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1,3-DIPOLAR CYCLOADDITION REACTION IN PORPHYRIN SYSTEMS WITH FUNCTIONALIZED ALKYL NITRILE OXIDES – SYNTHESIS OF ISOXAZOLINE-FUSED CHLORINS

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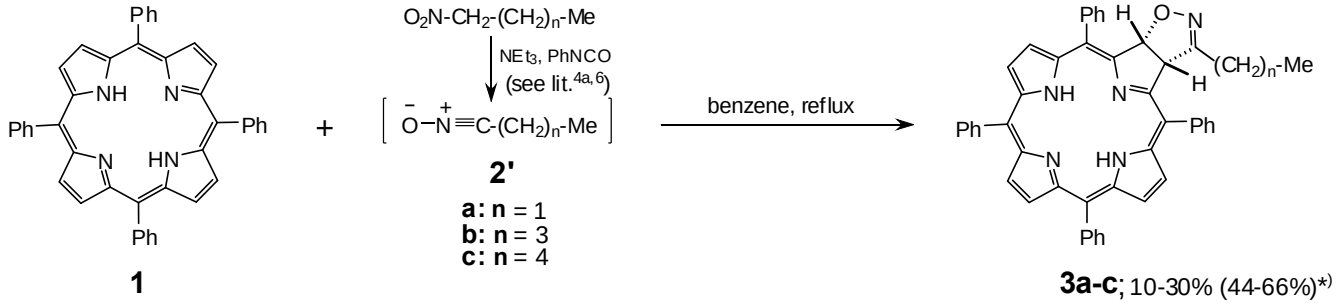
Abstract – *meso*-Tetraphenylporphyrin reacts at higher temperature with unstable alkyl nitrile oxides (R–C≡N→O) affording isoxazoline-fused chlorins according to dipolar [3+2]-cycloaddition pathway. The respective nitrile oxides were *in situ* generated from the corresponding functionalized nitroalkanes in the presence of base (NEt_3, DABCO) and dehydrating agent (PhNCO, $(Boc)_2O$). Substituent **R** bearing diverse of functionality allows synthesis of very attractive moieties which may be of potential use as sensitizers in photodynamic therapy. The products obtained are also suitable intermediates for further derivatization of porphyrins.

In the past decade numerous investigations oriented towards the synthesis and utilization of chlorins and bacteriochlorins have been undertaken. These compounds may be considered as second generation photosensitizers in antitumor photodynamic therapy (PDT)[1] due to their characteristic strong absorption bands shifted to the red region of visible spectrum (630-780 nm).

The attractive chlorin systems can be synthesized by various methods.[2] One of the approaches involves 1,3-dipolar cycloaddition reaction of peripheral β,β-double bonds of porphyrin moiety with some 1,3-dipoles. Among others, nitrile oxides could be used for this purpose. In the recent past we reported our preliminary results concerning this type of cycloaddition with the use of alkyl nitrile oxides,[3] generation of which is relatively difficult, and which are generally less stable[4] as compared to the aryl ones. It was one of the first three published works in which synthesis of fused porphyrin-isoxazoline derivatives was described.[3,5a,b]

Herein we report our further investigations oriented towards the synthesis of diversely functionalized chlorins. Studies on the scope and limitations of this derivatization method and exploring other possibilities of generation this type of alkyl nitrile oxides (and their applications in the above cycloaddition) were attempted. The previous reactions of *meso*-tetraphenylporphyrin (**1**) with an excess of alkyl nitrocompounds **2a-c**, carried out in the presence of NEt_3 and PhNCO in refluxing benzene (Mukaiyama's method[4a]), gave the expected isoxazoline-fused chlorins (**3a-c**)[3] (Scheme 1).



*) yields in brackets were calculated for recovered **1**

Scheme 1

The reactions were carried out in benzene due to a good solubility of the reagents in this solvent. The generated *in situ* nitrile oxides readily enter into the cycloaddition to β,β-double bond, which exhibits considerable olefinic character. Every 3 hours new portions of the substrates were supplied and the reaction mixtures were heated up to *ca* 50 hours. Due to the various difficulties, *e.g*. addition of new portions of R-NO_2, NEt_3, and PhNCO (to supplement the loss of the formed *in situ* nitrile oxide), long reaction time, and fast degradation of nitrile oxides, the yields of the chlorins were rather low or moderate (10-30%), and we recovered considerable amounts of the starting porphyrin. The prolonged reaction time did not give higher yields, because in these conditions the progressive degradation of the products was observed. Thus, some attempts concerning optimization of the reaction conditions were undertaken by changing the temperature, solvent, base, and dehydrating agent. These results are listed in Table 1.

Table 1. Optimization of the reaction conditions ([3+2]-cycloaddition of **1** with aliphatic nitrile *N*-oxides)

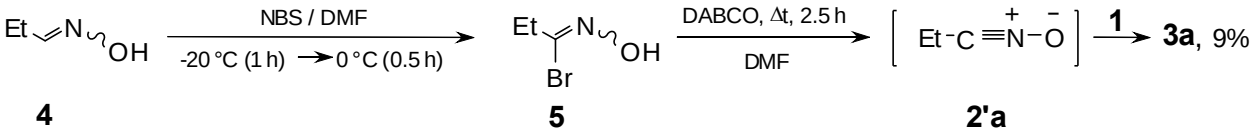
R-NO_2	Base	Dehydrating agent	Solvent	Temperature	Reaction time [h]	Yield [%][a)]
n-$C_3H_7NO_2$	NEt_3	PhNCO	toluene	111 ºC	14	11
n-$C_3H_7NO_2$	NEt_3	PhNCO	benzene	80 ºC	50	16 (66)
n-$C_3H_7NO_2$	NEt_3	$POCl_3$	benzene	80 ºC	5	–
n-$C_3H_7NO_2$	DABCO	PhNCO	1,2,4-TCB[b)]	120 ºC	11	<1
n-$C_3H_7NO_2$	DABCO	$POCl_3$	toluene	111 ºC	2	–
n-$C_3H_7NO_2$	DABCO	–	$CHCl_3$	61 ºC	20	–
n-$C_3H_7NO_2$	K_2CO_3	PhNCO	toluene	111 ºC	20	<1
n-$C_3H_7NO_2$	NEt_3	PhNCO	cyclooctane	149 ºC	2	15 (25)
n-$C_5H_{11}NO_2$	NEt_3	PhNCO	benzene	80 ºC	50	10 (44)
n-$C_5H_{11}NO_2$	CaH_2	PhNCO	DMSO	120 ºC	19	<1

[a)] in brackets – yields for the recovered substrate; [b)] 1,2,4-trichlorobenzene

It is known that most of the cycloaddition reactions in porphyrin systems usually takes place at higher temperature.[2d,7] In our case, the raising of the temperature did not give better yields; however, it allows shortening the reaction time (from 50 h to 2 h, see entries 2 and 8 in Table 1). Probably the most important limitation herein is the moderate reactivity of the porphyrin as dipolarophile. Nevertheless, this synthesis is a challenging task because the chlorins prepared by the above method, bearing lipophilic alkyl

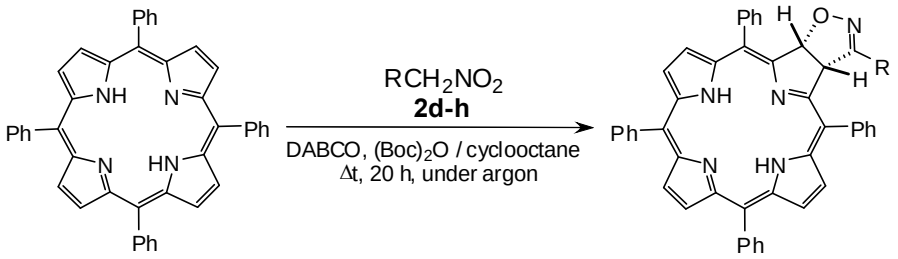
chains, can be transformed into hydrophilic ketones, amines, alcohols, etc.,[8] and therefore may lead to very attractive amphiphilic systems,[9] which are sought in many fields of this chemistry.

In the next step, some attempts concerning generation of the nitrile *N*-oxides were undertaken. Historically, the first method involves elimination of hydrogen halides from the aliphatic aldoxime derivatives. The starting halogeno-aldoximes are rather unstable, thus they are usually used in the reactions as solutions, directly after their preparation. However, in our case, we could not improve the yields by using these precursors (Scheme 2).



Scheme 2

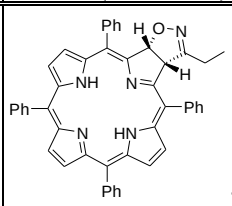
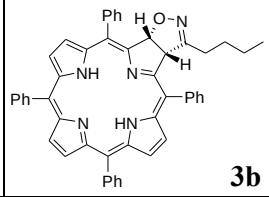
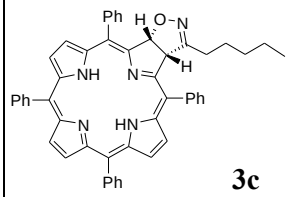
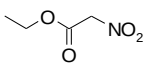
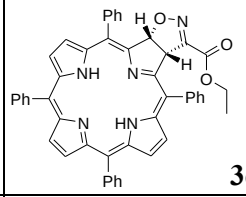
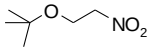
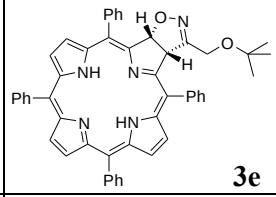
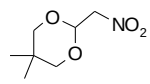
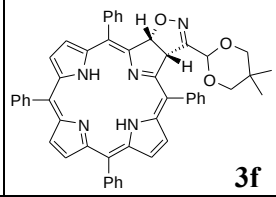
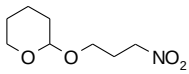
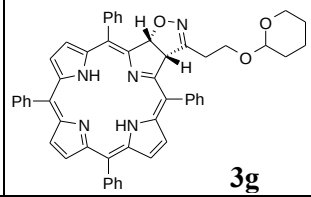
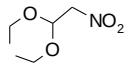
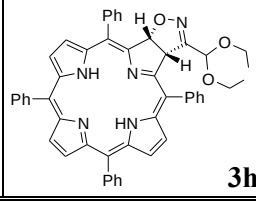
Also the literature method[10] involving chloramine-T (with the use of oxime **4**) completely failed. The same result was observed for application of nitrolic acids[11] (for example $PhCH_2C(NO_2)$=N-OH; toluene/reflux or DMSO/120 ºC; 10-20 h). None of the product was formed in these cases, even with activated porphyrins: *meso*-tetrakis(2,6-dichlorophenyl)porphyrin and *meso*-tetrakis(pentafluorophenyl)porphyrin.[12] Finally, we applied the modification described by Basel and Hassner (DMAP, $(Boc)_2O$).[13] From the several solvents tested (*e.g.* toluene, cyclooctane, $CHCl_3$) we choose cyclooctane, and the base DMAP was exchanged for DABCO. Under these conditions we carried out the remaining reactions with nitroalkanes bearing highly functionalized groups **R** (see Scheme 3 and Table 2).



Scheme 3

The chlorins **3a-h** were identified by ^{1}H NMR, MS, and UV-Vis methods. The ^{1}H NMR spectra reveal characteristic broad singlets at *ca* -1.75 ÷ -2.00 ppm originating from NH protons (deshielded as compared to porphyrins). The more diagnostic signals of H^β-protons in reduced pyrrole ring (H^β-chlorin) were always found as two doublets (J = 9.2 ÷ 10.0 Hz) in the region 6.50–7.80 ppm. The remaining signals of H^β-protons usually appear as several doublets and one singlet (2H; opposite site to the 'chlorin junction') in the region 7.92–8.68 ppm. The COSY spectrum measured for compound **3a** also confirmed the proposed structure.

Table 2. [3+2]-Cycloaddition reaction of porphyrin **1** with aliphatic nitrile *N*-oxides

Starting Nitroalkane	Procedure[a)]	Chlorin (Number)	Yield[b)] [%]
$Me\text{-}(CH_2)_2\text{-}NO_2$	A	 **3a**	66
$Me\text{-}(CH_2)_4\text{-}NO_2$	A C	 **3b**	44 35
$Me\text{-}(CH_2)_5\text{-}NO_2$	A B	 **3c**	55 8
	C	 **3d**	31
	C	 **3e**	24
	C	 **3f**	40
	C	 **3g**	63
	C	 **3h**	*ca* 1%

a) *Procedure A*: benzene, NEt_3, PhNCO, reflux, 50 h, protected with $CaCl_2$ tube, under argon; *Procedure B*: toluene, NEt_3, PhNCO, reflux, 30 h, under argon; *Procedure C*: cyclooctane, DABCO, $(Boc)_2O$, reflux, 20 h, under argon; b) yields are given for recovered **1**.

The yields of the products were moderate or low but the chlorins obtained are very attractive moieties. They are esters (**3d**), ethers (**3e**), acetals (**3f-h**), etc.; thus may be further transformed to novel diversely decorated chlorins of increased polarity. Additionally, the fused isoxazoline ring conceivably may be also easily cleaved[8] to polar functionalities. Such chlorins are sought in antitumor PDT, because in their structures all the desired properties were deposited.

CONCLUSIONS

We presented herein an approach to fused isoxazoline-type chlorins by dipolar [3+2]-cycloaddition of unstable alkyl nitrile oxides to *meso*-tetraphenylporphyrin. This reaction may well receive future attention in the area of porphyrin skeleton modifications. The products obtained are potentially attractive and versatile intermediates for the further derivatization of *meso*-arylchlorins designed as second generation photosensitizers[1a] in PDT. They could be practically applied in this therapy because they absorb low-energy UV-Vis light, and subsequently may be easily converted to soluble in physiological milieu moieties.

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 MARINER PerSeptive Biosystems (ESI-TOF) spectrometer (ESI method), 4000 Q-TRAP Applied Biosystems spectrometer (APPI method), and GCT Premier Waters (FD-TOF) spectrometer (FD method); *m/z* intensity values for peaks are given as % of relative intensity. UV-Vis spectra were measured with a Beckman DU-68 spectrometer. TLC analysis was performed on aluminium foil plates pre-coated with silica gel (60F 254, Merck); the products have lower R_f values as compared to the starting porphyrin **1** (TLC: $CHCl_3$/*n*-hexane). Silica gel, 230-400 mesh (Merck AG), was used for column chromatography. Molecular formulas of the compounds synthesised were confirmed by HR-MS (ESI and FD) and by comparing the molecular isotope patterns (theoretical and experimental).

All the nitroalkanes used were commercial products.

Procedure A. To a stirred solution of *meso*-tetraphenylporphyin (**1**; 100 mg, 0.163 mmol) and nitrocompound (**2a-c**; 4.2 mmol) in anhydrous benzene (4 mL), triethylamine (320 μL, 2.30 mmol) was added, and the mixture was stirred for 15 min at room temperature. Then, the reaction mixture was heated to reflux, and a solution of phenyl isocyanate (395 mg, 360 μL, 3.31 mmol) in benzene (1 mL) was added dropwise *via* syringe (septum) over a period of *ca* 15 min. The new portions of nitroalkane, NEt_3, and PhNCO were added every 3 h. The reaction was carried out under argon in a light-shielded flask equipped with a reflux condenser protected at the top with $CaCl_2$ tube. After 50 h the reaction mixture was cooled to room temperature, the precipitate was filtered off, and the residue was chromatographed (eluent: $CHCl_3$/*n*-hexane (2:1), then $CHCl_3$) to give the desired product: **3a** – 17.7 mg, 16% (66% for recovered **1**); **3b** – 11.8 mg, 10% (44%); **3c** – 35.4 mg, 30% (55%).

Procedure B. To a boiling solution of *meso*-tetraphenylporphyrin (**1**; 390 mg, 0.634 mmol) and PhNCO (219 mg, 200 μL, 1.84 mmol) in anhydrous toluene (10 mL), a mixture of nitrohexane (84 mg, 0.64 mmol) and NEt_3 (130 μL, 0.93 mmol) in toluene (0.5 mL) was added dropwise *via* syringe (septum) over a period of *ca* 15 min. The reaction was carried out under argon in a light-shielded flask equipped with a reflux condenser protected at the top with $CaCl_2$ tube. The new portions of nitrohexane (84 mg, 0.64 mmol) and NEt_3 (130 μL, 0.93 mmol) were added every 1 h, and PhNCO (219 mg, 200 μL, 1.84 mmol) – every 6 h. After 30 h the reaction mixture was cooled to room temperature and transferred quantitatively to separatory funnel filled with 100 mL of water. The product was extracted with chloroform (3×25 mL). The combined organic layers were washed with water (100 mL) and dried over anhydrous $MgSO_4$. After evaporating the solvent, chlorin **3c** was isolated by column chromatography (eluent: $CHCl_3$/*n*-hexane, from 2:1 to 4:1). Yield: 37 mg (8%).

Procedure C. To a boiling solution of *meso*-tetraphenylporphyrin (**1**; 123 mg, 0.200 mmol), DABCO (90 mg, 0.80 mmol), and $(Boc)_2O$ (660 mg, 3.02 mmol) in anhydrous cyclooctane (8 mL), a solution of nitroalkane **2b**,**d-h** (2.0 mmol) in cyclooctane (2 mL) was added dropwise *via* syringe (septum) over a period of *ca* 30 min. The reaction was carried out under argon in a light-shielded flask equipped with a reflux condenser protected at the top with $CaCl_2$ tube. The new portions of nitroalkane (2.0 mmol), DABCO (90 mg, 0.80 mmol), and $(Boc)_2O$ (660 mg, 3.02 mmol) were added every 5 h. After 20 h the reaction mixture was cooled to room temperature, poured onto 100 mL of water, and extracted with chloroform (5×20 mL). The combined organic layers were dried over anhydrous $MgSO_4$. After evaporating the solvent, the products were isolated by column chromatography (eluent: $CHCl_3$/*n*-hexane,

from 1:1 to 4:1). The desired chlorins (**3b**,**d-h**) were found in the second more polar fraction, eluted after the first fraction containing the recovered porphyrin **1**. These chlorins were rechromatographed (eluent: $CHCl_3$/*n*-hexane, 3:1) to give analytically pure products: **3b** – 18.6 mg, 13% (35% for recovered **1**); **3d** – 13.2 mg, 9% (31%); **3e** – 12.0 mg, 8% (24%); **3f** – 15.6 mg, 10% (40%); **3g** – 16.4 mg, 10% (63%); **3h** – 0.6 mg, < 1%.

Chlorin 3a: mp > 300 °C. ^{1}H NMR ($CDCl_3$, 400 MHz), δ [ppm]: 8.65 (apparent d, *J* ~ 4.9 Hz, 2H, 2×H$^\beta$), 8.56 (d, *J* = 7.7 Hz, 1H, H-C_6H_5), 8.49 (s, 2H, 2×H$^\beta$), 8.39-8.15 (m, 6H, 2×H$^\beta$ and 4H of H-C_6H_5), 8.09-7.97 (m, 2H, H-C_6H_5), 7.87-7.63 (m, 12H, 11H of H-C_6H_5 and CH [7.67 (d, *J* = 9.6 Hz)]), 7.62-7.55 (m, 2H, H-C_6H_5), 6.50 (d, *J* = 9.6 Hz, 1H, CH), 1.86-1.69 (m, 2H, CH_2), 0.58 (t, *J* = 7.4 Hz, 3H, CH_3), -1.75 (s, 1H, NH), -1.79 (s, 1H, NH). UV-Vis ($CHCl_3$), λ_{max} [nm] (lg ε): 645.5 (4.17), 594 (3.69), 548 (3.99), 519.5 (3.98), 414 (4.84, Soret). MS (ESI), *m/z* (% rel. int.): 688 (5), 687 (38), 686 (100) [isotope $(M+H)^+$]. HR-MS (ESI) calcd for $C_{47}H_{36}N_5O$ $[(M+H)^+]$: 686.2920, found: 686.2925.

Chlorin 3b: This compound has been already described in the earlier literature[3]; the respective ^{1}H NMR spectrum is given here for more detailed and accurate characterization of the product. ^{1}H NMR ($CDCl_3$, 400 MHz), δ [ppm]: 8.63 (apparent d, *J* ~ 4.8 Hz, 2H, 2×H$^\beta$), 8.54 (d, *J* = 7.4 Hz, 1H, H-C_6H_5), 8.47 (s, 2H, 2×H$^\beta$), 8.39-7.92 (m, 8H, 2×H$^\beta$ and 6H of H-C_6H_5), 7.89-7.12 (m, 14H, 13H of H-C_6H_5 and CH [7.65 (d, *J* = 10.0 Hz)]), 6.51 (d, *J* = 10.0 Hz, 1H, CH), 1.80-1.17 (m, 6H, 3×CH_2), 0.64 (t, *J* = 7.0 Hz, 3H, CH_3), -1.79 (broad s, 2H, 2×NH).

Chlorin 3c: mp > 300 °C. ^{1}H NMR ($CDCl_3$, 400 MHz), δ [ppm]: 8.64 (apparent d, *J* ~ 4.8 Hz, 2H, 2×H$^\beta$), 8.55 (d, *J* = 7.6 Hz, 1H, H-C_6H_5), 8.48 (s, 2H, 2×H$^\beta$), 8.38-7.95 (m, 8H, 2×H$^\beta$ and 6H of H-C_6H_5), 7.85-7.53 (m, 14H, 13H of H-C_6H_5 and CH [7.65 (d, *J* = 9.6 Hz)]), 6.50 (d, *J* = 9.6 Hz, 1H, CH), 1.82-1.63 (m, 2H, CH_2), 1.10-0.78 (m, 6H, 3×CH_2), 0.70 (t, *J* = 7.0 Hz, 3H, CH_3), -1.75 (s, 1H, NH), -1.79 (s, 1H, NH). UV-Vis ($CHCl_3$), λ_{max} [nm] (lg ε): 645 (3.68), 593 (3.22), 548 (3.52), 519 (3.51), 416 (4.59, Soret). MS (ESI), *m/z* (% rel. int.): 730 (9), 729 (36), 728 (100) [isotope $(M+H)^+$]. HR-MS (ESI) calcd for $C_{50}H_{42}N_5O$ $[(M+H)^+]$: 728.3389, found: 728.3397.

Chlorin 3d: mp > 300 °C. ^{1}H NMR ($CDCl_3$, 400 MHz), δ [ppm]: 8.68 (d, *J* = 4.8 Hz, 1H, H$^\beta$), 8.63-8.52 (m, 2H, 1H$^\beta$ and 1H of H-C_6H_5), 8.50 and 8.49 (AB, *J* = 4.5 Hz, 2H, 2×H$^\beta$), 8.40-8.31 (m, 2H, 1H$^\beta$ and 1H of H-C_6H_5), 8.23-7.94 (m, 6H, 1H$^\beta$ and 5H of H-C_6H_5), 7.84 (d, 1H, *J* = 7.3 Hz, H-C_6H_5), 7.79-7.60 (m, 10H, CH and 9H of H-C_6H_5), 7.56-7.47 (m, 3H, H-C_6H_5), 6.77 (d, *J* = 9.2 Hz, 1H, CH), 4.02 (q, *J* = 7.2 Hz, 2H, CH_2), 1.16 (t, *J* = 7.2 Hz, 3H, CH_3), -1.93 (s, 1H, NH), -1.99 (s, 1H, NH). UV-Vis ($CHCl_3$), λ_{max} [nm] (lg ε): 643 (4.09), 590.5 (3.57), 545.5 (3.84), 517 (3.87), 417 (4.99, Soret). MS (APPI), *m/z* (% rel. int.): 732 (19), 731 (61), 730 (100) [isotope $(M+H)^+$]. HR-MS (ESI) calcd for $C_{48}H_{36}N_5O_3$ $[(M+H)^+]$: 730.2818, found: 730.2787.

Chlorin 3e: mp > 300 °C. ^{1}H NMR ($CDCl_3$, 400 MHz), δ [ppm]: 8.63 (apparent d, *J* ~ 4.8 Hz, 2H, 2×H$^\beta$), 8.52 (d, *J* = 7.6 Hz, 1H, H-C_6H_5), 8.48 (s, 2H, 2×H$^\beta$), 8.35-8.15 (m, 6H, 2×H$^\beta$ [8.34 (apparent d, *J* = 4.8 Hz)] and 4H of H-C_6H_5), 8.10-7.95 (m, 2H, H-C_6H_5), 7.83-7.62 (m, 12H, 11H of H-C_6H_5 and CH [7.65 (d, *J* = 9.7 Hz)]), 7.60-7.51 (m, 2H, H-C_6H_5), 6.57 (d, *J* = 9.7 Hz, 1H, CH), 3.64 and 3.48 (AB, *J* = 14.5 Hz, 2H, CH_2), 0.83 (s, 9H, $C(CH_3)_3$), -1.81 (s, 1H, NH), -1.83 (s, 1H, NH). UV-Vis ($CHCl_3$), λ_{max} [nm] (lg ε): 647 (3.85), 594 (3.37), 548 (3.68), 519 (3.66), 418 (4.77, Soret). MS (ESI), *m/z* (% rel. int.): 746 (13), 745 (55), 744 (100) [isotope $(M+H)^+$]. HR-MS (ESI) calcd for $C_{50}H_{42}N_5O_2$ $[(M+H)^+]$: 744.3339, found: 744.3300.

Chlorin 3f: mp > 300 °C. ^{1}H NMR ($CDCl_3$, 400 MHz), δ [ppm]: 8.64-8.59 (m, 2H, 2×H$^\beta$), 8.51 (d, *J* = 7.4 Hz, 1H, H-C_6H_5), 8.47 (s, 2H, 2×H$^\beta$), 8.33 (d, *J* = 5.0 Hz, 1H, H$^\beta$), 8.29 (d, *J* = 4.7 Hz, 1H, H$^\beta$),

8.25-7.92 (m, 6H, H-C_6H_5), 7.84-7.63 (m, 12H, 11H of H-C_6H_5 and CH [7.68 (d, J = 9.5 Hz)]), 7.60-7.52 (m, 2H, H-C_6H_5), 6.65 (d, J = 9.5 Hz, 1H, CH), 4.45 (s, 1H, C*H*(OCH_2-)$_2$), 3.34 (dd, J = 11.3, 2.7 Hz, 1H, H^{ax} of CH_2), 3.22 (dd, J = 11.1, 2.7 Hz, 1H, H^{ax} of CH_2), 3.14 (d, J = 11.3 Hz, 1H, H^{eq} of CH_2), 3.00 (d, J = 11.1 Hz, 1H, H^{eq} of CH_2), 0.94 (s, 3H, CH_3), 0.59 (s, 3H, CH_3), -1.77 (s, 1H, NH), -1.80 (s, 1H, NH). UV-Vis ($CHCl_3$), λ_{max} [nm] (lg ε): 647 (3.91), 594.5 (3.41), 549 (3.75), 520 (3.71), 417 (4.85, Soret). MS (FD), *m/z* (% rel. int.): 774 (3), 773 (15), 772 (58), 771 (100) [isotope M^+]. HR-MS (FD) calcd for $C_{51}H_{41}N_5O_3$ [M^+]: 771.3209, found: 771.3203.

Chlorin 3g: mp > 300 °C. ^{1}H NMR ($CDCl_3$, 400 MHz), δ [ppm]: 8.63 (apparent d, J ~ 4.8 Hz, 2H, 2×H^{β}), 8.52 (d, J = 7.7 Hz, 1H, H-C_6H_5), 8.47 (s, 2H, 2×H^{β}), 8.36-8.15 (m, 6H, 2×H^{β} and 4H of H-C_6H_5), 8.08-7.93 (m, 2H, H-C_6H_5), 7.84-7.63 (m, 12H, 11H of H-C_6H_5 and CH [7.65 (d, J = 9.6 Hz)]), 7.62-7.55 (m, 2H, H-C_6H_5), 6.50 (apparent t, 'J' ~ 10.3 Hz, 1H, CH), 4.18-4.14 (m, 1H, C*H*(OCH_2-)$_2$), 3.50-3.34 (m, 2H, OCH_2), 3.15-3.00 (m, 2H, OCH_2), 2.16-1.96 (m, 2H, CH_2), 1.76-1.43 and 1.39-1.15 (2×m, 6H, 3×CH_2), -1.78 (s, 1H, NH), -1.82 (s, 1H, NH). UV-Vis ($CHCl_3$), λ_{max} [nm] (lg ε): 647 (4.15), 594.5 (3.64), 548.5 (3.97), 519.5 (3.94), 416.5 (5.06, Soret). MS (FD), *m/z* (% rel. int.): 788 (7), 787 (26), 786 (70), 785 (100) [isotope M^+]. HR-MS (FD) calcd for $C_{52}H_{43}N_5O_3$ [M^+]: 785.3366, found: 785.3334.

Chlorin 3h: This compound was obtained in small amounts (below 1 mg); its structure was proposed on the basis of MS and UV-Vis spectra. UV-Vis ($CHCl_3$), λ_{max} [nm]: 647, 594.5, 548.5, 521, 419 (Soret). MS (FD), *m/z* (% rel. int.): 762 (4), 761 (18), 760 (59), 759 (100) [isotope M^+]. HR-MS (FD) calcd for $C_{50}H_{41}N_5O_3$ [M^+]: 759.3209, found: 759.3179. The molecular formula was also confirmed by comparing the theoretical and experimental isotope patterns for the M^+ ion ($C_{50}H_{41}N_5O_3$); it was found to be identical within the experimental error limits.

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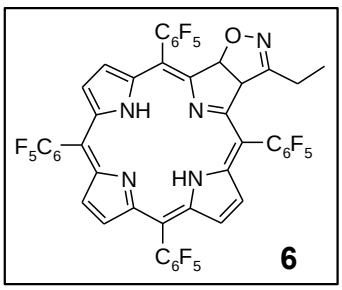

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