Supporting information

New Asymmetric Approach to β-Trifluoromethyl Isoserines

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X-ray crystallography:

Crystals were each mounted on a Hampton cryo-loop for indexing and intensity data collection at 100 K on a Bruker D8 APEX II CCD using Mo-Kα radiation (λ = 0.71073 Å). Lorentz and polarization corrections were applied, and an absorption correction was performed using the SADABS program.

Direct methods were used for structure solution of all structures (SHELXS-97). Structural refinement was obtained from successive Fourier maps (SHELXL-97). All heavy atoms (C, N, O, S, F) were refined anisotropically whereas the hydrogen atoms were found through calculated constrained positions. The crystallographic data for **6** and **4b** are summarized in Table S1.

Table S1**. Crystal data**

Compound	**6**	**4b**
Empirical formula	C9H16F3NO4S	C14H24F3NO6S
Formula weight, g/mol	291.29	391.40
Crystal system	Orthorhombic	Orthorhombic
Space group	$P2_12_12_1$	$P2_12_12$
a, Å	10.706(2)	25.049(2)
b, Å	14.746(3)	8.4762(7)
c, Å	16.870(4)	8.8991(8)
α, °	90.00	90.00
β, °	90.00	90.00
γ, °	90.00	90.00
Volume, Å^3	2663.3(10)	1889.5(3)
Z	8	4
D_{calc}, g/cm^3	1.453	1.376
Absorption coefficient	0.285	0.228
F(000)	1216	824
Crystal size, mm	0.4 x 0.4 x 0.3	0.3 x 0.3 x 0.2
Theta range for data collection, °	3.57 – 30.51	3.42 – 28.43
Reflections collected	166854	97622
Independent reflections	8110	4664
R(int)	0.0696	0.0541
Observed (I > 2σ(I))	7699	4491
Goodness-of-fit on F2	1.026	1.017
R_1[I > 2σ(I)][a]	0.0242	0.0455
wR_2 (all data)[b]	0.0601	0.1251
Flack Parameter	-0.03(3)	0.02(10)

[a] $R = \Sigma||F_o| - |F_c||/\Sigma|F_o|$. [b] $R_w = [\Sigma w(F_o^2 - F_c^2)^2/\Sigma w(F_o^2)^2]^{1/2}$.

Figures S1 and S2 are Mercury[1] images for the respective crystal structures.

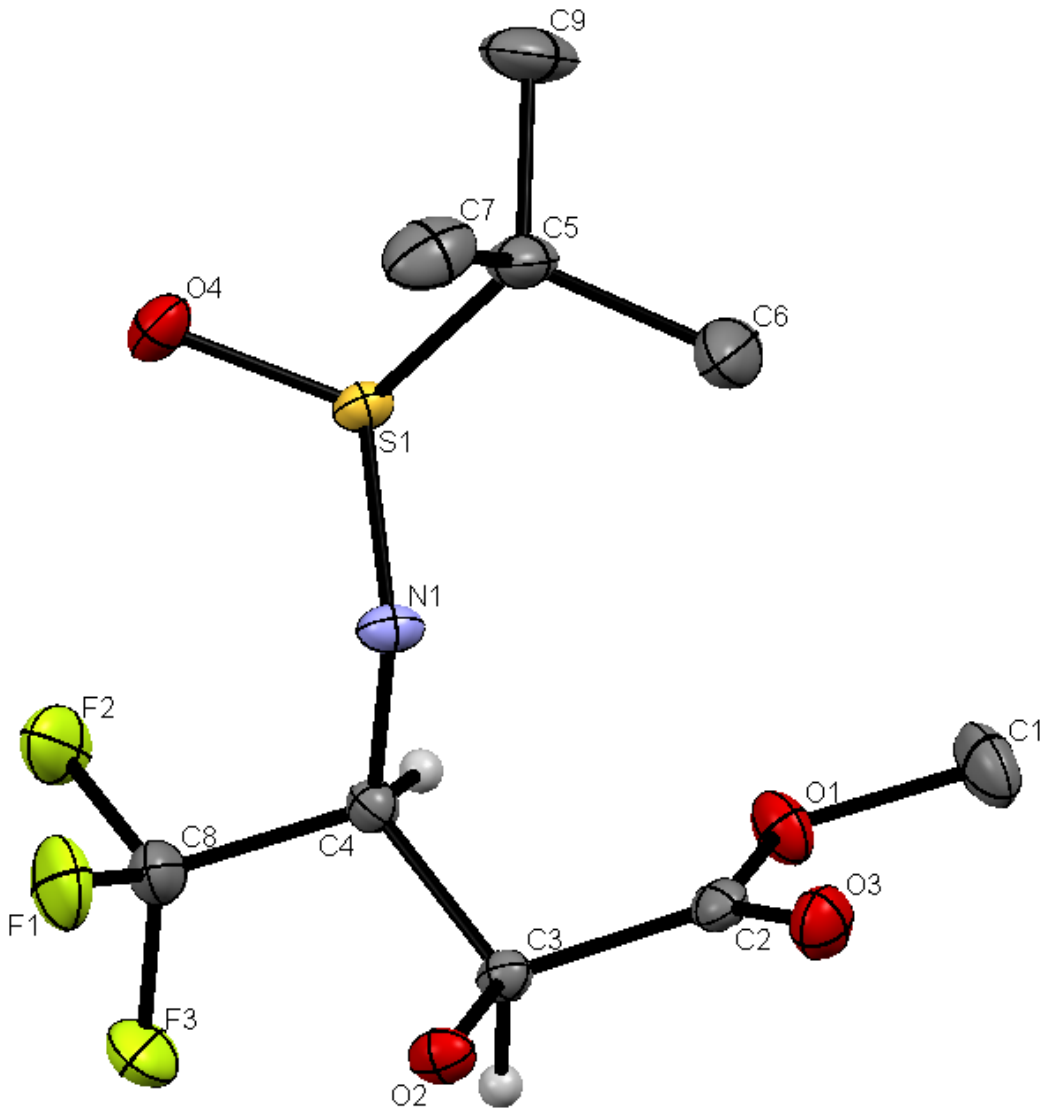

Figure 1. CCDC 910363. Mercury representation for crystal structure of **6** (derivative of "major diastereomer"). Hydrogens, except of those at chiral centers, are omitted for clarity.

[1] Mercury CSD 2.0 - New Features for the Visualization and Investigation of Crystal Structures. C. F. Macrae, I. J. Bruno, J. A. Chisholm, P. R. Edgington, P. McCabe, E. Pidcock, L. Rodriguez-Monge, R. Taylor, J. van de Streek and P. A. Wood, *J. Appl. Cryst.*, 2008, **41**, 466-470. DOI: 10.1107/S0021889807067908

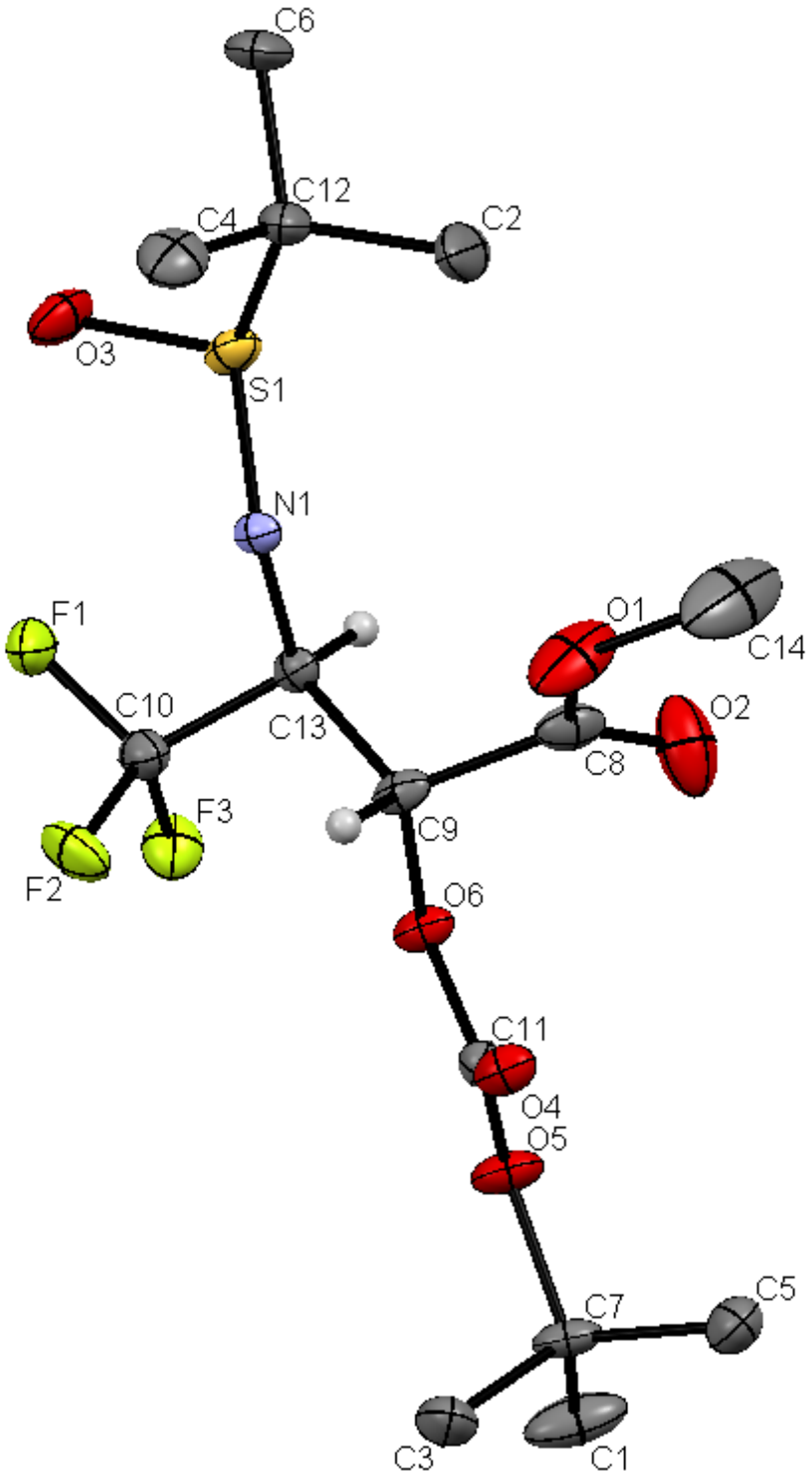

Figure 2. CCDC 910364. Mercury representation for crystal structure of **4b** ("minor diastereomer"). Hydrogens, except of those at chiral centers, are omitted for clarity.

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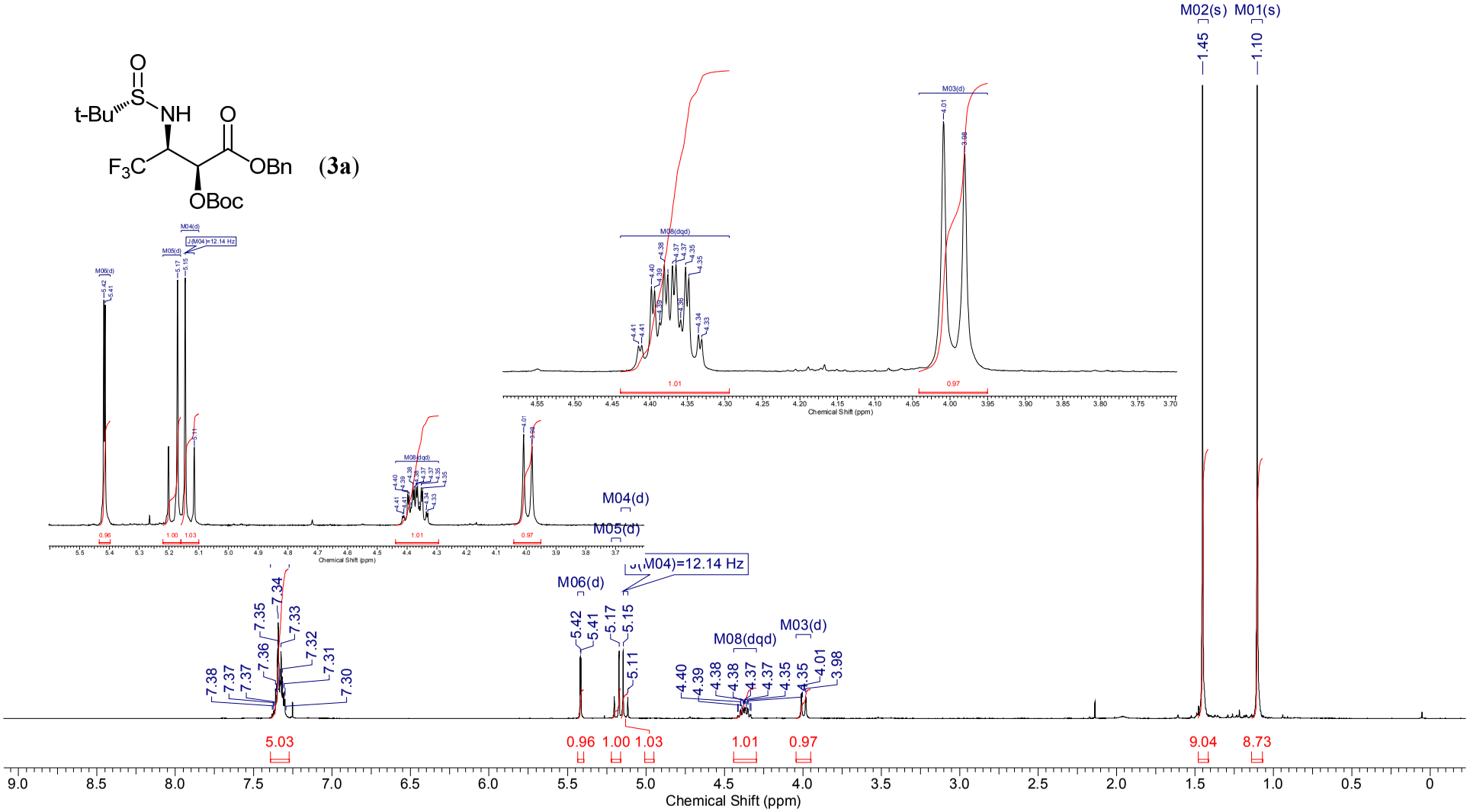
Temperature (degree C)	22.500								



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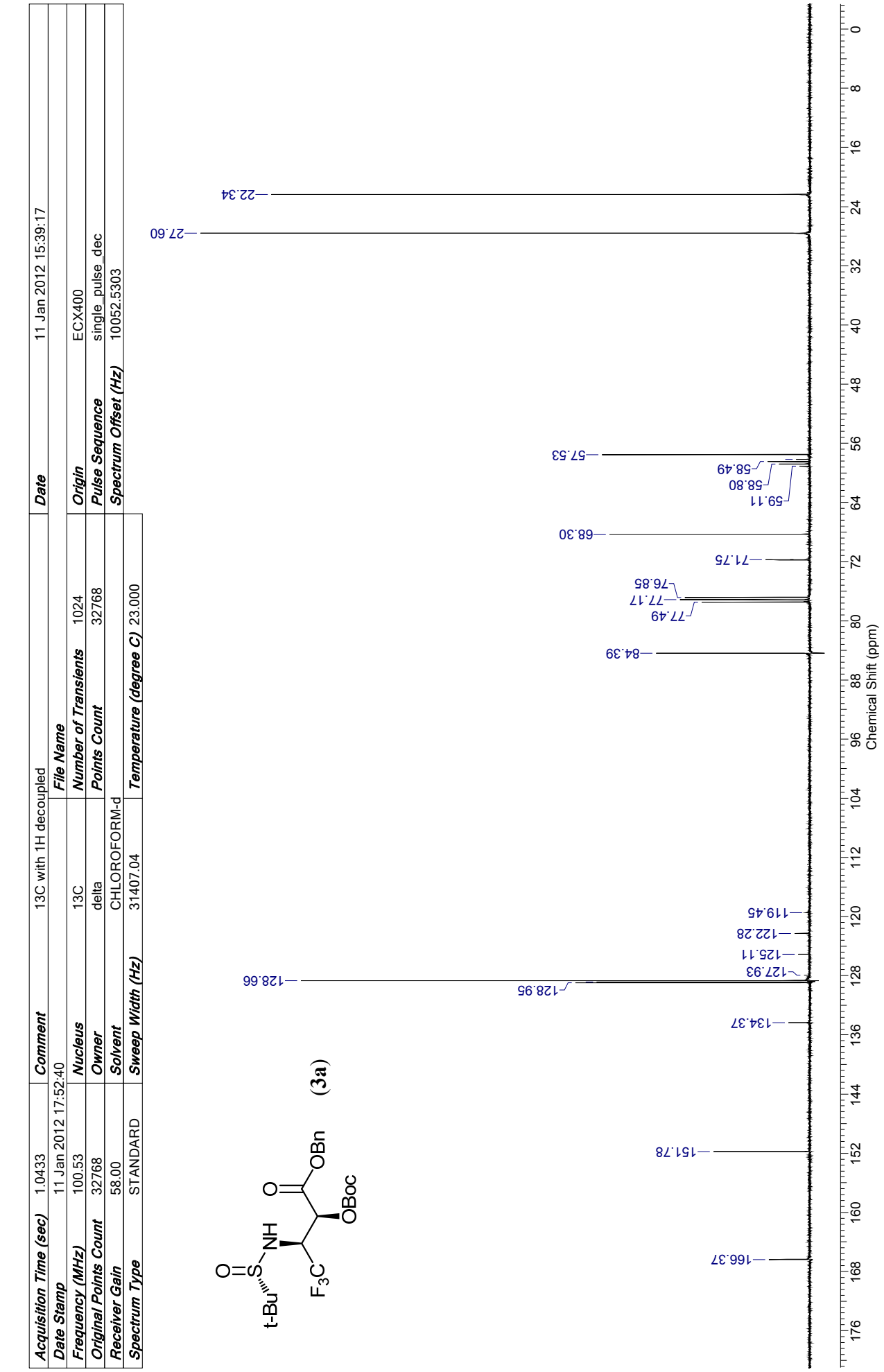

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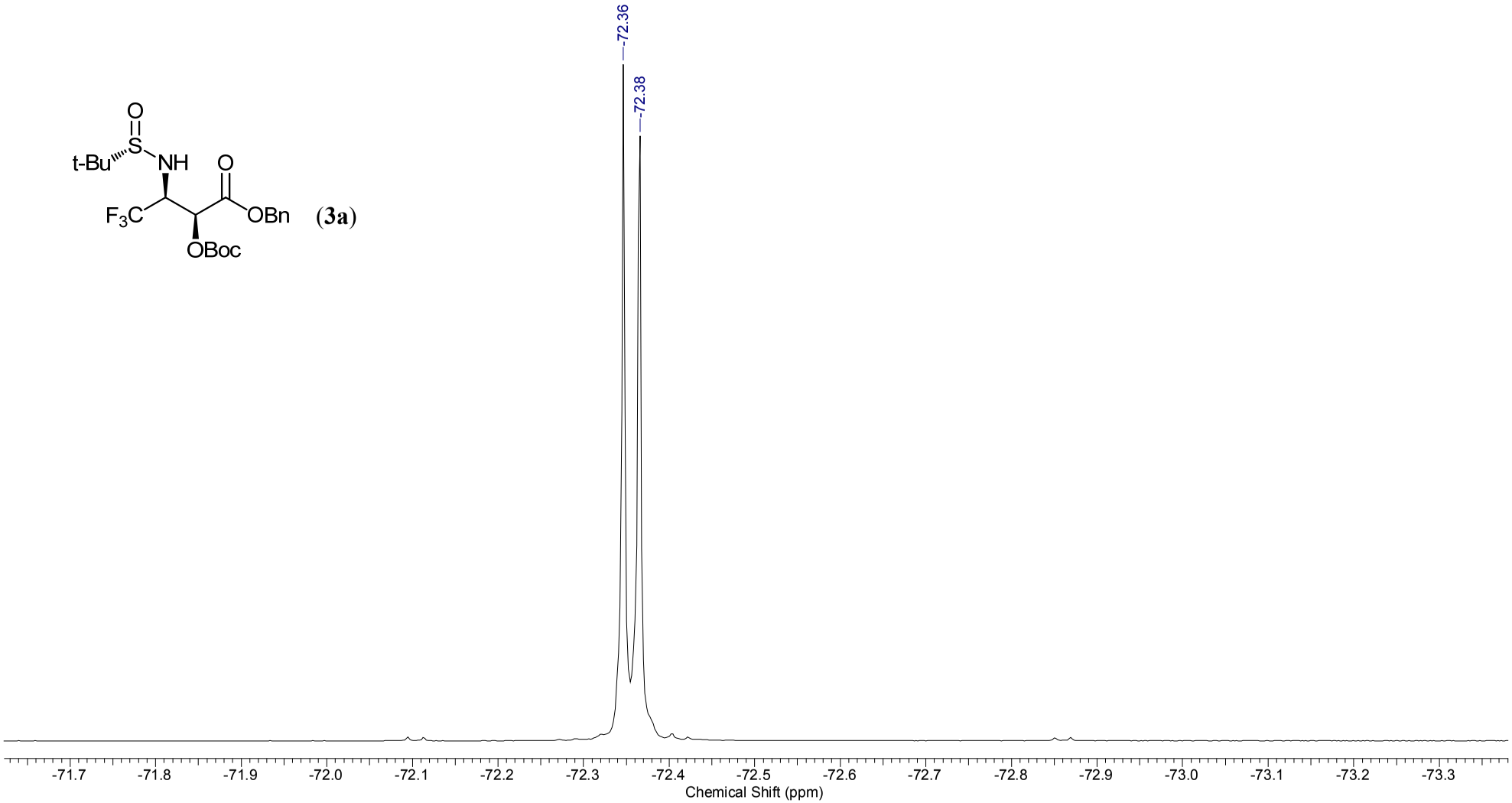
(3a)



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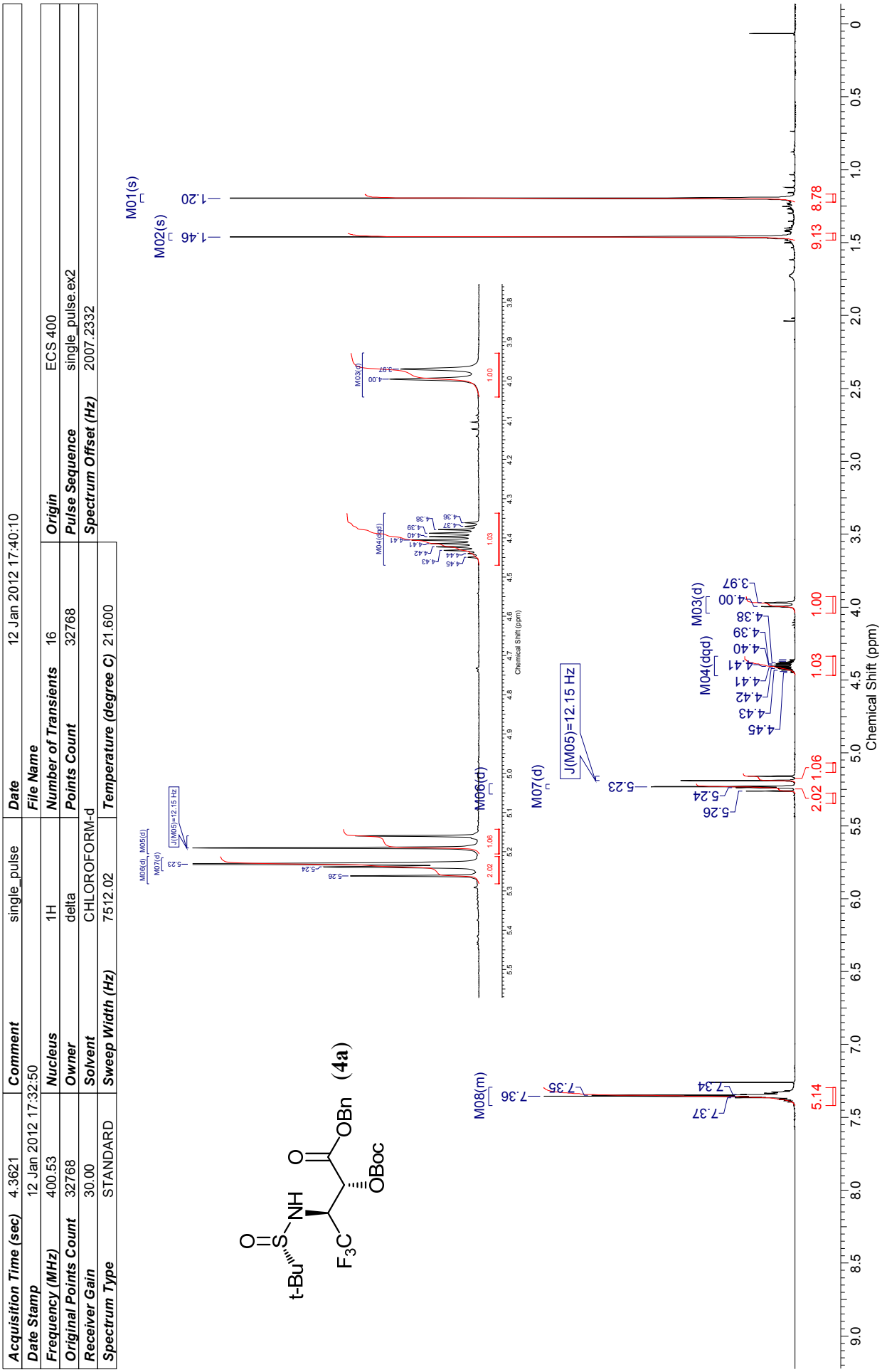

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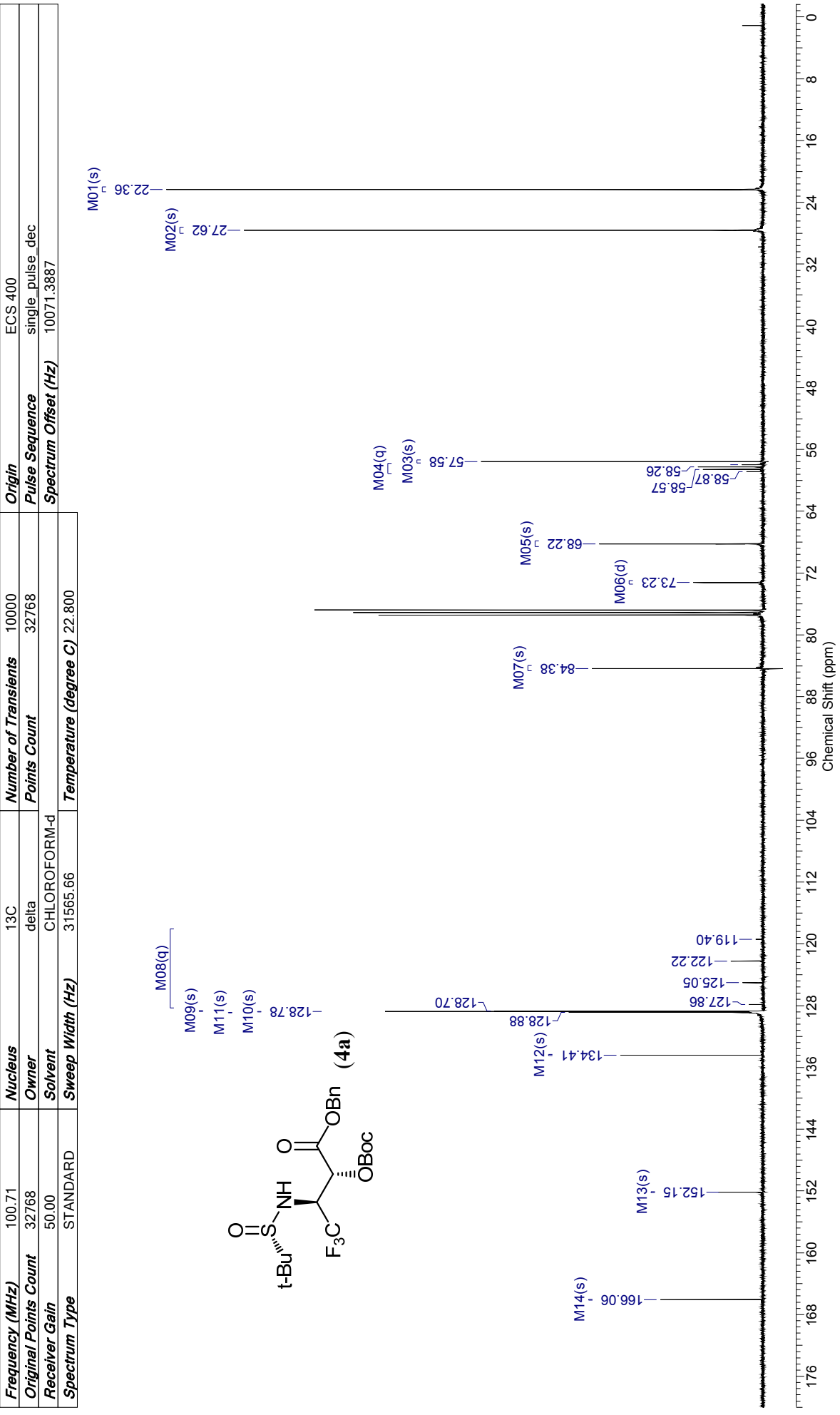

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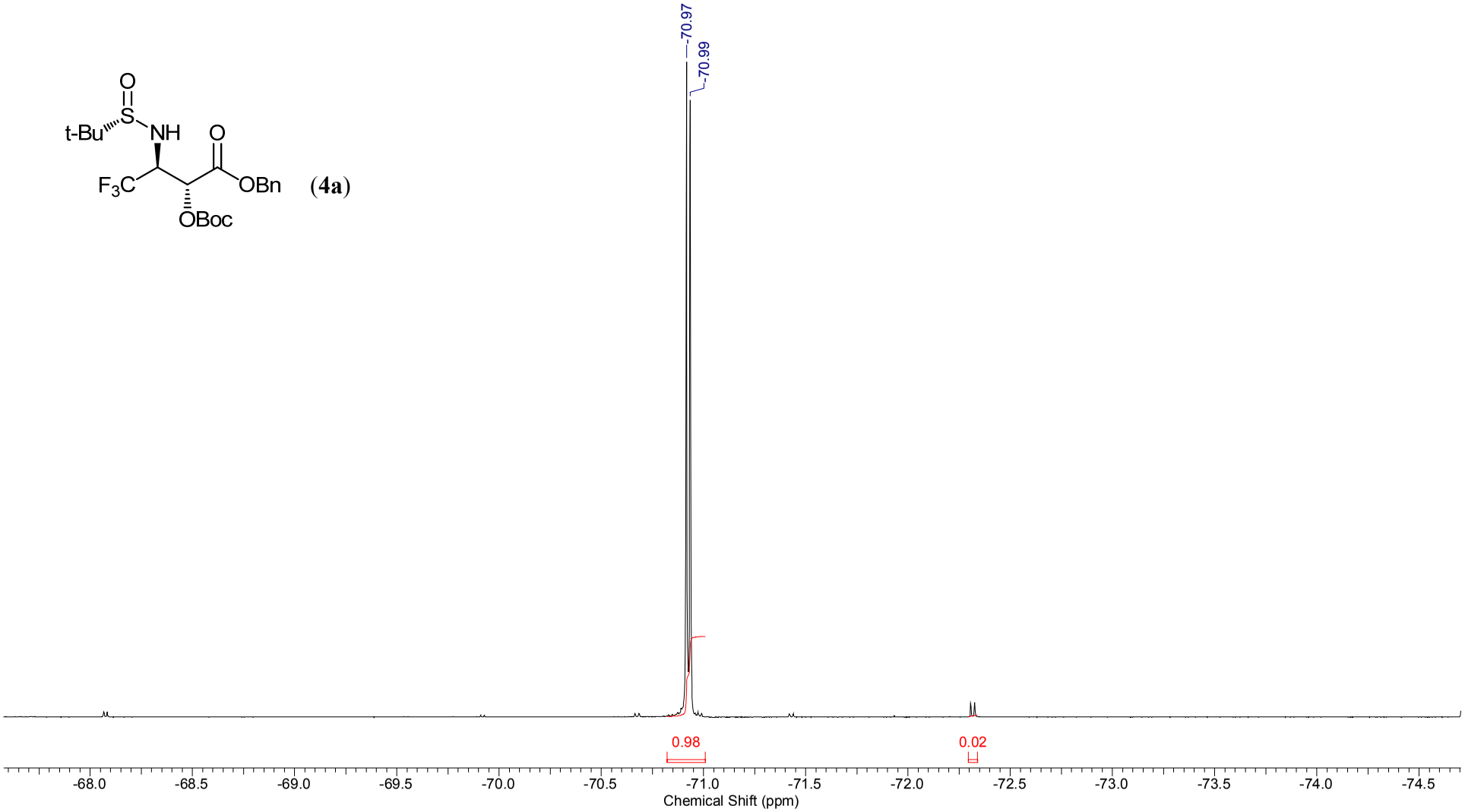
(4a)



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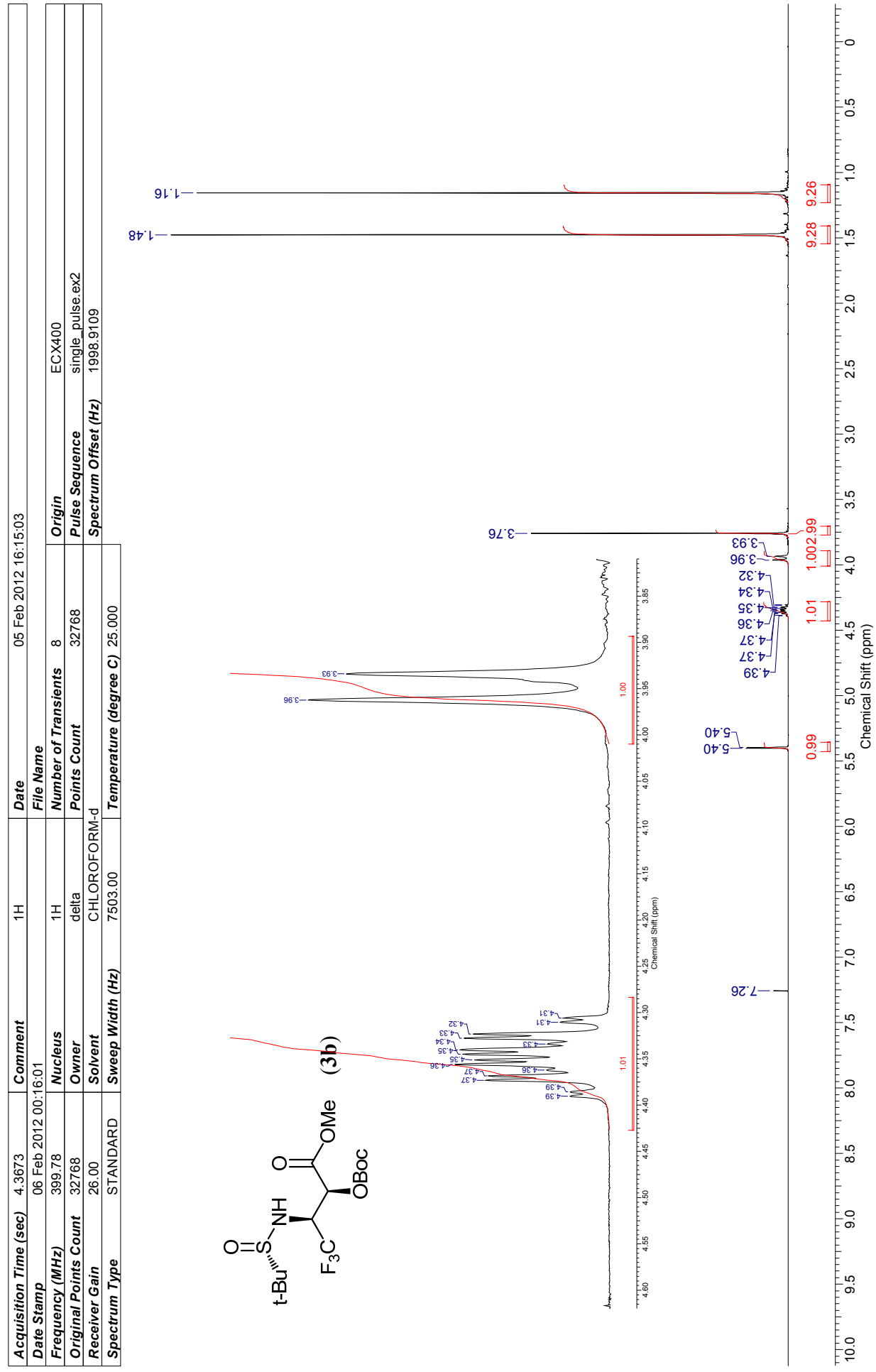

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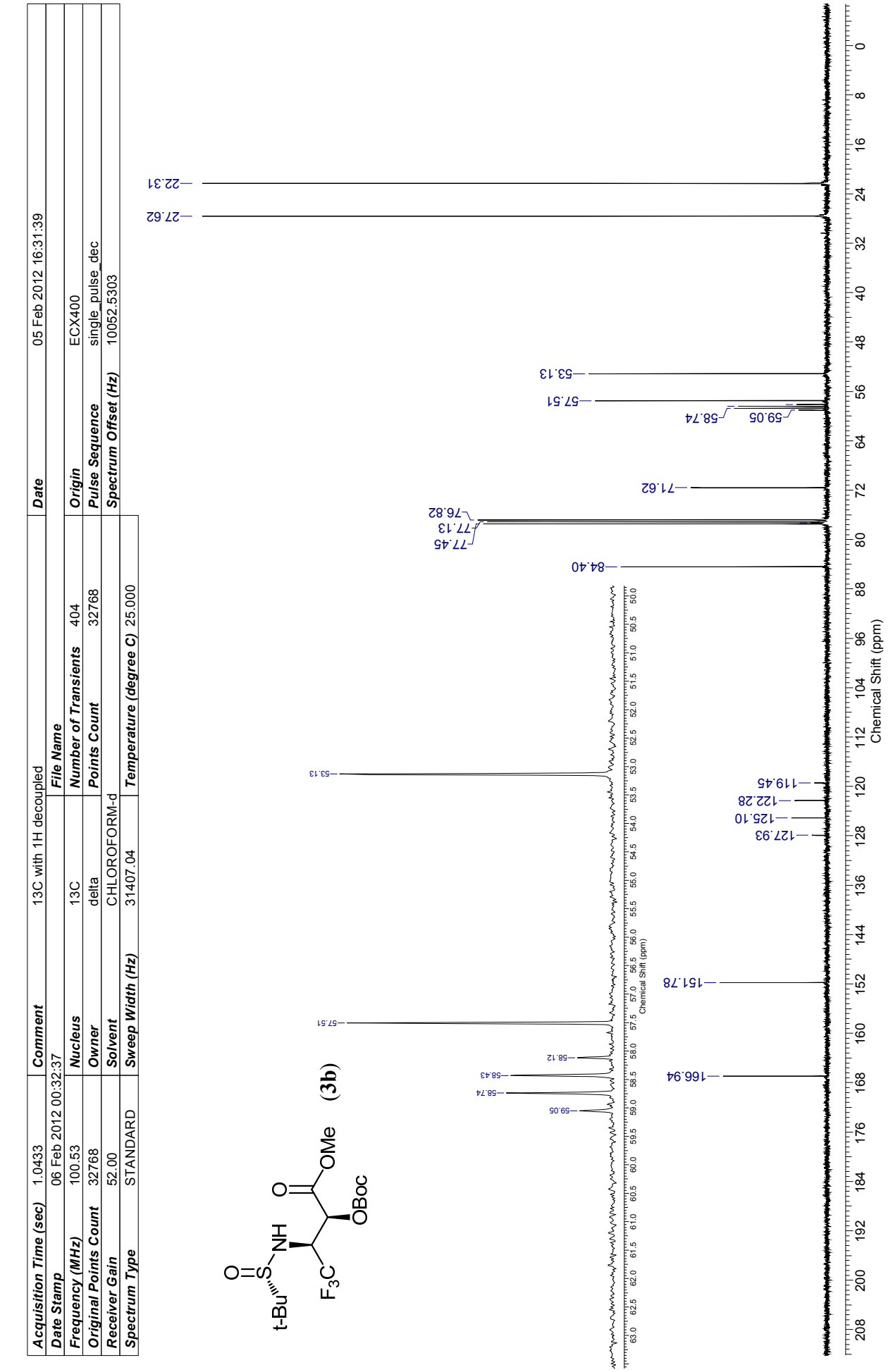

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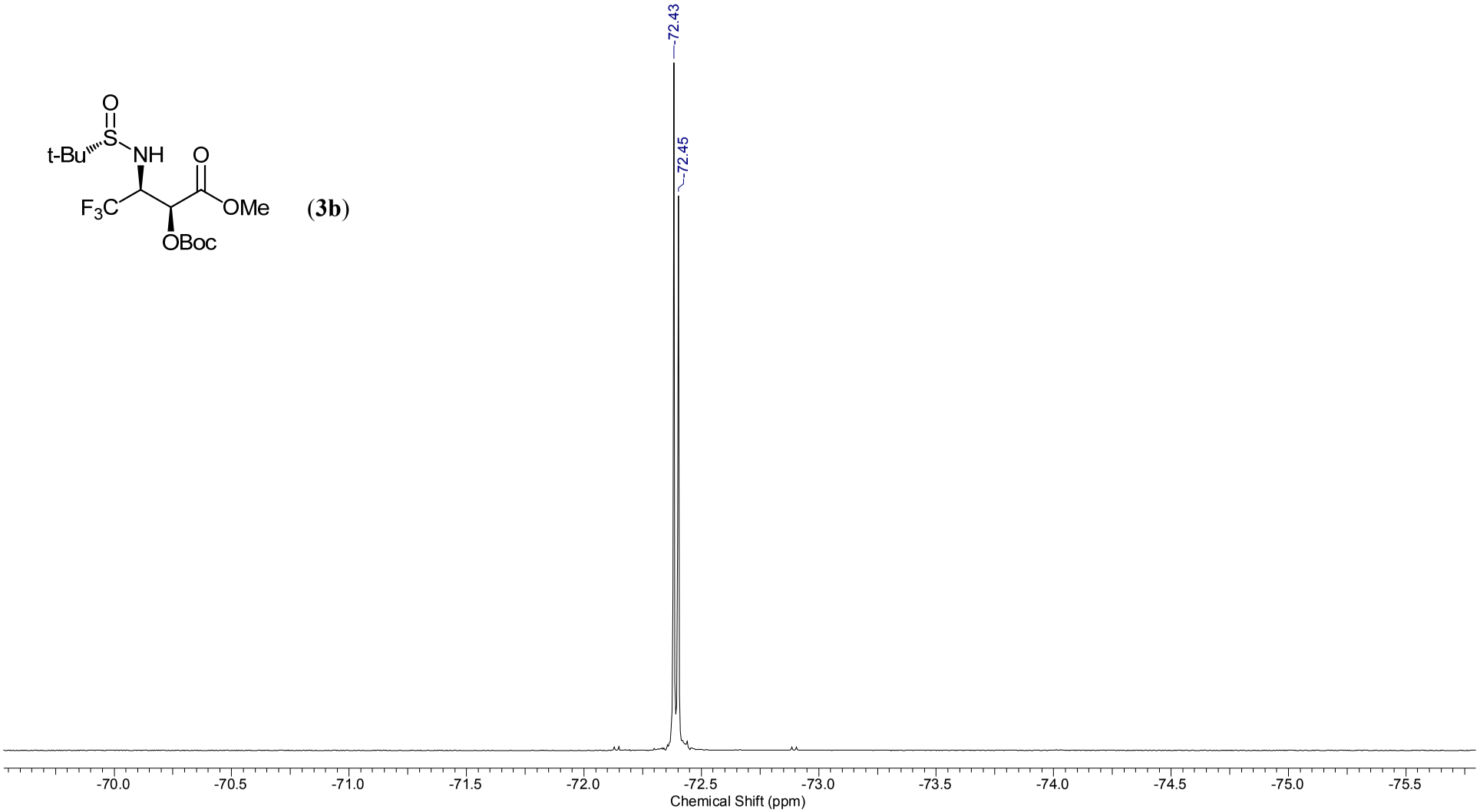
(3b)



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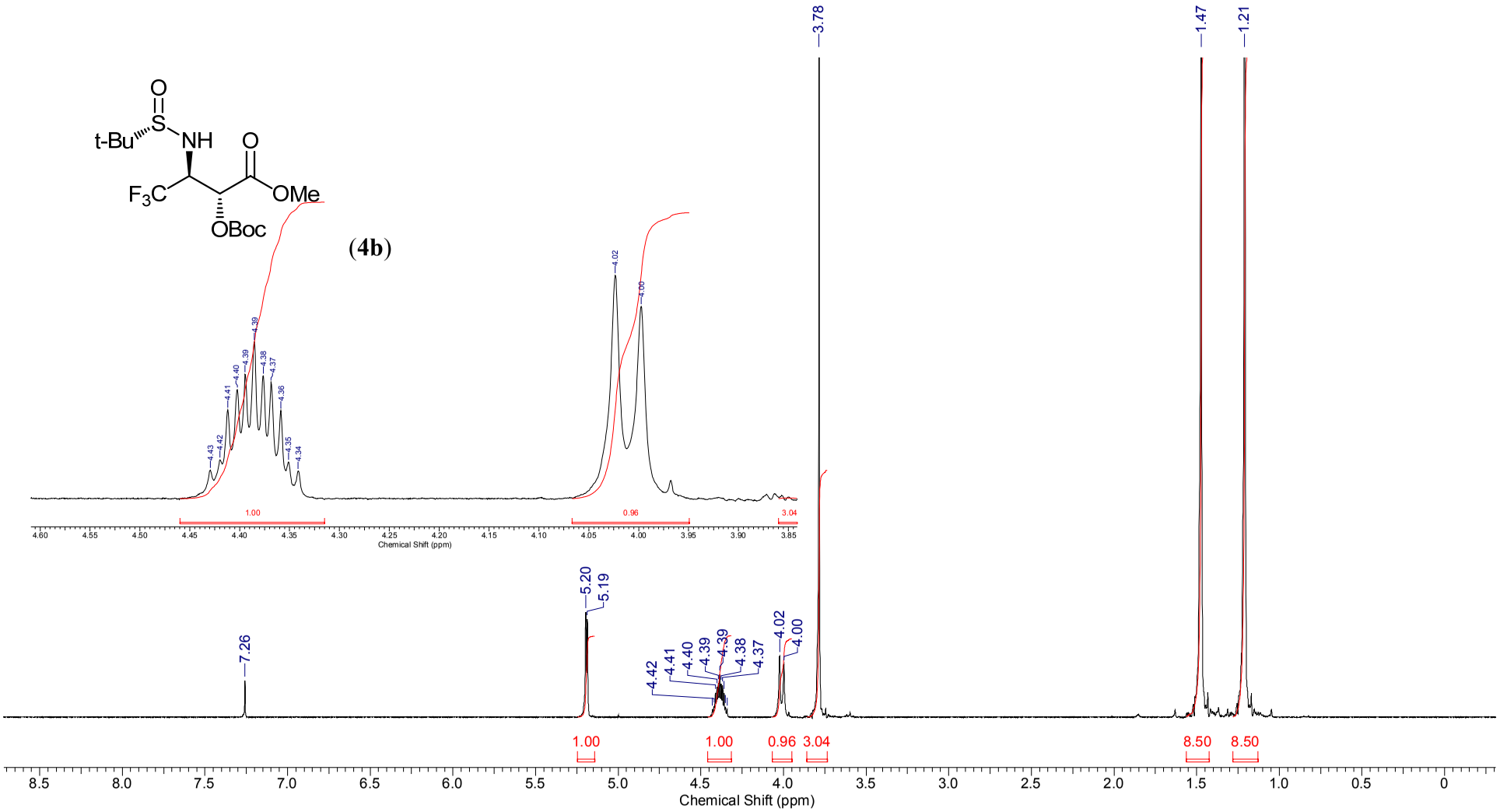

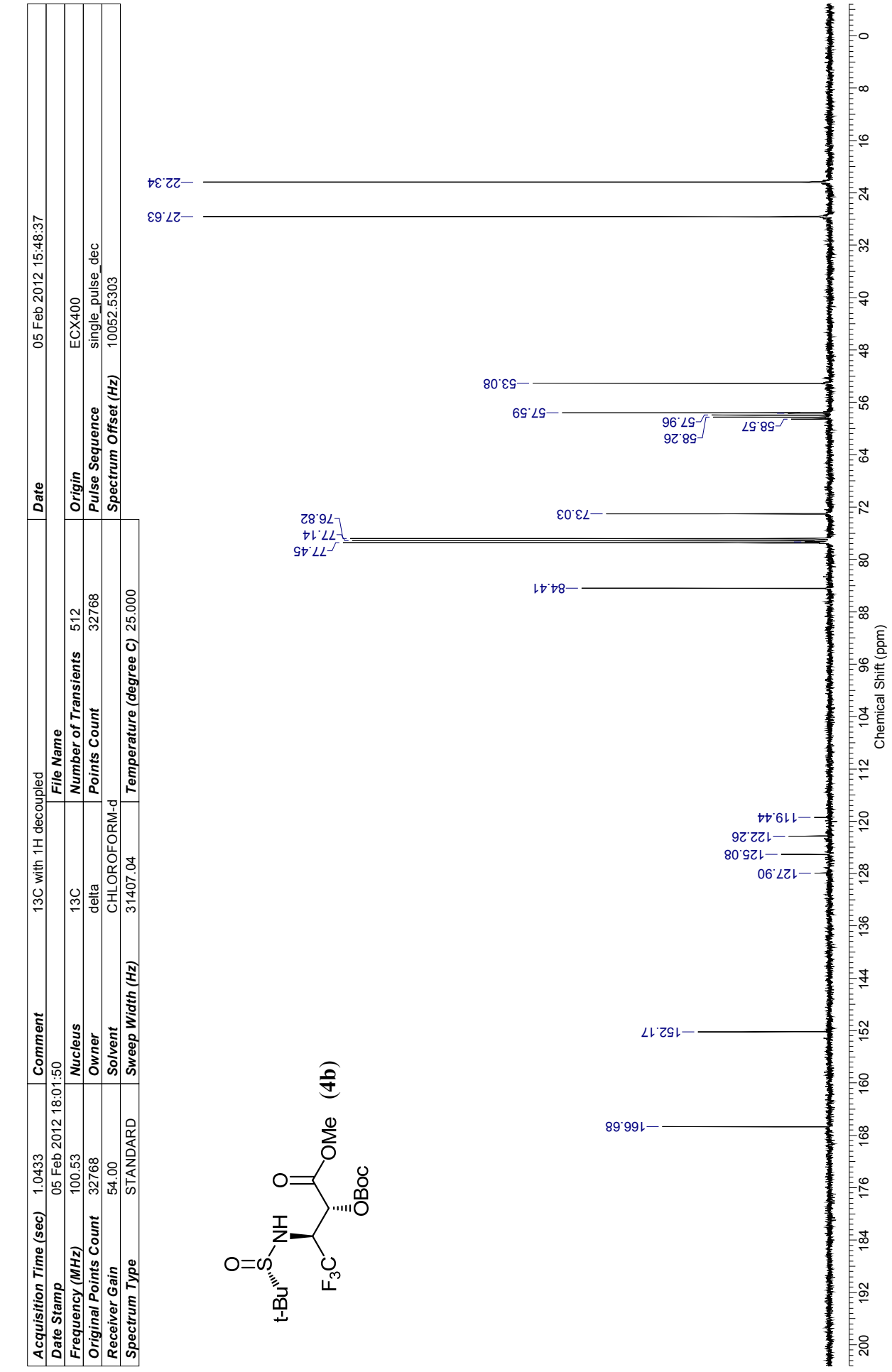
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(4b)
t-Bu
NH
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58.57
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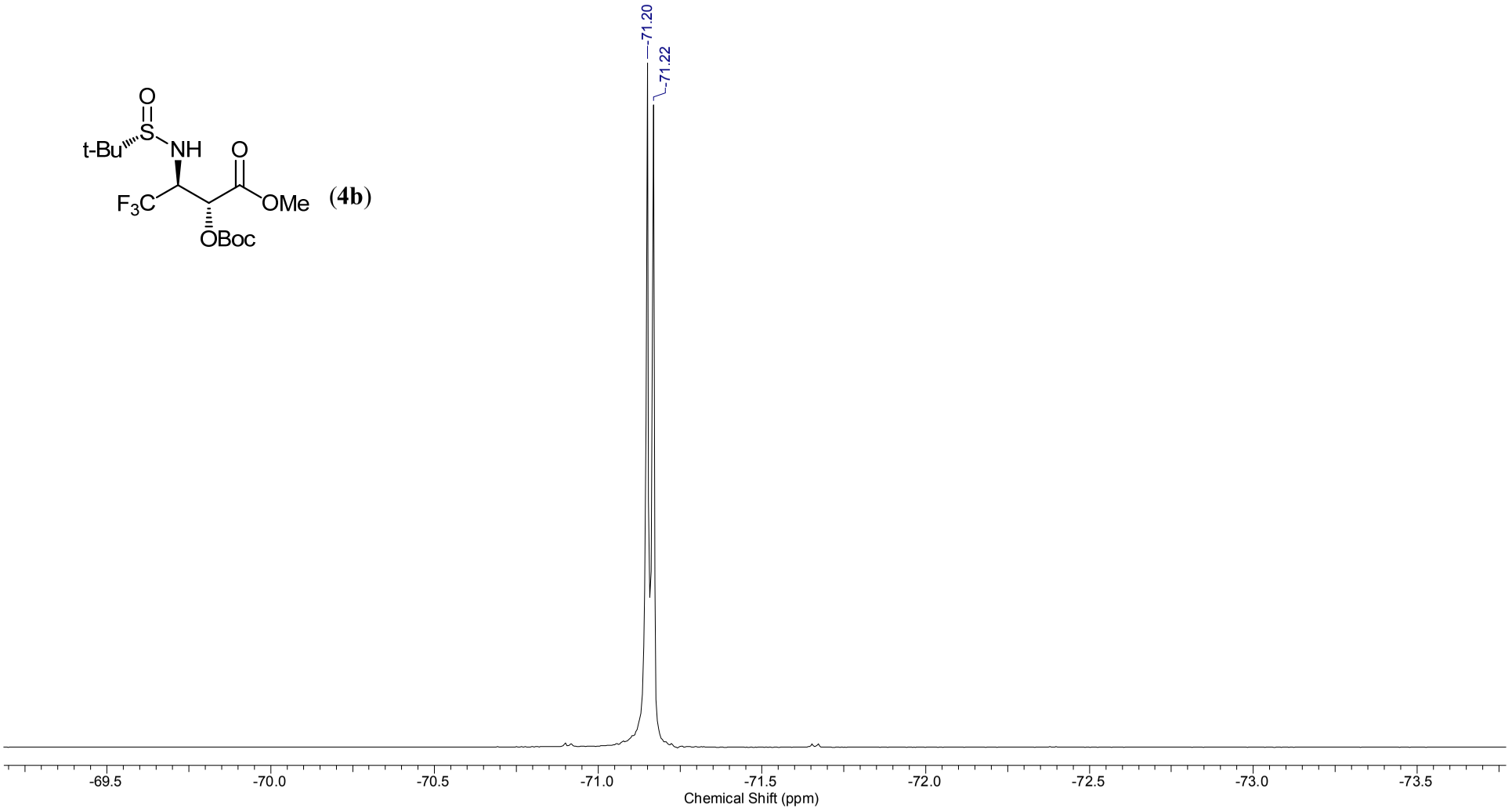

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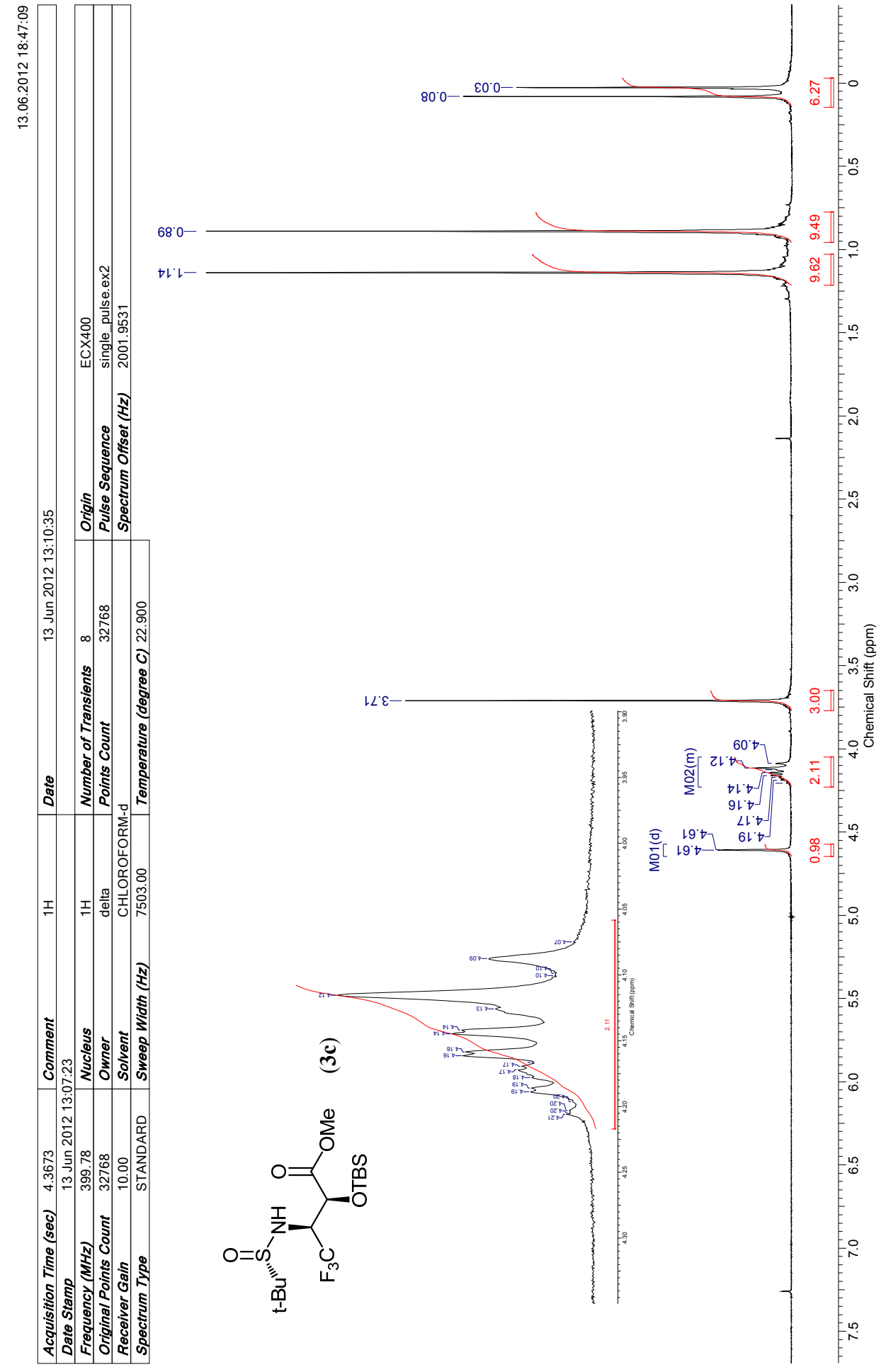

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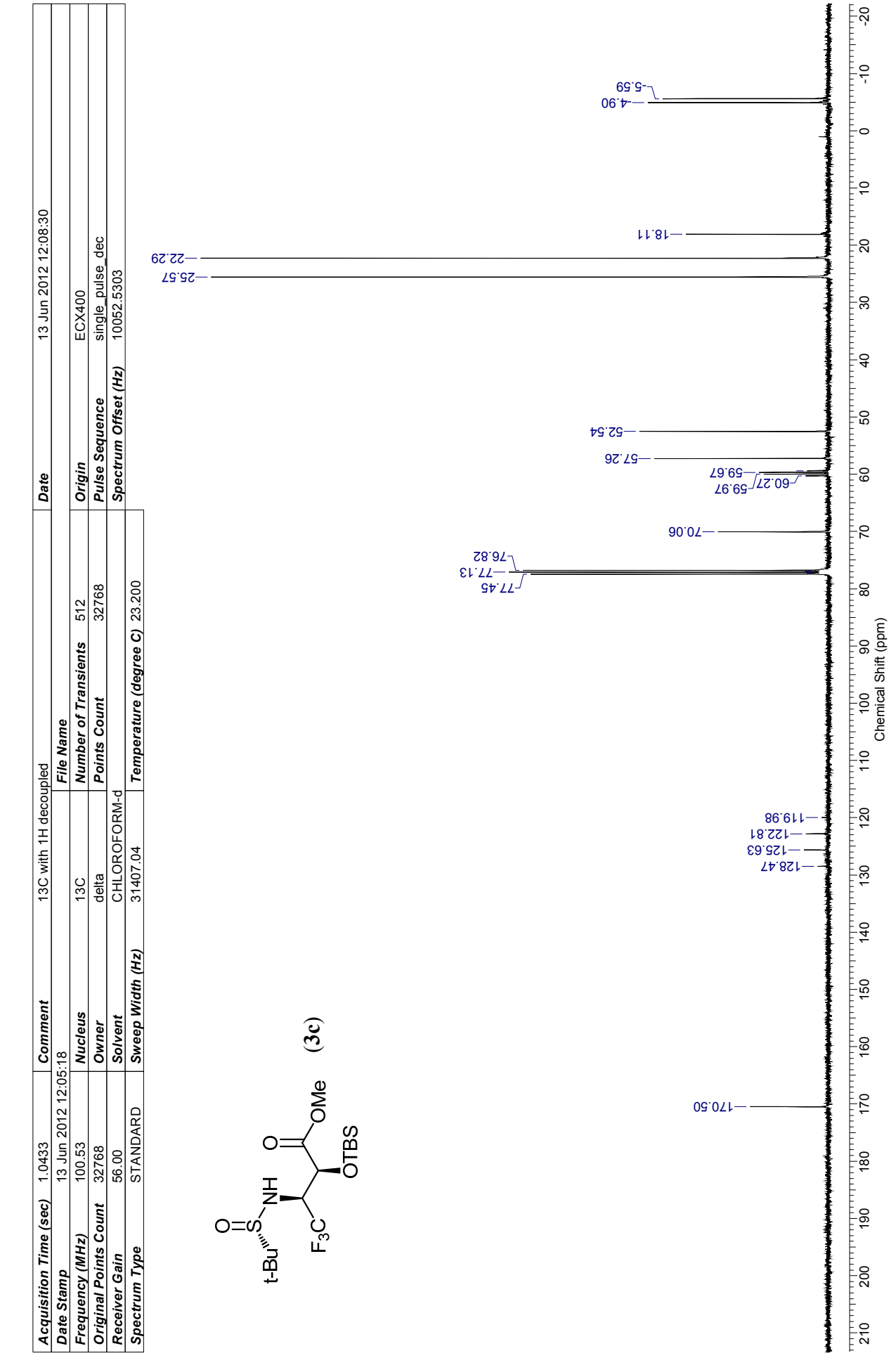

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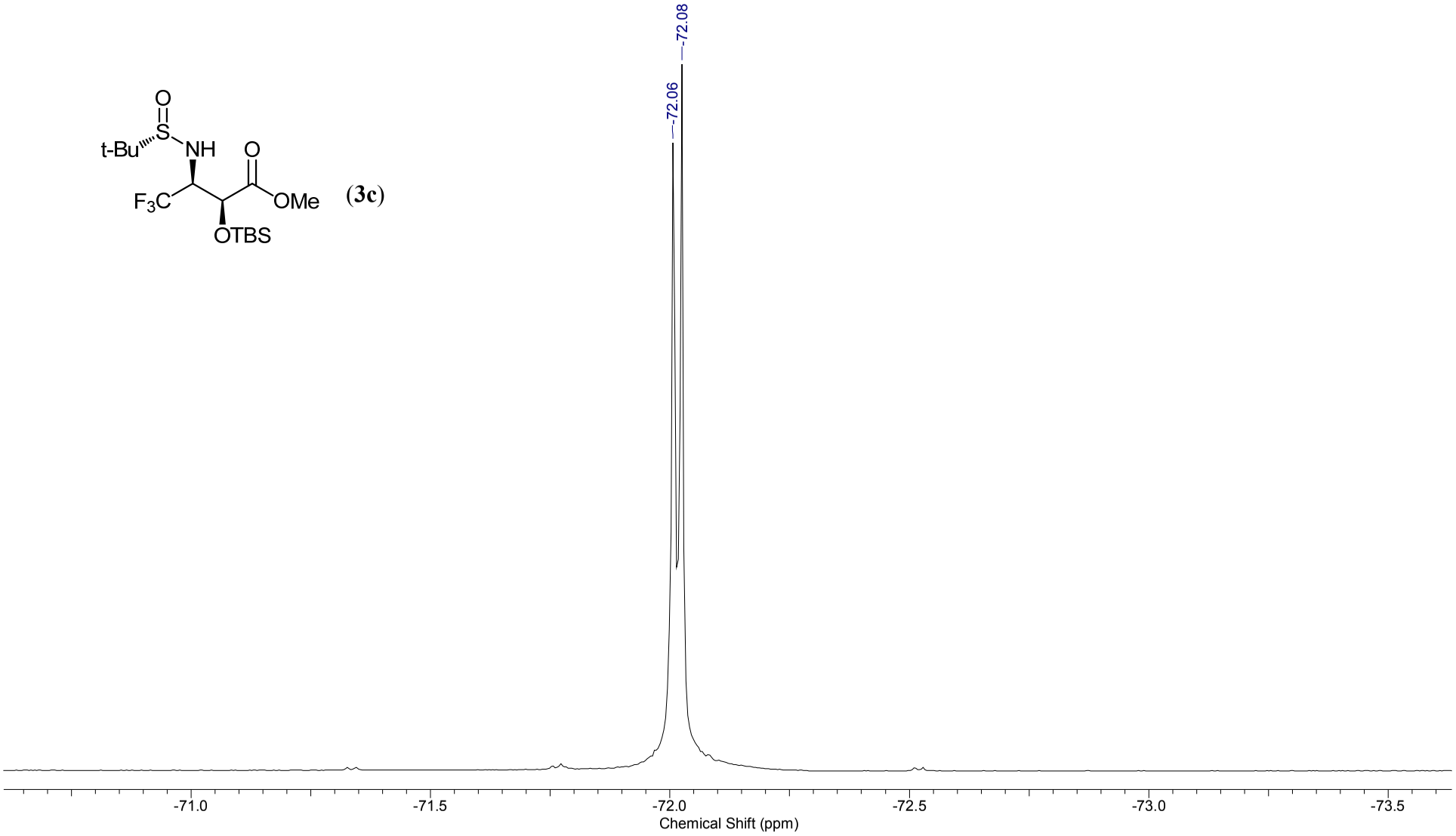

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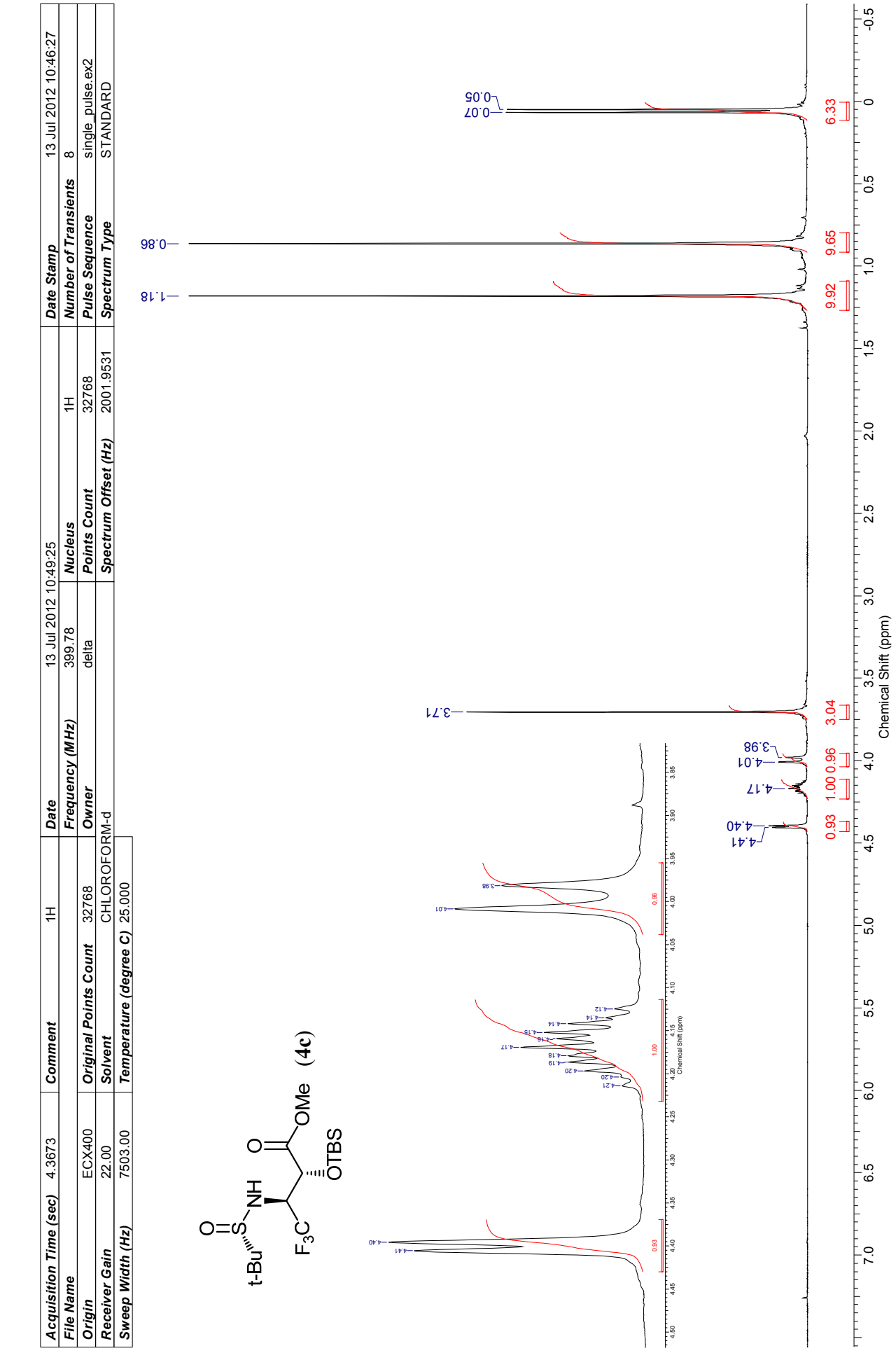

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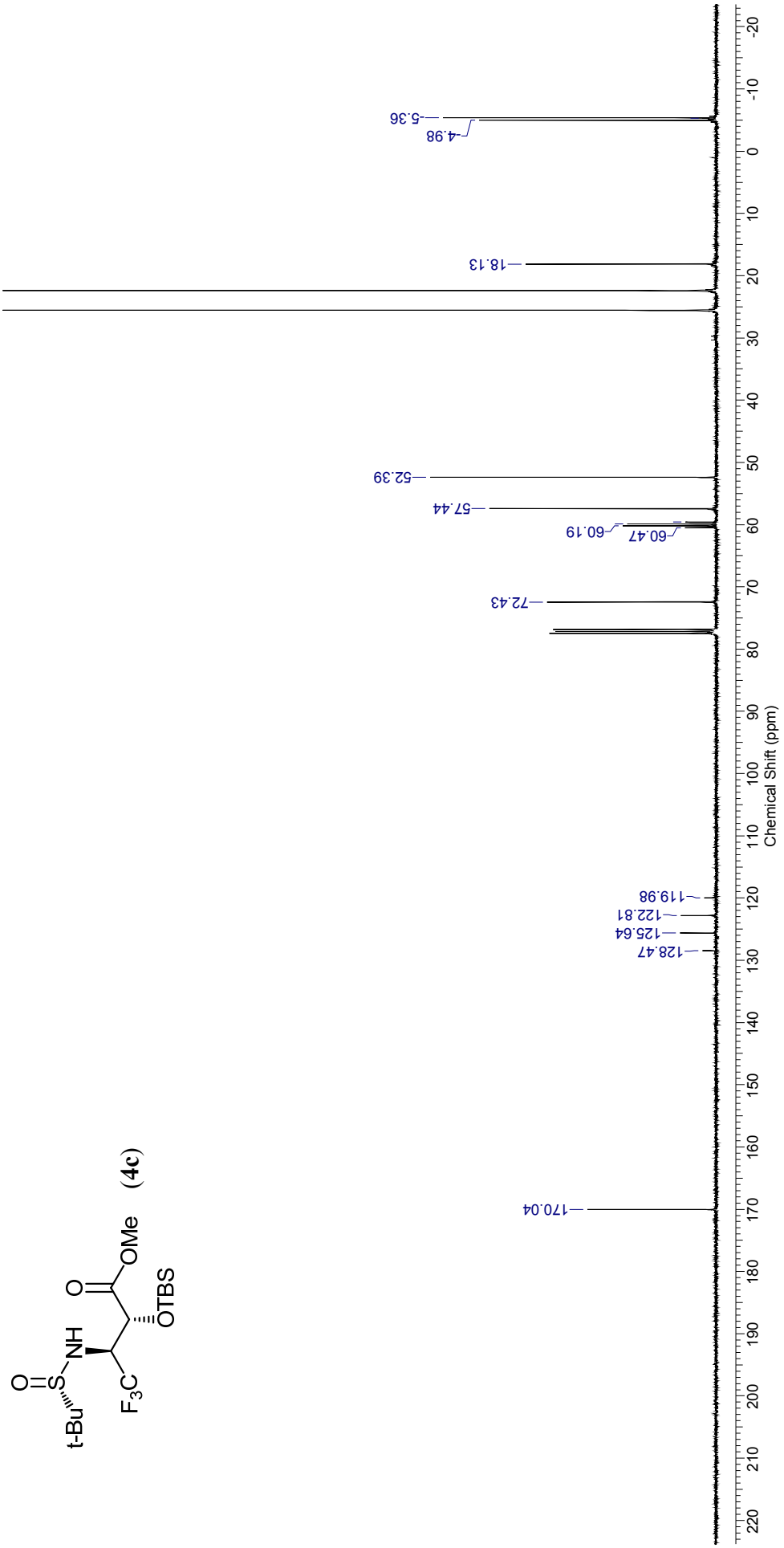

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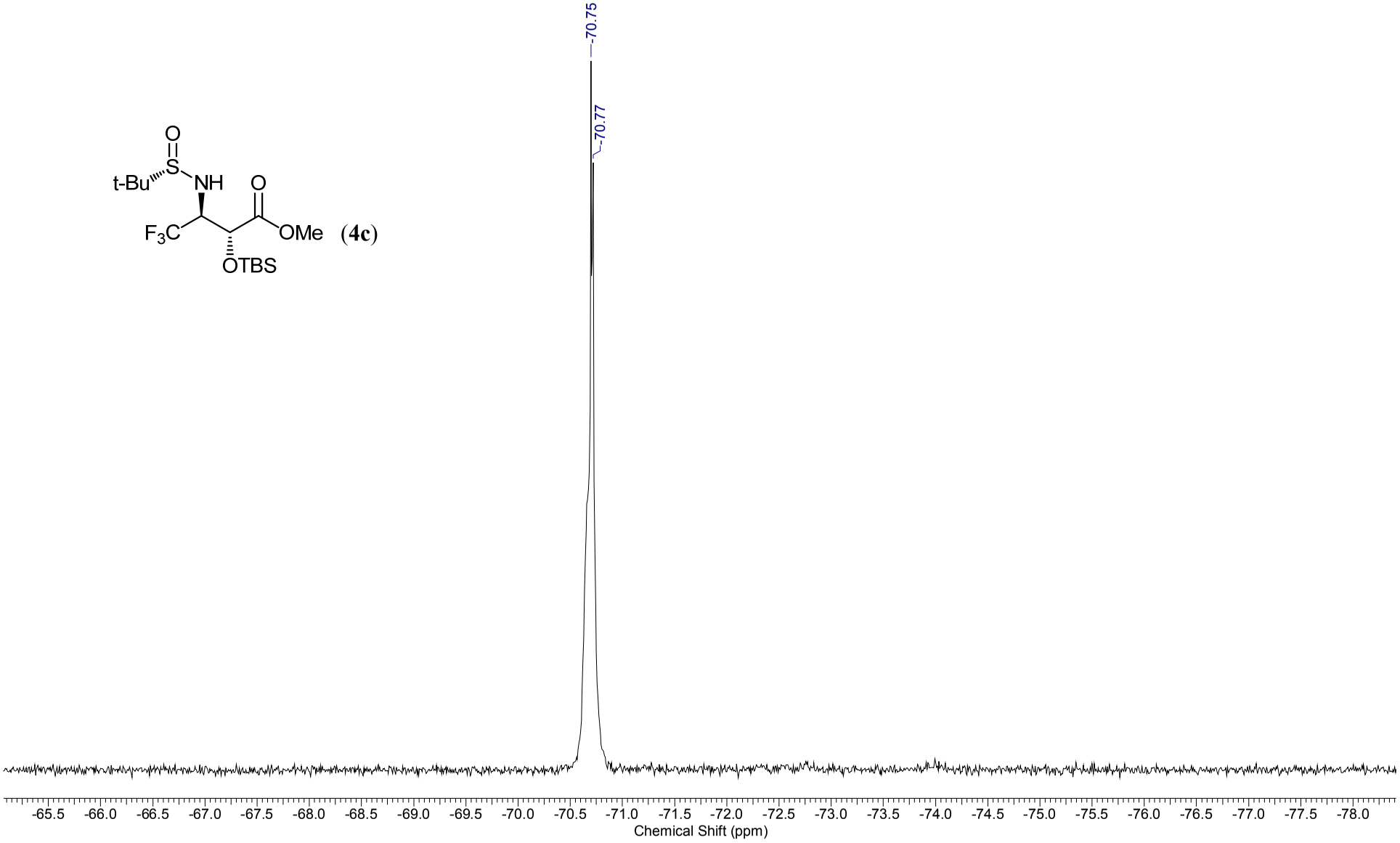
(4c)



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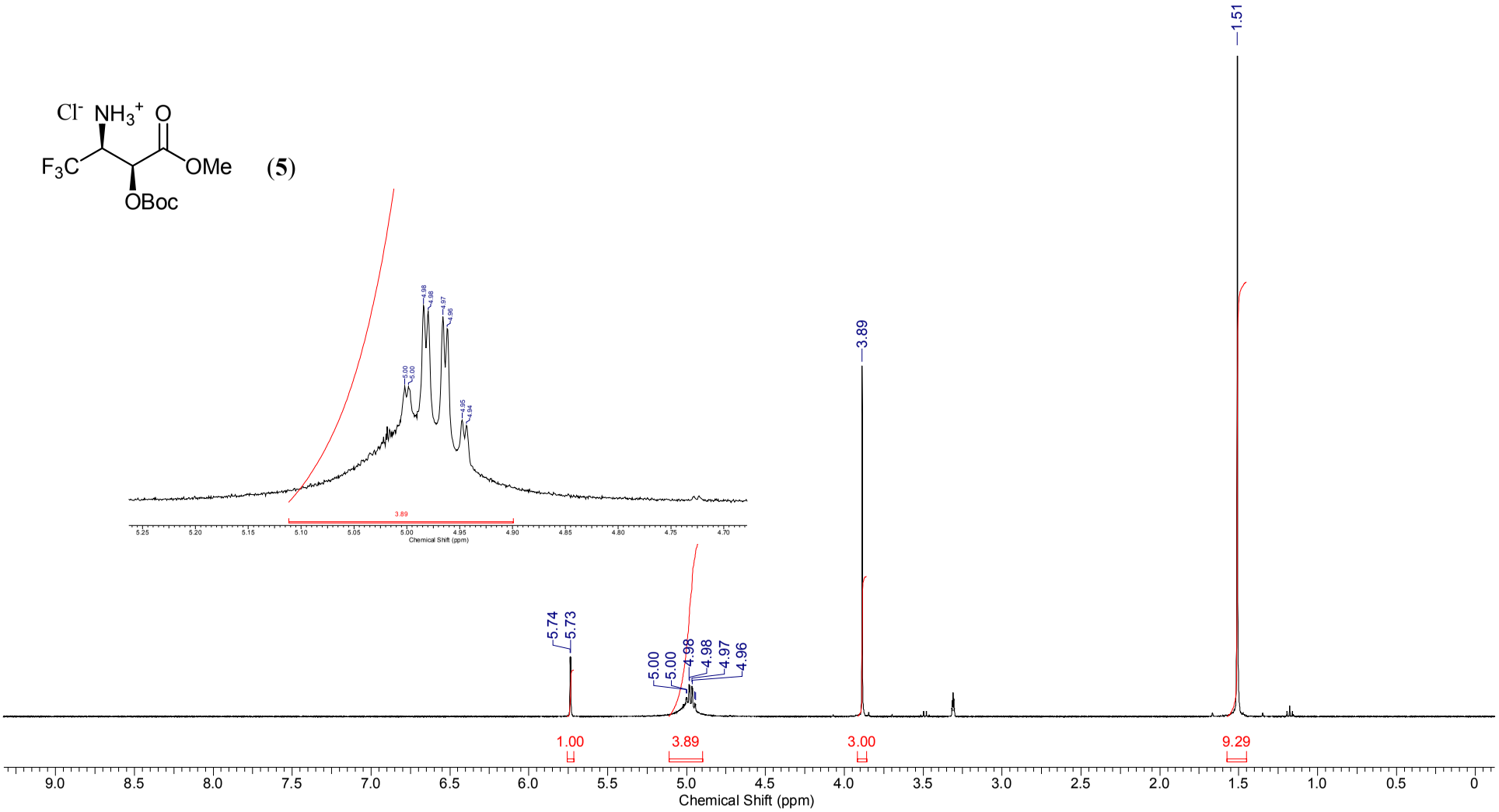

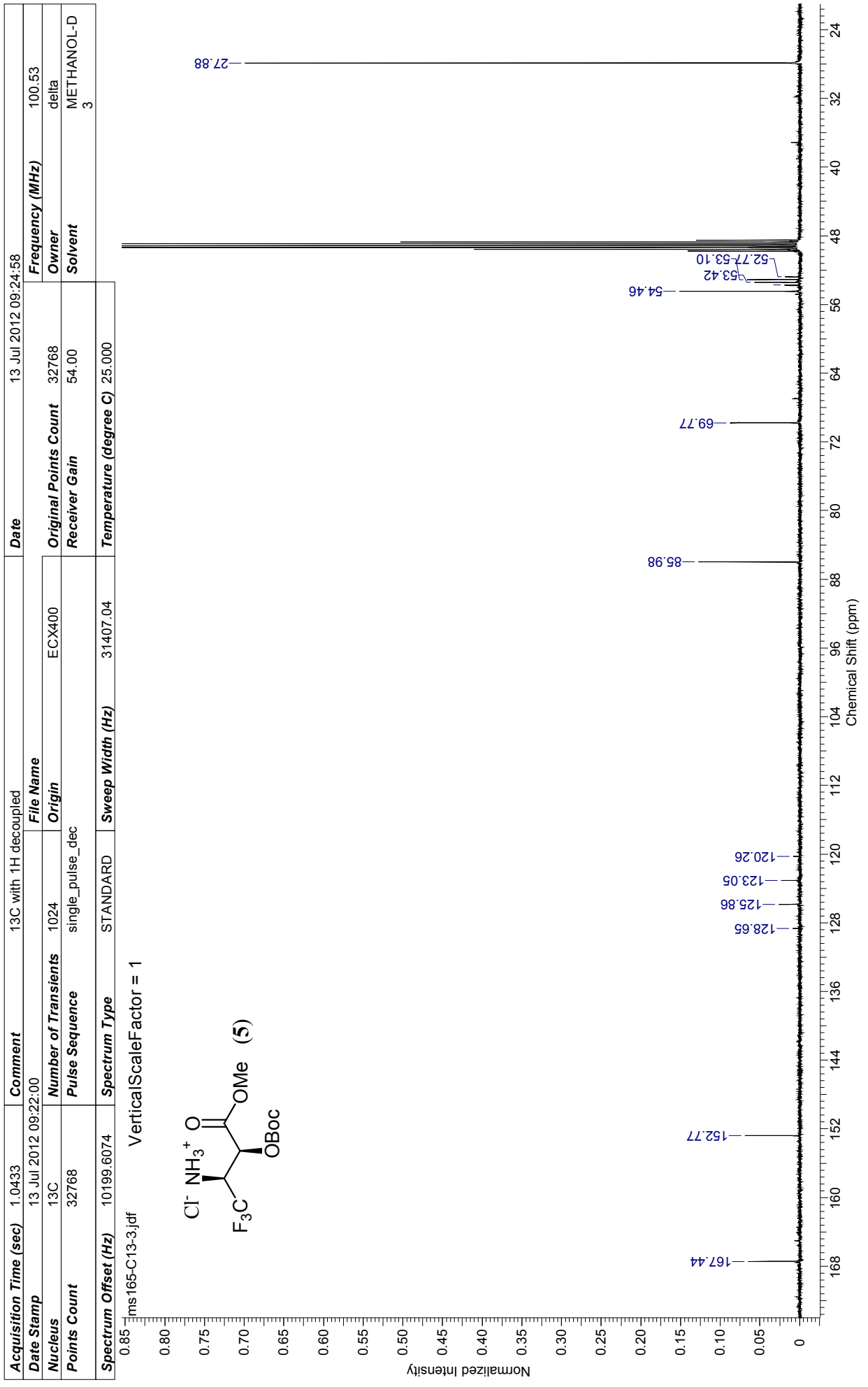

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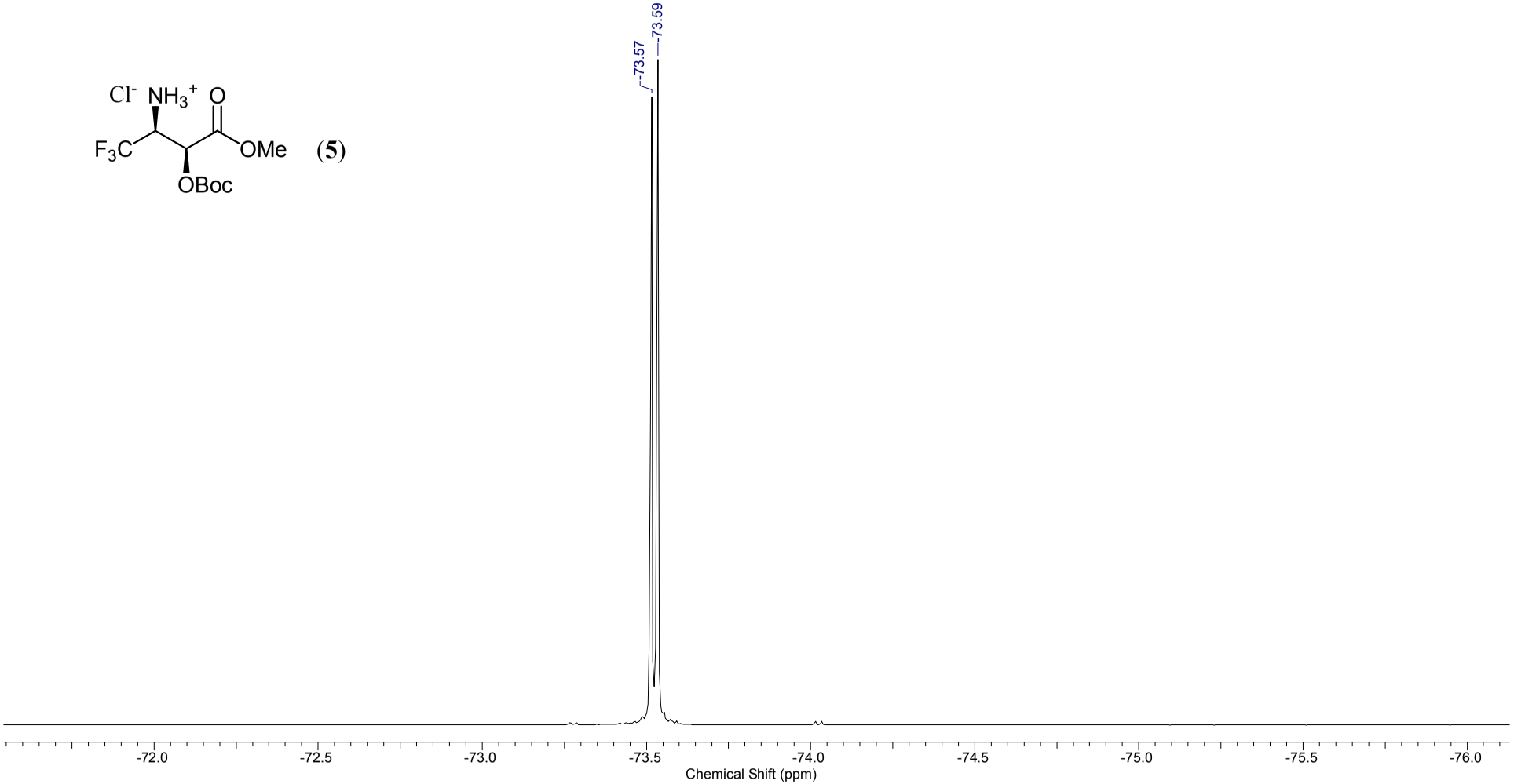
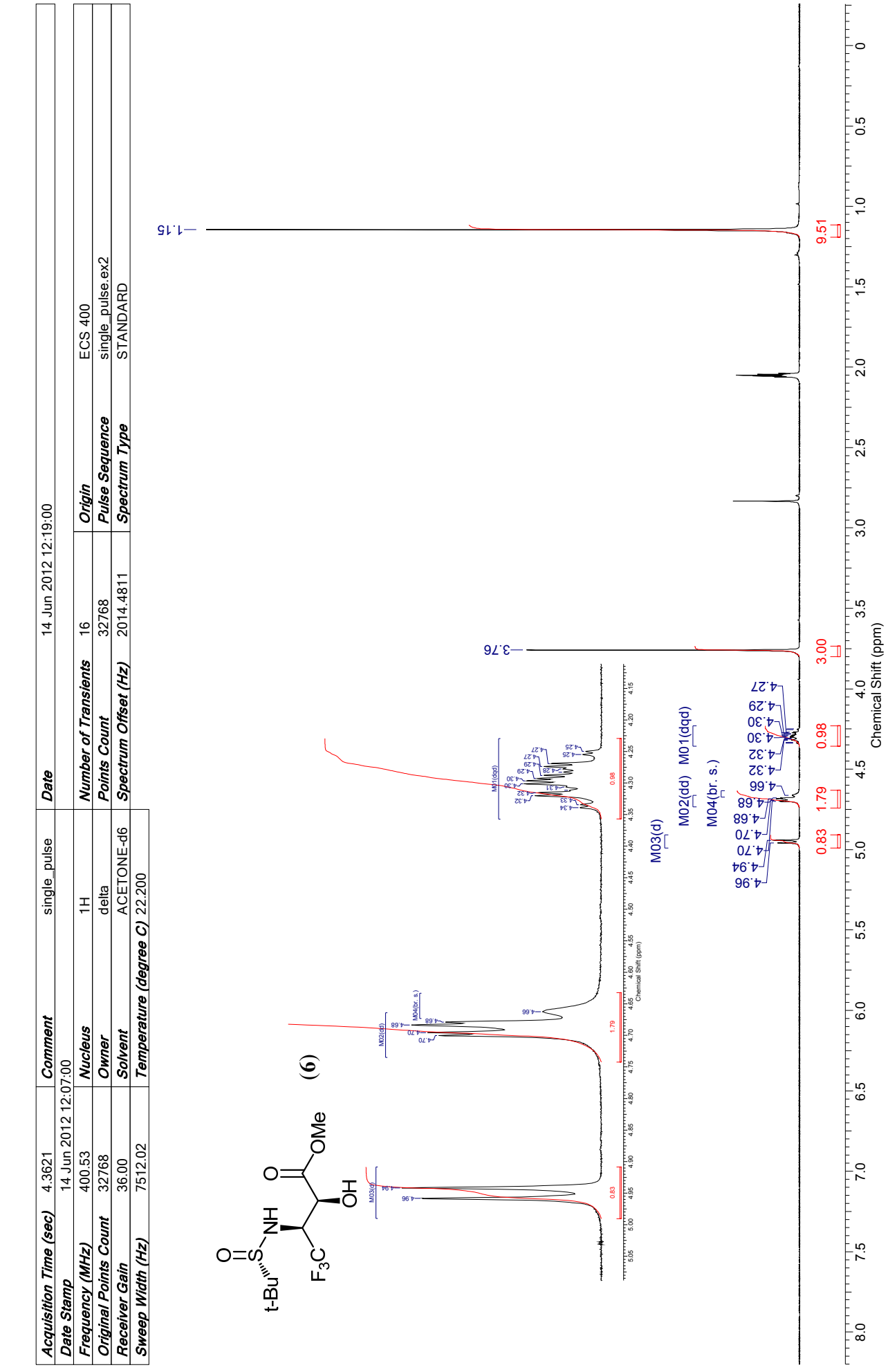
Original Points Count	131072	***Owner***	delta	***Points Count***	131072	***Pulse Sequence***	single_pulse.ex2
Receiver Gain	32.00	***Solvent***	METHANOL-D3			***Spectrum Offset (Hz)***	0.0000
Spectrum Type	STANDARD	***Sweep Width (Hz)***	189393.94	***Temperature (degree C)***	22.800		

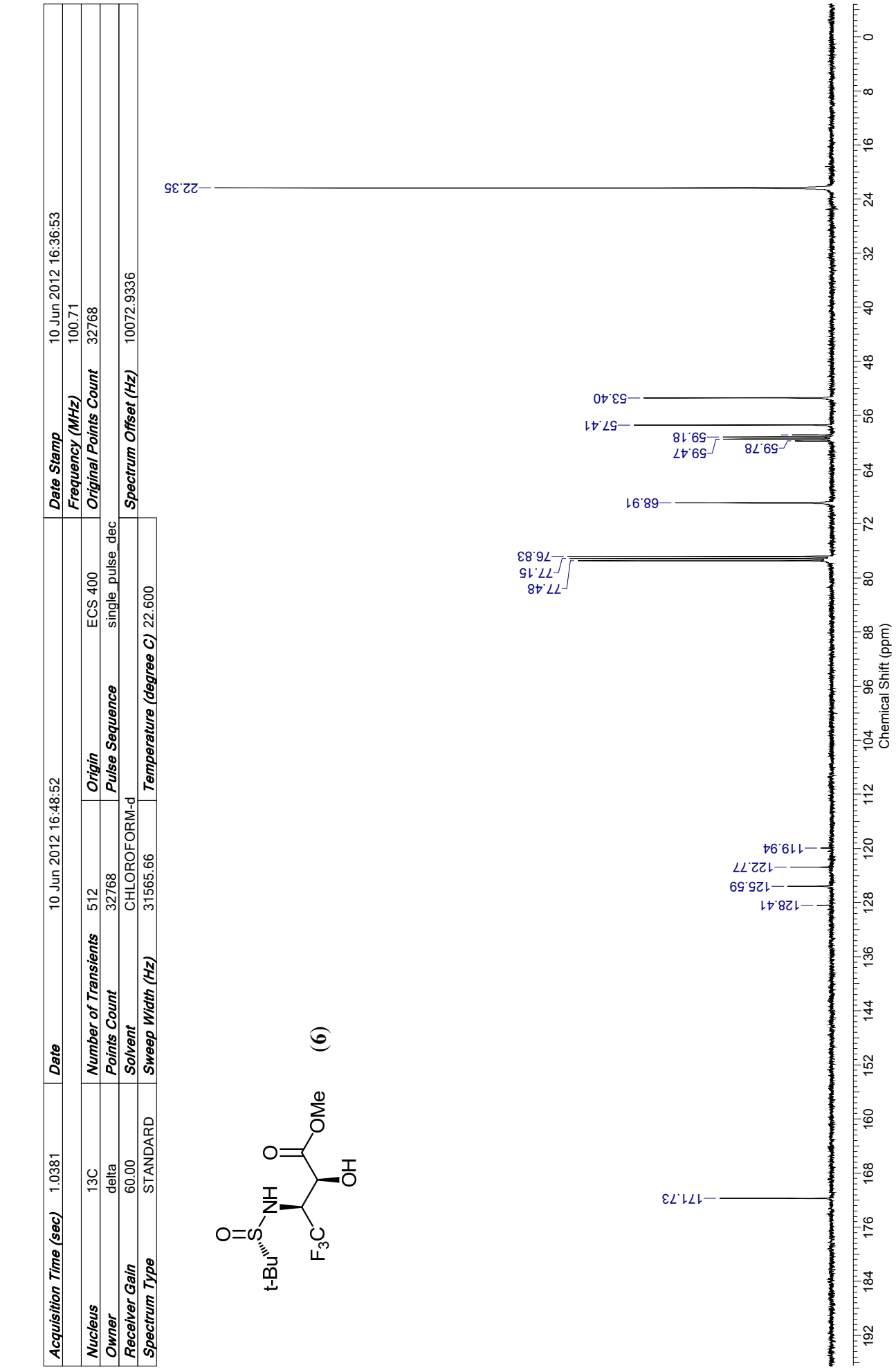
(**5**)



Acquisition Time (sec)	4.3621	***Comment***	single_pulse	***Date***	14 Jun 2012 12:19:00		
Date Stamp	14 Jun 2012 12:07:00						
Frequency (MHz)	400.53	***Nucleus***	1H	***Number of Transients***	16	***Origin***	ECS 400
Original Points Count	32768	***Owner***	delta	***Points Count***	32768	***Pulse Sequence***	single_pulse.ex2
Receiver Gain	36.00	***Solvent***	ACETONE-d6	***Spectrum Offset (Hz)***	2014.4811	***Spectrum Type***	STANDARD
Sweep Width (Hz)	7512.02	***Temperature (degree C)***	22.200				



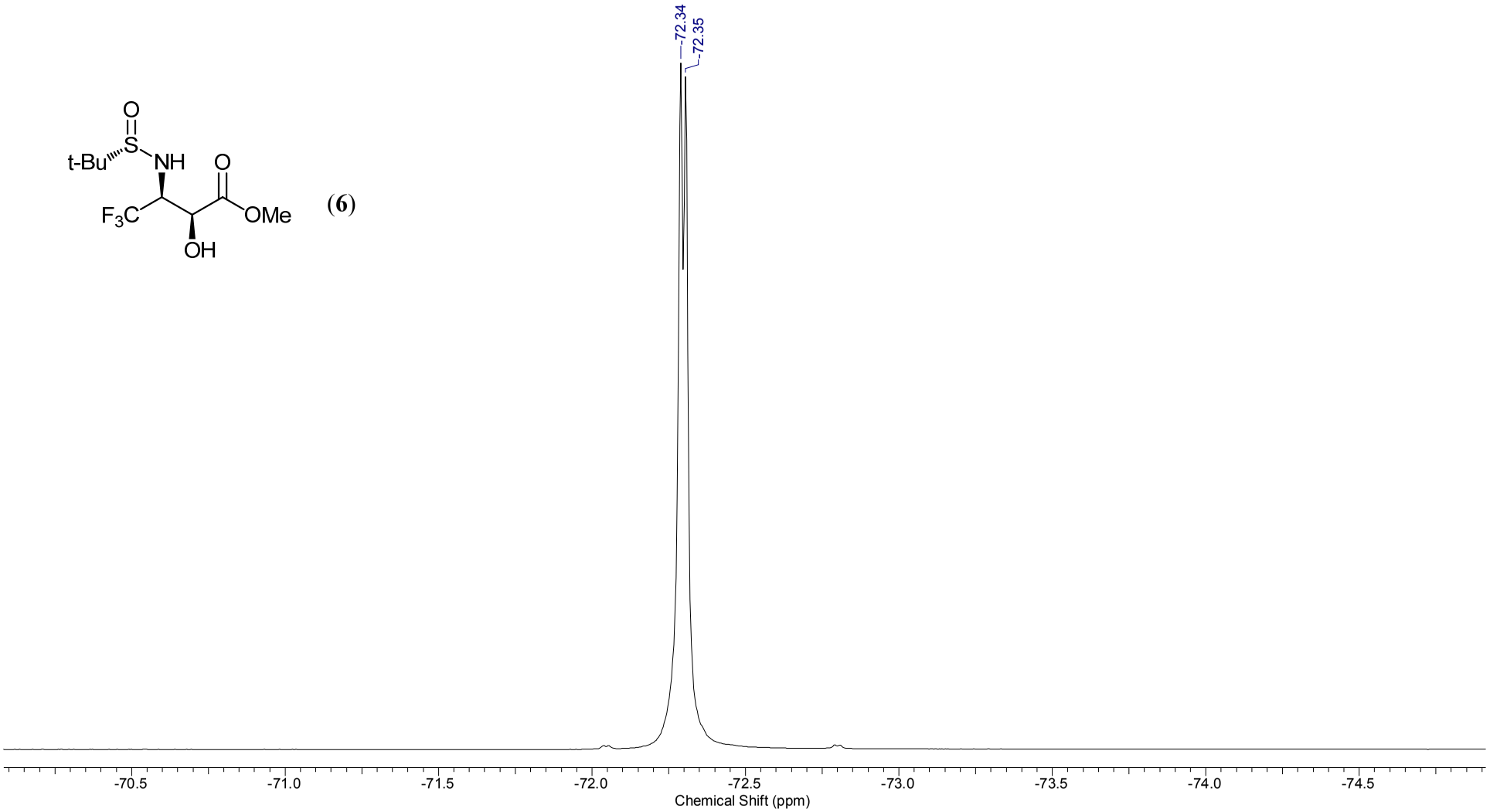
Acquisition Time (sec)	1.0381	***Date***	10 Jun 2012 16:48:52	***Date Stamp***	10 Jun 2012 16:36:53
				Frequency (MHz)	100.71
Nucleus	13C	***Number of Transients***	512	***Origin***	ECS 400
Owner	delta	***Points Count***	32768	***Pulse Sequence***	single_pulse_dec
Receiver Gain	60.00	***Solvent***	CHLOROFORM-d		
Spectrum Type	STANDARD	***Sweep Width (Hz)***	31565.66	***Temperature (degree C)***	22.600
				Original Points Count	32768
				Spectrum Offset (Hz)	10072.9336



(6)

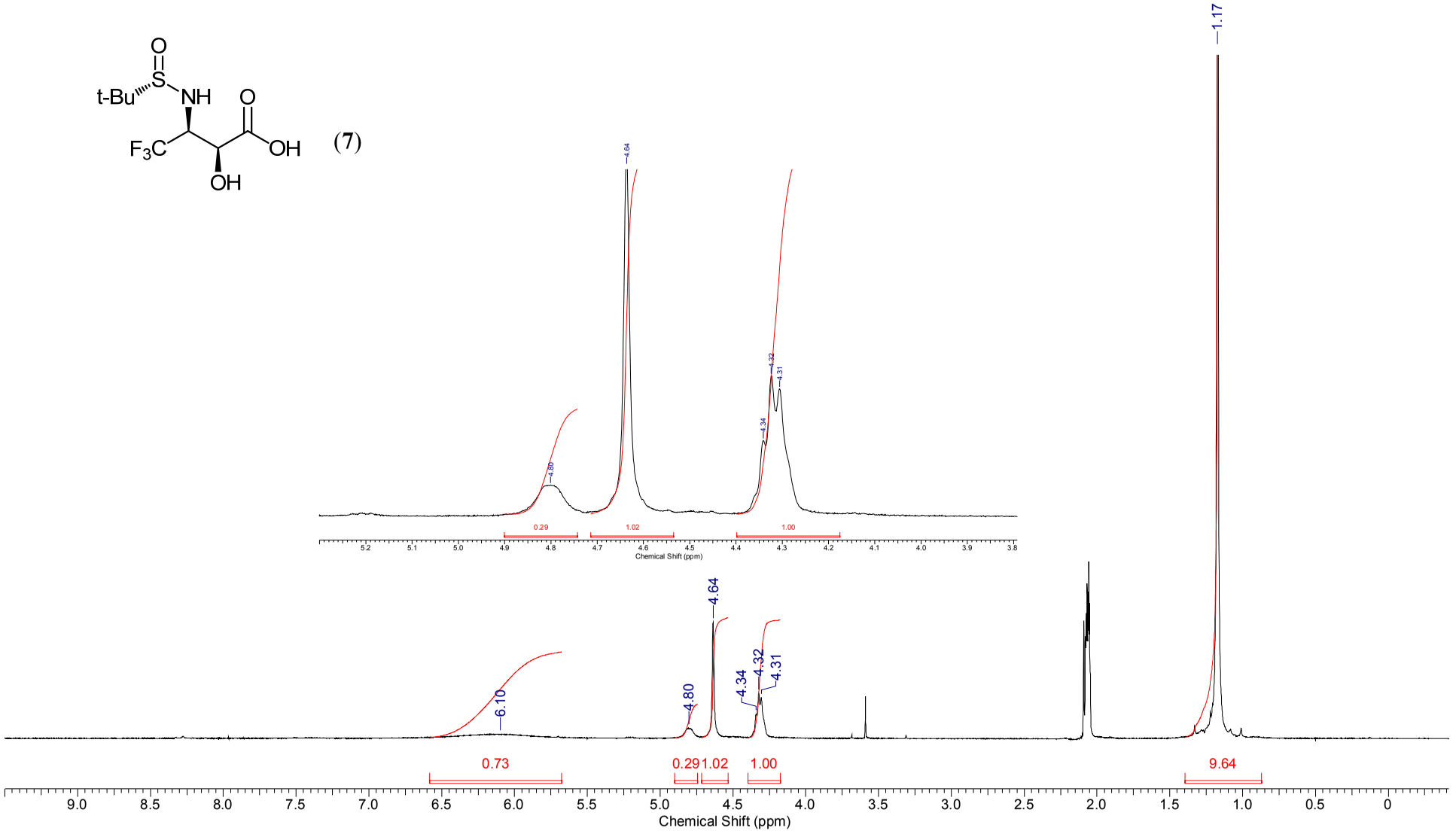
Acquisition Time (sec)	0.6921	***Comment***	single_pulse	***Date***	10 Jun 2012 16:52:20		
Date Stamp	10 Jun 2012 16:40:21			***File Name***			
Frequency (MHz)	376.88	***Nucleus***	19F	***Number of Transients***	16	***Origin***	ECS 400
Original Points Count	131072	***Owner***	delta	***Points Count***	131072	***Pulse Sequence***	single_pulse.ex2
Receiver Gain	28.00	***Solvent***	CHLOROFORM-d			***Spectrum Offset (Hz)***	0.0000
Spectrum Type	STANDARD	***Sweep Width (Hz)***	189393.94	***Temperature (degree C)***	22.100		

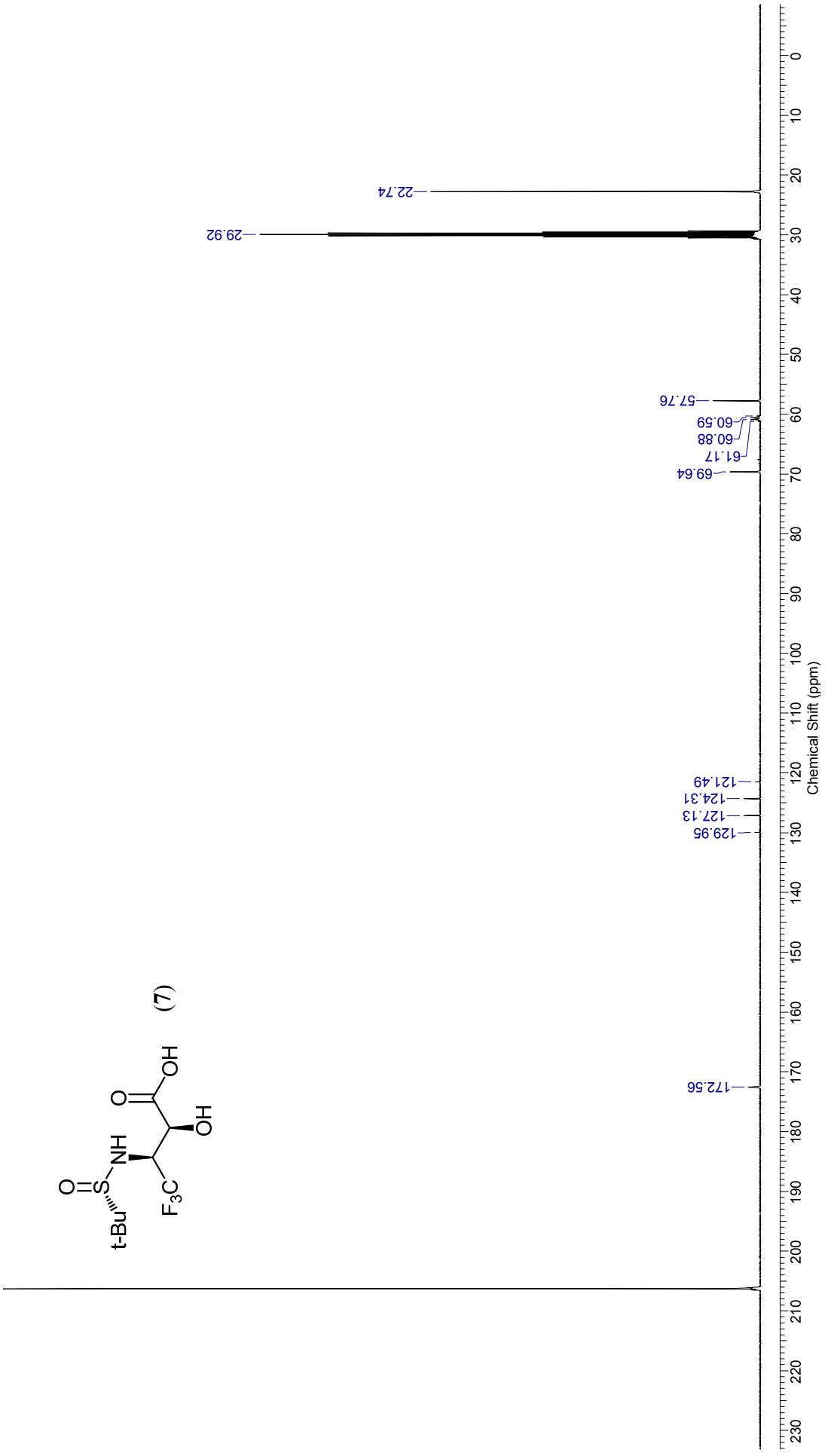
(6)



Acquisition Time (sec)	1.5000	***Comment***	Acetone	***Date***	Nov 29 2012	***Date Stamp***	Nov 29 2012		
File Name				***Frequency (MHz)***	400.08	***Nucleus***	1H	***Number of Transients***	8
Original Points Count	12000	***Points Count***	16384	***Pulse Sequence***	s2pul	***Receiver Gain***	18.00	***Solvent***	Acetone
Spectrum Offset (Hz)	3199.9270	***Spectrum Type***	STANDARD	***Sweep Width (Hz)***	8000.00	***Temperature (degree C)***	AMBIENT TEMPERATURE		

(7)

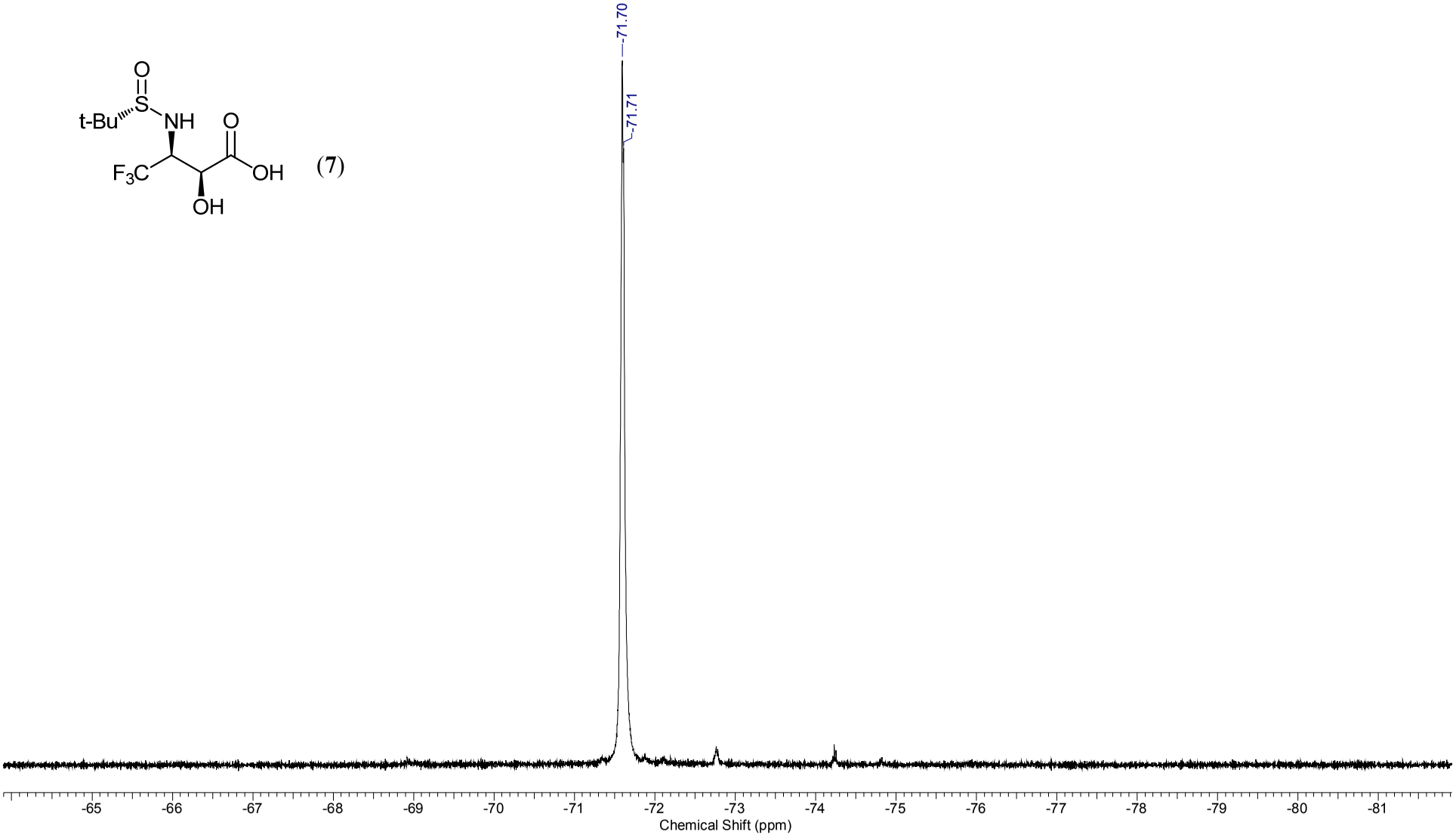




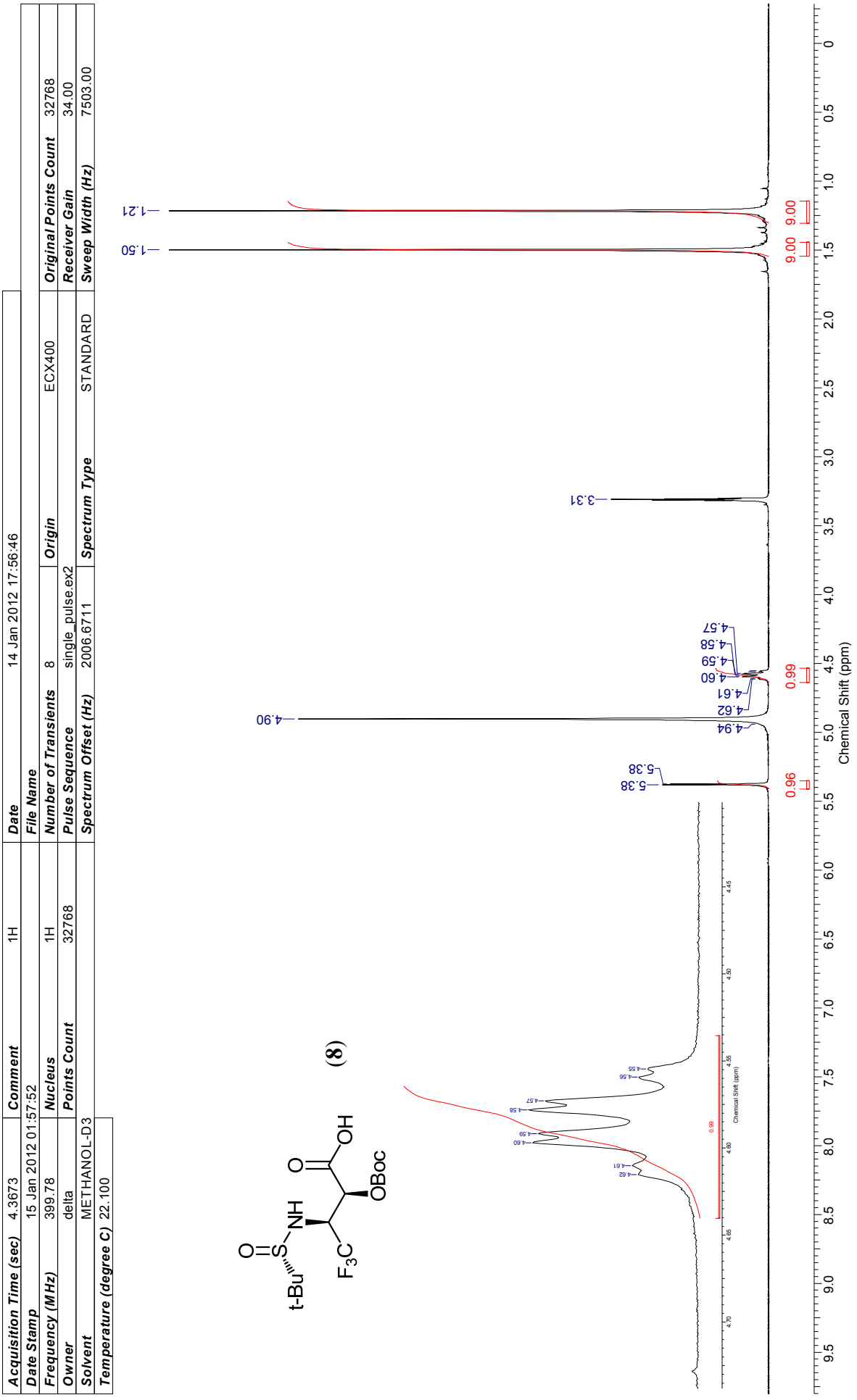
Acquisition Time (sec)	0.3864	***Date***	Dec 4 2012	***Date Stamp***	Dec 4 2012	***File Name***	
Frequency (MHz)	376.30	***Nucleus***	19F	***Number of Transients***	4	***Original Points Count***	32000
Pulse Sequence	s2pul	***Receiver Gain***	22.00	***Solvent***		***Spectrum Offset (Hz)***	-38745.2578
Sweep Width (Hz)	82815.73	***Temperature (degree C)***	AMBIENT TEMPERATURE				

Points Count	1048576		
Spectrum Type	STANDARD		

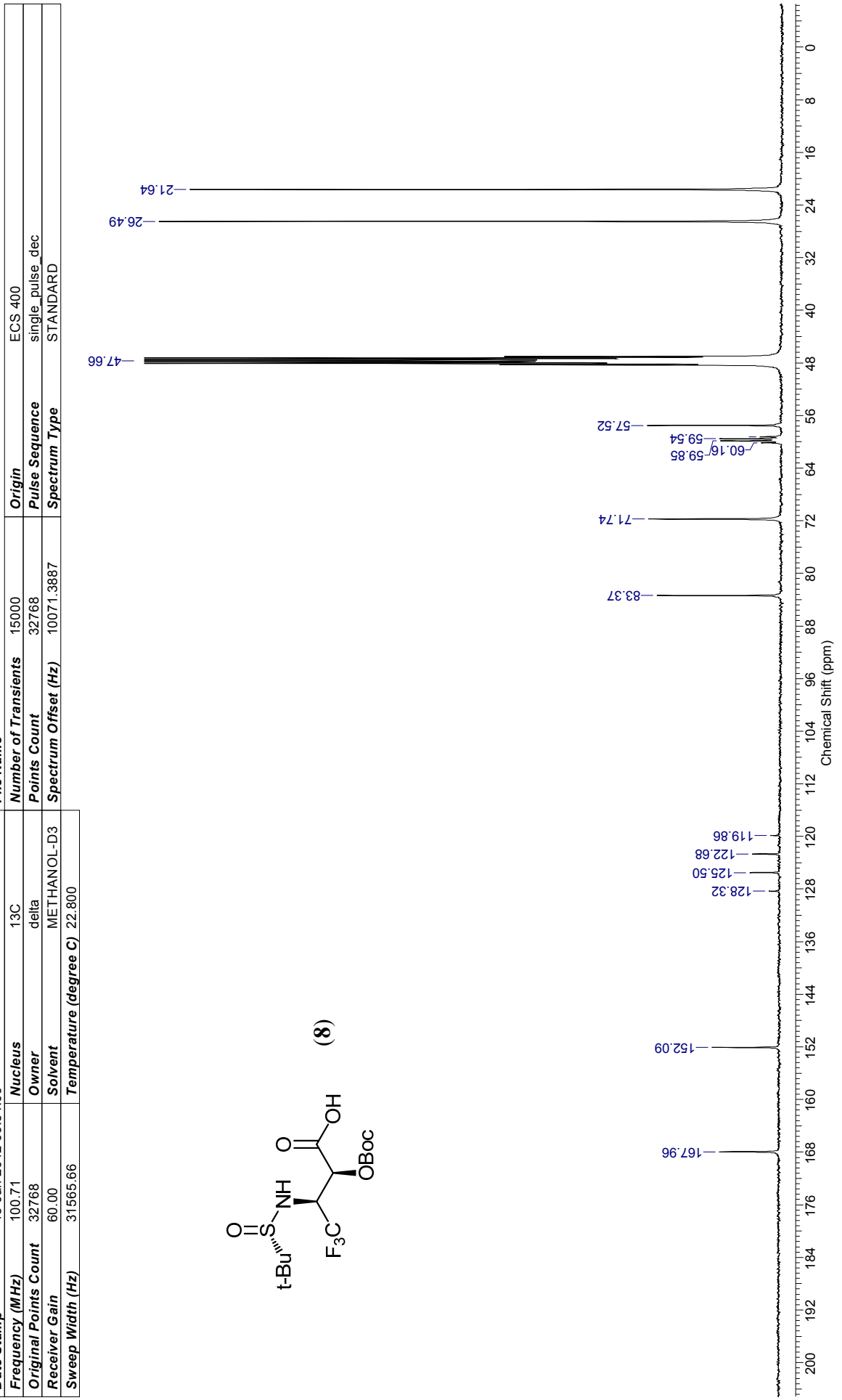
(7)



Acquisition Time (sec)	4.3673	***Comment***	1H	***Date***	14 Jan 2012 17:56:46		
Date Stamp	15 Jan 2012 01:57:52			***File Name***			
Frequency (MHz)	399.78	***Nucleus***	1H	***Number of Transients***	8	***Origin***	ECX400	***Original Points Count***	32768
Owner	delta	***Points Count***	32768	***Pulse Sequence***	single_pulse.ex2			***Receiver Gain***	34.00
Solvent	METHANOL-D3			***Spectrum Offset (Hz)***	2006.6711	***Spectrum Type***	STANDARD	***Sweep Width (Hz)***	7503.00
Temperature (degree C)	22.100								



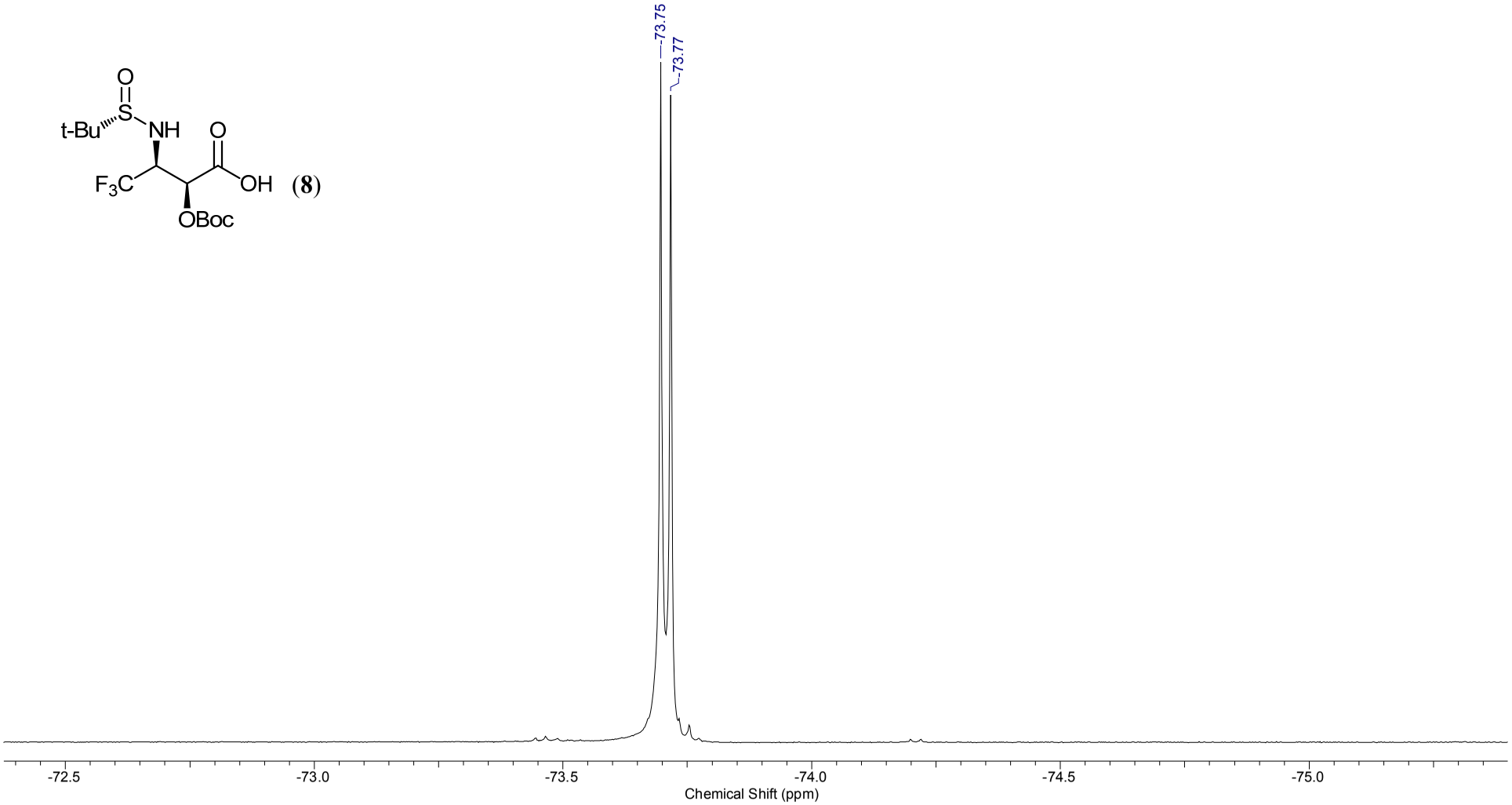
Acquisition Time (sec)	1.0381	Comment	single pulse decoupled gated NOE	Date	15 Jan 2012 09:41:28
Date Stamp	15 Jan 2012 09:34:09	File Name			
Frequency (MHz)	100.71	Nucleus	13C	Number of Transients	15000	Origin	ECS 400
Original Points Count	32768	Owner	delta	Points Count	32768	Pulse Sequence	single_pulse_dec
Receiver Gain	60.00	Solvent	METHANOL-D3	Spectrum Offset (Hz)	10071.3887	Spectrum Type	STANDARD
Sweep Width (Hz)	31565.66	Temperature (degree C)	22.800				



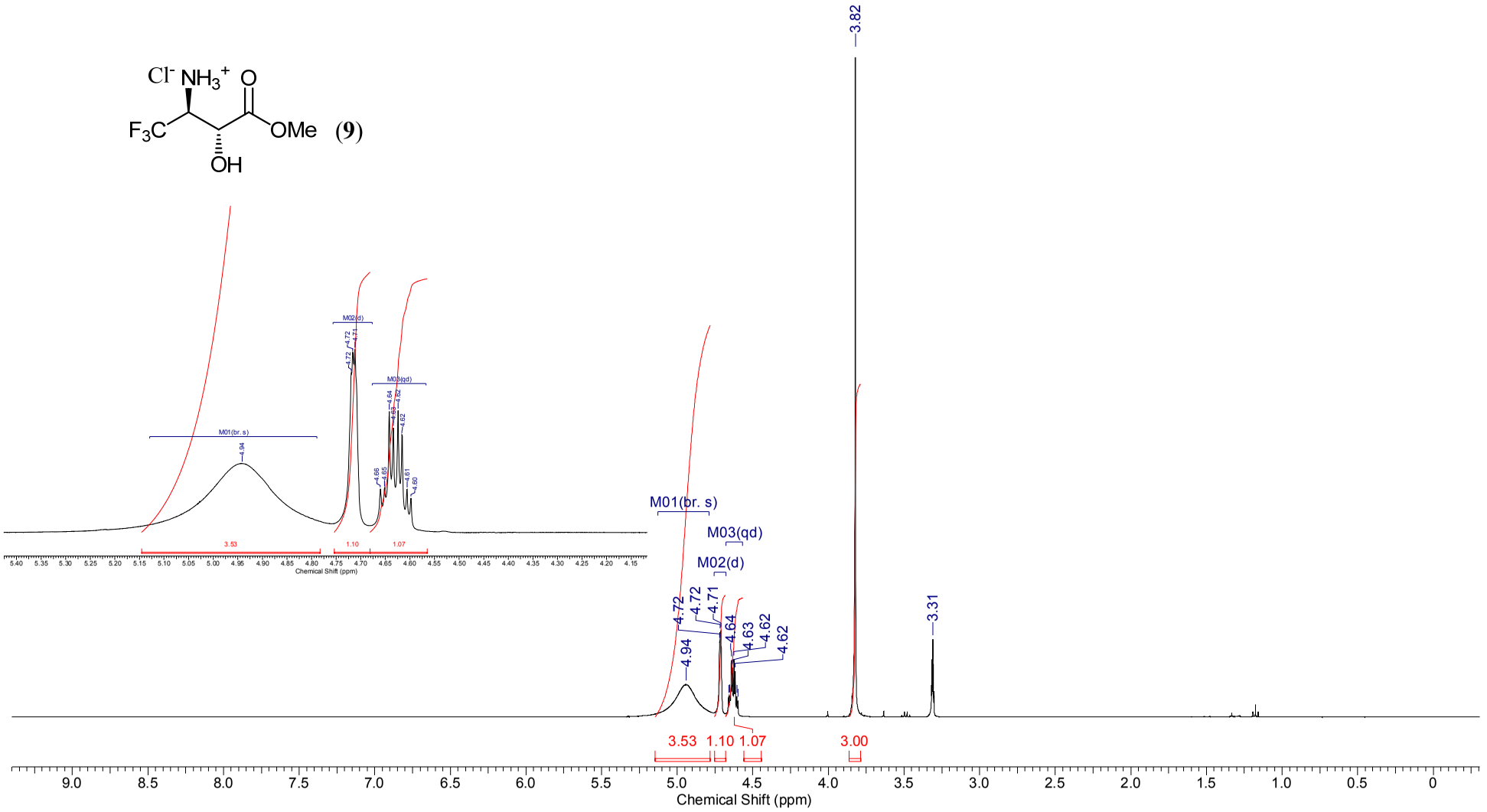
(8)

Acquisition Time (sec)	1.3841	***Comment***	19F	***Date***	14 Jan 2012 17:54:21				
Date Stamp	15 Jan 2012 01:55:27			***File Name***					
Frequency (MHz)	376.17	***Nucleus***	19F	***Number of Transients***	16	***Origin***	ECX400	***Original Points Count***	262144
Owner	delta	***Points Count***	262144	***Pulse Sequence***	single_pulse.ex2			***Receiver Gain***	30.00
Solvent	METHANOL-D3			***Spectrum Offset (Hz)***	0.0000	***Spectrum Type***	STANDARD	***Sweep Width (Hz)***	189393.95
Temperature (degree C)	22.100								

(8)

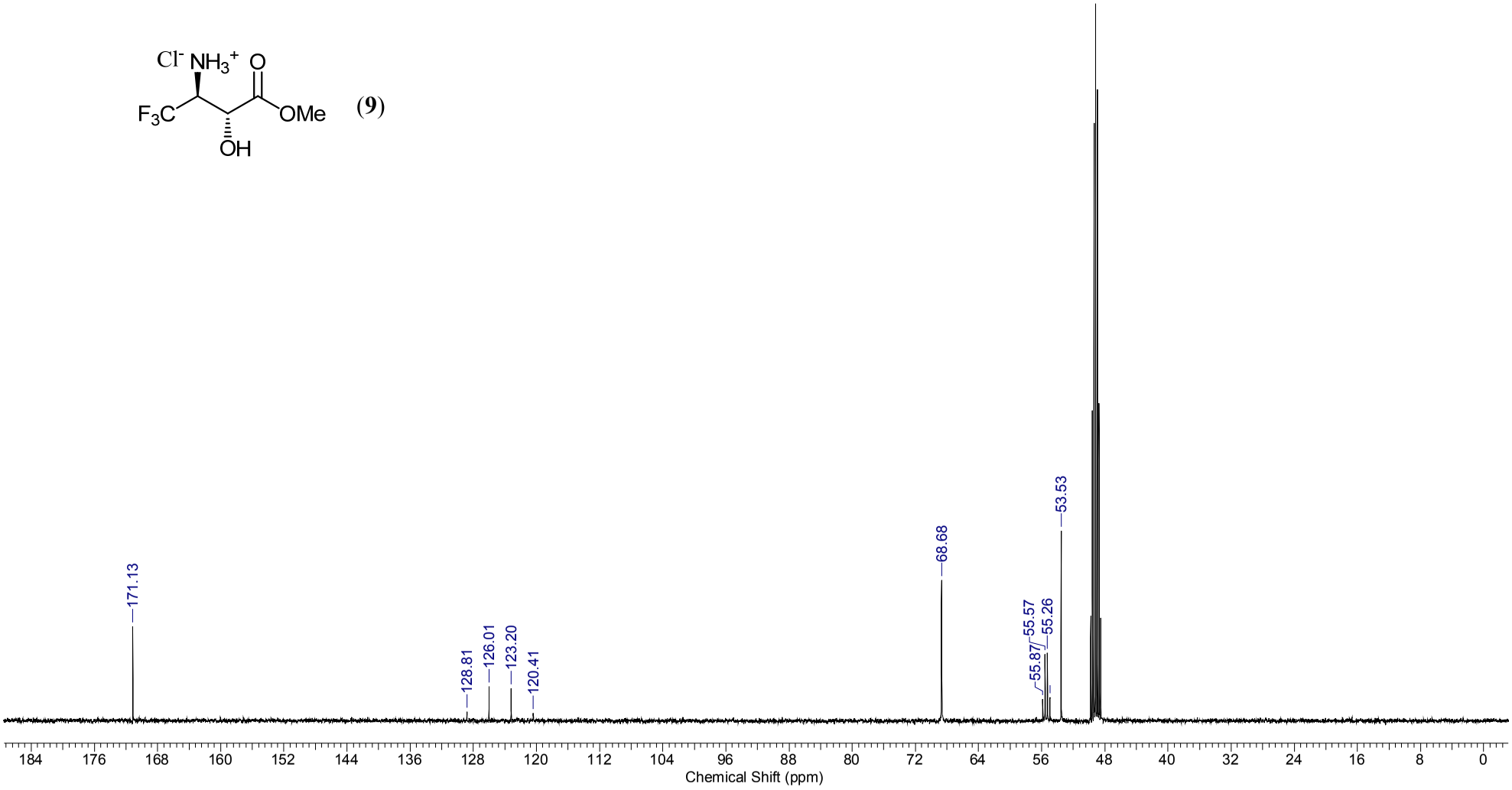


Acquisition Time (sec)	4.3621	***Comment***	single_pulse	***Date***	14 Jun 2012 09:16:32		
Date Stamp	14 Jun 2012 09:04:32			***File Name***			
Frequency (MHz)	400.53	***Nucleus***	1H	***Number of Transients***	16	***Origin***	ECS 400
Original Points Count	32768	***Owner***	delta	***Points Count***	32768	***Pulse Sequence***	single_pulse.ex2
Receiver Gain	30.00	***Solvent***	METHANOL-D3			***Spectrum Offset (Hz)***	2013.6431
Spectrum Type	STANDARD	***Sweep Width (Hz)***	7512.02	***Temperature (degree C)***	22.400		



Acquisition Time (sec)	1.0381	***Comment***	single pulse decoupled gated NOE			***Date***	14 Jun 2012 09:38:15
Date Stamp	14 Jun 2012 09:26:15						
Frequency (MHz)	100.71	***Nucleus***	13C	***Number of Transients***	512	***Origin***	ECS 400
Original Points Count	32768	***Owner***	delta	***Points Count***	32768	***Pulse Sequence***	single_pulse_dec
Receiver Gain	60.00	***Solvent***	METHANOL-D3	***Spectrum Offset (Hz)***	10219.0586	***Spectrum Type***	STANDARD
Sweep Width (Hz)	31565.66	***Temperature (degree C)***	23.100				

(9)



Acquisition Time (sec)	0.6921	***Comment***	single_pulse	***Date***	14 Jun 2012 09:40:47		
Date Stamp	14 Jun 2012 09:28:47			***File Name***			
Frequency (MHz)	376.88	***Nucleus***	19F	***Number of Transients***	16	***Origin***	ECS 400
Original Points Count	131072	***Owner***	delta	***Points Count***	131072	***Pulse Sequence***	single_pulse.ex2
Receiver Gain	28.00	***Solvent***	METHANOL-D3			***Spectrum Offset (Hz)***	0.0000
Spectrum Type	STANDARD	***Sweep Width (Hz)***	189393.94	***Temperature (degree C)***	22.600		

(**9**)