Electronic supplementary materials *Mendeleev Commun.*, 2025, **35**, 664–666

A novel natural chlorin metal complex containing gold(I) in the macrocycle periphery

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Contents:

Gold(I) complex with 13^1-thiocarbonyl derivative of pyropheophorbide A within the macrocycle cavity (**3**).
Pyropheophorbide *a* thioketone (**2**) (35 mg, 0.062 mol) was dissolved in toluene, and chloro(dimethyl sulfide)gold(I) (18 mg, 0.062 mmol) was added. The mixture was stirred for 2 hours in an argon atmosphere in the dark. The reaction mass was dried on a rotary evaporator and purified by preparative thin-layer chromatography in the CH_2Cl_2/CH_3OH (10/1) system. The output of the target product was 15%. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.40 (s, 1H, 10-H), 9.29 (s, 1H, 5-H), 8.52 (s, 1H, 20-H), 7.94 (dd, 1H, *J* = 17.8, 11.6 Hz, 3^1-H), 6.24 (d, 1H, *J* = 17.8 Hz, 3^2-H$_a$), 6.13 (d, 1H, *J* = 11.5 Hz, 3^2-H$_b$), 5.25 (d, 1H, *J* = 20.2 Hz, 13^2 -CH$_{2a}$), 5.09 (d, 1H, *J* = 20.0 Hz, 13^2 -CH$_{2b}$), 4.46 (q, *J* = 7.0 Hz, 1H, 18-H), 4.28 (m, 1H, 17-H), 3.63 (m, 2H, 8^2-CH$_2$), 3.60 (s, 3H, 12-CH$_3$), 3.37 (s, 3H, 17^3-COOCH$_3$), 3.18 (s, 3H, 2^1-CH$_3$), 2.98 (s, 3H, 7^1-CH$_3$), 2.63 (m, 2H, 17^1-CH$_2$), 2.32 (m, 2H, 17^2-CH$_2$), 1.80 (d, 3H, *J*=7.2 Hz, 18^1-CH$_3$), 1.65 (t, 3H, *J*=7.5 Hz, 8^2-CH$_3$). ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.65 (C13^1), 177.51 (C17^3), 171.43 (C19), 160.24 (C16), 155.27 (C6), 150.72 (C9), 149.03 (C14), 144.98 (C8), 141.60 (C1), 137.76 (C12), 136.24 (C7), 136.05 (C4), 135.80 (C3), 131.62 (C11), 130.26 (C2), 129.14 (C3^1), 128.29 (C13), 122.55 (C3^2), 105.93 (C15), 104.09 (C10), 97.10 (C5), 93.04 (C20), 51.47 (C17), 49.95 (C17^5), 47.97 (C18), 30.71 (C13^2), 29.61(C17^2), 23.16 (C17^1), 22.83 (C18^1), 19.42(C8^1), 17.46 (C8^2), 12.13 (C2^1), 12.05 (C12^1), 11.23 (C7^1). ESI *m*/*z*: $[M+H]^+$: 758.2, 759.2, 760.2, 761.2, 762.2, 763.1, (calc. for $C_{34}H_{34}AuN_4O_2S$, *m*/*z*: 759.21, 760.21, 761.21, 761.20, 762.21, 760.20). Elemental Analysis: C, 51.36; H, 4.31; Au, 24.77; Cl, 4.46; N, 7.05; O, 4.02; S, 4.03. Found (%): C, 51.32; H, 4.36; N, 7.02; S, 4.01. Calc. for $C_{34}H_{34}AuN_4O_2S$ (%): C, 51.36; H, 4.31; N, 7.05; S, 4.03. UV/Vis λ_{max} nm: 414 (25,473), 663(11,518).

Gold(I) metal complex of thiocarbonyl derivative of pyropheophorbide A on the periphery of the macrocycle (**4**). Pyropheophorbide *a* thioketone (**2**) (35 mg, 0.062 mol) was dissolved in anhydrous ethyl alcohol, and KOH (4 mg, 0.078 mol) was added. After 5 minutes, chloro(dimethyl sulfide)gold (I) (15 mg, 0.052 mmol) was added. The mixture was stirred for 48 hours in an argon atmosphere in the dark. The reaction mass was dried on a rotary evaporator and purified by preparative thin-layer chromatography in the CH_2Cl_2/CH_3OH (10/1) system. The product yield was 23%. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.46 (s, 1H, 10-H), 9.35 (s, 1H, 5-H), 8.56 (s, 1H, 20-H), 7.98 (dd, 1H, *J* = 17.8, 1.5 Hz, 3^1-CH), 6.28 (d, 1H, *J* = 17.8 Hz, 3^2- H_a), 6.16 (d, 1H, *J* = 11.6 Hz, 3^2-H_b), 5.21 (m, 2H, 13^2-CH_2), 4.50 (q, *J* = 7.0 Hz, 1H, 18-H), 4.42 (d, 1H, *J* = 10.1 Hz, 17-H), 3.66 (m, 5H, 8^1-CH_2, 12-CH_3), 3.41 (s, 3H, 17^3-$COOCH_3$), 3.21 (s, 3H, 2^1-CH_3), 3.04 (s, 3H, 7^1-CH_3), 2.86 (s, 6H, -S(CH3)2), 2.63 (m, 2H, 17^1-CH_2), 2.25 (m, 2H, 17^2-CH_2), 1.82 (d, 3H, *J*= 7.3 Hz, 18^1-CH_3), 1.68 (t, 3H, J= 7.6 Hz, 8^2-CH_3), 0.87 (s, NH), -1.73 (s, NH). ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.18 ($C13^1$), 171.01 (C19), 169.03 ($C17^3$), 168.29 (C16), 159.64 (C6), 155.23 (C9), 150.79 (C14), 148.96 (C8), 145.01 (C1), 141.56 (C12), 137.87 (C7), 136.18 (C4), 136.08 (C3), 135.84 (C11), 131.59 (C2), 130.56 ($C3^1$), 129.19 (C13), 128.36 ($C3^2$), 122.55 ($C13^2$), 106.12 (C15), 104.14 (C10), 97.22 (C5), 93.06 (C20), 51.03 (C17), 49.85 ($C17^5$), 47.95 (C18), 29.69 (SCH_3), 28.23 (SCH_3), 25.60 ($C17^2$), 23.07($C17^1$), 19.46 ($C18^1$), 17.43 ($C8^1$), 14.12 ($C8^2$), 12.10 ($C2^1$), 12.05 ($C12^1$), 11.23 ($C7^1$). ESI *m*/*z*: $[M+H]^+$: 822.5, 823.3, 823.9, 824.3, 825.3, 826.3, 826.8., (calc. for $C_{36}H_{43}AuN_4O_2S_2$, *m*/*z*: 822.23, 823.24, 824.23, 824.24, 825.23, 823.23, 825.24). Found (%): C, 52.52; H, 5.07; N, 6.79; S, 7.75. Calc. for $C_{36}H_{43}AuN_4O_2S_2$ (%): C, 52.55; H, 5.02; N, 6.81; S, 7.79. UV/Vis λ_{max} nm: 388 (22,673), 663(13,518), 669 (18,518).

Preparation of micellar solutions of compound **1** and **4**. A solution of compound in dichloromethane was added dropwise under continuous argon bubbling to freshly prepared 4% aqueous solution of Kolliphor ELP (5 ml) heated to 45°C. The bubbling was continued until vigorous foaming began. A clear solution with a concentration of 0.25 mg/ml was obtained, which was then filtered through a PTFE filter. The concentration of the resulting solution was controlled spectrophotometrically.

Molecular docking studies were conducted using HEX 8.0.0 software (Dave Ritchie, Paris, France). The crystal structure of B-DNA (PDB ID: 1BNA) was obtained from the Protein Data Bank (http://www.rcsb.org./pdb). The following parameters were used for docking: correlation type Shape+Electro, post-processing OPLS Minimisation, FFT 3D mode, grid size 0.6, receptor range 180, ligand range 180, rotation range 360, and distance range 40.

DNA Binding Test

Single-stranded DNA (ss-DNA) was dissolved in deionized water by stirring for 12 hours at pH 7.0 and stored at 4 °C. The buffer solution was prepared using deionized water (20 mM NaH_2PO_4–Na_2HPO_4 phosphate buffer, pH 7.2). The DNA concentration was determined according to the Bouguer-Lambert-Baer law, based on a molar absorption coefficient of 6600 M-1 cm-1 (at a wavelength of 261 nm). The studied compounds were dissolved in 70% ethanol. Absorption in the ultraviolet-visible region was measured at a constant concentration of compounds, while the concentration of the DNA solution varied from 1.25 to 5.0 mM. To exclude absorption signals from the DNA itself, control samples with the same volume of DNA of a given concentration were used when measuring control samples. Before the experiment, the solutions of the complexes were incubated with DNA for about 5 minutes at room temperature. Absorption spectra were recorded in quartz cuvettes (1 cm) at room temperature (25 ± 1 °C) in 1 nm increments over three scans.

Table S1. Intensity of the long-wavelength absorption band in 4% micellar solutions of Kolliphor ELP

Time	pH	Compound **4** in 4% micellar solutions of Kolliphor ELP		Compound **4** in 4% micellar solutions of Kolliphor ELP with the addition of 0.1% Twin 80.	
		Intensity at 669 nm	Content %	Intensity at 669 nm	Content %
0 min	4	0.274	100%	0,843	100%
	7	0.751		0,843	
	9	0.678		0,843	
4 hours	4	0.07	25%	0,363	43%
	7	0.709	**94%**	0,839	**99.5%**
	9	0.274	40%	0,816	96,8%
24 hours	4	0.034	12%	0,160	19%
	7	0.124	16%	0,818	**97%**
	9	0.273	**40%**	0,808	**95.9%**

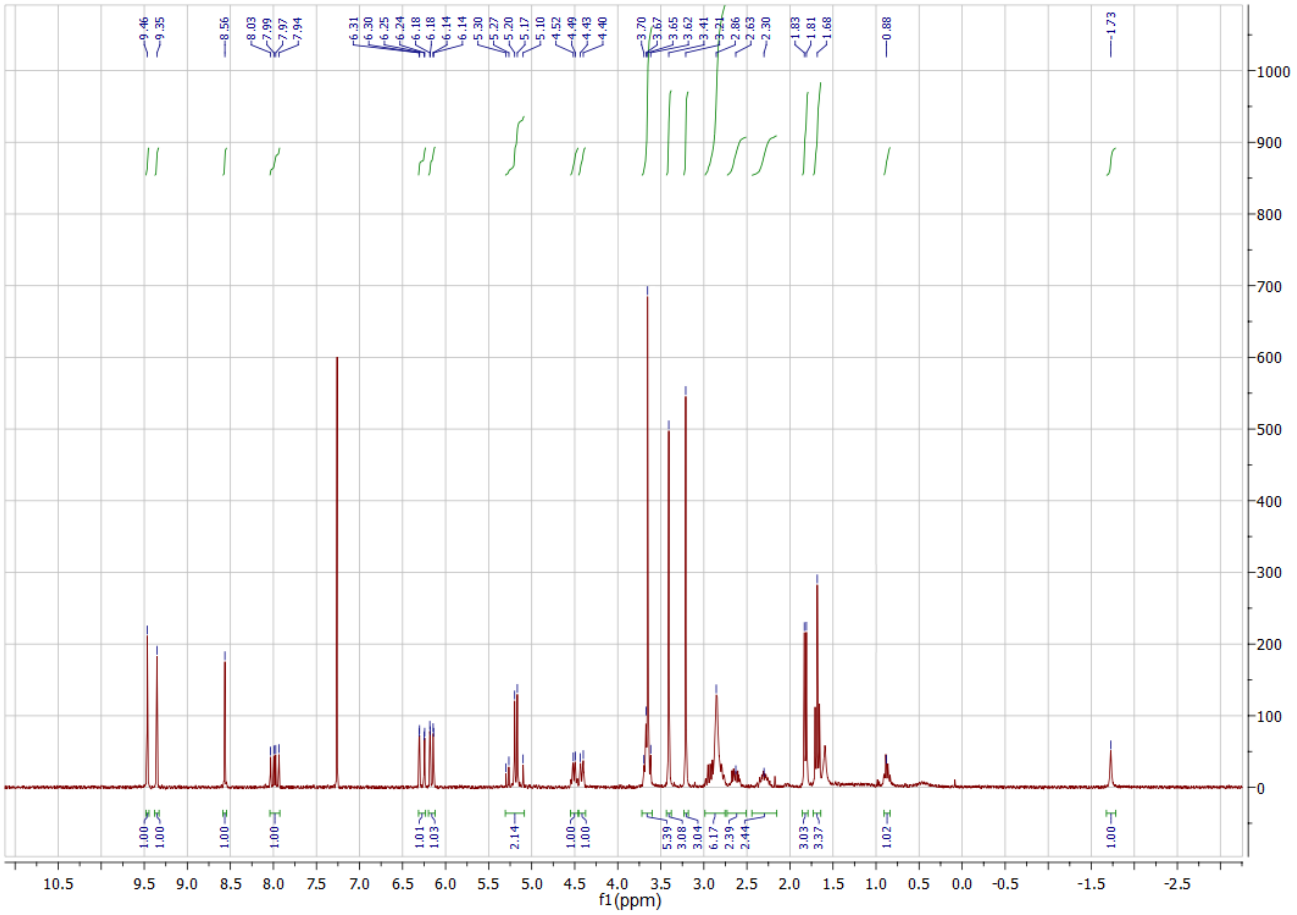

Figure S1. ^{1}H NMR spectrum of compound **4**

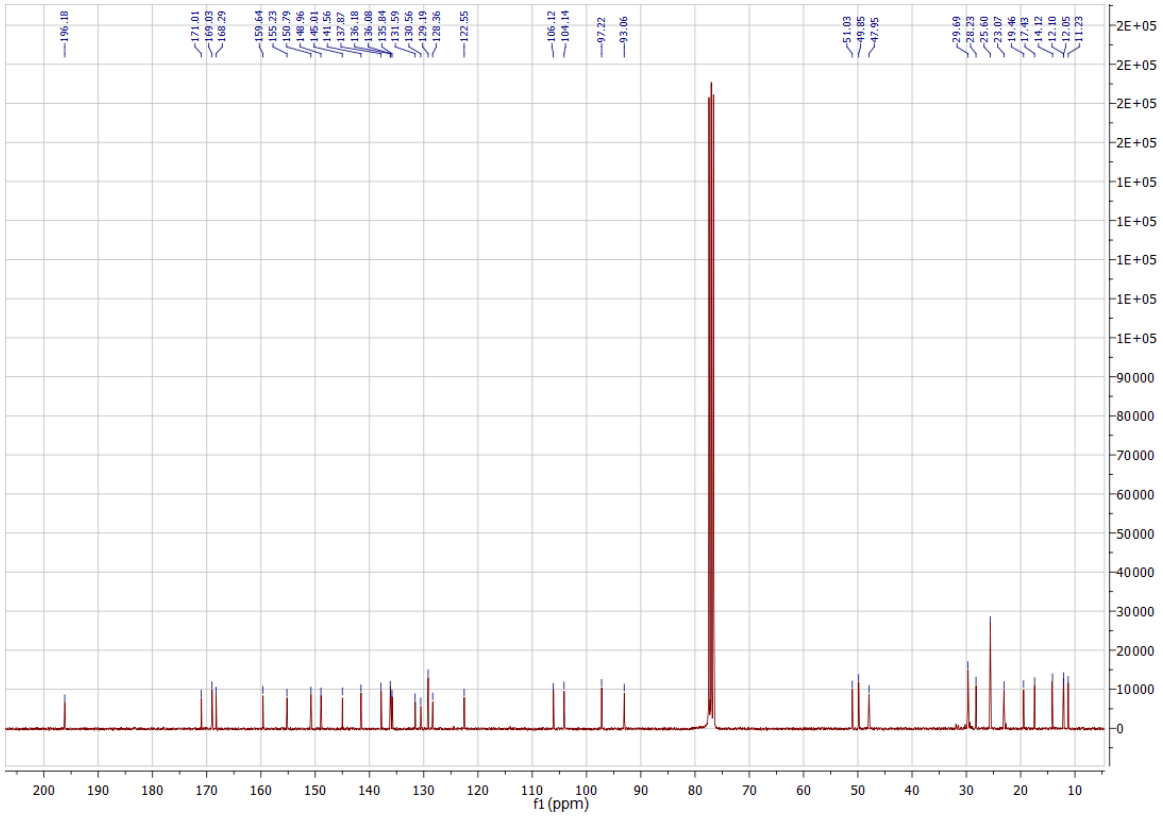

Figure S2. ^{13}C NMR spectrum of compound **4**

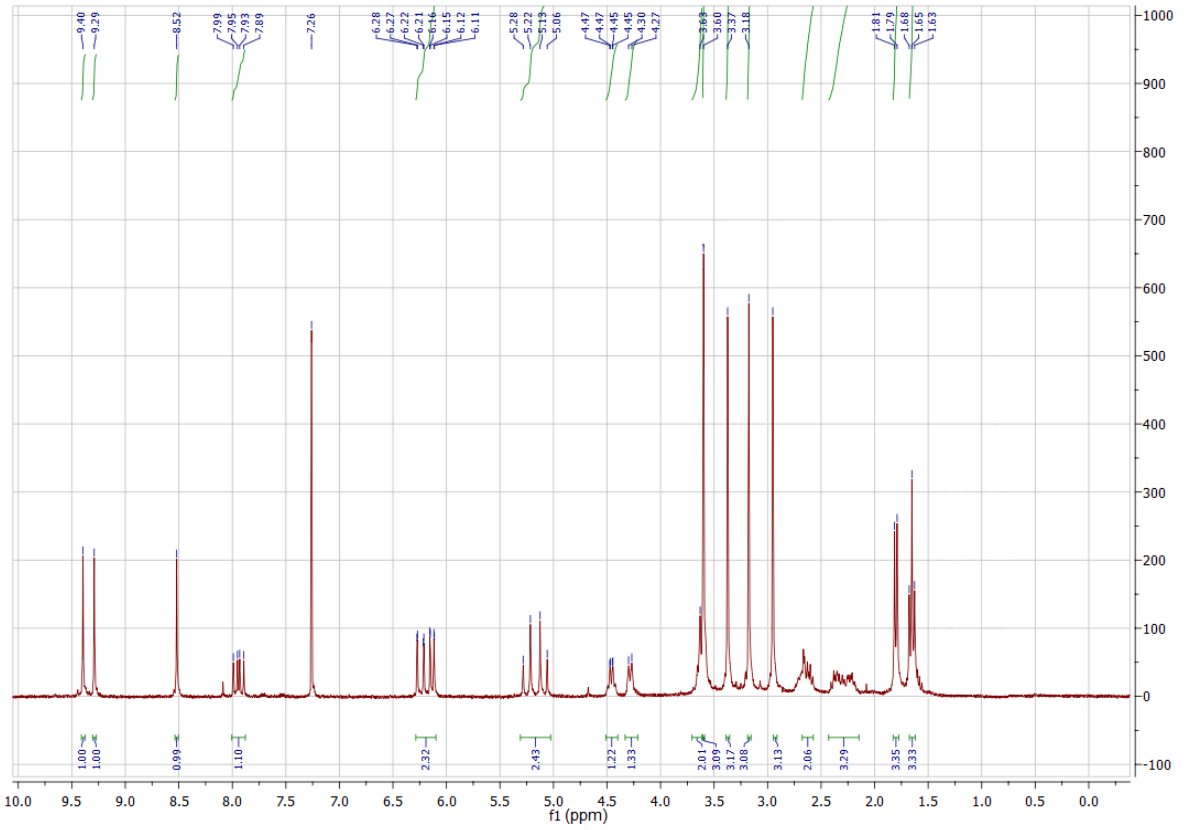

Figure S3. ^{1}H NMR spectrum of compound **3**

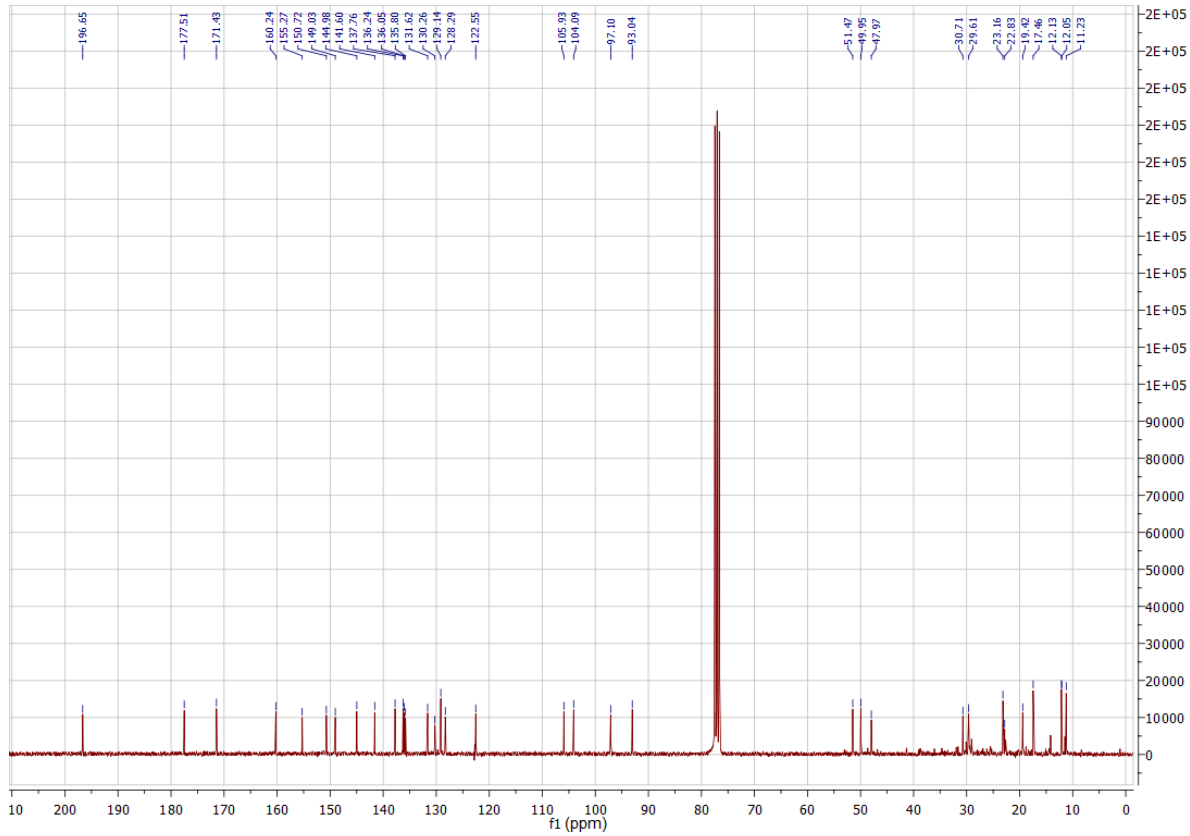

Figure S4. ^{13}C NMR spectrum of compound **3**