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Supporting Information

69451 Weinheim, Germany

Potent Small-Molecule Suppression of Oxacillin Resistance in Methicillin-Resistant *Staphylococcus aureus***

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Biological assay protocols and data

Bacterial strains, media, and antibiotics

Staphylococcus aureus strains were obtained from the ATCC (43300, 33591, 700789, BAA-1753, BAA-811, BAA-1770, BAA-1685, BAA-44, BAA-1556) or the Network on Antimicrobial Resistance in *Staphylococcus aureus* (NARSA) (JE-2, NE-218, NE-147, NE-958, NE-481, NE-262, NE-618, NE-554, NE-823, NE-873, NE-210, NE-820, NE-839, NE-49, NE-116, NE-95, NE-423) and colonies grown on solid media as instructed. Mueller-Hinton broth (MHB) (cat # 275710) was purchased from BD Diagnostics. Vancomycin (cat # 861987) and streptomycin (cat # S1567) were purchased from Sigma Aldrich. Oxacillin (cat # O0353) was purchased from TCI. Chloramphenicol (cat # B20841) was purchased from Alfa Aesar. All assays were run in duplicate and repeated at least two separate times. All compounds were dissolved as their HCl salts in molecular biology grade DMSO as 100 mM stock solutions.

Broth microdilution method for determination of minimum inhibitory concentrations

S. aureus was grown in MHB for 6-8 h and this culture was used to inoculate fresh MHB (5 x 10^5 CFU/mL). The resulting bacterial suspension was aliquoted (5 mL) into culture tubes and compound, from a 100 mM or 10 mM DMSO stock, was added. Inoculated media not treated with compound served as the control. From each sample, 1 mL was transferred to a new culture tube and antibiotic, from water stock, was added. Rows 2-12 of a 96-well microtiter plate were filled at 100 μL/well from the remaining inoculated media, allowing the concentration of compound to be kept uniform throughout the antibiotic dilution procedure. The samples containing antibiotic were then aliquoted (200 μL) into the corresponding first row wells of the microtiter plate. Row 1 wells were mixed 6 to 8 times then 100 μL was transferred to row 2. Row 2 wells were mixed 6 to 8 times, followed by a 100 μL transfer from row 2 to row 3. This procedure was repeated to serially dilute the rest of the rows of the microtiter plate, with the exception of the final row, to which no antibiotic was added (to check for growth of bacteria in the presence of compound alone). The plate was then covered with a lid and incubated under stationary conditions at 37 ˚C. After 16 h, minimum inhibitory concentration (MIC) values were recorded as the lowest concentration of antibiotic at which no visible growth of bacteria was observed.

Time kill curves

S. aureus was grown in MHB overnight and this culture was used to inoculate fresh MHB (5 x 10^5 CFU/mL). Inoculated media was aliquoted (3 mL) into culture tubes and compound and/or oxacillin were added, untreated inoculated media served as the control. Tubes were incubated at 37 ˚C with shaking. Samples were taken at 2, 4, 6, 8, and 24 h time points, serially diluted in fresh MHB and plated on tryptic soy agar. Plates were incubated at 37 ˚C overnight and the number of colonies enumerated.

Hemolysis assay

Hemolysis assays were performed on mechanically difibrinated sheep blood (Hemostat Labs: DSB100). Difibrinated blood (1.5 mL) was placed into a microcentrifuge tube and centrifuged for 10 min at 10,000 rpm. The supernatant was then removed and then the cells were

resuspended in 1 mL of phosphate-buffered saline (PBS). The suspension was centrifuged, the supernatant was removed and cells were resuspended two additional times. The final cell suspension was then diluted 10-fold. Test compound solutions were made in PBS in small culture tubes and then added to aliquots of the 10-fold suspension dilution of blood. PBS was used as a negative control and a zero hemolysis marker. Triton X (a 1% sample) was used as a positive control serving as the 100% lysis marker. Samples were then placed in an incubator at 37 ˚C while being shaken at 200 rpm for one hour. After one hour, the samples were transferred to microcentrifuge tubes and centrifuged for 10 min at 10,000 rpm. The resulting supernatant was diluted by a factor of 40 in distilled water. The absorbance of the supernatant was then measured with a UV spectrometer at a 540 nm wavelength.

Bacterial membrane permeabilization assay

The BacLight assay (Invitrogen) was used to assess membrane permeability. *S. aureus* was grown overnight in MHB at 37 °C with shaking. The culture was diluted 1:40 in MHB and grown to an optical density at 600nm (OD_{600}) of ~1.0 (~4 h growth). The cultures were centrifuged at 10,000g for 15 min, and the cell pellet was washed once with sterile water, resuspended to 1/10 of the original volume and diluted 1:20 into either water or water containing test compounds. Suspensions were incubated at 37 °C with shaking for 1 h then centrifuged at 10,000g for 10 min, washed once with sterile water, and resuspended in water. A 1:1 mixture of SYTO-9 and propidium iodide were added to the suspension (3 μL/mL) and mixed well. 100 μL of the suspension was added to each well of a 96-well plate. And the plates were incubated in the dark for 15 min at room temperature. Green fluorescence (SYTO-9) was read at 530 nm, and red fluorescence (propidium iodide) was read at 645 nm (excitation wavelength,485nm). The ratio of green to red fluorescence was expressed as a percentage of the control.

Description of Mutant Strains

Strain Name	**Gene Name**	**Gene Description**
BAA-1556		
JE2		USA300 JE2- PARENT STRAIN
NE218		sensor histidine kinase family protein
NE147		sensor histidine kinase
NE958	-	two-component response regulator
NE481		DNA-binding response regulator
NE262		DNA-binding response regulator, LuxR family
NE618	phoR	sensory box histidine kinase PhoR
NE554	vraR	DNA-binding response regulator
NE823	vraS	two-component sensor histidine kinase
NE873	agrC	accessory gene regulator protein C
NE210		staphylococcal accessory regulator
NE820	-	sensor histidine kinase
NE839	-	methicillin-resistance MecR1 regulatory protein
NE49		DNA-binding response regulator, AraC family
NE116		putative sensor histidine kinase
NE95	agrB	accessory gene regulator protein B
NE423	kdpD	sensor histidine kinase, KdpD

Antibiotic MIC without/with compound 7d

Antibiotic	MIC/MIC with 7d[a] (μg/mL)				
	JE2	NE554	NE823	NE49	NE116
Oxacillin	32/0.5	4/4	4/4	32/16	32/32
Vancomycin	1/0.25	0.5/0.5	0.5/0.5	1/1	1/1
Streptomycin	8/4	8/4	4/4	8/4	4/4
Chloramphenicol	8/4	8/8	8/8	8/8	8/8

[a]Compound 7d used at 40% MIC (5 μM for JE2, 2.5 μM for all other strains)

24 Hour Log Reduction

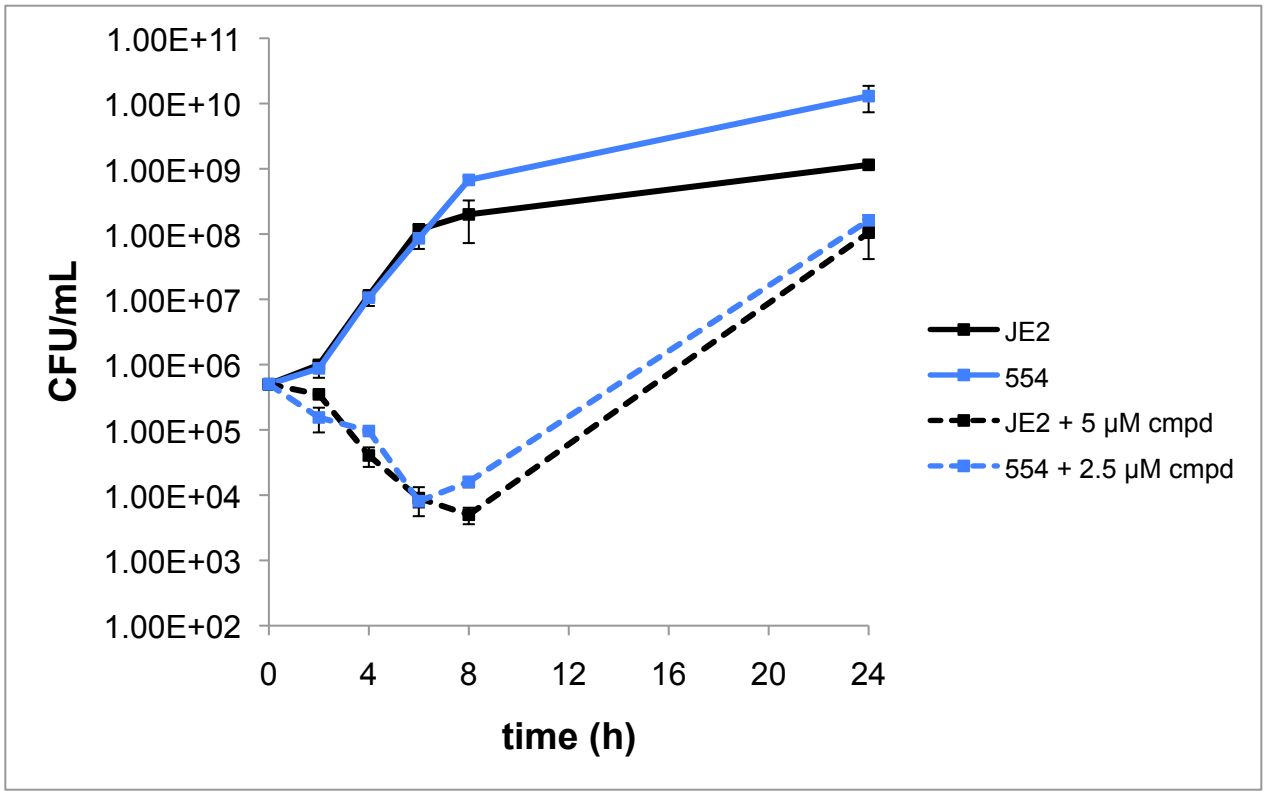
Oxacillin Concentration (μg/mL)	Log reduction in CFU/mL[a]	
	In absence of 7d	In presence of 5 μM 7d
-		1.08 ± 0.28
64	1.19 ± 0.03	7.49 ± 0.38
16	0.31 ± 0.21	6.41 ± 0.08
4	0.12 ± 0.04	5.54 ± 0.12
1	0.13 ± 0.04	4.38 ± 0.03

[a]Strain JE2, 24 h time point.

MIC reduction for ATCC MRSA strains

Strain	Oxacillin MIC (μg/mL)	Oxacillin MIC (μg/mL) in the presence of 7d (5 μM)	Fold reduction in oxacillin MIC
43300	32	1	32
33591	256	≤0.5	512
700789	64	8	8
BAA-1753	256	64	4
BAA-811	64	1	64
BAA-1770	32	≤0.5	64
BAA-1685	256	64	4
BAA-44	512	microbicidal	-

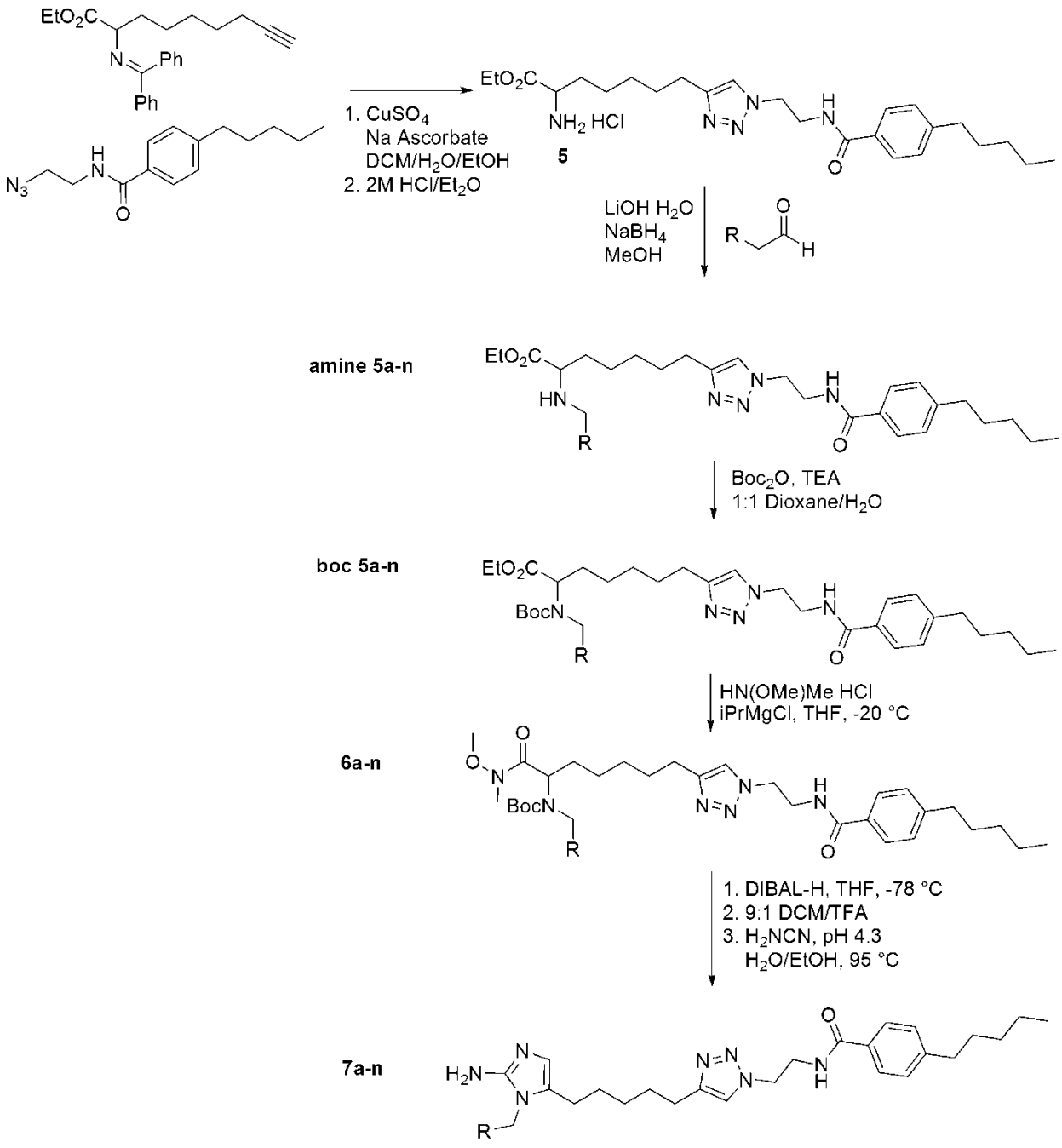
Time kill curve for JE2 and NE554 with compound 7d



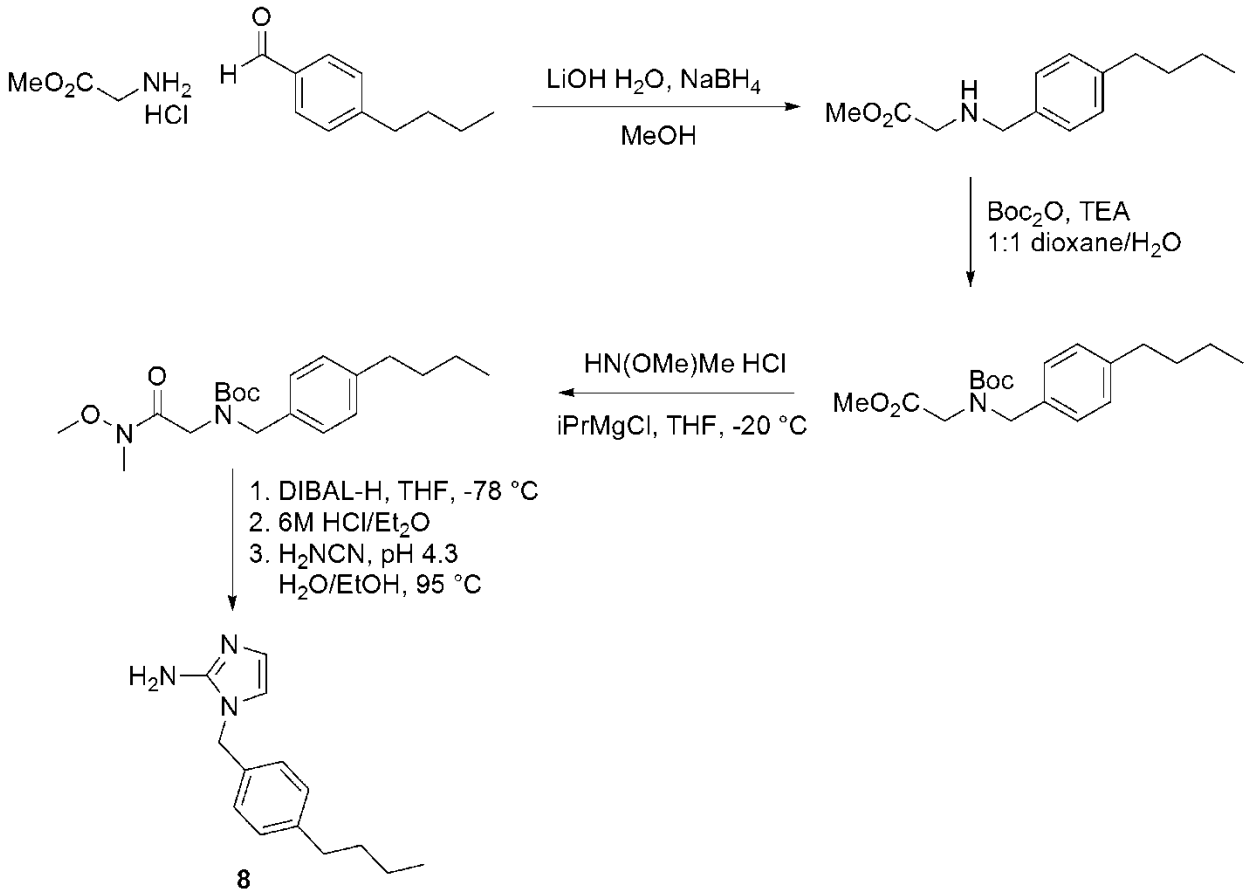
Experimental

All reagents used for chemical synthesis were purchased from commercially available sources and used without further purification. Chromatography was performed using 60A˚ mesh standard grade silica gel from Sorbtech (Atlanta, GA, USA). NMR solvents were obtained from Cambridge Isotope Labs and used as is. ^{1}H NMR (300 MHz or 400 MHz) and ^{13}C NMR (300 MHz or 400 MHz) spectra were recorded at 25 ℃ on Varian Mercury spectrometers. Chemical shifts (*d*) are given in ppm relative to tetramethylsilane or the respective NMR solvent; coupling constants (*J*) are in Hertz (Hz). Abbreviations used are s = singlet, br s = broad singlet, d = doublet, dd = doublet of doublets, t = triplet, dt = doublet of triplets, q = quartet, qn = quintet, sp = septet, sx = sextet, and m = multiplet. Mass spectra were obtained at the NCSU Department of Chemistry Mass Spectrometry Facility. Infrared spectra were obtained on a FT/IR-4100 spectrophotometer (ν_{max} in cm^{-1}). UV absorbance was recorded on a Genesys 10 scanning UV/visible spectrophotometer (λ_{max} in nm).

Synthesis of 1,5-substituted 2-aminoimidazoles



Synthesis of control compound



General synthetic procedure for reductive amination

5 was dissolved in methanol (30 mL). $LiOH.H_2O$ was added to the solution and stirred at room temperature for 30 minutes. The respective aldehyde was added dropwise, and stirred for 2 hours. Sodium borohydride was then added portionwise, and the solution was allowed to stir for 1 hour. The solvent was removed under reduced pressure and the resulting solid was dissolved in ethyl acetate (75 mL), and washed with saturated sodium bicarbonate (3 x 75 mL). The organic layer was then dried over sodium sulfate. The solvent was removed under reduced pressure, and the crude product was purified via flash column chromatography (20% → 40% acetone/hexanes).

General synthetic procedure for Boc-protection

The **amine 5a - n** was dissolved in 1:1 dioxane/water (20 mL) and triethylamine was added. Di-tert-butyl dicarbonate was added and the solution was stirred at room temperature overnight (16 hours). The solvent was removed under reduced pressure, and the crude product was then dissolved in water (50 mL) and extracted with diethyl ether (3 x 50 mL). The combined organic layers were washed with brine (100 mL) and then dried over sodium sulfate. Following the removal of the solvent under reduced pressure, the crude product was purified via flash column chromatography (40% → 75% ethyl acetate/hexanes) .

General synthetic procedure for weinreb amide

Boc 5a - n was stirred in dry tetrahydrofuran (15 mL) under nitrogen gas. To this solution, *O,N*-dimethylhydroxylamine hydrochloride was added and then cooled to -20 °C. 2.0*M* isopropylmagnesium chloride solution in tetrahydrofuran was added dropwise and the reaction was allowed to warm to room temperature. After 18 hours, the solution was cooled to 0 °C and saturated ammonium chloride (15 mL) was added dropwise. The aqueous layer was then extracted with ethyl acetate (3 x 25 mL) and the combined organic layers were dried over sodium sulfate. The solvent was removed under reduced pressure, and the crude product was purified via flash column chromatography (20% → 40% acetone/hexanes).

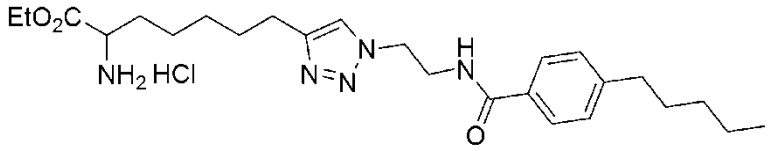
General synthetic procedure for cyanamide cyclization

A solution of **6a - n** was stirred in dry tetrahydrofuran (8 mL) and then cooled to -78 °C under nitrogen gas. To this solution, 1.0*M* diisobutylaluminium hydride (DIBAL-H) in hexanes was added and the reaction was stirred until completion by TLC analysis (approximately 2 hours). The reaction was quenched with aqueous 0.35 M sodium bisulfate (15 mL), then extracted with diethyl ether (3 x 20 mL). The combined organic fractions were then washed with aqueous 1M HCl (2 x 30 mL), followed by aqueous saturated sodium bicarbonate (2 x 30 mL), and then with brine (2 x 30 mL). The organic layer was then dried over sodium sulfate, and the solvent was removed under reduced pressure.

The crude product was dissolved in 9:1 dichloromethane:trifluoroacetic acid (15 mL). This was stirred for 15 minutes and upon completion by TLC analysis the solvent was removed under reduced pressure. Following the removal of the solvent, the crude product was dissolved in 1:1 ethanol/water (8 mL) and the pH of the solution was adjusted to 4.3 with aqueous 2M sodium hydroxide. To this, cyanamide was added and the reaction was stirred at reflux (95 °C) for 3 hours. The solvent was removed under reduced pressure and the crude product was purified via flash column chromatography (4% → 10% methanol(saturated ammonia)/dichloromethane). The pure product was dissolved in methanol (3 mL) and concentrated HCl (0.3 mL) was added. The HCl salt was obtained upon the removal of solvent under reduced pressure.

Characterization of novel compounds

ethyl 2-amino-7-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)heptanoate hydrochloride (5)



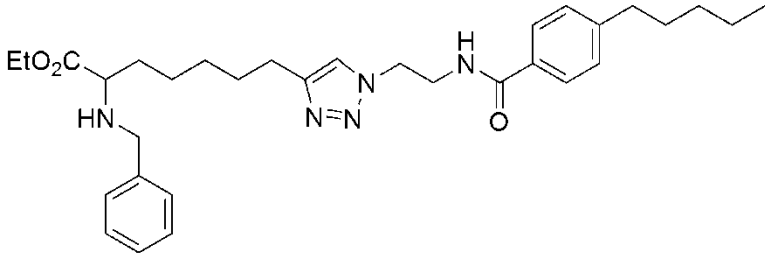
Ethyl 2-(diphenylmethyleneamino)non-8-ynoate was synthesized as described by Su *et al.*[1] N-(2-azidoethyl)-4-pentylbenzamide was synthesized as described by Rogers *et al.*[2] Ethyl 2-(diphenylmethyleneamino)non-8-ynoate (10 mmol) and N-(2-azidoethyl)-4-pentylbenzamide (10 mmol) were stirred in 1:1:1 DCM/H_2O/EtOH (100 mL). To this solution, copper(II)sulfate (1.5 mmol) and sodium ascorbate (4.5 mmol) were added and the reaction stirred at room temperature for 3 hours. Upon completion of the reaction, H_2O (200 mL) was added. The aqueous layer was

extracted with DCM (3 x 200 mL). The combined organic fractions were dried over sodium sulfate, and the solvent was removed under reduced pressure.

The crude product was dissolved in 1:1 diethyl ether/2M aqueous HCl (150 mL). The reaction stirred at room temperature for 2 hours. Upon completion, H_2O (75 mL) was added to the solution and the aqueous layer was washed with diethyl ether (3 x 150 mL). H_2O was then removed under reduced pressure and without further purification **5** was isolated as the HCl salt.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.67 (s, 1H), 7.72 (d, 2H, *J* = 8.1 Hz), 7.30 (d, 2H, *J* = 8.1 Hz), 4.88 (t, 2H, *J* = 5.3 Hz), 4.31 (q, 2H, *J* = 7.2 Hz), 4.06 - 3.95 (m, 3H), 2.93 (t, 2H, *J* = 7.4 Hz), 2.68 (t, 2H, *J* = 7.7 Hz), 1.95 - 1.17 (m, 17H), 0.92 (t, 3H, *J* = 6.8 Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ 170.6, 170.5, 148.8, 145.4, 132.2, 129.8, 128.9, 128.6, 63.7, 54.5, 54.0, 40.5, 36.8, 32.6, 32.2, 31.3, 29.2, 28.8, 25.5, 24.0, 23.7, 14.6, 14.5; IR (KBr) *v*(cm^{-1}) 3448, 1645, 1239; λ_{max} = 205 nm, 232 nm; HRMS (ESI): *m/z*: Calcd for $C_{25}H_{39}N_5O_3$: 458.3126 $[M+H]^+$, found: 458.3129.

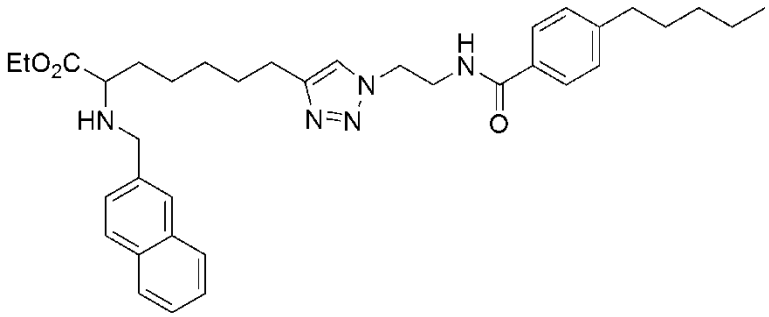
ethyl 2-(benzylamino)-7-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)heptanoate (amine 5a)



Amine 5a was synthesized as described in the general procedure using the α-amino ethyl ester HCl salt (1 mmol), $LiOH.H_2O$ (1.1 mmol), benzaldehyde (1 mmol), sodium borohydride (2 mmol). Following purification via flash column chromatography, **amine 5a** was obtained as a clear oil (33% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, 2H, *J* = 8.4 Hz), 7.34 - 7.20 (m, 8H), 7.00 (br s, 1H), 4.55 (t, 2H, *J* = 5.6 Hz), 4.18 (q, 2H, *J* = 7.2 Hz), 3.95 (t, 2h, *J* = 5.6 Hz), 3.82 (d, 1H, *J* = 12.8 Hz), 3.68 (d, 1H, *J* = 22.0 Hz), 3.24 (t, 1H, *J* = 6.6 Hz), 2.68 - 2.60 (m, 4H), 2.16 (br s, 1H), 1.67 - 1.26 (m, 17H), 0.88 (t, 3H, *J* = 7.0 Hz) ; ^{13}C NMR (400 MHz, $CDCl_3$) δ 175.2, 167.8, 148.2, 147.2, 139.4, 131.1, 128.6, 128.4, 128.3, 127.1, 127.0, 121.8, 60.6, 60.5, 52.0, 49.3, 39.8, 35.7, 33.2, 31.3, 30.8, 29.1, 28.8, 25.4, 25.3, 22.5, 14.3, 14.0; IR (KBr) *v*(cm^{-1}) 3431, 2989, 1733, 1270; λ_{max} = 230 nm; HRMS (ESI): *m/z*: Calcd for $C_{32}H_{45}N_5O_3$: 548.3595 $[M+H]^+$, found: 548.3597.

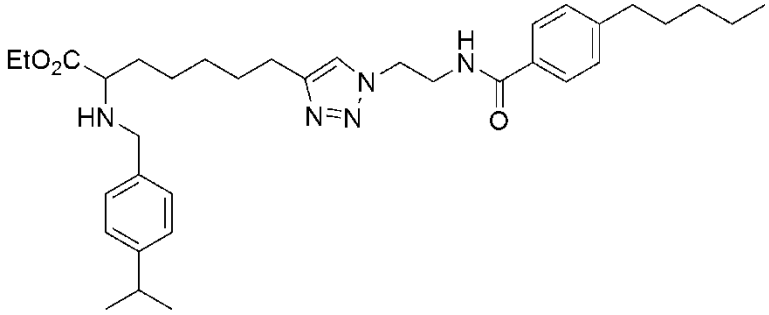
ethyl 2-(naphthalen-2-ylmethylamino)-7-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)heptanoate (amine 5b)



Amine 5b was synthesized as described in the general procedure using the α-amino ethyl ester HCl salt (1 mmol), $LiOH.H_2O$ (1.1 mmol), 2-naphthaldehyde (1 mmol), sodium borohydride (2 mmol). Following purification via flash column chromatography, **amine 5b** was obtained as a clear oil (76% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 - 7.67 (m, 6H), 7.47 - 7.44 (m, 3H), 7.25 (s, 1H), 7.20 (d, 2H, *J* = 8.4 Hz), 7.09 (br s, 1H), 4.52 (t, 2H, *J* = 5.6 Hz), 4.18 (q, 2H, *J* = 7.1 Hz), 4.00 - 3.71 (m, 4H), 3.29 (m, 1H), 2.66 - 2.59 (m, 4H), 2.37 (br s, 1H), 1.66 - 1.25 (m, 17H), 0.88 (t, 3H, *J* = 7.0 Hz) ; ^{13}C NMR (400 MHz, $CDCl_3$) δ 175.2, 167.8, 148.1, 147.2, 136.8, 133.3, 132.7, 131.0, 128.6, 128.0, 127.7, 127.0, 126.7, 126.0, 125.6, 121.8, 60.7, 60.4, 52.1, 51.7, 49.3, 39.8, 35.7, 33.2, 31.3, 30.8, 29.1, 28.8, 25.3, 22.4, 14.3, 14.0; IR (KBr) *v*(cm^{-1}) 3328, 2937, 1733, 1540, 1236; λ_{max} = 227 nm; HRMS (ESI): *m/z*: Calcd for $C_{36}H_{47}N_5O_3$: 598.3752 $[M+H]^+$, found: 598.3759.

ethyl 2-(4-isopropylbenzylamino)-7-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)heptanoate (amine 5c)

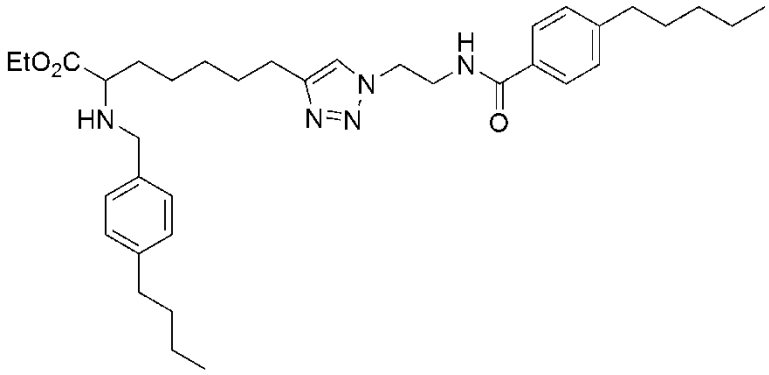


Amine 5c was synthesized as described in the general procedure using the α-amino ethyl ester HCl salt (1 mmol), $LiOH.H_2O$ (1.1 mmol), 4-isopropylbenzaldehyde (1 mmol), sodium borohydride (2 mmol). Following purification via flash column chromatography, **amine 5c** was obtained as a clear oil (32% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, 2H, *J* = 8.8 Hz), 7.65 (t, 1H, *J* = 5.8 Hz), 7.26 - 7.13 (m, 7H), 4.51 (t, 2H, *J* = 5.8 Hz), 4.13 (q, 2H, *J* = 7.2 Hz), 3.88 (m, 2H), 3.72 (d, 1H, *J* = 12.4 Hz), 3.56 (d, 1H, *J* = 12.8 Hz), 3.20 (t, 1H, *J* = 6.6 Hz), 2.85 (sp, 1H, *J* = 7.0 Hz), 2.60 - 2.57 (m, 4H), 1.98 (br s, 1H), 1.56 - 1.19 (m, 23H), 0.85 (t, 3H, *J* = 6.8 Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ 175.3, 167.8, 147.7, 147.4, 146.8, 137.0, 131.0, 128.3, 128.0, 127.0, 126.2, 121.7, 60.5, 60.3, 51.7, 49.0, 39.8, 35.6, 33.6, 33.2, 31.2, 30.7, 29.0, 28.7, 25.2, 23.8, 23.8, 22.3, 14.2, 13.8; IR

(KBr) ν(cm^{-1}) 3349, 2946, 1722, 1644, 1164; λ_{max} = 203 nm; HRMS (ESI): *m/z*: Calcd for $C_{35}H_{51}N_5O_3$: 590.4065 $[M+H]^+$, found: 590.4065.

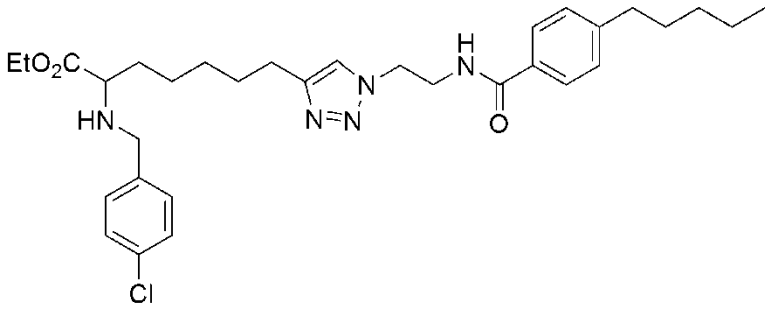
ethyl 2-(4-butylbenzylamino)-7-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)heptanoate (amine 5d)



Amine 5d was synthesized as described in the general procedure using the α-amino ethyl ester HCl salt (1 mmol), $LiOH.H_2O$ (1.1 mmol), 4-butylbenzaldehyde (1 mmol), sodium borohydride (2 mmol). Following purification via flash column chromatography, **amine 5d** was obtained as a clear oil (29% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67 (d, 2H, *J* = 8.1 Hz), 7.29 - 7.11 (m, 7H), 6.92 (t, 1H, *J* = 5.6 Hz), 4.55 (t, 2H, *J* = 7.4 Hz), 4.17 (q, 2H, *J* = 7.2 Hz), 3.95 (m, 2H), 3.76 (d, 1H, *J* = 12.6 Hz), 3.59 (d, 1H, *J* = 12.6 Hz), 3.23 (t, 1H, *J* = 6.8 Hz), 2.70 - 2.56 (m, 6H), 1.87 (br s, 1H), 1.66 - 1.25 (m, 21H), 0.94 - 0.86 (m, 6H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 175.5, 167.8, 148.1, 147.1, 141.6, 136.9, 131.1, 128.5, 128.3, 128.1, 127.0, 121.7, 60.6, 60.5, 51.8, 49.2, 39.8, 35.7, 35.2, 33.6, 33.3, 31.3, 30.8, 29.1, 28.9, 25.4, 25.4, 22.4, 22.3, 14.3, 13.9, 13.8; IR (KBr) ν(cm^{-1}) 3313, 2932, 1728, 1667, 1187; λ_{max} = 221 nm; HRMS (ESI): *m/z*: Calcd for $C_{36}H_{53}N_5O_3$: 604.4221 $[M+H]^+$, found: 604.4242.

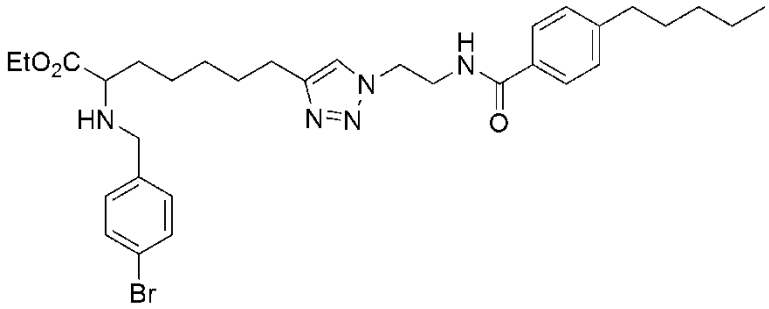
ethyl 2-(4-chlorobenzylamino)-7-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)heptanoate (amine 5e)



Amine 5e was synthesized as described in the general procedure using the α-amino ethyl ester HCl salt (1 mmol), $LiOH.H_2O$ (1.1 mmol), 4-chlorobenzaldehyde (1 mmol), sodium borohydride (2 mmol). Following purification via flash column chromatography, **amine 5e** was obtained as a clear oil (73% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, 2H, *J* = 8.4 Hz), 7.28 - 7.17 (m, 8H), 4.53 (t, 2H, *J* = 5.8 Hz), 4.16 (q, 2H, *J* = 7.2 Hz), 3.92 (m, 2H), 3.75 (d, 1H, *J* = 13.2 Hz), 3.55 (d, 1H, *J* = 13.2 Hz), 3.12 (t, 1H, *J* = 6.6 Hz), 2.64 - 2.58 (m, 4H), 1.95 (br s, 1H), 1.63 - 1.24 (m, 17H), 0.86 (t, 3H, *J* = 7.0 Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ 175.3, 167.8, 148.0, 147.1, 138.3, 132.6, 131.1, 129.5, 128.5, 128.3, 127.0, 121.7, 60.5, 60.4, 51.3, 49.2, 39.8, 35.7, 33.3, 31.3, 30.8, 29.1, 28.8, 25.4, 25.3, 22.4, 14.3, 13.9; IR (KBr) *ν*(cm^{-1}) 3301, 2926, 1733, 1644, 754; λ_{max} = 224 nm; HRMS (ESI): *m/z*: Calcd for $C_{32}H_{44}ClN_5O_3$: 582.3205 $[M+H]^+$, found: 582.3209.

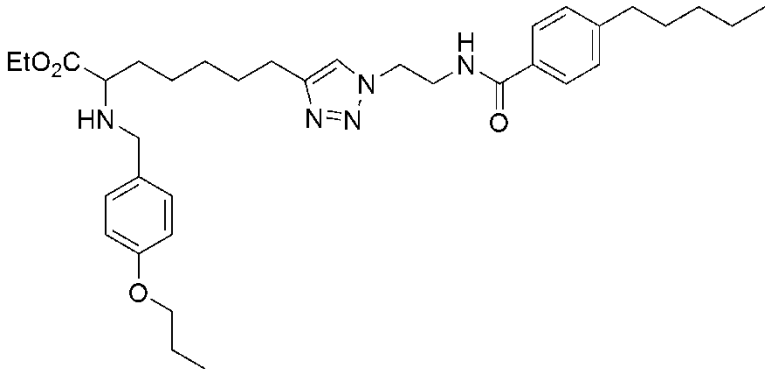
ethyl 2-(4-bromobenzylamino)-7-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)heptanoate (amine 5f)



Amine 5f was synthesized as described in the general procedure using the α-amino ethyl ester HCl salt (1 mmol), $LiOH.H_2O$ (1.1 mmol), 4-bromobenzaldehyde (1 mmol), sodium borohydride (2 mmol). Following purification via flash column chromatography, **amine 5f** was obtained as a clear oil (52% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, 2H, *J* = 8.0 Hz), 7.41 - 7.17 (m, 8H), 4.53 (t, 2H, *J* = 5.8 Hz), 4.15 (q, 2H, *J* = 7.0 Hz), 3.92 (m, 2H), 3.74 (d, 1H, *J* = 13.2 Hz), 3.54 (d, 1H, *J* = 13.2 Hz), 3.15 (t, 1H, *J* = 6.6 Hz), 2.64 - 2.58 (m, 4H), 1.97 (br s, 1H), 1.63 - 1.25 (m, 17H), 0.86 (t, 3H, *J* = 7.0 Hz) ; ^{13}C NMR (400 MHz, $CDCl_3$) δ 175.3, 167.8, 148.0, 147.1, 138.8, 131.3, 131.1, 129.9, 128.5, 127.0, 121.7, 120.7, 60.5, 60.4, 51.6, 51.3, 49.2, 39.8, 35.7, 33.3, 31.3, 30.7, 29.1, 28.8, 25.4, 22.4, 14.3, 13.9; IR (KBr) *ν*(cm^{-1}) 3319, 2932, 1726, 1653, 702; λ_{max} = 225 nm; HRMS (ESI): *m/z*: Calcd for $C_{32}H_{44}BrN_5O_3$: 626.2700 $[M+H]^+$, found: 626.2691.

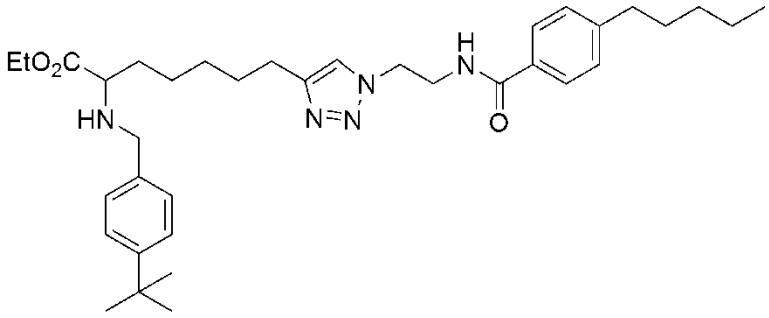
ethyl 7-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)-2-(4-propoxybenzylamino)heptanoate (amine 5g)



Amine 5g was synthesized as described in the general procedure using the α-amino ethyl ester HCl salt (1 mmol), $LiOH.H_2O$ (1.1 mmol), 4-propoxybenzaldehyde (1 mmol), sodium borohydride (2 mmol). Following purification via flash column chromatography, **amine 5g** was obtained as a clear oil (41% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, 2H, J = 8.0 Hz), 7.31 - 7.17 (m, 6H), 6.82 (d, 2H, J = 8.4 Hz), 4.52 (t, 2H, J = 5.4 Hz), 4.16 (q, 2H, J = 7.2 Hz), 3.93 - 3.86 (m, 4H), 3.70 (m, 1H), 3.53 (m, 1H), 3.20 (m, 1H), 2.63 - 2.58 (m, 4H), 2.07 (br s, 1H), 1.82 - 1.24 (m, 19H), 1.00 (t, 3H, J = 7.4 Hz), 0.86 (t, 3H, J = 7.0 Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ 175.4, 167.8, 158.2, 148.0, 147.0, 131.5, 131.1, 129.3, 128.5, 127.0, 121.7, 114.2, 69.4, 60.4, 60.3, 51.5, 51.4, 49.2, 39.8, 35.7, 33.2, 31.3, 30.7, 29.1, 28.8, 25.3, 22.5, 22.4, 14.3, 13.9, 10.4; IR (KBr) ν(cm^{-1}) 3402, 2937, 1726, 1504, 1239; λ_{max} = 201 nm, 226 nm; HRMS (ESI): *m/z*: Calcd for $C_{35}H_{51}N_5O_4$: 606.4014 $[M+H]^+$, found: 606.4013.

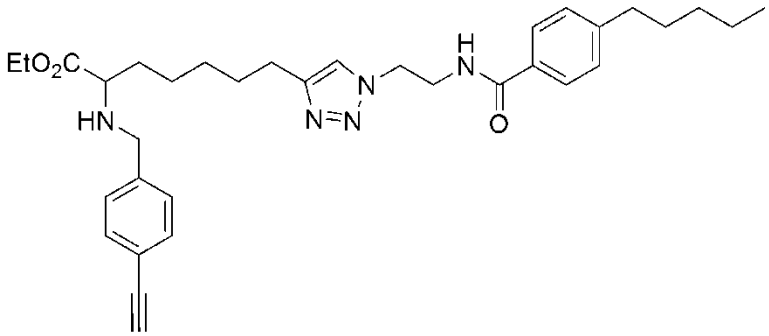
ethyl 2-(4-tert-butylbenzylamino)-7-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)heptanoate (amine 5h)



Amine 5h was synthesized as described in the general procedure using the α-amino ethyl ester HCl salt (1 mmol), $LiOH.H_2O$ (1.1 mmol), 4-tert-butylbenzaldehyde (1 mmol), sodium borohydride (2 mmol). Following purification via flash column chromatography, **amine 5h** was obtained as a clear oil (71% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, 2H, J = 8.4 Hz), 7.34 - 7.18 (m, 8H), 4.53 (t, 2H, J = 5.6 Hz), 4.16 (q, 2H, J = 7.1 Hz), 3.92 (m, 2H), 3.76 (d, 1H, J = 12.8 Hz), 3.61 (d, 1H, J = 12.8 Hz), 3.24 (t, 1H, J = 6.6 Hz), 2.65 - 2.59 (m, 4H), 2.41 (br s, 1H), 1.64 - 1.24 (m, 26H), 0.88 (t, 3H, J = 7.0 Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ 175.2, 167.8, 149.9, 148.0, 147.1, 136.3, 131.1, 128.5, 128.0, 127.0, 125.2, 121.7, 60.6, 60.5, 51.6, 49.2, 39.8, 35.7, 34.3, 33.2, 31.3, 31.2, 30.8, 29.1, 28.8, 25.4, 25.3, 22.4, 14.3, 13.9; IR (KBr) ν(cm^{-1}) 3368, 2926, 1733, 1641, 1186; λ_{max} = 202 nm, 220 nm; HRMS (ESI): *m/z*: Calcd for $C_{36}H_{53}N_5O_3$: 604.4221 $[M+H]^+$, found: 604.4203.

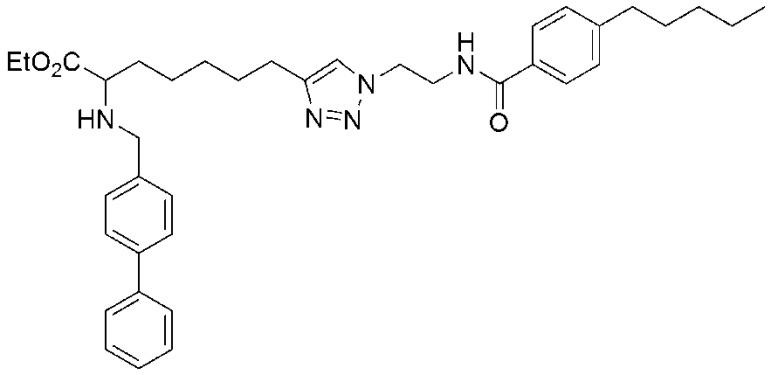
ethyl 2-(4-ethynylbenzylamino)-7-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)heptanoate (amine 5i)



Amine 5i was synthesized as described in the general procedure using the α-amino ethyl ester HCl salt (1 mmol), $LiOH.H_2O$ (1.1 mmol), 4-ethynylbenzaldehyde (1 mmol), sodium borohydride (2 mmol). Following purification via flash column chromatography, **amine 5i** was obtained as a clear oil (27% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, 2H, *J* = 8.1 Hz), 7.46 - 7.20 (m, 7H), 6.92 (br s, 1H), 4.55 (t, 2H, *J* = 5.6 Hz), 4.17 (q, 2H, *J* = 7.0 Hz), 3.95 (m, 2H), 3.83 (d, 1H, *J* = 13.2 Hz), 3.62 (d, 1H, *J* = 13.2 Hz), 3.20 (t, 1H, *J* = 6.6 Hz), 3.06 (s, 1H), 2.70 - 2.60 (m, 4H), 2.17 (br s, 1H), 1.66 - 1.21 (m, 17H), 0.88 (t, 3H, *J* = 6.8 Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ 176.0, 168.5, 148.7, 147.8, 141.3, 132.7, 131.8, 129.2, 128.8, 127.7, 122.4, 121.3, 84.2, 77.6, 61.3, 61.2, 52.3, 49.9, 40.5, 36.4, 34.0, 32.0, 31.5, 29.8, 29.5, 29.4, 26.1, 23.1, 15.0, 14.6; IR (KBr) ν(cm^{-1}) 3301, 2937, 2264, 1728, 1191; λ_{max} = 206 nm, 238 nm; HRMS (ESI): *m/z*: Calcd for $C_{34}H_{45}N_5O_3$: 572.3595 $[M+H]^+$, found: 572.3584.

ethyl 2-(biphenyl-4-ylmethylamino)-7-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)heptanoate (amine 5j)

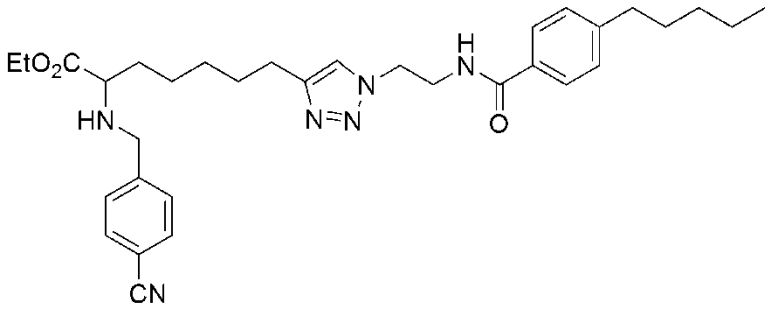


Amine 5j was synthesized as described in the general procedure using the α-amino ethyl ester HCl salt (1 mmol), $LiOH.H_2O$ (1.1 mmol), biphenyl-4-carbaldehyde (1 mmol), sodium borohydride (2 mmol). Following purification via flash column chromatography, **amine 5j** was obtained as a clear oil (40% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, 2H, *J* = 8.0 Hz), 7.59 - 7.27 (m, 10H), 7.20 (d, 2H, *J* = 8.4 Hz), 4.53 (t, 2H, *J* = 5.6 Hz), 4.19 (q, 2H, *J* = 7.2 Hz), 3.95 - 3.90 (m, 2H), 3.87 (d, 1H, *J* = 13.2 Hz), 3.69 (d, 1H, *J* = 13.2 Hz), 3.27 (t, 1H, *J* = 6.6 Hz), 2.67 - 2.59 (m, 4H), 1.68 - 1.24 (m, 18H), 0.88 (t, 3H, *J* = 7.0 Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ 175.2, 167.8, 148.1, 147.1, 140.8, 140.0, 138.5, 131.1, 128.7, 128.6, 128.5, 127.2, 127.1, 127.0, 126.9, 121.7, 60.6, 60.5, 51.6, 49.2,

39.8, 35.7, 33.2, 31.3, 30.8, 29.1, 28.8, 25.4, 25.3, 22.4, 14.3, 13.9; IR (KBr) ν(cm^{-1}) 3372, 2927, 1672, 1541, 1168; λ_{max} = 210 nm, 244 nm; HRMS (ESI): *m/z*: Calcd for $C_{38}H_{49}N_5O_3$: 624.3908 $[M+H]^+$, found: 624.3888.

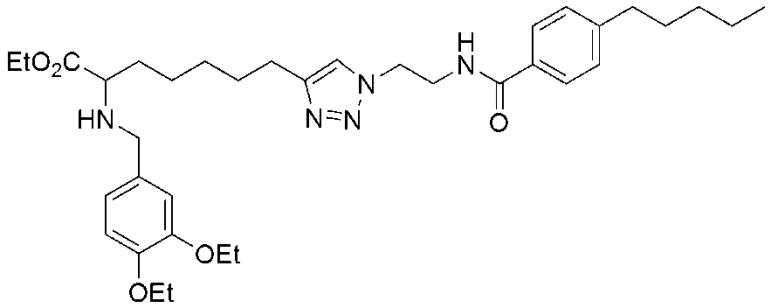
ethyl 2-(4-cyanobenzylamino)-7-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)heptanoate (amine 5k)



Amine 5k was synthesized as described in the general procedure using the α-amino ethyl ester HCl salt (1 mmol), $LiOH.H_2O$ (1.1 mmol), 4-formylbenzonitrile (1 mmol), sodium borohydride (2 mmol). Following purification via flash column chromatography, **amine 5k** was obtained as a clear oil (40% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, 2H, *J* = 8.4 Hz), 7.57 (d, 2H, *J* = 8.4 Hz), 7.43 (d, 2H, *J* = 8.4 Hz), 7.29 (s, 1H), 7.23 (br s, 1H), 7.18 (d, 2H, *J* = 8.8 Hz), 4.53 (t, 2H, *J* = 5.8 Hz), 4.16 (q, 2H, *J* = 7.1 Hz), 3.90 (m, 2H, 3.71 - 3.62 (m, 2H), 3.15 (t, 1H, *J* = 6.6 Hz), 2.66 - 2.57 (m, 4H), 2.55 (br s, 1H), 1.64 - 1.21 (m, 17H), 0.85 (t, 3H, *J* = 7.0 Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ 175.0, 167.8, 148.0, 147.1, 145.3, 132.3, 131.0, 128.7, 128.4, 127.0, 121.7, 118.8, 110.7, 60.6, 60.5, 51.4, 49.2, 39.7, 35.6, 33.2, 31.2, 30.7, 29.0, 28.8, 25.4, 25.3, 22.3, 14.2, 13.9; IR (KBr) ν(cm^{-1}) 3415, 2929, 2231, 1634, 1150; λ_{max} = 202 nm, 230 nm; HRMS (ESI): *m/z*: Calcd for $C_{33}H_{44}N_6O_3$: 573.3548 $[M+H]^+$, found: 573.3548.

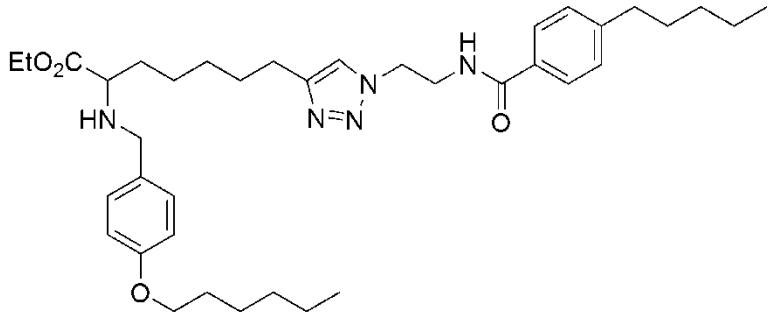
ethyl 2-(3,4-diethoxybenzylamino)-7-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)heptanoate (amine 5l)



Amine 5l was synthesized as described in the general procedure using the α-amino ethyl ester HCl salt (1 mmol), $LiOH.H_2O$ (1.1 mmol), 3,4-diethoxybenzaldehyde (1 mmol), sodium borohydride (2 mmol). Following purification via flash column chromatography, **amine 5l** was obtained as a clear oil (35% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, 2H, *J* = 8.0 Hz), 7.42 - 7.15 (m, 4H), 6.85 - 6.77 (m, 3H), 4.50 (t, 2H, *J* = 5.2 Hz), 4.17 - 3.49 (m, 10H), 3.17 (t, 1H, *J* = 6.6 Hz), 2.69 - 2.57 (m, 4H), 1.96 (br s, 1H), 1.58 - 1.22 (m, 23H), 0.85 (t, 3H, *J* = 6.4 Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ 175.3, 167.8, 148.5, 147.9, 147.6, 147.0, 132.4, 131.1, 128.4, 127.0, 121.6, 120.4, 113.5, 113.2, 64.4, 64.2, 60.3, 51.7, 49.1, 39.7, 35.6, 33.2, 31.2, 31.0, 30.7, 30.6, 29.0, 28.8, 25.3, 25.2, 22.3, 14.7, 14.2, 13.8; IR (KBr) ν(cm^{-1}) 3405, 2936, 1634, 1262; λ_{max} = 204 nm; 230 nm; HRMS (ESI): *m/z*: Calcd for $C_{36}H_{53}N_5O_5$: 636.4119 $[M+H]^+$, found: 636.4123.

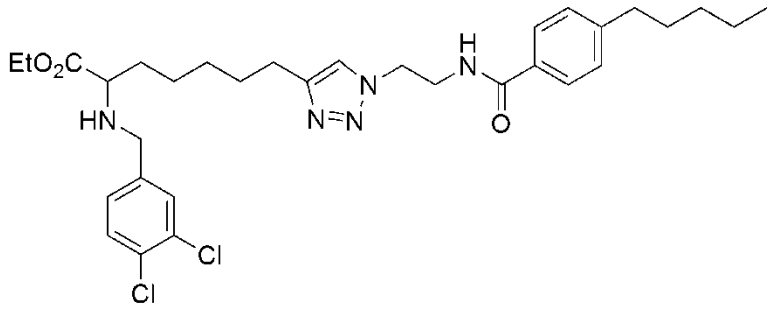
ethyl 2-(4-(hexyloxy)benzylamino)-7-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)heptanoate (amine 5m)



Amine 5m was synthesized as described in the general procedure using the α-amino ethyl ester HCl salt (1 mmol), $LiOH.H_2O$ (1.1 mmol), 4-(hexyloxy)benzaldehyde (1 mmol), sodium borohydride (2 mmol). Following purification via flash column chromatography, **amine 5m** was obtained as a clear oil (63% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, 2H, *J* = 8.4 Hz), 7.30 - 7.19 (m, 5H), 7.00 (t, 1H, *J* = 5.4 Hz), 6.82 (d, 2H, *J* = 8.7 Hz), 4.54 (t, 2H, *J* = 5.6 Hz), 4.17 (q, 2H, *J* = 7.2 Hz), 3.97 - 3.90 (m, 4H), 3.73 (d, 1H, *J* = 12.6 Hz), 3.56 (d, 1H, *J* = 12.6 Hz), 3.21 (t, 1H, *J* = 6.6 Hz), 2.68 - 2.59 (m, 4H), 2.07 (br s, 1H), 1.80 - 1.24 (m, 25H), 0.91 - 0.85 (m, 6H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 175.2, 167.8, 158.1, 147.7, 146.8, 131.3, 131.0, 129.2, 128.3, 127.0, 121.6, 114.1, 67.7, 60.3, 60.2, 51.3, 49.0, 39.8, 35.2, 33.1, 31.3, 31.2, 30.6, 29.0, 28.9, 28.7, 25.5, 25.2, 25.1, 22.4, 22.2, 14.1, 13.8, 13.7; IR (KBr) ν(cm^{-1}) 3411, 2934, 1702, 1219; λ_{max} = 202 nm, 226 nm; HRMS (ESI): *m/z*: Calcd for $C_{38}H_{57}N_5O_4$: 648.4483 $[M+H]^+$, found: 648.4483.

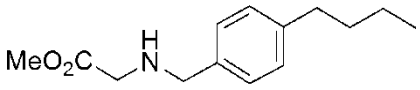
ethyl 2-(3,4-dichlorobenzylamino)-7-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)heptanoate (amine 5n)



Amine 5n was synthesized as described in the general procedure using the α-amino ethyl ester HCl salt (1 mmol), $LiOH.H_2O$ (1.1 mmol), 3,4-dichlorobenzaldehyde (1 mmol), sodium borohydride (2 mmol). Following purification via flash column chromatography, **amine 5n** was obtained as a clear oil (43% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, 2H, *J* = 8.0 Hz), 7.46 - 7.17 (m, 6H), 6.96 (br s, 1H), 4.55 (t, 2H, *J* = 5.6 Hz), 4.18 (q, 2H, *J* = 7.1 Hz), 3.98 - 3.93 (m, 2H), 3.80 (d, 1H, *J* = 13.6 Hz), 3.59 (d, 1H, *J* = 13.6 Hz), 3.19 (t, 1H, *J* = 6.6 Hz), 2.69 - 2.60 (m, 4H), 2.17 (br s, 1H), 1.66 - 1.26 (m, 17H), 0.88 (t, 3H, *J* = 6.8 Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ 174.7, 167.8, 148.0, 147.1, 139.4, 132.3, 131.1, 130.2, 130.1, 128.5, 127.7, 127.6, 127.0, 121.8, 60.8, 60.3, 50.6, 49.3, 39.8, 35.7, 33.0, 31.3, 30.8, 29.6, 29.0, 28.7, 25.3, 22.4, 14.3, 13.9; IR (KBr) ν(cm^{-1}) 3326, 2924, 1644, 751; λ_{max} = 202 nm, 226 nm; HRMS (ESI): *m/z*: Calcd for $C_{32}H_{43}Cl_2N_5O_3$: 616.2816 $[M+H]^+$, found: 616.2818.

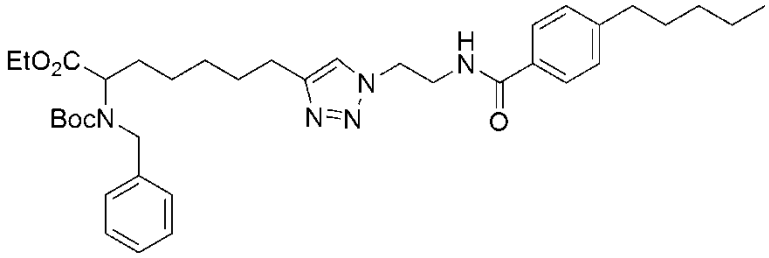
methyl 2-(4-butylbenzylamino)acetate



Methyl 2-(4-butylbenzylamino)acetate was synthesized as described in the general procedure using glycine methyl ester hydrochloride (1 mmol), $LiOH.H_2O$ (1.1 mmol), 4-butylbenzaldehyde (1 mmol), sodium borohydride (2 mmol). Following purification via flash column chromatography, methyl 2-(4-butylbenzylamino)acetate was obtained as a clear oil (49% yield)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (d, 2H, *J* = 8.0 Hz), 7.15 (d, 2H, *J* = 8.0 Hz), 3.78 (s, 2H), 3.73 (s, 3H), 3.43 (s, 2H), 2.60 (t, 2H, *J* = 7.8 Hz), 2.17 (br s, 1H), 1.60 (qn, 2H, *J* = 7.6 Hz), 1.36 (sx, 2H, *J* = 7.6 Hz), 0.93 (t, 3H, *J* = 7.2 Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ 172.9, 141.8, 136.5, 128.5, 128.2, 53.0, 51.7, 49.9, 35.3, 33.6, 22.3, 13.9; IR (KBr) ν(cm^{-1}) 3459, 2942, 1721, 1189; λ_{max} = 219 nm, 260 nm; HRMS (ESI): *m/z*: Calcd for $C_{14}H_{21}NO_2$: 236.1645 $[M+H]^+$, found: 236.1637.

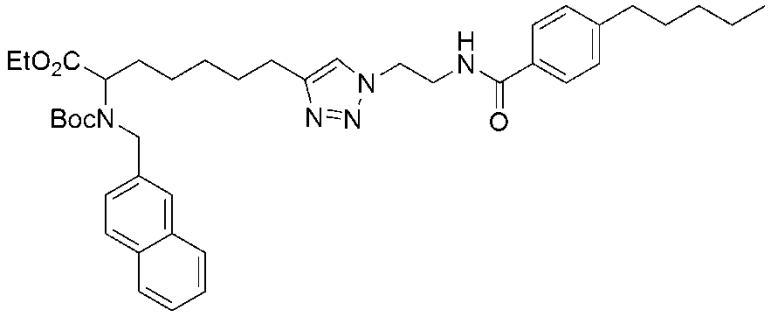
ethyl 2-(benzyl(tert-butoxycarbonyl)amino)-7-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)heptanoate (boc 5a)



Boc 5a was synthesized as described in the general procedure using **amine 5a** (0.25 mmol), triethylamine (0.33 mmol), di-tert-butyl dicarbonate (0.75 mmol). Following completion of the reaction via TLC, the crude product was purified via flash column chromatography. **Boc 5a** was obtained as a clear oil (75% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, 2H, *J* = 8.4 Hz), 7.30 - 7.21 (m, 8H), 6.93 (br s, 1H), 4.63 - 3.92 (m, 9H), 2.65 - 2.60 (m, 4H), 1.90 - 1.17 (m, 26H), 0.89 (t, 3H, *J* = 7.0 Hz) ; ^{13}C NMR (400 MHz, $CDCl_3$) δ 171.7 and 171.5 (rotamers), 167.8, 155.8 and 155.6 (rotamers), 147.9, 147.0, 138.8 and 138.0 (rotamers), 131.0, 128.4, 128.1, 127.2, 127.1, 127.0, 121.7, 80.4, 60.8, 59.5 and 58.9 (rotamers), 51.0 and 49.7 (rotamers), 49.2, 39.8, 35.6, 31.2, 30.8, 30.1, 29.3, 28.7 and 28.5 (rotamers), 28.2, 26.2 and 26.0 (rotamers), 25.3, 22.3, 13.9, 13.8; IR (KBr) *v*(cm^{-1}) 3317, 2926, 1697, 1536, 1166; λ_{max} = 202 nm, 232 nm; HRMS (ESI): *m/z*: Calcd for $C_{37}H_{53}N_5O_5$: 648.4119 $[M+H]^+$, found: 648.4134.

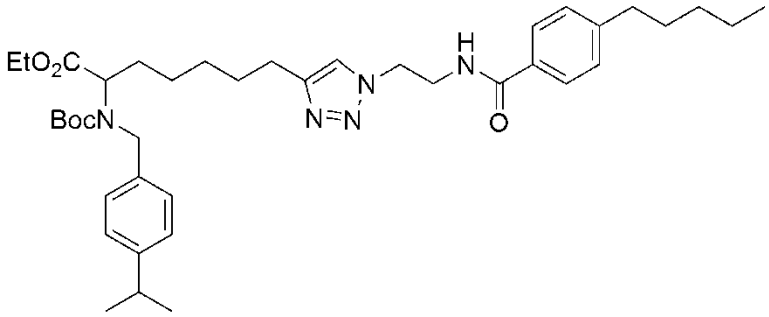
ethyl 2-(tert-butoxycarbonyl(naphthalen-2-ylmethyl)amino)-7-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)heptanoate (boc 5b)



Boc 5b was synthesized as described in the general procedure using **amine 5b** (0.25 mmol), triethylamine (0.33 mmol), di-tert-butyl dicarbonate (0.75 mmol). Following completion of the reaction via TLC, the crude product was purified via flash column chromatography. **Boc 5b** was obtained as a clear oil (73% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 - 7.39 (m, 10H), 7.15 (d, 2H, *J* = 8.0 Hz), 7.11 (s, 1H), 4.78 - 4.42 (m, 5H), 4.00 - 3.85 (m, 4H), 2.57 (t, 2H, *J* = 7.8 Hz), 2.40 (br s, 2H), 1.87 - 1.11 (m, 26H), 0.84 (t, 3H, *J* = 6.8 Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ 171.6 and 171.4 (rotamers), 167.7, 155.6 and 155.5 (rotamers), 147.6, 146.8, 136.1 and 135.4 (rotamers), 132.9, 132.5 and 132.3 (rotamers), 131.0, 128.3, 127.8, 127.6, 127.4, 127.0, 126.8, 126.6, 125.8, 125.5, 121.5, 80.4, 60.7, 59.4 and 58.9 (rotamers), 51.6 and 51.2 (rotamers), 49.9 and 49.5 (rotamers), 49.0, 39.7, 35.5, 31.1, 30.6, 29.9 and 29.2 (rotamers), 28.7 and 28.4 (rotamers), 28.1, 25.9, 25.0, 22.2, 13.8, 13.7; IR (KBr) *v*(cm^{-1}) 3270, 2926, 1733, 1686, 1155; λ_{max} = 226 nm; HRMS (ESI): *m/z*: Calcd for $C_{41}H_{44}N_5O_5$: 698.4276 $[M+H]^+$, found: 698.4274.

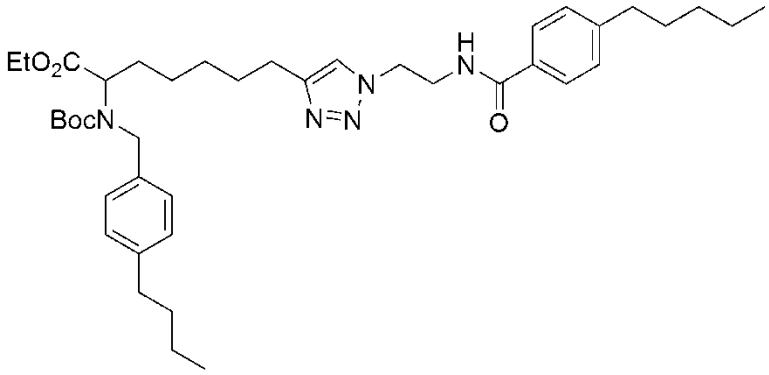
ethyl 2-(tert-butoxycarbonyl(4-isopropylbenzyl)amino)-7-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)heptanoate (boc 5c)



Boc 5c was synthesized as described in the general procedure using **amine 5c** (0.25 mmol), triethylamine (0.33 mmol), di-tert-butyl dicarbonate (0.75 mmol). Following completion of the reaction via TLC, the crude product was purified via flash column chromatography. **Boc 5c** was obtained as a clear oil (70% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67 (d, 2H, *J* = 8.1 Hz), 7.28 - 7.13 (m, 7H), 6.95 (br s, 1H), 4.57 - 4.42 (m, 4H), 3.98 - 3.92 (m, 4H), 3.71 (s, 1H), 2.86 (sp, 1H, *J* = 6.9 Hz) , 2.65 - 2.59 (m, 4H), 1.98 - 1.13 (m, 32H), 0.88 (t, 3H, *J* = 6.8 Hz); ^{13}C NMR (300 MHz, $CDCl_3$) δ 171.6, 167.8, 155.7 and 155.5 (rotamers), 147.9, 147.7 and 147.5 (rotamers), 147.0, 136.0 and 135.2 (rotamers), 131.0, 128.4, 127.5, 127.0, 126.0, 121.6, 80.3, 66.9, 60.7, 59.4 and 58.7 (rotamers), 50.7 and 49.5 (rotamers), 49.2, 39.8, 35.6, 33.6, 31.3, 30.8, 29.0, 28.8 and 28.6 (rotamers), 28.2, 26.1 and 26.0 (rotamers), 25.3, 23.9, 22.3, 13.9, 13.8; IR (KBr) *v*(cm^{-1}) 3419, 2921, 1713, 1686, 1161; λ_{max} = 203 nm, 220; HRMS (ESI): *m/z*: Calcd for $C_{40}H_{59}N_5O_5$: 690.4589 $[M+H]^+$, found: 690.4605.

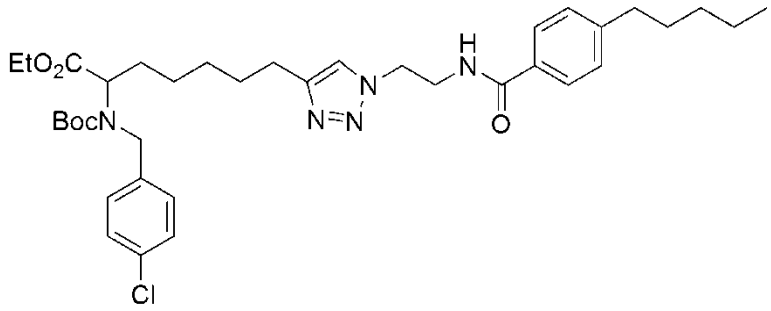
ethyl 2-(tert-butoxycarbonyl(4-butylbenzyl)amino)-7-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)heptanoate (boc 5d)



Boc 5d was synthesized as described in the general procedure using **amine 5d** (0.25 mmol), triethylamine (0.33 mmol), di-tert-butyl dicarbonate (0.75 mmol). Following completion of the reaction via TLC, the crude product was purified via flash column chromatography. **Boc 5d** was obtained as a clear oil (81% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, 2H, *J* = 7.6 Hz) 7.42 (br s, 1H), 7.19 - 7.14 (m, 5H), 7.07 (d, 2H, *J* = 7.6 Hz) 4.53 - 4.19 (m, 5H), 4.05 - 3.86 (m, 4H), 2.62 - 2.54 (m, 6H), 1.91 - 1.13 (m, 30H), 0.89 - 0.84 (m, 6H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 171.7 and 171.6 (rotamers), 167.8, 155.7 and 155.5 (rotamers), 147.9, 147.0, 141.7 and 141.5 (rotamers), 135.8 and 135.0 (rotamers), 131.0, 128.4, 128.1, 127.3, 127.0, 121.6, 80.3, 60.7, 59.3 and 58.8 (rotamers), 50.7 and 49.5 (rotamers), 49.2, 39.8, 35.6, 35.1, 33.5, 31.2, 30.7, 30.0, 29.2 and 29.0 (rotamers), 28.7 and 28.5 (rotamers), 28.1, 26.1 and 25.9 (rotamers), 25.2, 22.3, 22.1, 13.9, 13.8, 13.7; IR (KBr) *v*(cm^{-1}) 3422, 2932, 1686, 1634, 1165; λ_{max} = 206 nm, 221 nm; HRMS (ESI): *m/z*: Calcd for $C_{41}H_{61}N_5O_5$: 704.4745 $[M+H]^+$, found: 704.4758.

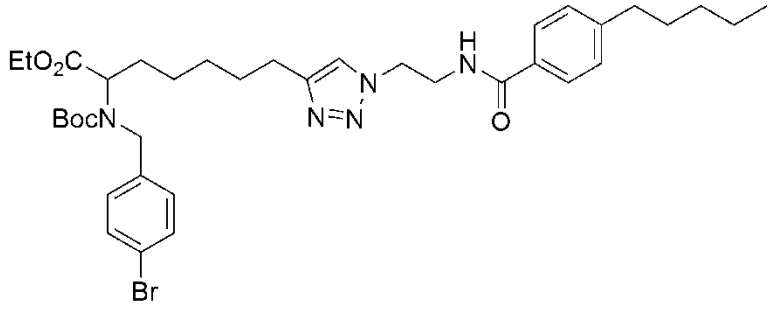
ethyl 2-(tert-butoxycarbonyl(4-chlorobenzyl)amino)-7-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)heptanoate (boc 5e)



Boc 5e was synthesized as described in the general procedure using **amine 5e** (0.25 mmol), triethylamine (0.33 mmol), di-tert-butyl dicarbonate (0.75 mmol). Following completion of the reaction via TLC, the crude product was purified via flash column chromatography. **Boc 5e** was obtained as a clear oil (74% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, 2H, J = 8.0 Hz), 7.42 - 7.06 (m, 8H), 4.60 (t, 2H, J = 5.6 Hz), 4.50 - 3.95 (m, 7H), 2.68 - 2.61 (m, 4H), 1.72 - 1.18 (m, 26H), 0.89 (t, 3H, J = 7.0 Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ 171.4 and 171.2 (rotamers), 167.7, 155.4, 147.6, 146.8, 137.4 and 136.6 (rotamers), 132.6 and 132.3 (rotamers), 131.0, 129.5, 128.2, 128.0, 127.0, 121.6, 80.5, 60.7, 59.6 and 58.8 (rotamers), 50.1, 49.0, 39.7, 35.5, 31.1, 30.6, 29.9, 29.2, 28.9 and 28.5 (rotamers), 28.0, 26.0, 25.1, 22.2, 13.8, 13.7; IR (KBr) v(cm^{-1}) 3308, 2918, 1728, 1634, 732; λ_{max} = 227 nm; HRMS (ESI): *m/z*: Calcd for $C_{37}H_{52}ClN_5O_5$: 682.373 $[M+H]^+$, found: 682.3719.

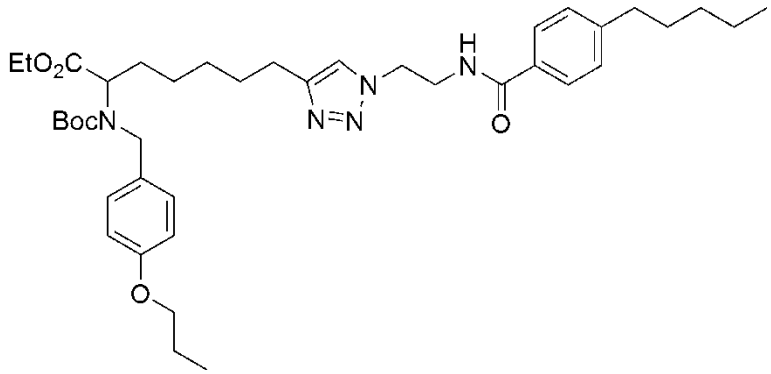
ethyl 2-((4-bromobenzyl)(tert-butoxycarbonyl)amino)-7-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)heptanoate (boc 5f)



Boc 5f was synthesized as described in the general procedure using **amine 5f** (0.25 mmol), triethylamine (0.33 mmol), di-tert-butyl dicarbonate (0.75 mmol). Following completion of the reaction via TLC, the crude product was purified via flash column chromatography. **Boc 5f** was obtained as a clear oil (79% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, 2H, J = 8.0 Hz), 7.51 (br s, 1H), 7.36 - 7.33 (m, 4H), 7.15 - 7.09 (m, 3H), 4.51 - 3.86 (m, 9H), 2.58 - 2.51 (m, 4H), 1.87 - 1.12 (m, 26H), 0.83 (t, 3H, J = 6.6 Hz) ; ^{13}C NMR (400 MHz, $CDCl_3$) δ 171.5 and 171.2 (rotamers), 167.8, 155.4, 147.7, 146.9, 137.9 and 137.1 (rotamers), 131.0, 129.9, 128.8, 128.3, 127.0, 121.6, 120.8 and 120.4 (rotamers), 80.5, 60.8, 59.7 and 58.9 (rotamers), 50.2, 49.1, 39.7, 35.5, 31.2, 30.6, 29.9, 29.4, 28.9 and 28.6 (rotamers), 28.0, 26.0 and 25.9 (rotamers), 25.2, 22.2, 13.9, 13.8; IR (KBr) v(cm^{-1}) 3318, 2937, 1686, 1161, 492; λ_{max} = 202 nm, 226 nm; HRMS (ESI): *m/z*: Calcd for $C_{37}H_{52}BrN_5O_5$: 726.3225 $[M+H]^+$, found: 726.3215.

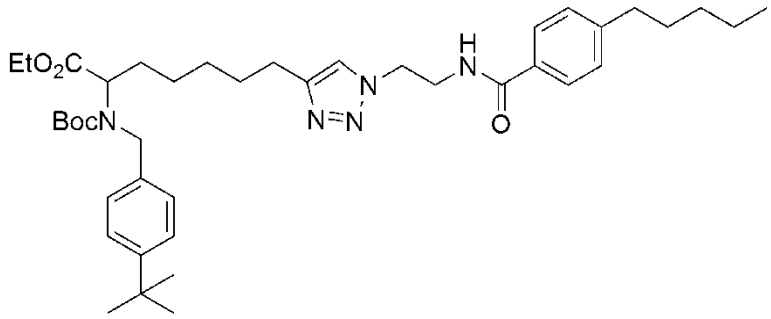
ethyl 2-(tert-butoxycarbonyl(4-propoxybenzyl)amino)-7-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)heptanoate (boc 5g)



Boc 5g was synthesized as described in the general procedure using **amine 5g** (0.25 mmol), triethylamine (0.33 mmol), di-tert-butyl dicarbonate (0.75 mmol). Following completion of the reaction via TLC, the crude product was purified via flash column chromatography. **Boc 5g** was obtained as a clear oil (66% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, 2H, *J* = 8.4 Hz), 7.28 (d, 2H, *J* = 6.8 Hz), 7.22 - 7.05 (m, 4H), 6.81 (d, 2H, *J* = 8.4 Hz), 4.56 - 3.88 (m, 11H), 2.64 - 2.60 (m, 4H), 1.79 - 1.16 (m, 28H), 1.00 (t, 3H, *J* = 7.6 Hz), 0.88 (t, 3H, *J* = 7.0 Hz) ; ^{13}C NMR (400 MHz, $CDCl_3$) δ 171.6, 167.8, 158.3, 155.5, 147.9, 147.0, 131.0, 129.7, 128.6, 128.4, 127.0, 121.7, 114.1, 80.4 and 80.3 (rotamers), 69.4, 60.7, 59.2 and 58.8 (rotamers), 51.7, 50.5, 49.2, 39.7, 35.6, 31.2, 30.7, 29.0 and 28.7 (rotamers), 28.5, 28.2, 26.1, 25.2, 22.4, 22.3, 13.9, 13.8, 10.3; IR (KBr) ν(cm^{-1}) 3459, 2942, 1697, 1514, 1249; λ_{max} = 205 nm, 227 nm; HRMS (ESI): *m/z*: Calcd for $C_{40}H_{59}N_5O_6$: 706.4538 $[M+H]^+$, found: 706.4541.

ethyl 2-(tert-butoxycarbonyl(4-tert-butylbenzyl)amino)-7-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)heptanoate (boc 5h)

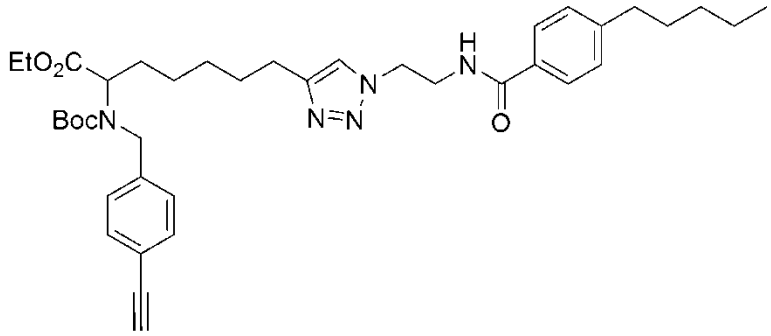


Boc 5h was synthesized as described in the general procedure using **amine 5h** (0.25 mmol), triethylamine (0.33 mmol), di-tert-butyl dicarbonate (0.75 mmol). Following completion of the reaction via TLC, the crude product was purified via flash column chromatography. **Boc 5h** was obtained as a clear oil (62% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, 2H, *J* = 8.4 Hz), 7.30 - 7.18 (m, 8H), 4.53 - 4.18 (m, 5H), 4.08 - 3.86 (m, 4H), 2.62 - 2.56 (m, 4H), 1.92 - 1.11 (m, 26H), 0.86 (t, 3H, *J* = 6.8 Hz) ; ^{13}C NMR (400 MHz, $CDCl_3$) δ 171.6, 167.8, 155.9 and 155.7 (rotamers), 149.9, 148.0, 147.1, 135.6

and 134.9 (rotamers), 131.1, 128.5, 127.3, 127.0, 125.0, 121.7, 80.4, 60.7, 59.4 and 58.8 (rotamers), 51.7 and 50.6 (rotamers), 49.2, 39.8, 35.7, 34.3, 31.3, 31.2, 30.8, 30.0, 29.1, 28.8 and 28.6 (rotamers), 28.2, 26.2 and 26.0 (rotamers), 25.3, 22.4, 13.9, 13.8; IR (KBr) ν(cm^{-1}) 3374, 2926, 1692, 1161; λ_{max} = 204 nm, 219 nm; HRMS (ESI): *m/z*: Calcd for $C_{41}H_{61}N_5O_5$: 704.4745 $[M+H]^+$, found: 704.4739.

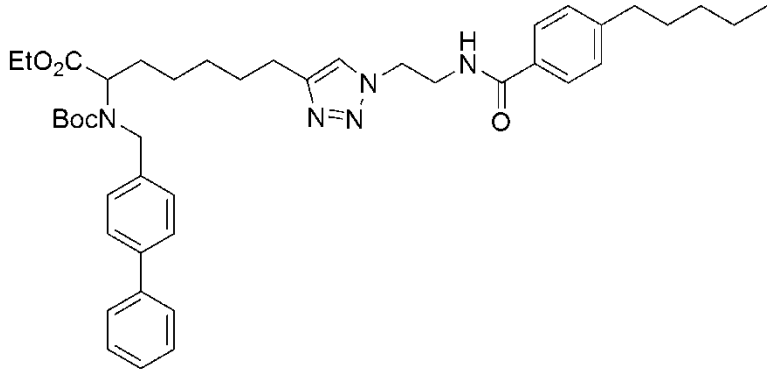
ethyl 2-(tert-butoxycarbonyl(4-ethynylbenzyl)amino)-7-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)heptanoate (boc 5i)



Boc 5i was synthesized as described in the general procedure using **amine 5i** (0.25 mmol), triethylamine (0.33 mmol), di-tert-butyl dicarbonate (0.75 mmol). Following completion of the reaction via TLC, the crude product was purified via flash column chromatography. **Boc 5i** was obtained as a clear oil (75% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, 2H, *J* = 8.0 Hz), 7.40 (d, 2H, *J* = 8.0 Hz), 7.29 - 7.13 (m, 6H), 4.56 - 3.91 (m, 9H), 3.07 (s, 1H), 2.63 - 2.57 (m, 4H), 1.91 - 1.16 (m, 26H), 0.87 (t, 3H, *J* = 6.8 Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ 171.7, 167.8, 155.8, 148.0, 147.1, 140.0 and 139.2 (rotamers), 131.9, 131.1, 128.5, 128.2, 127.0, 121.8, 120.7, 83.5, 80.7, 60.9, 59.8 and 59.0 (rotamers), 51.8 and 51.0 (rotamers), 49.3, 39.8, 35.7, 31.3, 30.8, 30.1, 29.4, 29.0, 28.6, 28.2, 26.0, 25.3, 22.4, 14.0, 13.9; IR (KBr) ν(cm^{-1}) 3296, 2926, 2358, 1697, 1165; λ_{max} = 203 nm, 231 nm; HRMS (ESI): *m/z*: Calcd for $C_{39}H_{53}N_5NaO_5$: 694.3939 $[M+Na]^+$, found: 694.3933.

ethyl 2-((biphenyl-4-ylmethyl)(tert-butoxycarbonyl)amino)-7-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)heptanoate (boc 5j)

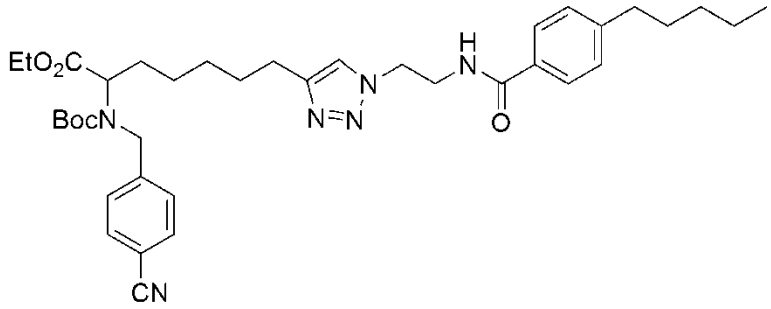


Boc 5j was synthesized as described in the general procedure using **amine 5j** (0.25 mmol), triethylamine (0.33 mmol), di-tert-butyl dicarbonate (0.75 mmol). Following completion of the

reaction via TLC, the crude product was purified via flash column chromatography. **Boc 5j** was obtained as a clear oil (63% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, 2H, *J* = 8.0 Hz), 7.57 - 7.12 (m, 11H), 6.98 (br s, 1H), 4.65 - 4.28 (m, 5H), 4.08 - 3.90 (m, 4H), 2.64 - 2.56 (m, 4H), 1.95 - 1.18 (m, 26H), 0.88 (t, 3H, *J* = 7.0 Hz) ; ^{13}C NMR (400 MHz, $CDCl_3$) δ 171.9, 167.8, 155.8, 148.1, 147.2, 140.7 and 139.7 (rotamers), 137.7 and 137.3 (rotamers), 131.1, 128.9, 128.7, 128.6, 127.8, 127.2, 127.0, 126.9, 126.7, 121.6, 80.6, 60.9, 59.8 and 59.1 (rotamers), 50.8 and 49.9 (rotamers), 49.3, 39.7, 35.7, 31.3, 30.8, 30.1, 29.1, 28.8, 28.3, 26.2, 25.4, 22.4, 14.0, 13.9; IR (KBr) ν(cm^{-1}) 3380, 2931, 1541, 1159; λ_{max} = 204 nm, 244 nm; HRMS (ESI): *m/z*: Calcd for $C_{43}H_{57}N_5O_5$: 724.4432 $[M+H]^+$, found: 724.4417.

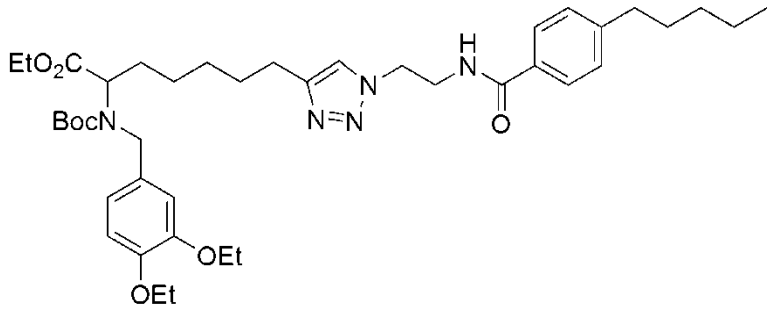
ethyl 2-(tert-butoxycarbonyl(4-cyanobenzyl)amino)-7-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)heptanoate (boc 5k)



Boc 5k was synthesized as described in the general procedure using **amine 5k** (0.25 mmol), triethylamine (0.33 mmol), di-tert-butyl dicarbonate (0.75 mmol). Following completion of the reaction via TLC, the crude product was purified via flash column chromatography. **Boc 5k** was obtained as a clear oil (90% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68 (d, 2H, *J* = 8.4 Hz), 7.59 (d, 2H, *J* = 8.1 Hz), 7.42 (br s, 2H), 7.31 (s, 1H), 7.22 (d, 2H, *J* = 8.4 Hz), 6.98 (br s, 1H), 4.62 - 3.95 (m, 9H), 2.65 - 2.60 (m, 4H), 1.93 - 1.18 (m, 26H), 0.88 (t, 3H, *J* = 6.8 Hz) ; ^{13}C NMR (400 MHz, $CDCl_3$) δ 171.5 and 171.1 (rotamers), 167.7, 155.4, 147.7, 146.9, 144.9 and 144.0 (rotamers), 132.3, 131.0, 128.3, 127.4, 126.9, 121.6, 118.6, 110.6 and 110.3 (rotamers), 80.9, 60.9, 60.1 and 58.9 (rotamers), 51.8 and 50.3 (rotamers), 49.1, 39.7, 35.5, 31.2, 30.6, 29.9 and 29.4 (rotamers), 28.9, 28.5, 28.0, 26.1 and 25.9 (rotamers), 25.2, 22.2, 13.9, 13.8; IR (KBr) ν(cm^{-1}) 3422, 2932, 2234, 1640, 1161; λ_{max} = 202 nm, 232 nm; HRMS (ESI): *m/z*: Calcd for $C_{38}H_{52}N_6O_5$: 673.4072 $[M+H]^+$, found: 673.0471.

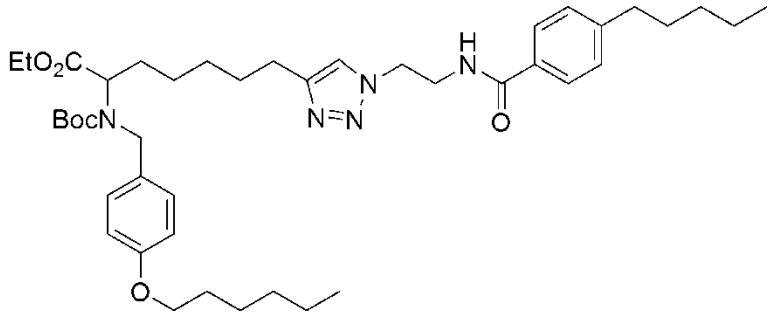
ethyl 2-(tert-butoxycarbonyl(3,4-diethoxybenzyl)amino)-7-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)heptanoate (boc 5l)



Boc 5l was synthesized as described in the general procedure using **amine 5l** (0.25 mmol), triethylamine (0.33 mmol), di-tert-butyl dicarbonate (0.75 mmol). Following completion of the reaction via TLC, the crude product was purified via flash column chromatography. **Boc 5l** was obtained as a clear oil (68% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, 2H, J = 8.0 Hz), 7.42 (br s, 1H), 7.28 (s, 1H), 7.14 (d, 2H, J = 8.0 Hz), 6.90 - 6.74 (m, 3H), 4.50 - 3.82 (m, 13H), 2.58 - 2.53 (m, 4H), 1.91 - 1.11 (m, 32H), 0.83 (t, 3H, J = 6.8 Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ 171.5, 167.7, 155.5, 148.4 and 147.6 (rotamers), 147.8, 146.9, 131.3 and 130.6 (rotamers), 131.0, 128.3, 127.0, 121.7, 120.8, 119.8, 113.8, 112.9, 80.2, 64.4, 64.2, 60.7, 59.2 and 58.9 (rotamers), 50.7 and 49.6 (rotamers), 49.1, 39.7, 35.6, 31.2, 30.7, 30.0, 28.9, 28.6 and 28.5 (rotamers), 28.1, 26.1, 25.2, 22.3, 14.6, 14.6, 13.9, 13.8; IR (KBr) ν(cm^{-1}) 3396, 2925, 1686, 1262, 1164; λ_{max} = 210 nm, 230 nm; HRMS (ESI): *m/z*: Calcd for $C_{41}H_{61}N_5O_7$: 736.4644 $[M+H]^+$, found: 736.4641.

ethyl 2-(tert-butoxycarbonyl(4-(hexyloxy)benzyl)amino)-7-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)heptanoate (boc 5m)

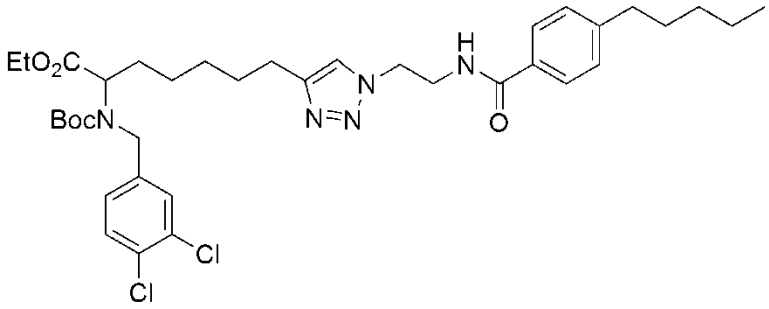


Boc 5m was synthesized as described in the general procedure using **amine 5m** (0.25 mmol), triethylamine (0.33 mmol), di-tert-butyl dicarbonate (0.75 mmol). Following completion of the reaction via TLC, the crude product was purified via flash column chromatography. **Boc 5m** was obtained as a clear oil (88% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.69 (d, 2H, J = 8.4 Hz), 7.32 - 7.08 (m, 6H), 6.81 (d, 2H, J = 8.4 Hz), 4.59 - 3.89 (m, 11H), 2.66 - 2.60 (m, 4H), 1.97 - 1.16 (m, 34H), 0.92 - 0.86 (m, 6H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 171.5, 167.8, 158.2 and 158.0 (rotamers), 155.4, 147.6, 146.9, 131.0, 130.3 and 129.6 (rotamers), 128.5, 128.3, 127.0, 121.8, 114.0, 80.2, 67.8, 60.6, 59.1 and 58.8 (rotamers), 50.4 and 49.4 (rotamers), 49.2, 39.7, 35.6, 31.4, 31.2, 30.7, 30.0, 29.0, 28.9, 28.6 and 28.5 (rotamers), 28.1, 26.0, 25.5, 25.1, 22.4, 22.3, 13.9, 13.8, 13.7; IR (KBr) ν(cm^{-1}) 3389, 2922,

1718, 1499, 1218; λ_{max} = 228 nm; HRMS (ESI): *m/z*: Calcd for $C_{43}H_{65}N_5O_6$: 747.5008 $[M+H]^+$, found: 747.5006.

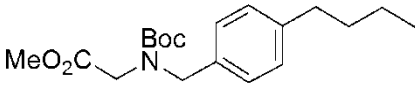
ethyl 2-(tert-butoxycarbonyl(3,4-dichlorobenzyl)amino)-7-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)heptanoate (boc 5n)



Boc 5n was synthesized as described in the general procedure using **amine 5n** (0.25 mmol), triethylamine (0.33 mmol), di-tert-butyl dicarbonate (0.75 mmol). Following completion of the reaction via TLC, the crude product was purified via flash column chromatography. **Boc 5n** was obtained as a clear oil (76% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, 2H, *J* = 8.0 Hz), 7.45 - 7.07 (m, 7H), 4.58 - 3.88 (m, 9H), 2.62 - 2.57 (m, 4H), 1.60 - 1.16 (m, 26H), 0.85 (t, 3H, *J* = 6.8 Hz) ; ^{13}C NMR (400 MHz, $CDCl_3$) δ 171.4 and 171.1 (rotamers), 167.8, 155.4, 147.4, 147.0, 139.4 and 138.6 (rotamers), 132.0, 130.9, 129.9, 129.0, 128.4, 127.5, 127.1, 126.4, 122.2, 80.9, 61.0, 59.9 and 59.0 (rotamers), 49.8 and 48.6 (rotamers), 49.6, 39.7, 35.6, 31.2, 30.7, 29.9 and 29.4 (rotamers), 28.9, 28.7 and 28.5 (rotamers), 28.1, 26.0, 25.0, 22.3, 13.9, 13.8; IR (KBr) *v*(cm^{-1}) 3334, 2922, 1672, 761; λ_{max} = 204 nm, 222 nm; HRMS (ESI): *m/z*: Calcd for $C_{37}H_{51}Cl_2N_5O_5$: 716.3340 $[M+H]^+$, found: 716.3347.

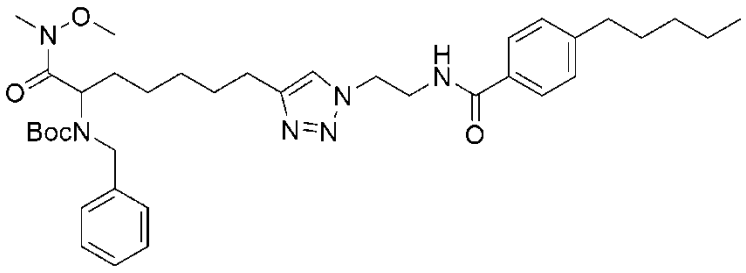
methyl 2-(tert-butoxycarbonyl(4-butylbenzyl)amino)acetate



Methyl 2-(tert-butoxycarbonyl(4-butylbenzyl)amino)acetate was synthesized as described in the general procedure using methyl 2-(4-butylbenzylamino)acetate (0.25 mmol), triethylamine (0.33 mmol), di-tert-butyl dicarbonate (0.75 mmol). Following completion of the reaction via TLC, the crude product was purified via flash column chromatography. Methyl 2-(tert-butoxycarbonyl(4-butylbenzyl)amino)acetate was obtained as a clear oil (91% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 - 7.14 (m, 4H), 4.51 and 4.48 (2 x s, 2H, rotamers), 3.92 and 3.78 (2 x s, 2H, rotamers), 3.71 (s, 3H), 2.59 (t, 2H, *J* = 7.6 Hz), 1.60 - 1.33 (m, 13H), 0.93 (t, 3H, *J* = 7.4 Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ 170.5 and 170.4 (rotamers), 155.8 and 155.5 (rotamers), 142.1, 134.6 and 134.4 (rotamers), 128.6, 128.1 and 127.5 (rotamers), 80.5 and 80.3 (rotamers), 51.9 and 51.8 (rotamers), 51.1 and 50.6 (rotamers), 47.7 and 47.2 (rotamers), 35.2, 33.6, 28.3 and 28.2 (rotamers), 22.3, 13.9; IR (KBr) *v*(cm^{-1}) 3458, 2932, 1759, 1187; λ_{max} = 220 nm, 262 nm; HRMS (ESI): *m/z*: Calcd for $C_{19}H_{29}NNaO_4$: 358.1989 $[M+Na]^+$, found: 358.1987.

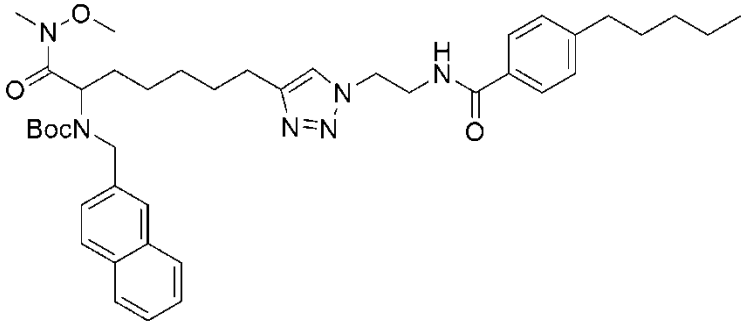
tert-butyl benzyl(1-(methoxy(methyl)amino)-1-oxo-7-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)heptan-2-yl)carbamate (6a)



6a was synthesized as described in the general procedure using **boc 5a** (0.20 mmol), *O,N*-dimethylhydroxylamine hydrochloride (1.00 mmol), and 2.0*M* isopropylmagnesium chloride solution in tetrahydrofuran (1.6 mmol). Upon completion of the reaction via TLC analysis, the crude product was purified via flash column chromatography. **6a** was obtained as a clear oil (71% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, 2H, J = 8.0 Hz), 7.53 (br s, 1H), 7.26 - 7.11 (m, 8H), 5.18 and 4.87 (2 x br s, 1H, rotamers), 4.54 - 4.27 (m, 4H), 3.87 - 3.83 (m, 2H), 3.63 and 3.54 (2 x br s, 3H, rotamers), 2.92 and 2.78 (2 x br s, 3H, rotamers), 2.59 - 2.52 (m, 4H), 1.77 - 1.18 (m, 23H), 0.83 (t, 3H, J = 6.8 Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ 171.9 and 170.9 (rotamers), 167.8, 155.7, 147.8, 146.9, 139.5 and 138.7 (rotamers), 131.0, 128.3, 127.8, 127.0, 126.7, 126.5 and 126.3 (rotamers), 121.6, 80.0, 61.5, 54.5 and 53.5 (rotamers), 49.0, 47.0 and 46.4 (rotamers), 39.8, 35.6, 31.7, 31.2, 30.7, 29.2 and 28.9 (rotamers), 28.6, 28.2, 28.0, 25.5, 25.2, 22.3, 13.8; IR (KBr) ν(cm^{-1}) 3437, 2932, 1660, 1160; λ_{max} = 235 nm; HRMS (ESI): *m/z*: Calcd for $C_{37}H_{54}N_6O_5$: 663.4228 $[M+H]^+$, found: 663.423.

tert-butyl 1-(methoxy(methyl)amino)-1-oxo-7-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)heptan-2-yl(naphthalen-2-ylmethyl)carbamate (6b)

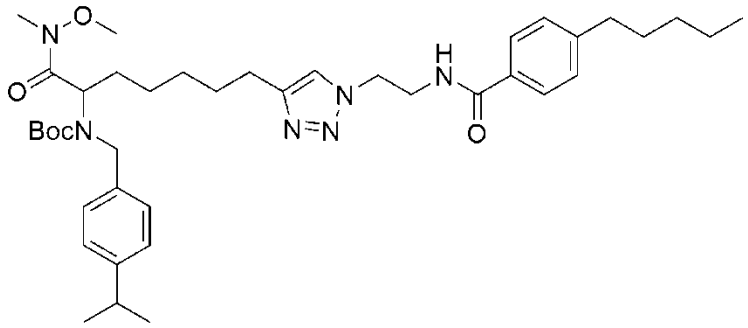


6b was synthesized as described in the general procedure using **boc 5b** (0.20 mmol), *O,N*-dimethylhydroxylamine hydrochloride (1.00 mmol), and 2.0*M* isopropylmagnesium chloride solution in tetrahydrofuran (1.6 mmol). Upon completion of the reaction via TLC analysis, the crude product was purified via flash column chromatography. **6b** was obtained as a clear oil (63% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 - 7.32 (m, 10H), 7.17 - 7.14 (m, 3H), 5.28 and 4.89 (2 x br s, 1H, rotamers), 4.72 - 4.47 (m, 4H), 3.89 - 3.84 (m, 2H), 3.68 and 3.56 (2 x br s, 3H, rotamers),

2.91 and 2.75 (2 x br s, 3H, rotamers), 2.58 (t, 2H, J = 7.8 Hz), 2.49 (t, 2H, J = 7.4 Hz), 1.80 - 1.16 (m, 23H), 0.85 (t, 3H, J = 6.8 Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ 171.9 and 171.0 (rotamers), 167.7, 155.8, 147.8, 146.9, 137.0 and 136.4 (rotamers), 133.0, 132.2, 131.0, 128.3, 127.4, 127.0, 126.1, 126.0, 125.7, 125.6, 125.2, 125.1, 121.6, 80.1, 61.5, 54.9 and 53.6 (rotamers), 49.0, 47.1 and 46.6 (rotamers), 39.7, 35.6, 31.8, 31.2, 30.7, 29.3, 28.9 and 28.6 (rotamers), 28.3, 28.0, 25.5, 25.1, 22.3, 13.8; IR (KBr) ν(cm^{-1}) 3395, 2937, 1689, 1537, 1169; λ_{max} = 224 nm; HRMS (ESI): *m/z*: Calcd for $C_{41}H_{56}N_6O_5$: 713.4385 $[M+H]^+$, found: 713.4381.

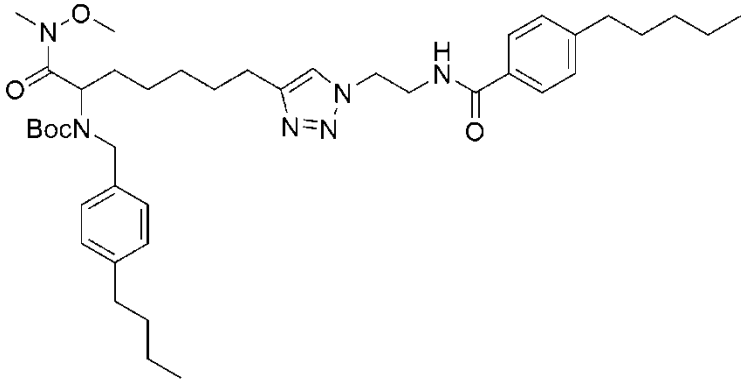
tert-butyl 4-isopropylbenzyl(1-(methoxy(methyl)amino)-1-oxo-7-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)heptan-2-yl)carbamate (6c)



6c was synthesized as described in the general procedure using **boc 5c** (0.20 mmol), *O,N*-dimethylhydroxylamine hydrochloride (1.00 mmol), and 2.0*M* isopropylmagnesium chloride solution in tetrahydrofuran (1.6 mmol). Upon completion of the reaction via TLC analysis, the crude product was purified via flash column chromatography. **6c** was obtained as a clear oil (87% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (br s, 1H), 7.70 (d, 2H, J = 8.4 Hz), 7.15 - 7.08 (m, 7H), 5.15 and 4.85 (2 x br s, 1H, rotamers), 4.51 - 4.23 (m, 4H), 3.86 - 3.82 (m, 2H), 3.61 and 3.53 (2 x br s, 3H, rotamers), 2.87 - 2.77 (m, 4H), 2.59 - 2.51 (m, 4H), 1.71 - 1.15 (m, 29H), 0.83 (t, 3H, J = 7.0 Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ 171.7 and 170.8 (rotamers), 167.7, 155.6, 147.6, 146.9, 146.7, 136.6 and 135.9 (rotamers), 131.0, 128.2, 127.6, 126.9, 125.6, 121.5, 79.8, 61.3, 54.4 and 53.4 (rotamers), 48.9, 46.6 and 46.0 (rotamers), 39.7, 35.5, 33.4, 31.5, 31.1, 30.6, 29.0, 28.9, 28.5, 28.1, 27.9, 25.4 and 25.1 (rotamers), 23.7, 22.2, 13.7; IR (KBr) ν(cm^{-1}) 3416, 2941, 1678, 1541, 1152; λ_{max} = 219 nm; HRMS (ESI): *m/z*: Calcd for $C_{40}H_{60}N_6O_5$: 705.4698 $[M+H]^+$, found: 705.4699.

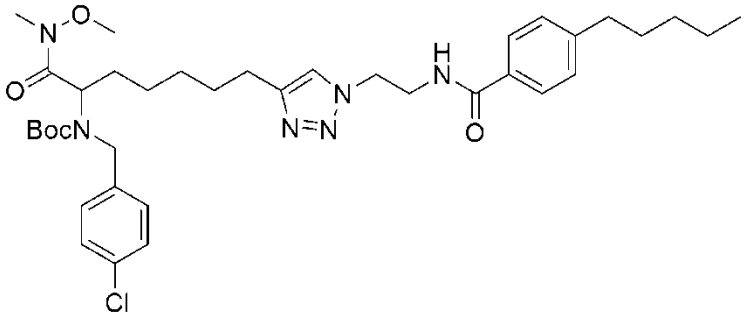
tert-butyl 4-butylbenzyl(1-(methoxy(methyl)amino)-1-oxo-7-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)heptan-2-yl)carbamate (6d)



6d was synthesized as described in the general procedure using **boc 5d** (0.20 mmol), *O,N*-dimethylhydroxylamine hydrochloride (1.00 mmol), and 2.0*M* isopropylmagnesium chloride solution in tetrahydrofuran (1.6 mmol). Upon completion of the reaction via TLC analysis, the crude product was purified via flash column chromatography. **6d** was obtained as a clear oil (66% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, 2H, *J* = 8.0 Hz), 7.34 - 7.03 (m, 8H), 5.18 and 4.85 (2 x br s, 1H, rotamers), 4.52 (t, 2H, *J* = 5.6 Hz), 4.45 - 4.20 (m, 2H), 3.92 - 3.88 (m, 2H), 3.63 and 3.55 (2 x br s, 3H, rotamers), 2.92 and 2.82 (2 x br s, 3H, rotamers), 2.62 - 2.51 (m, 6H), 1.62 - 1.22 (m, 27H), 0.89 - 0.84 (m, 6H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 171.9, 167.8, 155.8, 148.0, 147.0, 141.0, 136.6 and 135.9 (rotamers), 131.1, 128.4, 127.9, 127.0, 126.9, 121.7, 80.0, 61.5, 54.5 and 53.6 (rotamers), 49.2, 46.8 and 46.2 (rotamers), 39.8, 35.7, 35.1, 33.6, 31.8, 31.3, 30.8, 29.2 and 29.0 (rotamers), 28.7, 28.3, 28.1, 25.5, 25.3, 22.4, 22.1, 13.9, 13.8; IR (KBr) ν(cm^{-1}) 3297, 2947, 1692, 1540, 1165; λ_{max} = 230 nm; HRMS (ESI): *m/z*: Calcd for $C_{41}H_{62}N_6O_5$: 719.4854 $[M+H]^+$, found: 719.4833.

tert-butyl 4-chlorobenzyl(1-(methoxy(methyl)amino)-1-oxo-7-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)heptan-2-yl)carbamate (6e)

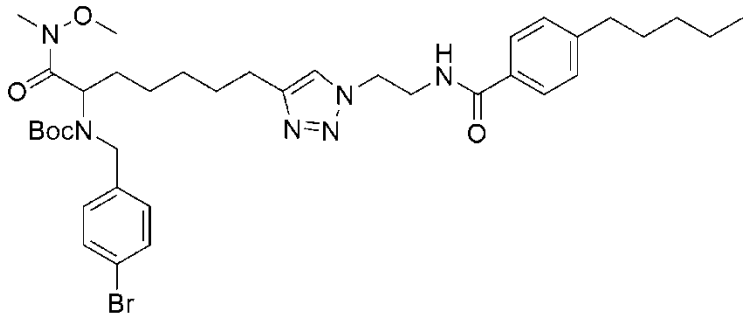


6e was synthesized as described in the general procedure using **boc 5e** (0.20 mmol), *O,N*-dimethylhydroxylamine hydrochloride (1.00 mmol), and 2.0*M* isopropylmagnesium chloride solution in tetrahydrofuran (1.6 mmol). Upon completion of the reaction via TLC analysis, the crude product was purified via flash column chromatography. **6e** was obtained as a clear oil (84% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, 2H, *J* = 8.4 Hz), 7.29 - 7.10 (m, 8H), 5.23 and 4.92 (2 x br s, 1H, rotamers), 4.55 (t, 2H, *J* = 5.6 Hz), 4.50 - 4.29 (m, 2H), 3.96 - 3.92 (m, 2H), 3.69 and

3.60 (2 x br s, 3H, rotamers), 2.98 and 2.86 (2 x br s, 3H, rotamers), 2.65 - 2.60 (m, 4H), 1.75 - 1.25 (m, 23H), 0.87 (t, 3H, J = 7.0 Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ 171.8 and 170.9 (rotamers), 167.7, 155.5, 147.8, 146.9, 137.4 and 136.9 (rotamers), 132.1 and 131.9 (rotamers), 131.1, 129.1, 128.3, 127.8, 127.0, 121.6, 80.2, 61.5 and 61.2 (rotamers), 54.6 and 53.4 (rotamers), 49.1, 46.3 and 45.7 (rotamers), 39.8, 35.6, 31.7, 31.2, 30.7, 29.5 and 29.2 (rotamers), 28.6, 28.2, 28.0, 25.5, 25.2, 22.3, 13.8; IR (KBr) ν(cm^{-1}) 3322, 2932, 1697, 1165, 733; λ_{max} = 223 nm; HRMS (ESI): *m/z*: Calcd for $C_{37}H_{53}ClN_6NaO_5$: 719.3658 $[M+Na]^+$, found: 719.3659.

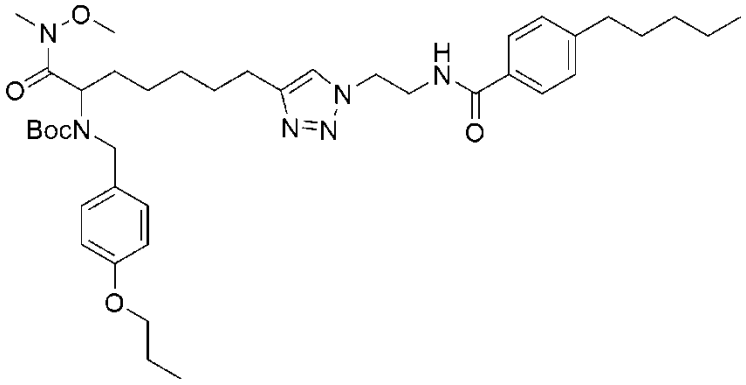
tert-butyl 4-bromobenzyl(1-(methoxy(methyl)amino)-1-oxo-7-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)heptan-2-yl)carbamate (6f)



6f was synthesized as described in the general procedure using **boc 5f** (0.20 mmol), *O,N*-dimethylhydroxylamine hydrochloride (1.00 mmol), and 2.0*M* isopropylmagnesium chloride solution in tetrahydrofuran (1.6 mmol). Upon completion of the reaction via TLC analysis, the crude product was purified via flash column chromatography. **6f** was obtained as a clear oil (63% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68 (d, 2H, J = 8.1 Hz), 7.39 - 6.99 (m, 8H), 5.25 and 4.94 (2 x br s, 1H, rotamers), 4.56 (t, 2H, J = 5.4 Hz), 4.49 - 4.23 (m, 2H), 3.98 - 3.93 (m, 2H), 3.69 and 3.61 (2 x br s, 3H, rotamers), 2.99 and 2.88 (2 x br s, 3H, rotamers), 2.67 - 2.60 (m, 4H), 1.82 - 1.25 (m, 23H), 0.88 (t, 3H, J = 6.8 Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ 171.9 and 170.9 (rotamers), 167.8, 155.6, 148.0, 147.0, 138.8 and 138.0 (rotamers), 131.1, 130.9, 129.5, 128.5, 127.0, 121.7, 120.4 and 120.0 (rotamers), 80.3, 61.6 and 61.3 (rotamers), 54.3 and 53.4 (rotamers), 49.2, 46.4 and 45.8 (rotamers), 39.8, 35.6, 31.8, 31.3, 30.7, 29.3 and 29.0 (rotamers), 28.7, 28.3, 28.1, 25.5, 25.3, 22.3, 13.9; IR (KBr) ν(cm^{-1}) 3354, 2932, 1655, 1171, 749; λ_{max} = 226 nm; HRMS (ESI): *m/z*: Calcd for $C_{37}H_{53}BrN_6O_5$: 741.3334 $[M+H]^+$, found: 741.3332.

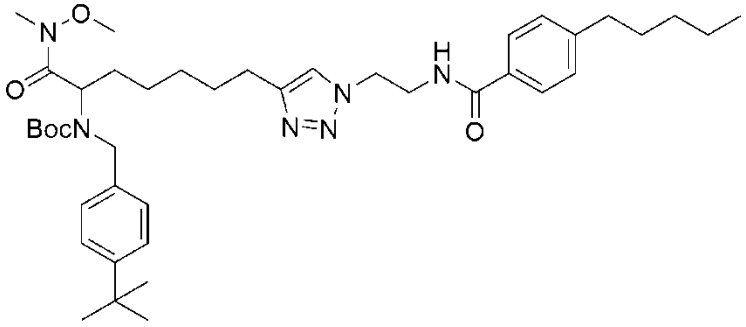
tert-butyl 1-(methoxy(methyl)amino)-1-oxo-7-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)heptan-2-yl(4-propoxybenzyl)carbamate (6g)



6g was synthesized as described in the general procedure using **boc 5g** (0.20 mmol), *O,N*-dimethylhydroxylamine hydrochloride (1.00 mmol), and 2.0*M* isopropylmagnesium chloride solution in tetrahydrofuran (1.6 mmol). Upon completion of the reaction via TLC analysis, the crude product was purified via flash column chromatography. **6g** was obtained as a clear oil (59% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.69 (d, 2H, *J* = 8.1 Hz), 7.29 - 7.11 (m, 6H), 6.79 (d, 2H, *J* = 8.4 Hz), 5.20 and 4.89 (2 x br s, 1H, rotamers), 4.55 (t, 2H, *J* = 5.6 Hz), 4.48 - 4.39 (m, 2H), 4.0 - 3.85 (m, 4H), 3.64 and 3.55 (2 x br s, 3H, rotamers), 3.00 and 2.88 (2 x br s, 3H, rotamers), 2.65 - 2.60 (m, 4H), 1.81 - 1.25 (m, 25H), 1.00 (t, 3H, *J* = 7.4 Hz), 0.88 (t, 3H, *J* = 6.9 Hz) ; ^{13}C NMR (400 MHz, $CDCl_3$) δ 172.2 and 171.8 (rotamers), 168.1, 158.1, 156.1, 148.3, 147.3, 131.7 and 131.4 (rotamers), 129.6, 128.8, 128.6, 127.4, 122.0, 114.2, 80.3, 69.7, 61.8 and 61.5 (rotamers), 55.0 and 53.9 (rotamers), 49.5, 46.7 and 46.3 (rotamers), 40.1, 36.0, 32.2, 31.6, 31.1, 29.9, 29.5 and 29.4 (rotamers), 29.0, 28.5, 25.9, 25.6, 22.8, 22.7, 14.2, 10.7; IR (KBr) *ν*(cm^{-1}) 3318, 2932, 1676, 1241; λ_{max} = 226 nm; HRMS (ESI): *m/z*: Calcd for $C_{40}H_{60}N_6O_6$: 721.4647 $[M+H]^+$, found: 721.4639.

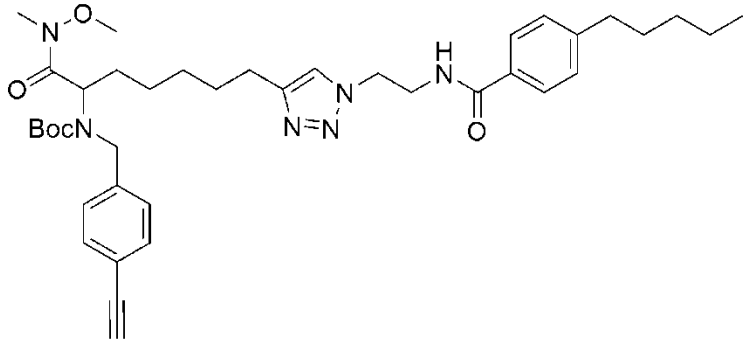
tert-butyl 4-tert-butylbenzyl(1-(methoxy(methyl)amino)-1-oxo-7-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)heptan-2-yl)carbamate (6h)



6h was synthesized as described in the general procedure using **boc 5h** (0.20 mmol), *O,N*-dimethylhydroxylamine hydrochloride (1.00 mmol), and 2.0*M* isopropylmagnesium chloride solution in tetrahydrofuran (1.6 mmol). Upon completion of the reaction via TLC analysis, the crude product was purified via flash column chromatography. **6h** was obtained as a clear oil (88% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, 2H, *J* = 8.0 Hz), 7.32 - 7.17 (m, 8H), 5.18 and 4.76 (2 x br s, 1H, rotamers), 4.57 (t, 2H, *J* = 5.6 Hz), 4.49 - 4.27 (m, 2H), 3.98 - 3.93 (m, 2H), 3.65 and 3.57 (2 x br s, 3H, rotamers), 2.91 and 2.82 (2 x br s, 3H, rotamers), 2.67 - 2.61 (m, 2H), 1.76 - 1.28 (m, 32H), 0.89 (t, 3H, *J* = 7.0 Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ 171.9 and 171.0 (rotamers), 167.8, 155.8, 149.3, 148.0, 147.0, 136.4 and 135.7 (rotamers), 131.1, 128.4, 127.5, 127.0, 124.7, 121.7, 80.0, 61.5, 54.7 and 53.6 (rotamers), 49.2, 46.7 and 46.1 (rotamers), 39.8, 35.7, 34.2, 31.8, 31.3, 31.2, 29.6, 29.2 and 29.0 (rotamers), 28.7, 28.3, 28.1, 25.5, 25.3, 22.4, 13.9; IR (KBr) *v*(cm^{-1}) 3429, 2921, 1686, 1452; λ_{max} = 228 nm; HRMS (ESI): *m/z*: Calcd for $C_{41}H_{62}N_6O_5$: 719.4854 $[M+H]^+$, found: 719.4837.

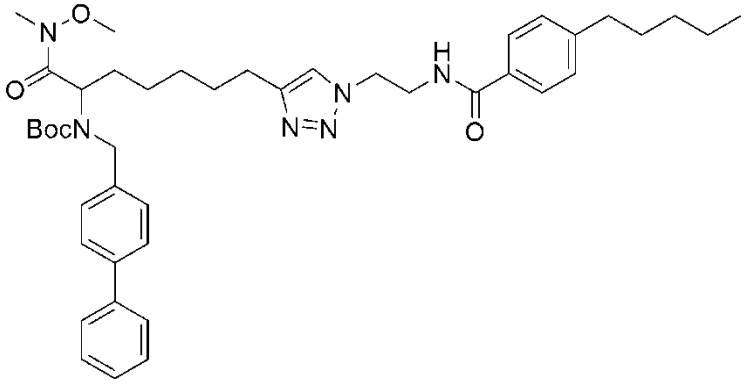
tert-butyl 4-ethynylbenzyl(1-(methoxy(methyl)amino)-1-oxo-7-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)heptan-2-yl)carbamate (6i)



6i was synthesized as described in the general procedure using **boc 5i** (0.20 mmol), *O,N*-dimethylhydroxylamine hydrochloride (1.00 mmol), and 2.0*M* isopropylmagnesium chloride solution in tetrahydrofuran (1.6 mmol). Upon completion of the reaction via TLC analysis, the crude product was purified via flash column chromatography. **6i** was obtained as a clear oil (52% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70 (d, 2H, *J* = 7.8 Hz), 7.39 - 7.15 (m, 8H), 5.23 and 4.88 (2 x br s, 1H, rotamers), 4.62 (t, 2H, *J* = 5.1 Hz), 4.46 (s, 2H), 3.97 - 3.94 (m, 2H), 3.70 and 3.61 (2 x br s, 3H, rotamers), 3.05 (s, 1H), 3.01 and 2.88 (2 x br s, 3H, rotamers), 2.72 - 2.61 (m, 4H), 1.76 - 1.26 (m, 23H), 0.89 (t, 3H, *J* = 6.5 Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ 172.0, 167.8, 155.7, 148.0, 147.1, 140.8 and 140.0 (rotamers), 131.7 and 131.1 (rotamers), 128.5, 127.7, 127.0, 126.7, 121.8, 120.0, 83.6, 80.3, 61.7, 54.8 and 53.5 (rotamers), 49.4, 46.9 and 46.2 (rotamers), 39.8, 35.7, 31.9, 31.3, 30.8, 29.6, 29.4, 29.0 and 28.7 (rotamers), 28.3, 28.1, 25.6, 25.3, 22.4, 13.9; IR (KBr) *v*(cm^{-1}) 3281, 2937, 2322, 1686, 1165; λ_{max} = 238 nm; HRMS (ESI): *m/z*: Calcd for $C_{39}H_{54}N_6O_5$: 687.4228 $[M+H]^+$, found: 687.424.

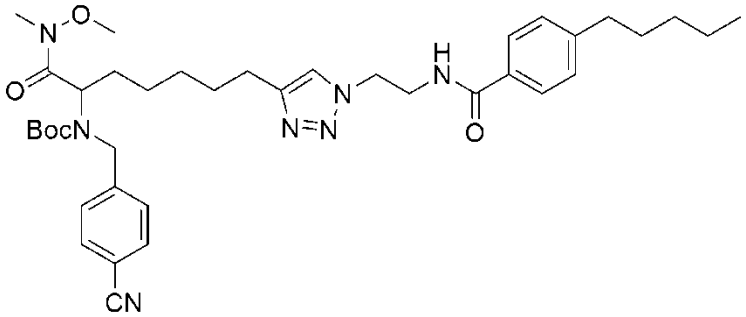
tert-butyl biphenyl-4-ylmethyl(1-(methoxy(methyl)amino)-1-oxo-7-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)heptan-2-yl)carbamate (6j)



6j was synthesized as described in the general procedure using **boc 5j** (0.20 mmol), *O,N*-dimethylhydroxylamine hydrochloride (1.00 mmol), and 2.0*M* isopropylmagnesium chloride solution in tetrahydrofuran (1.6 mmol). Upon completion of the reaction via TLC analysis, the crude product was purified via flash column chromatography. **6j** was obtained as a clear oil (56% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, 2H, *J* = 8.0 Hz), 7.56 - 7.18 (m, 13H), 5.32 an 4.88 (2 x br s, 1H, rotamers), 4.63 - 4.46 (m, 4H), 3.91 - 3.87 (m, 2H), 3.67 and 3.60 (2 x br s, 3H, rotamers), 2.98 and 2.87 (2 x br s, 3H, rotamers), 2.63 - 2.58 (m, 4H), 1.82 - 1.24 (m, 23H), 0.87 (t, 3H, *J* = 7.0 Hz) ; ^{13}C NMR (400 MHz, $CDCl_3$) δ 172.0, 167.8, 155.8, 147.9, 147.1, 140.7, 139.2, 138.8 and 138.1 (rotamers), 131.1, 128.7, 128.5, 128.2, 127.4, 127.0, 126.8, 126.5, 121.8, 80.2, 61.6 and 61.3 (rotamers), 54.7 and 53.7 (rotamers), 49.3, 46.8 and 46.3 (rotamers), 39.7, 35.7, 31.8, 31.3, 30.8, 29.3, 29.0 and 28.8 (rotamers), 28.4, 28.2, 25.6, 25.3, 22.4, 13.9; IR (KBr) *ν*(cm^{-1}) 3427, 2932, 2120, 1644, 1171; λ_{max} = 244 nm; HRMS (ESI): *m/z*: Calcd for $C_{43}H_{58}N_6O_5$: 739.4541 $[M+H]^+$, found: 739.4542.

tert-butyl 4-cyanobenzyl(1-(methoxy(methyl)amino)-1-oxo-7-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)heptan-2-yl)carbamate (6k)

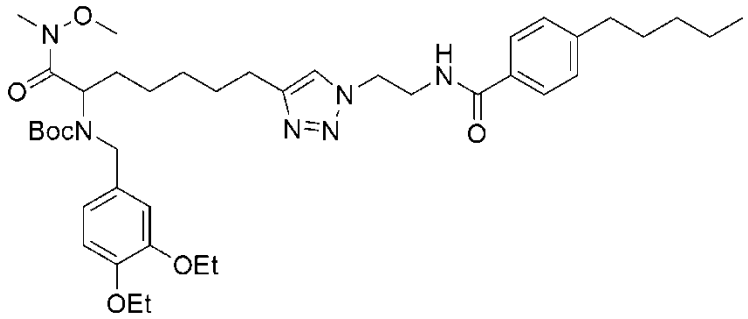


6k was synthesized as described in the general procedure using **boc 5k** (0.20 mmol), *O,N*-dimethylhydroxylamine hydrochloride (1.00 mmol), and 2.0*M* isopropylmagnesium chloride solution in tetrahydrofuran (1.6 mmol). Upon completion of the reaction via TLC analysis, the crude product was purified via flash column chromatography. **6k** was obtained as a clear oil (88% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68 (d, 2H, *J* = 8.1 Hz), 7.57 (d, 2H, *J* = 7.5 Hz), 7.33 - 7.21 (m, 5H), 7.00 (br s, 1H), 5.28 and 4.97 (2 x br s, 1H, rotamers), 4.60 - 4.37 (m, 4H), 3.99 - 3.94 (m,

2H), 3.74 and 3.66 (2 x br s, 3H, rotamers), 3.01 and 2.86 (2 x br s, 3H, rotamers), 2.69 - 2.61 (m, 4H), 1.81 - 1.26 (m, 23H), 0.89 (t, 3H, J = 6.9 Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ 171.9 and 170.9 (rotamers), 167.8, 155.5, 147.9, 147.1, 145.7 and 144.7 (rotamers), 131.8, 131.1, 128.5 and 128.0 (rotamers), 127.2, 127.0, 121.7, 118.9, 110.1, 80.6, 61.7 and 61.4 (rotamers), 54.5 and 53.3 (rotamers), 49.2, 46.9 and 46.1 (rotamers), 39.8, 35.6, 31.8, 31.2, 30.7, 29.4, 29.0 and 28.7 (rotamers), 28.3, 28.0, 25.5, 25.3, 22.3, 13.9; IR (KBr) ν(cm^{-1}) 3426, 2932, 2223, 1655, 1166; λ_{max} = 234 nm; HRMS (ESI): *m/z*: Calcd for $C_{38}H_{53}N_7O_5$: 688.4181 $[M+H]^+$, found: 688.4175.

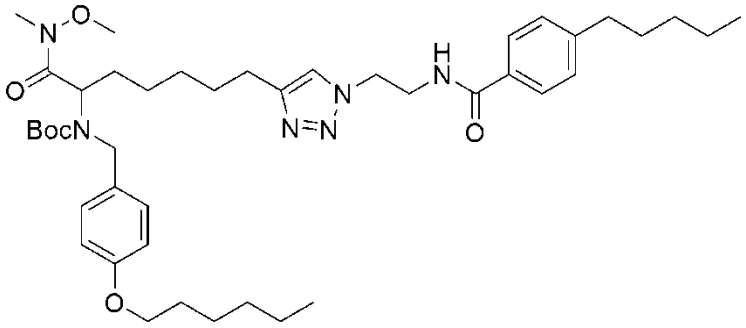
tert-butyl 3,4-diethoxybenzyl(1-(methoxy(methyl)amino)-1-oxo-7-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)heptan-2-yl)carbamate (6l)



6l was synthesized as described in the general procedure using **boc 5l** (0.20 mmol), *O,N*-dimethylhydroxylamine hydrochloride (1.00 mmol), and 2.0*M* isopropylmagnesium chloride solution in tetrahydrofuran (1.6 mmol). Upon completion of the reaction via TLC analysis, the crude product was purified via flash column chromatography. **6l** was obtained as a clear oil (95% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, 2H, J = 8.0 Hz), 7.41 (br s, 1H), 7.15 (d, 2H, J = 8.0 Hz), 6.91 - 6.70 (m, 4H), 5.18 and 4.86 (2 x br s, 1H, rotamers), 4.51 (t, 2H, J = 5.6 Hz), 4.40 - 3.85 (m, 8H), 3.60 and 3.51 (2 x br s, 3H, rotamers), 2.90 and 2.82 (2 x br s, 3H, rotamers), 2.59 - 2.54 (m, 4H), 1.59 - 1.18 (m, 29H), 0.83 (t, 3H, J = 6.8 Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ 171.9, 167.7, 155.6, 148.1, 147.8, 147.1, 146.9, 132.2 and 131.7 (rotamers), 131.0, 128.4, 127.0, 121.7, 120.3 and 119.5 (rotamers), 113.3 and 113.0 (rotamers), 112.6, 79.9, 64.4, 64.1 and 64.0 (rotamers), 61.4, 54.5 and 53.6 (rotamers), 49.2, 46.6 and 46.1 (rotamers), 39.7, 35.6, 31.8, 31.2, 30.7, 29.2, 28.9, 28.7, 28.2, 25.5, 25.2, 22.3, 14.7, 14.6, 13.8; IR (KBr) ν(cm^{-1}) 3378, 2922, 1672, 1233, 1138; λ_{max} = 230 nm; HRMS (ESI): *m/z*: Calcd for $C_{41}H_{62}N_6O_7$: 751.1753 $[M+H]^+$, found: 751.4757.

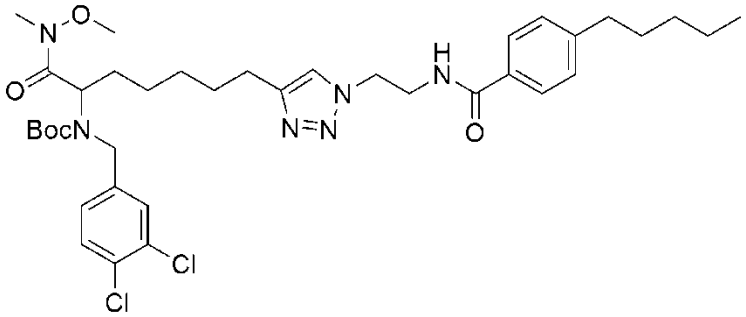
tert-butyl 4-(hexyloxy)benzyl(1-(methoxy(methyl)amino)-1-oxo-7-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)heptan-2-yl)carbamate (6m)



6m was synthesized as described in the general procedure using **boc 5m** (0.20 mmol), *O,N*-dimethylhydroxylamine hydrochloride (1.00 mmol), and 2.0*M* isopropylmagnesium chloride solution in tetrahydrofuran (1.6 mmol). Upon completion of the reaction via TLC analysis, the crude product was purified via flash column chromatography. **6m** was obtained as a clear oil (55% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 (d, 2H, *J* = 7.8 Hz), 7.42 - 7.11 (m, 6H), 6.79 (d, 2H, *J* = 7.8 Hz), 5.19 and 4.88 (2 x br s, 1H, rotamers), 4.61 (t, 2H, *J* = 5.3 Hz), 4.56 - 4.17 (m, 4H), 3.97 - 3.89 (m, 4H), 3.64 and 3.56 (2 x br s, 3H, rotamers), 2.97 and 2.89 (2 x br s, 3H, rotamers), 2.71 - 2.60 (m, 4H), 1.77 - 1.26 (m, 31H), 0.92 - 0.86 (m, 6H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 172.0, 167.8, 157.7, 155.8, 147.9, 147.0, 131.1, 129.2, 128.4, 128.2, 127.0, 121.8, 113.9, 80.0, 67.9, 61.5 and 61.2 (rotamers), 54.3 and 53.6 (rotamers), 49.3, 46.4 and 45.9 (rotamers), 39.8, 35.6, 31.8, 31.5, 31.3, 30.7, 29.2 and 29.0 (rotamers), 29.1, 28.7, 28.2, 28.1, 25.6, 25.5, 25.2, 22.5, 22.3, 13.9, 13.8; IR (KBr) *ν*(cm^{-1}) 3401, 2932, 1644, 1236, 1151; λ_{max} = 229 nm; HRMS (ESI): *m/z*: Calcd for $C_{43}H_{66}N_6O_6$: 763.5117 $[M+H]^+$, found: 763.5105.

tert-butyl 3,4-dichlorobenzyl(1-(methoxy(methyl)amino)-1-oxo-7-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)heptan-2-yl)carbamate (6n)

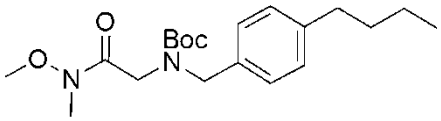


6n was synthesized as described in the general procedure using **boc 5n** (0.20 mmol), *O,N*-dimethylhydroxylamine hydrochloride (1.00 mmol), and 2.0*M* isopropylmagnesium chloride solution in tetrahydrofuran (1.6 mmol). Upon completion of the reaction via TLC analysis, the crude product was purified via flash column chromatography. **6n** was obtained as a clear oil (79% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.69 (d, 2H, *J* = 8.4 Hz), 7.37 - 7.03 (m, 7H), 5.26 and 4.97 (2 x br s, 1H, rotamers), 4.60 (t, 2H, *J* = 5.4 Hz), 4.41 (s, 2H), 4.05 - 3.97 (m, 2H), 3.72 and 3.65 (2 x br s, 3H, rotamers), 3.04 and 2.95 (2 x br s, 3H, rotamers), 2.72 - 2.61 (m, 4H), 1.82 - 1.26 (m, 23H), 0.89 (t, 3H, *J* = 6.8 Hz) ; ^{13}C NMR (400 MHz, $CDCl_3$) δ 171.8, 167.8, 155.5, 147.7, 147.1,

140.2, 131.9, 131.0, 129.8, 129.4, 128.7, 128.5, 127.0, 126.2, 122.0, 80.6, 61.6, 54.2 and 53.3 (rotamers), 49.5, 46.0 and 45.4 (rotamers), 39.7, 35.7, 31.8, 31.3, 30.8, 29.3, 29.0 and 28.7 (rotamers), 28.3, 28.1, 25.5, 25.1, 22.4, 13.9; IR (KBr) ν(cm^{-1}) 3321, 2926, 1668, 755; λ_{max} = 221 nm; HRMS (ESI): *m/z*: Calcd for $C_{37}H_{52}Cl_2N_7O_5$: 731.3449 $[M+H]^+$, found: 731.3442.

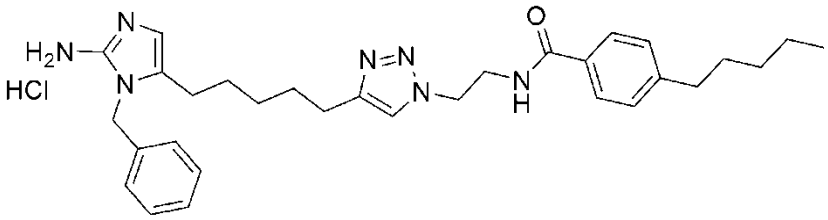
tert-butyl 4-butylbenzyl(2-(methoxy(methyl)amino)-2-oxoethyl)carbamate



Tert-butyl 4-butylbenzyl(2-(methoxy(methyl)amino)-2-oxoethyl)carbamate was synthesized as described in the general procedure using methyl 2-(tert-butoxycarbonyl(4-butylbenzyl)amino)acetate (0.20 mmol), *O,N*-dimethylhydroxylamine hydrochloride (1.00 mmol), and 2.0*M* isopropylmagnesium chloride solution in tetrahydrofuran (1.6 mmol). Upon completion of the reaction via TLC analysis, the crude product was purified via flash column chromatography. Tert-butyl 4-butylbenzyl(2-(methoxy(methyl)amino)-2-oxoethyl)carbamate was obtained as a clear oil (77% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 - 7.12 (m, 4H), 4.53 and 4.51 (2 x s, 2H, rotamers), 4.08 and 3.95 (2 x s, 2H, rotamers), 3.63 and 3.58 (2 x s, 3H, rotamers), 3.17 (s, 3H), 2.59 (t, 2H, *J* = 7.8 Hz), 1.60 - 1.34 (m, 13H), 0.92 (t, 3H, *J* = 7.4 Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ 170.4 and 170.1 (rotamers), 156.1 and 155.9 (rotamers), 141.9, 135.1 and 134.9 (rotamers), 128.4, 128.0 and 127.4 (rotamers), 80.1 and 79.9 (rotamers), 61.1 and 61.0 (rotamers), 51.1 and 50.5 (rotamers), 46.7 and 46.5 (rotamers), 35.2, 33.6, 32.3 and 32.2 (rotamers), 28.3 and 28.2 (rotamers), 22.2, 13.8; IR (KBr) ν(cm^{-1}) 3464, 2958, 1671, 1171; λ_{max} = 223 nm, 261 nm; HRMS (ESI): *m/z*: Calcd for $C_{20}H_{32}N_2NaO_4$: 387.2254 $[M+Na]^+$, found: 387.2247.

N-(2-(4-(5-(2-amino-1-benzyl-1H-imidazol-5-yl)pentyl)-1H-1,2,3-triazol-1-yl)ethyl)-4-pentylbenzamide hydrochloride (7a)

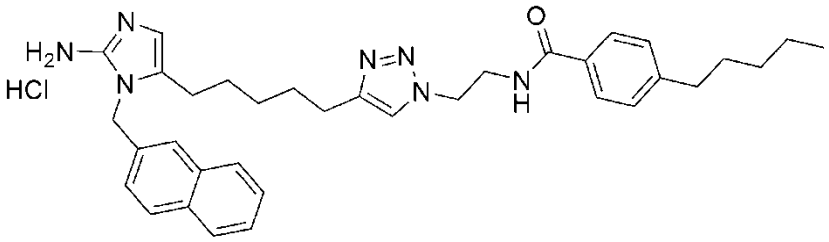


7a was synthesized as described in the general procedure using **6a** (0.1 mmol), DIBAL-H (0.15 mmol), and cyanamide (0.5 mmol). Upon completion of the reaction, the crude product was purified via flash column chromatography. Methanol and aqueous concentrated HCl were added, following the removal of the solvent the HCl salt **7a** was obtained as a pale yellow solid (50% yield).

^{1}H NMR (400 MHz, CD_3OD) δ 7.69 - 7.65 (m, 3H), 7.33 - 7.22 (m, 5H), 7.06 (d, 2H, *J* = 7.2 Hz), 6.29 (s, 1H), 4.99 (s, 2H), 4.60 (t, 2H, *J* = 6 Hz), 3.82 (t, 2H, *J* = 5.9 Hz), 2.65 - 2.58 (m, 4H), 2.30 (t, 2H, *J* = 7.6 Hz), 1.63 - 1.26 (m, 12H), 0.90 (t, 3H, *J* = 6.8 Hz); ^{13}C NMR (400 MHz, CD_3OD) δ 170.5, 150.6, 149.1, 148.6, 138.5, 132.8, 129.9, 129.7, 128.9, 128.6, 128.5, 127.4,

123.8, 120.1, 50.4, 46.4, 41.2, 36.8, 32.7, 32.2, 30.2, 29.6, 29.0, 26.1, 25.2, 23.7, 14.5; IR (KBr) ν(cm^{-1}) 3423, 2921, 1687; λ_{max} = 232 nm; HRMS (ESI): *m/z*: Calcd for $C_{31}H_{41}N_7O$: 528.3445 $[M+H]^+$, found: 528.3447.

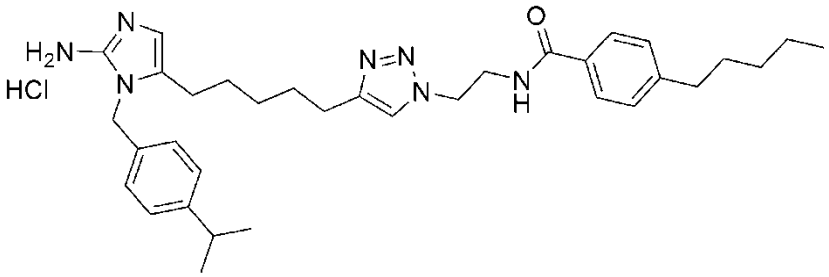
N-(2-(4-(5-(2-amino-1-(naphthalen-2-ylmethyl)-1H-imidazol-5-yl)pentyl)-1H-1,2,3-triazol-1-yl)ethyl)-4-pentylbenzamide hydrochloride (7b)



7b was synthesized as described in the general procedure using **6b** (0.1 mmol), DIBAL-H (0.15 mmol), and cyanamide (0.5 mmol). Upon completion of the reaction, the crude product was purified via flash column chromatography. Methanol and aqueous concentrated HCl were added, following the removal of the solvent the HCl salt **7b** was obtained as a pale yellow solid (38% yield).

^{1}H NMR (400 MHz, CD_3OD) δ 7.81 - 7.65 (m, 5H), 7.48 (s, 1H), 7.43 - 7.40 (m, 3H), 7.25 (dd, 1H, *J* = 5.9 Hz, *J* = 8.6 Hz), 7.19 (d, 2H, *J* = 8.4 Hz), 6.32 (s, 1H), 5.13 (s, 2H), 4.55 (t, 2H, *J* = 5.8 Hz), 3.79 (t, 2H, *J* = 5.8 Hz), 2.58 (t, 2H, *J* = 7.6 Hz), 2.48 (t, 2H, *J* = 7.2 Hz), 2.30 (t, 2H, *J* = 7.6 Hz), 1.56 - 1.21 (m, 12H), 0.88 (t, 3H, *J* = 7.0 Hz); ^{13}C NMR (400 MHz, CD_3OD) δ 170.4, 150.7, 149.1, 148.5, 136.1, 134.9, 134.3, 132.7, 129.8, 129.7, 128.9, 128.9, 128.5, 128.5, 127.6, 127.2, 125.8, 125.6, 123.7, 120.3, 50.3, 41.1, 36.8, 32.6, 32.2, 30.1, 29.5, 29.0, 26.1, 25.2, 23.7, 14.5; IR (KBr) ν(cm^{-1}) 3256, 2931, 1748; λ_{max} = 229 nm; HRMS (ESI): *m/z*: Calcd for $C_{35}H_{43}N_7O$: 578.3602 $[M+H]^+$, found: 578.3592.

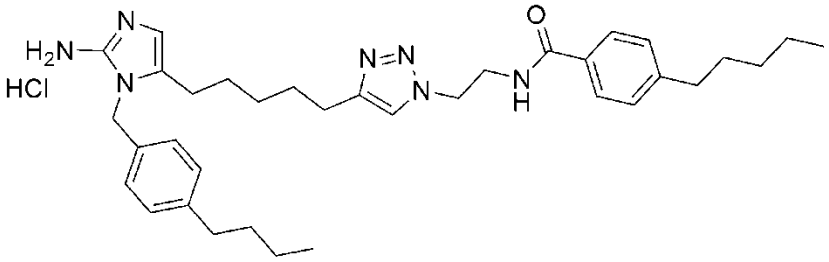
N-(2-(4-(5-(2-amino-1-(4-isopropylbenzyl)-1H-imidazol-5-yl)pentyl)-1H-1,2,3-triazol-1-yl)ethyl)-4-pentylbenzamide hydrochloride (7c)



7c was synthesized as described in the general procedure using **6c** (0.1 mmol), DIBAL-H (0.15 mmol), and cyanamide (0.5 mmol). Upon completion of the reaction, the crude product was purified via flash column chromatography. Methanol and aqueous concentrated HCl were added, following the removal of the solvent the HCl salt **7c** was obtained as a pale yellow solid (38% yield).

^{1}H NMR (400 MHz, CD_3OD) δ 7.68 (s, 1H), 7.65 (d, 2H, *J* = 4.4 Hz), 7.23 (d, 2H, *J* = 8.4 Hz), 7.18 (d, 2H, *J* = 8 Hz), 6.99 (d, 2H, *J* = 8 Hz), 6.27 (s, 1H), 4.49 (s, 2H), 4.60 (t, 2H, *J* = 5.8 Hz), 3.82 (t, 2H, *J* = 6.2 Hz), 2.86 (sp, 1H *J* = 7 Hz), 2.65 - 2.57 (m, 4H), 2.31 (t, 2H, *J* = 7.6 Hz), 1.65 - 1.19 (m, 18H), 0.90 (t, 3H, *J* = 6.8 Hz) ; ^{13}C NMR (400 MHz, CD_3OD) δ 170.5, 150.6, 149.6, 149.2, 148.6, 135.9, 132.8, 129.7, 128.9, 128.5, 127.9, 127.4, 123.8, 120.2, 50.4, 46.2, 41.2, 36.8, 35.2, 32.7, 32.3, 30.2, 29.6, 29.1, 26.1, 25.3, 24.6, 23.7, 14.5; IR (KBr) *v*(cm^{-1}) 3321, 2915, 1701; λ_{max} = 221 nm; HRMS (ESI): *m/z*: Calcd for $C_{34}H_{47}N_7O$: 570.3915 $[M+H]^+$, found: 570.3898.

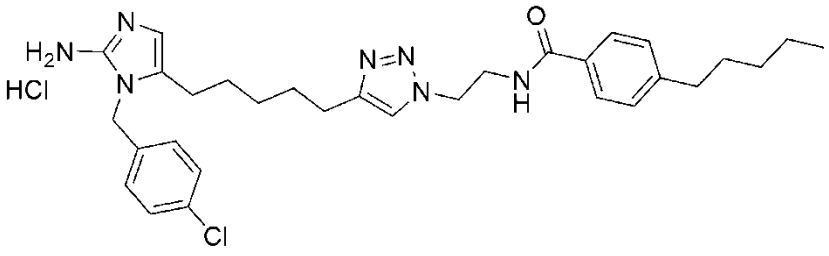
N-(2-(4-(5-(2-amino-1-(4-butylbenzyl)-1H-imidazol-5-yl)pentyl)-1H-1,2,3-triazol-1-yl)ethyl)-4-pentylbenzamide hydrochloride (7d)



7d was synthesized as described in the general procedure using **6d** (0.1 mmol), DIBAL-H (0.15 mmol), and cyanamide (0.5 mmol). Upon completion of the reaction, the crude product was purified via flash column chromatography. Methanol and aqueous concentrated HCl were added, following the removal of the solvent the HCl salt **7d** was obtained as a pale yellow solid (62% yield).

^{1}H NMR (400 MHz, CD_3OD) δ 7.67 (d, 2H, *J* = 6.8 Hz), 7.65 (s, 1H), 7.23 (d, 2H, *J* = 8.4 Hz), 7.13 (d, 2H, *J* = 8 Hz), 6.97 (d, 2H, *J* = 8 Hz), 6.27 (s, 1H), 4.94 (s, 2H), 4.60 (t, 2H, *J* = 5.8 Hz), 3.82 (t, 2H, *J* = 6.2 Hz), 2.65 (m, 6H), 2.30 (t, 2H, *J* = 7.4 Hz), 1.63 - 1.26 (m, 16H), 0.91 (m, 6H); ^{13}C NMR (400 MHz, CD_3OD) δ 170.5, 150.6, 149.2, 148.6, 143.5, 135.7, 132.7, 130.0, 129.7, 128.9, 128.5, 127.4, 123.8, 120.2, 50.4, 46.3, 41.1, 36.8, 36.3, 35.0, 32.7, 32.3, 30.2, 29.6, 29.0, 26.1, 25.3, 23.7, 23.4, 14.6, 14.4; IR (KBr) *v*(cm^{-1}) 3305, 2934, 1687; λ_{max} = 225 nm; HRMS (ESI): *m/z*: Calcd for $C_{35}H_{49}N_7O$: 584.4071 $[M+H]^+$, found: 584.4070.

N-(2-(4-(5-(2-amino-1-(4-chlorobenzyl)-1H-imidazol-5-yl)pentyl)-1H-1,2,3-triazol-1-yl)ethyl)-4-pentylbenzamide hydrochloride (7e)

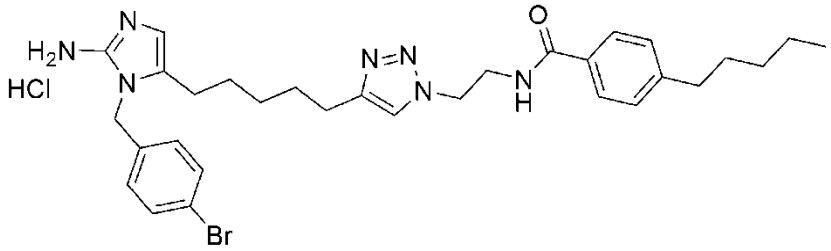


7e was synthesized as described in the general procedure using **6e** (0.1 mmol), DIBAL-H (0.15 mmol), and cyanamide (0.5 mmol). Upon completion of the reaction, the crude product was purified via flash column chromatography. Methanol and aqueous concentrated HCl were

added, following the removal of the solvent the HCl salt **7e** was obtained as a yellow solid (48% yield).

^{1}H NMR (400 MHz, CD_3OD) δ 7.67 - 7.65 (m, 3H), 7.33 (d, 2H, *J* = 8.8 Hz), 7.25 (d, 2H, *J* = 8.4 Hz), 7.05 (d, 2H, *J* = 8.8 Hz), 6.31 (s, 1H), 4.99 (s, 2H), 4.61 (t, 2H, *J* = 6 Hz), 3.83 (t, 2H, *J* = 5.8 Hz), 2.67 - 2.61 (m, 4H), 2.31 (t, 2H, *J* = 7.6 Hz), 1.64 - 1.28 (m, 12H), 0.91 (t, 3H, *J* = 7.2 Hz) ; ^{13}C NMR (400 MHz, CD_3OD) δ 170.6, 150.6, 149.2, 148.6, 137.4, 134.4, 132.8, 130.0, 129.7, 129.1, 128.8, 128.5, 123.8, 119.9, 50.4, 45.8, 41.2, 36.8, 32.7, 32.3, 30.2, 29.6, 29.0, 26.1, 25.2, 23.7, 14.5; IR (KBr) *v*(cm^{-1}) 3411, 2924, 1678, 764; λ_{max} = 220 nm; HRMS (ESI): *m/z*: Calcd for $C_{31}H_{40}ClN_7O$: 562.3056 $[M+H]^+$, found: 562.3062.

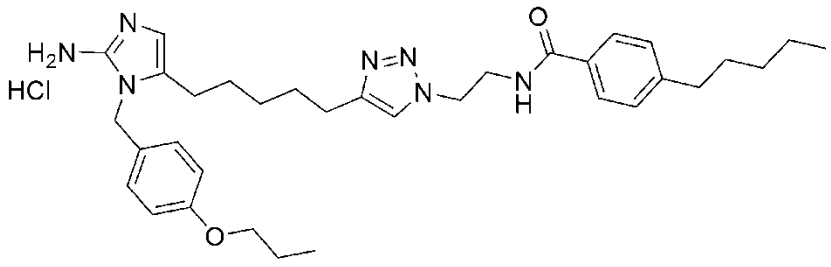
N-(2-(4-(5-(2-amino-1-(4-bromobenzyl)-1H-imidazol-5-yl)pentyl)-1H-1,2,3-triazol-1-yl)ethyl)-4-pentylbenzamide hydrochloride (7f)



7f was synthesized as described in the general procedure using **6f** (0.1 mmol), DIBAL-H (0.15 mmol), and cyanamide (0.5 mmol). Upon completion of the reaction, the crude product was purified via flash column chromatography. Methanol and aqueous concentrated HCl were added, following the removal of the solvent the HCl salt **7f** was obtained as a yellow solid (42% yield).

^{1}H NMR (400 MHz, CD_3OD) δ 7.68 (s, 1H), 7.67 (d, 2H, *J* = 8.4 Hz), 7.48 (d, 2H, *J* = 8.4 Hz), 7.24 (d, 2H, *J* = 8.8 Hz), 7.0 (d, 2H, *J* = 8.4 Hz), 6.30 (s, 1H), 4.97 (s, 2H), 4.62 (t, 2H, *J* = 5.8), 3.83 (t, 2H, *J* = 6 Hz), 2.67 - 2.61 (m, 4H), 2.30 (t, 2H, *J* = 7.6 Hz), 1.65 - 1.28 (m, 12H), 0.91 (t, 2H, *J* = 7 Hz); ^{13}C NMR (400 MHz, CD_3OD) δ 170.6, 150.5, 149.2, 148.6, 137.9, 133.0, 132.8, 129.7, 129.4, 128.8, 128.5, 123.8, 122.3, 119.8, 50.4, 45.9, 41.2, 36.8, 32.7, 32.3, 30.2, 29.6, 29.0, 26.1, 25.2, 23.7, 14.5; IR (KBr) *v*(cm^{-1}) 3378, 2936, 1703, 622; λ_{max} = 228 nm; HRMS (ESI): *m/z*: Calcd for $C_{31}H_{40}BrN_7O$: 606.255 $[M+H]^+$, found: 606.2548.

N-(2-(4-(5-(2-amino-1-(4-propoxybenzyl)-1H-imidazol-5-yl)pentyl)-1H-1,2,3-triazol-1-yl)ethyl)-4-pentylbenzamide hydrochloride (7g)

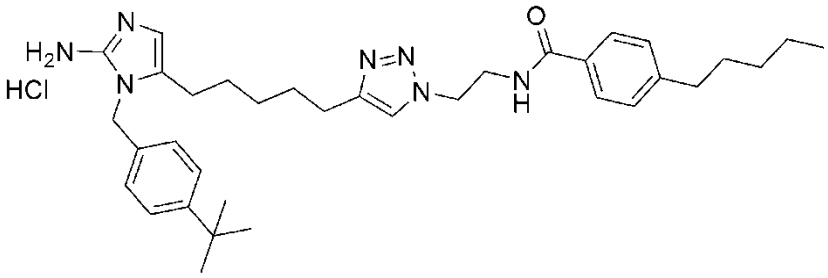


7g was synthesized as described in the general procedure using **6g** (0.1 mmol), DIBAL-H (0.15 mmol), and cyanamide (0.5 mmol). Upon completion of the reaction, the crude product was

purified via flash column chromatography. Methanol and aqueous concentrated HCl were added, following the removal of the solvent the HCl salt **7g** was obtained as a yellow oil (50% yield).

^{1}H NMR (400 MHz, CD_3OD) δ 7.67 (d, 2H, *J* = 8.2 Hz), 7.66 (s, 1H), 7.24 (d, 2H, *J* = 8.4 Hz), 7.00 (d, 2H, *J* = 8.8 Hz), 6.86 (d, 2H, *J* = 8.8 Hz), 6.30 (s, 1H), 4.61 (t, 2H, *J* = 5.8 Hz), 3.89 (t, 2H, *J* = 6.4 Hz), 3.83 (t, 2H, *J* = 5.8 Hz), 2.65 - 2.60 (m, 4H), 2.32 (t, 2H, *J* = 7.6 Hz), 1.78 - 1.30 (m, 14H), 1.02 (t, 3H, *J* = 7.2 Hz), 0.91 (t, 3H, *J* = 6.8 Hz) ; ^{13}C NMR (400 MHz, CD_3OD) δ 170.6, 160.2, 150.3, 149.2, 148.6, 132.8, 130.0, 129.7, 129.1, 128.7, 128.5, 123.8, 119.0, 115.9, 70.7, 50.4, 46.1, 41.2, 36.8, 32.7, 32.3, 30.2, 29.6, 28.9, 26.1, 25.2, 23.8, 23.7, 14.5, 11.0; IR (KBr) ν(cm^{-1}) 3462, 2926, 1733, 1243; λ_{max} = 229 nm; HRMS (ESI): *m/z*: Calcd for $C_{34}H_{47}N_7O_2$: 586.3864 $[M+H]^+$, found: 586.3861.

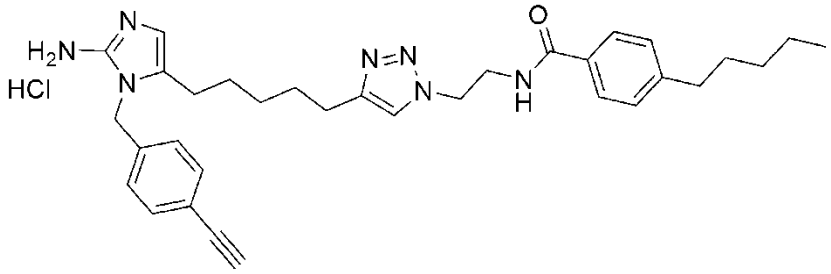
N-(2-(4-(5-(2-amino-1-(4-tert-butylbenzyl)-1H-imidazol-5-yl)pentyl)-1H-1,2,3-triazol-1-yl)ethyl)-4-pentylbenzamide hydrochloride (7h)



7h was synthesized as described in the general procedure using **6h** (0.1 mmol), DIBAL-H (0.15 mmol), and cyanamide (0.5 mmol). Upon completion of the reaction, the crude product was purified via flash column chromatography. Methanol and aqueous concentrated HCl were added, following the removal of the solvent the HCl salt **7h** was obtained as a yellow solid (40% yield).

^{1}H NMR (400 MHz, CD_3OD) δ 7.66 (d, 2H, *J* = 8 Hz), 7.65 (s, 1H), 7.39 (d, 2H, *J* = 8.4 Hz), 7.24 (d, 2H, *J* = 8 Hz), 7.00 (d, 2H, *J* = 8.4 Hz), 6.27 (s, 1H), 4.96 (s, 2H), 4.61 (t, 2H, *J* = 5.8 Hz), 3.83 (t, 2H, *J* = 5.8 Hz), 2.66 - 2.60 (m, 4H), 2.32 (t, 2H, *J* = 7.6 Hz), 1.64 - 1.26 (m, 21H), 0.91 (t, 3H, *J* = 7.2 Hz); ^{13}C NMR (400 MHz, CD_3OD) δ 170.6, 152.6, 148.8, 148.6, 145.8, 133.2, 132.4, 130.5, 129.8, 128.5, 128.5, 127.2, 127.2, 110.2, 54.3, 46.5, 40.5, 36.8, 35.6, 32.7, 32.3, 31.8, 29.2, 29.0, 27.8, 24.6, 24.1, 23.7, 14.5; IR (KBr) ν(cm^{-1}) 3405, 2942, 1644; λ_{max} = 218 nm; HRMS (ESI): *m/z*: Calcd for $C_{35}H_{49}N_7O$: 584.4071 $[M+H]^+$, found: 584.4089.

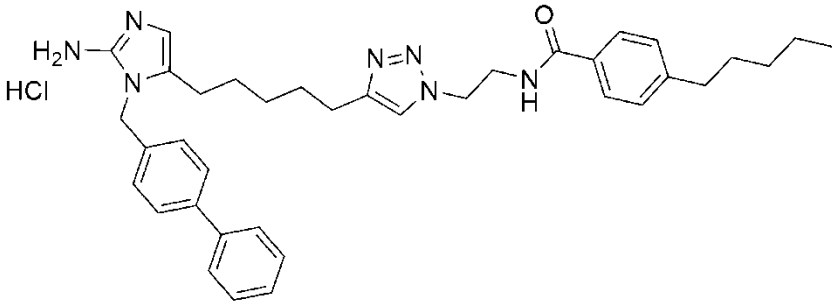
N-(2-(4-(5-(2-amino-1-(4-ethynylbenzyl)-1H-imidazol-5-yl)pentyl)-1H-1,2,3-triazol-1-yl)ethyl)-4-pentylbenzamide hydrochloride (7i)



7i was synthesized as described in the general procedure using **6i** (0.1 mmol), DIBAL-H (0.15 mmol), and cyanamide (0.5 mmol). Upon completion of the reaction, the crude product was purified via flash column chromatography. Methanol and aqueous concentrated HCl were added, following the removal of the solvent the HCl salt **7i** was obtained as a pale yellow solid (28% yield).

^{1}H NMR (400 MHz, CD_3OD) δ 7.66 (s, 1H), 7.65 (d, 2H, *J* = 8.4 Hz), 7.42 (d, 2H, *J* = 8 Hz), 7.24 (d, 2H, *J* = 8.4 Hz), 7.04 (d, 2H, *J* = 8.4 Hz), 6.29 (s, 1H), 5.00 (s, 2H), 4.61 (t, 2H, *J* = 5.8 Hz), 3.83 (t, 2H, *J* = 5.8 Hz), 3.49 (s, 1H), 2.66 - 2.60 (m, 4H), 2.30 (t, 2H, *J* = 7.6 Hz), 1.62 - 1.29 (m, 12H), 0.91 (t, 3H, *J* = 7.2 Hz); ^{13}C NMR (400 MHz, CD_3OD) δ 169.3, 149.1, 147.8, 147.3, 137.8, 132.3, 131.5, 128.4, 127.7, 127.2, 126.2, 122.5, 121.9, 117.5, 82.8, 77.9, 49.1, 44.9, 39.8, 35.5, 31.4, 31.0, 28.9, 28.2, 27.6, 24.8, 23.8, 22.4, 13.2; IR (KBr) ν(cm^{-1}) 3296, 2929, 2318, 1699; λ_{max} = 234 nm; HRMS (ESI): *m/z*: Calcd for $C_{22}H_{41}N_7O$: 552.3445 $[M+H]^+$, found: 552.3442.

N-(2-(4-(5-(2-amino-1-(biphenyl-4-ylmethyl)-1H-imidazol-5-yl)pentyl)-1H-1,2,3-triazol-1-yl)ethyl)-4-pentylbenzamide hydrochloride (7j)

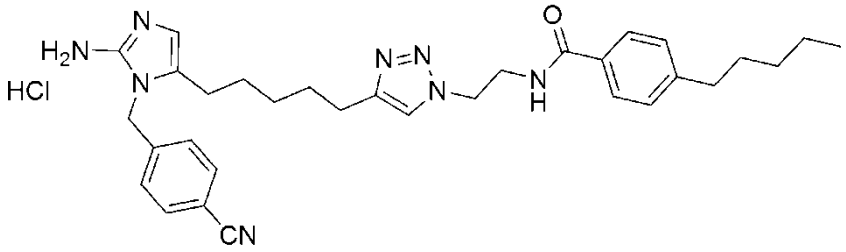


7j was synthesized as described in the general procedure using **6j** (0.1 mmol), DIBAL-H (0.15 mmol), and cyanamide (0.5 mmol). Upon completion of the reaction, the crude product was purified via flash column chromatography. Methanol and aqueous concentrated HCl were added, following the removal of the solvent the HCl salt **7j** was obtained as a pale yellow solid (72% yield).

^{1}H NMR (400 MHz, CD_3OD) δ 7.67 - 7.14 (m, 14H), 6.30 (s, 1H), 5.04 (s, 2H), 4.57 (t, 2H, *J* = 8 Hz), 3.80 (t, 2H, *J* = 8 Hz), 2.66 - 2.58 (m, 4H), 2.35 (t, 2H, *J* = 10 Hz), 1.64 - 1.26 (m, 12H), 0.90 (t, 3H, *J* = 9.2 Hz); ^{13}C NMR (400 MHz, CD_3OD) δ 170.5, 150.7, 149.2, 148.6, 141.9, 141.8, 137.7, 132.8, 130.1, 129.7, 128.9, 128.6, 128.5, 128.5, 128.0, 127.9, 123.8, 120.4, 50.4, 46.2, 41.1, 36.8, 32.7, 32.2, 30.2, 29.6, 29.1, 26.1, 25.3, 23.7, 14.5; IR (KBr) ν(cm^{-1}) 3386,

2918, 1675; λ_{max} = 242 nm; HRMS (ESI): *m/z*: Calcd for $C_{37}H_{45}N_7O$: 604.3758 $[M+H]^+$, found: 604.3756.

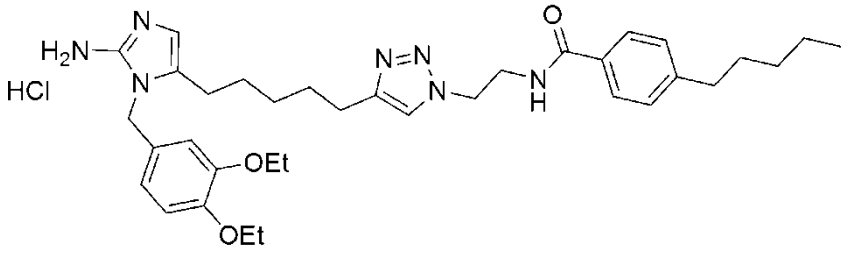
N-(2-(4-(5-(2-amino-1-(4-cyanobenzyl)-1H-imidazol-5-yl)pentyl)-1H-1,2,3-triazol-1-yl)ethyl)-4-pentylbenzamide hydrochloride (7k)



7k was synthesized as described in the general procedure using **6k** (0.1 mmol), DIBAL-H (0.15 mmol), and cyanamide (0.5 mmol). Upon completion of the reaction, the crude product was purified via flash column chromatography. Methanol and aqueous concentrated HCl were added, following the removal of the solvent the HCl salt **7k** was obtained as a yellow oil (44% yield).

^{1}H NMR (400 MHz, CD_3OD) δ 7.70 - 7.65 (m, 4H), 7.24 (d, 2H, *J* = 8.4 Hz), 7.21 (d, 2H, *J* = 8.4 Hz), 6.30 (s, 1H), 5.09 (s, 2H), 4.61 (t, 2H, *J* = 6 Hz), 3.83 (t, 2H, *J* = 5.8 Hz), 2.66 - 2.60 (m, 4H), 2.29 (t, 2H, *J* = 7.4 Hz), 1.64 - 1.30 (m, 12H), 0.91 (t, 3H, *J* = 7.0 Hz); ^{13}C NMR (400 MHz, CD_3OD) δ 170.6, 150.7, 149.1, 148.6, 144.5, 133.8, 132.8, 129.7, 128.7, 128.5, 128.4, 123.8, 120.4, 119.6, 112.4, 61.7, 46.1, 41.2, 36.8, 32.7, 32.3, 30.9, 29.6, 26.1, 25.1, 23.7, 21.0, 14.5; IR (KBr) *v*(cm^{-1}) 3406, 2922, 2214, 1643; λ_{max} = 228 nm; HRMS (ESI): *m/z*: Calcd for $C_{32}H_{40}N_8O$: 553.3398 $[M+H]^+$, found: 553.3397.

N-(2-(4-(5-(2-amino-1-(3,4-diethoxybenzyl)-1H-imidazol-5-yl)pentyl)-1H-1,2,3-triazol-1-yl)ethyl)-4-pentylbenzamide hydrochloride (7l)

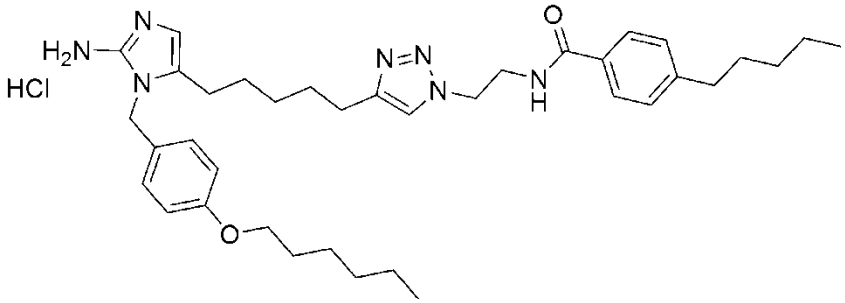


7l was synthesized as described in the general procedure using **6l** (0.1 mmol), DIBAL-H (0.15 mmol), and cyanamide (0.5 mmol). Upon completion of the reaction, the crude product was purified via flash column chromatography. Methanol and aqueous concentrated HCl were added, following the removal of the solvent the HCl salt **7l** was obtained as a yellow oil (29% yield).

^{1}H NMR (400 MHz, CD_3OD) δ 7.68 (s, 1H), 7.66 (d, 2H, *J* = 8.4 Hz), 7.25 (d, 2H, *J* = 8.6 Hz), 6.89 (d, 1H, *J* = 8.1 Hz), 6.69 (d, 1H, *J* = 2.8 Hz), 6.58 (dd, 1H, *J* = 8.3 Hz, *J* = 2.8 Hz), 6.27 (s, 1H), 4.88 (s, 2H), 4.61 (t, 2H, *J* = 8.0 Hz), 4.06 - 3.95 (m, 4H), 3.82 (t, 2H, *J* = 8.0 Hz), 2.66 - 2.59 (m, 4H), 2.33 (t, 2H, *J* = 7.4 Hz), 1.65 - 1.28 (m, 18H), 0.91 (t, 3H, *J* = 6.9 Hz); ^{13}C NMR

(300 MHz, CD_3OD) δ 170.5, 150.4, 149.5, 149.1, 148.6, 132.7, 131.3, 129.7, 128.9, 128.5, 123.8, 120.2, 119.9, 118.0, 115.2, 113.2, 65.9, 65.8, 50.4, 46.1, 41.1, 36.8, 32.7, 32.2, 30.2, 29.6, 29.1, 26.2, 25.2, 23.7, 15.3, 15.2, 14.5; IR (KBr) ν(cm^{-1}) 3386, 2938, 1691, 1124; λ_{max} = 228 nm; HRMS (ESI): *m/z*: Calcd for $C_{35}H_{49}N_7O_3$: 616.3970 $[M+H]^+$, found: 616.3967.

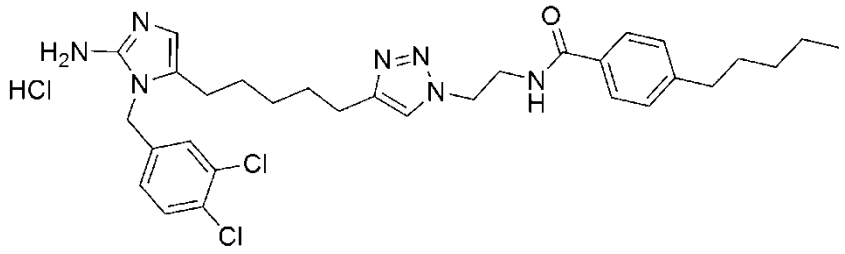
N-(2-(4-(5-(2-amino-1-(4-(hexyloxy)benzyl)-1H-imidazol-5-yl)pentyl)-1H-1,2,3-triazol-1-yl)ethyl)-4-pentylbenzamide hydrochloride (7m)



7m was synthesized as described in the general procedure using **6m** (0.1 mmol), DIBAL-H (0.15 mmol), and cyanamide (0.5 mmol). Upon completion of the reaction, the crude product was purified via flash column chromatography. Methanol and aqueous concentrated HCl were added, following the removal of the solvent the HCl salt **7m** was obtained as a yellow oil (77% yield).

^1H NMR (400 MHz, CD_3OD) δ 7.66 (d, 2H, *J* = 7.2 Hz), 7.65 (s, 1H), 7.24 (d, 2H, *J* = 8.4 Hz), 6.99 (d, 2H, *J* = 8.8 Hz), 6.86 (d, 2H, *J* = 8.4 Hz), 6.27 (s, 1H), 4.91 (s, 2H), 4.61 (t, 2H, *J* = 6.0 Hz), 3.93 (t, 2H, *J* = 6.4 Hz), 3.83 (t, 2H, *J* = 5.8 Hz), 2.66 - 2.60 (m, 4H), 2.32 (t, 2H, *J* = 7.6 Hz), 1.76 - 1.30 (m, 20H), 0.94 - 0.89 (m, 6H); ^{13}C NMR (400 MHz, CD_3OD) δ 170.5, 164.9, 160.0, 149.2, 148.6, 132.7, 130.1, 129.7, 128.7, 128.5, 123.8, 119.9, 118.0, 115.9, 69.2, 50.4, 46.0, 41.1, 36.8, 32.9, 32.6, 32.2, 30.4, 30.2, 29.6, 29.0, 26.9, 26.1, 25.2, 23.8, 23.6, 14.5, 14.5; IR (KBr) ν(cm^{-1}) 3332, 2906, 1614, 1108; λ_{max} = 229 nm; HRMS (ESI): *m/z*: Calcd for $C_{37}H_{53}N_7O_2$: 628.4334 $[M+H]^+$, found: 628.4330.

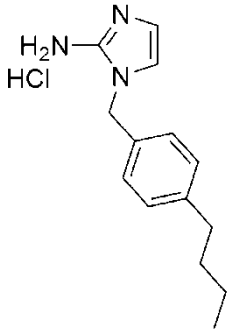
N-(2-(4-(5-(2-amino-1-(3,4-dichlorobenzyl)-1H-imidazol-5-yl)pentyl)-1H-1,2,3-triazol-1-yl)ethyl)-4-pentylbenzamide hydrochloride (7n)



7n was synthesized as described in the general procedure using **6n** (0.1 mmol), DIBAL-H (0.15 mmol), and cyanamide (0.5 mmol). Upon completion of the reaction, the crude product was purified via flash column chromatography. Methanol and aqueous concentrated HCl were added, following the removal of the solvent the HCl salt **7n** was obtained as a pale yellow solid (46% yield).

^{1}H NMR (400 MHz, CD_3OD) δ 7.66 (s, 1H), 7.65 (d, 2H, *J* = 8.8 Hz), 7.48 (d, 1H, *J* = 8.4 Hz), 7.24 (d, 2H, *J* = 8.4 Hz), 7.19 (d, 1H, *J* = 2.0 Hz), 6.99 (dd, 1H, *J* = 8.4 Hz, *J* = 2.0 Hz), 6.31 (s, 1H), 4.99 (s, 2H), 4.61 (t, 2H, *J* = 5.8 Hz), 3.83 (t, 2H, *J* = 5.8 Hz), 2.66 - 2.61 (m, 4H), 2.31 (t, 2H, *J* = 7.6 Hz), 1.64 - 1.29 (m, 12H), 0.91 (t, 3H, *J* = 7.0 Hz) ; ^{13}C NMR (400 MHz, CD_3OD) δ 170.6, 164.9, 150.5, 149.2, 148.7, 139.4, 133.8, 132.5, 132.0, 129.7, 129.4, 128.4, 127.3, 123.8, 120.0, 117.9, 50.4, 45.4, 41.1, 36.8, 32.6, 32.2, 30.2, 29.5, 28.9, 26.1, 25.1, 23.6, 14.5; IR (KBr) *v*(cm^{-1}) 3304, 2941, 1636, 724; λ_{max} = 226 nm; HRMS (ESI): *m/z*: Calcd for $C_{31}H_{39}Cl_2N_7O$: 596.2666 $[M+H]^+$, found: 596.2665.

1-(4-butylbenzyl)-1H-imidazol-2-amine (8)



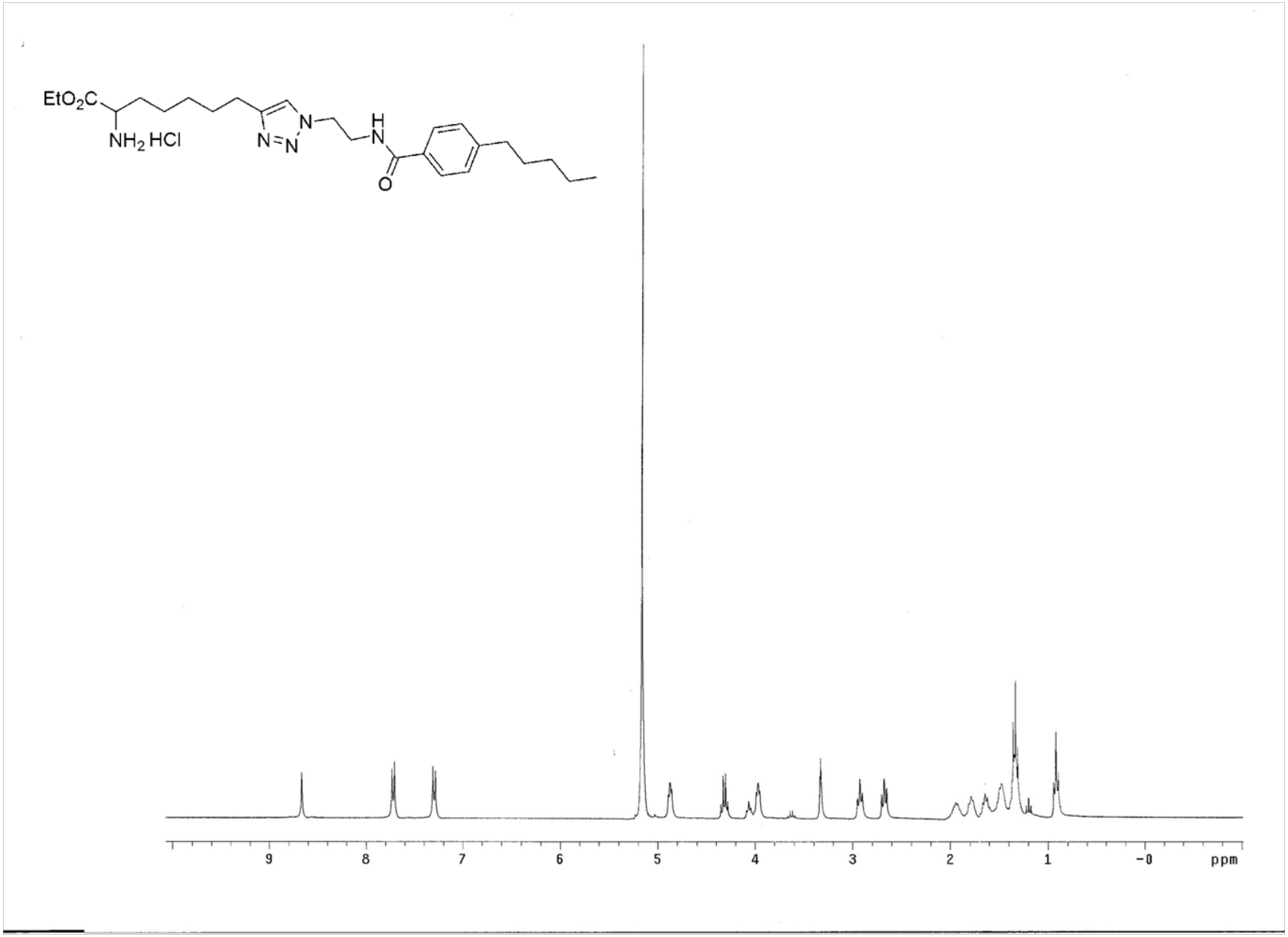
8 was synthesized as described in the general procedure using Tert-butyl 4-butylbenzyl(2-(methoxy(methyl)amino)-2-oxoethyl)carbamate (0.1 mmol), DIBAL-H (0.15 mmol), and cyanamide (0.5 mmol). Upon completion of the reaction, the crude product was purified via flash column chromatography. Methanol and aqueous concentrated HCl were added, following the removal of the solvent the HCl salt **8** was obtained as a pale yellow solid (39% yield).

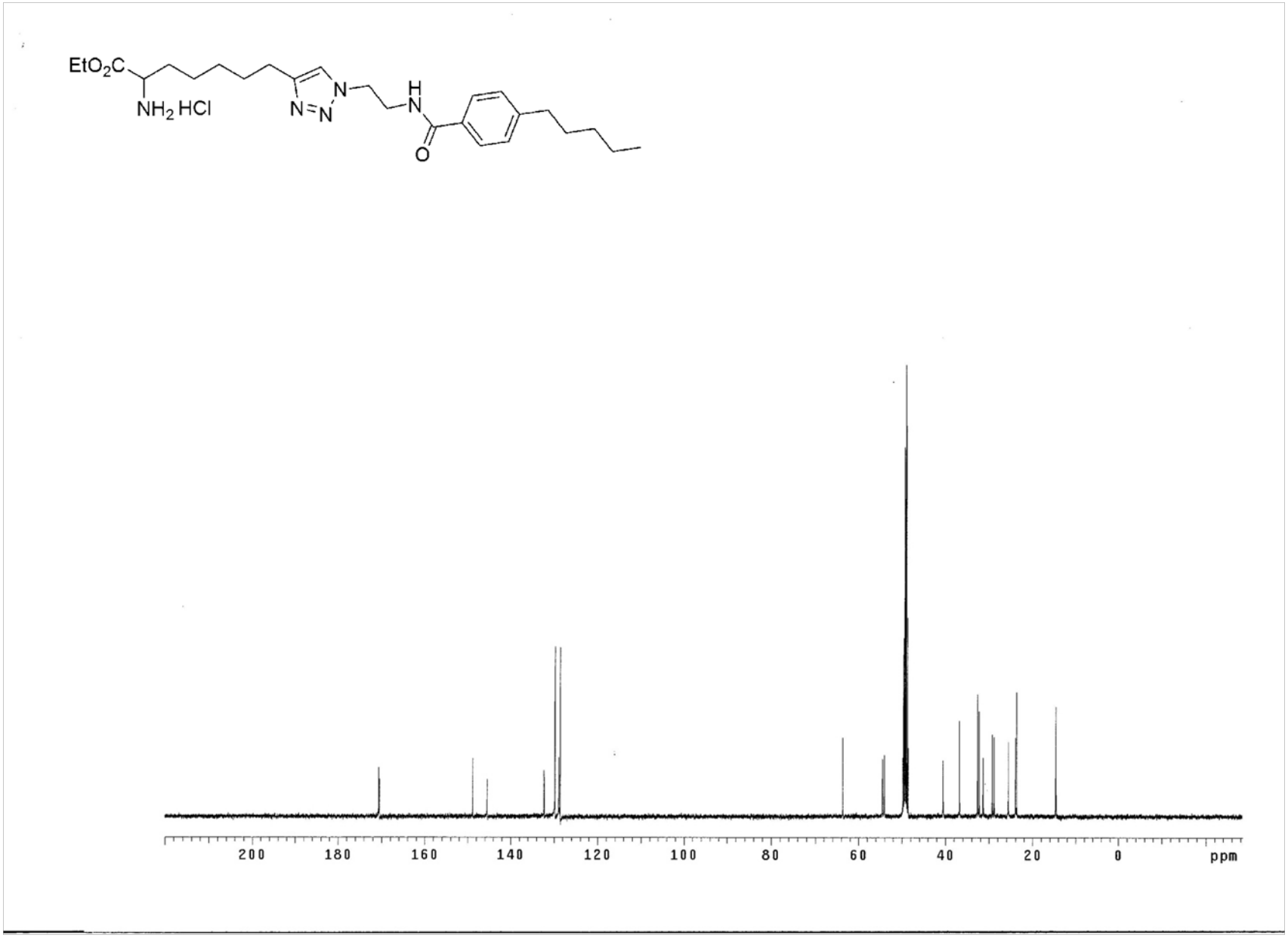
^{1}H NMR (400 MHz, CD_3OD) δ 7.18 (d, 2H, *J* = 8.0 Hz), 7.12 (d, 2H, *J* = 8.0 Hz), 6.55 (d, 1H, *J* = 2.0 Hz), 6.51 (d, 1H, *J* = 2.0 Hz), 4.93 (s, 2H), 2.61 (t, 2H, *J* = 7.8 Hz), 1.60 (qn, 2H, *J* = 7.6 Hz), 1.36 (sx, 2H, *J* = 7.6 Hz), 0.95 (t, 3H, *J* = 7.4 Hz); ^{13}C NMR (400 MHz, CD_3OD) δ 165.0, 143.8, 130.0, 128.4, 124.0 120.1, 48.9, 36.4, 35.0, 23.4, 14.4; IR (KBr) *v*(cm^{-1}) 3421, 2946; λ_{max} = 218 nm; HRMS (ESI): *m/z*: Calcd for $C_{14}H_{19}N_3$: 230.1652 $[M+H]^+$, found: 230.1649.

References

1. Su, Z.; Peng, L.; Worthington, R. J.; Melander, C.*ChemMedChem* **2011**, *6*, 2243.
2. Rogers, S. A.; Bero, J. D.; Melander, C. *ChemBioChem* **2010**, *11*, 396.

^{1}H and ^{13}C NMR Spectra

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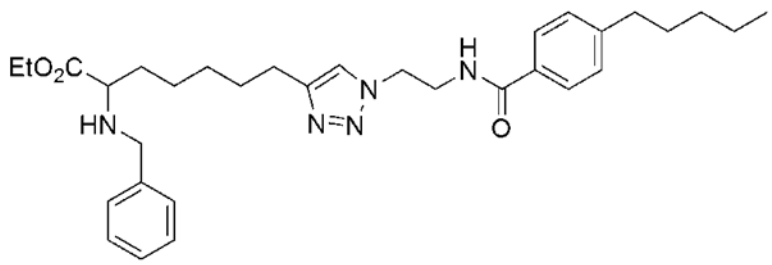
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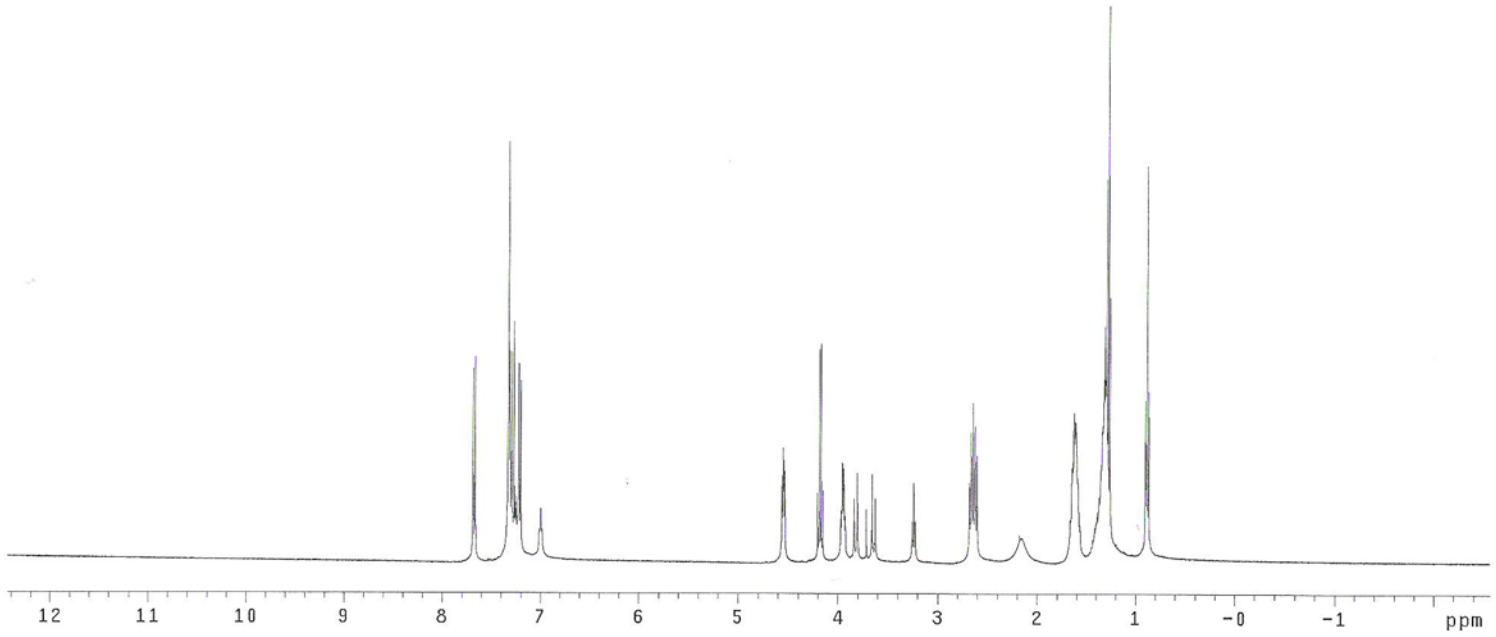
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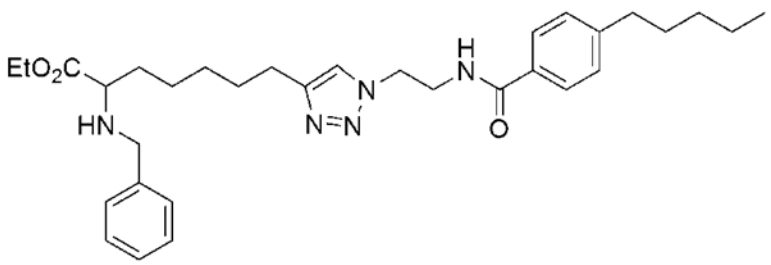
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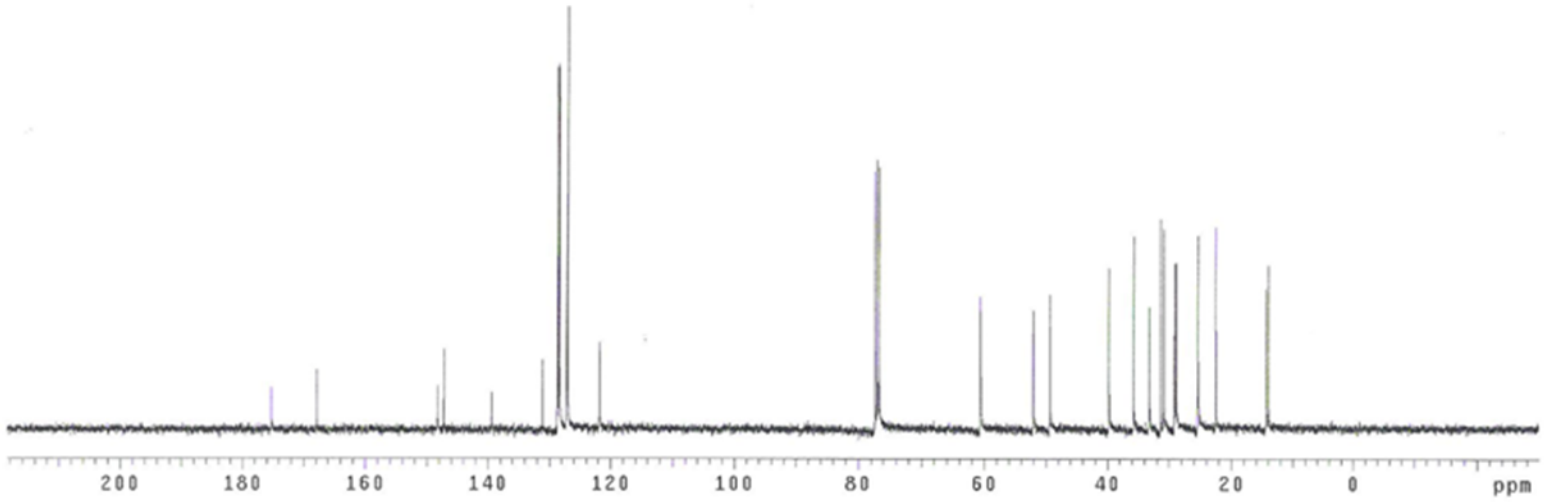
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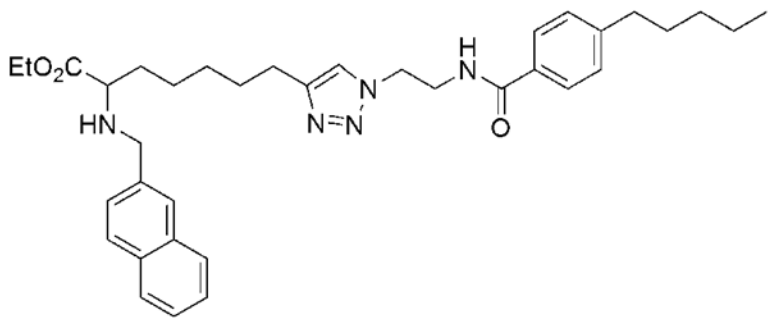
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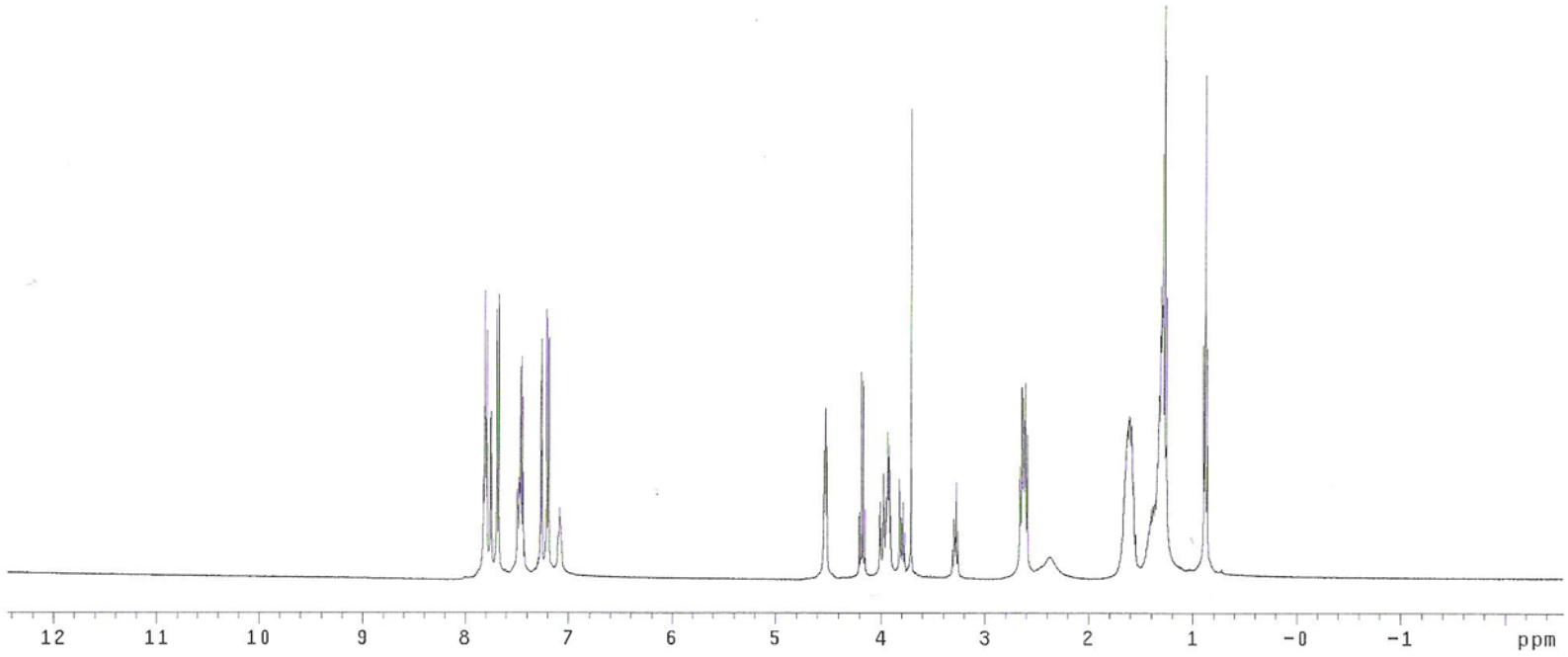
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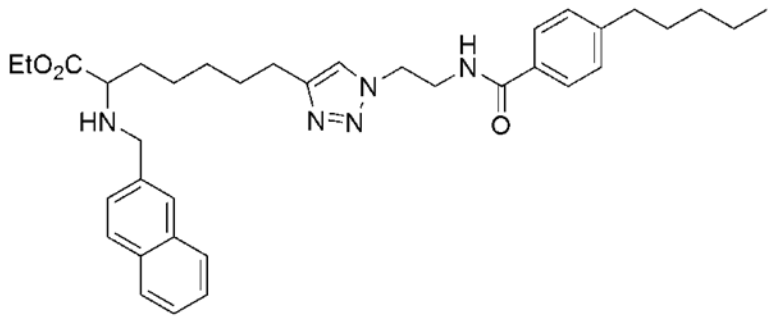
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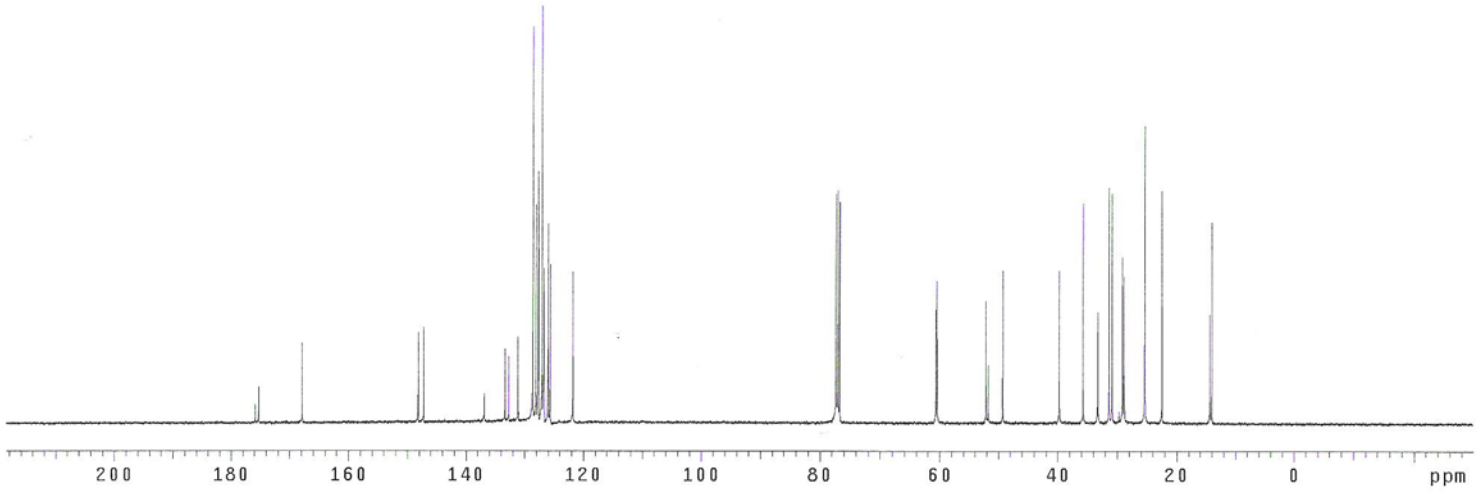
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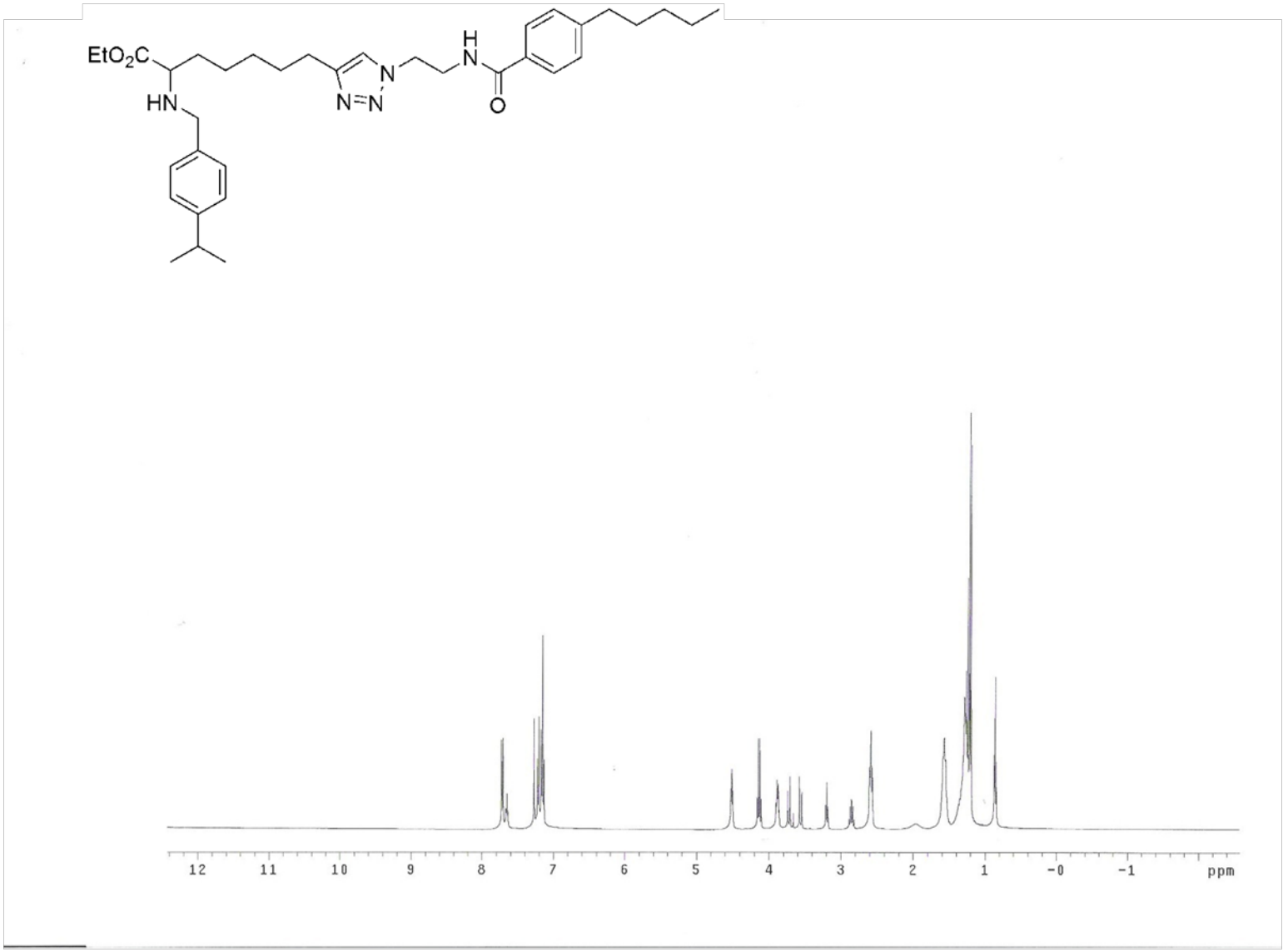
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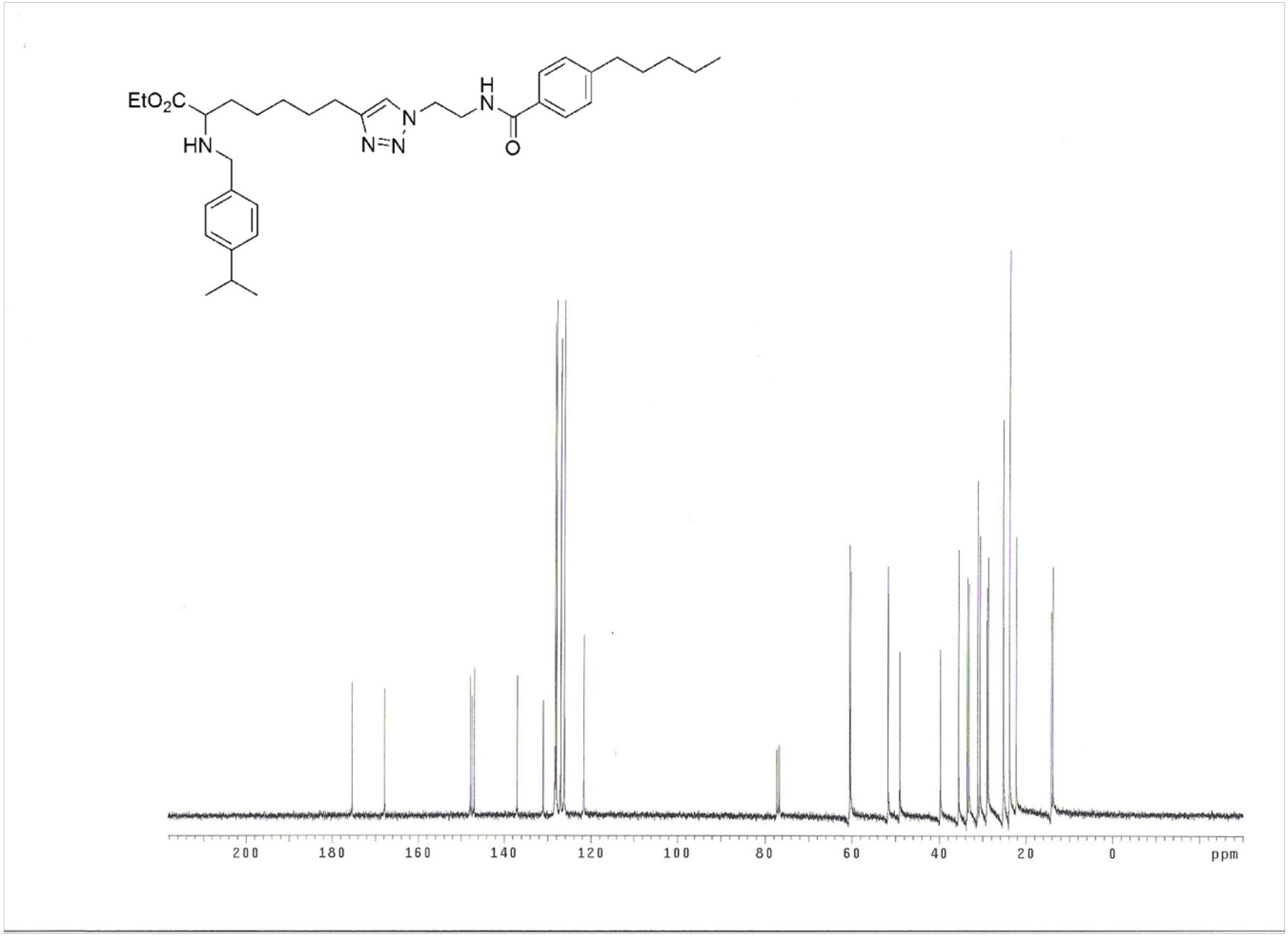
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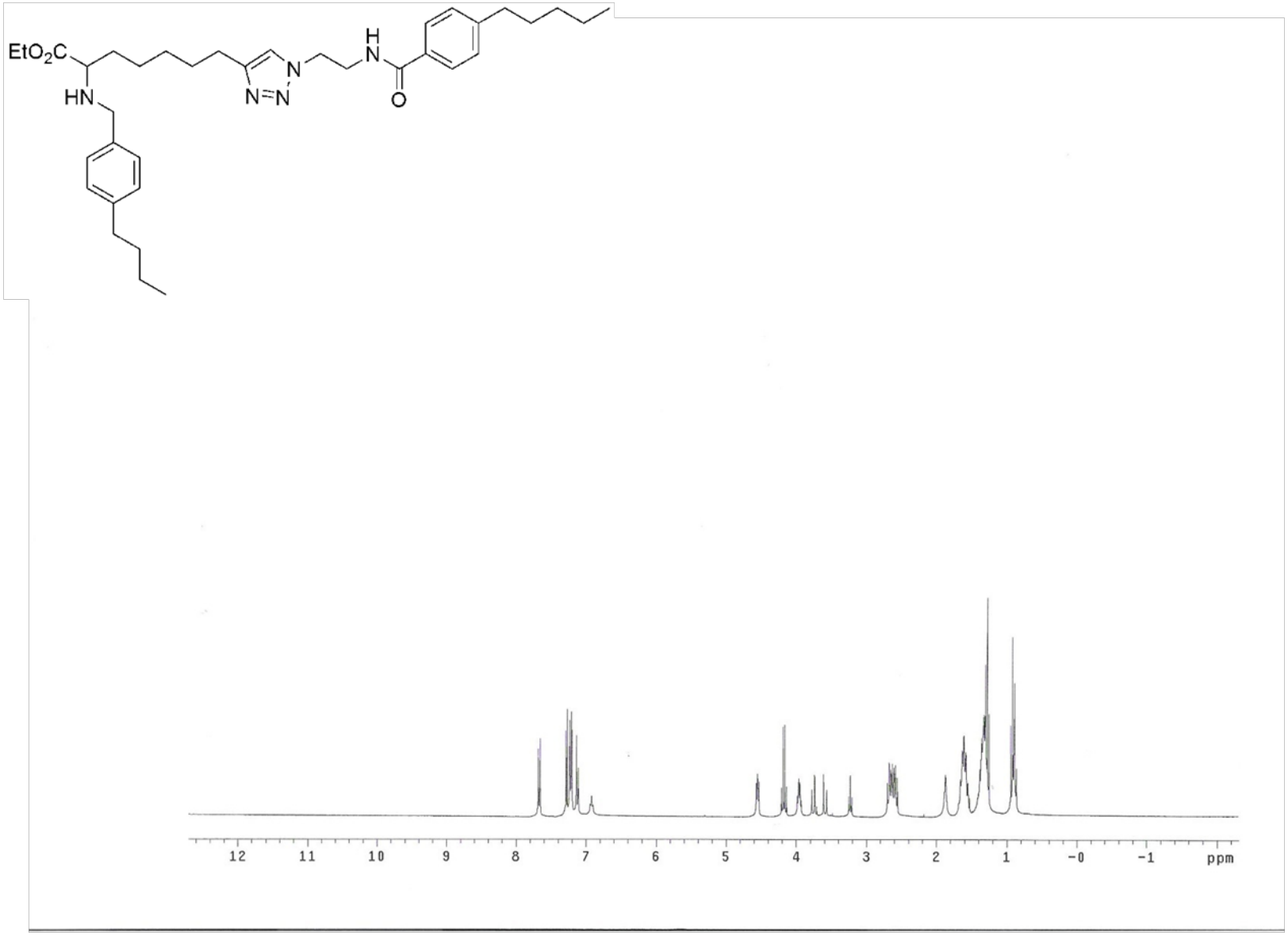
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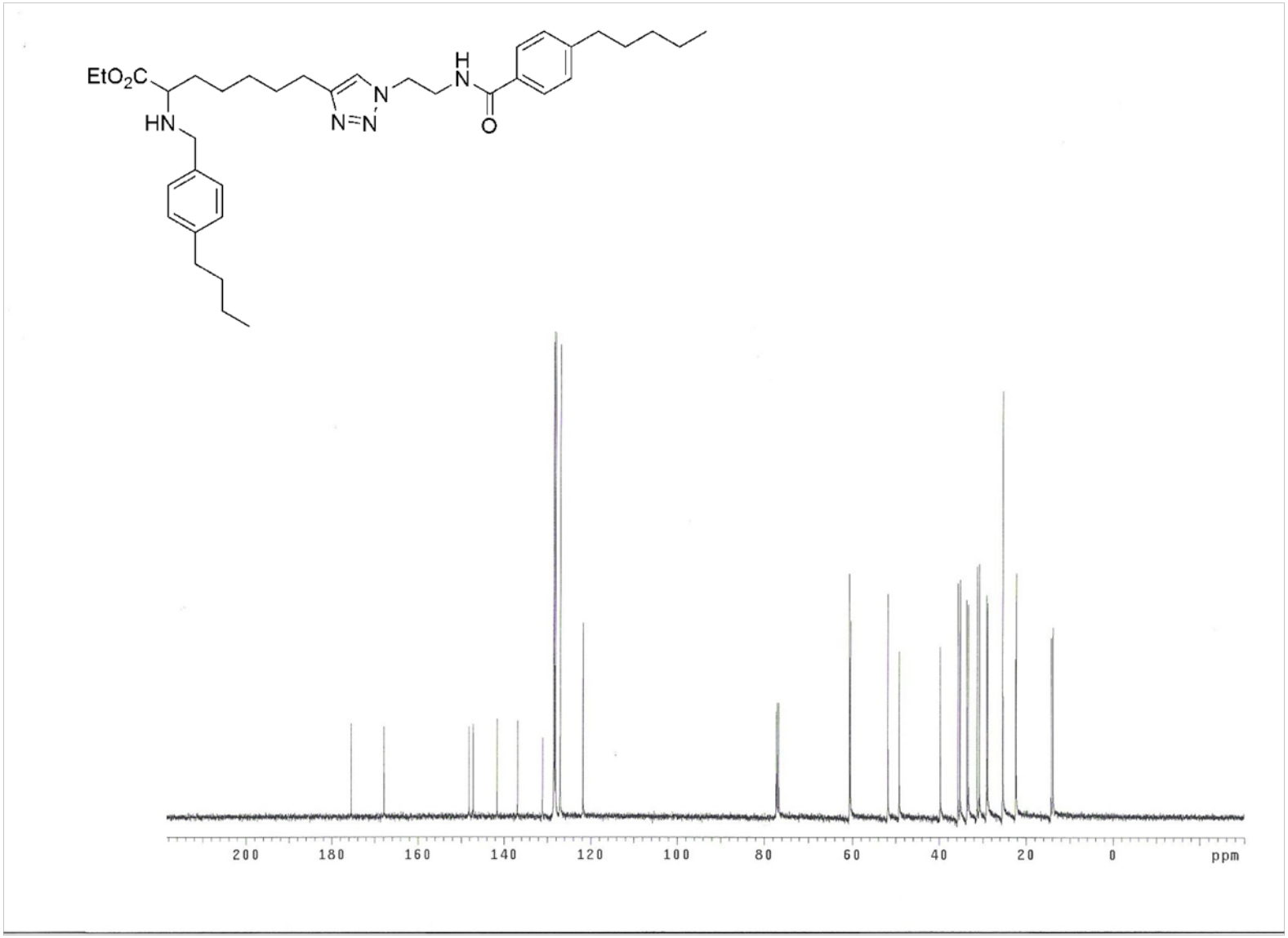
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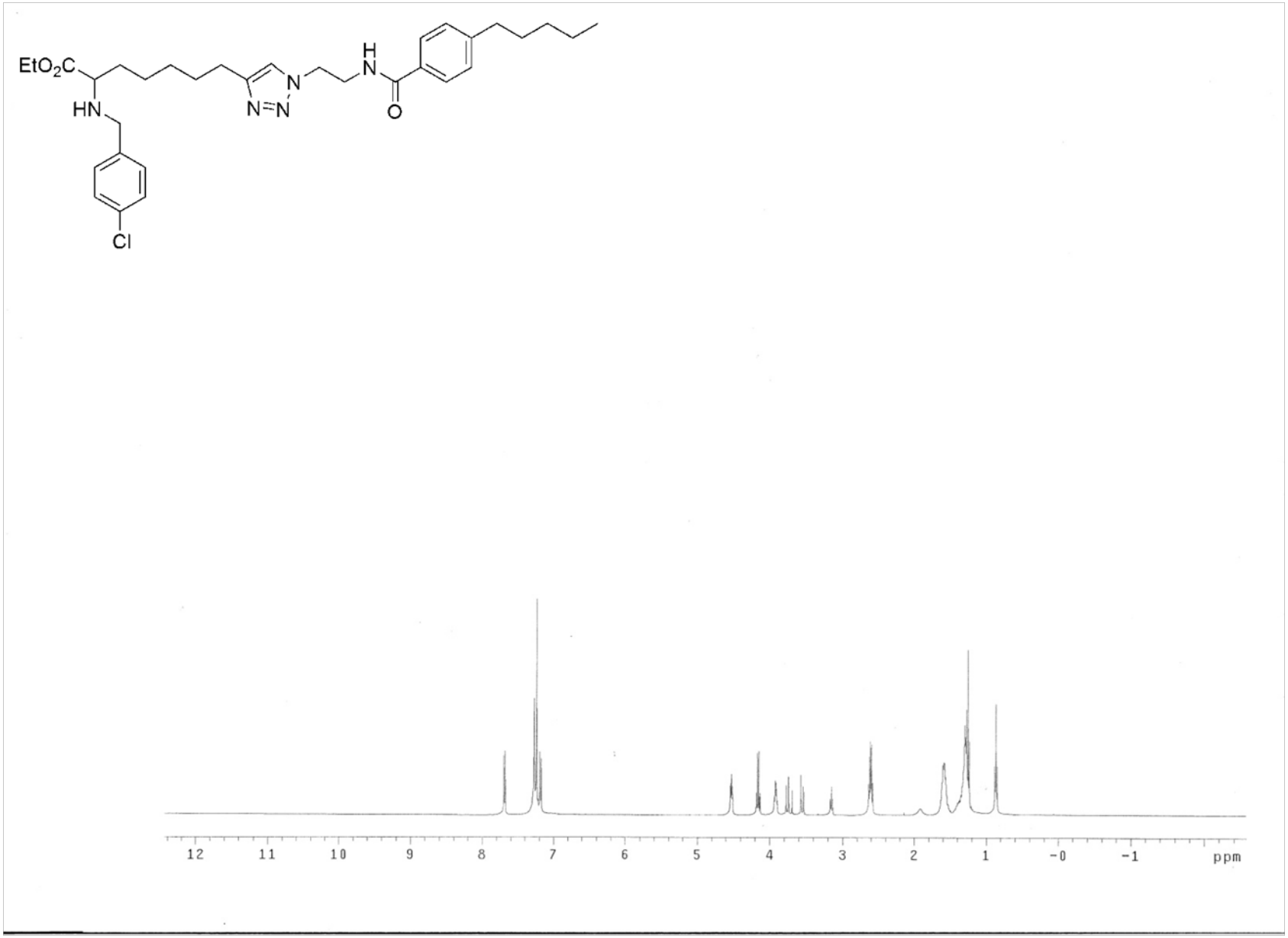
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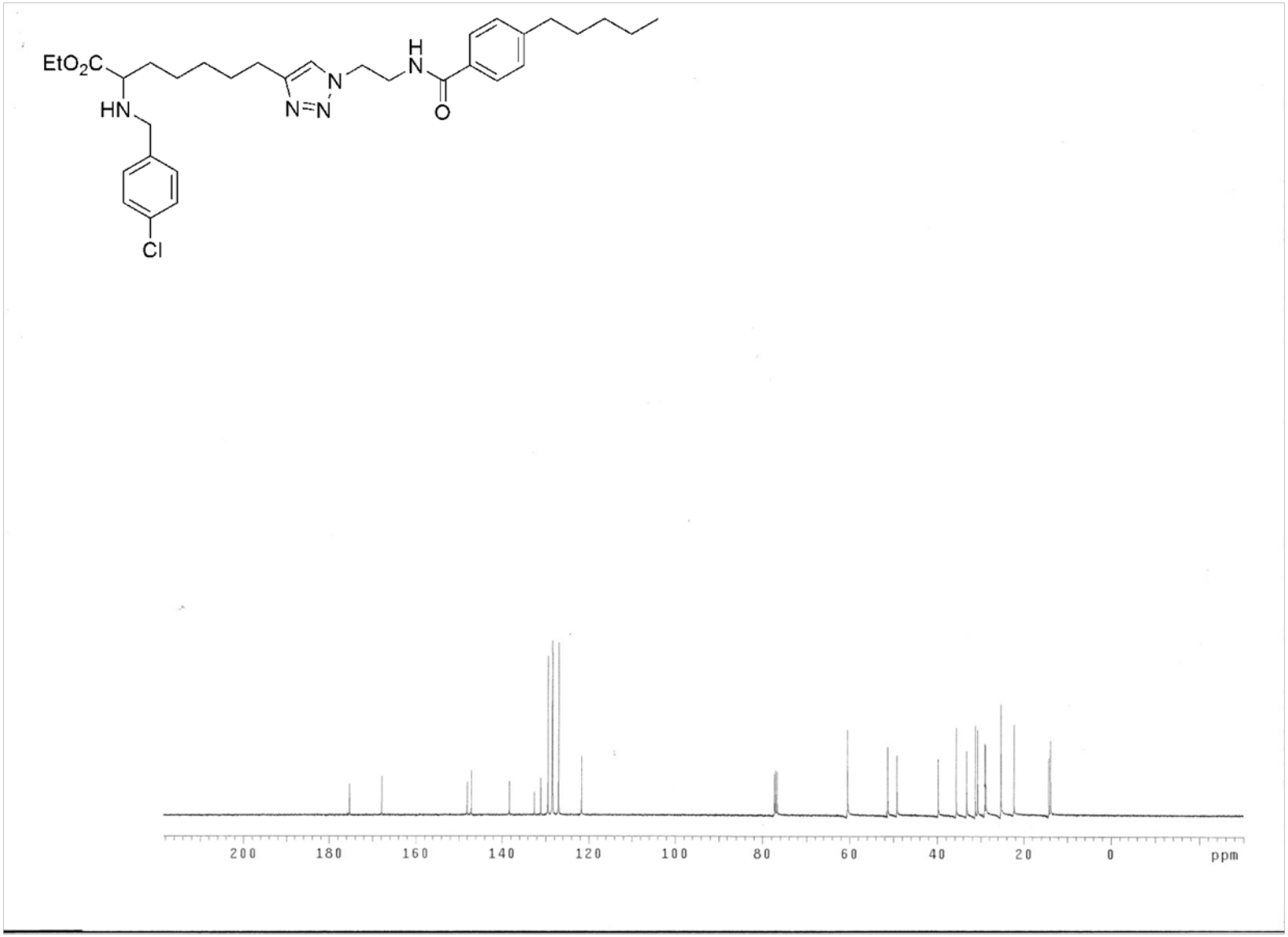
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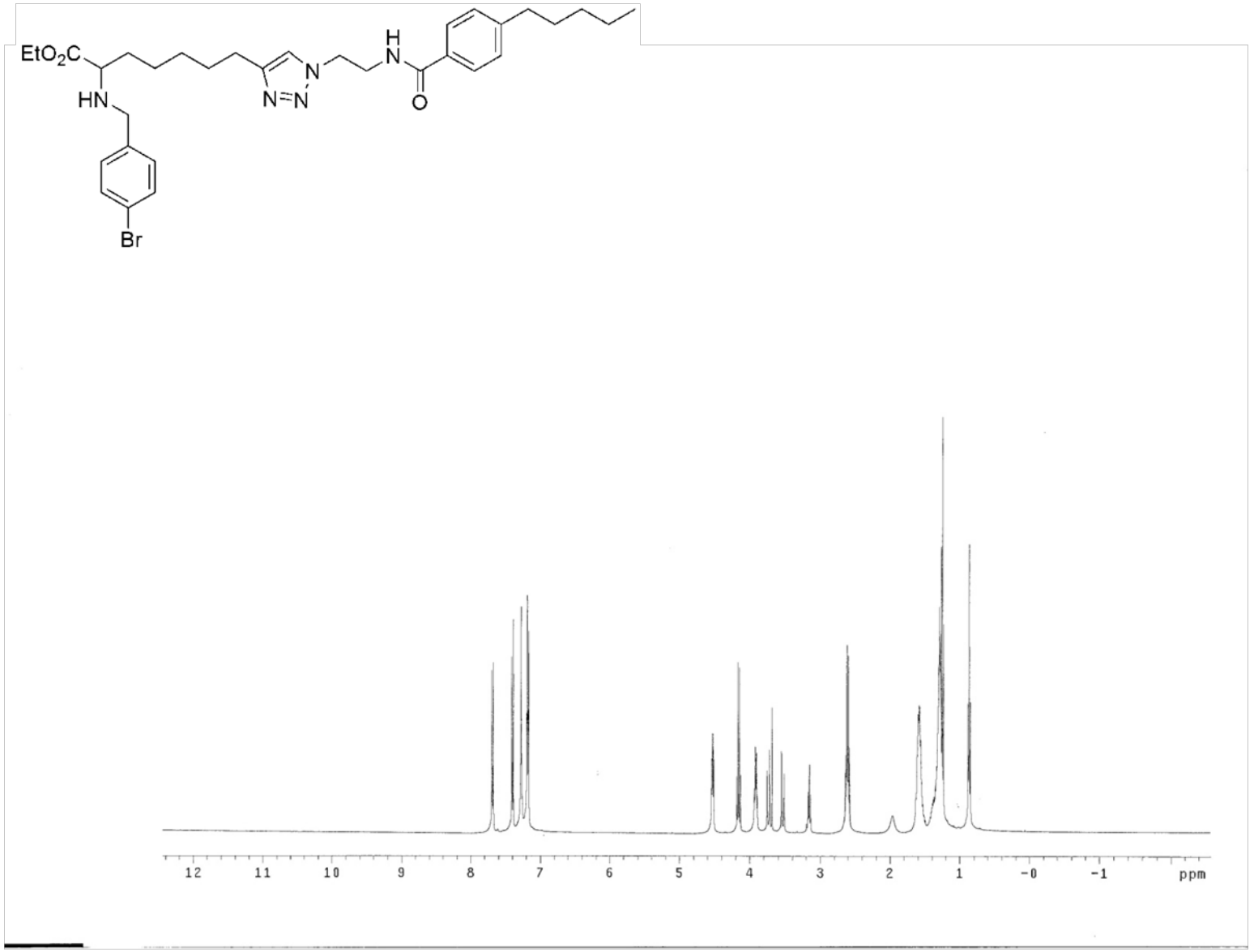
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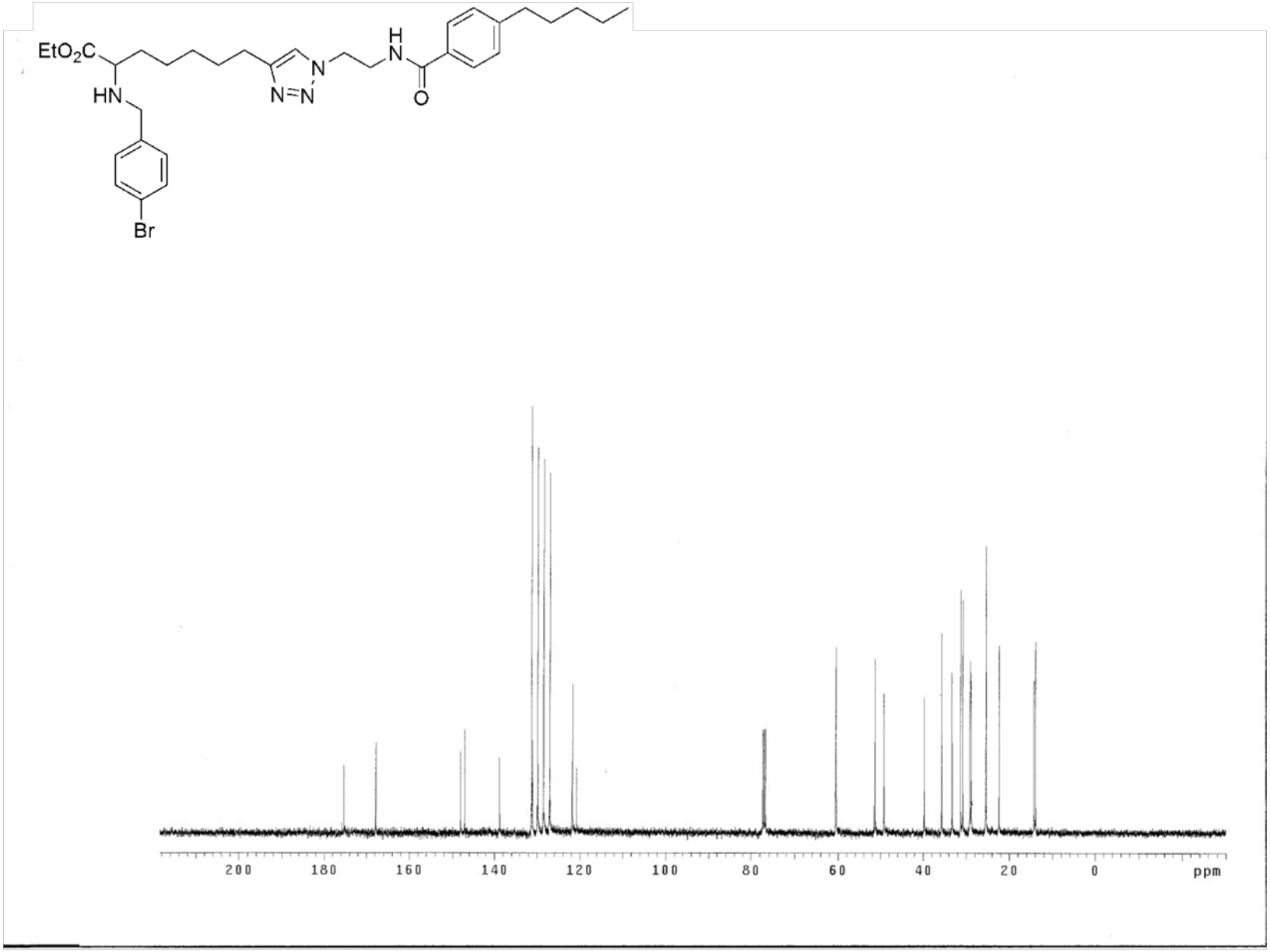
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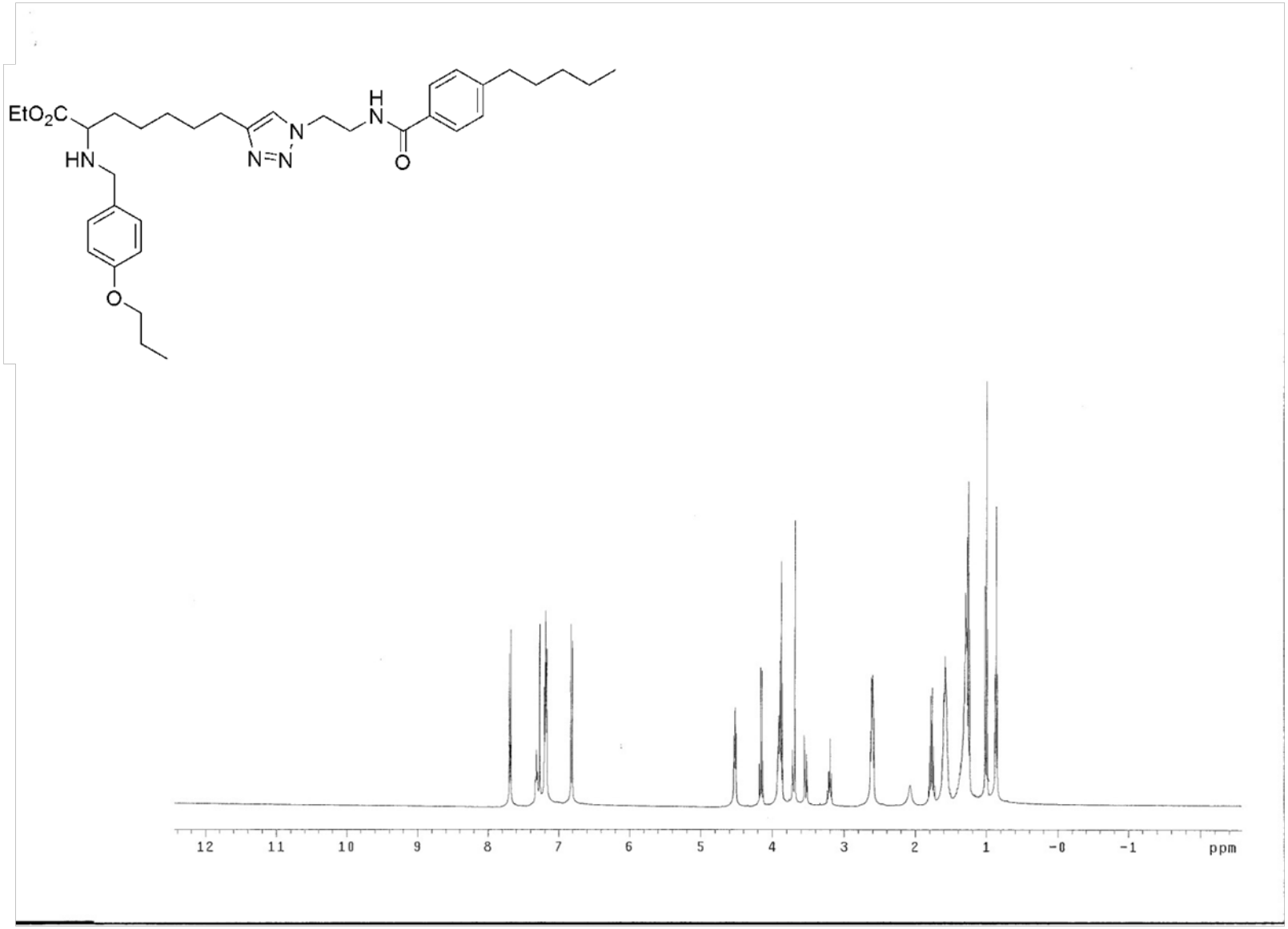
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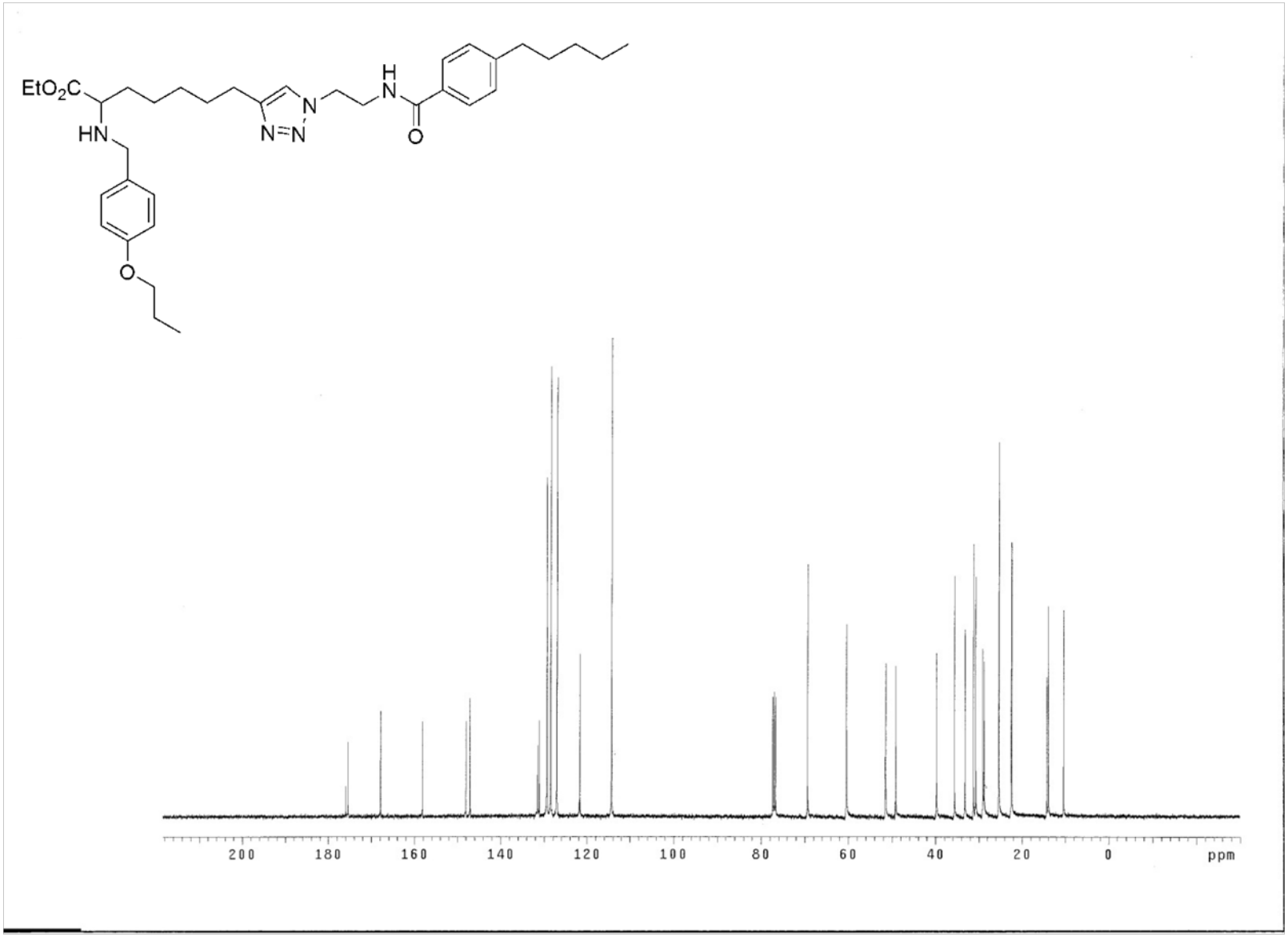
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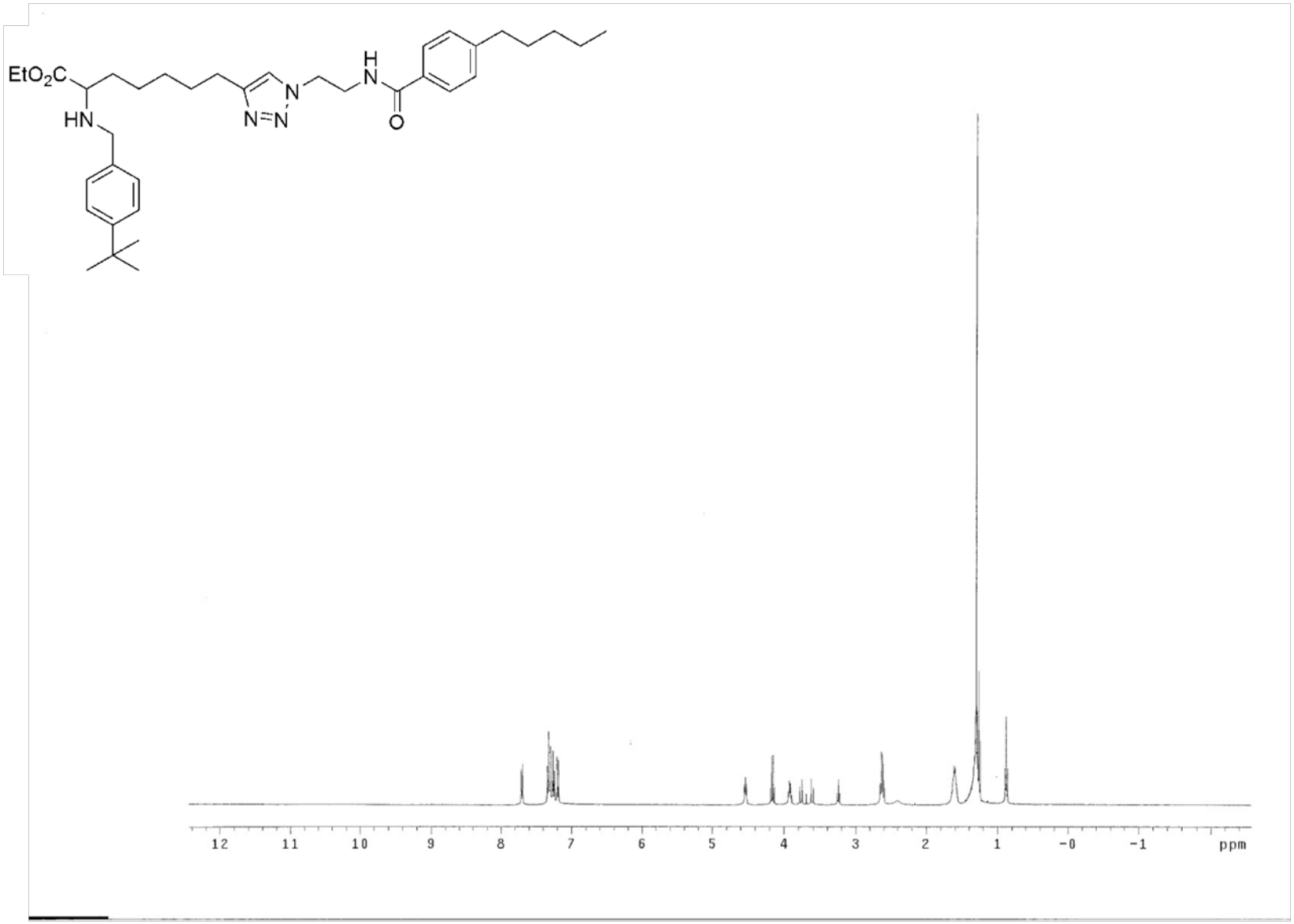
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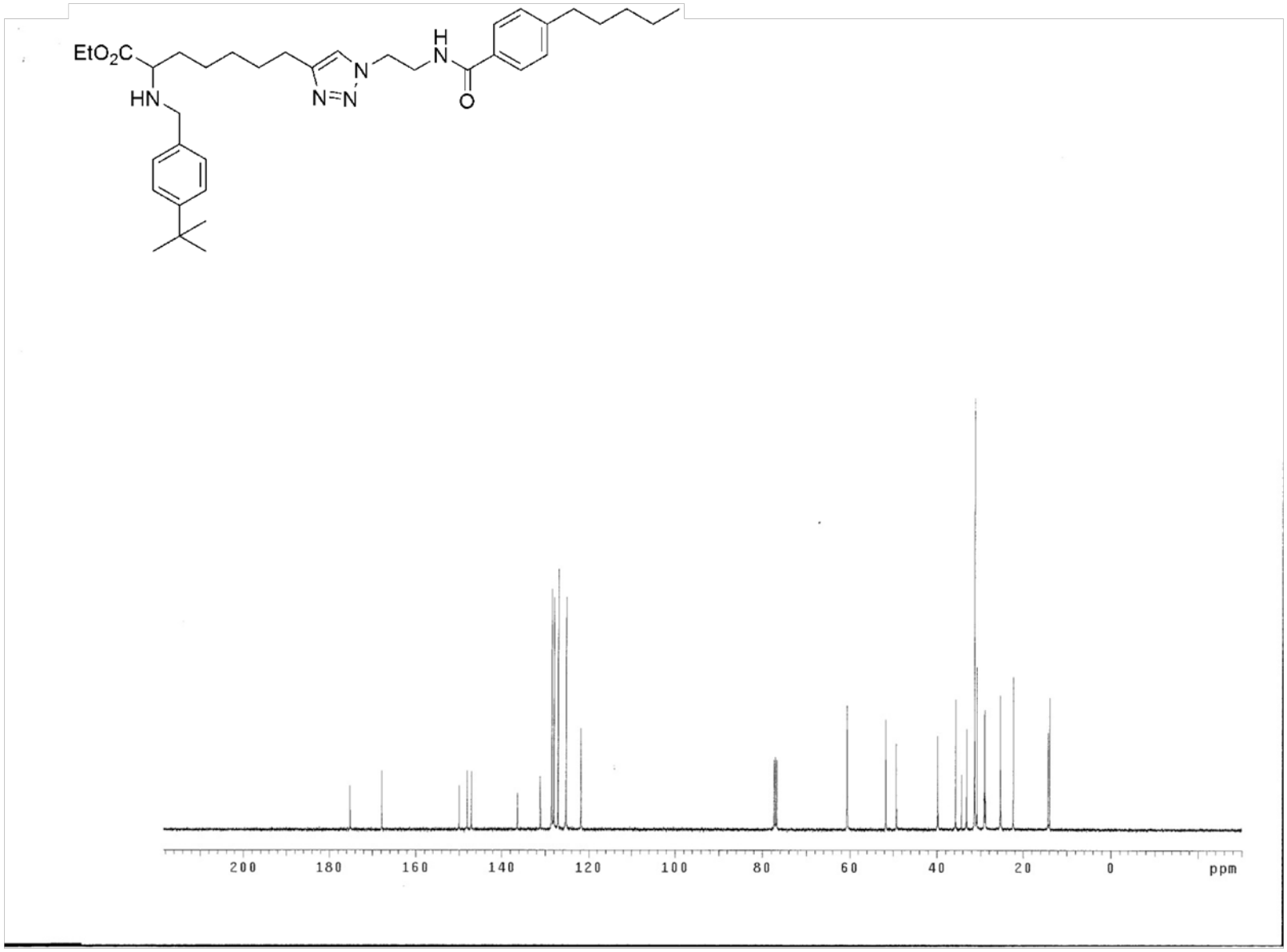
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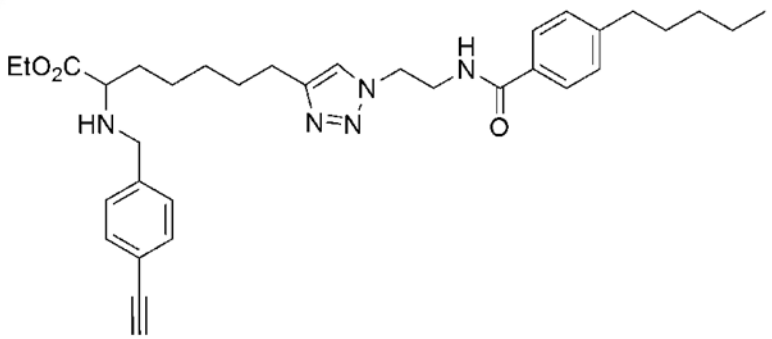
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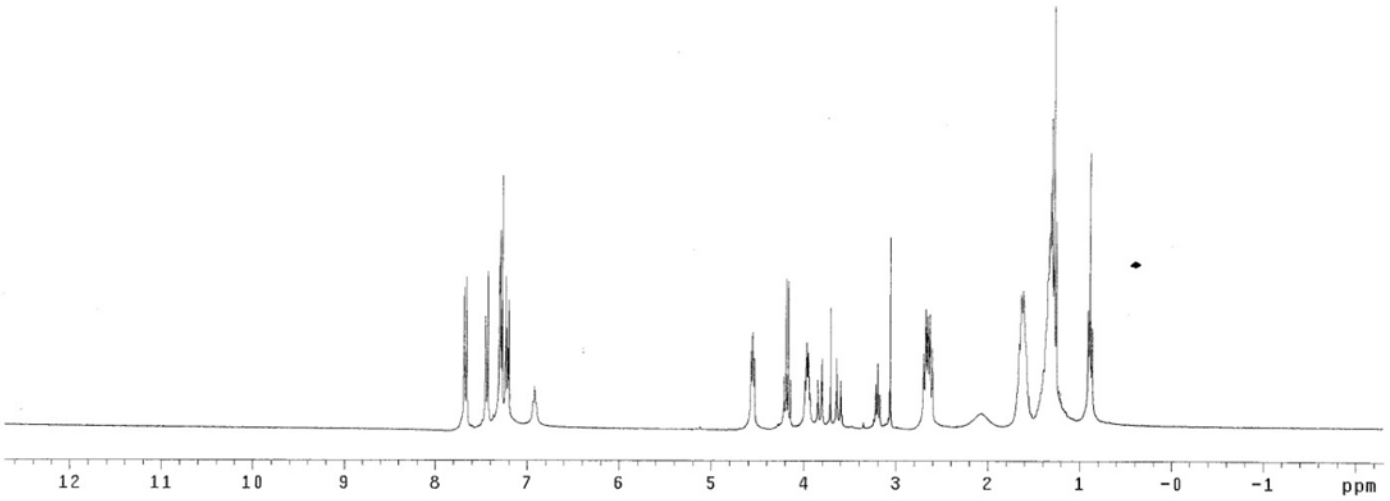
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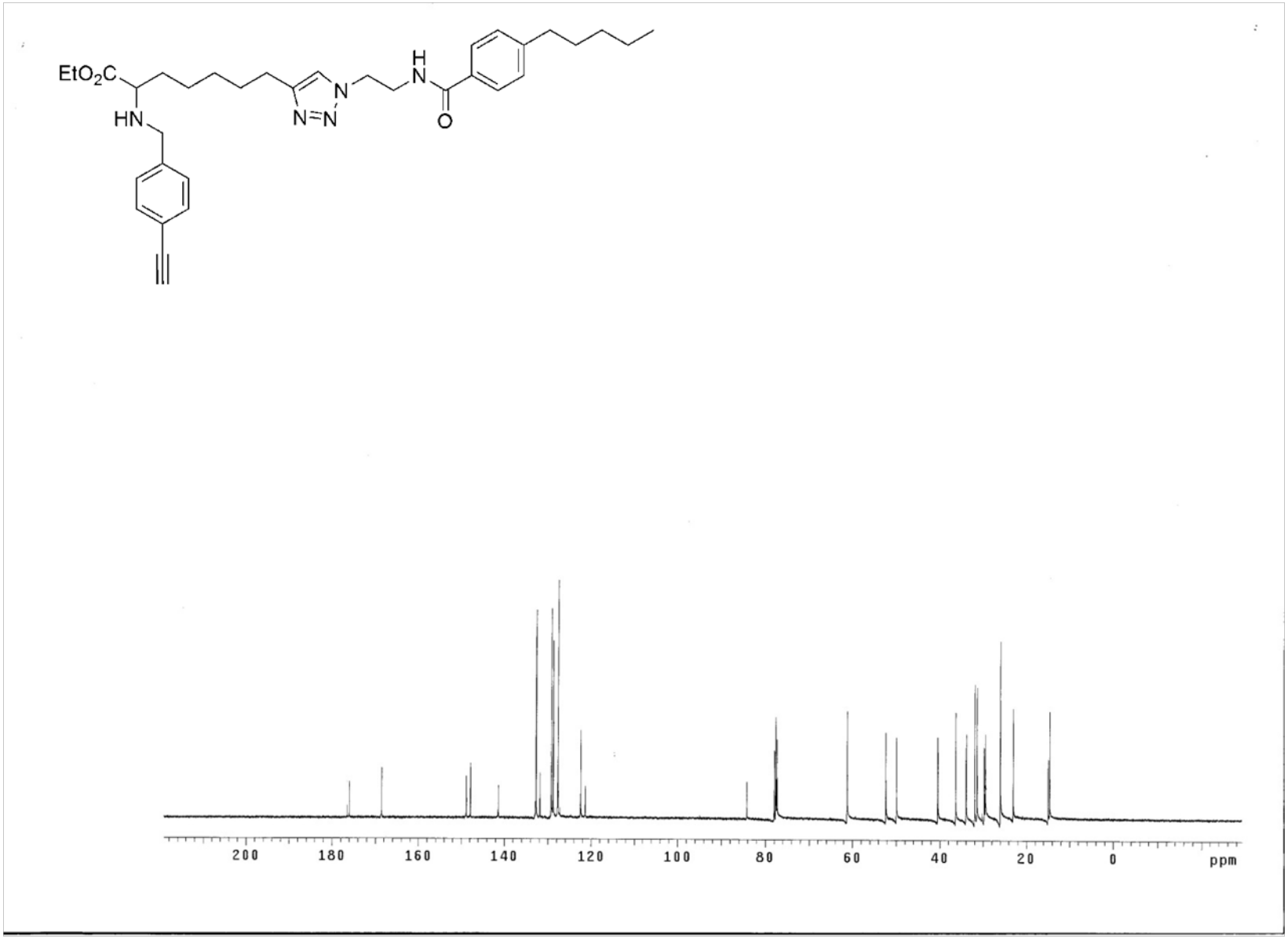
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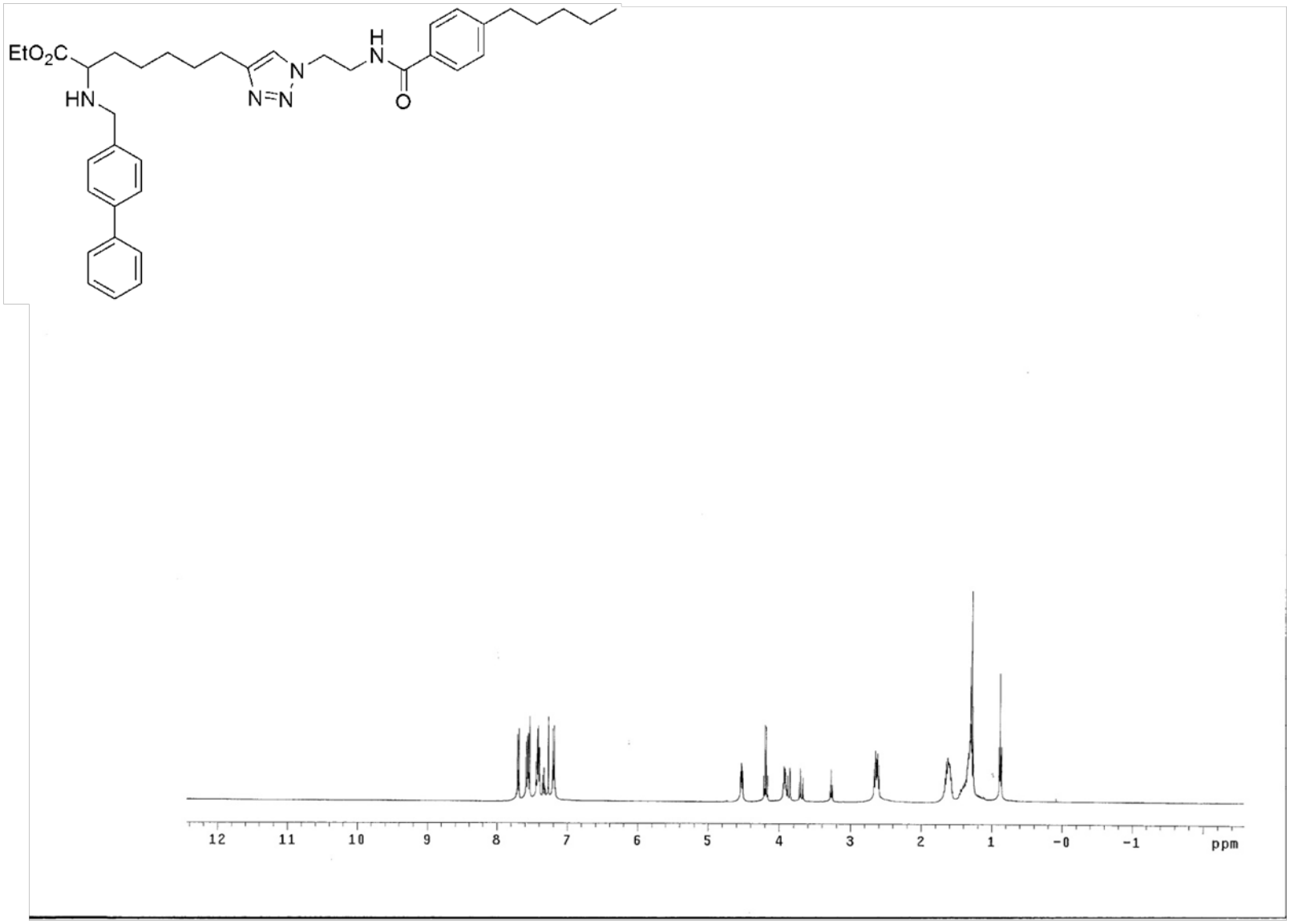
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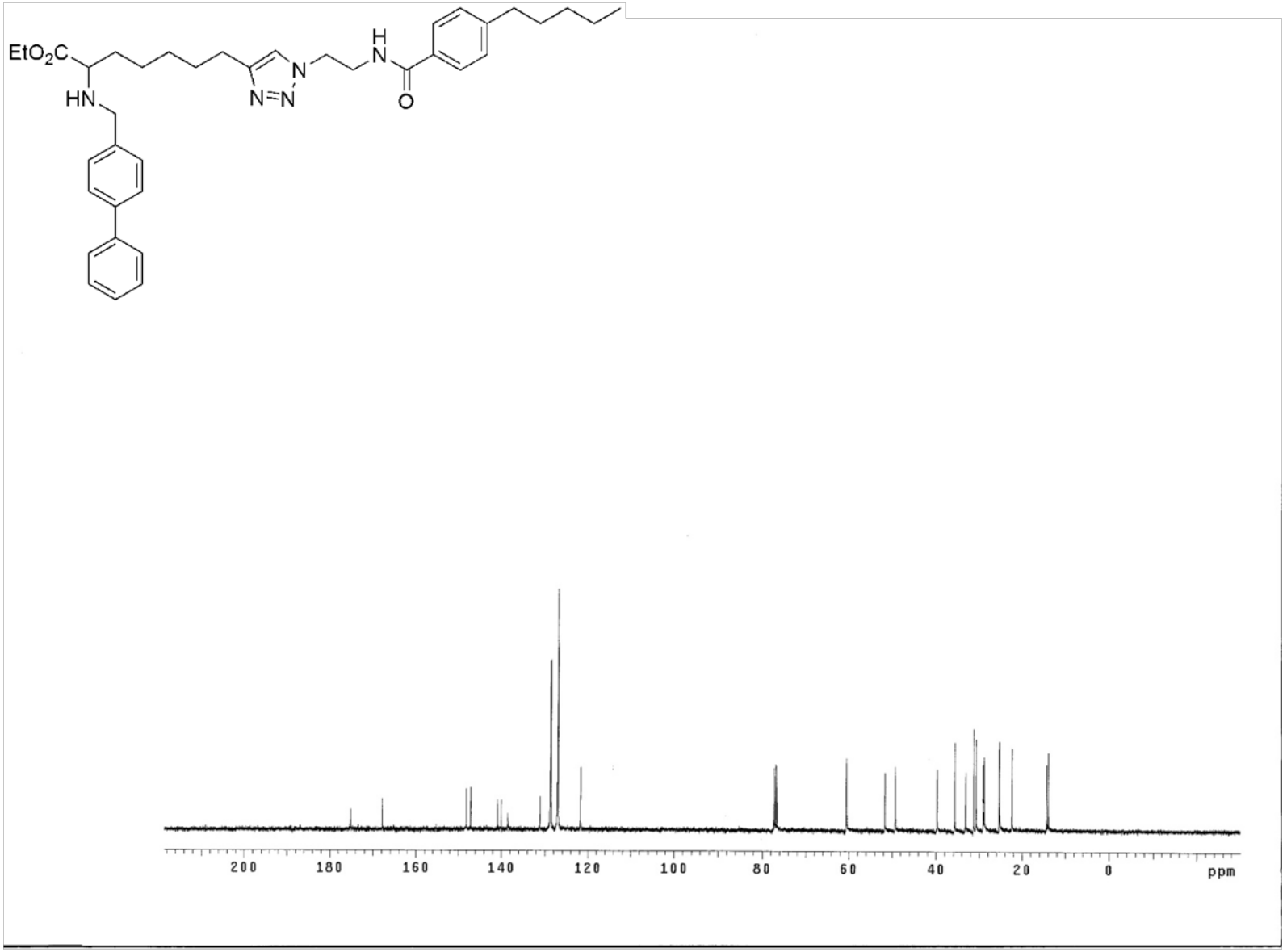
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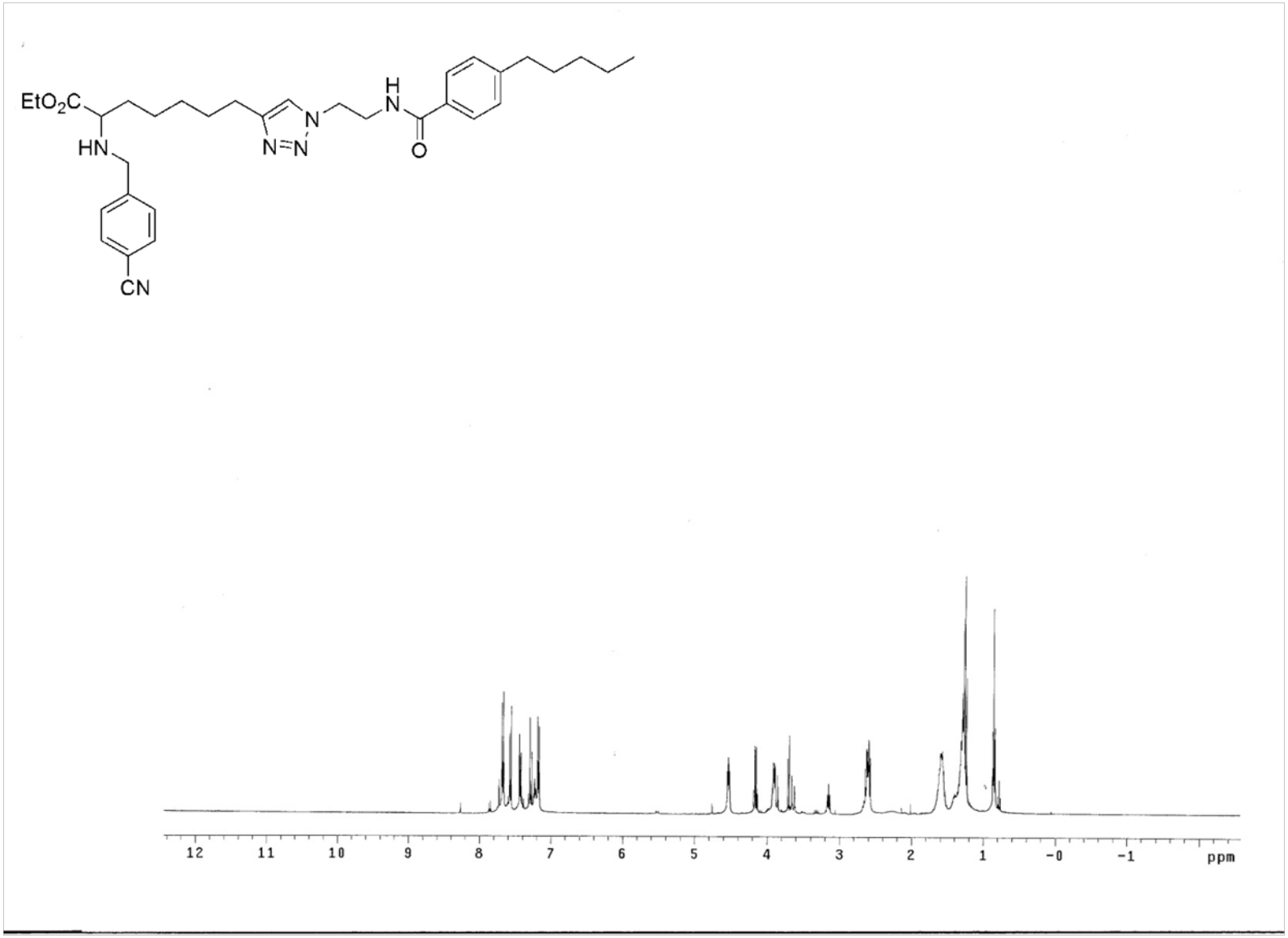
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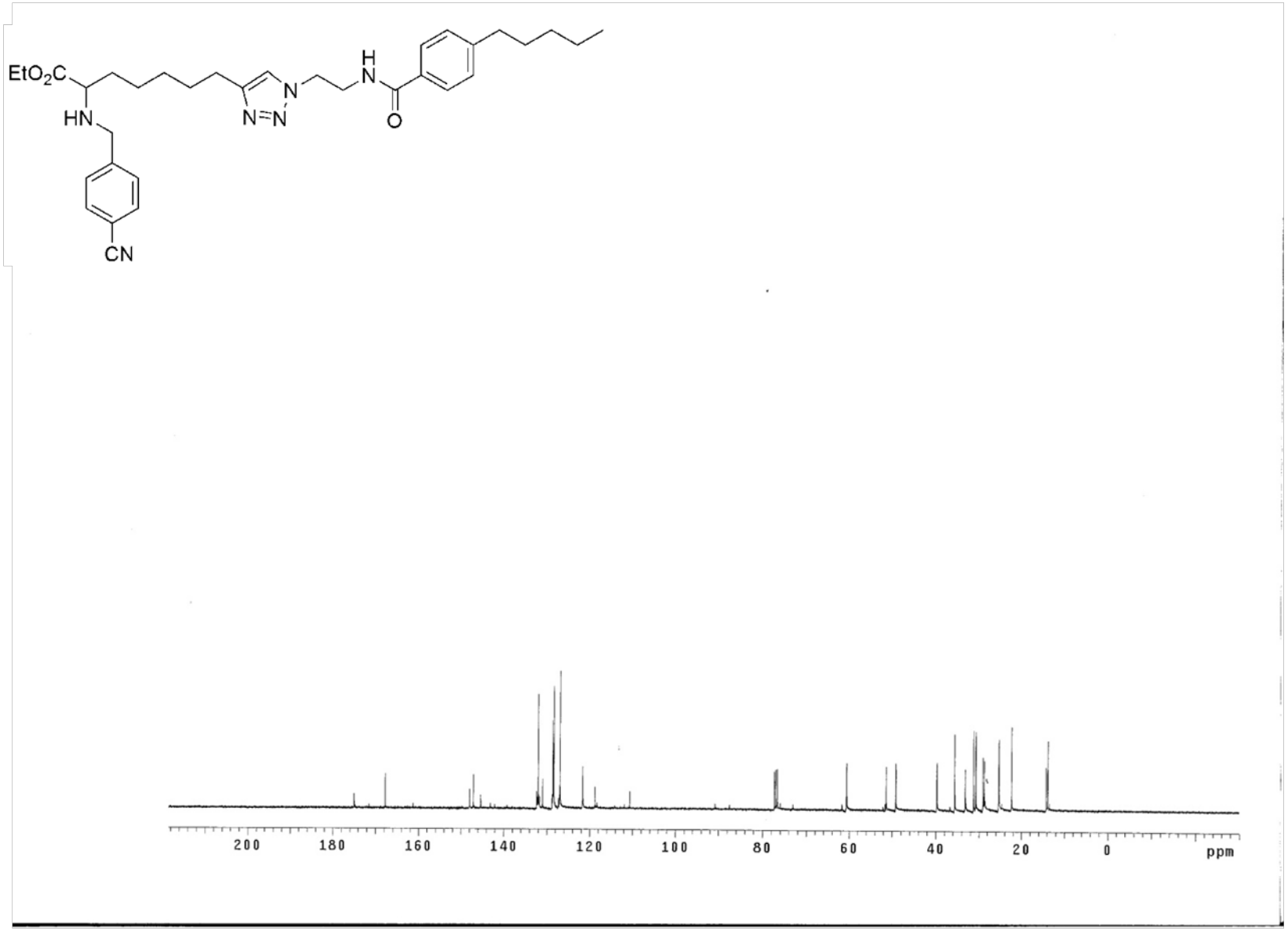
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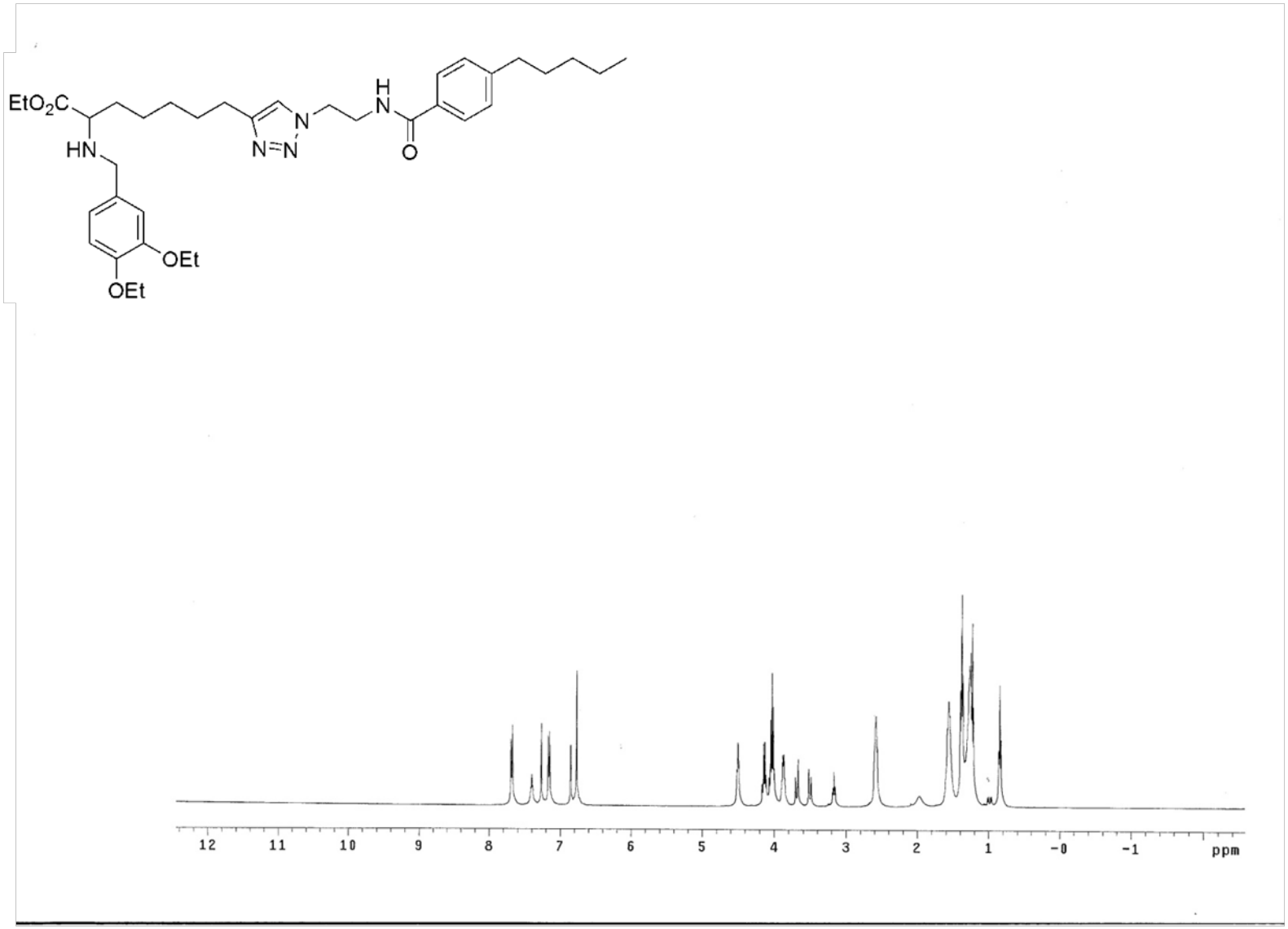
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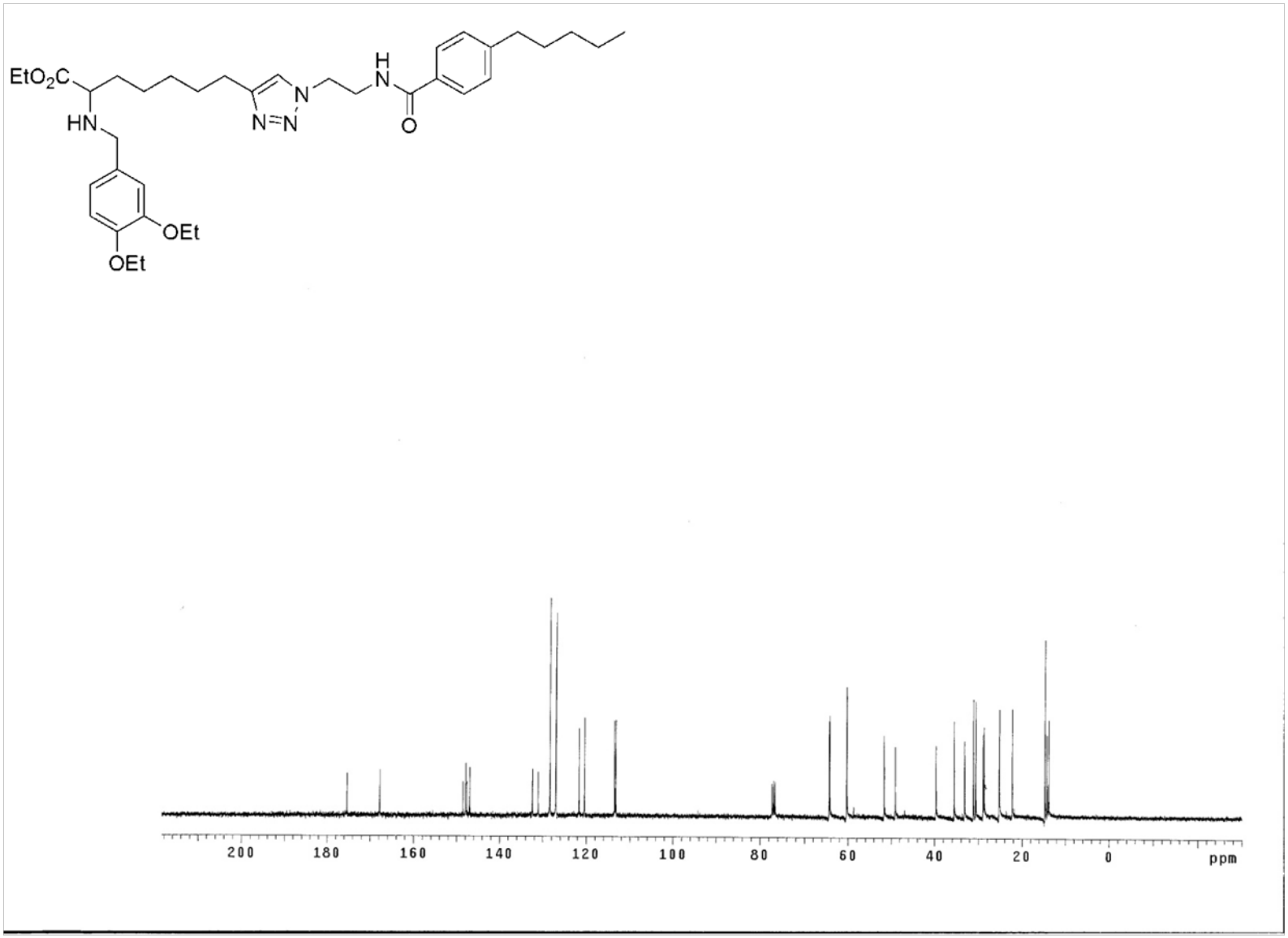
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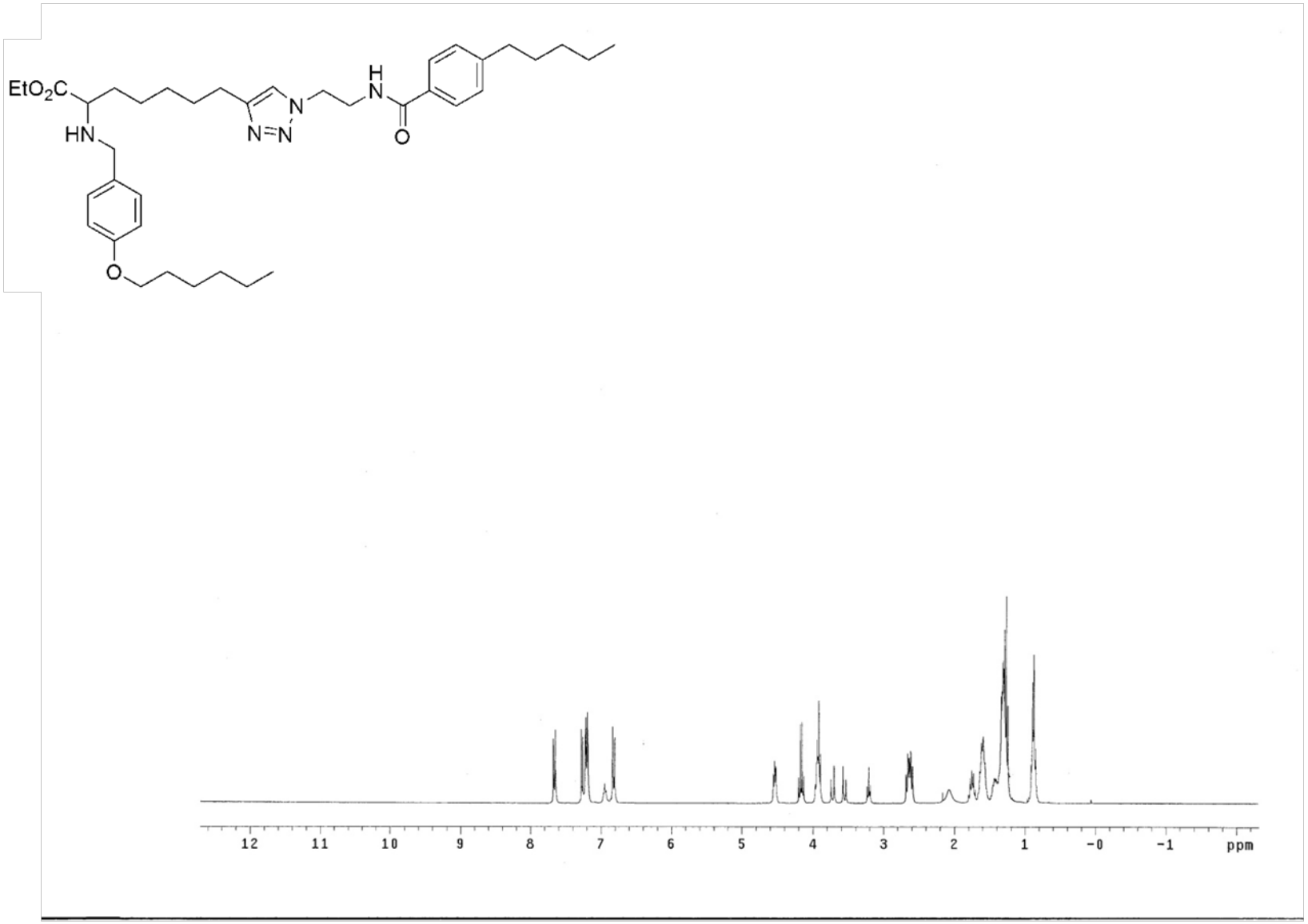
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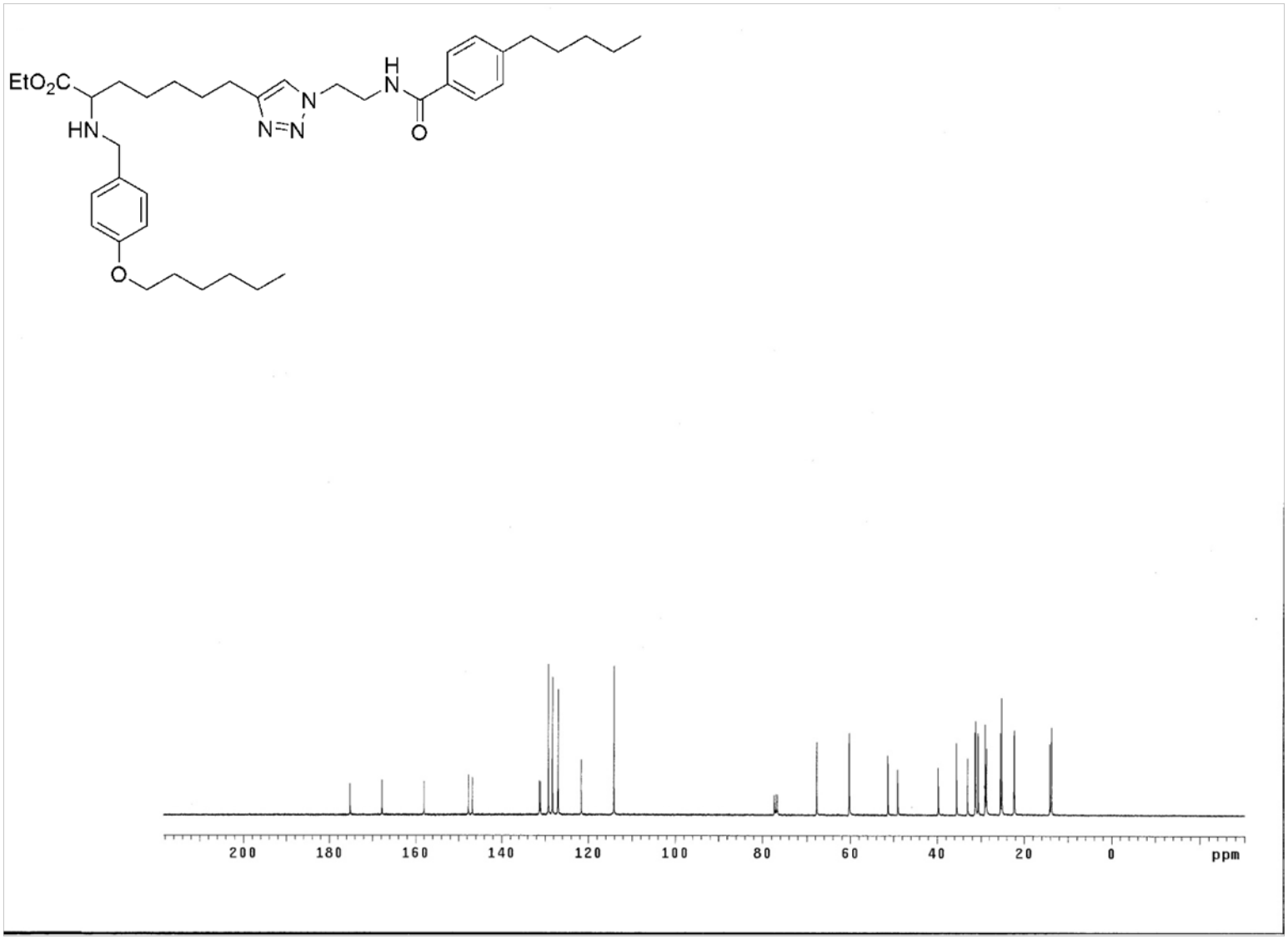
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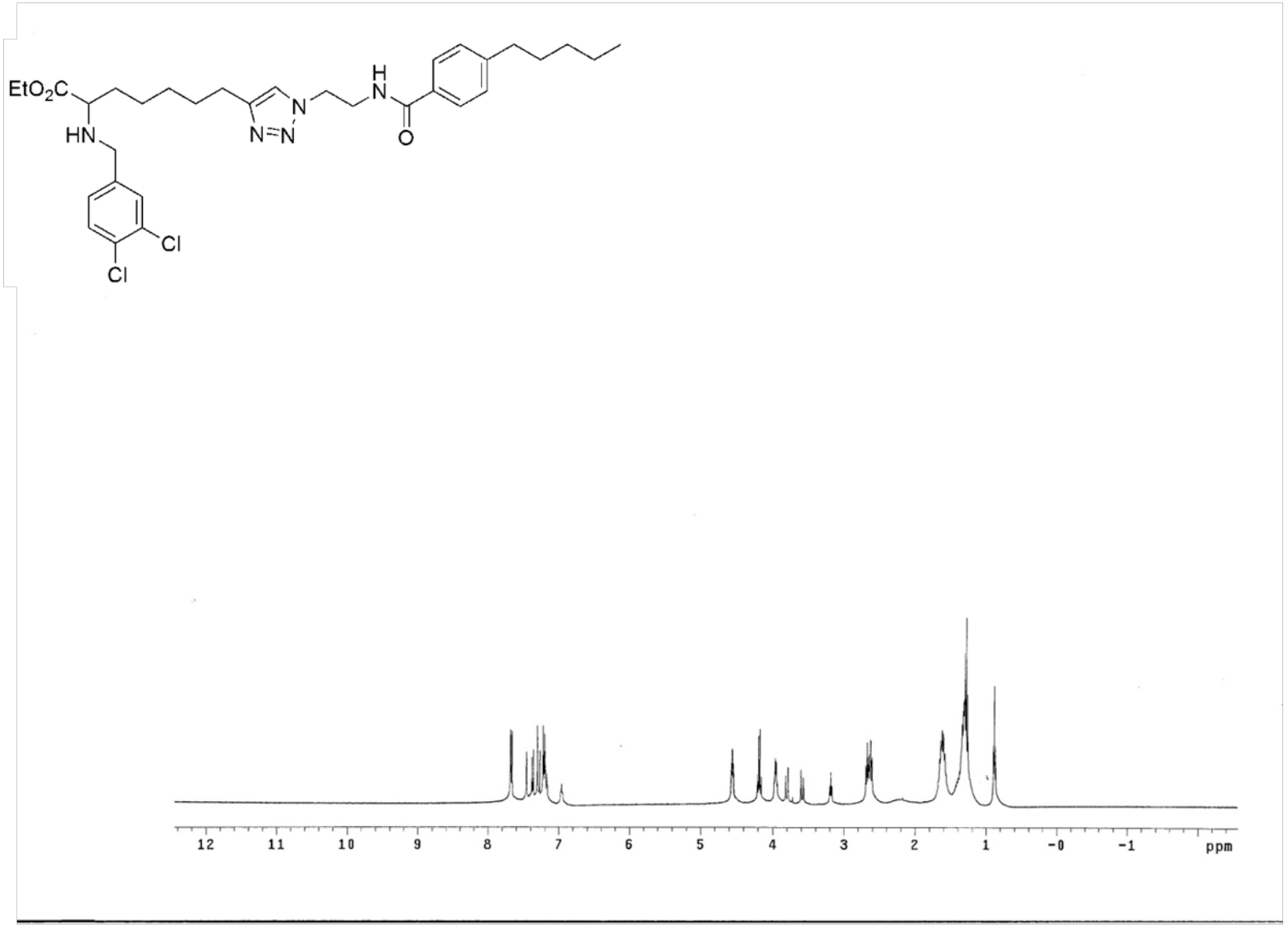
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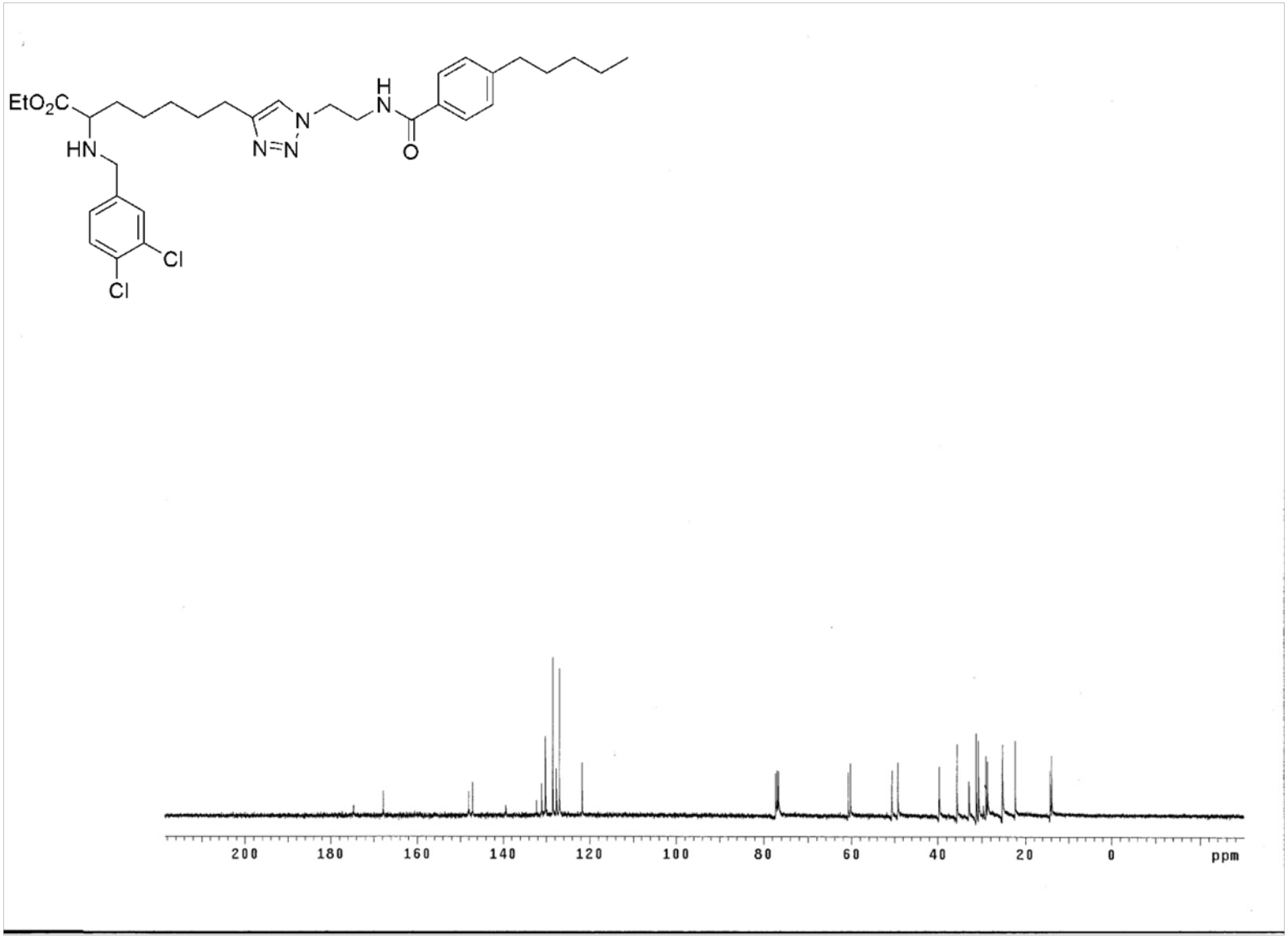
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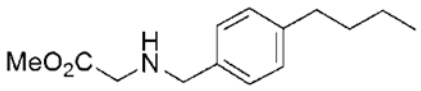
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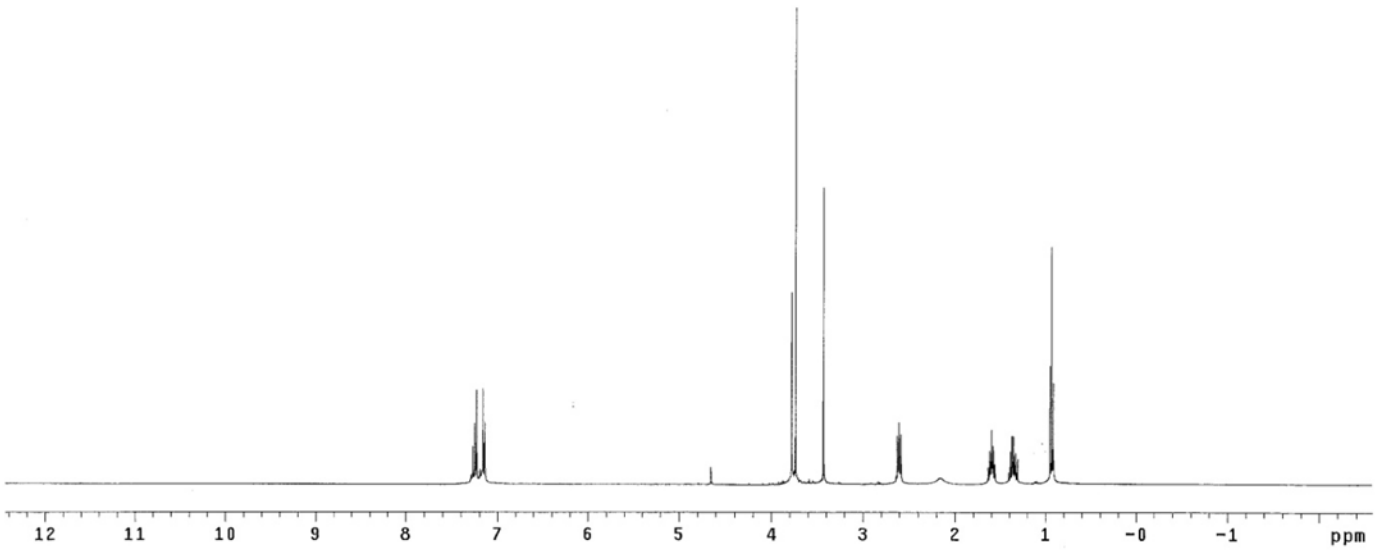
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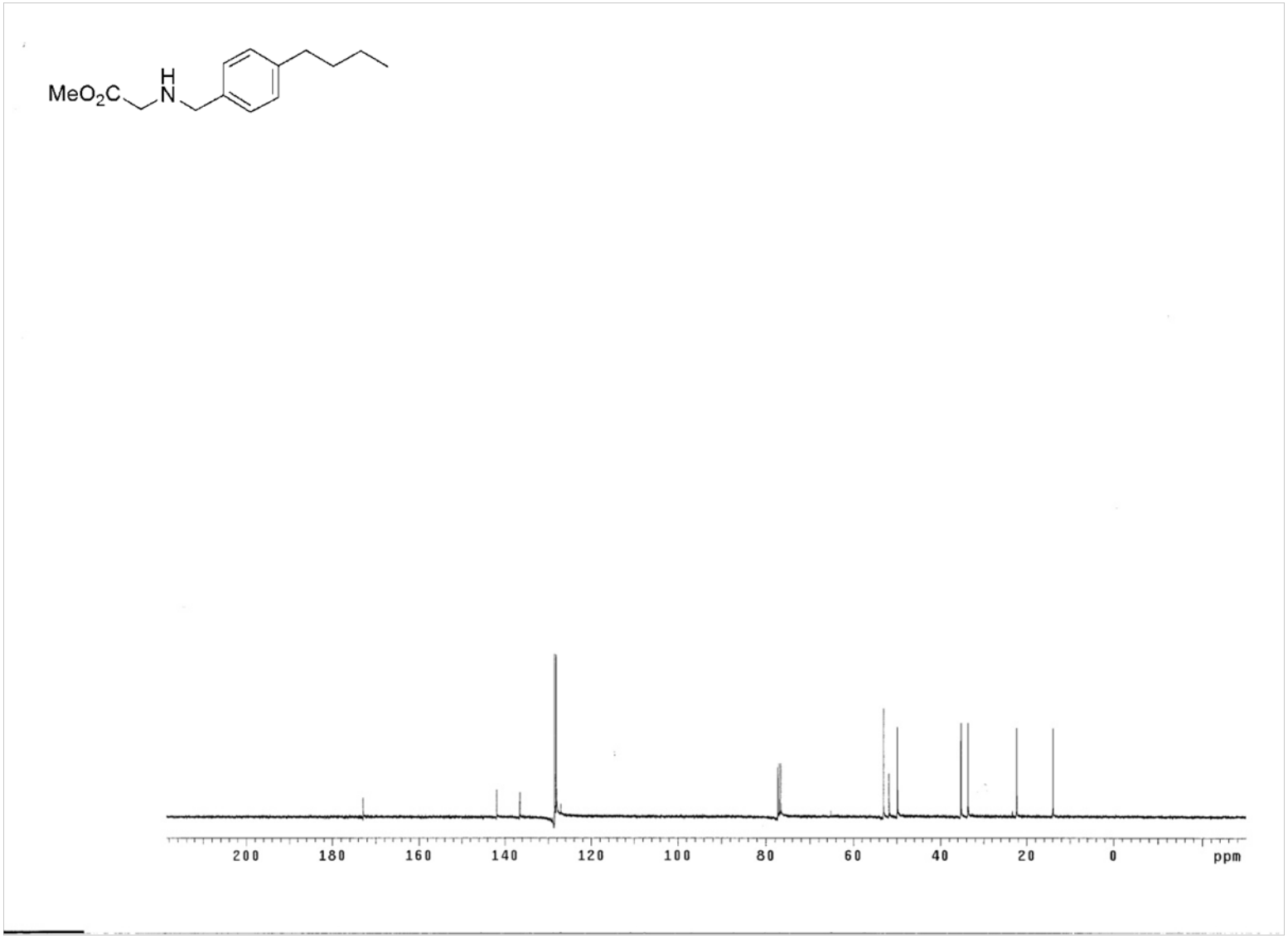
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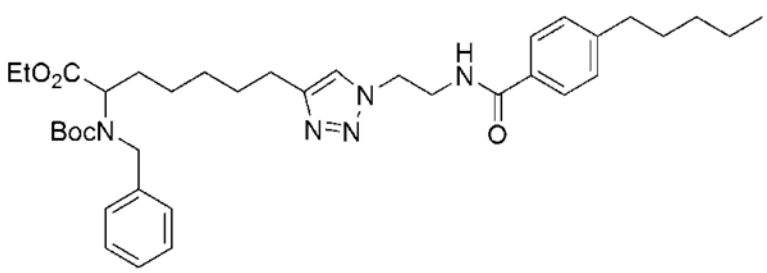
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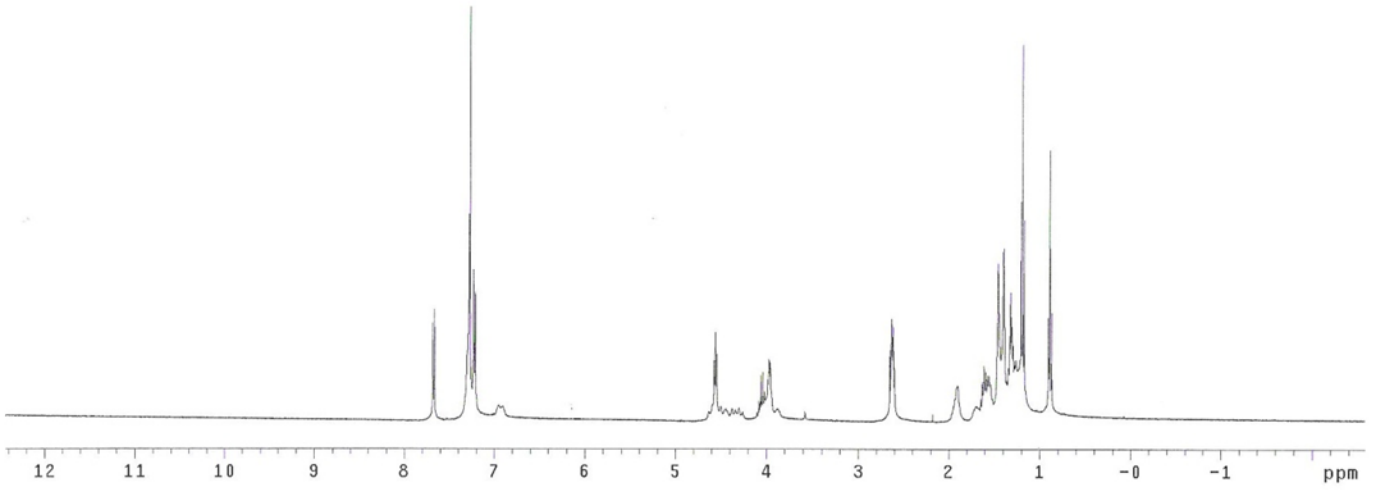
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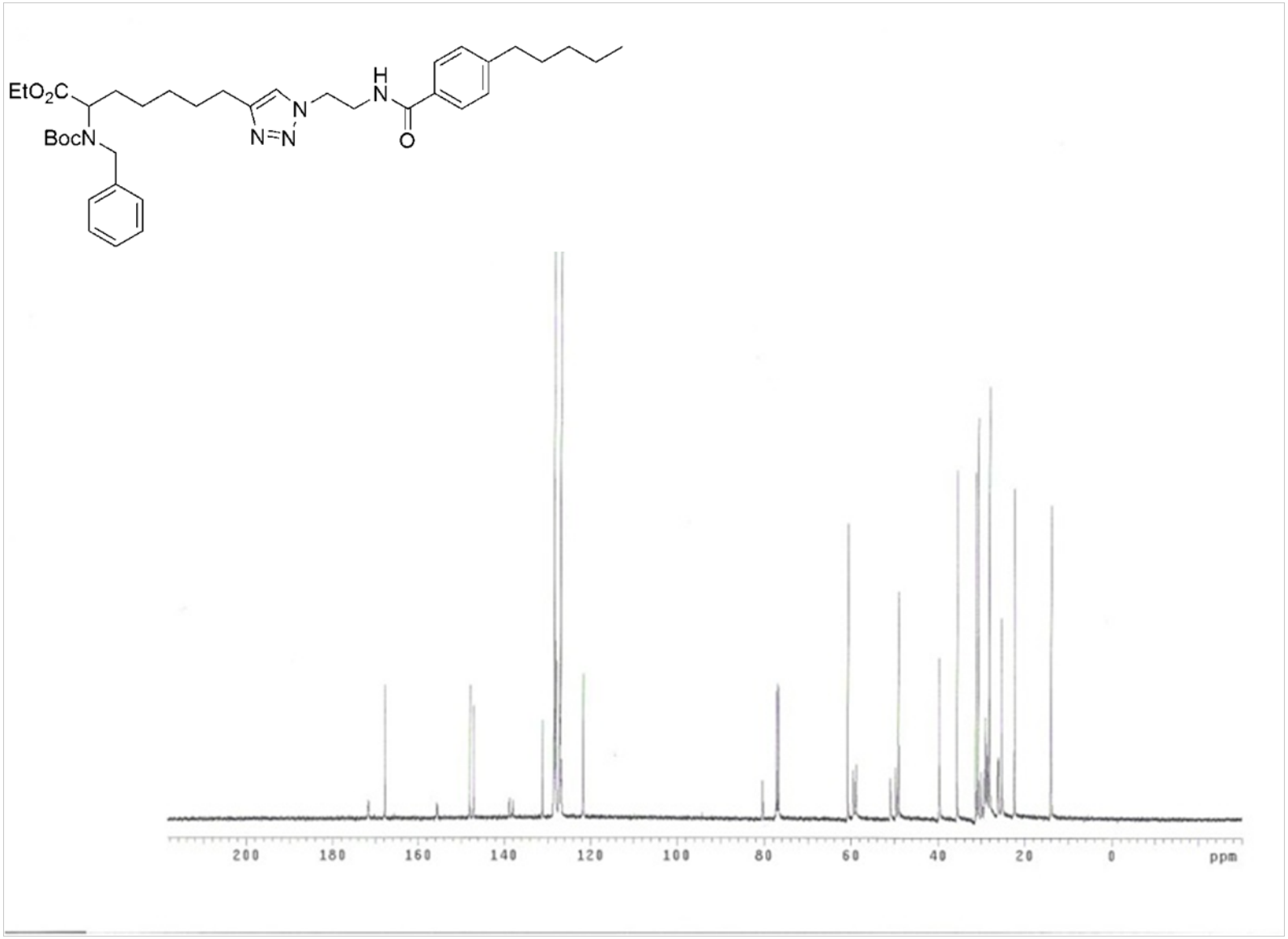
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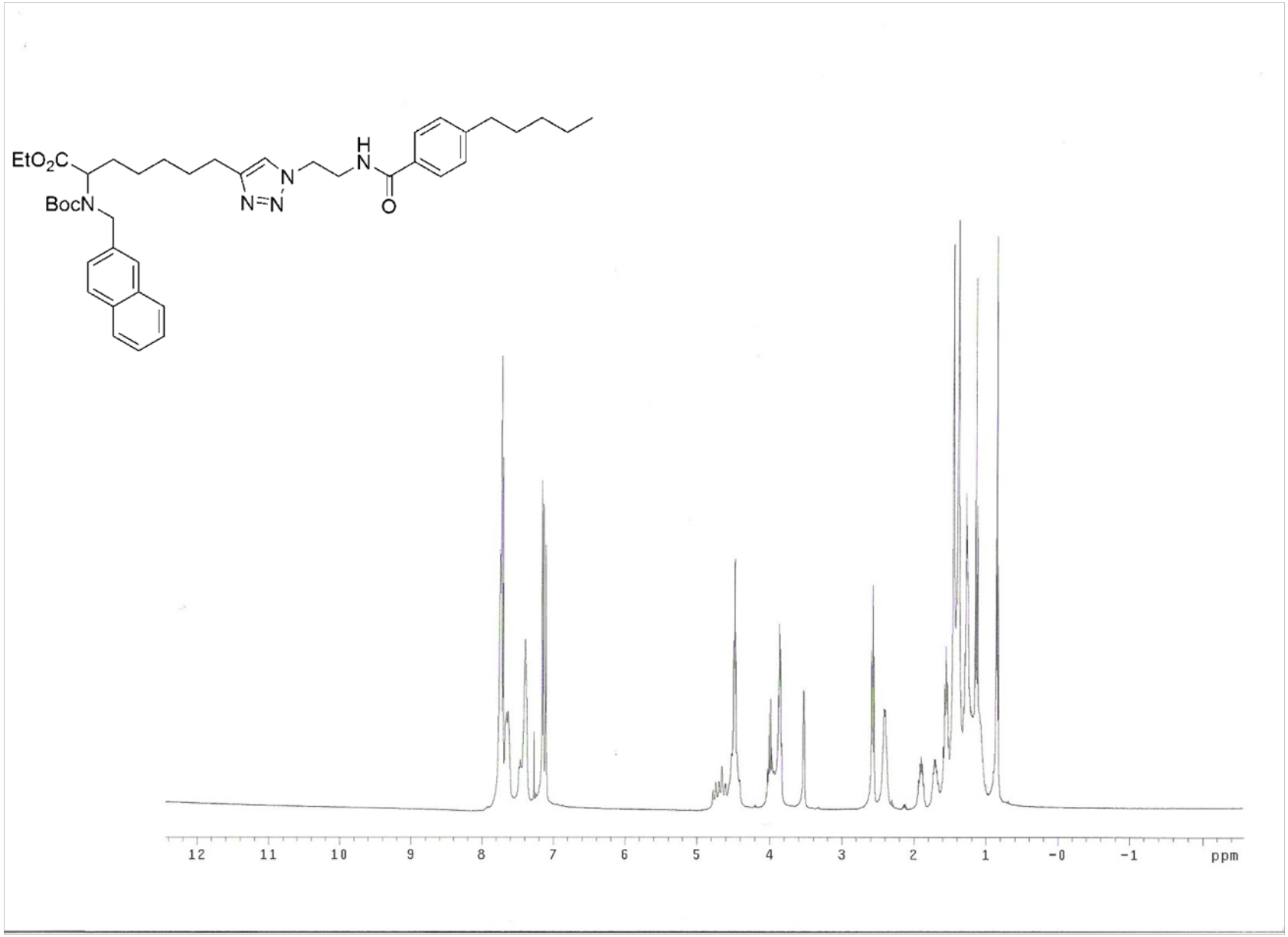
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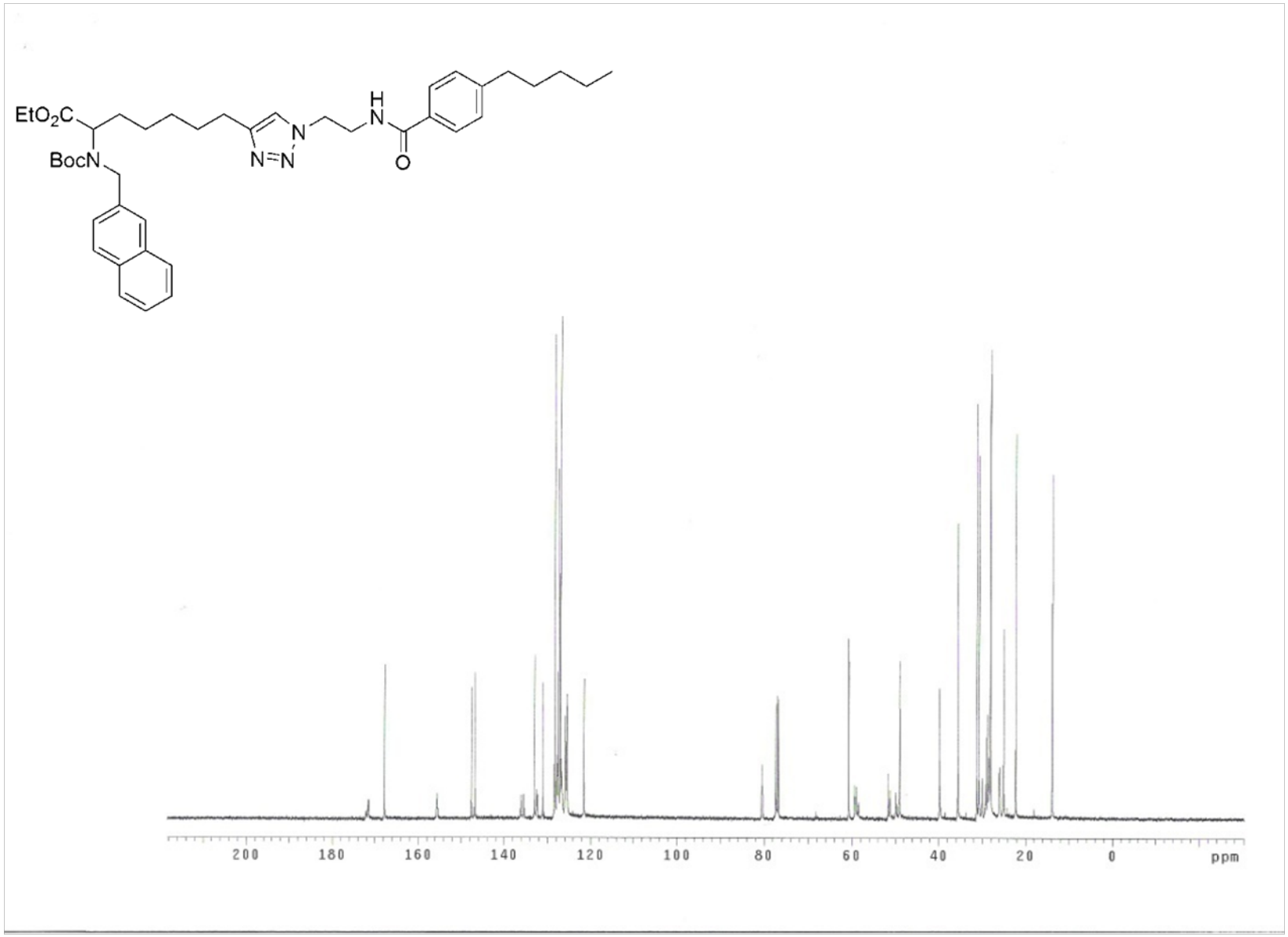
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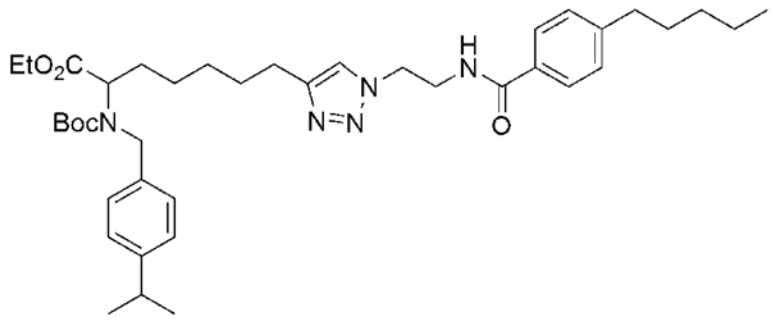
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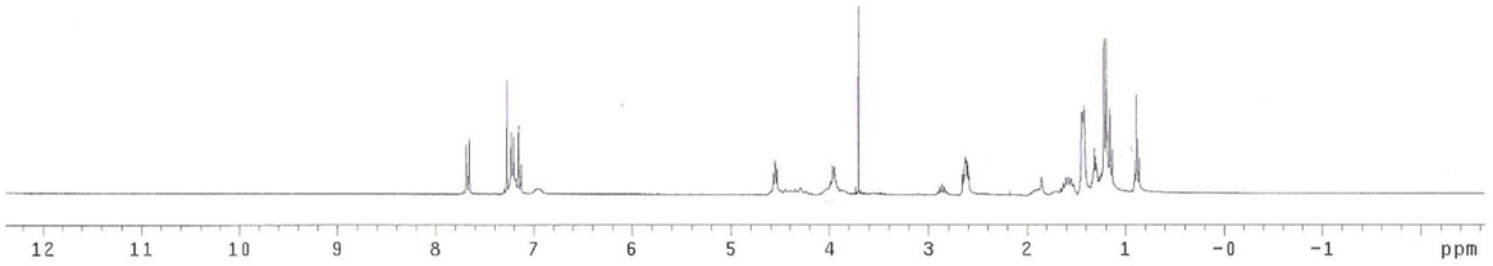
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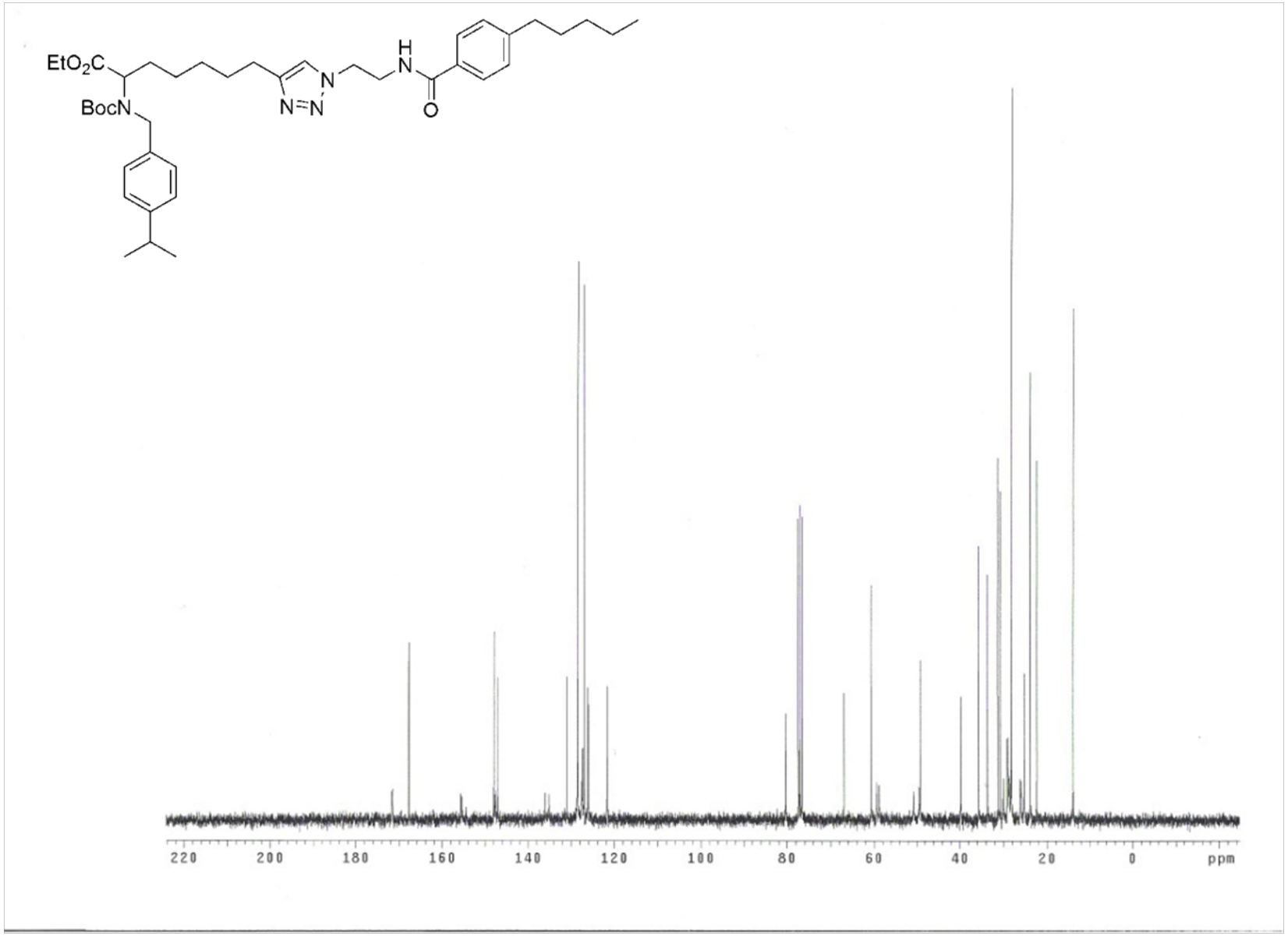
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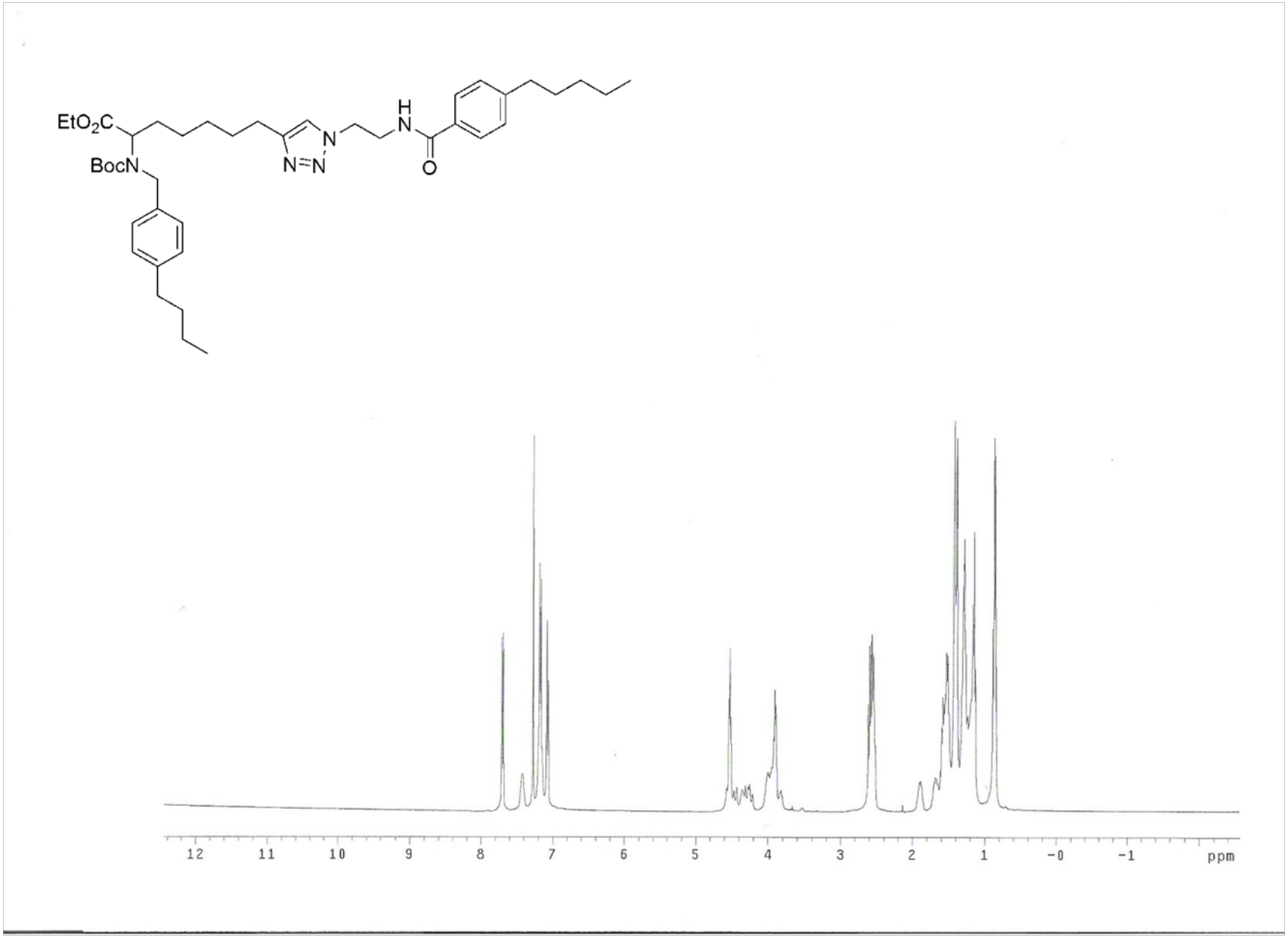
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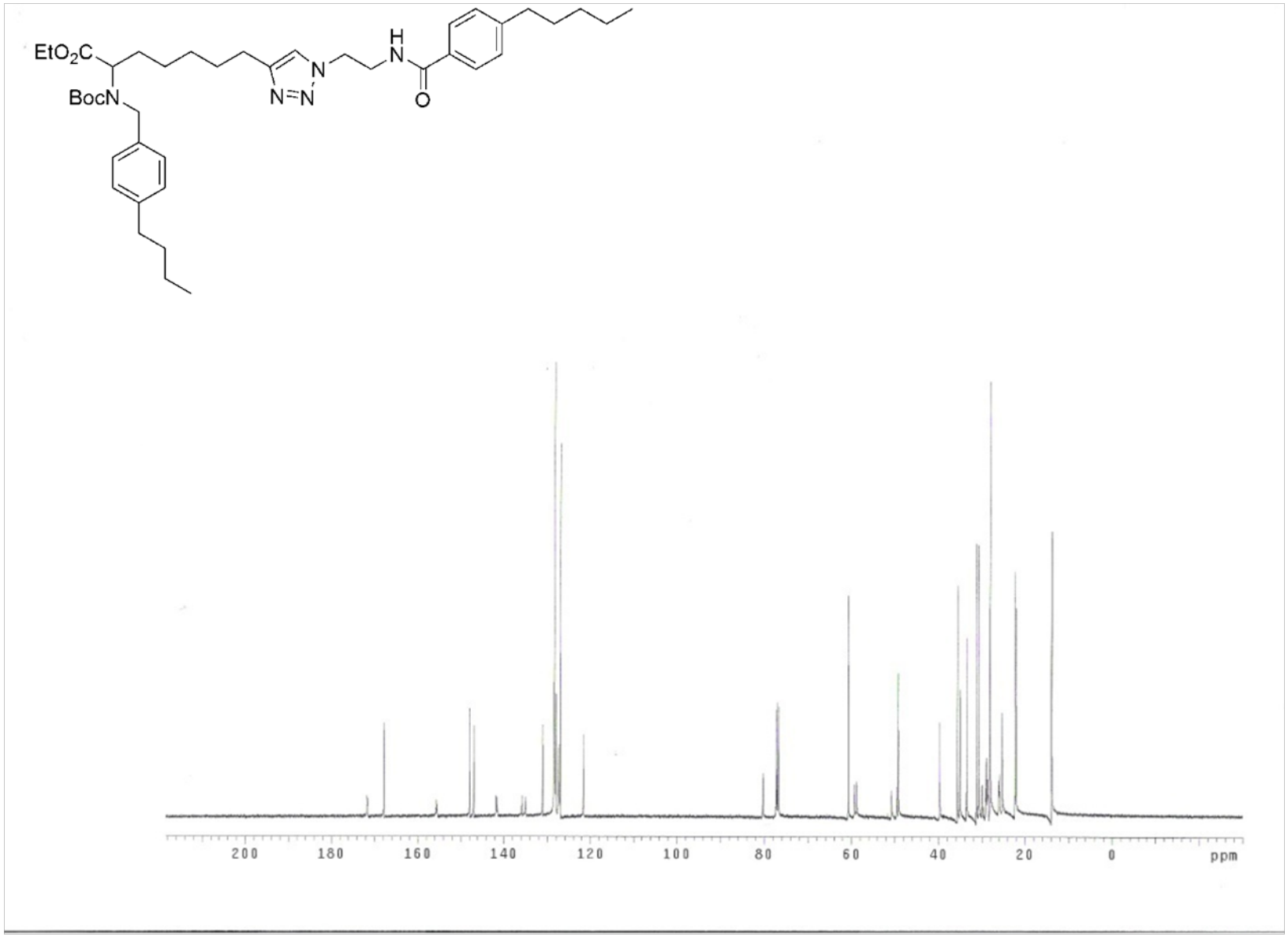
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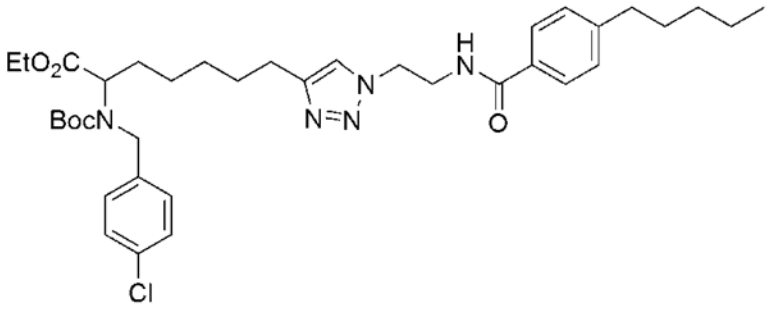
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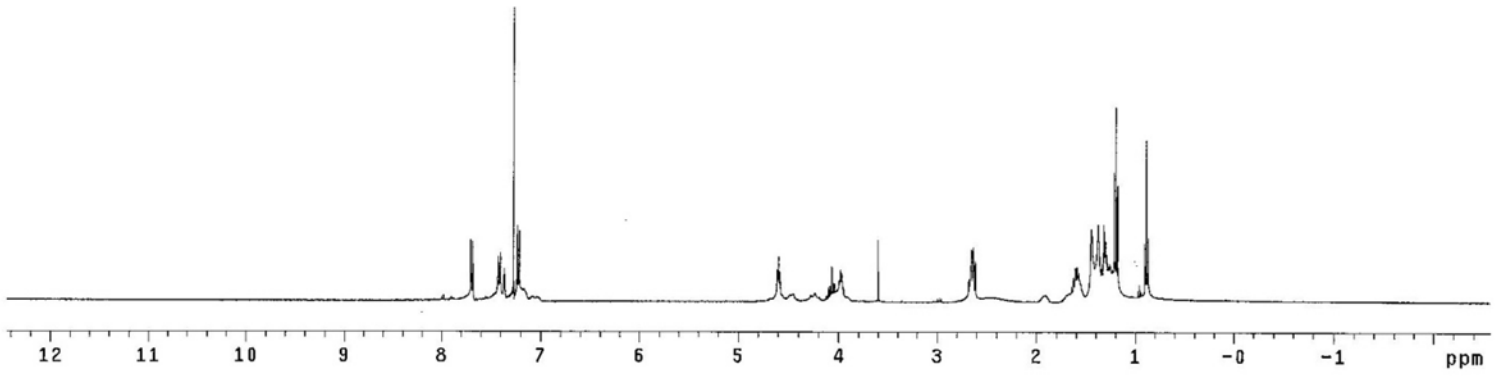
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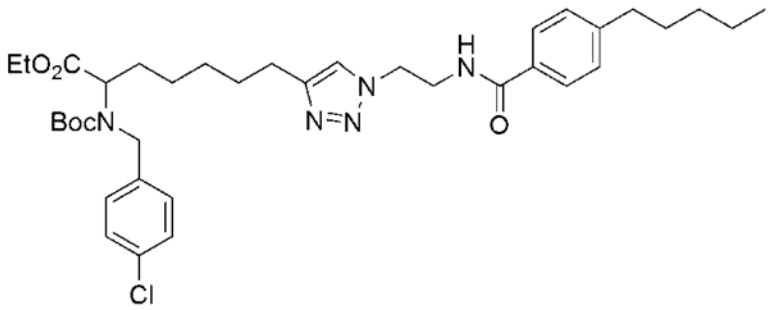
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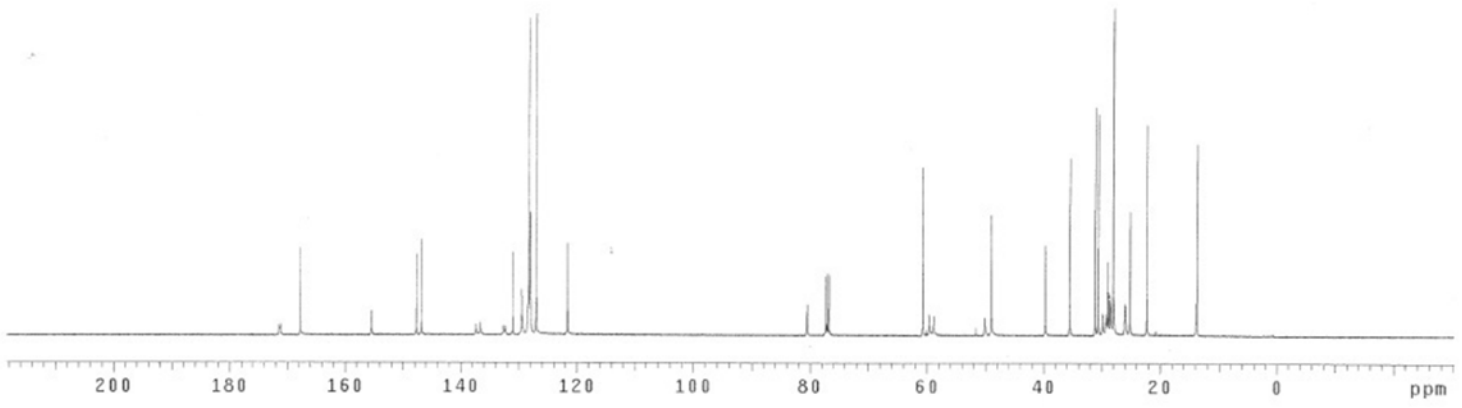
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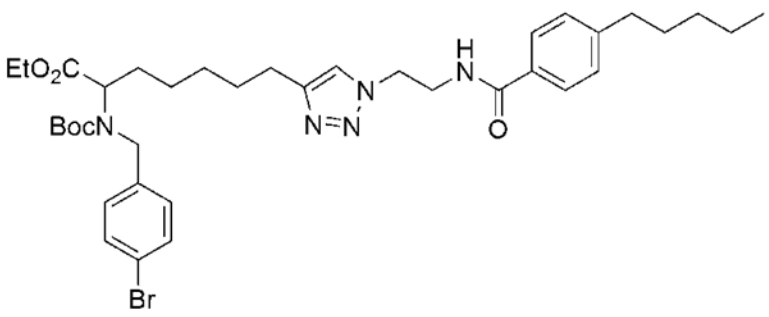
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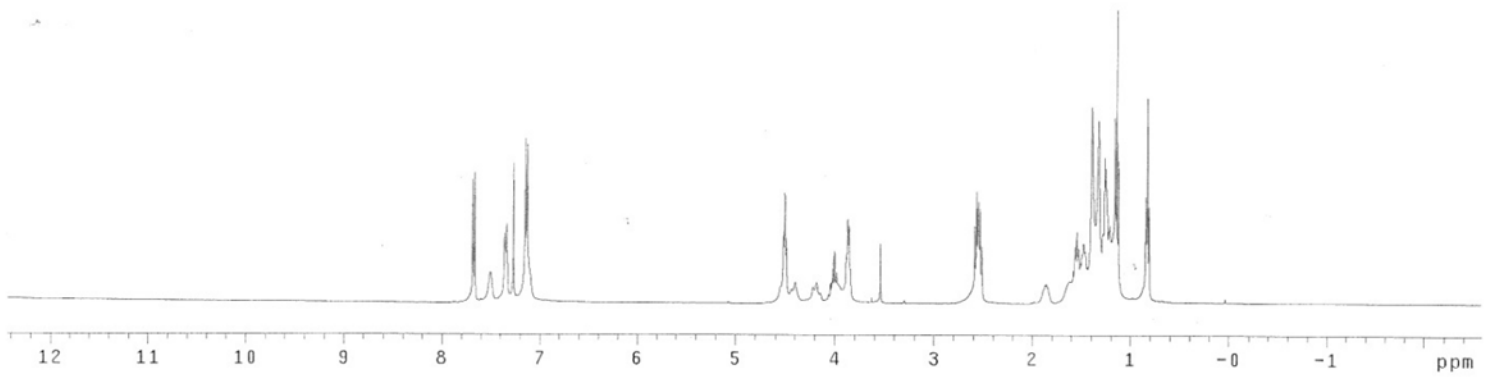
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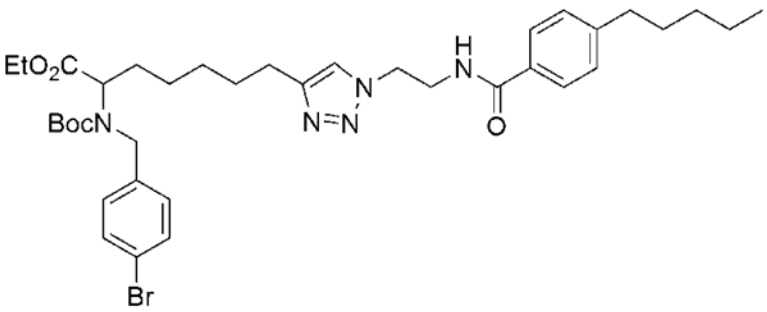
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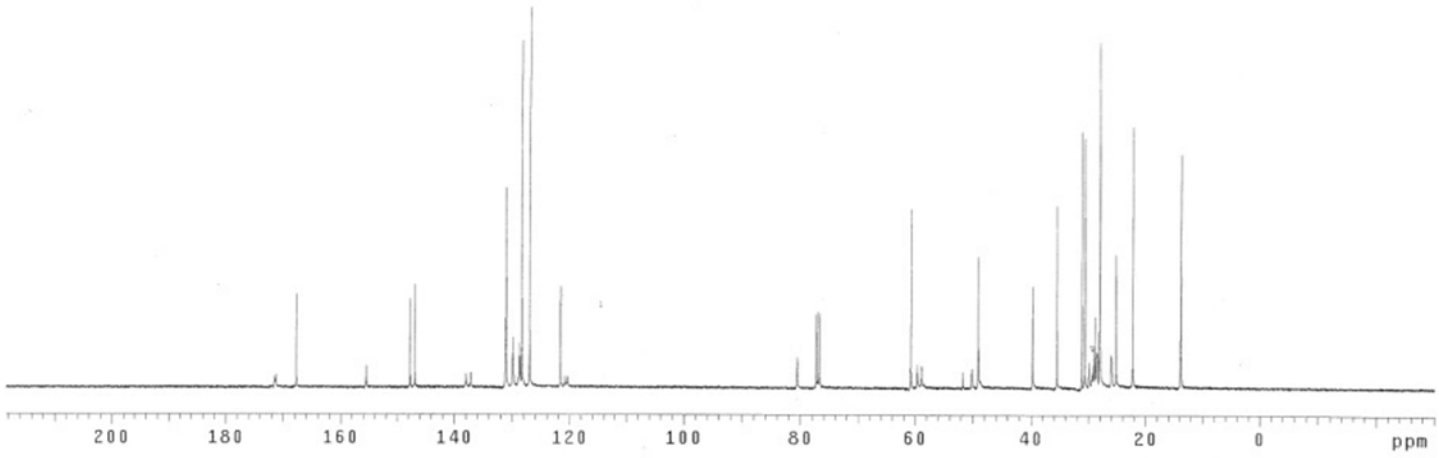
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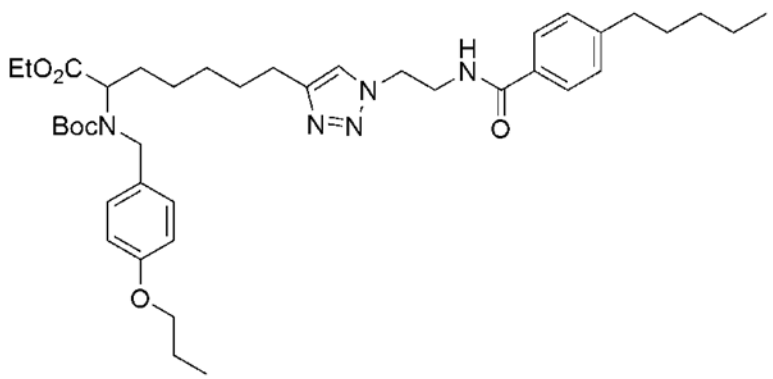
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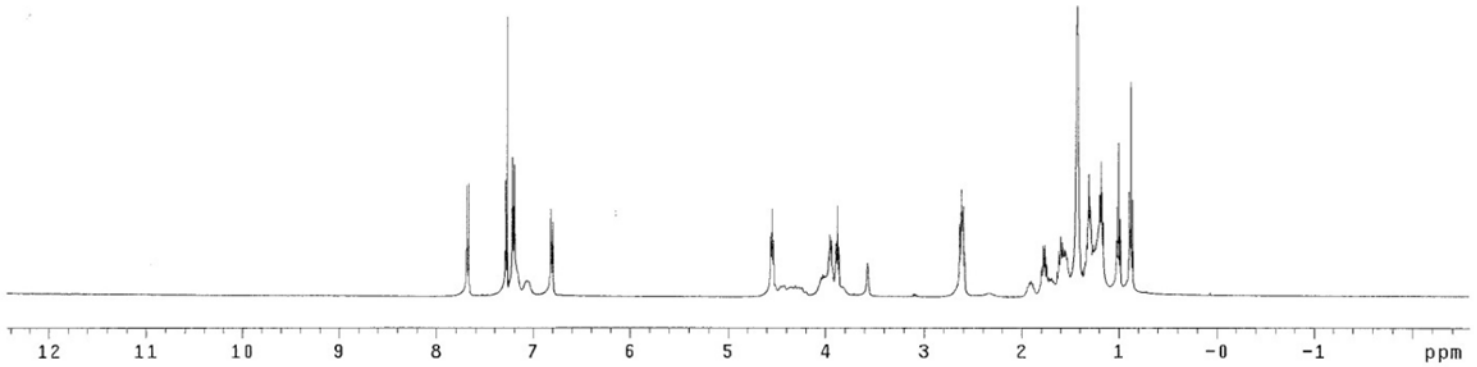
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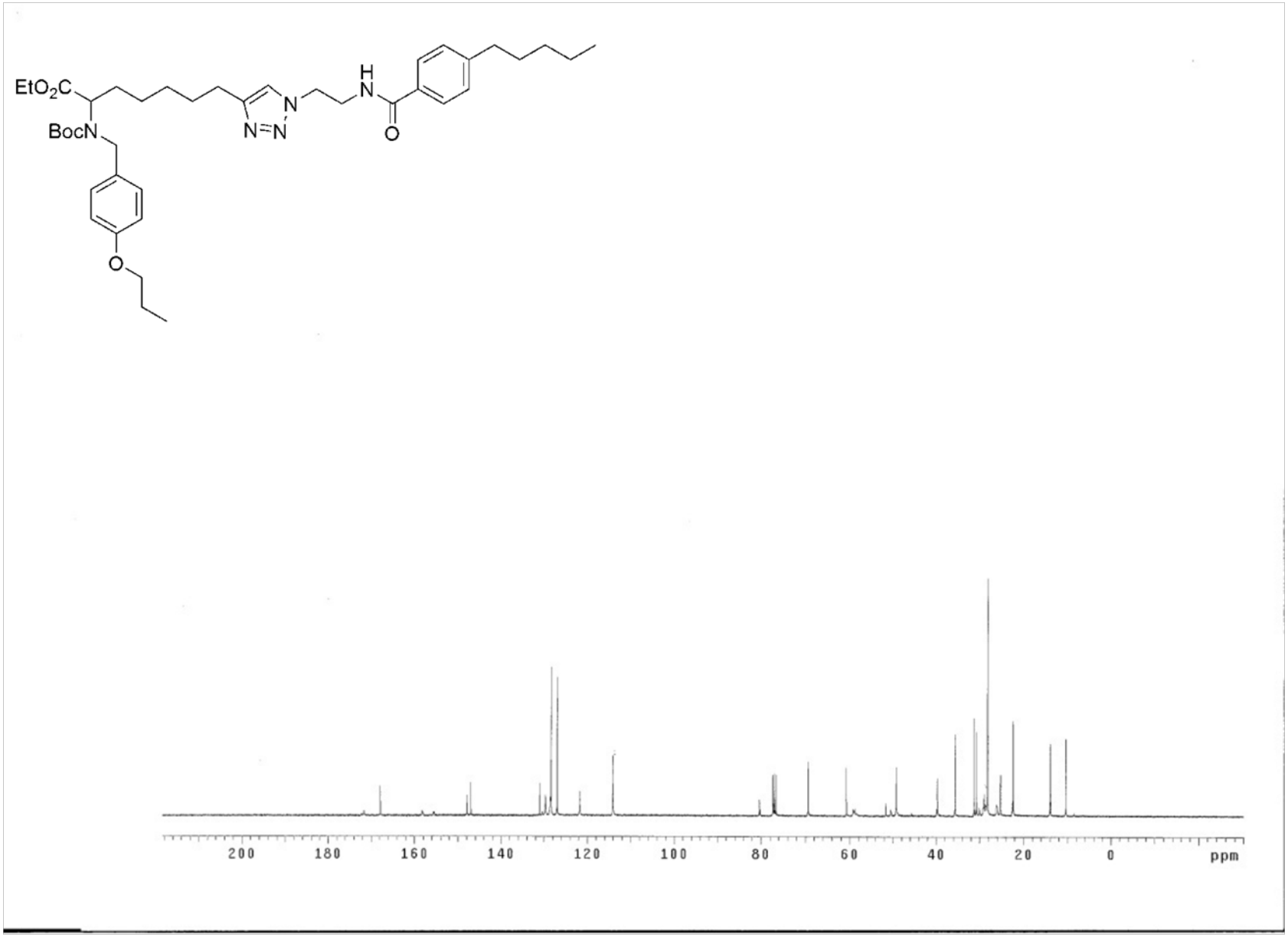
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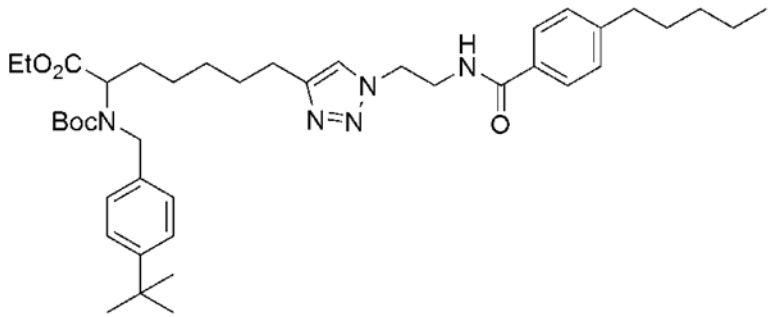
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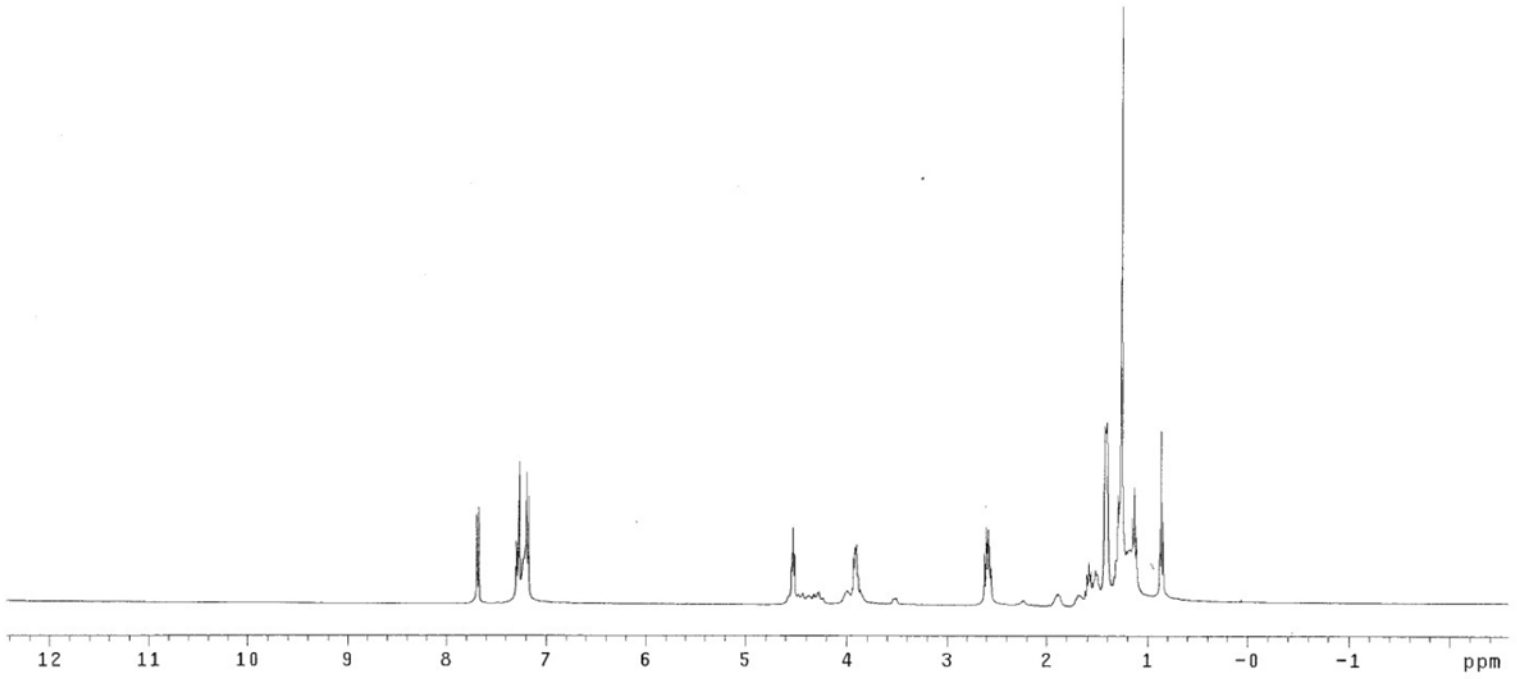
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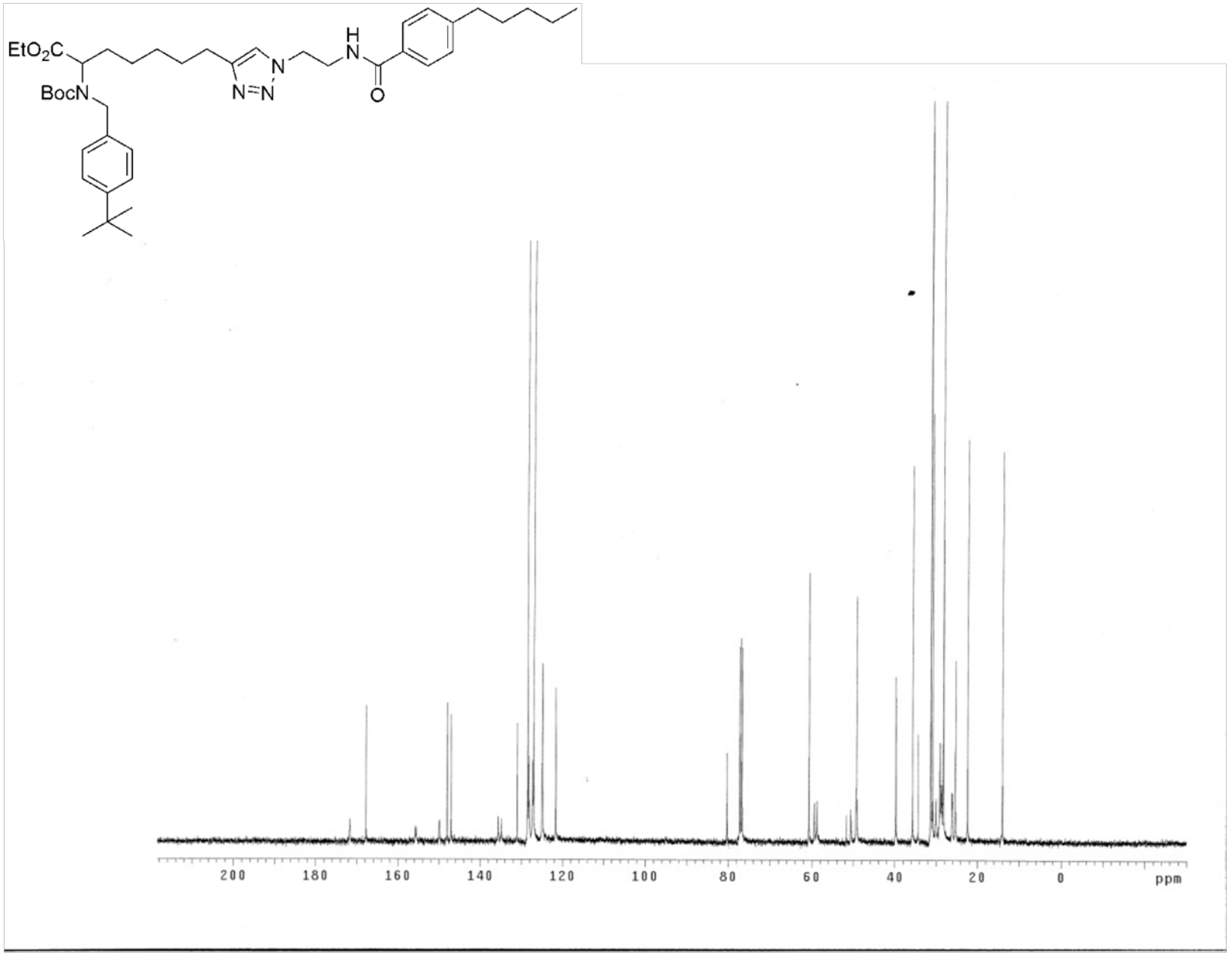
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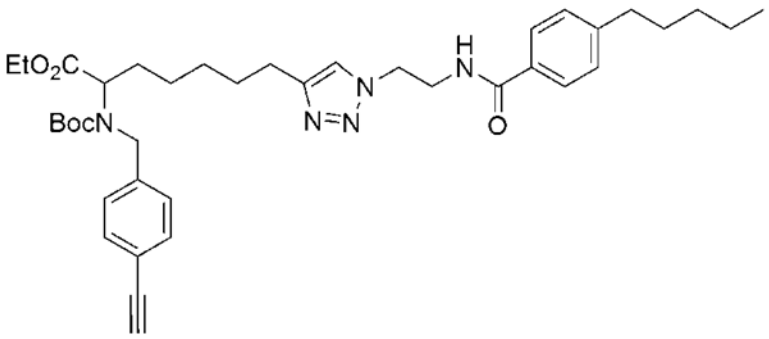
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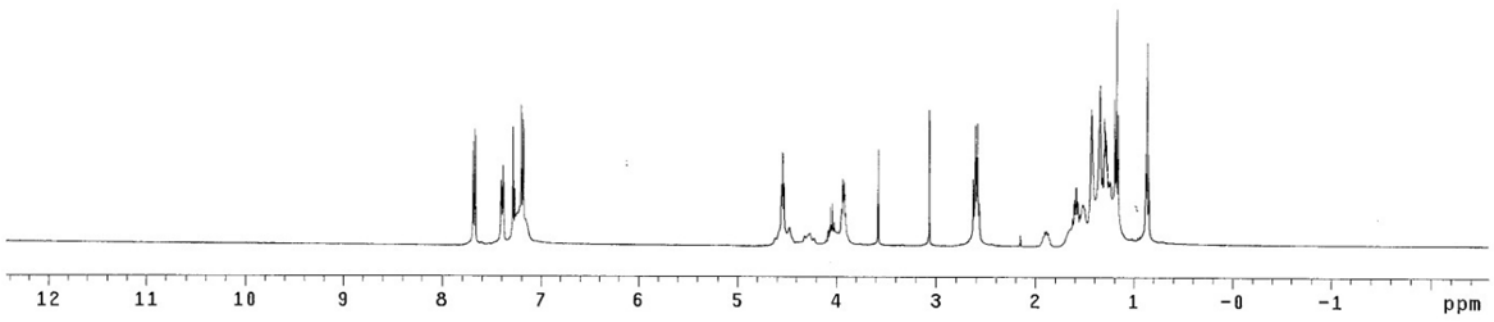
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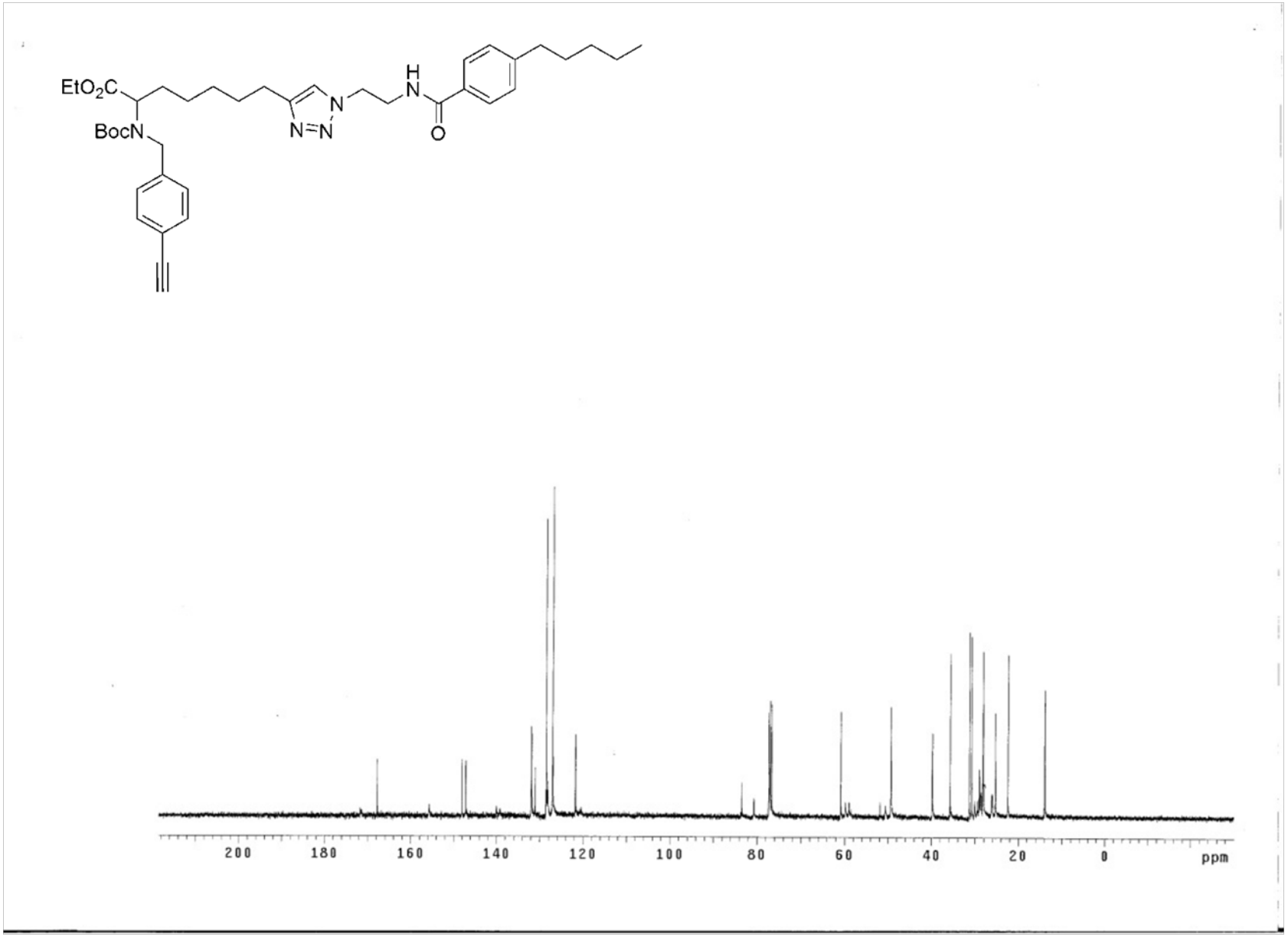
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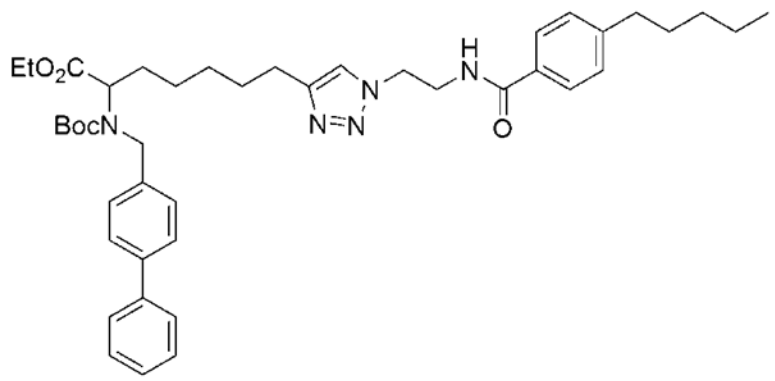
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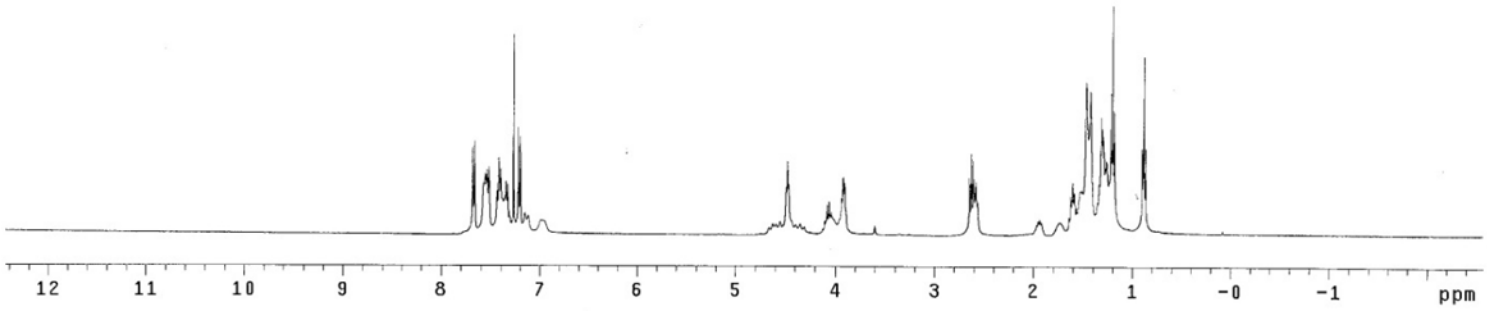
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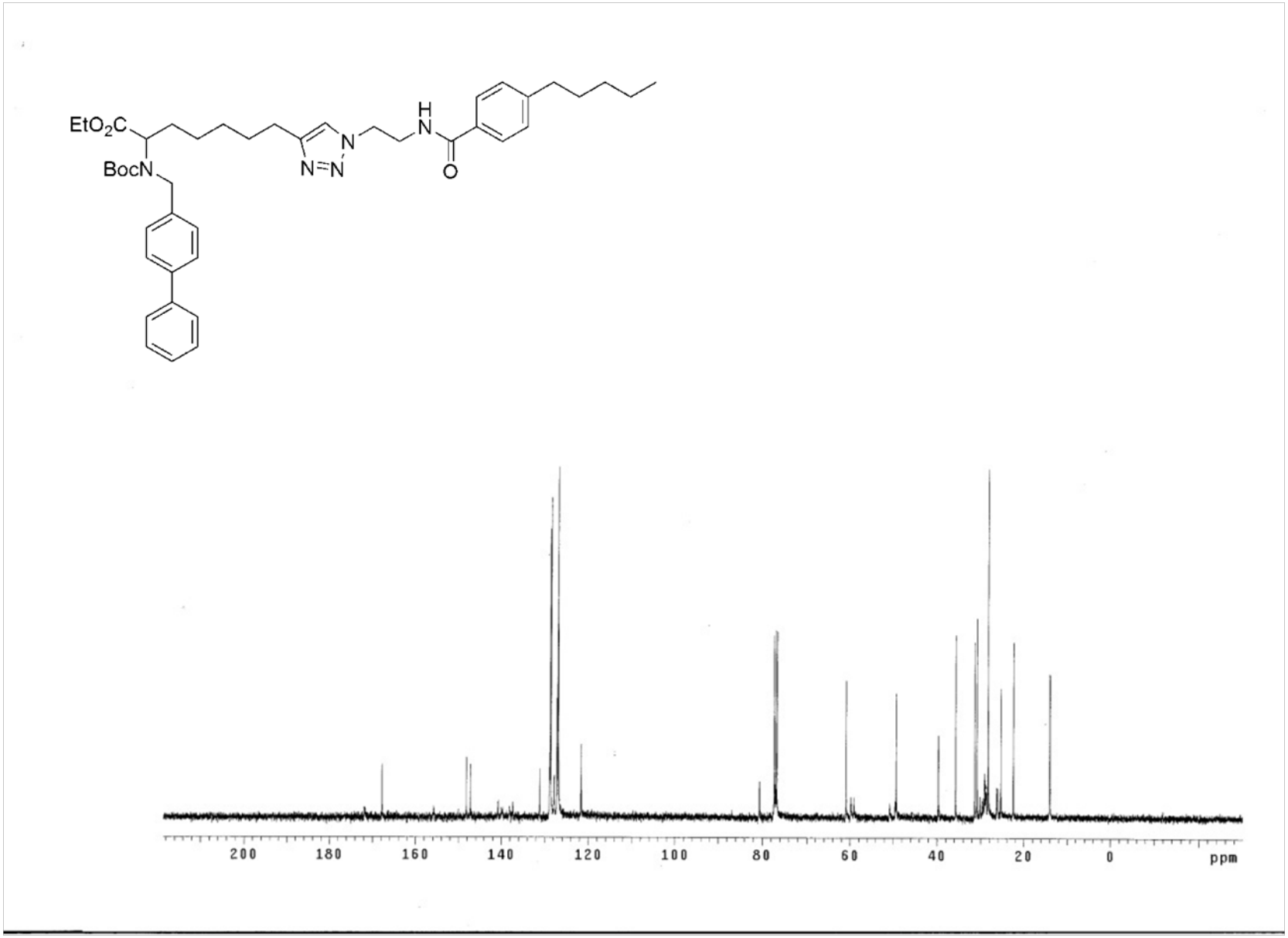
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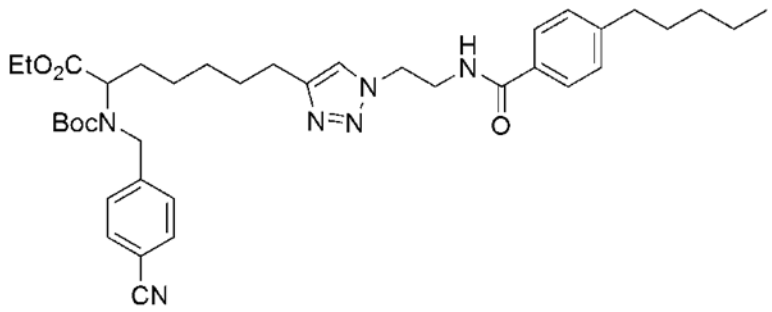
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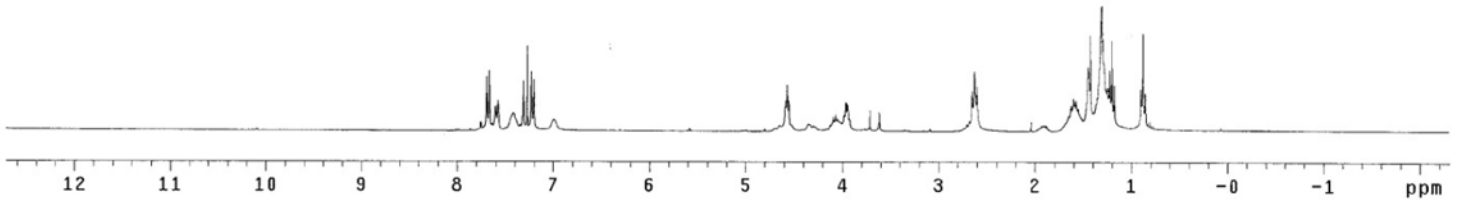
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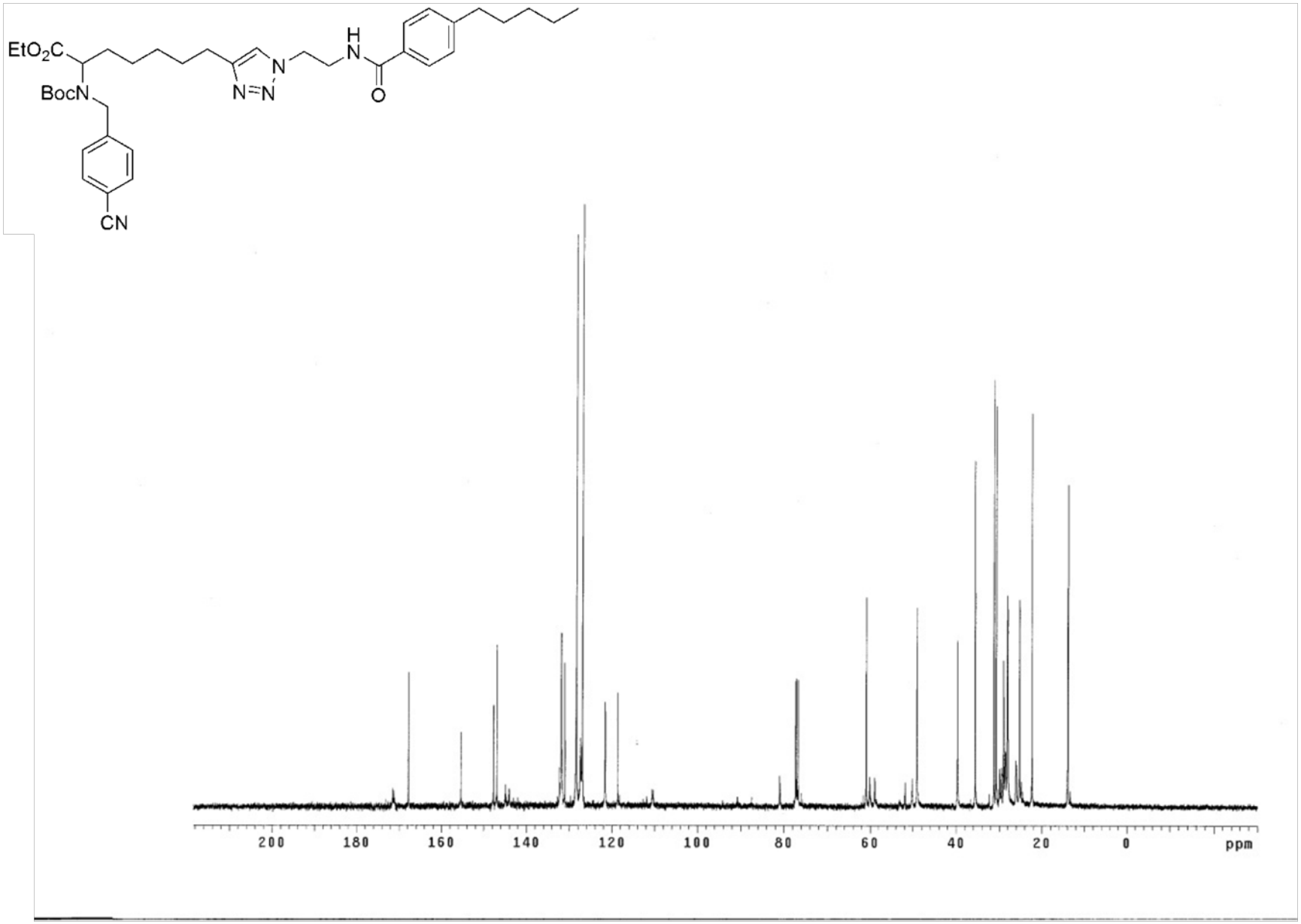
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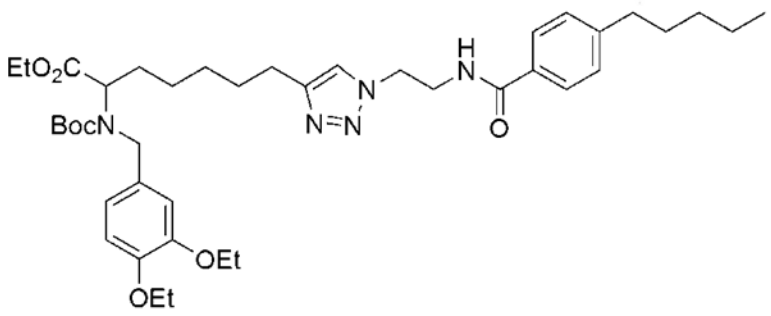
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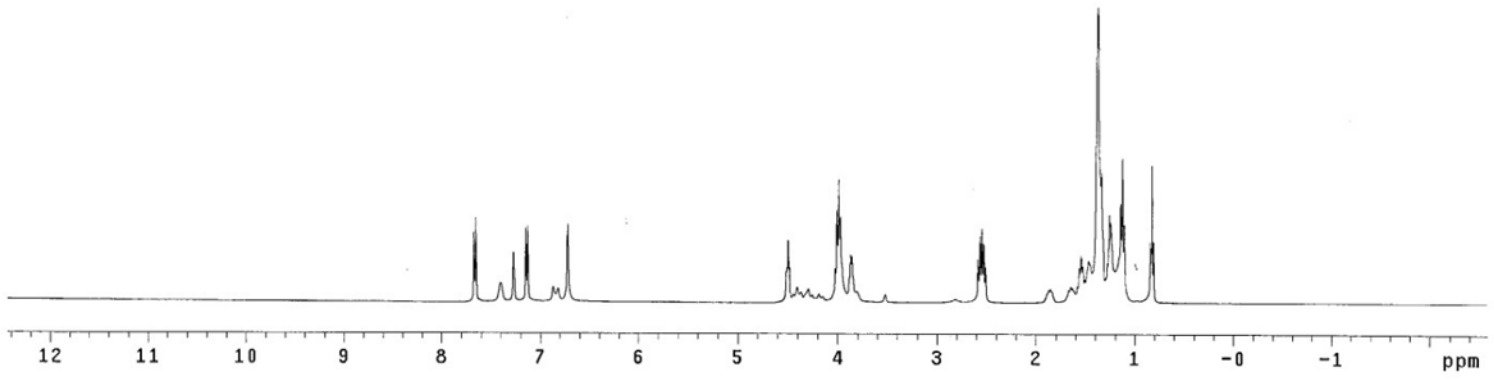
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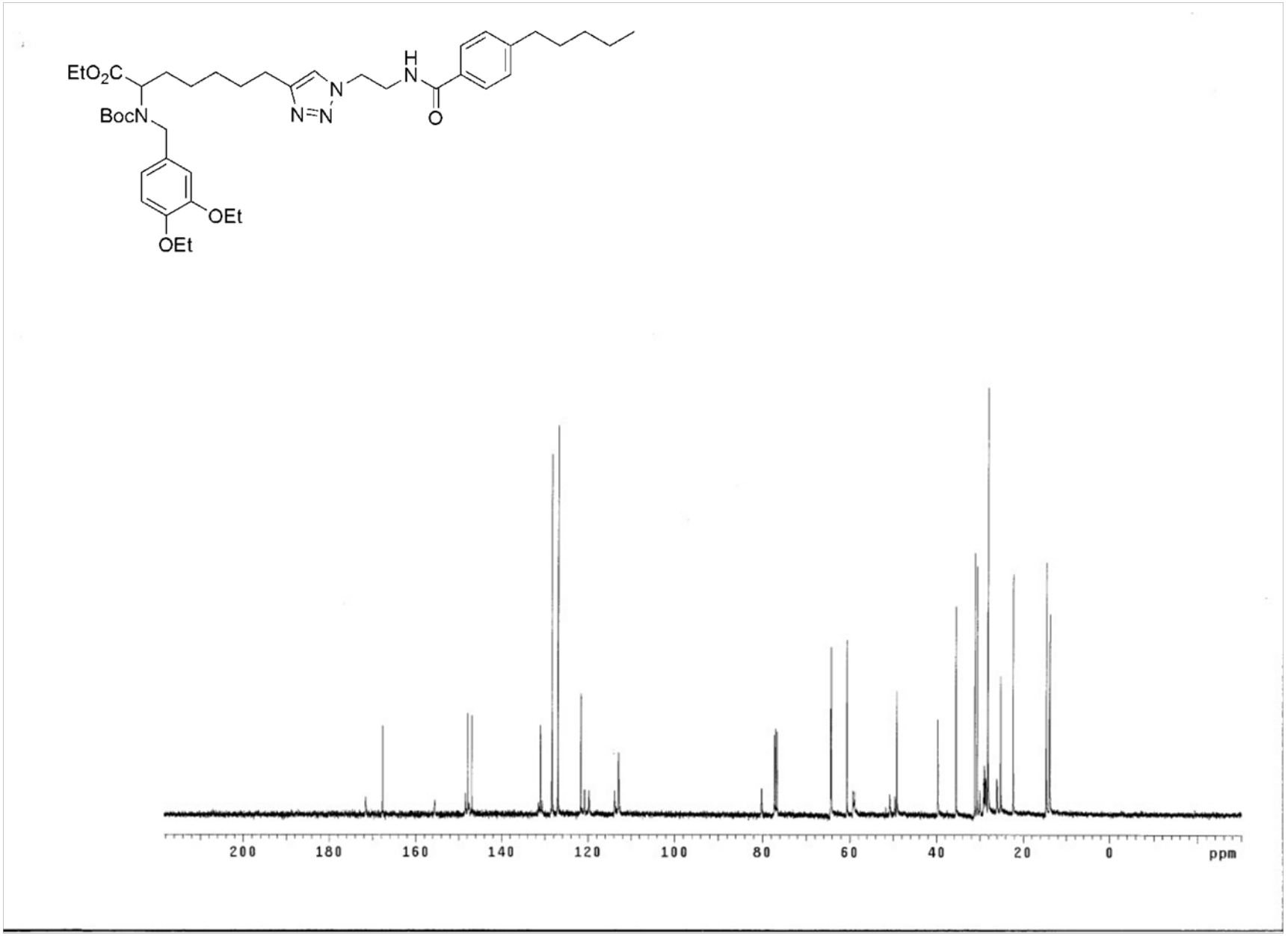
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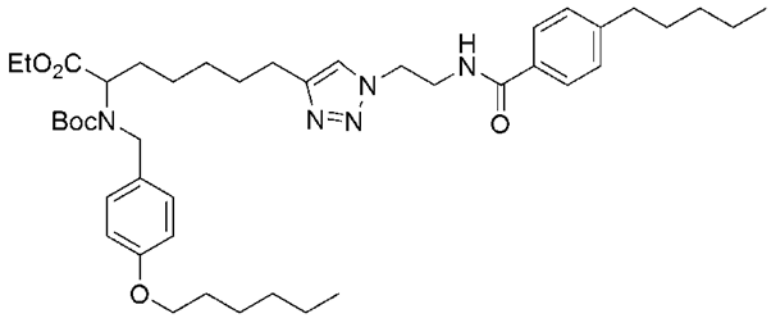
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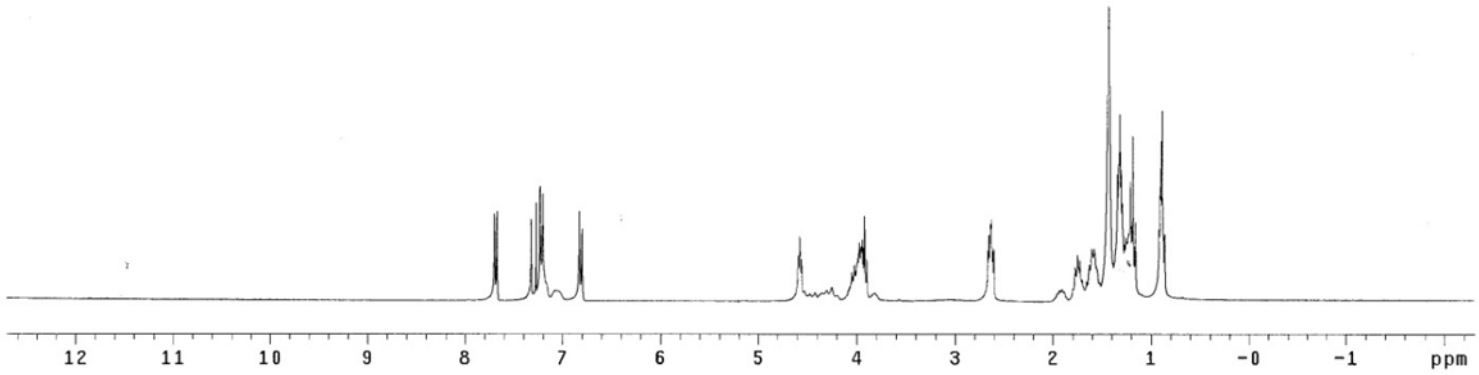
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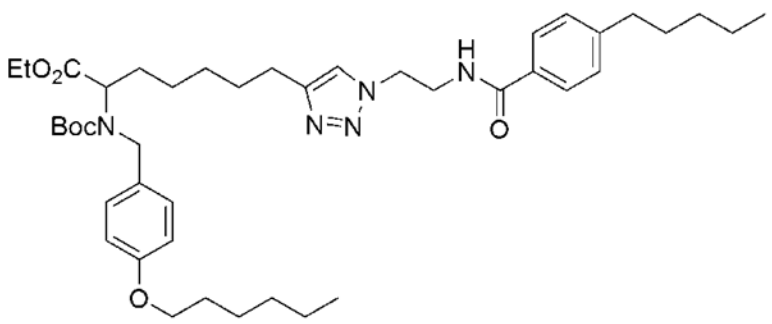
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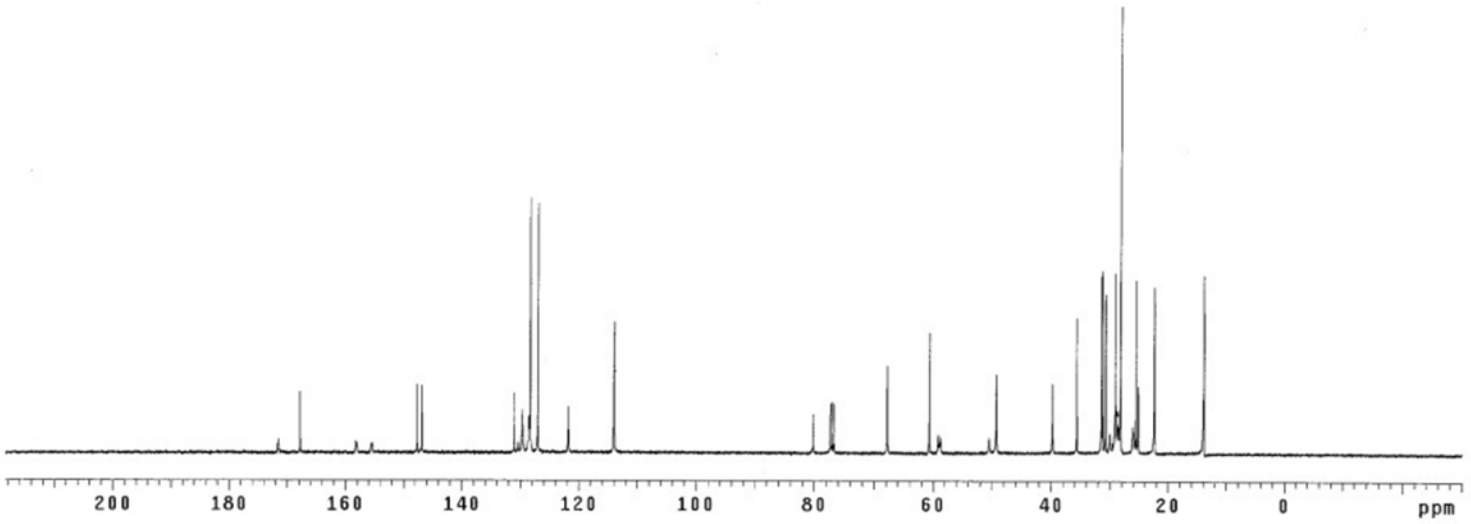
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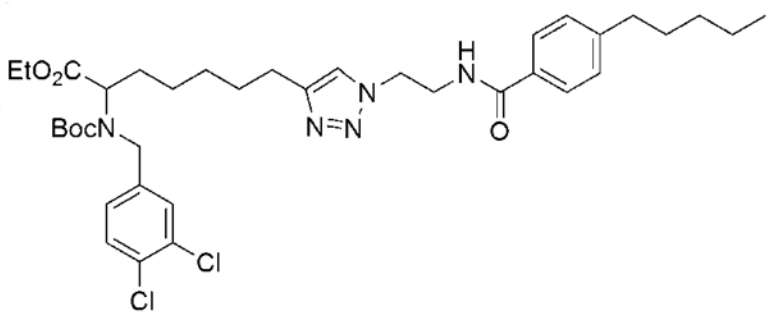
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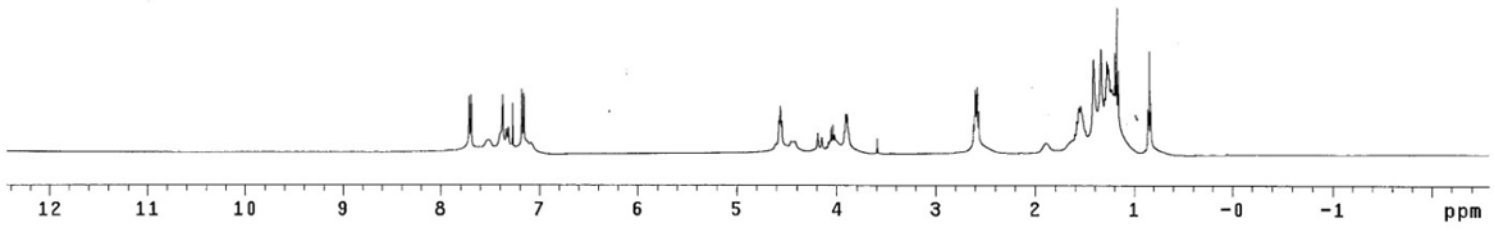
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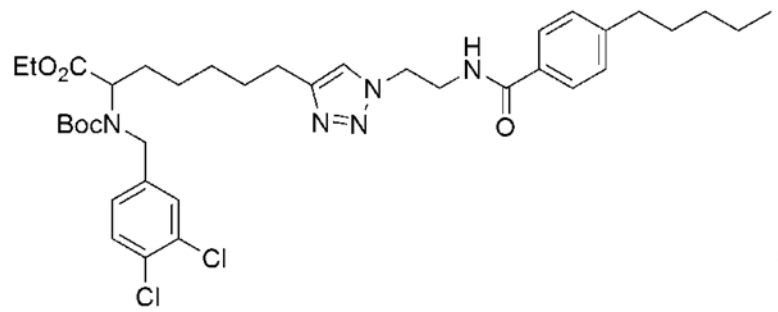
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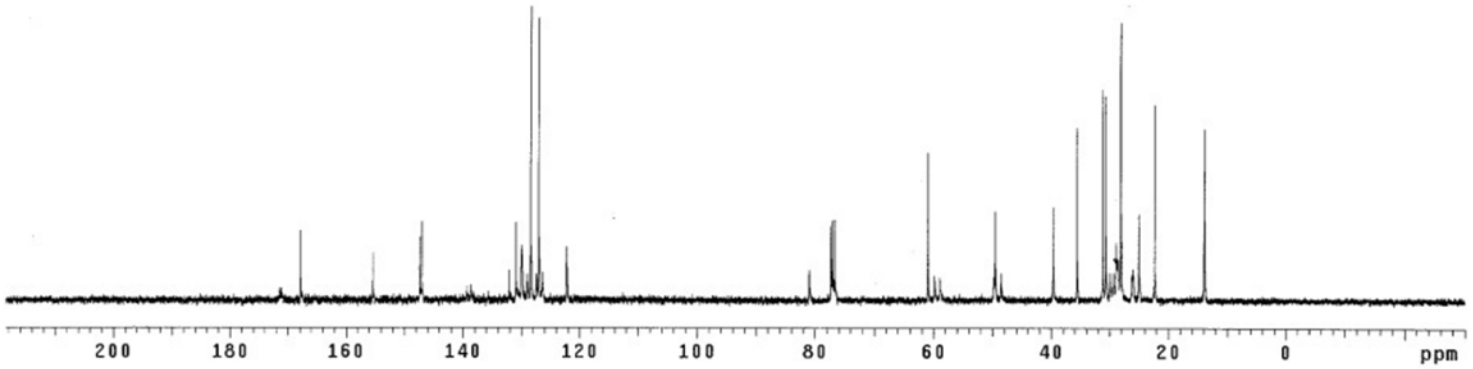
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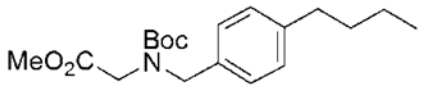
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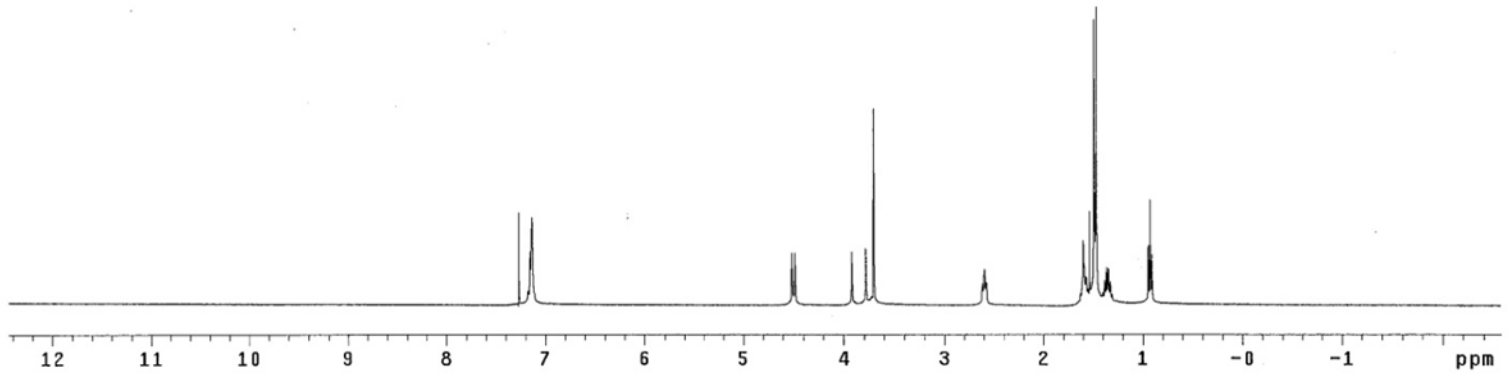
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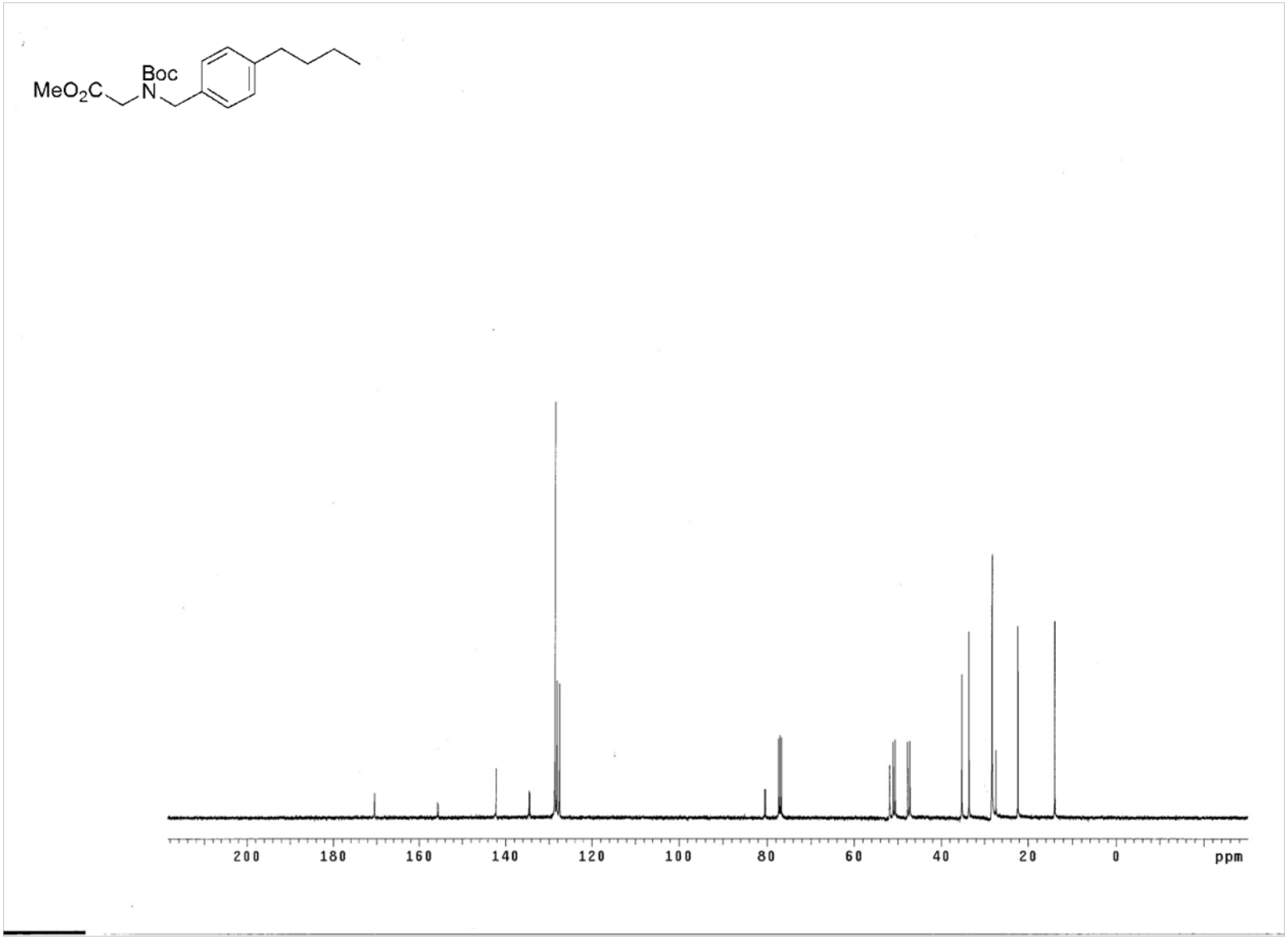
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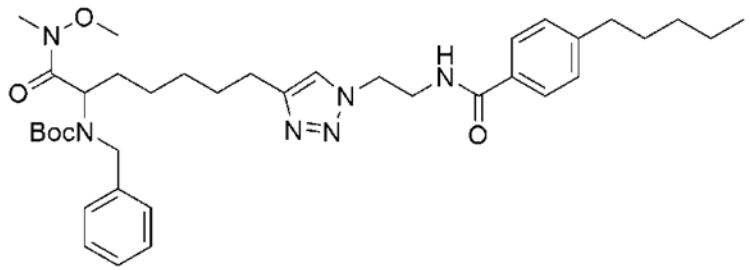
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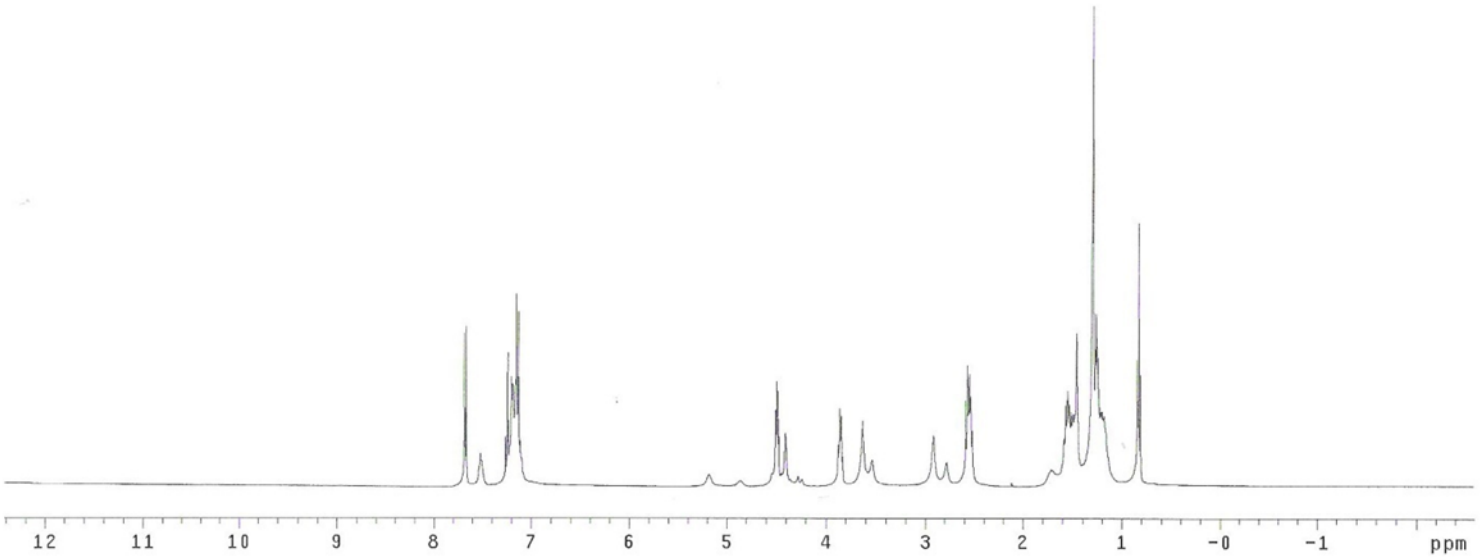
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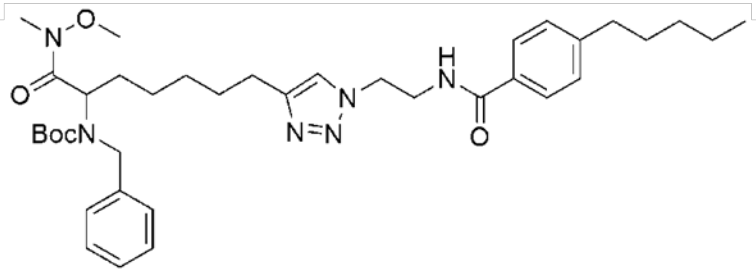
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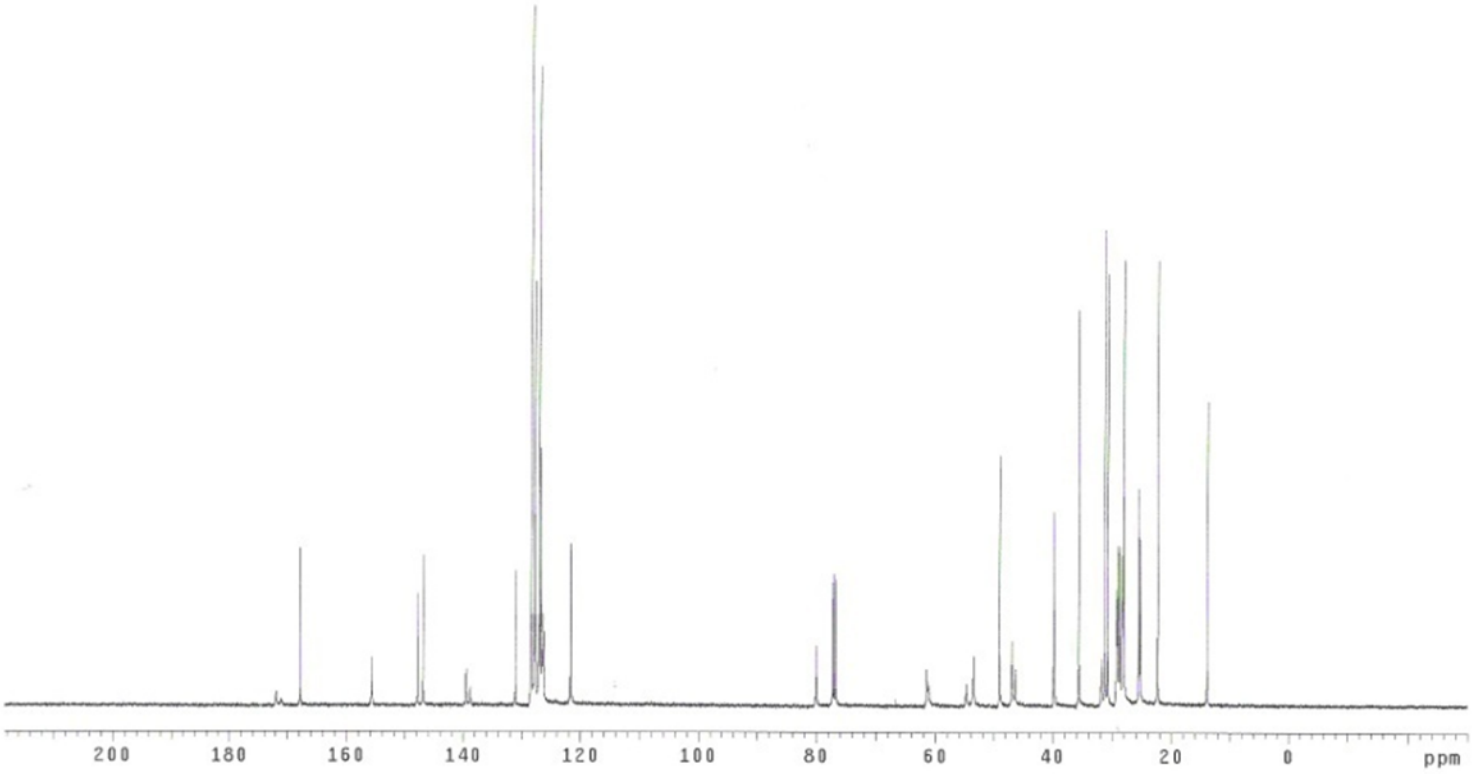
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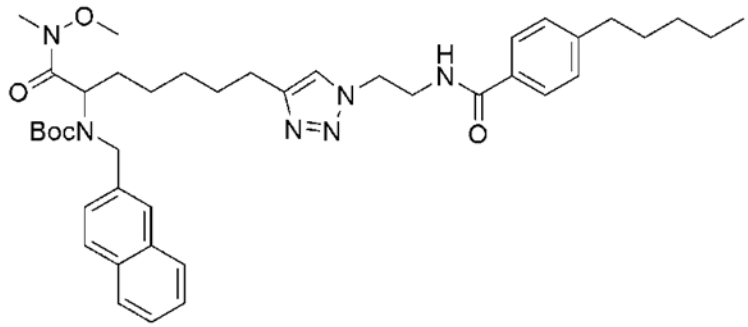
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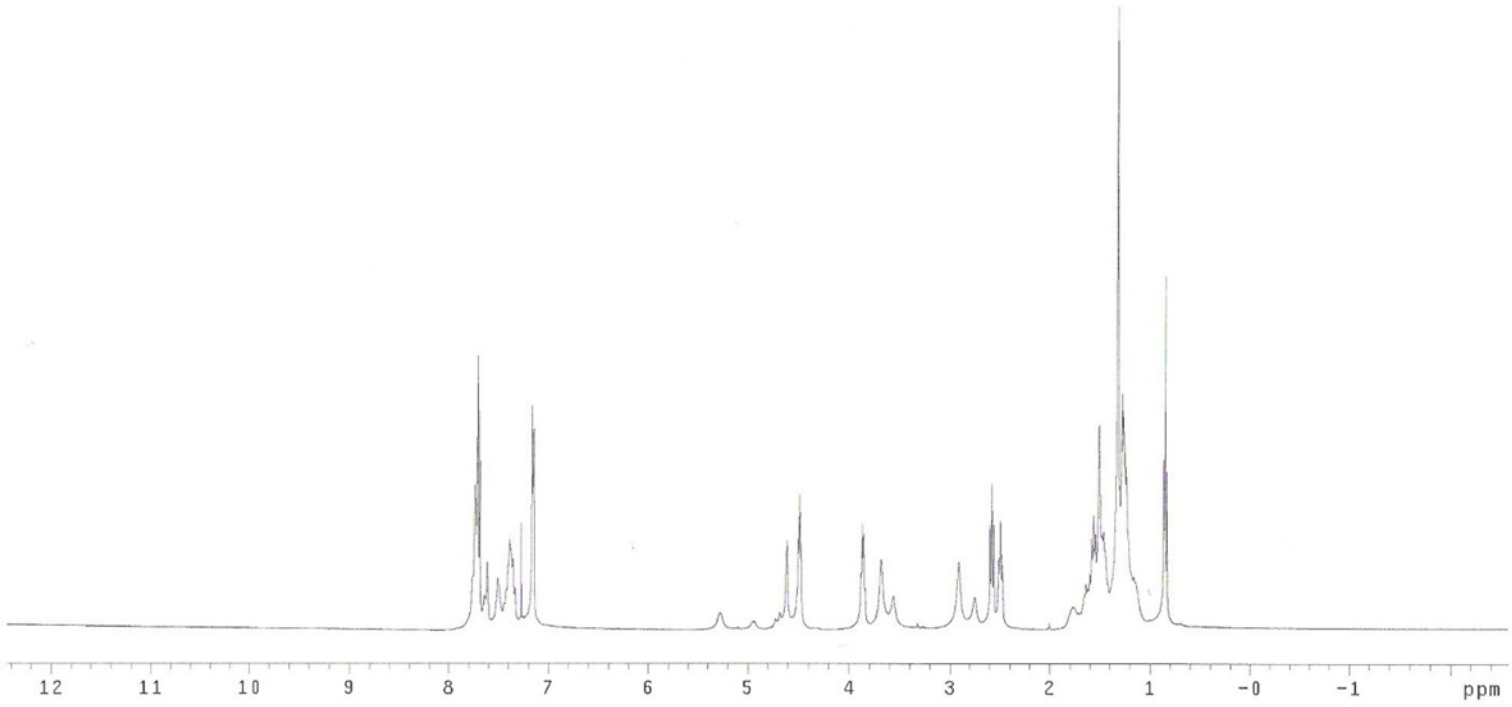
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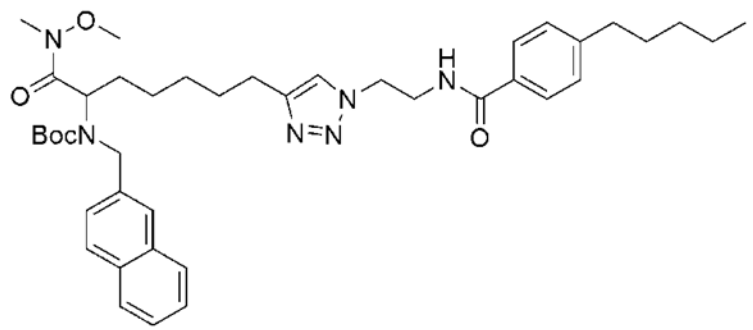
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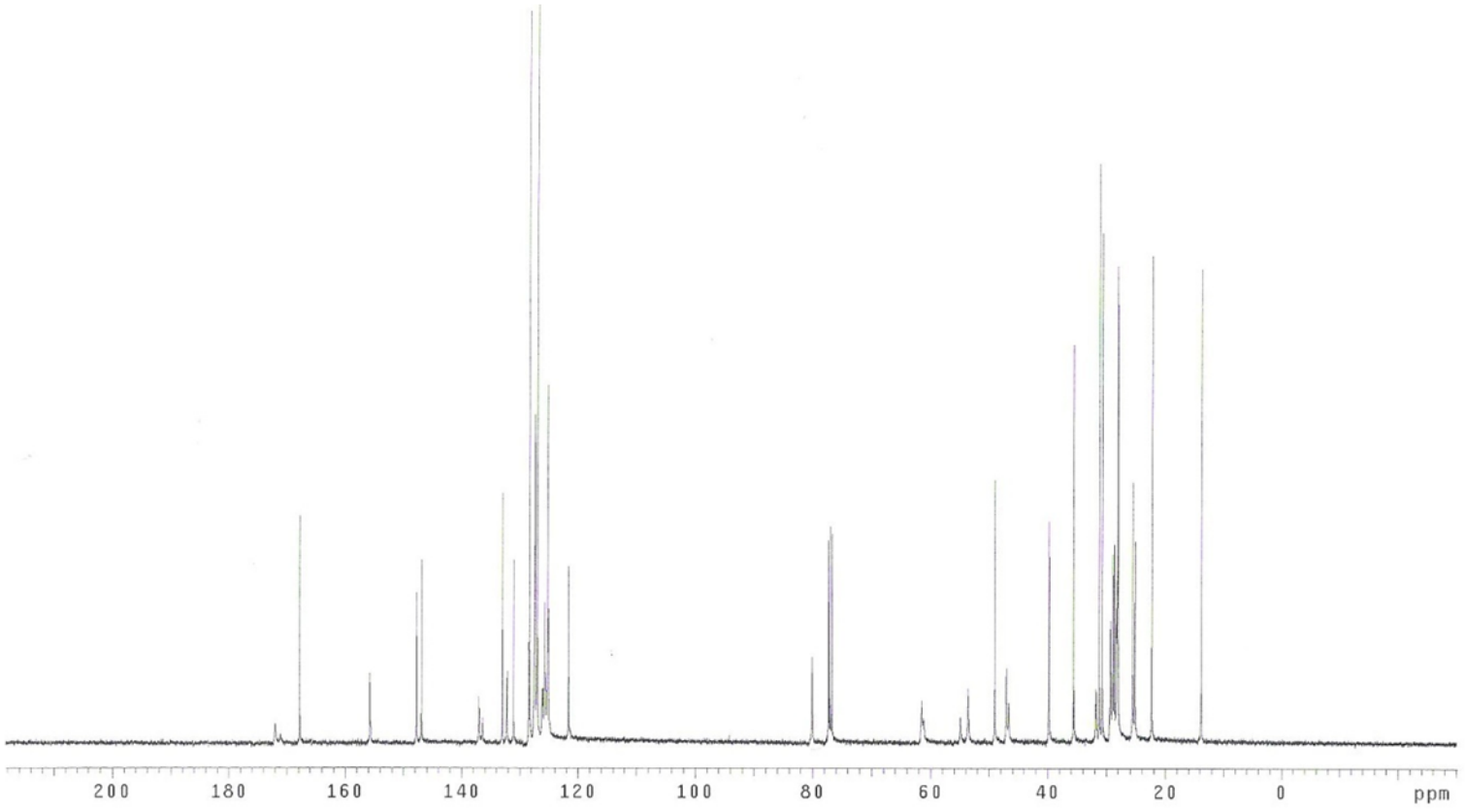
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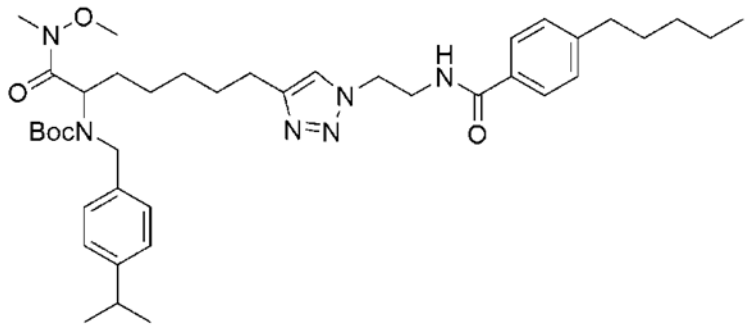
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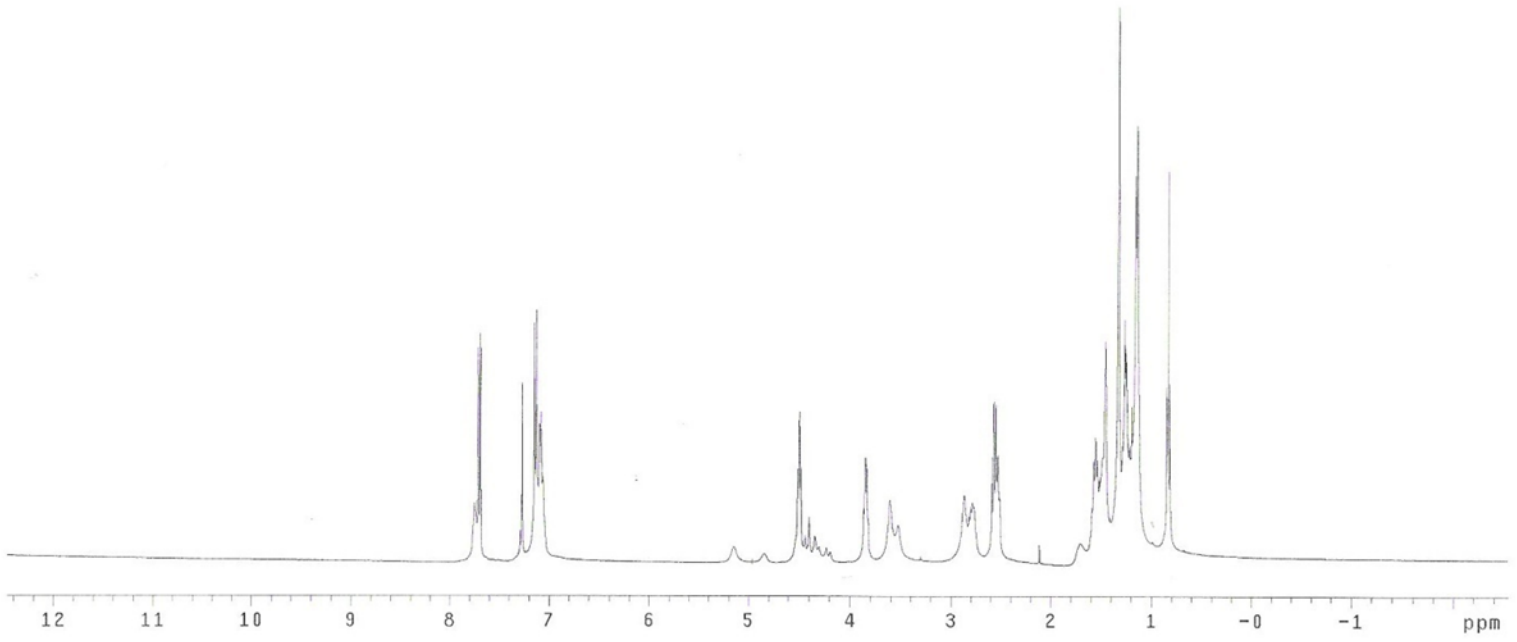
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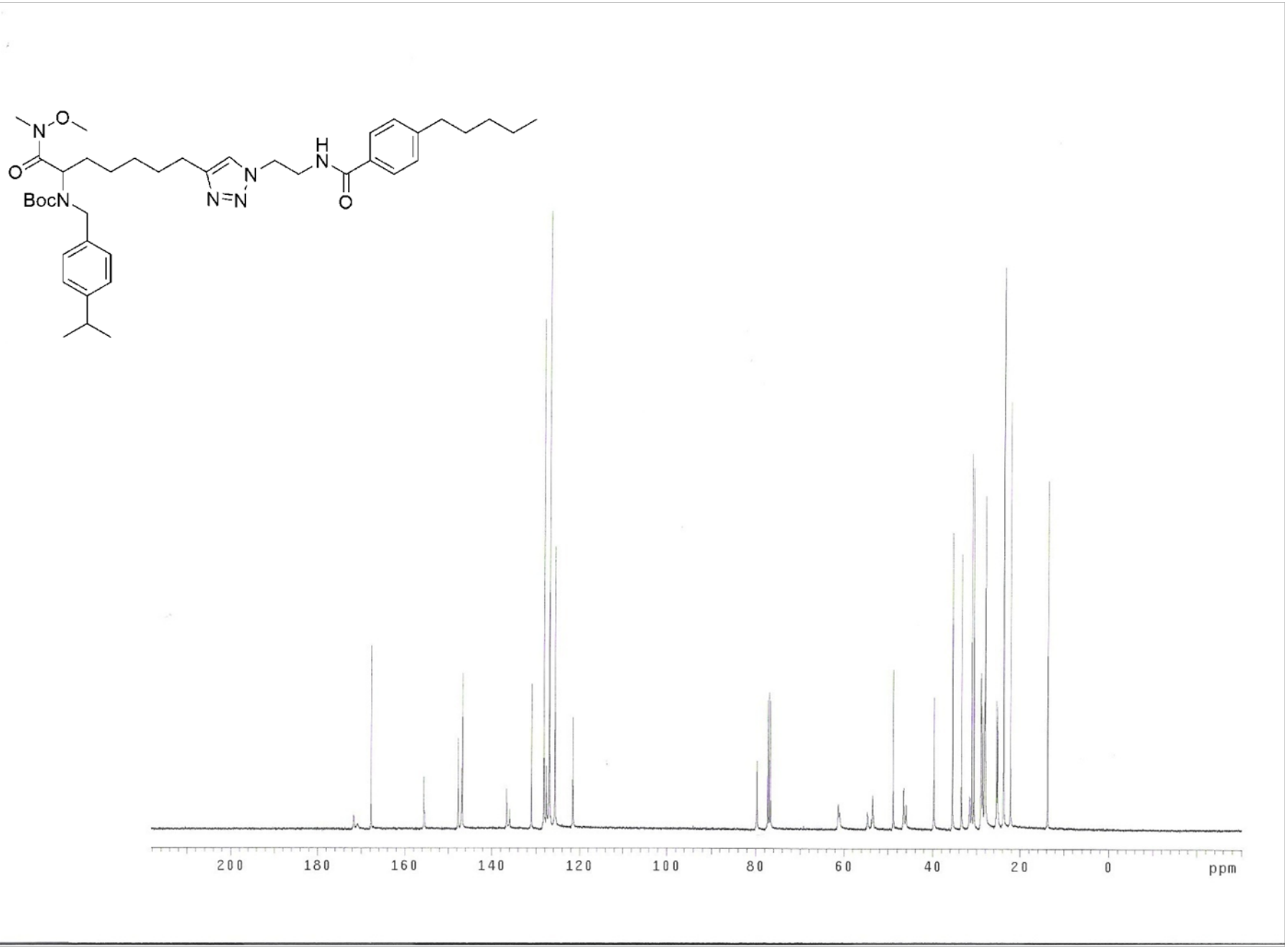
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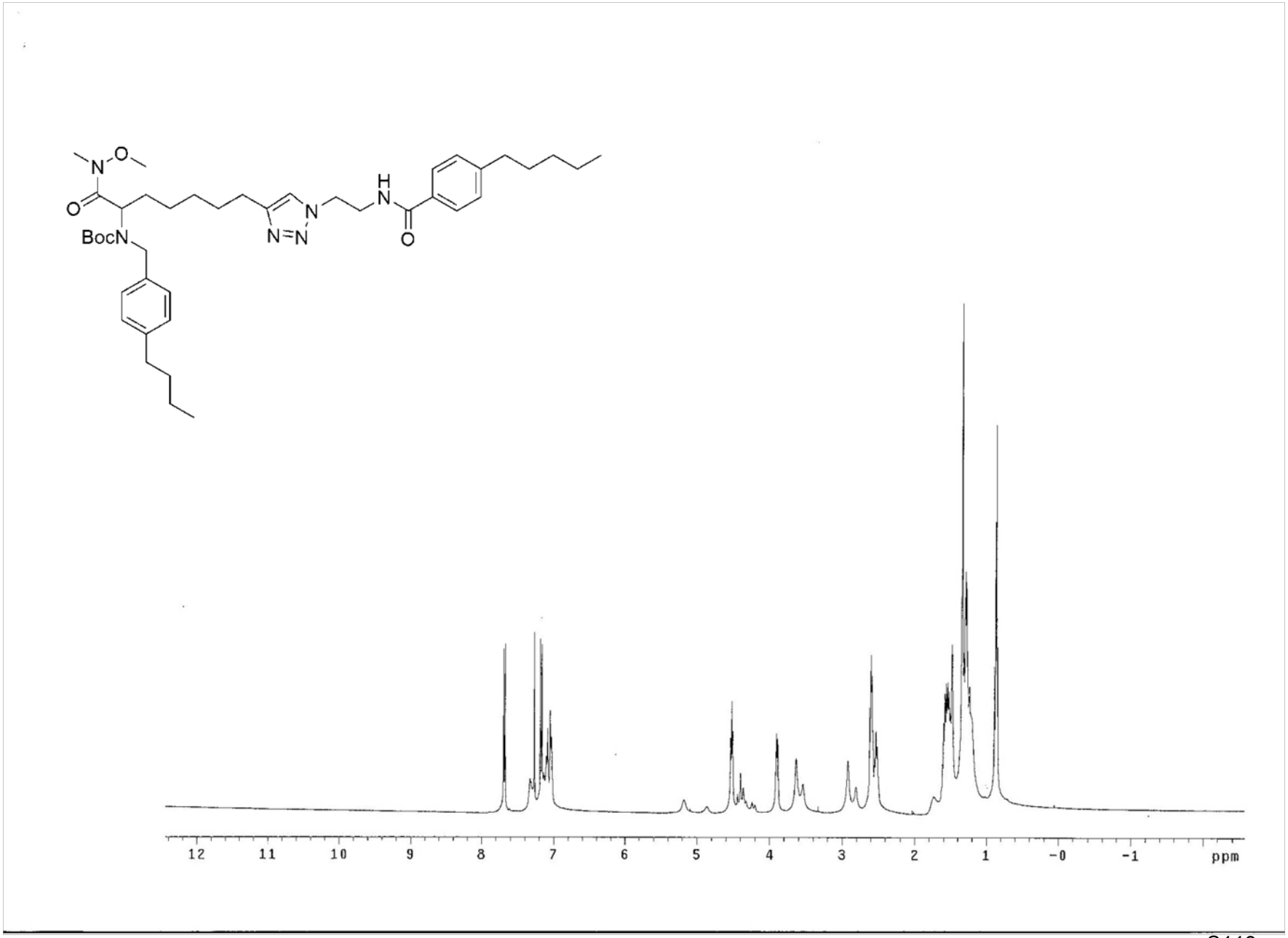
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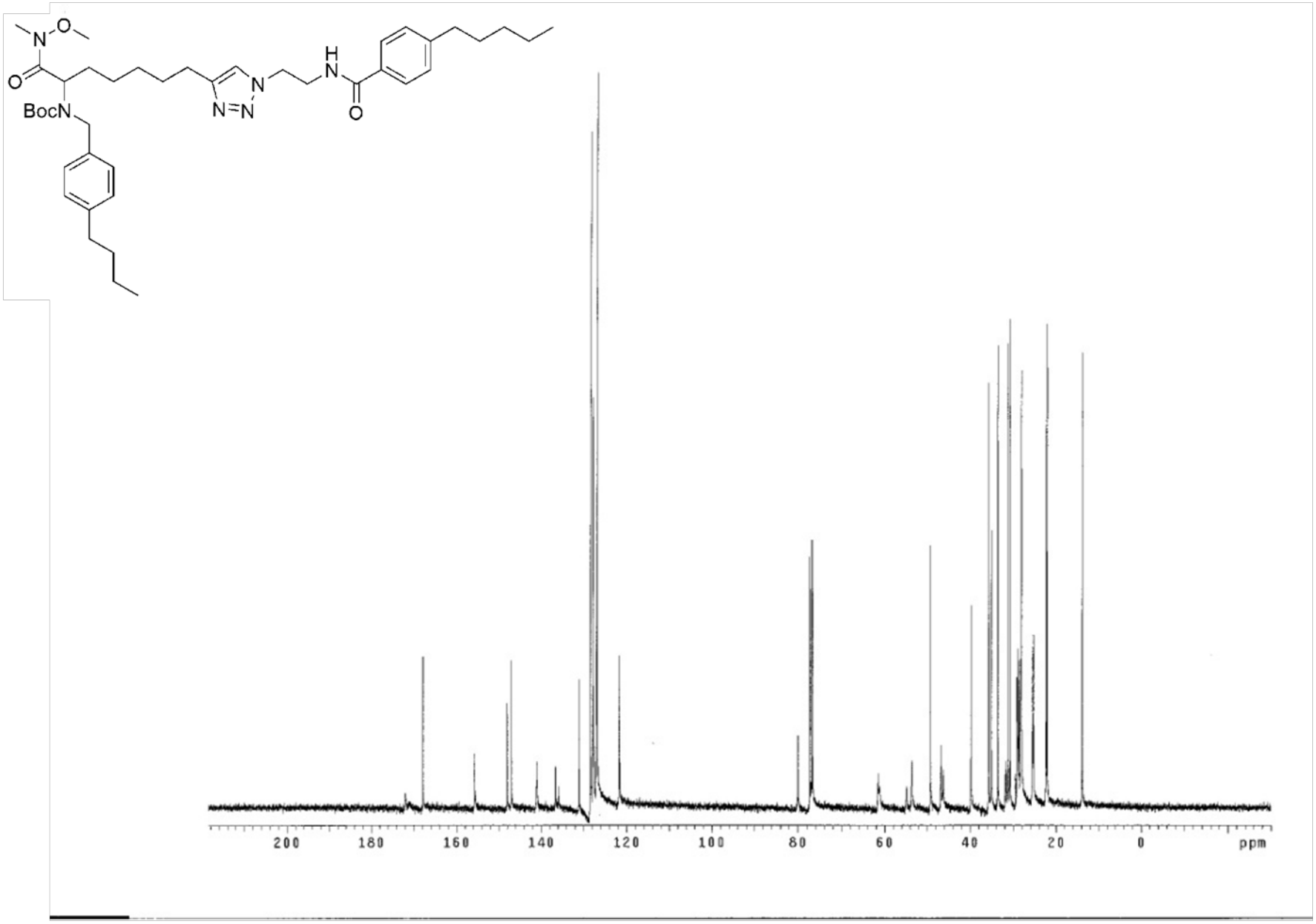
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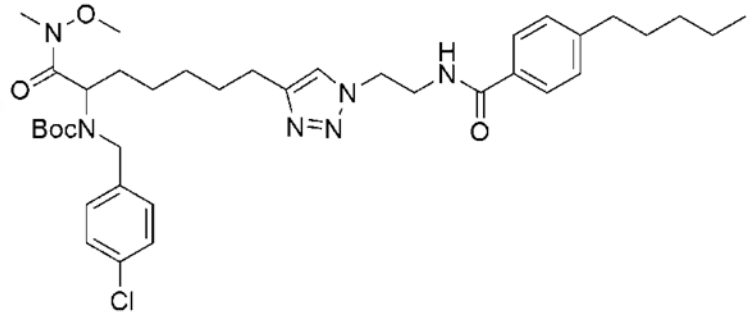
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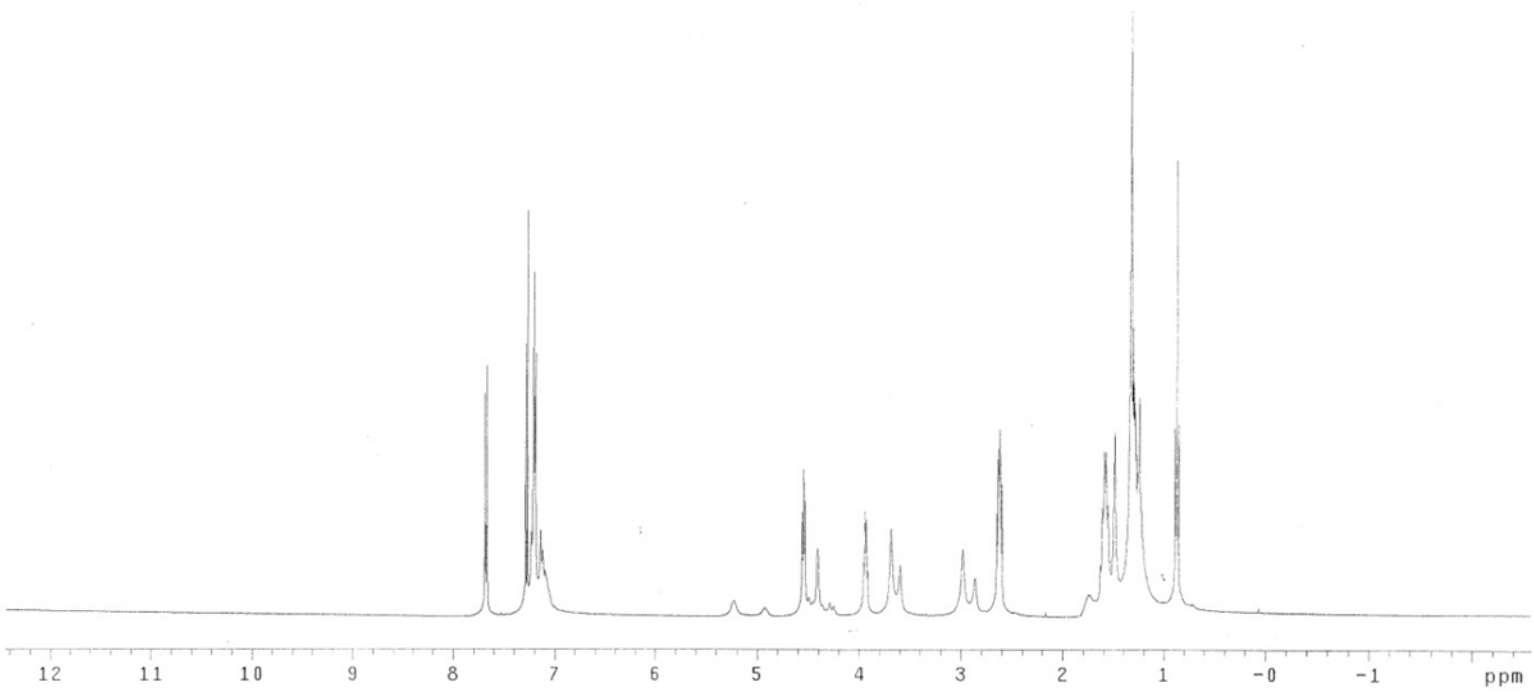
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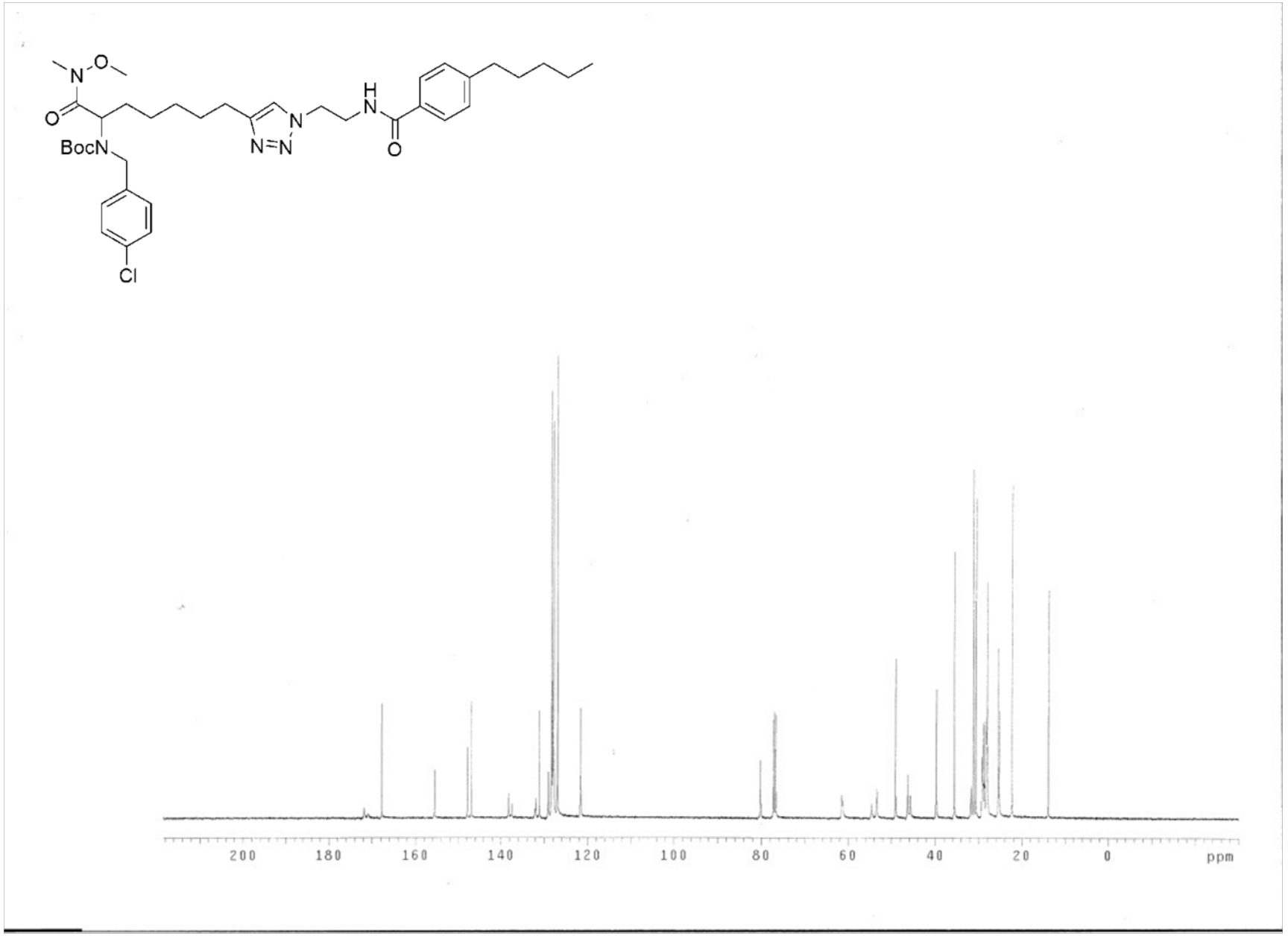
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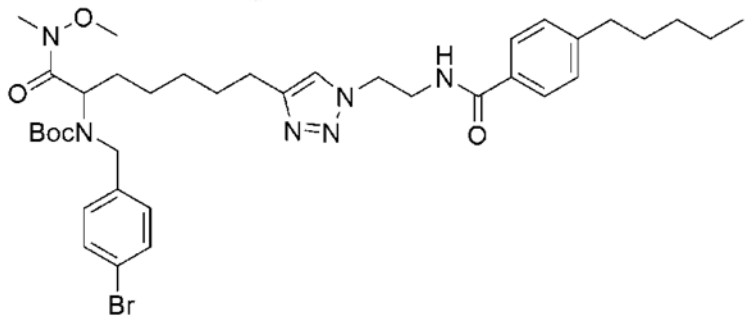
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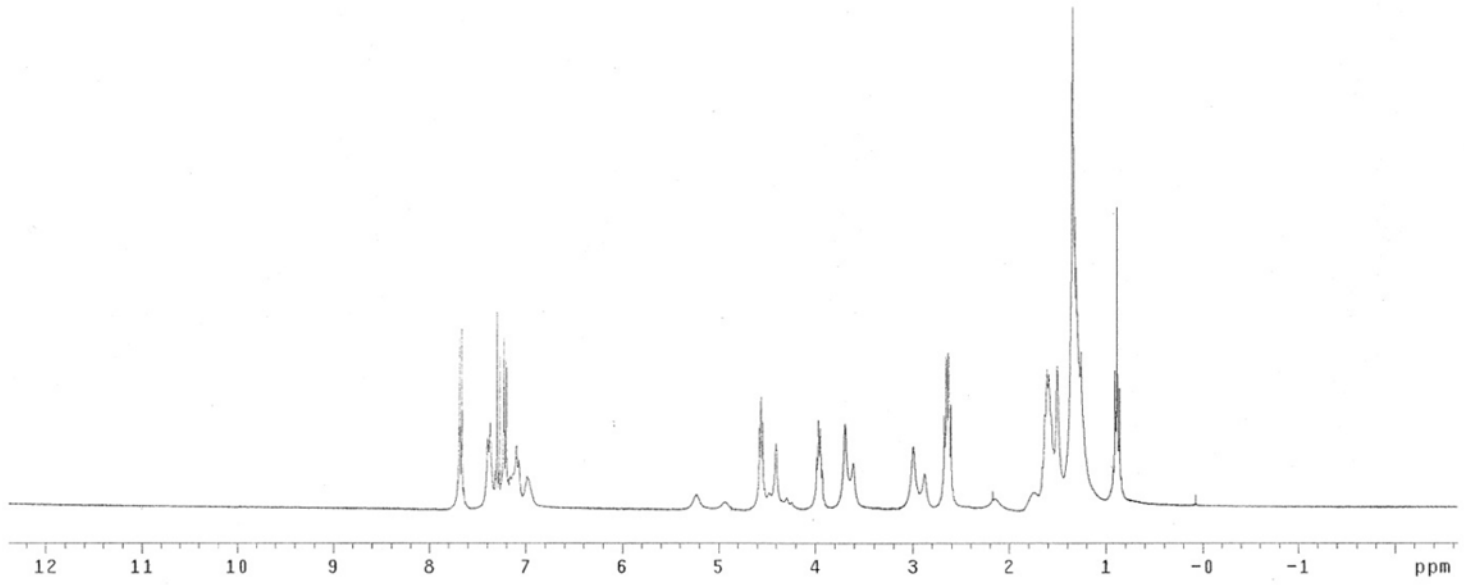
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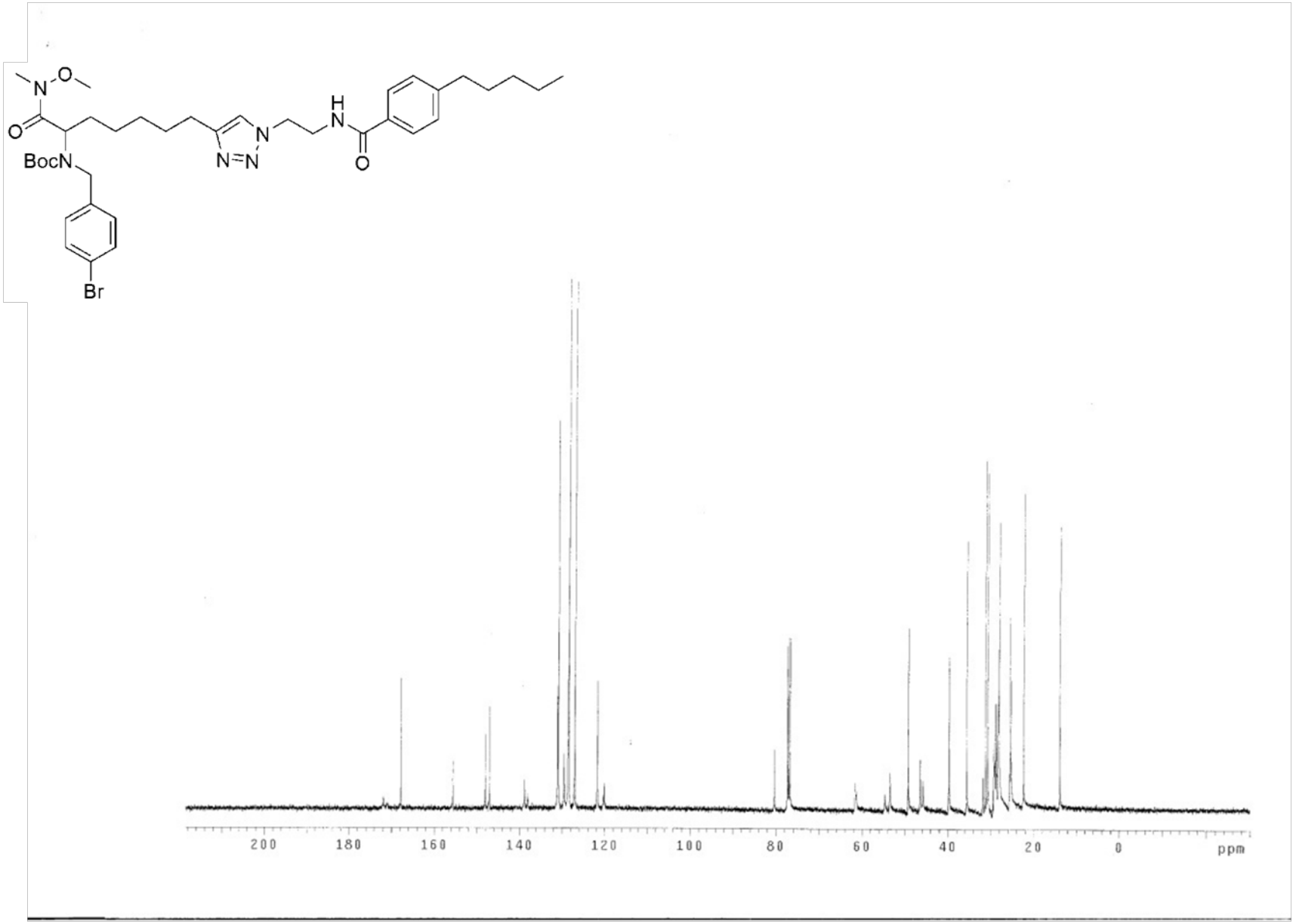
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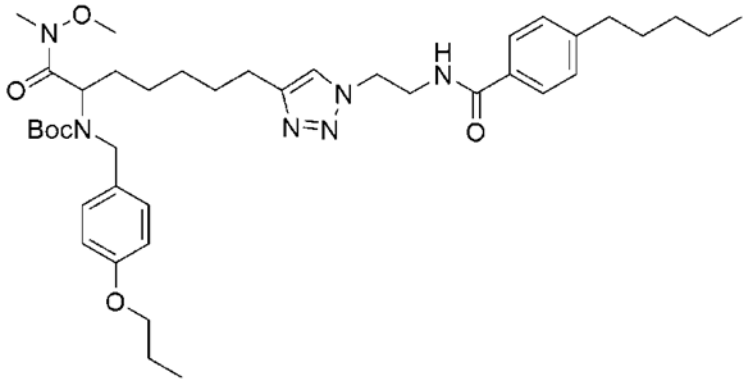
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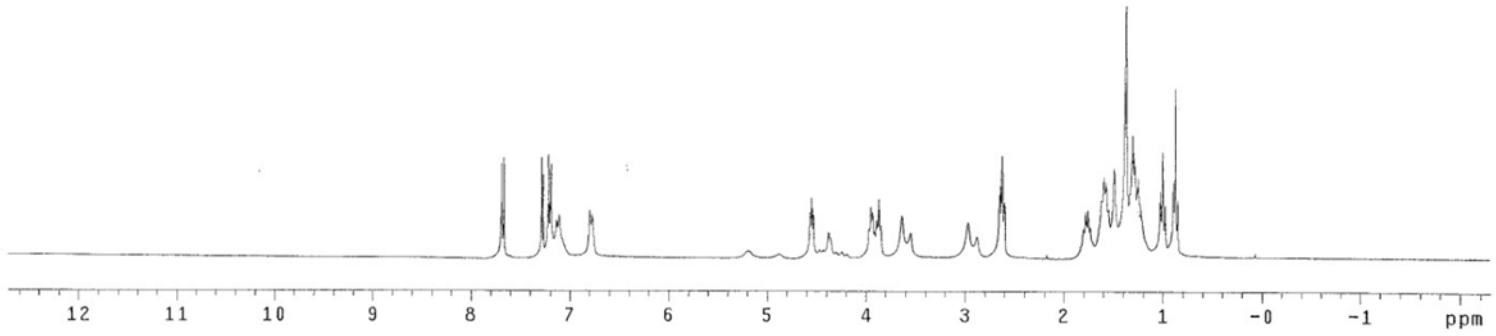
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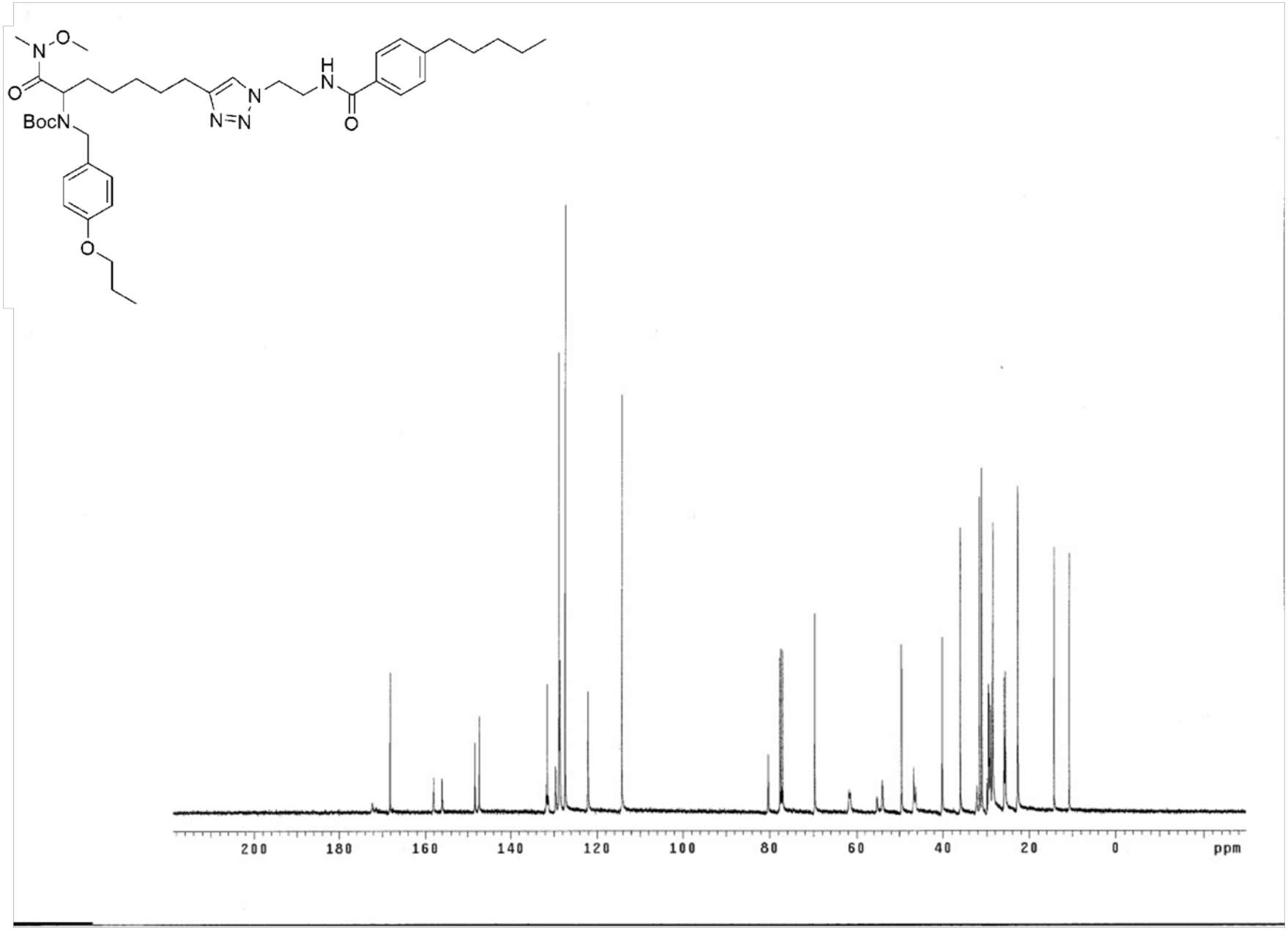
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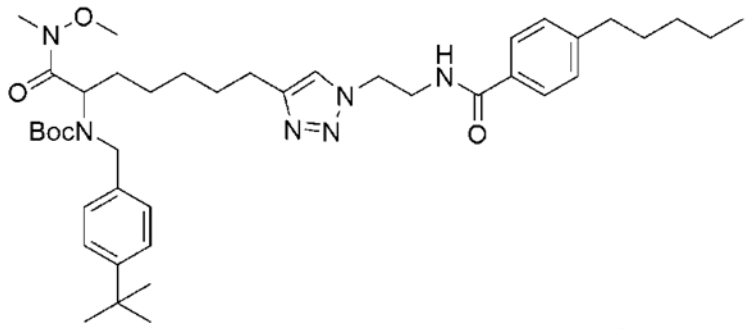
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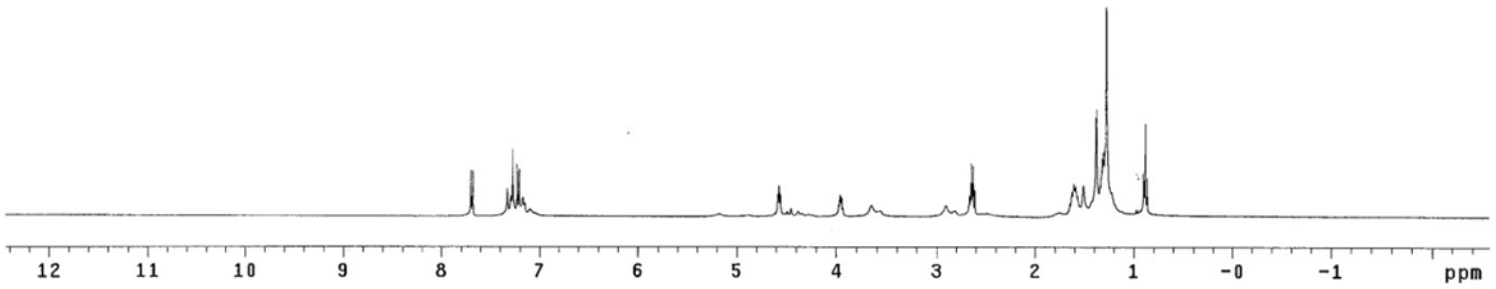
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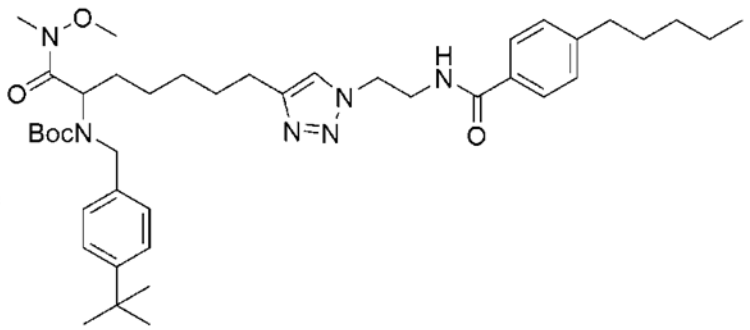
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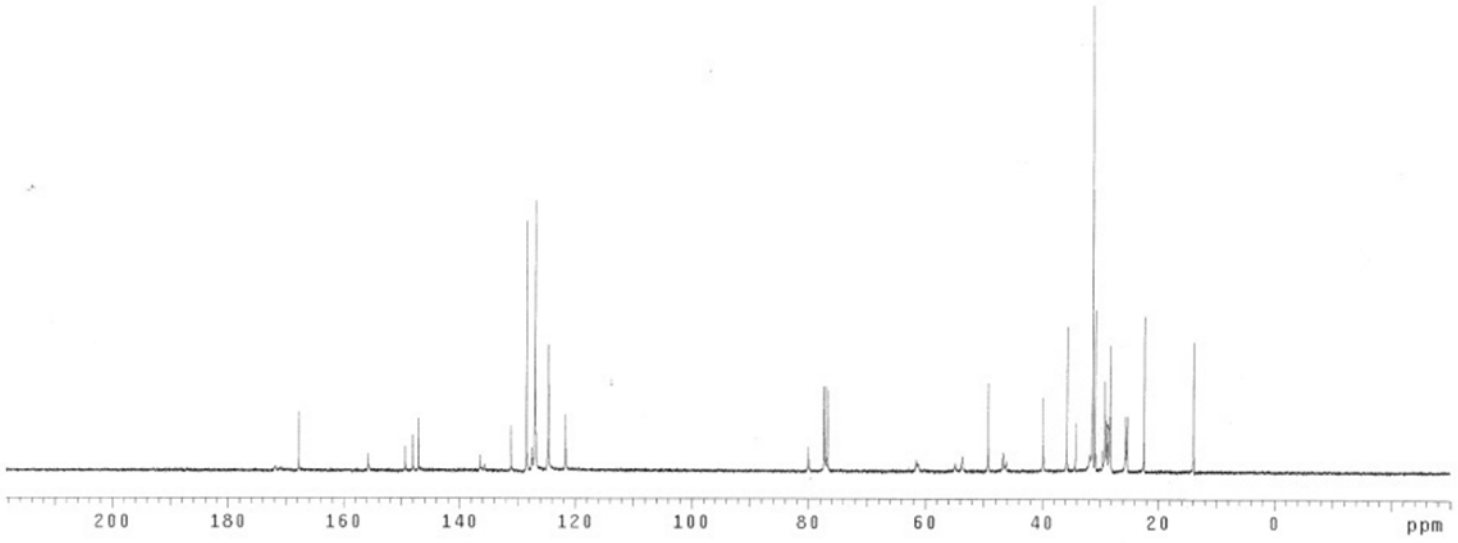
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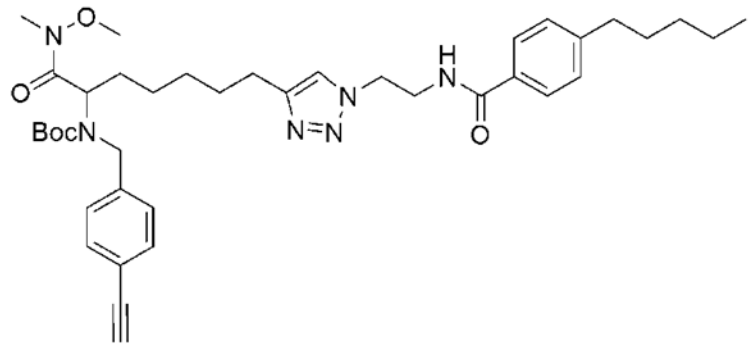
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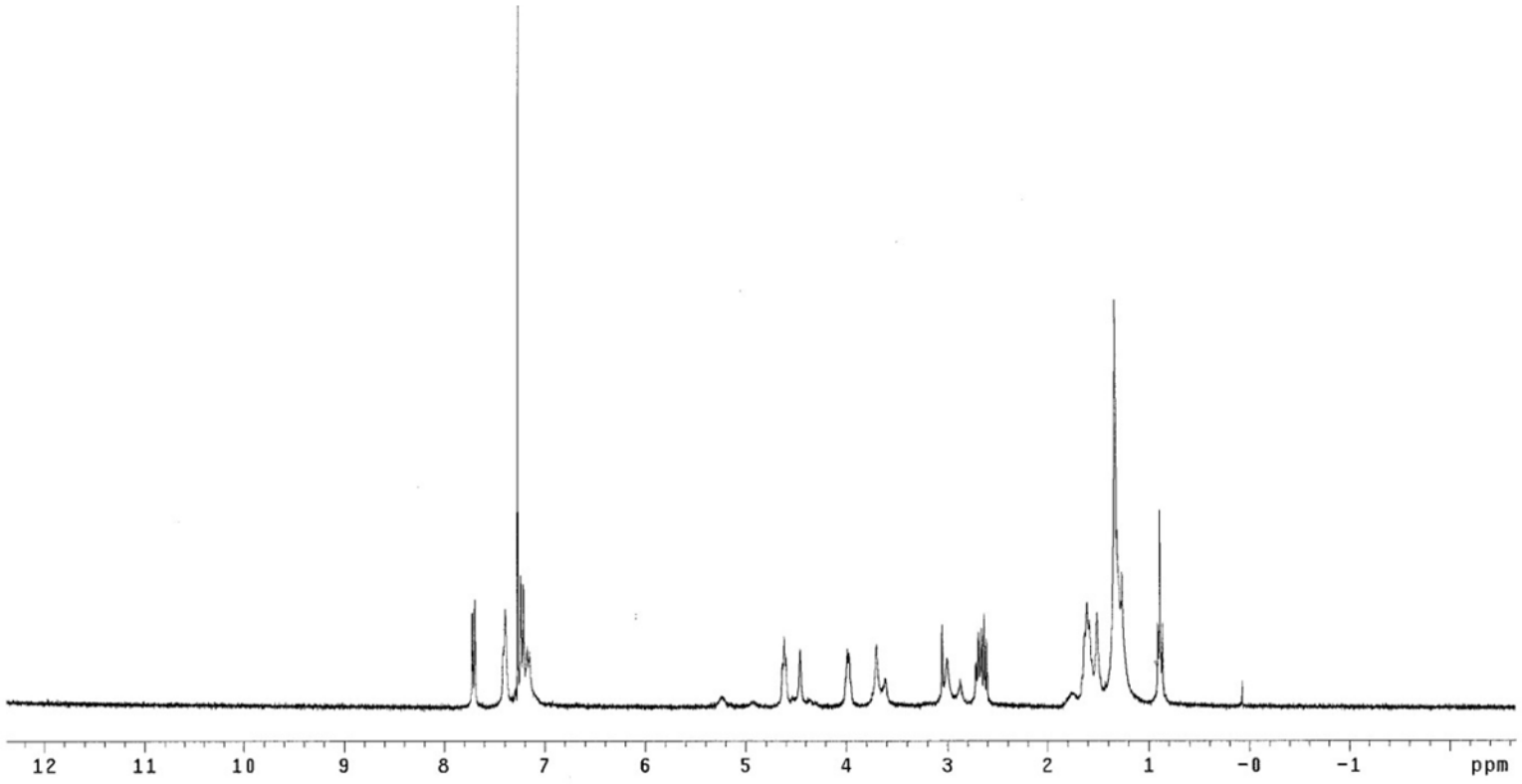
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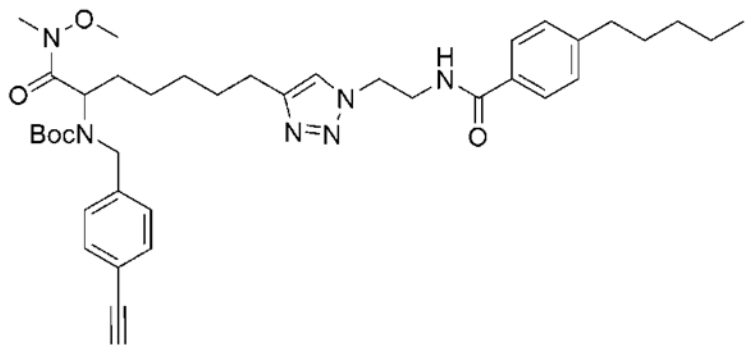
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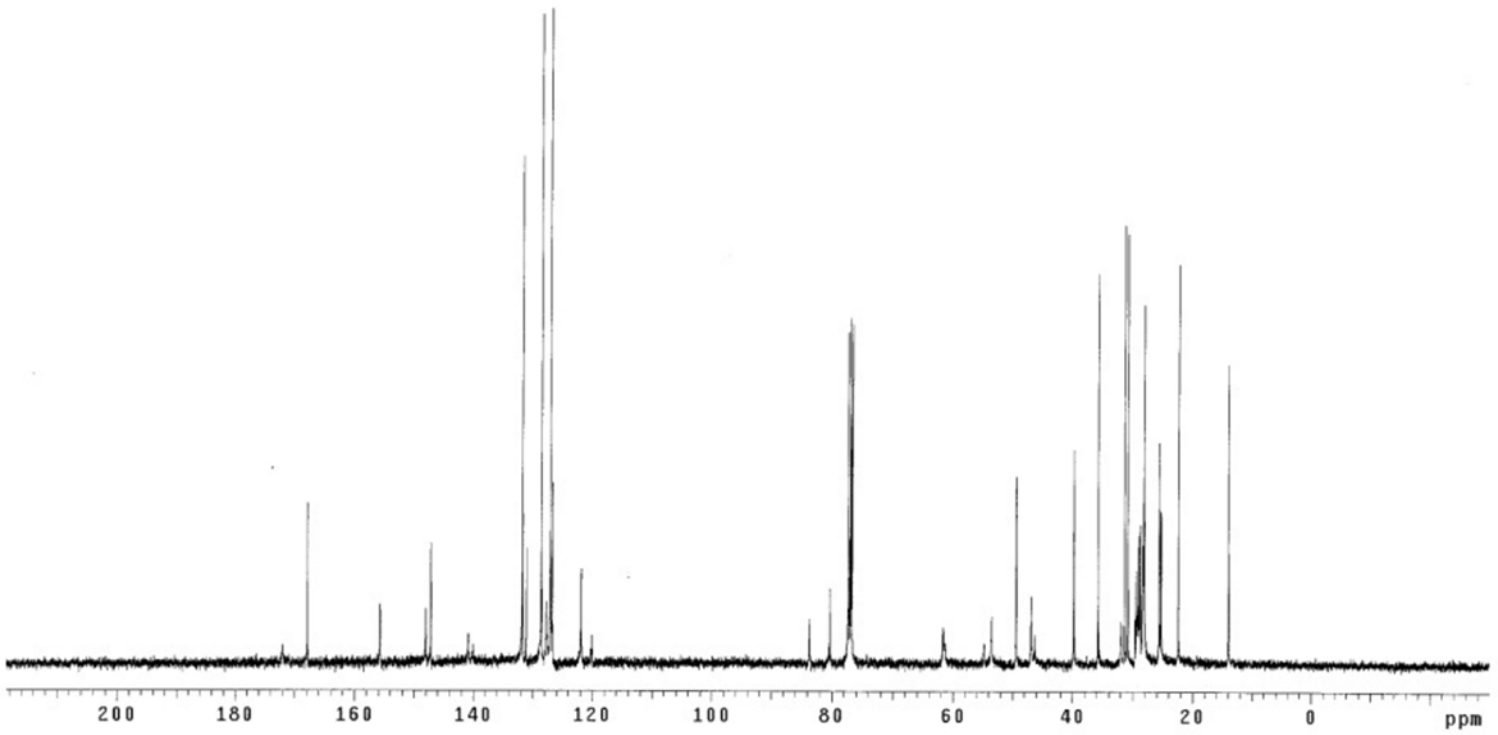
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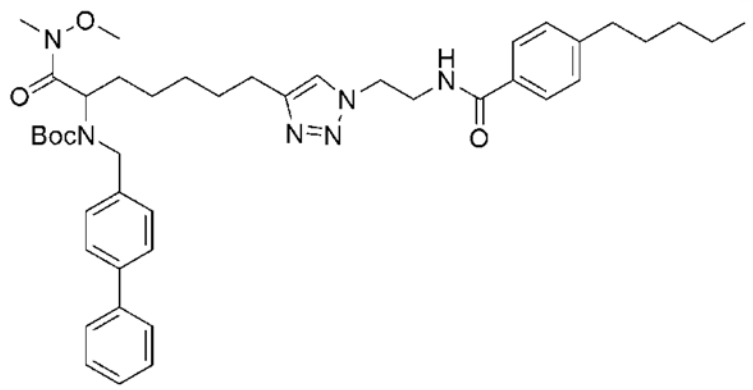
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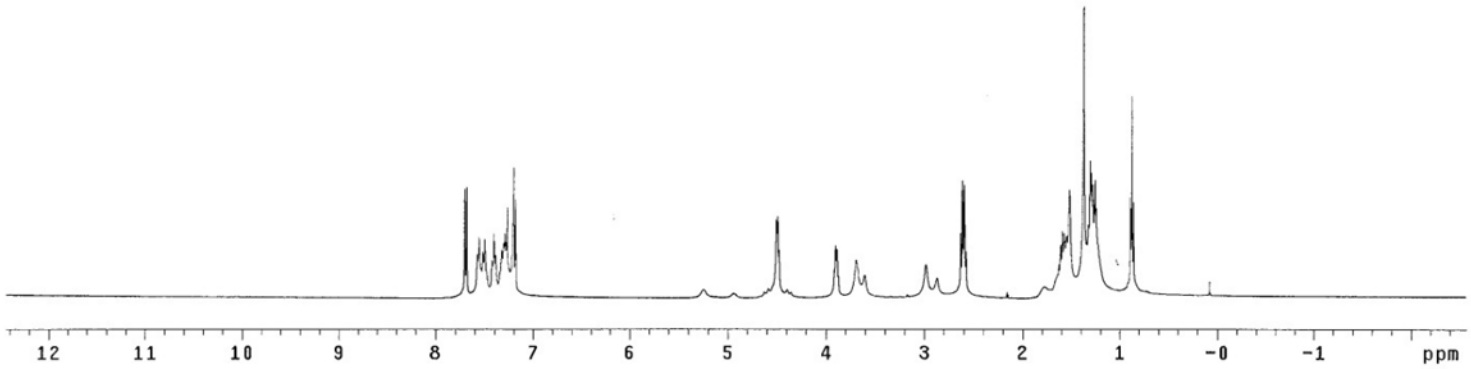
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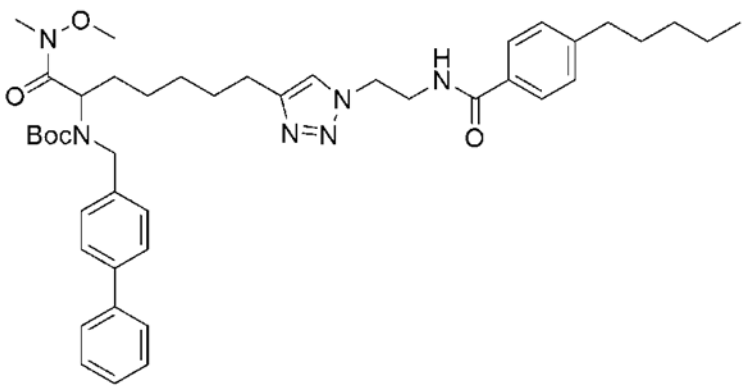
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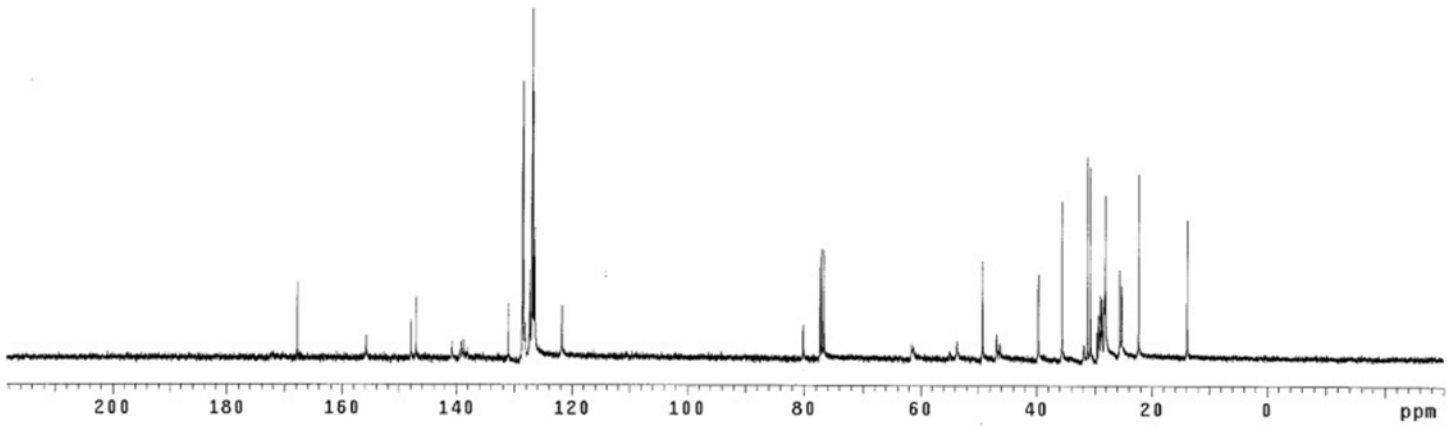
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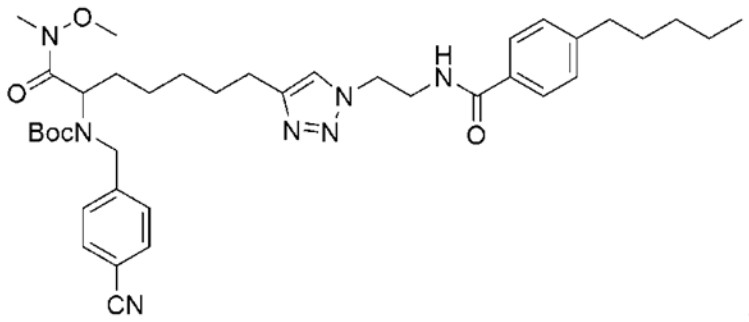
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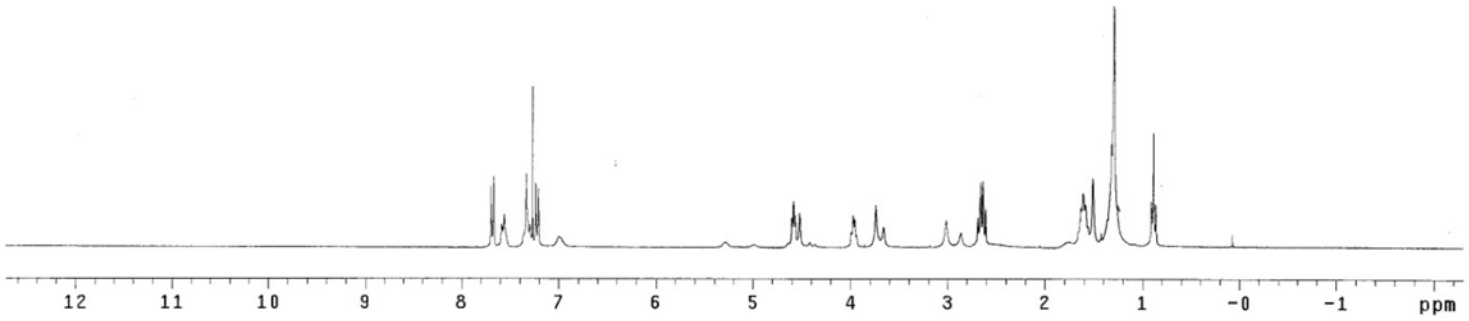
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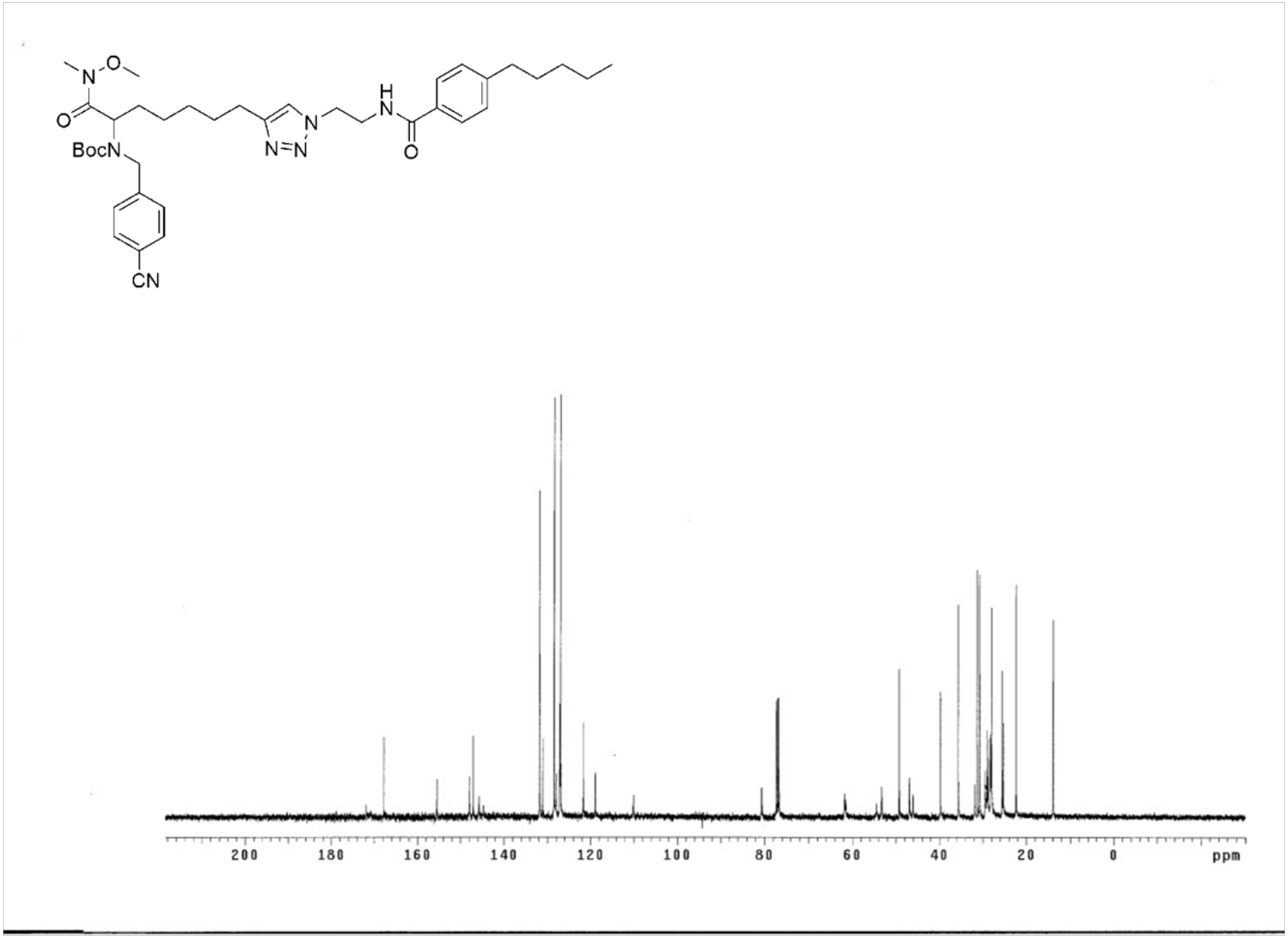
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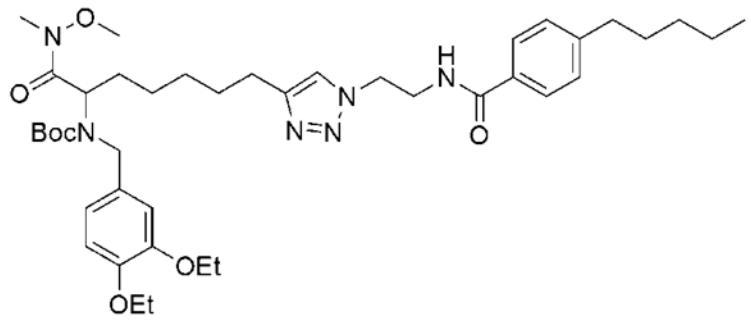
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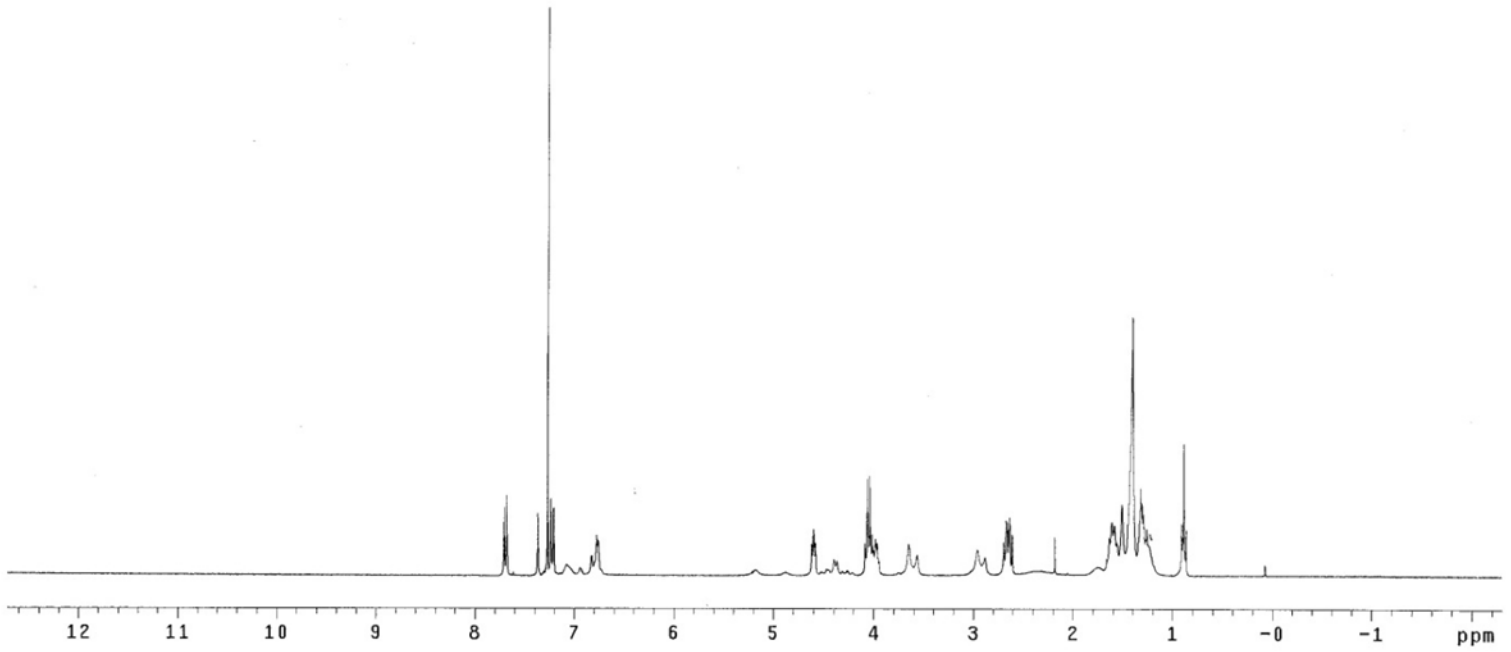
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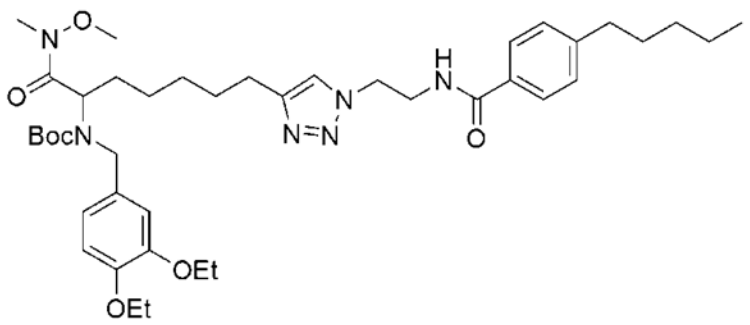
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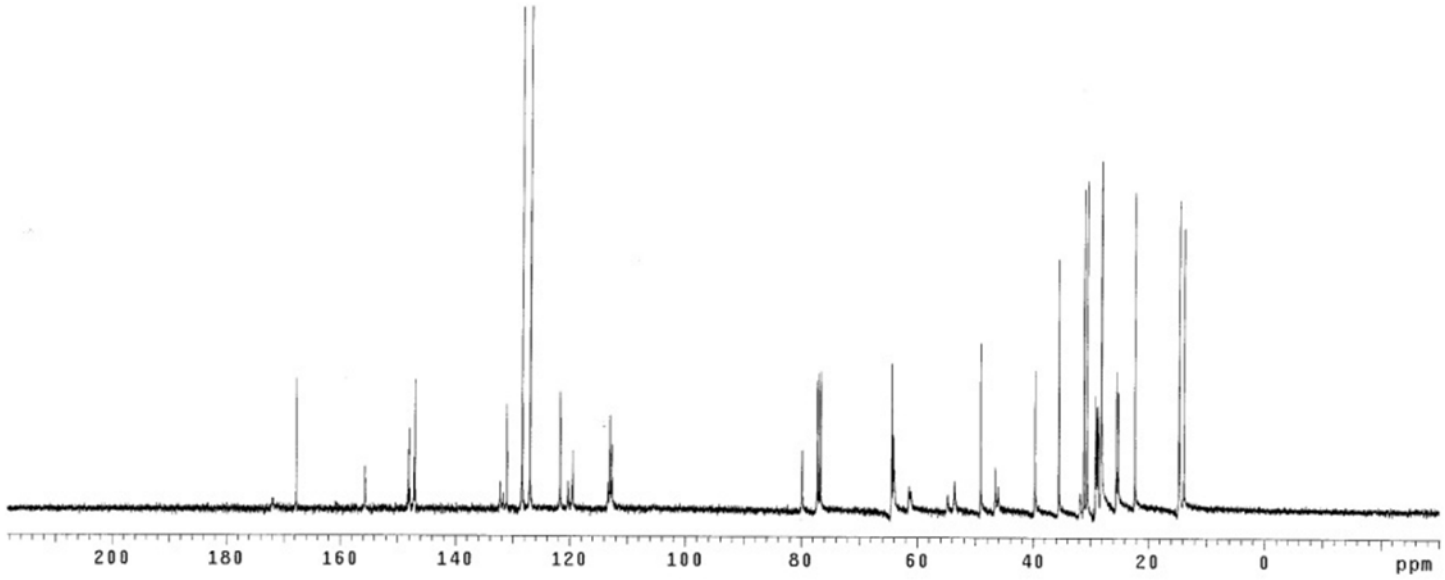
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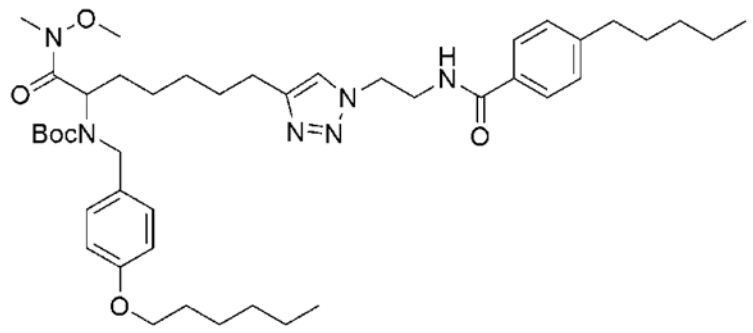
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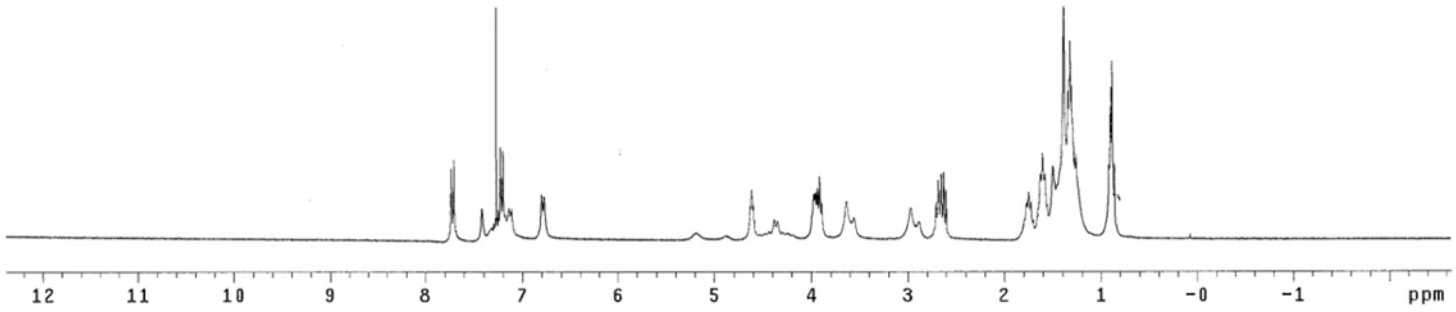
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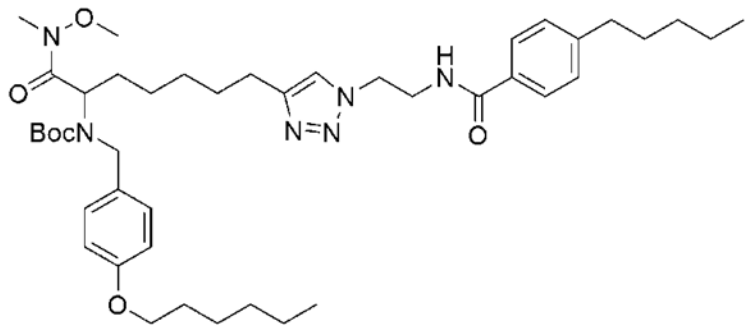
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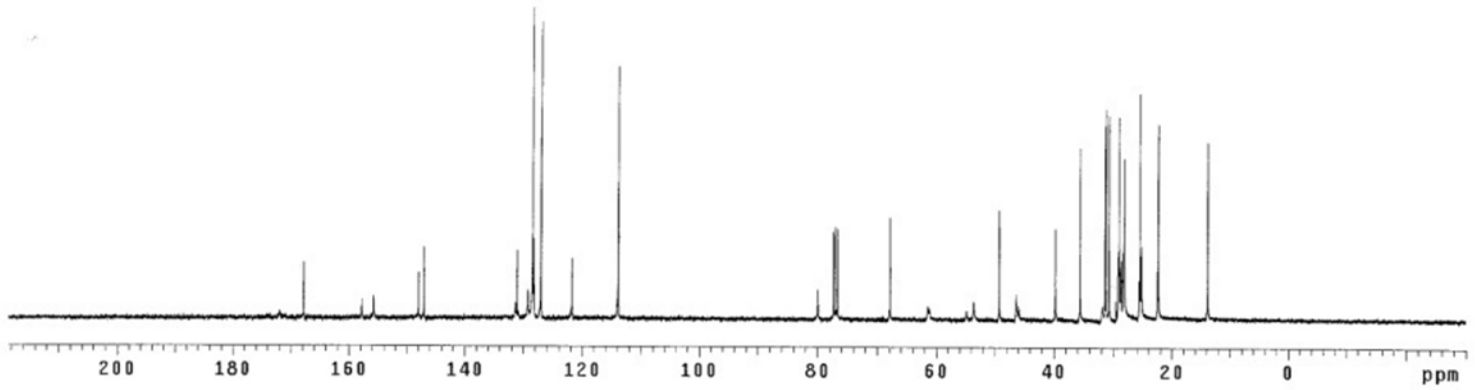
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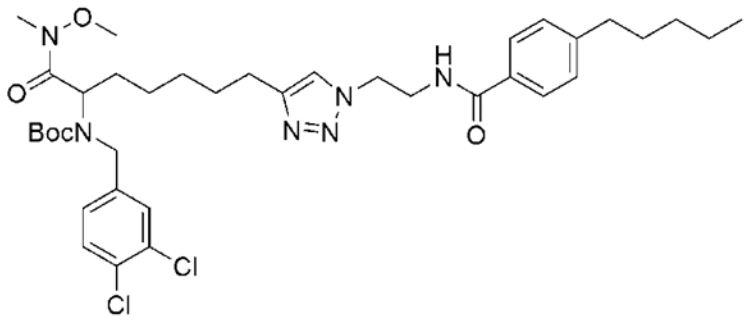
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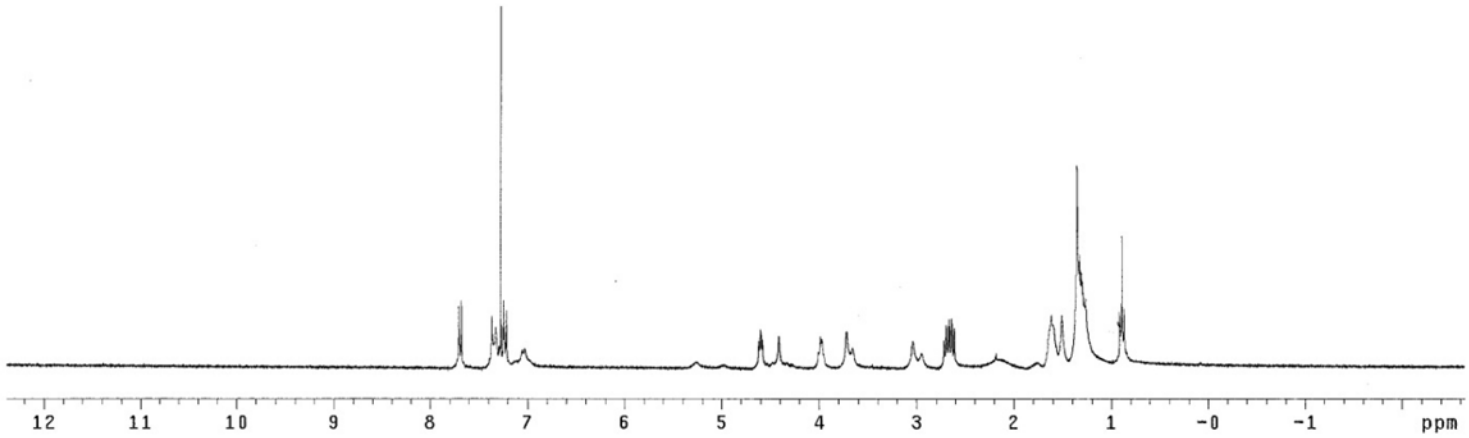
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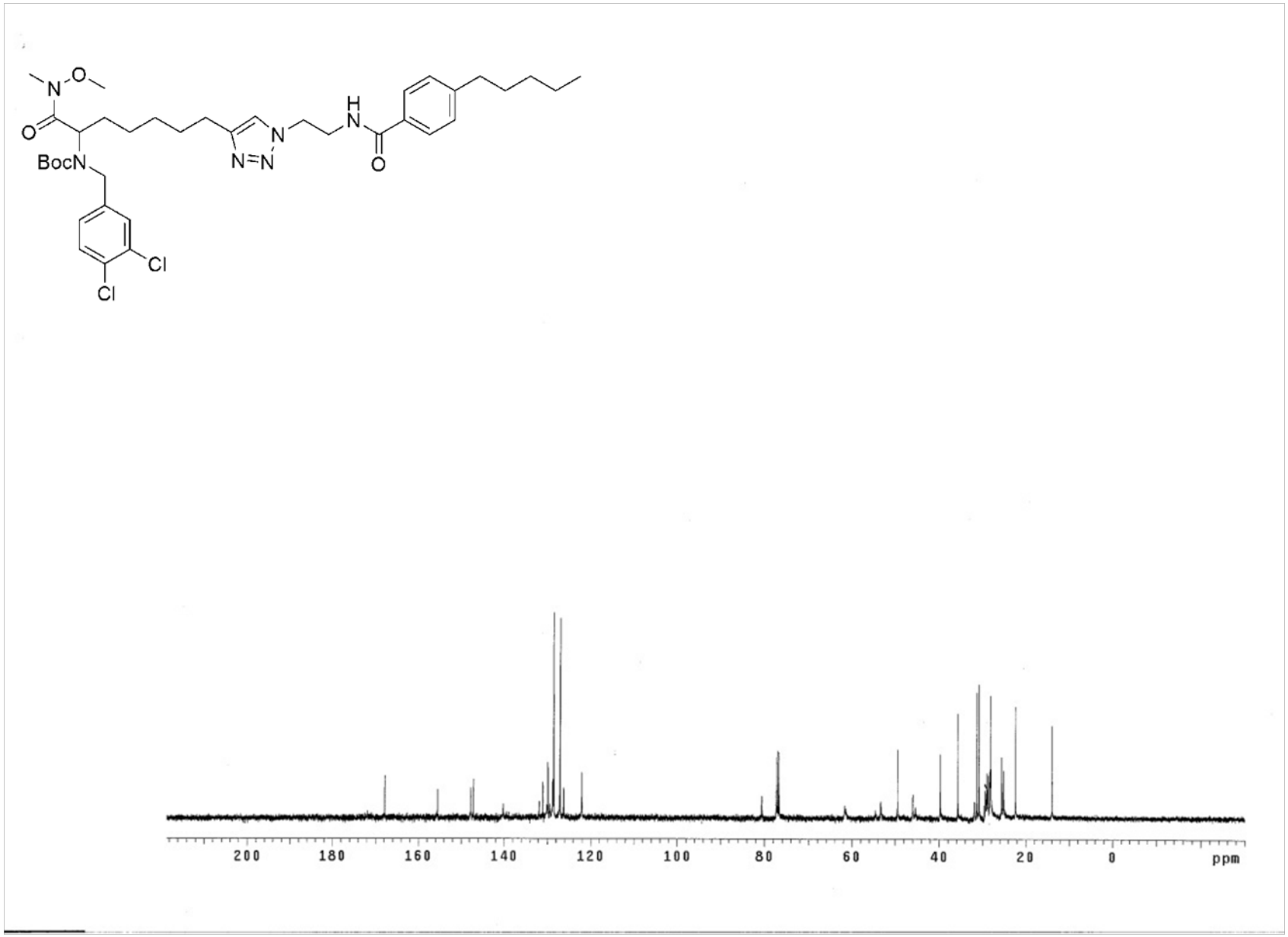
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BocN
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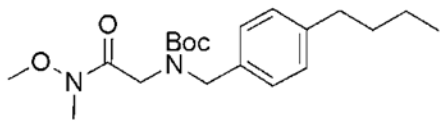
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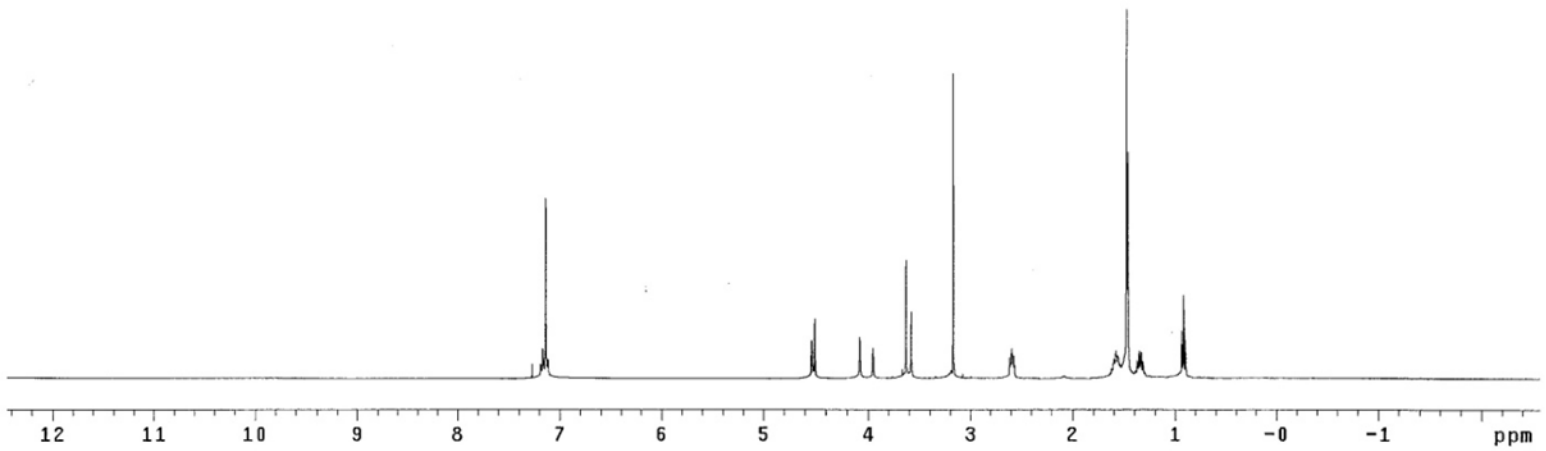
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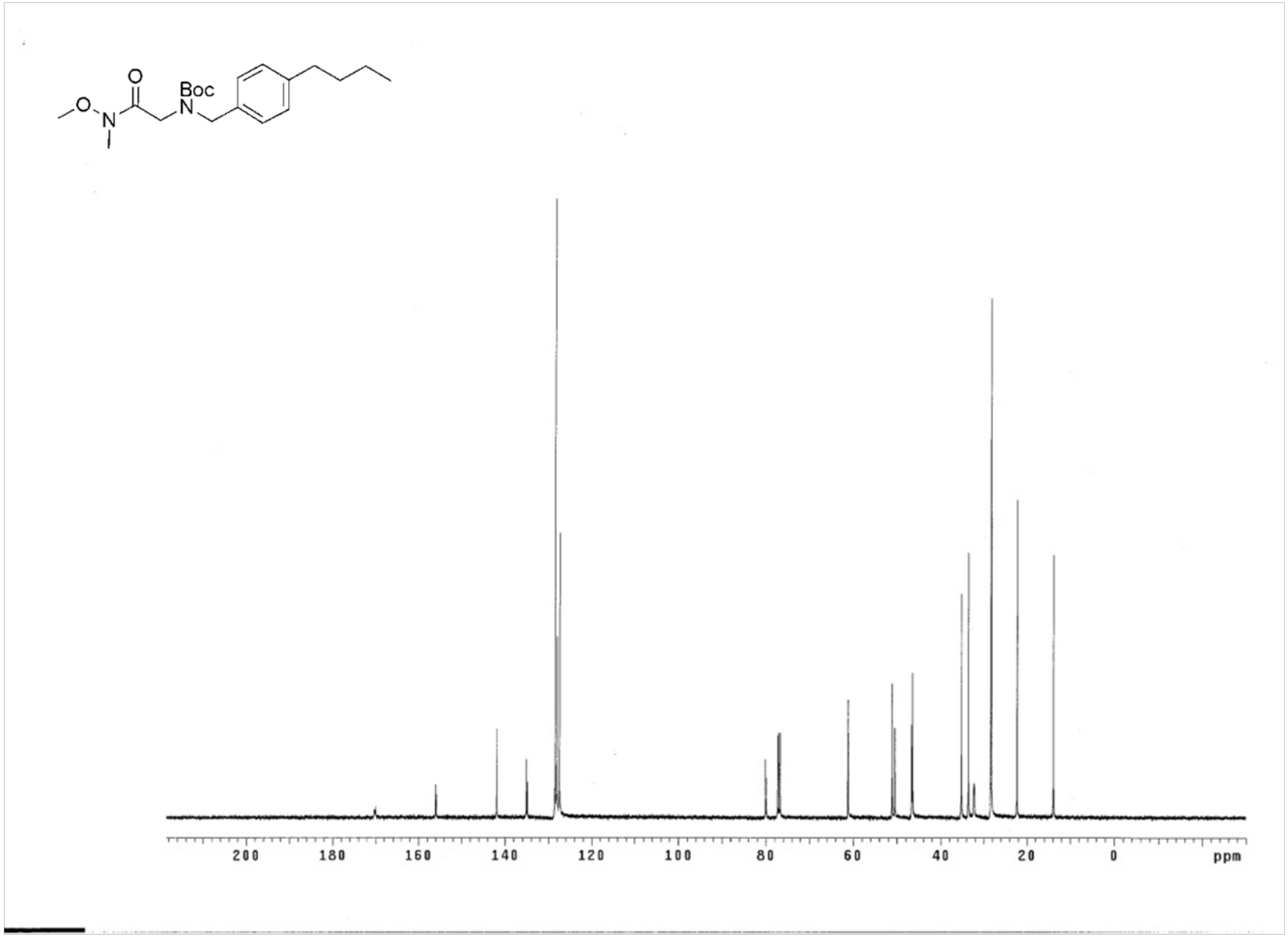
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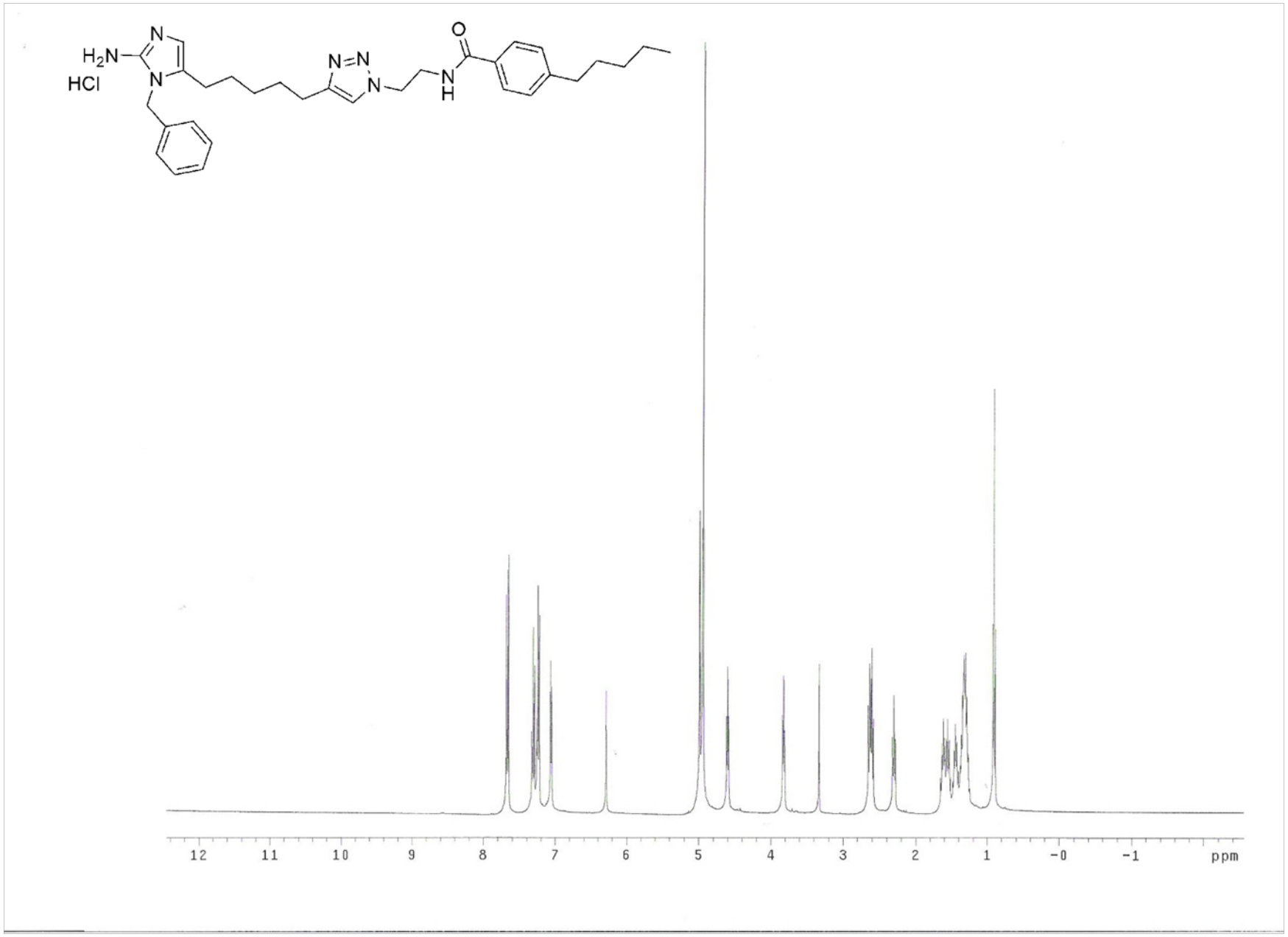
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HCl
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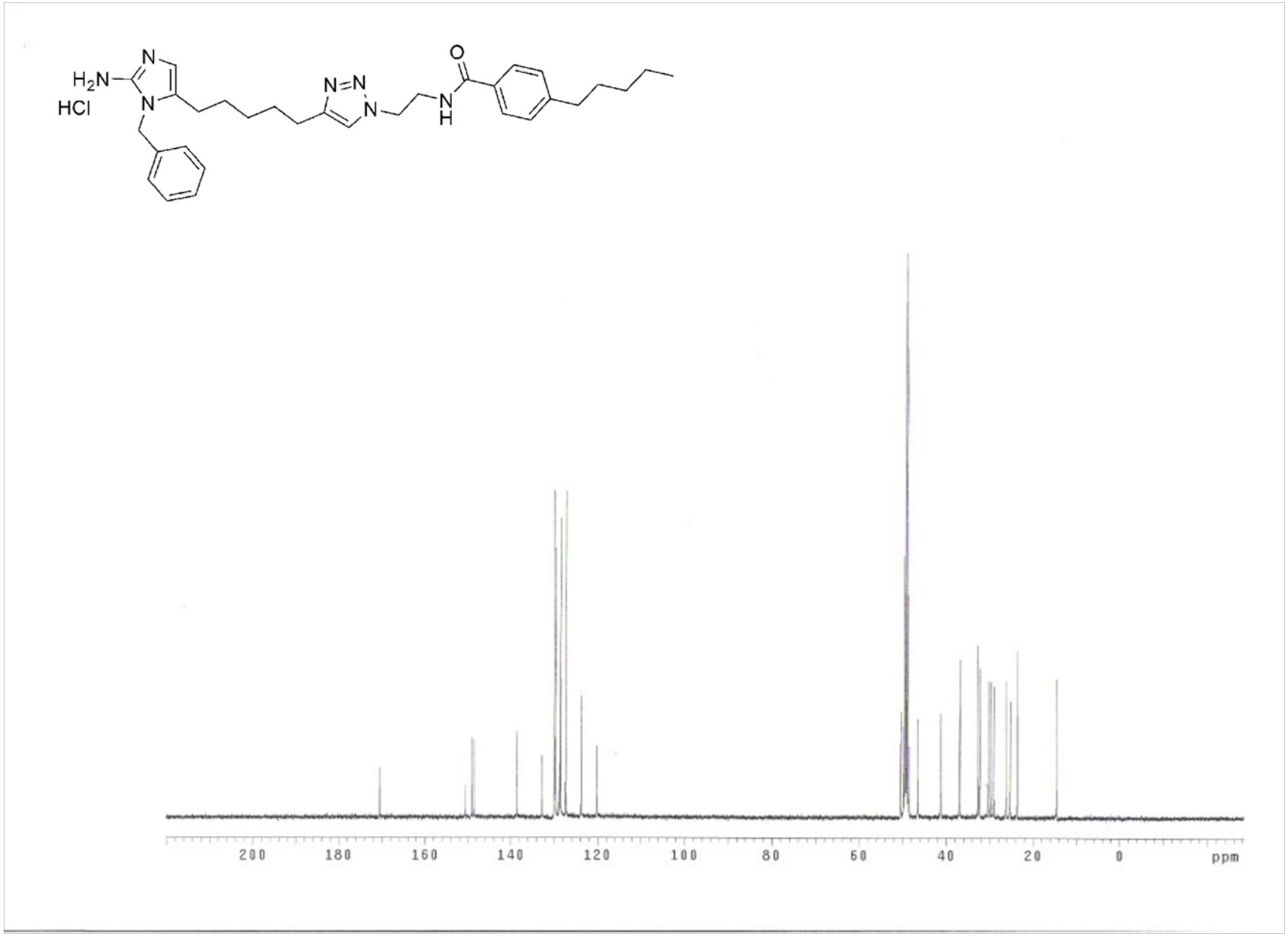
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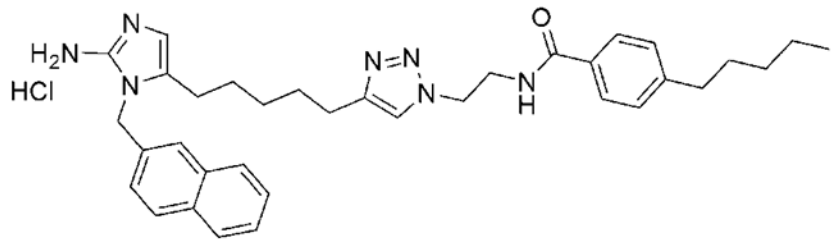
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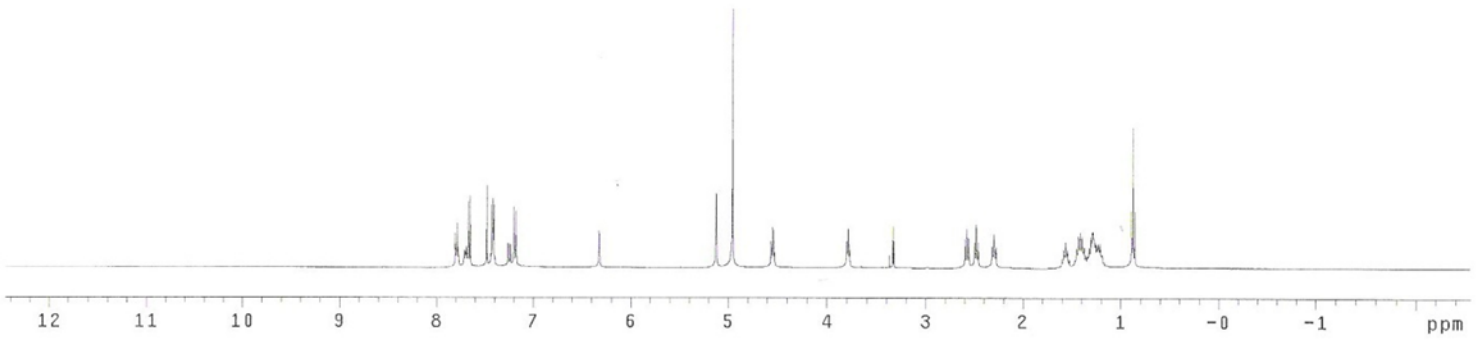
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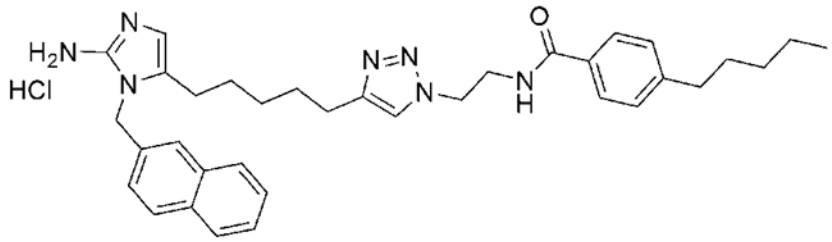
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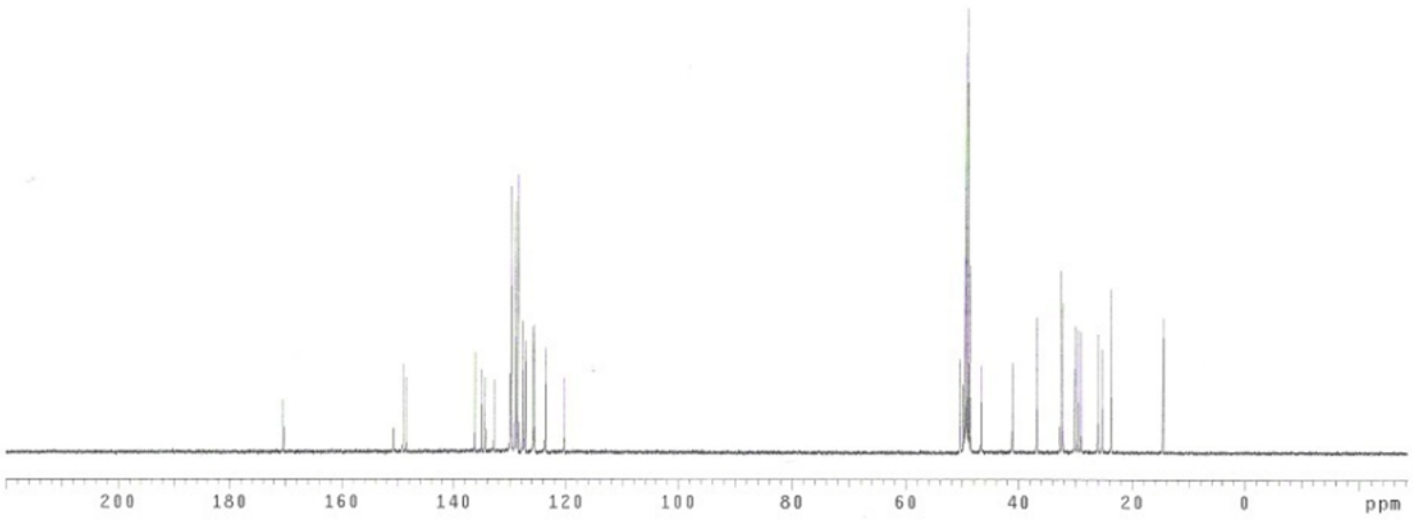
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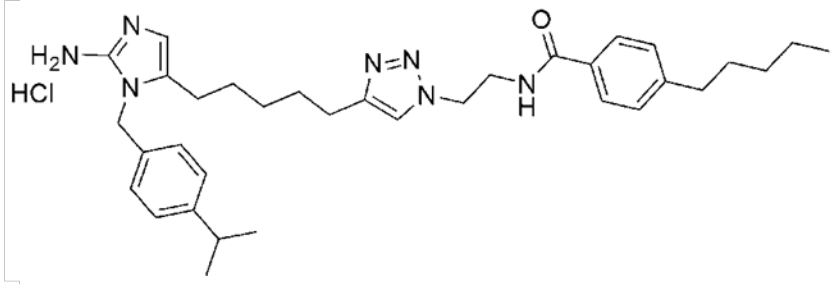
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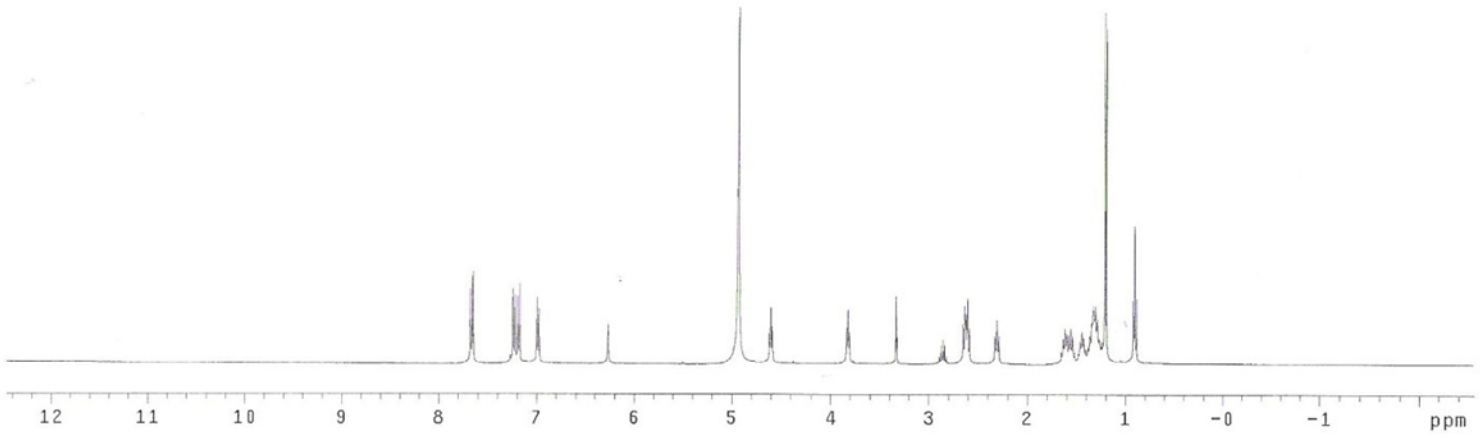
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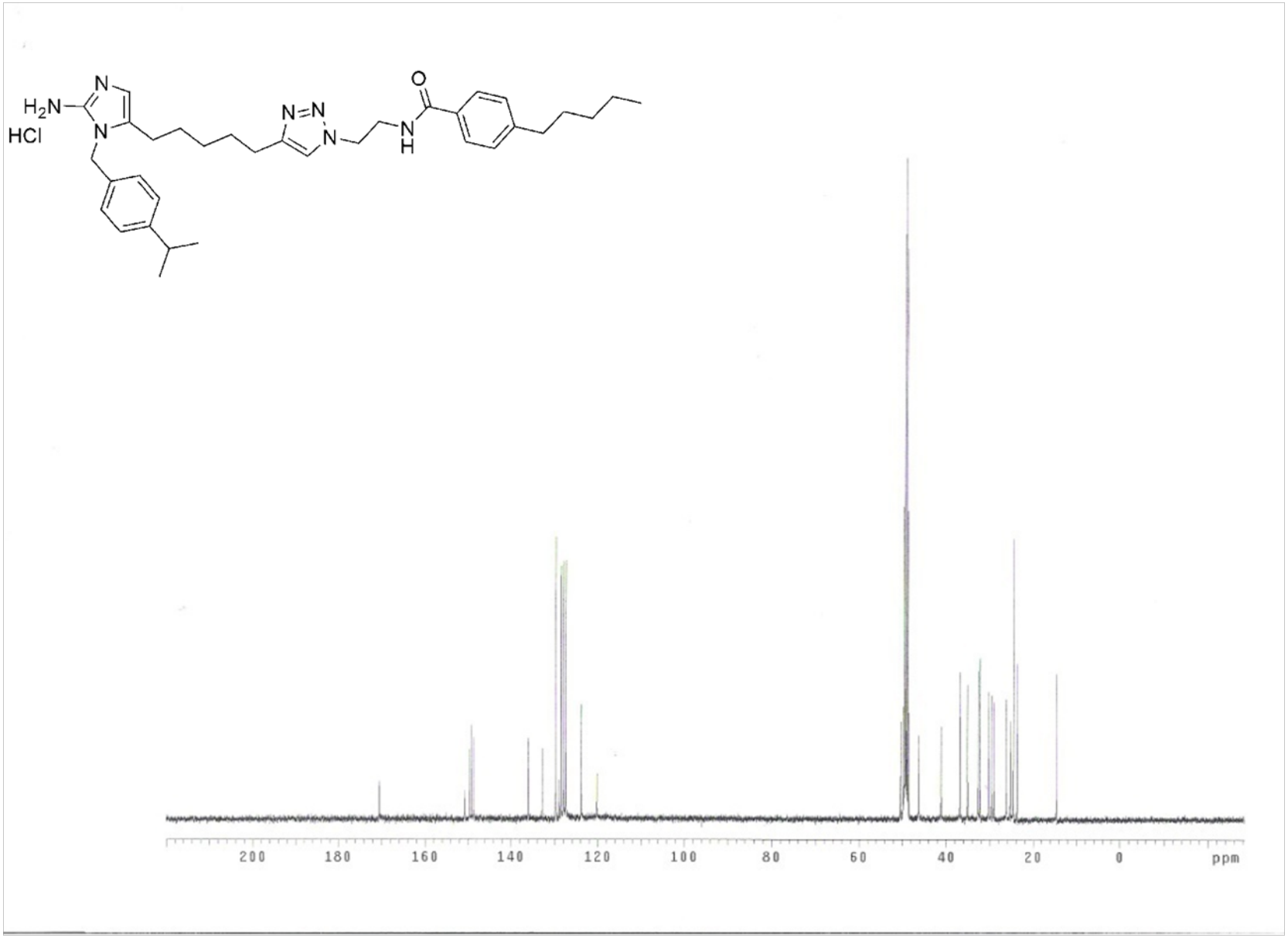
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HCl
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N
H
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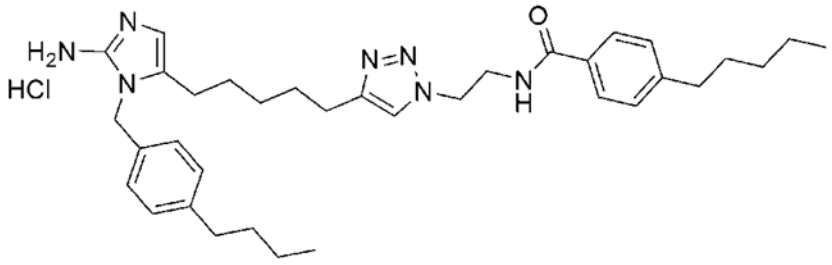
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H
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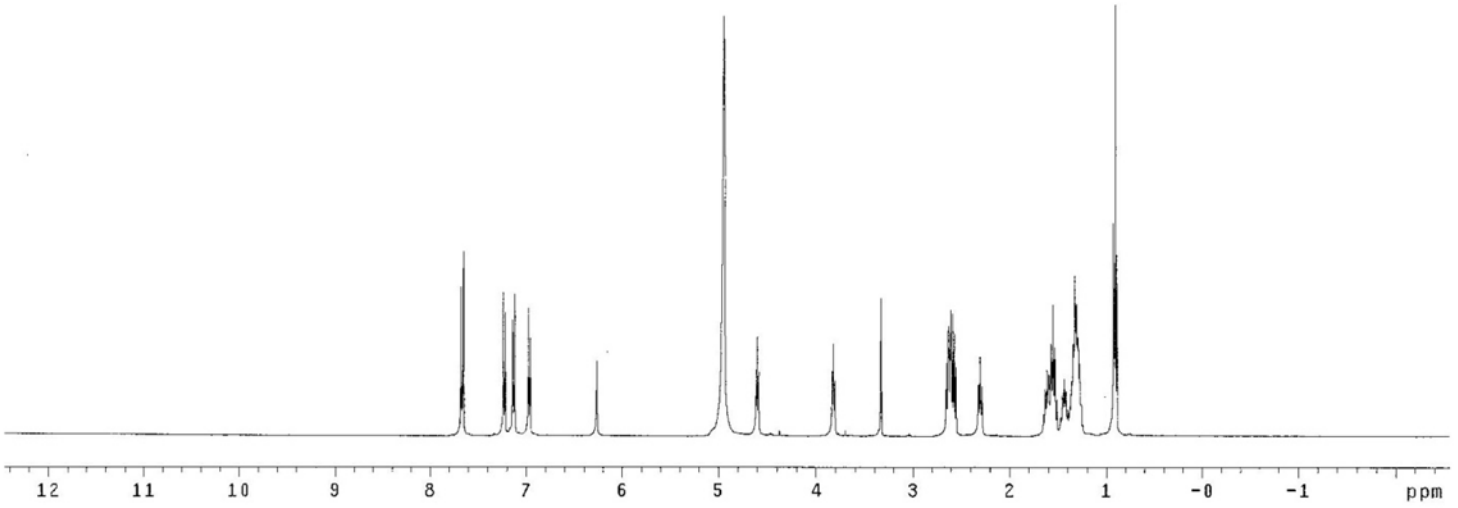
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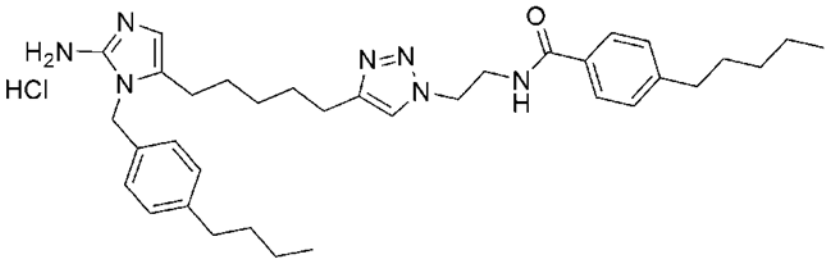
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H
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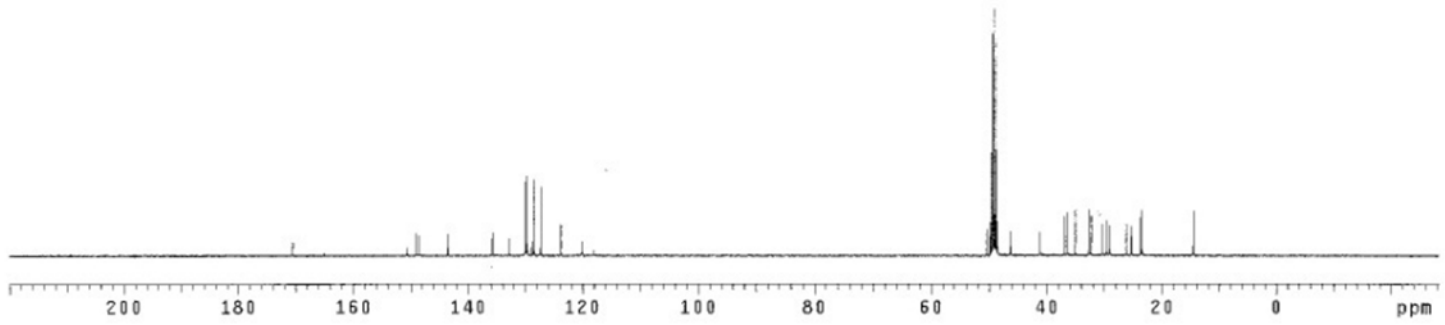
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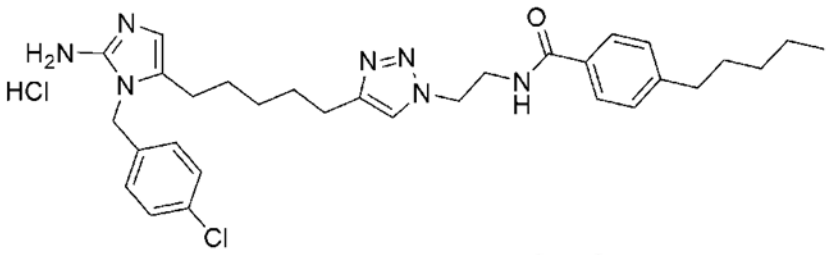
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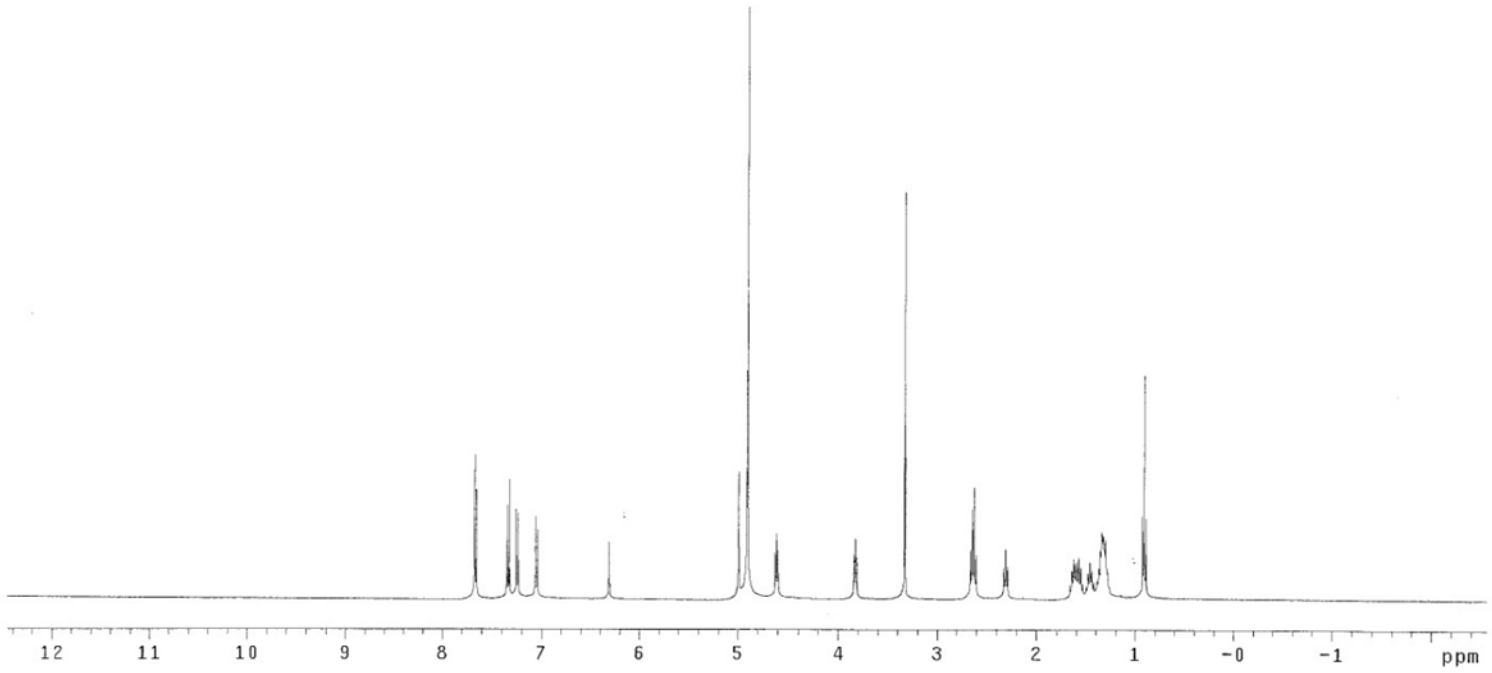
H
O
Cl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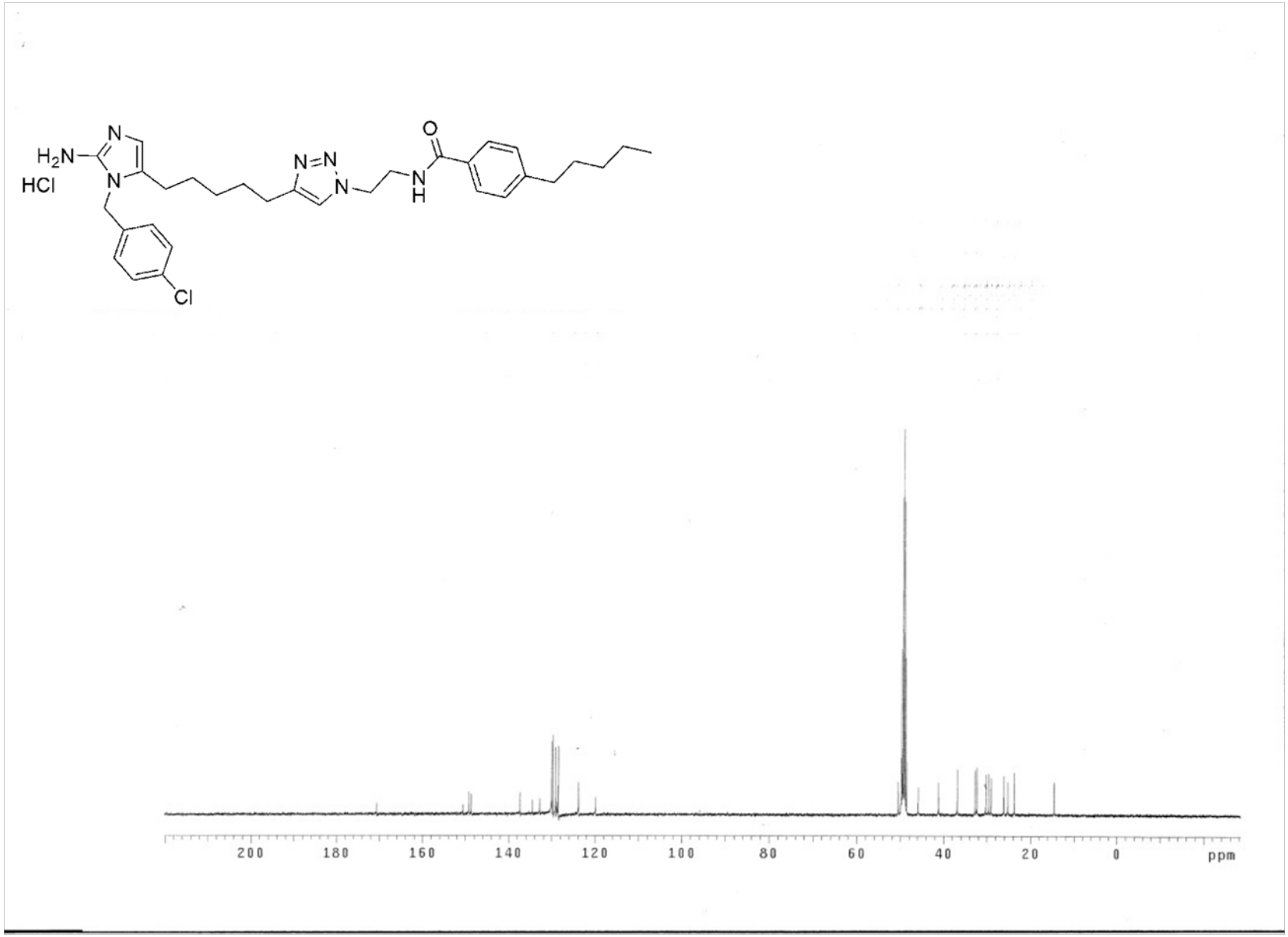
H2N
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Cl
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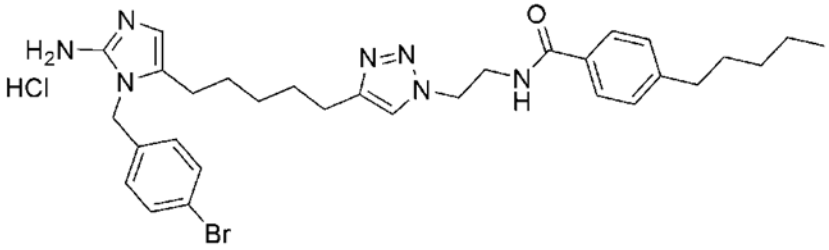
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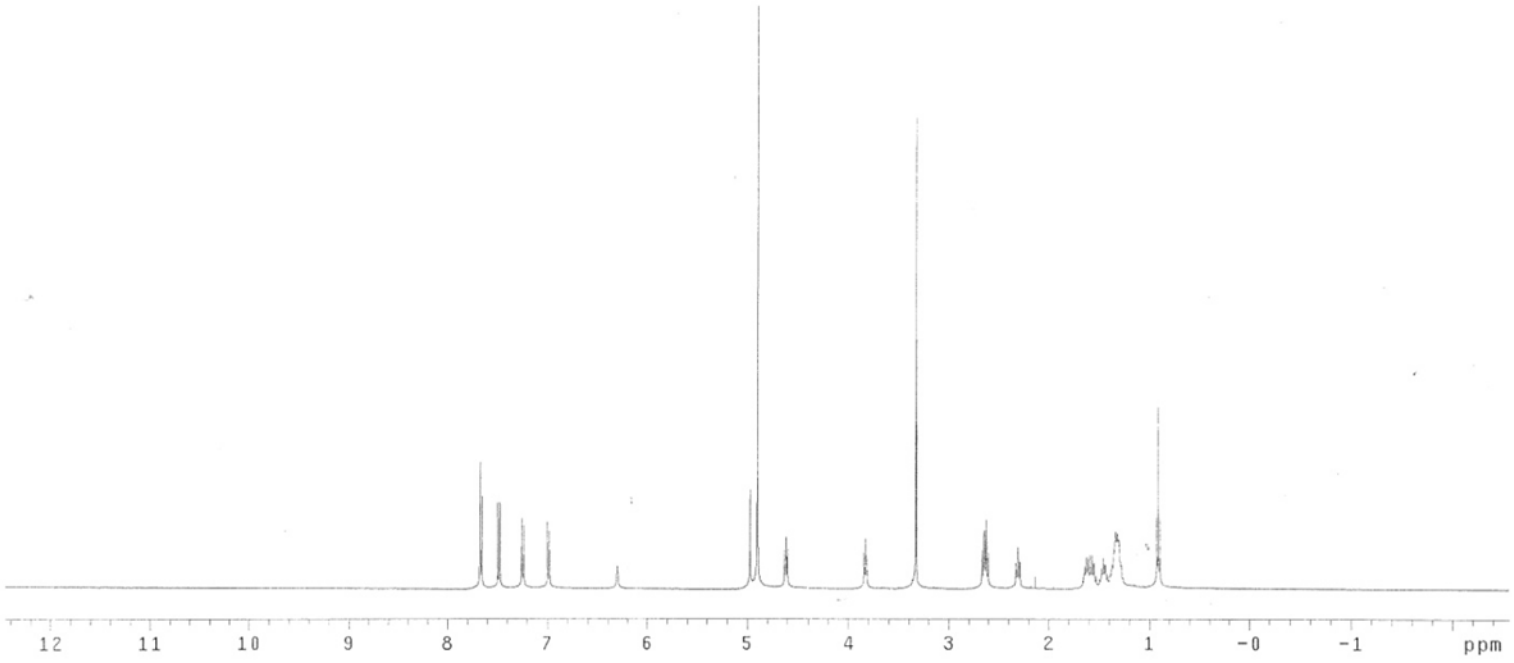
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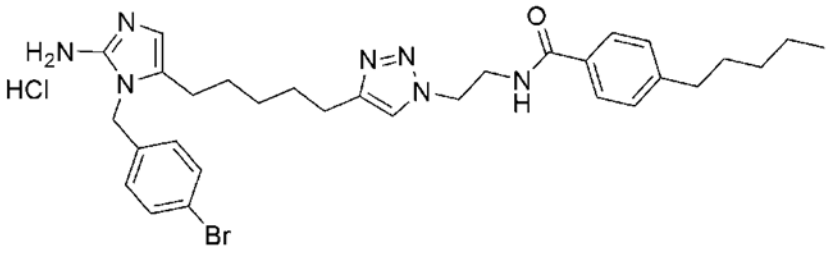
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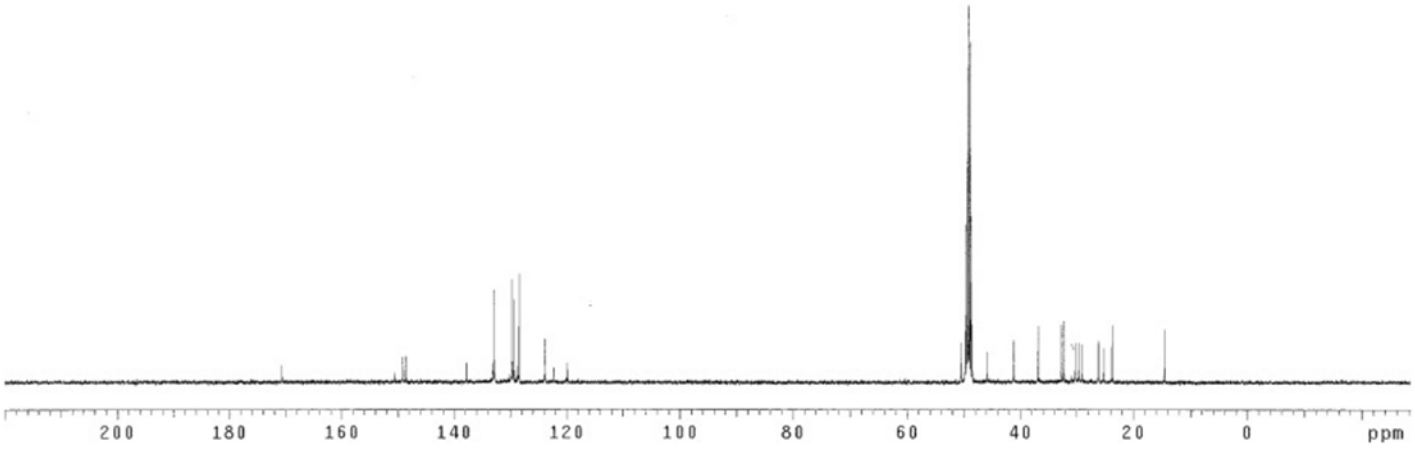
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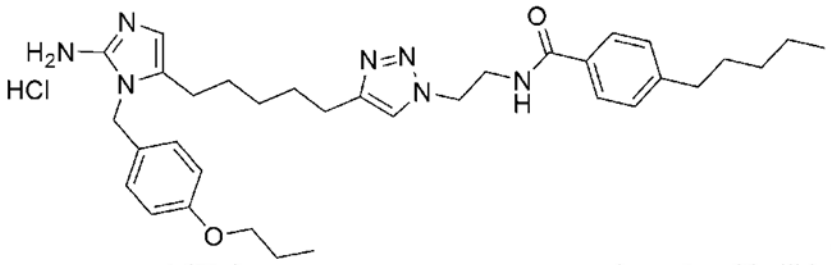
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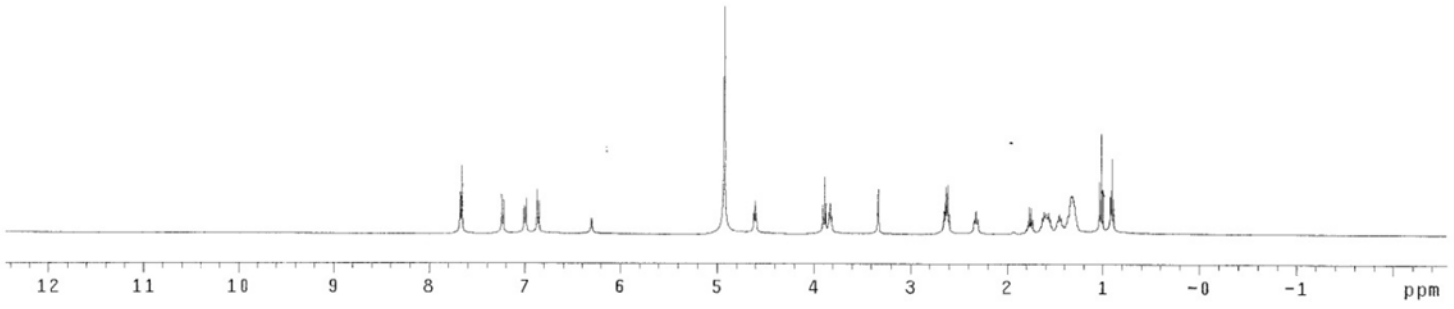
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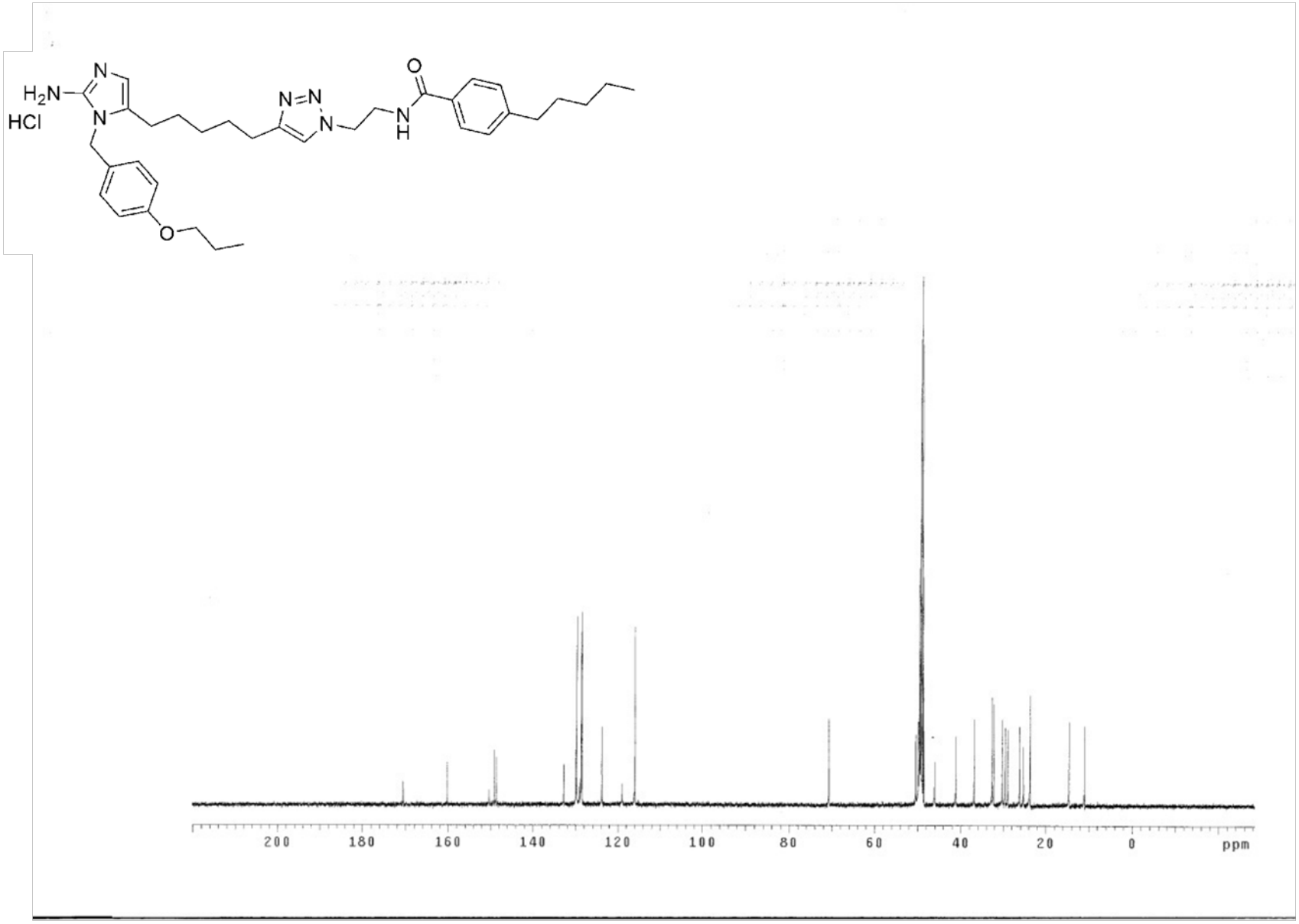
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HCl
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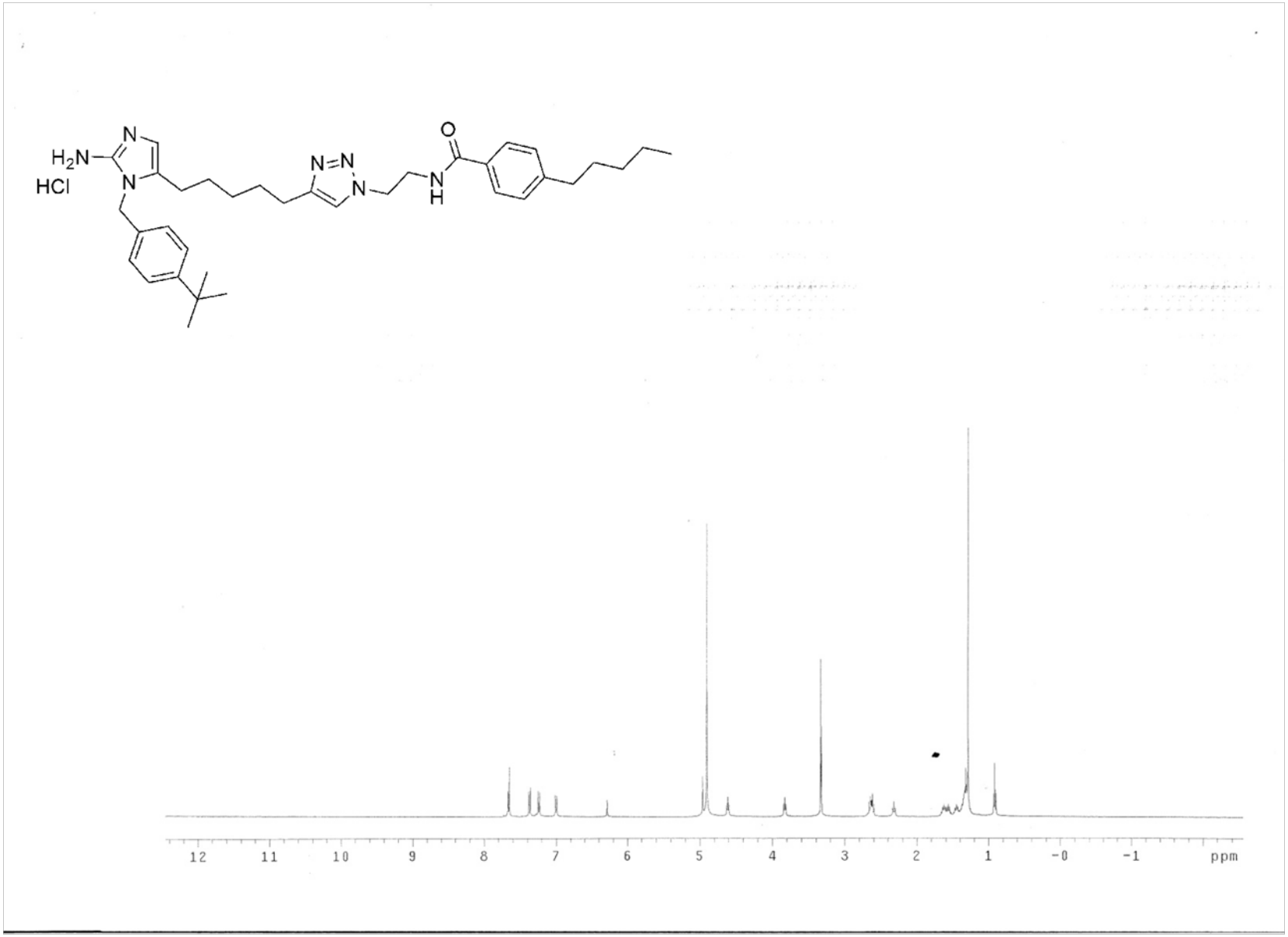
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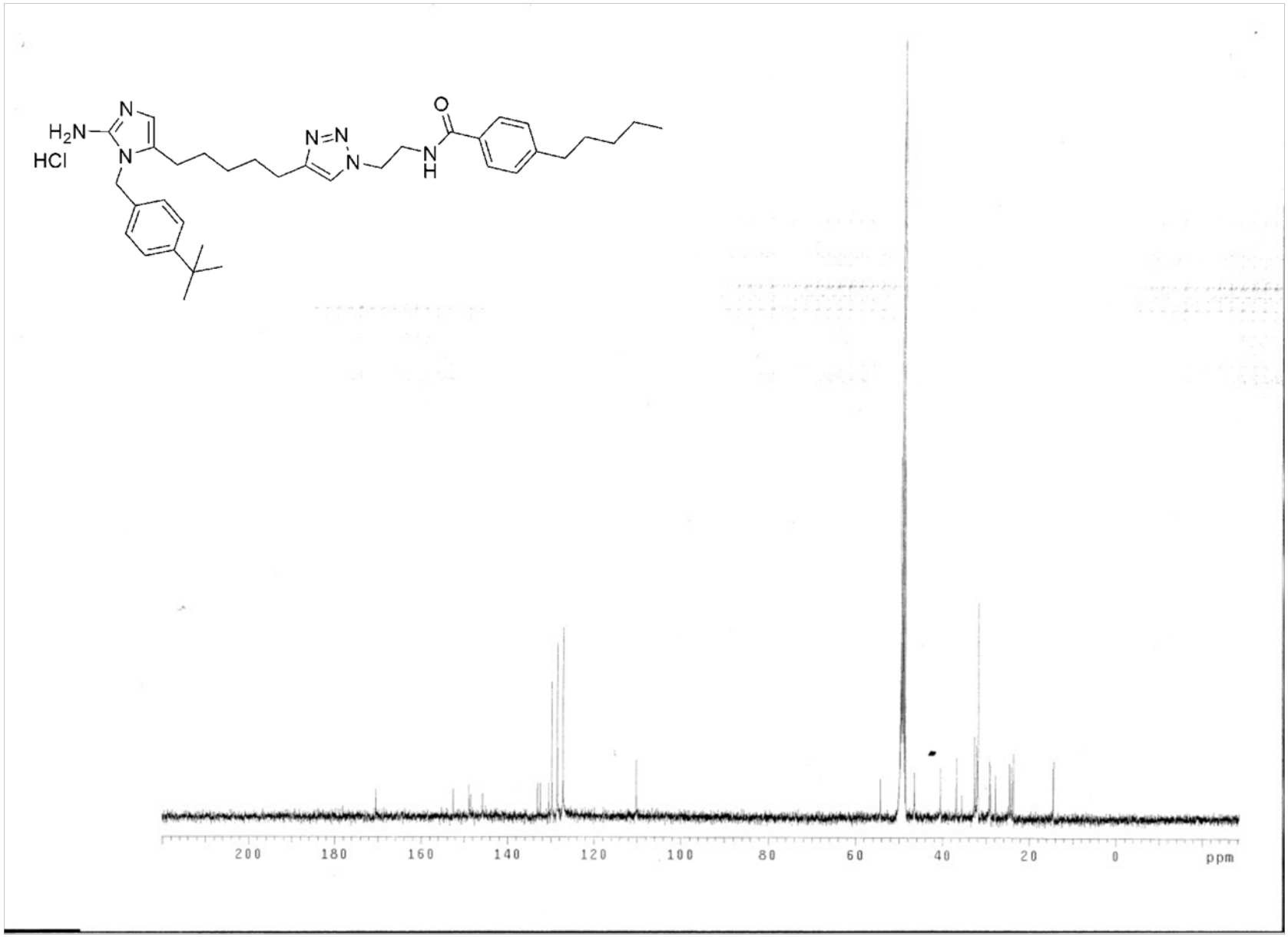
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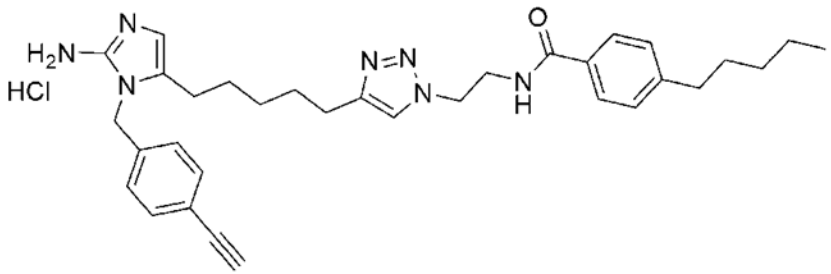
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HCl
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H
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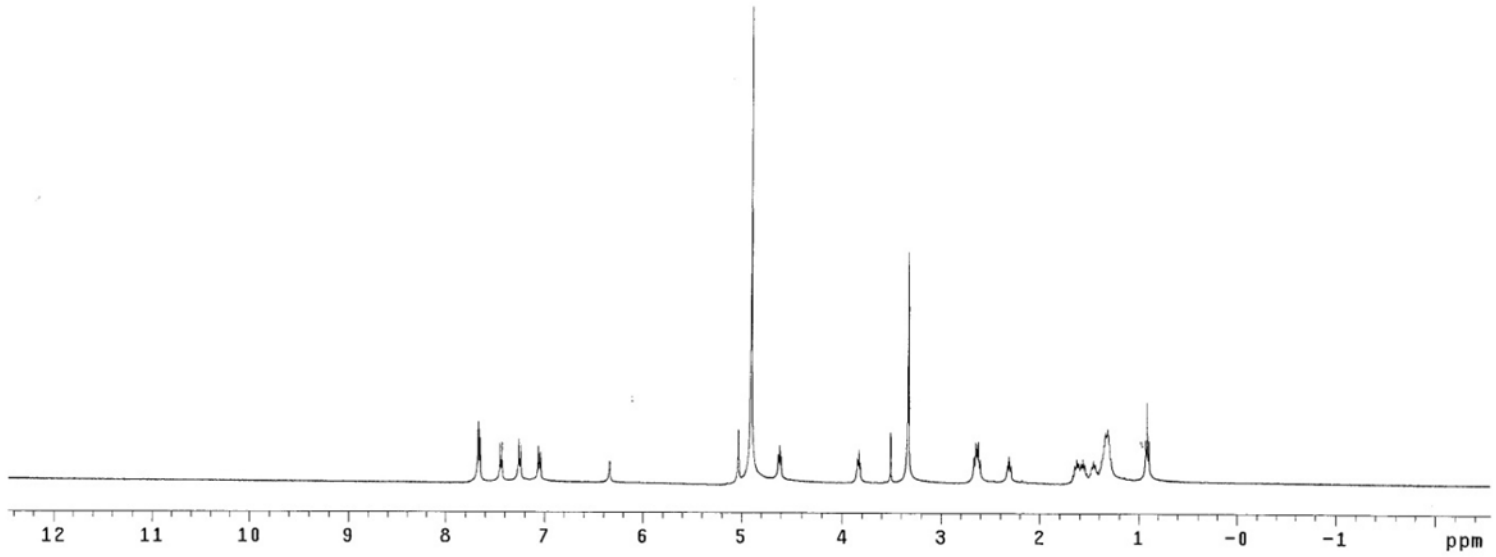
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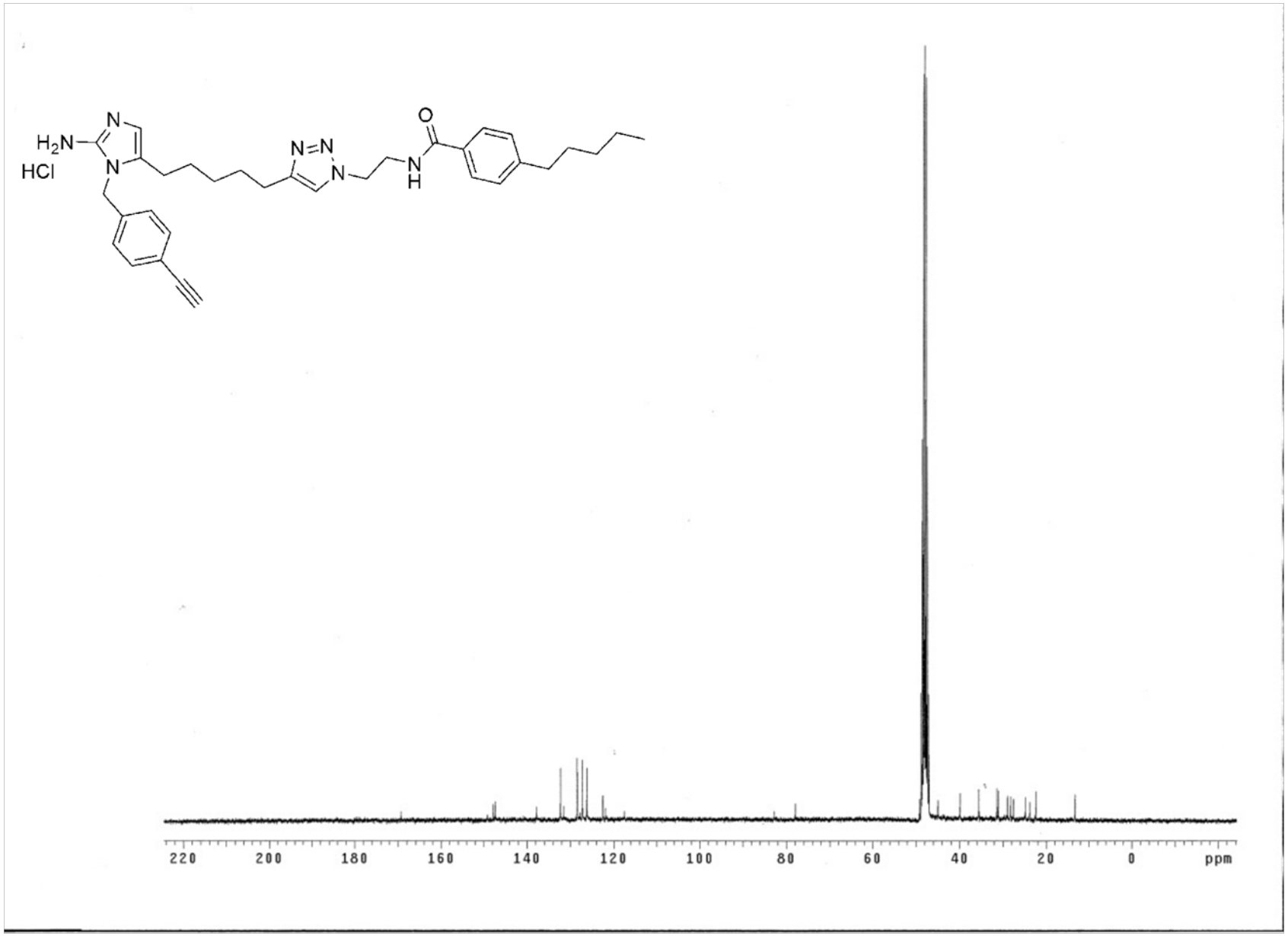
-1
ppm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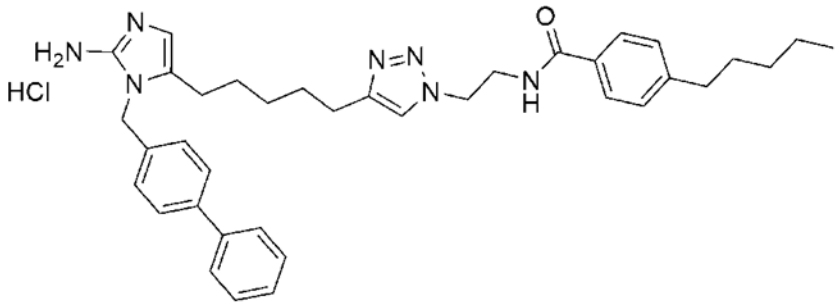
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HCl
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N
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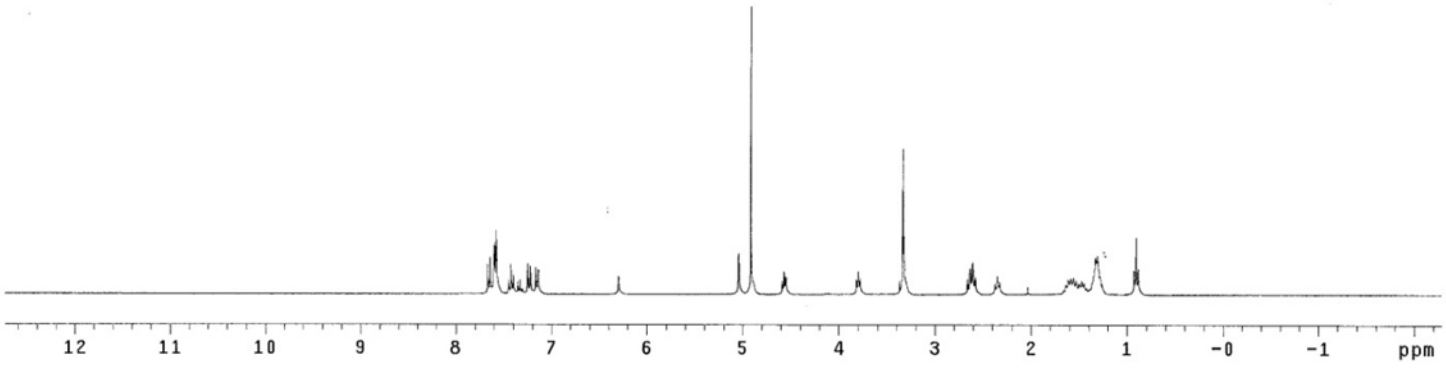
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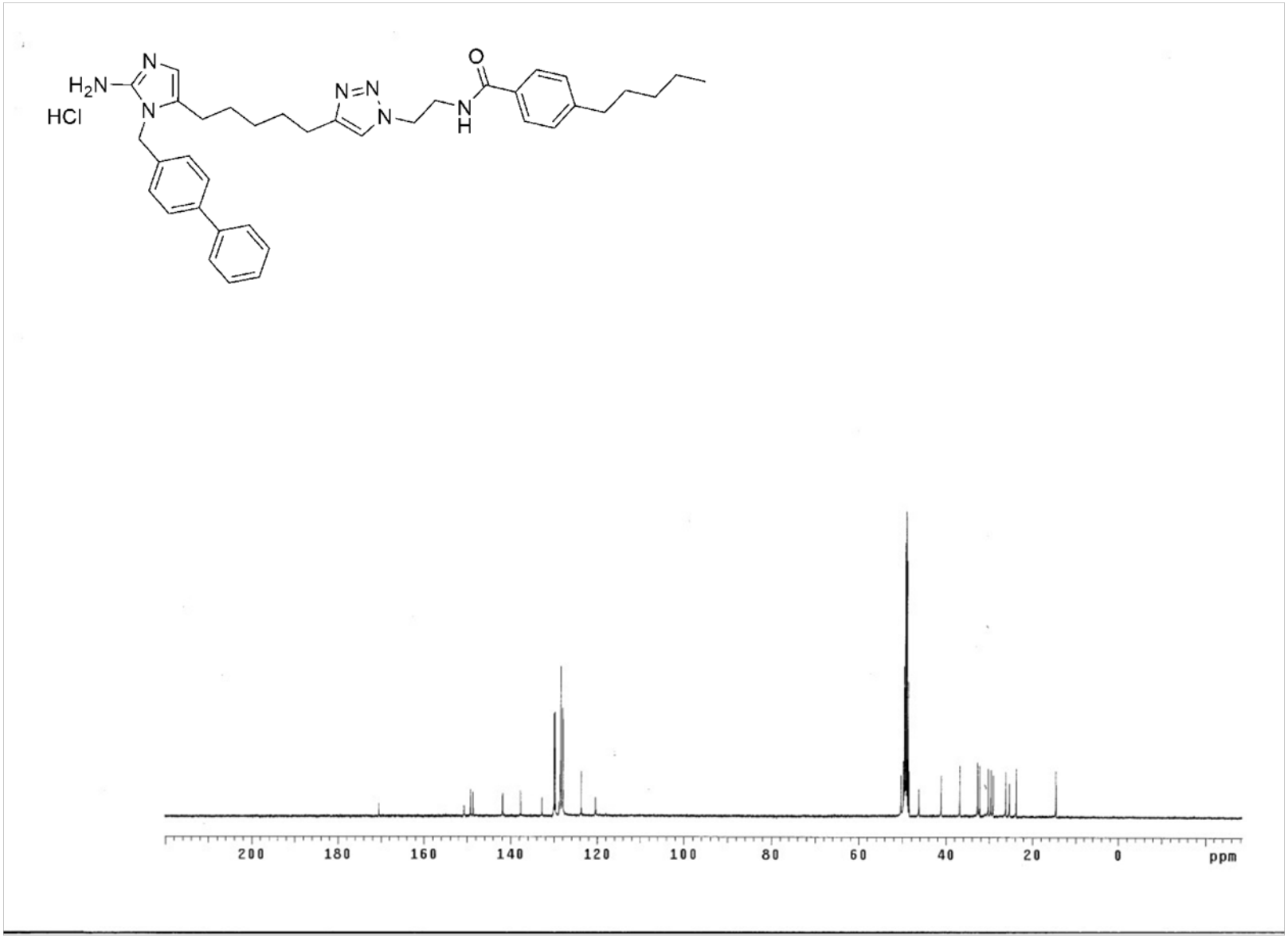
-1
ppm


H2N
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H
O
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100
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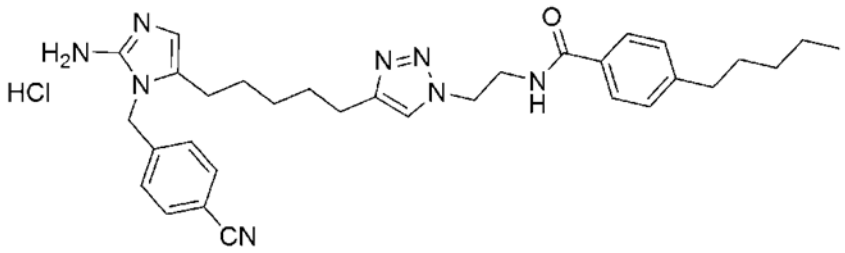
ppm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HCl
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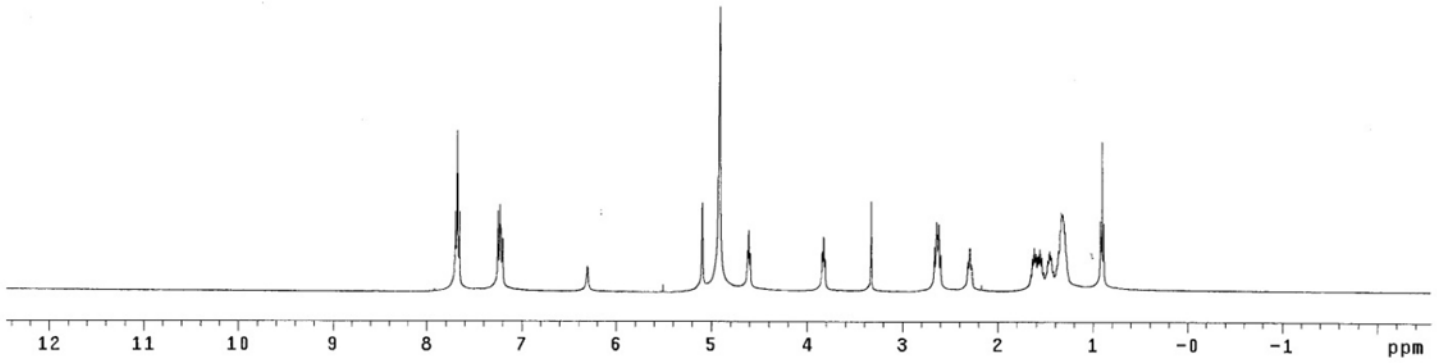
O
CN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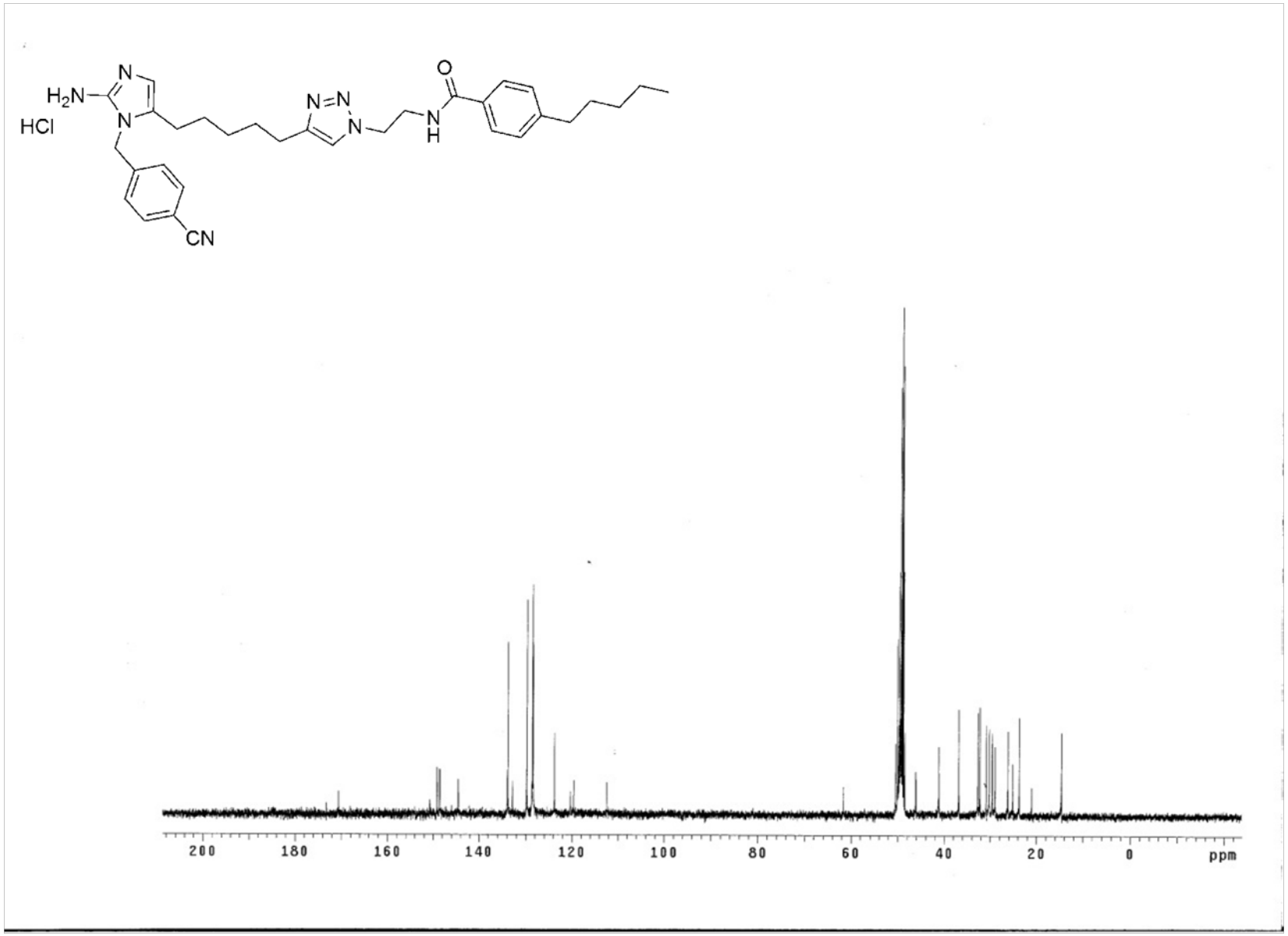
H2N
HCl
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CN
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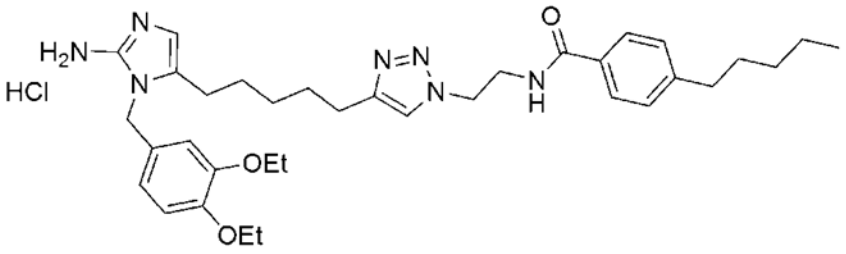
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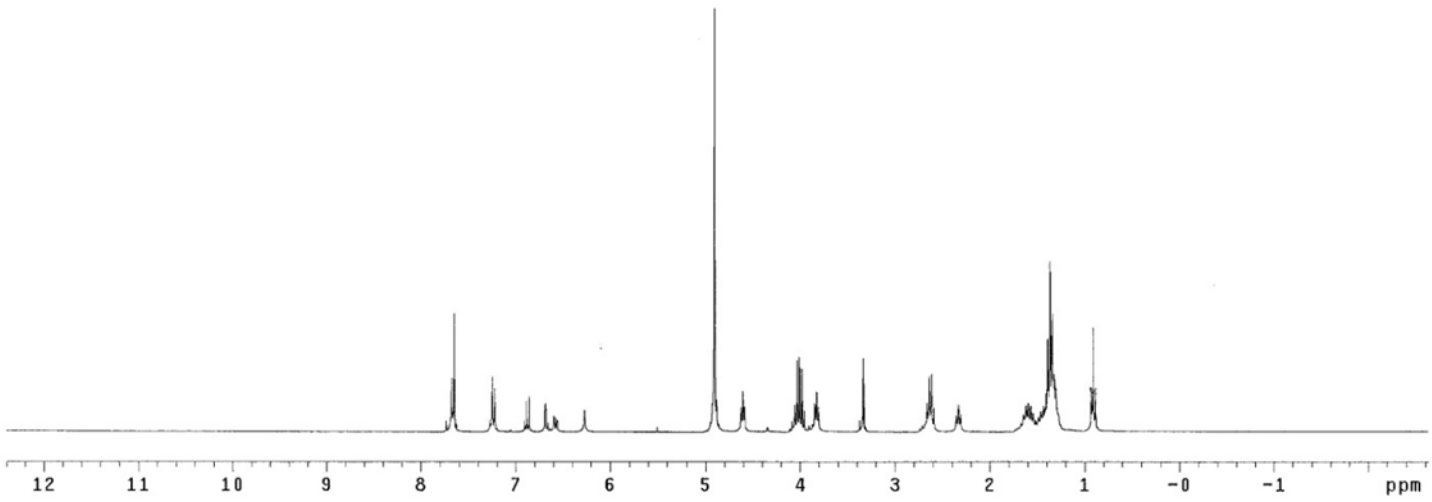
OEt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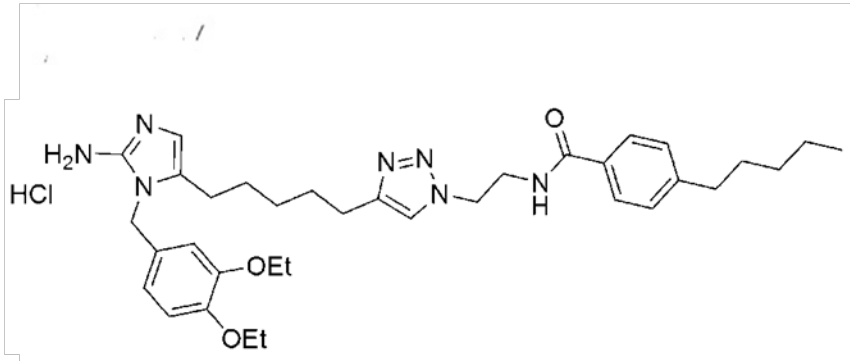
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HCl
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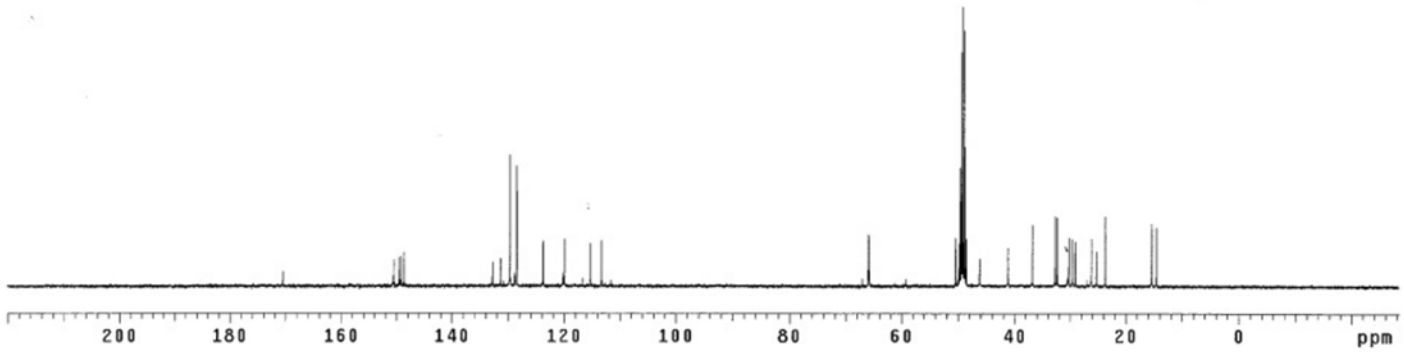
OEt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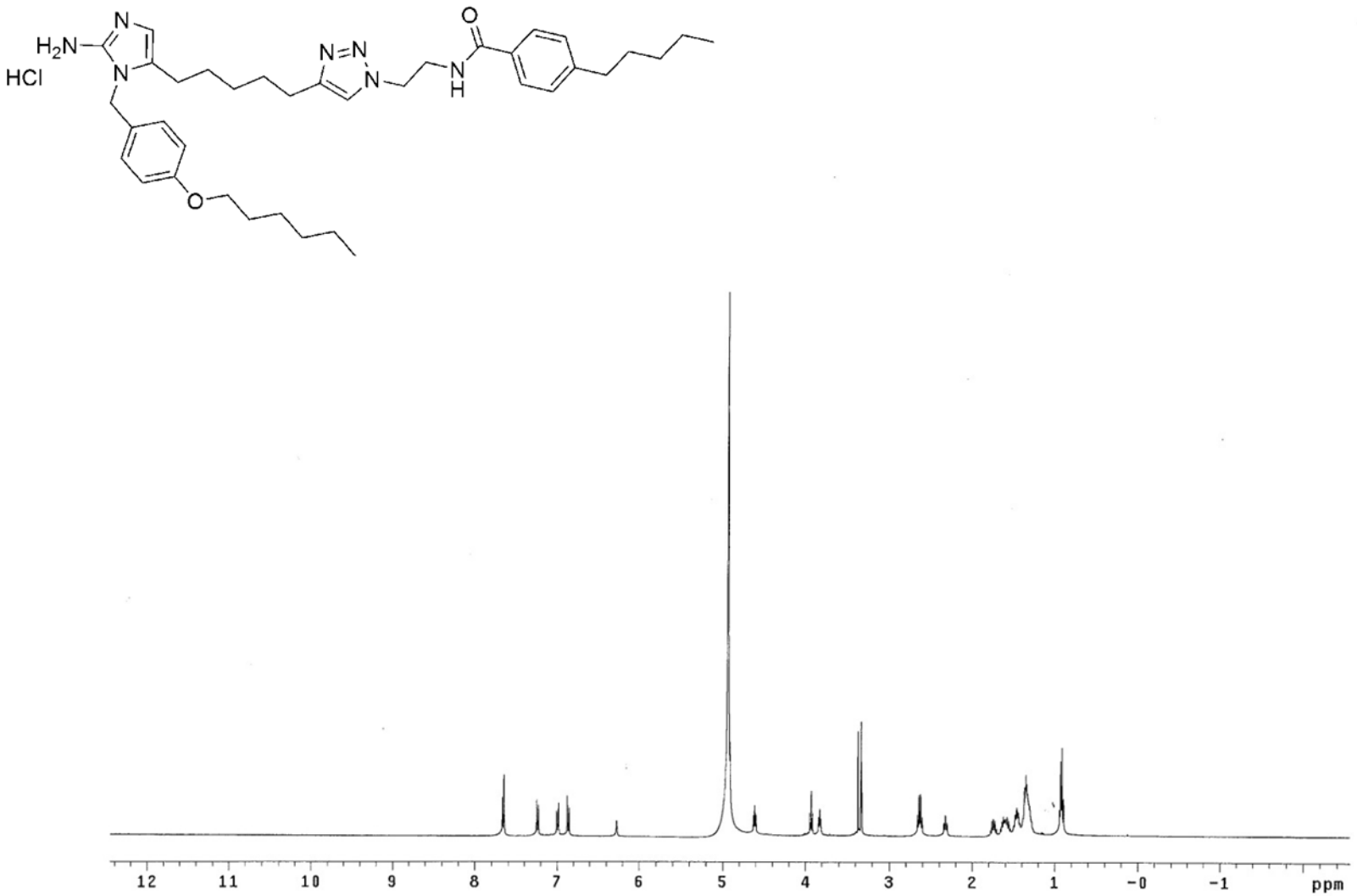
H2N
HCl
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N
N=N
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H
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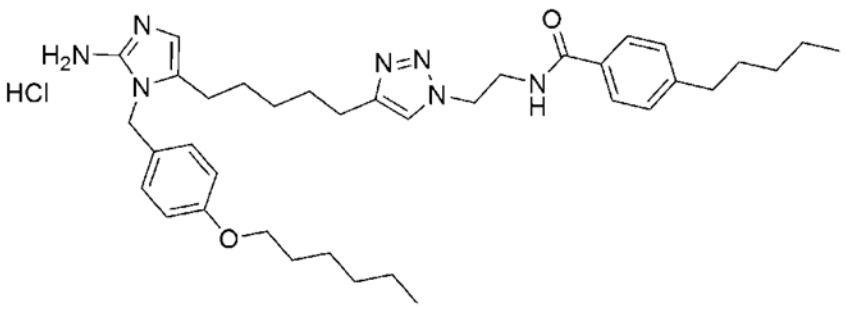
ppm


HCl
H_2N
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N
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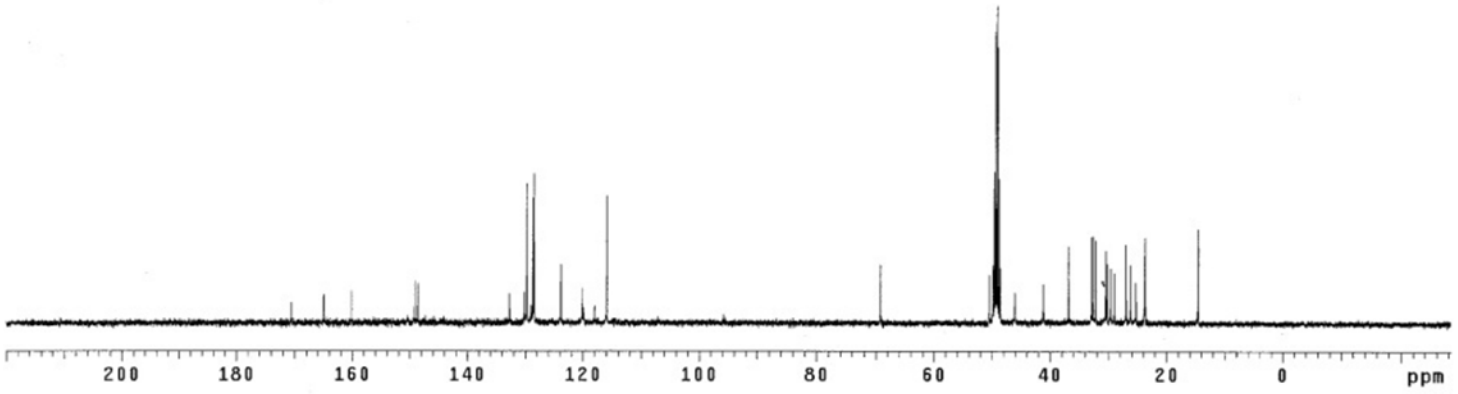
O
O


200
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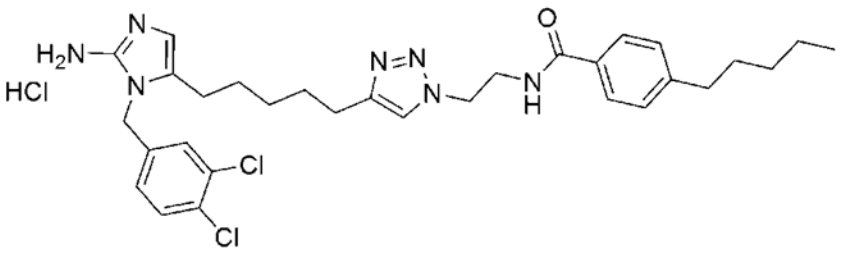
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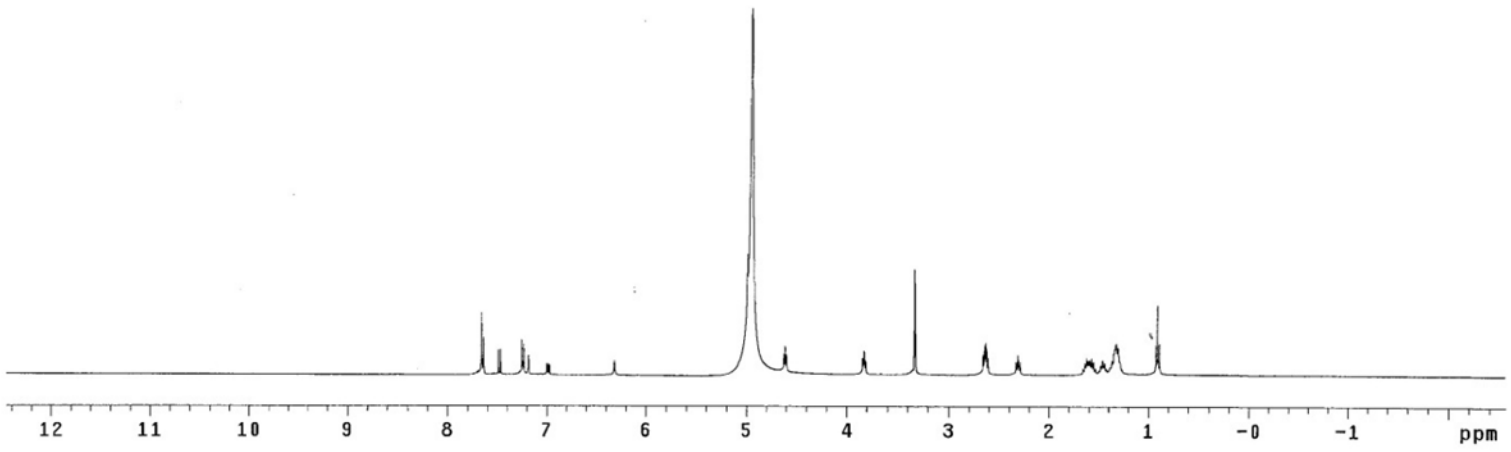
HCl
N
N=N
N
O
N
H
Cl
Cl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9
8
7
6
5
4
3
2
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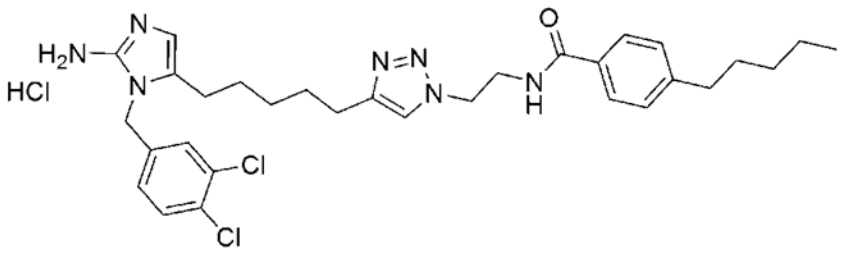
-0
-1
ppm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HCl
N
N
N=N
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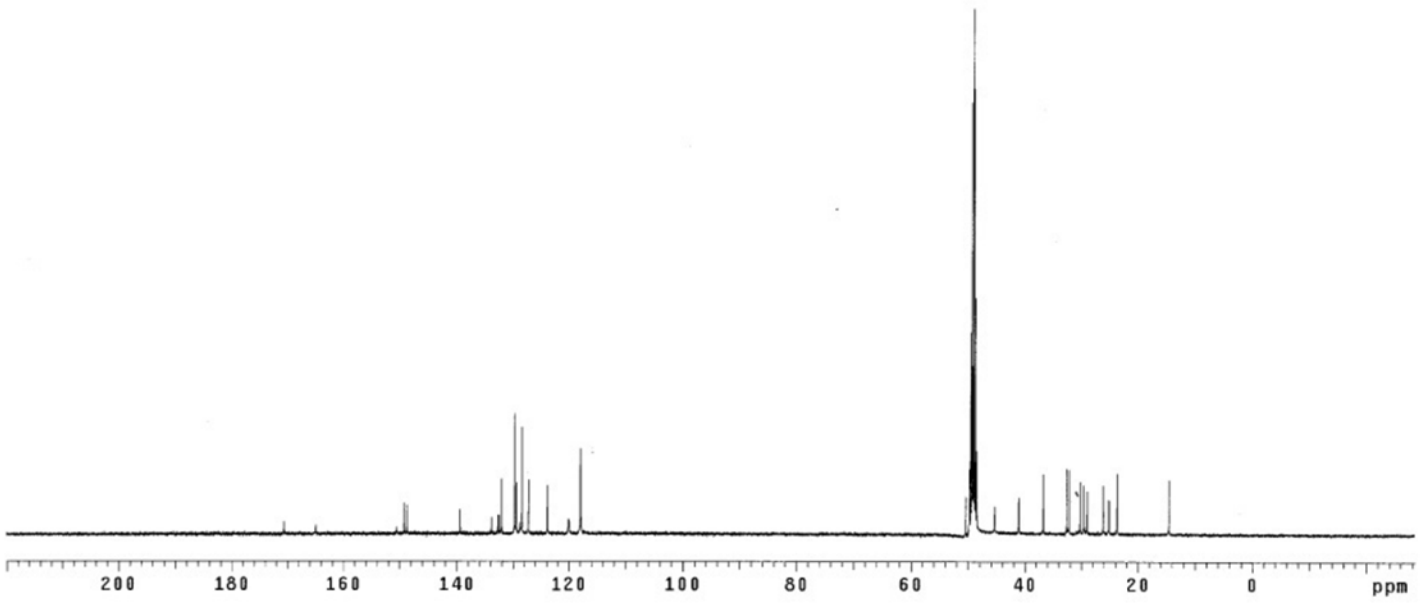
N
H
O
Cl
Cl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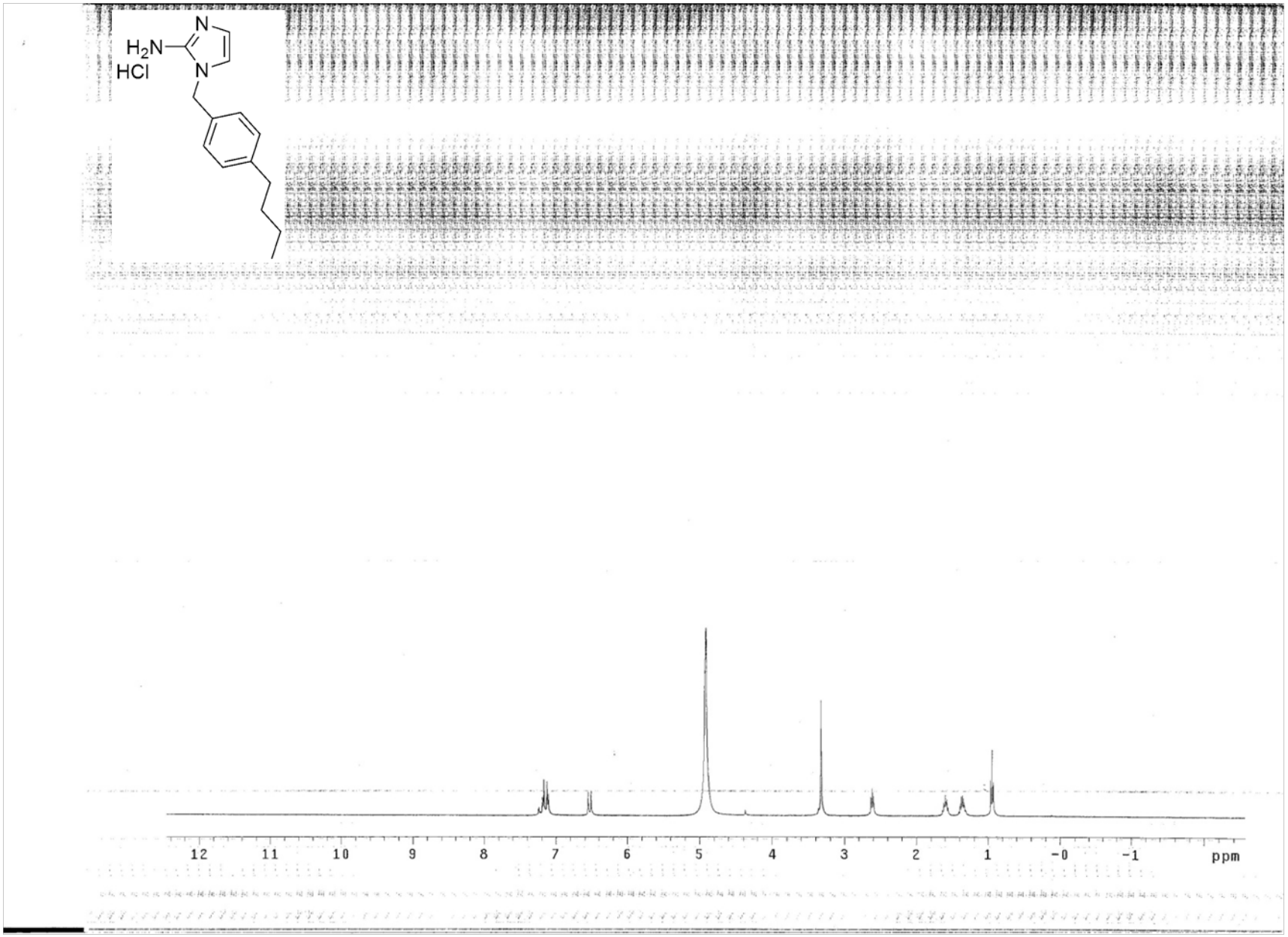
140
120
100
80
60
40
20
0
ppm


H2N
HCl
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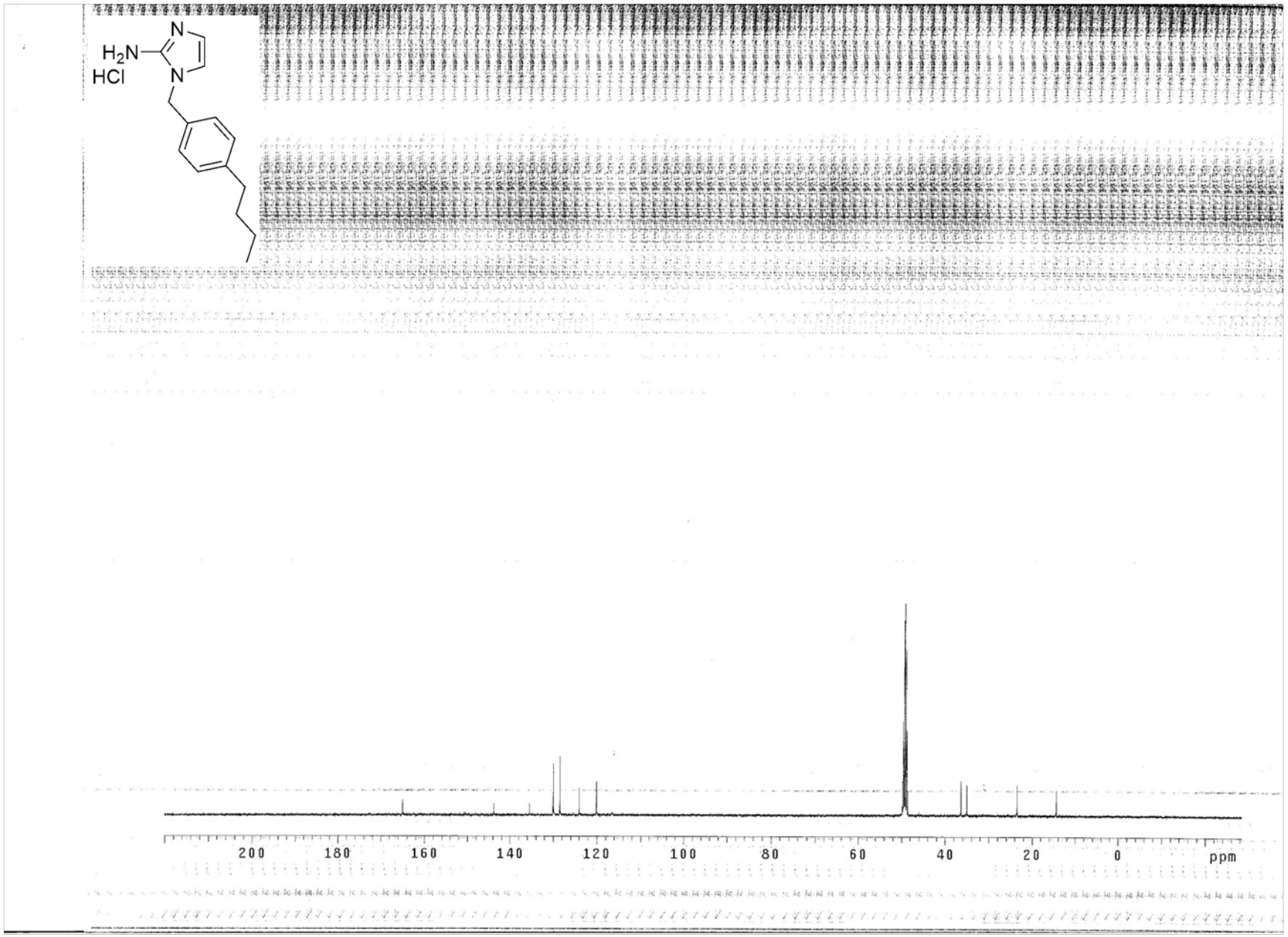
ppm


N
H2N
HCl
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200
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