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Synthesis of Locked meso-β-Substituted Chlorins via 1,3-Dipolar Cycloaddition

Michał Gałęzowski and Daniel T. Gryko*

Institute of Organic Chemistry of the Polish Academy of Sciences, Warsaw, Poland

daniel@icho.edu.pl

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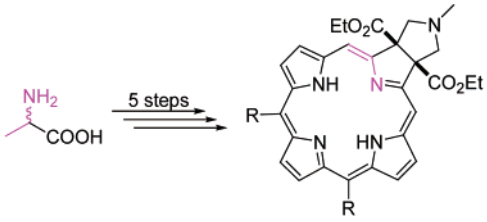

A novel approach toward "locked" chlorins with increased stability has been studied in detail. The chlorin skeleton is assembled in a convergent fashion from two fragments via a porphyrin forming reaction, followed by 1,3-dipolar cycloaddition of azomethine ylides, which are formed in situ. Central to the success of the process is the presence of two electron-withdrawing groups in vicinal positions at the perimeter of the porphyrin. As a result, the 1,3-dipolar cycloaddition took place regioselectively, on the bond activated by two electron-withdrawing groups. Moreover, the chlorins formed are locked and hence more stable because of the presence of two quaternary carbon atoms. Overall, in just six steps locked chlorins were constructed from easily available materials. The large array of functionalities tolerated in this approach validates it for a broad use in more advanced studies. The correlation between the results of the 1,3-dipolar cycloaddition and dipolarophile (porphyrin) LUMO energy was extensively studied. There was a definite correlation between the reaction time and the LUMO energy level, and a partial correlation between the reaction yield and the distribution of the LUMO. Additionally, various approaches toward crucial building blocks, namely 3,4-disubstituted-2,5-diformylpyrroles, were investigated.

Introduction

The green color of leaves has intrigued humans for millennia. It was not until the twentieth century that chlorin was discovered to be the basic structural element responsible for this color. Being involved in one of the most elaborate nanobiological machines, the natural photosynthetic system,[1] chlorins were intensively studied and synthesized for more than a century.[2] Recently, many studies have been focused on the use of artificial photosynthesis to develop light-energy conversion systems.[3] Although porphyrins lack some crucial photophysical features they are often used instead of chlorins in the energy and electron-transfer studies. The photophysical development of chlorins is hampered by the lack of a reasonable methodology to construct suitable chlorin building blocks.

Another promising area of chlorins applications is photodynamic therapy (PDT); a method utilizing visible or ultraviolet light in combination with a photosensitizing agent to induce a phototoxic reaction, which results in cell damage or death. With a growing importance of PDT,[4] which seems to be endowed with several favorable features also for the treatment of localized microbial[5] and fungi infections,[6] there is a need for the

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development of new agents. One potential advantage of chlorins in PDT stems from their photophysical properties, the red shift of the longest wavelength Q band (which enables lower energy light to be used) along with the increased molar extinction of this band. The majority of second generation PDT sensitizers are chlorins.[7−9]

The major obstacle preventing broader use of chlorins in PDT and artificial photosynthesis is the lack of their efficient synthesis. Routes to chlorins for materials and biological chemistry applications typically employ one of three strategies: (1) derivatization of naturally occurring chlorins,[2] (2) transformation of synthetic porphyrins,[10,11] or (3) total syntheses. The first route provides access to large quantities of starting materials, but restricts control over the pattern of substituents. The transformation of synthetic porphyrins is compatible with diverse substituents, yet it often suffers from adventitious dehydrogenation that regenerates the porphyrin.[10,12] In total syntheses, it is possible to incorporate quaternary carbon atoms in the reduced ring, thereby precluding adventitious dehydrogenation and "locking" the chlorin oxidation state. However, the total syntheses of such stable chlorins are rare and lengthy. Typically they comprise 11−17 steps with the overall yield in the range 0.04−1.1%.[13−15] Despite further remarkable progress in chlorin chemistry over the past decade, mainly due to the work of Lindsey and co-workers,[16] the task of developing novel strategies for the preparation of these tetrapyrrole macrocycles remains a challenge to state-of-the-art synthesis. This fact provided us with the motivation to develop a simpler procedure for the synthesis of inherently stable chlorins.

In our preliminary communication we presented a successful realization of our idea of locked chlorin synthesis via regioselective 1,3-dipolar cycloaddition.[17] Here, we present the full account which outlines the scope and limitations of this method, the building block synthesis, and the relationship between the structure of porphyrins and the efficiency of chlorin formation.

Results and Discussion

Design. Several issues merit particular consideration when contemplating the synthesis of complex chlorins. From the standpoint of synthetic economy, it is desirable to avoid the protecting group manipulations which have come to dominate traditional syntheses. Stabilization of the compounds can be achieved by the introduction of a quaternary carbon atom(s) at the reduced bond. To reduce the total number of steps, while maintaining the 'lock', we considered various strategies. Eventually we chose an approach based on Cavailero's discovery that simple meso-substituted A_4-porprhyrins could act as dienophiles in the Diels−Alder reaction and as dipolarophiles in the 1,3-dipolar cycloaddition.[18] In these reactions, chlorins were formed as the main products but with bacteriochlorin and isobacteriochlorin side products. These interesting results were expanded[19] to also include corroles, sapphyrins, hexaphyrins, and octaphyrins.[20] However, Cavaleiro's approach has some drawbacks: (1) the reaction is not regioselective, (2) chlorins (and bacteriochlorins) formed are intrinsically unstable and can easily oxidize back to porphyrins, and (3) separation could often only be accomplished by preparative TLC. We envisioned that if two electron-withdrawing groups were placed in vicinal positions at the perimeter of the porphyrins, two problems could be solved at the same time. First, the reaction might take place regioselectively, on the bond activated by the two electron-withdrawing groups. Second, the chlorins formed would be locked because of the presence of two quaternary carbon atoms. Such chlorins would be very interesting candidates for various studies provided that (1) the synthesis of respective porphyrins was straightforward, and (2) a potentially broad variety of functional groups could be introduced. An alternative approach, involving only one electron-withdrawing group placed at the β position, was rejected because of uncertain regioselectivity, the

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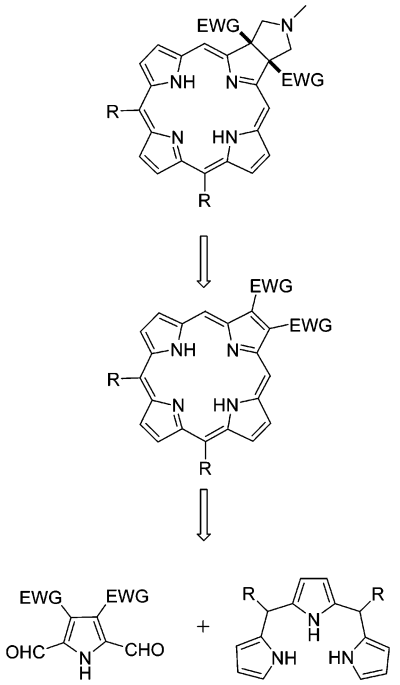
SCHEME 1



formation of two enantiomers, and the equally difficult preparation of the required porphyrins.[21]

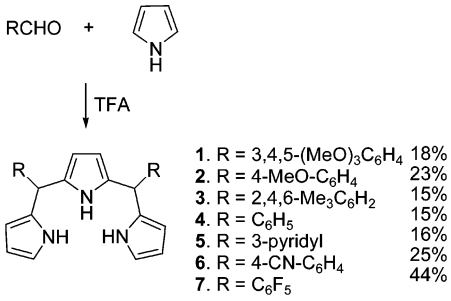
Since porphyrins with such a pattern of substituents were not previously known, we had to devise a method for their synthesis (Scheme 1). We selected porphyrins bearing two meso and two β substituents at designated places (i.e., 2, 3, 10, and 15). In principle, the required porphyrins could be synthesized via a [3 + 1] approach[22] from tripyrranes and 3,4-disubstituted-2,5-pyrroledicarboxaldehydes. Further retrosynthetic disconnection of the required subunits produced pyrrole, aldehydes, and β-ketoesters.

In a preliminary account,[17] we showed that this strategy works for a few combinations of substituents located at β and meso positions. However, a study of the scope and limitations of this promising approach was necessary before applying it to energy/electron-transfer studies and PDT. We designed a very broad group of target porphyrins for the following reasons:

(1) We would like to establish the range of substituents that provide reasonable yields for the porphyrin to chlorin transformation.

(2) We would like to determine if there are any correlations between the results of the final chlorin-forming cycloaddition and the energy of the LUMO orbital and its local distribution. To determine which structural differences do not interfere with the cycloaddition, we prepared a complementary set of porphyrins (bearing the following substituents: 3,4,5-trimethoxyphenyl, 4-methoxyphenyl, mesityl-, phenyl, 4-cyanophenyl, 3-pyridyl, pentafluorophenyl and trifluoromethyl) and evaluated their reactivity. The substituents used span a great range of

SCHEME 2



electron-withdrawing and electron-donating character. At the same time, they form convenient handles for further chemical transformations. Since regioselectivity was a crucial issue in this approach, we felt it was very important to have strong electron-withdrawing subunits, which might cause the formation of two chlorins.

(3) We would like to optimize the efficiency of the building block synthesis and the possible introduction of other electron-withdrawing groups on the pyrrole unit. Various esters, cyano, and keto functionalities were chosen for this study.

Building Block Synthesis. Facile generation of the pivotal porphyrin core, endowed with suitable functionality for further elaboration, relies on the availability of tripyrranes and pyrrole-2,5-dicarboxaldehydes possessing additional electron-withdrawing groups at positions 3 and 4. A broad range of tripyrranes can be synthesized directly from aldehydes and pyrrole via acid-mediated condensation. This reaction however is not selective, and it gives a mixture of dipyrromethanes, tripyrranes, and tetrapyrranes etc. The yields of tripyrranes can be optimized via changing the ratio of aldehyde to pyrrole. Using such a procedure,[23] we synthesized tripyrranes **1**−**7** in 15−44% yield (Scheme 2). The required tripyrranes were separated by column chromatography but were very difficult to purify especially on a larger scale. The limited stability and the existence of the tripyrranes as a mixture of diastereomers and regioisomers contributed to the purification problems. Consequently, they were often used in a partially purified state. The only exception was tripyrrane **8** (Table 2) possessing trifluoromethyl groups, which was synthesized according to the new procedure developed by Dmowski et al.,[24] and was a solid that could be purified by recrystallization.

The synthesis of the second crucial building block, the dialdehydes, represented a significant challenge, since the presence of four electron-withdrawing groups excluded most of the simple routes based on electrophilic substitution. We finally settled on a simple synthesis based on the Paal−Knorr condensation (Scheme 3). Esters of acetoacetic acid **9**−**11** were oxidatively dimerized using I_2[25] or cerium ammonium nitrate (CAN)[26] to give corresponding 1,4-diketones **12**−**14** (yield 22−75%) bearing additional ester functionality. The Paal−Knorr condensation[27] gave symmetrically substituted pyrroles **15**−**17**, respectively, in 73−100% yield. Central to the success of this strategy was the selective oxidation of methyl groups to formyl groups. The model compound **16** was tested with a variety of

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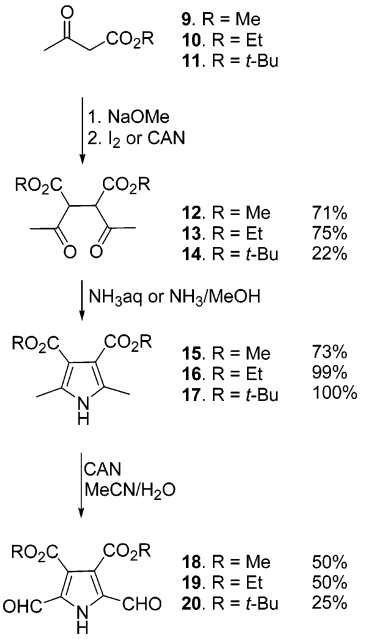
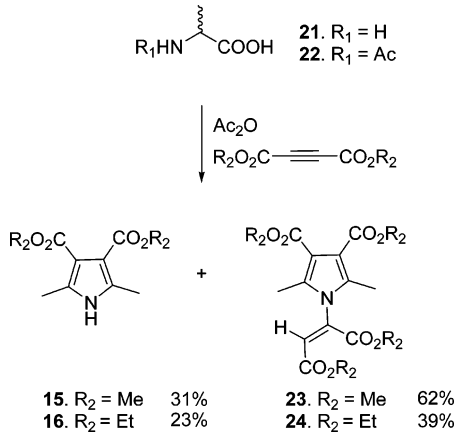
SCHEME 3



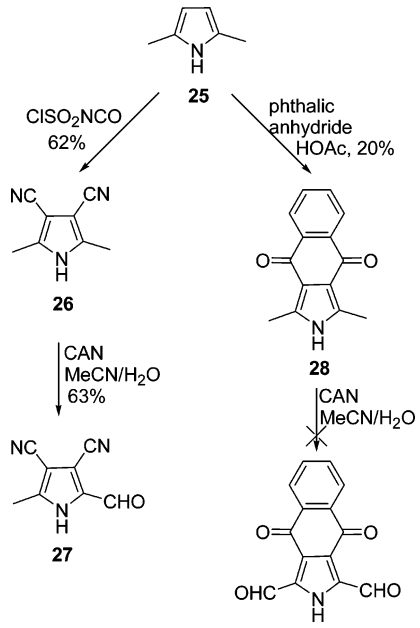
reagents, such as $PbO_2/Pb(CH_3COO)_4$,[28] $Pb(CH_3COO)_4$,[29] 2-iodoxybenzoic acid (IBX), and PCC. In the end, we found that the only reagent capable of oxidizing **16** to dialdehyde **19** was CAN,[30] although extensive modifications had to be made to the existing procedure in order to obtain a reasonable yield. Both original procedures ($MeCN/H_2O$−RT and $HOAc/THF/H_2O$−RT) resulted in the formation of numerous sideproducts and unsatisfactory yields of dialdehyde **19** (<25%). In contrast, performing the reaction in $MeCN/H_2O$ at reflux temperature resulted in a much cleaner reaction, higher yield of product (50%), and, most importantly, easy separation. Application of the optimized method to methyl and *tert*-butyl esters **15** and **17** led smoothly to the dialdehydes **18** and **20** in 25% and 50% yield, respectively (Scheme 3). These fragments, that is, **18**, **19**, and **20**, were thus prepared in three steps with the overall yield of 26%, 37%, and 6%, respectively.

To install the necessary pyrrole building blocks in an even more concise fashion, we employed a Huisgen 1,3-dipolar cycloaddition of azlactones to esters of acetylenedicarboxylic acid.[31] Using this cascade reaction, pyrrole **16** could, in principle, be synthesized from alanine and acetic anhydride. However, Huisgen wrote that the reaction of azlactones derived from α-amino acids bearing aliphatic side chains could not be stopped at the level of compound **16**, and Michael addition of a second molecule of acetylenedicarboxylate occurred to give exclusively **24**.[32] We felt that pyrrole **16** could have been overlooked because of the separation method used by Huisgen and co-workers. To our delight, the exposure of *N*-acetyl-D,L-alanine

SCHEME 4



SCHEME 5



(**22**) to acetic anhydride in the presence of 2 equiv of diethyl acetylenedicarboxylate furnished the expected **24**, accompanied by **16** in 23% yield (Scheme 4). Puzzled with this result we resolved to repeat the reaction with dimethyl acetylenedicarboxylate and performed exactly according to the original Huisgen procedure (D,L-alanine (**21**), 4 equiv of alkyne, 140 °C, 30 min). We obtained ester **15** in 31% yield accompanied by adduct **23** (Scheme 4). While this shorter route to esters **15** and **16** is not comparable in terms of efficiency with previous procedures, it can be very useful for the synthesis of unsymmetrically substituted pyrrole building blocks.

Obviously the replacement of the ester group by another moiety with a stronger electron-withdrawing effect could be beneficial for both regioselectivity and efficiency of the 1,3-dipolar addition. In this context we attempted to synthesize pyrrole-2,5-dialdehydes with cyano or keto groups at positions 3 and 4. One of the most promising routes started from 3,4-dicyano derivative **26,** easily accessed from 2,5-dimethylpyrrole (**25**) as described by Dolphin et al. (Scheme 5).[33] The latter one in turn was subjected to our refined conditions for the CAN-

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TABLE 1. Optimization of the Conditions for the Condensation of Aldehyde 19 with Tripyrrane 6 Leading to Porphyrin 35[a]

entry	TFA concn [M]	substrate concn [mM]	solvent	yield of porphyrin **35**[b] (%)
1	0.026	40	CH_2Cl_2	0
2	0.001	1	CH_2Cl_2	3.4
3	0.01	1	CH_2Cl_2	8.3
4	0.1	1	CH_2Cl_2	17.7
5	0.5	1	CH_2Cl_2	19
6	0.1	1	$CHCl_3$	26
7	0.1	1	$CHCl_3$ + 2.5% EtOH	18.5
8	0.1	1	MeCN	5.7
9[c]	0.1	1	$CHCl_3$	4
10	0.1	10	$CHCl_3$	10.8
11	1.0	10	$CHCl_3$	14
12	1.0	10	$CHCl_3$	26

[a] All reactions were performed under the following constant conditions: 1st step, 15 min, room temperature; 2nd step, 20 min NEt_3, room temperature; 3rd step, 20 min, DDQ (1 equiv versus substrates), room temperature. [b] Isolated yields. [c] TFA was replaced with $BF_3{\cdot}Et_2O$. [d] Each substrate was dissolved in $CHCl_3$ (concentration, 125 mM) and then simultaneously syringed into a stirred solution of TFA in solvent over 15 min.

mediated oxidation. Unfortunately, we obtained monoaldehyde **27** as the only isolable product in 63% yield (Scheme 5). All attempts to further oxidize this compound to dialdehyde using PCC, IBX, SeO_2, or $Pb(OAc)_4$ or directly oxidize **26** to dialdehyde using the same reagents failed. Other unsuccessful approaches to the corresponding dialdehyde are described in the Supporting Information.

Furthermore, keto groups, on the condition that they would not interfere with formyl groups during the porphyrin-forming step, were another interesting option to be considered. One of the promising building blocks was diketone **28**, easily synthesized via the two-step procedure described by Treibs and Jacob[34] (Scheme 5). We tried to transform dimethyl derivative **28** into the corresponding dialdehyde using CAN, PCC, IBX, or $Pb(OAc)_4$ without any success (monoaldehyde was detected using MS). Taken together, these last results show that CAN cannot oxidize methylpyrroles bearing a few strongly electron-withdrawing groups.

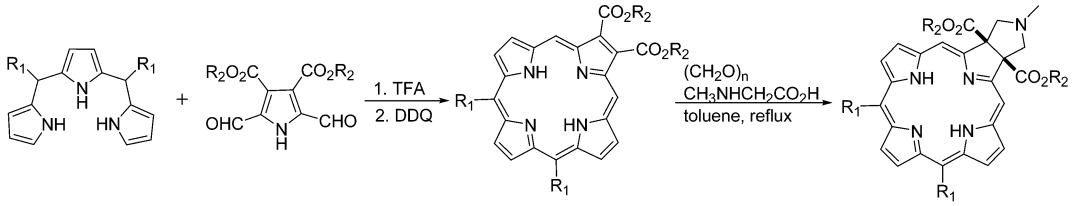
Synthesis of Porphyrins and Chlorins. The next stage of our synthesis involved the construction of the porphyrin ring via a [3 + 1] route. This strategy was extensively studied by Lash,[35] but there are almost no examples for the use of β-unsubstituted tripyrranes in this reaction. Therefore the condensation of model reagents (tripyrrane **6** with aldehyde **19**) was initially performed using the reaction conditions that were developed during our study on the condensation of 5-pentafluorophenyldipyrromethane and aldehydes leading to corroles.[36] Since porphyrin **35** was not detected in this case, we modified the reaction conditions by changing the concentration of TFA and reagents. Various conditions were tested, and the results are shown in Table 1. The increase in the concentration of TFA combined with the dilution of the reaction mixture led to porphyrin **35** in 3.4% yield. A further increase in acid concentration gave the product in an appreciable yield of 19% (Table 1, entry 3−5). The next improvement (26%) was reached with a change in the solvent to $CHCl_3$ which might be attributed to the presence of EtOH in commercially available $CHCl_3$; however, further addition of EtOH to 2.5% led to a decrease in the yield of porphyrin **35**. Changes of solvent and type of acid did not improve the outcome of the process (Table 1, entries 8 and 9). Since the optimal conditions (entry 6) would require large solvent volumes for preparative-scale synthesis, we attempted to increase the reaction concentration. We observed that a 10-fold increase in concentration gave porphyrin **35** in much lower yield (Table 1, entry 10). This trend was overcome to a certain extent by an increase in TFA concentration (entry 11). Finally, simultaneous addition of two reagents into a stirred solution of TFA in a relatively small volume of $CHCl_3$ solved the problem (Table 1, entry 12). One of the most important modifications which we were forced to apply was to replace triethylamine as the neutralizing agent with another base. Reaction quenching with triethylamine always created intractable and persistent emulsions. The use of triethanolamine eliminated this problem because the trifluoroacetate salt of triethanoloamine precipitated from solution after 20 min at room temperature. A simple filtration then removed the byproduct.

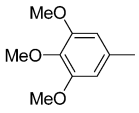
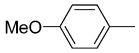
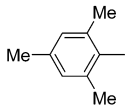
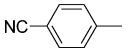
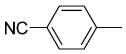
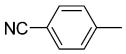
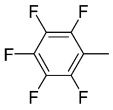
Model aldehyde **19**, bearing ethyl ester functionalities, was used in reactions with all remaining tripyrranes **1**−**5** and **7**−**8** (Table 2). All porphyrin forming reactions proceeded smoothly, and they gave porphyrins **29**−**33**, **37**, and **38** in 7−30% yield. Either electron-donating or electron-withdrawing groups could be used with no significant differences in the results obtained (Table 2). An exceptionally low yield was obtained for porphyrin **38**. This result was attributed to low reactivity of tripyrrane **8** imparted by strongly electron-withdrawing groups. Aldehydes **18** and **20** were coupled with tripyrrane **6** to afford porphyrins **34** and **36** in yields lower (17% and 11%) than for ethyl ester aldehyde **19** (Table 2).

The stage was set for the pivotal cycloaddition reaction, which we approached with some trepidation because of the regioselectivity issue; in principle three regioisomeric chlorins could be formed in this reaction. In this final step, we chose 1,3-dipolar cycloaddition rather than the Diels−Alder reaction for the following reasons: (1) Substrates are commercially available and cheap (1,3-dipoles are generated in situ by thermal decarboxylation of immonium salts obtained from condensation of *N*-methylglycine and paraformaldehyde, in contrast to reactive diene precursors used to date in the Diels−Alder reaction with porphyrins). (2) The presence of a pyrrolidine ring in the product imparts some polarity which should facilitate separation from possible unreacted porphyrin. Our first model, porphyrin **35**, gave excellent results with 100% conversion and 30% yield of the isolated purified product, utilizing slightly modified Cavaleiro's conditions (Table 2). To achieve full conversion of porphyrin **35** we had to increase the reaction time and amounts of dipole precursors. We tried to improve the yield by performing the reaction with other forms of formaldehyde and in different solvents. The reaction in toluene with trioxane gave 32% yield, whereas reactions carried out in DMF in the presence of paraformaldehyde, trioxane, and formaline gave chlorin **45** in 0%, 0%, and 21% yield, respectively. Results revealed that the desired chlorin **45** formed with full regioselectivity. The structure of chlorin **45** was confirmed by the analysis of the ^1H NMR spectrum and mass spectrometry. The formation of bacteriochlorin and isobacteriochlorin was not observed. All other porphyrins **29**−**34** and **36**−**38** were subjected to the same conditions and gave chlorins **39**−**48** in 10−57% yield (Table

(34) Treibs, A.; Jacob, K. *Liebigs Ann. Chem.* **1970**, *740*, 196−199.
(35) Lash, T. D. In *Porphyrin Handbook*; Kadish, K. M., Smith, K. M., Guilard, R., Eds.; Academic Press: San Diego, CA, 2000; Vol. 2, pp 125−199.
(36) Gryko, D. T.; Koszarna, B. *Synthesis* **2004**, 2205−2209.

TABLE 2. Results of the Synthesis of Porphyrins 29−38 and Chlorins 39−48, as Well as LUMO Energy of Chlorins



Tripyrrane	R_1	R_2	Porphyrin	Yield	Chlorin	Yield	Reaction Time	LUMO (eV)
1		Et	**29**	12%	**39**	42%	1 week	-2.54
2		Et	**30**	11%	**40**	47%	48h	-2.54
3		Et	**31**	30%	**41**	57%	72h	-2.57
4		Et	**32**	16%	**42**	21%	24h	-2.57
5		Et	**33**	17%	**43**	42%	48h	-2.76
6		Me	**34**	17%	**44**	35%	24h	-2.98
6		Et	**35**	26%	**45**	43%	24h	-2.95
6		*t*-Bu	**36**	11%	**46**	47%	24h	-2.92
7		Et	**37**	15%	**47**	30%	10h	-2.96
8	CF_3	Et	**38**	7%	**48**	10%	2h	-3.07

2). Reactions were always carried out until the disappearance of the starting porphyrin. Depending on the substituents present, this meant reaction times varied from 2 h to 1 week. The presence of strongly electron-donating groups at meso positions 10 and 15 greatly lowered the rates of these reactions, with full conversion taking 1 week under these conditions. The electronic character of the meso substituent appears to dictate the yield, with the strongest electron-donating groups affording the highest yields. Cavaleiro and co-workers showed that the presence of electron-withdrawing groups at meso positions increased the yield of the cycloaddition reactions to the porphyrin.[18c] Our examples prove that, if electron-withdrawing groups are introduced at β positions, the presence of electron-withdrawing groups at meso position is no longer necessary for the successful 1,3-dipolar cycloaddition. To demonstrate the practical potential of the approach, selected examples were examined under preparative scale conditions, furnishing 200 mg of chlorins **45** and **47**.

Numerous attempts to obtain X-ray quality crystals of any of 10 prepared chlorins failed. Finally, we were able to obtain crystals of chlorin **45** × TFA suitable for single-crystal X-ray diffraction analysis (Figure 1). This analysis fully confirms the expected structure of this molecule. Chlorin ring is slightly deformed from planarity.

One of our fundamental objectives to be established before this methodology would be implemented on a larger scale was the relationship between the structure of the porphyrin and the yield of the chlorin. In this context, DFT calculations of the energy of the lowest unoccupied molecular orbital (LUMO) of the dipolarophile (porphyrin) were performed. The geometry of the molecule was first optimized (B3LYP 3-21G*) and then the LUMO was calculated using B3LYP 6-311G*. It is well-known that azomethine ylide dipoles are characterized by a high-lying highest occupied molecular orbital (HOMO) and LUMO. Consequently, the dominant interaction is between the dipole HOMO and the dipolarophile LUMO. The LUMO energy of all porphyrins used is presented in Scheme 7 (and in Figure S1 in Supporting Information). The correlation between the energy of the dipole LUMO and the reaction time is clearly visible. The gap between the dipolarophile LUMO and the dipole HOMO is the smallest for porphyrin **38** bearing two CF_3 groups (reaction time 2 h). On the antipode we have porphyrin **29** with

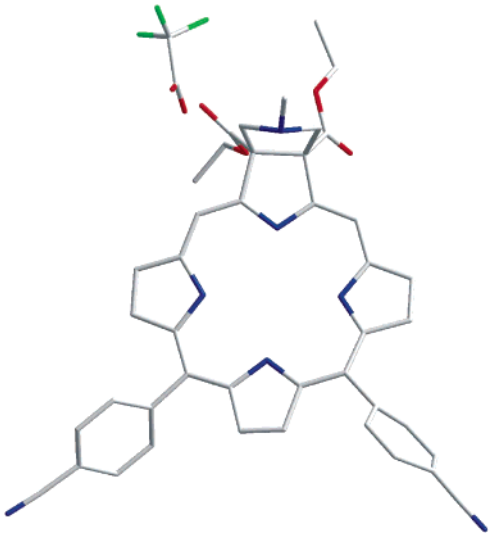


FIGURE 1. X-ray structure of chlorin **45** × TFA (hydrogens were omitted for clarity).

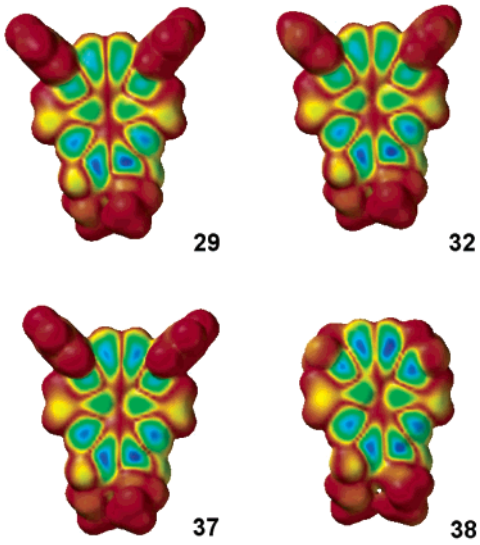


FIGURE 2. LUMO maps of porphyrins **29**, **32**, **37**, and **38** calculated at the B3LYP/6-31G* level of DFT with a G-31G* basis set using Spartan′04 for Windows.

a LUMO that is 0.53 eV higher and needed 1 week to react completely.

We also decided to calculate the so-called "LUMO-map", in which the absolute value of the LUMO is mapped onto a size surface. The LUMO-map (Figure 2) shows which regions of the molecule are most electron deficient (blue color) and, hence, most subject to nucleophilic attack.[37] For the most interesting case, porphyrin **38**, it can be seen that there is an equal probability of the reaction occurring in two different positions, yet only one regioisomer is formed in this reaction. In fact, the yield of chlorins is the lowest in this case and the highest when the difference of the local LUMO between two double bonds—the one activated by two ester groups and the opposite one—is the highest (porphyrins **29**−**31**, Table 2).

(37) Hehre, W. J. *A Guide to Molecular Mechanics and Quantum Chemical Calculations*; Wavefunction Inc.: Irvine, CA, 2003.

Visual observations revealed that chlorins bearing electron-withdrawing or sterically hindered groups at meso positions are green, while other chlorins were distinctly violet-green. The UV−vis spectra of these compounds (see Supporting Information) provided an explanation of this phenomenon. The absorption spectrum of chlorins **41**, **47**, and **48** shows that the ratio of a Soret band (∼408 nm) to last Q band (∼641 nm), is ∼3.5 while for the rest of the chlorins it is ∼5 (Figure 2, Supporting Information). The last Q band is significantly stronger than in the case of chlorins **45** and **46.**

Conclusions. The chemistry described herein demonstrates the power of 1,3-dipolar cycloaddition with porphyrins to construct inherently stable (locked) chlorins. Our studies have clearly documented the ability of this strategy to assemble chlorin skeletons with excellent regioselective control. By using this optimized sequence, chlorins could be prepared from commercially available reagents in just six steps in a higher overall yield than any previous approach based on total synthesis. The scope of this approach proved to be remarkably broad: all substituents studied were tolerated and could be used at meso positions around the chlorin scaffold. This should allow for fine-tuning of the photophysical properties for energy transfer and PDT studies. The yield of cycloaddition was found to be surprisingly dependent upon the electron-withdrawing and electron-donating substituents located at the meso positions. The exploration of the chemistry of pyrroles allowed us to obtain key building blocks in very good overall yields. Additionally, the utility and limitations of CAN-mediated oxidation of methylpyrroles has been demonstrated. In terms of efficiency, the standard ethyl ester group placed on the β positions generally offered the best yield for both substrate synthesis and porphyrin and chlorin formation. We found that the yield of porphyrins strongly depended on the concentration of reagents and TFA. The optimized conditions differ from the typical ones used for β-substituted tripyrranes in that the concentration of TFA is much higher ([TFA] = 1.00 M). Chlorins bearing strongly electron-withdrawing or sterically hindered substituents were found to possess significantly stronger last Q band than the rest of the studied chlorins. Furthermore the extraordinary ease with which the starting materials for these reactions can be prepared, coupled with the striking complexity which is attainable in one step, makes this protocol ideal for the generation of a range of chlorins. Applications of this knowledge to the synthesis of complex chlorins should facilitate their further evaluation with regard to their chemistry and medicine.

Experimental Section

6,12-Bis(3,4,5-trimethoxyphenyl)tripyrrane (1). The solution of 3,4,5-trimethoxybenzaldehyde (10 mmol, 1.96 g) in pyrrole (50 mmol, 3.47 mL) was stirred for 5 min at room temperature under argon atmosphere, and then TFA (1 mmol, 77 μL) was added. The whole mixture was stirred for 30 min and then combined with aqueous NaOH (0.1 M, 10 mL) in order to quench the reaction. The mixture was extracted with CH_2Cl_2, and the organic layer was dried (Na_2SO_4). The solvents were removed under vacuum. Chromatography of the resulting dark brown oil (silica, CH_2Cl_2/ethyl acetate 95:5) afforded the product (0.5 g, 18%): R_f 0.51 (CH_2Cl_2/ethyl acetate, 9:1). HRMS (EI): calcd for $C_{32}H_{35}N_3O_6$ [M^+], 557.2526; found, 557.2520. Anal. Calcd for $C_{32}H_{35}N_3O_6$ C, 68.92; H, 6.33; N, 7.54. Found: C, 68.78; H, 6.44; N, 7.72.

6,12-Dimesityltripyrrane (3). The solution of mesitaldehyde (10 mmol, 1.47 mL) in pyrrole (50 mmol, 3.47 mL) was stirred for 10 min at room temperature under argon atmosphere, and then TFA

(1 mmol, 77 μL) was added. The whole mixture was stirred for 30 min and then combined with aqueous NaOH (0.1 M, 10 mL) in order to quench the reaction. The mixture was extracted with CH_2Cl_2, and the organic layer was dried (Na_2SO_4). The solvent was removed under vacuum, and the resulting dark brown oil was distilled under vacuum. 5-Mesityldipyrromethane was distilled off at 180−200 °C (0.5 mmHg). Chromatography (silica, ethyl acetate/hexane, 1:9) of the remaining black solid afforded the product (0.35 g, 15%): R_f, 0.60 (ethyl acetate/hexane, 1:3). HRMS (EI): calcd for $C_{32}H_{35}N_3$ [M^+], 461.2831; found, 461.2821.

6,12-Bis-(3-pyridyl)tripyrrane (5). The solution of 3-pyridinecarboxaldehyde (75 mmol, 7.15 mL) in pyrrole (1.0 mol, 70 mL) was heated in 85 °C for 24 h. After the mixture was cooled, pyrrole was evaporated under vacuum. Chromatography of the residue (silica, CH_2Cl_2/MeOH, 99:1) afforded 5-(3-pyridyl)dipyrromethane (10.3 g, 62%) and the desired product **5** (2.28 g, 16%): R_f, 0.37 (CH_2Cl_2 /MeOH, 9:1). HRMS (EI): calcd for $C_{10}H_{10}NO_6$ [M^+], 379.1797; found, 379.1790.

3,4-Diacetylsuccinic Acid Di-*t*-butyl Ester (14). After sodium metal (0.1 mol, 2.3 g) was dissolved in warm *tert*-butyl alcohol, *tert*-butyl acetoacetate (0.1 mol, 16.6 mL) was added, and the mixture was stirred in a homogeneous state for 1 h. Subsequently *tert*-butyl alcohol was removed in vacuo, the residue was suspended in dry ether (150 mL), and a solution of iodine (0.05 mol, 12.7 g) in dry THF (50 mL) was added dropwise with vigorous stirring until the reaction mixture started to get purple. Next the reaction mixture was filtered, and the solvent was evaporated. Crystallization from AcOEt/hexane afforded the pure product (3.45 g, 22%): mp 87−89 °C (ethyl acetate/hexane). IR ν_{max}/cm^{-1}: 3013, 2986, 2944, 1729, 1710, 1373, 1356, 1250, 1152, 1136. ^{1}H NMR (500 MHz, $CDCl_3$, Me_4Si, δ ppm): 1.43 (s, 18H), 2.40 (s, 6H), 4.35 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$, Me_4Si, δ ppm): 27.8, 59.0, 82.9, 166.2, 201.9. HRMS (ESI): calcd for $C_{16}H_{26}O_6Na$ [$M + Na^+$], 337.1622; found, 337.1636. Anal. Calcd for $C_{16}H_{26}O_6$: C, 61.13; H, 8.34. Found: C, 60.80; H, 8.52.

2,5-Dimethyl-pyrrole-3,4-dicarboxylic Acid Dimethyl Ester (15). Method A. 3,4-Diacetylsuccinic acid dimethyl ester **12**[26] (11.5 g, 0.05 mol) was dissolved in methanolic ammonia solution (50 mL, 2 M) and stirred for 1 h. Subsequently ethyl acetate (250 mL) was added, and the reaction mixture was extracted with aqueous HCl solution (5%), washed three times with water, and dried (Na_2SO_4). Next, solvent was evaporated, and the product was crystallized from AcOEt/hexane (7.7 g, 73%): mp 115−117 °C (ethyl acetate/hexane) (lit. 118−119 °C[38]).

Method B. D,L-Alanine (890 mg, 10 mmol) was suspended in Ac_2O (15 mL), and dimethyl acetylenedicarboxylate (5.0 mL, 41 mmol) was added. The reaction mixture was maintained at 140 °C for 30 min, cooled, and evaporated under reduced pressure. The oily residue was chromatographed (dry column vacuum chromatography[39] (DCVC), CH_2Cl_2 then CH_2Cl_2/MeOH, 99:1, 98:2) to afford compound **23** as yellowish crystals (2.17 g, 62% yield; mp 118−119 °C [lit. 119−120 °C][32]) and compound **15** as white crystals (647 mg, 31% yield; mp 116−118 °C [lit. 118−119 °C[38]]).

Diethyl 2,5-Dimethyl-pyrrole-3,4-dicarboxylate (16). This compound was obtained according to ref 27 and via 1,3-dipolar cycloaddition: *N*-Acetyl-D,L-alanine (1.31 g, 10 mmol) was suspended in Ac_2O (10 mL), and diethyl acetylenedicarboxylate (3.2 mL, 20 mmol) was added. The reaction mixture was maintained at 110 °C for 2 h, cooled, and evaporated under reduced pressure. The oily residue was dissolved in hot cyclohexane and left in the refrigerator overnight with crystal seeds. White needles of **16** were filtered (274 mg). The filtrate was evaporated and chromatographed (DCVC, CH_2Cl_2 then CH_2Cl_2/EtOH, 99:1, 98:2) to afford compound **24** as yellowish oil (1.58 g, 39% yield). ^{1}H NMR (500 MHz, $CDCl_3$, Me_4Si, δ ppm): 1.11 (t, J = 7.0 Hz, 3H), 1.26−1.38 (m, 9H), 2.20 (s, 6H), 4.10 (q, J = 7.0 Hz, 2H), 4.21−4.39 (m, 6H), 7.39 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, Me_4Si, δ ppm): 11.1, 13.6, 14.0, 14.2, 60.0, 61.9, 63.0, 113.2, 131.8, 134.0, 135.2, 162.2, 162.4, 165.2. HRMS (EI): calcd for $C_{20}H_{27}NO_8$ [M^+], 409.1737; found, 409.1727. Anal. Calcd for $C_{20}H_{27}NO_8$: C, 58.67; H, 6.65; N, 3.42. Found: C, 58.50; H, 6.63; N, 3.51. Also an additional crop of compound **16** as white needles was obtained (278 mg, overall yield 23%): mp 96−98 °C (lit. 94−97 °C).[38]

2,5-Dimethyl-pyrrole-3,4-dicarboxylic Acid Di-*t*-butyl Ester (17). 3,4-Diacetylsuccinic acid di-*tert*-butyl ester (**14**) (17 g, 0.054 mol) was suspended in aqueous ammonia solution (80 mL, 25%) and stirred for 1 h. Filtration and washing three times with water afforded pure product (16.0 g, 100%): mp. 220 °C (dec). IR ν_{max} (KBr)/cm^{-1}: 3315, 2979, 1705, 1447, 1365, 1302, 1179, 1100. ^{1}H NMR (500 MHz, $CDCl_3$, Me_4Si, δ ppm): 1.54 (s,18H), 2.30 (s, 6H), 8.35 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, Me_4Si, δ ppm): 12.4, 28.4, 80.0, 114.0, 131.3, 164.6. HRMS (EI): calcd for $C_{16}H_{25}NO_4$ [M^+], 295.1784;, found, 295.1772. Anal. Calcd for $C_{16}H_{25}NO_4$: C, 65.06; H, 8.53; N, 4.74. Found: C, 64.92; H, 8.72; N, 4.54.

2,5-Diformyl-pyrrole-3,4-dicarboxylic Acid Dimethyl Ester (18). 2,5-Dimethyl-pyrrole-3,4-dicarboxylic acid dimethyl ester (**15**) (5.28 g, 25 mmol) was dissolved in mixture of acetonitrile (750 mL) and water (125 mL). CAN (110 g, 0.2 mol) was added, and the mixture was stirred at 80 °C for 5 h. Then the reaction mixture was cooled to room temperature, and water (200 mL) was added. The layers were separated, and the aqueous layer was extracted with ethyl acetate (100 mL). The combined organic layers were washed again with water, dried (Na_2SO_4), and concentrated. After crystallization (hexane/ethyl acetate), the product was isolated. This solid was dried in vacuo (3.0 g, 50%): mp. 112−113 °C (ethyl acetate/hexane). IR ν_{max} (KBr)/cm^{-1}: 3267, 1735, 1717, 1682, 1508, 1292, 1227, 1104. ^{1}H NMR (500 MHz, $CDCl_3$, Me_4Si, δ ppm): 3.97 (s, 6H), 10.11 (s, 2H), 10.50 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, Me_4Si, δ ppm): 52.8, 122.8, 133.3, 162.4, 181.5. HRMS (EI): calcd for $C_{10}H_9NO_6$ [M^+], 239.0430; found, 239.0424.

2,5-Diformyl-pyrrole-3,4-dicarboxylic Acid Diethyl Ester (19). 2,5-Dimethyl-pyrrole-3,4-dicarboxylic acid diethyl ester **16**[27] (8.4 g, 35 mmol) was dissolved in a mixture of acetonitrile (1050 mL) and water (175 mL). Then CAN (172.7 g, 315 mmol) was added, and the resulting mixture was stirred at 80 °C for 5 h. Then it was cooled to room temperature, and water (200 mL) was added. The layers were separated, and the aqueous layer was extracted with ethyl acetate (100 mL). The combined organic layers were washed again with water, dried (Na_2SO_4), and concentrated. Column chromatography (silica, hexane/ethyl acetate, 3:2) afforded a pale yellow oil which was cooled in the refrigerator and then warmed back to room temperature. After this operation was repeated, oil turned into crystals of the product (4.7 g, 50%): mp 41−43 °C. IR (CH_2Cl_2)/cm^{-1}: 3229 (br), 2984, 1716, 1688, 1502, 1284, 1225, 1101. ^{1}H NMR (500 MHz, $CDCl_3$, Me_4Si, δ ppm): 1.33 (t, 6H, J = 7.1 Hz), 4.34 (q, 4H, J = 7.1 Hz, 4H), 10.02 (s, 2H), 10.47 (s,1H). ^{13}C NMR (125 MHz, $CDCl_3$, Me_4Si, δ ppm): 14.39, 62.70, 123.60, 134.24, 163.44, 182.61. HRMS (EI): calcd for $C_{12}H_{13}NO_6$ [M^+], 267.0743; found, 267.0732. Anal. Calcd for $C_{12}H_{13}NO_6$: C, 53.93; H, 4.90; N, 5.24. Found: C, 53.86; H, 5.08; N, 5.30.

2,5-Diformyl-pyrrole-3,4-dicarboxylic Acid Di-*t*-butyl Ester (20). 2,5-Dimethyl-pyrrole-3,4-dicarboxylic acid di-*tert*-butyl ester (**17**) (886 mg, 3 mmol) was dissolved in mixture of acetonitrile (90 mL) and water (15 mL). CAN (14.8 g, 27 mmol) was added, and the mixture was stirred at room temperature for 20 h. Then water (200 mL) was added. The layers were separated, and the aqueous layer was extracted with ethyl acetate (100 mL). The combined organic layers were washed again with water, dried (Na_2SO_4), and concentrated. After crystallization (hexane/ethyl acetate), product was isolated. This solid was dried in vacuo (240 mg, 25%): mp 143−145 °C (ethyl acetate/hexane). IR ν_{max} (KBr)/cm^{-1}: 3.145, 2981, 1732, 1709, 1687, 1498, 1370, 1298, 1234, 1161, 1108. ^{1}H NMR (500 MHz, $CDCl_3$, Me_4Si, δ ppm): 1.61 (s, 18H), 10.10

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(s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$, Me_4Si, δ ppm): 28.18, 83.30, 125.0, 132.7, 160.9, 181.6. HRMS (ESI): calcd for $C_{16}H_{25}NO_4Na$ [M + Na^+], 346.1261; found, 346.1266. Anal. Calcd for $C_{16}H_{21}NO_6$: C, 59.43; H, 6.55; N, 4.33. Found: C, 59.23; H, 6.42; N, 4.34.

3,4-Dicyano-2-formyl-5-methylpyrrole (27). 2,5-Dimethyl-3,4-dicyanopyrrole (435 mg, 3 mmol) was dissolved in mixture of acetonitrile (90 mL) and water (15 mL). Then CAN (4.5 equiv, 7.4 g) was added, and the mixture was stirred at 80 °C for 5 h. Then the reaction mixture was cooled to room temperature, and water (200 mL) was added. The layers were separated, and the aqueous layer was extracted with ethyl acetate (100 mL). The combined organic layers were washed again with water, dried (Na_2SO_4), and concentrated. Chromatography (toluene/ethyl acetate 4:1) afforded the product (300 mg, 63%): mp. 158−160 °C (ethyl acetate/hexane). IR ν_{max} (KBr)/cm^{-1}: 3201, 3131, 2249, 2239, 1677, 1517, 1421, 1257, 1257, 1016, 881. ^{1}H NMR (200 MHz, $(CD_3)_2SO$, δ ppm): 2.41 (s, 3H), 9.63 (s, 1H), 13.6 (s, 1H, br). ^{13}C NMR (50 MHz, $(CD_3)_2CO$, Me_4Si, δ ppm): 11.9, 95.8, 100.6, 112.1, 112.9, 135.4, 144.6, 178.2. HRMS: calcd for $C_8H_5N_3O$ [M^+], 159.0433; found, 159.0429.

General Procedure for the Synthesis of Porphyrins: To a vigorously stirred solution of TFA (7.7 mL, 0.1 mol) in chloroform (100 mL), solutions of tripyrrane (1 mmol) in chloroform (10 mL) and aldehyde (1 mmol) in chloroform (10 mL) were simultaneously added during 15 min. Then the reaction was stirred for 10 min, and the solution of DDQ (227 mg, 1 mmol) in toluene (2 mL) was added. After an additional 10 min of stirring, the reaction mixture was quenched using triethanoloamine (15.2 g, 0.1 mol). The reaction mixture was then cooled for 20 min in the refrigerator and filtered. Black crystals of salt (triethanoloammonium trifluoroacetate) were washed with ethyl acetate until they became pale green and solvent was evaporated. The purification details are described for each case as follows.

10,15-Dimesityl-22,24-dihydro-porphine-3,4-dicarboxylic Acid Diethyl Ester (31). Dry column vacuum chromatography (silica, toluene/ethyl acetate, 99:1) afforded product as a purple solid which was recrystallized from CH_2Cl_2/hexane (207 mg, 30%): R_f = 0.73 (silica, toluene/ethyl acetate 9:1). λ_{max} (toluene)/nm: 421 (ϵ/dm^3 mol^{-1} cm^{-1} 210000), 515 (13000), 553 (6000), 596 (4300), and 651 (4100). ^{1}H NMR (500 MHz, $CDCl_3$, Me_4Si, δ ppm): −2.96 (s, 2H), 1.73 (t, 6H, J = 7.2 Hz), 1.84 (s, 12H), 2.63 (s, 6H), 4.90 (q, 4H, J = 7.2 Hz), 7.28 (s, 4H), 8.60 (s, 2H), 8.87 (d, 2H, J = 2.7 Hz), 9.40 (d, 2H, J = 2.7 Hz), 10.70 (s, 2H). HRMS (ESI): calcd for $C_{44}H_{43}N_4O_4$ [M + H^+], 691.3279; found, 691.3250. Anal. Calcd for $C_{44}H_{42}N_4O_4$: C, 76.50, H, 6.13, N, 8.11; Found: C, 76.25, H, 6.32, N, 8.01.

10,15-Bis(3-pyridyl)-22,24-dihydro-porphine-3,4-dicarboxylic Acid Diethyl Ester (33). Dry column vacuum chromatography (silica, CH_2Cl_2/MeOH, 98:2) afforded the product as a purple solid which was recrystallized from CH_2Cl_2/hexane (103 mg, 17%): R_f = 0.65 (silica, CH_2Cl_2/MeOH 95:5). λ_{max} (toluene)/nm: 422 (ϵ/dm^3 mol^{-1} cm^{-1} 199000), 515 (12200), 553 (5270), 594 (4270), and 649 (3820). ^{1}H NMR (200 MHz, $CDCl_3$, Me_4Si, δ ppm): −3.23 (s, 2H), 1.75 (t, 6H, J = 7.1 Hz), 4.93 (q, 4H, J = 7.1 Hz), 7.77−7.83 (m, 2H), 8.51 (s, 2H), 8.79 (s, 2H), 9.03 (d, 2H, J = 4.7 Hz), 9.10 (dd, 2H, J = 4.9 Hz), 9.47 (s, 2H), 9.55 (d, 2H, J = 4.7 Hz), 10.83 (s, 2H). HRMS (EI): calcd for $C_{36}H_{29}N_6O_4$ [M + H^+], 609.2245; found, 609.2250.

10,15-Bis(trifluoromethyl)-22,24-dihydro-porphine-3,4-dicarboxylic Acid Diethyl Ester (38). Dry column vacuum chromatography (silica, toluene/ethyl acetate, 99:1) afforded product as purple solid which was recrystallized from CH_2Cl_2/hexane (41 mg, 7%): R_f = 0.5 (silica, toluene/ethyl acetate 9:1). λ_{max} (toluene)/nm: 413 (ϵ/dm^3 mol^{-1} cm^{-1} 106000), 515 (6660), 551 (10700), and 582 (5000). ^{1}H NMR (500 MHz, $CDCl_3$, Me_4Si, δ ppm): −4.47 (s, 2H), 1.77 (t, 6H, J = 7.2 Hz), 4.91 (q, 4H, J = 7.2 Hz), 9.25 (d, 2H, J = 4.4 Hz), 9.42 (s, 2H), 9.52 (s, 2H), 10.27 (s, 2H). HRMS: calcd for $C_{28}H_{21}F_6N_4O_4$ [M + H^+], 591.1462; found, 591.1484. Anal. Calcd for $C_{28}H_{20}F_6N_4O_4 \cdot 0.5H_2O$: C, 56.10; H, 3.53; N, 9.35. Found: C, 55.71; H, 3.33; N, 9.16.

General Procedure for the Synthesis of Chlorins: Porphyrin (0.1 mmol), paraformaldehyde (10 equiv), and sarcosine (4 equiv) were placed in dry toluene (20 mL). Then flask was flushed with argon and refluxed with Dean−Stark apparatus. Every 5 h the next portions of paraformaldehyde (10 equiv) and sarcosine (4 equiv) were added until all porphyrin disappeared. Subsequently, the reaction mixture was cooled, and the solvent was removed by rotary evaporation. The purification details are described for each case as follows.

Chlorin 41. Dry column vacuum chromatography [silica, toluene/ethyl acetate (9:1)] afforded the product as a green solid which was recrystallized from MeOH (43 mg, 57%): R_f = 0.5 (silica, toluene/ethyl acetate 4:1). λ_{max} (toluene)/nm: 413 (ϵ/dm^3 mol^{-1} cm^{-1} 119000), 507 (13300), 530 (5090), 587 (4760), and 637 (34000). ^{1}H NMR (500 MHz, $CDCl_3$, Me_4Si, δ ppm): −2.04 (s, 2H), 1.15 (t, 6H, J = 7.1 Hz), 1.79 (s, 6H), 1.89 (s, 6H), 2.24 (s,3H), 2.59 (s, 6H), 3.79 (d, 2H, J = 9.6 Hz), 4.07 (d, 2H, J = 9.6 Hz), 4.25 (q, 4H, J = 7.1 Hz), 7.22 (s, 2H), 7.23 (s, 2H), 8.29 (s, 2H), 8.61 (d, 2H, J = 4.5 Hz), 8.82 (d, 2H, J = 4.5 Hz), 9.09 (s, 2H). HRMS (ESI): calcd for $C_{47}H_{50}N_5O_4$ [M + H^+], 748.3857; found, 748.3848.

Chlorin 43. Dry column vacuum chromatography (silica, CH_2Cl_2/MeOH, 95:5) afforded the product as a purple solid which was recrystallized from CH_2Cl_2/hexane (28 mg, 42%): R_f = 0.63 (silica, CH_2Cl_2/MeOH 95:5). λ_{max} (toluene)/nm: 413 (ϵ/dm^3 mol^{-1} cm^{-1} 116000), 507 (10300), 587 (2840), and 637 (22700). ^{1}H NMR (500 MHz, $(CD_3)_2SO$, Me_4Si, 100 °C, δ ppm): −2.3 (s, 2H), 1.16 (t, 6H, J = 7.1 Hz), 2.19 (s, 3H), 3.77 (d, 2H, J = 10.0 Hz), 4.08 (d, 2H, J = 10.0 Hz), 4.30−4.22 (m, 4H), 7.84 (ddd, 2H, J_1 = 0.7 Hz, J_2 = 5.0 Hz, J_3 = 7.7 Hz), 8.44 (s,2H), 8.52 (m, 2H), 8.79 (d, 2H, J = 4.7 Hz), 9.02 (dd, 2H, J_1 = 1.6 Hz, J_2 = 5.0 Hz), 9.25 (d, 2H, J = 4.7 Hz), 9.27 (dd, 2H, J_1 = 0.7 Hz, J_2 = 2.2 Hz), 9.38 (s, 2H). HRMS (ESI): calcd for $C_{39}H_{36}N_7O_4$ [M + H^+], 666.2823; found, 666.2824.

Chlorin 48. Dry column vacuum chromatography (silica, toluene/ethyl acetate, 9:1) afforded the product as a purple-green solid which was recrystallized from CH_2Cl_2/hexane (4.5 mg, 7%): R_f = 0.38 (silica, toluene/ethyl acetate 4:1). λ_{max} (toluene)/nm: 400 (ϵ/dm^3 mol^{-1} cm^{-1} 128000), 501 (12900), 599 (5510), and 654 (40000). ^{1}H NMR (500 MHz, $CDCl_3$, Me_4Si, δ ppm): −2.97 (s, 2H), 1.14 (t, 6H, J = 7.1 Hz), 2.26 (s, 3H), 3.82 (d, 2H, J = 10.1 Hz), 4.13 (d, 2H, J = 10.1 Hz), 4.27 (q, 4H, J = 7.1 Hz), 9.18 (dd, 2H, J_1 = 1.5 Hz, J_2 = 4 Hz), 9.45 (s, 2H), 9.47 (m, 2H), 9.73 (m, 2H). HRMS (ESI): calcd for $C_{31}H_{28}F_6N_5O_4$ [M + H^+], 648.2040; found, 648.2065.

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Supporting Information Available: Description of unsuccessful attempts to synthesize 2,5-diformyl-3,4-dicyano-pyrrole; ^{1}H NMR spectra for compounds **18**, **27**, **29**, **30**, **32**, **33**, **35**, **37**−**48**; ^{13}C NMR spectra for compounds **18** and **27** as well as UV−vis spectra of chlorins **41**, **45**, **47**, and **48**. This material is available free of charge via the Internet at http://pubs.acs.org.

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