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1,3-Dipolar Cycloaddition Reactions of Porphyrins with Azomethine Ylides†

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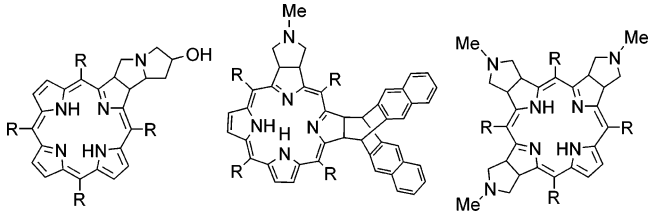

The behavior of porphyrins as dipolarophiles in 1,3-dipolar cycloadditions with azomethine ylides was studied. Depending on the nature of the substituent groups on the porphyrin macrocycles, the reaction can give monoadducts (chlorins) or bisadducts (isobacteriochlorins and bacteriochlorins). When a large excess of azomethine ylide is used, trisadducts can also be obtained. Mixed isobacteriochlorin derivatives were prepared from the reaction of azomethine ylides with the chlorin monoadducts previously obtained via Diels−Alder reactions.

Introduction

In recent years, great effort has been put forth toward the development and improvement of new methods to convert porphyrins into dihydroporphyrins (chlorins) and tetrahydroporphyrins (isobacteriochlorins and bacteriochlorins). This is mainly due to the potential use of such compounds in several scientific areas, with a special emphasis in medicine. Present medicinal formulations already being used in several countries include porphyrin derivatives as photosensitizers for the photodetection and treatment (photodynamic therapy, PDT) of cancer cells and for the treatment of the age-related macular degeneration. Amphiphilic structural features, simple synthesis, and absorptions near the infrared region are requirements to be fulfilled by any new potential photosensitizer; good books and reviews related to this subject have been published.[1]

We and others have shown that Diels−Alder reactions and 1,3-dipolar cycloadditions can be excellent tools for preparing novel derivatives containing such macrocyclic features.[2−5] In addition, the high versatility and the regio- and stereoselectivity found in those reactions[6] can be used to prepare new porphyrinic compounds with well-defined stereochemistry.

Now we report further progress in the cycloaddition reactions of porphyrinic macrocycles with azomethine ylides. The experimental conditions were optimized in order to favor mono- or bisaddition. The new products

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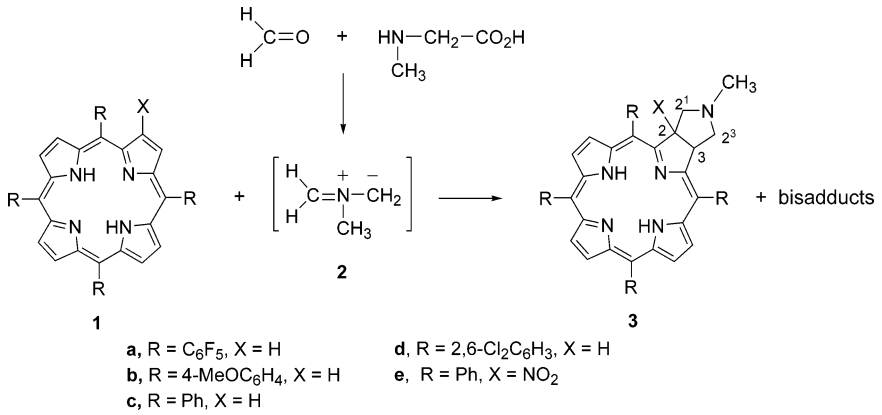
SCHEME 1



fulfill certain requirements for being considered as potential PDT photosensitizer candidates. If required, they can even be further derivatized into more promising PDT agents, namely, by converting them into cationic derivatives by simple alkylation procedures.

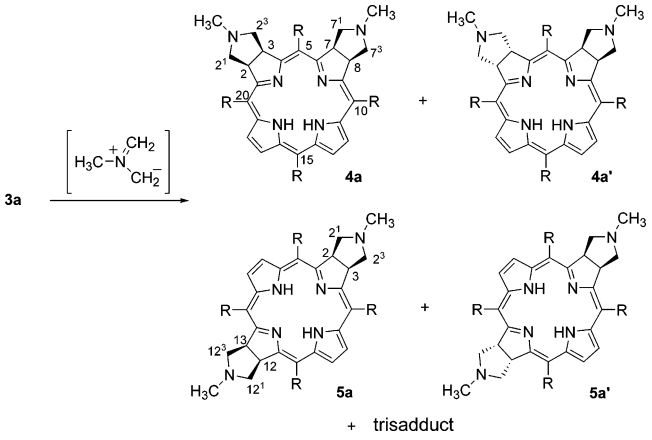
Results and Discussion

The 1,3-dipolar cycloaddition reactions of tetrapyrrolic macrocycles with azomethine ylides were, typically, carried out as follows: a toluene solution of the porphyrin derivative, paraformaldehyde, and an excess of amino acid was heated at reflux for 5 h under a nitrogen atmosphere. The reaction was monitored by TLC, and further portions of amino acid and paraformaldehyde could be added and the reflux prolonged for an extra period of 5 h in order to obtain better yields of the adducts.

The reaction of porphyrin **1a** with azomethine ylide **2** (generated in situ from sarcosine and paraformaldehyde) afforded chlorin **3a** in 61% yield and an isobacteriochlorin (a bisadduct) in 11% yield (Scheme 1).

To increase the amount of bisadducts, chlorin **3a** was treated with a large excess of precursors of the azomethine ylide **2** (Scheme 2). After 40 h at reflux and

SCHEME 2

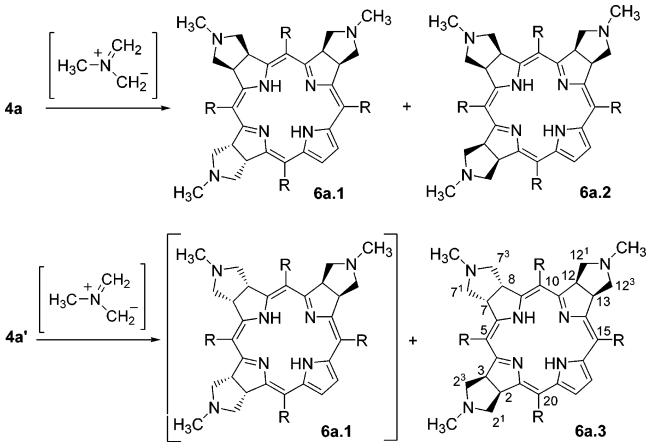


successive additions of small portions of sarcosine and paraformaldehyde, most of the chlorin **3a** was converted into bisadducts. Purification of the reaction mixture by preparative TLC afforded the isobacteriochlorin **4a′** (37% yield) as the main product of the reaction and four minor products: the diastereomeric isobacteriochlorin **4a** (5% yield), the two diastereomeric bacteriochlorins **5a** and **5a′** (trace amount), and a trisadduct (5% yield). These results suggest that the addition of a second azomethine ylide to chlorin **3a** occurs preferentially at the adjacent β-pyrrolic double bond (site selectivity) and at the anti face of the chlorin (diastereofacial selectivity), producing mainly the bisadduct with the two pyrrolidine-fused rings in adjacent positions and with "trans" configuration.

Insertion of Zn(II) into chlorin derivative **3a** does not change the outcome of the reaction. In fact, and despite awareness of the relatively lower reactivity of the Zn(II) complex, it was observed that the selectivity for the adjacent β-pyrrolic double bond remains, yielding mainly the Zn(II) complex of isobacteriochlorin **4a′**.

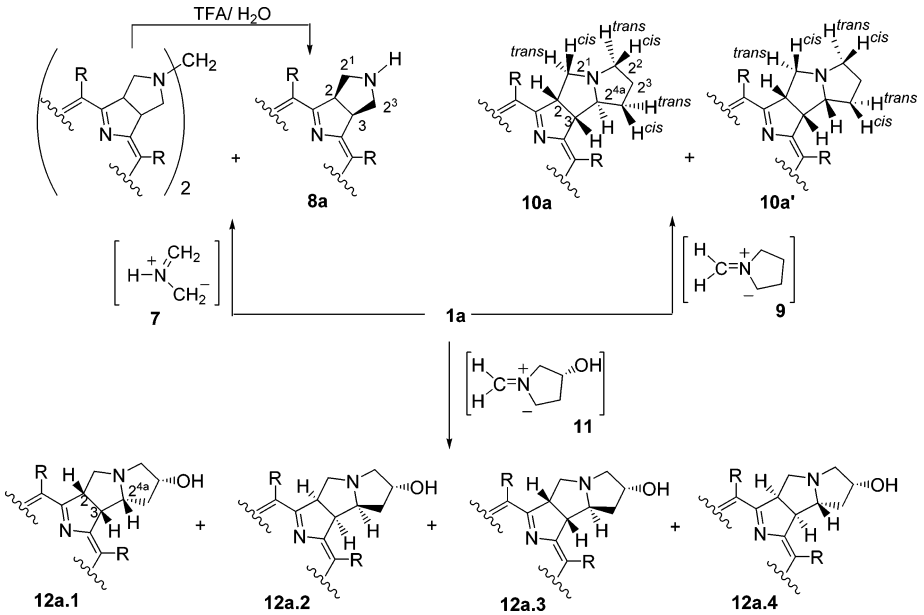
Interesting results were also obtained when the reaction of isobacteriochlorin **4a** or **4a′** was performed with an excess of azomethine ylide **2** (refluxing toluene, 30 h). With isobacteriochlorin **4a′**, the reaction afforded one trisadduct, while with isobacteriochlorin **4a**, the reaction gave two trisadducts. These trisadducts show similar UV−vis and mass spectra. Scheme 3 shows all possible diastereomers that could be formed in these reactions.

SCHEME 3



As shown in Scheme 3, compound **6a.1** can be obtained from **4a** or **4a′**. However, compounds **6a.2** and **6a.3** can be formed only from **4a** and **4a′**, respectively. Since isobacteriochlorin **4a** gave two trisadducts, this means that both trisadducts **6a.1** and **6a.2** are produced in this reaction. On the other hand, isobacteriochlorin **4a′** gave

SCHEME 4



only one trisadduct, which can be **6a.1** or **6a.3**. The ^{1}H NMR spectrum of the trisadduct obtained from **4a′** shows one doublet at δ 6.33 (J 2.1 Hz) corresponding to two β-pyrrolic protons, while the spectrum of the mixture of the two trisadducts obtained from **4a** shows two doublets, each corresponding to two β-pyrrolic protons: one at δ 6.36 (J 1.9 Hz) and another at δ 6.43 (J 2.5 Hz) (with relative intensities ca. 1:5, respectively). These data reveal that the trisadduct obtained from **4a′** is different from both trisadducts obtained from **4a**, and therefore it should correspond to compound **6a.3**. Furthermore, comparing the spectrum of **6a.3** and the one due to the trisadduct obtained in the reaction with chlorin **3a** allows to conclude that they have the same structure, and so compound **6a.3** is the main product of the trisaddition reaction.

During the course of this work we noticed that both bis- and trisadducts could be directly obtained from porphyrin **1a**. In fact, when a larger excess of the precursors of the azomethine ylide **2** was used and the reaction time was increased up to 60 h, a smaller amount of chlorin was isolated (24% yield) to the benefit of bis- and trisadducts (38% yield for isobacteriochlorin **4a′** and 13% yield for trisadduct **6a.3**).

Next, we turned our attention towards the cycloaddition reaction with other α-amino acids, namely, glycine, L-proline and *trans*-4-hydroxy-L-proline (Scheme 4). The reaction between porphyrin **1a** and azomethine ylide **7**, generated in situ from glycine and paraformaldehyde, yielded (after 30 h of reaction time) a mixture of two compounds: the major one was identified as the expected chlorin **8a** and the minor one probably corresponds to a dimer resulting from the reaction of **8a** with formaldehyde.[7] This dimer was hydrolyzed to **8a** by treatment of the crude reaction mixture with TFA/H_2O at room temperature. In this way, chlorin **8a** was obtained in 47% yield. We have also isolated, but in a trace amount, a bisadduct [$(M + H)^+$= 1061] of the isobacteriochlorin type (λ_{max} = 587 and 651 nm).

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The reaction of **1a** with azomethine ylide **9**, generated in situ from L-proline and paraformaldehyde, furnished (after 10 h of reaction time) a 1:1 *endo*/*exo* diastereomeric mixture of chlorins **10a** and **10a′** in combined 43% yield. Each chlorin **10a** and **10a′** should be a racemate. This reaction also furnished a trace amount of a mixture of isobacteriochlorins with $(M + H)^+ = 1141$ and $\lambda_{max} = 588$ and 649 nm.

When the cycloaddition reaction was carried out with porphyrin **1a**, paraformaldehyde, and *trans*-4-hydroxy-L-proline, we isolated only three chlorins (with a combined yield of 26%), although diastereomers **12a.1**−**12a.4** could be expected. No bisadducts were isolated from this reaction.

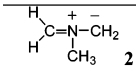
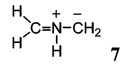
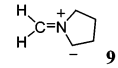
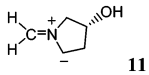
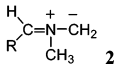
We have also tried to perform the cycloaddition between porphyrin **1a** and C,N-disubstituted azomethine ylides **2′**, generated in situ from sarcosine and several aldehydes such as benzaldehyde, 4-nitrobenzaldehyde, 4-methoxybenzaldehyde, acetaldehyde, phenylacetaldehyde, and chloral hydrate, but none of these experiments gave the expected adducts; in all cases, the starting porphyrin was recovered unchanged.

The conditions and the yields of the 1,3-dipolar cycloaddition reactions of porphyrin **1a** with azomethine ylides are summarized in Table 1.

The reaction of other *meso*- and β-substituted porphyrins with azomethine ylide **2**, in refluxing toluene or *o*-dichlorobenzene, was also carried out in order to find the effect of the substituents in the reactivity of the porphyrins (Scheme 1). The results are presented in Table 2. Better yields were obtained when the reactions were carried out at higher temperatures.

It is evident from these results that the presence of electron-withdrawing atoms in the aryl groups increases the reactivity of the porphyrin toward azomethine ylide **2**. In fact, *meso*-tetrakis(2,6-dichlorophenyl)porphyrin **1d** is more reactive than *meso*-tetraphenylporphyrin **1c**, which is more reactive than *meso*-tetrakis(4-methoxyphenyl)porphyrin **1b**. Actually, from this group of three porphyrins, only porphyrin **1d** gave bisadducts (isobacteriochlorins) with $(M + H)^+ = 1005$ and $\lambda_{max} = 594$ and

TABLE 1. Cycloaddition of Porphyrin 1a with Different Azomethine Ylides[a] in Refluxing Toluene

azomethine ylide	t (h)	yield (%) monoadducts	yield (%) bisadducts
 **2**	15	61	11
 **7**	30	47	trace amount
 **9**	10	43	trace amount
 **11**	20	26	not observed
 **2′**	32	not observed	not observed

[a] R = Me, Bn, CCl_3, Ph, 4-$NO_2C_6H_4$, 4-$MeOC_6H_4$.

654 nm. Electron-withdrawing groups in the β-pyrrolic position such as the nitro group in porphyrin **1e** also increase the reactivity of the macrocycle. In this case, as expected, the cycloaddition occurred selectively at the most activated double bond, yielding chlorin **3e** in 27% yield (Scheme 1). This chlorin is very stable and can be stored without any decomposition.

We have also considered the synthesis of mixed cycloadducts using as starting materials the chlorins **13** and **14**, which resulted from the Diels−Alder reaction of *meso*-tetrakis(pentafluorophenyl)porphyrin with *ortho*-benzoquinodimethane[2a] or pentacene,[2b] respectively (Scheme 5). As observed in the previous bisaddition experiments (Scheme 2), the reaction of chlorins **13** and **14** with azomethine ylide **2** gave mainly the isobacteriochlorins **15** and **16**, respectively (34% yield in both cases). Other bisadducts (bacteriochlorins) and trisadducts were also isolated but in minor amounts. These results show that the second addition to the macrocycle occurs preferentially at the β-pyrrolic double bond adjacent to the ring already fused to the macrocycle.

Structural Characterization. All mono-, bis-, and trisadducts synthesized were characterized by nuclear magnetic resonance, UV−vis spectroscopy, and high-resolution mass spectrometry or elemental analyses.

Figure 1 shows the electronic absorption spectra of adducts **3a**, **4a′**, **5a′**, and **6a.3**, measured in dichloromethane, at equimolar concentrations. As expected, the spectrum of monoadduct **3a** exhibits a characteristic chlorin band at 652 nm.

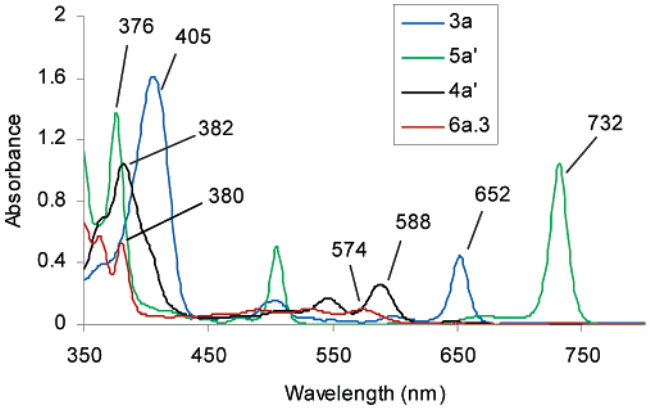
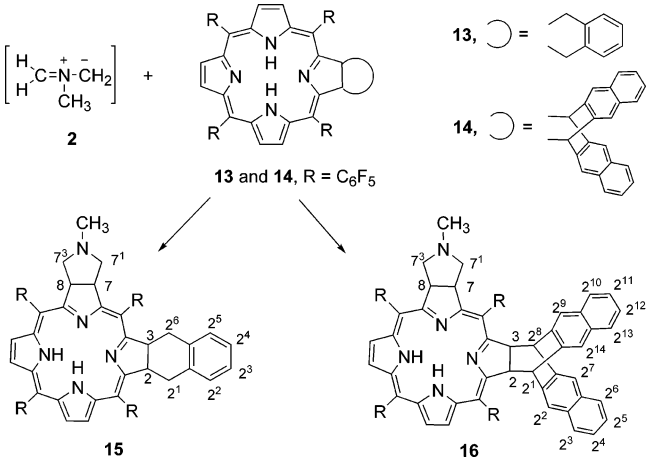


FIGURE 1. Electronic absorption spectra of adducts **3a**, **4a′**, **5a′**, and **6a.3** at equimolar concentrations (10 μM) in dichloromethane.

SCHEME 5



The UV−vis spectrum of bisadduct **4a′** is typical of an isobacteriochlorin: it shows three bands of increasing intensity between 510 and 588 nm and a less intense band at 645 nm. The absorption spectra of isobacteriochlorins **4a**, **15**, and **16** are very similar to this one.

The UV−vis spectrum of bisadduct **5a′**, which is similar to that of **5a**, shows a strong absorption band at 732 nm, which is characteristic of a bacteriochlorin derivative.

Finally, the UV−vis spectrum of trisadduct **6a.3** exhibits an absorption band near 380 nm and other broad absorption bands with relatively low intensities. Although the conjugation of the macrocycle ring in this derivative is formally interrupted, several resonance forms may be drawn, justifying the fact that these macrocycles show absorption bands similar to those of

TABLE 2. Cycloaddition of Different Porphyrins with Azomethine Ylide 2 in Refluxing Toluene

porphyrin	*meso*-substituent	β-substituent	*t* (h)	yield (%) monoadduct	yield (%) bisadduct
1a	C_6F_5	H	15	61	11
1b	4-$MeOC_6H_4$	H	20 (20)[a]	3 (7)[a]	not observed
1c	Ph	H	50 (20)[a]	12 (21)[a]	not observed
1d	2,6-$Cl_2C_6H_3$	H	35 (20)[a]	26 (45)[a]	6 (7)[a]
1e	Ph	NO_2	20	27	not observed

[a] In refluxing 1,2-dichlorobenzene.

TABLE 3. ^{1}H NMR Spectral Data for Adducts 3a, 4a′, 5a, 5a′, and 6a.3

adduct	pyrrolic β-H	β-H [C (sp^3)]	H-pyrrolidine	CH_3	NH
3a	8.40 (d, *J* 4.9), 8.48 (s), 8.71 (d, *J* 4.9)	5.26 (t, *J* 5.1)	2.52−2.56 (m), 3.11−3.16 (m)	2.21 (s)	−1.82 (s)
4a	7.120 (d, *J* 4.6), 7.125 (d, *J* 4.6), 7.56 (d, *J* 4.6)	4.14−4.23 (m), 4.29−4.38 (m)	2.37−2.43 (m), 2.85−2.96 (m)	2.27 (s)	4.08 (br s)
4a′	7.089 (d, *J* 4.6), 7.091 (d, *J* 4.6), 7.55 (d, *J* 4.6)	4.33−4.46 (m)	2.12−2.21 (m), 2.24−2.29 (m), 2.63−2.69 (m), 2.82−2.88 (m)	2.15 (s)	4.12 (br s)
5a	8.17 (s)	5.05−5.11 (m)	2.39−2.44 (m), 3.04−3.09 (m)	2.17 (s)	−1.85 (s)
5a′	8.26 (s)	5.24 (br s)	2.62−2.70 (m), 3.40−3.65 (m)	2.08 (s)	−2.09 (s)
6a.3	6.33 (d, *J* 2.1 Hz)	3.79−3.92 (m), 4.02−4.06 (m)	2.00−2.13 (m), 2.37−2.43 (m), 2.58−2.64 (m)	2.12 (s), 2.13 (s)	5.88 (s), 6.26 (s)

porphyrins.[8] The relative configuration or the nature of the rings fused to the macrocycle does not modify the outline of the UV−vis spectrum.

The FAB mass spectra of the adducts typically show the $[M + H]^+$ peak and minor value peaks presumably corresponding to fragments resulted from retrocycloadditions. Exceptional situations were found in the mass spectra of chlorin **3e**, where we observed the loss of HNO_2, and in adducts **3b**, **4a**, and **6a.3**, where only $[M + H]^+$ and $(M)^{\bullet+}$ were observed. The mass spectra of isobacteriochlorins **15** and **16** are particularly interesting: while the mass spectrum of **15** showed $[M + H]^+ = 1136$ and only one fragment at *m/z* 1079, corresponding to the loss of azomethine ylide, the mass spectrum of **16** showed $[M + H]^+ = 1310$ and two fragments at *m/z* 1032 and 975, corresponding to the loss of pentacene and subsequent loss of azomethine ylide. These results are easily explained by the fact that the loss of pentacene involves an energetically favorable process, with the transformation of a nonaromatic ring into an aromatic one, while the loss of *ortho*-benzoquinodimethane involves the loss of aromaticity in the benzene ring (an energetically unfavorable process).

The structures of the adducts were deduced from their ^{1}H NMR spectra. The chemical shifts and the multiplicity of the signals for the adducts obtained from porphyrin **1a** and the ylide **2** are summarized in Table 3.

From the values of the chemical shifts observed in the spectra of the mono- and bisadducts, we conclude that the β-pyrrolic protons linked to sp^2 or sp^3 carbon atoms are gradually shifted to higher fields due to the reduction of the ring current. These shifts are higher for the isobacteriochlorins, indicating that the ring current in these derivatives is lower than in bacteriochlorins, despite all being tetrahydroporphyrins. These observations are consistent with similar results obtained for other reduced porphyrins.[9] In trisadducts, these signals are even more shifted to higher fields since the conjugation of the macrocyclic system is formally interrupted. The effect of reduced ring current is also observed in the chemical shifts of the inner NH protons. Whereas in chlorins and bacteriochlorins the NH protons appear around δ −2 ppm, in isobacteriochlorins and trisadducts they appear around δ 4 and 6 ppm, respectively. The possible out-of-plane geometry of the NH bonds in the trisadducts may also contribute to such high δ values.[10−12]

The ^{1}H NMR spectra of the adducts gave also important information about the symmetry of the molecules. In chlorin **3a**, the six β-pyrrolic protons appear as two doublets and one singlet, which is typical of a chlorin with one plane of symmetry. In bacteriochlorins **5a** and **5a′**, the four β-pyrrolic protons appear as one singlet at δ 8.17 and 8.26, respectively. Such chemical shifts indicate that there is a reduced ring current in **5a**, which probably results from a deviation from planarity of the macrocycle brought by the "cis" relationship between the two pyrrolidine-fused rings. In contrast, in isobacteriochlorins **4a** and **4a′**, the four protons appear as three doublets with very similar chemical shifts. These compounds were identified mainly by the analysis of ^{19}F NMR spectra. These spectra showed, for both isobacteriochlorins, three sets of nonequivalent pentafluorophenyl rings, in a 1:2:1 ratio, expressed by the integral values of *para*-fluorine atoms (1F:2F:1F). From the spectrum of isobacteriochlorin **4a**, we concluded the following: (i) the resonances attributed to the two *ortho*-fluorine atoms of the 5-phenyl ring are very different from each other (δ −133.32 and −137.62 ppm, 1F each), where the former has a quite different environment relative to all of the other fluorine atoms in the molecule; (ii) the phenyl rings at positions 10 and 20 are equivalent, but again, in each ring, the two *ortho*-fluorine atoms are not equivalent (δ −136.66 and −139.73 ppm, 2F each); and (iii) the two *ortho*-fluorine atoms in the 15-phenyl ring are also not equivalent but have a similar environment (δ −139.26 and −139.53 ppm, 1F each). These results are only compatible with the structure of isobacteriochlorin **4a** having a "cis" configuration. The ^{19}F NMR spectrum of isobacteriochlorin **4a′** shows that its structure must be more symmetrical than **4a**, since only four signals (δ −136.98, −137.16, −139.27, and −139.67 ppm) are observed for the *ortho*-fluorine atoms: one signal for the two *ortho*-F atoms in the 5-phenyl ring, two signals for the two nonequivalent *ortho*-F atoms in the equivalent 10- and 20-phenyl rings, and one signal for the two *ortho*-F atoms in the 15-phenyl ring. This spectrum is in agreement with the structure of isobacteriochlorin **4a′** having a "trans" configuration.

In the ^{1}H NMR spectrum of trisadduct **6a.3**, the two β-pyrrolic protons appear as one doublet at δ 6.33, with *J* 2.1 Hz, due to coupling with the NH proton. This long-range coupling disappears after addition of D_2O to the solution. The ^{19}F NMR spectrum of **6a.3** reveals the presence of two signals at δ −152.16 and −154.98 ppm (2F each) for the *para*-fluorine atoms: one signal for the

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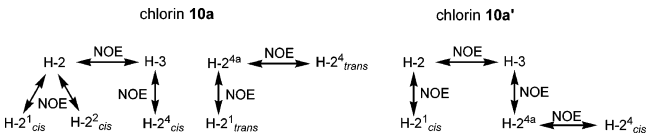

FIGURE 2. NOE cross-peaks found in the NOESY spectra of chlorins **10a** and **10a′**.

two *para*-F atoms in the phenyl rings at positions 5 and 10 and the other one for the two *para*-F atoms in the phenyl rings at positions 15 and 20. In the same spectrum, the three signals corresponding to the *ortho*-fluorine atoms are also very diagnostic: one signal at δ −137.90 ppm, corresponding to the four *ortho*-F atoms in the phenyl rings at positions 5 and 10, and two signals at δ −136.80 and −140.87 ppm, each one corresponding to one *ortho*-F atom in the 15-phenyl ring and one *ortho*-F atom in the 20-phenyl ring. These data are in agreement with the relative configuration indicated for trisadduct **6a.3**.

The ^{1}H NMR spectrum of chlorin **8a** is quite similar to that of chlorin **3a**; they only differ in the signal of the methyl group that is absent in chlorin **8a**.

The ^{1}H NMR spectra of chlorins **10a** and **10a′** are much more complex. The configuration of these chlorins was mainly established by the intense NOE cross-peaks found in their NOESY spectra (Figure 2).

In the NOESY spectrum, chlorin **10a** shows a NOE effect of H-2^{4a} with H-2$^4_{trans}$ and H-2$^1_{trans}$. In ^{1}H NMR spectrum, H-2^{4a} appears as one doublet at δ 3.80 ($J_{H2^{4a}-H3}$ 4.7 Hz), which is consistent with a trans configuration between H-2^{4a} and H-3. In contrast, chlorin **10a′** shows a NOE effect of H-2^{4a} with H-3 and H-2$^4_{cis}$. In addition, H-2^{4a} appears as one quartet, at δ 3.49 (J 8.6 Hz), which confirms the cis configuration for this chlorin. In general, the signals of the pyrrolizidine-fused ring protons for cis isomer **10a′** appear further downfield than the corresponding signals for the trans isomer due to the ring distortion found in chlorin **10a′**, which promotes a big influence of the porphyrinic ring in this chlorin.

On the basis of the multiplicity and coupling constants of the H-3 signal of chlorins **12**, we were able to establish the relative stereochemistry of protons H-3 and H-2^{4a}. In this way, H-3 in the chlorin with the higher R_f ($J_{H3-H2^{4a}}$ 5.3 Hz and J_{H3-H2} 8.9 Hz) as well as in the chlorin with the medium R_f ($J_{H3-H2^{4a}}$ 4.5 Hz and J_{H3-H2} 9.4 Hz) both appeaar sa double doublets, indicating a trans configuration for both chlorins **12a.3** and **12a.4**; in the chlorin with the lower R_f, H-3 appears as a triplet (J 8.9 Hz), indicating a cis configuration, which is consistent with structures **12a.1** or **12a.2**. Because of the high number of overlapping signals in the RMN spectra of these compounds, we were not able to establish the relative stereochemistry between H-2^{4a} and the OH group.

The aliphatic region of the ^{1}H NMR spectra of chlorins **3b**−**d** is very similar to that of chlorin **3a**. In the spectrum of chlorin **3e**, the chemical shifts of the protons in the pyrrolidine ring were assigned on the basis of the coupling constants and the electronegative effect of the nitro group. The triplet at δ 5.62 (J 9.0 Hz) was attributed to H-3; this proton presents correlation with two triplets at δ 2.13 and 3.16 (J 9.0 Hz), which were attributed to H-2$^3_{trans}$ and H-2$^3_{cis}$, respectively. Protons H-2$^1_{trans}$ and H-2$^1_{cis}$, which are neighbors of nitro group, appear as two doublets at δ 2.82 and 3.98, with a geminal coupling constant of 11.9 Hz.

The ^{1}H NMR spectra of mixed isobacteriochlorins **15** and **16** are relatively similar to the ones of the isobacteriochlorins **4**. Typically, the NH signals appear between δ 3.78 and 4.17 ppm, while the H-β-pyrrolic signals appear between δ 6.85 and 7.49 ppm.

Conclusion

Azomethine ylides react with *meso*-tetraarylporphyrins in 1,3-dipolar cycloadditions to yield chlorins (monoadducts) and isobacteriochlorins (bisadducts). Isobacteriochlorins can be the main products of the reaction if a large excess of precursors of the azomethine ylide is used. The bisaddition is selective, yielding mainly one of the four possible isomers. In those conditions, trisaddition can also occur but in a small scale, affording only one trisadduct. Further studies are underway to clarify such selectivity.

meso-Tetraarylporphyrins with electron-withdrawing groups (pentafluorophenyl and 2,6-dichlorophenyl groups) are the most reactive. The introduction of a nitro group in the β-pyrrolic position induces an increasing reactivity in the macrocycle. In this case, the reaction is site selective, yielding mainly the chlorin resulting from the attack of the azomethine ylide to the double bond bearing the nitro group.

Cycloaddition reactions with azomethine ylides can also be used as a strategy for the selective synthesis of novel mixed isobacteriochlorins.

All the chlorin monoadducts described here are stable compounds, are obtained in reasonable yields, and show absorption bands of medium intensity at ca. 650 nm, which make them potentially useful photosensitizers for PDT.

Experimental Section

^{1}H and ^{13}C solution NMR spectra were recorded at 300.13 and 75.47 MHz, respectively. $CDCl_3$ was used as the solvent and TMS as the internal reference; the chemical shifts are expressed in δ (ppm) and the coupling constants (J) in hertz [Hz]. Unequivocal ^{1}H assignments were made with aid of two-dimensional COSY (^{1}H/^{1}H) and NOESY spectra (mixing time of 800 ms), while ^{13}C assignments were made on the basis of two-dimensional HETCOR (^{1}H/^{13}C) (or HSQC) and HMBC (delays for long-range J C/H couplings were optimized for 7 Hz) experiments. C_6F_6 was used as a reference in the ^{19}F NMR spectra. Mass spectra and HRMS were recorded using $CHCl_3$ as the solvent and NBA as the matrix. Column chromatography was carried out using silica gel (35−70 mesh). Preparative thin-layer chromatography was carried out on 20 × 20 cm glass plates coated with silica gel (1 mm thick).

meso-Tetraarylporphyrins **1a**−**d** were prepared according to the literature.[13] β-Nitro-*meso*-tetraphenylporphyrin **1e** was prepared by nitration of *meso*-tetraphenylporphyrin with $Cu(NO_3)_2$ in acetic anhydride, followed by acid treatment.[14] Chlorins **13** and **14** were prepared by Diels−Alder reaction of *meso*-tetrakis(pentafluorophenyl)porphyrin with *ortho*-benzoquinodimethane or pentacene, respectively.[2] Light petroleum was the fraction of bp 40−60 °C.

General Procedure for the 1,3-Dipolar Cycloadditions. A toluene or *o*-dichlorobenzene (0.8−5 mL) solution of the porphyrinic macrocycle (5−42 mg), α-amino acid (2−20 equiv),

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and paraformaldehyde (5−25 equiv) was heated at reflux for 5 h under a nitrogen atmosphere. Depending on the reactivity of substrates, additional portions of α-amino acid and paraformaldehyde were added and the reaction mixture was refluxed for another 5 h period. After being cooled to room temperature, the reaction mixture was applied on the top of a silica gel column, and the adducts were eluted with the adequate solvents. The stereoisomeric isobacteriochlorins and bacteriochlorins were then separated by preparative TLC. The isolated compounds were crystallized from dichloromethane/hexane.

Cycloaddition of Porphyrin 1a with Azomethine Ylide 2. Successive additions of sarcosine (4.0 mg, 45.4 μmol) and paraformaldehyde (3.4 mg, 0.114 mmol) were made every 5 h, for 15 h, to a toluene (5 mL) solution of porphyrin **1a** (22.2 mg, 22.7 μmol) following the general procedure. The purification was carried out on a silica gel column using dichloromethane/light petroleum (4:1) as an eluent to give the unchanged porphyrin **1a** (4.4 mg, 20%) followed by chlorin **3a** (14.2 mg, 61%). Using dichloromethane as the eluent, a small amount of isobacteriochlorin (2.8 mg, 11%) was collected. Spectral data for **3a**: mp 247−248 °C; ^{1}H NMR data (see Table 1); ^{19}F NMR δ −136.62 (dd, 2 F, J 23.2 and 7.7, F_{ortho}-Ar), −138.17 (dd, 2 F, J 22.5 and 8.7, F_{ortho}-Ar), −138.25 (dd, 2 F, J 21.8 and 8.7, F_{ortho}-Ar), −138.63 (dd, 2 F, J 23.4 and 7.7, F_{ortho}-Ar), −152.66 (dd, 2 F, J 22.0 and 21.2, F_{para}-Ar), −153.01 (dd, 2 F, J 22.0 and 21.3, F_{para}-Ar), −161.39 (ddd, 2 F, J 23.2, 22.0, and 8.3, F_{meta}-Ar), −161.78 (ddd, 2 F, J 23.4, 22.1, and 8.3, F_{meta}-Ar), −162.73 (ddd, 2 F, J 22.5, 22.0, and 8.4, F_{meta}-Ar), −162.78 (ddd, 2 F, J 22.5, 21.3, and 8.4, F_{meta}-Ar); ^{13}C NMR δ 41.2 (CH_3), 53.1 (C-2 and C-3), 62.8 (CH_2), 96.8, 106.1, 123.9, 128.0, 132.3, 135.2, 140.3, 152.7, 168.8; UV−vis (CH_2Cl_2) λ_{max}/nm (log ϵ) 405 (5.29), 505 (4.26), 598 (3.77), 652 (4.72); MS FAB$^+$ m/z 1032 (M + H)$^+$, 1031 (M)$^{\bullet+}$, 975 [(M − C_3H_7N) + H]$^+$. Anal. Calcd for $C_{47}H_{17}N_5F_{20}$: C, 54.69; N, 6.49; H, 2.10. Found: C, 54.72; N, 6.79; H, 1.66.

Cycloaddition of Chlorin 3a with Azomethine Ylide 2. Successive additions of sarcosine (3.6 mg, 40.6 μmol) and paraformaldehyde (3.0 mg, 0.102 mmol) were made every 5 h, for 40 h, to a toluene (5 mL) solution of chlorin **3a** (21.0 mg, 20.3 μmol) as described in the general procedure. The purification was carried out on a silica gel column using dichloromethane/light petroleum (4:1) as the first eluent to give the unchanged chlorin **3a** (6.8 mg, 32%); then, using dichloromethane/acetone (3:1) as an eluent, a mixture of products was obtained. This mixture was further purified by preparative TLC (silica), using dichloromethane/acetone (30:1) as an eluent. Five fractions were collected. The first and the second ones (with higher R_f values) were identified as bacteriochlorins **5a** and **5a′**, respectively. These compounds were obtained in trace amounts. The following fraction was the isobacteriochlorin **4a′** (8.3 mg, 37%), and the next one was the isobacteriochlorin **4a** (1.2 mg, 5%). Finally, the last fraction (the one with lower R_f) was the trisadduct **6a.3** (1.2 mg, 5%). Spectral data for **4a**: mp 223−225 °C; ^{1}H NMR data (see Table 1); ^{19}F NMR δ −133.32 (d, 1 F, J 23.5, F_{ortho}-Ar), −136.66 (dd, 2 F, J 23.2 and 5.7, F_{ortho}-Ar), −137.62 (dd, 1 F, J 24.2 and 7.3, F_{ortho}-Ar), −139.26 (dd, 1 F, J 22.6 and 6.8, F_{ortho}-Ar), −139.53 (dd, 1 F, J 23.8 and 6.8, F_{ortho}-Ar), −139.73 (dd, 2 F, J 23.9 and 7.3, F_{ortho}-Ar), −151.80 (t, 1 F, J 20.5, F_{para}-Ar), −153.47 (t, 2 F, J 20.8, F_{para}-Ar), −153.69 (dd, 1 F, J 21.8 and 20.9, F_{para}-Ar), from −159.99 to −160.14 (m, 1 F, F_{meta}-Ar), from −161.14 to −161.51 (m, 3 F, F_{meta}-Ar), −162.05 (ddd, 2 F, J 22.6, 21.8 and 8.5, F_{meta}-Ar), from −162.66 to −162.92 (m, 2 F, F_{meta}-Ar); ^{13}C NMR δ 41.2 (CH_3), 48.2 and 52.4 (C-2, C-3, C-7, and C-8), 61.9 and 62.5 (CH_2), 91.6, 97.6, 113.0, 114.7, 121.5, 128.6, 139.7, 143.4, 148.7, 157.0; UV−vis (CH_2Cl_2) λ_{max}/nm (log ϵ) 381 (4.99), 509 (3.94), 546 (4.19), 588 (4.37); MS FAB$^+$ m/z 1089 (M + H)$^+$, 1088 (M)$^{\bullet+}$; HRMS (FAB) exact mass m/z for $C_{50}H_{25}N_6F_{20}$ (M + H)$^+$ calcd 1089.1821, found 1089.1832. Spectral data for **4a′**: mp 250−252 °C; ^{1}H NMR data (see Table 1); ^{19}F NMR δ −136.98 (dd, 2 F, J 23.3 and 6.8, F_{ortho}-Ar), −137.16 (dd, 2 F, J 23.2 and 7.1, F_{ortho}-Ar), −139.27 (dd, 2 F, J 22.9 and 7.6, F_{ortho}-Ar), −139.67 (dd, 2 F, J 22.9 and 7.8, F_{ortho}-Ar), −152.13 (t, 1 F, J 21.5, F_{para}-Ar), −153.55 (dd, 2 F, J 22.0 and 21.2, F_{para}-Ar), −153.77 (t, 1 F, J 21.3, F_{para}-Ar), −160.39 (ddd, 2 F, J 23.3, 21.5, and 8.0, F_{meta}-Ar), 161.78 (ddd, 2 F, J 23.2, 22.0, and 8.3, F_{meta}-Ar), −162.05 (ddd, 2 F, J 22.9, 21.2, and 8.6, F_{meta}-Ar), −162.83 (ddd, 2 F, J 22.0, 21.3, and 7.5, F_{meta}-Ar); ^{13}C NMR δ 41.0 (CH_3), 47.8 and 51.7 (C-2, C-3, C-7, and C-8), 61.6 and 62.4 (CH_2), 91.4, 97.6, 113.0, 114.8, 121.2, 128.4, 136.0, 139.6, 143.4, 146.7, 149.1, 156.9; UV−vis (CH_2Cl_2) λ_{max}/nm (log ϵ) 382 (5.09), 510 (4.04), 546 (4.30), 588 (4.49), 645 (3.37); MS FAB$^+$ m/z 1089 (M + H)$^+$, 1088 (M)$^{\bullet+}$, 1032 [(M − C_3H_7N) + H]$^+$, 975 [(M − 2 x C_3H_7N) + H]$^+$. Anal. Calcd for $C_{50}H_{24}N_6F_{20}$: C, 55.53; N, 7.45; H, 2.72. Found: C, 55.16; N, 7.72; H, 2.22. Spectral data for **5a**: mp > 300 °C; ^{1}H NMR data (see Table 1); ^{19}F NMR δ −159.16 (ddd, 4 F, J 22.6, 8.5 and 5.6, F_{ortho}-Ar), −161.16 (ddd, 4 F, J 22.6, 8.5, and 5.6, F_{ortho}-Ar), −175.43 (dd, 4 F, J 19.8 and 22.6, F_{para}-Ar), −184.00 (dddd, 4 F, J 25.4, 22.6, 8.5, and 5.6, F_{meta}-Ar), −184.35 (dddd, 4 F, J 25.4, 22.6, 8.5, and 5.6, F_{meta}-Ar); UV−vis (CH_2Cl_2) λ_{max}/nm (log ϵ) 375 (5.13), 505 (4.68), 733 (4.99); MS FAB$^+$ m/z 1089 (M + H)$^+$, 1088 (M)$^{\bullet+}$, 1032 [(M − C_3H_7N) + H]$^+$, 975 [(M − 2 x C_3H_7N) + H]$^+$; HRMS (FAB) exact mass m/z for $C_{50}H_{25}N_6F_{20}$ (M + H)$^+$ calcd 1089.1821, found 1089.1807. Spectral data for **5a′**: mp > 300 °C; ^{1}H NMR data (see Table 1); ^{19}F NMR δ −159.18 (ddd, 4 F, J 25.0, 8.0, and 5.6, F_{ortho}-Ar), −161.22 (ddd, 4 F, J 22.6, 8.5, and 5.6, F_{ortho}-Ar), −175.37 (dd, 4 F, J 19.8 and 22.6, F_{para}-Ar), −183.90 (dddd, 4 F, J 25.4, 19.8, 11.3, and 8.5, F_{meta}-Ar), −184.30 (dt, 4 F, J 22.6 and 8.5, F_{meta}-Ar); UV−vis (CH_2Cl_2) λ_{max}/nm (log ϵ) 376 (5.15), 504 (4.72), 732 (5.03); MS FAB$^+$ m/z 1089 (M + H)$^+$, 1088 (M)$^{\bullet+}$, 1032 [(M − C_3H_7N) + H]$^+$, 975 [(M − 2 x C_3H_7N) + H]$^+$; HRMS (FAB) exact mass m/z for $C_{50}H_{25}N_6F_{20}$ (M + H)$^+$ calcd 1089.1821, found 1089.1797.

Cycloaddition of Isobacteriochlorin 4a′ with Azomethine Ylide 2. Successive additions of sarcosine (1.6 mg, 18.4 μmol) and paraformaldehyde (1.4 mg, 46.0 μmol) were made every 5 h, for 30 h, to a toluene (0.8 mL) solution of isobacteriochlorin **4a′** (5.0 mg, 4.60 μmol) as described in the general procedure. The purification was carried out by preparative TLC, using dichloromethane/acetone (10:1) as an eluent, to give the unchanged isobacteriochlorin **4a′** (3.1 mg, 62%) and the trisadduct **6a.3** (1.8 mg, 34%). Spectral data for **6a.3**: mp > 300 °C; ^{1}H NMR data (see Table 1); ^{19}F NMR δ −136.80 (dd, 2 F, J 23.5 and 5.4, F_{ortho}-Ar), −137.90 (br s, 4 F, F_{ortho}-Ar), −140.87 (dd, 2 F, J 23.7 and 7.5, F_{ortho}-Ar), −152.16 (t, 2 F, J 20.0, F_{para}-Ar), −154.98 (t, 2 F, J 20.4, F_{para}-Ar), from −160.39 to −160.58 (m, 4 H, F_{meta}-Ar), from −162.30 to −162.67 (m, 4 H, F_{meta}-Ar); ^{13}C NMR δ 40.8 (CH_3), 41.1 (CH_3), 46.9, 53.7 (C-2, C-3, C-7, C-8, C-12, and C-13), 60.8, 61.7, 62.4 (CH_2), 92.4, 103.5, 112.4, 131.6, 153.6, 172.8; UV−vis (CH_2Cl_2) λ_{max}/nm (log ϵ) 380 (4.75), 489 (3.96), 530 (3.99), 574 (3.97); MS FAB$^+$ m/z 1146 (M + H)$^+$, 1145 (M)$^{\bullet+}$; MS-HRFAB exact mass m/z for $C_{53}H_{32}N_7F_{20}$ (M + H)$^+$ calcd 1146.2394, found 1146.2425.

Cycloaddition of Porphyrin 1a with Azomethine Ylide 7. Successive additions of glycine (3.5 mg, 46.6 μmol) and paraformaldehyde (3.5 mg, 0.116 mmol) were made every 5 h, for 30 h, to a toluene (5 mL) solution of porphyrin **1a** (22.8 mg, 23.3 μmol) by following the general procedure. The toluene was evaporated under vacuum, the residue was dissolved in dichloromethane and treated with a 2% solution of TFA in H_2O, at room temperature, for 2 h. The mixture was neutralized with sodium carbonate and extracted with dichloromethane. The organic fraction was dried (Na_2SO_4), and the mixture was purified on silica gel column using dichloromethane/light petroleum (4:1) as an eluent to afford the unchanged porphyrin **1a** (4.4 mg, 20%), followed by chlorin **8a** (11.3 mg, 47%). A trace amount of isobacteriochlorin was then eluted with dichloromethane. Spectral data for **8a**: mp

(14) Giraudeau, A.; Callot, H. J.; Jordan, J.; Ezhar, I.; Gross, M. *J. Am. Chem. Soc.* **1979**, *101*, 3857.

> 300 °C; ^{1}H NMR δ −1.83 (s, 2 H, NH), 3.13−3.18 (m, 2 H, H-pyrrolidine), 3.39−3.42 (m, 2 H, H-pyrrolidine), 5.21−5.24 (m, 2 H, H-2, 3), 8.40 (d, 2 H, *J* 4.9, H-β), 8.49 (s, 2 H, H-12, 13), 8.72 (d, 2 H, *J* 4.9, H-β); ^{13}C NMR δ 54.8, 55.4, 96.7, 123.9, 128.0, 132.4, 135.2, 140.4, 152.7, 169.0; UV−vis (CH_2Cl_2) λ_{max}/nm (log ϵ) 405 (5.14), 504 (4.10), 597 (3.61), 652 (4.55); EM FAB$^+$ *m/z* 1018 (M + H)$^+$, 1017 (M)$^{\bullet+}$, 975 [(M − C_2H_5N) + H]$^+$. Anal. Calcd for $C_{46}H_{15}F_{20}N_5\cdot H_2O$: C, 53.34; N, 6.76; H, 1.66; Found: C, 53.49; N, 6.79; H, 1.89.

Cycloaddition of Porphyrin 1a with Azomethine Ylide 9. Successive additions of L-proline (9.8 mg, 85.6 μmol) and paraformaldehyde (6.4 mg, 0.214 mmol) were made every 5 h, for 10 h, to a toluene (5 mL) solution of porphyrin **1a** (41.8 mg, 42.8 μmol) by following the general procedure. The purification was carried out on a silica gel column: the unchanged porphyrin **1a** (14.2 mg, 34%) was eluted with dichloromethane/light petroleum (1:1), chlorin **10a** (10.4 mg, 23%) was eluted with dichloromethane, and chlorin **10a′** (8.9 mg, 20%) was eluted with dichloromethane/acetone (9:1). A trace amount of an isobacteriochlorin was also eluted. Spectral data for **10a**: mp > 300 °C; ^{1}H NMR δ −1.82 (s, 2 H, NH), 1.29−1.35 (m, 1 H, H-2$^4_{cis}$), 1.85−1.90 (m, 3 H, H-2$^4_{trans}$ and H-2^3), 2.69−2.77 (m, 1 H, H-2$^2_{cis}$), 2.94−3.01 (m, 1 H, H-2$^2_{trans}$), 3.04 (dd, 1 H, *J* 11.7 and 8.0, H-2$^1_{trans}$), 3.36 (dd, 1 H, *J* 11.7 and 8.0, H-2$^1_{cis}$), 3.80 (d, 1 H, *J* 4.7, H-2^{4a}), 5.11 (dd, 1 H, *J* 8.9 and 4.7, H-3), 5.42 (dd, 1 H, *J* 8.9 and 8.0, H-2), 8.36 (d, 2 H, *J* 4.8, H-β), 8.48 (s, 2 H, H-12, 13), 8.70 (d, 2 H, *J* 4.8, H-β); ^{13}C NMR δ 25.8 (C-2^3), 31.8 (C-2^4), 53.1 (C-2^2), 53.9 (C-2), 59.4 (C-2^1), 62.0 (C-3), 73.2 (C-2^{4a}), 96.4 96.9, 106.1, 123.9 and 128.0 (C-7, 8, 17, 18), 132.3 (C-12, 13), 135.2, 140.2, 140.5, 152.6, 168.9, 169.6; UV−vis (CH_2Cl_2) λ_{max}/nm (log ϵ) 405 (5.29), 504 (4.23), 599 (3.74), 653 (4.72); MS FAB$^+$ *m/z* 1058 (M + H)$^+$, 1057 (M)$^{\bullet+}$, 975 [(M − C_5H_9N) + H]$^+$. Anal. Calcd for $C_{49}H_{19}F_{20}N_5\cdot{}^1/_2H_2O$: C, 55.15; N, 6.57; H, 1.89. Found: C, 55.46; N, 6.16; H 2.34. Spectral data for **10a′**: mp > 300 °C; ^{1}H NMR δ −1.83 (s, 2 H, NH), from −0.03 to 0.03 (m, 1 H, H-2$^4_{trans}$), 1.10−1.17 (m, 1 H, H-2$^4_{cis}$), 1.35−1.43 (m, 2 H, H-2^3), 2.83 (m, 3 H, H-2$^1_{trans}$, H-2^2), 3.29 (t, 1 H, *J* 9.2, H-2$^1_{cis}$), 3.49 (q, 1 H, *J* 8.6, H-2^{4a}), 5.42 (q, 1 H, *J* 9.2, H-2), 5.63 (dd, 1 H, *J* 9.2 and 8.6, H-3), 8.41−8.45 (m, 2 H, H-β), 8.50 (s, 2 H, H-12, 13), 8.73 (d, 2 H, *J* 4.2, H-β). ^{13}C NMR δ 22.1 (C-2^3), 24.5 (C-2^4), 51.1 (C-2^2), 53.7 (C-2), 55.5 (C-3), 58.2 (C-2^1), 69.7 (C-2^{4a}), 97.0, 97.4, 106.2, 124.0 and 124.2 and 128.1 (C-7, C-8, 17, 18), 132.5 (C-12, 13), 135.2, 135.3, 140.1, 140.3, 152.7, 167.7, 169.6; UV−vis (CH_2Cl_2) λ_{max}/nm (log ϵ) 405 (5.30), 504 (4.24), 599 (3.75), 653 (4.71); MS FAB$^+$ *m/z* 1058 (M + H)$^+$, 1057 (M)$^{\bullet+}$, 975 [(M −C_5H_9N) + H]$^+$. Anal. Calcd for $C_{49}H_{19}F_{20}N_5$: C, 55.62; N, 6.62; H, 1.81; Found: C, 55.87; N, 6.27; H, 2.15.

Cycloaddition of Porphyrin 1a with Azomethine Ylide 11. Successive additions of *trans*-4-hydroxy-L-proline (22.8 mg, 0.174 mmol) and paraformaldehyde (13.0 mg, 0.433 mmol) were made every 5 h, for 20 h, to a toluene (15 mL) solution of porphyrin **1a** (42.3 mg, 43.4 μmol) by following the general procedure. The purification was carried out on a silica gel column with dichloromethane to give the unchanged porphyrin **1a** (24.6 mg, 58%) and then with dichloromethane/acetone (9:1) to give a mixture of the two chlorins **12a.3** and **12a.4**, followed by the chlorin with the lower R_f **12a.1** or **12a.2** (4.8 mg, 10%). The mixture of the two chlorins **12a.3** and **12a.4** was further purified by preparative TLC with dichloromethane/ethyl acetate (4:1) as an eluent: the chlorin with the higher R_f (2.8 mg, 6%) and the middle R_f chlorin (4.7 mg, 10%) were separated in this way. Spectral data for **12** with the higher R_f (**12a.3** or **12a.4**): mp 242−244 °C; ^{1}H NMR δ −1.87 (s, 2 H, NH), 0.79−0.90, 1.16−1.29 and 1.87−1.96 (3 m, 3 H), 2.92 (dd, 1 H, *J* 10.0 and 3.5), 3.02−3.11 (m, 2 H), 3.40 (dd, 1 H, *J* 11.8 and 8.4), 3.90−3.98 (m, 1 H), 4.47−4.49 (m, 1 H), 5.10 (dd, 1 H, *J* 8.9 and 5.3, H-3), 5.46 (q, 1 H. *J* 8.9, H-2), 8.35 (d, 1 H, *J* 4.7, H-β), 8.37 (d, 1 H, *J* 4.7, H-β), 8.49 (s, 2 H. H-12, 13), 8.72 (d, 2 H, *J* 4.7, H-β); UV−vis (CH_2Cl_2) λ_{max}/nm (rel intensity) 405 (100%), 503 (11%), 598 (5%), 652 (28%); MS FAB$^+$ *m/z* 1075 (M + 2H)$^+$, 975 [(M − C_5H_9NO) + H]$^+$. Spectral data for **12** with middle R_f (**12a.3** or **12a.4**): mp 235−237 °C; ^{1}H NMR δ −1.83 (s, 2 H, NH), 0.83−0.90 and 1.25−1.43 (2 m, 2 H), 2.20−2.27 (m, 1 H), 2.78 (dd, 1 H, *J* 5.6 and 5.0), 3.04 (dd, 1 H, *J* 11.9 and 7.3), 3.26 (dd, 1 H, *J* 5.6 and 5.0), 3.49 (dd, 1 H, *J* 11.9 and 8.4), 3.76−3.81 (m, 1 H), 4.49−4.56 (m, 1 H), 5.39 (dd, 1 H, *J* 8.8 and 4.5, H-3), 5.49 (q, 1 H. *J* 8.8, H-2), 8.36 (d, 2 H, *J* 5.0, H-β), 8.48 (s, 2 H, H-12, H-13), 8.70 (d, 2 H, *J* 5.0, H-β); UV−vis (CH_2Cl_2) λ_{max}/nm (rel intensity) 406 (100%), 504 (12%), 599 (6%), 653 (30%); MS FAB$^+$ *m/z* 1075 (M + 2H)$^+$, 975 [(M − C_5H_9NO) + H]$^+$. Spectral data for **12** with the lower R_f (**12a.1** or **12a.2**): mp 251−253 °C; ^{1}H NMR δ −1.84 (s, 2 H, NH), 0.25−0.36, 0.82−0.90, 1.10−1.16 and 2.76−2.89 (4 m, 5 H), 3.02 (dd, 1 H, *J* 13.4 and 5.9), 3.47 (t, 1 H, *J* 9.5), 3.86−3.99 (m, 2 H), 5.42 (q, 1 H, *J* 8.9, H-2), 5.62 (t, 1 H, *J* 8.9, H-3), 8.41 (d, 1 H, *J* 4.9, H-β), 8.45 (d, 1 H, *J* 4.9, H-β), 8.50 (s, 2 H, H-12, 13), 8.72−8.75 (m, 2 H, H-β); UV−vis (CH_2Cl_2) λ_{max}/nm (rel intensity) 406 (100%), 504 (12%), 598 (5%), 653 (29%); MS FAB$^+$ *m/z* 1075 (M + 2H)$^+$, 975 [(M − C_5H_9NO) + H]$^+$. MS-HRFAB exact mass *m/z* for $C_{49}H_{20}N_5OF_{20}$ (M + H)$^+$ calcd 1074.13340, found 1074.13340.

Cycloaddition of Porphyrin 1b with Azomethine Ylide 2. Successive additions of sarcosine (4.3 mg, 48.5 μmol) and paraformaldehyde (3.6 mg, 0.121 mmol) were made every 5 h, for 20 h, to an *o*-dichlorobenzene (5 mL) solution of porphyrin **1b** (8.9 mg, 12.1 μmol) by following the general procedure. The reaction mixture was applied on a silica gel column. The *o*-dichlorobenzene was eluted with light petroleum, the unchanged porphyrin **1b** (7.7 mg, 86%) was eluted with dichloromethane, and chlorin **3b** (0.7 mg, 7%) was eluted with dichloromethane/acetone (4:1). Spectral data for **3b**: ^{1}H NMR δ −1.73 (s, 2 H, NH), 2.10 (s, 3 H, CH_3), 2.31−2.36 and 2.95−3.07 (2 m, 4 H, H-pyrrolidine), 4.04 and 4.06 (2 s, 12 H, 4 x OCH_3), 5.36−5.38 (m, 2 H, H-2, 3), 7.18−7.24 (m, 8 H, H$_{meta}$-Ar), 7.85 (d, 4 H, *J* 8.7, H$_{ortho}$-Ar), 8.00−8.06 (m, 4 H, H$_{ortho}$-Ar), 8.27 (d, 2 H, *J* 4.8, H-β), 8.47 (s, 2 H, H-12, 13), 8.62 (d, 2 H, *J* 4.8, H-β); UV−vis (CH_2Cl_2) λ_{max}/nm (log ϵ) 421 (5.34), 522 (4.18), 550 (4.18), 595 (3.87), 648 (4.41); MS FAB$^+$ *m/z* 792 (M + H)$^+$, 791 (M)$^{\bullet+}$; MS-HRFAB exact mass *m/z* for $C_{51}H_{46}N_5O_4$ (M + H)$^+$ calcd 792.3550, found 792.3579.

Cycloaddition of Porphyrin 1c with Azomethine Ylide 2. Successive additions of sarcosine (100 mg, 1.12 mmol) and paraformaldehyde (42.0 mg, 1.40 mmol) were made every 5 h, for 20 h, to an *o*-dichlorobenzene (5 mL) solution of porphyrin **1c** (34.3 mg, 55.9 μmol) by following the general procedure. The reaction mixture was applied on a silica gel column. The *o*-dichlorobenzene was eluted with light petroleum, the unchanged porphyrin **1c** (26.6 mg, 78%) was eluted with dichloromethane, and chlorin **3c** (7.8 mg, 21%) was eluted with dichloromethane/acetone (9:1). Spectral data for **3c**: mp > 300 °C; ^{1}H NMR δ −1.74 (s, 2 H, NH), 2.06 (s, 3 H, CH_3), 2.34−2.38 and 2.88−2.92 (2 m, 4 H, H-pyrrolidine), 5.34−5.37 (m, 2 H, H-2, 3), 7.62−7.70 (m, 12 H, H$_{meta+para}$-Ph), 7.93−7.98 and 8.08−8.15 (2 m, 8 H, H$_{ortho}$-Ph), 8.25 (d, 2 H, *J* 4.8, H-β), 8.44 (s, 2 H, H-12, 13), 8.60 (d, 2 H, *J* 4.8, H-β); ^{13}C NMR δ 41.4 (CH_3), 52.8 (C-2, 3), 64.8 (CH_2), 112.6, 122.6, 123.9, 126.6, 127.4, 127.6, 127.9, 128.1, 131.9, 132.1, 133.9, 134.1, 134.4, 135.3, 140.8, 142.0, 142.3, 152.6; UV−vis (CH_2Cl_2) λ_{max}/nm (log ϵ) 418 (5.33), 518 (4.22), 544 (4.10), 594 (3.82), 647 (4.51); MS FAB$^+$ *m/z* 672 (M + H)$^+$, 614 (M − C_3H_7N)$^{\bullet+}$. Anal. Calcd for $C_{47}H_{37}N_5$: C, 84.02; N, 10.42; H, 5.55. Found: C, 83.78; N, 10.16; H, 5.58.

Cycloaddition of Porphyrin 1d with Azomethine Ylide 2. Successive additions of sarcosine (51.0 mg, 0.573 mmol) and paraformaldehyde (21.5 mg, 0.716 mmol) were made every 5 h, for 20 h, to an *o*-dichlorobenzene (7 mL) solution of porphyrin **1d** (25.5 mg, 28.6 μmol) by following the general procedure. The reaction mixture was applied on a silica gel column. The *o*-dichlorobenzene was eluted with light petroleum, the unchanged porphyrin **1d** (11.7 mg, 46%) was eluted with dichloromethane, and chlorin **3d** (12.2 mg, 45%) was eluted with dichloromethane/acetone (9:1). A trace amount of isobacteriochlorin was also eluted. Spectral data for **3d**: ^{1}H

NMR δ −1.59 (s, 2 H, NH), 2.21 (s, 3 H, CH_3), 2.61−2.65 and 3.03−3.06 (2 m, 4 H, H-pyrrolidine), 5.17−5.24 (m, 2 H, H-2, 3), 7.58−7.66 and 7.71−7.77 (2 m, 12 H, H−Ar), 8.16 (d, 2 H, *J* 4.8, H-β), 8.29 (s, 2 H, H-12, 13), 8.48 (d, 2 H, *J* 4.8, H-β); ^{13}C NMR δ 41.5 (CH_3), 53.0 (C-2, 3), 62.3 (CH_2), 107.7, 116.6, 123.3, 127.1, 127.7, 128.4, 128.7, 130.3, 130.4, 131.4, 134.6, 137.8, 138.3, 138.4, 139.4, 139.7, 139.8, 152.0; UV−vis (CH_2Cl_2) λ_{max}/nm (log ϵ) 418 (5.32), 513 (4.25), 539 (3.85), 600 (3.78), 654 (4.68); MS FAB$^+$ *m/z* 948 $(M + H)^+$, 947 $(M)^{\bullet+}$, 890 $(M - C_3H_7N)^{\bullet+}$. Anal. Calcd for $C_{47}H_{29}N_5Cl_8 \cdot {}^1/_2H_2O$: C, 59.02; N, 7.32; H, 3.16. Found: C, 58.89; N, 7.15; H, 3.28.

Cycloaddition of Porphyrin 1e with Azomethine Ylide 2. Successive additions of sarcosine (5.5 mg, 61.3 μmol) and paraformaldehyde (4.6 mg, 0.153 mmol) were made every 5 h, for 20 h, to a toluene (5 mL) solution of porphyrin **1e** (10.1 mg, 15.3 μmol) by following the general procedure. The purification was carried out on a silica gel column with dichloromethane to give the unchanged porphyrin **1e** (5.0 mg, 50%), followed by the chlorin **3e** (3.0 mg, 27%). A trace amount of a site-isomeric adduct was then eluted with dichloromethane/acetone (9:1). Spectral data for **3e**: mp > 300 °C; ^{1}H NMR δ −2.06 (s, 2 H, NH), 2.13 (t, 1 H, *J* 9.0, H-2^3_{trans}), 2.22 (s, 3 H, CH_3), 2.82 (d, 1 H, *J* 11.9, H-2^1_{trans}), 3.16 (t, 1 H, *J* 9.0, H-2^3_{cis}), 3.98 (d, 1 H, *J* 11.9, H-2^1_{cis}), 5.62 (t, 1 H, *J* 9.0, H-3), 7.57−7.76 (m, 13 H, H-Ph), 7.85−7.88, 7.90−7.96, 7.99−8.03 and 8.08−8.16 (4 m, 7 H, H-Ph), 8.17 (dd, 1 H, *J* 4.9 and 1.6, H-β), 8.37 (dd, 1 H, *J* 4.9 and 1.6, H-β), 8.51 (AB, 2 H, *J* 4.9, H-12, H-13), 8.64 (dd, 1 H, *J* 4.9 and 1.6, H-β), 8.70 (dd, 1 H, *J* 4.9 and 1.6, H-β); ^{13}C NMR δ 41.2 (CH_3), 63.8, 64.7, 67.0, 105.5, 112.1, 112.5, 123.0, 124.0, 124.8, 125.1, 126.7, 127.4, 127.8, 127.9, 128.1, 128.5, 128.7, 132.3, 132.8, 133.1, 133.2, 133.9, 134.0, 134.1, 135.6, 136.2, 138.7, 140.6, 140.8, 141.57, 141.62, 141.8, 153.0, 153.8, 156.3, 159.5; UV−vis (CH_2Cl_2) λ_{max}/nm (log ϵ) 412 (5.26), 514 (4.16), 541 (4.16), 588 (3.84), 640 (4.39); MS FAB$^+$ *m/z* 717 $(M + H)^+$, 716 $(M)^{\bullet+}$, 669 $(M - HNO_2)^{\bullet+}$; MS-HRFAB exact mass *m/z* for $C_{47}H_{37}N_6O_2$ $(M + H)^+$ calcd 717.2972, found 717.2964.

Cycloaddition of Chlorin 13 with Azomethine Ylide 2. Successive additions of sarcosine (8.1 mg, 91.3 μmol) and paraformaldehyde (6.8 mg, 0.228 mmol) were made every 5 h, for 10 h, to a toluene (5 mL) solution of chlorin **13** (24.6 mg, 22.8 μmol) by following the general procedure. The purification was carried out by preparative TLC using dichloromethane/light petroleum (7:3) as an eluent. Four fractions were collected. The first fraction, with the higher R_f, was the unchanged chlorin **13** (6.6 mg, 27%), and the second one was the isobacteriochlorin **15** (8.7 mg, 34% yield). The third and fourth fractions were identified as a bacteriochlorin [0.8 mg, 3% yield, $(M + H)^+$ = 1136, λ_{max} = 740 nm] and a trisadduct [3.7 mg, 14% yield, $(M + H)^+$ = 1193, λ_{max} = 587, 653 and 736 nm (low-intensity broad bands)], respectively. Spectral data for **15**: mp 217−219 °C; ^{1}H NMR δ 2.05 (t, 1 H, *J* 8.3, H-pyrrolidine), 2.11 (s, 3 H, CH_3), 2.18 (t, 1 H, *J* 8.3, H-pyrrolidine), 2.52−2.76 and 2.82 [m and t (*J* 8.3), 6 H, H-2^1, 3^1, and H-pyrrolidine], 4.09−4.17 and 4.32−4.50 (2 m, 6 H, H-2, 3, 17, 18 and N*H*), 6.85−6.93 and 7.02−7.06 (2 m, 6 H, H−Ar and H-β), 7.49 (d, 2 H, *J* 4.1, H-β); UV−vis (CH_2Cl_2) λ_{max}/nm (log ϵ): 383 (5.03), 513 (3.96), 548 (4.23), 591 (4.41); MS FAB$^+$ *m/z* 1136 $(M + H)^+$, 1135 $(M)^{\bullet+}$, 1079 $[(M - \text{azomethine ylide}) + H]^+$. MS-HRFAB exact mass *m/z* for $C_{55}H_{26}N_5F_{20}$ $(M + H)^+$ calcd 1136.1863, found 1136.1871.

Cycloaddition of Chlorin 14 with Azomethine Ylide 2. Successive additions of sarcosine (4.1 mg, 46.0 μmol) and paraformaldehyde (3.4 mg, 0.115 mmol) were made every 5 h, for 10 h, to a toluene (5 mL) solution of chlorin **14** (14.4 mg, 11.5 μmol) by following the general procedure. The purification was carried out by preparative TLC using dichloromethane/light petroleum (7:3) as an eluent. Five fractions were collected. The first fraction, with the higher R_f, was the unchanged chlorin **14** (4.2 mg, 29%), and the second one was the isobacteriochlorin **16** (5.1 mg, 34% yield). The third, fourth, and fifth fractions were identified as a minor isobacteriochlorin (1.0 mg, 7% yield, $(M + H)^+$ = 1310, λ_{max} = 591, 652 nm), a bacteriochlorin [1.5 mg, 10% yield, $(M + H)^+$ = 1310, λ_{max} = 738 nm], and a trisadduct [3.0 mg, 19% yield, $(M + H)^+$ = 1367, λ_{max} = 581, 656, 737 nm (low-intensity broad bands)], respectively. Spectral data for **16**: mp 237−240 °C; ^{1}H NMR δ 1.97 (t, 1 H, *J* 8.5, H-pyrrolidine), 2.06−2.13 (m, 1 H, H-pyrrolidine), 2.11 (s, 3 H, CH_3), 2.60 (t, 1 H, *J* 8.5, H-pyrrolidine), 2.86 (t, 1 H, *J* 8.5, H-pyrrolidine), 3.78 (br s, 2 H, NH), 4.30, 4.36−4.44 and 4.52−4.61 (1 br s and 2 m, 6 H, H-2, 3, 2^1, 2^8, 17, 18), 6.99, 7.00−7.09, 7.34−7.48 [1 d (*J* 4.5) and 2 m, 14 H, H-β and H-naphthalene], 7.79 (dd, 2 H, *J* 6.2 and 3.3, H-naphthalene); UV−vis (CH_2Cl_2) λ_{max}/nm (log ϵ) 386 (5.03), 513 (3.97), 549 (4.23), 591 (4.40); MS FAB$^+$ *m/z* 1310 $(M + H)^+$, 1309 $(M)^{+\bullet}$, 1032 $[(M - \text{pentacene}) + H]^+$, 975 $[(1032 - \text{azomethine ylide}) + H]^+$. MS-HRFAB exact mass *m/z* for $C_{69}H_{32}N_5F_{20}$ $(M + H)^+$ calcd 1310.2333, found 1310.2350.

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