Supporting information

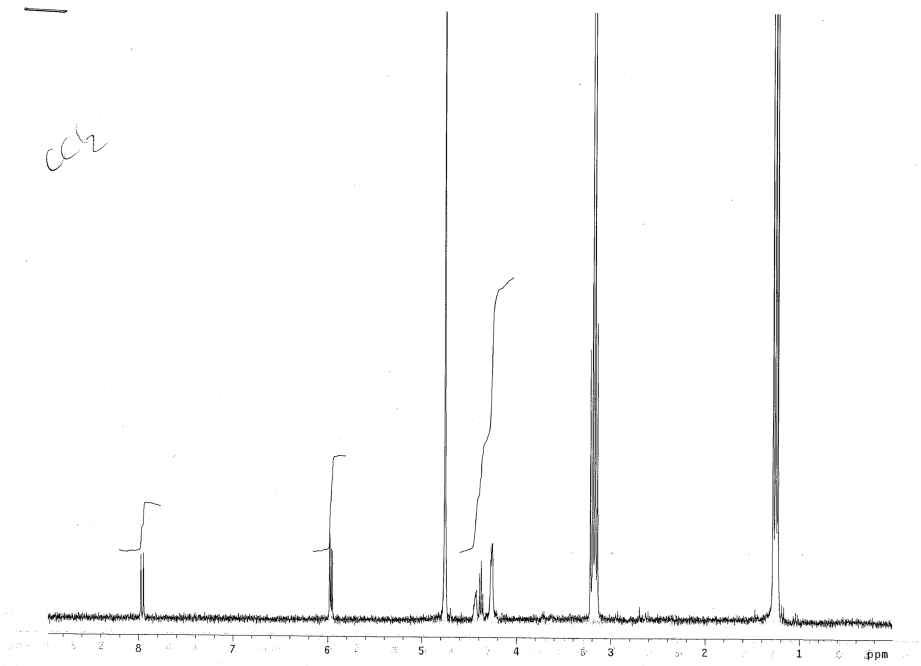
Pyrimidine Nucleotides with 4-Alkyloxyimino and Terminal Phosphate Ester Modifications as Selective Agonists of the $P2Y_4$ Receptor

Hiroshi Maruoka, M.P. Suresh Jayasekara, Matthew O. Barrett, Derek A. Frankin, Sonia de Castro, Nathaniel Kim, Stefano Costanzi, T. Kendall Harden, and Kenneth A. Jacobson

Contents: page

Uridine-5′-β,γ-dichloromethylene triphosphate ammonium salt (10)

^{1}H NMR



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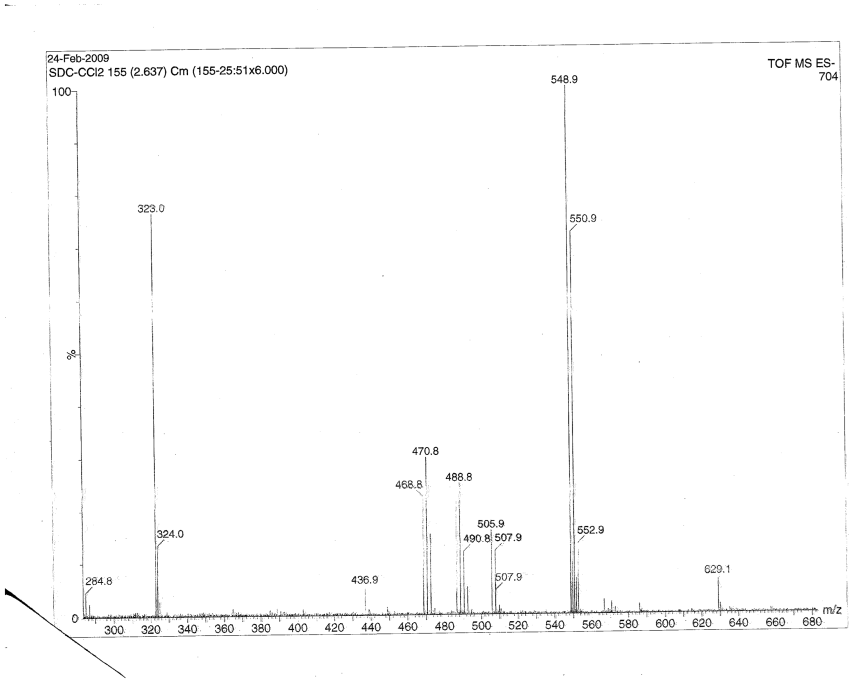

***N*^{4}-**

Methoxycytidine-5′-triphosphate triethylammonium salt (11)

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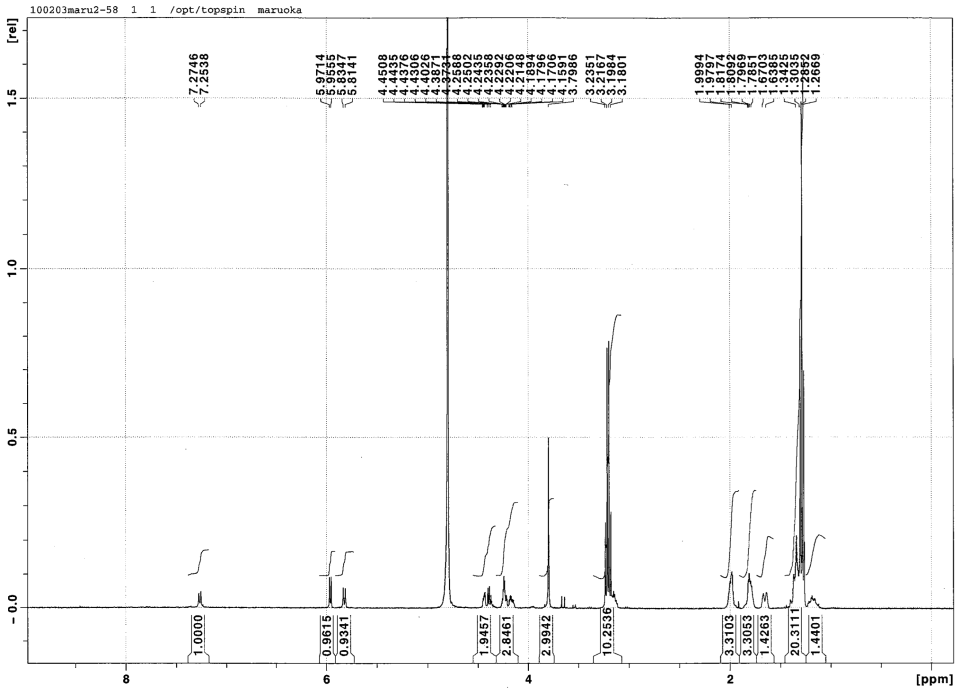
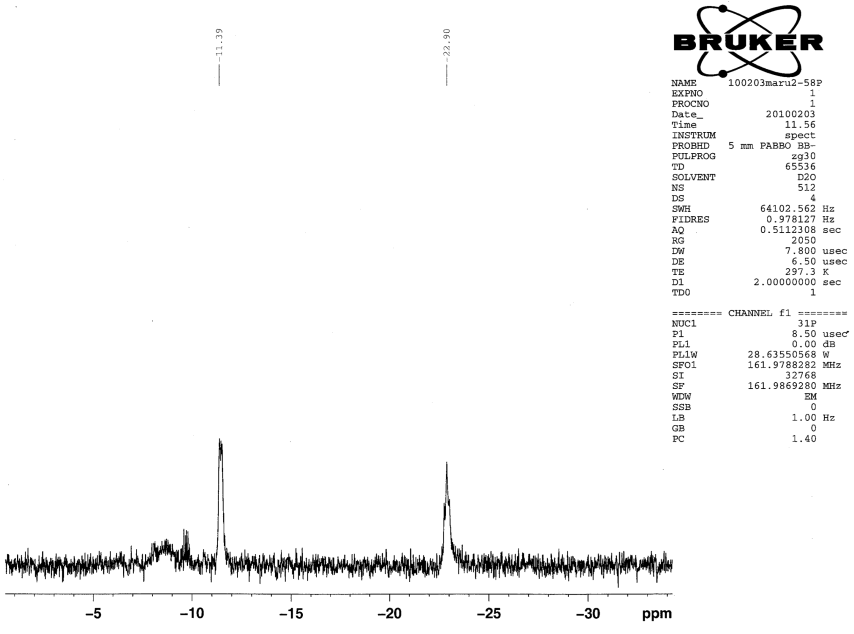


^{31}P NMR



N^4-Ethoxycytidine-5′-triphosphate triethylammonium salt (12)

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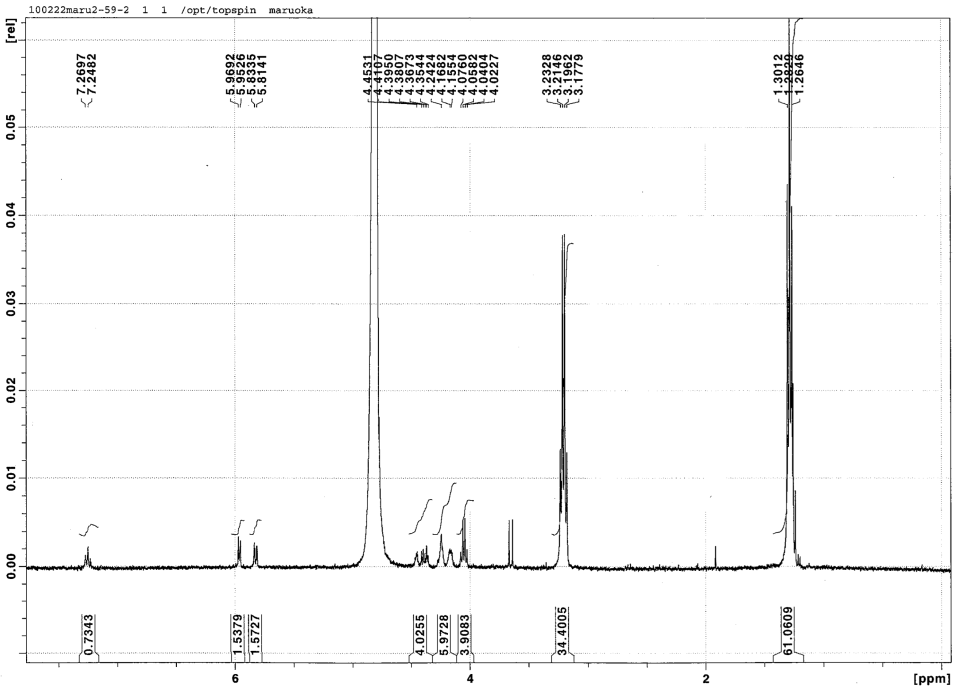

N^4-*tert*-Butyloxycytidine-5′-triphosphate triethylammonium salt (13)

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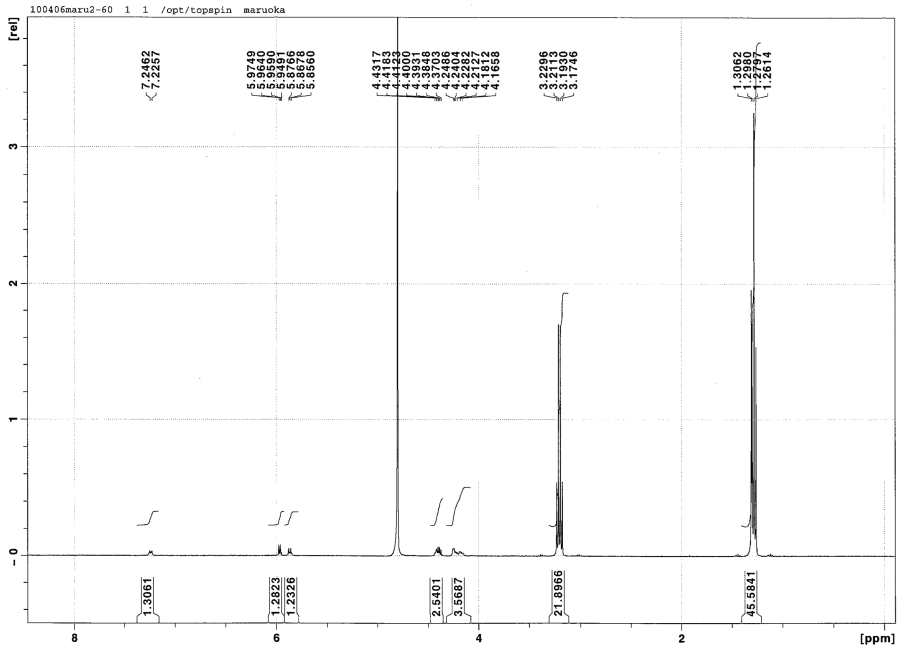

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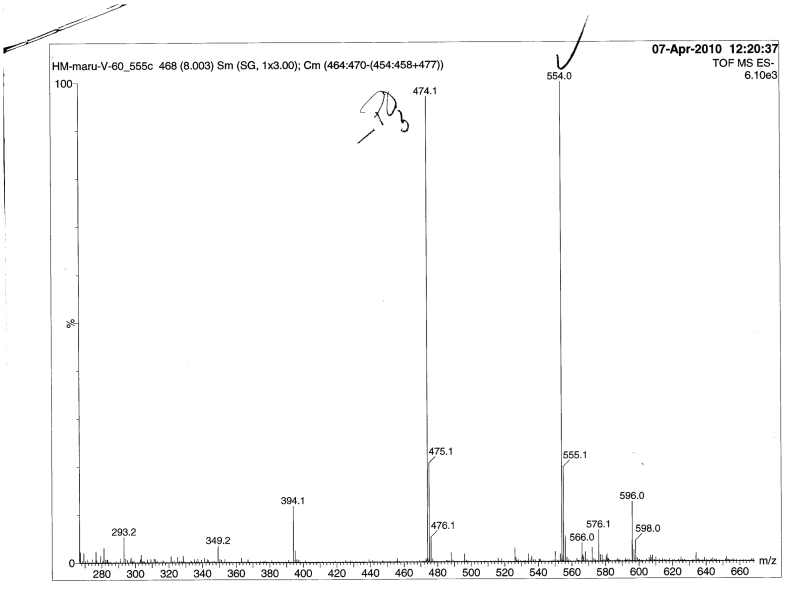

N^4-Benzyloxycytidine-5′-triphosphate triethylammonium salt (14)

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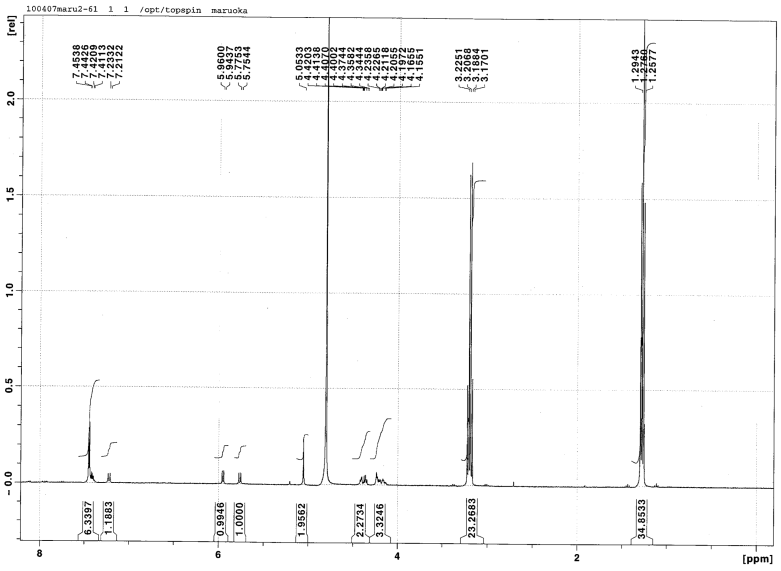

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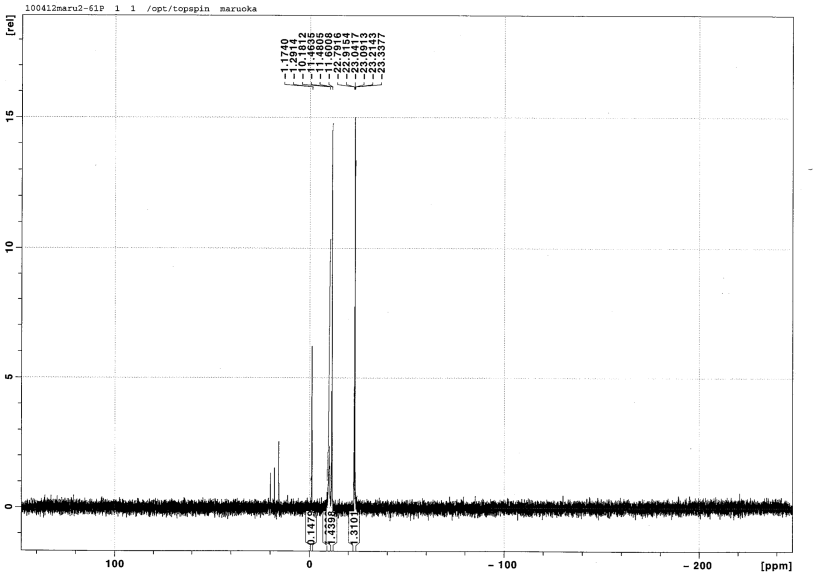

N^4-Phenylethoxycytidine-5′-triphosphate triethylammonium salt (15)

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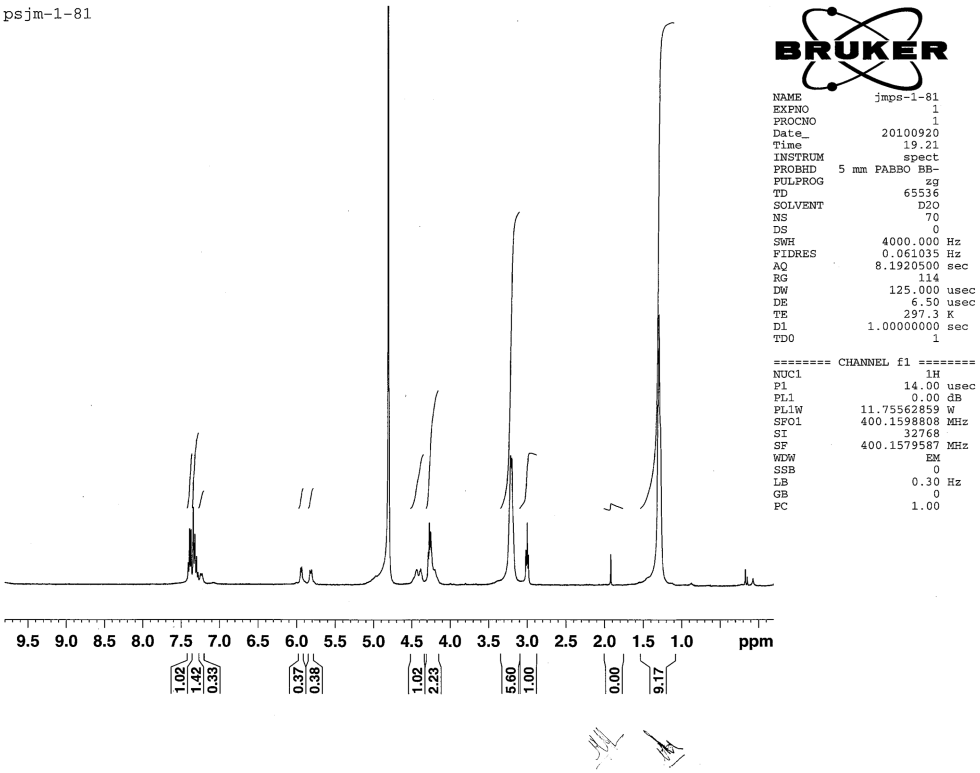

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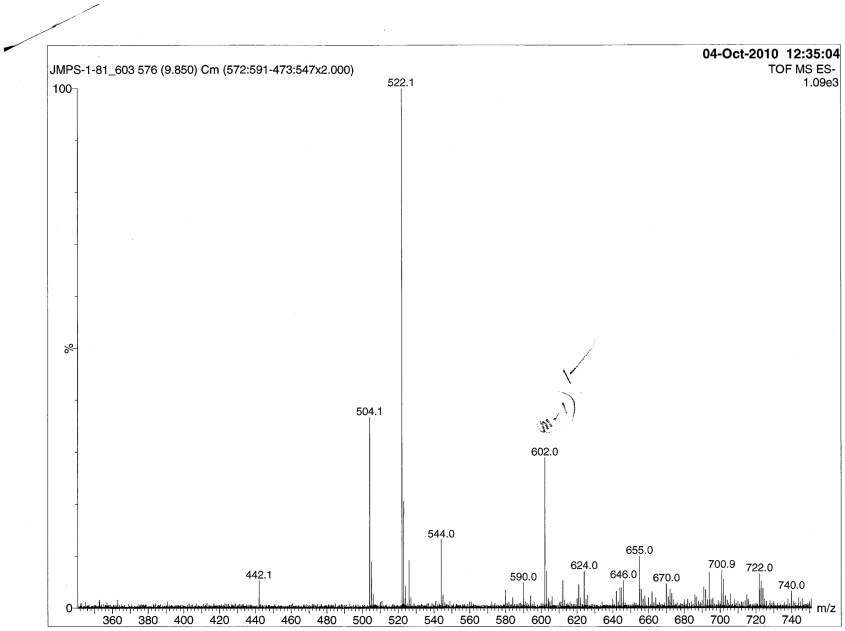

N^4-Phenylpropoxycytidine-5′-triphosphate triethylammonium salt (16)

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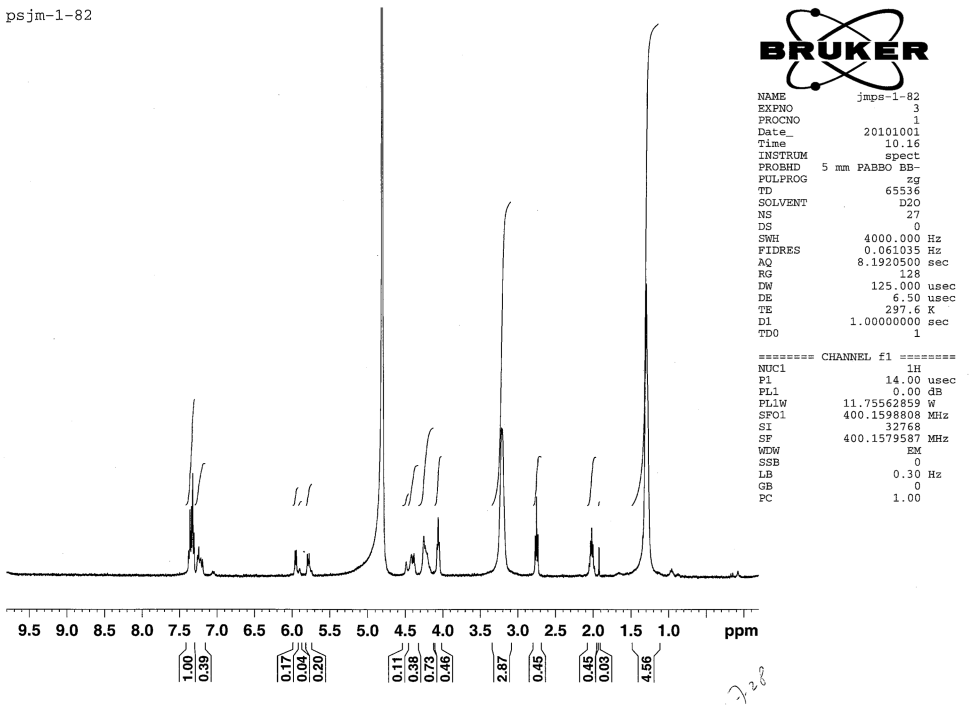

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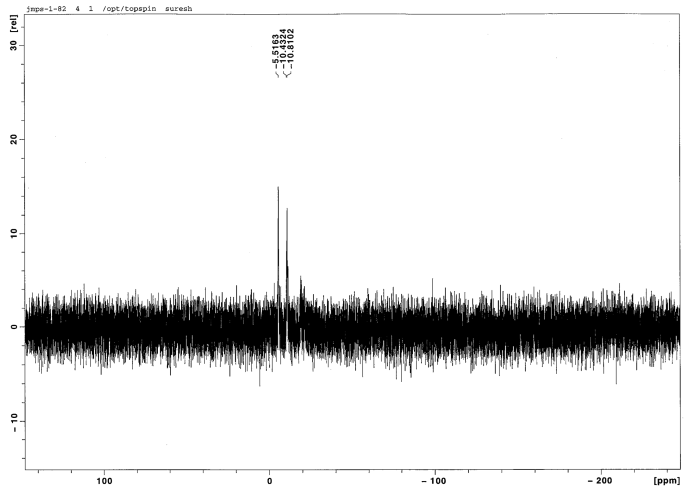

Uridine-5′-(4-chlorophenyl)- tetraphosphate triethylammonium salt (20)

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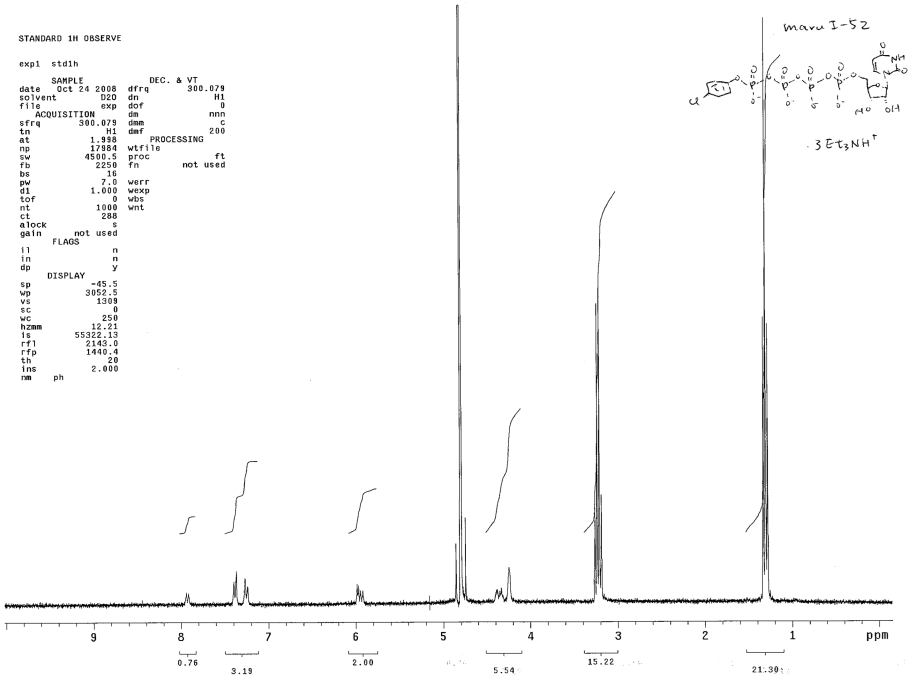
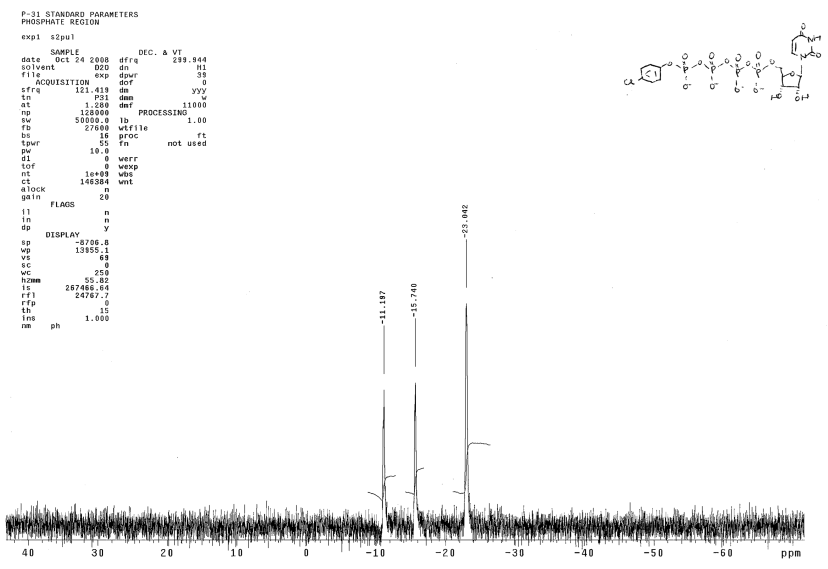
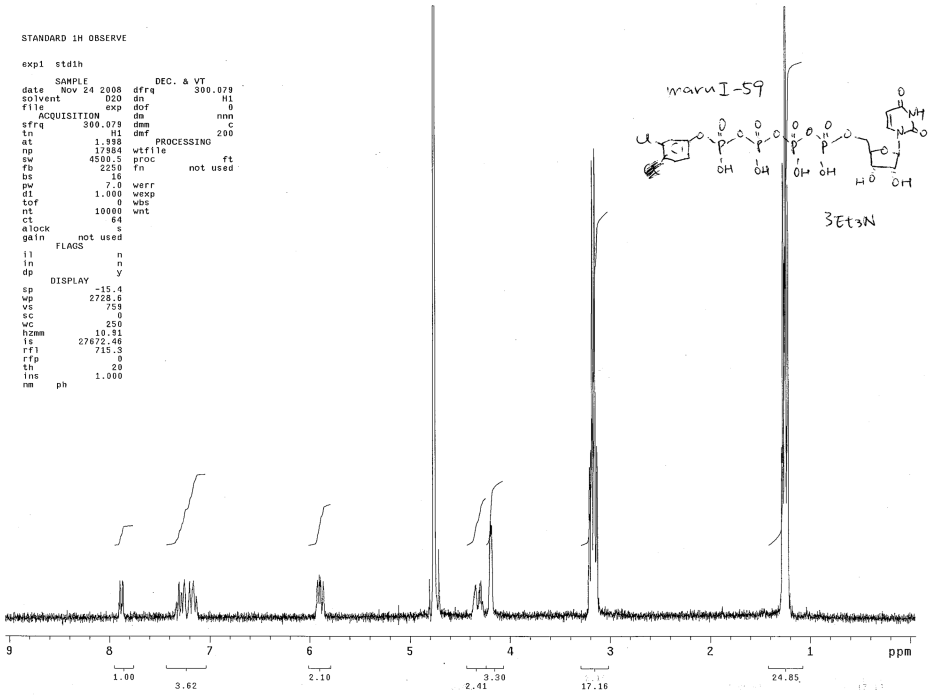


^{31}P NMR

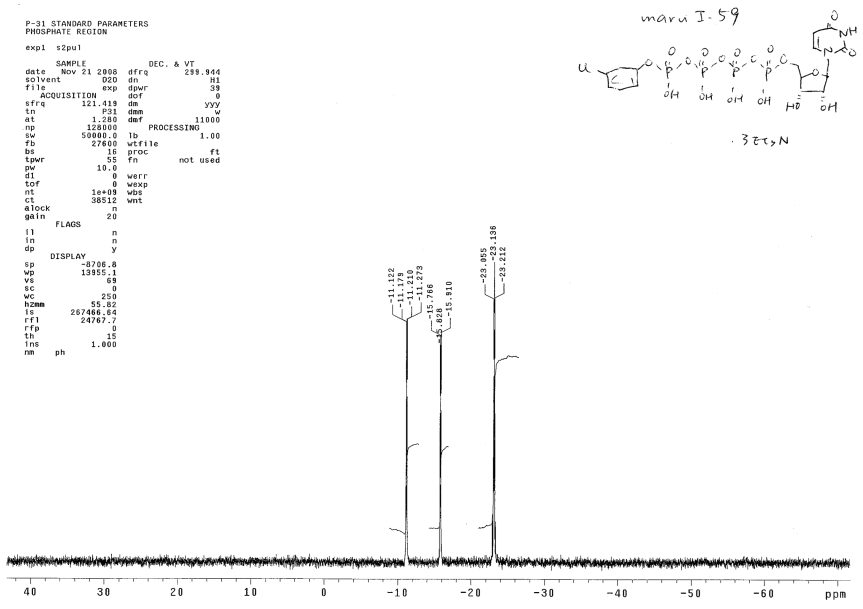


Uridine-5′-(3-chlorophenyl)- tetraphosphate triethylammonium salt (21)

^{1}H NMR



^{31}P NMR



Uridine-5′-(4-methoxyphenyl)- tetraphosphate triethylammonium salt (22)

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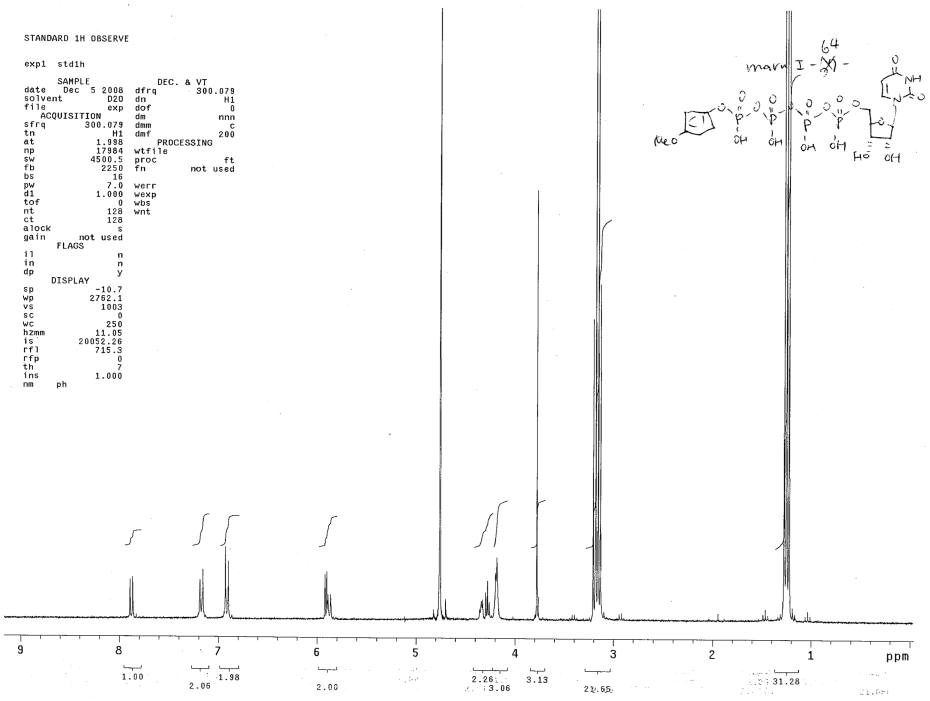

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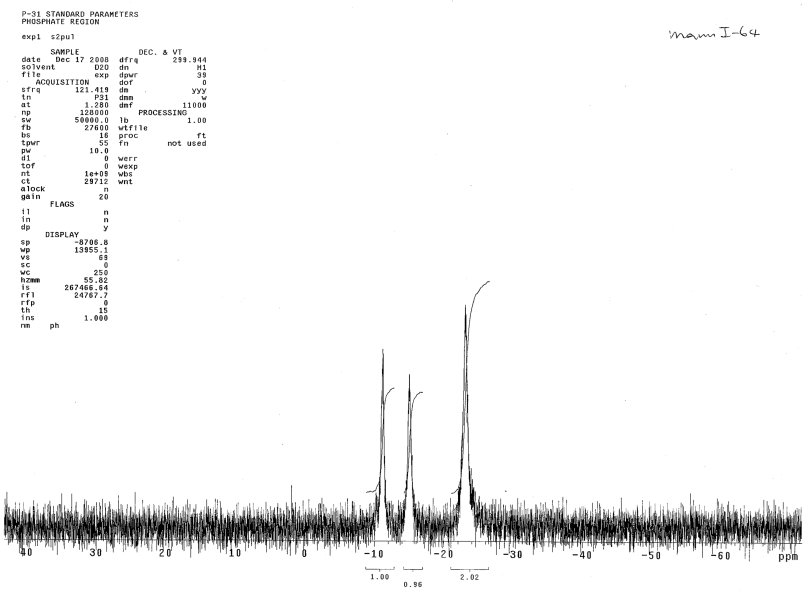

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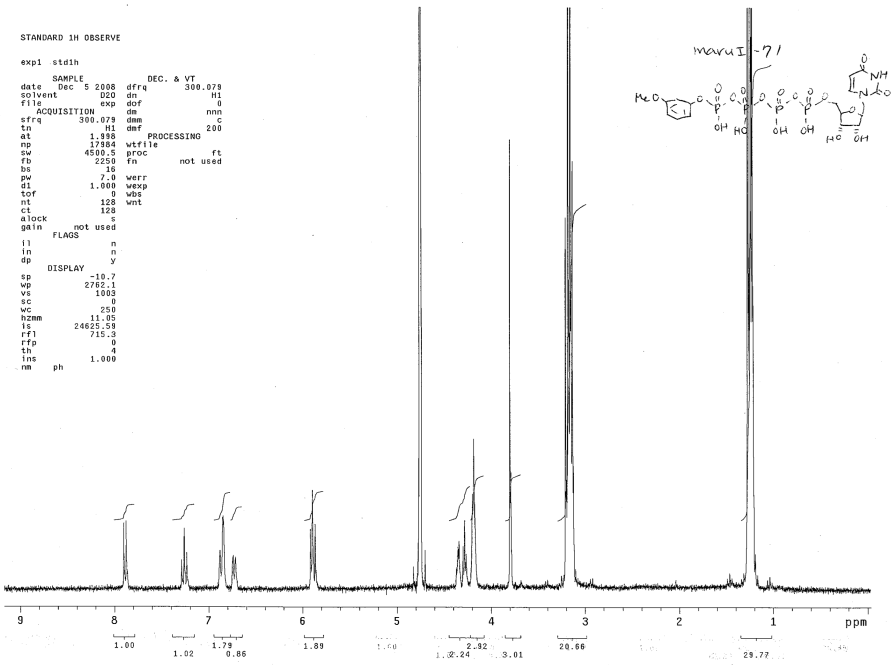
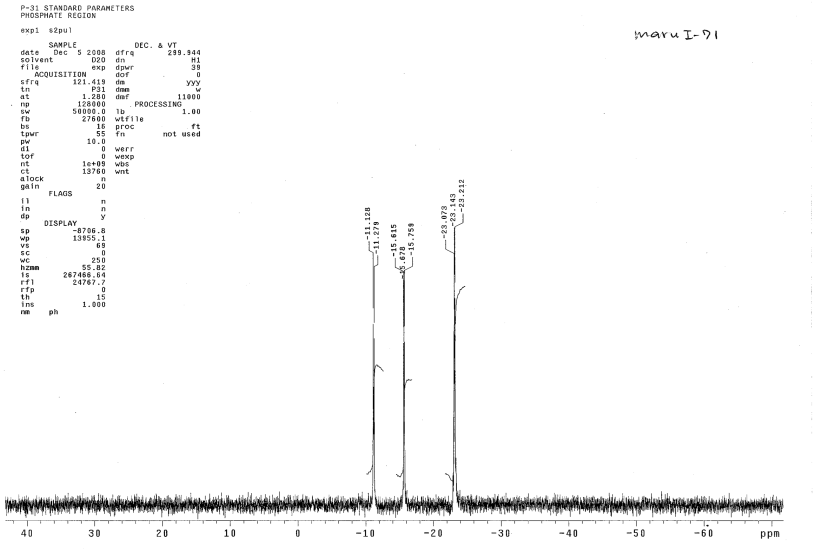


^{31}P NMR



Uridine-5′-(4-nitrophenyl)- tetraphosphate triethylammonium salt (24)

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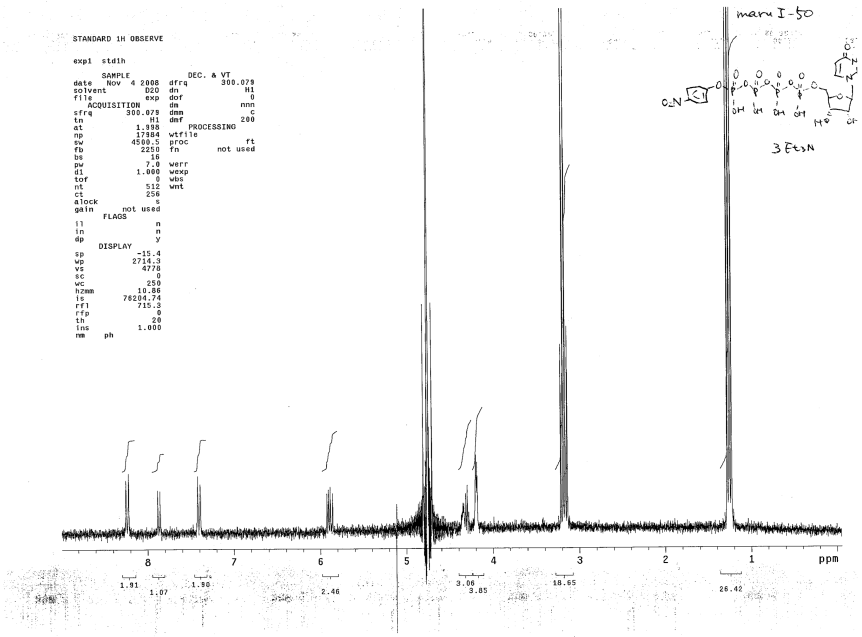

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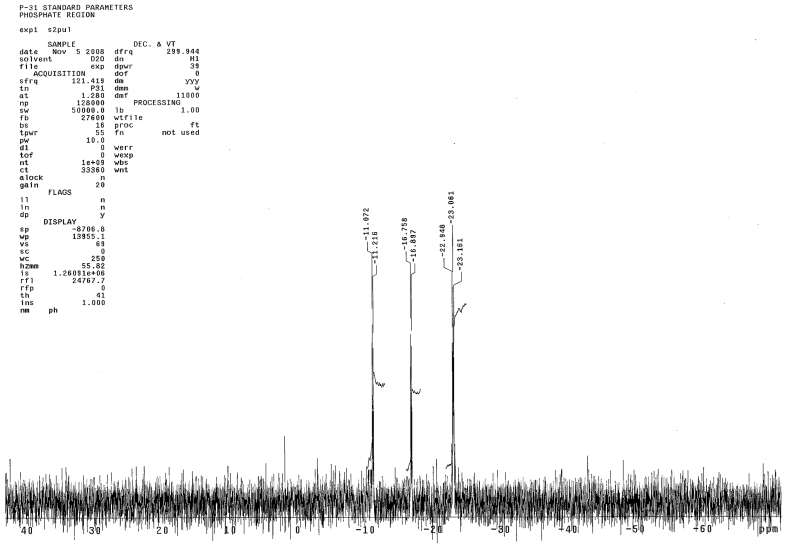
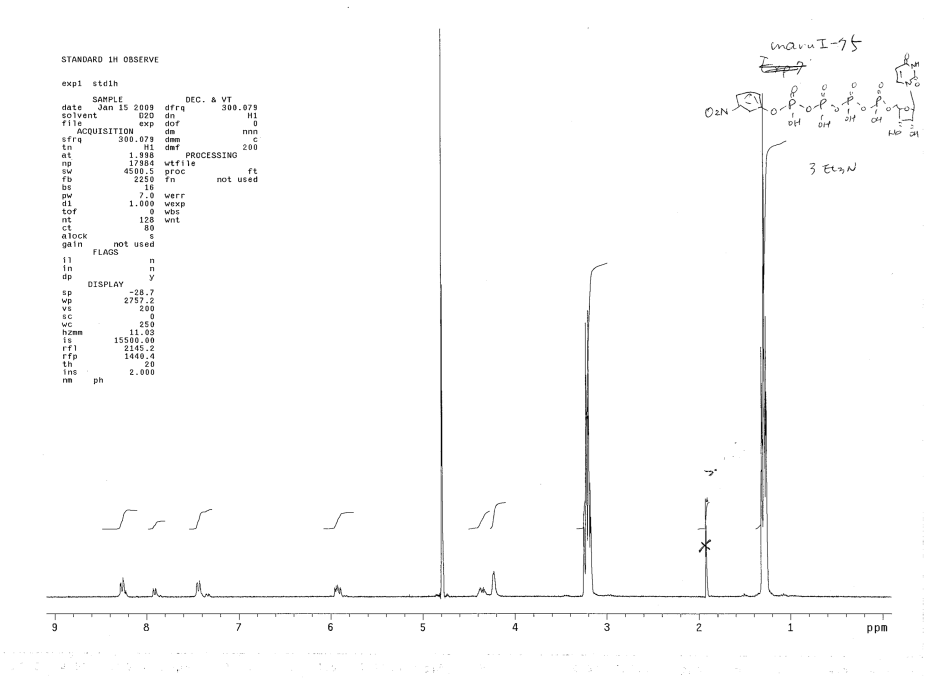


Uridine-5′-(3-nitrophenyl)- tetraphosphate triethylammonium salt (25)

^{1}H NMR



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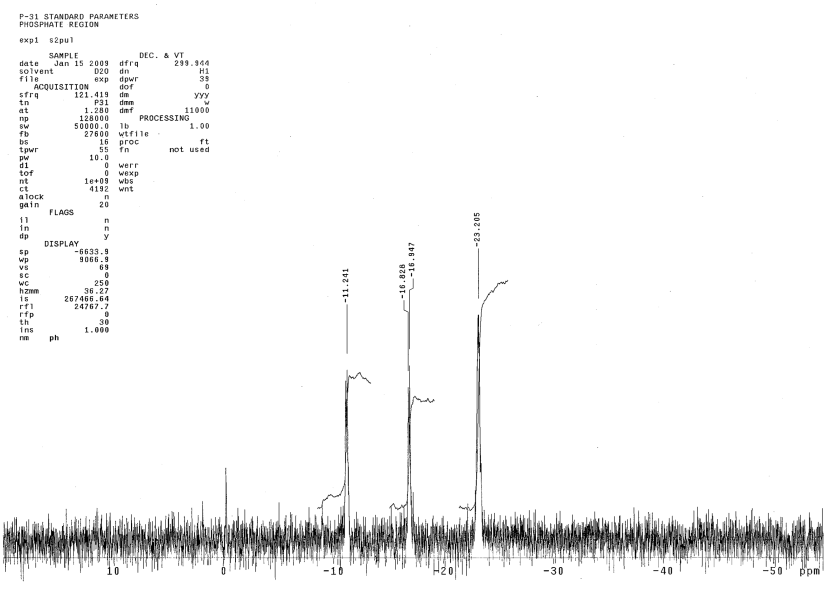
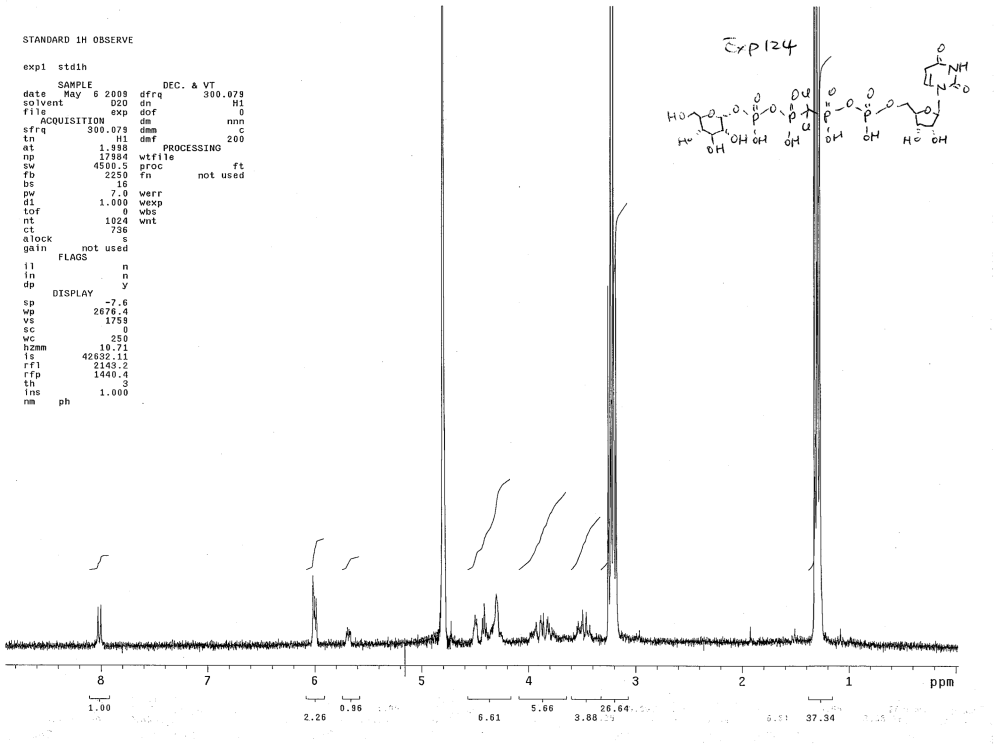


Uridine-5′-glucose-1′-β,γ-dichloromethylene tetraphosphate triethylammonium salt (26)

^{1}H NMR



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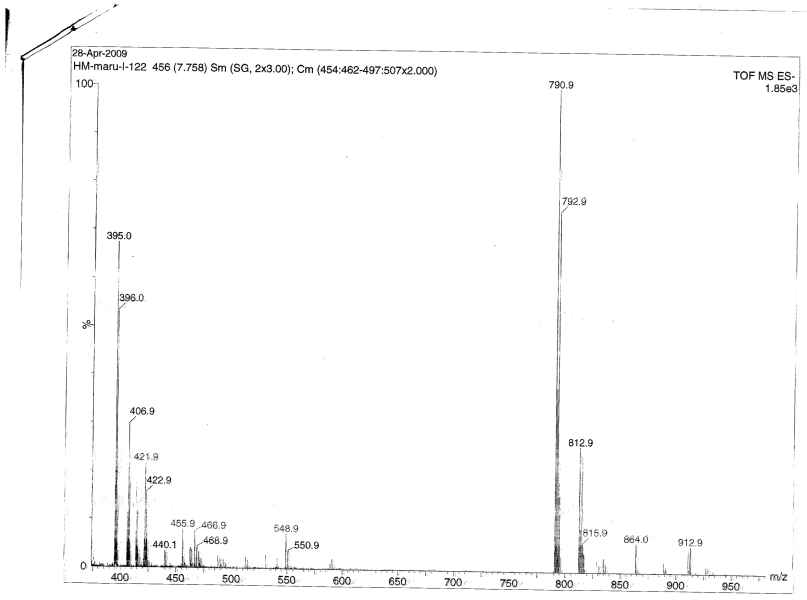
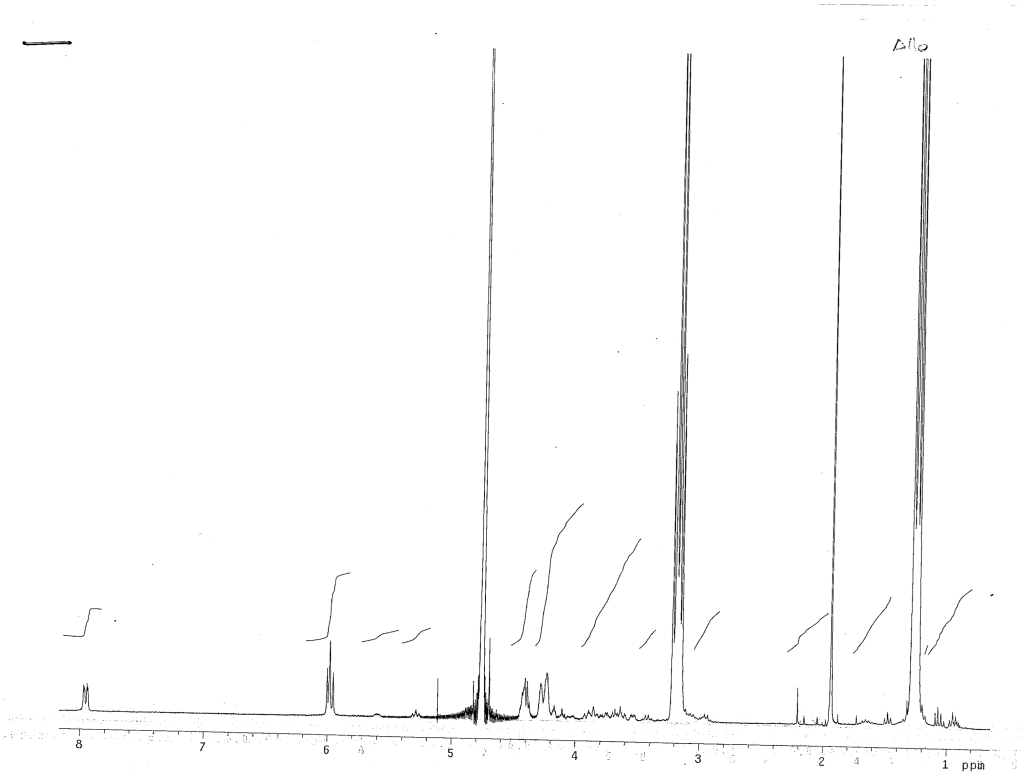


Uridine-5′-allose-1′-tetraphosphate triethylammonium salt (28)

^{1}H NMR



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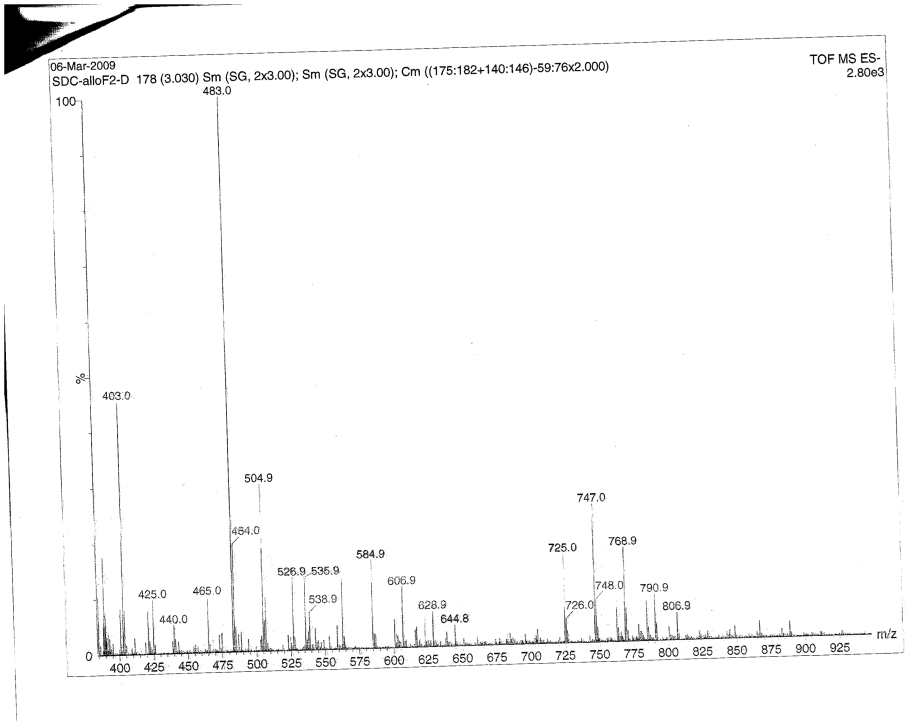
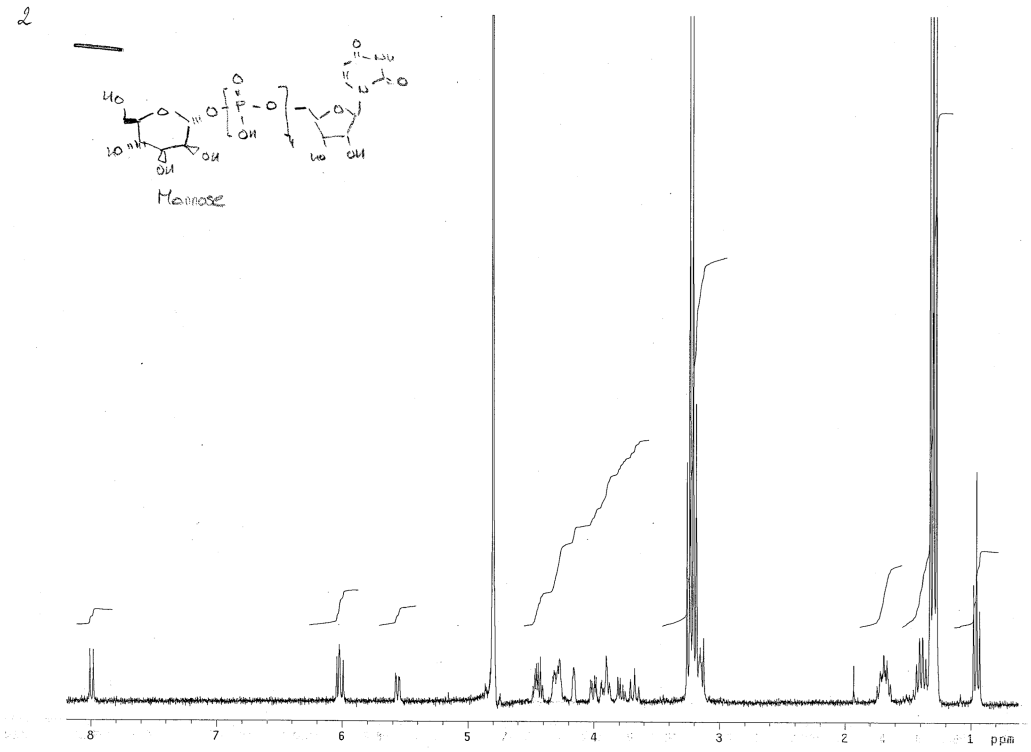


Uridine-5′-mannose-1′-tetraphosphate triethylammonium salt (29)

^{1}H NMR



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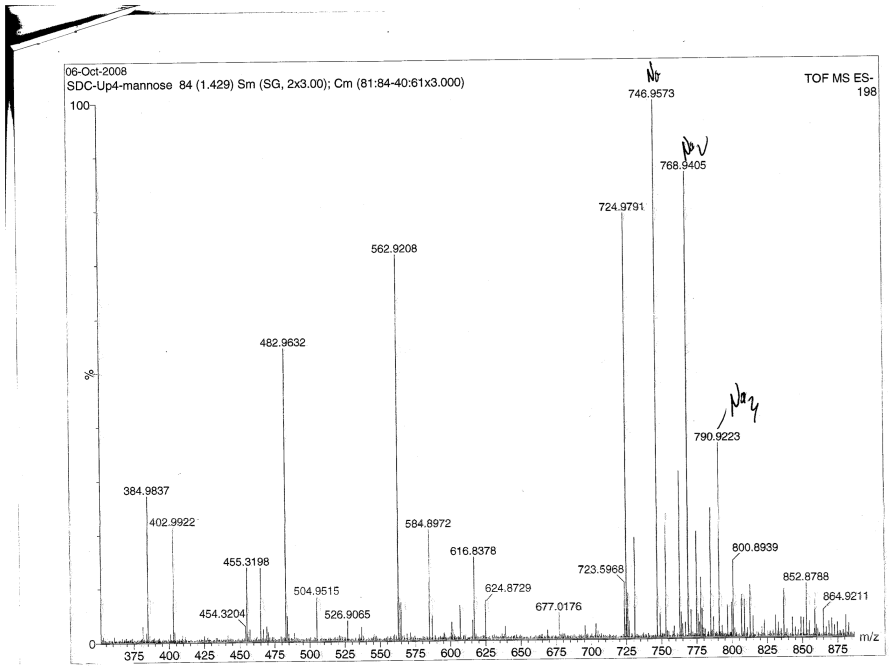

Uridine-5′-xylose-1′-tetraphosphate triethylammonium salt (30)

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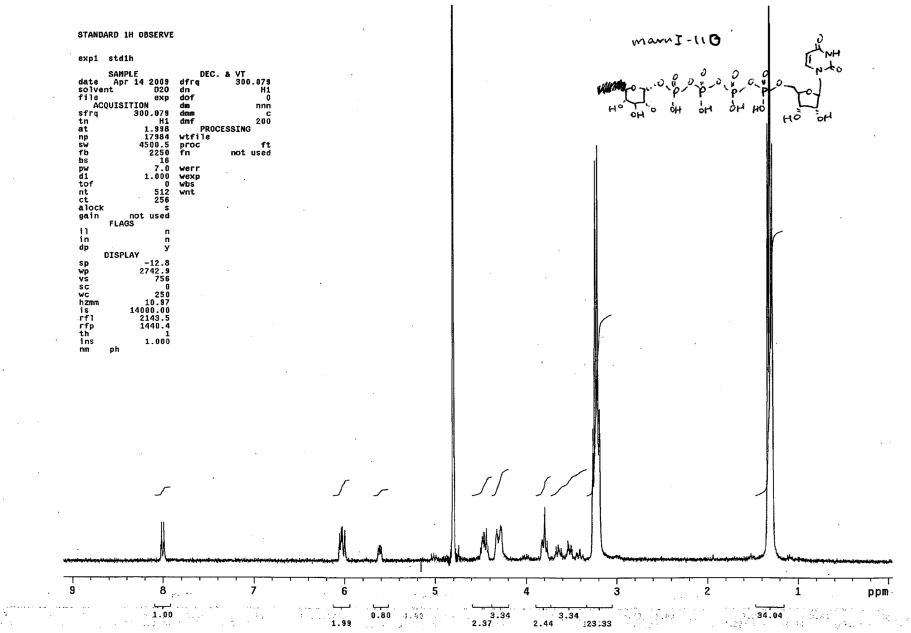

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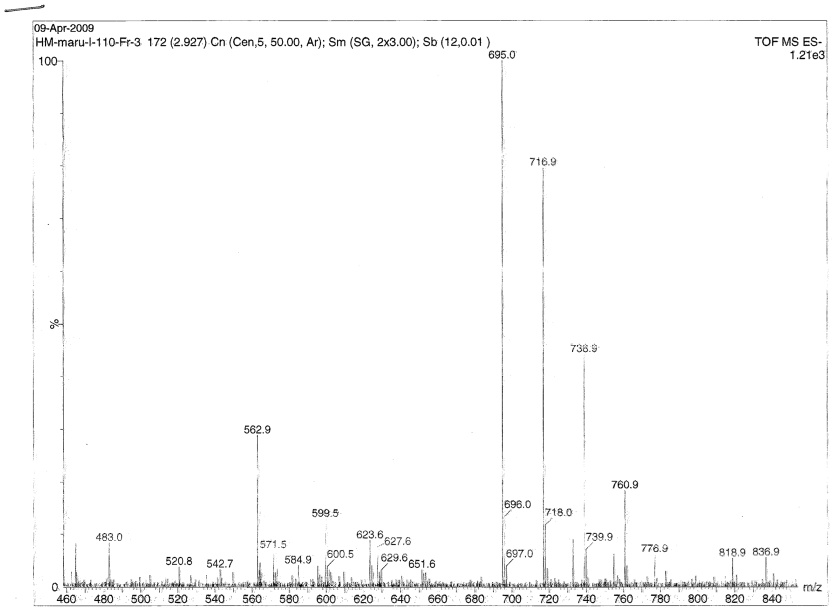
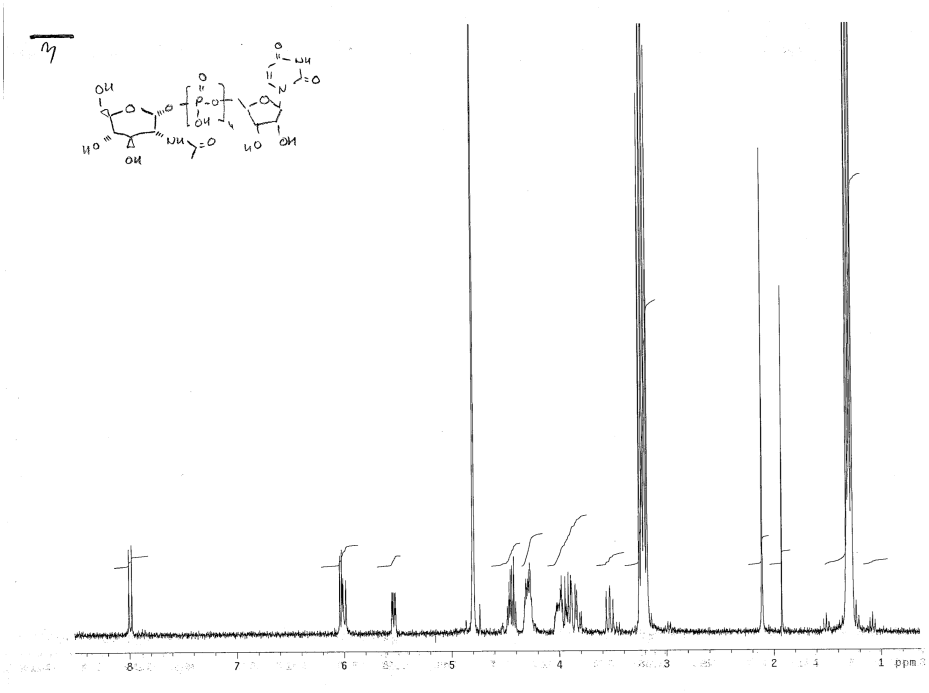
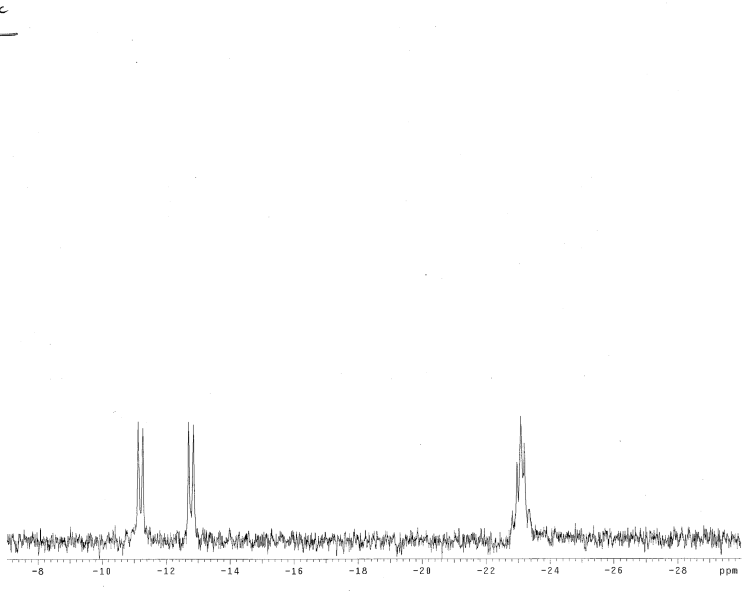


P^1-(Uridine-5′-)P^4-(2’-deoxy-2′-acetaminoglucose-1′-)tetraphosphate triethylammonium salt (31)

^{1}H NMR

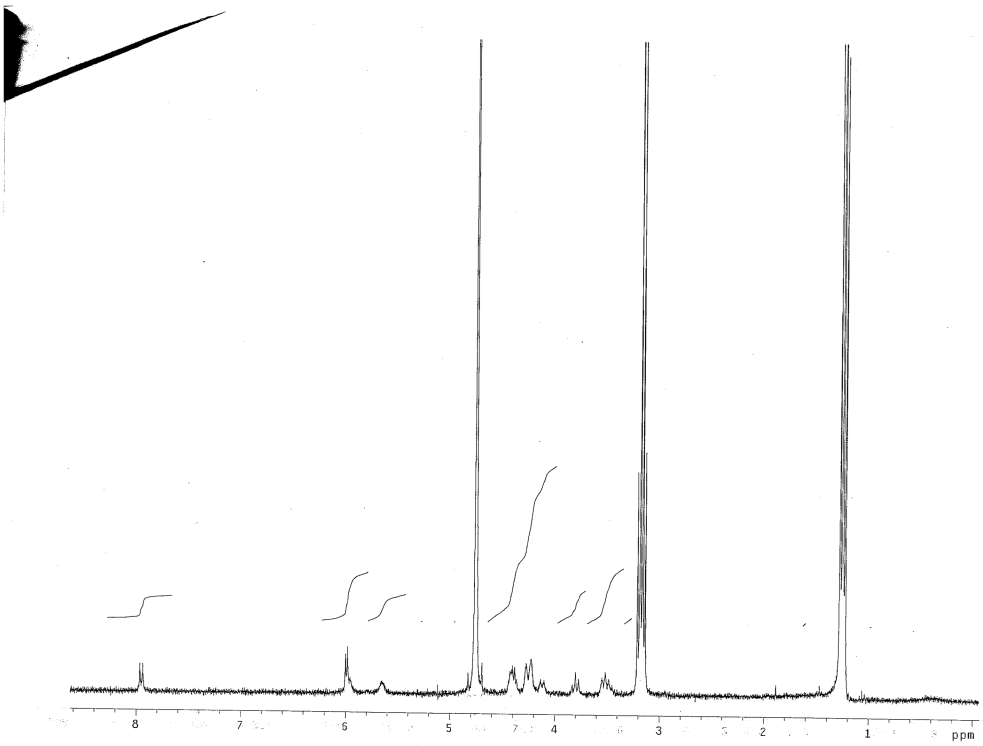


^{19}F NMR



P^1-(Uridine-5′-)P^4-(glucuronic acid-1′-)tetraphosphate triethylammonium salt (32)

^{1}H NMR



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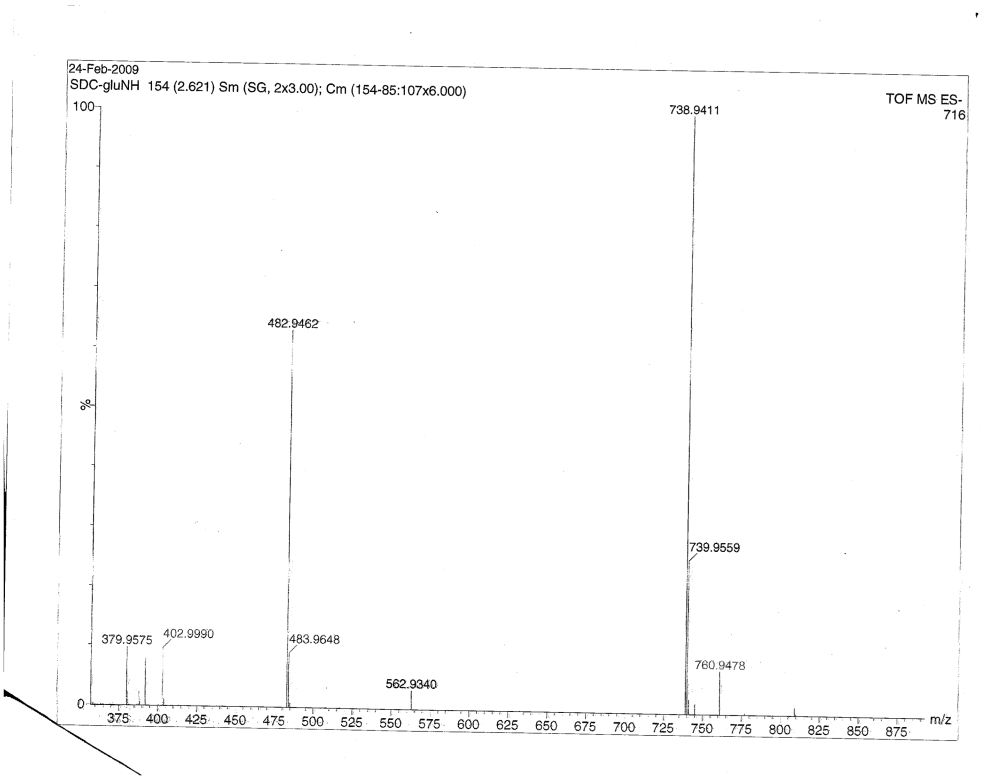
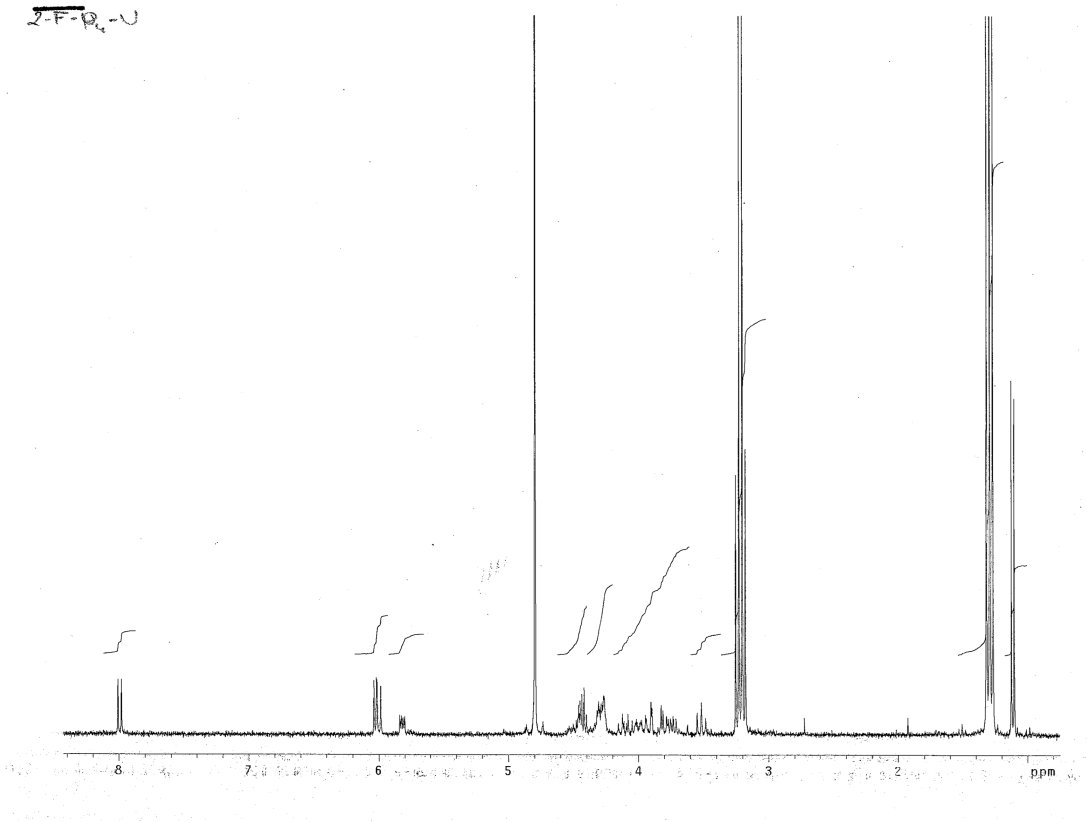


P^1-(Uridine-5′-)P^4-(2′-deoxy-2′-fluoroglucose-1′-)tetraphosphate triethylammonium salt (33)

^{1}H NMR



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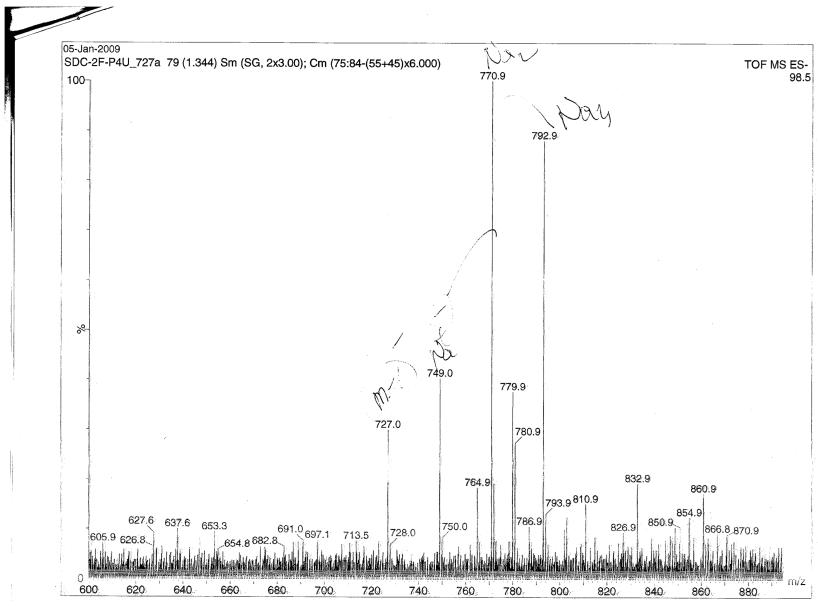
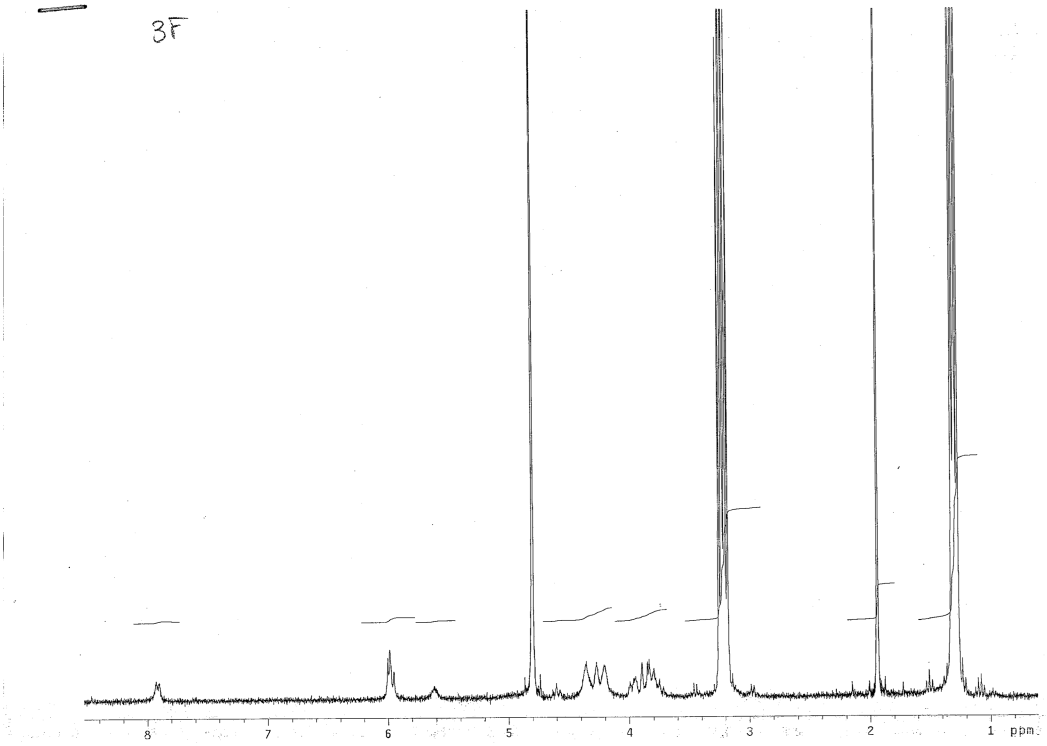


P^1-(Uridine-5′-)P^4-(3′-deoxy-3′-fluoroglucose-1′-)tetraphosphate triethylammonium salt (34)

^{1}H NMR



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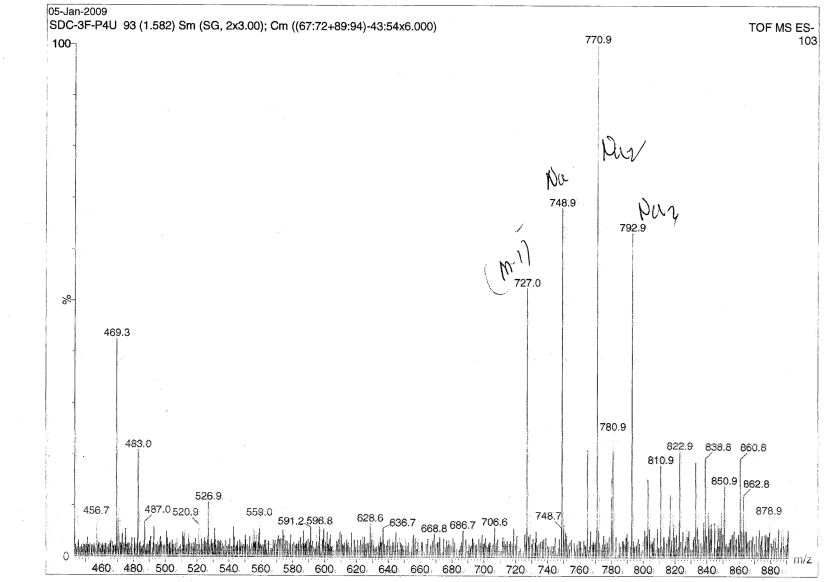
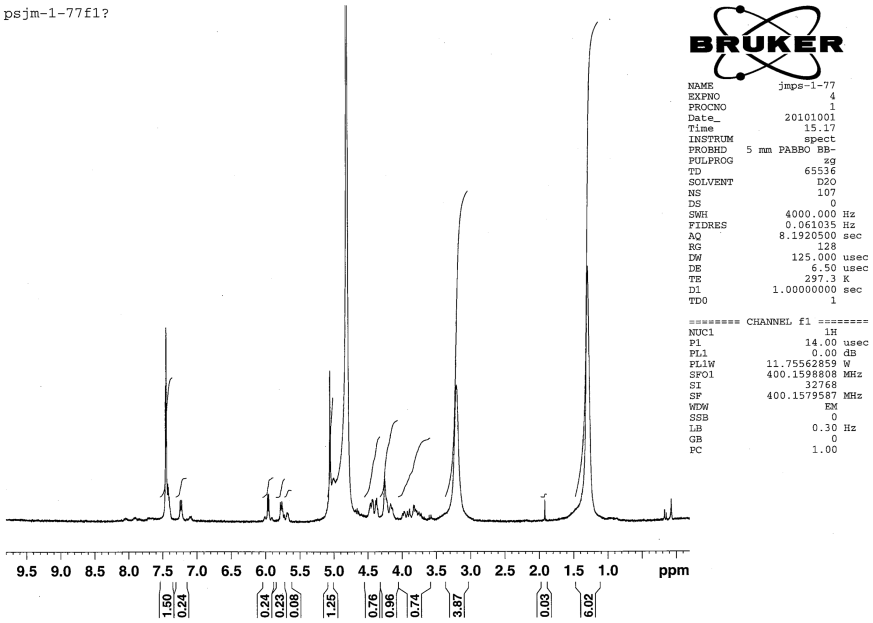


P^1-(N^4-Benzyloxycytidine-5′-)P^4-(3′-deoxy-3′-fluoroglucose-1′-)tetraphosphate triethylammonium salt (35)

^{1}H NMR



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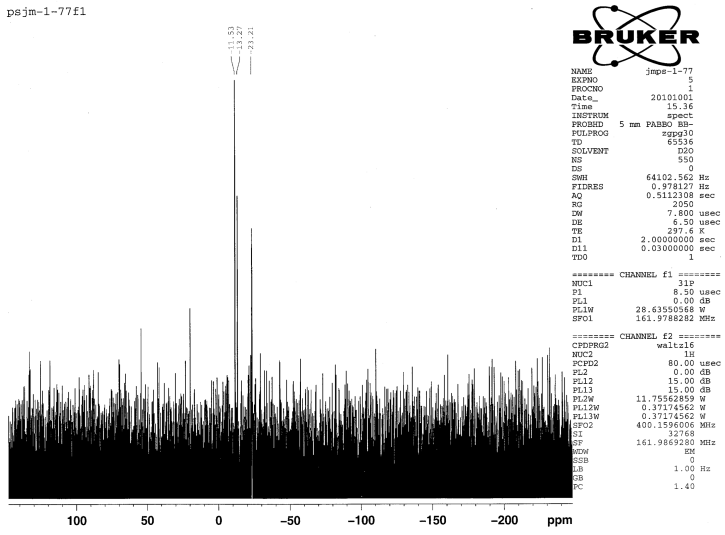
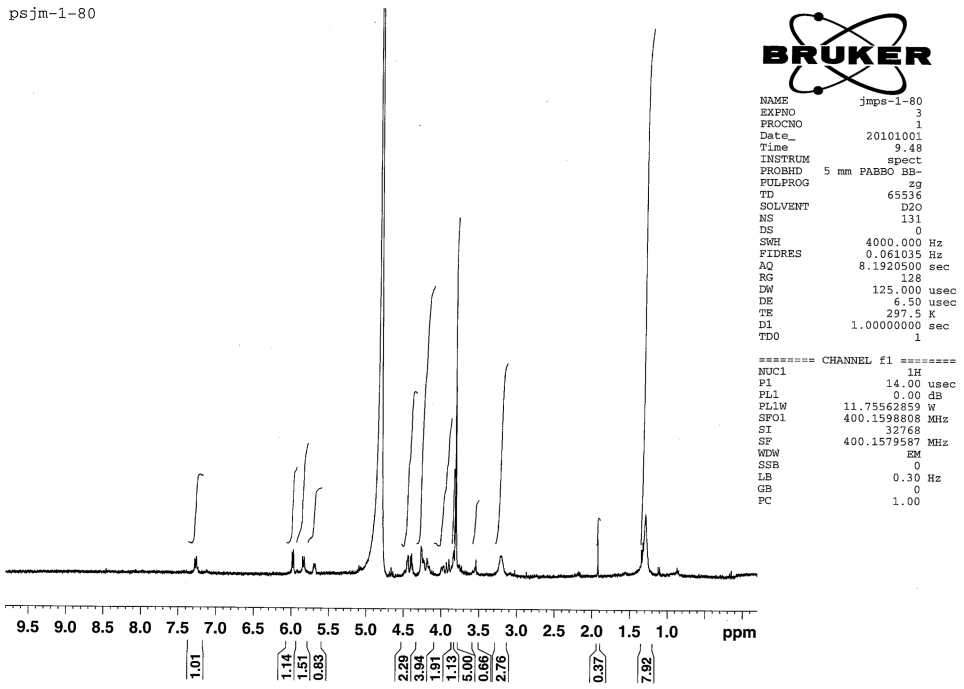


P^1-(N^4-Methoxycytidine-5′-)P^4-(3′-deoxy-3′-fluoroglucose-1′-)tetraphosphate triethylammonium salt (36)

^{1}H NMR



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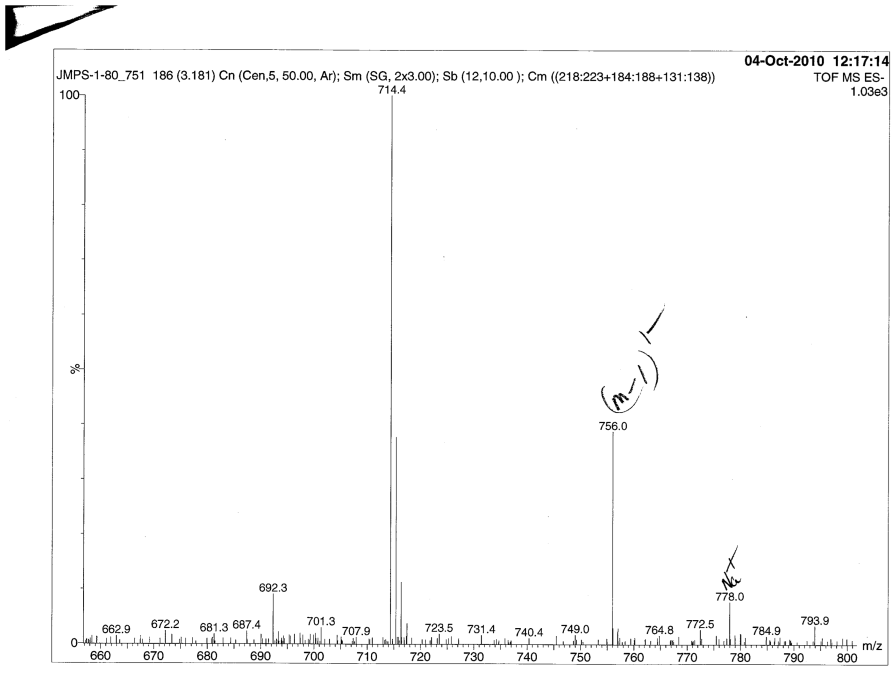
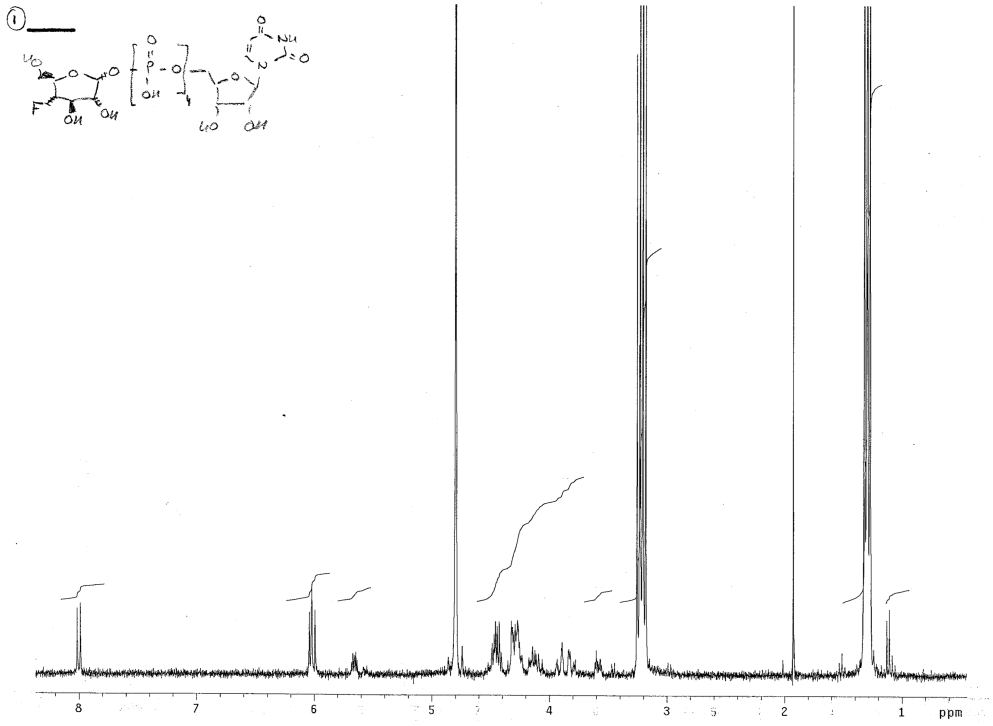


P^1-(Uridine-5′-)P^4-(4′-deoxy-4′-fluoroglucose-1′-)tetraphosphate triethylammonium salt (37)

^{1}H NMR



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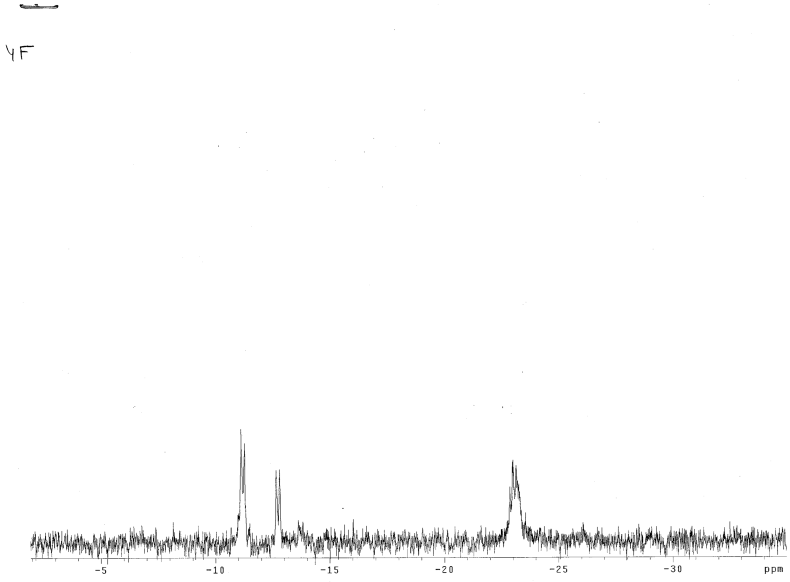


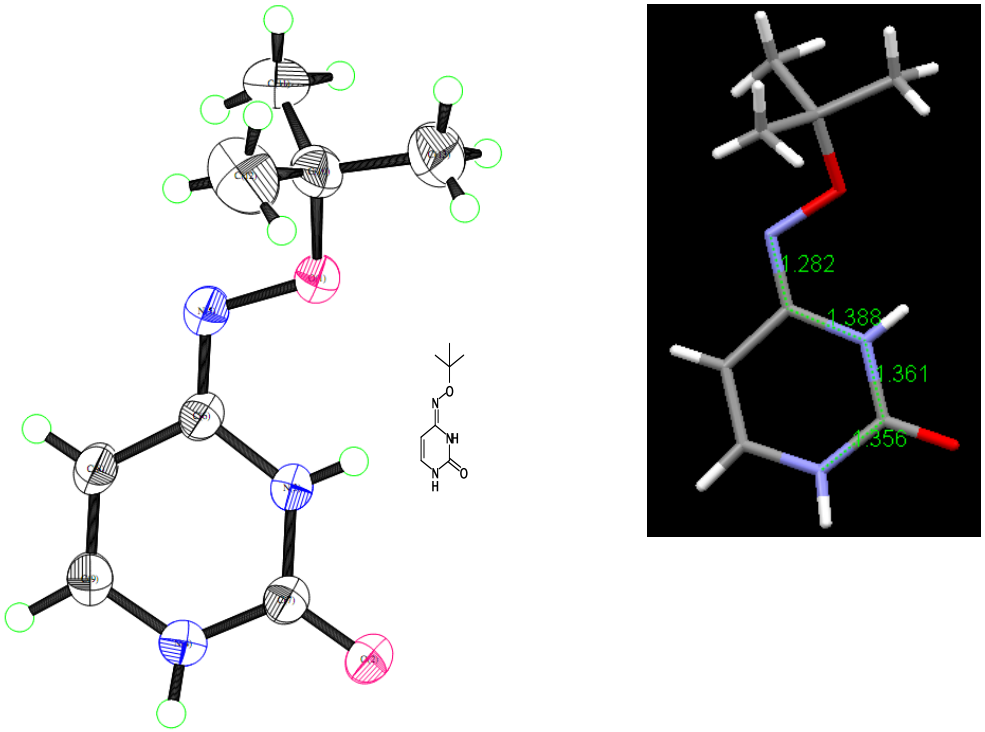


Figure 1. Structure of N^4-*t*-BuO-cytosine determined by x-ray crystallography (bond lengths in Å).

Table 1. Crystal data and structure refinement for 1.

Identification code	SMX10004
Empirical formula	C8 H13 N3 O2
Formula weight	183.21
Temperature	296.2 K
Wavelength	0.7107 A
Crystal system	Monoclinic
Space group	C 2/c
Unit cell dimensions	a = 21.98(1) A alpha = 90 deg.
	b = 7.543(5) A beta = 105.16(2) deg.
	c = 12.120(6) A gamma = 90 deg.
Volume	1939(2) A^3
Z	8
Density (calculated)	1.255 Mg/m^3
Absorption coefficient	0.092 mm^-1
F(000)	784
Crystal size	0.60 x 0.60 x 0.40 mm
Theta range for data collection	3.22 to 27.48 deg.
Index ranges	-28<=h<=28, -9<=k<=9, -15<=l<=15
Reflections collected	9631
Independent reflections	2221 [R(int) = 0.01460]
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2221 / 0 / 118
Goodness-of-fit on F^2	1.081
Final R indices [I>2sigma(I)]	R1 = 0.0534, wR2 = 0.1651
R indices (all data)	R1 = 0.0584, wR2 = 0.1707
Largest diff. peak and hole	.378 and -.259 e.A^-3

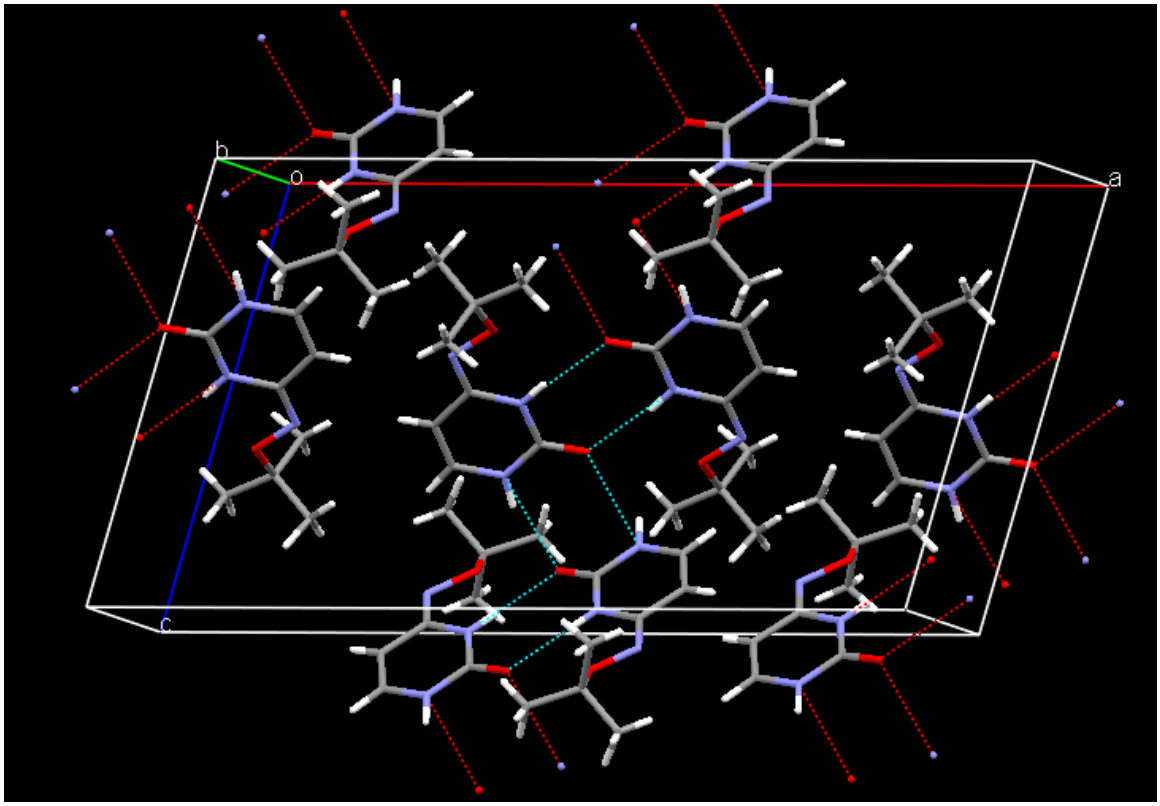


Figure 2. Crystal lattice of N^4-*t*-BuO-cytosine determined by x-ray crystallography.

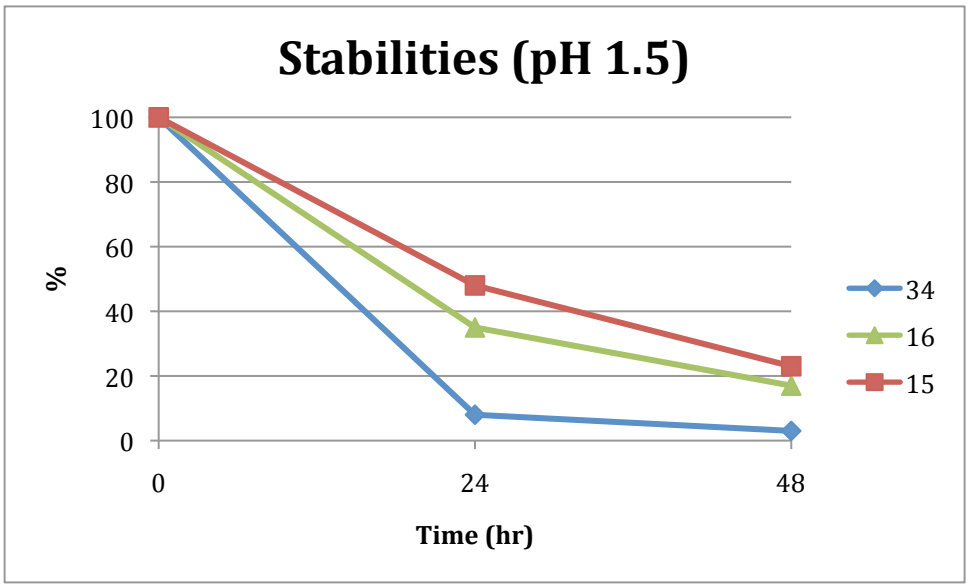
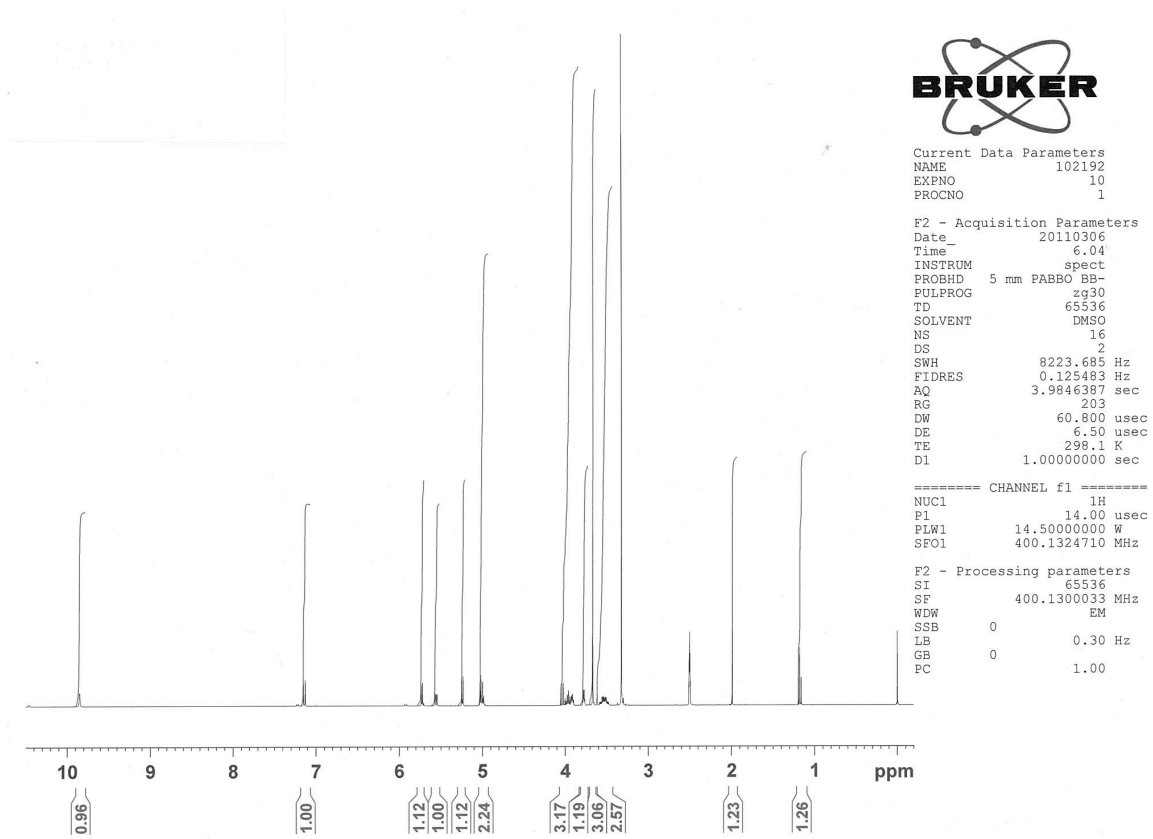
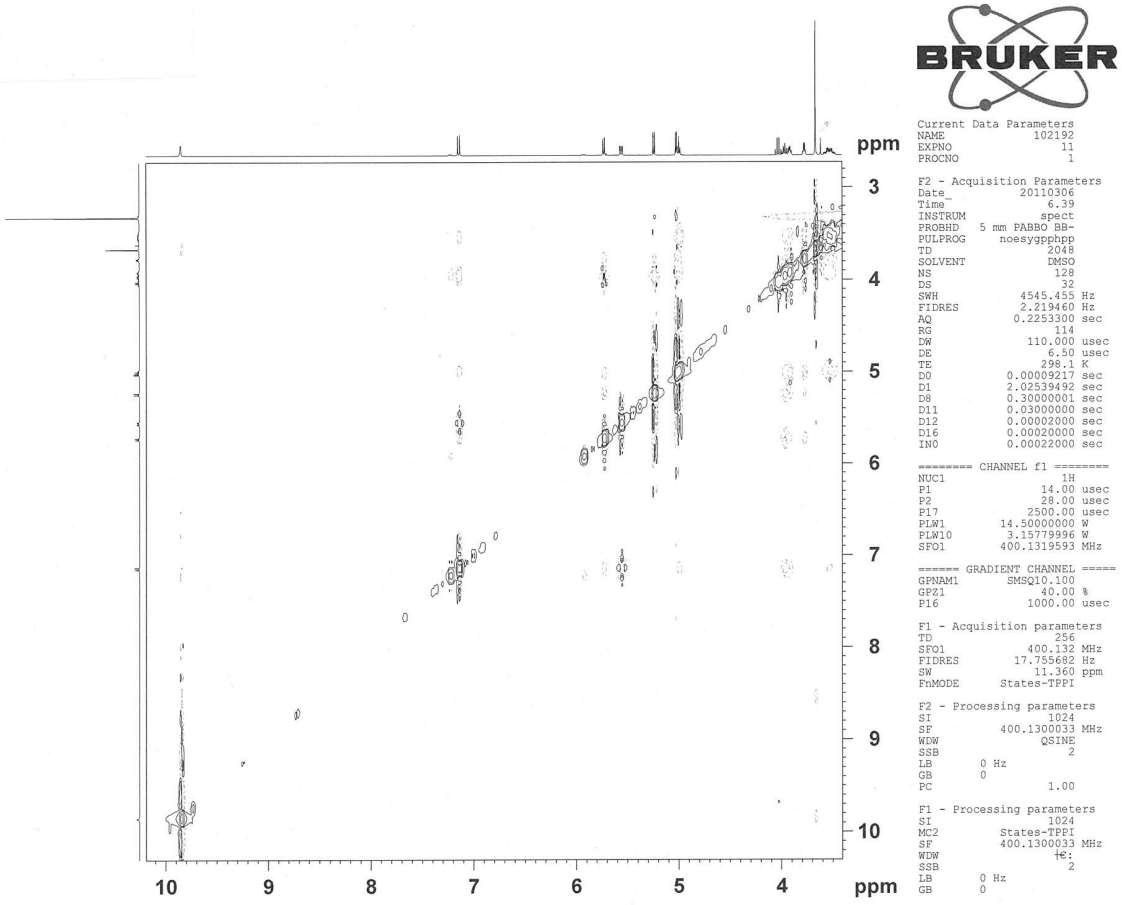
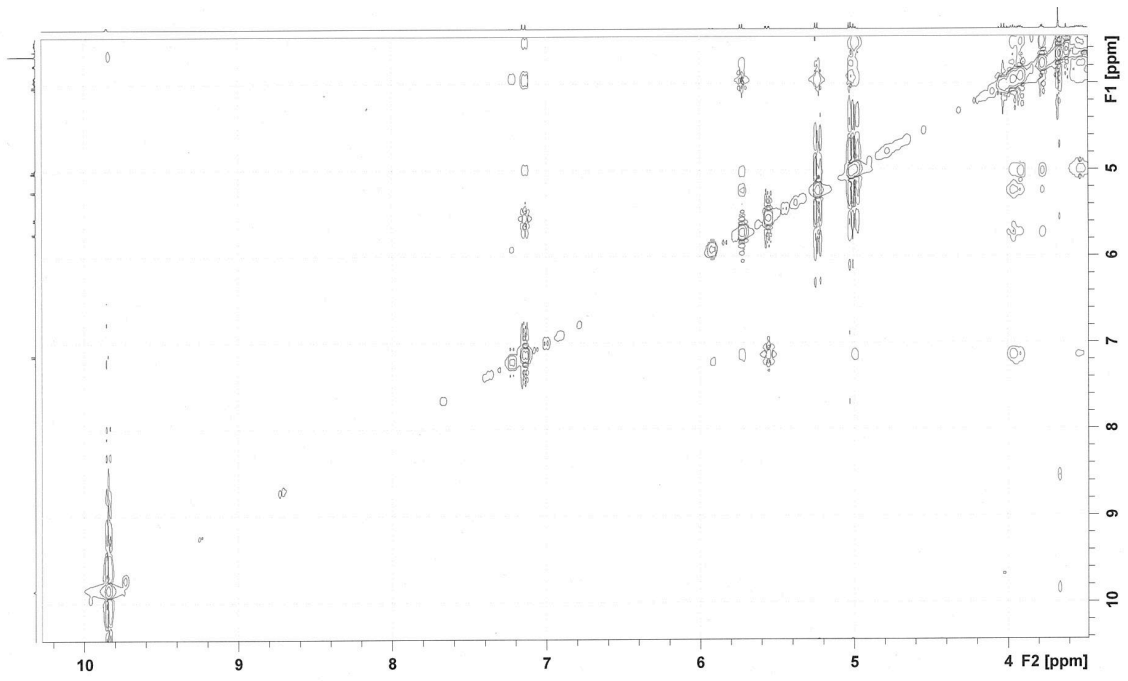


Figure 3. Stability data at pH 1.5 (37˚C) for compounds **15**, **16**, and **34**.

Figure 4. NOESY experiment for compound **39**




BRUKER
Current Data Parameters
NAME 102192
EXPNO 11
PROCNO 1
F2 - Acquisition Parameters
Date_ 20110306
Time 6.39
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG noesygpphpp
TD 2048
SOLVENT DMSO
NS 128
DS 32
SWH 4545.455 Hz
FIDRES 2.219460 Hz
AQ 0.2253300 sec
RG 114
DW 110.000 usec
DE 6.50 usec
TE 298.1 K
D0 0.00009217 sec
D1 2.02539492 sec
D8 0.30000001 sec
D11 0.03000000 sec
D12 0.00002000 sec
D16 0.00020000 sec
IN0 0.00022000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 14.00 usec
P2 28.00 usec
P17 2500.00 usec
PLW1 14.50000000 W
PLW10 3.15779996 W
SFO1 400.1319593 MHz
====== GRADIENT CHANNEL =====
GPNAM1 SMSQ10.100
GPZ1 40.00 %
P16 1000.00 usec
F1 - Acquisition parameters
TD 256
SFO1 400.132 MHz
FIDRES 17.755682 Hz
SW 11.360 ppm
FnMODE States-TPPI
F2 - Processing parameters
SI 1024
SF 400.1300033 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0
PC 1.00
F1 - Processing parameters
SI 1024
MC2 States-TPPI
SF 400.1300033 MHz
WDW
SSB 2
LB 0 Hz
GB 0
ppm
3
4
5
6
7
8
9
10
10 9 8 7 6 5 4 ppm


F1 [ppm]
5
6
7
8
9
10
10 9 8 7 6 5 4 F2 [ppm]