Supporting materials

Cationic lipophosphoramidates with two different lipid chains: synthesis and evaluation as gene carriers.

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Summary

S1 NMR spectra (non-symmetric phosphite – method 1 and 2)

Method 1

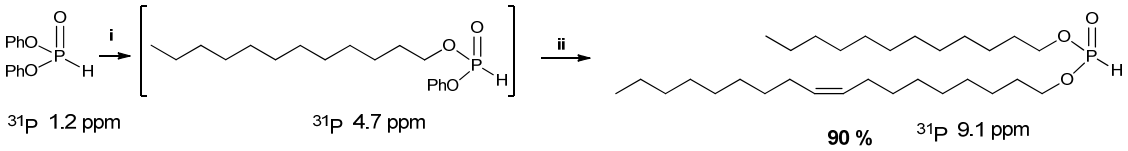


Figure S1-1: Attempts to produce non-symmetric dialkylphosphite from diphenylphosphite. i) pyridine (0.9 eq) ; $C_{12}H_{25}OH$ (0.9 eq), 20°C, 2h ; ii) pyridine (1 eq) ; Oleyl-OH (1 eq) 3h, 20°C.

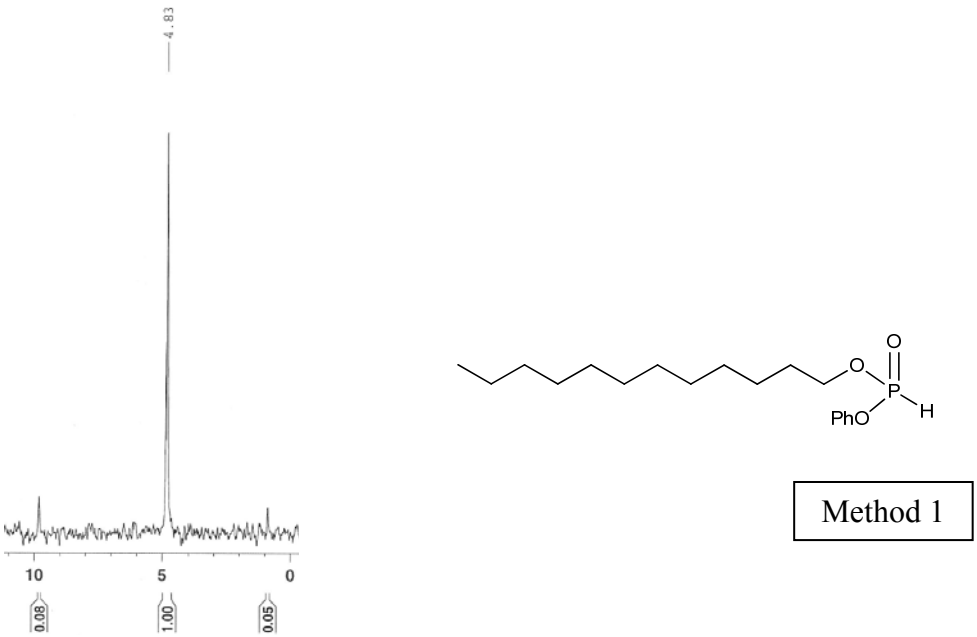


Figure S1-2 : ^{31}P NMR of alkylarylphosphite synthesised by method **1**.

Method 2

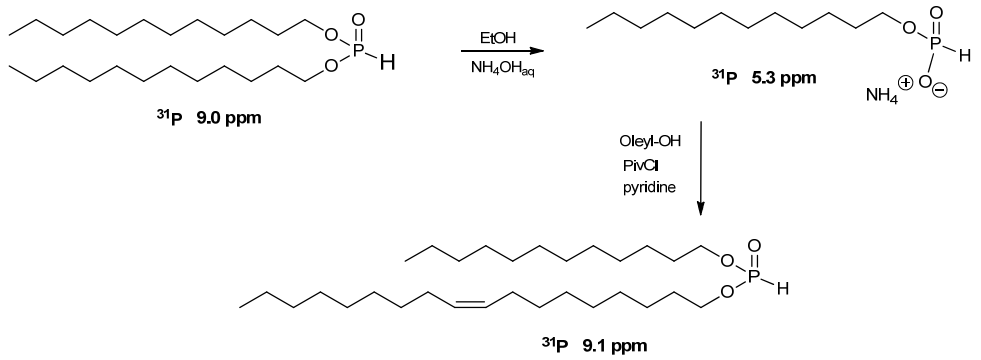


Figure S1-3 : Synthesis of non-symmetric dialkylphosphite from symmetric dialkylphosphite.

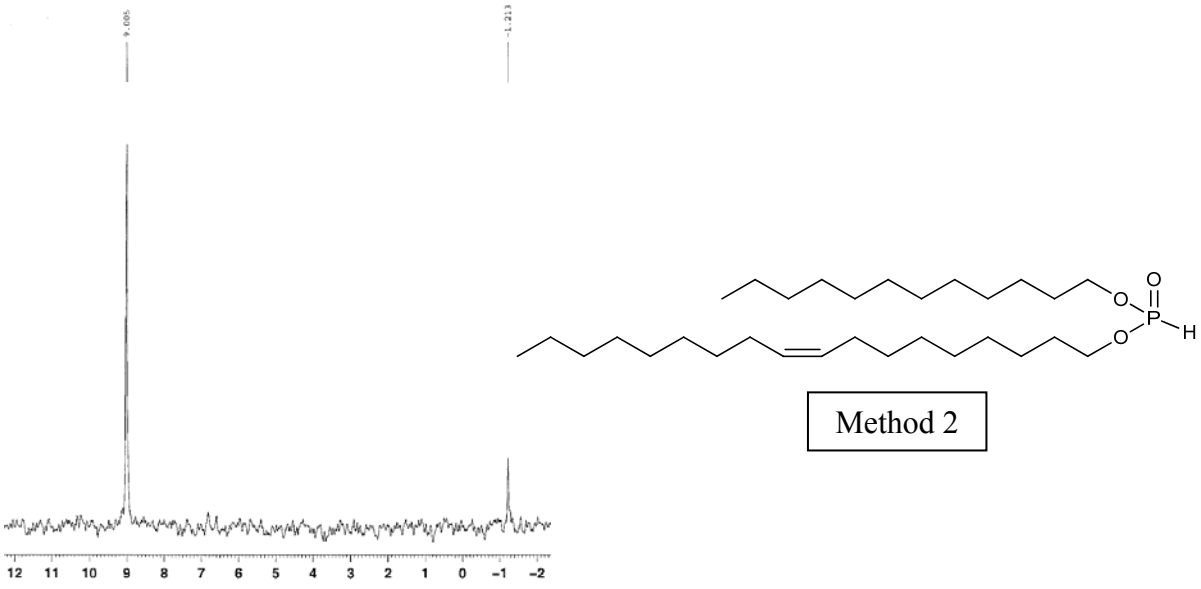


Figure S1-4 : ^{31}P NMR of non-symmetric dialkylphosphite synthesised by method **2**.

S2 NMR spectra ($POCl_3$ method)

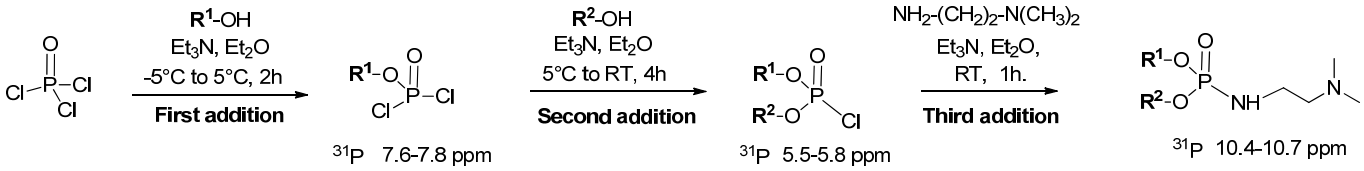


Figure S2-1 : One-pot procedure for the synthesis of non-symmetric lipophosphoramide (R1≠R2).

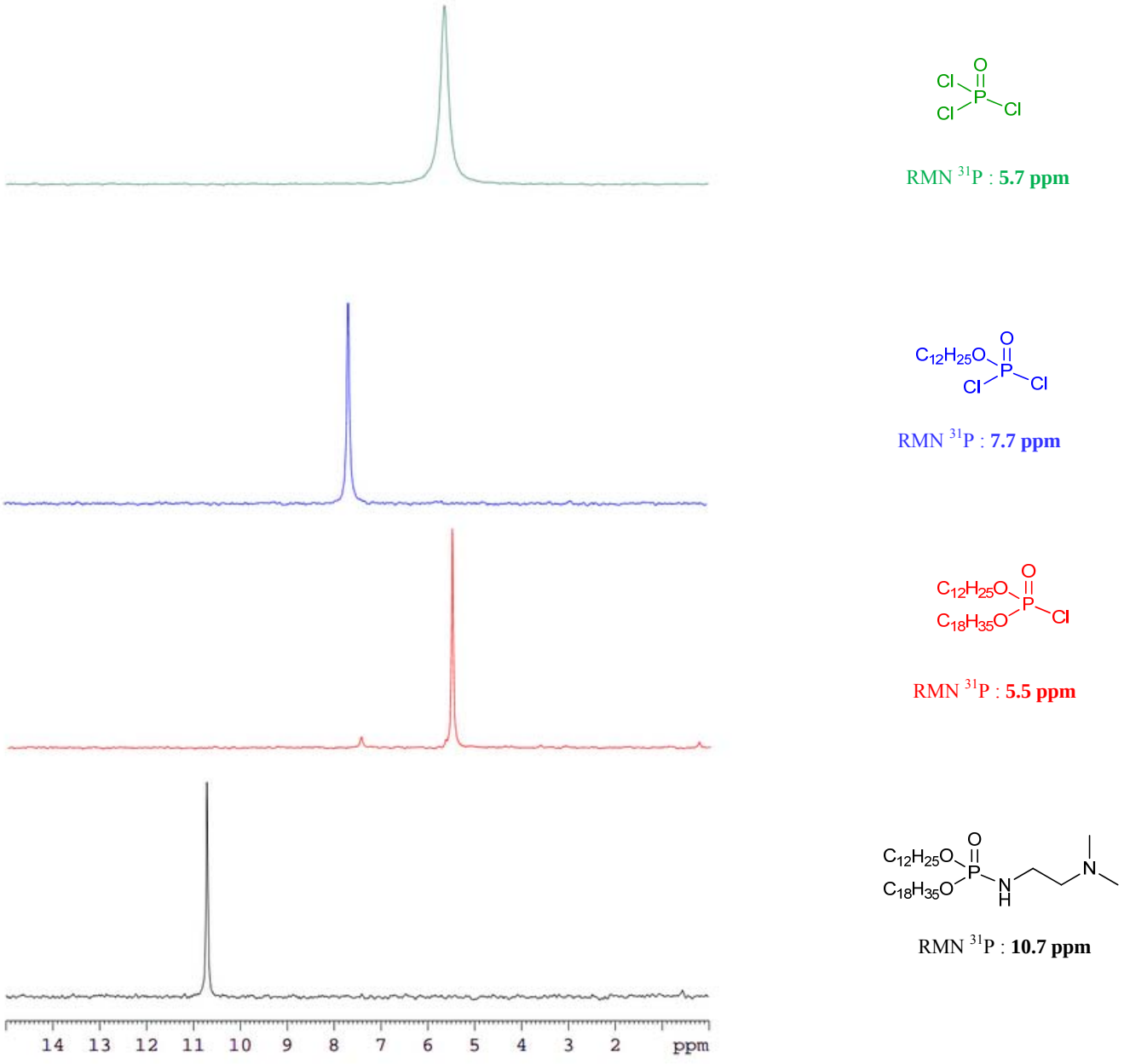


Figure S2-2 : ^{31}P NMR ($CDCl_3$) spectrum of **$POCl_3$ method**

S3 NMR spectra

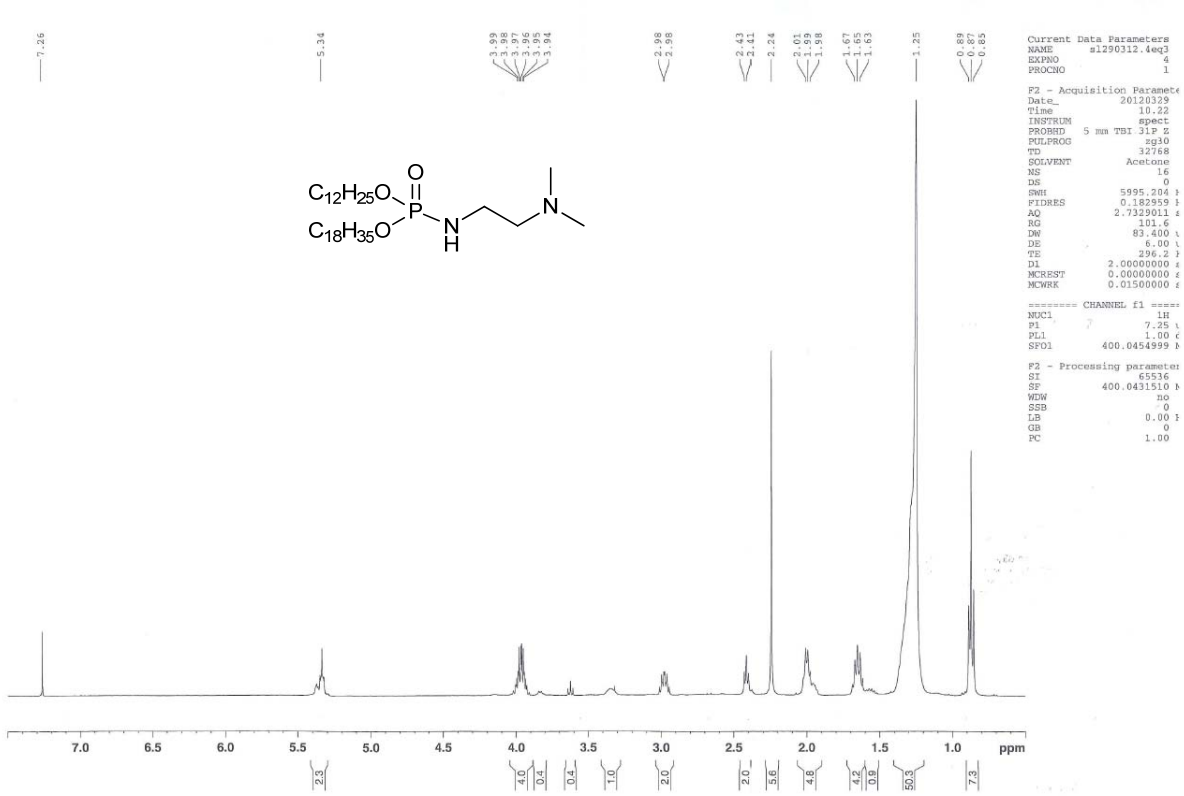


Figure S3-1: ^{1}H NMR ($CDCl_3$) spectrum of compound **1**.

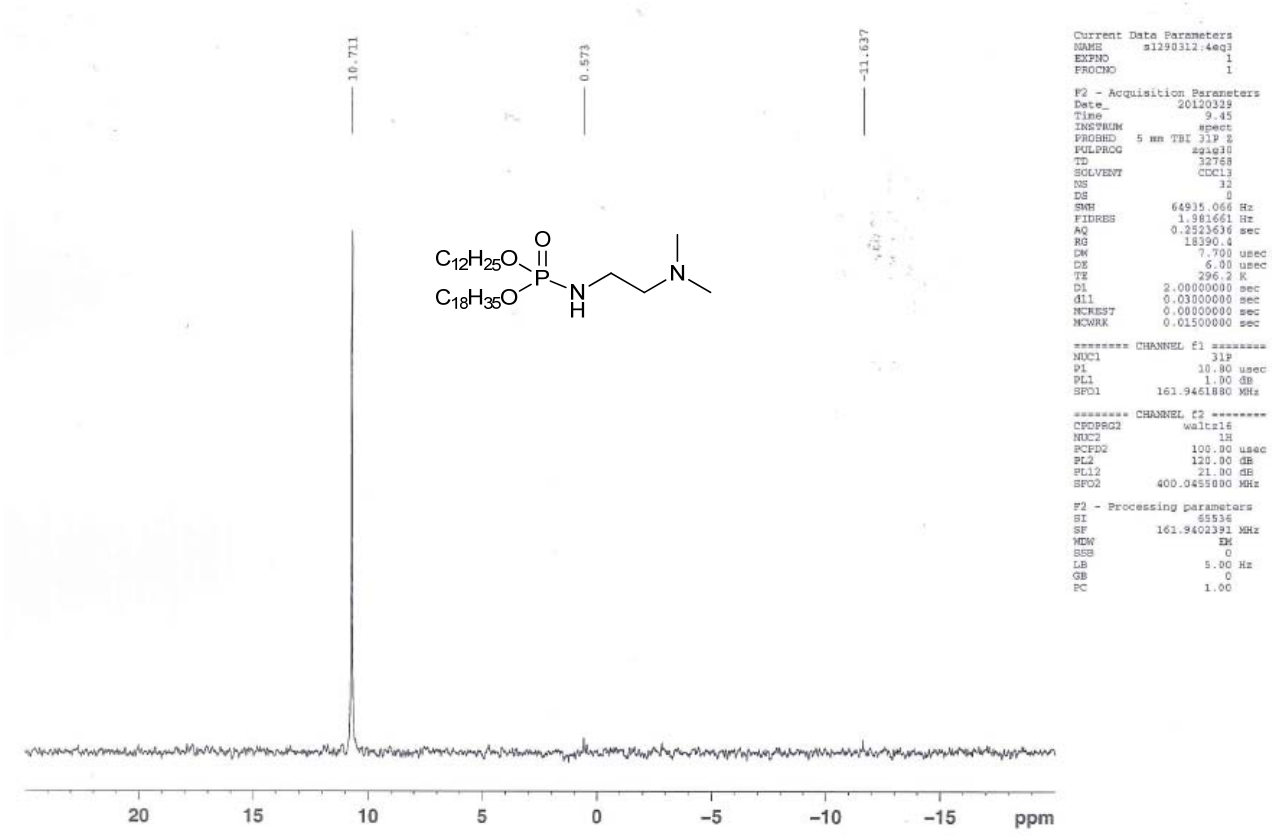


Figure S3-2: ^{31}P NMR ($CDCl_3$) spectrum of compound **1**.

Supporting materials

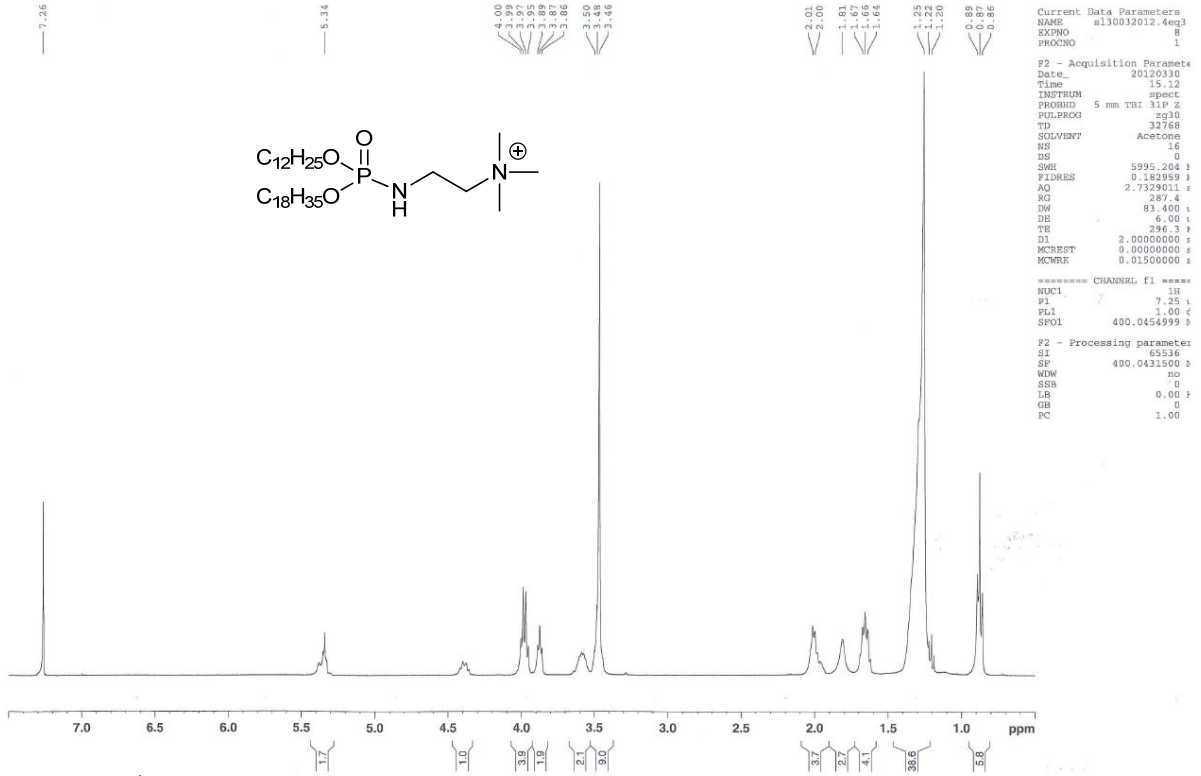


Figure S3-3: ^{1}H NMR ($CDCl_3$) spectrum of compound **2**.

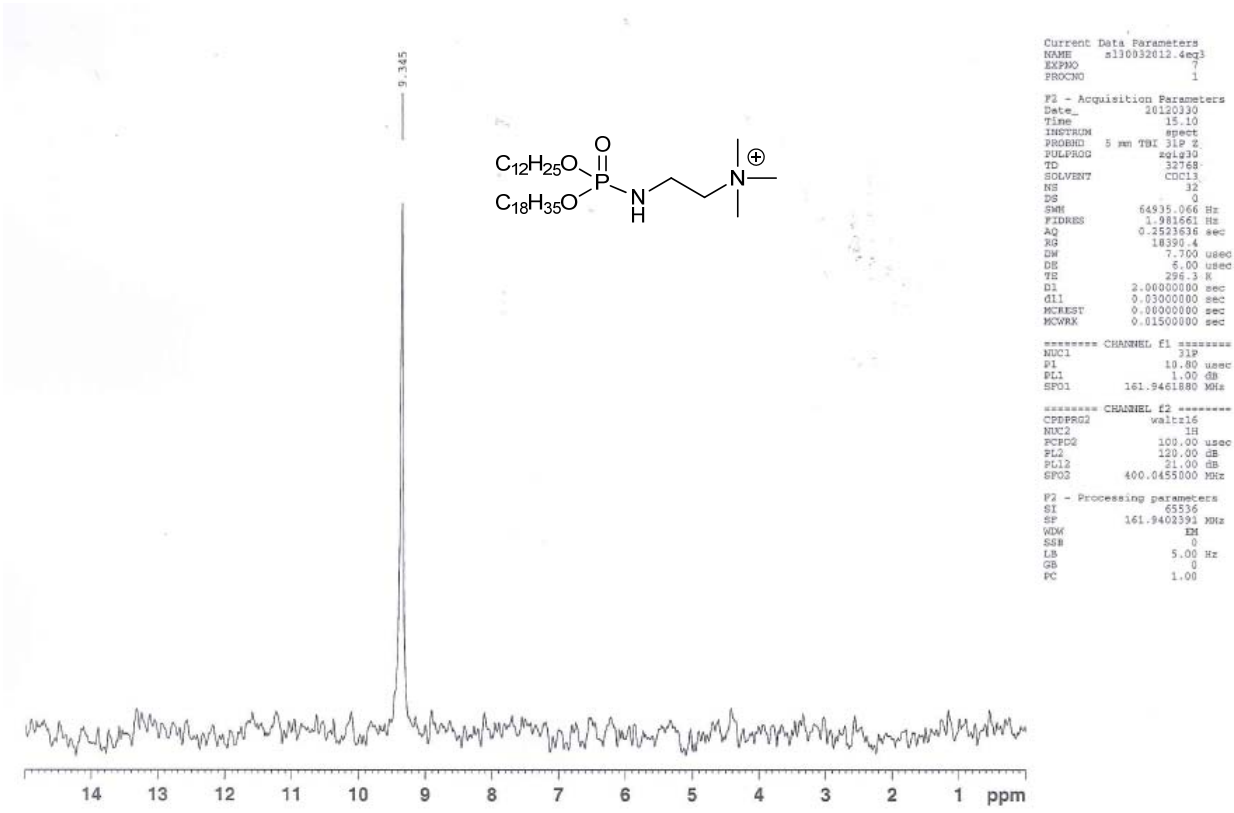


Figure S3-4: ^{31}P NMR ($CDCl_3$) spectrum of compound **2**.

Supporting materials

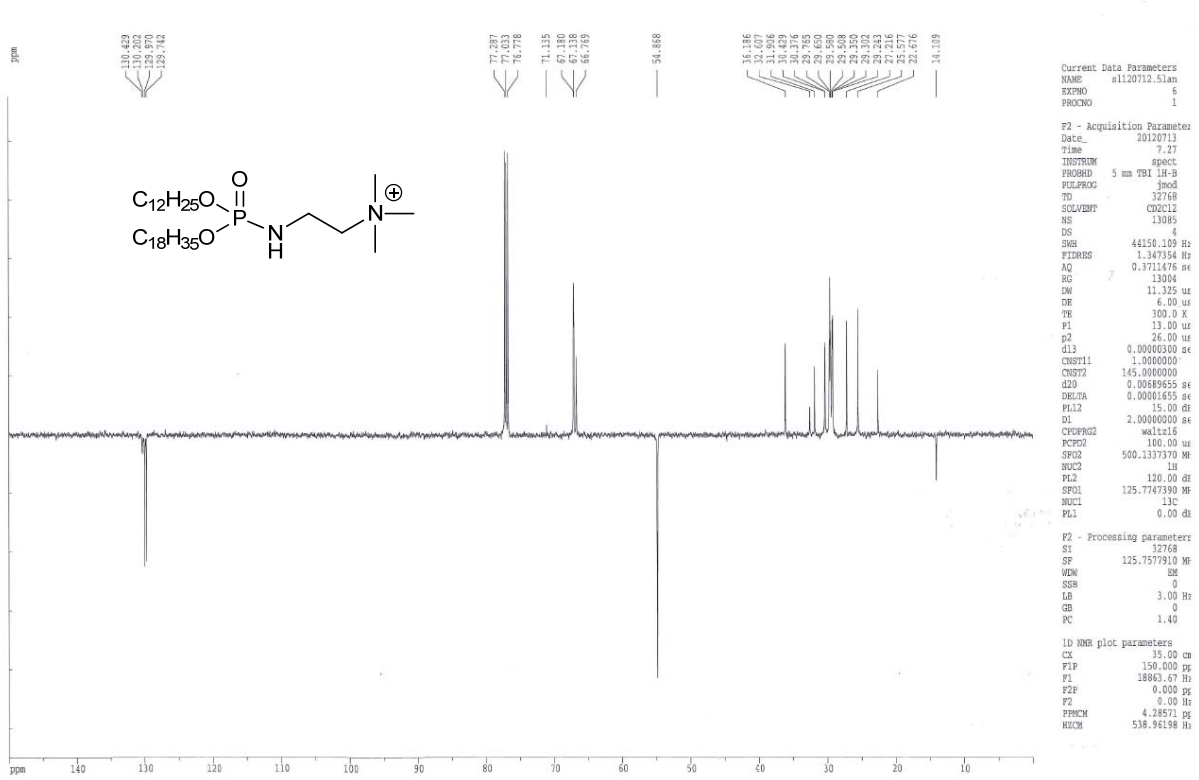


Figure S3-5: ^{13}C jmod ($CDCl_3$) spectrum of compound **2**.

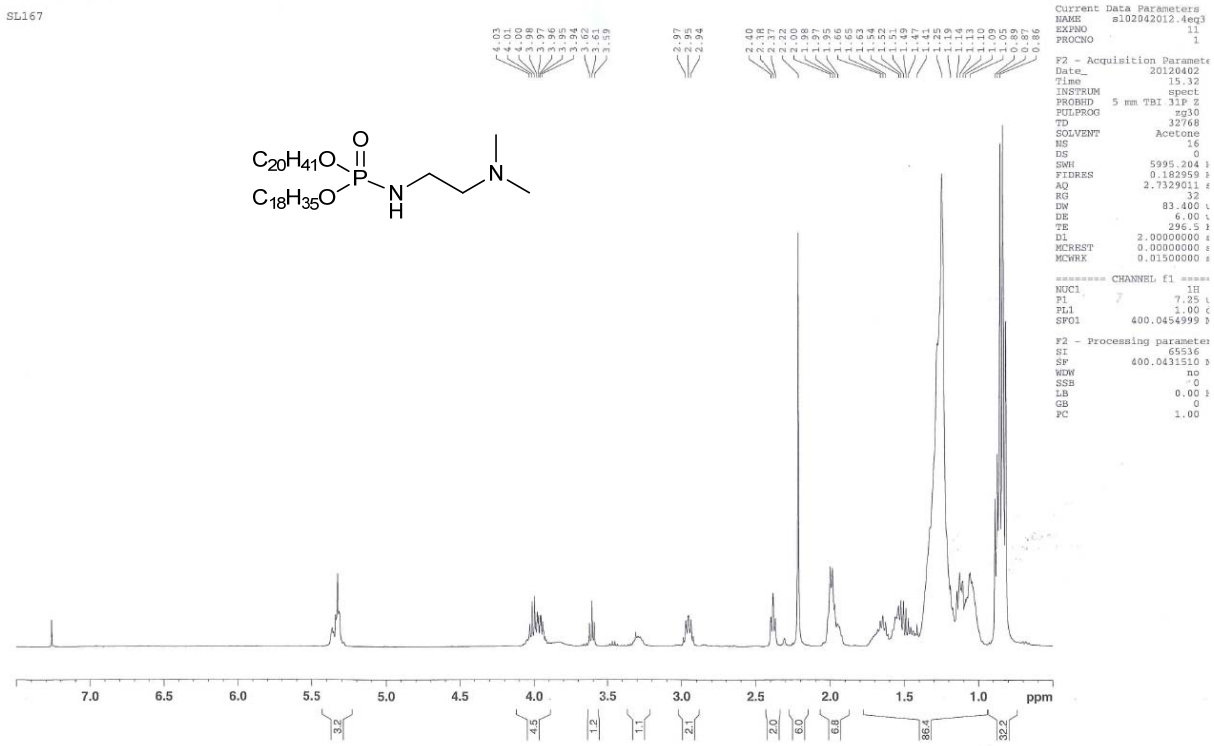


Figure S3-6: ^{1}H NMR ($CDCl_3$) spectrum of compound **3**.

Supporting materials

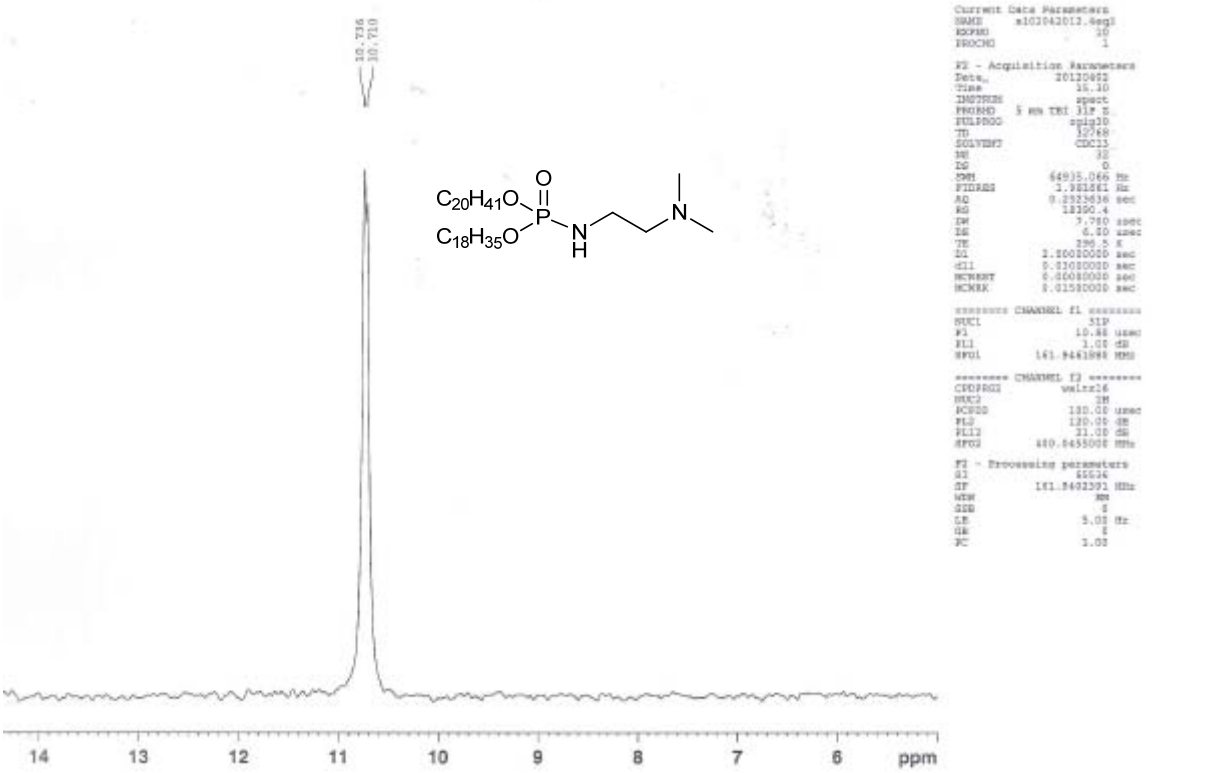


Figure S3-7: ^{31}P NMR ($CDCl_3$) spectrum of compound **3**.

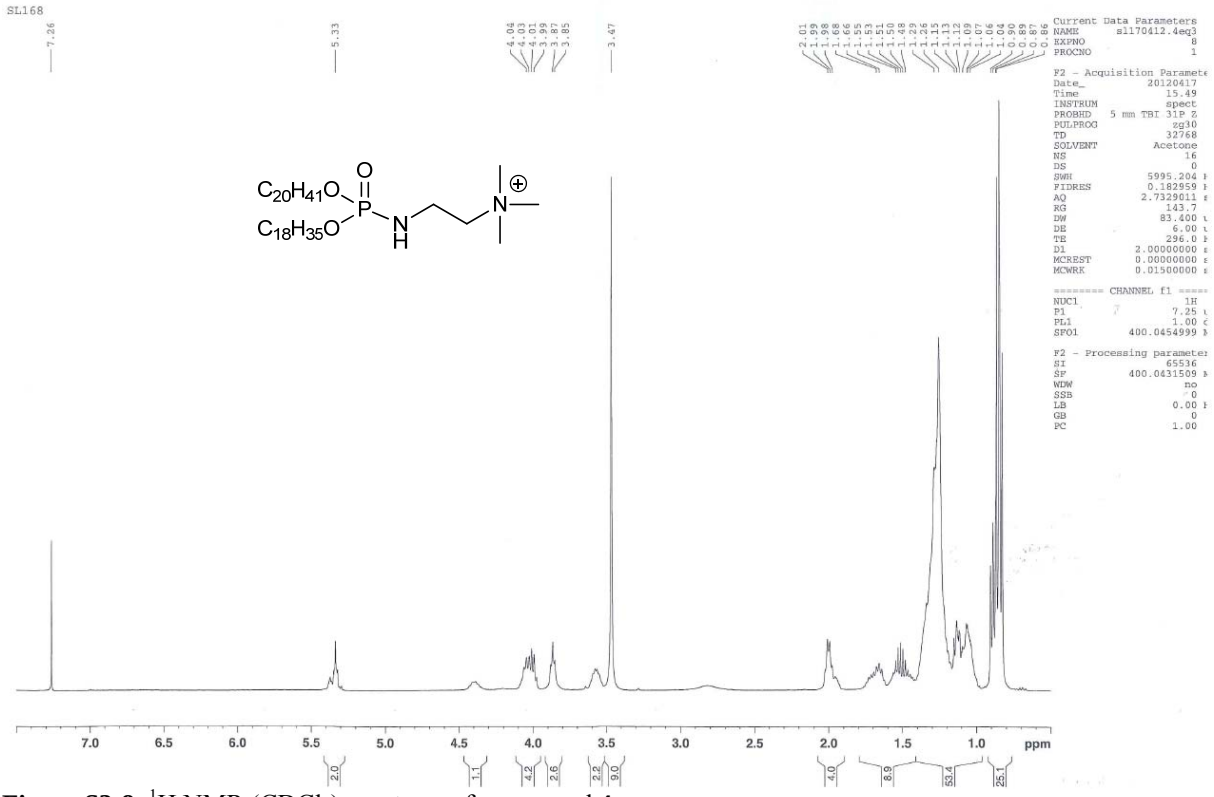


Figure S3-8: ^{1}H NMR ($CDCl_3$) spectrum of compound **4**.

Supporting materials

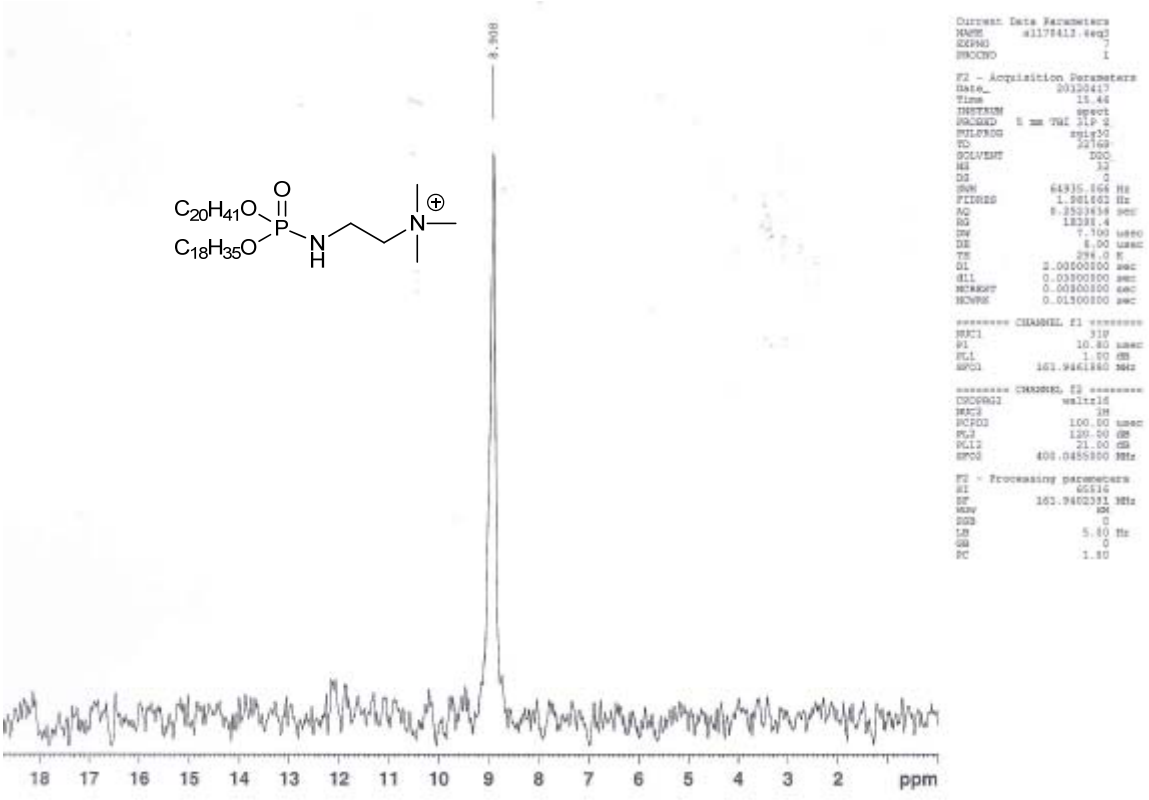


Figure S3-9: ^{31}P NMR ($CDCl_3$) spectrum of compound **4**.

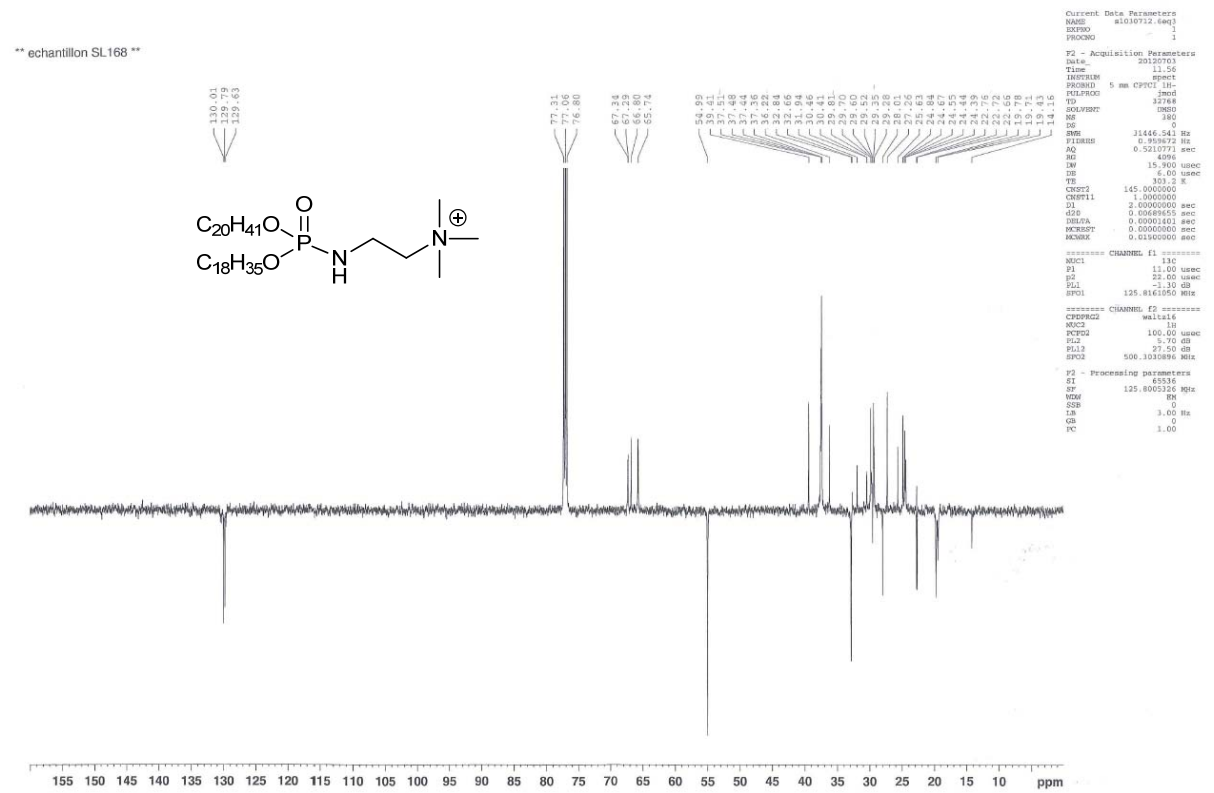


Figure S3-10: ^{13}C jmod ($CDCl_3$) spectrum of compound **4**.

Supporting materials

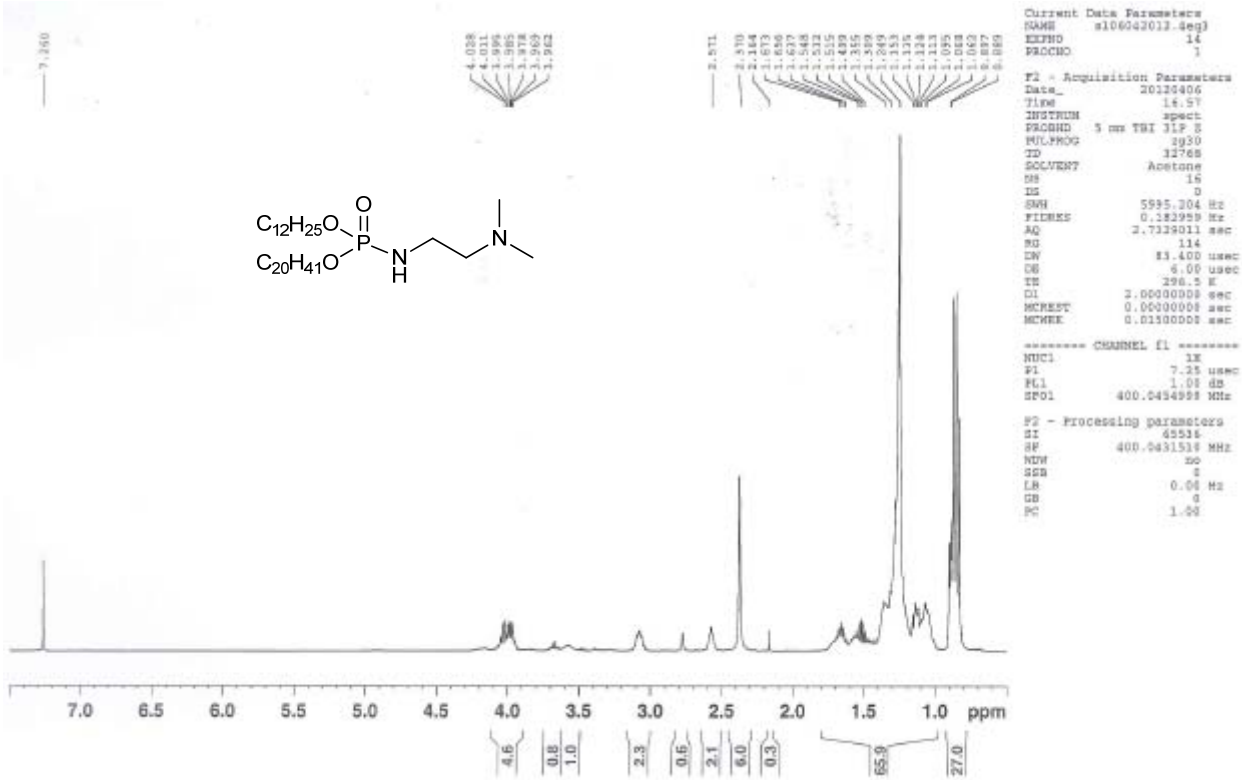


Figure S3-11: ^{1}H NMR ($CDCl_3$) spectrum of compound **5**.

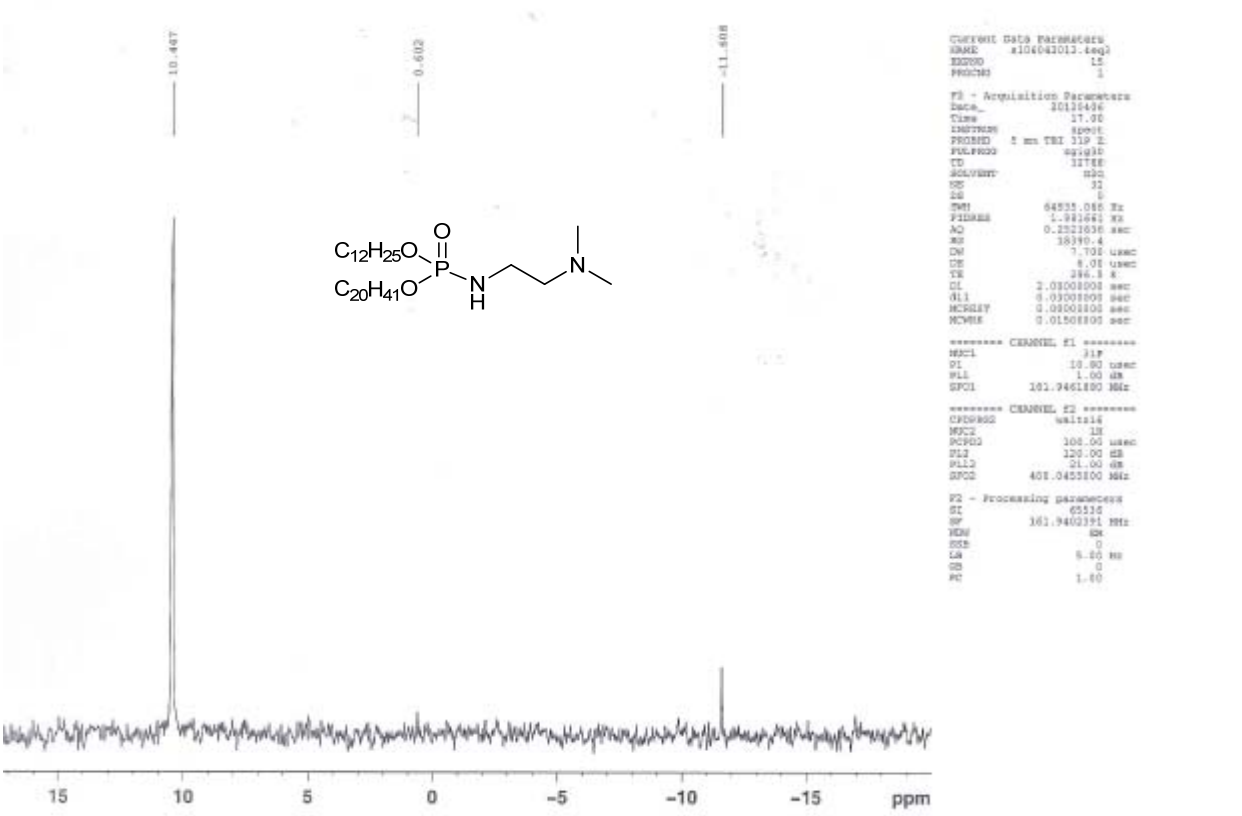


Figure S3-12: ^{31}P NMR ($CDCl_3$) spectrum of compound **5**.

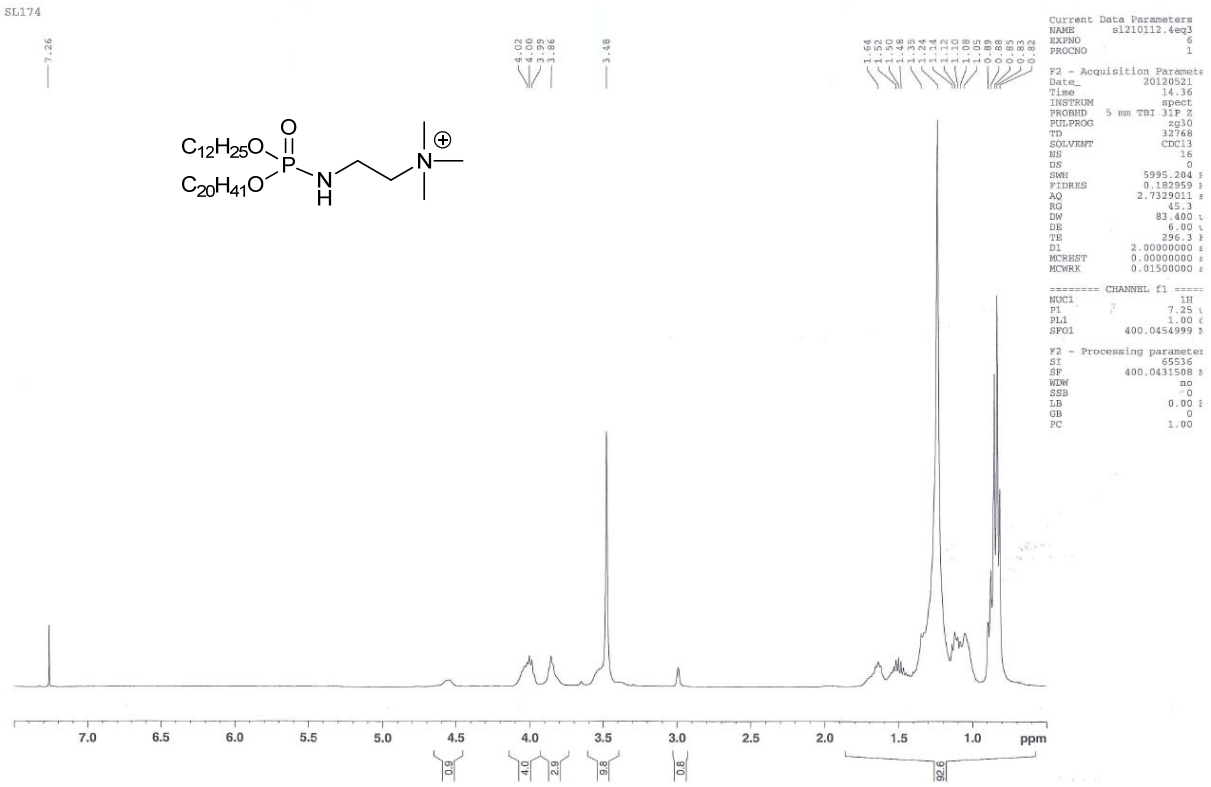


Figure S3-13: ^{1}H NMR ($CDCl_3$) spectrum of compound **6**.

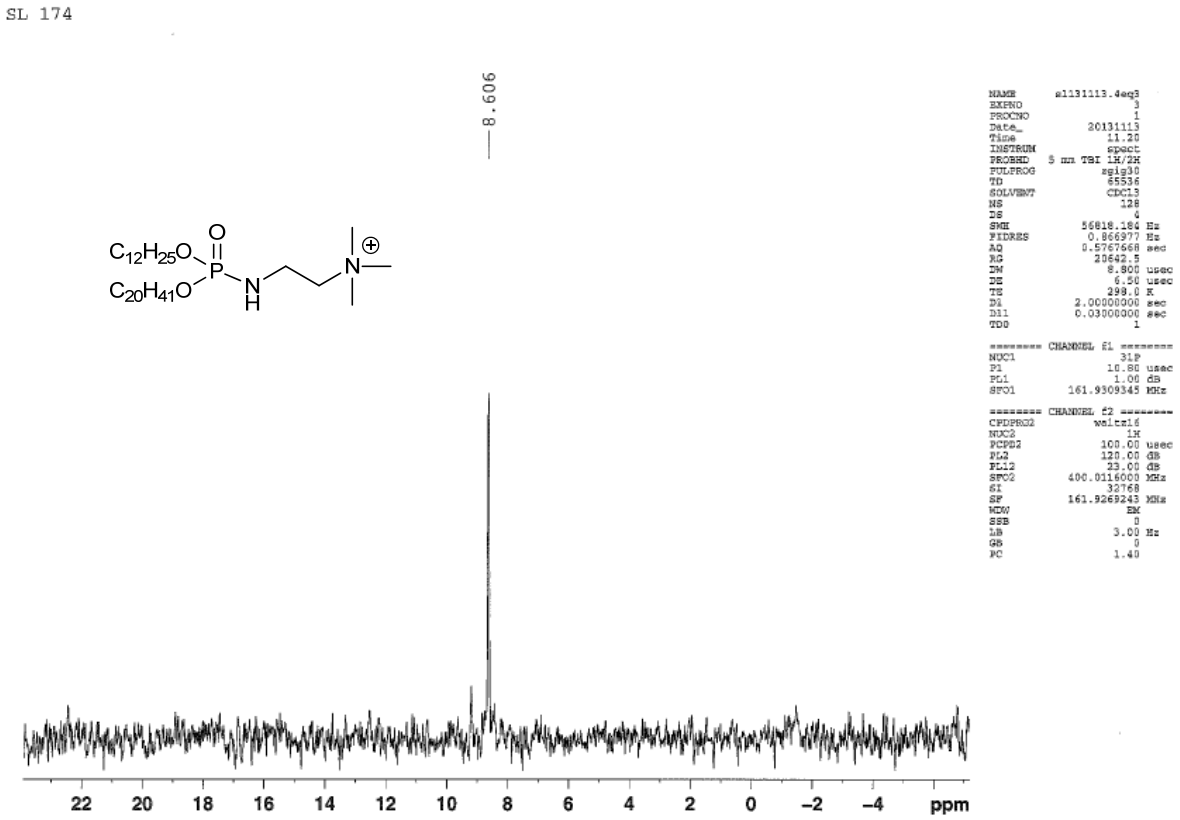


Figure S3-14: ^{31}P NMR ($CDCl_3$) spectrum of compound **6**.

Supporting materials

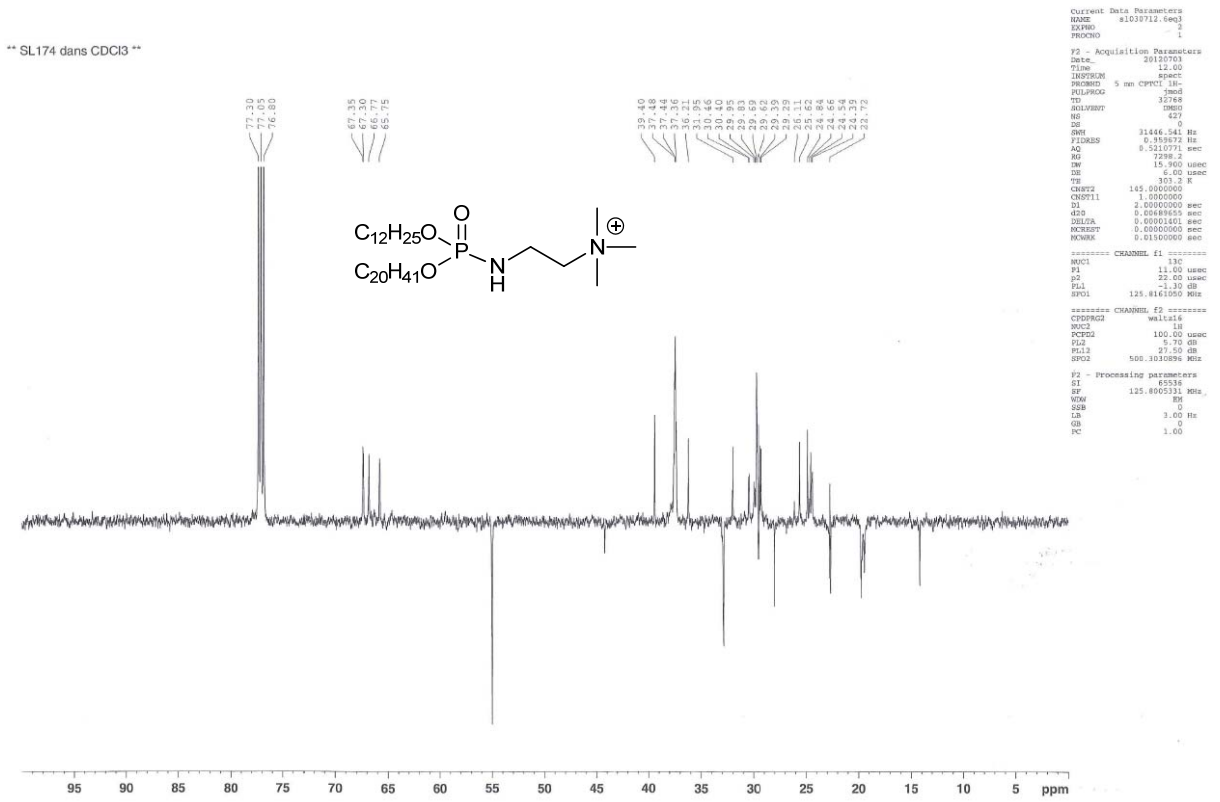


Figure S3-15: ^{13}C jmod ($CDCl_3$) spectrum of compound **6**.

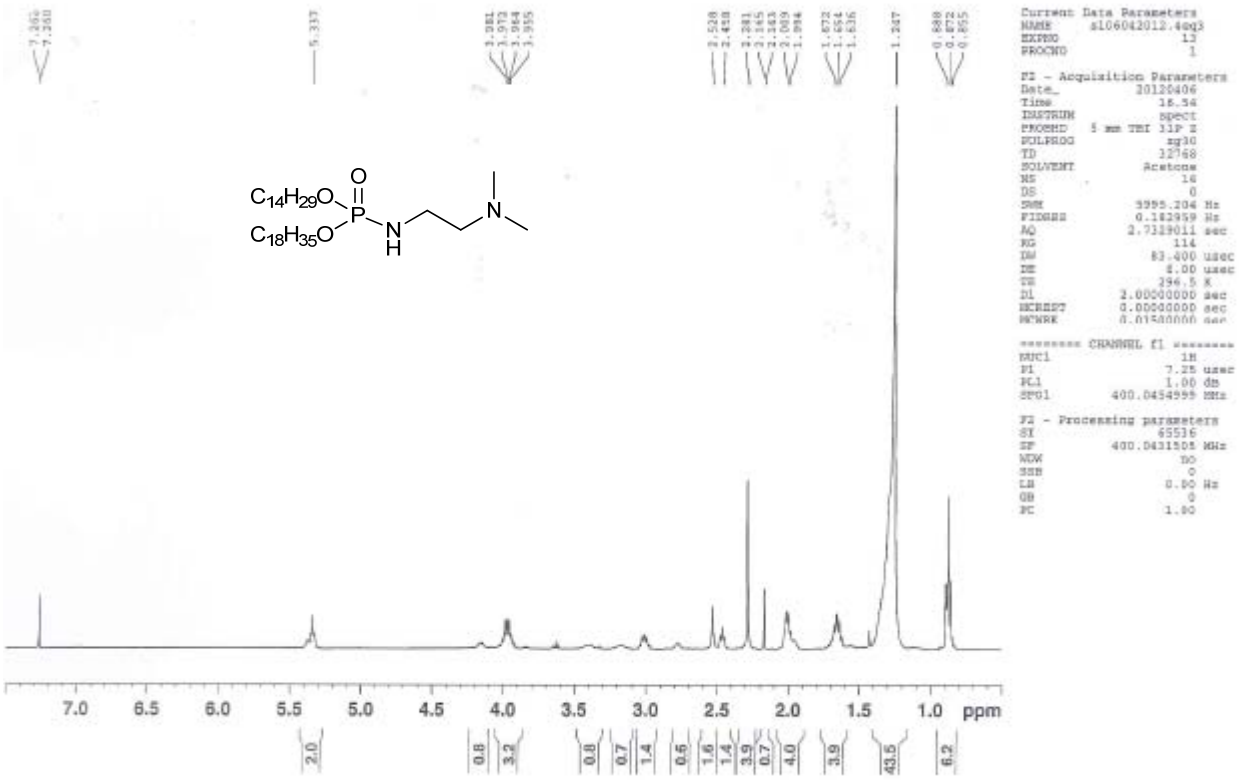


Figure S3-16: ^{1}H NMR ($CDCl_3$) spectrum of compound **7**.

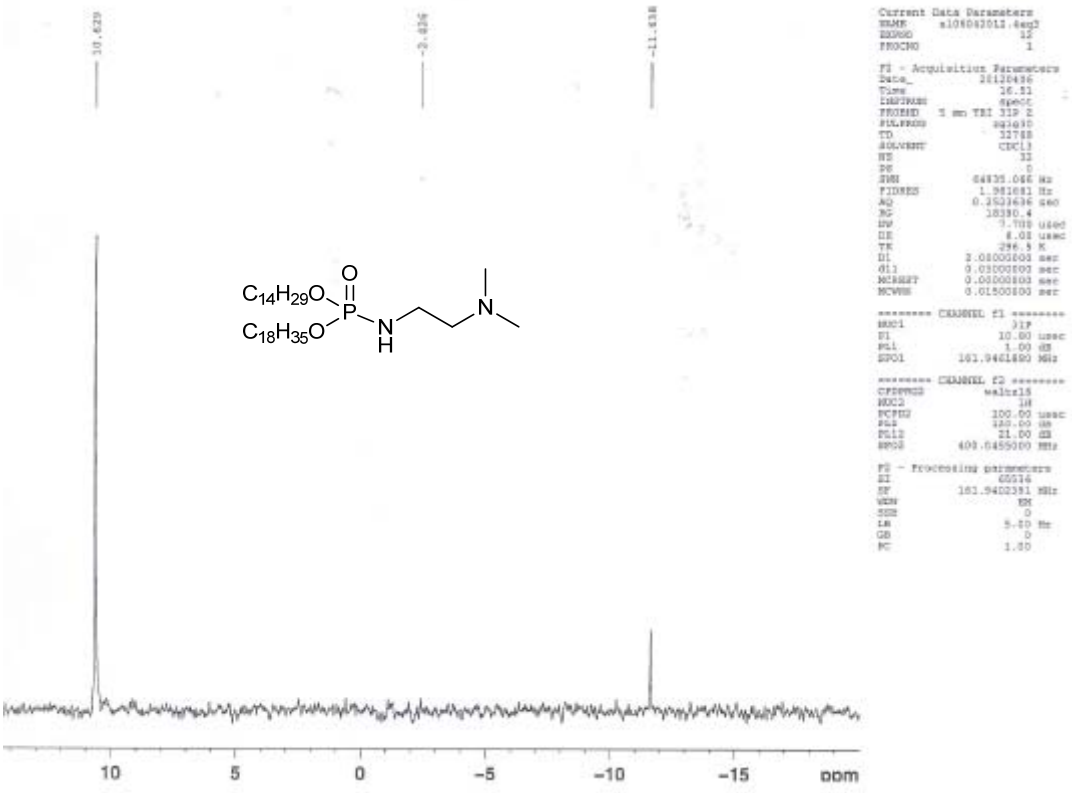


Figure S3-17: ^{31}P NMR ($CDCl_3$) spectrum of compound **7**.

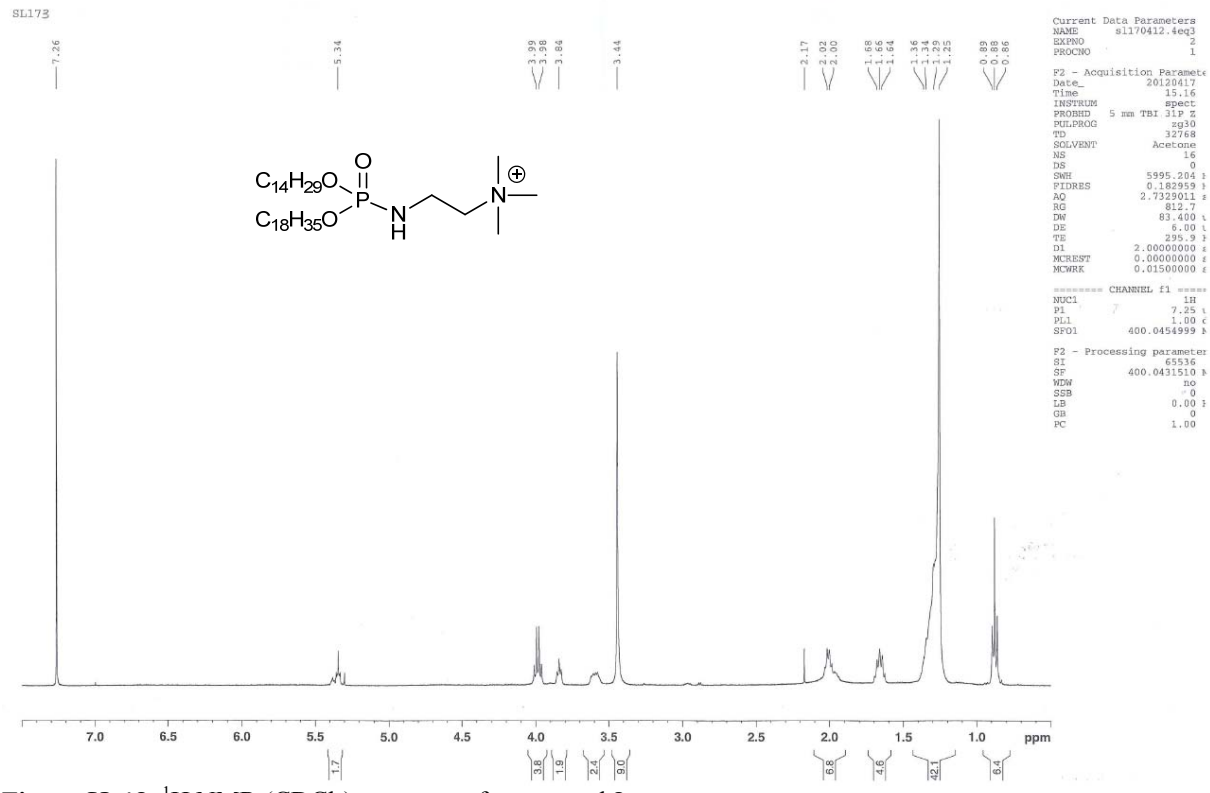


Figure S3-18: ^{1}H NMR ($CDCl_3$) spectrum of compound **8**.

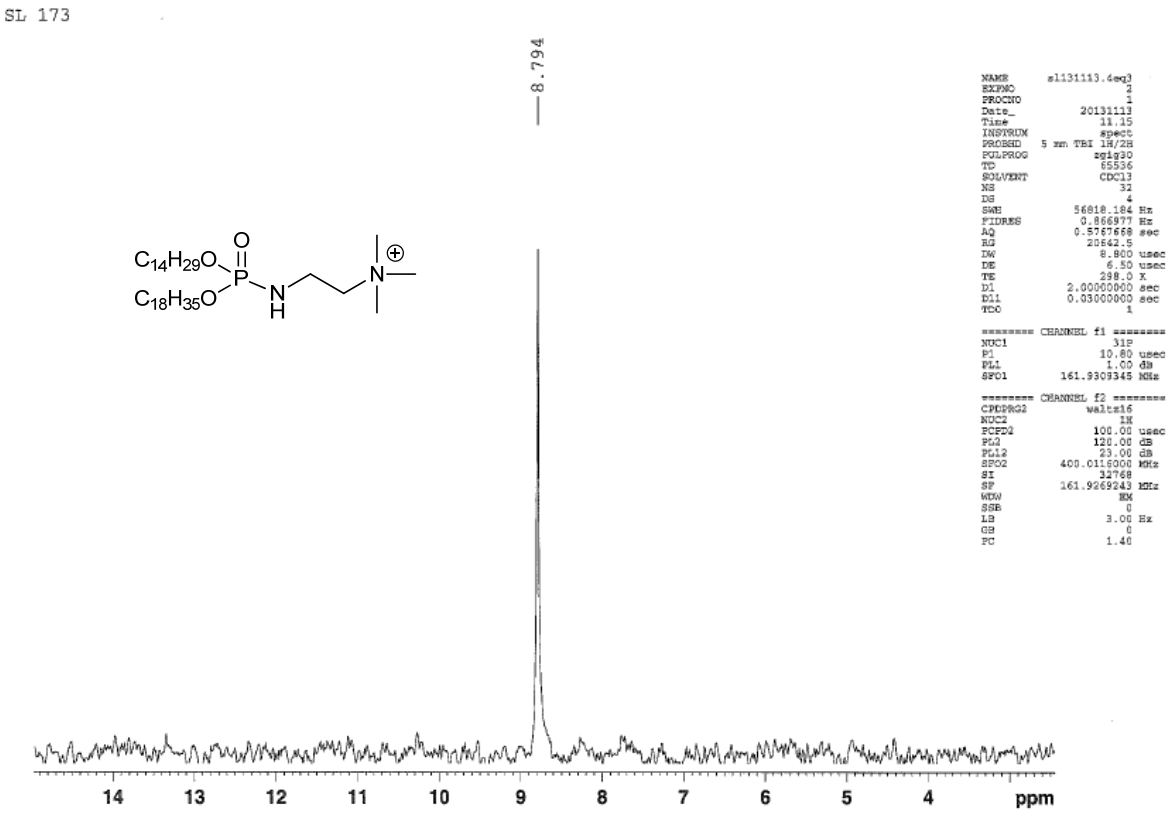


Figure S3-19 : ^{31}P NMR ($CDCl_3$) spectrum of compound **8**.

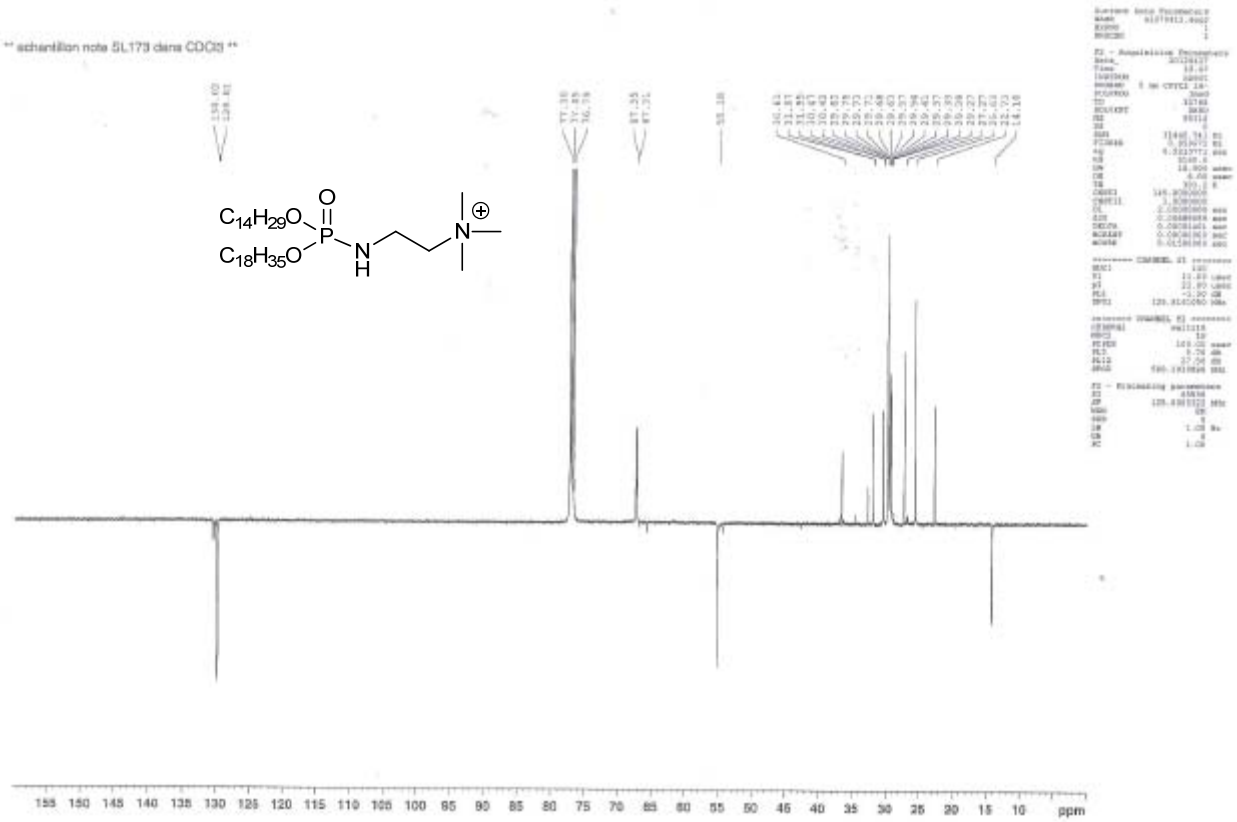


Figure S3-20: ^{13}C jmod ($CDCl_3$) spectrum of compound **8**.

Supporting materials

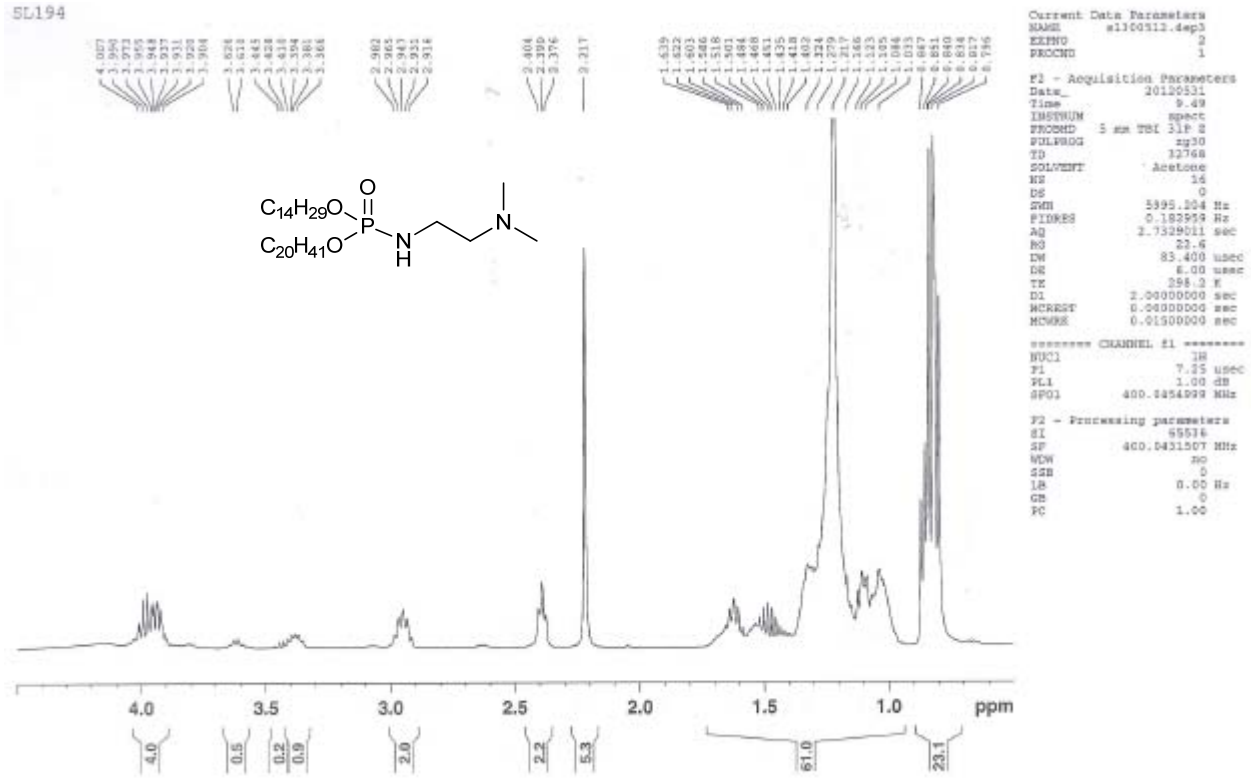


Figure S3-21: ^{1}H NMR ($CDCl_3$) spectrum of compound **9**.

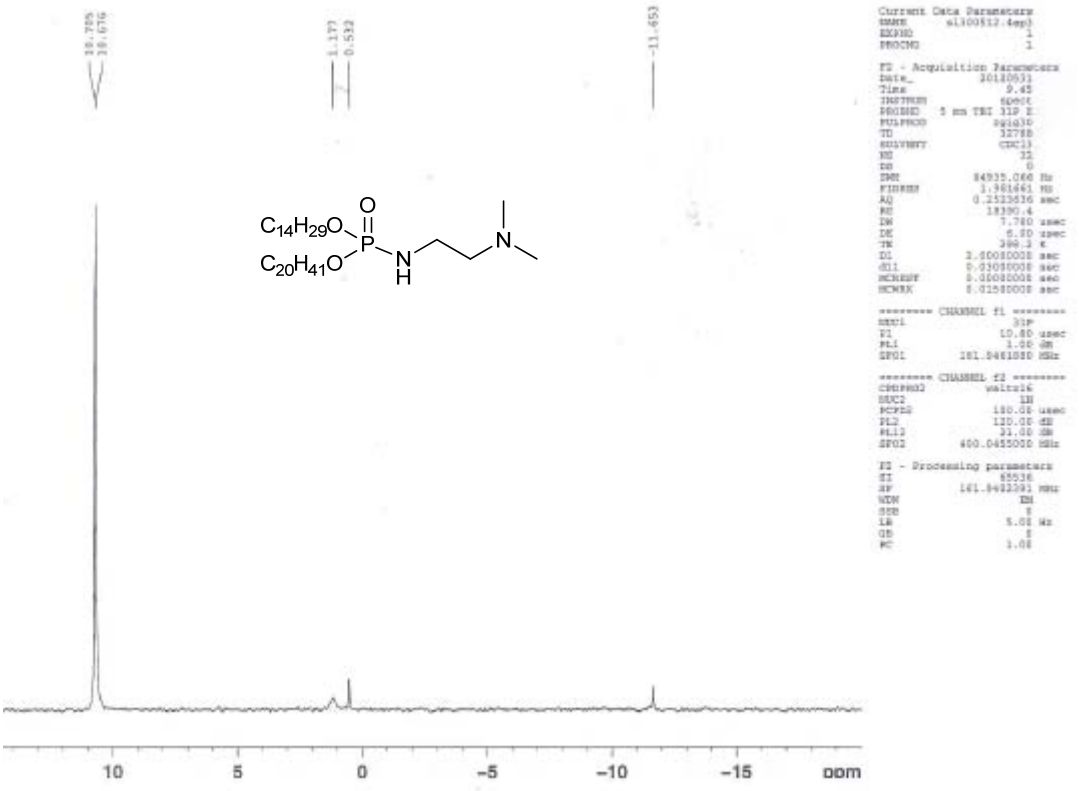


Figure S3-22: ^{31}P NMR ($CDCl_3$) spectrum of compound **9**.

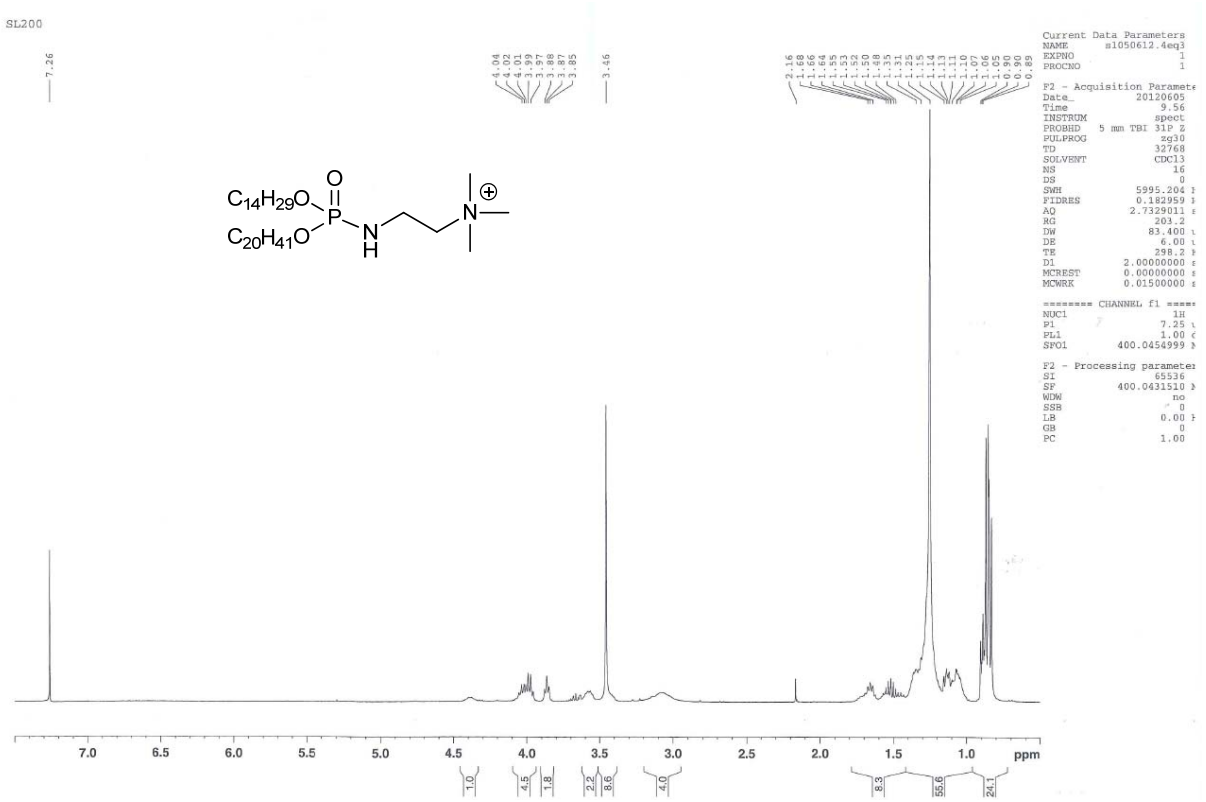


Figure S3-23: ^{1}H NMR ($CDCl_3$) spectrum of compound **10**.

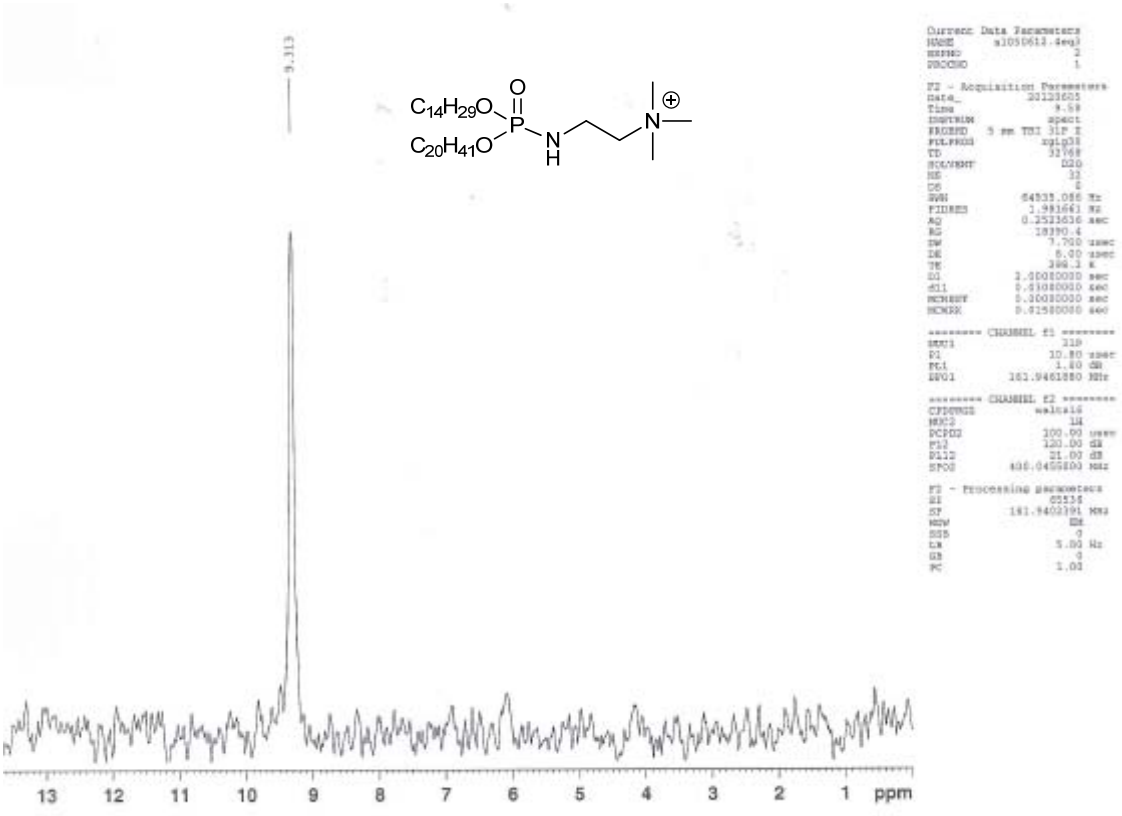


Figure S3-24: ^{31}P NMR ($CDCl_3$) spectrum of compound **10**.

Supporting materials

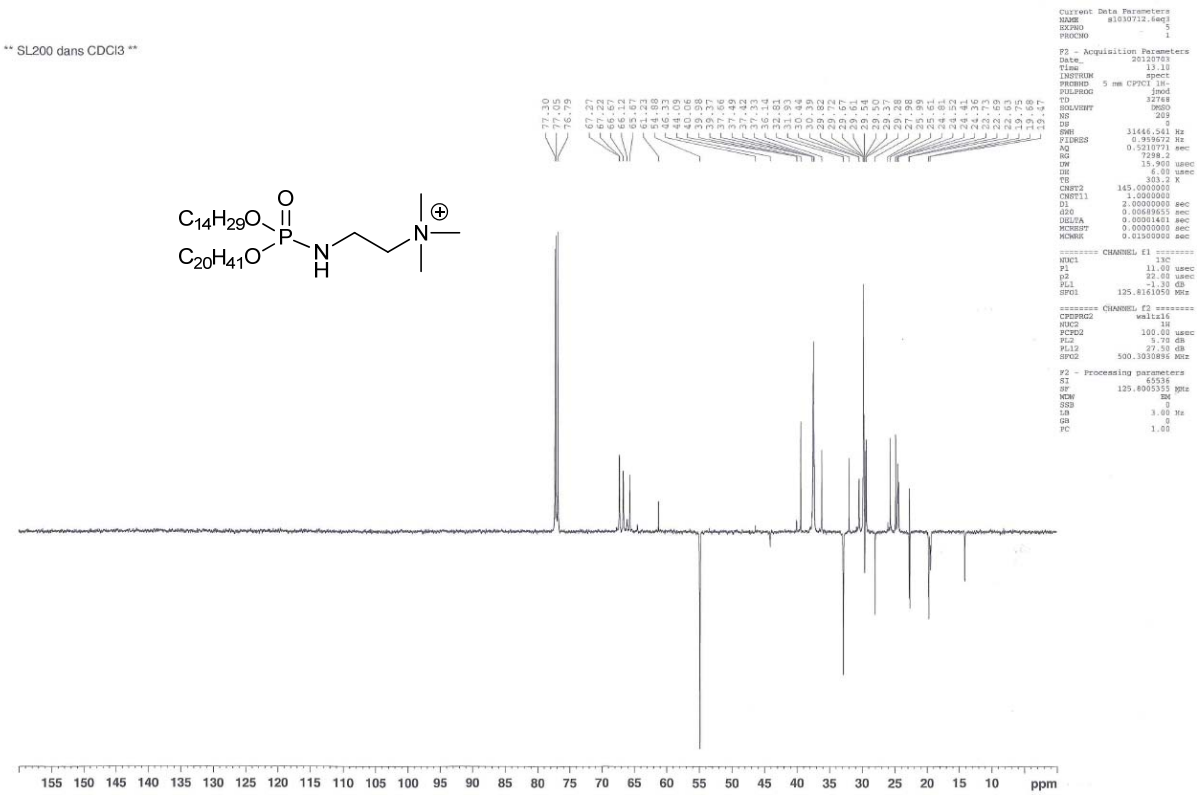


Figure S3-25: ^{13}C jmod ($CDCl_3$) spectrum of compound **10**.

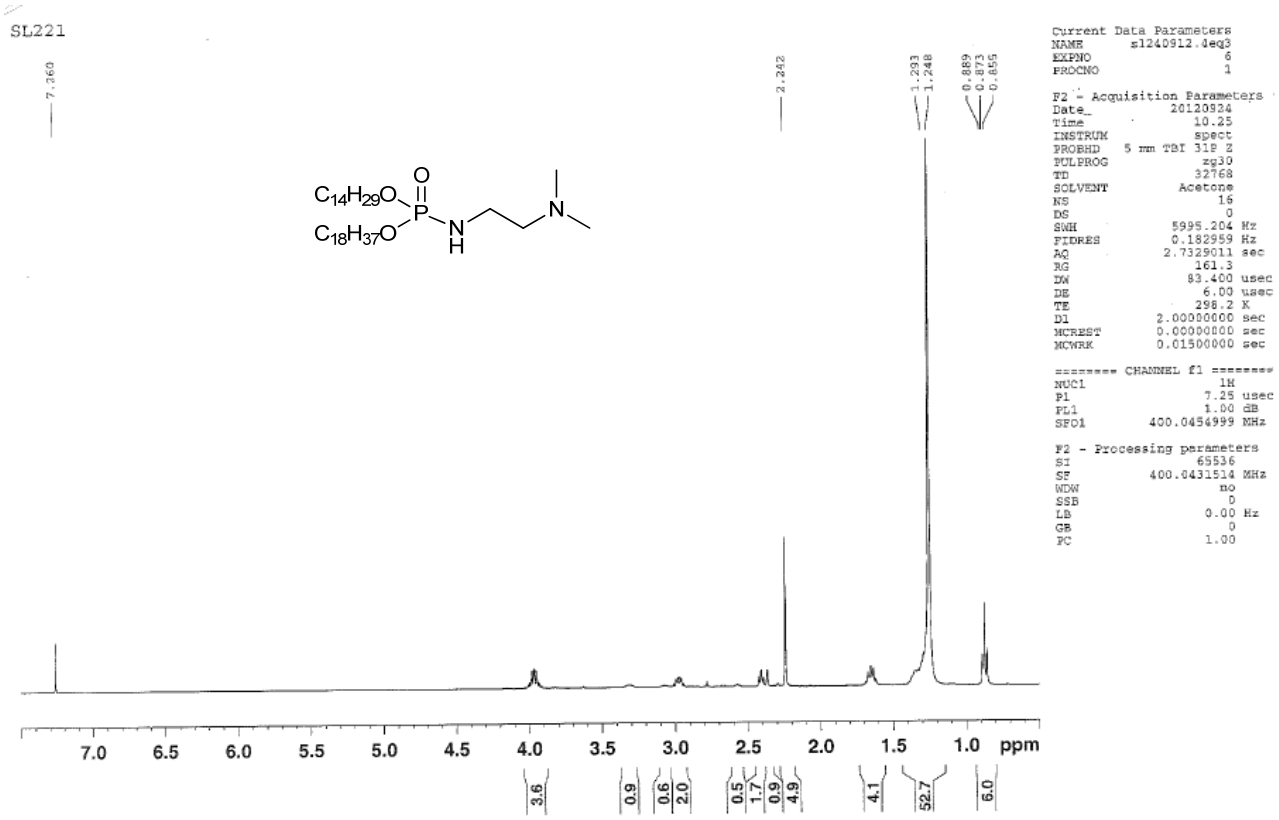


Figure S3-26: ^{1}H NMR ($CDCl_3$) spectrum of compound **11**.

Supporting materials

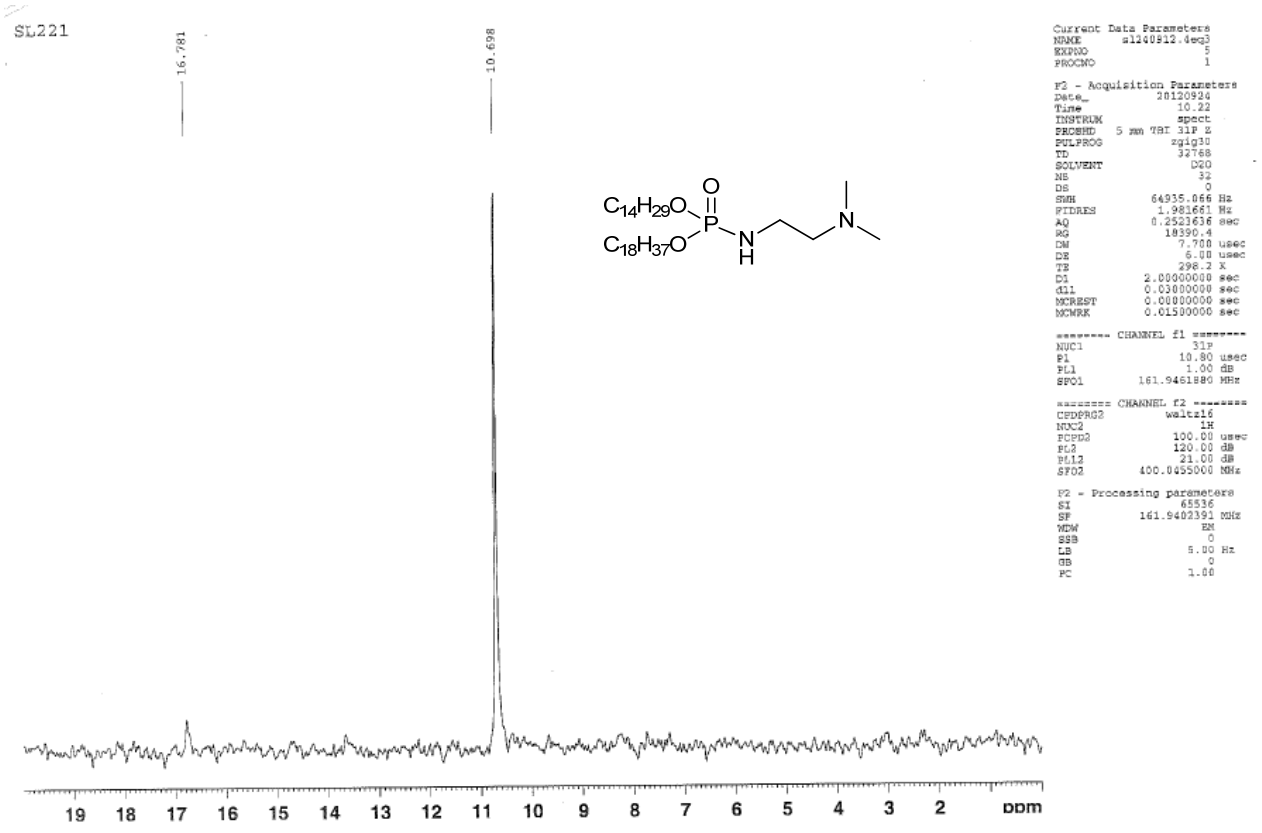


Figure S3-27: ^{31}P NMR ($CDCl_3$) spectrum of compound **11**.

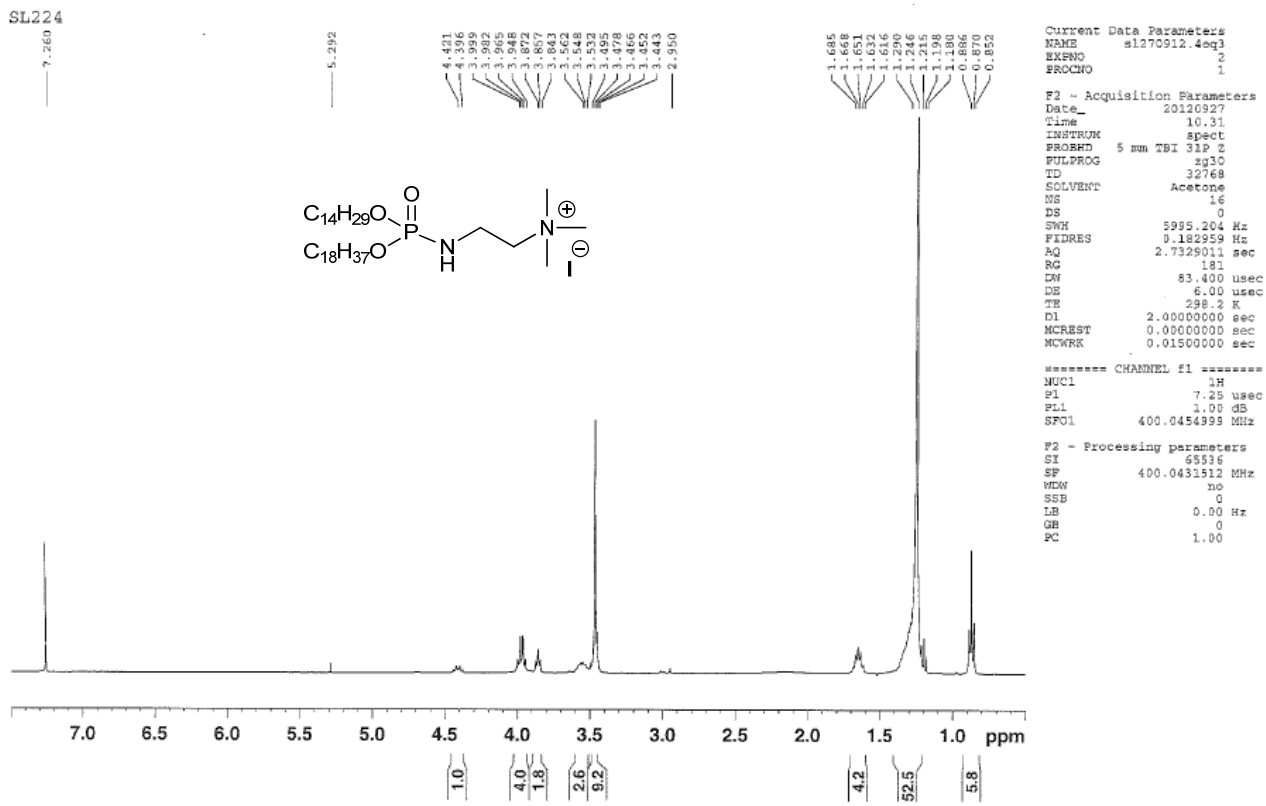


Figure S3-28: ^{1}H NMR ($CDCl_3$) spectrum of compound **12.**

Supporting materials

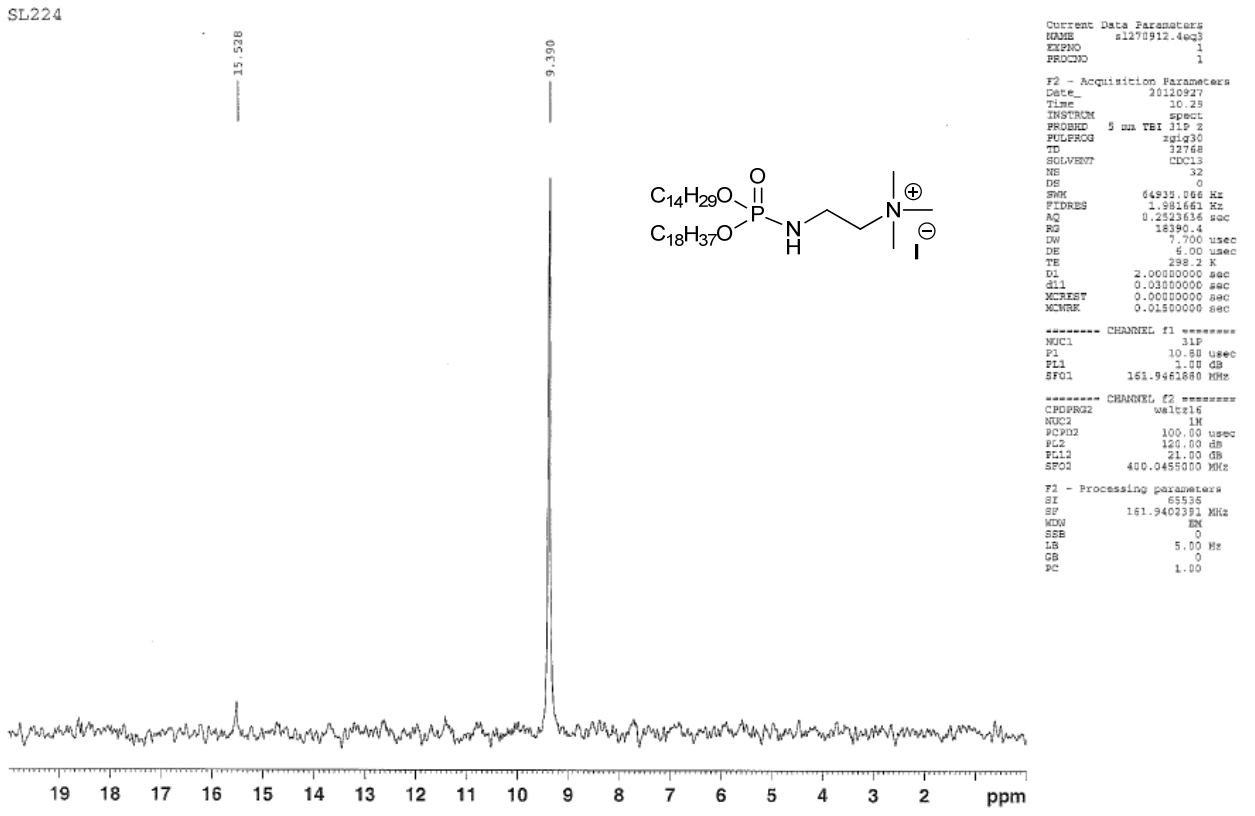


Figure S3-29: ^{31}P NMR ($CDCl_3$) spectrum of compound **12.**

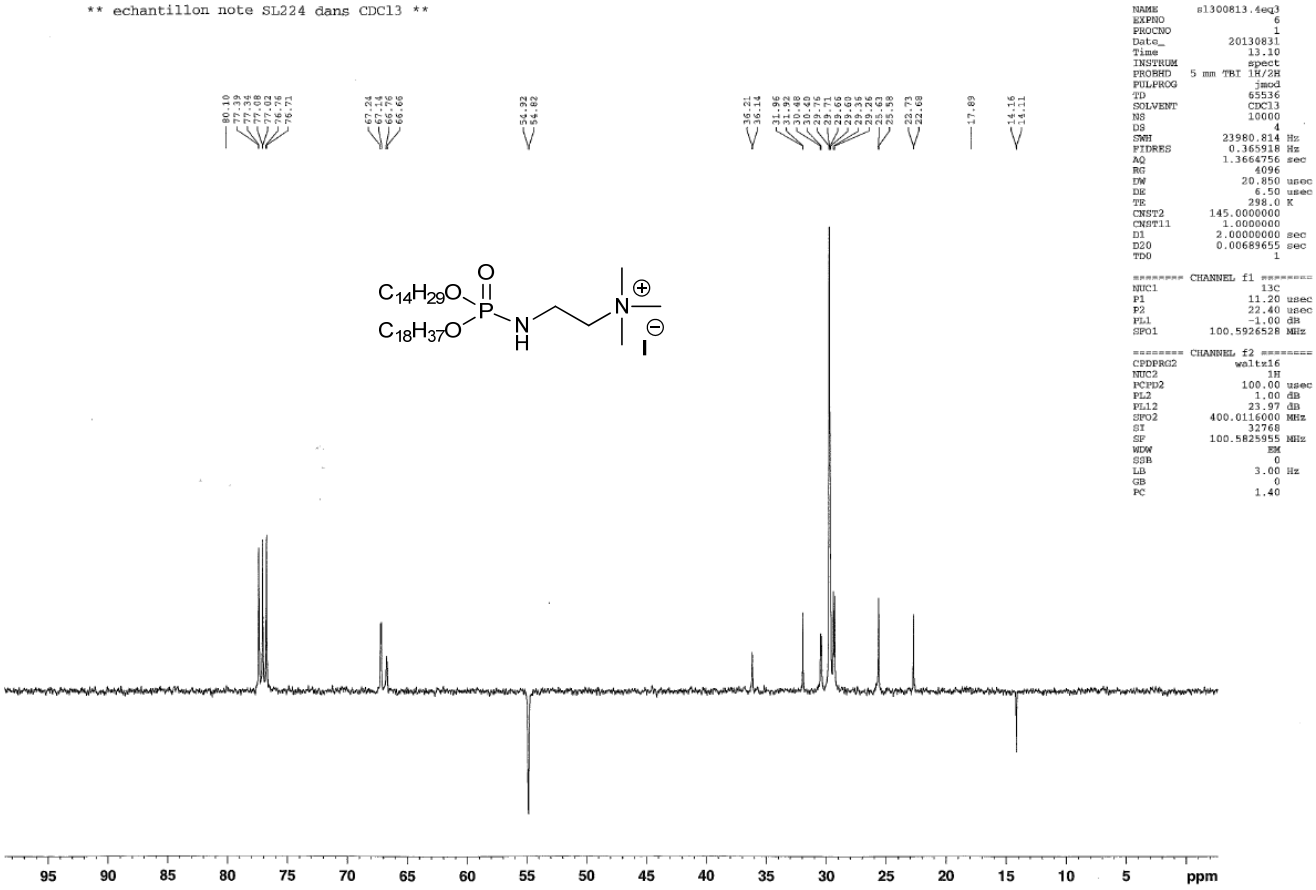


Figure S3-30: ^{13}C jmod ($CDCl_3$) spectrum of compound **12**.

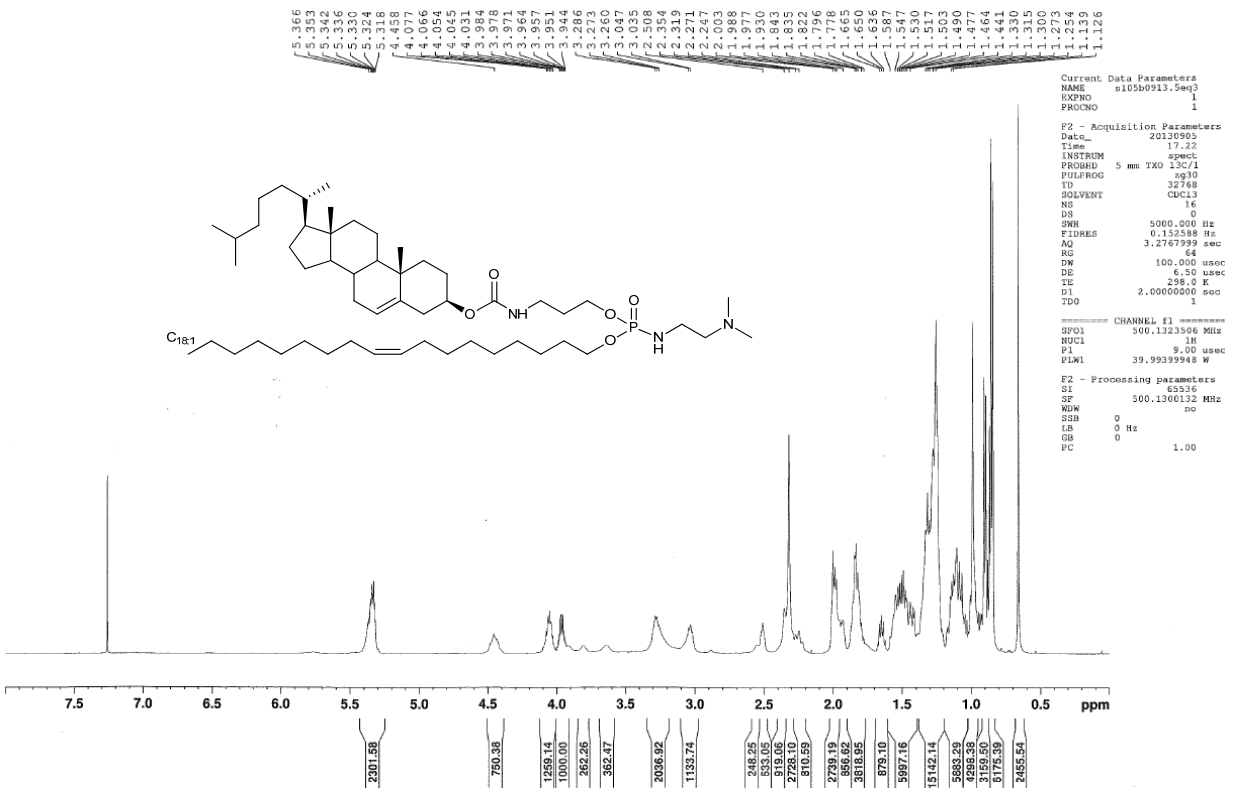


Figure S3-31: ^{1}H NMR ($CDCl_3$) spectrum of compound **13.**

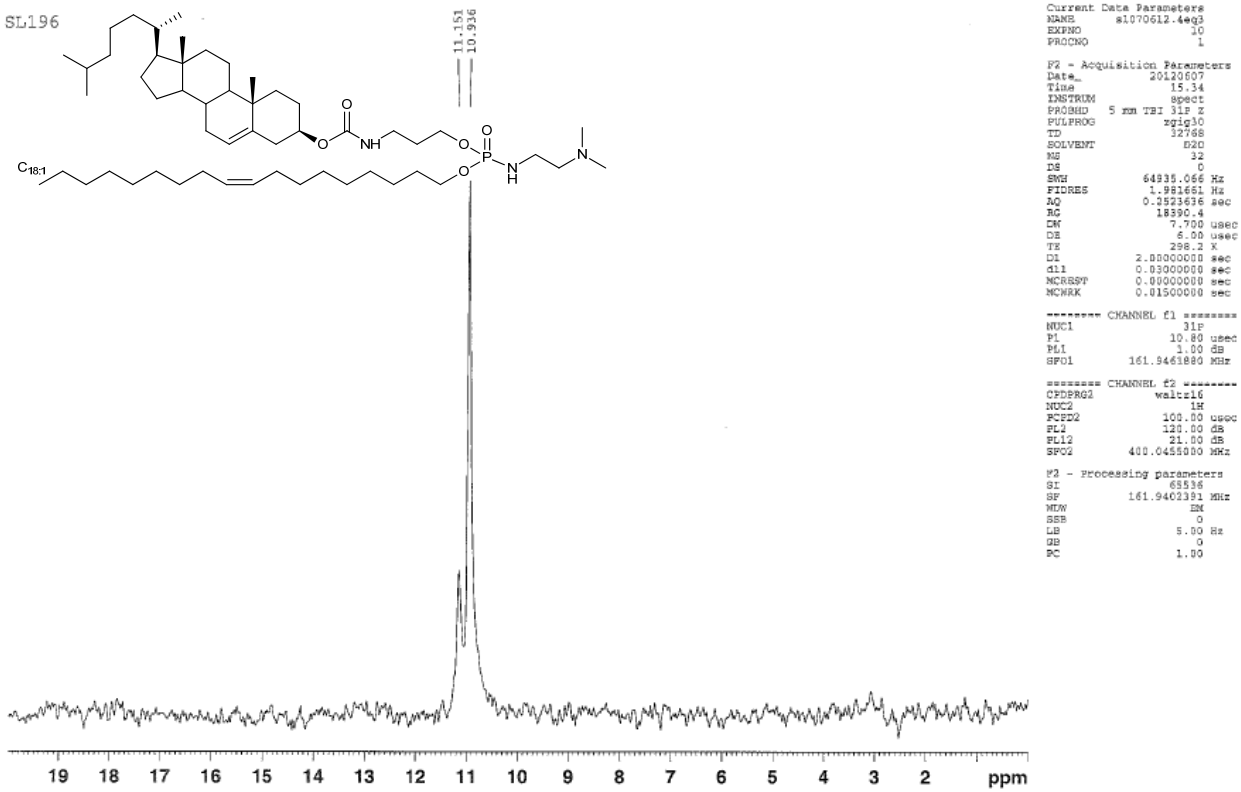


Figure S3-32: ^{31}P NMR ($CDCl_3$) spectrum of compound **13.**

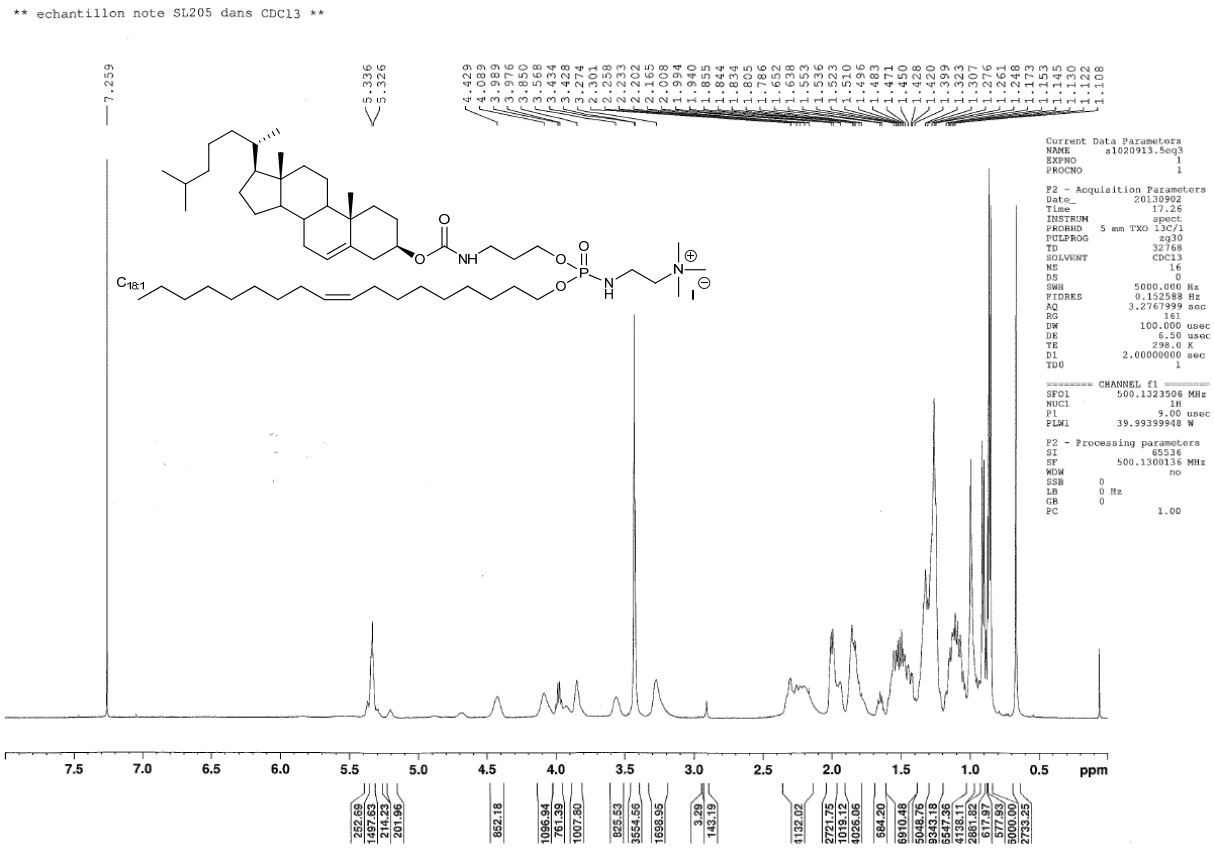


Figure S3-33: ^{1}H NMR ($CDCl_3$) spectrum of compound **14.**

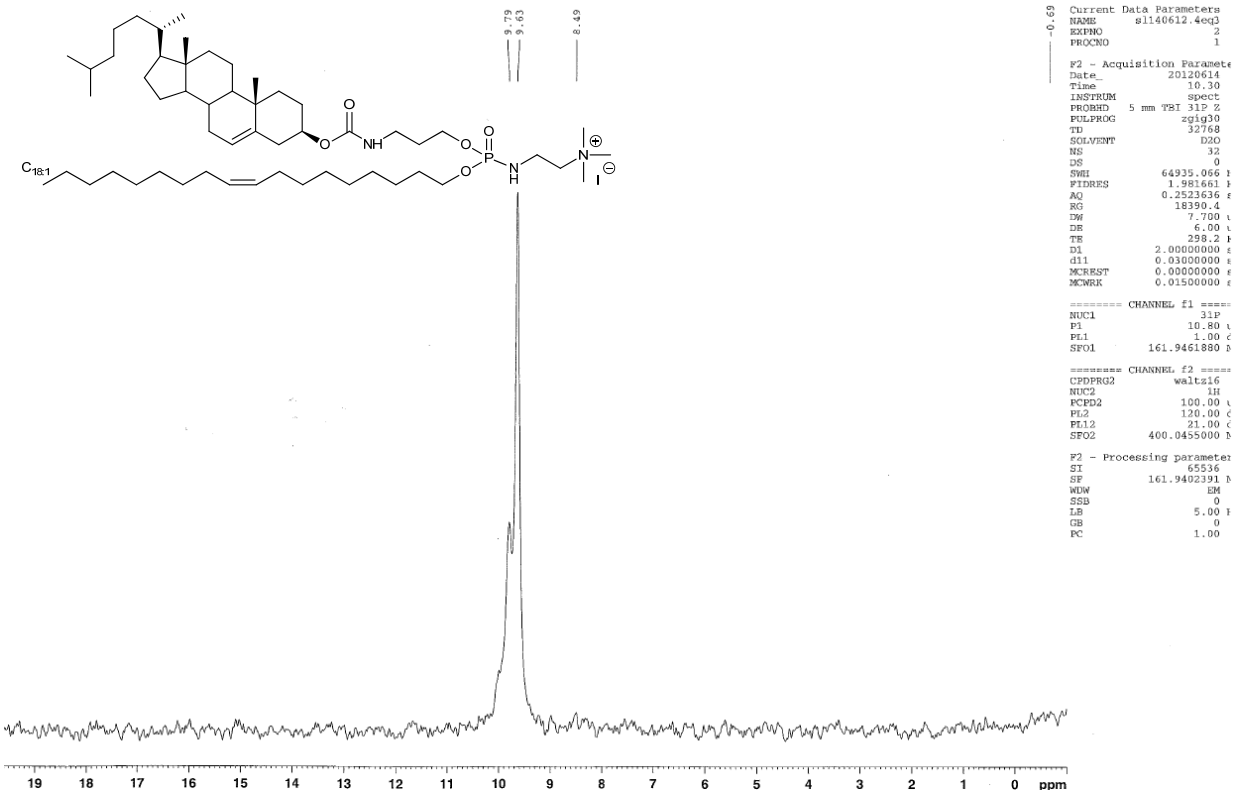


Figure S3-34: ^{31}P NMR ($CDCl_3$) spectrum of compound **14.**

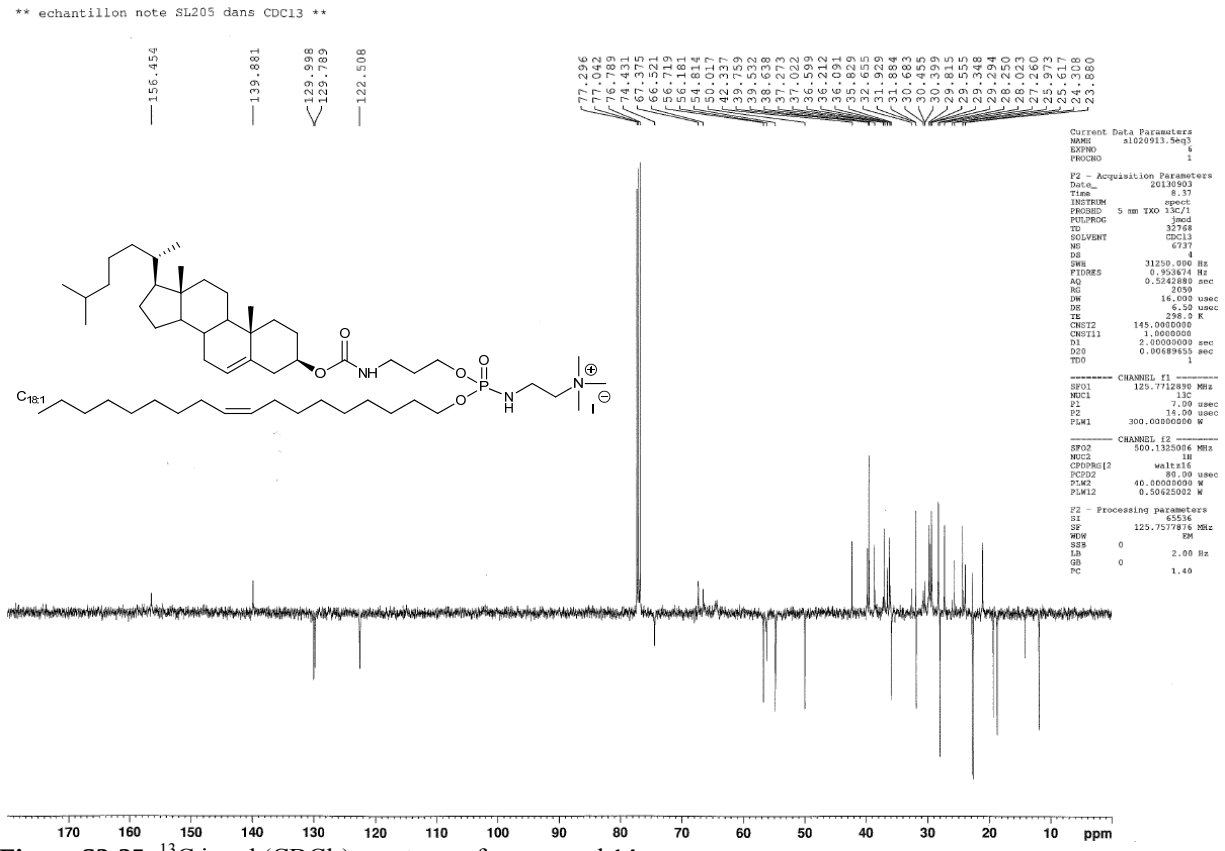


Figure S3-35: ^{13}C jmod ($CDCl_3$) spectrum of compound **14**.

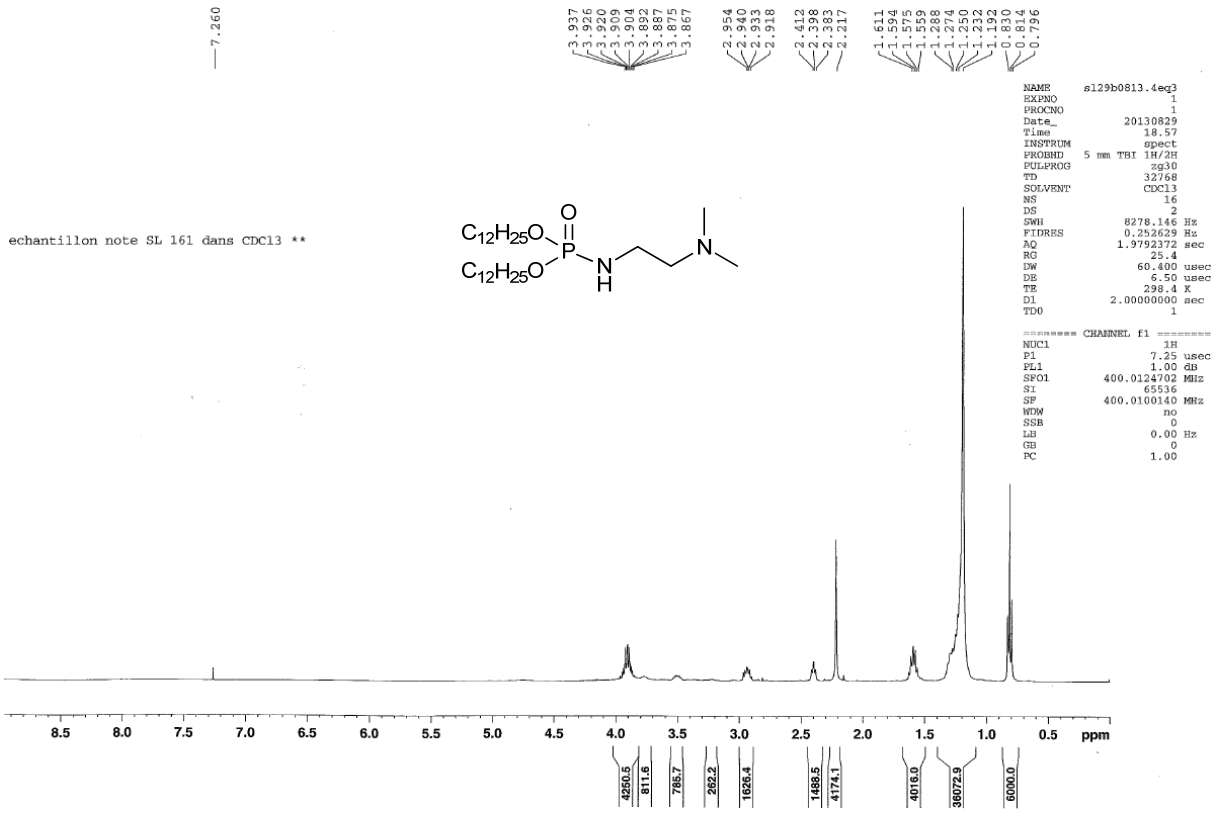


Figure S3-36: ^{1}H NMR ($CDCl_3$) spectrum of compound **15.**

Supporting materials

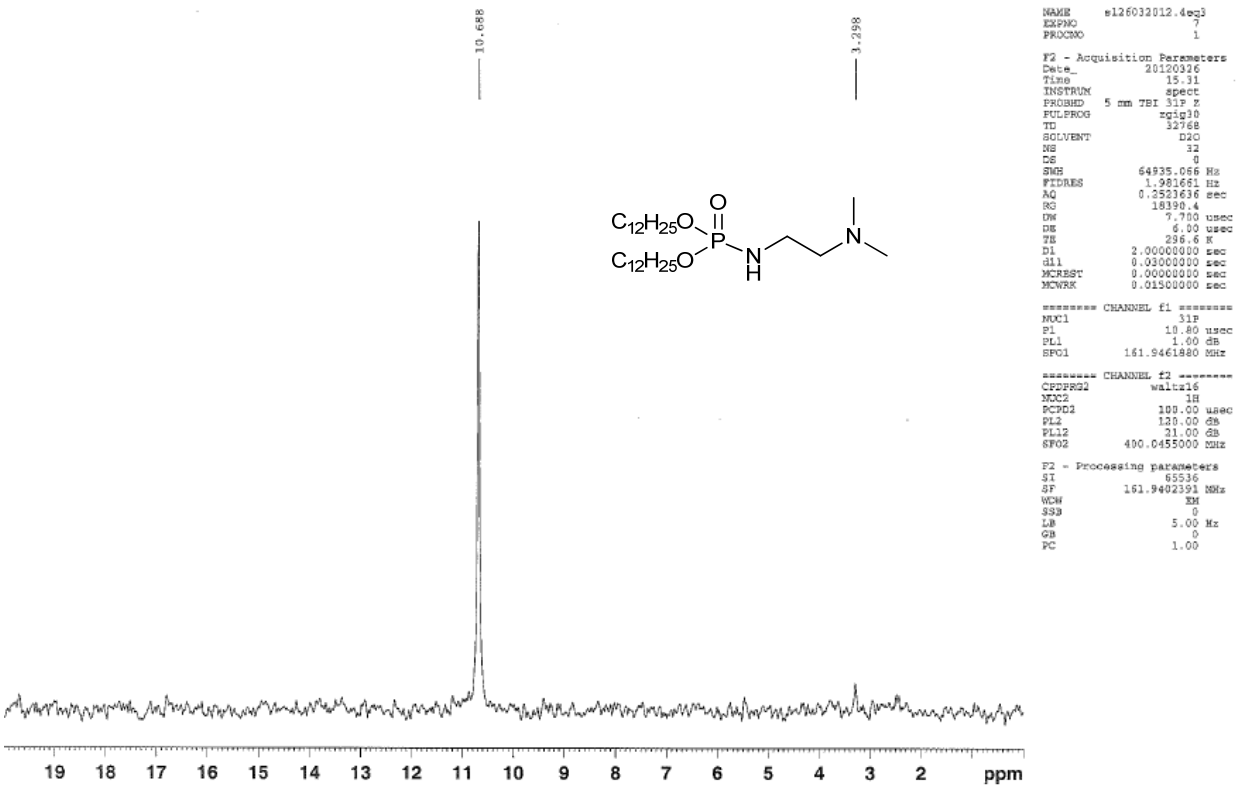


Figure S3-37: ^{31}P NMR ($CDCl_3$) spectrum of compound **15.**

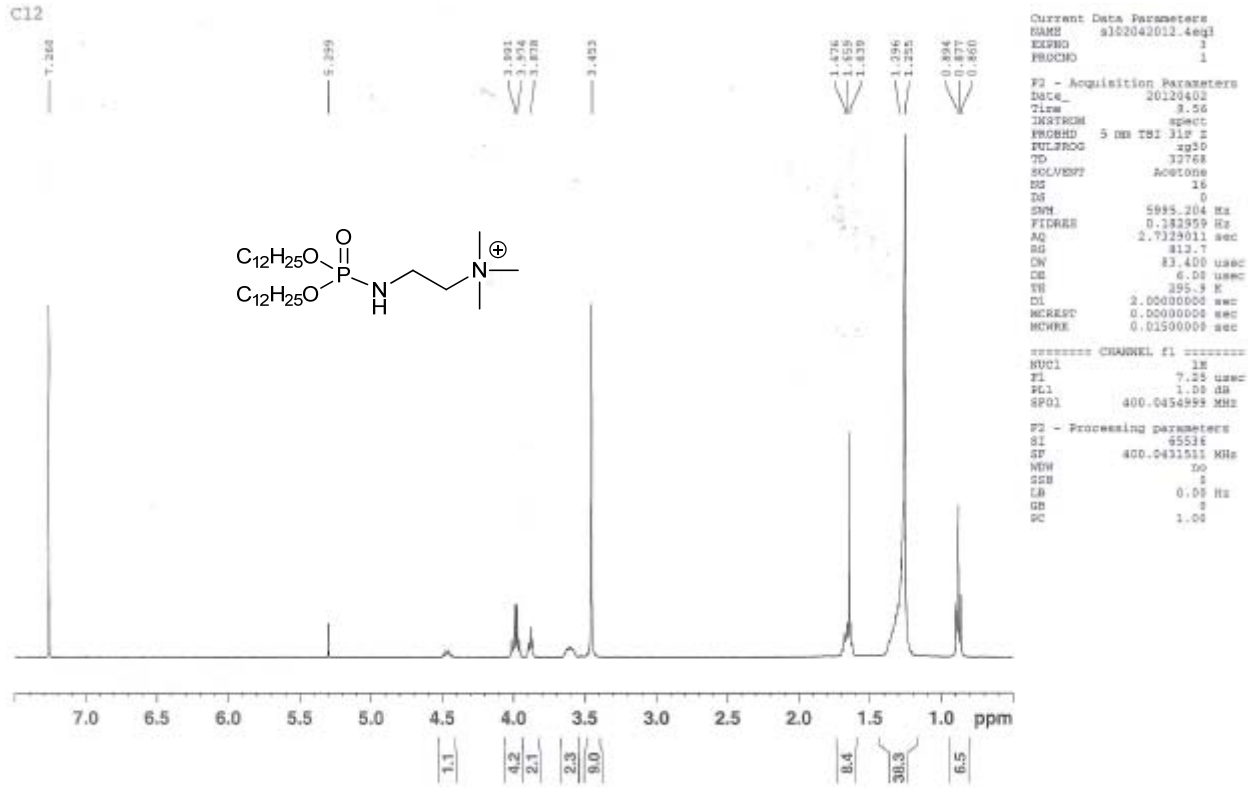


Figure S3-38: ^{1}H NMR ($CDCl_3$) spectrum of compound **16.**

Supporting materials

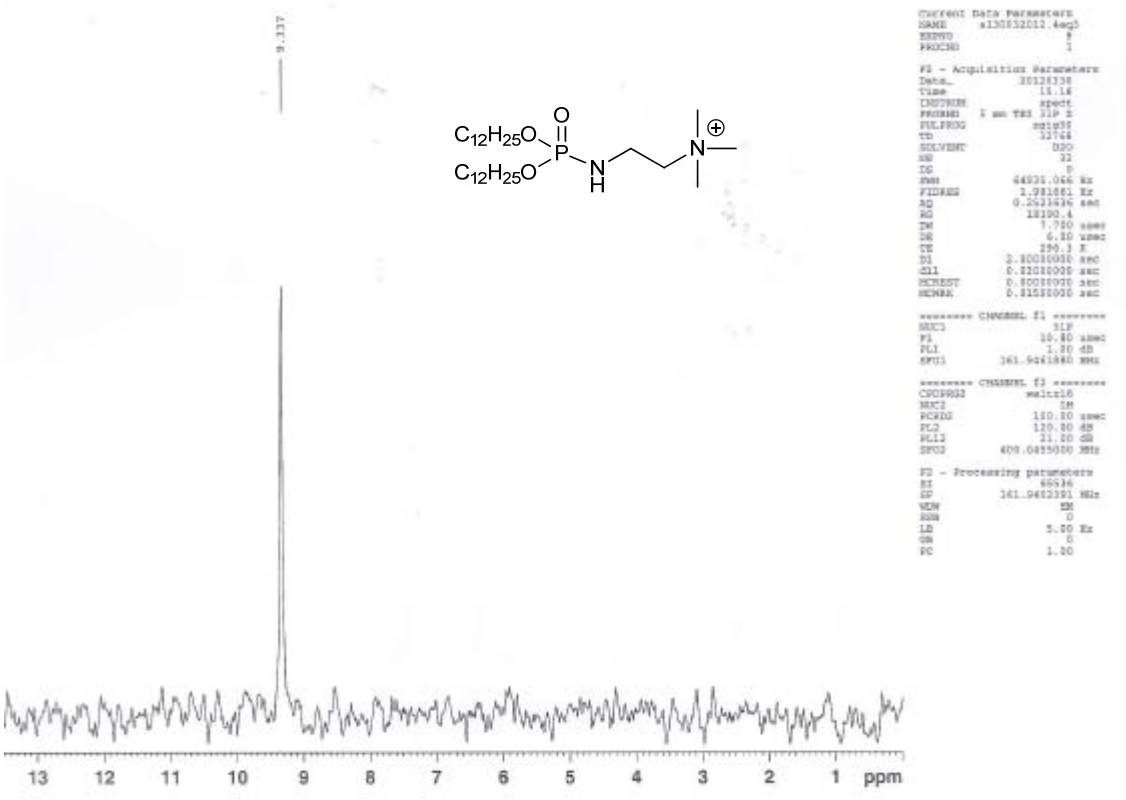


Figure S3-39: ^{31}P NMR ($CDCl_3$) spectrum of compound **16.**

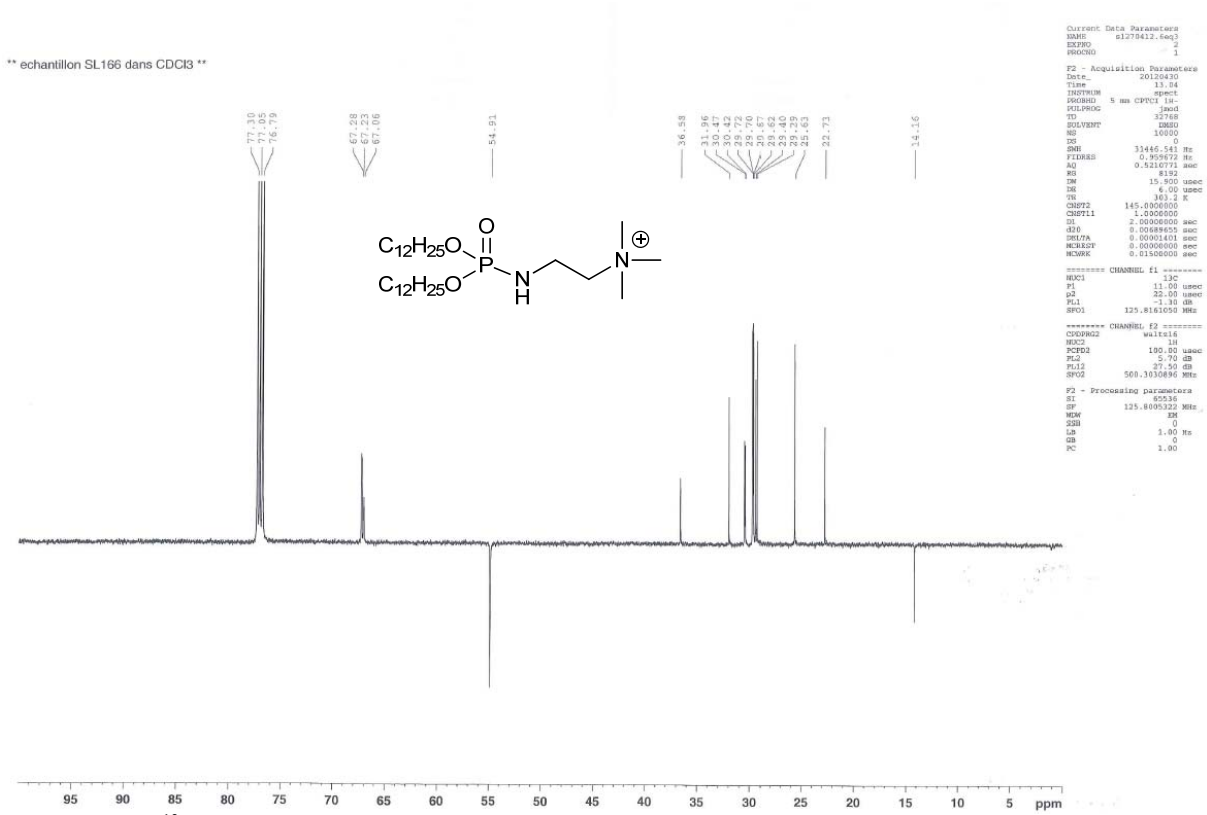


Figure S3-40: ^{13}C jmod ($CDCl_3$) spectrum of compound **16**.

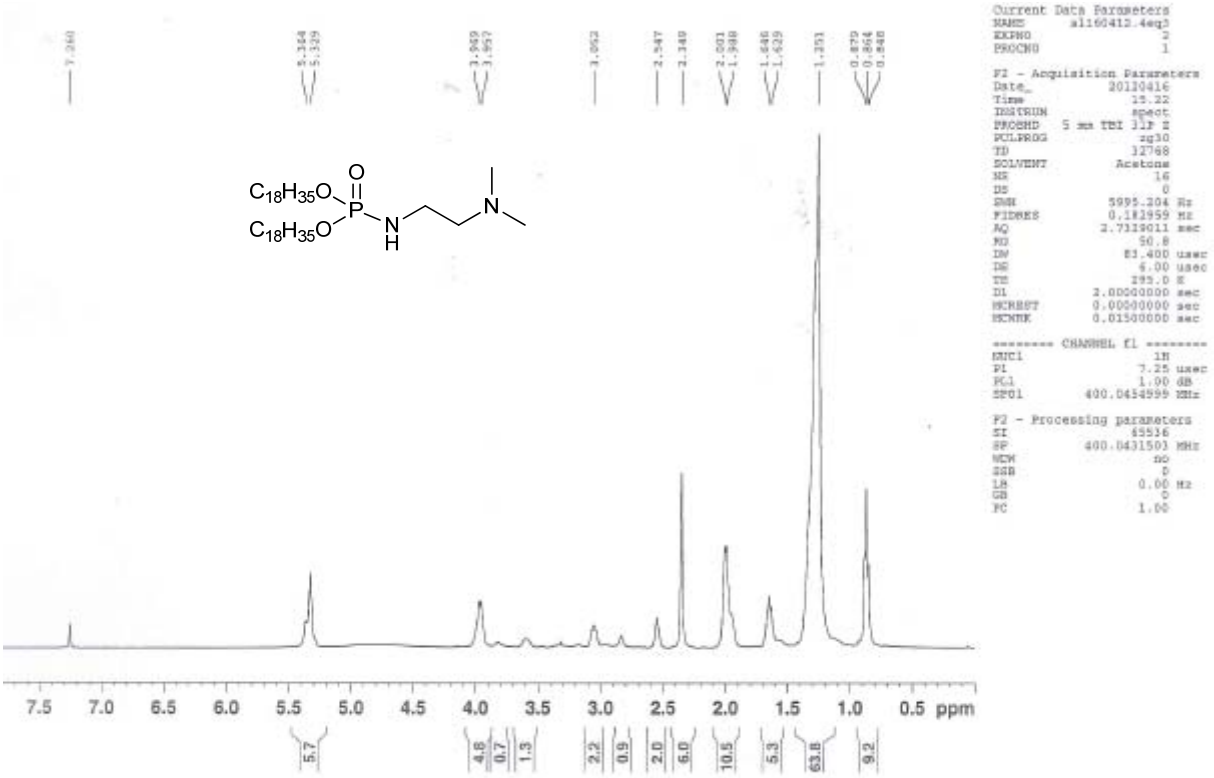


Figure S3-41: ^{1}H NMR ($CDCl_3$) spectrum of compound **17.**

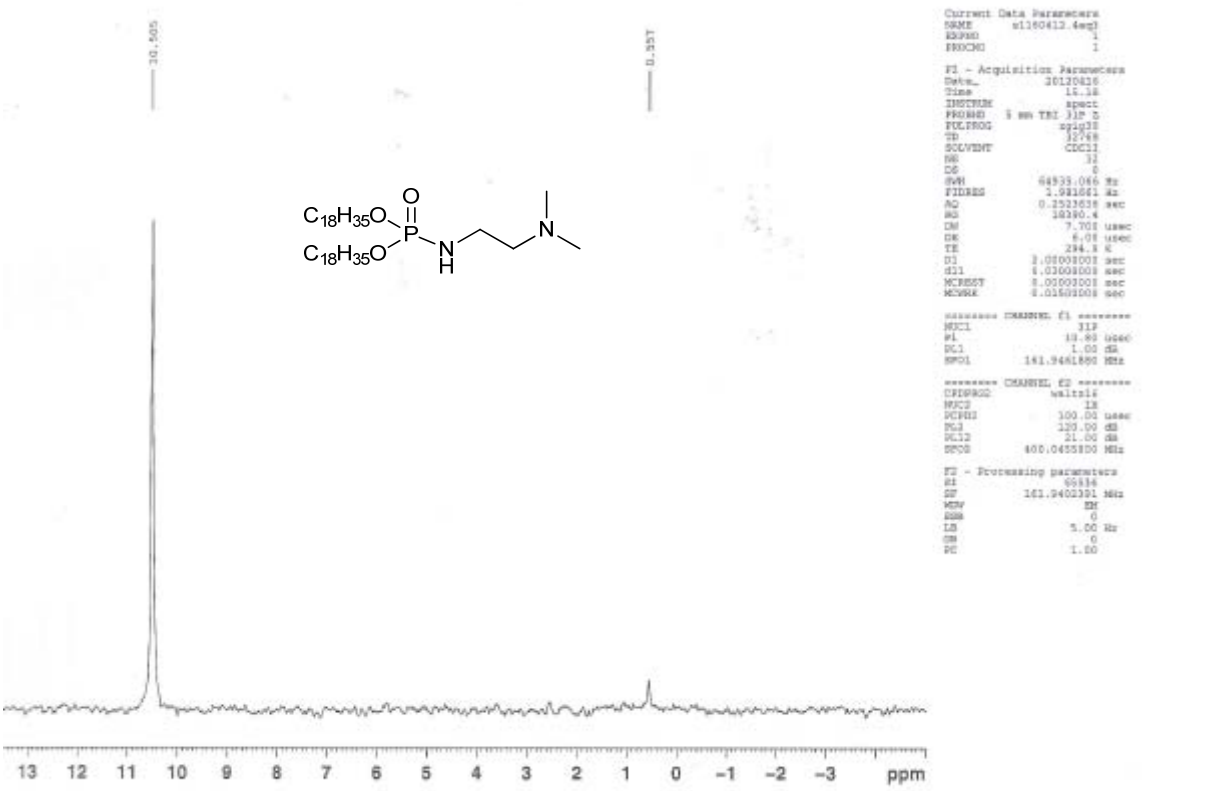


Figure S3-42: ^{31}P NMR ($CDCl_3$) spectrum of compound **17.**

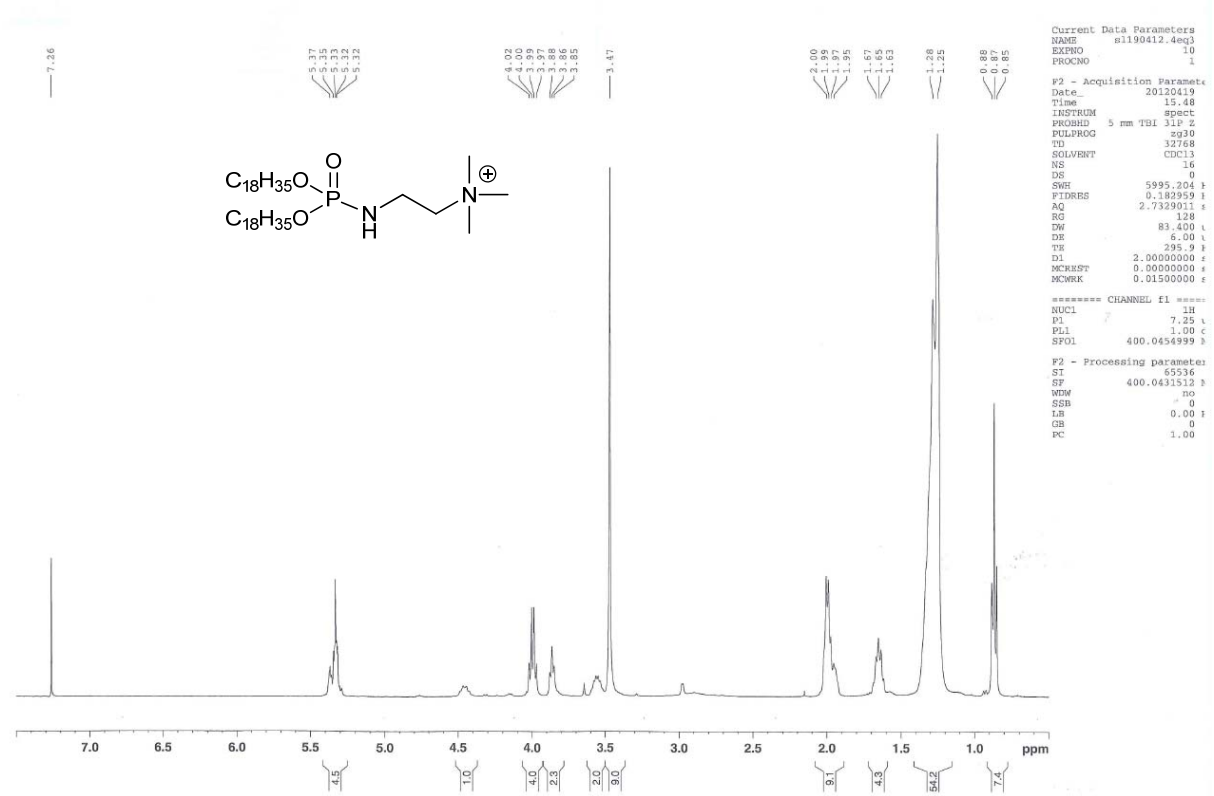


Figure S3-43: ^{1}H NMR ($CDCl_3$) spectrum of compound **18.**

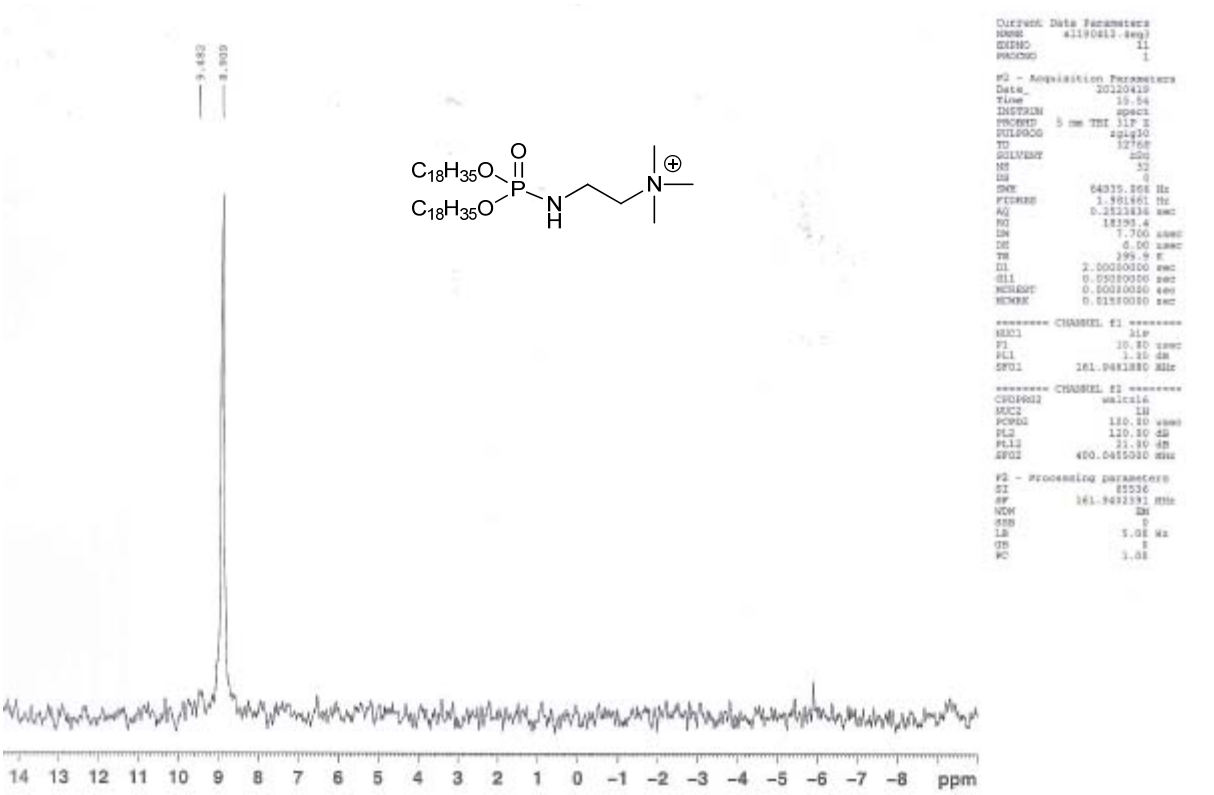


Figure S3-44: ^{31}P NMR ($CDCl_3$) spectrum of compound **18.**

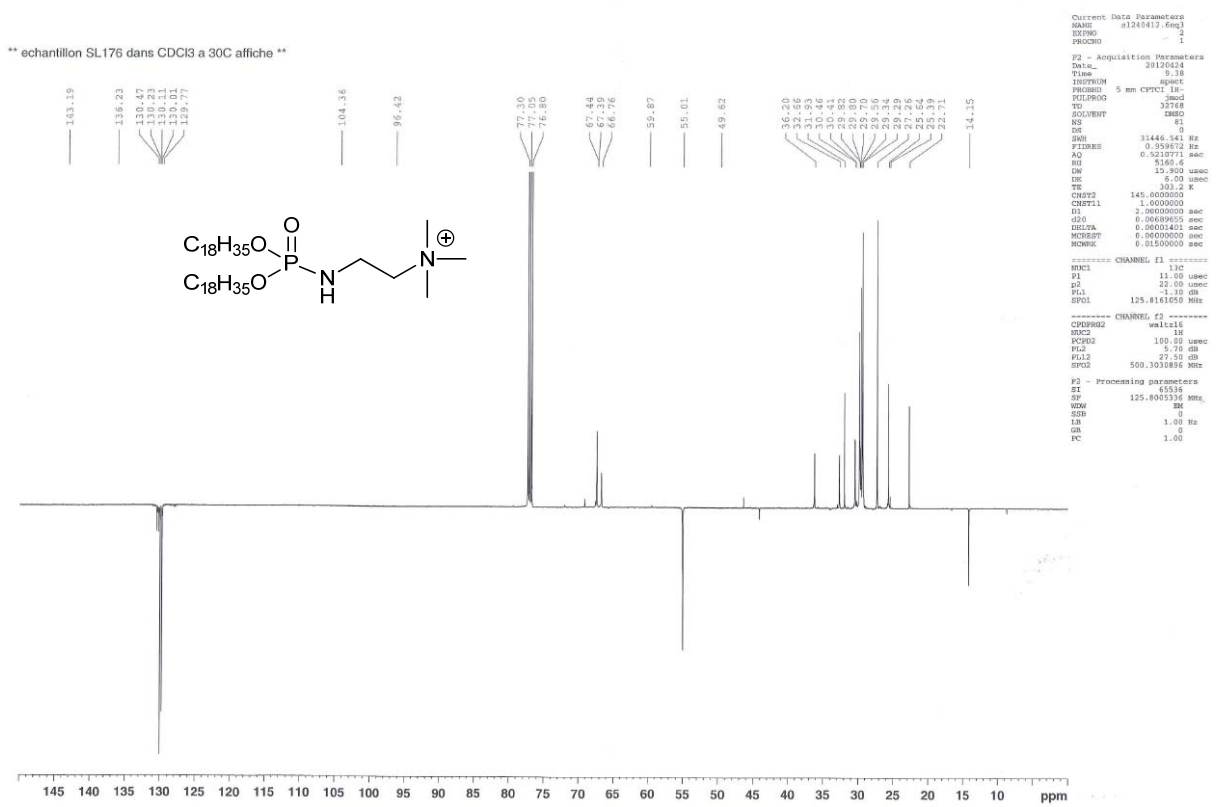


Figure S3-45: ^{13}C jmod ($CDCl_3$) spectrum of compound **18**.

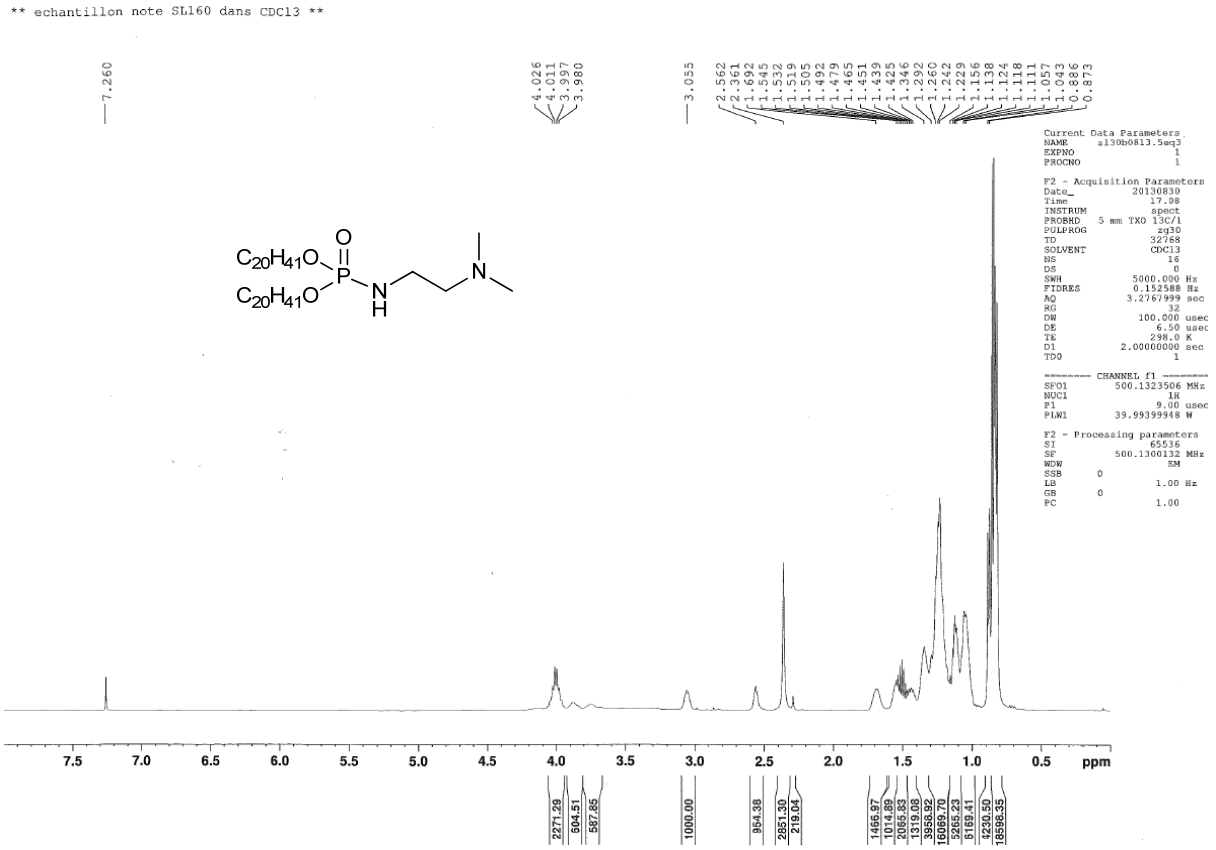


Figure S3-46: ^{1}H NMR ($CDCl_3$) spectrum of compound **19.**

Supporting materials

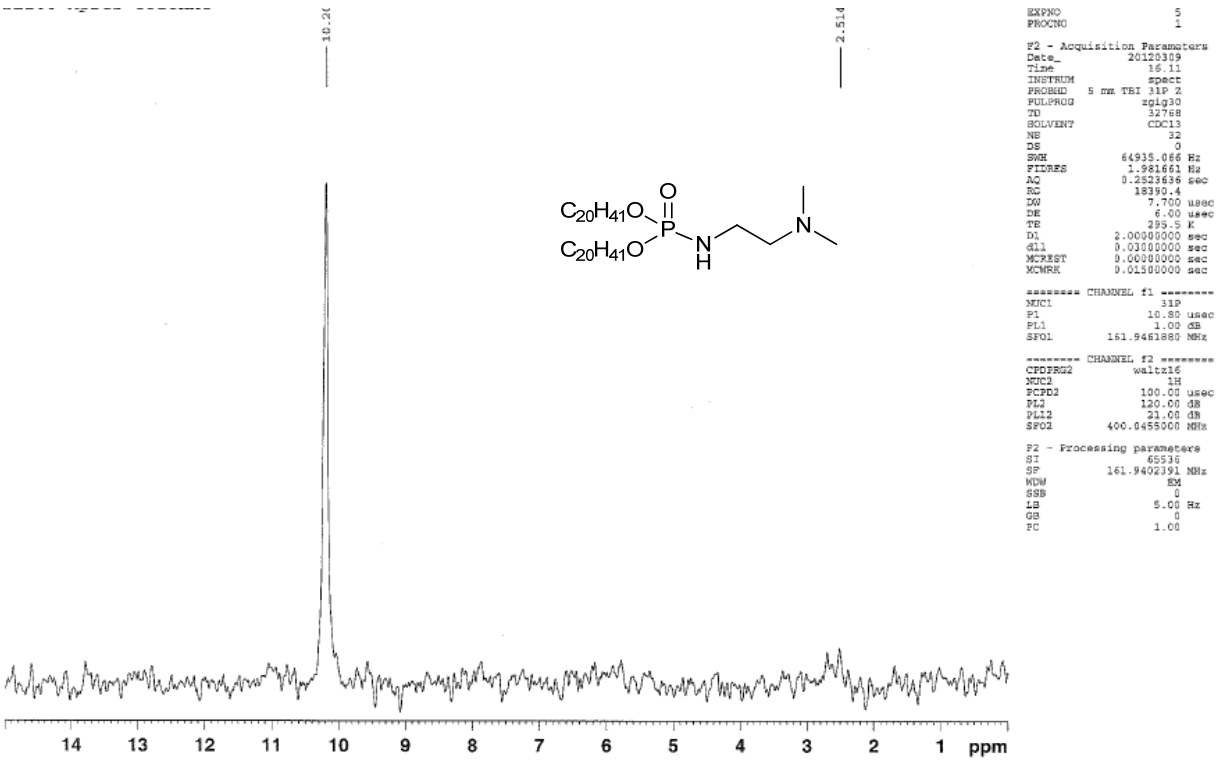


Figure S3-47: ^{31}P NMR ($CDCl_3$) spectrum of compound **19.**

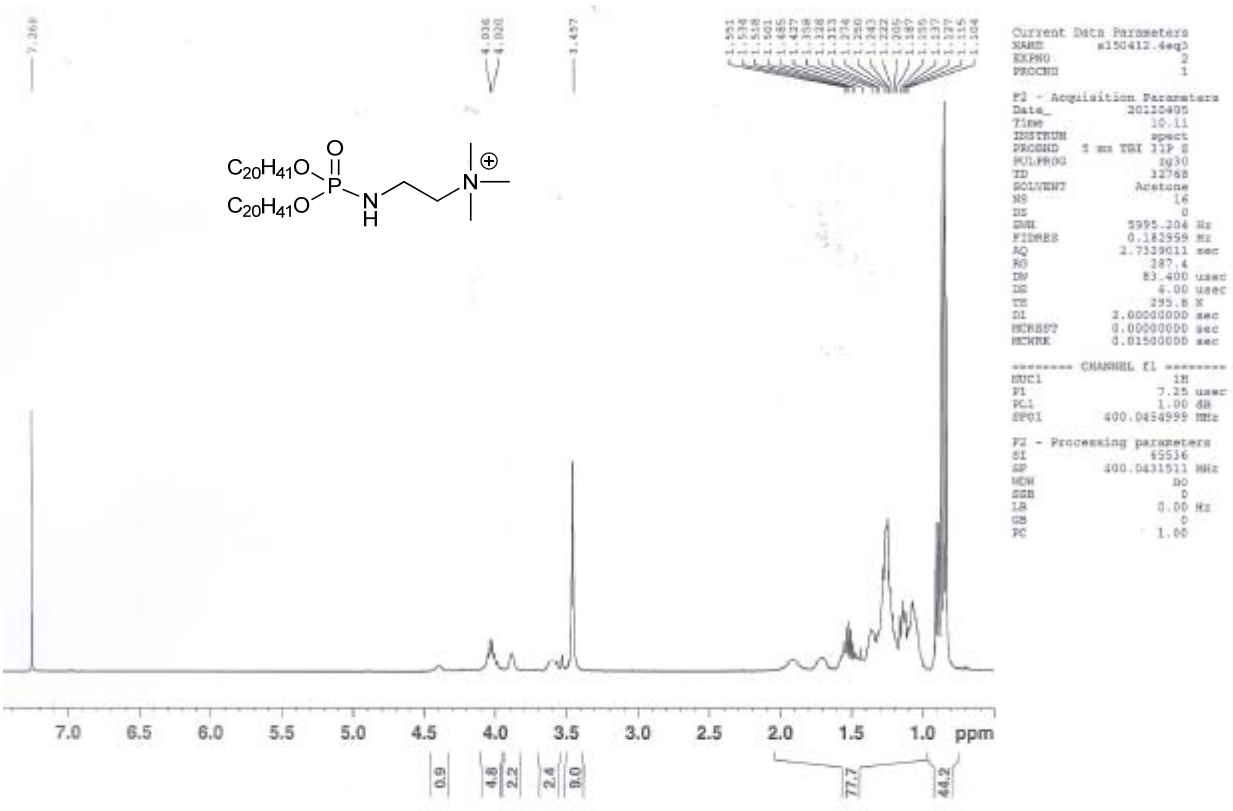


Figure S3-48: ^{1}H NMR ($CDCl_3$) spectrum of compound **20.**

Supporting materials

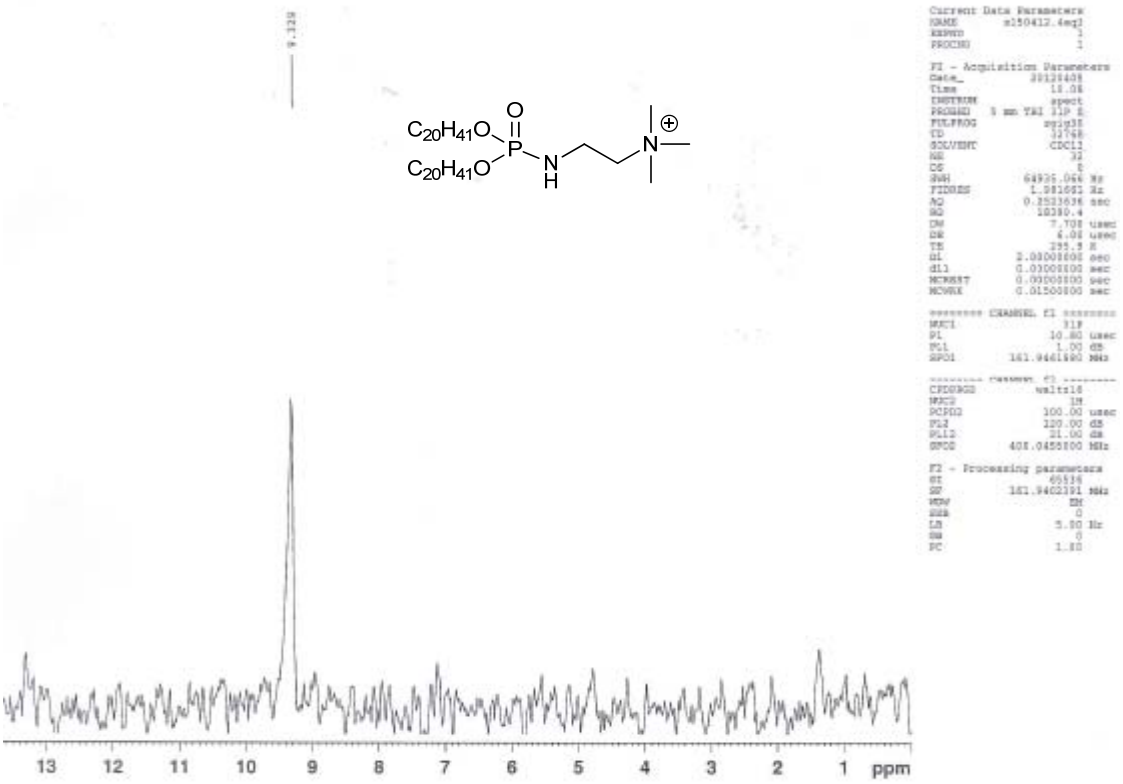


Figure S3-49: ^{31}P NMR ($CDCl_3$) spectrum of compound **20.**

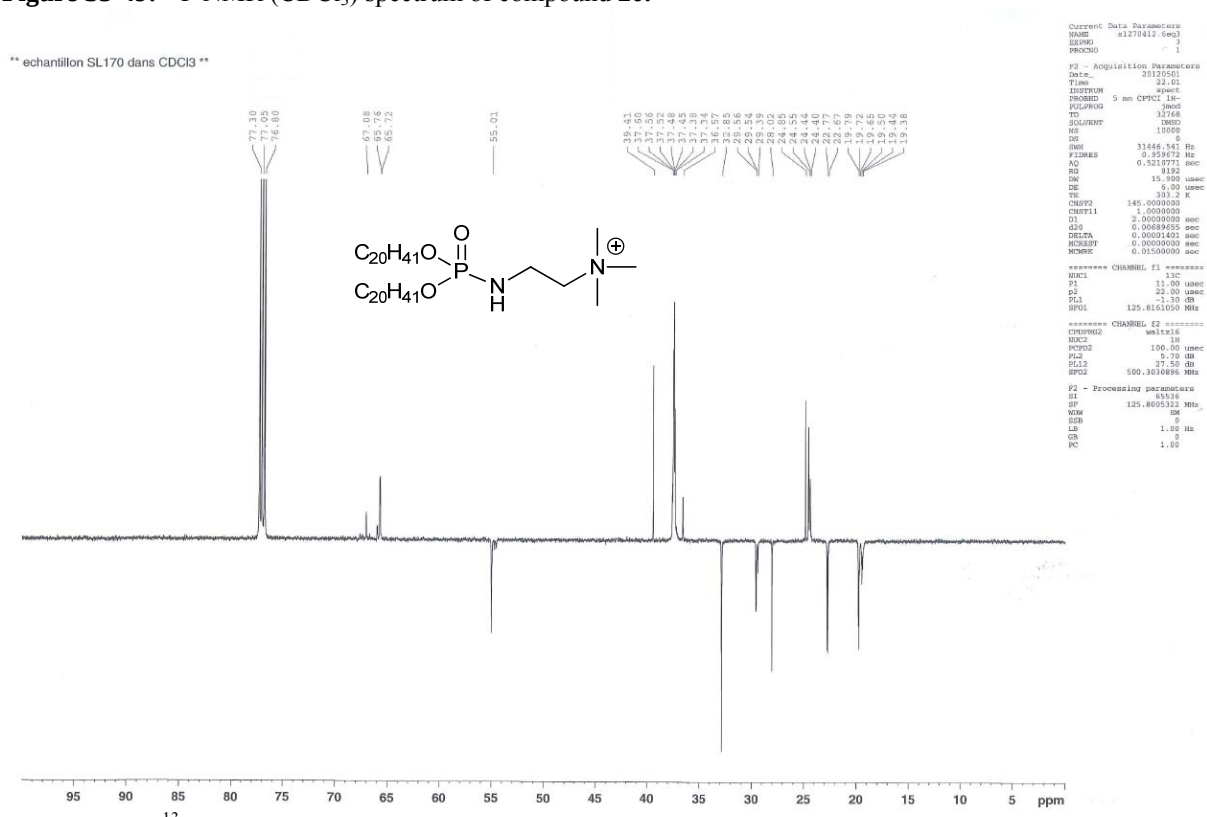


Figure S3-50: ^{13}C jmod ($CDCl_3$) spectrum of compound **20**.

Supporting materials

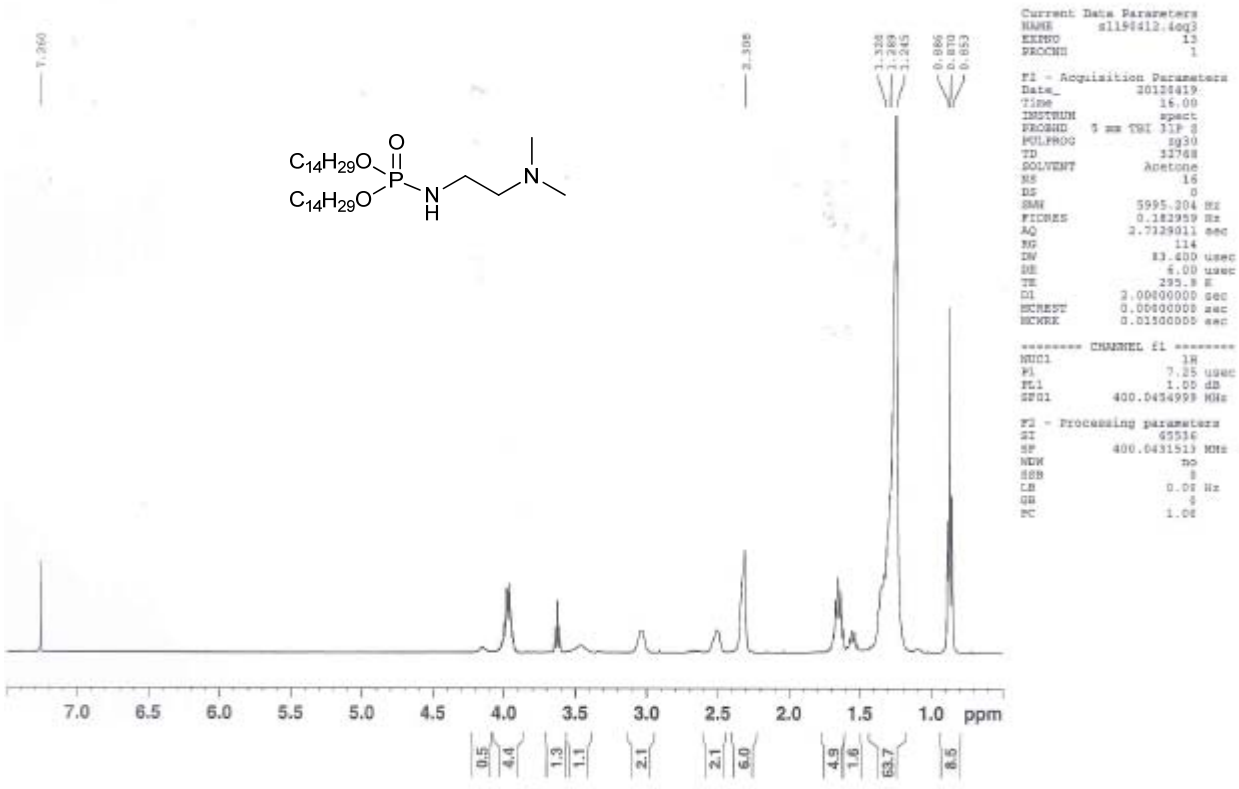


Figure S3-51: ^{1}H NMR ($CDCl_3$) spectrum of compound **21.**

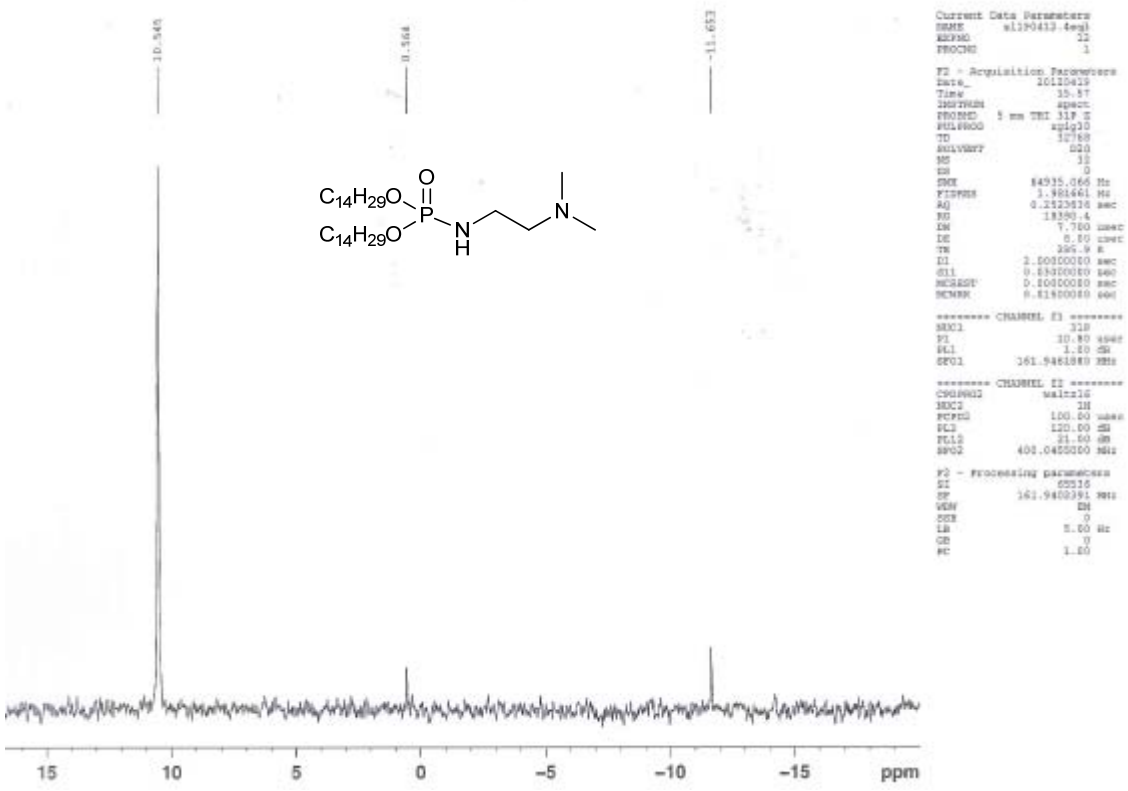


Figure S3-52: ^{31}P NMR ($CDCl_3$) spectrum of compound **21.**

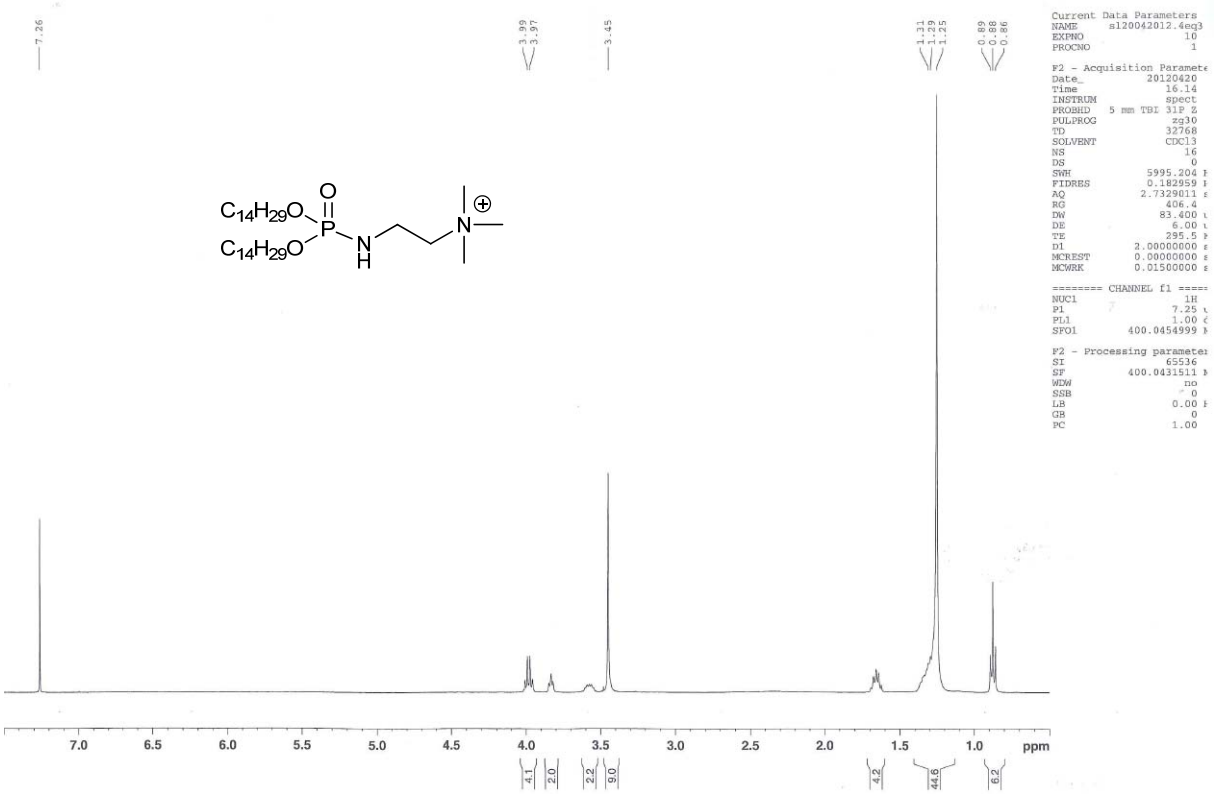


Figure S3-53: ^{1}H NMR ($CDCl_3$) spectrum of compound **22.**

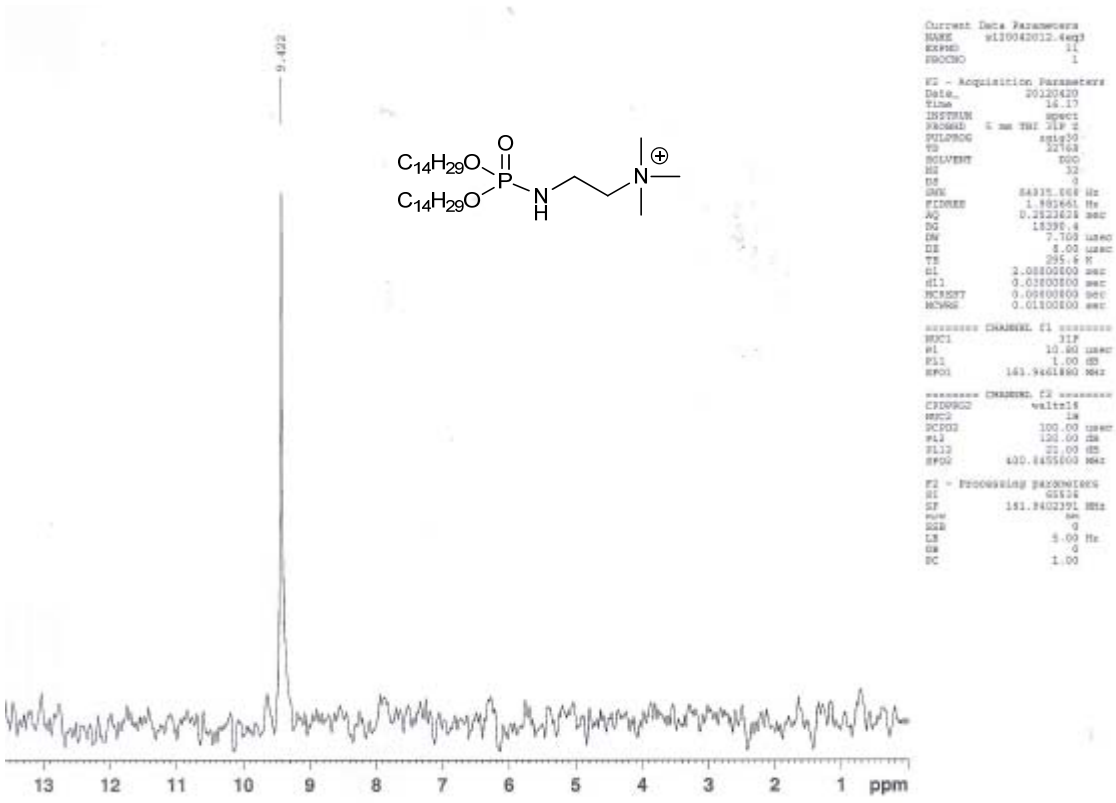


Figure S3-54: ^{31}P NMR ($CDCl_3$) spectrum of compound **22.**

Supporting materials

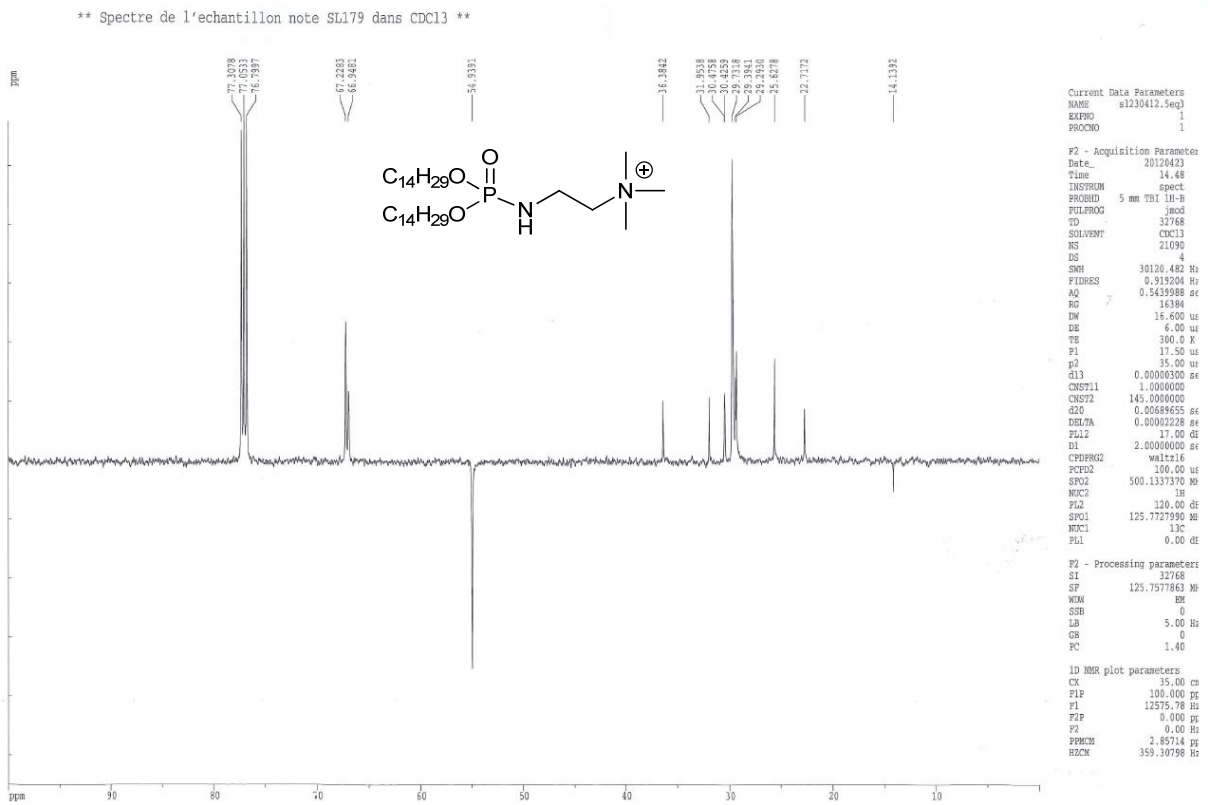


Figure S3-55: ^{13}C jmod ($CDCl_3$) spectrum of compound **22**.

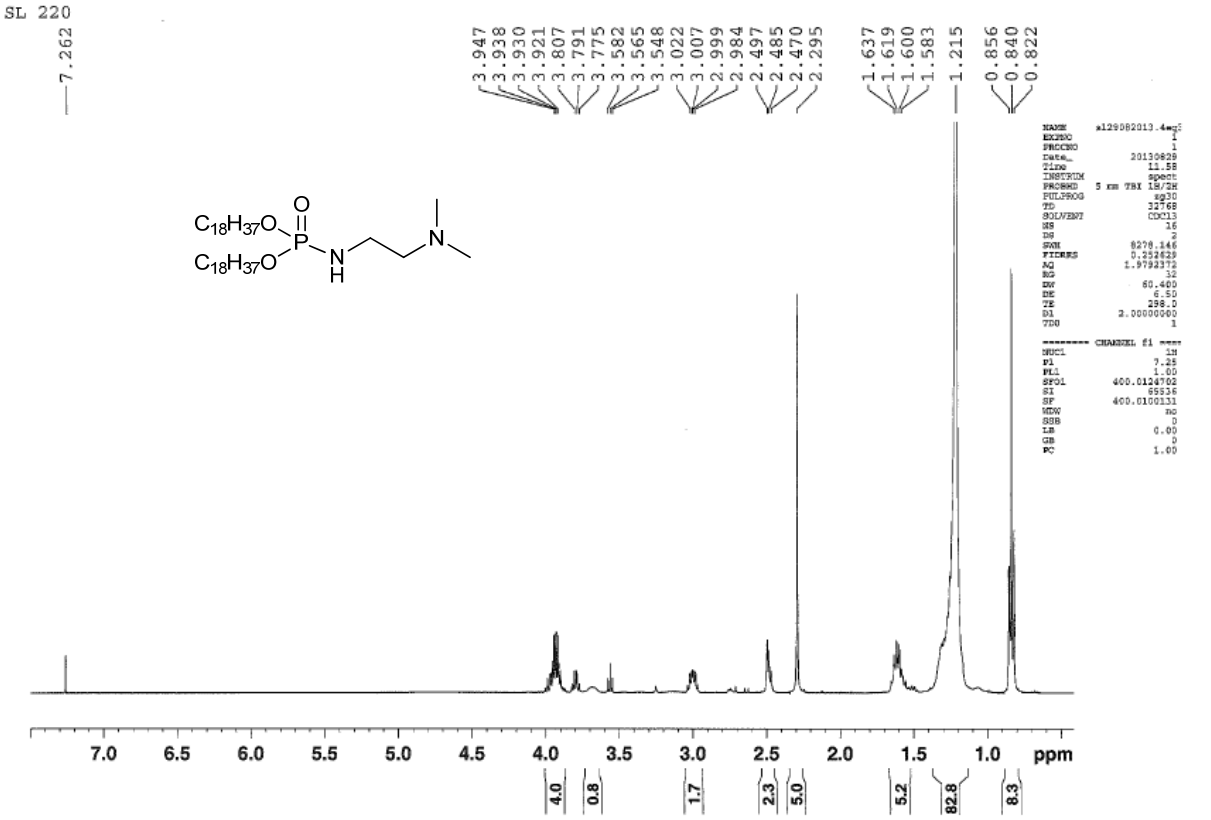


Figure S3-56: ^{1}H NMR ($CDCl_3$) spectrum of compound **23.**

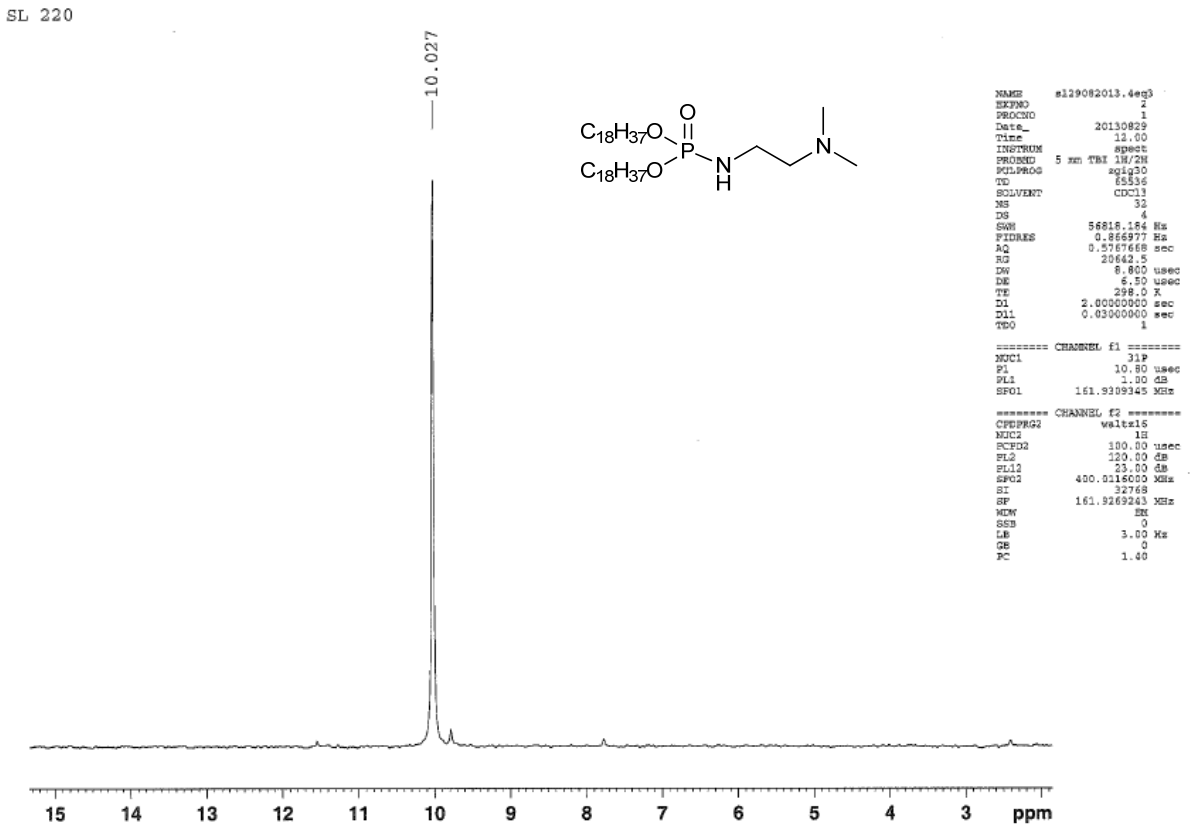


Figure S3-57: ^{31}P NMR ($CDCl_3$) spectrum of compound **23.**

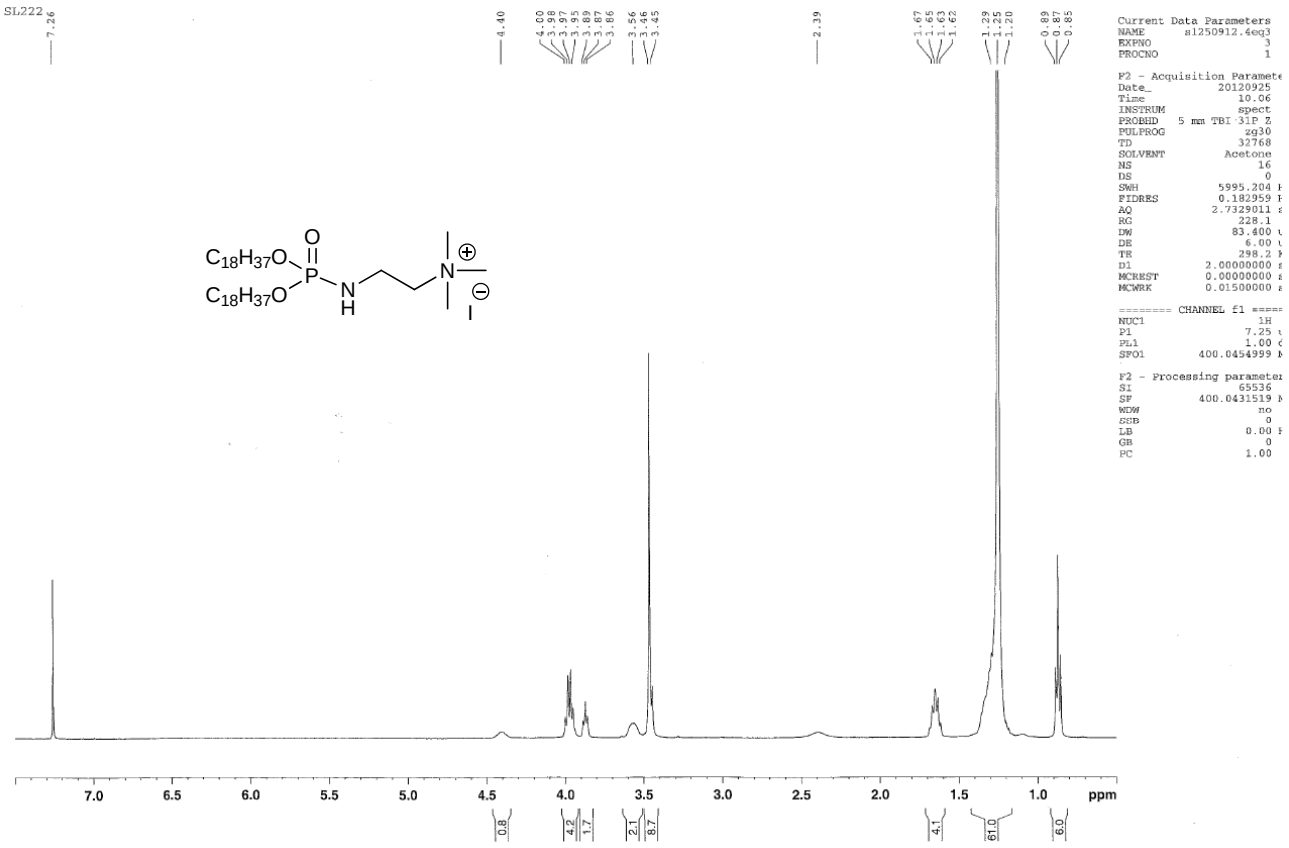


Figure S3-58: ^{1}H NMR ($CDCl_3$) spectrum of compound **24.**

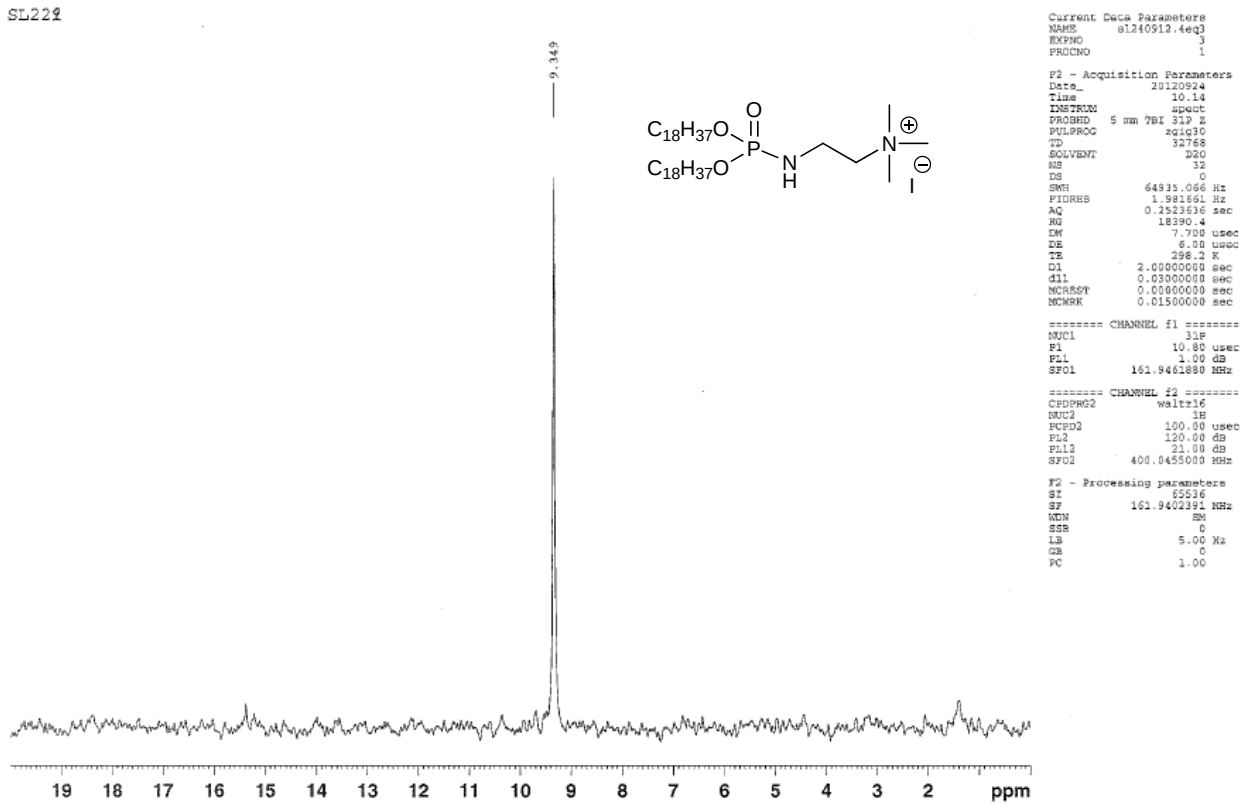


Figure S3-59: ^{31}P NMR ($CDCl_3$) spectrum of compound **24.**

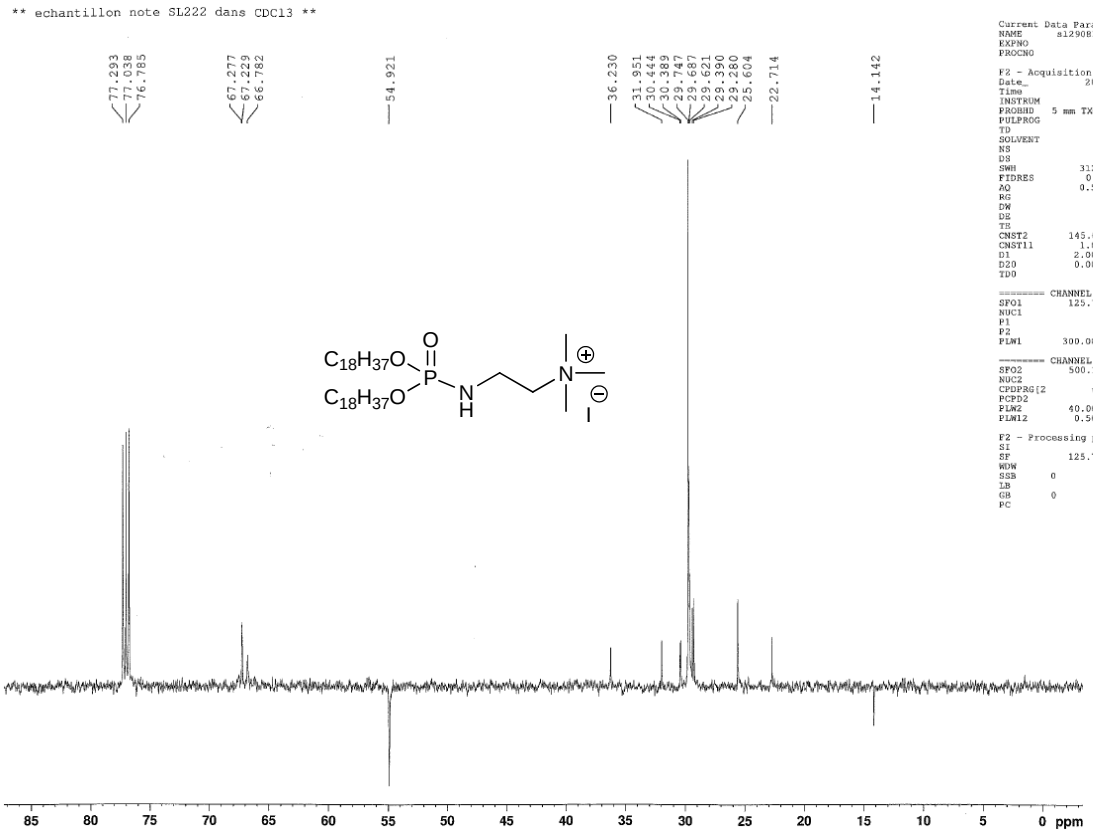
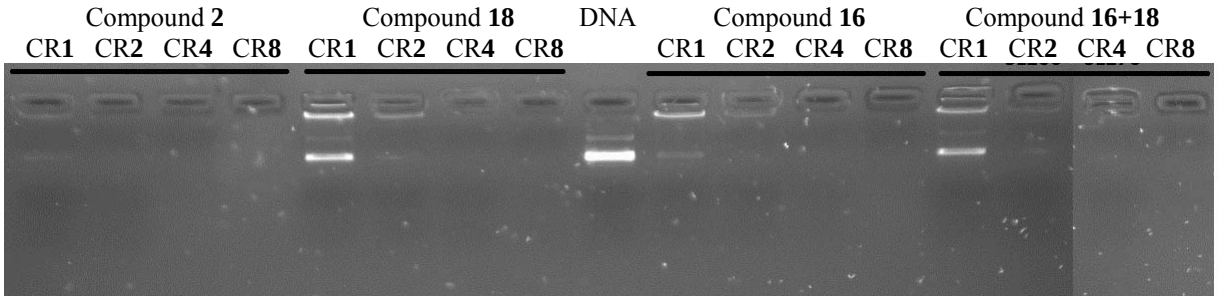


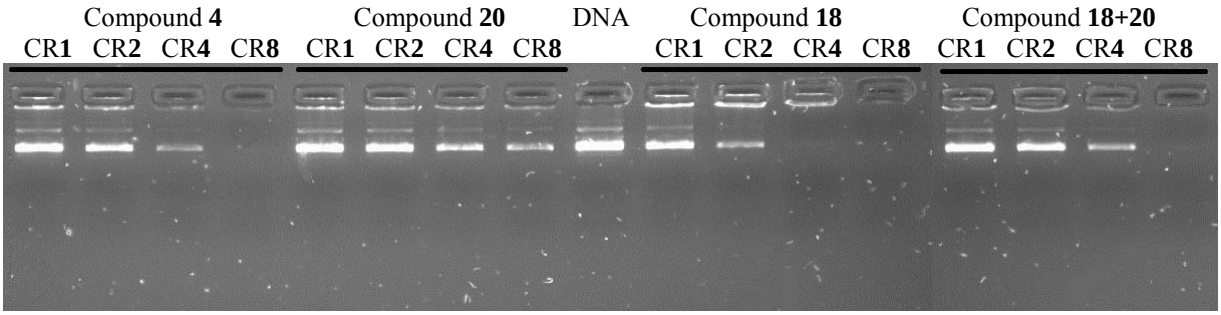
Figure S3-60: ^{13}C jmod ($CDCl_3$) spectrum of compound **24**.

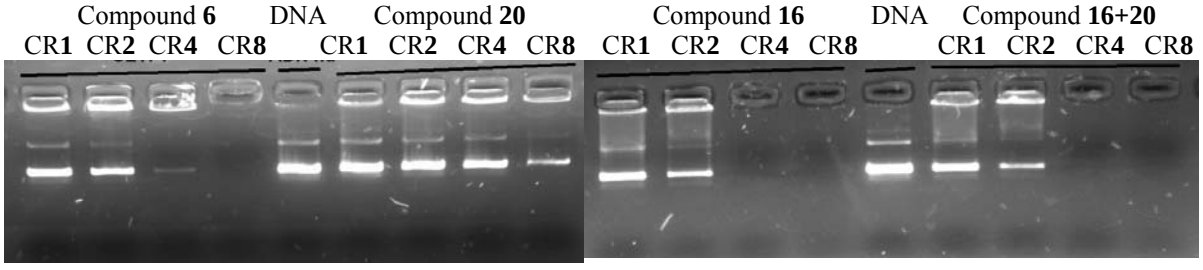
S4 Size, Zeta

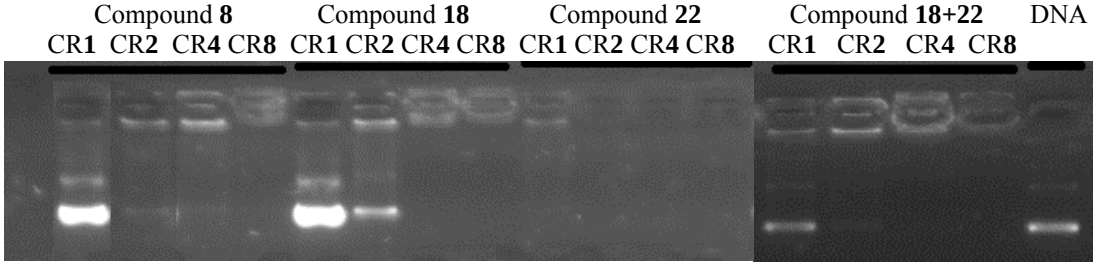
Series	Compound[a]	Size (nm)	Index Poly	Zeta (mV)
1	Non-symmetric $C_{12:0}/C_{18:1}$ (**2**)	112.8	0.563	49.3
	Symmetric $C_{12:0}$ (**16**)	162.8	0.742	63.5
	Symmetric $C_{18:1}$ (**18**)	66.7	0.352	37.3
	Mixture of **16** and **18** (1/1 ratio)	183.7	0.504	50.8
2	Non-symmetric $C_{20:0}/C_{18:1}$ (**4**)	131.5	0.311	9.1
	Symmetric $C_{18:1}$ (**18**)	63.9	0.393	70.2
	Symmetric $C_{20:0}$ (**20**)	194.7	0.304	45.1
	Mixture of **18** and **20** (1/1 ratio)	204.0	0.269	53.7
3	Non-symmetric $C_{12:0}/C_{20:0}$ (**6**)	170.0	0.242	39.1
	Symmetric $C_{12:0}$ (**16**)	120.8	0.362	51.7
	Symmetric $C_{20:0}$ (**20**)	178.4	0.315	31.2
	Mixture of **16** and **20** (1/1 ratio)	266.7	0.488	46.0
4	Non-symmetric $C_{14:0}/C_{18:1}$ (**8**)	154.8	0.204	52.3
	Symmetric $C_{18:1}$ (**18**)	125.0	0.273	50.1
	Symmetric $C_{14:0}$ (**22**)	242.3	0.376	66.9
	Mixture of **18** and **22** (1/1 ratio)	107.3	0.390	49.1
5	Non-symmetric $C_{14:0}/C_{20:0}$ (**10**)	262.1	0.387	46.7
	Symmetric $C_{20:0}$ (**20**)	156.4	0.193	33.5
	Symmetric $C_{14:0}$ (**22**)	242.3	0.376	66.9
	Mixture of **20** and **22** (1/1 ratio)	173.6	0.255	49.1
6	Non-symmetric $C_{14:0}/C_{18:0}$ (**12**)	169.9	0.277	44.4
	Symmetric $C_{18:0}$ (**24**)	172.7	0.349	44.3
	Symmetric $C_{14:0}$ (**22**)	213.4	0.302	40.6
	Mixture of **24** and **22** (1/1 ratio)	179.9	0.409	53.1
7	Non-symmetric $C_{holest}/C_{18:1}$ (**14**)	210.3	0.406	38.3
	Symmetric $C_{18:1}$ (**18**)	**208.7**	**0.372**	**40.5**

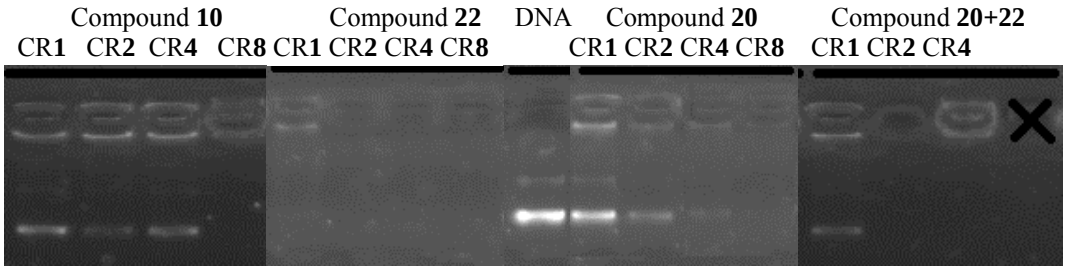
S5 DNA binding ability of cationic lipids

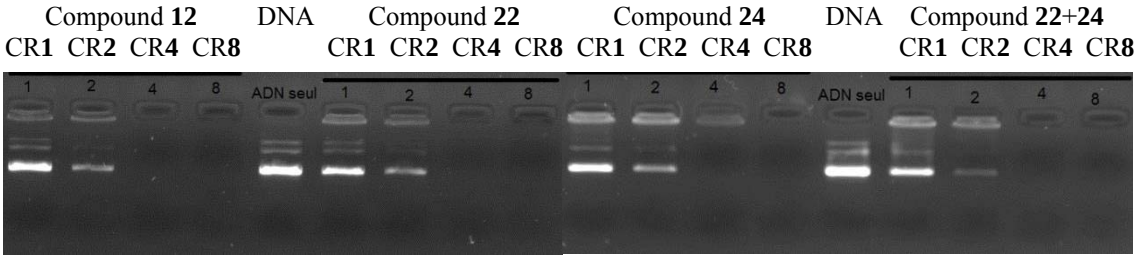




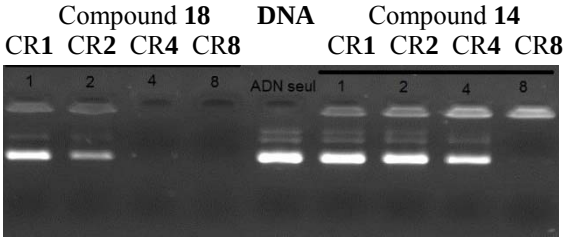






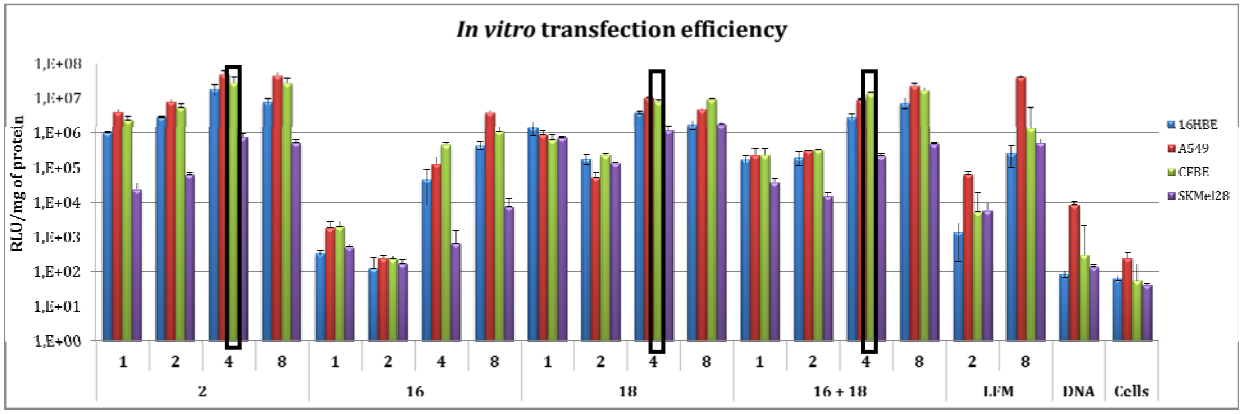


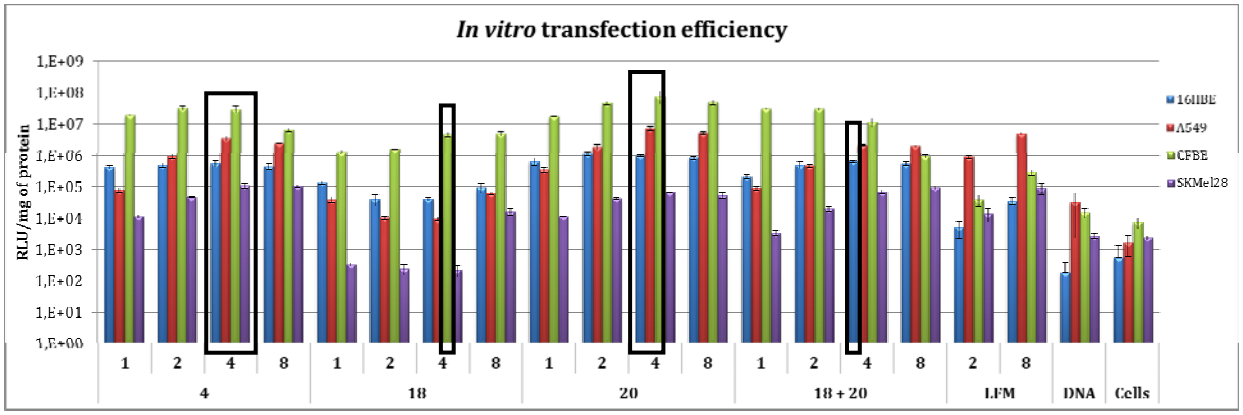
Supporting materials

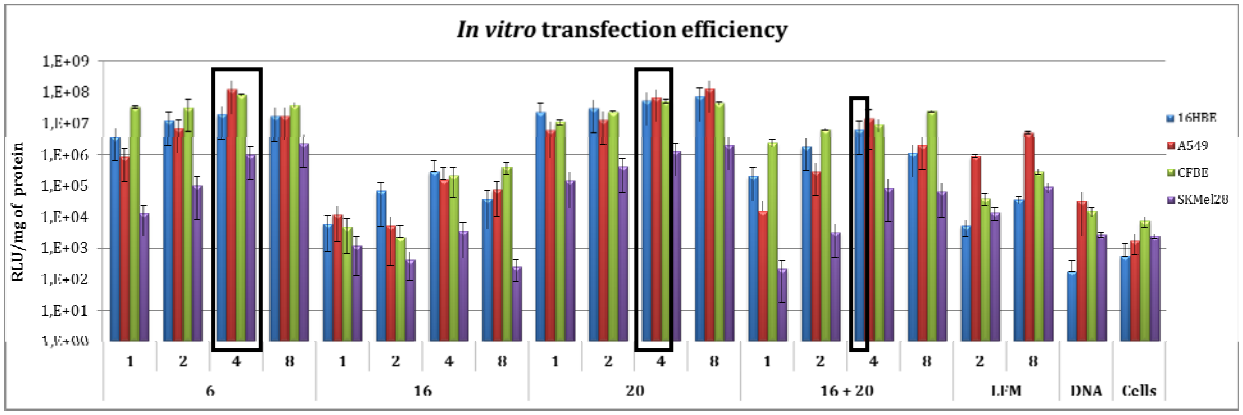


S6 *In vitro* transfection assays

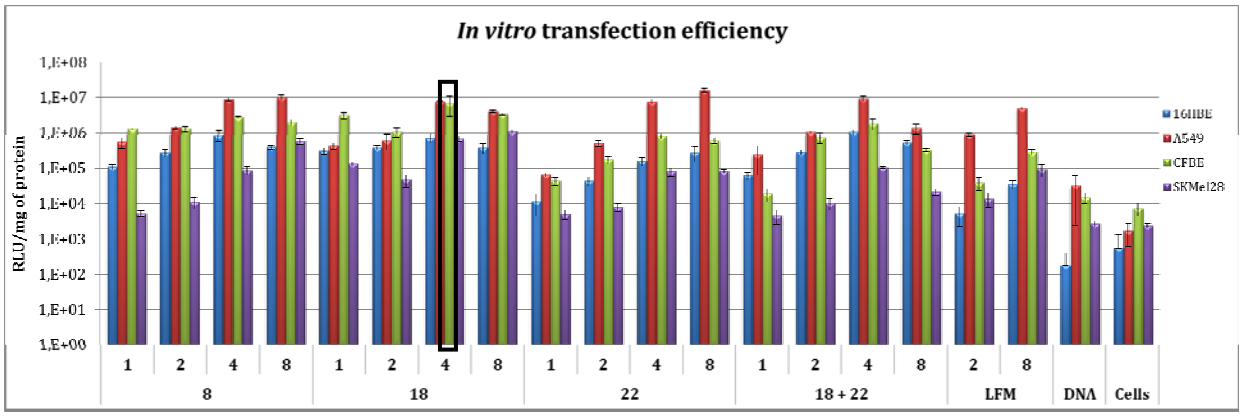
For details see the experimental procedure.

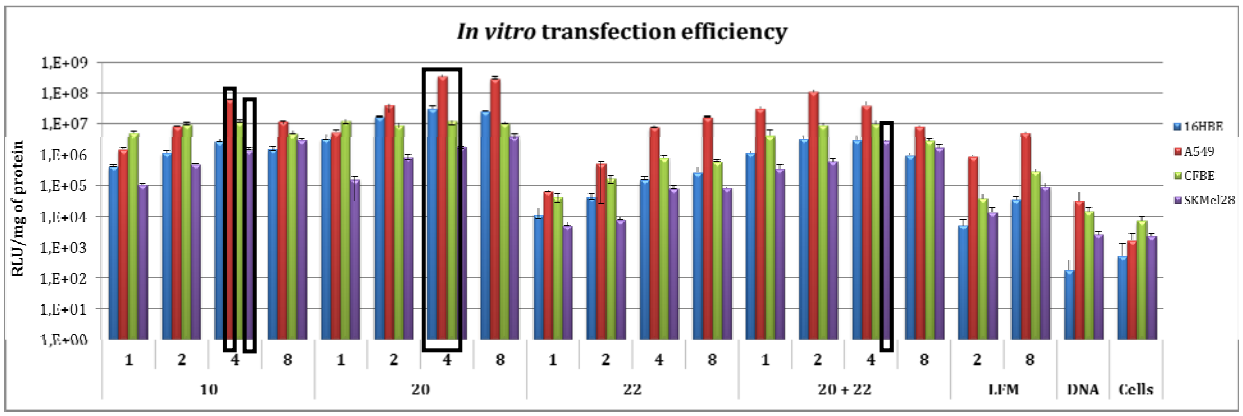


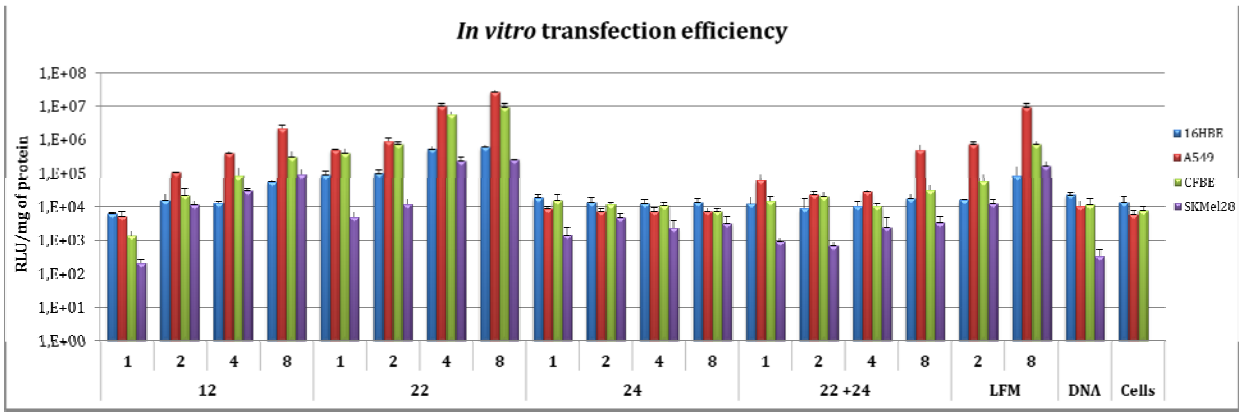


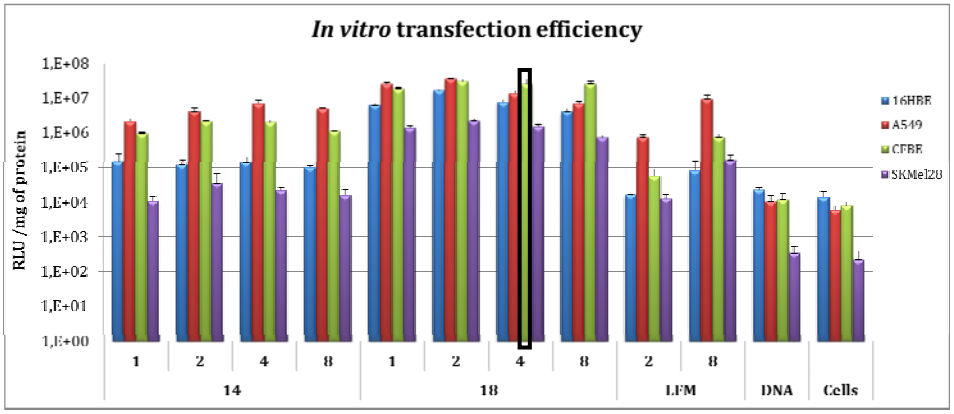


Supporting materials



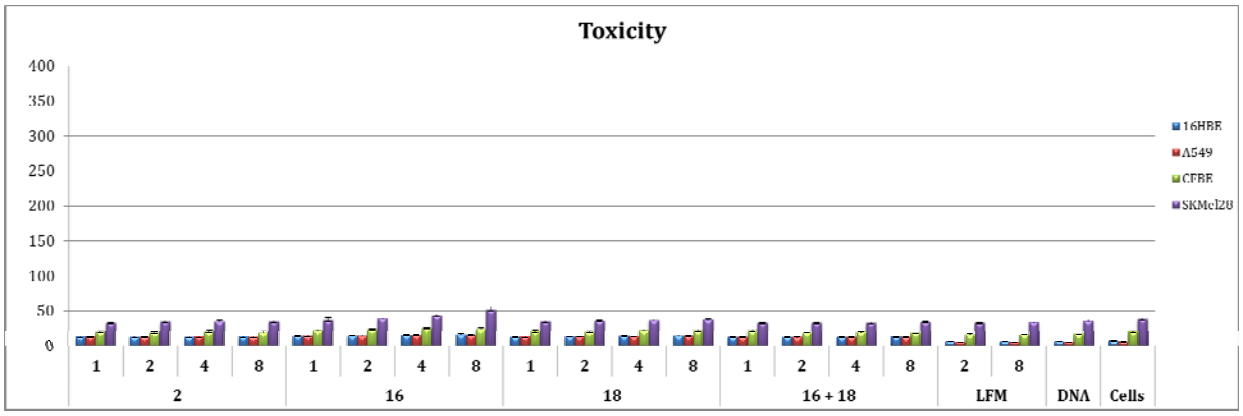


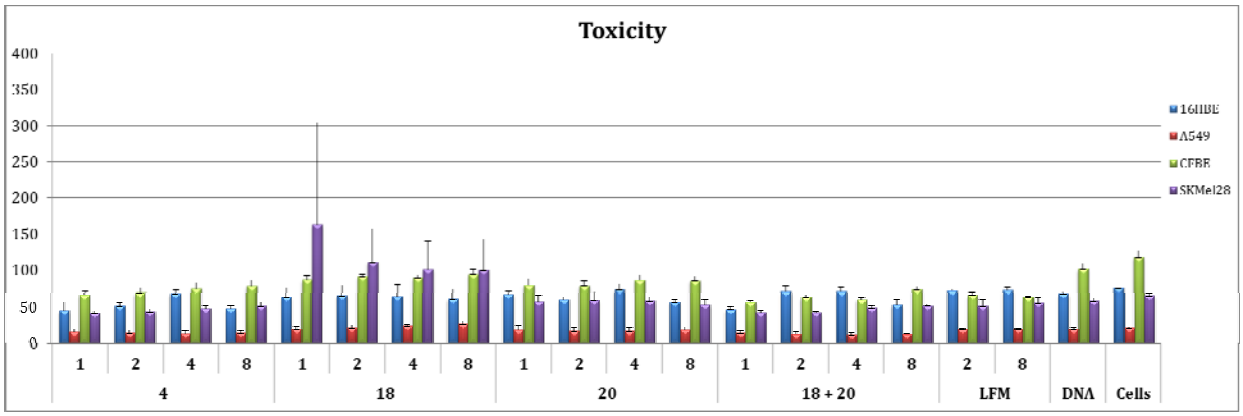


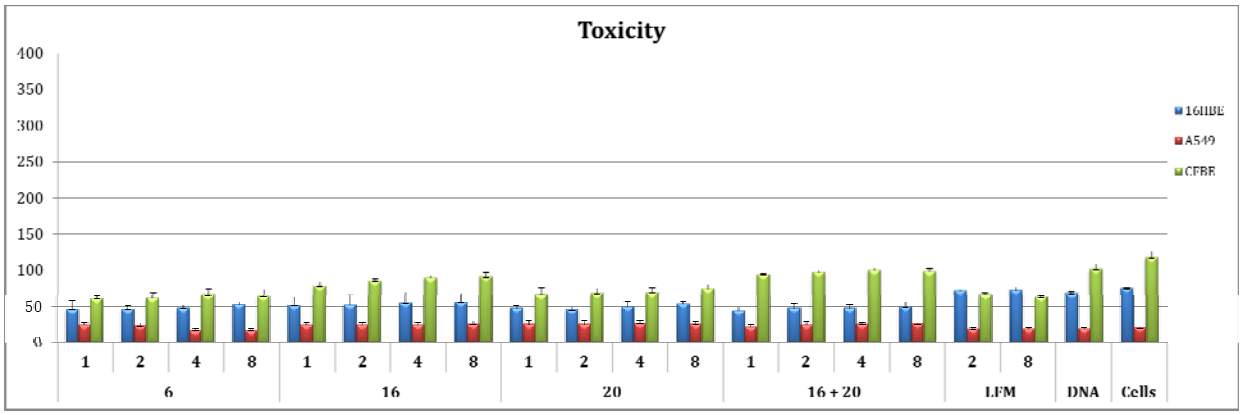


S7 Evaluation of toxicity

The toxicity of the different lipid/DNA complexes was determined by using a chemiluminescent assay (Toxilight - Cambrex, Liège, Belgium). For details see experimental procedure.







Supporting materials