

Sustainable synthesis of enantiopure fluorolactam derivatives by a selective direct fluorination - amidase strategy

Nicky J. Willis,^a Craig A. Fisher,^b Catherine M. Alder,^a Antal Harsanyi,^b Lena Shukla^{*a} Joseph P. Adams,^a and Graham Sandford^{*b}

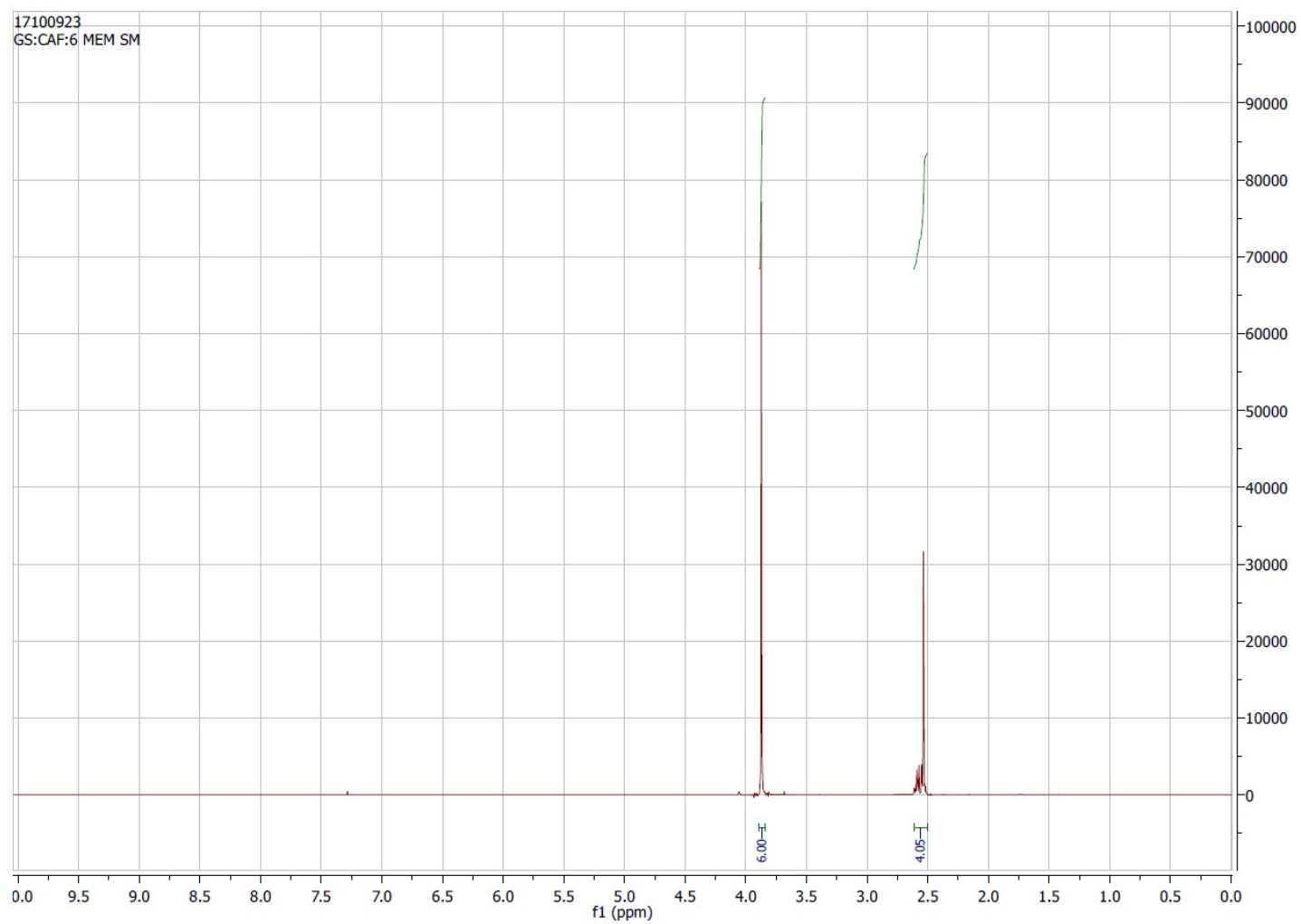
SUPPORTING INFORMATION 5

NMR Spectra

SI-5.1	Dimethyl 2-(2-cyanoethyl)-2-fluoromalonate 4b	2
SI-5.2	Dimethyl 2-(3-aminopropyl)-2-fluoromalonate, hydrochloride salt 4c	5
SI-5.3	Methyl 3-fluoro-2-oxo-3-piperidine carboxylate 4d	8
SI-5.4	3-Fluoro-2-oxopiperidine-3-carboxylic acid 5	11
SI-5.5	(S)-Methyl 3-fluoro-2-oxo-3-piperidine carboxylate 2b	14

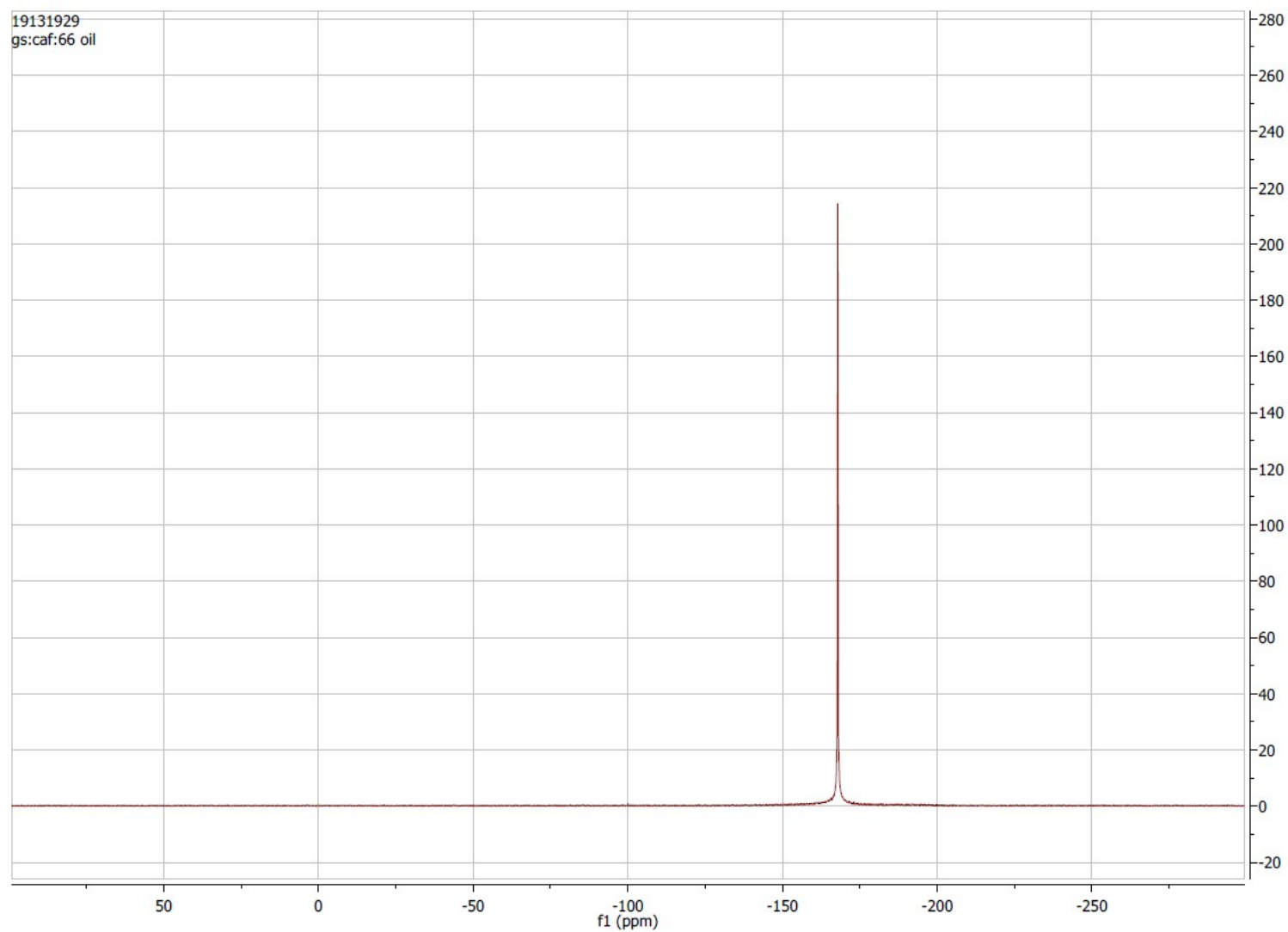
SI-5.1 Dimethyl 2-(2-cyanoethyl)-2-fluoromalonate **4b**

^1H NMR spectrum



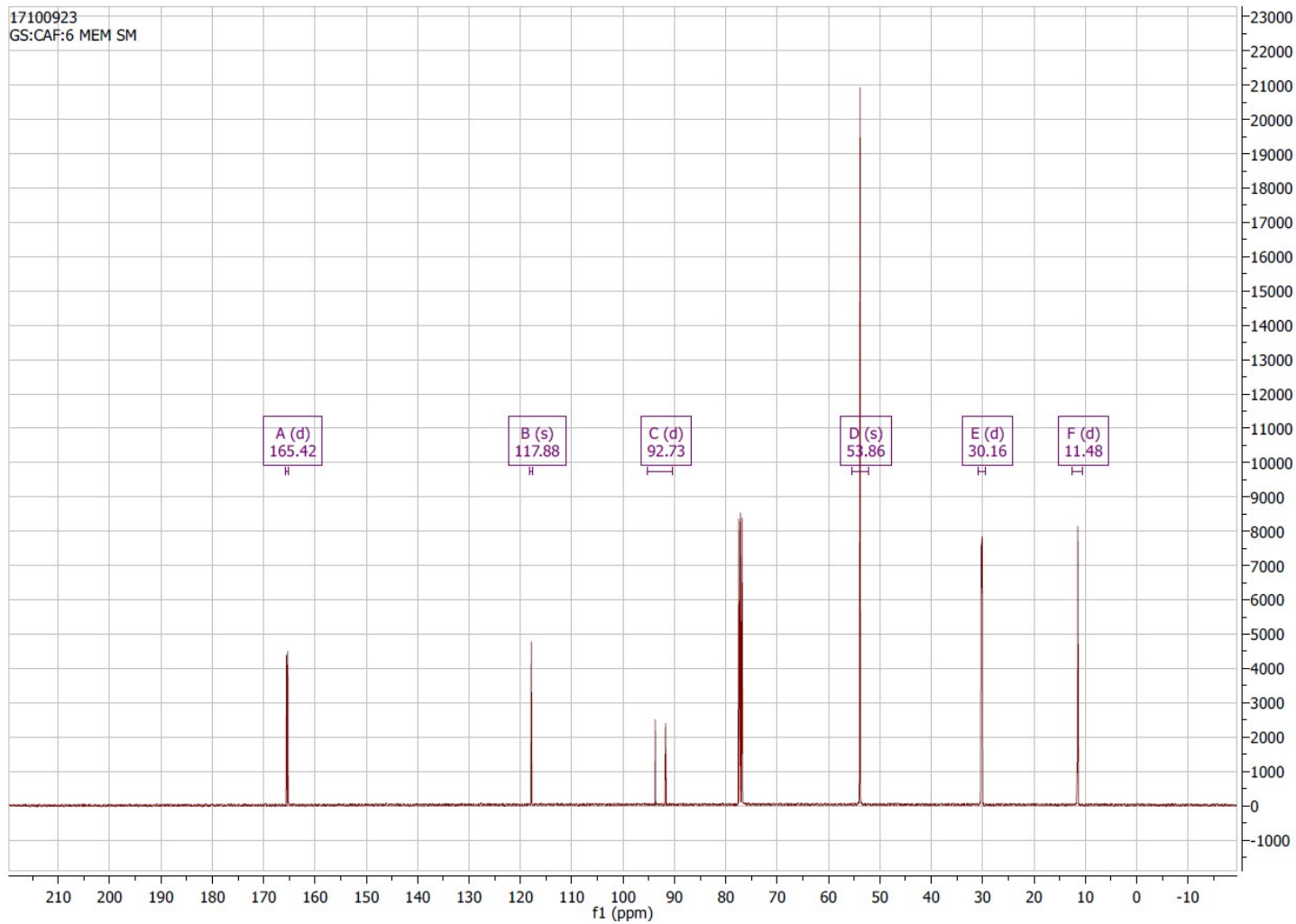
Dimethyl 2-(2-cyanoethyl)-2-fluoromalonate **4b**

^{19}F NMR spectrum



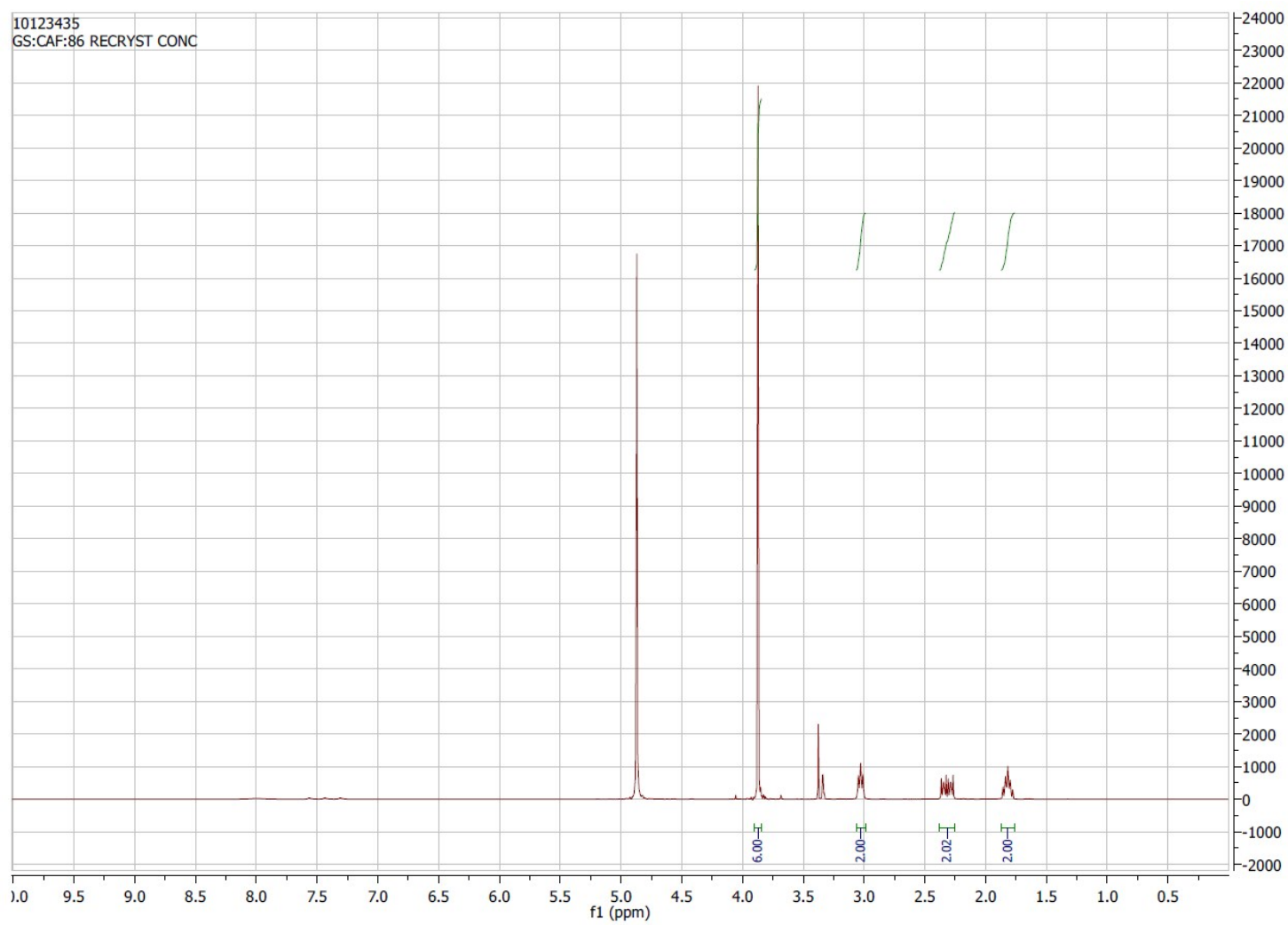
Dimethyl 2-(2-cyanoethyl)-2-fluoromalonate **4b**

^{13}C NMR spectrum



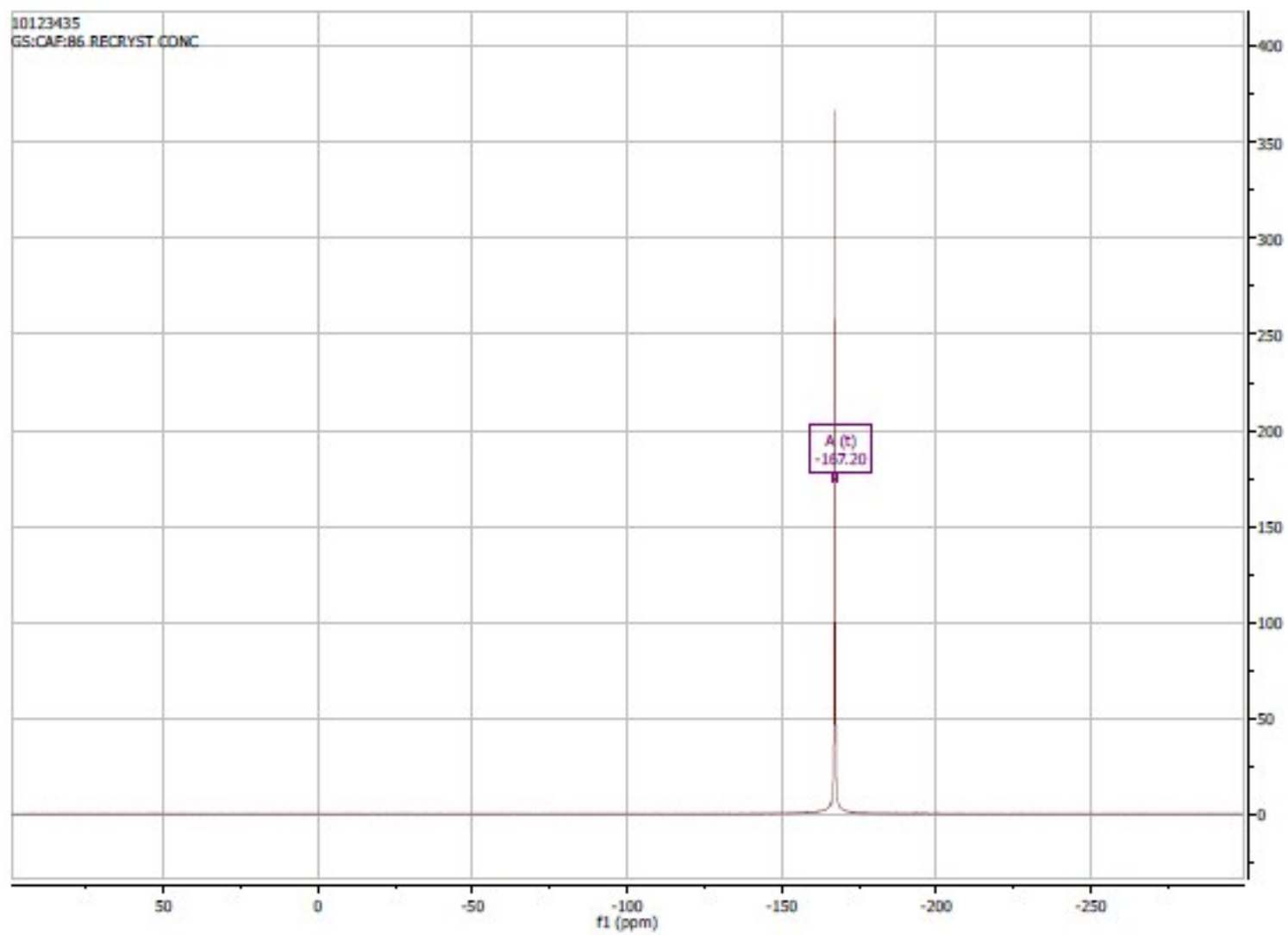
SI-5.2 Dimethyl 2-(3-aminopropyl)-2-fluoromalonate, hydrochloride salt **4c**

^1H NMR spectrum



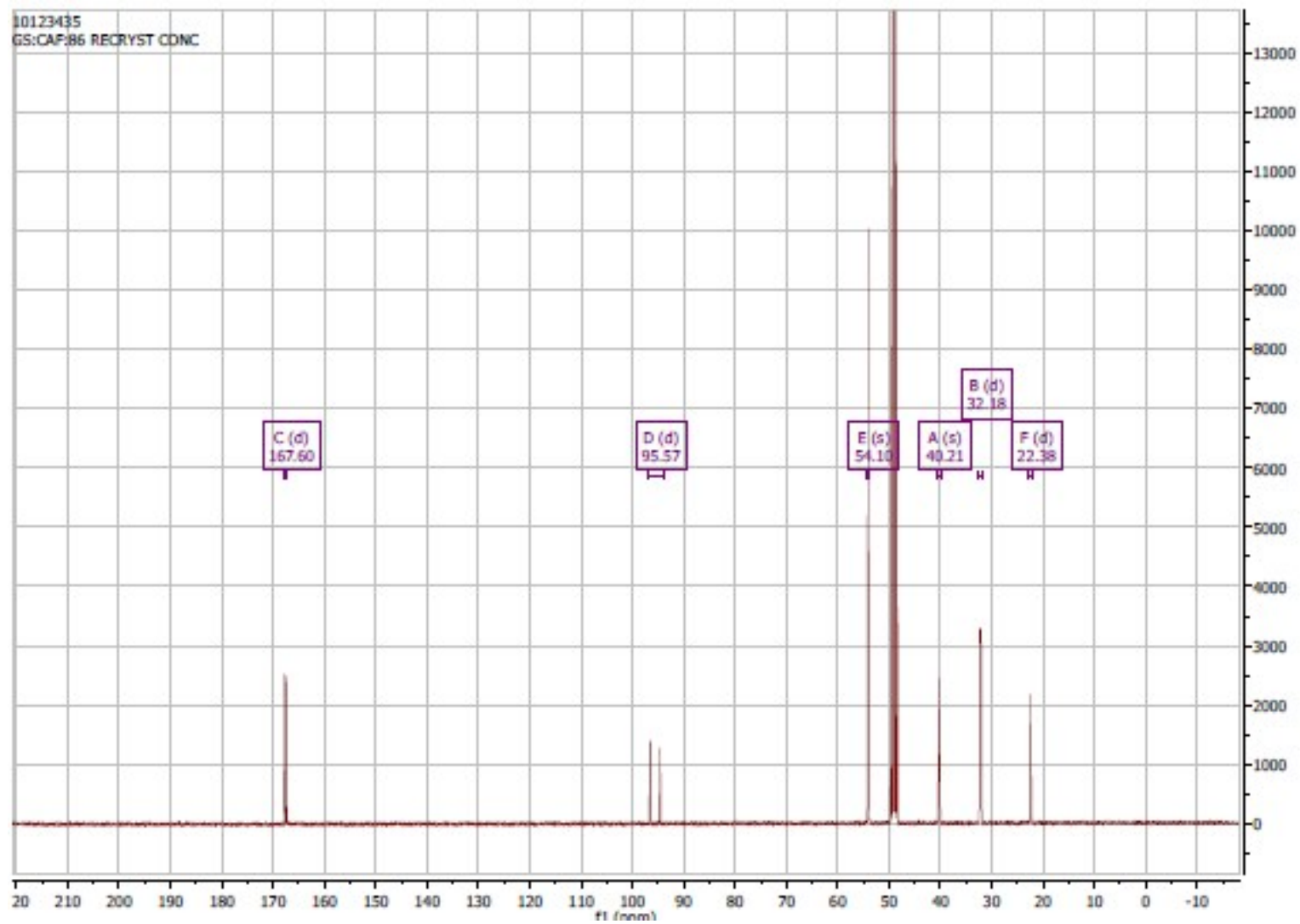
Dimethyl 2-(3-aminopropyl)-2-fluoromalonate, hydrochloride salt **4c**

^{19}F NMR spectrum



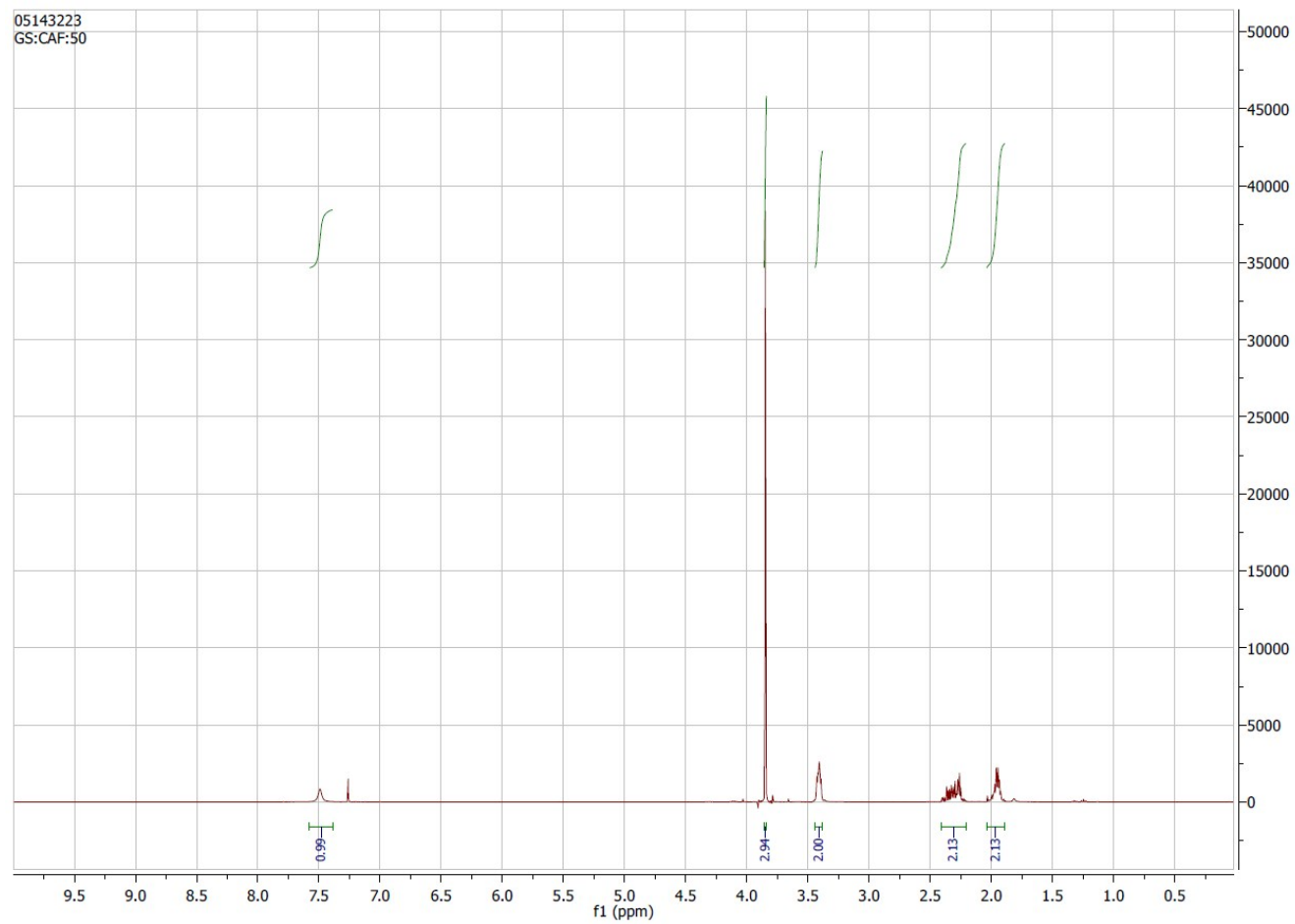
Dimethyl 2-(3-aminopropyl)-2-fluoromalonate, hydrochloride salt **4c**

^{13}C NMR spectrum



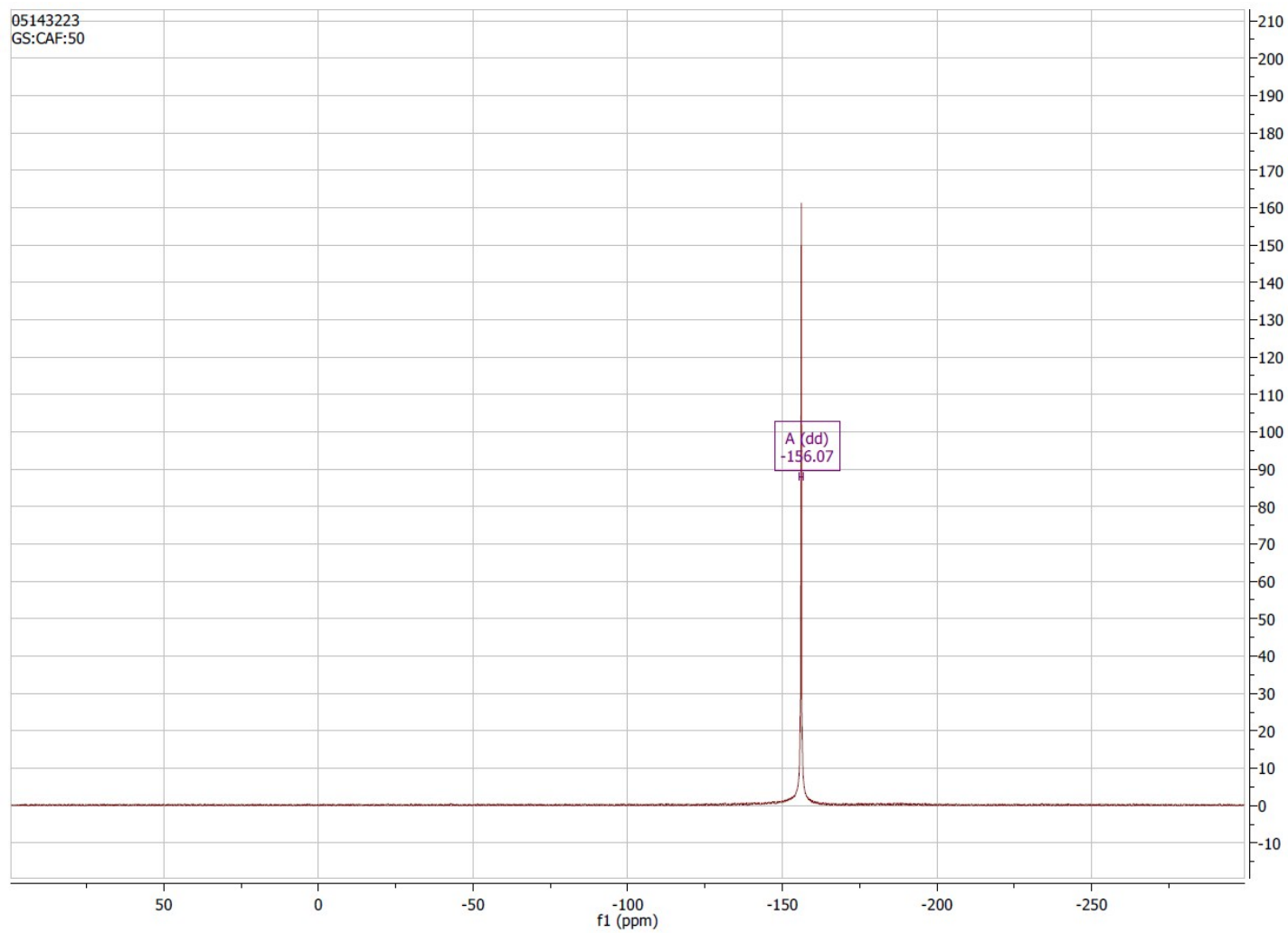
SI-5.3 Methyl 3-fluoro-2-oxo-3-piperidinecarboxylate **4d**

^1H NMR spectrum



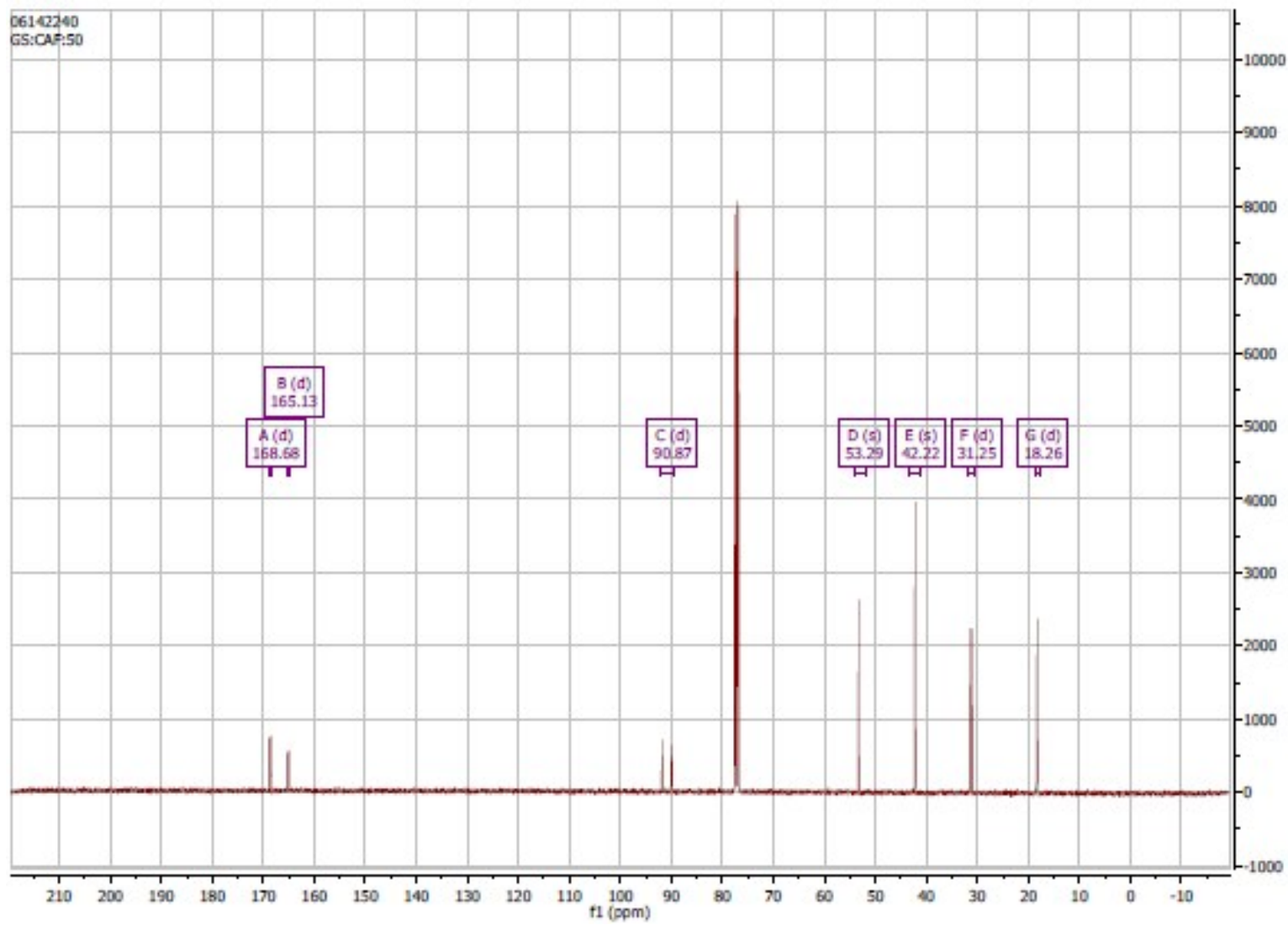
Methyl 3-fluoro-2-oxo-3-piperidinecarboxylate **4d**

^{19}F NMR spectrum



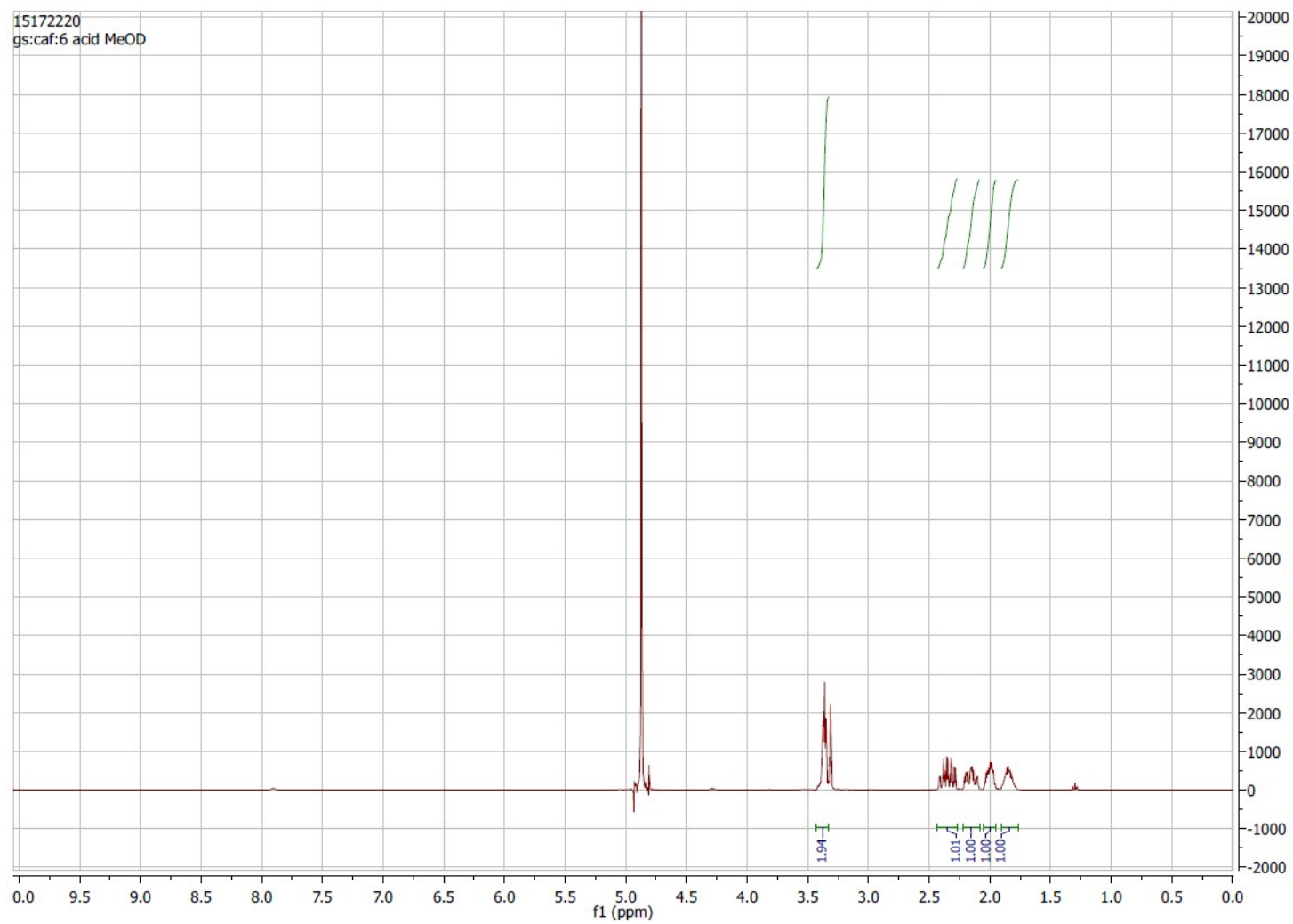
Methyl 3-fluoro-2-oxo-3-piperidinecarboxylate **4d**

^{13}C NMR spectrum



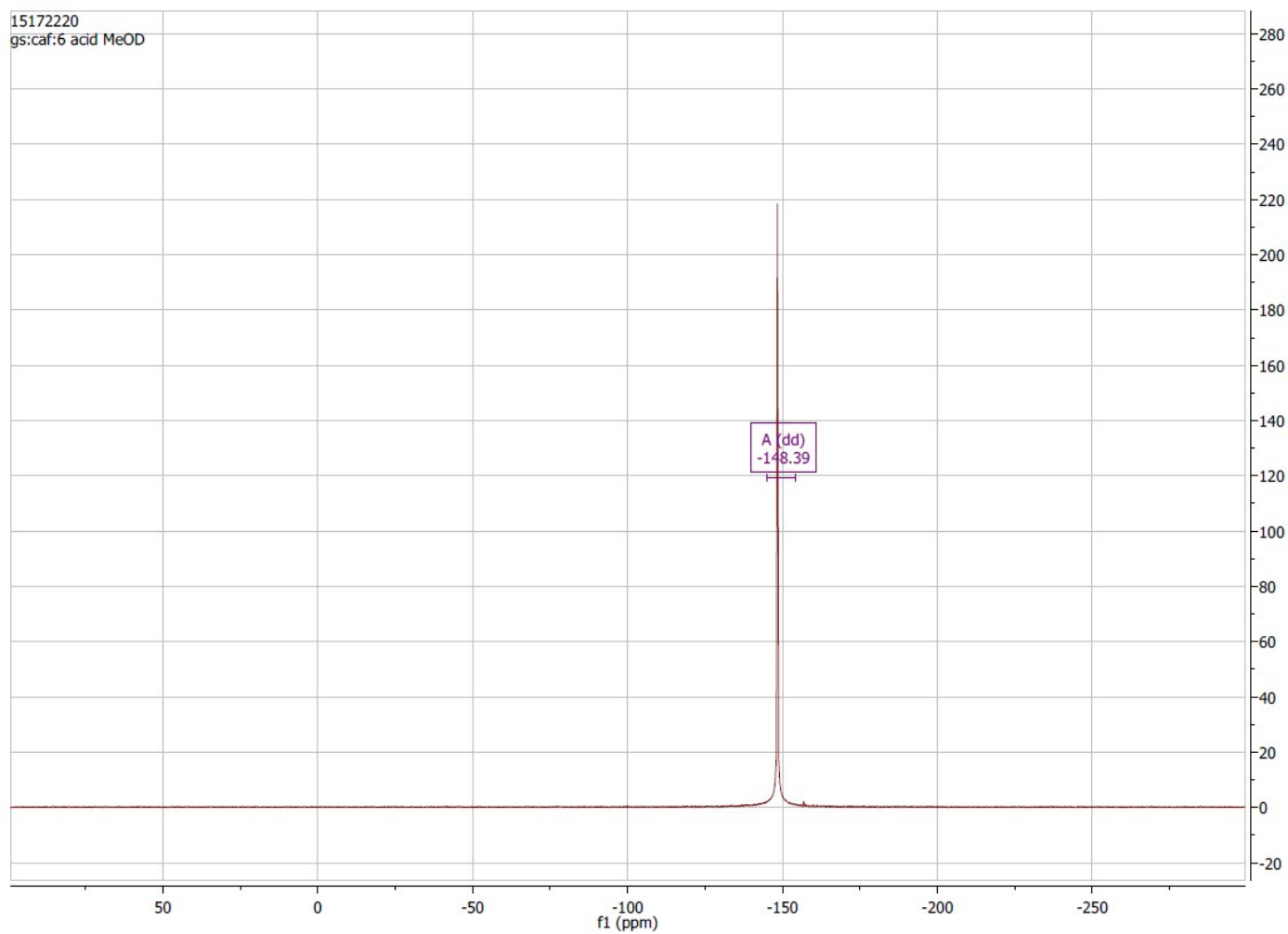
SI-5.4 3-Fluoro-2-oxopiperidine-3-carboxylic acid **5**

^1H NMR spectrum



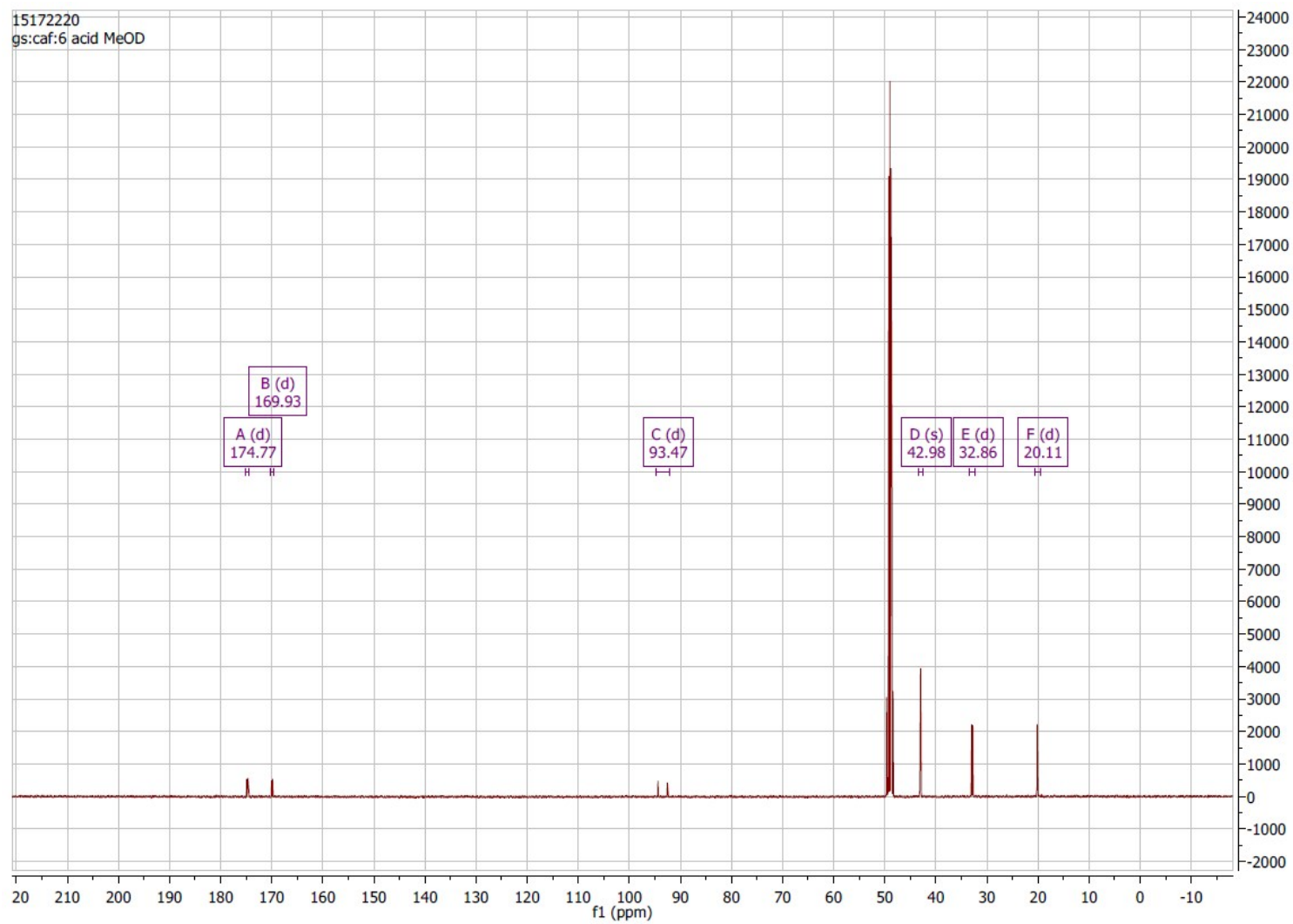
3-Fluoro-2-oxopiperidine-3-carboxylic acid **5**

^{19}F NMR spectrum



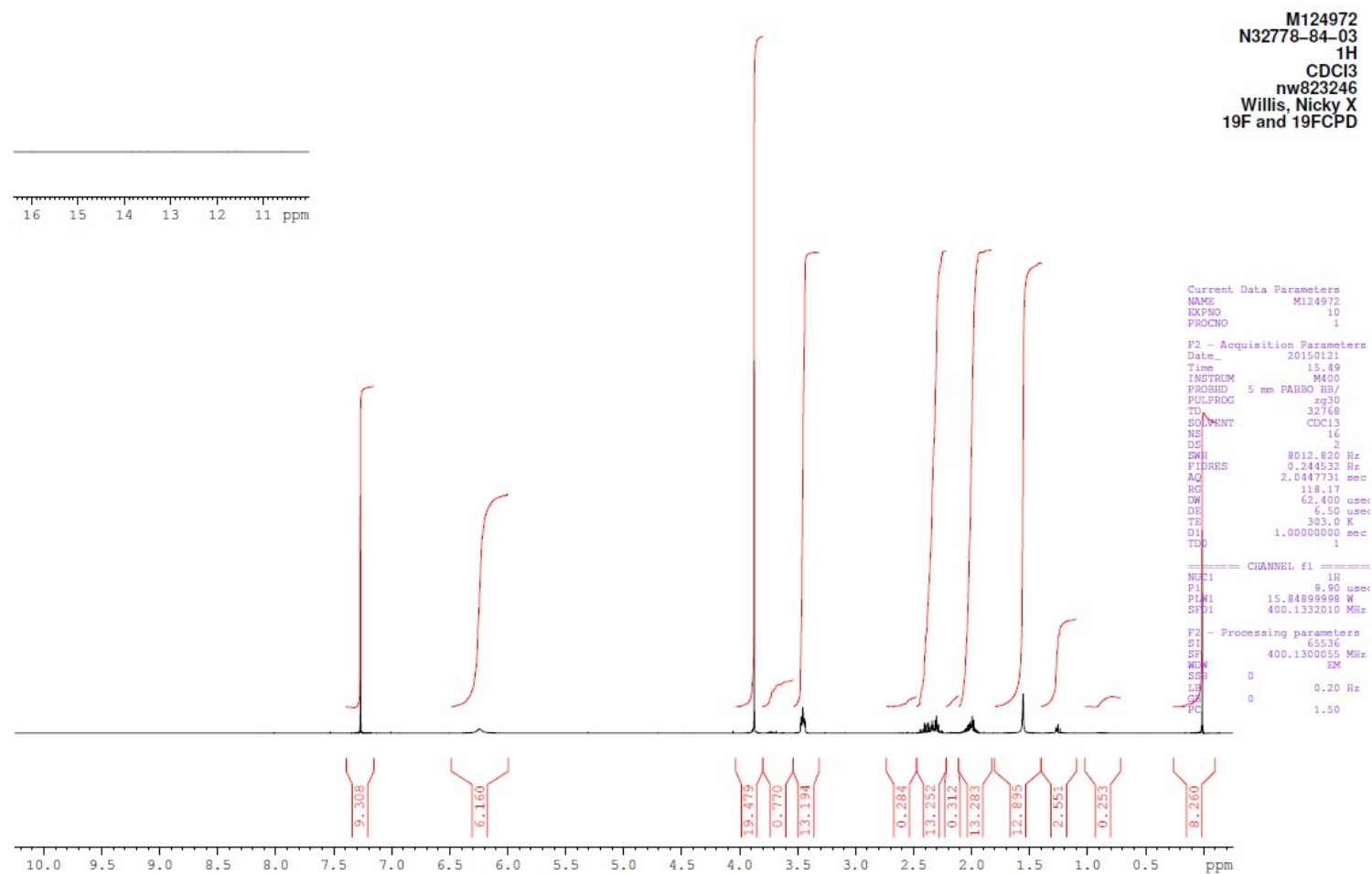
3-Fluoro-2-oxopiperidine-3-carboxylic acid **5**

^{13}C NMR spectrum



SI-5.5 (S)-Methyl 3-fluoro-2-oxopiperidine-3-carboxylate **2b**

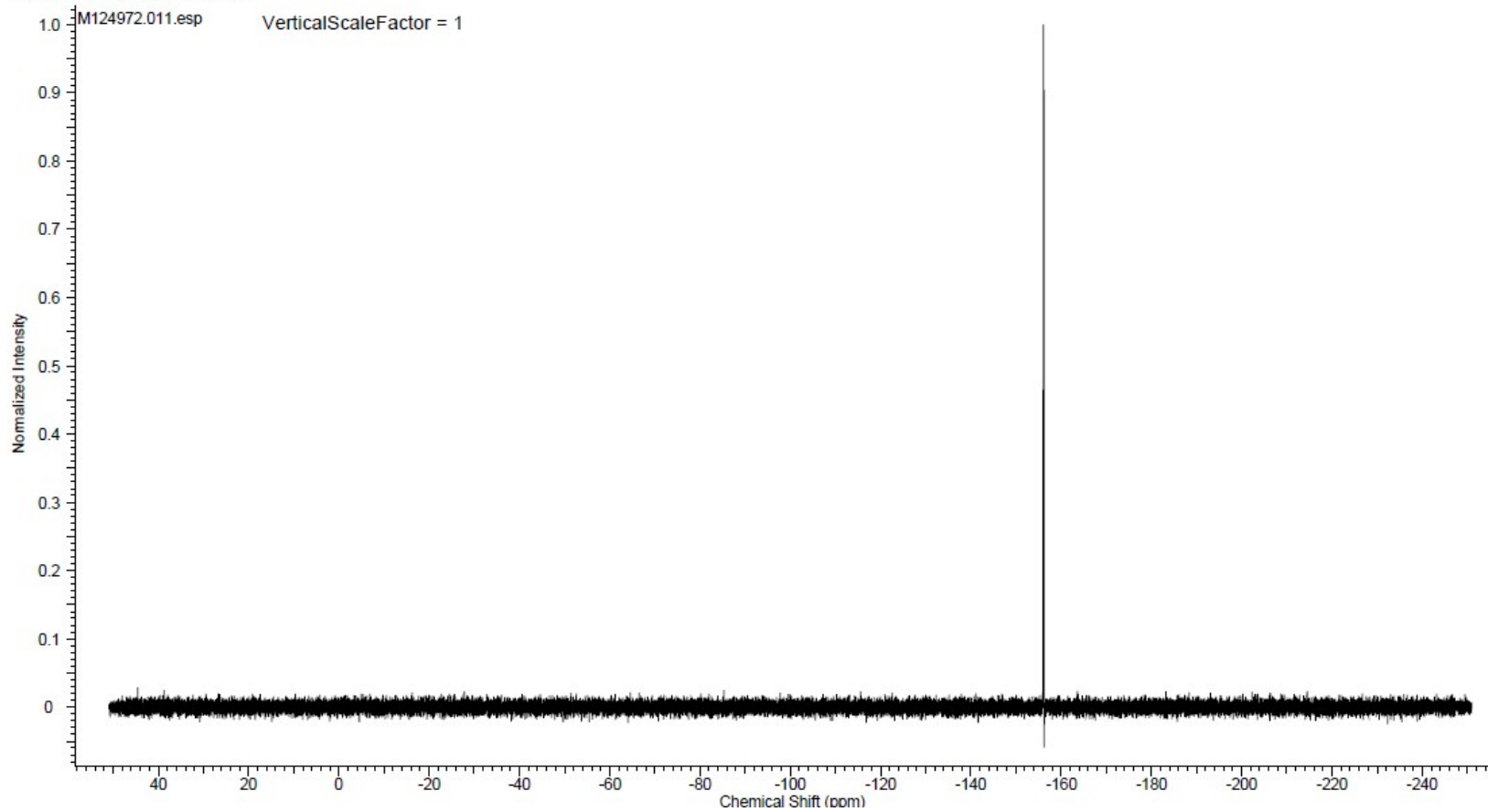
^1H NMR spectrum



(S)-Methyl 3-fluoro-2-oxopiperidine-3-carboxylate **2b**

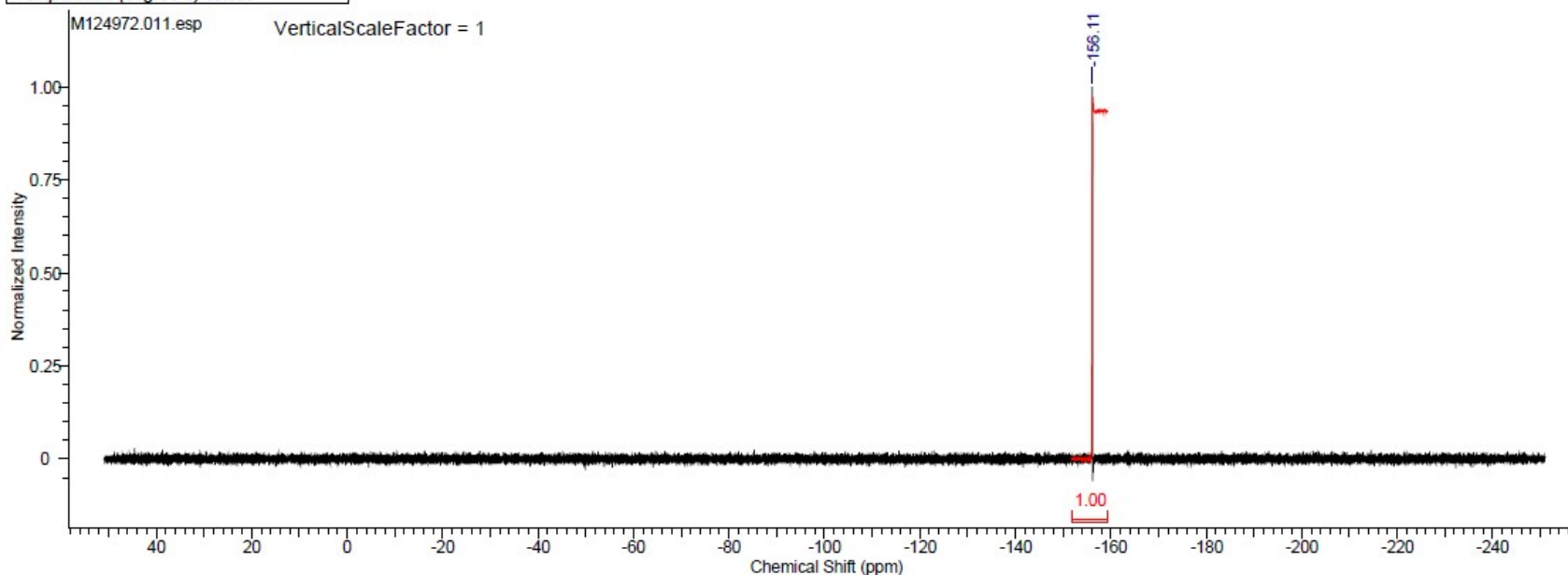
^{19}F NMR spectrum

Number of Nuclei 0 F's					
Acquisition Time (sec)	0.2884	Comment M124972 N32778-84-03 19F CDCl3 nw823246 Willis, Nicky X 19F and 19FCPD			
Date	21 Jan 2015 15:57:52	Date Stamp		21 Jan 2015 15:57:52	
File Name	C:\USERS\CMS26237\APPDATA\LOCAL\TEMP\M124972\11\FID	Frequency (MHz)	376.46	Nucleus	19F
Number of Transients	32	Origin	M400	Original Points Count	32768
Points Count	32768	Pulse Sequence	zg30	Receiver Gain	192.79
Solvent	CHLOROFORM-d	Spectrum Offset (Hz)	-37649.8359	SW(cyclical) (Hz)	113636.36
Temperature (degree C)	30.005	Spectrum Type	STANDARD	Sweep Width (Hz)	113632.89



Number of Nuclei 0 F's

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Temperature (degree C)	30.005	Spectrum Type	STANDARD	Sweep Width (Hz)	113632.89



No.	(ppm)	Value	Absolute Value	Non-Negative Value
1	-156.18	-58795.4	58795.4	58795.4
2	-156.12	-58774.6	58774.6	58774.6
3	-156.11	-58767.7	58767.7	58767.7
4	-156.06	-58750.3	58750.3	58750.3

^1H and ^{19}F NMR spectra of (S)-methyl 3-fluoro-2-oxopiperidine-3-carboxylate **2b** prepared by scaled-up process.

