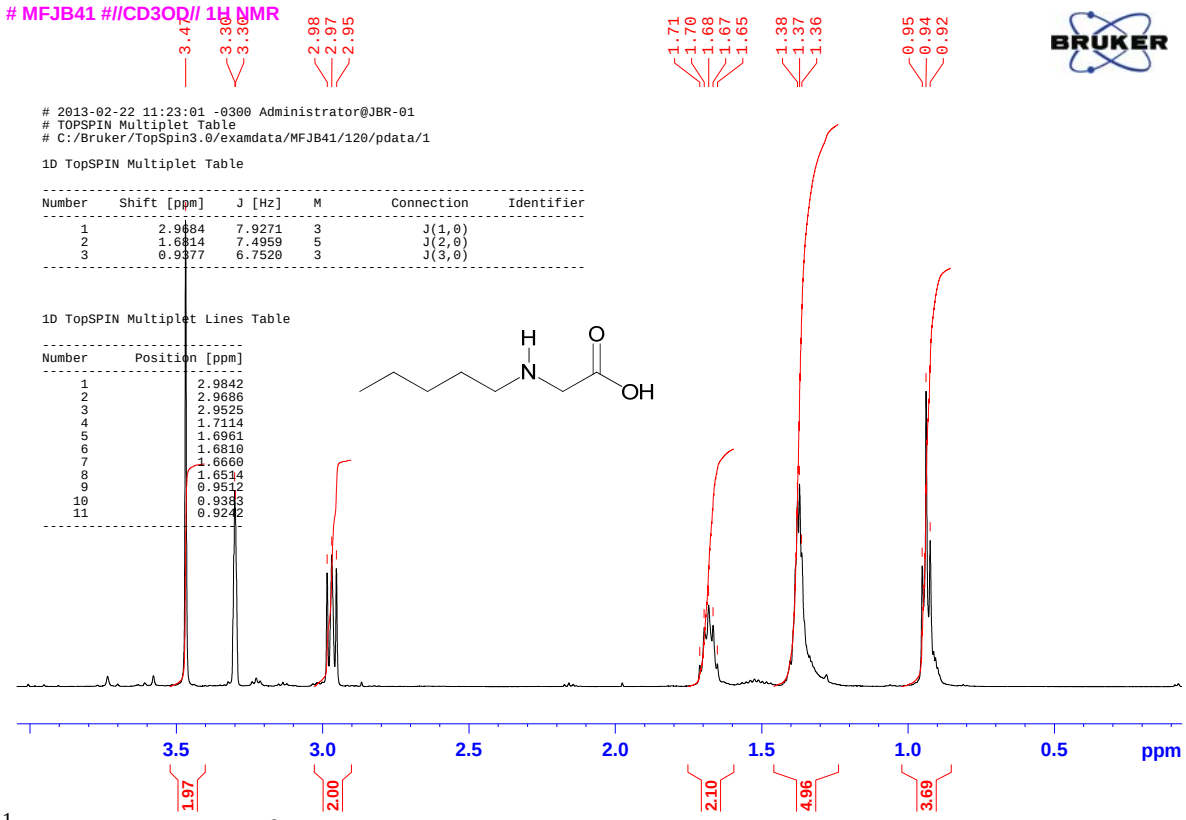
Supporting Information

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

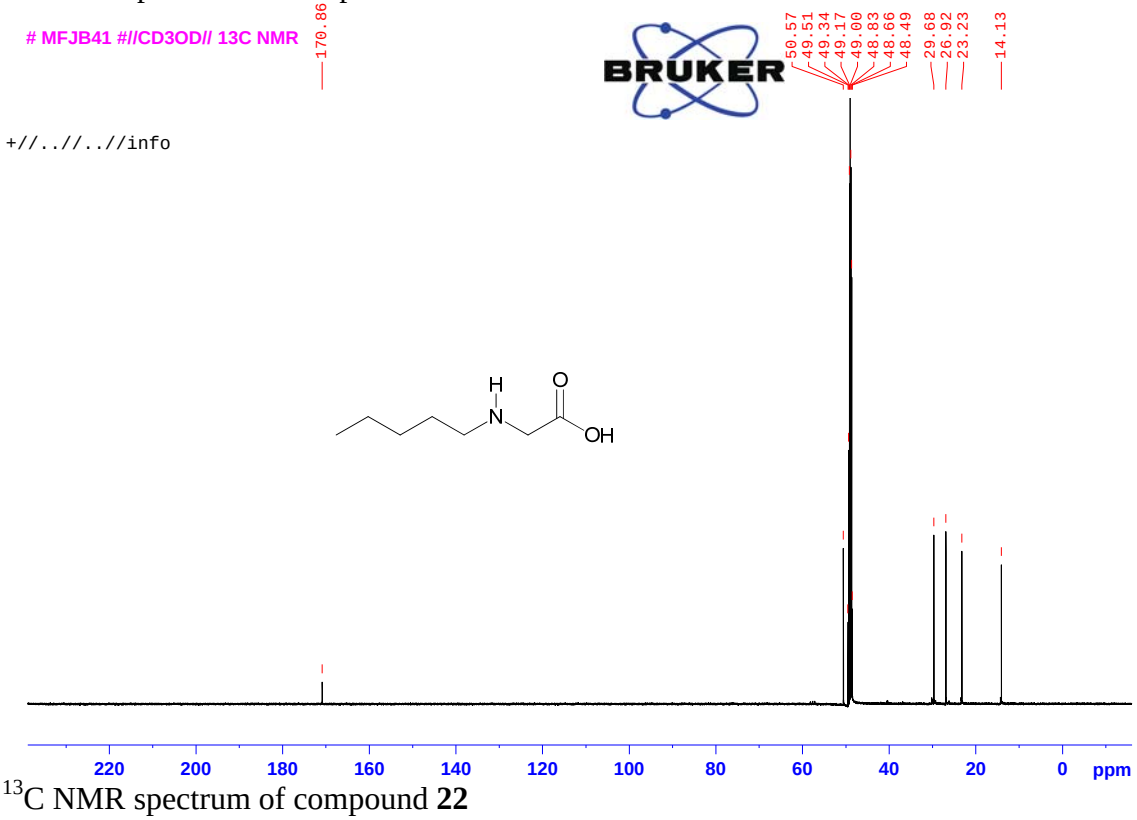
Mariana Ferrer-Casal,[a] Catherine Li,[b] Melina Galizzi,[b] Carlos A. Stortz,[c] Sergio H. Szajnman,[a] Roberto Docampo,[b] Silvia N. J. Moreno,[b] and Juan B. Rodriguez[a,*]

[a]Departamento de Química Orgánica and UMYMFOR (CONICET–FCEyN), Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Pabellón 2, Ciudad Universitaria, C1428EHA, Buenos Aires, Argentina, [b]Center for Tropical and Emerging Global Diseases and Department of Cellular Biology, University of Georgia, Athens, Georgia, 30602, USA, [c]Departamento de Química Orgánica and CIHIDECAR, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Pabellón 2, Ciudad Universitaria, C1428EHA, Buenos Aires, Argentina

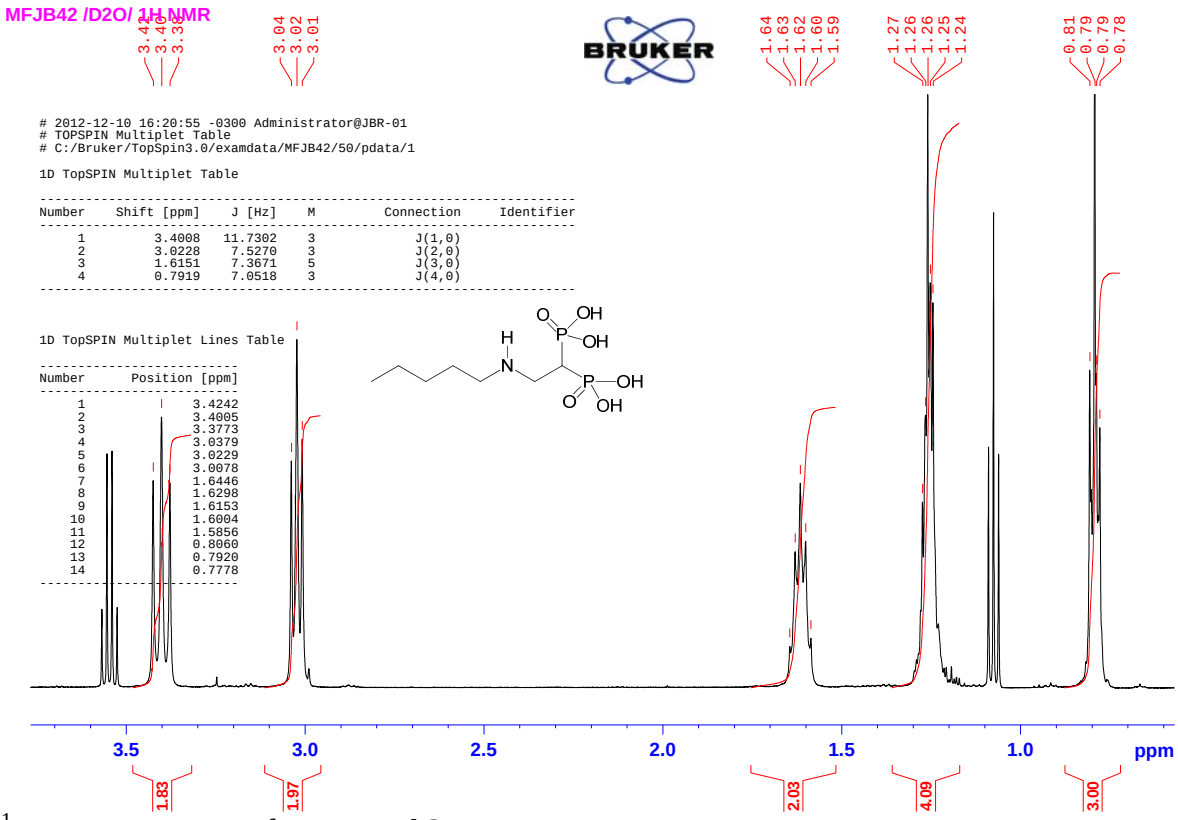
List of Contents



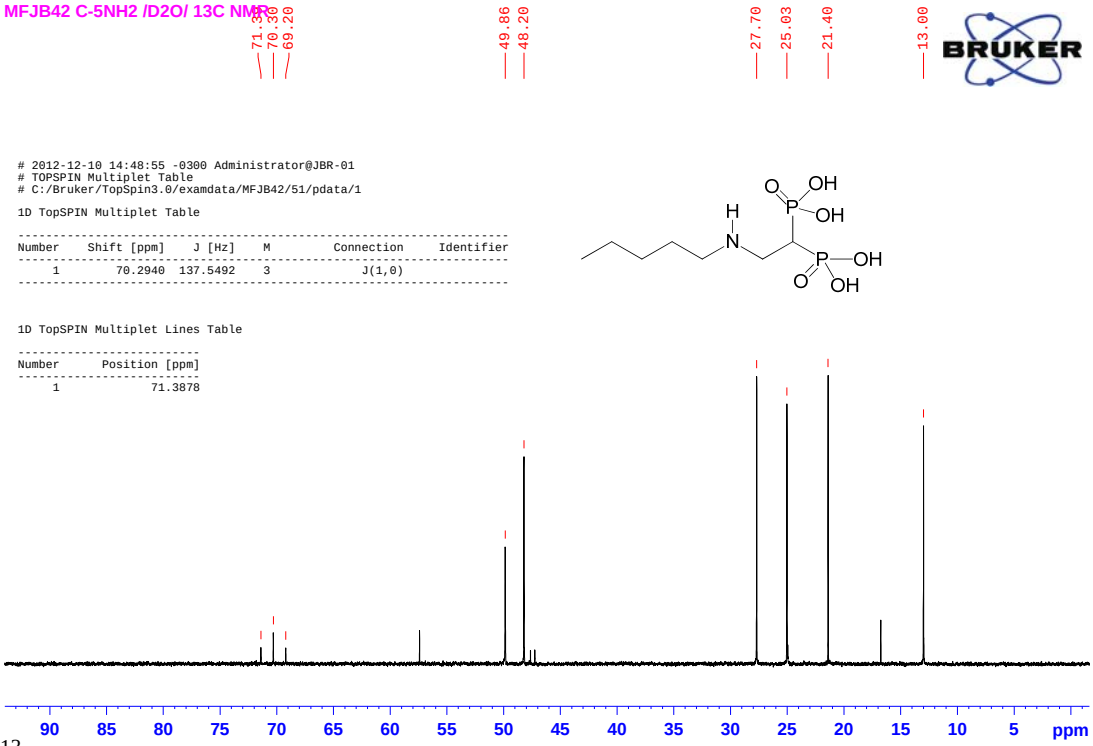
^{1}H NMR spectrum of compound **22**



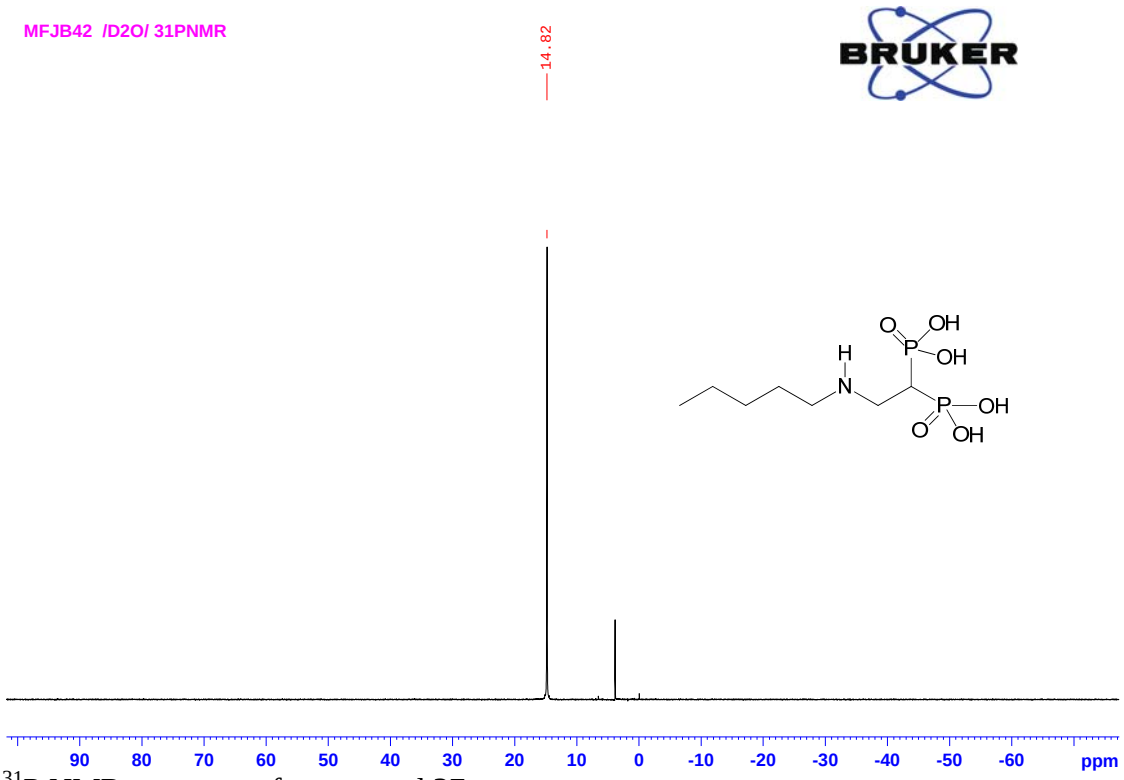
^{13}C NMR spectrum of compound **22**



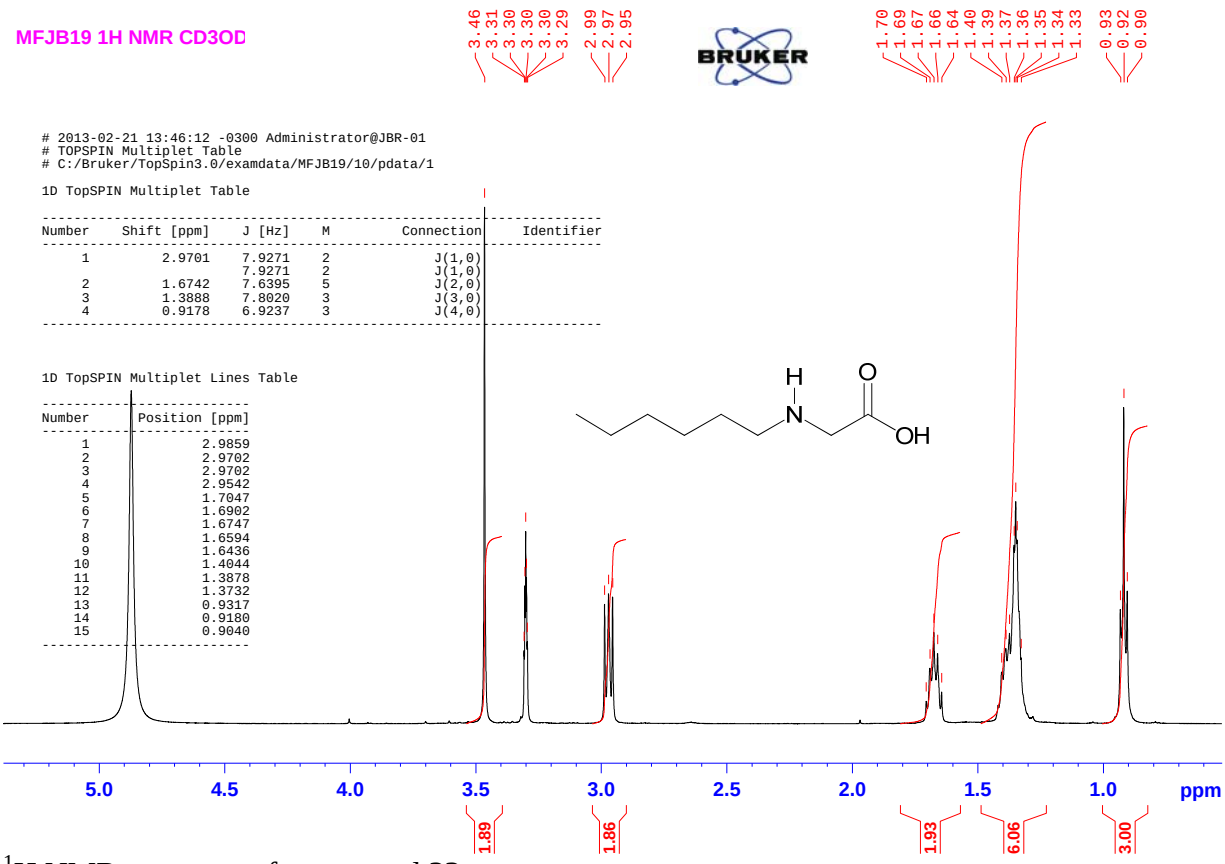
^{1}H NMR spectrum of compound **27**



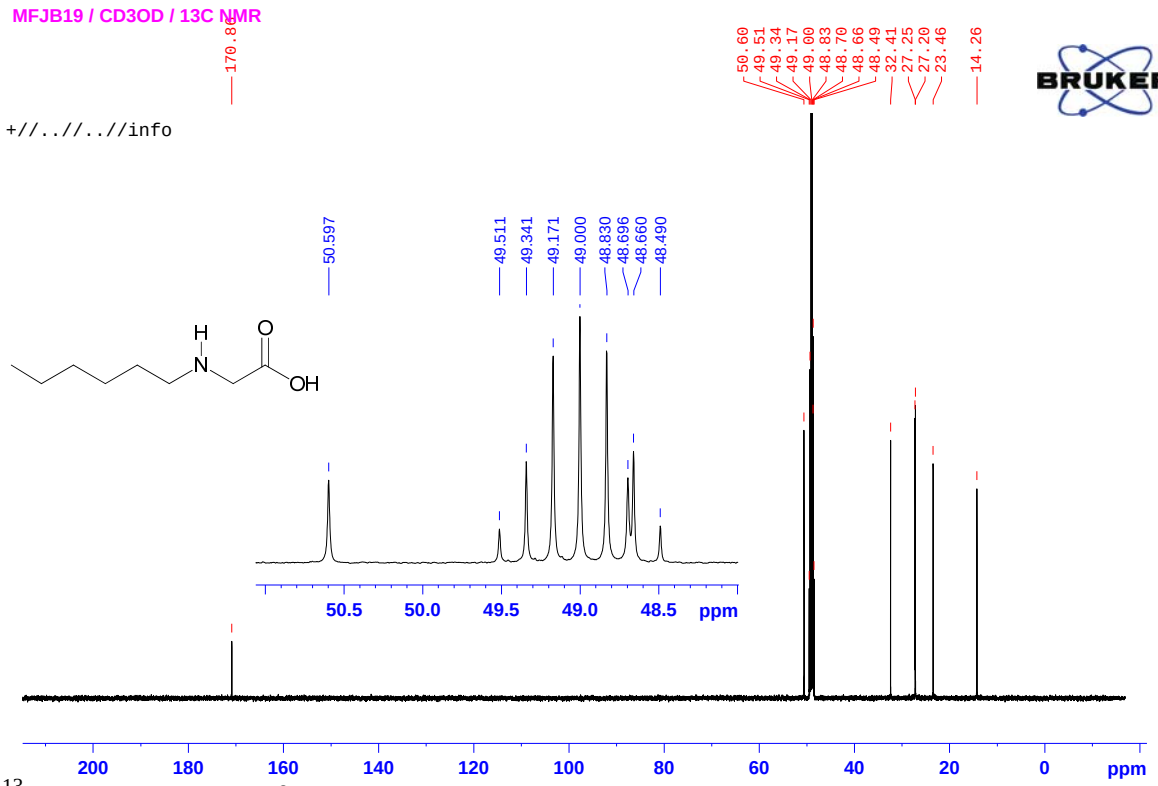
^{13}C NMR spectrum of compound **27**.



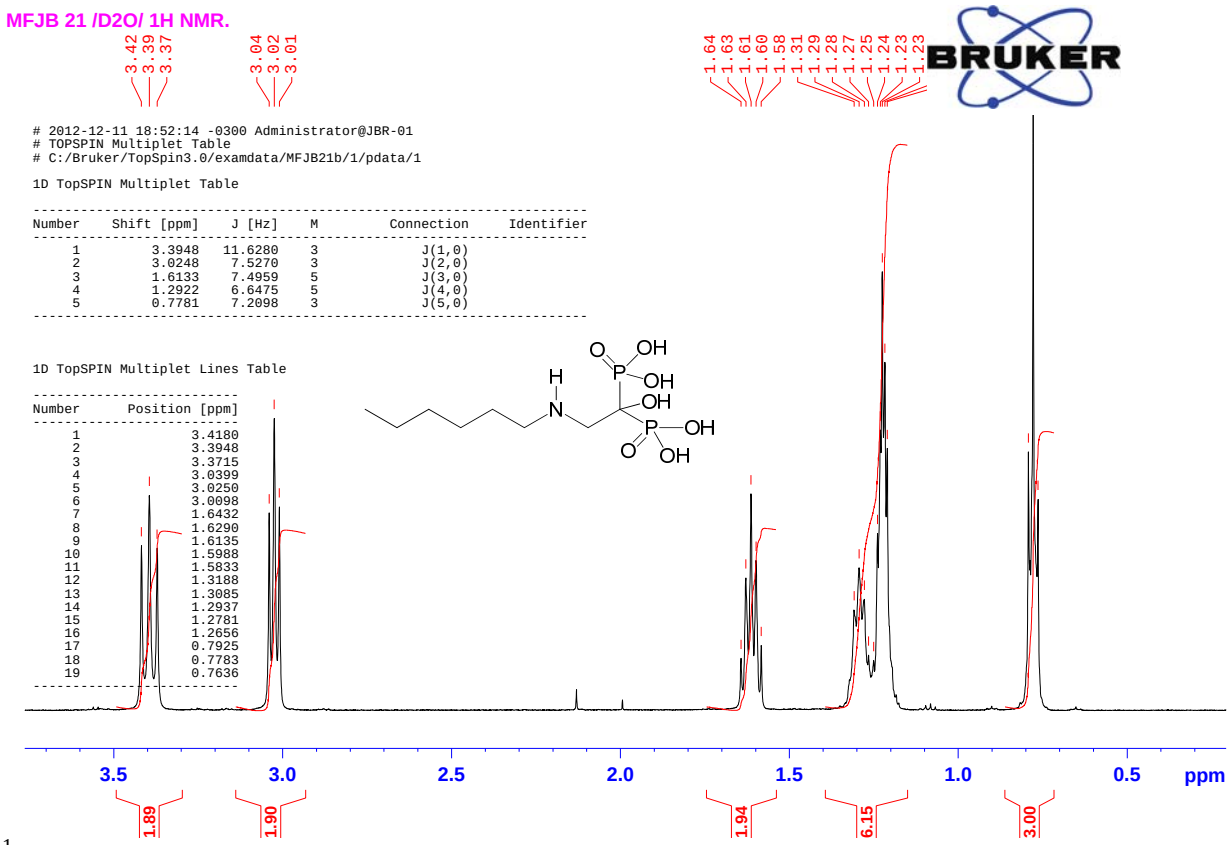
^{31}P NMR spectrum of compound **27**



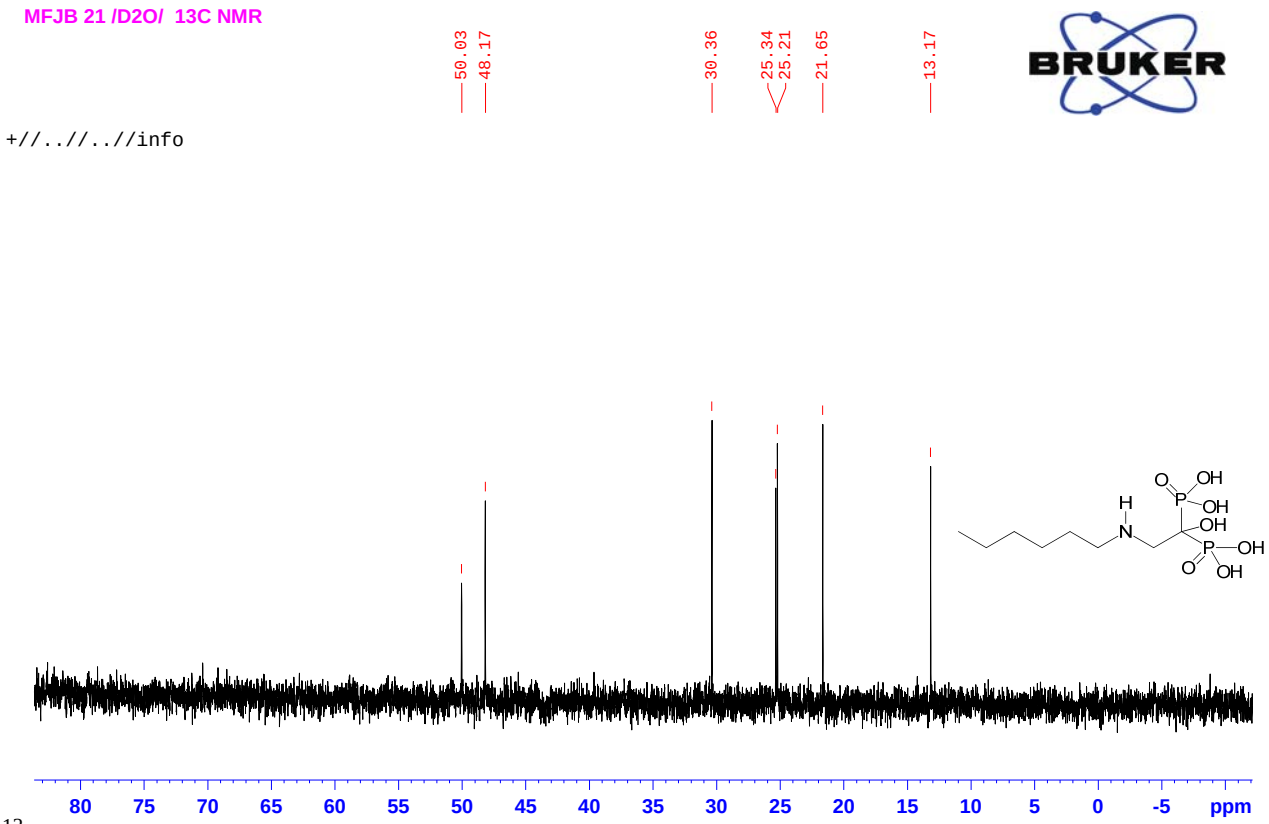
^{1}H NMR spectrum of compound **23**.



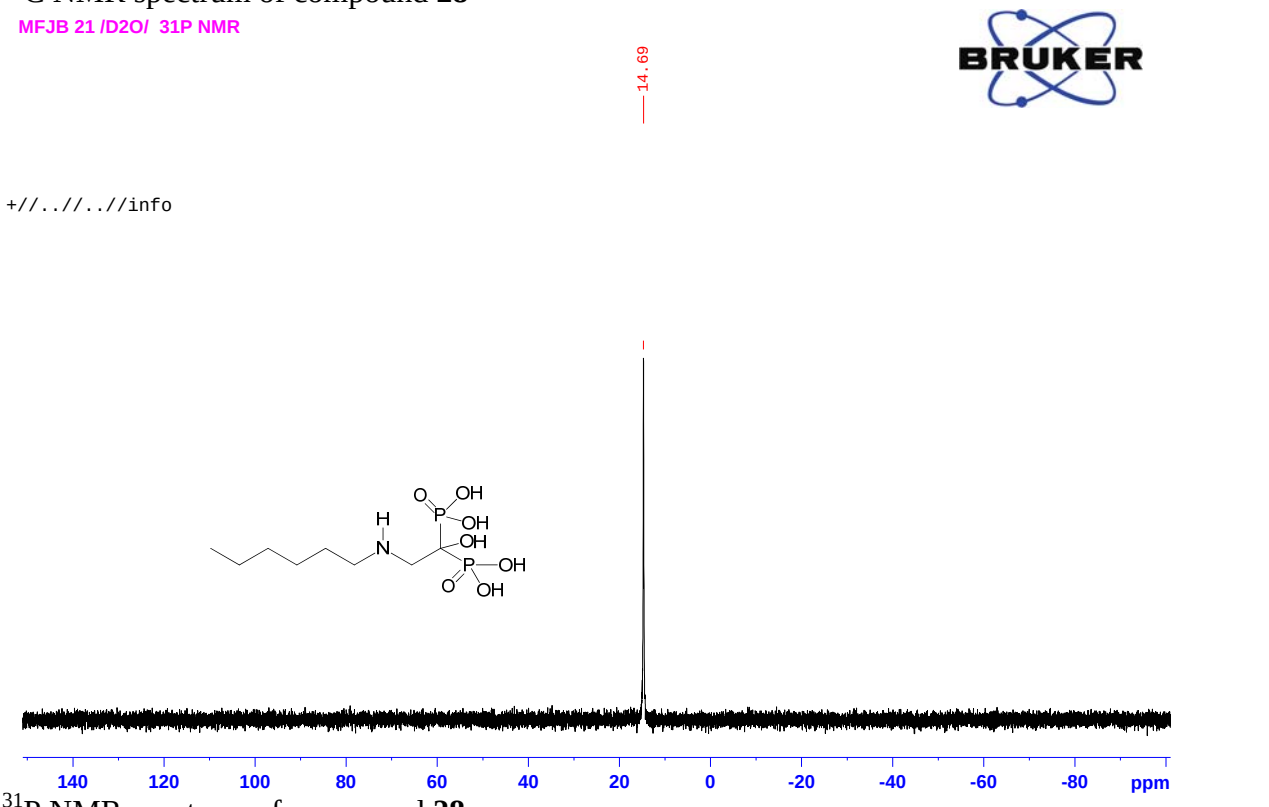
^{13}C NMR spectrum of compound **23**.



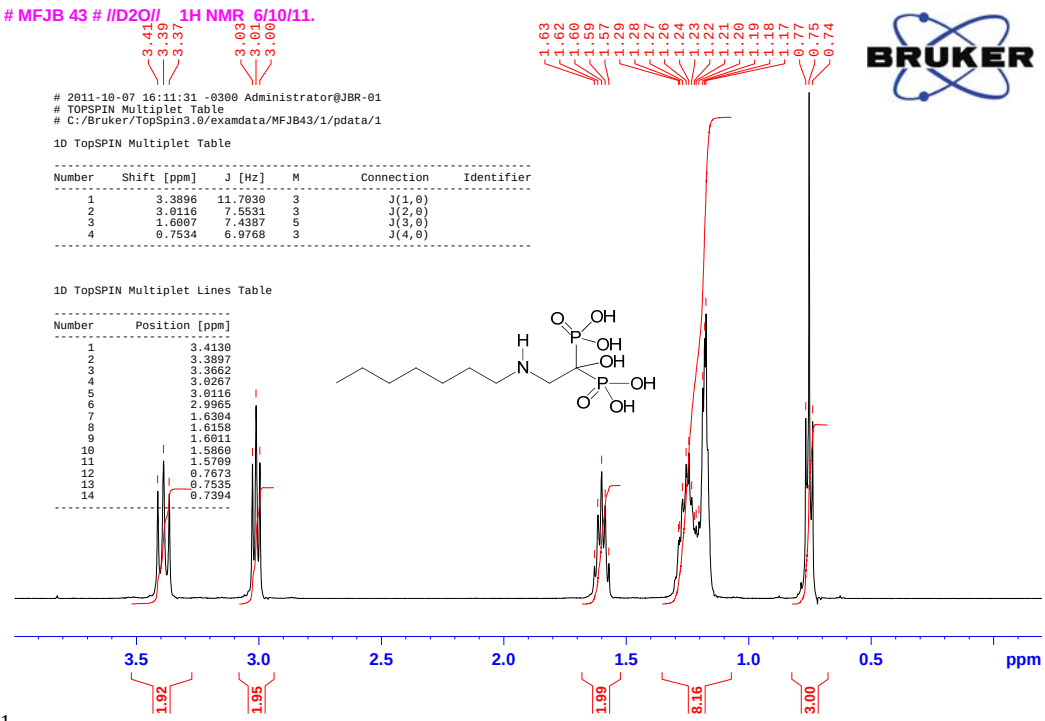
^{1}H NMR spectrum of compound **28**.



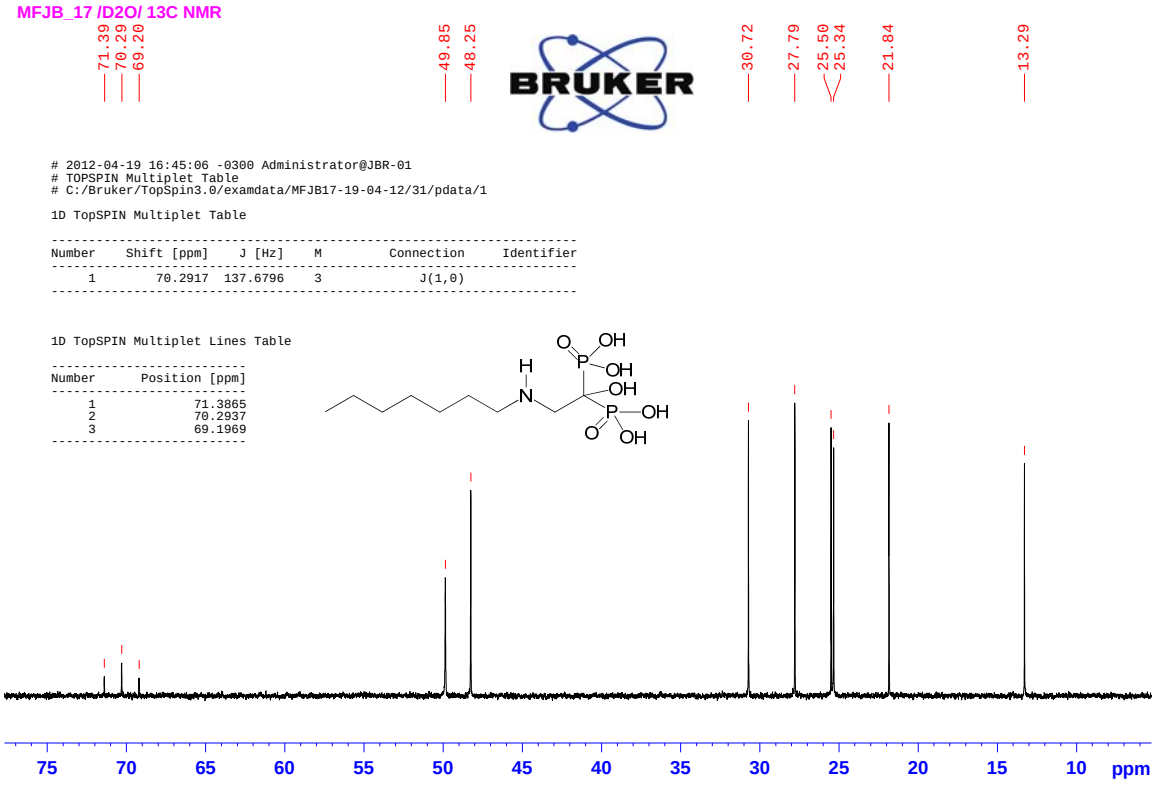
^{13}C NMR spectrum of compound **28**



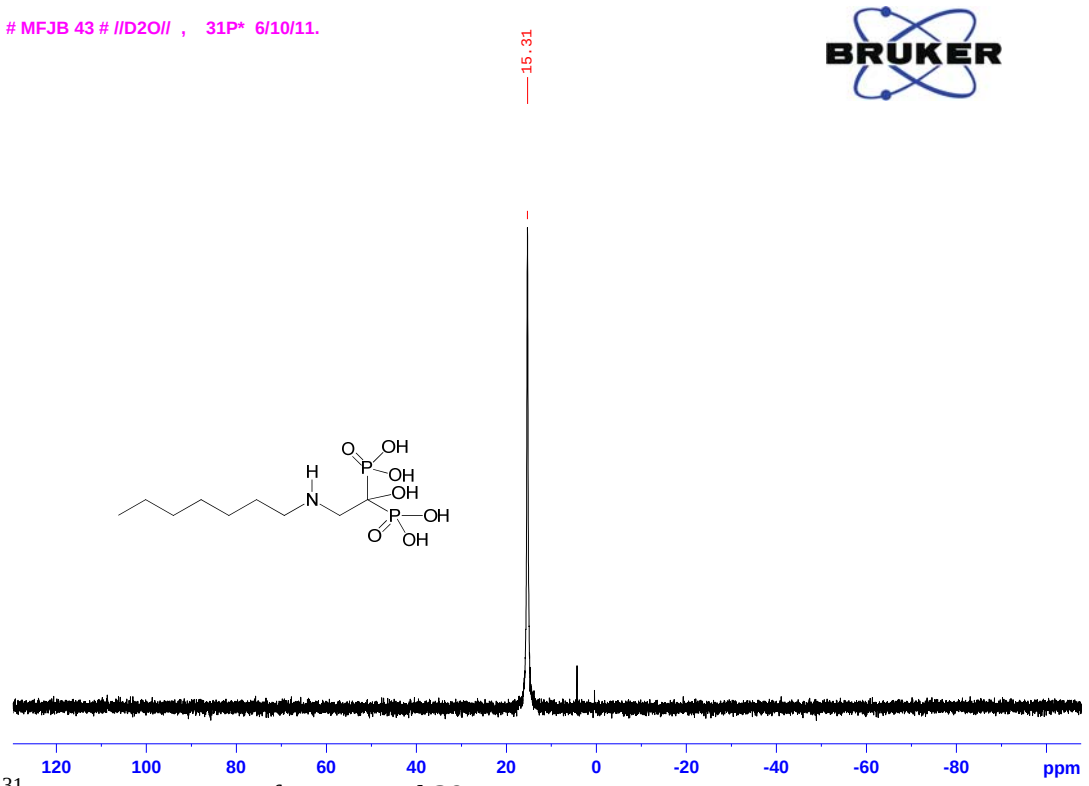
^{31}P NMR spectrum of compound **28**.



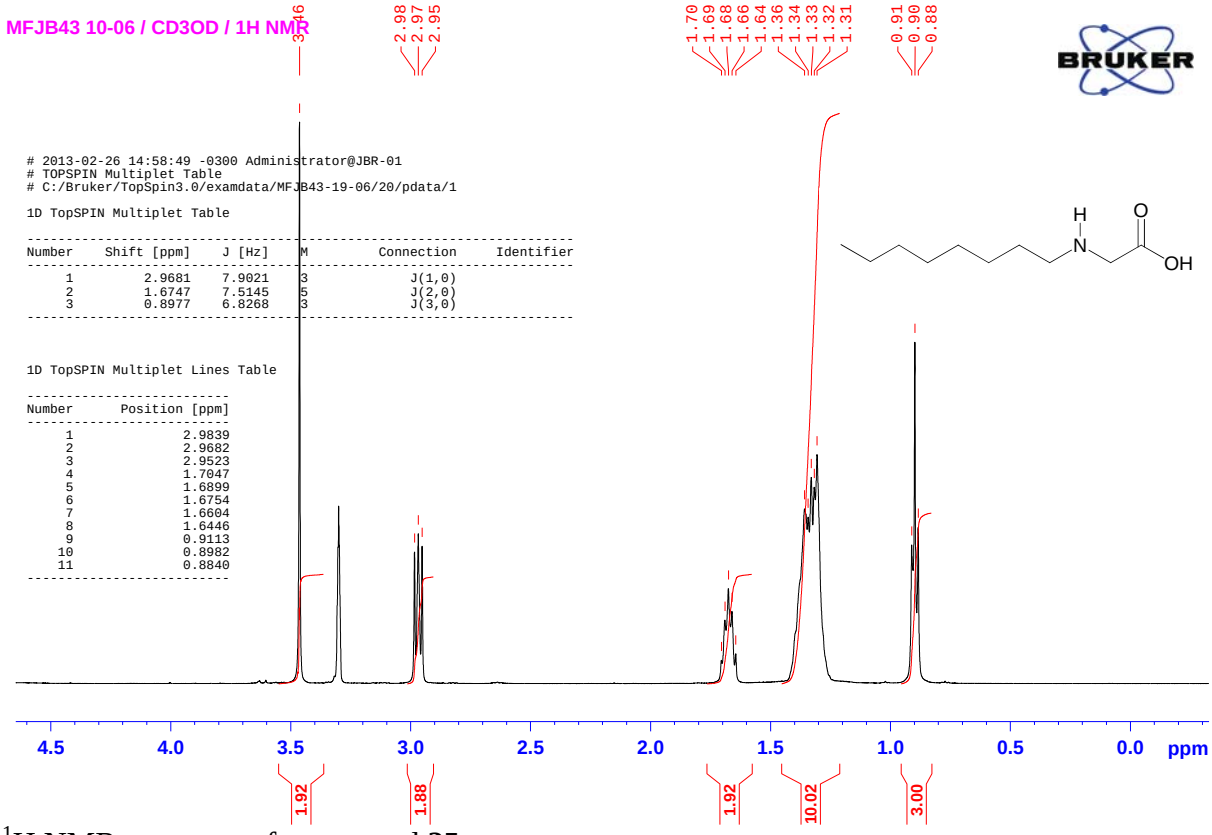
^{1}H NMR spectrum of compound **29**.



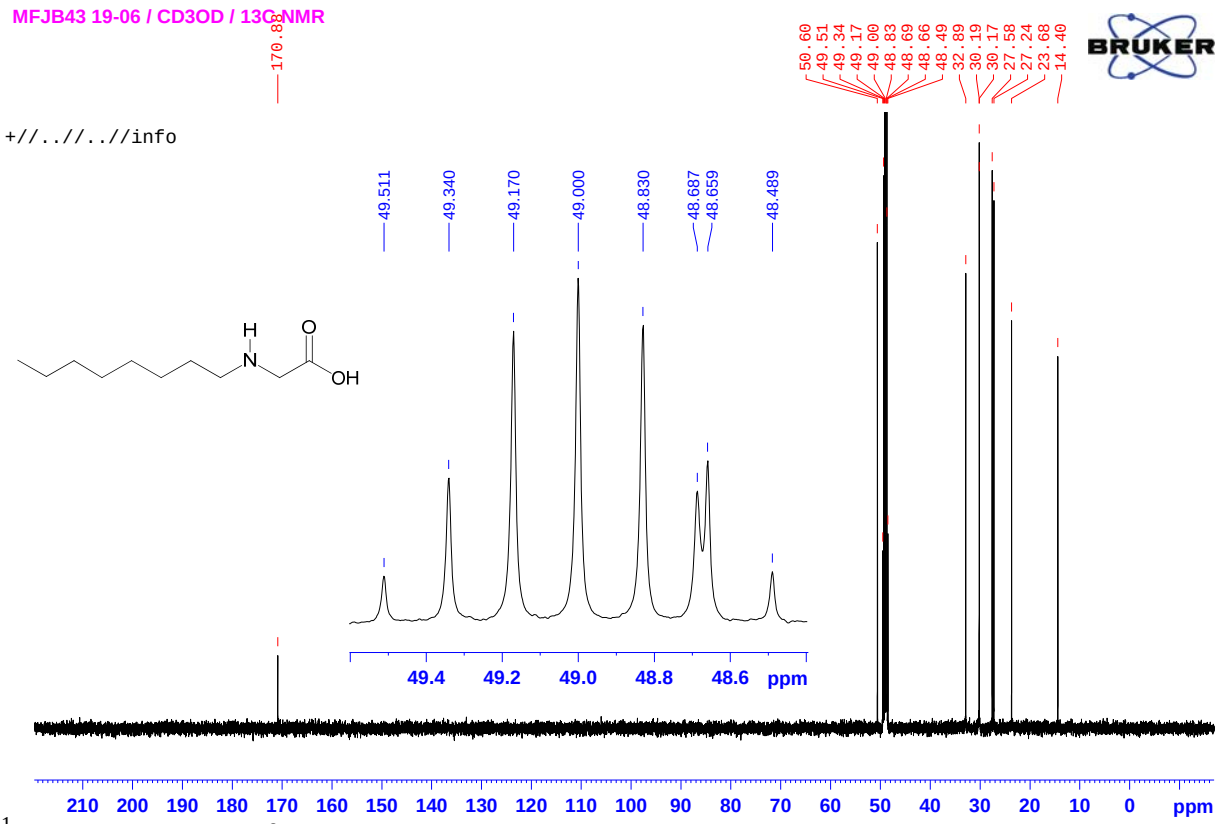
^{13}C NMR spectrum of compound **29**.



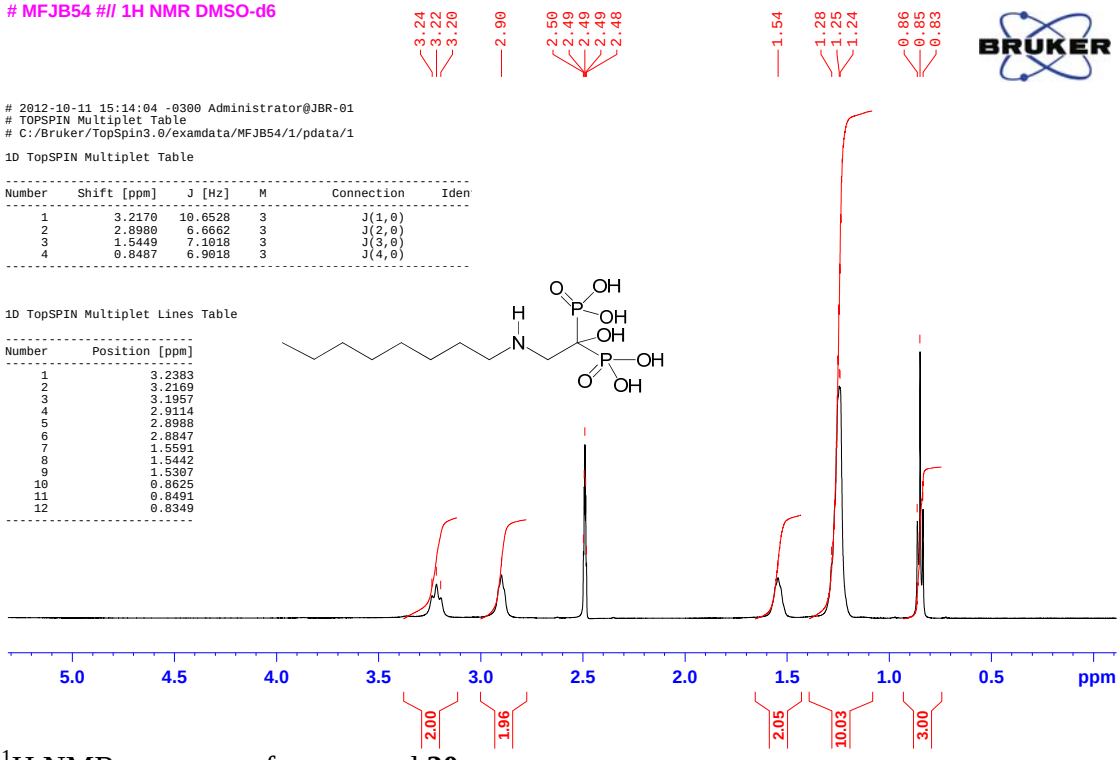
^{31}P NMR spectrum of compound **29**.



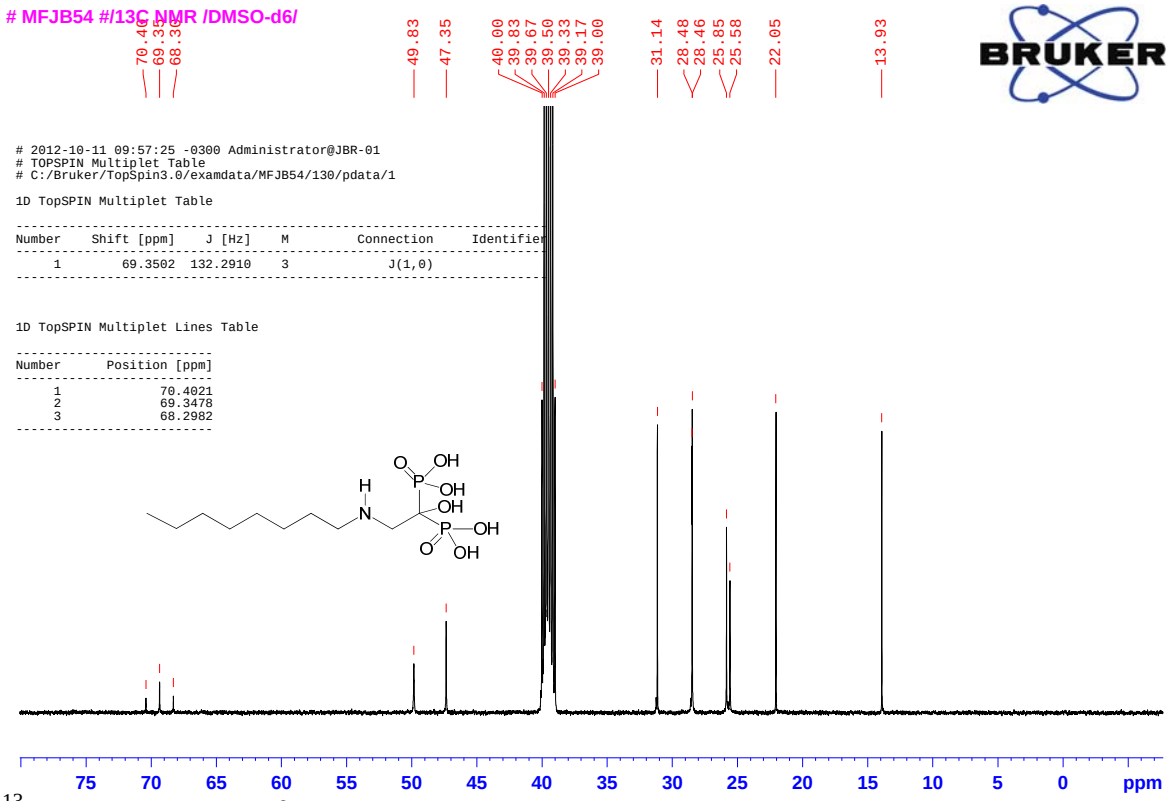
^{1}H NMR spectrum of compound **25**.



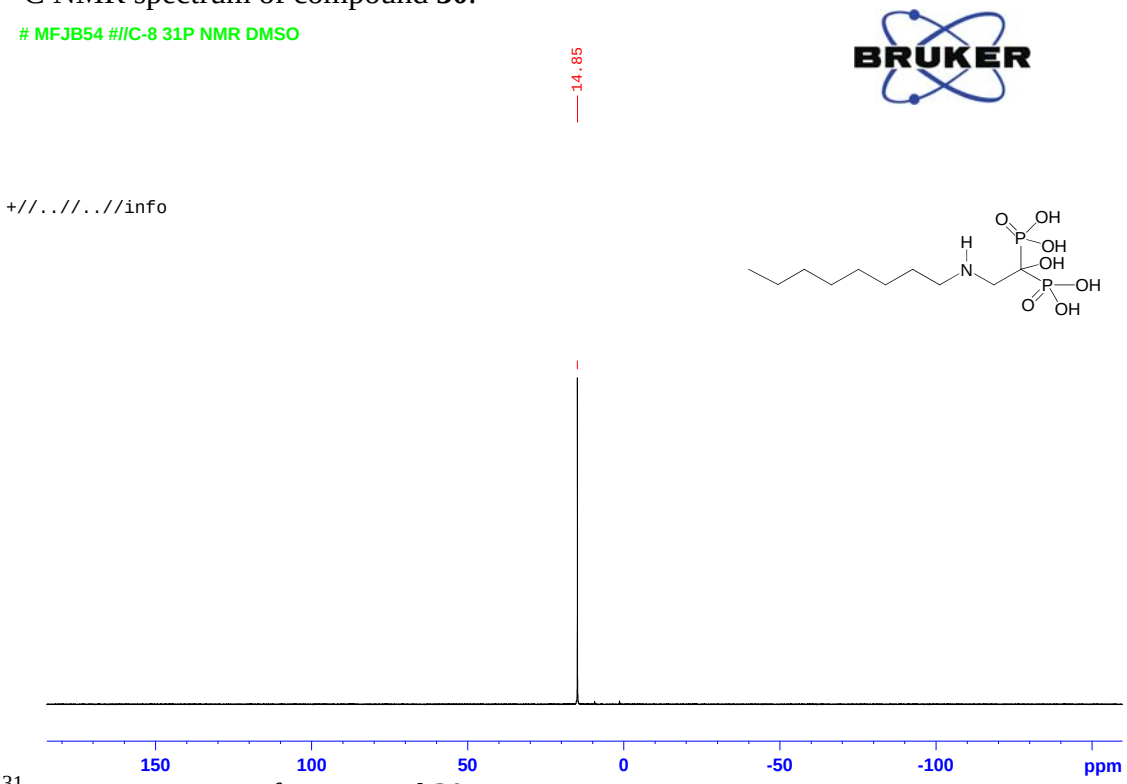
^{1}H NMR spectrum of compound **25**.



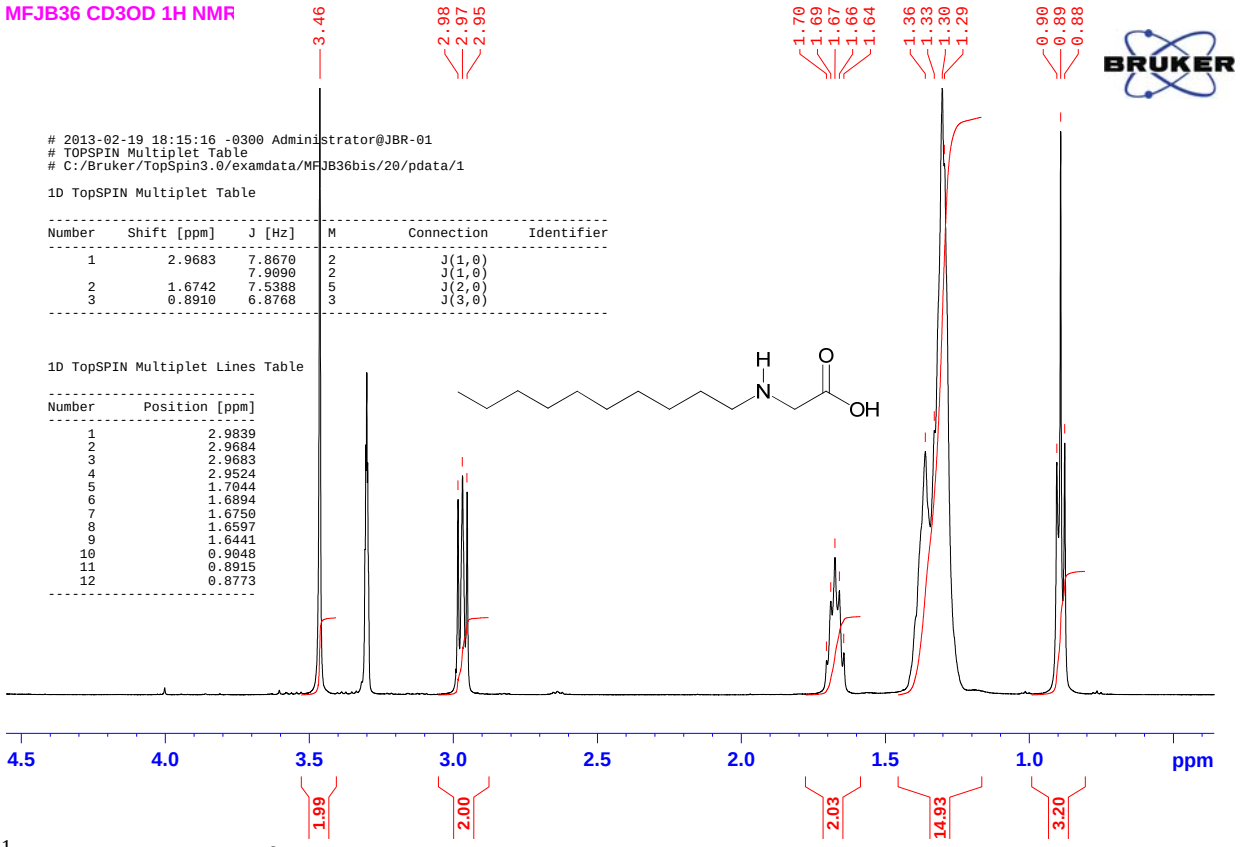
^{1}H NMR spectrum of compound **30**.



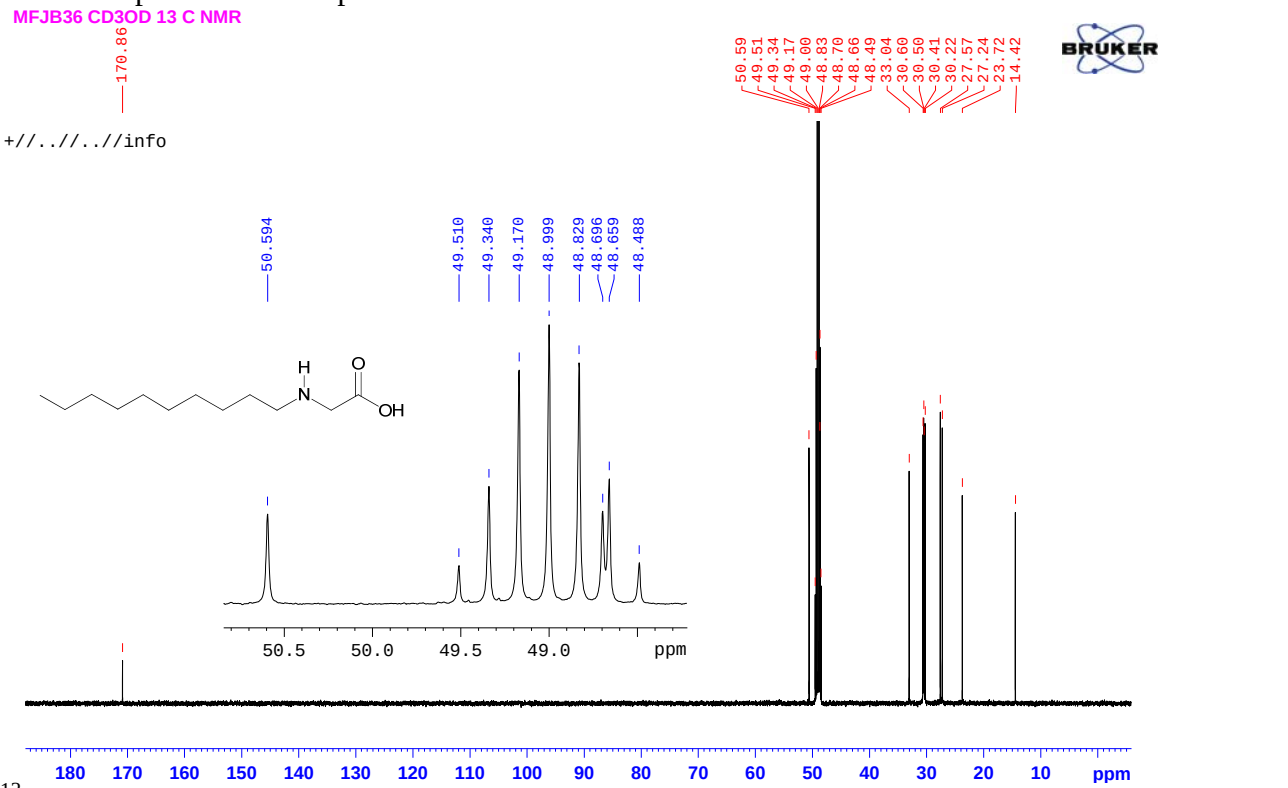
^{13}C NMR spectrum of compound **30**.



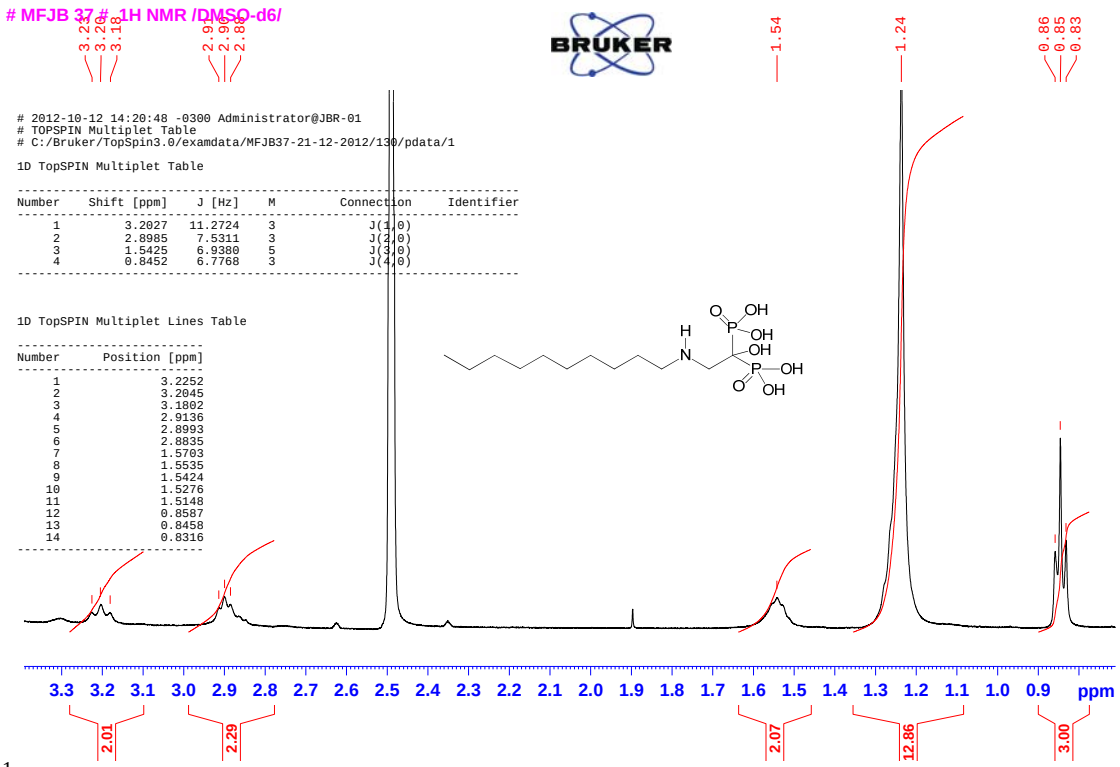
^{31}P NMR spectrum of compound **30**.



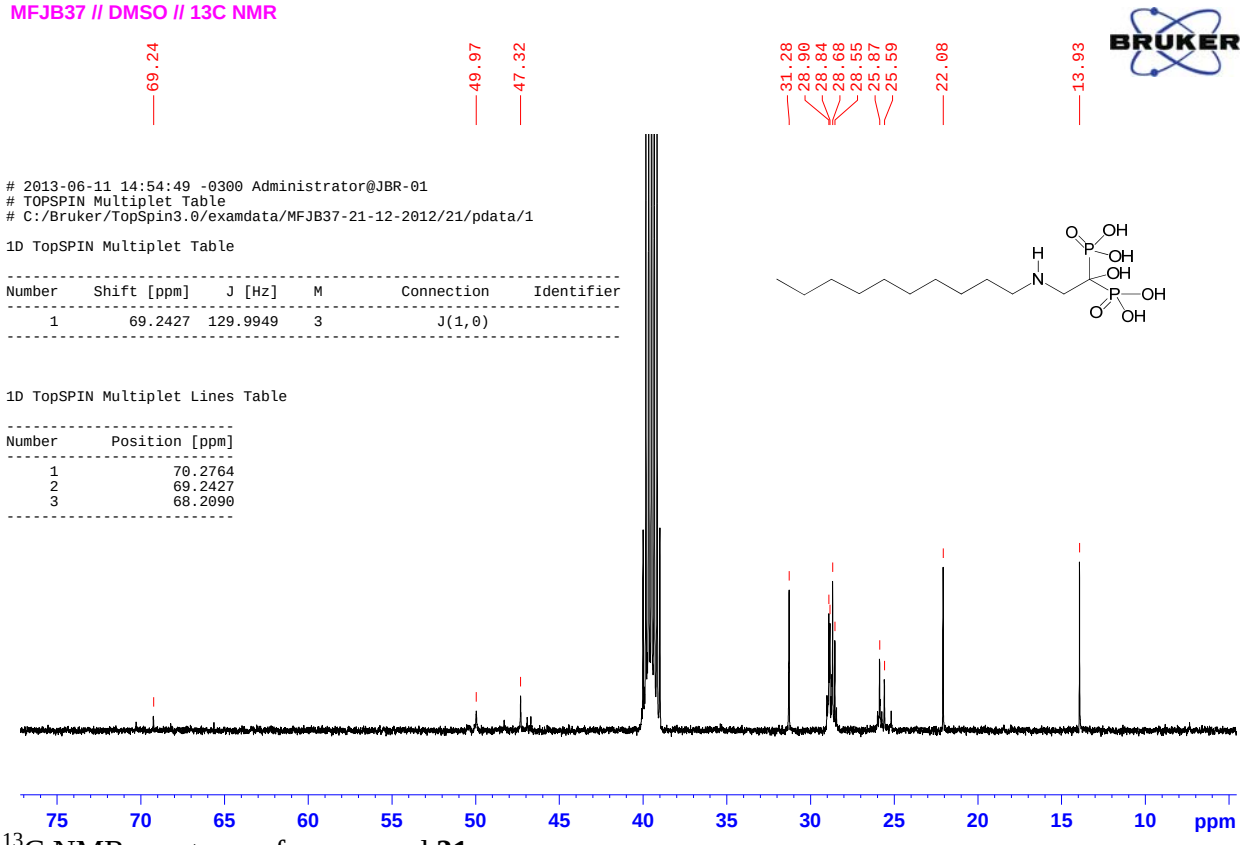
^{1}H NMR spectrum of compound **26**.



^{13}C NMR spectrum of compound **26**.

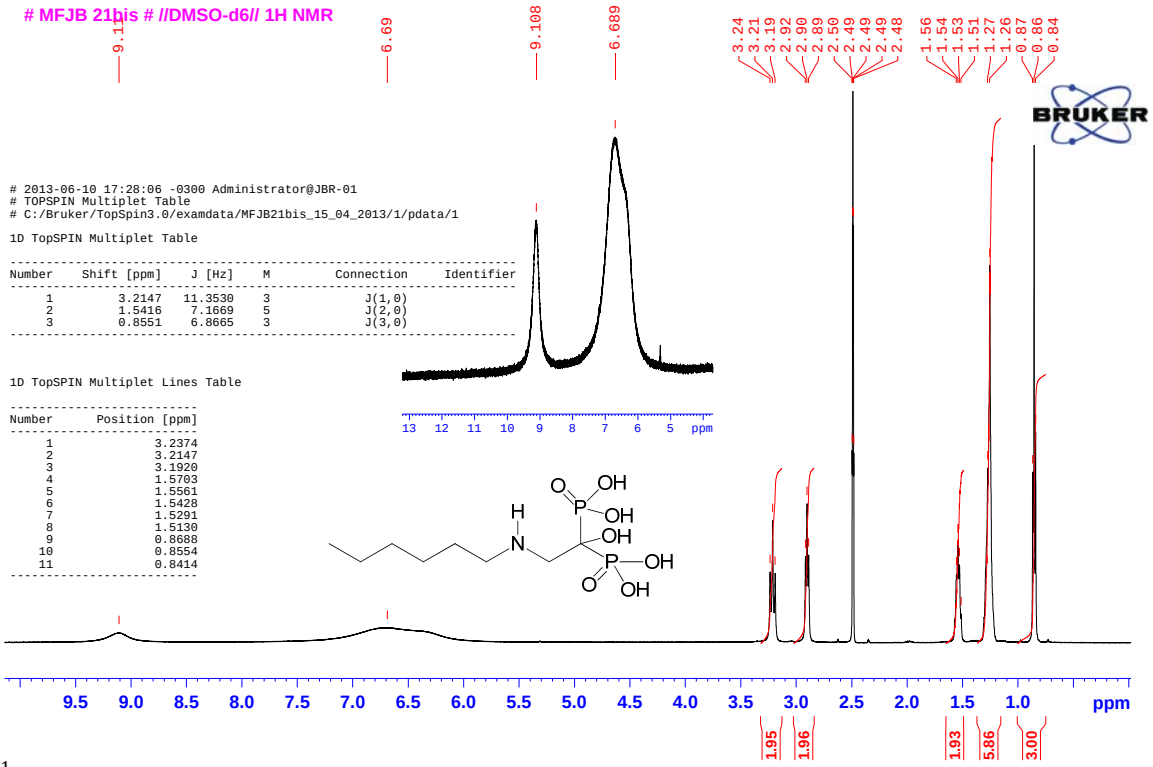


^{1}H NMR spectrum of compound **31**.

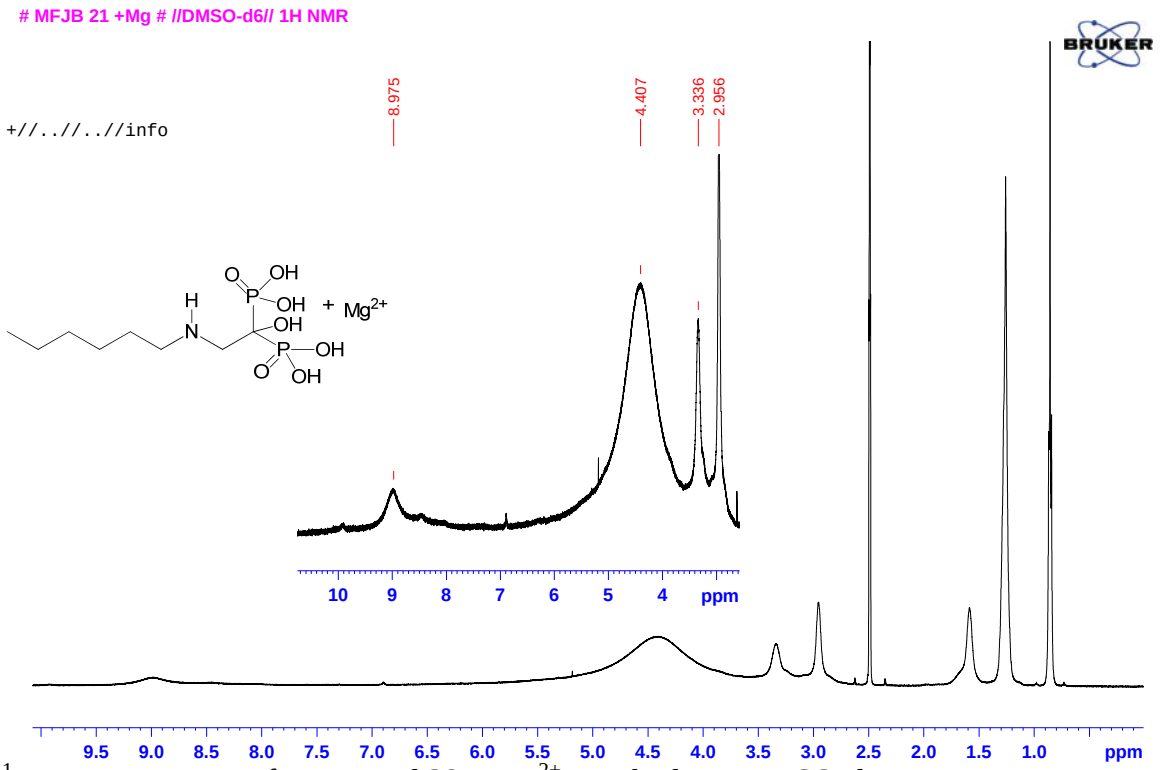


^{13}C NMR spectrum of compound **31**.

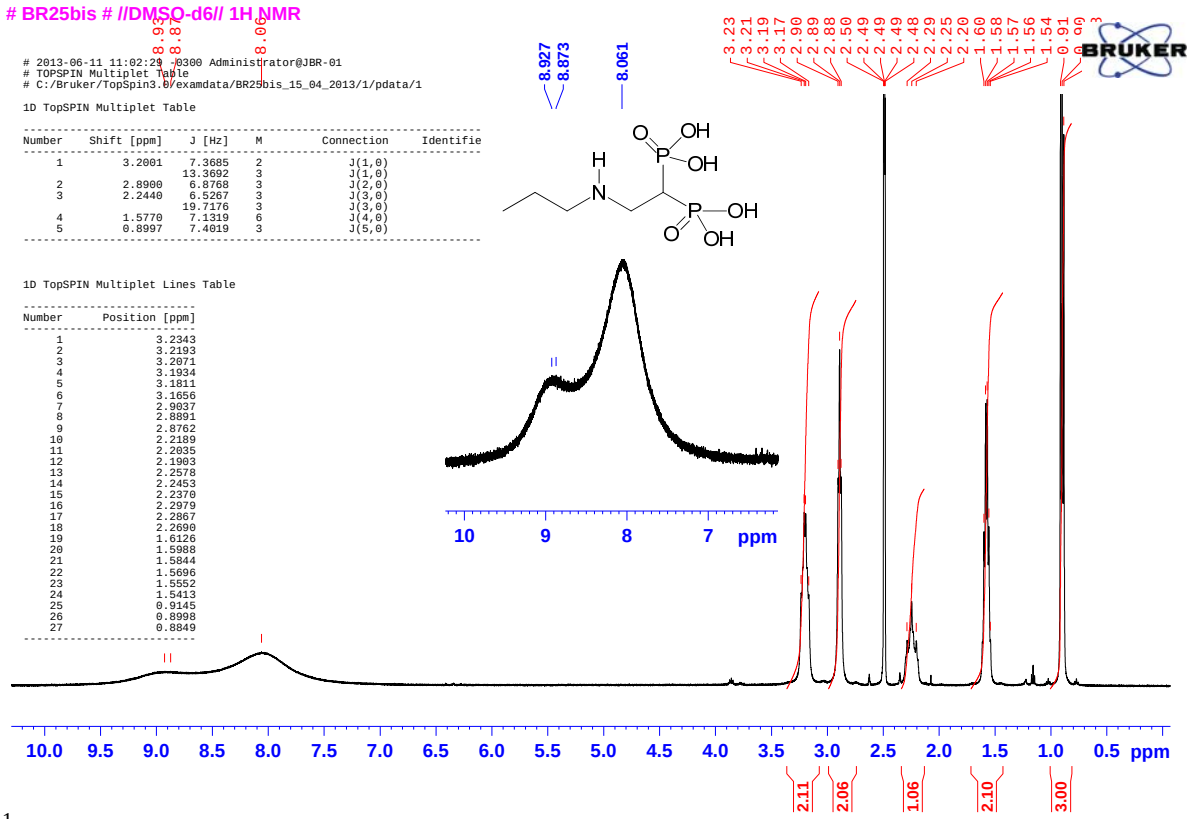
^{31}P NMR spectrum of compound **31**.



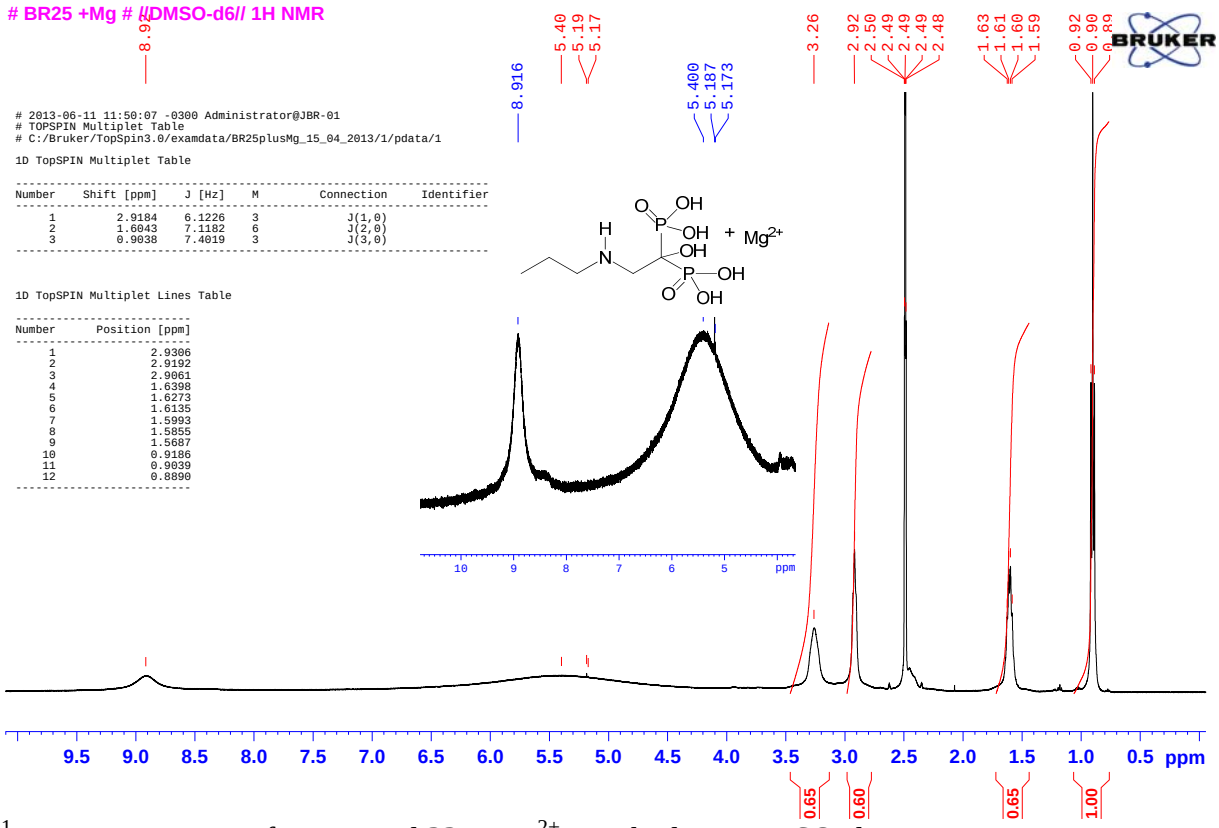
^{1}H NMR spectrum of compound **28** in anhydrous DMSO-d_6.



^{1}H NMR spectrum of compound **28** + Mg^{2+} in anhydrous DMSO-d_6.



^{1}H NMR spectrum of compound **33** in anhydrous DMSO-d_6.



^{1}H NMR spectrum of compound **33** + Mg^{2+} in anhydrous DMSO-d_6.

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
```