Spectroscopic evidence of the interaction of titanium (IV) coordination complexes with phosphate head group in phospholipids

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Supporting Information

Contents

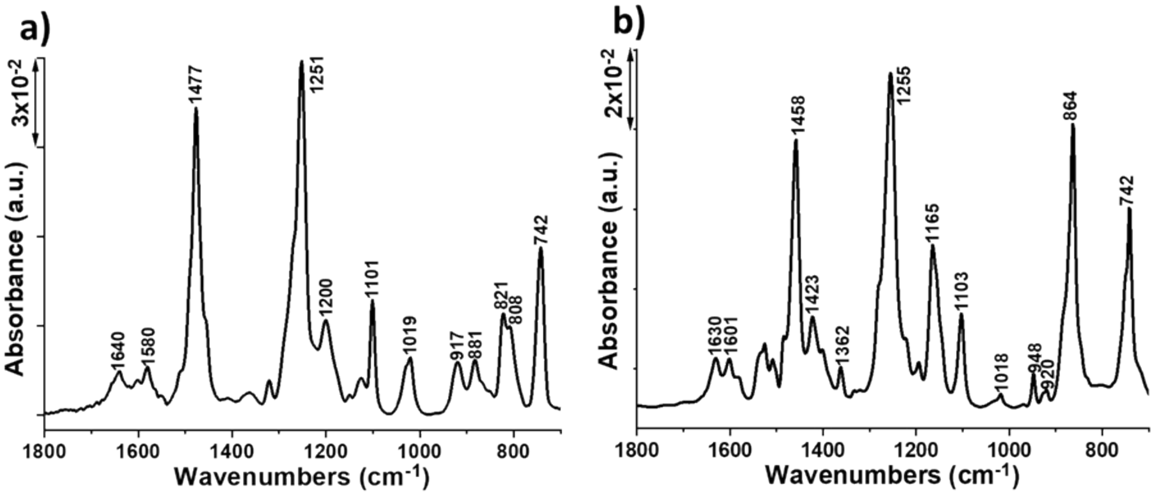

Figure S1. ATR-FTIR spectra of the titanium complexes (a) complex **1** and (b) complex **2** as dry film from solutions in methanol (10 mM).

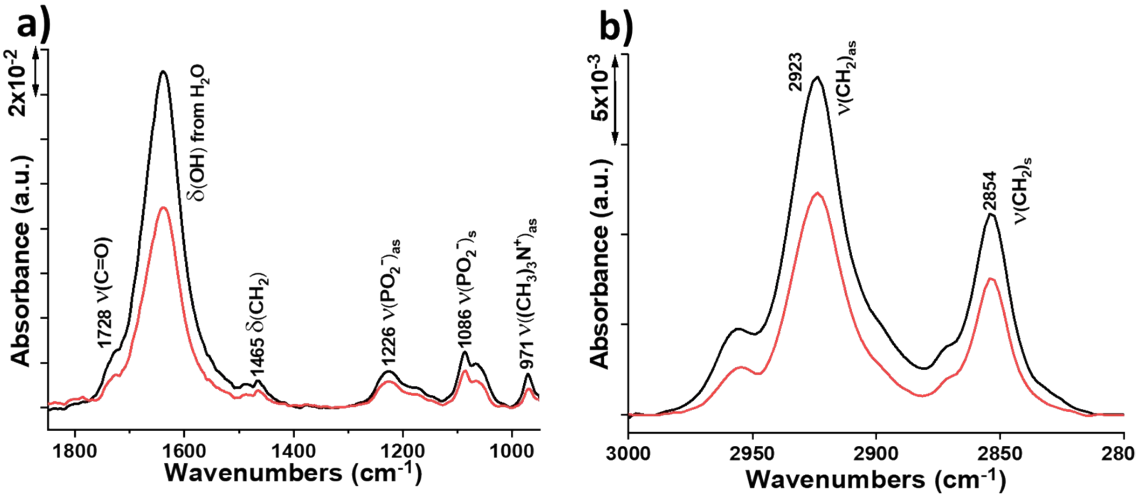

Figure S2. ATR-FTIR spectra on diamond crystal of DOPC lipid multi-bilayers hydrated by H_2O. The spectra were recorded with a parallel (black curve) and a perpendicular (red curve) polarization. (a) Spectral range characteristic for the C=O and PO_2^- stretching modes (b) Spectral range characteristic for the CH_2 stretching modes.

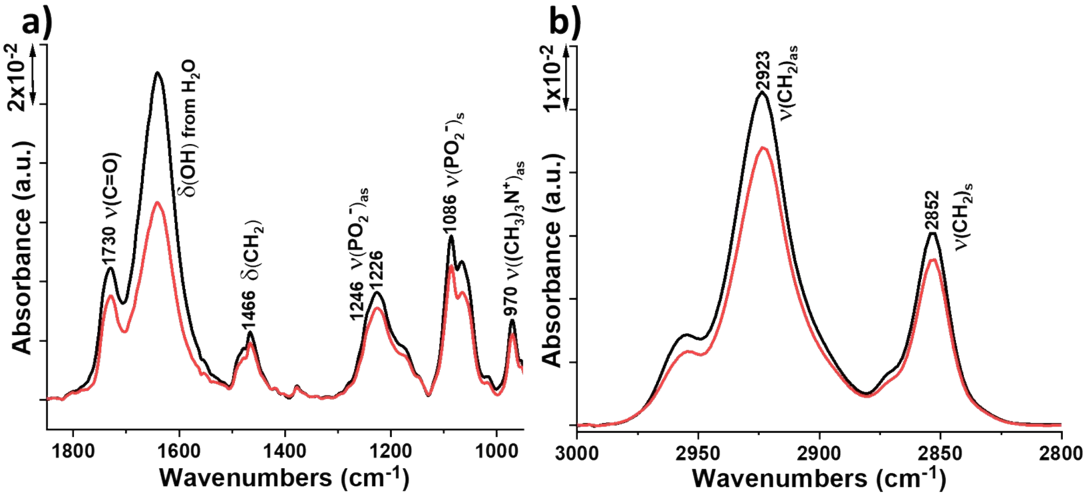

Figure S3. ATR-FTIR spectra of complex **1**/DOPC multi-bilayers hydrated by H_2O at a complex **1**/lipid ratio of 1/20. The spectra were recorded with a parallel (black curve) and a perpendicular (red curve) polarization. (a) Spectral range characteristic for the C=O and PO_2^- stretching modes (b) Spectral range characteristic for the CH_2 stretching modes.

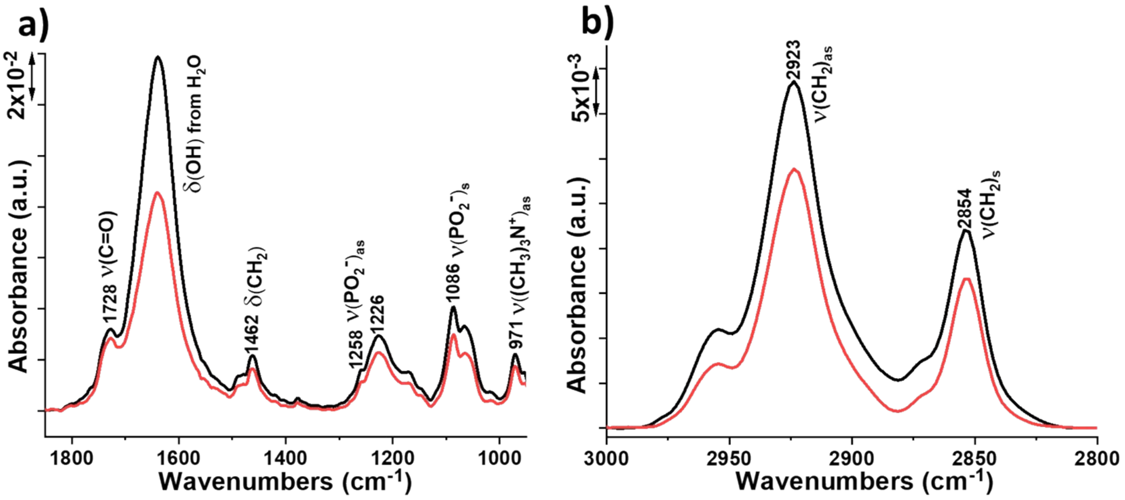

Figure S4. ATR-FTIR spectra of complex **2**/DOPC multi-bilayers hydrated by H_2O at a complex **2**/lipid ratio of 1/20. The spectra were recorded with a parallel (black curve) and a perpendicular (red curve) polarization. (a) Spectral range characteristic for the C=O and PO_2^- stretching modes (b) Spectral range characteristic for the CH_2 stretching modes.

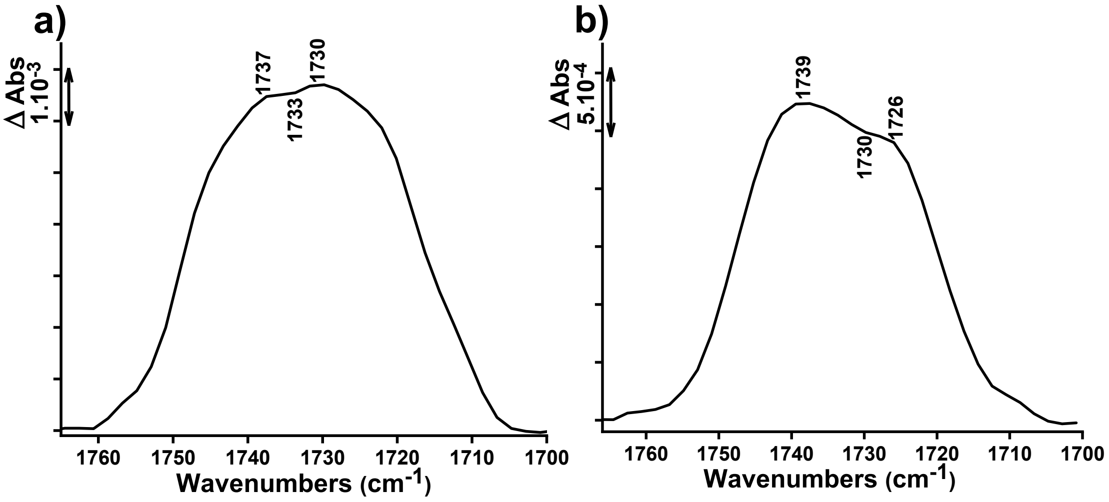

Figure S5. ATR-FTIR difference spectra of the C=O ester carbonyl stretching in the 1770-1700 cm^{-1} spectral range, calculated by subtracting the spectrum of DOPC multi-bilayers from the spectra of complex **1**/DOPC (a) and complex **2**/DOPC multi-bilayers (b). To account for differences in lipid concentration in mixtures samples, the subtraction of the spectra have been normalized with respect to the area of the antisymmetric $(CH_3)_3N^+$ stretching band present in the DOPC and Ti(IV) complexes/DOPC spectra.

Experimental part – Additional procedures and analyses

The syntheses of complexes **1** and **2** have previously been reported in refs [1] and [2], respectively.

In a 25 mL reaction flask, the diol (3.04 mmol, catechol H_2Cat: 335 mg; 2,3-dihydroxynaphtalene H_2Napht: 487 mg) was first dissolved in dry toluene (10 mL) by gentle heating under argon atmosphere, and $Ti(OiPr)_4$ (0.3 mL, 1.00 mmol) was added dropwise. The resulting mixture was heated at 80 °C for 3 h. The suspension was allowed to cool at room temperature and the solvent was evaporated. The residue was washed with toluene (2 x 5 mL) and pentane (5 mL). The precipitate was then dried *in vacuo* to afford a dark reddish powder (**1**: 122 mg, 32%; **2**: 136 mg, 26%).

Complex **1**: ^{1}H NMR (300 MHz, DMSO-d_6): δ 6.44 (m, 6H), 6.12 (m, 6H). ESI$^-$-MS: *m/z* 109.03 ([HCat]$^-$, 100%), 295.01 ([Ti(Cat)$_2$(OMe)]$^-$, 59%), 373.02 ([Ti(Cat)$_2$(HCat)]$^-$, 27%).

Complex **2**: ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.48 (m, 6H), 7.07 (m, 6H), 6.50 (s, 6H). ESI$^-$-MS: *m/z* 319.11 ([(H_2Napht)(HNapht)]$^-$, 100%), 523.07 ([Ti(Napht)$_2$(HNapht)]$^-$, 48%).

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[1] Y. Chi, P.-F. Hsu, J.-W. Lan, C.-L. Chen, S.-M. Peng and G.-H. Lee, *J. Phys. Chem. Solids*, 2001, **62**, 1871–1879.

[2] A. Sugawara, Jpn. Pat., 2006335835A, 2006.

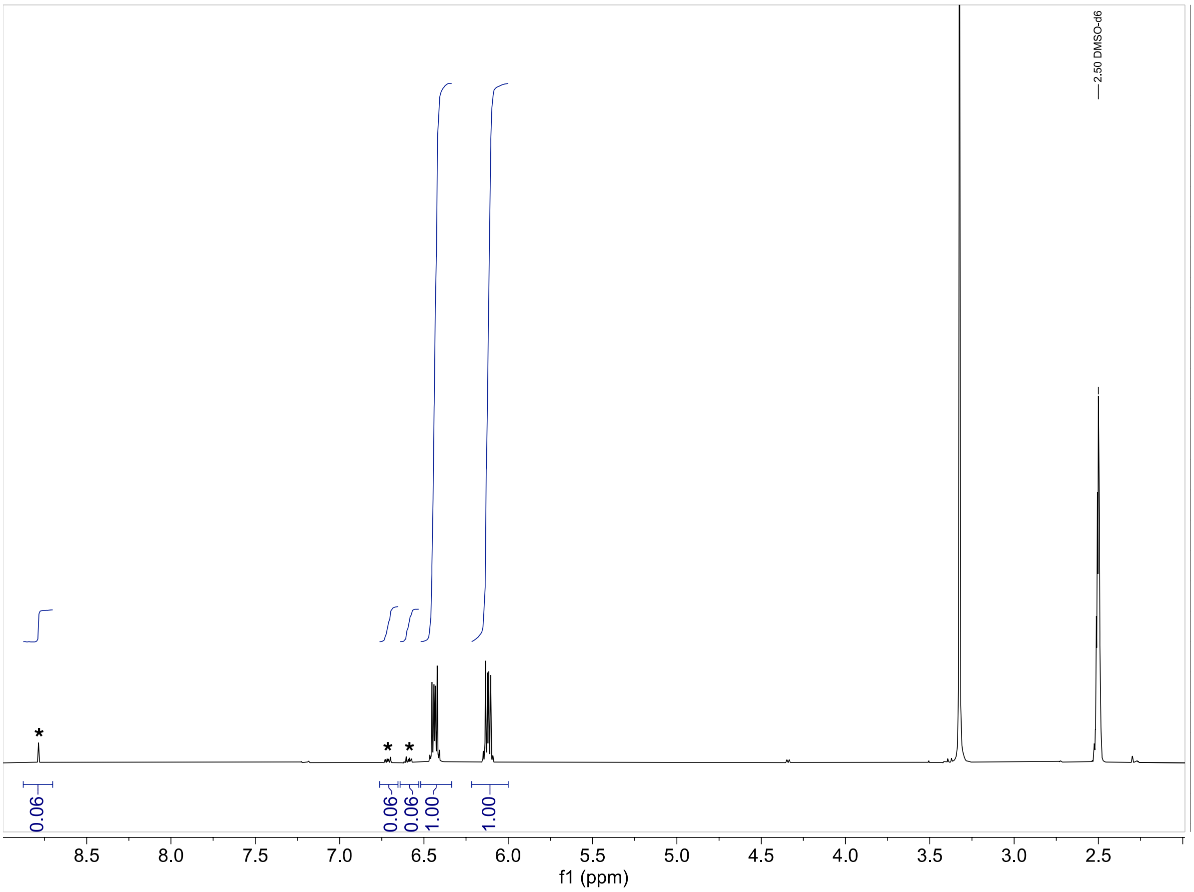


Figure S6. ^{1}H NMR spectrum of complex **1** in DMSO-*d*$_6$ (300 MHz). Residual free catechol signals are marked by asterisks.

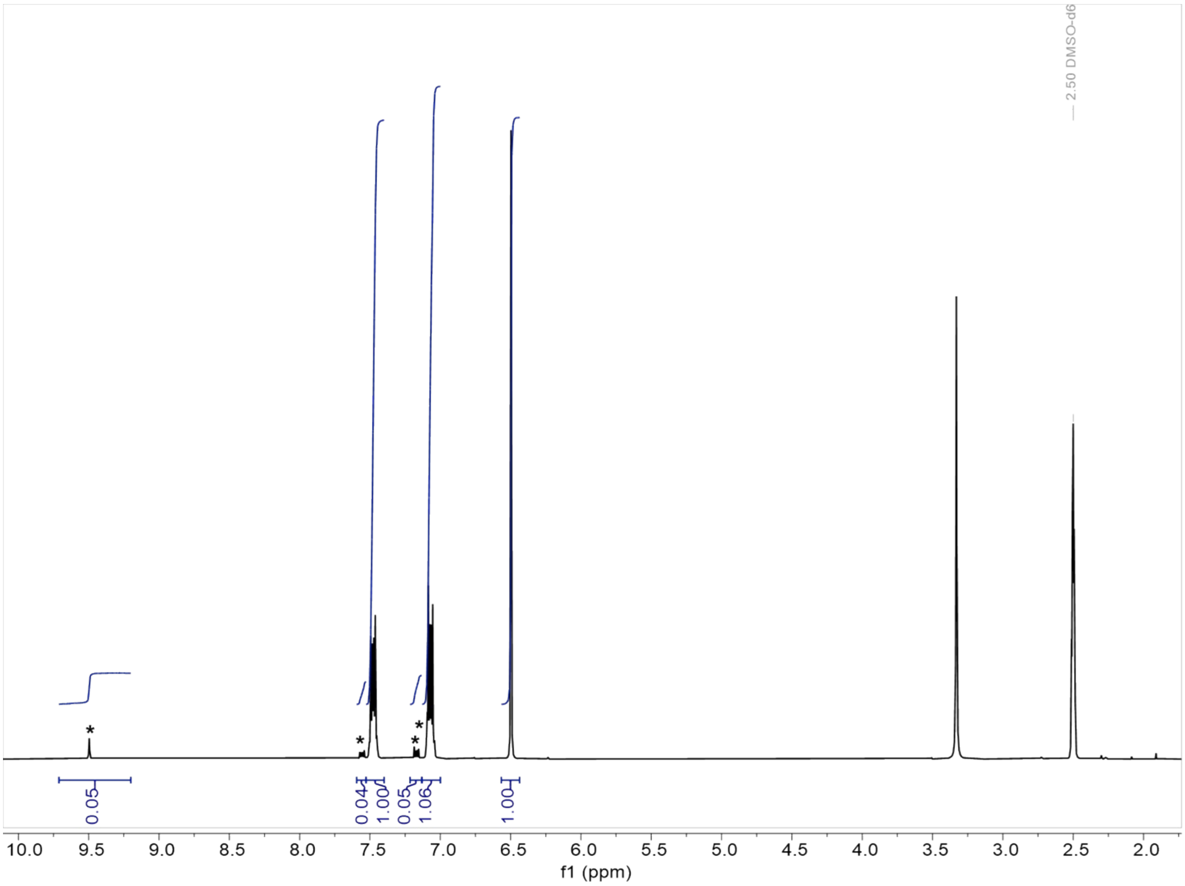


Figure S7. ^{1}H NMR spectrum of complex **2** in DMSO-d_6 (300 MHz). Residual free 2,3-dihydroxy-naphthalene signals are marked by asterisks.

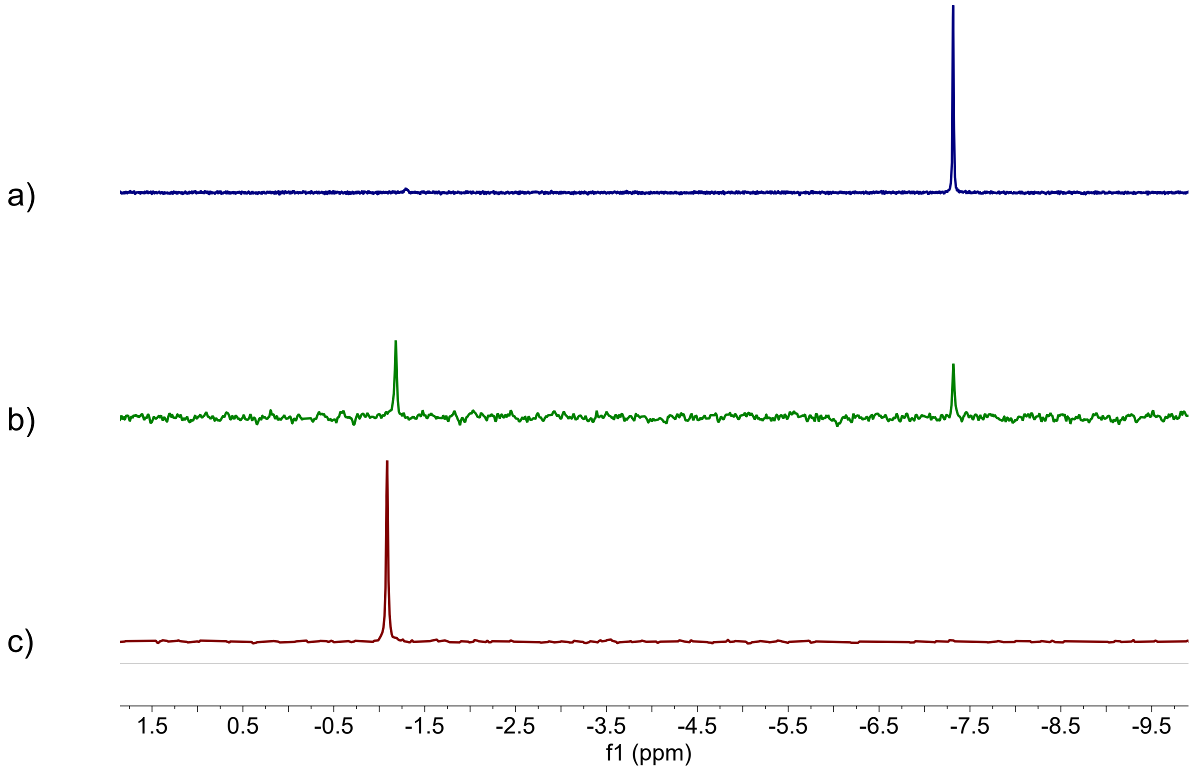


Figure S8. $^{31}P\{^{1}H\}$ NMR spectra in DMSO-d_6 of (a) solution **B** (202 MHz); (b) solution **A** (121 MHz); (c) DOPC (121 MHz).

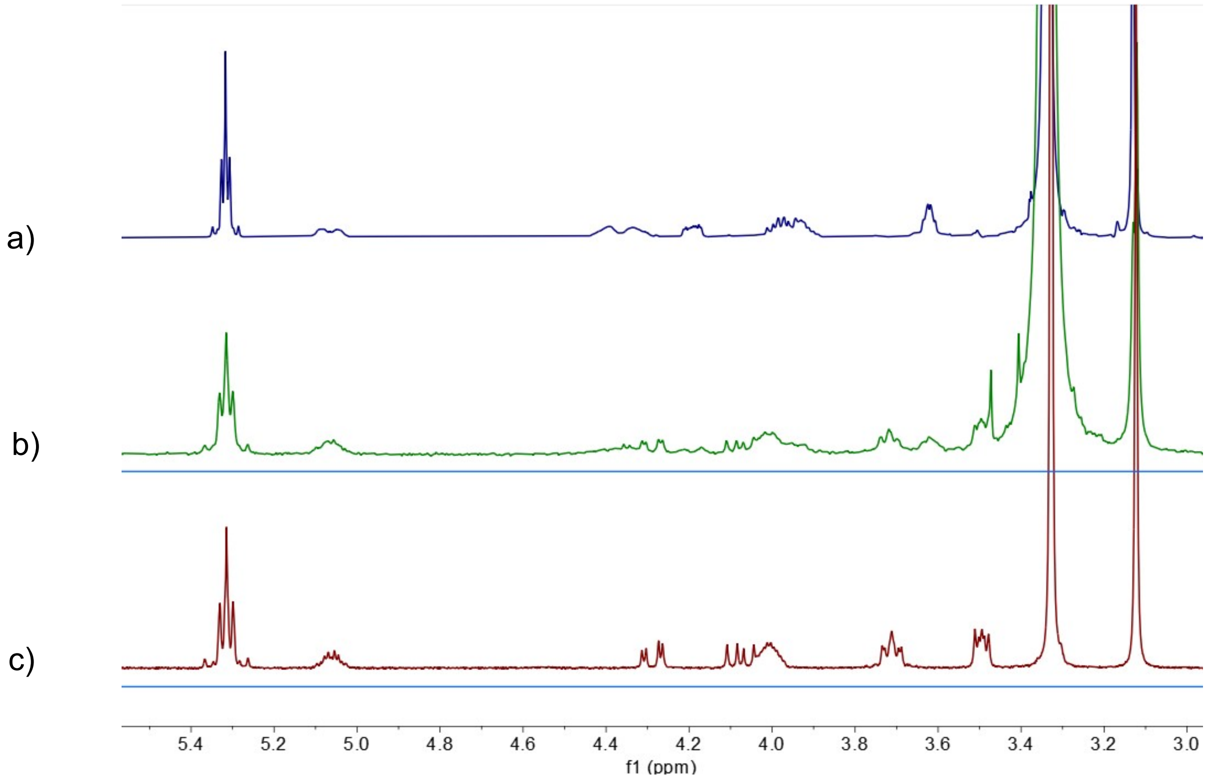


Figure S9. Sections of the ^{1}H NMR spectra in DMSO-d_6 of (a) solution **B** (500 MHz); (b) solution **A** (300 MHz); (c) DOPC (300 MHz).

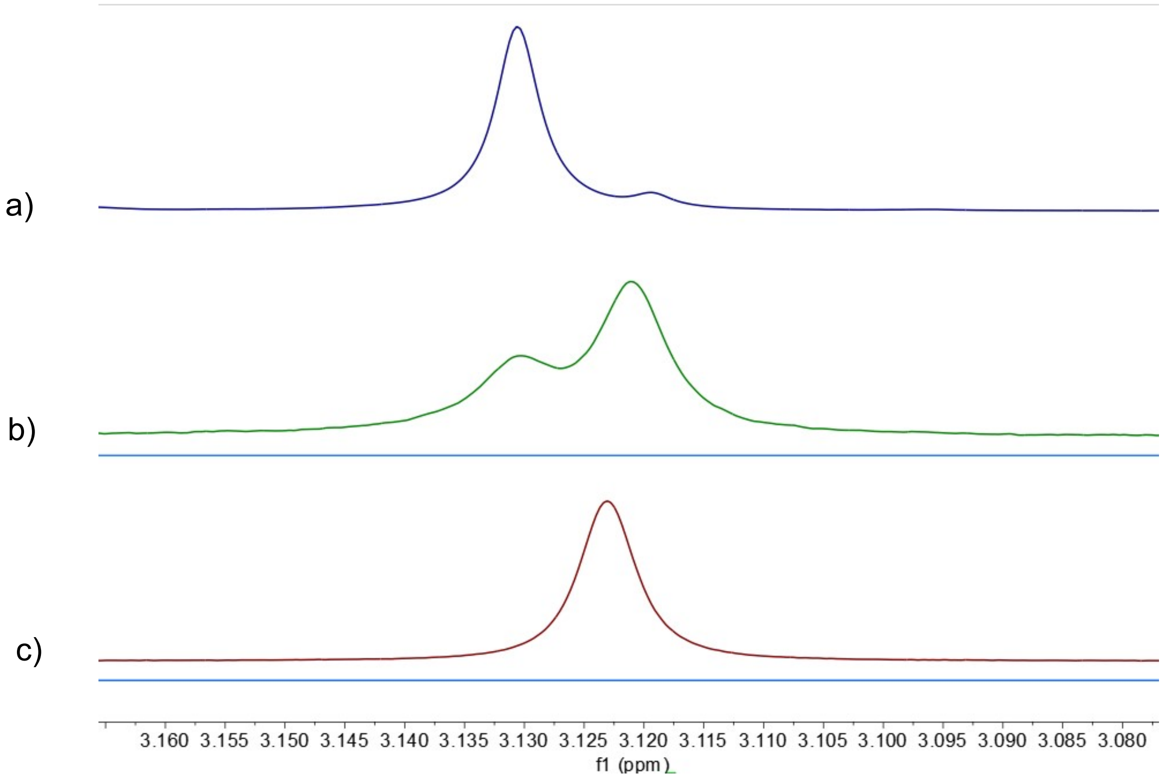
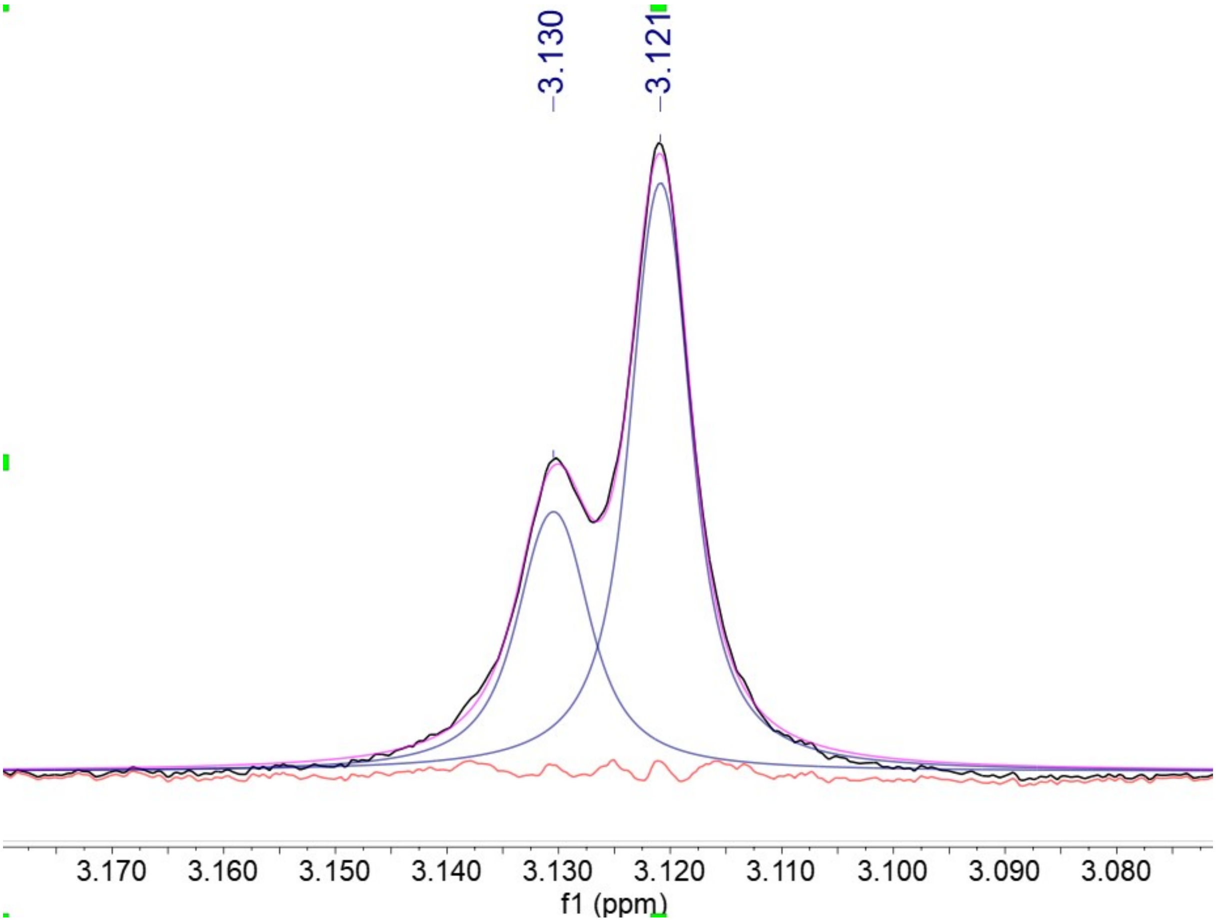
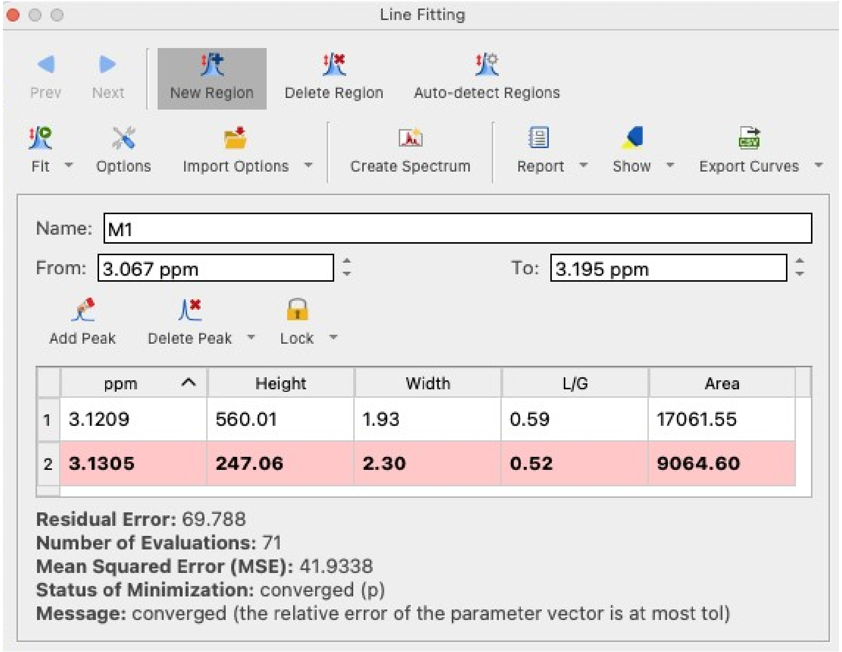


Figure S10. Zooms of figure **S9**: trimethylammonium signals on the ^{1}H NMR spectra in DMSO-d_6.





Name: M1

From: 3.067 ppm To: 3.195 ppm

	ppm	Height	Width	L/G	Area
1	3.1209	560.01	1.93	0.59	17061.55
2	**3.1305**	**247.06**	**2.30**	**0.52**	**9064.60**

Residual Error: 69.788
Number of Evaluations: 71
Mean Squared Error (MSE): 41.9338
Status of Minimization: converged (p)
Message: converged (the relative error of the parameter vector is at most tol)

Figure S11. Deconvolution of the trimethylammonium signals of solution **A** (Fig. S10b).

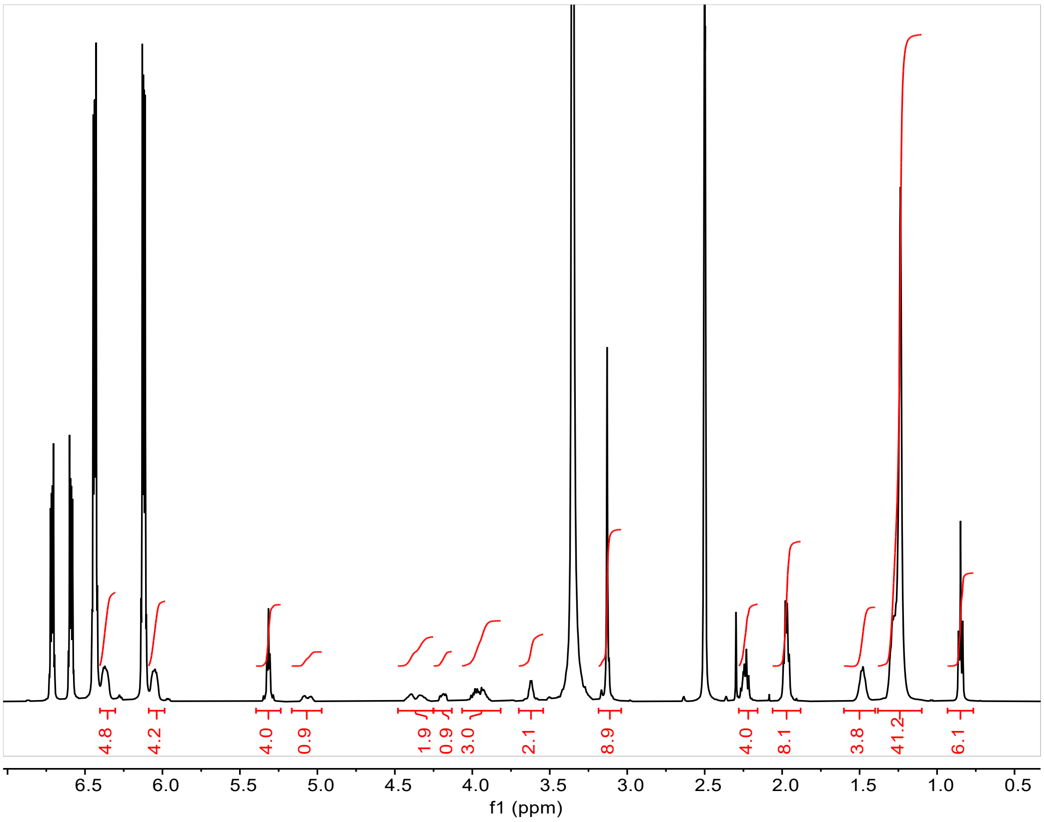


Figure S12. ^{1}H NMR spectrum of solution **B** recorded in DMSO-d_6 (500 MHz); the signals of complex **3** have been integrated.

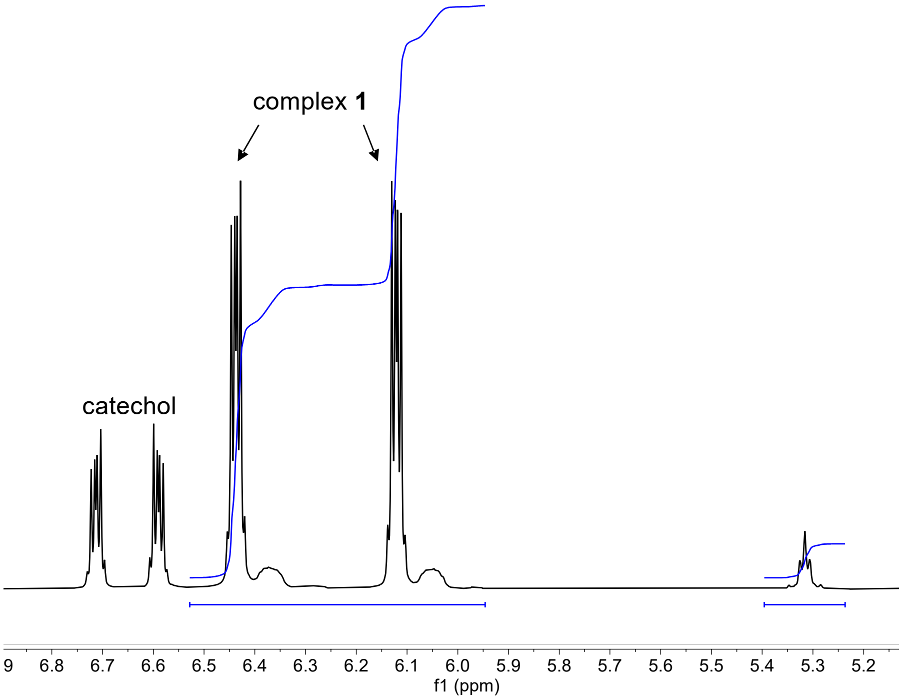
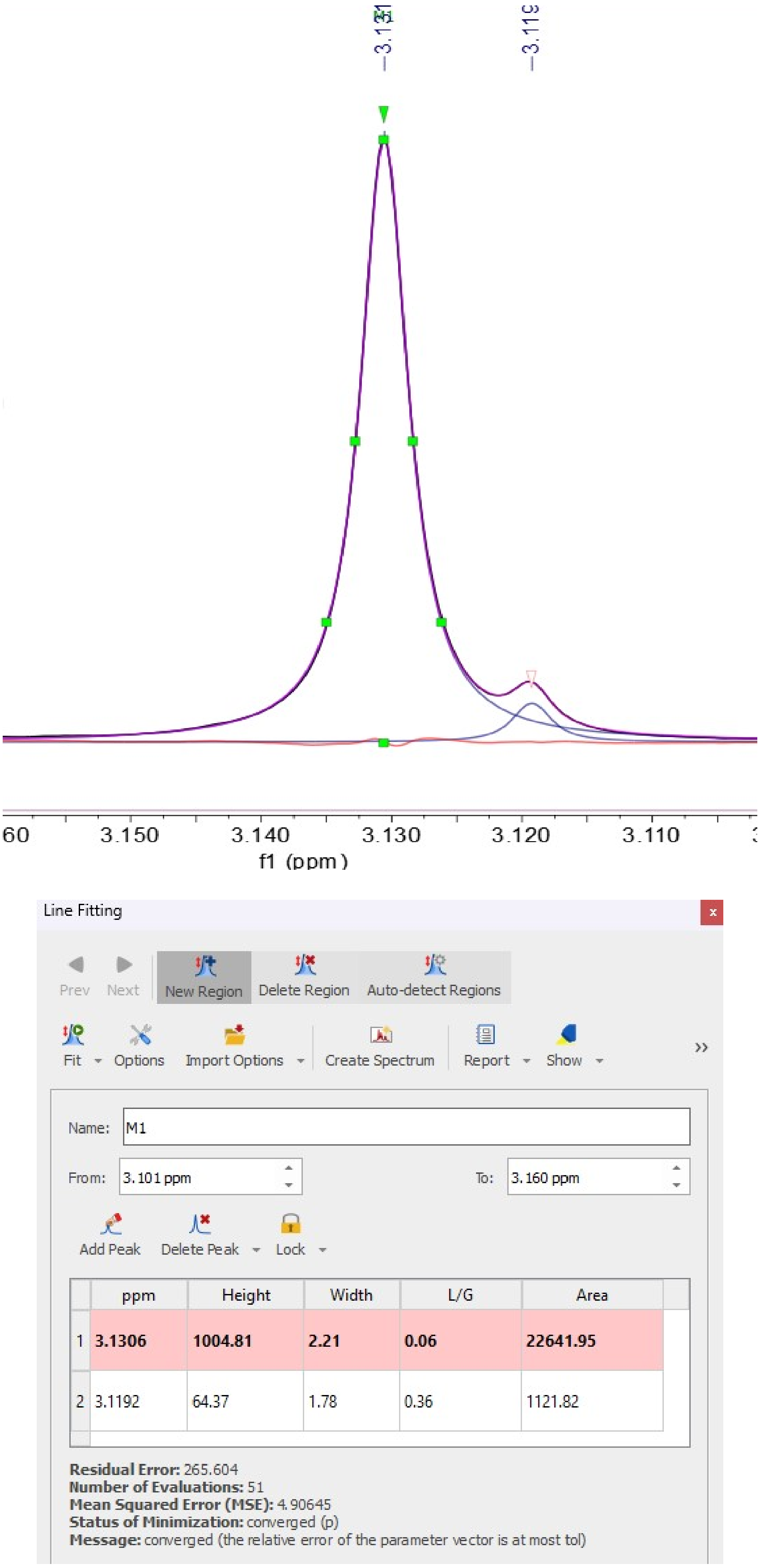


Figure S13. Zoom of figure S12 showing that the integrals of the signals at 6.40-6.34 ppm, 6.08-6.02 and 5.35-5.28 are equal, integrating each for 4H.



Name: M1

From: 3.101 ppm To: 3.160 ppm

	ppm	Height	Width	L/G	Area
1	**3.1306**	**1004.81**	**2.21**	**0.06**	**22641.95**
2	3.1192	64.37	1.78	0.36	1121.82

Residual Error: 265.604
Number of Evaluations: 51
Mean Squared Error (MSE): 4.90645
Status of Minimization: converged (p)
Message: converged (the relative error of the parameter vector is at most tol)

Figure S14. Deconvolution of the trimethylammonium signals of solution **B** (Fig. S10a).

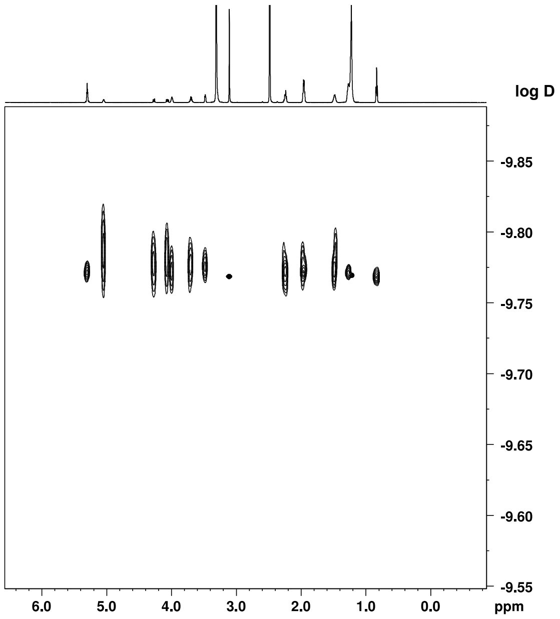


Figure S15. ^{1}H NMR DOSY spectrum of DOPC in DMSO-d_6.

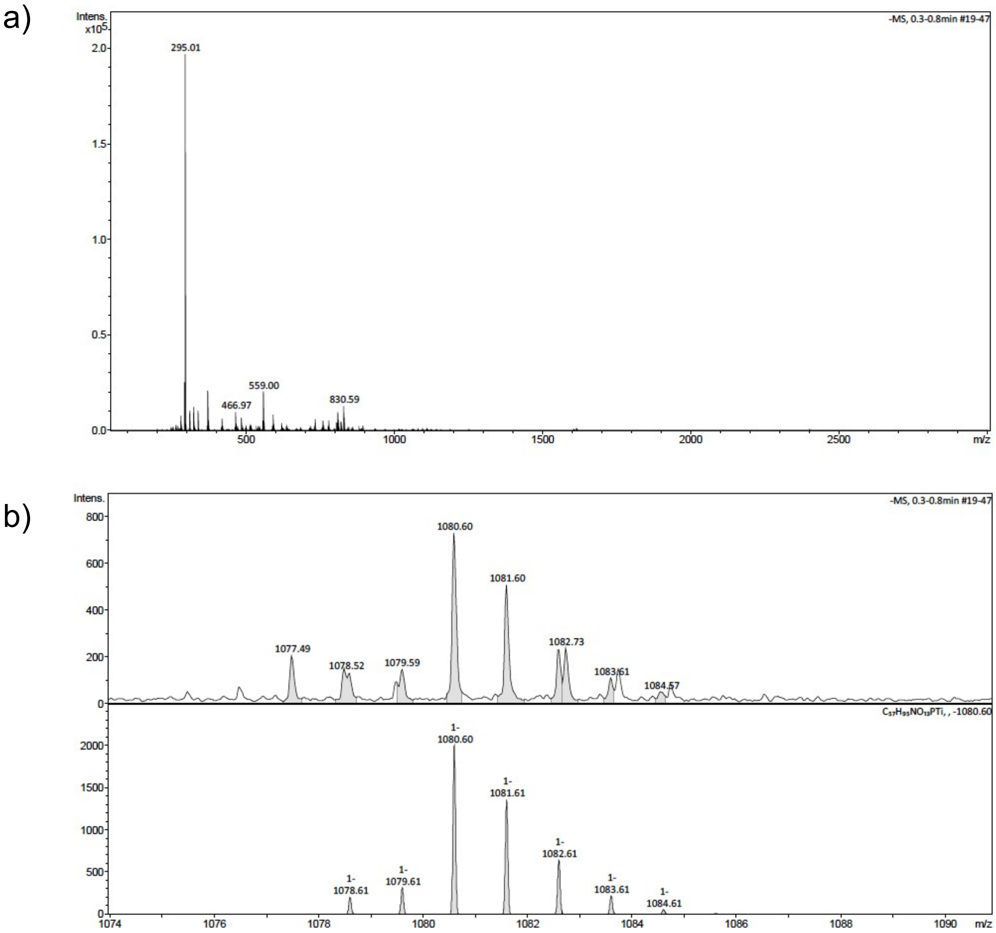


Figure S16. Negative-mode electrospray ionization mass analysis of the mixture resulting from the stoichiometric reaction of complex **1** with DOPC in methanol. (a) Whole spectrum; (b) Zoom on $[\mathrm{Ti(cat)_2(DOPC)(OMe)}]^-$ (top): experimental spectrum; bottom: simulated pattern).

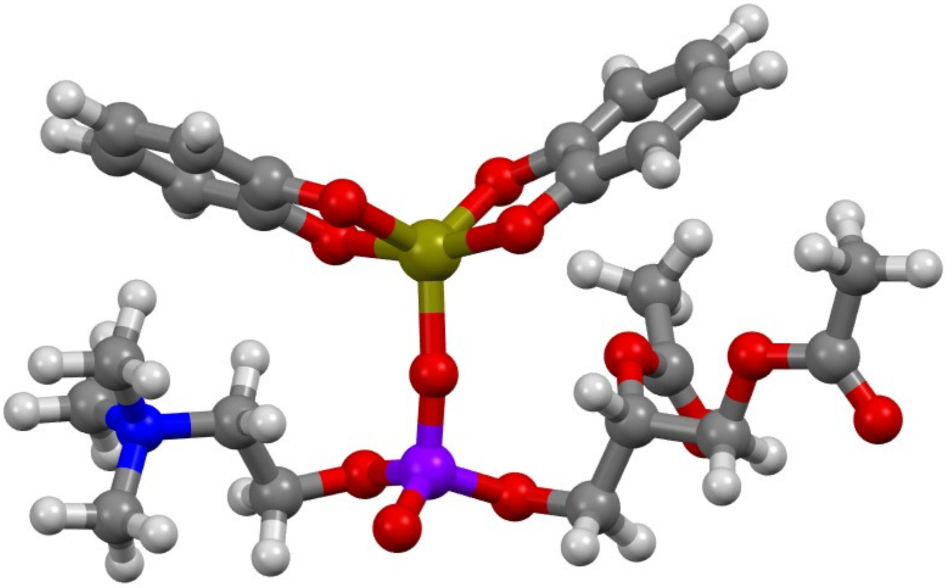


Figure S17. 3D optimized geometry of complex **4** obtained by DFT calculation. Colour code: carbon, dark grey; hydrogen, light grey; nitrogen, blue; oxygen, red; phosphorus, violet; titanium, khaki. Absolute configurations : C, *R*; P, *S*.

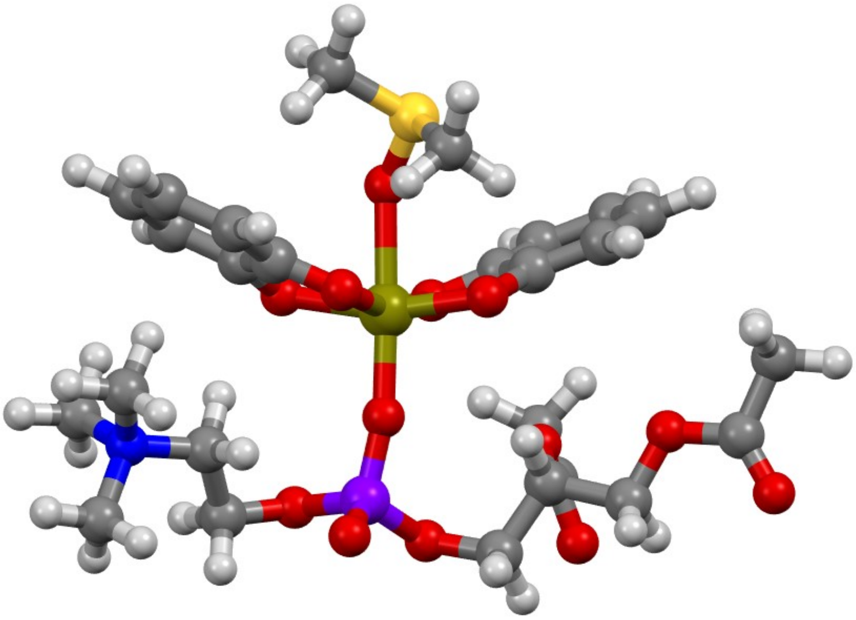


Figure S18. 3D optimized geometry of complex **5** obtained by DFT calculation. Colour code: carbon, dark grey; hydrogen, light grey; nitrogen, blue; oxygen, red; phosphorus, violet; sulfur, yellow; titanium, khaki. Absolute configurations : C, *R*; P, *S*.

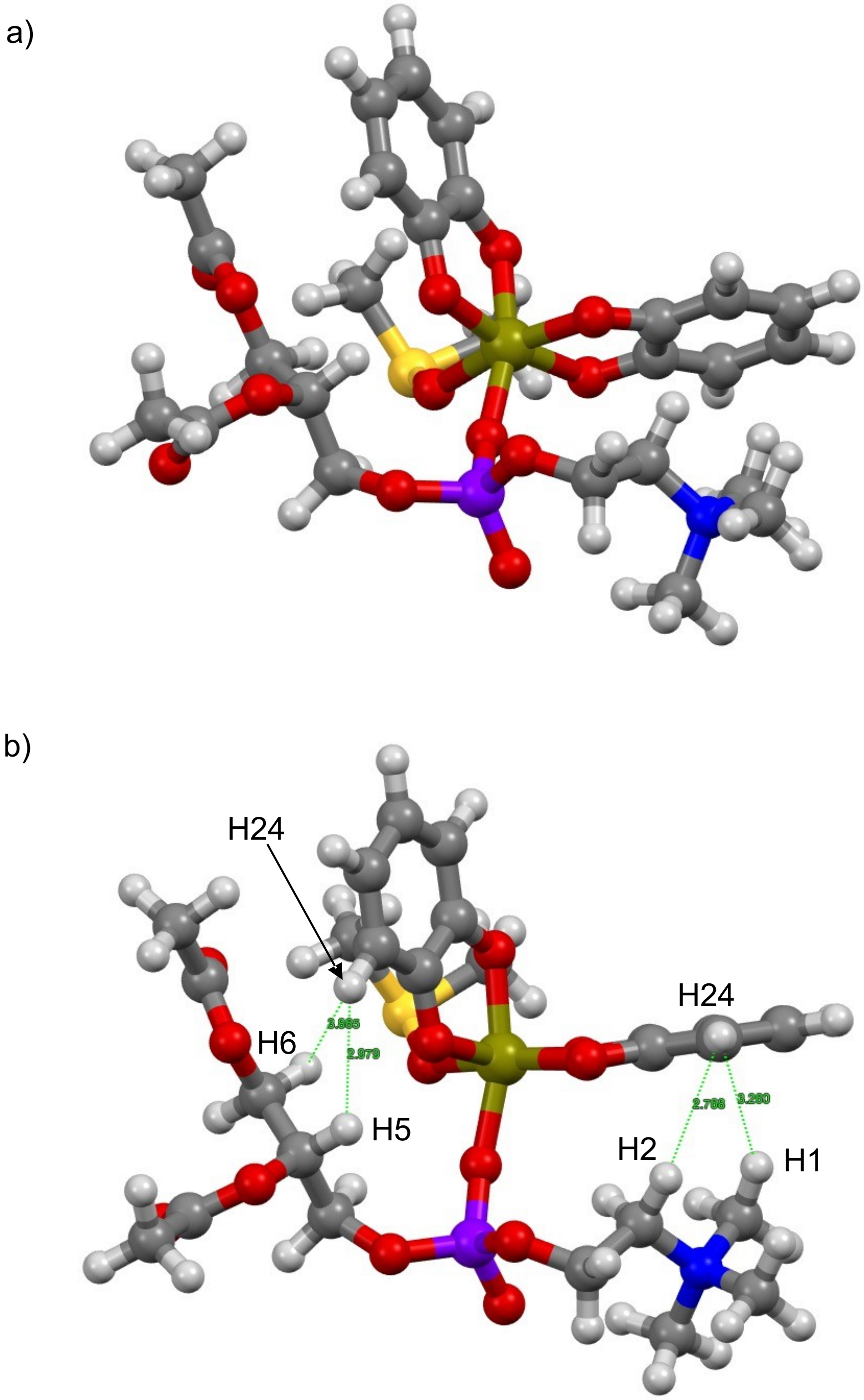


Figure S19. (a) 3D optimized geometry of complex **6** obtained by DFT calculation. Colour code: carbon, dark grey; hydrogen, light grey; nitrogen, blue; oxygen, red; phosphorus, violet; sulfur, yellow; titanium, khaki. Absolute configurations : C, *R*; P, *S*; Ti, *Δ*. (b) View of complex **6** exhibiting interligands spatial distances in Å, in agreement with the NOE cross-peaks represented Fig. 4a,b (for the atom numbering, see Fig 4c).

Estimation of Ti-DOPC binding constant from ^{1}H NMR analysis of solution B

The chemical equilibrium leading to the Ti-DOPC adduct, *viz.* complex **3**, can be written as:

$$\text{complex } \mathbf{1} + \text{DOPC} + \text{DMSO-}d_6 = \text{complex } \mathbf{3} + \text{CatH}_2$$

The equilibrium constant is:

$$K = \frac{[complex\ 3][CatH2]}{[DOPC][complex\ 1][DMSO]}$$

DMSO being the solvent, it is convenient to determine constant *K'*:

$$K^{'} = K[DMSO] \ = \frac{[complex\ 3][CatH2]}{[DOPC][complex\ 1]}$$

In solution **B**, the [complex **3**]/[DOPC] ratio has been determined as 95/5 = 19 as stated in the text of the article; the [$CatH_2$]/[complex **1**] ratio has been calculated as 0.37 from the integration of the aromatic catechol signals depicted below (see similar figure S13), from which *K'* = 7.0 at room temperature.