

**Electronic Supplementary Information (ESI)**

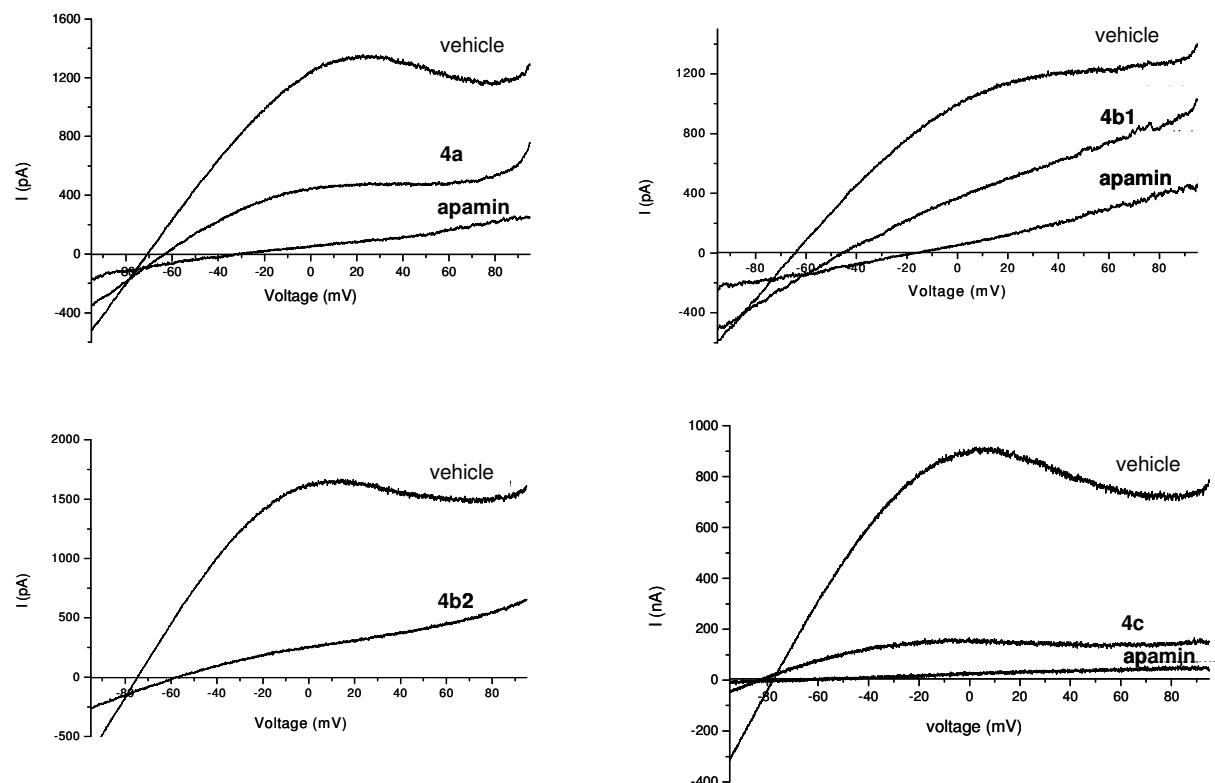
**Glyco-Phospho-Glycero Ether Lipid (GPGEL): synthesis and evaluation as Small Conductance  $\text{Ca}^{2+}$ -Activated  $\text{K}^+$  Channels (SK3) inhibitor.**

**Charlotte M. Sevrain, Jean-Pierre Haelters, Aurélie Chantôme, Hélène Couthon-Gourvès,  
Alban Girault, Christophe Vandier and Paul-Alain Jaffrè**

**Summary**

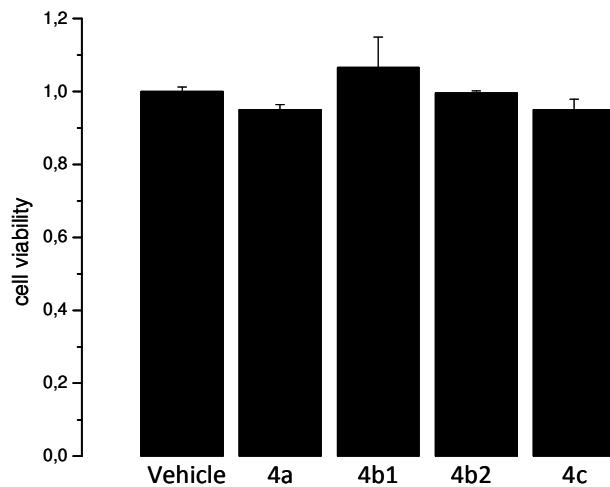
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## ESI-1 Patch-Clamp Data



**Figure S1:** Examples of whole cell K<sup>+</sup> currents recorded in HEK293 T cells expressing recombinant SK3 channels before and after application of 10  $\mu$ M **4a**, **4b1**, **4b2** and **4c** compounds with or without 10 nM apamin (specific pore blocker of SKCa channel) during three minutes. Currents were generated by ramp protocol from +100 mV to -100 mV in 500 ms from a holding potential of 0 mV.

## ESI-2 MTT assays



**Figure S2:** Cell viability of compounds **4** determined with the tetrazolium salt reduction method (MTT). HEK293T cells expressing recombinant SK3 channel were either treated with vehicle (0.6% ethanol/0.4% DMSO) or 10 µM GPGEL for 48h. Results from 3 independents experiments performed in triplicate are expressed as mean ± S.E.M.

## ESI-3 NMR Data

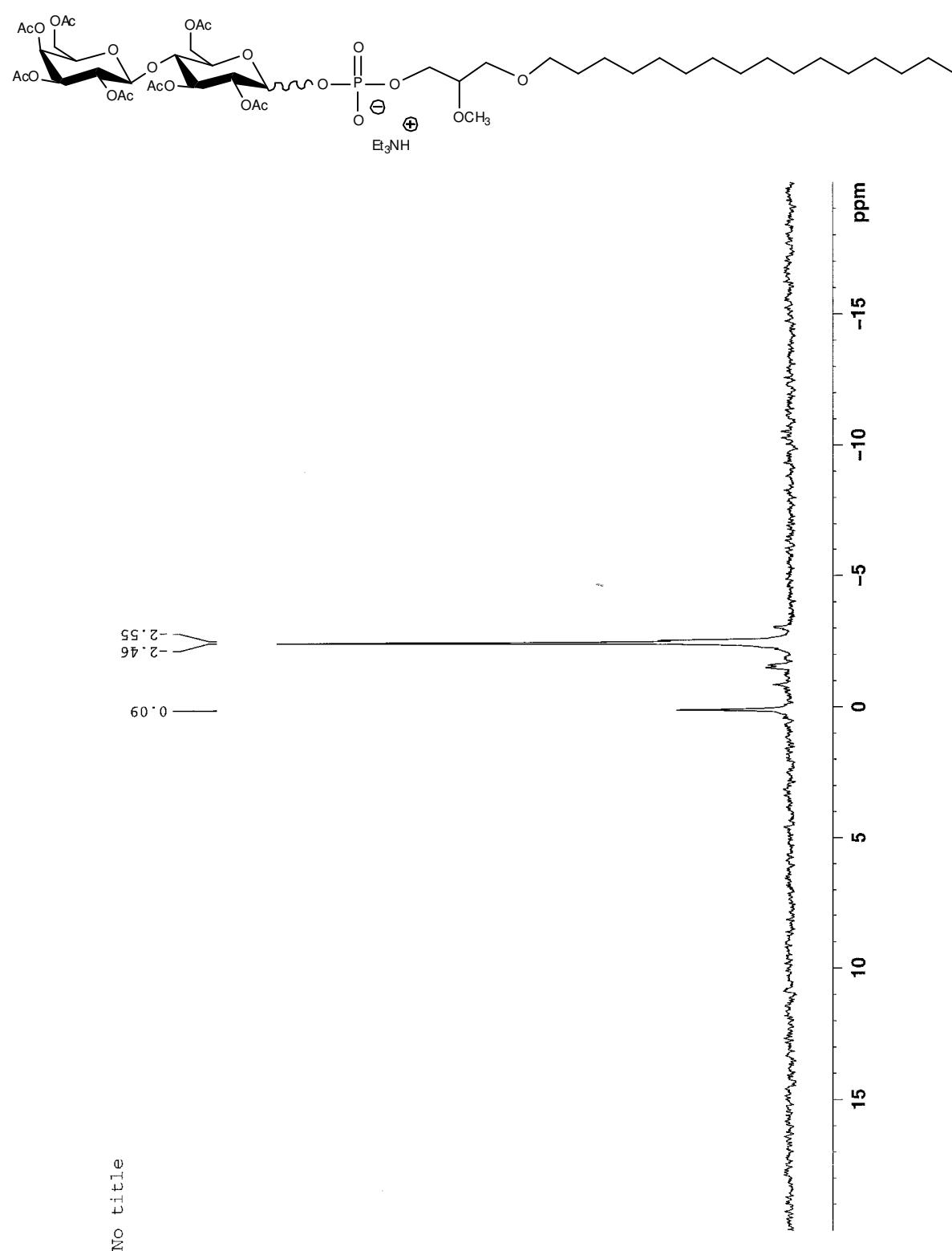
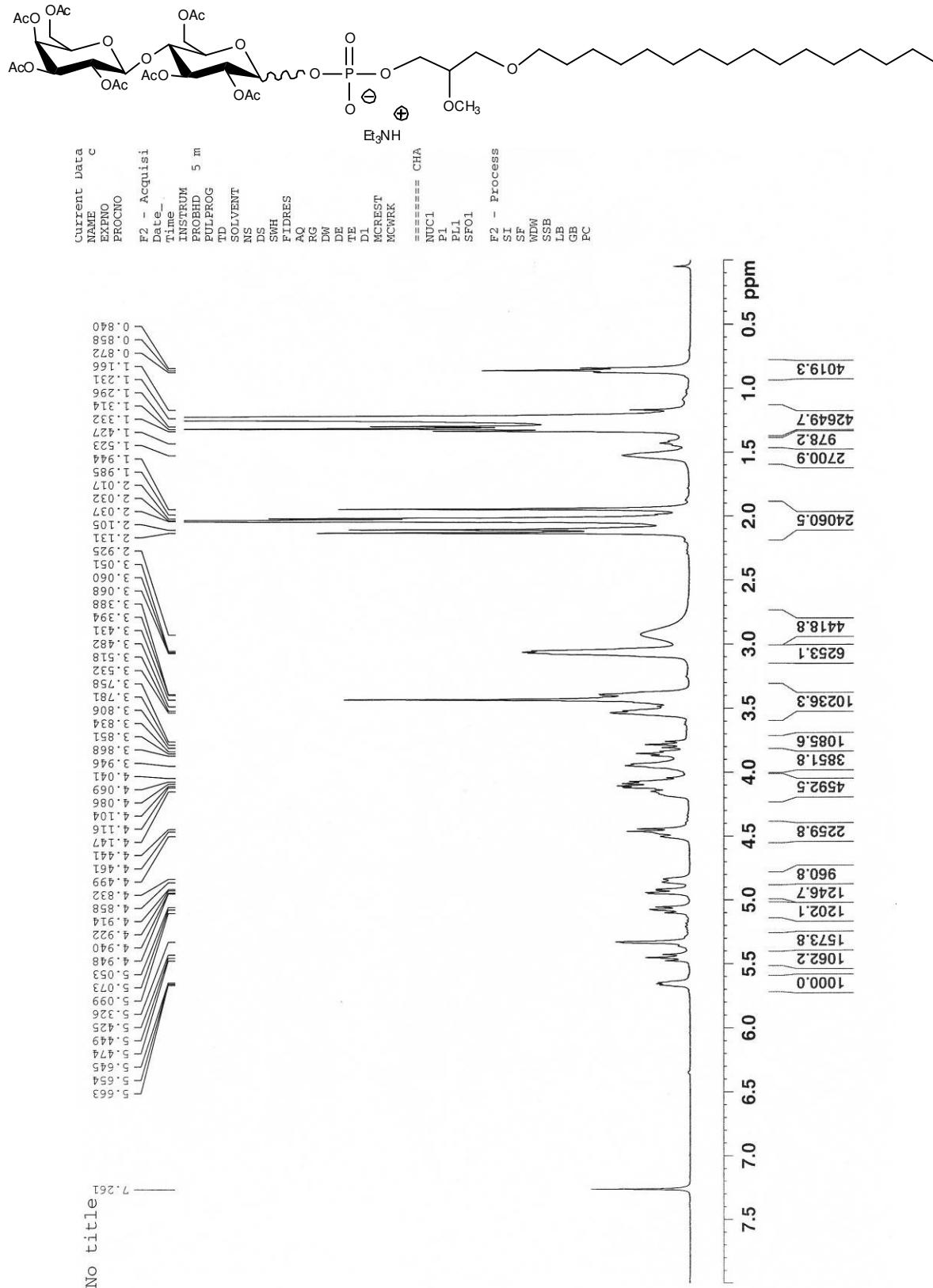
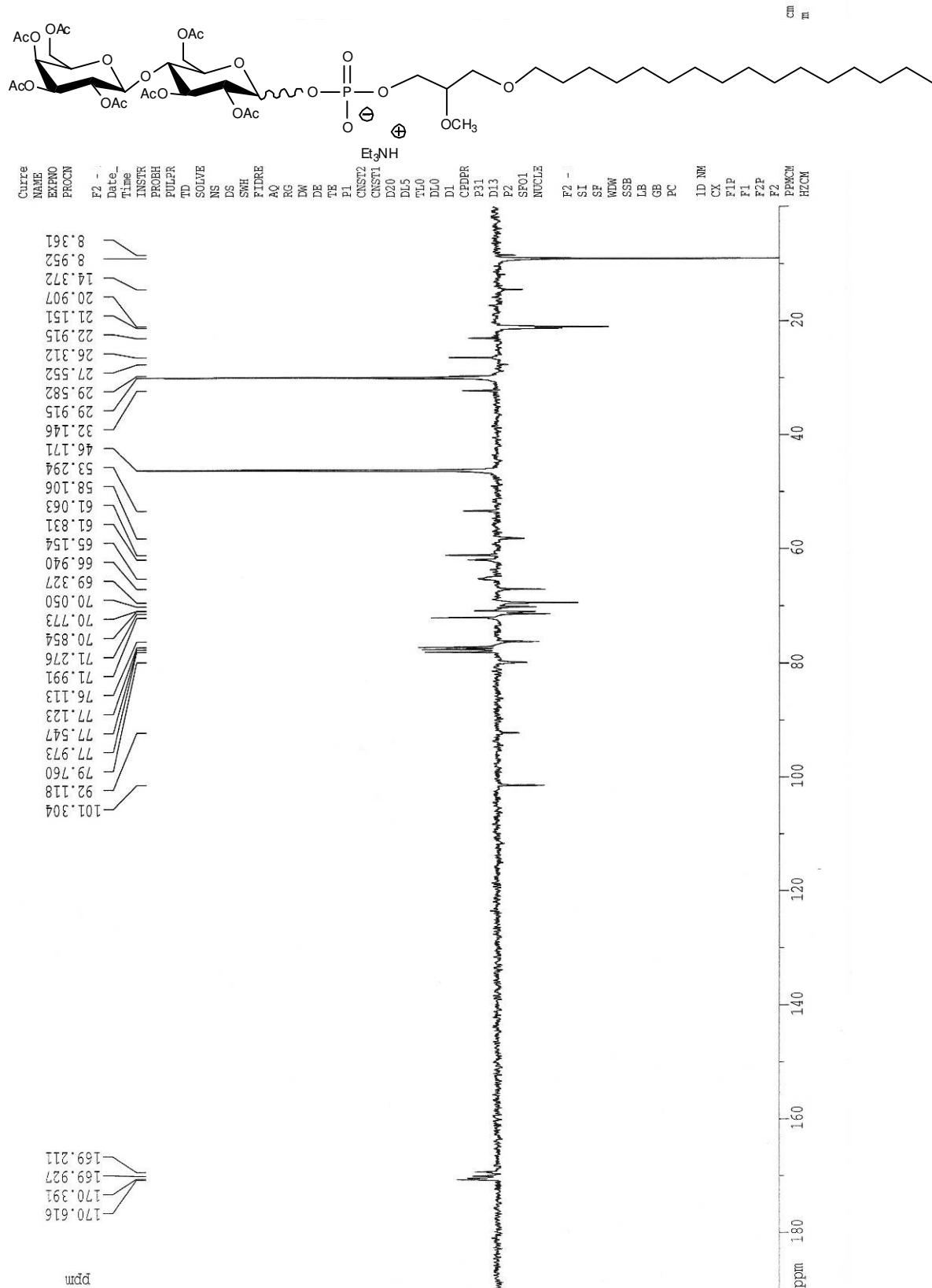


Figure S3-1:  $^{31}\text{P}$  NMR ( $\text{CDCl}_3$ ) spectrum of compound 3a.



**Figure S3-2:**  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ) spectrum of compound 3a.



**Figure S3-3:**  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ) spectrum of compound 3a.

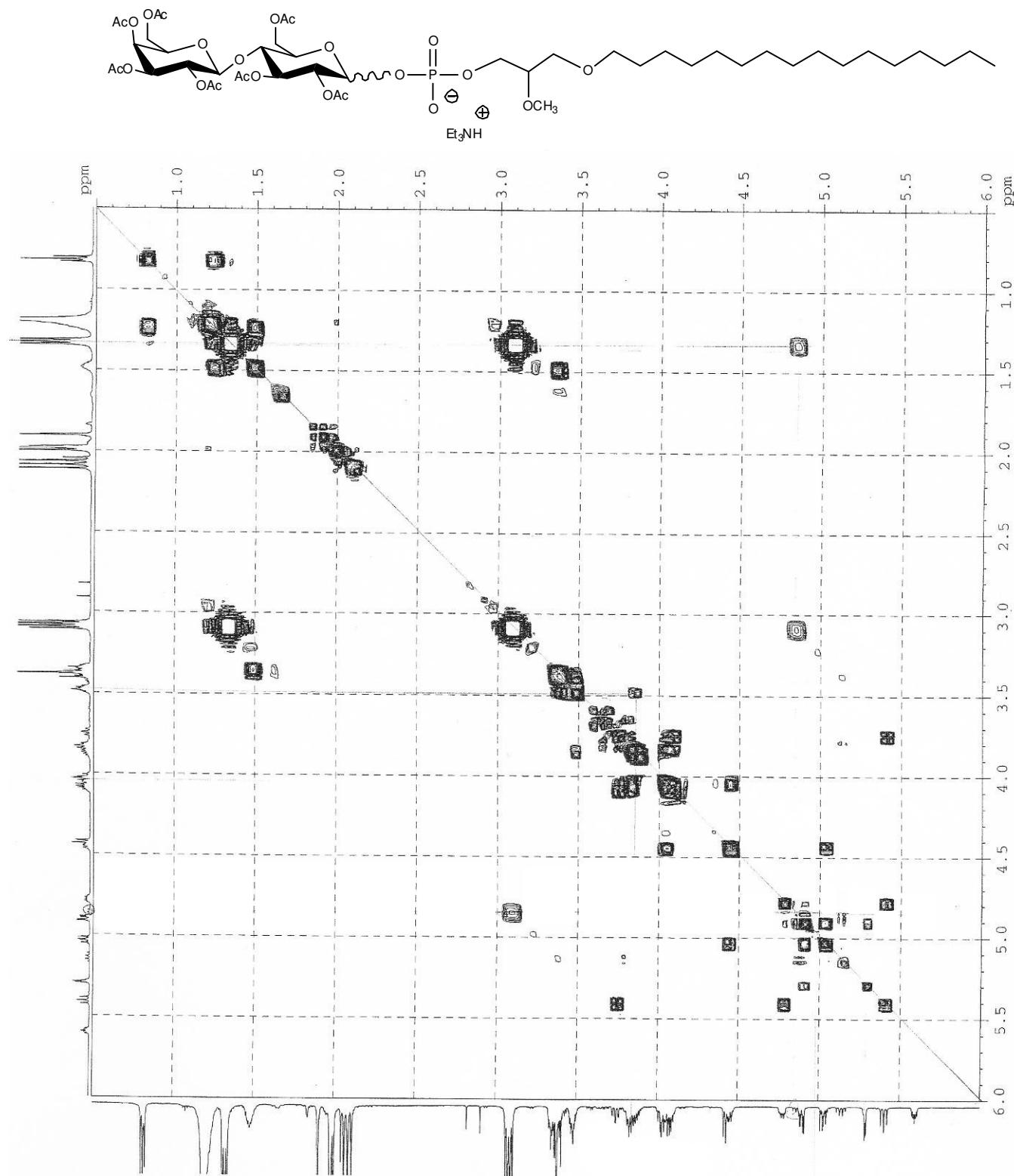


Figure S3-4: 2D NMR - COSY ( $\text{CDCl}_3$ ) spectrum of compound 3a.

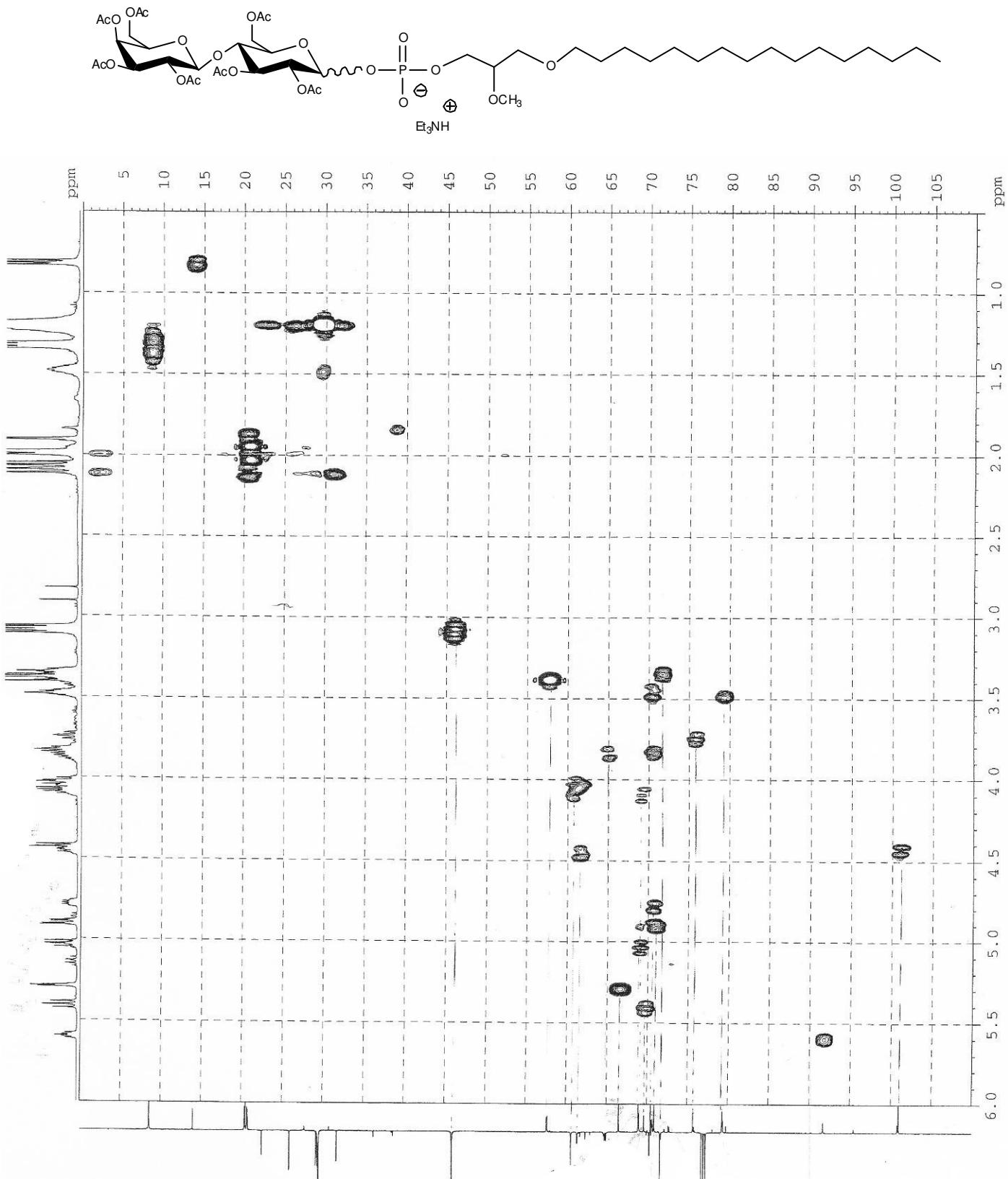


Figure S3-5: 2D NMR - HMQC ( $\text{CDCl}_3$ ) spectrum of compound 3a.

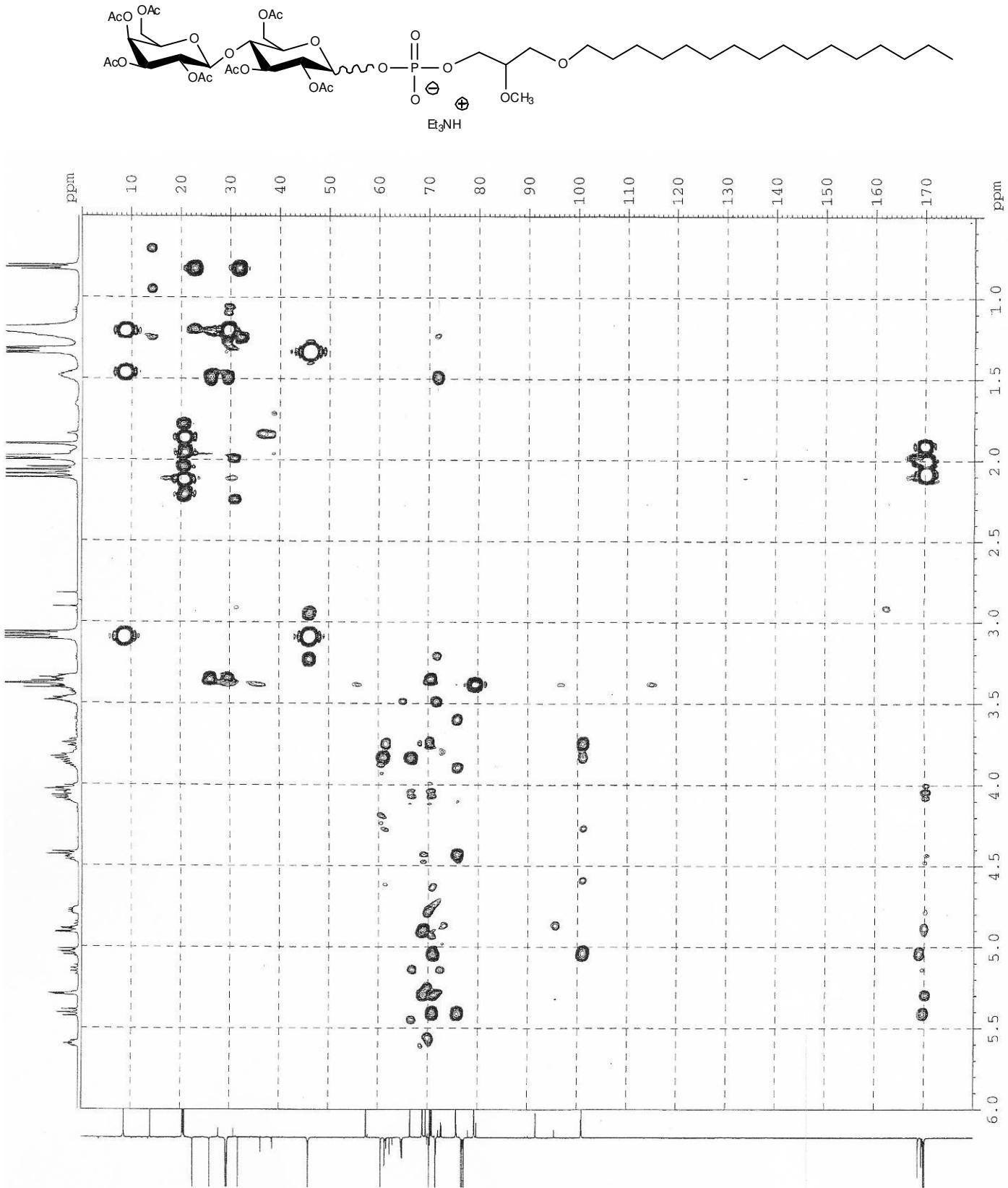


Figure S3-6: 2D NMR - HMBC ( $\text{CDCl}_3$ ) spectrum of compound 3a.

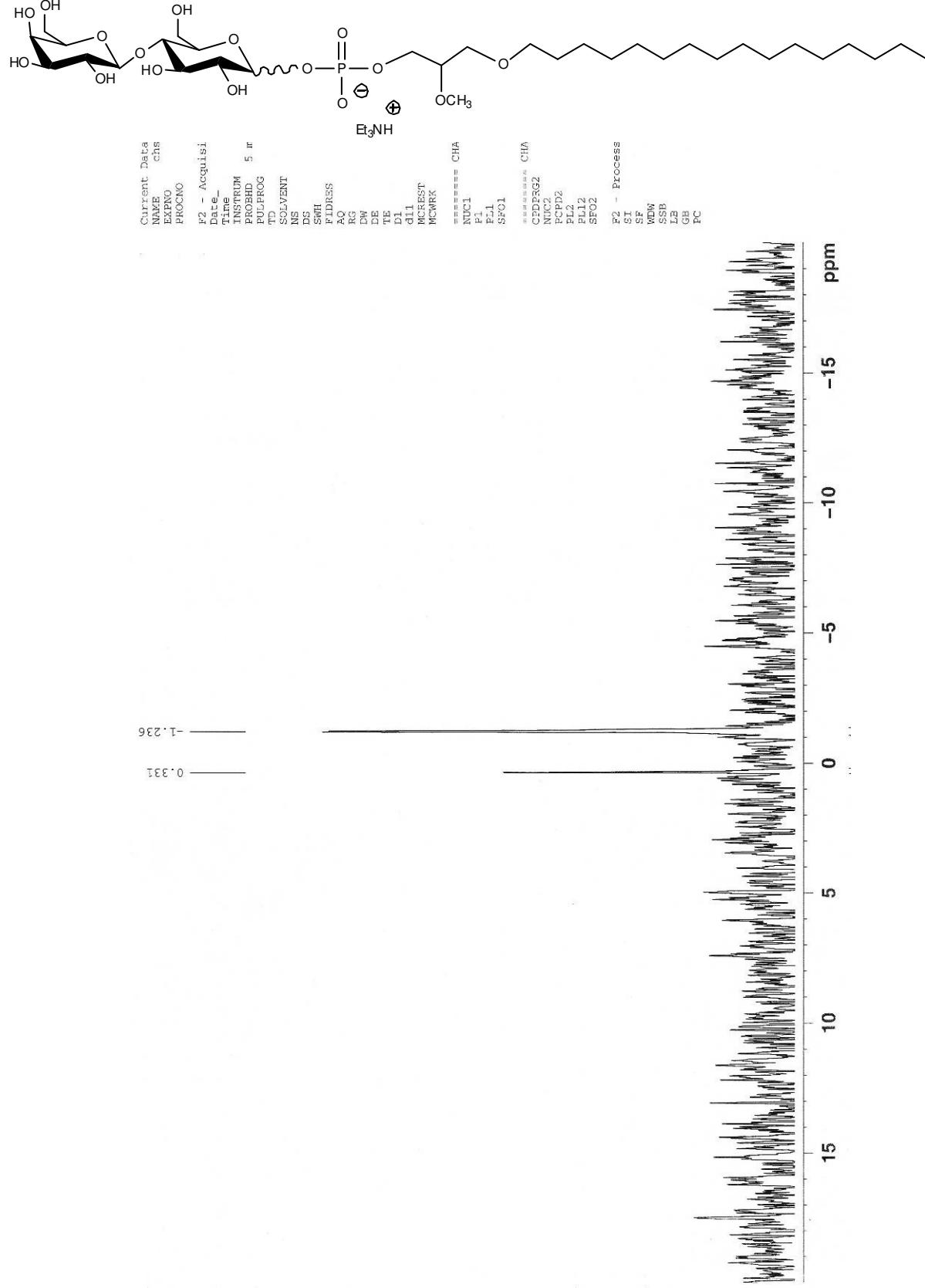
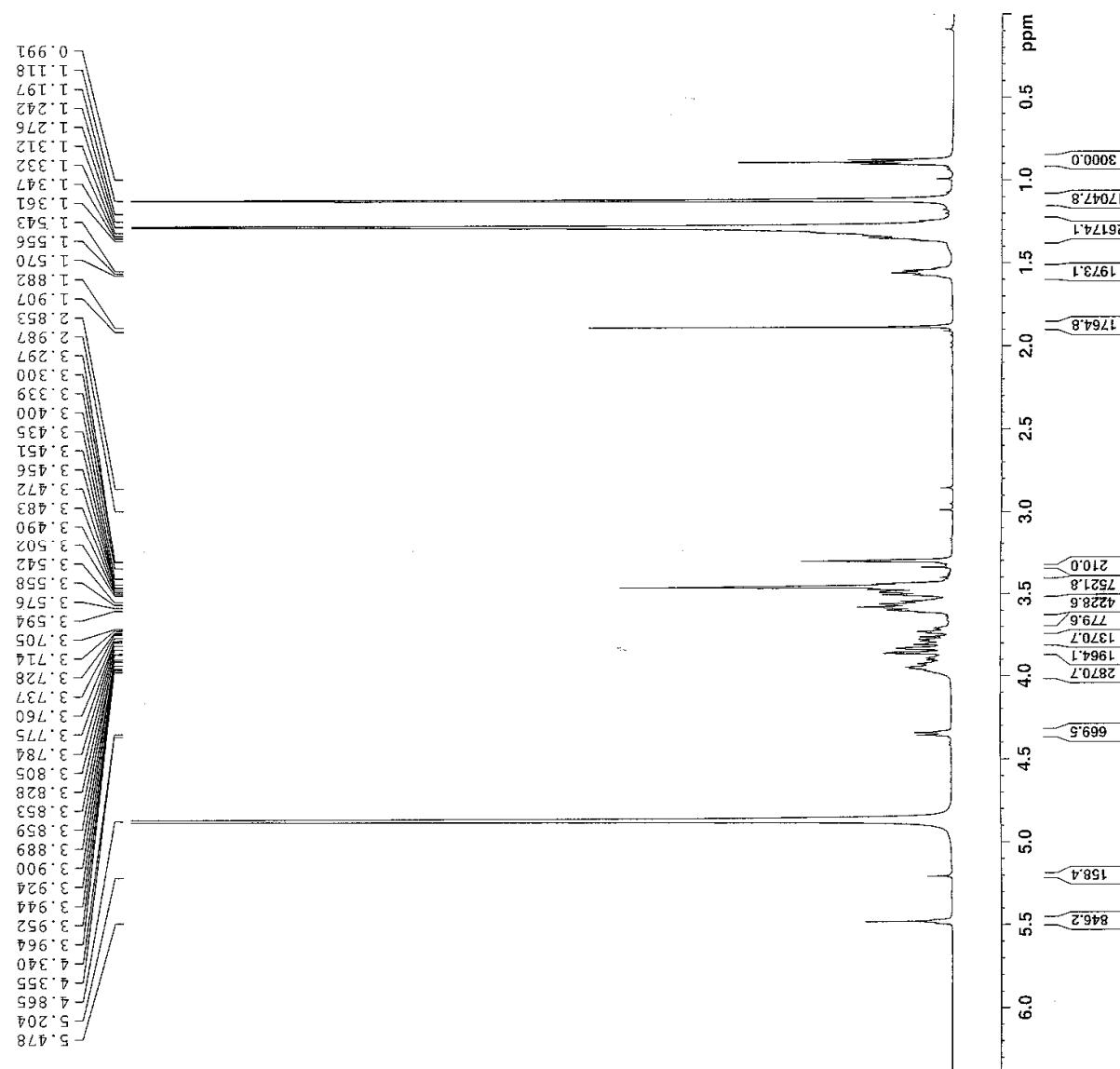
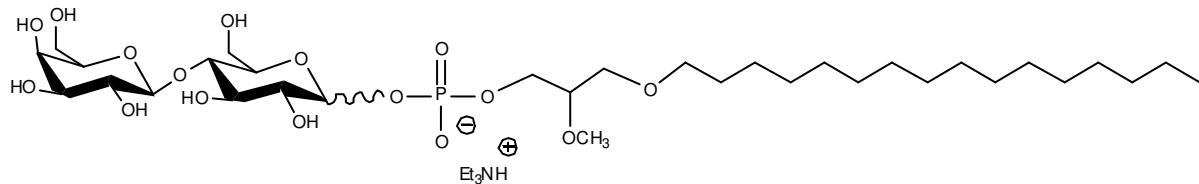
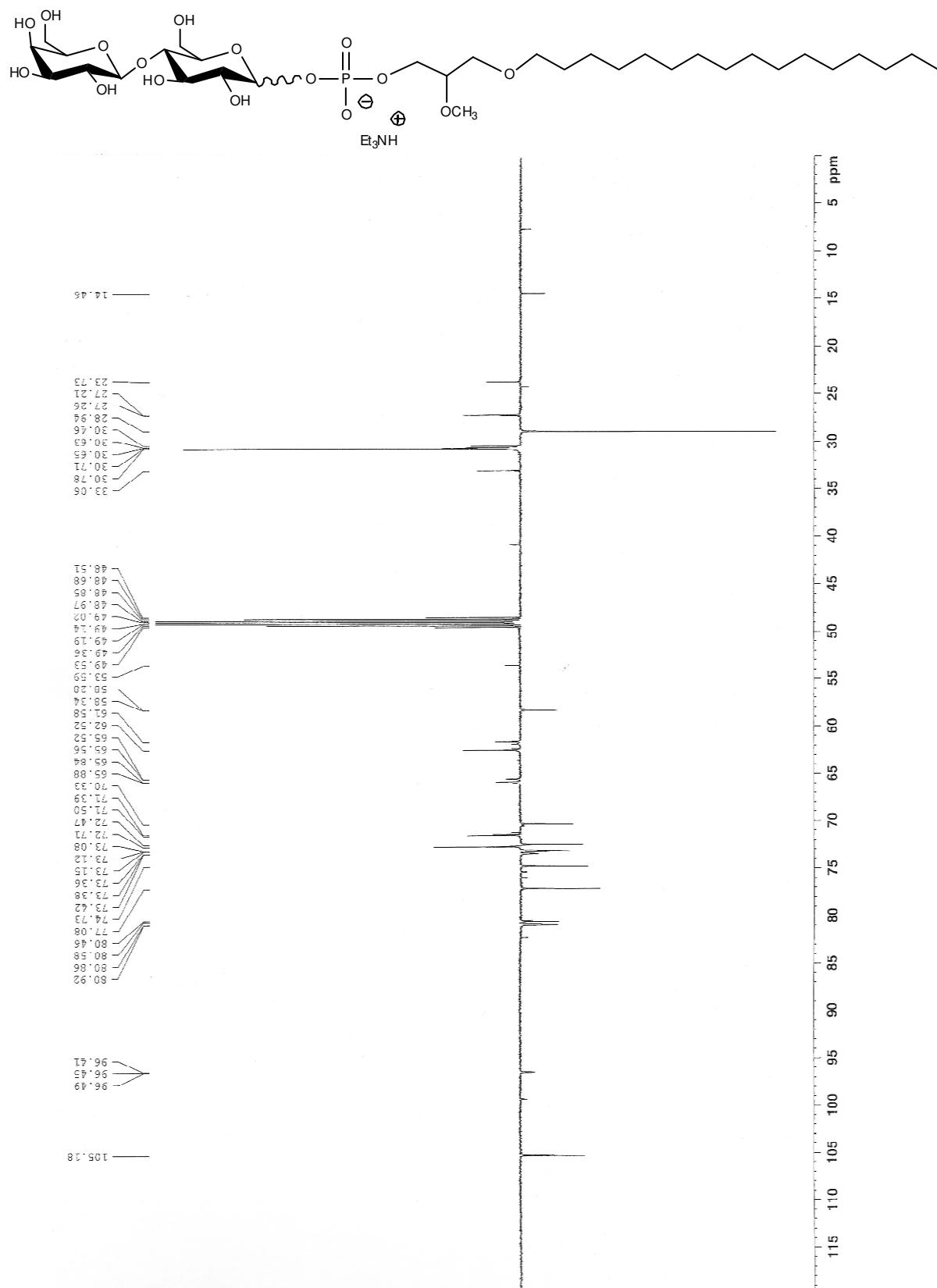


Figure S3-7:  $^{31}\text{P}$  NMR ( $\text{CD}_3\text{OD}$ ) spectrum of compound 4a.



**Figure S3-8:**  $^1\text{H}$  NMR ( $\text{CD}_3\text{OD}$ ) spectrum of compound 4a.



**Figure S3-9:**  $^{13}\text{C}$  NMR ( $\text{CD}_3\text{OD}$ ) spectrum of compound 4a.

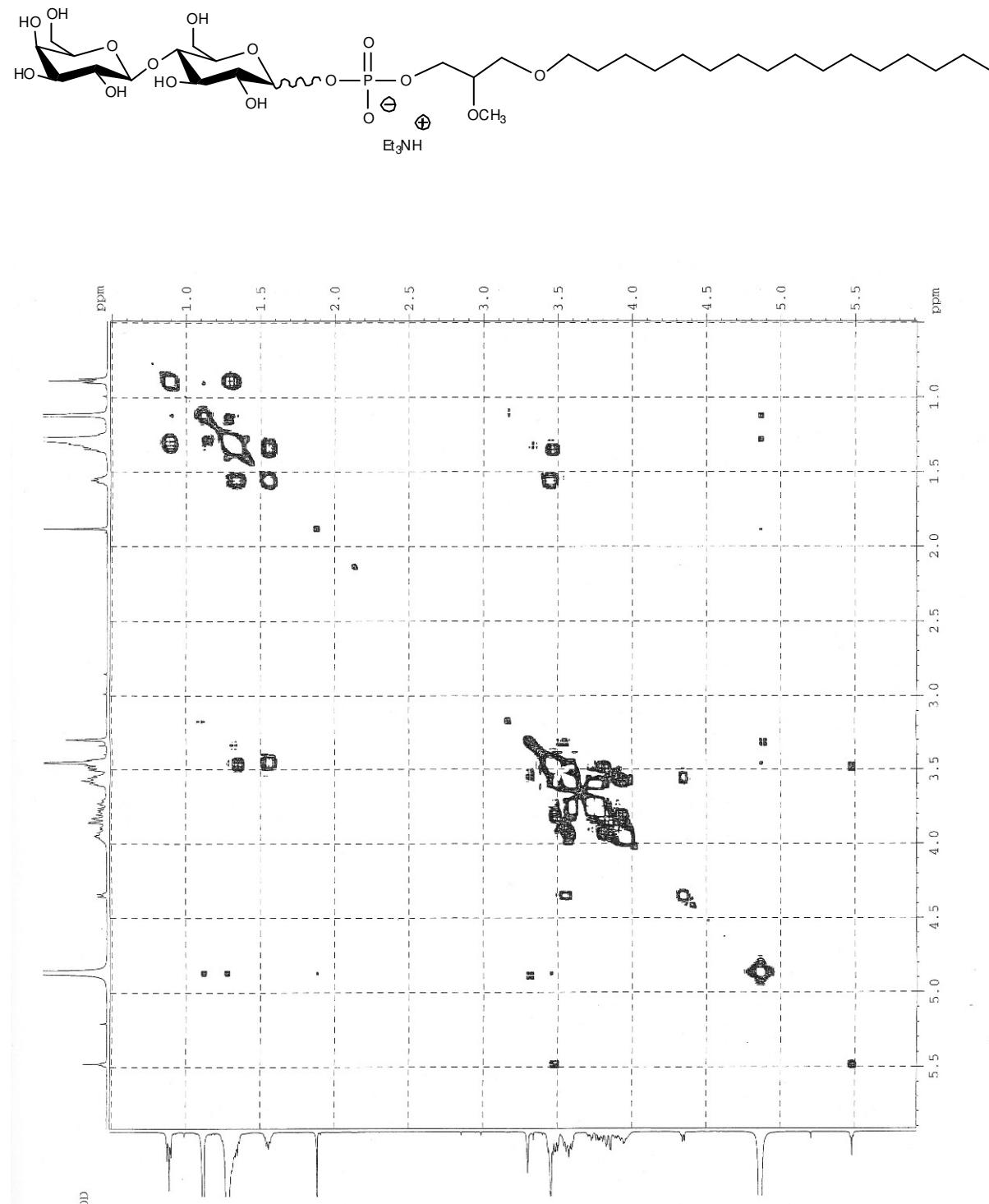


Figure S3-10: 2D NMR - COSY ( $\text{CD}_3\text{OD}$ ) spectrum of compound 4a.

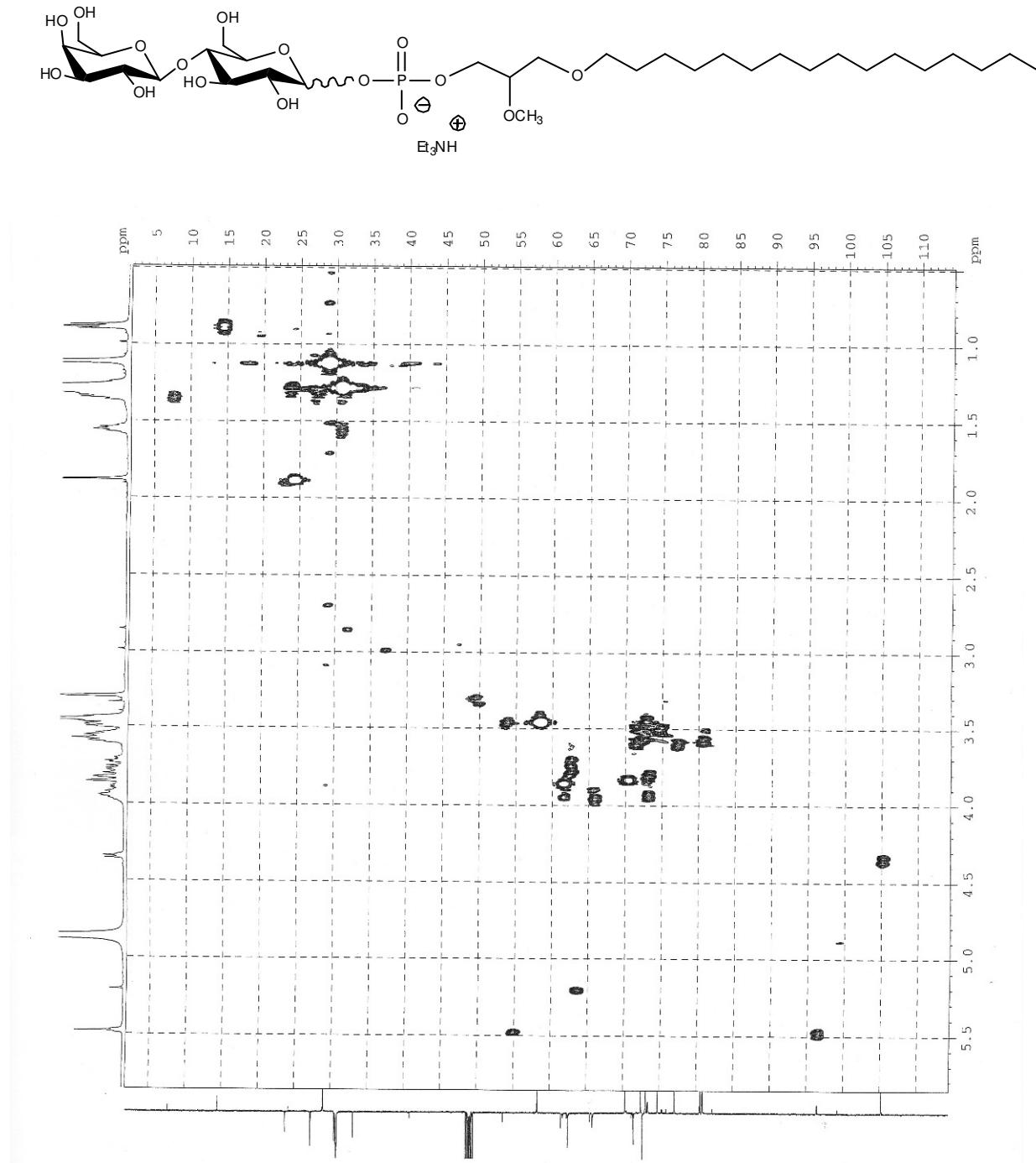


Figure S3-11: 2D NMR - HMQC ( $\text{CD}_3\text{OD}$ ) spectrum of compound 4a.

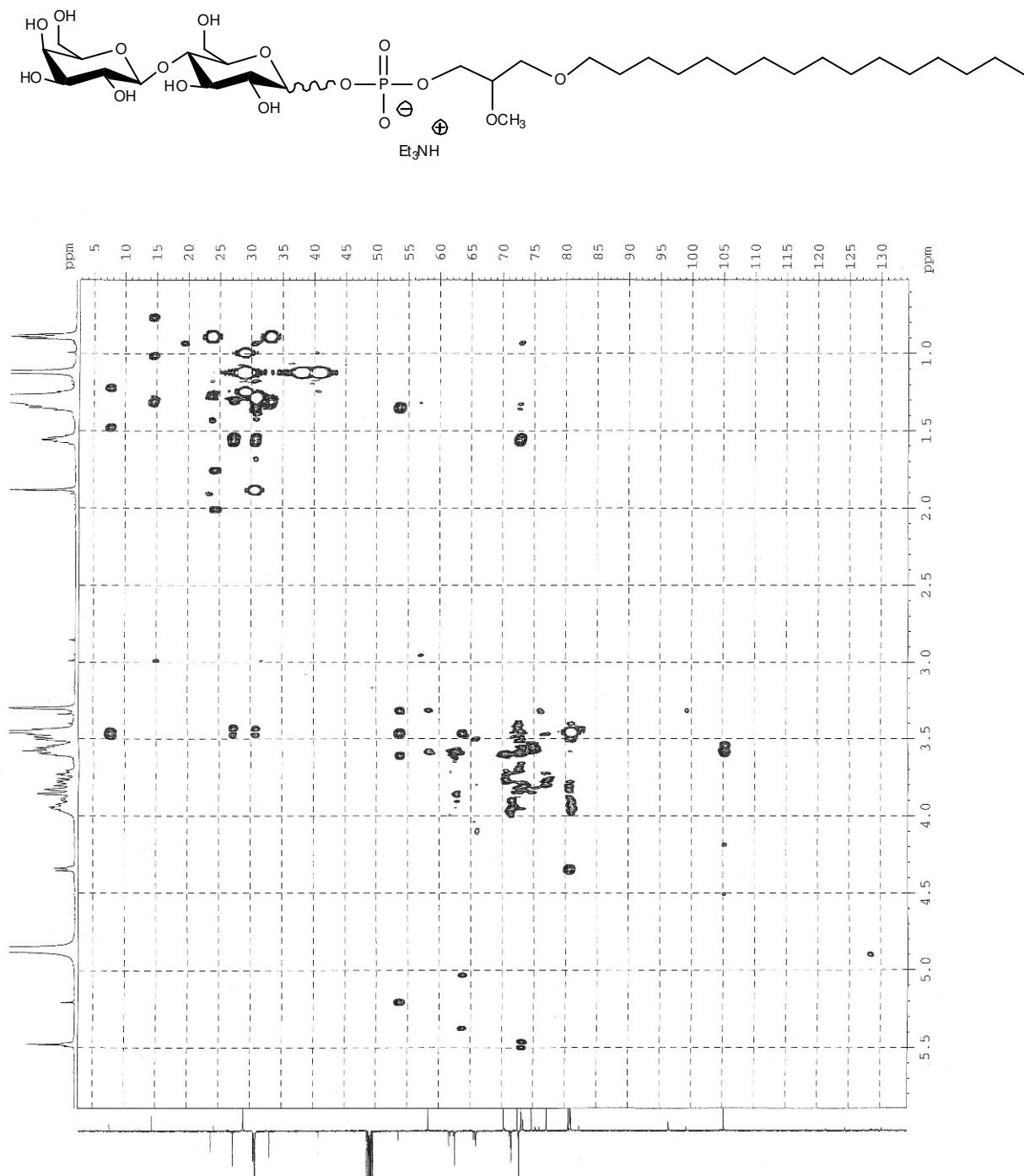
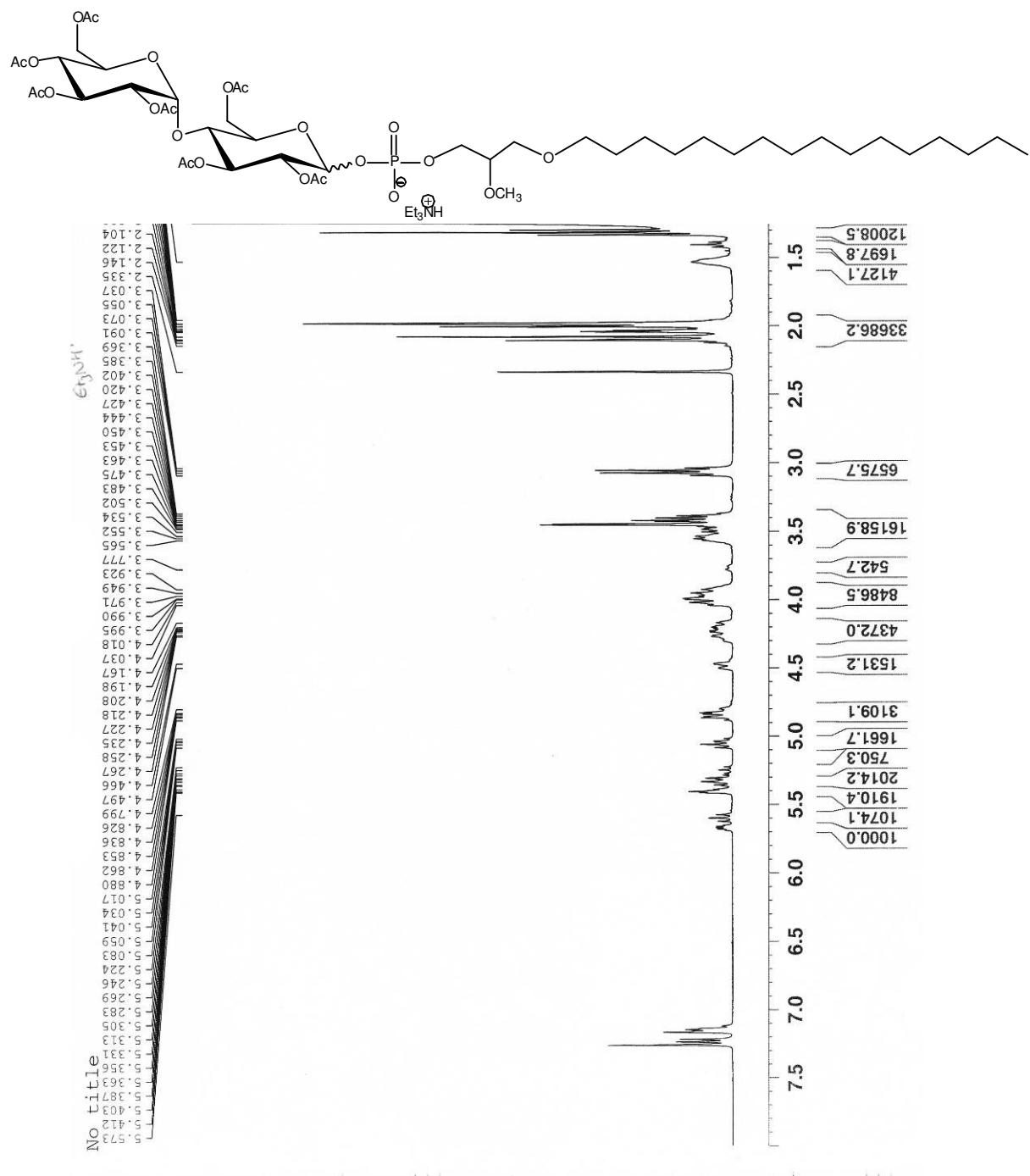


Figure S3-12: 2D NMR - HMBC ( $\text{CD}_3\text{OD}$ ) spectrum of compound 4a.



Figure S3-13:  $^{31}\text{P}$  NMR ( $\text{CDCl}_3$ ) spectrum of compound 3b1.



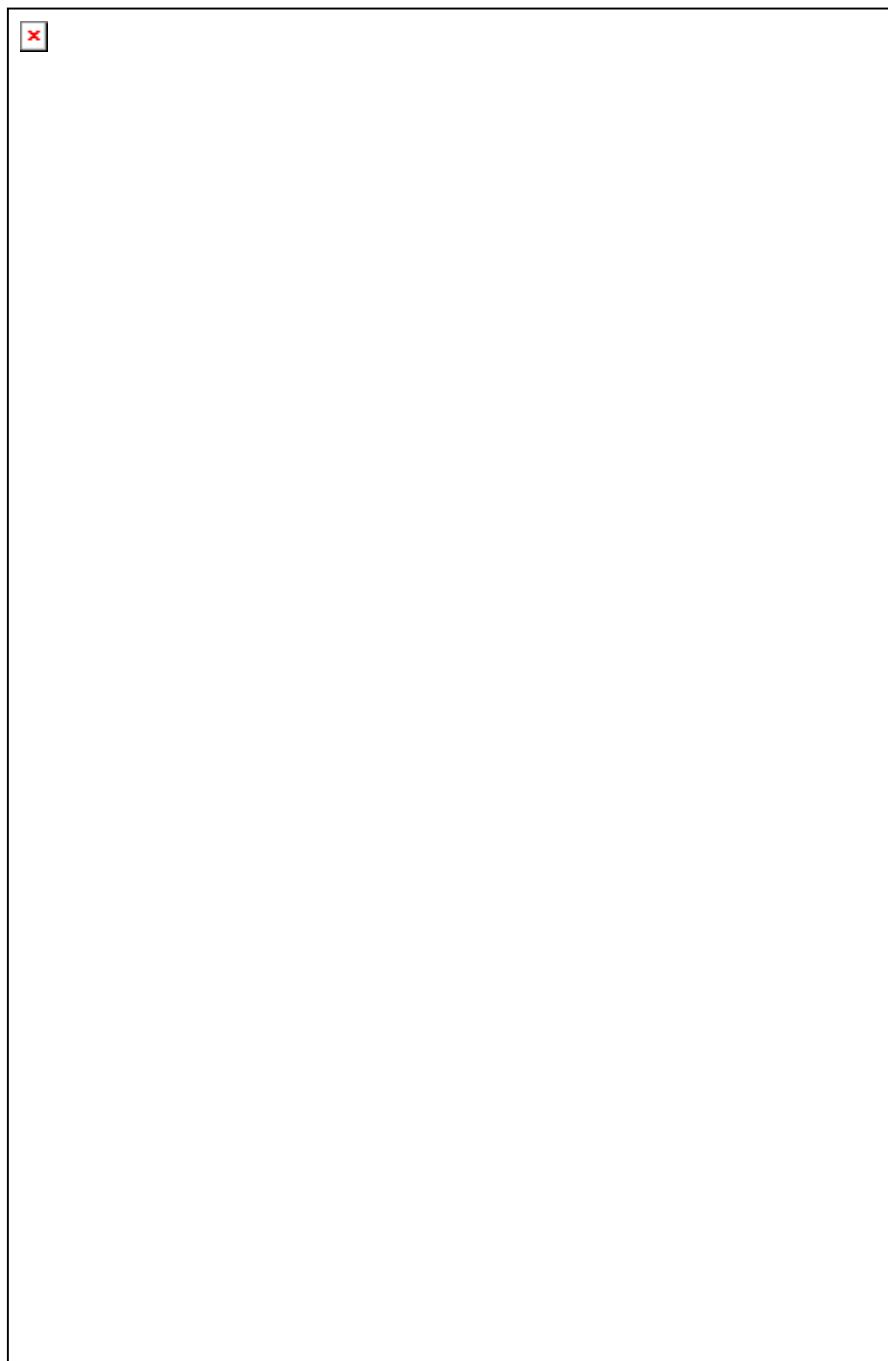
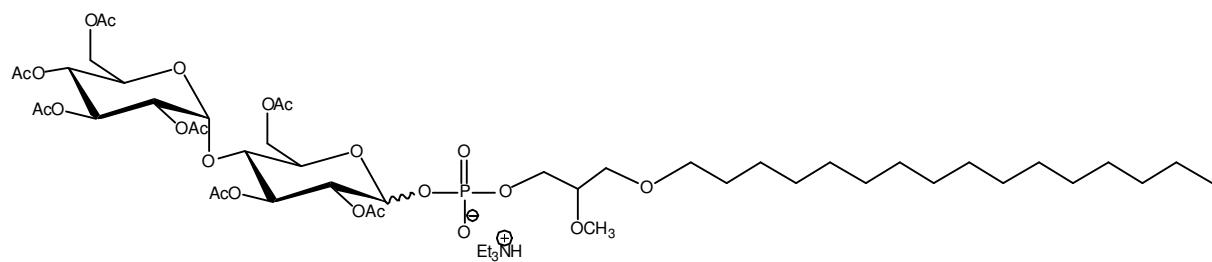


Figure S3-15:  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ) spectrum of compound 3b1.

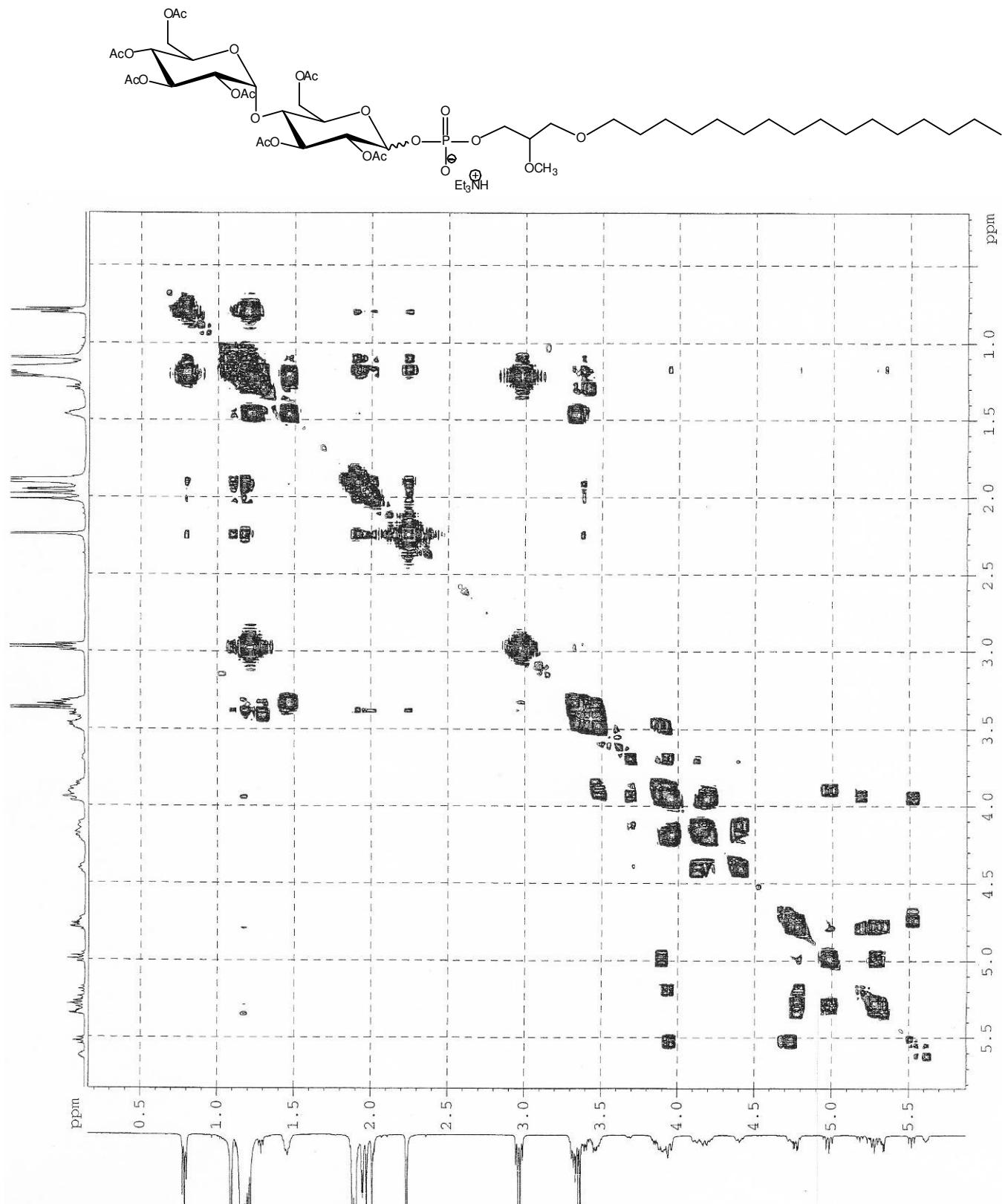


Figure S3-16: 2D NMR - COSY ( $\text{CDCl}_3$ ) spectrum of compound 3b1.

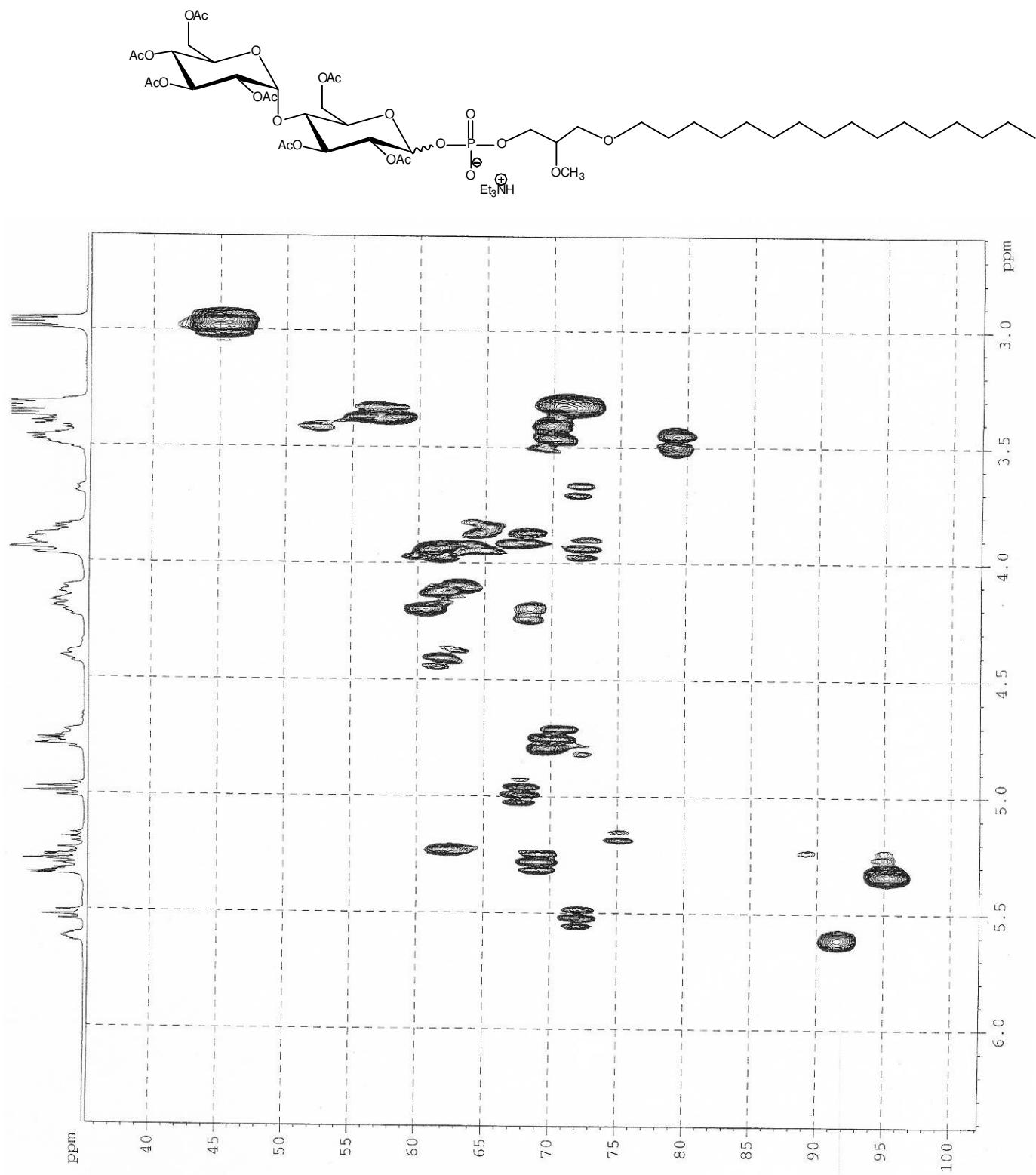


Figure S3-17: 2D NMR - HMQC ( $\text{CDCl}_3$ ) spectrum of compound 3b1.

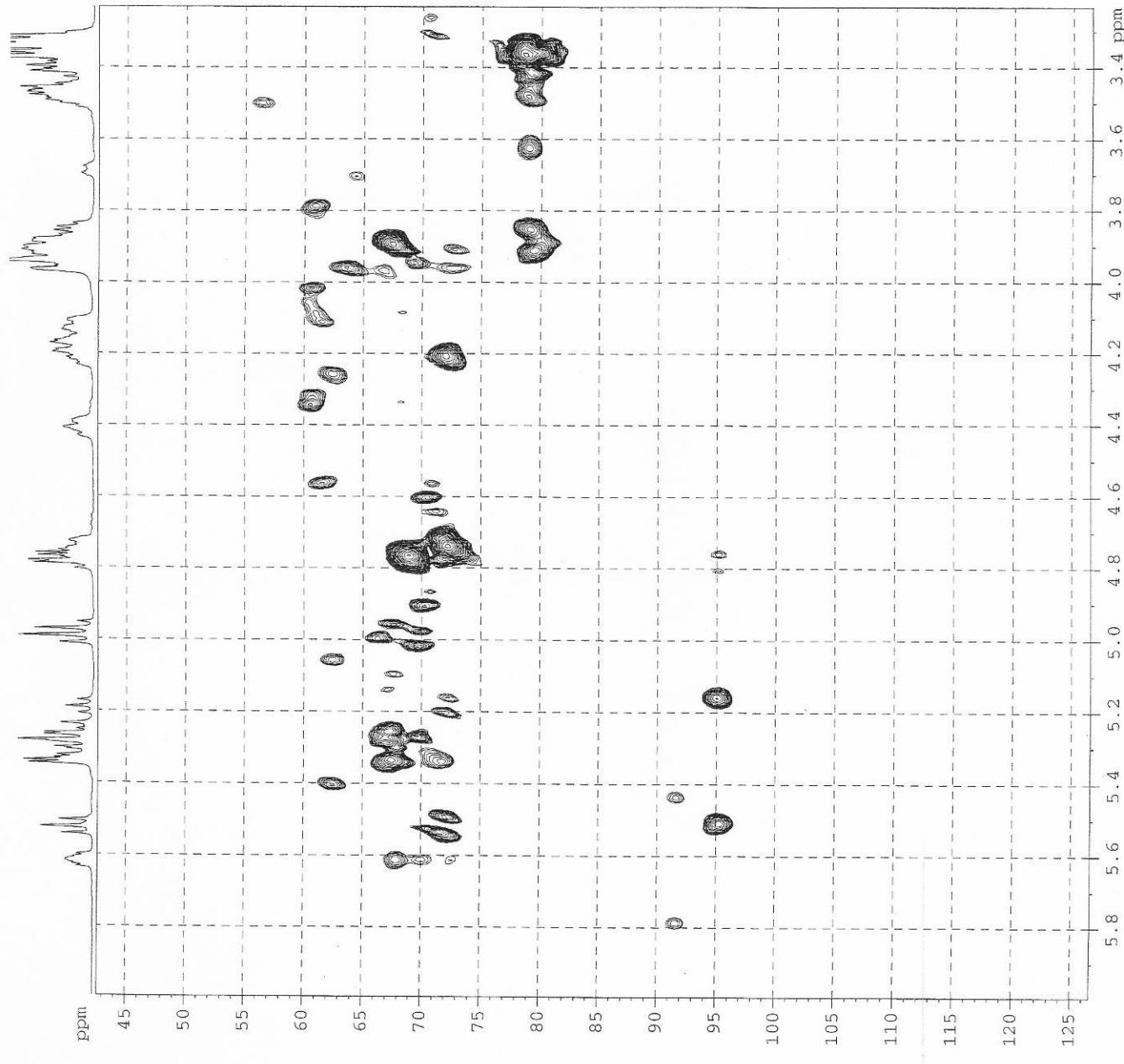
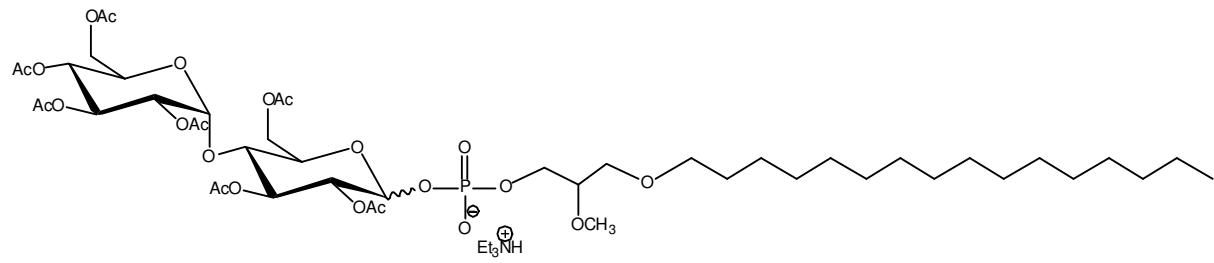


Figure S3-18: 2D NMR - HMBC ( $\text{CDCl}_3$ ) spectrum of compound 3b1.

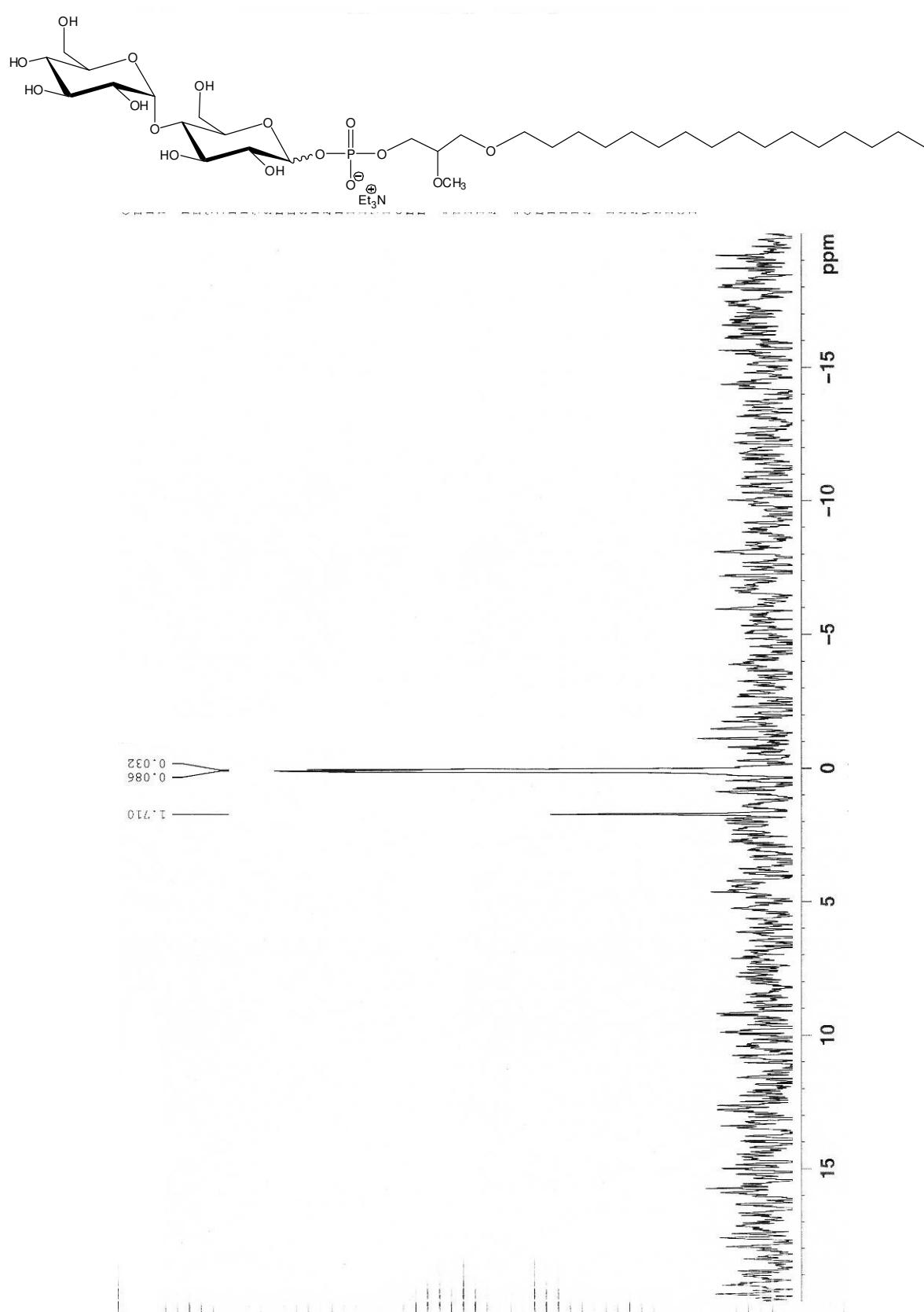
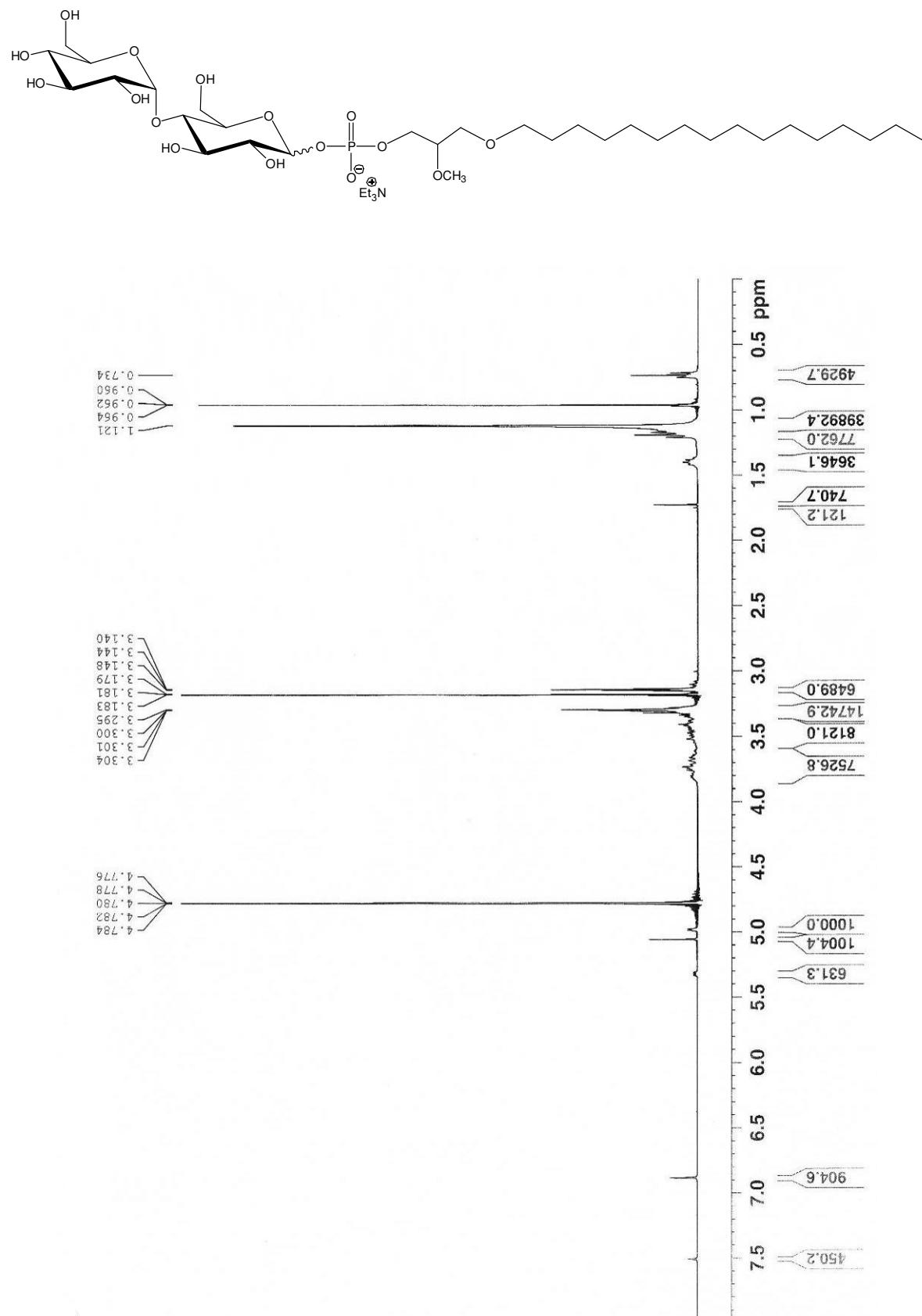


Figure S3-19:  $^{31}\text{P}$  NMR ( $\text{CD}_3\text{OD}$ ) spectrum of compound 4b1.



**Figure S3-20:**  $^1\text{H}$  NMR ( $\text{CD}_3\text{OD}$ ) spectrum of compound 4b1.

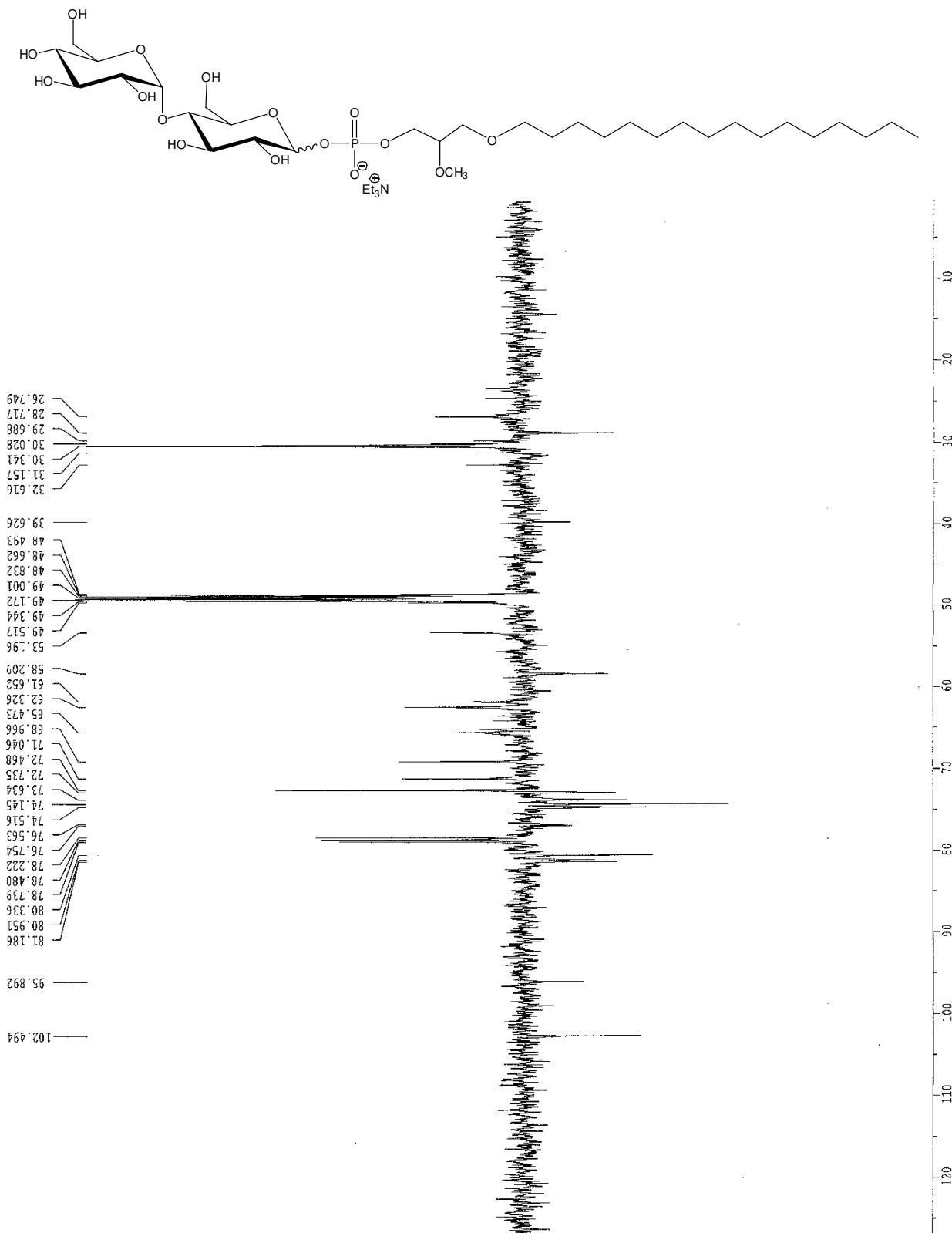
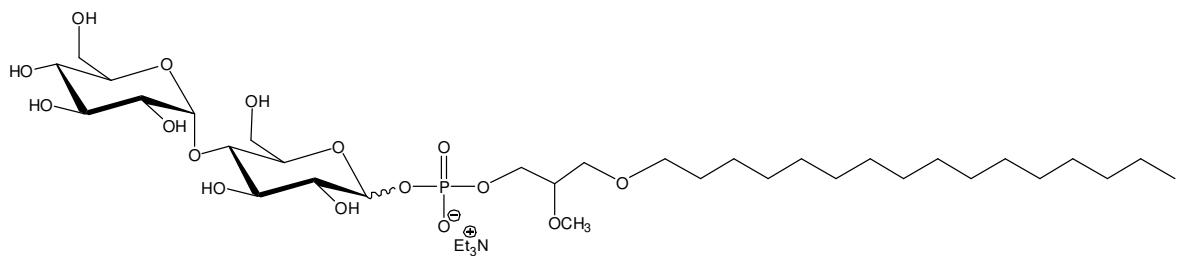


Figure S3-21:  $^{13}\text{C}$  NMR ( $\text{CD}_3\text{OD}$ ) spectrum of compound 4b1.



**Figure S3-22: 2D NMR - COSY( $\text{CD}_3\text{OD}$ ) spectrum of compound 4b1.**

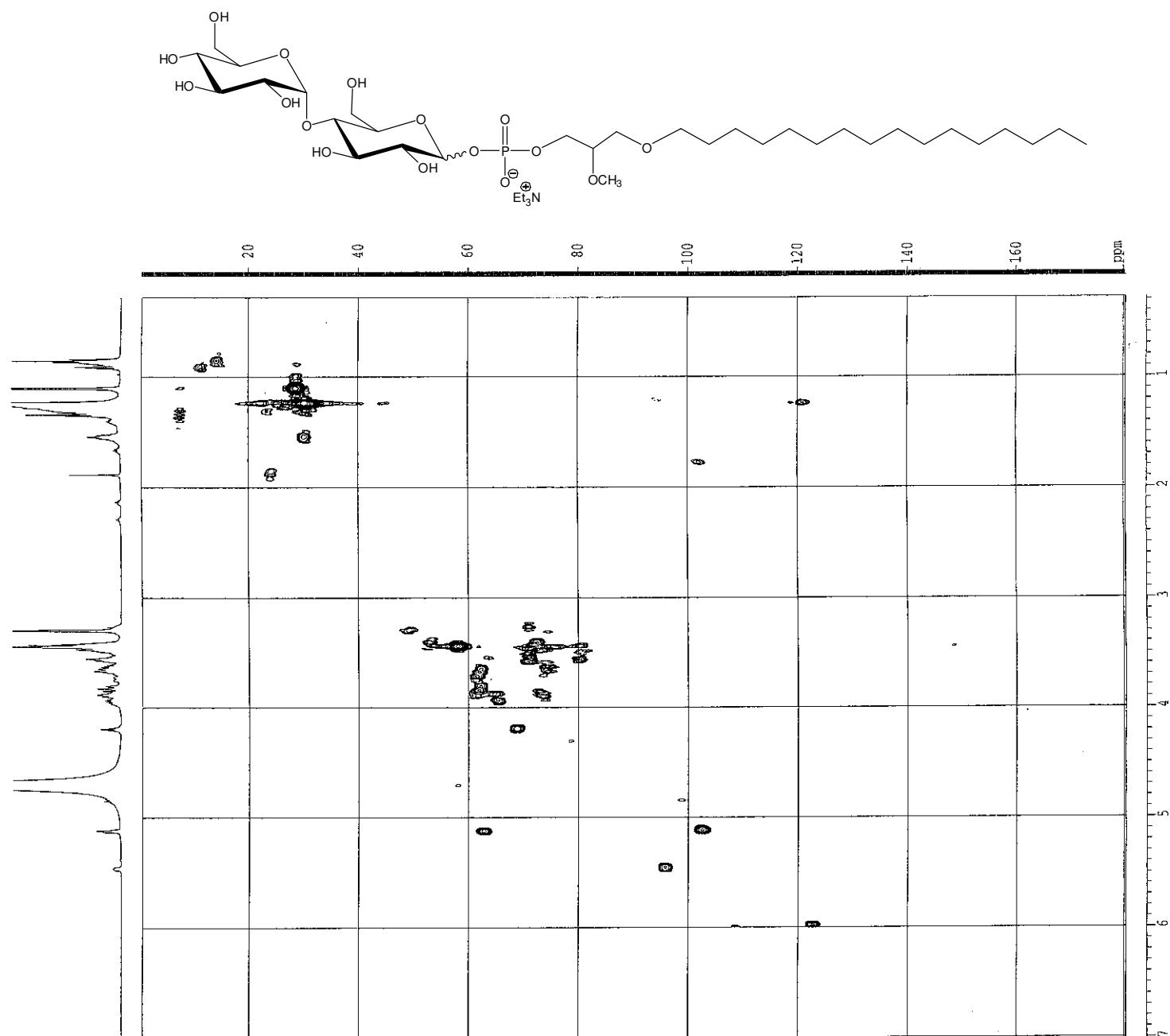


Figure S3-23: 2D NMR - HMQC( $\text{CD}_3\text{OD}$ ) spectrum of compound 4b1.

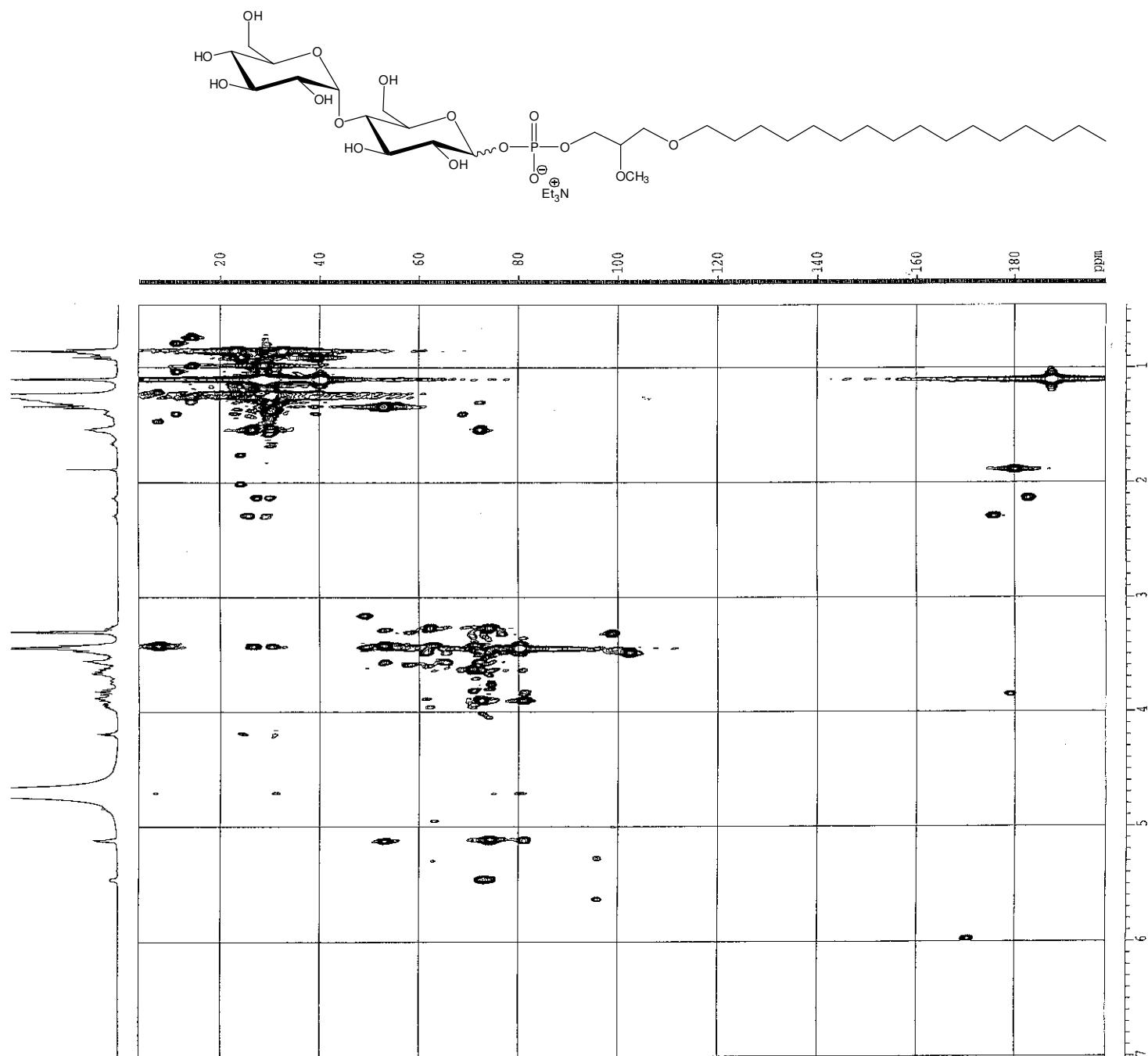


Figure S3-24: 2D NMR - HMBC( $\text{CD}_3\text{OD}$ ) spectrum of compound 4b1.

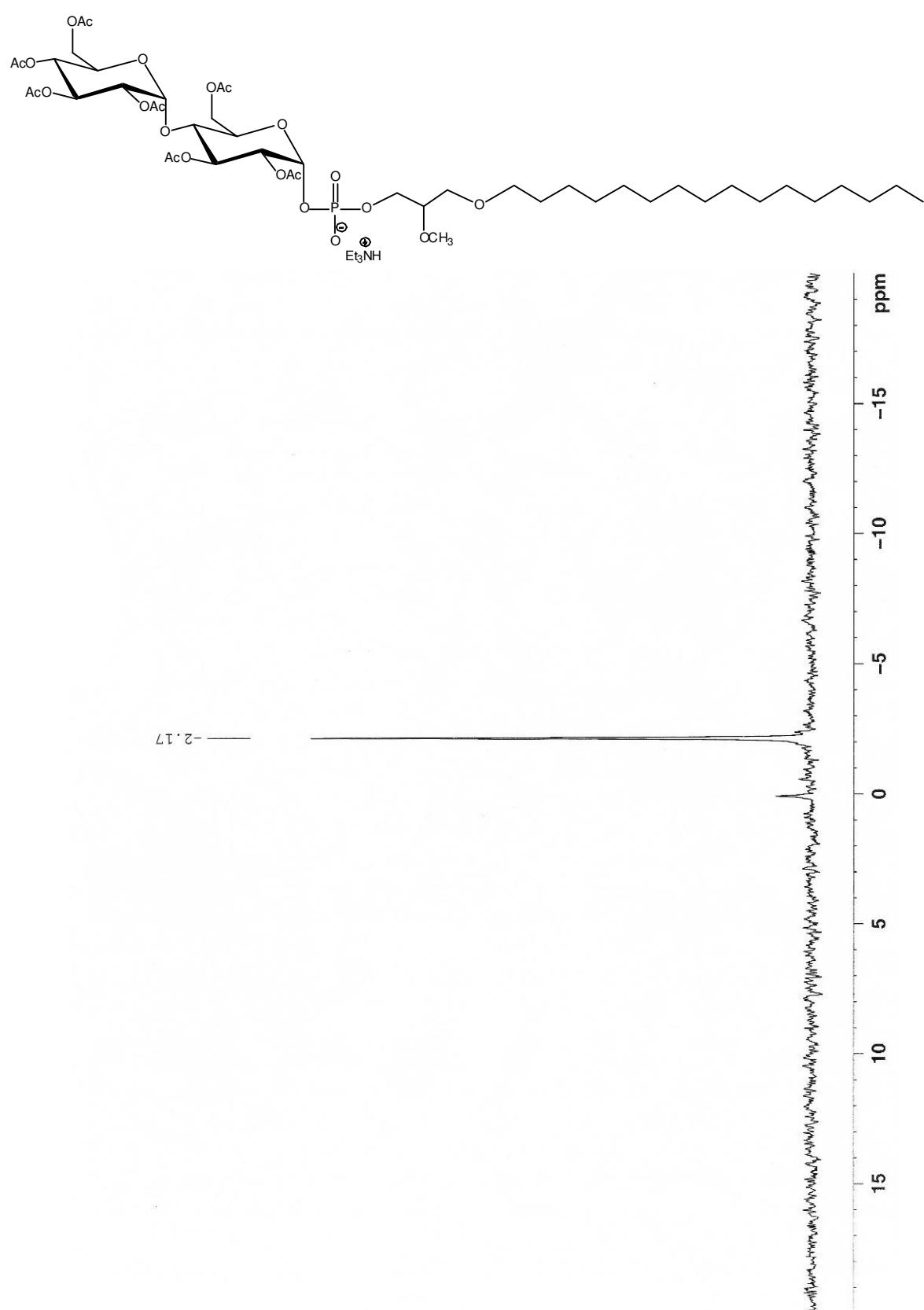
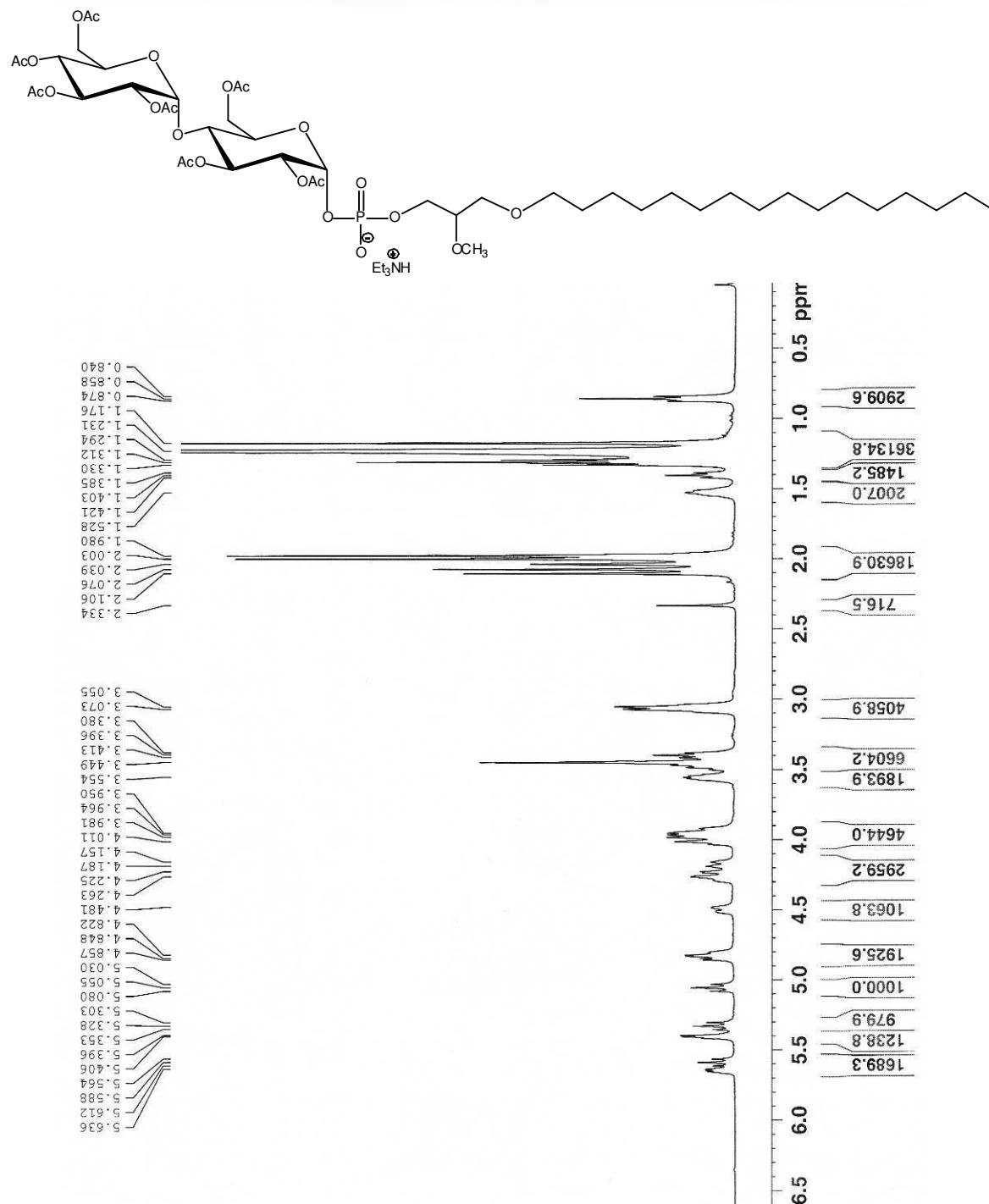


Figure S3-25:  $^{31}\text{P}$  NMR ( $\text{CDCl}_3$ ) spectrum of compound 3b2.



**Figure S3-26:**  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ) spectrum of compound 3b2.

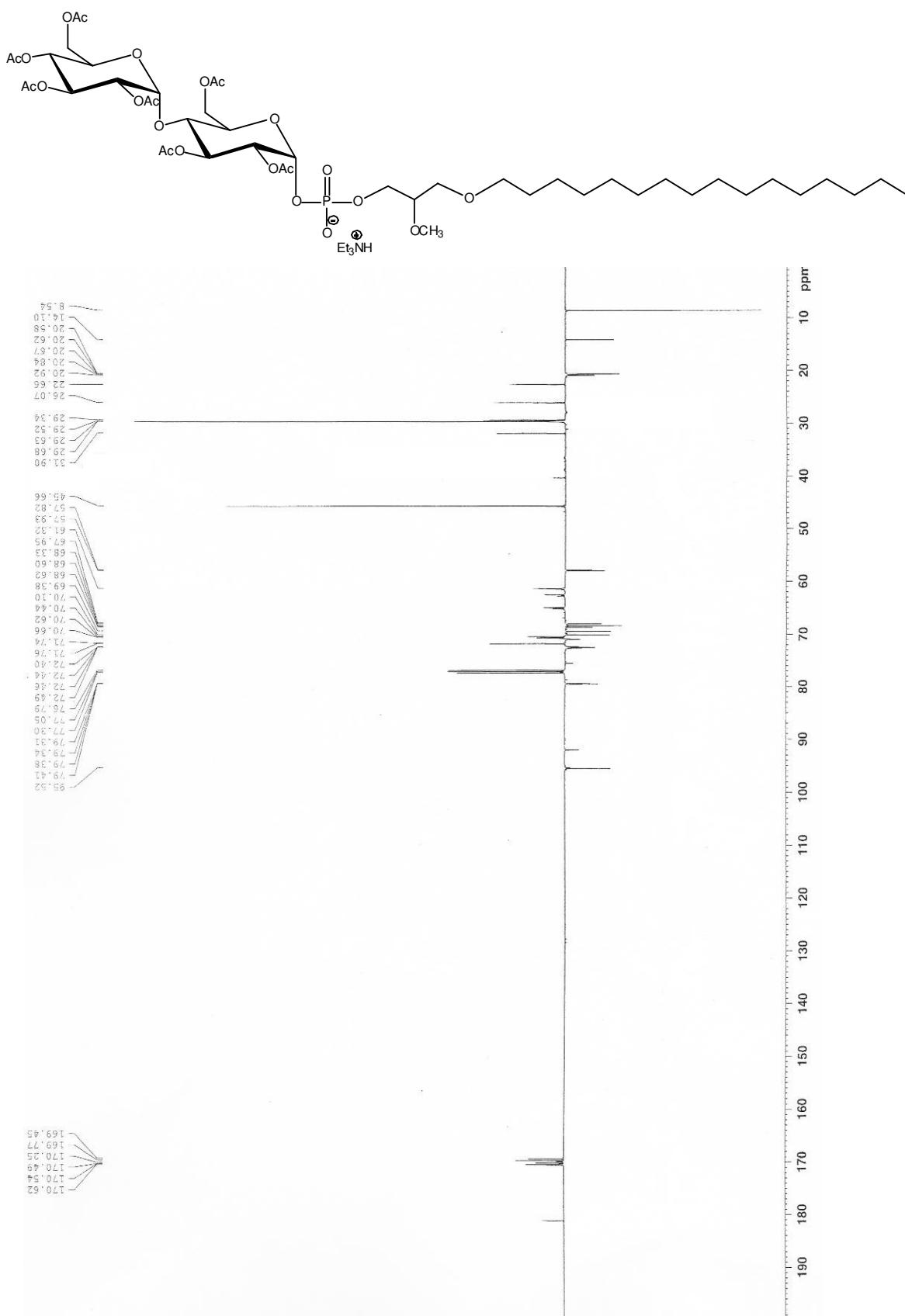


Figure S3-27:  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ) spectrum of compound 3b2.

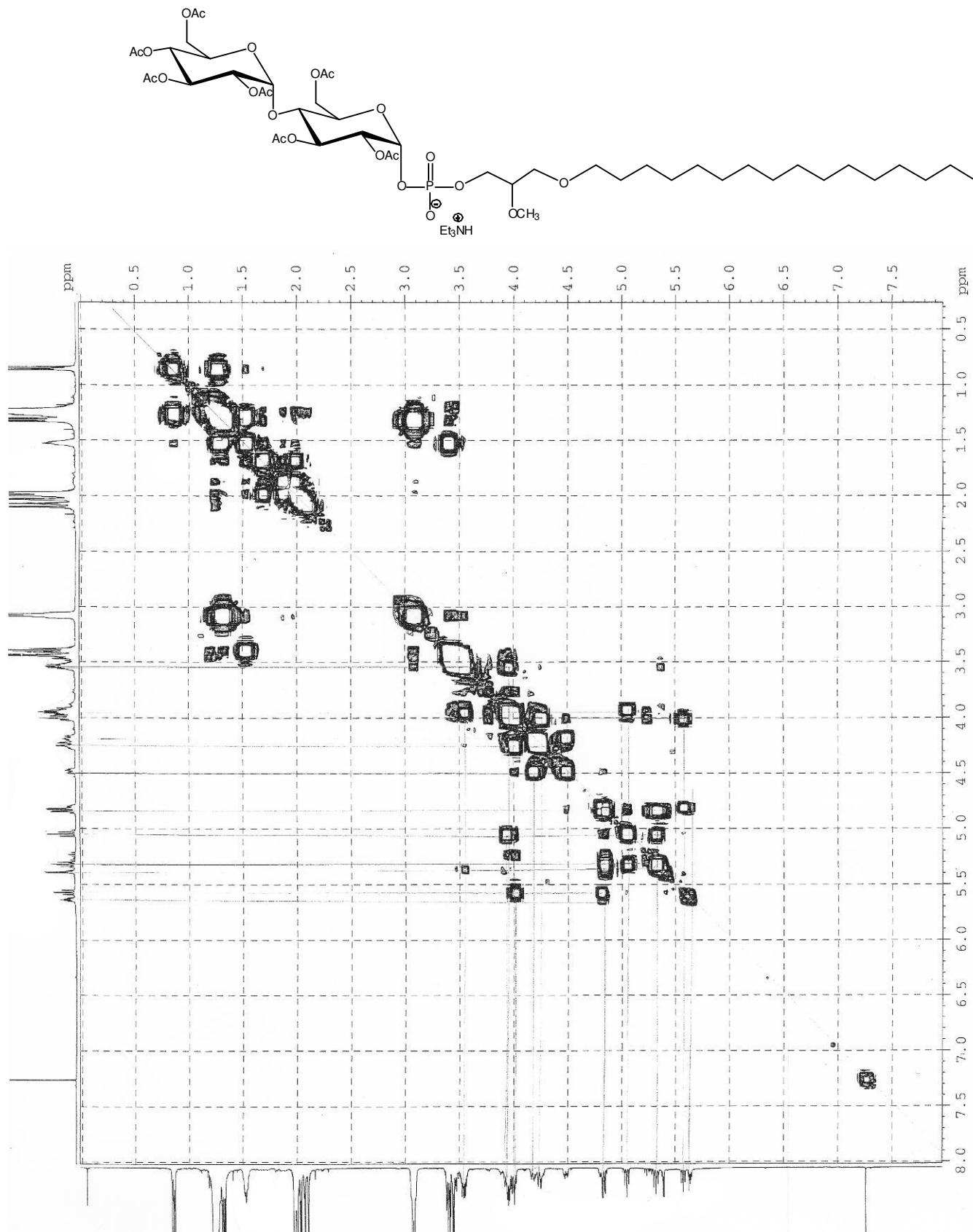


Figure S3-28: 2D NMR - COSY ( $\text{CDCl}_3$ ) spectrum of compound 3b2.

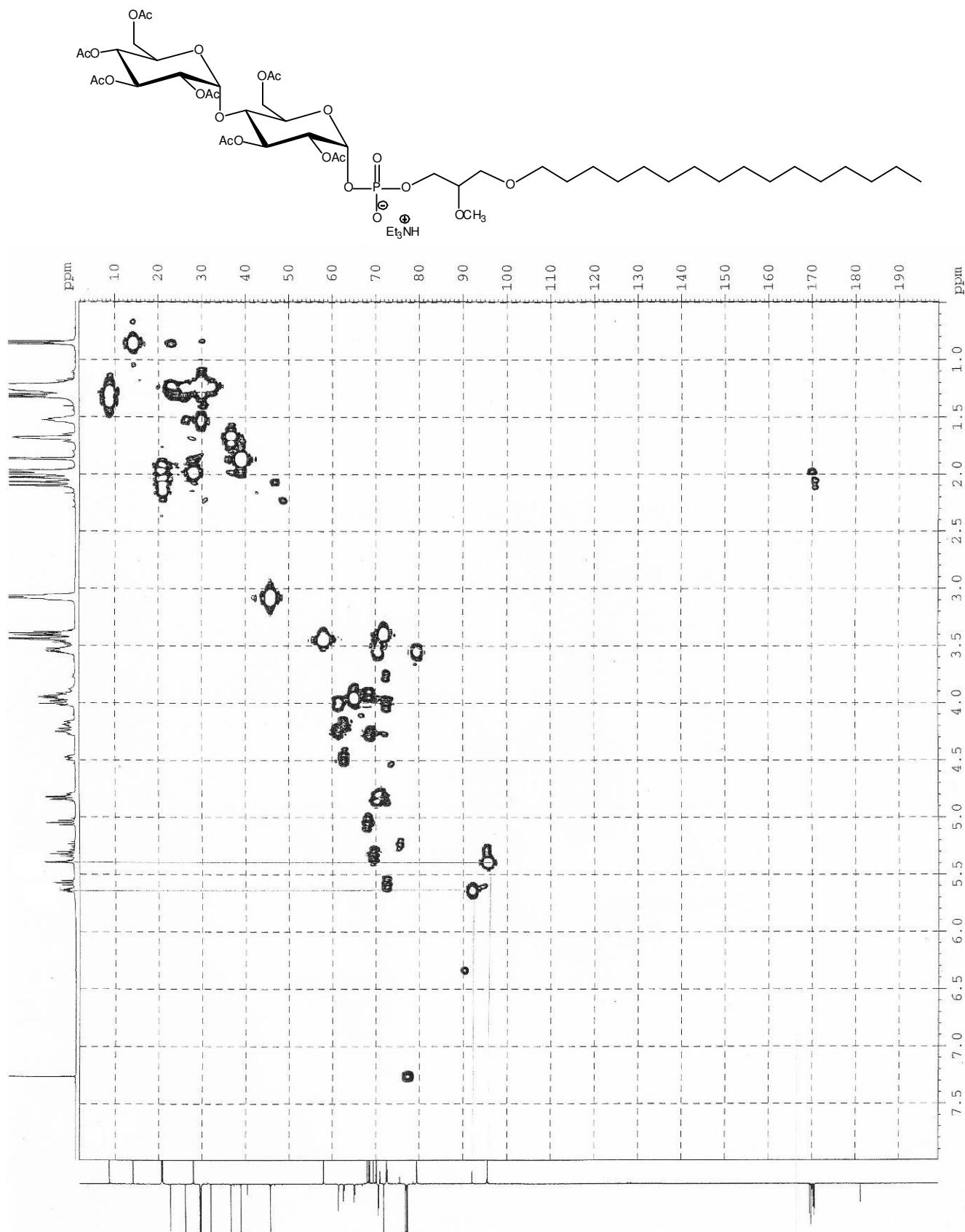


Figure S3-29: 2D NMR - HMQC ( $\text{CDCl}_3$ ) spectrum of compound 3b2.

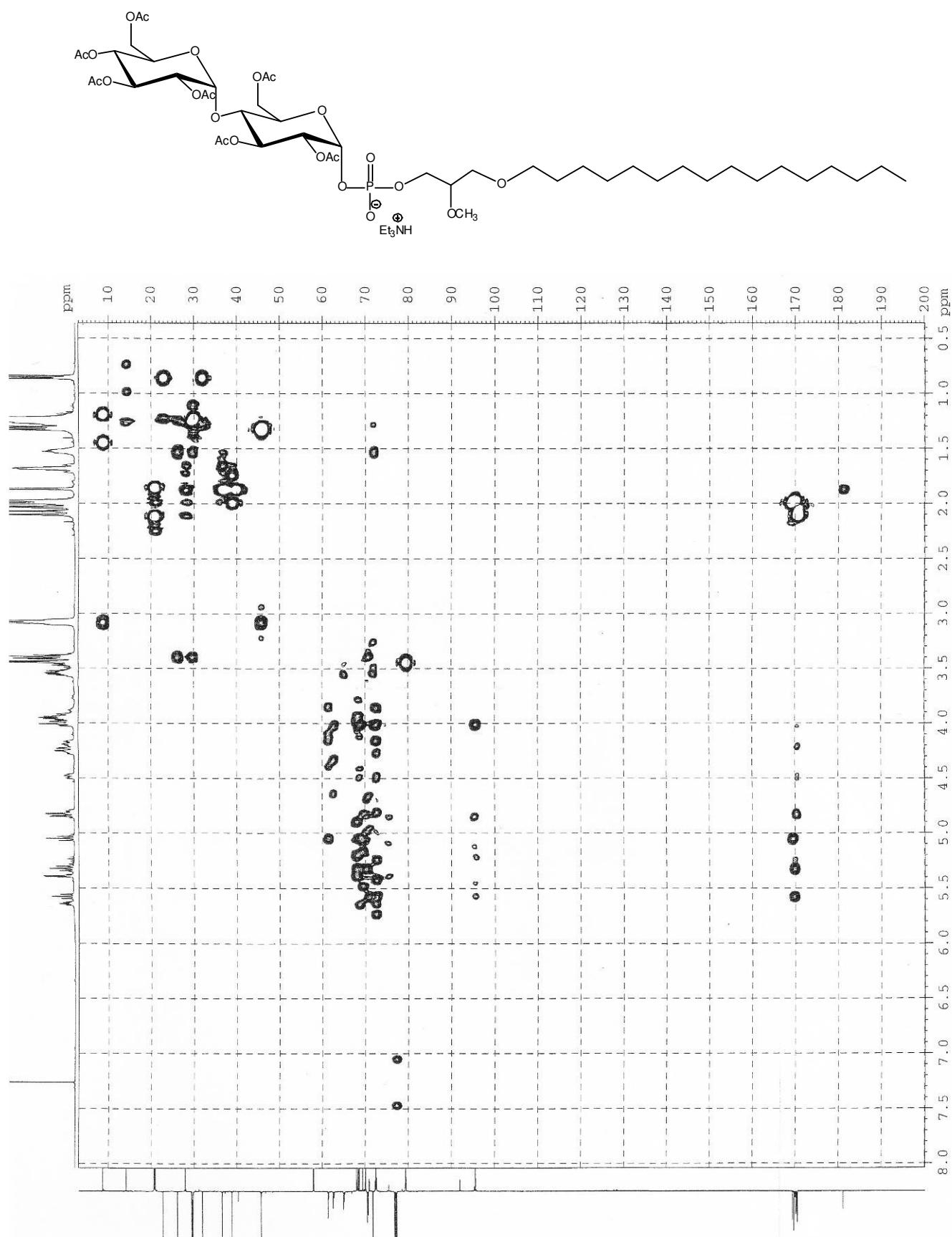
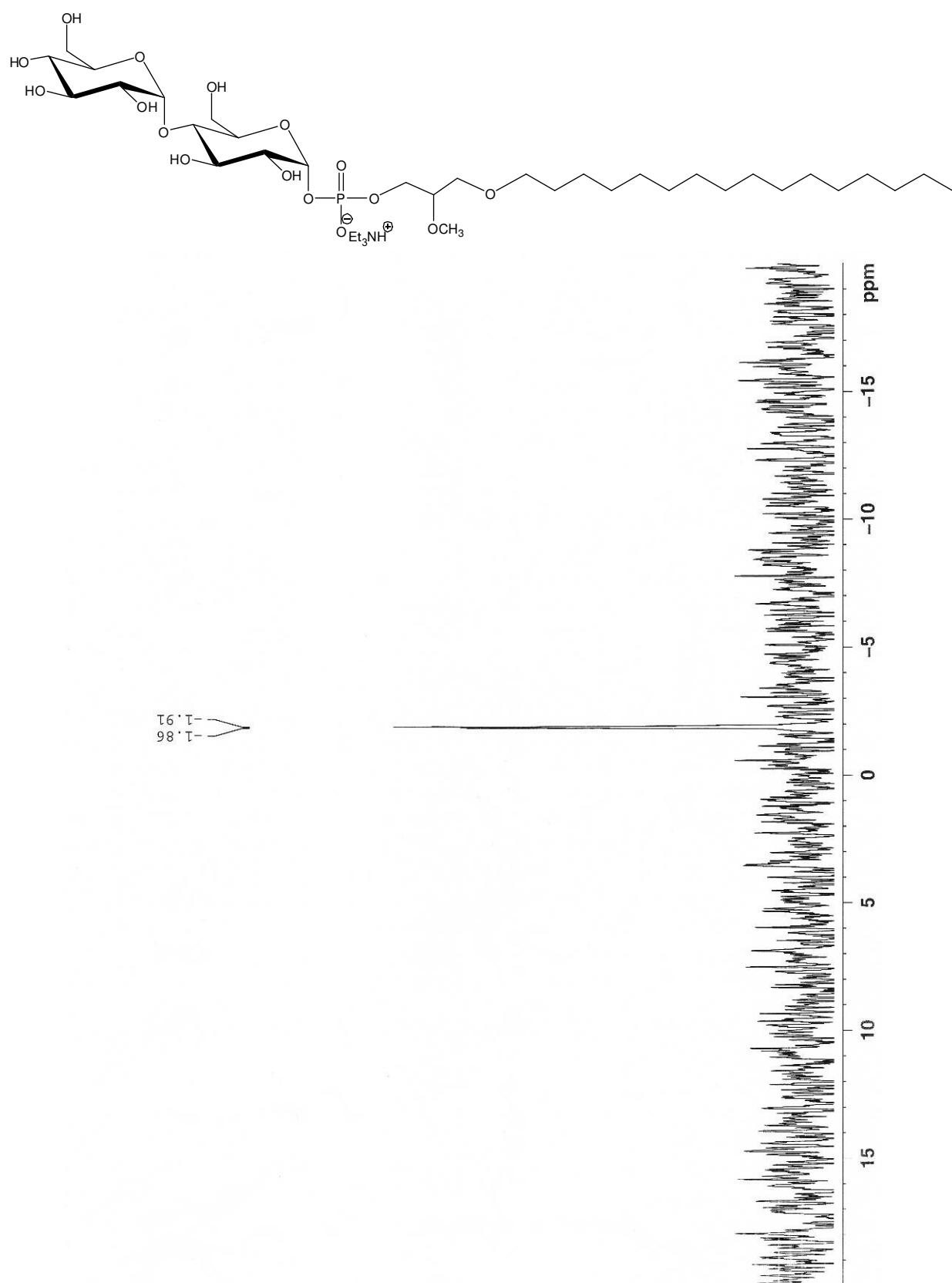
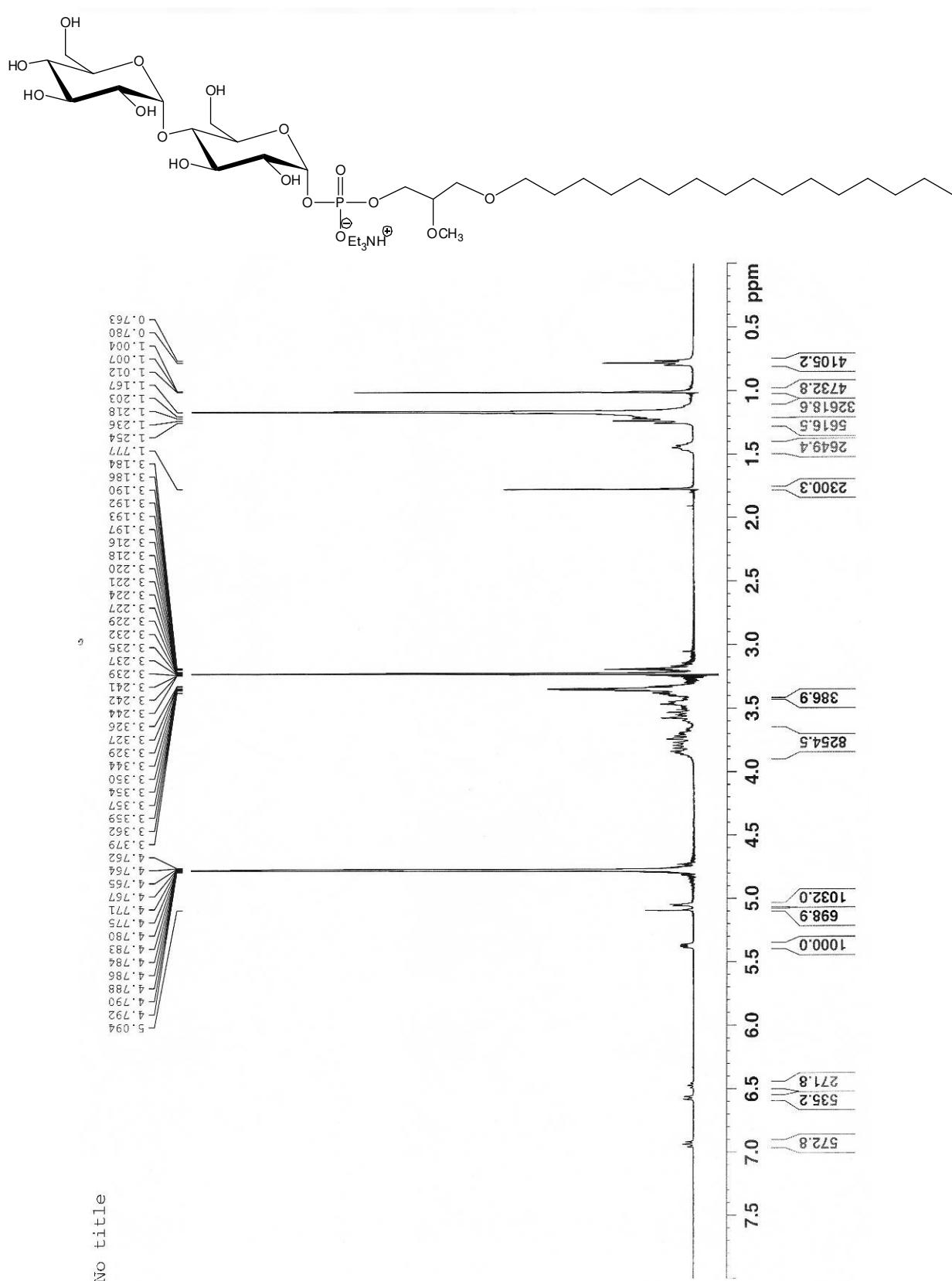


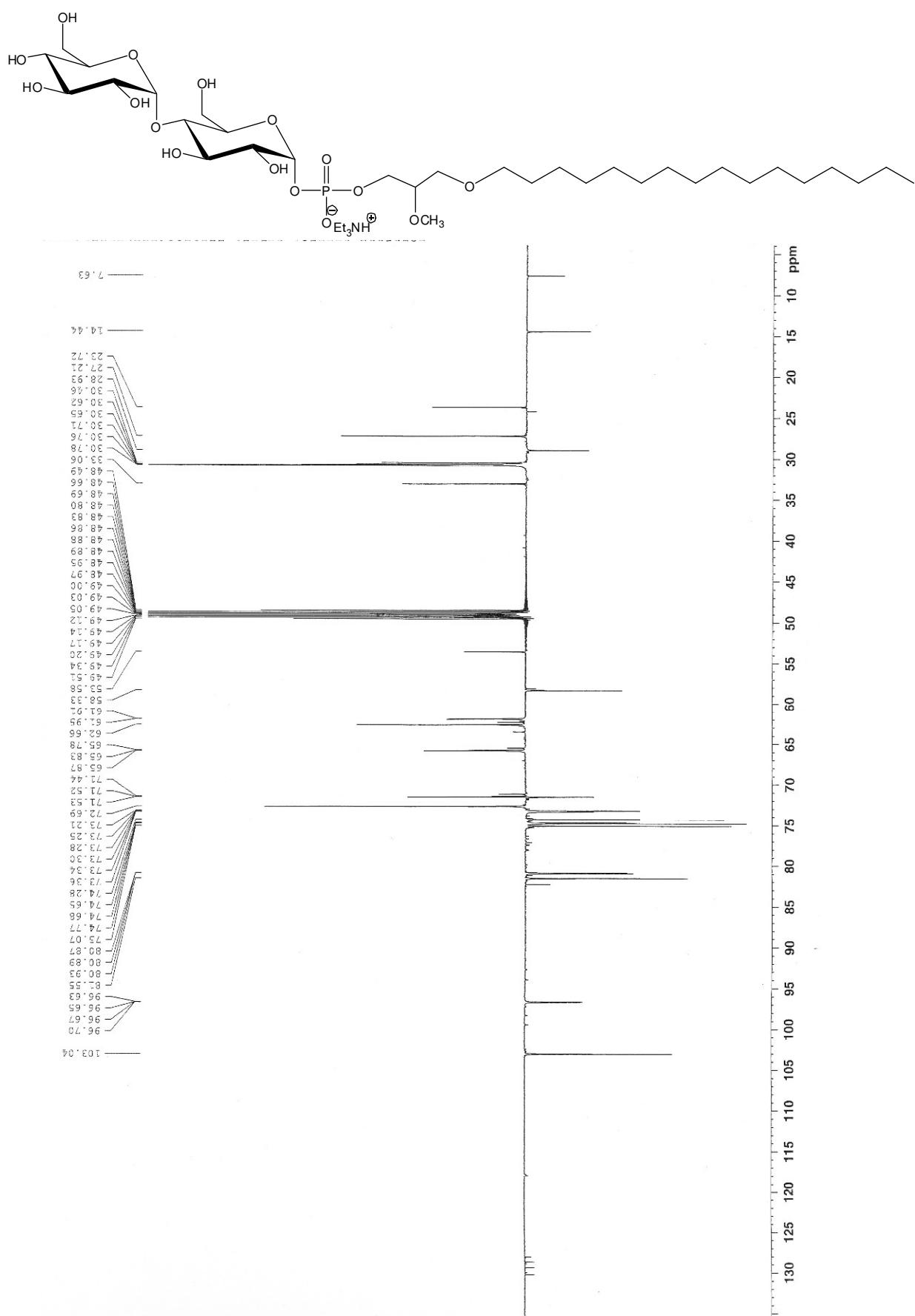
Figure S3-30: 2D NMR - HMBC ( $\text{CDCl}_3$ ) spectrum of compound 3b2.



**Figure S3-31:**  $^{31}\text{P}$  NMR ( $\text{CD}_3\text{OD}$ ) spectrum of compound 4b2.



**Figure S3-32:**  $^1\text{H}$  NMR ( $\text{CD}_3\text{OD}$ ) spectrum of compound 4b2.



**Figure S3-33:**  $^{13}\text{C}$  NMR ( $\text{CD}_3\text{OD}$ ) spectrum of compound 4b2.

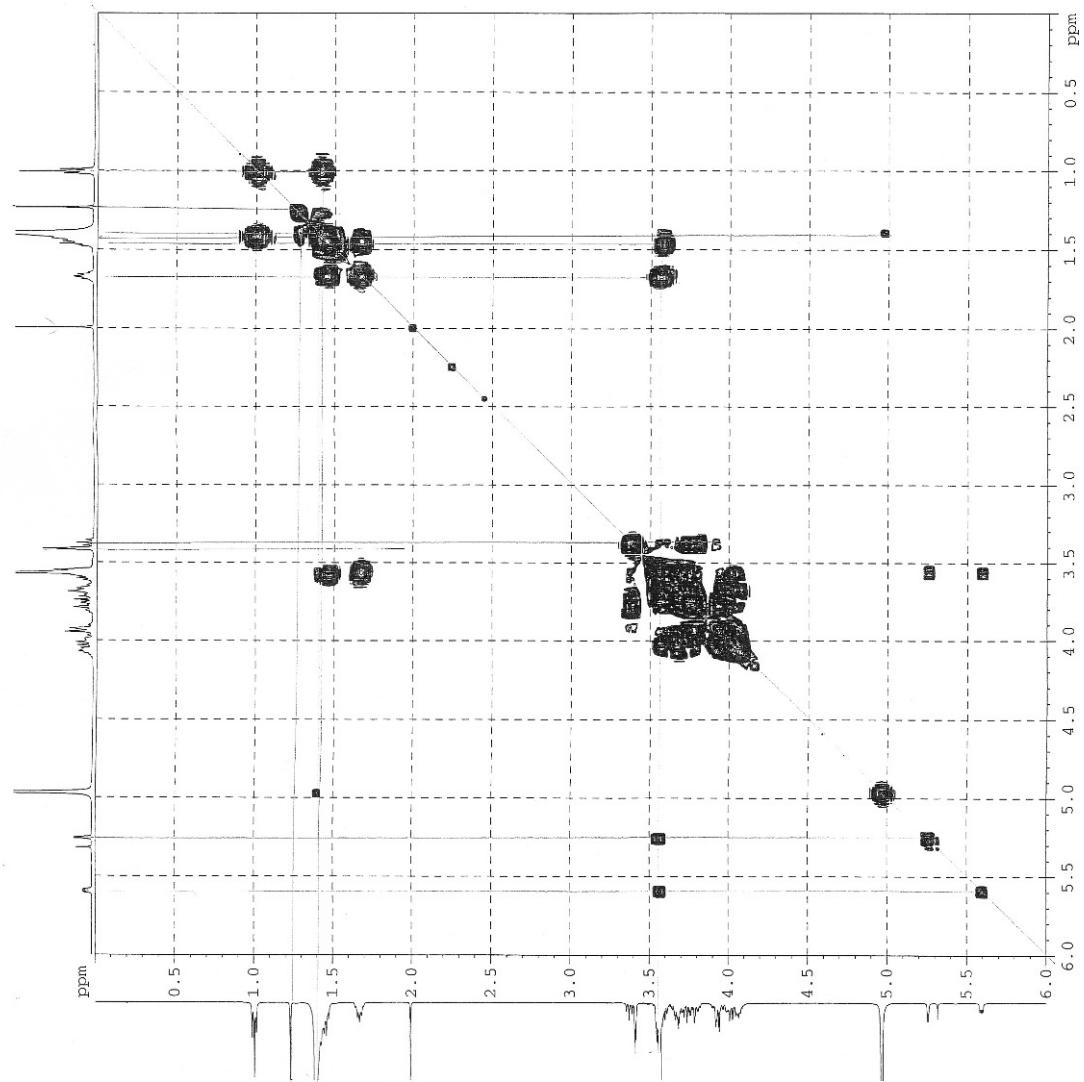
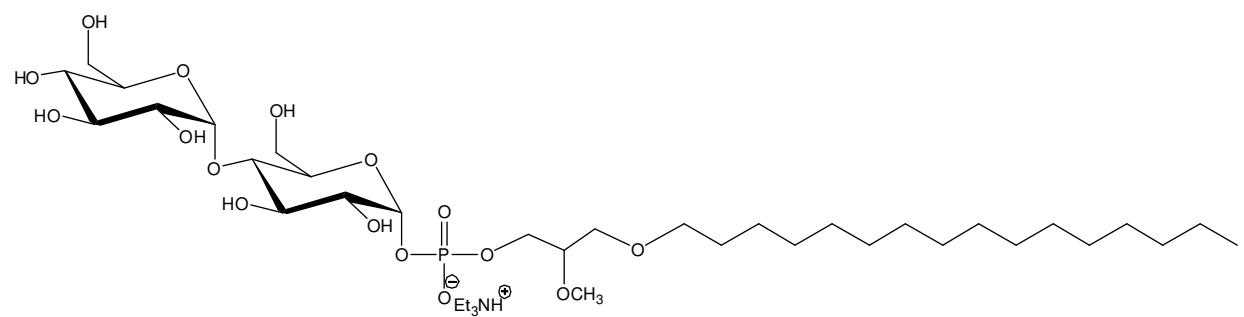


Figure S3-34: 2D-COSY NMR ( $\text{CD}_3\text{OD}$ ) spectrum of compound 4b2.

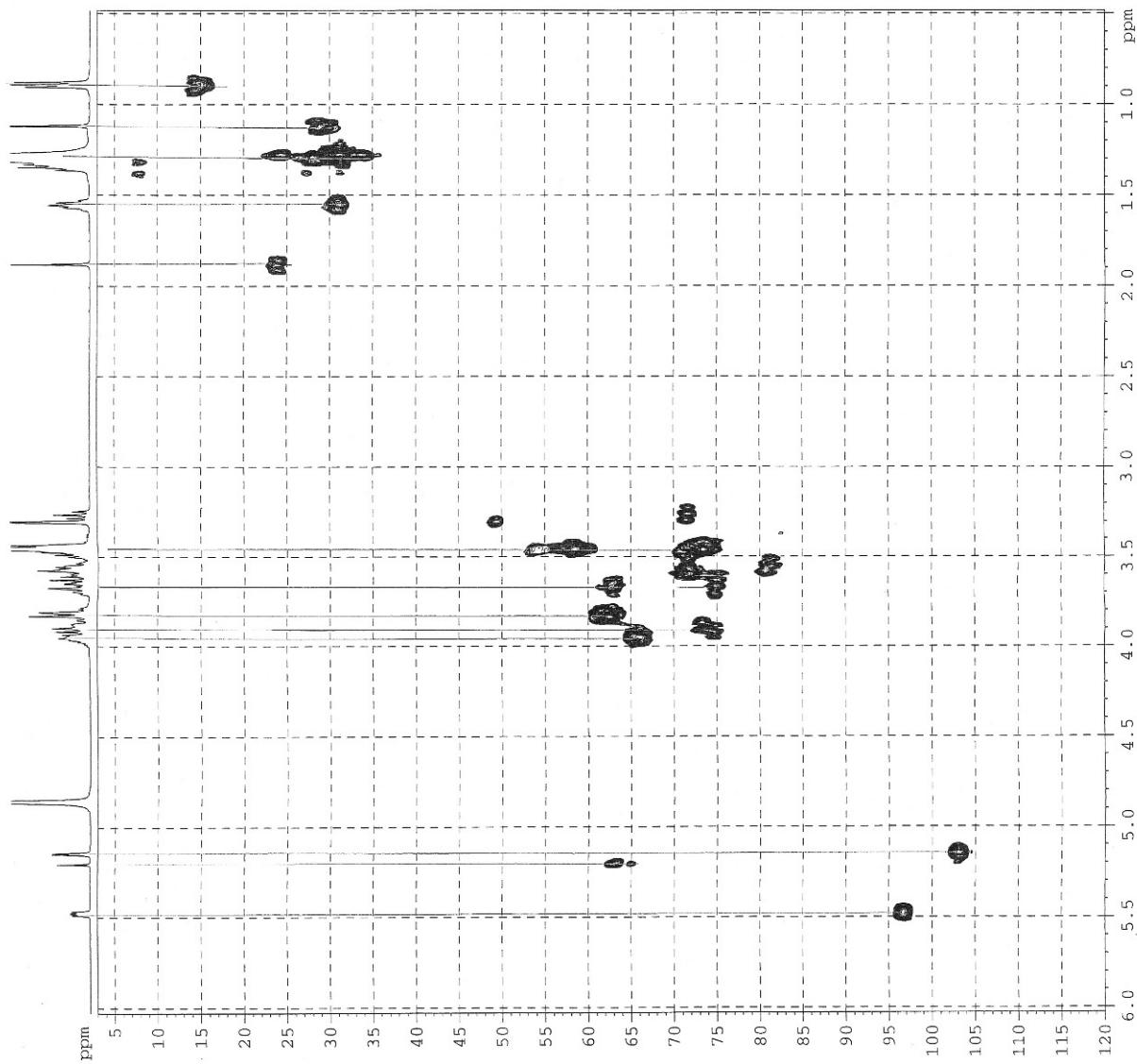
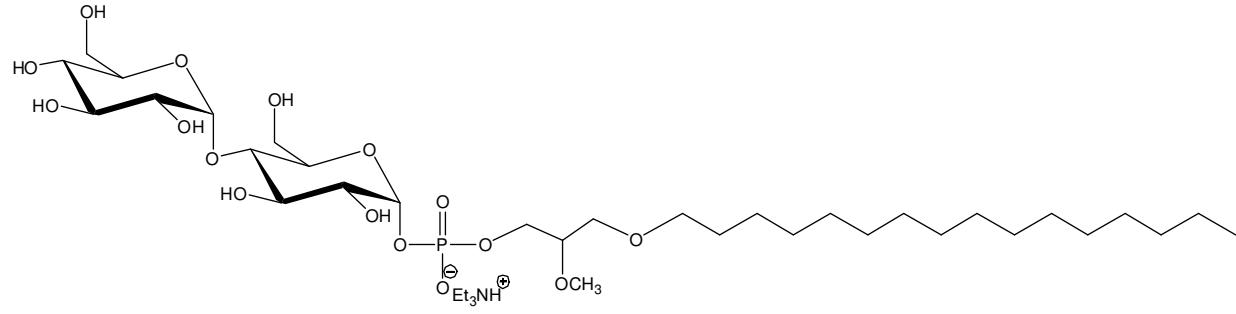


Figure S3-35: 2D-HMQC NMR ( $\text{CD}_3\text{OD}$ ) spectrum of compound 4b2.

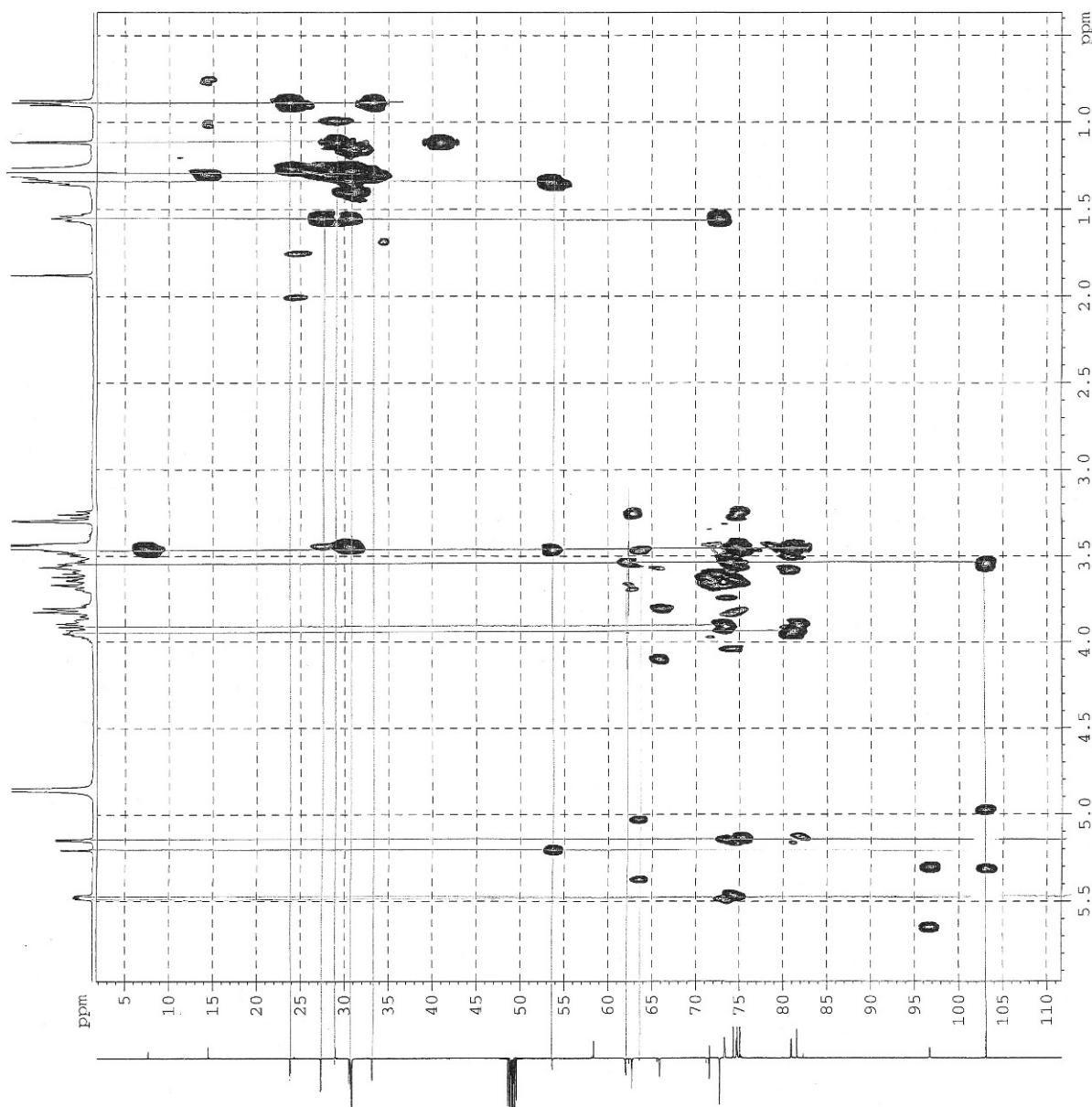
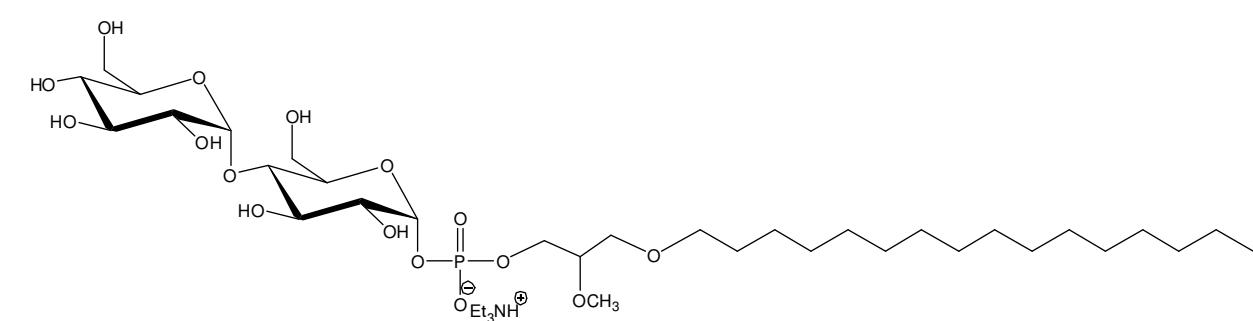


Figure S3-36: 2D-HMBC NMR (CD<sub>3</sub>OD) spectrum of compound 4b2.

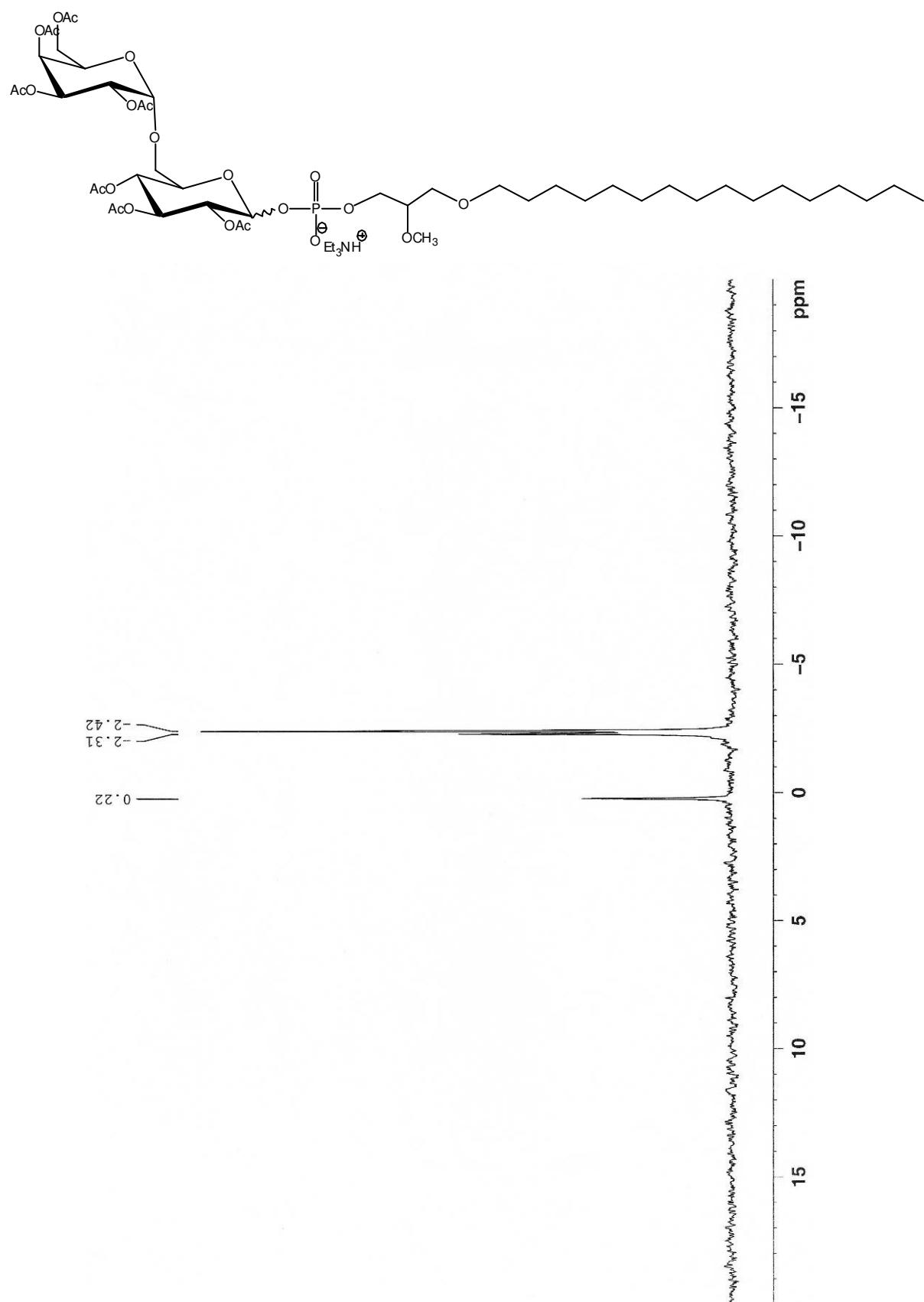
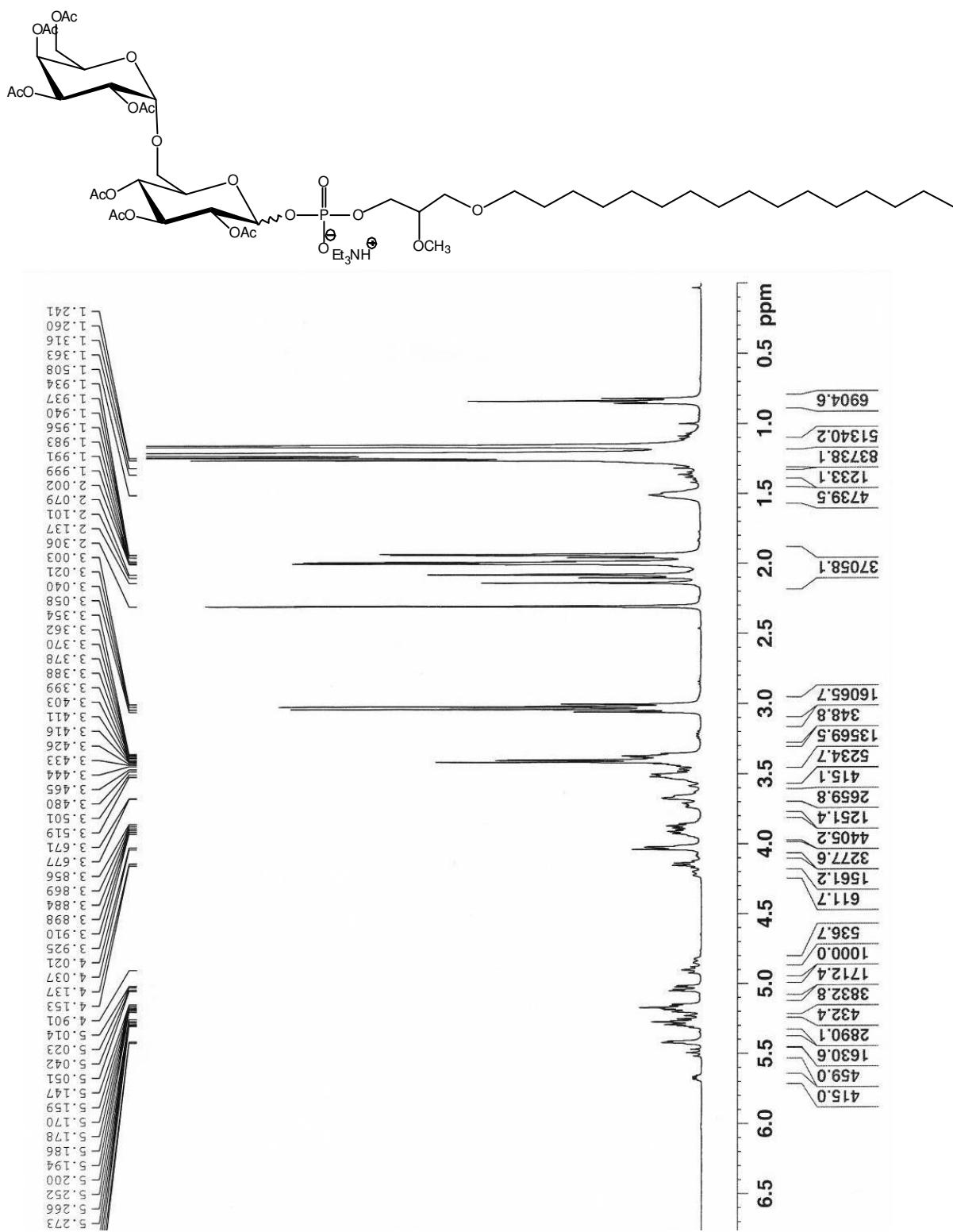
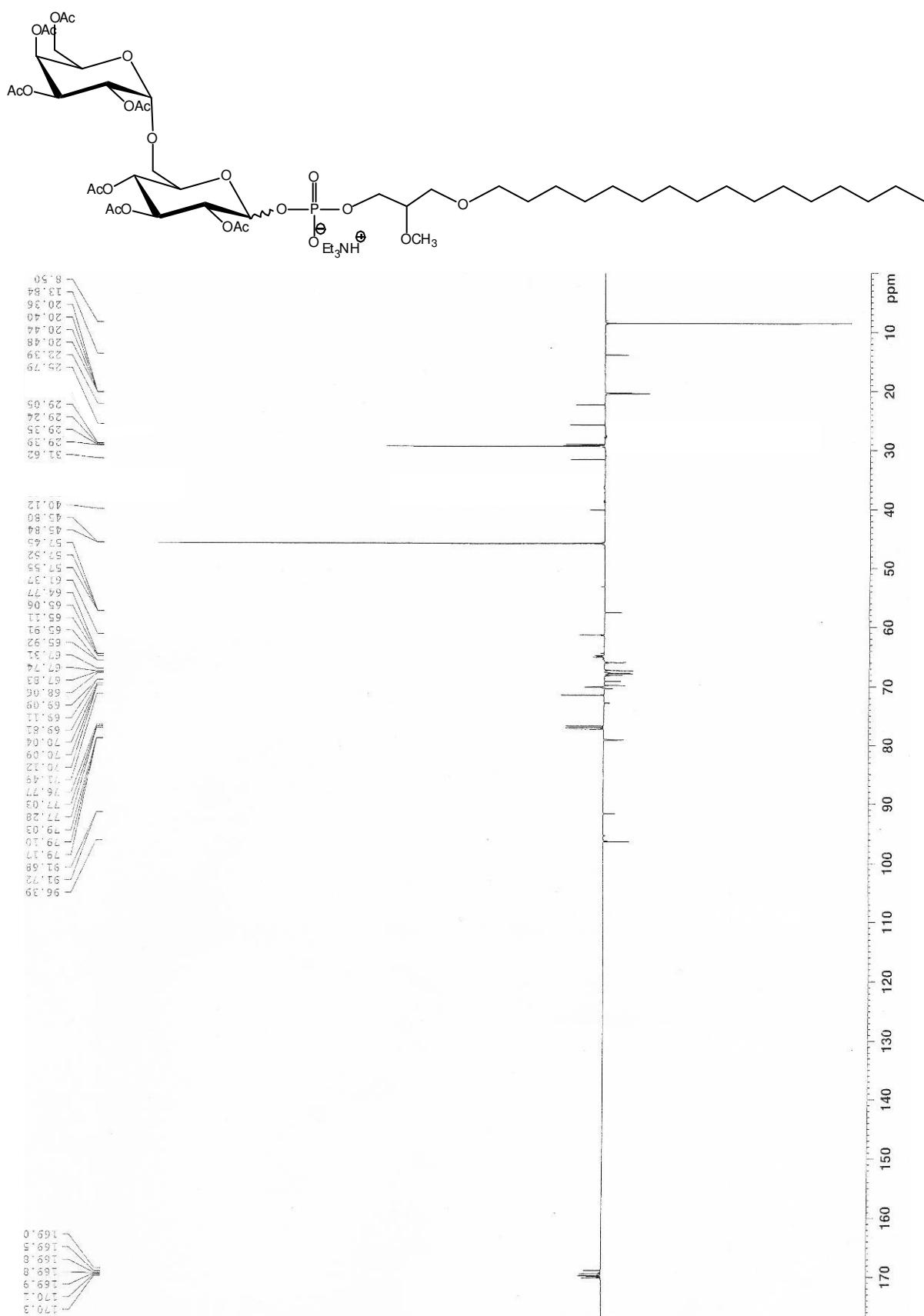


Figure S3-37:  $^{31}\text{P}$  NMR ( $\text{CDCl}_3$ ) spectrum of compound 3c.



**Figure S3-38:**  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ) spectrum of compound 3c.



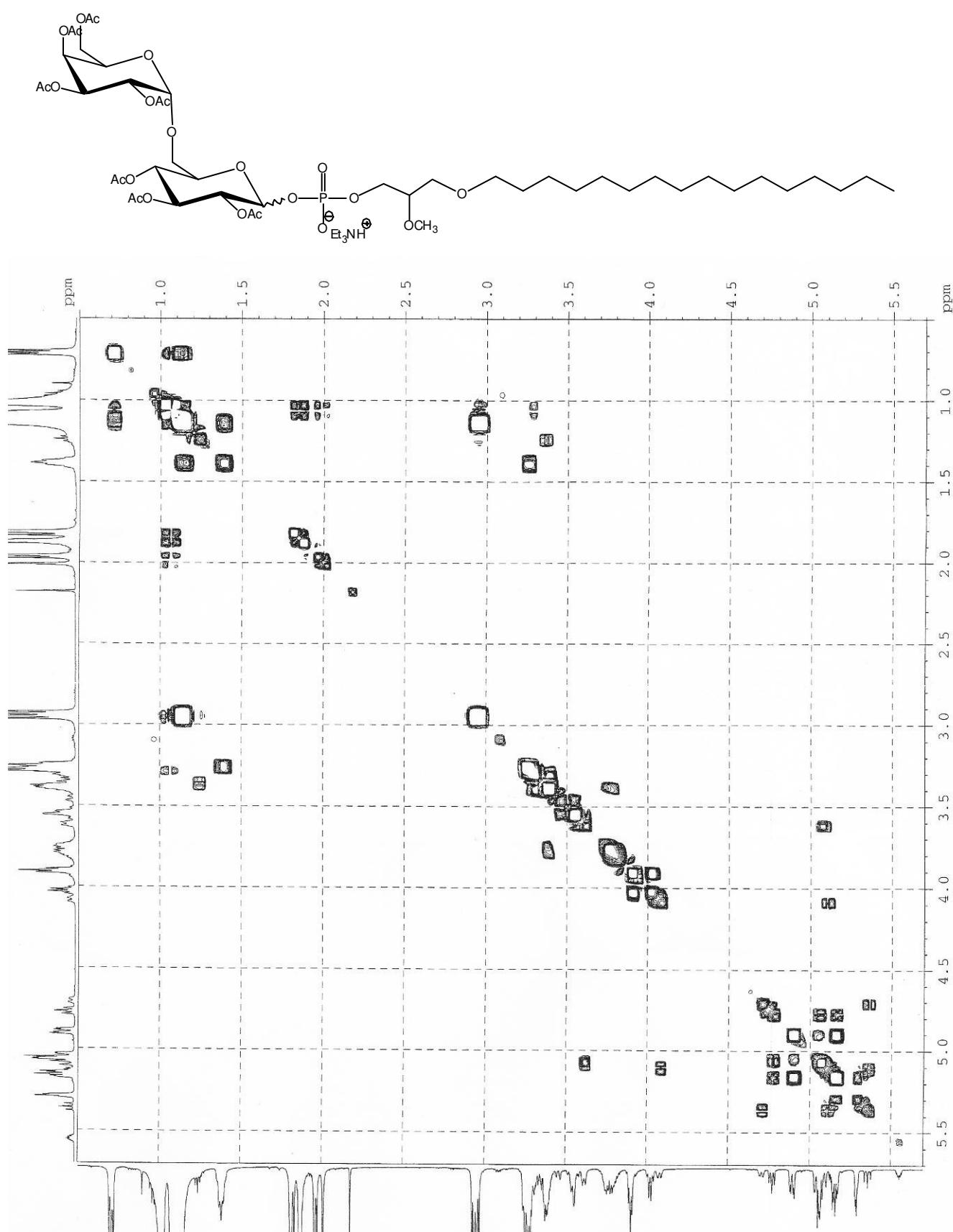


Figure S3-40: 2D NMR - COSY ( $\text{CDCl}_3$ ) spectrum of compound 3c.

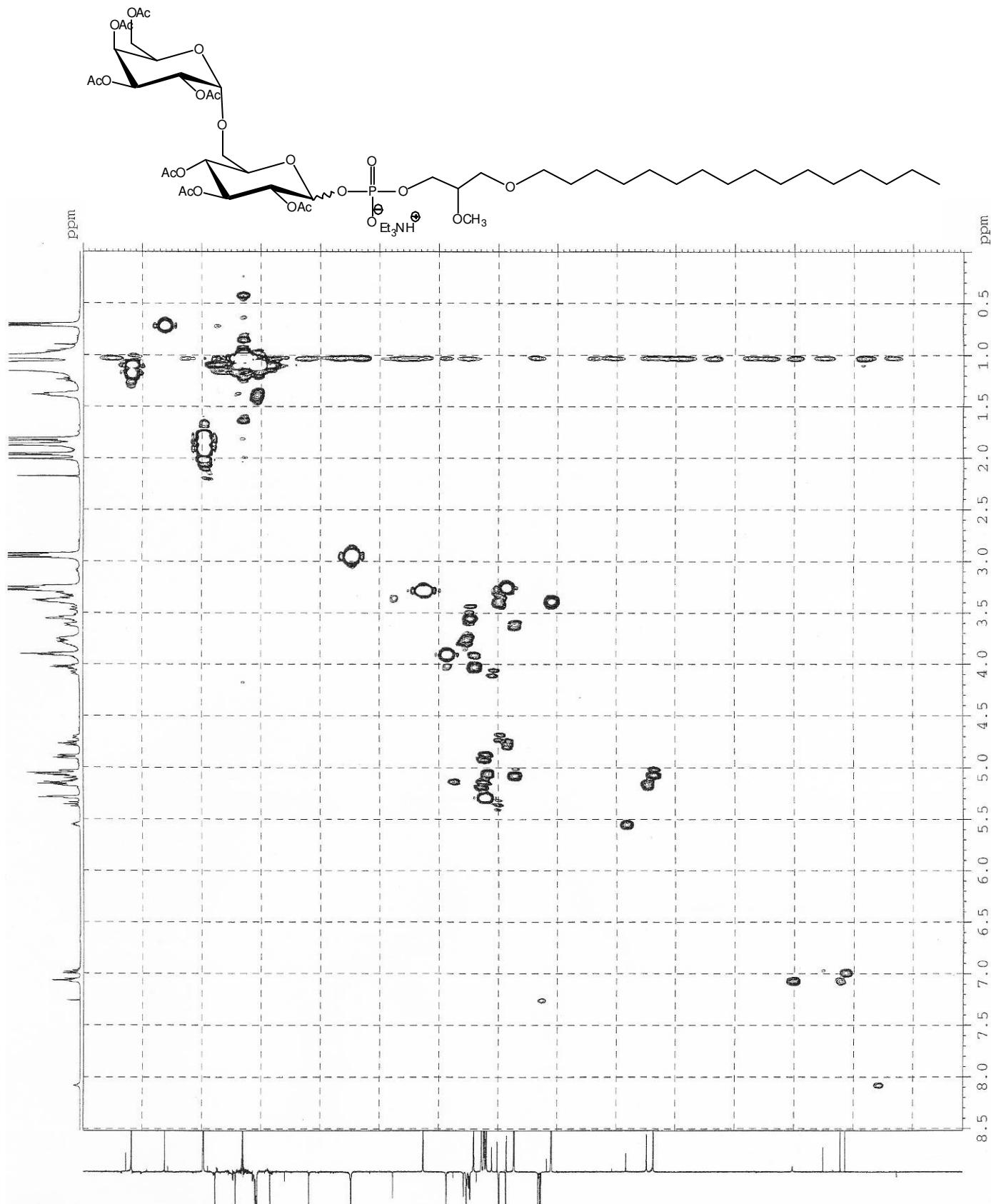


Figure S3-41: 2D NMR - HMQC ( $\text{CDCl}_3$ ) spectrum of compound 3c.

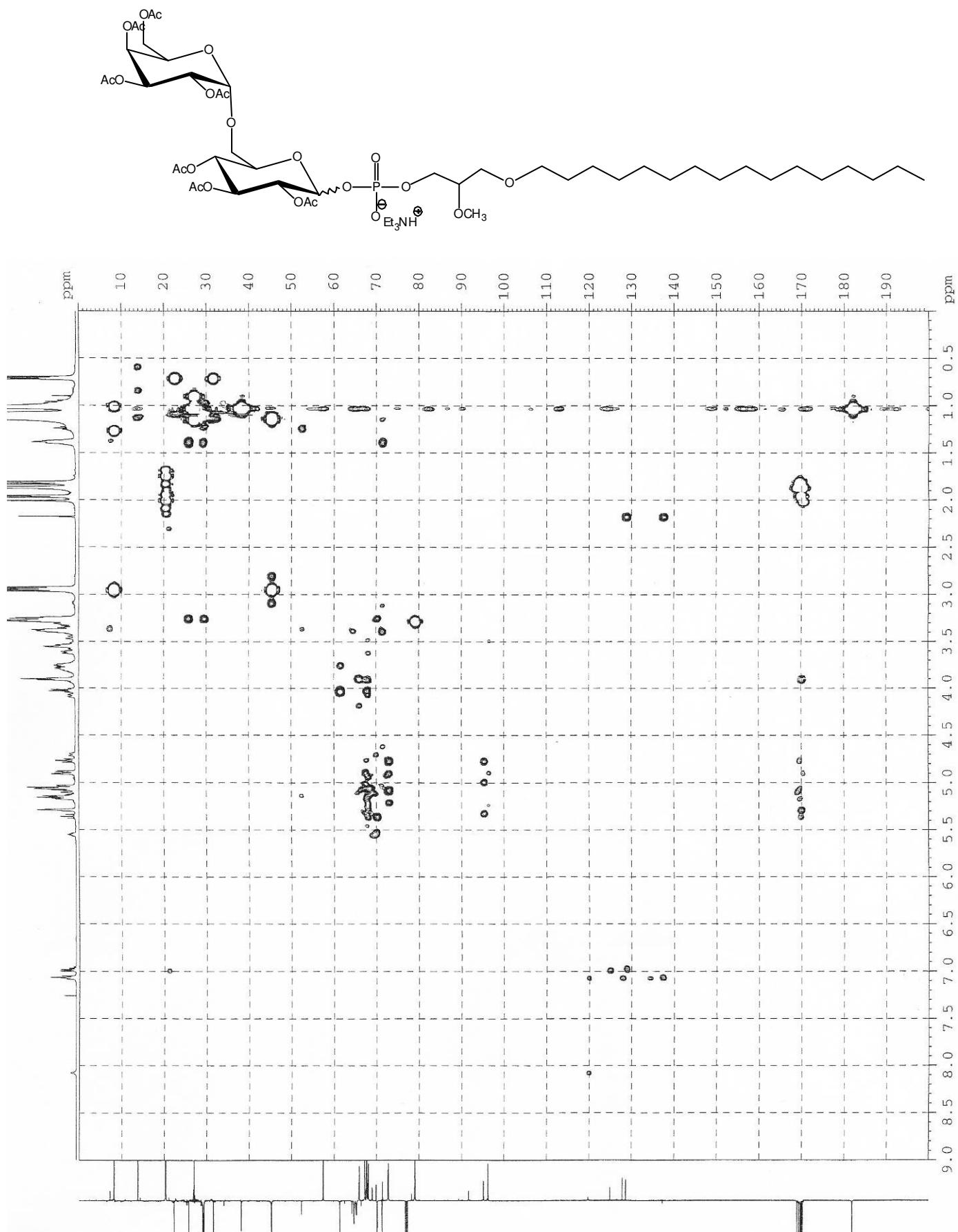


Figure S3-42: 2D NMR - HMBC ( $\text{CDCl}_3$ ) spectrum of compound 3c.

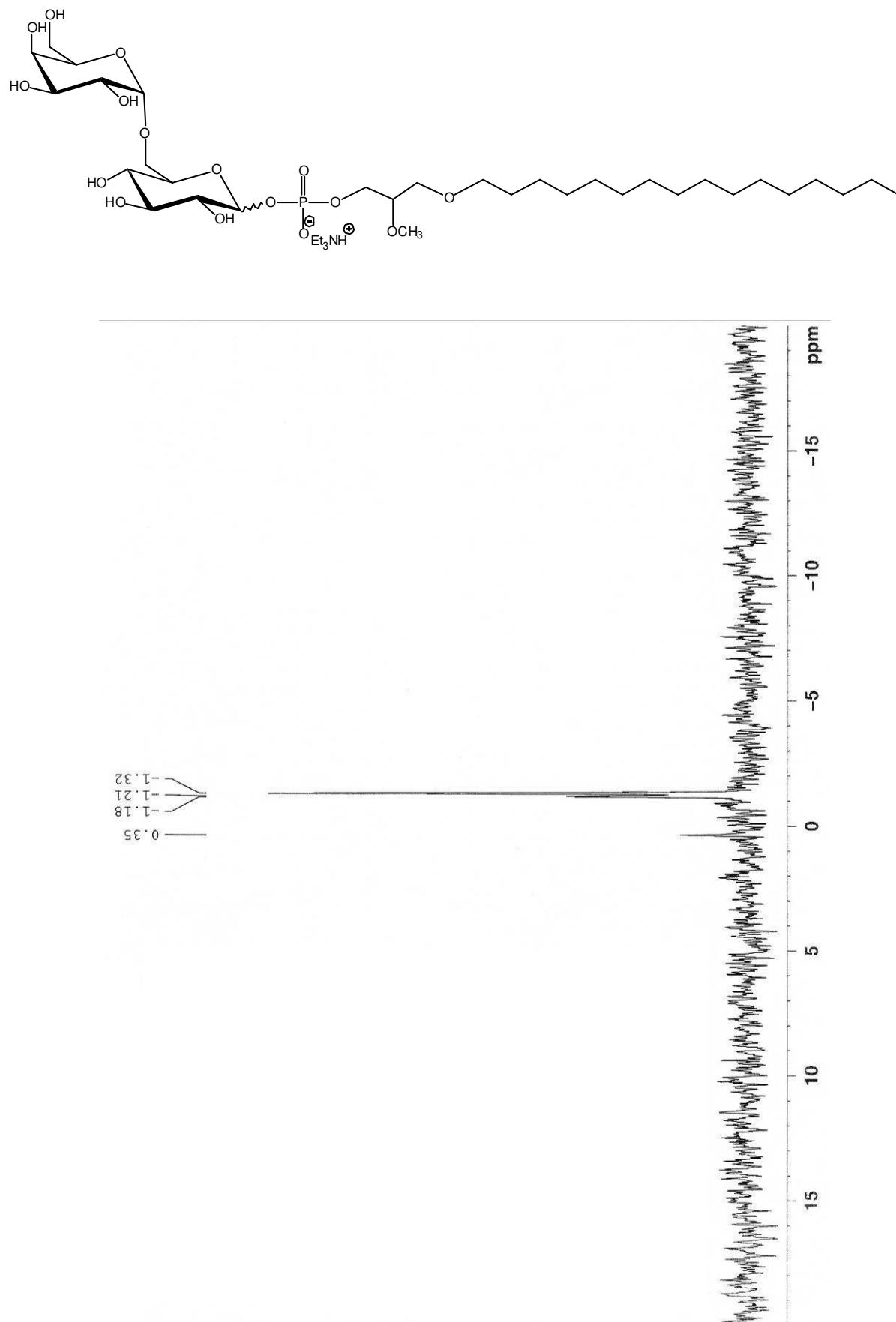


Figure S3-43:  $^{31}\text{P}$  NMR ( $\text{CD}_3\text{OD}$ ) spectrum of compound 4c.

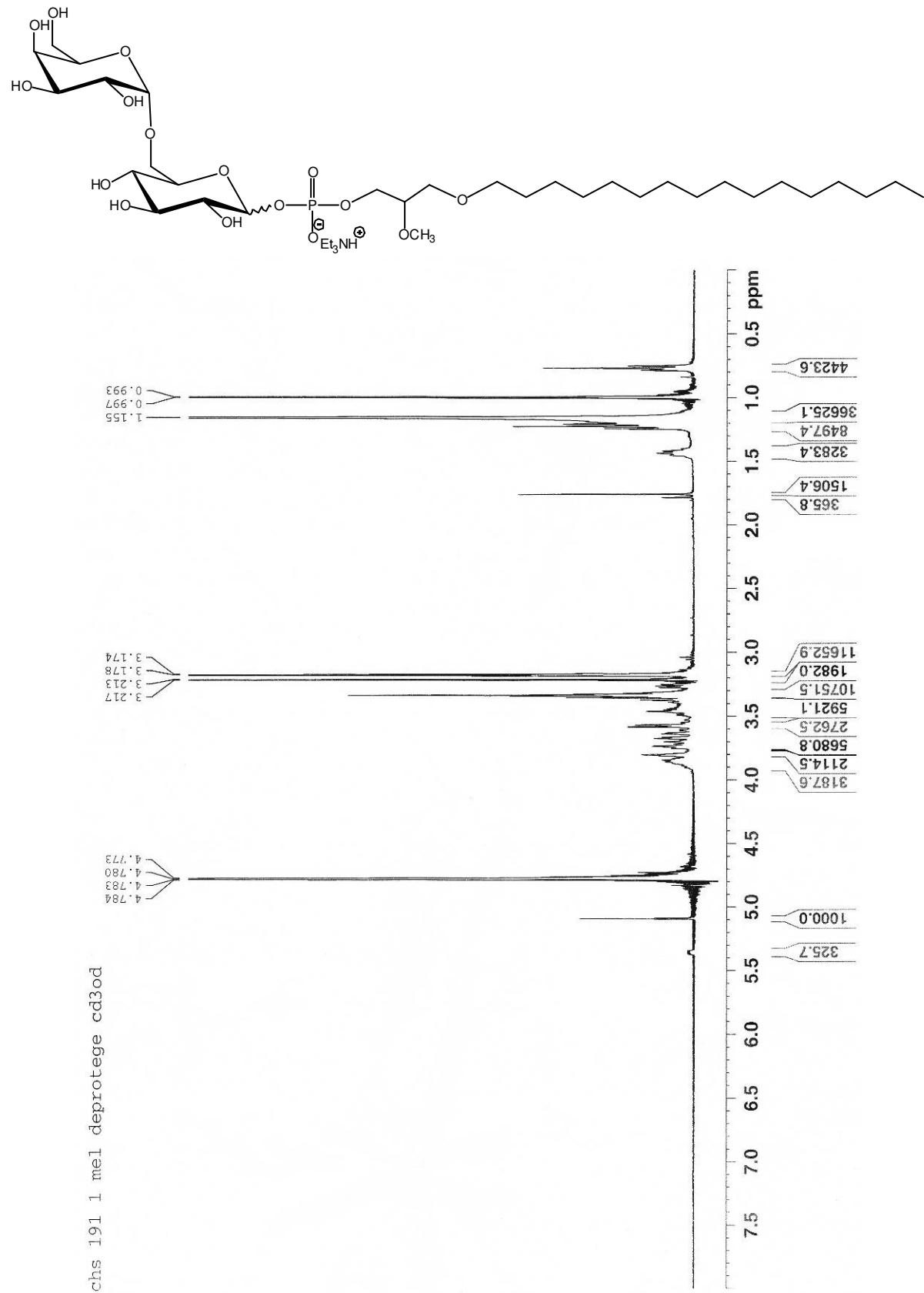
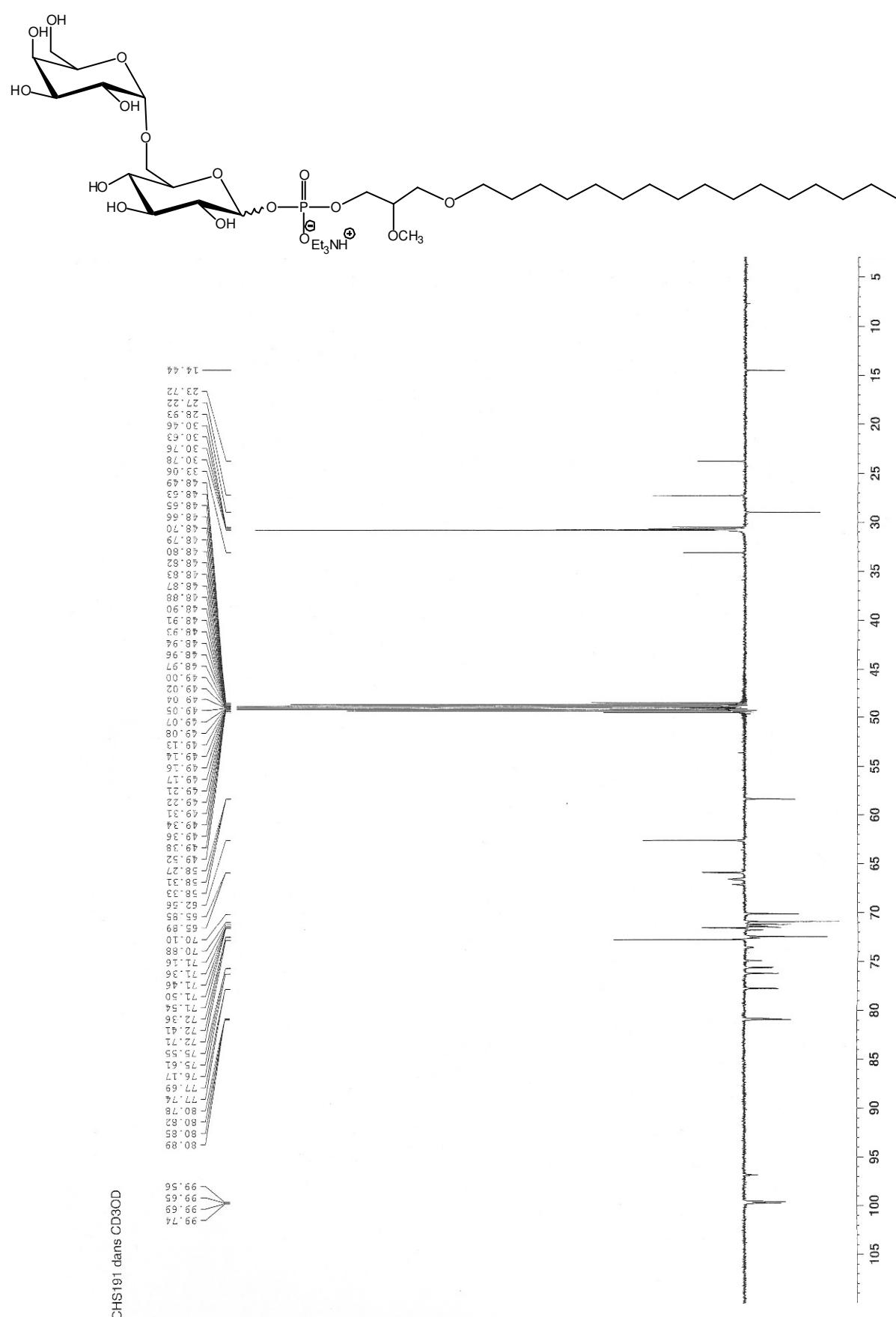


Figure S3-44: <sup>1</sup>H NMR ( $\text{CD}_3\text{OD}$ ) spectrum of compound 4c.



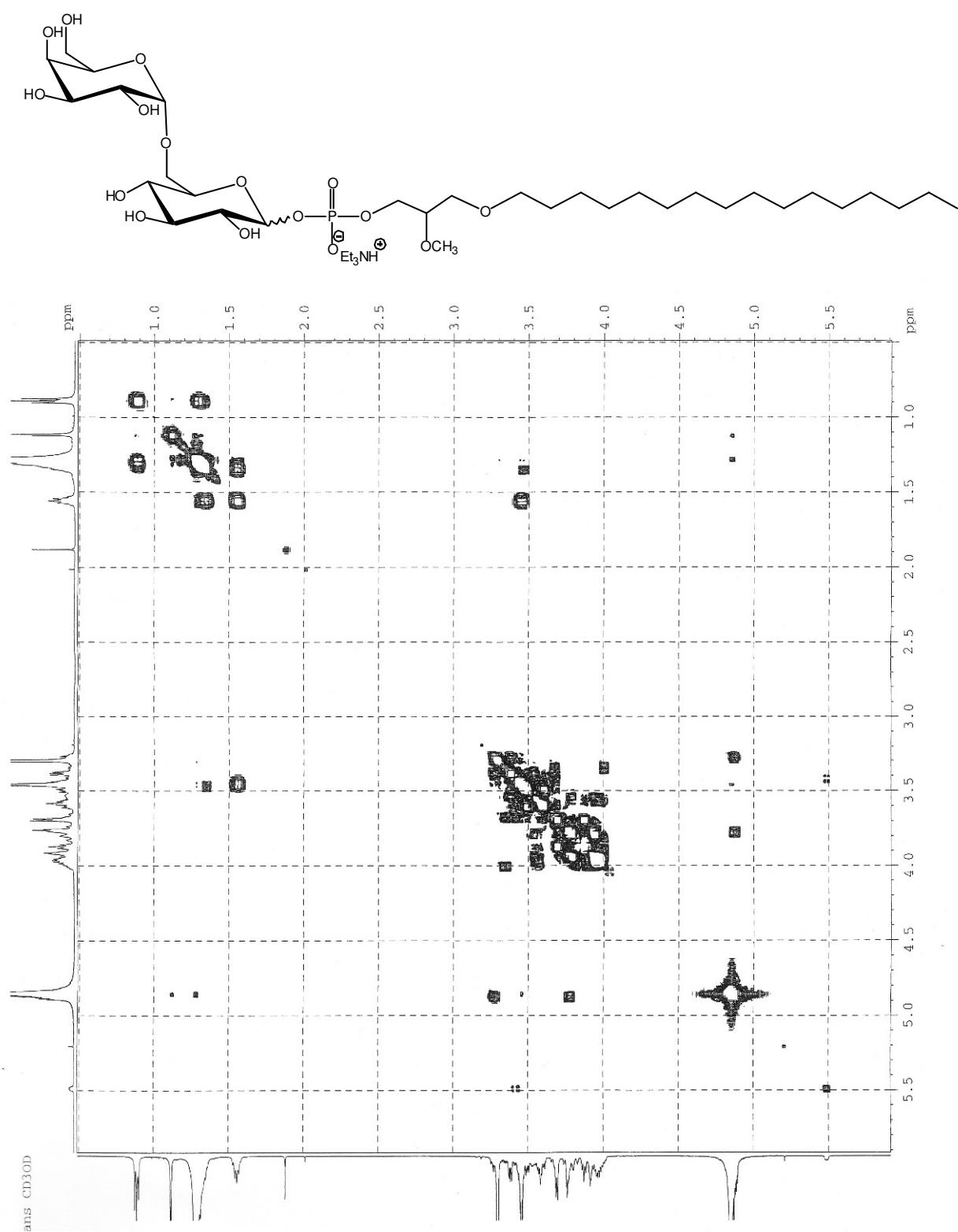


Figure S3-46: 2D-COSY NMR ( $\text{CD}_3\text{OD}$ ) spectrum of compound 4c.

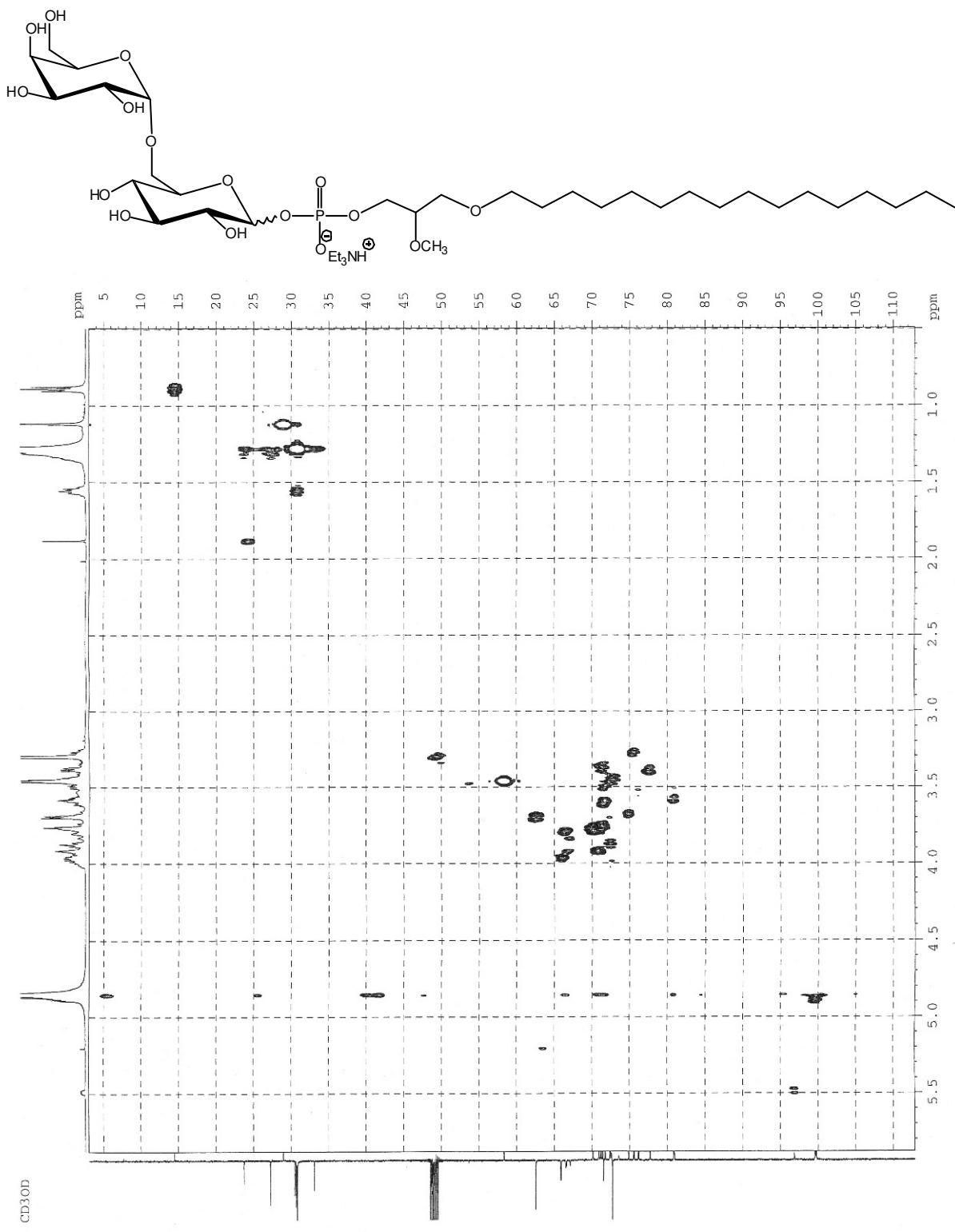


Figure S3-47: 2D-HMQC NMR ( $\text{CD}_3\text{OD}$ ) spectrum of compound 4c.

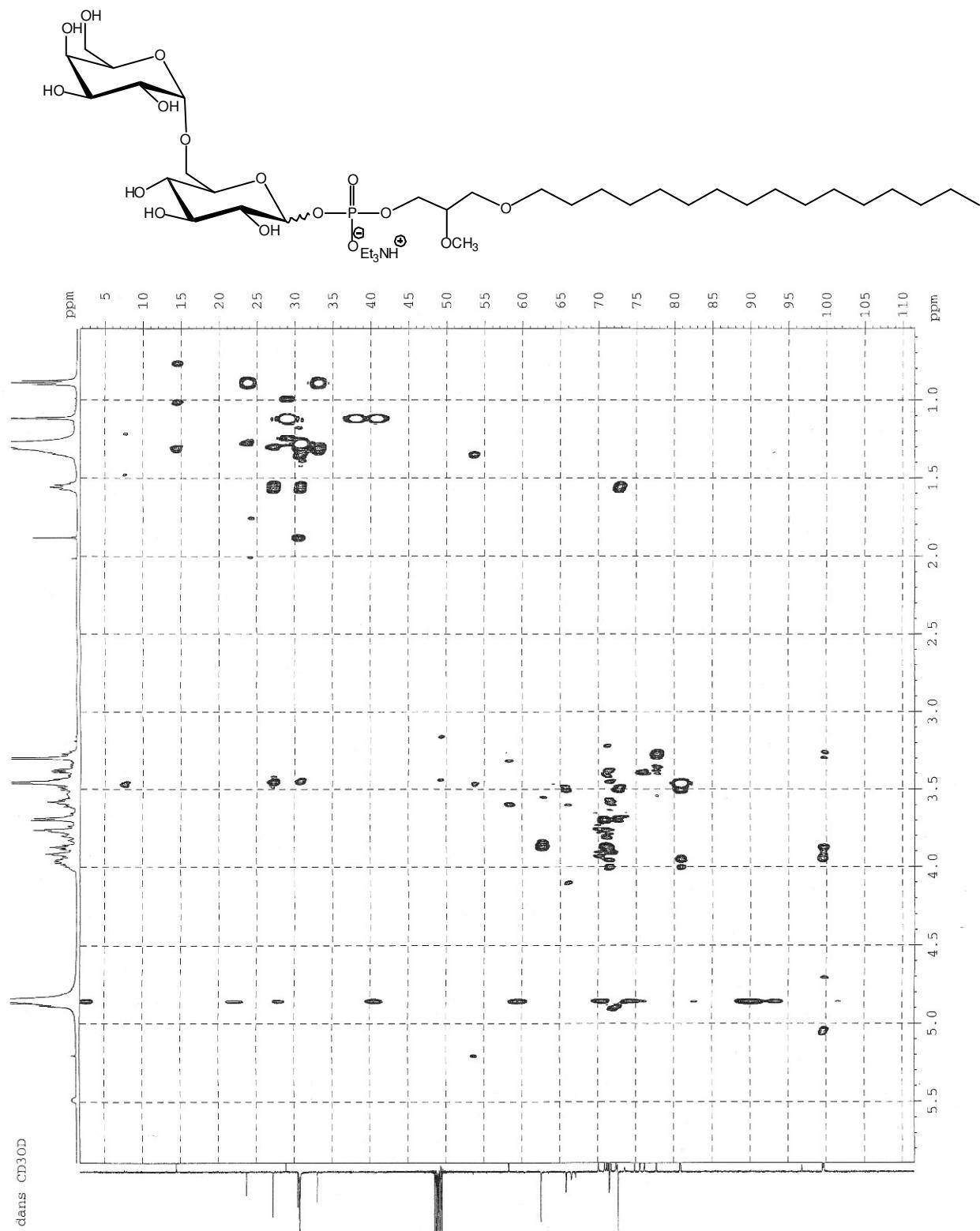


Figure S3-48: 2D-HMBC NMR ( $\text{CD}_3\text{OD}$ ) spectrum of compound 4c.

## ESI-4 IR Data

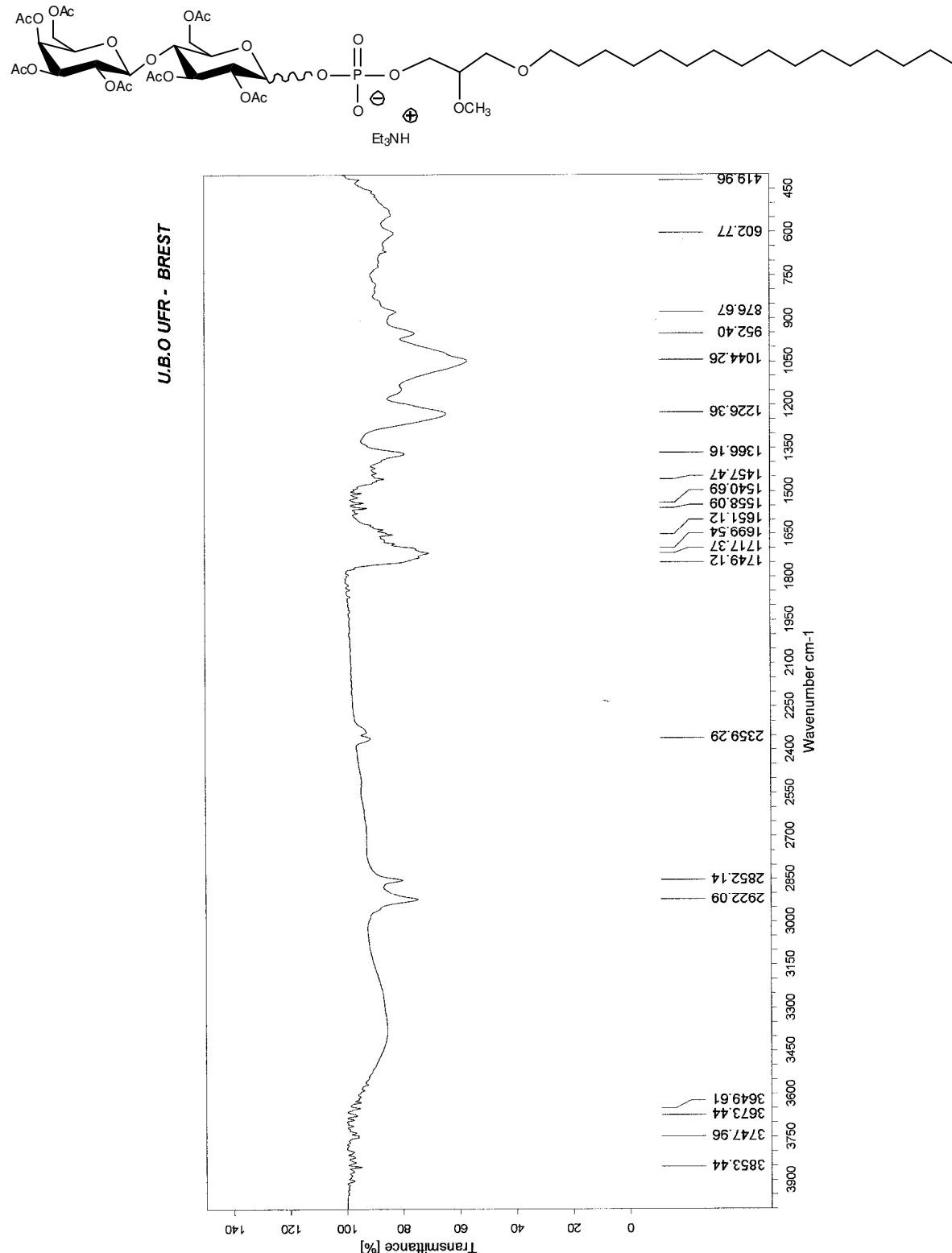


Figure S4-1: IR spectrum of compound 3a.

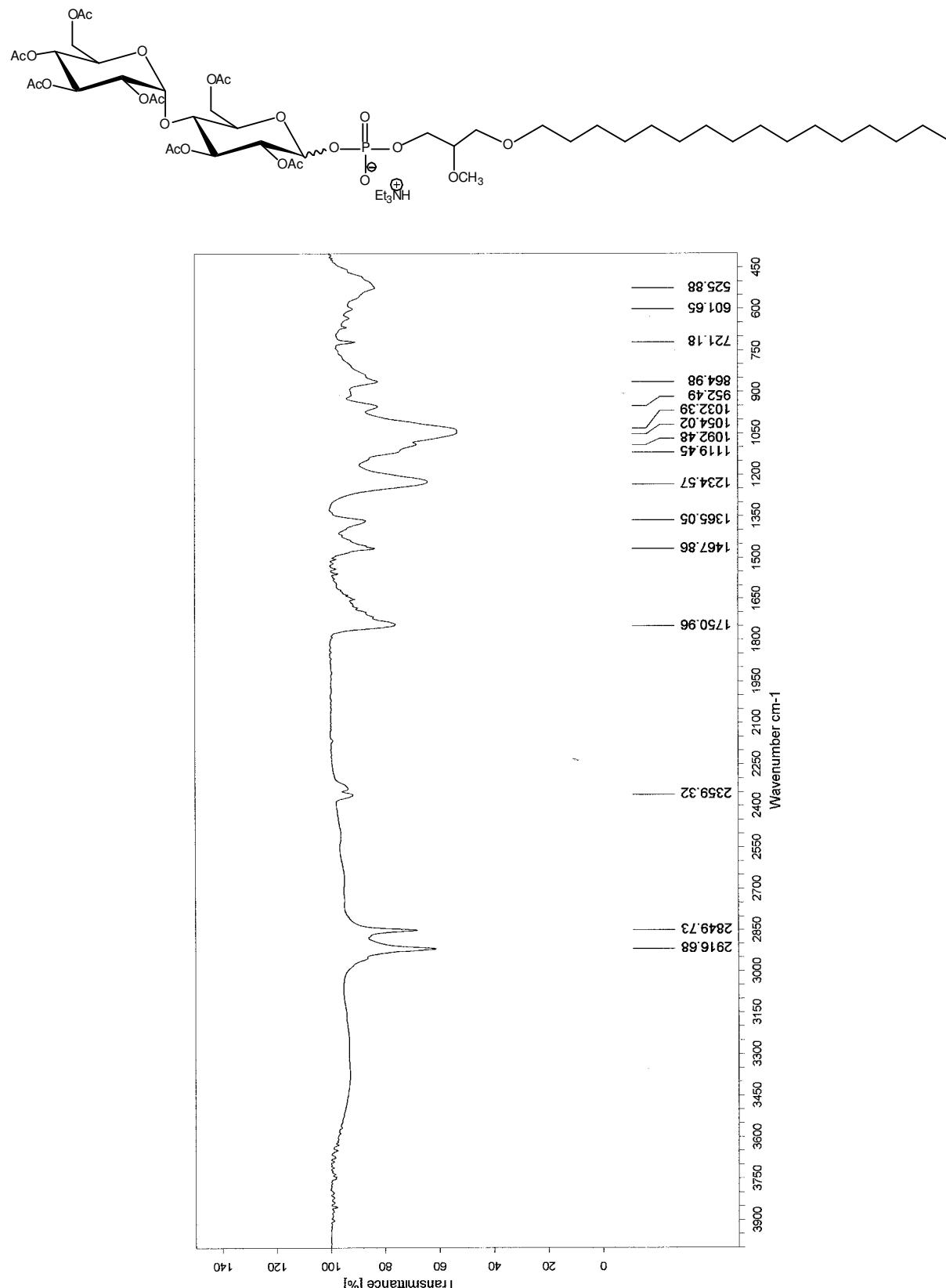


Figure S4-2: IR spectrum of compound 3b1.

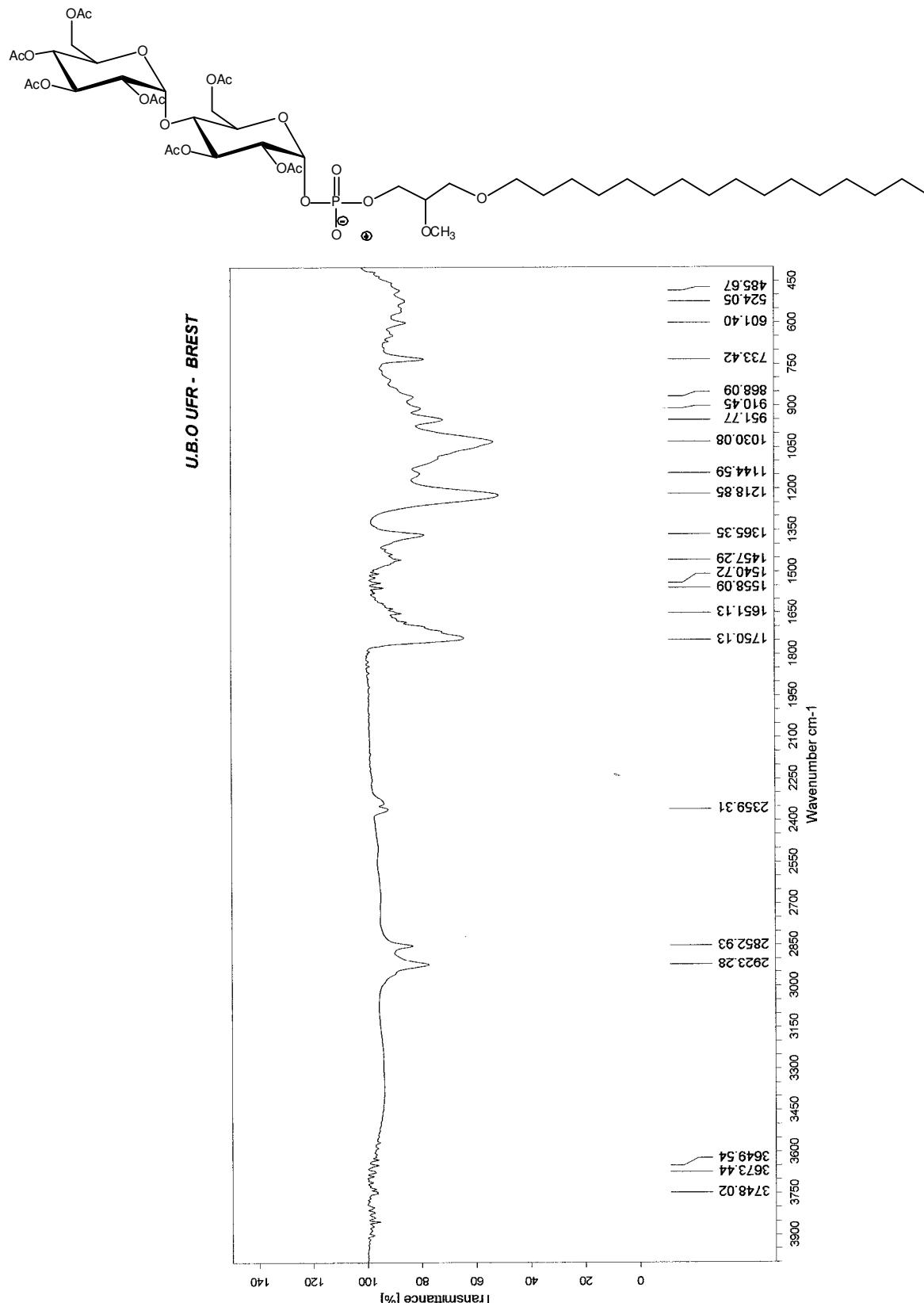


Figure S4-3: IR spectrum of compound 3b2.

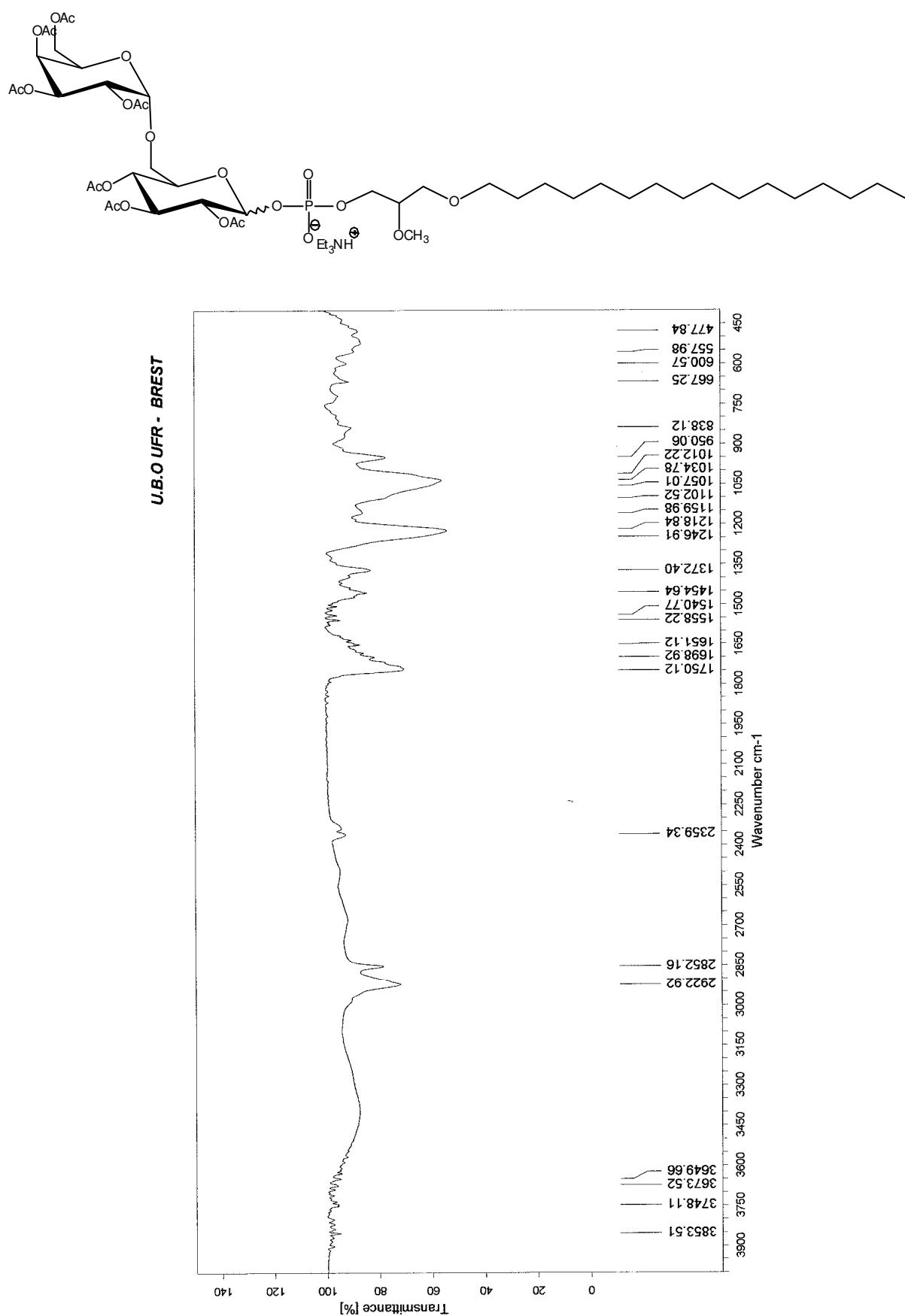
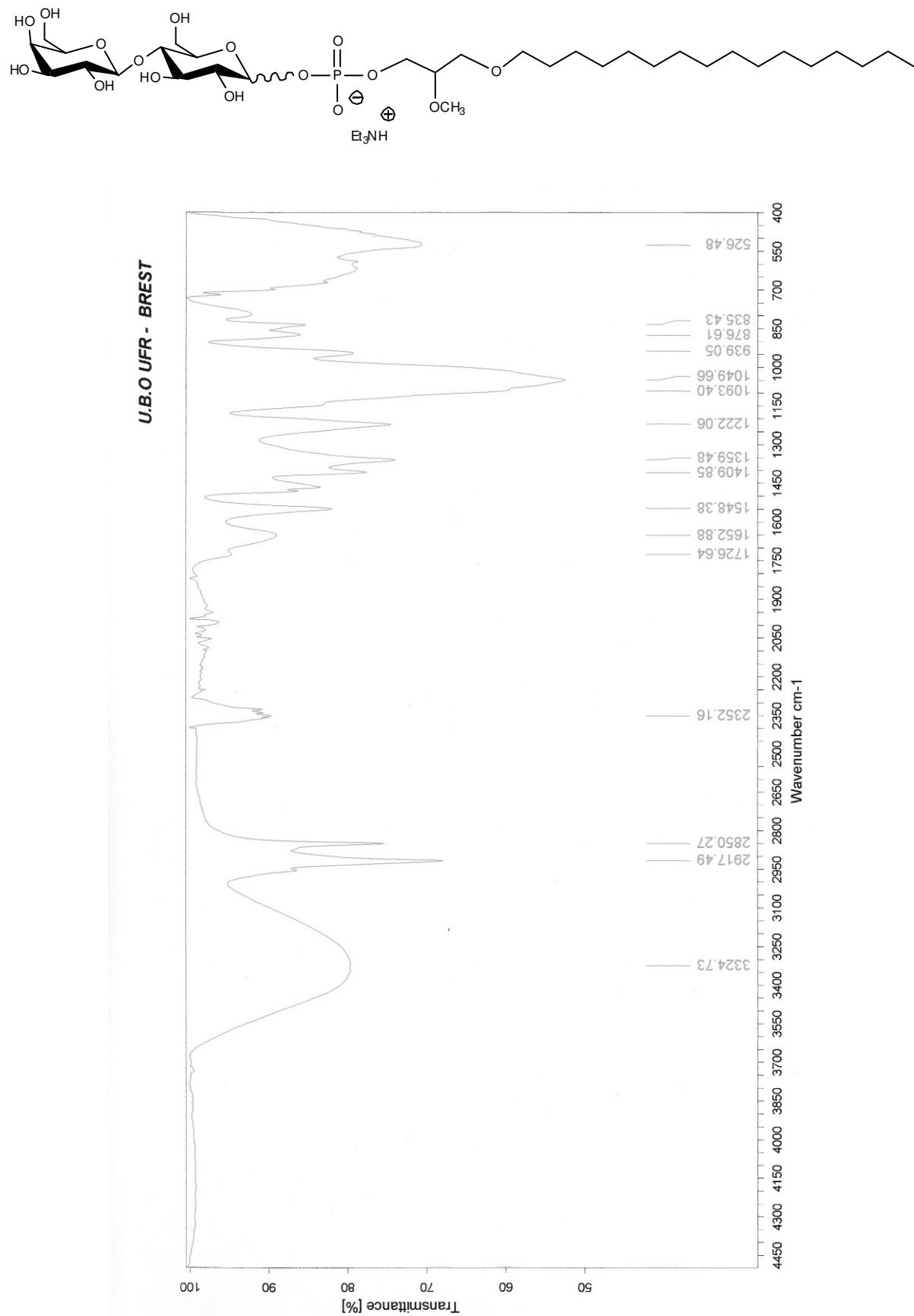


Figure S4-4: IR spectrum of compound 3c.



**Figure S4-5:** IR spectrum of compound 4a.

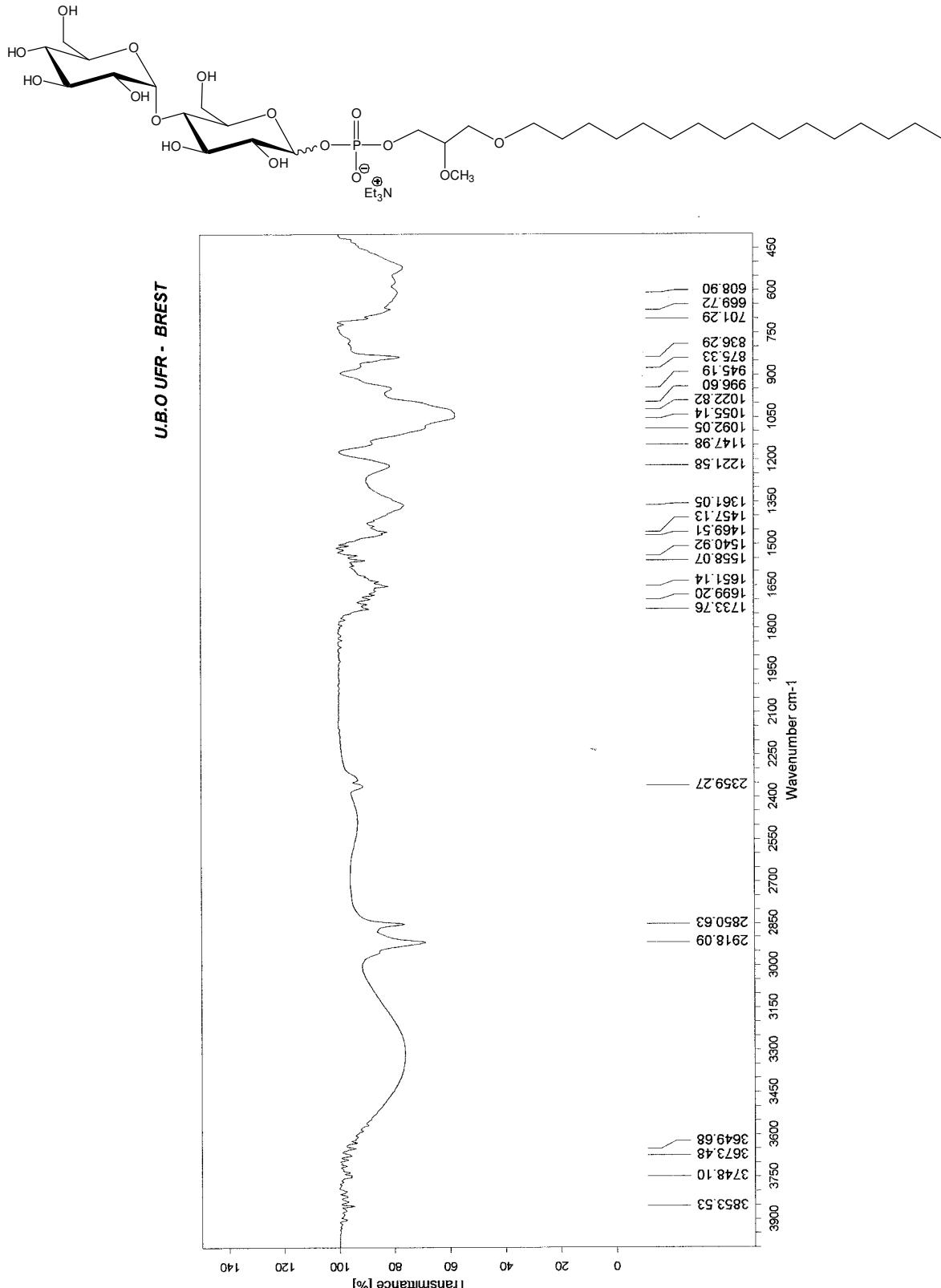


Figure S4-6: IR spectrum of compound 4b1.

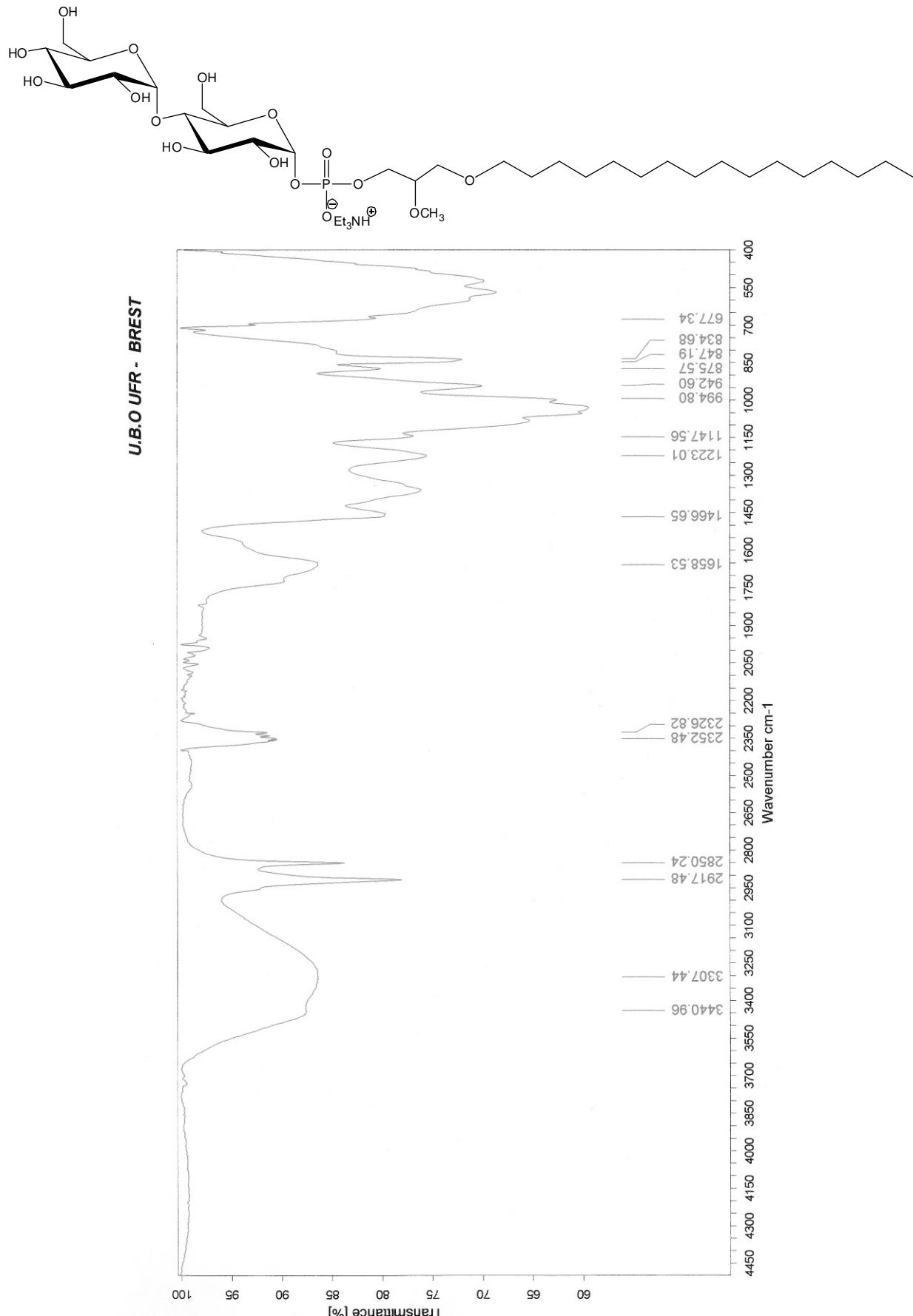


Figure S4-7: IR spectrum of compound 4b2.

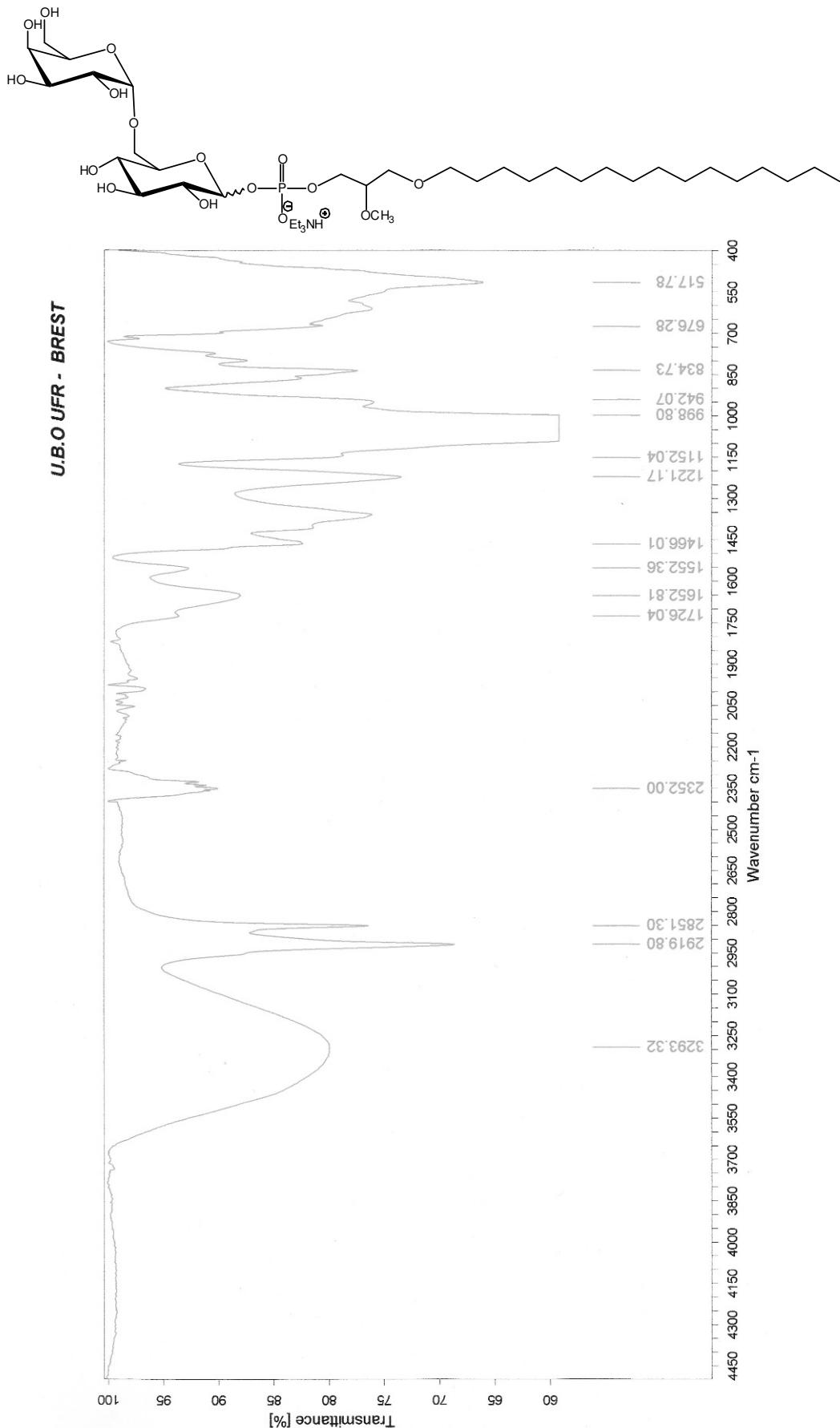


Figure S4-8: IR spectrum of compound 4c.