



**DESIGN AND SYNTHESIS OF NOVEL *P. falciparum* GDH INHIBITORS FOR USE AS  
POTENTIAL ANTIMALARIAL AGENTS**

By

**Edward Kumbirai Kasonde**  
**B.Sc. (Hons), M.Sc., Pg. Cert. (FHEA)**

**School of Human Sciences**

**A thesis submitted in partial fulfilment of the requirements of London Metropolitan  
University for the degree of Doctor of Philosophy**

**December 2020**

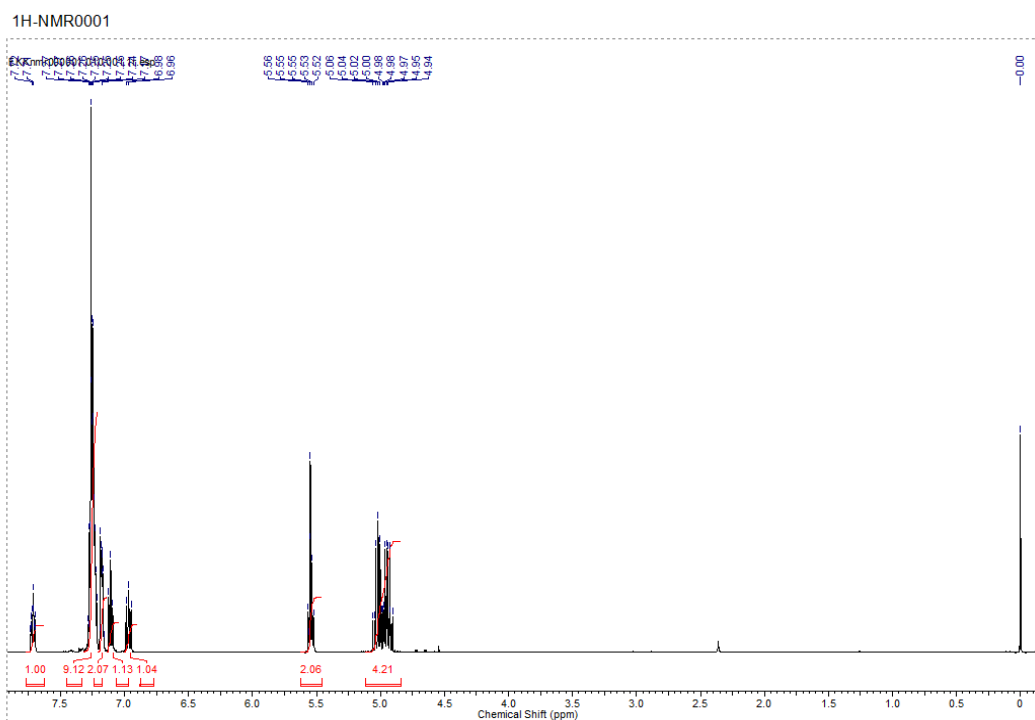
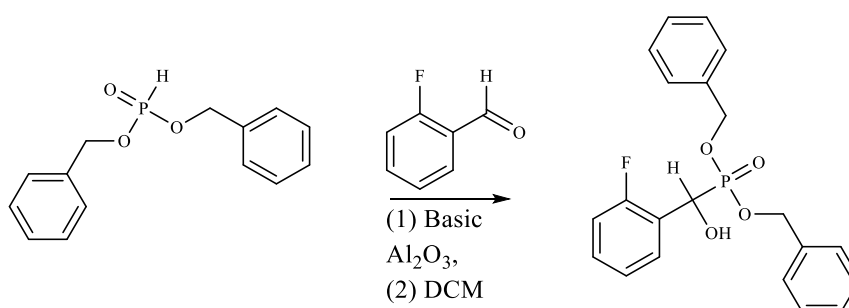
# 1 APPENDIX

$^1\text{H}$ -NMR,  $^{13}\text{C}$ -NMR,  $^{13}\text{C}$ -DEPT-135,  $^{31}\text{P}$ -NMR, MS and FT-IR

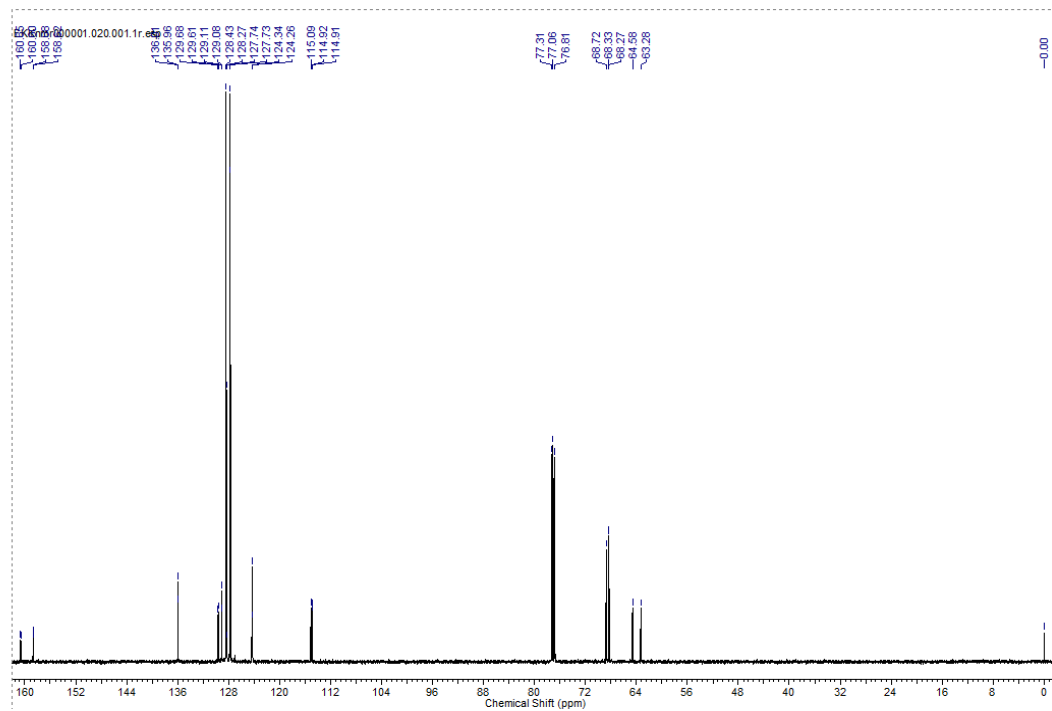
## 1 SUBSTITUTED BENZYL- $\alpha$ -HYDROXY

### PHOSPHONATES

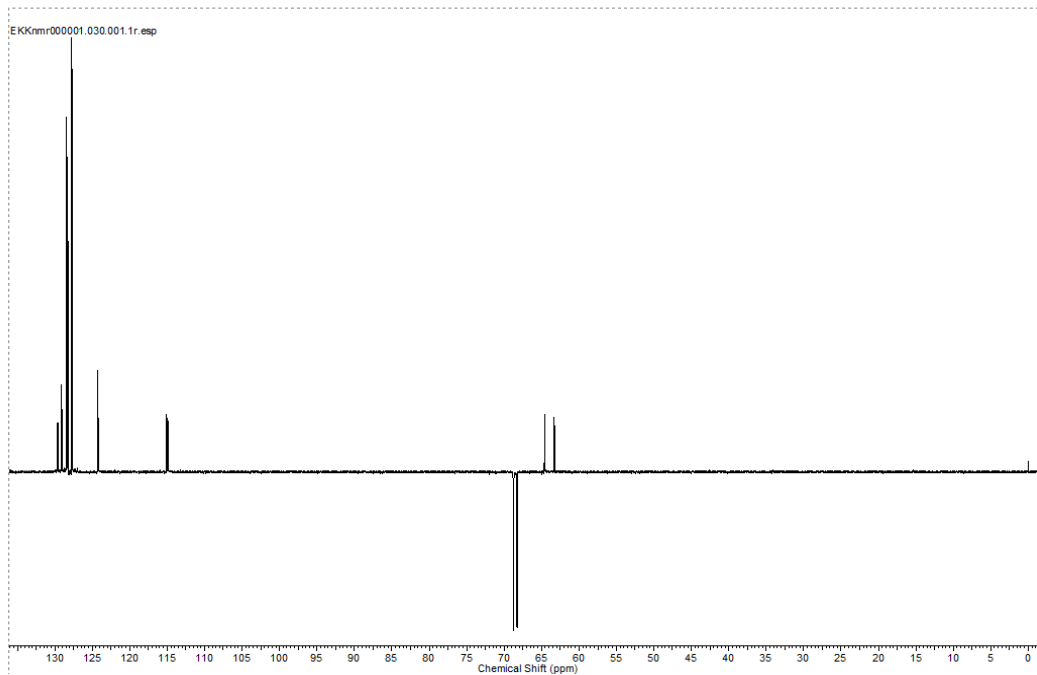
#### 1.1 2-Fluorobenzyl- $\alpha$ -hydroxy-dibenzyl phosphonate (6)



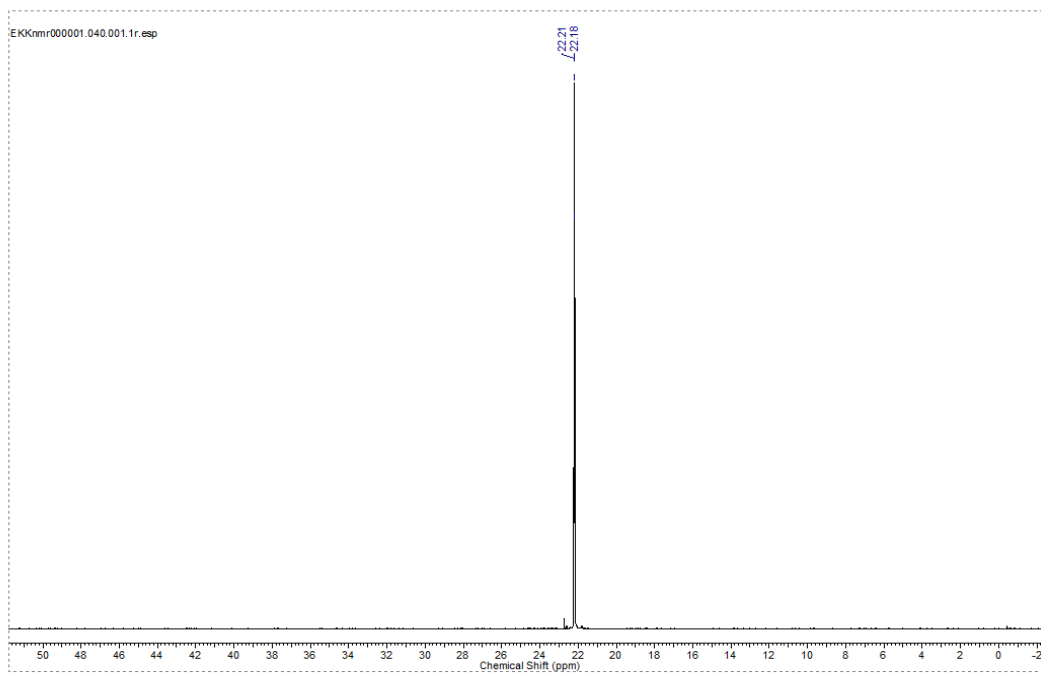
13C-NMR0001



13C-NMR0001

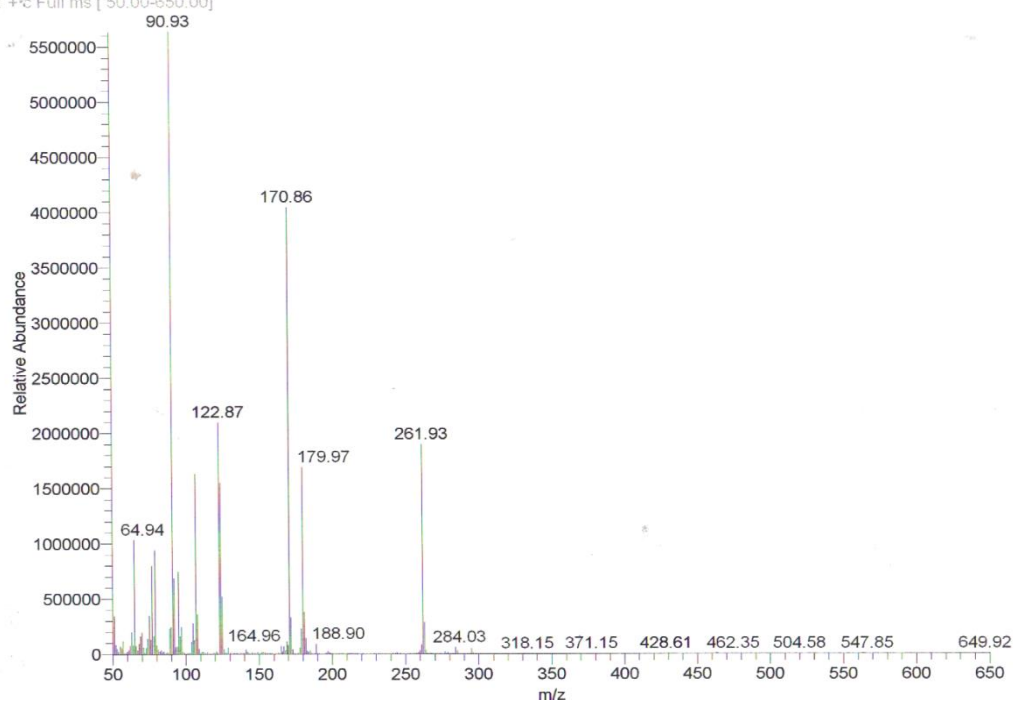


31P-NMR0001

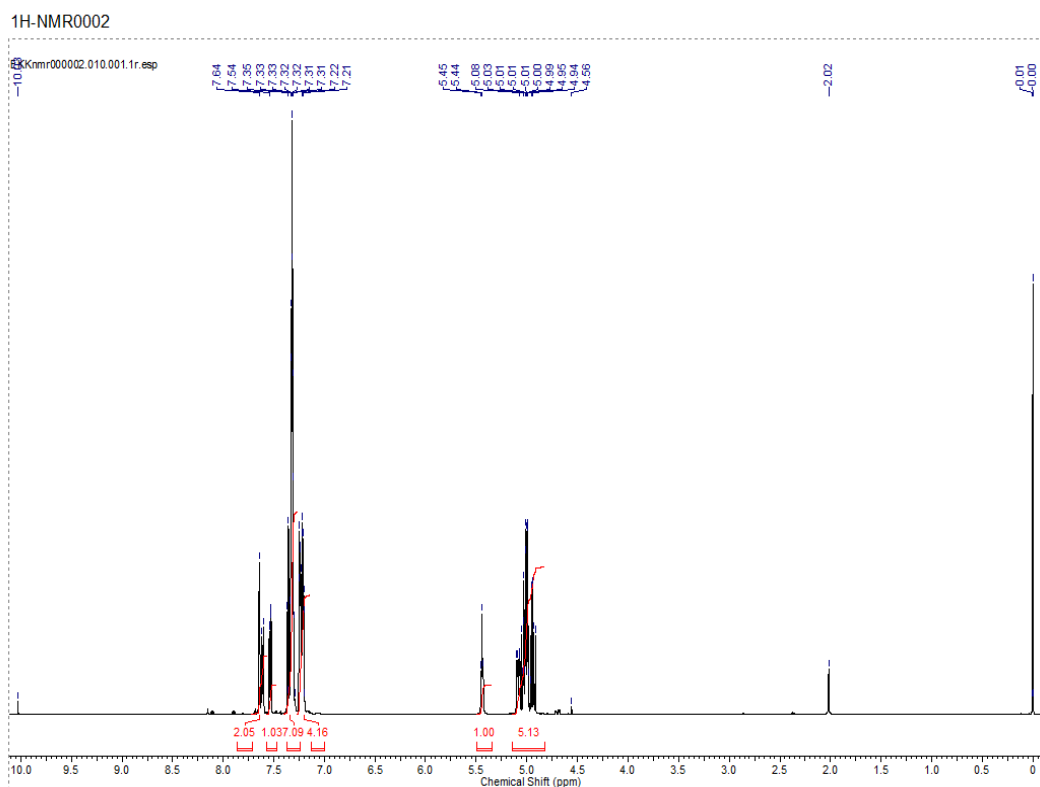
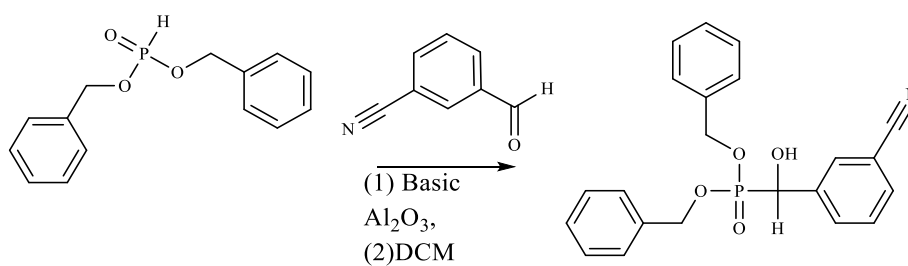


2:\Xcalibur\...2014\February\EKKms0001  
Edward Kumbira Kasonda sample MS000001  
EKKms0001 #52 RT: 1.29 AV: 1 NL: 5.64E6  
Γ: +c Full ms [ 50.00-650.00]

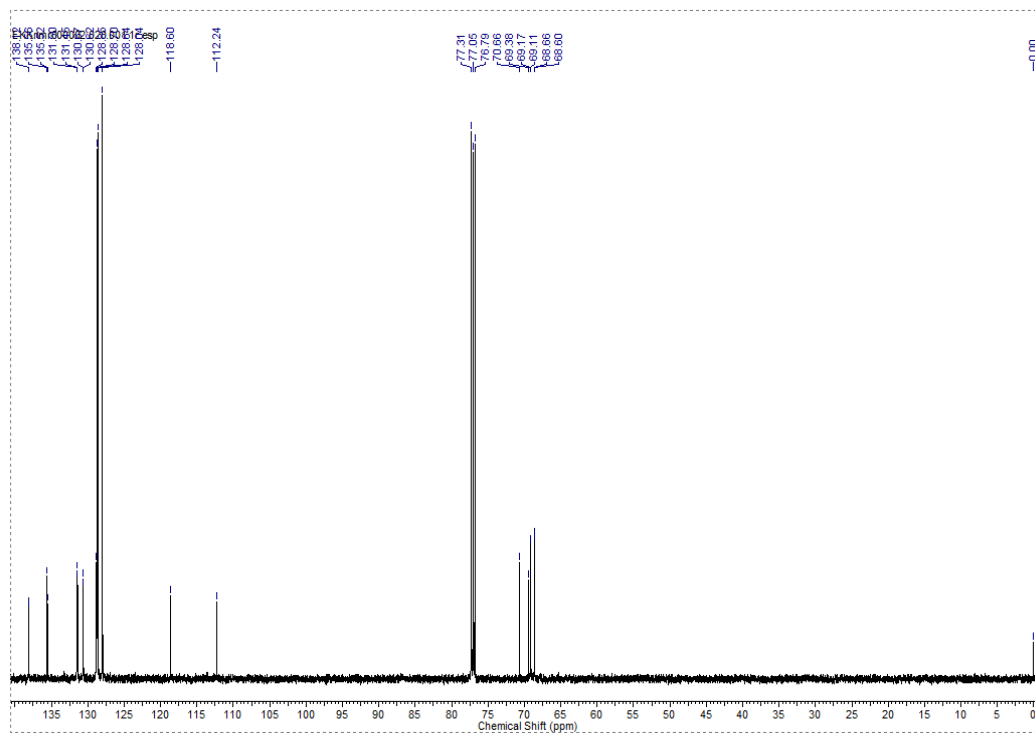
2/19/2008 9:46:47 AM



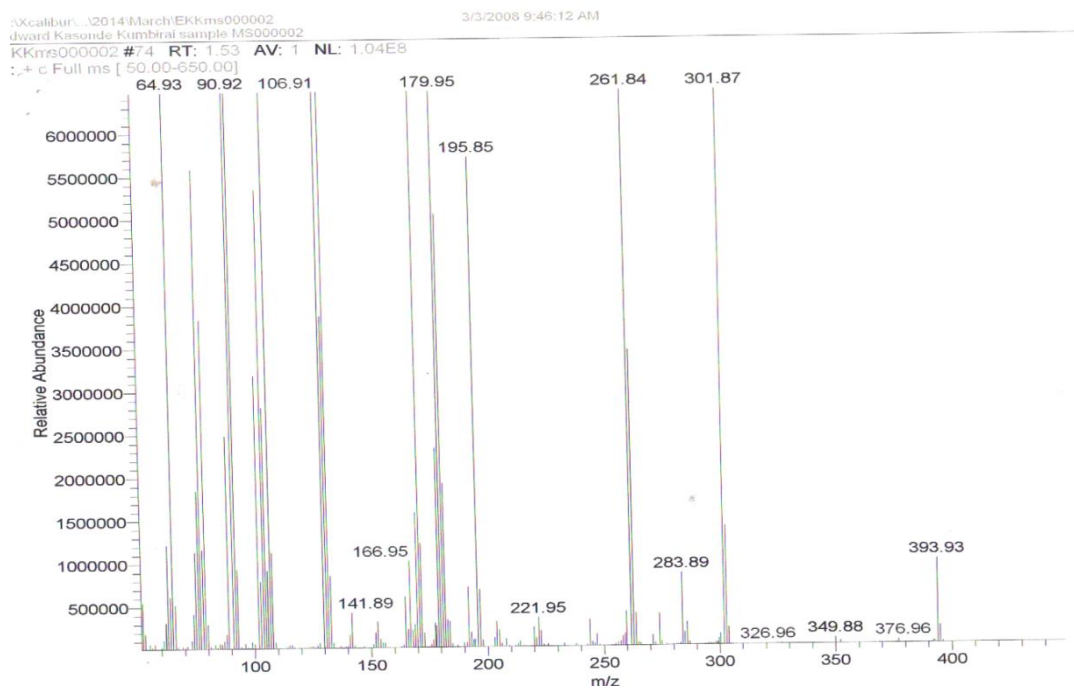
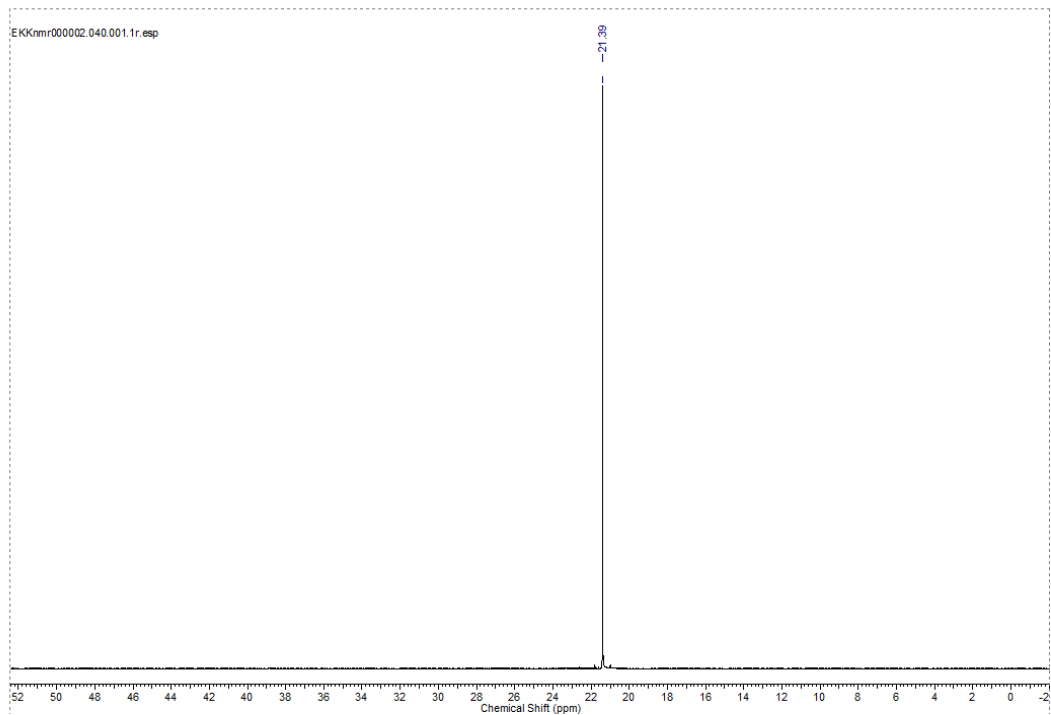
## 1.2 3-Cyano benzyl- $\alpha$ - hydroxy dibenzyl phosphonate (7)



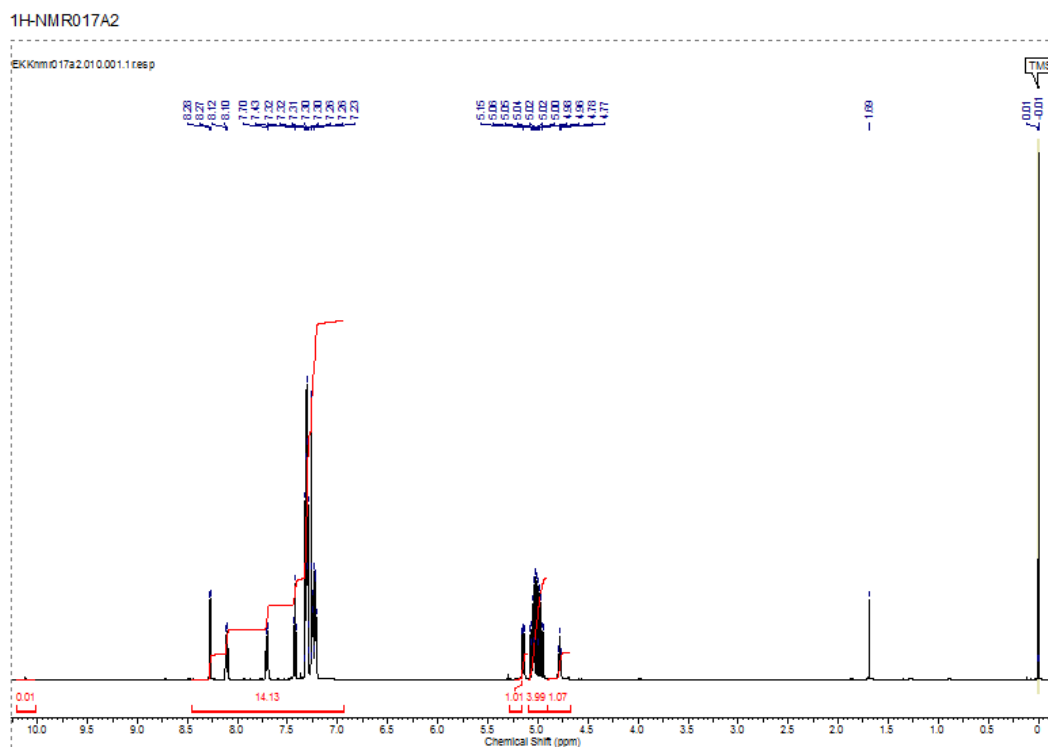
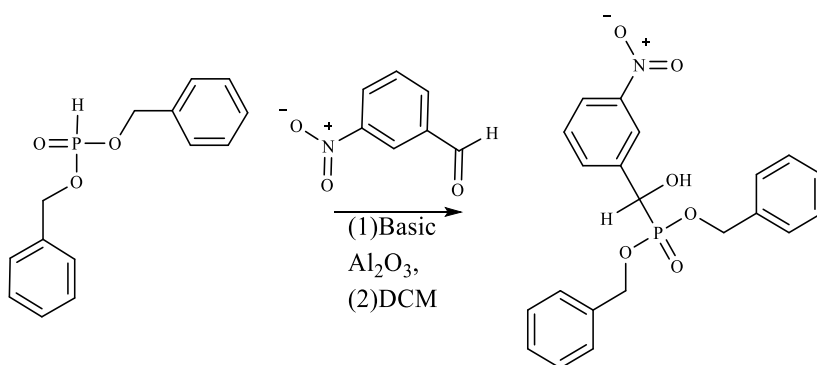
13C-NMR0002



# 31P-NMR0002

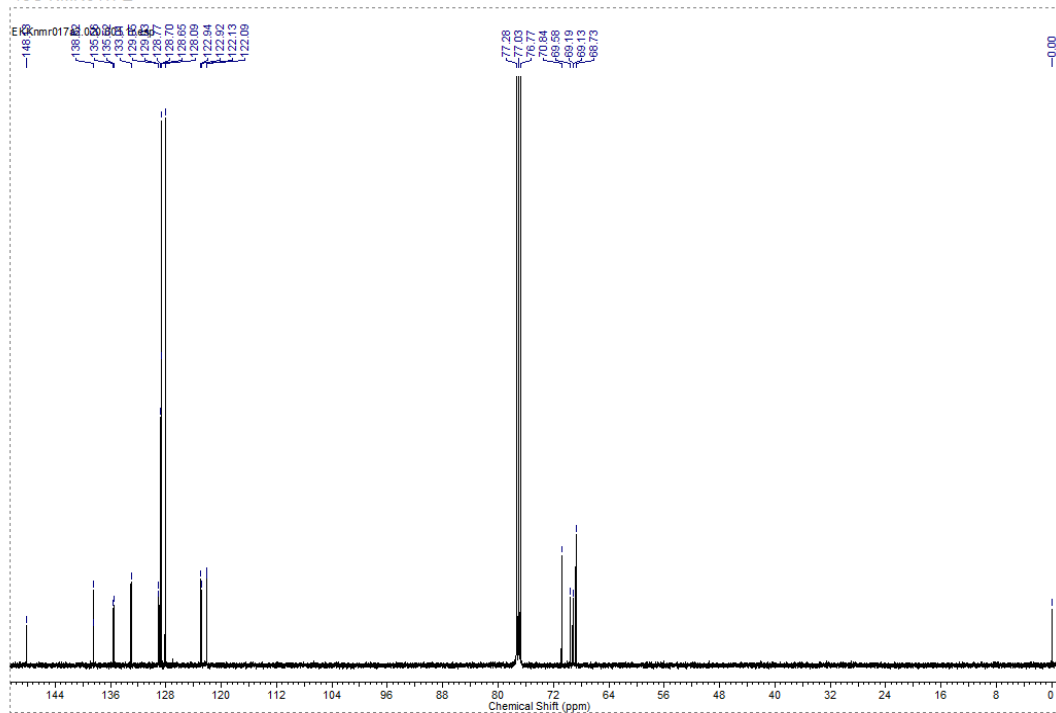


### 1.3 3-Nitrobenzyl- $\alpha$ -hydroxy dibenzyl phosphonate (8)

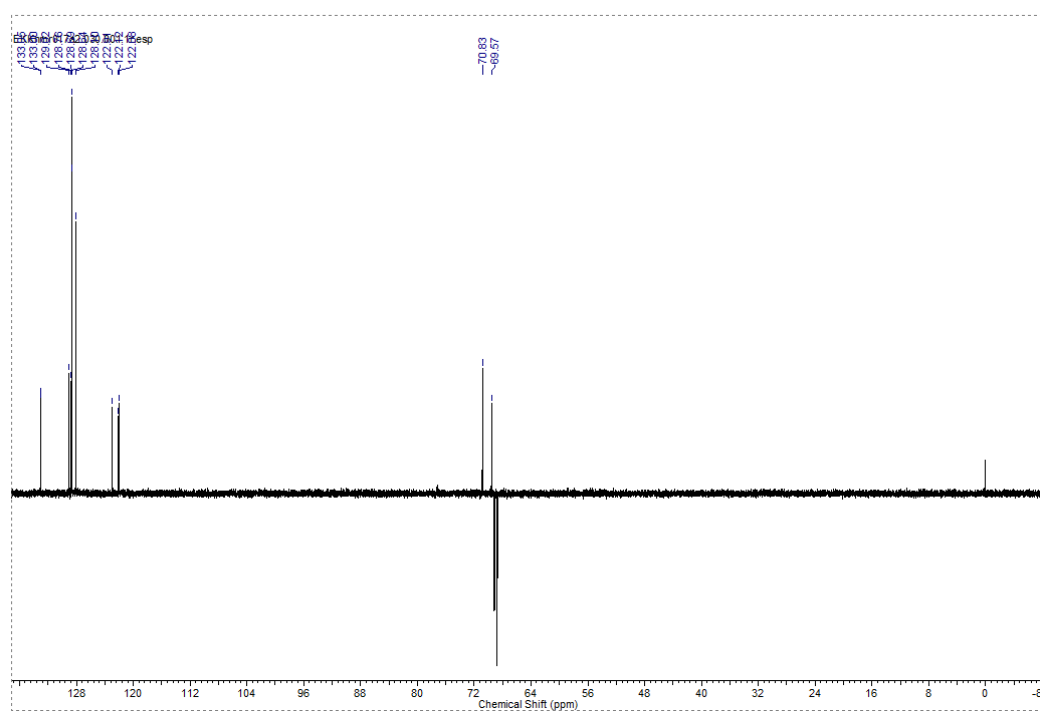




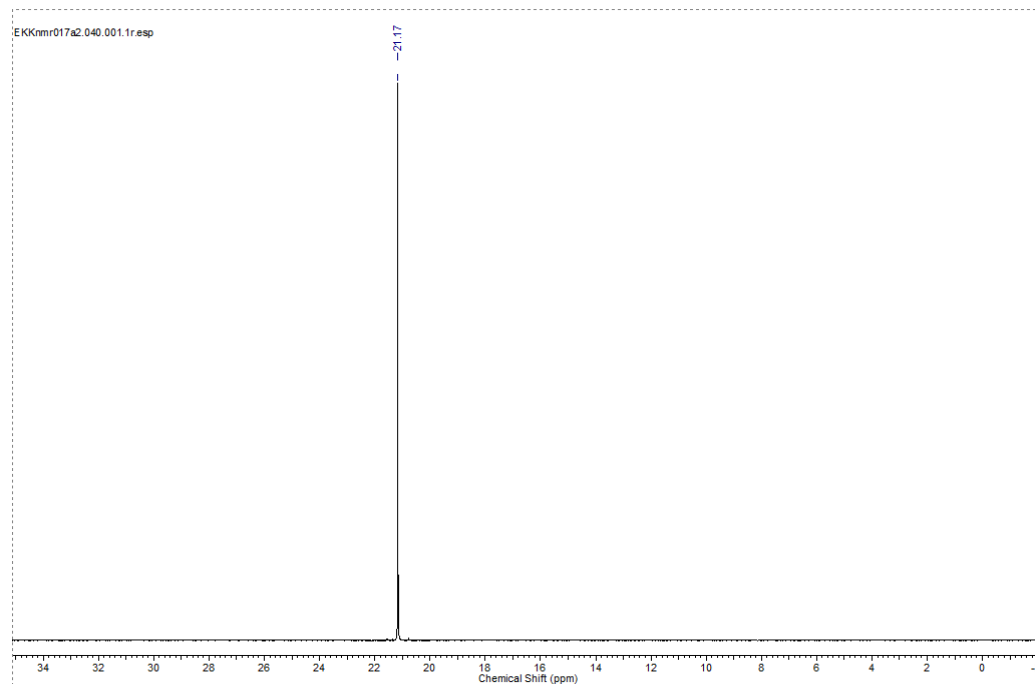
13C-NMR017A2



13C-NMR017A2-DEPT



31P-NMR017A2

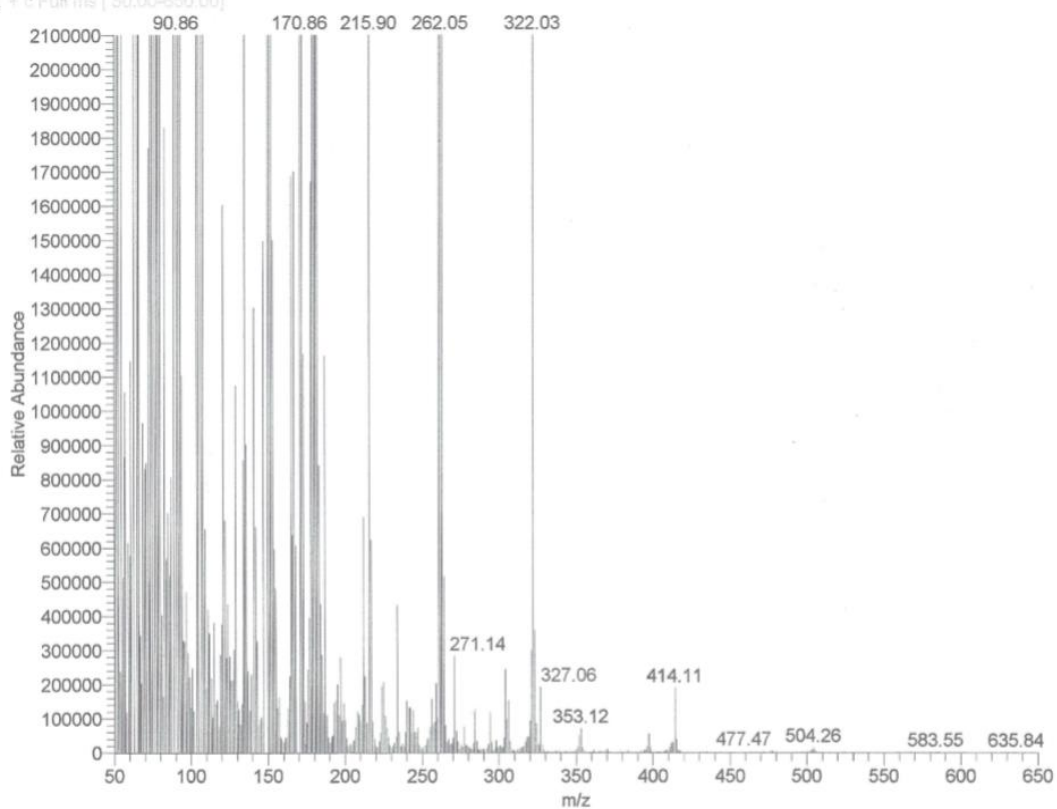


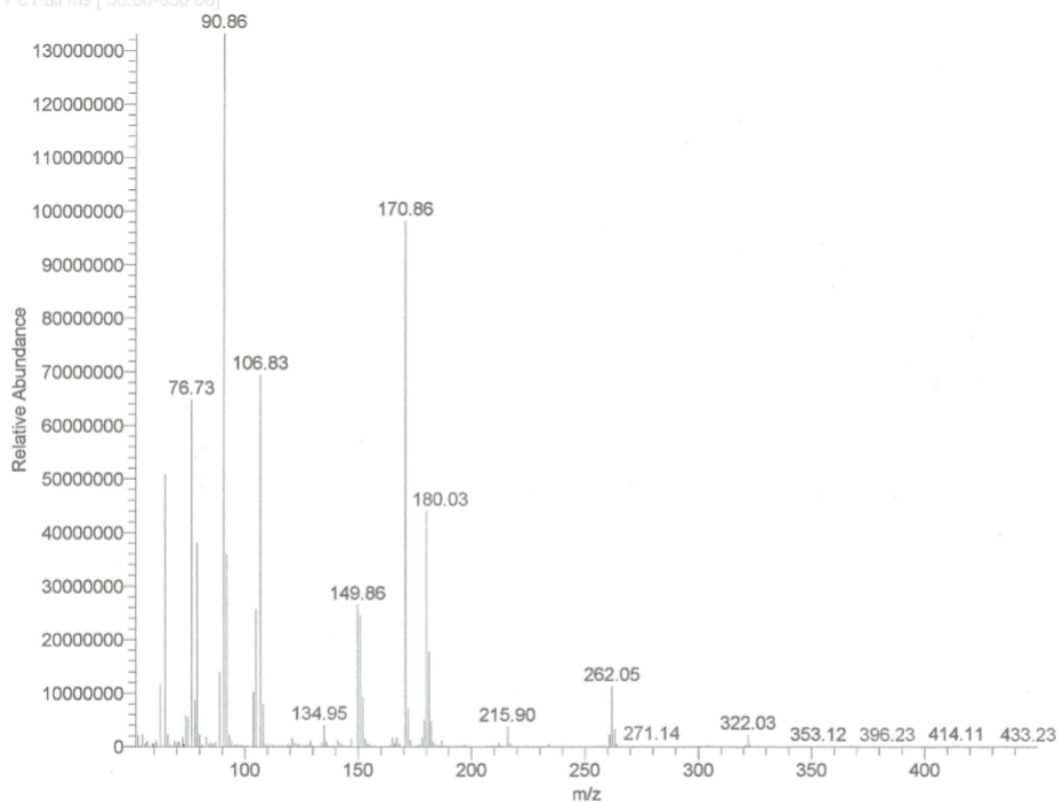
C:\Xcalibur\...2016\November\EKKmr017a1  
edcra-1 Kuratinal Kasande sample MS017A1

11/30/2019 11:17:22 AM

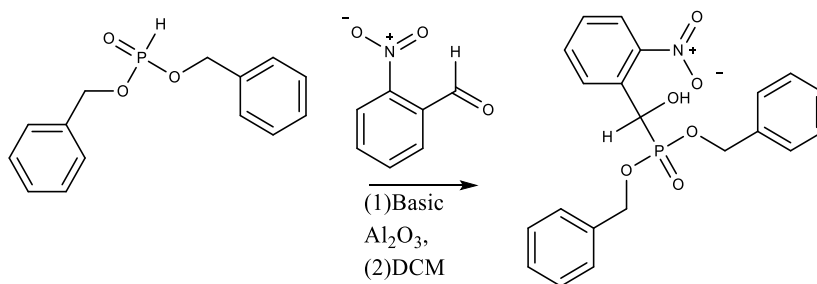
EKKmr017a1 #33 RT: 1.31 AV: 1 NL: 2.69E8

T: 7°C Full ms [50.00-650.00]

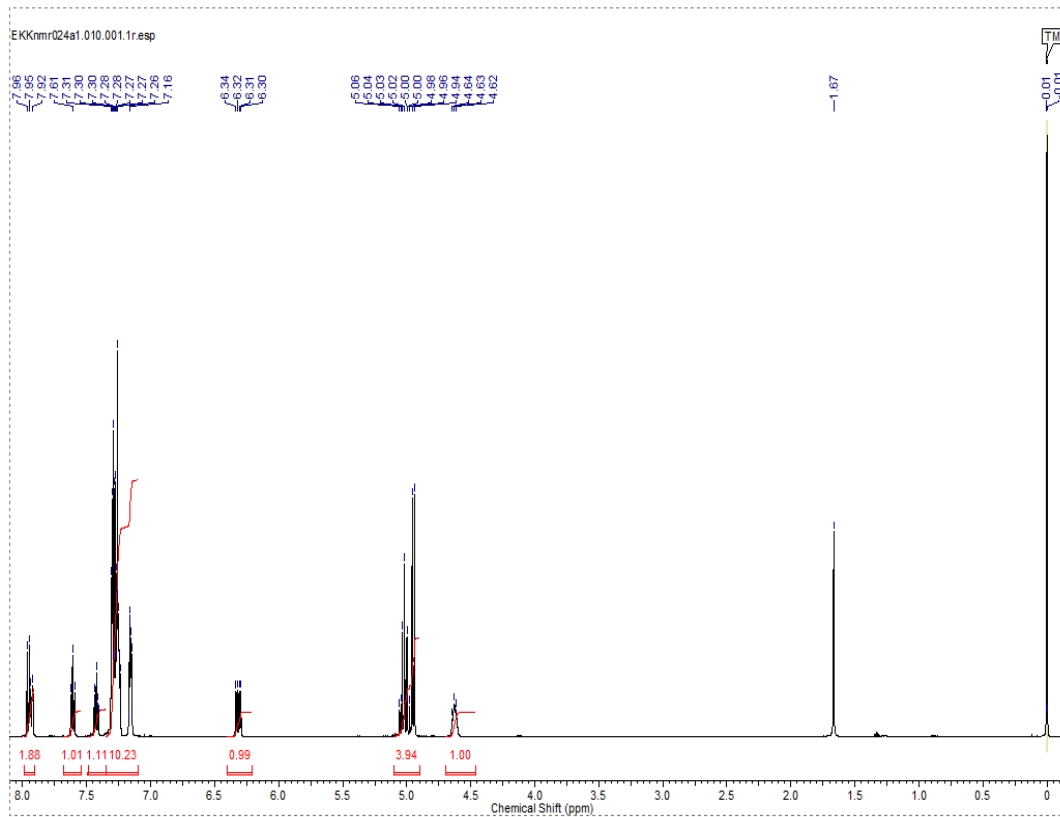




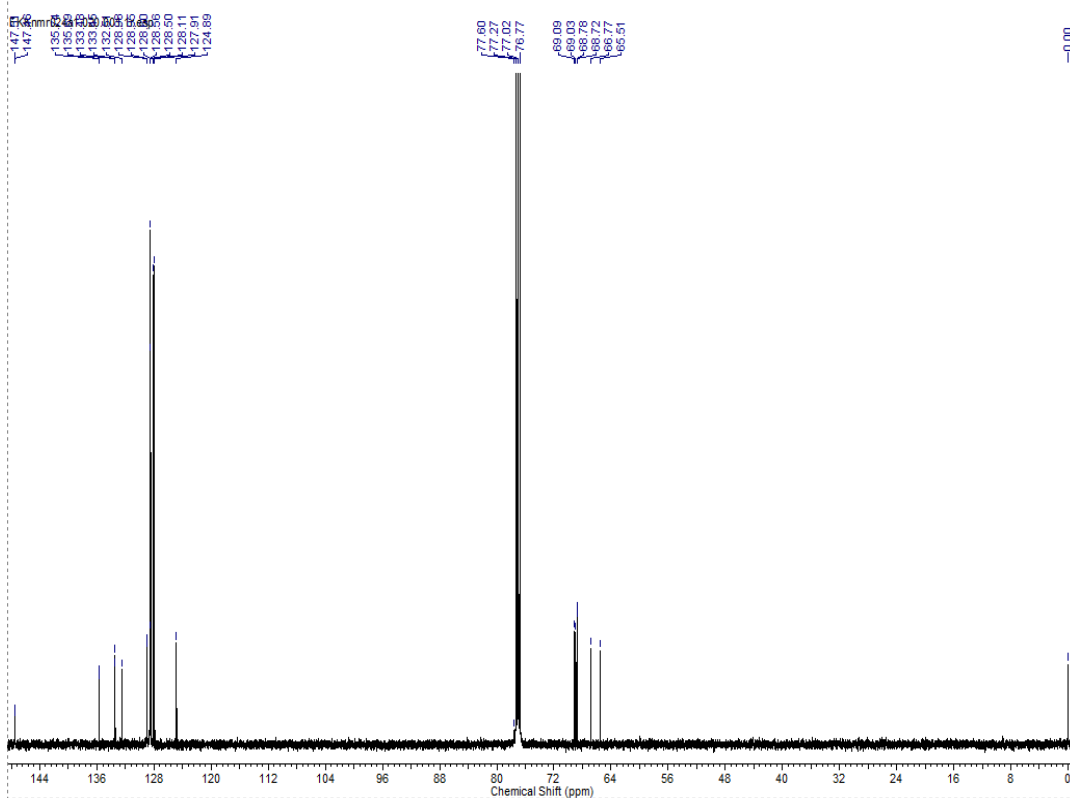
## 1.4 2-Nitrobenzyl- $\alpha$ -hydroxy dibenzyl phosphonate (9)



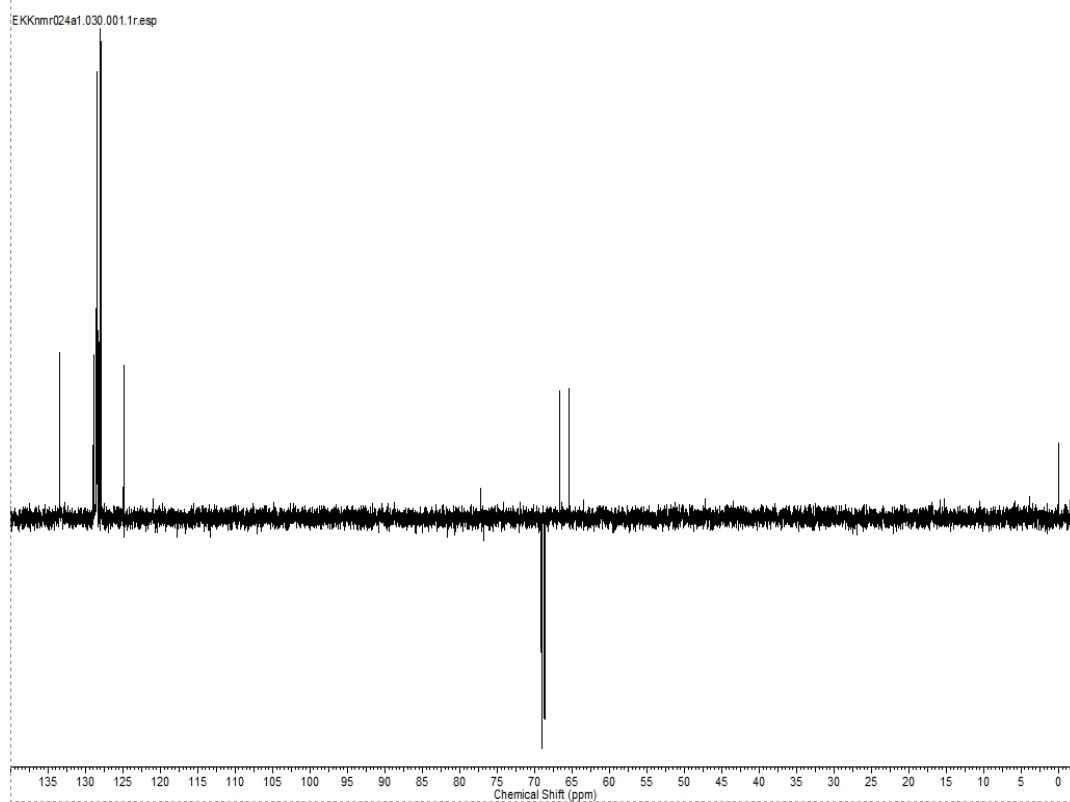
<sup>1</sup>H-NMR024A1



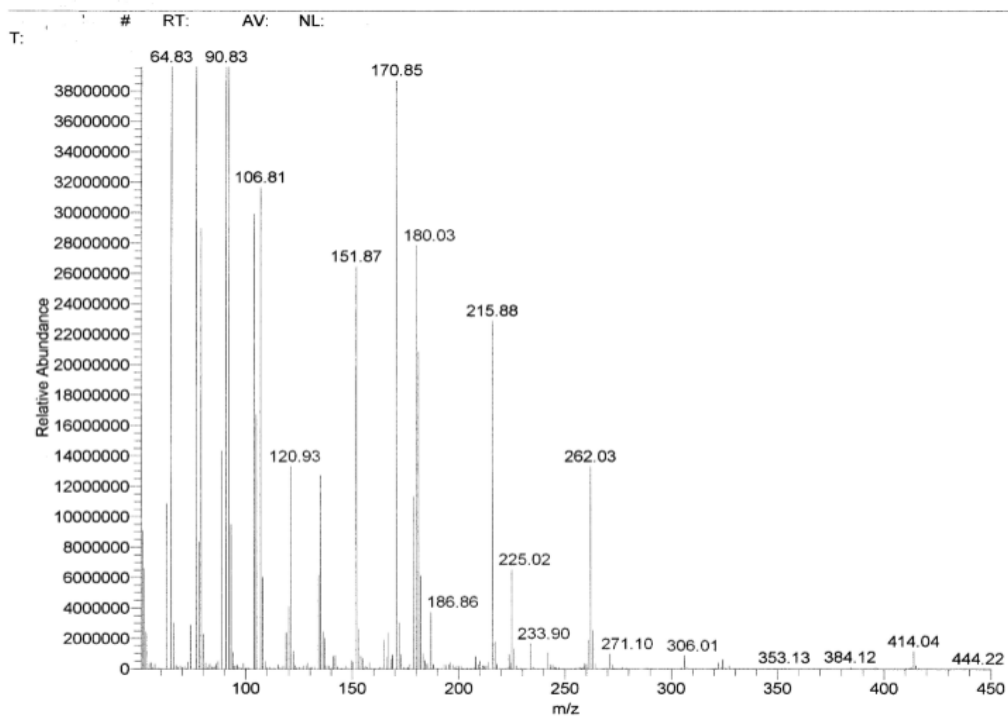
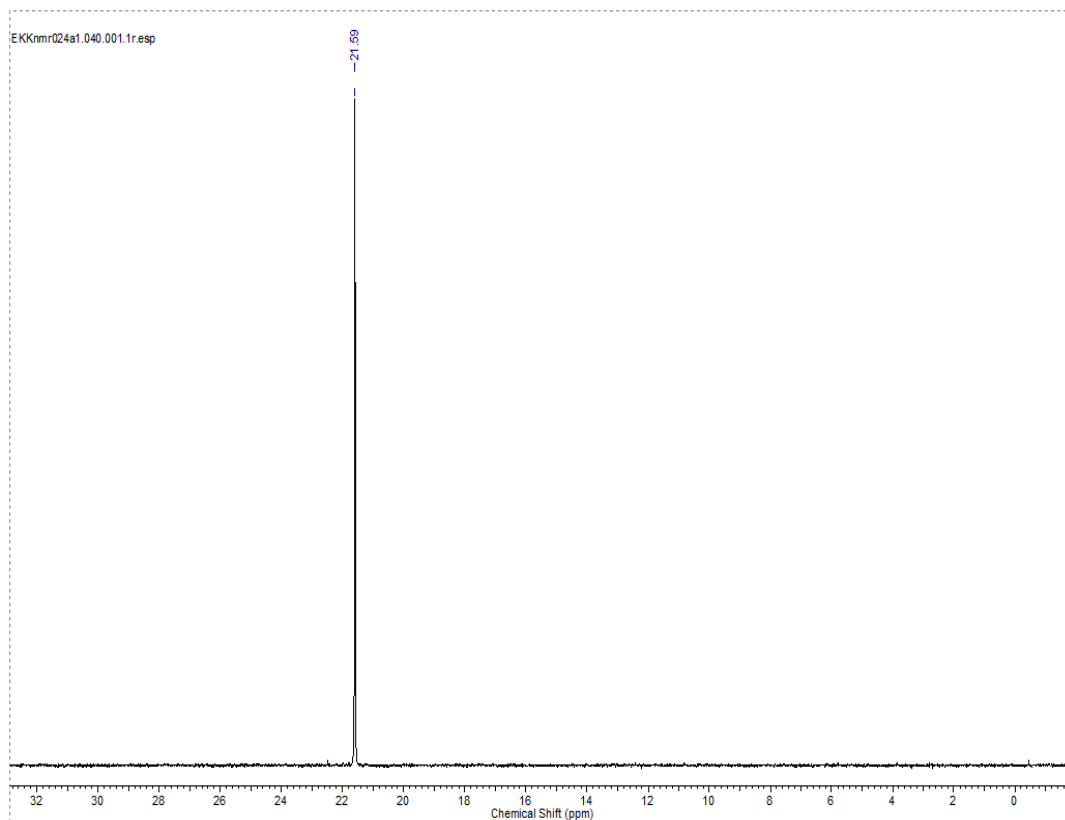
13C-NMR024A1



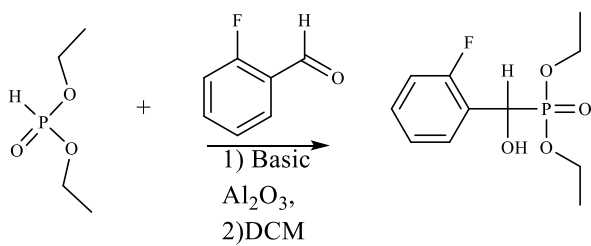
13C-NMR024A1-DEPT



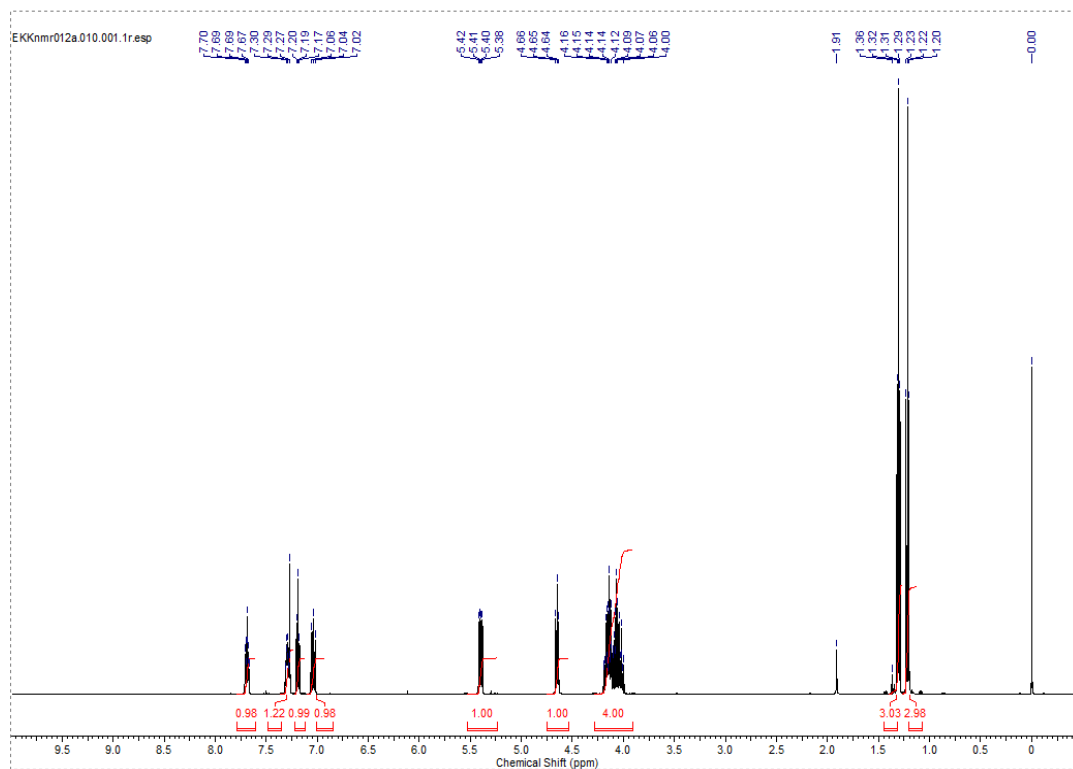
31P-NMR024A1



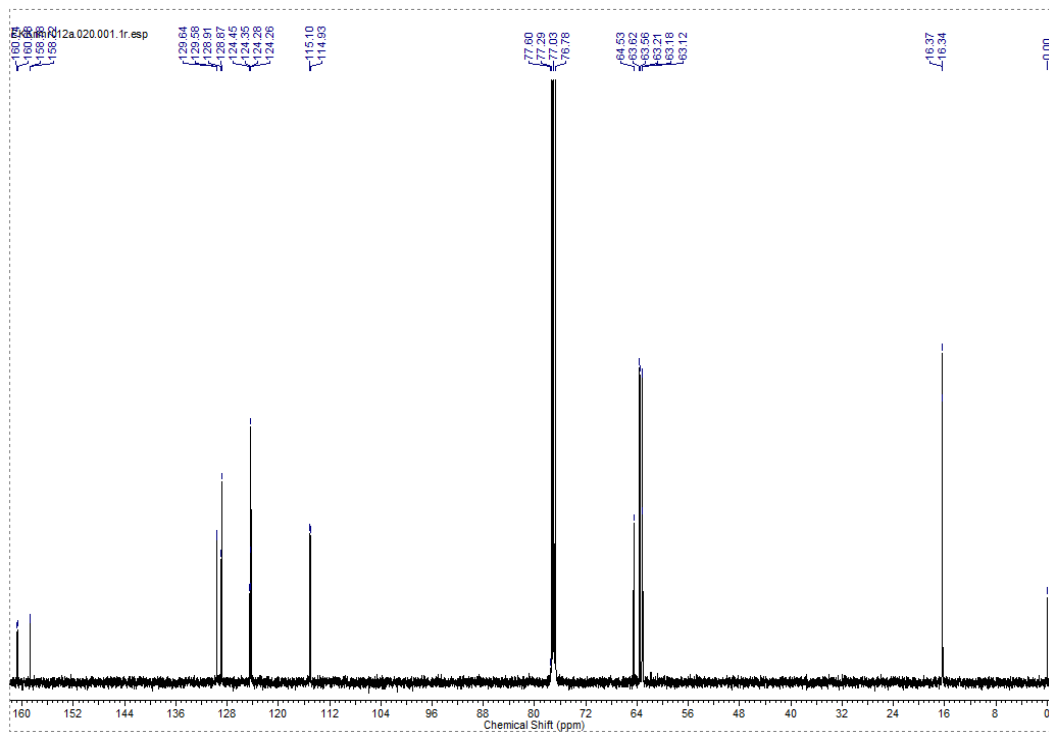
## 1.5 2-Fluorobenzyl- $\alpha$ -hydroxy diethyl phosphonate (12)



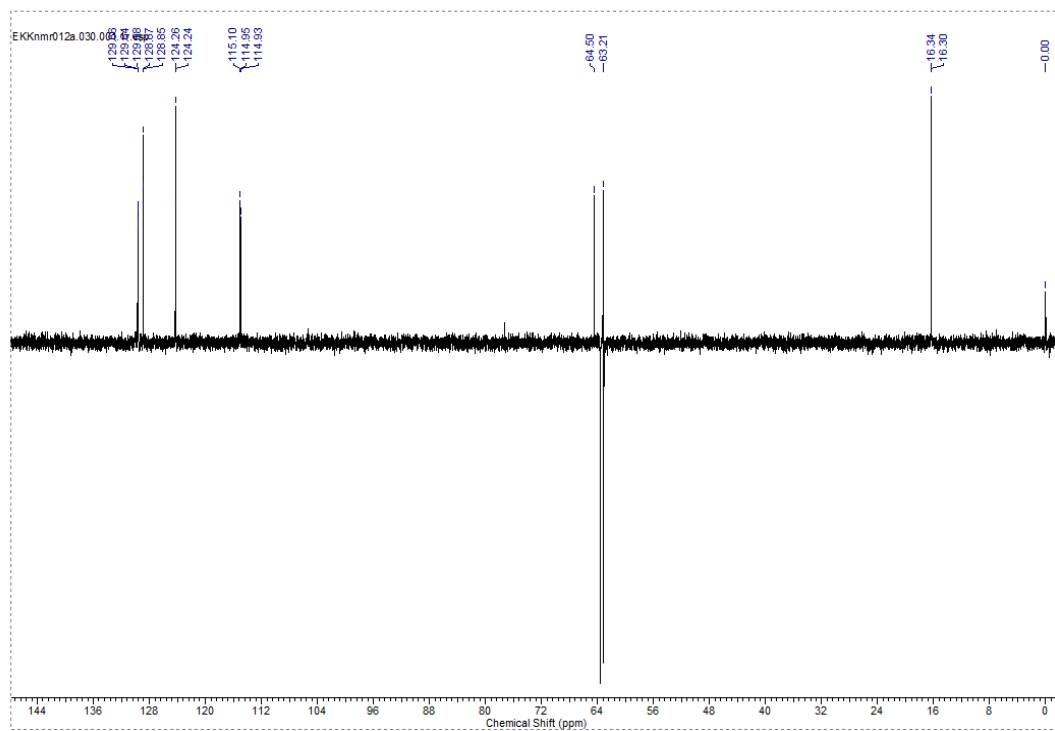
H-NMR0012A 2-FLUOROBENZYL- HYDROXY- DIETHYLPHOSPHITE



<sup>13</sup>C-NMR012A1



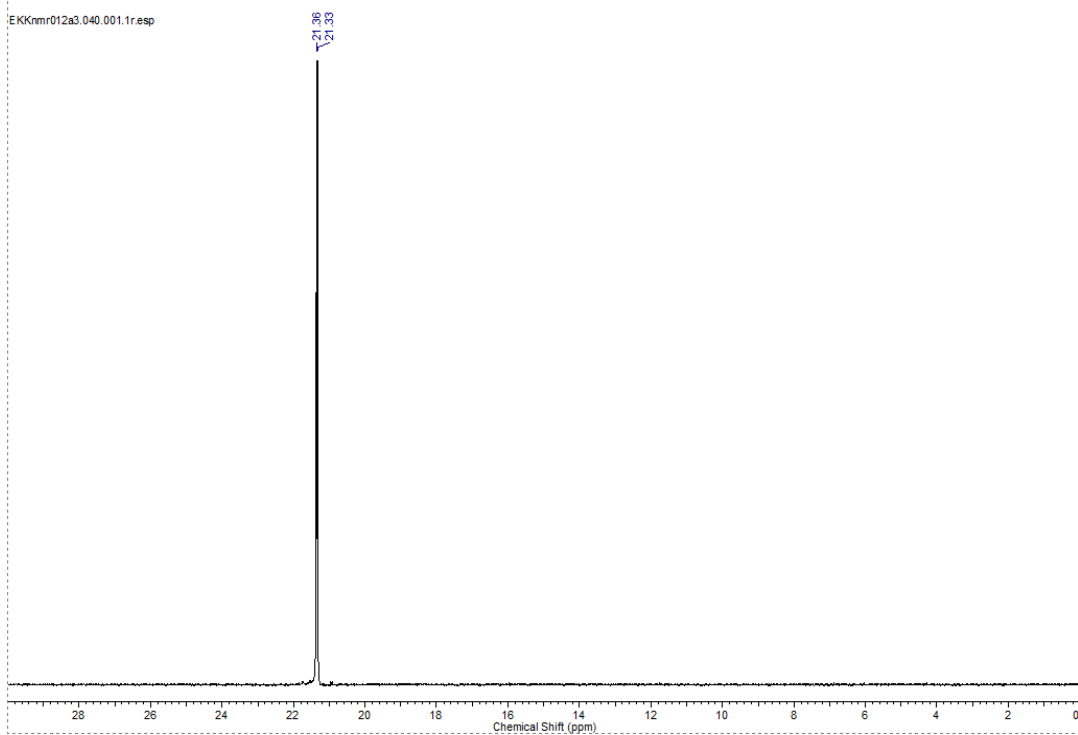
<sup>13</sup>C-NMR012ADEPT





# 31P-NMR012A

EKKmr012a3.040.001.1r.esp

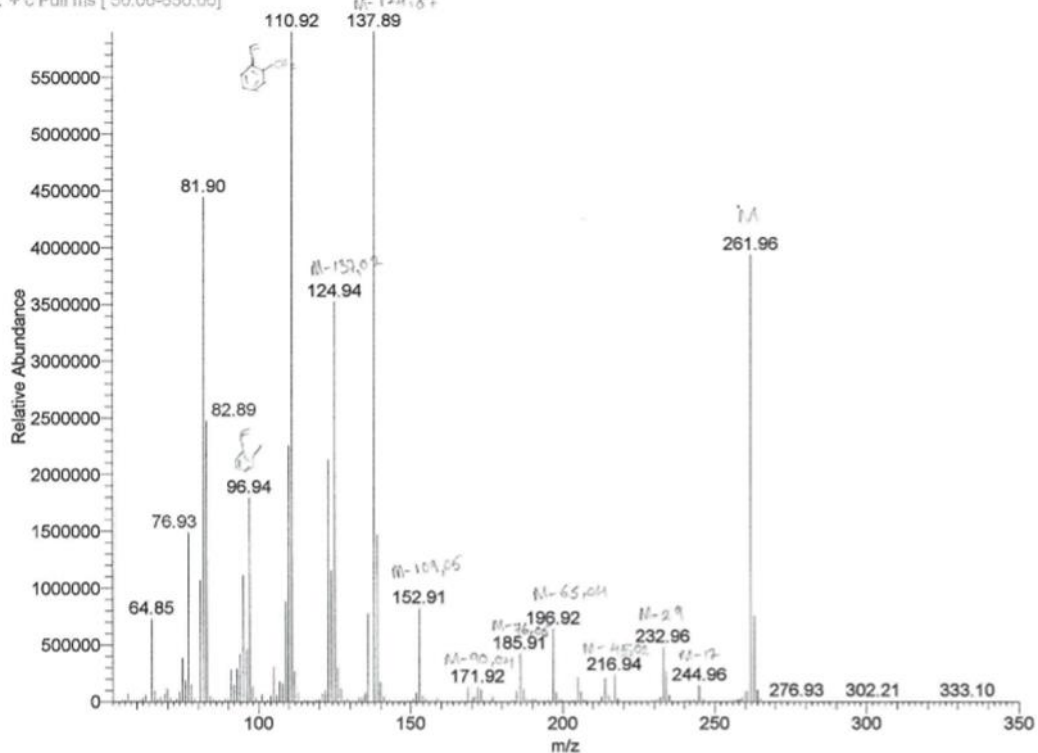


C:\Xcalibur\...2016 August EKKms012a  
Edward Kumbhrai Kasode sample MS012A

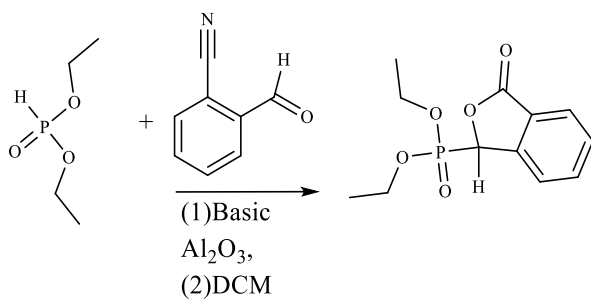
8/4/2008 1:32:53 PM

EKKms012a #51 RT: 1.06 AV: 1 NL: 1.20E7

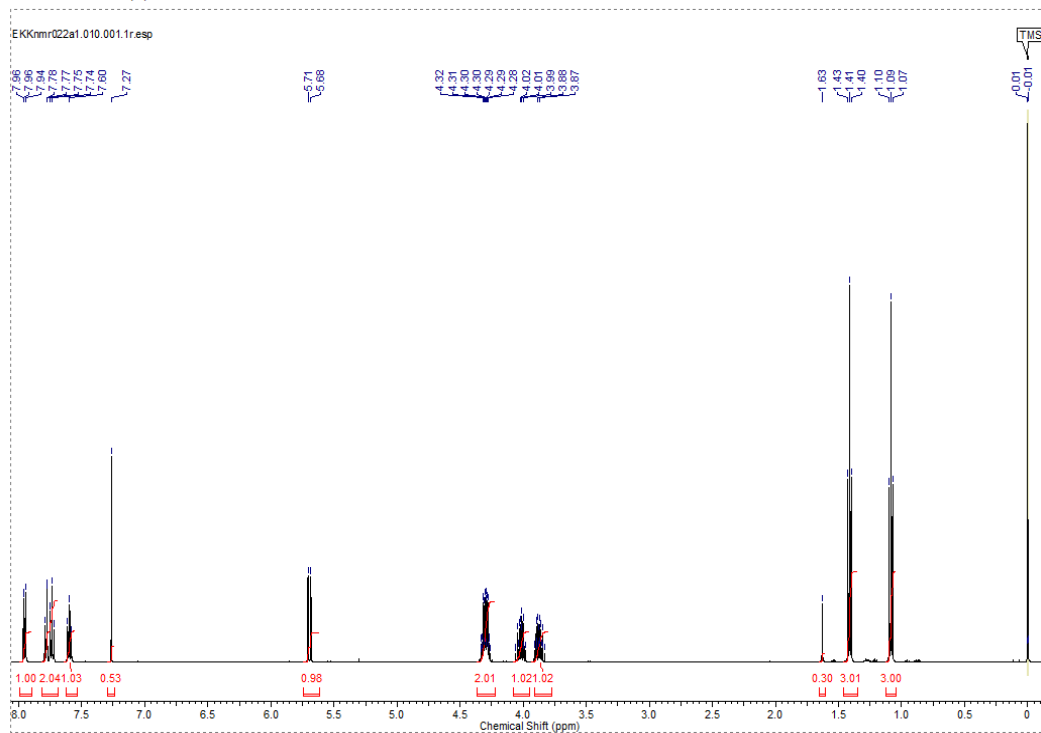
T: + c Full ms [ 50.00-650.00]



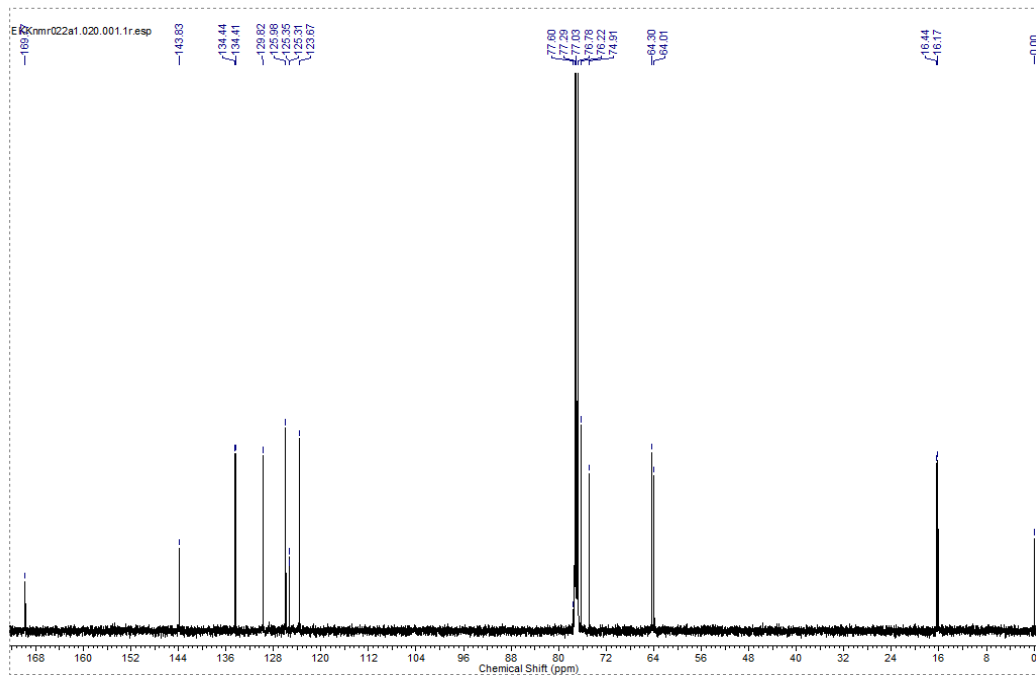
**1.6 1,2-Benzyl- $\gamma$ -lactone-2-diethyl phosphonate (18) (Menear, K. A, *et al* 2012, US008247416B2).**



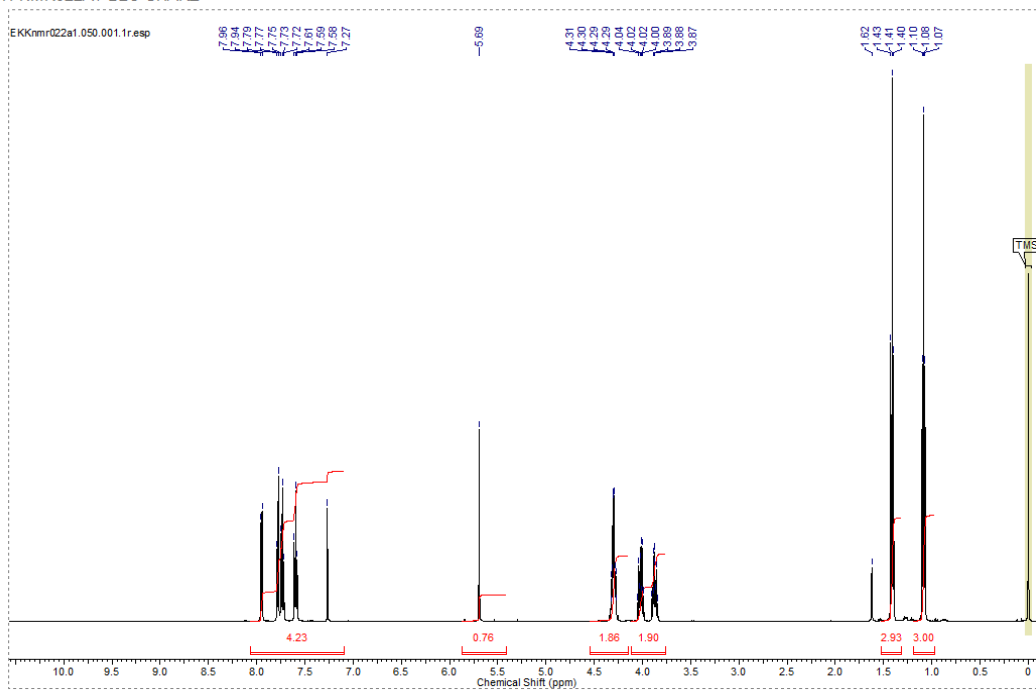
1-H-NMR022A1 (2)



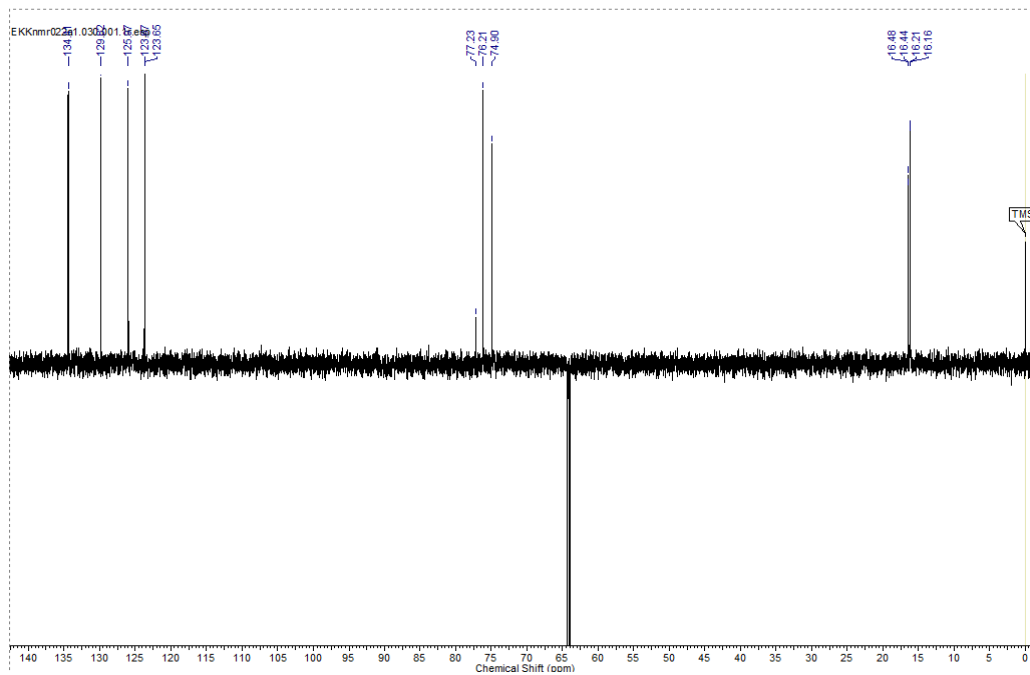
13C-NMR022A1



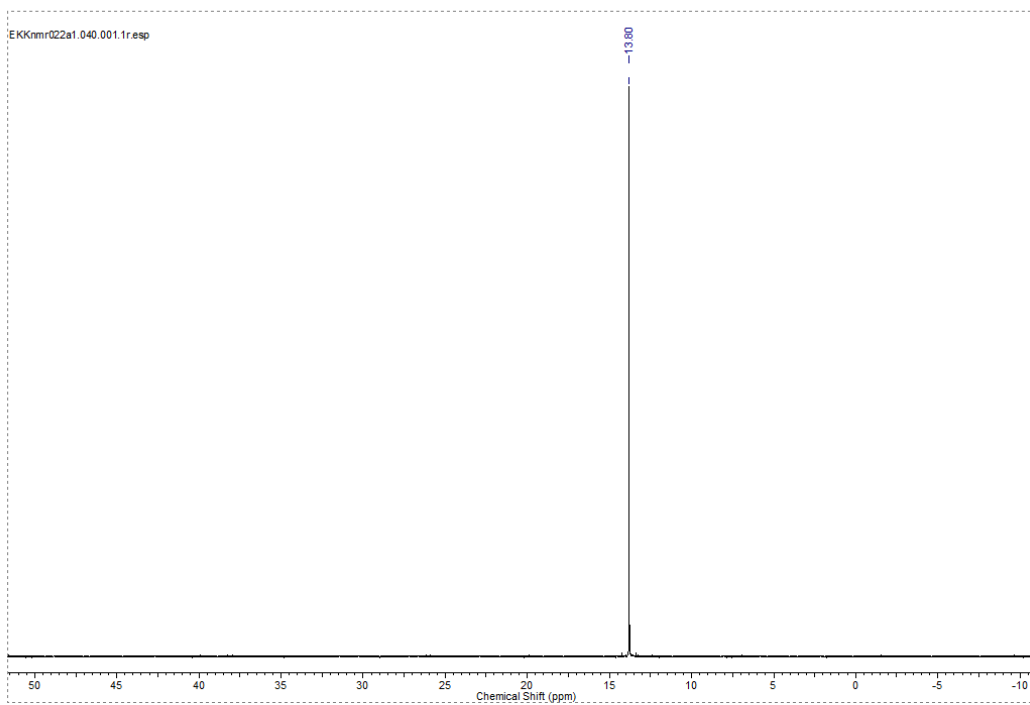
1H-NMR022A1-D2O SHAKE

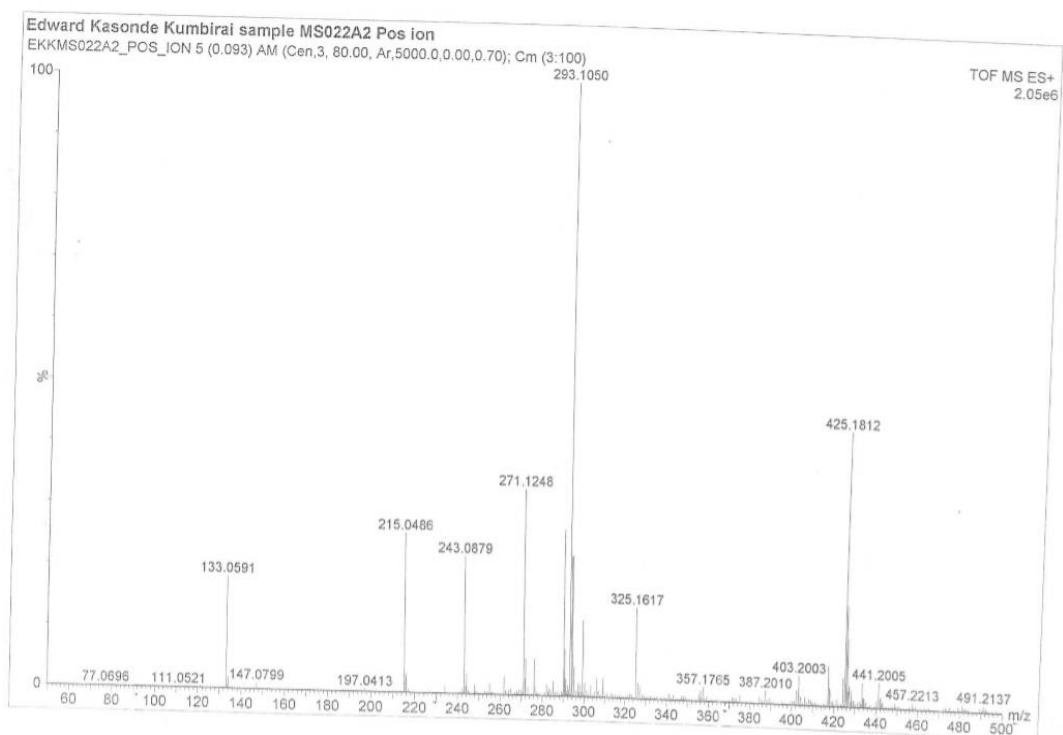
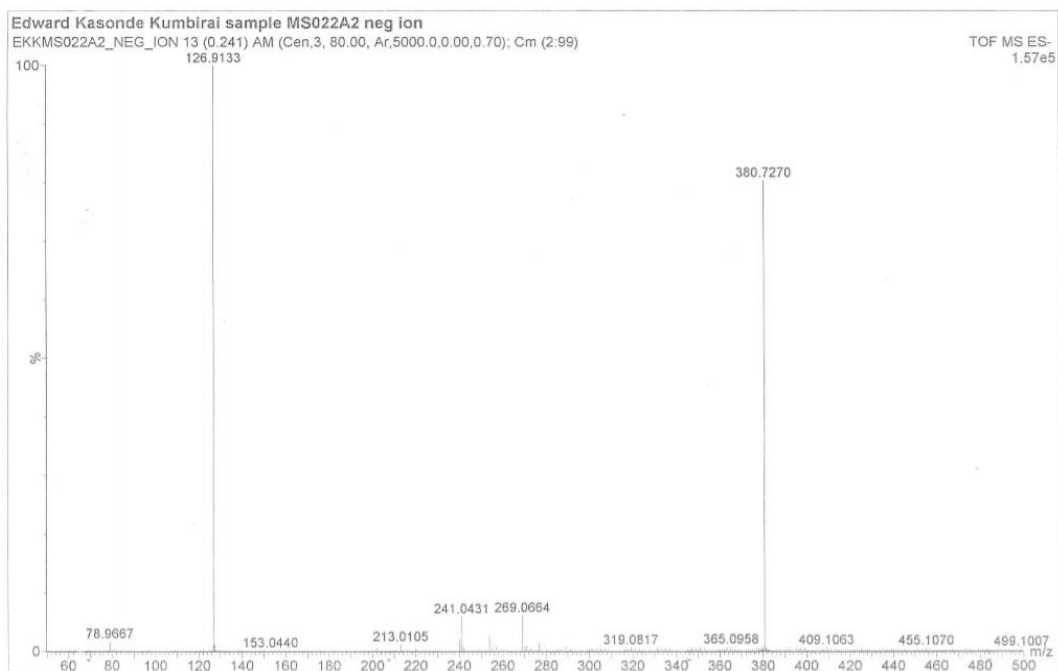


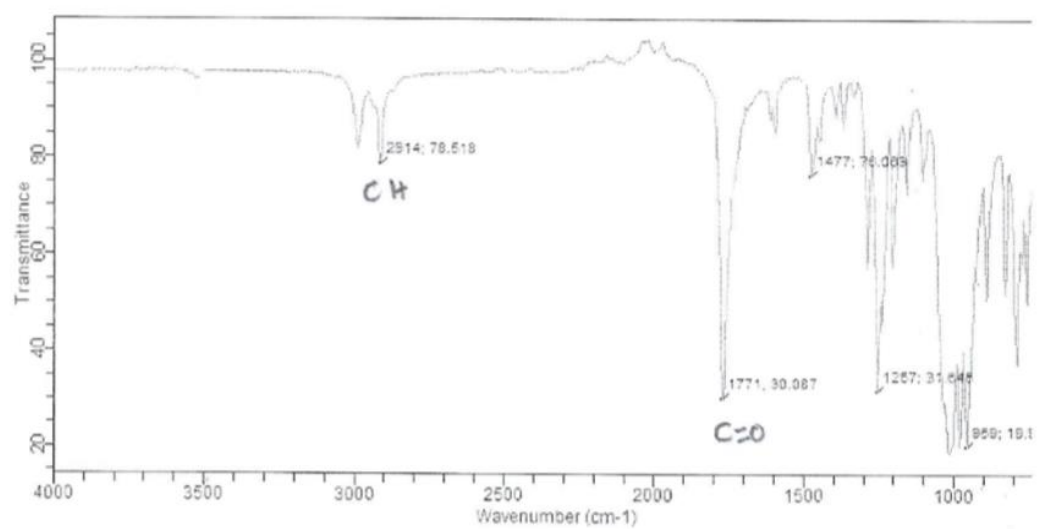
13C-NMR022A1-DEPT



31P-NMR022A1

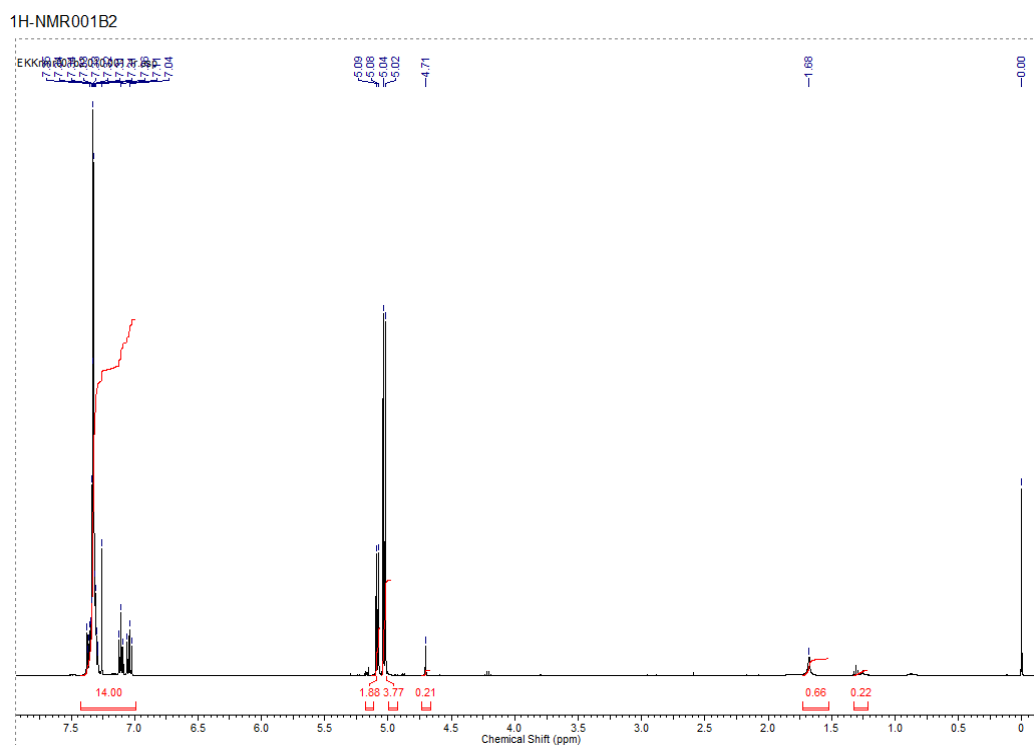
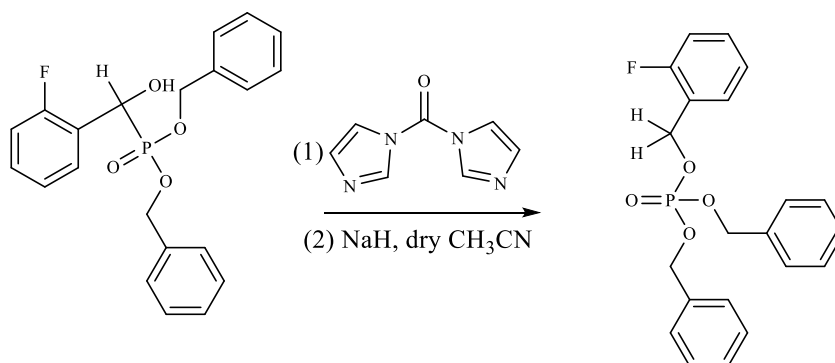


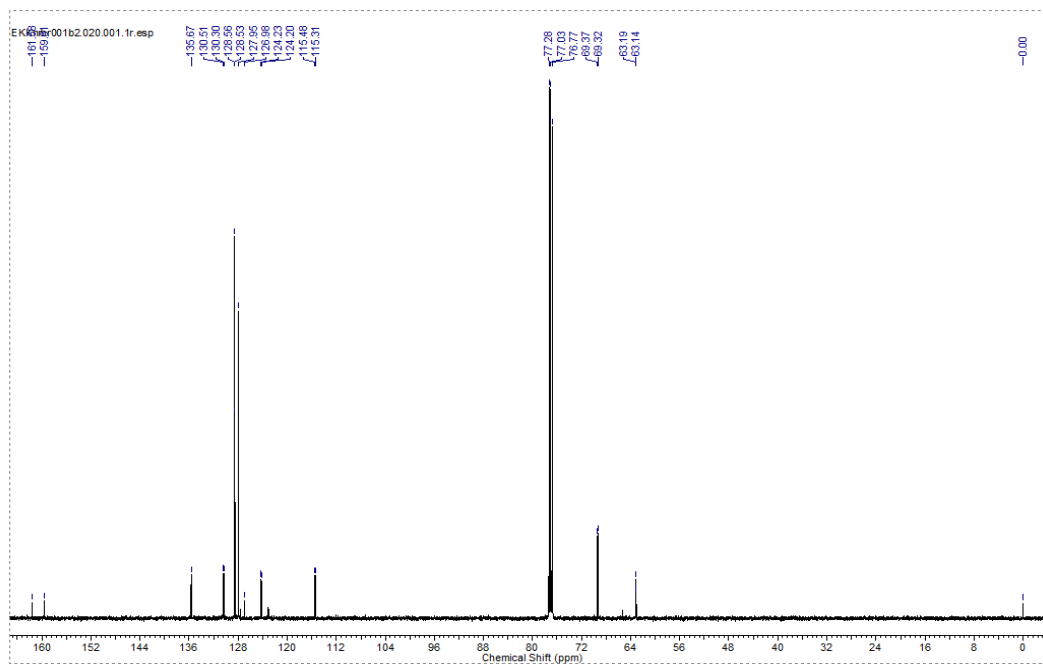




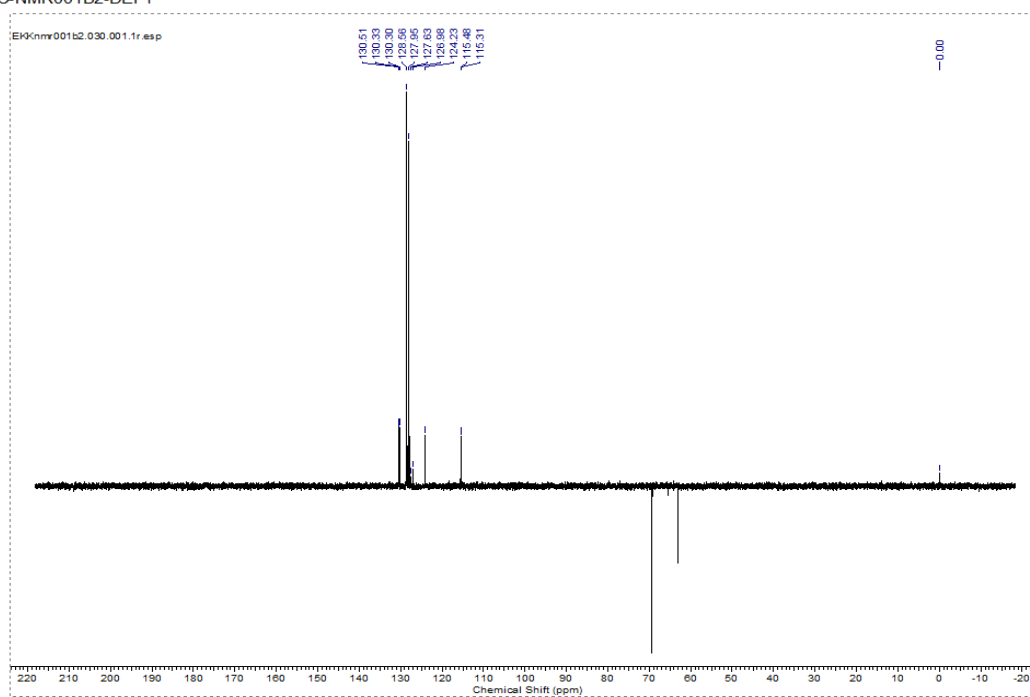
## 2 CONVERSION OF THE BENZYL- $\alpha$ -HYDROXY TO THE BENZYL- $\alpha$ -METHYLENE PHOSPHONATES/PHOSPHATES

### 2.1 2-Fluorobenzyl-dibenzyl phosphate (19)





13C-NMR001B2-DEPT





31P-NMR001B2

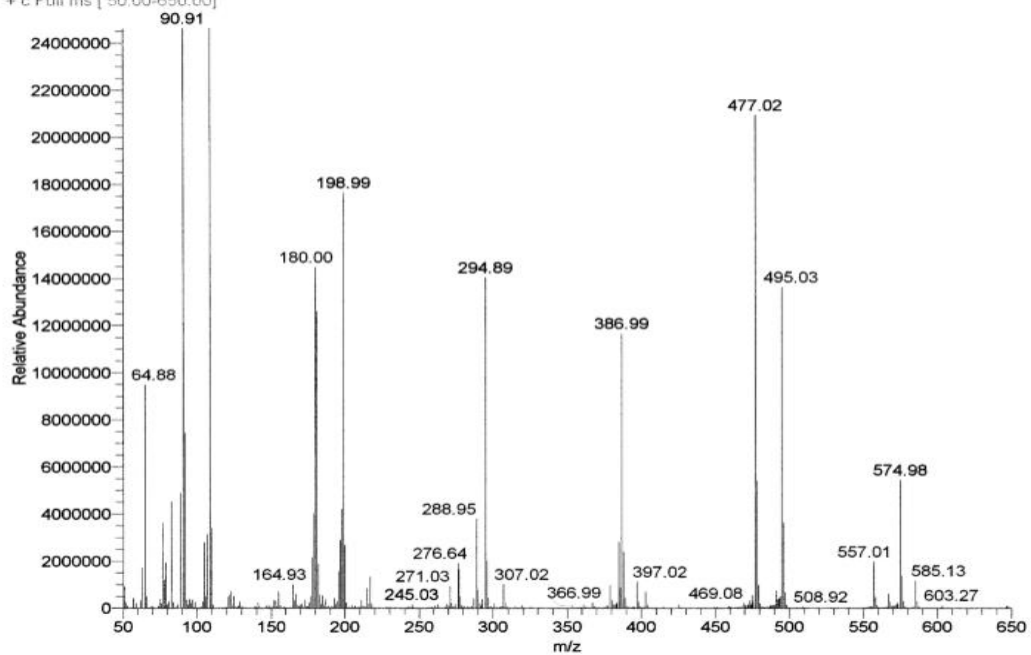
EKKms001b2.040.001.fr.esp

-0.51

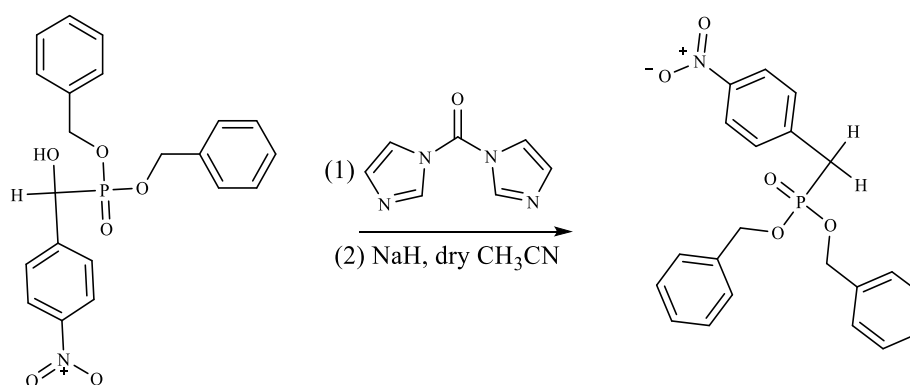
GCXcalibur 3.2015 July EKKms001b2  
Edward Kumbhat Kasonde sample MS001B2

7/12/2009 11:09:31 AM

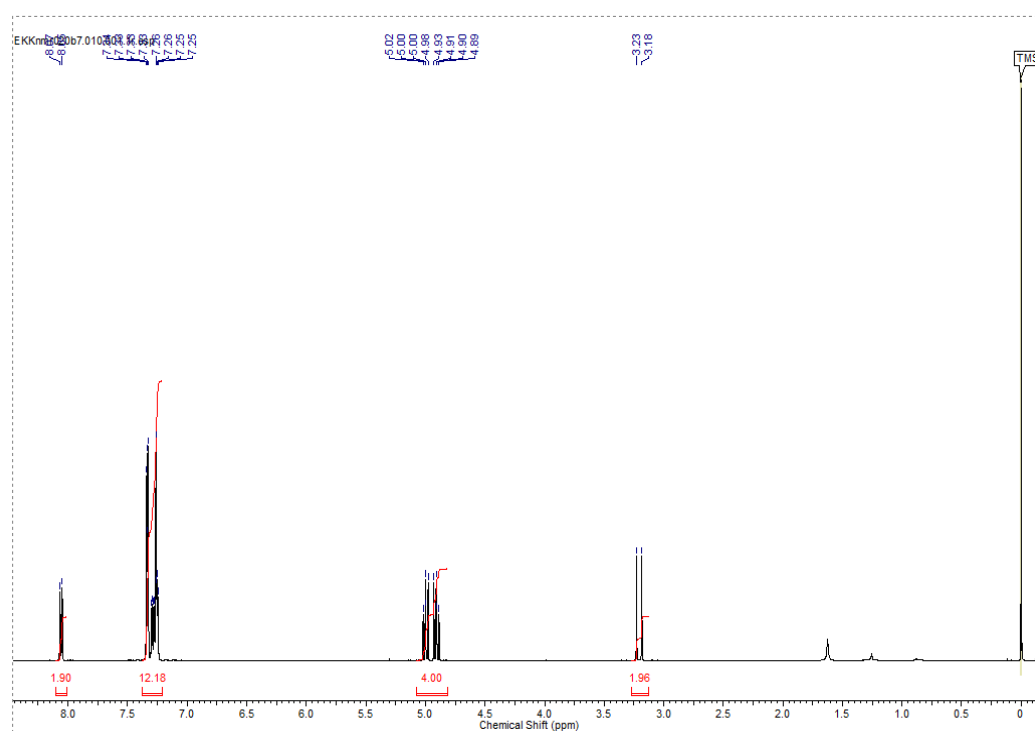
EKKms001b2 #69 RT: 1.44 AV: 1 NL: 9.85E7  
T: + c Full ms [ 50.00-650.00]



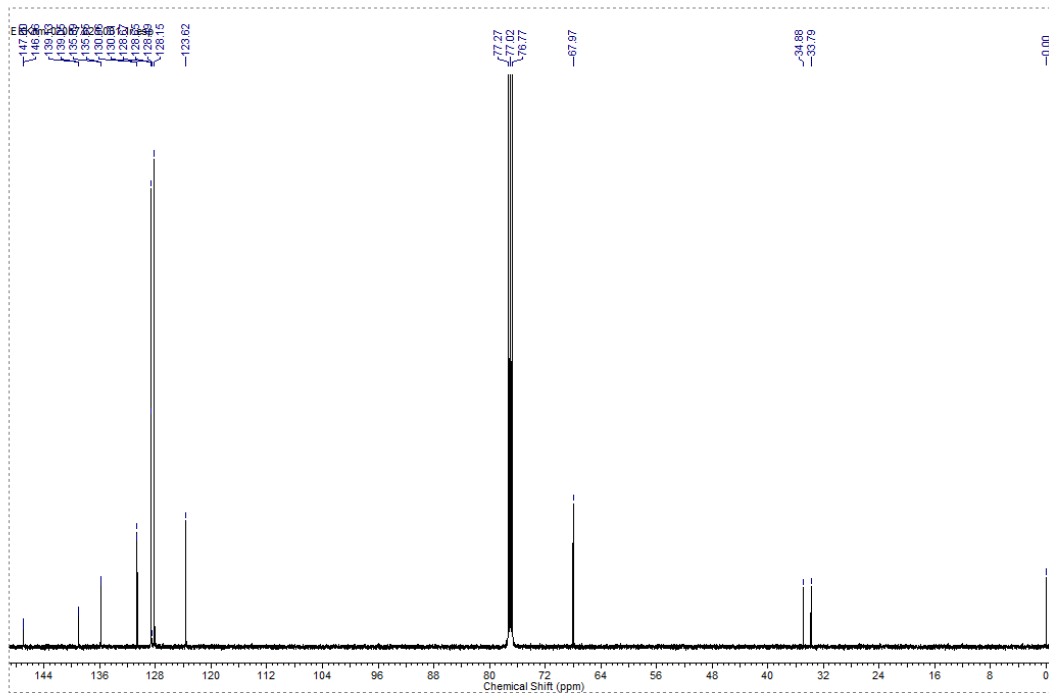
## 2.2 4-Nitrobenzyl- $\alpha$ -methylene-dibenzyl phosphonate (24)



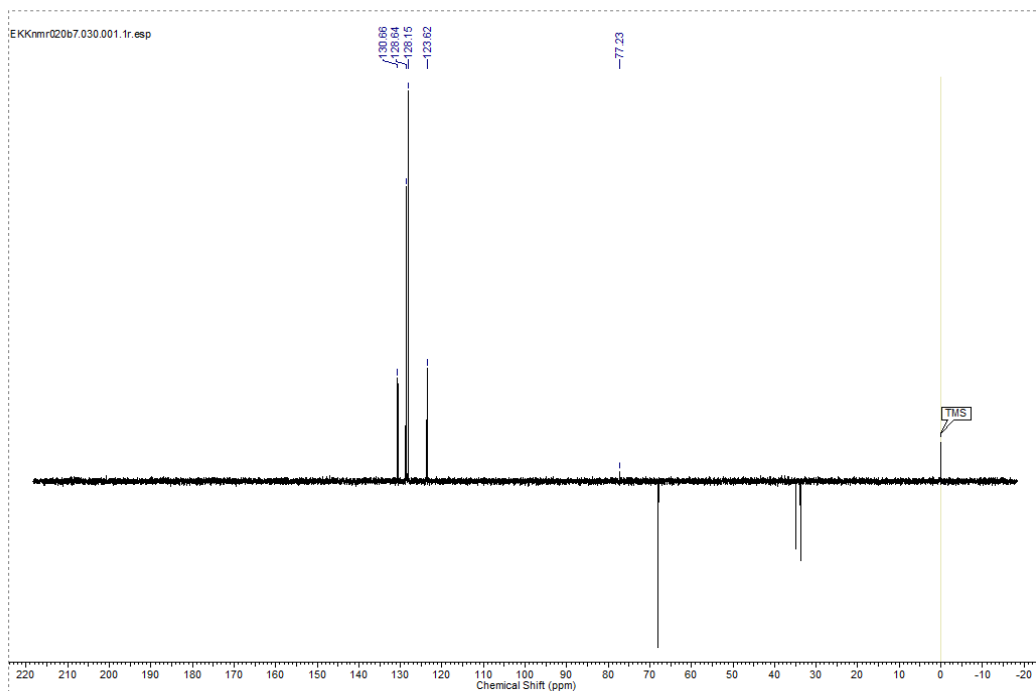
<sup>1</sup>H-NMR020B7



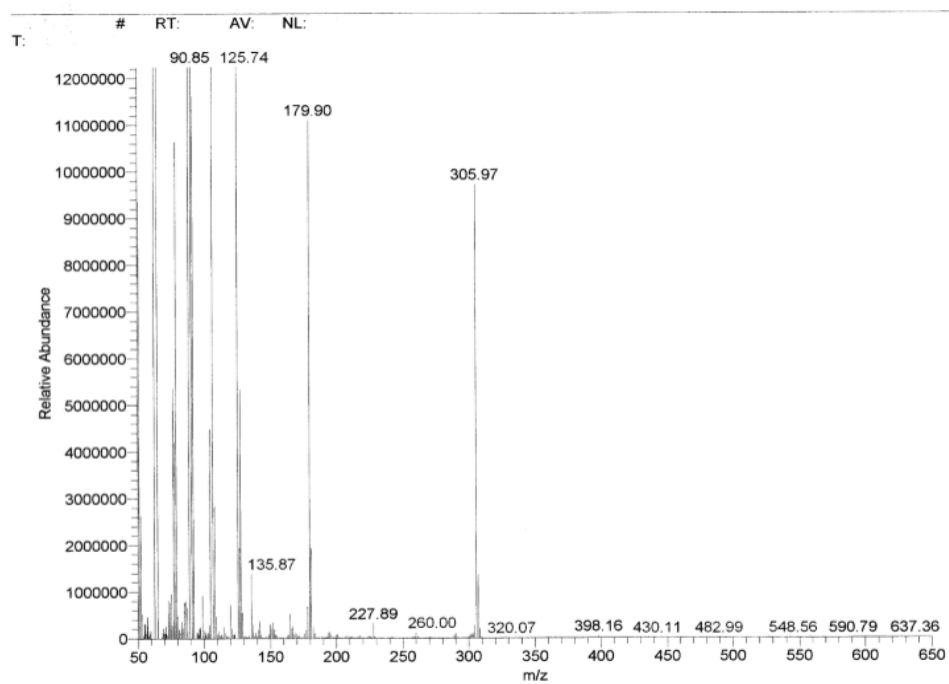
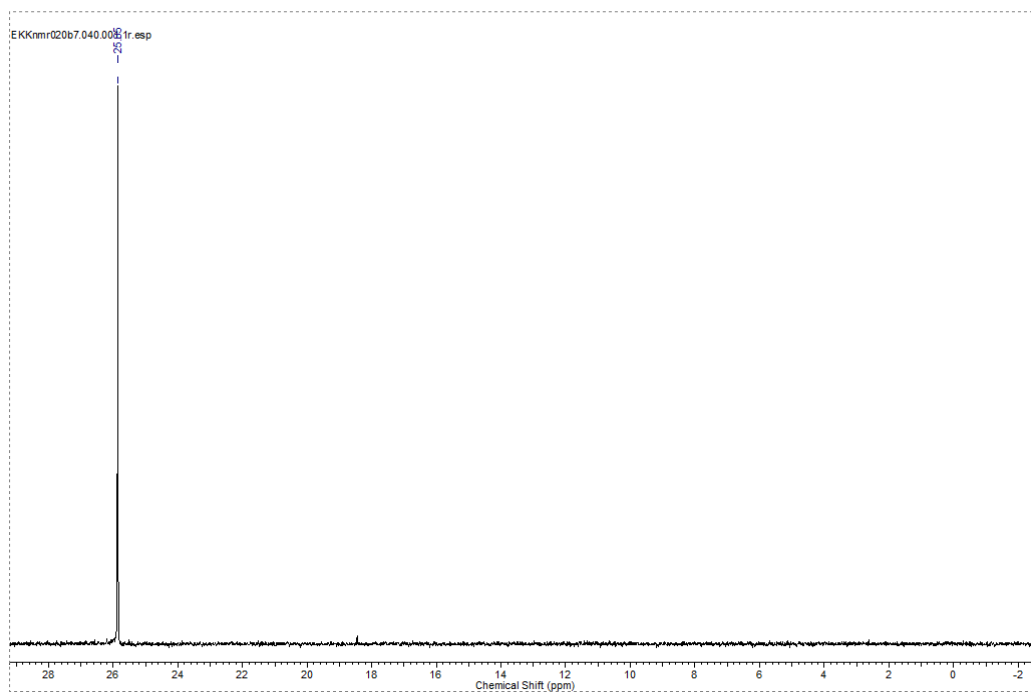
13C-NMR020B7



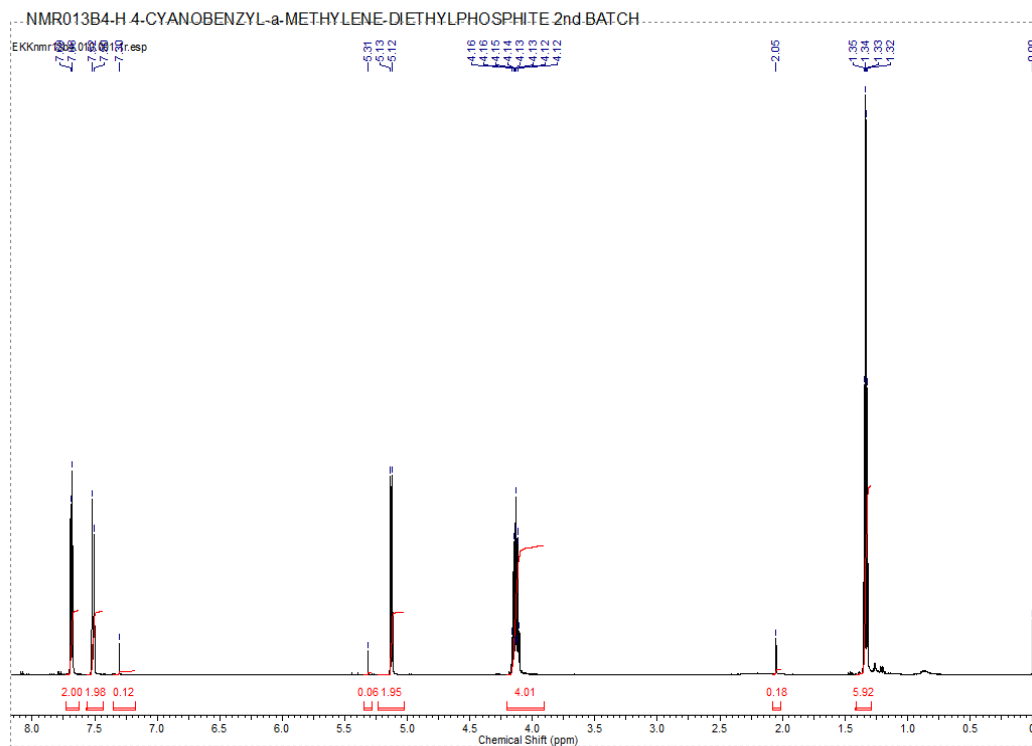
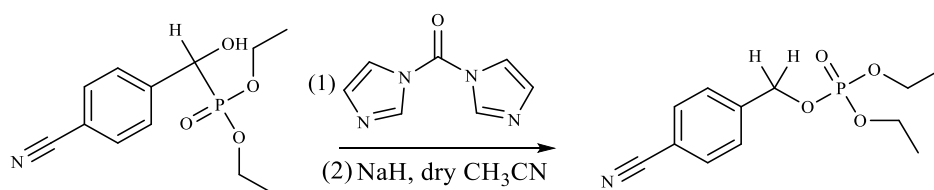
13C-NMR020B7-DEPT



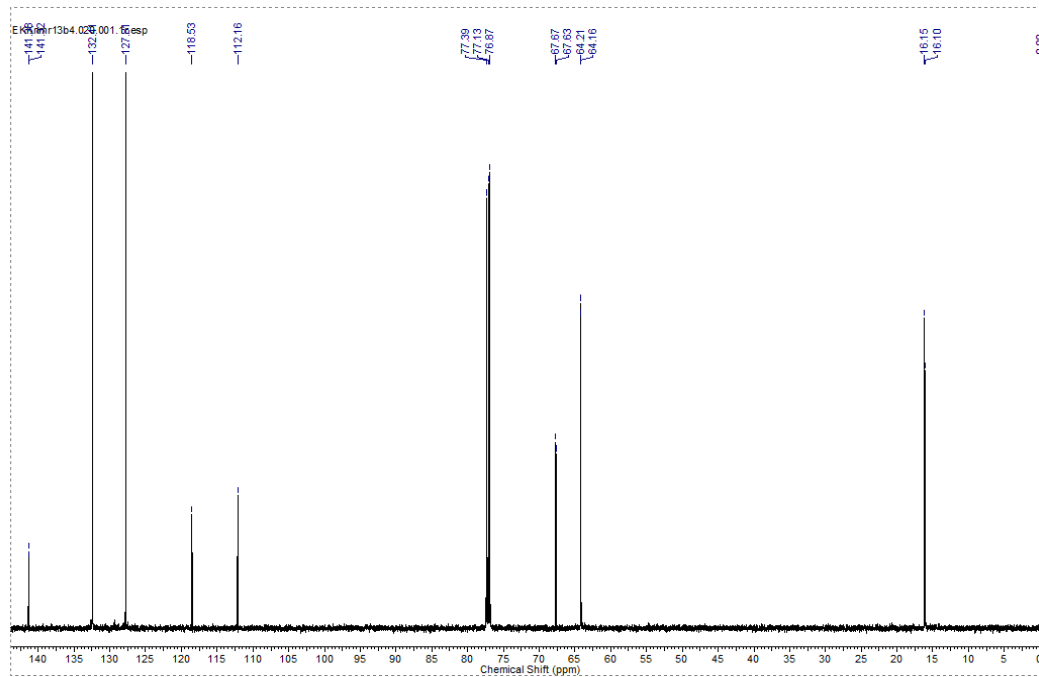
# 31P-NMR020B7



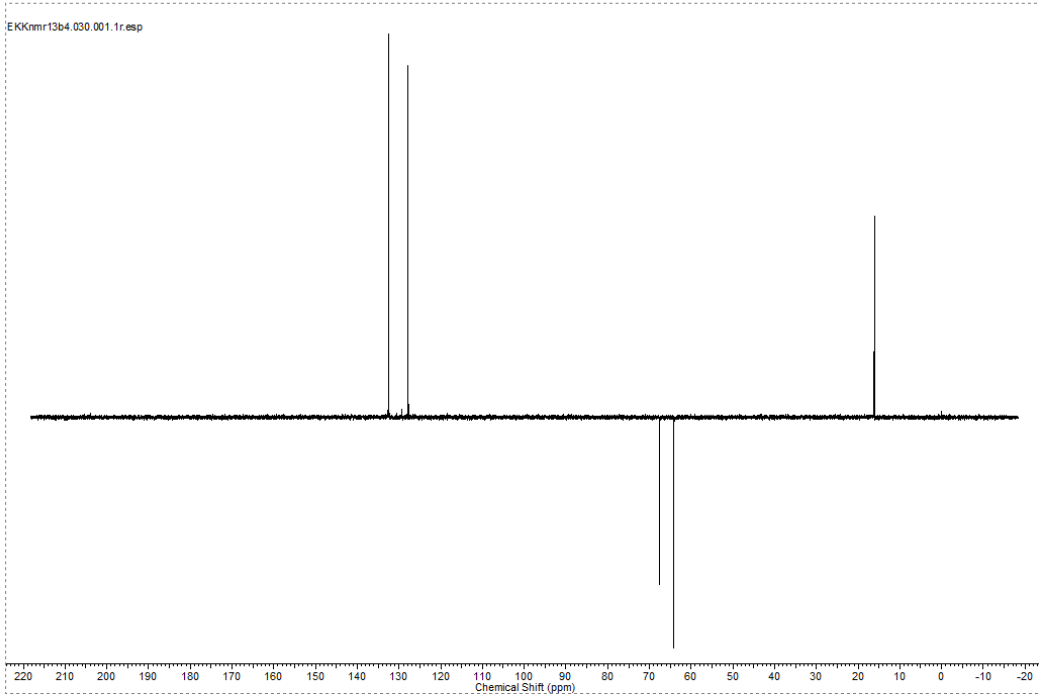
## 2.3 4-Cyanobenzyl-diethyl phosphate (22)



13C-NMR013B4

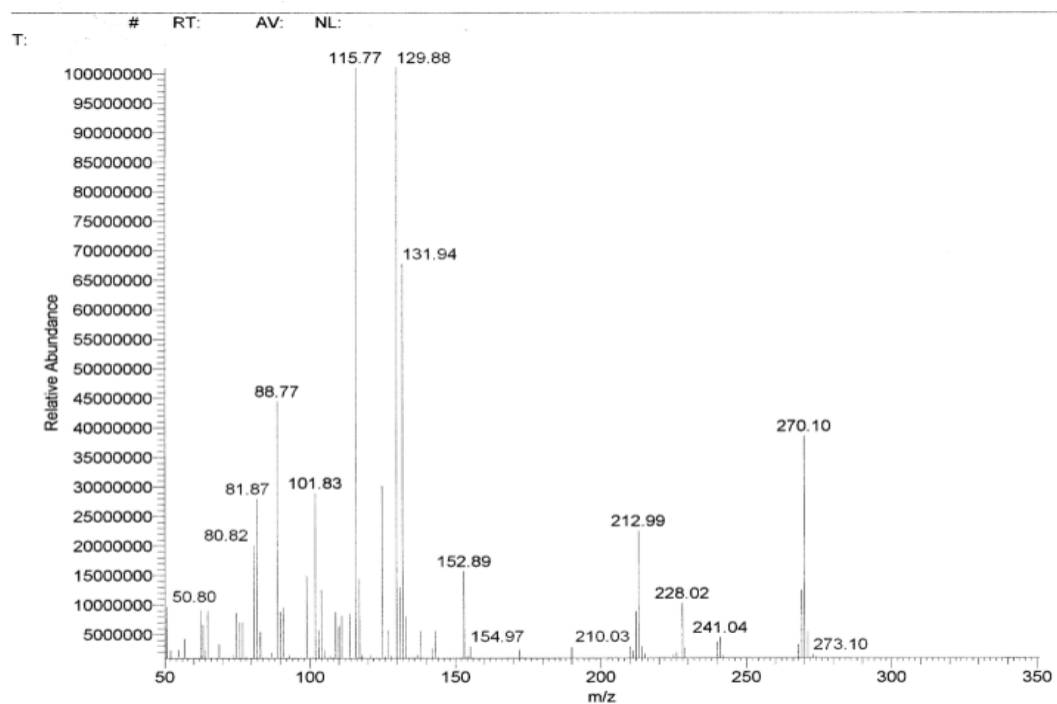
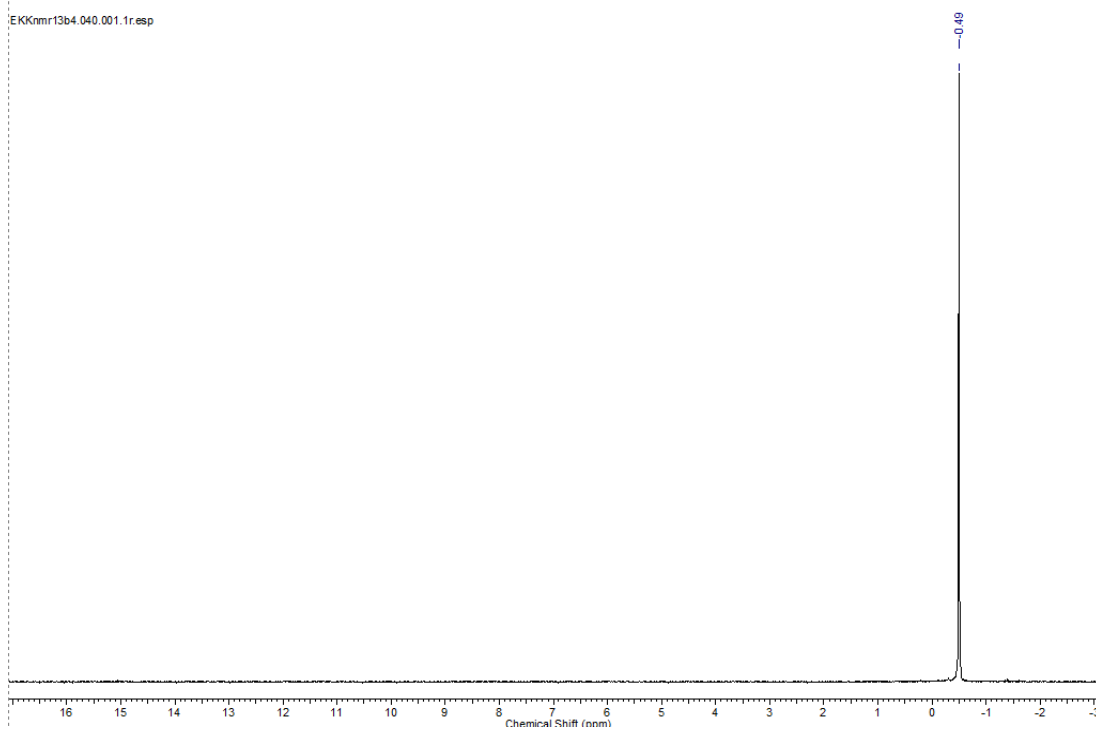


NMR013B4-13C DEPT

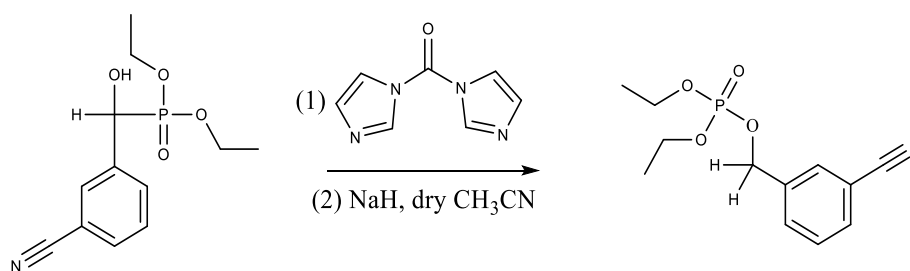


31P- NMR013B4

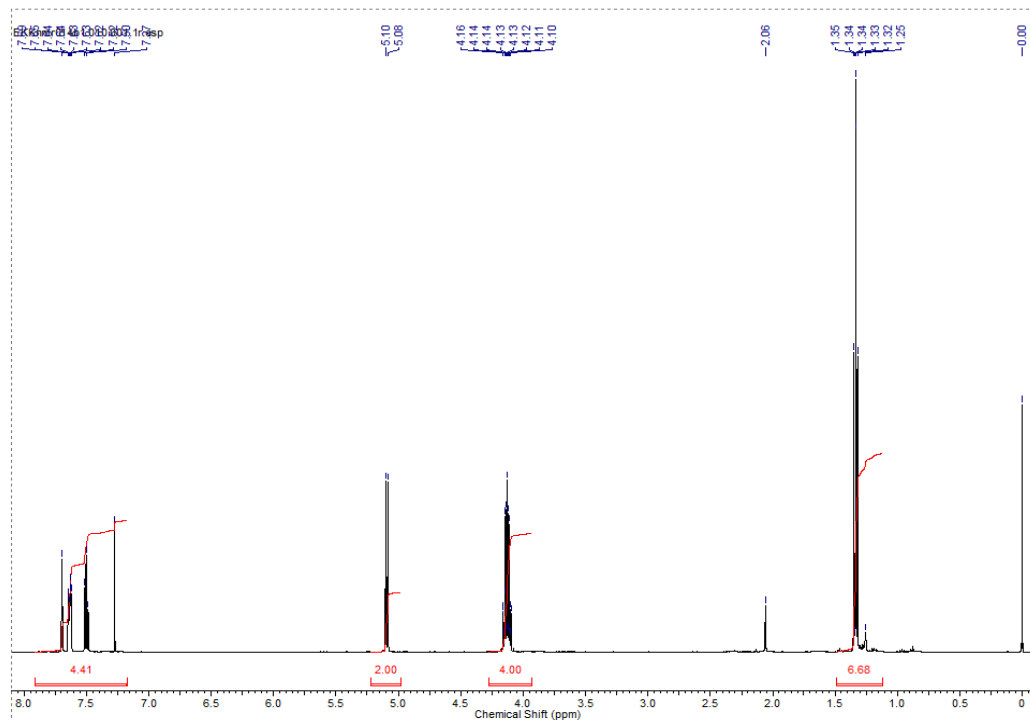
EKKnmr13b4.040.001.1r.esp



## 2.4 3-Cyanobenzyl-diethyl phosphate (21)

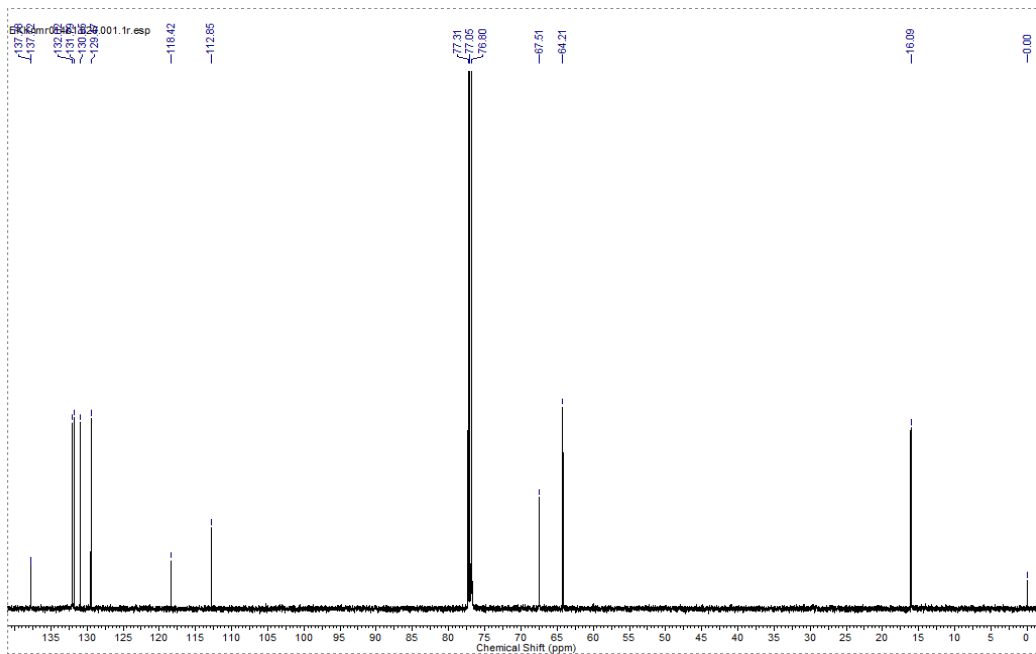


1H-NMR014B1

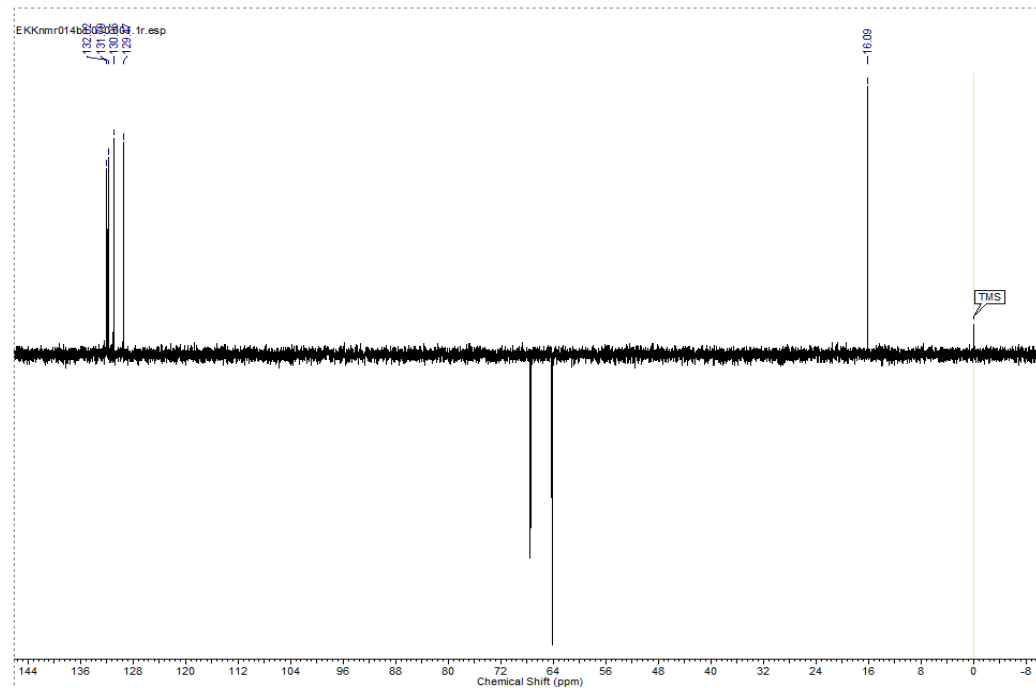




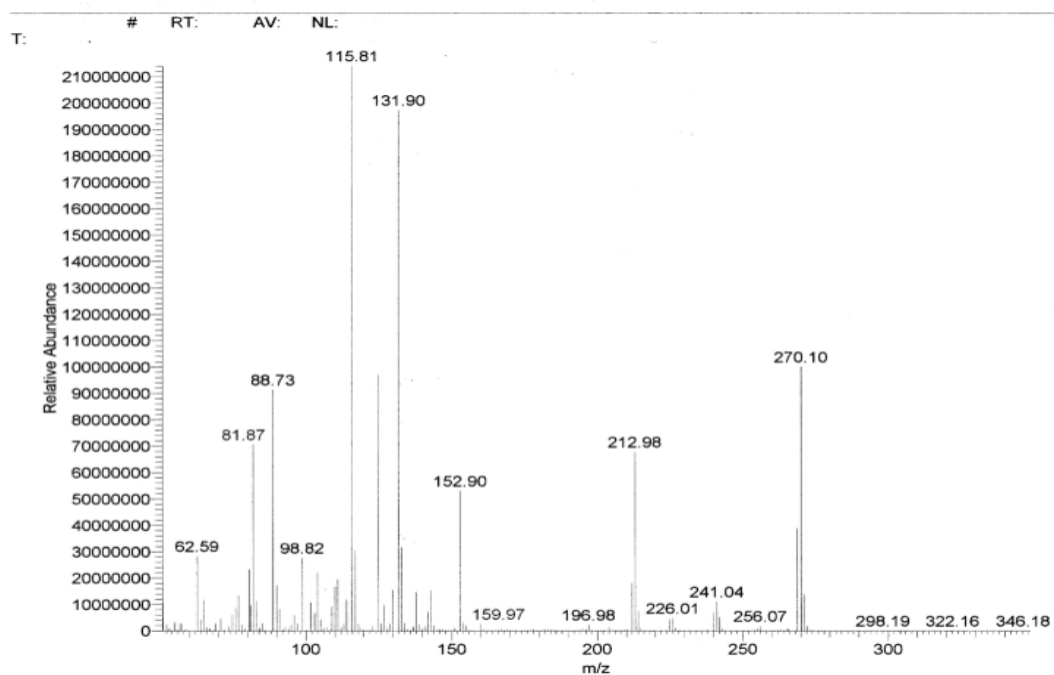
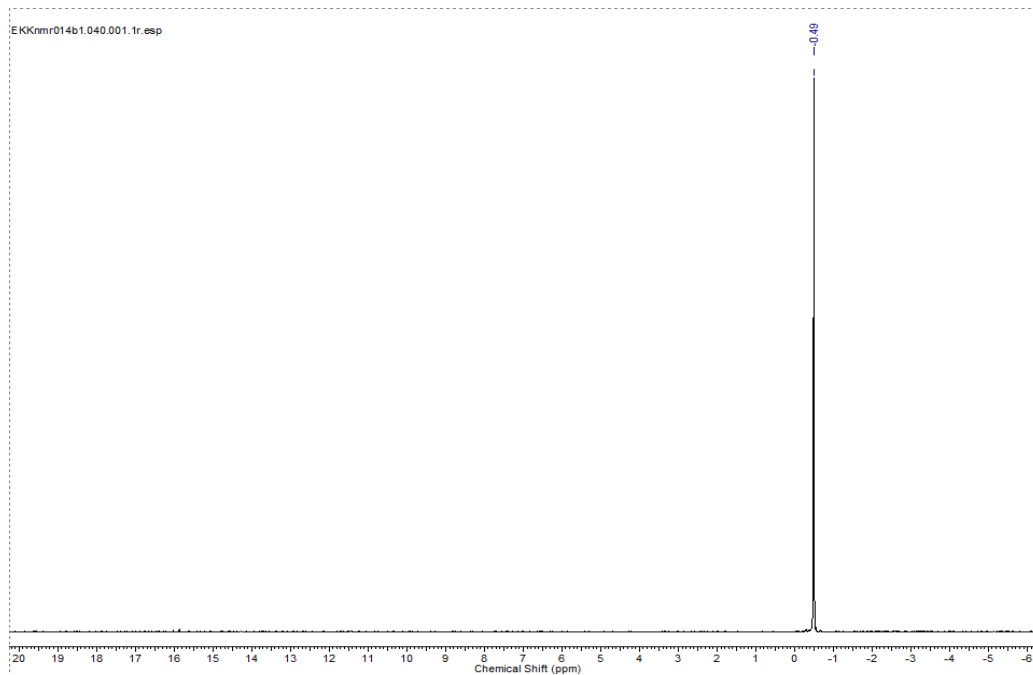
13C-NMR014B1



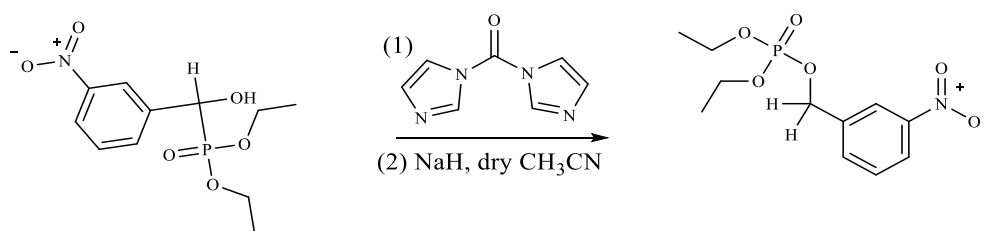
13C-NMR014B1-DEPT



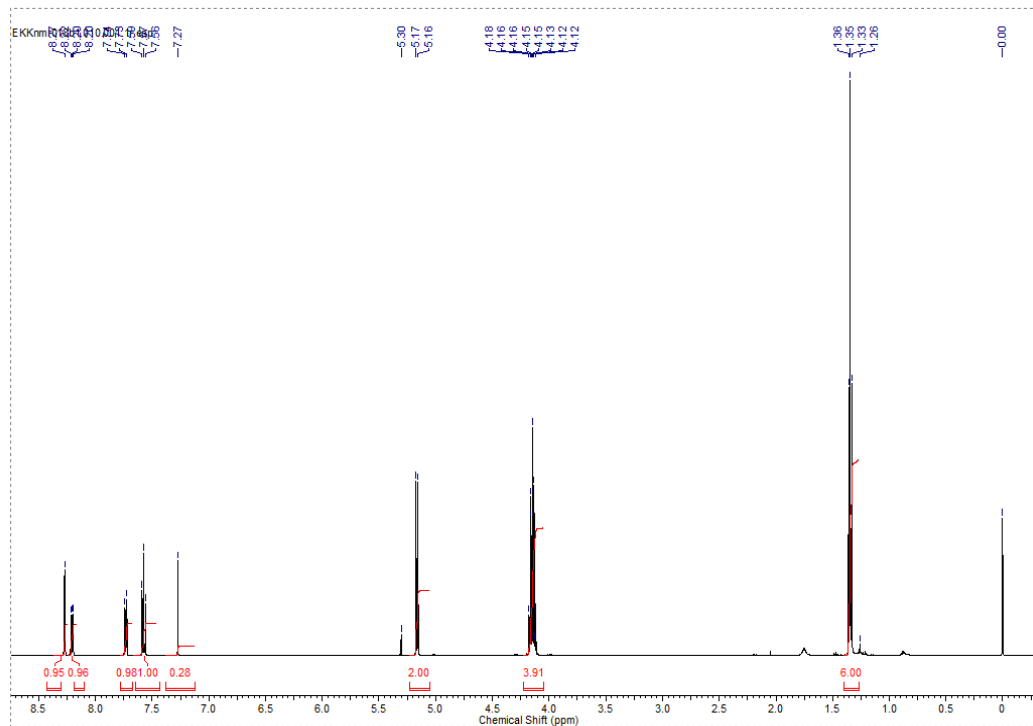
31P-NMR014B1



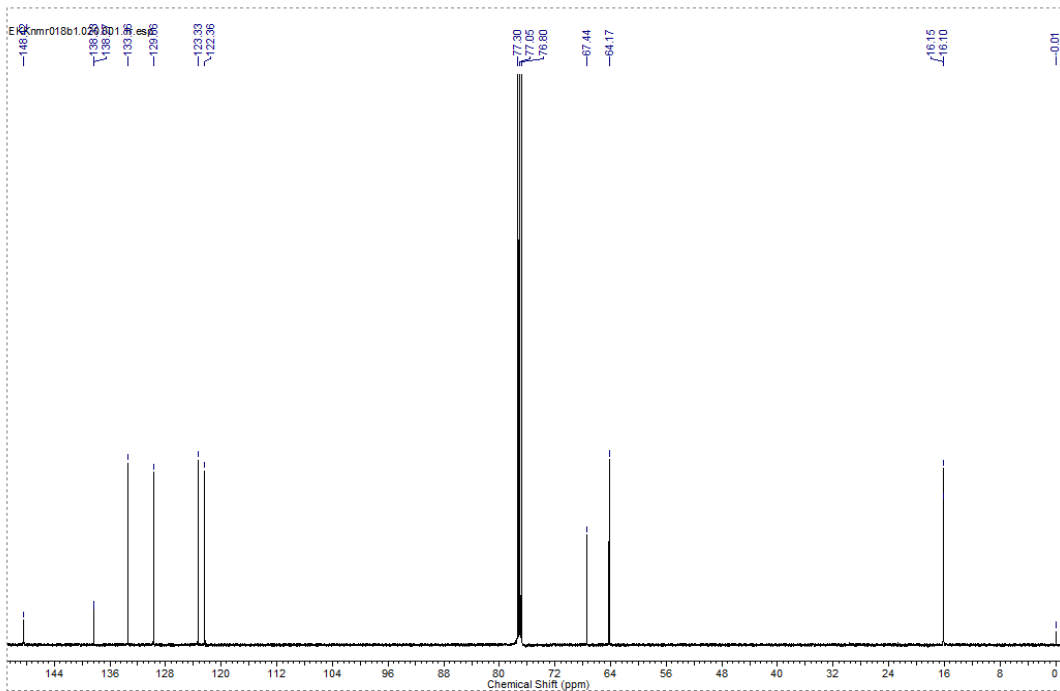
## 2.5 3-Nitrobenzyl-diethyl phosphate (23)



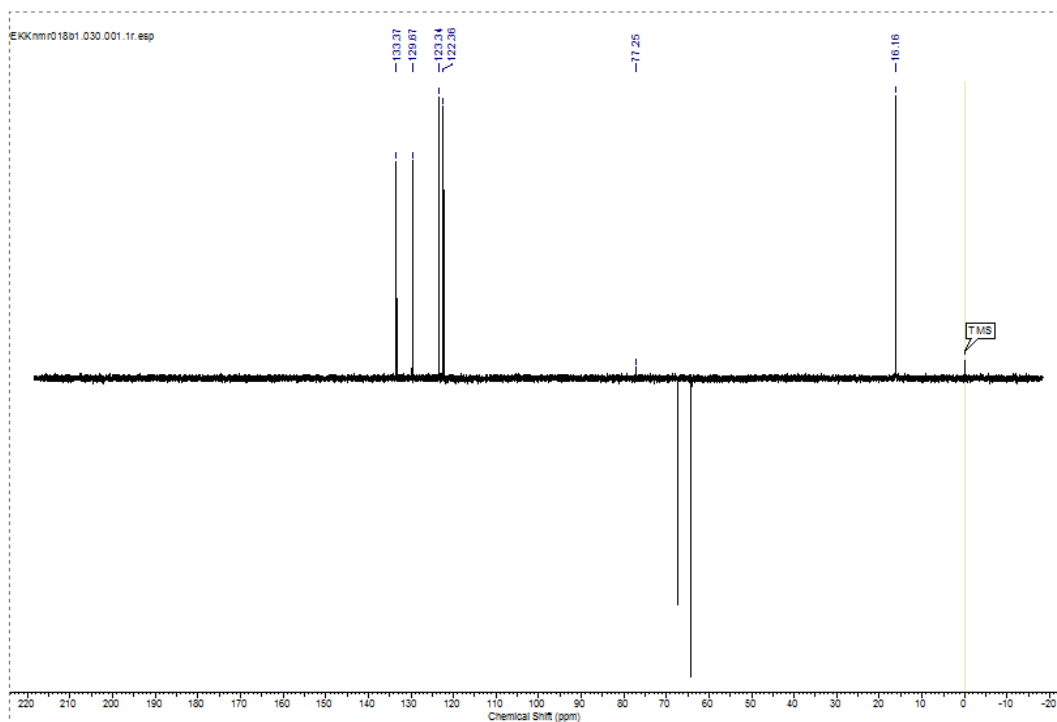
1H-NMR018B1



13C-NMR018B1

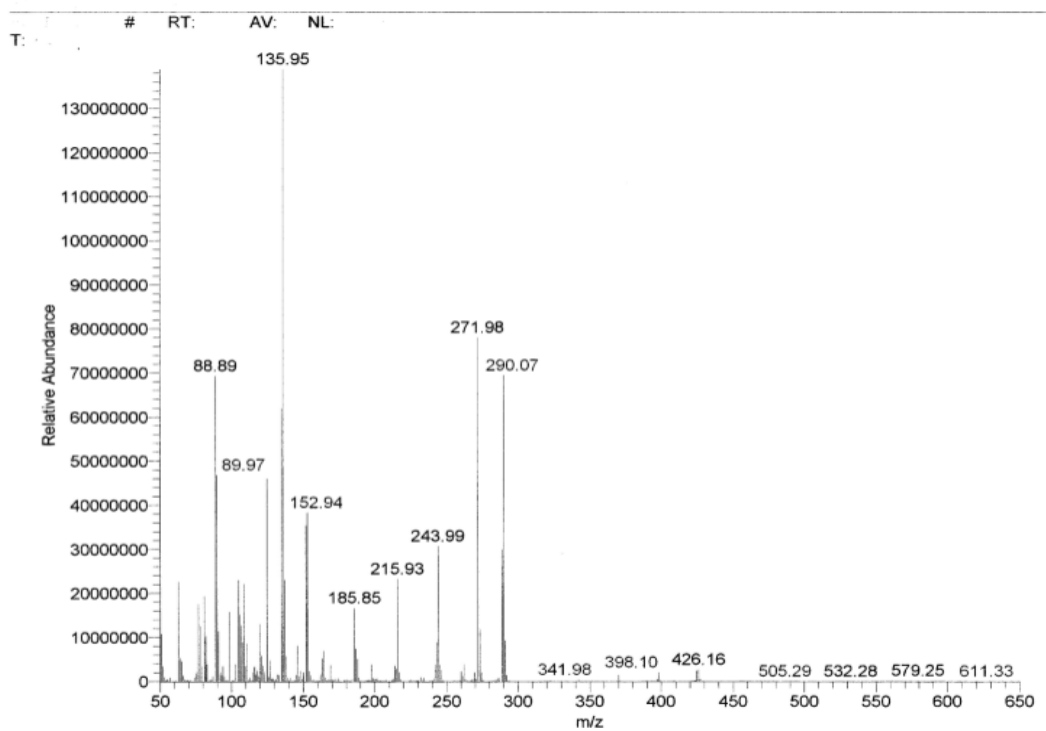
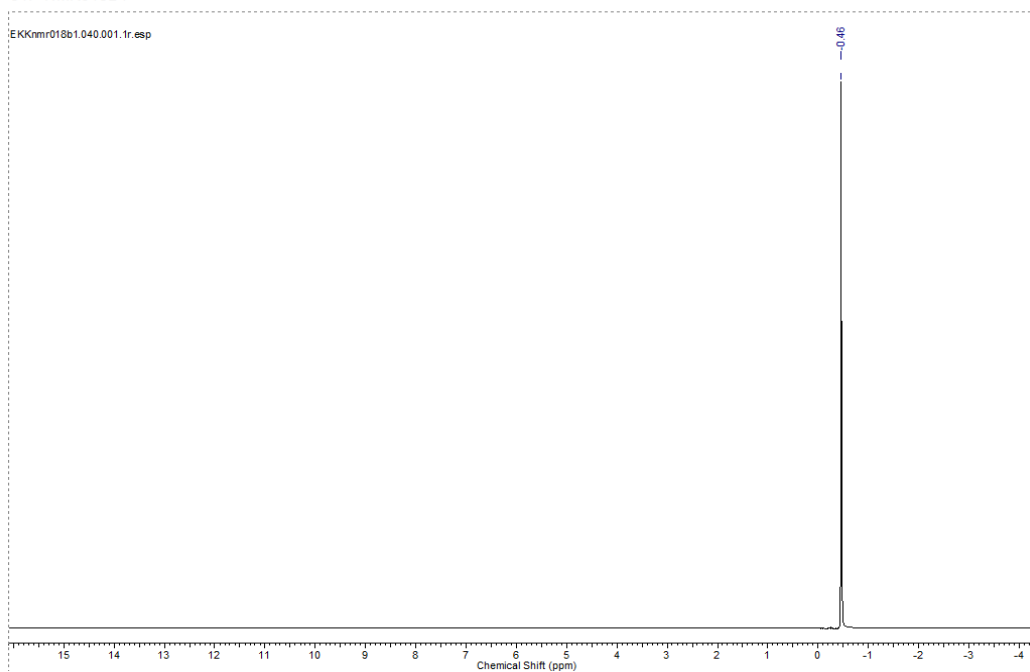


13C-NMR018B1-DEPT



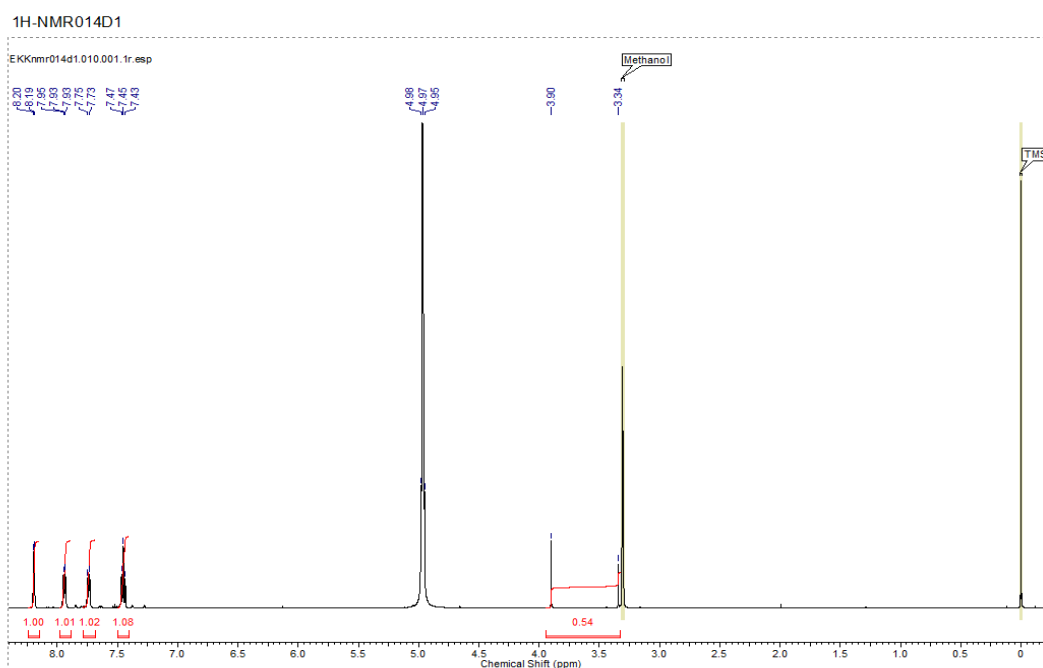
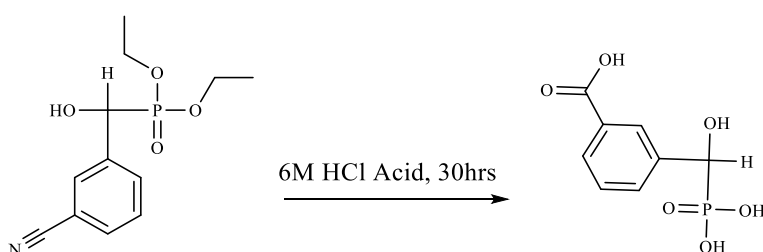
31P-NMR018B1

EKKnmr018b1.040.001.1r.esp

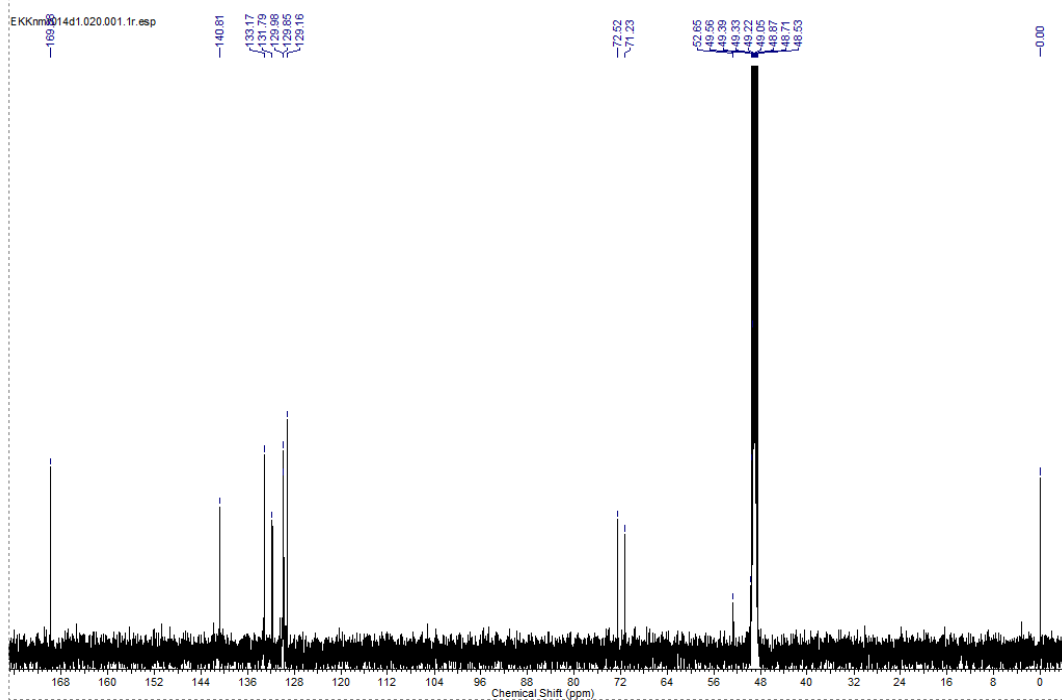


### 3 SYNTHESIS OF SUBSTITUTED BENZYL- $\alpha$ - HYDROXY PHOSPHONIC ACIDS FROM THEIR DIETHYLPHOSPHONATE PRECURSORS.

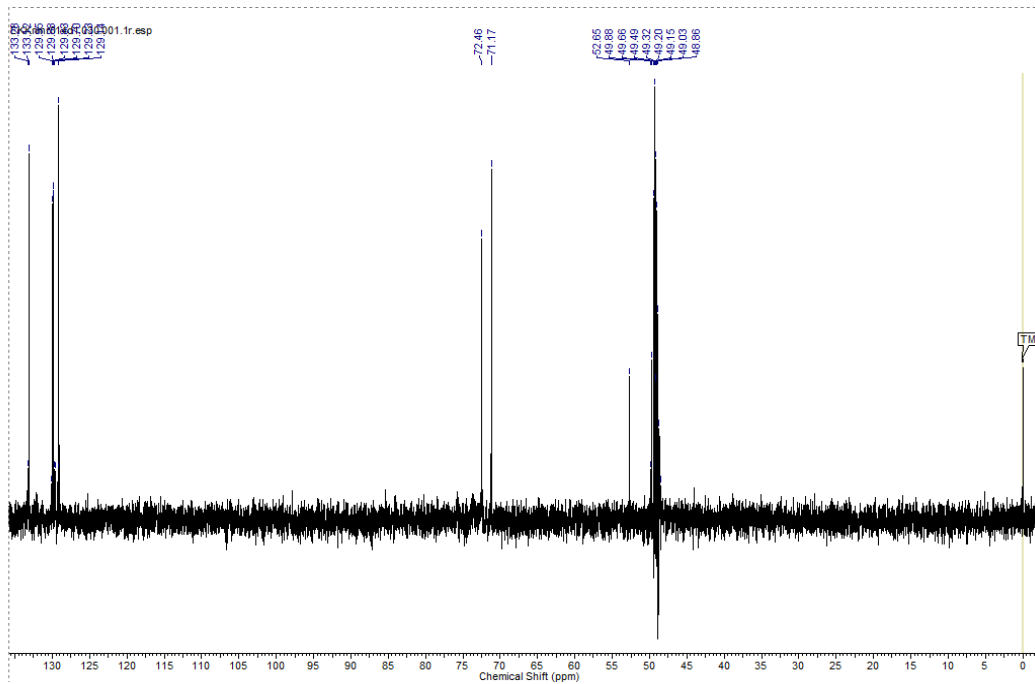
#### 3.1 3-Carboxy benzyl- $\alpha$ -hydroxy phosphonic acid (26)



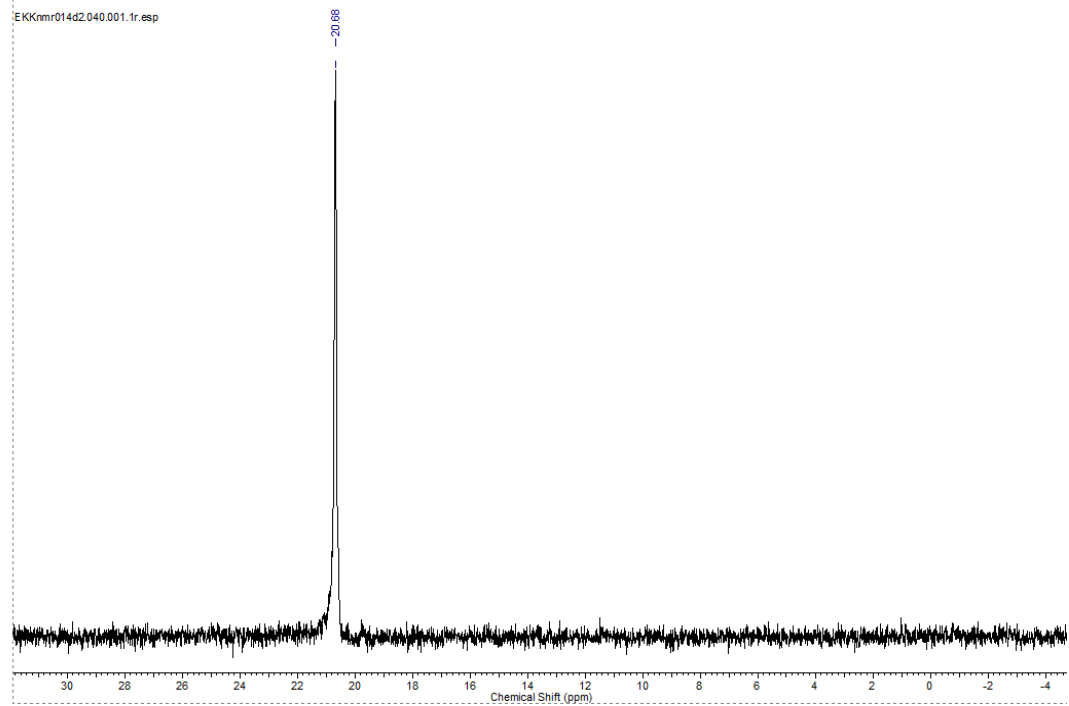
13C-NMR014D1



13C-NMR014D1-DEPT



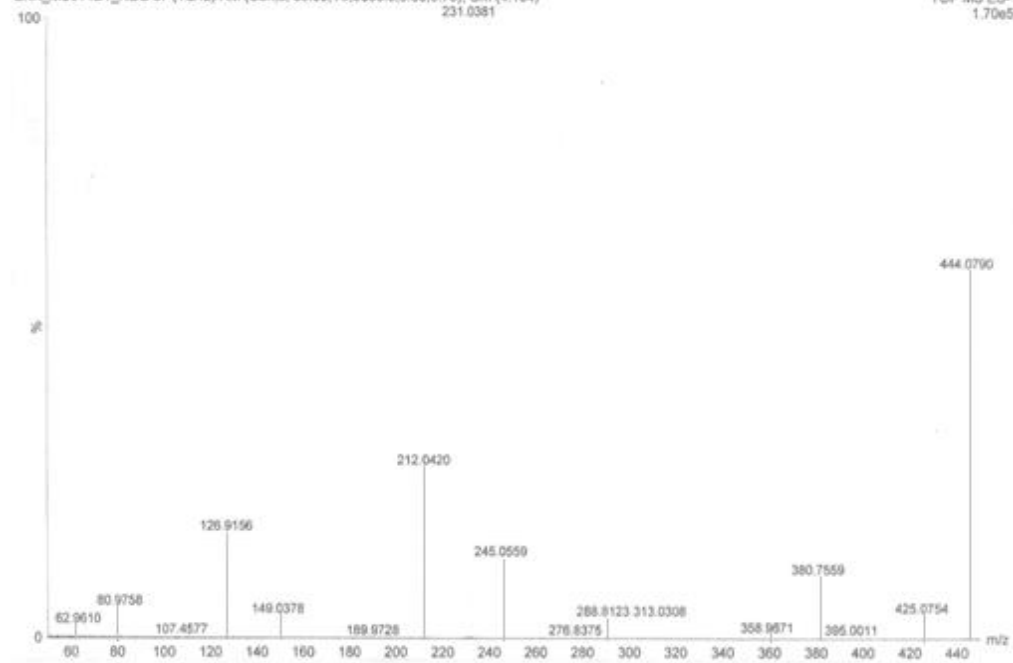
# 31P-NMR014D1



## Edward Kasonde Kumbirai sample MS014D1 neg ion

EKK\_MS014D1\_NEG 67 (1.242) AM (Cen\_3, 80.00, Ar.5000.0.0.00,0.70); Cm (4.104)  
231.0381

TOF MS ES-  
1.70e5

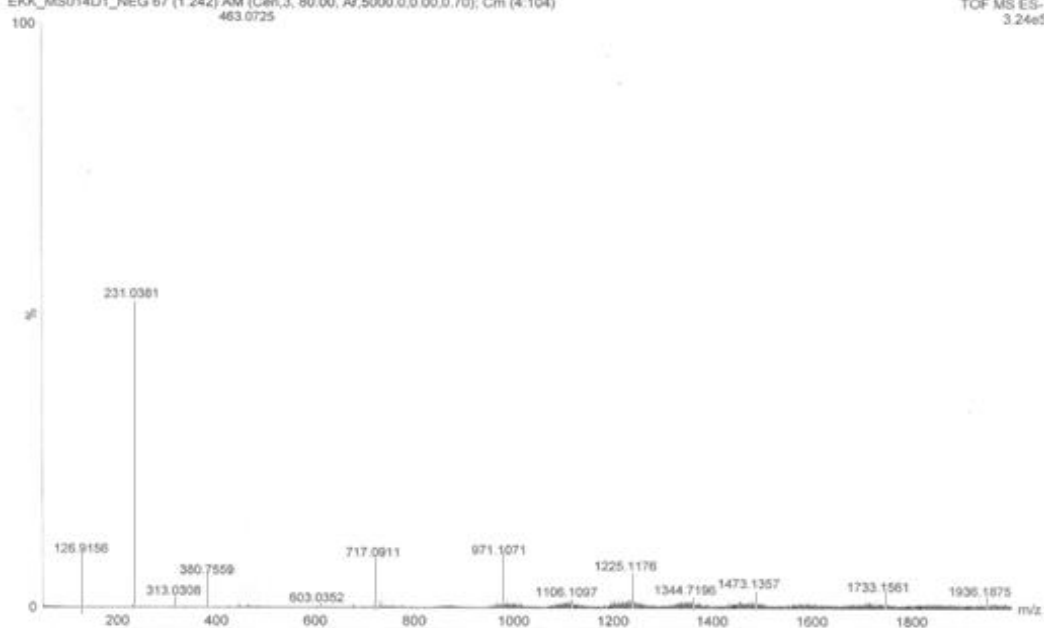




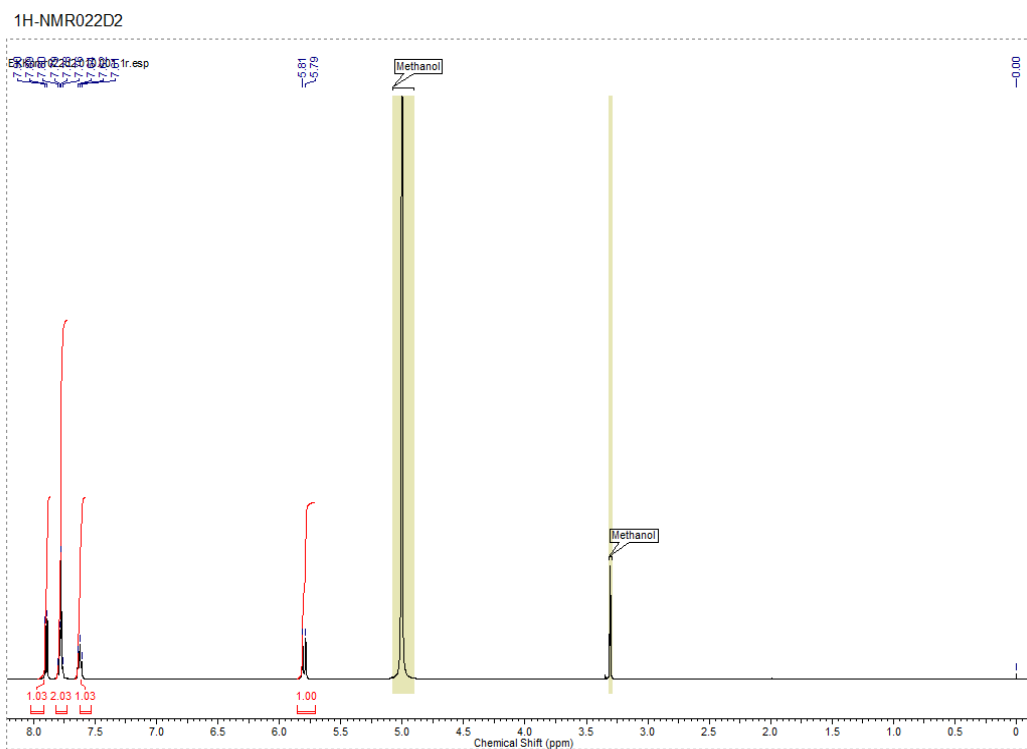
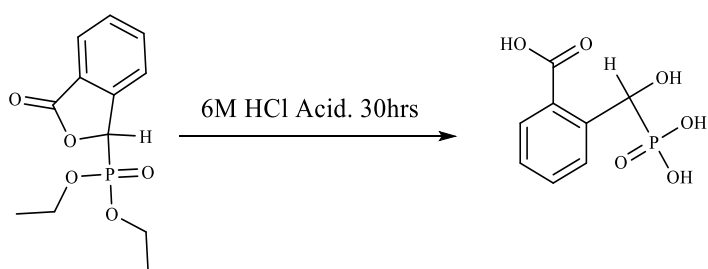
Edward Kasonde Kumbirai sample MS014D1 neg ion

EKK\_MS014D1\_NEG 67 (1.242) AM (Cen,3, 80.00, Ar,5000.0,0.00,0.70); Cm (4:104)

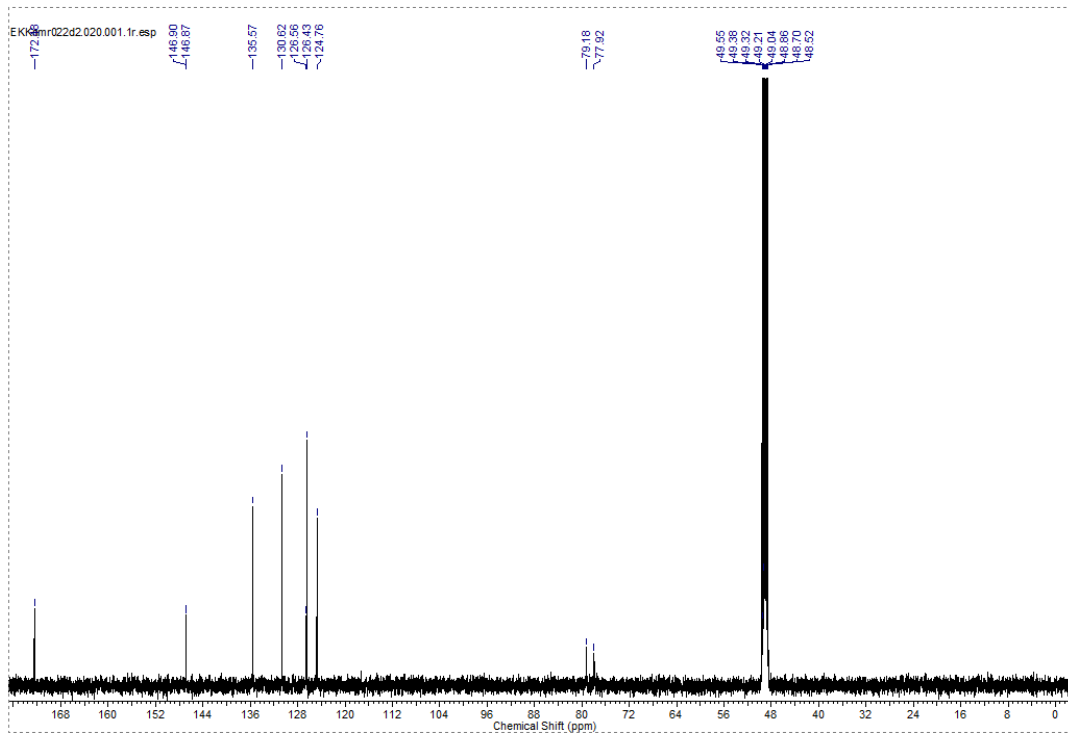
TOF MS ES-  
3.24e5



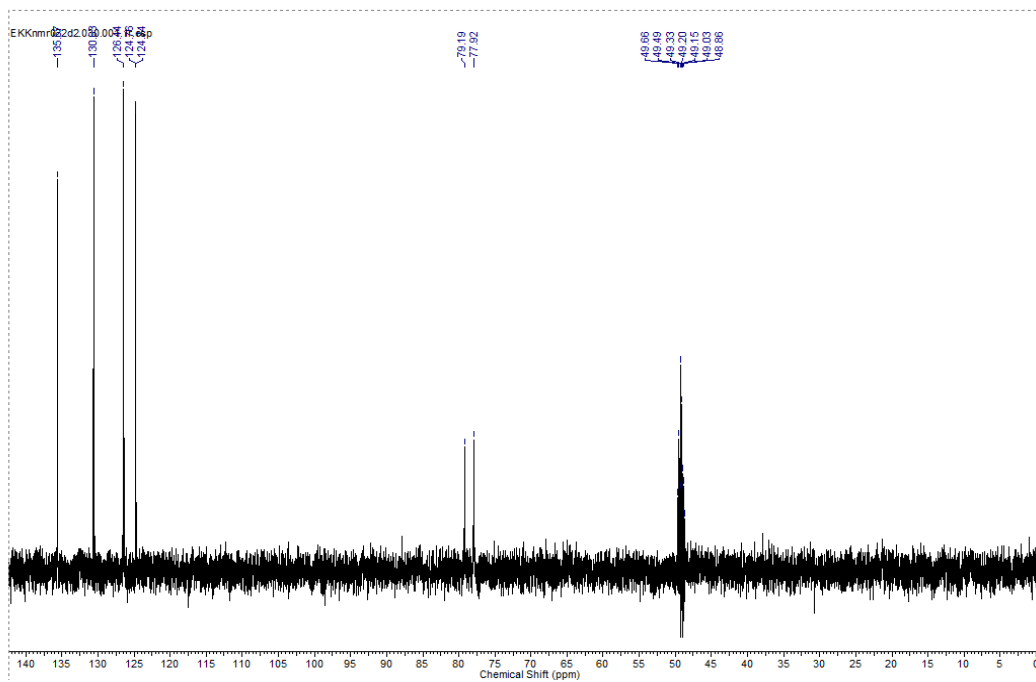
### 3.2 2-Carboxybenzyl- $\alpha$ -hydroxy phosphonic acid (27)



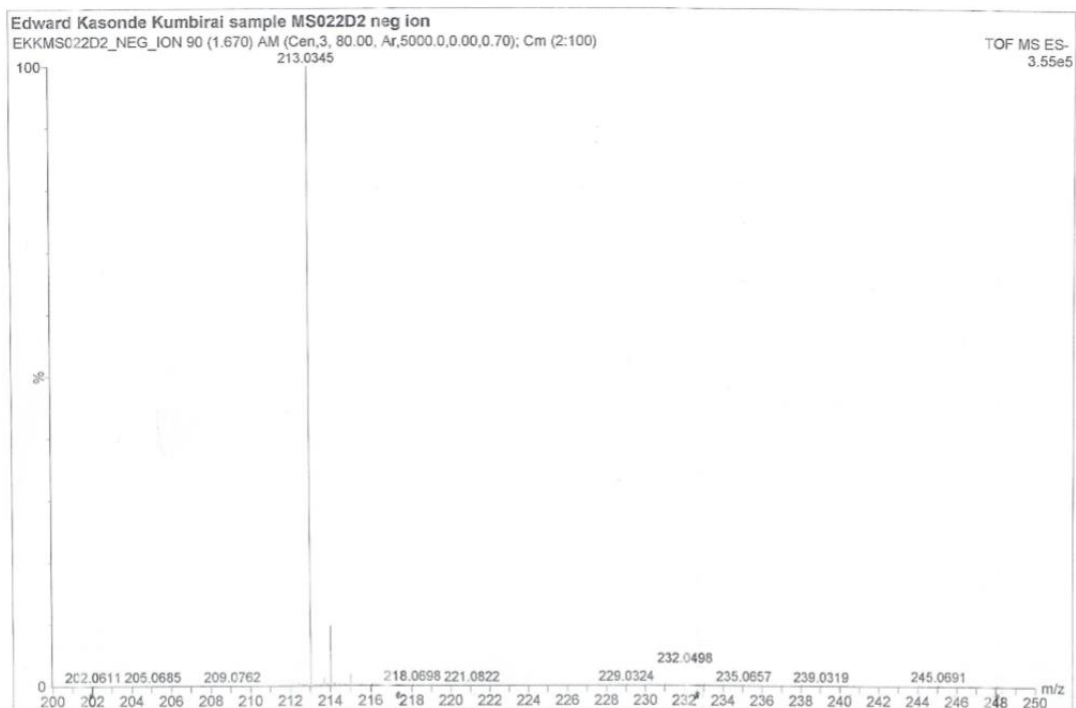
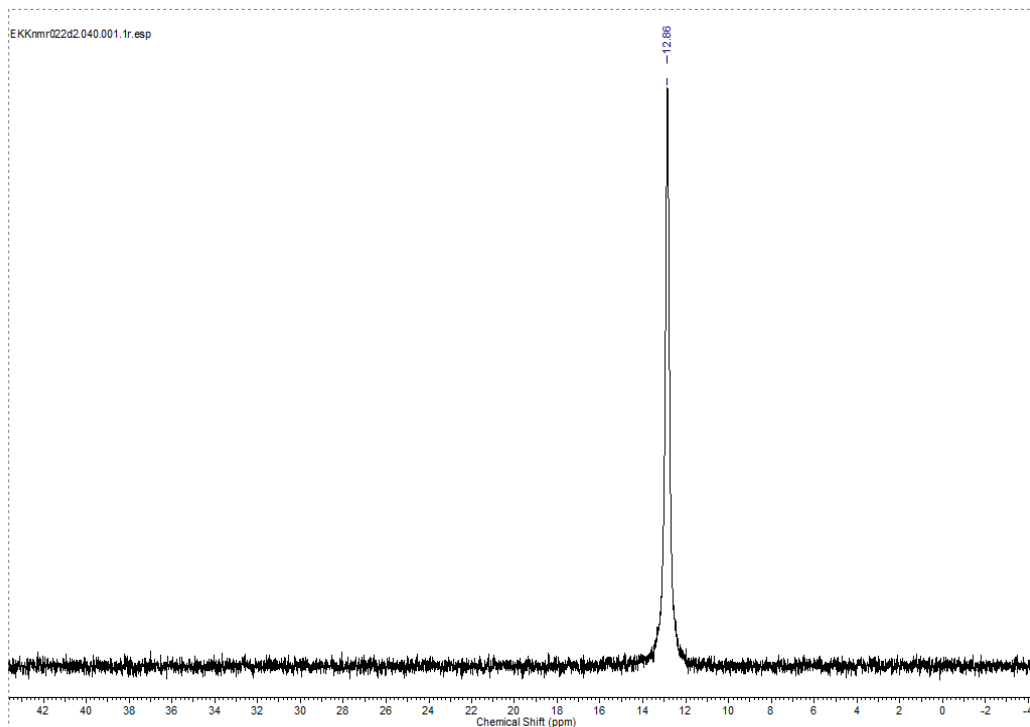
13C-NMR022D2

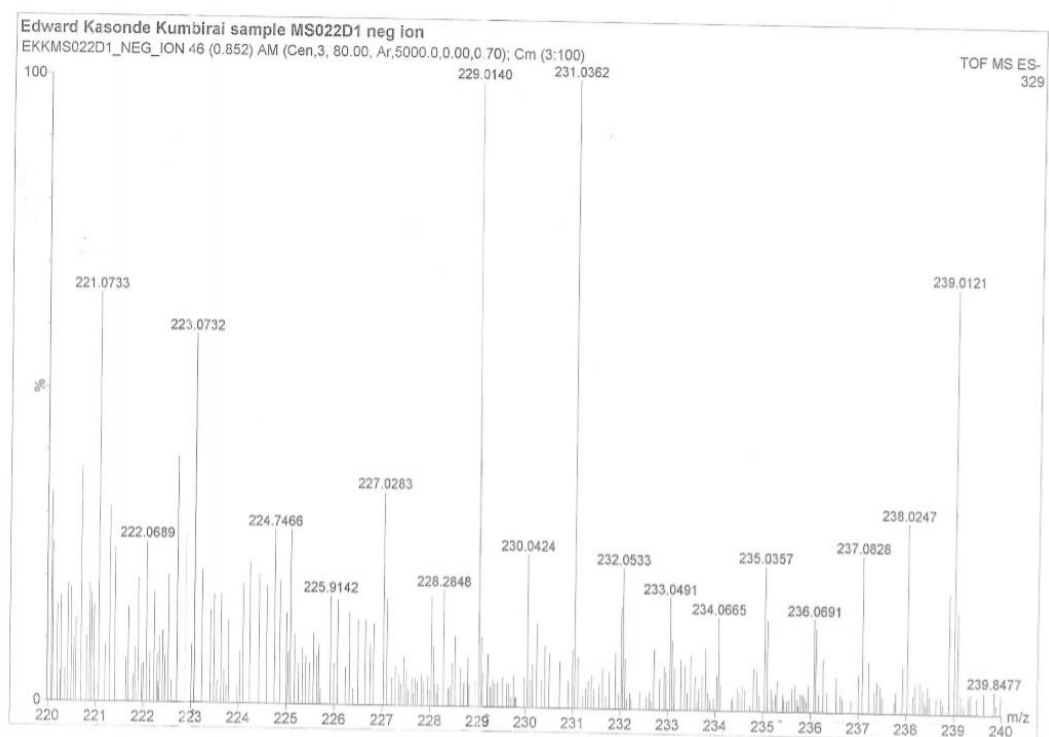


13C-NMR022D2-DEPT



# 31P-NMR022D2

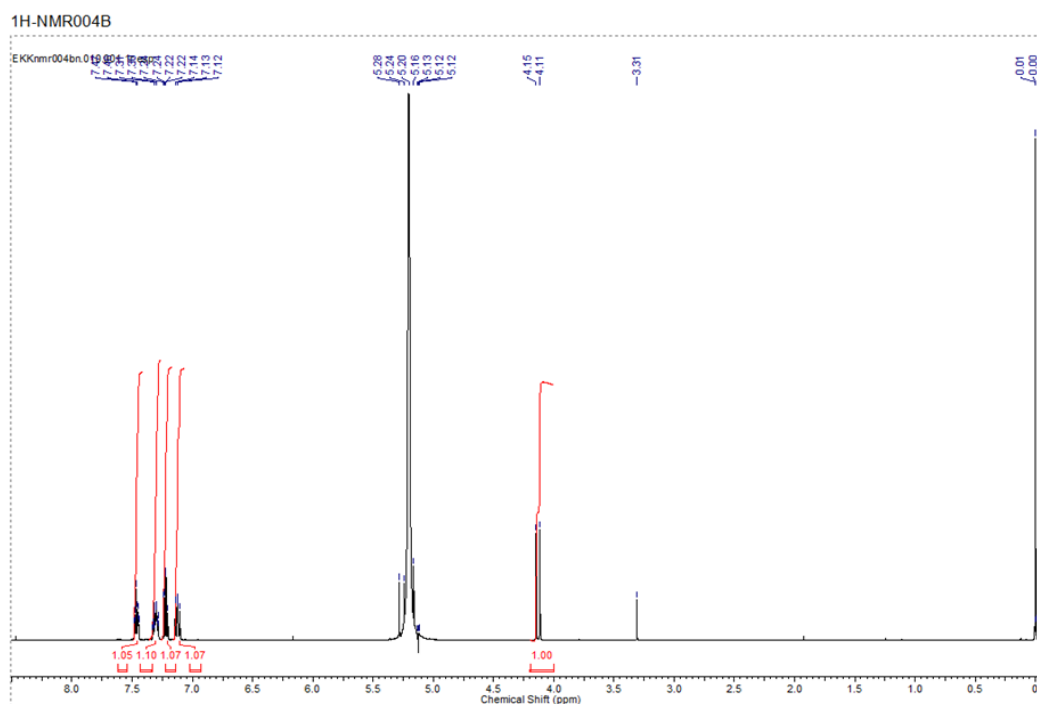
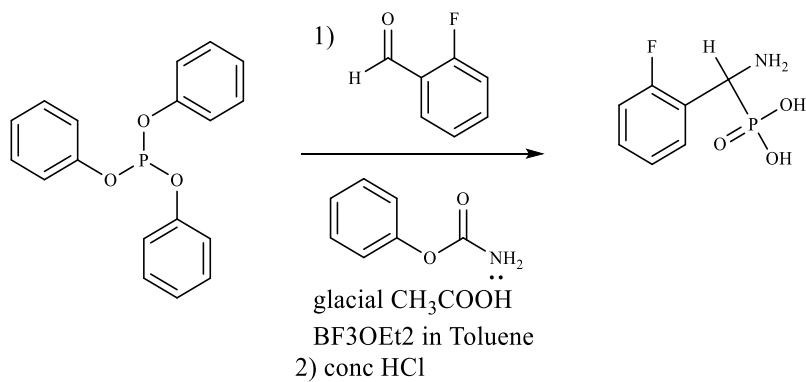




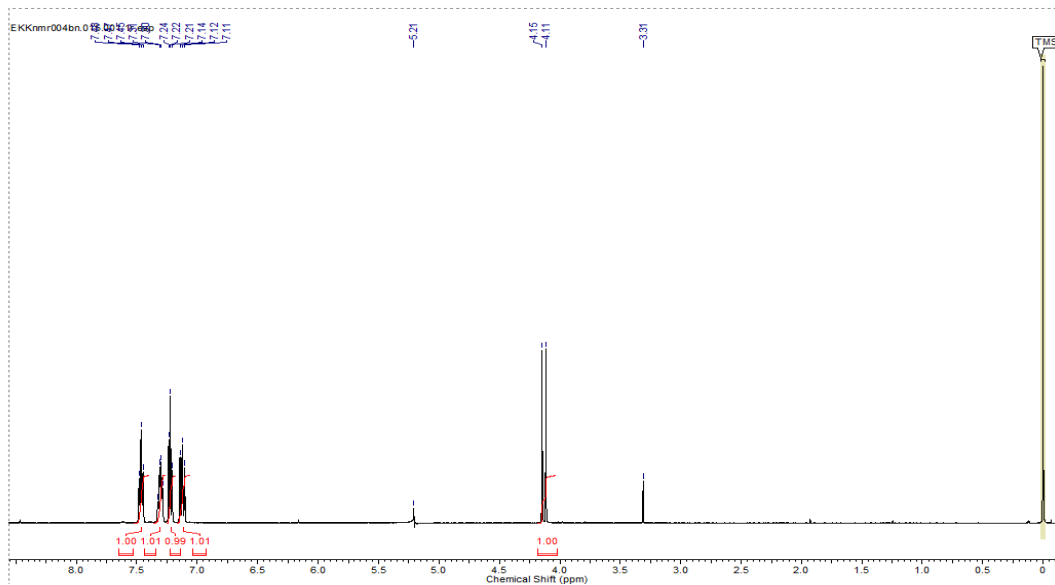
## 4 SYNTHESIS OF BENZYL- $\alpha$ -AMINO

### PHOSPHONIC ACIDS

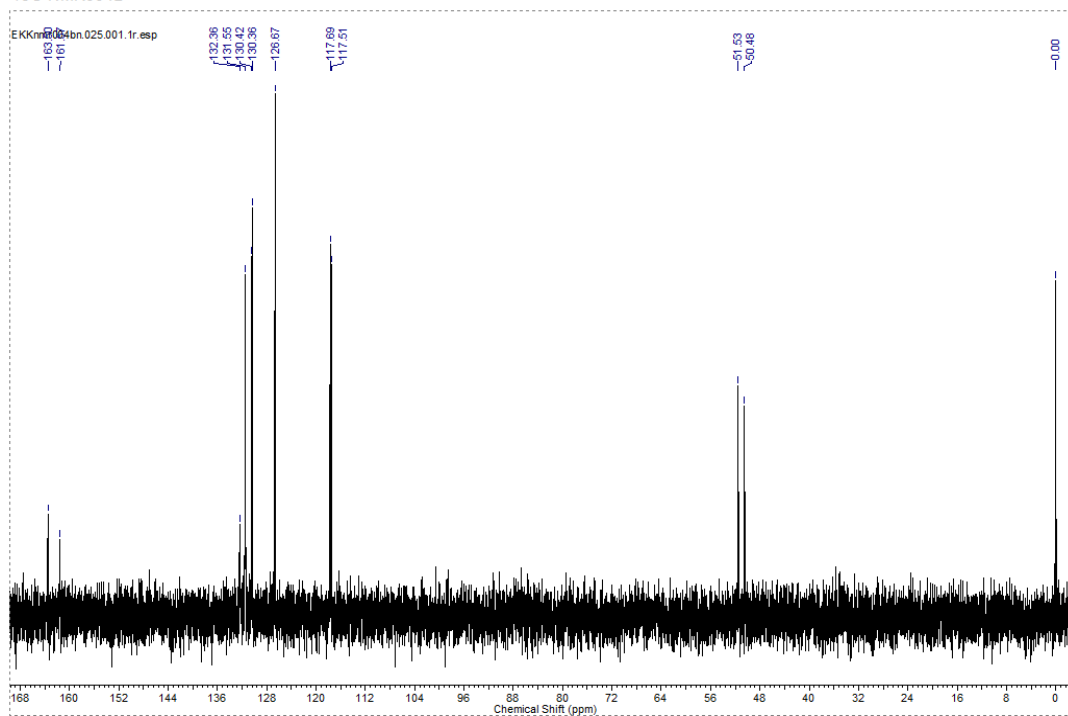
#### 4.1 2-Fluoro benzyl- $\alpha$ -amino phosphonic acids (34).



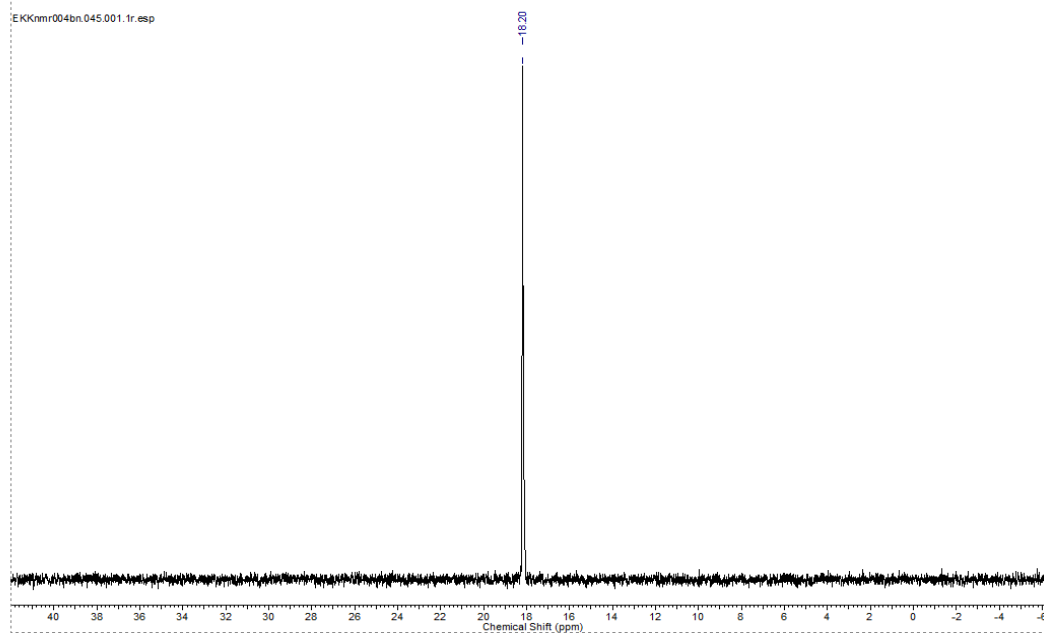
1H-NMR004B D2O SUPPRESSED



13C-NMR004B



# 31P-NMR004B



\\Xcalibur\...DATA\2014\March\EKMS4B  
Edward Kasonde Kumbira sample MS0004B

3/20/2008 12:56:24 PM

EKMS4B #113 RT: 2.33 AV: 1 NL: 1.22E7  
[+ c Full ms [ 50.00-650.00]]

