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# Synthesis, Spectroscopic, and in Vitro Photosensitizing Efficacy of Ketobacteriochlorins Derived from Ring-B and Ring-D Reduced Chlorins via Pinacol−Pinacolone Rearrangement

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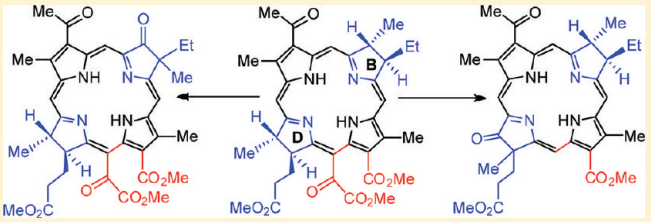
Supporting Information

**ABSTRACT:** In this report, we present a regioselective oxidation of a series bacteriochlorins, which on reacting with either ferric chloride ($FeCl_3$) or 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) yielded the corresponding ring-B or ring-D reduced chlorins. The effect of the number of electron-withdrawing groups present at the peripheral position, with or without a fused isocyclic ring (ring-E), did not make any significant difference in regioselective oxidation of the pyrrole rings. However, depending on the nature of substituents, the intermediate bis-dihydroxy bacteriochlorins on subjecting to pinacol−pinacolone reaction conditions gave various ketochlorins. The introduction of the keto-group at a particular position in the molecule possibly depends on the stability of the intermediate carbocation species. The newly synthesized bacteriochlorins show strong long-wavelength absorption and produced significant in vitro (Colon26 cells) photosensitizing ability. Among the compounds tested, the bacteriochlorins containing a keto-group at position 7 of ring-B with cleaved five-member isocyclic ring showed the best efficacy.




## INTRODUCTION

In developing effective agents for photodynamic therapy (PDT), the structure−activity relationship (SAR) and quantitative structure−activity relationship (QSAR) studies have been proven to be extremely useful.[1−3] The Roswell Park Cancer Institute (RPCI) group was the first to investigate the SAR and QSAR studies on a series of the alkyl ether analogues of pyropheophorbide-a (chlorophyll-a derivative) and observed a parabolic relationship between overall lipophilicity and PDT efficacy.[4,5] Among the compounds investigated, 3-(1′-hexyloxyethyl) derivative (HPPH) showed the best PDT efficacy without any significant toxicity and is currently undergoing phase I/II clinical trials for several indications.[6−8] The SAR approach has also been found useful in developing other systems, for example, phthalocyanines,[9] -tetra (*m*-hydroxyphenyl) chlorins,[10] extended porphyrins (texaphyrins),[11] porphyceins,[12] purpurinimides[13−15] and bacteriopurpurinimides,[16] and other bacteriochlorin analogues.[17,18] The biological studies have indicated that besides overall lipophilicity, the position of the substituents present in the photosensitizer(s) makes a tremendous difference in long-term PDT efficacy.

Bacteriochlorins are a class of the tetrapyrrolic system in which two pyrrole rings diagonal to each other are reduced.[19] These chromophores exhibit long-wavelength absorption in the range of 720−800 nm depending on the nature of substituents present at the peripheral positions of the molecules. In recent years, enormous interest has been generated due to the utility of bacteriochlorins in the bacterial photosynthetic reaction center[20] and in the treatment of cancer by PDT. There are several bacteriochlorophyll-a analogues, which are currently under advanced human clinical trials (e.g., Tookad)[21] or at the advanced preclinical studies (bacteriopurpurinimides) for the treatment of cancer.[22] The only naturally occurring bacteriochlorin that is not involved in photosynthesis is the tolyporphyrin isolated by Prinsep et al. from the blue-green alga *Tolypothrix nodosa*.[23] This compound, which enhances the cytotoxicity of adriamycin or viablastine in SK-VLB cells at doses as low as 1 mg/mL, is characterized as a multidrug resistance (MDR) reversing agent. Kishi's group at Harvard University synthesized the tolyporphyrin by the extension of the Eschenmoser sulfide contraction/iminoester cyclization method with long-wavelength absorption near 675 nm ($\varepsilon$ = 22000).[24] However, there are no reports regarding the in vivo photosensitizing ability of this novel compound. Lindsey and co-workers[25] have also reported facile syntheses of certain bacteriochlorins starting from pyrroles with variable lipophilicity following multistep synthetic methodologies. Some of these compounds exhibit interesting photophysical properties and could be potential candidates for PDT.

One of the simplest methods that has been used extensively for the conversion of porphyrins/chlorins to the corresponding

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*vic*-dihydroxy chlorins and bacteriochlorins, respectively, is the osmium tetroxide-mediated oxidation.[26] These intermediate "diols" on reacting under acidic conditions produce the corresponding keto-chlorins and keto-bacteriochlorins, respectively. The position of the keto-group in the resulting chlorins and bacteriochlorins depends on the stability of the intermediate carbocation, which is also influenced by the nature of the substituents (electron withdrawing or electron donating) present in the molecules (Scheme 1).

Chang and Sotiriou[27] were the first to show that free-base octaethylchlorin or its metalated analogue upon reaction with osmium tetroxide can be converted into the corresponding keto-bacteriochlorins in a reasonable yield. Bonnett et al.[28] employed this approach to prepare bacteriochlorin diols by reacting ketoethyl chlorin with osmium tetroxide. Some of these analogues showed considerable PDT efficacy in vitro. Pandey et al. in collaboration with Smith and co-workers extended this approach to the pyropheophorbide-a, purpurin-18, and purpurinimide systems, and a series of stable keto-bacteriochlorin analogues were synthesized.[29] Most of the resulting bacteriochlorins showed long-wavelength absorption in the range of 730−800 nm, and some of them were effective both in vitro and in vivo.

So far, most of the keto-bacteriochlorins [the keto-group is present at either position 7 or position 8 (ring-B)] investigated for PDT efficacy are derived from ring-D reduced chlorins.[30] The main objectives of the work presented herein were (i) to develop an efficient synthetic approach for ring-B reduced chlorins from certain selected bacteriochlorins derived from naturally occurring bacteriochlorophyll-a and then convert them into the corresponding ring-D ketobacteriochlorins (17-keto- and 18 keto-) and (ii) to compare the photophysical and photosensitizing abilities of these novel structures.

## RESULTS AND DISCUSSION

For our present study, two types of bacteriochlorins **6** and **13** containing either a fused five-member isocyclic ring system or a methoxycarbonyl group present at position 13 (ring-C pyrrole) were used as a substrate, and these were obtained from bacteriochlorophyll-a by following the literature procedure.[31] We have recently reported an efficient regioselective preparation of ring-B and ring-D reduced chlorins from bacteriochlorins.[32] We extended this approach for bacteriopyropheophorbide-a, which on treating with DDQ at room temperature produced mainly D-ring reduced chlorin **5**, whereas on treating **6** with ferric chloride ($FeCl_3$) produced ring-B reduced chlorin **7** in excellent yields (Scheme 2). Analysis of the NMR data confirmed the structures of both isomers. One of the distinct differences was the resonances of the $-CH_2$ protons of the five-member fused isocyclic ring, which showed an ABX pattern at 5.22 ppm in compound **5** due to reduced ring-D, whereas these protons appeared as a singlet at 5.44 ppm in compound **7** (ring-D oxidized).

For determining the photophysical and photosensitizing abilities of various keto-bacteriochlorin isomers, the keto-group was regioselectively introduced in either the ring-B or the ring-D pyrrole ring of the bacteriochlorin system. For the synthesis of the desired analogues, the ring-D and ring-B reduced chlorins **5** and **7** were individually reacted with $OsO_4$, and the resulting diols **8** and **10** (both as isomeric mixtures, *cis*-diol up and *cis*-diol down with respect to the diagonal reduced ring) were isolated in 60% yield. Reaction of these diols independently with concentrated sulfuric acid under pinacol−pinacolone conditions produced some interesting results. For example, diol **8** gave 7-keto-bacteriochlorin **9** as a major and **9a** as a minor product, and it is exactly matched with the previously reported procedure,[26c] whereas diol **10** under similar reaction conditions gave mainly 18-keto-bacteriochlorin **11**. These results suggest that the formation of intermediate carbocation species is certainly directing the position of the keto-group, which is possibly also being influenced by the electron-withdrawing acetyl group[26] present at position 3 of the 7,8- and 17,18-dihydroxybacteriochlorins (Scheme 3).

For investigating the effect of the variable number of electron-withdrawing groups in bacteriochlorin diols under pinacol−pinacolone rearrangement conditions, the isocyclic ring in methyl bacteriopheophorbide-a **12** was cleaved on reacting with sodium methoxide, and the resulting bacteriochlorin **13** was obtained in excellent yield.[33] Subsequent treatment of **13** with collidine at refluxing temperature gave rhodobacteriochlorin **14** as the minor (15%) and the corresponding ring-B reduced chlorin **15** as the major product (85%), which on reacting with osmium tetraoxide/pyridine yielded 17,18-dihydroxybacteriochlorin diol **16** as an isomeric mixture (*cis*-hydroxy groups up or down relative to ring-B). Further treatment of **16** with concentrated sulfuric acid gave 18-keto-bacteriochlorin **17** as a major product (Scheme 4). As expected, the oxidation of bacteriochlorin **13** with DDQ and $FeCl_3$ afforded the corresponding ring-D and ring-B reduced chlorins **18** and **22**, respectively, which on reacting with osmium tetroxide produced the corresponding diols **19** and **23** in quantitative yields. Interestingly, further reaction of these diols with concentrated sulfuric acid gave a mixture of 7-keto-bacteriochlorin **20** and 8-keto-bacteriochlorin **21** (from **19**) as an isomeric mixture. Separation of these mixtures (**20**/**21**) by the usual chromatographic technique was not successful. Finally, the isomeric mixture was separated by HPLC (column, Luna; eluting solvent, using ethyl acetate and hexane as the eluting solvents) delivered the pure regioisomer 8-keto-isomer **20** and regioisomer 7-keto-isomer **21** were isolated in 19 and 25%, respectively. Whereas diol **23** in which the *cis*-hydroxyl groups were present in ring-D yielded only 18-keto-bacteriochlorin **17** (in which the $\beta$-ketoester functionality present at position 15 was cleaved) as a major product. The elimination of $\beta$-keto-ester functionality was not observed on treating **19** under similar reaction conditions, and these results were surprising (Scheme 5). The results presented herein confirm our previous findings,[34] which suggests that the position and presence of the number of electron-withdrawing groups present at the peripheral position of chlorin diols makes a significant impact in the stability of the intermediate carbocation during the pinacol−pinacolone reaction, which obviously determines the formation of the resulting keto-chlorins under acid-catalyzed rearrangement. Therefore, in our study to investigate the effect of more than two electron-withdrawing groups under acid-catalyzed conditions, methyl bacteriopheophorbide-a **12** containing a methoxycarbonyl group at position $13^2$ of the fused isocyclic ring was used as a substrate, which on reacting with DDQ and $FeCl_3$ produced exclusively the ring-D reduced **24** and ring-B reduced chlorins **25**, respectively (Scheme 6). Unfortunately, the corresponding bacteriochlorin diols obtained by reacting **24** and **25** with $OsO_4$/pyridine as such or under acidic conditions at room temperature were not stable and produced complex mixtures, which were not characterized.

The mechanism of the formation of keto-chlorins under pinacol−pinacolone reaction is well established. However, the


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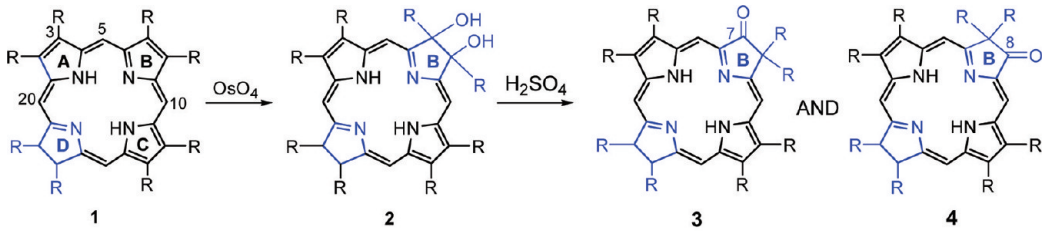
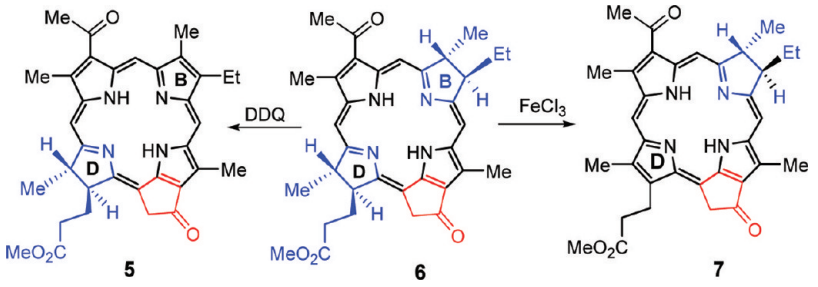
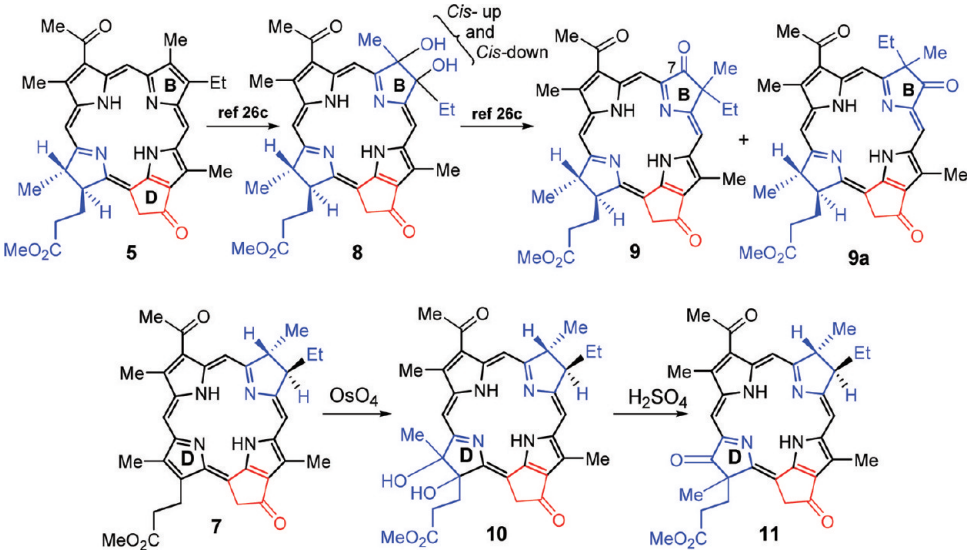
**Scheme 1. Conversion of Chlorins to Keto-bacteriochlorins**




**Scheme 2. Regioselective Synthesis of Ring-D and Ring-B Chlorins (5 and 7, Respectively) from Bacteriochlorin 6**




**Scheme 3. Synthesis of Ring-B and Ring-D Reduced Ketobacteriochlorins from Ring-B and Ring-D Reduced Chlorins**




compounds investigated in this study shows some interesting results, and the mechanism for the formation of these analogues is illustrated in Scheme 7. In brief, in the *vic*-dihydroxy analogue containing methyl and ethyl groups present at adjacent positions, the migration of the methyl group was preferred over the ethyl group, and the ethyl group migrated product was isolated in a minor quantity. Interestingly, the *vic*-dihydroxy analogues containing methyl and propionic ester functionality at adjacent positions on treating under similar acidic conditions gave only the methyl migrated product (18-keto-), which of course depends upon the stability of intermediate carbocation species. The previous studies from others[26c] and our own laboratory[34] suggest that in the porphyrin system the number of electron-withdrawing groups present at the peripheral position of the porphyrin skeleton makes a remarkable difference in the stability of intermediate cabocation(s), which dictates the formation of the corresponding keto-analogues.

The purity of ketobacteriochlorins **11**, **17**, **20**, and **21** was ascertained by HPLC, and the structures were assigned by NMR and mass spectrometry analyses. The bacteriochlorins **20** and **21**, which were initially isolated as isomeric mixture, were separated into individual isomers by HPLC using Luna column, eluted with 30% ethyl acetate−hexane. The retention times for bacteriochlorins **11**, **17**, **20**, and **21** were 12.20, 10.76, 21.13, and 18.47 min, respectively (Figure 1). A slight shoulder in the HPLC chromatogram of **21** could be due to repeated use of the HPLC column for a long time. The purity of the product was also confirmed by using a reverse phase HPLC column (Symmetry C18 column, dimensions 4.6 mm × 150 mm), eluted with 90% $CH_3OH$ and 10% $H_2O$, and the flow rate was adjusted to 1.0 mL/min. For details, see the Supporting Information.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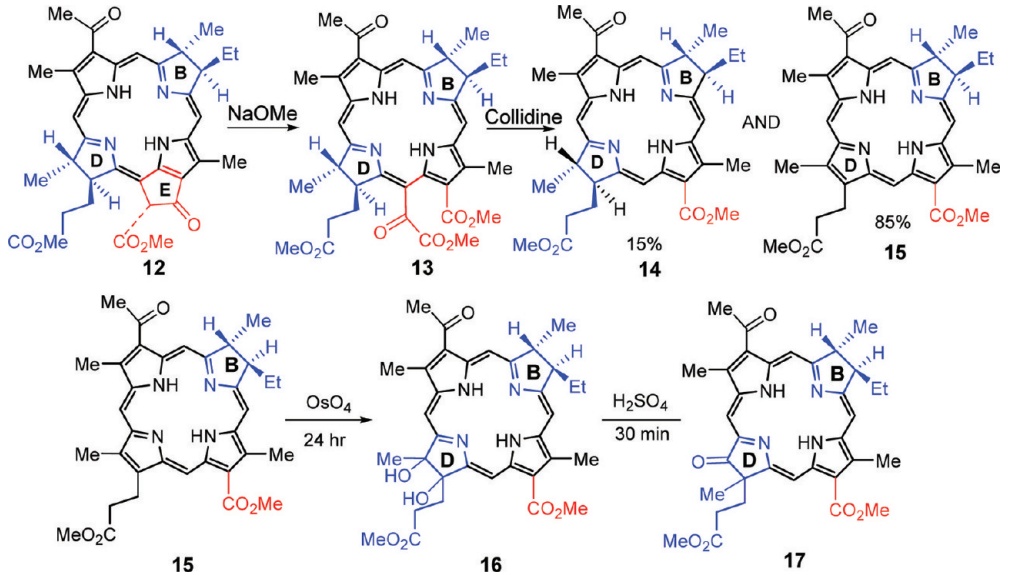
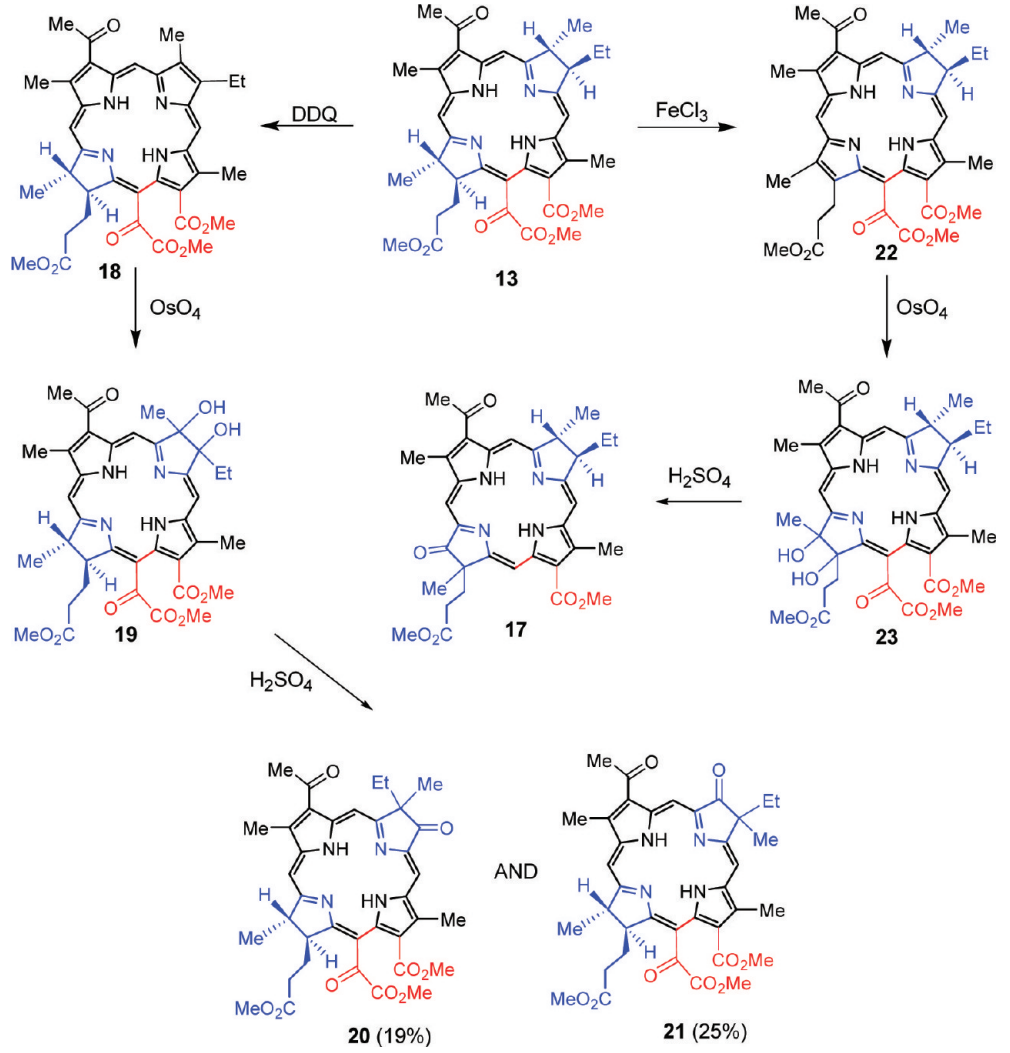
**Scheme 4. Synthesis of Rhodobacteriochlorin 14 and the Corresponding 18-Keto-bacteriochlorin 16**




**Scheme 5. Synthesis of 7-Keto- and 8-Keto-Ring-D Reduced and 18-Keto-Ring-B Reduced Bacteriochlorins**




A detailed NMR study confirmed the structures of the proposed bacteriochlorins. As can be seen from the results summarized in Figure 2 (only partial NMR Spectra are shown) the *meso*-protons at positions 5, 10, and 20 for bacteriochlorins **11**, **17**, **20**, and **21** show a significant shift, which could be due to variation in electron density at these positions. Furthermore,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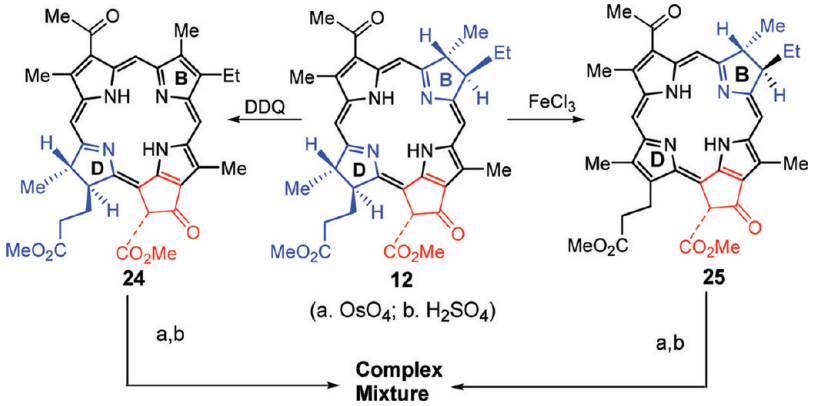
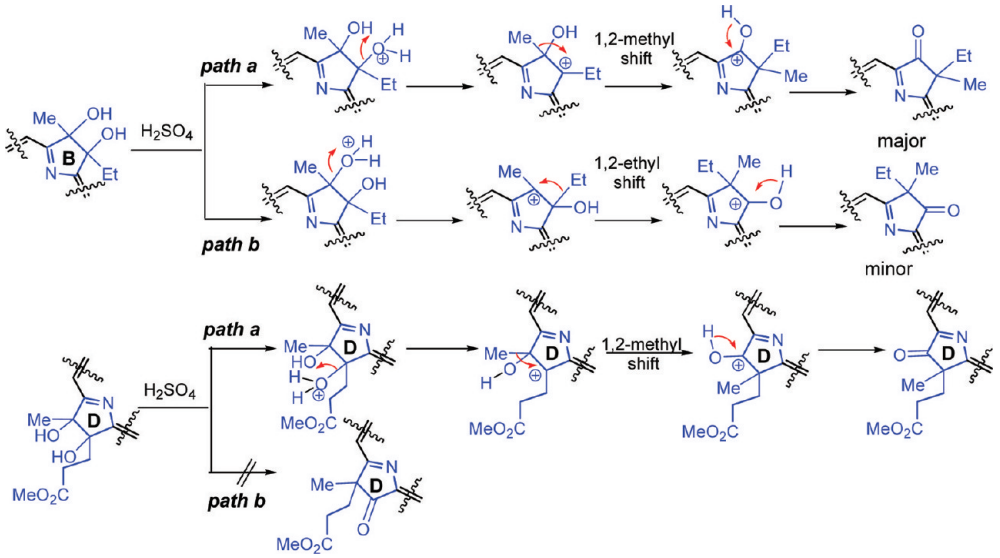
**Scheme 6. Ring-B and Ring-D Reduced Chlorins Derived from Methyl Bacteriopheophorbide-a on Reacting with $OSO_4/H_2SO_4$ Gave a Complex Mixture**




**Scheme 7. Proposed Mechanism for the Formation Ring-B and Ring-D Reduced Keto-bacteriochlorins Obtained from Their Corresponding Diols under Pinacol−Pinacolone Reaction Conditions**



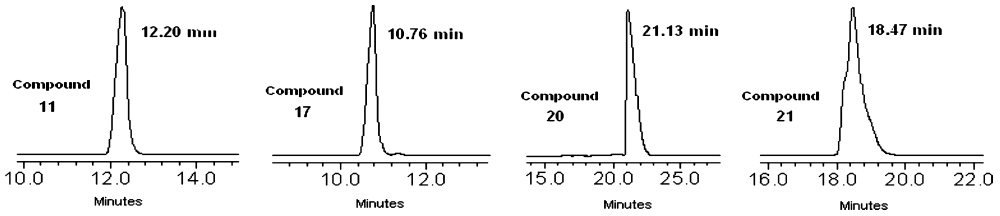




**Figure 1.** HPLC chromatogram of bacteriochlorin **11**, **17**, **20**, and **21** (for details, see the Supporting Information).

in 8-keto-bacteriochlorin **20**, the $7^1$-$CH_3$ protons appeared as a triplet around 0.5 ppm, whereas for the other isomer **21**, these protons were observed as a multiplet at 0.45−0.51 ppm, which could be due to the presence of epimeric mixture. In compound **20**, the 7-$CH_3$ was observed as a singlet at 1.82 ppm, while in compound **21**, it exhibited two singlets around 1.90/1.92 ppm (epimeric mixture) for 8-$CH_3$. The 7-$CH_2$ and 8-$CH_2$ in isomer **20** and **21** appeared as nice quartets at 2.56 and 2.62 ppm, respectively. These assignments were further confirmed by 2D NMR studies.

To confirm the position of dialky groups (methyl/ethyl) or methyl/propionic ester of the major regioisomers, NOESY experiment was performed on isomers **11**, **17**, and **21**. In the case of compound **21**, the resonances for the ethyl group at position C-8 were chosen as a starting point for the interpretation of the NOESY results. A peak at $\delta$ 2.62 for the $CH_2CH_3$ protons showed NOE correlation with the adjacent *meso*- proton at $\delta$ 8.97, which is *C*-10; the $-CH_3$protons of the ethyl group also showed a strong interaction with the methyl proton, which is attached to the same carbon (C-8) as well as adjacent *meso*-10-H proton. No correlation was observed between the $CH_3$ protons and the acetyl protons (C-3), which further confirmed the proposed structural assignment for **21**. Following a similar approach, the structures of compound **11** and **17** were also established (Figure 3).

**Spectroscopic Properties of Keto-Bacteriochlorins.** The absorption and fluorescence characteristics of keto-bacteriochlorins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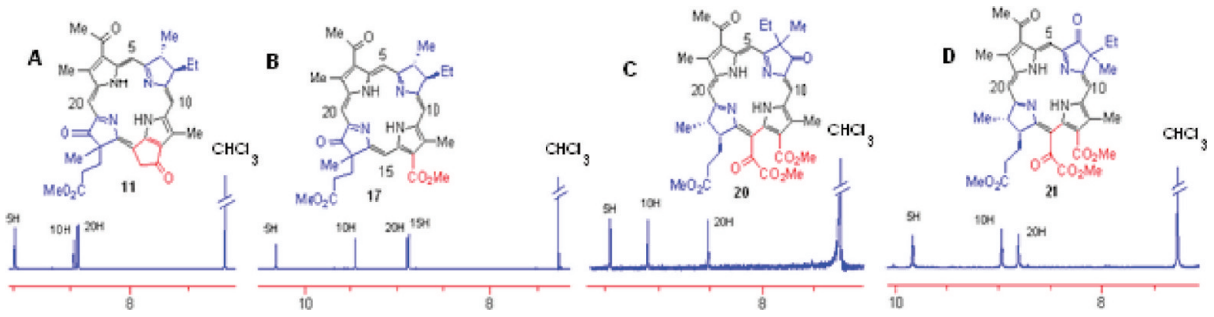



**Figure 2.** Partial $^1$H NMR of keto-bacteriochlorins **11**, **17**, **20**, and **21** (only *meso*-regions are shown). For details, see the Experimental Section and Supporting Information.

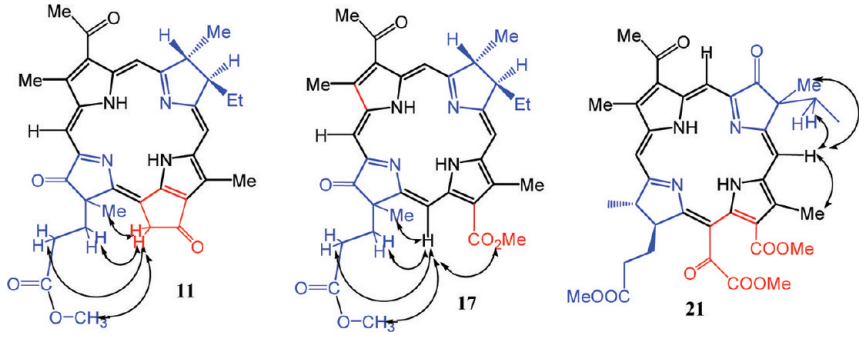
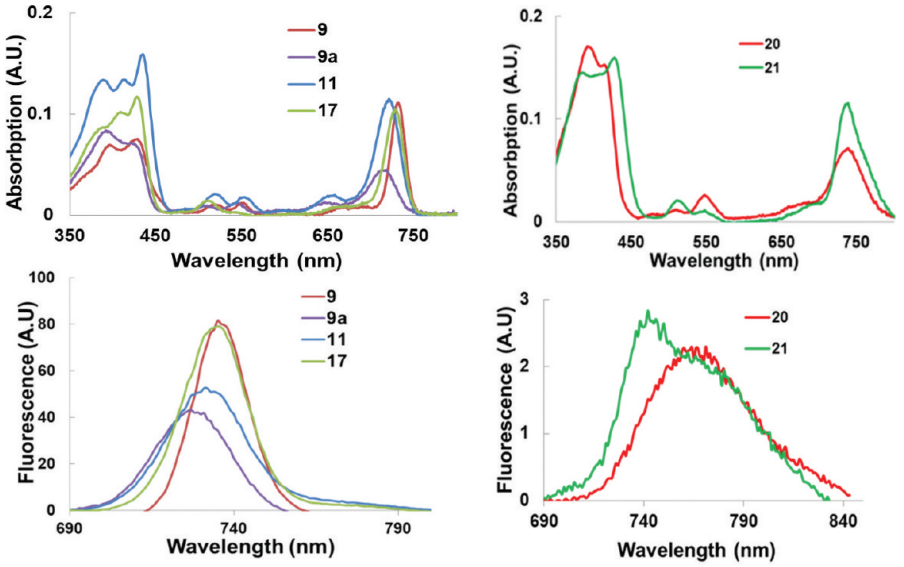



**Figure 3.** NOE correlations of ketobacteriochlorins **11**, **17**, and **21**.




| Compounds | 9 | 9a | 11 | 17 | 20 | 21 |
|---|---|---|---|---|---|---|
| Absorbance | 725 | 714 | 715 | 731 | 737 | 732 |
| Fluorescence Emission | 736 | 727 | 732 | 735 | 765 | 741 |
| Stokes shift (nm) | 11 | 13 | 17 | 4 | 28 | 9 |

**Figure 4.** Electronic absorption spectra and fluorescence emission spectra of keto-bacteriochlorins **9**, **9a**, **11**, **17**, **20**, and **21** at equimolar concentration (1.2 $\mu$M in $CH_2Cl_2$).

**9**, **9a**, **11**, **17**, **20**, and **21** as epimeric mixtures were measured in dichloromethane. These bacteriochlorins exhibited the long-wavelength absorptions at 725, 714, 715, 731, 737, and 732 nm and fluorescence at 736, 727, 732, 735, 765, and 741, respectively. Among all of the analogues, the 18-keto-bacteriochlorin **20** exhibited the largest Stokes shift (28 nm), whereas bacteriochlorin **17** lacked the five-member ring but, instead, containing a methoxycarbonyl- functionality at position 13, showed a much smaller shift of 4 nm. The observed shift was in the order of **20** > **11** > **9a** > **9** > **21** > **17** (Figure 4).

**In Vitro Photosensitizing Efficacy.** The keto-bacteriochlorins **9**, **9a**, **11**, and **17** and **20** and **21** (as an isomeric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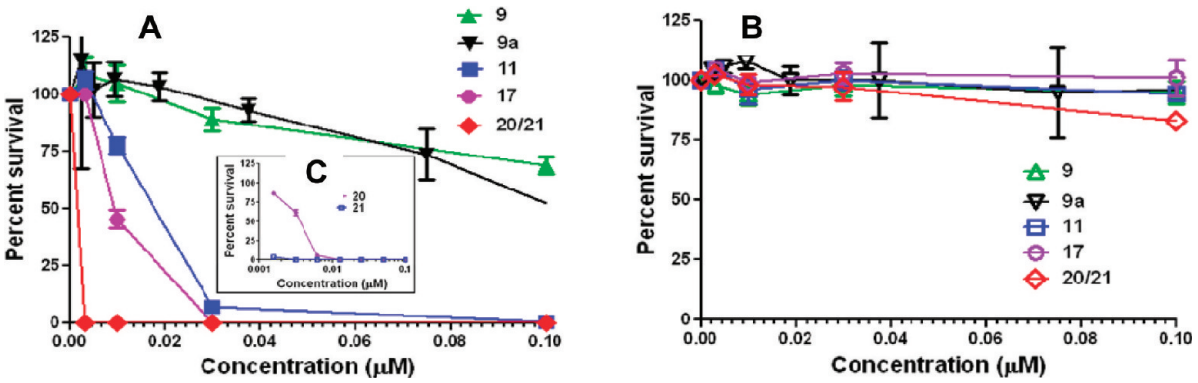


**Figure 5.** (A) In vitro photosensitizing efficacy of bacteriochlorins **9**, **9a** (containing a keto-group in ring-B), **11** (containing a keto-group in ring-D), **17**, and **20**/**21** isomeric mixture (bearing keto-groups in ring-B) at variable concentrations and light doses. The Colon26 tumor cells were exposed to light at 1 J/cm$^2$ at 24 h postincubation, and the MTT assay was performed after 48 h. (B) In vitro dark toxicity of photosensitizers **9**, **9a**, **11**, **17**, and **20**/**21** incubated in Colon26 tumor cells for 24 h but not exposed to light. (C) The inset figure shows the PDT efficacy of the separated isomers **20** and **21** at similar concentrations as the parent mixture and exposed to light (dose, 1 J/cm$^2$).

mixture and as individual isomers) were evaluated for in vitro PDT efficacy in Colon26 tumor cells. The cells were incubated with increasing concentrations of the photosensitizers (3−100 nM) for 24 h and were then exposed to variable light doses (0−2 J/cm$^2$) at an appropriate wavelength corresponding to the long-wavelength absorption of each compound formulated in 17% BCS in PBS. The MTT assay[35] was performed after 48 h (for details, see the Experimental Section). Among the photosensitizers evaluated, the bacteriochlorins **9** and **9a** containing a keto-group in ring-B were less effective than bacteriochlorins **11** and **17** containing a keto-group in ring-D. However, the photosensitizer containing a fused five-member isocyclic ring showed lower activity than **17** bearing a $-CO_2Me$ group at position 13. In contrast, bacteriochlorins **20** and **21** (as a 43:57 mixture) containing a keto-group in ring-B showed enhanced activity than **11** and **17**. To investigate the efficacy of the individual isomer, the isomeric mixture of **20** and **21** was duly separated into individual isomers by HPLC (see Figure 1 and the Supporting Information), and the in vitro photosensitizing efficacy of both the isomers was investigated under similar experimental conditions except that the cells were exposed to light at the appropriate long-wavelength absorptions of the photosensitizers (bacteriochlorin **20**: $\lambda_{max}$, 737 nm; and **21**: $\lambda_{max}$, 732 nm). Under similar parameters, isomer **21** showed significantly higher efficacy than the isomer **20** (see the inset in Figure 5C). As mentioned earlier, isomer **21** constitutes a major part of the mixture **20**/**21** (Scheme 5), which could explain the reason for similar PDT efficacy of the mixture as compared to isomer **21**.

The in vitro results depicted in Figure 5 suggest that besides the position of the keto-group (ring-B vs ring-D), the nature of the substituents present at the periphery of bacteriochlorin system makes a significant impact in PDT efficacy. However, further study with a series of analogues is required to establish a "true" SAR, and these studies are currently in progress. Efforts are also underway to investigate a correlation between the cell uptake, intracellular localization, and STAT-3 dimerization[36] with in vitro/in vivo PDT efficacy, and these results will be published in an appropriate journal.

## CONCLUSION

In summary, the work discussed in this manuscript describes an efficient approach for the synthesis of ring-B and ring-D reduced chlorins from naturally occurring bacteriochlorophyll-a, which are otherwise difficult to synthesize. As compared to naturally occurring bacteriochlorins, the keto-bacteriochlorins obtained from the respective chlorins showed enhanced stability with significant in vitro photosensitizing efficacy. The acetyl group present at position 3 of the chlorin systems provides a unique opportunity to alter the overall lipophilicity of the molecules to investigate the effect of such modifications in in vivo clearance and PDT efficacy. Easy access to these molecules should also generate a great interest in developing new supramolecular structures and synthetic models for understanding the bacterial photosynthetic reaction centers.

## EXPERIMENTAL SECTION

All reactions were carried out in heat gun-dried glassware under an atmosphere of nitrogen with magnetic stirring. Thin-layer chromatography (TLC) was done on precoated silica gel GF PE sheets (layer thickness, 0.25 mm) and aluminum oxide NF PE sheets. Column chromatography was performed either over silica gel 60 (70−230 mesh) or neutral alumina. In some cases, preparative TLC plates were also used for the purification. Solvents were purified as follows: trace amounts of water and oxygen from THF were removed by refluxing over sodium under an inert atmosphere. Dichloromethane was dried over $P_2O_5$. Anhydrous DMF, triethylamine, pyridine, and other common chromatographic solvents were obtained from commercial suppliers and used without further purification. NMR spectra were recorded on a 400 MHz spectrometer. All chemical shifts are reported in parts per million ($\delta$). $^1$H NMR (400 MHz) spectra were recorded at room temperature in $CDCl_3$ or $CD_3OD$ solutions and referenced to residual $CHCl_3$ (7.26 ppm) or TMS (0.00 ppm). EI-mass spectra were carried out on a ion-trap mass spectrometer equipped with a pneumatically assisted electrospray ionization source, operating in positive mode. UV−visible spectra were recorded on FT UV−visible spectrophotometer using dichloromethane/THF as solvent. All photophysical experiments were carried out using spectroscopic grade solvents.

**HPLC Method.** HPLC analysis of final products was carried out using a Waters Delta 600 System consisting of the 600 Controller, 600 Fluid Handling Unit, and 2998 Photodiode Array Detector equipped with a Phenomenex Luna column, 5 $\mu$m particle size, with dimensions 4.6 mm × 250 mm. A gradient mobile phase program was used as follows: starting at 30% ethyl acetate/70% hexane linear gradient to 70% ethyl acetate/30% hexane over 80 min; the flow rate was 1.0 mL/min.

**Methyl 3-Acetyl-17,18-dihydroxybacteriopyropheophorbide-a (10).** Compound 7 (50.0 mg, 0.09 mmol) was taken in a round-bottom flask (100 mL) and dissolved in 30 mL of dry dichloromethane. To this were added $OsO_4$ (100.0 mg) and pyridine


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(1.0 mL), and the reaction mixture was stirred vigorously at room temperature for 24 h. The reaction was monitored by UV−vis and TLC. $H_2S$ gas was then bubbled into the reaction mixture for 5 min, and then, the excess of $H_2S$ was removed by bubbling $N_2$ gas for another 30 min. Water was added to the reaction mixture and then extracted with dichloromethane (100 mL), and the organic layer was separated, washed with water, dried over sodium sulfate, and concentrated. The crude thus obtained was chromatographed over silica gel using 0.5−1% $CH_3OH/CH_2Cl_2$ mixture as an eluent to give **10** as a mixture of *cis*-diols (49:51). Yield, 23.0 mg (44%). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 9.08 and 9.02 (s, 1H, 5-H), 8.67 and 8.64 (s, 1H, 10-H), 8.30 and 7.96 (s, 1H, 20-H), 5.24 (dd, 1H, 13CHH, $J$ = 20 Hz), 4.89 (dd, 1H, 13CHH), 4.30−4.25 (m, 1H, 8-H), 4.05 and 3.96 (m, 1H, 7-H), 3.45 and 3.43 (s, 3H, $CO_2Me$), 3.38 and 3.34 (s, 3H, 12-$CH_3$), 3.04 and 2.97 (s, 3H, 2-$CH_3$), 2.89 and 2.24 (s, 3H, $COCH_3$), 2.96−2.88 (m, 2H, 17$^1$-$CH_2$), 2.67−2.62 (m, 2H, 17$^2$-$CH_2$), 2.41−2.36 (m, 2H, 8-$CH_2$-$CH_3$), 2.15 and 2.12 (s, 3H, 18-$CH_3$), 1.95 and 1.72 (d, 3H, 7-$CH_3$, $J$ = 7.2 and 7.6 $H_z$), 1.11 and 1.02 (t, 3H, 8-$CH_2CH_3$, $J$ = 7.2 and 7.6 Hz), −0.09 and −0.03 (brs, 1H, NH), −1.26 and −1.23 (brs, 1H, NH). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 199.0, 198.9, 196.1, 196.0, 174.2, 174.1, 170.6, 170.7, 164.8, 164.6, 164.2, 164.0, 154.8, 154.6, 146.9, 146.7, 139.6, 139.1, 137.2, 136.9, 136.6, 136.5, 136.4, 136.1, 132.3, 132.2, 130.3, 129.6, 121.7, 120.9, 109.6, 109.4, 99.2, 99.0, 97.9, 97.8, 94.6, 94.4, 84.3, 83.8, 83.75, 83.74, 55.29, 55.28, 51.8, 51.7, 48.6, 48.5, 47.9, 47.8, 33.24, 33.2, 33.1, 33.0, 30.7, 30.1, 30.0, 28.9, 28.8, 23.1, 22.9, 20.9, 20.7, 11.0, 10.8, 10.7, 10.4. EIMS ($m/z$): 621 ($M^+$ + Na). HRMS: calcd for $C_{34}H_{39}N_4O_6$ $[MH]^+$, 599.2870; found, 599.2880.

**Methyl 3-Acetyl-18-keto-bacteriopyropheophorbide-a (11).** Compound **10** (15.0 mg, 0.02 mmol) was taken in a round-bottom flask (100 mL) and dissolved in 15 mL of concentrated $H_2SO_4$. The reaction mixture was stirred vigorously at room temperature for 30 min and then poured into ice−water. The reaction mixture was then extracted with dichloromethane (100 mL), and the organic layer was separated, washed with water, dried over sodium sulfate, and concentrated. The crude thus obtained was chromatographed over silica gel using 1−3% $CH_3OH/CH_2Cl_2$ mixture as an eluent to get **11**. Yield, 6.0 mg (42.8%). UV−vis (THF, $\lambda_{max}$ (nm) ($\varepsilon$): 715 (9.27 × 10$^4$), 650 (2.19 × 10$^4$), 518 (2.19 × 10$^4$), 432 (1.48 × 10$^5$), and 385 (1.39 × 10$^5$). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 9.06 (s, 1H, 5-H), 8.55 (s, 1H, 10-H), 8.51 (s, 1H, 20-H), 5.32 (s, 2H, 13-$CH_2$), 4.38−4.33 (m, 1H, 7-H), 4.07−4.11 (m, 1H, 8-H), 3.56 (s, 3H, $CO_2Me$), 3.46 (s, 3H, 12-$CH_3$), 3.38 (s, 3H, 2-$CH_3$), 3.18 (s, 3H, $COCH_3$), 2.86−2.80 (m, 2H, 17$^1$-$CH_2$), 2.41−2.35 (m, 1H, 8-CHH−$CH_3$), 2.17 - 2.06 (m, 3H, 17$^2$-$CH_2$ and 1H of 8-CHH−$CH_3$), 1.89/1.88 (s, 3H, 17-$CH_3$), 1.83 (d, 3H, 7-$CH_3$ $J$ = 6.4 Hz), 1.10−1.15 (distorted triplet, 3H, 8-$CH_2CH_3$), 0.2 (brs, 1H, NH), −0.88 (brs, 1H, NH). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 207.7, 199.0, 196.5, 173.1, 165.9, 165.6, 144.9, 141.9, 138.7, 138.2, 138.1, 134.0, 133.8, 128.0, 122.2, 115.0, 112.9, 99.3, 97.6,94.0, 55.0, 54.7, 51.4, 49.2, 47.9, 33.3, 32.4, 30.1, 28.9, 22.8, 22.4, 13.6, 11.5, 10.7. EIMS ($m/z$): 603 ($M^+$ + Na). HRMS: calcd for $C_{34}H_{37}N_4O_5[MH]^+$, 581.2764; found, 581.2770.

**Methyl Bacteriopheophorbide-a (12).** *Rhodobacter sphaeroides* [containing bacteriochlorophyll *a* (**6**)] biomass (~500 g) was suspended in 1-propanol (2 L) and stirred at room temperature in dark with constant nitrogen bubbling for 12 h. The blue-green extract was filtered, and aqueous 0.5 N HCl (150−200 mL) was added to the filtrate. After it was stirred for 25 min, the solution began to turn reddish. The reaction mixture was then diluted with aqueous 5% NaCl (1.5 L) and extracted with dichloromethane. The combined extracts were washed with water, dried, and rotavaporated. The residue was precipitated from hexanes to give crude bacteriopheophytin-*a* **6** (2 g) with purity sufficient to proceed to the next step. Compound **6** was dissolved in aqueous 80% TFA (300 mL) and stirred in the dark under $N_2$ at 0 °C for 2 h. The solution was then diluted with ice/water (600 mL) and extracted with dichloromethane. The combined organic extracts were washed with water, treated with diazomethane, and evaporated to dryness. The crude residue was precipitated from hexanes to obtain the title compound (1.20 g); mp 222−224 °C. UV−vis [ethyl ether, $\lambda_{max}$ nm ($\varepsilon$)]: 358 (11.8 × 10$^4$), 385 (6.76 × 10$^4$), 525 (2.89 × 10$^4$), 680 (1.22 × 10$^4$), 749 (6.75 × 10$^4$); (in $CH_2Cl_2$): 362 (10.8 × 10$^4$), 389 (5.81 × 10$^4$), 530 (2.84 × 10$^4$), 683 (1.11 × 10$^4$), 754 (6.27 × 10$^4$). $^1$H NMR $\delta$ (in $CDCl_3$): 8.98 (s, 1H, 5-H), 8.49 (s, 1H, 10-H), 8.41 (s, 1H, 20-H), 6.08 (s, 1H, 13$^2$-H), 4.27 (m, 2H, 1H for 7-H, 1H for 8-H), 4.02 (m, 2H, 1H for 17-H, 1H for 18-H), 3.85 (s, 3H, 12-$CH_3$), 3.59 (s, 3H, 2-$CH_3$), 3.49 (s, 3H, 13$^2$-$COOCH_3$), 3.45 (s, 3H, 17-$CH_2CH_2$ $COOCH_3$), 3.16 (s, 3H, 3-$COCH_3$), 2.52 (m, 2H, 17-$CH_2CH_2COOCH_3$), 2.34 (m, 2H, 17-$CH_2$-$CH_2COOCH_3$), 2.25 (m, 2H, 8-$CH_2CH_3$), 1.80 (d, $J$ = 7.4 Hz, 3H, 7-$CH_3$), 1.73 (d, $J$ = 7.9 Hz, 3H, 18-$CH_3$), 1.12 (t, $J$ = 7.2 Hz, 3H, 8-$CH_2CH_3$), 0.47 (s, 1H, NH), −0.95 (s, 1H, NH). EIMS ($m/z$): 626 (M + 1). HRMS: calcd for $C_{36}H_{41}N_4O_6$ $[MH]^+$, 625.3026; found, 625.3043.

**3-Acetyl-bacteriochlorin 15-Glyoxilic Acid Trimethyl Ester (13).** Methyl bacteriopheophorbide-a **12** (100 mg, 016 mmol) was taken in a round-bottom flask (100 mL), and dry THF (30 mL) was added. A 0.3 mL amount of NaOMe (25% in $CH_3OH$) was dissolved in 10 mL of dry THF and added slowly via syringe to the reaction mixture under vigorous stirring. The reaction mixture was stirred at room temperature for 4 h and was quenched with 5% acetic acid−$H_2O$ and extracted with dichloromethane (100 mL). The organic layer separated, washed with brine, dried over sodium sulfate, and concentrated to dryness. A trace of acetic acid was removed under high vacuum. The crude product was redissolved in dichloromethane and treated with diazomethane. The reaction mixture was stirred for 10 min, and then, an excess of diazomethane was removed by bubbling $N_2$ gas. The reaction mixture concentrated and chromatographed over silica gel using 1−3% $CH_3OH$/dichloromethane gradient as an eluent to obtain the compound as a major product. Slow moving brown-red band on silica. Yield, 40.0 mg (37.2%); mp > 260 °C (decomp.). UV−vis $\lambda_{max}$ (in $CH_2Cl_2$): 782 nm ($\varepsilon$ 5.19 × 10$^4$), 748 (10.4 × 10$^4$), 543 (3.12 × 10$^4$), 410 (5.27 × 10$^4$) and 363 (7.61 × 10$^4$).$^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 9.14 (s, 1H, *meso*-H), 8.68 (s, 1H, *meso*-H), 8.54 (s, 1H, *meso*-H), 4.48 (m, 1H, 17-H), 4.26 (m, 1H, 8-H), 4.22 (m, 1H, 18-H), 4.10 (s, 3H, $CO_2Me$), 4.07 (m, 1H, 7-H), 3.91 (s, 3H, $CO_2Me$), 3.53 (s, 3H, $CO_2Me$), 3.51 (s, 3H, 12-$CH_3$), 3.44 (s, 3H, 2-$CH_3$), 3.15 (s, 3H, $COCH_3$), 2.31 (m, 2H, 17$^2$-$CH_2$), 2.06−2.00 (m, 3H, 8-$CH_2CH_3$ and 17$^1$-$CH_2$), 1.83 (d, 3H, 7-$CH_3$, $J$ = 7.2 Hz), 1.76 (d, 3H, 18-$CH_3$, $J$ = 7.6 Hz), 1.72 (m, 1H, 17$^1$-$CH_2$), 1.06 (t, 3H, 8-$CH_2CH_3$, $J$ = 7.6 Hz), −0.45 (brs, 1H, NH), −0.53 (brs, 1H, NH). EIMS ($m/z$): 671.3 (M + H). HRMS: calcd for $C_{37}H_{42}N_4O_8$, 670.3002; found, 670.3030.

**Ring-B Reduced Chlorin (15).** 3-Acetyl-bacteriochlorin 15-glyoxilic acid trimethyl ester **13** (100.0 mg, 0.15 mmol) was refluxed in collidine (15 mL) for 30 min. The progress of the reaction was monitored by UV−vis and TLC. After completion, the reaction mixture was concentrated to dryness using high vacuum and purified on alumina (G-III) column using dichloromethane−hexane mixture as the eluent. Yield, 50.0 mg (57.6%). UV−vis ($CH_2Cl_2$, $\lambda_{max}$, nm, ($\varepsilon$): 410.0 (8.16 × 10$^4$), 509.0 (7.50 × 10$^3$), 683.1 (4.16 × 10$^4$). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 10.50 (s, 1H, *meso*-H), 9.71 (s, 1H, *meso*-H), 9.60 (s, 1H, *meso*-H), 8.95 (s, 1H, *meso*-H), 4.60 (m, 1H, 8-H), 4.40 (s, 3H, $CO_2Me$), 4.36 (m, 1H, 7-H), 4.12 (t, 2H, 17$^1$-$CH_2$, $J$ = 7.6 Hz), 3.77 (s, 3H, ring-$CH_3$), 3.75 (s, 3H, ring-$CH_3$), 3.70 (s, 3H, $CO_2Me$), 3.35 (s, 3H, ring-$CH_3$), 3.26 (s, 3H, $COCH_3$), 3.18 (t, 2H, 17$^2$-$CH_2$, $J$ = 7.6 Hz), 2.51−2.46 (m, 1H, 8-CHHCH$_3$), 2.20−2.15 (m, 1H, 8-CHHCH$_3$), 1.92 (d, 3H, 7-$CH_3$, $J$ = 7.6 Hz), 1.13 (t, 3H, 8-$CH_2CH_3$, $J$ = 7.6 Hz), −1.79 (brs, 2H, NH). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 198.8, 173.5, 171.5, 168.9, 166.5, 152.7, 151.9, 140.8, 138.7, 138.1, 137.9, 137.3, 137.2, 133.5, 132.1, 130.1, 124.3, 101.9, 100.9, 96.7, 94.9, 57.4, 51.6, 47.8, 37.0, 33.3, 30.2, 29.6, 23.8, 21.9, 14., 13.2, 11.5, 10.8. EIMS ($m/z$): 583.8 ($M^+$ + 1). HRMS: calcd for $C_{34}H_{39}N_4O_5$ $[MH]^+$, 583.2920; found, 583.2938.

**Rhodobacteriochlorin (14).** The second band from the column. Yield, 9.0 mg (10.2%). UV−vis ($CH_2Cl_2$, $\lambda_{max}$, nm, ($\varepsilon$): 355.0 (1.05 × 10$^5$), 521.0 (2.22 × 10$^4$), 760 (8.43 × 10$^4$). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 9.58 (s, 1H, *meso*-H), 9.32 (s, 1H, *meso*-H), 8.72 (s, 1H, *meso*-H), 8.65 (s, 1H, *meso*-H), 4.43−4.33 (m, 3H, 8-H, 17-H, 18-H), 4.31 (s, 3H, $CO_2Me$), 4.19−4.16 (m, 1H, 7-H), 3.63 (s, 3H, $CO_2Me$),

3.62 (s, 3H, ring-$CH_3$), 3.58 (s, 3H, ring-$CH_3$), 3.20 (s, 3H, $COCH_3$), 2.67−2.56 (m, 2H, $17^2$-$CH_2$), 2.42−2.35 (m, 3H, 8-$\underline{CH_2}CH_3$ and $17^1$-$C\underline{H}H$), 2.13−2.07 (m, 1H, $17^1$-$CH\underline{H}$), 1.83 (d, 3H, 7-$CH_3$, $J$ = 4.4 Hz), 1.81 (d, 3H, 18-$CH_3$, $J$ = 4.4 Hz), 1.11 (t, 3H, 8-$CH_2\underline{CH_3}$, $J$ = 7.6 Hz), −1.39 (brs, 1H, NH), −1.44 (brs, 1H, NH). EIMS ($m/z$): 584.5 ($M^+$). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 198.8, 173.8, 168.5, 166.9, 166.0, 164.8, 164.6, 135.6, 135.0, 134.6, 133.9, 133.7, 132.2, 129.7, 119.7, 98.6, 98.5, 97.2, 96.3, 56.8, 54.8, 51.5, 47.6, 47.5, 33.2, 32.1, 30.9, 30.2, 29.6, 23.6, 23.5, 13.6, 13.2, 10.8. HRMS: calcd for $C_{34}H_{41}N_4O_5$ $[MH]^+$, 585.3077; found, 585.3059.

**3-Acetyl-17,18-bis Hydroxyl-Ring-B Reduced Chlorin (16).** Acetyl-chlorin-dimethyl ester **15** (50.0 mg, 0.08 mmol) was taken in a round-bottom flask (100 mL) and dissolved in 30 mL of dry dichloromethane. To this were added $OsO_4$ (100.0 mg) and pyridine (1.0 mL), and the reaction mixture was stirred vigorously at room temperature for 24 h. The reaction was monitored UV−vis and TLC. $H_2S$ gas was then bubbled into the reaction mixture for 5 min, and then, the excess of $H_2S$ was removed by bubbling $N_2$ gas for 30 min. Water was added to the reaction mixture and extracted with dichloromethane (100 mL), and the organic layer was separated, washed with water, dried over sodium sulfate, and concentrated. The crude reaction product thus obtained was chromatographed over silica gel using 0.5−1% $CH_3OH/CH_2Cl_2$ mixture as an eluent to give product as a mixture of *cis*-diols (44:56). Yield, 30.0 mg (57%). UV−vis $\lambda_{max}$ (in $CH_2Cl_2$) ($\varepsilon$): 358.1 nm ($7.88 \times 10^4$), 388.1 nm ($7.35 \times 10^4$), 524 nm ($2.49 \times 10^4$), 751.9 nm ($7.88 \times 10^4$). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 9.72 and 9.69 (s, 1H, *meso*-H), 9.34 and 9.33 (s, 1H, *meso*-H), 8.83 and 8.79 (s, 1H, *meso*-H), 8.71 and 8.64 (s, 1H, *meso*-H), 4.43−4.36 (m, 1H, 8-H), 4.27 and 4.20 (m, 1H, 7-H), 4.12 and 4.10 (s, 3H, $CO_2Me$), 3.67 and 3.61 (s, 3H, $CO_2Me$), 3.49 and 3.36 (s, 3H, ring-$CH_3$), 3.31 (s, 3H, ring-$CH_3$), 2.90 and 2.87 (s, 3H, $COCH_3$), 2.85 (m, 2H, $17^1$-$CH_2$), 2.76 and 2.66 (m, 2H, $17^2$-$CH_2$), 2.41 and 2.31 (m, 1H, 8-C$\underline{H}$H−$CH_3$), 2.11 and 2.00 (m, 1H, 8-CH$\underline{H}$-$CH_3$), 2.06 and 1.87 (s, 3H, 18-$CH_3$), 1.91 and 1.78 (d, 3H, 7-$CH_3$, $J$ = 7.6 Hz), 1.15 and 1.08 (t, 3H, 8-$CH_2\underline{CH_3}$, $J$ = 7.6 Hz), −1.30 and −1.37 (brs, 1H, NH), −1.42 and −1.44 (brs, 1H, NH). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 198.7, 198.6, 177.4, 177.3, 175.0, 170, 169.2, 169.1, 166.9, 166.3, 165.0, 163.9, 158.5, 158.4, 154.4, 154.2, 153.0, 143.0, 137.1, 137.0, 135.7,135.6, 135.5, 135.4, 134.9, 134.8, 133.3, 133.4, 120.0,119.9, 99.4, 99.2, 98.5, 98.3, 95.0, 96.1, 94.8, 94.2, 86.0, 86.4, 84.1, 84.0, 56.9, 57.1, 56.6, 56.5, 52.0, 51.9, 48.1, 47.8, 33.2, 33.1, 30.3, 30.2, 29.9, 30.0, 29.3, 29.2, 25.0, 25.1, 23.5, 23.3, 13.67, 13.64, 13.36, 13.14, 10.69, 10.64. EIMS ($m/z$): 617 ($M^+$+ 1). HRMS: calcd for $C_{34}H_{40}N_4O_7$ $[MH]^+$, 617.2975; found, 617.2980.

**3-Acetyl-18-keto-bacteriochlorin (17).** Bacteriochlorin diol **16** (25.0 mg, 0.04 mmol) was taken in a round-bottom flask (100 mL) and dissolved in 15 mL of concentrated $H_2SO_4$. The reaction mixture was stirred vigorously at room temperature for 30 min and then poured into ice−water. The reaction mixture was then extracted with dichloromethane (100 mL), and the organic layer was separated, washed with water, dried over sodium sulfate, and concentrated. Crude thus obtained was chromatographed over silica gel using 1−3% $CH_3OH/CH_2Cl_2$ mixture as an eluent to get the product; yield, 15.0 mg (61.9%). UV−vis [$CH_2Cl_2$, $\lambda_{max}$, nm, ($\varepsilon$)]: 403.1 ($7.68 \times 10^4$), 425.0 ($9.10 \times 10^4$), 507.0 ($1.17 \times 10^4$), 539.0 ($2.72 \times 10^3$), 725.00 ($8.70 \times 10^4$). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 10.30 (s, 1H, 5-H), 9.44 (s, 1H, 10-H), 8.88 (s, 1H, 20-H), 8.89 (s, 1H, 15-H), 4.48−4.51 (m, 1H, 7-H), 4.37 (s, 3H, 17-$CO_2Me$), 4.24−4.28 (m, 1H, 8-H), 3.69 (s, 3H, 13-$CO_2Me$), 3.68 (s, 3H, 2-$CH_3$), 3.32 (s, 3H, 12-$CH_3$), 3.24 (s, 3H, $COCH_3$), 2.99−2.95 (m, 2H, $17^1$-$CH_2$), 2.49−2.39 (m, 2H, 8-C$\underline{H}$H−$CH_3$ and 1H of $17^2$-$CH_2$), 2.20−2.10 (m, 2H, 8-CH$\underline{H}$-$CH_3$ and $17^2$-$CH_2$), 1.95/1.97 (singlets, 3H, 17-$CH_3$), 1.86 (d, 3H, 7-$CH_3$, $J$ = 7.2 Hz), 1.09−1.15 (m, 3H, 8-$CH_2\underline{CH_3}$,), −1.50 (brs, 1H, NH), −1.6 (brs, 1H, NH). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 208.6, 198.7, 173.1, 172.0, 166.5, 166.3, 162.8, 145.2, 136.8, 136.4, 135.1, 132.2, 131.5, 127.9, 123.4, 114.6, 98.6, 97.6, 94.6, 56.7, 53.4, 53.0, 52.2, 51.3, 48.3, 33.3, 30.4, 29.7, 28.8, 23.4, 23.0, 13.9, 12.9, 10.8; EIMS ($m/z$): 621.3 (M + Na). HRMS: calcd for $C_{34}H_{39}N_4O_6$ $[MH]^+$, 599.2870; obsd, 599.2882.

**3-Acetyl-chlorin-15-glyoxilic Acid Trimethyl Ester (18).** 3-Acetyl-bacteriochlorin 15-glyoxilic acid trimethyl ester **13** (45 mg, 0.06 mmol) was dissolved in dichloromethane (15 mL). To this mixture was added slowly a $CH_2Cl_2$ solution of DDQ (30 mg, 0.13 mmol). The resulting mixture was stirred at room temperature for 10 min and washed with water three times. The organic layer was separated and dried over anhydrous $Na_2SO_4$, and solvent was removed under vacuum. The residue obtained was purified with preparative plates using 2% acetone/dichloromethane. Yield, 35.0 mg (78.6%). UV−vis [$CH_2Cl_2$, $\lambda_{max}$, nm, ($\varepsilon$)]: 410.9 ($8.48 \times 10^4$), 504.9 ($7.24 \times 10^3$), 546 ($8.77 \times 10^3$), 692 ($2.79 \times 10^4$). $^1$H NMR $\delta$ (in $CDCl_3$): 9.94 (s, 1H, 5H), 9.68 (s, 1H, 10H), 8.70 (s, 1H, 20H), 4.66 (dd, 1H, 18 H, $J$ = 6.8 Hz), 4.35 (m, 1H, 17H, $J$ = 7.2 Hz), 4.15 (s, 3H, $CO_2Me$), 3.90 (s, 3H, $CO_2Me$), 3.72 (m, 3H, 8 $CH_2$ +$17^1$-$CH_2$), 3.66 (s, 3H, $CO_2Me$), 3.53 (s, 3H, 12 $CH_3$), 3.73 (s, 3H, 2 $CH_3$), 3.25 (s, 3H, 7-$CH_3$), 3.20 (s, 3H, $COCH_3$), 2.05- 2.17 (m, 3H, $17^2$-$CH_2$ +$17^1$-$CH_2$), 1.68 (t, 3H, 8$CH_3$, $J$ = 7.6 Hz), 1.81 (d, 3H, 18 $CH_3$, $J$ = 8 Hz), 1.68 (t, 3H, 8$CH_3$, $J$ = 7.6 Hz). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 198.5, 186.4, 173.2, 171.4, 167.4, 166.4, 163.5, 155.4, 150.1, 145.3, 140.6, 139.9, 137.4, 136.7, 135.6, 135.1, 135.0, 131.4, 121.1, 106.6, 105.4, 104.3, 94.7, 53.3, 52.8, 52.1, 51.5, 49.2, 33.2, 31.4, 30.9, 23.2, 19.4, 17.4, 13.4, 13.0, 11.1. EIMS ($m/z$): 691.1 ($M^+$ + Na). HRMS: calcd for $C_{37}H_{41}N_4O_8$ $[MH]^+$, 669.2924; found, 669.2916.

**3-Acetyl-7,8-dihydroxybacteriochlorin-15-glyoxilic Acid Trimethyl Ester (19).** Compound **18** (30.0 mg, 0.04 mmol) was taken in a round-bottom flask (100 mL) and dissolved in 30 mL of dry dichloromethane (DCM). To this were added $OsO_4$ (100 mg) and pyridine (1.0 mL), and the reaction mixture was stirred vigorously at room temperature for 24 h. The reaction was monitored UV−vis and TLC. $H_2S$ gas was then bubbled into the reaction mixture for 5 min, and then, an excess of $H_2S$ was removed by bubbling $N_2$ gas for 30 min. Water was added to the reaction mixture and extracted with DCM (100 mL), and the organic layer was separated, washed with water, dried over sodium sulfate, and concentrated. The crude thus obtained was purified with silica gel preparative plates using 5% $CH_3OH/CH_2Cl_2$ to give **19** as a mixture of *cis*-diols (38:62). Yield, 27.0 mg (64%). UV−vis [$CH_2Cl_2$, $\lambda_{max}$, nm, ($\varepsilon$)]: 761 ($7.1 \times 10^4$), 529 ($3.47 \times 10^4$), 386 ($9.9 \times 10^4$), 358 ($1.3 \times 10^5$). $^1$H NMR $\delta$ (in $CDCl_3$): 9.31 and 9.28 (s, 1H, 5H), 8.95 and 8.93 (s, 1H, 10H), 8.55 and 8.50 (s, 1H, 20H), 4.37−4.39 (m, 1H, 18 H), 4.25−4.26 (m, 1H, 17H), 4.09 and 4.07 (s, 3H, $CO_2Me$), 3.93 and 3.90 (s, 3H, $CO_2Me$), 3.72−3.60 (m, 3H, 8 $CH_2$ +$17^1$-$CH_2$), 3.56 and 3.53 (s, 3H, $CO_2Me$), 3.45 and 3.43 (s, 3H, 12 $CH_3$), 3.38 and 3.34 (s, 3H, 2 $CH_3$), 2.97 and 2.84 (s, 3H, 7 $CH_3$), 2.26−2.41 (m, 3H, $17^2$-$CH_2$ + $17^1$-$CH_2$), 2.10 and 2.22 (s, 3H, $COCH_3$), 1.67 and 1.80 (d, 3H, 18-$CH_3$, $J$ = 7.6 Hz), 0.68 and 0.86 (t, 3H, 8-$CH_3$, $J$ = 7.2 and 7.6 Hz), −0.41 and −0.44 (brs, 1H, NH), −0.49 and −0.53 (brs, 1H, NH). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 198.2, 198.1, 186.4, 186.3, 173.3, 173.1, 169.7, 168.8, 166.6, 166.5, 166.1, 166.0, 165.8, 165.7, 164.8, 164.3, 163.2, 163.3, 161.5, 160.4, 136.0, 136.1, 135.9, 135.7, 134.3, 133.2, 132.7, 132.4, 132.0, 131.9, 131.5, 131.2, 120.7, 120.1, 108.8, 108.7, 100.3, 100.2, 98.6, 97.1, 96.5, 86.3, 85.8, 84.9, 82.7, 82.4, 53.3, 52.8, 52.1, 52.0, 51.9, 51.7, 51.6, 51.5, 49.1, 49.0, 32.9, 32.8, 31.3, 31.2, 31.0, 30.9, 22.7, 22.6, 20.7, 20.0, 13.8, 13.7, 13.3, 13.2, 12.8, 12.7, 8.3, 8.2. EIMS ($m/z$): 703 (M + H). HRMS: calcd for $C_{37}H_{43}N_4O_{10}$ $[MH]^+$, 703.2979; found, 703.3000.

**3-Acetyl-8-keto- and 3-Acetyl-7-keto-bacteriochlorin-15-glyoxilic Acid Trimethyl Ester (20 and 21).** Compound **19** (20.0 mg, 0.04 mmol) was taken in a round-bottom flask (100 mL) and dissolved in 15 mL of concentrated $H_2SO_4$. The reaction mixture was stirred vigorously at room temperature for 30 min and then poured into ice−water. The reaction mixture was then extracted with dichloromethane (100 mL), and the organic layer was separated, washed with water, dried over sodium sulfate, and concentrated. The crude thus obtained was chromatographed using preparative plates using 50% ethyl acetate/hexane to give an isomeric mixture of **20** and **21** (43:57). This isomeric mixture was then separated by HPLC using the conditions described above in the Experimental Section to yield pure isomer of **20** and **21**.

**3-Acetyl-8-keto-bacteriochlorin-15-glyoxilic Acid Trimethyl Ester (20).** Yield, 3.8 mg (19%). UV−vis [$CH_2Cl_2$, $\lambda_{max}$, nm, ($\varepsilon$)]:


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392.1 (1.24 × $10^5$), 508.0 (1.0 × $10^4$), 546.0 (2.0 × $10^3$), 737.0 (5.1 × $10^4$). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 9.45 (s, 1H, 5-H), 9.10 (s, 1H, 10-H), 8.51 (s, 1H, 20-H), 4.43−4.45 (m, 1H, 18-H), 4.21- 4.27 (m, 1H, 17-H), 4.11 (s, 3H, $CO_2Me$), 3.91 (s, 3H, $CO_2Me$), 3.56, 3.53, and 3.51 (each s, 3H, 12-$CH_3$, 2-$CH_3$, and $CO_2Me$), 3.18 (s, 3H, $COCH_3$), 2.56 (q, 2H, 7-$CH_2$, $J$ = 8 Hz), 2.36−2.37 (m, 1H, 17$^1$-$CH_2$), 2.04−2.09 (m, 3H, 2H of 17$^2$-$CH_2$ and 1H of 17$^1$-$CH_2$), 1.82 (s, 3H, 7-$CH_3$), 1.74 (d, 3H, 18-$CH_3$, $J$ = 7.6 Hz), 0.50 (t, 3H, 7-$CH_2\underline{CH_3}$, $J$ = 8 Hz), 0.19 (brs, 1H, NH), 0.13 (brs, 1H, NH). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 209.2, 198.0, 185.8, 174.1, 173.2, 168.4, 166.4, 166.1, 163.25, 143.1, 140.39,137.8, 137.5, 137.4, 134.7, 133.8, 129.3, 127.8, 101.3, 98.4, 96.03, 55.1, 53.3, 52.0, 51.6, 49.9, 33.1, 31.5, 31.4, 31.2, 31.04, 30.9, 29.6, 22.6, 22.5, 13.4, 12.9, 12.8, 8.8. EIMS ($m/z$): 707.3 ($M^+$ + Na). HRMS: calcd for $C_{37}H_{41}N_4O_9$ $[MH]^+$, 685.2874; found, 685.2890.

**3-Acetyl-7-keto-bacteriochlorin-15-glyoxilic Acid Trimethyl Ester (21).** Yield, 4.5 mg (25%). UV−vis [$CH_2Cl_2$, $\lambda_{max}$, nm, ($\varepsilon$)]: 385 (1.19 × $10^5$), 428.0 (1.29 × $10^5$), 511.0 (1.96 × $10^4$), 544.0 (1.08 × $10^4$), 732.0 (9.1 × $10^4$). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 9.83 (s, 1H, 5-H), 8.97 (s, 1H, 10-H), 8.81 (s, 1H, 20-H), 4.49−4.52 (m, 1H, 18-H), 4.35−4.37 (m, 1H, 17-H), 4.15 (s, 3H, $CO_2Me$), 3.97/3.96 (s, 3H, $CO_2Me$), 3.58 and 3.54 (s, 9H, 12 $CH_3$, 2-$CH_3$ and $CO_2Me$), 3.29 (s, 3H, $COCH_3$), 2.62 (q, 2H, 8-$C\underline{H_2}CH_3$, $J$ = 7.8 Hz), 2.36−2.37 (m, 1H, 17$^1$ −$CH_2$), 2.05−2.09 (m, 3H, 2H of 17$^2$-$CH_2$ and 1H of 17$^1$-$CH_2$), 1.90/1.92 (s, 3H, 8-$CH_3$), 1.78−1.80 (m, 3H, 18-$CH_3$), 0.45−0.51 (m, 3H, 8-$CH_2\underline{CH_3}$), −1.07 (brs, 1H, NH), −1.01 (brs, 1H, NH). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 208.7, 198.1, 198.1, 186.4, 173.0, 169.2, 166.7, 166.3, 163.0, 162.95,162.93 147.7, 139.4, 136.7, 136.6, 135.6, 135.2, 134.6, 134.2, 133.3, 133.2, 98.9, 98.8, 97.3, 54.6, 53.2, 52.4, 51.6, 48.8, 33.3, 31.8, 31.7, 31.3, 30.5, 29.7, 23.2, 23.0, 22.9, 13.1, 13.0, 8.8, 8.7. EIMS ($m/z$): 707.3 ($M^+$ + Na). HRMS: calcd for $C_{37}H_{41}N_4O_9[MH]^+$, 685.2874; found, 685.2852.

**3-Acetyl-15-glyoxilic Acid-Ring-B Reduced Chlorin Trimethyl Ester (22).** Acetyl-bacteriochlorin 15-glyoxilic acid trimethyl ester **13** (45 mg, 0.06 mmol) was dissolved in dichloromethane (20 mL). To this mixture was added slowly a nitromethane solution of $FeCl_3{\cdot}6H_2O$ (72 mg, 0.267 mmol). The resulting mixture was stirred at room temperature for 30 min, quenched by the addition of 5 mL of methanol, and washed with water three times. The organic layer was separated and dried over anhydrous $Na_2SO_4$, and the solvent was removed under vacuum. The residue obtained was purified with preparative plates using 2% acetone/dichloromethane; yield, 39.0 mg (87.2%). UV−vis [$CH_2Cl_2$, $\lambda_{max}$, nm, ($\varepsilon$)]: 410.9 (8.09 × $10^4$), 512.1 (1.00 × $10^4$), 679 (3.28 × $10^4$). $^1$H NMR $\delta$ (in $CDCl_3$): 9.85 (s, 1H, 5H), 9.56 (s, 1H, 10H), 8.90 (s, 1H, 20H), 4.53 (q, 1H, 7-H, $J$ = 24 Hz), 4.35 (m, 1H, 8H), 4.15 (s, 3H, $CO_2Me$), 3.90 (s, 3H, $CO_2Me$), 3.80 (s, 3H, $CO_2Me$), 3.63 (s, 3H, 12 $CH_3$), 3.52 (s, 3H, 2 $CH_3$), 3.32 (s, 3H, 18 $CH_3$), 3.26 (s, 3H, $COCH_3$), 2.58−2.64 (m, 2H, 17$^1$-$CH_2$), 2.43−2.45 (m, 1H, 8-C$\underline{H}$H), 2.10−2.14 (m, 1H, 8-CH$\underline{H}$), 1.89 (d, 3H, 7$CH_3$, $J$ = 6.8 Hz), 1.08 (t, 3H, 8- $CH_2\underline{CH_3}$, $J$ = 7.6 Hz), −1.2 (brs, 1H, NH), −1.60 (brs, 1H, NH). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 198.4, 189.3, 173.0, 172.0, 169.9, 167.0, 161.8, 149.6, 149.4, 141.8, 138.5, 138.2, 137.8, 137.7, 137.4, 131.0, 130.8, 129.9, 127.5, 113.0, 102.8, 97.8, 96.0, 58.0, 54.0, 53.5, 51.6, 47.1, 35.0, 33.2, 30.0, 23.6, 23.4, 14.0, 12.6, 11.8, 10.8. EIMS ($m/z$): 691.1 ($M^+$ + Na). HRMS: calcd for $C_{37}H_{41}N_4O_8[MH]^+$, 669.2924; found, 669.2912.

**3-Acetyl-17,18-dihydroxy-15-glyoxilic Acid-Bacteriochlorin Trimethyl Ester (23).** Compound **22** (40.0 mg, 0.06 mmol) was taken in a round-bottom flask (100 mL) and dissolved in 30 mL of dry DCM. To this were added $OsO_4$ (75.0 mg) and pyridine (1.0 mL), and the reaction mixture was stirred vigorously at RT for 24 h. The reaction was monitored by UV−vis and TLC. $H_2S$ gas was then bubbled into the reaction mixture for 5 min, and then, an excess of $H_2S$ was removed by bubbling $N_2$ gas for another 30 min. Water was added to reaction mixture and extracted with dichloromethane (100 mL), and the organic layer was separated, washed with water, dried over sodium sulfate, and concentrated. The crude thus obtained was purified with silica gel preparative plates using 5% MeOH/$CH_2Cl_2$. Yield, 23 mg (55%). $^1$H NMR $\delta$ (in $CDCl_3$): 9.45 and 9.43 (s, 1H, 5H), 8.88 and 8.86 (s, 1H, 10H), 8.75 and 8.73 (s, 1H, 20H), 4.38−4.40 (m, 1H, 8 H), 4.28−4.29 (m, 1H, 7H), 4.16 and 4.15 (s, 3H, $CO_2Me$), 3.63 and 3.67 (s, 3H, $CO_2Me$), 3.51 and 3.50 (s, 3H, $CO_2Me$), 3.43 and 3.42 (s, 3H, 12 $CH_3$), 3.14 and 3.13 (s, 3H, 2 $CH_3$), 3.10 and 3.09 (s, 3H, 18 $CH_3$), 2.52 (s, 3H, 3$COCH_3$), 2.31−2.24 (m, 2H, 17-$CH_2$), 2.19−2.24 (m, 2H, 8-$CH_2$), 2.04−2.08 (m, 2H, 17-$CH_2$), 1.73 and 1.89 (d, 3H, 7 $CH_3$, $J$ = 7.2 and 7.6 Hz), 1.08 (t, 3H, 8$CH_3$, $J$ = 5.6 Hz), −0.354 and −0.415 (brs, 1H, NH), −0.52 and −0.60 (brs, 1H, NH). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 198.3, 198.4, 175.2 (2C ?), 174.4, 174.3, 171.0, 170.9, 170.1, 170.0, 167.2, 167.1, 166.2, 166.1, 160.2, 159.8, 159.5, 159.4, 158.2, 157.8, 153.0, 143.0, 137.4, 137.2, 135.6, 135.8, 134.1, 134.2, 133.6, 133.5, 131.6, 131.4, 131.3,129.8, 115.2, 115.0, 104.7, 104.3, 103.8, 103.9, 95.9, 96.0, 92.7, 92.8, 83.0, 83.2, 57.1, 57.0, 55.0, 52.6, 52.1, 52.0, 51.5, 51.5, 46.8, 47.4, 33.3, 33.5, 28.9, 29.5, 23.4, 23.3, 22.7,22.6, 19.2,19.3, 14.0, 14.1, 13.6, 13.5, 11.9, 11.8, 10.8, 10.7. EIMS ($m/z$): 725 ($M^+$ + Na). HRMS: calcd for $C_{37}H_{41}N_4O_{10}$ [M − H]$^+$, 701.2823; found, 701.2855.

**3-Acetyl-15-glyoxilic Acid-8-keto-bacteriochlorin Trimethyl Ester (17).** Compound **23** (15.0 mg, 0.02 mmol) was taken in a round-bottom flask (100 mL) and dissolved in 15 mL of concentrated $H_2SO_4$. The reaction mixture was stirred vigorously at room temperature for 30 min and then poured into ice−water. The reaction mixture was then extracted with dichloromethane (100 mL), and the organic layer was separated, washed with water, dried over sodium sulfate, and concentrated. The residue obtained was purified with silica gel preparative plates using 2% acetone/dichloromethane to give **17** as a mixture of *cis*-diols (47:53). Yield, 5.5 mg (43%). UV−vis [THF, $\lambda_{max}$, nm, ($\varepsilon$)]: 403.1(7.68 × $10^4$), 425.0 (9.10 × $10^4$), 507.0 (1.17 × $10^4$), 539.0 (2.72 × $10^3$), 725.00 (8.70 × $10^4$). $^1$H NMR (400 MHz, $CDCl_3$ $\delta$): 10.30 (s, 1H, *meso*-H), 9.44 (s, 1H, *meso*-H), 8.88 (s, 1H, *meso*-H), 4.48−4.51 (m, 1H, 8-H), 4.37 (s, 3H, $CO_2Me$), 4.24−4.28 (m, 1H, 7-H), 3.69 (s, 3H, $CO_2Me$), 3.68 (s, 3H, 12$CH_3$), 3.32 (s, 3H, 2-$CH_3$), 3.24 (s, 3H, $COCH_3$), 2.97−2.91 (m, 2H, 17$^1$-$CH_2$), 2.49−2.39 (m, 2H, 8-C$\underline{H}$H−$CH_3$ and 1H of 17$^2$-$CH_2$), 2.09−2.15 (m, 2H, 8-CH$\underline{H}$-$CH_3$ and 17$^2$-$CH_2$), 1.96 (d, 3H, 17-$CH_3$, $J$ = 7.2 Hz), 1.86 (d, 3H, 7-$CH_3$, $J$ = 7.2 Hz), 1.09−1.15 (m, 3H, 8-$CH_2\underline{CH_3}$), 1.50 (brs, 1H, NH), −1.6 (brs, 1H, NH). EIMS ($m/z$): 621.3 (M + Na).

**Ring-D Reduced Methyl Pheophorbide-a (24).** Methyl bacteriopheophorbide **12** (20 mg, 0.032 mmol) was dissolved in dichloromethane (5 mL) under Ar atm. To this mixture, a solution of DDQ (5.9 mg, 0.026 mmol) in dry $CH_2Cl_2$ was added slowly. The resulting mixture was stirred at room temperature for 5 min, and the entire reaction mixture was washed with water three times. The organic layer was separated and dried over anhydrous $Na_2SO_4$, and solvent was removed under vacuum. The residue obtained was purified with preparative plates using 3% acetone/DCM affording 17 mg of the methyl pheophorbide-a. Yield, 17.0 mg (85%). UV−vis [$CH_2Cl_2$, $\lambda_{max}$, nm, ($\varepsilon$)]: 691 (3.45 × $10^4$). $^1$H NMR $\delta$ (in $CDCl_3$): 9.95 (s, 1H, 5-H), 9.61 (s, 1H, 10-H), 8.77 (s, 1H, 20-H), 6.31 (s, 1H, 13$^2$-H), 4.53 (m, 1H for 18-H), 4.25 (m, 1H for 17-H), 3.89 (s, 3H, 12-$CH_3$), 3.72 (s, 3H, 2-$CH_3$), 3.63 (s, 3H, 13$^2$-$COOCH_3$), 3.57 (s, 3H, 17-$CH_2CH_2COO\underline{CH_3}$), 3.27 (s, 6H, 7-$CH_3$ and 3-$COCH_3$), 2.62 (m, 2H, 17-$C\underline{H_2}CH_2COOCH_3$), 2.28 (m, 4H, 2H of 17-$CH_2C\underline{H_2}COOCH_3$, 2H of 8-$C\underline{H_2}CH_3$), 1.83 (d, $J$ = 7.6 Hz, 3H, 18-$CH_3$), 1.70 (t, $J$ = 7.2 Hz, 3H, 8- $CH_2C\underline{H_3}$). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 199.2, 189.5, 173.2, 169.4, 162.0, 153.2, 151.9, 148.8, 145.0, 139.1, 137.6, 135.9, 135.6, 134.4, 130.4, 129.8, 105.7, 104.0, 100.7, 94.2, 64.8, 52.9, 51.6, 51.4, 49.8, 33.4, 31.0, 29.8, 23.2, 19.4, 17.3, 13.8, 13.4, 12.2, 11.4, 11.2. EIMS ($m/z$): 623 (M + 1). HRMS: calcd for $C_{36}H_{39}N_4O_6$ $[MH]^+$, 623.2870; found, 623.2864.

**Ring-B Reduced Methyl Pheophorbide-a (25).** Methyl bacteriopheophorbide **12** (20 mg, 0.032 mmol) was dissolved in dichloromethane (20 mL). To this mixture, a solution of $FeCl_3{\cdot}6H_2O$ (24 mg, 0.089 mmol) in nitromethane was added slowly. The resulting mixture was stirred at room temperature for 30 min, quenched by the addition of 5 mL of methanol, and washed with water three times. The organic layer was separated and dried over anhydrous $Na_2SO_4$, and solvent was removed under vacuum. The residue obtained was purified with silica gel preparative plates using 2% acetone/dichloromethane.Yield, 16.0 mg (80%). UV−vis [$CH_2Cl_2$, $\lambda_{max}$, nm, ($\varepsilon$)]: 682 (3.65 × $10^4$). $^1$H NMR $\delta$ (in $CDCl_3$): 9.51 (s, 1H, 5-H), 9.35


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(s, 1H, 10-H), 8.77 (s, 1H, 20-H), 6.67 (s, 1H, 13$^2$-H), 4.53 (m, 1H for 7-H), 4.30 (m, 1H for 8-H), 3.91 (m, 2H, 17-C$\underline{H}_2$CH$_2$COOCH$_3$), 3.81 (s, 3H, 12-CH$_3$), 3.72 (m, 6H, 3H of 18-CH$_3$ and 3H of 2-CH$_3$), 3.60 (s, 3H, 13$^2$-COOCH$_3$), 3.29 (s, 3H, 17-CH$_2$CH$_2$COOC$\underline{H}_3$), 3.23 (s, 3H, 3-COCH$_3$), 2.90 (m, 2H of 8-C$\underline{H}_2$CH$_3$), 2.08 (m, 2H, 17-CH$_2$C$\underline{H}_2$COOCH$_3$), 1.88 (d, $J$ = 7.2 Hz, 3H, 18-CH$_3$), 1.15 (t, $J$ = 7.2 Hz, 3H, 8-CH$_2$C$\underline{H}_3$). $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 203.3, 189, 172.9, 169.7, 166.4, 159.2, 155.4, 141.3, 140.2, 138.4, 133.3, 132.2, 127.9, 114.6, 113.3, 114.6, 100.1, 96.9, 96.2, 96.1, 66.2, 55.8, 53.1, 51.7, 48.3, 35.6, 33.3, 30.1, 29.2, 23.3, 22.1, 13.8, 11.9, 11.4, 10.8, 10.7. EIMS ($m/z$): 623 (M + 1). HRMS: calcd for $C_{36}H_{39}N_4O_6$ [MH]$^+$, 623.2870; found, 623.2828.

**In Vitro Photosensitizing Efficacy.** The photosensitizing activity of the compounds was determined as described previously.[30] The tumor cell lines used are Colon26 (mouse colon tumor). The Colon26 tumor cells were grown in RPMI-1640 medium supplemented with 10% fetal bovine serum, L-glutamine, penicillin, and streptomycin. Tumor cells were maintained in an atmosphere of 5% $CO_2$, 95% air, and 100% humidity at 37 °C. For determining the PDT efficacy of the compounds, the cells were plated in 96-well plates at a cell density of 3000 cell/well in complete media. After 16 h of incubation at 37 °C, the photosensitizers were added at variable concentrations and incubated at 37 °C for 24 h in the dark. Prior to light treatment, the cells were replaced with drug-free complete media. Cells were then illuminated with light from an argon-pumped dye laser set at 725−741 nm, respectively, for each of the drugs as per their absorption wavelength in 17% bovine calf serum (BCS) measured before, at a dose rate of 1.6 mW/cm$^2$ for 0−2 J/cm$^2$. After PDT, the cells were incubated for a further 48 h at 37 °C in the dark. Following the 48 h incubation, 10 $\mu$L of 5.0 mg/mL solution of 3-[4,5-dimethylthiazol-2-yl]-2−5-diphenyltetrazoliumbromide (MTT) in PBS (Sigma, St. Louis, MO) was added to each well. After 4 h of incubation at 37 °C, the MTT and the media were removed, and 100 $\mu$L of DMSO was added to solubilize the formazan crystals. The 96-well plate was read on a microtiter plate reader (BioTek Instruments, Inc., ELx800 Absorbance Microplate Reader) at an absorbance of 570 nm. The results were plotted as a percent survival of the corresponding dark (drug no light) control for each compound tested. Each data point represents the mean from two separate experiments, with six replicate wells, and the error bars are the standard deviation.

## ■ ASSOCIATED CONTENT

### Supporting Information

$^1$H and $^{13}$C NMR spectra of compounds **10**, **11**, and **14**−**25** and 2D NMR spectra of compounds **11**, **17**, and **21**. This material is available free of charge via the Internet at http://pubs.acs.org.

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