Electronic Supplementary Material (ESI) for RSC Advances.

Conformationally restricted glutamic acid analogues: stereoisomers of 1-aminospiro[3.3]heptane-1,6-dicarboxylic acid

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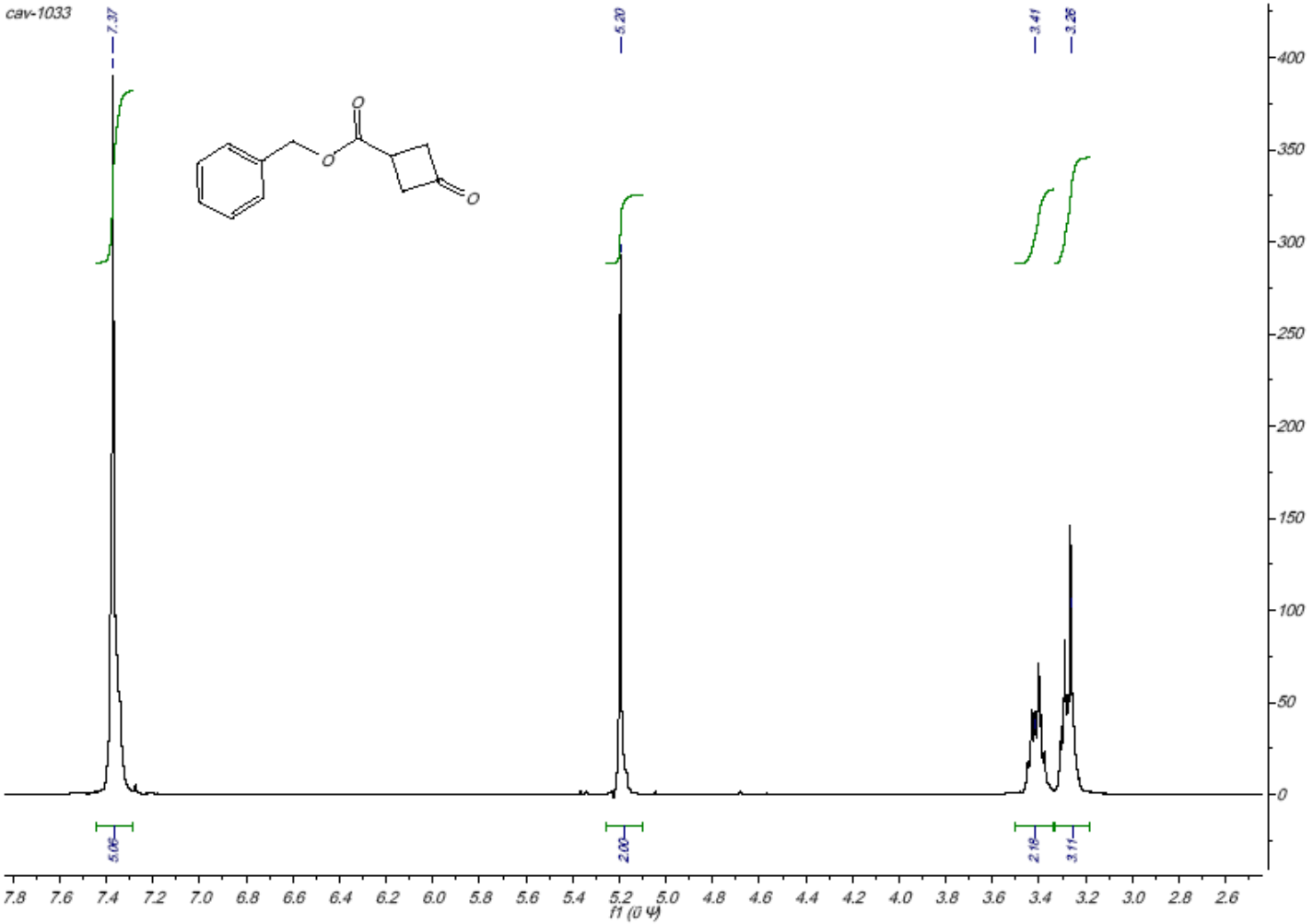
Table of contents.

^{1}H NMR spectrum of the compound **8**



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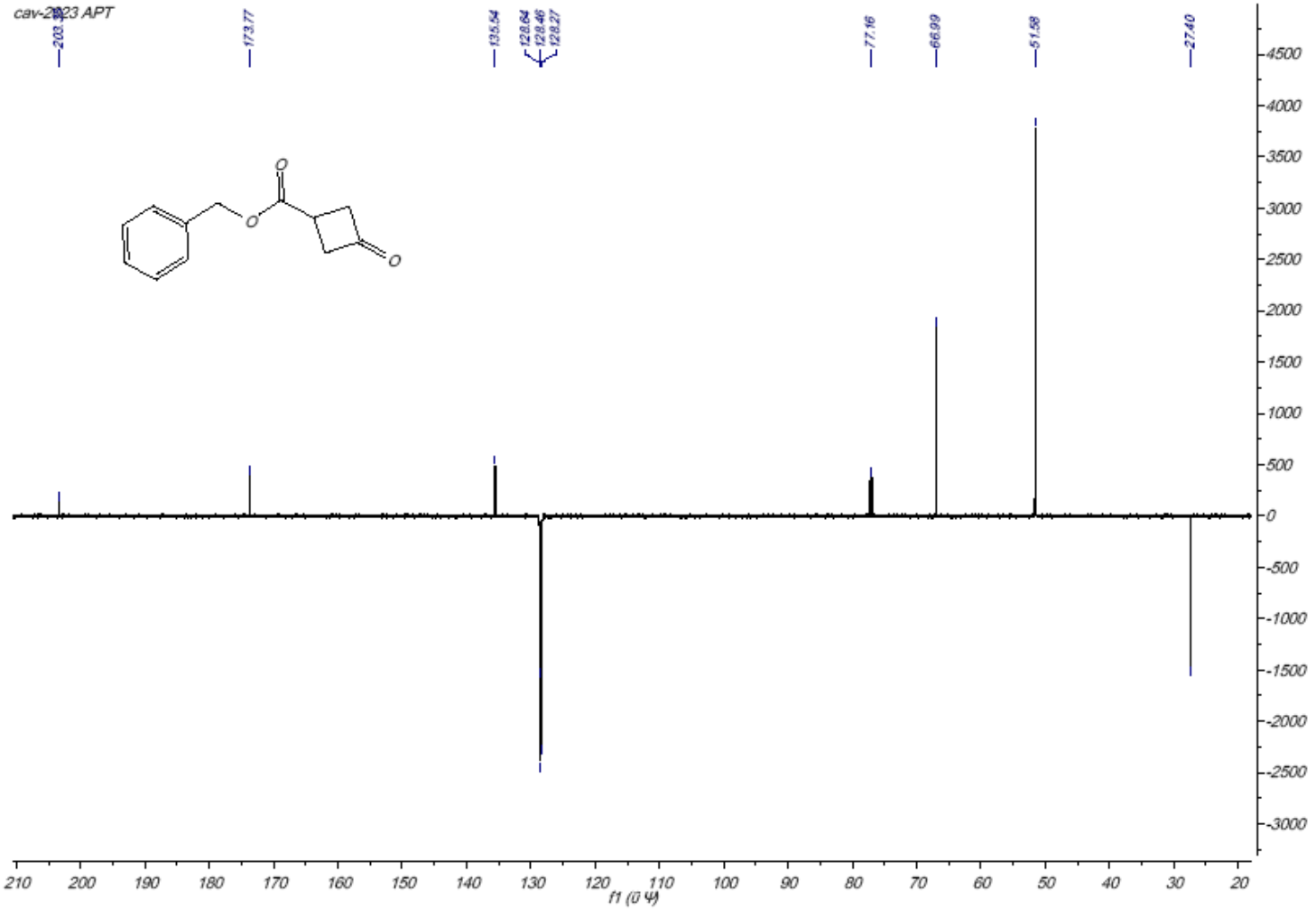

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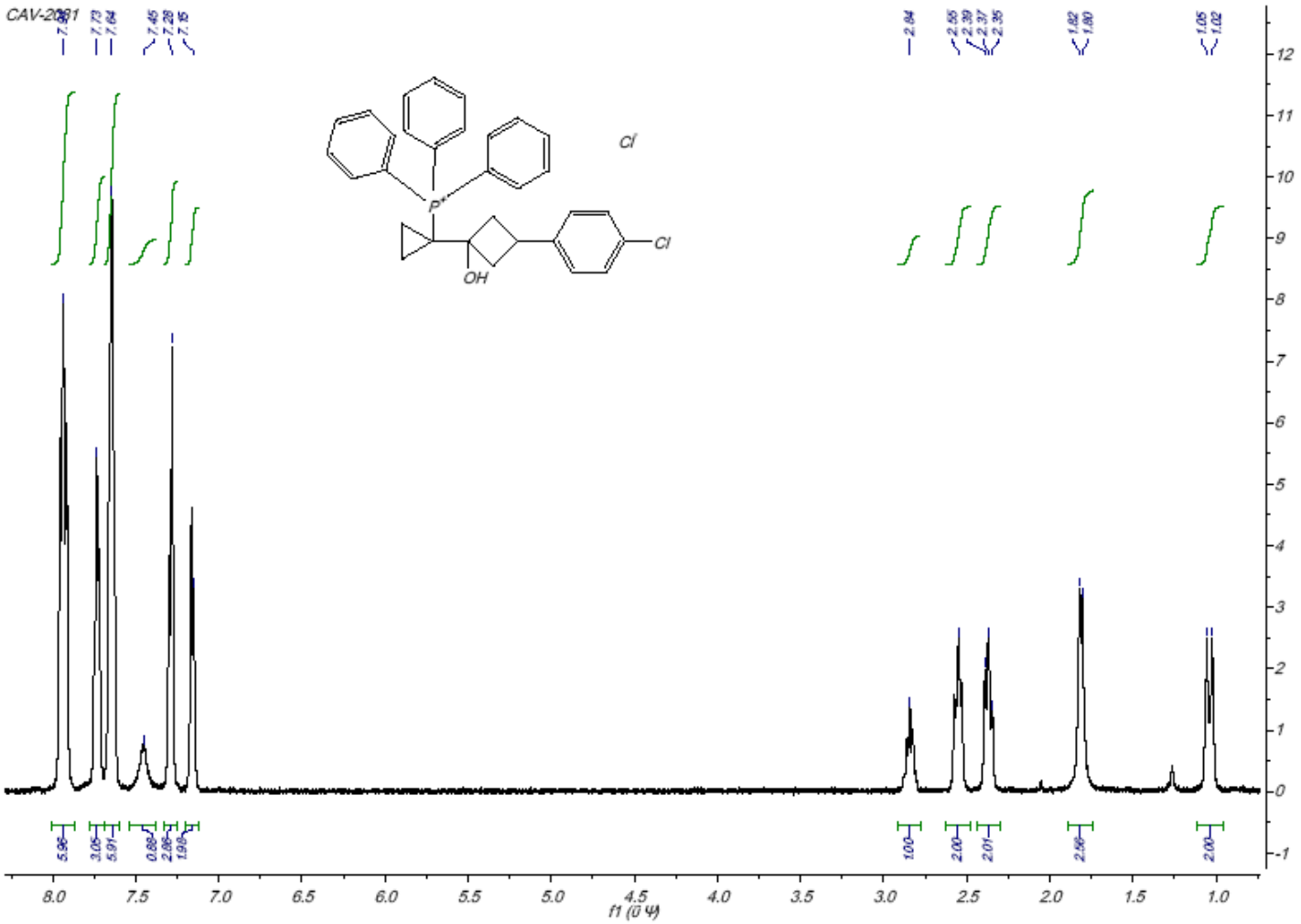

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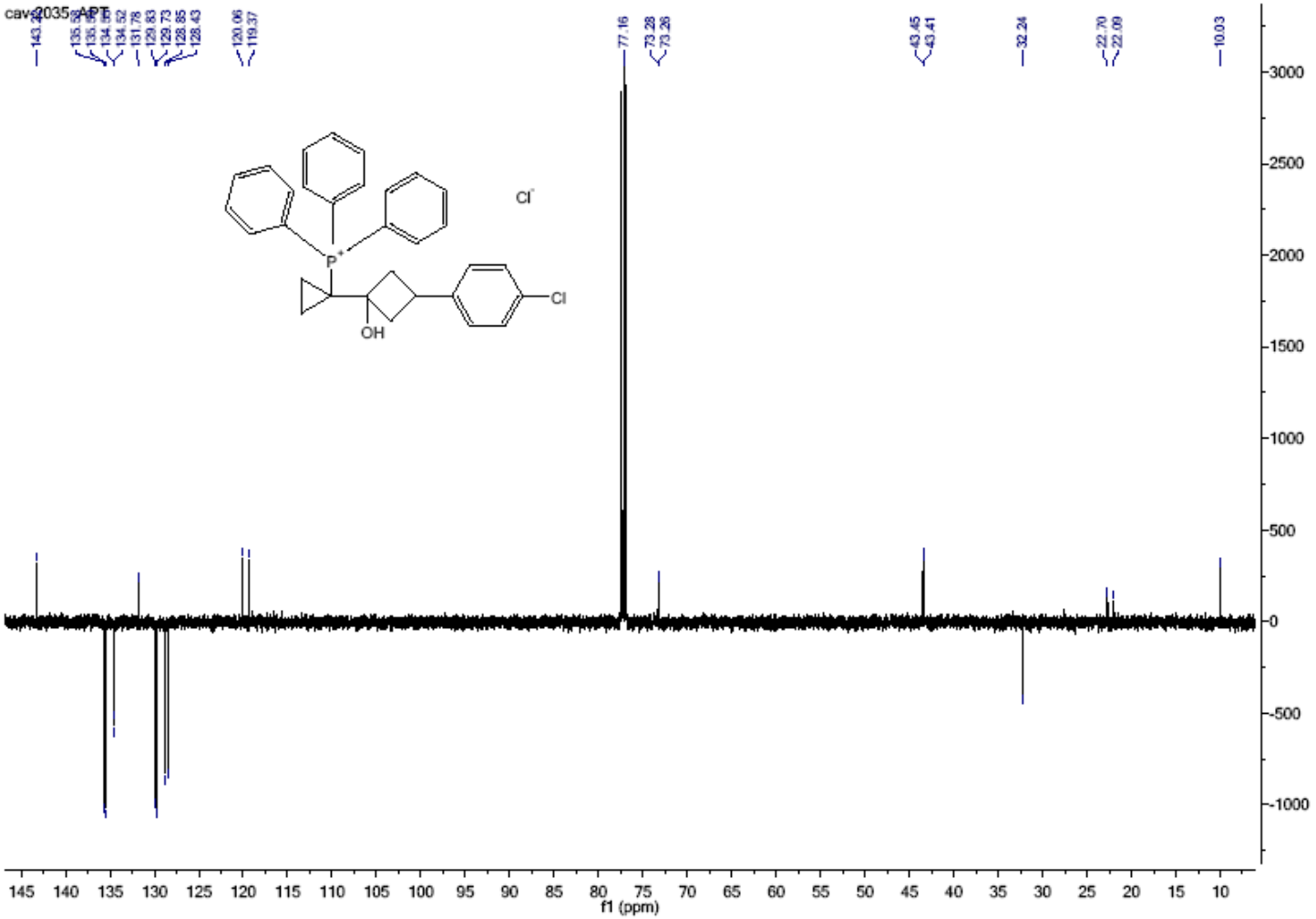

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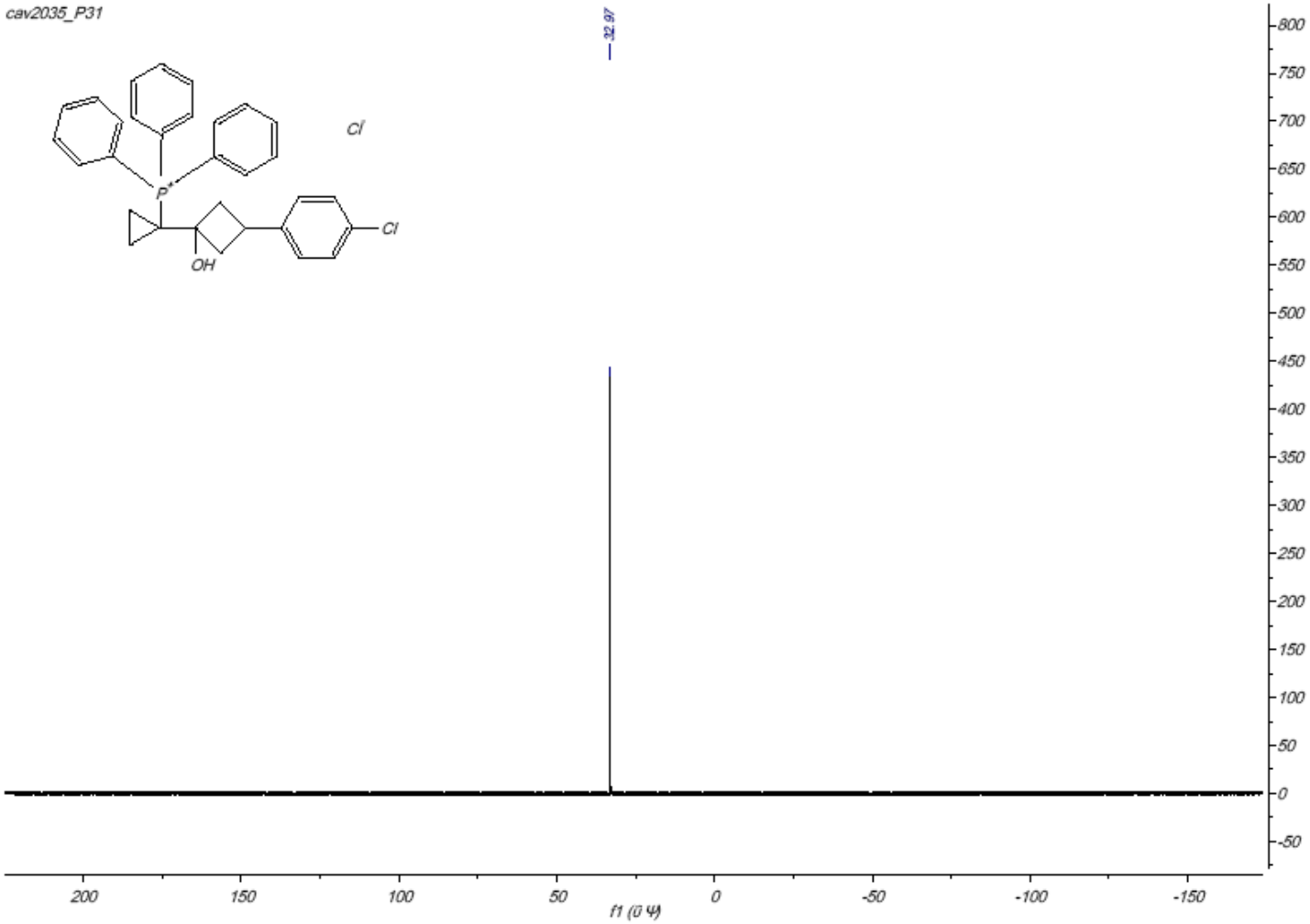

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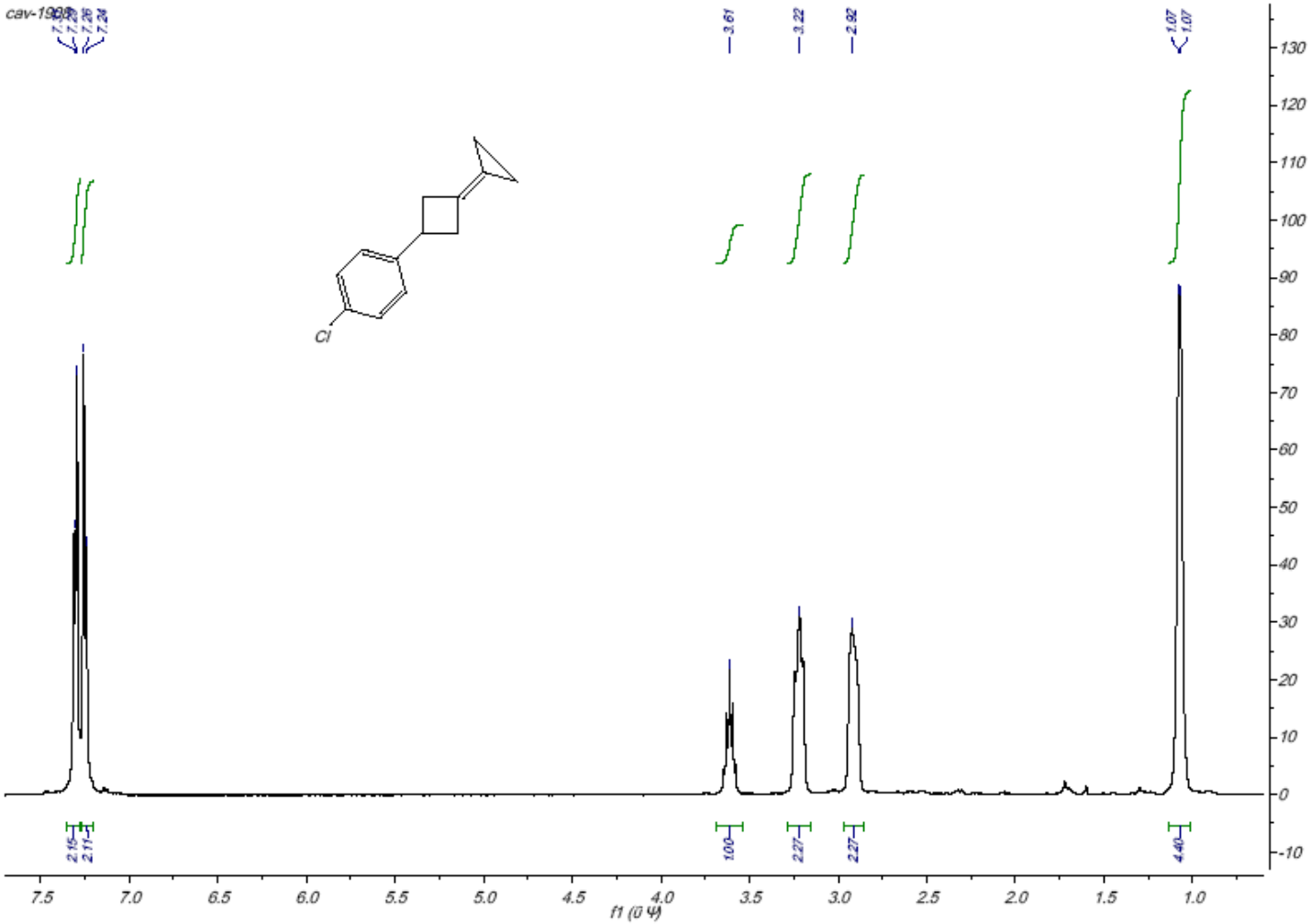

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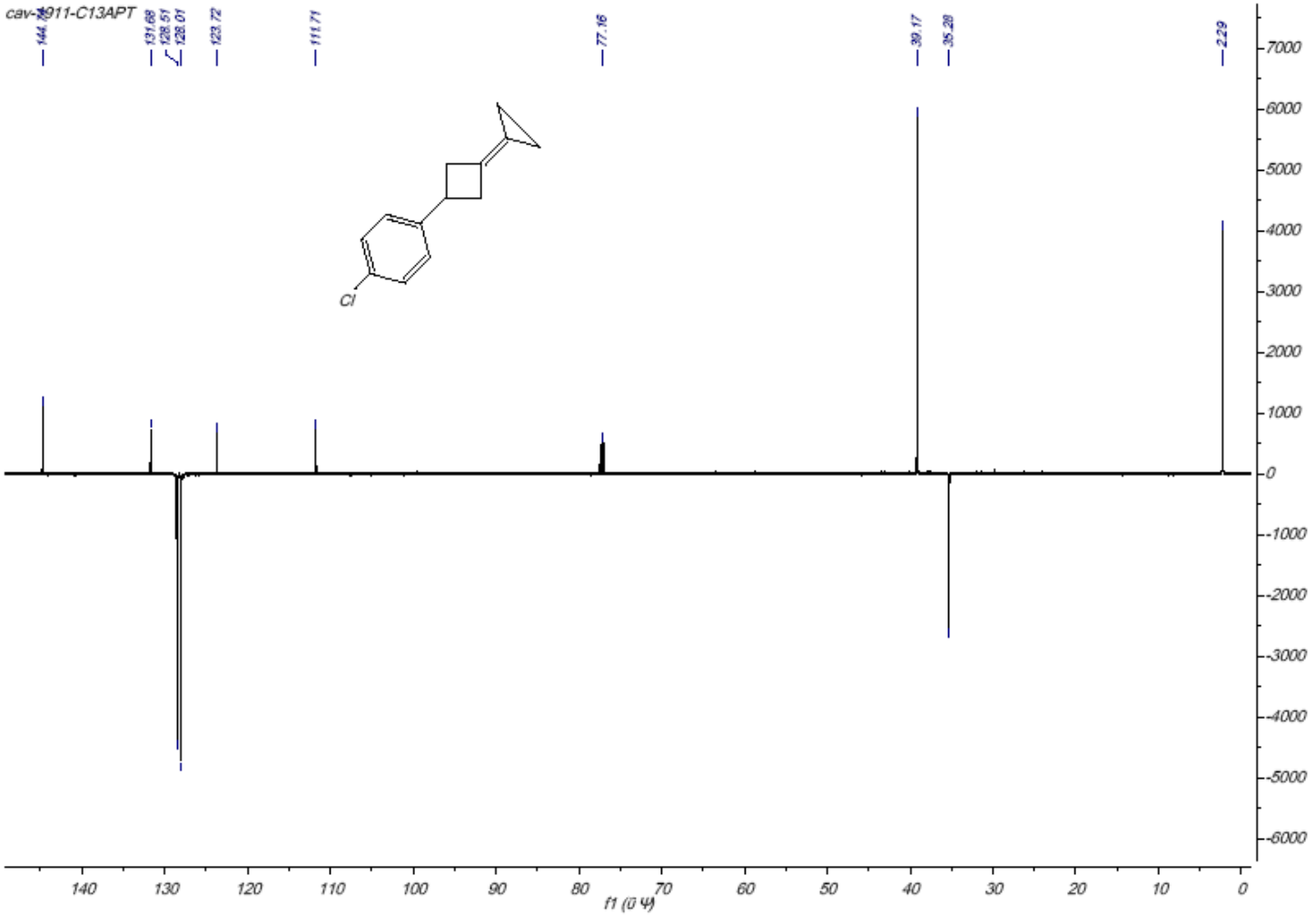

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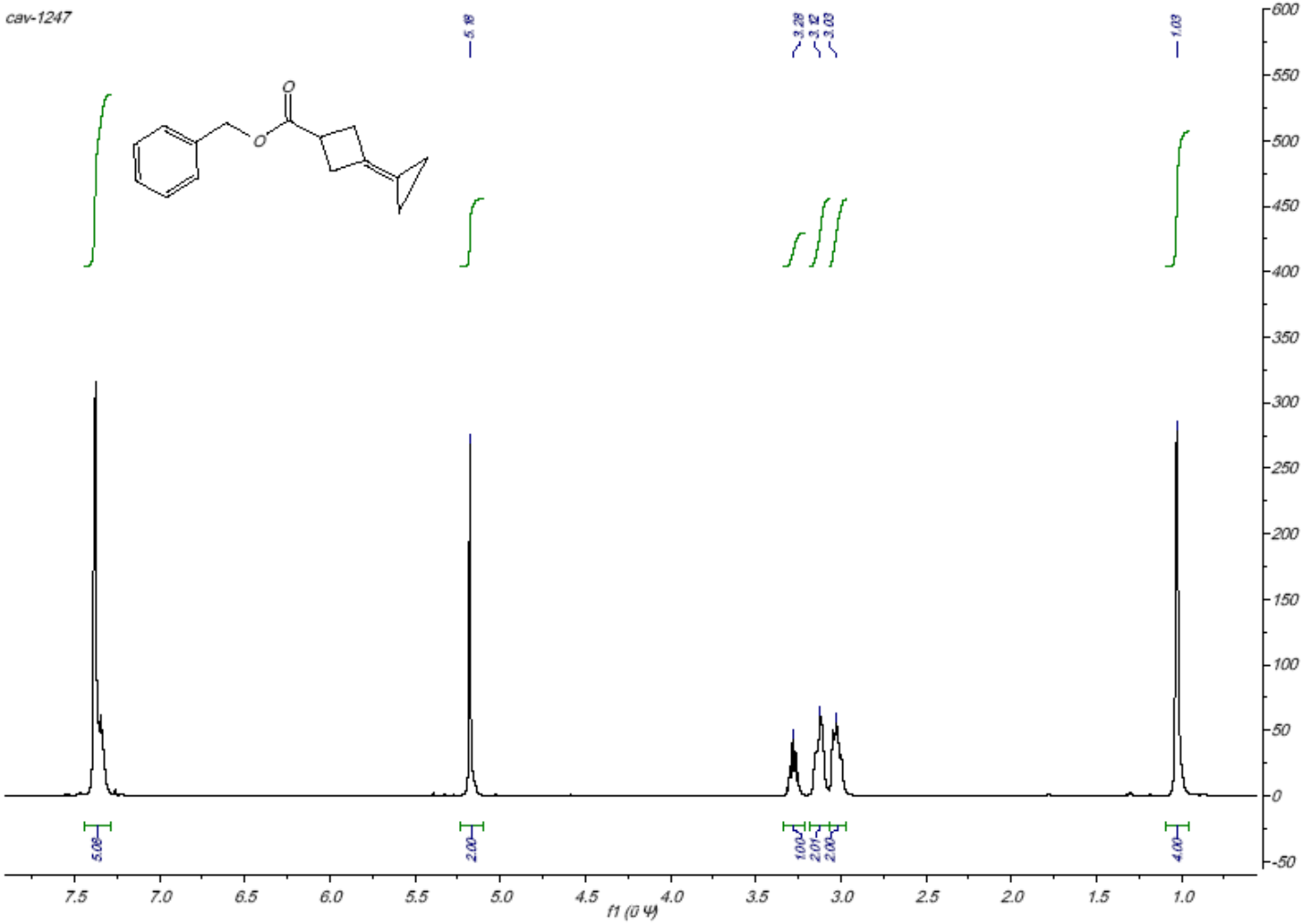

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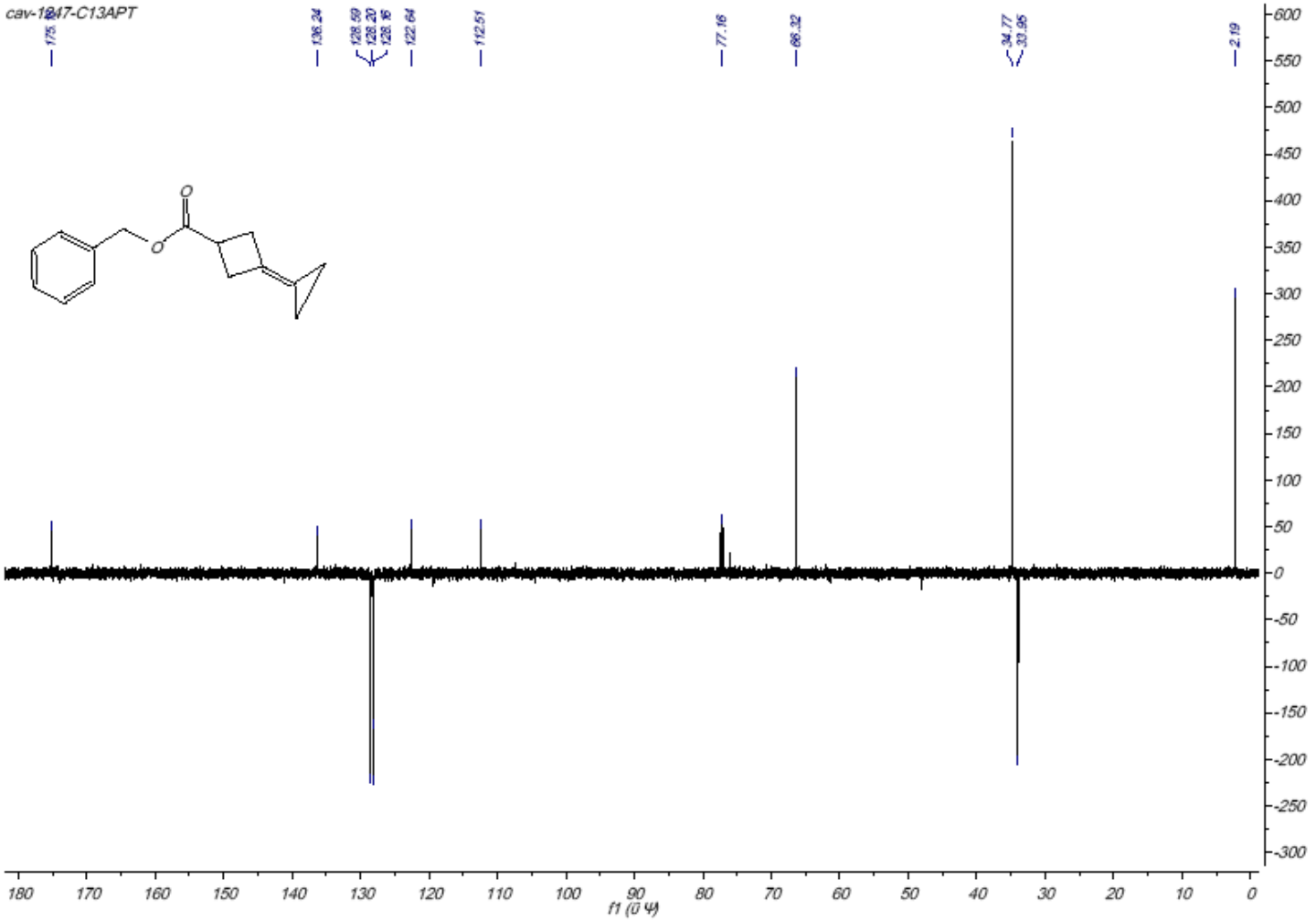

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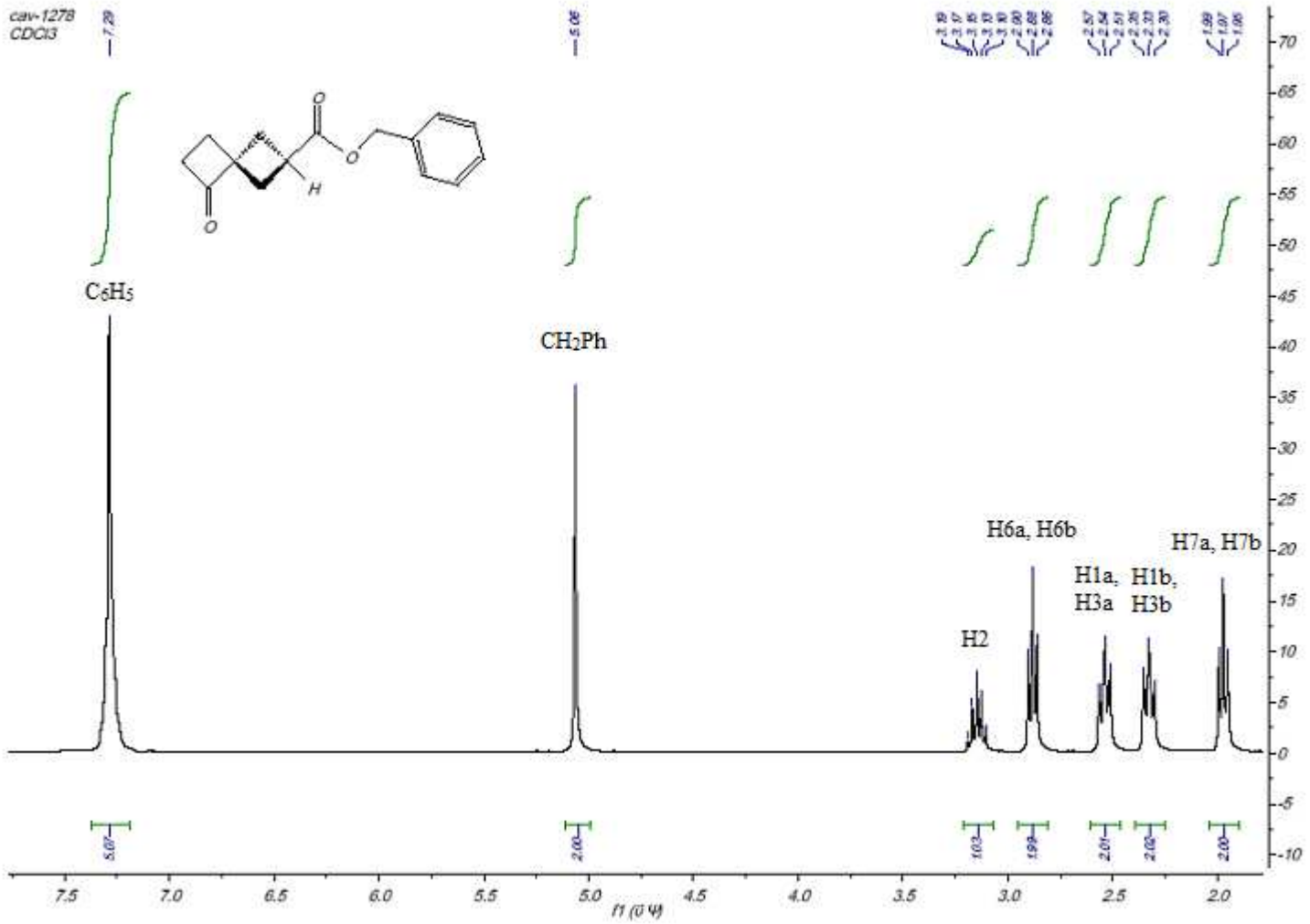

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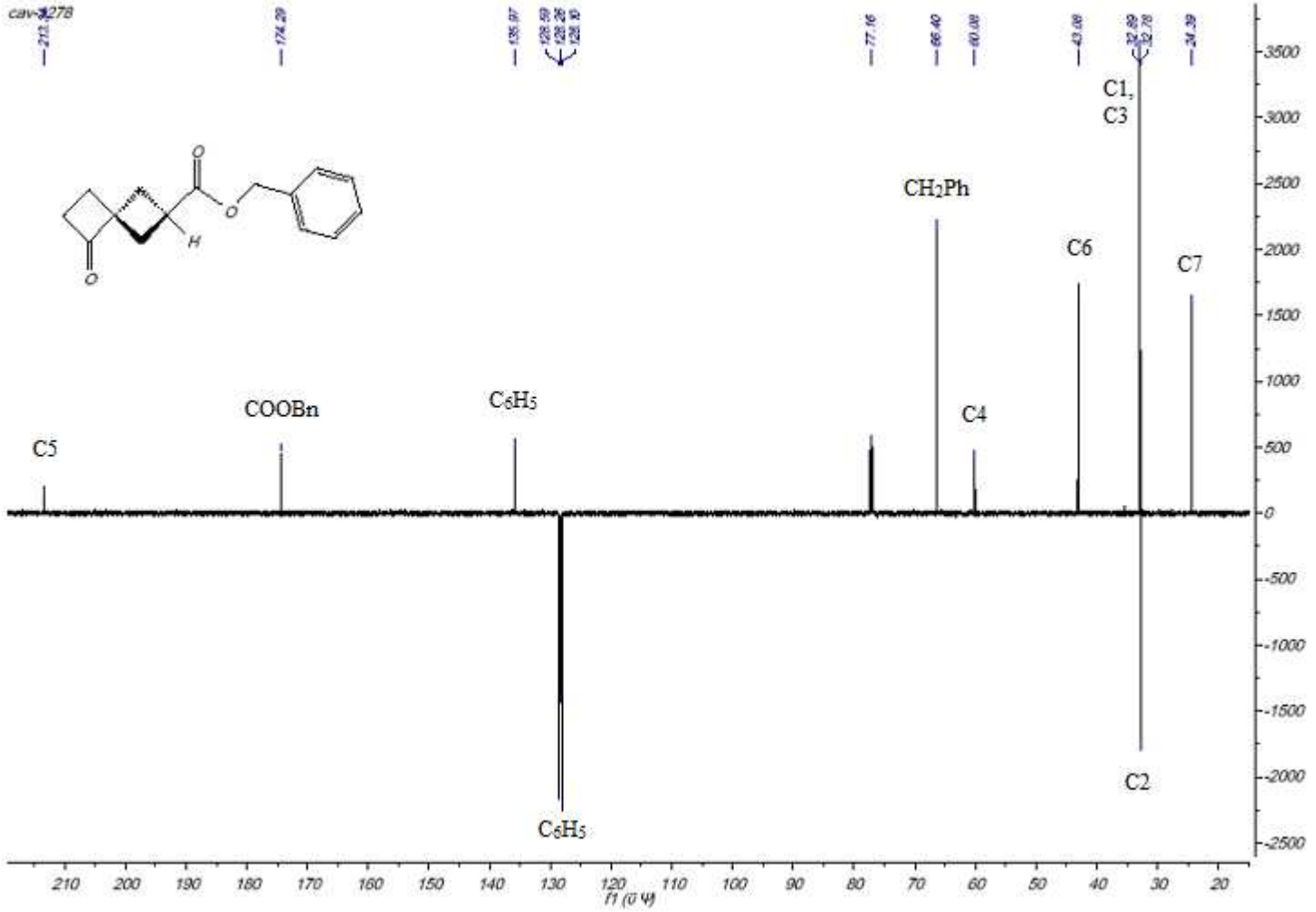

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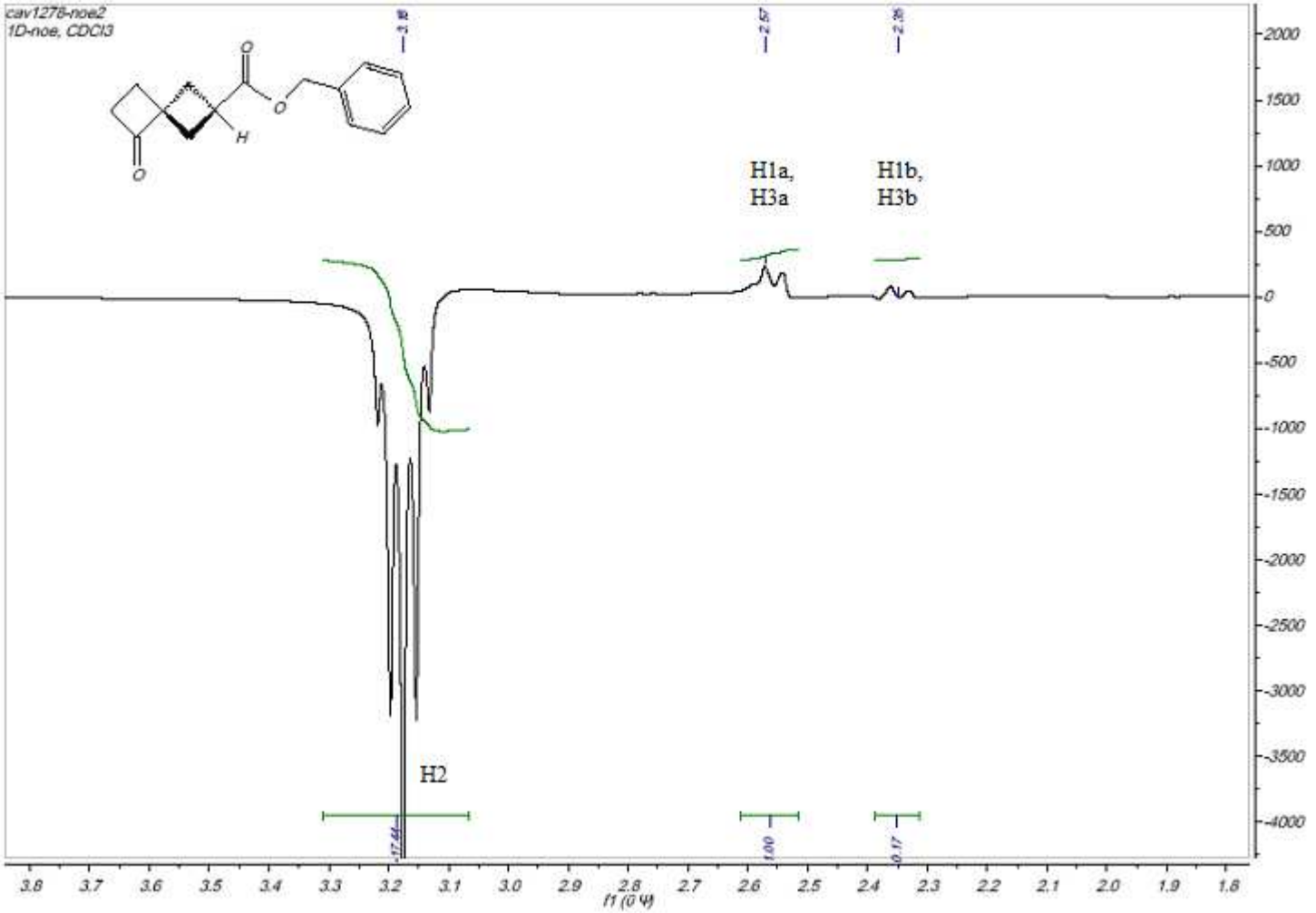

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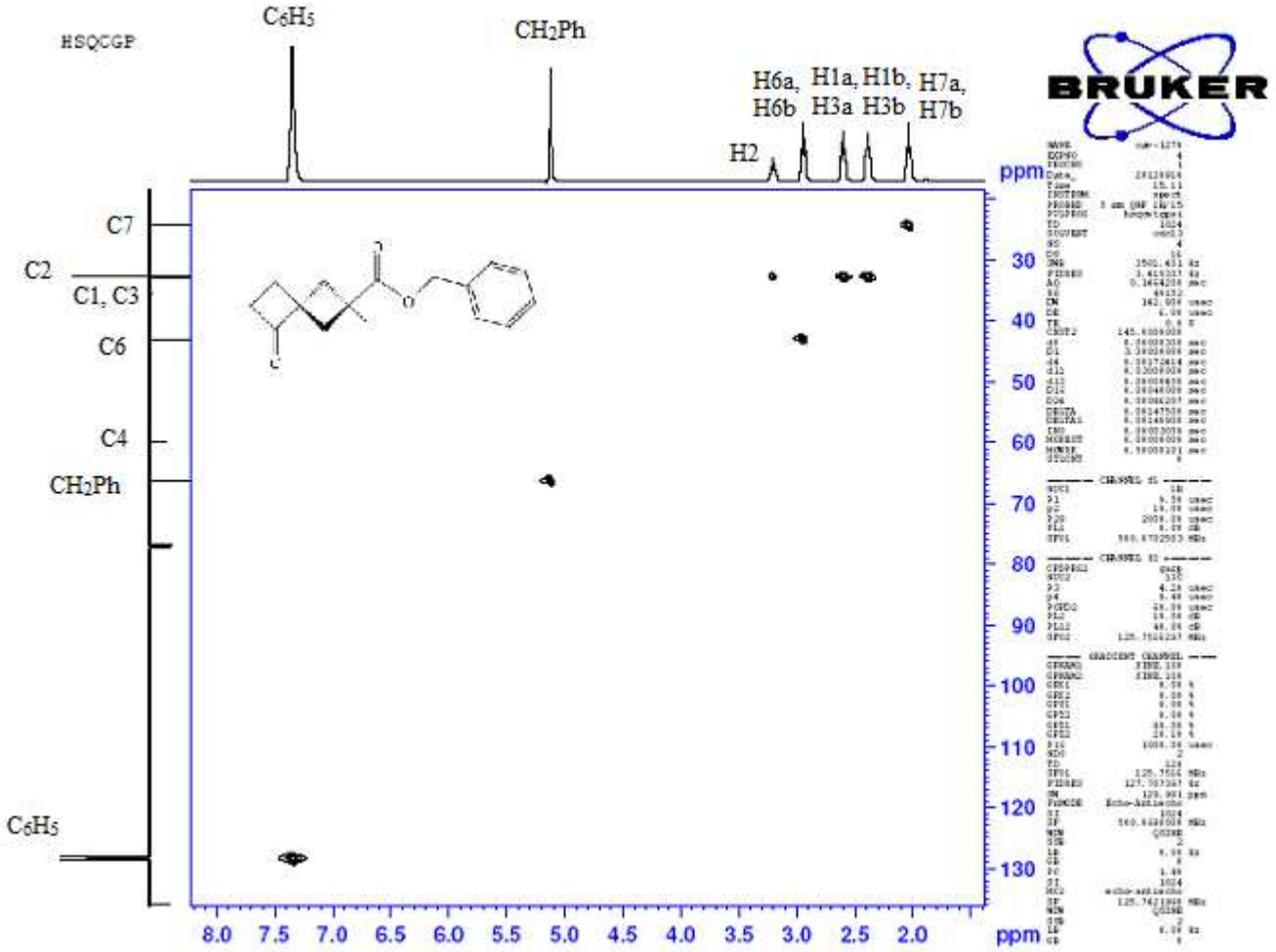

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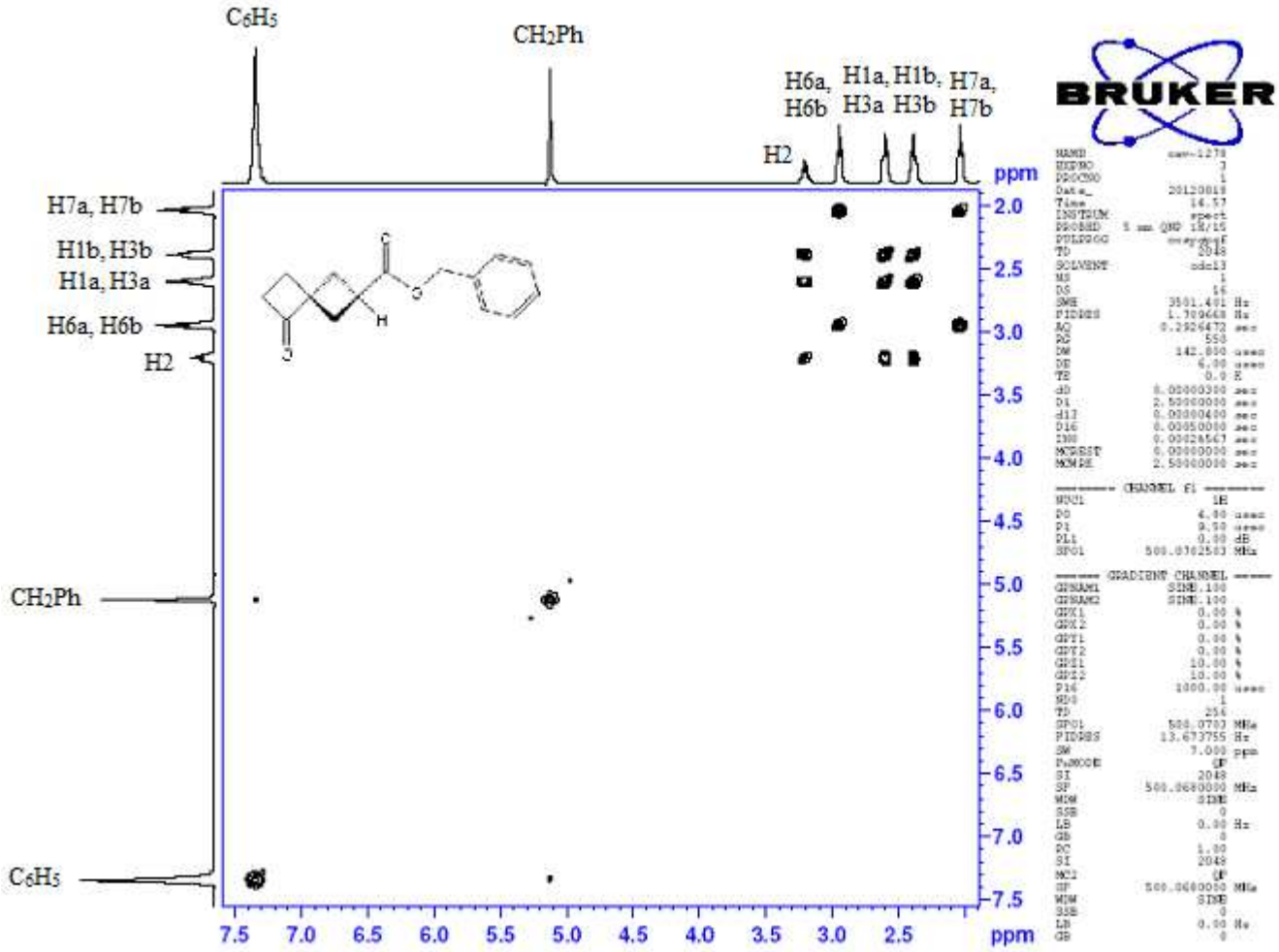

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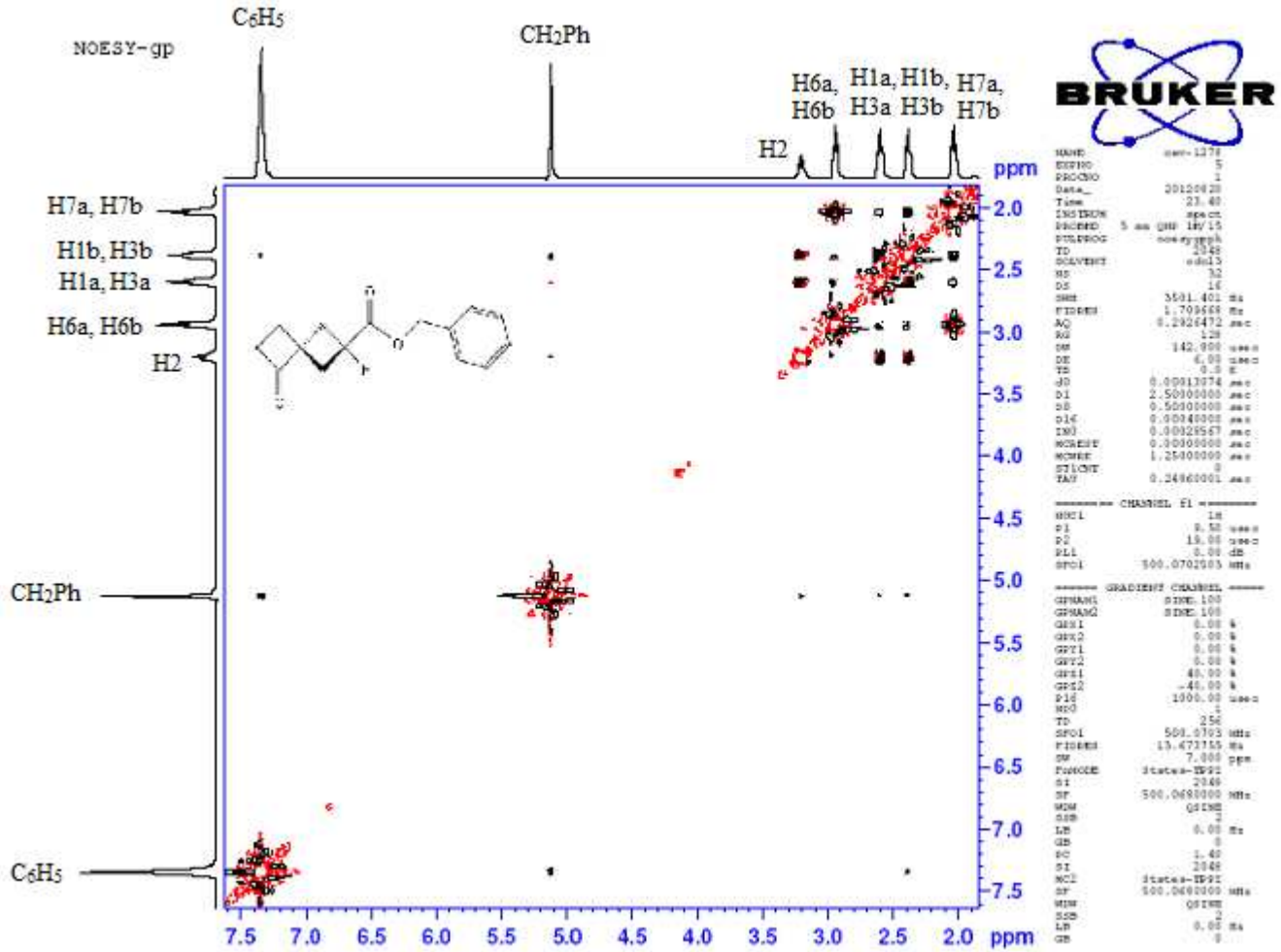

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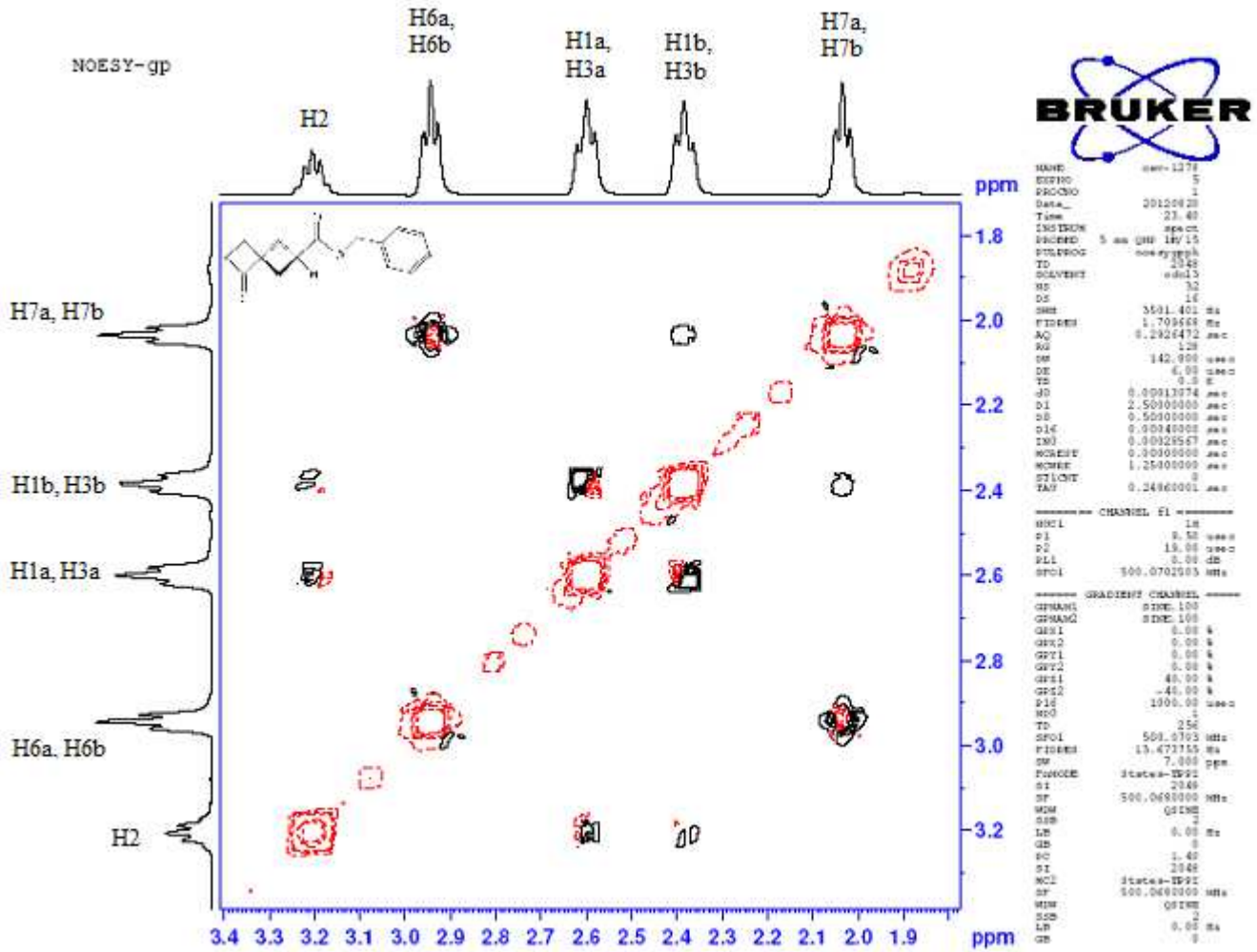

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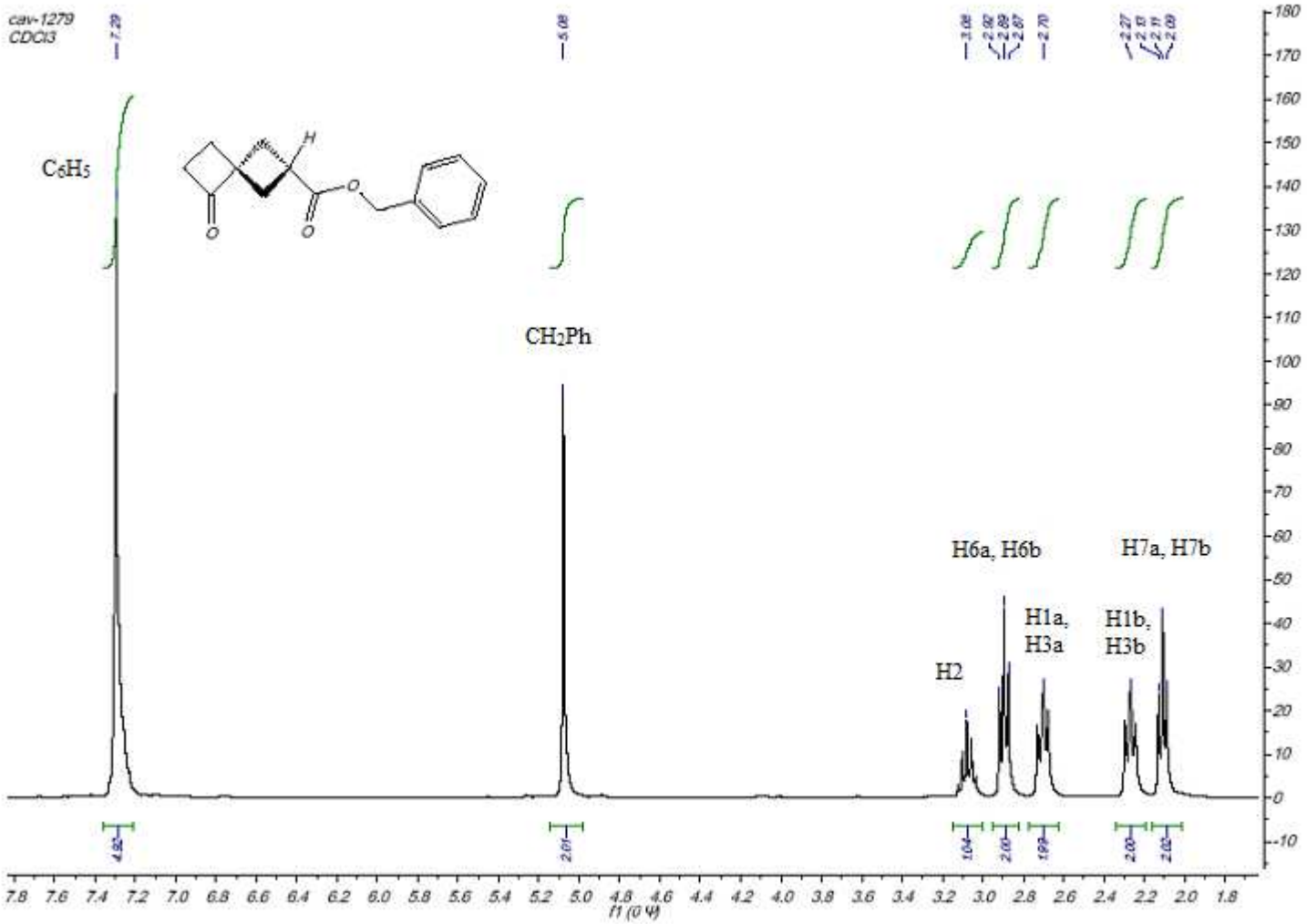

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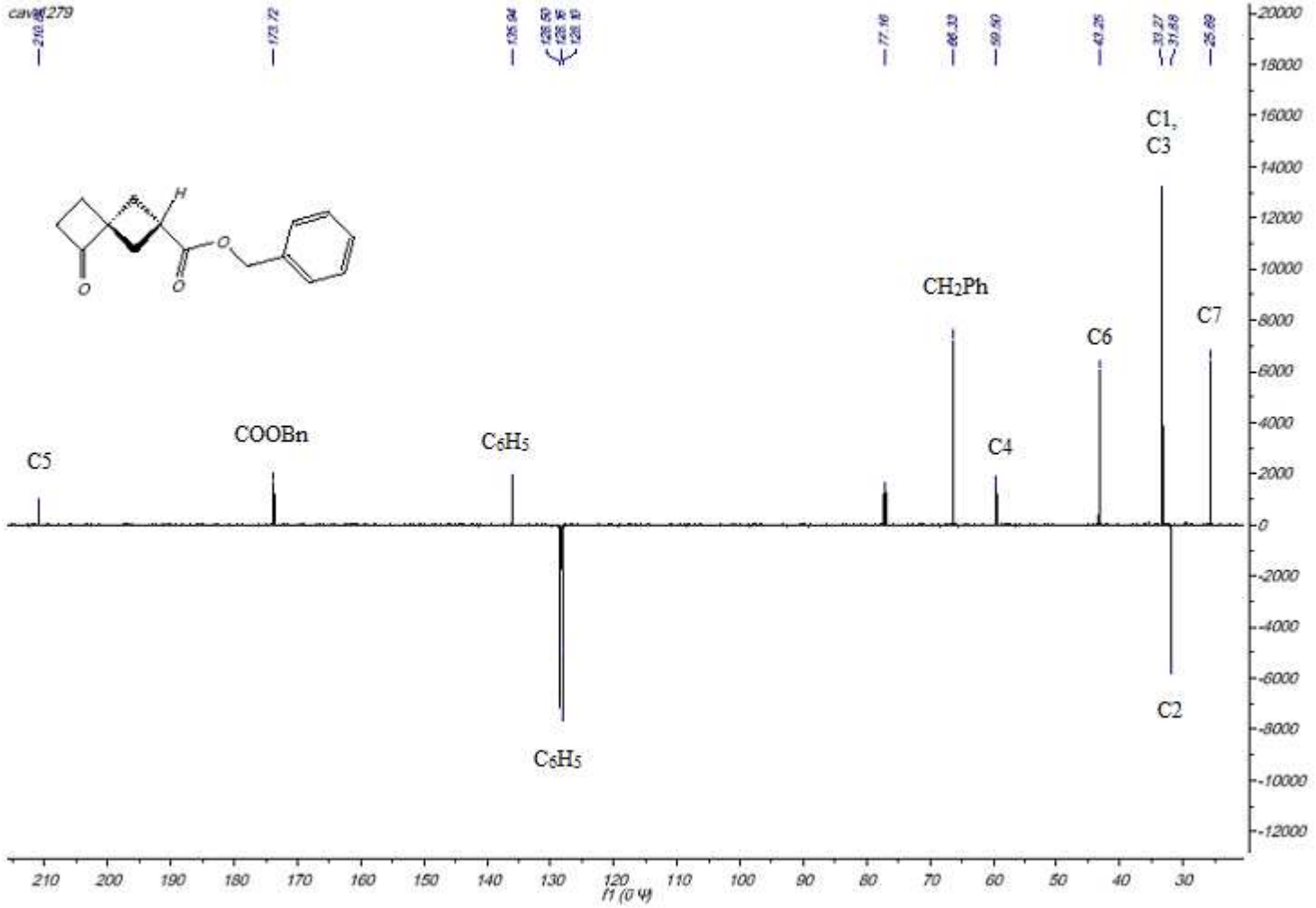

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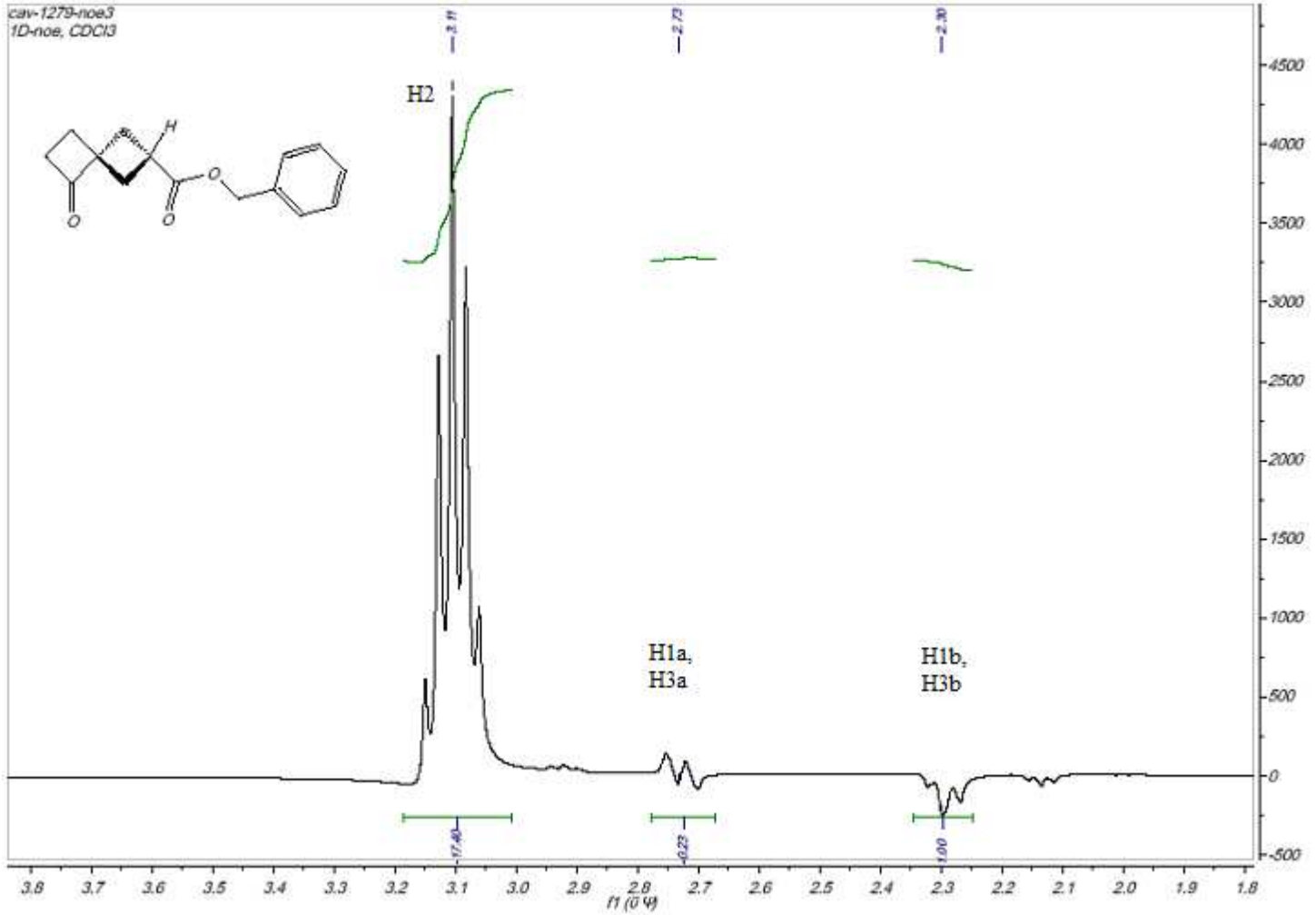

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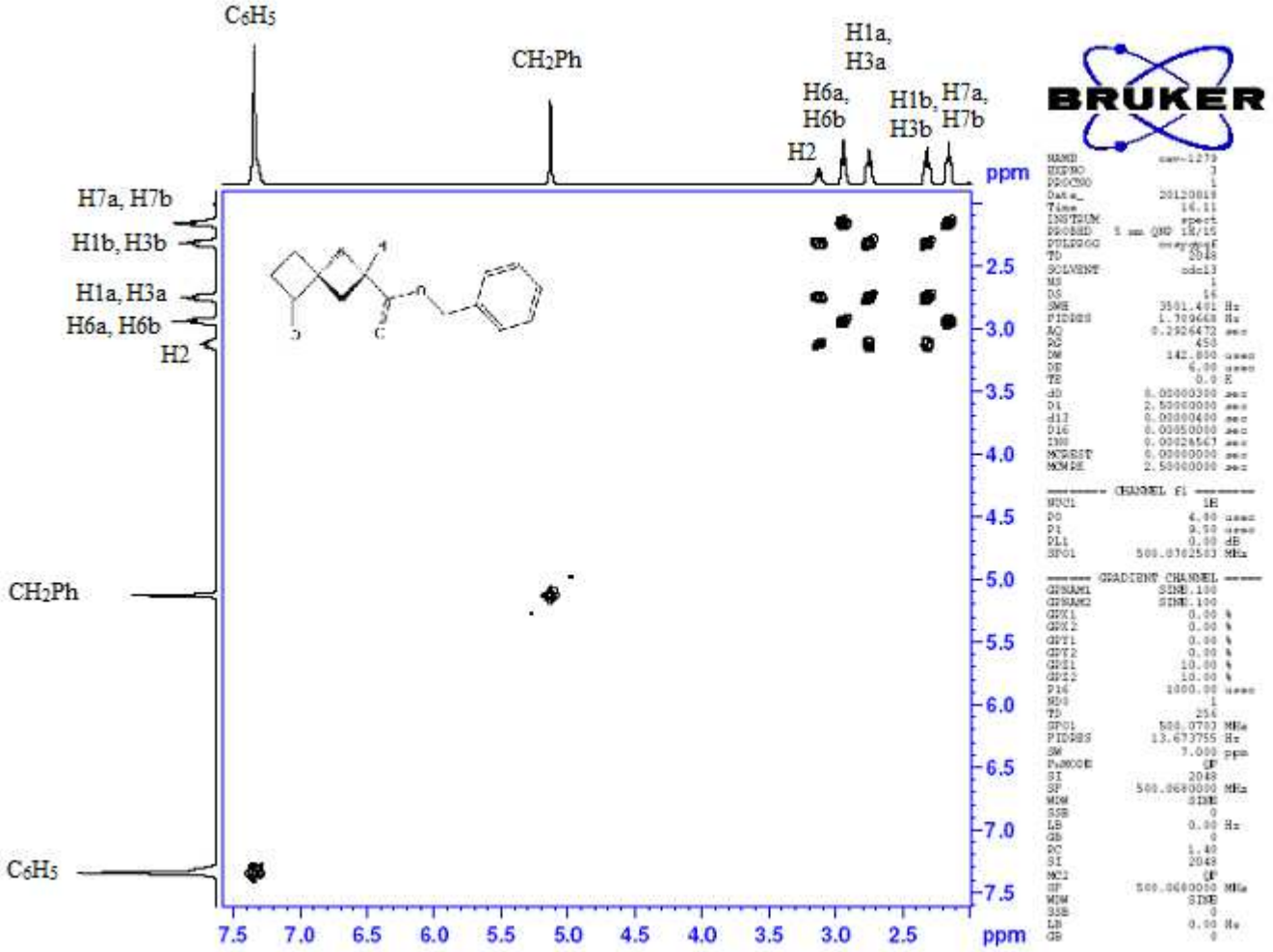

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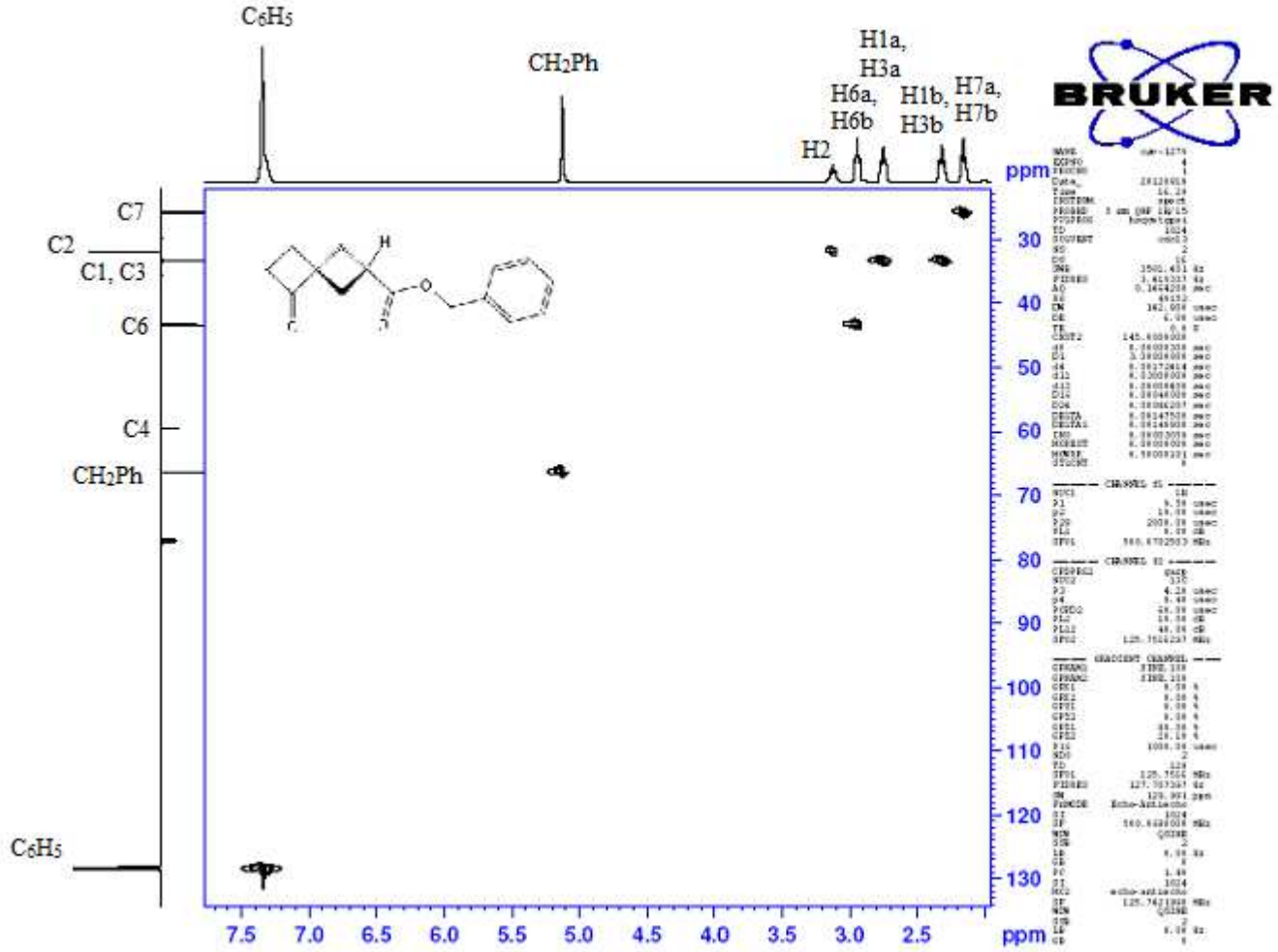

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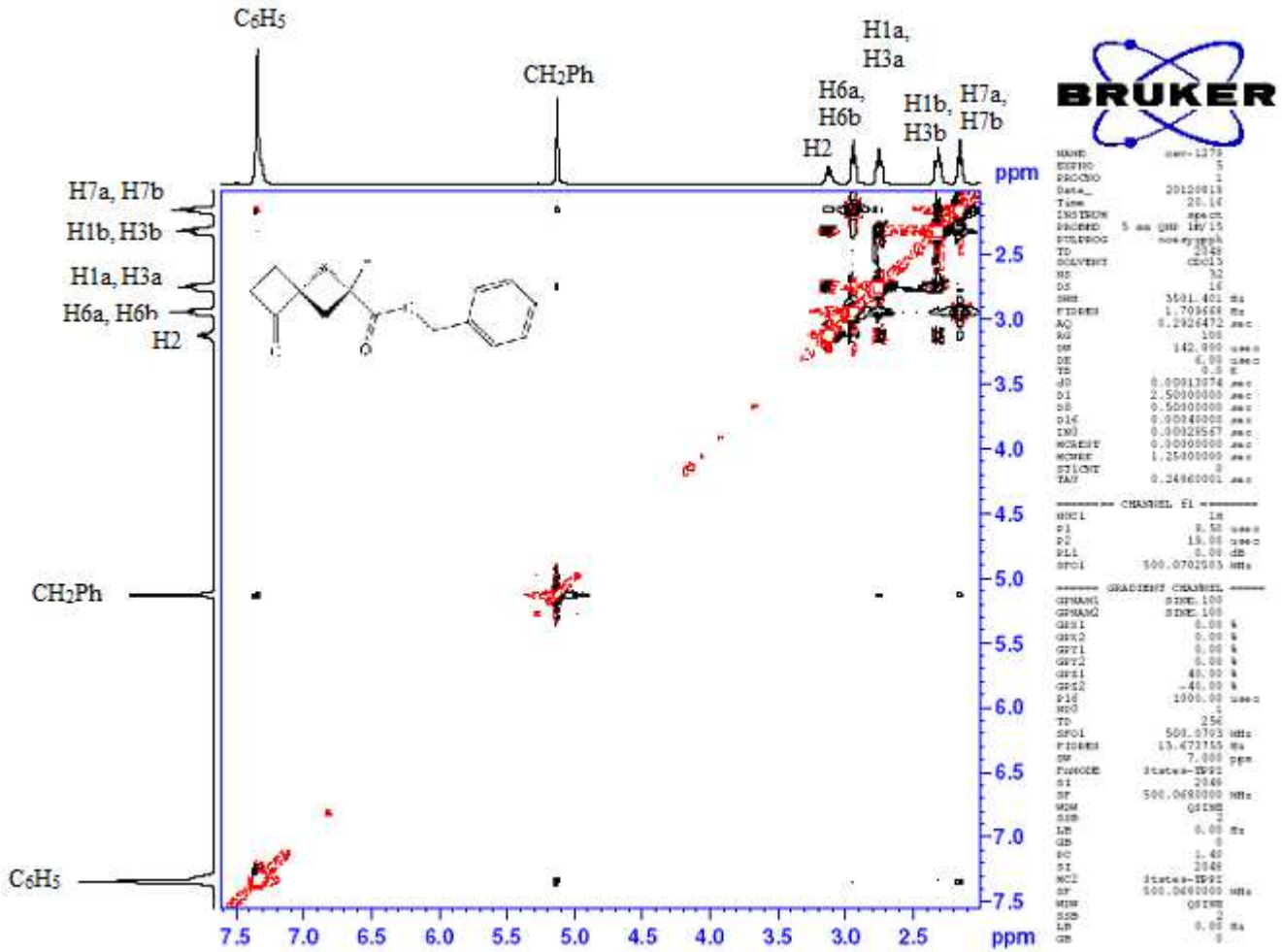
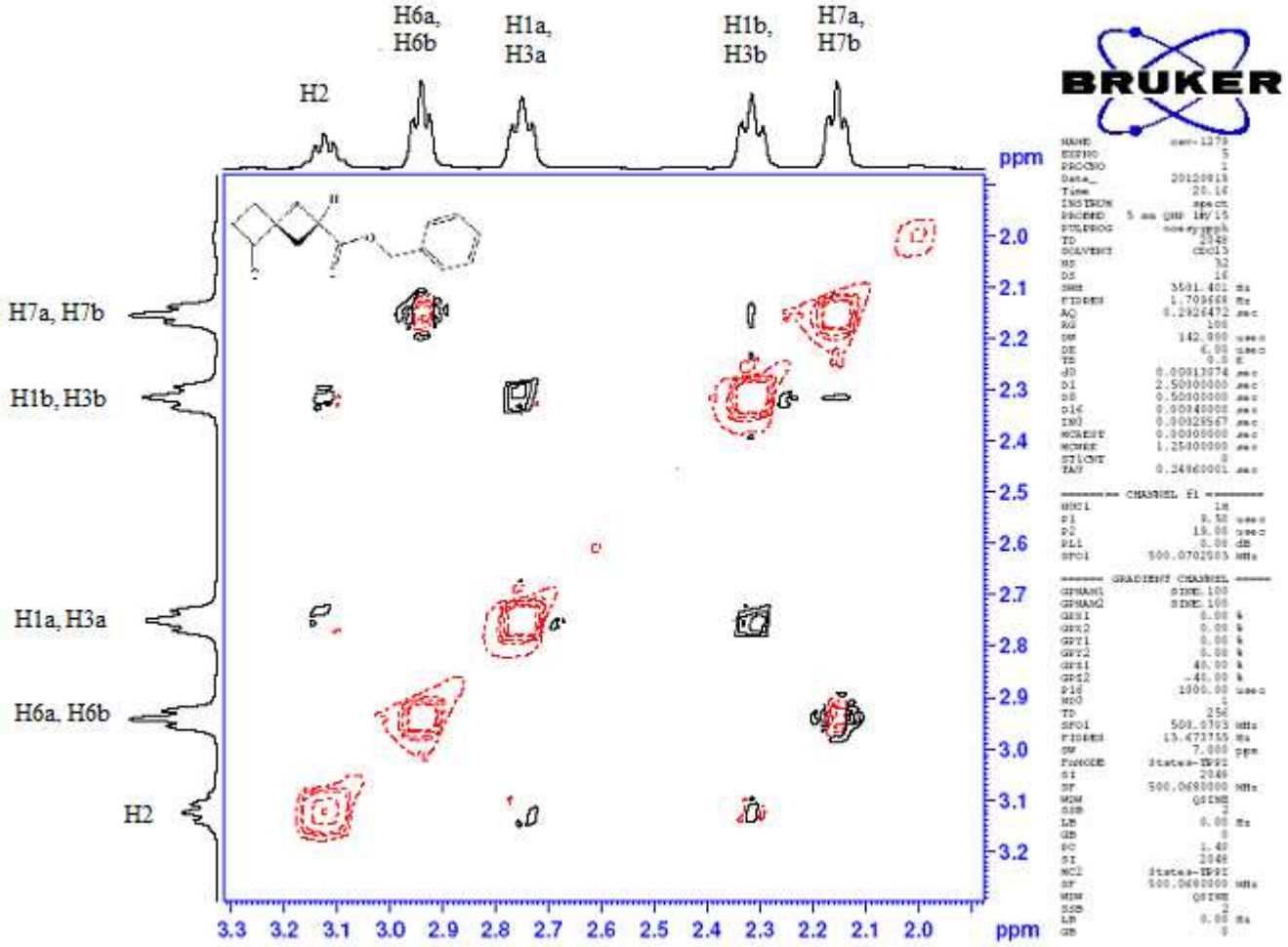


NOESY spectrum of the compound **11b** (fragment)



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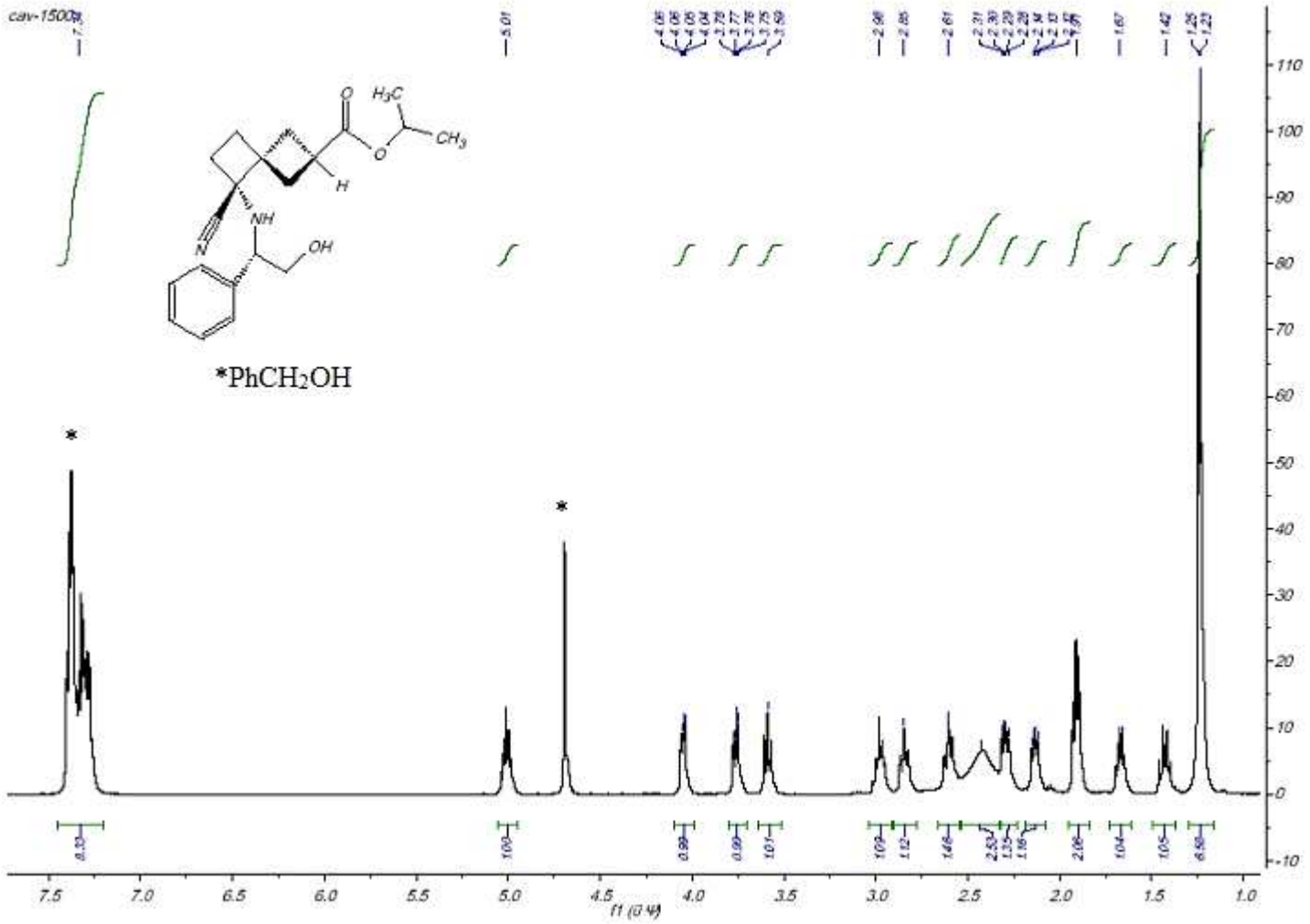

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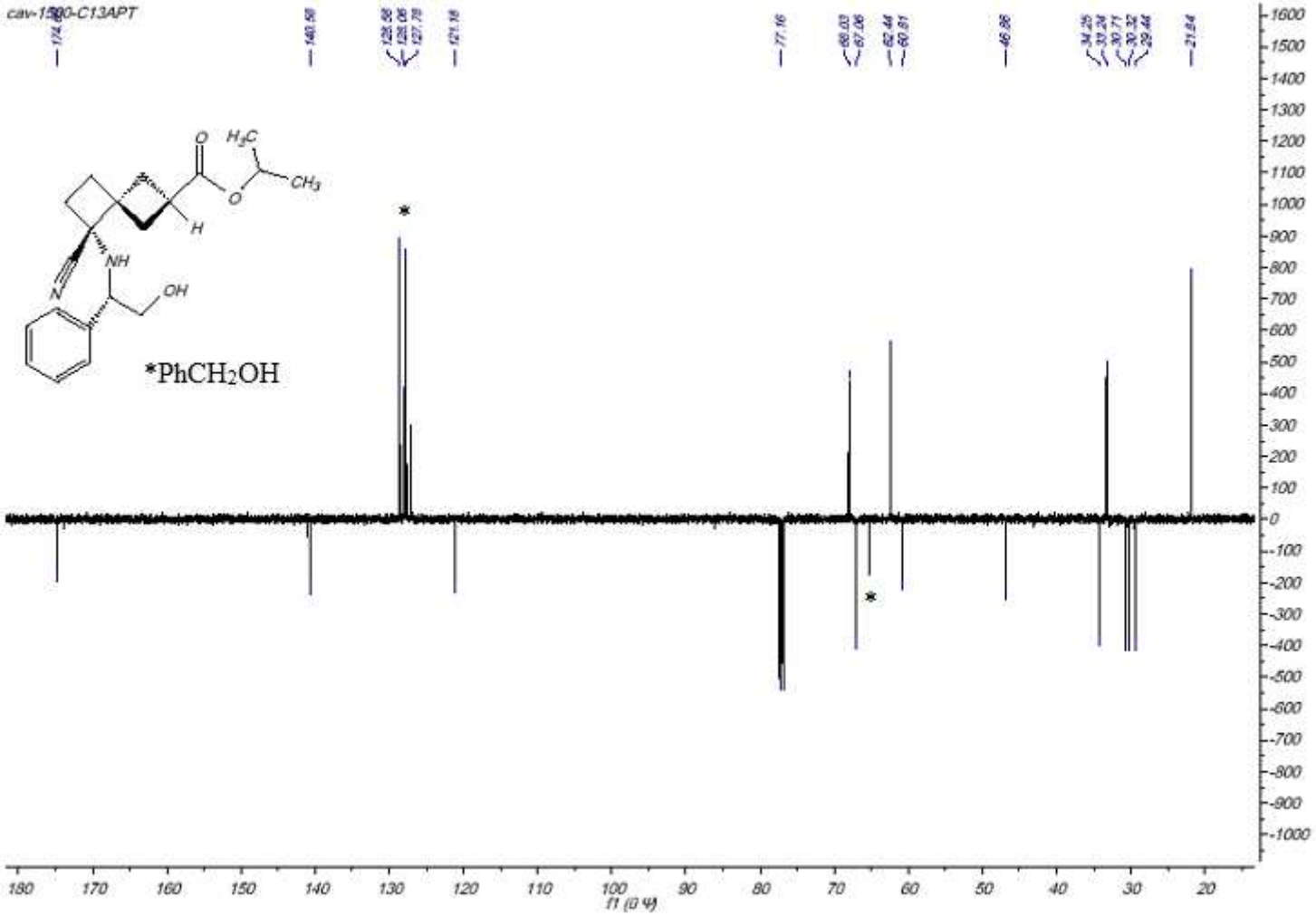

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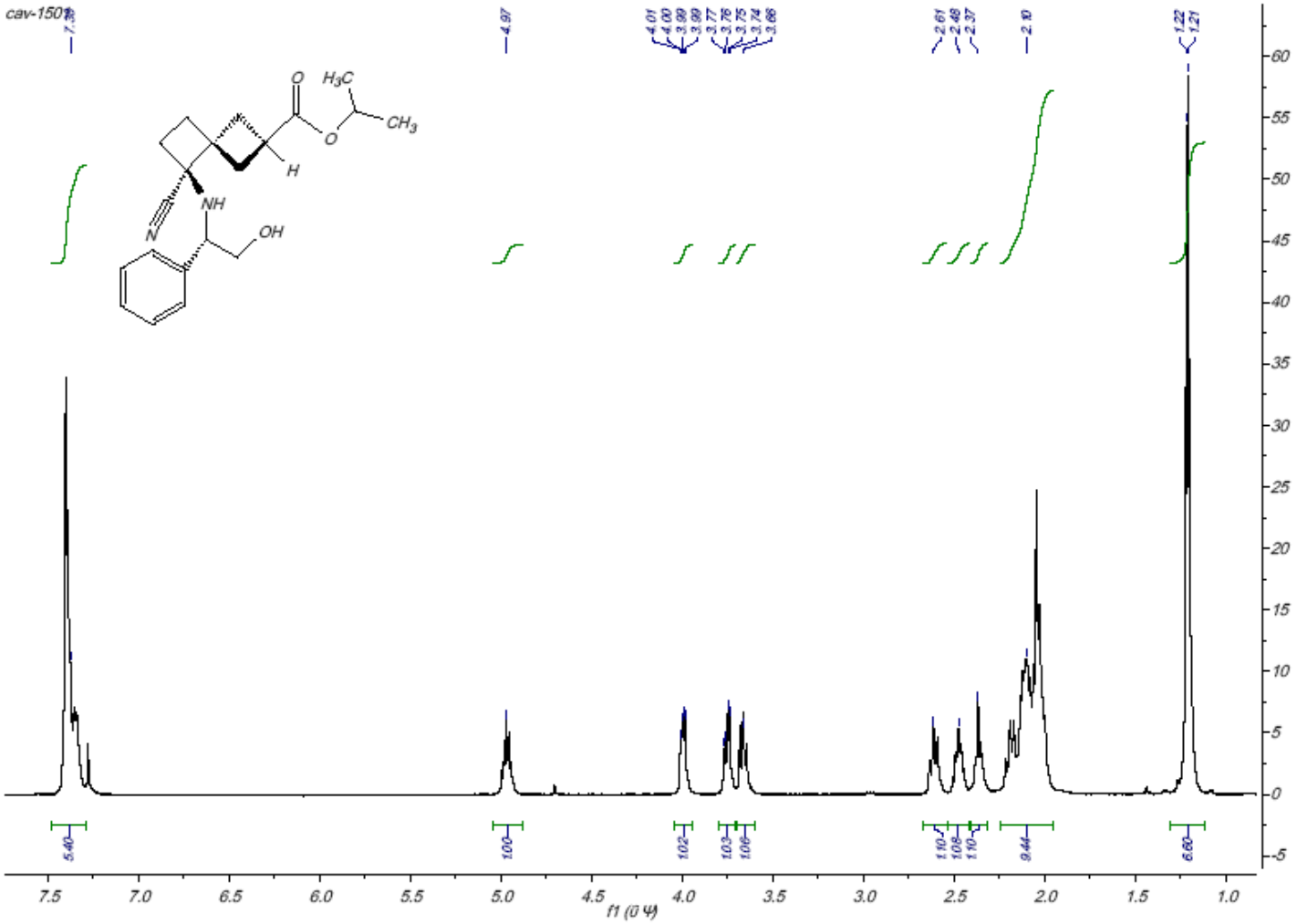

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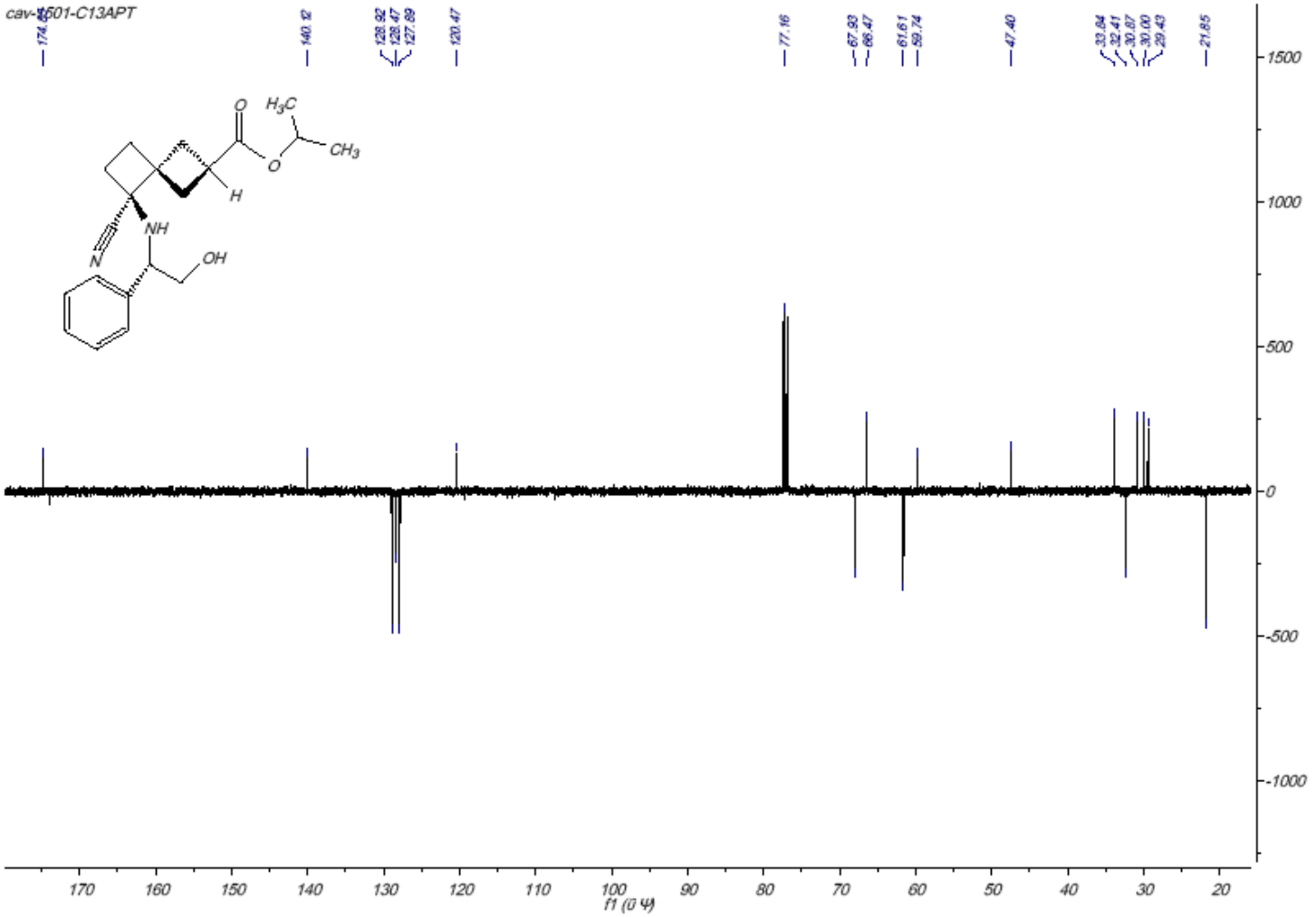

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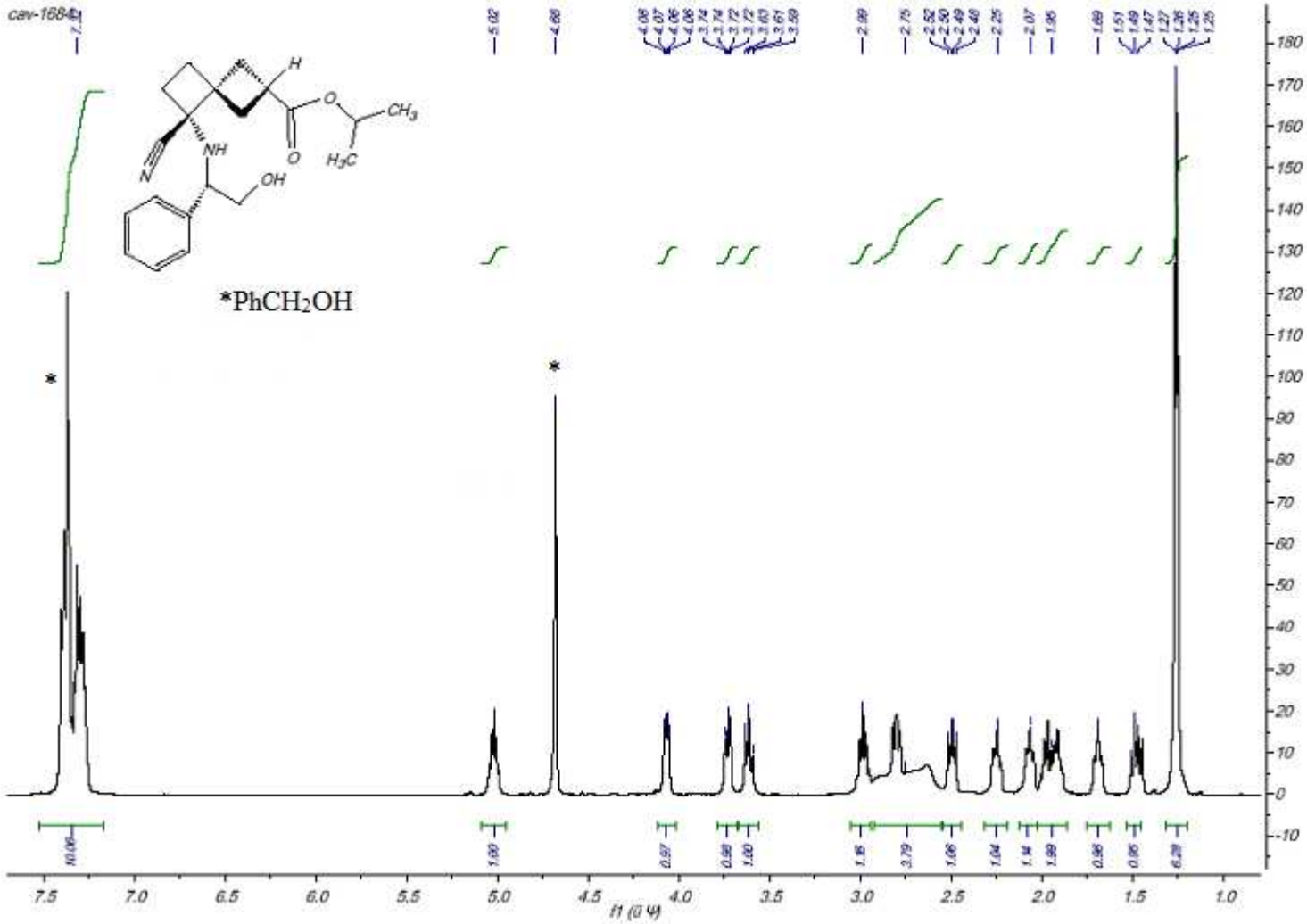

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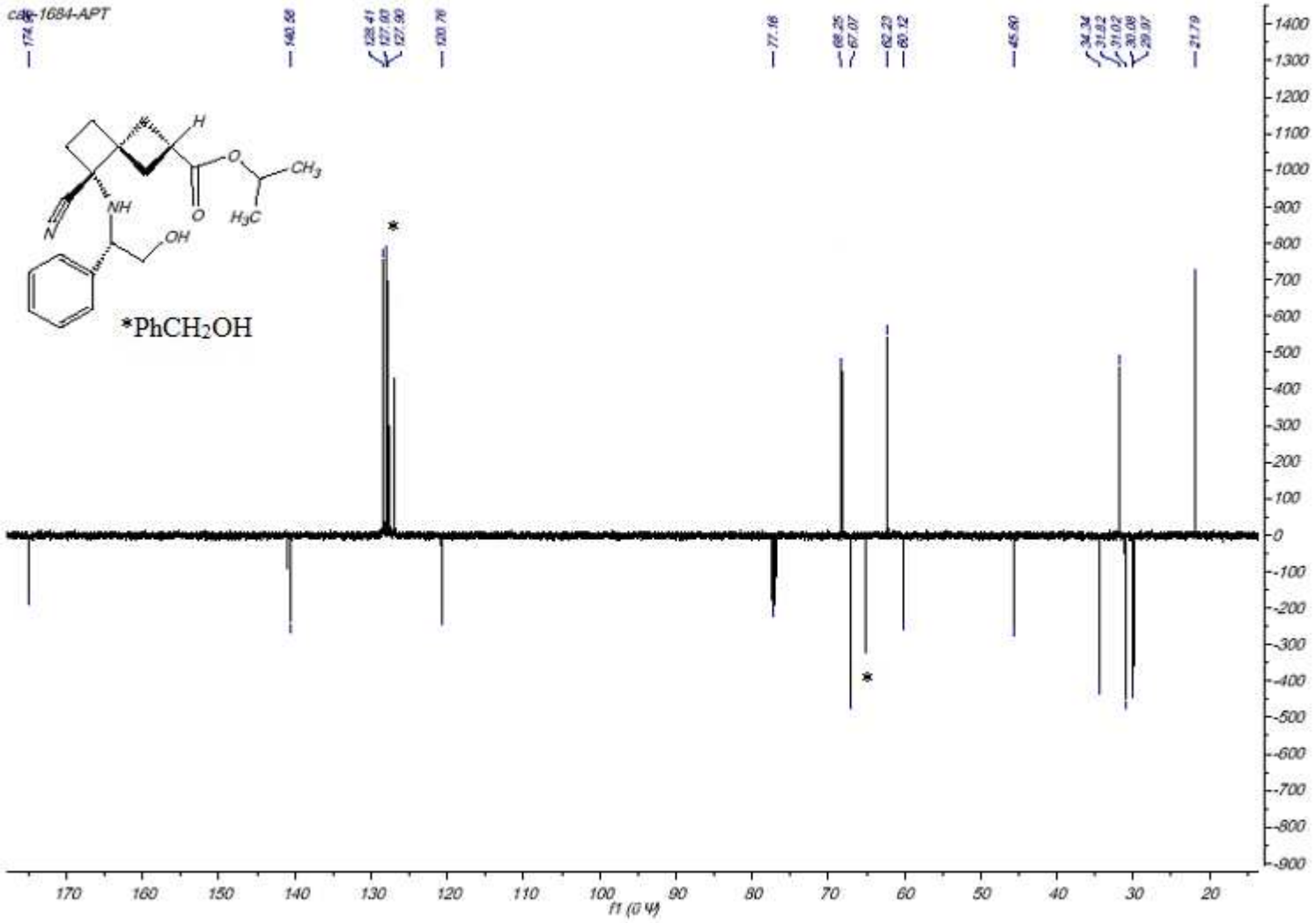

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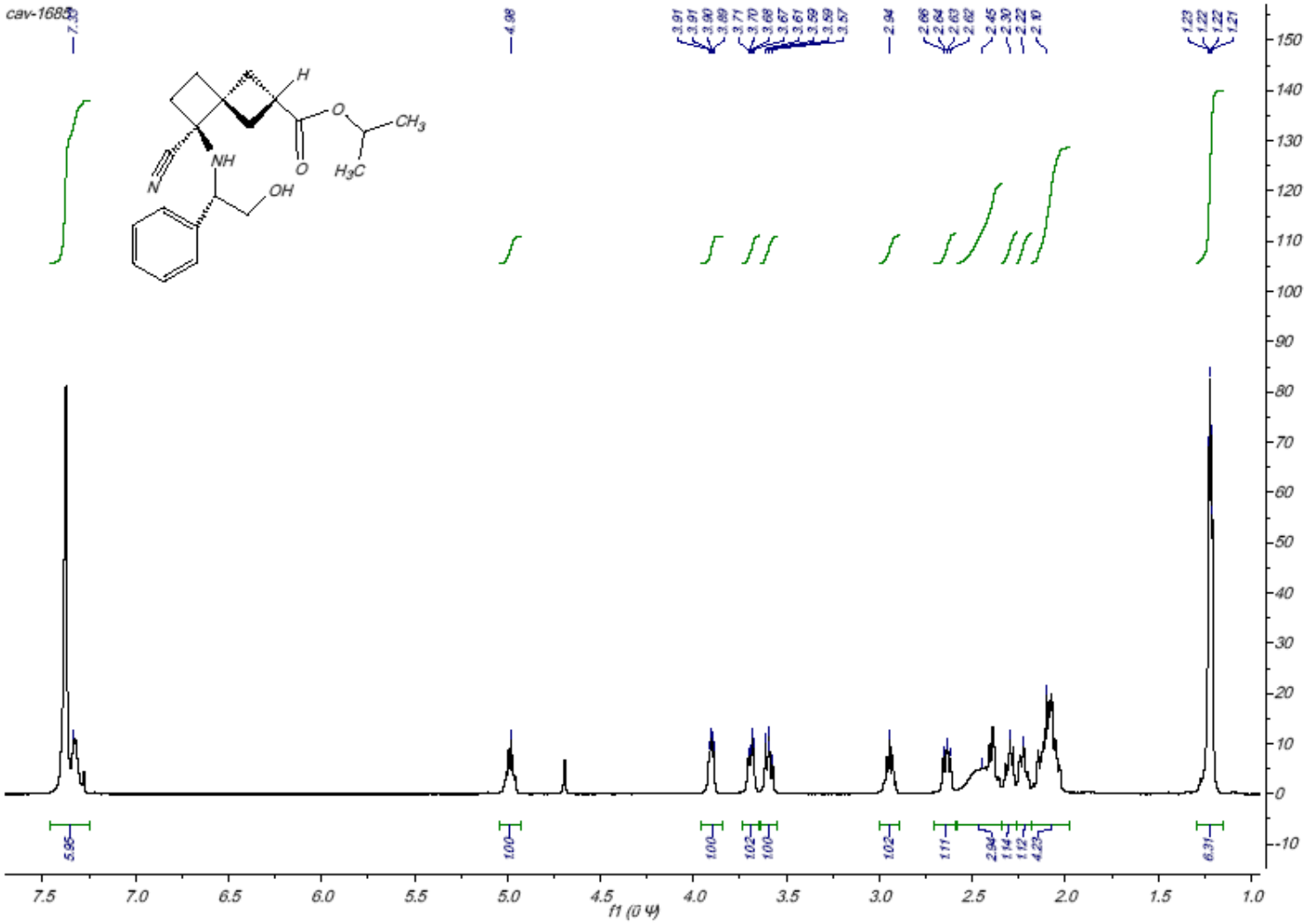

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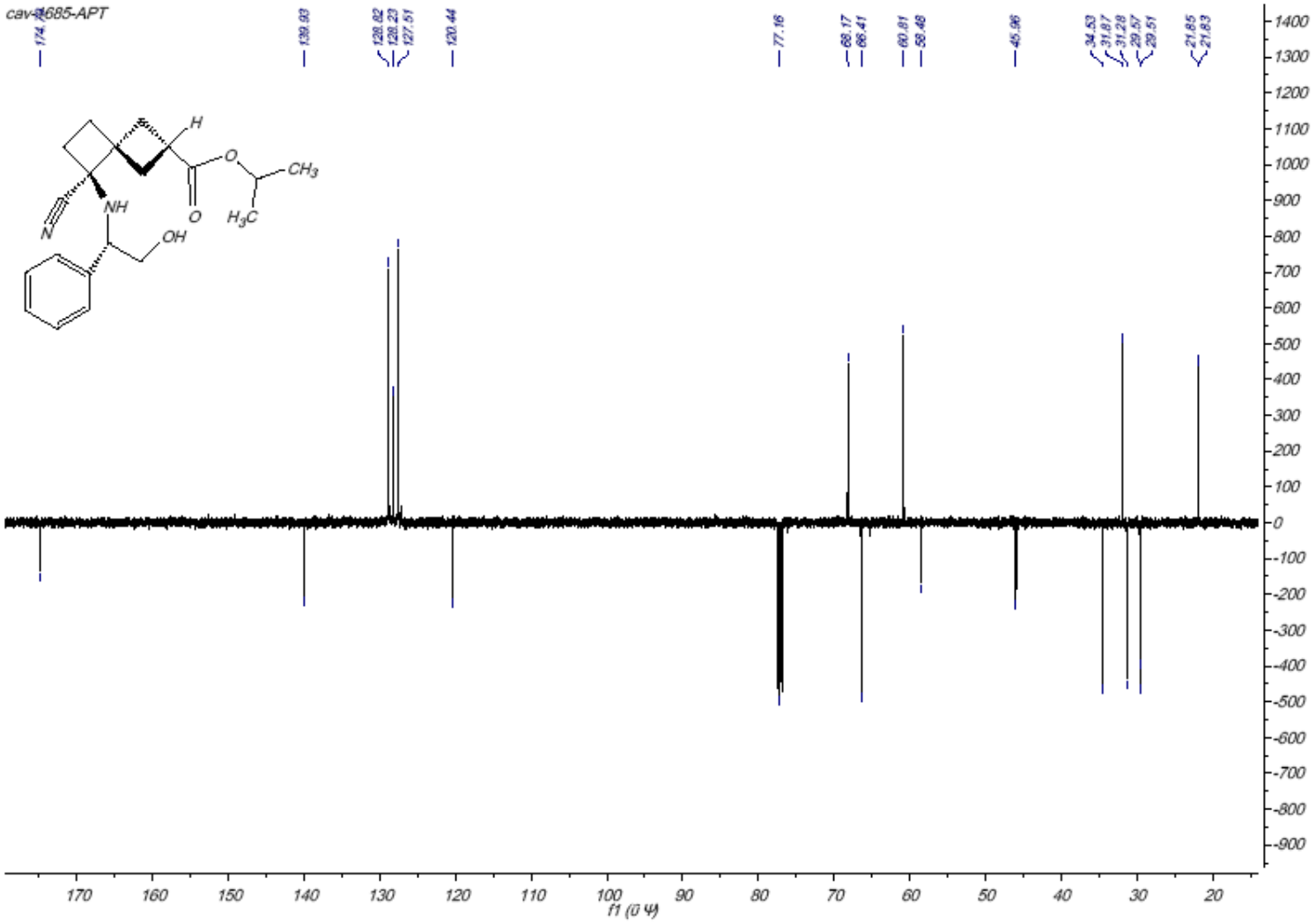

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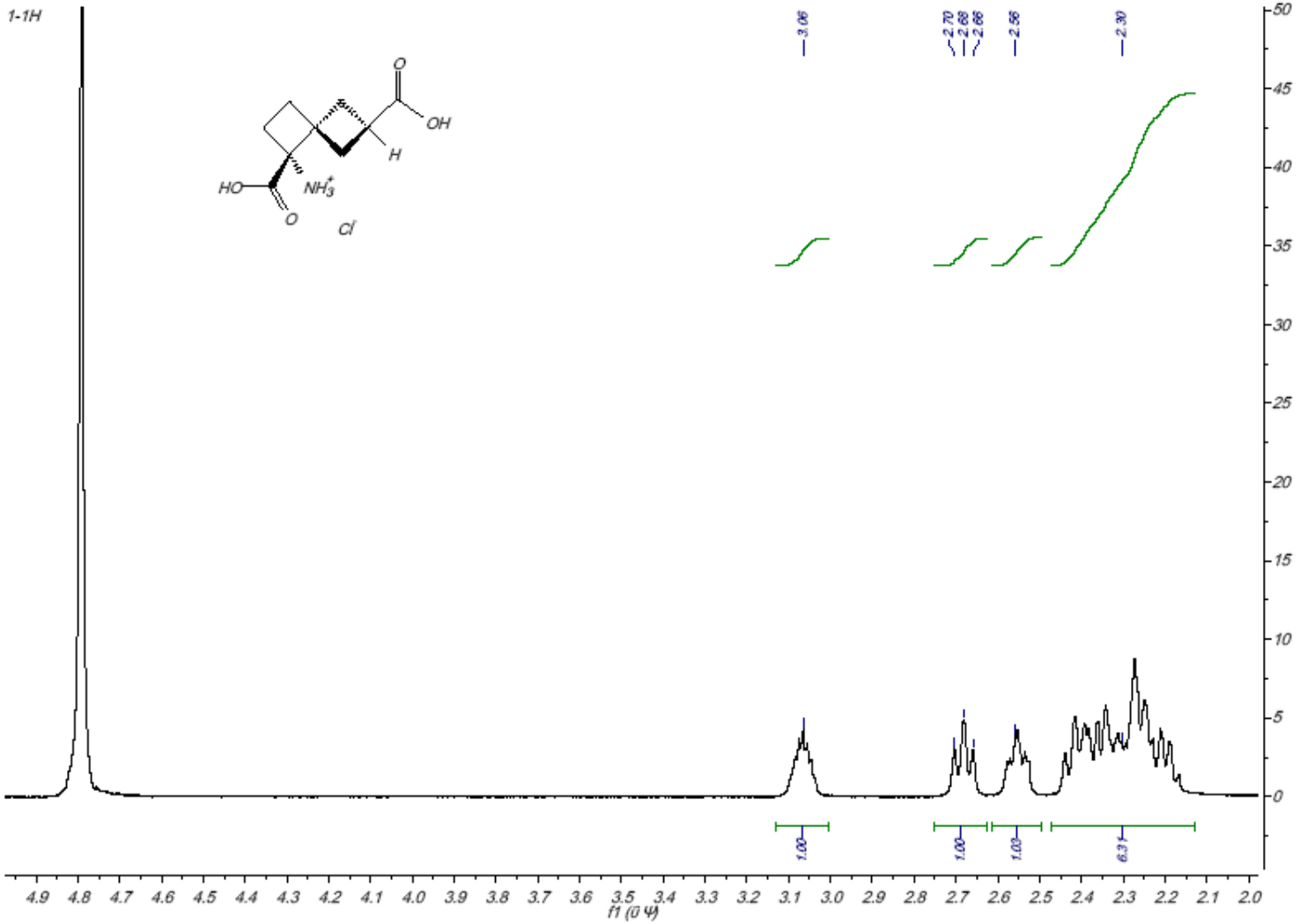

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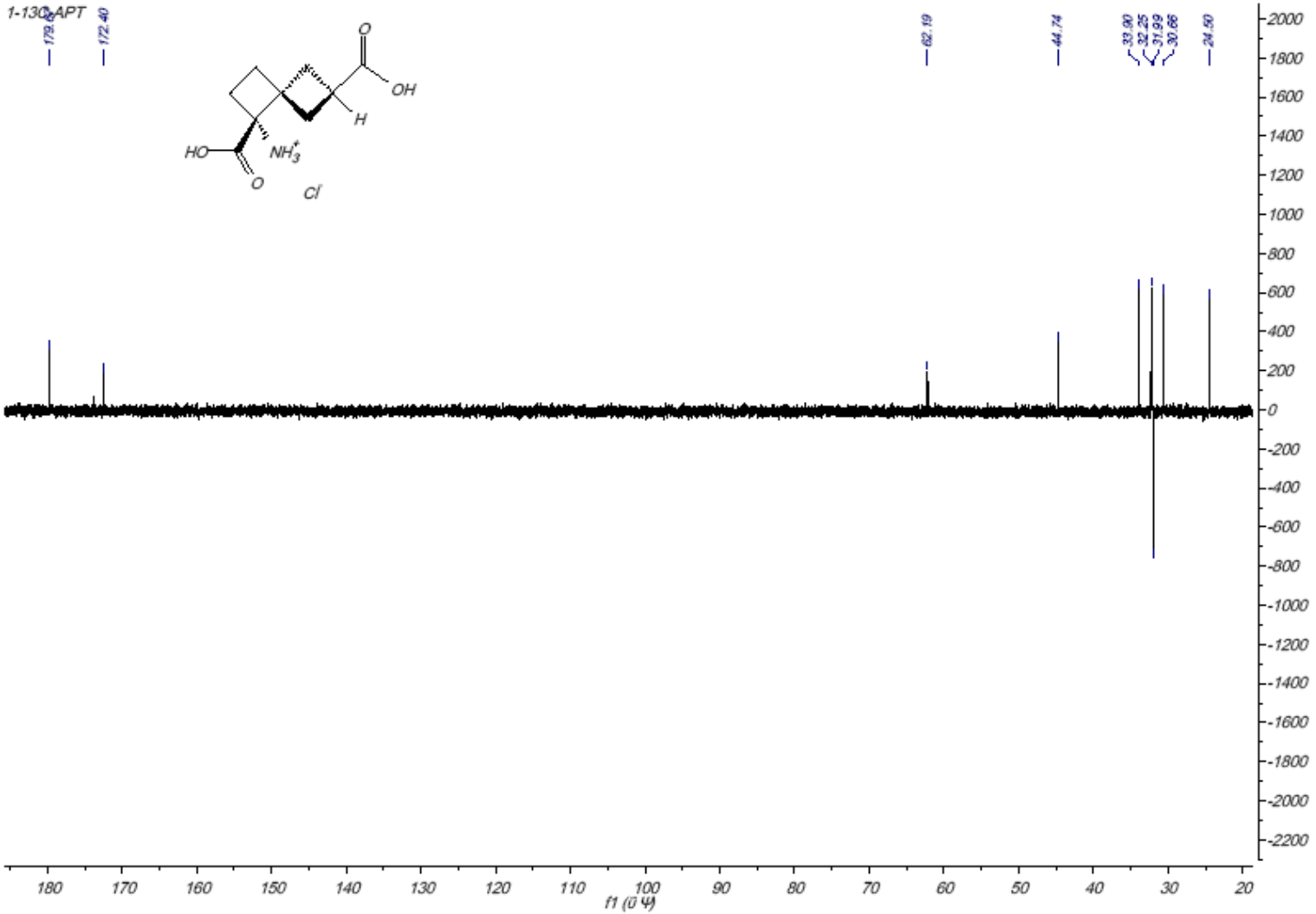

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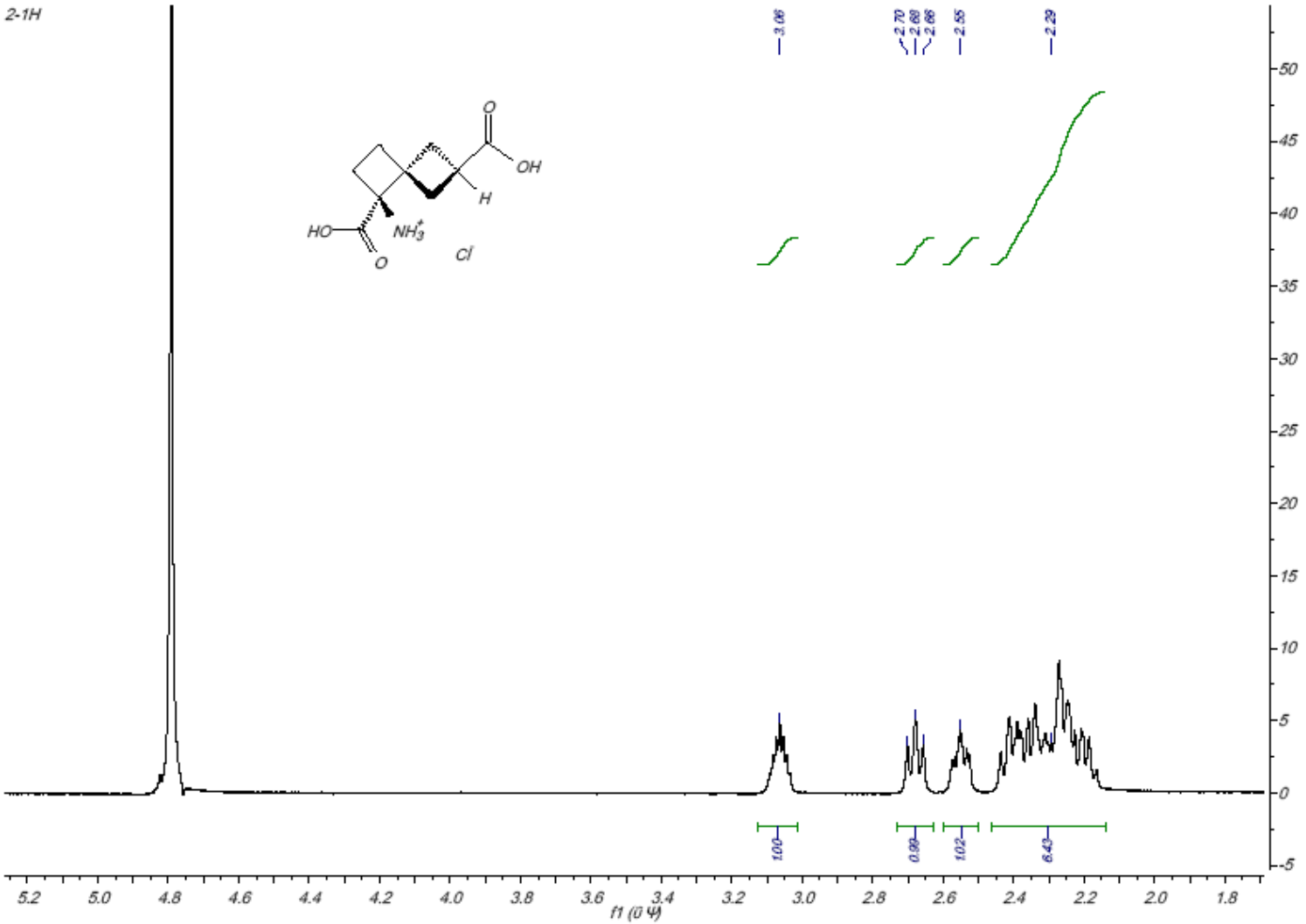

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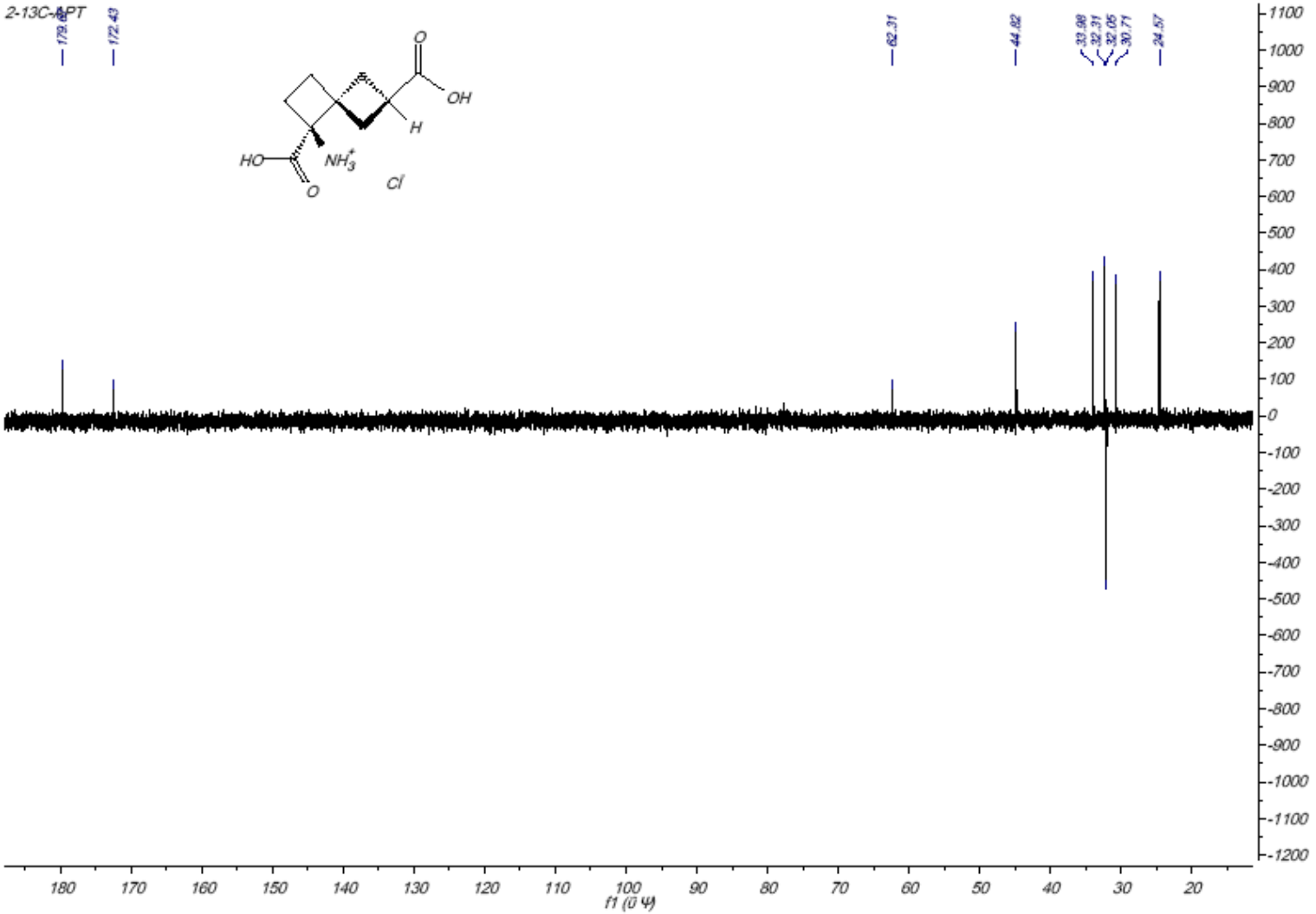

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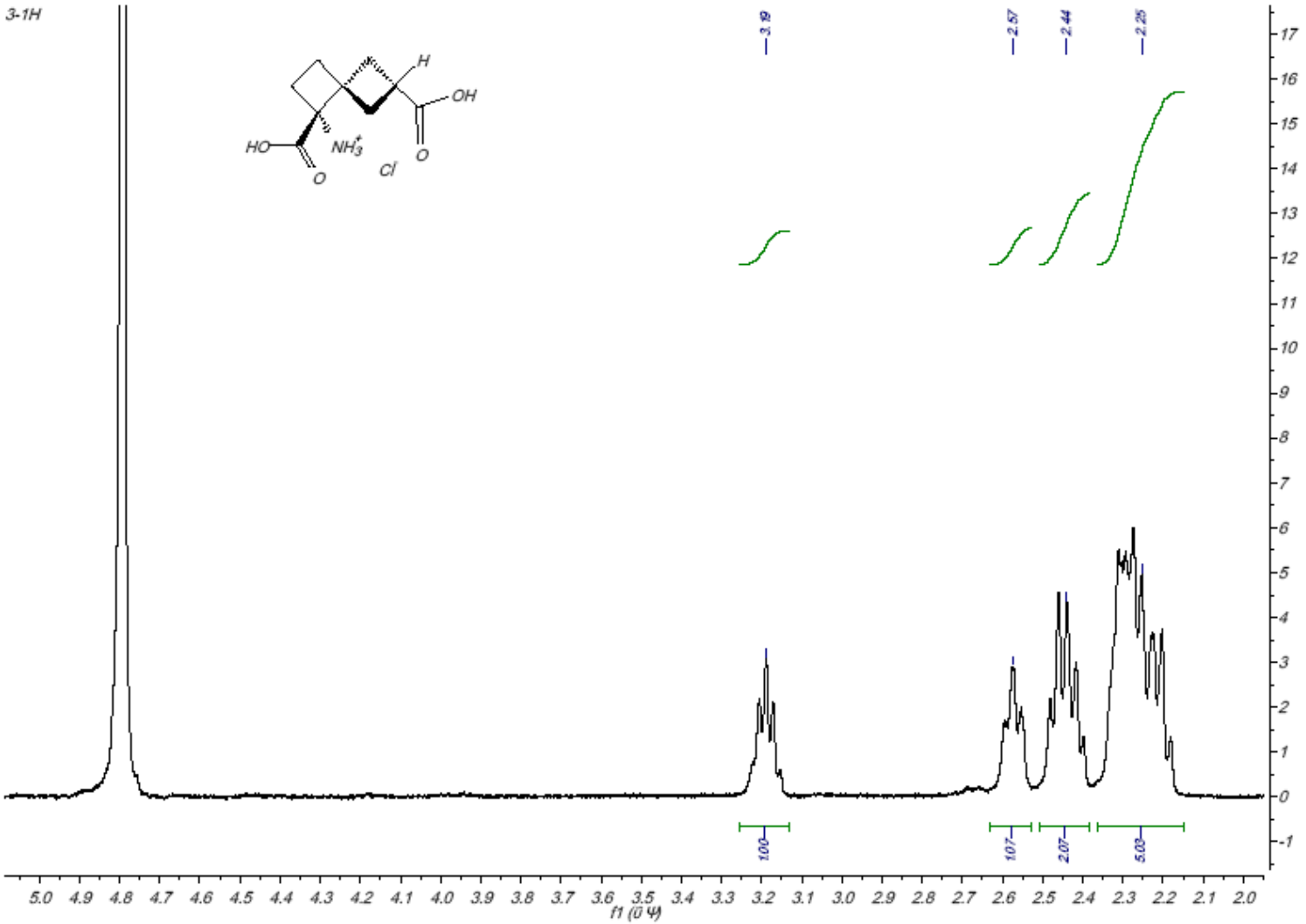

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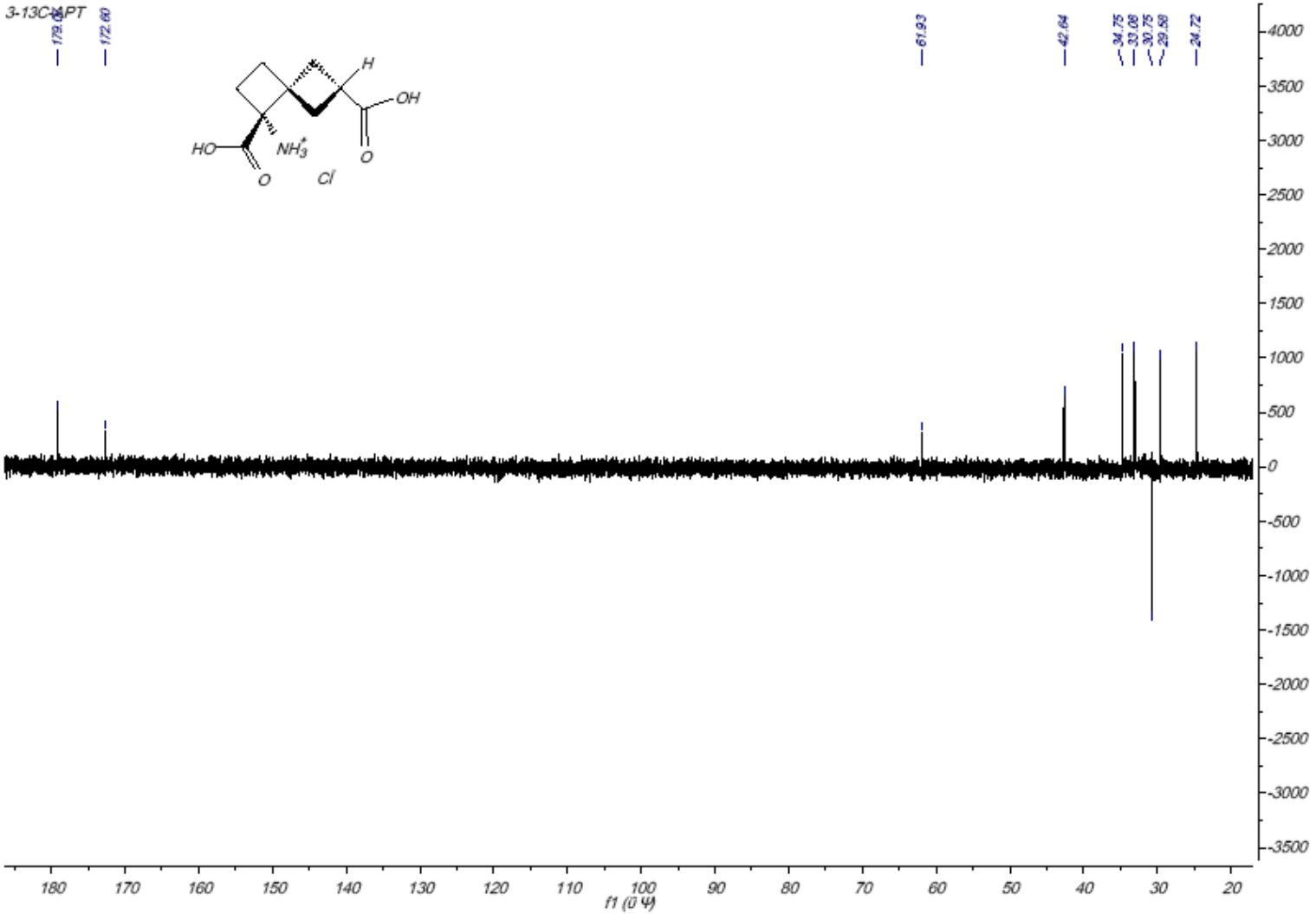

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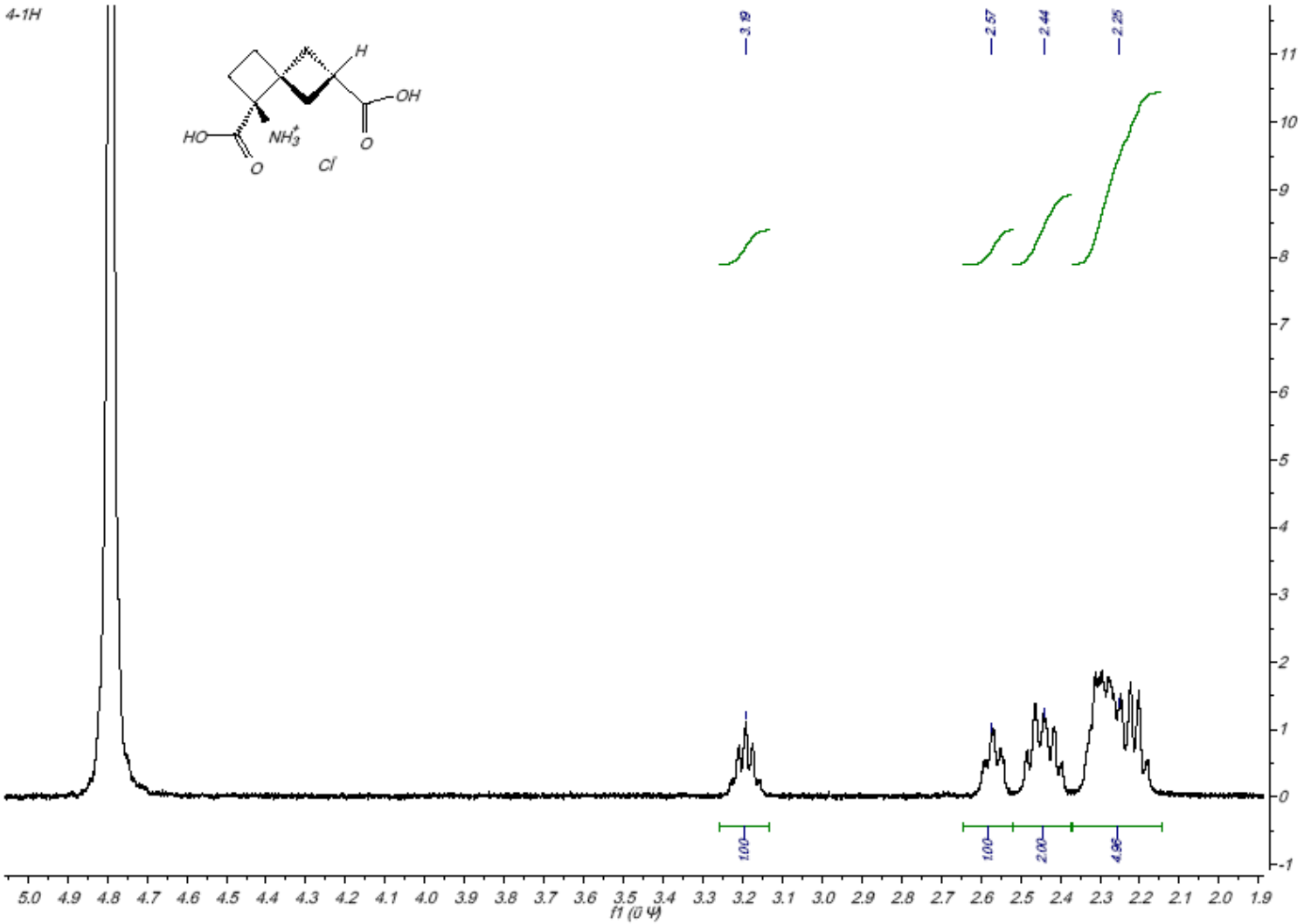

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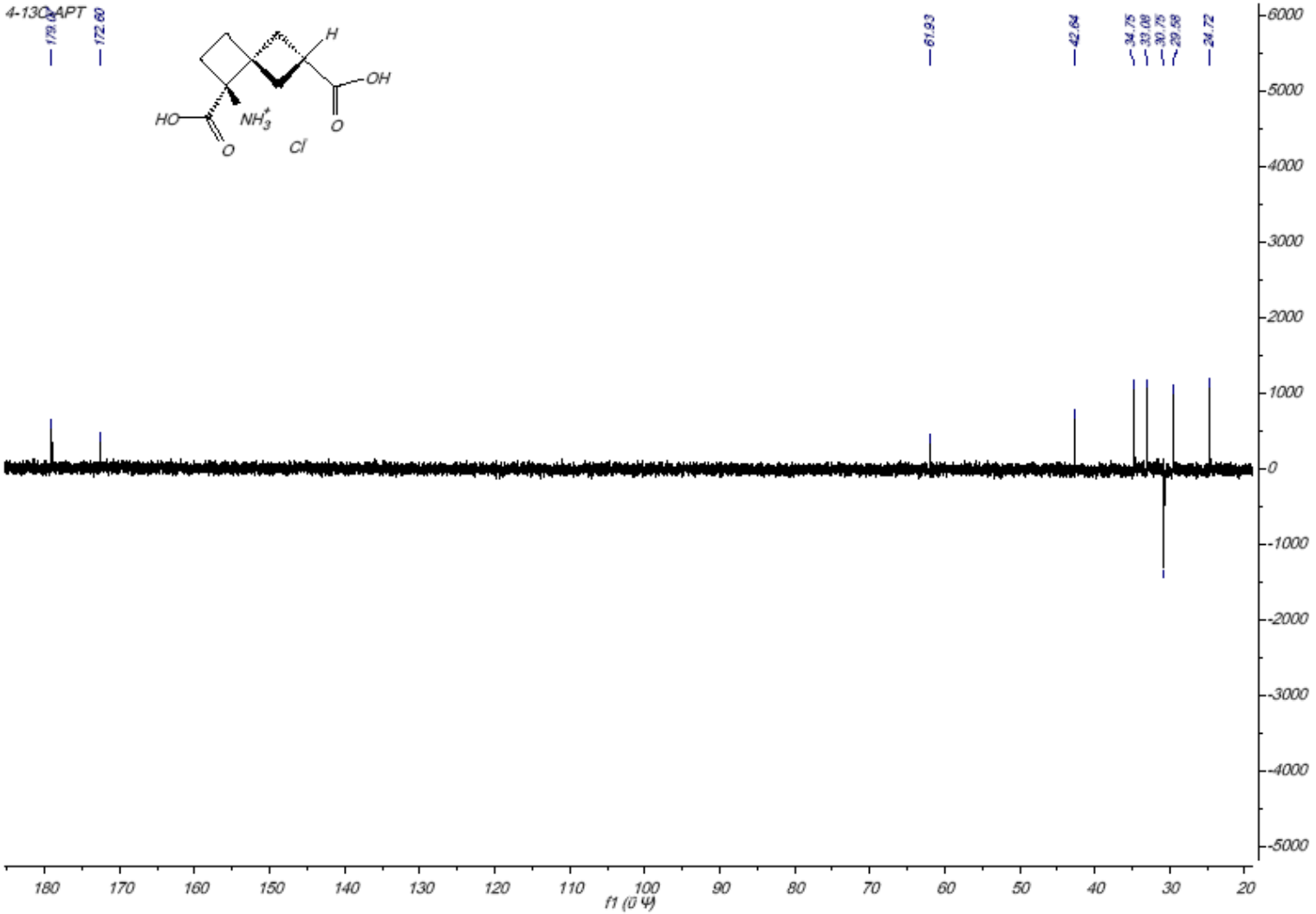

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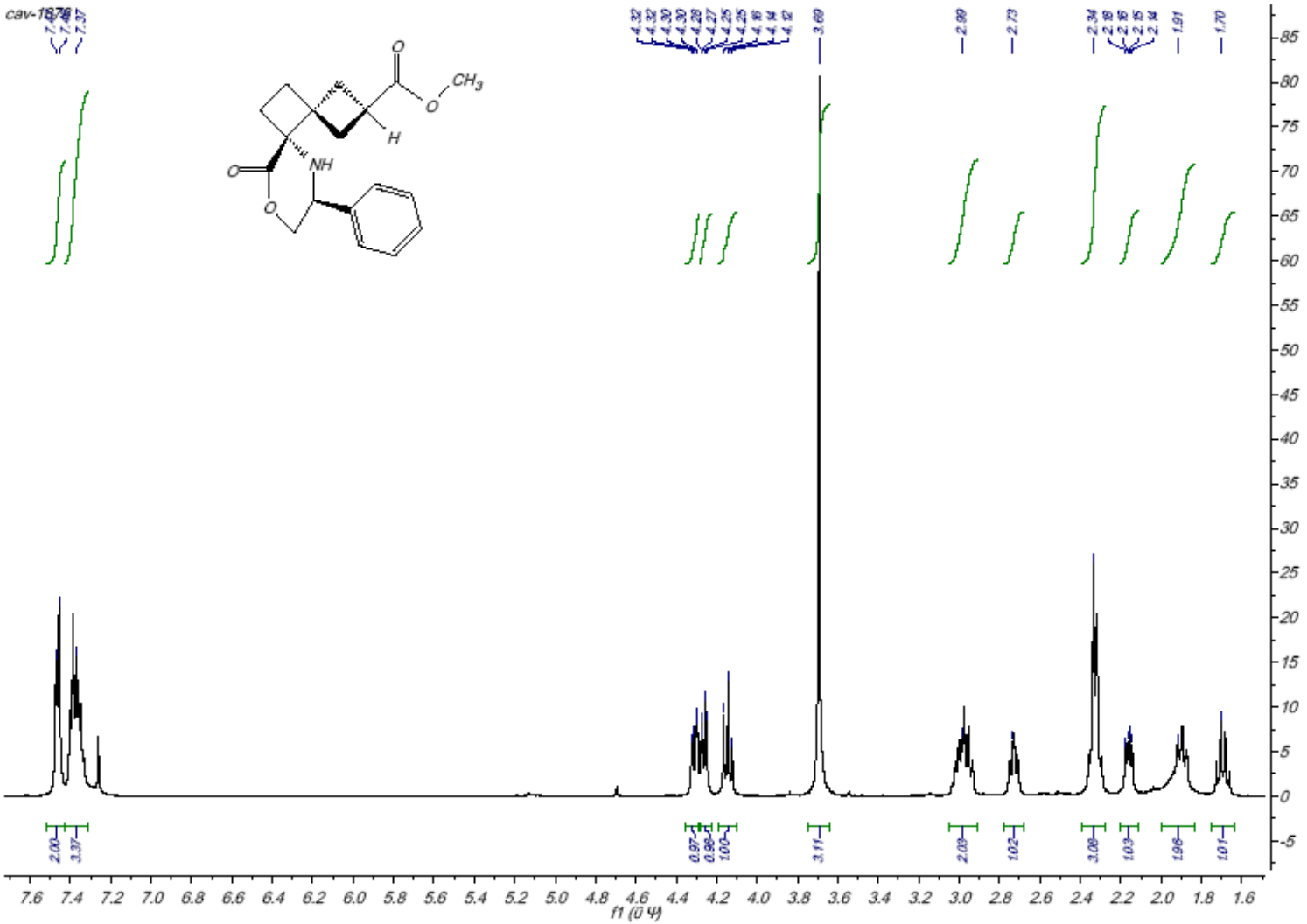

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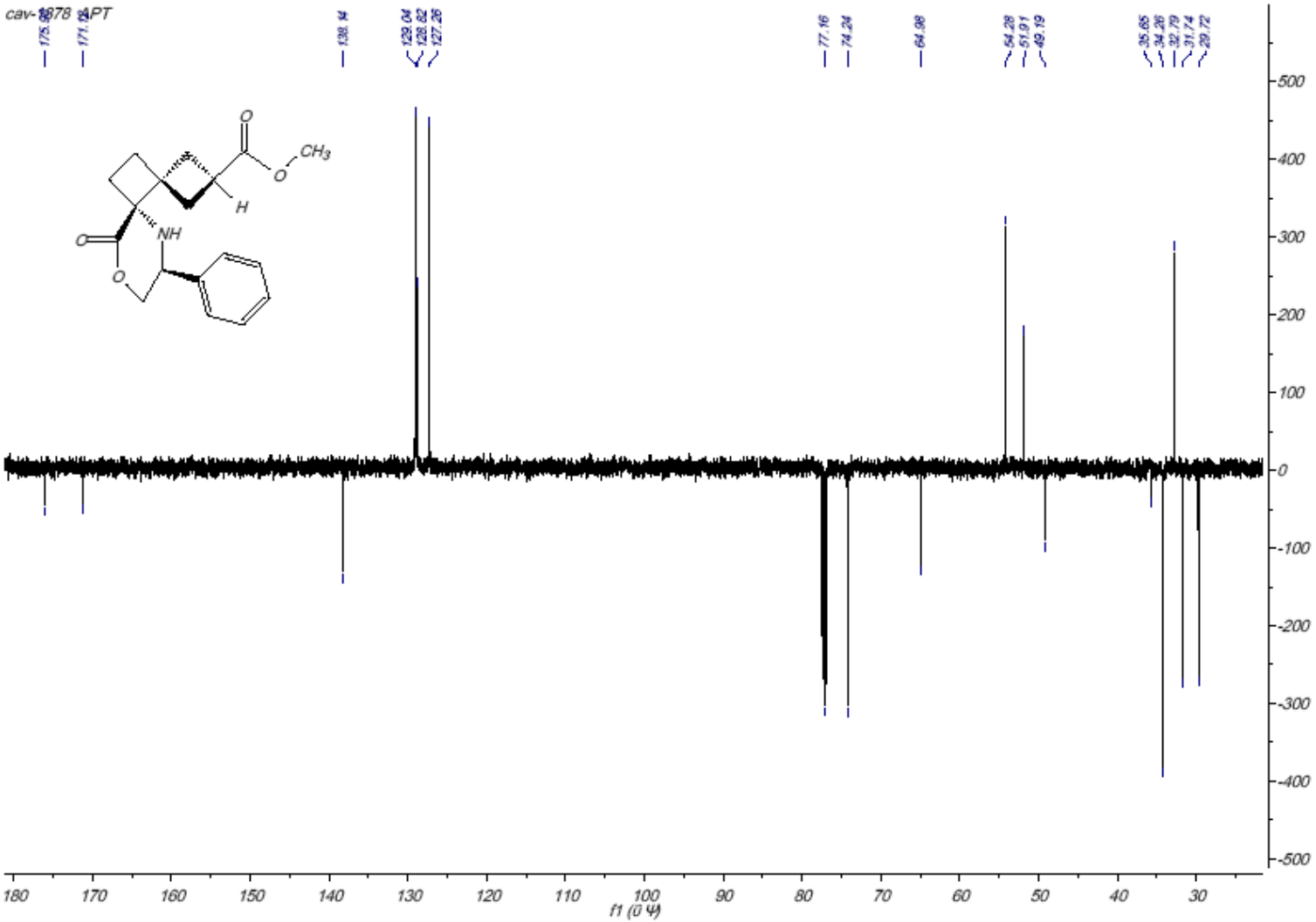

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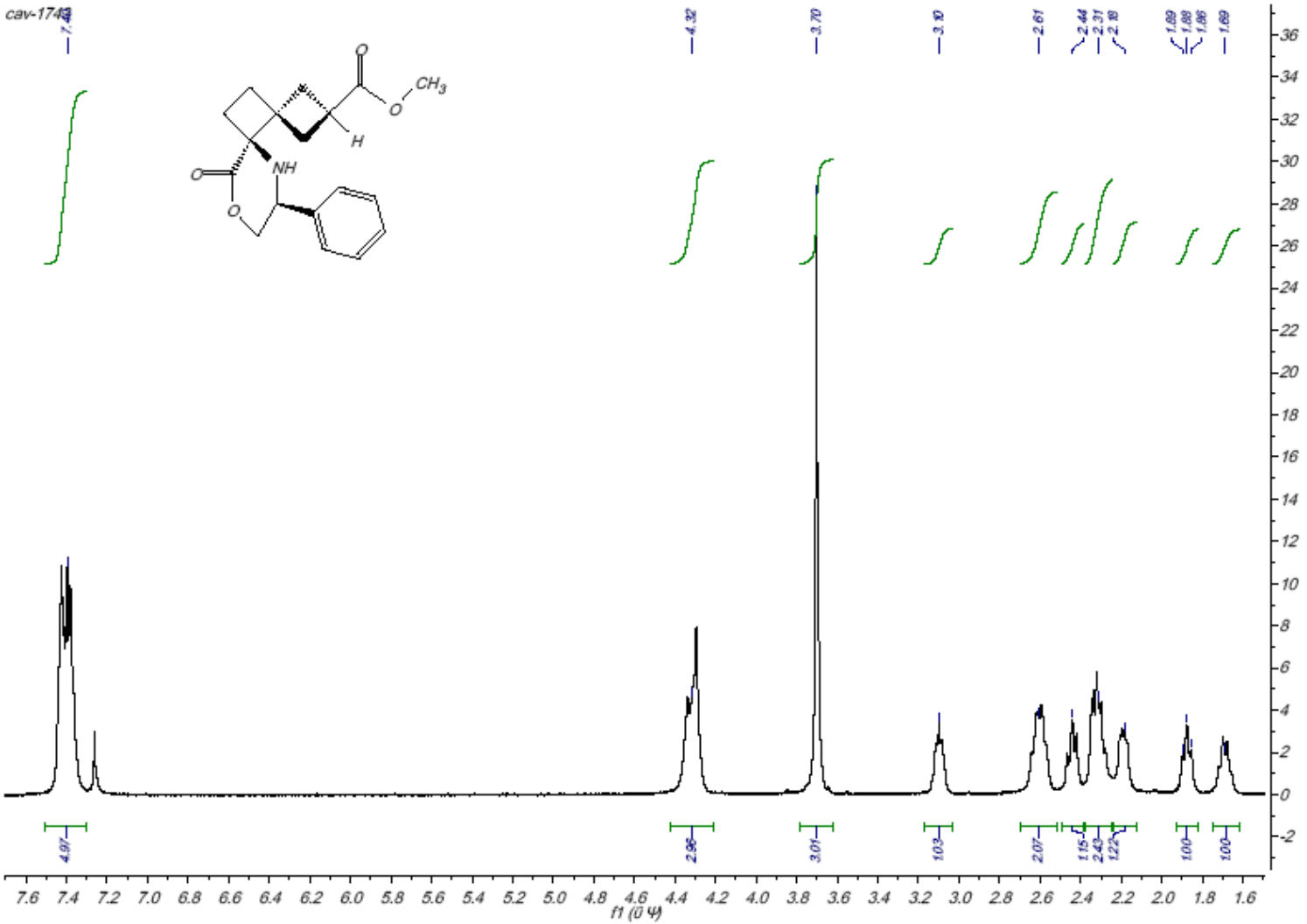

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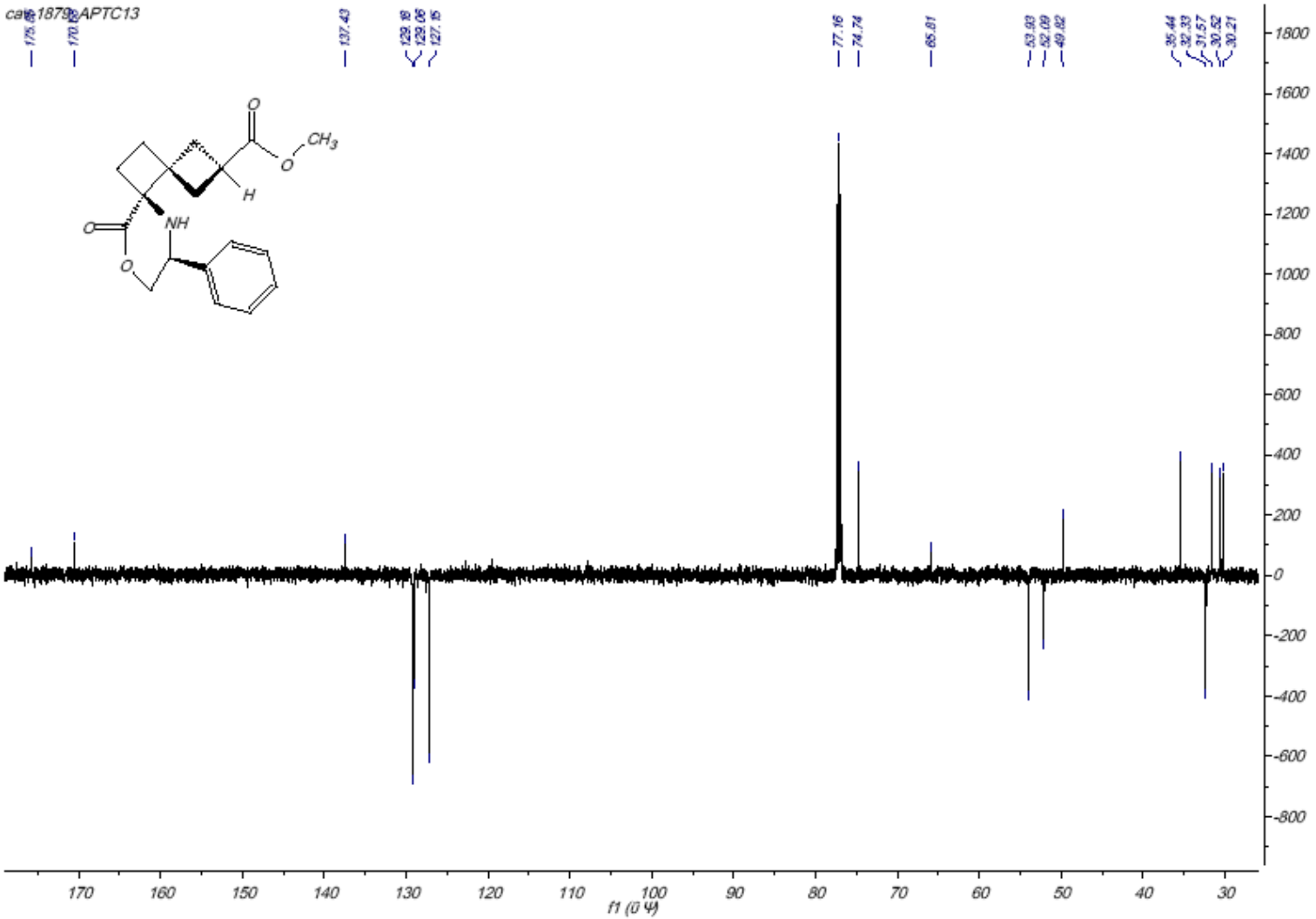

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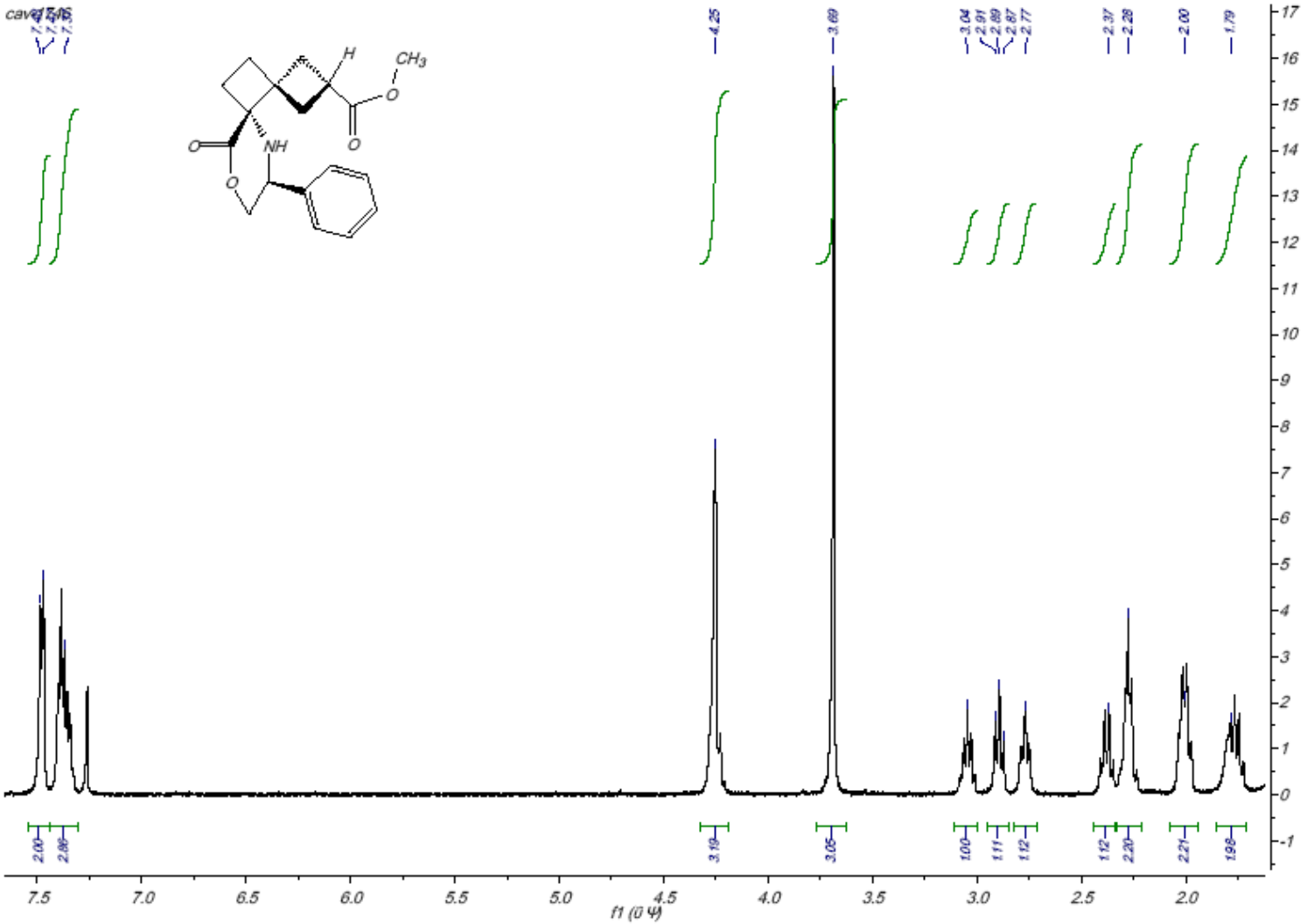

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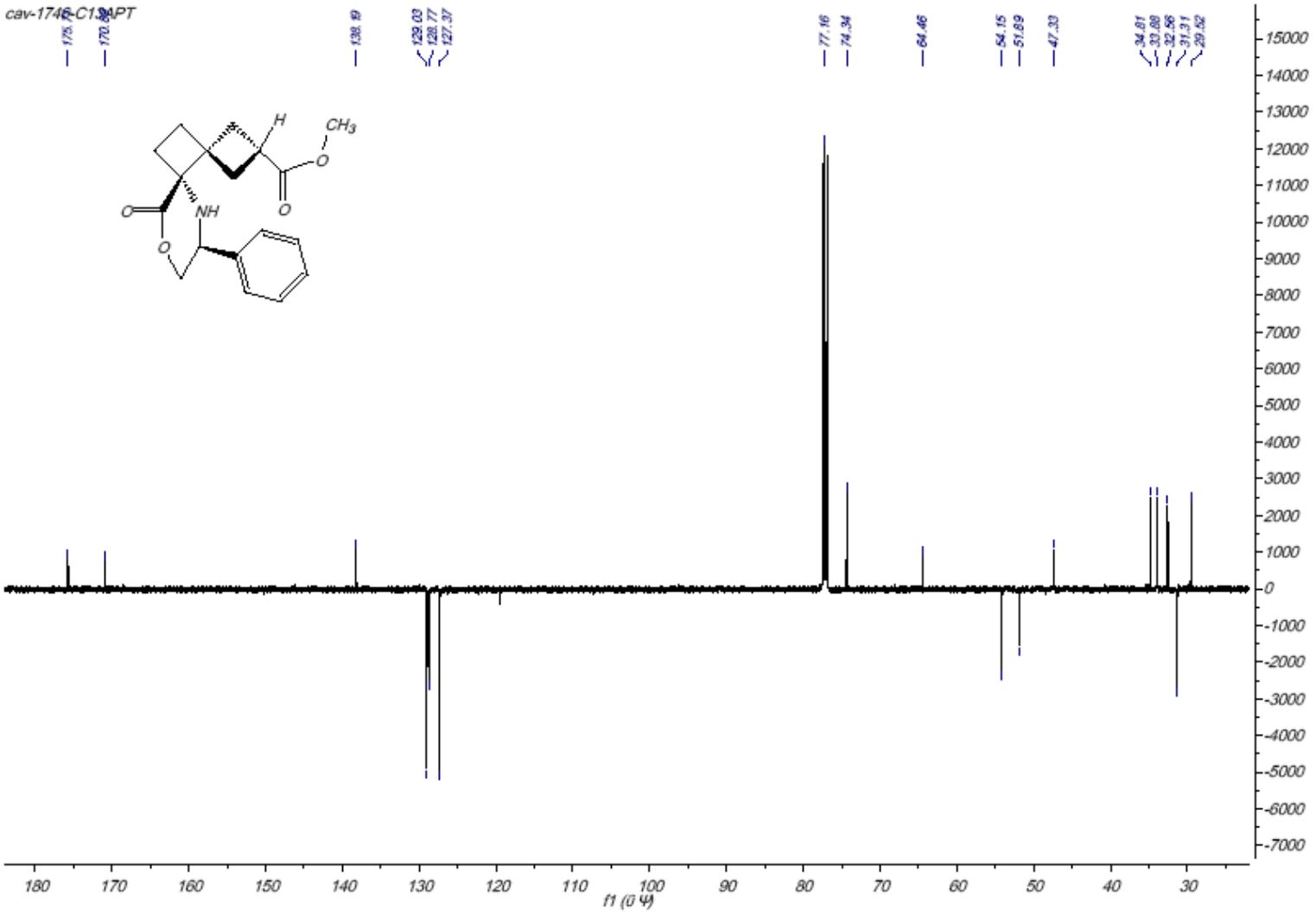

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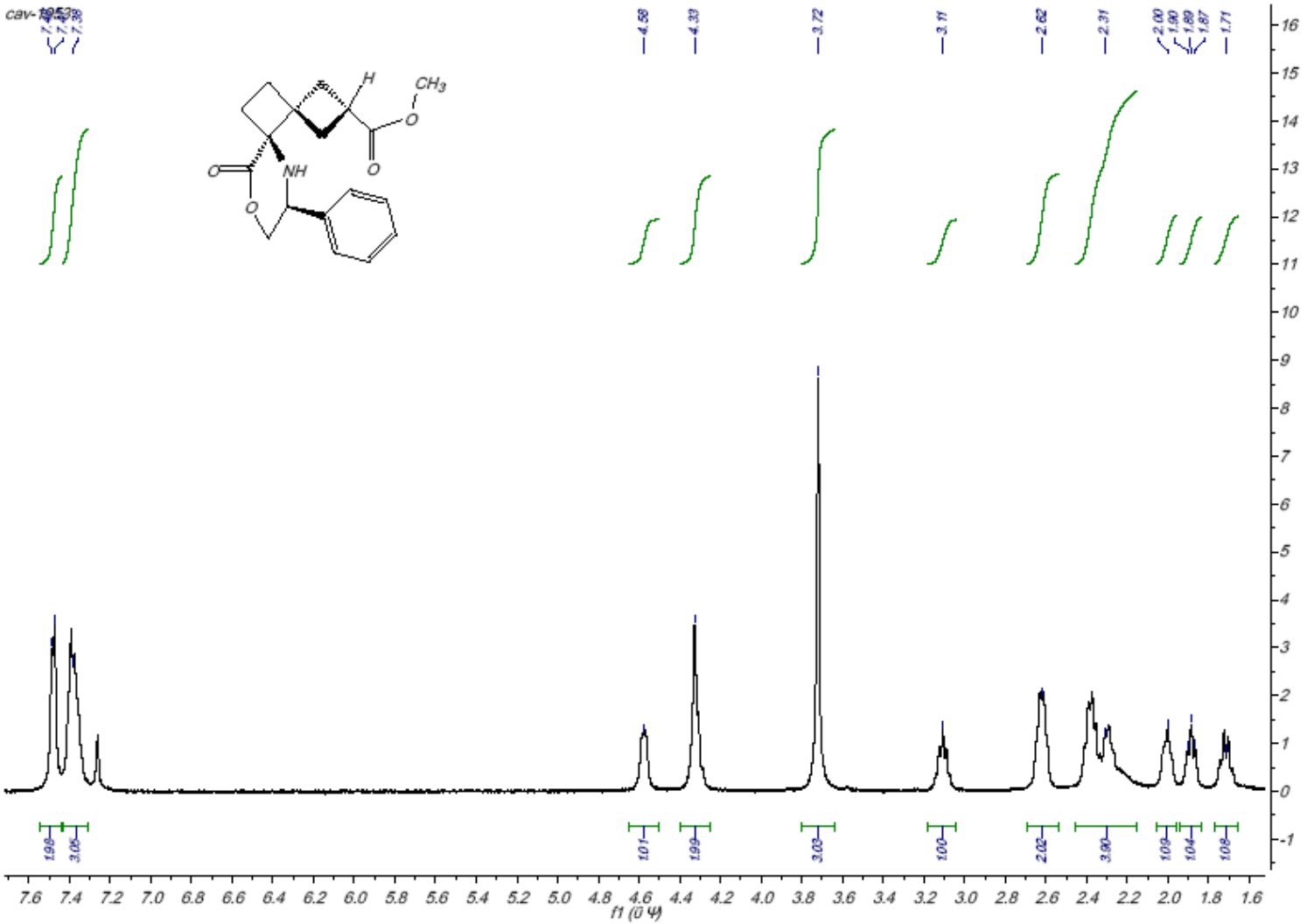

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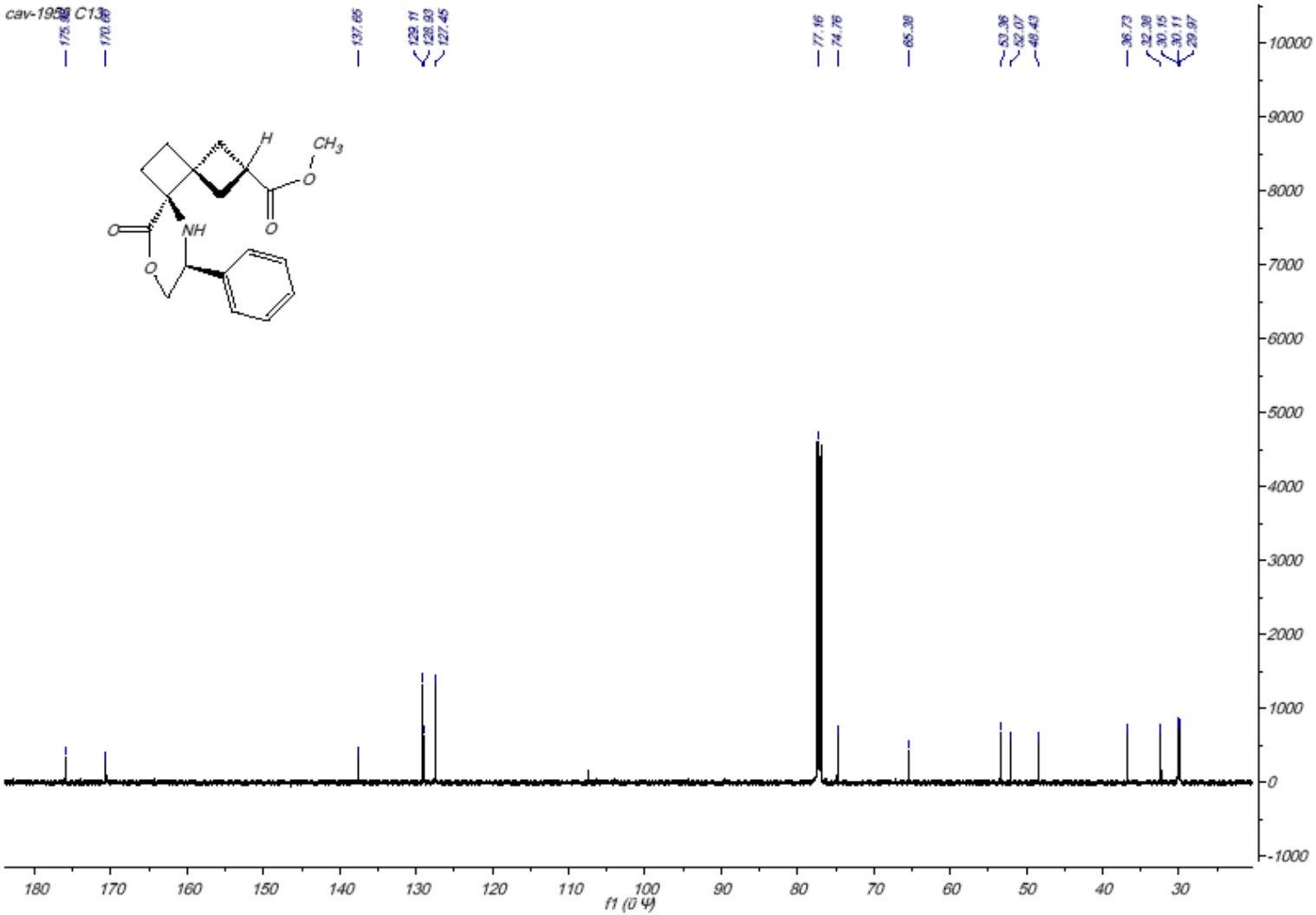

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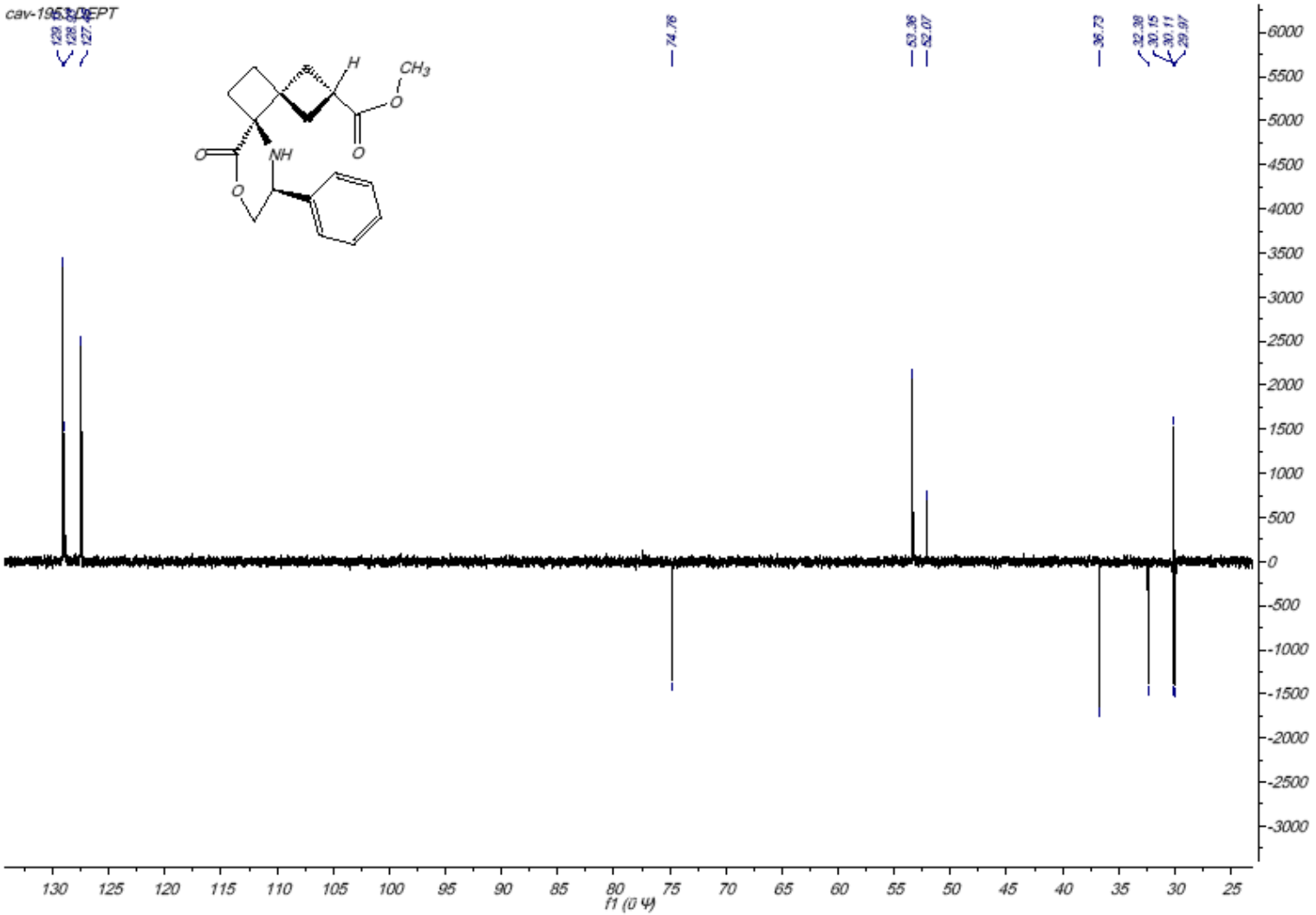

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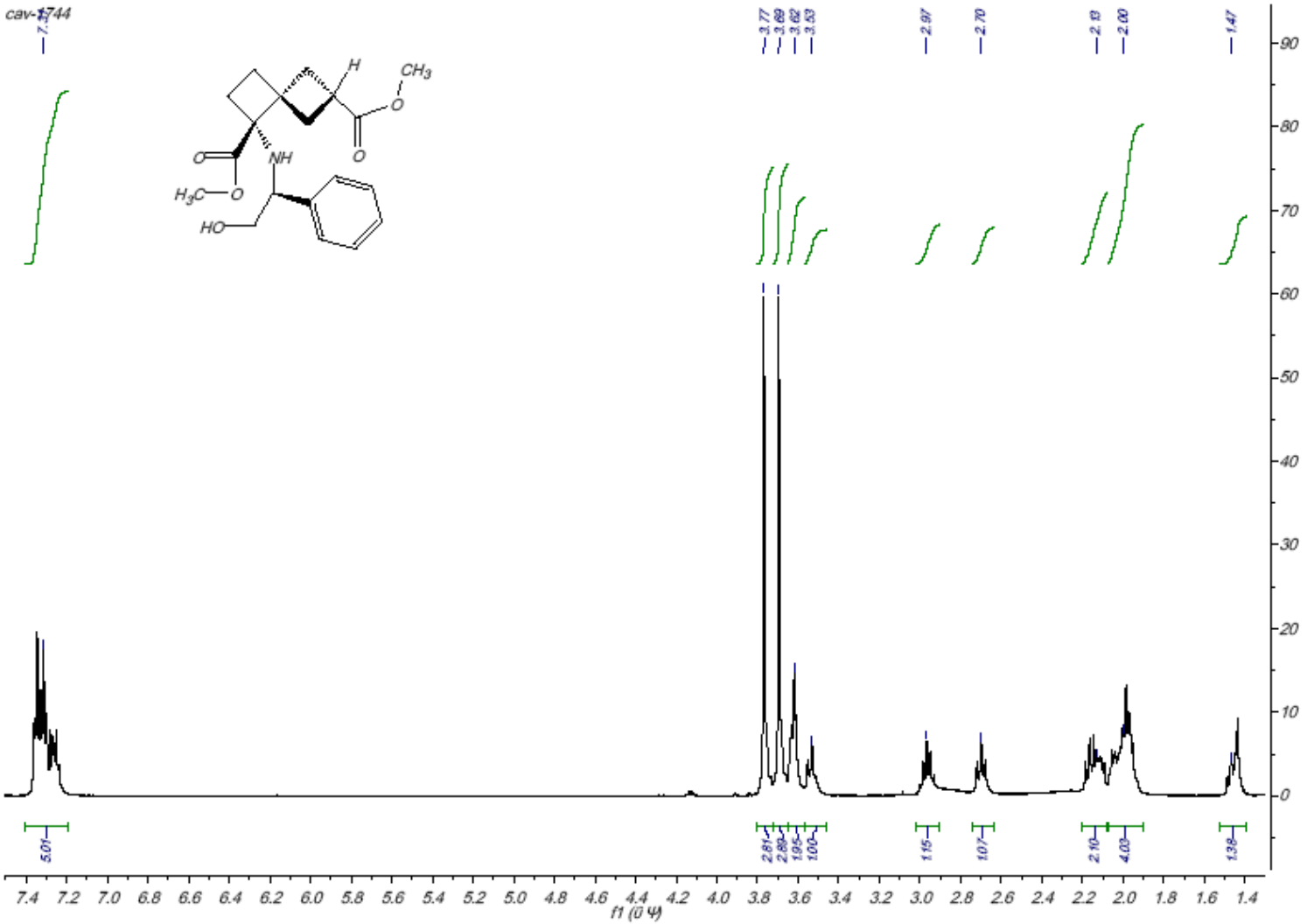

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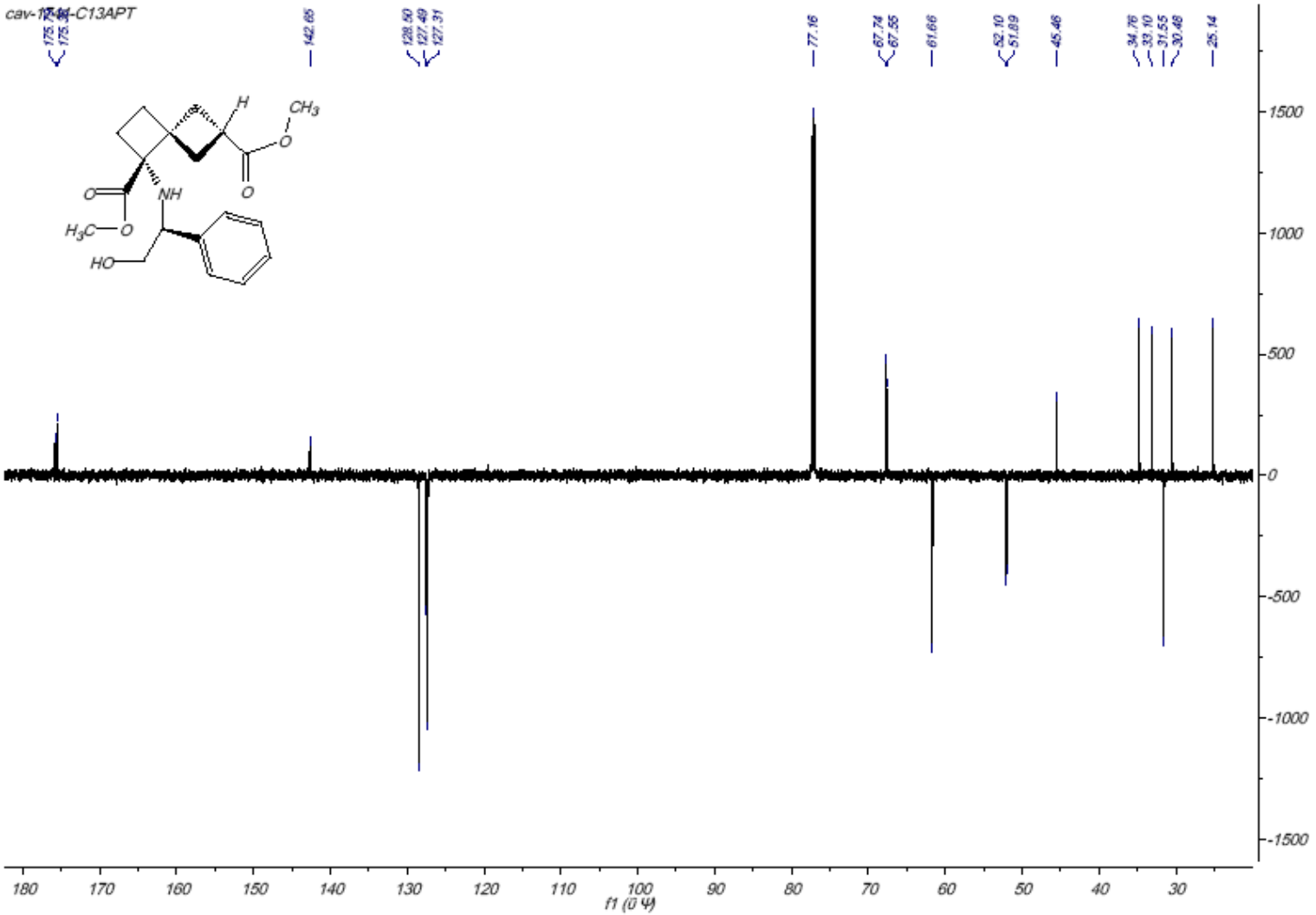


Stereochemical assignments of **1a-d**

The stereochemical assignment of the final compounds **1a-d** was done basing on several experiments: 1D- and 2D-NOESY for compounds **11a**,**b** (see above) and X-ray diffractional studies of three purposely synthesized compounds **18a**-**c**.

Before performing the NOE studies, we assigned the NMR signals in the spectra of **11a**,**b** using APT, HSQC, H,H-COSY experiments (see the spectra above). The H2 proton (which gives NMR signal at 3.15 ppm for **11a**, 3.08 ppm for **11b**), assigned reliably by its correlation with the C2 in the HSQC (the only tertiary carbon atom, 32.8 ppm for **11a**, 31.9 ppm for **11b**) was irradiated; NOE effect was observed for the proton with the chemical shift 2.54 ppm for **11a** and 2.19-2.34 ppm for **11b**. At the same time, strong NOE correlation was observed in the 2D-NOESY spectra for H7 (1.97 ppm (**11a**) and 2.11 ppm (**11b**)): with the signals H1b in **11a** (2.33 ppm) and H3b in **11b** (2.19-2.34 ppm). From these data we concluded that signals at 2.54 ppm (**11a**) and 2.63-2.77 ppm (**11b**) correspond to H1a and H3a. Hence, the keto-ester **11a** is the *trans*-isomer, because its H2 proton reveals strong NOE with H1a and H3a. Compound **11b** is the *cis*-isomer, because its H2 proton shows strong NOE with H1b and H3b.

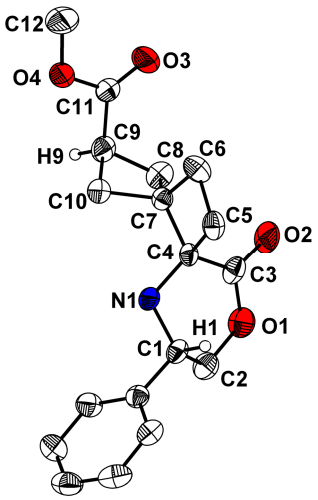
The crystallographic data, experimental parameters and CCDB deposition numbers are listed in Table S1. ORTEP diagrams of the compounds **18a–c** illustrate the absolute configuration of the stereocenters in these compounds.

Ideally, X-Ray analysis of all the four derivatives **18a-d** would give us enough information regarding the stereochemistry of **1a**-**d**, because compounds **16a-d** bear chiral auxiliary with the defined absolute configuration and transformed both into **1a**-**d** and **18a**-**d** without racemization at the stereocenters. However, compound **18d** did not give crystals suitable for the X-Ray study. Its absolute stereoconfiguration was deduced using the following reasoning. Compound **18d** is the only diastereomer of the four possible (the chiral auxiliary group was derived from the *S*-α-phenylglycinol for all the diastereomers); its absolute configuration at one of the stereocenter C2 (2*S*) should be the same as in its precursor **11b**, determined by 1D- and 2D-NOESY experiments. The other stereocenter C5 must have the stereoconfiguration reverse to that in its diastereomer **18c**, thus, 5*S*.

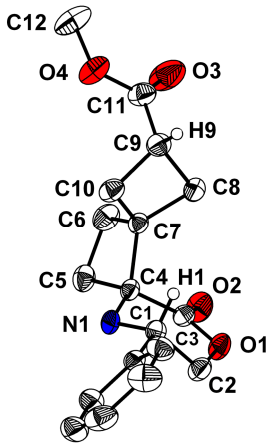
Table S1 Crystallographic data and experimental parameters for the compound **13** and **18a–c**

Parameter	**13**	**18a**	**18b**	**18c**
a, Å	8.9199(4)	6.0940(5)	6.1255(6)	10.260(3)
b, Å	18.9724(8)	15.418(2)	11.218(1)	5.820(2)
c, Å	17.167(1)	17.637(2)	24.188(2)	14.060(4)
α, deg	90.0	90.0	90.0	90.0
β, deg	100.522(5)	90.0	90.0	98.37(3)
γ, deg	90.0	90.0	90.0	90.0
V, $Å^3$	2856.4(3)	1657.1(3)	1662.1(3)	830.6(5)
T, K	293(2)	293(2)	293(2)	293(2)
F(000)	1132	672	672	336
Crystal system	Monoclinic	Rhombic	Rhombic	Monoclinic
Space group	$P2_1/n$	$P2_12_12_1$	$P2_12_12_1$	$P2_1$
Z	2	4	4	2
μ, mm^{-1}	0.307	0.089	0.089	0.089
d_{calc}, g/cm^3	1.256	1.264	1.260	1.261
$2\Theta_{max}$, deg	50	60	60	60
Reflection measured	19720	8562	13719	7469
Reflections independent	5018	4455	4755	4370
R_{int}	0.023	0.071	0.102	0.155
Reflections with F>4σ(F)	3827	1524	1883	836
R_1	0.098	0.048	0.055	0.066
wR_2	0.285	0.064	0.084	0.159
S	1.227	0.793	0.840	0.696
CCDC deposition number	**962474**	**962475**	**962476**	**962477**

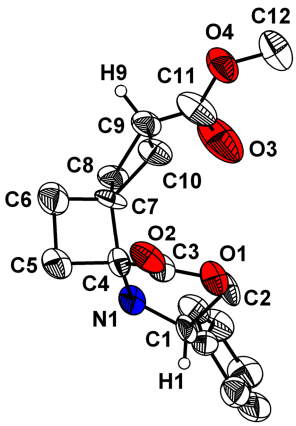
ORTEP diagrams of the compounds **18a–c**



18a



18b



18c