

Formation of vesicles with an organometallic amphiphile bilayer by supramolecular arrangement of metal carbonyl metallosurfactants

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1. General Information

All reactions were performed under nitrogen using standard Schlenk tube techniques. Tetrahydrofuran and methanol were distilled (respectively, over sodium/benzophenone and magnesium) and stored over 3Å molecular sieve. Pentane was dried with 3Å molecular sieve. Infrared spectra were recorded with a Perkin-Elmer 2000 FT spectrometer. The NMR spectra were recorded in the *Servei de Ressonància Magnètica Nuclear de la Universitat Autònoma de Barcelona* on Bruker DPX-250, DPX-360 and AV400 instruments. Microanalyses were performed by the *Servei d'Anàlisi Química del Departament de Química de la Universitat Autònoma de Barcelona*. Mass spectra and exact mass measurements were respectively obtained on an Esquire 3000 with electrospray ionization and an ion trap Bruker Daltonics and on a Bruker microTOFQ with electrospray ionization Apollo of Bruker by *Servei d'Anàlisi Química del Departament de Química de la Universitat Autònoma de Barcelona*.

The Dynamic Light Scattering measurements were performed in the *Departament de Fisicoquímica de la Facultat de Farmàcia de la Universitat de Barcelona* using a Malvern Zetasizer ZS90 (Malvern Instruments Ltd, Malvern, UK) equipped with an He-Ne laser. In this

device scattered light is detected at 90° and its intensity on the detector is automatically adjusted in order to achieve an optimal range. This fact allows the analysis of several orders of sample concentration, avoiding their dilution and, consequently, changes in the phase equilibrium. The DLS instrument used for these experiments can be used to characterize particles with diameters in the range 2 nm – 6 µm. All compounds were previously recrystallized. The water solutions of amphiphiles (**4**: 10.9 mM; **5**: 7.3 mM; **6**: 3.4 mM; **7**: 10.5 mM; **8**: 9.1 mM; **9**: 3.7 mM) were prepared with degassed Milli-Q water. The solutions were previously centrifuged for 2 – 3 minutes at 13000 rpm and then aged for at least 1 hour before measurements. For all DLS measurements the temperature was 25 ± 0.5 °C. Each data acquisition was a mean of 10 consecutive analyses and each experiment was repeated three times. The data were analyzed by cumulant method using the software provided by the manufacturer. Polydispersity index of the samples corresponded to polydisperse vesicles (**4**: 0.41 ± 0.05 ; **5**: 0.46 ± 0.02 ; **6**: 0.7 ± 0.2 ; **7**: 0.56 ± 0.06 ; **8**: 0.34 ± 0.05 ; **9**: 0.50 ± 0.01) in agreement with cryo-TEM microscopy analysis.

The microscopy studies were performed in the *Servei de Microscòpia Electrònica de la Universitat Autònoma de Barcelona*. Micrographs were obtained using a Jeol JEM-1400 electron microscope operating at 120 kV and equipped with a CCD multiscan camera (Gatan). The microscope was equipped with a Gatan cryoholder and the samples were maintained at -177°C during imaging. Micro drops (2 µL) of the water solutions of amphiphiles were blotted onto holey carbon grids (Quantifoil) previously glow discharged in an BAL-TEC MSC 010 glow discharger unit, which were immediately plugged into liquid ethane at -180 °C using a Leica EM CPC cryoworkstation.

2. Synthesis of Complexes 4-9

Complexes 4, 5, 6: The phosphine $\text{Ph}_2\text{P}(\text{CH}_2)_n\text{SO}_3\text{Na}$ {0.22 mmol (0.070 g for **4**, 0.082 g for **5** and 0.095 g for **6**)} was dissolved in dry methanol (10 mL for **4** and **5**; 15 mL for **6**) and this solution was added at room temperature to a solution of $[\text{Mo}(\text{CO})_6]$ (0.584 g, 2.21 mmol) in freshly distilled THF (40 mL). The resulting solution was protected from light and heated with a bath at 80 °C for 15 hours under nitrogen atmosphere. The obtained yellow solution was cooled, getting dark as temperature decreases and becoming black at room temperature. Next, solvent was evaporated under reduced pressure to dryness to yield a black solid that was washed (3×20 mL) with dry pentane in order to remove $[\text{Mo}(\text{CO})_6]$ excess. Dry methanol (50 mL for **4** and **5**; 75 mL for **6**) was added to the residual solid and after vigorous stirring the resulting mixture was

centrifuged (5000 rpm) and filtered with Celite. The complexes were isolated as brown solids after evaporation of filtrate to dryness under reduced pressure.

[Mo(CO)₅(1)](4): The above procedure leads to 85 mg of **4** (70 %). IR (CH₂Cl₂, cm⁻¹): 2073, 1990, 1945 {ν(CO)}. ³¹P{¹H}-NMR (CD₃OD, δ in ppm): 26.7 (s). ¹H-NMR (CD₃OD, δ in ppm): 2.62 – 2.73 (m, PCH₂), 2.89 – 3.00 (m, CH₂S), 7.45 – 7.69 (m, Ph). MS-ESI (negative mode, *m/z*): 446.8 ([M-3CO-Na]⁻, 100 %), 474.8 ([M-2CO-Na]⁻, 15 %). HRMS (ESI) calcd for C₁₉H₁₄MoO₈PS ([M-Na]⁻) 530.9209, found 530.9199. Anal. Found: C, 41.12; H, 2.60; S, 5.63. Calcd for C₁₉H₁₄MoNaO₈PS: C, 41.32; H, 2.56; S, 5.81.

[Mo(CO)₅(2)](5): The above procedure leads to 90 mg of **5** (67 %). IR (CH₂Cl₂, cm⁻¹): 2072, 1988, 1944 {ν(CO)}. ³¹P{¹H}-NMR (CD₃OD, δ in ppm): 27.2 (s). ¹H-NMR (CD₃OD, δ in ppm): 1.32 – 1.49 (m, PCH₂CH₂CH₂CH₂), 1.56 – 1.70 (m, CH₂CH₂S), 2.41 – 2.56 (m, PCH₂), 2.70 – 2.80 (m, CH₂S), 7.42 – 7.68 (m, Ph). MS-ESI (negative mode, *m/z*): 586.9 ([M-Na]⁻, 100 %), HRMS (ESI) calcd for C₂₃H₂₂MoO₈PS ([M-Na]⁻) 586.9836, found 586.9820. Anal. Found: C, 45.28; H, 3.53; S, 5.12. Calcd for C₂₃H₂₂MoNaO₈PS: C, 45.41; H, 3.64; S, 5.27.

[Mo(CO)₅(3)](6): The above procedure leads to 84 mg of **6** (57 %). IR (CH₂Cl₂, cm⁻¹): 2071, 1988, 1943 {ν(CO)}. ³¹P{¹H}-NMR (CD₃OD, δ in ppm): 27.4 (s). ¹H-NMR (CD₃OD, δ in ppm): 1.13 – 1.47 (m, PCH₂(CH₂)₇), 1.71 – 1.82 (m, CH₂CH₂S), 2.41 – 2.50 (m, PCH₂), 2.73 – 2.82 (m, CH₂S), 7.44 – 7.59 (m, Ph). MS-ESI (negative mode, *m/z*): 642.9 ([M-Na]⁻, 100 %). HRMS (ESI) calcd for C₂₇H₃₀MoO₈PS ([M-Na]⁻) 643.0464, found 643.0447. Anal. Found: C, 48.45; H, 4.37; S, 4.56. Calcd for C₂₇H₃₀MoNaO₈PS: C, 48.40; H, 4.55; S, 4.83.

Complexes 7, 8, 9: The phosphine Ph₂P(CH₂)_nSO₃Na {0.119 g (0.37 mmol) for **7**, 0.208 g (0.56 mmol) for **8**, 0.219 g (0.51 mmol) for **9**} was dissolved in dry methanol (10 mL for **7** and **8**; 20 mL for **9**) and this solution was slowly added at room temperature to a solution of *cis*-[Mo(CO)₄(pip)₂] (pip = piperidine, 0.070 g, 0.19 mmol) in dry THF (10 mL). The resulting solution was protected from light and allowed to stir at room temperature for 3 hours under nitrogen atmosphere. At this point, a clear yellow solution should be obtained. If some turbidity was observed, it can be related with the use of solvents that were not dry enough. This clear yellow solution was evaporated under reduced pressure to dryness to yield a yellow solid. Dry methanol (0.5 mL for **7** and **8**; 1.5 mL for **9**) was added to this solid and after vigorous stirring the resulting mixture was centrifuged (13000 rpm). Freshly distilled diethyl ether was dropwise added to the filtrate until the precipitation of a yellow solid is complete (≈ 2 mL). The precipitate was isolated by centrifugation (13000 rpm), washed with diethyl ether (2 × 1 mL) and dried under reduced pressure. Complexes **7, 8, 9** were isolated as yellow solids.

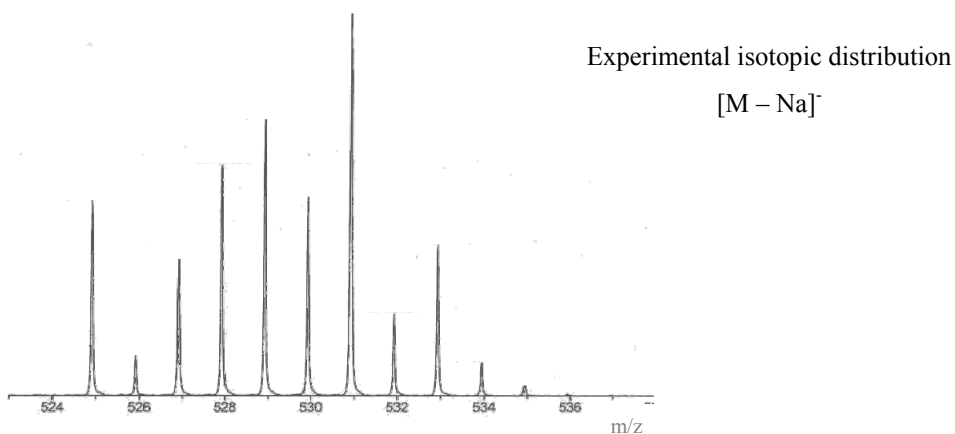
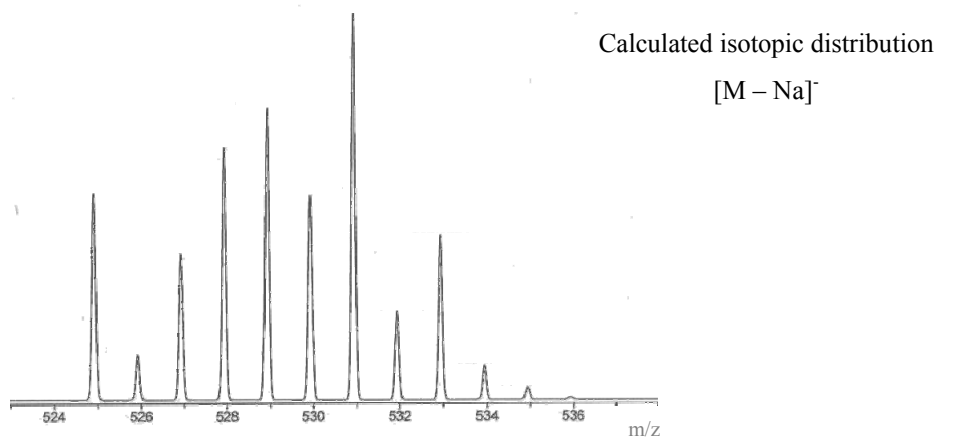
cis-[Mo(CO)₄(**1**)₂](**7**): The above procedure leads to 127 mg of **7** (82 %). IR (CH₂Cl₂, cm⁻¹): 2020, 1925, 1897 {ν(CO)}. ³¹P{¹H}-NMR (CD₃OD, δ in ppm): 25.6 (s). ¹H-NMR (CD₃OD, δ in ppm): 2.43 – 2.62 (m, PCH₂), 2.69 – 2.84 (m, CH₂S), 7.24 – 7.90 (m, Ph). ¹³C-NMR (CD₃OD, δ in ppm): 28.3 (AXX', 3 lines, ¹J_{C-P}+³J_{C-P'} = 20.4 Hz, PCH₂), 46.4 (s, CH₂S), 128.2-135.7 (multiple signals, Ph), 209.3 (t, ²J_{C-P} = 9.4 Hz, CO cis to the two P atoms), 214.8 (AXX', 3 lines, ²J_{C-P}+²J_{C-P'} = 15.8 Hz, CO trans and cis to P atoms). MS-ESI (negative mode, *m/z*): 818.8 ([M-Na]⁻, 55 %). HRMS (ESI) calcd for C₃₂H₂₈MoNaO₁₀P₂S₂ ([M-Na]⁻) 818.9550, found 818.9550. Anal. Found: C, 45.34; H, 3.56; S, 7.31. Calcd for C₃₂H₂₈MoNa₂O₁₀P₂S₂·0.5CH₄O: C, 45.57; H, 3.53; S, 7.49.

cis-[Mo(CO)₄(**2**)₂](**8**): The above procedure leads to 150 mg of **8** (85 %). IR (CH₂Cl₂, cm⁻¹): 2015, 1914, 1896, 1868 {ν(CO)}. ³¹P{¹H}-NMR (CD₃OD, δ in ppm): 26.3 (s). ¹H-NMR (CD₃OD, δ in ppm): 1.07 – 1.16 (m, PCH₂CH₂), 1.16 – 1.25 (m, PCH₂CH₂CH₂CH₂), 1.59 – 1.69 (m, CH₂CH₂S), 2.00 – 2.08 (m, PCH₂), 2.66 – 2.73 (m, CH₂S), 7.31 – 7.41 (m, Ph). ¹³C-NMR (CD₃OD, δ in ppm): 23.9 (s, PCH₂CH₂), 24.4 (s, CH₂CH₂S), 28.0 (s, CH₂CH₂CH₂S), 30.3 (AXX', 3 lines, ²J_{C-P}+⁴J_{C-P'} = 12.8 Hz, PCH₂CH₂CH₂), 32.2 (AXX', 3 lines, ¹J_{C-P}+³J_{C-P'} = 21.7 Hz, PCH₂), 51.0 (s, CH₂S), 127.9-137.1 (multiple signals, Ph), 210.0 (t, ²J_{C-P} = 9.4 Hz, CO cis to the two P atoms), 215.3 (AXX', 3 lines, ²J_{C-P}+²J_{C-P'} = 15.9 Hz, CO trans and cis to P atoms). MS-ESI (negative mode, *m/z*): 931.0 ([M-Na]⁻, 70 %). HRMS (ESI) calcd for C₄₀H₄₄MoNaO₁₀P₂S₂ ([M-Na]⁻) 931.0805, found 931.0795. Anal. Found: C, 49.78; H, 5.02; S, 6.28. Calcd for C₄₀H₄₄MoNa₂O₁₀P₂S₂·CH₄O: C, 50.00; H, 4.91; S, 6.51.

[Mo(CO)₅(**3**)](**9**): The above procedure leads to 149 mg of **9** (76 %). IR (CH₂Cl₂, cm⁻¹): 2018, 1917, 1900, 1875 {ν(CO)}. ³¹P{¹H}-NMR (CD₃OD, δ in ppm): 26.5 (s). ¹H-NMR (CD₃OD, δ in ppm): 1.01 – 1.31 (m, PCH₂(CH₂)₆), 1.31 – 1.47 (m, CH₂CH₂CH₂S), 1.70 – 1.82 (m, CH₂CH₂S), 1.97 – 2.08 (m, PCH₂), 2.73 – 2.81 (m, CH₂S), 7.27 – 7.49 (m, Ph). ¹³C-NMR (CD₃OD, δ in ppm): 23.7 (s, PCH₂CH₂), 24.5 (s, CH₂CH₂S), 28.3 (s, CH₂CH₂CH₂S), 28.6-28.9 {four singlets, PCH₂CH₂CH₂(CH₂)₄}, 30.3 (AXX', 3 lines, ²J_{C-P}+⁴J_{C-P'} = 12.5 Hz, PCH₂CH₂CH₂), 32.2 (AXX', 3 lines, ¹J_{C-P}+³J_{C-P'} = 21.6 Hz, PCH₂), 51.3 (s, CH₂S), 127.9-137.3 (multiple signals, Ph), 210.0 (t, ²J_{C-P} = 9.7 Hz, CO cis to the two P atoms), 215.3 (AXX', 3 lines, ²J_{C-P}+²J_{C-P'} = 16.0 Hz, CO trans and cis to P atoms). MS-ESI (negative mode, *m/z*): 1043.1 ([M-Na]⁻, 63 %, 510.0 ([M-2Na]²⁻, 100 %). HRMS (ESI) calcd for C₄₈H₆₀MoNaO₁₀P₂S₂ ([M-Na]⁻) 1043.2032, found 1043.2032. Anal. Found: C, 53.73; H, 5.77; S, 5.69. Calcd for C₄₈H₆₀MoNa₂O₁₀P₂S₂·0.5 CH₄O: C, 53.89; H, 5.78; S, 5.93.

3. High Resolution Mass Spectrometry

a) Calculated and experimental isotopic distribution for $[\text{Mo}(\text{CO})_5(\mathbf{1})](\mathbf{4})$

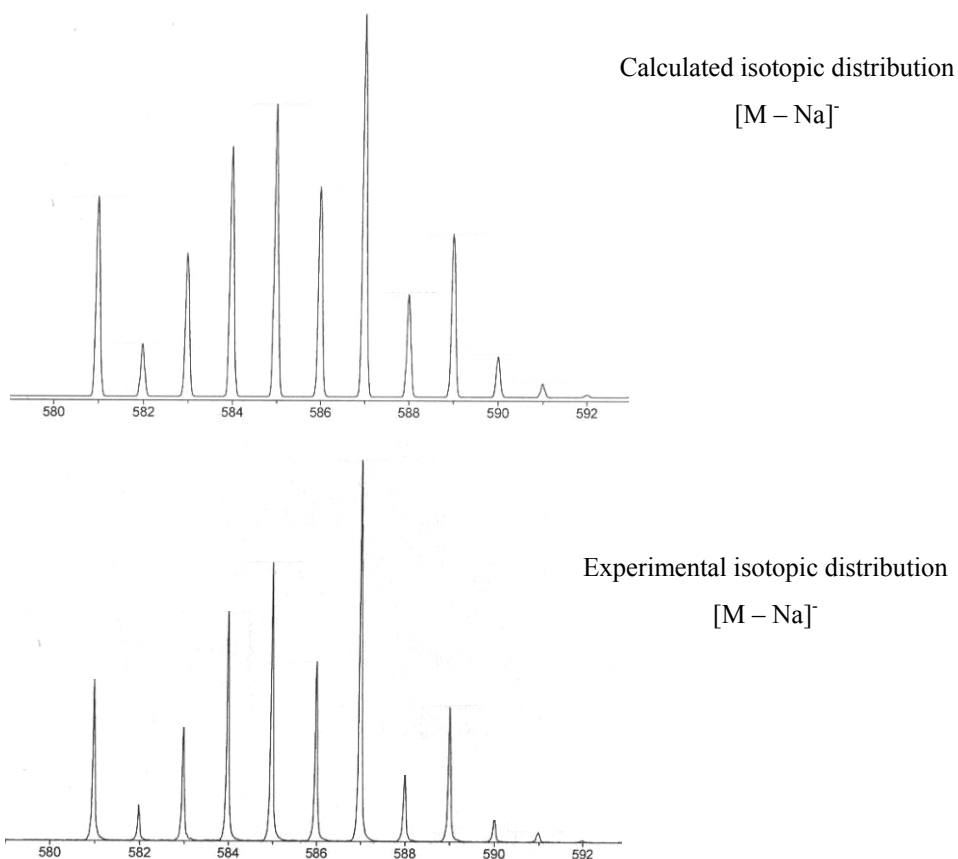


$[\text{M} - \text{Na}]^+ : \text{C}_{19}\text{H}_{14}\text{MoO}_8\text{PS}$

Calculated: 524.9221, 525.9253, 526.9206, 527.9214, 528.9207, 529.9218, 530.9209, 531.9235, 532.9224, 533.9255, 534.9231.

Experimental: 524.9214, 525.9236, 526.9199, 527.9205, 528.9198, 529.9211, 530.9199, 531.9231, 532.9215, 533.9246, 534.9240.

b) Calculated and experimental isotopic distribution for $[\text{Mo}(\text{CO})_5(\mathbf{2})](\mathbf{5})$

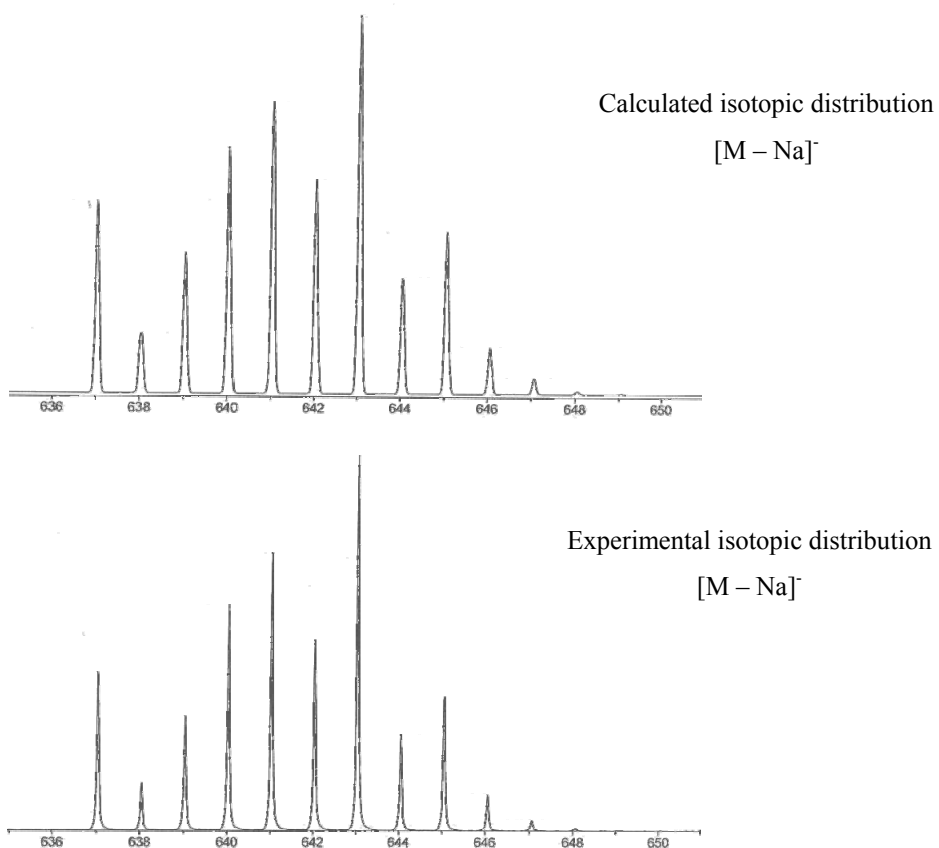


[M – Na]⁺ : C₂₃H₂₂MoO₈PS

Calculated: 580.9847, 581.9879, 582.9833, 583.9841, 584.9834, 585.9845, 586.9836, 587.9863, 588.9852, 589.9882, 590.9864.

Experimental: 580.9830, 581.9857, 582.9805, 583.9823, 584.9816, 585.9826, 586.9820, 587.9831, 588.9821, 589.9836, 590.9734.

c) Calculated and experimental isotopic distribution for $[\text{Mo}(\text{CO})_5(\mathbf{3})](\mathbf{6})$

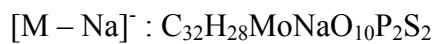
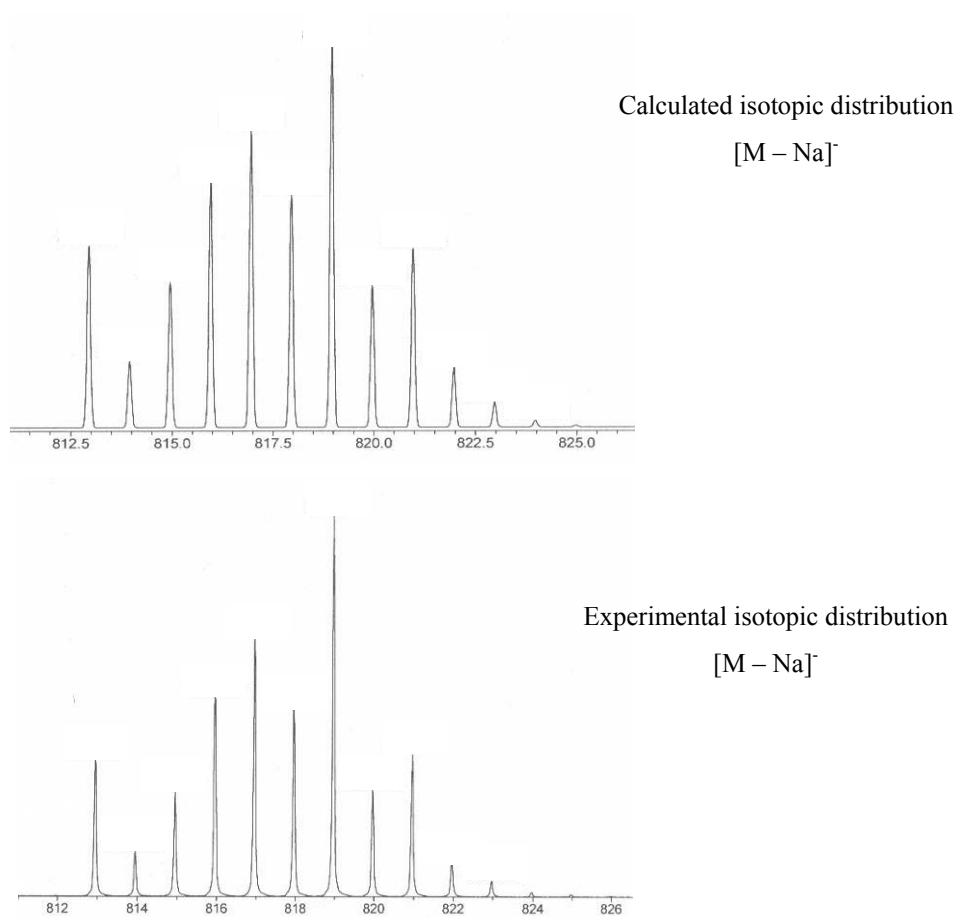


$[\text{M} - \text{Na}]^+ : \text{C}_{27}\text{H}_{30}\text{MoO}_8\text{PS}$

Calculated: 637.0473, 638.0506, 639.0460, 640.0467, 641.0462, 642.0473, 643.0464, 644.0490, 645.0479, 646.0509, 647.0497.

Experimental: 637.0460, 638.0484, 639.0445, 640.0449, 641.0445, 642.0451, 643.0447, 644.0473, 645.0464, 646.0492, 647.0489.

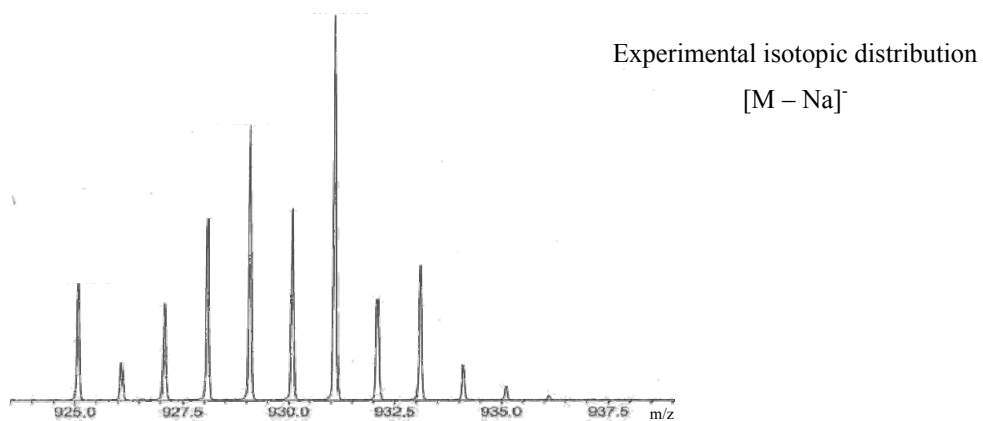
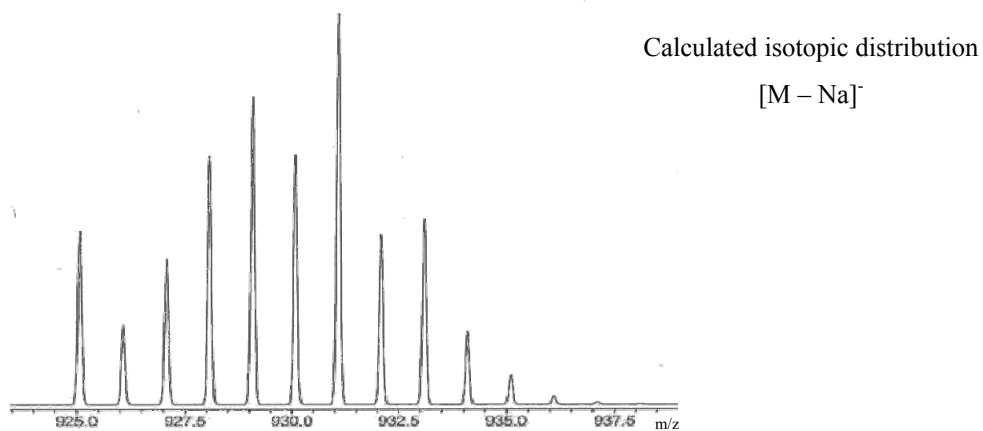
d) Calculated and experimental isotopic distribution for *cis*-[Mo(CO)₄(**1**)₂](**7**)



Calculated: 812.9559, 813.9592, 814.9548, 815.9555, 816.9550, 817.9559, 818.9550, 819.9573, 820.9562, 821.9590, 822.9572.

Experimental: 812.9556, 813.9593, 814.9543, 815.9554, 816.9549, 817.9561, 818.9550, 819.9576, 820.9559, 821.9591, 822.9580.

e) Calculated and experimental isotopic distribution for *cis*-[Mo(CO)₄(**2**)₂](**8**)

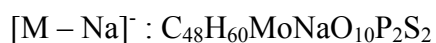
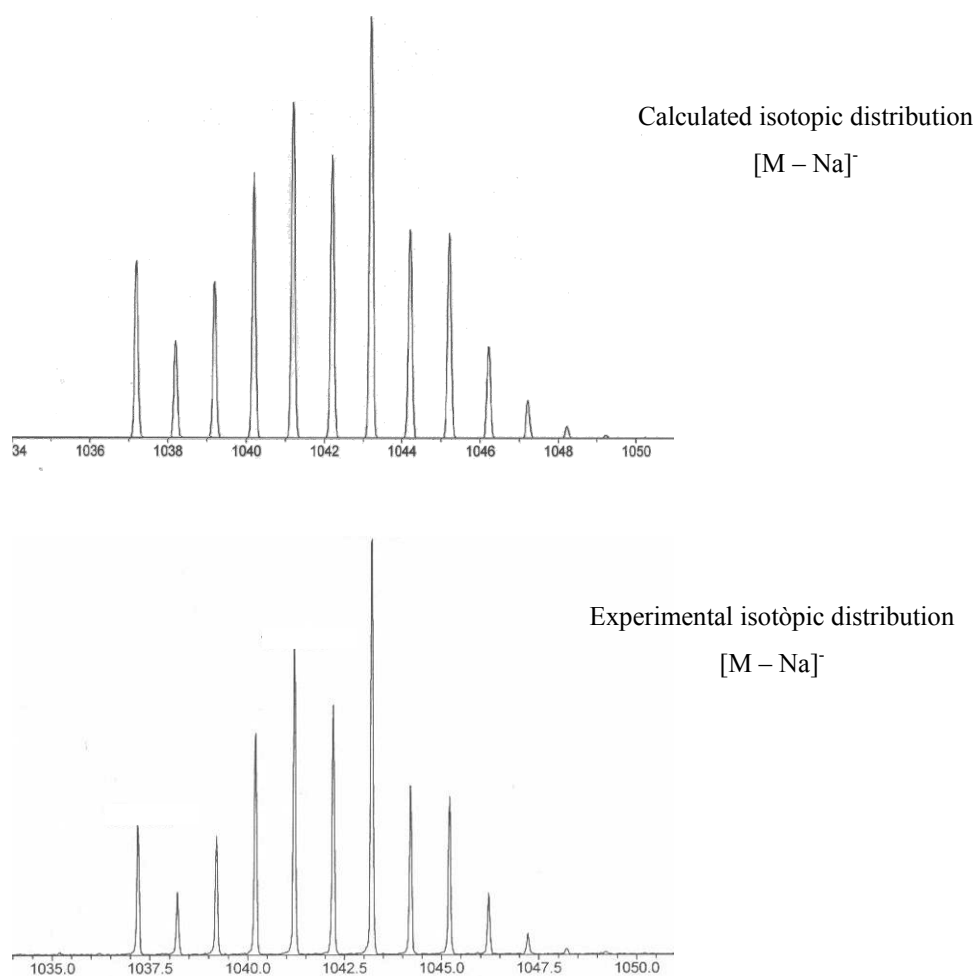


[M – Na]⁺ : C₄₀H₄₄MoNaO₁₀P₂S₂

Calculated: 925.0811, 926.0844, 927.0803, 928.0808, 929.0805, 930.0814, 931.0805, 932.0828, 933.0818, 934.0843, 935.0834.

Experimental: 925.0785, 926.0813, 927.0779, 928.0788, 929.0781, 930.0792, 931.0795, 932.0816, 933.0803, 934.0824, 935.0815.

f) Calculated and experimental isotopic distribution for *cis*-[Mo(CO)₄(**3**)₂](**9**)

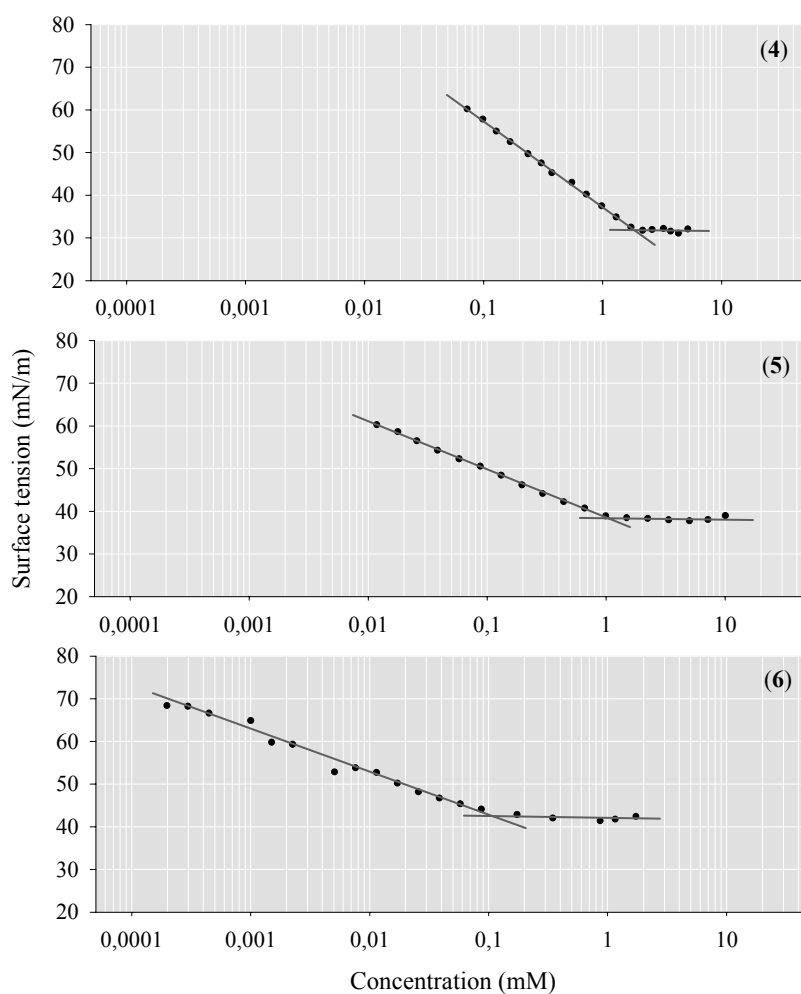


Calculated: 1037.2063, 1038.2096, 1039.2059, 1040.2062, 1041.2059, 1042.2068, 1043.2059, 1044.2082, 1045.2073, 1046.2097, 1047.2095, 1048.2103.

Experimental: 1037.2021, 1038.2072, 1039.2021, 1040.2029, 1041.2029, 1042.2029, 1043.2032, 1044.2042, 1045.2028, 1046.2067, 1047.2075, 1048.2011.

4. Surface Tension Measurements. The surface tension measurements of the aqueous solutions were performed in the *Departament de Tecnologia de Tensioactius de l'Institut de Química Avançada de Catalunya (IQAC-CSIC)* at 25 °C with a Krüss K-12 automatic tensiometer (Hamburg, Germany) equipped with a Wilhelmy plate. All compounds were previously recrystallized and lyophilized. The water solutions of amphiphiles were prepared with degassed Milli-Q water. The different solutions were prepared by dilution of a concentrated sample and then aged for at least 30 min before the determinations. The stability criterion for surface tension values was tuned to ± 0.1 mN/m for five consecutive measurements. The cmc values were taken from the intersection of two linear sections obtained in the graphical plots of surface tension versus logarithm of the concentration. The area occupied per molecule adsorbed at the water/air interface, expressed in $\text{\AA}^2$, was obtained from the equation $A = 10^{16}/N_A\Gamma$, where N_A is Avogadro's number and Γ the surface excess concentration in mol/cm^2 , calculated according to the Gibbs equation: $\Gamma = -(d\gamma/d\log C)/2.303nRT$, where n is the number of molecular species in solution ($n = 2$ for compounds **4-6** and $n = 3$ for compounds **7-9**), and $(d\gamma/d\log C)$ is the slope of the linear part of the graph obtained immediately below the cmc.

a) Surface tension measurements for complexes (4-6)



b) Surface tension measurements for complexes (7-9)

