

Supporting Information

New Insights into Molecular Recognition of 1,1-Bisphosphonic Acids by Farnesyl Pyrophosphate Synthase

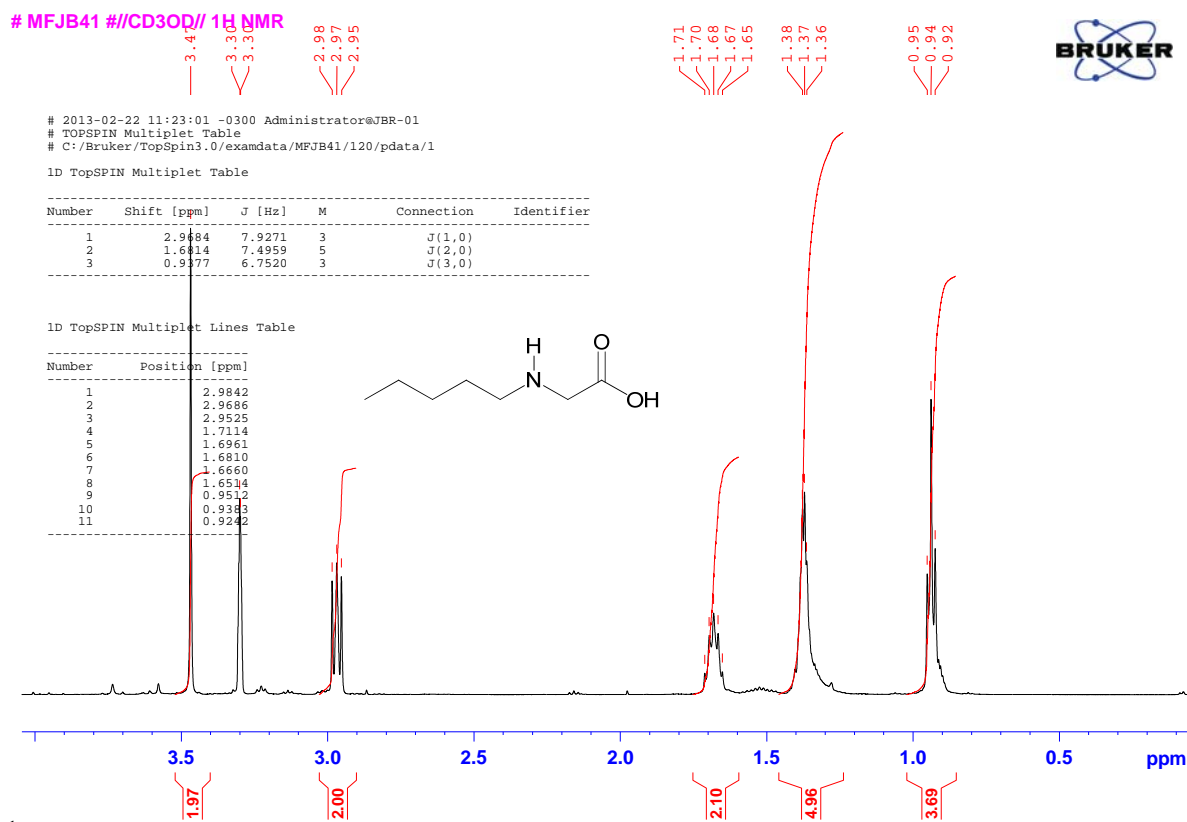
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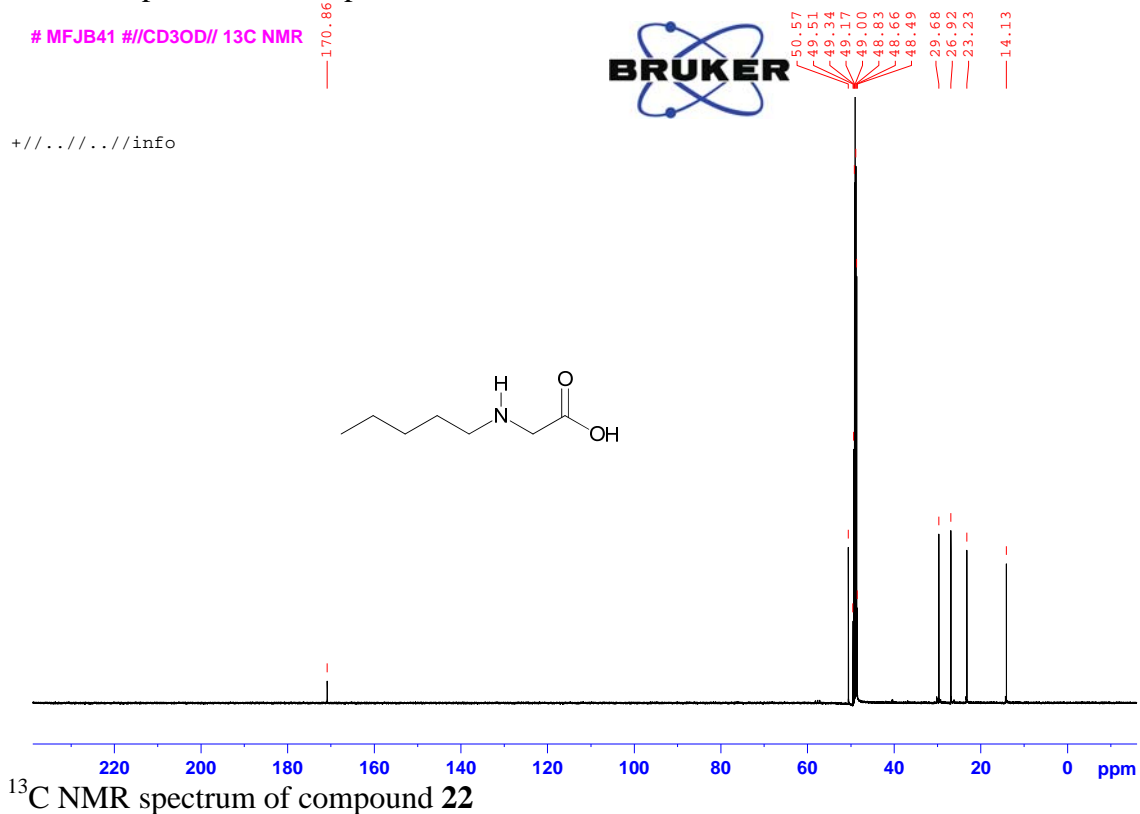
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MFJB41 #/CD3OD// 1H NMR



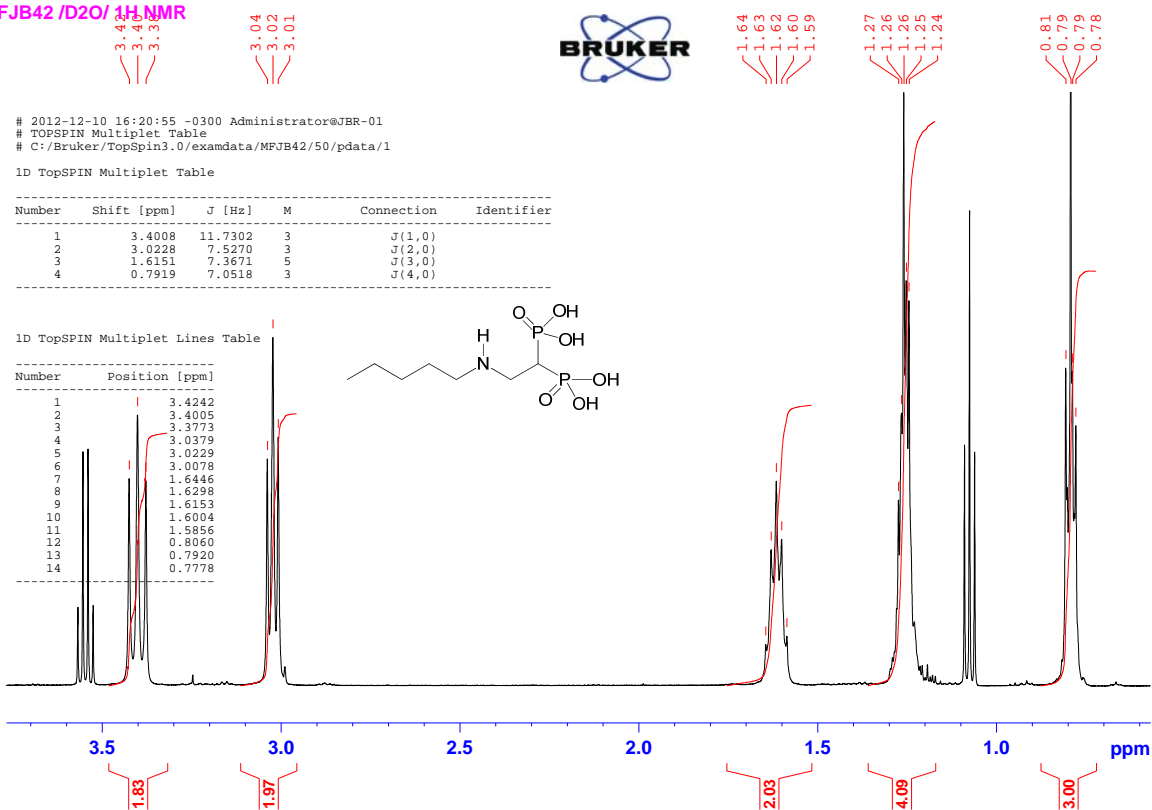
¹H NMR spectrum of compound 22

MFJB41 #/CD3OD// 13C NMR



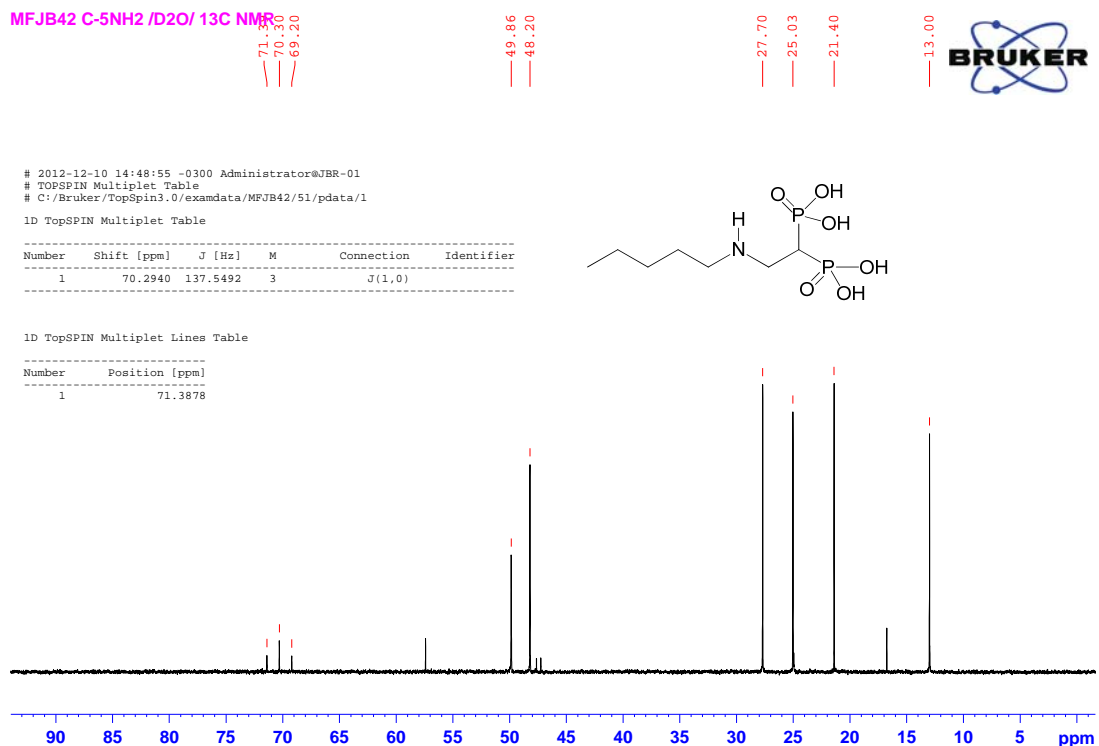
¹³C NMR spectrum of compound 22

MFJB42 /D2O/ ¹H NMR



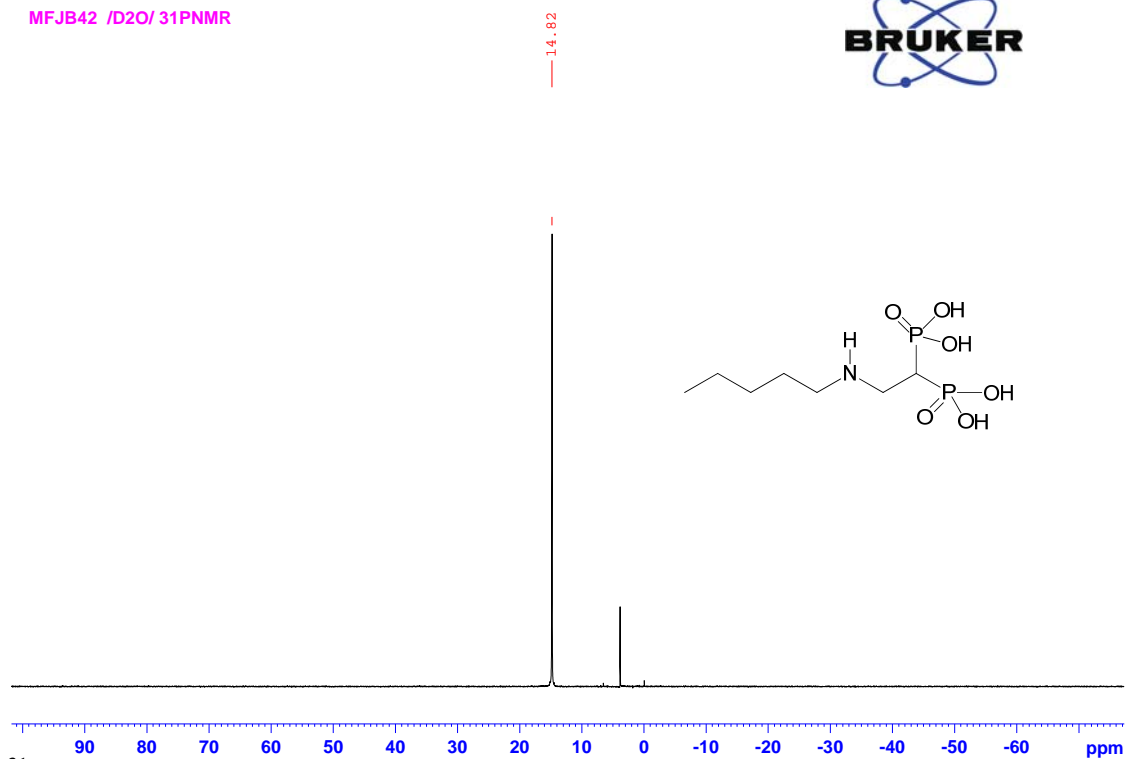
¹H NMR spectrum of compound 27

MFJB42 C-5NH2 /D2O/ ¹³C NMR



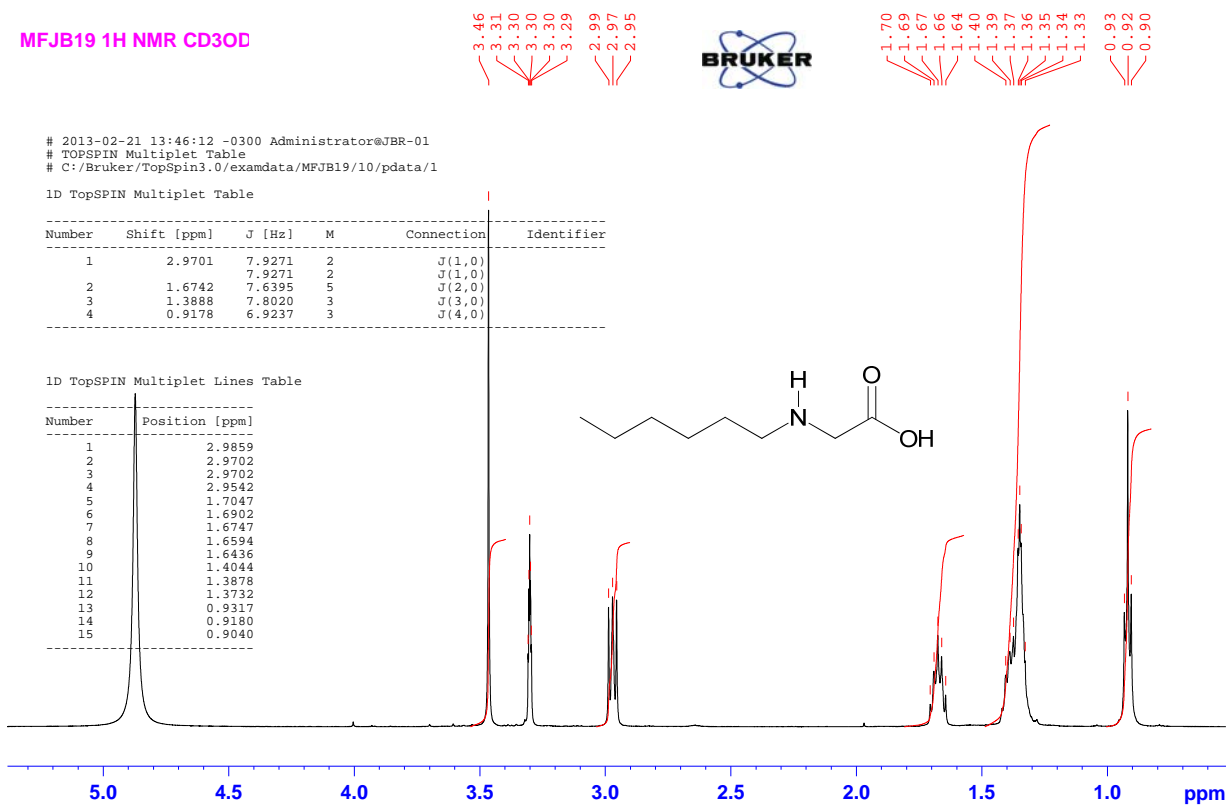
¹³C NMR spectrum of compound 27.

MFJB42 /D2O/ 31PNMR



³¹P NMR spectrum of compound 27

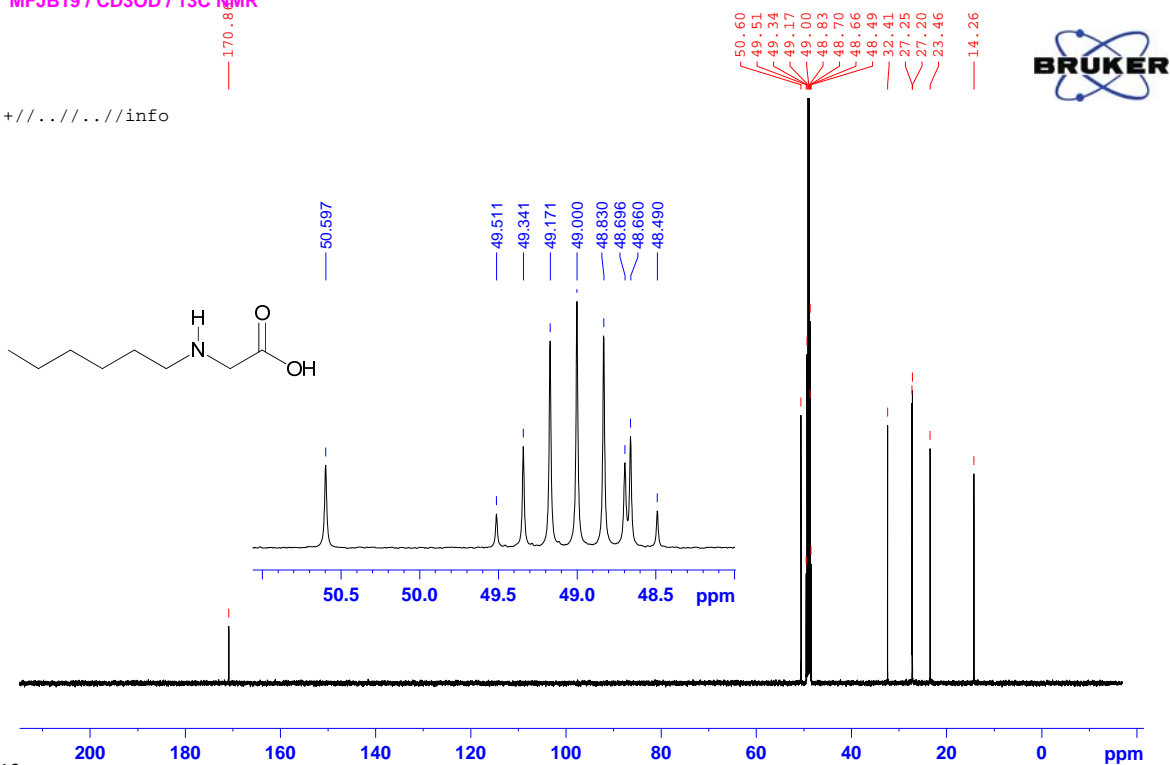
MFJB19 1H NMR CD3OD



¹H NMR spectrum of compound 23.

MFJB19 / CD3OD / ¹³C NMR

+//...//info



¹³C NMR spectrum of compound 23.

MFJB 21 / D2O / ¹H NMR.

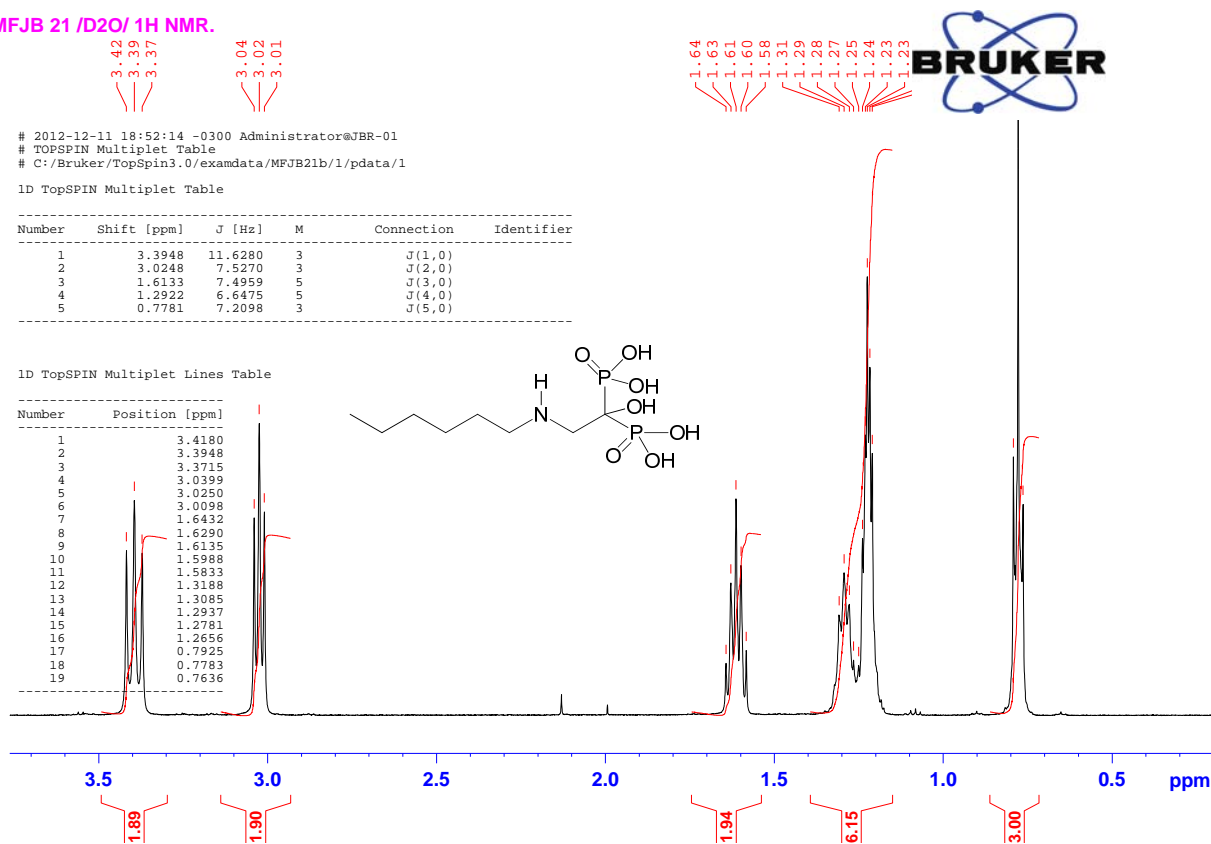
2012-12-11 18:52:14 -0300 Administrator@JBR-01
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1D TopSPIN Multiplet Table

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1	3.3948	11.6280	3	J(1,0)	
2	3.0248	7.5270	3	J(2,0)	
3	1.6133	7.4959	5	J(3,0)	
4	1.2922	6.6475	5	J(4,0)	
5	0.7781	7.2098	3	J(5,0)	

1D TopSPIN Multiplet Lines Table

Number	Position [ppm]
1	3.4180
2	3.3948
3	3.3715
4	3.0399
5	3.0250
6	3.0098
7	1.6432
8	1.6290
9	1.6135
10	1.5988
11	1.5833
12	1.5188
13	1.3085
14	1.2937
15	1.2781
16	1.2656
17	0.7925
18	0.7783
19	0.7636



¹H NMR spectrum of compound 28.

MFJB 21 /D2O/ 13C NMR

50.03
48.17

30.36

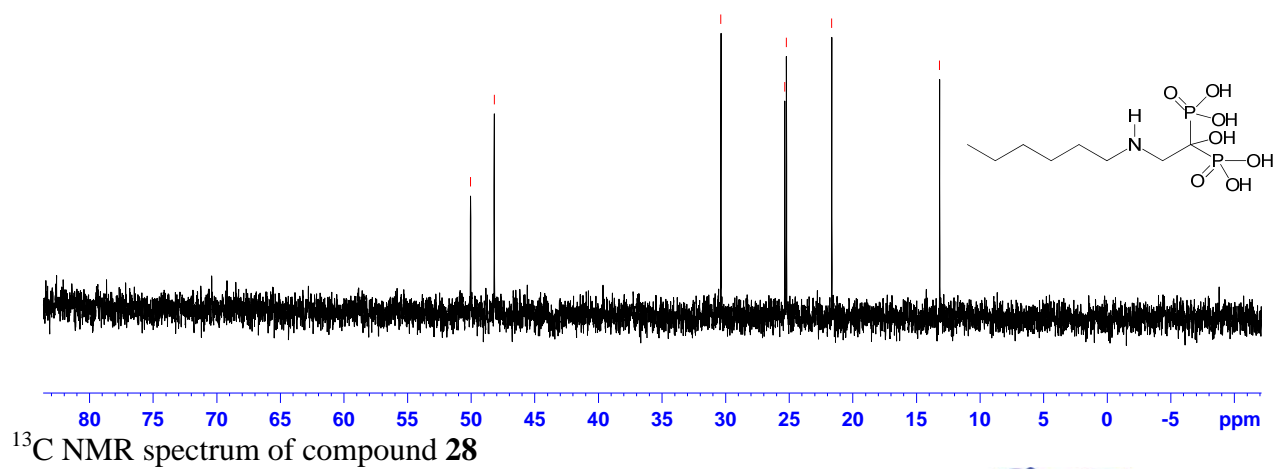
25.34
25.21

21.65

13.17



+//...//...//info

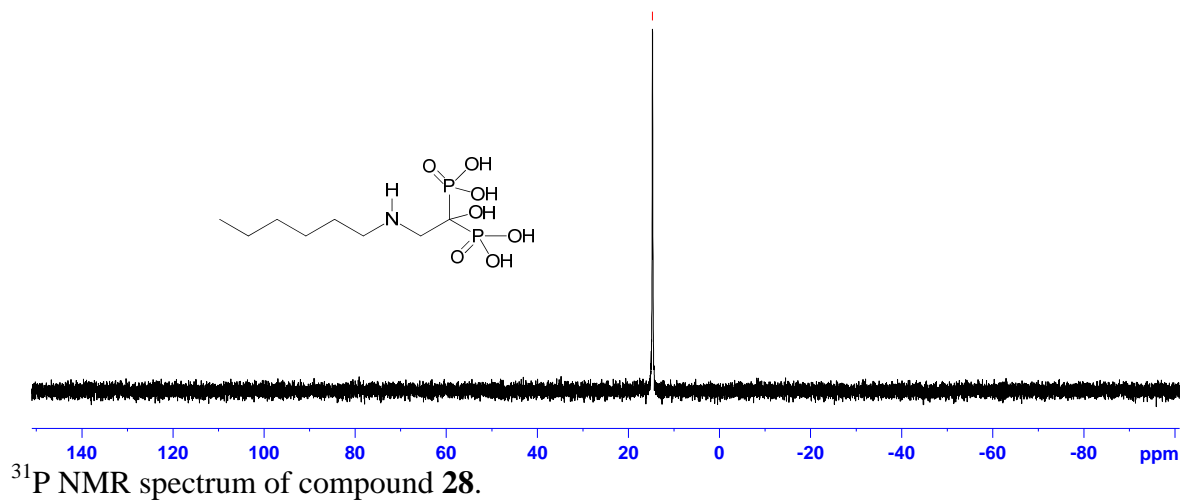


MFJB 21 /D2O/ 31P NMR

14.69



+//...//...//info



MFJB 43 # //D2O// ¹H NMR 6/10/11.

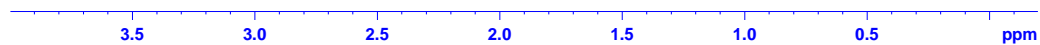
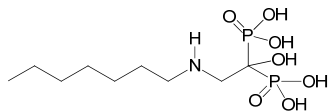
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1	3.3896	11.7030	3	J(1,0)	
2	3.0116	7.5531	3	J(2,0)	
3	1.6007	7.4387	5	J(3,0)	
4	0.7534	6.9768	3	J(4,0)	

1D TopSPIN Multiplet Lines Table

Number	Position [ppm]
1	3.4130
2	3.3897
3	3.1662
4	3.0267
5	3.0116
6	2.9965
7	1.6304
8	1.6158
9	1.6011
10	1.5860
11	1.5709
12	0.7673
13	0.7535
14	0.7394



¹H NMR spectrum of compound **29**.

MFJB_17 /D2O/ ¹³C NMR

71.39
70.29
69.20

49.85
48.25



30.72
27.79
25.50
25.34
21.84

13.29

2012-04-19 16:45:06 -0300 Administrator@JBR-01

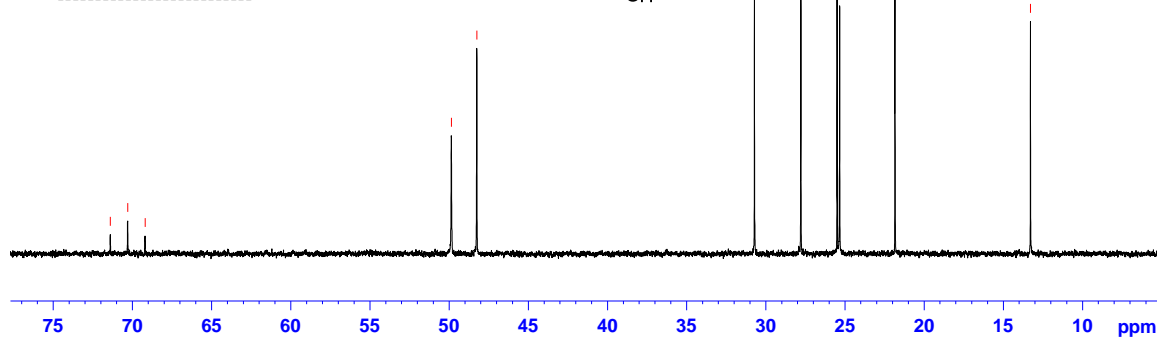
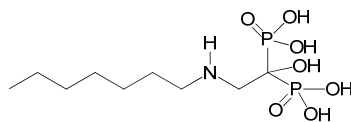
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Number	Shift [ppm]	J [Hz]	M	Connection	Identifier
1	70.2917	137.6796	3	J(1,0)	

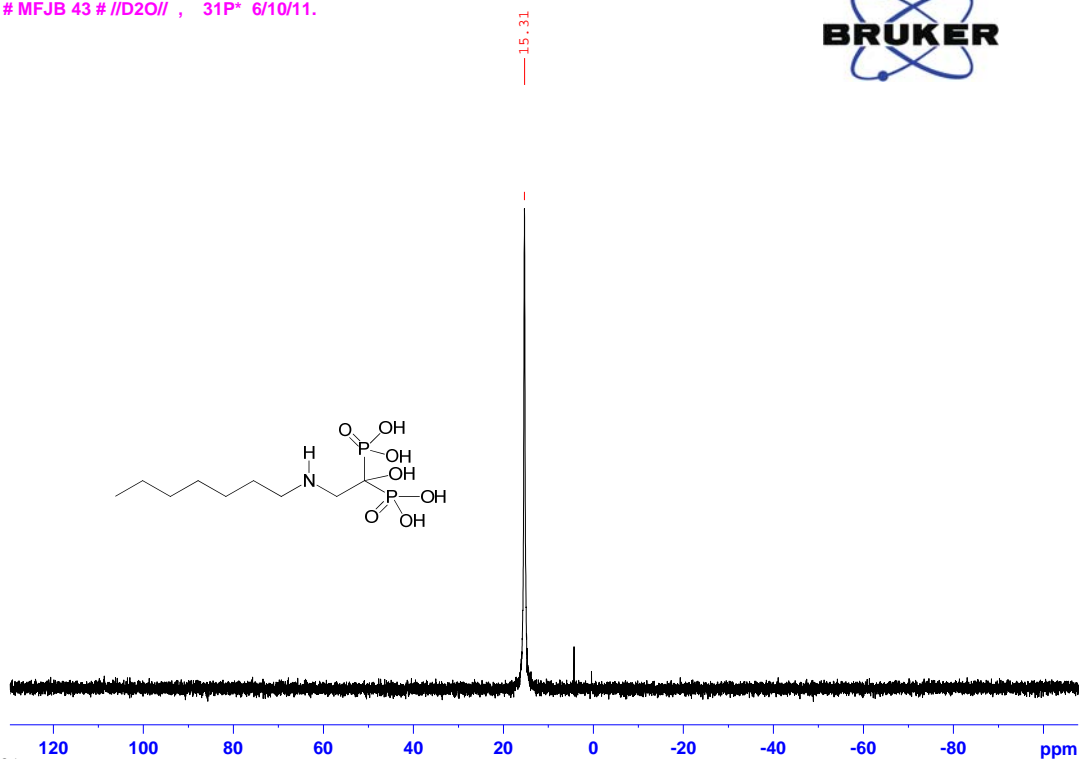
1D TopSPIN Multiplet Lines Table

Number	Position [ppm]
1	71.3865
2	70.2937
3	69.1969



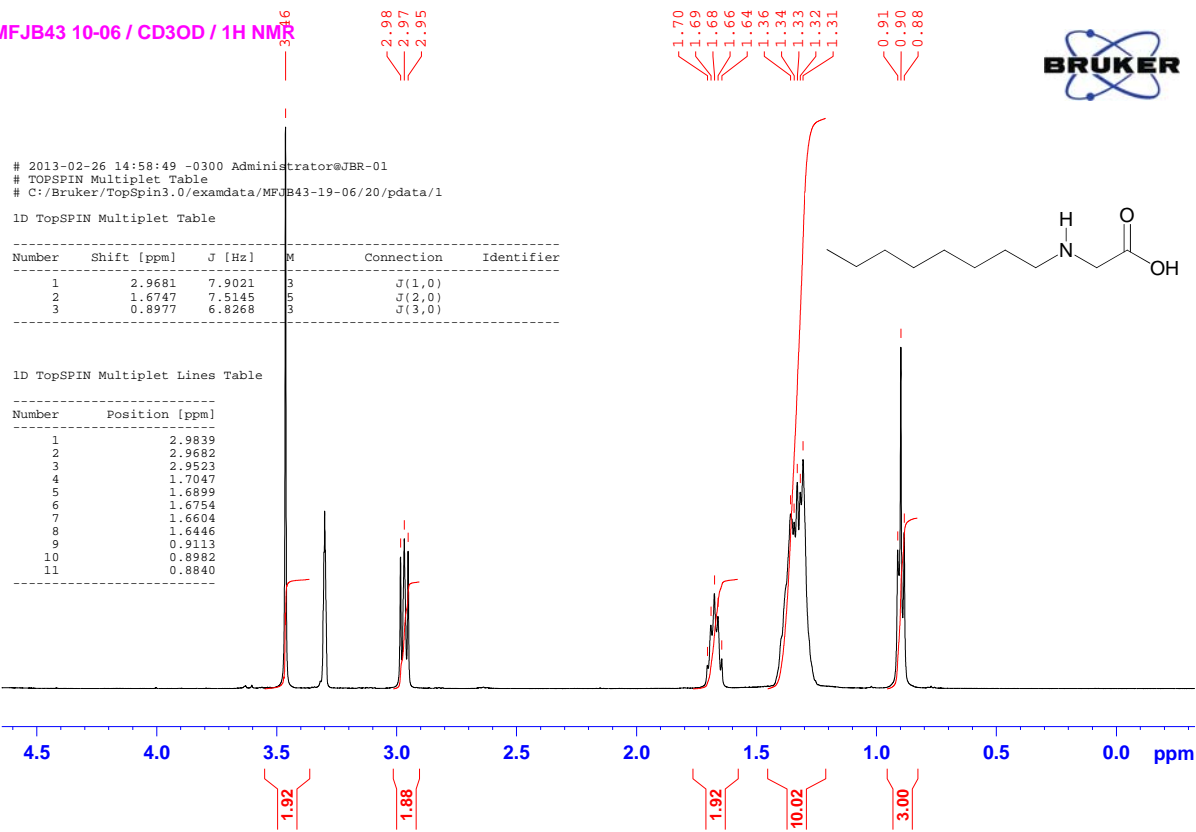
¹³C NMR spectrum of compound **29**.

#MFJB 43 #/D2O// , 31P* 6/10/11.



³¹P NMR spectrum of compound **29**.

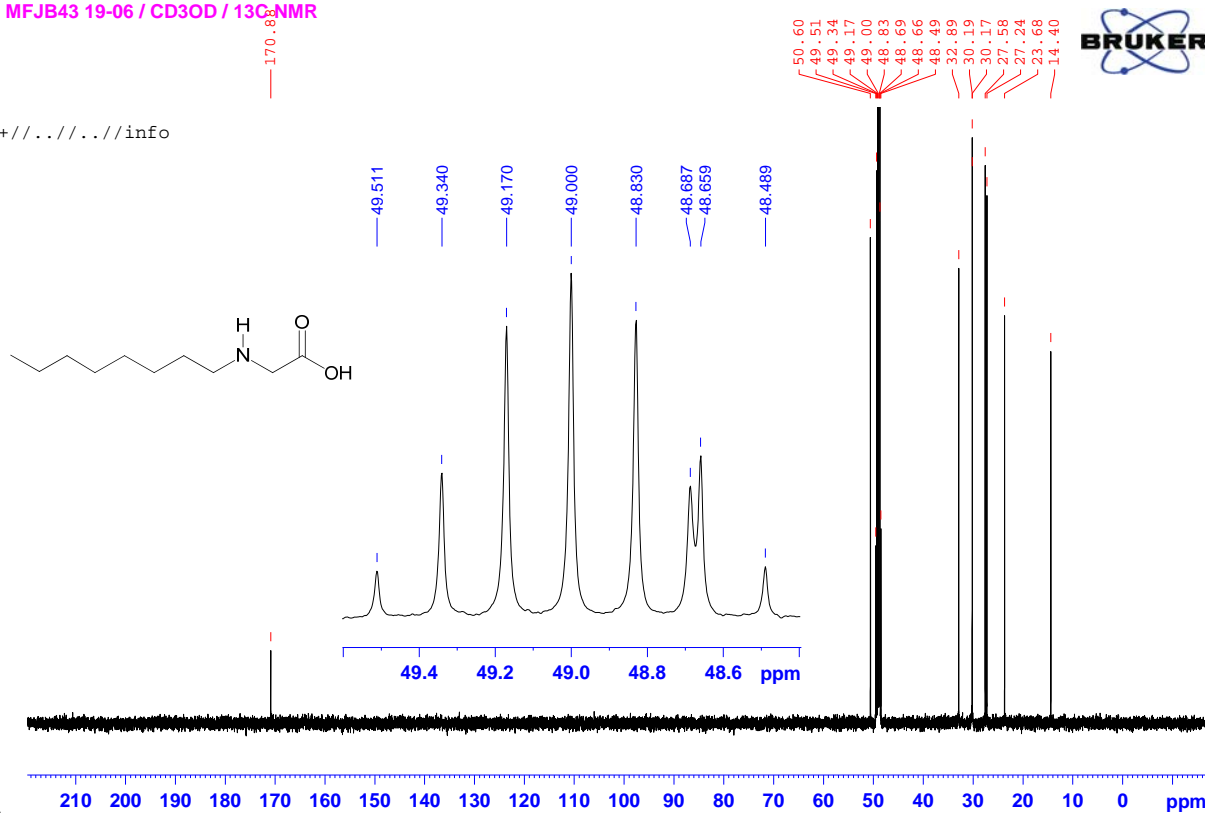
MFJB43 10-06 / CD3OD / 1H NMR



¹H NMR spectrum of compound **25**.

MFJB43 19-06 / CD3OD / ¹³C NMR

+//...//info



¹H NMR spectrum of compound 25.

MFJB54 #// ¹H NMR DMSO-d6

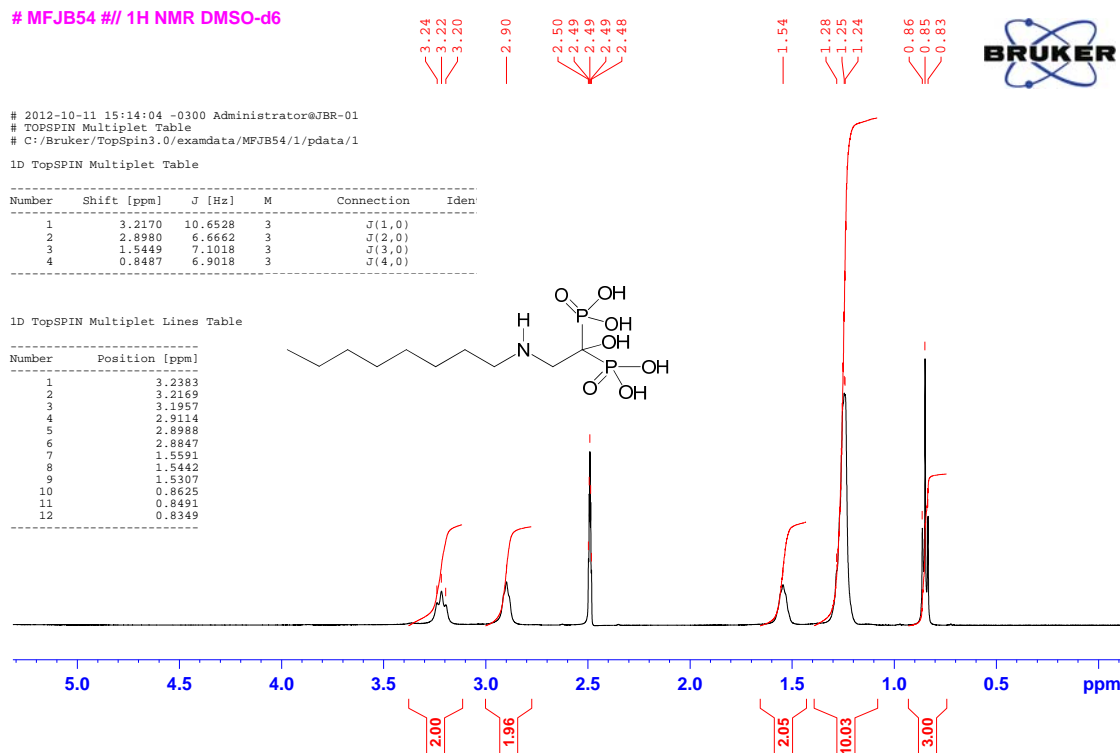
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1D TopSPIN Multiplet Table

Number	Shift [ppm]	J [Hz]	M	Connection	I den
1	3.2170	10.6528	3	J(1,0)	
2	2.8980	6.6662	3	J(2,0)	
3	1.5449	7.1018	3	J(3,0)	
4	0.8487	6.9018	3	J(4,0)	

1D TopSPIN Multiplet Lines Table

Number	Position [ppm]
1	3.2383
2	3.2169
3	3.1957
4	2.9114
5	2.8988
6	2.8847
7	1.5591
8	1.5442
9	1.5307
10	0.8625
11	0.8491
12	0.8349



¹H NMR spectrum of compound 30.

MFJB54 #/¹³C NMR /DMSO-d6/

70.46
69.34
68.38

49.83
47.35

40.00
39.83
39.67
39.50
39.33
39.17
39.00

31.14
28.48
28.46
25.85
25.58
22.05

13.93



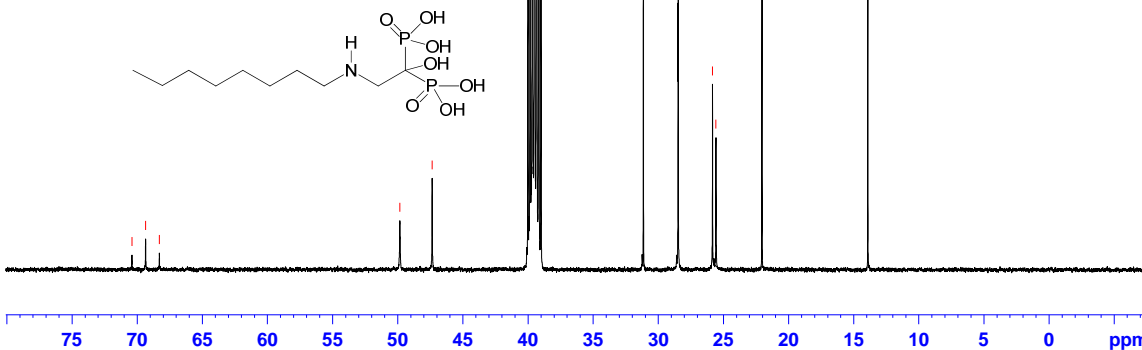
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Number	Shift [ppm]	J [Hz]	M	Connection	Identifier
1	69.3502	132.2910	3	J(1,0)	

1D TopSPIN Multiplet Lines Table

Number	Position [ppm]
1	70.4021
2	69.3478
3	68.2982



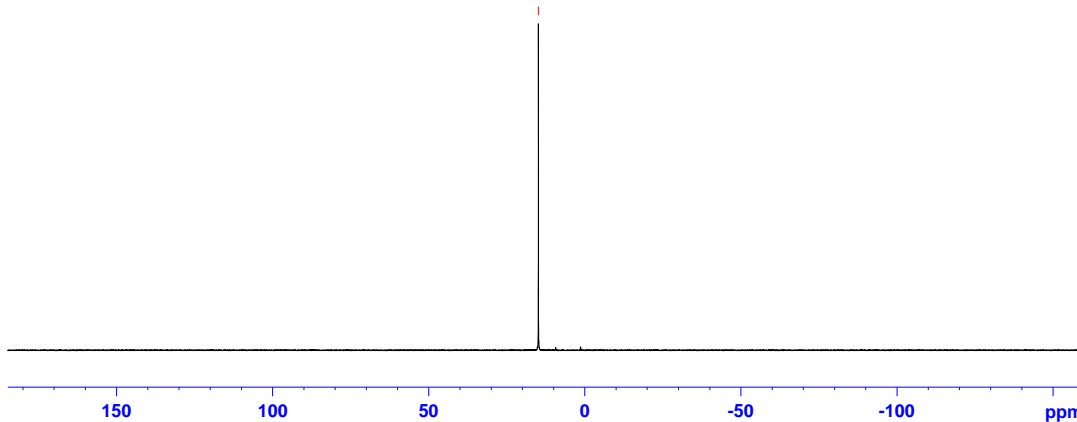
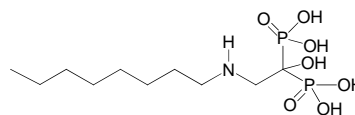
¹³C NMR spectrum of compound 30.

MFJB54 #/³¹P NMR DMSO

14.85

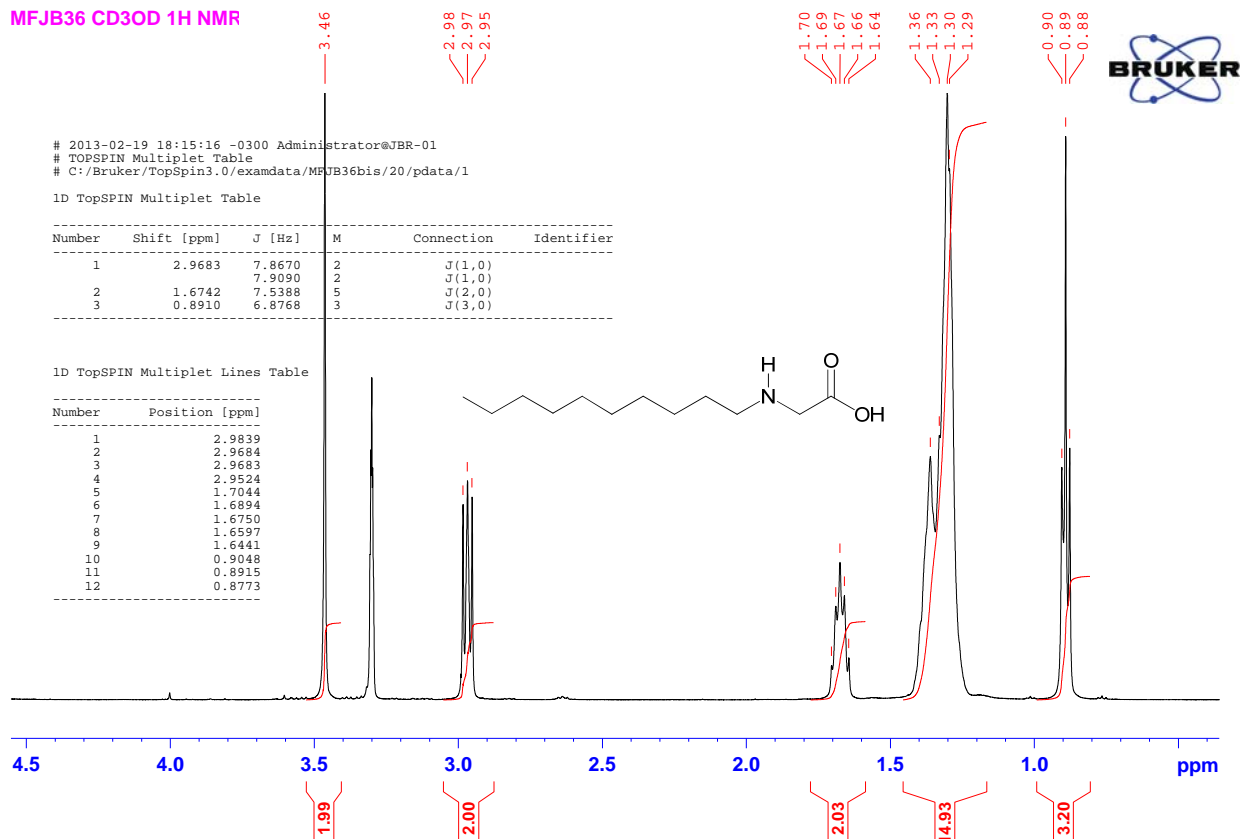


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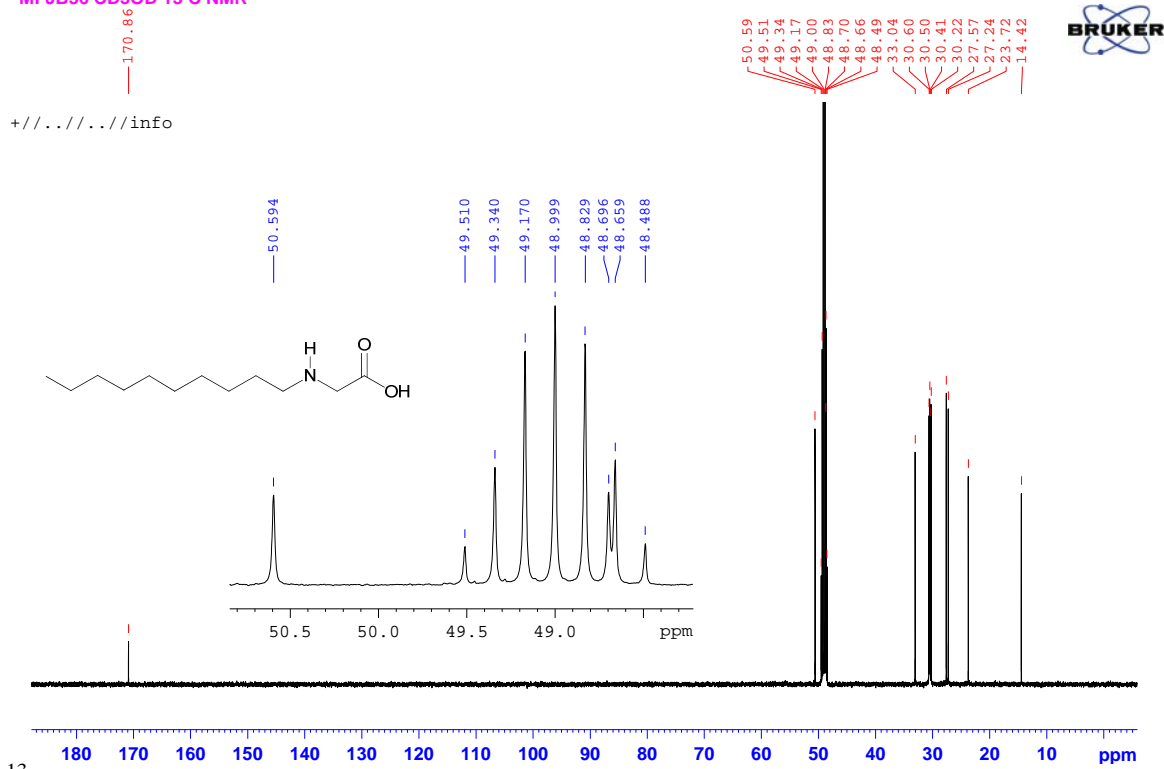
³¹P NMR spectrum of compound 30.

MFJB36 CD3OD 1H NMR



¹H NMR spectrum of compound 26.

MFJB36 CD3OD 13 C NMR



¹³C NMR spectrum of compound 26.

MFJB 37 # ¹H NMR / DMSO-d₆/



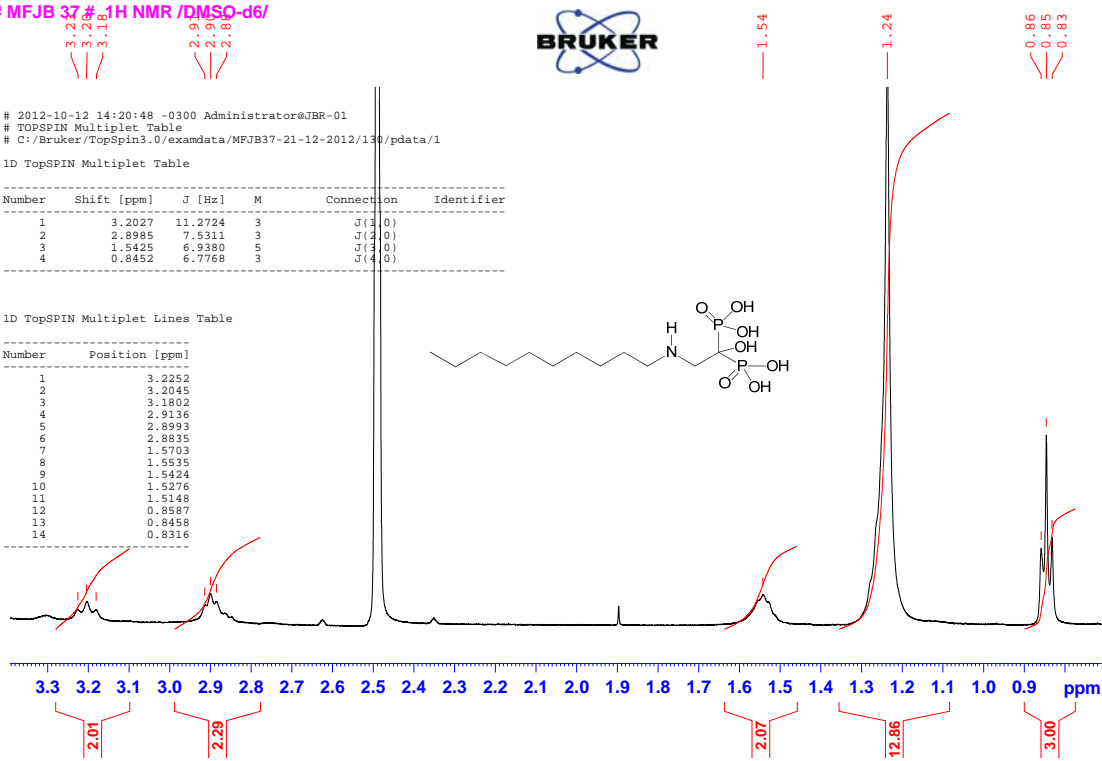
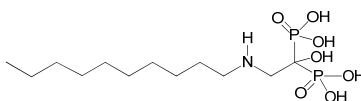
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1D TopSPIN Multiplet Table

Number	Shift [ppm]	J [Hz]	M	Connection	Identifier
1	3.2027	11.2724	3	J(1,0)	
2	2.8985	7.5311	3	J(2,0)	
3	1.5425	6.9380	5	J(3,0)	
4	0.8452	6.7768	3	J(4,0)	

1D TopSPIN Multiplet Lines Table

Number	Position [ppm]
1	3.2252
2	3.2045
3	3.1802
4	2.9136
5	2.8993
6	2.8835
7	1.5703
8	1.5535
9	1.5424
10	1.5276
11	1.5148
12	0.8587
13	0.8458
14	0.8316



¹H NMR spectrum of compound **31**.

MFJB37 // DMSO // ¹³C NMR



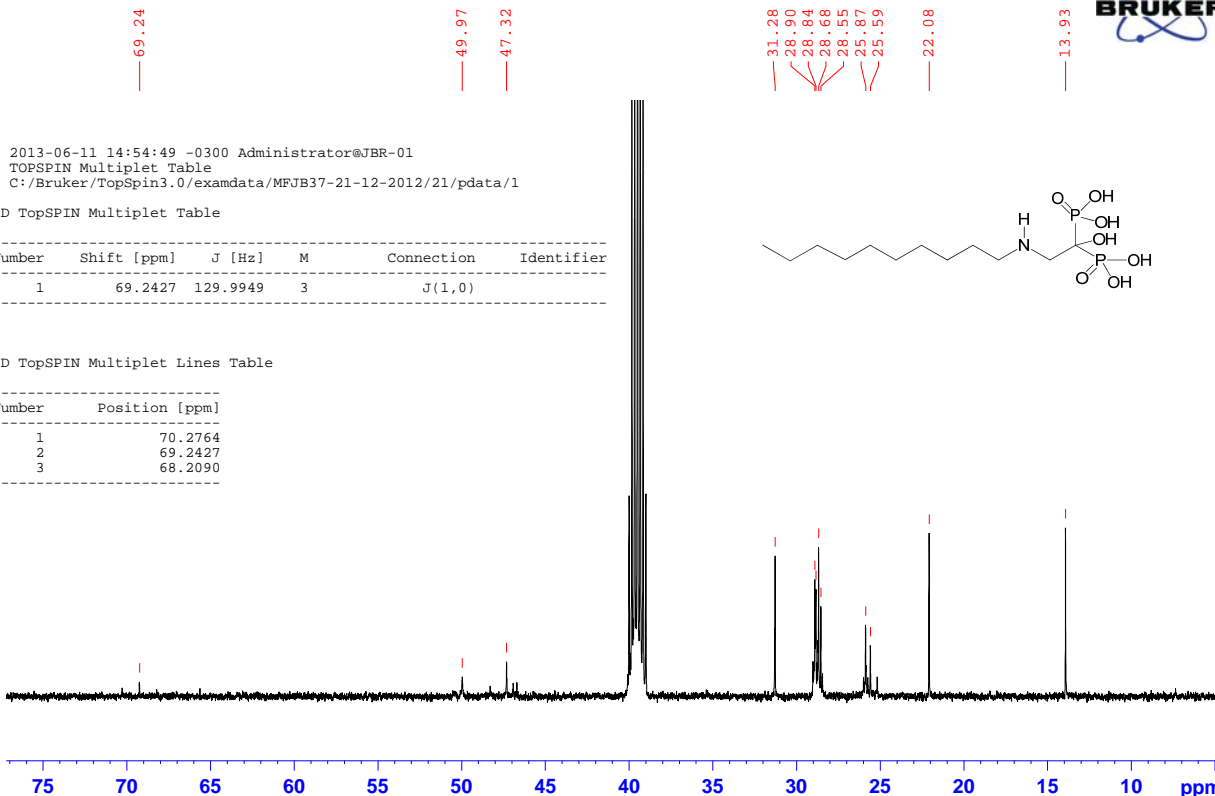
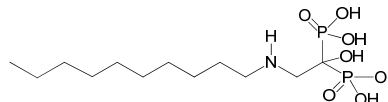
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1D TopSPIN Multiplet Table

Number	Shift [ppm]	J [Hz]	M	Connection	Identifier
1	69.2427	129.9949	3	J(1,0)	

1D TopSPIN Multiplet Lines Table

Number	Position [ppm]
1	70.2764
2	69.2427
3	68.2090

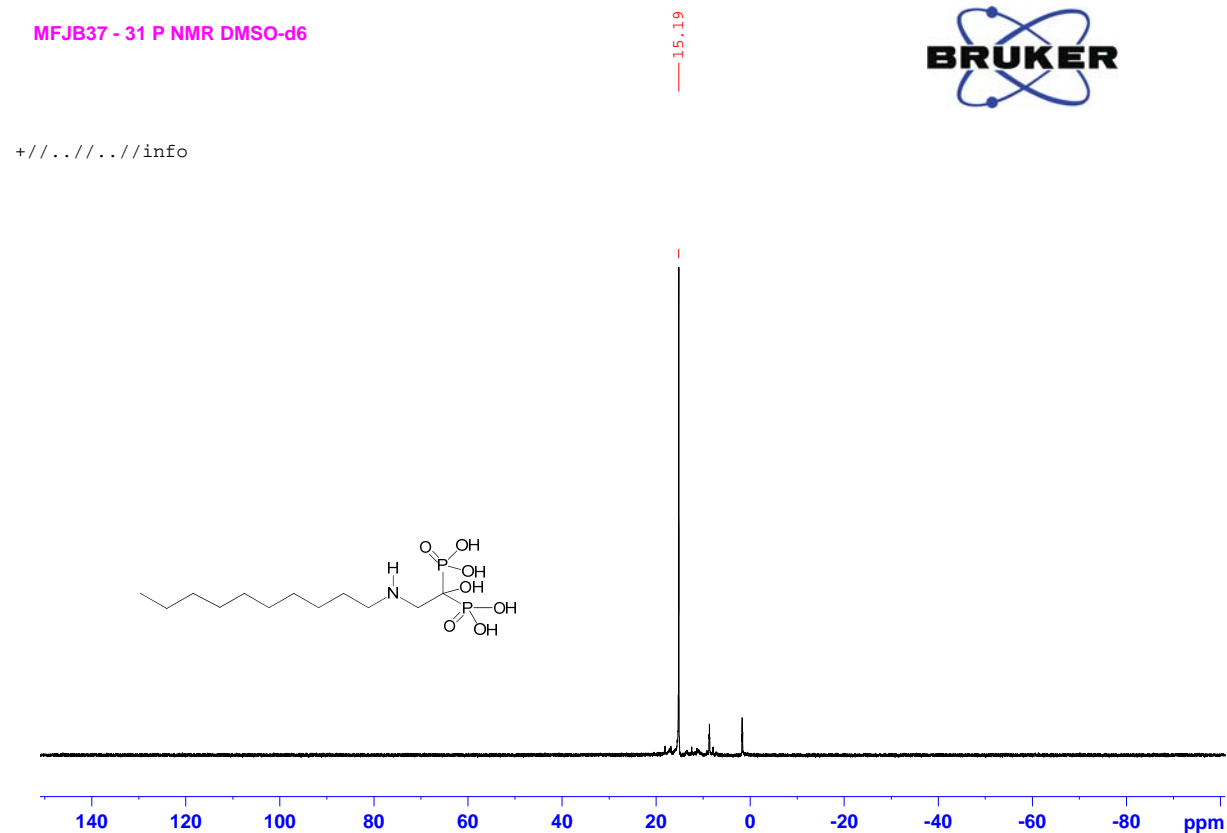


¹³C NMR spectrum of compound **31**.

MFJB37 - 31 P NMR DMSO-d6

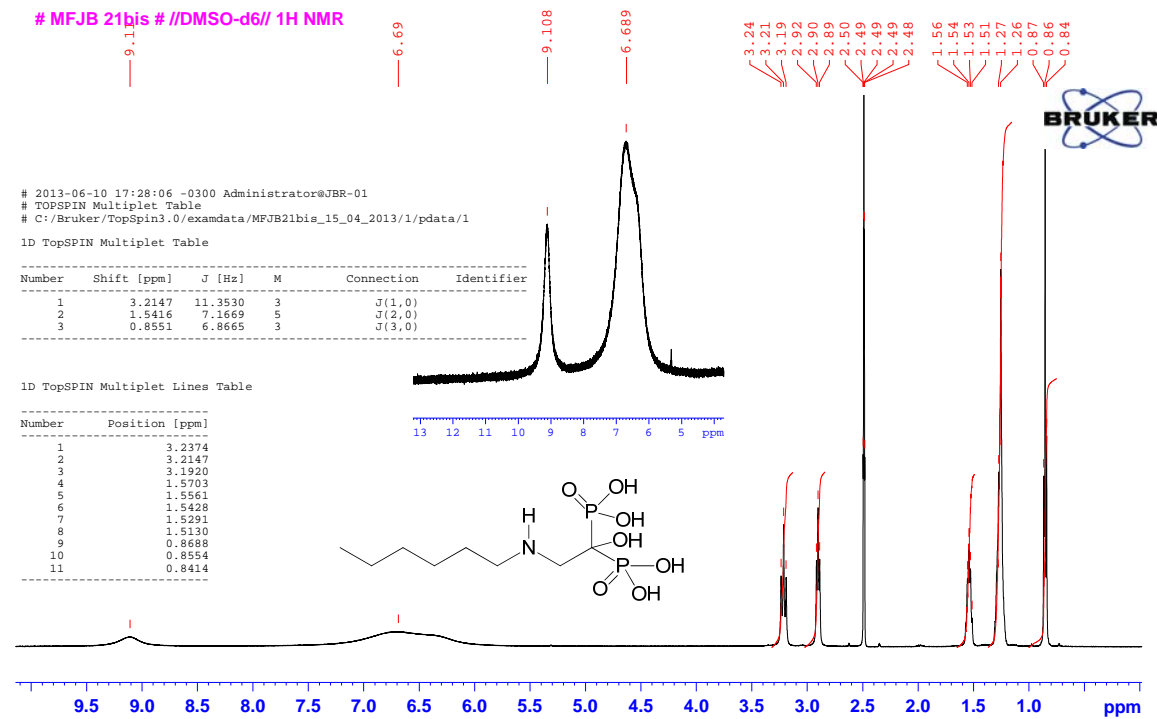


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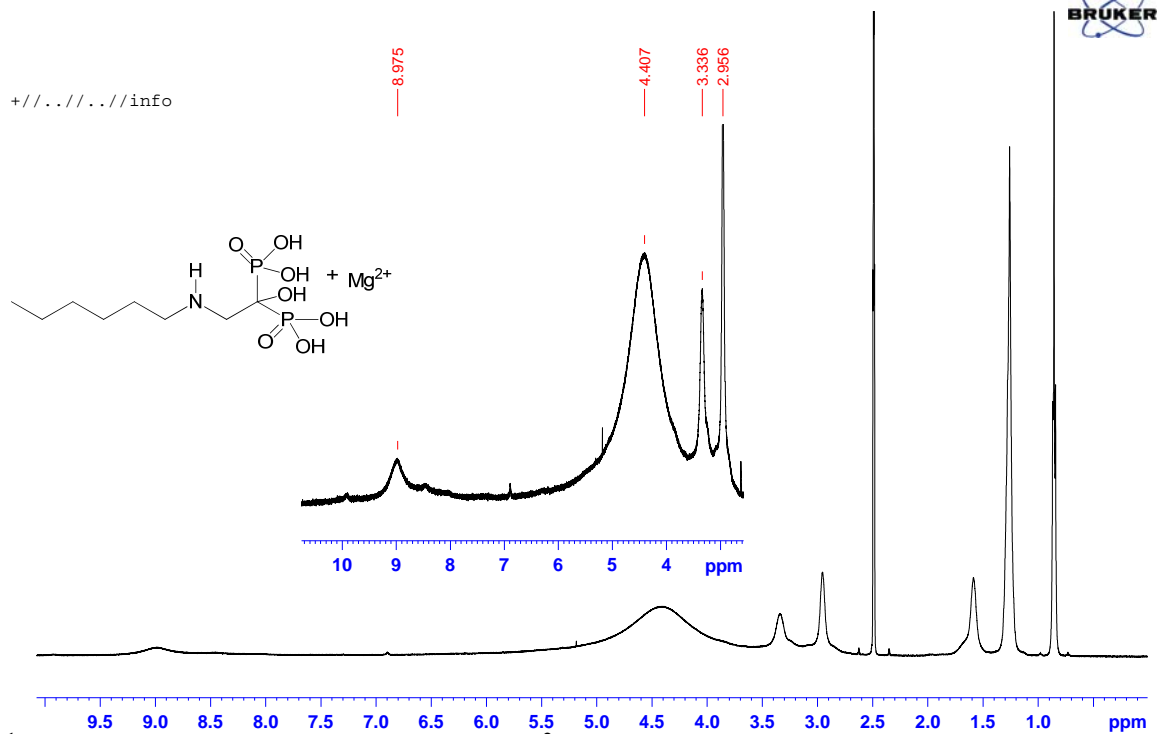
³¹P NMR spectrum of compound 31.

MFJB 21bis # //DMSO-d6// 1H NMR



¹H NMR spectrum of compound 28 in anhydrous DMSO-d₆.

MFJB 21 +Mg # //DMSO-d6// 1H NMR



¹H NMR spectrum of compound 28 + Mg²⁺ in anhydrous DMSO-d₆.

BR25bis # //DMSO-d6// 1H NMR

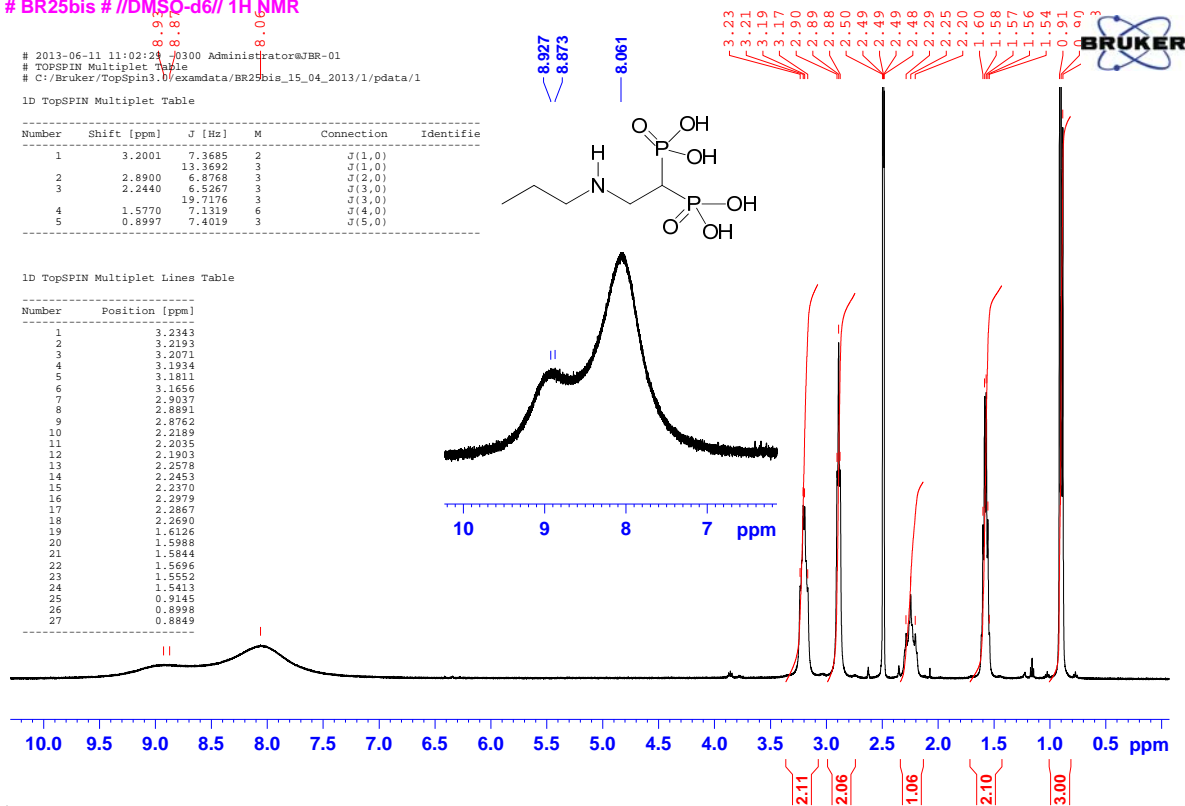
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Number	Shift [ppm]	J [Hz]	M	Connection	Identifie
1	3.2001	7.3685	2	J(1,0)	
2	2.8900	13.3692	3	J(1,0)	
3	2.2440	6.8768	3	J(2,0)	
4	1.5770	6.5267	3	J(3,0)	
5	0.8997	19.7176	3	J(3,0)	
		7.1319	6	J(4,0)	
		7.4019	3	J(5,0)	

ID TopSPIN Multiplet Lines Table

Number	Position [ppm]
1	3.2243
2	3.2193
3	3.2071
4	3.1934
5	3.1811
6	3.1656
7	2.9037
8	2.8921
9	2.8762
10	2.2189
11	2.2035
12	2.1903
13	2.2578
14	2.2453
15	2.2370
16	2.2979
17	2.2867
18	2.2690
19	1.6126
20	1.5988
21	1.5848
22	1.5696
23	1.5552
24	1.5413
25	0.9145
26	0.8998
27	0.8849



¹H NMR spectrum of compound 33 in anhydrous DMSO-d₆.

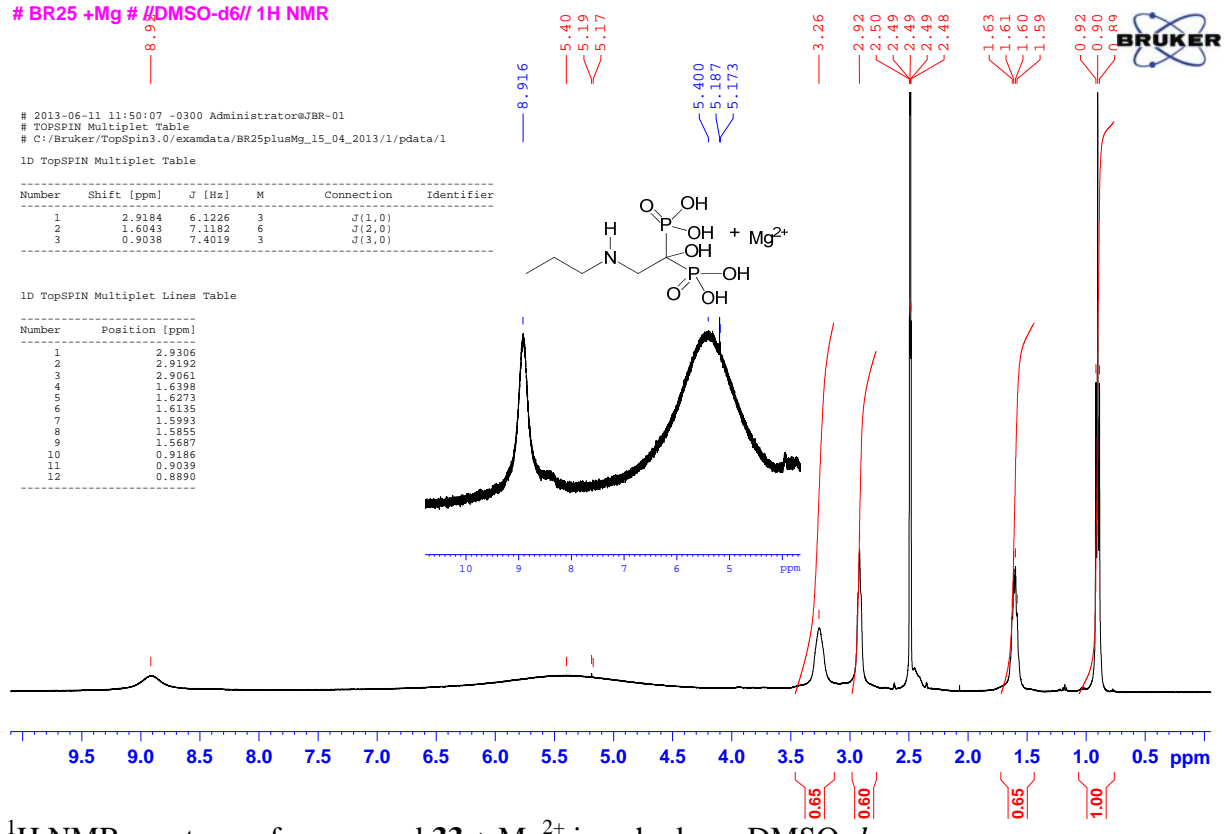
BR25 +Mg # DMSO-d6// 1H NMR

2013-06-11 11:50:07 -0300 Administrator@BR-01
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Number	Shift [ppm]	J [Hz]	M	Connection	Identifier
1	2.9184	6.1226	3	J(1,0)	
2	1.6043	7.1182	6	J(2,0)	
3	0.9038	7.4019	3	J(3,0)	

ID TopSPIN Multiplet Lines Table

Number	Position [ppm]
1	2.9306
2	2.9192
3	2.9061
4	1.6398
5	1.6273
6	1.6135
7	1.5993
8	1.5855
9	1.5687
10	0.9186
11	0.9039
12	0.8890



¹H NMR spectrum of compound **33** + Mg²⁺ in anhydrous DMSO-d₆.

Table 2. Cartesian coordinates of compounds **12a** and **27a**, as calculated by B3LYP/6-311+G(d,p) with SCRF=PCM (water)

Compound 12a

Charge= 0

Conformer 1

Energy: -1509.2521684 H

C	-0.334544	0.346275	-0.480262
C	-1.700473	0.987886	-0.164000
N	-2.805636	0.148107	-0.676680
P	1.103209	1.408278	0.003429
P	-0.148401	-1.322221	0.312363
O	1.011953	1.434752	1.632389
O	1.007123	2.812329	-0.515676
O	2.364375	0.604824	-0.402304
O	0.024996	-1.118621	1.808830
O	1.005071	-2.078731	-0.387974
O	-1.517988	-2.082862	-0.057958
H	-0.243700	0.209646	-1.563621
H	-1.830339	1.076733	0.917430
H	-1.739328	1.999558	-0.583254
C	-4.127763	0.579924	-0.197134
H	-2.797702	0.188798	-1.693442
Mg	2.718612	-1.255415	-0.843654
H	-2.218639	-1.374659	-0.285484
H	0.750368	0.541381	1.966334
H	-4.897771	-0.030234	-0.671096
H	-4.329945	1.635879	-0.416329
H	-4.186506	0.432238	0.883114

Conformer 2

Energy: -1509.2512462 H

C	0.215972	0.530842	-0.591900
C	1.290829	1.256058	0.241465
N	2.641140	0.903155	-0.251716
P	0.368476	-1.312564	-0.478481
P	-1.523014	1.041890	-0.216187
O	0.204285	-1.707452	1.013034
O	1.897407	-1.589231	-0.909727
O	-0.610514	-1.955491	-1.438633
O	-2.358888	0.242355	-1.370823
O	-1.754139	2.515181	-0.375053
O	-1.895820	0.435109	1.159774
H	0.358994	0.785064	-1.648238
H	1.123063	2.338875	0.211046
H	1.232466	0.945259	1.287139
H	2.786261	1.365209	-1.146428
C	3.718958	1.302067	0.666128

H	2.429022	-0.759618	-0.665494
H	-1.983050	-0.656022	-1.517489
Mg	-1.194980	-1.042752	2.202257
H	4.681976	1.090163	0.199407
H	3.646341	0.717110	1.585412
H	3.681572	2.367443	0.926847

Conformer 3

Energy: -1509.2419860 H

C	0.505819	0.328366	-0.171611
C	1.772737	0.926491	0.516650
N	3.055409	0.414415	0.039912
P	0.266002	-1.464751	0.237374
P	-1.044638	1.241301	0.234627
O	-0.966267	-1.949418	-0.566805
O	-0.128430	-1.434762	1.823099
O	1.525058	-2.268361	0.072942
O	-0.741581	2.822389	-0.025344
O	-1.346295	1.056471	1.704177
O	-2.129660	0.818016	-0.780240
Mg	-2.484602	-1.025036	-1.353296
H	0.619889	0.380295	-1.258864
H	1.768222	2.010391	0.374442
H	1.707359	0.747389	1.592835
H	3.038654	-0.601216	0.088807
C	3.419667	0.836084	-1.313241
H	-0.675983	-0.641796	2.030908
H	-0.854511	3.083860	-0.948812
H	4.394526	0.414638	-1.568581
H	3.507296	1.925952	-1.346277
H	2.709496	0.531432	-2.097727

Conformer 4

Energy: -1509.2388717 H

C	-0.391115	0.244051	-0.324914
C	-1.788607	0.722828	0.127969
N	-2.850289	0.169758	-0.712582
P	0.931823	1.429693	0.192976
P	-0.081547	-1.535885	0.080950
O	0.817858	1.851494	1.630765
O	0.645737	2.716599	-0.795360
O	2.280988	0.880570	-0.307632
O	0.052416	-1.603656	1.718219
O	1.323483	-1.917704	-0.417480
O	-1.241272	-2.374130	-0.385601
H	-0.369444	0.271906	-1.420985
H	-1.931205	0.490447	1.196386
H	-1.837648	1.813236	0.045431
H	-2.772578	-0.844544	-0.697814
C	-4.181896	0.575828	-0.264593

H	0.251007	3.454105	-0.313956
H	-0.791700	-1.780114	2.152272
Mg	2.950774	-0.896462	-0.698556
H	-4.938909	0.092505	-0.885909
H	-4.296881	1.658358	-0.376540
H	-4.388005	0.324588	0.788913

Compound 27a

Charge= -1

Conformer 1

Energy: -1584.0230468 H

C	0.396725	0.270074	-0.278165
C	1.766716	0.735120	0.262210
N	2.836759	0.067745	-0.489066
P	0.034652	-1.487390	0.286516
P	-0.997392	1.437601	0.278887
O	-1.312452	-1.909819	-0.364202
O	-0.197755	-1.319746	1.886564
O	1.187295	-2.432061	0.041173
O	-0.581134	2.875507	0.009094
O	-1.217132	1.064856	1.767976
O	-2.236902	1.005853	-0.598276
Mg	-2.749904	-0.795600	-1.036748
O	0.457380	0.282308	-1.715806
H	1.856313	1.811398	0.089534
H	1.827073	0.565545	1.346037
H	2.818954	-0.925344	-0.265967
C	4.165704	0.625643	-0.242833
H	-0.660767	-0.431057	2.034064
H	1.406989	0.146399	-1.904827
H	4.907756	0.062430	-0.813068
H	4.458683	0.604853	0.818203
H	4.198359	1.665386	-0.580046

Conformer 2

Energy: -1584.0202747 H

C	0.303676	-0.342938	-0.288856
C	1.629815	-0.947481	0.211290
N	2.785676	-0.253612	-0.394306
P	-1.176440	-1.439421	0.223795
P	0.187548	1.431947	0.282526
O	-0.929415	-2.027796	1.606646
O	-1.220589	-2.424455	-0.960483
O	-2.437810	-0.491159	0.205368
O	0.271077	1.505471	1.788575
O	-1.040777	2.124441	-0.364590
O	1.482976	2.125489	-0.425793
O	0.310305	-0.347797	-1.736563

Mg	-2.796313	1.289537	-0.389620
H	1.693565	-0.845056	1.295590
H	1.648436	-2.020937	-0.023209
C	4.071860	-0.689349	0.161333
H	2.767323	-0.446623	-1.392316
H	2.207720	1.430744	-0.421945
H	-0.181058	-1.165855	-1.958478
H	4.885416	-0.206576	-0.383293
H	4.212662	-1.778103	0.106566
H	4.137097	-0.389590	1.209989

Conformer 3

Energy: -1584.0196418 H

C	0.242957	-0.468839	0.426058
C	1.269162	-1.039410	-0.563616
N	2.659591	-0.722149	-0.169050
P	0.344734	1.412576	0.487096
P	-1.516774	-1.159157	0.068793
O	-0.111864	1.955173	-0.901896
O	1.941770	1.697536	0.597785
O	-0.362756	2.012741	1.676269
O	-2.105457	-1.215582	1.488623
O	-1.356142	-2.500376	-0.642793
O	-2.262269	-0.114832	-0.843940
O	0.583404	-0.966891	1.738694
Mg	-1.796326	1.504924	-1.737258
H	1.113021	-2.120662	-0.638840
H	1.097381	-0.611907	-1.555474
H	2.849206	-1.201515	0.707297
C	3.647876	-1.138799	-1.171743
H	2.442893	0.875478	0.270536
H	-0.285121	-1.101191	2.167566
H	4.653096	-0.953160	-0.789598
H	3.512827	-0.550044	-2.082085
H	3.562611	-2.202181	-1.433409

Conformer 4

Energy: -1584.0171791 H

C	0.356424	0.276183	-0.400729
C	1.736185	0.846605	-0.013982
N	2.869745	0.112917	-0.580927
P	0.125496	-1.465523	0.257137
P	-1.016466	1.416111	0.288822
O	-1.256004	-1.962489	-0.243761
O	0.045051	-1.209559	1.857338
O	1.280357	-2.388568	-0.044092
O	-0.699914	2.828700	-0.184052
O	-1.001798	1.173977	1.818314
O	-2.348405	0.872157	-0.354925
Mg	-2.806024	-0.938999	-0.798478

O	0.208771	0.179693	-1.832583
H	1.782396	1.880860	-0.373112
H	1.785637	0.899002	1.086568
H	2.763001	-0.874438	-0.359977
C	4.150652	0.605840	-0.082784
H	-0.405305	-0.318160	2.028873
H	0.237109	1.079858	-2.182805
H	4.960953	-0.007505	-0.484350
H	4.228822	0.601050	1.018171
H	4.311975	1.635028	-0.419471

Conformer 5

Energy: -1584.0153643 H

C	-0.327937	-0.359258	-0.554796
C	-1.458730	-0.945915	0.310738
N	-2.753048	-0.286285	0.145289
P	-0.028242	1.519050	-0.412546
P	1.256190	-1.256674	-0.094290
O	-0.069393	1.828550	1.129921
O	-1.126065	2.181292	-1.235688
O	1.405510	1.742511	-0.962749
O	2.363463	-0.633638	-1.097920
O	1.194917	-2.750362	-0.272803
O	1.570053	-0.767824	1.353535
O	-0.622104	-0.618244	-1.947918
Mg	1.144637	0.872318	2.304205
H	-1.524104	-2.017986	0.054906
H	-1.182680	-0.893485	1.367643
H	-2.948271	-0.187475	-0.845730
C	-3.837427	-1.036344	0.777124
H	2.171067	0.361706	-1.145638
H	-0.995829	0.206219	-2.297356
H	-4.790888	-0.543222	0.574809
H	-3.691507	-1.051601	1.861558
H	-3.907786	-2.082795	0.435433