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Nucleophilic Ring Opening of *meso*-Substituted 5-Oxaporphyrin by Oxygen, Nitrogen, Sulfur, and Carbon Nucleophiles

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Supporting Information

ABSTRACT: Nucleophilic ring opening of 23*H*-[21,23-didehydro-10,15,20-tris(4-methoxycarbonylphenyl)-5-oxaporphyrinato](trifluoroacetato)zinc(II) with various nucleophiles such as alkoxide, amine, thiolate, and enolate gave 19-substituted bilinone zinc complexes, and they were isolated as free base bilinones. An X-ray crystallographic study demonstrated that the product of 5-oxaporphyrin with sodium methoxide was 21*H*,23*H*-(4*Z*,9*Z*,15*Z*)-1,21-dihydro-19-methoxy-5,10,15-tris(4-methoxycarbonylphenyl)bilin-1-one with a helicoidal conformation. The structure of the product of 5-oxaporphyrin with an enolate of ethyl acetoacetate was 21*H*,22*H*,24*H*-(4*Z*,9*Z*,15*Z*,19*E*)-19-(1-ethoxycarbonyl-2-oxopropylidene)-5,10,15-tris(4-methoxycarbonylphenyl)-1,19,21,24-tetrahydrobilin-1-one, with three inner NH groups. The product with SH^- was also the same tautomer, 21*H*,22*H*,24*H*-19-thioxo-bilin-1-one, with three NH groups, while the products with RO^-, RNH_2, and RS^- nucleophiles were 21*H*,23*H*-bilin-1-ones with two inner NH groups. The first-order rate constants of the ring opening reaction of 5-oxaporphyrin with 1 M BnOH and BnSH in toluene at 303 K were 3.0×10^{-4} and 6.1×10^{-4} s^{-1}, respectively. The ratio of the rate of alcohol to thiol was much higher than that with methyl iodide, suggesting that 5-oxaporphyrin reacted as a hard electrophile in comparison to methyl iodide. UV−visible spectra of 19-substituted bilinones in $CHCl_3$ at 298 K showed that the absorption maximum of the lower energy band was red-shifted in increasing order of O-substituted (645 nm), S-substituted (668 nm), N-substituted (699 nm), and C-substituted bilinones (706 nm).

INTRODUCTION

Linear tetrapyrroles[1] are found in nature as the prosthetic group of photoreceptor proteins,[2] antenna pigments in photosynthesis,[3] and intermediates of heme and chlorophyll catabolism.[4,5] They are π-conjugated dye molecules, and absorption maxima are shifted by *Z*−*E* isomerization and intermolecular hydrogen bonding. Upon irradiation of light, photochemical *Z*−*E* isomerization at the C−D methine linkage occurs, inducing a hydrogen-bonding rearrangement and structural changes in the apoprotein.[2,6,7] When *Z*−*E* isomerization occurs, the structure of the photoreceptor protein around bilindione is changed through hydrogen bonding between the NH proton of bilindione and the apoprotein.[8] In addition, the extended π-electron system and the flexible framework of linear tetrapyrroles have been used as a chirality sensor[9] and an active layer of a molecular switch.[10] Bilindione has helical chirality, and there is dynamic interconversion between enantiomers.[9a,b,11] The dynamic chiral framework was employed as an element of the chirality amplification supramolecular system[9d,e,12] and as a dopant inducing a chiral nematic phase in liquid crystals.[9f] We previously reported that triarylbilindiones showed solvatochromism through hydrogen bonding with aprotic amines and amides.[6] There have been several investigations of metal complexes of bilindiones. Ribo's and Balch's groups reported the preparation and characterization of copper,[13] cobalt,[14] and iron complexes[15] of bilindiones, although bilindione metal complexes are unstable in air. Biliverdin has antivirus activity[16] and antioxidant action;[17] thus, biliverdin not only is an intermediate of heme catabolism but also is applicable to biomaterials and photonic and electronic materials.

There are two approaches to synthesize linear tetrapyrroles. One is chemical oxidation such as coupled oxidation of iron porphyrin[18,19] and cobalt porphyrin,[14,20] where a reaction proceeds analogously to that catalyzed by heme oxygenase, and the other is stepwise connection of pyrrole units, suitable for the preparation of unsymmetrical linear tetrapyrroles such as natural biliverdin.[21]

There is considerable interest in bilinones bearing a substituent at the 19-position. Kräutler and co-workers and Tanaka and co-workers demonstrated that 19-formylbilinone is one of the catabolites of chlorophyll, and elucidation of their biological roles has just started.[22] Bilinones substituted at the 19-position with alkoxy or amino groups have been synthesized by a ring-opening reaction of 5-oxaporphyrin metal complexes with alkoxides or amines.[23,24] For example, reactions of 5-oxaporphyrins with various nucleophiles such as alcohol,

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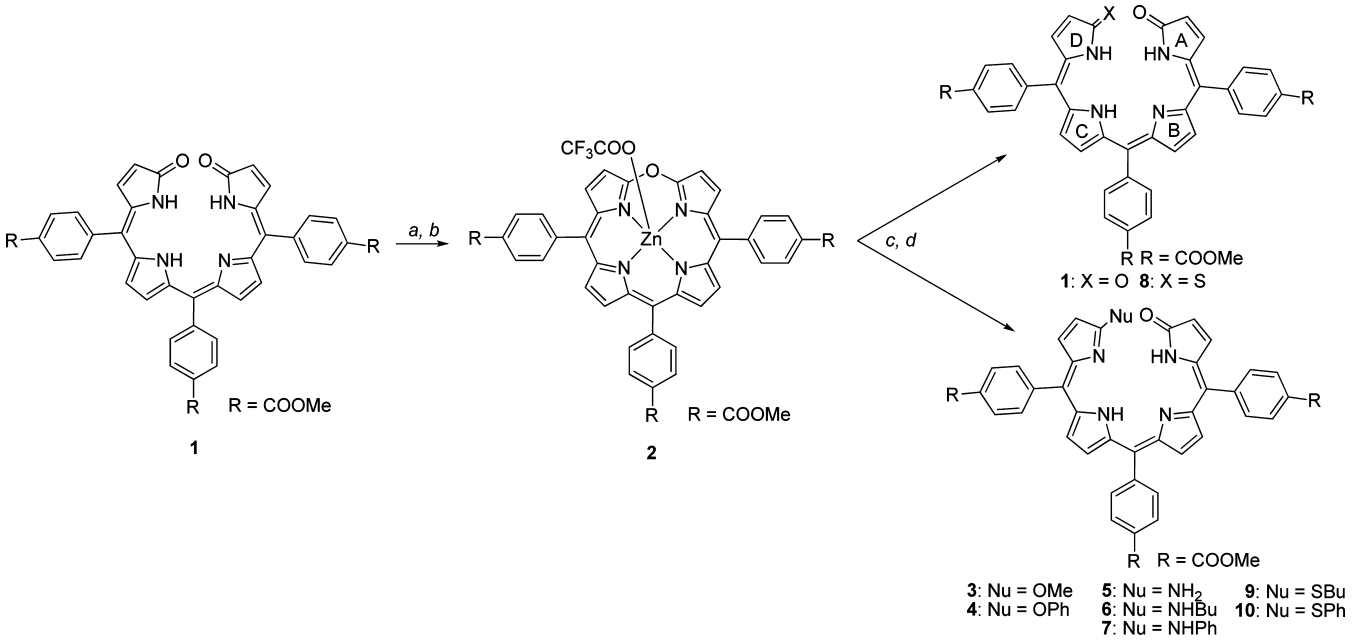
Scheme 1. Synthesis of 19-Substituted Bilinones 3−10[a]



[a]Reagents: (*a*) Ac_2O, $Zn(OAc)_2$, ethanol-free $CHCl_3$, reflux; (*b*) 0.1% TFA; (*c*) corresponding nucleophiles; (*d*) 1 M HCl.

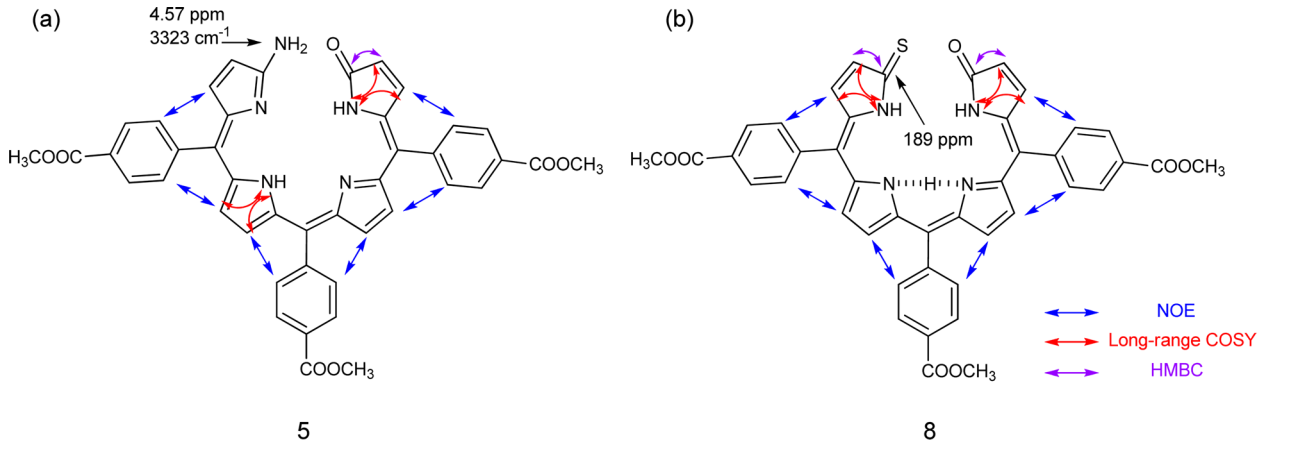


Figure 1. COSY, NOE, and HMBC correlations of bilinones **5** and **8**.

alkoxide, amine, and thiolate afforded 19-substituted bilinones.[24−28] Bilinones can also be obtained by oxidative ring-cleavage reactions of porphyrins.[29] Fuhrhop and co-workers reported that photooxidation of a *β*-octaethylporphyrin magnesium complex gave a 19-formylbilinone magnesium complex.[29] Smith, Cavaleiro, and Latos-Grazynski independently reported that the magnesium, cadmium, and thallium complexes of tetraphenylporphyrin, its dianion, or N-confused tetraphenylporphyrin dianion were photochemically oxidized to give 19-benzoyl-15-alkoxybilin-1-one.[30−32] We previously reported that coupled oxidation of the tetraarylporphyrin iron complex with dioxygen, ascorbic acid, and pyridine gave 1,15,21,24-tetrahydro-19-benzoyl-15-hydroxybilinone (biladienone) as the major product.[19] 1,15,21,24-Tetrahydro-19-benzoyl-15-hydroxybilinone was converted to 1,21-dihydro-19-benzoylbilinone by using acetic acid or mesoporous silica.[19,33] The metal complex of bilinone was more stable than that of bilindione in protic solvents, and the zinc, cobalt, and iron complexes of bilinone were reported by Balch and others.[9b,24,27,28]

We reported that *meso*-substituted bilindione reacted with acetic anhydride and zinc acetate in $CHCl_3$ to give the *meso*-substituted 5-oxaporphyrin zinc complex, and it was labile toward nucleophiles; a solution of *meso*-substituted 5-oxaporphyrin in alcohols readily afforded a ring-opened bilinone at room temperature.[24] We report herein that the ring-opening reactions of *meso*-tetrakis(methoxycarbonylphenyl)-5-oxaporphyrin with various nucleophiles such as nitrogen, oxygen, sulfur, and carbon nucleophiles give 19-substituted bilinones. Tautomeric structures and *π*-conjugated electronic structures can be controlled by the substituent introduced at the 19-position.

RESULTS AND DISCUSSION

Synthesis of 19-Substituted Bilinones. *meso*-Triarylbilindione **1** was prepared from [*meso*-tetrakis(methoxycarbonylphenyl)porphyrinato]iron(III) chloride by a coupled oxidation

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reaction.[19b] The *meso*-substituted 5-oxaporphyrin zinc complex **2** was synthesized in quantitative yield from **1** (Scheme 1).[24] 19-Substituted bilinones were synthesized from 5-oxaporphyrin **2** by ring-opening reactions with various nucleophiles. Acidic workup with 1 M HCl afforded the free base bilinones **3**−**10**. The preparation and characterization of bilindione **1** and 19-methoxybilinone **3** were reported elsewhere in detail.[19b,24]

19-Aminobilinone **5** was prepared by the reaction of **2** with ammonia. The MALDI-TOF mass spectrum of **5** showed a peak at m/z 731 (M^+, M = $C_{43}H_{33}N_5O_7$). In the ^{1}H NMR, the resonances of pyrrole β-protons of bilinone **5** appeared at 6.09, 6.27, 6.40, 6.45, 6.57, 6.85−6.87 (two overlapped doublets), and 7.05 ppm, the phenyl ortho protons at 7.52 and 7.63−7.65 ppm, and the phenyl meta protons at 8.10−8.16 ppm. According to the ROESY spectra, the following NOE correlations were found: the resonances of pyrrole β-protons at 6.45 and 7.05 ppm (H-7, H-3) with that of the ortho phenyl protons at 7.52 ppm, the resonances of pyrrole β-protons at 6.57 and 6.85−6.87 ppm (H-8, H-12 or H-13) with that of the ortho phenyl protons at 7.63−7.65 ppm, and the resonances of pyrrole β-protons at 6.40 and 6.85−6.87 ppm (H-17 and H-12 or H-13) with that of the ortho phenyl proton at 7.63−7.65 ppm. On the basis of these ROESY correlations, we identified that bilinone **5** was the 4*Z*,9*Z*,15*Z* geometric isomer (Figure 1a). The broad signal at 4.57 ppm (2H) in the ^{1}H NMR and the broad peak at 3323 cm^{-1} in the IR spectrum indicated that bilinone **5** has an amino group.

The product **8** ring-opened with NaSH was characterized with 1D and 2D NMR and MALDI-TOF mass spectroscopic studies. The MALDI-TOF mass spectrum of **8** showed a peak at m/z 748 (M^+, M = $C_{43}H_{32}N_4O_7S$). In the ^{1}H NMR, the resonances of pyrrole β-protons of bilinone **8** appeared at 6.08, 6.66, 6.72, 6.82, 7.04−7.06 (two overlapped doublets), 7.16, and 7.25 ppm, the phenyl ortho protons at 7.50, 7.63, and 7.74 ppm, and the phenyl meta protons at 8.10, 8.13, and 8.22 ppm. According to the ROESY spectra, following ROESY correlations were found: the resonances of pyrrole β-protons at 6.66 and 7.15 ppm (H-7, H-3) with that of the ortho phenyl protons at 7.50 ppm, the resonances of pyrrole β-protons at 6.82 and 7.04−7.06 ppm (H-12, H-8 or H-13) with that of the ortho phenyl protons at 7.71 ppm, and the resonances of pyrrole β-protons at 7.04−7.06 and 7.25 ppm (H-8 or H-13 and H-17) with that of the ortho phenyl protons at 7.71 ppm. These ROESY correlations suggested that bilinone **8** was the 4*Z*,9*Z*,15*Z* geometric isomer (Figure 1b). The resonance of the SH proton was not found; alternatively, the resonances of three NH protons of bilinone **8** appeared at 8.47, 11.63, and 12.17 ppm. The IR spectrum showed that there was no SH stretching peak. Therefore, **8** was identified as 19-thioxobilin-1-one.

For the ring-opened products with OH^-, NH_3, and SH^-, there are several tautomers, such as lactam−lactim tautomers, imine−enamine tautomers, and iminothiol−aminothione tautomers.[34] Tautomeric equilibria of bilinones **1**, **5**, and **8** are shown in Figure 2. 19-Hydroxybilinone is unstable, and the tautomeric equilibrium is shifted to bilindione. Generally, the imine tautomer is more stable than the enamine tautomer, although 2-aminopyridine is more stable than 2(1*H*)-pyridineimine.[35] The framework of the enamine in 19-aminobilinone **5** is similar to that of 2-aminopyridine. ^{1}H NMR and IR spectra indicated that 19-aminobilinone **5** had an amino group. Thus, the tautomeric equilibrium of 19-aminobilinone **5** was shifted to the enamine form. 19-Sulfanylbilinone **8** did not exhibit an SH proton in ^{1}H NMR

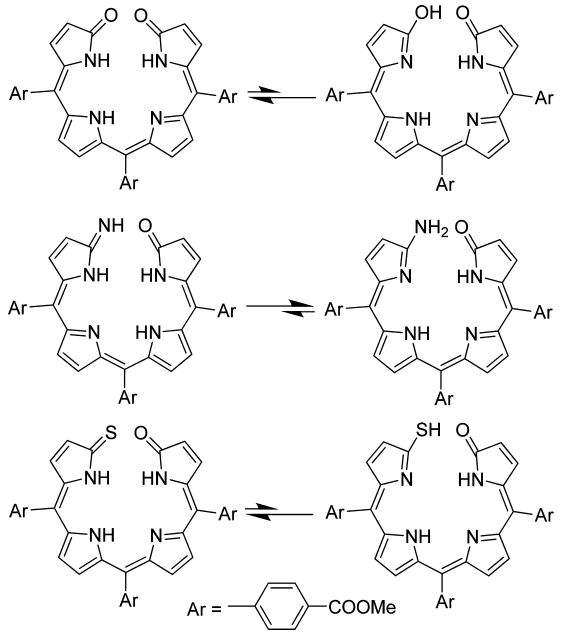

Figure 2. Tautomeric structures of 19-substituted bilinones.

or SH stretching in the IR spectra. The resonance of C-19 in the ^{13}C NMR of **8** appeared at 188.6 ppm, shifted downfield about 20 ppm in comparison to C-1 or C-19 of **5.** The chemical shift of the C═S carbon in 2(1*H*)-pyridinethione was 180 ppm,[36] similar to that of 19-C of **8**. Therefore, the tautomeric equilibrium of 19-surfanylbilinone **8** was shifted to the thioamide form. According to the ^{1}H NMR, however, the resonances of other tautomers were also observed and the signal integration indicates that the fraction of the major tautomer is about 85%. Other 19-substituted bilinones **4**, **6**, **7**, **9**, and **10** were also identified by 1D and 2D NMR and MALDI-TOF mass spectroscopy. To summarize the tautomeric structures, 21*H*,23*H* tautomers were formed when RO^-, RNH_2, and NH_3 were employed as nucleophiles (**3**−**7**, **9**, and **10**). When SH^- was employed (**8**), a mixture of 21*H*,23*H*,24*H* and 21*H*,22*H*,24*H* tautomers was formed.

X-ray Crystallographic Studies of 19-Methoxybilinone 3. Crystals of **3** were obtained by slow diffusion of cyclohexane into a solution of **3** in dichloromethane. An ORTEP view of **3** is shown in Figure 3 and Figure S21 (Supporting Information). The crystal structure of **3** demonstrated that it is a *ZZZ*,*syn*,*syn*,*syn* keto-methoxy isomer with a helicoidal conformation, and NOESY NMR indicated that **3** took this conformation in solution.[24] The phenyl groups were tilted: the C(pyrrole)−C(meso)−C(phenyl ipso)−C(phenyl ortho) dihedral angles are 47−54°. The A and B rings were almost coplanar, while the B−C rings and C−D rings were twisted. The methyl group in the methoxy group at the 19-position was under the A ring pyrrole and folded into the inside of the bilinone framework. In the unit cell, there are two bilinone molecules: one has a *P*- and the other an *M*-helix configuration. Bilinone molecules with the same chirality are stacked to form a column of helices in the crystal (see Figure S22 in the Supporting Information). For triphenylbilindione, the NH group of the A ring is hydrogen-bonded to the D ring carbonyl group of the neighboring molecule, to form a linear homochiral column.[19a] However, 19-methoxybilinone has no NH proton in the D ring, and there is no hydrogen bonding with the neighboring molecule. Therefore, 19-methoxybilinone formed a

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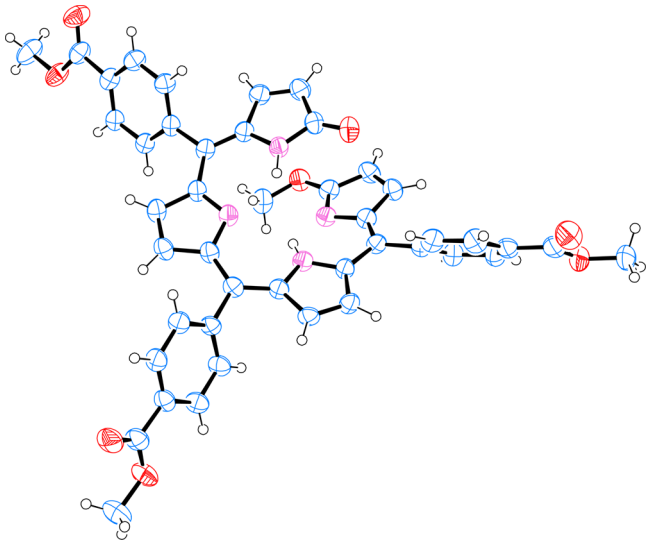


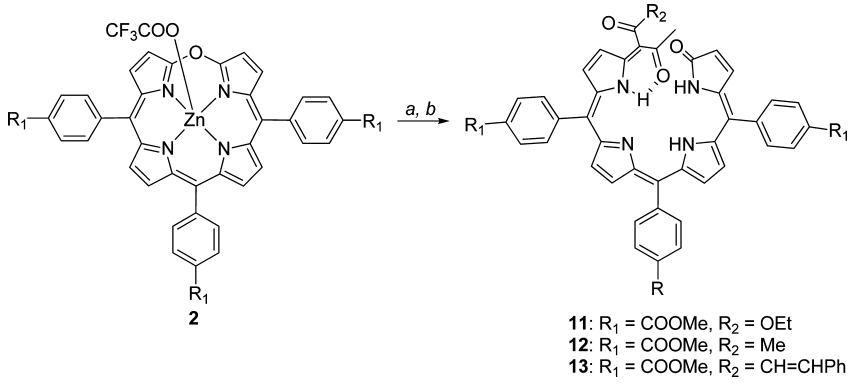
Figure 3. ORTEP view of 19-methoxybilinone **3**.

slant column in the crystal without intermolecular hydrogen bonding. In comparison to the bilinone with alkyl substituents at the β-positions of pyrrole,[37] **3** has a narrower helix with a larger helix pitch. The distance between C5 and C15 is 7.03 Å, longer than that of β-substituted bilinone (6.82 Å), and the distance between the C═O oxygen and the methoxy oxygen is 4.14 Å, longer than that of β-substituted bilinone (3.94 Å). Moreover, introduction of phenyl groups at the meso positions makes the C4−C5−C6, C9−C10−C11, and C14−C15−C16 bond angles smaller than those of β-substituted bilinone, leading to a better spatial overlap of the terminal A, D pyrroles. The average of the three bond angles around the meso carbons of **3** was 122.4°, while that of β-substituted bilinone was 126.7°. Therefore, the helical pitch of **3** is larger than that of β-substituted bilinone.

Reaction of 5-Oxaporphyrin 2 with Carbon Nucleophiles. A pyrylium salt reacts with cyanide,[38] Grignard reagents,[39] and enolates.[39a] Balch and co-workers reported that the zinc complex of β-octaethyl-5-oxaporphyrin reacted with tetrabutylammonium cyanide to give 19-cyanobilinone along with dicyanobilinones such as 10,19-dicyanobilinone and 15,19-dicyanobilinone.[40] We investigated the reaction of 5-oxaporphyrin **2** with carbon nucleophiles such as a Grignard reagent, acetylide, and enolates. The reaction of 10,15,20-triphenyl-5-oxaporphyrin[24] with 50 mM EtMgBr at −80 °C gave various colored products, and we failed to isolate 19-ethylbilinone. When 5-oxaporphyrin **2** was reacted with 20 mM LiC≡CTMS, the solution turned from green to brown, and acidic workup only gave bilindione **1**.

5-Oxaporphyrin **2** reacted with the enolate monoanions of ethyl acetoacetate, acetylacetone, and (*E*)-6-phenyl-5-hexene-2,4-dione to yield enolate-appended bilinones **11**−**13**, respectively (Scheme 2). The MALDI-TOF mass spectrum of **11** showed a peak at 845 (M + H$^+$, M = $C_{49}H_{40}N_4O_{10}$). In the ^{1}H NMR, the resonances of pyrrole β-protons of bilinone **11** appeared at 6.18, 6.65, 6.70, 6.85−6.89 (two overlapped doublets), 6.97, 7.07, and 7.48 ppm, the phenyl ortho protons at 7.54, 7.60, and 7.77 ppm, the phenyl meta protons at 8.03, 8.12, and 8.19 ppm, and the NH protons at 8.28, 11.61, and 11.89 ppm. The resonances at 1.24 (3H), 2.00 (3H), and 4.19 (2H) ppm indicate that **11** has an ethyl acetoacetate group. The signals at 1.24 and 4.19 ppm were assigned to the ethoxy group, and the singlet signal at 2.00 ppm was assigned to the acetyl group. The characteristic resonances in the ^{13}C NMR of **11** appeared at 103.9, 166.9, 167.9, 171.1, and 195.5 ppm. In order to identify the structure, COSY, HMBC, HMQC and ROESY experiments were carried out. The signal at 166.9 ppm in the ^{13}C NMR spectrum was correlated with the methyl ester protons in the phenyl groups at 3.88−3.96 ppm in the HMBC experiment; therefore, this signal was assigned to the ester carbonyl carbons in the phenyl groups. The signal at 167.9 ppm was correlated with methylene protons in the ethoxy group at 4.19 ppm in the HMBC experiment; therefore, this signal was assigned to the ester carbonyl carbons in the ethyl acetoacetate group. The signals at 195.5 and 103.9 ppm were correlated with the acetyl protons at 2.00 ppm in the HMBC experiment; therefore, the signal at 195.5 ppm was assigned to the acetyl carbonyl carbon in the ethyl acetoacetate group and the signal at 103.9 ppm was assigned to the methylene carbon between the two carbonyl carbons in the ethyl acetoacetate group. Furthermore, the HMBC experiments indicated that there was a long-range coupling between the resonances at 6.18 and 7.07 ppm in the ^{1}H NMR and the resonance at 171.1 ppm in the ^{13}C NMR. The signal at 171.1 ppm was assigned to the lactam carbonyl carbon; therefore, the signals at 6.18 and 7.07 ppm were assigned to the pyrrole β-protons at H-2 and H-3. According to the ROESY spectra, the following NOE correlations were found: the resonances of pyrrole β-protons at 6.70 and 7.07 ppm (H-7, H-3) with that of the ortho phenyl

Scheme 2. Synthetic Route to Enolate-Appended Bilinones[a]



[a]Reagents: (*a*) corresponding enolates; (*b*) 1 M HCl.

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protons at 7.54 ppm, the resonances of pyrrole β-protons at 6.65 and 6.58−6.89 ppm (H-12, H-8 or H-17) with that of the ortho phenyl protons at 7.60 ppm, and the resonances of pyrrole β-protons at 6.58−6.89 and 6.97 ppm (H-8 or H-17 and H-13) with that of the ortho phenyl proton at 7.77 ppm. In addition, the resonance of acetyl protons at 2.0 ppm showed an NOE correlation with the resonance of phenyl protons at 7.54 ppm (5-phenylene H-2′) in the ROESY spectrum. On the basis of these ROESY correlations, we concluded that bilinone **11** was a 4*Z*,9*Z*,15*Z*,19*E* geometric isomer. Scheme S2 (Supporting Information) shows possible tautomeric structures of enolate-appended bilinone **11**. The resonance of the methylene carbon between two carbonyl groups at 104 ppm was not correlated with any protons in the HMQC experiment; therefore, this carbon was a quaternary carbon. At this point, tautomers having a proton at the methylene carbon such as (*RS*)-β-diketo and O-alkylated products were excluded. Furthermore, according to the COSY experiment, the following COSY correlations were found: the resonances of β-protons at 6.18 and 7.07 ppm (H-2 and H-3) with that of the NH proton at 8.28 ppm, the resonances of β-protons at 6.70 and 6.85−6.89 ppm (H-7 and H-8) with that of the NH proton at 11.89 ppm, and the resonances of β-protons at 6.85−6.89 and 7.48 ppm (H-17 and H-18) with that of the NH proton at 11.61 ppm. Therefore, the major tautomer of enolate-appended bilinone **11** had the structure shown in Figure 4. Molecular modeling with ab initio B3LYP/6-31G(D) suggested that hydrogen bonding between the acetyl group and the D ring NH stabilized the conformation. In this conformation, the methyl group of the acetyl group was close to the ortho proton of the 5-phenyl group, consistent with the observed NOE. In the ^{1}H NMR, however, the resonances of other tautomers were also present in a fraction of about 10%. The other 19-enolate-substituted bilinones **12** and **13** were also identified by 1D and 2D NMR and MALDI-TOF mass spectra. Bilinone **11** had a 1-acetyl-2-oxopropylidene group at the 19-position. For bilinone **13**, we did not determine whether the 19*E* or 19*Z* form is the major isomer, owing to the complex ^{1}H NMR spectrum.

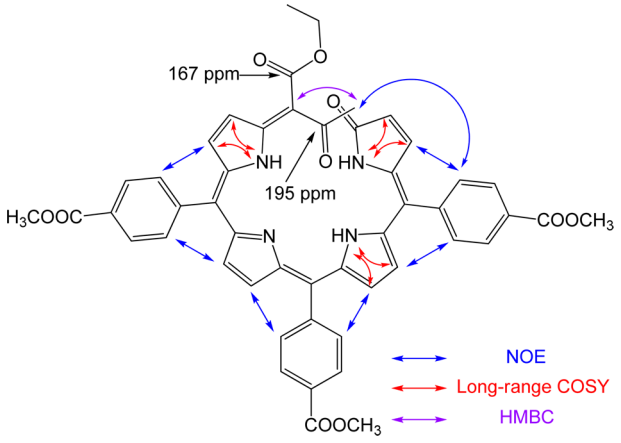

Figure 4. COSY and NOE correlations of enolate-appended bilinone **11**.

Kinetic Studies on Nucleophilic Ring Opening of *meso*-Substituted 5-Oxaporphyrin. We previously reported that *meso*-substituted 5-oxaporphyrins had higher reactivity than β-substituted species: *meso*-substituted 5-oxaporphyrins reacted with weak nucleophiles such as methanol, ethanol, and 2-propanol to give 19-alkoxybilinone zinc complexes, and the rate of this nucleophilic ring-opening reaction depended on the steric hindrance of the nucleophiles.[24] We compared the rates of the nucleophilic ring opening of 5-oxaporphyrin **2** with various nucleophiles such as BnOH, PhOH, $BnNH_2$, $PhNH_2$, BnSH, and PhSH. As a representative example, the UV−visible spectral changes of **2** in 1 M BnOH in toluene at 30 °C are shown in Figure 5. When **2** was dissolved in 1 M BnOH in toluene, the absorption of **2** at 398 and 645 nm decreased and new peaks developed at 324 and 800 nm. The spectral changes followed a first-order kinetic equation. The first-order rate constants of the ring-opening reaction with other nucleophiles were also determined at a concentration of 1 M in toluene except for $BnNH_2$, for which a concentration of 1 mM in toluene was employed due to its high reactivity. Table 1 summarizes the rate constants of the nucleophilic ring-opening reaction of **2** by BnOH, PhOH, $BnNH_2$, $PhNH_2$, BnSH, and PhSH at 30 °C. The reactivity of **2** toward nucleophiles decreases in the order $BnNH_2 \gg$ PhSH > $PhNH_2$ > BnSH >

Table 1. First-Order Rate Constants of Nucleophilic Ring Opening of 5-Oxaporphyrin 2 in 1 M BnOH, BnSH, PhOH, $PhNH_2$, and PhSH and in 1 mM $BnNH_2$ in Toluene at 30 °C

nucleophile	k/s^{-1}	nucleophile	k/s^{-1}
BnOH	$(3.0 \pm 0.2) \times 10^{-4}$	PhOH	$(2.6 \pm 0.2) \times 10^{-4}$
$BnNH_2$	$(3.6 \pm 0.4) \times 10^{-4}$	$PhNH_2$	$(1.2 \pm 0.2) \times 10^{-3}$
BnSH	$(6.1 \pm 0.6) \times 10^{-4}$	PhSH	$(5.2 \pm 0.1) \times 10^{-3}$

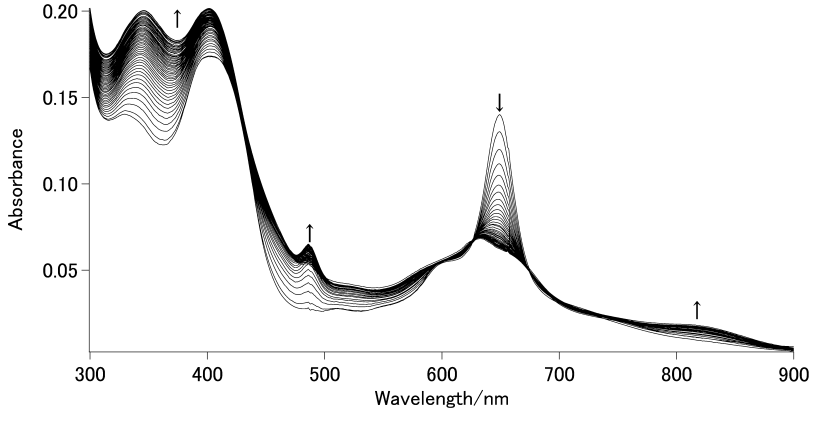

Figure 5. UV−visible spectral changes of 5×10^{-6} M 5-oxaporphyrin **2** in 1 M BnOH in toluene at 30 °C. Spectra were recorded every 5 min.

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BnOH > PhOH. The reaction of **2** with $BnNH_2$ was about 1000 times faster than those for other nucleophiles. Aniline, thiol, and alcohols reacted at a similar rate.

Pearson and co-workers compared the rate constants of methyl iodide with various nucleophiles.[41] The ratio of the rate constant of the reaction of methyl iodide with PhSH to that with methanol was 50000, and the ratio of the rate constant of reaction of methyl iodide with PhSH to that with $PhNH_2$ was 1.2. In contrast, the ratio of the rate constant of the reaction of **2** with PhSH to that with BnOH was 16 and the ratio of the rate constant of reaction of **2** with PhSH to that with $PhNH_2$ was 4.3. These comparisons indicate that the reaction of **2** with alcohol was notably faster in comparison to that for methyl iodide. According to the HSAB theory, BnOH and $BnNH_2$ are hard nucleophiles and BnSH is a soft nucleophile.[42] The relatively fast reaction of **2** toward alcohols in comparison with methyl iodide thus implies that 5-oxaporphyrin **2** is a harder electrophile than methyl iodide. The ring-opening reaction is a multistep reaction, much more complex than nucleophilic substitution of methyl iodide. Nucleophilic ring opening of 5-oxaporphyrin was proposed to proceed through a tetrahedral intermediate initially formed by nucleophilic attack of the nucleophiles to the carbon neighboring the oxygen atom, C4, and it was then directly converted to a helical ring-opened zinc complex.[40,43]

UV−Visible Spectra of 19-Substituted Bilinones. Figure 6 shows the UV−visible spectra of 19-substituted bilinones in $CHCl_3$ at 25 °C. The absorption maximum of the higher energy band of bilinones with a 21*H*, 23*H* tautomeric structure was red-shifted in the order of O-substituted, N-substituted, and S-substituted, while their lower energy bands were red-shifted in the order of O-substituted, S-substituted, and N-substituted. Enolate-appended bilinone **11** was a 21*H*,22*H*,24*H* tautomer, and its tautomeric structure was identical with that of bilindione **1**. The π-conjugated system of bilinone **11** was extended via the ethyl acetoacetate group. In comparison to bilindione **1**, the higher energy band and the lower energy band of the UV−visible spectrum of bilinone **11** were red-shifted by 64 nm from 399 to 463 nm and by 80 nm from 626 to 706 nm, respectively. The absorption maximum of bilinone **13**, in which the π-conjugated system was more extended via the phenylethenyl group, was red-shifted by 17 nm with respect to bilinone **11**.

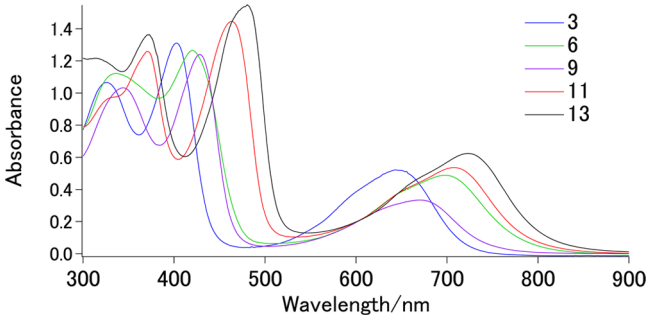

Figure 6. UV−visible spectra of 3×10^{-5} M 19-substituted bilinones in $CHCl_3$ at 25 °C.

CONCLUSIONS

[21,23-Didehydro-10,15,20-tris(4-methoxycarbonylphenyl)-23*H*-5-oxaporphyrinato](trifluoroacetato)zinc(II) (**2**) reacted with phenoxide, ammonia, butylamine, aniline, sodium hydrogensulfide, butanethiolate, benzenethiolate, enolate anions of ethyl acetoacetate, acetylacetone, and 6-phenyl-5-hexene-2,4-dione to give bilinone zinc complexes, and they were isolated as free base bilinones by acid treatment in yields ranging from 53 to 87%. An X-ray crystallographic study demonstrated that 19-methoxybilinone **3** is a *ZZZ,syn,syn,syn* keto-methoxy isomer with a helicoidal conformation. When RONa, NH_3, RNH_2, and RSNa were used as nucleophiles, 21*H*,23*H* tautomers were formed. When NaSH was used as a nucleophile, a 21*H*,22*H*,24*H* tautomer was formed. 1D and 2D NMR demonstrated that enolate-appended bilinone **11** is a *ZZZE*, β-diketo tautomer. 5-Oxaporphyrin **2** reacted with BnOH and BnSH at similar rates and with $BnNH_2$ 1000 times faster. The higher reactivity of **2** toward alcohol and amine relative to methyl iodide suggested that 5-oxaporphyrin **2** was a hard electrophile. UV−visible spectra of 19-substituted bilinones in $CHCl_3$ at 298 K showed that the higher energy band of the absorption maximum of bilinones was red-shifted in the increasing order of methoxybilinone **3**, butylaminobilinone **6**, butylsulfanylbilinone **9**, and enolate-appended bilinone **11**, while their lower energy bands were red-shifted in the increasing order of **3**, **9**, **6**, and **11**. The absorption maximum of enolate-appended bilinone **13** was red-shifted by 17 nm with respect to **11**. Finally, various *meso*-substituted bilinones having near-infrared absorption and helicity were easily obtained in good yields from *meso*-substituted 5-oxaporphyrin zinc complexes.

EXPERIMENTAL SECTION

Commercially available reagents were used as received. Chromatographic separation of 19-substituted bilinones was performed using silica gel 60N, spherical neutral with particle size 40−50 μm. The preparations of bilindione **1**, 5-oxaporphyrin **2**, and 19-methoxybilinone **3** were reported elsewhere.[19b,24] Tetramethylsilane was used as an internal standard for ^1H and ^{13}C NMR spectra. ^1H NMR and ^{13}C NMR signals were assigned using $^1H-^1H$ COSY, ROESY, HMBC, and HMQC spectra. High-resolution mass spectral data were obtained from a double-focusing, magnetic sector, high-resolution mass spectrometer. A blue needle crystal of methoxybilinone **3** was obtained by slow diffusion of cyclohexane into a solution of **3** in dichloromethane. Crystal data and data collection parameters are given in Table S1 (Supporting Information).

21*H*,23*H*-(4*Z*,9*Z*,15*Z*)-1,21-Dihydro-5,10,15-tris(4-methoxycarbonylphenyl)-19-phenoxybilin-1-one (4). 5-Oxaporphyrin **2** (122 mg, 0.137 mmol) was placed in a 100 mL three-necked flask, and dry THF (50 mL) was added. Phenol (129 mg, 1.37 mmol) and sodium hydride (60% oil dispersion, 60 mg, 1.50 mmol) were added to dry THF (10 mL). The phenoxide solution (2 mL) was added dropwise to the 5-oxaporphyrin solution, and the reaction mixture was stirred at room temperature for 5 min. Then chloroform (50 mL) was added to the reaction mixture, the chloroform solution was washed once with water, twice with 1 M HCl, and once again with water. The organic layer was dried over Na_2SO_4. Evaporation of the solvent under reduced pressure gave a blue-green solid. The product was purified on silica gel chromatography using dichloromethane/acetone (10/1) as eluent. Further purification by silica gel chromatography using chloroform yielded 89.7 mg of **4** (81%).

^1H NMR (500 MHz, $CDCl_3$): δ 3.95 (s, 3H; $COOCH_3$), 3.96 (s, 3H; $COOCH_3$), 3.97 (s, 3H; $COOCH_3$), 6.17 (two overlapped doublets, 2H; pyrrole H-2 and H-18), 6.32 (m, 1H; pyrrole H-12 or H-13), 6.38 (m, 1H; pyrrole H-12 or H-13), 6.41 (d, J = 4.60 Hz, 1H; pyrrole H-7), 6.83 (three overlapped doublets, 3H; pyrrole H-3, H-8, and H-17), 7.05 (m, 1H; phenyl), 7.15 (m, 4H; phenyl), 7.34 (d, J = 8.45 Hz, 2H; 5-phenylene H-2′), 7.60 (d, J = 8.45 Hz, 2H; 10 or 15-phenylene H-2′), 7.66 (d, J = 8.40 Hz, 2H; 10 and 15-phenylene H-

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2′), 8.09 (d, J = 8.45 Hz, 2H; 5-phenylene H-3′), 8.15 (m, 4H; 10 or 15-phenylene H-3′), 10.5 (s, 1H; NH), 13.1 (s, 1H; NH). ^{13}C NMR (125 MHz, $CDCl_3$): δ 52.3 ($COOCH_3$), 52.4 ($COOCH_3$), 117.7, 118.5 (pyrrole C-2 or C-8), 120.0 (phenoxy), 120.3 (pyrrole C-12 or C-13), 123.0 (pyrrole C-12 or C-13), 125.0 (phenoxy), 125.4 (pyrrole C-2 or C-18), 128.3 (pyrrole C-7), 129.06, 129.11, 129.3 (phenoxy), 129.7, 130.4, 131.0, 131.3, 131.4, 132.1, 132.2, 135.0 (pyrrole C-3 or C-8 or C-17), 136.8 (pyrrole C-3 or C-8 or C-17), 137.5 (pyrrole C-11 or C-14), 137.9 (pyrrole C-3 or C-8 or C-17), 138.3, 140.6 (pyrrole C-11 or C-14), 141.1, 141.2, 142.0, 142.3 (pyrrole C-4 or C-16), 148.3 (pyrrole C-4 or C-16), 152.6 (phenoxy), 154.1 (pyrrole C-9), 166.6 ($COOCH_3$), 166.8 ($COOCH_3$), 167.9 (pyrrole C-6), 170.9 (pyrrole C-1), 174.6 (pyrrole C-19). MS (MALDI-TOF): m/z 809 $[M + H]^+$. HRMS (FAB): calcd for $C_{49}H_{36}O_8N_4$ m/z 808.2533, found 808.2551. UV−vis ($CHCl_3$, 25 °C): λ_{max} (ε_{max}) 328 (3.84×10^4), 409 (5.05×10^4), 651 nm (1.52×10^4 M^{-1} cm^{-1}).

21*H*,23*H*-(4*Z*,9*Z*,15*Z*)-19-Amino-1,21-dihydro-5,10,15-tris(4-methoxycarbonylphenyl)bilin-1-one (5). 5-Oxaporphyrin **2** (25.0 mg, 0.0280 mmol) was placed in a 200 mL three-necked flask. Dry acetone (60 mL) was added, and NH_3 gas was bubbled at room temperature for 5 min. NH_3 gas was generated by heating 28% ammonia solution. Then chloroform (50 mL) was added to the reaction mixture, and the chloroform solution was washed twice with water, once with 1 M HCl, once with saturated aqueous sodium hydrogen carbonate, and once with brine. The organic layer was dried over Na_2SO_4. Evaporation of the solvent under reduced pressure gave a green solid. The product was purified by silica gel chromatography using chloroform as eluent to yield 16.0 mg of **5** (78%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 3.96−3.98 (three overlapped singlets, 9H; $COOCH_3$), 4.57 (s, 2H; NH_2), 6.09 (d, J = 5.75 Hz, 1H; pyrrole H-2), 6.27 (d, J = 4.60 Hz, 1H; pyrrole H-18), 6.40 (d, J = 4.00 Hz, 1H; pyrrole H-13), 6.45 (d, J = 4.00 Hz, 1H; pyrrole H-7), 6.57 (s, 1H; pyrrole H-12), 6.85−6.87 (two overlapped doublets, 2H; pyrrole H-8 and H-17), 7.05 (d, J = 5.75 Hz, 1H; pyrrole H-3), 7.52 (d, J = 8.05 Hz, 2H; 5-phenylene H-2′), 7.63−7.65 (two overlapped doublets, 2H; 10,15-phenylene H-2′), 8.10−8.16 (three overlapped doublets, 6H; 5,10,15-phenylene H-3′), 9.89 (s, 1H; NH), 13.16 ppm (s, 1H; NH). ^{13}C NMR (125 MHz, $CDCl_3$): δ 52.1 ($COOCH_3$), 52.2 ($COOCH_3$), 118.1, 118.8 (pyrrole C-13), 121.2 (pyrrole C-18), 124.4 (pyrrole C-12), 124.7 (pyrrole C-2), 127.0 (pyrrole C-7), 128.8, 128.9, 129.4, 129.7, 129.8, 130.7, 131.4, 132.0, 134.4 (pyrrole C-8), 135.7, 136.1 (pyrrole C-3), 138.5, 138.7 (pyrrole C-17), 139.7 (pyrrole C-4), 141.4, 141.7, 142.4, 143.2, 151.0 (pyrrole C-9), 153.3 (pyrrole C-16), 165.2 (pyrrole C-6), 166.6 ($COOCH_3$), 166.8 ($COOCH_3$), 167.6 (pyrrole C-19), 170.6 (pyrrole C-1). MS (MALDI-TOF): m/z 731 $[M]^+$. HRMS (FAB): calcd for $C_{43}H_{33}O_7N_5$ m/z 731.2380, found 731.2398. UV−vis ($CHCl_3$, 25 °C): λ_{max} (ε_{max}) 331 (3.57×10^4), 408 (4.51×10^4), 673 nm (1.59×10^4 M^{-1} cm^{-1}). IR (KBr): 3323, 2950, 2883, 1716, 1697, 1635, 1427, 1278, 1114, 962 cm^{-1}.

21*H*,23*H*-(4*Z*,9*Z*,15*Z*)-19-*N*-Butylamino-1,21-dihydro-5,10,15-tris(4-methoxycarbonylphenyl)bilin-1-one (6). 5-Oxaporphyrin **2** (26.2 mg, 0.0293 mmol) was placed in a 200 mL three-necked flask, and dry dichloromethane (100 mL) was added. Butylamine (1 mL) was added into the three-necked flask, and the reaction mixture was stirred at room temperature for 2 h. Then the dichloromethane solution was washed with 1 M HCl and with brine. The organic layer was dried over K_2CO_3. Evaporation of the solvent under reduced pressure gave a green solid. The product was purified by silica gel chromatography using chloroform as eluent to yield 20.1 mg of **6** (87%).

^{1}H NMR (500 MHz, acetone-d_6): δ 0.71 (t, J = 6.85 Hz, 3H), 1.12 (q, J = 6.85 Hz, 2H), 1.40 (m, 2H), 3.23 (bm, 1H), 3.94−3.95 (m, 9H), 6.13 (d, J = 5.70 Hz, 1H), 6.31 (d, J = 4.60 Hz, 1H), 6.36 (s, 1H), 6.54 (d, J = 4.00 Hz, 1H), 6.61 (bs, 1H), 6.74 (d, J = 4.55 Hz, 1H), 6.87 (d, J = 4.60 Hz, 1H), 6.98 (bs, 1H), 7.04 (d, J = 5.70 Hz, 1H), 7.57−7.75 (m, 6H), 8.11−8.18 (m, 6H), 10.38 (s, 1H; NH), 13.62 (s, 1H). ^{13}C NMR (125 MHz, acetone-d_6): δ 13.9, 20.7, 32.3, 43.0, 52.49, 52.56, 52.64, 117.4, 118.1, 121.1, 124.2, 125.3, 125.8, 127.5, 129.7, 129.9, 130.2, 130.5, 130.6, 131.9, 132.5, 133.3, 134.5, 135.8, 137.6, 138.1, 139.2, 142.4, 142.6, 143.6, 143.7, 145.1, 151.9, 156.0, 166.0, 166.97, 167.03, 167.1, 169.9, 170.7. MS (MALDI-TOF): m/z 788 $[M + H]^+$. HRMS (FAB): calcd for $C_{47}H_{42}O_7N_5$ m/z 788.3054, found 788.3084. UV−vis ($CHCl_3$, 25 °C): λ_{max} (ε_{max}) 336 (3.72×10^4), 420 (4.21×10^4), 699 nm (1.67×10^4 M^{-1} cm^{-1}).

21*H*,23*H*-(4*Z*,9*Z*,15*Z*)-1,21-Dihydro-5,10,15-tris(4-methoxycarbonylphenyl)-19-*N*-phenylaminobilin-1-one (7). 5-Oxaporphyrin **2** (27.0 mg, 0.0303 mmol) was placed in a 200 mL three-necked flask, and dry dichloromethane (100 mL) was added. Distilled aniline (9.15 mL, 0.100 mol) was added into the three-necked flask, and the reaction mixture was refluxed for 10 h. After it was cooled to room temperature, the reaction mixture was washed twice with 1 M HCl and twice with brine. The organic layer was dried over Na_2SO_4. Evaporation of the solvent under reduced pressure gave a green solid. The product was purified by silica gel chromatography using chloroform/acetone (17/3) as eluent. Further purification by silica gel column chromatography using chloroform yielded 20.8 mg of **7** (85%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 3.97 (three overlapped singlets, 9H; $COOCH_3$), 6.07 (d, J = 5.70 Hz, 1H), 6.42 (three overlapped doublets, 2H), 6.50 (d, J = 4.60 Hz 1H), 6.56 (d, J = 4.00 Hz, 1H), 6.85 (d, J = 5.70 Hz, 1H), 6.91 (three overlapped doublets, 3H), 7.05 (m, 2H), 7.12 (m, 4H), 7.68 (m, 4H), 8.01 (d, J = 8.00 Hz, 2H), 8.14 (m, 4H), 9.89 (s, 1H; NH), 13.0 (s, 1H; NH). ^{13}C NMR (125 MHz, $CDCl_3$): δ 52.26, 52.30, 52.4, 117.9, 119.2, 119.4, 123.4, 124.3, 124.6, 126.0, 127.7, 128.8, 129.0, 129.12, 129.16, 129.6, 129.9, 131, 131.5, 131.6, 132.4, 134.2, 136.4, 136.6, 137.8, 138.1, 139.1, 140.5, 141.3, 142.0, 142.5, 142.8, 151.5, 164.4, 165.7, 166.68, 166.77, 166.90, 170.2. MS (MALDI-TOF): m/z 808.0 $[M + H]^+$. HRMS (FAB): calcd for $C_{49}H_{38}O_7N_5$ m/z 808.2766, found 808.2766. UV−vis ($CHCl_3$, 25 °C): λ_{max} (ε_{max}) 366 (4.09×10^4), 433 (4.46×10^4), 706 nm (1.23×10^4 M^{-1} cm^{-1}).

(21*H*,23*H*,24*H*)-(4*Z*,9*Z*,15*Z*)-5,10,15-Tris(4-methoxycarbonylphenyl)-19-thioxo-1,19,21,24-tetrahydrobilin-1-one (8). 5-Oxaporphyrin **2** (25.0 mg, 0.0280 mmol) was placed in a 200 mL three-necked flask, and acetone (100 mL) was added. An aqueous solution of 2.6 M of sodium hydrogen sulfide (200 μL) was added to the solution of **2**, and the reaction mixture was stirred at room temperature for 30 s. Then chloroform (50 mL) was added to the reaction mixture, and the chloroform solution was washed with 1 M HCl and with brine. The organic layer was dried over Na_2SO_4. Evaporation of the solvent under reduced pressure gave a green solid. The product was purified by silica gel chromatography using chloroform as eluent. Thioxobilinone eluted in the latter fraction was further purified by silica gel column chromatography using dichloromethane/methanol (30/1). The thioxobilinone fraction was further purified by preparative silica gel TLC using dichloromethane/ethyl acetate (20/1) to yield 11.3 mg (54%) of **8**.

^{1}H NMR (500 MHz, $CDCl_3$): δ 3.92 (s, 3H; $COOCH_3$), 3.95 (s, 3H; $COOCH_3$), 4.00 (s, 3H; $COOCH_3$), 6.08 (d, J = 5.20 Hz, 1H; pyrrole H-2), 6.66 (d, J = 4.60 Hz, 1H; pyrrole H-7), 6.72 (d, J = 5.15 Hz, 1H; pyrrole H-18), 6.82 (d, J = 4.60 Hz, 1H; pyrrole H-12), 7.04−7.06 (two overlapped doublets, 2H; pyrrole H-8 and H-13), 7.16 (d, J = 5.20 Hz, 1H; pyrrole H-3), 7.26 (1H; pyrrole H-17, overlapped with $CHCl_3$), 7.51 (d, J = 8.00 Hz, 2H; 5-phenylene H-2′), 7.64 (d, J = 8.00 Hz, 2H; 10-phenylene H-2′), 7.74 (d, J = 8.60 Hz, 2H; 15-phenylene H-2′), 8.10 (d, J = 8.00 Hz, 2H; 5-phenylene H-3′), 8.14 (d, J = 8.00 Hz, 2H; 10-phenylene H-3′), 8.23 (d, J = 8.60 Hz, 2H; 15-phenylene H-3′), 11.05 (s, 1H; NH). ^{13}C NMR (125 MHz, $CDCl_3$): δ 52.3 ($COOCH_3$), 52.4 ($COOCH_3$), 117.3, 118.2 (pyrrole C-13), 123.25 (pyrrole C-2 or C-17), 123.31 (pyrrole C-2 or C-17), 124.6 (pyrrole C-12), 126.7, 129.4, 129.5, 129.6, 130.2, 130.4, 130.5, 130.6, 131.2, 131.8, 132.1 (pyrrole C-8), 134.4 (pyrrole C-17), 136.2, 138.1 (pyrrole C-3 or C-4), 138.2 (pyrrole C-3 or C-4), 140.6, 141.1, 142.9 (pyrrole C-9), 144.1(pyrrole C-16), 145.1 (pyrrole C-11 or C-14), 152.0 (pyrrole C-6), 152.9(pyrrole C-14), 166.5 ($COOCH_3$), 166.6 ($COOCH_3$), 170.6 (pyrrole C-1), 188.6 (pyrrole C-19). MS (MALDI-TOF): m/z 749 $[M + H]^+$. HRMS (FAB): calcd for $C_{43}H_{33}O_7N_4S$ m/z 749.2070, found 749.2059. UV−vis ($CHCl_3$, 25 °C): λ_{max} (ε_{max}) 332 (2.78×10^4), 360 (3.34×10^4), 444 (4.75×10^4),

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676 nm (1.62×10^4 M^{-1} cm^{-1}). IR (KBr): 3124, 2954, 2881, 1722, 1608, 1540, 1508, 1435, 1278, 1191, 1145, 1113, 966 cm^{-1}.

21*H*,23*H*-(4*Z*,9*Z*,15*Z*)-19-Butylsulfanyl-1,21-dihydro-5,10,15-tris(4-methoxycarbonylphenyl)bilin-1-one (9). 5-Oxaporphyrin **2** (25.2 mg, 0.0283 mmol) was placed in a 100 mL three-necked flask, and dry dichloromethane (20 mL) was added. Butanethiol (30 μL, 0.274 mmol) and sodium hydride (60% oil dispersion, 40 mg, 1.00 mmol) were added to dry THF (10 mL). The thiolate solution (2 mL) was added dropwise to the 5-oxaporphyrin solution, and the reaction mixture was stirred at room temperature for 1 min. Then the dichloromethane solution was washed with water, with 1 M HCl, and with brine. The organic layer was dried over Na_2SO_4. Evaporation of the solvent under reduced pressure gave a green solid. The product was purified on silica gel chromatography using chloroform as eluent to yield 14.3 mg of **9** (63%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 0.62 (t, *J* = 7.60 Hz, 3H; CH_3), 0.99 (septet, *J* = 7.60 Hz, 2H; CH_2), 1.37 (sextet, *J* = 7.60 Hz, 2H; CH_2), 2.57 (bs, 2H; SCH_2), 3.98−3.99 (three overlapped singlets, 9H; $COOCH_3$), 6.09 (d, *J* = 5.50 Hz, 1H; pyrrole H-2), 6.52 (d, *J* = 4.80 Hz, 1H; pyrrole H-18), 6.53 (m, 1H; pyrrole H-13), 6.59 (m, 1H; pyrrole H-12), 6.65 (d, *J* = 4.80 Hz, 1H; pyrrole H-7), 6.95 (d, *J* = 4.80 Hz, 1H; pyrrole H-17), 6.98 (d, *J* = 4.80 Hz, 1H; pyrrole H-8), 7.04 (d, *J* = 5.50 Hz, 1H; pyrrole H-3), 7.53 (d, *J* = 8.25 Hz, 2H; 5-phenylene H-2′), 7.68 (d, *J* = 8.95 Hz, 2H; 10-phenylene H-2′), 7.72 (d, *J* = 8.25 Hz, 2H; 15-phenylene H-2′), 8.15−8.18 (m, 6H; 5,10,15-phenylene H-3′), 9.63 (s, 1H; NH), 12.51 (s, 1H; NH). ^{13}C NMR (125 MHz, $CDCl_3$): δ 13.3 (CH_3), 22.2 (CH_2), 30.7 (CH_2) 31.2 (SCH_2), 52.31 ($COOCH_3$), 52.37 ($COOCH_3$), 52.42 ($COOCH_3$), 116.8, 120.6 (pyrrole C-13), 123.7 (pyrrole C-12), 124.9 (pyrrole C-2), 126.9 (pyrrole C-18), 128.3 (pyrrole C-7), 129.09, 129.12, 129.5, 129.9, 130.3, 131.1, 131.6, 132.5, 135.0 (pyrrole C-8), 136.4 (pyrrole C-17), 136.8 (pyrrole C-3), 137.4, 137.5 (pyrrole C-11 or C-14), 141.1, 141.3, 141.6 (pyrrole C-11 or C-14), 142.3 (pyrrole C-4), 152.2 (pyrrole C-9), 152.9 (pyrrole C-16), 166.6 ($COOCH_3$), 166.7 ($COOCH_3$), 166.8 ($COOCH_3$), 167.0 (pyrrole C-6), 170.1 (pyrrole C-1), 172.7 (pyrrole C-19). MS (MALDI-TOF): *m*/*z* 805 $[M + H]^+$. HRMS (FAB): calcd for $C_{47}H_{41}O_7N_4S$ *m*/*z* 805.2696, found 805.2721. UV−vis ($CHCl_3$, 25 °C): λ_{max} (ε_{max}) 346 (3.45×10^4), 427 (4.17×10^4), 668 nm (1.07×10^4 M^{-1} cm^{-1}).

21*H*,23*H*-(4*Z*,9*Z*,15*Z*)-1,21-Dihydro-5,10,15-tris(4-methoxycarbonylphenyl)-19-phenylsulfanylbilin-1-one (10). 5-Oxaporphyrin **2** (25.2 mg, 0.0283 mmol) was placed in a 100 mL three-necked flask, and dry dichloromethane (20 mL) was added. Thiophenol (28.8 μL, 0.281 mmol) and sodium hydride (60% oil dispersion, 40 mg, 1.00 mmol) were added to dry THF (10 mL). The thiolate solution (8 mL) was added dropwise to the 5-oxaporphyrin solution, and the reaction mixture was stirred at room temperature for 5 min. Then the dichloromethane solution was washed twice with water, twice with 1 M HCl, and once with water. The organic layer was dried over Na_2SO_4. Evaporation of the solvent under reduced pressure gave a green solid. The product was purified by silica gel chromatography using chloroform as eluent. Further purification by preparative silica gel TLC using dichloromethane/ethyl acetate (40/1) yielded 12.5 mg of **10** (53%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 3.96−3.98 (three overlapped singlets, 9H; $COOCH_3$), 6.11−6.13 (two overlapped doublets, 2H; pyrrole H-2 and H-18), 6.52−6.54 (two overlapped doublets, 2H; pyrrole H-7 and H-13), 6.57 (d, *J* = 3.45 Hz, 1H), 6.85 (d, *J* = 4.15 Hz, 1H; pyrrole H-17), 6.94 (d, *J* = 4.15 Hz; pyrrole H-8), 7.09 (d, *J* = 6.20 Hz, 1H; pyrrole H-3), 7.38−7.47 (m, 3H; phenyl), 7.43 (d, *J* = 7.60 Hz, 2H; phenyl), 7.54 (d, *J* = 8.25 Hz, 2H; 15-phenylene H-2′), 7.67 (d, *J* = 8.25 Hz, 2H; 10-phenylene H-2′), 7.69 (d, *J* = 8.25 Hz, 2H; 5-phenylene H-2′), 8.12−8.16 (m, 6H; 5,10,15-phenylene H-3′), 9.79 (s, 1H; NH), 12.76 (s, 1H; NH). ^{13}C NMR (125 MHz, chloroform-*d*): δ 52.3 ($COOCH_3$), 52.4 ($COOCH_3$), 117.8, 121.4 (pyrrole C-7 or C-13), 123.1 (pyrrole C-12), 124.8 (pyrrole C-18), 125.2 (pyrrole C-2), 128.8 (pyrrole C-7 or C-13), 129.07, 129.10, 129.2, 129.5, 129.8, 130.3, 130.4, 131.0, 131.4, 131.5, 131.7, 132.3, 134.4, 135.2 (pyrrole C-8), 135.8 (pyrrole C-17), 137.2 (pyrrole C-3), 138.2 (pyrrole C-11 or C-14), 140.5 (pyrrole C-11 or C-14), 141.3, 141.6, 142.3 (pyrrole C-4), 152.8 (pyrrole C-16), 152.9 (pyrrole C-9), 166.7 ($COOCH_3$), 166.8 ($COOCH_3$), 168.0 (pyrrole C-6), 170.8 (pyrrole C-1), 173.5 (pyrrole C-19). MS (MALDI-TOF): *m*/*z* 825 $[M + H]^+$. HRMS (FAB): calcd for $C_{49}H_{37}O_7N_4S$ *m*/*z* 825.2377, found 825.2389. UV−vis ($CHCl_3$, 25 °C): λ_{max} (ε_{max}) 342 (3.74×10^4), 430 (5.47×10^4), 667 nm (1.23×10^4 M^{-1} cm^{-1}).

21*H*,22*H*,24*H*-(4*Z*,9*Z*,15*Z*,19*E*)-19-(1-Ethoxycarbonyl-2-oxopropylidene)-5,10,15-tris(4-methoxycarbonylphenyl)-1,19,21,24-tetrahydrobilin-1-one (11). 5-Oxaporphyrin **2** (30.4 mg, 0.0341 mmol) was placed in a 100 mL three-necked flask, and dry THF (20 mL) was added. Ethyl acetoacetate (100 μL, 0.785 mmol) and sodium hydride (60% oil dispersion, 33.3 mg, 0.833 mmol) were added to dry THF (1 mL). The enolate suspension was added dropwise to the 5-oxaporphyrin solution, and the reaction mixture was stirred at room temperature for 10 min. Then chloroform (50 mL) was added to the reaction mixture, and the chloroform solution was washed with 1 M HCl and with water. The organic layer was dried over Na_2SO_4. Evaporation of the solvent under reduced pressure gave a green solid. The product was purified by silica gel chromatography using chloroform as eluent to yield 18.7 mg of **11** (66%).

^{1}H NMR (500 MHz, acetone-d_6): δ 1.24 (t, *J* = 6.90 Hz, 3H; CH_3), 2.00 (s, 3H; $COCH_3$), 3.88 (s, 3H; $COOCH_3$), 3.93 (s, 3H; $COOCH_3$), 3.96 (s, 3H; $COOCH_3$), 4.19 (q, *J* = 6.90 Hz, 3H; $COOCH_2$), 6.18 (d, *J* = 5.40 Hz, 1H; pyrrole H-2), 6.65 (d, *J* = 4.30 Hz, 1H; pyrrole H-12), 6.69−6.71 (m, 1H; pyrrole H-7), 6.85−6.89 (two overlapped doublets, 2H; pyrrole H-8 and H-17), 6.97 (d, *J* = 4.350 Hz, 1H; pyrrole H-13), 7.07 (d, *J* = 5.40 Hz, 1H; pyrrole H-3), 7.48 (d, *J* = 5.75 Hz, 1H; pyrrole H-18), 7.54 (d, *J* = 8.60 Hz, 2H; 5-phenylene H-2′), 7.60 (d, *J* = 8.60 Hz, 2H; 10-phenylene H-2′), 7.77 (d, *J* = 8.60 Hz, 2H; 15-phenylene H-2′), 8.03 (d, *J* = 8.60 Hz, 2H; 5-phenylene H-3′), 8.12 (d, *J* = 8.60 Hz, 2H; 10-phenylene H-3′), 8.19 (d, *J* = 8.60 Hz, 2H; 15-phenylene H-3′), 8.28 (s, 1H; NH), 11.61 (s, 1H; NH), 11.89 (s, 1H; NH). ^{13}C NMR (125 MHz, acetone-d_6): δ 14.6 (CH_3), 31.0 ($COCH_3$), 52.5 ($COOCH_3$), 52.6 ($COOCH_3$), 60.8 ($COOCH_2$), 103.9 (methylene), 116.6, 120.7 (pyrrole C-7), 122.5, 124.2 (pyrrole C-2), 127.2 (pyrrole C-8 and C12), 129.8, 129.9, 130.0, 130.9 (pyrrole C-18), 131.0, 131.8, 132.6 (pyrrole C-17), 132.8, 133.3, 134.2 (pyrrole C-13), 137.9, 138.2 (pyrrole C-3), 138.8 (pyrrole C-6 or C-9), 139.7 (pyrrole C-4), 142.5, 142.6, 143.0 (pyrrole C-16), 146.4 (pyrrole C-6 or C-9), 150.4 (pyrrole C-11), 157.8 (pyrrole C-19), 161.2 (pyrrole C-14), 166.9 ($COOCH_3$), 167.9 ($COOCH_2$), 171.1 (pyrrole C-1), 195.5 ($COCH_3$). MS (MALDI-TOF): *m*/*z* 845 $[M + H]^+$. HRMS (FAB): calcd for $C_{49}H_{41}O_{10}N_4$ *m*/*z* 845.2823, found 845.2824. UV−vis ($CHCl_3$, 25 °C): λ_{max} (ε_{max}) 371 (4.19×10^4), 463 (4.82×10^4), 706 nm (1.75×10^4 M^{-1} cm^{-1}).

21*H*,22*H*,24*H*-(4*Z*,9*Z*,15*Z*)-19-(1-Acetyl-2-oxopropylidene)-5,10,15-tris(4-methoxycarbonylphenyl)-1,19,21,24-tetrahydrobilin-1-one (12). 5-Oxaporphyrin **2** (20.7 mg, 0.0232 mmol) was placed in a 100 mL three-necked flask, and dry THF (20 mL) was added. Acetylacetone (100 μL, 0.984 mmol) and sodium hydride (60% oil dispersion, 40 mg, 1.00 mmol) were added to dry THF (1 mL). The enolate suspension was added dropwise to the 5-oxaporphyrin solution, and the reaction mixture was stirred at room temperature for 10 min. Then chloroform (50 mL) was added to the reaction mixture, and the chloroform solution was washed with 1 M HCl and then with water. The organic layer was dried over Na_2SO_4. Evaporation of the solvent under reduced pressure gave a green solid. The product was purified by silica gel chromatography using chloroform as eluent to yield 12.3 mg of **12** (65%).

^{1}H NMR (500 MHz, acetone-d_6): δ 1.99 (s, 3H; $COCH_3$), 2.34 (s, 3H; $COCH_3$), 3.93 (s, 3H; $COOCH_3$), 3.95 (s, 3H; $COOCH_3$), 3.96 (s, 3H; $COOCH_3$), 6.19 (d, *J* = 5.70 Hz, 1H; pyrrole H-2), 6.61 (d, *J* = 4.60 Hz, 1H; pyrrole H-12), 6.68−6.71 (m, 1H; pyrrole H-7), 6.84−6.89 (two overlapped doublets, 2H; pyrrole H-8 and H-17), 6.94 (d, *J* = 4.60 Hz, 1H; pyrrole H-13), 7.11 (d, *J* = 5.75 Hz, 1H; pyrrole H-3), 7.19 (d, *J* = 5.70 Hz, 1H; pyrrole H-18), 7.55 (d, *J* = 8.60 Hz, 2H; 5-phenylene H-2′), 7.60 (d, *J* = 8.60 Hz, 2H; 10-phenylene H-2′), 7.77 (d, *J* = 8.60 Hz, 2H; 15-phenylene H-2′), 8.04 (d, *J* = 8.60 Hz, 2H; 5-phenylene H-3′), 8.12 (d, *J* = 8.60 Hz, 2H; 10-phenylene H-3′), 8.19 (d, *J* = 8.60 Hz, 2H; 15-phenylene H-3′), 8.47 (s, 1H; NH), 11.63 (s,

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1H; NH), 12.17 (s, 1H; NH). ^{13}C NMR (125 MHz, acetone-d_6): δ 31.3 ($COCH_3$), 52.4 ($COOCH_3$), 52.5 ($COOCH_3$), 115.2 (methylene), 116.7, 120.4 (pyrrole C-12), 121.9, 124.4, 126.8 (pyrrole C-8), 127.2 (pyrrole C-12), 128.9 (pyrrole C-18), 129.9, 130.0, 130.9, 131.8, 132.6, 132.7, 132.9 (pyrrole C-17), 133.2, 134.3 (pyrrole C-13), 137.8, 138.2 (pyrrole C-3), 138.7 (pyrrole C-6 or C-9), 139.5, 139.6 (pyrrole C-4), 142.5, 143.0, 144.1 (pyrrole C-16), 146.2 (pyrrole C-6 or C-9), 150.6 (pyrrole C-11), 155.8 (pyrrole C-19), 161.9 (pyrrole C-14), 166.9 ($COOCH_3$), 171.3 (pyrrole C-1), 194.7 ($COCH_3$), 199.6 ($COCH_3$). MS (MALDI-TOF): m/z 814 $[M]^+$. HRMS (FAB): calcd for $C_{48}H_{38}O_9N_4$ m/z 814.2639, found 814.2657. UV−vis ($CHCl_3$, 25 °C): λ_{max} (ε_{max}) 331 (2.94×10^4), 371 (3.55×10^4), 459 (4.09×10^4), 706 nm (1.49×10^4 M^{-1} cm^{-1}).

21*H*,22*H*,24*H*-(4*Z*,9*Z*,15*Z*,19*E*)-19-((*E*)-1-Acetyl-2-oxo-4-phenyl-3-butenylidene)-5,10,15-tris(4-methoxycarbonylphenyl)-1,19,21,24-tetrahydrobilin-1-one (13). 5-Oxaporphyrin **2** (25.2 mg, 0.0283 mmol) was placed in a 100 mL three-necked flask, and dry THF (15 mL) was added. (*E*)-6-Phenyl-5-hexene-2,4-dione (56 mg, 0.298 mmol) and sodium hydride (60% oil dispersion, 40 mg, 1.00 mmol) were added to dry THF (5 mL). (*E*)-6-Phenyl-5-hexene-2,4-dione was synthesized according to the literature.[44] The enolate suspension was added dropwise to the 5-oxaporphyrin solution, and the reaction mixture was stirred at room temperature for 5 min. Then chloroform (50 mL) was added to the reaction mixture, and the chloroform solution was washed with 1 M HCl and with water. The organic layer was dried over Na_2SO_4. Evaporation of the solvent under reduced pressure gave a green solid. The product was purified by silica gel chromatography using chloroform/acetone (20/1) as eluent. Further purification by preparative silica gel TLC using dichloromethane/acetone (20/1) yielded 18.3 mg of **13** (72%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 2.07 (s, 3H; $COCH_3$), 3.92 (s, 3H; $COOCH_3$), 3.96 (s, 3H; $COOCH_3$), 4.00 (s, 3H; $COOCH_3$), 6.17 (dd, J = 5.50, 1.35 Hz, 1H; pyrrole H-2), 6.55 (d, J = 4.80 Hz, 1H; pyrrole H-12; pyrrole H-7), 6.76 (d, J = 4.80 Hz, 1H; pyrrole H-12), 6.79 (d, J = 15.8 Hz, 1H; C═CH), 6.87−6.88 (two overlapped doublets, 2H; pyrrole H-8 and H-17), 6.95 (d, J = 4.80 Hz, 1H; pyrrole H-13), 7.06 (d, J = 5.50 Hz, 1H; pyrrole H-3), 7.13 (d, J = 5.75 Hz, 1H; pyrrole H-18), 7.35−7.41 (m, 5H; phenyl), 7.52 (d, J = 15.8 Hz, 1H; C═CH), 7.54 (d, J = 8.25 Hz, 2H; 5-phenylene H-2′), 7.59 (d, J = 8.25 Hz, 2H; 10-phenylene H-2′), 7.73 (d, J = 8.25 Hz, 2H; 15-phenylene H-2′), 8.01 (d, J = 8.25 Hz, 2H; 5-phenylene H-3′), 8.13 (d, J = 8.25 Hz, 2H; 10-phenylene H-3′), 8.21 (d, J = 8.25 Hz, 2H; 15-phenylene H-3′), 11.36 (s, 1H; NH), 11.95 (s, 1H; NH). ^{13}C NMR (125 MHz, $CDCl_3$): δ 29.9 ($COCH_3$), 52.28 ($COOCH_3$), 52.34 ($COOCH_3$), 52.4 ($COOCH_3$), 113.0, 117.4, 121.3, 122.7 (pyrrole C-7), 123.7 (pyrrole C-2), 124.5 (pyrrole C-12), 127.5 (pyrrole C18), 128.1, 128.3, 128.5, 128.9, 129.0, 129.2 (pyrrole C-8 or C-17), 129.4, 130.21, 130.24, 130.6, 130.6, 131.0 (pyrrole C-13), 131.2, 131.7, 131.8, 132.0, 132.1, 132.4, 134.5 (pyrrole C-8 or C-17), 136.8, 137.1 (pyrrole C-3), 137.4 (pyrrole C-4), 141.1, 141.4, 141.7, 142.7 (pyrrole C-9), 143.1 (PhCH═), 145.8, (pyrrole C-10 or C-14), 151.5 (pyrrole C-6), 155.6 (pyrrole C-10 or C-14), 156.6 (pyrrole C-19), 166.53 ($COOCH_3$), 166.56 ($COOCH_3$), 155.60 ($COOCH_3$), 170.0 (pyrrole C-1), 191.7 (COCH═), 194.9 ($COCH_3$). MS (MALDI-TOF): m/z 903 $[M + H]^+$. HRMS (FAB): calcd for $C_{55}H_{43}O_9N_4$ m/z 903.3030, found 903.3039. UV−vis ($CHCl_3$, 25 °C): λ_{max} (ε_{max}) = 372 (4.54×10^4), 480 (5.18×10^4), 723 nm (2.12×10^4 M^{-1} cm^{-1}).

■ ASSOCIATED CONTENT

Supporting Information

An X-ray crystallographic file for **3** in CIF format, the numbering scheme of **1**−**13**, ^{1}H NMR and ^{13}C NMR spectra of **4**−**13**, UV−visible spectra of **1**, **4**, **5**, **7**, **8**, **10**, and **12**, tautomeric structures of **11**, and crystallographic data for **3**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

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