HETEROCYCLES, Vol. 71, No. 9, 2007, pp. 1929 - 1949. © The Japan Institute of Heterocyclic Chemistry
Received, 12th April, 2007, Accepted, 6th June, 2007, Published online, 8th June, 2007. COM-07-11077

CONVERSION OF BACTERIOCHLOROPHYLL-A TO BACTERIOPURPURIN-18: A USEFUL SYNTHON FOR THE CONSTRUCTION OF BIOACTIVE AGENTS FOR PHOTODYNAMIC THERAPY (PDT)

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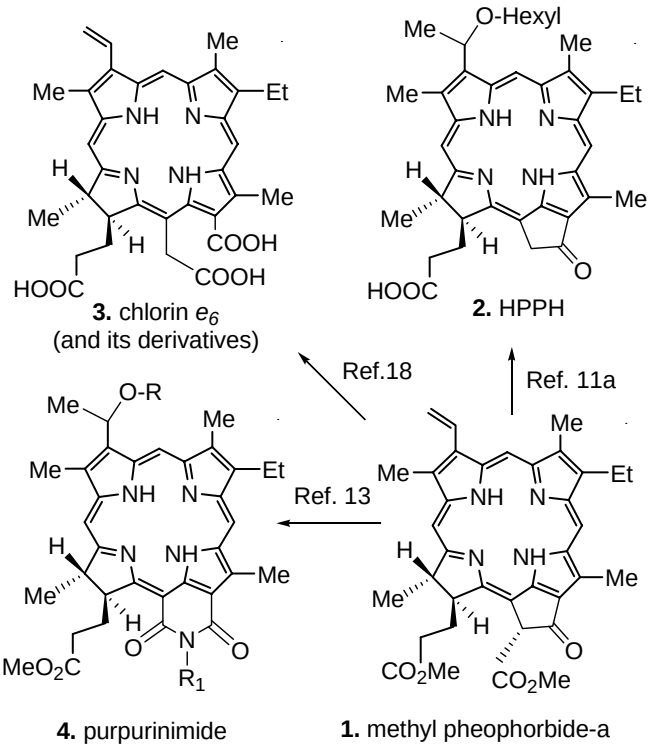
Abstract – Bacteriochlorophyll-a **5** present in *Rb. sphaeroides* was converted into bacteriopurpurin-18 methyl ester **10** by following three different approaches and was used as a substrate for the preparation of a series of stable bacteriochlorins with long wavelength absorptions ranging from 760 to 824 nm. Bacteriopurpurin p_6 **17**, obtained by the base hydrolysis of **10,** on reacting with L-aspartyl-di-*tert*-butyl ester in presence of EDCI and DMAP afforded the corresponding N-aspartyl-bacteriopurpurinimide **21** in high yield, possibly by the base-catalyzed intramolecular cyclization *via* the isoimide intermediate(s) **19** and **20**. A possible mechanism for the formation of **10** and bacteriochlorin 15-glyoxilic acid trimethyl ester **8** from **5** *via* hydroxylactone **11** is also discussed. Among the compounds synthesized, the bacteriochlorin **21** containing a fused cyclic imide ring system was found to be the most stable in various solvents at room temperature and exhibited the longest wavelength absorption at 824 nm in dichloromethane.

INTRODUCTION

Bacteriochlorophyll-a is the most abundant bacteriochlorin derivative in natural photosynthesis, and plays a significant role on the light-harvesting, energy-migrating and electron-transporting reactions at the initial stage of bacterial photosynthesis.[1] Bacteriochlorophyll-a has two reduced pyrrole rings diagonal to each other and the substituents are with *trans*-configuration. The 3-acetyl group in bacteriochlorophyll-a

strongly influences the position of Q_y absorption band in the electronic absorption spectrum. Due to their long wavelength absorption >750 nm and high singlet oxygen producing efficiency, the naturally occurring bacteriochlorophylls have also been evaluated for the use in photodynamic therapy (PDT).[2]

PDT is an FDA-approved minimally invasive medical treatment modality that utilizes light in the presence of oxygen to activate photosensitizing agents (photosensitizers) that are relatively more selective to neoplastic cells, resulting in cell death.[3-6] Among the types of compounds investigated for the use in PDT, porphyrins or porphyrin-types are most widely used agents due to their higher affinity to tumors and the ability to produce singlet oxygen (a key cytotoxic agent) after light exposure.[7] Efforts are underway in various laboratories to prepare long wavelength photosensitizers (> 660 nm), which may help in treating large and deeply seated tumors.[8] In general, two different approaches have been used for developing effective photosensitizers[9,10]: (i) to prepare the porphyrin, chlorin and bacteriochlorin skeleton in a multi-step process starting from pyrroles and then to modify their overall lipophilicity and (ii) to use chlorophyll-a and bacteriochlorophyll-*a* **5** as the substrates for further modifications.



Scheme 1: Some effective photosensitizers derived from methyl pheophorbide-a

In recent years, starting from methyl pheophorbide-a **1**, a series of photosensitizers have been synthesized. Some of these analogs, e.g. HPPH (Photochlor) **2**,[11] LS-11 (aspartic acid derivative of chlorin e_6 **3**)[12] and purpurinimide **4**[13] are at various stages of clinical trials. Inspired by the biological results *(both in vitro and in vivo)* obtained from HPPH and purpurinimides, we were interested to translate these structural parameters to the bacteriochlorin system for developing efficient photosensitizers with long wavelength absorption >750 nm and high singlet oxygen ($^1O_2$) producing ability.

Almost 20 years ago, Beems *et al.*[14] investigated the *in vitro* photosensitizing property of two water-soluble derivatives of bacteriochlorophylls. A few years later, Henderson, Dougherty and coworkers[15] were the first to investigate the utility of **5** in transplantable murine tumors and it was shown that the photodynamic effects were greatly influenced by its rapid degradation *in vivo*. Even at higher doses (5 & 10 μmol/kg) and at a shorter period (2 h post injection) of light treatment, limited tumor cure was observed. It was also noted that **5** rapidly demetallized *in vivo*, particularly in the liver and tumor.

Low efficiency may be a result of the rapid self-photodestruction of **5** compared to porphyrins as evidenced by their inability to inhibit this process *in vitro*, even in the presence of high concentrations of singlet oxygen traps (tryptophane or 1,3-diphenyl isobenzofuran). Therefore, our objective was to prepare more stable analogs of **5** and this manuscript describes the various synthetic routes that were used to achieve our goal.

RESULTS AND DISCUSSION

A. Preparation of bactertiopurpurin-18 methyl ester:

The introduction of electron withdrawing group(s) at the peripheral positions of the chlorin system generally diminishes its ability to photo-degrade. Among the chlorin analogs derived from methylpheophorbide-a, purpurin-18 (containing a fused six member anhydride ring system) was found to be most stable. Therefore, attempts were made to convert the **5** to bacteriopurpurin-18 methyl ester **10** by following three different approaches:

(a) In-situ conversion of bacteriochlorophyll-a to bacteriopurpurin methyl ester (Route 1):

In our previous studies with several chlorins we observed that introduction of a cyclic anhydride ring generally enhanced the stability of the compound towards oxidation. These results prompted us to investigate the effect of such a cyclic anhydride and naturally occurring bacteriochlorins. In our initial studies, **5** present in *Rb. sphaeroides,* was directly converted into **10** by optimizing the reactions conditions previously reported.[16] In brief, the n-propyl alcohol extract of *Rb. sphaeroides* was directly reacted with KOH/1-propanol. Air was continuously bubbled through the reaction mixture. The intermediate "unstable bacteriochlorin" was not isolated and was immediately treated with 1N HCl to produce mainly bacteriopurpurin carboxylic acid, which on reacting with diazomethane gave the corresponding methyl ester in 30-35% yield. This process however is very time consuming, the extraction and purification processes are tedious. The carotenoids and other impurities present in the reaction mixture produce emulsions and require a large amount of solvents, and is not suitable for a large scale synthesis. Therefore, we decided to first isolate methyl bacteriopheophorbide-a **7** from *Rb. sphaeroides* and then convert it into the desired analog.

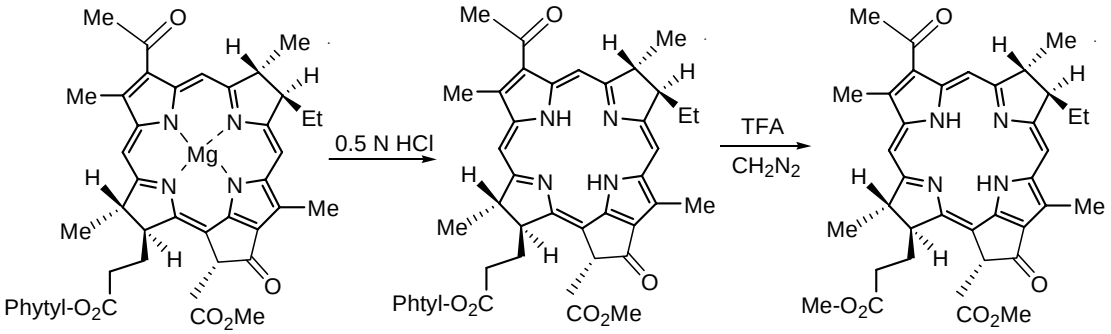
(b) Conversion of methyl bacteriopheophorbide-a to bacteriopurpurin methyl ester:

Compound **7** was isolated from *Rb. sphaerodes* biomass by suspending it in 1-propanol with constant nitrogen bubbling for 12 hrs. It was then filtered and treated with hydrochloric acid. The product was precipitated with n-hexane and treated with TFA to remove the phytyl ester. The crude carboxylic acid on reacting with diazomethane afforded the corresponding methyl ester and was purified by silica column chromatography. Compound **7** was then converted into **10** by following the foregoing procedure described

in approach (a) in 30% yield. Though there was not a significant difference in the overall yield of both the procedures, this method was less time consuming and easier to handle.

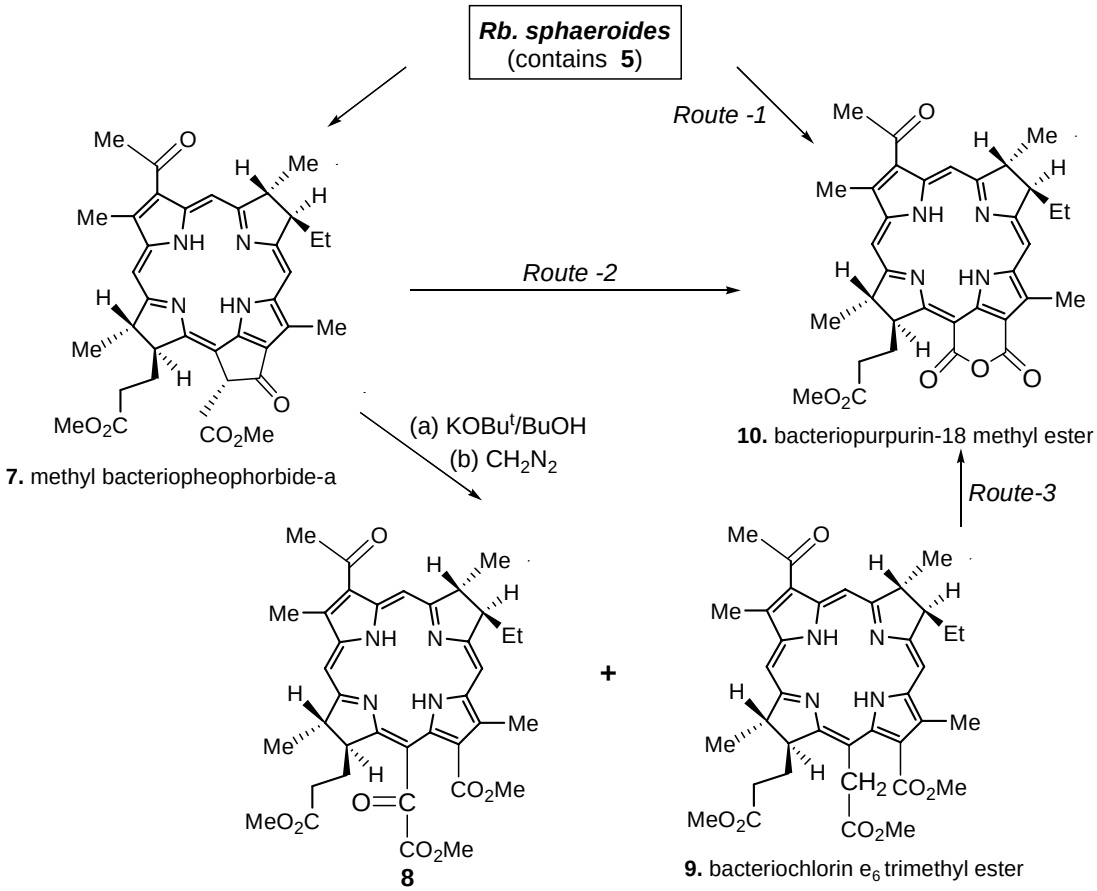
(c) Conversion of bacteriochlorin e_6 to bacteriopurpurin methyl ester:

In our recent approach to develop an industrial preparation of **2** we have shown[17] that commercially available chlorin e_6 **3**, under Dieckmann condensation[18,19] can be converted into the desired compound in excellent yield. However, if instead of maintaining an inert atmosphere, the air was bubbled through the reaction mixture, purpurin-18 containing a six-member anhydride ring system was isolated as major



5. bacteriochlorophyll-a **6.** bacteriopheophytin-a **7.** methyl bacteriopheophorbide-a

Scheme 2: Preparation of methyl bacteriopheophorbide-a from bacteriochlorophyll-a

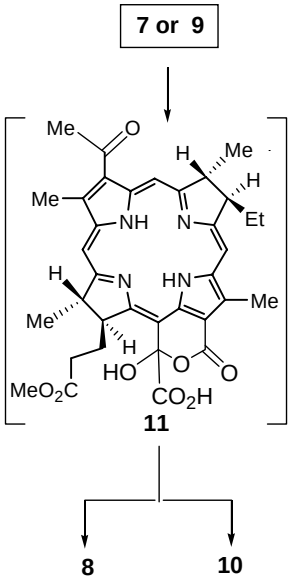


7. methyl bacteriopheophorbide-a **10.** bacteriopurpurin-18 methyl ester

8 **9.** bacteriochlorin e_6 trimethyl ester

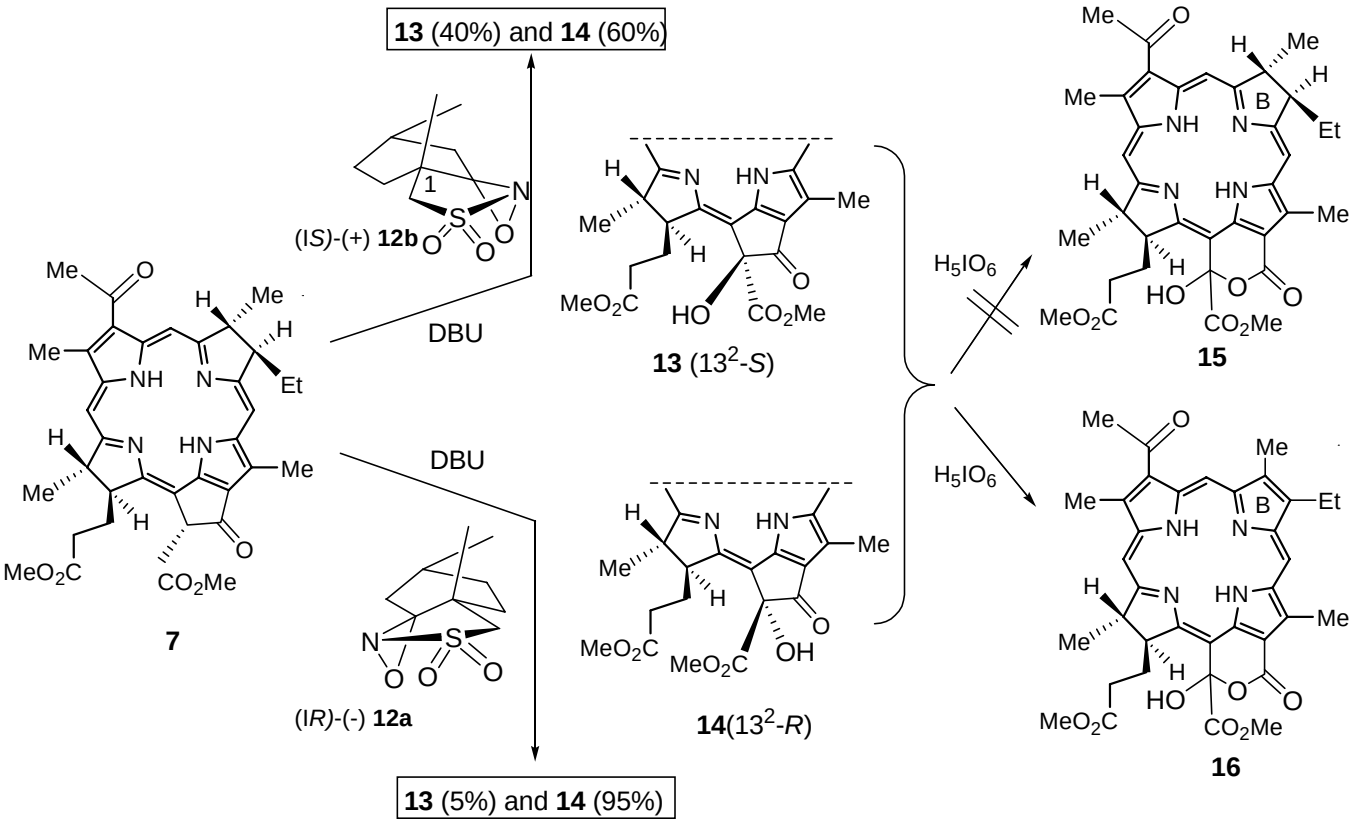
Scheme 3: Various synthetic routes for the conversion of methylbacteriochlorophyll-a to bacteriopurpurin 18 methyl ester

product. We noted that it would be worthwhile to extend this approach to the bacteriochlorin e_6 system. In our approach, **7** was converted into bacteriochlorin trimethyl ester **9** by following the methodology that has been successfully used for the preparation of **3**. In the bacteriopheophorbide system, this reaction gave us a mixture of the desired compound **9** and an unexpected 3-acetyl-bacteriochlorin-15-glyoxilic acid trimethyl ester **8**. The reaction was found to extremely sensitive to the reaction conditions used and an inert atmosphere was necessary for the formation of the desired bacteriochlorin **9**, which under modified Dieckmann condensation (for experimental details see the experimental section) gave **10** in 50% yield.



Scheme 4

On the basis of the studies performed in chlorophyll-a analogs, we envisaged that **7** or **9** was converted into **8** and **10** *via* the intermediacy of hydroxy lactonebacteriochlorin **11** (Scheme 4); In order to prove our hypothesis, we were interested in preparing the 13-hydroxybacteriochlorin **13** or **14**, which on oxidation could generate the desired intermediate **11**. It has been shown that **1**



Scheme 5: Hydroxy lactonechlorin from methyl bacteriopheophorbide-a

can be converted into methyl 13^2-hydroxypheophorbide-a on refluxing with zinc acetate and air[20]. However, this approach did not work in methyl bacteriopheophorbide *a.* and the dark red bacteriopheophorbide decomposed into a complex mixture of various chlorins. We then followed the synthetic strategy reported

by Ma and Dolphin[21] in chlorophyll-a based analogs. Reaction of methyl bacteriopheophorbide-a **7** with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) [a strong "non-nucleophilic" organic base for promoting the hydroxylation reaction], followed by oxidation with commercially available (-)-(*1R*)-(10-camphorsulfonyl)oxaziridine [(-) **12a**] at –25°C for 22 h gave a 55% yield of methyl 13^2-hydroxy bacteriopheophorbide-a **14** as a diasteromeric mixture with 95% 13^2 (*R*)-**14** and 5% 13^2(*S*)-**13** by NMR and reversed-phase HPLC analysis. Structure assignments for **13** (*S*) and **14**(*R*) were based on the anisotropic effect of the newly introduced 13^2-OH groups which caused downfield shifts in the *meso*- region proton ^{1}H NMR of 13^2(*S*)-**13** compared to the corresponding *R*-isomer **14**. The retention time for 13^2(*S*)-**13** and 13^2(*R*)-**14** in an analytical C-18 reverse phase HPLC column [solvent system: 0.1% TFA in CH_3CN (70%) and 0.1% TFA in water (30%), flow rate, 1.0 mL/min)] were 19.6 and 20.3 minutes respectively. Reaction of **7** with (+)-(*1S*)-(10-camphorsulfonyl) oxaziridine [(+) **12b**] under similar reaction conditions afforded a 50% yield of the *R*- and *S*- mixture with 40% 13^2(*S*)-**13** and 60% 13^2(*R*)-**14** as determined by the NMR and HPLC analyses**.**

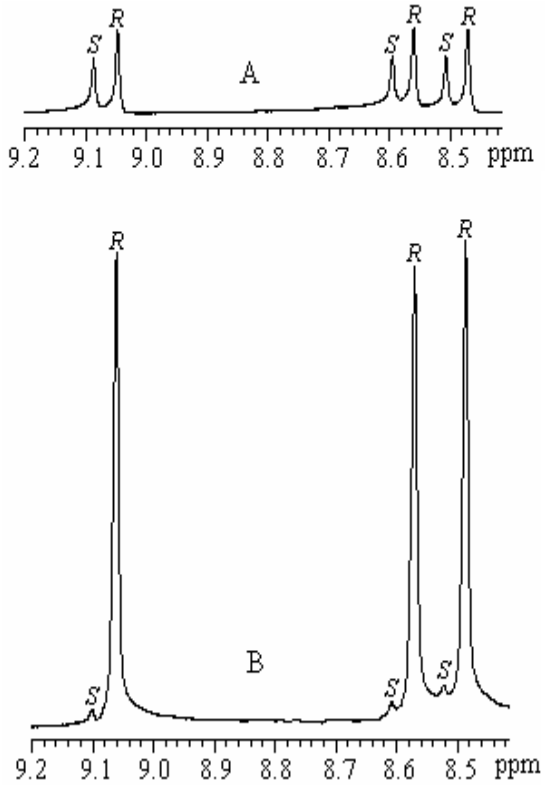


Figure 1: Partial NMR spectra (only the *meso* region is shown) of methyl 13^2-hydroxy bacteriopheophorbide-a. **A:** The diastereomeric mixture obtained by reacting **7** with (+)-(*1S*)-(10-camphorsulfonyl) oxaziridine[(+)**12b**]. The ratio of *R*- and *S*-isomers was 60 to 40. **B**: The diastereomeric mixture obtained by reacting **7** with (-)-(*1R*)-(10-camphorsulfonyl) oxaziridine [(-)**12a**]. The ratio of *R*- and *S*-isomers was 95 to 5.

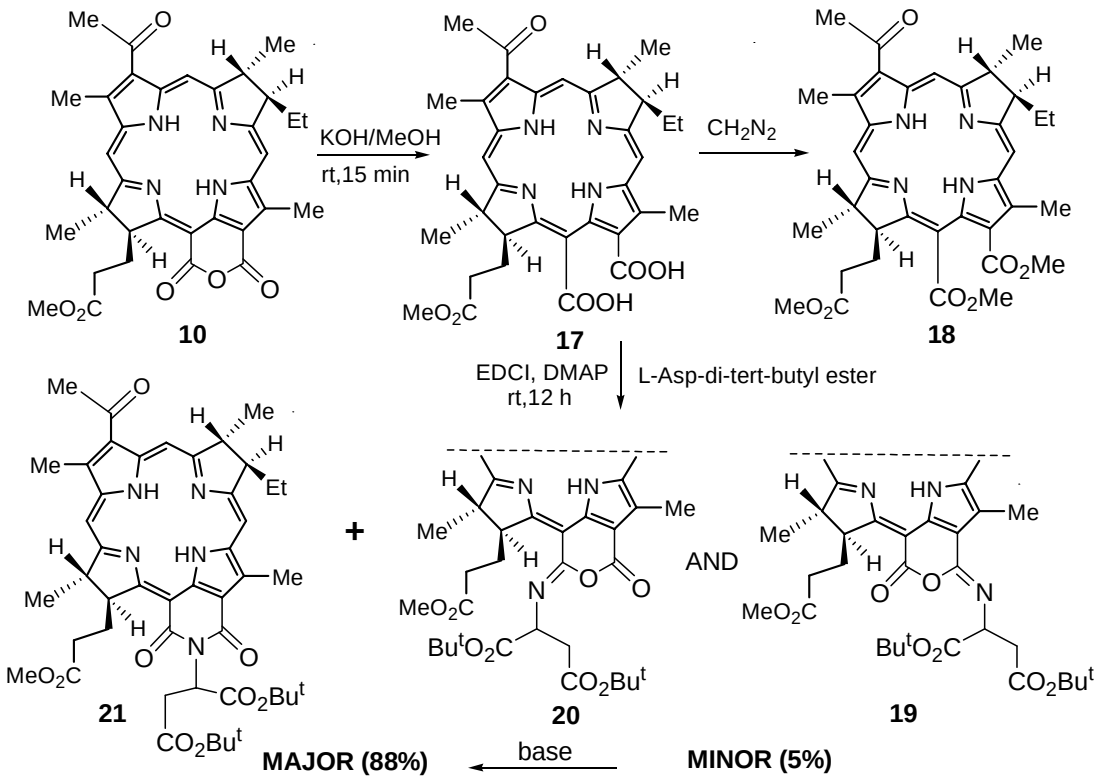
The partial proton NMR spectra (only the *meso*- region is shown) of the diastereomeric mixture obtained by chirally pure reagents are illustrated in Figure 1. The stereoselectivity during reaction of **7** with **12** or **12a** can be rationalized due to the effects of the 17-propionic group, which possibly hinders the bulky electrophile (+)**12b** from approaching the *re* face of the bacteriochlorin enolate.

Our next step was to convert the isomeric mixture **13** and **14** to the corresponding hydroxy bactonenacteriochlorin **11.** The periodate oxidation produced the hydroxylactone, but the resulting product

was found to be a chlorin **16** instead of expected bacteriochlorin **15** as evident by its electronic absorption spectra (689 nm). The NMR spectra further confirmed the proposed structure in which the ring B pyrrole unit of bacteriochlorin **15** was oxidized. The reaction product obtained after treating **16** under aq. acidic conditions (pH 2-3) gave a complex mixture, which on reacting with diazomethane gave purpurin-18 methyl ester as one of the reaction products (the other products could not be identified). These results suggest that the hydroxylactones **15** and **16** (as carboxylic acid analogs) could be the intermediate species formed during the conversion of methyl bacteriopheophorbide-a and methyl pheophorbide-a into the corresponding purpurin-18 analogs.

B. Further modification of Bacteriopurpurin-18

Bacteriopurpurin **10** exhibited the long wavelength absorption at 813 nm and showed significant *in vitro* photosensitizing efficacy in RIF tumor cells. However, it was found to be unstable *in vivo*, and produced bacteriochlorin p_6 **17** on cleaving the fused anhydride ring, causing a considerable blue shift (765 nm) in



Scheme 6: Conversion of bacteriopurpurin-18 to bacteriochlorin p_6, isoimide and imide

the electronic absorption spectrum (see Figure 3)[22] The *in vivo* structure of the metabolite was further confirmed by comparing the NMR data with the authentic sample obtained in a quantitative yield on base hydrlolysis of purpurin-18 methyl ester **10**. The diazomethane treatment of **17** gave the corresponding trimethyl ester analog **18**.

Certain amino acid analogs of porphyrin-based compounds, especially the aspartic acid derivative of chlorin e_6 have recently attracted great attention due to their remarkable ability to localize in more sensitive

sites of the tumor cells.[23] Therefore, in our quest to investigate the effect of the aspartic acid substituent in chlorin p_6 system, compound **17** was reacted with aspartic acid di-butyl ester in presence of EDCI and DMAP. To our surprise, instead of the expected aspartic derivative of bacteriochlorin p_6 (linked with an amide bond) as a sole product, an isomeric mixture of fused six member isomimides **19** and **20** (minor components) and the highly stable bacteriopurpurinimide **21** was obtained as a major product (yield: 88%). The isomides under base catalyzed conditions (KOH/MeOH) can be rearranged to the corresponding imide system in quantitative yield and the progress of the reaction can be monitored spectrophotometrically.

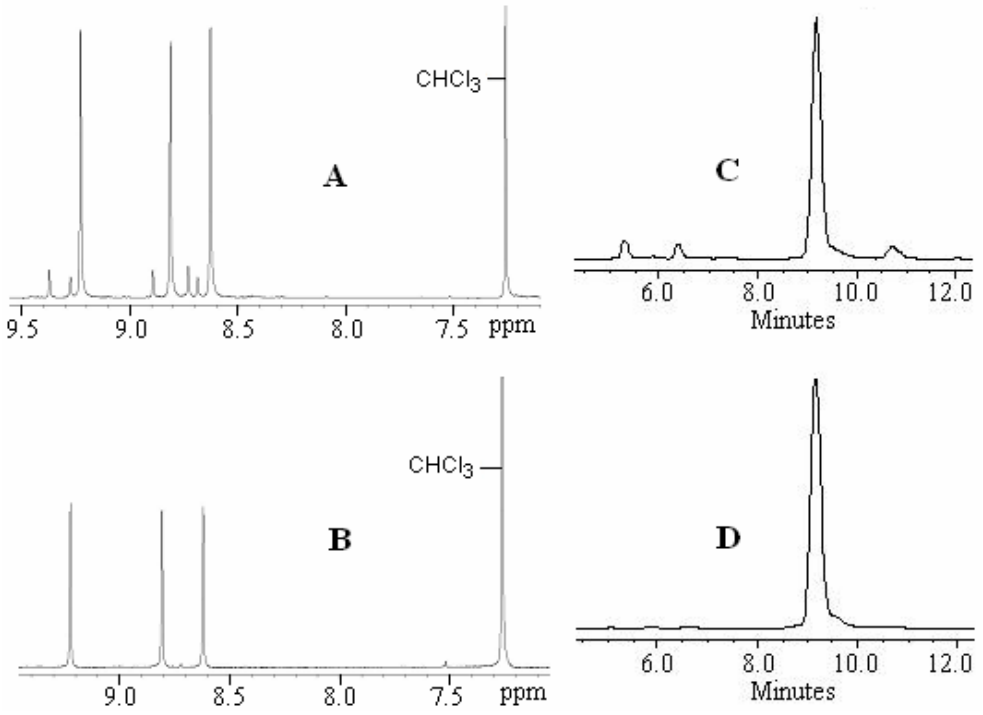
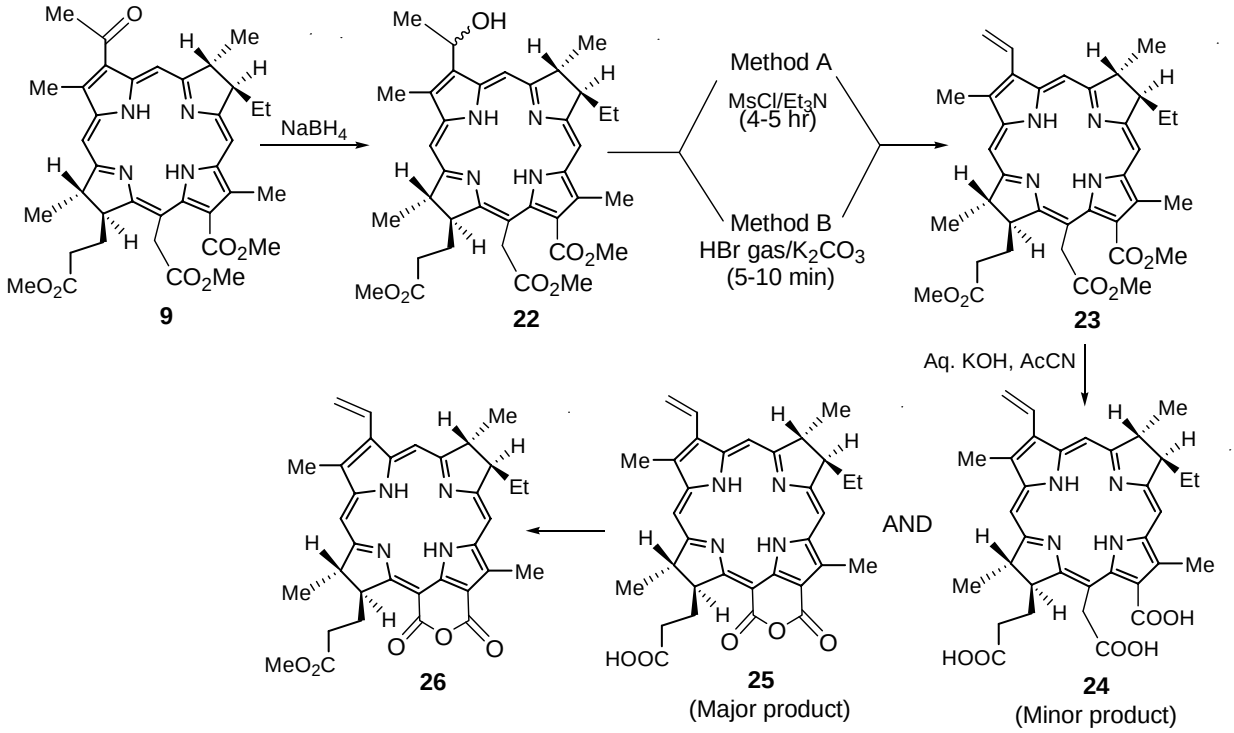


Figure 2: **A** and **B**: Partial NMR spectra (only the *meso*-region is shown) of crude reaction mixture obtained by reacting **17** with L-aspartyl-di-tert-butyl ester in the presence of EDCI and DMAP and the pure imide analog **21** and the **C** and **D** are the HPLC profiles (C-18 column, eluting solvent 90% methanol in water) of the crude and pure isomide **21** respectively (for details see the text).

The partial NMR spectra (only the *meso*- region is shown) and the HPLC profiles of the crude reaction mixture and the pure imide analog **21** are shown in Figure 2. The HPLC chromatogram of the reaction mixture showed mainly 4 peaks. The main component with retention time (rt) 9.18 min was identified as bacteriopurpurinimide **21** by NMR and mass spectrometry analyses. The eluents with rt 6.38 and 10.74 min had a long wavelength absorption at 804 nm, which corresponds to the isomeric mixture of isoimides **19** and **20**, whereas the compound that eluted at 5.3 min showed a long wavelength absorption at 760 nm, which could possibly relate to the non-cyclic bacteriochlorin-p_6 derivative. However, the minor components were not fully characterized.

Among the photosensitizers derived from chlorophyll-a, the aspartic acid derivative of chlorin e_6 (LS 11,[24] developed by Light Sciences, Seattle) is currently under phase I/II human clinical trials. Due to a close structural resemblance between chlorin e_6 (ring D is reduced) and bacteriochlorin e_6 (ring B and D are reduced), our interest was to prepare a similar analog by replacing the 3-acetyl group with the vinyl substituent and to prepare the corresponding aspartic acid derivative. Both aspartic acid analogs derived from chlorin e_6 and bacteriochlorin e_6 should have similar lipophilicity, however compared to chlorin e_6 (660 nm) the bacteriochlorin e_6 system provides an advantage due to its long wavelength absorption at 739 nm.

For synthesizing the bacteriochlorin with structural features similar to LS11, it was necessary to replace the 3-acetyl- functionality in **9** with a vinyl substituent. Therefore, bacteriochlorin **9** was reacted with sodium borohydride and the resulting 3-(1'-hydroxyethyl) derivative **22** as a mixture of diasteromers was obtained in quantitative yield. As shown in Scheme 7, two different approaches were used for the preparation of the bacteriochlorin **23**. Reaction of **22** with methane sulfonyl chloride and triethyl amine by following Tamiaki



Scheme 7: Bacteriochlorins with 3-vinyl substituents

reaction conditions[25] afforded the desired compound in 51.1 % whereas a brief treatment of the hydroxy derivative **22** with HBr gas in presence of anhydrous potassium carbonate afforded bacteriochlorin **23** in 68.7% yield.[26] The next step was to convert the ester groups to the corresponding carboxylic acids. Among the ester functionalities present in bacteriochlorin **23**, the methyl ester group directly attached to the pyrrole ring was difficult to hydrolyze and required strong reaction conditions. Due to the unstable

nature of bacteriochlorins under strong acid reaction conditions, bacteriochlorin **23** was dissolved in acetonitrile and reacted with aq. KOH at room temperature. The progress of reaction was monitored by HPLC. The product obtained after the usual work-up was found to be mainly 3-deacetyl-3-vinyl-bacteriopurpurin-18 **25** obtained by intramolecular cyclization via a probable intermediate species **11**. The structure of the corresponding methyl ester analog **26** obtained by diazomethane treatment of **25** was confirmed by NMR and mass spectrometry analyses. During the hydrolysis, the bacteriochlorin e_6 **24** (735 nm) was obtained as a minor product and the efforts are currently underway to optimize the reaction conditions for the preparation of this bacteriochlorin in a reasonable yield.

C. Absorption Characteristics of bacteriochlorophyll-a Analogs:

The bacteriochlorins derived from **5** exhibited the long wavelength absorption >750 nm. The absorption spectra of the selected bacteriochlorins in dichloromethane are shown in Figure 3. As can be seen, bacteriopurpurinimide **21** containing a fused imide ring system showed the longest wavelength absorption at 824 nm. Bacteriopurpurin **18** with an anhydride ring system also produced a similar spectrum with a small blue shift, whereas in case of bacteriochlorin p_6 (**18**) and e_6 (**9**), the long wavelength absorptions were observed at 768 and 755 nm respectively. A difference in the absorption between a series of bacteriochlorins clearly indicates that the presence of the electron-withdrawing substituents at the peripheral position(s) makes a significant impact in the absorption characteristics, especially on the long wavelength absorption.

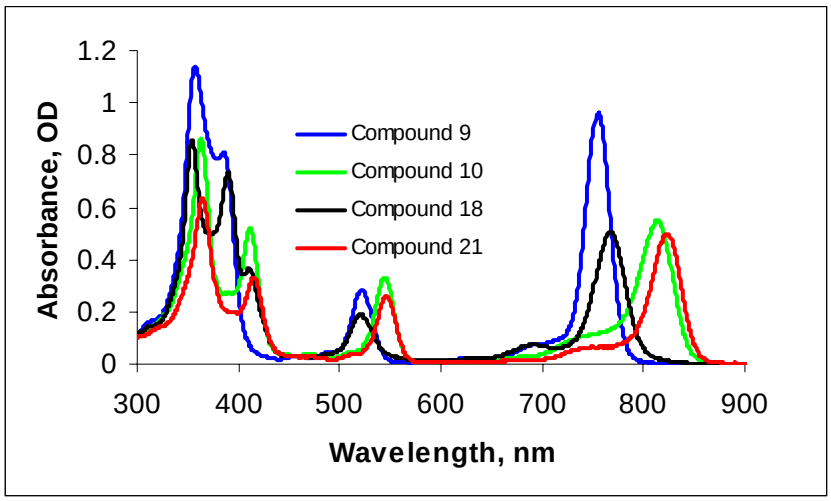


Figure 3: Electronic absorption spectra of selected bacteriochlorins in dichloromethane at equimolar concentrations (10 μM).

CONCLUSION

Most of the naturally occurring bacteriochlorins tested so far in our laboratory for *in vivo* photosensitizing

activity were quite unstable with regards to photooxidation, and thus the development of methods that efficiently construct stable bacteriochlorins has been a primary target in our group. In this manuscript we present an efficient method for the preparation of bacteriopurpurin-18 methyl ester, which can be converted into a series of bacteriochlorins with long-wavelength absorptions ranging from 750 to 824 nm. The long wavelength absorption of these photosensitizers could make PDT more efficient and practical because of increased tissue penetration and availability of less expensive diode lasers in this region. Further work on fine-tuning the molecule(s) with required overall lipophilicity for optimizing the *in vivo* efficacy are currently in progress and the biological results obtained from these studies will be published elsewhere.

EXPERIMENTAL

All reactions were carried out in flame-dried glassware under an atmosphere of nitrogen with magnetic stirring. Thin-layer chromatography (TLC) was done on Analtech precoated silica gel GF PE sheets (Cat. 159017, layer thickness 0.25 mm) and aluminum oxide NF PE sheets (Cat. 101016, layer thickness 0.2 mm). Column chromatography was performed either over Silica Gel 60 (70-230 mesh) or neutral Alumina (Brockmann grade III, 50 mesh). In some cases preparative TLC plates were also used for the purification (ANALTECH precoated silica gel GF glass plate, Cat. 02013, layer thickness 1.0 mm). Solvents were purified as follows: trace amounts of water and oxygen from THF were removed by refluxing over sodium under an inert atmosphere. Dichloromethane (CH_2Cl_2) was dried over P_2O_5. Anhydrous DMF, triethylamine (Et_3N), pyridine and other common chromatographic solvents were obtained from commercial suppliers (J.T. Baker®, EMD® and Aldrich®) and used without further purification. NMR spectra were recorded on a Bruker DRX 400 MHz spectrometer. All chemical shifts are reported in parts per million (δ). ^{1}H NMR (400 MHz) spectra were recorded at room temperature (rt) 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 Brucker Esquire ion-trap mass spectrometer equipped with a pneumatically assisted electrospray ionization source, operating in positive mode. The high-resolution mass spectrometry analyses were performed at the Mass Spectrometry Facility, Michigan State University. UV-visible spectrums were recorded on Varian Cary 50 Bio UV-visible spectrophotometer using CH_2Cl_2 as solvent. All photophysical experiments were carried out using spectroscopic grade solvents.

Methyl bacteriopheophorbide-a 7:

Rhodobacte sphaeroides (containing bacteriochlorophyll *a* **5**) biomass (200 mL, ~500 gram) was suspended in 1-propanol (1.5 L) and stirred at rt in the dark with constant nitrogen bubbling for 12h. The blue-green extract was filtered and aqueous 0.5 N HCl (200 mL) was added to the filtrate. After stirring for 2 to 4 min, the solution turned reddish. The reaction mixture was then diluted with aqueous 5% NaCl (1.5 L) and extracted with CH_2Cl_2. The combined extracts were washed with water, dried and

rotavaporated. The residue was precipitated from hexanes to give crude bacteriopheophytin *a* **6** (600 mg) with purity sufficient to proceed to the next step. Compound **6** was dissolved in aqueous 80% TFA (100 mL) and stirred in the dark at 0°C for 2h. The solution was then diluted with ice/water (600 mL) and extracted with CH_2Cl_2. The combined organic extracts were washed with water, treated with diazomethane and evaporated to dryness. The crude residue was chromatographed on silica (CH_2Cl_2 in acetone, gradient 3% to 7%). The major band was collected. Evaporation of the solvent gave the title compound (340 mg), mp 222-224 °C. UV-vis λ_{max} nm (ε, x10^4) (in ethyl ether) 358 (11.8), 385 (6.76), 525 (2.89), 680 (1.22), 749 (6.75). (in CH_2Cl_2) 362 (10.8), 389 (5.81), 530 (2.84), 683 (1.11), 754 (6.27). ^{1}H NMR δ (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 $COOC\underline{H}_3$), 3.16 (s, 3H, 3-$COCH_3$), 2.52 (m, 2H, 17-$C\underline{H}_2CH_2$ $COOCH_3$), 2.34 (m, 2H, 17-$CH_2C\underline{H}_2$ $COOCH_3$), 2.25 (m, 2H, 8-$C\underline{H}_2CH_3$), 1.80 (d, J= 7.4Hz, 3H, 7-CH_3), 1.73 (d, J= 7.9Hz, 3H, 18-CH_3), 1.12 (t, J= 7.2Hz, 3H, 8- $CH_2C\underline{H}_3$), 0.47 (s, 1H, NH), -0.95 (s, 1H, NH); HRMS: $C_{36}H_{40}N_4O_6$, Calcd $[MH]^+$ 625.3026. Obsd. 625.3043.

Bacteriopurpurin-18 methyl ester 10:

Route 1. Direct method:

In a 5 lit conical flask were added *Rh. sphaeroides* (500 g, ca. 20% dry weight), 1-propanol (1.5 L) and vigorously stirred at rt for 12 h under constant nitrogen bubbling. The deep blue-green colored extract was filtered on a paper filter, and the residue was washed with n-propanol (2 X 250 mL). Combined filtrates were taken in a 5 L conical flask, KOH (20.0 g dissolved in 200 mL 1-propanol) was added to it. Air was bubbled into the solution for 4 hr with intensive stirring at room temperature. The reaction mixture was then acidified with 5% sulfuric acid to pH 2-3 and was extracted with a CH_2Cl_2/THF (3:1) mixture (3 X 500 mL). Organic layers were separated and the combined extract was kept in dark for 74 h. UV-vis of the solution was shifted from 761 nm to 815 nm. Extract was then washed with water, dried over sodium sulfate and concentrated using high vacuo. Precipitation of residue with dichloromethane/hexane mix gave crude Bacteriopurpurin-18 (1.5 g), which was further treated with diazomethane and purified on silica column using 1-3 % MeOH/CH_2Cl_2 gradient to obtained bacteriopurpurine-18 methyl ester **10**. Yield: 0.5-0.6 gm.

Route 2. From methyl bacteriopheophorbide-a:

Bacteriopheophorbide-*a* methyl ester (100.0 mg, 0.16 mmol) was dissolved in Et_2O (200 mL), KOH (1.0 g, 17.8 mmol) in propanol (50 mL) and pyridine (10 mL). Air was bubbled into the solution for 0.5 h with vigorous stirring at rt. The solution was diluted with water (300 mL) and ether layer was removed. Water layer was treated with 1.0 N HCl and the pH was adjusted to 4.0 and extracted with dichloromethane/THF (3:1, 3 X 100 mL). Combined extracts were washed with water (2 X 300 mL) and treated with diazomethane. Reaction mixture was evaporated under vacuum and chromatographed on a silica column

using 1-3 % MeOH/CH_2Cl_2 gradient as eluent. Yield: 27.0 mg, (29.0 %).

Route 3. From Bacteriochlorin e_6:

Bacteriopurpurin e_6 trimethyl ester (46.0 mg, 0.07 mmol) was dissolved in dry pyridine (10.0 mL) and degassed four times with N_2. The reaction mixture was heated to 50^0C and a solution of potassium *tert*-butoxide in *t*-BuOH (1.0 M, 1.0 mL) was added drop wise to it. Reaction mixture was stirred at same temperature for 15 min, cooled to rt and air was bubbled for 2 h. Reaction mixture was then poured in to water and acidified with 10% H_2SO_4 to pH 2-3 and extracted with 100 mL of CH_2Cl_2/THF mix (3:1). 10 % H_2SO_4 (0.5 mL) was added to extract and refluxed for 2 h. UV-vis changed for 765 nm to 810 nm. Reaction mix was then washed with water (2 X 100 mL), organic layer separated, dried over sodium sulfate and concentrated. The crude product was dissolved in dichloromethane (20 mL) and treated with diazomethane, reaction mixture was concentrated after 10 min and the crude product thus obtained was chromatographed over silica using 1-3 % MeOH/CH_2Cl_2 gradient as eluent to afford Bacteriopurpurin-18 methyl ester. Yield: 21.0 mg (50.0 %).

Product **10** was recrystallized from CH_2Cl_2-hexane to give a title compound as fine purple crystals Mp 272 ^{0}C. UV-vis λ_{max} (in CH_2Cl_2): 364 nm (ε 8.91×10^4), 412 nm (ε 5.36×10^4), 545 nm (ε 3.4×10^4), 815 (ε 5.53×10^4). ^{1}HNMR (400 MHz, $CDCl_3$): δ 9.21 (s, 1H, meso-H), 8.80 (s, 1H, meso-H), 8.62 (s, 1H, meso-H), 5.13 (m, 1H, 17-H), 4.31 (m, 2H, 8-H & 18-H), 4.10 (m, 1H, 7-H), 3.66 (s, 3H, ring-CH_3), 3.60 (s, 3H, CO_2Me), 3.54 (s, 3H, ring-CH_3), 3.17 (s, 3H, $COCH_3$), 2.71 (m, 1H, 17^2-CH_2), 2.44 (m, 2H, 8-$\underline{CH_2}CH_3$), 2.36 (m, 1H, 17^2-CH_2), 2.09 (m, 1H, 17^1-CH_2), 1.96 (m, 1H, 17^1-CH_2), 1.82 (d, 3H, 7-CH_3, J = 7.6 Hz), 1.71 (d, 3H, 18-CH_3, J = 7.6 Hz), 1.11 (t, 3H, 8-$CH_2\underline{CH_3}$, J = 7.2 Hz), -0.29 (brs, 1H, NH), -0.66 (brs, 1H, NH). EIMS (m/z): 597.8(M+1). HRMS: Calcd for $C_{34}H_{36}N_4O_6$: 596.2635; Found: 596.2615.

3-Acetyl-bacteriochlorin 15-glyoxilic acid trimethyl ester* 8 and *3-acetyl-bacteriochlorin e_6 trimethyl ester 9:

Methyl bacteriopheophorbide-a **7** (100 mg, 016 mmol) was taken in a flame dried flask (100 mL) and dry THF (30 mL) added. The reaction mixture was stirred and degassed five times with N_2. 0.3 mL of NaOMe (25 % in MeOH) was dissolved in 10 mL of dry THF and added slowly via syringe to reaction mixture under vigorous stirring. The reaction mixture was degassed again after this addition and stirred at rt for 3 h. Reaction mixture was quenched with 5% acetic acid-H_2O and extracted with CH_2Cl_2 (100 mL). Organic layer separated, washed with brine, dried over sodium sulfate and concentrated to dryness. Trace of acetic acid was removed under high vacuum. The crude was re-dissolved in dichloromethane and treated with diazomethane. Reaction mixture was stirred for 10 min and then excess of diazomethane was removed by bubbling N_2. Reaction mixture concentrated and chromatographed over silica gel using 1-3% MeOH/CH_2Cl_2 gradient as eluent to obtained fast moving band as product.

***3-Acetyl-bacteriochlorin 15-glyoxilic acid trimethyl ester* 8:** Slow moving brown-red band on silica. Yield: 12.0 mg (11.0 %), mp > 260°C (decomp.); UV-vis λ_{max} (in CH_2Cl_2): 782 nm (ε 5.19 x 10^4), 748 (10.4 x 10^4), 543 (3.12 x 10^4), 410 (5.27 x 10^4) and 363 (7.61 x 10^4);. ^{1}HNMR (400 MHz, $CDCl_3$): δ 9.14 (s, 1H, meso-H), 8.68 (s, 1H, V), 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-$\underline{CH_2}CH_3$ & 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-$CH_2\underline{CH_3}$, J = 7.6 Hz), -0.45 (brs, 1H, NH), -0.53 (brs, 1H, NH). EIMS (*m/z*) 671.3 (M+1), HRMS: Calcd. For $C_{37}H_{42}N_4O_8$: 670.3002. Found: 670.3030.

3-Acetyl-bacteriochlorin e_6 trimethyl ester 9 Fast moving brown-red band on silica.Yield: 30.0 mg (29.0 %), UV-vis λ_{max} (CH_2Cl_2), 755 nm (ε 9.6 x 10^4), 523 nm (ε2.8 x 10^4), 386 nm (ε7.9 x 10^4), and 358 nm (ε11.2 x 10^4). ^{1}HNMR (400 MHz, $CDCl_3$): δ 9.29 (s, 1H, meso-H), 8.69 (s, 1H, meso-H), 8.63 (s, 1H, meso-H), 5.26 (d, 1H, 15^1-CH_2, J = 18.8 Hz), 5.16 (d, 1H, 15^1CH_2, J = 18.8 Hz), 4.34 (m, 1H, 17-H), 4.26 (m, 1H, 8-H), 4.22 (s, 3H, CO_2Me), 4.17 (m, 2H, 18-H & 7-H), 3.76 (s, 3H, CO_2Me), 3.65 (s, 3H, CO_2Me), 3.61 (s, 3H, 12-CH_3), 3.36 (s, 3H, 2-CH_3), 3.20 (s, 3H, $COCH_3$), 2.58 (m, 1H, 17^2-CH_2), 2.36 (m, 1H, 17^2-CH_2), 2.27-2.23 (m, 2H, 8-$\underline{CH_2}CH_3$), 2.07 (m, 1H, 17^1-CH_2), 1.88 (d, 3H, 7-CH_3, J = 7.6 Hz), 1.73 (m, 1H, 17^1-CH_2), 1.69 (d, 3H, 18-CH_3, J = 7.2 Hz), 1.10 (t, 3H, 8-$CH_2\underline{CH_3}$, J = 7.6 Hz), -1.06 (brs, 1H, NH), -1.16 (brs, 1H, NH). EIMS (*m/z*): 657 (M+Na), HRMS: Calcd. For $C_{37}H_{44}N_4O_7$: 656.3210. Found: 656.3214.

Methyl 13^2-Hydroxy bacteriopheophorbide-a 13 and 14:

A cold (-25 °C) solution of methyl bacteriopheophorbide-a **7** (90 mg, 0.14 mmol) in dry CH_2Cl_2 (15 mL) was blanketed with argon and stirred vigorously while DBU (0.08mL) was injected dropwise via a syringe. After 15 min at this temperature, a solution of (+) or (-)-(10-camphorsulfonyl)oxaziridine **12a** or **12b** (90 mg, 0.40 mmol) in cold dry CH_2Cl_2 (3 mL)was transferred into the reaction vessel via a cannula. This mixture was stirred at -25 °C for 12 h, and the reaction was quenched with saturated aqueous NH_4Cl. The aqueous phase was extracted with dichloromethane (2 x 100 mL), and the combined organic phases were dried over sodium sulfate, filtered, and evaporated in vacuum. The residue was purified by chromatography on silica, eluting with 4% MeOH/CH_2Cl_2. The product was crystallized from CH_2Cl_2/hexane to give violet-black crystals (44 mg, 50% yield), mp 250-252°C. UV-vis λ_{max} nm (ε, x10^4) (in CH_2Cl_2) 361 (7.9), 389 (4.43), 527 (2.11), 683 (0.90), 754 (4.66). ^{1}H NMR δ (in $CDCl_3$): For (13^2)-*R*-isomer: 9.05 (s, 1H, 5-H), 8.56 (s, 1H, 10-H), 8.47 (s, 1H, 20-H), 5.23 (s, 1H, 13^2-OH), 4.47 (m, 1H, 17-H), 4.31 (m, 2H, 1H for 7-H, 1H for 8-H), 4.06 (m, 1H, 18-H), 3.67 (s, 3H, 12-CH_3), 3.58 (s, 3H, 2-CH_3), 3.51 (s, 3H, 13^2-$COOCH_3$), 3.48 (s, 3H, 17-CH_2CH_2 $COO\underline{CH_3}$), 3.16 (s, 3H, 3-$COCH_3$), 2.42 (m, 2H, 17-$C\underline{H_2}CH_2$ $COOCH_3$), 2.08 (m, 4H, 2H for17-$CH_2C\underline{H_2}COOCH_3$, 2H for 8-$C\underline{H_2}CH_3$), 1.83 (d, J=

7.4Hz, 3H, 7-CH_3), 1.62 (d, J= 7.9Hz, 3H, 18-CH_3), 1.13 (t, J= 7.2Hz, 3H, 8- $CH_2C\underline{H}_3$), 0.35 (s, 1H, NH), -1.07 (s, 1H, NH); For (13^2)-*S*-isomer: 9.08 (s, 1H, 5-H), 8.59 (s, 1H, 10-H), 8.50 (s, 1H, 20-H), 5.30 (s, 1H, 13^2-OH), 4.47 (m, 1H, 17-H), 4.31 (m, 2H, 1H for 7-H, 1H for 8-H), 3.98 (m, 1H, 18-H), 3.67 (s, 3H, 12-CH_3), 3.62 (s, 3H, 2-CH_3), 3.51 (s, 3H, 13^2-$COOCH_3$), 3.48 (s, 3H, 17-CH_2CH_2 $COOC\underline{H}_3$), 3.16 (s, 3H, 3-$COCH_3$), 2.52 (m, 2H, 17-$C\underline{H}_2CH_2$ $COOCH_3$), 2.08 (m, 4H, 2H for17-$CH_2C\underline{H}_2COOCH_3$, 2H for 8-$C\underline{H}_2CH_3$), 1.83 (d, J= 7.4Hz, 3H, 7-CH_3), 1.53 (d, J= 7.9Hz, 3H, 18-CH_3), 1.13 (t, J= 7.2Hz, 3H, 8-$CH_2C\underline{H}_3$), 0.24 (s, 1H, NH), -1.19 (s, 1H, NH); MS: $C_{36}H_{40}N_4O_7$, calculated: 640.3. Found: 663.1 (M+Na). HRMS: Calcd. 640.2897. Found: 640.2900.

15^1-Hydroxypurpurin lactone 16:

A solution of the foregoing 13^2-hydroxy methyl bacteriopheophorbide-a mixture **13** and **14** (45mg, 0.07 mmol) in dioxane (20 mL) was stirred with periodic acid dehydrate (20 mg, 0.09 mmol) at rt for 20 h before the mixture was put into water and extracted with CH_2Cl_2 (2 x 40 mL). The combined organic phases were dried over sodium sulfate, filtered, and evaporated in vacuum. The residue was purified by chromatography on silica, eluting with 4% MeOH/CH_2Cl_2. The product was crystallized from CH_2Cl_2/hexane to give violet-black crystals (7 mg, 15% yield). Mp 230-232 ^oC. UV-vis λ_{max} nm (ε, x10^4) (in CH_2Cl_2) 406 (8.31), 504 (0.78), 539 (0.74), 633 (0.49), 689 (3.55). ^1H NMR δ (in $CDCl_3$): 10.13 (s, 1H, 5-H), 9.80 (s, 1H, 10-H), 8.89 (s, 1H, 20-H), 4.49 (m, 2H, 17-H and 18-H), 3.92 (m, 2H, 8-$C\underline{H}_2CH_3$), 3.77 (s, 6H, 2-CH_3 and 12-CH_3), 3.68 (s, 3H, 17-CH_2CH_2 $COOC\underline{H}_3$), 3.53 (s, 3H, 15^1-$COOCH_3$), 3.28 (s, 6H, 3-$COCH_3$ and 7-CH_3), 2.48 (m, 2H, 17-$C\underline{H}_2CH_2$ $COOCH_3$), 2.22 (m, 2H, for17-$CH_2C\underline{H}_2COOCH_3$), 1.73 (m, 3H, 18-$CH_3$), 1.62 (m, 8-$CH_2C\underline{H}_3$), 0.084 (s, 1H, NH), -1.42 (s, 1H, NH); MS: $C_{36}H_{38}N_4O_8$, calculated: 654.3. Found: 677.1 (M+Na). HRMS: Calcd 655.2768 (M + H). Found: 655.2772.

***Bacteriochlorin p6 di-carboxylic acid 17*:**

Two pellets of KOH were dissolved in MeOH (30 mL) and added to a solution of bacteriopurpurin-18 methyl ester (50.0 mg, 0.083 mmol) in THF (5.0 mL). Resultant mixture was stirred for 15 min under N_2 atm. UV-vis shift from 812 nm to 766 nm was indicative of completion of the reaction. Reaction mixture was neutralized with 2% acetic acid in water and extracted with CH_2Cl_2 (2 x 50 mL). Organic layers separated, combined, washed with water (50 mL), dried over sodium sulfate and concentrated to give crude **17**. Yield: 30.0 mg (58.2 %). UV-vis λmax (CH_2Cl_2): 354 nm (ε 7.72×10^4), 390 nm (ε 6.20×10^4), 521 nm (ε 1.90×10^4), 765 nm (ε 5.00×10^4). ^{1}HNMR (400 MHz, $CDCl_3$): δ 9.29 (s, 1H, meso-H), 8.75 (s, 1H, meso-H), 8.66 (s, 1H, meso-H), 5.11 (m, 1H, 17-H), 4.32 (m, 1H, 8-H), 4.17 (m, 2H, 18-H & 7-H), 3.61 (s, 3H, CO_2Me), 3.44 (s, 6H, 12-CH_3 & 2-CH_3), 3.19 (s, 3H, $COCH_3$), 2.40-2.35 (m, 3H, 17^2-CH_2 & 17^1-CH), 2.10 (m, 2H, 8-$C\underline{H}_2CH_3$), 1.96 (m, 1H, 17^1-CH), 1.86 (d, 3H, 7-CH_3, J = 7.2 Hz), 1.73 (d, 3H, 18-CH_3, J = 6.8 Hz), 1.09 (t, 3H, 8-$CH_2C\underline{H}_3$, J = 7.6 Hz), -0.95 (brs, 1H, NH), -1.10 (brs, 1H, NH). Mass: Calcd. for $C_{34}H_{38}N_4O_7$: 614/27. Found: EIMS (*m/z*), 637 (M+Na).

Bacteriochlorin p6 trimethyl ester 18:

Bacteriochlorin p6 di-acid **17** (10.0 mg, 0.061 mmol) was dissolved in CH_2Cl_2 (10 mL) and treated with diazomethane. The reaction mixture was stirred for 5 min and then concentrated to dryness. Crude thus obtained was purified on silica preparative plates using 2.5 % MeOH/CH_2Cl_2 mixture as mobile phase. Yield: 7.0 mg (67.0 %). mp > 260^0C (decomp.). UV-vis λmax (CH_2Cl_2): 354 nm (ε 7.69×10^4), 390 nm (ε 6.23×10^4), 522 nm (ε 2.01×10^4), 768nm (ε 5.03×10^4). ^{1}HNMR (400 MHz, $CDCl_3$): δ 9.29 (s, 1H, meso-H), 8.75 (s, 1H, meso-H), 8.66 (s, 1H, meso-H), 4.99 (m, 1H, 17-H), 4.32 (m, 1H, 8-H), 4.23 (m, 2H, 18-H & 7-H), 4.20 (s, 3H, CO_2Me), 4.15 (s, 3H, CO_2Me), 3.59 (s, 3H, 12-CH_3), 3.53 (s, 3H, CO_2Me), 3.47 (s, 3H, 2-CH_3), 3.19 (s, 3H, $COCH_3$), 2.40 (m, 2H, 17^2-CH_2), 2.25 (m, 1H, 17^1-CH_2), 2.12 (m, 3H, 8-$\underline{CH_2}CH_3$ & 17^1-CH_2), 1.85 (d, 3H, 7-CH_3, J = 7.2 Hz), 1.80 (d, 3H, 18-CH_3, J = 7.2 Hz), 1.10 (t, 3H, 8-$CH_2\underline{CH_3}$, J = 7.6 Hz), -1.09 (brs, 1H, NH), -1.10 (brs, 1H, NH). Anal. Calcd for $C_{36}H_{42}N_4O_7$: C, 67.27; H, 6.59; N, 8.72. Found: C, 67.08; H, 6.40; N, 8.62. HRMS: Calcd. for $C_{36}H_{42}N_4O_7$: 642.3053; Found: 642.3032

N-L-Aspartyl-(di-tert-butyl)-Bacteriopurpurinimide 21:

Bacteriochlorin p_6 diacid **17** (20.0 mg, 0.032 mmol) was dissolved in dry CH_2Cl_2 (20 mL). To this, were added L-Aspartic acid di-*t*-butyl ester.HCl (9.1 mg, 0.032 mmol), EDCI (9.36 mg, 0.048 mmol) and DMAP (6.0 mg, 0.048 mmol). Resultant mixture was stirred for 12 h, diluted with CH_2Cl_2 (50 ml) and extracted with brine (50 mL). Organic layer separated, dried over sodium sulfate and concentrated. Product was isolated as a mixture of imide and isoimide from silica column using 1-3 % MeOH/CH_2Cl_2 and re-purified by HPLC, which gave the title imide analog as the main product. Yield: 20.0 mg (74.6 %). UV-vis λ_{max} (CH_2Cl_2): 824 nm (ε 4.9×10^4), 758 nm (ε 1.4×10^4), 547 nm (ε 2.4×10^4), 416 nm (ε 3.7×10^4) and 365 nm (ε 7.8×10^4). ^{1}HNMR (400 MHz, $CDCl_3$): δ 9.22 (s, 1H, meso-H), 8.80 (s, 1H, meso-H), 8.62 (s, 1H, meso-H), 6.39 (t, 1H, Asp-α-H, J = 6.8 Hz), 5.23 (m, 1H, 17-H), 4.31-4.27 (m, 2H, 8-H & 18-H), 4.10 (m, 1H, 7-H), 3.68 (s, 3H, CO_2Me), 3.62 (s, 3H, ring-CH_3), 3.57 (dd, 1H, Asp-C$\underline{H}$H, J = 7.2 & 15.8 Hz), 3.54 (s, 3H, ring-CH_3), 3.17 (s, 3H, $COCH_3$), 3.05 (dd, 1H, Asp-CH$\underline{H}$, J = 7.2 & 16.0 Hz), 2.66 (m, 1H, 17^2-C$\underline{H}$H), 2.37 (m, 3H, 8-$\underline{CH_2}CH_3$, 17^2-CH$\underline{H}$), 2.09 (m, 1H, 17^1-CH_2), 1.94 (m, 1H, 17^1-CH_2), 1.81 (d, 3H, 7-CH_3, J = 7.2 Hz), 1.68 (d, 3H, 18-CH_3, J = 7.2 Hz), 1.45 (s, 9H, CO_2Bu^t), 1.40 (s, 9H, CO_2Bu^t), 1.11 (t, 3H, 8-$CH_2\underline{CH_3}$, J = 7.2 Hz), -0.46 (brs, 1H, NH), -0.71 (brs, 1H, NH). EIMS (*m/z*): 824 (M+H). HRMS: Calcd. for $C_{46}H_{57}N_5O_9$: 823.4156. Found: 823.4151.

3-(1-Hydroxyethyl)-bacteriochlorin e6 trimethyl ester 22:

Bacteriochlorin e_6 tri-methyl ester (50.0 mg, 0.076 mmol) was dissolved in 20 mL of MeOH/CH_2Cl_2 (1:3). Reaction mixture was degassed three times, added $NaBH_4$ (400.0 mg) to it and stirred vigorously at rt for 3-4 min. Reaction mixture turns green and shift in UV-vis from 753 nm to 726 nm indicates completion of reaction. Reaction mixture was quenched with water immediately and extracted with CH_2Cl_2 (100 mL),

organic layer separated, dried over sodium sulfate and concentrated. The crude product was chromatographed over silica gel using 1-4% acetone/CH_2Cl_2 gradient as eluent to obtained the title compound **22**. Yield: 30.0 mg (60.0%). UV-vis λ_{max} (relative peak area (%) in CH_2Cl_2), 728 (54), 664 (8), 505 (22), 378 (81) and 352 (100). Compound was isolated as isomeric mixture (1:4), ^{1}HNMR peaks are assigned for the major isomer: ^{1}HNMR (400 MHz, $CDCl_3$): δ 8.75 (splitted s, 1H, meso-H), 8.51 (s, 1H, meso-H), 8.36 (s, 1H, meso-H), 6.26 (m, 1H, $CH_3\underline{CH}OH$), 5.14 (d, 1H, 15^1-CH_2, J = 18.8Hz), 5.06 (d, 1H, 15^1-CH_2, J = 18.8 Hz), 4.23 (m, 1H, 17-H), 4.17 (s, 3H, CO_2Me), 4.16 (m, 2H, 8-H & 18-H), 4.09 (m, 1H, 7-H), 3.74 (s, 3H, CO_2Me), 3.62 (s, 3H, CO_2Me), 3.32 (s, 3H, 12-CH_3), 3.31 (s, 3H, 2-CH_3), 2.50 (m, 2H, 17^2-CH_2), 2.29 (m, 2H, 8-$\underline{CH_2}CH_3$), 2.14 (m, 1H, 17^1-CH_2), 2.98 (d, 3H, $\underline{CH_3}CHOH$, J = 6.8 Hz), 2.01 (m, 1H, 17^1-CH_2), 1.84 (d, 3H, 7-CH_3, J = 7.2 Hz), 1.66 (d, 3H, 18-CH_3, J = 7.2 Hz), 1.08 (t, 3H, 8-$CH_2\underline{CH_3}$, J = 8.0 Hz), -0.56 (brs, 1H, NH),-0.89 (brs, 1H, NH). Mass: Calcd for $C_{37}H_{46}N_4O_7$: 651.34EIMS (*m/z*):681 (M+Na).

***3-Vinyl-bacteriochlorin e6 trimethyl ester* 23:**

Method A: The hydroxyethyl bacteriochlorin **22** (30.0 mg, 0.045 mmol) was dissolved in dry CH_2Cl_2 (20 mL) and MsCl (10.4 mg, 0.091 mmol) in CH_2Cl_2 (5 mL) was added to reaction mixture slowly. Reaction mixture was stirred at rt for 30 min under N_2 atm. Et_3N (13.7 mg, 0.136 mmol) in CH_2Cl_2 (5 mL) was added to reaction mixture slowly and stirred for another 4 h. UV-vis shift from 726 nm to 736 nm indicated completion of reaction. Reaction mixture was poured onto dil HCl (2 %) and extracted with CH_2Cl_2 (100 mL). Organic layer separated, washed with sat. aqueous $NaHCO_3$ and brine subsequently, dried over sodium sulfate. The solvent was evaporated to dryness and the crude product thus obtained was chromatographed over silica gel column using 1-2 % acetone/CH_2Cl_2 gradient as eluent to obtain product **23**. Yield: 15.0 mg (51.5 %).

Method B: Bacteriochlorin **22** (15.0 mg, 0.022 mmol) was dissolved in dry CH_2Cl_2 (20 mL) and HBr gas was bubbled in it for 3-4 min. Reaction mixture was then concentrated in vacuo to dryness and re-dissolved in dry CH_2Cl_2 (20 mL). To this were added K_2CO_3 (500.0 mg) and alcohol **22** (15.0 mg, 0.022 mmol), the resultant mixture was stirred for 10 min. UV-vis shift from 726 nm to 736 nm indicated completion of reaction. Reaction mixture was diluted with CH_2Cl_2 (100 mL). Organic layer washed with brine, dried over sodium sulfate. Solvent was evaporated to dryness and crude thus obtained was chromatographed over silica gel column using 1-2 % acetone/ CH_2Cl_2 gradient as eluent to obtain product **23**. Yield: 20.0 mg (68.7 %). UV-vis λ_{max} (CH_2Cl_2, nm (ε), 739 (6.3 x 10^4), 670 (0.9 x 10^4), 510 (2.5 x 10^4), 380 (8.4 x 10^4), 355 (11.6 x 10^4). ^{1}HNMR (400 MHz, $CDCl_3$): δ 8.51 (s, 2H, meso-H), 8.41 (s, 1H, meso-H), 7.86 (dd, 1H, CH-vinyl, J = 11.6 Hz), 6.20 (d, 1H, $\underline{CH_2}$-vinyl, J = 17.6 Hz), 6.02 (d, 1H, $\underline{CH_2}$-vinyl, J = 12.0 Hz), 5.15 (d, 1H, 15^1-CH_2, J = 19.2 Hz), 5.09 (d, 1H, 15^1CH_2, J = 18.8 Hz), 4.24 (m, 1H, 17-H), 4.18 (s, 3H, CO_2Me), 4.16 (m, 2H, 8-H & 18-H), 4.09 (m, 1H, 7-H), 3.74 (s, 3H, CO_2Me),

3.63 (s, 3H, CO_2Me), 3.33 (s, 3H, ring-CH_3), 3.32 (s, 3H, ring-CH_3), 2.51 (m, 1H, 17^2-CH_2), 2.31 (m, 1H, 17^2-CH_2), 2.20 (m, 2H, 8-$\underline{CH_2}CH_3$), 2.04 (m, 1H, 17^1-CH_2), 1.84 (d, 3H, 7-CH_3, J = 7.2 Hz), 1.74 (m, 1H, 17^1-CH_2), 1.68 (d, 3H, 18-CH_3, J = 7.6 Hz), 1.09 (t, 3H, 8-$CH_2\underline{CH_3}$, J = 7.2 Hz), -0.65 (brs, 1H, NH), -0.89 (brs, 1H, NH). HRMS: Calcd. for $C_{37}H_{44}N_4O_6$: 640.3261. Found: 640.3264.

***3-Vinyl-bacteriopurpurin-18* (25):**

Bacteriochlorin e_6 tri-methyl ester **23** (15.0 mg, 0.023 mmol) was dissolved in taken in MeCN (10.0 mL). Reaction mixture was degassed five times with N_2 and aq. KOH (50.0 mg in 10 mL H_2O) was added. Resultant mixture was degassed again with N_2 and stirred at rt for 8 h. Reaction mixture was neutralized with 5 % acetic acid and extracted with 50 mL CH_2Cl_2/THF mix (3:1). The organic layer was separated, washed with brine, dried and concentrated. Crude thus obtained was purified on silica preparative plates using 7.5 % MeOH/CH_2Cl_2 mixture as mobile phase. Yield: 9.0 mg (68.1 %). UV-vis λ_{max} (CH_2Cl_2), nm (ε x 10^4) 777 nm (37%), 540 nm (38%), 416 nm (48%) and 363 nm (100%). ^{1}HNMR (400 MHz, $CDCl_3$-CD_3OD, 4:1): δ 10.81 (s, 1H, COOH), 8.50 (s, 1H, meso-H), 8.43 (s, 1H, meso-H), 8.30 (s, 1H, meso-H), 7.69 (dd, 1H, vinyl-CH, J = 11.6 & 17.6 Hz), 6.18 (d, 1H, $\underline{CH_2}$-vinyl, J = 18.0 Hz), 6.11 (d, 1H, vinyl-$\underline{CH_2}$, J = 11.6 Hz), 4.98 (d, 1H, 17-H, J = 9.2 Hz), 4.23 (m, 1H, 8-H), 4.14 (m, 1H, 18-H), 3.95 (m, 1H, 7-H), 3.51 (s, 3H, ring-CH_3), 3.22 (s, 3H, ring-CH_3), 2.67 (m, 1H, 17^2-CH_2), 2.41 (m, 2H, 8-$\underline{CH_2}CH_3$), 2.30 (m, 1H, 17^2-CH_2), 2.05-2.02 (m, 2H, 17^1-CH_2), 1.78 (d, 3H, 7-CH_3, J = 7.6 Hz), 1.68 (d, 3H, 18-CH_3, J = 7.2 Hz), 1.10 (t, 3H, 8-$CH_2\underline{CH_3}$, J = 7.2 Hz), 0.71 (brs, 1H, NH), -0.01 (brs, 1H, NH). Mass: Calcd for $C_{33}H_{34}N_4O_5$: 566.25. Found: EIMS (*m/z*), 589.3 (M+Na).

3-Vinyl-bacteriopurpurin-18 methyl ester (26):

3-Vinyl-bacteriopurpurin-18 **25** (8.0 mg, 0.014 mmol) was dissolved in CH_2Cl_2 (10 mL) and treated with diazomethane. Reaction mixture was stirred for 5 min and then concentrated to dryness. Crude thus obtained was purified on silica preparative plates using 3 % MeOH/CH_2Cl_2 as a mobile phase. Yield: 6.0 mg (73.2 %). UV-vis λ_{max} [nm, relative peak in CH_2Cl_2 (%)] 780 (38), 541 (40), 414 (47) and 365 (100). ^{1}HNMR (400MHz, $CDCl_3$): δ 8.55 (s, 1H, meso-H), 8.45 (s, 1H, meso-H), 8.31 (s, 1H, meso-H), 7.73 (dd, 1H, vinyl-CH, J = 11.6 & 17.6 Hz), 6.18 (d, 1H, vinyl-$\underline{CH_2}$, J = 17.6 Hz), 6.10 (d, 1H, $\underline{CH_2}$-vinyl, J = 12.0 Hz), 5.05 (d, 1H, 17-H, J = 11.6 Hz), 4.21 (m, 1H, 8-H), 4.16 (m, 1H, 18-H), 3.98 (m, 1H, 7-H), 3.60 (s, 3H, CO_2Me), 3.55 (s, 3H, ring-CH_3), 3.25 (s, 3H, ring-CH_3), 2.67 (m, 1H, 17^2-CH_2), 2.43 (m, 2H, 8-$\underline{CH_2}CH_3$), 2.32 (m, 1H, 17^2-CH_2), 2.05-1.95 (m, 2H, 17^1-CH_2), 1.78 (d, 3H, 7-CH_3, J = 7.2 Hz), 1.68 (d, 3H, 18-CH_3, J = 7.2 Hz), 1.10 (t, 3H, 8-$CH_2\underline{CH_3}$, J = 7.6 Hz), 0.43 (brs, 1H, NH), -0.04 (brs, 1H, NH). EIMS (*m/z*): 603.0 (M+Na), HRMS: Calcd. for $C_{34}H_{36}N_4O_5$: 580.2686. Found: 580.2688.

ACKNOWLEDGMENTS

The financial support from the NIH (CA55791, R21 CA109914, R21 CA114053), Oncologic Foundation

of Buffalo, Light Sciences Inc., Snoqualmie, WA (USA) and the shared resources of the RPCI support grant (P30CA16056) is highly appreciated. The mass spectrometry analyses were performed by the Mass Spectrometry facility, Michigan State University, East Lansing and the Biopolymer facility, RPCI, Buffalo.

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