Supporting Information

Nickel-Catalyzed Directed Sulfenylation of sp^2 and sp^3 C-H Bonds

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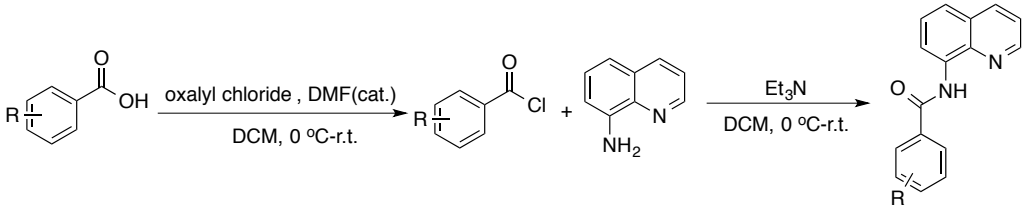
I. General Methods and Materials

All of the reactions dealing with air and/or moisture-sensitive reactions were carried out under an atmosphere of Ar using oven/flame-dried glassware and standard syringe/septa techniques. Unless otherwise noted, all commercial reagents and solvents were obtained from the commercial provider and used without further purification. ^{1}H NMR and ^{13}C NMR spectra were recorded on Agilent 400 MHz spectrometers. Chemical shifts were reported relative to internal tetramethylsilane (δ 0.00 ppm) or $CDCl_3$ (δ 7.26 ppm) for ^{1}H and $CDCl_3$ (δ 77.00 ppm) for ^{13}C. Flash column chromatography was performed on 230-430 mesh silica gel. Analytical thin layer chromatography was performed with precoated glass baked plates (250μ) and visualized by fluorescence and by charring after treatment with potassium permanganate stain. HRMS were recorded on Thermo Q-Exactive MS

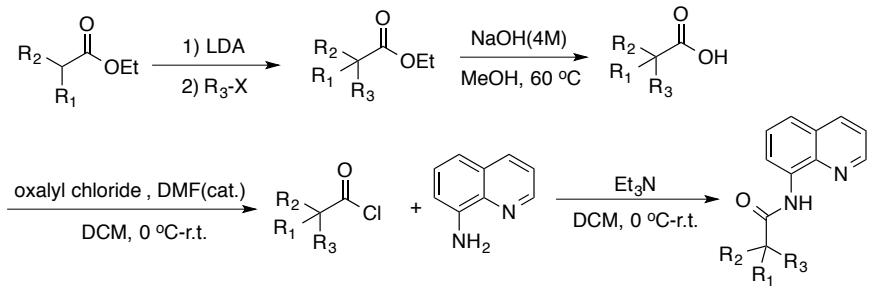
1.1 General Procedure for preparation of sp^2 starting materials



To the solution of carboxylic acid (10 mmol) and 10 drops of DMF in 30mL dry DCM at 0 °C, oxalyl chloride (20 mmol) was added dropwise under Ar. The mixture was then warm to r.t and stired for another 5h. The solvent was removed under vacuum to give crude acid cholid, which was used directly for next step without further purification.

To the mixuture of 8 aminoquinoline (10 mmol) and Et_3N (12 mmol) in dry DCM (30 mL) at 0 °C, the crude acid chloride obtained from previous step in 20 mL dry DCM was added dropwise. The mixture was then warm to r.t and stirred overnight. The reaction was quenched with H_2O. The mixture was extracted, washed with saturated $NaHCO_3$ solution. The combined organic layers were dried ($MgSO_4$), and concentrated in vacuum and then purified by silica gel chromatography with a mixture of hexanes and ethyl acetate as the eluent to afford the corresponding amide products.

1.2 General Procedure for preparation of sp^3 starting materials



The LDA solution was prepared freshly, by adding 2.5 M n-BuLi in hexane (10 mmol) into the THF solution (30 mL) of diisopropylamine (10 mmol) at -78 °C under Ar atmosphere. The ester (10 mmol) was then added at -78 °C. After stirring at same

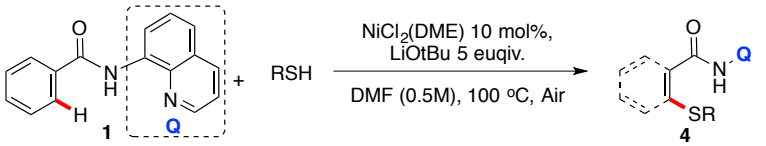
temperature for another 1h, Alkyl halide (15mmol) was then added. The mixture was warmed to r.t. and stirred overnight. The reaction was carefully quenched with the NH_4Cl solution. The aqueous phase was extracted with ether and the combined organic layers were dried ($MgSO_4$), and concentrated in vacuum, affording the crude ester. The crude ester used directly for next step without further purification.

NaOH (4M, 10 mL) was then adding into a solution of crude ester in 20mL MeOH. The mixture was then stirred at 60 ^oC overnight. The reaction was carefully acidified with 2M HCl. The aqueous phase was extracted with ether and the combined organic layers were dried ($MgSO_4$), and concentrated in vacuum, affording the crude acid. The crude acid used directly for next step without further purification.

To the solution of carboxylic acid (10 mmol) and 10 drops of DMF in 30mL dry DCM at 0 ^oC, oxalyl chloride (20 mmol) was added dropwise under Ar. The mixture was then warm to r.t and stired for another 5h. The solvent was removed under vacuum to give crude acid cholid, which was used directly for next step without further purification.

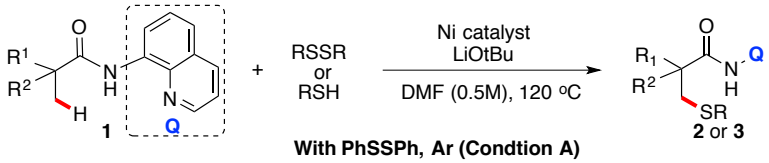
To the mixuture of 8 aminoquinoline (10 mmol) and Et_3N (12 mmol) in dry DCM (30 mL) at 0 ^oC, the crude acid chloride obtained from previous step in 20 mL dry DCM was added dropwise. The mixture was then warm to r.t and stirred overnight. The reaction was quenched with H_2O. The mixture was extracted, washed with saturated $NaHCO_3$ solution. The combined organic layers were dried ($MgSO_4$), and concentrated in vacuum and then purified by silica gel chromatography with a mixture of hexanes and ethyl acetate as the eluent to afford the corresponding amide products.

1.3 General Procedure for sp^2 C-H Sulfenylation.



A 10 mL tube was charged with the amides (0.3 mmol, 1.0 equiv.), LiOtBu (1.5 mmol, 5.0 equiv.) and $NiCl_2$(DME) (0.03 mmol, 10 mol%) in 0.6 mL anhydrous DMF. The benzenethiol (0.66 mmol, 2.2 equiv.) was then added into mixture slowly. After stirring at r.t for 15 min, the mixture was then heated at 100 ^oC. The reaction was monitored by TLC. After the reaction was completed, the solvent was removed under reduced pressure and the residue was purified by flash chromatography on silica gel (ethyl acetate/hexane = 15 : 1, V/V) to give desired sulfenylation product.

1.4 General Procedure for sp^3 C-H Sulfenylation.



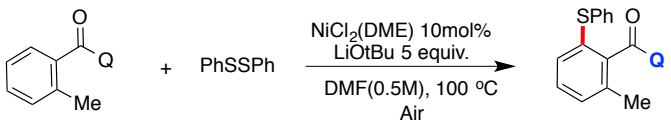
Condition A: A 10 mL sealed tube was charged with the amides (0.3 mmol, 1.0 equiv.), LiOtBu (1.5 mmol, 5.0 equiv.) and $Ni(OTf)_2$ (0.06 mmol, 20 mol%) in 0.6 mL anhydrous DMF. The disulfide (0.75 mmol, 2.5 equiv.) was then added into mixture slowly. The mixture was purged, protected under Ar , and then heated under 120 ^oC.

After the reaction was completed (20h), the solvent was removed under reduced pressure and the residue was purified by flash chromatography on silica gel (ethyl acetate/hexane = 15 : 1, V/V) to give desired sulfenylation product.

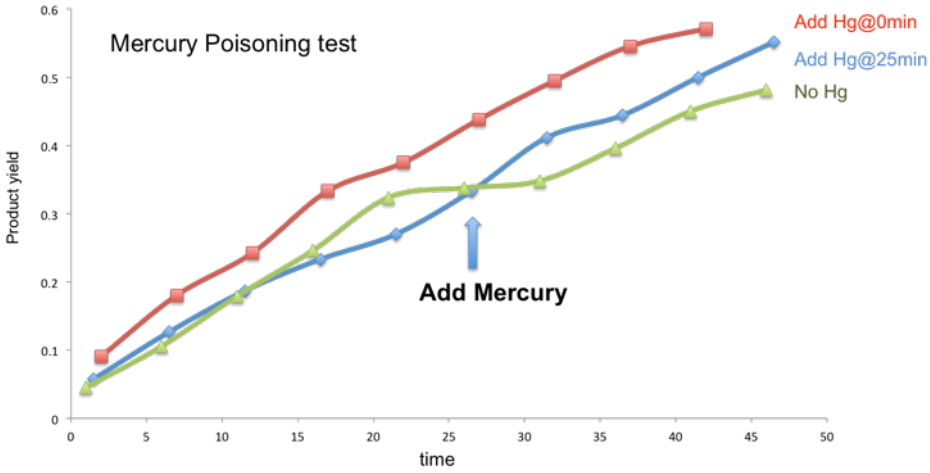
Condition B: A 10 mL sealed tube was charged with the amides (0.3 mmol, 1.0 equiv.), LiOtBu (2.1 mmol, 7.0 equiv.) and $NiCl_2$(DME) (0.06 mmol, 20 mol%) in 0.6 mL anhydrous DMF. The disulfide (1.2 mmol, 4 equiv.) was then added into mixture dropwise. The mixture was first stirred at r.t for 15min, and then heated under 120 ^{o}C. The reaction was monitored by TLC. After the completion of the reaction (5-6 h), the solvent was removed under reduced pressure and the residue was purified by flash chromatography on silica gel (ethyl acetate/hexane = 15 : 1, V/V) to give desired sulfenylation product.

II. Mercury poisoning experiment.

Excess Hg (100 equiv) was added to Nickel catalyzed sp^2 sulfenylation.



100 equiv. Hg(at t=0 or 25min)

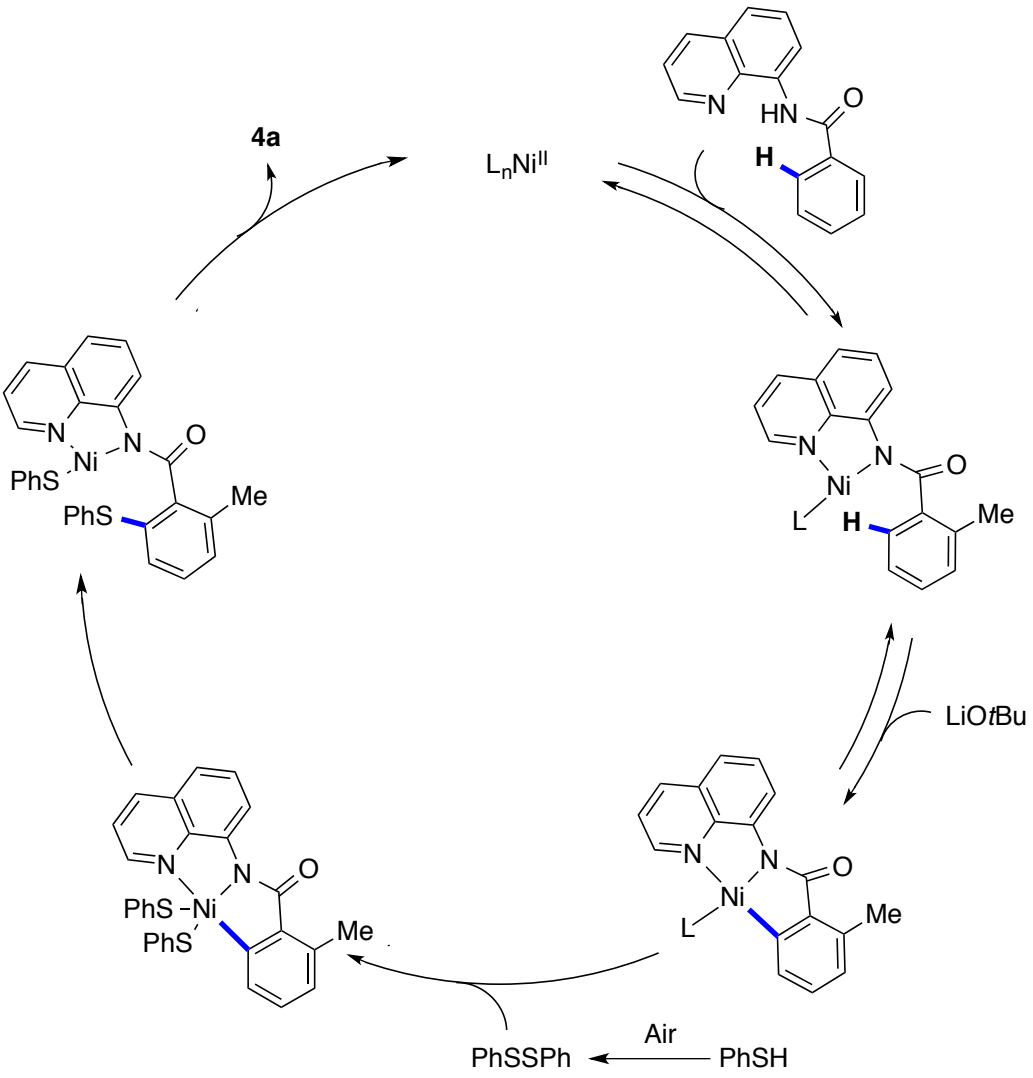


III. Competition experiment.

To a mixture of benzamide **1c** (0.20 mmol), **1f** (0.20 mmol), phenyldisulfide (0.10 mmol), $NiCl_2$(DME) (10.0 mol %) and LiOt-Bu (1.00 mmol) was added DMF (0.4 mL). The reaction mixture was stirred at 100 °C for 4 h. After cooling to room temperature, the reaction mixture was passed through a slica pad and washed by EtOAc. 1, 3, 5 trimethoxybenzene was then added as internal stardard. The mixture was concentrated under vacuum and analyzed by ^{1}HNMR

V. Proposed Reaction Mechanism

Here is one plausible reaction mechanism. Detailed mechanistic investigations are currently undergoing in our lab.



VI. ORTEP Drawing of the Crystal Structures

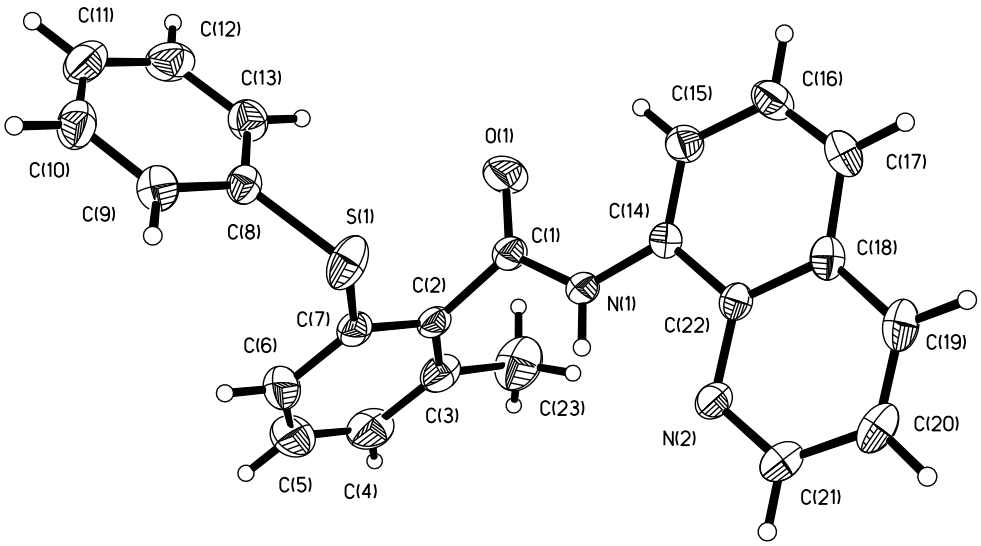


Figure 1. Perspective view of the molecular structure of $C_{23}H_{18}N_2OS$ with the atom labeling scheme. The thermal ellipsoids are scaled to enclose 30% probability. CCDC 1052404

Description of the X-ray Structural Analysis of $C_{23}H_{18}N_2OS$

A colorless crystal cleaved from a larger crystal of $C_{23}H_{18}N_2OS$ was washed with the perfluoropolyether PFO-XR75 (Lancaster) and wedged in a glass capillary. The sample was optically aligned on a Bruker AXS D8 Venture fixed-chi X-ray diffractometer equipped with a Triumph monochromator, a Mo Kα radiation source (λ = 0.71073 Å), and a PHOTON 100 CMOS detector. Two sets of 12 frames each were collected using the omega scan method with a 10 s exposure time. Integration of these frames followed by reflection indexing and least-squares refinement produced a crystal orientation matrix for the monoclinic crystal lattice.

Data collection consisted of the measurement of a total of 812 frames in two runs using omega scans with the detector held at 6.00 cm from the crystal. Frame scan parameters are summarized in Table 1 below:

Table 1. Data collection details for $C_{23}H_{18}N_2OS$.

Run	2θ	ω	φ	χ	Scan Width (º)	Frames	Exposure Time (sec)
1	17.51	-173.99	-77.17	54.79	0.50	406	10.00
2	17.51	-173.99	47.94	54.79	0.50	406	10.00

The APEX2 software program (version 2014.1-1)[1] was used for diffractometer control, preliminary frame scans, indexing, orientation matrix calculations, least-squares refinement of cell parameters, and the data collection. The frames were integrated with the Bruker SAINT software package using a narrow-frame algorithm. The integration of the data using a monoclinic unit cell yielded a total of 15986 reflections to a maximum θ angle of 27.50° (0.77 Å resolution), of which 4423 were independent (average redundancy 3.614, completeness = 99.3%, R_{int} = 2.40%, R_{sig} = 2.37%) and 3405 (76.98%) were greater than $2\sigma(F^2)$. The final cell constants of a = 16.2600(6) Å, b = 8.0578(3) Å, c = 16.7298(7) Å, β = 118.2165(10)°, volume = 1931.46(13) $Å^3$, are based upon the refinement of the XYZ-centroids of 9986 reflections above 20 σ(I) with 6.981° < 2θ < 58.02°. Data were corrected for absorption effects using the multi-scan method (SADABS). The ratio of minimum to maximum apparent transmission was 0.839. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.895 and 0.947.

The structure was solved by the direct methods and difference Fourier analysis using the programs provided by SHELXL-2013.[2] Idealized positions for the hydrogen atoms were included as fixed contributions using a riding model with isotropic temperature factors set at 1.2 times (aromatic hydrogens) or 1.5 (methyl hydrogens) times that of the adjacent carbon atom. The fractional coordinates and isotropic temperature factor for the H atom bound to N(1) was refined. The positions of the methyl hydrogen atoms were optimized by a rigid rotating group refinement with idealized angles. Full-

matrix least-squares refinement, based upon the minimization of $\Sigma w_i |F_o^2 - F_c^2|^2$, with weighting $w_i^{-1} = [\sigma^2(F_o^2) + (0.0393\ P)^2 + 0.09520\ P]$, where $P = (\text{Max}\ (F_o^2, 0) + 2\ F_c^2)/3$.[2] The final anisotropic full-matrix least-squares refinement on F^2 with 249 variables converged at R1 = 5.53%, for the observed data and wR2 = 12.65% for all data. The goodness-of-fit was 1.094.[3]

A correction for secondary extinction was not applied. The largest peak in the final difference electron density synthesis was 0.291 $e^-/Å^3$ and the largest hole was -0.373 $e^-/Å^3$ with an RMS deviation of 0.039 $e^-/Å^3$. The linear absorption coefficient, atomic scattering factors, and anomalous dispersion corrections were calculated from values found in the International Tables of X-ray Crystallography.[4]

References

1. APEX2 is a Bruker AXS crystallographic software package for single crystal data collection, reduction and preparation.
2. Sheldrick, G. M., SHELXL-2013, Crystallographic software package, Bruker AXS, Inc., Madison, Wisconsin, USA.
3. $R_1 = \sum(||F_o| - |F_c||) / \sum|F_o|$, $wR_2 = [\sum[w(F_o^2 - F_c^2)^2] / \sum[w(F_o^2)^2]]^{1/2}$, $R_{int.} = \sum|F_o^2 - F_o^2(\text{mean})|^2 / \sum[F_o^2]$, and $GOF = [\sum[w(F_o^2 - F_c^2)^2] / (n-p)]^{1/2}$, where n is the number of reflections and p is the total number of parameters which were varied during the last refinement cycle.
4. International Tables for X-ray Crystallography (1974). Vol. IV, p. 55. Birmingham: Kynoch Press. (Present distributor, D. Reidel, Dordrecht.).

Table 2. Crystal data for $C_{23}H_{18}N_2OS$.

Identification code	xs24cms	
Chemical formula	$C_{23}H_{18}N_2OS$	
Formula weight	370.45	
Temperature	296(2) K	
Wavelength	0.71073 Å	
Crystal size	0.304 x 0.435 x 0.623 mm	
Crystal system	monoclinic	
Space group	$P2_1/c$ (No. 14)	
Unit cell dimensions	a = 16.2600(6) Å	α = 90°
	b = 8.0578(3) Å	β = 118.2165(10)°
	c = 16.7298(7) Å	γ = 90°
Volume	1931.46(13) $Å^3$	
Z	4	
Density (calculated)	1.274 g/cm^3	
Absorption coefficient	0.182 mm^{-1}	
F(000)	776	

Table 3. Data collection and structure refinement for $C_{23}H_{18}N_2OS$.

Theta range for data analysis	2.88 to 27.50°	
Index ranges	$-20 \le h \le 21$, $-9 \le k \le 10$, $-21 \le l \le 21$	
Reflections collected	15986	
Independent reflections	4423 [R(int) = 0.0240]	
Coverage of independent reflections	99.3%	
Absorption correction	multi-scan	
Max. and min. transmission	0.947 and 0.895	
Refinement method	Full-matrix least-squares on F^2	
Refinement program	SHELXL-2013 (Sheldrick, 2013)	
Data / restraints / parameters	4423 / 0 / 249	
Goodness-of-fit on F^2	1.094	
Final R indices	3405 data; I>2σ(I)	R1 = 0.0553, wR2 = 0.1182
	all data	R1 = 0.0692, wR2 = 0.1265
Largest diff. peak and hole	0.291 and -0.373 $e^-/Å^3$	

Table 4. Atomic coordinates and equivalent isotropic atomic displacement parameters ($Å^2$) for $C_{23}H_{18}N_2OS$. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x/a	y/b	z/c	U(eq)
S1	0.26690(4)	0.41082(7)	0.03971(4)	0.0647(2)
O1	0.22416(12)	0.45723(19)	0.81527(13)	0.0750(5)
N1	0.27461(11)	0.1957(2)	0.86306(11)	0.0441(4)
N2	0.35986(11)	0.90485(19)	0.90311(11)	0.0454(4)
C1	0.21675(13)	0.3260(2)	0.84671(13)	0.0448(4)
C2	0.14006(12)	0.2976(2)	0.87108(13)	0.0426(4)
C3	0.05402(15)	0.2334(3)	0.80678(16)	0.0594(6)
C4	0.98443(16)	0.2174(3)	0.8317(2)	0.0787(8)
C5	0.99832(19)	0.2655(4)	0.9158(2)	0.0825(8)
C6	0.08256(17)	0.3275(3)	0.97851(18)	0.0676(6)
C7	0.15420(13)	0.3429(2)	0.95666(14)	0.0460(4)
C8	0.24392(12)	0.6148(2)	0.06322(12)	0.0429(4)
C9	0.26360(14)	0.6540(3)	0.15083(13)	0.0538(5)
C10	0.25035(16)	0.8128(3)	0.17219(16)	0.0637(6)
C11	0.21705(16)	0.9316(3)	0.1071(2)	0.0692(7)
C12	0.19655(18)	0.8942(3)	0.01921(19)	0.0696(6)
C13	0.21082(15)	0.7354(3)	0.99702(14)	0.0555(5)
C14	0.35532(12)	0.1834(2)	0.85317(11)	0.0392(4)
C15	0.39246(14)	0.3086(3)	0.82507(13)	0.0494(5)
C16	0.47608(15)	0.2825(3)	0.82110(15)	0.0573(5)
C17	0.52067(14)	0.1347(3)	0.84376(14)	0.0561(5)
C18	0.48374(13)	0.0022(2)	0.87168(12)	0.0448(4)
C19	0.52566(15)	0.8443(3)	0.89651(14)	0.0565(5)
C20	0.48539(16)	0.7253(3)	0.92308(15)	0.0595(6)
C21	0.40237(15)	0.7601(2)	0.92532(14)	0.0544(5)
C22	0.40020(12)	0.0256(2)	0.87656(11)	0.0381(4)
C23	0.0377(2)	0.1876(4)	0.71306(19)	0.0952(10)

Table 5. Interatomic distances (Å) for $C_{23}H_{18}N_2OS$.

S1-C8	1.7705(19)	S1-C7	1.783(2)
O1-C1	1.212(2)	N1-C1	1.349(2)
N1-C14	1.402(2)	N2-C21	1.316(2)
N2-C22	1.360(2)	C1-C2	1.501(3)
C2-C7	1.387(3)	C2-C3	1.400(3)
C3-C4	1.384(3)	C3-C23	1.507(4)
C4-C5	1.372(4)	C5-C6	1.366(4)
C6-C7	1.382(3)	C8-C13	1.377(3)
C8-C9	1.381(3)	C9-C10	1.373(3)
C10-C11	1.356(4)	C11-C12	1.378(4)
C12-C13	1.382(3)	C14-C15	1.368(3)
C14-C22	1.426(2)	C15-C16	1.408(3)
C16-C17	1.352(3)	C17-C18	1.409(3)
C18-C19	1.410(3)	C18-C22	1.412(3)
C19-C20	1.350(3)	C20-C21	1.397(3)

Table 6. Bond angles (°) for $C_{23}H_{18}N_2OS$.

C8-S1-C7	102.18(8)	C1-N1-C14	129.27(17)
C21-N2-C22	117.14(17)	O1-C1-N1	124.35(18)
O1-C1-C2	121.11(17)	N1-C1-C2	114.54(16)
C7-C2-C3	120.53(18)	C7-C2-C1	119.11(17)
C3-C2-C1	120.29(18)	C4-C3-C2	117.7(2)
C4-C3-C23	121.6(2)	C2-C3-C23	120.7(2)
C5-C4-C3	121.4(2)	C6-C5-C4	120.7(2)
C5-C6-C7	119.6(2)	C6-C7-C2	120.0(2)
C6-C7-S1	120.38(18)	C2-C7-S1	119.51(14)
C13-C8-C9	119.91(19)	C13-C8-S1	121.30(15)
C9-C8-S1	118.73(16)	C10-C9-C8	120.2(2)
C11-C10-C9	120.1(2)	C10-C11-C12	120.4(2)
C11-C12-C13	120.1(2)	C8-C13-C12	119.2(2)
C15-C14-N1	125.37(17)	C15-C14-C22	120.00(16)
N1-C14-C22	114.62(16)	C14-C15-C16	119.94(19)
C17-C16-C15	121.4(2)	C16-C17-C18	120.29(18)
C17-C18-C19	124.00(19)	C17-C18-C22	119.38(18)
C19-C18-C22	116.62(19)	C20-C19-C18	119.73(19)
C19-C20-C21	119.45(19)	N2-C21-C20	123.8(2)
N2-C22-C18	123.29(17)	N2-C22-C14	117.68(15)
C18-C22-C14	119.02(17)		

Table 7. Anisotropic atomic displacement parameters ($Å^2$) for $C_{23}H_{18}N_2OS$. The anisotropic atomic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2} U_{11}$

$+ ... + 2\ h\ k\ a^{*}\ b^{*}\ U_{12}]$.

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
S1	0.0490(3)	0.0584(4)	0.0677(4)	-0.0115(3)	0.0119(3)	0.0207(3)
O1	0.0789(11)	0.0509(9)	0.1191(14)	0.0367(9)	0.0665(11)	0.0218(8)
N1	0.0474(9)	0.0319(8)	0.0613(10)	0.0036(7)	0.0327(8)	0.0035(7)
N2	0.0497(9)	0.0348(8)	0.0516(9)	-0.0023(7)	0.0238(7)	0.0011(7)
C1	0.0451(10)	0.0365(10)	0.0546(11)	0.0036(8)	0.0250(9)	0.0046(8)
C2	0.0408(9)	0.0281(8)	0.0602(11)	0.0013(8)	0.0250(8)	0.0041(7)
C3	0.0486(11)	0.0459(12)	0.0754(14)	-0.0082(10)	0.0225(10)	-0.0017(9)
C4	0.0441(12)	0.0650(16)	0.121(2)	-0.0143(15)	0.0340(14)	-0.0135(11)
C5	0.0627(16)	0.0771(18)	0.130(3)	-0.0016(17)	0.0644(18)	-0.0063(13)
C6	0.0709(15)	0.0639(15)	0.0883(17)	0.0019(13)	0.0543(14)	0.0094(12)
C7	0.0434(10)	0.0346(9)	0.0629(12)	0.0012(8)	0.0275(9)	0.0058(8)
C8	0.0347(9)	0.0452(10)	0.0464(10)	-0.0033(8)	0.0173(8)	0.0042(8)
C9	0.0494(11)	0.0623(13)	0.0457(10)	-0.0009(9)	0.0191(9)	0.0023(10)
C10	0.0556(12)	0.0728(16)	0.0626(13)	-0.0239(12)	0.0279(11)	-0.0070(12)
C11	0.0594(13)	0.0500(13)	0.1005(19)	-0.0219(13)	0.0395(14)	-0.0059(11)
C12	0.0730(15)	0.0481(13)	0.0901(18)	0.0165(12)	0.0406(14)	0.0053(11)
C13	0.0597(12)	0.0586(13)	0.0504(11)	0.0056(9)	0.0279(10)	0.0045(10)
C14	0.0402(9)	0.0394(9)	0.0396(9)	-0.0014(7)	0.0202(7)	0.0020(8)
C15	0.0532(11)	0.0461(11)	0.0532(11)	0.0088(9)	0.0285(9)	0.0053(9)
C16	0.0562(12)	0.0640(14)	0.0625(13)	0.0096(10)	0.0370(11)	-0.0020(11)
C17	0.0453(11)	0.0722(15)	0.0594(12)	0.0005(11)	0.0319(10)	0.0035(10)
C18	0.0415(10)	0.0516(11)	0.0394(9)	-0.0050(8)	0.0175(8)	0.0056(8)
C19	0.0480(11)	0.0609(13)	0.0570(12)	-0.0057(10)	0.0219(10)	0.0155(10)
C20	0.0615(13)	0.0436(11)	0.0619(13)	-0.0024(10)	0.0198(11)	0.0164(10)
C21	0.0615(13)	0.0364(10)	0.0611(12)	-0.0011(9)	0.0254(10)	0.0021(9)
C22	0.0392(9)	0.0389(9)	0.0338(8)	-0.0048(7)	0.0153(7)	0.0010(7)
C23	0.0804(18)	0.101(2)	0.0782(18)	-0.0321(17)	0.0160(15)	-0.0080(17)

Table 8. Hydrogen atom coordinates and isotropic atomic displacement parameters ($Å^2$) for $C_{23}H_{18}N_2OS$.

	x/a	y/b	z/c	U(eq)
H1N	0.2634(15)	0.107(3)	0.8832(14)	0.053(6)
H4	-0.0730	0.1731	0.7905	0.094
H5	-0.0501	0.2559	0.9303	0.099
H6	0.0916	0.3591	1.0356	0.081
H9	0.2859	0.5725	1.1955	0.065
H10	0.2642	0.8390	1.2314	0.076
H11	0.2080	1.0390	1.1218	0.083
H12	0.1731	0.9760	0.9747	0.083
H13	0.1982	0.7102	0.9381	0.067
H15	0.3625	0.4108	0.8086	0.059
H16	0.5011	0.3687	0.8025	0.069
H17	0.5760	0.1205	0.8409	0.067
H19	0.5808	-0.1777	0.8946	0.068
H20	0.5127	-0.3791	0.9398	0.071
H21	0.3756	-0.3237	0.9436	0.065
H23A	-0.0218	0.1338	0.6806	0.143
H23B	0.0861	0.1136	0.7177	0.143
H23C	0.0385	0.2861	0.6812	0.143

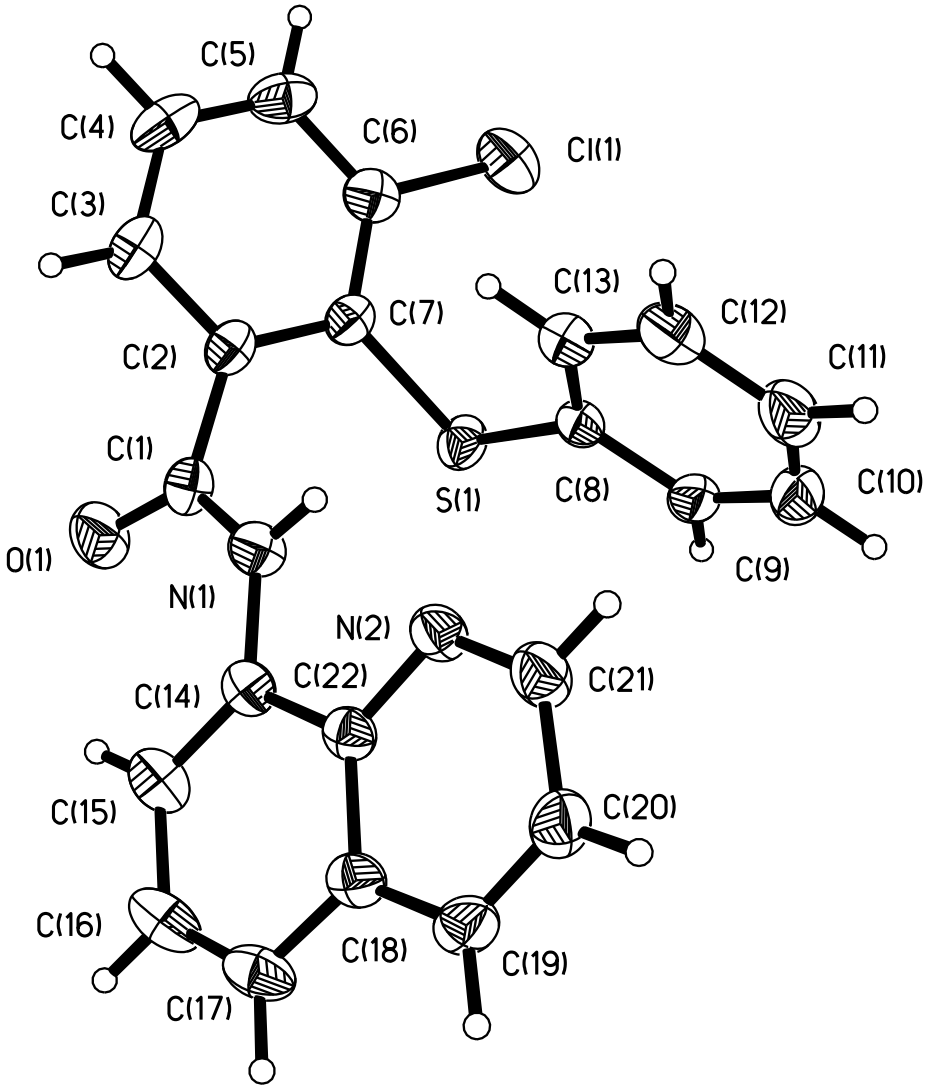


Figure 1. Perspective view of the molecular structure of $C_{22}H_{15}N_2ClSO$ with the atom labeling scheme for the non-hydrogen atoms. The thermal ellipsoids are scaled to enclose 30% probability. CCDC 1052405

Description of the X-ray Structural Analysis of $C_{22}H_{15}N_2ClSO$

A light yellow crystalline fragment of $C_{22}H_{15}N_2ClSO$ was washed with the perfluoropolyether PFO-XR75 (Lancaster) and wedged in a glass capillary. The sample was optically aligned on a Bruker AXS D8 Venture fixed-chi X-ray diffractometer equipped with a Triumph monochromator, a Mo Kα radiation source (λ = 0.71073 Å), and a PHOTON 100 CMOS detector. Two sets of 12 frames each were collected using the omega scan method with a 10 s exposure time. Integration of these frames followed by reflection indexing and least-squares refinement produced a crystal orientation matrix for the monoclinic setting of the crystal lattice that was used for the structural analysis.

Data collection consisted of the measurement of a total of 1472 frames in four runs using omega scans with the detector held at 5.00 cm from the crystal. Frame scan parameters are summarized in Table 1 below:

Table 1. Data collection details for $C_{22}H_{15}N_2ClSO$.

Run	2θ	ω	φ	χ	Scan Width (º)	Frames	Exposure Time (sec)
1	21.65	-160.35	0.00	54.74	0.50	368	20.00
2	21.65	-160.35	120.00	54.74	0.50	368	20.00
3	21.65	-160.35	-120.00	54.74	0.50	368	20.00
4	21.65	-160.35	60.00	54.74	0.50	368	20.00

The APEX2 software program (version 2014.1-1)[1] was used for diffractometer control, preliminary frame scans, indexing, orientation matrix calculations, least-squares refinement of cell parameters, and the data collection. The frames were integrated with the Bruker SAINT software package using a narrow-frame algorithm. The integration of the data using a monoclinic unit cell yielded a total of 28740 reflections to a maximum θ angle of 27.50° (0.77 Å resolution), of which 4214 were independent (average redundancy 6.820, completeness = 99.5%, R_{int} = 3.02%, R_{sig} = 1.82%) and 3444 (81.73%) were greater than $2\sigma(F^2)$. The final cell constants of $\underline{a}$ = 12.0459(5) Å, $\underline{b}$ = 10.3781(5) Å, $\underline{c}$ = 15.4051(7) Å, β = 107.3945(12)°, volume = 1837.78(14) $Å^3$, are based upon the refinement of the XYZ-centroids of 9974 reflections above 20 σ(I) with 6.444° < 2θ < 65.16°. Data were corrected for absorption effects using the multi-scan method (SADABS). The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.809 and 0.843.

The structure was solved by direct methods and difference Fourier analysis using the programs provided by SHELXL-2014.[2] Idealized positions for the hydrogen atoms were included as fixed contributions using a riding model with isotropic temperature factors set at 1.2 times (N-H and aromatic hydrogens) of the adjacent non-hydrogen atom. Full-matrix least-squares refinement, based upon the minimization of $\Sigma w_i |F_o^2 - F_c^2|^2$, with weighting $w_i^{-1} = [\sigma^2(F_o^2) + (0.0835\ P)^2 + 1.1019\ P]$, where $P = (\text{Max}\ (F_o^2, 0) + 2\ F_c^2)/3$.[2] The final anisotropic full-matrix least-squares refinement on F^2 with 244

variables converged at R1 = 5.60%, for the 3444 observed data with $I > 2\sigma(I)$ and wR2 = 16.76% for all data. The goodness-of-fit was 1.055.[3]

A correction for secondary extinction was not applied. The largest peak in the final difference electron density synthesis was 0.559 $e^-/Å^3$ and the largest hole was -0.380 $e^-/Å^3$ with an RMS deviation of 0.058 $e^-/Å^3$. The linear absorption coefficient, atomic scattering factors, and anomalous dispersion corrections were calculated from values found in the International Tables of X-ray Crystallography.[4]

References

1. APEX2 is a Bruker AXS crystallographic software package for single crystal data collection, reduction and preparation.
2. Sheldrick, G. M., SHELXL-2014, Crystallographic software package, Bruker AXS, Inc., Madison, Wisconsin, USA.
3. $R_1 = \sum(||F_o| - |F_c||) / \sum|F_o|$, $wR_2 = [\sum[w(F_o^2 - F_c^2)^2] / \sum[w(F_o^2)^2]]^{1/2}$, $R_{int.} = \sum|F_o^2 - F_o^2(mean)|^2 / \sum[F_o^2]$, and $GOF = [\sum[w(F_o^2 - F_c^2)^2] / (n-p)]^{1/2}$, where n is the number of reflections and p is the total number of parameters which were varied during the last refinement cycle.
4. International Tables for X-ray Crystallography (1974). Vol. IV, p. 55. Birmingham: Kynoch Press. (Present distributor, D. Reidel, Dordrecht.).

Table 2. Crystal data for $C_{22}H_{15}N_2ClSO$.

Identification code	xs32cms	
Chemical formula	$C_{22}H_{15}N_2ClSO$	
Formula weight	390.87 g/mol	
Temperature	293(2) K	
Wavelength	0.71073 Å	
Crystal size	0.526 x 0.607 x 0.660 mm	
Crystal system	monoclinic	
Space group	P 2_1/n (No. 14, non-standard setting)	
Unit cell dimensions	a = 12.0459(5) Å	α = 90°
	b = 10.3781(5) Å	β = 107.3945(12)°
	c = 15.4051(7) Å	γ = 90°
Volume	1837.78(14) $Å^3$	
Z	4	
Density (calculated)	1.413 g/cm^3	
Absorption coefficient	0.336 mm^{-1}	
F(000)	808	

Table 3. Data collection and structure refinement for $C_{22}H_{15}N_2ClSO$.

Theta range for data used in the structural refinement	2.77 to 25.00°	
Index ranges	$-15 \le h \le 15$, $-13 \le k \le 13$, $-20 \le l \le 20$	
Reflections	28740	
Independent reflections	4214 [R(int) = 0.0302]	
Coverage of independent reflections	99.5%	
Absorption correction	multi-scan	
Max. and min. transmission	0.843 and 0.809	
Refinement method	Full-matrix least-squares on F^2	
Refinement program	SHELXL-2014 (Sheldrick, 2014)	
Data / restraints / parameters	4214 / 0 / 244	
Goodness-of-fit on F^2	1.055	
Final R indices	3444 data; I>2σ(I)	R1 = 0.0560, wR2 = 0.1495
	all data	R1 = 0.0679, wR2 = 0.1676
Largest diff. peak and hole	0.559 and -0.380 $e^-/Å^3$	

Table 4. Atomic coordinates and equivalent isotropic atomic displacement parameters ($Å^2$) for $C_{22}H_{15}N_2ClSO$. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x/a	y/b	z/c	U(eq)
Cl1	0.33168(7)	0.52839(8)	0.11672(5)	0.0787(3)
S1	0.59522(5)	0.48751(6)	0.23561(4)	0.0533(2)
O1	0.67933(18)	0.13640(19)	0.32607(14)	0.0748(6)
N1	0.69058(17)	0.31069(19)	0.41662(13)	0.0507(4)
N2	0.75732(17)	0.49700(18)	0.53759(13)	0.0505(4)
C1	0.6362(2)	0.2325(2)	0.34750(15)	0.0478(5)
C2	0.51317(19)	0.2684(2)	0.29605(14)	0.0453(5)
C3	0.4261(2)	0.1793(3)	0.29601(17)	0.0580(6)
C4	0.3126(2)	0.2025(3)	0.24305(19)	0.0681(8)
C5	0.2845(2)	0.3098(3)	0.18969(18)	0.0647(7)
C6	0.3705(2)	0.3964(2)	0.18859(16)	0.0540(5)
C7	0.48536(19)	0.3786(2)	0.24198(14)	0.0450(5)
C8	0.58105(18)	0.6120(2)	0.31105(15)	0.0451(5)
C9	0.6468(2)	0.7222(2)	0.31205(18)	0.0560(6)
C10	0.6445(2)	0.8216(3)	0.3706(2)	0.0700(8)
C11	0.5769(3)	0.8130(3)	0.4284(2)	0.0752(9)
C12	0.5109(2)	0.7043(3)	0.42684(19)	0.0657(7)
C13	0.5122(2)	0.6038(2)	0.36840(17)	0.0538(5)
C14	0.80788(19)	0.3082(2)	0.47011(14)	0.0454(5)
C15	0.8889(2)	0.2174(3)	0.46488(16)	0.0582(6)
C16	0.0041(2)	0.2301(3)	0.52041(18)	0.0683(8)
C17	0.0392(2)	0.3291(3)	0.57955(16)	0.0618(7)
C18	0.95850(19)	0.4227(2)	0.58741(14)	0.0489(5)
C19	0.9862(2)	0.5283(3)	0.64795(17)	0.0587(6)
C20	0.9026(2)	0.6126(3)	0.65187(18)	0.0639(7)
C21	0.7883(2)	0.5935(3)	0.59484(18)	0.0627(7)
C22	0.84156(18)	0.4121(2)	0.53288(13)	0.0436(5)

Table 5. Interatomic distances (Å) for $C_{22}H_{15}N_2ClSO$.

Cl1-C6	1.735(3)	S1-C7	1.765(2)
S1-C8	1.780(2)	O1-C1	1.215(3)
N1-C1	1.344(3)	N1-C14	1.407(3)
N2-C21	1.313(3)	N2-C22	1.362(3)
C1-C2	1.504(3)	C2-C7	1.396(3)
C2-C3	1.399(3)	C3-C4	1.387(4)
C4-C5	1.365(4)	C5-C6	1.376(4)
C6-C7	1.394(3)	C8-C13	1.384(3)
C8-C9	1.389(3)	C9-C10	1.377(4)
C10-C11	1.377(5)	C11-C12	1.376(4)
C12-C13	1.381(4)	C14-C15	1.376(3)
C14-C22	1.424(3)	C15-C16	1.402(4)
C16-C17	1.355(4)	C17-C18	1.405(3)
C18-C22	1.412(3)	C18-C19	1.413(4)
C19-C20	1.349(4)	C20-C21	1.408(4)

Table 6. Bond angles (°) for $C_{22}H_{15}N_2ClSO$.

C7-S1-C8	102.03(10)	C1-N1-C14	128.3(2)
C21-N2-C22	117.5(2)	O1-C1-N1	124.4(2)
O1-C1-C2	119.7(2)	N1-C1-C2	116.0(2)
C7-C2-C3	119.7(2)	C7-C2-C1	122.75(19)
C3-C2-C1	117.2(2)	C4-C3-C2	119.5(2)
C5-C4-C3	121.3(2)	C4-C5-C6	119.2(2)
C5-C6-C7	121.6(2)	C5-C6-Cl1	117.6(2)
C7-C6-Cl1	120.76(19)	C6-C7-C2	118.6(2)
C6-C7-S1	120.71(18)	C2-C7-S1	120.51(17)
C13-C8-C9	119.5(2)	C13-C8-S1	124.42(18)
C9-C8-S1	116.07(18)	C10-C9-C8	120.1(3)
C9-C10-C11	120.5(3)	C12-C11-C10	119.5(3)
C11-C12-C13	120.8(3)	C12-C13-C8	119.7(2)
C15-C14-N1	125.7(2)	C15-C14-C22	119.7(2)
N1-C14-C22	114.57(18)	C14-C15-C16	119.4(2)
C17-C16-C15	122.3(2)	C16-C17-C18	119.9(2)
C17-C18-C22	119.2(2)	C17-C18-C19	124.1(2)
C22-C18-C19	116.7(2)	C20-C19-C18	120.0(2)
C19-C20-C21	119.0(2)	N2-C21-C20	123.7(2)
N2-C22-C18	123.0(2)	N2-C22-C14	117.41(18)

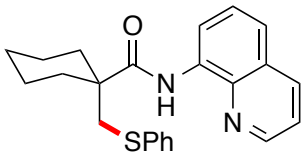
Table 7. Anisotropic atomic displacement parameters ($Å^2$) for $C_{22}H_{15}N_2ClSO$. The anisotropic atomic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2} U_{11} + ... + 2 h k a^* b^* U_{12}]$.

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
Cl1	0.0830(5)	0.0780(5)	0.0704(5)	0.0082(3)	0.0158(4)	0.0228(4)
S1	0.0582(4)	0.0474(3)	0.0622(4)	0.0003(2)	0.0303(3)	-0.0063(2)
O1	0.0807(13)	0.0544(11)	0.0793(13)	-0.0221(9)	0.0089(10)	0.0097(9)
N1	0.0509(10)	0.0531(11)	0.0458(10)	-0.0112(8)	0.0110(8)	0.0047(8)
N2	0.0501(10)	0.0493(10)	0.0455(10)	-0.0056(8)	0.0042(8)	0.0063(8)
C1	0.0589(12)	0.0433(11)	0.0416(11)	-0.0016(9)	0.0157(9)	-0.0045(9)
C2	0.0546(11)	0.0452(11)	0.0391(10)	-0.0100(8)	0.0183(9)	-0.0097(9)
C3	0.0719(16)	0.0532(13)	0.0535(13)	-0.0064(10)	0.0259(12)	-0.0199(11)
C4	0.0605(15)	0.0824(19)	0.0669(16)	-0.0204(14)	0.0273(13)	-0.0318(14)
C5	0.0475(13)	0.0859(19)	0.0592(15)	-0.0194(14)	0.0136(11)	-0.0090(12)
C6	0.0552(13)	0.0595(14)	0.0471(12)	-0.0093(10)	0.0151(10)	0.0021(10)
C7	0.0486(11)	0.0454(11)	0.0446(11)	-0.0076(8)	0.0194(9)	-0.0063(9)
C8	0.0394(10)	0.0419(10)	0.0482(11)	0.0044(8)	0.0041(8)	0.0041(8)
C9	0.0425(11)	0.0504(13)	0.0664(15)	0.0100(11)	0.0032(10)	-0.0015(9)
C10	0.0603(15)	0.0490(14)	0.0835(19)	-0.0017(13)	-0.0048(14)	-0.0028(11)
C11	0.0702(17)	0.0615(16)	0.0769(19)	-0.0199(14)	-0.0039(14)	0.0138(13)
C12	0.0597(14)	0.0718(17)	0.0610(15)	-0.0076(13)	0.0109(12)	0.0148(13)
C13	0.0485(12)	0.0519(13)	0.0596(13)	0.0002(10)	0.0140(10)	0.0027(10)
C14	0.0518(11)	0.0492(11)	0.0355(10)	0.0044(8)	0.0137(8)	0.0048(9)
C15	0.0700(15)	0.0625(15)	0.0432(11)	0.0009(10)	0.0186(10)	0.0176(12)
C16	0.0657(15)	0.089(2)	0.0532(14)	0.0138(13)	0.0218(12)	0.0344(14)
C17	0.0495(12)	0.0871(19)	0.0458(12)	0.0168(12)	0.0098(10)	0.0155(12)
C18	0.0477(11)	0.0587(13)	0.0374(10)	0.0134(9)	0.0082(8)	0.0013(10)
C19	0.0546(13)	0.0647(15)	0.0458(12)	0.0083(11)	-0.0014(10)	-0.0083(11)
C20	0.0716(16)	0.0524(13)	0.0531(13)	-0.0047(11)	-0.0036(12)	-0.0057(12)
C21	0.0651(15)	0.0529(14)	0.0587(14)	-0.0084(11)	0.0012(11)	0.0093(11)
C22	0.0457(10)	0.0471(11)	0.0370(10)	0.0074(8)	0.0105(8)	0.0031(8)

Table 8. Hydrogen atom coordinates and isotropic atomic displacement parameters ($Å^2$) for $C_{22}H_{15}N_2ClSO$.

	x/a	y/b	z/c	U(eq)
H1	0.6483	0.3698	0.4299	0.061
H3	0.4440	0.1050	0.3312	0.07
H4	0.2546	0.1439	0.2439	0.082
H5	0.2081	0.3241	0.1545	0.078
H9	0.6924	0.7288	0.2731	0.067
H10	0.6888	0.8951	0.3712	0.084
H11	0.5760	0.8800	0.4682	0.09
H12	0.4649	0.6985	0.4656	0.079
H13	0.4670	0.5309	0.3676	0.065
H15	0.8674	0.1483	0.4249	0.07
H16	1.0584	0.1683	0.5165	0.082
H17	1.1165	0.3351	0.6149	0.074
H19	1.0621	0.5397	0.6851	0.07
H20	0.9201	0.6823	0.6916	0.077
H21	0.7316	0.6526	0.5979	0.075

VI. Compounds Characterization



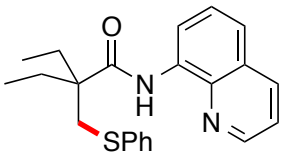
2a

2a: 1-((phenylthio)methyl)-N-(quinolin-8-yl)cyclohexanecarboxamide was prepared following the general procedure **1.4 Condition A** and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as colorless oil; Isolated yield 86%;

^{1}H NMR (400 MHz; $CDCl_3$): δ 10.40 (s, 1H), 8.82 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.71 (dd, *J* = 5.8, 3.3 Hz, 1H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.50-7.44 (m, 3H), 7.32-7.29 (m, 2H), 7.08-7.04 (m, 2H), 7.01-6.97 (m, 1H), 3.32 (s, 2H), 2.35-2.30 (m, 2H), 1.74-1.55 (m, 7H), 1.43-1.37 (m, 1H).

^{13}C NMR (101 MHz; $CDCl_3$): δ 173.4, 148.2, 138.8, 136.7, 136.2, 134.3, 129.9, 128.6, 127.8, 127.3, 125.9, 121.47, 121.29, 116.4, 49.1, 44.5, 33.8, 25.7, 22.8.

HRMS Calculated for $[C_{23}H_{25}N_2OS]^+$: 377.1682, Found: 377.1687



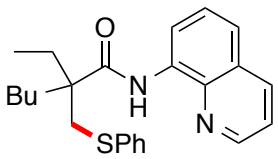
2b

2b: 2-ethyl-2-((phenylthio)methyl)-N-(quinolin-8-yl)butanamide was prepared following the general procedure **1.4 Condition A** and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as colorless oil; Isolated yield 74%;

^{1}H NMR (400 MHz; $CDCl_3$): δ 10.32 (s, 1H), 8.81 (dd, *J* = 4.3, 1.7 Hz, 1H), 8.76 (dd, *J* = 7.0, 2.0 Hz, 1H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.54-7.40 (m, 6H), 7.21-7.17 (m, 2H), 7.12-7.10 (m, 1H), 3.41 (s, 2H), 2.04-1.89 (m, 4H), 0.93 (t, *J* = 7.4 Hz, 6H).

^{13}C NMR (101 MHz; $CDCl_3$): δ 173.8, 148.2, 138.8, 136.9, 136.2, 134.3, 132.4, 130.0, 128.7, 127.9, 127.4, 126.0, 121.5, 121.3, 116.3, 52.0, 38.6, 28.0, 8.6.

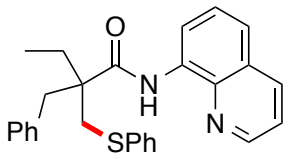
HRMS Calculated for $[C_{22}H_{25}N_2OS]^+$: 365.1682, Found: 365.1684.



2c

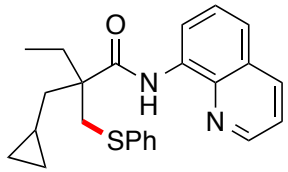
2c: 2-ethyl-2-((phenylthio)methyl)-N-(quinolin-8-yl)heptanamide was prepared following the general procedure **1.4 Condition A** and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as colorless oil; Isolated yield 87%;

^{1}H NMR (400 MHz; $CDCl_3$):δ 10.33 (s, 1H), 8.81 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.75 (dd, *J* = 7.0, 1.9 Hz, 1H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.52-7.41 (m, 5H), 7.22-7.18 (m, 2H), 7.12 (m, 1H), 3.45-3.38 (ABq, *J* = 12.8 Hz, 2H), 2.05-1.78 (m, 5H), 1.31-1.26 (m, 5H), 0.93 (t, *J* = 7.4 Hz, 3H), 0.85 (t, *J* = 6.9 Hz, 3H).
^{13}C NMR (101 MHz; $CDCl_3$): δ 173.9, 148.2, 138.8, 137.0, 136.2, 134.3, 130.0, 128.7, 127.9, 127.4, 126.0, 121.5, 121.3, 116.3, 51.7, 38.9, 35.3, 28.4, 26.3, 23.1, 13.9, 8.6
HRMS Calculated for $[C_{24}H_{29}N_2OS]^+$: 393.1995, Found: 393.2000.



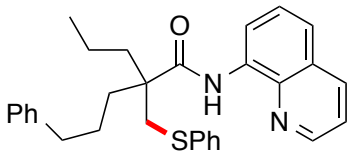
2d

2d: 2-benzyl-2-((phenylthio)methyl)-N-(quinolin-8-yl)butanamide was prepared following the general procedure **1.4 Condition A** and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as colorless oil; Isolated yield 75%;
^{1}H NMR (400 MHz; $CDCl_3$): δ 10.27 (s, 1H), 8.75-8.73 (m, 2H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.55-7.49 (m, 2H), 7.45-7.39 (m, 3H), 7.25-7.10 (m, 8H), 3.40-3.21 (m, 4H), 1.97 (q, *J* = 7.4 Hz, 2H), 1.02 (t, *J* = 7.4 Hz, 3H).
^{13}C NMR (101 MHz; $CDCl_3$): δ 172.9, 148.2, 138.7, 136.74, 136.68, 136.2, 130.08, 129.93, 128.8, 128.2, 127.98, 127.87, 127.4, 126.6, 126.0, 121.52, 121.41, 116.4, 53.1, 41.0, 38.6, 28.2, 8.8.
HRMS Calculated for $[C_{27}H_{27}N_2OS]^+$: 427.1839, Found: 427.1845.



2e

2e: 2-(cyclopropylmethyl)-2-((phenylthio)methyl)-N-(quinolin-8-yl)butanamide was prepared following the general procedure **1.4 Condition A** and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as colorless oil; Isolated yield 71%;
^{1}H NMR (400 MHz; $CDCl_3$): δ 10.34 (s, 1H), 8.81 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.76 (dd, *J* = 7.1, 1.9 Hz, 1H), 8.16 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.53-7.50 (m, 2H), 7.47-7.41 (m, 3H), 7.23-7.19 (m, 2H), 7.12 (d, *J* = 7.4 Hz, 1H), 3.54 (d, *J* = 0.9 Hz, 2H), 2.05 (dt, *J* = 17.2, 7.2 Hz, 2H), 1.86 (dd, *J* = 6.8, 3.4 Hz, 2H), 0.95 (t, *J* = 7.4 Hz, 3H), 0.72-0.68 (m, 1H), 0.41-0.38 (m, 2H), 0.21-0.11 (m, 2H).
^{13}C NMR (101 MHz; $CDCl_3$): δ 173.9, 148.2, 138.8, 137.0, 136.3, 134.3, 129.8, 128.7, 127.9, 127.4, 125.9, 121.5, 121.3, 116.4, 52.4, 40.3, 38.8, 28.3, 8.6, 6.4, 4.4, 4.1
HRMS Calculated for $[C_{24}H_{27}N_2OS]^+$: 391.1839, Found: 391.1840.



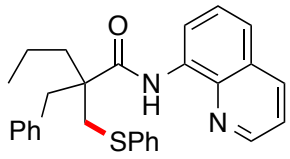
2f

2f: 2-ethyl-5-phenyl-2-((phenylthio)methyl)-N-(quinolin-8-yl)pentanamide was prepared following the general procedure **1.4 Condition A** and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as colorless oil; Isolated yield 75%;

^{1}H NMR (400 MHz; $CDCl_3$): δ 10.29 (s, 1H), 8.79 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.72 (dd, *J* = 6.7, 2.3 Hz, 1H), 8.16 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.52-7.40 (m, 5H), 7.19-7.07 (m, 8H), 3.41 (s, 2H), 2.58 (t, *J* = 7.6 Hz, 2H), 2.00-1.96 (m, 1H), 1.92-1.84 (m, 2H), 1.82-1.74 (m, 1H), 1.65-1.60 (m, 2H), 1.32-1.24 (m, 2H), 0.87 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz; $CDCl_3$): δ 173.8, 148.2, 141.9, 138.8, 136.9, 136.2, 134.3, 130.1, 128.8, 128.34, 128.18, 127.9, 127.4, 126.1, 125.7, 121.53, 121.34, 116.4, 51.5, 39.4, 38.2, 36.1, 35.4, 25.9, 17.5, 14.4

HRMS Calculated for $[C_{30}H_{33}N_2OS]^+$: 469.2308, Found: 469.2315.



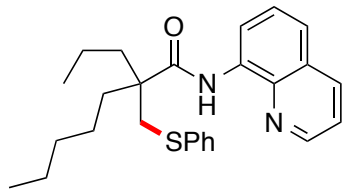
2g

2g: 2-benzyl-2-((phenylthio)methyl)-N-(quinolin-8-yl)pentanamide was prepared following the general procedure **1.4 Condition A** and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as colorless oil; Isolated yield 88%;

^{1}H NMR (400 MHz; $CDCl_3$): δ 10.28 (s, 1H), 8.75-8.72 (m, 2H), 8.14 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.55-7.48 (m, 2H), 7.44-7.39 (m, 3H), 7.25-7.09 (m, 8H), 3.38-3.26 (m, 4H), 1.91-1.82 (m, 2H), 1.46-1.40 (m, 2H), 0.90 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz; $CDCl_3$): δ 173.0, 148.2, 138.7, 136.71, 136.70, 136.2, 134.1, 130.07, 129.91, 128.8, 128.2, 127.9, 127.4, 126.6, 126.0, 121.51, 121.39, 116.4, 52.8, 41.4, 38.9, 37.9, 17.7, 14.3

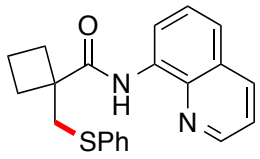
HRMS Calculated for $[C_{28}H_{29}N_2OS]^+$: 441.1995, Found: 441.2001.



2h: 2-((phenylthio)methyl)-2-propyl-N-(quinolin-8-yl)heptanamide was prepared following the general procedure **1.4 Condition A** and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as colorless oil; Isolated yield 72%;

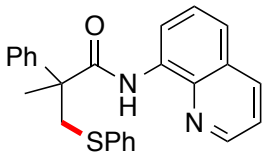
^{1}H NMR (400 MHz; $CDCl_3$): δ 10.32 (s, 1H), 8.81 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.74 (dd, *J* = 7.0, 2.0 Hz, 1H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.54-7.41 (m, 3H), 7.23-7.19 (m, 2H),

7.14-7.10 (m, 1H), 3.42 (s, 2H), 1.97-1.89 (m, J = 5.7 Hz, 2H), 1.85-1.76 (m, J = 5.3 Hz, 2H), 1.36-1.24 (m, 8H), 0.89 (t, J = 7.3 Hz, 3H), 0.83-0.80 (m, 3H).
^{13}C NMR (101 MHz; $CDCl_3$): δ 174.1, 148.2, 138.8, 137.0, 136.2, 134.4, 130.0, 128.7, 127.9, 127.4, 126.0, 121.5, 121.3, 116.4, 51.5, 39.3, 38.4, 35.9, 32.2, 23.8, 22.4, 17.5, 14.5, 14.0
HRMS Calculated for $[C_{26}H_{33}N_2OS]^+$: 421.2308, Found: 421.2315



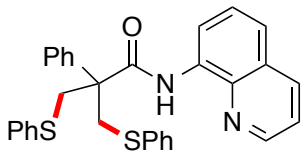
2i

2i: 1-((phenylthio)methyl)-N-(quinolin-8-yl)cyclobutanecarboxamide was prepared following the general procedure **1.4 Condition A** and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as colorless oil; Isolated yield 63%;
^{1}H NMR (400 MHz; $CDCl_3$): δ 10.19 (s, 1H), 8.82 (dd, J = 4.2, 1.7 Hz, 1H), 8.69 (dd, J = 5.6, 3.4 Hz, 1H), 8.16 (dd, J = 8.3, 1.7 Hz, 1H), 7.50-7.44 (m, 3H), 7.35-7.33 (m, 2H), 7.09-7.05 (m, 2H), 7.02-7.00 (m, 1H), 3.56 (s, 2H), 2.67 (ddd, J = 12.7, 9.5, 7.5 Hz, 2H), 2.30-2.23 (m, 2H), 2.04 (ddt, J = 19.6, 10.7, 5.1 Hz, 2H).
^{13}C NMR (101 MHz; $CDCl_3$): δ 174.2, 148.2, 138.7, 136.2, 134.2, 130.0, 128.6, 127.8, 127.3, 126.0, 121.49, 121.37, 116.3, 50.3, 42.9, 30.3, 15.1
HRMS Calculated for $[C_{21}H_{21}N_2OS]^+$: 349.1369, Found: 349.1373.



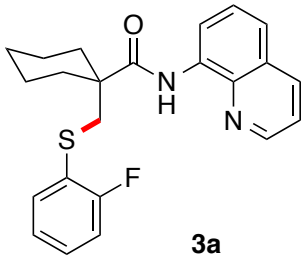
2j

2j: 2-methyl-2-phenyl-3-(phenylthio)-N-(quinolin-8-yl)propanamide was prepared following the general procedure **1.4 Condition A** and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as colorless oil; Isolated yield 53%;
^{1}H NMR (400 MHz; $CDCl_3$): δ 9.91 (s, 1H), 8.75 (dd, J = 7.5, 1.5 Hz, 1H), 8.58 (dd, J = 4.2, 1.7 Hz, 1H), 8.08 (dd, J = 8.3, 1.7 Hz, 1H), 7.54-7.44 (m, 4H), 7.40-7.29 (m, 6H), 7.20-7.16 (m, 2H), 7.12-7.08 (m, 1H), 3.86-3.71 (ABq, J = 12.8 Hz, 2H), 1.97 (s, 3H).
^{13}C NMR (101 MHz; $CDCl_3$): δ 173.8, 148.1, 141.7, 138.6, 137.4, 136.1, 134.4, 129.8, 128.80, 128.71, 127.8, 127.6, 127.2, 126.9, 126.0, 121.47, 121.44, 116.1, 52.9, 44.9, 23.2
HRMS Calculated for $[C_{25}H_{23}N_2OS]^+$: 399.1526, Found: 399.1530.



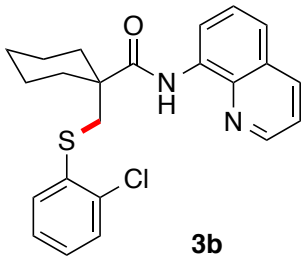
2j-di

2j-di: 2-phenyl-3-(phenylthio)-2-((phenylthio)methyl)-N-(quinolin-8-yl)propanamide was prepared following the general procedure **1.4 Condition A** and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as colorless oil; Isolated yield 27%;
^{1}H NMR (400 MHz; $CDCl_3$): δ 9.93 (s, 1H), 8.64 (dd, *J* = 7.2, 1.8 Hz, 1H), 8.53 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.06 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.50-7.43 (m, 5H), 7.37-7.31 (m, 3H), 7.30 (s, 4H), 7.08-6.98 (m, 5H), 4.03 (s, 4H).
^{13}C NMR (101 MHz; $CDCl_3$): δ 171.4, 148.0, 139.8, 138.5, 136.2, 135.9, 134.1, 130.5, 129.4, 128.79, 128.59, 128.0, 127.22, 127.18, 126.2, 121.47, 121.37, 116.3, 56.7, 41.7
HRMS Calculated for $[C_{31}H_{27}N_2OS_2]^+$: 507.1559, Found: 507.1568.



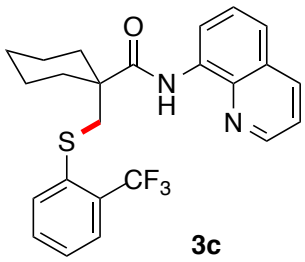
3a

3a: 1-(((2-fluorophenyl)thio)methyl)-N-(quinolin-8-yl)cyclohexanecarboxamide was prepared following the general procedure **1.4 Condition B** and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as colorless oil; Isolated yield 80%;
^{1}H NMR (400 MHz; $CDCl_3$): δ 10.37 (s, 1H), 8.82 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.66 (t, *J* = 4.5 Hz, 1H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.48-7.44 (m, 3H), 7.34-7.30 (m, 1H), 6.99-6.94 (m, 1H), 6.81-6.76 (m, 2H), 3.30 (s, 2H), 2.34-2.30 (m, 2H), 1.75-1.58 (m, 7H), 1.43-1.38 (m, 1H).
^{13}C NMR (101 MHz; $CDCl_3$): δ 173.2, 161.5 (d, *J* = 244.4 Hz), 148.2, 138.8, 136.1, 134.3, 132.93 (d, *J* = 1.9 Hz), 128.26, 128.18, 127.8, 127.3, 124.08 (d, *J* = 3.7 Hz), 123.24, 121.5, 121.3, 116.4, 115.34 (d, *J* = 22.2 Hz), 49.0, 43.6, 33.7, 25.7, 22.8
HRMS Calculated for $[C_{23}H_{24}FN_2OS]^+$: 395.1588, Found: 395.2595.



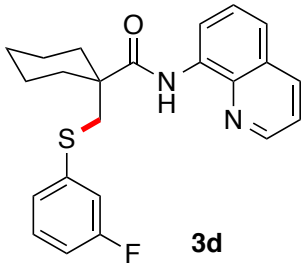
3b

3b: 1-(((2-chlorophenyl)thio)methyl)-N-(quinolin-8-yl)cyclohexanecarboxamide was prepared following the general procedure **1.4 Condition B** and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as colorless oil; Isolated yield 78%;
^{1}H NMR (400 MHz; $CDCl_3$): δ 10.40 (s, 1H), 8.81 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.69 (dd, *J* = 5.4, 3.6 Hz, 1H), 8.13 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.48-7.42 (m, 3H), 7.34 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.10 (dd, *J* = 7.9, 1.4 Hz, 1H), 6.99-6.95 (m, 1H), 6.89 (td, *J* = 7.6, 1.6 Hz, 1H), 3.32 (s, 2H), 2.39-2.34 (m, 2H), 1.78-1.58 (m, 7H), 1.45-1.39 (m, 1H).
^{13}C NMR (101 MHz; $CDCl_3$): δ 173.2, 148.2, 138.8, 136.1, 135.5, 134.39, 134.29, 130.3, 129.3, 127.8, 127.3, 126.80, 126.66, 121.47, 121.35, 116.5, 48.8, 43.12, 33.8, 25.7, 22.8.
HRMS Calculated for $[C_{23}H_{24}ClN_2OS]^+$: 411.1292, Found: 411.1297.



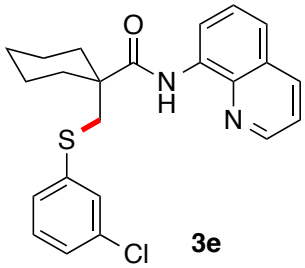
3c

3c: N-(quinolin-8-yl)-1-(((2-(trifluoromethyl)phenyl)thio)methyl)cyclohexanecarboxamide was prepared following the general procedure **1.4 Condition B** and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as colorless oil; Isolated yield 42%;
^{1}H-NMR (400 MHz; $CDCl_3$): δ 10.40 (s, 1H), 8.80 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.71 (dd, *J* = 5.7, 3.3 Hz, 1H), 8.14 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.55 (d, *J* = 7.9 Hz, 1H), 7.52-7.40 (m, 3H), 7.31-7.28 (m, 1H), 7.10-7.05 (m, 1H), 3.36 (s, 2H), 2.37-2.31 (m, 2H), 1.79-1.57 (m, 7H), 1.43-1.36 (m, 1H).
^{13}C NMR (101 MHz; $CDCl_3$): δ 173.3, 148.3, 138.8, 136.1, 134.3, 132.3, 131.8, 127.8, 127.3, 126.38 (q, *J* = 5.8 Hz), 125.8, 125.0, 123.7 (q, *J* = 272.3 Hz), 121.51, 121.44, 116.5, 49.0, 45.01, 44.99, 33.6, 25.7, 22.8
HRMS Calculated for $[C_{24}H_{24}F_3N_2OS]^+$: 445.1556, Found: 455.1559



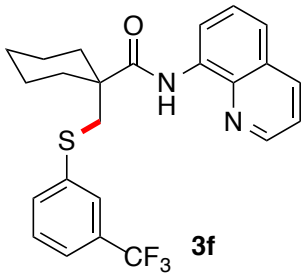
3d

3d: 1-(((3-fluorophenyl)thio)methyl)-N-(quinolin-8-yl)cyclohexanecarboxamide was prepared following the general procedure **1.4 Condition B** and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as colorless oil; Isolated yield 75%;
^{1}H-NMR (400 MHz; $CDCl_3$): δ 10.38 (s, 1H), 8.82 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.70 (dd, *J* = 5.2, 3.8 Hz, 1H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.49-7.43 (m, 3H), 7.05-6.95 (m, 3H), 6.66-6.61 (m, 1H), 3.31 (s, 2H), 2.34 (dd, *J* = 12.9, 4.5 Hz, 2H), 1.72-1.56 (m, 8H).
^{13}C NMR (101 MHz; $CDCl_3$): δ 173.1, 163.48 (d, *J* = 246.6 Hz), 148.2, 139.00 (d, *J* = 7.6 Hz), 138.796, 136.2, 134.2, 129.72 (d, *J* = 8.5 Hz), 127.9, 127.3, 124.976 (d, *J* = 2.8 Hz), 121.50, 121.38, 116.39, 116.24 (d, *J* = 23.2 Hz), 112.66 (d, *J* = 21.2 Hz), 49.0, 44.1, 33.9, 25.7, 22.8.
HRMS Calculated for $[C_{23}H_{24}FN_2OS]^+$: 395.1588, Found: 395.1590.



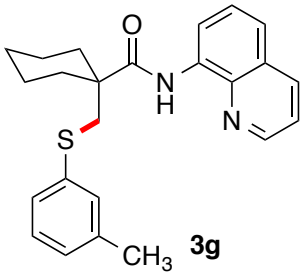
3e

3e: 1-(((3-chlorophenyl)thio)methyl)-N-(quinolin-8-yl)cyclohexanecarboxamide was prepared following the general procedure **1.4 Condition B** and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as colorless oil; Isolated yield 81%;
^{1}H-NMR (400 MHz; $CDCl_3$): δ 10.37 (s, 1H), 8.82 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.68 (t, *J* = 4.5 Hz, 1H), 8.14 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.49-7.43 (m, 3H), 7.24 (t, *J* = 1.8 Hz, 1H), 7.14 (dt, *J* = 7.5, 1.5 Hz, 1H), 6.95-6.87 (m, 2H), 3.31 (s, 2H), 2.38-2.32 (m, 2H), 1.70-1.59 (m, 8H), 1.42-1.38 (m, 1H).
^{13}C NMR (101 MHz; $CDCl_3$): δ 173.0, 148.3, 138.78, 138.60, 136.2, 134.25, 134.17, 129.46, 129.26, 127.9, 127.7, 127.3, 125.9, 121.49, 121.38, 116.4, 48.9, 44.2, 33.9, 25.7, 22.8
HRMS Calculated for $[C_{23}H_{24}ClN_2OS]^+$: 411.1292, Found: 411.1203.



3f

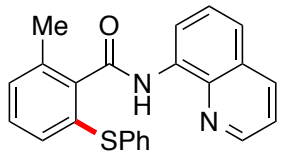
3f: N-(quinolin-8-yl)-1-(((3-(trifluoromethyl)phenyl)thio)methyl)cyclohexanecarboxamide was prepared following the general procedure **1.4 Condition B** and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as colorless oil; Isolated yield 70%;
^{1}H-NMR (400 MHz; $CDCl_3$): δ 10.38 (s, 1H), 8.81 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.65 (dd, *J* = 5.6, 3.4 Hz, 1H), 8.14 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.50-7.42 (m, 5H), 7.12 (dt, *J* = 17.2, 8.3 Hz, 2H), 3.34 (s, 2H), 2.37 (dd, *J* = 15.4, 7.3 Hz, 2H), 1.72-1.56 (m, 7H), 1.44-1.36 (m, 1H).
^{13}C NMR (101 MHz; $CDCl_3$): δ 172.9, 148.2, 138.7, 138.0, 136.2, 134.1, 132.5, 131.0-130.7 (q, *J* = 32.1 Hz), 128.8, 127.8, 127.3, 125.98 (q, *J* = 5.8 Hz), 123.6 (q, *J* = 271.6 Hz), 122.390 (q, *J* = 5.8 Hz), 121.50, 121.41, 116.3, 48.9, 44.1, 33.9, 25.7, 22.8
HRMS Calculated for $[C_{24}H_{27}N_2OS]^+$: 445.1556, Found: 455.1564.



3g

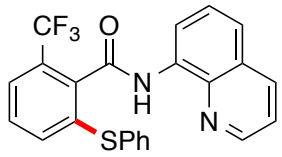
3g: N-(quinolin-8-yl)-1-((m-tolylthio)methyl)cyclohexanecarboxamide was prepared following the general procedure **1.4 Condition B** and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as colorless oil; Isolated yield 37%;
^{1}H-NMR (400 MHz; $CDCl_3$): δ 10.38 (s, 1H), 8.82 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.70 (dd, *J* = 5.7, 3.3 Hz, 1H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.49-7.43 (m, 3H), 7.12-7.08 (m, 2H), 6.94 (t, *J* = 7.6 Hz, 1H), 6.77-6.75 (m, 1H), 3.30 (s, 2H), 2.36-2.32 (m, 3H), 2.07 (s, 3H), 1.73-1.58 (m, 7H), 1.39 (dd, *J* = 5.9, 4.2 Hz, 1H).

^{13}C NMR (101 MHz; $CDCl_3$): δ 173.4, 148.2, 138.8, 138.3, 136.26, 136.17, 134.4, 130.6, 128.4, 127.8, 127.3, 127.0, 126.7, 121.4, 121.2, 116.4, 49.0, 44.6, 33.8, 25.8, 22.9, 21.0
HRMS Calculated for $[C_{24}H_{27}N_2OS]^+$: 391.1837, Found: 391.1848.



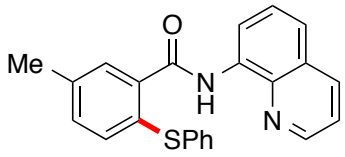
4a

4a: 2-methyl-6-(phenylthio)-N-(quinolin-8-yl)benzamide was prepared following the general procedure **1.3** and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as colorless soild; Isolated yield 89%;
^{1}H-NMR (400 MHz; $CDCl_3$): δ 9.94 (s, 1H), 8.96 (dd, *J* = 7.4, 1.6 Hz, 1H), 8.68 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.61-7.53 (m, 2H), 7.41 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.34-7.31 (m, 2H), 7.25-7.12 (m, 6H), 2.47 (s, 3H).
^{13}C NMR (101 MHz; $CDCl_3$): δ 166.94, 166.94, 148.13, 148.13, 140.11, 140.11, 138.46, 138.46, 136.22, 136.22, 136.13, 136.13, 135.68, 135.68, 134.28, 134.28, 133.00, 133.00, 131.31, 131.31, 130.41, 130.41, 129.65, 129.65, 129.55, 129.55, 129.06, 129.06, 127.92, 127.92, 127.39, 127.39, 127.05, 127.05, 121.93, 121.93, 121.54, 121.54, 116.87, 116.87, 19.59, 19.59.
HRMS Calculated for $[C_{23}H_{19}N_2OS]^+$: 371.1213, Found: 371.1217.



4b

4b: 2-(phenylthio)-N-(quinolin-8-yl)-6-(trifluoromethyl)benzamide was prepared following the general procedure **1.3** and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as colorless solid; Isolated yield 85%;
^{1}H-NMR (400 MHz; $CDCl_3$): δ 10.07 (s, 1H), 8.96 (dd, *J* = 7.1, 1.8 Hz, 1H), 8.73 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.17 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.63-7.57 (m, 3H), 7.46-7.41 (m, 5H), 7.30-7.25 (m, 3H).
^{13}C NMR (101 MHz; $CDCl_3$): δ 164.0, 148.2, 138.4, 137.6, 136.3, 134.8, 134.1, 133.5, 133.0, 129.8, 129.5, 128.32 (q, *J* = 31.2 Hz), 128.28, 128.0, 127.4, 124.6 (q, *J* = 4.7 Hz), 123.4 (q, *J* = 272.4 Hz), 122.3, 121.6, 117.1.
HRMS Calculated for $[C_{23}H_{16}F_3N_2OS]^+$: 425.0930, Found: 425.0939



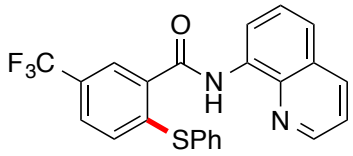
4c

4c: 5-methyl-2-(phenylthio)-N-(quinolin-8-yl)benzamide was prepared following the general procedure **1.3** and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as colorless oil; Isolated yield 78%;

^{1}H-NMR (400 MHz; $CDCl_3$): δ 10.51 (s, 1H), 8.91 (dd, *J* = 7.3, 1.6 Hz, 1H), 8.74 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.17 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.63-7.62 (m, 1H), 7.59-7.52 (m, 2H), 7.44 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.39-7.36 (m, 2H), 7.27-7.25 (m, 2H), 7.24-7.19 (m, 3H), 2.41 (s, 3H).

^{13}C NMR (101 MHz; $CDCl_3$): δ 166.5, 148.2, 137.34, 137.16, 136.3, 135.4, 134.6, 132.4, 132.11, 132.00, 131.82, 129.27, 129.19, 127.9, 127.42, 127.35, 121.8, 121.6, 116.8, 21.0

HRMS Calculated for $[C_{23}H_{19}N_2OS]^+$: 371.1213, Found: 371.1221.



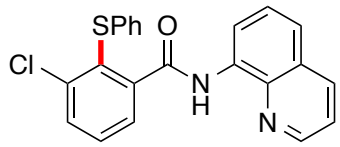
4d

4d: 2-(phenylthio)-N-(quinolin-8-yl)-5-(trifluoromethyl)benzamide was prepared following the general procedure **1.3** and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as colorless oil; Isolated yield 65%;

^{1}H-NMR (400 MHz; $CDCl_3$): δ 10.55 (s, 1H), 8.93 (dd, *J* = 6.7, 2.3 Hz, 1H), 8.82 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.21 (dd, *J* = 8.3, 1.7 Hz, 1H), 8.00 (t, *J* = 0.7 Hz, 1H), 7.64-7.58 (m, 2H), 7.55-7.47 (m, 4H), 7.41-7.38 (m, 3H), 7.12 (d, *J* = 8.4 Hz, 1H).

^{13}C NMR (101 MHz; $CDCl_3$): δ 165.0, 148.4, 143.9, 138.6, 136.4, 134.96, 134.76, 134.2, 132.0, 129.8, 129.27, 129.23, 128.0, 127.7 (q, *J* = 33.3 Hz), 127.40, 127.3 (q, *J* = 3.5 Hz), 125.0 (q, *J* = 3.5 Hz), 123.7 (q, *J* = 271.0 Hz), 122.3, 121.8, 117.0

HRMS Calculated for $[C_{23}H_{15}F_3N_2OSNa]^+$: 447.0749, Found: 447.0749



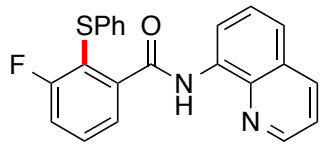
4e

4e: 3-chloro-2-(phenylthio)-N-(quinolin-8-yl)benzamide was prepared following the general procedure **1.3** and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as colorless solid; Isolated yield 81%;

^{1}H-NMR (400 MHz; $CDCl_3$): δ 10.25 (s, 1H), 8.80 (dd, *J* = 6.4, 2.6 Hz, 1H), 8.62 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.14 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.64 (ddd, *J* = 13.6, 7.8, 1.4 Hz, 2H), 7.55-7.51 (m, 2H), 7.46 (d, *J* = 7.7 Hz, 1H), 7.43-7.39 (m, 2H), 7.17-7.10 (m, 4H), 7.07-7.03 (m, 1H).

^{13}C NMR (101 MHz; $CDCl_3$): δ 165.8, 148.1, 144.5, 140.8, 138.4, 136.2, 135.7, 134.2, 131.9, 130.3, 129.9, 128.9, 128.7, 127.8, 127.3, 126.2, 122.0, 121.6, 116.8

HRMS Calculated for $[C_{22}H_{16}ClN_2OS]^+$: 391.0666, Found: 391.0678.



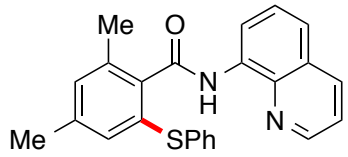
4f

4f: 3-fluoro-2-(phenylthio)-N-(quinolin-8-yl)benzamide was prepared following the general procedure **1.3** and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as colorless soild; Isolated yield 80%;

^{1}H-NMR (400 MHz; $CDCl_3$): δ 10.42 (s, 1H), 8.63 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.14 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.62-7.58 (m, 1H), 7.56-7.46 (m, 3H), 7.41 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.27-7.22 (m, 3H), 7.17-7.13 (m, 2H), 7.11-7.07 (m, 1H).

^{13}C NMR (101 MHz; $CDCl_3$): δ 165.2, 162.91 (d, *J* = 248.8 Hz), 148.2, 143.3, 138.5, 136.2, 135.5, 134.3, 130.92 (d, *J* = 9.0 Hz), 129.02 (d, *J* = 23.7 Hz), 127.9, 127.3, 126.5, 124.55 (d, *J* = 3.8 Hz), 122.1, 121.6, 119.50, 119.30, 117.91 (d, *J* = 23.9 Hz), 116.8

HRMS Calculated for $[C_{22}H_{16}FN_2OS]^+$: 375.0962, Found: 375.0969.



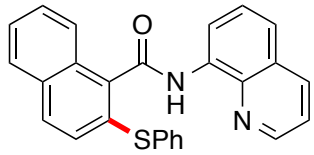
4g

4g: 2,4-dimethyl-6-(phenylthio)-N-(quinolin-8-yl)benzamide was prepared following the general procedure **1.3** and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as colorless solid; Isolated yield 91%;

^{1}H-NMR (400 MHz; $CDCl_3$): δ 9.91 (s, 1H), 8.94 (dd, *J* = 7.4, 1.6 Hz, 1H), 8.66 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.60-7.52 (m, 2H), 7.41 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.32-7.30 (m, 2H), 7.21-7.15 (m, 2H), 7.15-7.11 (m, 1H), 7.07-7.03 (m, 2H), 2.43 (s, 3H), 2.29 (s, 3H).

^{13}C NMR (101 MHz; $CDCl_3$): δ 167.2, 148.1, 139.7, 138.5, 137.9, 136.19, 136.11, 136.03, 134.4, 132.3, 131.2, 130.9, 130.7, 129.0, 127.9, 127.4, 126.8, 121.8, 121.5, 116.8, 21.1, 19.5

HRMS Calculated for $[C_{24}H_{21}N_2OS]^+$: 385.1369, Found: 385.1376.

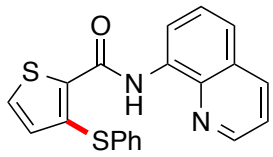


4h

4h: 2-(phenylthio)-N-(quinolin-8-yl)-1-naphthamide was prepared following the general procedure **1.3** and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as colorless solid; Isolated yield 90%;

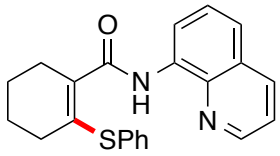
^{1}H-NMR (400 MHz; $CDCl_3$): δ 10.21 (s, 1H), 9.11 (dd, *J* = 7.5, 1.4 Hz, 1H), 8.63 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.16 (dd, *J* = 8.3, 1.6 Hz, 1H), 8.06-8.04 (m, 1H), 7.86-7.81 (m, 2H), 7.66-7.56 (m, 3H), 7.53-7.49 (m, 2H), 7.42-7.38 (m, 4H), 7.27-7.18 (m, 4H).

^{13}C NMR (101 MHz; $CDCl_3$): δ 166.5, 148.2, 138.5, 137.5, 136.2, 134.4, 132.4, 131.5, 130.78, 130.63, 130.0, 129.34, 129.15, 128.08, 127.97, 127.7, 127.44, 127.24, 126.8, 125.3, 122.1, 121.6, 117.0.
HRMS Calculated for $[C_{26}H_{19}N_2OS]^+$: 407.1212, Found: 407.1190.



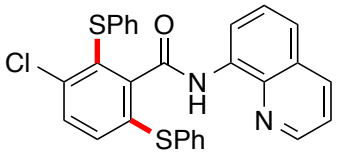
4i

4i: 3-(phenylthio)-N-(quinolin-8-yl)thiophene-2-carboxamide was prepared following the general procedure **1.3** and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as colorless oil; Isolated yield 72%;
^{1}H-NMR (400 MHz; $CDCl_3$): δ 11.71 (s, 1H), 8.89 (dd, *J* = 7.3, 1.7 Hz, 1H), 8.74 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.14 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.55-7.49 (m, 3H), 7.45-7.40 (m, 3H), 7.32-7.24 (m, 3H), 6.98 (d, *J* = 5.2 Hz, 1H).
^{13}C NMR (101 MHz; $CDCl_3$): δ 159.8, 148.3, 139.0, 138.3, 136.1, 135.1, 134.9, 133.4, 131.8, 130.3, 129.44, 129.27, 128.0, 127.35, 127.33, 121.9, 121.5, 117.3
HRMS Calculated for $[C_{20}H_{15}N_2OS_2]^+$: 363.0620, Found: 363.0627



4j

4j: 2-(phenylthio)-N-(quinolin-8-yl)cyclohex-1-enecarboxamide was prepared following the general procedure **1.3** and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as colorless oil; Isolated yield 82%;
^{1}H-NMR (400 MHz; $CDCl_3$): δ 10.24 (s, 1H), 8.87 (dd, *J* = 7.5, 1.5 Hz, 1H), 8.72 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.14 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.53-7.47 (m, 4H), 7.44-7.40 (m, 1H), 7.35-7.27 (m, 3H), 2.66 (tt, *J* = 6.1, 2.3 Hz, 2H), 2.21 (tt, *J* = 6.1, 2.3 Hz, 2H), 1.80-1.68 (m, 4H).
^{13}C NMR (101 MHz; $CDCl_3$): δ 167.8, 148.0, 136.9, 136.6, 136.3, 134.6, 133.7, 132.7, 131.5, 129.4, 128.9, 127.9, 127.5, 121.49, 121.41, 116.6, 77.3, 77.0, 76.7, 31.3, 28.4, 23.3, 21.9
HRMS Calculated for $[C_{22}H_{21}N_2OS]^+$: 361.1369, Found: 361.1371.



4k

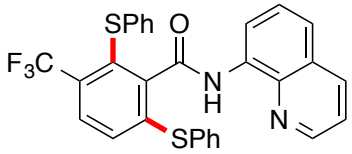
4k: 3-chloro-2,6-bis(phenylthio)-N-(quinolin-8-yl)benzamide was prepared following the general procedure **1.3** with 4 equiv. PhSH, 7 equiv. Li*O*t*B*U, and 15 mol%

$NiCl_2$(DME) and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as colorless oil; Isolated yield 77%;

^{1}H-NMR (400 MHz; $CDCl_3$): δ 9.97 (s, 1H), 8.98 (dd, *J* = 7.2, 1.7 Hz, 1H), 8.68 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.20 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.65-7.58 (m, 2H), 7.52-7.45 (m, 4H), 7.38-7.28 (m, 5H), 7.23-7.20 (m, 2H), 7.16-7.12 (m, 1H).

^{13}C NMR (101 MHz; $CDCl_3$): δ 164.4, 148.0, 145.7, 139.3, 138.3, 136.1, 135.4, 134.7, 134.0, 133.6, 133.3, 132.8, 131.4, 130.4, 129.5, 128.92, 128.87, 128.2, 127.8, 127.4, 126.4, 122.1, 121.5, 117.0

HRMS Calculated for $[C_{28}H_{19}ClN_2OS_2Na]^+$: 521.0520, Found: 521.0527.



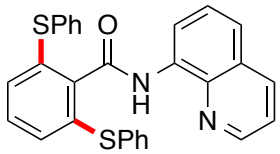
4l

4l: 2,6-bis(phenylthio)-N-(quinolin-8-yl)-3-(trifluoromethyl)benzamide was prepared following the general procedure **1.3** with 4 equiv. PhSH, 7 equiv. Li*O*t*BU, and 15 mol% $NiCl_2$(DME) and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as colorless oil; Isolated yield 72%;

^{1}H-NMR (400 MHz; $CDCl_3$): δ 9.80 (s, 1H), 8.83 (dd, *J* = 6.8, 2.2 Hz, 1H), 8.62 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.12 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.64 (d, *J* = 8.6 Hz, 1H), 7.56-7.49 (m, 4H), 7.41-7.34 (m, 4H), 7.10 (dd, *J* = 8.5, 0.6 Hz, 1H), 7.06-7.03 (m, 2H), 7.00-6.95 (m, 2H).

^{13}C NMR (101 MHz; $CDCl_3$): δ 163.8, 148.0, 144.3, 143.5, 138.3, 136.7, 136.1, 134.7, 134.0, 131.6 (q, *J* = 30.0 Hz), 131.2, 130.03 (q, *J* = 1.6 Hz), 129.9, 129.33, 129.16, 128.8, 128.5, 127.83 (q, *J* = 5.5 Hz), 127.77, 127.3, 126.1, 123.3 (q, *J* = 271.0 Hz),122.1, 121.5, 116.9

HRMS Calculated for $[C_{29}H_{20}F_3N_2OS_2]^+$: 533.0964, Found: 533.0969.



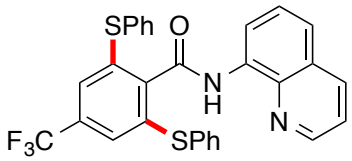
4m

4m: 2,6-bis(phenylthio)-N-(quinolin-8-yl)benzamide was prepared following the general procedure **1.3** with 4 equiv. PhSH, 7 equiv. Li*O*t*BU, and 15 mol% $NiCl_2$(DME) and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as colorless oil; Isolated yield 83%;

^{1}H-NMR (400 MHz; $CDCl_3$): δ 10.05 (s, 1H), 8.97 (dd, *J* = 7.4, 1.4 Hz, 1H), 8.69 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.15 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.60-7.53 (m, 2H), 7.43-7.40 (m, 5H), 7.27-7.12 (m, 9H).

^{13}C NMR (101 MHz; $CDCl_3$): δ 165.2, 148.1, 138.5, 136.2, 135.7, 134.38, 134.23, 132.5, 130.16, 130.08, 129.3, 127.91, 127.75, 127.5, 122.0, 121.5, 117.0.

HRMS Calculated for $[C_{28}H_{21}N_2OS_2]^+$: 465.1098, Found: 465.1090.



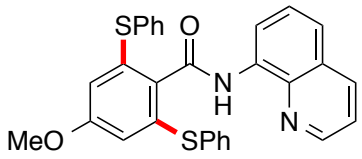
4n

4n: 2,6-bis(phenylthio)-*N*-(quinolin-8-yl)-4-(trifluoromethyl)benzamide was prepared following the general procedure **1.3** with 4 equiv. PhSH, 7 equiv. Li*O*t*BU*, and 15 mol% $NiCl_2$(DME) and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as yellow solid; Isolated yield 81%;

^{1}H-NMR (400 MHz; $CDCl_3$): δ 10.12 (s, 1H), 8.96 (dd, *J* = 7.0, 2.0 Hz, 1H), 8.74 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.18 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.62-7.56 (m, 2H), 7.47-7.43 (m, 5H), 7.33-7.28 (m, 6H), 7.26-7.22 (m, 3H).

^{13}C NMR (101 MHz; $CDCl_3$): δ 164.0, 148.6, 148.2, 138.5, 138.0, 136.6, 136.3, 136.2, 133.9, 133.3, 132.5, 131.1, 129.66, 129.51, 128.7, 128.02-127.98(q, *J* = 4.4 Hz), 127.9, 127.4, 125.1(q, *J* = 3.7 Hz), 123.1(q, *J* = 265.6 Hz), 122.4, 121.7, 121.60-121.23 (q, *J* = 37.3 Hz), 117.2

HRMS Calculated for $[C_{29}H_{20}F_3N_2OS_2]^+$: 533.0963, Found: 533. 0977.



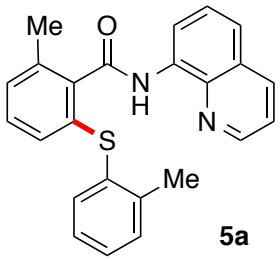
4o

4o: 4-methoxy-2,6-bis(phenylthio)-N-(quinolin-8-yl)benzamide was prepared following the general procedure **1.3** with 4 equiv. PhSH, 7 equiv. Li*O*t*BU*, and 15 mol% $NiCl_2$(DME) and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as yellow solid; Isolated yield 77%;

^{1}H-NMR (400 MHz; $CDCl_3$): δ 10.07 (s, 1H), 8.95 (dd, *J* = 7.4, 1.5 Hz, 1H), 8.69 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.14 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.59-7.51 (m, 2H), 7.45-7.39 (m, 5H), 7.29-7.20 (m, 6H), 6.60 (s, 2H), 3.59 (s, 3H).

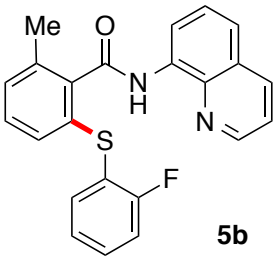
^{13}C NMR (101 MHz; $CDCl_3$): δ 165.2, 160.1, 148.0, 138.5, 137.3, 136.2, 134.3, 133.9, 132.8, 132.3, 129.3, 127.93, 127.88, 127.4, 121.8, 121.5, 116.9, 115.1, 55.3

HRMS Calculated for $[C_{29}H_{23}N_2O_2S_2]^+$: 495.1196, Found: 495.1203.



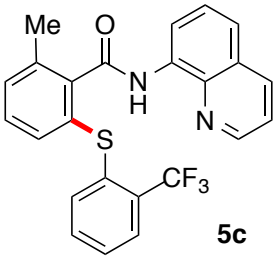
5a

5a: 2-methyl-N-(quinolin-8-yl)-6-(o-tolylthio)benzamide was prepared following the general procedure **1.3** and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as yellow solid; Isolated yield 86%;
^{1}H-NMR (400 MHz; $CDCl_3$): δ 9.98 (s, 1H), 8.98 (dd, *J* = 7.4, 1.6 Hz, 1H), 8.70 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.16 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.62-7.54 (m, 2H), 7.43 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.35-7.33 (m, 1H), 7.20-7.10 (m, 5H), 6.94 (dd, *J* = 7.7, 0.6 Hz, 1H), 2.47 (s, 3H), 2.29 (s, 3H).
^{13}C NMR (101 MHz; $CDCl_3$): δ 19.59, 20.60, 116.88, 121.55, 121.91, 126.73, 127.42, 127.91, 128.29, 128.72, 129.58, 130.48, 133.35, 133.63, 133.76, 134.36, 136.10, 136.24, 138.51, 138.83, 140.12, 148.14, 166.95, 20.6, 19.6
HRMS Calculated for $[C_{24}H_{21}N_2OS]^+$: 385.1369, Found: 385.1373.



5b

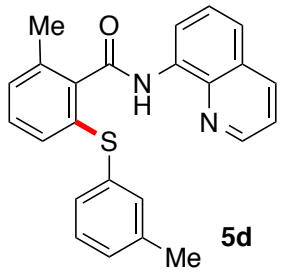
5b: 2-((2-fluorophenyl)thio)-6-methyl-N-(quinolin-8-yl)benzamide was prepared following the general procedure **1.3** and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as colorless oil; Isolated yield 84%;
^{1}H-NMR (400 MHz; $CDCl_3$): δ 9.98 (s, 1H), 8.96 (dd, *J* = 7.4, 1.6 Hz, 1H), 8.69 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.15 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.61-7.53 (m, 2H), 7.41 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.32-7.25 (m, 2H), 7.22-7.13 (m, 3H), 7.02-6.93 (m, 2H), 2.47 (s, 3H).
^{13}C NMR (101 MHz; $CDCl_3$): δ 166.7, 161.15 (d, *J* = 246.3 Hz) 148.1, 140.2, 138.5, 136.2, 134.3, 133.74, 133.73, 131.5, 130.2, 129.84, 129.71, 129.33, 129.25, 127.9, 127.4, 124.635(d, *J* = 3.8 Hz), 122.0, 121.6, 116.9, 115.78(d, *J* = 22.0 Hz), 19.6
HRMS Calculated for $[C_{23}H_{18}FN_2OS]^+$: 389.1118, Found: 389.1122.



5c

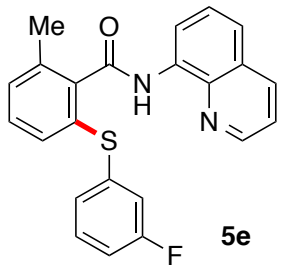
5c: 2-methyl-N-(quinolin-8-yl)-6-((2-(trifluoromethyl)phenyl)thio)benzamide was prepared following the general procedure **1.3** at 120 ^oC and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as colorless oil; Isolated yield 73%;
^{1}H-NMR (400 MHz; $CDCl_3$): δ 9.90 (s, 1H), 8.91 (dd, *J* = 7.1, 1.9 Hz, 1H), 8.66 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.59-7.51 (m, 3H), 7.43-7.34 (m, 3H), 7.32 (s, 3H), 7.21-7.18 (m, 1H), 2.49 (s, 3H).

^{13}C NMR (101 MHz; $CDCl_3$): δ 166.6, 148.1, 141.8, 138.5, 136.5, 136.3, 134.1, 132.8, 132.5, 132.2, 131.0, 130.8, 130.0, 127.9, 127.4, 126.4 (q, *J* = 3.7 Hz), 126.21, 123.6(q, *J* = 273.6 Hz), 122.0, 121.5, 117.0, 19.6
HRMS Calculated for $[C_{24}H_{18}F_3N_2OS]^+$: 439.1086, Found: 439.1093.



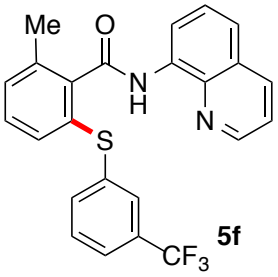
5d

5d: 2-methyl-N-(quinolin-8-yl)-6-(m-tolylthio)benzamide was prepared following the general procedure **1.3** and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as colorless oil; Isolated yield 88%;
^{1}H-NMR (400 MHz; $CDCl_3$): δ 9.91 (s, 1H), 8.97 (dd, *J* = 7.4, 1.5 Hz, 1H), 8.68 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.16 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.62-7.53 (m, 2H), 7.42 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.24-7.18 (m, 2H), 7.15-7.14 (m, 2H), 7.08 (dd, *J* = 9.9, 5.7 Hz, 1H), 6.94 (d, *J* = 7.2 Hz, 1H), 2.47 (s, 3H), 2.17 (s, 3H).
^{13}C NMR (101 MHz; $CDCl_3$): δ 167.0, 148.1, 138.9, 138.5, 136.26, 136.08, 135.2, 134.3, 133.4, 132.2, 130.3, 129.58, 129.40, 128.9, 128.7, 128.0, 127.4, 121.9, 121.5, 116.9, 21.2, 19.6
HRMS Calculated for $[C_{24}H_{21}N_2OS]^+$: 385.1369, Found: 385.1370.



5e

5e: 2-((3-fluorophenyl)thio)-6-methyl-*N*-(quinolin-8-yl)benzamide was prepared following the general procedure **1.3** and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as colorless oil; Isolated yield 84%;
^{1}H-NMR (400 MHz; $CDCl_3$): δ 9.87 (s, 1H), 8.93 (dd, *J* = 7.3, 1.6 Hz, 1H), 8.65 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.15 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.60-7.53 (m, 2H), 7.42 (t, *J* = 4.1 Hz, 1H), 7.31-7.28 (m, 3H), 7.12-7.08 (m, 1H), 7.01 (dt, *J* = 7.8, 1.3 Hz, 1H), 6.94 (dt, *J* = 9.3, 2.1 Hz, 1H), 6.76 (tdd, *J* = 8.3, 2.5, 0.9 Hz, 1H), 2.48 (s, 3H).
^{13}C NMR (101 MHz; $CDCl_3$): δ 166.7, 162.87 (d, *J* = 246.8 Hz), 148.1, 141.4, 139.1, 138.4, 136.5, 136.2, 134.2, 132.0, 130.78, 130.66, 130.11 (d, *J* = 8.3 Hz), 129.88, 127.9, 127.37, 127.34, 125.465 (d, *J* = 3.0 Hz), 122.0, 121.6, 116.8, 116.6, 113.504 (d, *J* = 21.2 Hz), 19.6
HRMS Calculated for $[C_{23}H_{18}FN_2OS]^+$: 389.1118, Found: 389.1112.



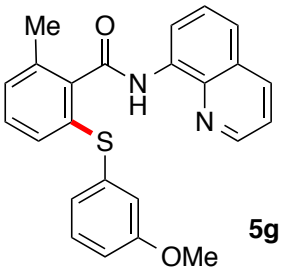
5f

5f: 2-methyl-N-(quinolin-8-yl)-6-((3-(trifluoromethyl)phenyl)thio)benzamide was prepared following the general procedure **1.3** at 120 ^{o}C and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as colorless oil; Isolated yield 75%;

^{1}H-NMR (400 MHz; $CDCl_3$): δ 9.80 (s, 1H), 8.90 (dd, *J* = 7.2, 1.8 Hz, 1H), 8.57 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.14 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.59-7.52 (m, 2H), 7.44-7.34 (m, 5H), 7.26-7.22 (m, 2H), 2.50 (s, 3H).

^{13}C NMR (101 MHz; $CDCl_3$): δ 166.6, 148.1, 142.6, 142.3, 138.2, 136.9, 136.2, 134.0, 133.1, 131.4, 130.1,129.2, 128.4, 127.87, 127.78, 127.34, 127.31, 126.6, 125.70 (q, *J* = 3.7 Hz), 124.0 (q, *J* = 270. 2 Hz), 122.1, 116.8, 19.6

HRMS Calculated for $[C_{24}H_{18}F_3N_2OS]^+$: 439.1086, Found: 439.1091.



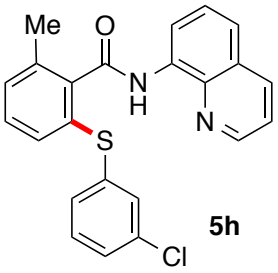
5g

5g: 2-((3-methoxyphenyl)thio)-6-methyl-N-(quinolin-8-yl)benzamide was prepared following the general procedure **1.3** and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as colorless oil; Isolated yield 80%;

^{1}H-NMR (400 MHz; $CDCl_3$): δ 9.90 (s, 1H), 8.97 (dd, *J* = 7.4, 1.6 Hz, 1H), 8.66 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.15 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.61-7.53 (m, 2H), 7.41 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.28-7.26 (m, 2H), 7.21 (td, *J* = 4.4, 0.9 Hz, 1H), 7.10 (t, *J* = 8.0 Hz, 1H), 6.90 (ddd, *J* = 7.7, 1.7, 0.9 Hz, 1H), 6.84 (dd, *J* = 2.4, 1.7 Hz, 1H), 6.65 (ddd, *J* = 8.3, 2.5, 0.9 Hz, 1H), 3.63 (s, 3H), 2.47 (s, 3H).

^{13}C NMR (101 MHz; $CDCl_3$): δ 166.9, 159.9, 148.1, 140.4, 138.4, 137.0, 136.20, 136.18, 134.3, 132.5, 130.8, 129.81, 129.79, 129.65, 127.9, 127.4, 123.3, 121.9, 121.5, 116.8, 116.0, 113.1, 55.1, 19.6

HRMS Calculated for $[C_{24}H_{21}N_2O_2S]^+$: 401.1318, Found: 401.1320.



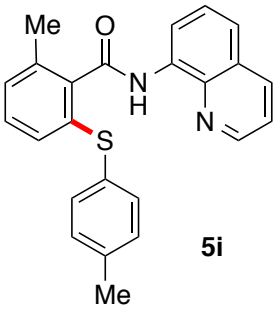
5h

5h: 2-((3-chlorophenyl)thio)-6-methyl-N-(quinolin-8-yl)benzamide was prepared following the general procedure **1.3** and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as colorless oil; Isolated yield 72%;

^{1}H-NMR (400 MHz; $CDCl_3$): δ 9.85 (s, 1H), 8.92 (dd, *J* = 7.4, 1.6 Hz, 1H), 8.65 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.13 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.59-7.51 (m, 2H), 7.40 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.32-7.24 (m, 3H), 7.21 (q, *J* = 1.2 Hz, 1H), 7.13-7.09 (m, 1H), 7.06-7.01 (m, 2H), 2.52-2.42 (m, 3H).

^{13}C NMR (101 MHz; $CDCl_3$): δ 166.7, 148.1, 141.3, 138.6, 138.4, 136.5, 136.2, 134.7, 134.1, 131.9, 130.9, 130.6, 129.90, 129.88, 129.7, 128.2, 127.9, 127.4, 126.7, 122.0, 121.6, 116.8, 19.6

HRMS Calculated for $[C_{23}H_{18}ClN_2OS]^+$: 405.0823, Found: 405.0828.



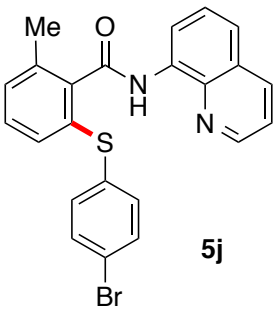
5i

5i: 2-methyl-N-(quinolin-8-yl)-6-(p-tolylthio)benzamide was prepared following the general procedure **1.3** and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as colorless oil; Isolated yield 90%;

^{1}H-NMR (400 MHz; $CDCl_3$): δ 9.94 (s, 1H), 8.98 (dd, *J* = 7.4, 1.5 Hz, 1H), 8.70 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.61-7.53 (m, 2H), 7.42 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.29-7.19 (m, 3H), 7.15-7.11 (m, 2H), 7.02-7.00 (m, 2H), 2.46 (s, 3H), 2.24 (s, 3H).

^{13}C NMR (101 MHz; $CDCl_3$): δ 167.0, 148.1, 139.2, 138.5, 137.5, 136.2, 135.9, 134.34, 134.32, 132.4, 131.4, 129.9, 129.5, 129.3, 129.0, 127.9, 127.4, 121.9, 121.5, 116.9, 21.0, 19.6

HRMS Calculated for $[C_{24}H_{21}N_2OS]^+$: 385.1369, Found: 385.1373.



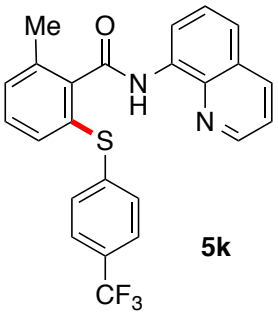
5j

5j: 2-((4-bromophenyl)thio)-6-methyl-N-(quinolin-8-yl)benzamide was prepared following the general procedure **1.3** and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as colorless oil; Isolated yield 83%;

^{1}H-NMR (400 MHz; $CDCl_3$): δ 8.94 (dd, *J* = 7.3, 1.7 Hz, 1H), 8.65 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.14 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.58-7.54 (m, 2H), 7.42 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.30-7.29 (m, 2H), 7.26-7.23 (m, 3H), 7.12-7.10 (m, 2H), 2.47 (s, 3H).

^{13}C NMR (101 MHz; $CDCl_3$): δ 166.7, 148.2, 141.0, 138.3, 136.5, 136.2, 135.6, 134.1, 132.04, 131.92, 131.53, 131.45, 130.4, 129.8, 127.9, 127.3, 122.0, 121.6, 120.8, 116.7, 19.6

HRMS Calculated for $[C_{23}H_{18}BrN_2OS]^+$: 449.0318, Found: 449.0322.



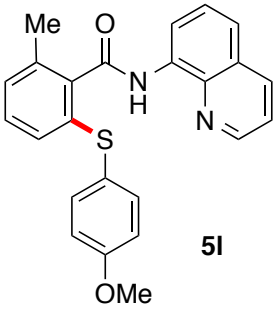
5k

5k: 2-methyl-N-(quinolin-8-yl)-6-((4-(trifluoromethyl)phenyl)thio)benzamide was prepared following the general procedure **1.3** at 120 °C and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as colorless oil; Isolated yield 65%;

^{1}H-NMR (400 MHz; $CDCl_3$): δ 9.86 (s, 1H), 8.92 (dd, *J* = 7.2, 1.7 Hz, 1H), 8.62 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.15 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.58-7.55 (m, 2H), 7.49 (s, 1H), 7.41 (dd, *J* = 8.3, 4.1 Hz, 2H), 7.28-7.26 (m, 5H), 2.49 (s, 3H).

^{13}C NMR (101 MHz; $CDCl_3$): δ 166.6, 148.1, 141.4, 138.35, 138.24, 136.7, 136.3, 134.1, 133.16, 133.15, 131.9, 131.3 (q, *J* = 31.7 Hz), 130.8, 130.6, 130.0, 129.4, 127.9, 127.4, 126.4 (q, *J* = 3.9 Hz), 123.3 (q, *J* = 3.9 Hz), 122.9-121.8 (q, *J* = 113 Hz), 122.1, 121.6, 116.8, 19.6

HRMS Calculated for $[C_{24}H_{18}F_3N_2OS]^+$: 439.1086, Found: 439.1093.



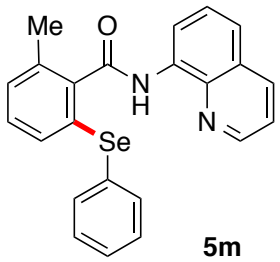
5l

5l: 2-((4-methoxyphenyl)thio)-6-methyl-N-(quinolin-8-yl)benzamide was prepared following the general procedure **1.3** and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as colorless oil; Isolated yield 85%;

^{1}H-NMR (400 MHz; $CDCl_3$): δ 9.97 (s, 1H), 9.01 (dd, *J* = 7.5, 1.5 Hz, 1H), 8.72 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.16 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.62-7.54 (m, 2H), 7.44-7.37 (m, 3H), 7.18 (t, *J* = 7.7 Hz, 1H), 7.10 (d, *J* = 7.6 Hz, 1H), 7.01 (t, *J* = 8.5 Hz, 1H), 6.78-6.76 (m, 2H), 3.72 (s, 3H), 2.45 (s, 3H).

^{13}C NMR (101 MHz; $CDCl_3$): δ 167.0, 159.7, 148.2, 138.5, 138.2, 136.2, 135.8, 135.2, 134.3, 129.4, 128.4, 128.0, 127.4, 126.6, 124.6, 121.9, 121.6, 116.9, 114.8, 114.3, 55.2, 19.5

HRMS Calculated for $[C_{24}H_{21}N_2O_2S]^+$: 401.1318, Found: 401.1323.



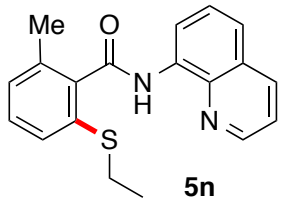
5m

5m: 2-methyl-6-(phenylselanyl)-N-(quinolin-8-yl)benzamide was prepared following the general procedure **1.3** wirh 1.5 equiv. diphenylselenium and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as colorless oil; Isolated yield 81%;

^{1}H-NMR (400 MHz; $CDCl_3$): δ 9.93 (s, 1H), 8.98 (dd, *J* = 7.4, 1.5 Hz, 1H), 8.69 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.17 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.63-7.54 (m, 2H), 7.50-7.48 (m, 2H), 7.43 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.29 (t, *J* = 4.5 Hz, 1H), 7.20-7.17 (m, 5H), 2.49 (s, 3H).

^{13}C NMR (101 MHz; $CDCl_3$): δ 167.5, 148.2, 140.6, 138.5, 136.3, 135.9, 134.3, 133.9, 131.6, 130.9, 129.8, 129.58, 129.46, 129.2, 128.0, 127.56, 127.43, 122.0, 121.6, 116.9, 19.9

HRMS Calculated for $[C_{23}H_{19}N_2OSe]^+$: 419.0657, Found: 419.0655.



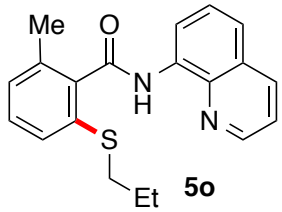
5n

5n: 2-(ethylthio)-6-methyl-N-(quinolin-8-yl)benzamide was prepared following the general procedure **1.3** with 1.5 equiv. disulfide and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as colorless oil; Isolated yield 70%;

^{1}H-NMR (400 MHz; $CDCl_3$): δ 9.95 (s, 1H), 9.01 (dd, *J* = 7.5, 1.5 Hz, 1H), 8.74 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.18 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.63-7.55 (m, 2H), 7.44 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.35-7.31 (m, 2H), 7.15 (dt, *J* = 7.3, 0.7 Hz, 1H), 2.94 (q, *J* = 7.4 Hz, 2H), 2.44 (s, 3H), 1.26 (t, *J* = 7.4 Hz, 4H).

^{13}C NMR (101 MHz; $CDCl_3$): δ 167.4, 148.2, 140.0, 138.6, 136.3, 135.8, 134.5, 133.3, 129.3, 128.6, 128.3, 128.0, 127.5, 121.9, 121.6, 116.9, 29.1, 19.5, 14.3

HRMS Calculated for $[C_{19}H_{19}N_2OS]^+$: 323.1213, Found: 323.1216.

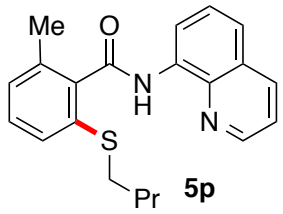


5o

5o: 2-methyl-6-(propylthio)-N-(quinolin-8-yl)benzamide was prepared following the general procedure **1.3** with 1.5 equiv. disulfide and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as colorless oil; Isolated yield 72%;

^{1}H-NMR (400 MHz; $CDCl_3$): δ 9.94-9.94 (m, 1H), 9.01 (dd, *J* = 7.5, 1.5 Hz, 1H), 8.74 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.18 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.64-7.55 (m, 2H), 7.44 (dd, *J* =

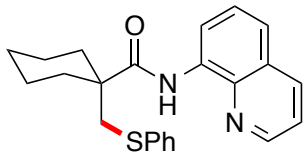
8.3, 4.2 Hz, 1H), 7.35-7.29 (m, 2H), 7.14 (ddd, *J* = 7.4, 1.3, 0.7 Hz, 1H), 2.88 (t, *J* = 7.3 Hz, 2H), 2.43 (s, 3H), 1.66-1.57 (m, 2H), 0.93 (t, *J* = 7.3 Hz, 3H).
^{13}C NMR (101 MHz; $CDCl_3$): δ 162.0, 148.2, 140.0, 139.5, 136.3, 135.8, 134.5, 133.6, 129.3, 128.51, 128.41, 128.0, 127.5, 121.9, 121.6, 116.9, 37.2, 22.6, 19.5, 13.4
HRMS Calculated for $[C_{20}H_{21}N_2OS]^+$: 337.1369, Found: 323.1371.



5p

5p: 2-(butylthio)-6-methyl-N-(quinolin-8-yl)benzamide was prepared following the general procedure **1.3** with 1.5 equiv. disulfide and purified by flash chromatography (Hexane-EtOAc, v/v 20/1) as colorless oil; Isolated yield 73%;
^{1}H-NMR (400 MHz; $CDCl_3$): δ 9.95 (s, 1H), 9.01 (dd, *J* = 7.5, 1.4 Hz, 1H), 8.73 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.17 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.63-7.54 (m, 2H), 7.43 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.30 (dt, *J* = 14.8, 7.4 Hz, 2H), 7.14 (dd, *J* = 7.4, 0.5 Hz, 1H), 2.91 (t, *J* = 7.5 Hz, 2H), 2.43 (s, 3H), 1.61-1.53 (m, 2H), 1.37 (dt, *J* = 15.0, 7.4 Hz, 2H), 0.83 (t, *J* = 7.4 Hz, 3H).
^{13}C NMR (101 MHz; $CDCl_3$): δ 167.4, 148.2, 139.9, 138.5, 136.3, 135.7, 134.5, 133.8, 129.3, 128.4, 128.2, 128.0, 127.5, 121.9, 121.6, 116.8, 34.8, 31.2, 21.9, 19.5, 13.6
HRMS Calculated for $[C_{20}H_{21}N_2OS]^+$: 351.1526, Found: 351.1530.

VII. NMR spectra data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SPh

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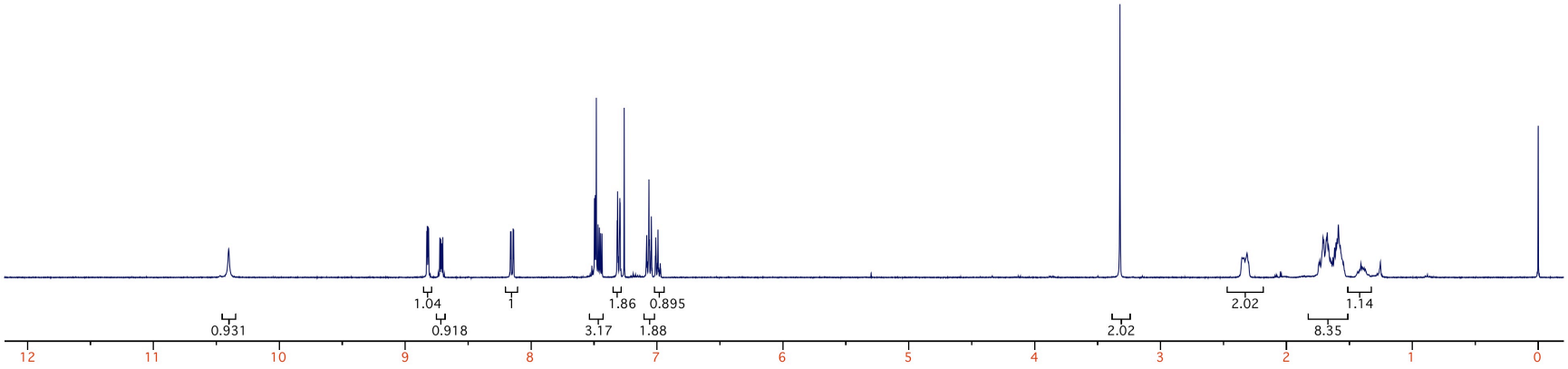
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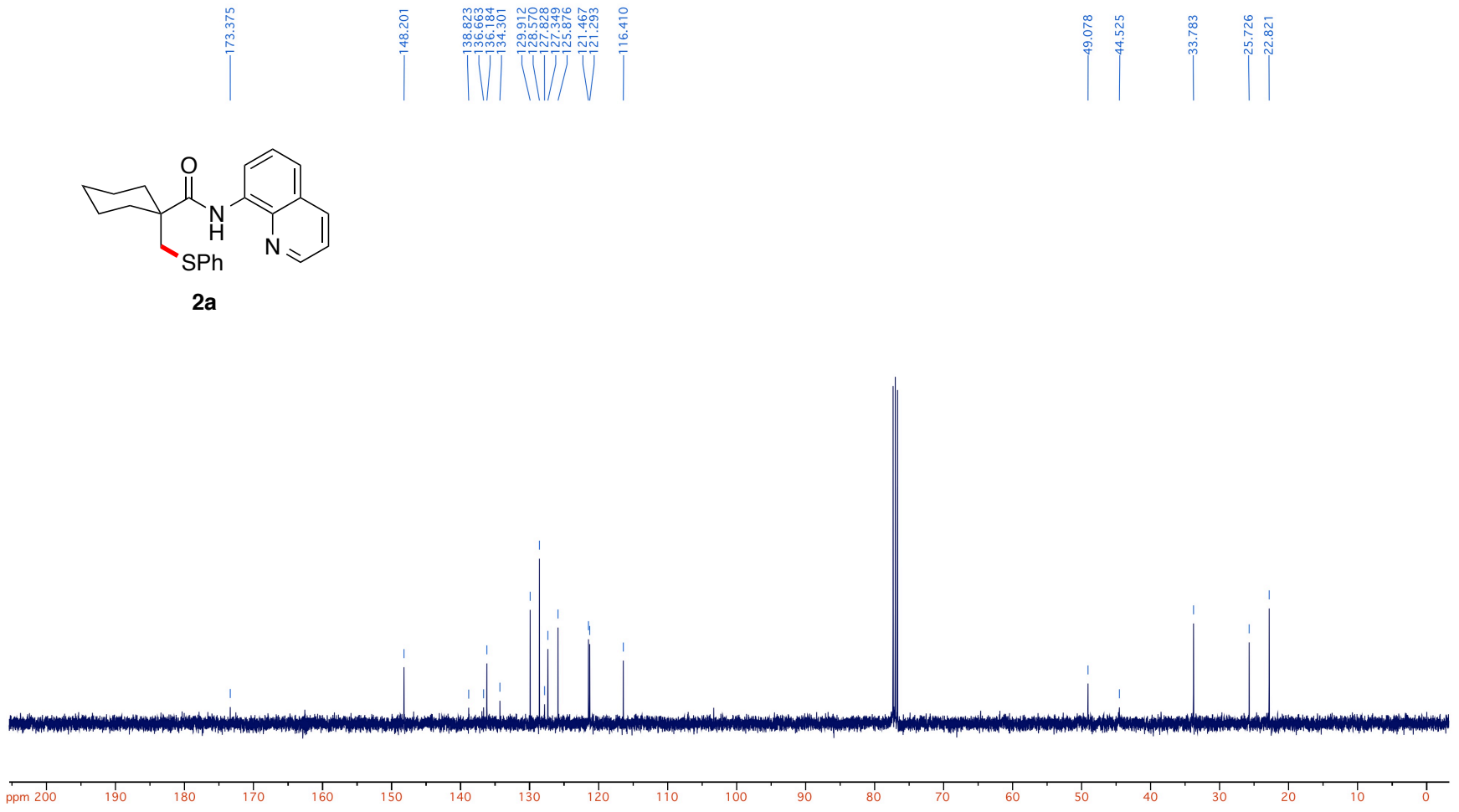
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25.726
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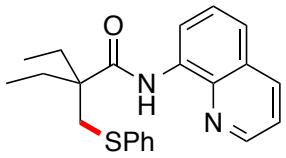
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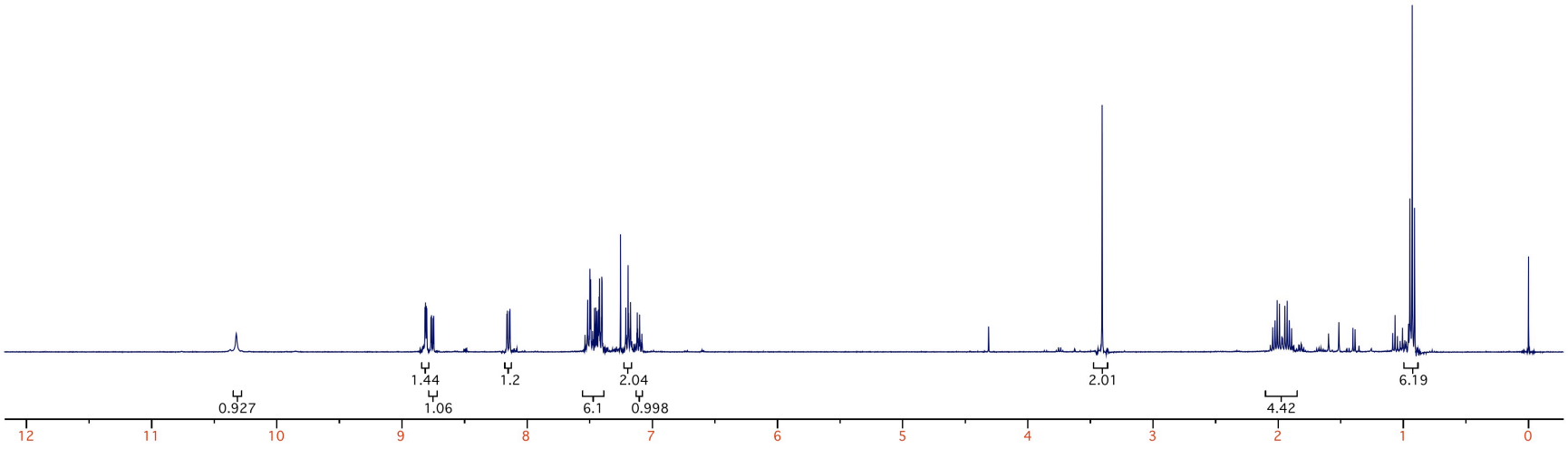
H
N
SPh

2b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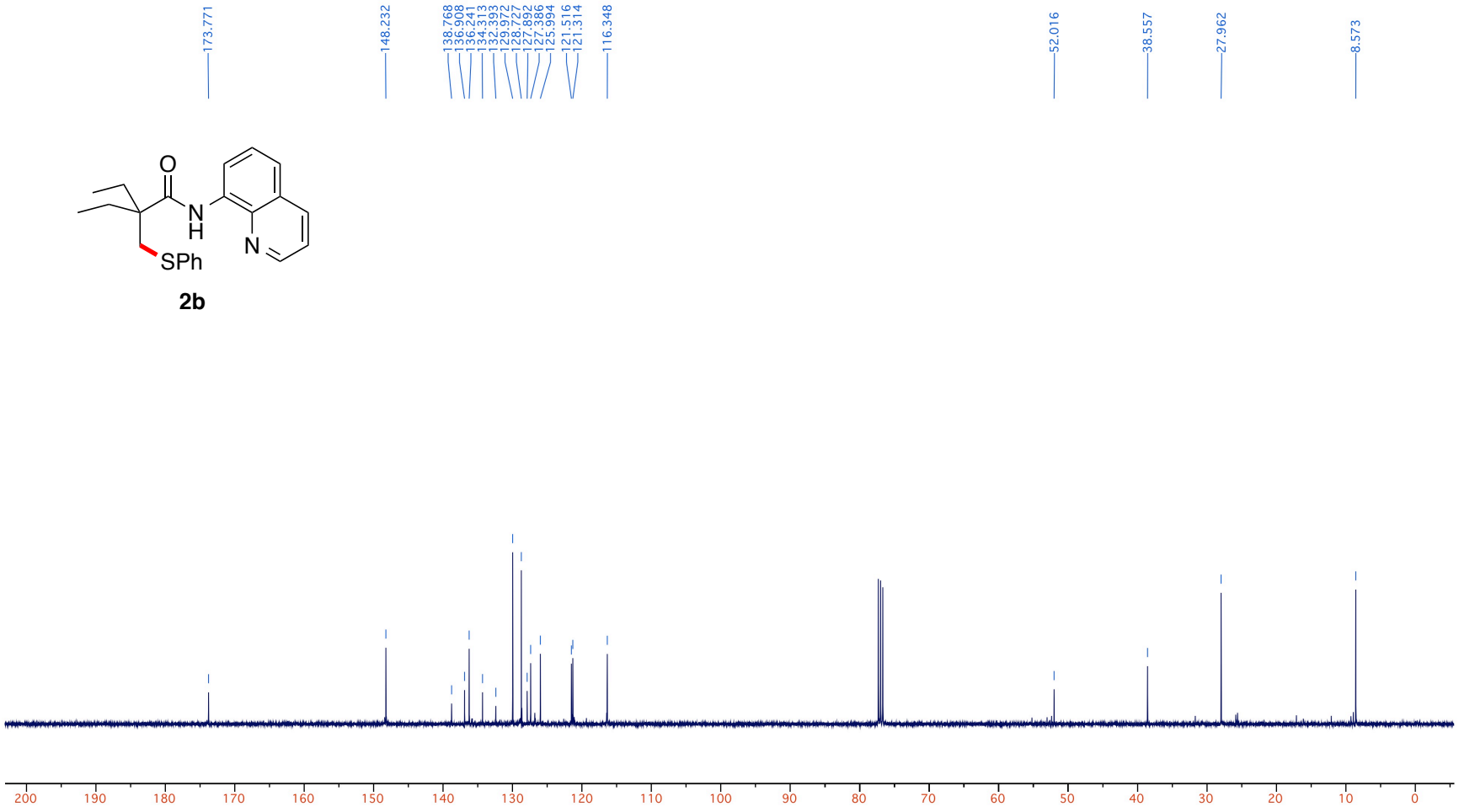
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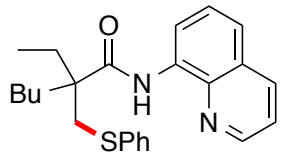
2b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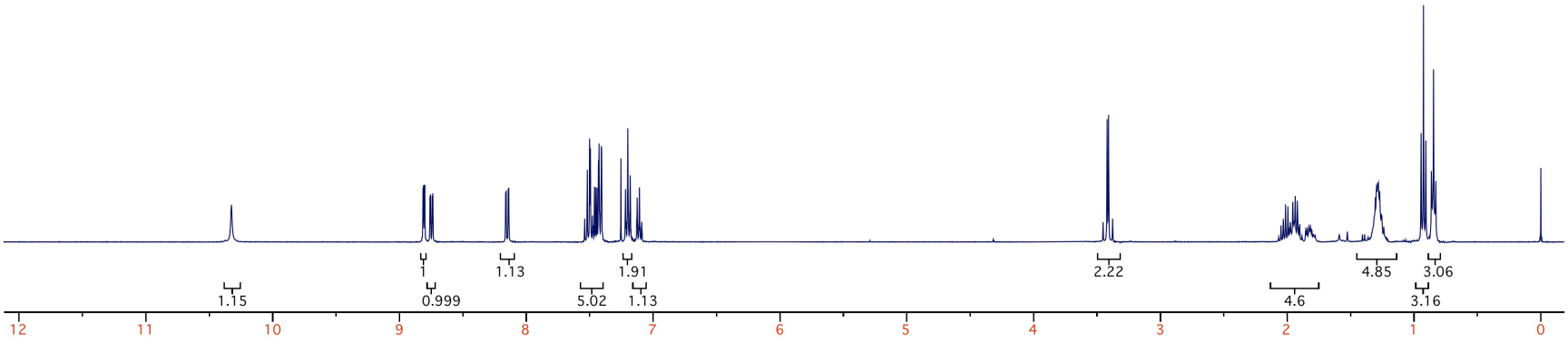
H
Bu
SPh
N

2c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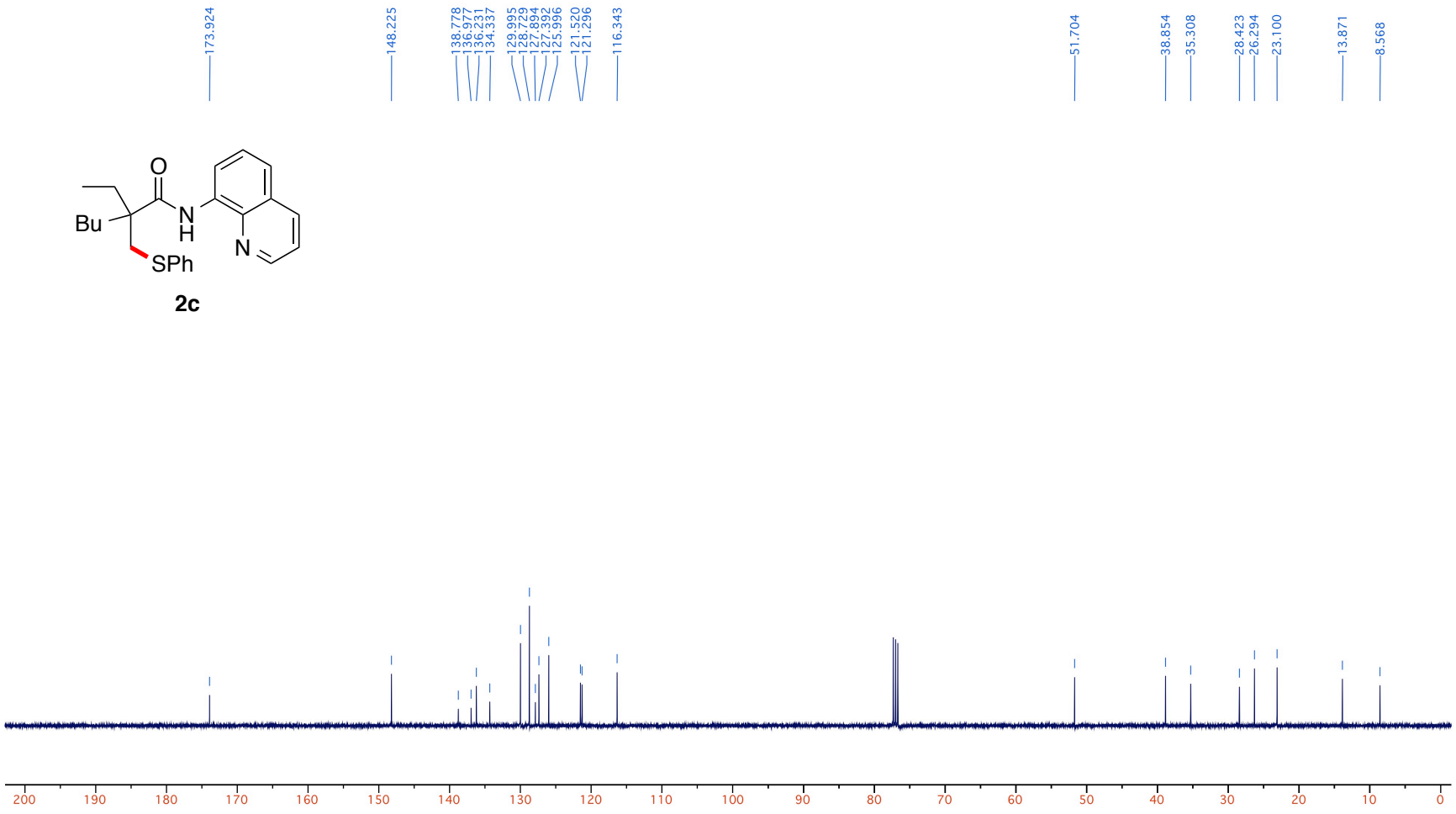
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H
Bu
SPh
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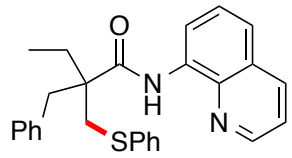
2c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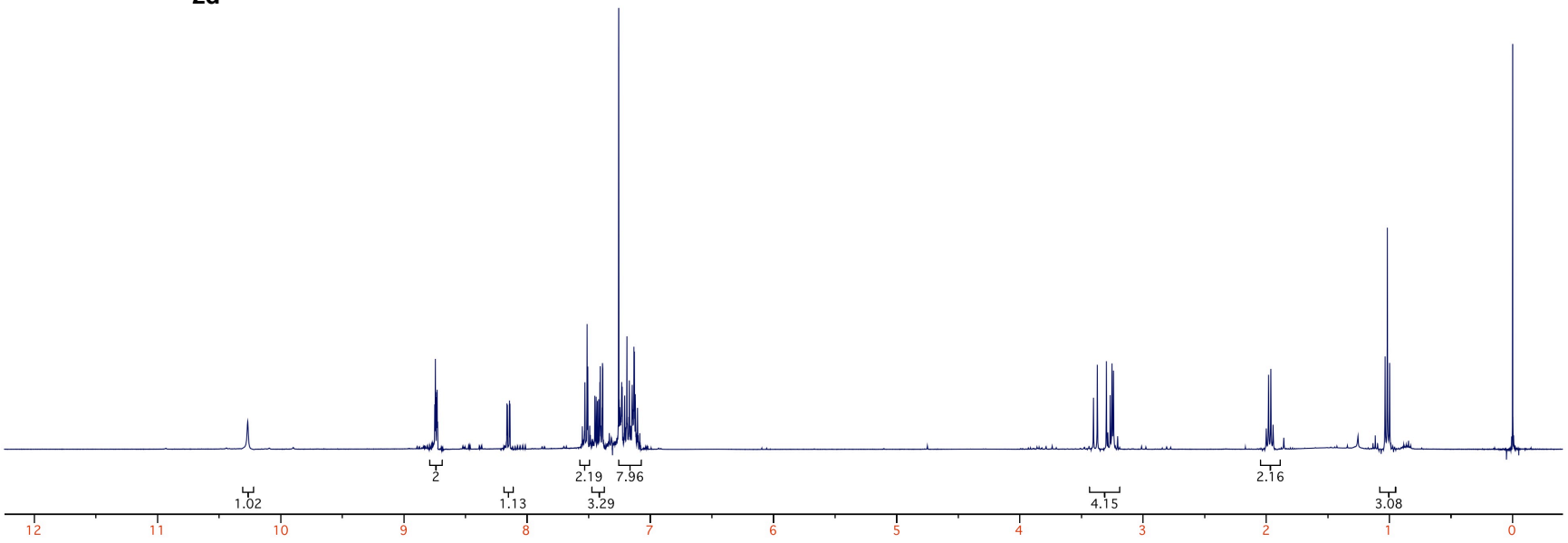
H
N
Ph
SPh

2d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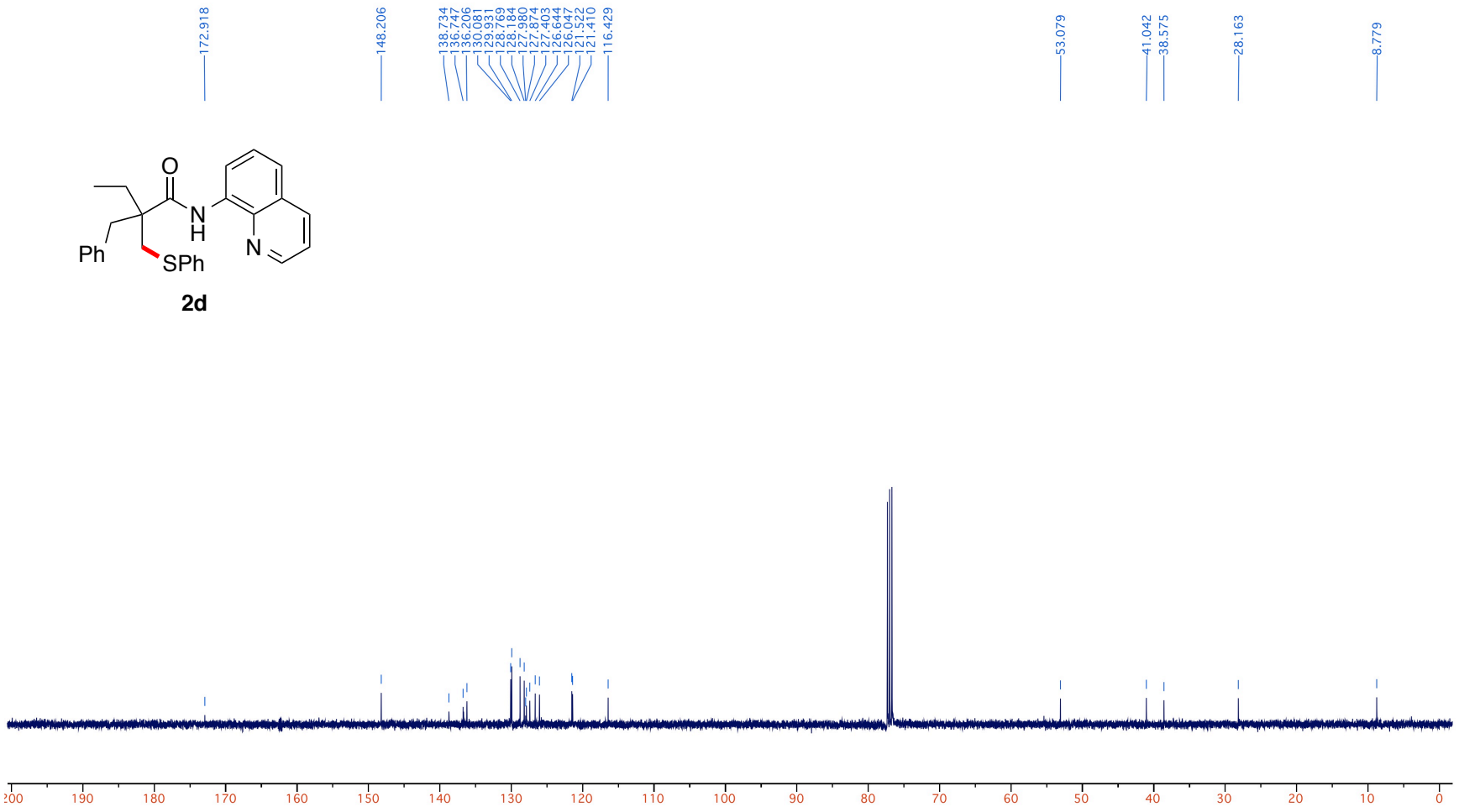
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SPh
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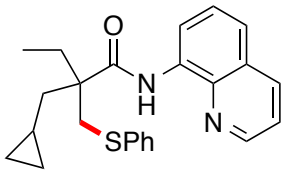
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SPh

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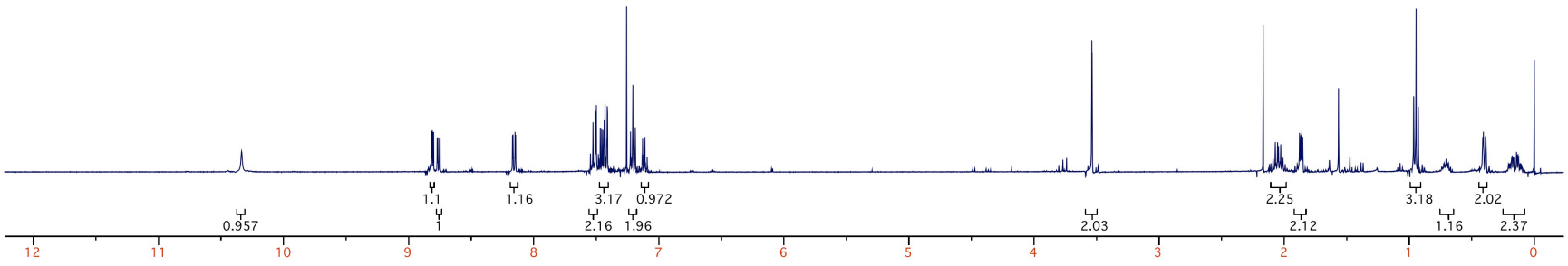
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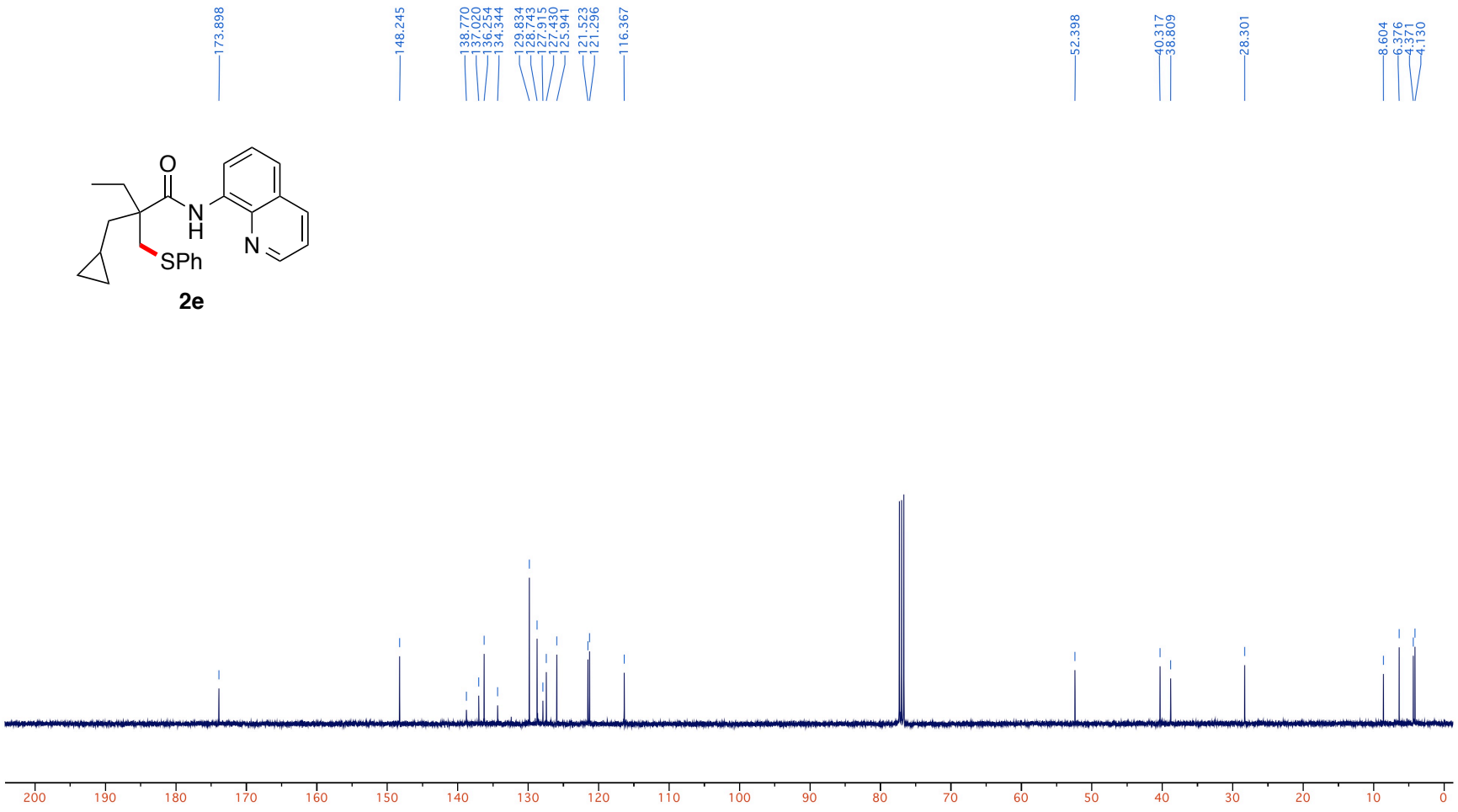
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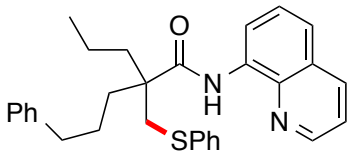
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Ph
SPh

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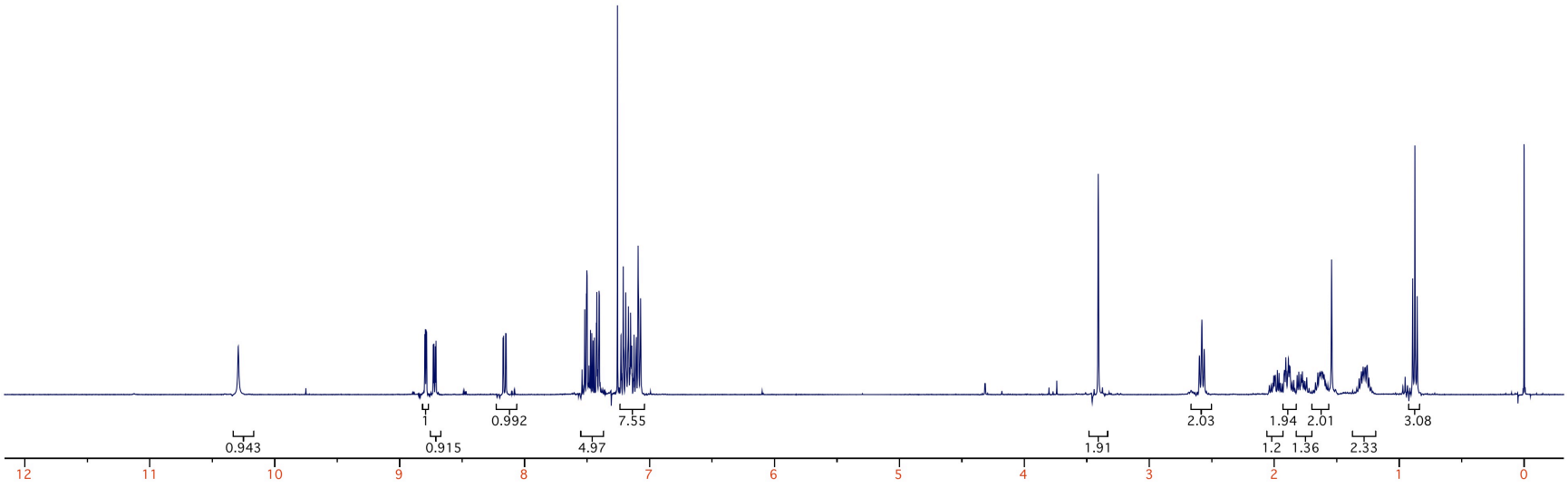
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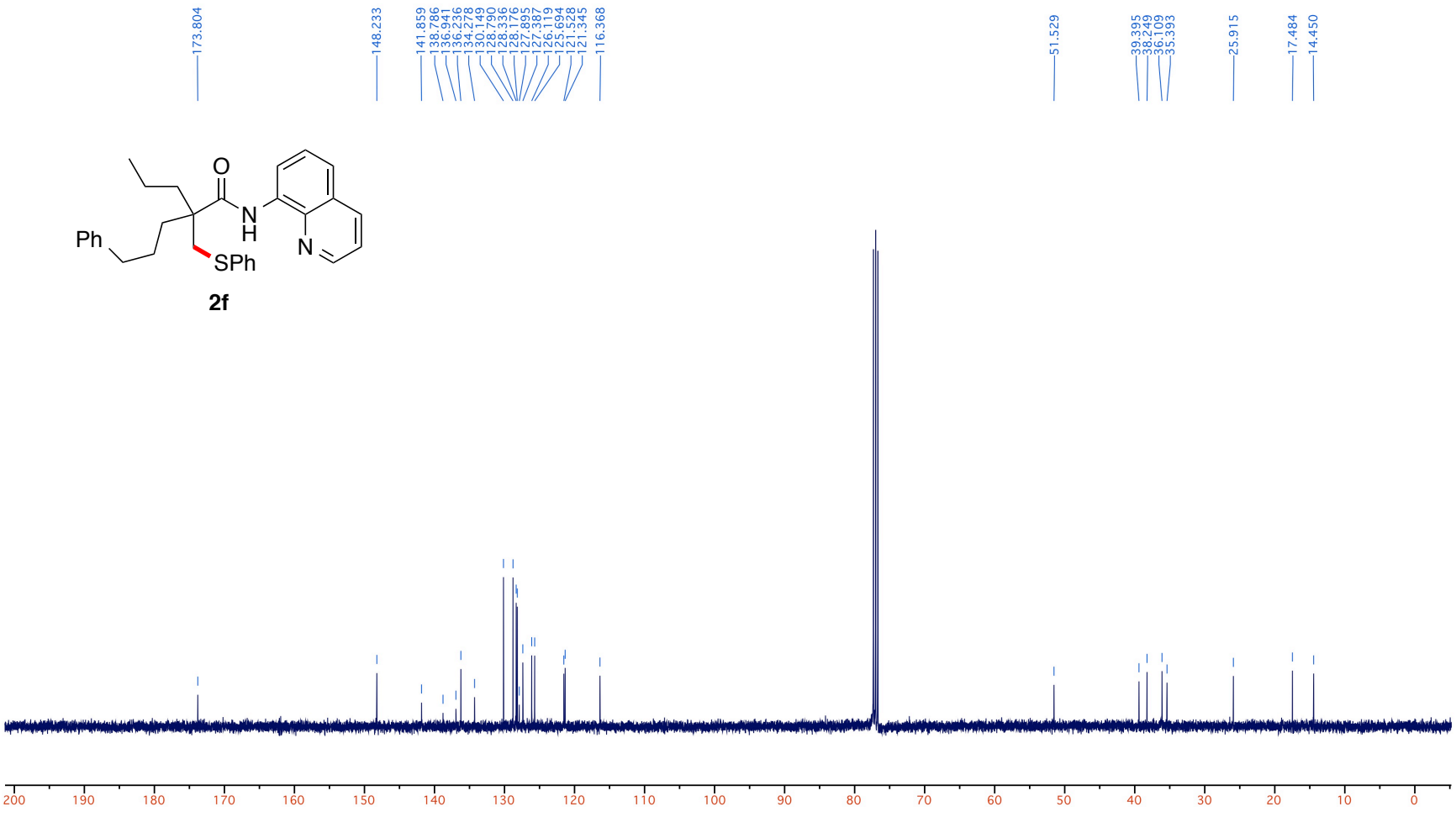
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H
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Ph
SPh
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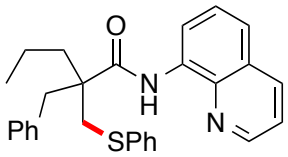
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SPh

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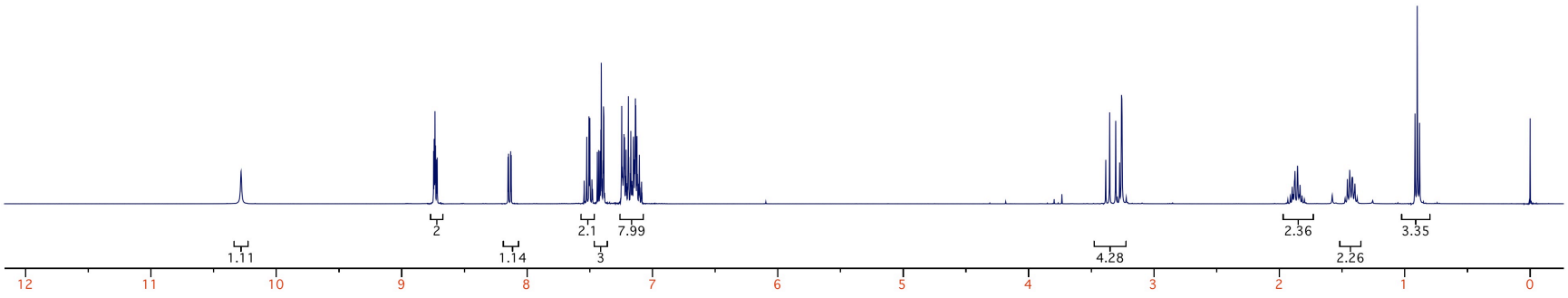
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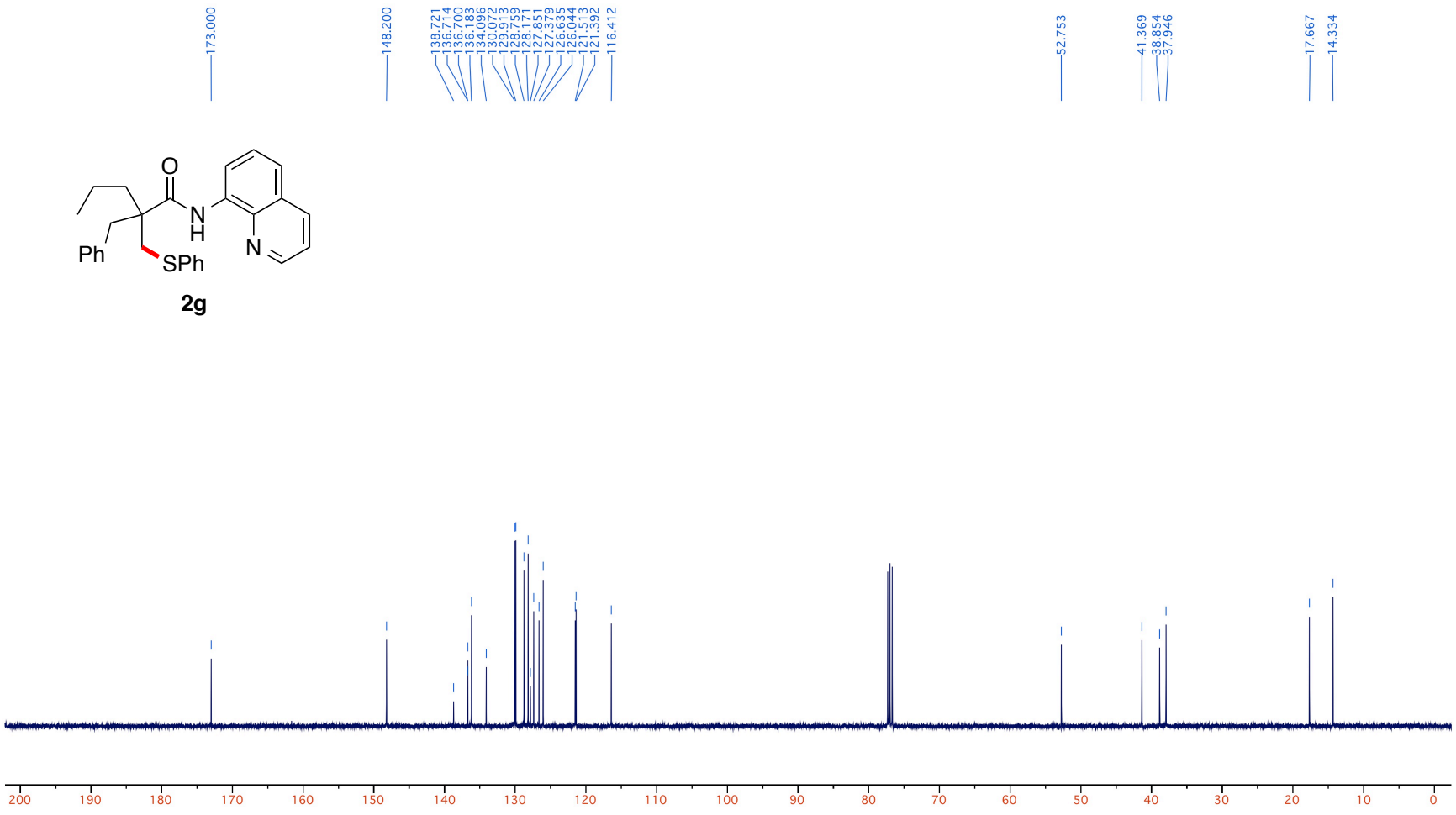
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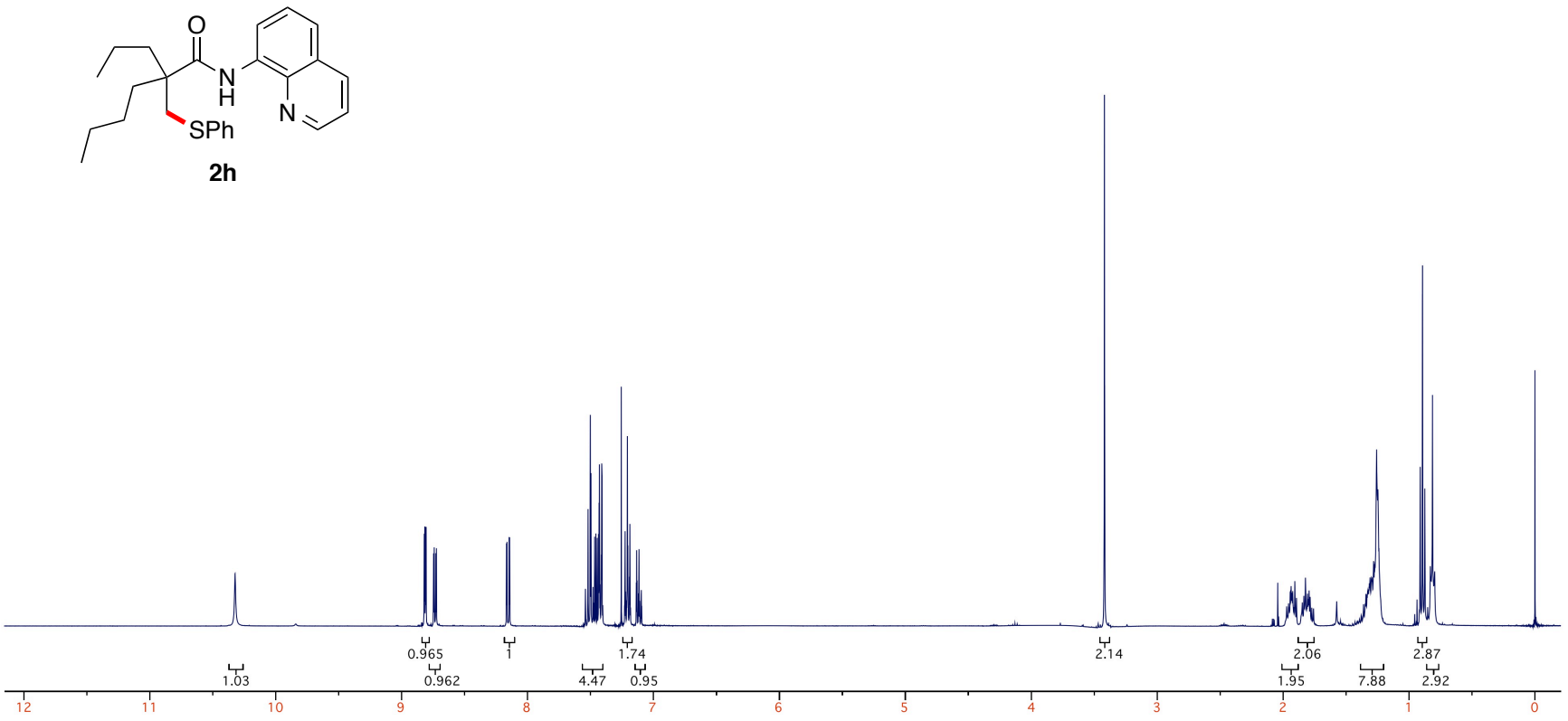
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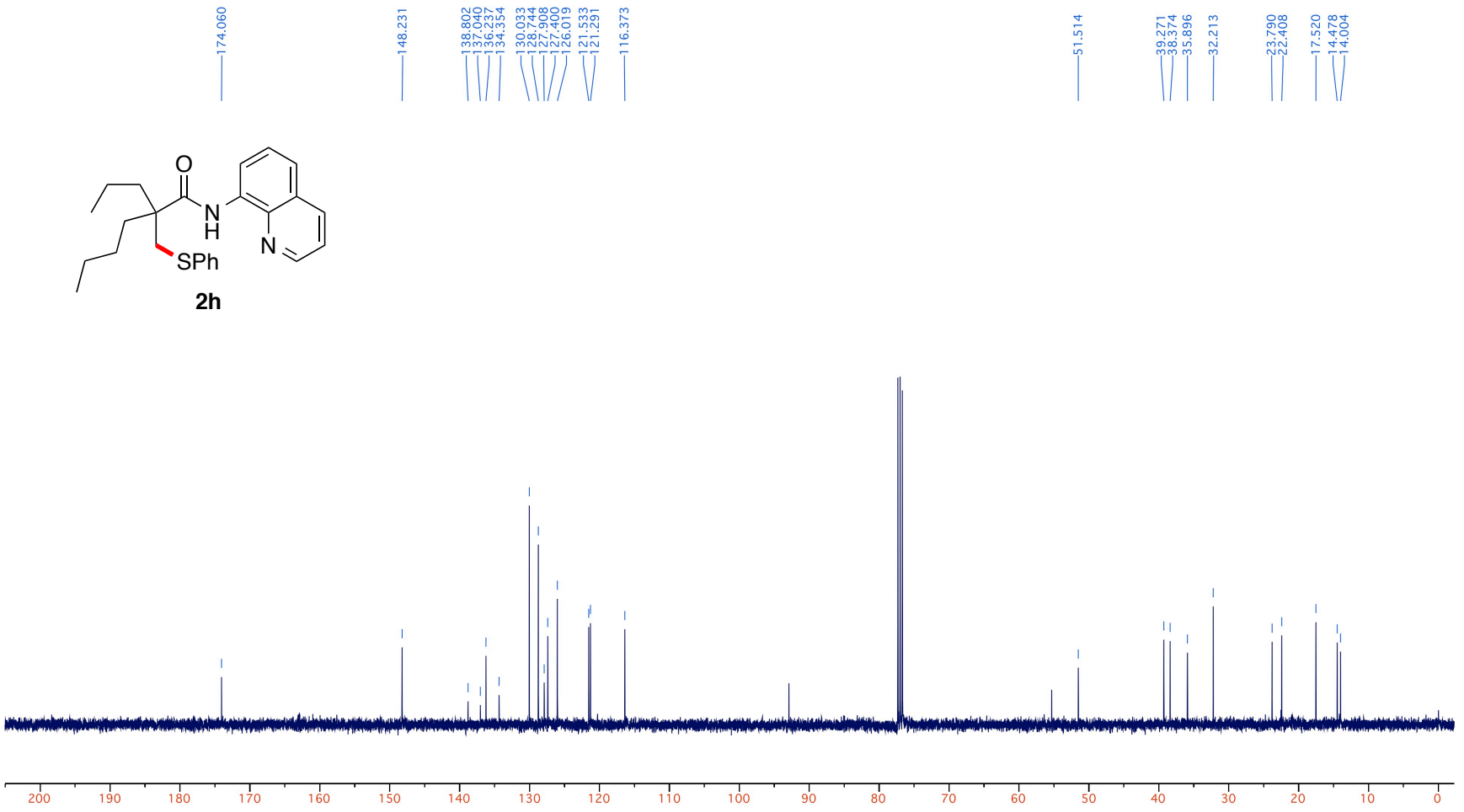
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H
N
SPh
2h
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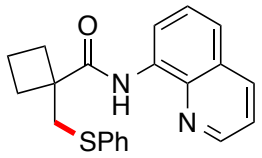
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SPh

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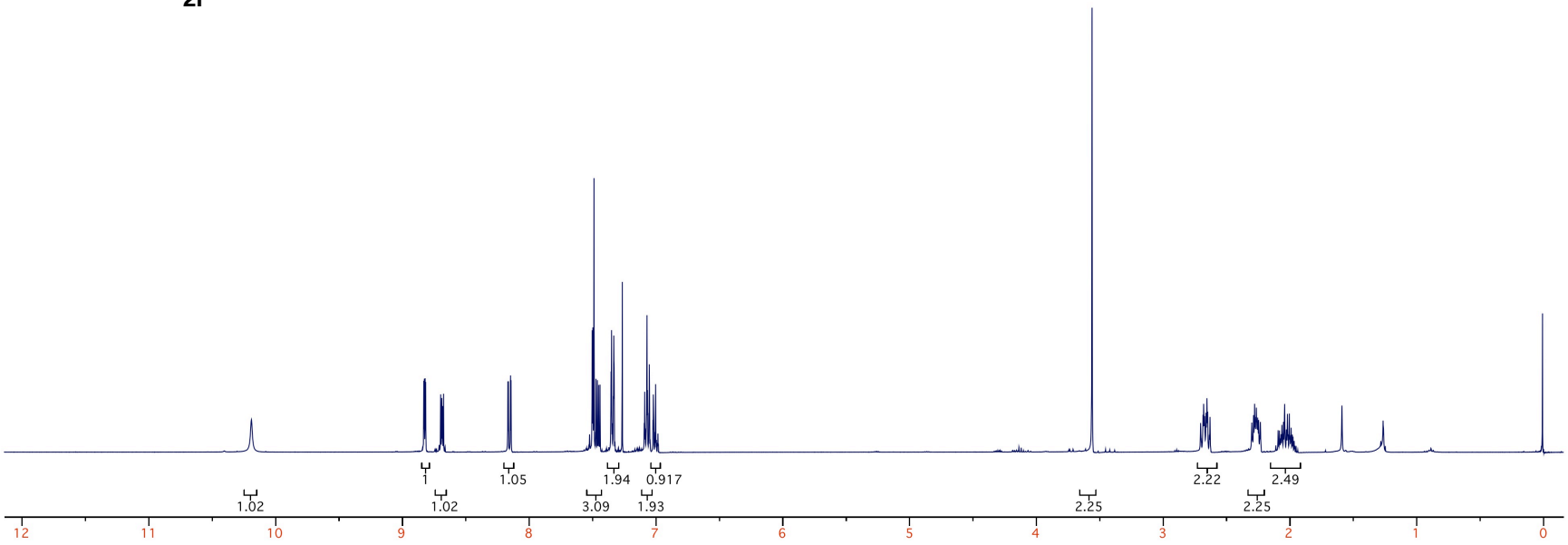
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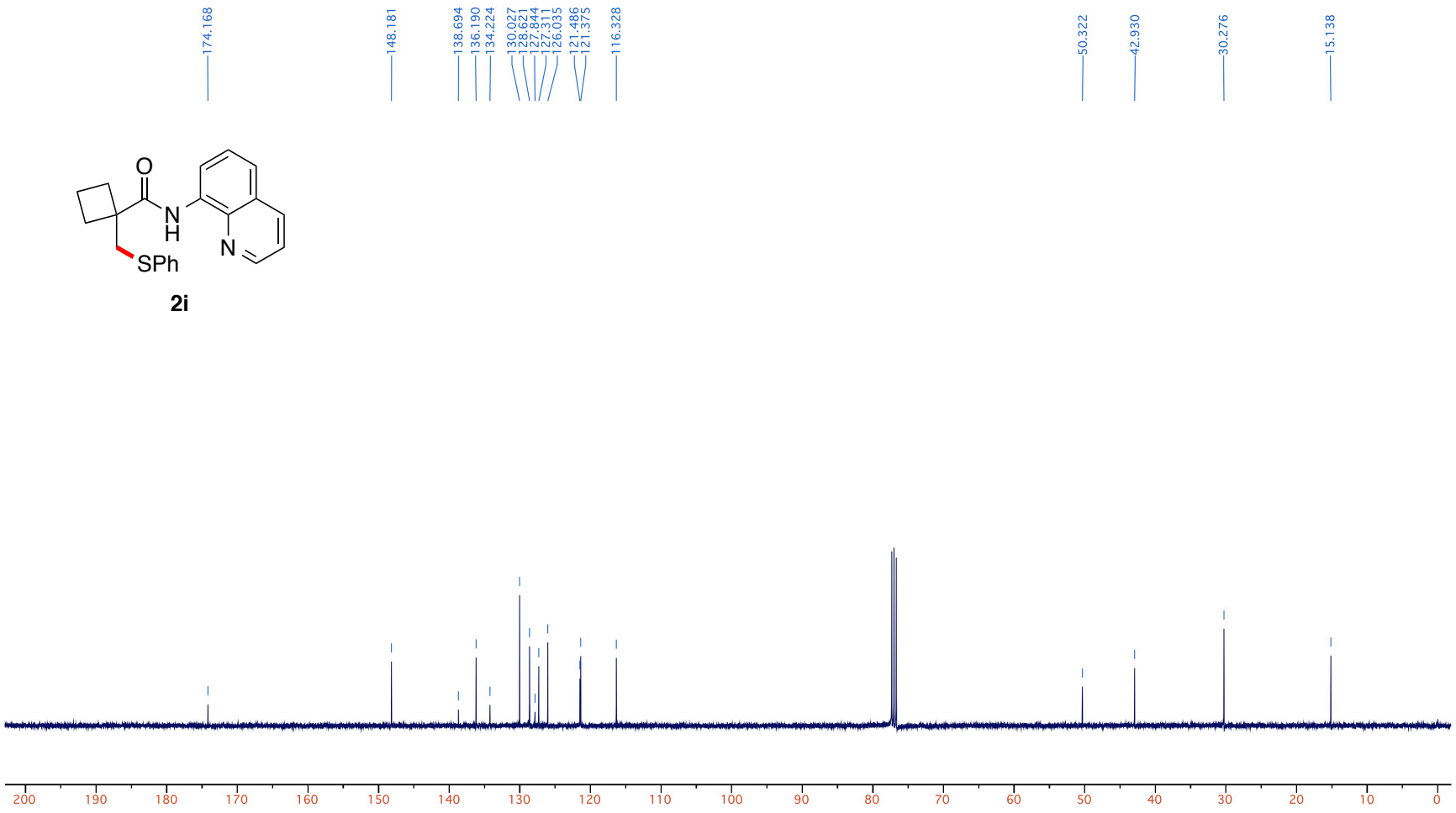
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30.276
15.138
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N
H
N
SPh
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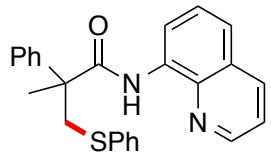
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SPh

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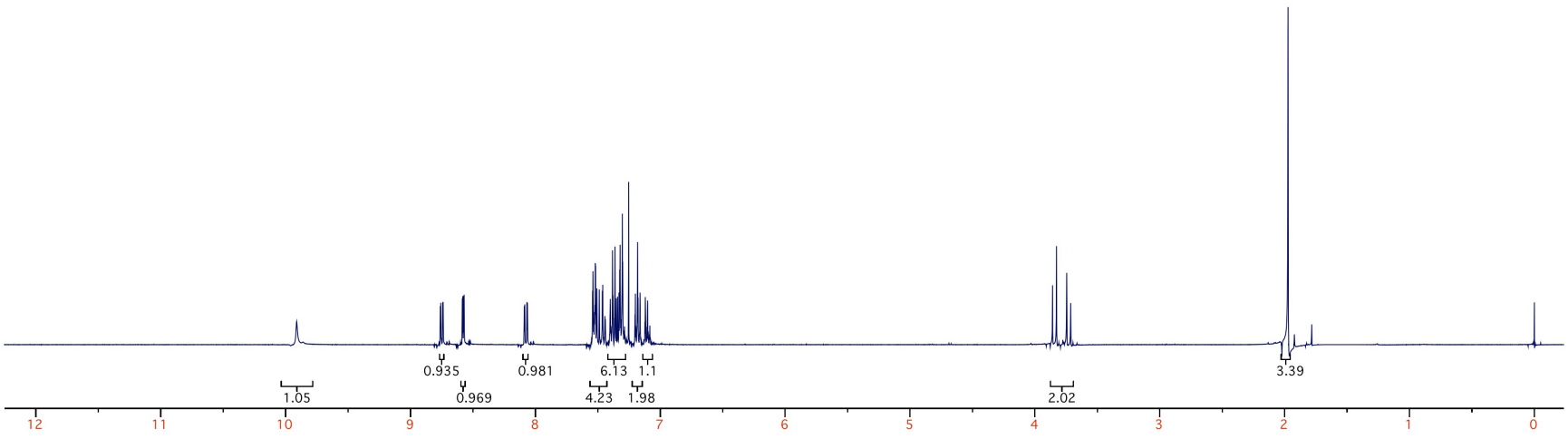
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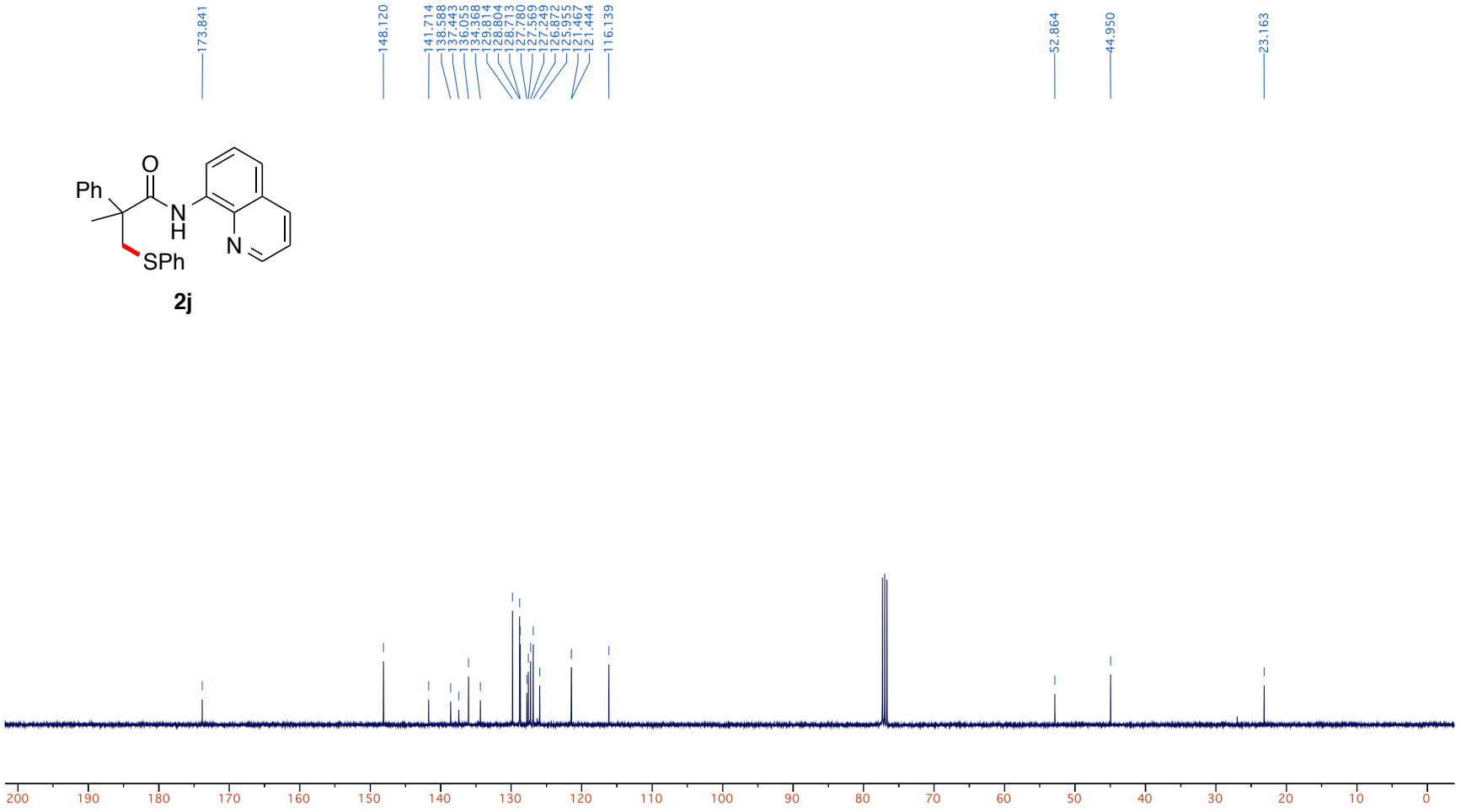
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125.955
121.467
121.444
116.139
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44.950
23.163
Ph
O
N
H
SPh
N
2j
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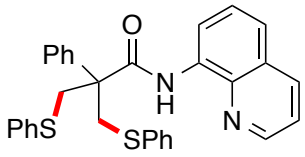
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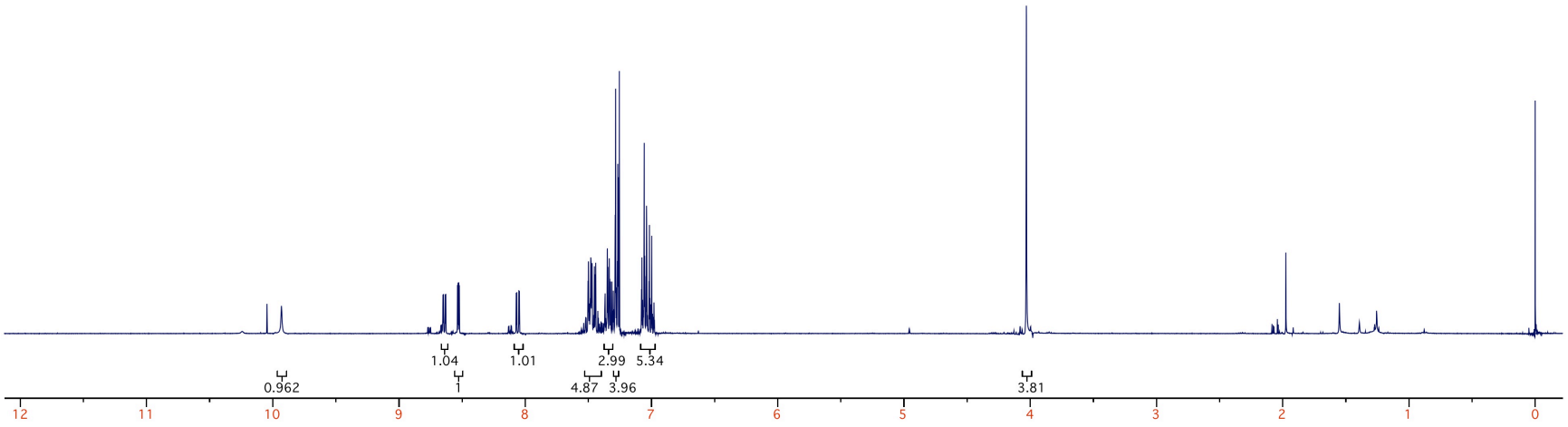
SPh
N

2j-di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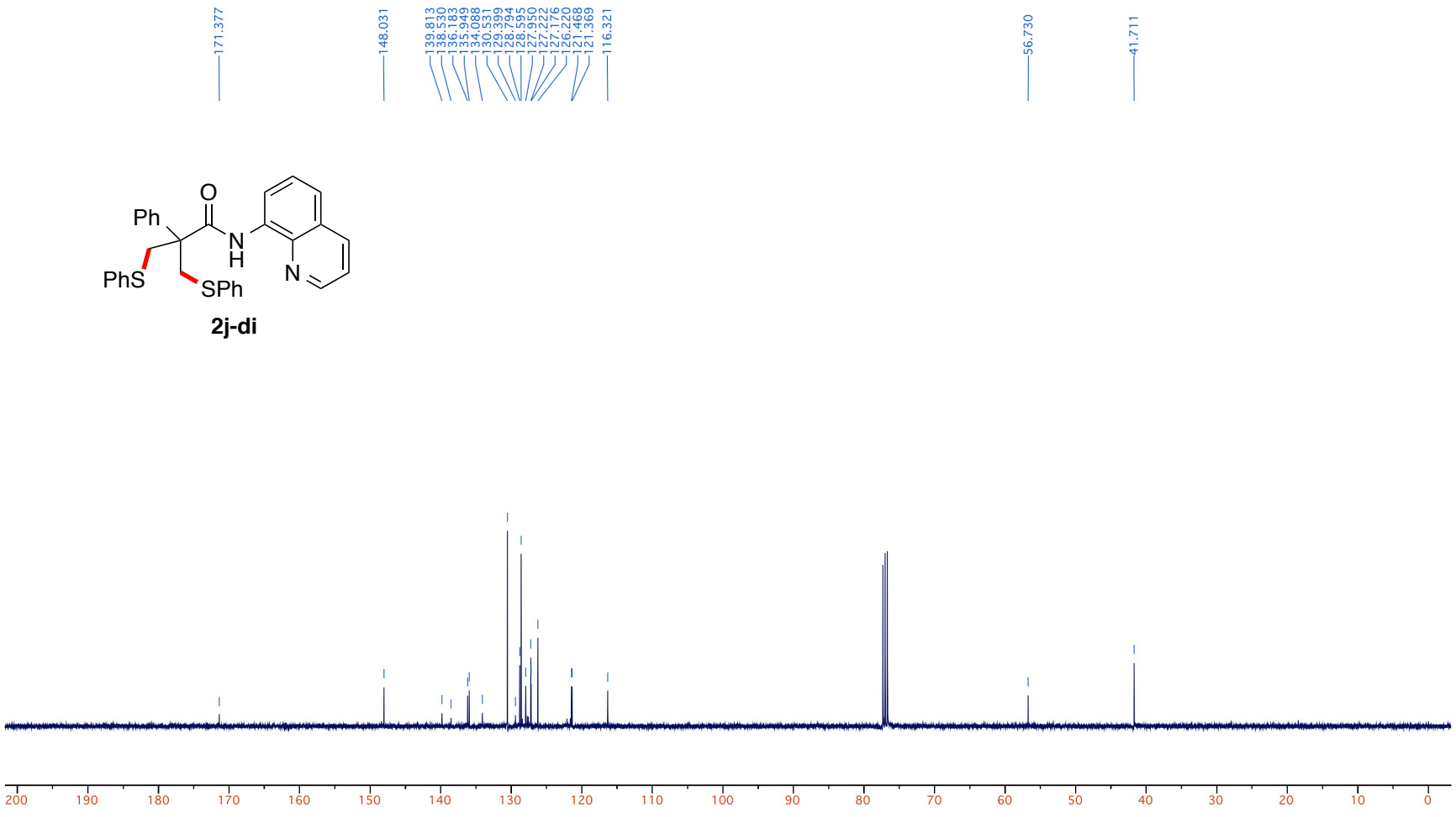
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127.222
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126.220
121.468
121.369
116.321
56.730
41.711
O
Ph
N
H
PhS
SPh
N
2j-di
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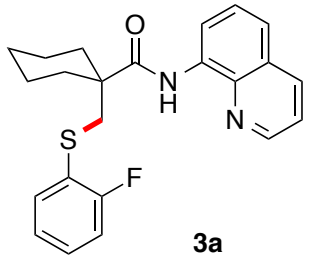
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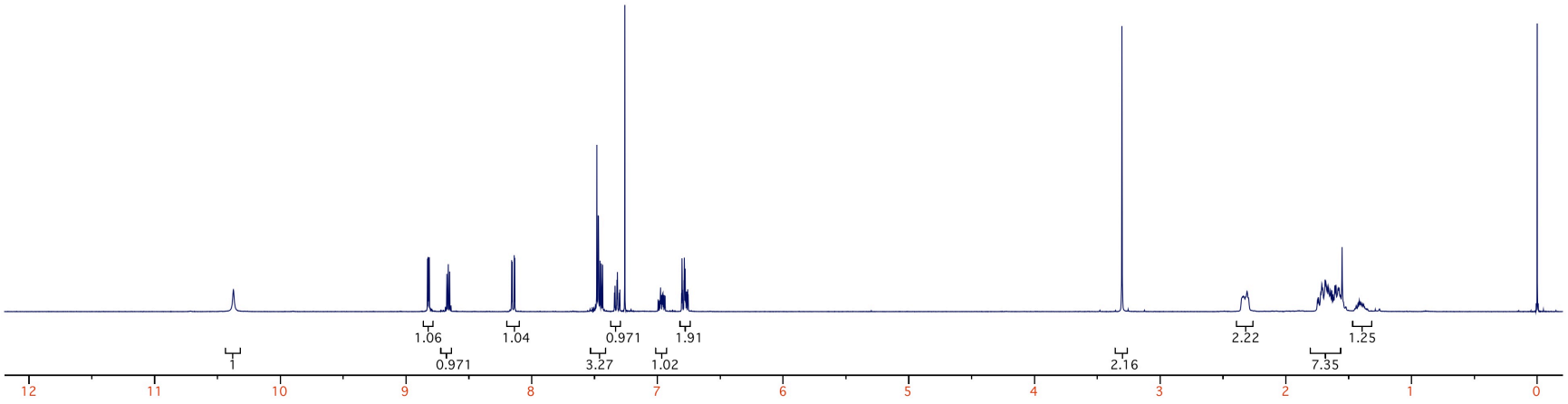
H
N
S
F

3a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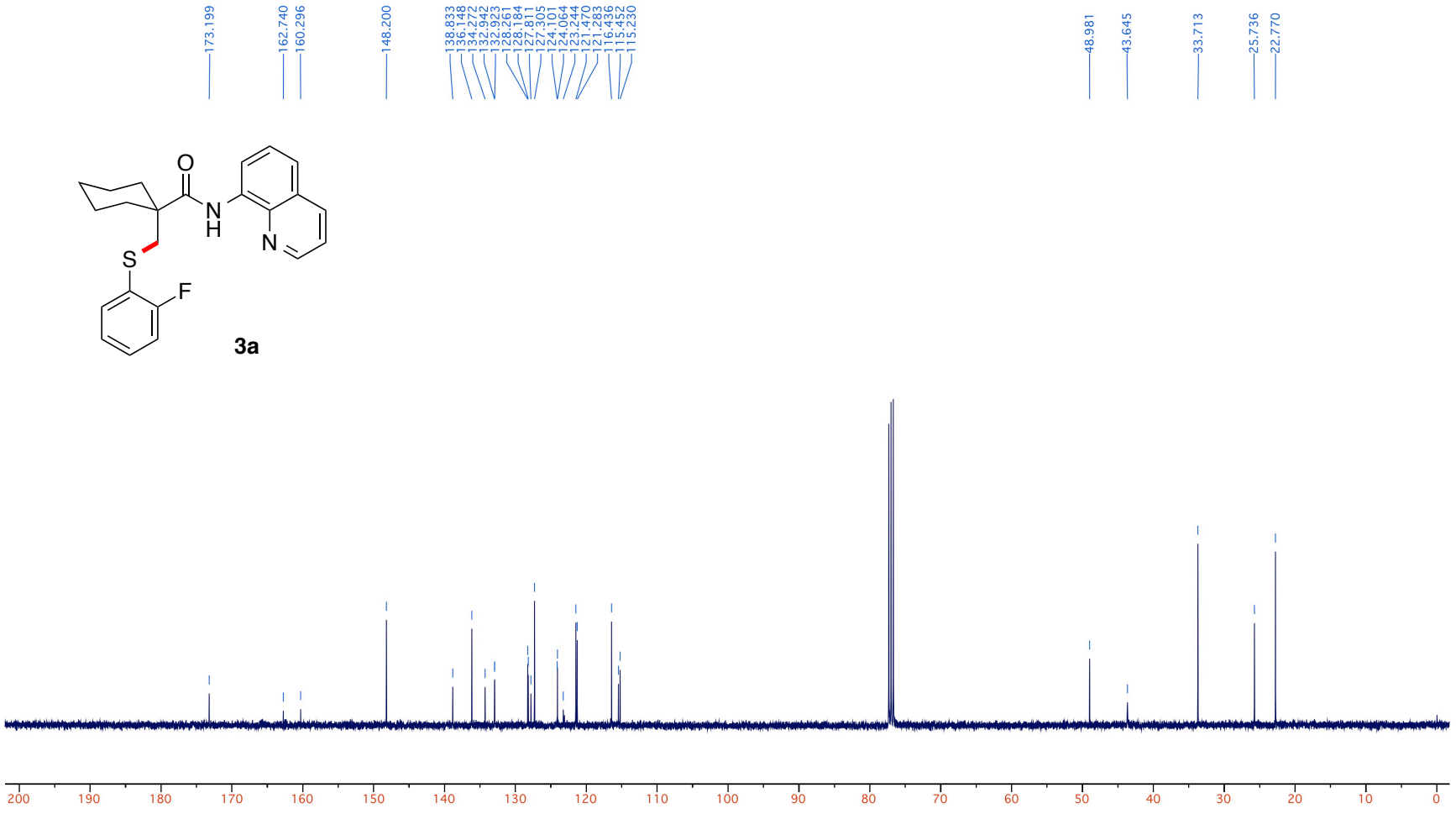
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124.064
123.244
121.470
121.283
116.436
115.452
115.230
48.981
43.645
33.713
25.736
22.770
O
N
H
N
S
F
3a
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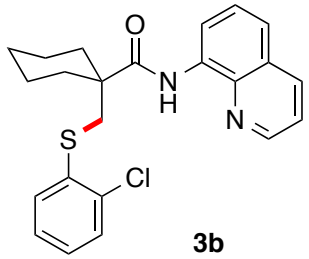
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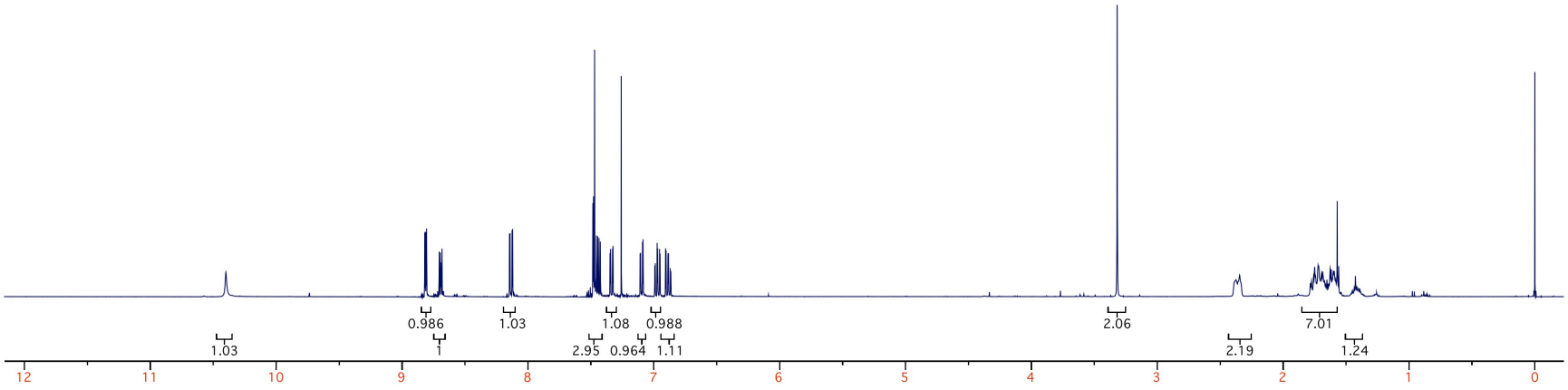
H
N
S
Cl

3b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2.95
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2.19
1.24
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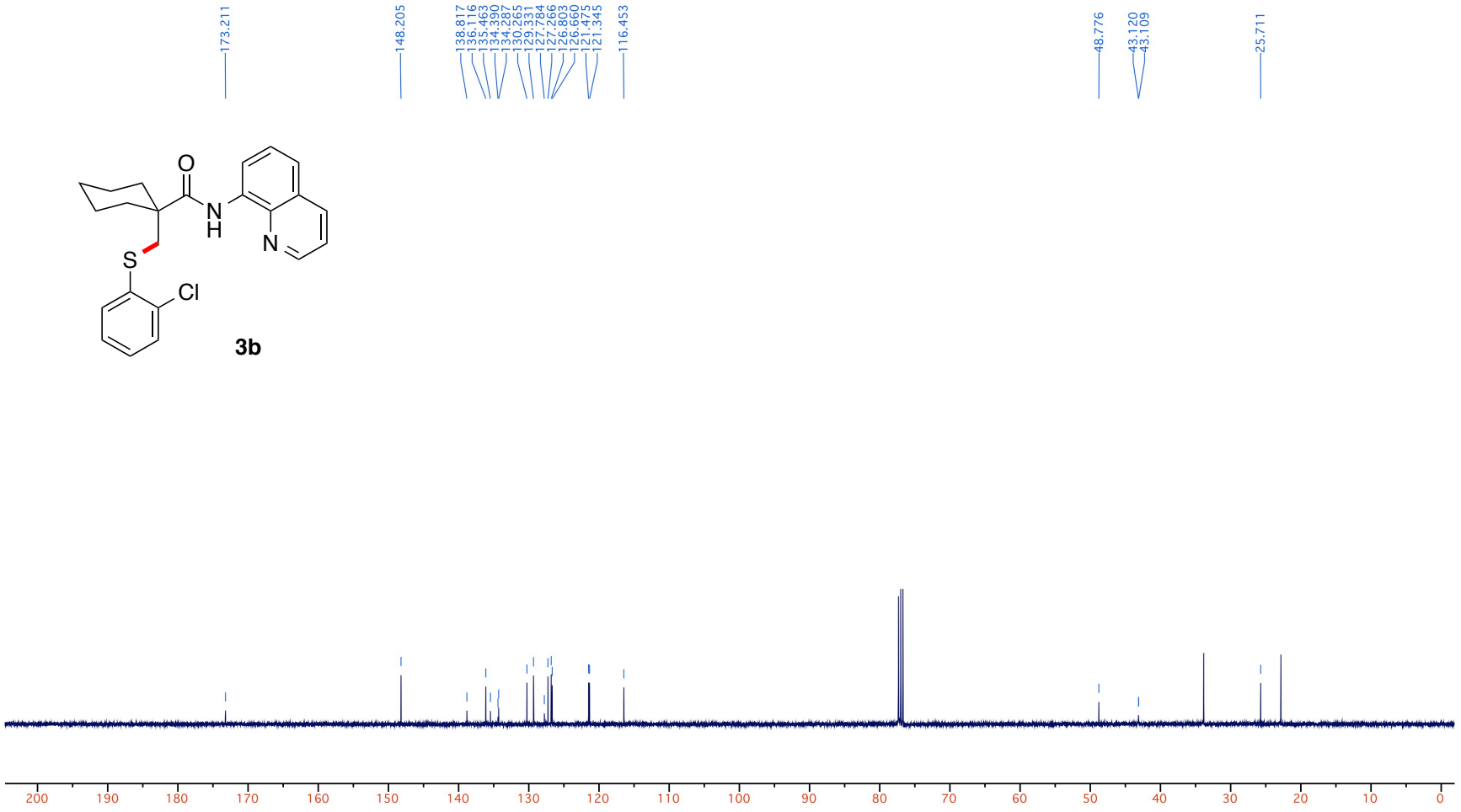
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43.109
25.711
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N
H
N
S
Cl
3b
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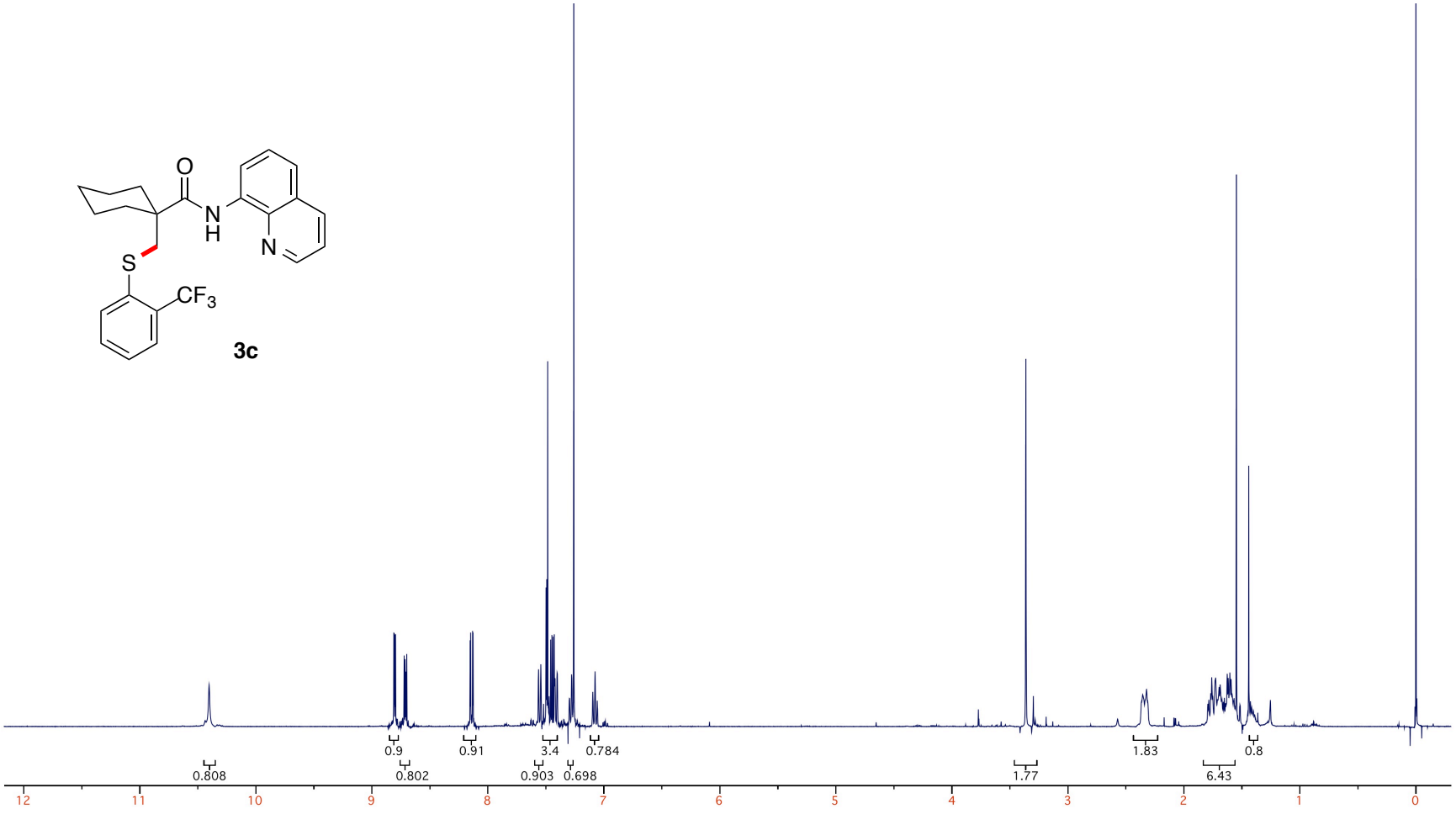
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H
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S
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0.903
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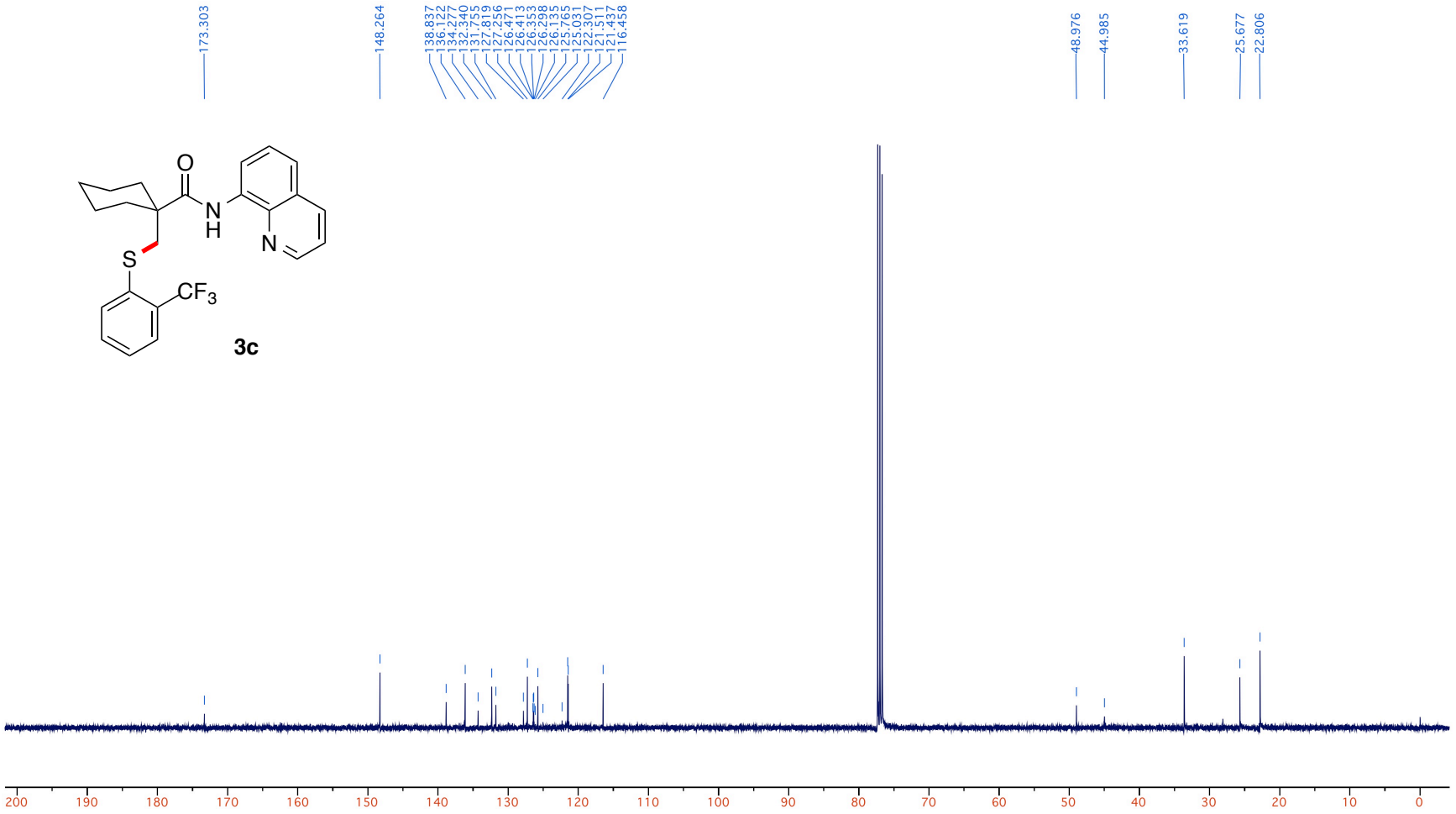
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121.511
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22.806
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H
N
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CF3
3c
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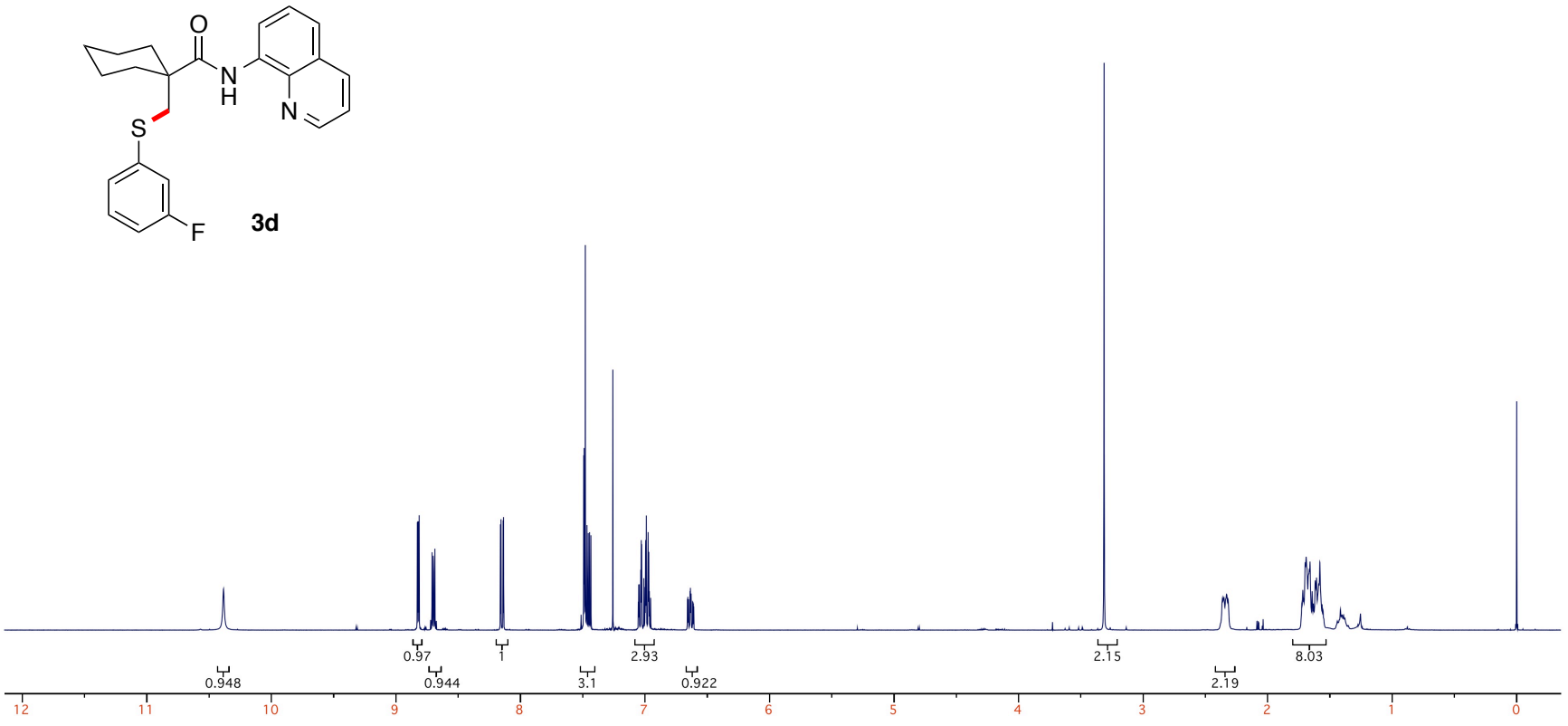
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H
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S
F
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0.922
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7
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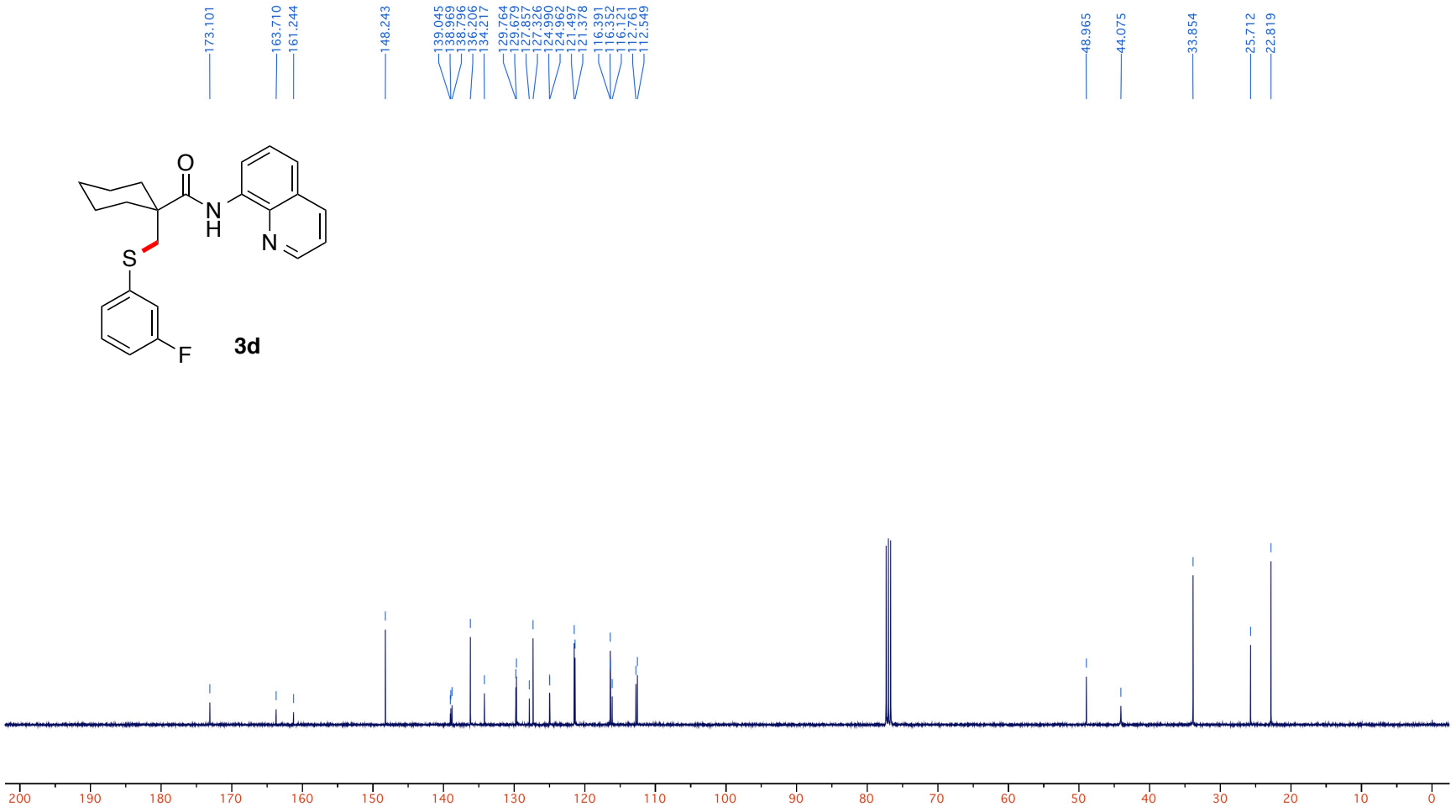
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N
S
F
3d
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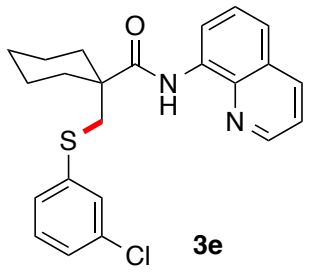
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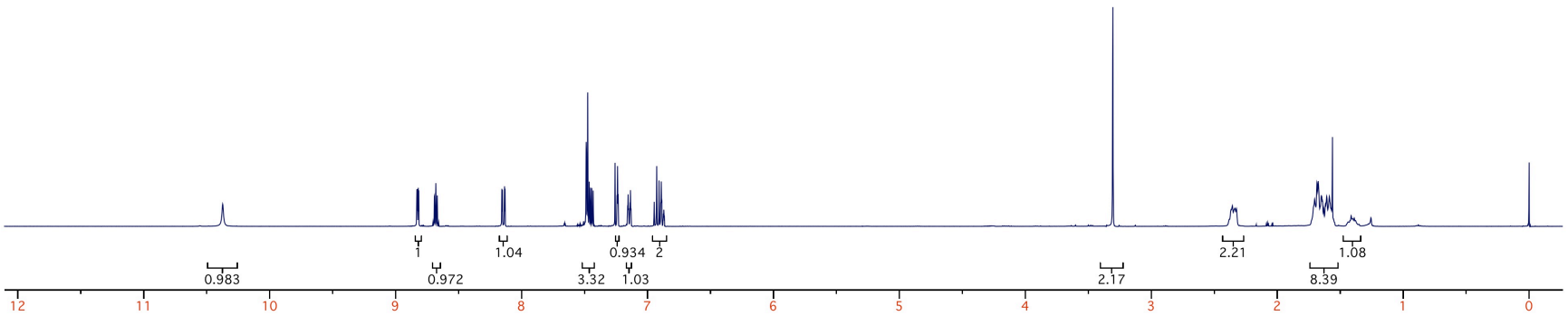
N
S
Cl

3e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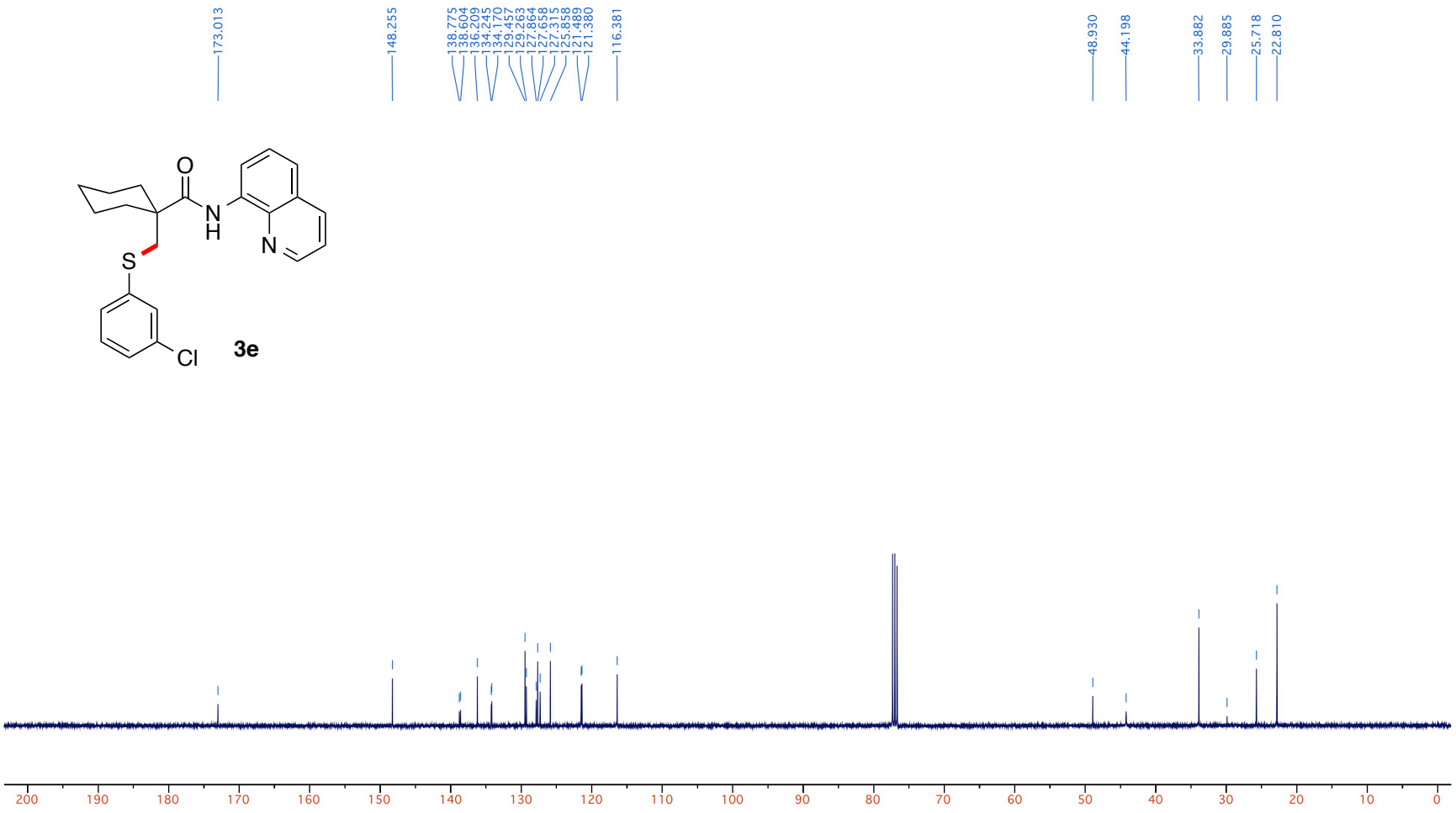
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125.858
121.489
121.380
116.381
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29.885
25.718
22.810
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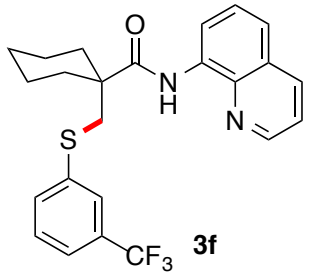
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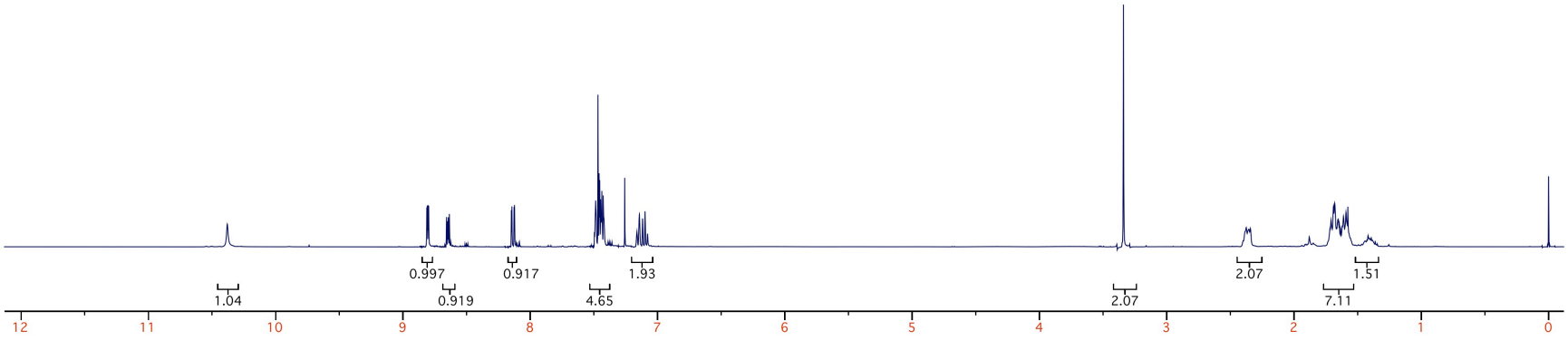
N
S
CF3

3f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1
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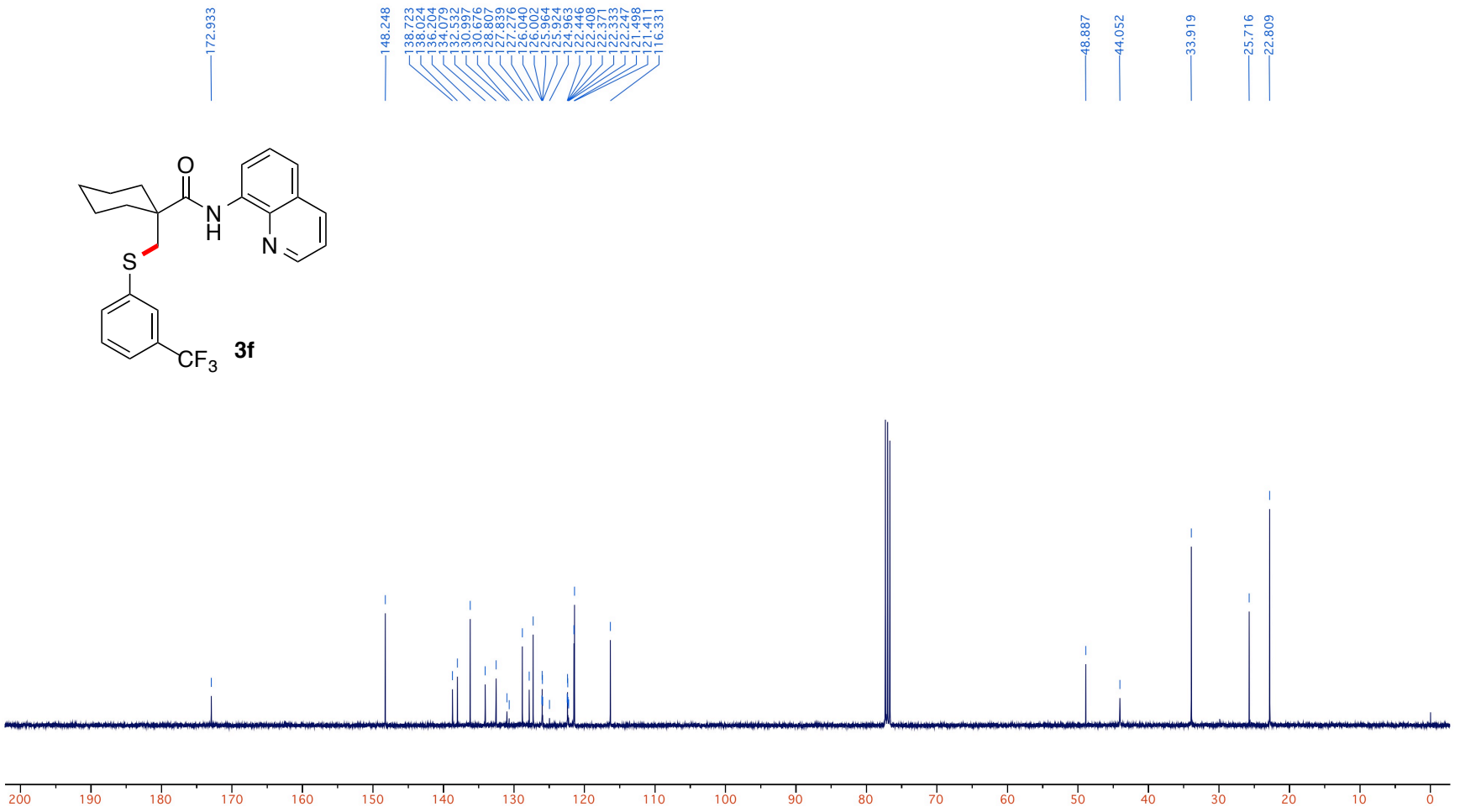
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44.052
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25.716
22.809
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H
N
S
CF3
3f
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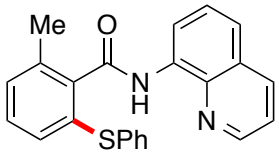
Me
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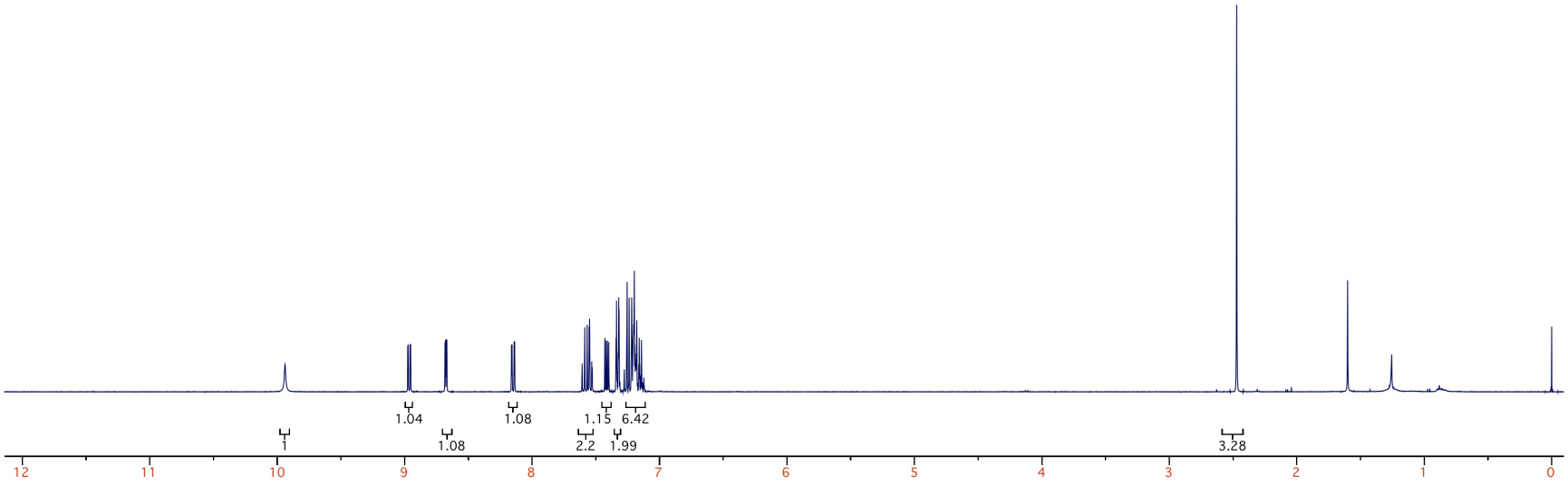
H
N
SPh

4a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7
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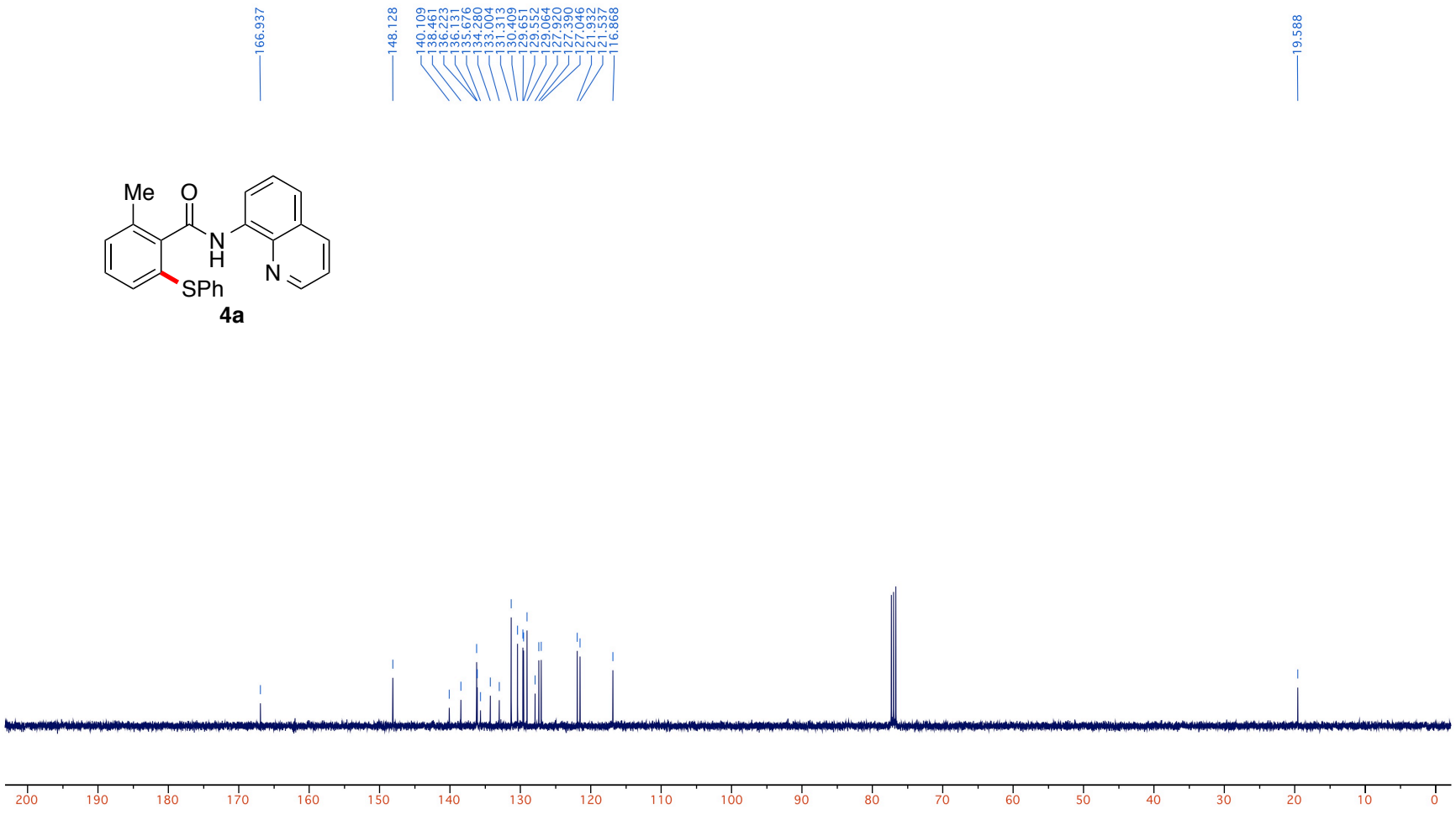
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127.924
127.390
127.046
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121.537
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19.588
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H
SPh
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4a
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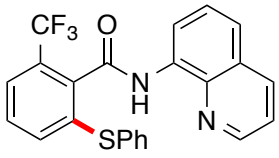
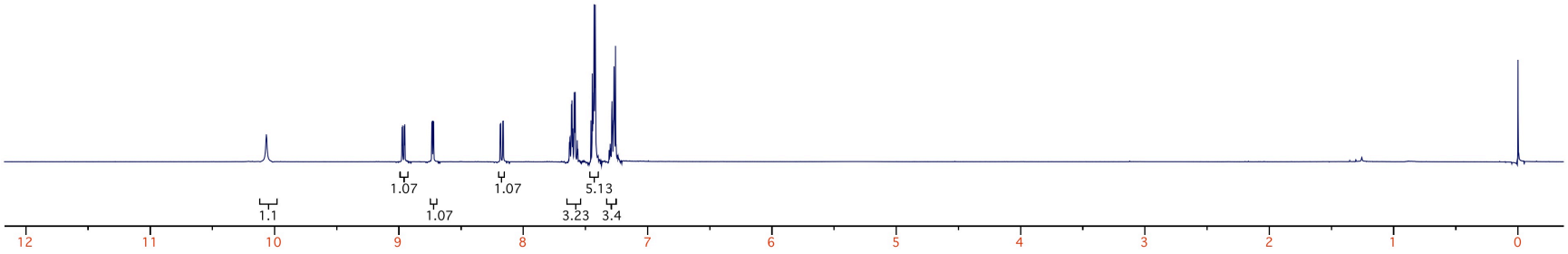
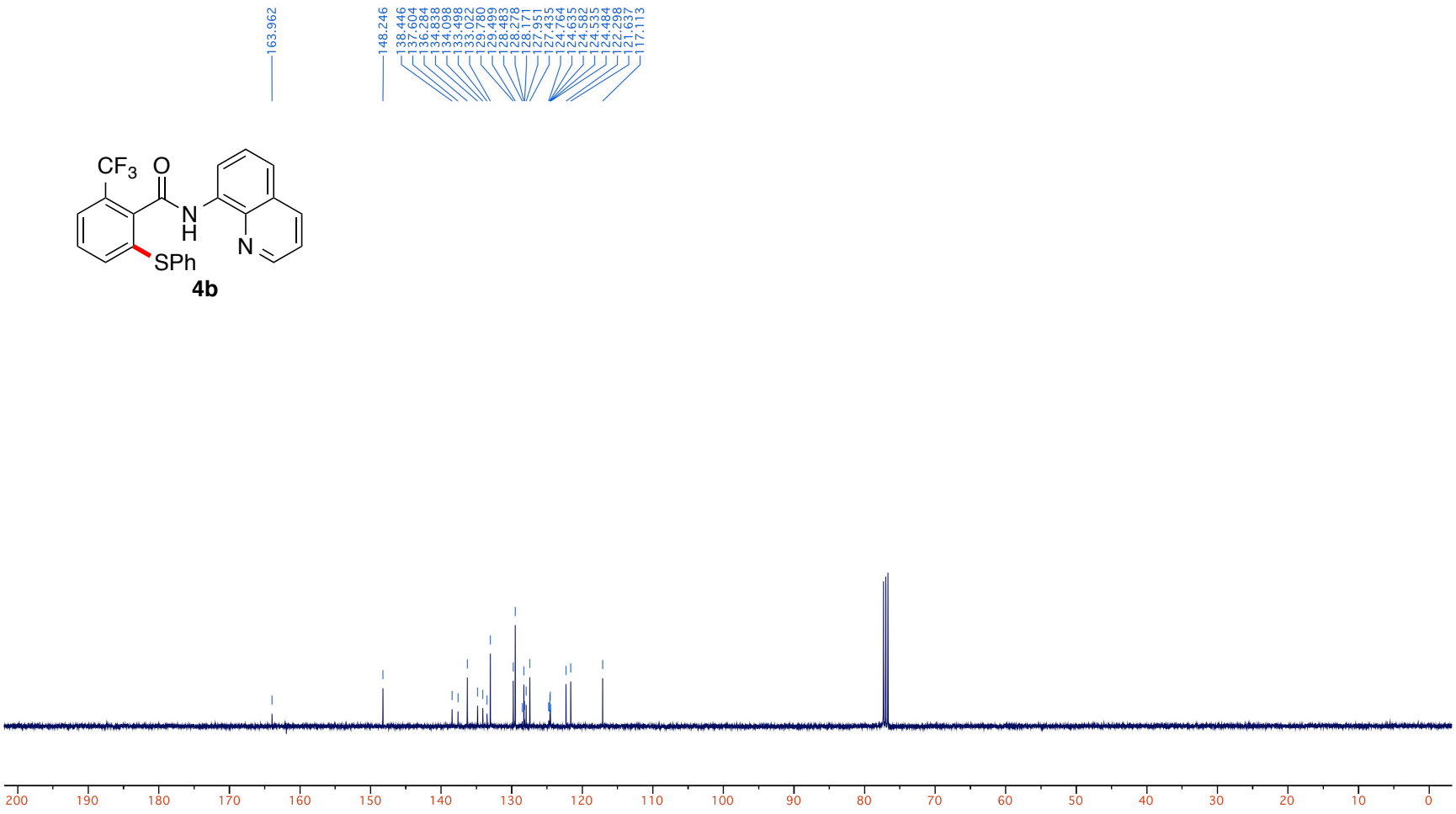


4b

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128.171
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127.435
124.764
124.635
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124.484
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121.637
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CF3
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H
N
SPh
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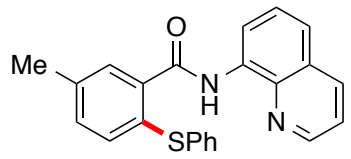
Me
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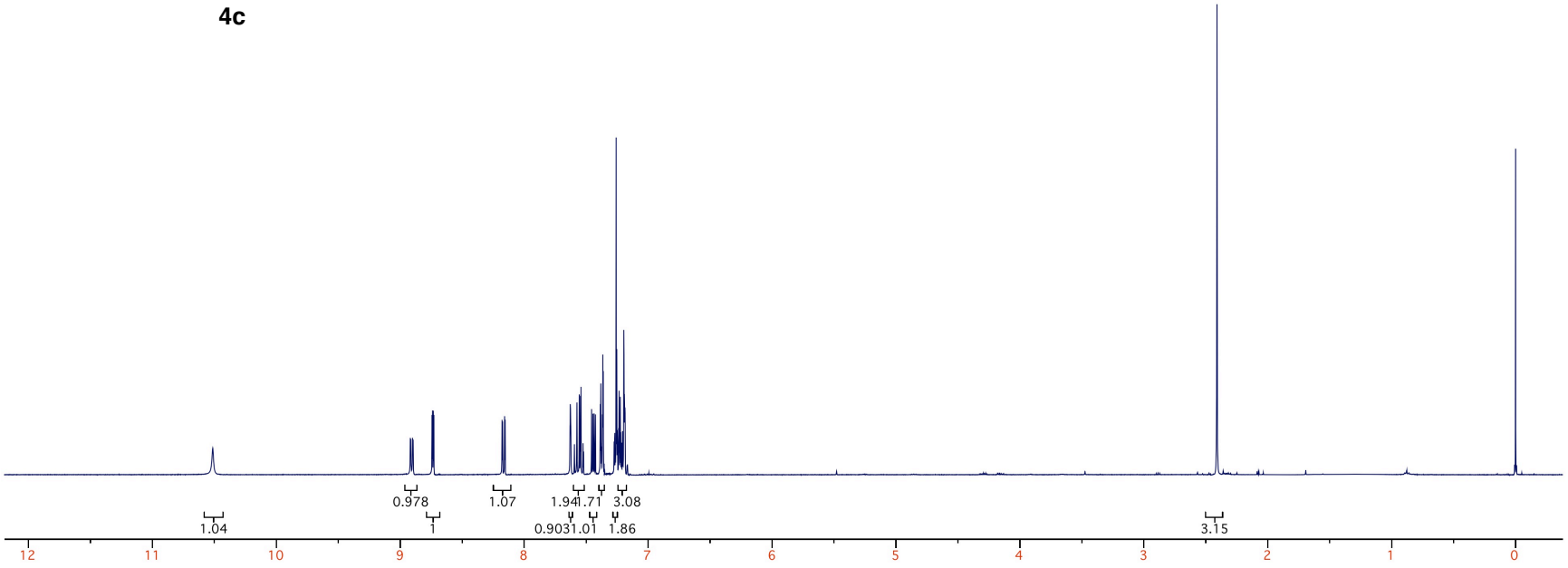
N
H
N
SPh

4c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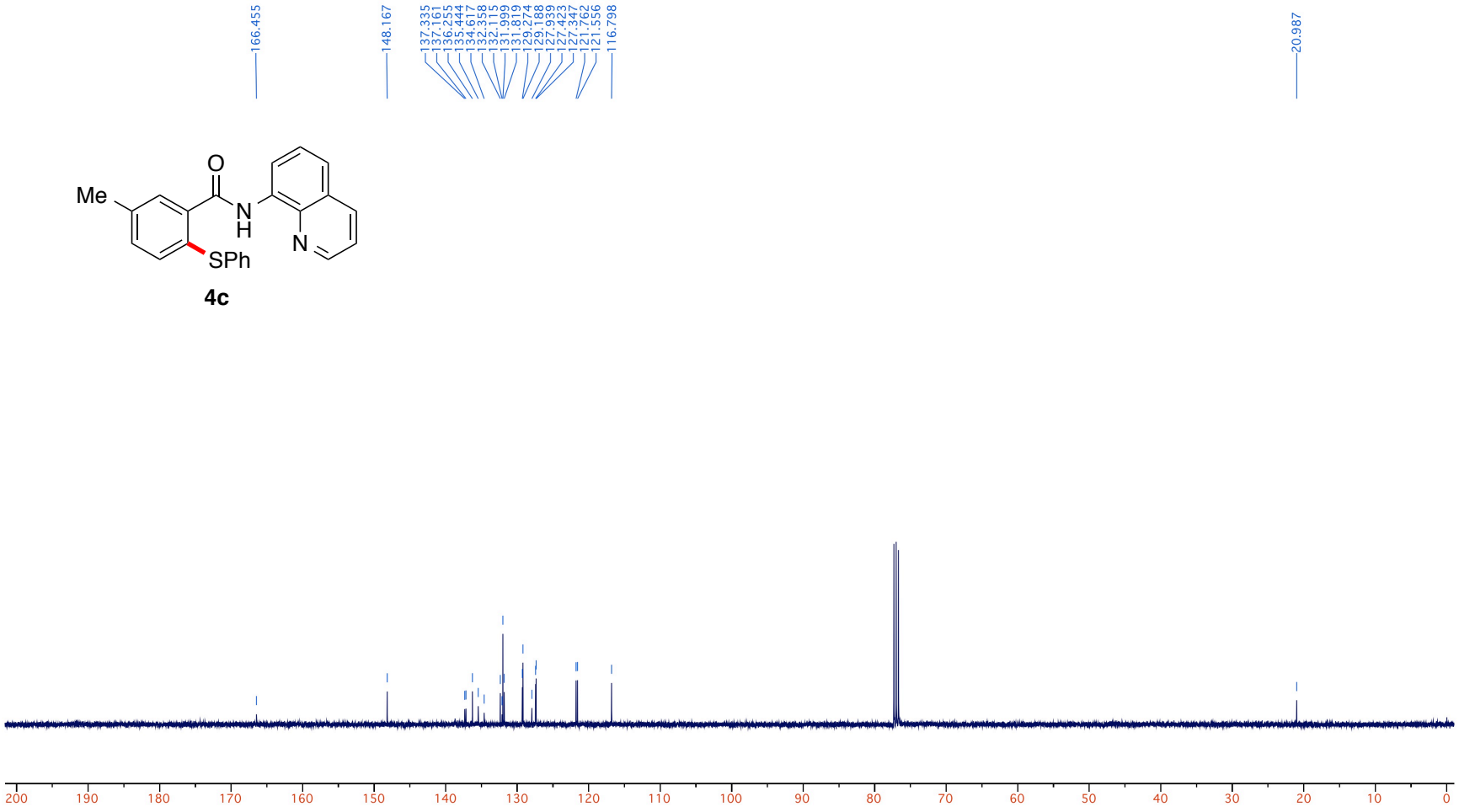
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20.987
Me
O
N
H
N
SPh
4c
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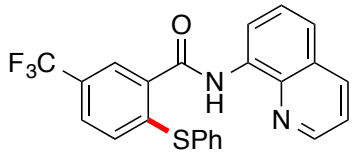
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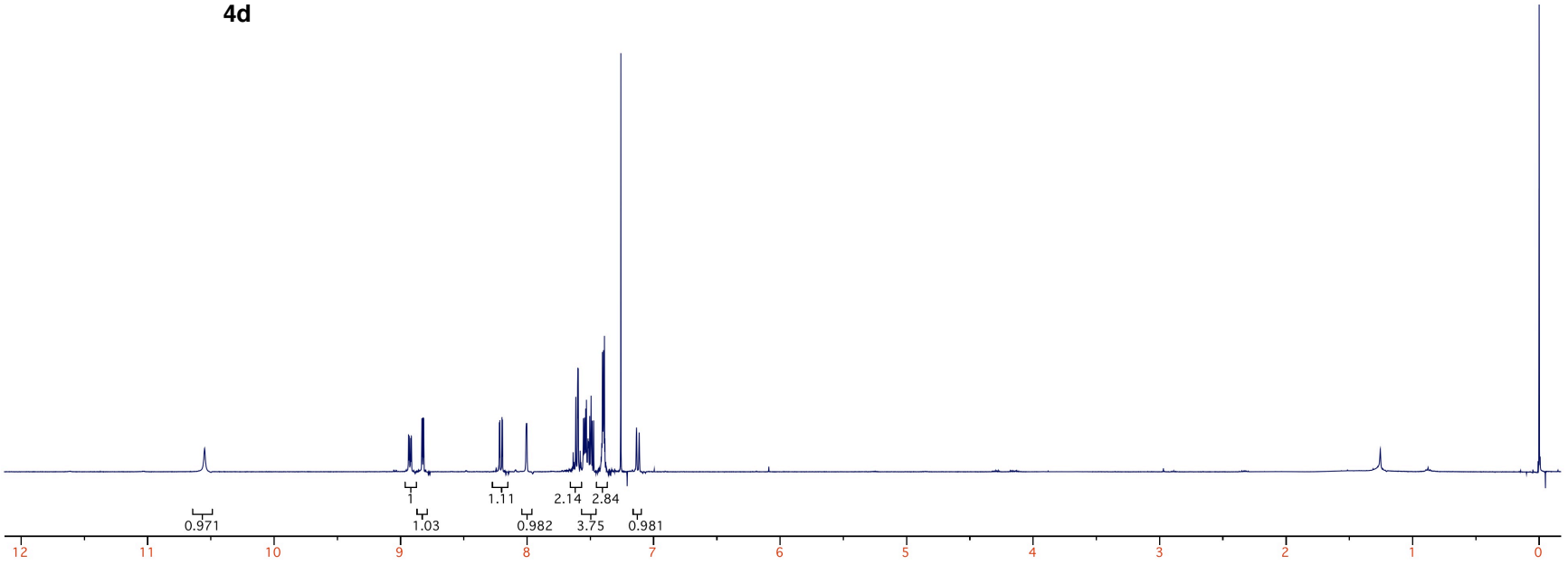
SPh

4d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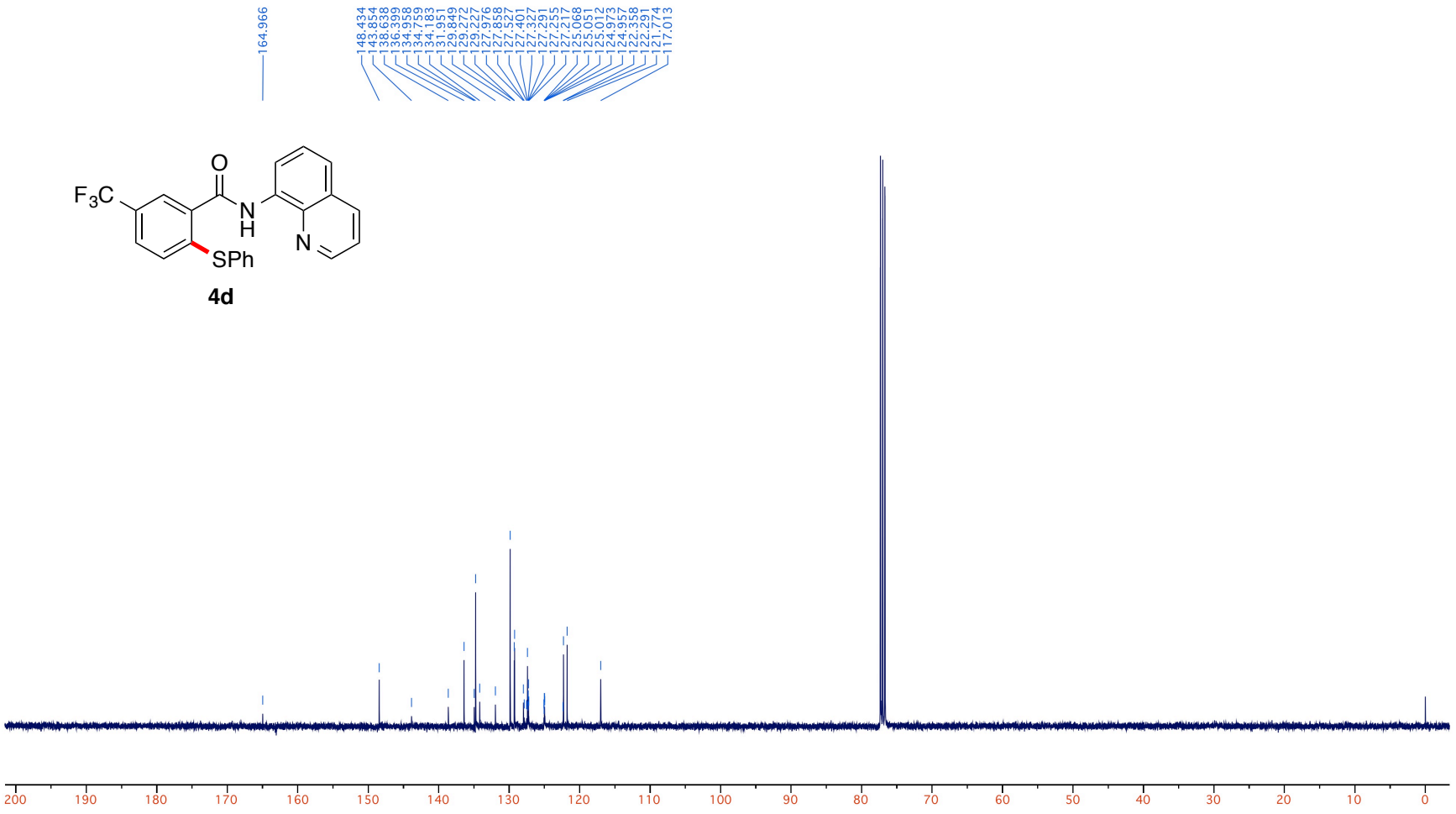
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127.401
127.327
127.291
127.255
127.217
125.068
125.051
125.012
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122.358
122.291
121.774
117.013
O
F3C
N
H
N
SPh
4d
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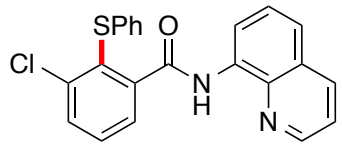
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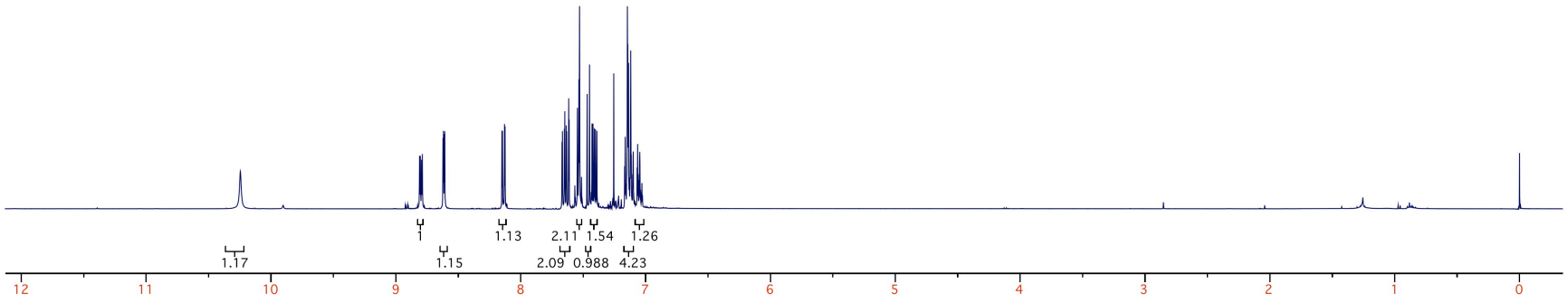
N

4e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1.17
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7
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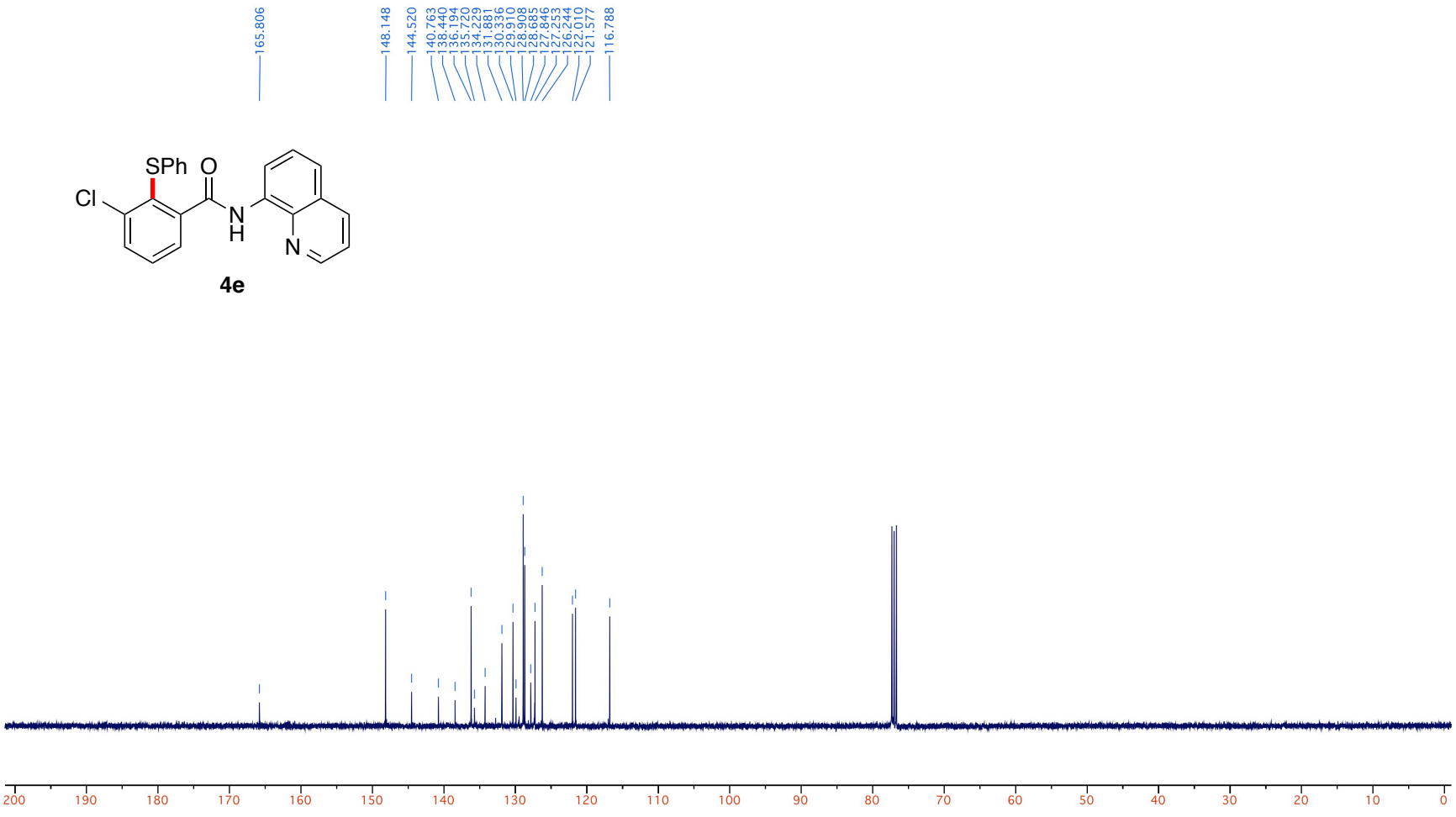
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134.229
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130.316
129.910
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128.685
127.846
127.253
126.244
122.010
121.577
116.788
SPh
O
Cl
N
H
N
200
190
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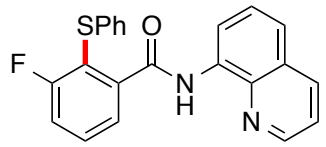
0

4e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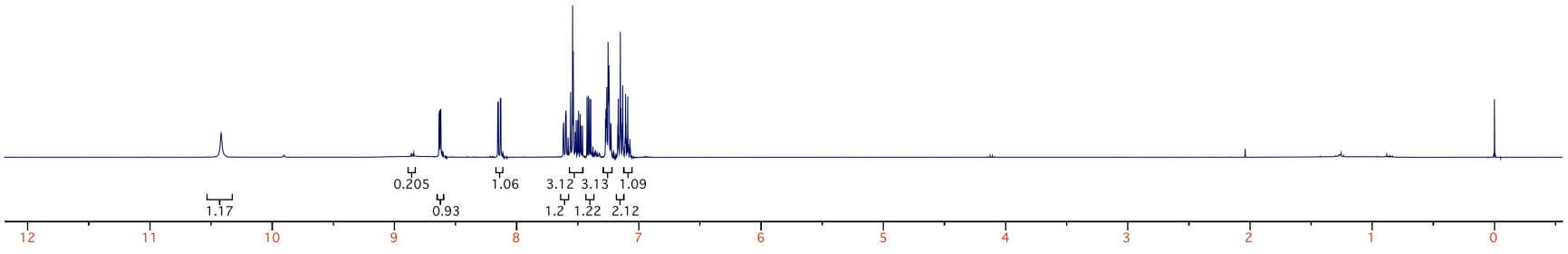
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1.09
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3
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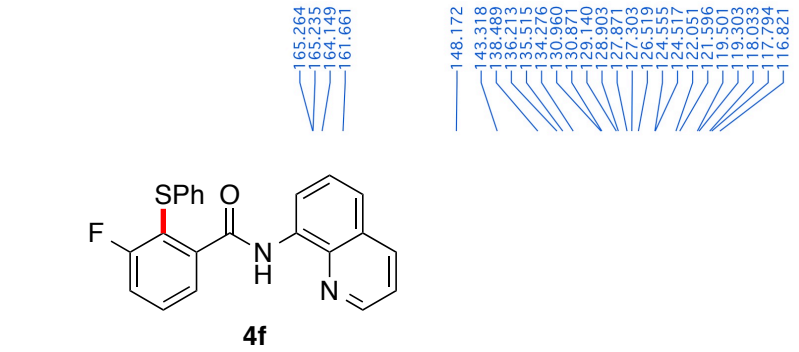
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130.960
130.871
129.140
128.903
127.871
127.303
126.519
124.555
124.517
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119.303
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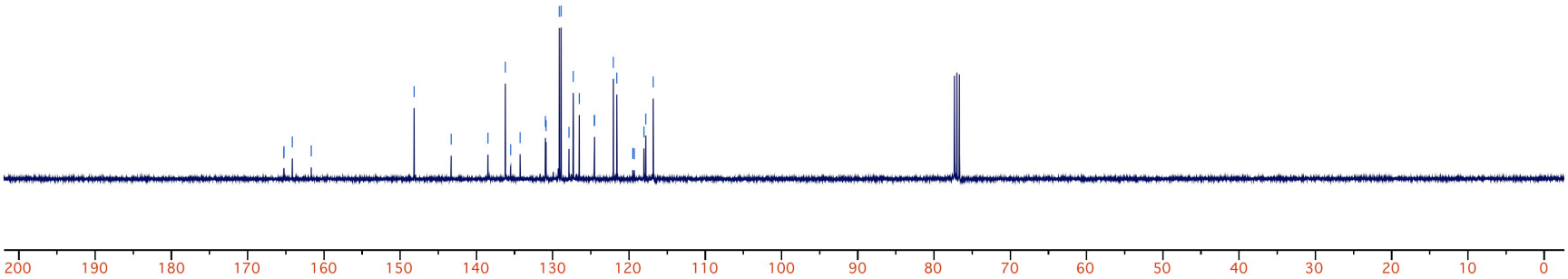
N
H
N

4f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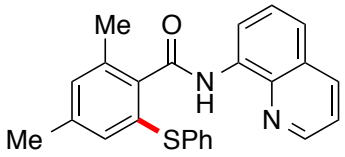
10
0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O
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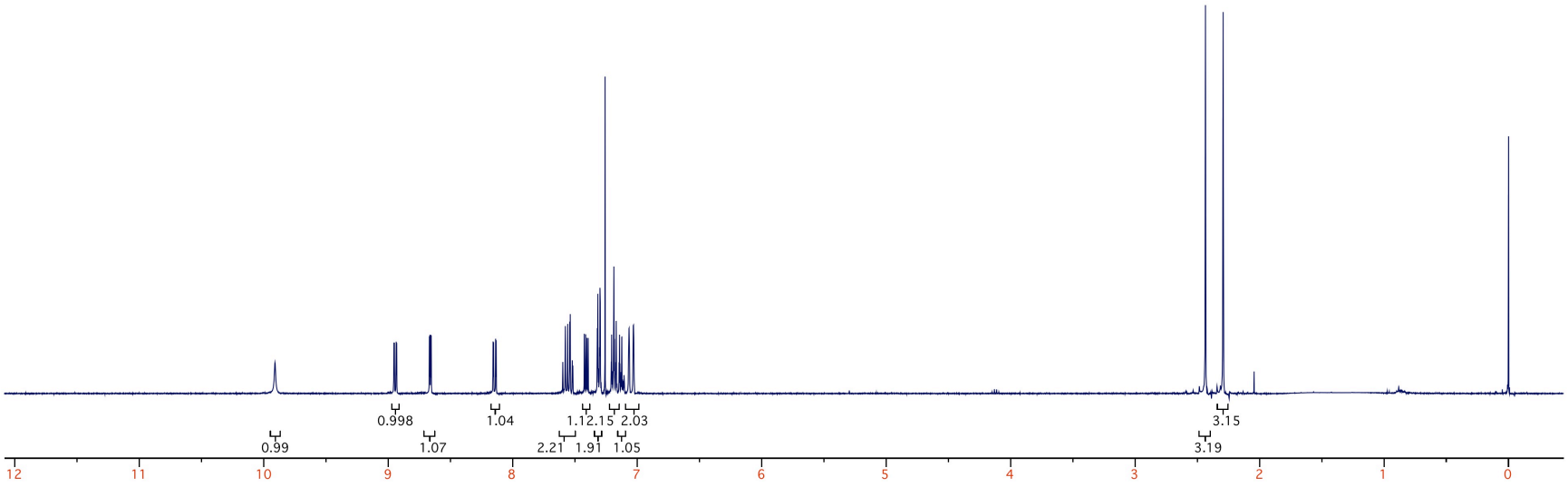
H
N
Me
SPh

4g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1.07
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1.05
3.19
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1
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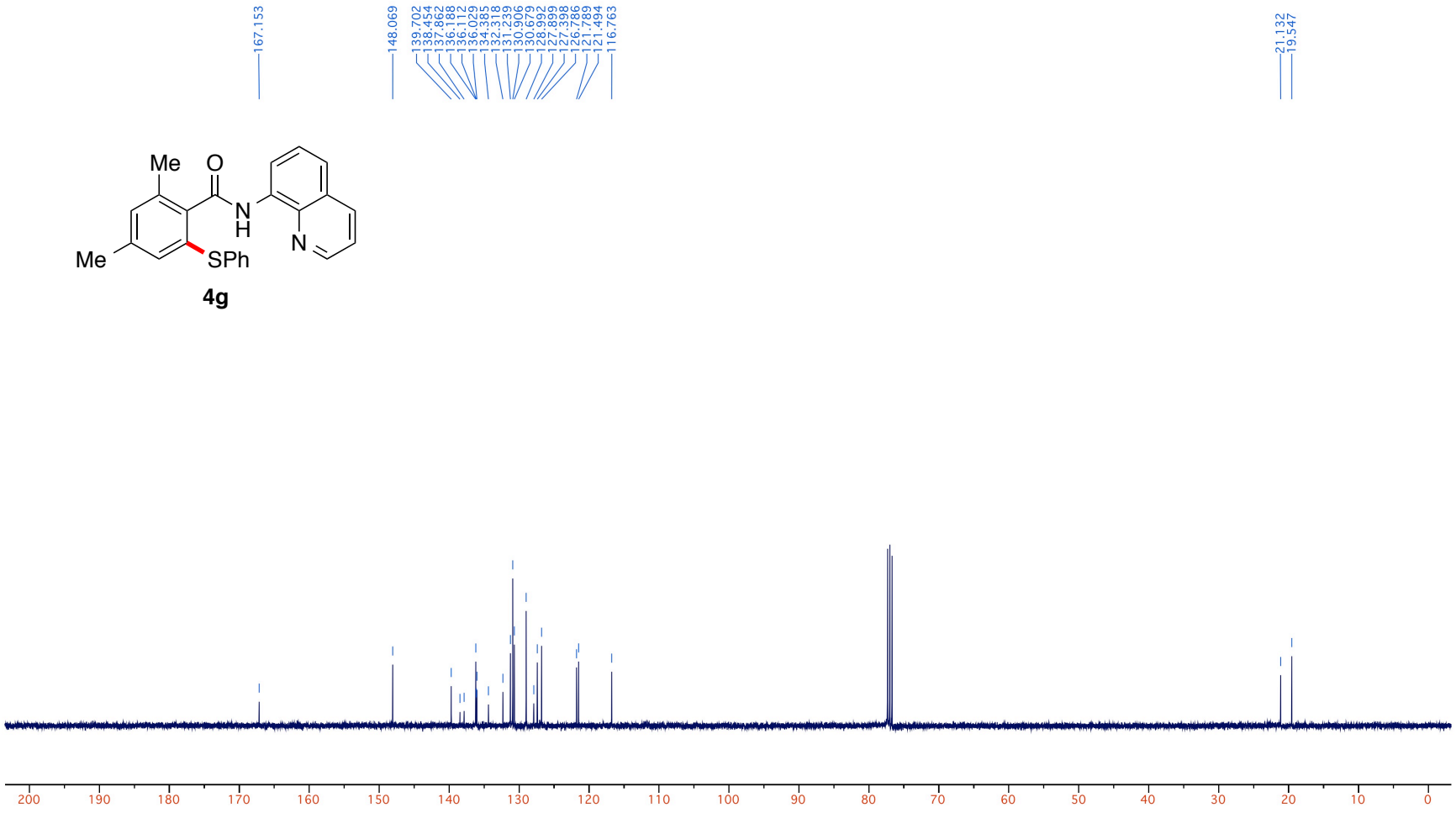
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130.679
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127.398
126.786
121.789
121.494
116.763
21.132
19.547
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O
N
H
N
Me
SPh
4g
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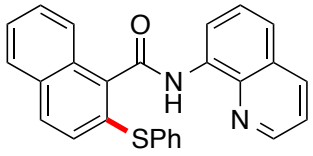

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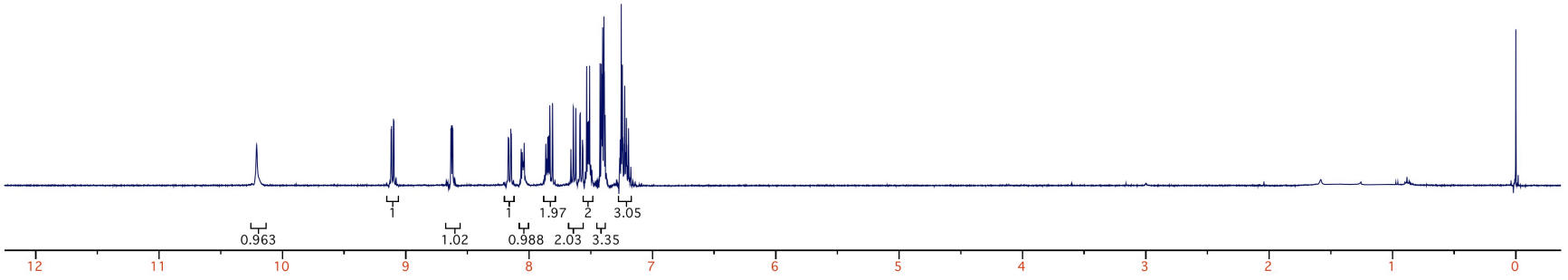

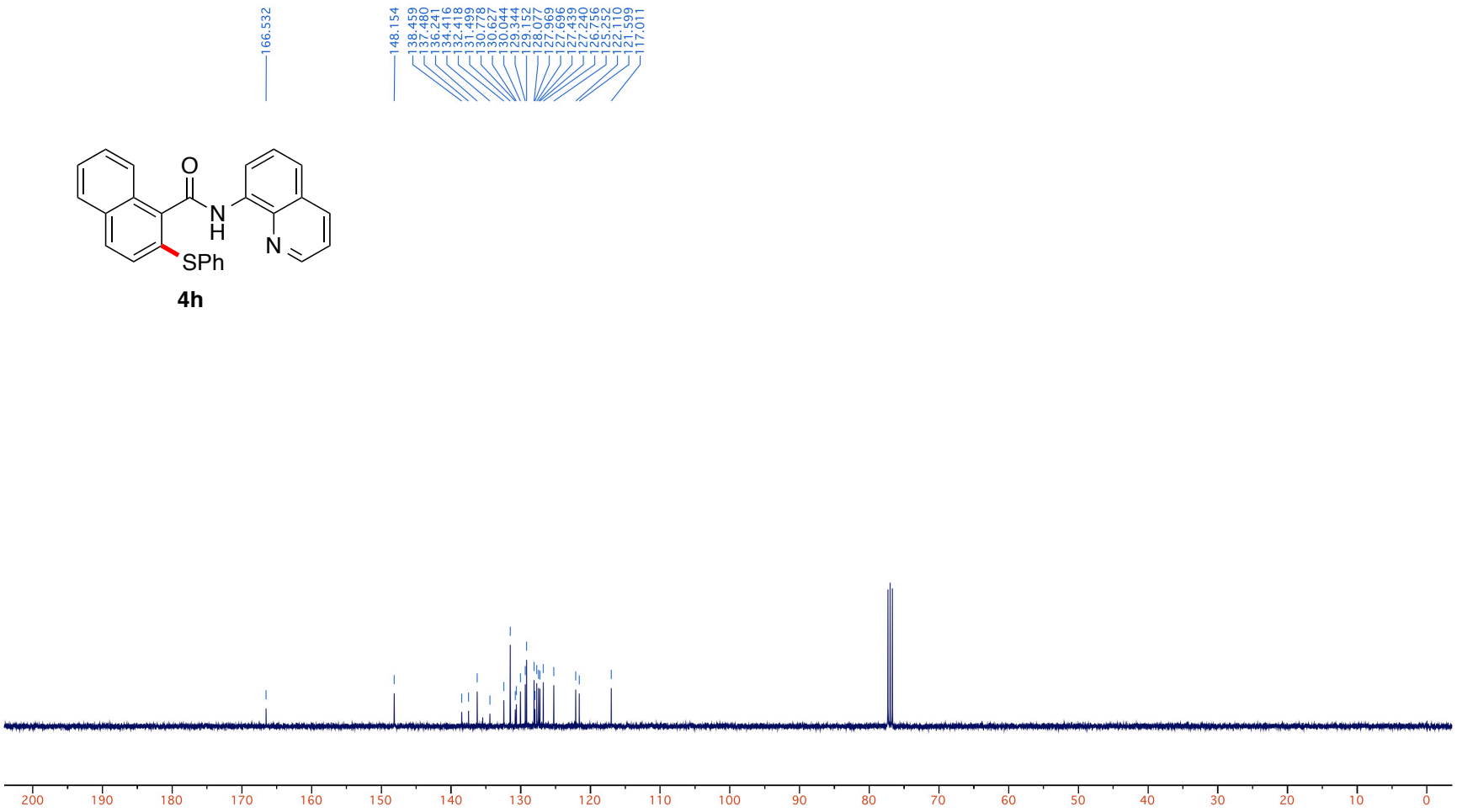
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129.152
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127.969
127.696
127.439
127.240
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123.252
122.110
121.599
117.011
O
N
H
N
SPh
200
190
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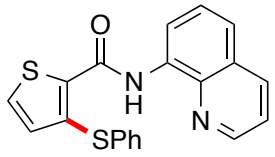
4h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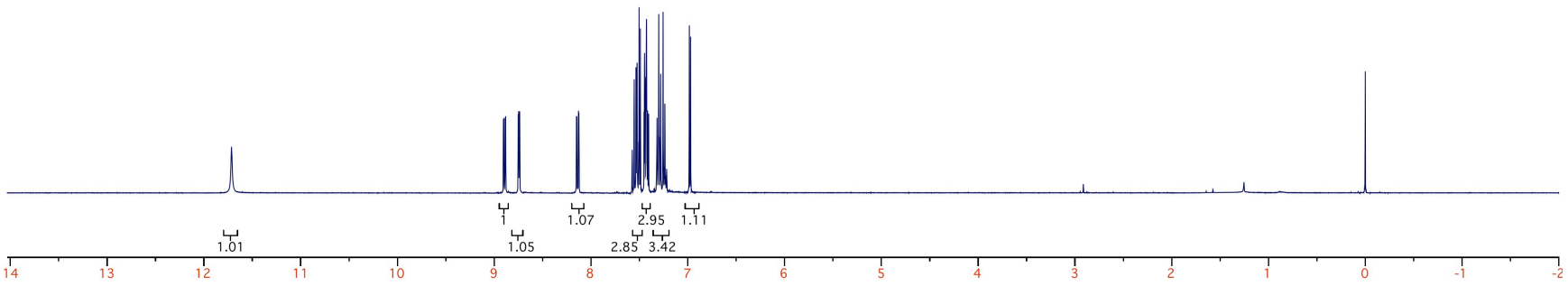
S
N
H
N
SPh

4i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2.95
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12
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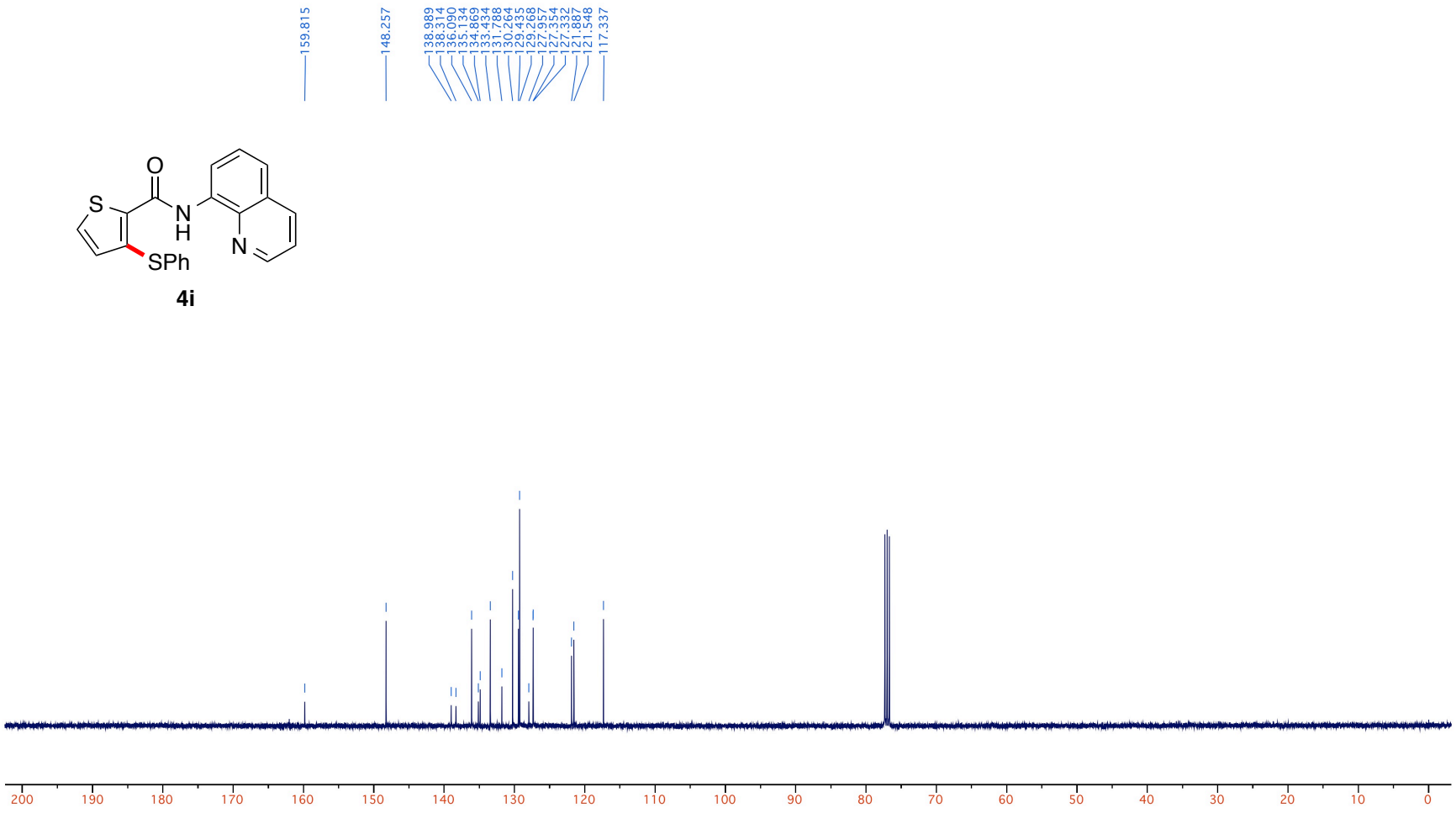
-2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131.788
130.264
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129.268
127.957
127.354
127.332
121.887
121.548
117.337
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S
N
H
N
SPh
200
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100
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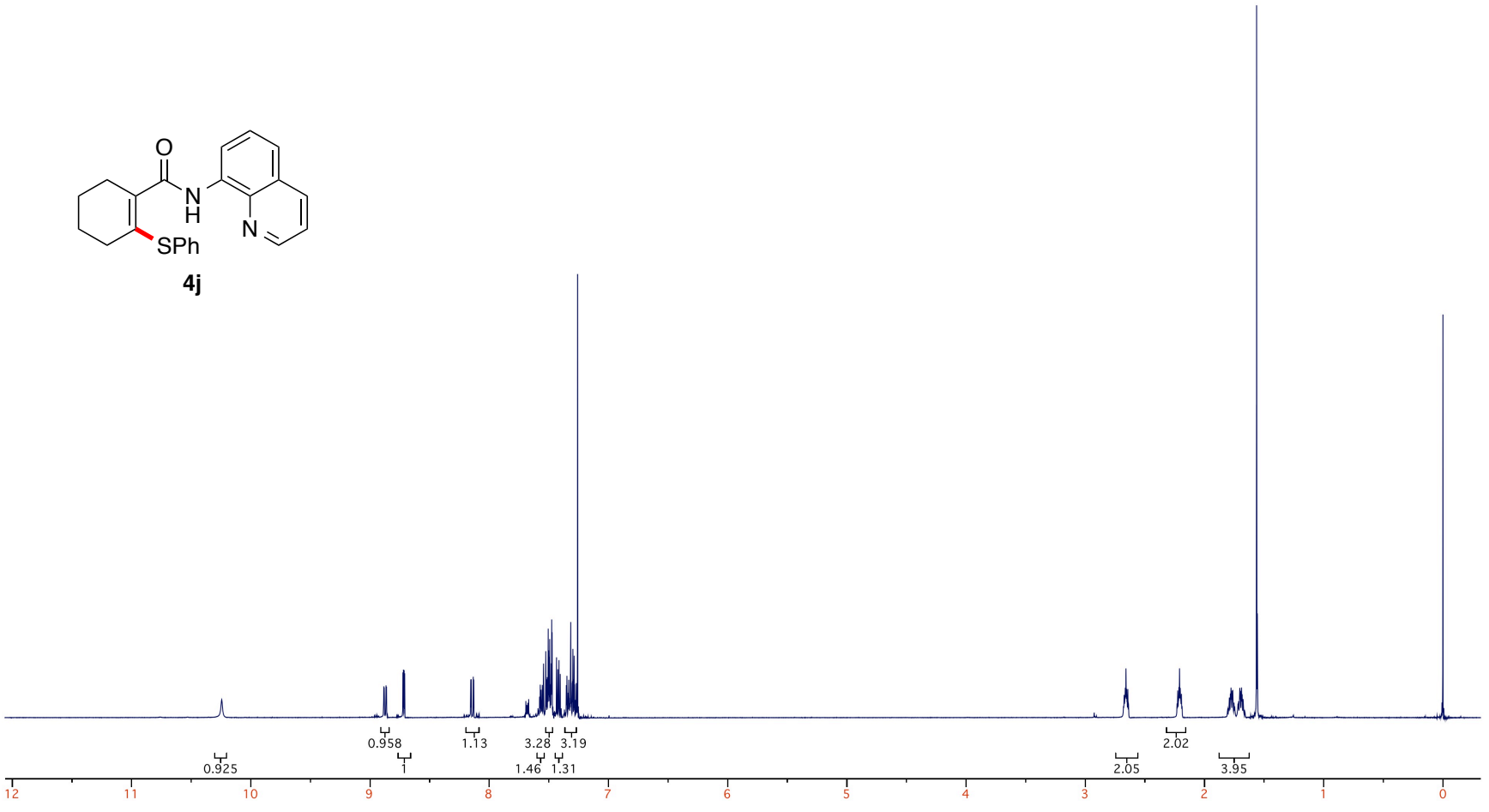
0

4i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N
H
N
SPh
4j
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0.958
1
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1.46
3.28
1.31
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2.02
3.95
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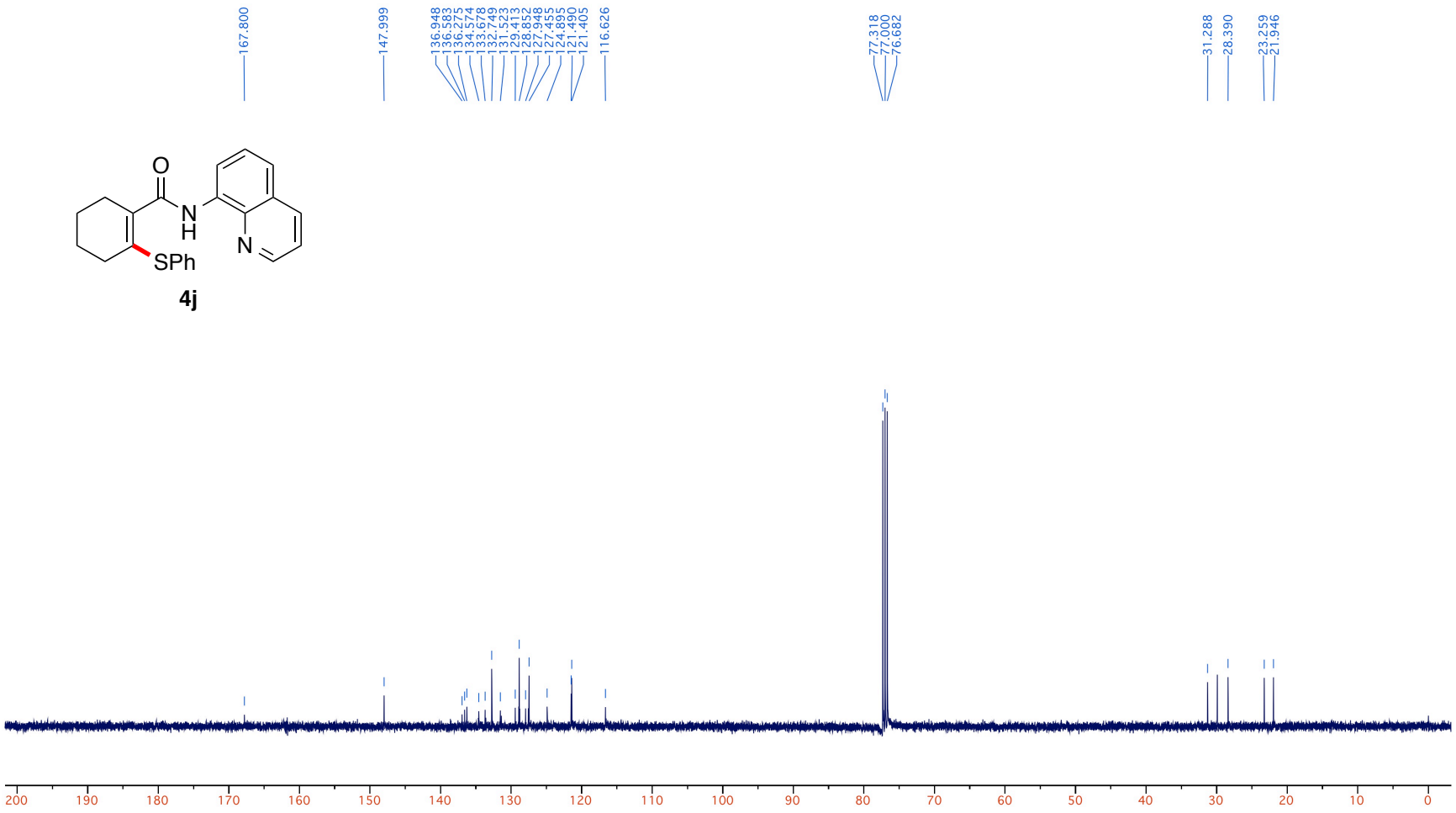
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121.490
121.405
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77.000
76.682
31.288
28.390
23.259
21.946
O
N
H
SPh
N
4j
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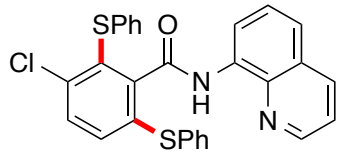
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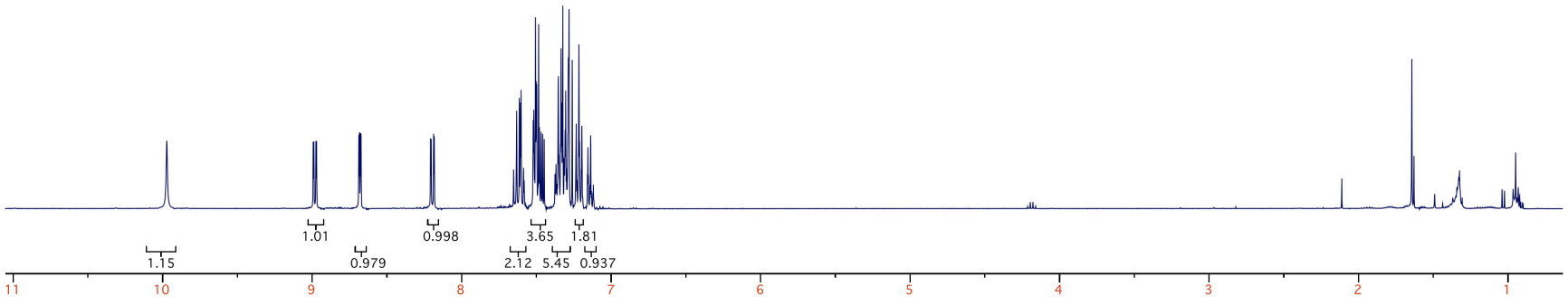
Cl
N
H
N
SPh

4k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8
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5
4
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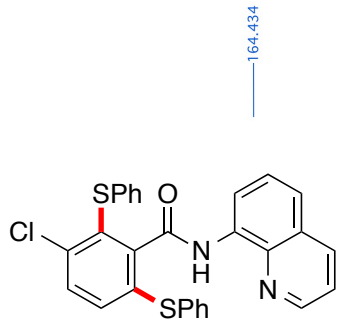
2
1


SPh
O
Cl
N
H
N
SPh

4k

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130.390
129.479
128.925
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128.190
127.824
127.370
126.374
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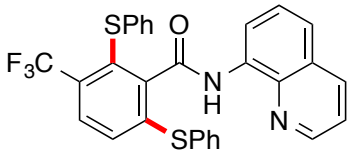
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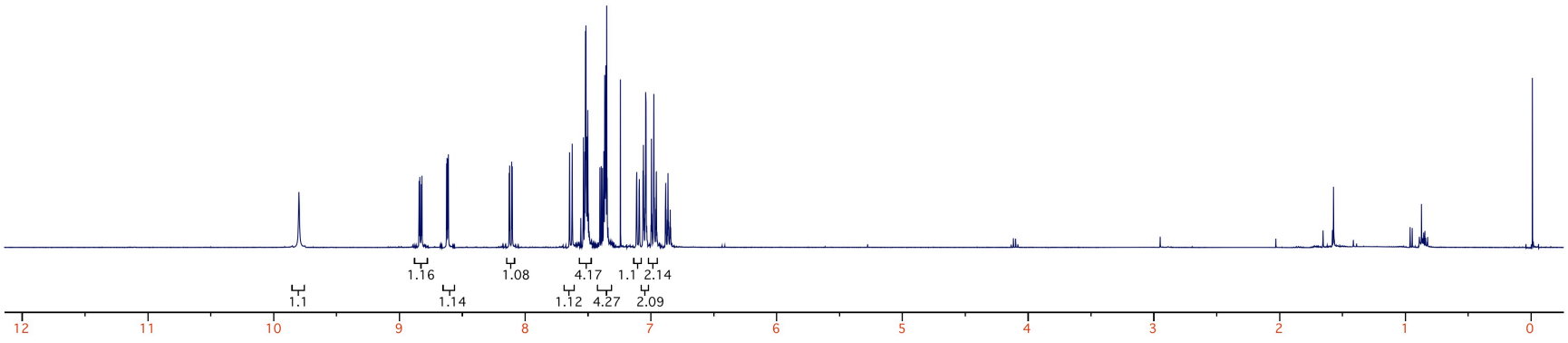
H
N
SPh

4l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1.1
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11
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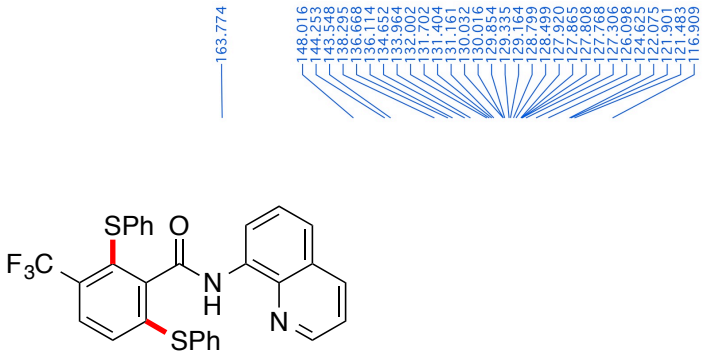
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128.499
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127.865
127.808
127.768
127.306
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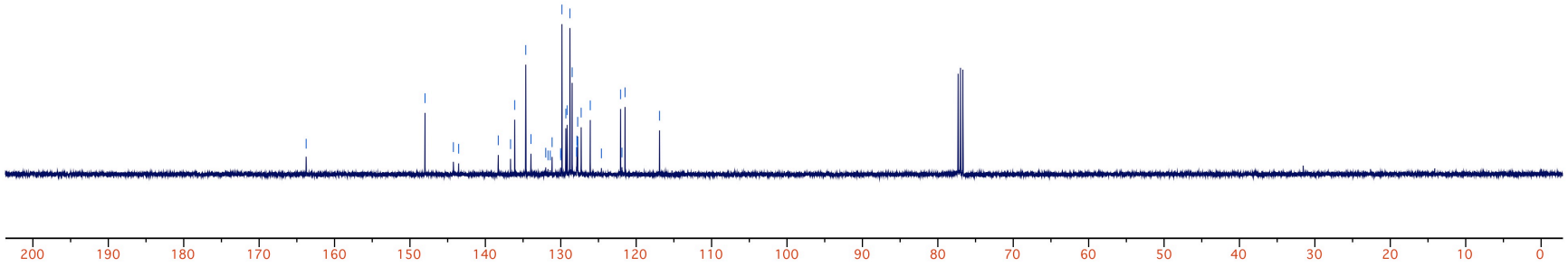
F3C
N
H
N
SPh

4l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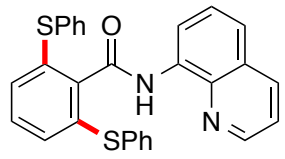
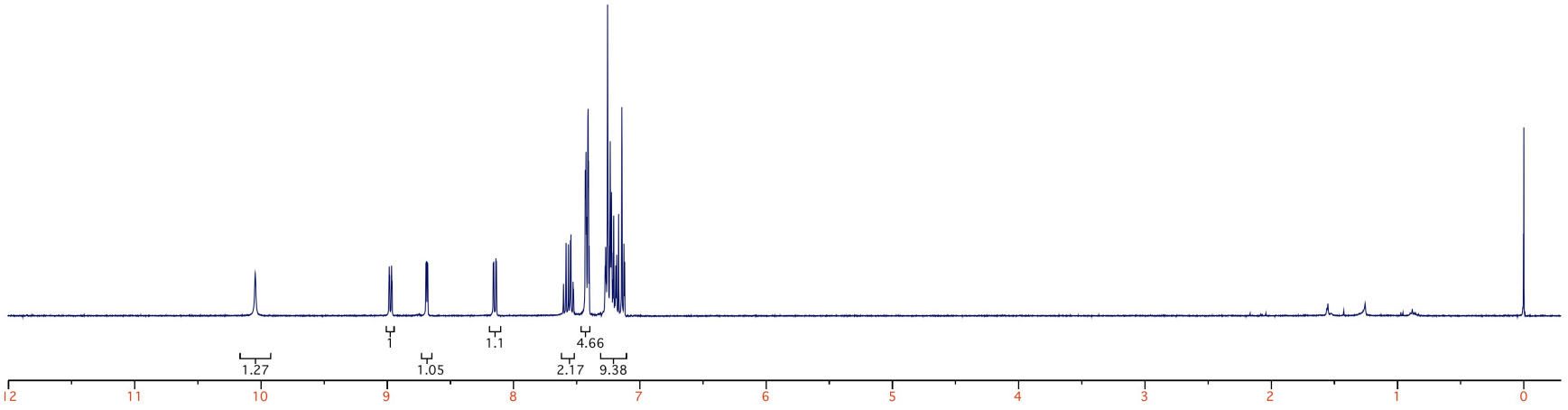
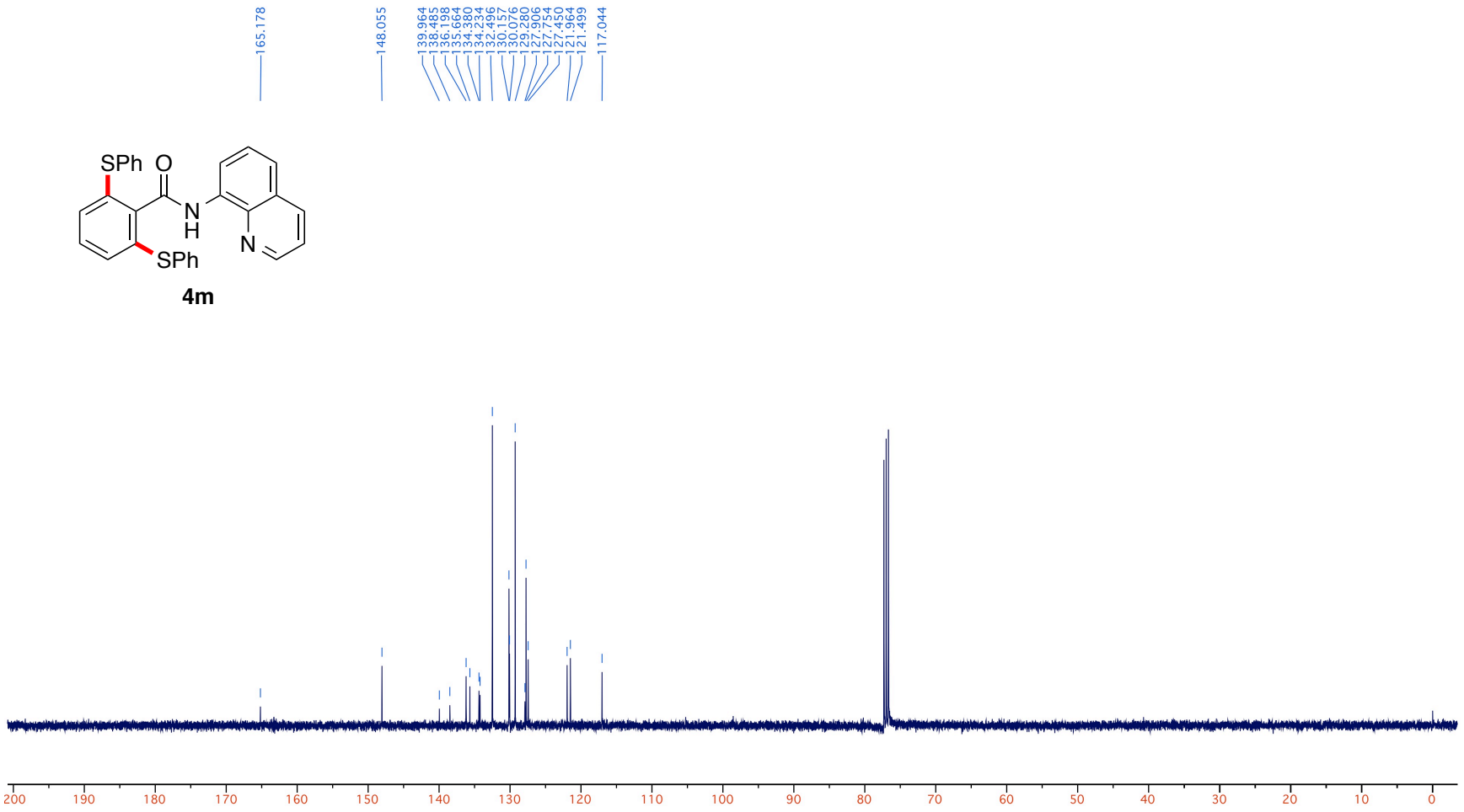


4m

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130.076
129.280
127.906
127.754
127.450
121.964
121.499
117.044
SPh
O
N
H
SPh
N
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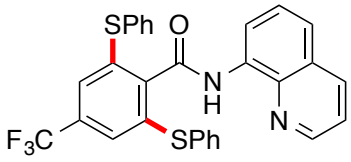
4m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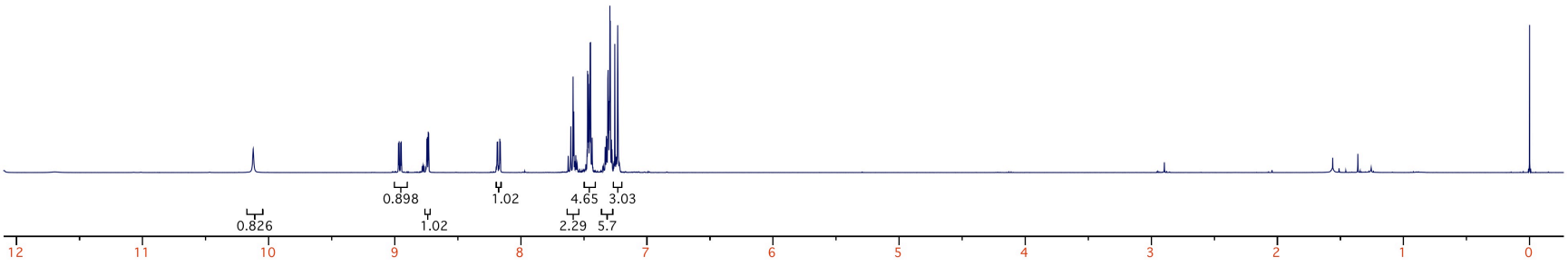
N
H
N
F3C
SPh

4n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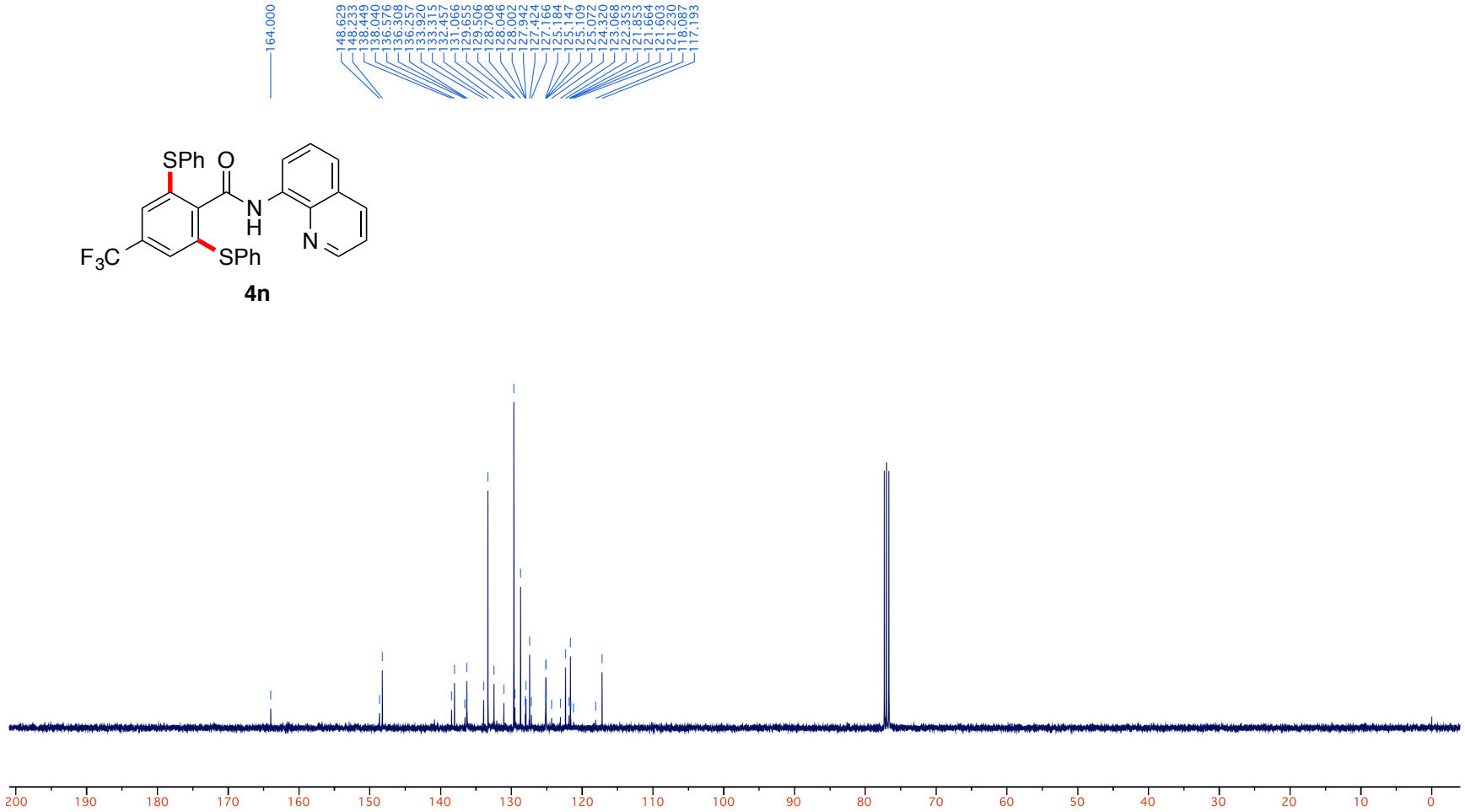
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119.087
117.193
SPh
O
N
H
N
F3C
SPh
4n
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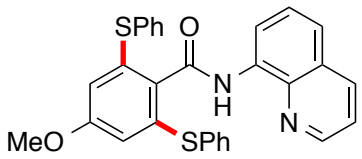
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MeO
SPh

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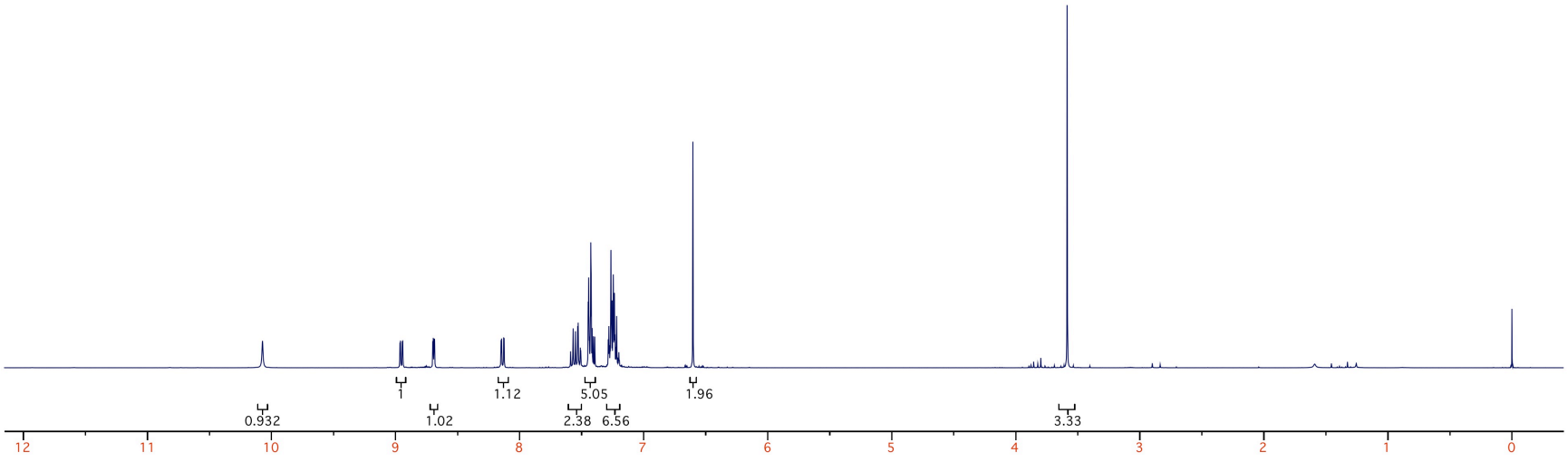
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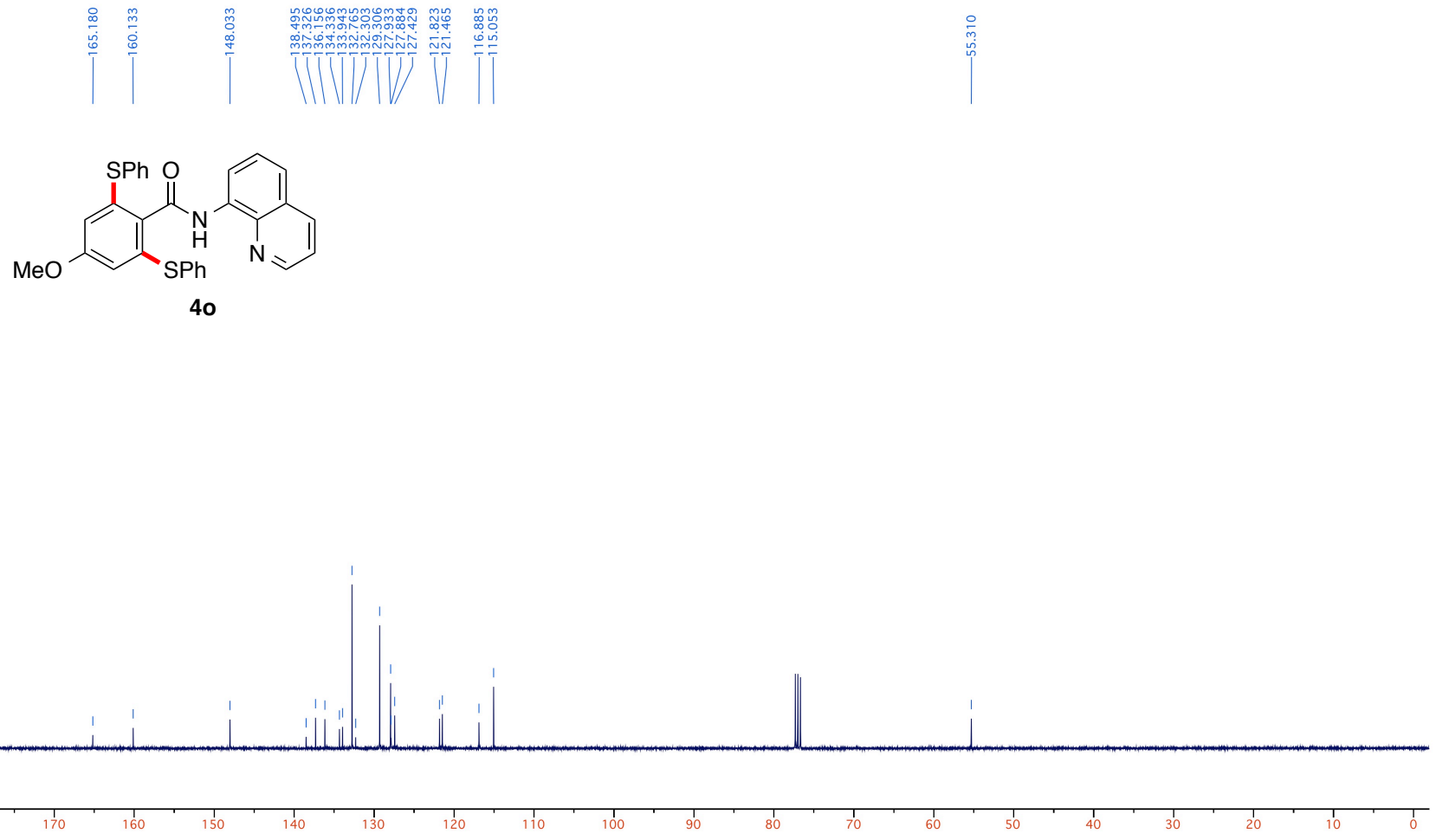
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121.465
116.885
115.053
55.310
SPh
O
N
H
N
MeO
SPh
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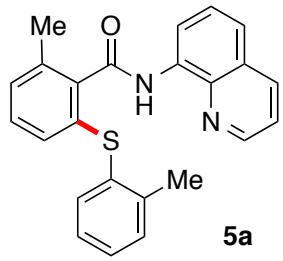
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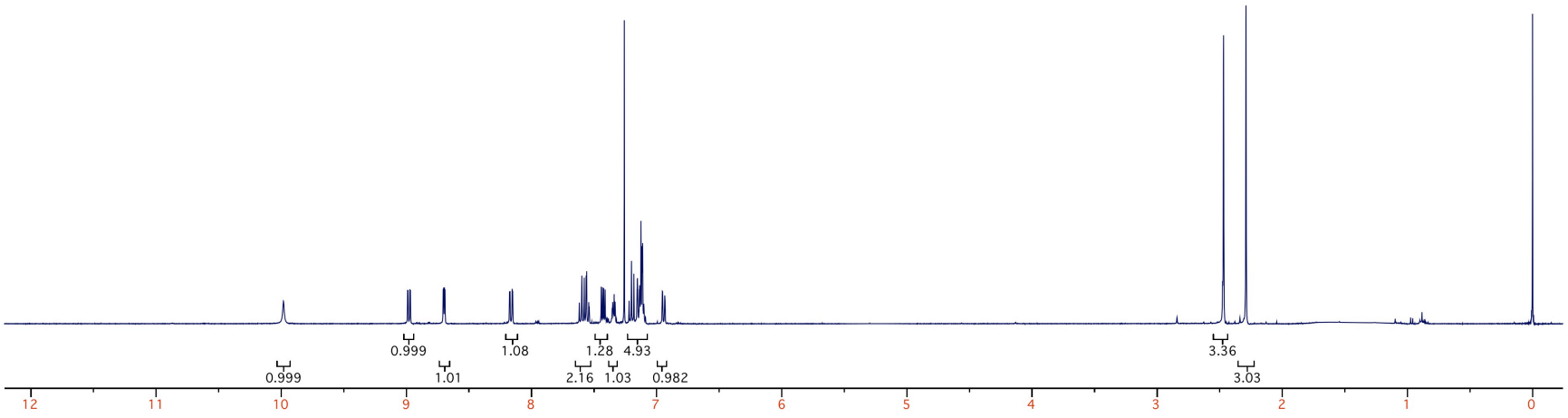
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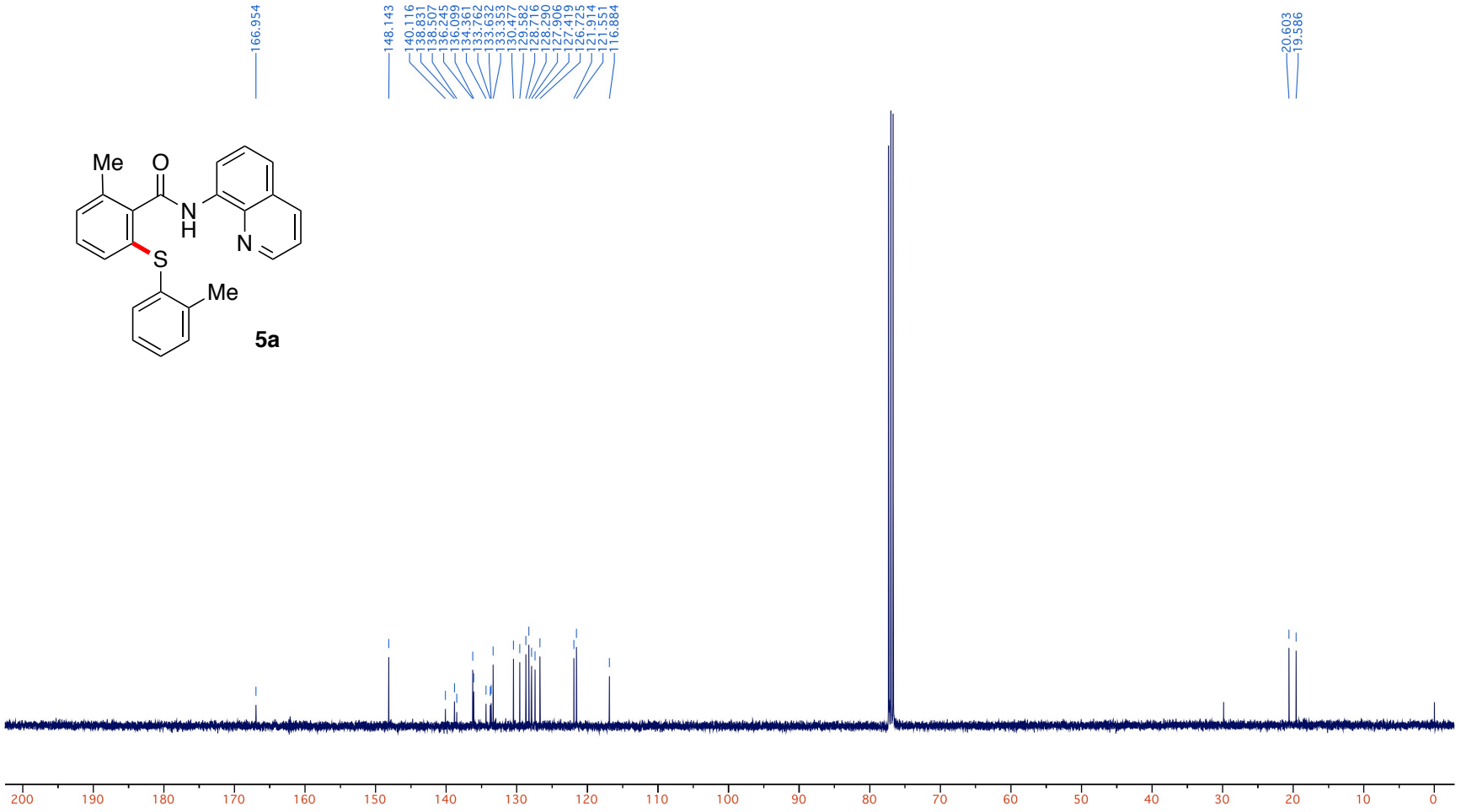
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H
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S
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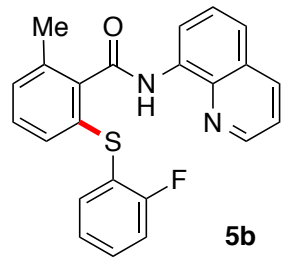
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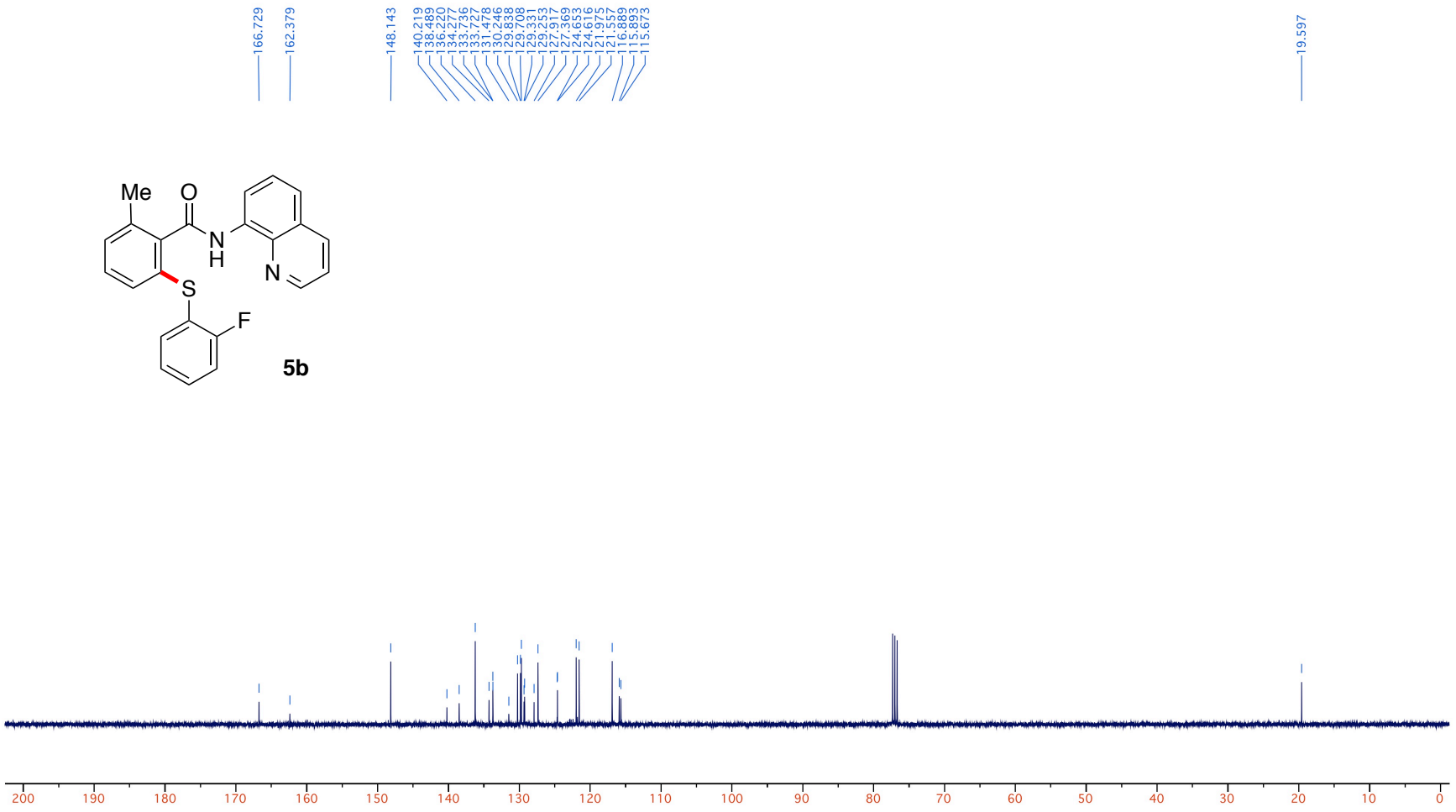
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H
N
S
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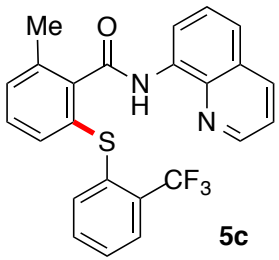
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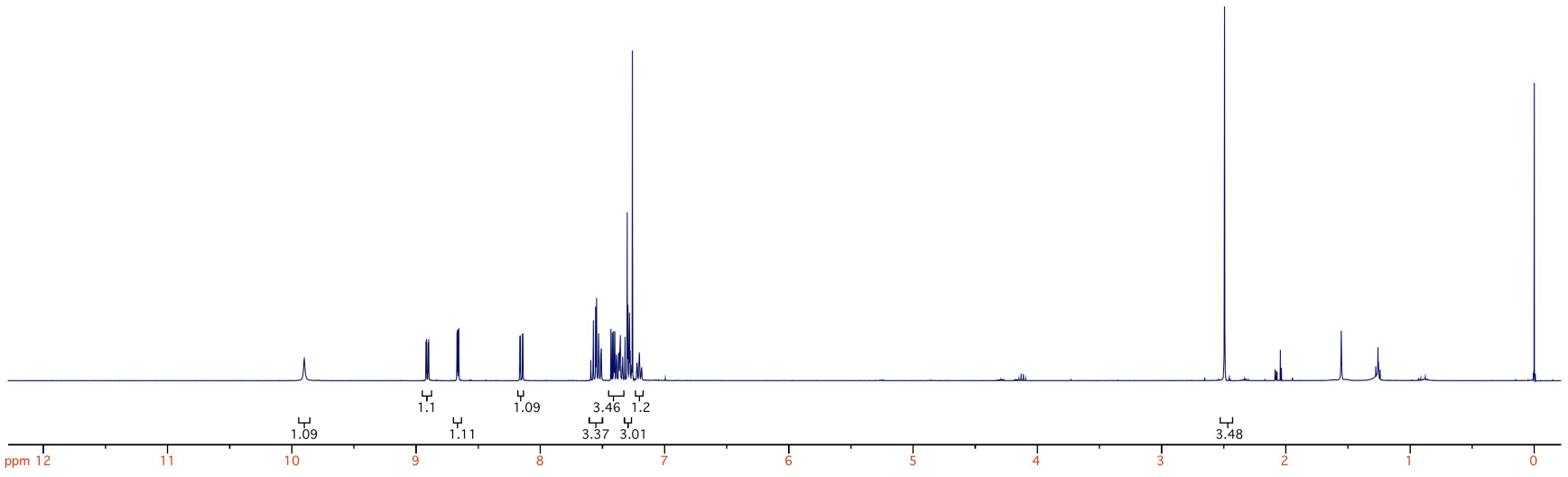
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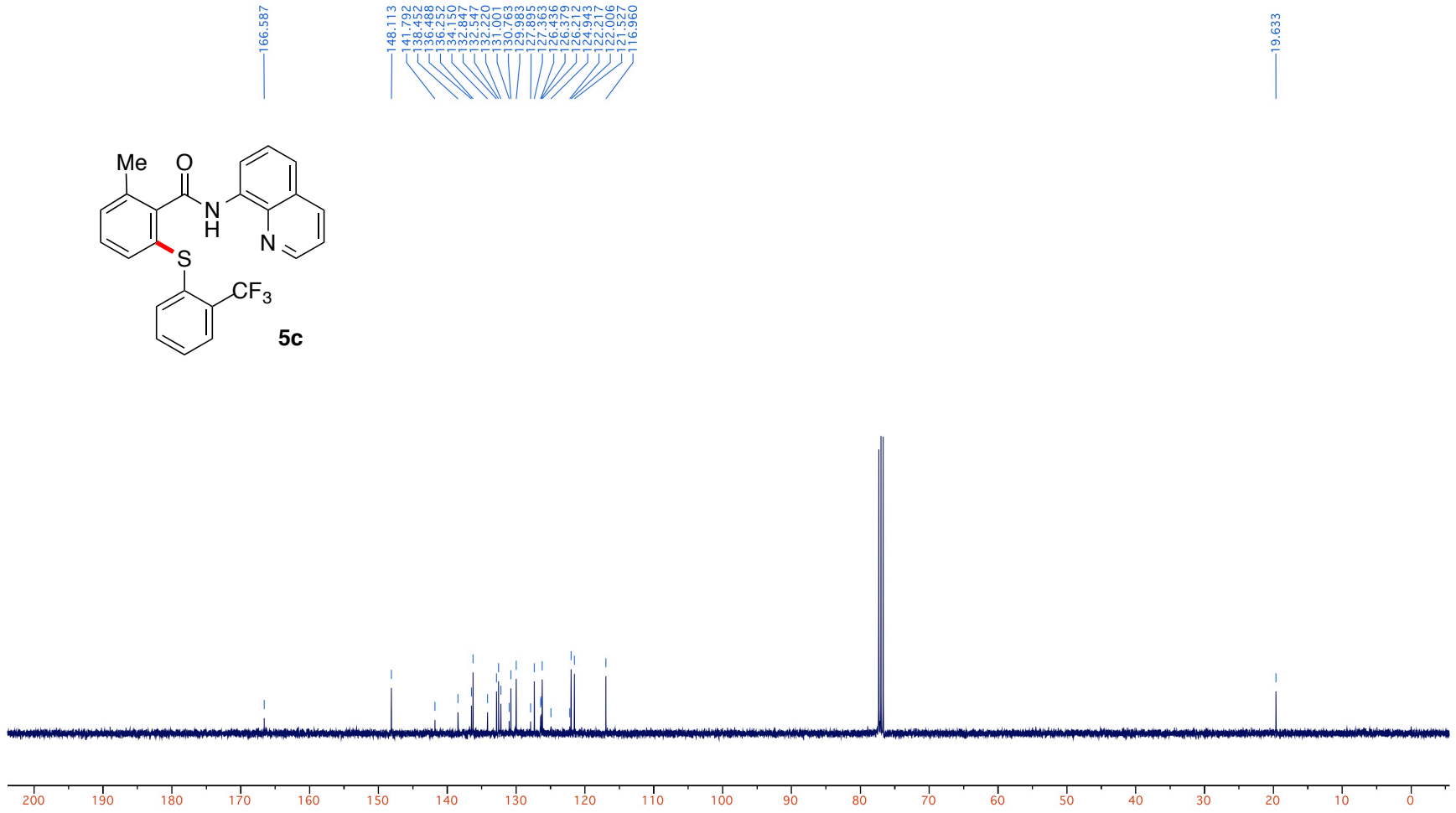
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S
CF3
5c
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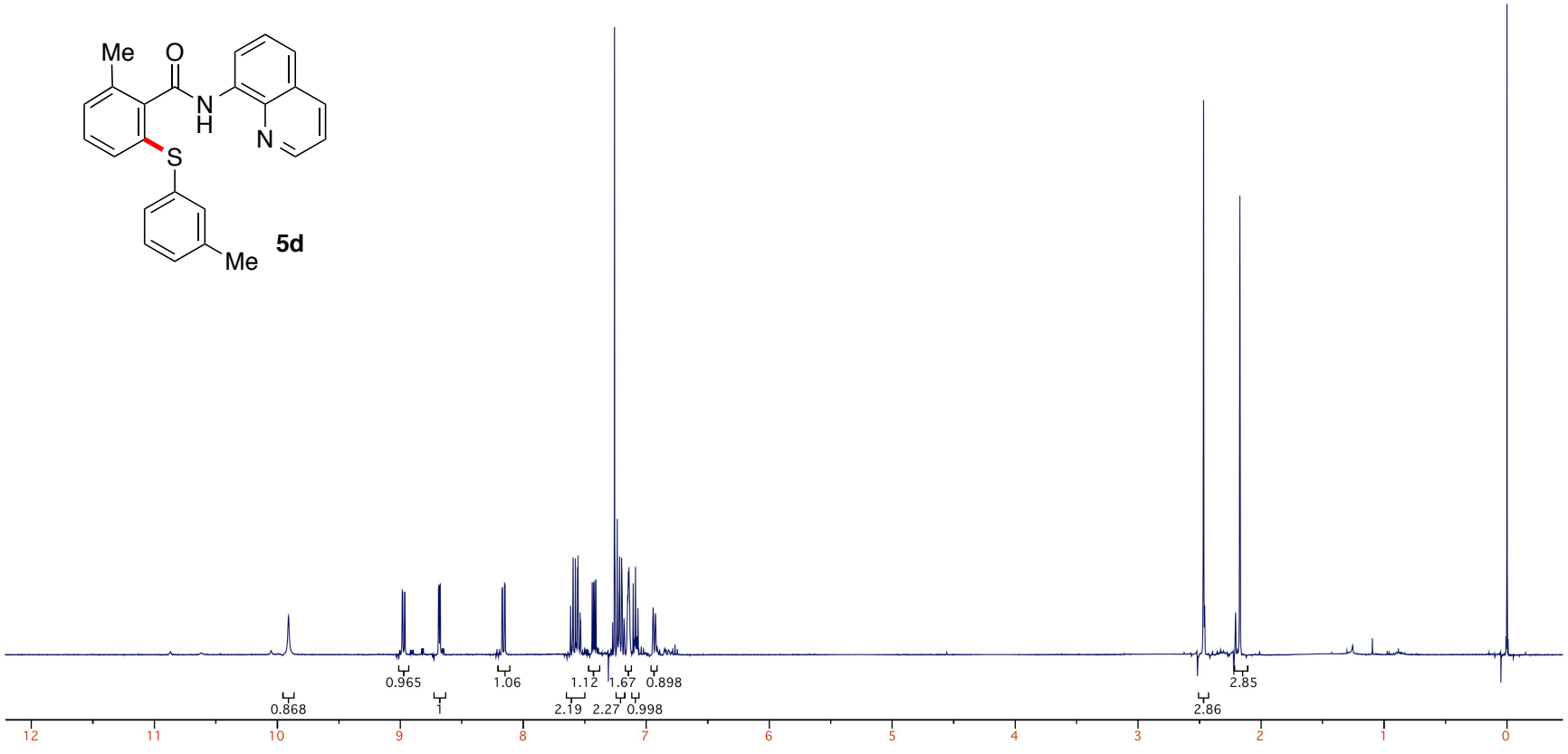
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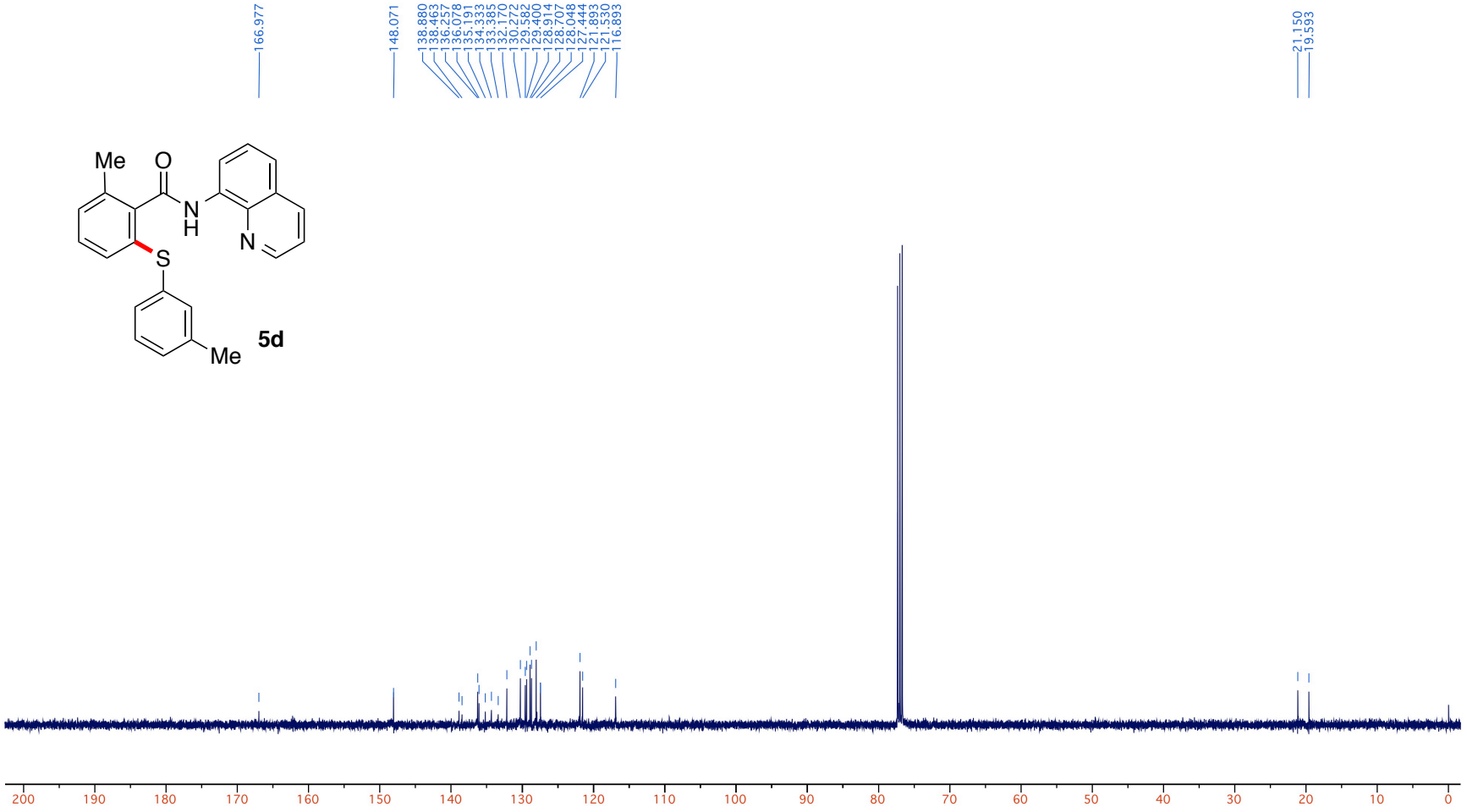
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H
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Me
5d
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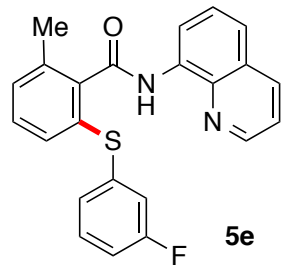
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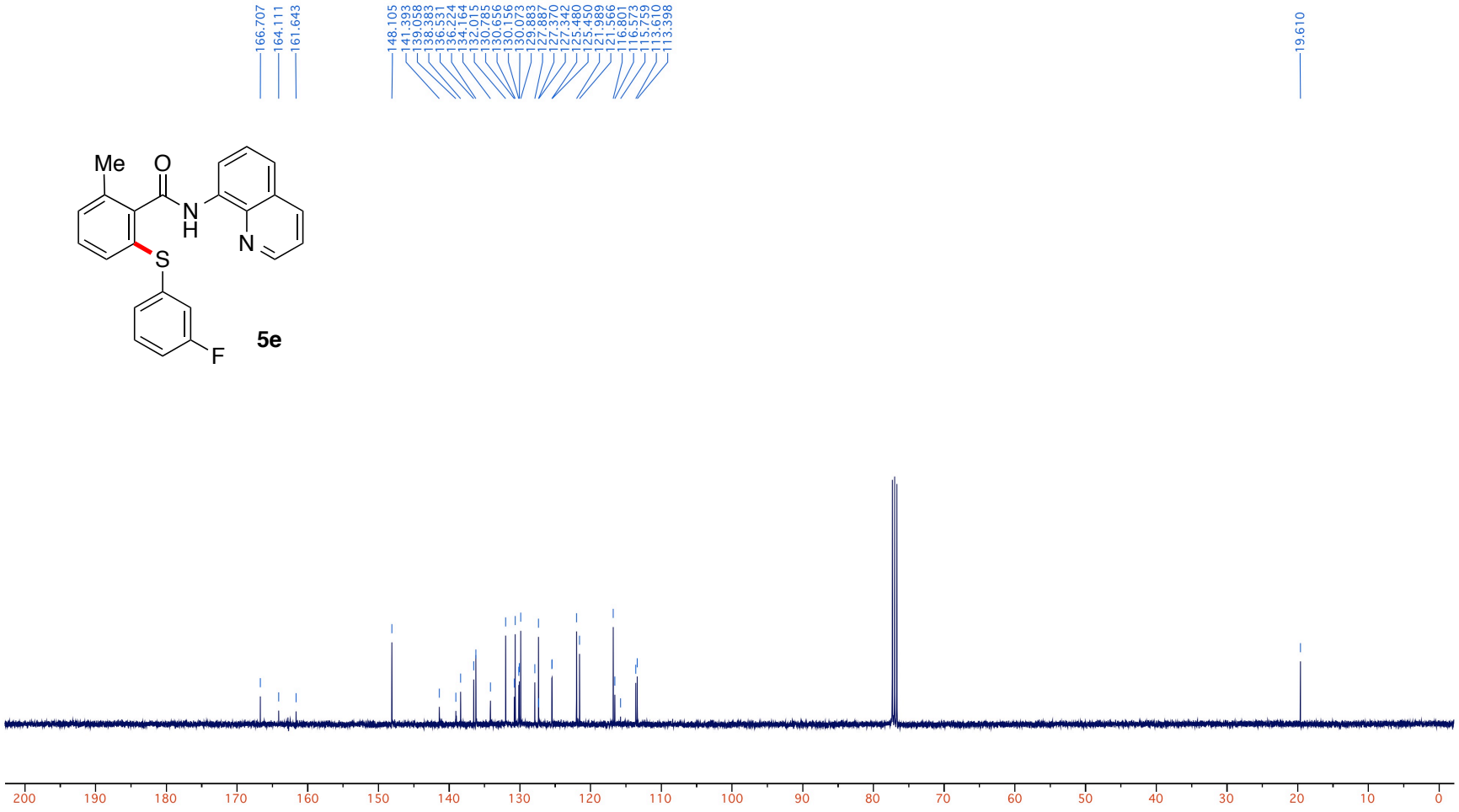
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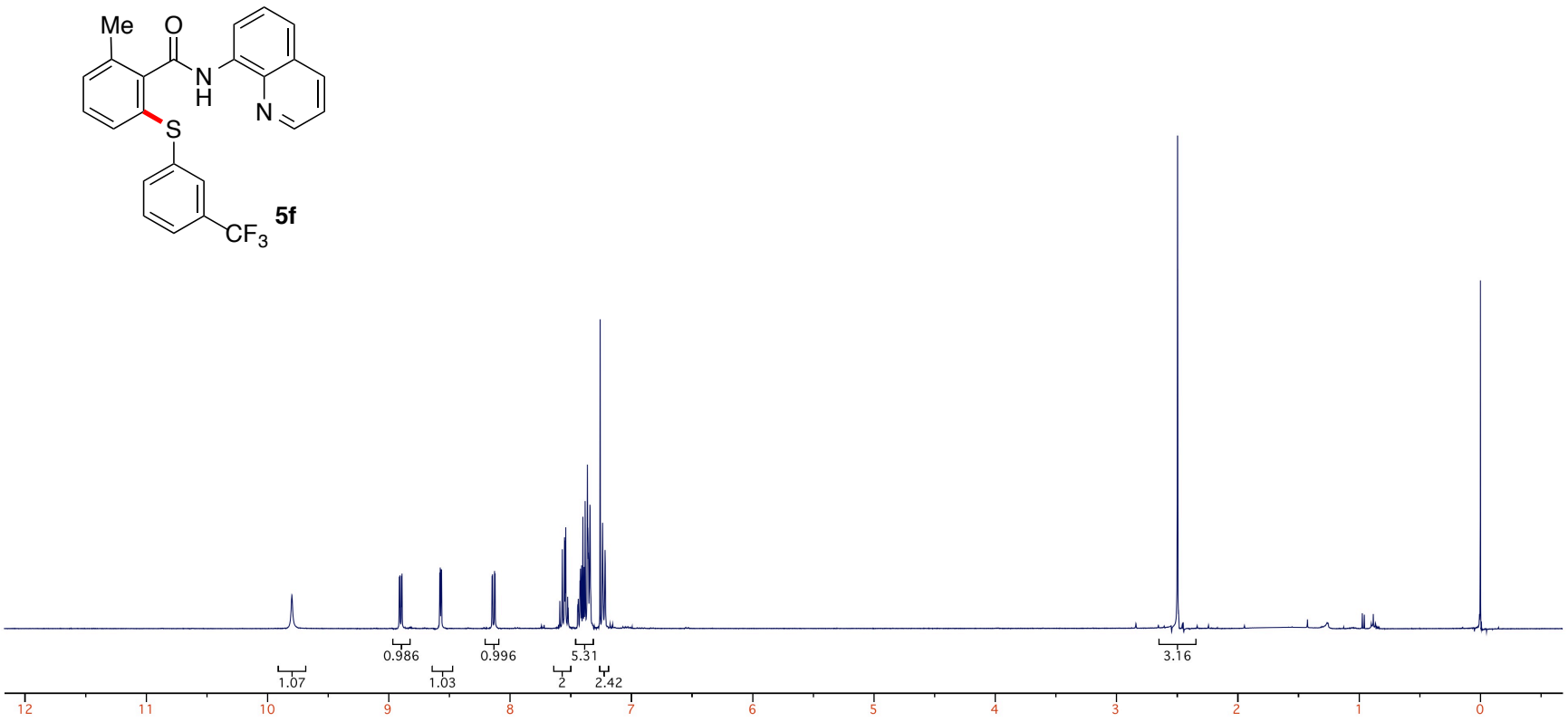
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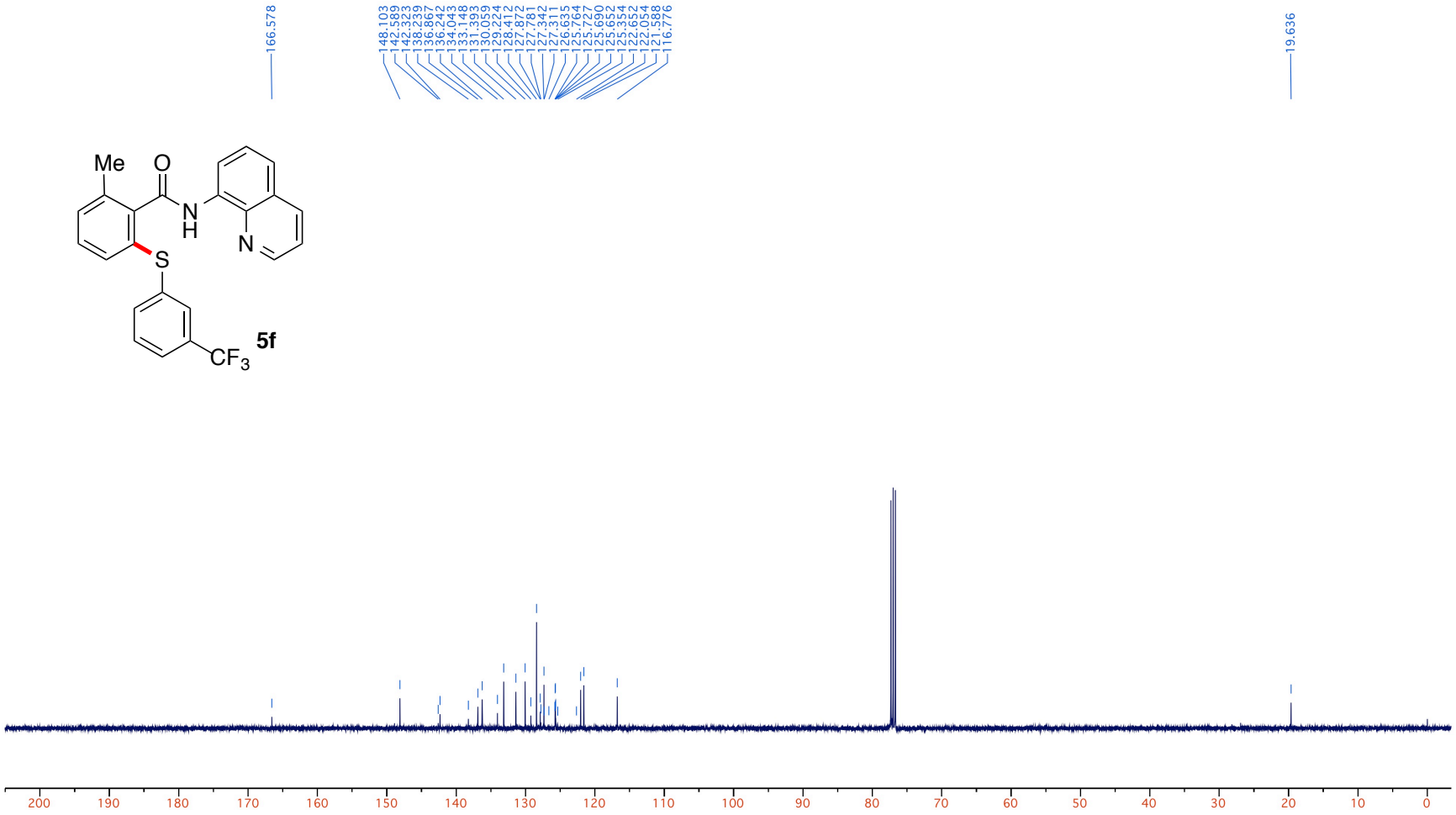
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19.636
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S
CF3
5f
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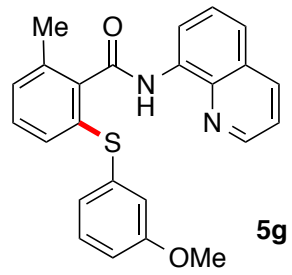
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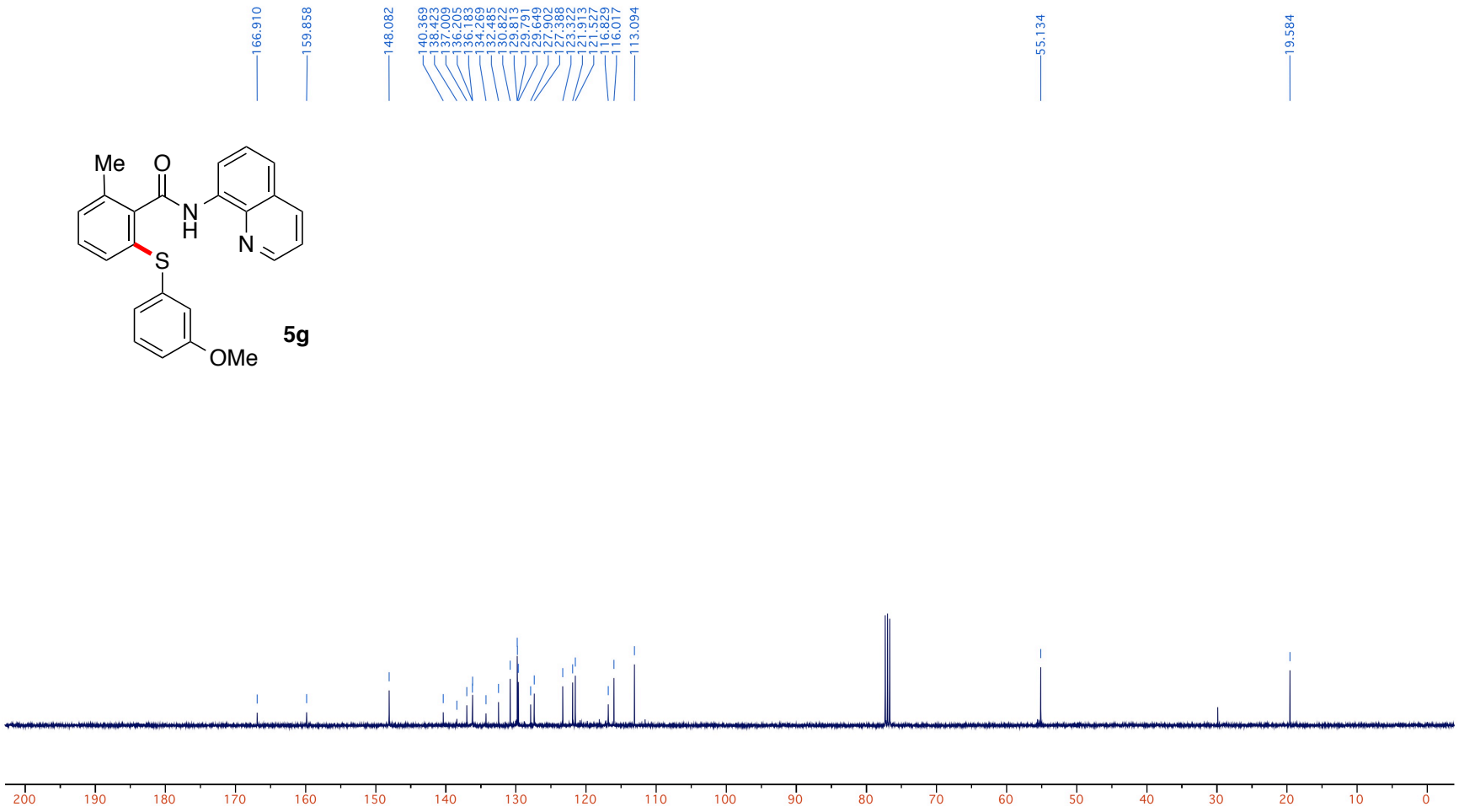
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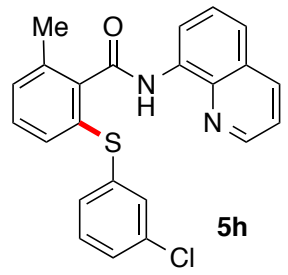
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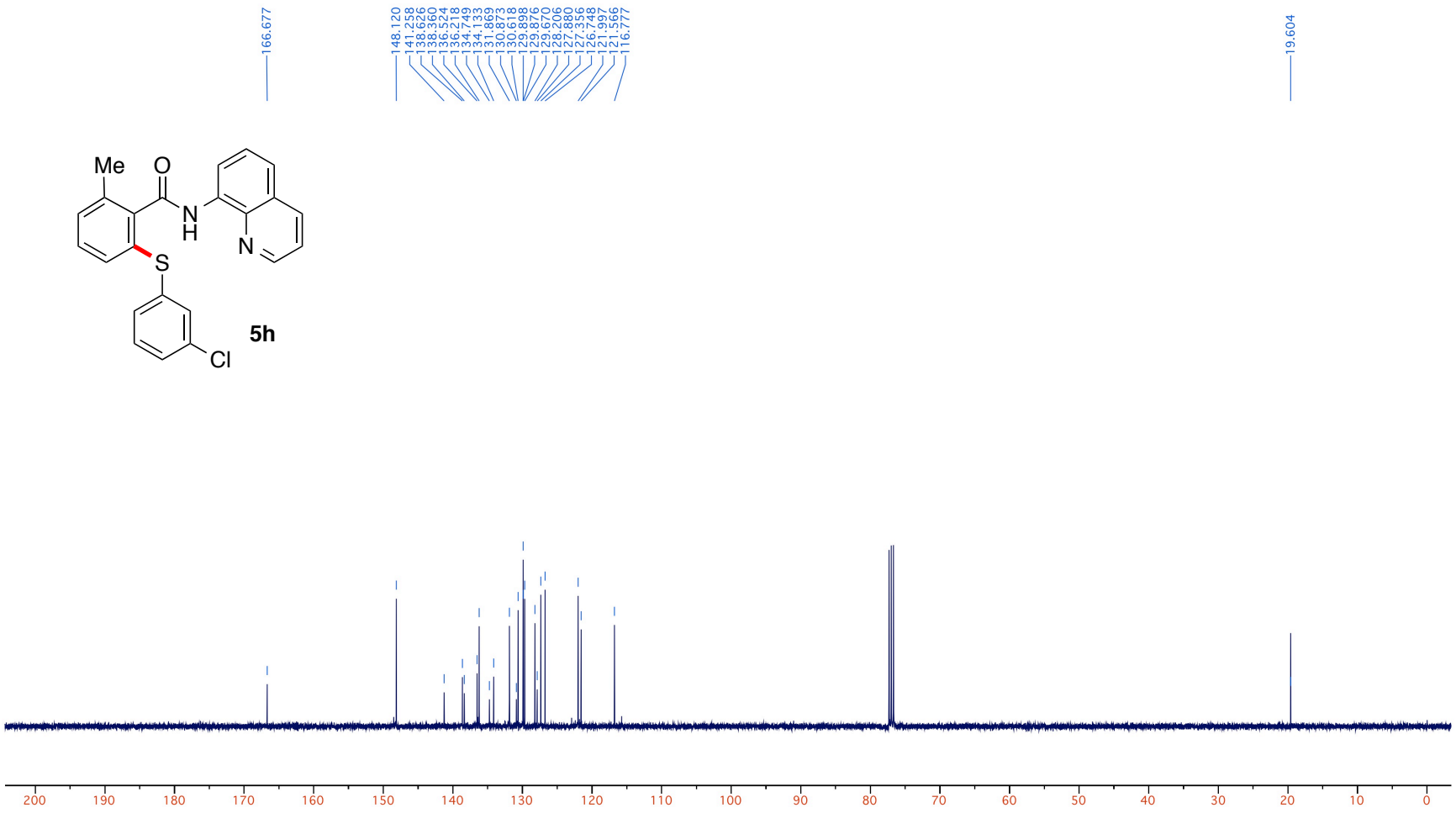
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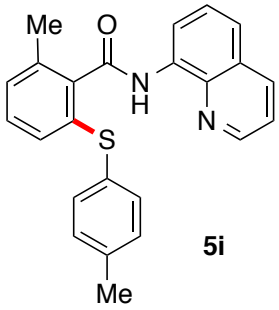
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Me

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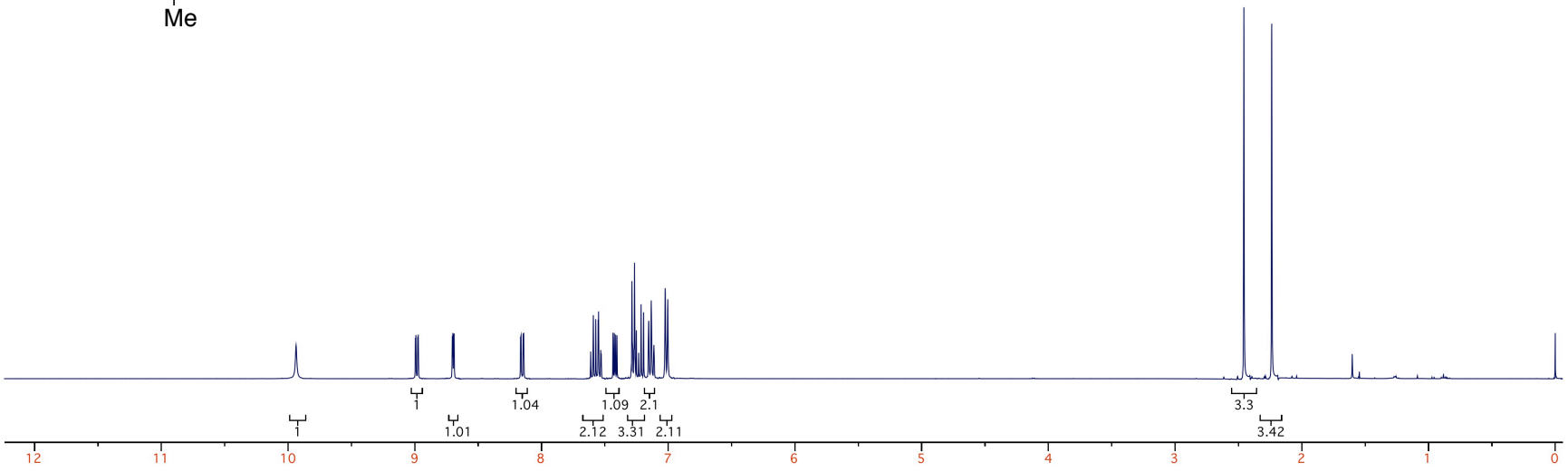
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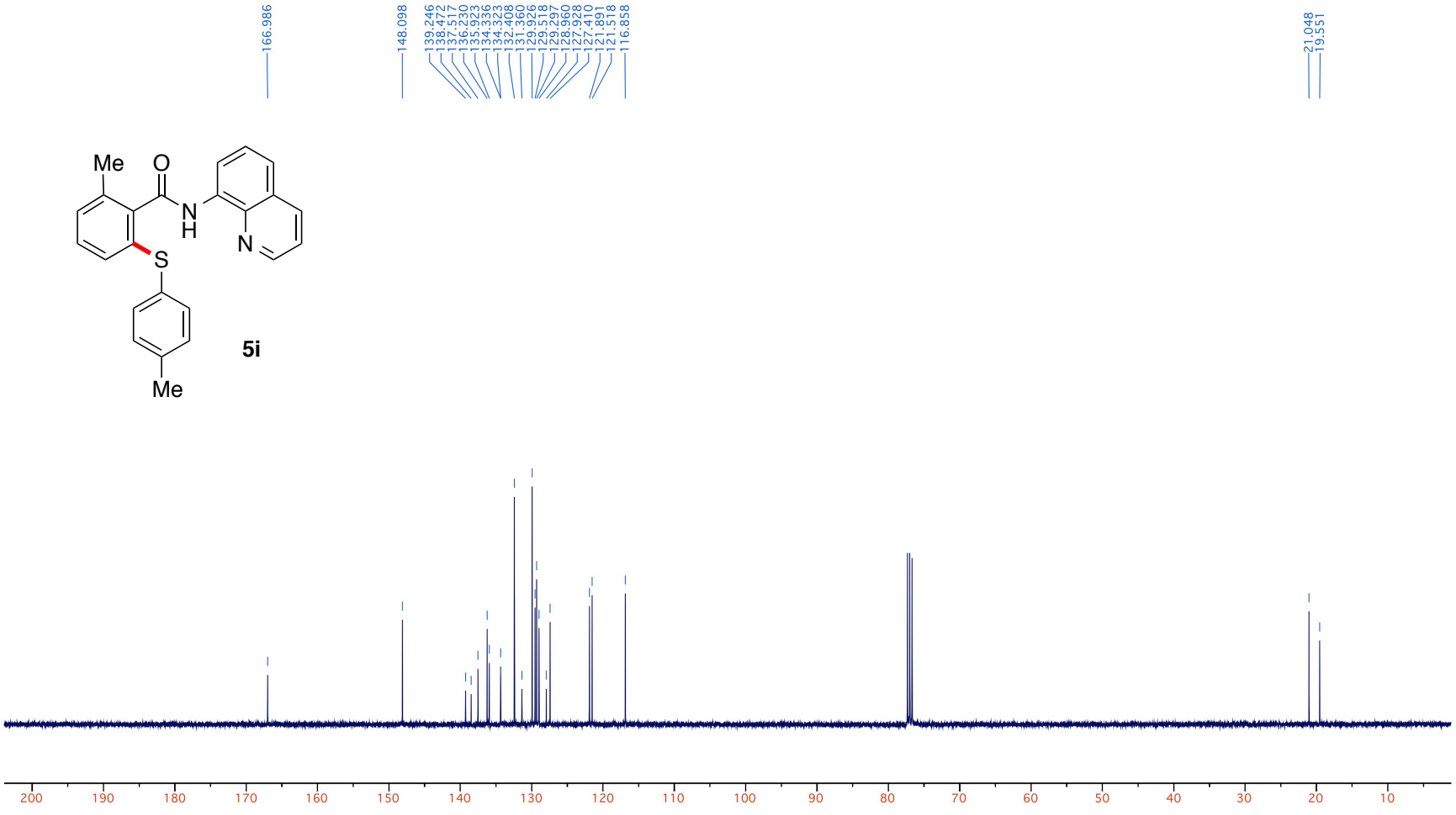
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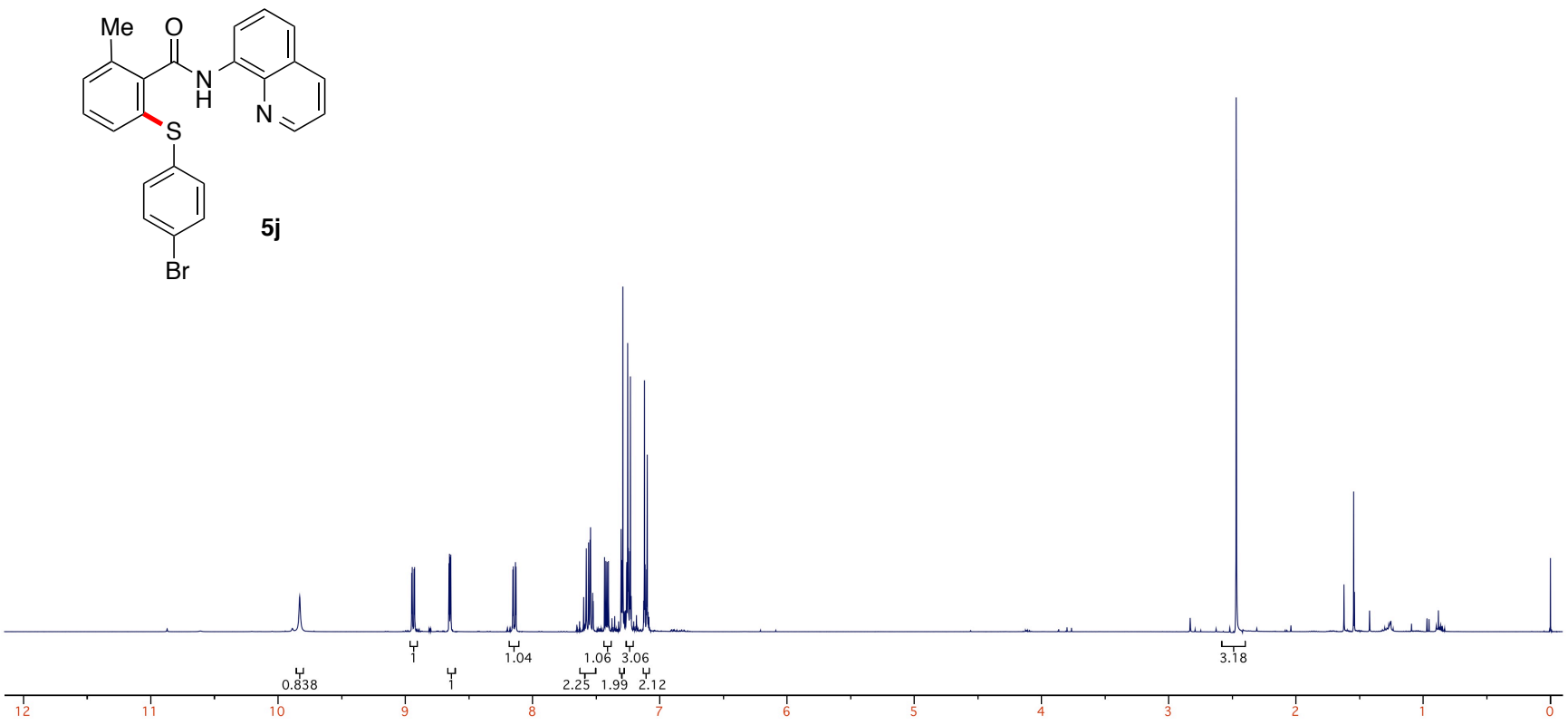
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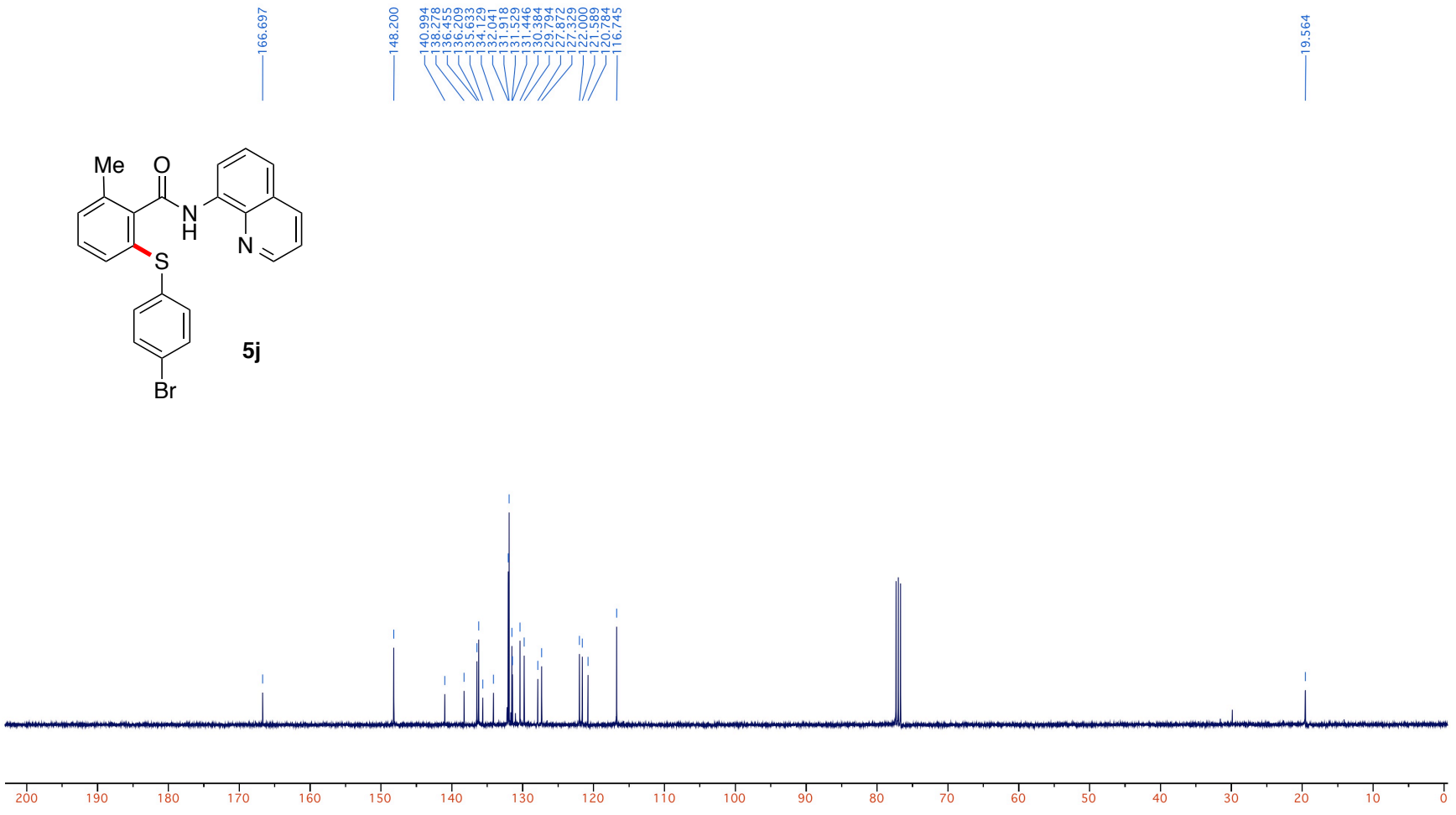
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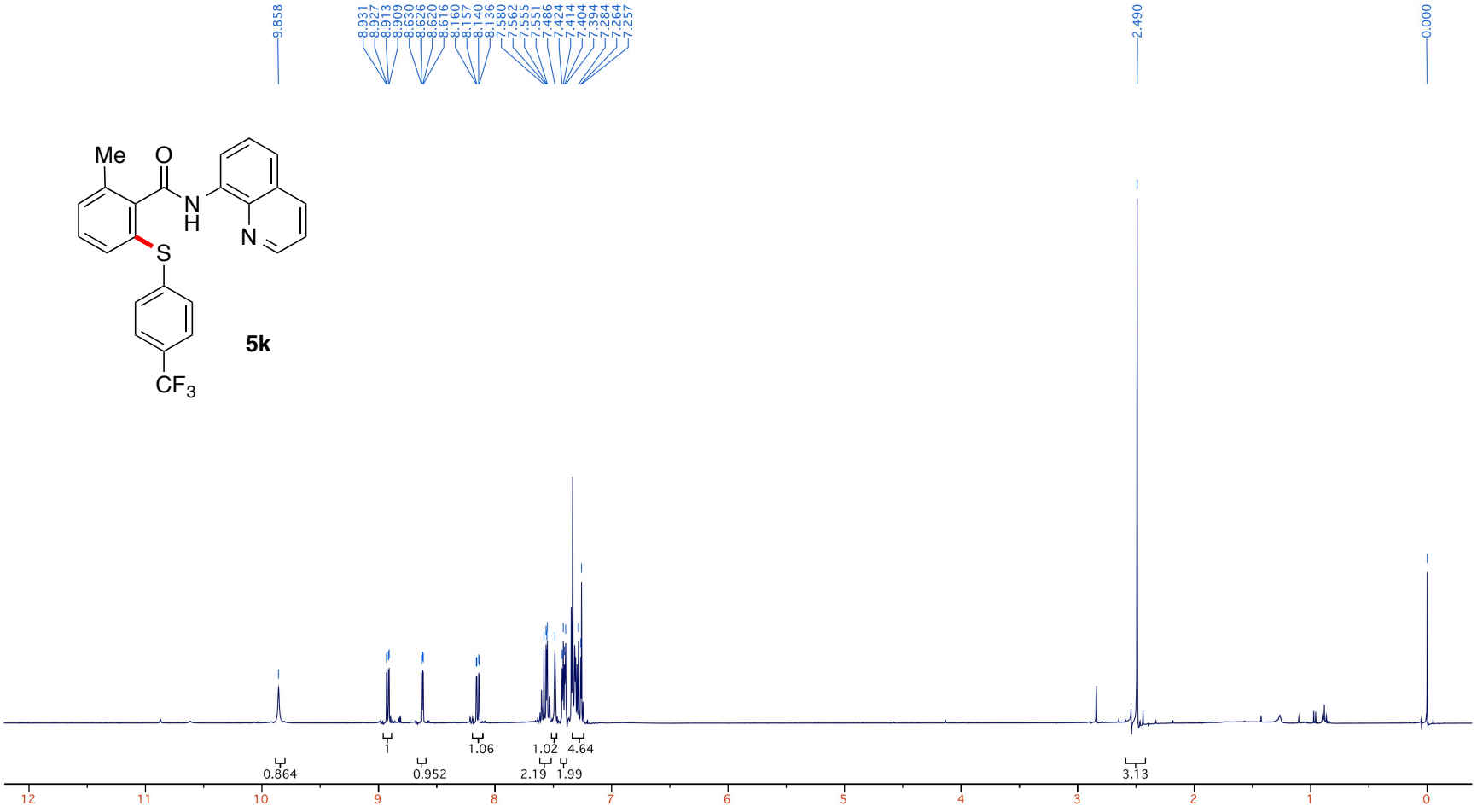
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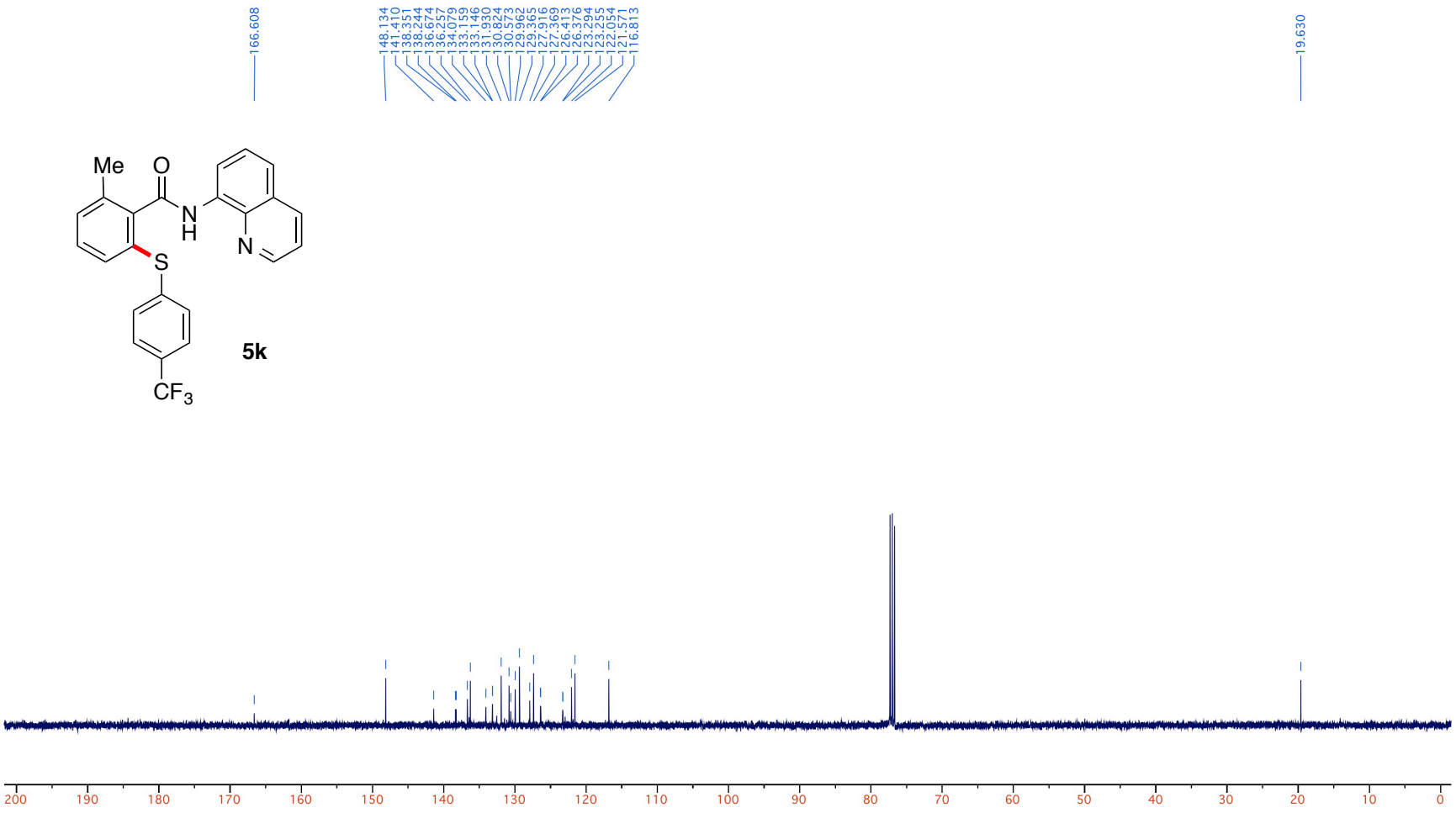
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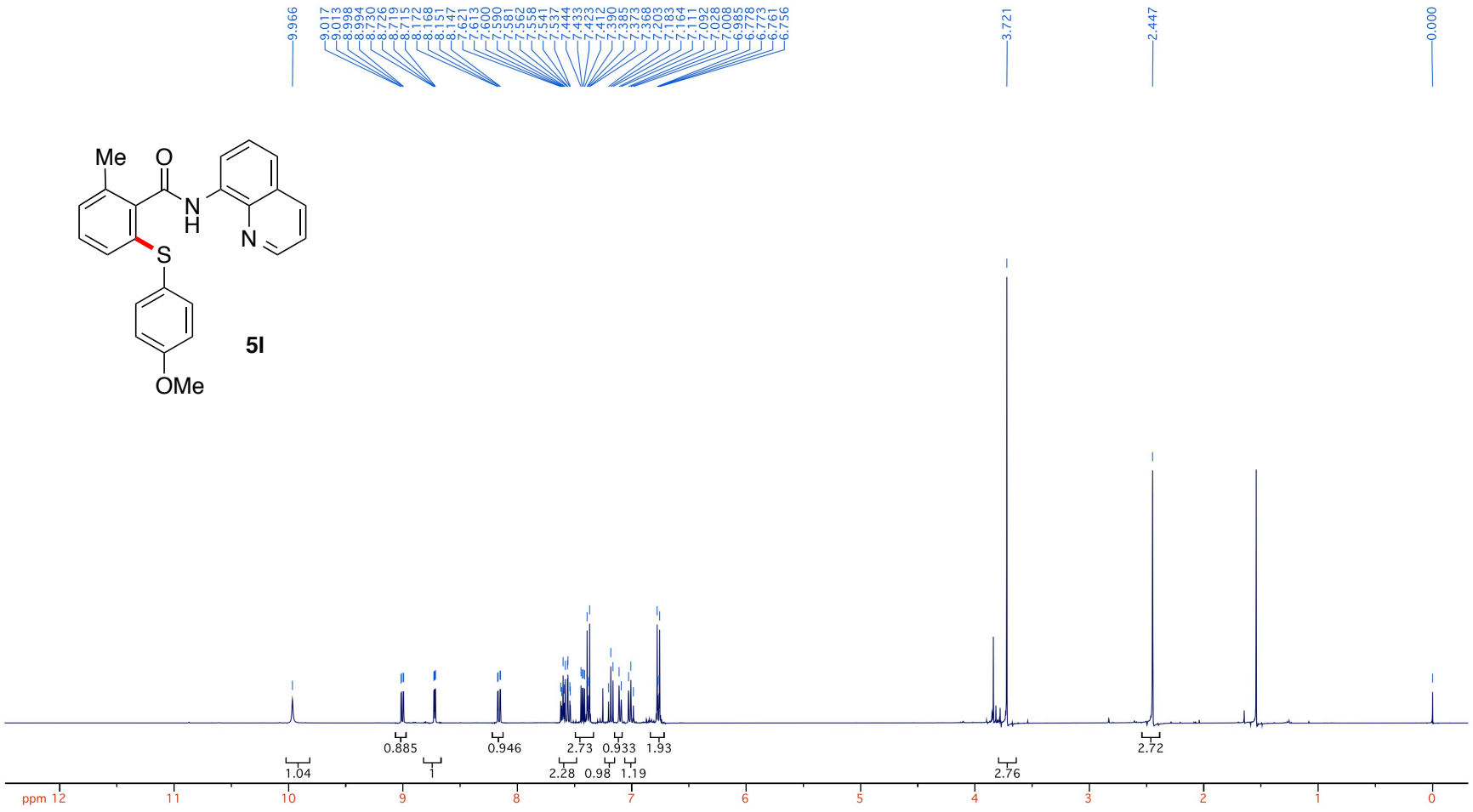
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5l
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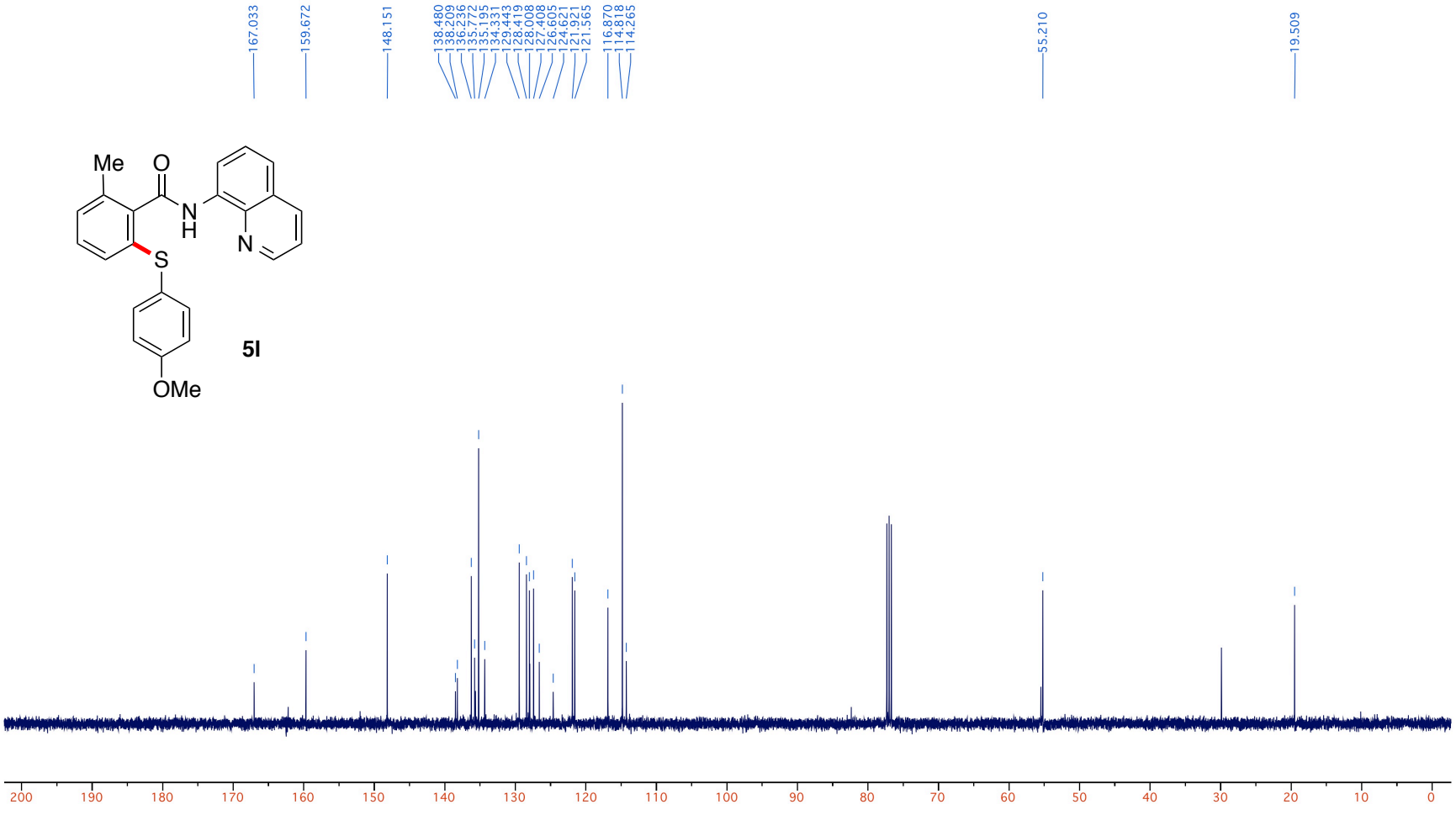
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OMe
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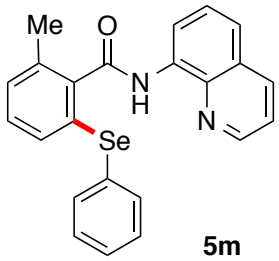
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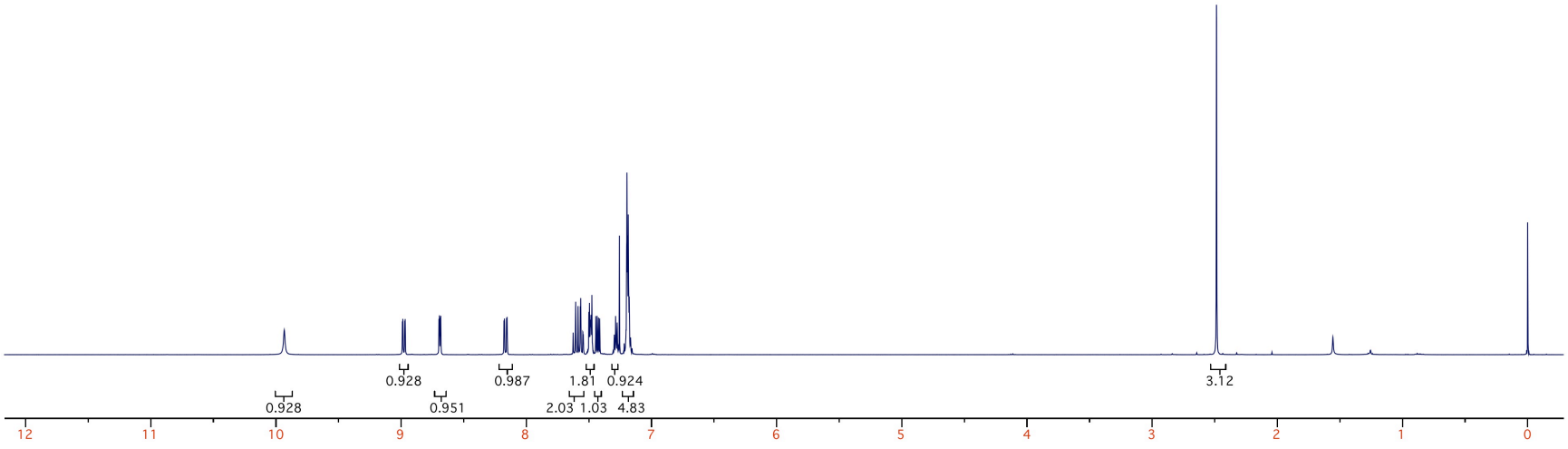
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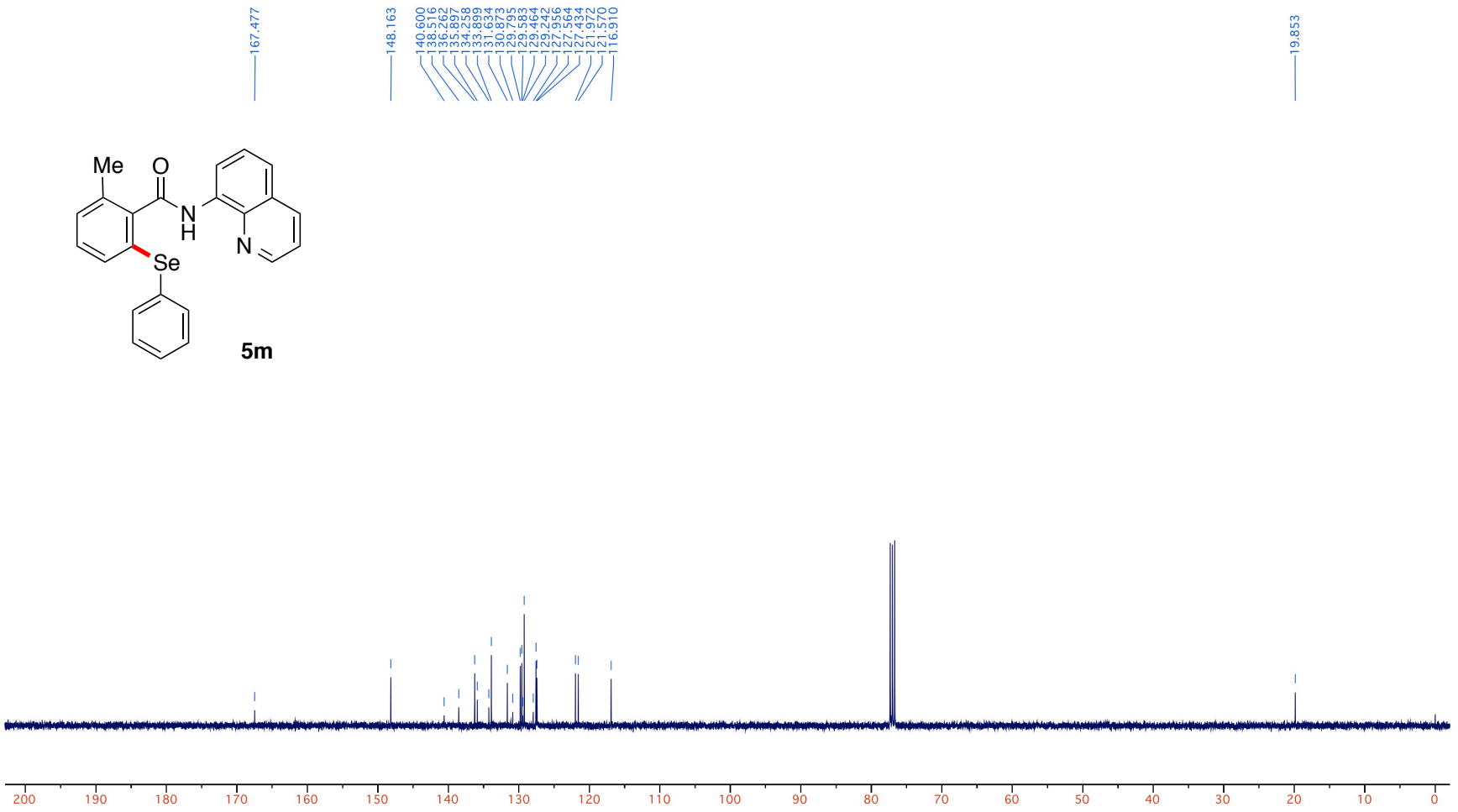
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N
H
N
Se
5m
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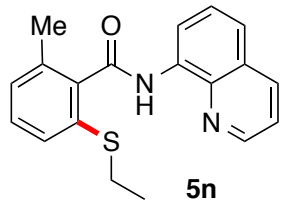
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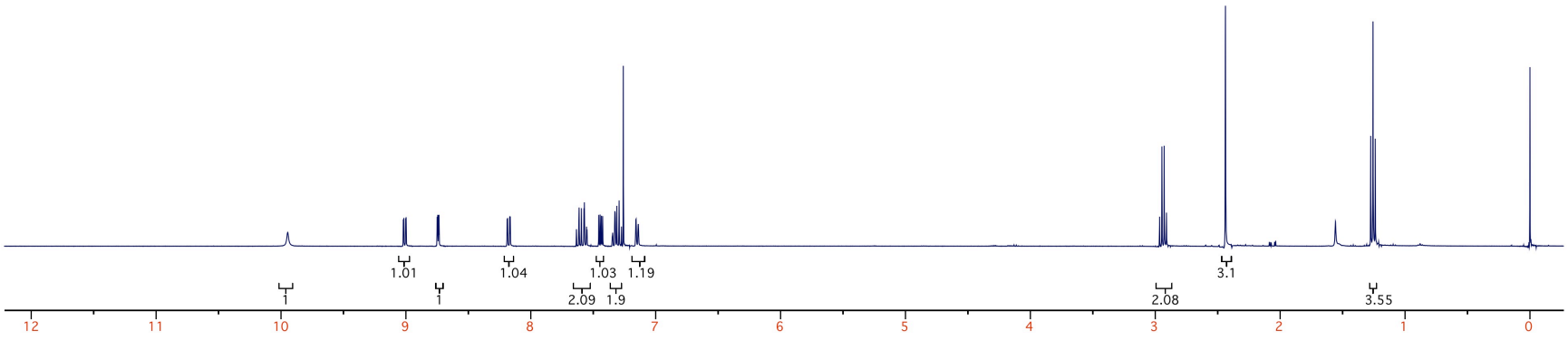
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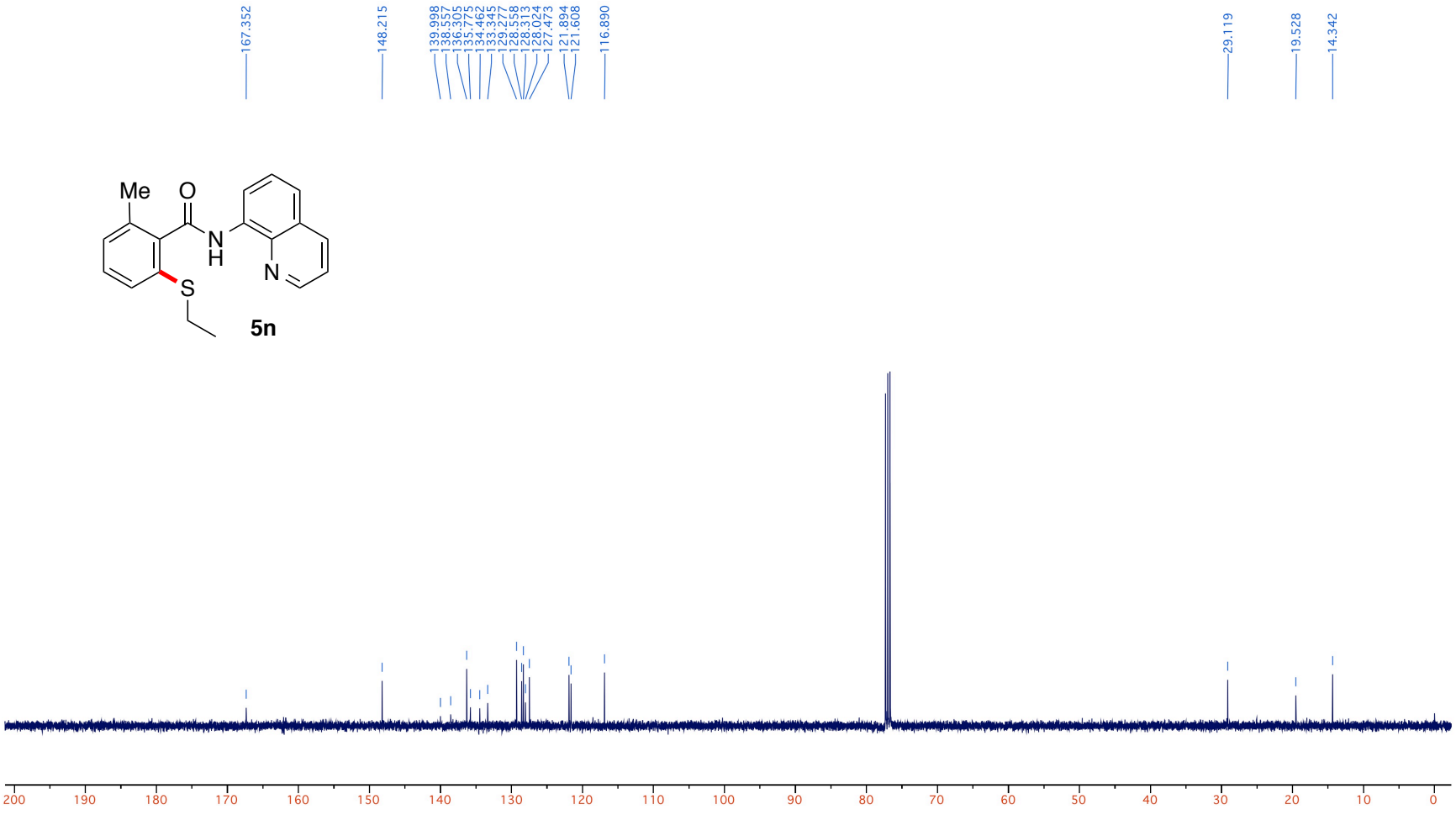
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H
N
S
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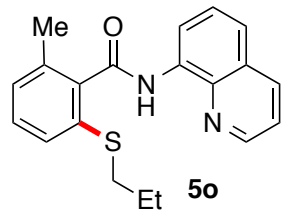
Me
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Et

5o

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0.987
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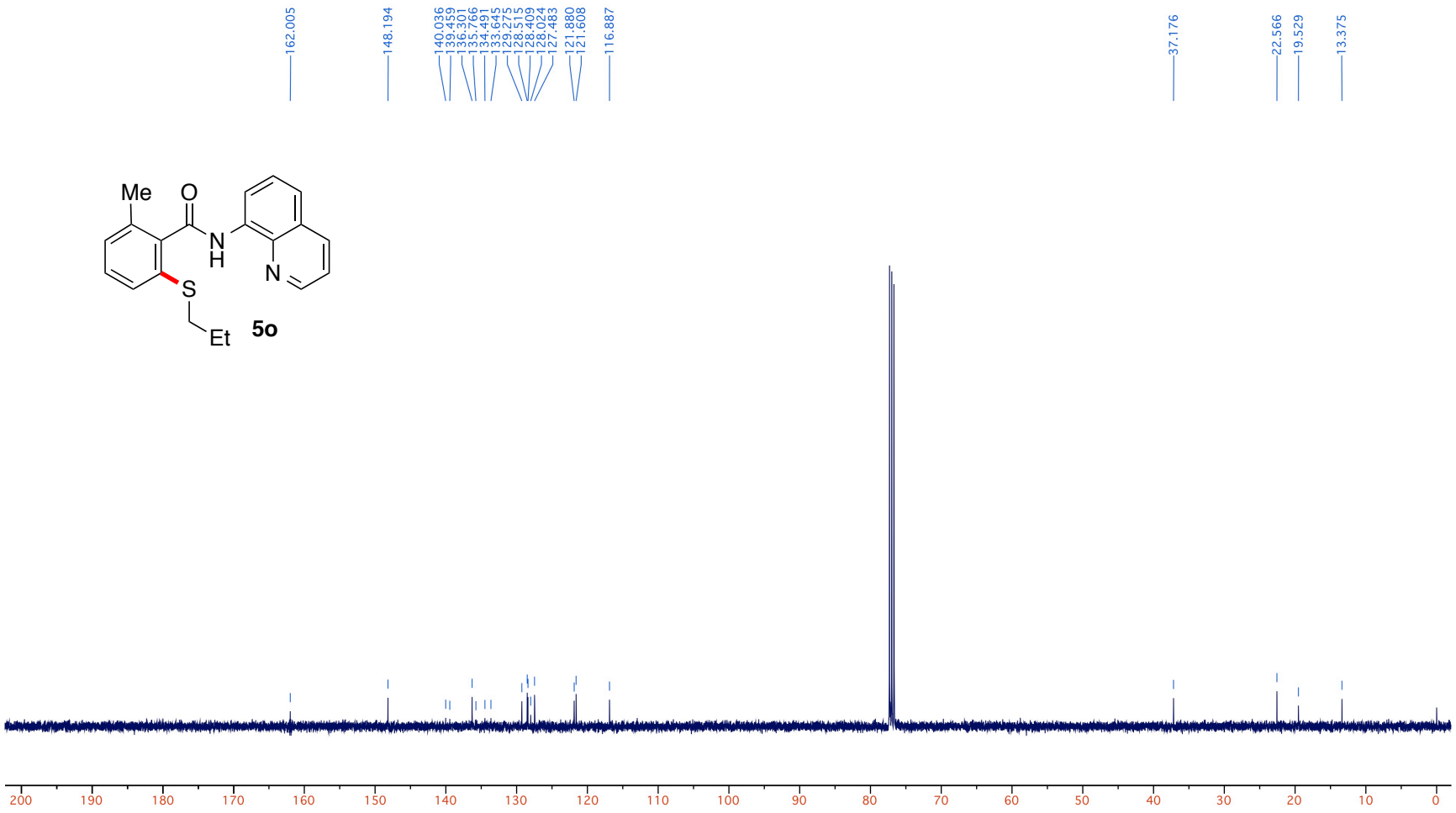
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127.483
121.880
121.608
116.887
37.176
22.566
19.529
13.375
Me
O
N
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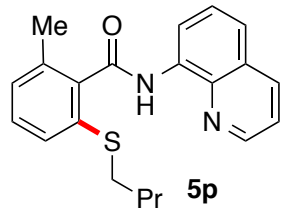
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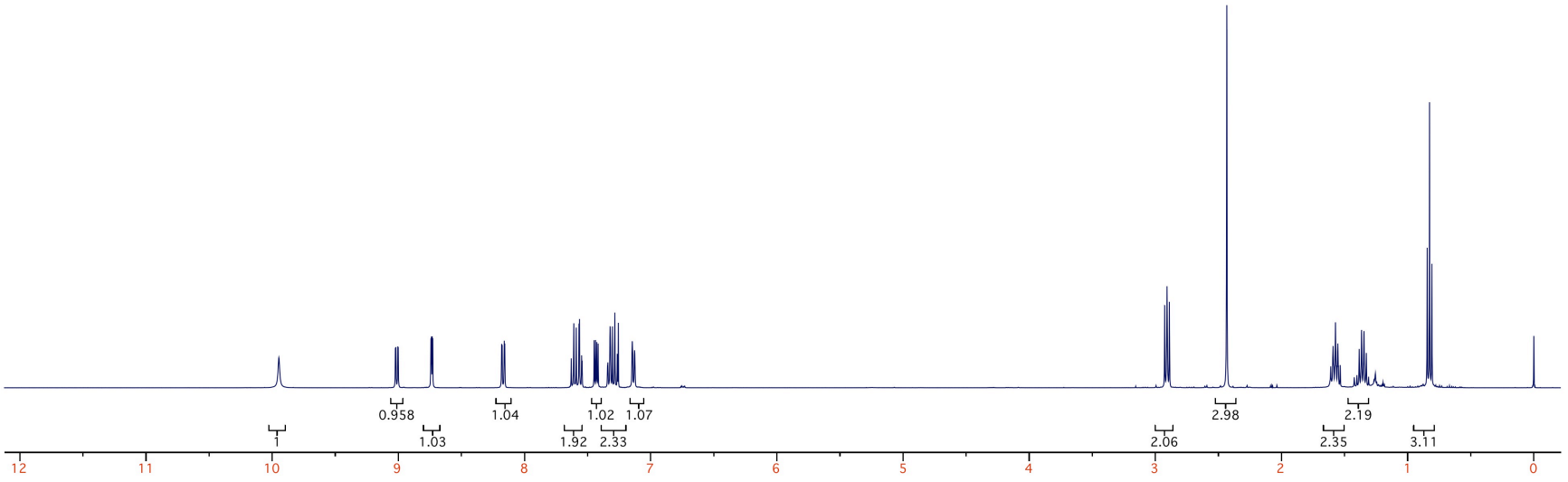
Pr

5p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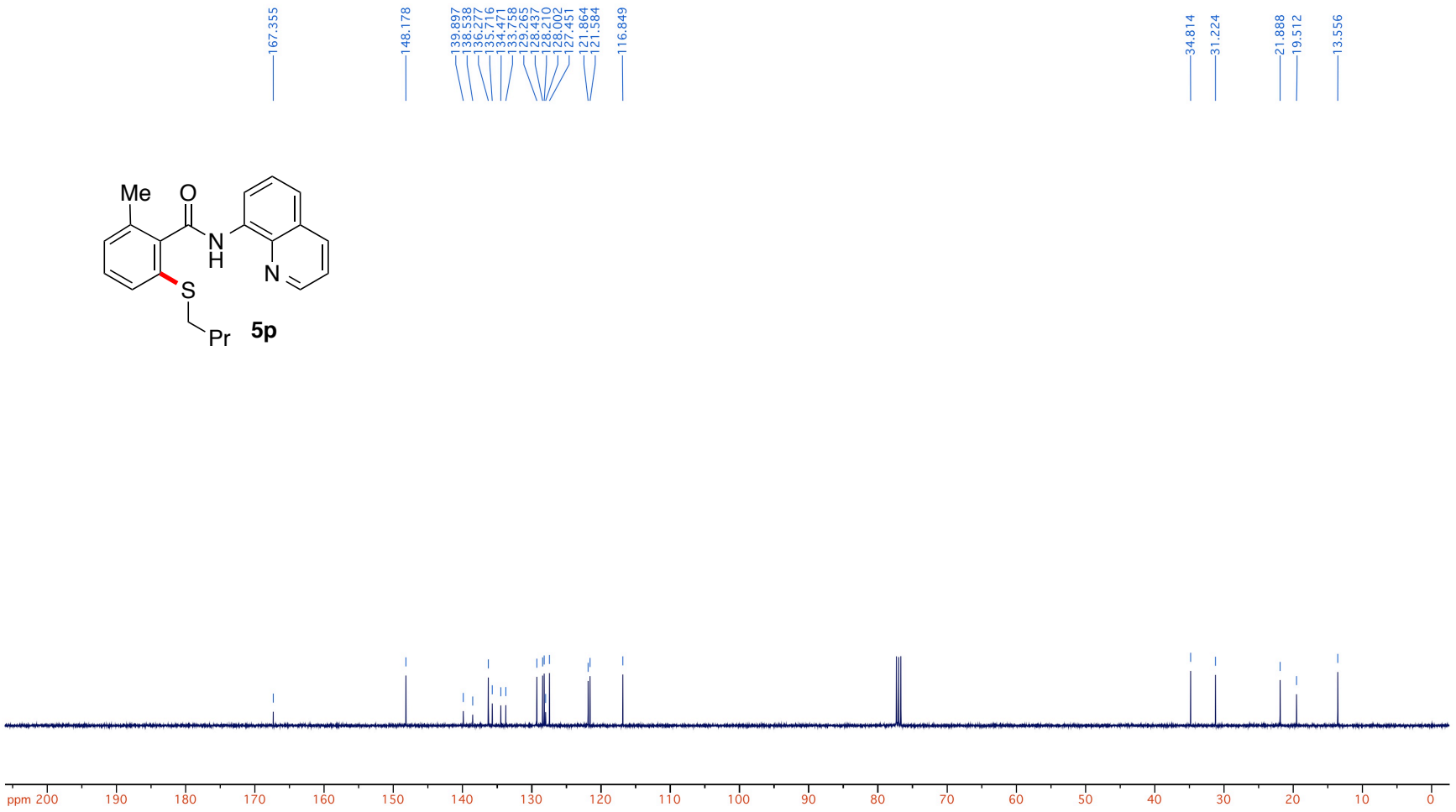
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Pr
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