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Synthesis of Functionalized *trans*-A_2B_2-Porphyrins Using Donor–Acceptor Cyclopropane-Derived Dipyrromethanes

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Dedicated to Professor Dr. Harry Kurreck on occasion of his 80th birthday.

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Abstract: *meso*-Substituted *trans*-A_2B_2-porphyrins bearing specific patterns of substituents are crucial building blocks in porphyrin-based biomimetic systems and molecular materials and can be used for the construction of well-defined porphyrin-based architectures. A new stepwise and rational synthesis of functionalized *trans*-A_2B_2-porphyrins is reported in which for the first time donor–acceptor-substituted cyclopropane precursors (d–a cyclopropanes) are exploited. The three presented d–a cyclopropanes are readily accessible in a multi-gram scale and serve as aldehyde equivalents in the reaction with an excess of pyrrole to afford the corresponding dipyrromethanes (DPMs). The three DPMs were synthesized in yields of 60–74%. They are stable in purified form in the absence of light and air and were subsequently condensed with a wide range of aliphatic and aromatic aldehydes bearing electron-donating or electron-withdrawing substituents followed by oxidation to form the corresponding *trans*-A_2B_2-porphyrins. Fourteen functionalized porphyrins were synthesized in yields of 14–31%, indicating the broad scope of the synthetic procedure. The possibility to introduce key functional groups is emphasized, which enables subsequent modification of these porphyrins with moieties inducing biological activity. Modification of the tetrapyrroles may occur by addition to one of the porphyrin peripheral double bonds, the use of substituents of the aryl groups or *via* the methoxycarbonyl group at two of the *meso*-substituents. Three examples of porphyrins were converted into the corresponding 7,8-dihydroxychlorins by osmium-mediated dihydroxylation and one of the resulting chlorins was subjected to saponification to give a highly polar chlorin dicarboxylic acid. A 4-bromophenyl-substituted d–a cyclopropane was prepared by rhodium-catalyzed cyclopropanation and then transformed into a DPM which was subsequently condensed to a porphyrin. Its Zn complex allowed a Heck reaction to afford the functionalized bis(alkenyl)-substituted *trans*-A_2B_2-Zn-porphyrin.

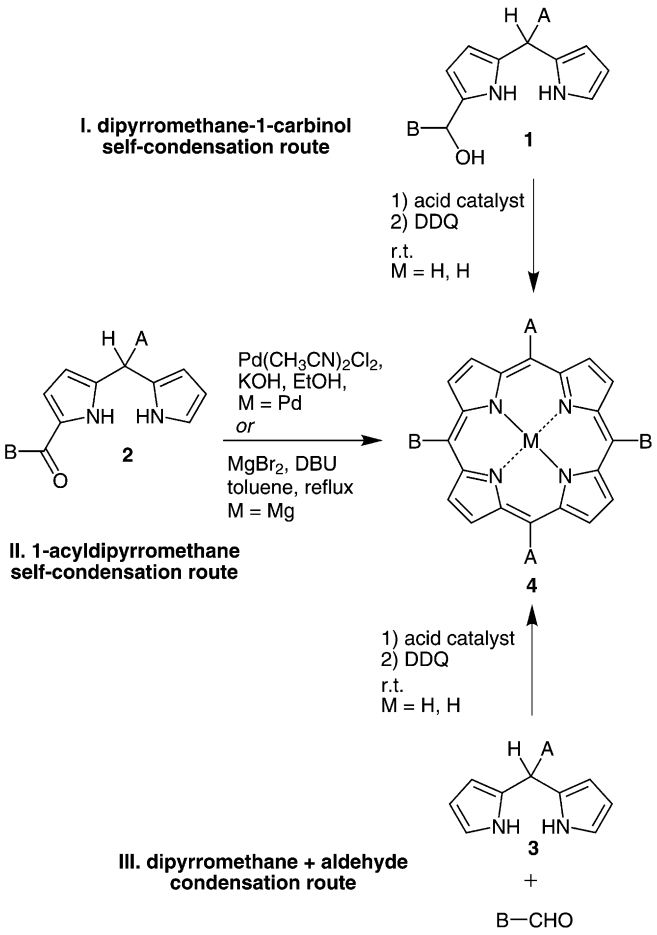
Keywords: cross-coupling; cyclopropanes; dihydroxylation; dipyrromethanes (dipyrranes); macrocycles; porphyrinoids; tetrapyrroles

Introduction

meso-Substituted *trans*-A_2B_2-porphyrins bearing distinct patterns of functional groups are valuable key components found in a wide range of model systems in biomimetic and material chemistry.[1,2] The level of architectural complexity that can be achieved in such systems is closely dependent upon the availability of suitable porphyrin building blocks. A *trans*-porphyrin provides a substitution pattern that can be used for the construction of porphyrin-based systems with a well-defined linear structure. Recent applications of *trans*-A_2B_2-porphyrins include enzyme models,[3] materials with non-linear optical properties,[4] charge sep-

aration devices that mimic photosynthesis,[5] multiporphyrin arrays for light harvesting applications and dye-sensitized solar cells (DSSC),[6] chiral sensors,[7] chiral catalysts,[8] optoelectronic devices,[9] amplified two-photon absorption,[10] synthetic receptors for small molecules,[11] liquid crystals,[12] and bilayer lipid membrane spanning arrays.[13]

Efficient synthetic methods for preparing specifically functionalized *trans*-A_2B_2-porphyrins are essential for the construction of materials and devices mentioned above. Often reported protocols are not compatible with key functional groups or the yields of purified porphyrins are very low. They may also result in metalloporphyrins which require harsh conditions for demetallation. Although *trans*-A_2B_2-porphyrins can in principle quite easily be obtained by condensation of pyrrole and two different aldehydes, this approach is in practice still limited because this 'mixed' condensation usually results in a statistical mixture of six porphyrins and consequently difficulties arise in separation and identification of products. Alternatively, porphyrins with a specific substitution pattern can also be prepared more rational by a step-by-step protocol.[14] However, more simple condensation reactions have the advantage of a faster access to porphyrin structures. Therefore, due to their easy availability DPM (dipyrrane) derivatives play a key role in the synthesis of regiospecifically pure *trans*-A_2B_2-porphyrins by pre-designating the orientation of *meso*-substituents. *trans*-A_2B_2-(metallo)porphyrins could be obtained from three described pathways *via* [2+2]-type building block approaches (Scheme 1).[15] (i) The acid-catalyzed self-condensation of an AB-substituted DPM-monocarbinol **1** which in its scope is limited with regard to functional groups tolerance. The reason is that the mentioned monocarbinol derivatives are prepared by treatment of a *meso*-substituted DPM with not easily available pyridyl thioesters and reactive Grignard reagents to yield the corresponding 1-acyldipyrromethane which then requires the subsequent reduction step using $NaBH_4$.[16] (ii) Reaction of 1-acyldipyrromethane **2** with PdX_2 or $MgBr_2$ under reflux conditions to give the palladium(II)- or magnesium(II)-porphyrins **4**, respectively;[17,18] again, the 1-acyldipyrromethanes are prepared by treatment of a *meso*-substituted DPM with pyridyl thioesters and reactive Grignard reagents, which limits the scope of functional group tolerance. In addition, the primary products are metalloporphyrins from which the metal may sometimes not easily be removed. (iii) Acid-catalyzed condensation reaction of a *meso*-substituted DPM **3** with an aldehyde;[19] in contrast to the former mentioned pathways, in this approach there is a wider functional group tolerance. In practice, similar as in acid-catalyzed reactions involving polypyrromethanes, the acid catalysis conditions required for this condensation introduce the possibility of scrambling which is



Scheme 1. Three possible [2+2] building block approaches for the synthesis of *trans*-A_2B_2-(metallo)porphyrins of type **4**.

the result of an acid-catalyzed fragmentation followed by an altered recombination of *meso*-substituents. However, Linsday et al. have shown optimized conditions which diminish or even suppress the ever-present possibility of scrambling.[20]

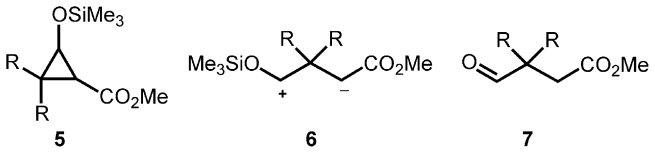
Results and Discussion

As a part of an ongoing project directed towards the synthesis of functionalized pyrrole-based macrocycles using d–a cyclopropanes as precursors,[21] we planned to design *trans*-A_2B_2-porphyrin systems employing sterically less hindered cyclopropane-derived DPMs. They should allow the synthesis of novel functionalized porphyrins that are not readily accessible *via* the known alternative strategies.

meso- or 5-substituted DPMs can simply be obtained in multi-gram scales by the condensation of an excess of pyrrole and the desired aldehyde and, for some examples, even more efficient synthetic protocols have also been reported.[22] DPMs are important

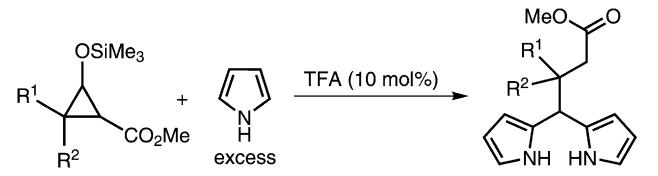
precursors for the synthesis of *meso*-substituted porphyrins, corroles, expanded and reduced porphyrins and related compounds such as dipyrrins, calixpyrroles (porphyrinogens) and chlorins.[23] Hence, we considered approach (iii) (*vide supra* and Scheme 1) to be also feasible for the synthesis *trans*-A_2B_2-porphyrin systems based on d–a cyclopropane-derived DPMs.

Cyclopropane derivatives vicinally substituted by donor and acceptor groups are particularly suitable for synthetic applications, since the electronic effects of the substituents activate the strained compound and provide high versatility of the respective products after ring cleavage.[24] Compounds such as methyl 2-siloxycyclopropanecarboxylates **5** serve as 1,3-zwitterionic synthons **6** and – in the presence of protic solvents, mild acids or fluoride ions – *in situ* generate products of type **7** carrying two carbonyl functionalities in 1,4 distance (Scheme 2).[25]



R = H or alkyl

Scheme 2. The d–a cyclopropanes **5** serving as 1,3-zwitterionic synthons **6** and leading to 1,4-dicarbonyl compounds **7**.



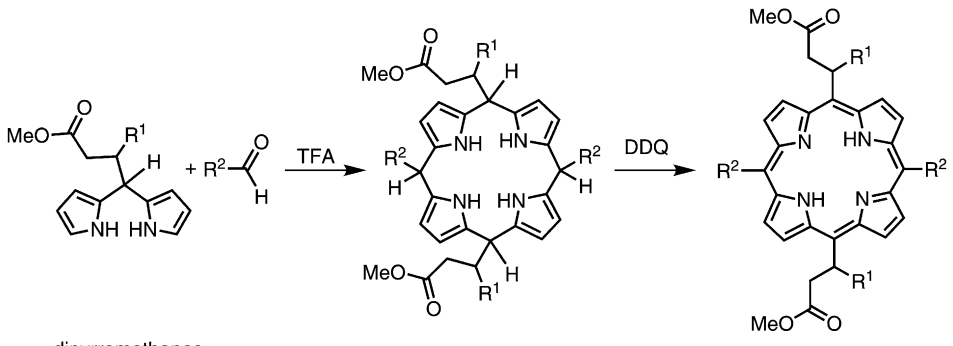
R^1 = H, R^2 = H **5a**
R^1 = H, R^2 = Me **5b**
R^1 = Me, R^2 = Me **5c**

R^1 = H, R^2 = H **8a**, 74%
R^1 = H, R^2 = Me **8b**, 65%
R^1 = Me, R^2 = Me **8c**, 61%

Scheme 3. Condensation of d–a cyclopropanes **5a–c** with an excess of pyrrole in a solvent-free condensation reaction leading to functionalized DPMs **8a–c**.

For the synthesis of DPMs **8a** and **8b**, d–a cyclopropanes **5a** and **5b** were treated with an excess of pyrrole in the presence of a catalytic amount of trifluoroacetic acid (TFA) (10 mol%).[19a] After performing the work up, the stable DPMs **8a** and **8b** were obtained in 74 and 65% yields, respectively (Scheme 3). Performing the two reaction steps in one pot (ring opening of the cyclopropane and condensation with excess pyrrole) and purifying only at the final step reduces the experimental effort and allows a good overall yield.[28] We have also prepared the sterically more congested DPM **8c** from d–a cyclopropane **5c** by the same method and utilized it recently for the synthesis of functionalized, *meso*-hydrogenated, oxidation-resistant calix[4]- and calix[6]phyrins.[21] The three aldehydes **7a–c** incorporated into DPMs **8a–c** are fairly elusive species and hard to prepare by alternative methods.

With multi-gram amounts of DPMs **8a** and **8b** in hand, we planned to react these compounds with different aldehydes in acid-catalyzed condensations to form calixpyrroles followed by oxidation to give the corresponding functionalized *trans*-A_2B_2-porphyrin systems (Scheme 4). Therefore, as a test reaction, DPM **8a** was condensed with benzaldehyde in a 1:1



dipyrromethanes (dipyrranes)

R^1 = H **8a**
R^1 = Me **8b**

calixpyrroles

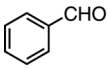
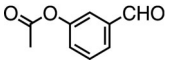
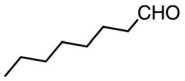
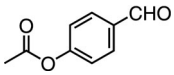
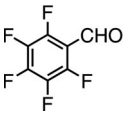
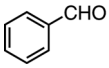
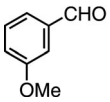
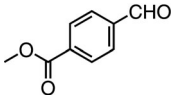
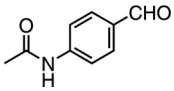
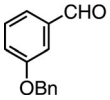
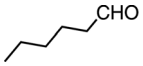
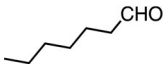
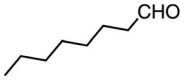
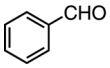
R^1 = H **9a–e**
R^1 = Me **10a–h**

trans-A_2B_2-porphyrins

R^1 = H **11a–e**
R^1 = Me **12a–h**, *dr* 1:1
R^2 = *cf.* Table 1
14–31%

Scheme 4. Acid-catalyzed condensation of d–a cyclopropane-derived DPMs **8a** and **8b** with aldehydes (1:1 ratio) forming functionalized *trans*-A_2B_2-porphyrins **11a–e** and **12a–h** *via* calixpyrrole intermediates **9a–e** and **10a–h**.

Table 1. TFA-catalyzed (20 mol%) condensation of DPMs **5a** and **5b** with different aldehydes (1:1 ratio, 2 mmol scale, room temperature, CH_2Cl_2) to functionalized *trans*-A_2B_2-porphyrins **11** and **12**.

Entry	DPM[a]	Aldehyde	Product	Time [h][b]	Yield [%][c]
1	**8a**		**11a**	16	19
2	**8a**		**11b**	15	14
3	**8a**		**11c**	18	21
4	**8a**		**11d**	17	16
5	**8a**		**11e**	16	14
6	**8b**		**12a**	22	26
7	**8b**		**12b**	18	24
8	**8b**		**12c**	18	22
9	**8b**		**12d**	18	29
10	**8b**		**12e**	18	31
11	**8b**		**12f**	18	15
12	**8b**		**12g**	18	20
13	**8b**		**12h**	17	18
14[d]	**8a**		**11a**	22	15

[a] Dipyrromethane.
[b] Time for condensation step.
[c] Yield of purified product.
[d] The reaction was performed on a 15 mmol scale.

ratio at room temperature in the presence of a catalytic amount of TFA (20 mol%) in dichloromethane (DCM) as described for other DPM condensations[29] to furnish the corresponding calixpyrrole **9a**. After subsequent oxidation with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ),[30] the purple crystalline product **11a** was isolated after column chromatography in 19% yield.

To the best of our knowledge, this is the first report in which d–a cyclopropane-derived DPMs are utilized in the synthesis of porphyrin systems. By this method *meso*-substituted alkyl chains carrying a terminal functional group could easily be incorporated into the porphyrin periphery. Following these promising results, we tested the generality and functional group tolerance of this procedure for the synthesis of other *trans*-A_2B_2-porphyrins. Therefore, we examined the reaction of a range of substituted aromatic and aliphatic aldehydes with DPMs **8a** or **8b** in a 1:1 ratio under the conditions used for the synthesis of **11a** to obtain the corresponding *trans*-A_2B_2-porphyrins **11a–e** and **12a–h**, some of which are functionalized at all four *meso*-bridges (Table 1).

As shown in Table 1, steric and electronic variations of the aldehydes bearing electron-donating or electron-withdrawing substituents did not change the efficacy of the reaction and resulted in the formation of the desired functionalized *trans*-A_2B_2-porphyrins **11a–e** and **12a–h** in acceptable yields (14–31%). For example, several key functional groups such as acetoxy, methoxy, methoxycarbonyl and acetamido are tolerated under the fairly mild reaction conditions (Table 1, entries 2, 3 and 7–9). In addition, other substituents such as pentafluorophenyl (allowing a variety of further functionalizations such as nucleophilic aromatic substitutions)[31] or benzyloxyphenyl and alkyl substituents were also readily introduced into the porphyrin skeleton (Table 1, entries 4, 5 and 10–13). Since chiral DPM **8b** was used as a racemate, each of the products **12a–h** (entries 6–13) was obtained as a 1:1 mixture of diastereomers. To examine the feasibility of this method on a larger preparative scale, the model reaction leading to **11a** was also performed on a 15 mmol scale. The transformation proceeded similarly to the small-scale experiment and provided the desired porphyrin in 15% yield after 22 h (Table 1, entry 14).

In addition, the effect of TFA loading was investigated for the model reaction (DPM **8a** with benzaldehyde in a 1:1 ratio). There is an ascending trend (Figure 1), that is, increasing the acid loading from 10 mol% to 100 mol% leads to an increase of the yield of the product **11a** from 15% to 34%. Using a stoichiometric amount of acid catalyst also the A_3B-type by-product 5-(2-methoxycarbonylethyl)-10,15,20-triphenylporphyrin resulting from scrambling (*vide supra*) could be isolated in 2% yield (see Supporting Information). In general, however, the DPMs **8a** and **8b** seem to be remarkably resistant to scrambling. These results suggest that in cases where interference of the acid catalyst with functional groups is not an issue, a higher loading of acid catalyst can be applied to achieve even better yields than those in Table 1. In a separate experiment under the same conditions as described for the model reaction, the addition of TFA

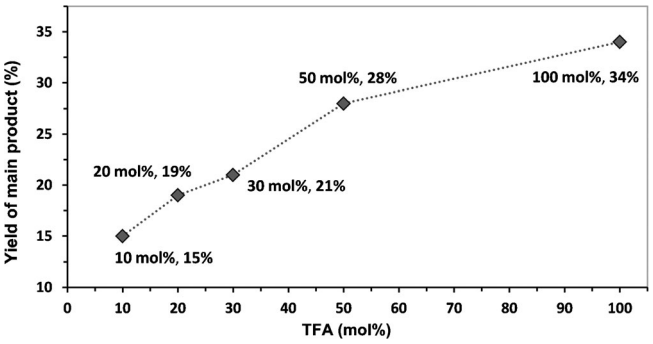
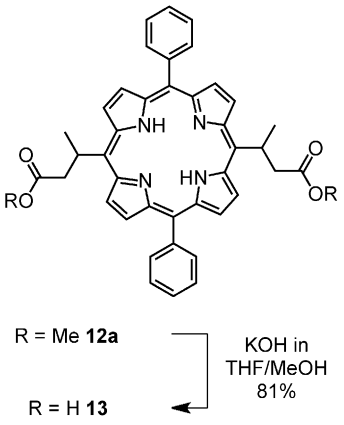


Figure 1. Effect of TFA loading on the yield of *trans*-A_2B_2 porphyrin **11a**.

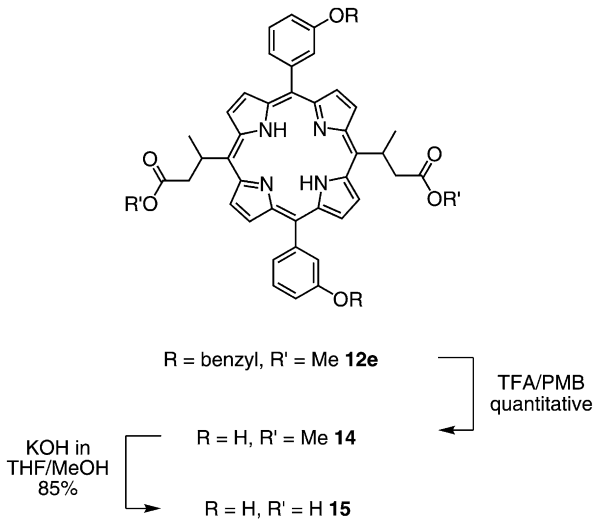
(20 mol%) was performed gradually during 8 h using syringe pump and a slightly improved yield of product was observed (23%).

The possibility to introduce and vary functional groups of the porphyrins should be emphasized here. They offer the option of a variety of additional transformations and enable the connection of these functionalized macrocycles to other interesting compounds. As an example, diester **12a** was subjected to alkaline hydrolysis using potassium hydroxide in a mixture of THF/MeOH (3:2) as solvent to give the polar porphyrindicarboxylic acid **13** (*d.r.* 1:1) in 81% yield (Scheme 5).

In a second example, compound **12e** underwent a selective *O*-debenzylation using TFA and pentamethylbenzene (PMB) as benzyl cation scavenger to give porphyrin **14** with two free phenolic hydroxy groups in quantitative yield (Scheme 6). This selective *O*-debenzylation method is orthogonal to the reactivity of the methoxycarbonyl groups.[32] In the following step, **14** was subjected to alkaline hydrolysis of the diester which furnished the polar bis(3-hydroxylphenyl)-substituted porphyrindicarboxylic acid **15** in 85% yield, exemplifying the possibility to selectively functionalize the presented *trans*-A_2B_2-porphyrins at their *meso*-residues.



Scheme 5. Saponification of **12a** to *trans*-A_2B_2-porphyrindicarboxylic acid **13**.

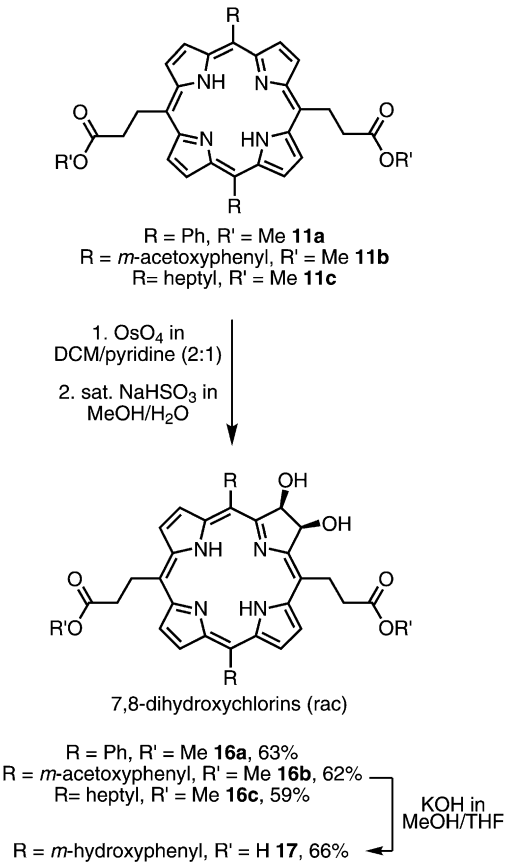


Scheme 6. Transformations of **12e** by selective *O*-debenzylation using TFA/PMB and subsequent saponification of **14** to furnish *trans*-A_2B_2-porphyrin dicarboxylic acid **15**.

A manipulation of the porphyrinic chromophore leading to an increase of the extinction coefficient ($\log\varepsilon$) or to a red-shift of the longest absorption wavelength (λ_{max}) is interesting as the resulting porphyrinoids are useful for a number of applications.[33] In order to accomplish such a modification, porphyrins **11a–c** were converted into the corresponding 7,8-dihydroxychlorins[34] by the well-known OsO_4-mediated dihydroxylation of one of the porphyrin peripheral double bonds.[35] The initially formed osmate esters were reduced using sodium bisulfite.[36] As a result compounds **16a–c** were obtained with 63, 62 and 59% yields, respectively (Scheme 7). Product **16b** was further subjected to alkaline hydrolysis resulting in simultaneous hydrolysis of the alkyl ester as well as the acetoxyphenyl substituents yielding the highly polar compound **17**. These chlorins exhibit typical differences in their absorption spectra compared to the porphyrins.

As an illustration for the absorption properties of these compounds the UV/Vis spectra of **11a** and **16a** are shown in Figure 2. Chlorin **16a** shows a splitting of the Soret band ($\lambda_{max}=407.5$ and $\lambda_{max}=423$) compared to **11a** ($\lambda_{max}=416.5$). In addition, the longest absorption wavelength of **16a** at $\lambda_{max}=647.5$ nm has a higher extinction coefficient [$\log\varepsilon$ ($L\,mol^{-1}\,cm^{-1}$) = 4.34] compared to that of **11a**, $\lambda_{max}=650.5$ nm [$\log\varepsilon$ ($L\,mol^{-1}\,cm^{-1}$) = 3.55].

In order to prepare a more complex *trans*-A_2B_2-porphyrin, the novel d–a cyclopropane **22**[37] carrying a *para*-bromophenyl group adjacent to the ethoxycarbonyl functionality was prepared from the corresponding diazo compound **20**[38] and silyl enol ether



Scheme 7. OsO_4-mediated dihydroxylations of **11a–c** to 7,8-dihydroxychlorins **16a–c** followed by saponification of **16b** to dihydroxylated *trans*-A_2B_2-chlorindicarboxylic acid **17**.

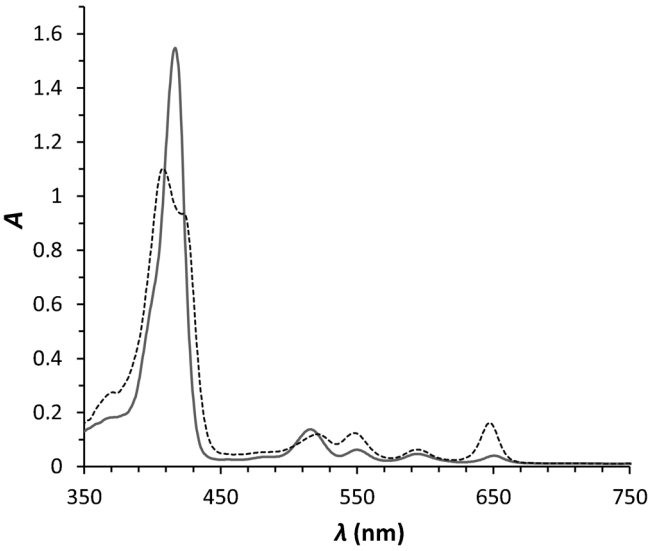


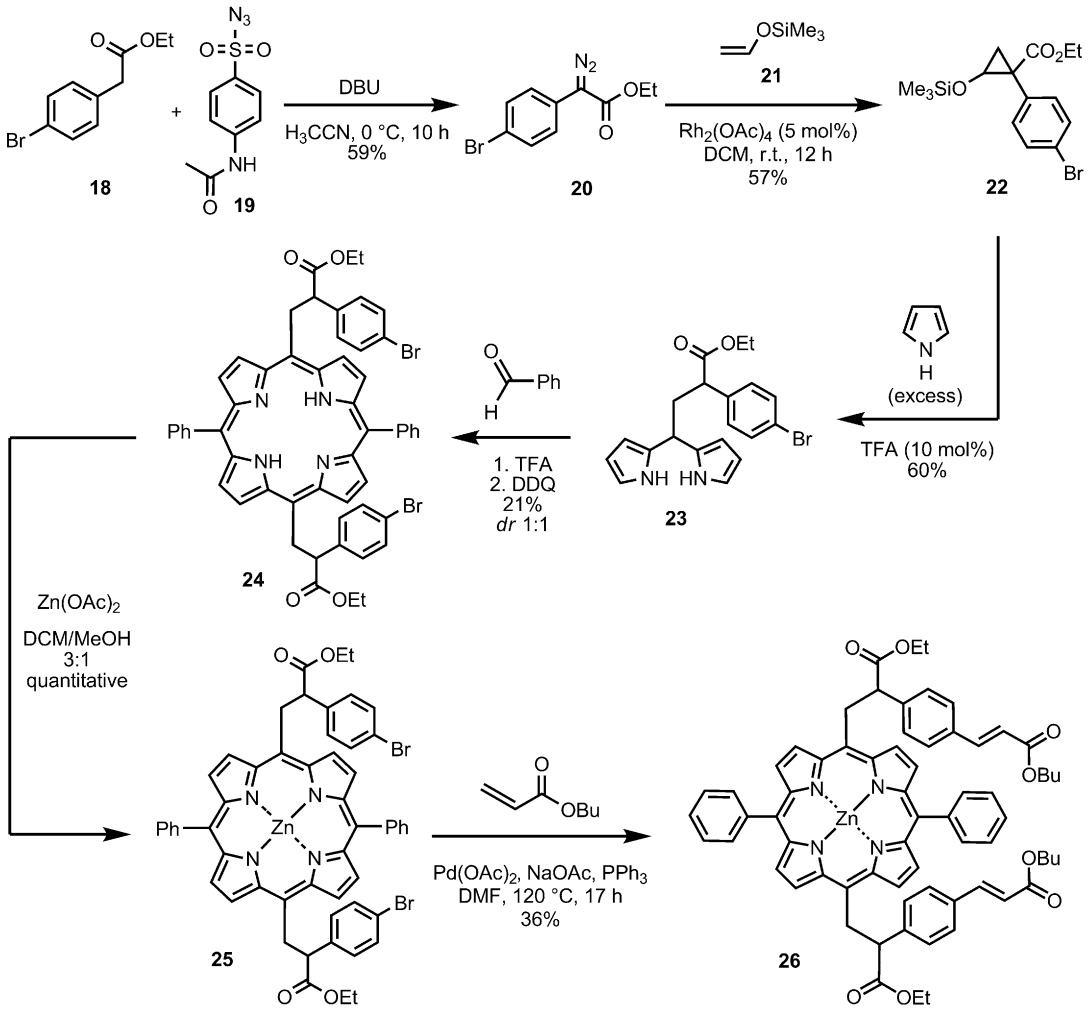
Figure 2. UV/Vis spectra of porphyrin **11a** (solid line) and 7,8-dihydroxychlorin **16a** (dashed line) recorded in CH_2Cl_2 (room temperature, 7.66×10^{-6} M).

21. Precursor **20** was obtained by reaction of ethyl 2-(4-bromophenyl)acetate (**18**) with 4-acetamidobenzenesulfonyl azide (**19**) in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU). Aryl-substituted diazoacetate **20** underwent $Rh_2(OAc)_4$-catalyzed cyclopropanation[39] of trimethylsilyl enol ether **21** to furnish d–a cyclopropane **22** in 57% yield (Scheme 8). This compound was then treated with an excess of pyrrole in the presence of TFA (10 mol%). After work up, the stable DPM **23** was obtained in 60% yield. Acid-catalyzed condensation of DPM **23** with benzaldehyde as a model substrate afforded *trans*-A_2B_2-porphyrin **24** as 1:1 mixture of diastereomers in 21% yield.

Porphyrin **24** was subsequently metallated[40] using zinc acetate to mask the inner core. The resulting bis(4-bromophenyl)-functionalized *trans*-A_2B_2-Zn-porphyrin **25** was coupled with butyl acrylate by a Heck reaction in moderate yield.[41] This process provided only the (*E,E*)-isomer of the highly functionalized bis-(alkenyl)-substituted *trans*-A_2B_2-Zn-porphyrin **26**. The multi-step synthesis of **26** illustrates the option of late stage functionalizations at d–a cyclopropane-derived moieties. Employing different aldehydes and olefins, this approach could certainly be used to prepare a variety of complex porphyrin systems. Other cross-coupling reactions such as the Negishi, Suzuki, Stille or Sonogashira reaction could further increase the diversity of specifically substituted and functionalized porphyrins available by this approach.

Conclusions

The field of tetrapyrrole chemistry is constantly expanding but the synthesis of porphyrins bearing distinct functionalized *meso*-substituents still presents a number of challenges. Simple and straightforward synthetic approaches are required. We have presented herein the first examples of applications of d–a cyclopropanes as precursors for the synthesis of functionalized porphyrin systems. These were utilized in acid-catalyzed porphyrin condensation reactions with a series of aromatic and aliphatic aldehydes affording an efficient and highly flexible entry and direct access to novel A_2B_2-porphyrins bearing functional groups in strongly defined *trans*-substitution patterns. Porphyrins carrying two different functional groups in their *meso* positions were thus easily obtained. As examples for further modifications, selected porphyrin products were converted into the corresponding 7,8-dihydroxychlorins *via* the osmium-mediated dihydroxylation as well as a selective *O*-debenzylation reaction. In addition, through a multi-step synthesis, a highly functionalized bis(alkenyl) *trans*-A_2B_2-Zn-porphyrin was prepared using a Heck-type reaction. This variety of modifications renders the d–a cyclopropane-derived dipyrromethanes and their corresponding porphyrins as valuable tools for the synthesis of advanced tetrapyrrole systems for material sciences, optoelectronics or biomedical applications.



Scheme 8. Multi-step synthesis of functionalized *trans*-A_2B_2-Zn-porphyrin **26** by $Rh_2(OAc)_4$-catalyzed synthesis of d–a cyclopropane **22** conversion into DPM **23** and porphyrin **24** followed by metallation to **25** and Heck-reaction to bis(alkenyl)-substituted *trans*-A_2B_2-Zn-porphyrin **26**.

Experimental Section

General Remarks

Reactions were generally performed under argon in oven-dried flasks. Reagents were added with syringes. Solvents were dried by using standard procedures. Dichloromethane (DCM) was distilled and stored over molecular sieves (4 Å) under an atmosphere of argon. Other reagents were purchased and were used as received without further purification unless otherwise stated. Products were purified by chromatography on silica gel (40–63 μm, Fluka, No. 60752, containing 0.1% Ca) and detection was carried out with a CAMAG variable UV detector ($\lambda = 254/366$ nm). Yields refer to chromatographically purified products, unless otherwise stated. Reactions were monitored by thin layer chromatography (TLC) analysis. NMR spectra were recorded with Bruker (AC 250, AC 500, AVIII 700) and JOEL (Eclipse 500) instruments. Chemical shifts are reported relative to tetramethylsilane (TMS, ^{1}H: $\delta = 0.00$ ppm), $CHCl_3$ (^{1}H: $\delta = 7.26$ ppm), and $CDCl_3$ (^{13}C: $\delta = 77.0$ ppm) in $CDCl_3$ solution. Integrals are in accordance with assignments; coupling constants are given in Hz. All ^{13}C NMR spectra are proton decoupled. Multiplicity is indicated as follows: s (singlet), d (doublet), t (triplet), m (multiplet), dd (doublet of doublets), td (triplet of doublets), q (quartet), br. s (broad singlet). For detailed peak assignments, 2D spectra were measured (^{1}H-^{1}H COSY, ^{1}H-^{13}C HMQC, and ^{1}H-^{13}C HMBC). IR spectra were measured with a Jasco FT/IR-4100 spectrometer equipped with an attenuated total reflectance (ATR) attachment (PIKE MIRacle). The UV/Vis spectra were measured with a SPECORD S300 VIS UV/Vis spectrometer (Analytik Jena, Jena, Germany) with DCM as the solvent and quartz cuvettes of 1 cm path length. HR-MS analyses were performed with an Agilent 6210 ESI-TOF instrument (Agilent Technologies, Santa Clara, CA, USA). The solvent flow rate was adjusted to 4 μL min^{-1} and the spray voltage was 4 kV. The drying gas flow rate was 15 psi (1 bar). All other parameters were adjusted for maximum abundance of the respective $[M+H]^+$ ions (ESI-TOF = electrospray ionization/time of flight). Elemental analyses were carried out in CHN mode with a Vario EL instrument (Ele-

mentar Analysensysteme GmbH). Melting points were measured with a Reichert Thermovar apparatus and are uncorrected. Methyl 3-(trimethylsiloxy)-1-cyclopropanecarboxylate (**5a**),[26] methyl 2-methyl-3-(trimethylsiloxy)-1-cyclopropanecarboxylate (**5b**)[26] and ethyl 1-(4-bromophenyl)-2-(trimethylsiloxy)cyclopropane-1-carboxy-late (**22**)[37] were prepared according to known procedures and their spectroscopic data were compared with those reported in the literature see the Supporting Information for the ^{1}H NMR spectrum of **22**).

Synthesis of 5-(3-Methoxy-3-oxopropyl)dipyrromethane (8a)

The reaction was performed in a 250-mL, three-necked, round-bottom flask fitted with a septum port, a bubble counter, and a gas inlet port. A solution of methyl 3-(trimethylsiloxy)-1-cyclopropanecarboxylate (**5a**) (1.36 g, 7.21 mmol) and pyrrole (25 mL, 362 mmol) was degassed by bubbling with argon for 10 min, then TFA (0.05 mL, 0.72 mmol) was added. The solution was stirred for 1.5 h at room temperature, and the progress of the reaction was monitored by TLC analysis. The TLC plates were developed in a solvent mixture of DCM/hexanes/NEt_3 (85:14:1) and the bands were visualized by exposure of the air-dried TLC plate to bromine vapor on which the unreacted pyrrole looks dark grey and dipyrromethane **8a** looks pink when diluted and dark red when concentrated. Then, the reaction mixture was diluted with DCM (200 mL) and washed with aqueous NaOH (0.1 N, 20 mL), followed by washing with water (3 × 200 mL) and was then dried with anhydrous Na_2SO_4. The solvent was removed under reduced pressure and then the unreacted pyrrole was removed by a rotary evaporator (10 mbar, 60 °C). The resulting dark viscous oil was dissolved in a minimal quantity of the eluent (DCM/hexanes/NEt_3 (85:14:1)) and was purified by silica column chromatography using DCM/hexanes/NEt_3 (85:14:1) as eluent. Any remaining pyrrole elutes first, followed slowly by the dipyrromethane **8a** (R_F 0.43) and followed later by tailing materials. Colorless oil; yield: 1.24 g (5.34 mmol, 74%). IR (ATR): υ_{max} = 3375 (N–H), 3100 (C–H pyrrole), 2955 (C–H), 2875 (CH_3), 1725 (C=O), 1560 (N–H), 1435 (CH_2), 1370 (CH_3), 1325 (C–N), 1215 (C–O), 1155 (C–O), 1115 (C–N), 1095 (C–H pyrrole), 1025 (C–H pyrrole), 885 (C–H pyrrole), 790 (C–H), 720 (C–H) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.22–2.28 (m, 2H, CHC*H*$_2$), 2.29–2.35 (m, 2H, C*H*$_2$CO), 3.64 (s, 3H, OC*H*$_3$), 4.01 (t, J = 7.6 Hz, 1H, *meso-H*), 6.05–6.08 (m, 2H, pyrrole-*H*), 6.12–6.15 (m, 2H, pyrrole-*H*), 6.60–6.63 (m, 2H, pyrrole-*H*), 7.82 ppm (br. s, 2H, 2 × N*H*); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 29.7 (CH*C*H$_2$), 32.0 (*C*H$_2$CO), 37.0 (*meso-C*), 51.7 (O*C*H$_3$), 105.9 (pyrrole-*C*), 108.2 (pyrrole-*C*), 117.5 (pyrrole-*C*), 132.5 (pyrrole-*C*), 174.0 ppm (*C*=O); HR-MS (ESI-TOF): m/z = 233.1278, calcd. for $C_{13}H_{17}N_2O_2$ $[M+H]^+$: 233.1290; m/z = 255.1109, calcd. for $C_{13}H_{16}N_2NaO_2$ $[M+Na]^+$: 255.1109; m/z = 271.0836, calcd. for $C_{13}H_{16}KN_2O_2$ $[M+K]^+$: 271.0849; elemental anal. calcd. (%) for $C_{13}H_{16}N_2O_2$ (232.1): C 67.22, H 6.94, N 12.06; found: C 66.55, H 6.69, N 11.81.

General Procedure for the Synthesis of *trans*-A_2B_2-Porphyrin Derivatives 11a–e and 12a–h

A standard reaction was performed in a 1-L, three-necked, round-bottom flask fitted with a septum port, bubble counter, and a gas inlet port with argon flow. 5-(3-Methoxy-3-oxopropyl)-dipyrromethane (**8a**) (465 mg, 2.00 mmol) or 5-(3-methoxy-1-methyl-3-oxopropyl)-dipyrromethane (**8b**) (493 mg, 2.00 mmol) and the appropriate aldehyde (2.00 mmol) were dissolved in dry DCM (500 mL). The resulting solution was degassed by bubbling with an argon flow for 10 min, and TFA (30 μL, 0.40 mmol) was added by a syringe with vigorous stirring. The reaction mixture was stirred under argon in the dark at room temperature for the specified time as indicated for each individual experiment in Table 1. After the indicated time, the calixpyrrole intermediate was subjected to oxidation for 2 h by the addition of DDQ (690 mg, 3.00 mmol), followed by neutralization of TFA with NEt_3 (500 μL, 3.60 mmol). The reaction mixture was filtered through a sintered glass Büchner funnel loaded with silica gel and eluted with a mixture of DCM/EtOAc (ratio depending on product, see individual procedures) to afford the crude product. After concentration of the filtrate under reduced pressure, the residue was dissolved in a minimum volume of solvent and applied to gravity silica gel column chromatography with DCM/hexanes(/EtOAc) (ratio depending on product, see individual procedures) for further purification. Recrystallization of the product gave the desired pure comound. The main products as *trans*-A_2B_2-porphyrin **11** and **12** were obtained in yields between 14–31% (see Table 1).

5,15-Diphenyl-10,20-bis(3-methoxy-3-oxopropyl)-porphyrin (11a)

According to the general procedure 5-(3-methoxy-3-oxopropyl)-dipyrromethane (**8a**) (465 mg, 2.00 mmol) and benzaldehyde (20 μL, 2.00 mmol) were reacted in dry DCM (500 mL) using TFA (30 μL, 0.40 mmol) as catalyst. After 16 h the calixpyrrole intermediate was subjected to oxidation for 2 h by addition of DDQ (690 mg, 3.00 mmol), followed by neutralization of TFA with NEt_3 (500 μL, 3.60 mmol). The reaction mixture was filtered and eluted with a mixture of DCM/EtOAc (95:5) to afford the crude products. After concentration of the filtrate under reduced pressure, the residue was dissolved in a minimum volume of solvent and applied to gravity silica gel column chromatography with DCM/hexanes (80:20) for further purification and *trans*-A_2B_2-porphyrin **11a** was obtained as the main product. Recrystallization from a DCM/MeOH mixture gave the pure product as purple crystals; yield: 121 mg, (0.19 mmol, 19%); mp 257 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = –2.74 (br. s, 2H, 2 × N*H*), 3.51–3.54 (m, 4H, 2 × CH$_2$C*H*$_2$CO), 3.77 (s, 6H, 2 × OC*H*$_3$), 5.32–5.36 (m, 4H, 2 × C*H*$_2$CH$_2$CO), 7.76–7.84 (m, 6H, Ar), 8.19–8.21 (m, 4H, Ar), 8.90 (d, J = 4.8 Hz, 4H, β-pyrrole-*H*), 9.46 ppm (d, J = 4.8 Hz, 4H, β-pyrrole-*H*); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 30.5 (2 × *C*H$_2$CH$_2$CO), 41.9 (2 × CH$_2$*C*H$_2$CO), 52.0 (2 × O*C*H$_3$), 117.0 (Ar), 119.6 (Ar), 126.73 (Ar), 127.67 (Ar), 127.9 (Ar), 132.3 (Ar), 134.6 (Ar), 142.4 (Ar), 173.2 (2 × *C*=O); HR-MS (ESI-TOF): m/z = 635.2661, calcd. for $C_{40}H_{35}N_4O_4$ $[M+H]^+$: 635.2658; m/z = 657.2488, calcd. for $C_{40}H_{34}N_4NaO_4$ $[M+Na]^+$: 657.7258; m/z = 673.2217, calcd.

for $C_{40}H_{34}KN_4O_4$ $[M+K]^+$: 673.2217; UV/Vis (CH_2Cl_2): λ_{max} [log ε ($L\,mol^{-1}\,cm^{-1}$)] = 416.5 [5.27], 516.0 [4.20], 550.0 [3.73], 594.5 [3.52], 650.5 nm [3.38].

5,15-Diphenyl-10,20-bis(2-carboxy-1-methylethyl)-porphyrin (13)

5,15-Diphenyl-10,20-bis(3-methoxy-1-methyl-3-oxopropyl)-porphyrin (**12a**) (40 mg, 0.06 mmol) was dissolved in THF (15 mL). Then a solution of potassium hydroxide (270 mg, 4.81 mmol) dissolved in hot methanol (10 mL) and three drops of water were added, and the mixture was stirred for 22 h at room temperature. The evolution of the reaction was monitored by TLC. After 22 h the solvents of the mixture were evaporated using a rotary evaporator. The residue was dissolved in 100 mL of EtOAc, transferred to a 500 mL separatory funnel and to the organic phase was added water (100 mL) and the solution was neutralized by adding 25% hydrochloric acid. The organic phase was washed with water (3 × 100 mL) (one spatula of NH_4Cl was added into this mixture for a better phase separation), and dried with anhydrous Na_2SO_4. The drying agent was removed and the organic phase was evaporated to dryness. The residue was dissolved in a minimum volume of DCM/MeOH (90:10) and applied to gravity silica gel column chromatography with DCM/MeOH (90:10) for further purification. Recrystallization of **13** from a DCM/MeOH mixture gave the desired pure product as purple crystals; yield: 31 mg (0.05 mmol, 81%); mp > 300 °C; 1:1 *dr*. ^{1}H NMR (500 MHz, DMSO-d_6): δ = −2.70 (s, 2H, 2 × N*H*), 2.36 (d, *J* = 7.2 Hz, 6H, 2 × CHC*H*$_3$), 3.69–3.81 (m, 4H, 2 × CHC*H*$_2$), 5.90–5.98 (m, 2H, 2 × C*H*CH$_2$), 7.81–7.85 (m, 4H, Ar), 7.85–7.89 (m, 2H, Ar), 8.17–8.21 (m, 4H, Ar), 8.75 (d, *J* = 5.0 Hz, 4H, *β*-pyrrole-*H*), 9.75 (d, *J* = 5.0 Hz, 4H, *β*-pyrrole-*H*), 12.14 (br. s, 2H, 2 × CO_2H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 27.75 (CH*C*H$_3$), 27.77 (CH*C*H$_3$), 36.7 (2 × *C*HCH$_2$), 46.8 (2 × *C*H$_2$CO), 100.0 (Ar), 104.5 (Ar), 108.6 (Ar), 114.3 (Ar), 119.2 (Ar), 124.1 (Ar), 127.3 (Ar), 128.6 (Ar), 132.4 (Ar), 134.5 (Ar), 138.6 (Ar), 142.8 (Ar), 148.5 (Ar), 174.1 (2 × *C*=O); HR-MS (ESI-TOF): *m/z* = 635.2609, calcd. for $C_{40}H_{35}N_4O_4$ $[M+H]^+$: 635.2658; UV/Vis spectrum in CH_2Cl_2: λ_{max} [log ε ($L\,mol^{-1}\,cm^{-1}$)] = 417.0 [4.86], 515.5 [3.82], 549.0 [3.66], 593.5 [3.63], 650.5 nm [3.60].

5,15-Bis(3-hydroxyphenyl)-10,20-bis(3-methoxy-1-methyl-3-oxopropyl)-porphyrin (14)

5,15-Bis(3-benzyloxyphenyl)-10,20-bis(2-methoxycarbonyl-1-methylethyl)-porphyrin (**12e**) (305 mg, 0.35 mmol) was dissolved in trifluoroacetic acid (6 mL). To the resulting green solution was added pentamethylbenzene (206 mg, 1.39 mmol). The reaction mixture was stirred at room temperature overnight. After this time, the reaction mixture was transferred to a separatory funnel and crushed ice was added, followed by EtOAc (200 mL) and water (150 mL). NaOH (20%) was added to attain a pH of 5–6 in the aqueous phase, the color of the organic phase changing from green to purple. The phases were separated and the organic phase was then washed with water (4 × 200 mL) until neutral pH was reached. The organic phase was dried with anhydrous Na_2SO_4. The drying agent was removed and the organic phase was evaporated to dryness. The remaining solid was washed with hexanes, after that, the residue was taken up in a minimum volume of solvent and applied to silica gel column chromatography for further purification using DCM/MeOH (9:1) as the eluent. Recrystallization of the isolated fraction from a DCM/hexanes mixture afforded the pure product **14**. Purple crystals; yield: 240 mg (0.35 mmol, quantitative); mp 290 °C (decomp.); 1:1 *dr*. ^{1}H NMR (500 MHz, acetone-d_6): δ = −2.50 (s, 2H, 2 × N*H*), 2.39 (d, *J* = 7.4 Hz, 6H, 2 × CHC*H*$_3$), 3.83–3.85 (m, 4H, 2 × CHC*H*$_2$), 6.01–6.09 (m, 2H, 2 × C*H*CH$_2$), 7.33–7.35 (m, 2H, Ar), 7.60–7.63 (m, 2H, Ar), 7.67–7.70 (m, 4H, Ar), 8.90 (d, *J* = 4.9 Hz, 4H, *β*-pyrrole-*H*), 8.91 (br. s, 2H, 2 × O*H*), 9.69 (d, *J* = 4.9 Hz, 4H, *β*-pyrrole-*H*); ^{13}C NMR (126 MHz, acetone-d_6): δ = 26.60 (CH*C*H$_3$), 26.61 (CH*C*H$_3$), 36.5 (2 × *C*HCH$_2$), 46.08 (*C*H$_2$CO), 46.10 (*C*H$_2$CO), 50.9 (2 × CO_2CH_3), 115.0 (Ar), 119.1 (Ar), 121.9 (Ar), 123.1 (Ar), 126.2 (Ar), 127.6 (Ar), 128.5 (Ar), 129.2 (Ar), 132.0 (Ar), 144.2 (Ar), 155.8 (Ar), 172.6 (2 × *C*=O); HR-MS (ESI-TOF): *m/z* = 695.2877, calcd. for $C_{42}H_{39}N_4O_6$ $[M+H]^+$: 695.2870; UV/Vis (acetone): λ_{max} [log ε ($L\,mol^{-1}\,cm^{-1}$)] = 415.5 [5.47], 514.0 [4.18], 547.0 [3.76], 593.5 [3.67], 649.0 nm [3.49].

5,15-Bis(2-carboxy-1-methylethyl)-10,20-bis(3-hydroxyphenyl)-porphyrin (15)

5,15-Bis(3-hydroxyphenyl)-10,20-bis(3-methoxy-1-methyl-3-oxopropyl)-porphyrin (**14**) (100 mg, 0.14 mmol) was dissolved in THF (15 mL). To this solution were added a solution of potassium hydroxide (270 mg, 4.81 mmol) dissolved in hot methanol (10 mL) and three drops of water, and the solution was stirred for 24 h at room temperature. The evolution of the reaction was monitored by TLC. Once no further progress of the reaction was detectable (after 24 h), the solvents in the reaction mixture were evaporated using a rotary evaporator. Then, the residue was dissolved in EtOAc (100 mL) and was transferred into a 500 mL separatory funnel and to the organic phase water was added (100 mL) and the solution was neutralized by adding 25% hydrochloric acid. After neutralization, the organic phase was washed with water (3 × 100 mL) (one spatula of NH_4Cl was added into this mixture for a better phase separation), and dried with anhydrous Na_2SO_4. The drying agent was removed and the organic phase was evaporated to dryness. The residue was dissolved in a minimum volume of DCM/MeOH (70:30) and applied to gravity silica gel column chromatography with DCM/MeOH (70:30) for further purification. Recrystallization of the product **15** from a DCM/MeOH mixture gave the desired pure crystalline form of the product as purple crystals; yield: 82 mg (0.12 mmol, 85%); mp > 300 °C; 1:1 *dr*. ^{1}H NMR (700 MHz, DMSO-d_6): δ = −2.72 (br. s, 2H, 2 × N*H*), 2.37 (d, *J* = 7.2 Hz, 6H, 2 × CHC*H*$_3$), 3.71–3.75 (m, 2H, 2 × CHC*H*HCO), 3.78–3.81 (m, 2H, 2 × CHCH*H*CO), 5.91–5.96 (m, 2H, 2 × C*H*CH$_2$), 7.26–7.28 (m, 2H, Ar), 7.54–7.61 (m, 6H, Ar), 8.61 (br. s, 2H, 2 × C$_6$H$_4$O*H*), 8.83 (d, *J* = 4.8 Hz, 4H, *β*-pyrrole-*H*), 9.74 (d, *J* = 4.9 Hz, 4H, *β*-pyrrole-*H*), 9.89 (br. s, 2H, 2 × CO_2H); ^{13}C NMR (176 MHz, DMSO-d_6): δ = 27.60 (CH*C*H$_3$), 27.62 (CH*C*H$_3$), 36.6 (2 × *C*HCH$_2$), 46.71 (*C*H$_2$CO), 46.73 (*C*H$_2$CO), 110.0 (Ar), 115.5 (Ar), 119.2 (Ar), 122.2 (Ar), 123.9 (Ar), 126.1 (Ar), 128.1 (Ar), 129.4 (Ar), 132.3 (Ar), 143.8 (Ar), 146.7 (Ar), 156.1 (Ar), 174.0 (2 × *C*=O); HR-MS (ESI-TOF): *m/z* = 667.2559, calcd. for $C_{40}H_{35}N_4O_6$ $[M+H]^+$:

667.2557; UV/Vis (MeOH): λ_{max} [log ε ($L\,mol^{-1}\,cm^{-1}$)] = 417.0 [5.19], 514.5 [3.97], 552.5 [3.73], 594.0 [3.58], 648.0 nm [3.27].

5,15-Diphenyl-10,20-bis(3-methoxy-3-oxopropyl)-7,8-*cis*-dihydroxychlorin (16a)

CAUTION: OsO_4 is highly poisonous, even at low exposure levels, and must be handled with appropriate precautions. OsO_4 also stains the human cornea, which can lead to blindness if proper safety precautions are not observed.

Under standard reaction conditions, in a 250-mL, three-necked, round-bottom flask equipped with a gas inlet port with argon flow and a stir bar, 5,15-diphenyl-10,20-bis(3-methoxy-3-oxopropyl)-porphyrin (**11a**) (520 mg, 0.82 mmol) (this amount was calculated from the commercially available 250 mg OsO_4 packed in a glass ampoule) was dissolved in dry DCM (30 mL) and freshly distilled pyridine (15 mL). Then, the argon flow was temporarily closed and the ampoule containing 1.2 equivalents of OsO_4 (250 mg, 0.98 mmol) was opened by snapping off the glass top at the neck using glass ampoule cracker and was immediately along with the glass ampoule residues transferred into the reaction mixture (***caution: use gloves, eye protection, and fume hood***). Using an argon balloon, the flask was stoppered under argon atmosphere, shielded from light with aluminum foil, and the contents stirred at ambient temperature. The evolution of the reaction was monitored by TLC. Once no further progress of the reaction was detectable (after 22 h) a saturated MeOH/H_2O (1:1) solution of $NaHSO_3$ (50 mL) was added to the crude reaction mixture. The flask was stoppered and wrapped in aluminum foil, and the biphasic solution was vigorously stirred at ambient temperature for 24 h. Then, the mixture was filtered through a short plug of diatomaceous earth (Celite) and washed with MeOH and then the solvent in the filtrate was minimized using a rotary evaporator. Then, the residue was transferred into a 250 mL separatory funnel and EtOAc was added. The organic phase (EtOAc) was washed with water (3×200 mL) (one spatula of NH_4Cl was added into this mixture for a better phase separation), and dried with anhydrous Na_2SO_4. Then, the organic fraction was evaporated to dryness. A gentle stream of argon for 30 min ensured that the crude material was thoroughly dried. The residue was dissolved in a minimum volume of DCM/EtAOc (80:20) and applied to gravity silica gel column chromatography with DCM/EtAOc (80:20) for further purification. After the recovery of a small amount of the low polarity starting material **11a** (14%) (purple in color), as the second major fraction dihydroxychlorin **16a** (red in color on TLC plate) was obtained. Recrystallization of the product from a DCM/MeOH mixture gave the desired pure crystalline form of the product aseddish-brown crystals; yield: 346 mg (0.52 mmol, 63%); mp 261 °C; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = -1.91$ (br. s, 1H, N*H*), −1.74 (br. s, 1H, N*H*), 2.81 (br. s, 1H, CHO*H*), 3.24–3.32 (m, 1H, CH_2CHHCO), 3.39 (t, J = 8.3 Hz, 2H, CH_2CHHCO, CH_2CHHCO), 3.43–3.51 (m, 1H, CH_2CHHCO), 3.73 (s, 3H, OCH_3), 3.74 (s, 3H, OCH_3), 4.29 (br. s, 1H, CHO*H*), 4.65–4.73 (m, 1H, $CHHCH_2CO$), 4.87–4.94 (m, 1H, $CHHCH_2CO$), 5.02–5.09 (m, 2H, $CHHCH_2CO$, $CHHCH_2CO$), 6.31 (d, J = 7.2 Hz, 1H, C*H*OH), 6.57 (d, J = 7.3 Hz, 1H, C*H*OH), 7.69–7.78 (m, 6H, Ar), 7.92–7.95 (m, 1H, Ar), 8.02–8.05 (m, 1H, Ar), 8.06–8.09 (m, 2H, Ar), 8.32 (d, J = 4.9 Hz, 1H, β-pyrrole-*H*), 8.52 (d, J = 4.5 Hz, 1H, β-pyrrole-*H*), 8.71 (d, J = 4.9 Hz, 1H, β-pyrrole-*H*), 9.02 (d, J = 5.0 Hz, 1H, β-pyrrole-*H*), 9.08 (d, J = 4.6 Hz, 1H, β-pyrrole-*H*), 9.22 (d, J = 5.0 Hz, 1H, β-pyrrole-*H*); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 28.8 (CH_2CH_2CO), 30.2 (CH_2CH_2CO), 39.9 (CH_2CH_2CO), 41.2 (CH_2CH_2CO), 51.86 (OCH_3), 51.94 (OCH_3), 73.3 (*C*HOH), 74.2 (*C*HOH), 120.0 (Ar), 121.3 (Ar), 122.6 (Ar), 124.6 (Ar), 125.0 (Ar), 126.8 (Ar), 127.80 (Ar), 127.89 (Ar), 128.2 (Ar), 128.4 (Ar), 128.9 (Ar), 129.4 (Ar), 132.3 (Ar), 133.7 (Ar), 134.0 (Ar), 134.8 (Ar), 135.5 (Ar), 140.1 (Ar), 140.8 (Ar), 141.5 (Ar), 142.1 (Ar), 152.3 (Ar), 153.2 (Ar), 160.5 (Ar), 162.9 (Ar), 173.2 (*C*=O), 174.1 (*C*=O); HR-MS (ESI-TOF): *m/z*669.2688, calcd. for $C_{40}H_{37}N_4O_6$ $[M+H]^+$: 669.2713, *m/z* = 691.2506, calcd. for $C_{40}H_{36}N_4NaO_6$ $[M+Na]^+$: 691.2513, *m/z* = 707.2239, calcd. for $C_{40}H_{36}KN_4O_6$ $[M+K]^+$: 707.2272; UV/Vis (CH_2Cl_2): λ_{max} [log ε ($L\,mol^{-1}\,cm^{-1}$)] = 407.5 [5.16], 423.0_{shldr} [5.09], 521.5 [4.10], 548.0 [4.12], 594.0 [3.71], 647.5 nm [4.26].

5,15-Bis(2-carboxyethyl)-10,20-bis(3-hydroxyphenyl)-7,8-*cis*-dihydroxychlorin (17)

5,15-Bis(3-acetoxyphenyl)-10,20-bis(3-methoxy-3-oxopropyl)-7,8-*cis*-dihydroxychlorin (**16b**) (140 mg, 0.178 mmol) was dissolved in THF (20 mL). To this solution was added a solution of potassium hydroxide (400 mg, 7.13 mmol) dissolved in hot methanol (10 mL), and the solution was stirred for 12 h at room temperature. The evolution of the reaction was monitored by TLC. Once no further progress of the reaction was detectable (after 12 h), the solvents in the reaction mixture were evaporated using a rotary evaporator. Then, the residue was dissolved in 200 mL EtOAc, then transferred into a 1 L separatory funnel and to the organic phase water was added (200 mL) and the solution was neutralized by adding 25% hydrochloric acid. After neutralization, the organic phase was washed with water (3×200 mL) (one spatula of NH_4Cl was added into this mixture for a better phase separation), and dried with anhydrous Na_2SO_4. The drying agent was removed and the organic phase was evaporated to dryness. The residue was dissolved in a minimum volume of DCM/EtAOc/MeOH (70:25:5) and applied to gravity silica gel column chromatography with DCM/EtAOc/MeOH (70:25:5) for further purification. After the recovery of a small amount of the low polarity starting material **16b** (4%) as the second major fraction the dihydroxychlorin dicarboxylic acid **17** was obtained. Recrystallization of the product **17** from a DCM/MeOH mixture gave the desired pure crystalline form of the product as dark reddish-brown crystals; yield: 79 mg (0.118 mmol, 66%); mp >300 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.20–3.25 (m, 3H, 2× $CHHCO$, $CHHCO$), 3.40–3.45 (m, 1H, $CHHCO$), 4.47–4.75 (m, 4H, 2×CH_2CH_2CO), 6.12–6.14 and 6.22–6.23 (2×m, 1H, C*H*OH), 6.38–6.43 and 6.49–6.52 (2×m, 1H, C*H*OH), 7.12–7.16 (m, 1H, Ar), 7.20–7.22 (m, 1H, Ar), 7.31–7.56 (m, 6H, Ar), 8.30–8.32 (m, 1H, β-pyrrole-*H*), 8.37–8.41 (m, 1H, β-pyrrole-*H*), 8.68–8.70 (m, 1H, β-pyrrole-*H*), 8.86–8.92 (m, 1H, β-pyrrole-*H*), 8.98–9.04 (m, 1H, β-pyrrole-*H*), 9.13–9.19 ppm (m, 1H, β-pyrrole-*H*); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 28.5 ($C_{meso}CH_2$), 31.4 ($C_{meso}CH_2$), 39.6 ($C_{meso}CH_2CH_2$), 40.9 ($C_{meso}CH_2CH_2$), 72.9 (*C*HOH), 73.0

(*C*HOH), 100.0 (Ar), 111.1 (Ar), 113.6 (Ar), 114.4 (Ar), 114.7 (Ar), 119.2 (Ar), 119.5 (Ar), 121.1 (Ar), 121.5 (Ar), 121.8 (Ar), 123.9 (Ar), 124.4 (Ar), 125.1 (Ar), 126.1 (Ar), 127.5 (Ar), 127.8 (Ar), 128.0 (Ar), 128.8 (Ar), 132.2 (Ar), 134.4 (Ar), 135.3 (Ar), 140.3 (Ar), 142.9 (Ar), 143.1 (Ar), 144.4 (Ar), 150.5 (Ar), 155.8 (Ar), 156.0 (Ar), 156.3 (Ar), 162.0 (Ar), 164.1 (Ar), 174.9 (*C*=O), 175.9 (*C*=O); HR-MS (ESI-TOF): $m/z = 673.2319$, calcd. for $C_{38}H_{33}N_4O_8$ $[M+H]^+$: 673.2298; $m/z = 695.2126$, calcd. for $C_{38}H_{32}N_4NaO_8$ $[M+Na]^+$: 695.2118; $m/z = 711.1854$, calcd. for $C_{38}H_{32}KN_4O_8$ $[M+K]^+$: 711.1857; UV/Vis (MeOH): λ_{max} [log ε ($L\,mol^{-1}\,cm^{-1}$)] = 406.5 [5.14], 420.5_{Shldr} [5.08], 519.0 [4.08], 546.0 [4.08], 595.0 [3.78], 647.5 nm [4.21].

Synthesis of 5-[2-(4-Bromophenyl)-3-ethoxy-3-oxopropyl]dipyrromethane (23)

A solution of ethyl 1-(4-bromophenyl)-2-(trimethylsiloxy)cyclopropane-1-carboxylate (**22**) (2.58 g, 7.21 mmol) and pyrrole (25 mL, 362 mmol) was degassed by bubbling with argon for 10 min, then TFA (0.05 mL, 0.72 mmol) was added. The solution was stirred for 3 h at room temperature, and the progress of reaction was monitored by TLC analysis. The TLC plates were developed in a solvent mixture of DCM/EtOAc/NEt_3 (95:4:1) and the bands were visualized by exposure of the air-dried TLC plate to bromine vapor as described for **8a**. Then, the reaction mixture was diluted with DCM (200 mL) and washed with aqueous NaOH (0.1 N, 20 mL), followed by washing with water (3×200 mL) and was then dried with anhydrous Na_2SO_4. The solvent was removed under reduced pressure and then the unreacted pyrrole was removed by a rotary evaporator (10 mbar, 60 °C). The resulting dark viscous oil was dissolved in a minimal quantity of the eluent (DCM/EtOAc/NEt_3 (95:4:1)) and was purified by silica column chromatography using DCM/EtOAc/NEt_3 (95:4:1) as eluent. Any remaining pyrrole elutes first, followed slowly by the dipyrromethane **23** (R_F 0.57) and followed later by tailing materials; colorless oil; yield: 1.79 g (4.47 mmol, 62%). IR (ATR): $\upsilon_{max} = 3375$ (N–H), 3095 (C–H pyrrole), 2975 (C–H), 2895 (CH_3), 1715 (C=O), 1560 (N–H), 1485 (CH_2), 1440 (N–H pyrrole), 1370 (CH_3), 1340 (C–N), 1175 (C–O), 1150 (C–O), 1115 (C–N), 1095 (C–H pyrrole), 1025 (C–H pyrrole), 1010 (Ar-Br), 790 (C–H), 720 cm^{-1} (C–H); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta =$ 1.17 (t, $J = 7.1$ Hz, 3H, CH_2CH_3), 2.36–2.41 (m, 1H, CHC*H*HCHCO), 2.62–2.68 (m, 1H, CHCH*H*CHCO), 3.48 (t, $J = 7.6$ Hz, 1H, C*H*CO), 3.81 (dd, $J = 9.0$, 6.7 Hz, 1H, *meso-H*), 4.00–4.12 (m, 2H, CH_2CH_3), 6.01–6.03 (m, 1H, pyrrole-*H*), 6.05–6.07 (m, 1H, pyrrole-*H*), 6.12–6.15 (m, 2H, pyrrole-*H*), 6.58–6.59 (m, 1H, pyrrole-*H*), 6.63–6.64 (m, 1H, pyrrole-*H*), 7.12–7.14 (m, 2H, Ar), 7.42–7.45 (m, 2H, Ar), 7.69 (br s, 1H, N*H*), 7.74 ppm (br. s, 1H, N*H*); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta = 14.2$ (CH_2CH_3), 35.4 (5-*meso*-*C*), 37.7 (CHCH_2CH), 48.7 (*C*HCO), 61.2 (CH_2CH_3), 105.4 (pyrrole-*C*), 106.5 (pyrrole-*C*), 108.2 (pyrrole-*C*), 108.3 (pyrrole-*C*), 117.5 (pyrrole-*C*), 117.8 (pyrrole-*C*), 121.4 (Ar), 130.0 (Ar), 131.7 (Ar), 131.9 (Ar), 132.6 (Ar), 137.8 (Ar), 173.4 (*C*=O); HR-MS (ESI-TOF): $m/z = 401.0844$, calcd. for $C_{20}H_{22}BrN_2O_2$ $[M+H]^+$: 401.0865; $m/z = 423.0671$, calcd. for $C_{20}H_{21}BrN_2NaO_2$ $[M+Na]^+$: 423.0684; elemental anal. calcd. (%) for $C_{20}H_{21}BrN_2O_2$ (400.1): C 59.86, H 5.27, N 6.98; found: C 58.97, H 5.01, N 6.61.

5,15-Bis[2-(4-bromophenyl)-3-ethoxy-3-oxopropyl]-10,20-diphenylporphyrin (24)

The reaction was performed according to the general procedure. 5-[2-(4-Bromophenyl)-3-ethoxy-3-oxopropyl]-dipyrromethane (**23**) (803 mg, 2.00 mmol) and benzaldehyde (20 μL, 2.00 mmol) were dissolved in dry DCM (500 mL). The resulting solution was degassed by bubbling with an argon flow for 10 min, and TFA (30 μL, 0.40 mmol) was added by syringe with vigorous stirring. The reaction mixture was stirred under argon in the dark at room temperature for 16 h. Then, the calixpyrrole intermediate was subjected to oxidation for 2 h by the addition of DDQ (690 mg, 3.00 mmol), followed by neutralization of TFA with NEt_3 (500 μL, 3.60 mmol). The reaction mixture was filtered through a sintered glass Büchner funnel loaded with silica gel and eluted with a mixture of DCM/EtOAc (90:10) to afford the crude products. After concentration of the filtrate under reduced pressure, the residue was dissolved in a minimum volume of solvent and applied to gravity silica gel column chromatography with DCM/EtOAc (98:2) for further purification and *trans*-A_2B_2-porphyrin **24** as the main product was obtained. Recrystallization of the product from a DCM/MeOH mixture gave the desired pure crystalline form of the product as purple crystals; yield: 205 mg (0.21 mmol, 21%); mp 244 °C; 1:1 *dr*. ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = -2.81$ (br. s, 2H, 2×N*H*), 0.88 (t, $J = 7.2$ Hz, 6H, 2×CH_3), 3.89–4.02 (m, 4H, 2×CH_2CH_3), 4.72 (t, $J =$ 7.0 Hz, 2H, 2×C*H*), 5.24–5.28 (m, 2H, 2×C*H*HCH), 5.82 (dd, $J = 14.8$, 7.5 Hz, 2H, 2×CH*H*CH), 7.19 (d, $J = 8.1$ Hz, 4H, 2×Ar [*meta* to Br]), 7.32 (d, $J = 8.3$ Hz, 4H, 2×Ar [*ortho* to Br]), 7.74–7.82 (m, 6H, 2×Ar), 8.15–8.18 (m, 4H, 2×Ar), 8.00–8.81 (m, 4H, *β*-pyrrole-*H*), 9.26–9.27 (m, 4H, *β*-pyrrole-*H*); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta = 13.9$ (2×CH_3), 39.1 (2×CH_2CH), 58.6 (2×*C*H), 61.2 (2×CH_2CH_3), 115.3 (Ar), 119.7 (Ar), 121.6 (Ar), 126.7 (Ar), 127.8 (Ar), 129.9 (Ar), 131.9 (Ar), 134.6 (Ar), 138.2 (Ar), 142.4 (Ar), 173.4 ppm (2×*C*=O); HR-MS (ESI-TOF): $m/z = 971.1822$, calcd. for $C_{54}H_{45}Br_2N_4O_4$ $[M+H]^+$: 971.1808; UV/Vis (CH_2Cl_2): λ_{max} [log ε ($L\,mol^{-1}\,cm^{-1}$)] = 418.5 [5.38], 517.5 [4.16], 551.0 [4.47], 595.0 [3.40], 651.0 nm [3.25].

{5,15-Bis[2-(4-bromophenyl)-3-ethoxy-3-oxopropyl]-10,20-diphenyl-porphyrinato}zinc(II) (25)

A standard reaction was performed using a 100-mL, round-bottom flask in which 5,15-bis[2-(4-bromophenyl)-3-ethoxy-3-oxopropyl]-10,20-diphenylporphyrin (**24**) (98 mg, 0.10 mmol) was dissolved in DCM/MeOH (4:1; 25 mL). Then, zinc acetate dihydrate (133 mg, 0.60 mmol) was predissolved in MeOH (5 mL) and was added to the reaction mixture at room temperature. The evolution of the reaction was monitored by TLC. Once no further progress of the reaction was detectable (after 2 h), the solvents were evaporated using a rotary evaporator and to the crude reaction mixture was added DCM (100 mL) and then the reaction mixture was washed with water (3×150 mL) and dried with anhydrous Na_2SO_4. The organic phase was finally evaporated to dryness by rotary evaporation. The residue was dissolved in a minimum volume of DCM/EtAOc (90:10) and applied to gravity silica gel column chromatography with DCM/EtAOc (90:10) for further purification. The product **25** was obtained and recrystallization of the product from

a DCM/MeOH mixture gave the desired pure crystalline form of the product as reddish-pink crystals; yield: 104 mg, 010 mmol, quantitative); mp 160 °C; 1:1 *dr*. ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 0.80$–0.83 (m, 6H, 2×CH_3), 3.82–3.93 (m, 4H, 2×CH_2CH$_3$), 4.66 (t, $J = 7.1$ Hz, 2H, 2×CH), 5.13 (dd, $J = 13.9$, 6.7 Hz, 2H, 2×CHHCH), 5.66 (dd, $J = 14.9$, 7.7 Hz, 2H, 2×CHHCH), 7.15 (d, $J = 8.3$ Hz, 4H, 2×Ar [*meta* to Br]), 7.33 (dd, $J = 8.4$, 1.9 Hz, 4H, 2×Ar [*ortho* to Br]), 7.76–7.84 (m, 6H, Ar), 8.12–8.15 (m, 4H, Ar), 8.83 (d, $J = 4.7$ Hz, 4H, β-pyrrole-H), 9.20–9.24 (m, 4H, β-pyrrole-H); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta = 13.70$ (CH_3), 13.72 (CH_3), 39.2 (2×CH$_2$CH), 58.6 (2×CH), 61.0 (2×CH$_2$CH$_3$), 100.0 (Ar), 116.0 (Ar-Br), 120.4 (Ar), 121.5 (Ar), 126.53 (Ar-Br), 126.57 (Ar-Br), 126.61 (Ar-Br), 127.5 (Ar), 128.9 (Ar-Br), 129.8 (Ar), 131.7 (Ar), 132.4 (Ar), 134.4 (Ar), 134.50 (Ar), 134.58 (Ar), 138.2 (Ar), 142.7 (Ar-Br), 149.5 (Ar), 150.1 (Ar), 173.3 (2×C=O); HR-MS (ESI-TOF): $m/z = 1033.0917$, calcd. for $C_{54}H_{43}Br_2N_4O_4Zn$ $[M+H]^+$: 1033.0943; UV/Vis (CH_2Cl_2): λ_{max} [log ε (L mol^{-1} cm^{-1})] = 420.0 [5.16], 552.0 [4.33], 589.0 nm [3.70].

{5,15-Bis[(*E*)-2-(4-(3-butoxy-3-oxoprop-1-en-1-yl)-phenyl)-3-ethoxy-3-oxopropyl]-10,20-diphenylporphyrinato}zinc(II) (26)

A standard reaction was performed in a 100-L, three-necked, round-bottom flask fitted with a septum port, bubble counter, and a gas inlet port with argon flow. Zn-porphyrin **25** (104 mg, 0.10 mmol) was dissolved in dry DMF (15 mL) under argon atmosphere in a Schlenk flask and was transferred to the flask. To the resulting solution were added palladium acetate (3.4 mg, 0.015 mmol, 15 mol-%), triphenylphosphine (15.7 mg, 0.06 mmol), NaOAc (16.4 mg, 0.20 mmol) and butyl acrylate (574 μL, 4.00 mmol). The temperature was raised to 120 °C for 17 h. The evolution of the reaction was monitored by TLC using DCM/EtAOc (80:20) as eluent. Then, the solvent was evaporated using a rotary evaporator and to the crude reaction mixture was added DCM (100 mL) and then the reaction mixture was washed with water (3×150 mL) and dried with anhydrous Na_2SO_4. The organic phase was finally evaporated to dryness by rotary evaporation. The residue was dissolved in a minimum volume of DCM/EtAOc (80:20) and applied to gravity silica gel column chromatography with DCM/EtAOc (80:20) for further purification. The product **26** was obtained and recrystallization of the product from a DCM/MeOH mixture gave the desired pure crystalline form of the product. purple crystals, yield: 41 mg (0.036 mmol, 36%); mp 135 °C; 1:1 *dr*. ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 0.78$–0.83 (m, 6H, 2×COCH$_2$CH_3), 0.94–0.97 (m, 6H, 2×CH$_2$CH$_2$CH_3), 1.38–1.46 (m, 4H, 2×CH$_2$CH_2CH$_3$), 1.63–1.69 (m, 4H, 2×CH_2CH$_2$CH$_3$), 3.84–3.95 (m, 4H, 2×COCH_2CH$_3$), 4.12–4.16 (m, 4H, 2×CO$_2$CH_2CH$_2$), 4.78 (t, $J = 7.0$ Hz, 2H, 2×CH$_2$CH), 5.31 (dd, $J = 14.9$, 6.0 Hz, 2H, 2×CHHCH), 5.83 (dd, $J = 14.7$, 7.7 Hz, 2H, 2×CHHCH), 6.30 (d, $J = 16.0$ Hz, 1H, CHCHCO$_2$), 6.31 (d, $J = 16.0$ Hz, 1H, CHCHCO$_2$), 7.33–7.35 (m, 8H, 2×CHC$_6H_4$CHCHCO), 7.53 (d, $J = 16.0$ Hz, 1H, CHCHCO$_2$), 7.54 (d, $J = 16.0$ Hz, 1H, CHCHCO$_2$), 7.72–7.80 (m, 6H, Ar), 8.11–8.15 (m, 4H, Ar), 8.87 (d, $J = 4.7$ Hz, 4H, β-pyrrole-H), 9.32–9.37 (m, 4H, β-pyrrole-H); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta = 13.80$ (CO$_2$CH$_2$CH_3), 13.82 (CO$_2$CH$_2$CH_3), 13.85 (2×CH$_2$CH$_2$CH_3), 19.3 (2×CH$_2$CH_2CH$_3$), 30.8 (2×CH_2CH$_2$CH$_3$), 39.5 (2×CH_2CH), 59.2 (2×CH$_2$CH), 61.2 (2×CO$_2$CH_2CH$_2$CH$_3$), 64.5 (2×CO$_2$CH_2CH$_2$), 116.28 (CHCHCO$_2$), 116.31 (CHCHCO$_2$), 118.24 (CHCHCO$_2$), 118.26 (CHCHCO$_2$), 120.5 (Ar), 126.59 (Ph), 126.62 (Ph), 126.65 (Ph), 127.6 (Ph), 128.44 (Ar*), 128.46 (Ar*), 128.8 (Ar*), 129.2 (Ar*), 132.6 (Ar), 133.70 (Ar), 133.73 (Ar), 134.47 (Ar), 134.53 (Ar), 134.57 (Ar), 141.58 (Ar), 141.60 (Ar),142.8 (Ar), 144.1 (Ar), 149.7 (Ar), 150.4 (Ar), 167.2 (2×CHCHC=O), 173.5 (2×CH$_2$CHC=O), *=carbons in 1,4-disubstituted phenyls; HR-MS (ESI-TOF): $m/z = 1129.4078$, calcd. for $C_{68}H_{65}N_4O_8Zn$ $[M+H]^+$: 1129.4094; UV/Vis (CH_2Cl_2): λ_{max} [log ε (L mol^{-1} cm^{-1})] = 421.0 [5.52], 552.0 nm [4.24].

Supporting Information

Preparation and characterization data of compounds **8b**, **11b–e**, **12a–h**, **16b**, **16c** and **20**; copies of the ^{1}H NMR spectrum of compound **22**; ^{1}H and ^{13}C NMR spectra of compounds **8a**, **8b**, **11b–e**, **12a–h**, and **13–26**; copies of the COSY ^{1}H-^{1}H, HMQC ^{1}H-^{13}C and HMBC ^{1}H-^{13}C correlated NMR spectra of compound **11a** as the parent compound are available as Supporting Information.

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