stained with APC-streptavidin (0.18 μg/100 μL, Biolegend). After incubation at 4 °C for 40 min, the cells were pelleted to remove the supernatant, washed twice with 1 mL PBS and resuspended in 250 μL of PBS, followed by CytoFLEX flow cytometric analysis (Beckman Coulter). Data were analyzed with Kaluza software (Beckman Coulter, v2.1).

For Western blot analysis, the cell pellets (2.5×10^6 cells) were then lysed in 50 μL of RIPA buffer. After the samples were rotated at 4 °C for 30 min, and then sonicated for 60 sec, laemmli SDS-PAGE sample buffer (non-reduce,1:1 volume) was added and the resulting sample was then heated for 5 min at 95 °C. 20 μL of each sample was then analyzed by Western blot. After gel electrophoresis was performed, gels were transferred from precast cassettes to PVDF membranes. The membrane was then blocked for 60 min in Block Ace. The membrane was then washed three times with PBS-T and incubated with HRP conjugated Streptavidin (5000× dilution in PBS-T) at room temperature for 1h. The membrane was then washed three times with PBS-T. After treatment with ECL prime western blotting detection reagent, the membrane was then imaged using ImageQuant LAS 4010 (Cytiva).

Targeted labeling of TNFR2 on TNFR2-expressing Ramos Blue cells for flow cytometry analysis

By a procedure identical with that described for the analysis using CD30-expressing Ramos Blue cells, the flow cytometry analysis for targeted labeling of TNFR2 on TNFR2-expressing Ramos Blue cells was carried out.

Targeted labeling of MR1 on MR1-expressing HeLa cells for flow cytometry analysis

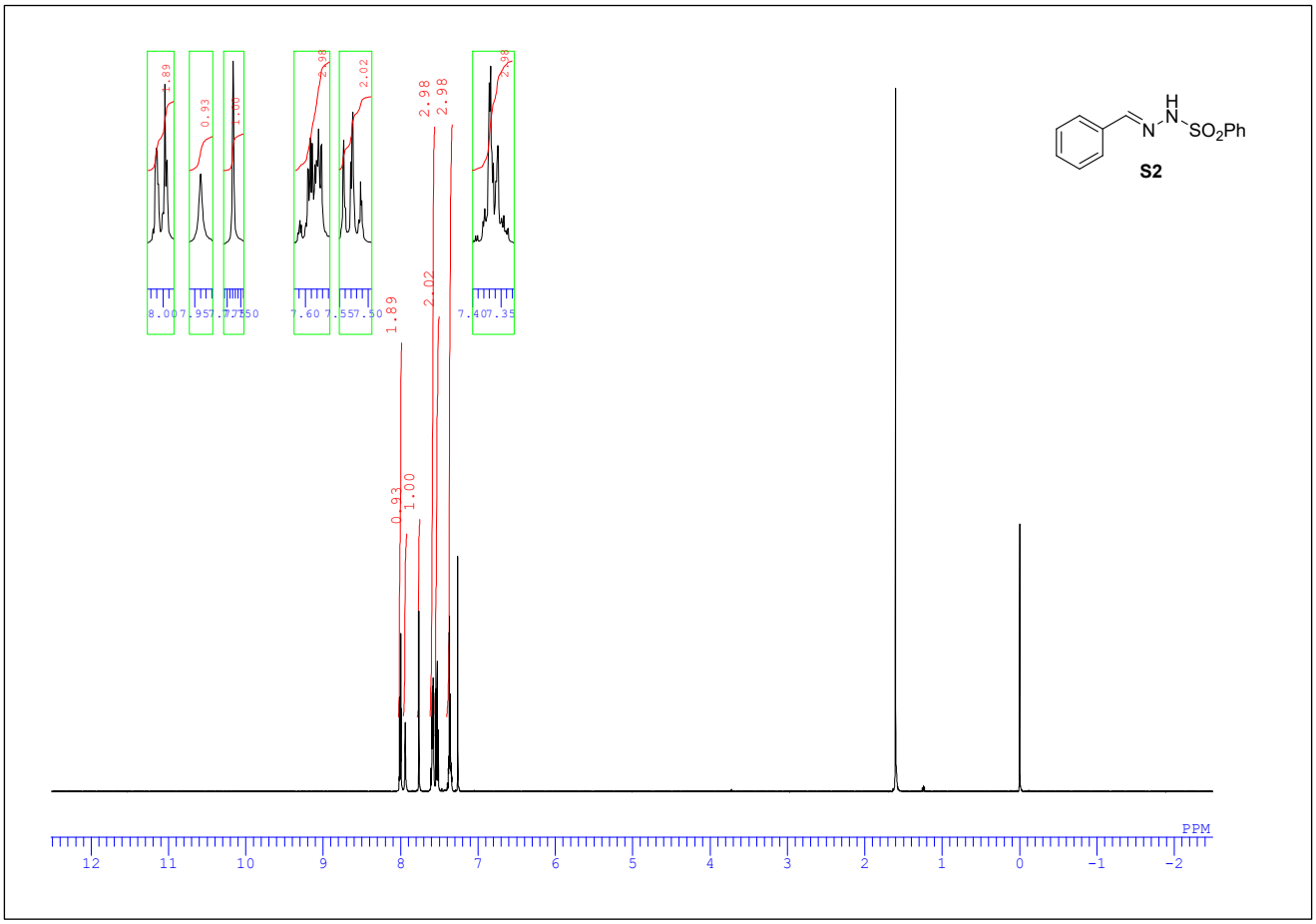
The MR1-expressing HeLa cells were incubated for 8 h in 200 μL medium (RPMI 1640) with or without 1 μM of Ac-6-FP. The cells were removed from culture, washed twice in cold PBS and resuspended in PBS at 1×10^6 cells/mL. The cells were pelleted, the supernatant removed, washed with 1 mL of PBS and treated with 2.5 μg of anti-MR1 antibody (Biolegend, 361102). After incubation at 4 °C for 30 min, the cells were pelleted to remove the supernatant, washed twice with 1 mL PBS and treated with 5 μg of photocatalyst (**S12**)-conjugated anti-mouse IgG polyclonal antibody or 5 μg of **S13**-conjugated anti-mouse IgG polyclonal antibody. After incubation at 4 °C for 30 min, the cells were pelleted to remove the supernatant, washed twice with 1 mL PBS and resuspended in 50 μM of biotin-tetrazole **6** in PBS (1 mL). The labeling reactions were carried out at room temperature for 1 h with irradiation from a 40 W blue LED light using an EvoluChem™ PhotoRedOx Box. After irradiation, the cells were then pelleted to remove the supernatant. The cells were subsequently stained with APC-streptavidin (0.18 μg/100 μL, Biolegend). After incubation at 4 °C for 40 min, the cells were pelleted to remove the supernatant, washed twice with 1 mL PBS and resuspended in 250 μL of PBS, followed by CytoFLEX flow cytometric analysis (Beckman Coulter). Data were analyzed with Kaluza software (Beckman Coulter, v2.1).

Targeted labeling of MR1 on MR1-expressing HEK293 cells for flow cytometry analysis

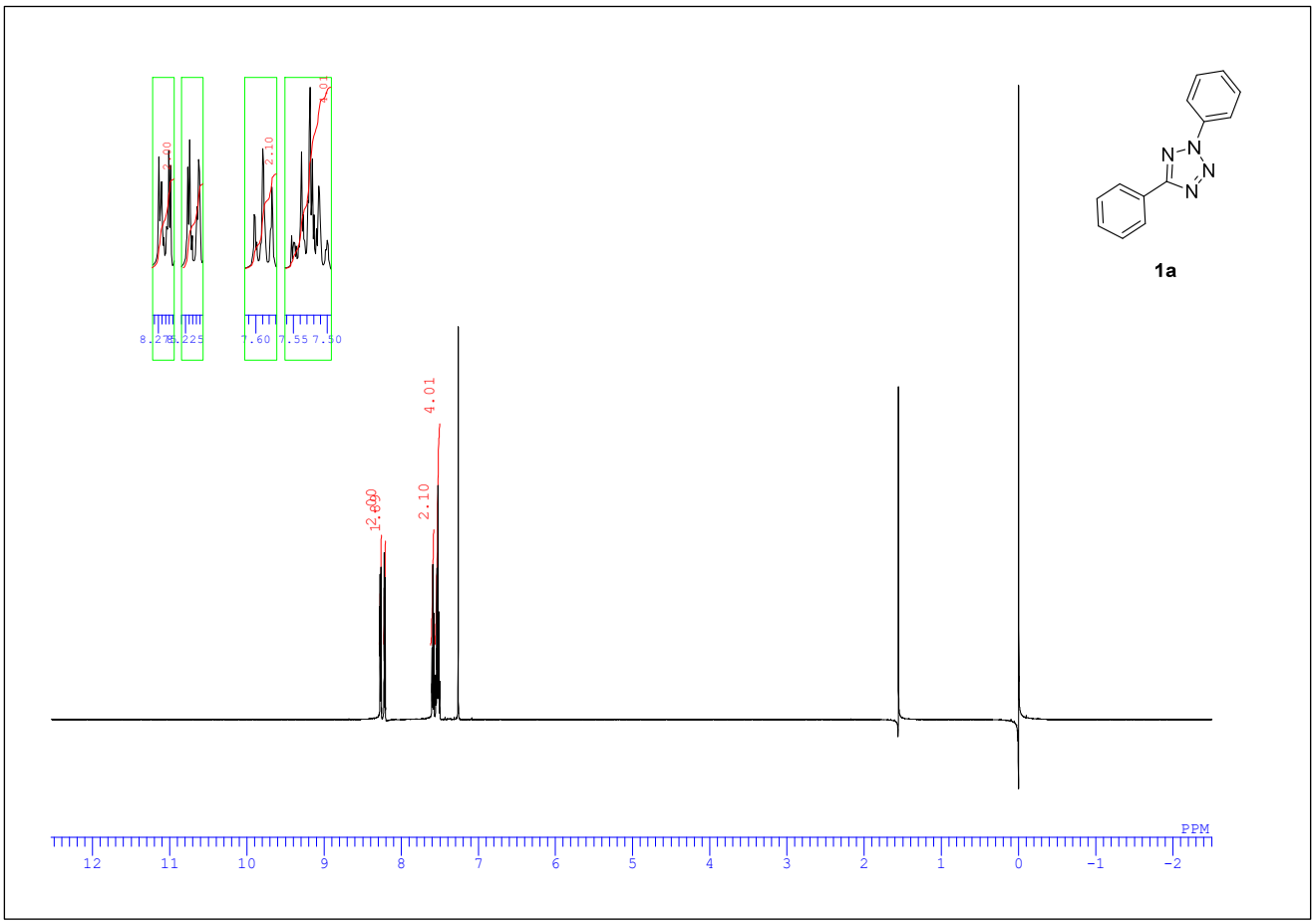
By a procedure identical with that described for the analysis using MR1-expressing HeLa cells, the flow cytometry analysis for targeted labeling of MR1 on MR1-expressing HEK293 cells was carried out.

IV. ^{1}H and ^{13}C NMR spectra

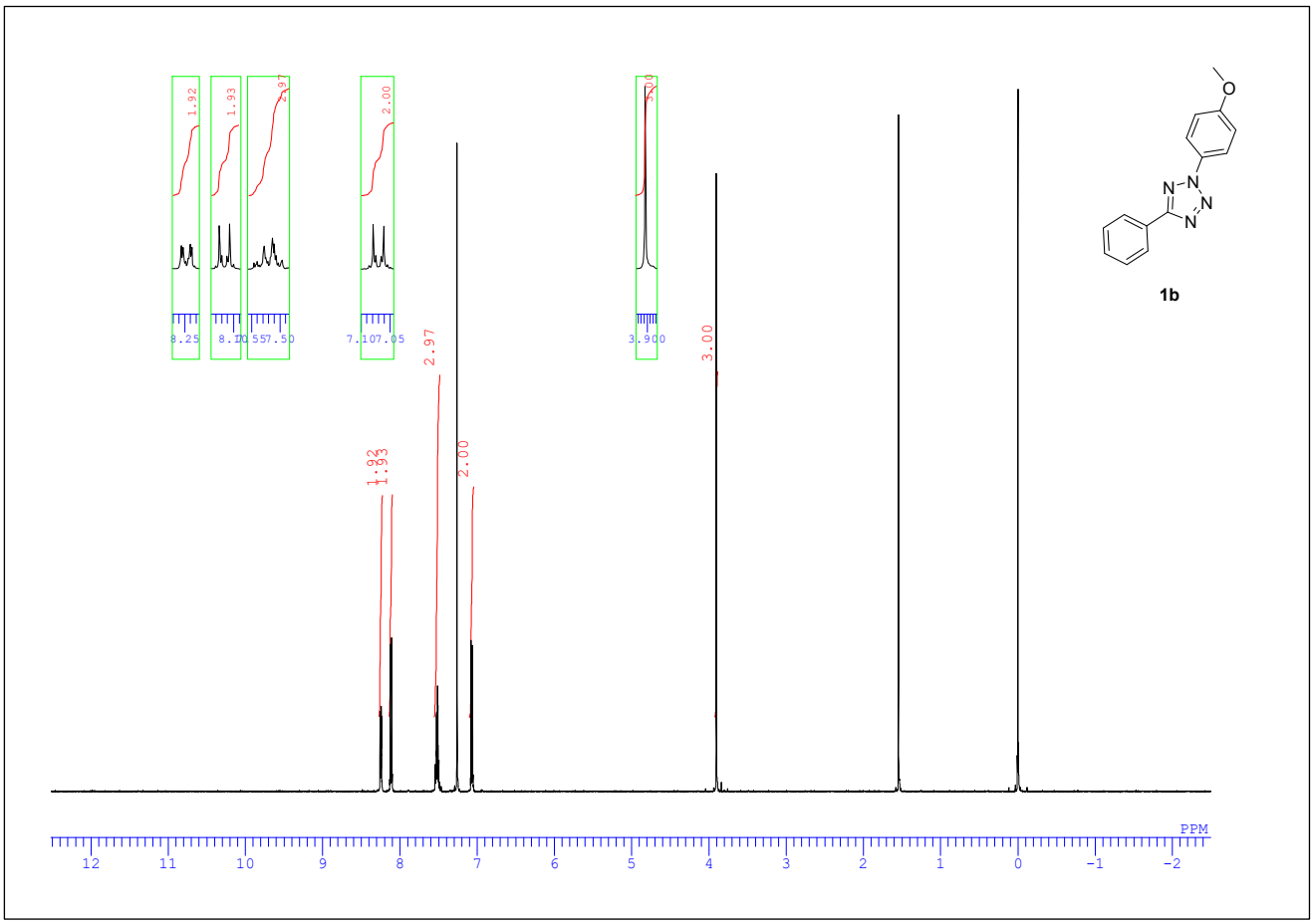
^{1}H NMR spectrum for compound **S2**



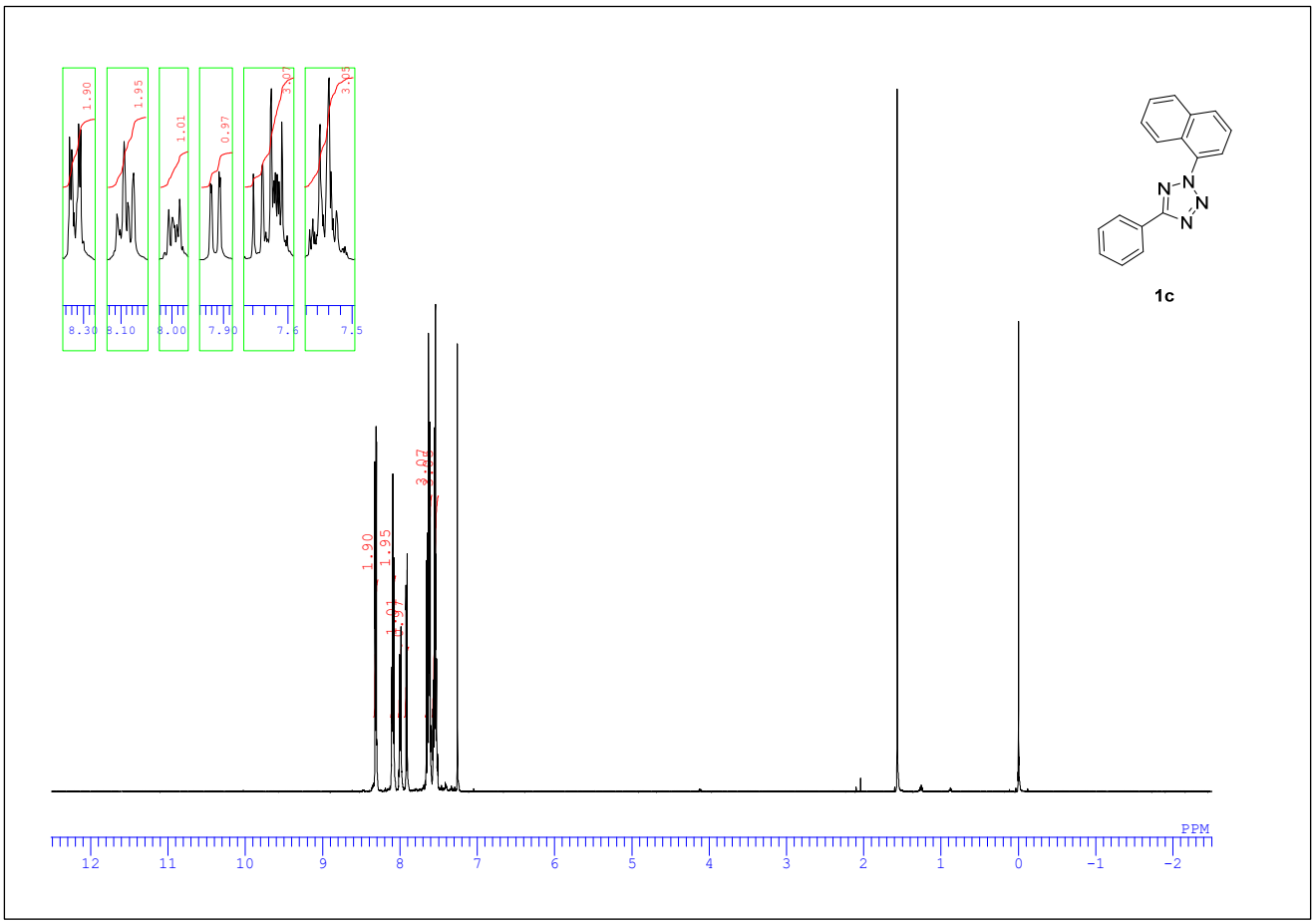
^{1}H NMR spectrum for compound **1a**



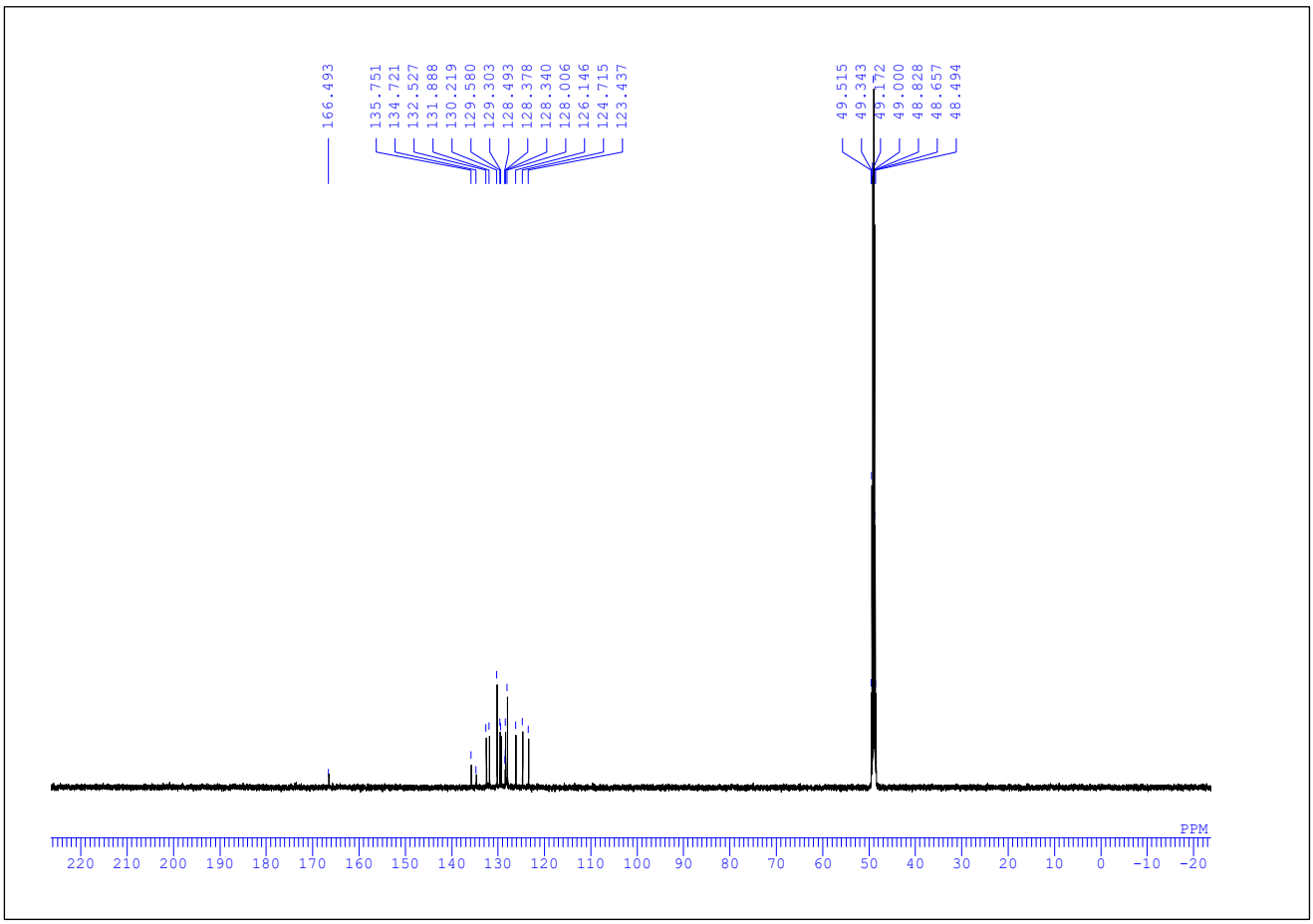
^{1}H NMR spectrum for compound **1b**



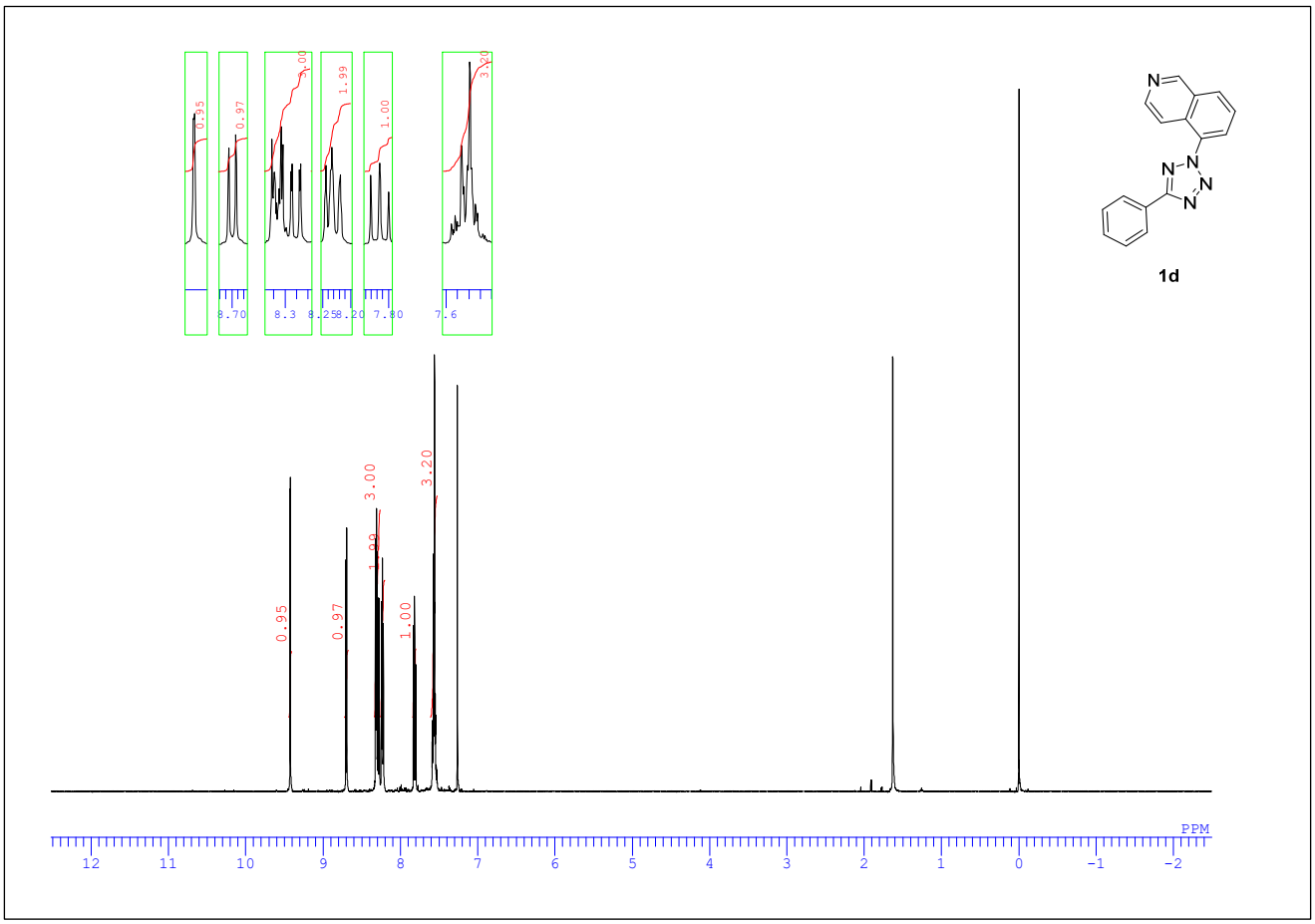
^{1}H NMR spectrum for compound **1c**



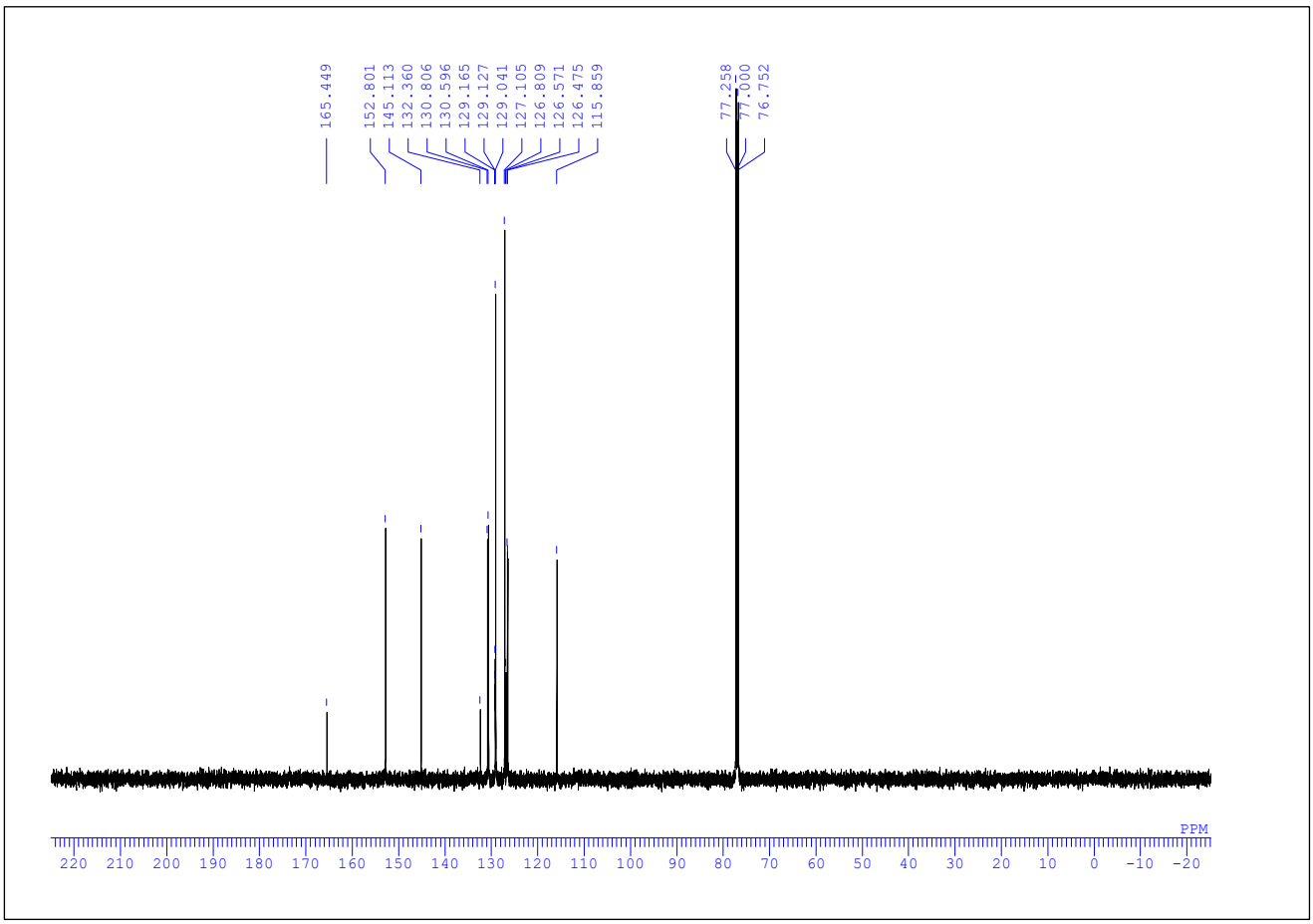
^{13}C NMR spectrum for compound **1c**



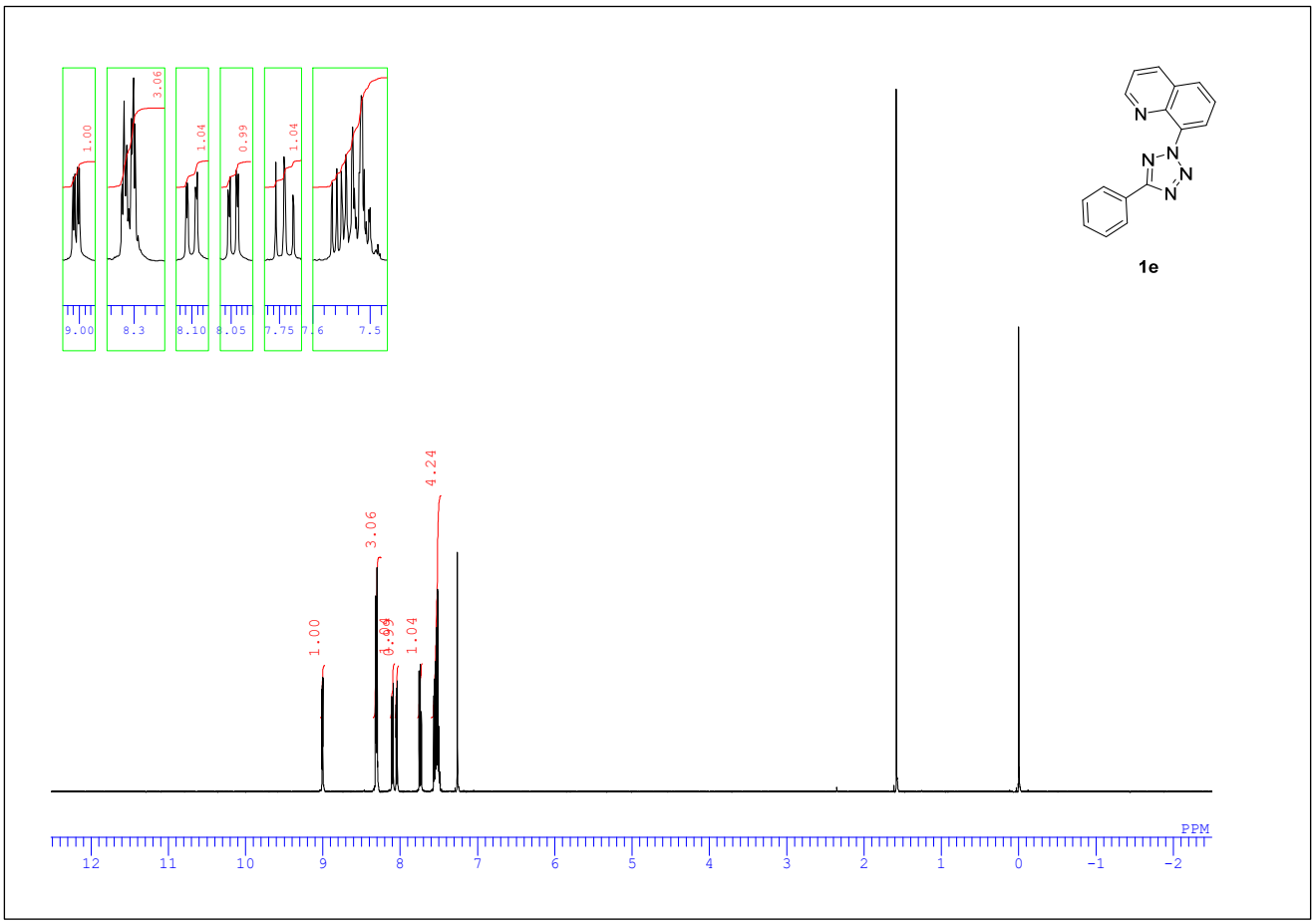
^{1}H NMR spectrum for compound **1d**



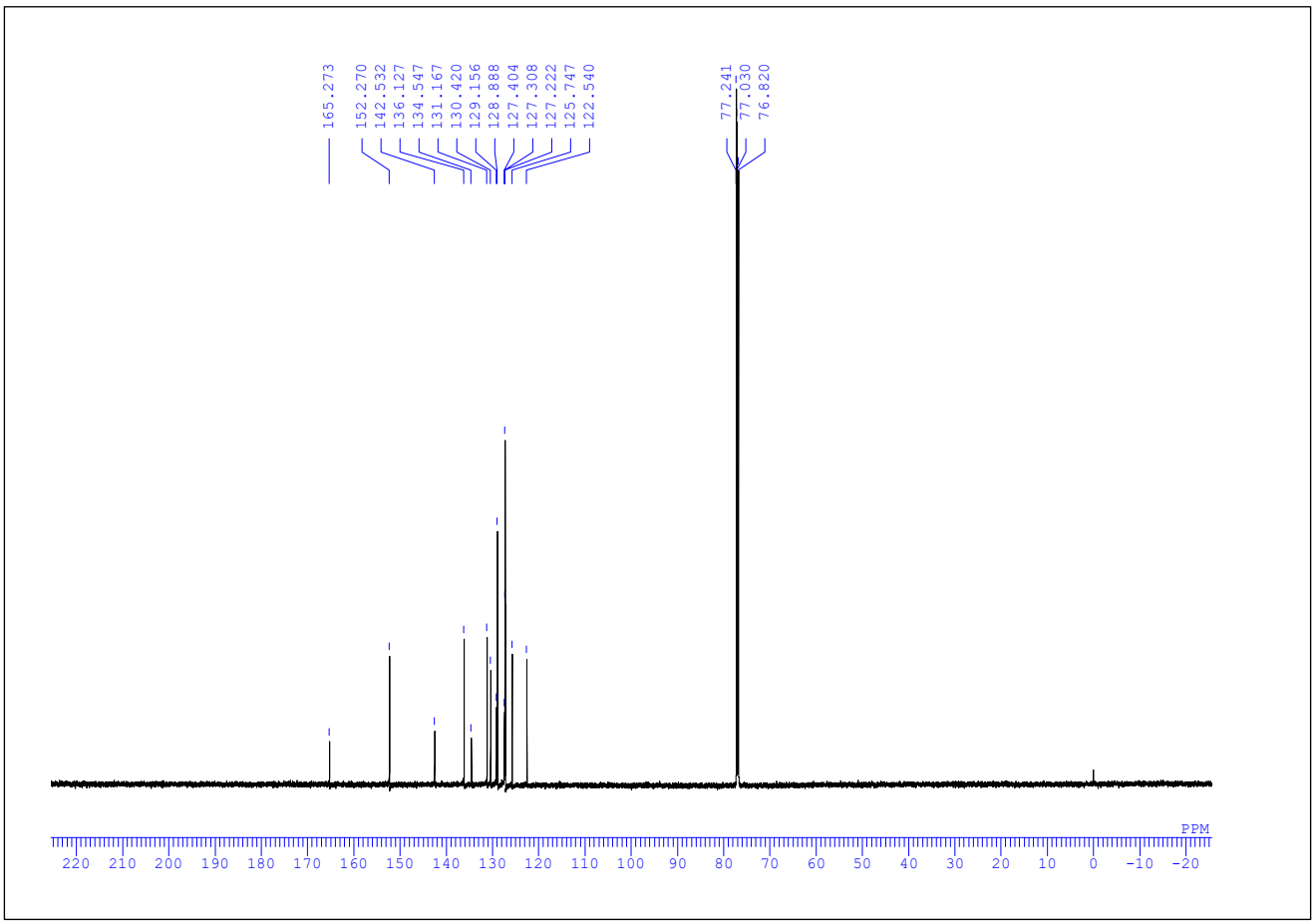
^{13}C NMR spectrum for compound **1d**



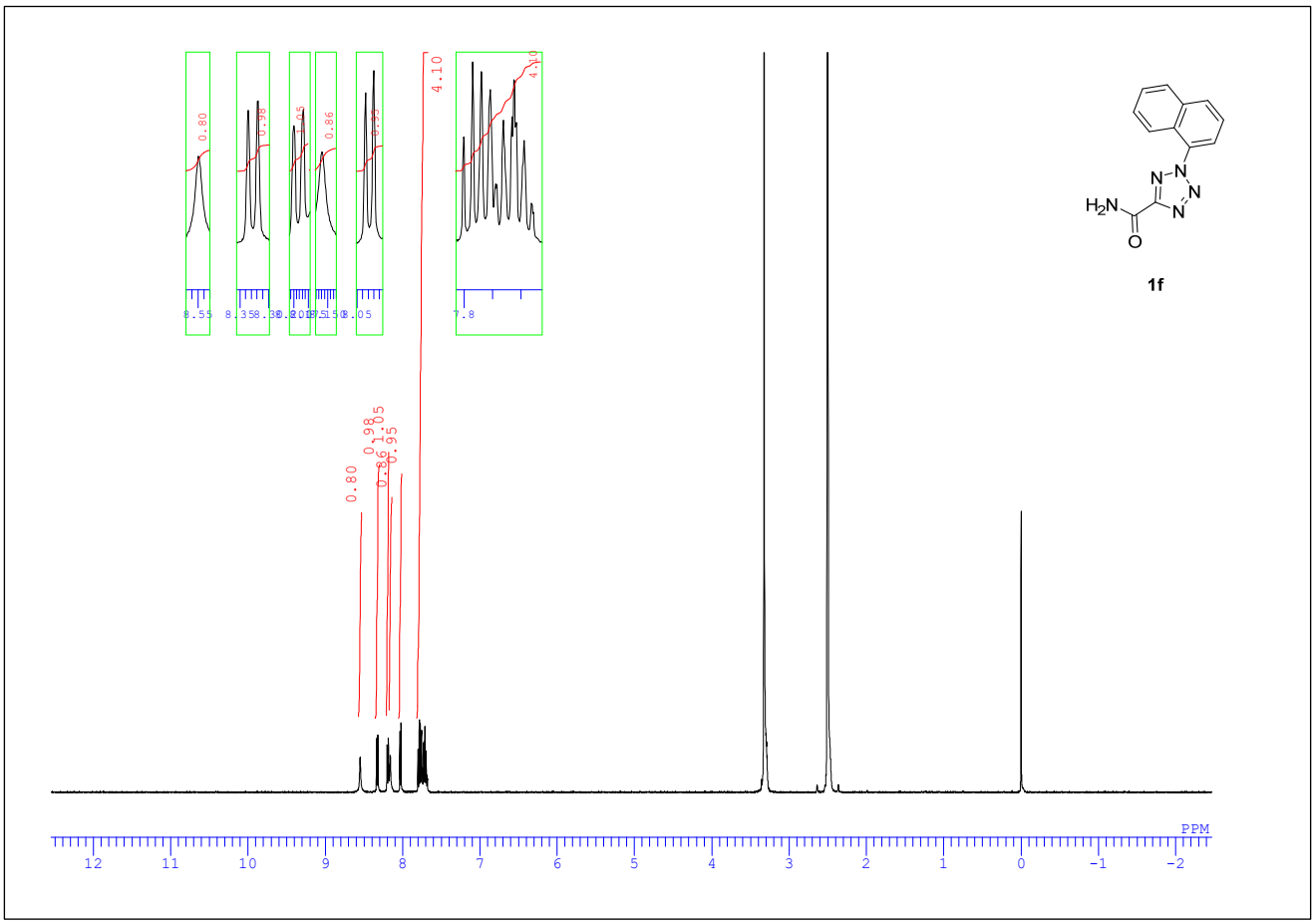
^{1}H NMR spectrum for compound **1e**



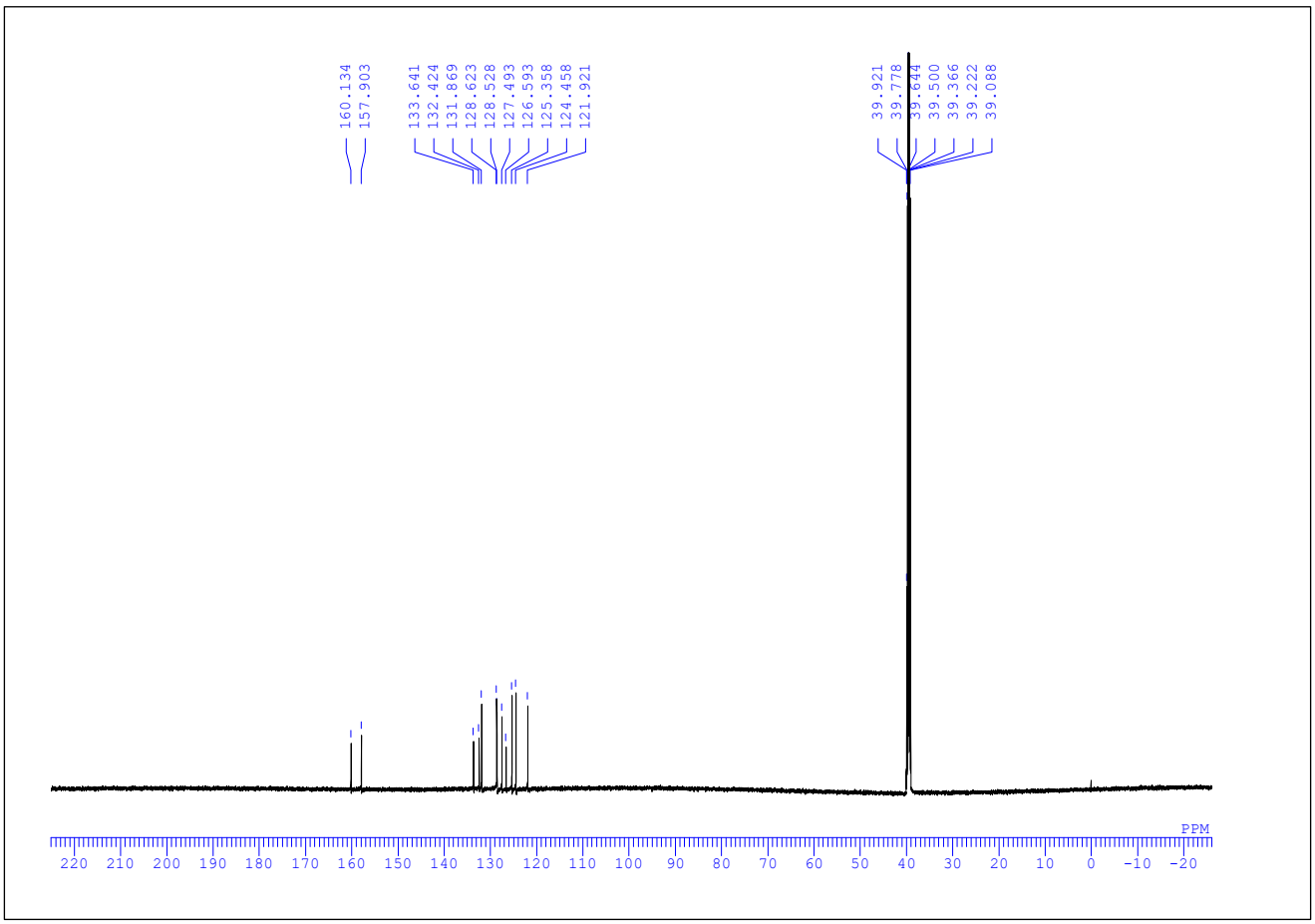
^{13}C NMR spectrum for compound **1e**



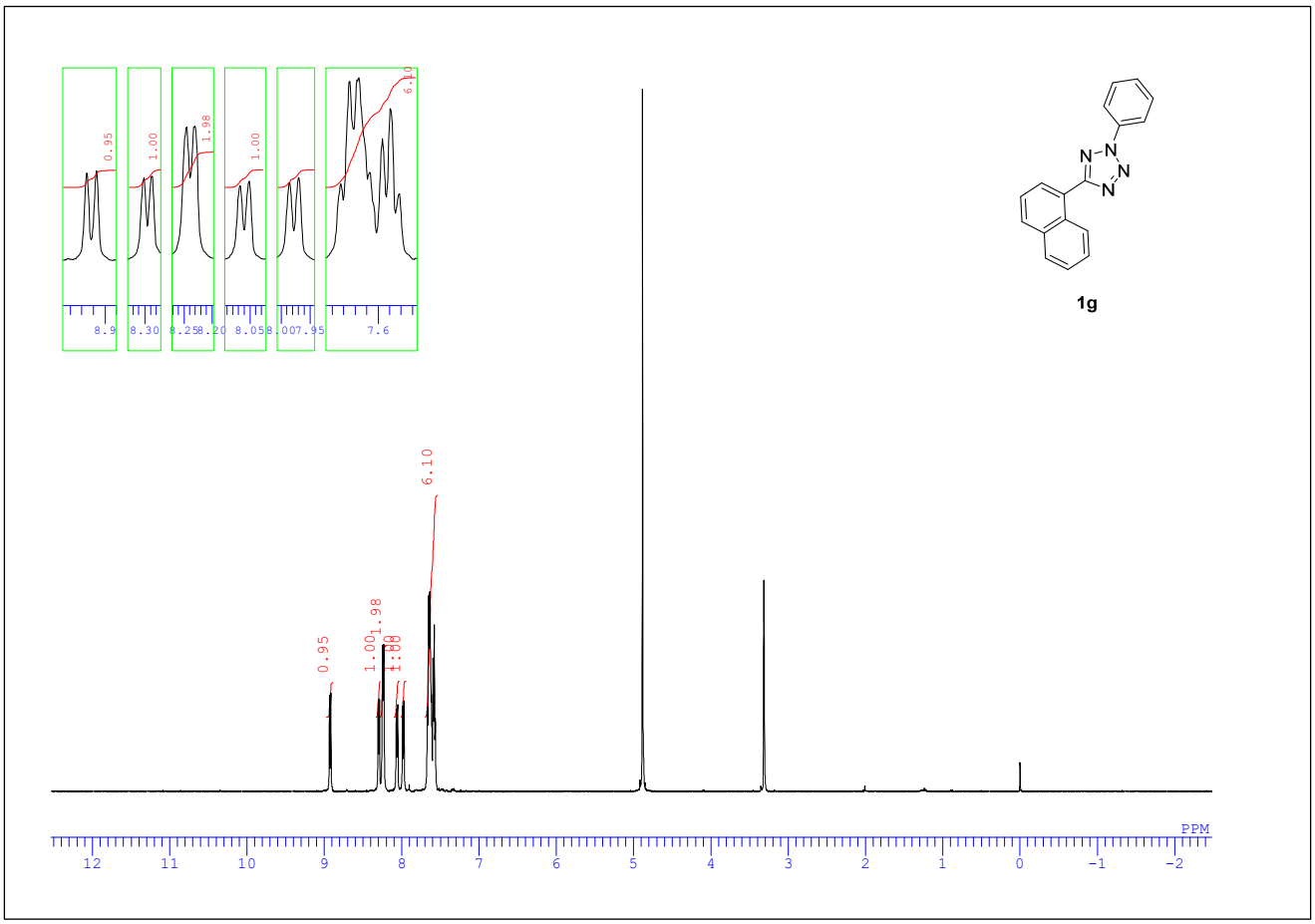
^{1}H NMR spectrum for compound **1f**



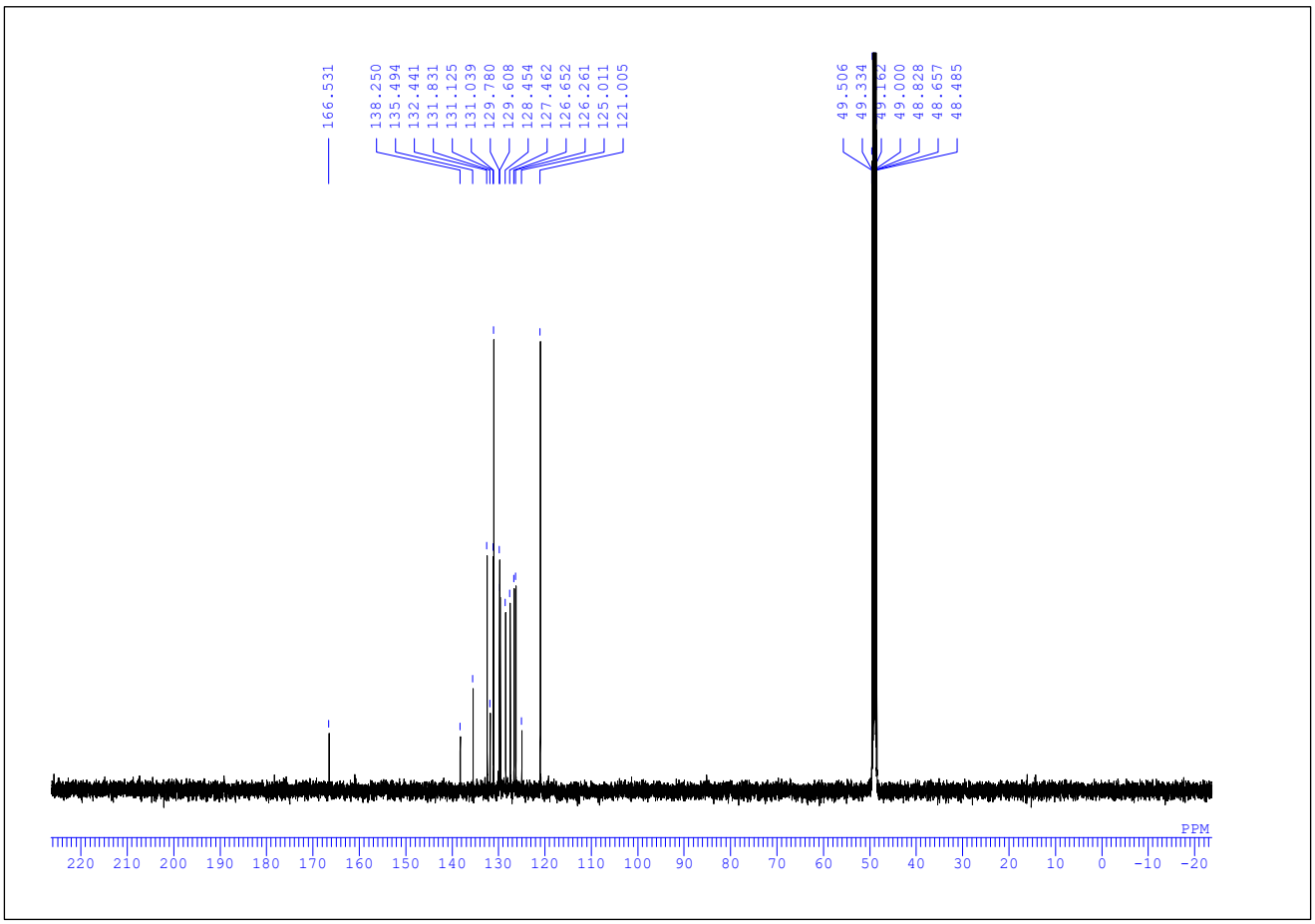
^{13}C NMR spectrum for compound **1f**



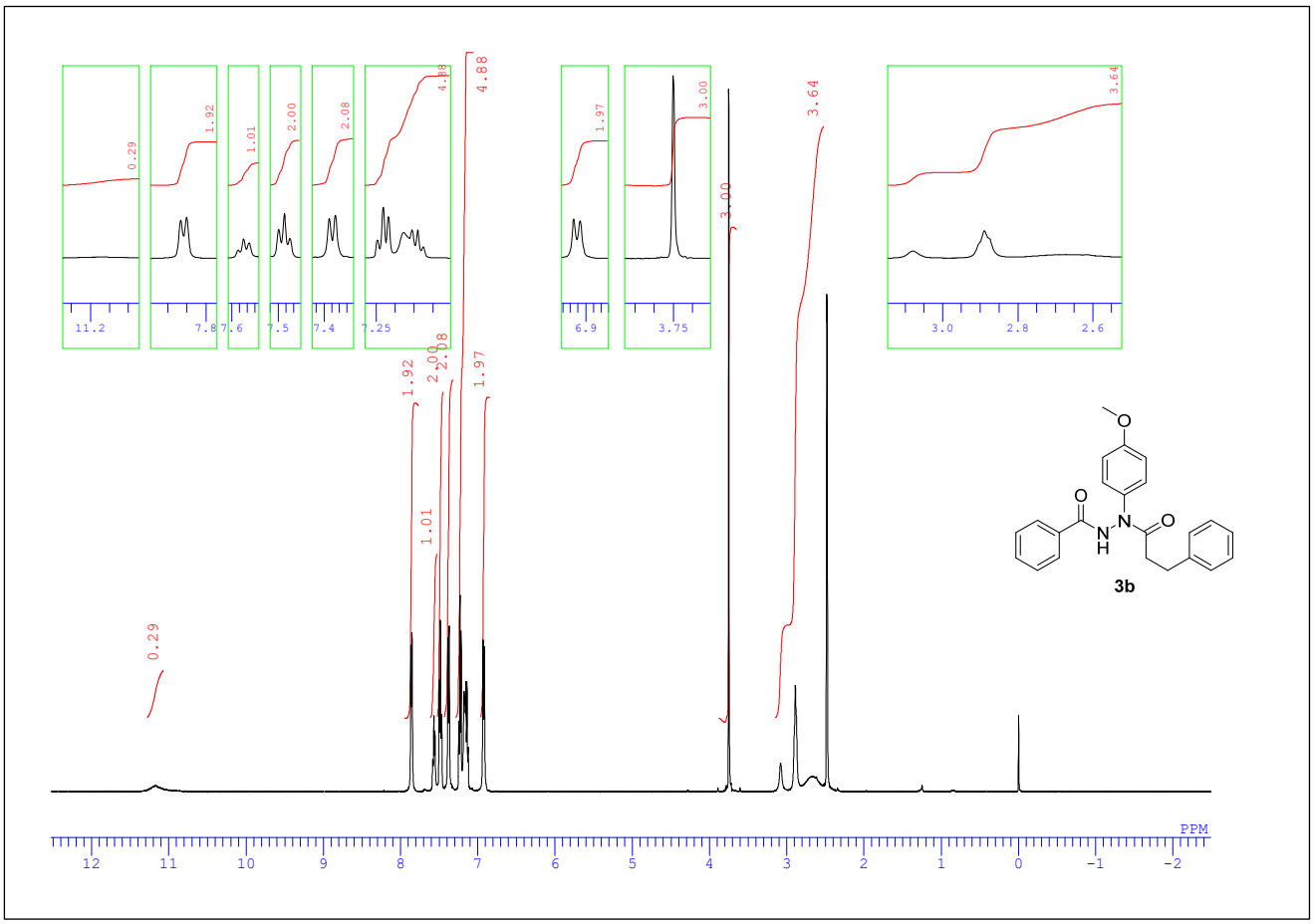
^{1}H NMR spectrum for compound **1g**



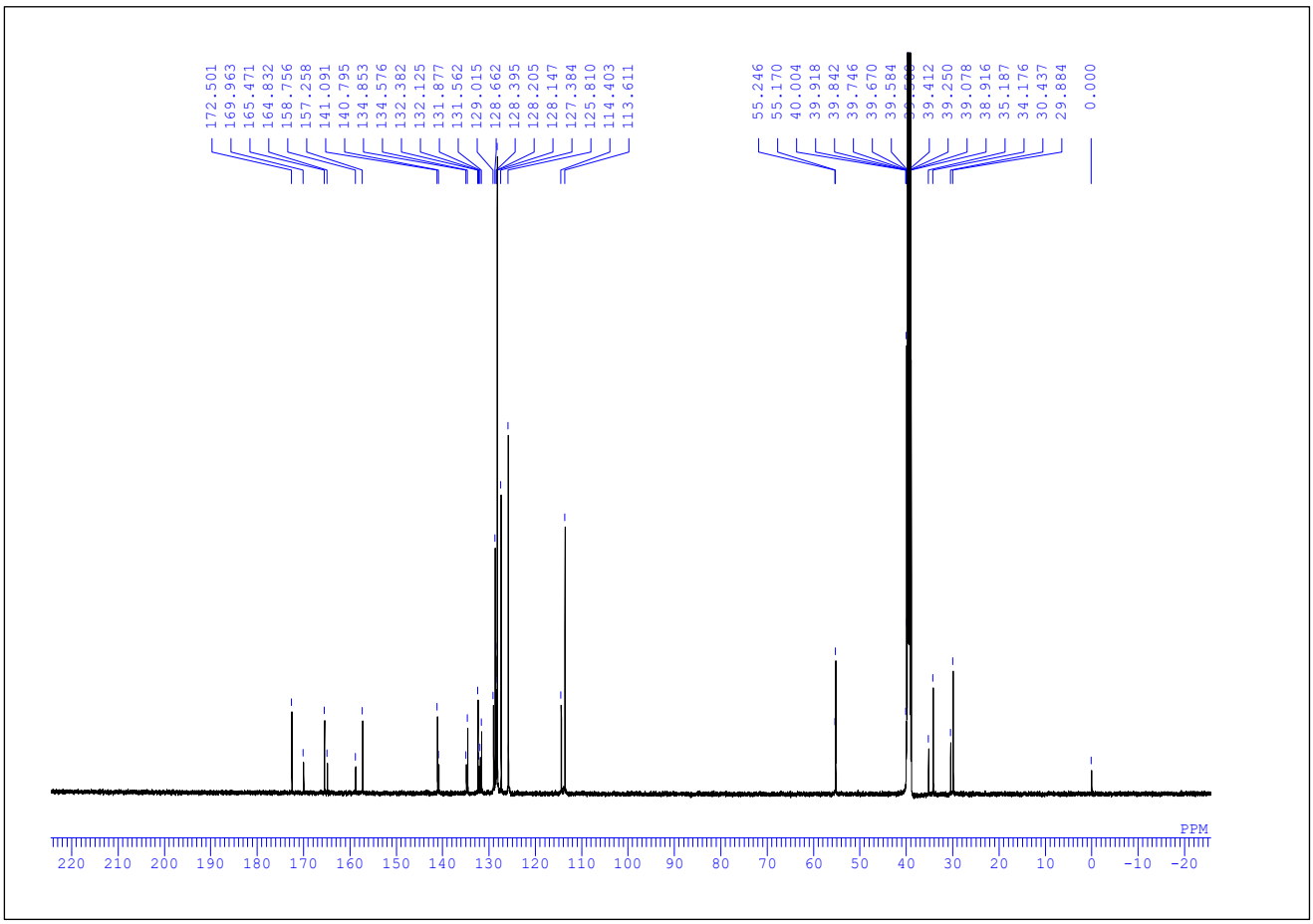
^{13}C NMR spectrum for compound **1g**



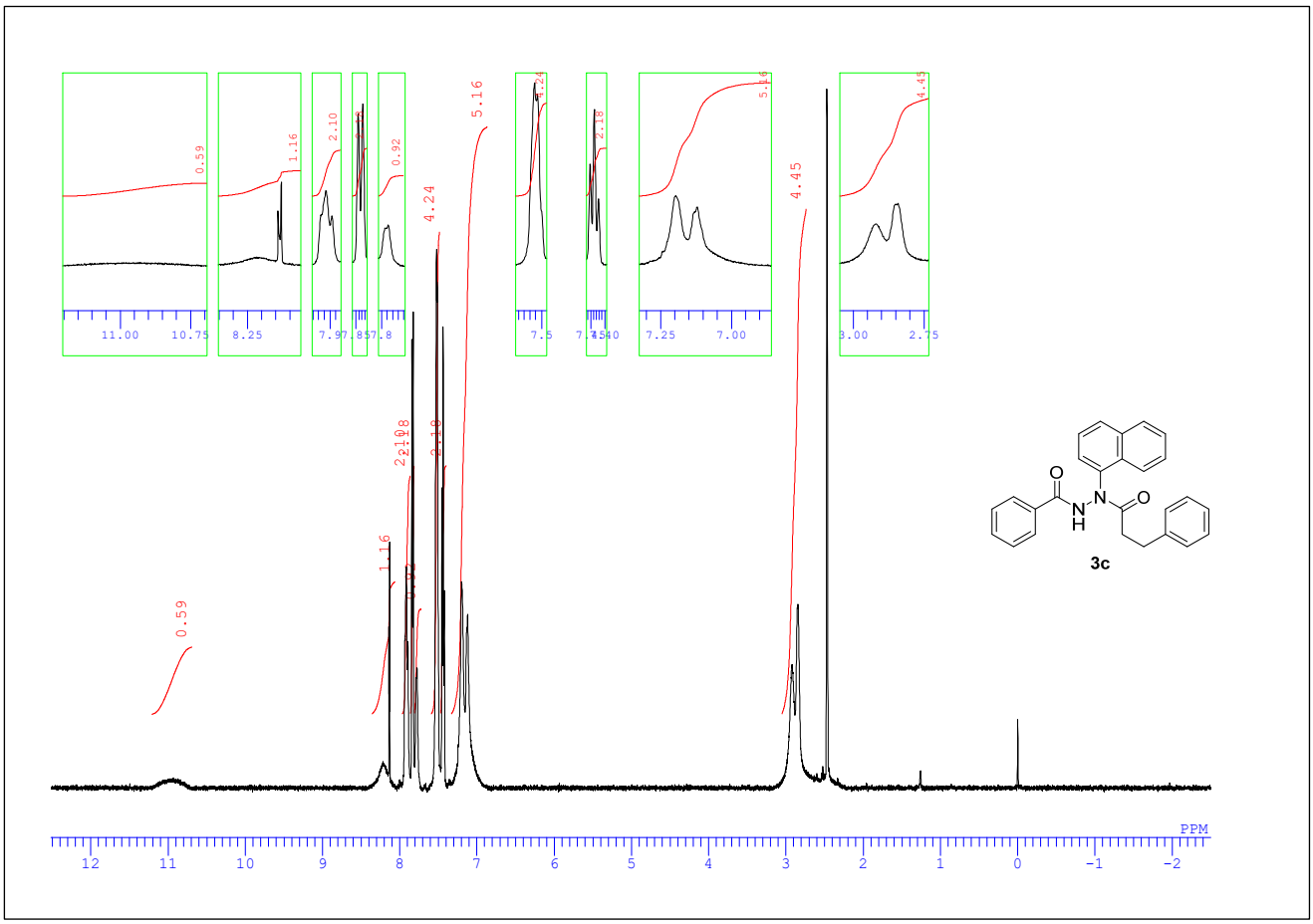
^{1}H NMR spectrum for compound **3b**



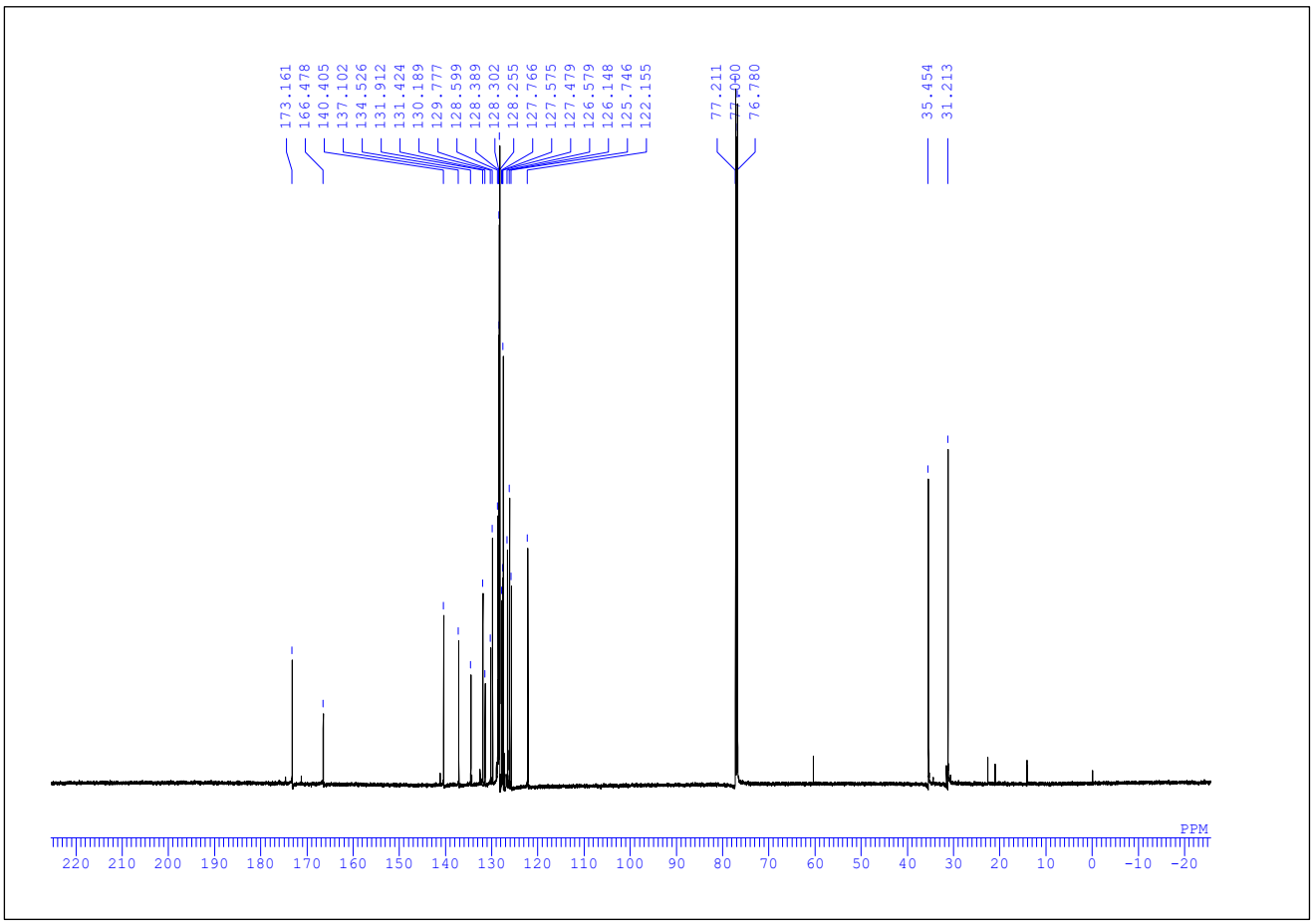
^{13}C NMR spectrum for compound **3b**



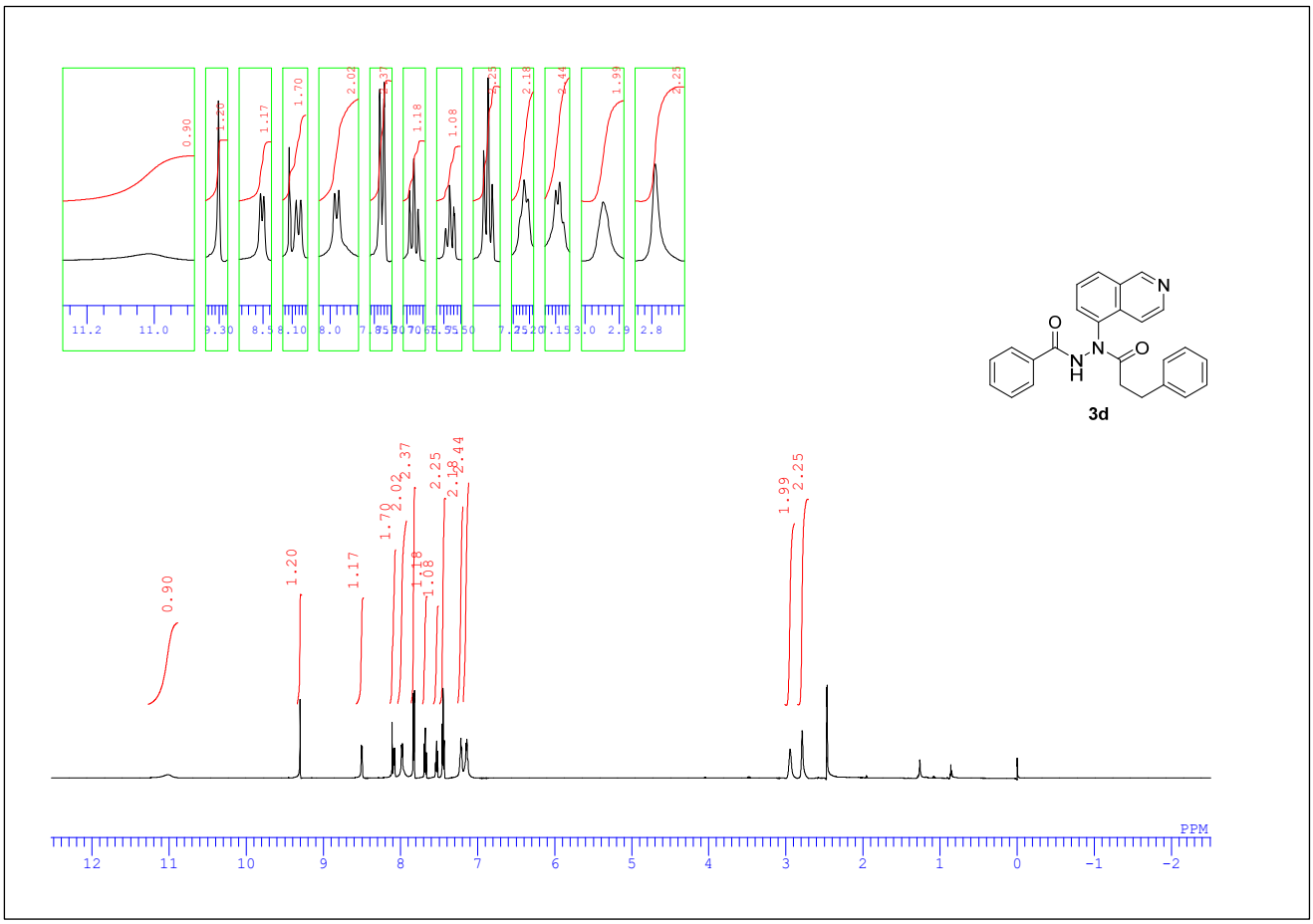
^{1}H NMR spectrum for compound **3c**



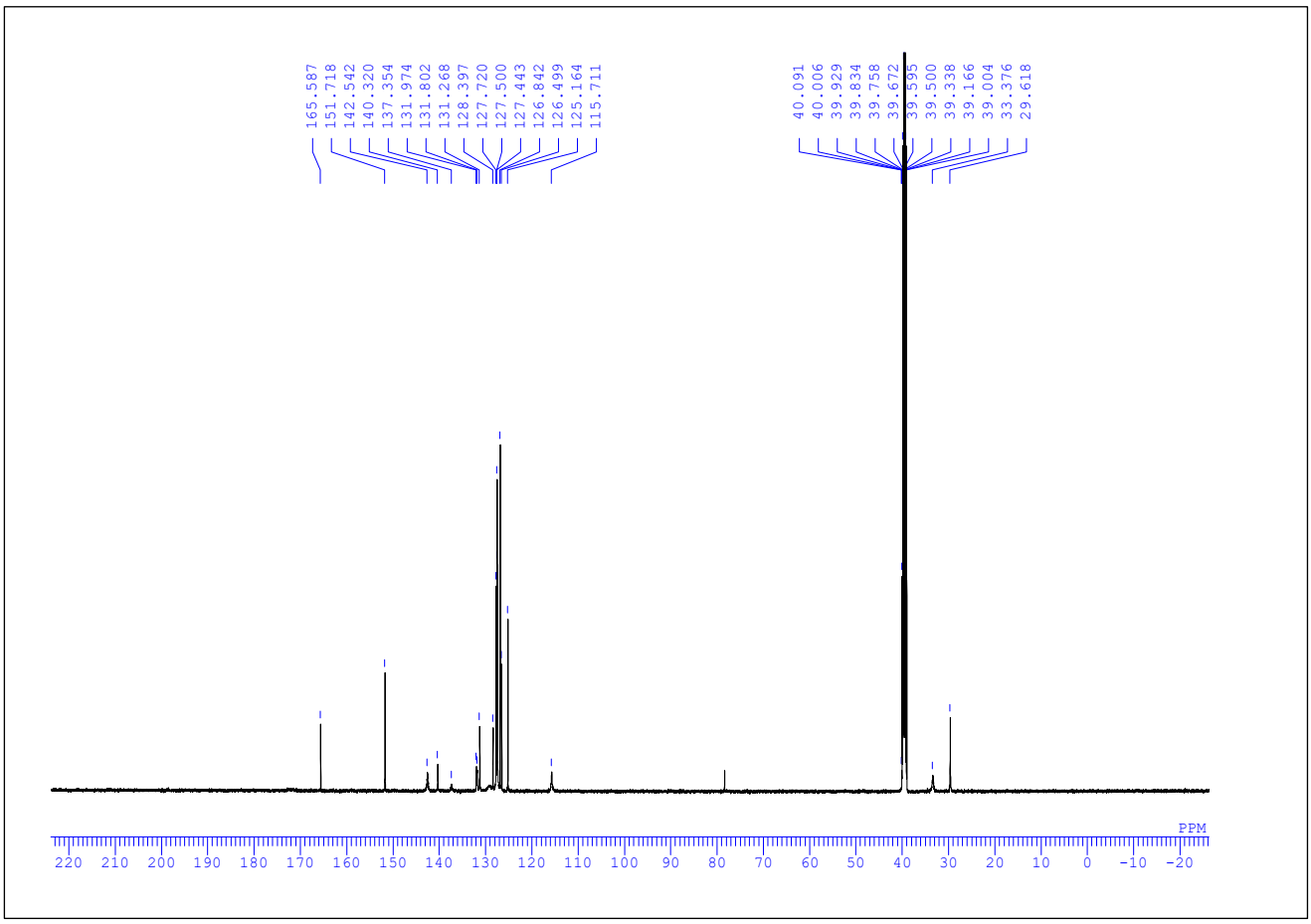
^{13}C NMR spectrum for compound **3c**



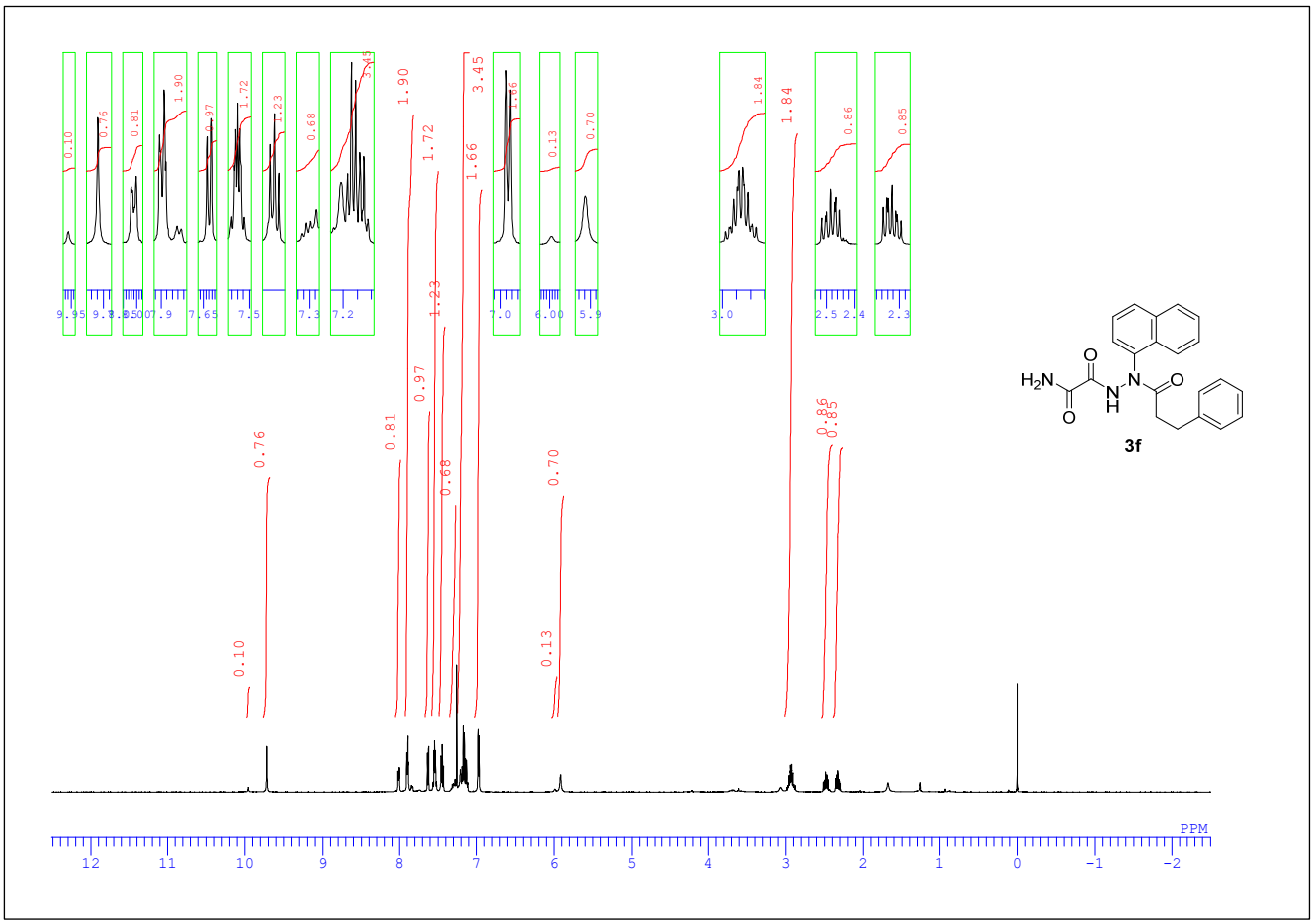
^{1}H NMR spectrum for compound **3d**



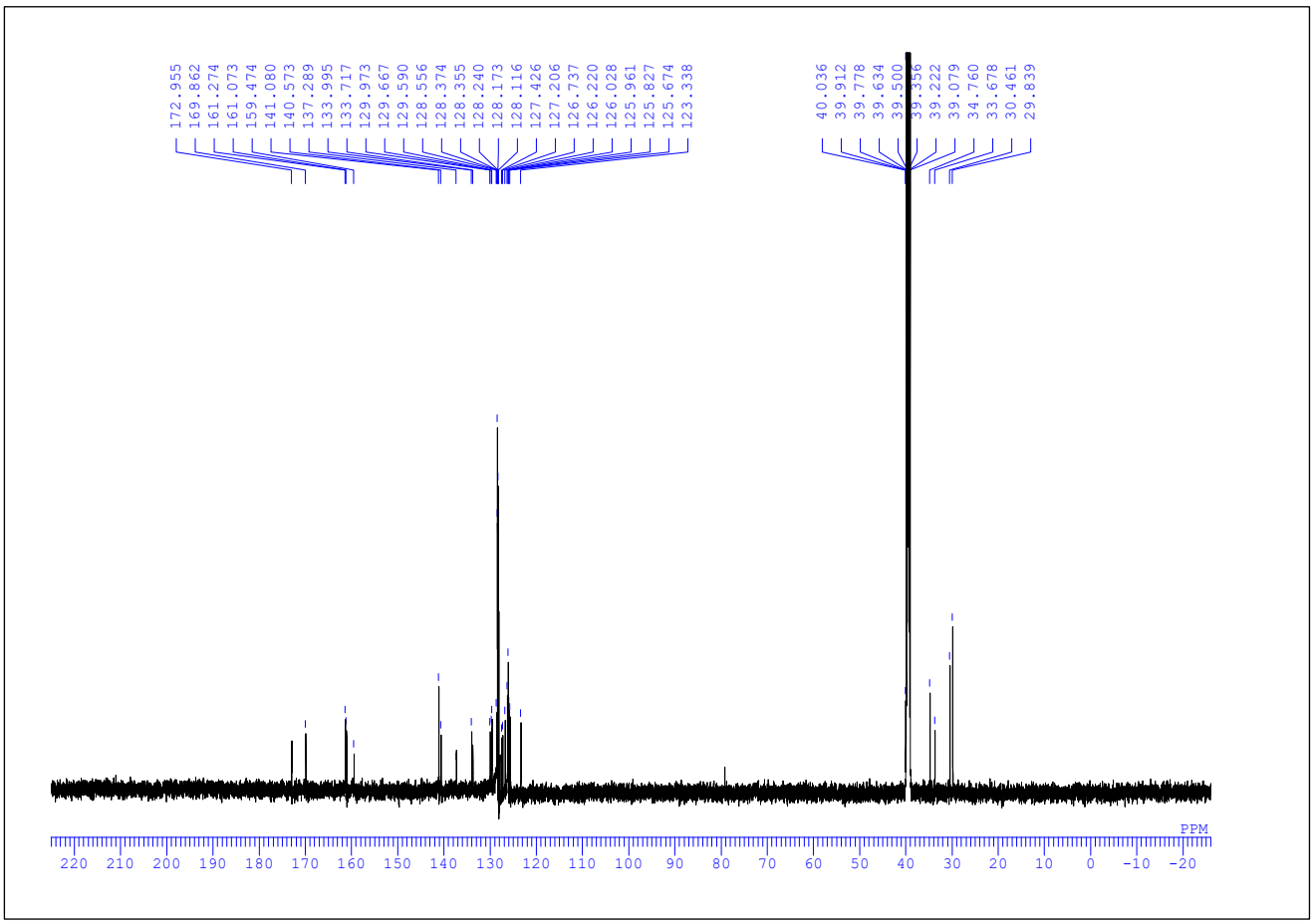
^{13}C NMR spectrum for compound **3d**



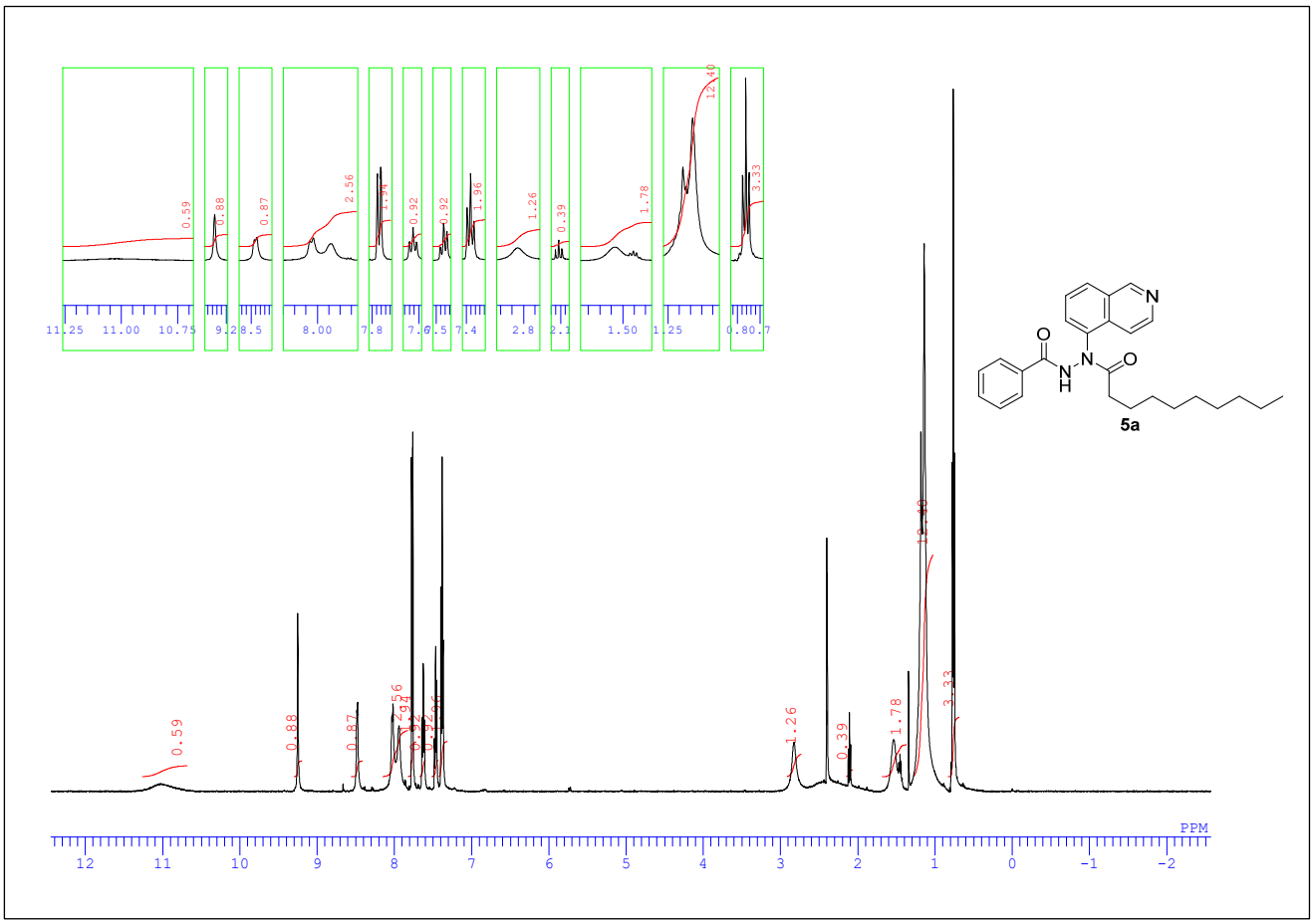
^{1}H NMR spectrum for compound **3f**



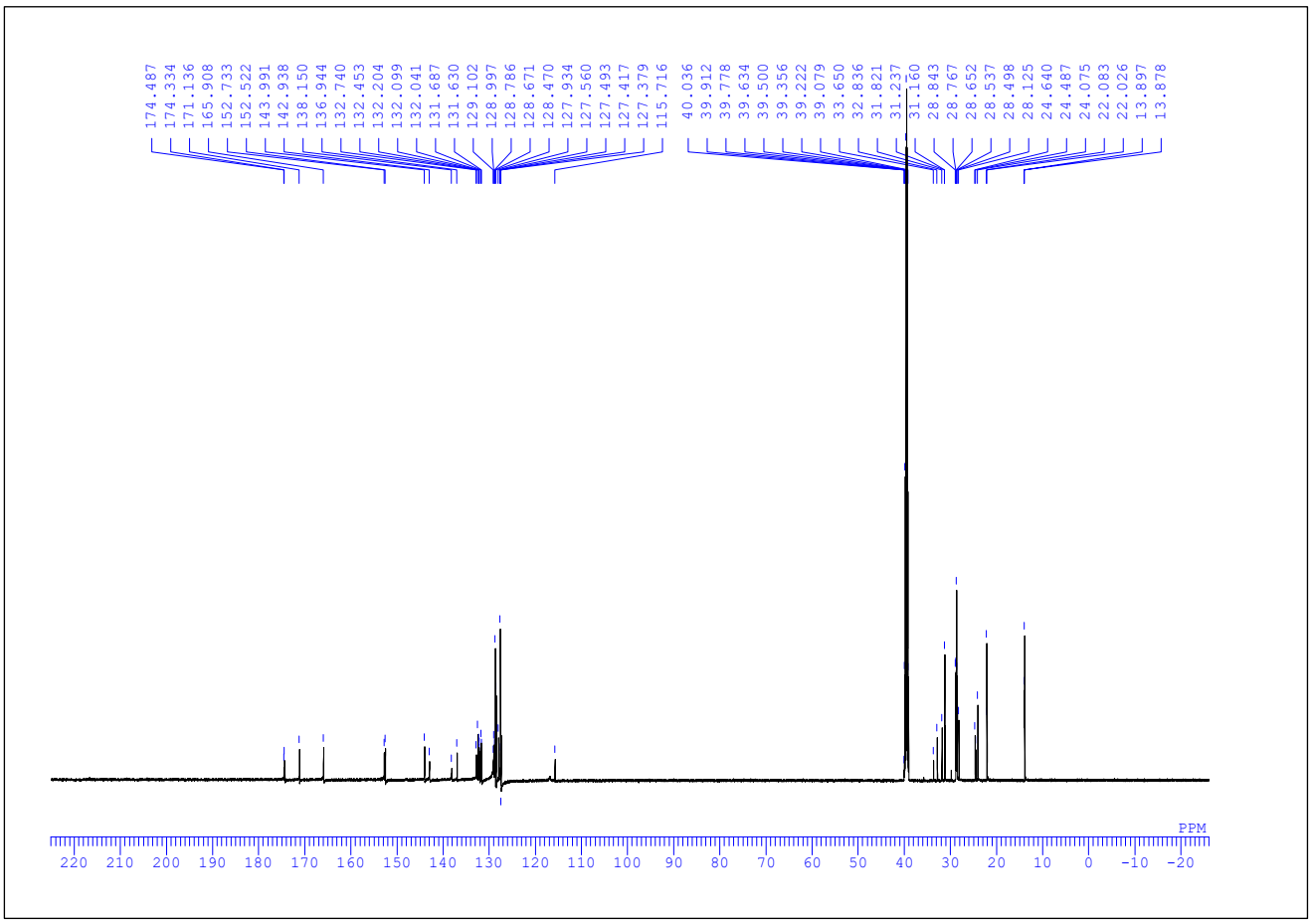
^{13}C NMR spectrum for compound **3f**



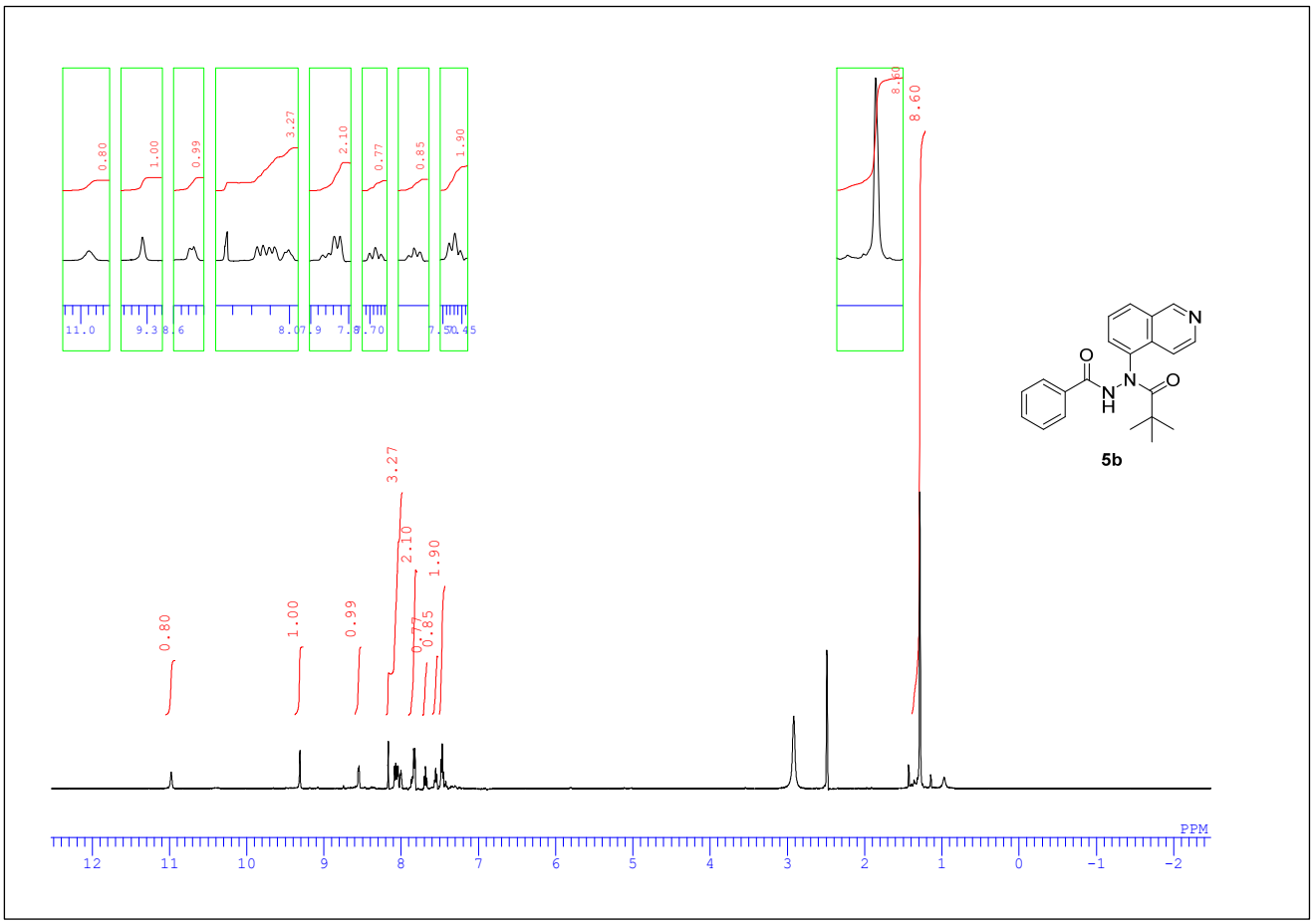
^{1}H NMR spectrum for compound **5a**



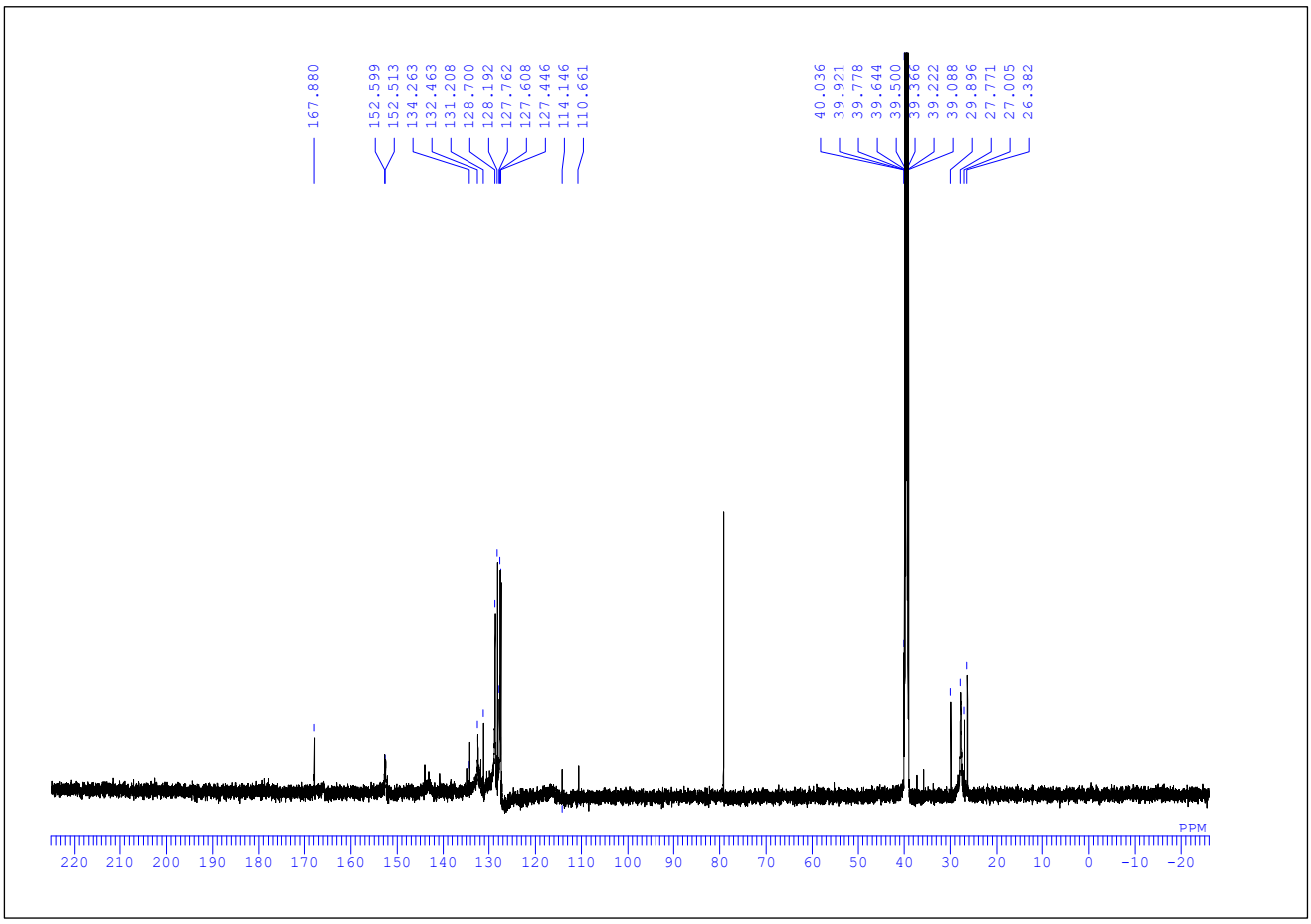
^{13}C NMR spectrum for compound **5a**



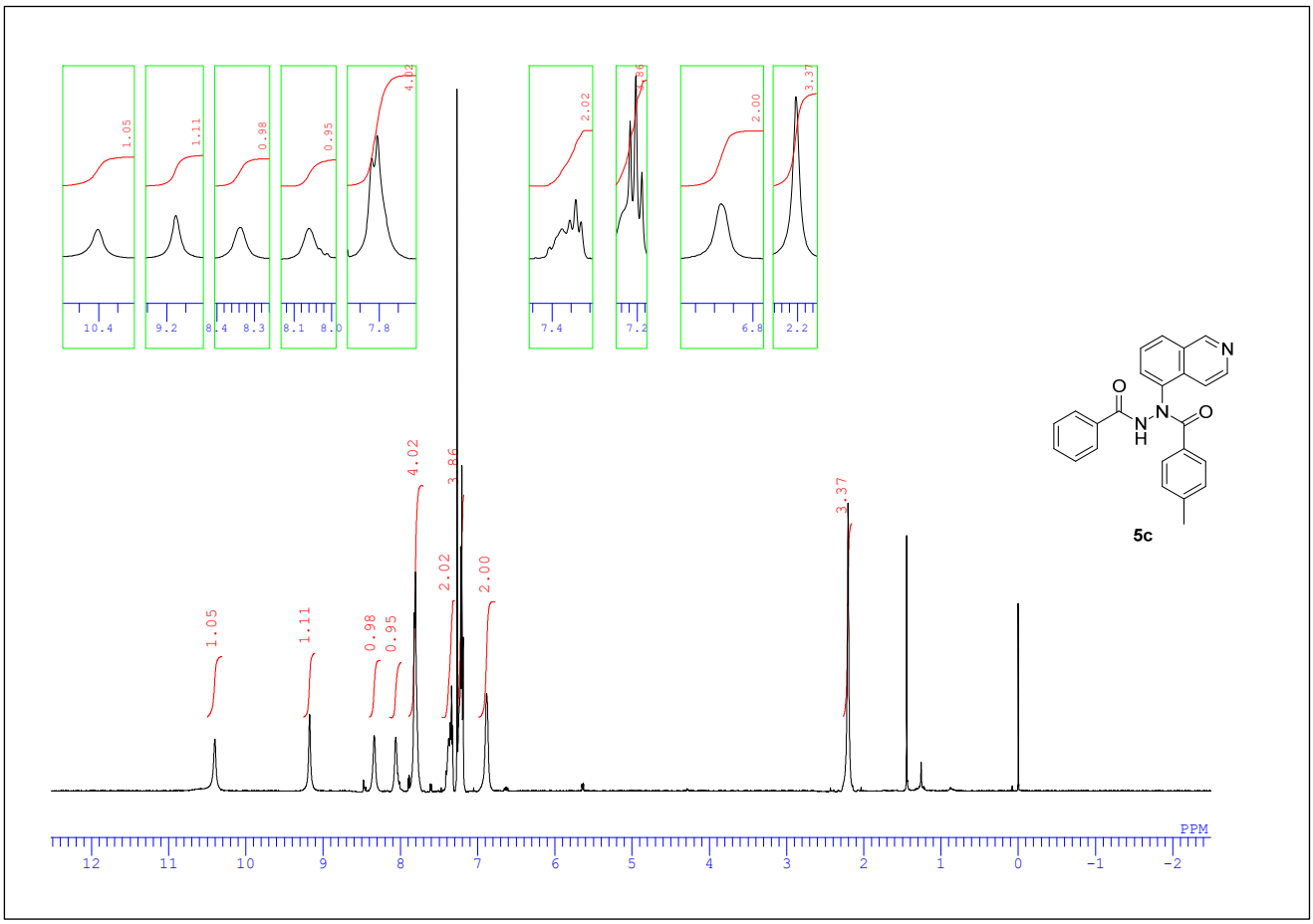
^{1}H NMR spectrum for compound **5b**



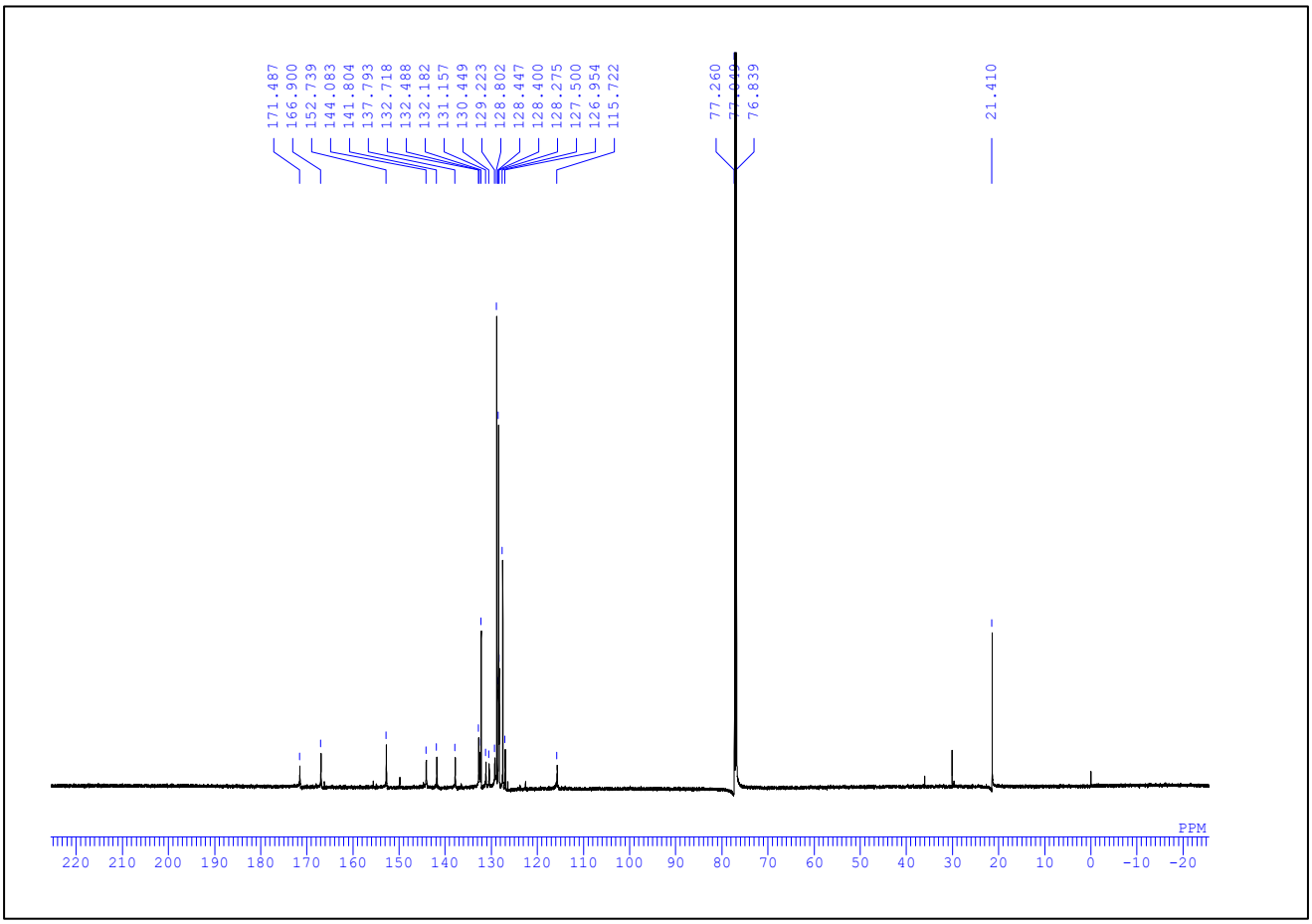
^{13}C NMR spectrum for compound **5b**



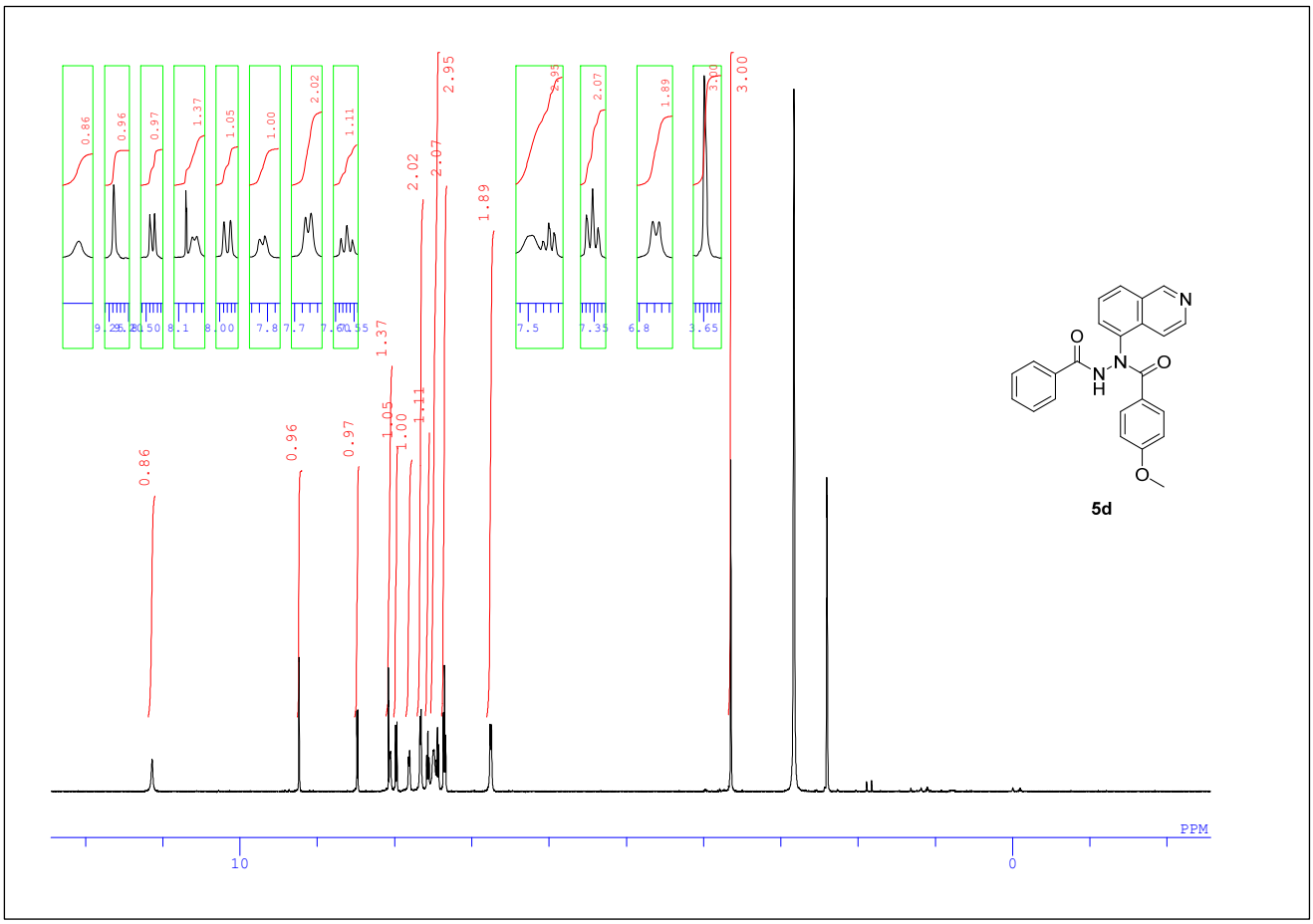
^{1}H NMR spectrum for compound **5c**



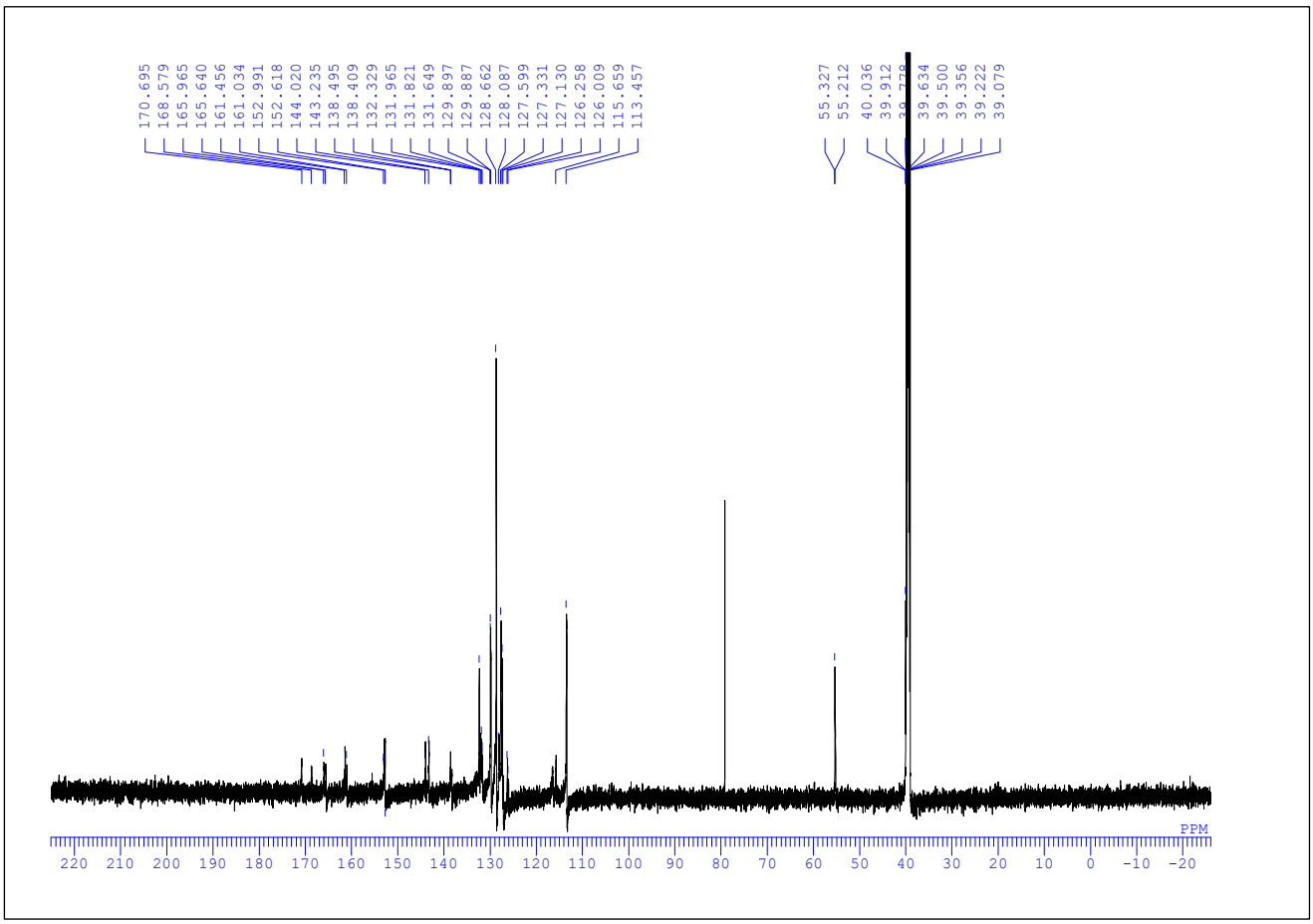
^{13}C NMR spectrum for compound **5c**



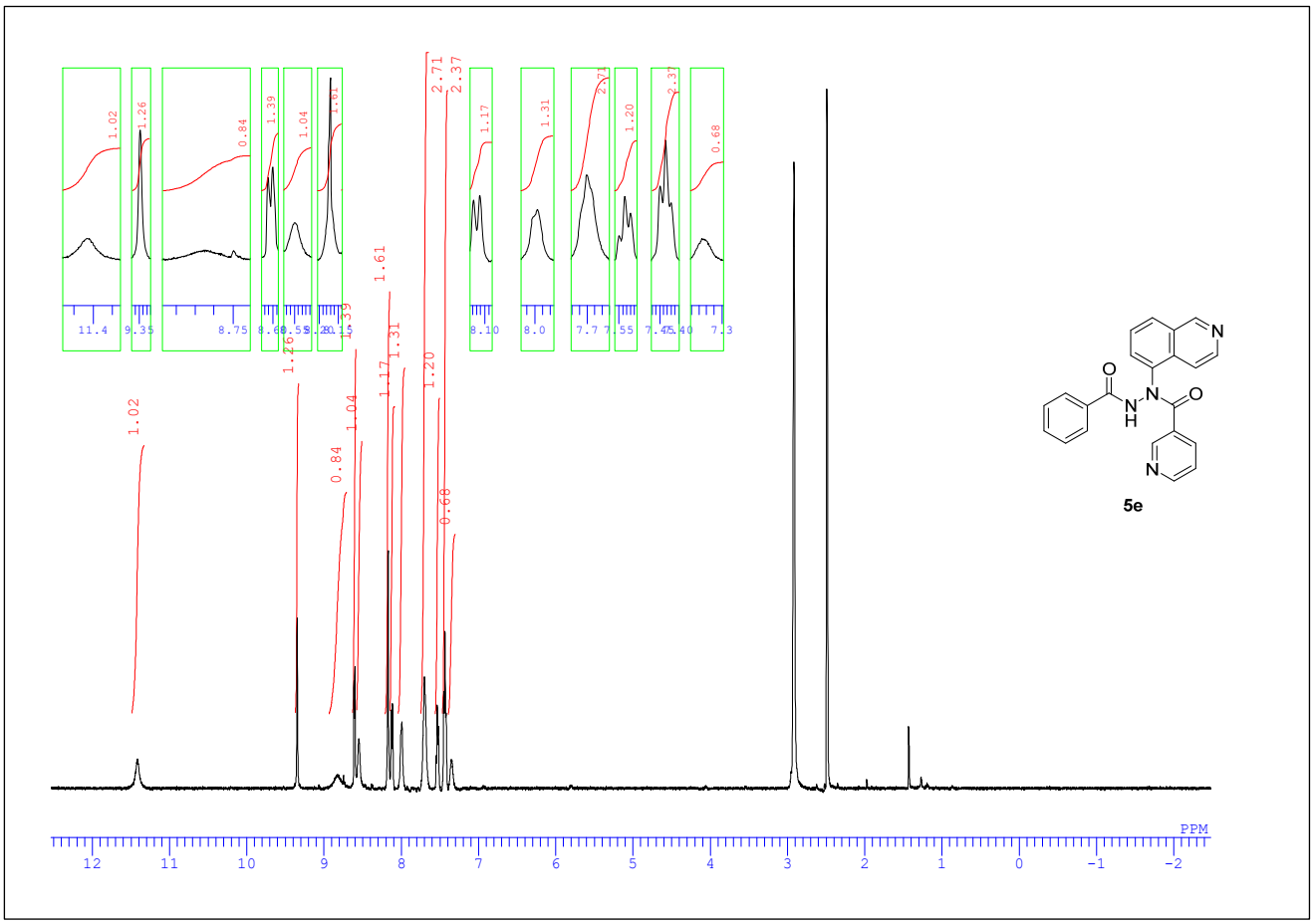
^{1}H NMR spectrum for compound **5d**



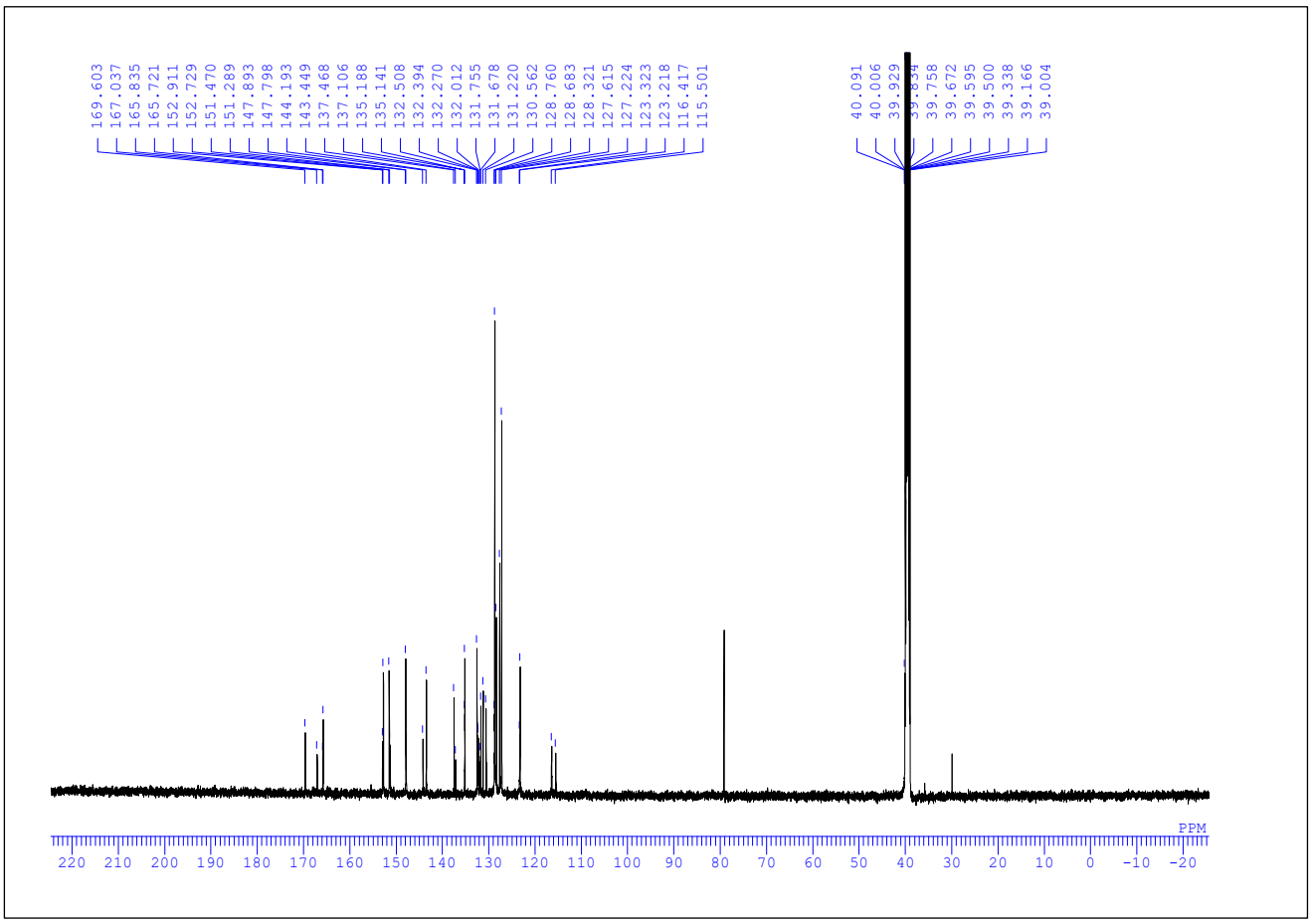
^{13}C NMR spectrum for compound **5d**



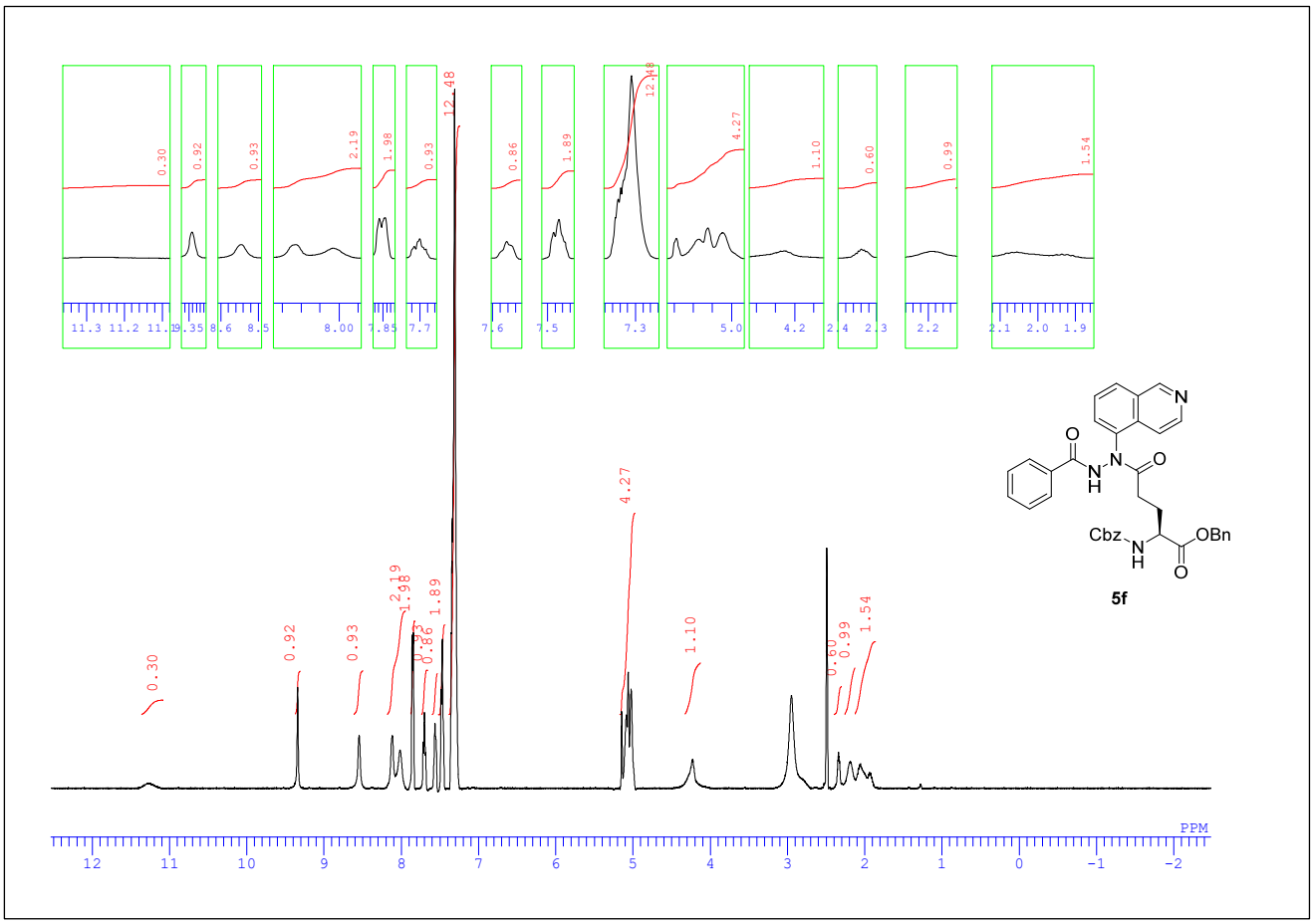
^{1}H NMR spectrum for compound **5e**



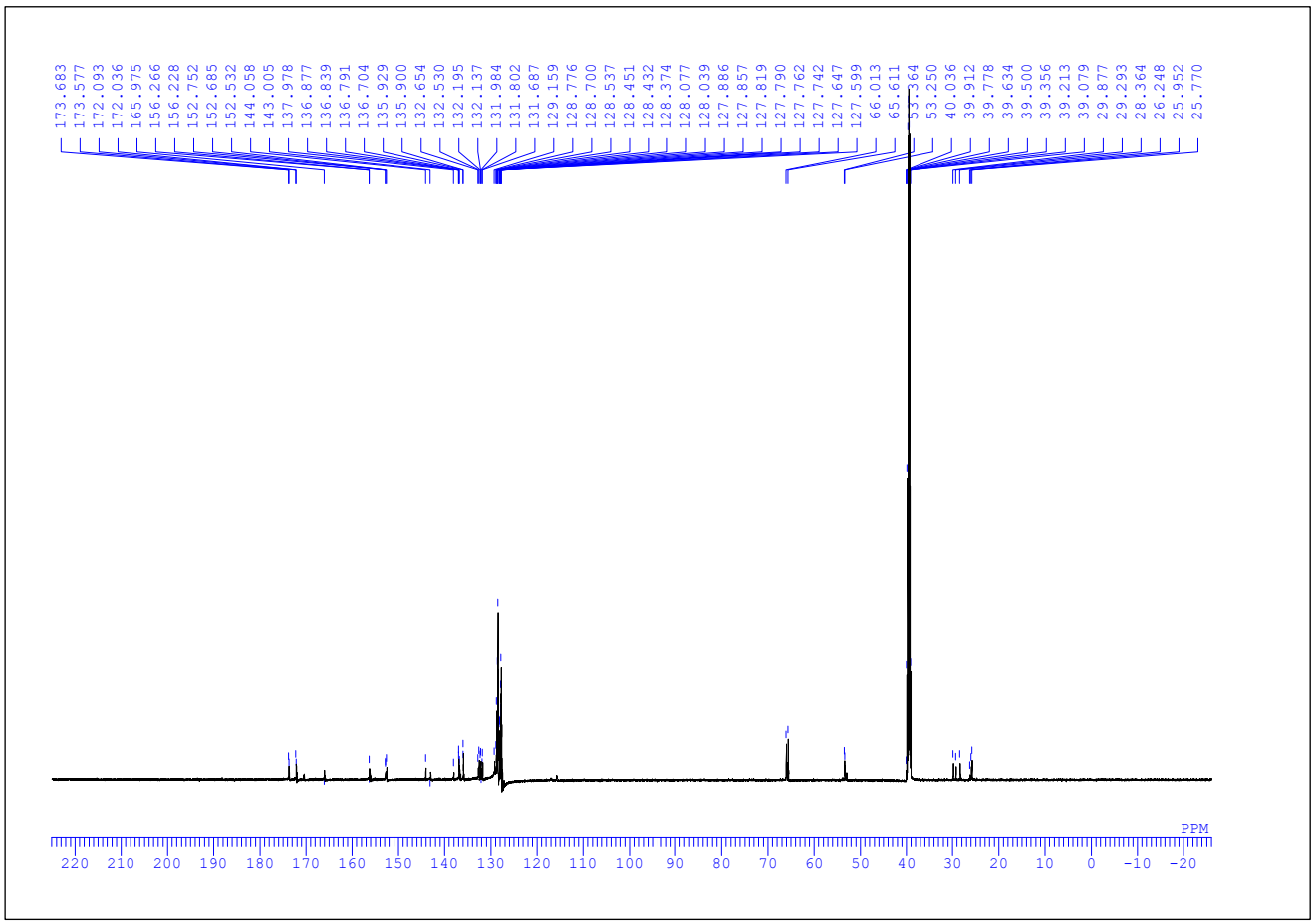
^{13}C NMR spectrum for compound **5e**



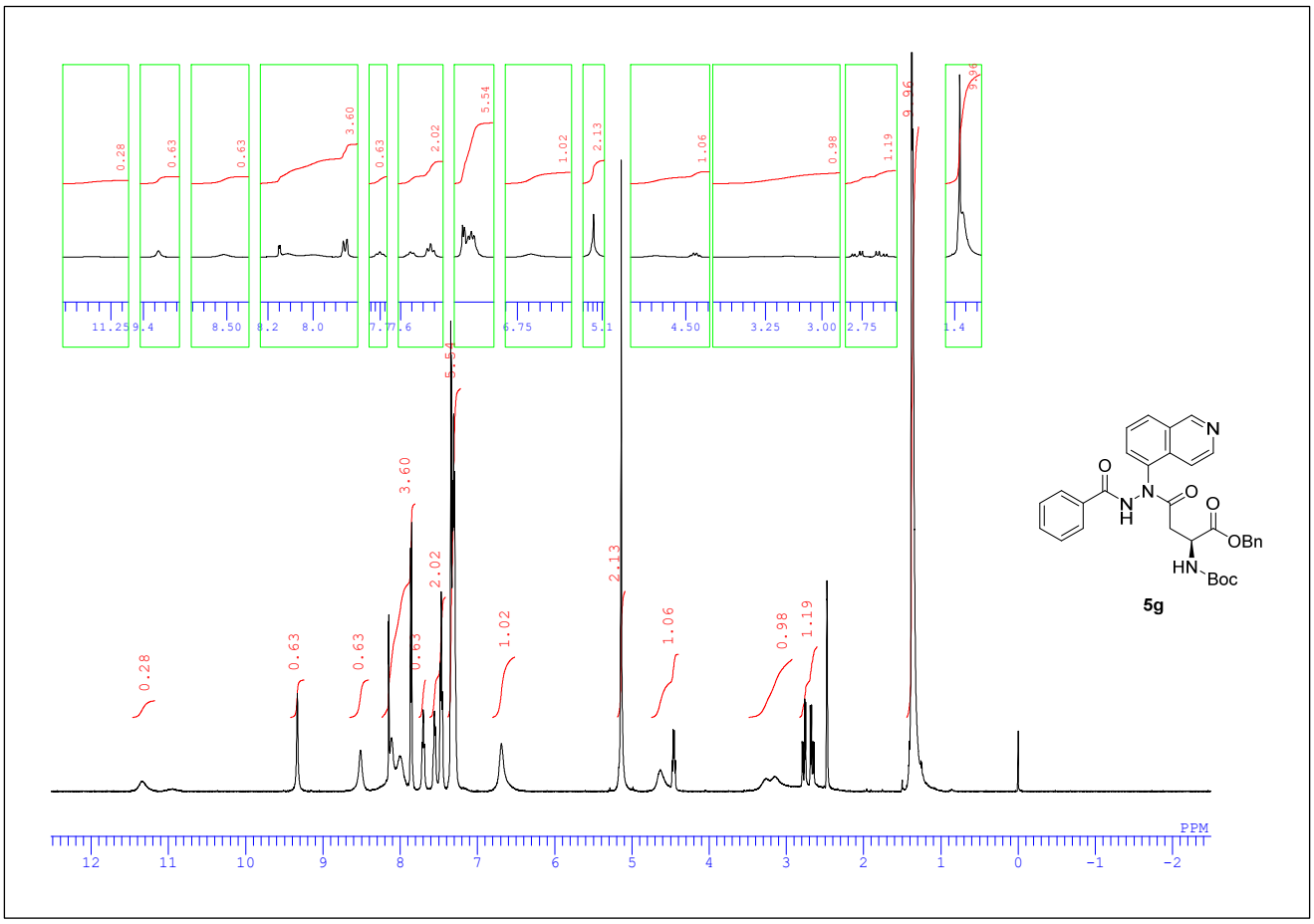
^{1}H NMR spectrum for compound **5f**



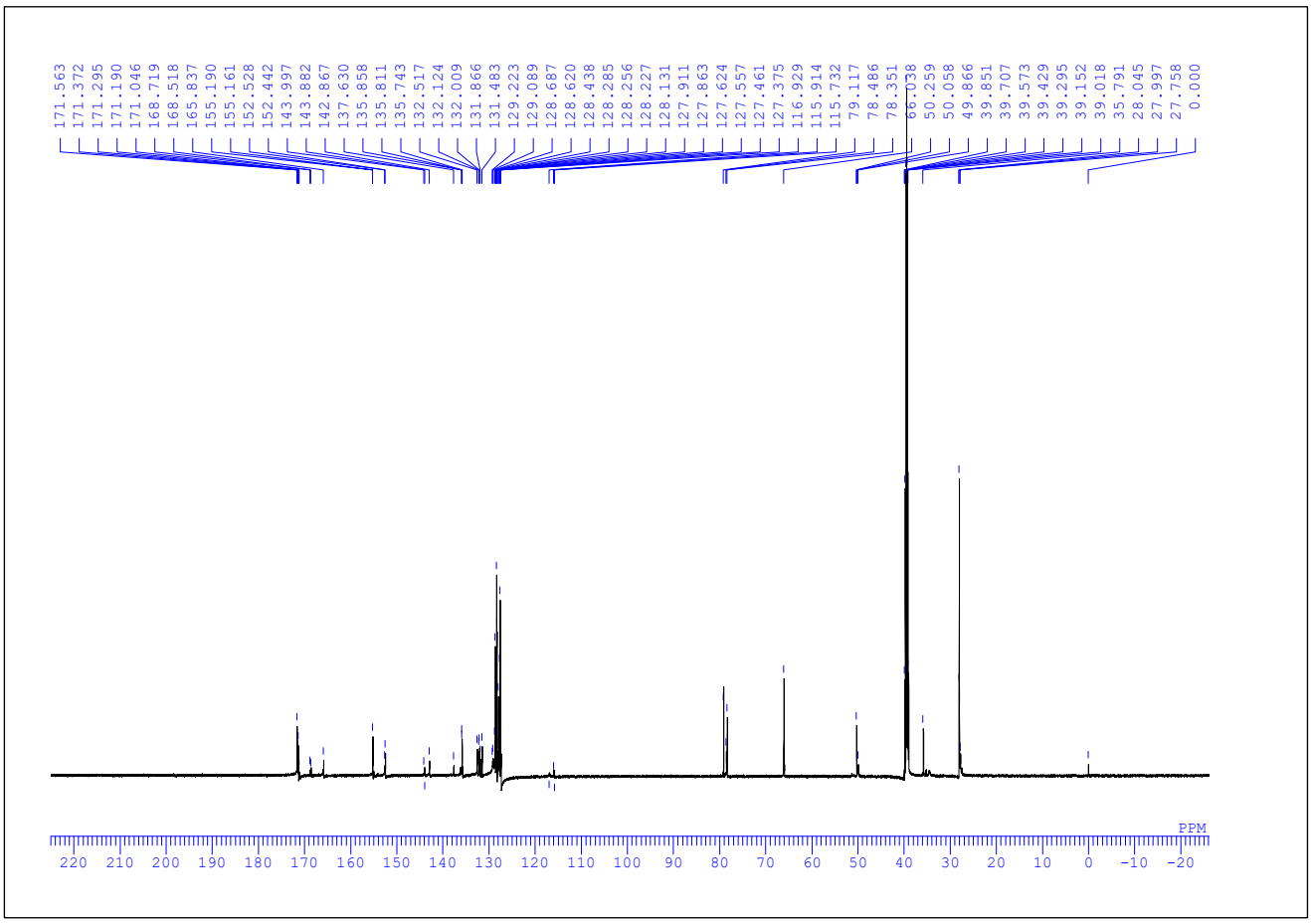
^{13}C NMR spectrum for compound **5f**



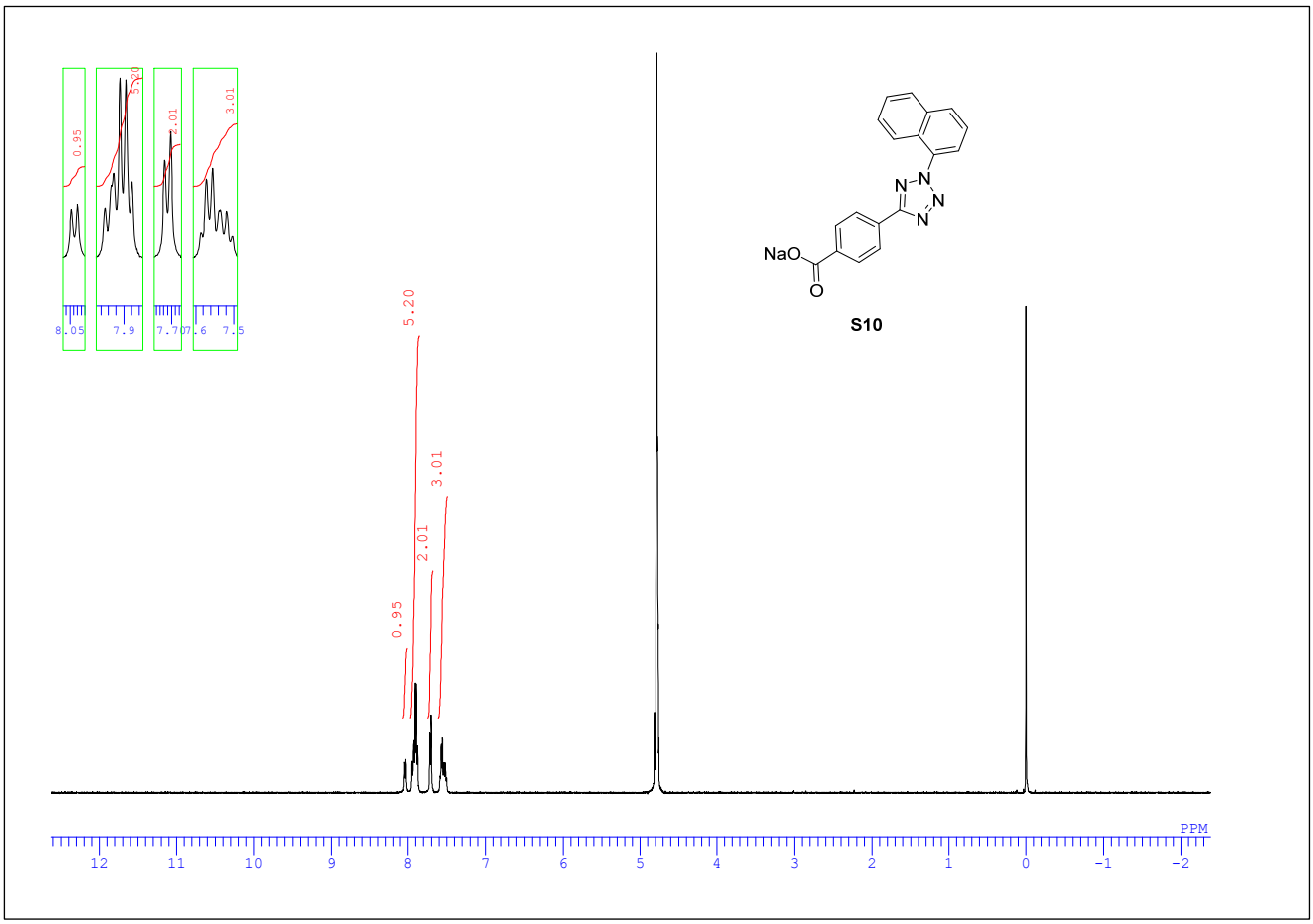
^{1}H NMR spectrum for compound **5g**



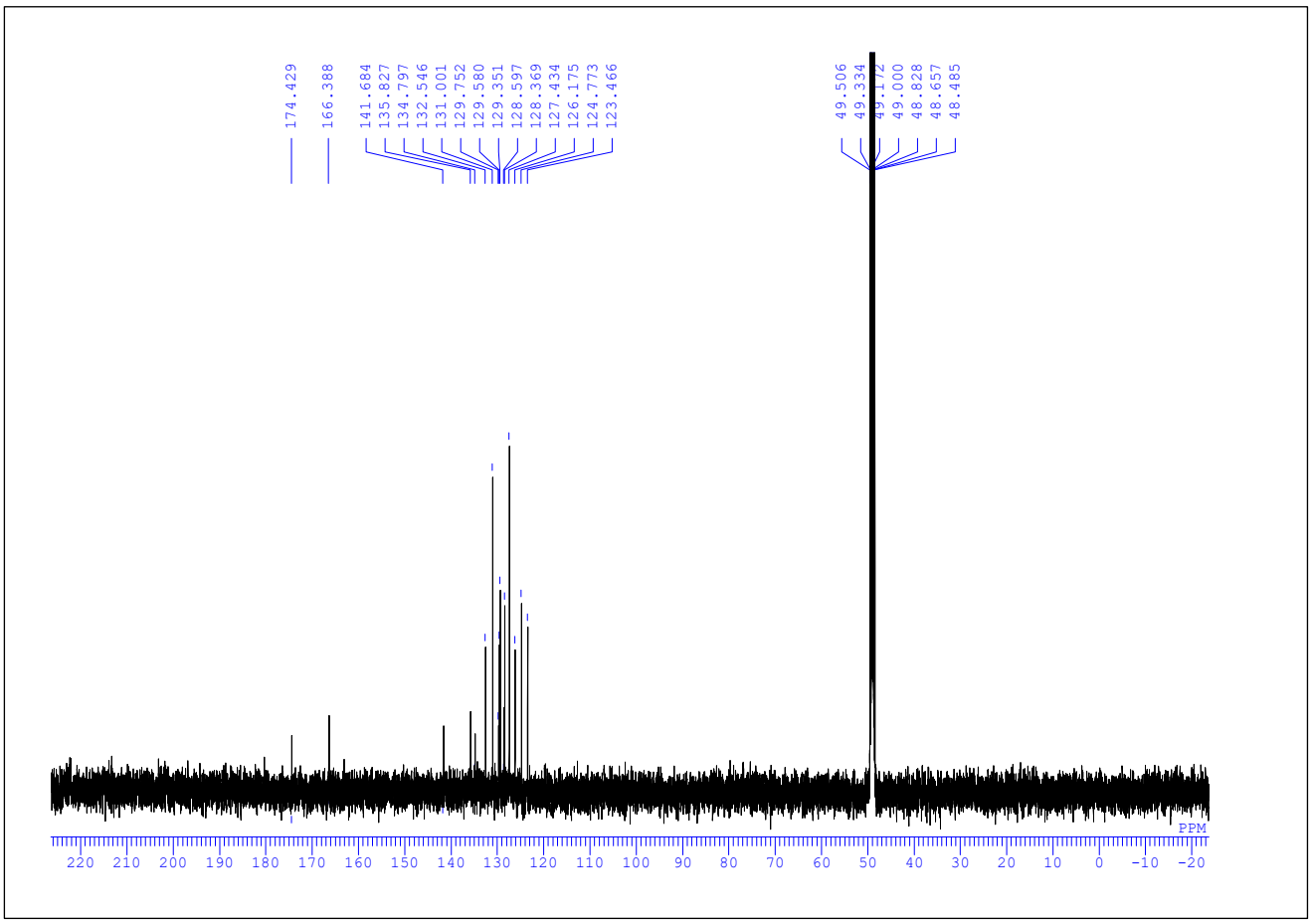
^{13}C NMR spectrum for compound **5g**



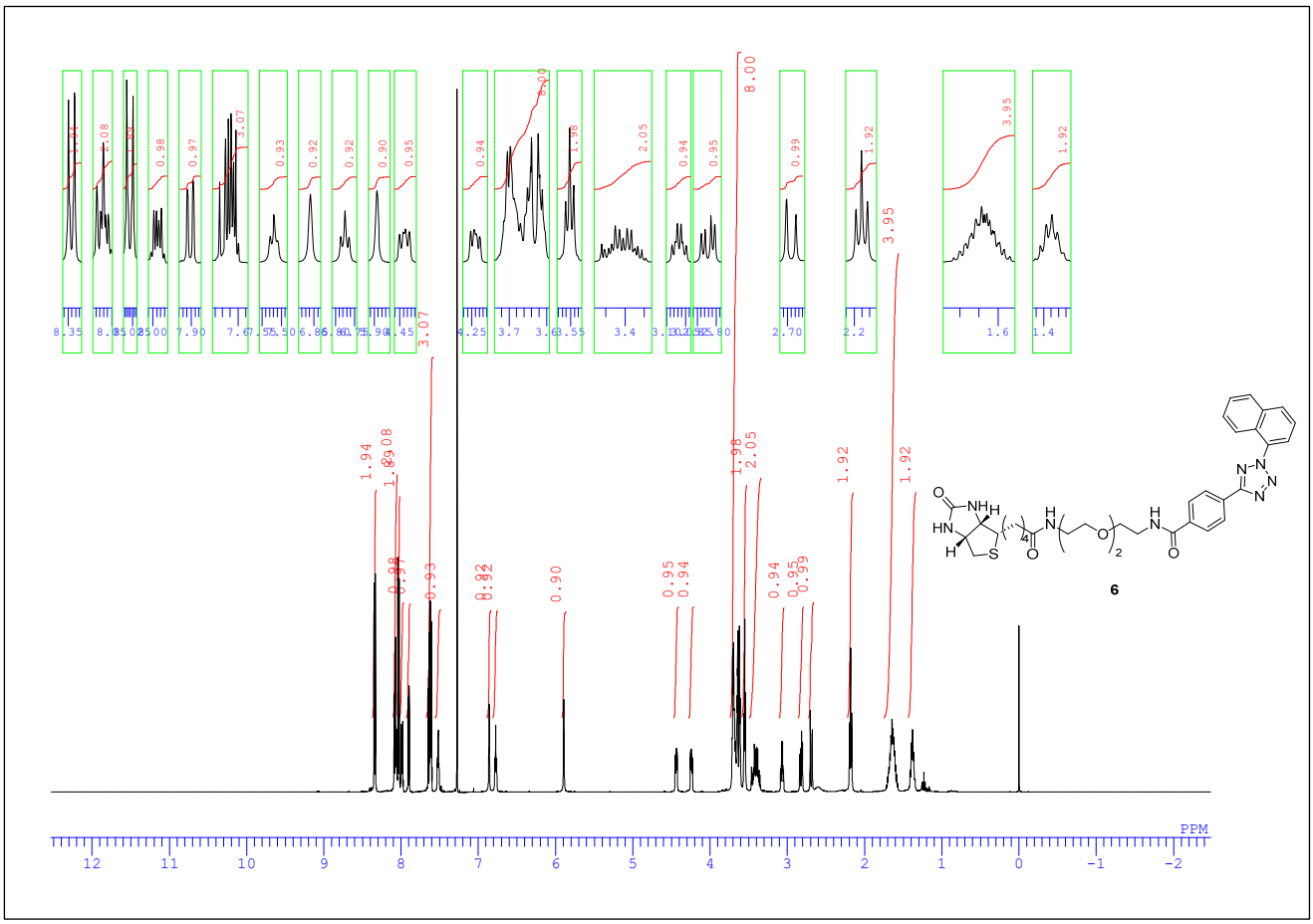
^{1}H NMR spectrum for compound **S10**



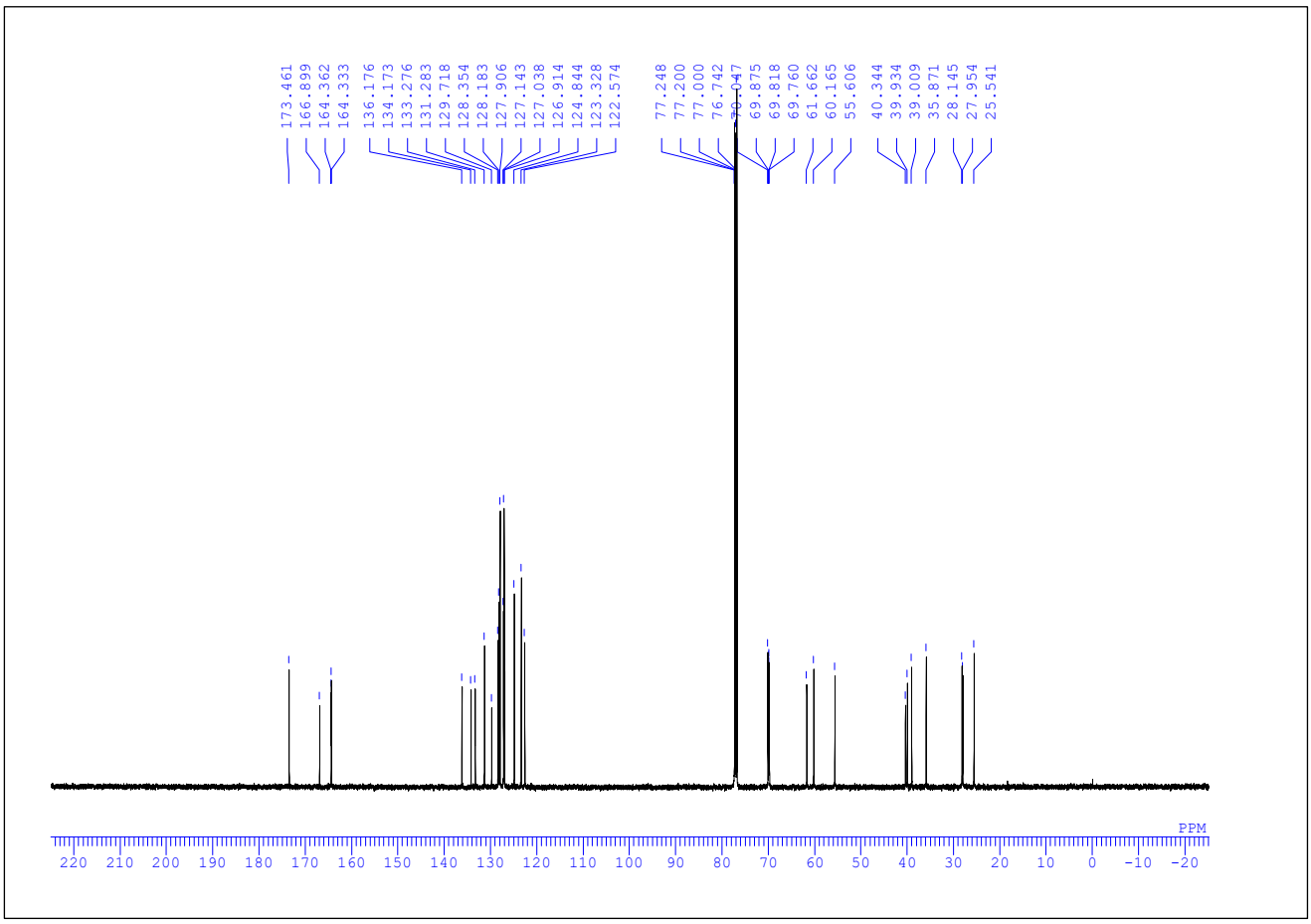
^{13}C NMR spectrum for compound **S10**



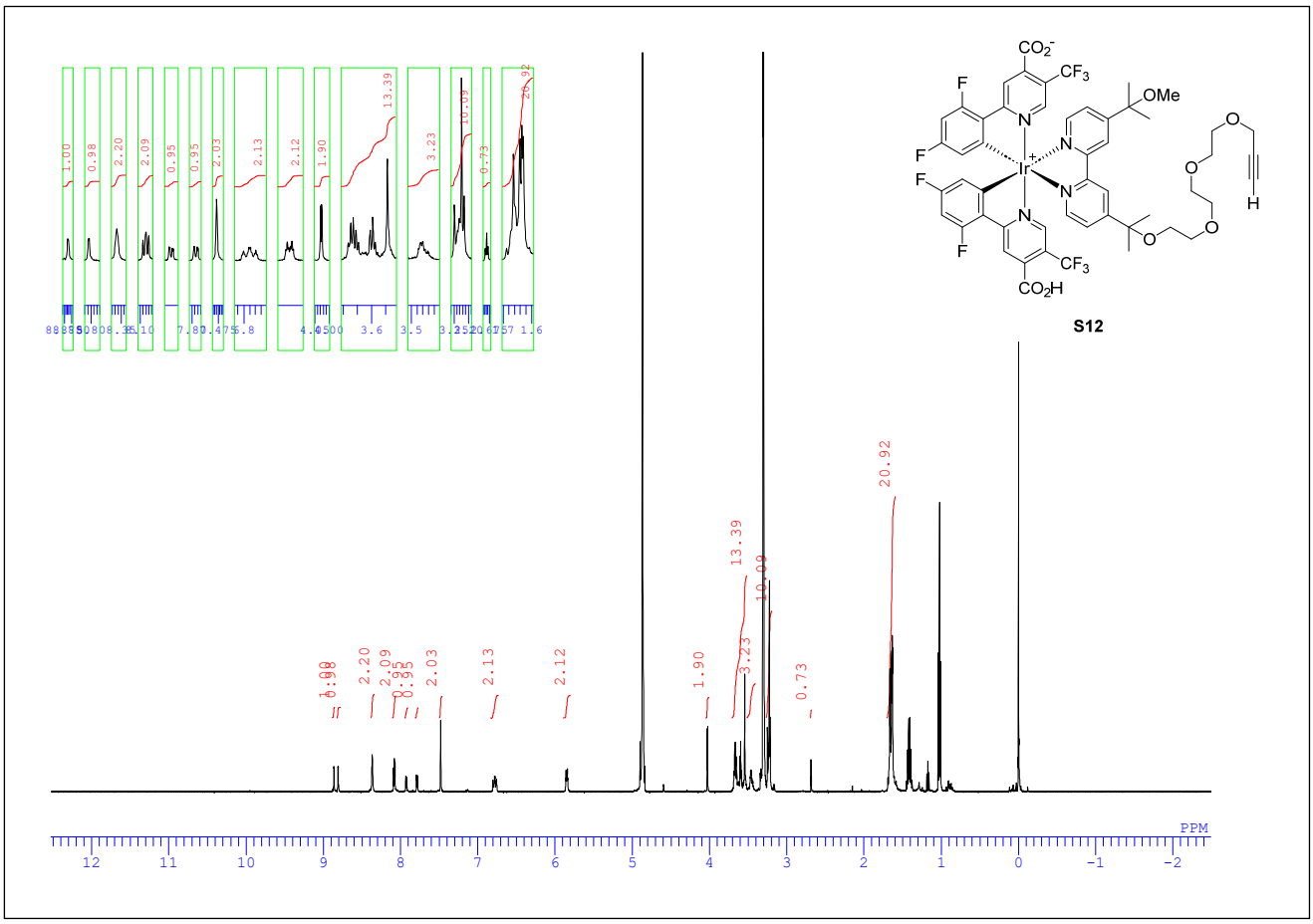
^{1}H NMR spectrum for compound **6**



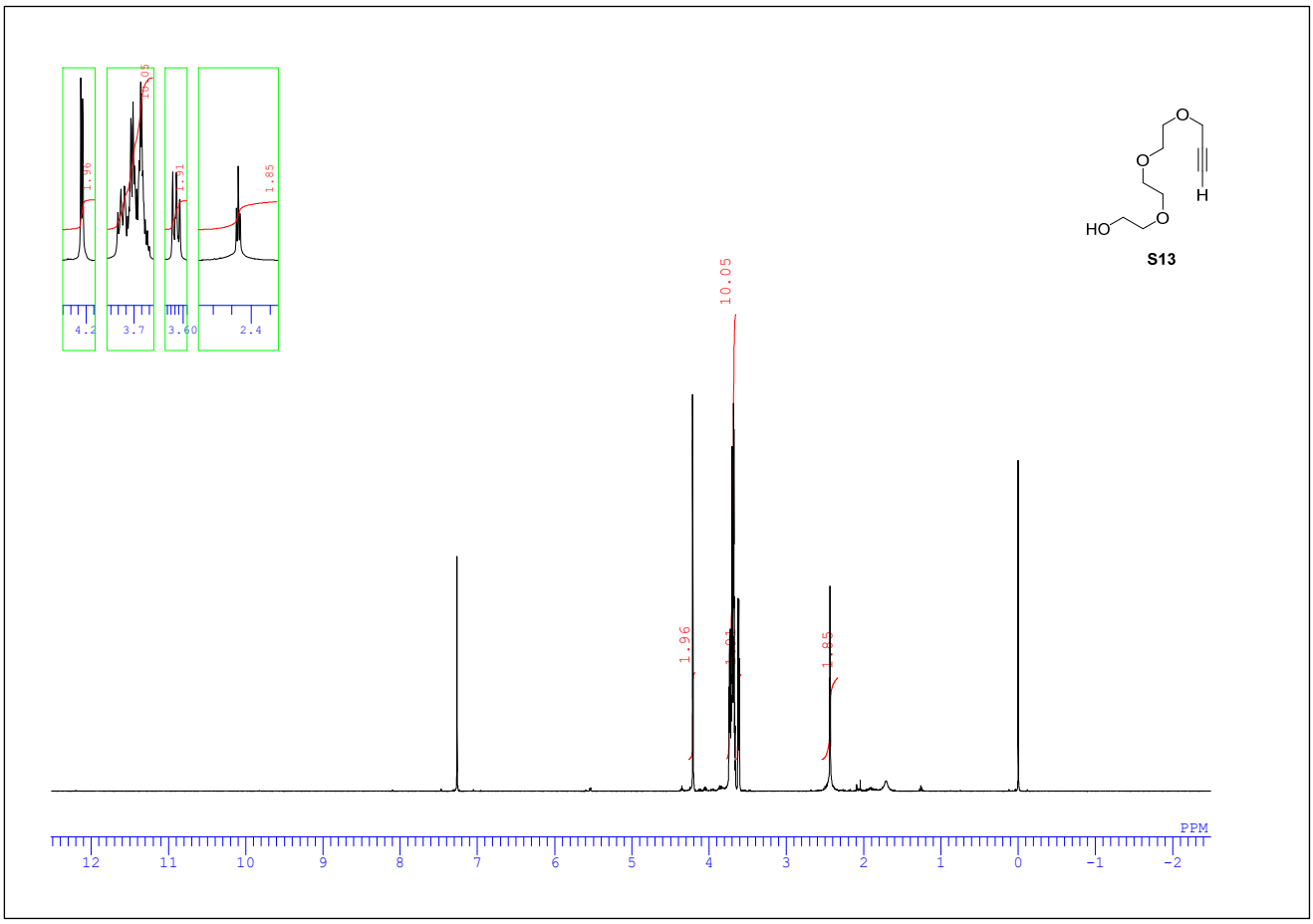
^{13}C NMR spectrum for compound **6**



^{1}H NMR spectrum for compound **S12**



^{1}H NMR spectrum for compound **S13**



V. Computational Studies

General

All calculations were performed using the Gaussian 16 program package.[11] All structures were optimized at the B3LYP level[12] of theory in combination with D3 dispersion corrections.[13] Unrestricted B3LYP-D3 was employed for the calculation of the triplet state. For geometry optimization, all atoms were described with the def2-SVP basis set,[14] in which solvent effects were included implicitly using the SMD model[15] for acetonitrile. Vibrational frequency analyses at the same level of theory were performed on all the optimized geometries to characterize stationary points as local minima (no imaginary frequency). The electronic energy was then refined using def2-TZVPP basis set[12] at the B3LYP-D3 level on the optimized geometries in combination with SMD solvation model. The given Gibbs free energies in acetonitrile were calculated in **Table S3** according to the formula: $G_{sol} = TCG + E_{sol}$ (kcal/mol). E_T was calculated based on the difference between G_{sol} in the singlet ground state (S_0) and G_{sol} in the triplet excited state (T_1).

Compound energies of all stationary points

Table S3. Thermal correction to Gibbs free energies (***TCG***, in Hartree), thermal correction to enthalpies (***TCH***, in Hartree), sum of electronic and thermal free energies (***G***, in Hartree), Sum of electronic and thermal enthalpies (***H***, in Hartree), and single point energies in acetonitrile computed at the B3LYP-D3/def2-TZVPP level (E_{sol}, in Hartree).

Compound	Energy state	***TCG***/a.u.	***TCH***/a.u.	***G***/a.u.	***H***/a.u.	E_{sol}/a.u.
1a	S_0	0.167235	0.222792	−719.72472	−719.669163	−720.67936
	T_1	0.162737	0.218394	−719.62137	−719.565718	−720.57472
1b	S_0	0.197097	0.257816	−834.13918	−834.078461	−835.2566
	T_1	0.192314	0.254237	−834.04271	−833.981735	−835.15857
1c	S_0	0.21253	0.272488	−873.22034	−873.160379	−874.38245
	T_1	0.206318	0.268737	−873.13778	−873.075357	−874.29343
1d	S_0	0.201143	0.260691	−889.25216	−889.192614	−890.42403
	T_1	0.194406	0.256662	−889.16975	−889.107495	−890.33451
1g	S_0	0.211679	0.272521	−873.21994	−873.159094	−874.38007
	T_1	0.206462	0.268849	−873.13702	−873.074634	−874.29124

Computed coordinates of all stationary points

1a_S_0

N	0.01766800	0.33353200	0.00001500
C	-1.02444900	-0.49426500	-0.00002200
N	-0.61334400	-1.79296200	-0.00010600
N	0.68595600	-1.77635000	-0.00008000
N	1.04838200	-0.49825300	-0.00002600
C	2.41099600	-0.07266600	-0.00000800
C	-2.43021100	-0.07057300	0.00000200
C	-2.76337500	1.29612400	0.00004900
C	-4.10218900	1.69089900	0.00007100
C	-5.12041700	0.72957600	0.00004500
C	-4.79326000	-0.63146100	-0.00000200
C	-3.45591600	-1.03285800	-0.00002400
C	2.69896100	1.29733600	-0.00011700
C	4.03382200	1.70813100	-0.00009500
C	5.06696900	0.76479400	0.00003000
C	4.76108300	-0.60114300	0.00013600
C	3.43296000	-1.03088600	0.00012100
H	-1.96908000	2.04562700	0.00006900
H	-4.35270300	2.75480700	0.00010800
H	-6.16810800	1.04139400	0.00006200
H	-5.58455700	-1.38551600	-0.00002300
H	-3.19855100	-2.09379900	-0.00006100
H	1.88775900	2.02534800	-0.00021800
H	4.26409300	2.77627700	-0.00018000
H	6.10916300	1.09295500	0.00004500
H	5.56260400	-1.34385400	0.00023700
H	3.18891900	-2.09304500	0.00021000

1a_T_1

N	0.00957200	0.40043700	-0.00000100
C	-1.03080300	-0.48054800	0.00000000
N	-0.63533900	-1.78057500	0.00000000
N	0.65071200	-1.85919500	0.00000000
N	1.07672800	-0.40549400	0.00000000
C	2.36822800	-0.04114800	0.00000000
C	-2.41468800	-0.07587500	0.00000000
C	-2.75276000	1.30007400	0.00000000
C	-4.08862700	1.68979300	0.00000000
C	-5.10487500	0.72293600	0.00000000
C	-4.77932000	-0.64372200	0.00000000

C	-3.44882200	-1.04497900	0.00000000
C	2.73239500	1.34932500	0.00000000
C	4.06776800	1.69743800	0.00000000
C	5.07793300	0.70676600	0.00000000
C	4.72229500	-0.65810800	0.00000000
C	3.39540300	-1.04764600	0.00000000
H	-1.95630300	2.04609000	0.00000000
H	-4.34516000	2.75194600	0.00000000
H	-6.15284500	1.03330200	0.00000000
H	-5.57375700	-1.39397300	0.00000000
H	-3.18675200	-2.10426100	0.00000000
H	1.94423400	2.10215700	0.00000000
H	4.34731600	2.75402700	0.00000000
H	6.13015300	0.99921800	0.00000100
H	5.50440500	-1.42151500	0.00000000
H	3.11223300	-2.09903100	-0.00000100

1b_ S_0

N	-0.82388000	0.27250700	0.01091100
C	-1.89829100	-0.51503900	-0.03033400
N	-1.53888300	-1.82369200	-0.11325900
N	-0.23714400	-1.85656300	-0.12838200
N	0.17324300	-0.59629300	-0.05142000
C	-3.28630200	-0.03705500	0.00870300
C	-3.56537300	1.34012600	0.07508600
C	-4.88748600	1.78670200	0.11079900
C	-5.94311700	0.86716100	0.08089700
C	-5.66999600	-0.50424800	0.01505500
C	-4.34970400	-0.95716500	-0.02100500
C	1.54897300	-0.22284100	-0.03813700
C	1.90100700	1.12704500	-0.18624100
C	3.24151100	1.48908300	-0.17175300
C	4.24807500	0.51561500	-0.01375400
C	3.88265500	-0.83516700	0.13256500
C	2.53550600	-1.19994500	0.12273600
O	5.51808700	0.96718300	-0.01430300
C	6.58832500	0.04472500	0.14112700
H	-2.74190700	2.05708500	0.09776000
H	-5.09559000	2.85854100	0.16186900
H	-6.97756500	1.21935900	0.10891500
H	-6.49056000	-1.22599600	-0.00830800
H	-4.13448900	-2.02628400	-0.07220100

H	1.12567900	1.88288400	-0.31297800
H	3.53761800	2.53384400	-0.28601700
H	4.63678400	-1.61123900	0.26036400
H	2.25495800	-2.24653200	0.24347900
H	7.51307600	0.63666400	0.11129500
H	6.53092800	-0.48528400	1.10789300
H	6.60832800	-0.69619700	-0.67706200

1b_ T_1

N	-0.83321400	0.34482000	0.00000300
C	-1.88378000	-0.49030000	0.00000100
N	-1.53274300	-1.80289200	-0.00000100
N	-0.23163400	-1.89927200	0.00000000
N	0.21731400	-0.52160500	0.00000200
C	-3.27228000	-0.04126900	0.00000000
C	-3.57545800	1.33667200	0.00000200
C	-4.90329700	1.76399200	0.00000100
C	-5.94568200	0.82805200	-0.00000100
C	-5.65220400	-0.54293000	-0.00000200
C	-4.32775800	-0.97759900	-0.00000200
C	1.50846700	-0.18685400	0.00000300
C	1.90888000	1.20321600	0.00000400
C	3.23666100	1.52089800	-0.00000100
C	4.24303600	0.49786200	-0.00000600
C	3.85750200	-0.87219900	-0.00000400
C	2.52768100	-1.21942900	0.00000100
O	5.50362700	0.93389000	-0.00001500
C	6.59157500	0.00738800	0.00001100
H	-2.76128200	2.06400700	0.00000300
H	-5.12846100	2.83366800	0.00000200
H	-6.98532200	1.16575600	-0.00000100
H	-6.46320900	-1.27582200	-0.00000400
H	-4.09512200	-2.04401700	-0.00000300
H	1.13935400	1.97416400	0.00001000
H	3.56711200	2.56179000	-0.00000100
H	4.61321300	-1.65815800	-0.00000600
H	2.22102100	-2.26369300	0.00000400
H	7.50645700	0.61322500	0.00003600
H	6.56953200	-0.62719900	0.90115100
H	6.56957700	-0.62719200	-0.90113500

1c_ S_0

N	0.66241100	-0.17519100	0.28513200
C	1.80077500	-0.65042400	-0.21784600
N	1.57119600	-1.75090200	-0.98579100
N	0.28847000	-1.96242900	-0.97036700
N	-0.24024100	-1.01154300	-0.20707600
C	-1.63811000	-0.95733100	0.08870900
C	3.12751500	-0.06806800	0.02298600
C	-2.24416900	-2.11694800	0.53045500
C	-3.62683900	-2.12252600	0.82570600
C	-4.36849200	-0.96895400	0.68424600
C	-3.76824000	0.23716900	0.22425900
C	-2.36648800	0.25991200	-0.09806900
C	4.26843000	-0.65021400	-0.55754900
C	5.53017700	-0.09703100	-0.32986600
C	5.66641500	1.03875200	0.47691000
C	4.53282000	1.62133500	1.05701500
C	3.26871800	1.07320300	0.83312400
C	-4.53352500	1.42661500	0.05773700
C	-3.95099500	2.58215000	-0.41805800
C	-2.57371300	2.59593400	-0.75403000
C	-1.79692200	1.46563200	-0.59753400
H	-1.64598700	-3.02078800	0.65761700
H	-4.09460400	-3.04479500	1.17719900
H	-5.43560500	-0.96414900	0.92096500
H	4.15972100	-1.53569400	-1.18687600
H	6.41196400	-0.55514200	-0.78513700
H	6.65521100	1.47012100	0.65349000
H	4.63411900	2.50816400	1.68783300
H	2.38440800	1.52706500	1.28549400
H	-5.59677900	1.40177900	0.31069900
H	-4.54864000	3.48857800	-0.54331100
H	-2.12151800	3.51218000	-1.14213700
H	-0.73927800	1.49790600	-0.85827600

1c_T_1

N	0.64316100	-0.07995500	-0.00004000
C	1.80781700	-0.73258500	-0.00008400
N	1.62816600	-2.07960200	-0.00021300
N	0.35182300	-2.31241000	-0.00024900
N	-0.26017200	-1.07167600	-0.00014100
C	-1.62487500	-0.95096400	-0.00009900
C	3.12033600	-0.08517200	0.00001900

C	-2.37672000	-2.21226400	0.00001400
C	-3.74159300	-2.20119800	0.00030900
C	-4.46507200	-0.97631100	0.00044600
C	-3.77701900	0.27700500	0.00019600
C	-2.33033700	0.32519900	-0.00012400
C	4.29279100	-0.86614200	-0.00017700
C	5.54534600	-0.25175500	-0.00007100
C	5.64557700	1.14535500	0.00023400
C	4.48344200	1.92709800	0.00043300
C	3.22726700	1.31930500	0.00032800
C	-4.50252600	1.48221200	0.00021900
C	-3.85510500	2.73572200	-0.00010600
C	-2.47234100	2.78497800	-0.00046000
C	-1.71448600	1.58754700	-0.00046200
H	-1.81877200	-3.14486600	-0.00010600
H	-4.28851700	-3.14722600	0.00042900
H	-5.55691700	-0.98116500	0.00068600
H	4.21189800	-1.95476100	-0.00041400
H	6.44949600	-0.86592000	-0.00022500
H	6.62817500	1.62430200	0.00031800
H	4.55716300	3.01762400	0.00067500
H	2.32239800	1.93027400	0.00049500
H	-5.59455300	1.43465100	0.00048500
H	-4.44833400	3.65336500	-0.00008100
H	-1.94747300	3.74306100	-0.00072800
H	-0.63044200	1.64797500	-0.00072700

1d_ S_0

N	-0.65527900	-0.16787200	0.27276900
C	-1.79705100	-0.67112600	-0.19322400
N	-1.57233300	-1.81375900	-0.89953800
N	-0.29030700	-2.02394400	-0.88312800
N	0.24401500	-1.03062400	-0.17860600
C	1.64277700	-0.95431000	0.09433000
C	-3.12232000	-0.07695900	0.02438100
C	-4.26598400	-0.68778500	-0.52019900
C	-5.52652900	-0.12329300	-0.31486900
C	-5.65868800	1.05213100	0.43366600
C	-4.52232600	1.66317300	0.97799500
C	-3.25935100	1.10414300	0.77605300
C	2.28711100	-2.10128900	0.51724100
C	3.67595900	-2.08485000	0.78426900

C	4.39562400	-0.91801900	0.63552200
C	3.75171700	0.26956900	0.19616400
C	2.34971700	0.27276500	-0.09629800
C	4.46959600	1.48778800	0.01299000
N	3.92731600	2.60539700	-0.41886000
C	2.59966200	2.59433100	-0.71171800
C	1.78732900	1.48871300	-0.57021100
H	-4.16046600	-1.60420100	-1.10410900
H	-6.41054600	-0.60355600	-0.74208700
H	-6.64658000	1.49221900	0.59290900
H	-4.62063000	2.58095100	1.56335300
H	-2.37303000	1.58017400	1.20086000
H	1.71193600	-3.01891600	0.65140600
H	4.16455000	-3.00195200	1.11993300
H	5.46712900	-0.88989200	0.84931100
H	5.54291500	1.49772200	0.24243800
H	2.17826200	3.53596900	-1.07928800
H	0.72911000	1.55722000	-0.81974300

1d_T_1

N	-0.63669000	-0.08517300	-0.00000500
C	-1.80126500	-0.73379500	0.00000600
N	-1.61923600	-2.08487100	0.00002400
N	-0.34637300	-2.31373400	0.00002500
N	0.26232800	-1.07613500	0.00000800
C	1.62823100	-0.95266400	0.00000300
C	-3.11333800	-0.08822700	0.00000000
C	-4.28437300	-0.87140300	-0.00001300
C	-5.53727000	-0.25794600	-0.00001900
C	-5.63797900	1.13901400	-0.00001200
C	-4.47680200	1.92263500	0.00000100
C	-3.22039200	1.31638800	0.00000700
C	2.39524600	-2.20266400	-0.00000100
C	3.75908600	-2.16961800	-0.00001300
C	4.46967000	-0.93228300	-0.00001800
C	3.76087700	0.30501000	-0.00001000
C	2.31695300	0.33157800	0.00000200
C	4.44474800	1.53481200	-0.00001000
N	3.84524200	2.74586100	0.00000100
C	2.52449800	2.76261600	0.00001300
C	1.71481200	1.59336200	0.00001300
H	-4.20255300	-1.95990300	-0.00001900

H	-6.44104300	-0.87250400	-0.00002900
H	-6.62096400	1.61711400	-0.00001700
H	-4.55202100	3.01296800	0.00000700
H	-2.31591200	1.92791800	0.00001800
H	1.85107800	-3.14355100	0.00000300
H	4.32018600	-3.10720100	-0.00001800
H	5.56150700	-0.92176000	-0.00002800
H	5.54048700	1.52762200	-0.00001900
H	2.03211600	3.74212800	0.00002200
H	0.63400400	1.69463300	0.00002200

1g_ S_0

N	-1.00974000	0.55569500	0.04725500
C	0.12949300	-0.08912900	-0.21272400
N	-0.12582100	-1.38187100	-0.56281400
N	-1.41557500	-1.54123600	-0.52250500
N	-1.92835100	-0.37283300	-0.15795000
C	-3.33000000	-0.15026400	-0.00099000
C	1.44858100	0.56833400	-0.15557500
C	1.46840700	1.95569700	-0.25787200
C	2.67501800	2.68616800	-0.21111000
C	3.87506500	2.02530900	-0.06085700
C	3.91202700	0.60827900	0.05551900
C	2.68760500	-0.15071400	0.01164500
C	-4.21520000	-1.23028800	-0.11065200
C	-5.58346100	-0.99892000	0.04108900
C	-6.06216600	0.29039300	0.30169100
C	-5.16339300	1.35707400	0.41039900
C	-3.79119500	1.14556600	0.25891500
C	5.15302300	-0.07097900	0.22407100
C	5.20071000	-1.44219500	0.35477000
C	3.99891100	-2.19162400	0.32416600
C	2.77871600	-1.56682000	0.15669600
H	0.52682500	2.49204500	-0.38875100
H	2.64762100	3.77471600	-0.30126900
H	4.81689000	2.57970400	-0.02834500
H	-3.83578500	-2.23247500	-0.30967300
H	-6.27944700	-1.83705400	-0.04306200
H	-7.13457300	0.46301300	0.42057100
H	-5.52936500	2.36647600	0.61315800
H	-3.08374900	1.97083000	0.33965900
H	6.07063600	0.52303700	0.25101200

H	6.15875800	-1.95208900	0.48503300
H	4.03668700	-3.27869700	0.43428000
H	1.86908300	-2.16311200	0.12440800

1g_T_1

N	-1.02541400	0.56623600	-0.00014900
C	0.14306600	-0.11894500	-0.00001800
N	-0.11790800	-1.47335700	0.00025200
N	-1.39806800	-1.62241400	0.00029500
N	-1.93264100	-0.39662600	0.00004900
C	-3.33637200	-0.16637800	0.00002600
C	1.42182400	0.52539100	-0.00011800
C	1.40218400	2.00145600	-0.00023500
C	2.55625900	2.72368300	-0.00012800
C	3.82961000	2.06976100	0.00005400
C	3.91504000	0.64193500	0.00004800
C	2.71038400	-0.16200800	-0.00007000
C	-4.21810000	-1.25691800	-0.00021900
C	-5.59238700	-1.01478600	-0.00023500
C	-6.08506300	0.29592400	-0.00002100
C	-5.19189600	1.37303700	0.00021700
C	-3.81319900	1.15138800	0.00024600
C	5.16653700	0.00154400	0.00013400
C	5.27997500	-1.41028000	0.00008000
C	4.13441700	-2.18068400	-0.00006500
C	2.85640400	-1.55761200	-0.00014300
H	0.43358300	2.50055500	-0.00038700
H	2.51766800	3.81615600	-0.00018900
H	4.75039700	2.65696600	0.00015000
H	-3.83018700	-2.27530800	-0.00039900
H	-6.28327700	-1.86142200	-0.00042800
H	-7.16266200	0.47675400	-0.00004200
H	-5.56791700	2.39903600	0.00039000
H	-3.11076800	1.98473700	0.00044100
H	6.07021300	0.61683100	0.00024200
H	6.26924600	-1.87459700	0.00014800
H	4.19314200	-3.27172500	-0.00011800
H	1.96667800	-2.18389700	-0.00025200

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