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ON SELECTIVE FUNCTIONALIZATION OF *meso*-TETRAPHENYLPORPHYRIN DERIVATIVES BY VICARIOUS NUCLEOPHILIC SUBSTITUTION OF HYDROGEN

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Abstract - The studies on selective derivatization of meso*-tetraphenylporphyrin (TPP) using nitration and Vicarious Nucleophilic Substitution of Hydrogen (VNS) are reported. TPP, its metal complexes and N,N-dimethyl substituted derivatives do not enter the VNS reaction. On the other hand,* meso*-substituted TPP results in the mono-nitration of one phenyl ring and the intermediate obtained, after simple transformation to its metal complex, reacts with carbanions bearing leaving groups at the carbanionic center, according to VNS scheme. This gives new opportunities for the peripheral functionalization of porphyrins. In this work the copper and zinc complexes were investigated.*

Introduction

Some porphyrin derivatives are used as photosensitizers in Photodynamic Theraphy (PDT).[1] PDT is a treatment modality using photosensitising drugs and light to kill neoplastic cells.[1b] This simple technique is currently evaluated in multiple clinical trials with promising results.[2] The clinical use of PDT requires the presence of a photosensitizing agent, oxygen, and light of a specific wavelenght, which matches the absorption characteristic of the photosensitizer. Then, the photosensitizer is activated by an appropriate wavelenght of light, and the energy is transferred through inter system crossing (ISC) to molecular oxygen. This forms a toxic, short-lived species (singlet oxygen, $^1O_2$), which is thought to mediate cellular death.[1b]

Unsymmetrical, functionalized porphyrins have been also covalently incorporated into polymer backbones[3] and are known to serve as a useful synthetic precursors to monooxygenase and allosteric enzyme model systems.[4,5] In oncology, the development of PDT has a potential to become an integral part

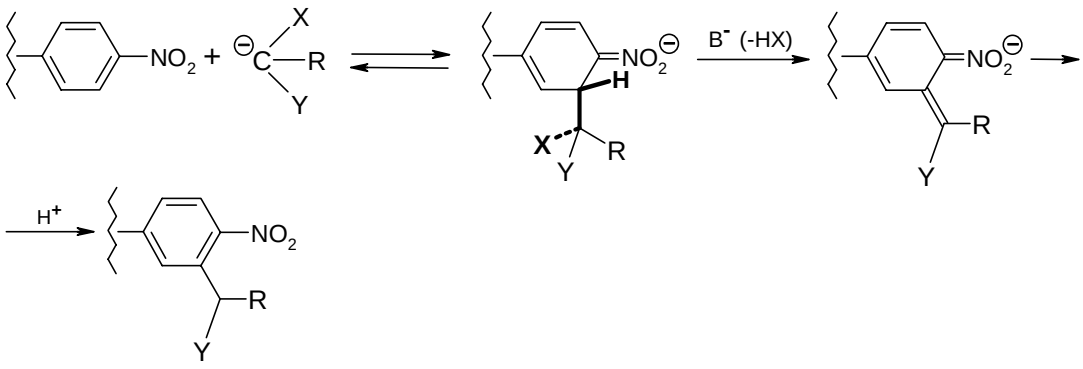
of cancer treatment in the future. This is relatively new technique, and is based on the administration of tumor-localizing photosensitizers and their subsequent activation by visible light to destroy cancer cells. However, their mode of action is still not clear. It has been known that human serum albumin (HSA) binding affinity to various photosensitizers plays an important role in their biodistribution within the tumor stroma,[6] and the distribution of porphyrins among serum proteins is dependent upon their chemical structure.[7]

In light of this knowledge, the preparation of newer photosensitizers which would allow greater depth of tissue penetration, is of particular interest. In spite of numerous studies in this field, new methods for synthesis and derivatization of hydrophilic, lipophilic and amphiphilic porphyrins, especially unsymmetrical ones, are continuously sought.

Results and Discussion

Herein, we present our studies on selective derivatization of porphyrins using Vicarious Nucleophilic Substitution of Hydrogen (VNS).[8] This reaction involves addition of a carbanion, bearing a leaving group X at the carbanionic center, to a nitroarene (or other electrophilic aromatic or heteroaromatic compound) followed by base induced β-elimination of HX, and protonation as a final step. This leads to the substitution of hydrogen product (Scheme 1).

Scheme 1



As model compounds to investigate the possibility of VNS in porphyrin systems easily available *meso*-tetraphenylporphyrin (TPP, **1**)[9] and its derivatives (**2-6**) were selected (Figure 1). However, it is well known that the VNS reaction proceeds smoothly and with high yield in electrophilic aromatic compounds where free OH or NH-acidic groups are ”blocked” (*e.g.* with Me, CH_2Ph, tetrahydropyranyl, etc.[10,11]). Unsuccessful results of VNS attempts in **1** and **3** with carbanion of chloromethyl *para*-tolylsulphone $ClCH_2SO_2Tol$ (the standard nucleophile for this reaction) supports this hypothesis.

Afterwards, it was found that the *meso*-tetraphenylporphyrin (the compound without any additional activating substituents, *e.g.* NO_2) is not active enough to enter the above reaction. This was confirmed by the use of the TPP derivative (**4**) in which the free NH-positions were protected with methyl groups.

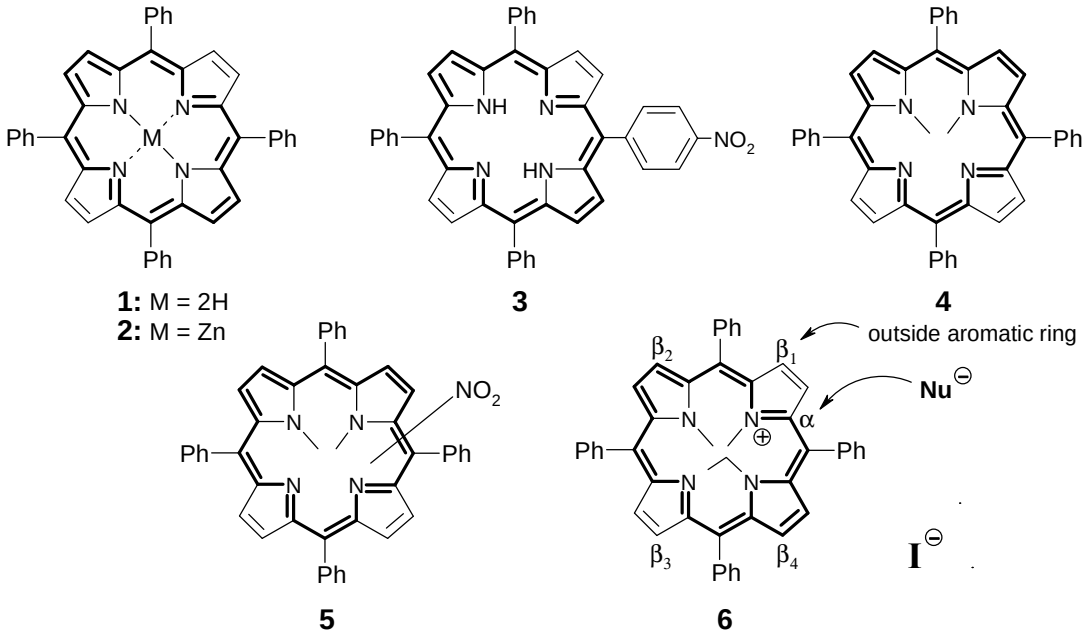


Figure 1

In this case, in the reaction of **4** with the carbanion of $ClCH_2SO_2Tol$ we did not isolate any product. However, we can postulate the formation of small amounts of the expected VNS compound as in ^1H NMR spectrum of the post-reaction mixture a diagnostic signal of AB spectral system at δ = 5.21 ppm was observed (J ~ 10 Hz). This could be originating from the methylene group of CH_2SO_2Tol substituent attached to pyrrole(s) in TPP (Figure 2).

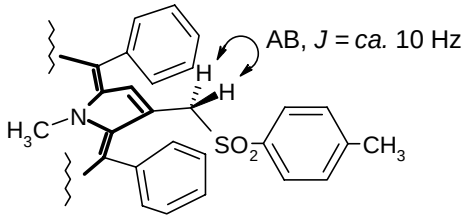


Figure 2

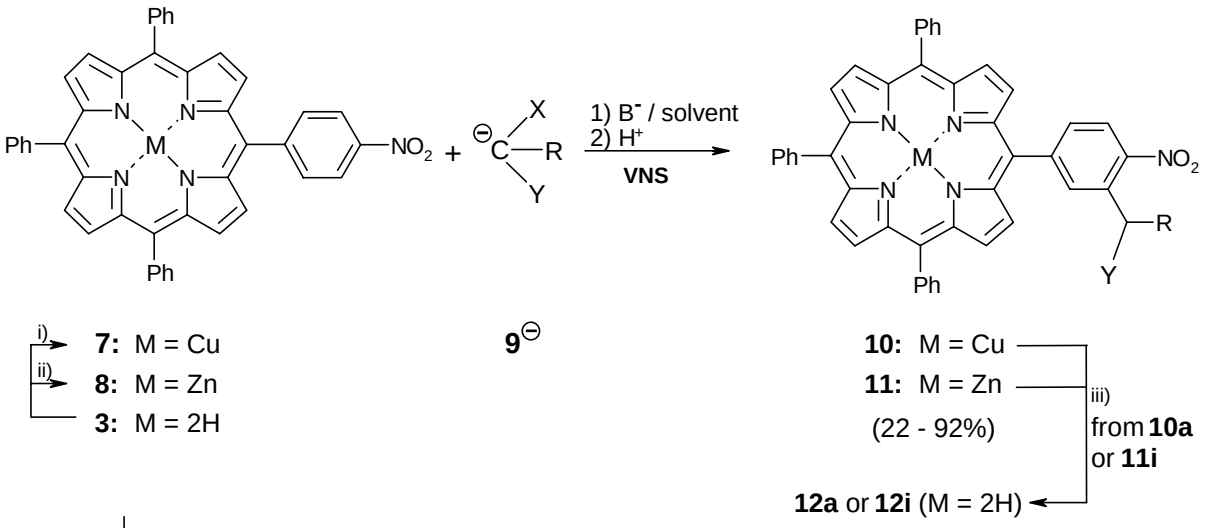
Next, the *N*,*N*-dimethyl derivative (**4**) was converted into the *N*,*N*,*N*-trialkyl porphyrinium salt (**6**).[12] This compound, being of higher electrophilicity than **4**, should react with nucleophiles smoothly. In this case, the possible addition of carbanion to porphyrin could take place at one of electronically equivalent activated positions: α, β_1, β_2, β_3 or β_4 (Figure 1). All β-positions bearing hydrogen could enter VNS. However, β_1 and β_3 are outside the aromatic system and the carbanion did not react in these vinylic-like positions. It could react in conjugated positions β_2 and β_4, which are in the aromatic framework; but they are far away from the activating, positively charged, quarternary nitrogen atom. Additionally, they are also strongly deactivated by *N*-alkyl fragments. Due to above reasons they are less active for nucleophilic addition than position α-. No doubt, the addition is concidered to take place at position α- of pyrrole ring, destroying

[18π] electron system of porphyrin aromaticity, and due to lack of hydrogen in this position the VNS reaction was not observed. Finally, the degradation (ring opening) of the macrocyclic moiety, under the reaction conditions, occurred, and no defined products were isolated. Nevertheless, it is worth mentioning that the *N*-alkyl substitution is not convenient protection for our purpose as the *N*-alkyl groups are not labile ones and it is rather difficult to remove them, sometimes almost impossible.

Hence, in all investigated instances of the compounds (**1**, **2**, **3**, **4**, and **6**), the VNS reaction was not occurred. We tried to check another model compound (of type **5**) having protected NH-centers and NO_2 electron-withdrawing activating group in phenyl ring or in β-position of pyrrole unit. Unfortunately, the nitration of dimethyl compound (**4**) proved somewhat troublesome, and, due to selectivity problem, we could not prepare the single defined nitro derivative from **4**.

On the other hand, the nitration of *meso*-tetraphenylporphyrin (**1**) results in the mononitration in position *para*- of one phenyl ring[13] and in this case the transformation of the two NH-centers in the macrocyclic ring into the metal complex, where the central metal cation is playing the role of a convenient protective group for VNS reaction, allows the direct substitution of hydrogen. Thus, the intermediate (**3**), after subsequent transformation to its copper complex, readily enters the VNS with good yield. This approach was exemplified by preparation of a few porphyrin derivatives and it was described in the previous communication.[14] We found that the metallation[15] offers very labile protection of NH functions and can be easily removed after reaction, if needed.[16]

Scheme 2



9 - 12	a	b	c	d	e	f	g	h	i	j
X	Cl	Cl	OC_6H_4Cl-*p*	STol	SO_2Tol	Cl	Cl	F	Cl	Cl
Y	SO_2Tol	SO_2Tol	CN	CN	SPh	SO_2Ph	SO_2Ph	SO_2Ph	SO_2NMe_2	SO_2Bu-*t*
R	H	Me	H	H	H	Ph	H	H	H	H

i) $Cu(OAc)_2xH_2O$, $CHCl_3$/MeOH, reflux, *ca.* 10 h, 92%;

ii) $Zn(OAc)_2x2H_2O$, $CHCl_3$/MeOH, reflux, 4 h, quantitatively;

iii) CF_3CO_2H, H_2SO_4, rt, 3 h[16]

Table 1. Products and the yields.

Entry	**CH-acid & Product**	Method [a]	Yield [b] [%]
1	**9a**, **10a**	A	58[c]
2	**9a**, **11a**	A	88
3	**9a**, **11a**	B	71
4	**9b**, **11b**	C	13 (60)
5	**9c**, **11c**	A	66[c]
6	**9c**, **11c**	B	31 (86)
7	**9d**, **11c**	A	-
8	**9d**, **11c**	D	29 (57)
9	**9c**, **10c**	A	50[c]
10	**9e**, **11e**	D	-
11	**9e**, **13**	A	traces
12	**9f**, -	A	-
13	**9g**, **11g**	A	79
14	**9h**, **11g**	B	< 5
15	**9h**, **11g**	A	22 (66)
16	**9i**, **11i**[d]	A	92
17	**9j**, **11j**	A	76

[a] see Experimental: **A** – *t*-BuOK / DMSO, rt; **B** – NaOH / DMSO, rt; **C** – *t*-BuOK / DMF, -40°C; **D** - *t*-BuOK/NH_3 (liq.), [b] (in brackets) yields given for consumed porphyrins, [c] see ref. [14], [d] the crude product **11i** was directly demetallated[16] and characterirized as **12i**, the yield is given for 2 steps.

The use of Cu complex, due to paramagnetic effect of the copper cation involved, caused difficulty in following the reaction sequence by NMR technique. However, we synthesized and characterized (by MS and UV-VIS methods) two compounds of this type (**10a**, **10c**, Table 1). In the case of **10a** full characterization could be finaly given for the demetallated product (**12a**). Most of the examples demonstrating the possibility of VNS reaction were performed with the use of a zinc complex - easy obtainable from the corresponding 5-(4-nitrophenyl)-10,15,20-triphenylporphyrin (**3**) with almost quantitative yield.

Thus, nitro-porphyrin complexes (**7**,**8**) react in the presence of *t*-BuOK with carbanions, bearing leaving groups at the carbanionic center ($\mathbf{9}^-$), in DMSO, DMF or in liquid ammonia, giving in most cases, good yields of the desired products. The substitution takes place selectively in the phenyl ring in the *ortho*-position to NO_2. The use of heterogeneous system, namely powdered NaOH in DMSO at room temperature (Entry 3, Table 1), also gave a satisfactory yield (71%). In the case of poor leaving groups, such as **X** = OAr or F, the conversion in the NaOH/DMSO system was moderate or low (Entries 6,14). For the carbanion bearing poor leaving group **X** = SAr ($\mathbf{9d}^-$), a similar yield of the desired product was obtained (this was only observed in the *t*-BuOK / liquid ammonia reaction system; Entry 8).

By this method we synthesized a series of new TPP derivatives, substituted with α-functionalized alkyl groups, *e.g.* arylsulphonylmethyl- (**10a**, **11a,g**), cyanomethyl- (**10c, 11c**), *N,N*-dimethyl-sulphonamide (**11i**), etc. Some of the products give opportunities for further transformations and can be easily converted into other derivatives, *e.g.* **11c** to carboxylic acid and its esters.

Reactions with tertiary carbanions were unsuccessful due to steric hindrances. Bulky carbanions of low nucleophilicity, *e.g.* generated from α-phenyl-(chloromethyl)phenylsulphone (**9f**), did not give any product. Better results were obtained for α-chloroethyl *para*-tolylsulphone (**9b**), under the conditions described earlier in the literature for unstable at higher temperature tertiary carbanions (*t*-BuOK/DMF, -40°C[17]). However, in this case most of the starting material was recovered and the product (**11b**) was isolated in 50% yield, calculated for consumed starting porphyrin (**8**).

In the reaction with phenylthiomethyl *para*-tolylsulphone (**9e**) we could not isolate any product. When the crude post-reaction mixture was examined by Liquid Secondary Ions Mass Spectrometry [LSIMS (+)], the molecular ion of the product of oxidative substitution of hydrogen (**13**) was identified (*m/z* = 998; M+H, 2.5%). In this case the initial addition of the carbanion to porphyrin (**8**) occurred; but SPh and SO_2Tol are poor leaving groups[18] and one could expect the difficulties in the elimination step. Finally, the formation of small amounts of **13** was observed.

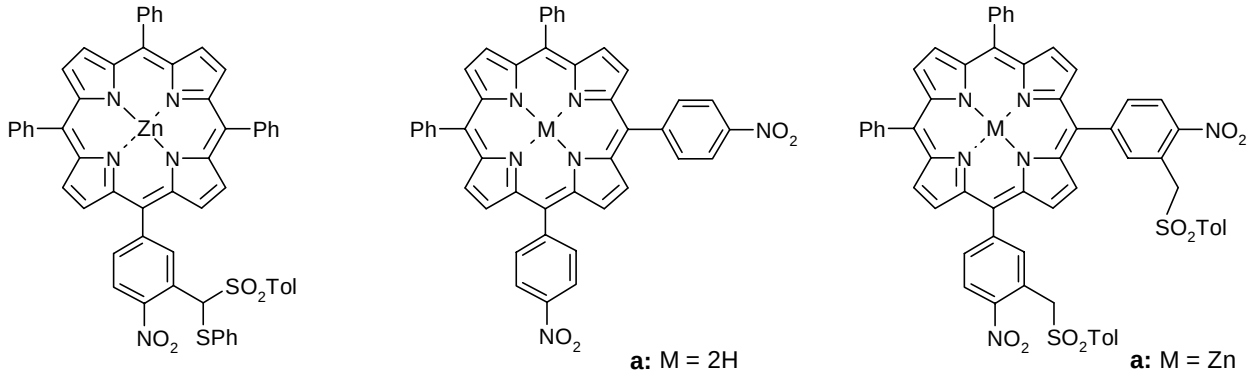


Figure 3

The VNS reaction in [5,10-bis(4-nitrophenyl)-15,20-diphenylporphyrinato]zinc(II) (**14b**) allows the introduction of two α-functionalized substituents in two different phenyl rings. However, the zinc complex (**14b**) and the compound (**15a**) are relatively unstable; hence, in the applied reaction conditions, the product (**15a**) underwent partial decomposition to **15b**. This was investigated by UV-VIS and MS method.

Conclusions

The ability to access new types of porphyrin derivatives is of great importance due to biological activity of these systems. In this paper we applied an useful nucleophilic methodology for their peripheral functionalization. The VNS can be a new tool in this field for direct substitution of hydrogen in nitro-substituted derivatives. It was also shown that the central metal cation in porphyrin complexes can play a role as a labile and convenient protective group for the VNS process, and it can be easily removed after reaction, if needed. Some of the compounds synthesized (**10a**; **11a,b,g,j**; **12a**) could have potential bioactive properties (earlier, several sulphonyl TPP derivatives reavealed anti-cancer activity[19]).

EXPERIMENTAL

^{1}H NMR spectra were recorded with a Varian GEMINI-200 and Varian 360 spectrometers operating at 200 MHz and 360 MHz, correspondingly. Coupling constants *J* are expressed in hertz. MS spectra were measured with a Shimadzu GC MS-QD 5050A mass spectrometer using a direct insertion probe and an AMD 604 (AMD Intectra GmbH, Germany) spectrometer (electron impact method); *m/z* intensity values for peaks are given as a % of relative intensity. UV-VIS spectra were measured with Perkin Elmer UV spectrophotometer Lambda 20. TLC analysis was performed on aluminium foil plates precoated with silica gel (60F 254, Merck AG). Silica gel, 200-300 mesh (Merck AG), was used for column chromatography.

N_a,N_b-Dimethyl-*meso*-tetraphenylporphyrin (**4**) and N_c-ethyl-N_a,N_b-dimethyl-*meso*-tetraphenylporphyrin iodide (**6**) were prepared from TPP by the method described earlier in the literature.[12] 5-(4-Nitrophenyl)-10,15,20-triphenylporphyrin (**3**) was obtained by nitration of TPP with HNO_3 (d = 1.5, Aldrich) according to the known procedure[13] with 66% yield. 5,10-Bis(4-nitrophenyl)-15,20-diphenylporphyrin (**14a**) was obtained as a by-product in the above nitration of TPP;[13] 4% yield.

[5-(4-Nitrophenyl)-10,15,20-triphenylporphyrinato]copper(II) (7): - 5-(4-Nitrophenyl)-10,15,20-triphenylporphyrin (**3**; 24 mg, 0.036 mmol) and $Cu(OAc)_2$ x H_2O (100 mg, 0.5 mmol) in $CHCl_3$ (10 mL) and MeOH (1 mL) were refluxed for 2 h. After cooling, the reaction mixture was concentrated to dryness and the residue was chromatographed ($CHCl_3$ / n-hexane - 1:1) to give the desired product (24 mg, 92%). - mp >300°C. - UV-VIS (CH_2Cl_2), λ_{max} (log ε): 578 (3.74), 539 (4.05), 485 (3.75), 415 (5.11, Soret), 357 (3.83), 308 nm (3.97). - MS (EI), *m/z* (% rel. int.): 722 (41) and 720 (100) [isotopic $M^{+\cdot}$]; HR-MS calcd for $C_{44}H_{27}N_5O_2Cu$ - 720.1461, found - 720.1460.

[5-(4-Nitrophenyl)-10,15,20-triphenylporphyrinato]zinc(II) (8): - 5-(4-Nitrophenyl)-10,15,20-triphenylporphyrin (**3**; 320 mg, 0.485 mmol) and $Zn(OAc)_2$ x $2H_2O$ (888 mg, 4.0 mmol) in $CHCl_3$ (90 mL) and MeOH (10 mL) were refluxed for 4 h. After cooling the reaction mixture was concentrated to dryness and the residue was chromatographed (at the beginning with $CHCl_3$ / n-hexane - 1:1, then with $CHCl_3$) to give the desired product (350 mg, quantitatively). - mp >300°C. - ^{1}H NMR ($CDCl_3$, 200 MHz): 8.99 (d, *J* = 4.7 Hz, 2H, H^β-pyrrole), 8.96 (s, 4H, H^β-pyrrole), 8.84 (d, *J* = 4.7 Hz, 2H, H^β-pyrrole), 8.63 and 8.40 (AA'XX', 4H, H-Ar(NO_2)), 8.25-8.17 (m, 6H, H-Ph), 7.81-7.70 (m, 9H, H-Ph). - UV-VIS (CH_2Cl_2), λ_{max} (log ε): 589 (3.73), 548 (4.24), 513 (3.66), 419 (5.31, Soret), 348 nm (4.01). - MS (EI), *m/z* (% rel. int.): 725 (28), 723 (40), 721 (56) [isotopic $M^{+\cdot}$], 675 (7), 661 (14), 660 (51), 659 (100), 613 (9), 598 (7), 361 (7), 330 (12), 300 (6), 298 (7); HR-MS calcd for $C_{44}H_{27}N_5O_2Zn$ - 721.1456, found - 721.1462.

[5,10-Bis(4-nitrophenyl)-15,20-diphenylporphyrinato]zinc(II) (14b): - This compound was obtained from 5,10-bis(4-nitrophenyl)-15,20-diphenylporphyrin (**14a**; 14 mg, 0.020 mmol) and $Zn(OAc)_2$ x

$2H_2O$ (56 mg, 0.25 mmol) according to the above procedure. After 4 h of reflux, additional 20 mg of $Zn(OAc)_2$ x $2H_2O$ (0.09 mmol) was added and it was refluxed for the next 2 h. Chromatography with $CHCl_3$ gave **14b** – 7 mg (46%); unstable. This was checking by UV-VIS (characteristic intensive band of the complex; λ_{max} = 550 nm) and MS, and it was used directly in the next step; - UV-VIS (CH_2Cl_2), λ_{max} (log ε): 590 (3.69), 550 (4.28), 5.14 (3.54), 418 (5.36, Soret), 350 (4.05), 291 nm (4.24). - MS (EI), *m/z* (% rel. int.): 770 (12), 768 (17) and 766 (25) [isotopic $M^{+\cdot}$], 721 (6), 720 (6), 674 (5), 598 (6), 523 (5), 459 (13), 293 (10), 248 (8), 246 (10), 207 (20), 149 (39), 91 (49), 77 (62), 55 (62), 44 (100).

Vicarious Nucleophilic Substitution. General Procedures.

Procedure A. *t*-BuOK/DMSO: - To a stirred solution of *t*-BuOK (112 mg, 1.0 mmol) in andydrous DMSO (3.5 mL, under argon) a solution of porphyrin derivative (**7**, **8** or **14b**; 0.15 mmol) and a carbanion precursor (**9a**, **9c-j**; 0.30 mmol) in DMSO (1.5 mL) was added dropwise *via* syringe at room temp. during *ca.* 10 min. After additional 20 min of stirring (50 min for **5c**) the mixture was poured into 3% HCl with ice (50 mL). The precipitate was filtered, washed with water, and then dissolved in $CHCl_3$. After drying with anhydrous Na_2SO_4 and evaporation of the solvent the products were isolated by column chromatography (eluent: $CHCl_3$ or $CHCl_3$/MeOH – 100:1); yields - see Table 1.

Procedure B. NaOH/DMSO: - To a stirred suspension of powdered NaOH (165 mg, 4.1 mmol) in andydrous DMSO (5 mL, under argon) a solution of porphyrin derivative (**8**; 108 mg, 0.15 mmol) and a carbanion precursor (**9a**, **9c**, **9h**; 0.30 mmol) in DMSO (1 mL) was added dropwise *via* syringe at room temp. during *ca.* 1 min. After additional 1 h of stirring at room temp. the mixture was poured into 3% HCl with ice (50 mL) and worked-up as in Procedure A (eluent for chromatography - $CHCl_3$).

Procedure C. *t*-BuOK/DMF: - To a stirred solution of *t*-BuOK (56 mg, 0.5 mmol) in anhydrous DMF (2 mL, under argon) a solution of porphyrin derivative (**8**; 54 mg, 0.075 mmol) and α-chloroethyl *p*-tolyl sulphone (**9b**; 37 mg, 0.17 mmol) in DMF (1mL) was added dropwise *via* syringe at -40°C during *ca* 10 min. After additional 50 min of stirring the mixture was poured into 3% HCl with ice (25 mL) and worked-up as in Procedure A (eluent for chromatography: $CHCl_3$ to $CHCl_3$/MeOH – 100:1) to give 42 mg of the starting porphyrin (**8**; 77%) and 9 mg of the desired product (**11b**; 13%).

Procedure D. *t*-BuOK/NH_3 (liq.): - To a stirred solution of *t*-BuOK (56 mg, 0.5 mmol) in liquid ammonia (10 mL, under argon) a solution of porphyrin derivative (**8**; 54 mg, 0.075 mmol) and a carbanion precursor (**9d** or **9e**; 0.20 mmol) in THF (1.5 mL) was added dropwise *via* syringe during *ca.* 5 min. The reaction was continued for additional 30 min, then it was completed by addition of NH_4Cl (*ca.* 300 mg, in portions). The ammonia was evaporated and water (3 mL) and $CHCl_3$ (10 mL) were added to the residue. The organic layer was separated and the water phase was extracted with $CHCl_3$ (2 x 3 mL). The combined organic layers were dried over anhydrous Na_2SO_4. After evaporation of the solvent the

products were isolated by column chromatography (eluent: $CHCl_3$) to give 28 mg (52%) of the starting porphyrin (**8**) and 17 mg of the desired product (**11c**; 30%).

{5-[4-Nitro-3-(toluene-4-sulphonylmethyl)phenyl]-10,15,20-triphenylporphyrinato}copper(II) (10a): - mp >300°C. The crude compound (**10a**) was analyzed by UV-VIS method (characteristic bands of porphyrin complex; λ_{max}: 576, 540, 490, 415 nm (Soret)), then it was demetallated and fully characterized as a free base (**12a**).

{[2-Nitro-5-(10,15,20-triphenylporphyrinato-5-yl)phenyl]acetonitrile}copper(II) (10c): - mp >300°C. - UV-VIS (CH_2Cl_2), λ_{max} (log ε): 576 (3.96), 540 (4.27), 490 (3.97), 415 nm (5.30, Soret). - MS (EI), *m/z* (% rel. int.): 762 (24) and 760 (52) [isotopic M + H], 761 (56) and 759 (100) [isotopic $M^{+\cdot}$], 742 (3), 718 (5), 713 (5), 712 (5), 636 (8), 635 (9), 559 (5), 380 (3); HR-MS calcd for $C_{46}H_{28}N_6O_2Cu$ - 759.1570, found - 759.1569.

{5-[4-Nitro-3-(toluene-4-sulphonylmethyl)phenyl]-10,15,20-triphenylporphyrinato}zinc(II) (11a): - mp >300°C. - ^{1}H NMR ($CDCl_3$, 200 MHz): 9.02 (d, *J* = 4.8 Hz, 2H, H^{β}-pyrrole), 8.98 (s, 4H, H^{β}-pyrrole), 8.83 (d, *J* = 4.8 Hz, 2H, H^{β}-pyrrole), 8.37 (s, 1H, H-Ar(NO_2)), 8.30-8.17 (m, 8H, 2H of H-Ar(NO_2) and 6H of H-Ph), 7.84-7.68 (m, 9H, H-Ph), 7.66 (apparent d, *J* = 8.5 Hz, 2H, H-Tol), 7.38 (apparent d, *J* = 8.5 Hz, 2H, H-Tol), 5.08 (s, 2H, CH_2), 2.29 (s, 3H, CH_3). - UV-VIS (CH_2Cl_2), λ_{max} (log ε): 590 (3.62), 549 (4.02), 420 (5.19, Soret), 348 nm (3.90). - MS (EI), *m/z* (% rel. int.): 893 (21), 891 (27), 889 (34) [isotopic $M^{+\cdot}$], 739 (3), 737 (5), 735 (9), 723 (6), 721 (10), 719 (15), 691 (9), 613 (5), 306 (4), 299 (4), 173 (14), 156 (14), 139 (10), 106 (15), 92 (52), 91 (100), 77 (10), 65 (27), 64 (53); HR-MS calcd for $C_{52}H_{35}N_5O_4SZn$ - 889.1701, found - 889.1699.

{5-{4-Nitro-3-[1-(toluene-4-sulphonyl)ethyl]phenyl}-10,15,20-triphenylporphyrinato}zinc(II) (11b): - mp >300°C. - ^{1}H NMR ($CDCl_3$, 200 MHz): 9.10 (d, *J* = 4.9 Hz, 2H, H^{β}-pyrrole), 9.00-8.96 (m, 4H, H^{β}-pyrrole), 8.81 (d, *J* = 4.9 Hz, 2H, H^{β}-pyrrole), 8.70 (d , *J* = 1.4 Hz, 1H, H-Ar(NO_2)), 8.32 (part of AB coupled with another proton, *J* = 8.3,1.4 Hz, 1H, H-Ar(NO_2)), 8.28-8.16 (m, 7H, 1H of H-Ar(NO_2) and 6H of H-Ph), 7.82-7.70 (m, 11H, 9H of H-Ph and 2H of H-Tol), 7.35 (apparent d, *J* = 8.4 Hz, 2H, H-Tol), 5.83 (q, *J* = 7.2 Hz, 1H, **CH**CH_3), 2.42 (s, 3H, CH_3-Tol), 1.90 (d, *J* = 7.2 Hz, 3H, CH**CH_3**). - UV-VIS (CH_2Cl_2), λ_{max} (log ε): 590 (3.89), 549 (4.18), 514 (3.87), 420 (5.27, Soret), 350 (4.02), 311 nm (4.10). - MS (EI), *m/z* (% rel. int.): 907 (10), 905 (13), 903 (17) [isotopic $M^{+\cdot}$], 736 (12), 734 (17), 721 (22), 719 (34), 717 (42), 689 (5), 675 (5), 598 (6), 359 (7), 156 (20), 139 (11), 124 (24), 91 (100), 64 (29), 59 (34); HR-MS calcd for $C_{53}H_{37}N_5O_4SZn$ - 903.1858, found - 903.1861.

{[2-Nitro-5-(10,15,20-triphenylporphyrinato-5-yl)phenyl]acetonitrile}zinc(II) (11c): - mp >300°C. - ^{1}H NMR ($CDCl_3$, 200 MHz): 9.03 (d, *J* = 4.7 Hz, 2H, H^{β}-pyrrole), 8.99 (s, 4H, H^{β}-pyrrole), 8.83 (d, *J* = 4.7 Hz, 2H, H^{β}-pyrrole), 8.60 (d, *J* = 8.8 Hz, 1H, H-Ar(NO_2)), 8.58 (s, 1H, H-Ar(NO_2)), 8.43 (dd , *J* =

8.8,1.4 Hz, 1H, H-Ar(NO_2)), 8.29-8.21 (m, 6H, H-Ph), 7.83-7.74 (m, 9H, H-Ph), 4.50 (s, 2H, CH_2CN). - UV-VIS (CH_2Cl_2), λ_{max} (log ε): 591 (3.77), 549 (4.23), 5.12 (3.72), 420 (5.41, Soret), 351 (4.03), 302 nm (4.14). - MS (EI), *m/z* (% rel. int.): 764 (42), 762 (70), 760 (100) [isotopic $M^{+\cdot}$], 719 (47), 636 (12), 380 (7), 299 (12), 149 (10), 91 (10); HR-MS calcd for $C_{46}H_{28}N_6O_2Zn$ - 760.1565, found - 760.1566.

{5-[4-Nitro-3-(phenylsulphonylmethyl)phenyl]-10,15,20-triphenylporphyrinato}zinc(II) (11g): - mp >300°C. - ^{1}H NMR ($CDCl_3$, 200 MHz): 9.11-8.80 (m, 8H, H^{β}-pyrrole), 8.48-8.15 (m, 11H, H-Ar), 7.94-7.47 (m, 12H, H-Ar), 5.22 (s, 2H, CH_2). - UV-VIS ($CHCl_3$), λ_{max} (log ε): 597 (3.82), 555 (4.30), 424 (5.56, Soret), 313 nm (4.28). - MS (EI), *m/z* (% rel. int.): 879 (6), 878 (5), 877 (8), and 875 (12) [isotopic $M^{+\cdot}$], 719 (2), 369 (5), 295 (8), 237 (21), 115 (17), 97 (51), 78 (36), 77 (33), 65 (12), 64 (39), 44 (100); HR-MS (ESI) calcd for $C_{51}H_{33}N_5O_4SZn$ - 875.1545, found - 875.1543.

{5-[4-Nitro-3-(*tert*-butylsulphonylmethyl)phenyl]-10,15,20-triphenylporphyrinato}zinc(II) (11j): - mp >300°C. - ^{1}H NMR ($CDCl_3$, 200 MHz): 9.04-8.94 (m, 8H, H^{β}-pyrrole), 8.54 (d, *J* = 8.5 Hz, 1 H, H-Ar(NO_2)), 8.48 (d, *J* = 1.6 Hz, 1H, H-Ar(NO_2)), 8.41 (dd, *J* = 8.5, 1.6 Hz, 1H, H-Ar(NO_2)), 8.27-8.15 (m, 6H, H-Ph), 7.81-7.70 (m, 9H, H-Ph), 5.11 (s, 2H, CH_2), 1.58 (s, 9H, $C(CH_3)_3$). - UV-VIS ($CHCl_3$), λ_{max} (log ε): 598 (3.70), 554 (4.20), 423 nm (5.48, Soret). - MS (EI), *m/z* (% rel. int.): 859 (2), 857 (2), and 855 (3) [isotopic $M^{+\cdot}$], 737 (2), 736 (2), 735 (4), 720 (1), 719 (1), 689 (1), 674 (1), 613 (1), 64 (94), 56 (43), 48 (35), 40 (100); HR-MS (ESI) calcd for $C_{49}H_{37}N_5O_4SZn$ - 855.1858, found - 855.1852.

{5,10-Bis[4-nitro-3-(toluene-4-sulphonylmethyl)phenyl]-15,20-diphenylporphyrinato}zinc(II) (15a). This compound was obtained according to Method A (contaminated with **15b**). - ^{1}H NMR ($CDCl_3$, 200 MHz): 8.98-8.85 (m, 6H, H^{β}-pyrrole), 8.79 (d, *J* = 5.0 Hz, 2H, H^{β}-pyrrole), 8.58 (d, *J* = 8.2 Hz, 2H, H-Ar(NO_2)), 8.45-8.16 (m, 8H, 4H of H-Ar(NO_2) and 4H of H-Ph), 7.84-7.68 (m, 10H, 6H of H-Ph and 4H of H-Tol), 7.33 (apparent d, *J* = 8.0 Hz, 4H, H-Tol), 5.21 (br s, 4H, 2xCH_2), 2.34 (br s, 6H, 2xCH_3). - UV-VIS (CH_2Cl_2), λ_{max}: 647, 590, 553, 517, 421 nm (Soret); log ε values are not given as the product was partially demetallated. - MS (EI), *m/z* (% rel. int.): 1102 (<1, $M^{+\cdot}$), 947 (1, M-SO_2Tol). LSIMS (+), *m/z* (% rel. int.); the molecular ion of **15a** was not detected, the ion of demetallated disubstituted compound (**15b**) ($C_{60}H_{44}N_6O_8S_2$) was identified: 1041 (1%, M+1).

Demetallation of the porphyrin complexes. – To a stirred solution of porphyrin complex (**10a** or **11i**; 0.03 mmol) in CF_3CO_2H (5 mL) concentrated H_2SO_4 (1 drop) was added and the reaction mixture was stirred at rt for 3 h. The reaction mixture was poured into water with ice (30 mL), the precipitate was filtered, washed with water, and then dissolved in CH_2Cl_2. After drying with anhydrous Na_2SO_4 and evaporation of the solvent, the products (**12a**, **12i**) were isolated by column chromatography (eluent: $CHCl_3$ to $CHCl_3$/MeOH – 100:1); quantitative yields.

5-[4-Nitro-3-(toluene-4-sulphonylmethyl)phenyl]-10,15,20-triphenylporphyrin (12a): - mp >300°C.

- ^{1}H NMR ($CDCl_3$, 200 MHz): 8.83 (d, *J* = 4.9 Hz, 2H, H^β-pyrrole), 8.78 (s, 4H, H^β-pyrrole), 8.66 (d, *J* = 4.9 Hz, 2H, H^β-pyrrole), 8.29 (part of AB, *J* = 8.3 Hz, 1H, H-Ar(NO_2)), 8.25 (part of AB coupled with another proton, *J* = 8.3,1.8 Hz, 1H, H-Ar(NO_2)), 8.17 (d, *J* = 1.8 Hz, 1H, H-Ar(NO_2)), 8.16-8.08 (m, 6H, H-Ph), 7.72-7.64 (m, 11H, 9H of H-Ph and 2H of Tol), 7.21 (apparent d, *J* = 7.8 Hz, 2H, H-Tol), 5.12 (s, 2H, CH_2), 2.20 (s, 3H, CH_3), -2.88 (s, 2 H, 2xNH). - UV-VIS (CH_2Cl_2), λ_{max} (log ε): 646 (3.93), 590 (3.98), 551 (4.05), 516 (4.25), 419 (5.37, Soret), 301 nm (4.18). - MS (EI), *m/z* (% rel. int.): 828 (31, M+H), 827 (53, $M^{+\cdot}$), 687 (9), 673 (30), 657 (30), 644 (11), 629 (14), 156 (34), 139 (17), 92 (75), 91 (100), 65 (37), 64 (64); HR-MS calcd for $C_{52}H_{37}N_5O_4S$ - 827.2566, found - 827.2561.

***N,N*-Dimethyl-*C*-{[2-nitro-5-(10,15,20-triphenylporphyrinato-5-yl)phenyl]methanesulphonamide}-zinc(II) (12i):** - mp >300°C. - ^{1}H NMR ($CDCl_3$, 200 MHz): 8.93 (d, *J* = 4.9 Hz, 2H, H^β-pyrrole), 8.86 (s, 4H, H^β-pyrrole), 8.83 (d, *J* = 4.9 Hz, 2H, H^β-pyrrole), 8.51 (d, *J* = 1.4 Hz, 1H, H-Ar(NO_2)), 8.46 (part of AB, *J* = 8.4 Hz, 1H, H-Ar(NO_2)), 8.38 (part of AB coupled with another proton, *J* = 8.4,1.4 Hz, 1H, H-Ar(NO_2)), 8.26-8.17 (m, 6H, H-Ph), 7.83-7.70 (m, 9H, H-Ph), 5.03 (s, 2H, CH_2), 2.95 (s, 6H, $N(CH_3)_2$), -2.80 (s, 2H, 2xNH). - UV-VIS ($CHCl_3$), λ_{max} (log ε): 653 (3.70), 591 (3.83), 553 (4.02), 516 (4.33), 420 nm (5.64, Soret). - MS (EI), *m/z* (% rel. int.): 782 (7), 781 (18), and 780 (34) [isotopic $M^{+\cdot}$], 721 (14), 676 (3), 675 (3), 656 (2), 655 (3), 628 (4), 627 (3), 626 (3), 369 (8), 295 (14), 281 (9), 221 (24), 121 (100), 91 (29), 78 (26), 57 (35), 55 (28), 44 (40), 40 (48); HR-MS calcd for $C_{47}H_{36}N_6O_4S$ - 780.2519, found - 780.2526.

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