

Cationic dialkylarylphosphate: new family of bio-inspired cationic lipids for gene delivery.

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S1 Size and Zeta measurements

Compound	Size – nm % of population^a	polydispersity Index	Zeta (mV)
10	78 (+/- 52)	0.274	42.1 (+/- 5)
11	101 (+/- 52) ; 91% 22 (+/- 6) ; 9%	0.292	50.3 (+/- 5)
12	64 (+/- 34)	0.249	40.9 (+/- 5)
17	124 (+/- 60) ; 60 % 647 (+/- 329) ; 40%	0.209	66.0 (+/- 8)
18	110 (+/- 57) ; 64% 941 (+/- 519) ; 36%	0.413	81.1 (+/- 8)
19	160 (+/- 75)	0.261	47.5 (+/- 5)
20	111 (+/- 47)	0.214	80.5 (+/- 5)
21	246 (+/- 81)	0.343	81.1 (+/- 7)
22	136 (+/- 71)	0.344	84.5 (+/- 8)

a) % of each population if the main population has an abundance below 95 %

S2 DNA Condensation experiments

Lipoplexes were prepared by mixing pDNA (3,7kb, pCMV-Luc) with a liposomal solution. Shortly, 1 μ g of pDNA in OptiMem (Gibco) were added to cationic lipids (liposomal solution) at concentrations corresponding to the +/- charge ratios ranging from 1 to 8. These mixtures were incubated for 30 min at RT. The complexes were subjected to electrophoresis in 0.8% agarose gel at 100 V, 90 mA. The gel was stained with ethidium bromide (10 mg/mL) and then visualized using an UV transilluminator

Figure S2-1 Monocationic dialkyl-arylphosphate

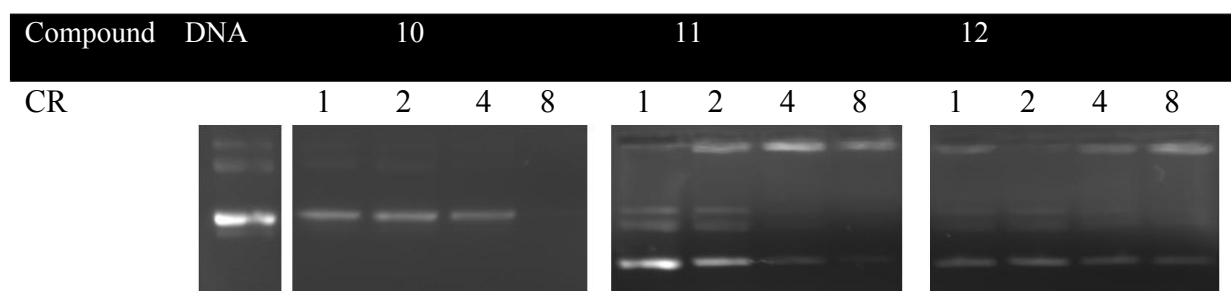
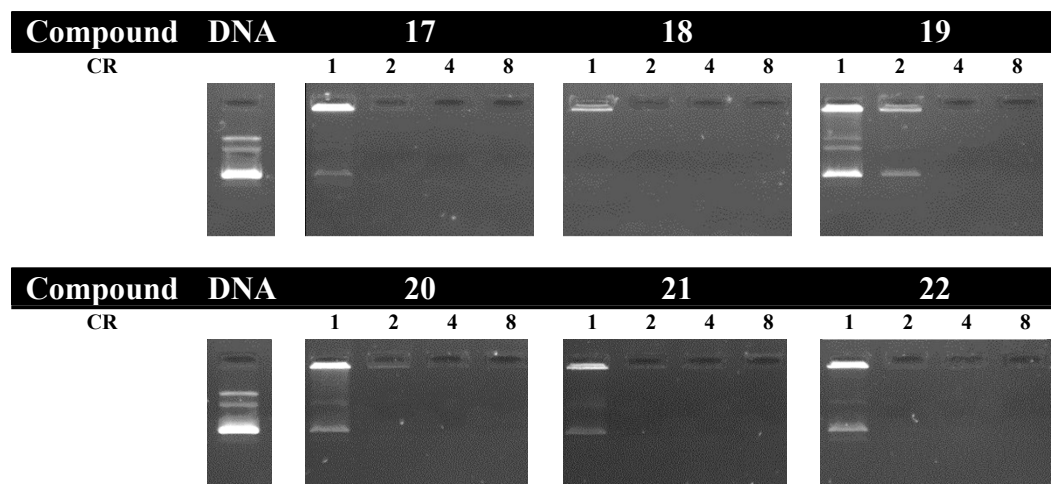
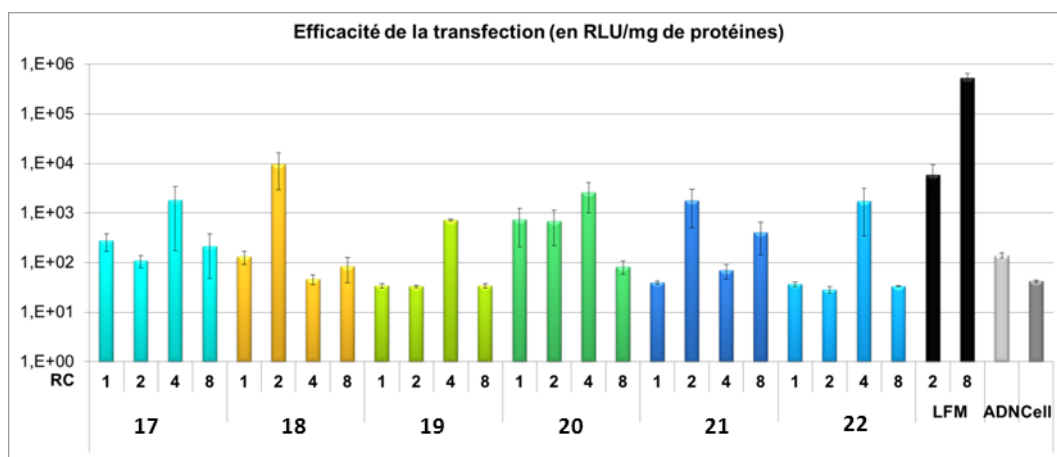


Figure S2-2 Dicationic dialkyl-arylphosphate



S3 In vitro transfection assays – SKMel28

Transfection efficacies of dicationic dialkylarylphosphate as determined using a luciferase-encoding pDNA and SKMel28 cell line. The CRs used were either 1, 2, 4, and 8. The transfection efficacy was expressed in RLU/mg of proteins.



S4 Comparison of transfection efficacy and toxicity of monocationic lipid 11 and di-cationic lipid 19.

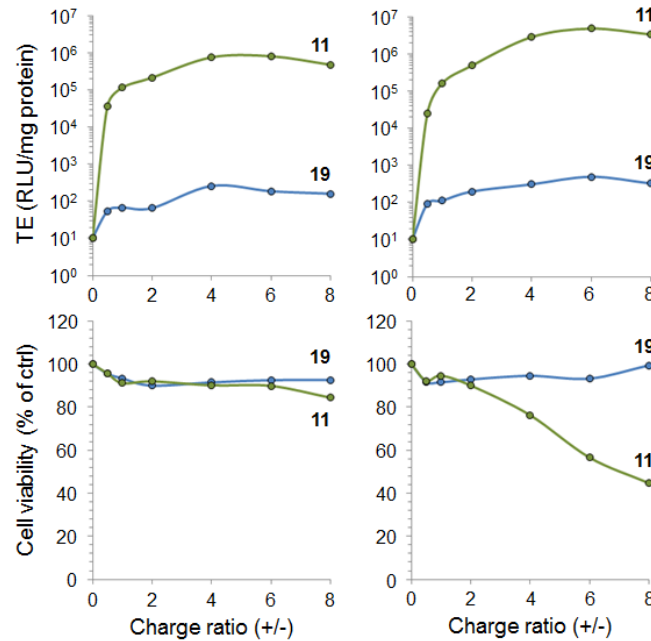
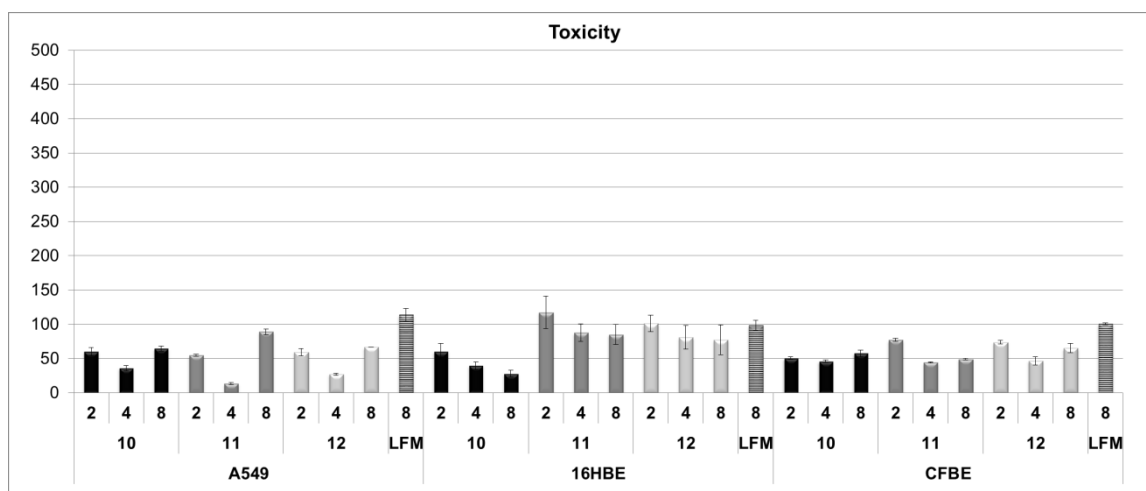


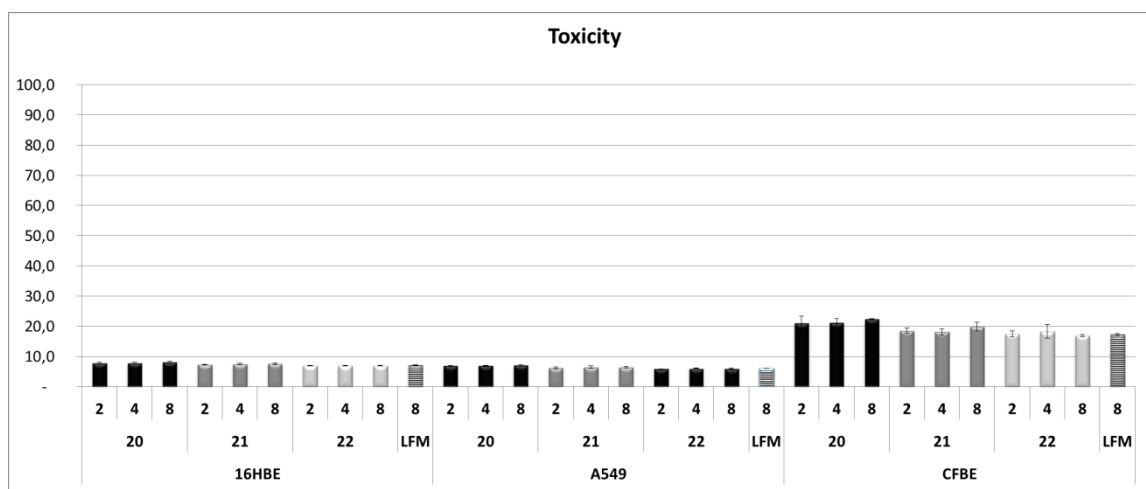
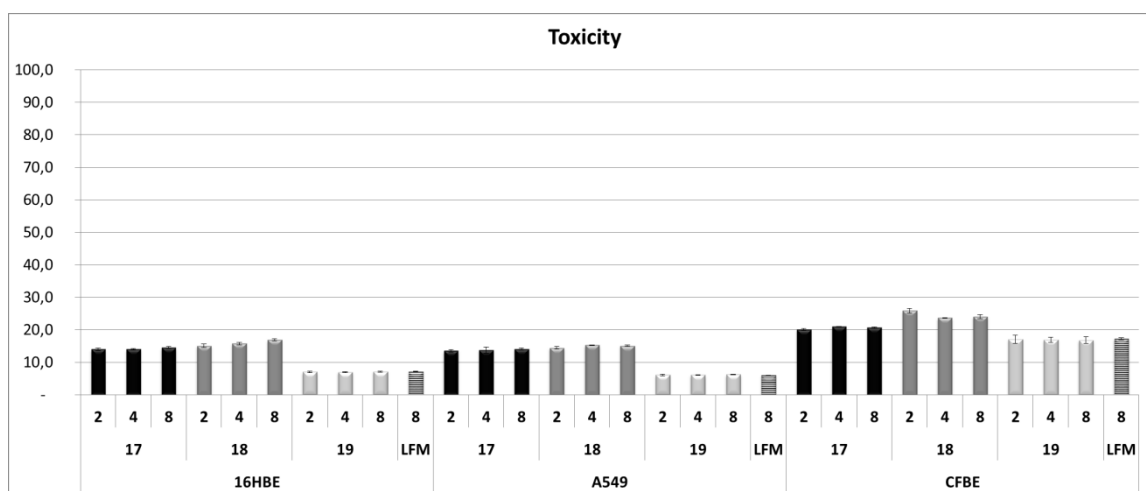
Figure S4 *In vitro* transfection efficiency (TE, top panels) and cell viability (bottom panels) following treatment with monocationic **11** and dicationic **19**-based lipoplexes. Cell viability was determined thanks to the Vialight Kit (Lonza) according to the manufacturer's recommendations. Left panels, 16HBE cell line, and right panels, CFBE cell line.

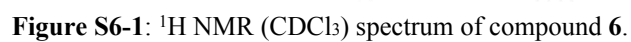
S5 Evaluation of toxicity

- Monocationic dialkyl-arylphosphate

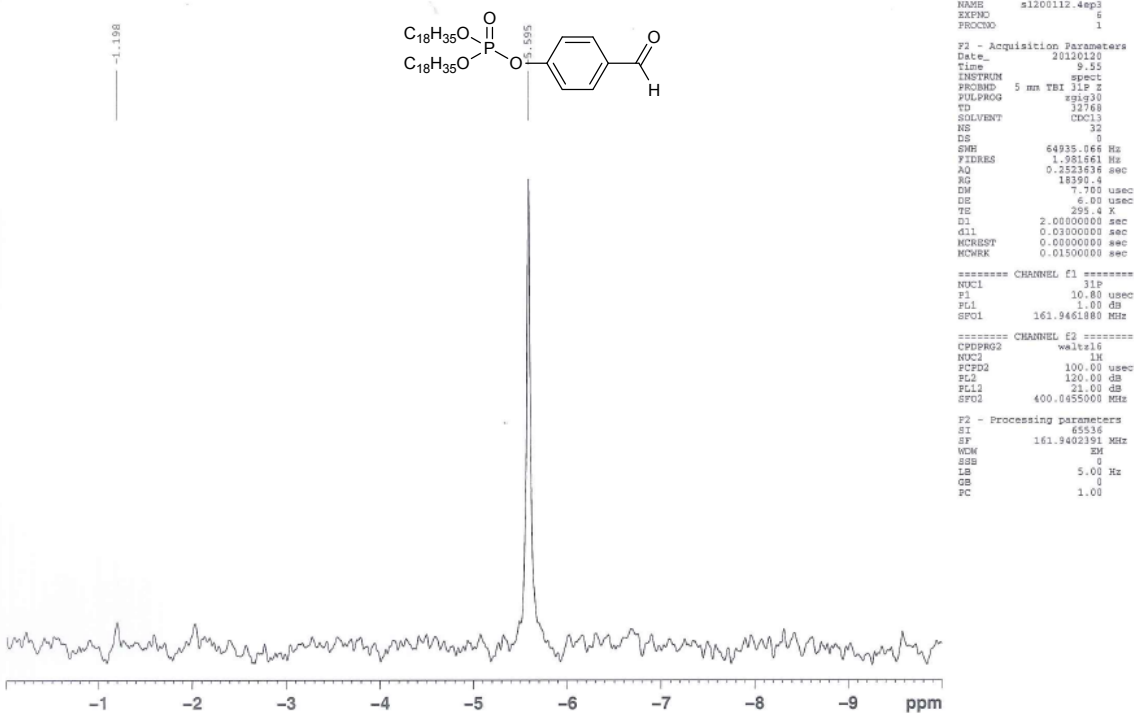


- Dicationic dialkyl-arylphosphate





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Figure S6-2: ³¹P NMR (CDCl₃) spectrum of compound 6.

Supporting materials

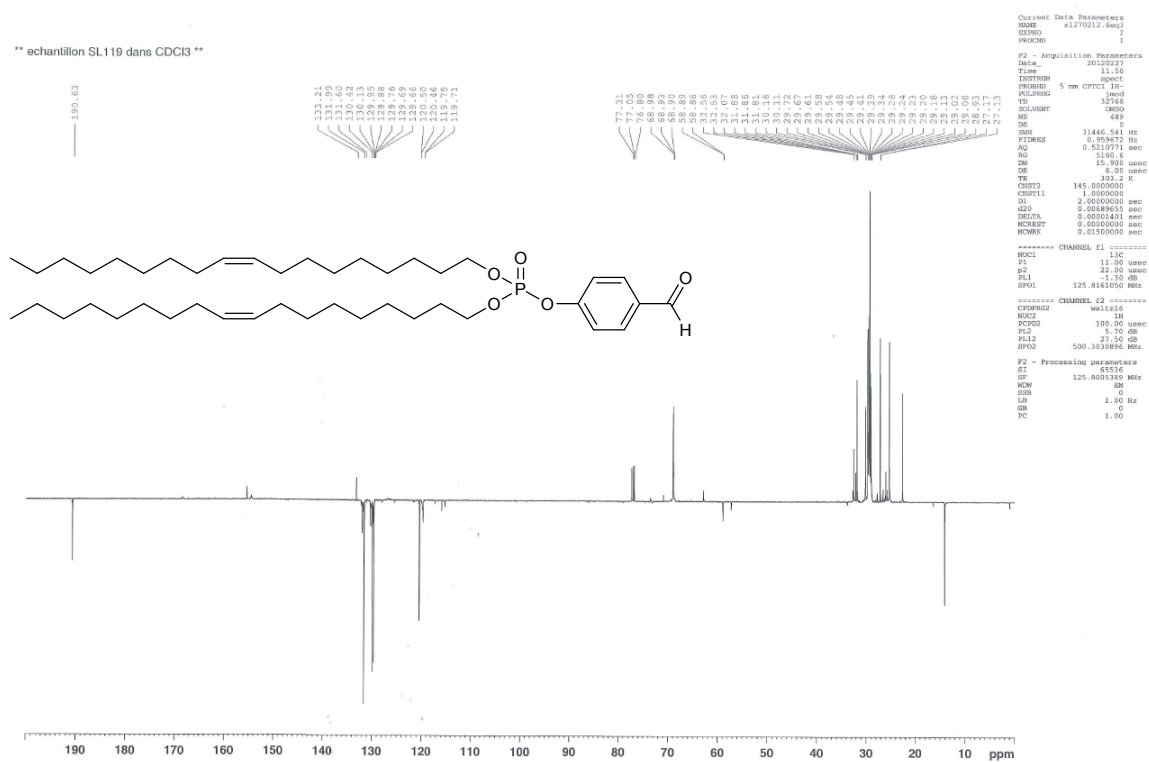
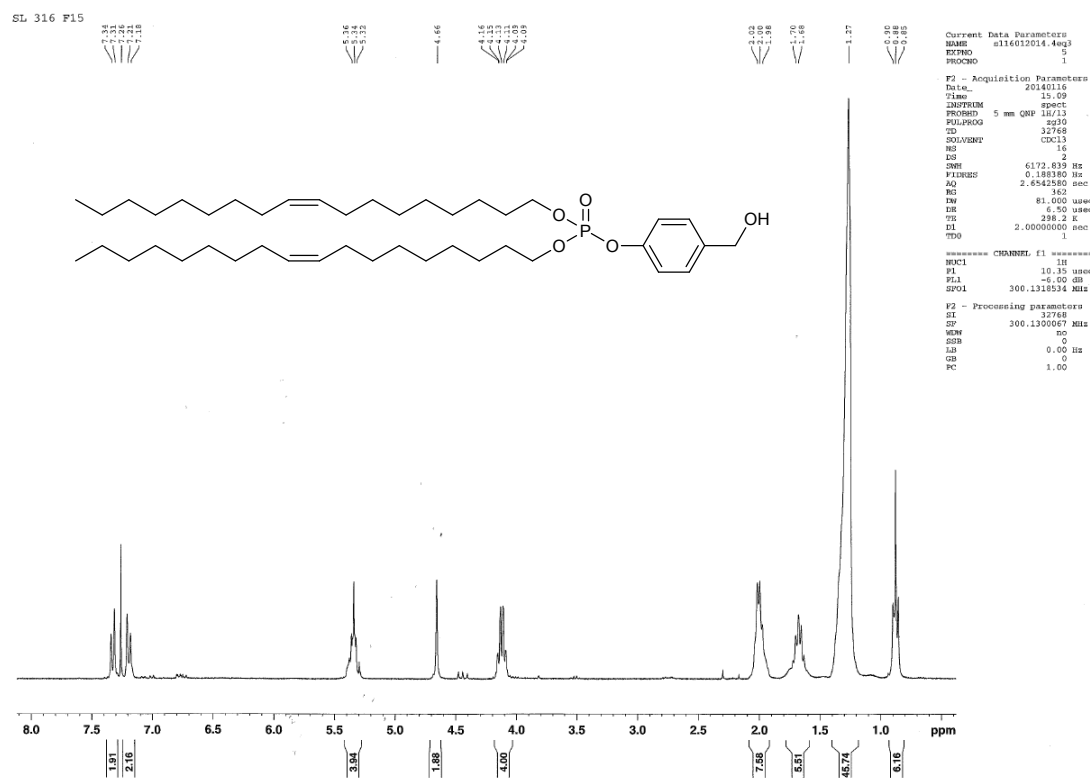


Figure S6-3: ^{13}C jmod (CDCl_3) spectrum of compound **6**.



S6-4: ^1H NMR (CDCl_3) spectrum of compound 7.



Supporting materials

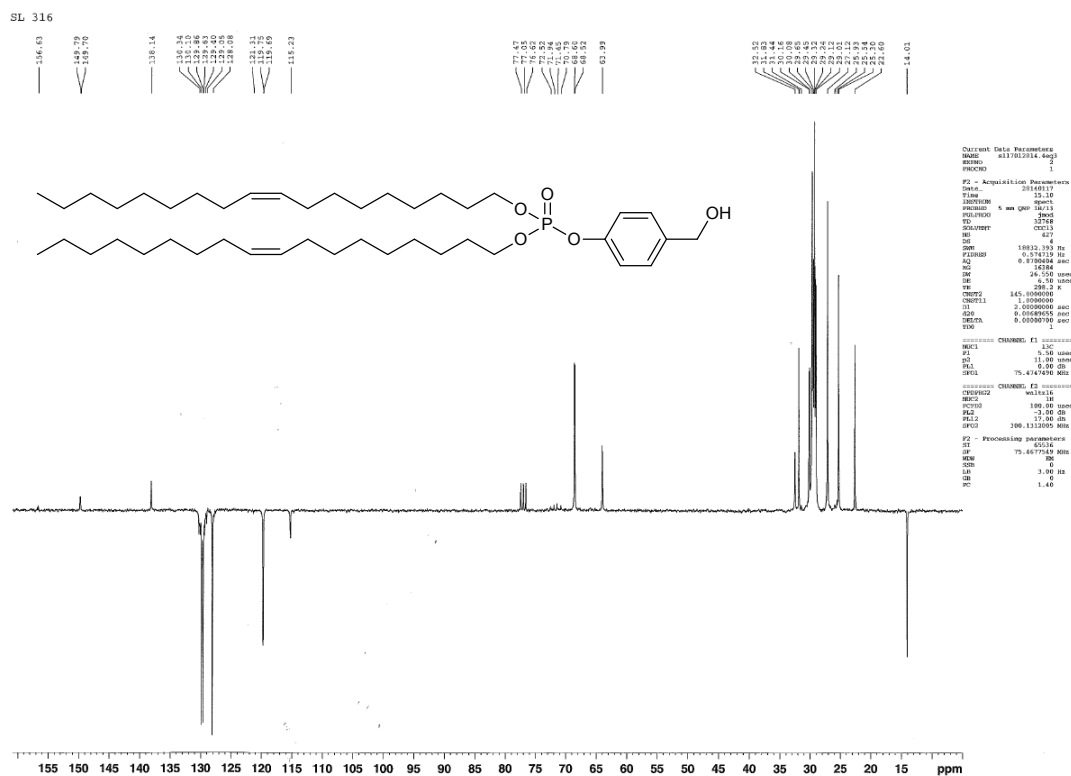


Figure S6-6: ¹³C jmod (CDCl₃) spectrum of compound 7.

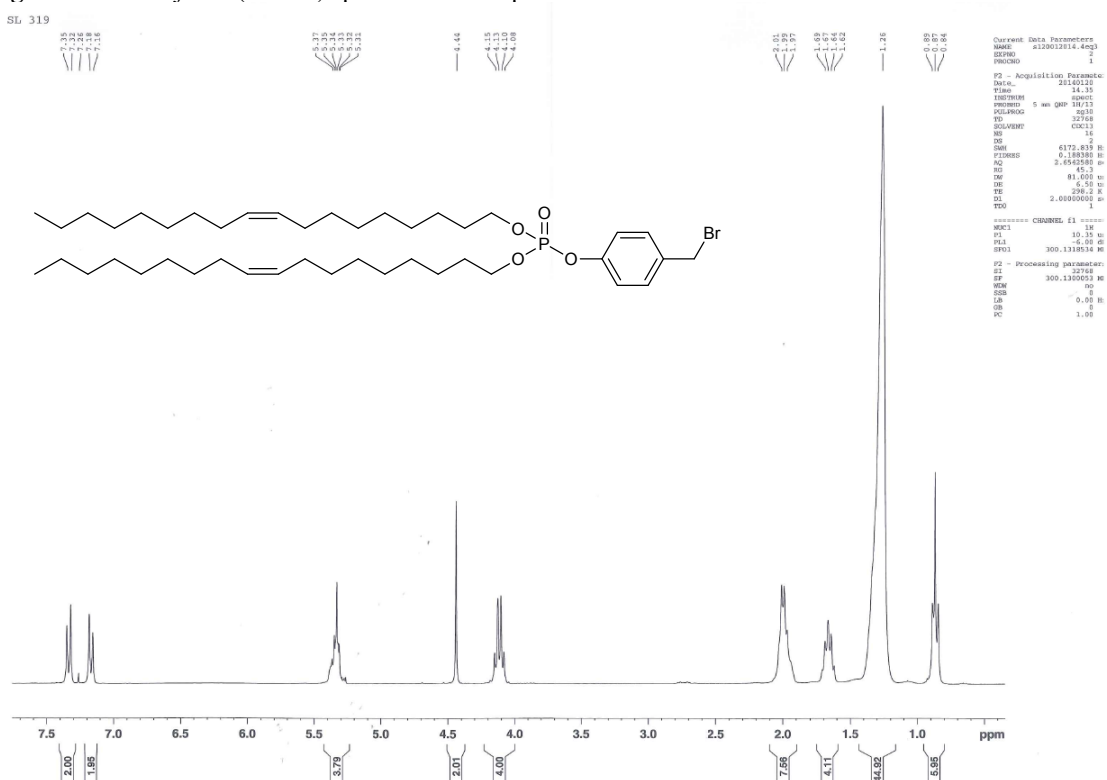


Figure S6-7: ¹H NMR (CDCl₃) spectrum of compound 8.

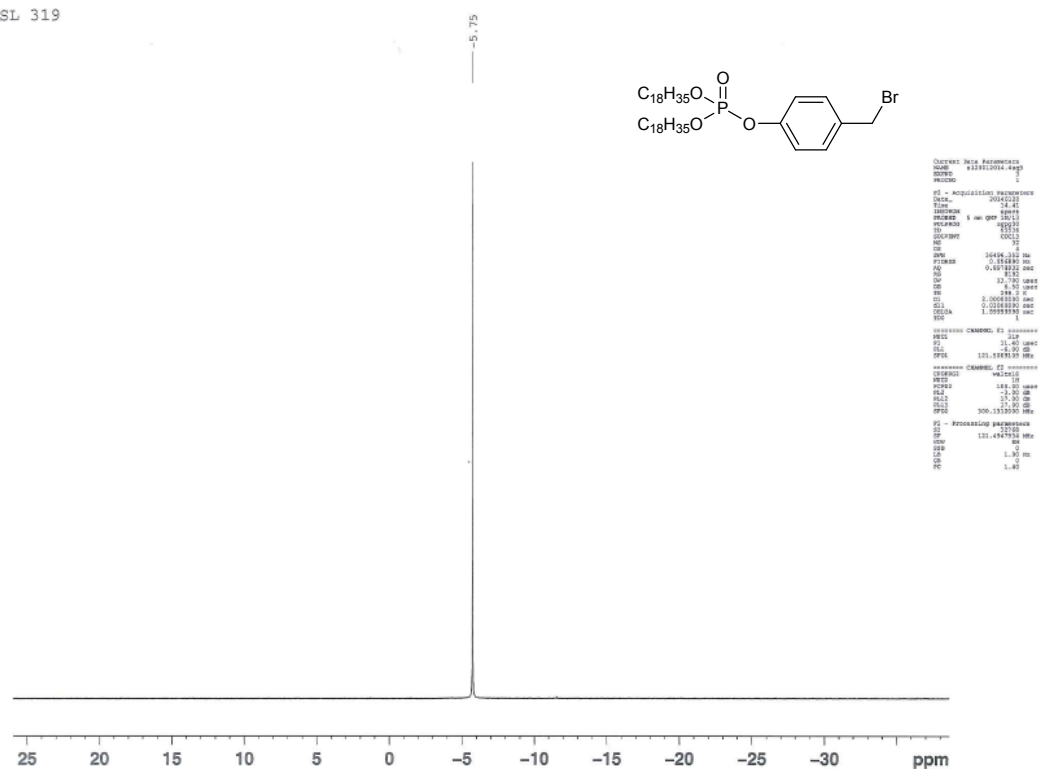


Figure S6-8: ^{31}P NMR (CDCl_3) spectrum of compound **8**.

Supporting materials

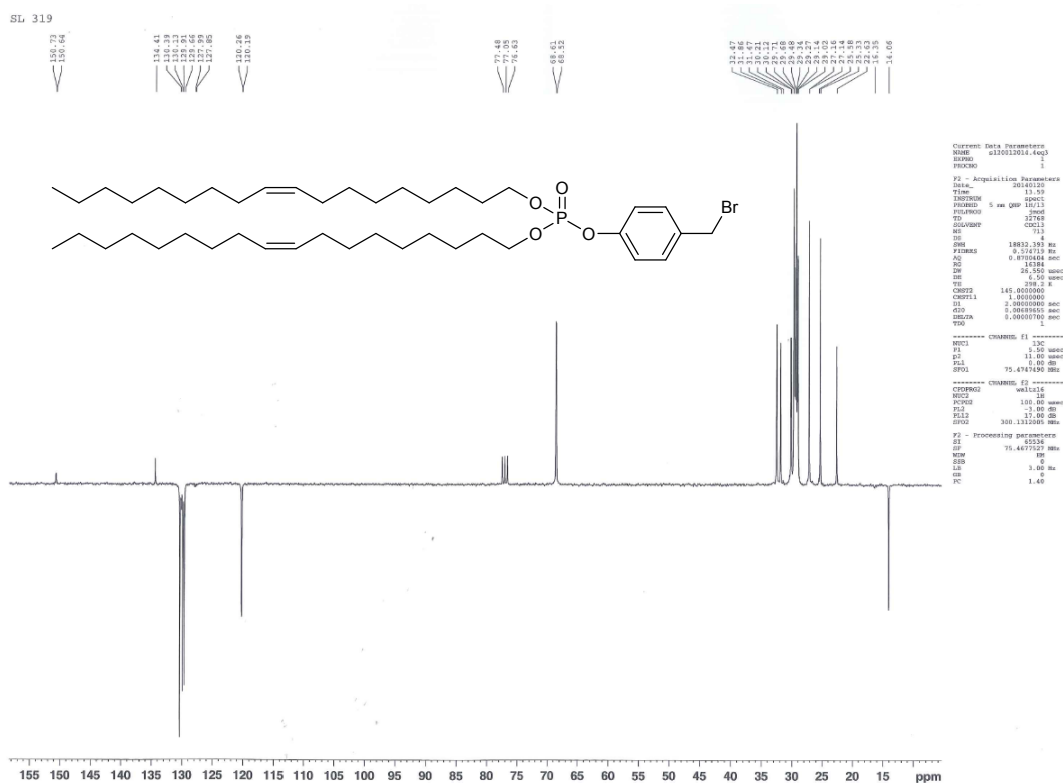


Figure S6-9: ^{13}C jmod (CDCl_3) spectrum of compound 8.

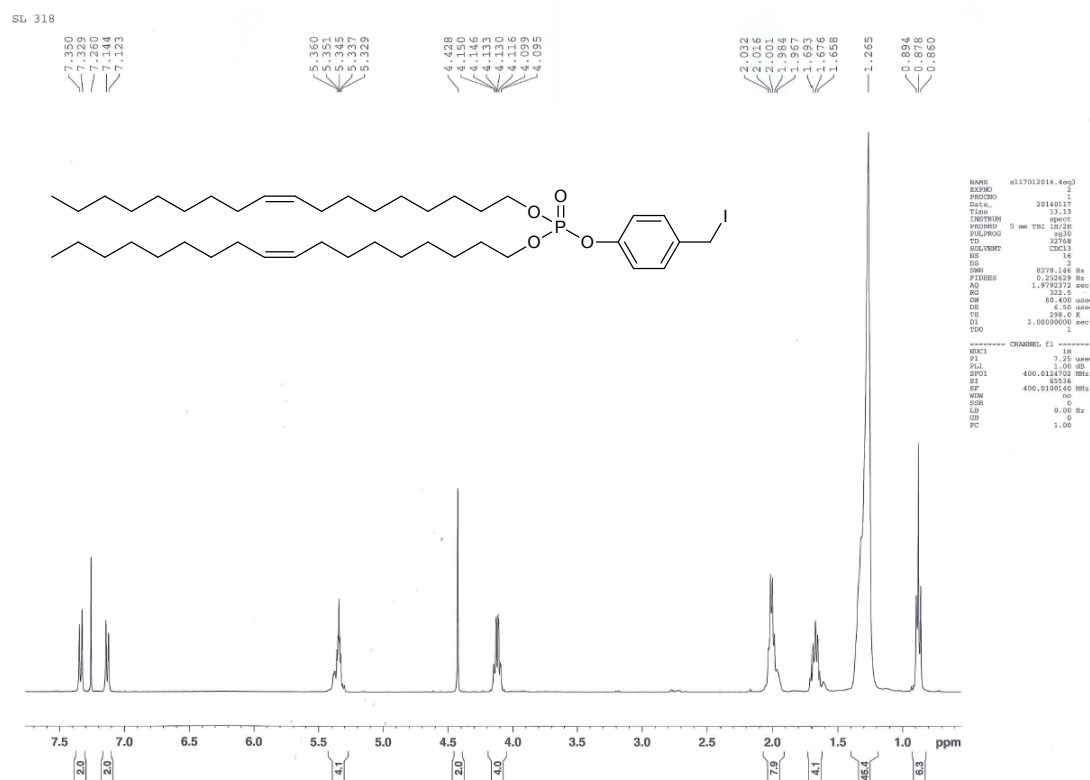


Figure S6-10: ^1H NMR (CDCl_3) spectrum of compound 9.

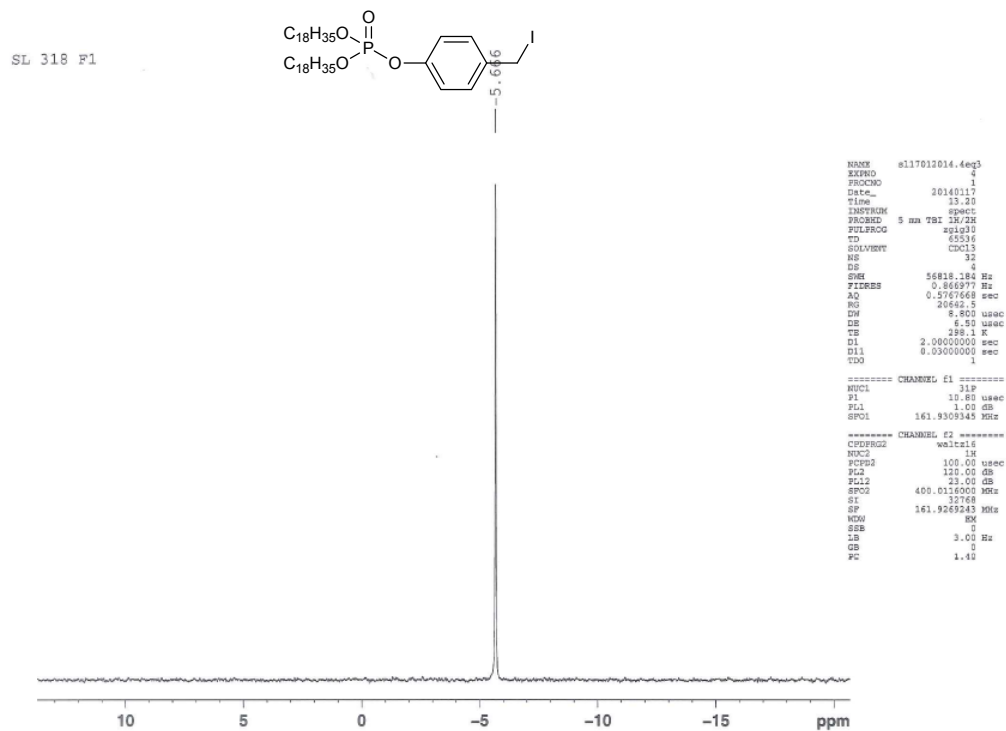


Figure S6-11: ^{31}P NMR (CDCl_3) spectrum of compound **9**.

Supporting materials

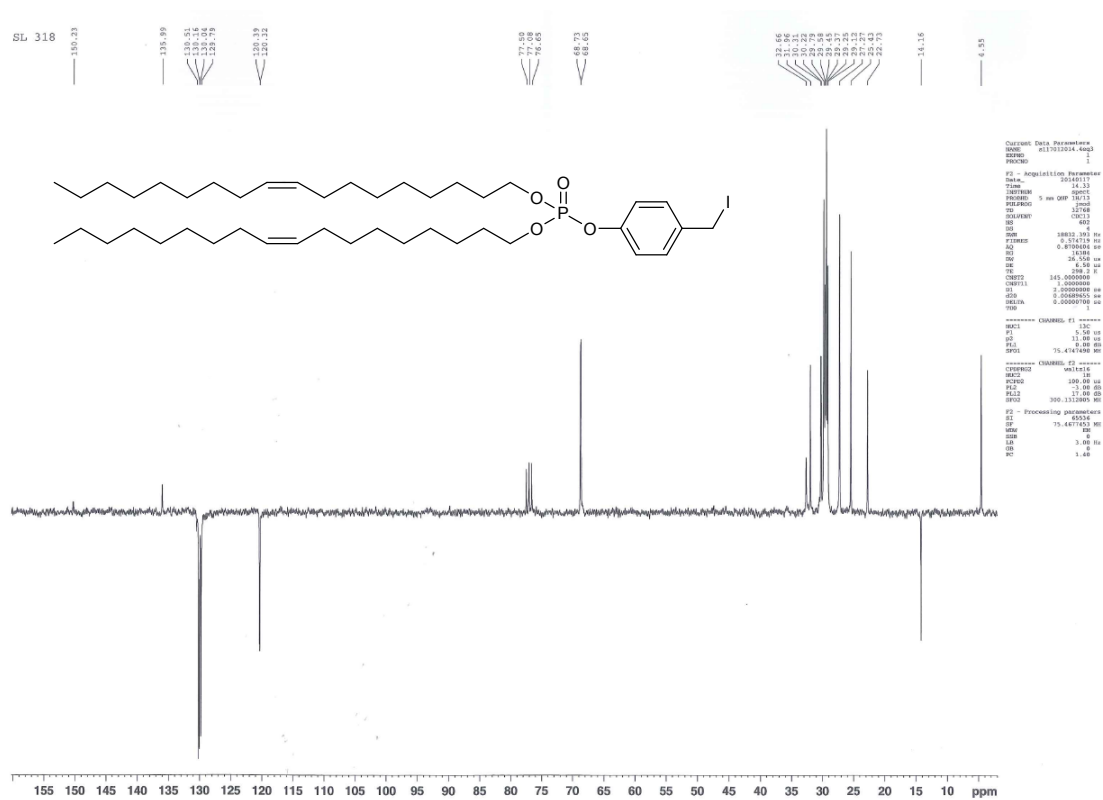


Figure S6-12: ^{13}C jmod (CDCl_3) spectrum of compound **9**.

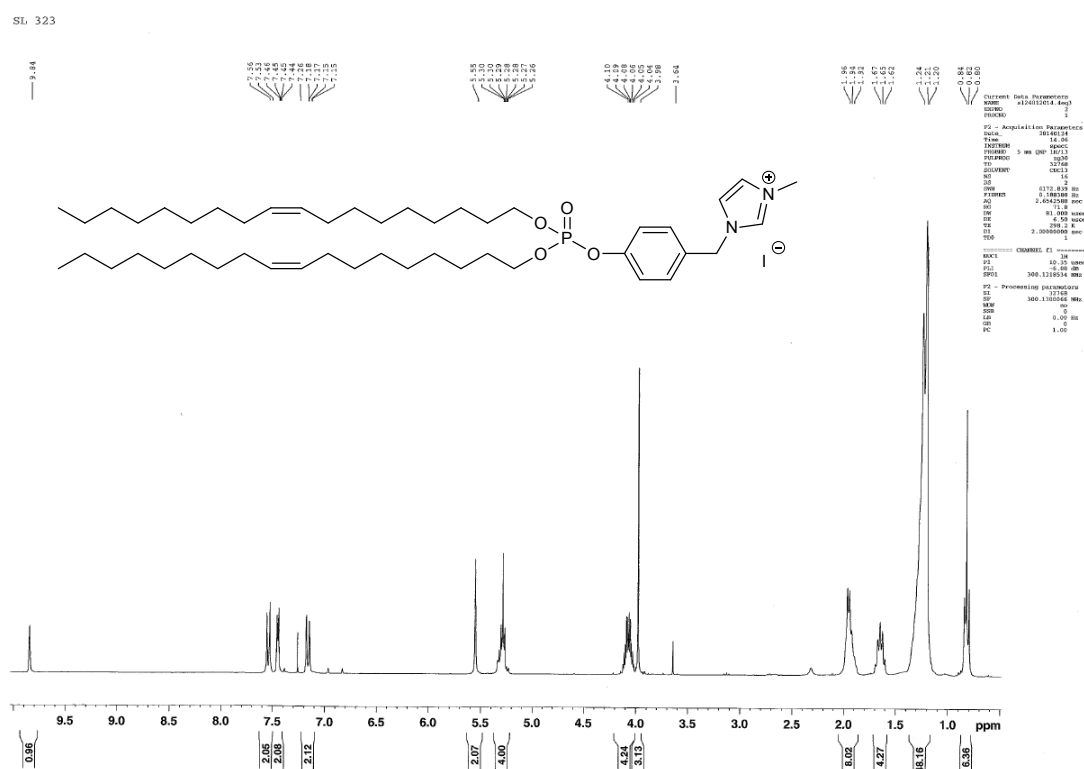
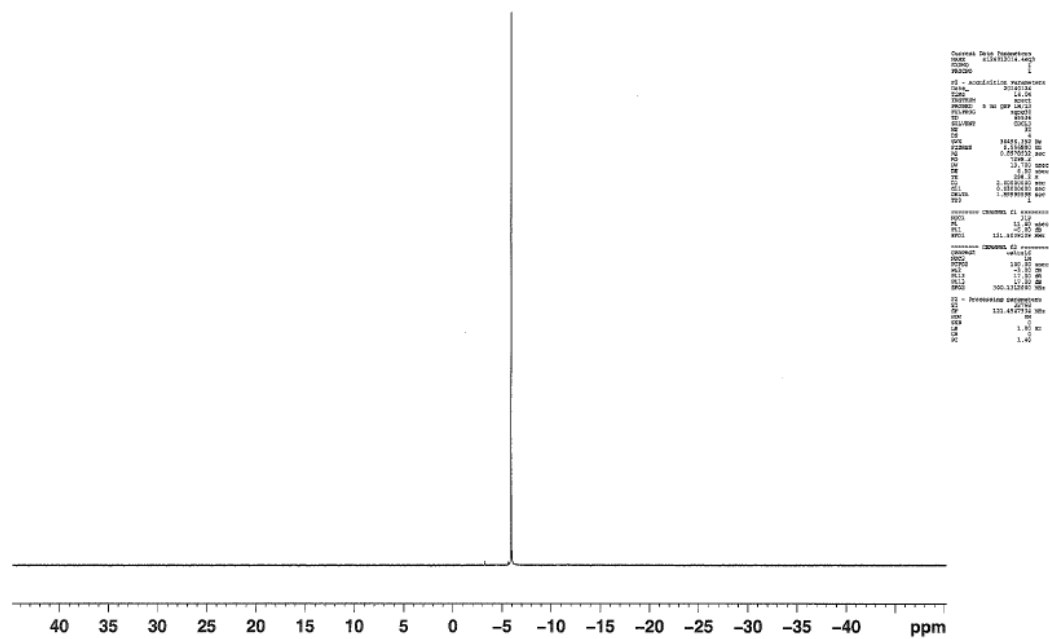
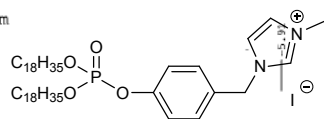


Figure S6-13: ^1H NMR (CDCl_3) spectrum of compound **10**.

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Figure S6-14: ³¹P NMR (CDCl₃) spectrum of compound 10.

Supporting materials

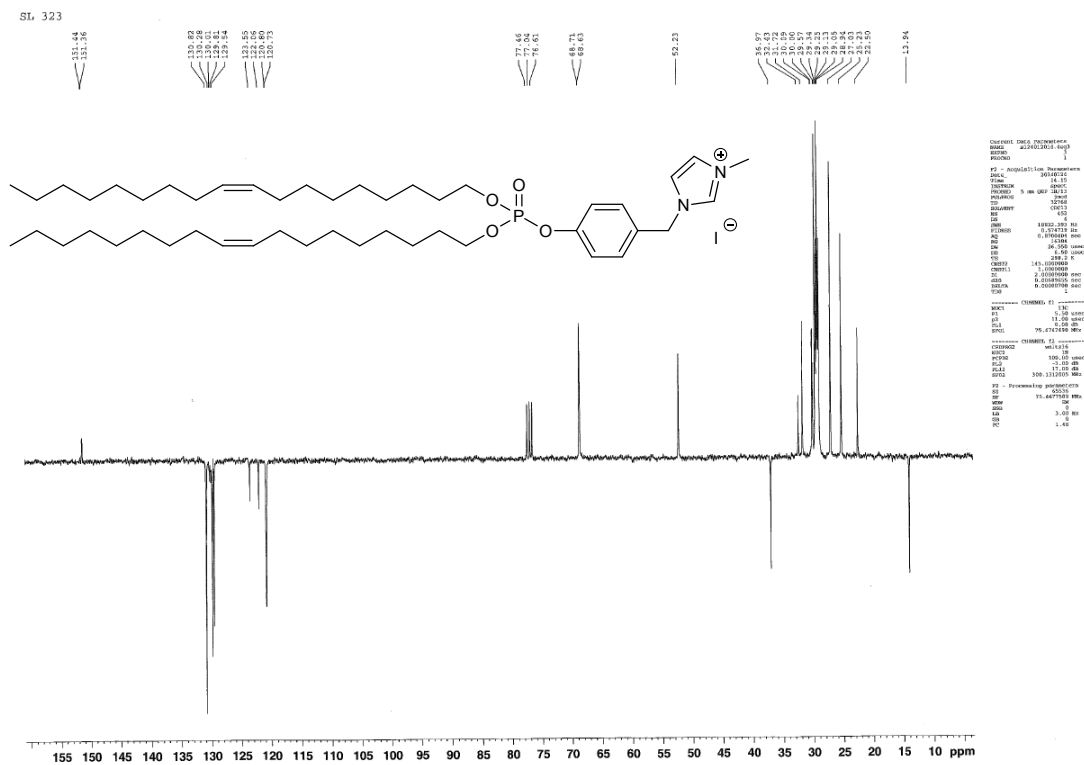


Figure S6-15: ^{13}C jmod (CDCl_3) spectrum of compound **10**.

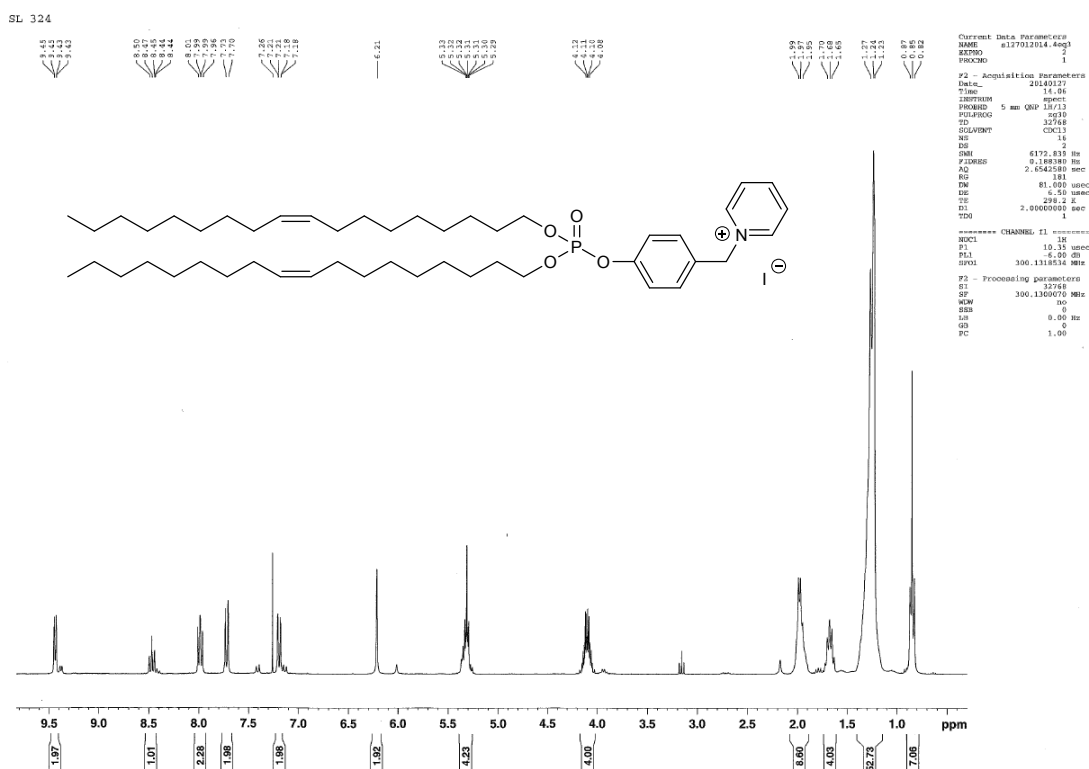
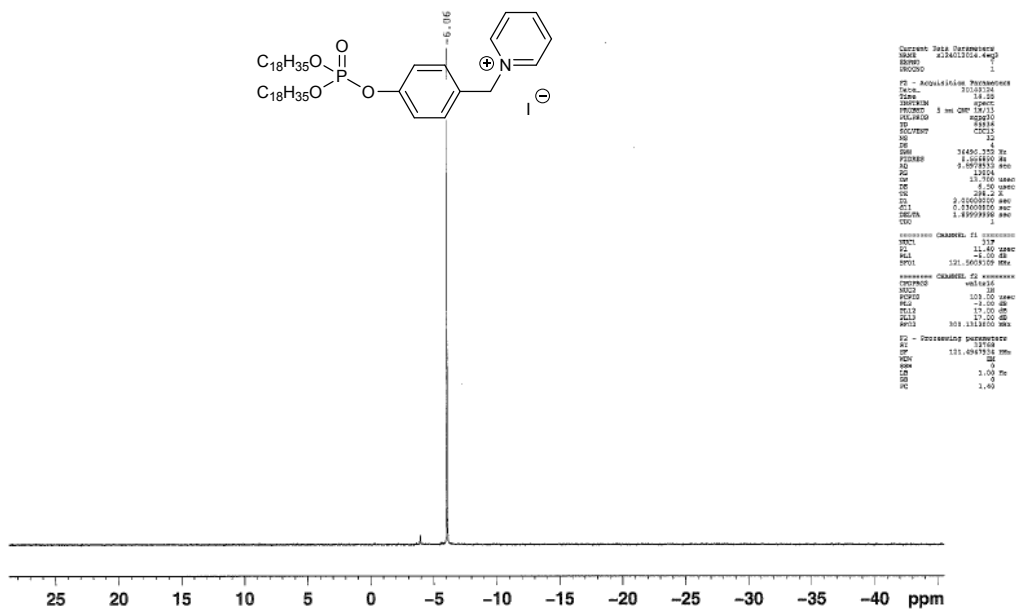


Figure S6-16: ^1H NMR (CDCl_3) spectrum of compound **11**.

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Supporting materials

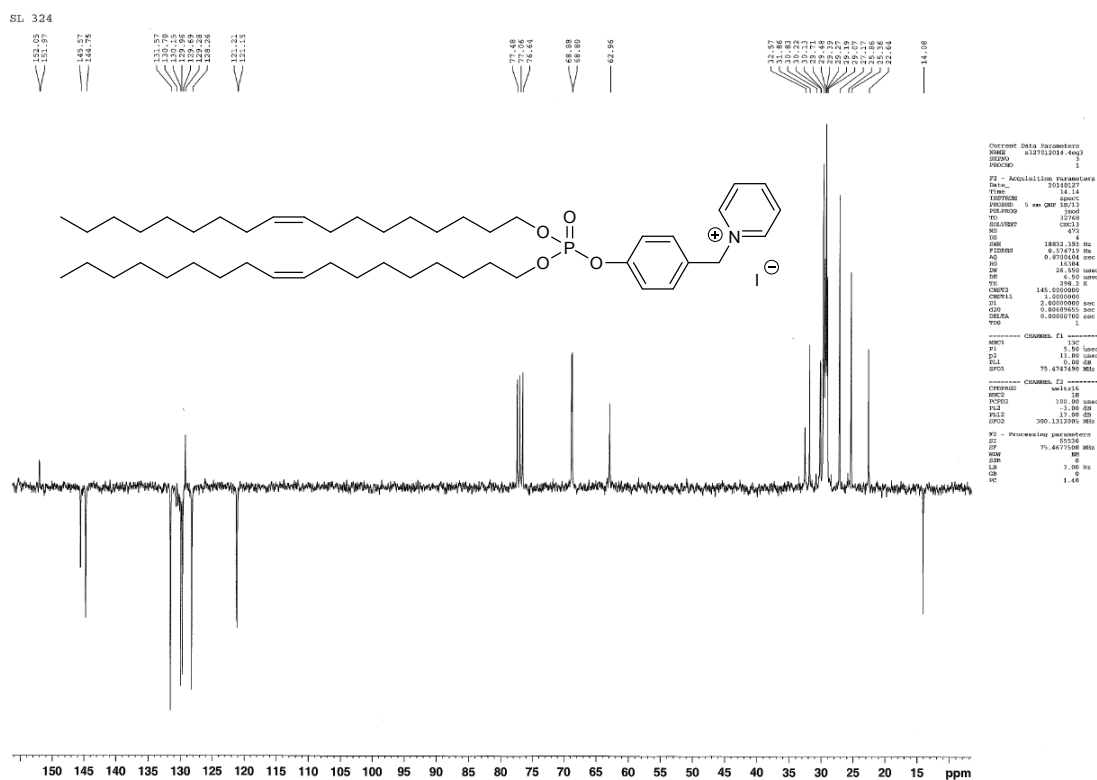


Figure S6-18: ^{13}C jmod (CDCl_3) spectrum of compound **11**.

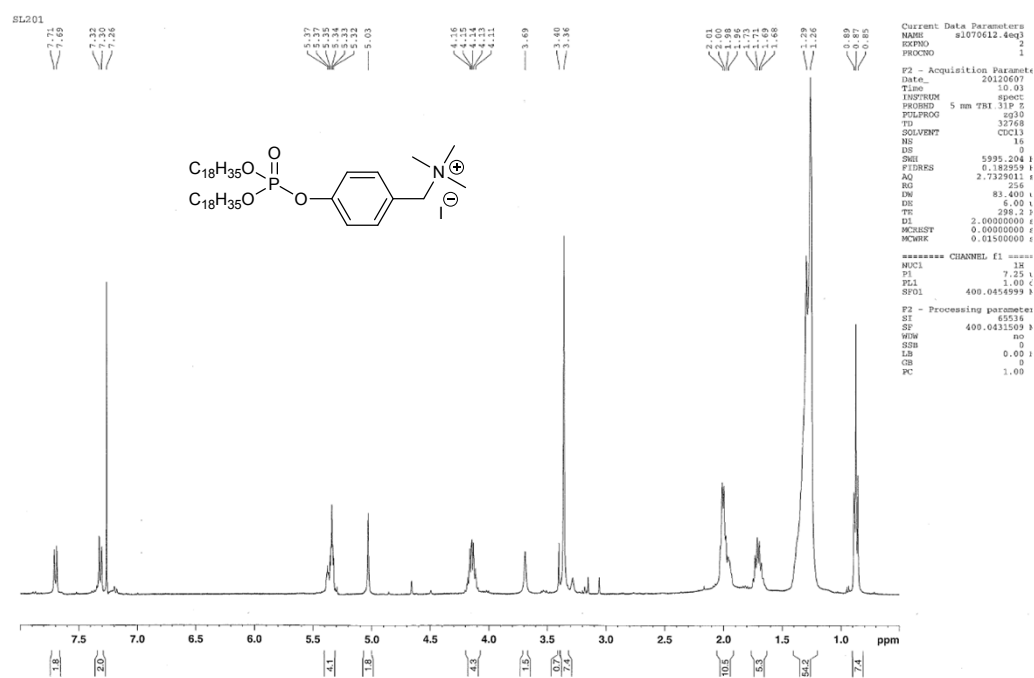
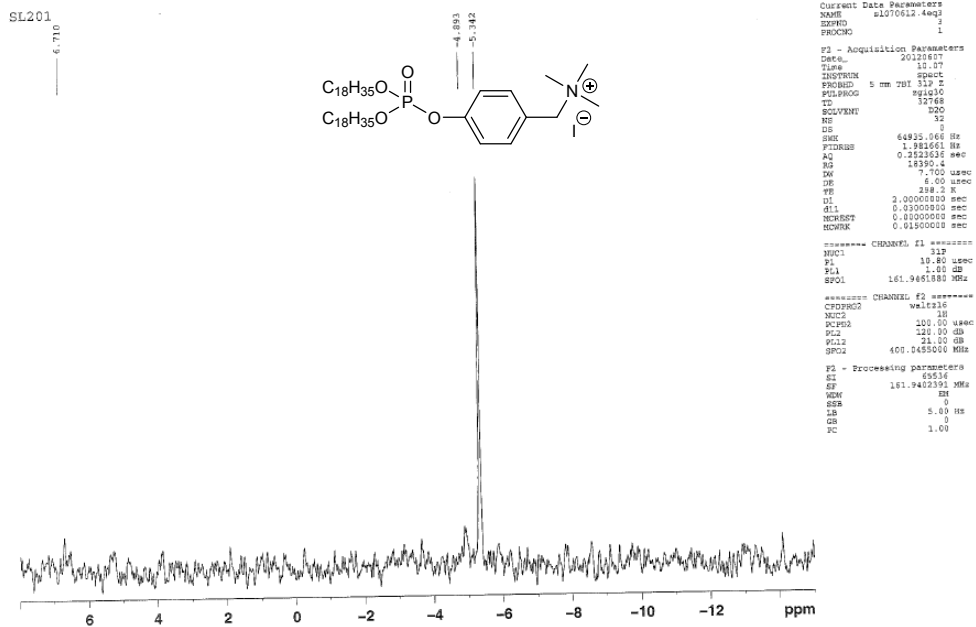


Figure S6-19: ^1H NMR (CDCl_3) spectrum of compound **12**.

Figure S6-20: ^{31}P NMR (CDCl_3) spectrum of compound 12.

Supporting materials

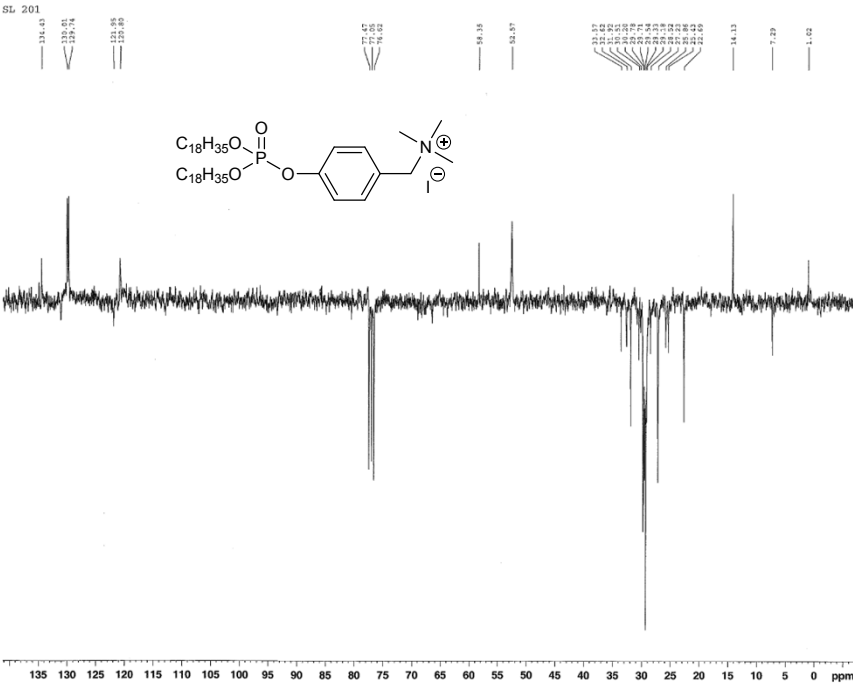
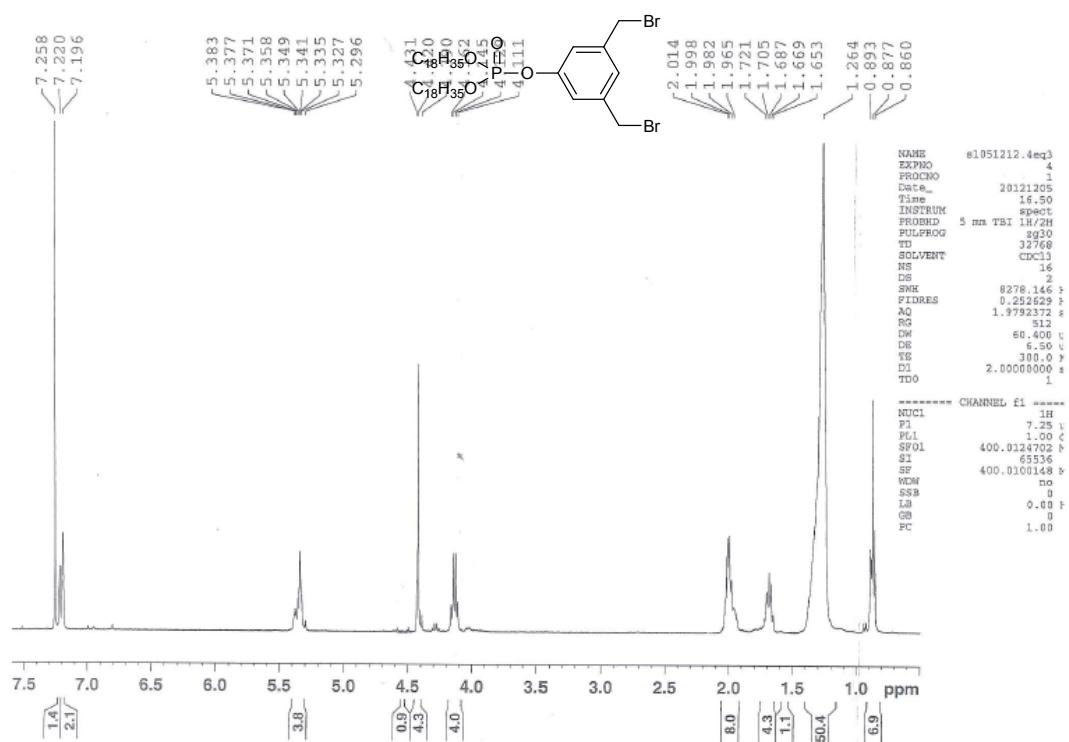
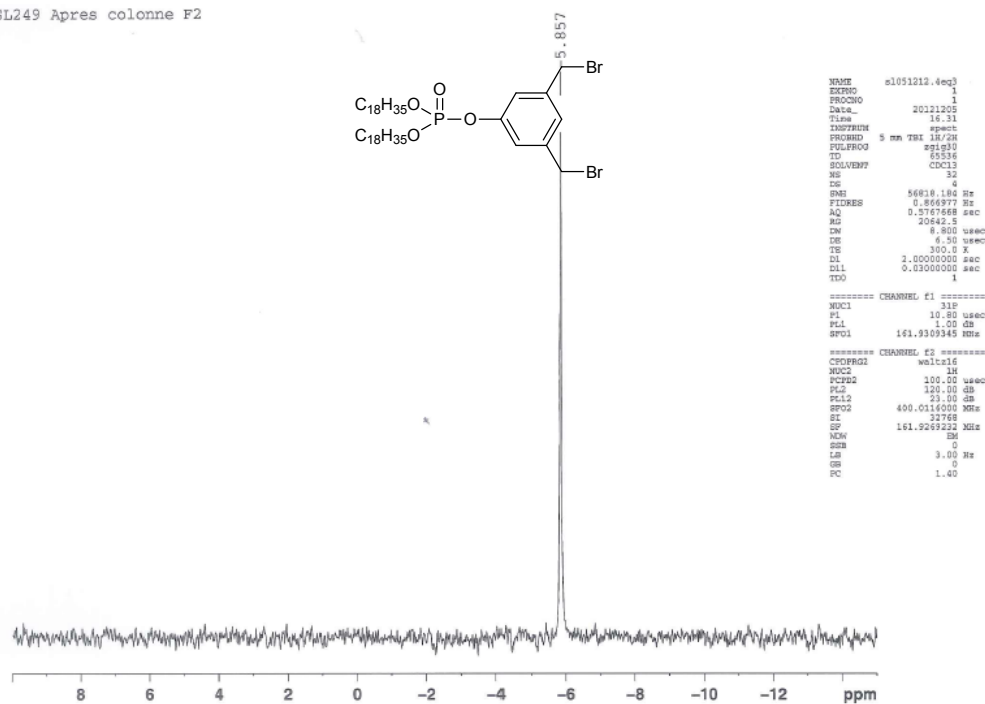
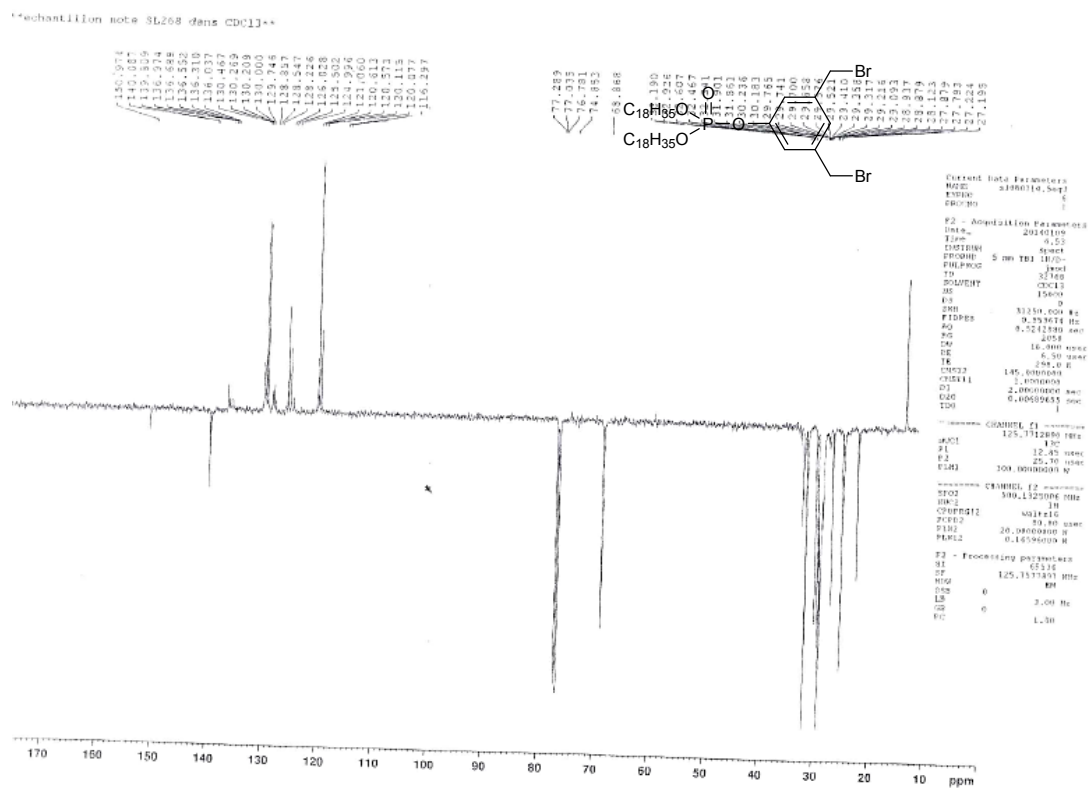


Figure S6-21: ^{13}C jmod (CDCl_3) spectrum of compound **12**.

Figure S6-22: ¹H NMR (CDCl₃) spectrum of compound 14.

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Figure S6-23: ³¹P NMR (CDCl₃) spectrum of compound 14.

Figure S6-24: ^{13}C jmod (CDCl_3) spectrum of compound 14.

Supporting materials

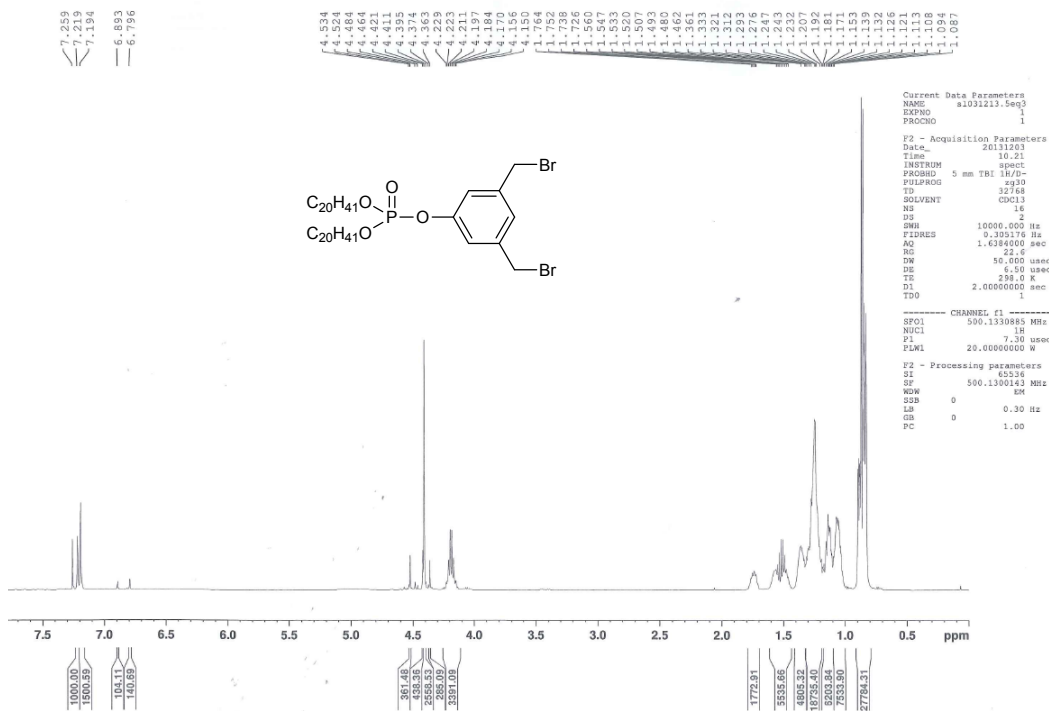


Figure S6-25: ^1H NMR (CDCl_3) spectrum of compound **15**.

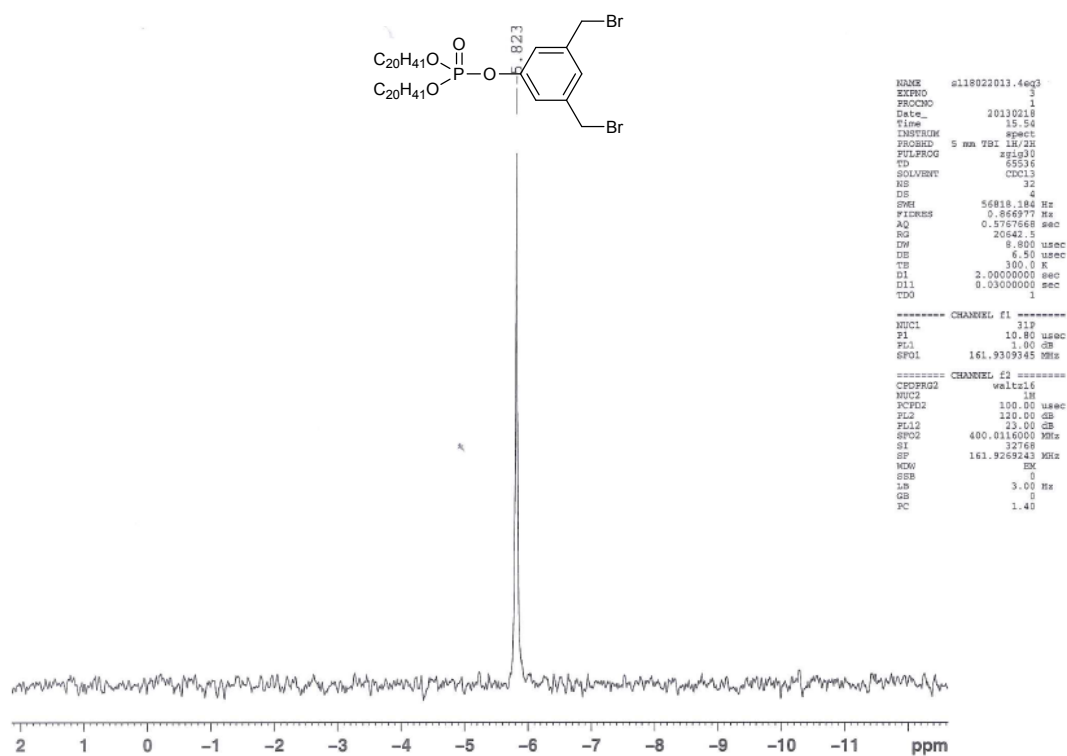


Figure S6-26: ³¹P NMR (CDCl₃) spectrum of compound 15.

Supporting materials

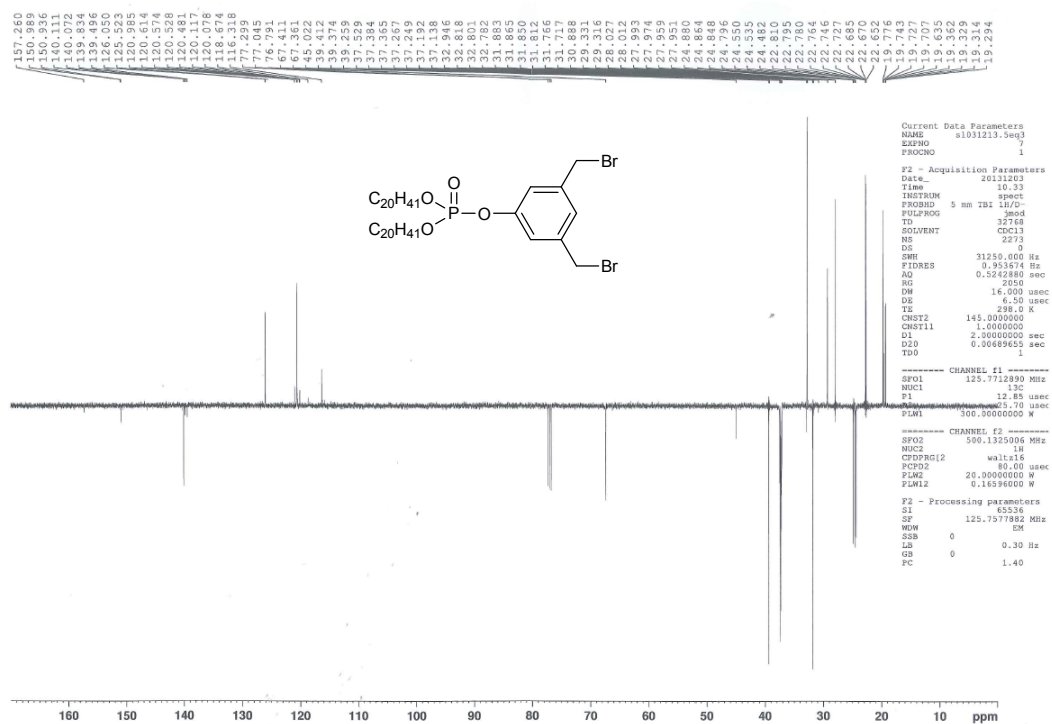
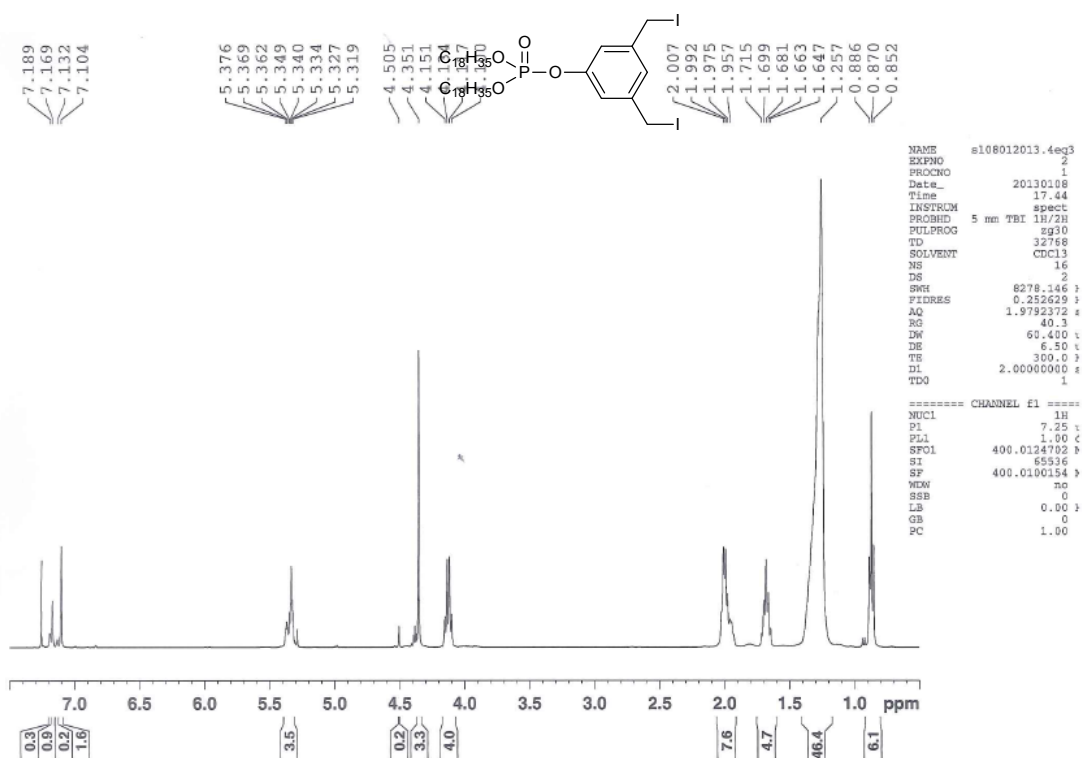
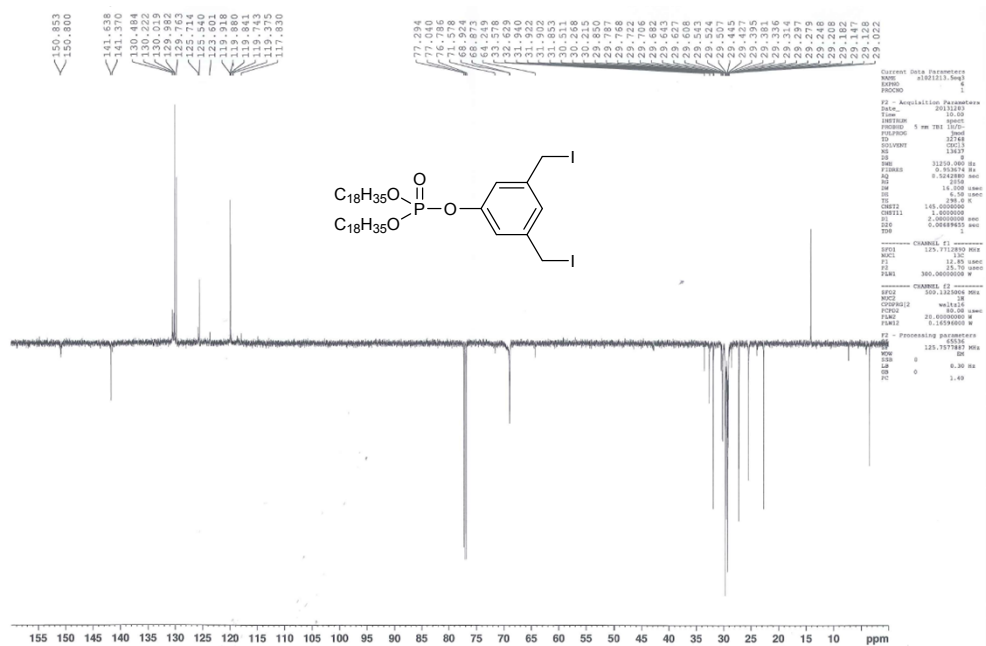
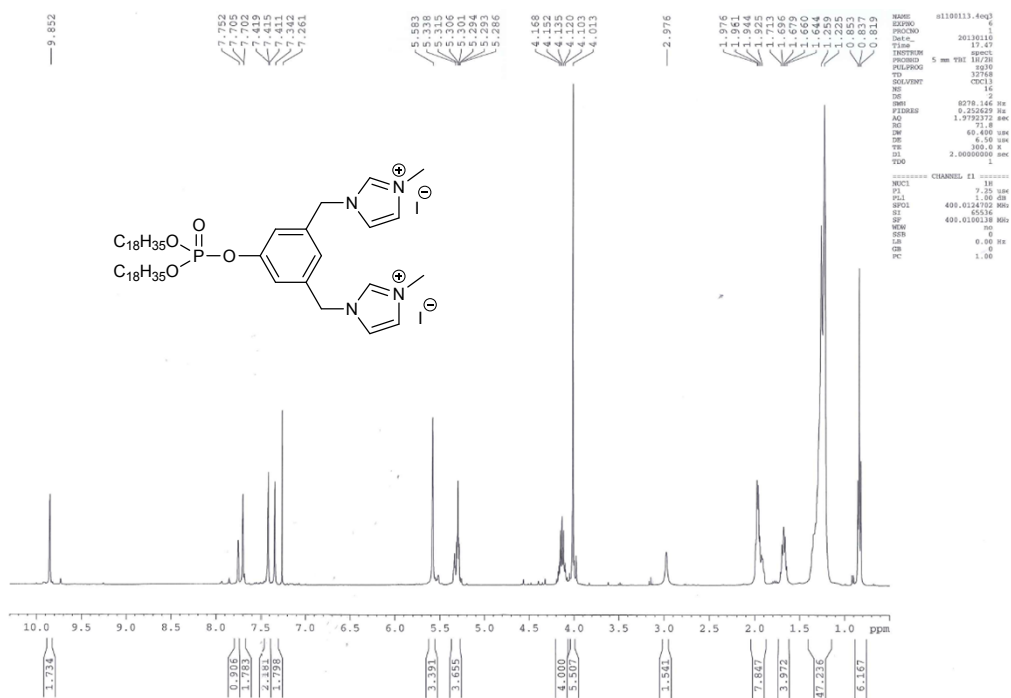
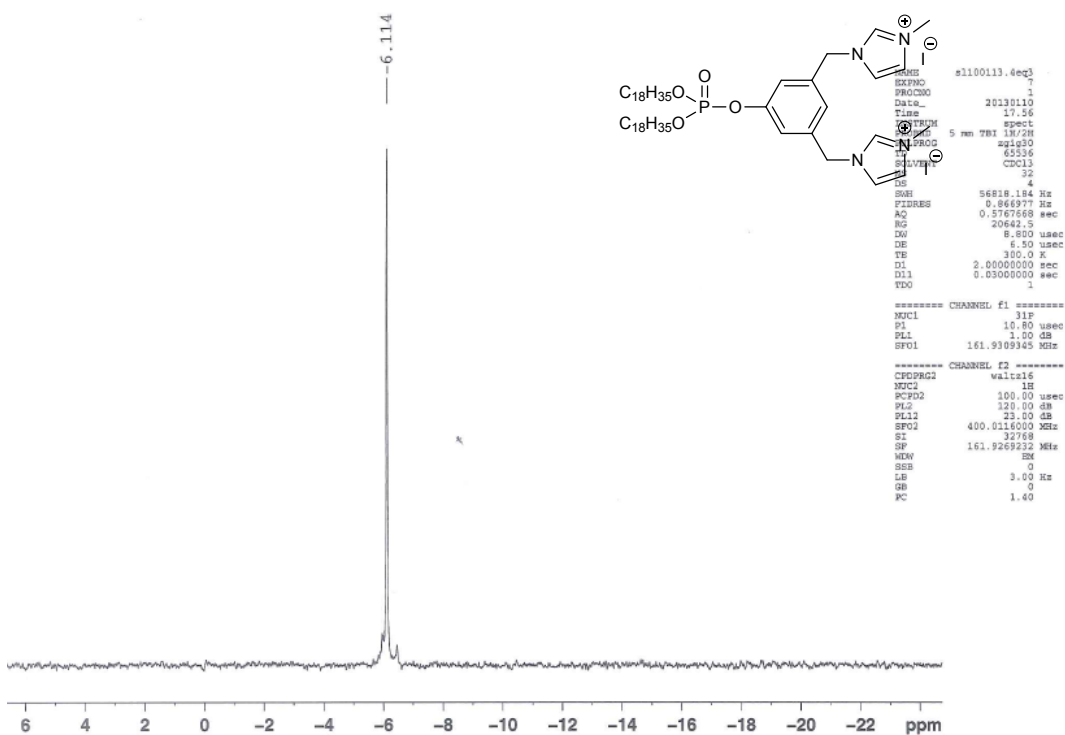


Figure S6-27: ¹³C jmod (CDCl₃) spectrum of compound 15.

Figure S6-28: ¹H NMR (CDCl₃) spectrum of compound 16.



Figure S6-30: ¹³C jmod (CDCl₃) spectrum of compound 16.Figure S6-31: ¹H NMR (CDCl₃) spectrum of compound 17.

Figure S6-32: ³¹P NMR (CDCl₃) spectrum of compound 17.

Supporting materials

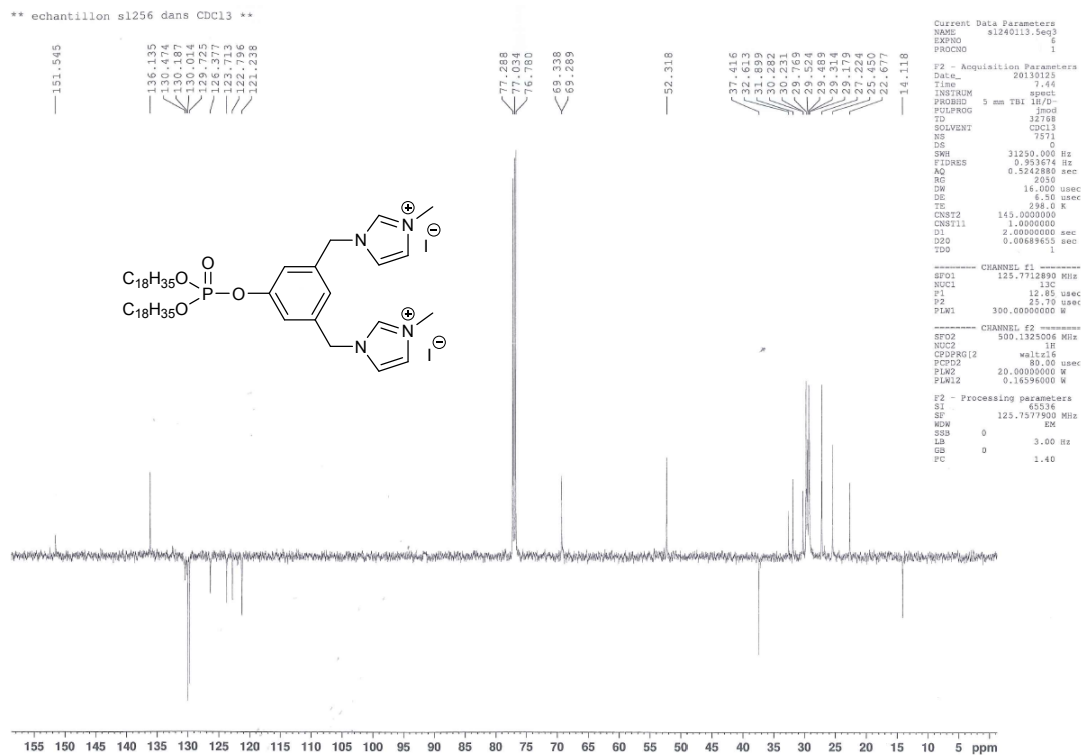


Figure S6-33: ^{13}C jmod (CDCl_3) spectrum of compound **17**.

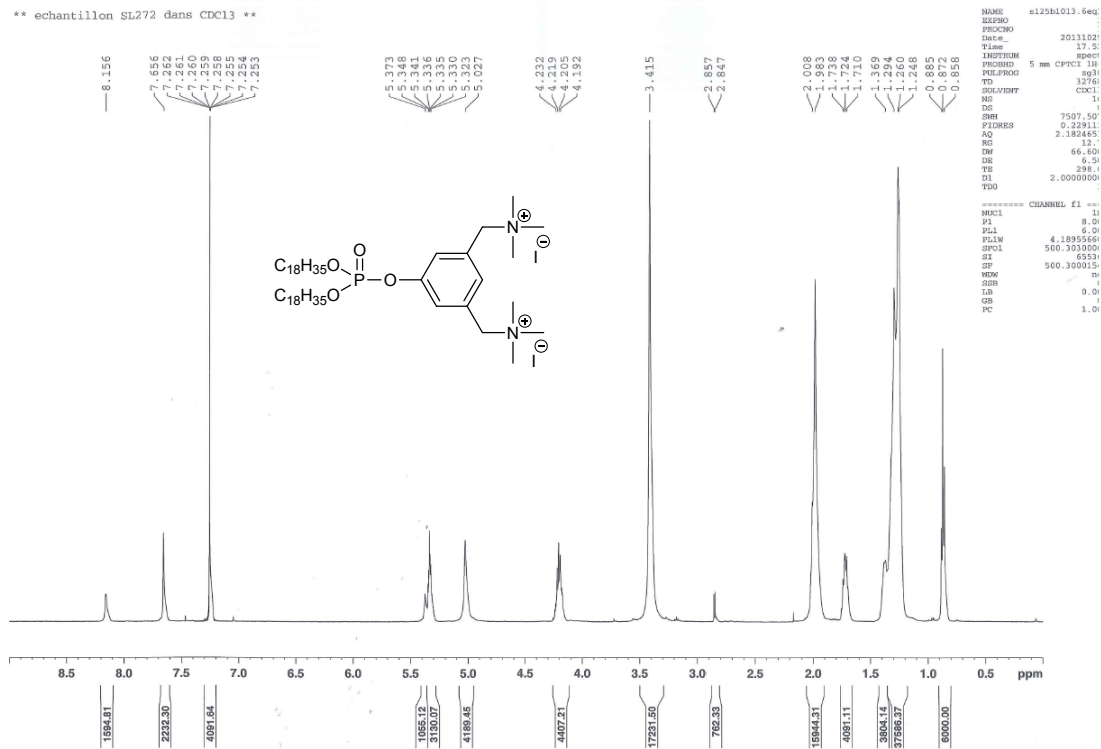


Figure S6-34: ^1H NMR (CDCl_3) spectrum of compound **18**.

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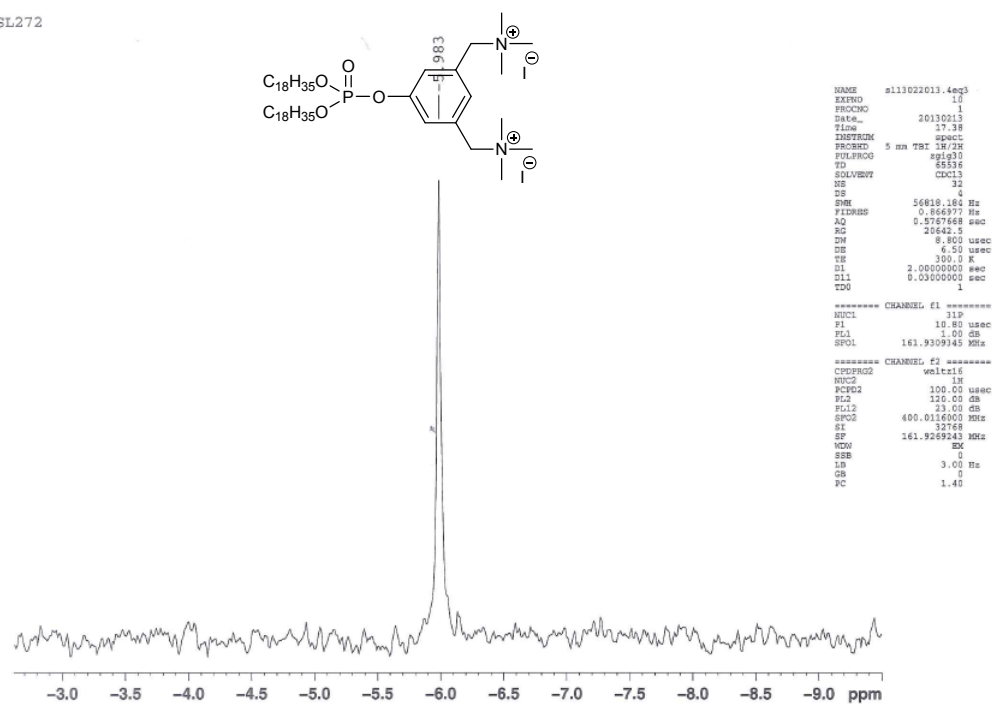


Figure S6-35: ^{31}P NMR (CDCl_3) spectrum of compound **18**.

Supporting materials

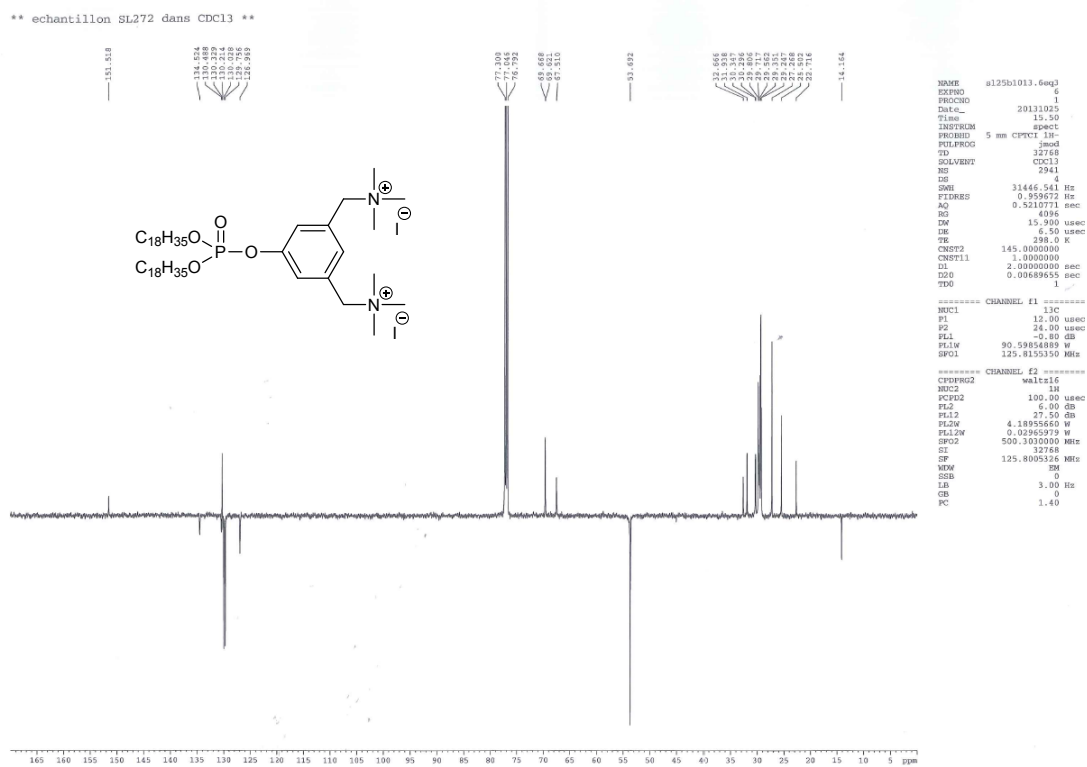


Figure S6-36: ^{13}C jmod (CDCl_3) spectrum of compound **18**.

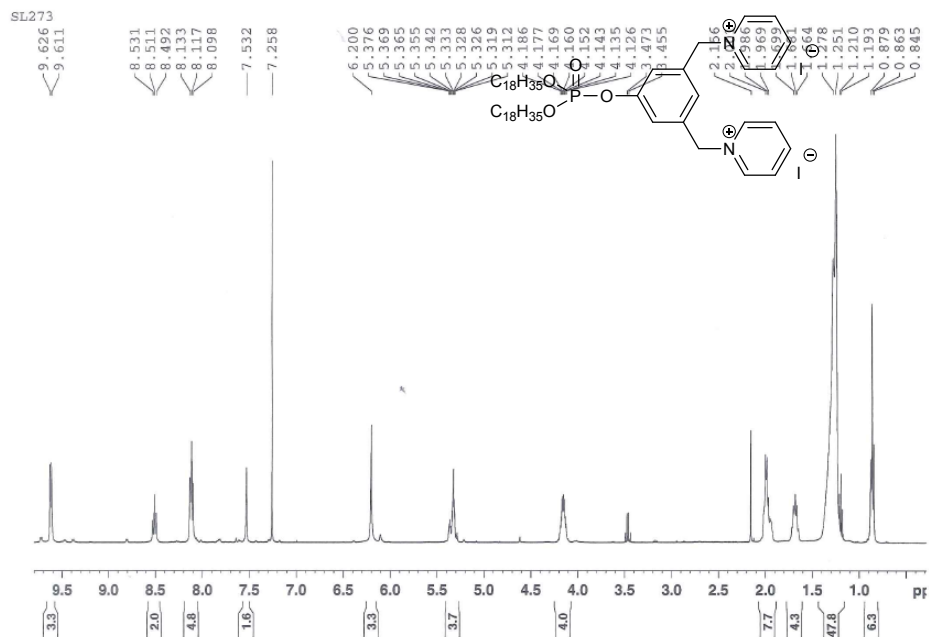
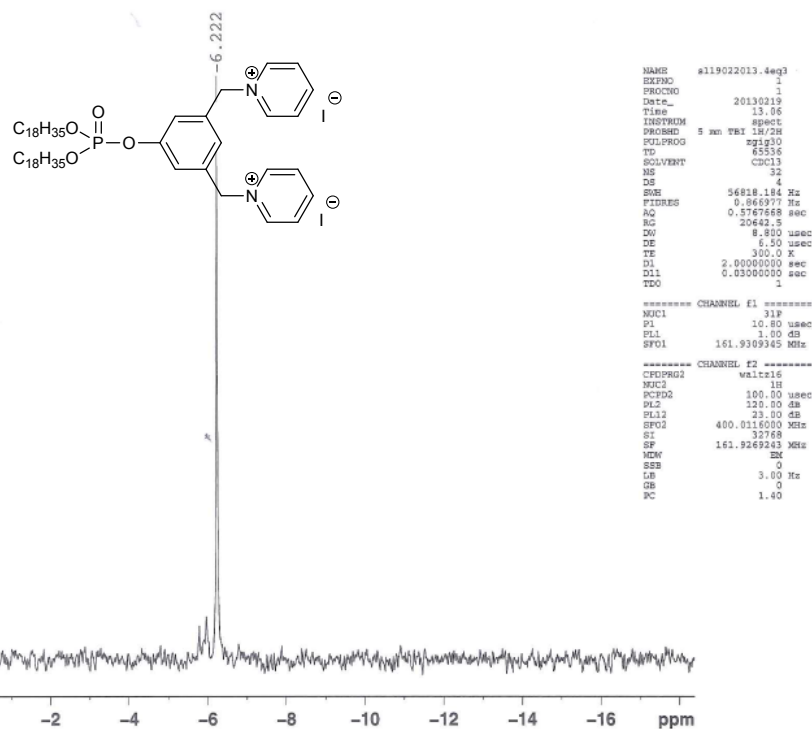


Figure S6-37: ^1H NMR (CDCl_3) spectrum of compound **19**.**Figure S6-38:** ^{31}P NMR (CDCl_3) spectrum of compound **19**.

Supporting materials

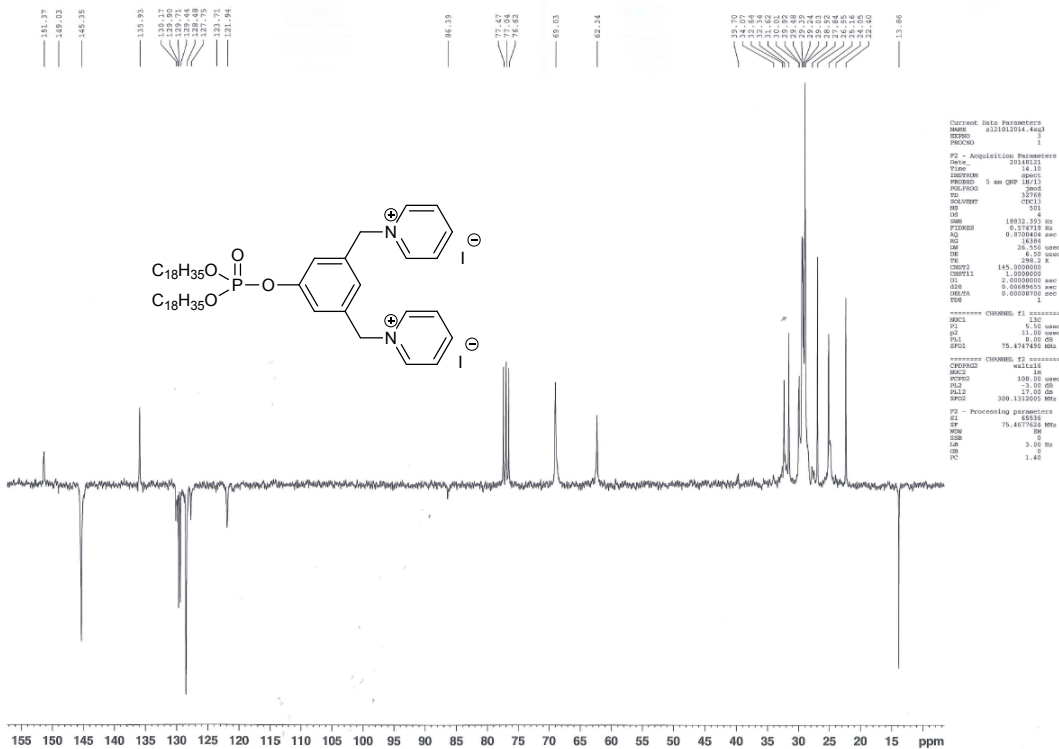
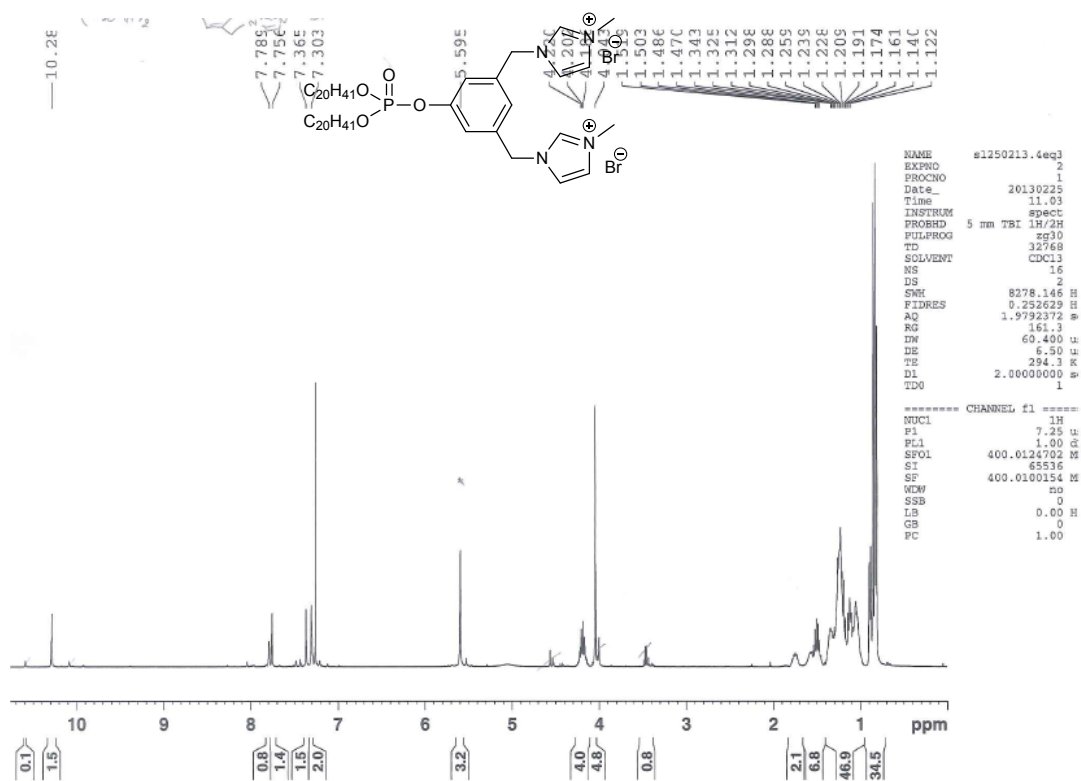


Figure S6-39: ^{13}C jmod (CDCl_3) spectrum of compound **19**.

Figure S6-40: ¹H NMR (CDCl₃) spectrum of compound 20.

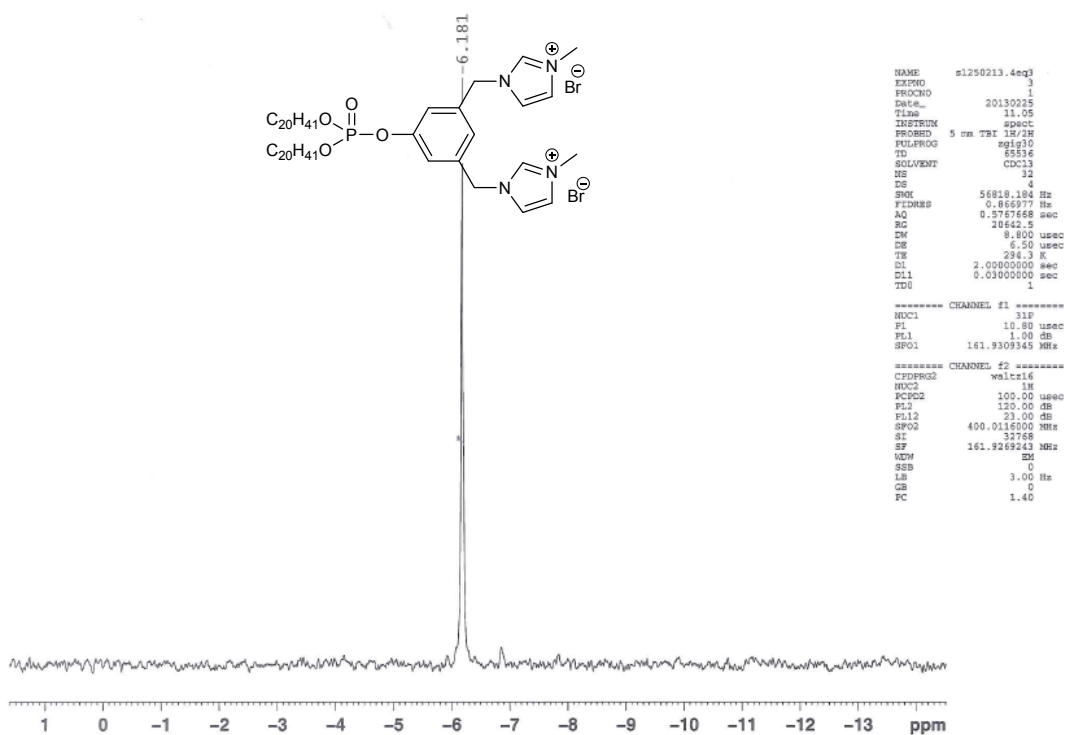


Figure S6-41: ³¹P NMR (CDCl₃) spectrum of compound 20.

Supporting materials

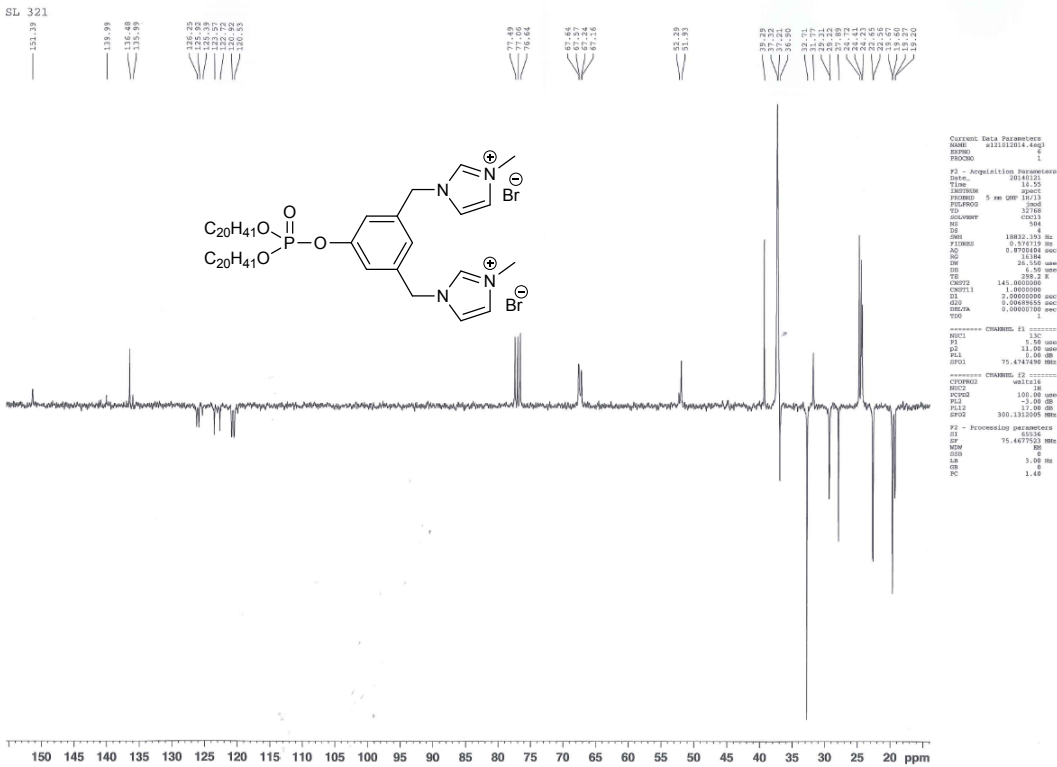


Figure S6-42: ^{13}C jmod (CDCl_3) spectrum of compound **20**.

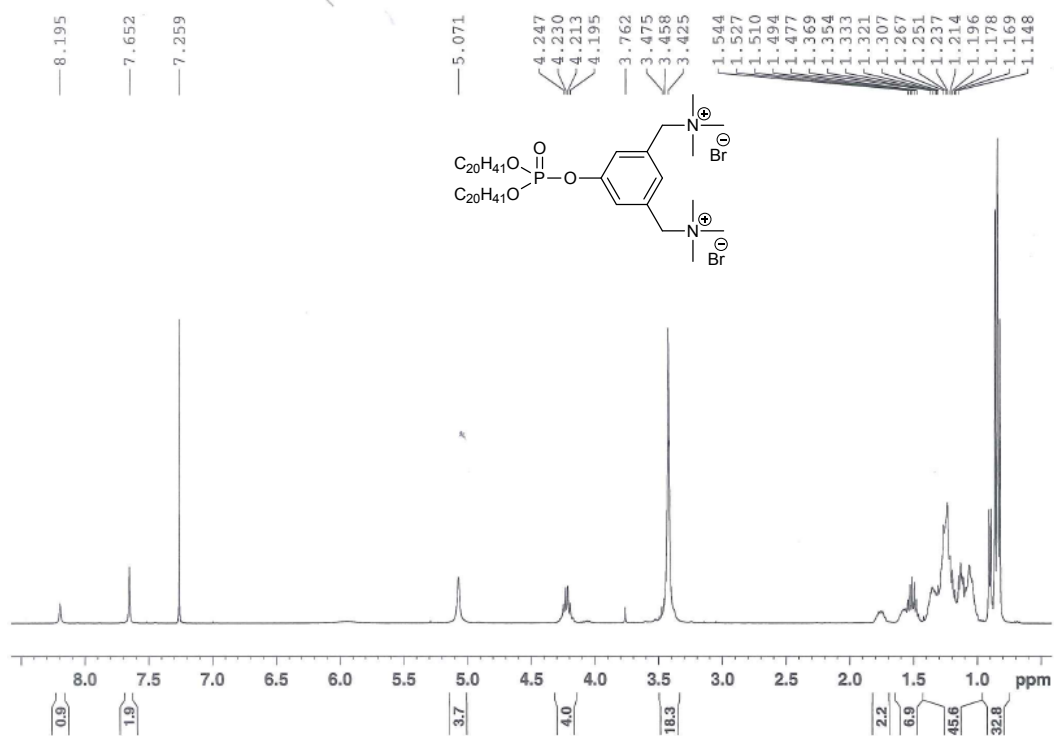


Figure S6-43: ¹H NMR (CDCl₃) spectrum of compound **21**.

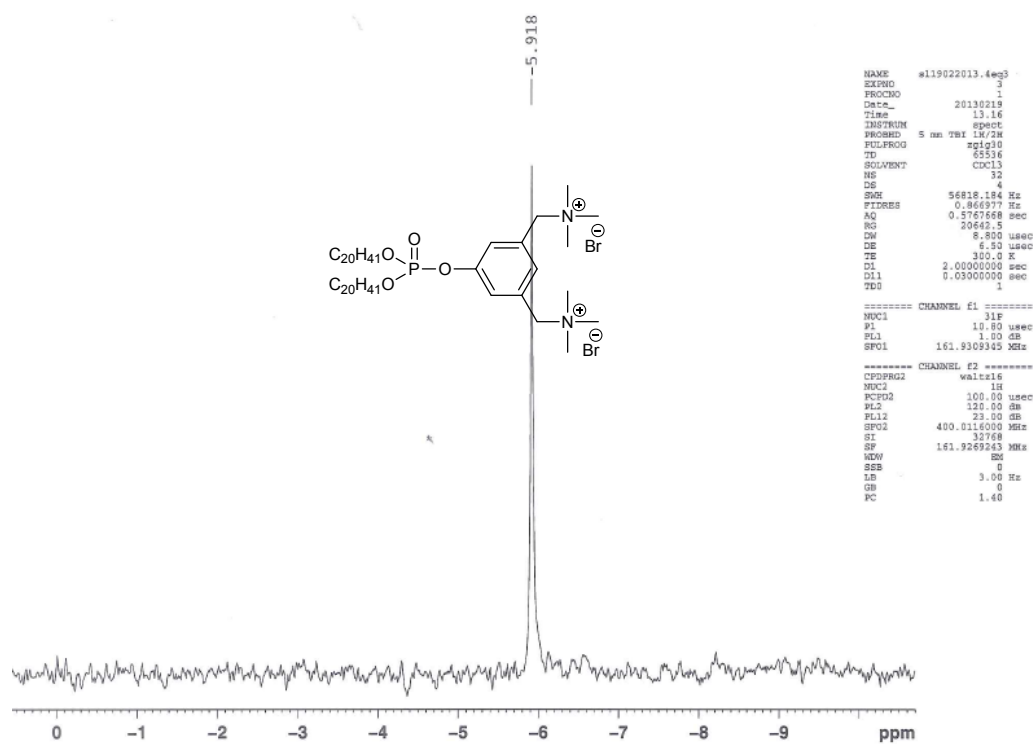


Figure S6-44: ^{31}P NMR (CDCl₃) spectrum of compound 21.

Supporting materials

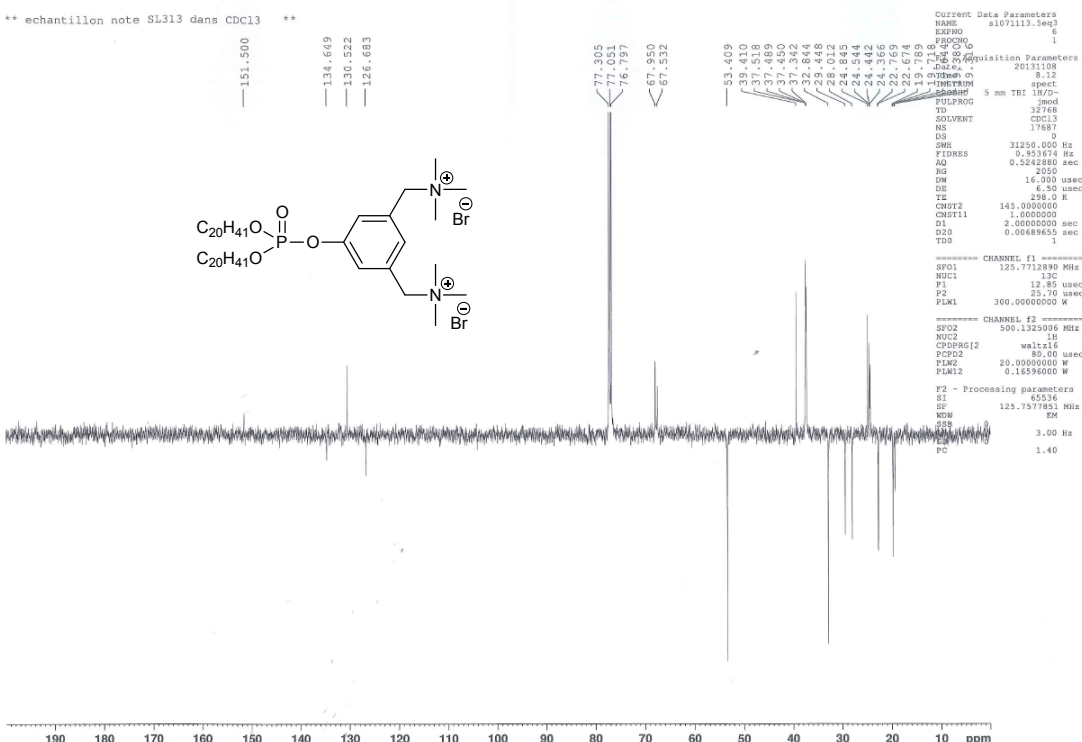


Figure S6-45: ^{13}C jmod (CDCl_3) spectrum of compound **21**.

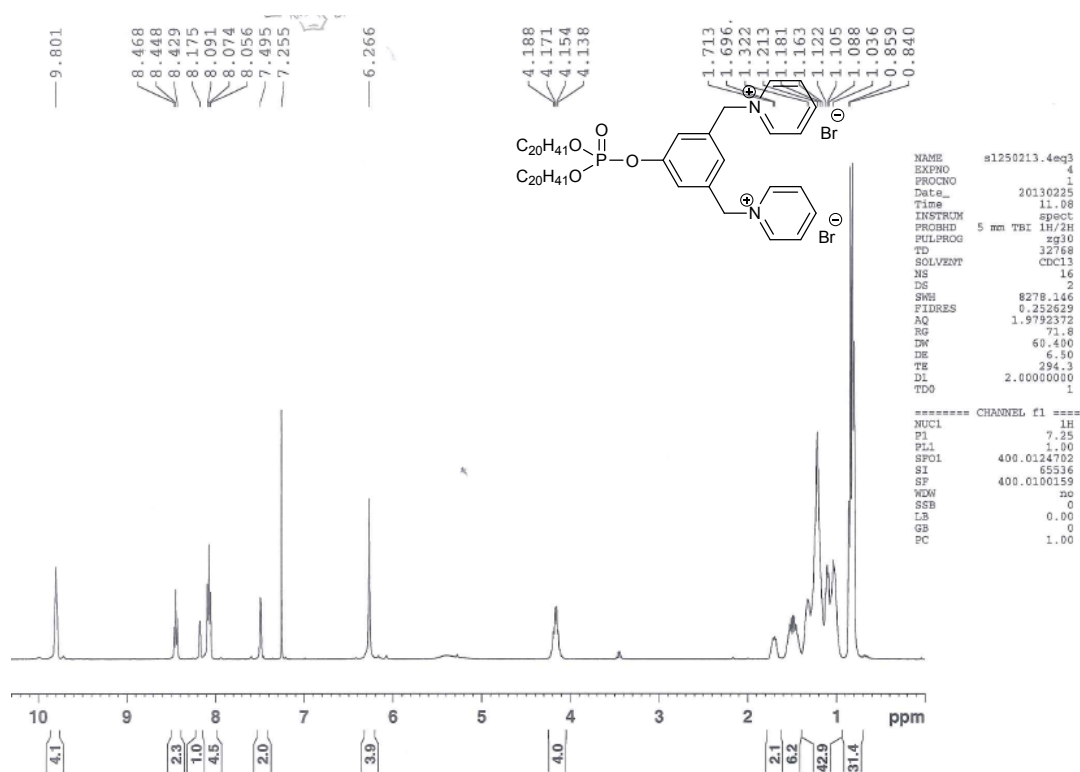
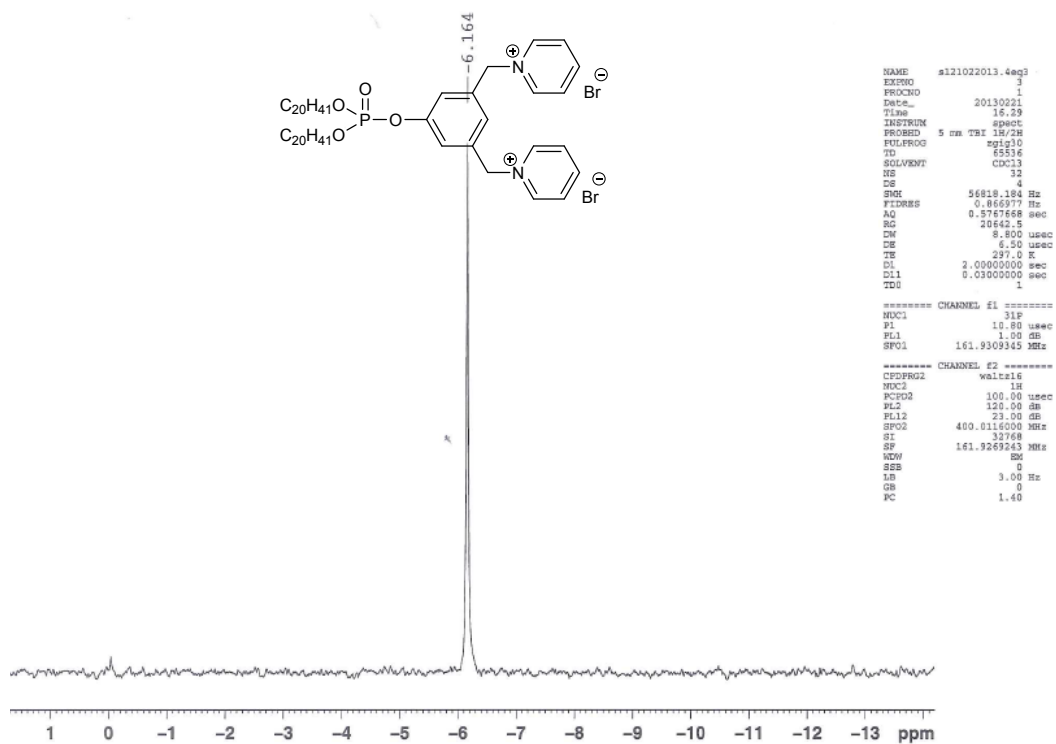


Figure S6-46: ^1H NMR (CDCl_3) spectrum of compound 22.

Figure S6-47: ^3P NMR (CDCl₃) spectrum of compound 22.

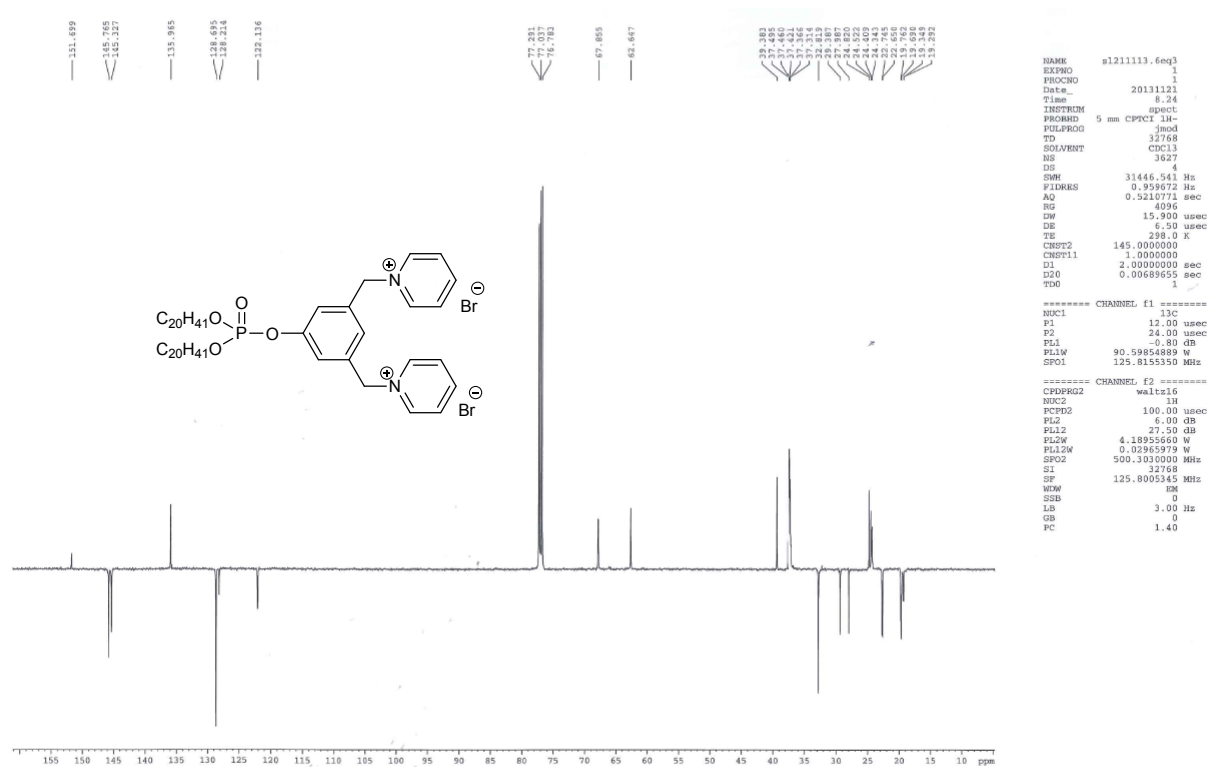


Figure S6-48: ^{13}C jmod (CDCl_3) spectrum of compound **22**.