Electronic Supplementary Information

Tetrahydrofuranyl and Tetrahydropyranyl Protection of Amino Acid Side-Chains Enables Synthesis of Hydroxamate-Containing Aminoacylated tRNA

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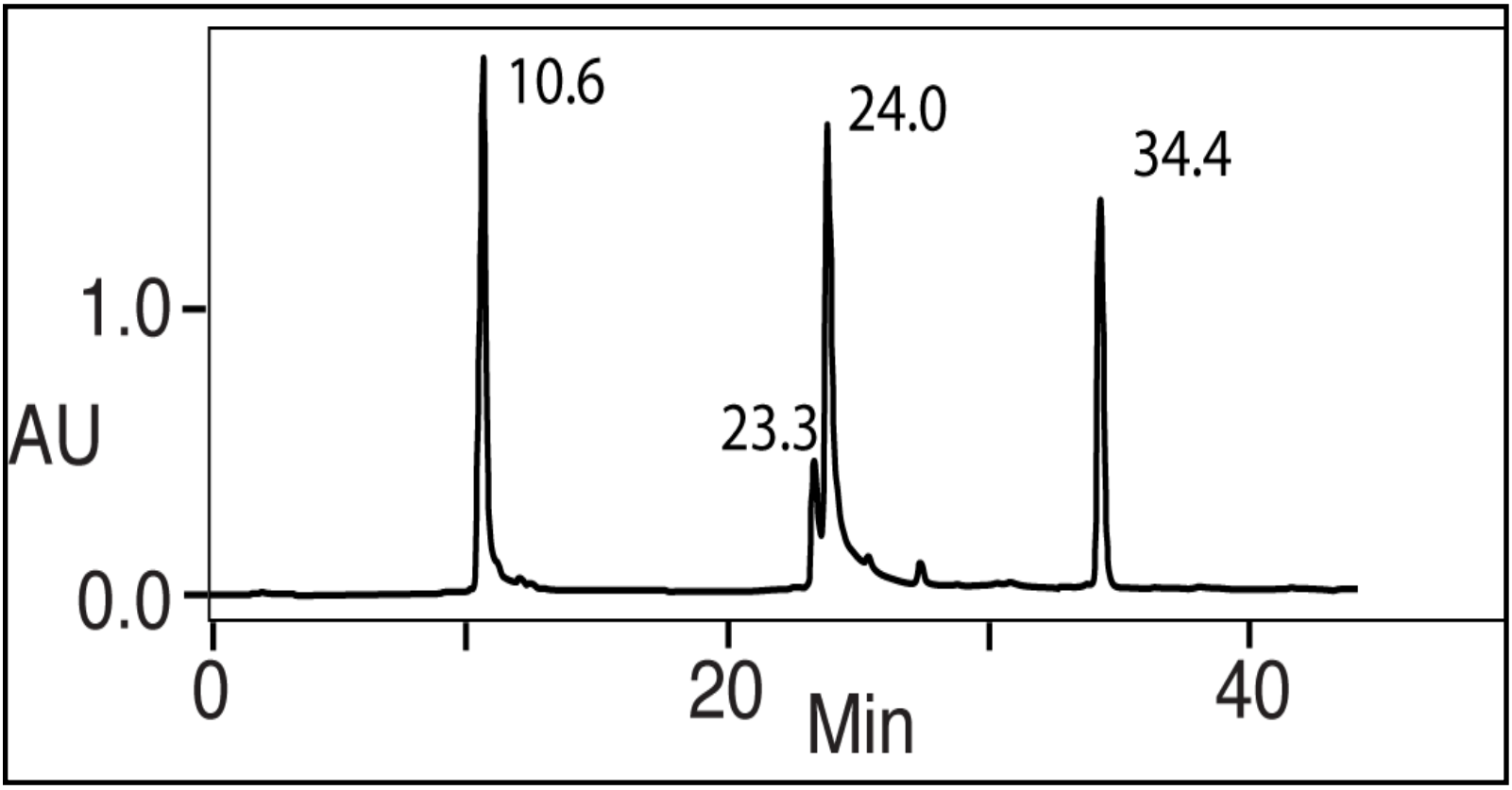


Figure S1. Reverse phase HPLC analysis of aminoacylation reaction showing progress in the synthesis of pdCpA aminoacylated with the tetrahydrofuranyl hydroxamate **8b**. (Waters Nova-Pac® 3.9 × 1500 mm developed with a linear gradient from 1-25% CH3CN over 30 minutes in 50 mM NaOAc, pH 4.5, at 0.8 mL/min monitored at 260 nm). The hybrid dinucleotide pdCpA elutes at 10.5 min and 2' 3' O-monoaminoacylated product **8b** elutes at 23-24 min. Unreacted amino acid cyanomethyl ester **7b** elutes at 34.4 min. Aminoacylation results in a mixture of 2' 3' O- isomers that are not separable using this protocol. Peak impurities at 25 min represent bisaminoacylated hybrid dinucleotide species.[1]

1) Duca, M., Chen, S. and Hecht S.M. (2008) Aminoacylation of tRNAs with one and two amino acids. Methods. 43, 87-99.

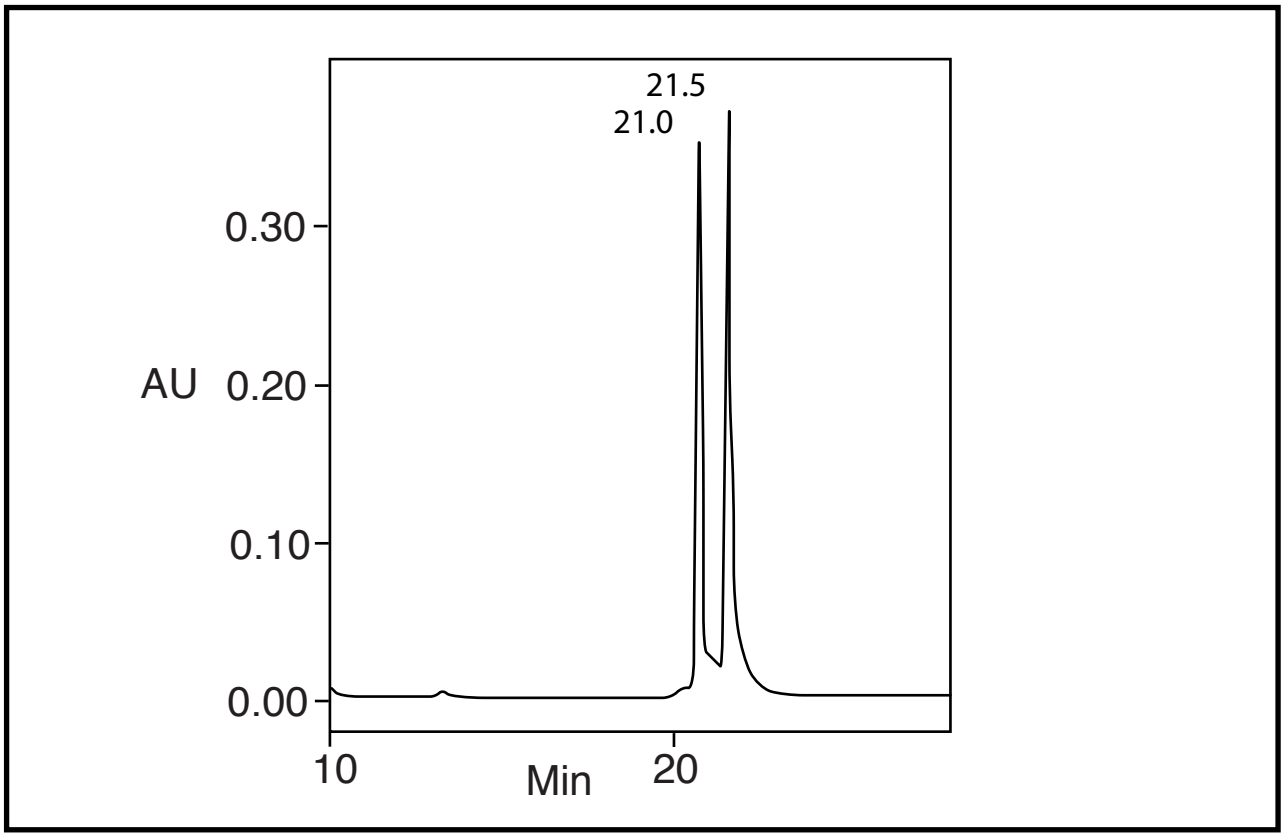
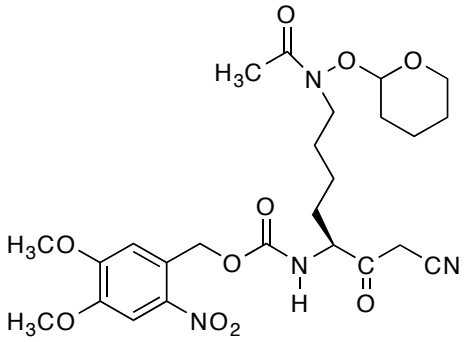


Figure S2**.** Reverse phase HPLC analysis of aminoacylation reaction post purification showing integrity and purity of deprotected pdCpA aminoacylated with the hydroxamate **9**.

The HPLC conditions were Waters Nova-Pac® 3.9 × 1500 mm developed with a linear gradient from 1-25% CH3CN over 30 minutes in 50 mM NaOAc, pH 4.5, at 0.8 mL/min monitored at 260 nm. The deprotected and aminoacylated product **9** elutes as isomers at 20-22 min.



7a

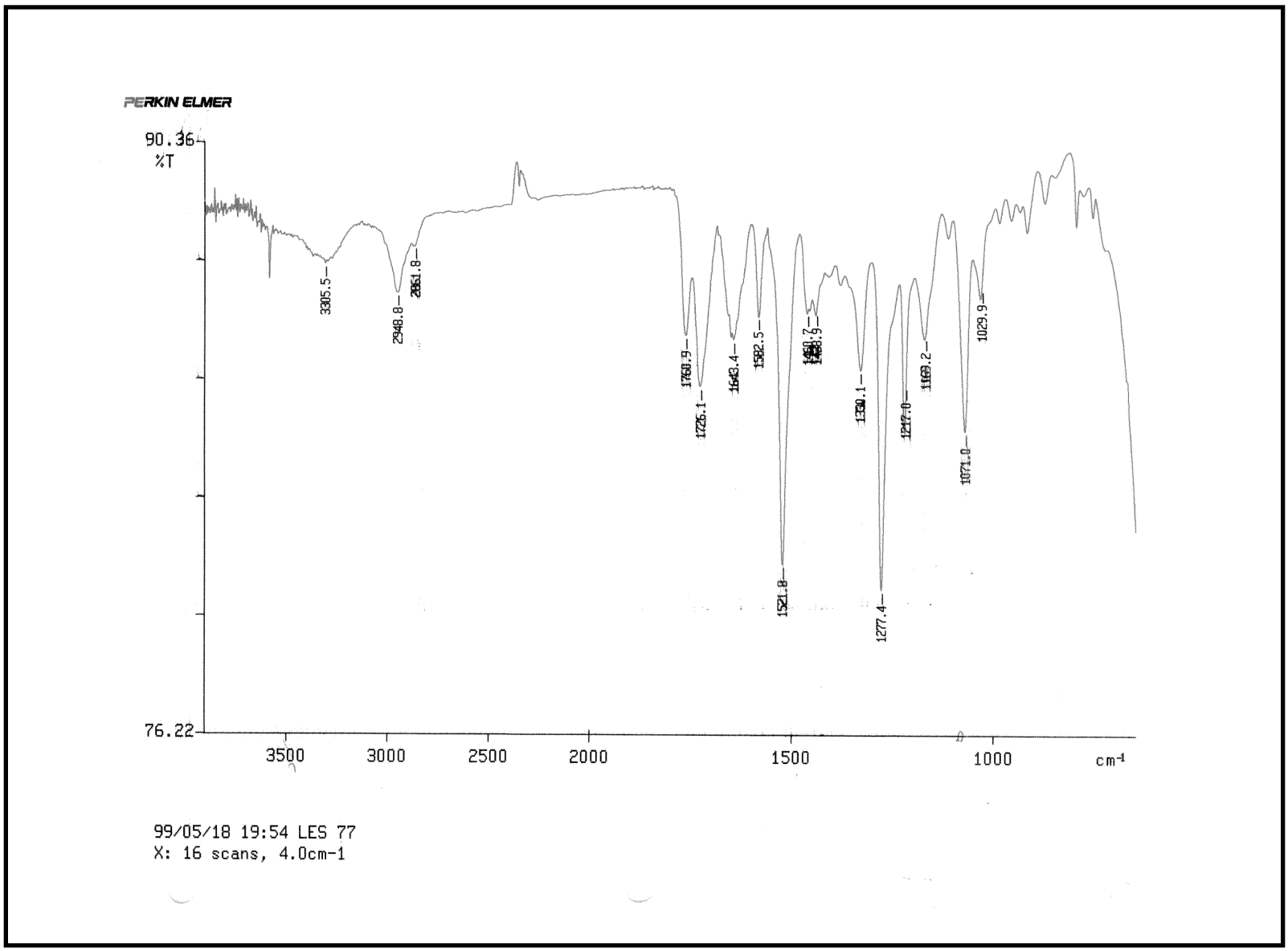
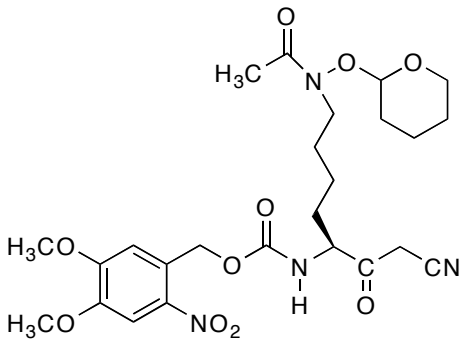


Figure S3. IR spectrum of **7a**.



7a

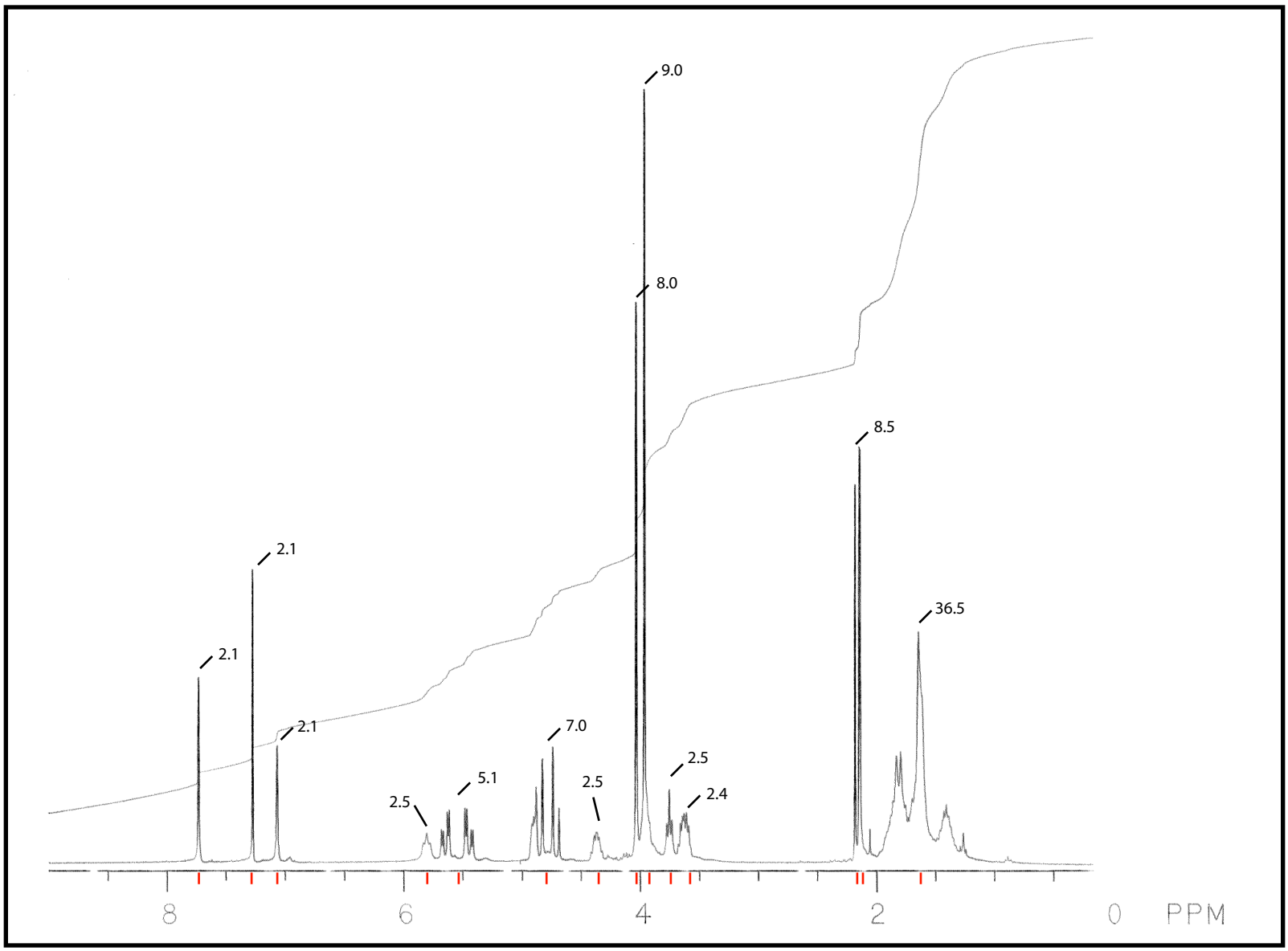
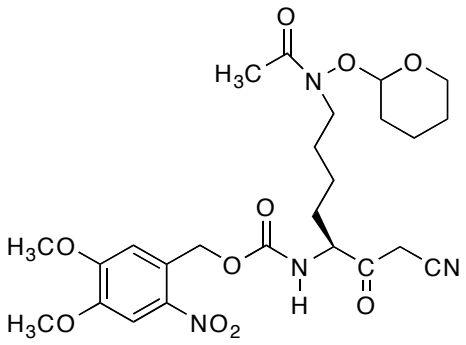


Figure S4. 1H NMR spectrum of **7a (**integrated area is indicated).



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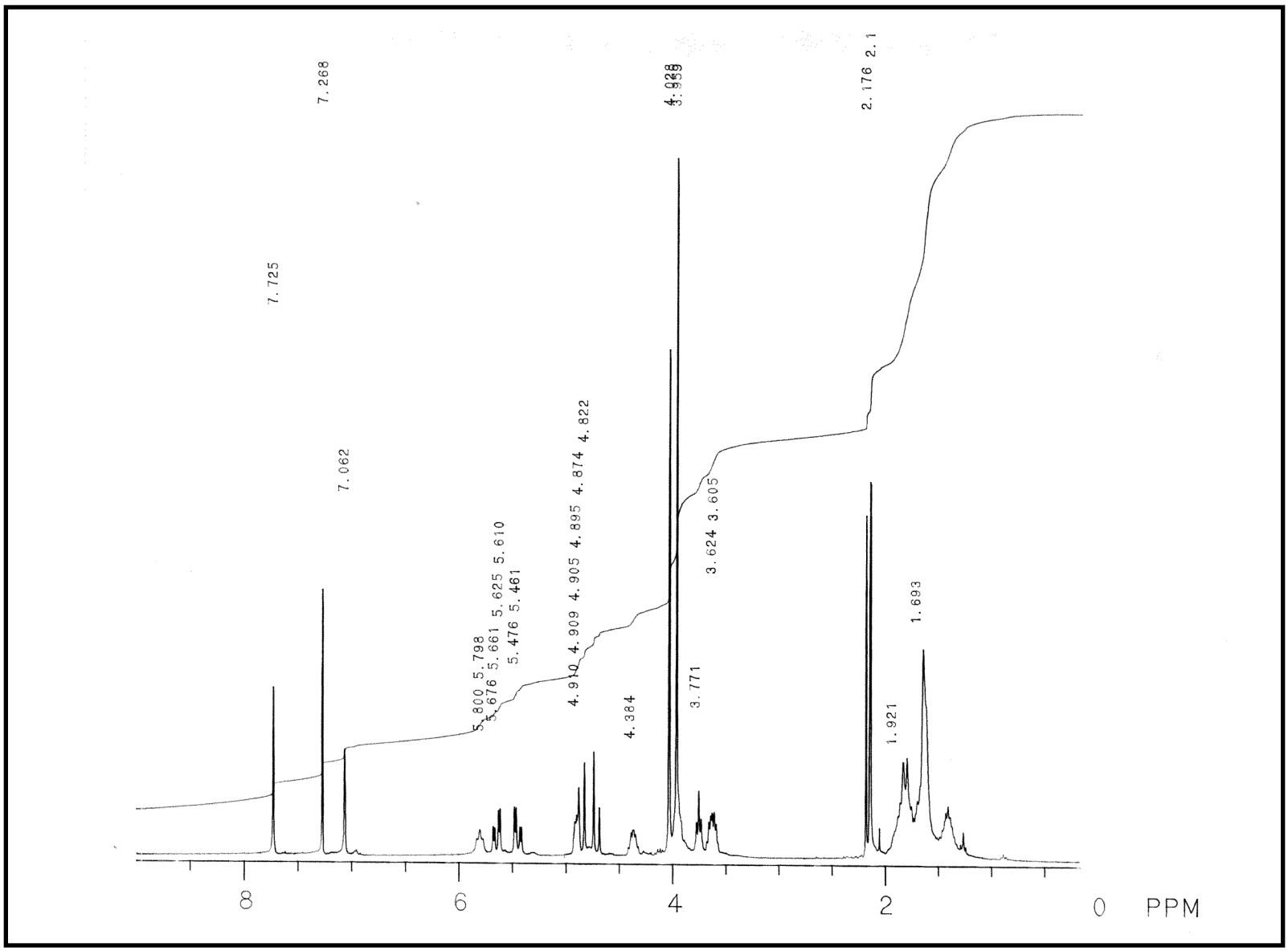
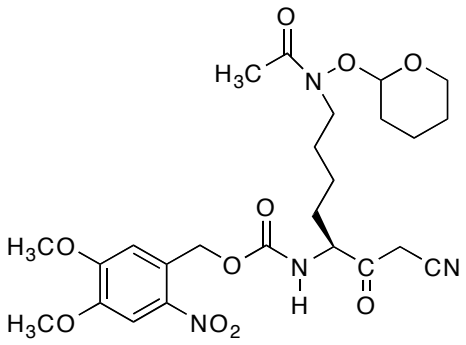


Figure S5. 1H NMR spectrum of **7a (**chemical shifts).



7a

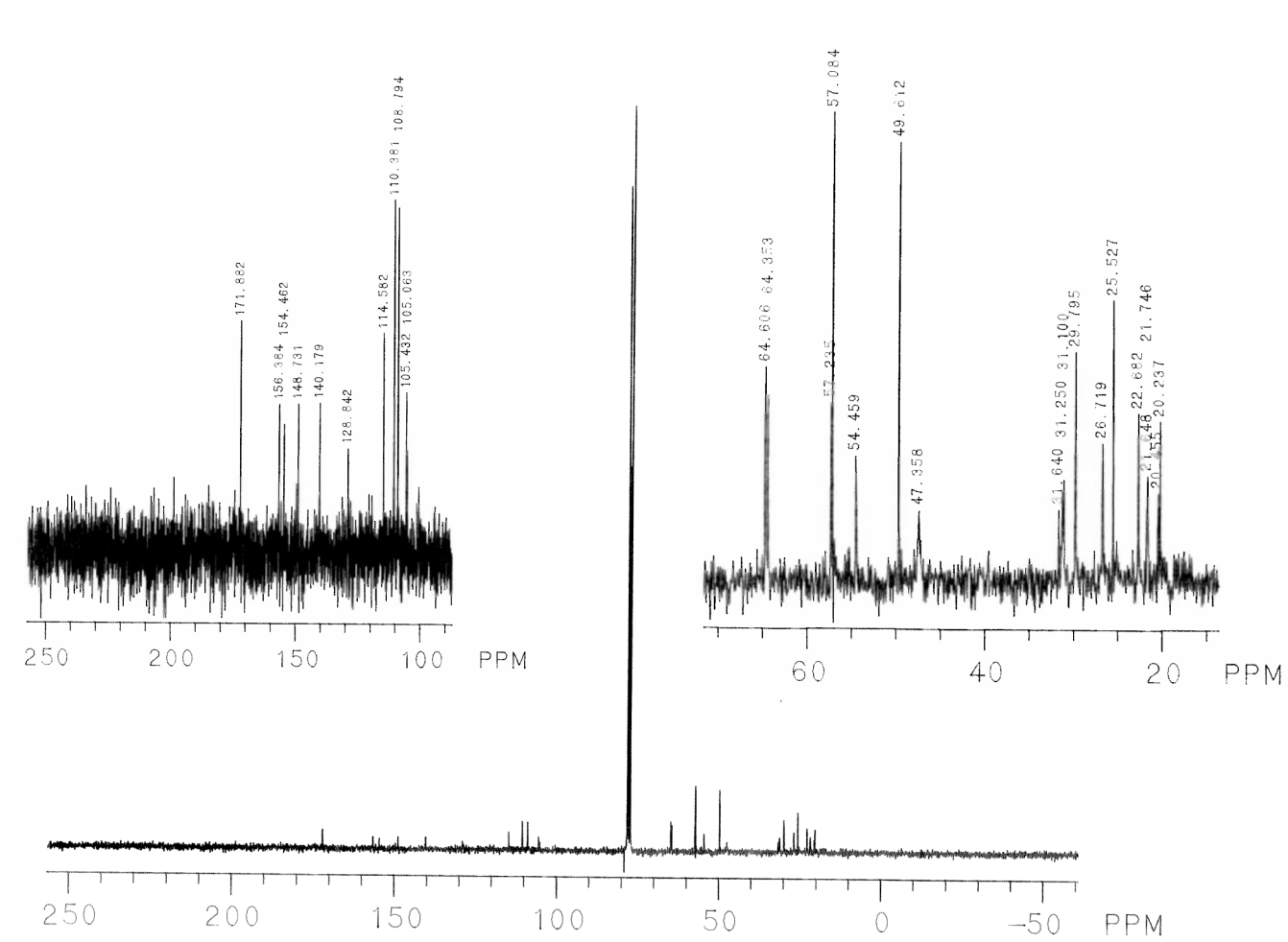
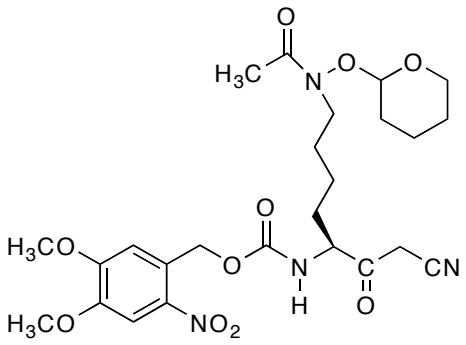


Figure S6. 13C NMR spectrum of **7a (**chemical shifts).



7a

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Sample: THP
Note : in NBA
Inlet : Direct                         Ion Mode : FAB+
RT : 0.69 min                          Scan#: (1,11)
Elements : C 40/0, H 84/0, O 13/0, N 6/0
Mass Tolerance      : 5mmu
Unsaturation (U.S.) : -0.5 - 12.0

Observed m/z Int%   Err[ppm / mmu]    U.S.  Composition
  567.2265    40.0     -6.6 /  -3.7   10.5  C 25 H 35 O 11 N 4
                       +0.5 /  +0.3    6.5  C 20 H 35 O 13 N 6
```

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[ Theoretical Ion Distribution ]                                 Page: 1
Molecular Formula : C25 H35 N4 O11
                    (m/z   567.2302, MW   567.5731, U.S. 10.5)
Base Peak :   567.2302, Averaged MW :   567.5743(a),   567.5750(w)

    m/z       INT.
  567.2302 100.0000 ************************************************************
  568.2333  30.2193 ******************
  569.2358   6.6138 ****
  570.2383   1.0791 *
  571.2408   0.1471
  572.2432   0.0172
  573.2456   0.0018
  574.2480   0.0002
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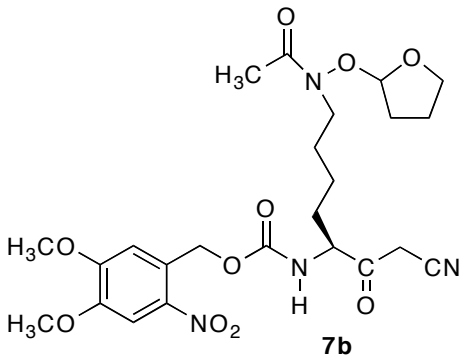
Figure S7. HRMS (FAB) mass spectrum analysis of **7a**.



7b

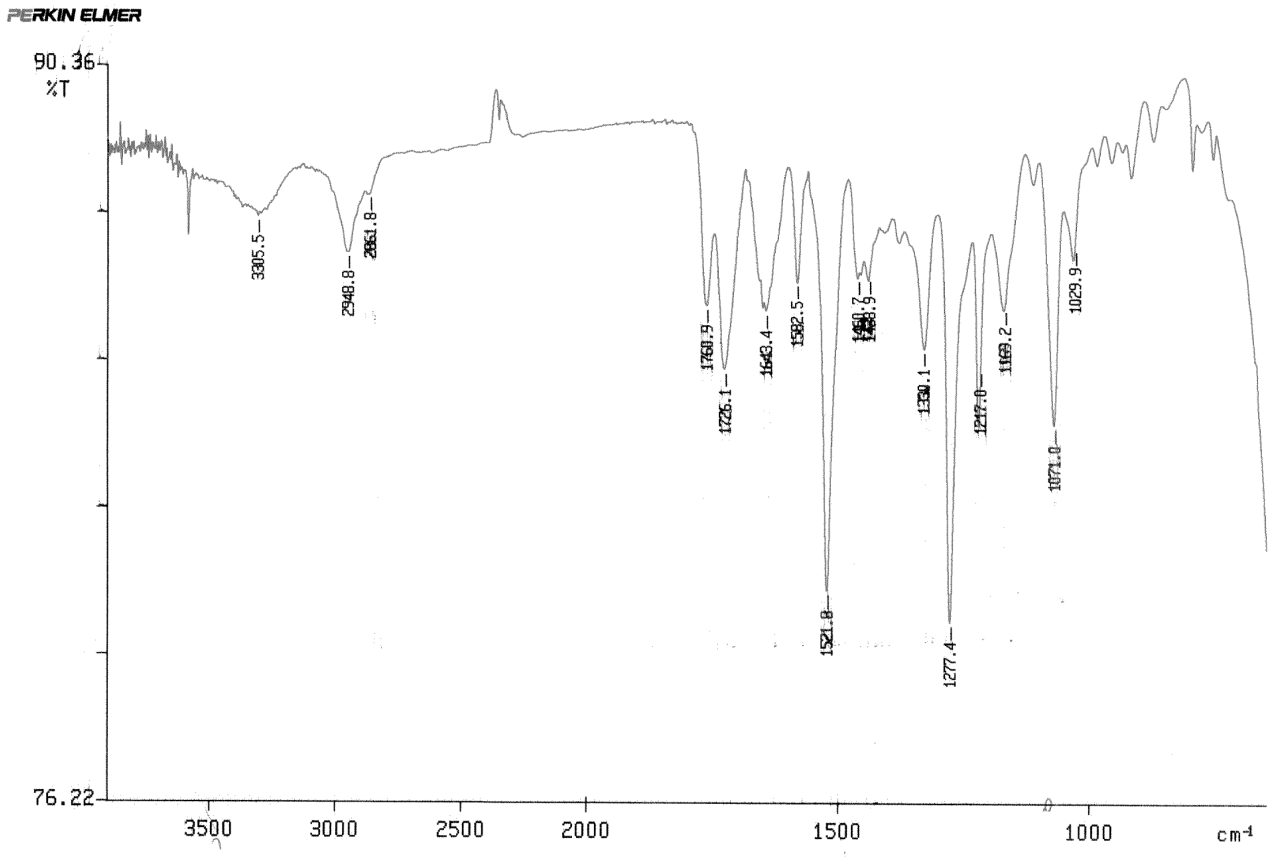
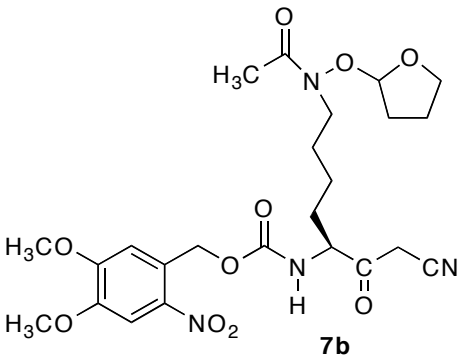


Figure S8. IR spectrum of **7b**.



7b

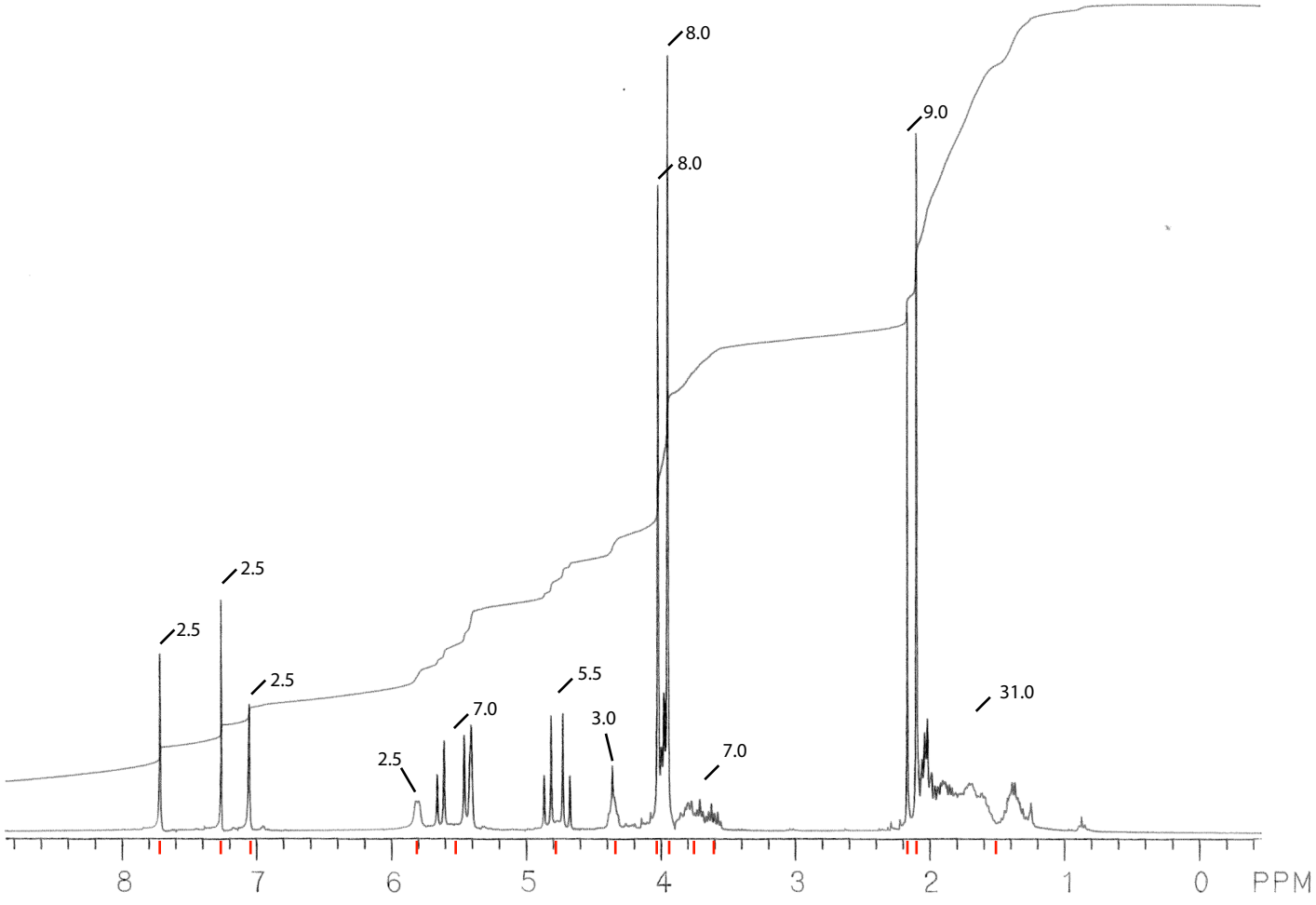
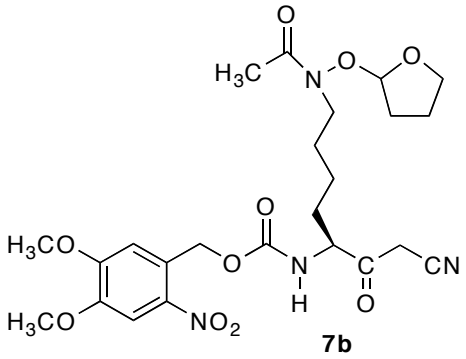


Figure S9. 1H NMR spectrum of **7b (**integrated area is indicated).



7b

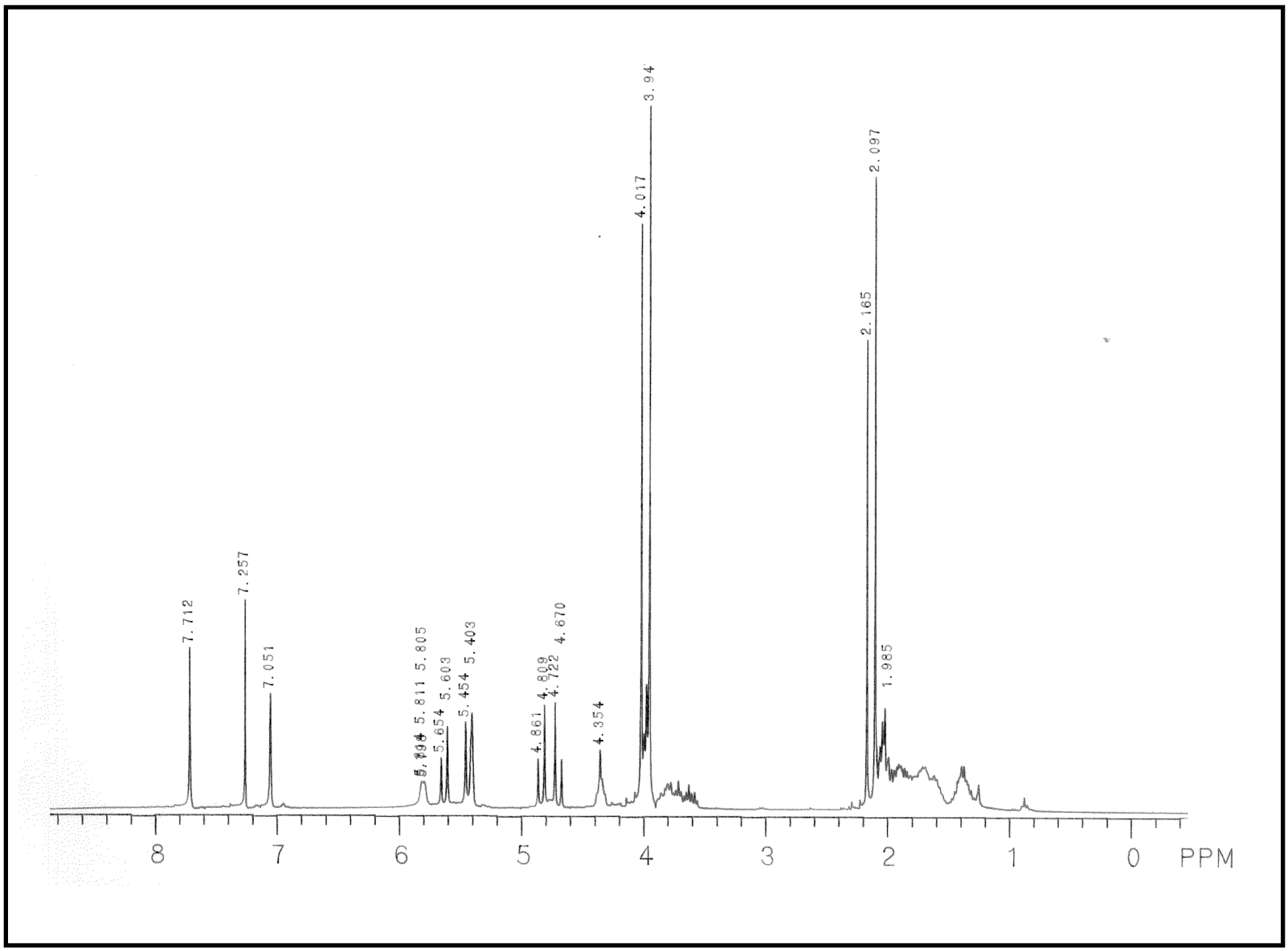
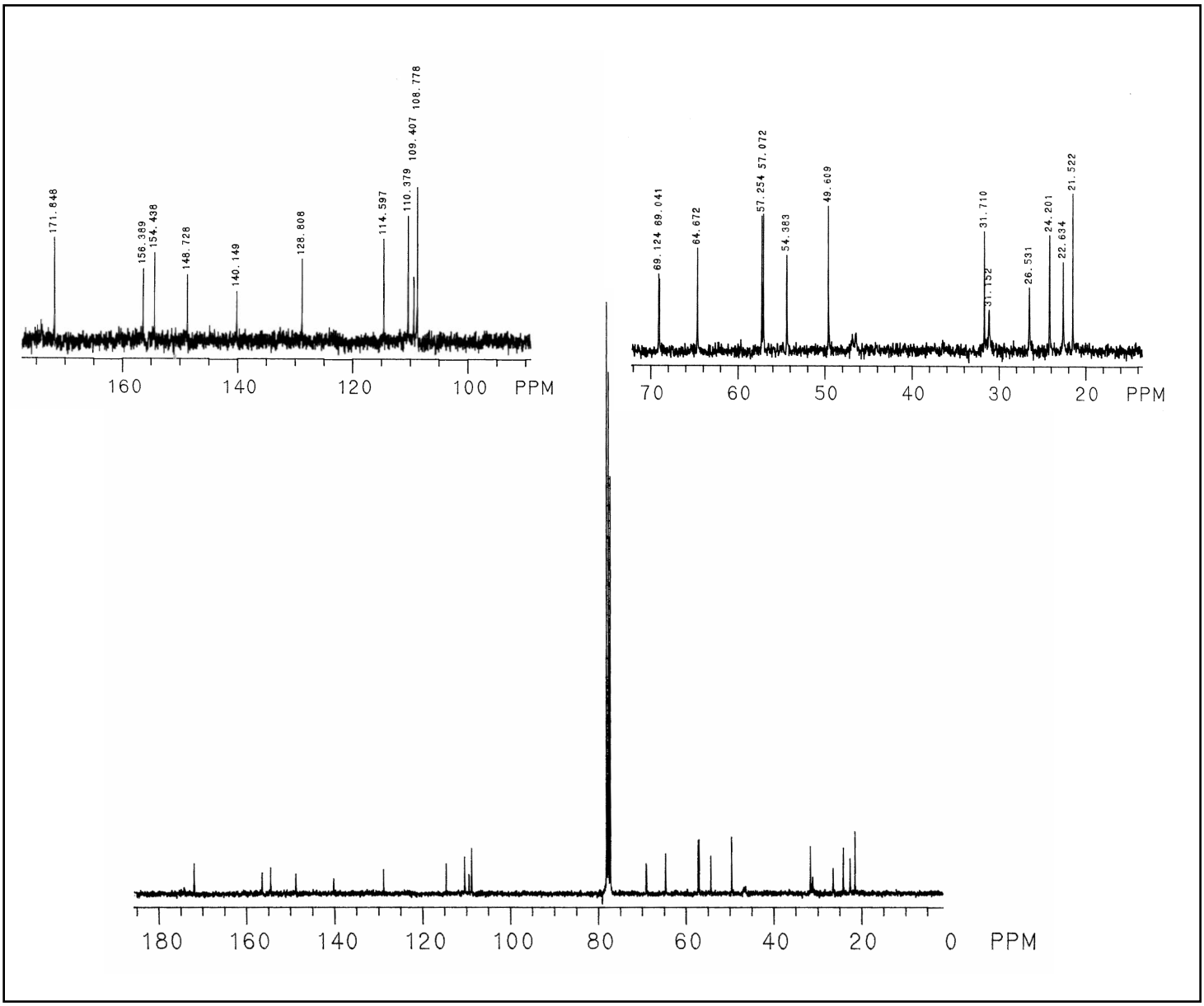
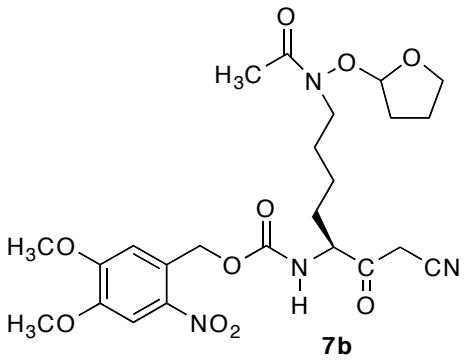


Figure S10. 1H NMR spectrum of **7b (**chemical shifts).



7b

Figure S11. 13C NMR spectrum of **7b (**chemical shifts).



7b

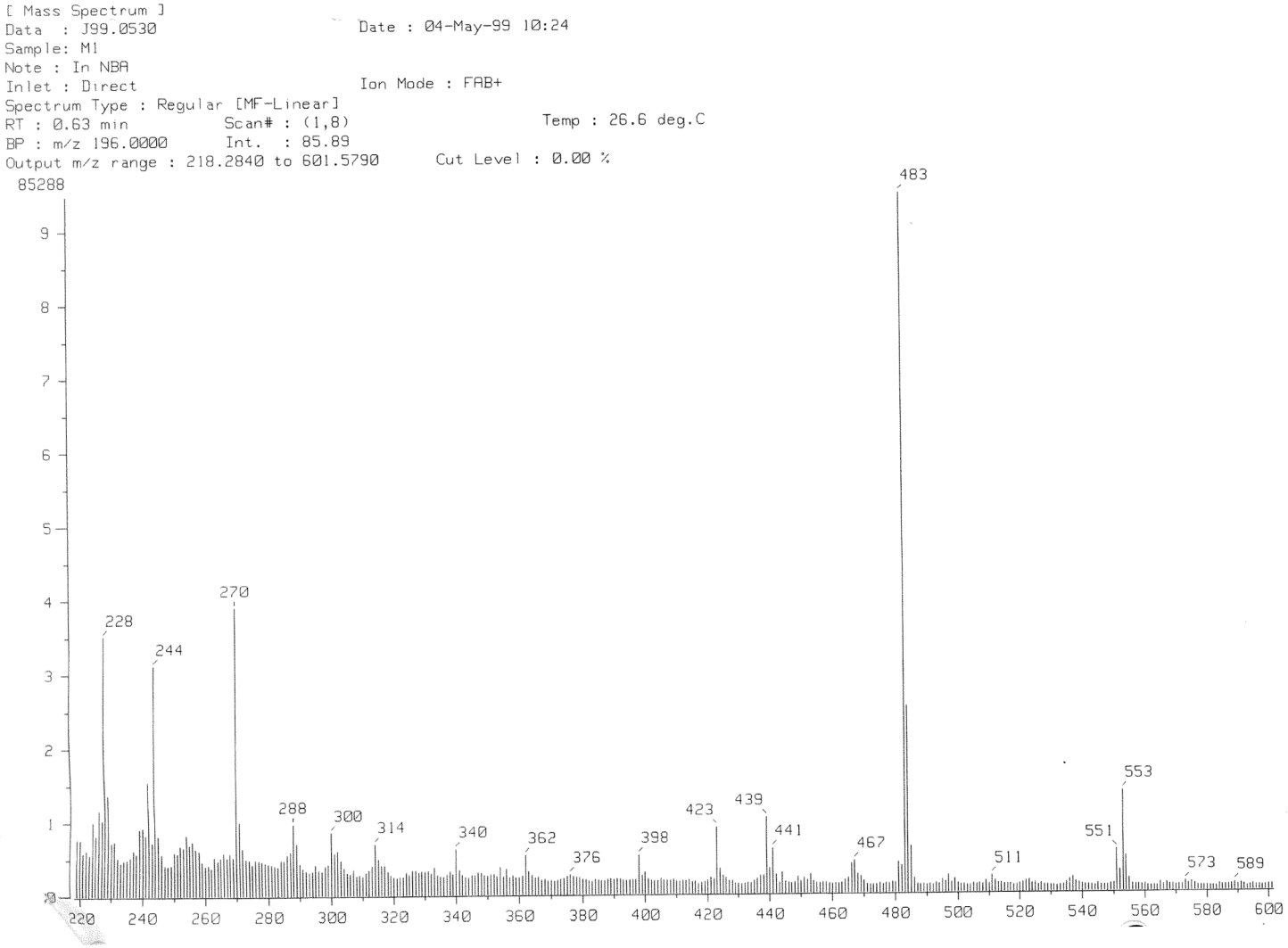
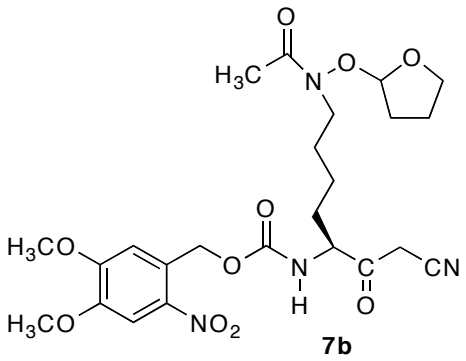


Figure S12. FAB mass spectrum of **7b**.



7b

Elemental Composition] Page: 1

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Note : in NBA
Inlet : Direct Ion Mode : FAB+
RT : 0.82 min Scan#: (1,13)
Elements : C 40/0, H 84/0, O 13/0, N 6/0
Mass Tolerance : 3mmu
Unsaturation (U.S.) : -0.5 - 12.0

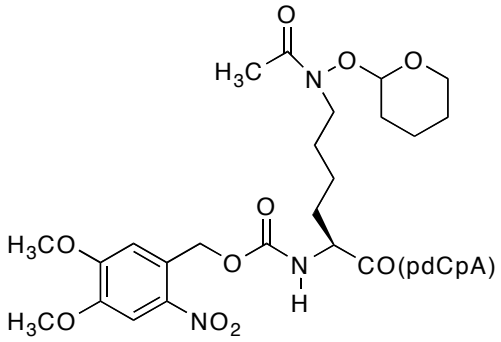
Observed m/z	Int%	Err[ppm / mmu]	U.S.	Composition
553.2141	100.0	-3.3 / -1.8	10.0	C 26 H 35 O 12 N
		-0.9 / -0.5	10.5	C 24 H 33 O 11 N 4

Theoretical Ion Distribution] Page: 1

Molecular Formula : C24 N4 O11 H33
(m/z 553.2146, MW 553.5462, U.S. 10.5)
Base Peak : 553.2146, Averaged MW : 553.5473(a), 553.5480(w)

m/z	INT.	
553.2146	100.0000	**********
554.2177	29.0771	**********
555.2201	6.2814	****
556.2226	1.0072	*
557.2250	0.1356	
558.2274	0.0157	
559.2298	0.0016	
560.2322	0.0001	

Figure S13. HRMS (FAB) mass spectrum analysis of **7b**.



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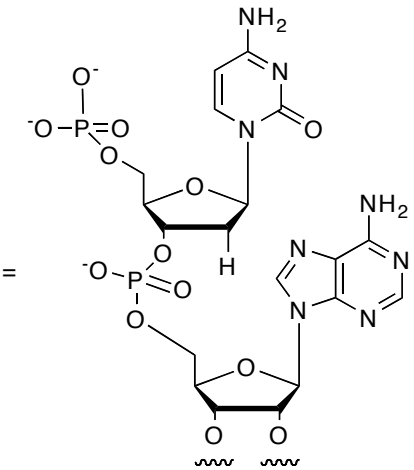


8a

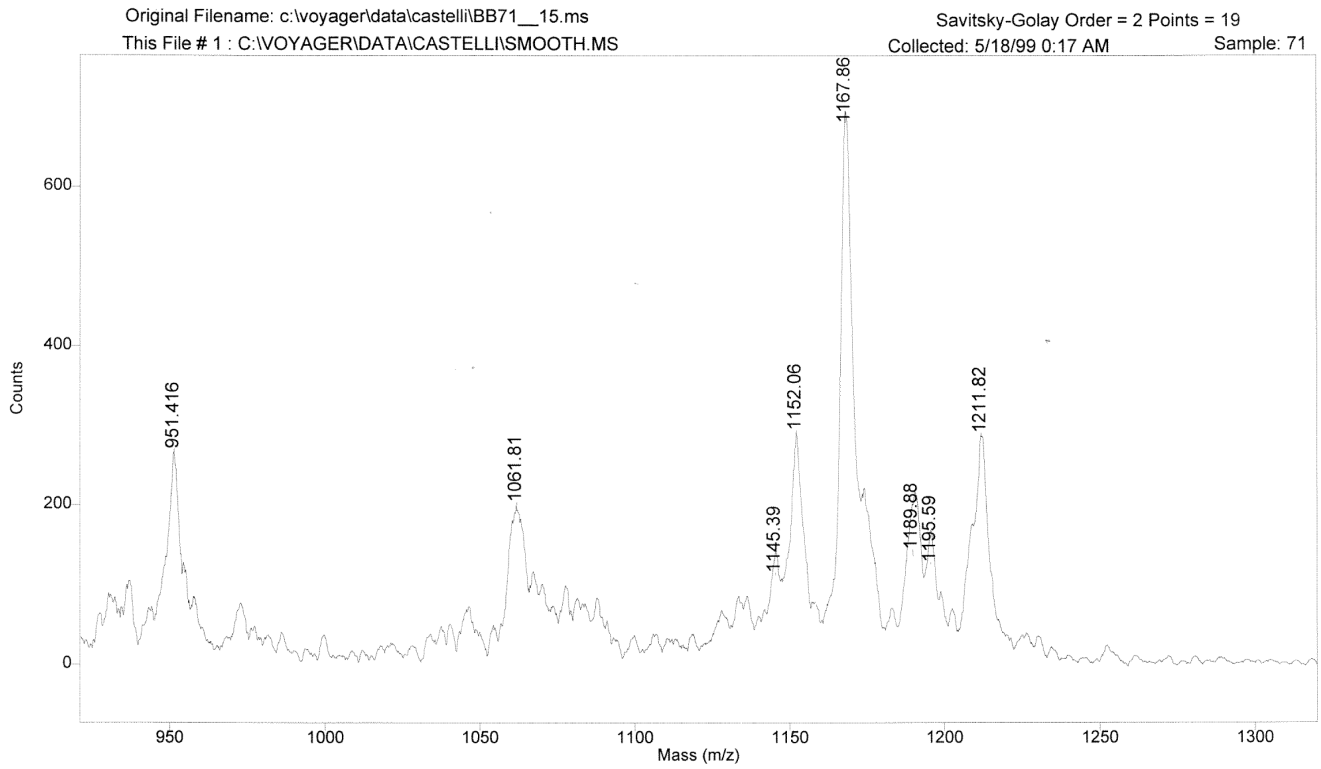
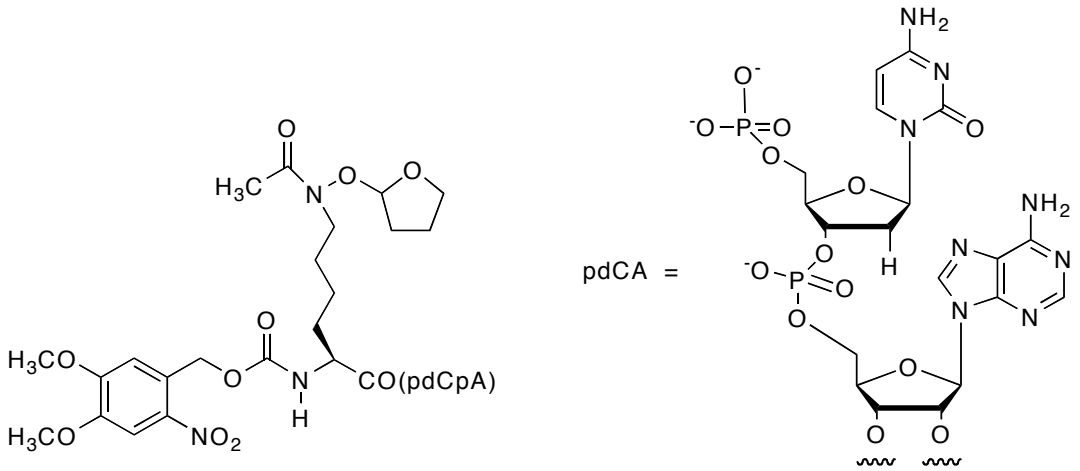


Figure S14. MALDI mass spectrum of **8a**.



8b

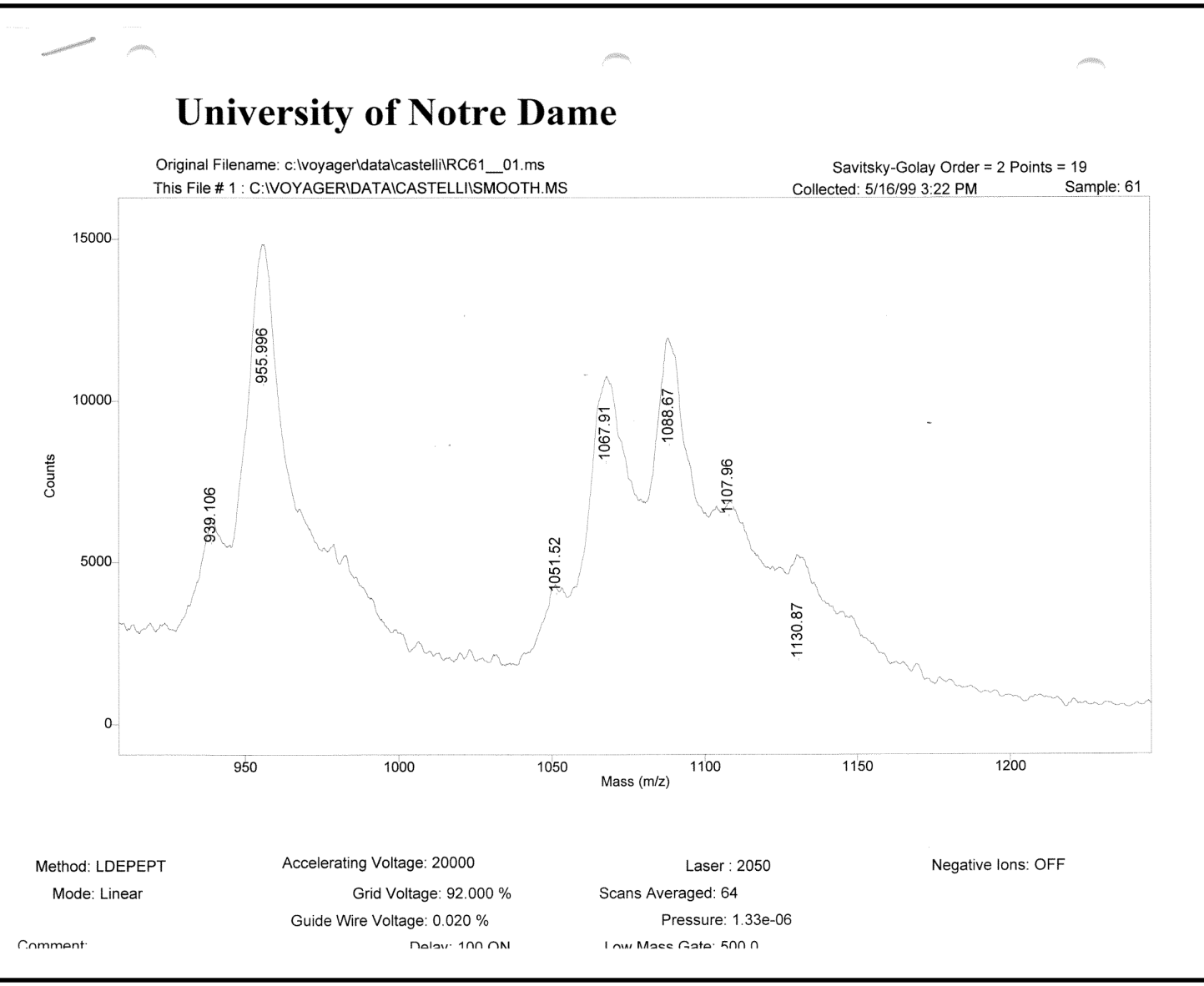
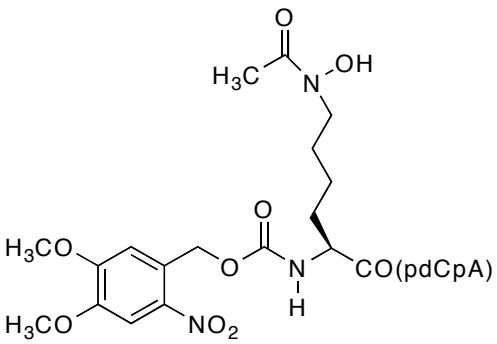


Figure S15 MALDI mass spectrum of **8b**.



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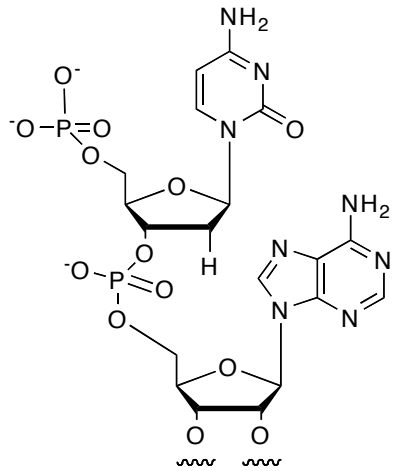

9

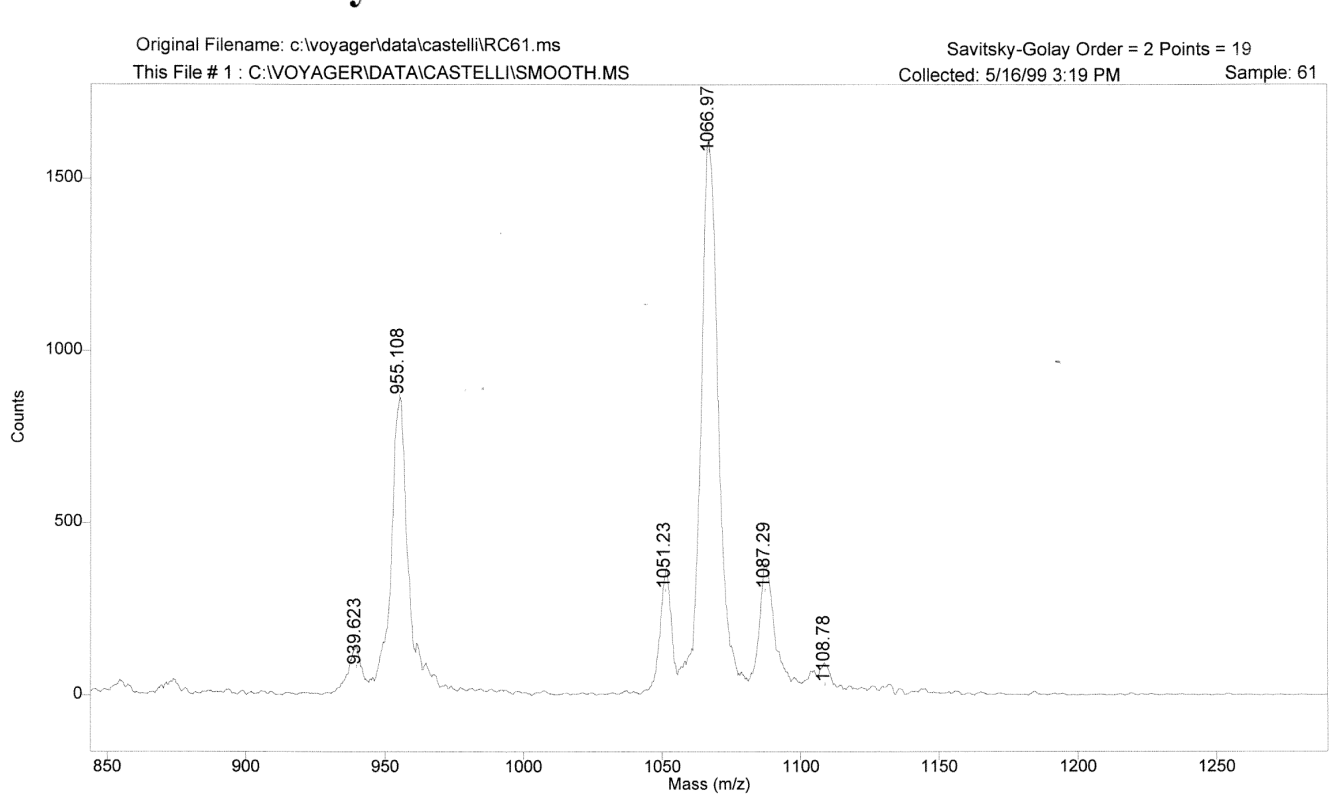

Figure S16 MALDI mass spectrum of **9**.