Development of a Factory Process for Omecamtiv Mecarbil, a Novel Cardiac Myosin Activator

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Supporting Information

Table of Contents:

1. ^{1}H NMR spectrum of **5**-phopshate in DMSO-d_6

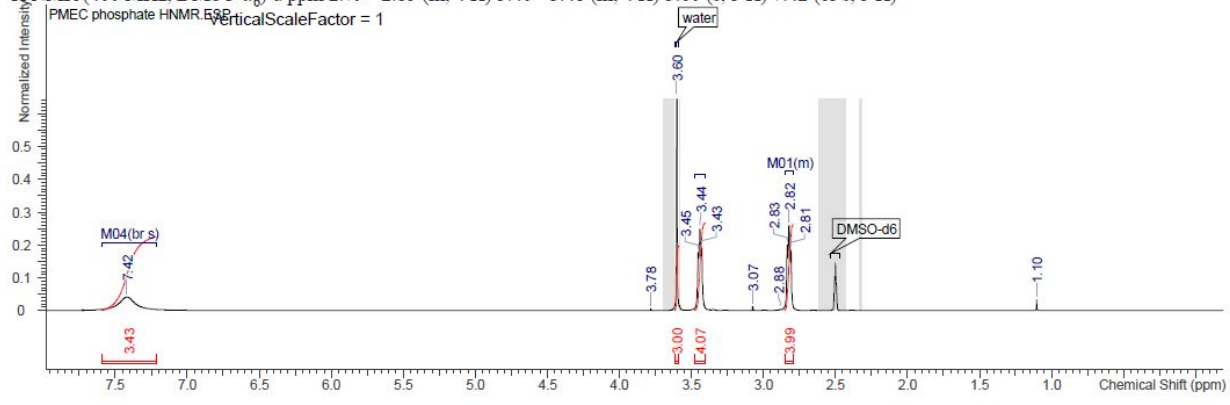
2/1/2019 9:13:07 AM

OriginalDateForRelativeTime 2019-01-31T17:50:29				*Sample ID*	ashi01-270-1	*ESP Filename*	ashi01-270-1_10.ESP
Notebook	ashi01-270-1	*User*	xianqing	*Notebook Reference*	ashi01-270-1	*Number of Nuclei*	14 H's
Multiplets Integrals Sum	14.49	*Labile*	yes	*RMS of Noise*	797.2739	*MINSN*	81.360977

Acquisition Time (sec)	4.8234	*Comment*	xianqing	*D*	0.06	*D1*	1	*DE*	6.5
DS	2	*Date*	31 Jan 2019 17:50:29			*Date Stamp*	31 Jan 2019 17:50:29		
ExpNo	10	*File Name*	D:\ACD\proc\as_data\xianqing\nmr\ashi01-270-1\10\pdata\1\1r					*Frequency (MHz)*	400.1300
GB	0	*INSTRUM*	<spect>	*LB*	0.3	*NS*	16	*Nucleus*	1H
Number of Transients	16	*Origin*	spect	*Original Points Count*	32768	*Owner*	shr-ato-nmr1		
PC	1	*PROBHD*	<5 mm PABBO BB-1H/D Z-GRD Z104450/0062 >			*PULPROG*	<zg30>	*Points Count*	32768
Pulse Sequence	zg30	*Receiver Gain*	203.00	*SF*	400.13	*SFO1*	400.132880936		
SI	32768	*SSB*	0	*SW(cyclical) (Hz)*	6793.48	*SWH*	6793.47826086957		
Solvent	DMSO-d6	*Spectrum Offset (Hz)*	2879.5815	*Spectrum Type*	standard	*Sweep Width (Hz)*	6793.27	*TD*	65536
TD0	1	*TE*	300	*Temperature (degree C)*	27.000	*UNC1*	<1H>	*WDW*	1

User Notes xianqing

^{1}H NMR (400 MHz, DMSO-d_6) d ppm 2.79 - 2.85 (m, 4 H) 3.40 - 3.48 (m, 4 H) 3.60 (s, 3 H) 7.42 (br s, 3 H)



2. ^{13}C {^{1}H} NMR spectrum of **5**-phopshate in DMSO-d_6

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Number of Transients	512	*Acquisition Time (sec)*	1.1534	*Points Count*	32768
Solvent	DMSO-d6	*Spectrum Offset (Hz)*	12024.6553	*Sweep Width (Hz)*	28408.22
Temperature (degree C)	27.000	*Owner*	shr-ato-nmr1		

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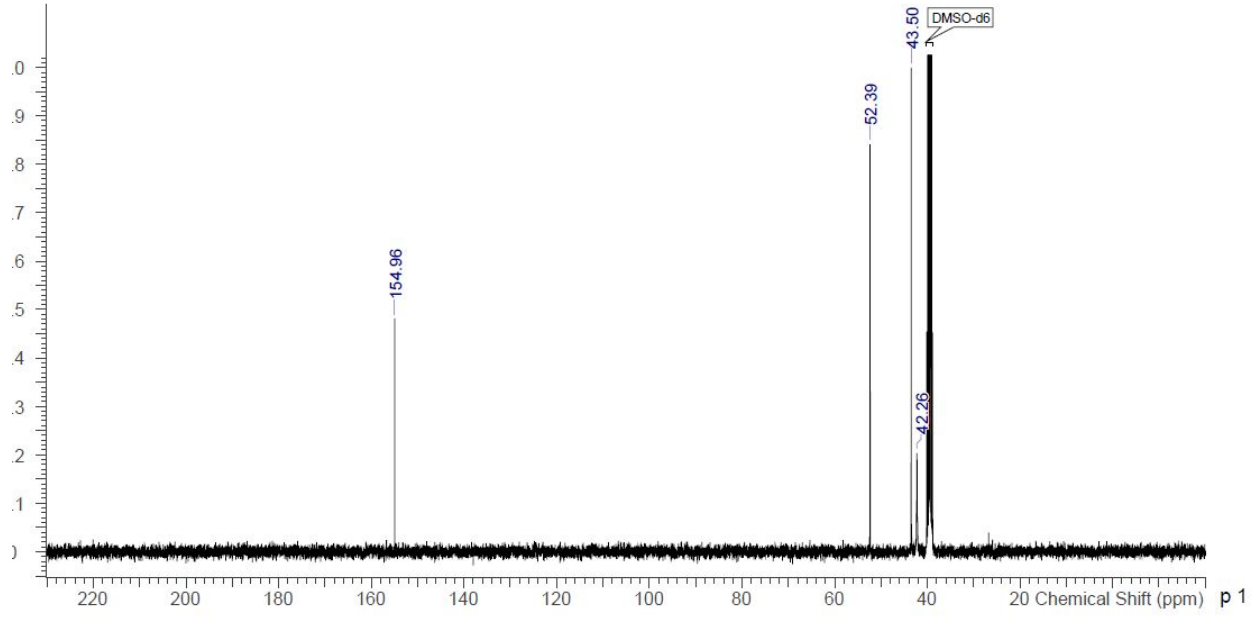
^{13}C NMR (101 MHz, DMSO-d_6) d ppm 42.26 (s, 1 C) 43.50 (s, 1 C) 52.39 (s, 1 C) 154.96 (s, 1 C)



3. ^{1}H NMR spectrum of **14-HCl** in DMSO-d_6

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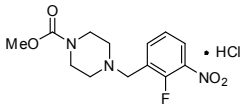
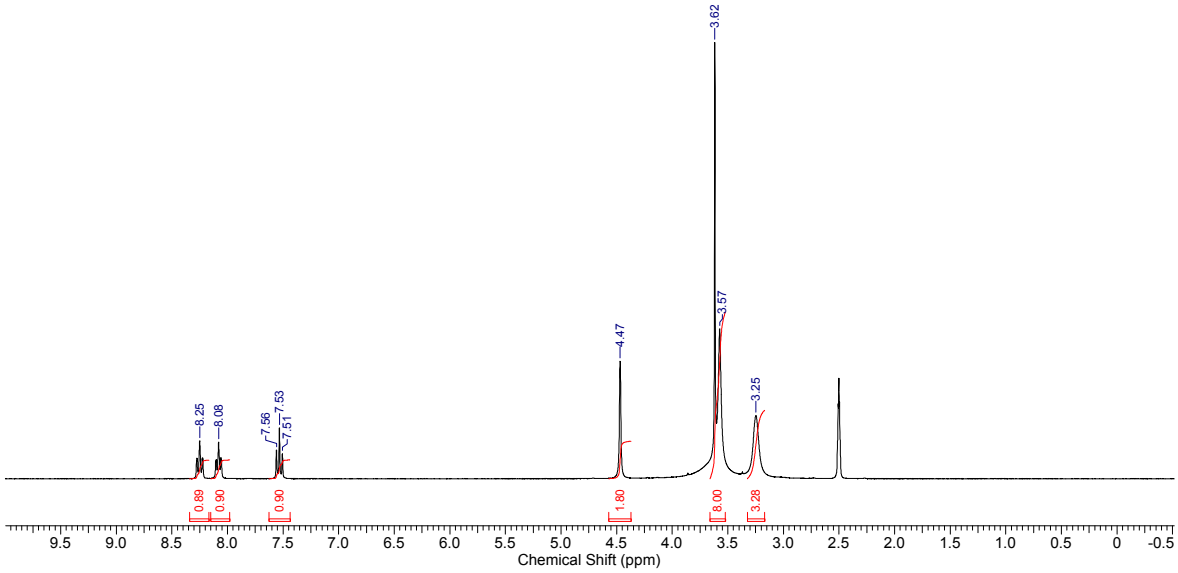
Date	27 Apr 2010 09:58:10		
Date Stamp	27 Apr 2010 09:58:10		
File Name	\\scone\nmr-archive\JCAMP\CBERNARD\2010\102151-40-17_11.DX		
Frequency (MHz)	300.13	***Nucleus***	1H
Number of Transients	32	***Origin***	Bruker BioSpin GmbH
Original Points Count	32768	***Owner***	shr-ato-nmr1
Points Count	32768	***SW(cyclical) (Hz)***	4789.27
Solvent	DMSO-d6	***Spectrum Offset (Hz)***	1801.0266
Sweep Width (Hz)	4789.13	***Temperature (degree C)***	27.100



Piperazine Nitro-HCl



4. ^{13}C {^{1}H} NMR spectrum of **14-HCl** in DMSO-d_6

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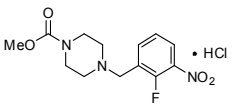
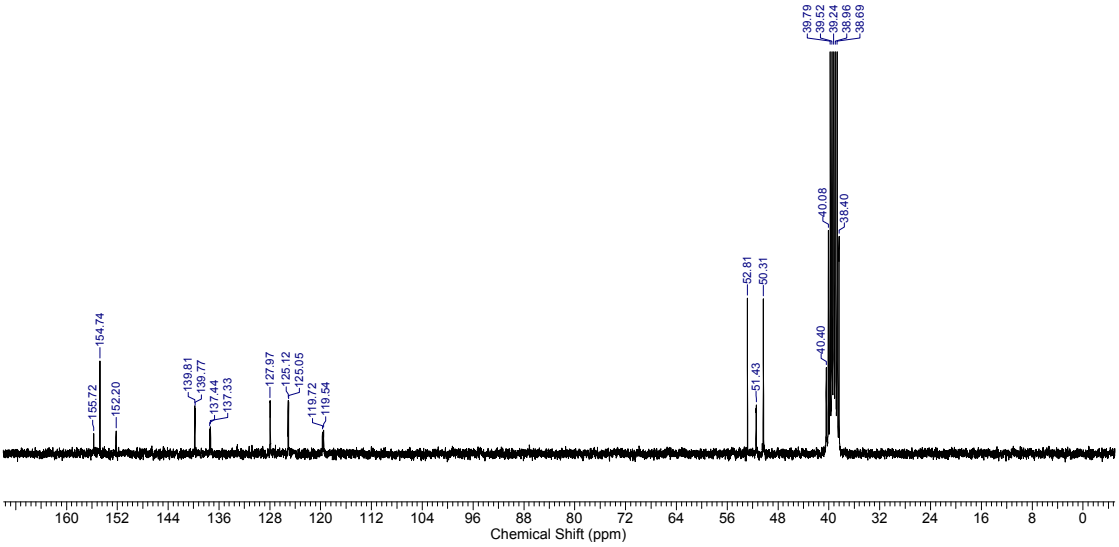
Date	27 Apr 2010 20:36:34		
Date Stamp	27 Apr 2010 20:36:34		
File Name	\\scone\nmr-archive\JCAMP\CBERNARD\2010\102151-40-17_14.DX		
Frequency (MHz)	75.48	***Nucleus***	13C
Number of Transients	2048	***Origin***	Bruker BioSpin GmbH
Original Points Count	32768	***Owner***	shr-ato-nmr1
Points Count	32768	***SW(cyclical) (Hz)***	21231.42
Solvent	DMSO-d6	***Spectrum Offset (Hz)***	9020.6133
Sweep Width (Hz)	21230.77	***Temperature (degree C)***	27.000



Piperazine Nitro-HCl



5. ^{1}H NMR spectrum of **12** in $CDCl_3$

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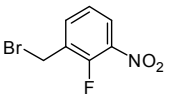
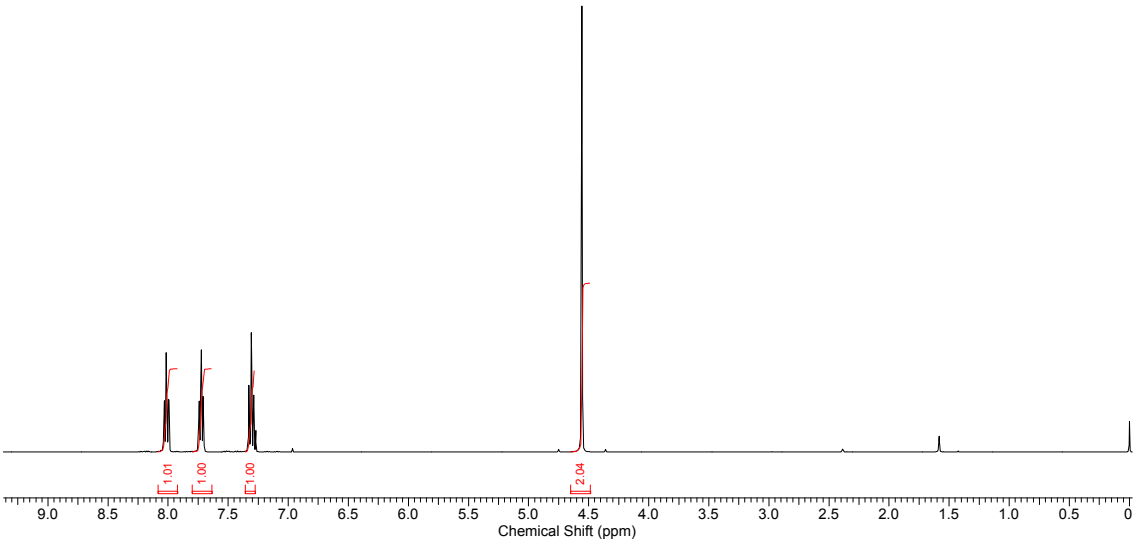
Date	26 Feb 2010 01:59:00		
File Name	\\scone\NMR-Archive\JCAMP\SCAILLE\2010\103097-91-1_10.DX		
Frequency (MHz)	400.13	***Nucleus***	1H
Number of Transients	32	***Origin***	Bruker BioSpin GmbH
Original Points Count	32768	***Owner***	shr-ato-nmr1
Points Count	32768	***SW(cyclical) (Hz)***	6410.06
Solvent	CHLOROFORM-d		
Spectrum Offset (Hz)	2395.1680	***Sweep Width (Hz)***	6409.86
Temperature (degree C)	25.000		

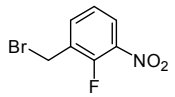


FN-Bromide

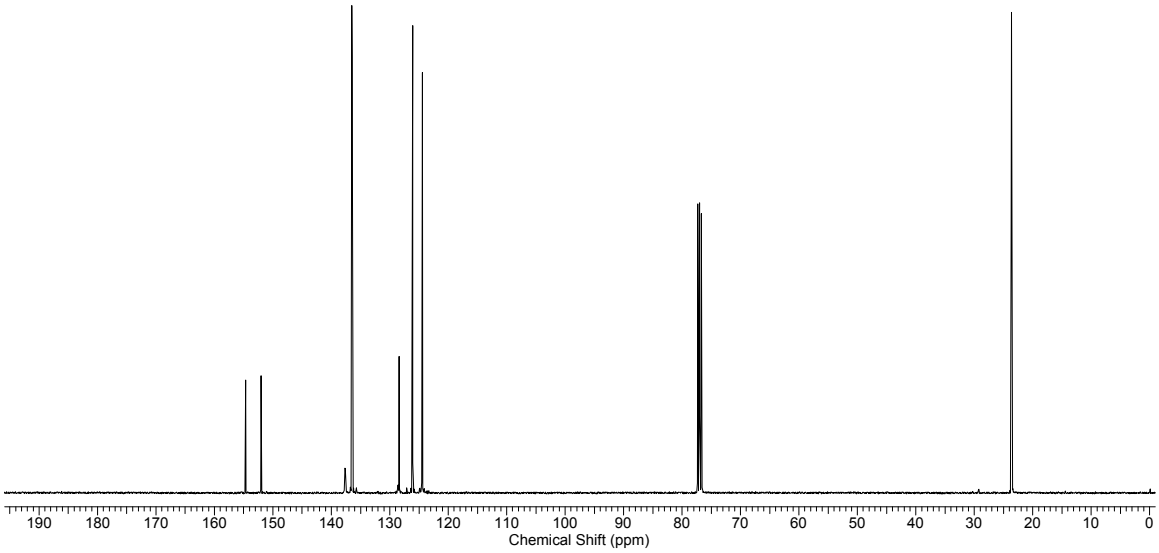


6. ^{13}C {^{1}H} NMR spectrum of **12** in $CDCl_3$

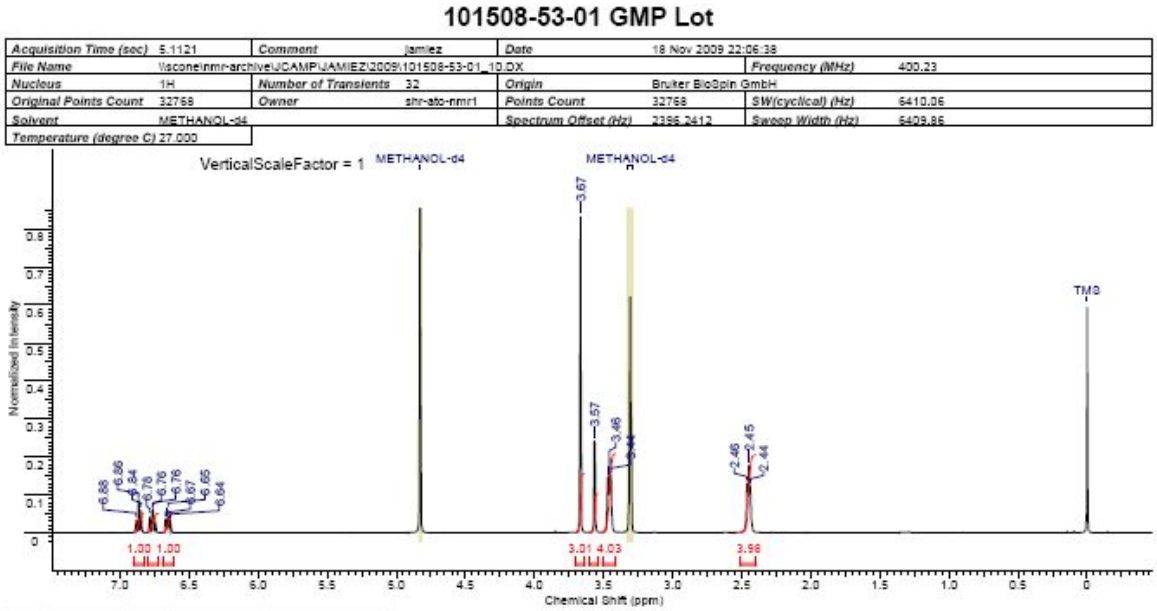
Acquisition Time (sec)	1.1535	***Comment***	scaille
Date	26 Feb 2010 09:38:48		
File Name	\\scone\NMR-Archive\JCAMP\SCAILLE\2010\103097-91-2_10.DX		
Frequency (MHz)	100.62	***Nucleus***	13C
Number of Transients	4096	***Origin***	Bruker BioSpin GmbH
Original Points Count	32768	***Owner***	shr-ato-nmr1
Points Count	32768	***SW(cyclical) (Hz)***	28408.22
Solvent	CHLOROFORM-d		
Spectrum Offset (Hz)	12060.7568	***Sweep Width (Hz)***	28407.36
Temperature (degree C)	25.000		



FN-Bromide



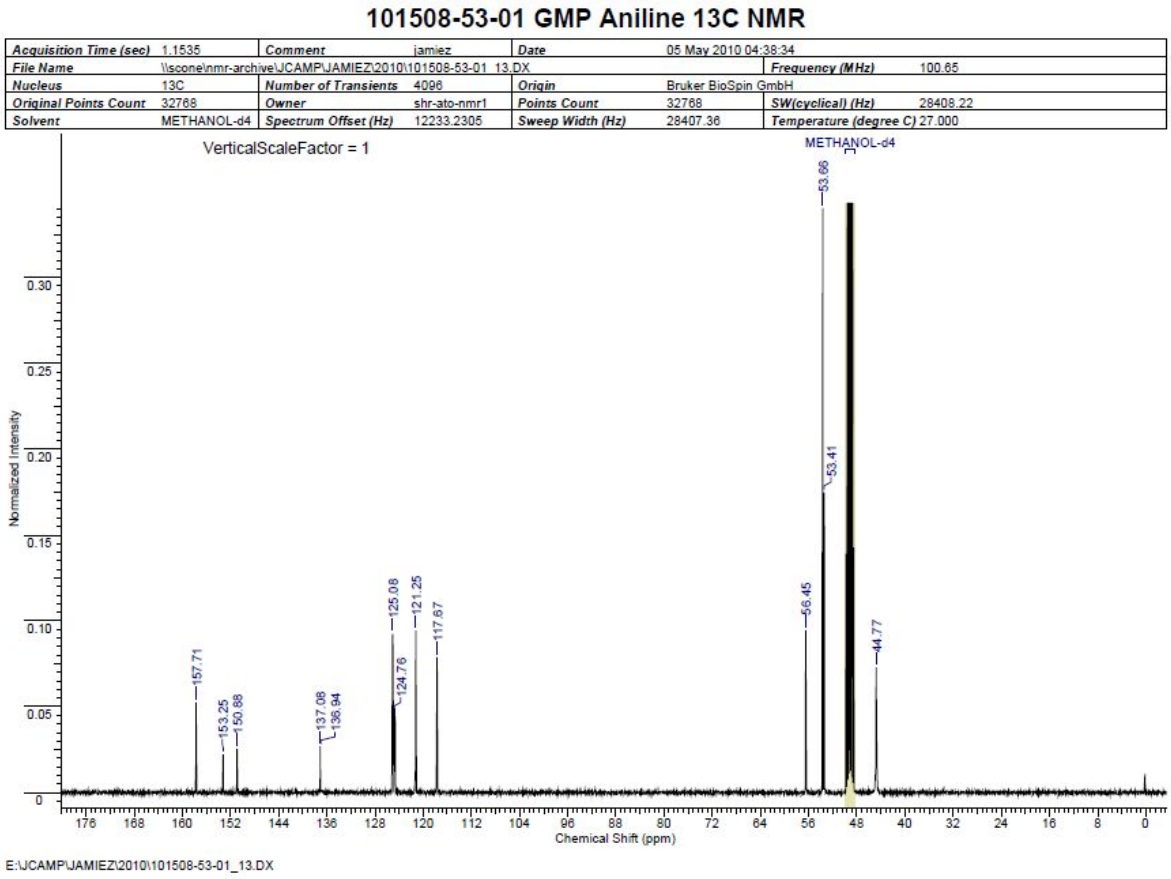
7. ^{1}H NMR spectrum of **2** in MeOH-d_4



No.	(ppm)	Value	Absolute Value	Non-Negative Value
1	[2.39 .. 2.51]	3.980	2.92434e+9	3.980
2	[3.41 .. 3.51]	4.030	2.96116e+9	4.030
3	[3.54 .. 3.60]	1.998	1.46805e+9	1.998
4	[3.64 .. 3.70]	3.010	2.21152e+9	3.010
5	[6.62 .. 6.69]	0.997	7.32691e+8	0.997
6	[6.72 .. 6.80]	0.983	7.21858e+8	0.983
7	[6.83 .. 6.90]	1.000	7.34675e+8	1.000

E:\JCAMP\JAMIEZ\2009\101508-53-01_10.DX

8. ^{13}C {^{1}H} NMR spectrum of **2** MeOH-d_4



9. ^{1}H NMR spectrum of **4-HCl** DMSO-d_6

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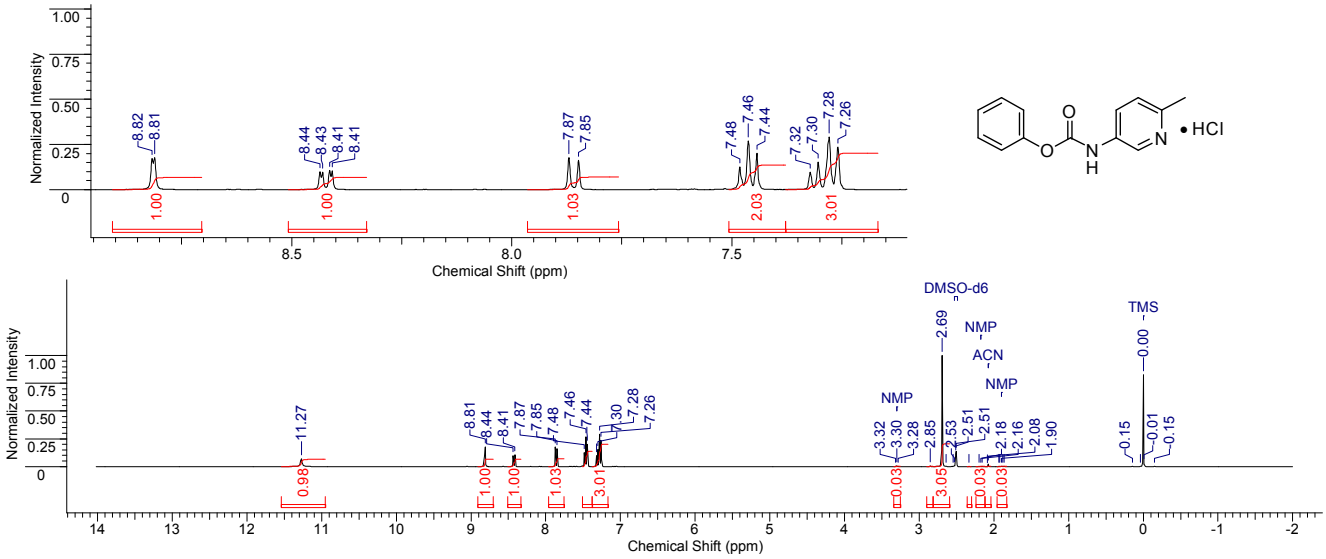
File Name	\\scone\NMR-archive\jcamp\RCROCK01\2009\95887-01-1_10.DX					***Frequency (MHz)***	400.23
Nucleus	1H	***Number of Transients***	32	***Origin***	Bruker BioSpin GmbH		
Original Points Count	32768	***Owner***	shr-ato-nmr1	***Points Count***	32768	***SW(cyclical) (Hz)***	6410.06
Solvent	DMSO-d6	***Spectrum Offset (Hz)***	2405.4353	***Sweep Width (Hz)***	6409.86	***Temperature (degree C)***	27.000



10. ^{13}C {^{1}H} NMR spectrum of **4-HCl** DMSO-d_6

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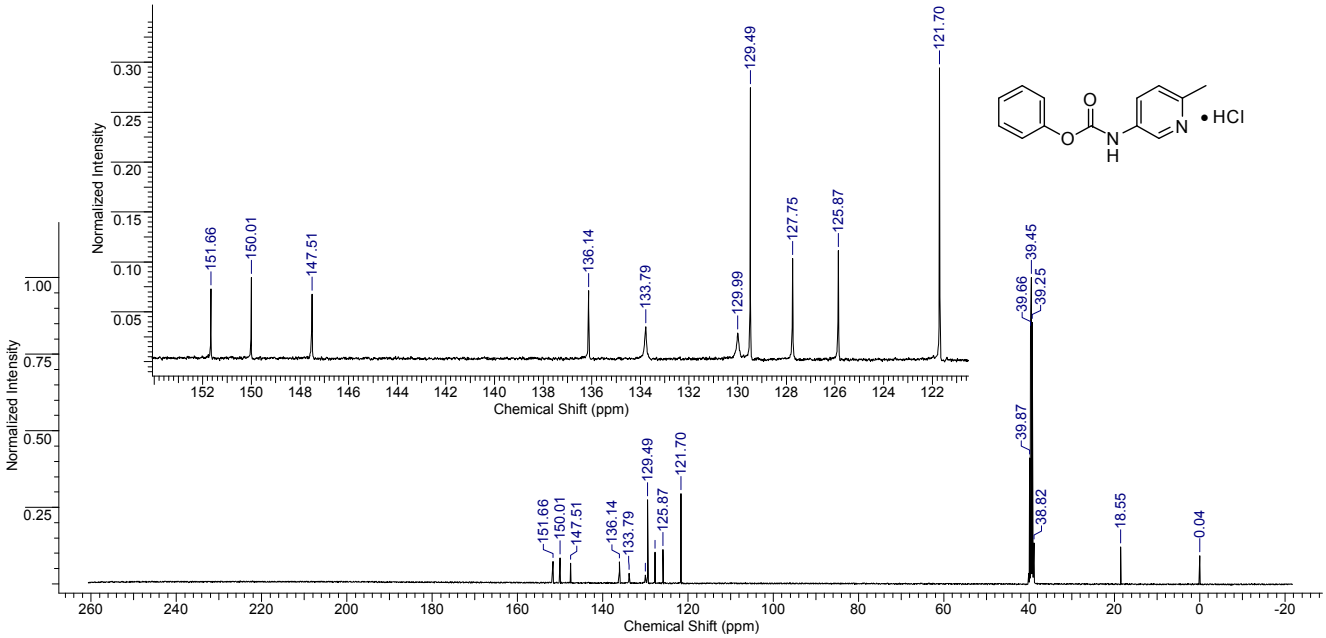
File Name	\\scone\NMR-archive\jcamp\RCROCK01\2010\103827-38-13_10.DX					***Frequency (MHz)***	100.62
Nucleus	13C	***Number of Transients***	4096	***Origin***	Bruker BioSpin GmbH		
Original Points Count	32768	***Owner***	shr-ato-nmr1	***Points Count***	32768	***SW(cyclical) (Hz)***	28408.22
Solvent	DMSO-d6	***Spectrum Offset (Hz)***	12019.0615	***Sweep Width (Hz)***	28407.36	***Temperature (degree C)***	25.000



11. ^{1}H NMR spectrum of **1** in DMSO-d_6

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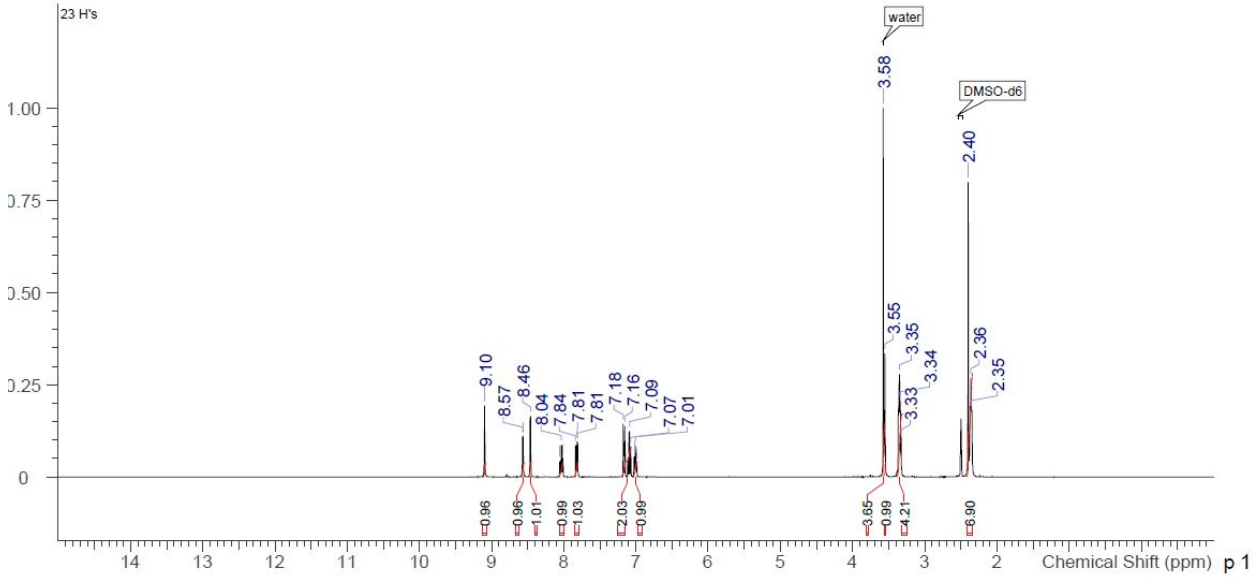
Comment	xianqing	*Date*	31 Jan 2019 18:22:27		
Nucleus	1H	*Frequency (MHz)*	400.1300	*Pulse Sequence*	zg30
Number of Transients	16	*Acquisition Time (sec)*	4.8234	*Points Count*	32768
Solvent	DMSO-d6	*Spectrum Offset (Hz)*	2879.3743	*Sweep Width (Hz)*	6793.27
Temperature (degree C)	27.000	*Owner*	shr-ato-nmr1		

I.ESP

^{1}H NMR (400 MHz, DMSO-d_6) d ppm 2.34 - 2.42 (m, 7 H) 3.31 - 3.39 (m, 4 H) 3.56 - 3.59 (m, 4 H) 7.01 (t, *J*=6.80 Hz, 1 H) 7.09 (t, *J*=7.87 Hz, 1 H) 7.17 (d, *J*=8.50 Hz, 1 H) 7.82 (dd, *J*=8.40, 2.59 Hz, 1 H) 8.03 (t, *J*=7.26 Hz, 1 H) 8.46 (d, *J*=2.49 Hz, 1 H) 8.57 (d, *J*=2.28 Hz, 1 H) 9.10 (s, 1 H)



12. ^{13}C {^{1}H} NMR spectrum of **1** in DMSO-d_6

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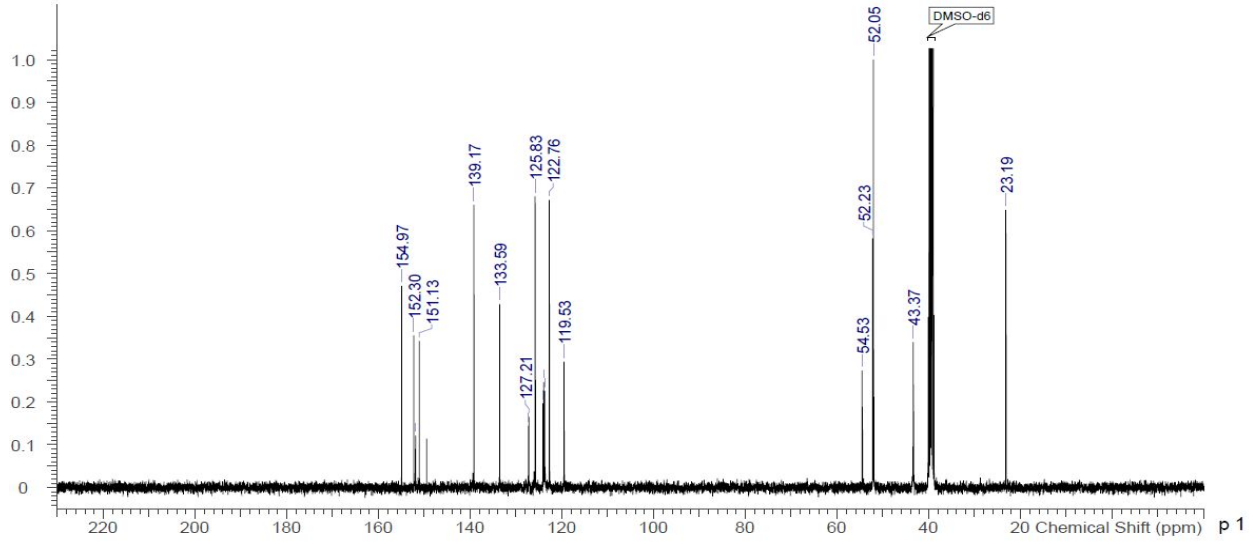
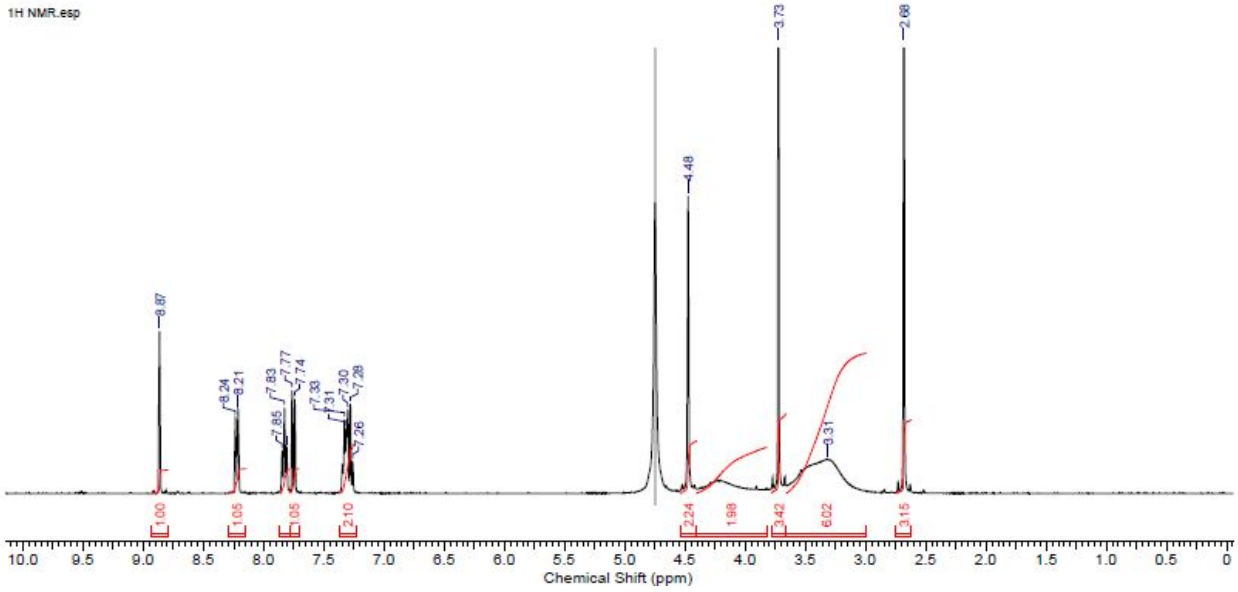
Nucleus	13C	*Frequency (MHz)*	100.6128	*Pulse Sequence*	zgpg30
Number of Transients	512	*Acquisition Time (sec)*	1.1534	*Points Count*	32768
Solvent	DMSO-d6	*Spectrum Offset (Hz)*	12023.7881	*Sweep Width (Hz)*	28408.22
Temperature (degree C)	27.000	*Owner*	shr-ato-nmr1		

.ESP

^{13}C NMR (101 MHz, DMSO-d_6) d ppm 23.19 (s, 1 C) 43.37 (s, 1 C) 52.05 (s, 1 C) 52.23 (s, 1 C) 54.53 (s, 1 C) 119.53 (s, 1 C) 122.76 (s, 1 C) 123.76 (s, 1 C) 124.01 (s, 1 C) 124.14 (s, 1 C) 125.83 (s, 1 C) 127.21 (s, 1 C) 127.32 (s, 1 C) 133.59 (s, 1 C) 139.17 (s, 1 C) 151.13 (s, 1 C) 151.93 (s, 1 C) 152.30 (s, 1 C) 154.97 (s, 1 C)



13. ^{1}H NMR spectrum of omecamtiv mecarbil (**1**) dihydrochloride hydrate in D_2O



14. ^{13}C {^{1}H} NMR spectrum of omecamtiv mecarbil (**1**) dihydrochloride hydrate in D_2O