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Porphyrin Complexes with Highly Electronegative Metals – A New Chapter in Nucleophilic Substitution of Hydrogen?

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Abstract: The attempts of direct substitution of hydrogen in porphyrin macrocyclic systems, with carbanions of weak nucleophilicity, are described. Porphyrins, when converted into the corresponding metal chelates, were reacted with the above mentioned carbanions, and the coordinated central metal atom (*e.g.*, Au^{III}, Sn^{IV}), which reveals considerable electronegativity, played a role of activating group. It could be easily removed from the system after reaction. A number of attempts to substitute hydrogen by carbon nucleophiles led to various products (addition of nucleophile to porphyrin ring, ligands substitution at metal center, etc.). These investigations were successfully finalized for *meso*-tetraphenylporphyrin–dichlorotin(IV) complex. Further development of this idea *may open a new chapter in the functionalization of porphyrins.*

Keywords: Porphyrins, Gold and tin complexes, Nucleophilic substitution of hydrogen, Carbanions.

1. Introduction

The selective functionalization of porphyrins is intensively studied in recent years.[1] Earlier, we published several examples of the reactions of weak nucleophiles (carbanions) with these compounds leading to substitution of hydrogen products, however, the macrocycle was activated by the strong electronwithdrawing groups, *e.g.* NO_2, which needs to be introduced to the porphyrin system before the reaction.[2] We set up the hypothesis that the same role could be played by the central metal atom when porphyrins are converted into corresponding chelates. This approach has one considerable advantage. The metal can be easily removed (often with almost quantitative yield) from the system after the H-substitution reaction. This metal should reveal enough high electronegativity (***e***). The natural candidates for this purpose are metals of ***e*** higher than 2.0; *e.g.*, Au (*e* = 2.54), Sb (2.05), W (2.36), Ge (2.01) (Pauling scale). *So, their corresponding porphyrin complexes could be able to react even with weak carbanions. The solution of this problem may open a new chapter in the functionalization of porphyrins.*

Herein, the studies on possibility of direct substitution of hydrogen in the porphyrin ring, activated by the highly electronegative central metal atom when porphyrins are converted into corresponding chelates, are described.

2. Results and discussion

2.1. Gold complexes. Electronegativity of gold is relatively high, *e* = 2.54. Thus, at the beginning, we tested 5,10,15,20-tetraphenylporphyrin–gold(III) chloride (*meso*-tetraphenylporphyrin–gold(III) chloride) (**1**) which can be easily prepared according to literature prescriptions.[3] This porphyrinate was purified by column chromatography and the yield was even higher (76%) as compared to that described previously.[3a] However, its reaction with carbanion of $ClCH_2SO_2Tol$, which usually allows nucleophilic substitution of hydrogen in electrophilic aromatic compounds according to vicarious nucleophilic substitution mechanism (VNS),[4] herein, in *t*-BuOK/THF system, led to a complicated mixture of several products. They were probably an effect of ligand-exchange processes. Some modifications of the procedure and the reaction conditions did not give better results (see Experimental). Next, we have undertaken some attempts to enhance the electrophilicity of the parent system by exchanging Cl^- ligand for CN^-. However, in this case, CN^- instead of exchange chloride Cl^- anion entered immediately the addition to *meso*-carbon atom, thus giving phlorin moiety **3** (80%; Scheme 1). Similar reactions (with OH^-) for gold(III) and for antimony(V) porphyrin complexes were observed by Segawa[5] and Knör.[6]

We also tried to use another model, 2,3,7,8,12,13, 17,18-octaethylporphyrin complex ([OEP-Au(III)]Cl,

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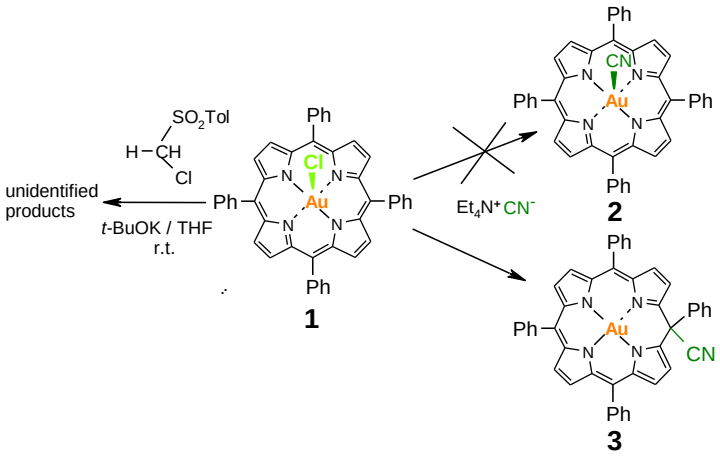


Scheme 1

4; having unsubstituted *meso*-positions). In this case, the synthesis of the substrate was somewhat troublesome. When the reaction was carried-out in $CHCl_3$/AcOH mixture (OEP+$KAuCl_4$+AcONa, 19 h, reflux), unexpectedly the only product obtained (with very small yield; 7.7%) was the acetoxy-derivative **5** (Figure 1). It was probably formed *via* tandem chlorination / $Cl^- \rightarrow AcO^-$ exchange processes (source of chlorine: $KAuCl_4$). At higher temperature (130°C) in DMF/$CHCl_3$, after shortening the reaction time to 13 h, the chlorinated product **6** was isolated in poor yield (7.8%), along with a large amount of the starting octaethylporphyrin (63%). Its *meso*-Cl structure was elucidated by HR-MS and ^{1}H NMR measurements. Finally, in the reaction carried-out in chloroform/methanol mixture (60°C, 20 h) both the above products were identified. In all the experiments the conversion rate was rather low and a lot of substrate OEP was recovered. In some reactions we also observed a pink, very polar spot on TLC which after longer period of time of refluxing disappeared. Analysis of the reaction mixture (after 3 h of heating in $CHCl_3$/AcOH) allowed us to identify this new compound(s). Probably this is a mixture of gold complex chloride of octaethylporphyrin (**4**; on the basis of HR-MS (ESI): *m/z* = 729.3239 [(M(**4**)–Cl)$^+$]; $C_{36}H_{44}N_4Au$) and its derivative **7** with additional Cl tethered to CH_2CH_3 chain or introduced to the *meso*-position (*m/z* = 763.2869 [(M(**7**)–Cl)$^+$]; $C_{36}H_{43}N_4ClAu$).

The attempts to obtain the desired complex **4** directly by the macrocyclization, in which from the beginning of the reaction an excess of $KAuCl_4$ was added to cause a template effect, also failed. Due to the above problems with the synthesis of the desired gold substrate the investigations were temporarily suspended. It is worth mentioning that Jamin and Iwamoto observed similar difficulties when trying complexation of etioporphyrin with $KAuCl_4$.[7]

2.2. Tin complexes: *meso*-tetraphenylporphyrin–dichlorotin(IV) and octaethylporphyrin–dichlorotin(IV) systems. We tried to verify the above concept

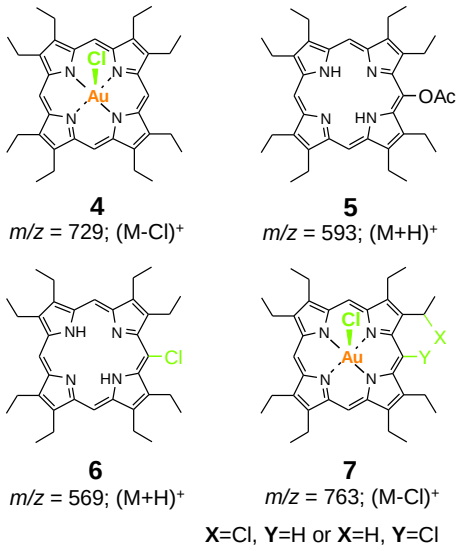


Figure 1

using another relatively easily available porphyrin complexes (dichlorotin derivatives; e_{Sn} = 1.96): octaethylporphyrin–dichlorotin(IV) (**8**) and *meso*-tetraphenylporphyrin–dichlorotin(IV) (**9**). They were synthesized on the basis of two literature reports.[8,9] Nevertheless, some modifications were introduced (sulfolane as a solvent, 170–200°C, *ca* 1 h, 68–100%; see Experimental). Confirmation of their structures was not a trivial problem. In MS spectrum of product **8** (ESI(+), in MeOH) instead of molecular and pseudomolecular ions M^+ or $(M+H)^+$, we observed another ions, probably formed during the measurements (*m/z* = 665 and *m/z* = 679; see Figure 2). Their formation can be explained easily by the ligand-exchange and ligand-losing processes. This is rather characteristic in the chemistry of such labile chelates and we observed it earlier.[10] In MS-FD spectrum the only observed peaks also were originating from the fragmentation ions and multi-charged ions. Thus, the structure cannot be confirmed definitively on the basis of these data.

Some verifications came from the ^{1}H NMR studies. The spectrum was in agreement with the structure.

The diagnostic singlet at δ = 10.48 ppm (4H), originating from *meso*-protons, and triplet/quartet pattern [2.04 ppm (24 H) and 4.21 ppm (16 H); 8×Et] confirm the structure of the expected porphyrinate. Additionally, the signal at δ = -3,73 ppm (characteristic for the inner NH-protons in substrate) disappeared, thus providing evidence for full conversion of octaethylporphyrin into complex **8**.

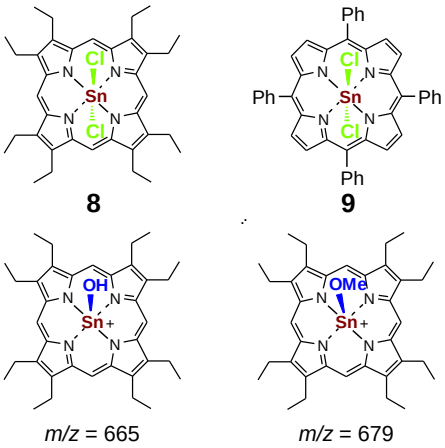
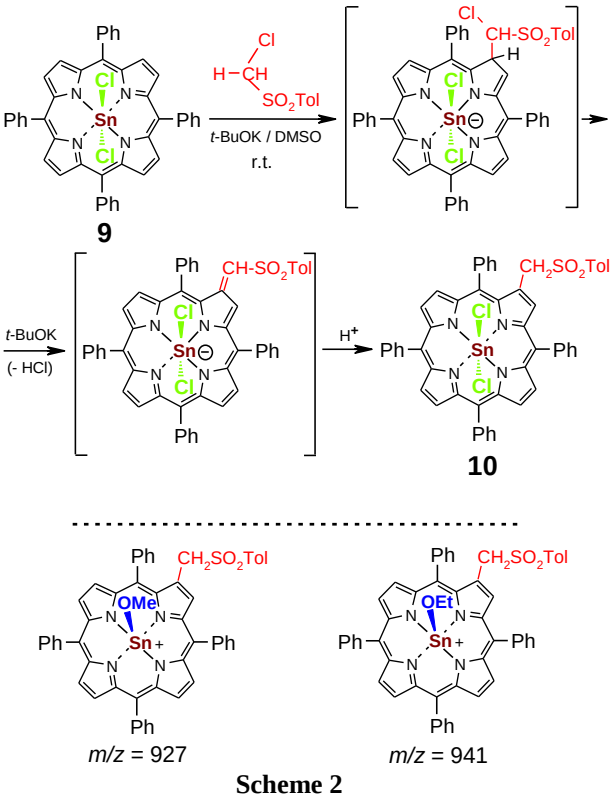


Figure 2

The complex obtained **8** was reacted, in the presence of base, with $^{-}$CH(Br)SO_2Tol carbanion, and we expected nucleophilic substitution of hydrogen[4] in *meso*-position. It could be an exceptional example of direct substitution of hydrogen with a carbanion nucleophile in porphyrinoid system. However, the reaction failed to afford the desired product. When analyzing the post-reaction mixture by MS method (APPI–photospray(+) in AcOEt), we observed only the fragmentation ions as a result of ligand-exchange and ligand-losing process in the substrate (*m/z* = 683, $OEPSnCl^+$, and *m/z* = 707, $OEPSn(OAc)^+$). There were no ions originated from the substitution of hydrogen product. The outcome of the reaction with carbanion of *para*-chlorophenoxyacetonitrile ($^{-}$CH(CN)$OC_6H_4Cl^p$), which is stronger nucleophile as compared to $^{-}$CH(Br)SO_2Tol, was similar (degradation of the reagents occurred).

Finally, in the reaction of 5,10,15,20-tetraphenylporphyrin–dichlorotin(IV) (**9**) with halomethyl *para*-tolyl sulphone carbanion ($^{-}$CH(Cl)SO_2Tol; *t*-BuOK/DMSO, r.t.) we observed the formation of new product (TLC monitoring). One can suppose it was a VNS product, formed due to substitution of hydrogen at the β-position. Initially, we couldn't confirm its molecular formula directly by MS method; however, we found in the spectrum (ESI(+), in CH_3OH) an ion peak *m/z* = 927 originating from the product **10** (see Scheme 2 and Experimental). This ion is a result of ligand-exchange/ligand-losing process which is possible during the MS measurement. We supported this hypothesis when the sample of product was dissolved and measured in ethanol. The formation of the analogous ion *m/z* = 941 was observed. It seems these ions are rather strong evidence for the structure of the desired product because such an easy spontaneous conversion of dichlorotin porphyrin complexes into dialkoxy- and diphenoxy-tin moieties was reported earlier by Arnold.[11] Similar observations were made in our previous studies.[10]

Nevertheless, finally we also detected the molecular ion of the examined compound by MS-FD method (*m/z* = 966; $C_{52}H_{36}N_4O_2SCl_2Sn$). Independently, we confirmed its structure by ^{1}H NMR. All the diagnostic signals were found in the spectrum: 2.21 (s, 3H, CH_3–Tol), 4.62 (s, 2H, CH_2), 6.89/7.18 (2×d, 4 H, *J* = 8.2 Hz, H–Tol), and 9.05-9.24 (m, 7H$^{\beta}$).



Scheme 2

Decomplexation of the product obtained with lithium in ethylenediamine (reflux, 3 h)[12] leads to the free base porphyrin moiety substituted with CH_2SO_2Tol group at the β-position (**11**, *m/z* = 782, M^+, $C_{52}H_{38}N_4O_2S_1$); and this is one more proof for the structure **10**.

3. Conclusions

We reported herein the attempts of direct nucleophilic substitution of hydrogen in porphyrin systems, activated by the coordinated central metal atom (of increased electronegativity), when porphyrins are converted into the corresponding chelates. Complexes of Au(III) and Sn(IV), and their reactions with carbanions of weak nucleophilicity, were examined. These investigations were successfully finalized for *meso*-tetraphenylporphyrin–dichlorotin(IV) complex.

The above mentioned metal atom played a role of activating moiety, as well as a labile protective group

for the inner NH-protons, and after reaction can be easily removed from the system, if needed. We believe that our concept involving complexation/de-complexation procedure and new type of activation for nucleophilic attack will receive future attention in the area of porphyrin skeleton functionalizations. Further development of this idea *may also open a new chapter in nucleophilic substitution of hydrogen in aromatic and heteroaromatic compounds*.

Experimental

General. ^{1}H NMR spectra were recorded with a Varian MR-400 spectrometer operating at 400 MHz. Coupling constants *J* are expressed in hertz [Hz]. Mass spectra were measured with a GCT Premier (Waters, FD-TOF) spectrometer (FD method), MARINER (PerSeptive Biosystems, ESI-TOF) spectrometer (ESI method), and 4000-QTRAP (Applied Biosystems) spectrometer (ESI–turbo-spray and APPI–photospray methods); *m/z* intensity values for peaks are given as a % of relative intensity. UV-Vis spectra were measured with a Beckman DU-68, Metertech SP-8001, and UV-3600 Shimadzu spectrophotometers. TLC analysis was performed on aluminium foil plates pre-coated with silica gel (60 F-254, Merck AG). All the products were isolated by column chromatography (silica gel, 230-400 mesh; Merck AG); some compounds and fractions were isolated or rechromatographed on preparative TLC plates (silica gel, 60 F-254, 0.5 mm; Merck AG).

Molecular formulas of new compounds were confirmed by elemental analysis, HR-MS (ESI and FD), and by comparing the isotope molecular patterns (theoretical and experimental).

Porphyrinate **1** was obtained according to known procedure described in the previous literature[3] (modification: in AcOH/$CHCl_3$, 3:2). It was isolated by column chromatography (eluent: $CHCl_3$/MeOH, 1:1), yield, 76%; lit.,[3a] 70%.
Also octaethylporphyrin was obtained according to known procedure.[13] Octaethylporphyrin–dichloro-tin(IV) complex (**8**) was prepared therefrom according to modified procedure described in the literature for similar compounds[8,9] [Octaethylporphyrin (50 mg, 0.094 mmol) and $SnCl_2{\times}2H_2O$ (31 mg, 0.137 mmol) in sulfolane (4 mL) were heated (under argon) at 170°C in a round-bottomed light-shielded flask equipped with a reflux condenser over a period of 1.5 h. Then, the reaction mixture was cooled to room temperature and to this mixture $CHCl_3$ (30 mL) was added. The organic layer was washed with water (4×40 mL) and dried with anhydrous $MgSO_4$. After evaporating the solvent, the column chromatography was performed using gradient mixture as eluent (from $CHCl_3$ to $CHCl_3$/MeOH, 20:1) to give product **8**; yield – 46 mg (68%)].

Similarly, 5,10,15,20-tetraphenylporphyrin–dichloro-tin(IV) (**9**) was obtained (reaction temp. 200°C, 1 h); yield – 100%, lit.,[8] 85%.

***Data for substrates*:**

(5,10,15,20-Tetraphenylporphyrinato)gold(III) chloride (1): Its ^{1}H NMR and UV-Vis spectra were in agreement with those reported earlier in the literature.[3a] MS (APPI–photospray(+)); *m/z* (% rel. int.): 811 (16), 810 (56), 809 (100) [isotope M–Cl (*m*-TPPAu$^+$)]. MS (APPI–photospray(-)); *m/z* (% rel. int.): 343 (5), 341 (21), 339 (42), 337 (34) [isotope $(AuCl_4)^-$]; 271 (14), 269 (68), 267 (100) [isotope $(AuCl_2)^-$].

Dichloro(octaethylporphyrinato)tin(IV) (8): M.p. > 300°C. ^{1}H NMR ($CDCl_3$, 400 MHz); δ_H [ppm]: 10.48 (s, 4H, H-*meso*), 4.21 (q, *J* = 7.6 Hz, 16H, 8×CH_2), 2.04 (t, *J* = 7.6 Hz, 24H, 8×CH_3). UV-Vis ($CHCl_3$); λ_{max} [nm] (log ε): 575.5 (3.82), 538 (3.84), 408 (5.12; Soret band), 355 (4.03). MS (ESI(+), CH_3OH); *m/z* (% rel. int.): 685 (23), 684 (42), 683 (100), 682 (59), 681 (88), 680 (42), 679 (45) [isotope $OEPSn(OCH_3)^+$]; 671 (22), 670 (38), 669 (94), 668 (54), 667 (79), 666 (39), 665 (42) [isotope $OEPSn(OH)^+$]. MS (FD); *m/z* (% rel. int.): 1952 (2.6), 1951 (2.9), 1950 (3.4), 1949 (4.0), 1948 (4.9), 1947 (4.0), 1946 (4.7), 1945 (4.4), 1944 (2.5) [isotope $(OEPSn)_3^+$]; 1303 (6.7), 1302 (8.8), 1301 (7.1), 1300 (8.7), 1299 (11), 1298 (12), 1297 (10), 1296 (10) [isotope $(OEPSn)_2^+$]; 975.7 (3.7), 975.2 (4.5), 974.8 (6.7), 974.3 (5.6), 973.7 (4.8), 973.2 (4.8), 972.7 (6.4), 972.2 (5.5) [isotope $(OEPSn)_3^{2+}$]; 655 (9), 654 (18), 653 (29), 652 (67), 651 (54), 650 (100), 649 (62), 648 (73), 647 (32), 646 (37) [isotope $(M–2{\times}HCl)^{+\cdot}$]; 327.6 (1.2), 327.1 (1.6), 326.6 (2.7), 326.1 (6.0), 325.6 (4.8), 325.1 (10.4), 324.6 (5.9), 324.1 (6.4), 323.6 (2.2), 323.1 (3.4) [isotope $(M–2{\times}HCl)^{2+}$ and $(M–2{\times}Cl)^{2+}$]. The molecular formula was confirmed by comparing the theoretical and experimental isotope patterns for the $(M–2{\times}HCl)^+$ ion ($C_{36}H_{42}N_4Sn$); it was found to be identical within the experimental error limits.

Dichloro(5,10,15,20-tetraphenylporphyrinato)-tin(IV) (9); unstable, known compound.[8,11,14] Its ^{1}H NMR, UV-Vis, and MS spectra were in agreement with those described earlier.[8,14] The spectroscopic data are given below for more detailed and accurate characterization of the product. M.p. > 300°C. ^{1}H NMR ($CDCl_3$, 400 MHz); δ_H [ppm]: 9.14 (s) and 9.14 (d, $^4J_{Sn-H}$ = 10.4 Hz) [8H, H^β-pyrrole],[15] 8.36–8.32 (m, 8H, H-Ph), 7.86–7.79 (m, 12H, H-Ph). UV-Vis ($CHCl_3$); λ_{max} [nm] (log ε): 600.5 (3.99), 561 (4.21), 523 (3.46), 426 (5.35; Soret band). MS (FD); *m/z* (% rel. int.): 809 (4), 808 (8), 807 (10), 806 (24), 805 (20), 804 (46), 803 (43), 802 (86), 801 (44), 800 (54), 799 (21), 798 (20) [isotope $M^{+\cdot}$]; 773 (5), 772 (5), 771 (11), 770 (10), 769 (24), 768 (31), 767 (74), 766

(38), 765 (49), 764 (18), 763 (21) [isotope $(M–Cl)^+$]; 737 (8), 736 (15), 735 (7), 734 (19), 733 (40), 732 (100), 731 (57), 730 (78), 729 (40), 728 (38) [isotope $(M–2\times Cl)^{+\cdot}$]; 368.5 (1.0), 368 (2.1), 367.5 (2.1), 367 (4.2), 366.5 (7.5), 366 (15), 365.5 (10), 365 (12), 364.5 (7.4), 364 (7.8) [isotope $(M–2\times Cl)^{2+}$]. The molecular formula was confirmed by comparing the theoretical and experimental isotope patterns for the M^+ ion ($C_{44}H_{28}N_4SnCl_2$); it was found to be identical within the experimental error limits. *Other MS investigations*: MS (ESI, CH_3OH); *m/z* (% rel. int.): 769 (5), 768 (8), 767 (15), 766 (12), 765 (26), 764 (54), 763 (100), 762 (57), 761 (70), 760 (32), 759 (27) [isotope *m*-$TPPSn(OCH_3)^+$]. MS (ESI–turbo-spray, CH_3OH/CH_2Cl_2); *m/z* (% rel. int.): 769 (4), 768 (10), 767 (20), 766 (11), 765 (28), 764 (52), 763 (100), 762 (62), 761 (85), 760 (45), 759 (43) [isotope *m*-$TPPSn(OCH_3)^+$]. MS (ESI–turbo-spray, $(CH_3)_2CHOH/CH_2Cl_2$); *m/z* (% rel. int.): 797 (3), 796 (9), 795 (17), 794 (9), 793 (27), 792 (52), 791 (100), 790 (59), 789 (74), 788 (40), 787 (39) [isotope *m*-$TPPSn(OCH(CH_3)_2)^+$]. MS (APPI–photospray, AcOEt /CH_2Cl_2; after treatment of **9** with H_2O); *m/z* (% rel. int.): 796 (4), 795 (10), 794 (6), 793 (14), 792 (26), 791 (51), 790 (29), 789 (37), 788 (19), 787 (18) [isotope *m*-$TPPSn(OAc)^+$]; 770 (3), 769 (8), 768 (10), 767 (21), 766 (11), 765 (18), 764 (18), 763 (31) [isotope *m*-$TPPSnCl^+$, M–Cl]; 755 (3), 754 (8), 753 (19), 752 (9), 751 (26), 750 (50), 749 (100), 748 (57), 747 (71), 746 (37), 745 (40) [isotope $(M+H)^+$ of side product formed *via* partial spontaneous hydrolysis of **9** followed by dehydration; *m*-TPP(Sn=O)]. Elemental anal. calculated for $C_{44}H_{28}N_4SnCl_2\times 2H_2O$ (838.36): C, 63.04; H, 3.85; N, 6.68. Found: C, 63.36; H, 4.40; N, 5.96.

Reaction of 1 with carbanion of $ClCH_2SO_2Tol$ in *t*-BuOK/THF system

Procedure A: In a round-bottomed flask *t*-BuOK (50 mg, 0.45 mmol) was stirred in anhydrous THF (7 mL; under argon) at room temperature for *ca* 5 min. To this solution a mixture of porphyrin–gold(III) chloride (**1**; 50 mg, 0.059 mmol) and chloromethyl *para*-tolyl sulphone (98 mg, 0.479 mmol) in THF (5 mL) was added dropwise *via* syringe. After 30 min of stirring, the mixture was poured into 3% HCl containing ice (10 mL) and extracted with $CHCl_3$ (3×15 mL). The combined organic layers were washed with water (3×50 mL) and dried with anhydrous $MgSO_4$. Several products were observed (TLC monitoring). After evaporation of the solvent, the column chromatography was performed using gradient mixture as eluent (from $CHCl_3$ to $CHCl_3$/MeOH, 20:1). None of the defined products were isolated.

Procedure B: In a round-bottomed flask chloromethyl *para*-tolyl sulphone (87 mg, 0.425 mmol) was stirred in anhydrous THF (3 mL; under argon) at room temperature for *ca* 2 min. To this solution *t*-BuOK (50 mg, 0.45 mmol) in THF (3 mL) was added and the stirring was continued for the next 5 min. Then, porphyrin–gold(III) chloride (**1**; 45 mg, 0.053 mmol) in THF (5 mL) was added dropwise *via* syringe. After additional 30 min of stirring, the reaction mixture was concentrated *in vacuo* to 1/3 of the initial volume, 20 mL of $CHCl_3$ was added, and washed with water (3×30 mL). The aqueous layers were extracted with $CHCl_3$ (3×30 mL) and all the combined organic layers were dried with anhydrous $MgSO_4$. After evaporating the solvent, the residue was recrystallized from $CHCl_3$ and various CCl_4/CH_2Cl_2 mixtures. Neither the VNS product nor the addition of carbanion product, or moiety with exchanged Cl ligand for carbon ligand, has been isolated. Always, the mixture of several products was crystallized.

Reaction of [5,10,15,20-tetraphenylporphyrinato]-gold(III) chloride (1) with tetraethylammonium cyanide ($Et_4N^+CN^–$)

Porphyrinate **1** (50 mg, 0.059 mmol) and $Et_4N^+CN^–$ (98 mg, 0.627 mmol) were dissolved in $CHCl_3$ (60 mL) and stirred at room temperature for *ca* 1 min. Then, the reaction mixture was washed with water (5×70 mL) and the organic layer was dried with anhydrous $MgSO_4$. After evaporating the solvent, the residue was purified by column chromatography (eluent: $CHCl_3$) to give 39.5 mg of phlorin **3** (80%).
M.p. > 300°C. ^1H NMR ($CDCl_3$, 400 MHz); δ_H [ppm]: 7.94–7.85 (m, 3H, H-Ph), 7.61 (d, J = 4.1 Hz, 2H, H^β-pyrrole), 7.60–7.44 (m, 12H, H-Ph), 7.39 (d, J = 4.1 Hz, 2H, H^β-pyrrole), 7.30 (d, J = 5.2 Hz, 2H, H^β-pyrrole), 7.13 (d, J = 5.2 Hz, 2H, H^β-pyrrole), 7.05–6.96 (m, 3H, $H_{m,p}$ of H-Ph), 6.57 (apparent d, J = 8.0 Hz, 2H, H_o of H-Ph). UV-Vis ($CHCl_3$); λ_{max} [nm] (log ε): 742.5 (3.99), 521 (4.00), 436 (4.50), 409 (5.20; Soret band), 304 (4.32). MS (FD); *m/z* (% rel. int.): 837 (11), 836 (47), 835 (82) [isotope M^+]; 811 (11), 810 (46), 809 (100) [isotope $(M–CN)^+$]. MS (APPI–photospray, AcOEt/CH_2Cl_2); *m/z* (% rel. int.): 838 (8), 837 (29), 836 (59) [isotope $(M+H)^+$]; 811 (18), 810 (60), 809 (100) [isotope $(M–CN)^+$]. HR-MS (FD): calculated for $C_{45}H_{28}N_5Au$ (M^+) – 835.2010, found – 835.1997.

Attempts of complexation of octaethylporphyrin with gold(III) cation

Procedure A: In a round-bottomed flask, equipped with a reflux condenser, $KAuCl_4$ (35 mg, 0.093 mmol) and AcONa (46 mg, 0.56 mmol) were heated to reflux (under argon) in acetic acid (6 mL) for *ca* 15 min. Then, octaethylporphyrin (40 mg, 0.075 mmol) in $CHCl_3$ (10 mL) was added and the reaction was continued at reflux for the next 19 h. To this mixture (cooled to room temperature), $CHCl_3$ (10 mL) was added and it was washed with water (3×30 mL). The organic layer was dried with anhydrous $MgSO_4$. After evaporating the solvent, the residue was

subjected to column chromatography (eluent: $CHCl_3$/*n*-hexane, 2:1); 3.4 mg of product **5** was isolated (7.7%), along with the recovery of 5.4 mg of octaethylporphyrin (13.5%).

Procedure B: In a round-bottomed flask, equipped with a reflux condenser, $KAuCl_4$ (37 mg, 0.098 mmol) and AcONa (46 mg, 0.56 mmol) were preheated to reflux (under argon) in DMF (4 mL) for *ca* 20 min. Then, octaethylporphyrin (40 mg, 0.075 mmol) dissolved in DMF-$CHCl_3$ mixture (24 mL; 1:2) was added and the reaction was continued at 130°C for the next 13 h. To this mixture (cooled to room temperature), $CHCl_3$ (40 mL) was added and it was washed with water (3×40 mL). Isolation of the product – as in *Procedure A* (eluent for chromatography – $CHCl_3$/*n*-hexane, 2:1; then $CHCl_3$): recovery of octaethylporphyrin, 25 mg (63%); product **6**, 3.3 mg (7.8%).

Procedure C: As in *Procedure A*. Reagents: $KAuCl_4$ (40 mg, 0.106 mmol) and AcONa (46 mg, 0.56 mmol) in $CHCl_3$/MeOH (4 mL; 1:1) were heated to reflux for *ca* 5 min; octaethylporphyrin (40 mg, 0.075 mmol) dissolved in $CHCl_3$/MeOH (16 mL; 3:1); reaction time – 20 h (at 60°C). Recovery of octaethylporphyrin, 25.6 mg (64%); product **6**, 3.9 mg (9.1%); product **5**, 4.0 mg (9.0%).

When the reaction was carried out according to *Procedure A* and the time was shortened to 3 h (heating at reflux) a mixture of products **4** and **7** was isolated (by preparative TLC, eluent: $CHCl_3$, five times developed); yield below 5%.

5: M.p. > 300°C. ^{1}H NMR ($CDCl_3$, 400 MHz); δ_H [ppm]: 10.65 (s, 1H, H-*meso*), 10.12 (s, 2H, H-*meso*), 4.20–4.05 (m, 16H, 8×CH_2), 2.31 (s, $OCOCH_3$), 1.96–1.90 (m, 24H, 8×CH_3), -3.70 (broad s, 2H, 2×NH). UV-Vis spectrum was not recorded because this compound still was contaminated with small amounts of other by-products. MS (ESI); *m/z* (% rel. int.): 595 (11), 594 (43), 593 (100) [isotope $(M+H)^+$]. MS (ESI): calculated for $C_{38}H_{49}N_4O_2$ [$(M+H)^+$] – 593.39, found – 593.40. The molecular formula was also confirmed by comparing the theoretical and experimental isotope patterns for the $(M+H)^+$ ion ($C_{38}H_{49}N_4O_2$); it was found to be identical within the experimental error limits.

6: M.p. > 300°C. ^{1}H NMR ($CDCl_3$, 400 MHz); δ_H [ppm]: 10.09 (s, 2H, H-*meso*), 9.88 (s, 1H, H-*meso*), 4.22 (q, *J* = 7.5 Hz, 4H, 2×CH_2), 4.14–3.99 (m, 8 lines, 12H, 6×CH_2), 1.94–1.83 (m, 6 lines, 24H, 8×CH_3). UV-Vis ($CHCl_3$); λ_{max} [nm] (log ε): 630 (3.00), 577 (3.64), 541.5 (3.63), 507 (4.07), 408.5 (5.15; Soret band). MS (ESI); *m/z* (% rel. int.): 1143 (0.7), 1142 (1.6), 1141 (3.3), 1140 (5.1), 1139 (7.8), 1138 (7.4), 1137 (8.2) [isotope $(2×M+H)^+$]; 573 (4), 572 (15), 571 (39), 570 (44), 569 (100) [isotope $(M+H)^+$]. HR-MS (ESI): calculated for $C_{36}H_{46}N_4Cl$ [$(M+H)^+$] – 569.3411, found – 569.3423. The molecular formula was also confirmed by comparing the theoretical and experimental isotope patterns for the $(M+H)^+$ ion ($C_{36}H_{46}N_4Cl$); it was found to be identical within the experimental error limits.

Mixture of compounds 4 and 7; their structures were proposed on the basis of MS spectrum: MS (ESI, CH_3OH/CH_2Cl_2); *m/z* (% rel. int.): 766 (5), 765 (11), 764 (13), 763 (28) [compound **7**; isotope $(M(\mathbf{7})–Cl)^+$]; 731 (10), 730 (46), 729 (100) [compound **4**; isotope $(M(\mathbf{4})–Cl)^+$]. HR-MS (ESI): compound **7**, calculated for $C_{36}H_{43}N_4ClAu$ [$(M(\mathbf{7})–Cl)^+$] – 763.2842, found – 763.2869; compound **4**, calculated for $C_{36}H_{44}N_4Au$ [$(M(\mathbf{4})–Cl)^+$] – 729.3232, found – 729.3239.

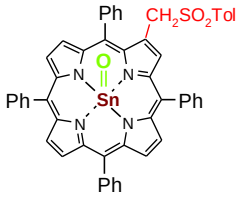
Substitution of hydrogen in porphyrin systems with carbanions of halomethyl *para*-tolyl sulphones (XCH_2SO_2Tol)

In a round-bottomed light-shielded flask *t*-BuOK (88 mg, 0.78 mmol, for **8**; 41 mg, 0.37 mmol, for **9**) was stirred under argon in anhydrous THF (16 mL, for **8**) or in DMSO (3.5 mL, for **9**) at room temperature. To this solution, a mixture of porphyrinate (**8**: 57 mg, 0.079 mmol; **9**: 41.1 mg, 0.051 mmol) and $BrCH_2SO_2Tol$ (44 mg, 0.177 mmol; for **8**) or $ClCH_2SO_2Tol$ (22.5 mg, 0.110 mmol; for **9**) in THF (12 mL; for **8**) or in DMSO (2.0 mL; for **9**) was added dropwise *via* syringe (septum) over a period of *ca* 5 min. After 0.5–1.5 h of intensive stirring (TLC monitoring; $CHCl_3$/MeOH, 15:1), the mixture was poured into 3% HCl containing ice (50 mL) and extracted with $CHCl_3$ (5×25 mL). The combined organic layers were washed with water (4×40 mL) and dried with anhydrous $MgSO_4$. After evaporating the solvent, the residue was analyzed by TLC and MS. In the mixture obtained from **8** none of the defined products were observed and ions originating from the substrate were identified only in MS spectrum [APPI–photospray(+) in AcOEt; *m/z* (% rel. int.): 715 (3.3), 714 (2.4), 713 (4.1), 712 (5.0), 711 (12), 710 (6.5), 709 (8.9), 708 (4.1), 707 (4.5) [isotope $OEPSn(OAc)^+$]; 693 (6.7), 692 (7.3), 691 (18), 690 (14), 689 (45), 688 (46), 687 (100), 686 (52), 685 (72), 684 (30), 683 (33) [isotope $OEPSnCl^+$]].

The crude mixture obtained from **9** was subjected to column chromatography using gradient mixture as eluent ($CHCl_3$/*n*-hexane, 2:1; $CHCl_3$; then $CHCl_3$/MeOH, from 20:1 to 5:1); 13 mg of the substrate was recovered (32%); then, 21.5 mg of product **10** was isolated (43.5%).

M.p. > 300°C. ^{1}H NMR ($CDCl_3$, 400 MHz); δ_H [ppm]: 9.24–9.05 (m, 7H, H^β-pyrrole), 8.40–8.15 (m, 8H, H-Ph), 7.90–7.70 (m, 12H, H-Ph), 7.18 (d, *J* = 8.2 Hz, 2H of H-Tol), 6.89 (d, *J* = 8.2 Hz, 2H of H-Tol), 4.62 (s, 2H, CH_2), 2.21 (s, 3H, CH_3). UV-Vis spectrum was not recorded because this compound was contaminated with small amounts of side

products formed *via* spontaneous hydrolysis and subsequent dehydration; see MS investigations below. MS (FD); *m/z* (% rel. int.): 976 (10), 975 (9), 974 (11), 973 (10), 972 (12), 971 (17), 970 (22), 969 (18), 968 (9), 967 (8), 966 (11) [isotope M^+]; 939 (7), 938 (9), 937 (11), 936 (15), 935 (22), 934 (10), 933 (12), 932 (18), 931 (16) [isotope $(M–Cl)^+$]; 838 (18), 837 (30), 836 (32), 835 (80), 834 (100), 833 (49), 832 (80), 931 (42), 830 (57) [isotope $(M–2×HCl–SO_2)^+$]; 781 (15), 780 (25), 779 (41), 778 (74), 777 (28), 776 (48) [isotope $(M–Cl–SO_2Tol)^+$]; 749 (20), 748 (35), 747 (31), 746 (41), 745 (43), 744 (95), 743 (60), 742 (52), 741 (30), 740 (48) [isotope $(M–Cl–HCl–SO_2Tol)^+$]. *Other MS investigations*: MS (ESI, CH_3OH); *m/z* (% rel. int.): 937 (11), 936 (15), 935 (22), 934 (20), 933 (39), 932 (63), 931 (100), 930 (57), 929 (63), 928 (32), 927 (22) [isotope $(M–2×Cl+OCH_3)^+$; $C_{53}H_{39}N_4O_3SSn$]. The molecular formula was confirmed by comparing the theoretical and experimental isotope patterns for the $(M–2×Cl+OCH_3)^+$ ion ($C_{53}H_{39}N_4O_3SSn$); it was found to be identical within the experimental error limits. MS (ESI, C_2H_5OH); *m/z* (% rel. int.): 951 (12), 950 (17), 949 (23), 948 (24), 947 (42), 946 (66), 945 (100), 944 (61), 943 (69), 942 (36), 941 (30) [isotope $(M–2×Cl+OC_2H_5)^+$; $C_{54}H_{41}N_4O_3SSn$]. MS (ESI–turbo-spray, $CH_3CN/CHCl_3$; when left for a longer period of time, compound **12** was formed *via* spontaneous hydrolysis and subsequent dehydration); *m/z* (% rel. int.): 923 (6), 922 (11), 921 (21), 920 (14), 919 (36), 918 (56), 917 (100), 916 (87), 915 (99), 914 (49), 913 (43) [isotope $(M+H)^+$ of **12**; $(TPP(SnO)CH_2SO_2Tol+H)^+$]. The molecular formula was confirmed by comparing the theoretical and experimental isotope patterns for the $(M+H)^+$ ion ($C_{52}H_{37}N_4O_3SSn$); it was found to be identical within the experimental error limits.



12

m/z = 913; $(M+H)^+$

Decomplexation of VNS product 10

A crude sample of product **10** (6.4 mg) in ethylenediamine (4 mL) was preheated to reflux (under argon) in a round-bottomed flask equipped with a reflux condenser. After 1 h, 34 mg of lithium was added (as thin wires) and the reaction was continued at reflux for the next 3 h. Then, the post-reaction mixture was poured into water (30 mL) and extracted with $CHCl_3$ (3×20 mL). The combined organic layers were washed with water (3×30 mL) and dried with anhydrous $MgSO_4$. After evaporation of the solvent, the residue was analyzed by MS method. The molecular ion originating from the desired product **11** was observed. MS (APPI–photospray(+), $AcOEt/CH_2Cl_2$); *m/z* (% rel. int.), among other ions: 787 (2.3), 786 (2.0), 785 (4.2), 784 (3.9), 783 (7.4), 782 (6.0) [isotope M^+ and $(M+H)^+$ of **11**; $C_{52}H_{38}N_4O_2S$].

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