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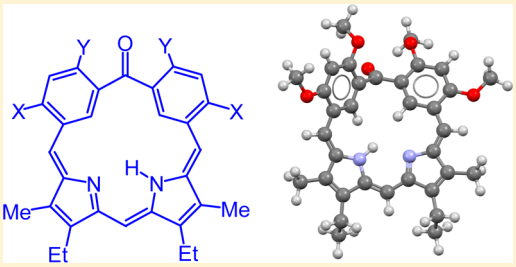
# Dicarbaporphyrinoid Systems. Synthesis of Oxo-*adj*-dibenziphlorins

Deyaa I. AbuSalim, Michelle L. Merfeld, and Timothy D. Lash*

Department of Chemistry, Illinois State University, Normal, Illinois 61790-4160, United States

Supporting Information

**ABSTRACT:** A series of diformylbenzophenones were generated by sequentially reacting protected bromobenzaldehydes with *n*-butyllithium and ethyl *N*,*N*-dimethylcarbamate. The acetal protective groups were cleaved with refluxing formic acid. Vilsmeier−Haack formylation of 2,2′,4,4′-tetramethoxybenzophenone also afforded a related dialdehyde. MacDonald "2 + 2" condensation of three benzophenone dialdehydes with a dipyrrylmethane gave oxophlorin analogues constructed from two benzene and two pyrrole rings. The free base oxodibenziphlorins were rather unstable in solution, and in most cases these porphyrinoids were isolated as the corresponding trifluoroacetate salts. The spectroscopic properties of 6-oxo-*adj*-dibenziphlorins are consistent with a nonaromatic ring system. DFT calculations indicated that the macrocycles considerably diverge from planarity, particularly when methoxy substituents are present on the arene rings.



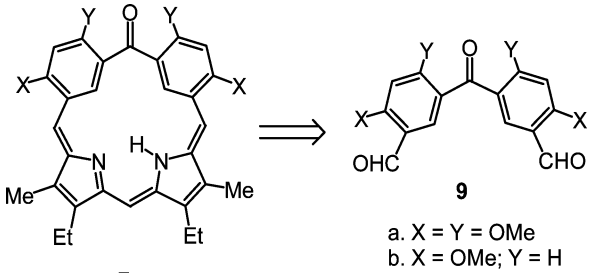

## INTRODUCTION

Carbaporphyrinoids are porphyrin analogues where one or more of the internal nitrogen atoms have been replaced by carbons.[1] N-confused porphyrins[2] and other monocarbaporphyrinoid systems with one interior carbon atom have been extensively studied over the last 20 years,[3] but far less work has been carried out on dicarbaporphyrinoids.[4−10] The spectroscopic properties and aromatic characteristics of these porphyrinoid macrocycles are very much dependent upon the identity of the individual subunits.[1] For instance, monocarbaporphyrin structures with cyclopentadiene or indene subunits are highly diatropic and have spectroscopic properties that closely resemble those of true porphyrins.[1] However, azuliporphyrins, which have one azulene and three pyrrolic subunits, have much reduced diatropic character and exhibit UV−vis and NMR spectra that are quite different from those of the porphyrins.[1] Dicarbaporphyrinoids with two indene subunits (structure **1**),[4] two azulenes (structure **2**),[5] one indene and one azulene (structures **3** and **4**),[6,7] and one indene and one benzene moiety (structure **5**)[8] have been reported, and these again show a wide range of aromatic properties and diverse spectroscopic characteristics. Benziporphyrins (**6**), carbaporphyrinoids with a benzene ring in place of a pyrrolic subunit,[11,12] have proven to be an important class of carbaporphyrinoids. Although the free base structures are nonaromatic, the corresponding diprotonated species show significant diatropic character.[13] This is enhanced by the presence of electron-donating methoxy groups.[14] Furthermore, 2-hydroxybenziporphyrins undergo a keto−enol type tautomerization to afford fully aromatic oxybenziporphyrins[15] and further oxidized species have also been described. Benziporphyrins readily undergo metalation reactions to form organometallic derivatives,[12] and a related system has been developed as a zinc cation sensor.[16] The possibility of preparing dibenziporphyrins, conjugated dicarbaporphyrinoids consisting of two benzene and two pyrrole rings, has not been investigated previously. In fact, the formation of conjugated macrocycles of this type is complicated by the fact that the arene subunits are likely to interrupt any conjugation pathways. With this in mind, a series of oxophlorin analogues **7** were targeted for investigation. Oxophlorins **8** are the keto tautomers of 5-hydroxyporphyrins[17] and are implicated in the breakdown of heme to form biliverdin IX$\alpha$.[18] Oxodibenziphlorins **7** would have a continuous arrangement of sp$^2$-hybridized atoms but would not be expected to exhibit any aromatic characteristics. An efficient route to this system has been developed, and the properties of these novel dibenziporphyrinoids are reported.[19]

## RESULTS AND DISCUSSION

A retrosynthetic analysis of the oxodibenziphlorin system indicates that benzophenone dialdehydes **9** would be well suited as late-stage intermediates (Scheme 1). With this in mind, syntheses of benzophenones **9** were developed starting from 3-bromobenzaldehydes **10** (Scheme 2). The bromo derivative **10a**

**Scheme 1**

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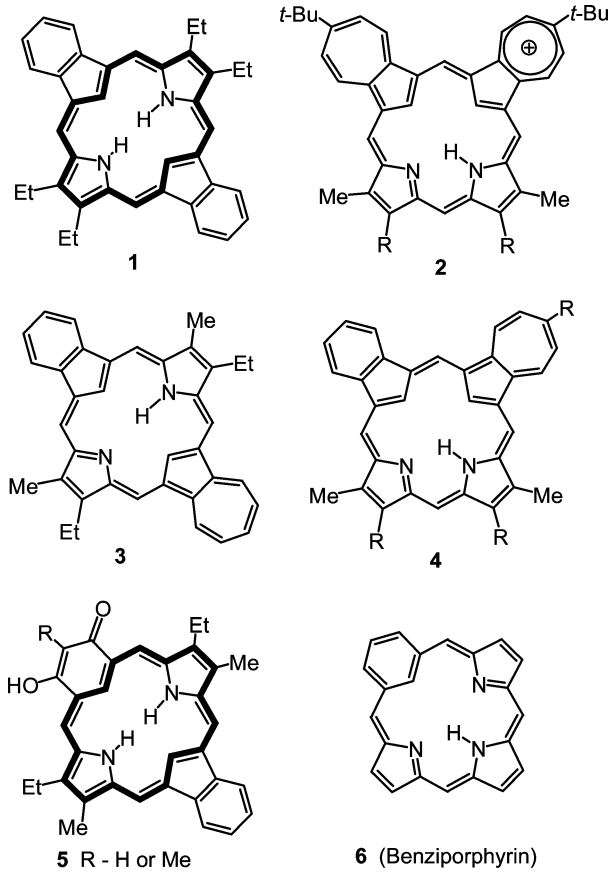
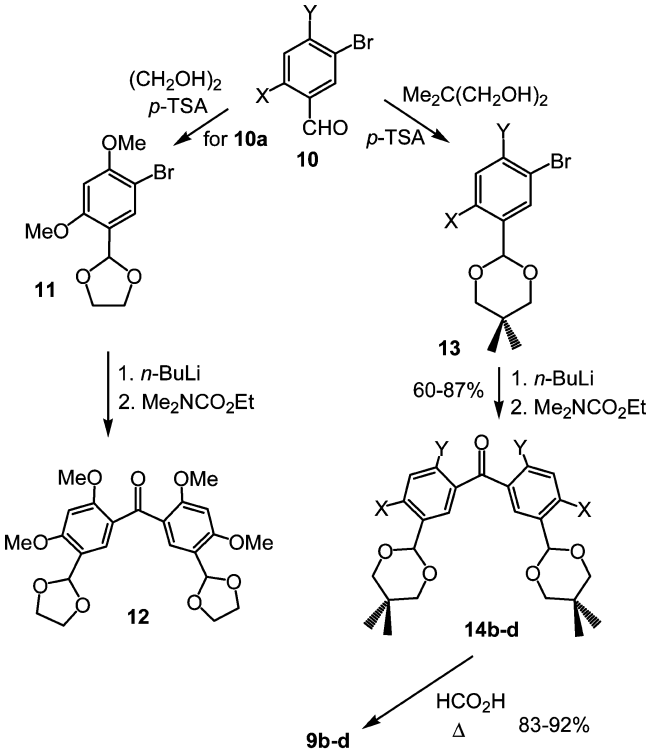



was prepared in 86% yield by reacting 2,4-dimethoxybenzaldehyde with bromine in acetic acid. Initially, we attempted to protect the aldehyde group with ethylene glycol to give acetal **11**. This chemistry was carried out using Dean–Stark conditions with *p*-toluenesulfonic acid as the catalyst, and the acetal could be isolated in 95% yield. Unfortunately, **11** proved to be somewhat unstable and gave poor results in subsequent reactions. Metal–halogen exchange with *n*-butyllithium, followed by reaction with ethyl *N*,*N*-dimethylcarbamate, afforded the protected benzophenone **12** in up to 28% yield. However, the results were very variable and much lower yields were obtained in many cases. Cleavage of the acetal group was accomplished in refluxing formic acid to give benzophenone dialdehyde **9a** in 57% yield. Due to the difficulties in preparing **12**, aldehyde **10a** was protected with neopentyl glycol (2,2-dimethyl-1,3-propanediol) to give the corresponding acetal **13a**. This species proved to be very robust and could easily be recrystallized from ethanol to give **13a** as a white powder in 86% yield. This method was also used to protect benzaldehydes **10b–d** and afforded the corresponding acetals **13b–d** in 84–97% yield. Unfortunately, acetal **13a** could not be taken on to the corresponding diaryl ketone, as its very poor solubility in ether solvents prevented metal–halogen

**Scheme 2**

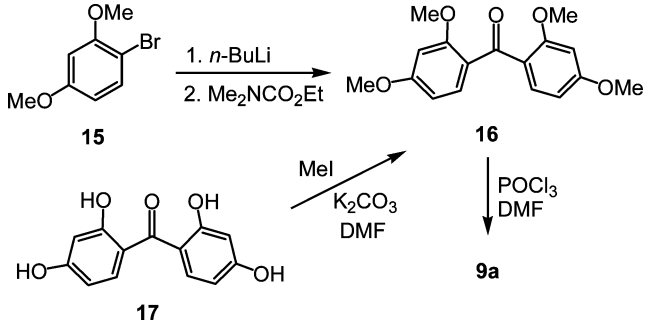



a. X = Y = OMe; b. X = OMe; Y = H; c. X = H; Y = OMe; d. X = Y = H

exchange. However, acetals **13b–d** have suitable solubilities and reacted with *n*-butyllithium, followed by ethyl *N*,*N*-dimethylcarbamate, to give good yields of the protected dialdehydes **14b–d**. Deprotection was accomplished in yields of 83–92% by refluxing the diacetals in formic acid.

An alternative strategy was devised to synthesize **13a** (Scheme 3). Monobromination of 1,3-dimethoxybenzene with *N*-

**Scheme 3**




bromosuccinimide gave the bromo derivative **15** in virtually quantitative yield.[20] Treatment with *n*-butyllithium, followed by addition of ethyl *N*,*N*-dimethylcarbamate, afforded tetramethoxybenzophenone (**16**) in 63% yield. Alternatively, **16** can be prepared by reacting tetrahydroxybenzophenone (**17**) with methyl iodide and potassium carbonate in DMF.[21] Vilsmeier–Haack formylation of **16** with $POCl_3$–DMF then gave the required dialdehyde **9a** in 84% yield. The intermediates were fully characterized by spectroscopic techniques and elemental analysis. The IR data for **9a–d** showed some interesting trends. For unsubstituted benzophenone dialdehyde **9d**, the aldehyde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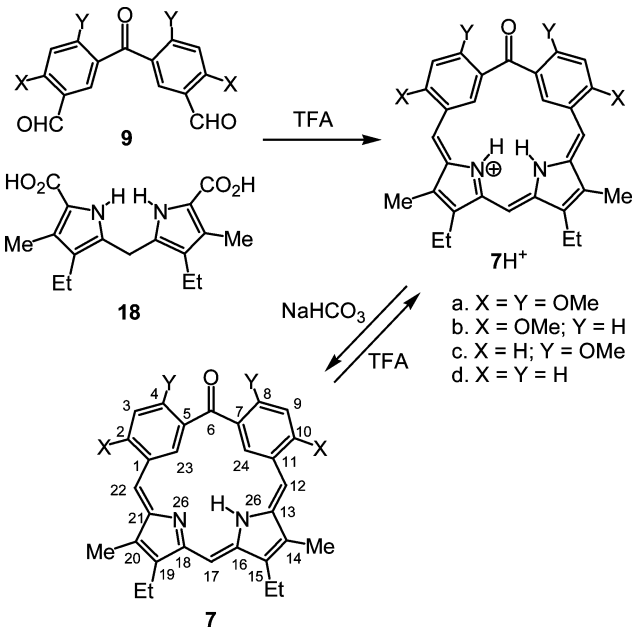
C═O stretch was observed at 1691 $cm^{-1}$, while the bridge C═O was present at 1655 $cm^{-1}$ (Table 1). Dimethoxy ketone **9b** showed a significant decrease in the frequency for the aldehydic carbonyl, which shifted to 1677 $cm^{-1}$, but the bridge carbonyl showed only a small decrease in frequency. On the other hand, the isomeric dialdehyde **9c** showed a significant shift to lower frequency for the bridge C═O, but the aldehyde units were essentially unaffected. Not surprisingly, the tetramethoxy system **9a** showed that both carbonyl groups had shifted to lower wavenumbers. The decreased frequencies are due to the electron-donating methoxy groups, and resonance contributors can be drawn to illustrate these changes. However, the effects only appear to be significant when the methoxy group is ortho, rather than para, to the affected carbonyl moiety. These changes give insights into the bond strength and reactivity of these carbonyl compounds.

**Table 1. Carbonyl Stretching Frequencies ($cm^{-1}$) in the Infrared Spectra for Benzophenone Dialdehydes 9a–d**

| | aldehyde C═O | bridge C═O |
|---|---|---|
| **9a** | 1668 | 1635 |
| **9b** | 1677 | 1650 |
| **9c** | 1692 | 1635 |
| **9d** | 1691 | 1655 |

Dialdehydes **9a–d** were reacted with dipyrrylmethanedicarboxylic acid **18** in a "2 + 2" MacDonald-type condensation[22] in the presence of catalytic trifluoroacetic acid (Scheme 4). Initially,

**Scheme 4**




**9a** was reacted under these conditions and the reaction solution was washed with aqueous sodium bicarbonate solution to remove acid. Following column chromatography on neutral grade 3 alumina, a deep purple band was collected corresponding to the macrocyclic product **7a**. Recrystallization from chloroform–hexanes gave the oxo-*adj*-dibenziphlorin as a dark purple solid in 35% yield. However, attempts to isolate oxophlorin analogues from the reaction of **18** with **9b–d** were unsuccessful. Column fractions that corresponded to the oxodibenziphlorins were observed in each case, but these proved to be rather unstable and rapidly underwent decomposition. A small amount of impure **7c** was obtained, but the product could not be fully characterized due to its instability. During the course of these studies, it was noted that these porphyrinoids were far more stable in protonated form. Hence, conditions were investigated where the macrocycles could be isolated as protonated species. The crude reaction mixture was evaporated under reduced pressure and taken up in chloroform, and the products were precipitated with hexanes. This simple strategy gave **7b**·TFA and **7d**·TFA as purple powders in 82% and 49% yields, respectively. Column chromatography could also be performed on silica gel using mixtures of TFA, methanol, and chloroform as the eluent. However, pure porphyrinoid **7c** could not be isolated under any of the conditions investigated. Nevertheless, the strategy could be used to prepare **7a**·TFA, which was isolated in an improved yield of 40%. The proton NMR spectra for the oxodibenziphlorins were straightforward and, as would be expected, showed no signs of overall aromatic character. The free base form of **7a** showed the bridging methine resonances in the olefinic region as a 1H singlet at 5.53 ppm and a 2H singlet at 6.54 ppm (Figure 1).

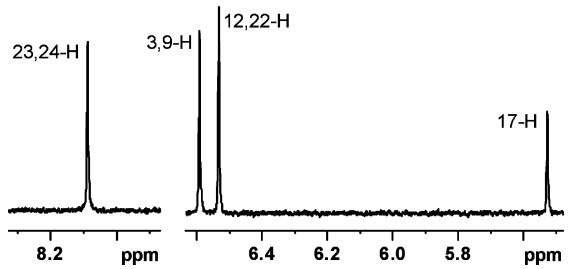



**Figure 1.** Partial 400 MHz proton NMR spectrum of **7a** in $CDCl_3$.

In TFA-$CDCl_3$, the *meso*-CH protons appeared as two singlets at 5.64 (1H) and 6.62 ppm (2H), while the interior and exterior arene protons gave rise to singlets at 7.73 and 6.92 ppm, respectively. The proton and carbon-13 NMR spectra also demonstrated that these macrocycles possess a plane of symmetry. In the case of free base **7a**, this apparent symmetry must be due to rapid NH tautomerization. The UV–vis spectra for the free base forms of **7a,b,d** were broad and showed no resemblance to porphyrin-type spectra. The spectrum of **7d** in 2.5% $Et_3N$–$CHCl_3$ showed absorptions at 339, 491, and 568 nm (Figure 2). However, in TFA–chloroform very different spectra were observed, due to the formation of the protonated species **7d**$H^+$. In 5% TFA–chloroform, absorption peaks were noted at 339, 526, 563, and 618 nm, where the peak at 563 nm dominated the spectrum (Figure 2). Minor changes were observed as the concentration of TFA was increased. The UV–vis spectrum for **7b** in 1% $Et_3N$–chloroform was similar to that for **7d**, showing broad absorption bands at 492 and 567 nm. Addition of TFA led to major changes, but in this case, a series of weak absorptions were observed between 450 and 650 nm and this spectrum showed no resemblance to that obtained for **7d**$H^+$. The results for tetramethoxyoxodibenziphlorin **7a** were even more distinctive. Free base **7a** in chloroform showed a band at 364 nm and a broad absorption centered on 580 nm (Figure 2). In 1% TFA–chloroform, a moderately strong absorption was noted at 311 nm and a broad absorption appeared at 649 nm (Figure 2). This spectrum was attributed to the monoprotonated cation **7a**$H^+$. Further changes were also noted at higher concentrations of TFA (Figure 2), and in 90% TFA–chloroform, a peak at 441 nm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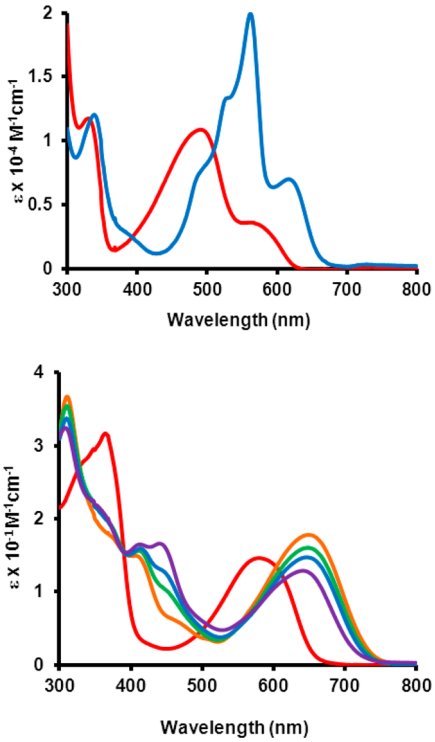
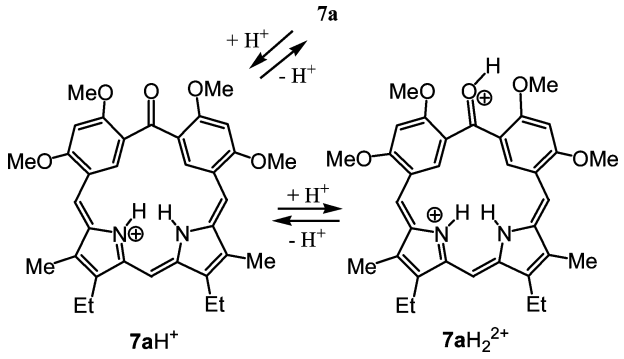



**Figure 2.** UV−vis spectra of oxodibenziphlorins **7a,d**: (top) spectra of **7d** in 2.5% $Et_3N$−chloroform (free base, red line) and 5% TFA−chloroform (cation **7d**$H^+$, blue line); (bottom) spectra of **7a** in chloroform (free base, red line), 1% TFA−$CHCl_3$ (orange line), 5% TFA−$CHCl_3$ (green line), 10% TFA−$CHCl_3$ (blue line), and 50% TFA−$CHCl_3$ (purple line). The latter spectra show the emergence of a diprotonated species.

emerged. This may be due to the diprotonated species **7a**$H_2^{2+}$ (Scheme 5) arising from protonation onto the carbonyl oxygen.

**Scheme 5**




This second protonation is likely to be more favored in this case due to stabilization by intramolecular hydrogen bonding to an adjacent methoxy group. The IR spectra for the macrocycles were difficult to interpret. The carbonyl stretch for **7a** was observed at 1655 $cm^{-1}$, demonstrating that the macrocyclic C═O moiety is not highly polarized, as this is a higher frequency than is observed for the bridge C═O in its benzophenone precursor **9a**. The protonated macrocycles **7**·TFA gave mixed results. The macrocycle **7d**·TFA gave a carbonyl stretch at 1656 $cm^{-1}$, again indicating minimal conjugation effects due to macrocycle formation. However, it was difficult to identify the C═O peaks for **7a**·TFA and **7b**·TFA, as no strong peaks were present above 1600 $cm^{-1}$. **7b**·TFA gave a medium peak at 1779 $cm^{-1}$, while **7a**·TFA afforded two medium peaks at 1740 and 1780 $cm^{-1}$ (see the Supporting Information), but the origins of these signals were not clear. It is worth noting, however, that the carbon-13 NMR spectra for **7a,b,d** in TFA−$CDCl_3$ show resonances for the carbonyl groups at 194.6, 194.9, and 193.5 ppm, respectively, which is typical for aromatic ketones.

Although we were unable to structurally characterize the new porphyrinoids by X-ray crystallography, the conformations of **7a−d** were assessed using density functional theory (DFT) with the B3LYP functional and a 6-311++G(2df, 2p) basis set. The results from these calculations show that the optimal conformations for these oxophlorin analogues are nonplanar and the degree of distortion increases with the addition of methoxy substituents (Figure 3). For **7d**, the benzene rings are twisted in opposite directions relative to the mean macrocyclic plane. The dihedral angles of the 4,5-bond relative to the carbonyl unit is −28.9°, while the dihedral angle for the 7,8-bond relative to the C═O is −12.6° (Table 2). Dimethoxy derivative **7b** shows distortions similar to those of **7d**, but these are greatly magnified in the tetramethoxyporphyrinoid **7a**. In this case, the twist of one benzene ring relative to the carbonyl, measured as the dihedral angle for $C_4C_5C_6O_{6'}$, is −71.5°, while the other benzene unit gives a dihedral angle for $C_8C_7C_6O_{6'}$ of 41.0°. The related dimethoxy structure **7c** has dihedral angles similar to those of **7a**, but the twist of the benzene rings relative to the carbonyl moiety is slightly larger. However, it is unlikely that these differences could account for the diminished stability of porphyrinoid **7c**. The dihedral angle for one of the benzene rings relative to the carbonyl group, as measured for $C_4C_5C_6O_{6'}$, is −73.9°, while the remaining benzene unit gives a dihedral angle for $C_8C_7C_6O_{6'}$ of 44.3°. In all four structures, the dipyrromethene unit is relatively planar, but only structures **7a,c** have one of the benzene units lying in the same plane as the dipyrrolic moiety. The second benzene ring has dihedral angles of 29.6 and 28.4°, respectively, relative to the adjacent pyrrole unit, and similar values were obtained for both arene rings in structures **7b,d**. These results demonstrate that two six-membered rings cannot easily be accommodated in a planar conformation within this porphyrinoid framework.

## CONCLUSION

Three examples of oxo-*adj*-dibenziphlorins have been synthesized by application of the MacDonald "2 + 2" methodology. The free base structures proved to be unstable, and only one example could be isolated in this form. However, the TFA salts for these porphyrinoids could be isolated in good to excellent yields. These structures are nonaromatic, and DFT calculations indicate that the macrocycles are substantially distorted from planarity. This new class of compounds represents a hybrid between carbaporphyrinoids and calix[4]arenes, in particular tetraoxacalixarenes such as **19a,b**.[23] These structures also relate to heterocyclic analogues such as calixpyridines **19c**,[24] xanthoporphyrinogens **20**,[25] and related systems such as **21** and **22**.[26] Hence, these structures are of interest not only as examples of dicarbaporphyrinoids but also as macrocyclic relatives of modified calixarene structures. Further investigations in this area are likely to show additional connections between these important research areas.

## EXPERIMENTAL SECTION

Melting points are uncorrected. IR spectra were obtained on a FT-IR spectrometer equipped with an attenuated total reflectance (ATR)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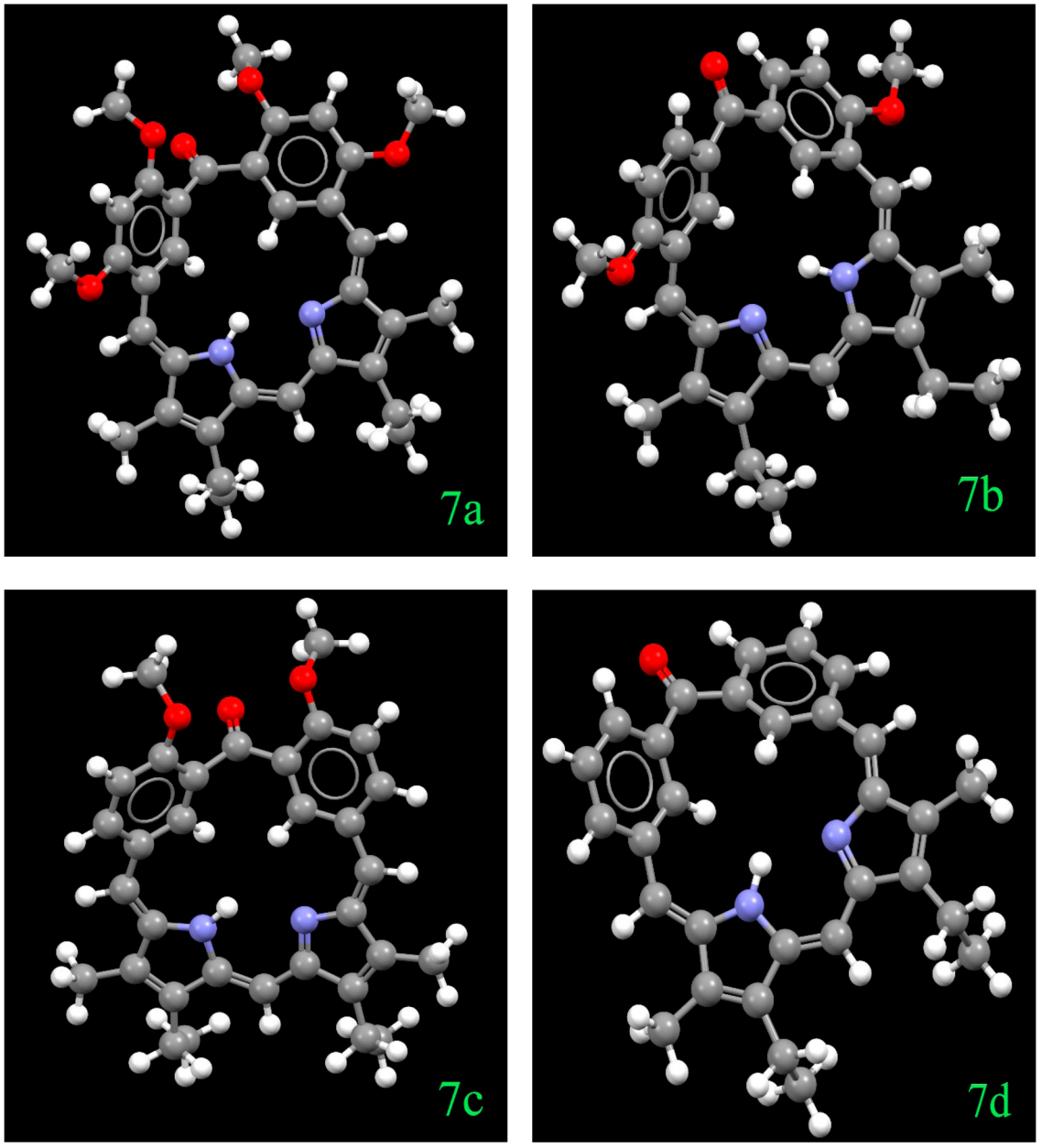
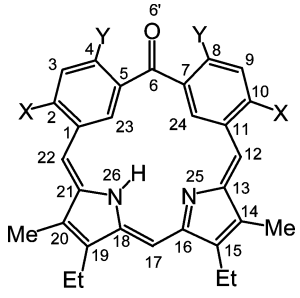



**Figure 3.** DFT calculated conformations for oxodibenziphlorins **7a–d** rendered with Mercury 3.1.

**Table 2. Selected Dihedral Angles (deg) for Oxodibenziphlorins 7a–d**




| molecule | $C_4C_5C_6O_{6'}$ | $C_8C_7C_6O_{6'}$ | $C_{23}C_5C_7C_{24}$ | $C_1C_{23}C_{21}N_{26}$ | $C_{11}C_{24}C_{13}N_{25}$ |
|---|---|---|---|---|---|
| **7d** | −28.9 | −12.6 | −43.7 | 26.2 | 25.0 |
| **7c** | −73.9 | 44.3 | −24.0 | 28.4 | 1.7 |
| **7b** | −23.3 | −18.4 | −44.6 | 27.9 | 29.2 |
| **7a** | −71.5 | 41.0 | −26.1 | 29.6 | −0.5 |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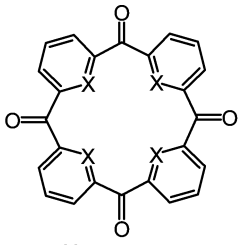
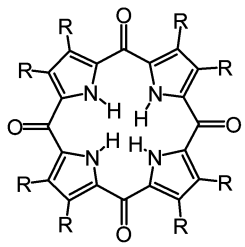
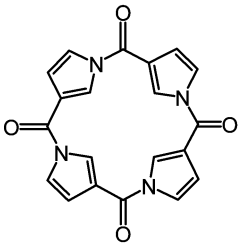


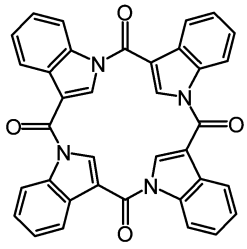
**19** a. X = CH
b. X = C-OH
c. X = N



**20** (Xanthoporphyrinogens)



**21**



**22**

diamond cell. NMR spectra were recorded using a 400 or 500 MHz NMR spectrometer. $^1$H NMR values are reported as chemical shifts $\delta$, relative integral, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; dd, doublet of doublets; dt, doublet of triplets; br, broad peak), and coupling constant ($J$). Chemical shifts are reported in parts per million (ppm) relative to $CDCl_3$ ($^1$H residual $CHCl_3$ $\delta$ 7.26, $^{13}$C $CDCl_3$ triplet $\delta$ 77.23), and coupling constants were taken directly from the spectra. NMR assignments were made with the aid of $^1$H−$^1$H COSY, HSQC, DEPT-135, and NOE difference proton NMR spectroscopy. 2D experiments were performed by using standard software. High-resolution mass spectra (HRMS) were carried out by using a double-focusing magnetic sector instrument. $^1$H and $^{13}$C NMR spectra for all new compounds are reported in the Supporting Information. Theoretical calculations were performed using Spartan '10 running on a Windows platform, as provided by Wavefunction, Inc., 18401 Von Karman Ave., Suite 370, Irvine, CA 92612 (www.wavefun.com). Equilibrium geometry optimization calculations of the molecules were performed at the density functional theory (DFT) level of theory with the B3LYP functional and a 6-311++G(2df,2p) basis set. Mercury 3.1 running on an OS X platform, as provided by the CCDC (www.ccdc.cam.ac.uk/mercury/), was used to visualize the optimized structures. The resulting Cartesian coordinates of the molecules can be found in the Supporting Information.

**5-Bromo-2,4-dimethoxybenzaldehyde (10a).** Bromine (9.70 g, 60.7 mmol) was added dropwise to a solution of 2,4-dimethoxybenzaldehyde (10.00 g, 60.2 mmol) in glacial acetic acid (200 mL), and the resulting mixture was stirred in a water bath at 70 °C for 2 h. The contents of the flask were then poured into 500 mL of ice/water. The resulting precipitate was filtered and recrystallized from ethanol to give 5-bromo-2,4-dimethoxybenzaldehyde (12.74 g, 52.0 mmol, 86%) as a white solid, mp 142−144 °C (lit.[27] mp 140−142 °C). $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 3.93 (3H, s), 3.97 (3H, s) (2 × $OCH_3$), 6.43 (1H, s, 3-H), 7.98 (1H, s, 6-H), 10.22 (1H, s, CHO). $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 56.0, 56.6, 95.7, 103.4, 119.3, 132.6, 161.7, 163.1, 187.0.

**2-(3-Bromophenyl)-5,5-dimethyl-1,3-dioxane (13d).** $p$-Toluenesulfonic acid (6 mg) was added to a solution of 2,2-dimethyl-1,3-propanediol (4.05 g, 38.9 mmol) and 3-bromobenzaldehyde (6.00 g, 32.4 mmol) in benzene (50 mL), and the resulting mixture was stirred under reflux using a Dean−Stark apparatus overnight. The resulting solution was diluted with ether and consecutively washed with saturated sodium bicarbonate, water, and brine. The resulting organic layer was dried over sodium sulfate and the solvent evaporated under reduced pressure to yield the protected bromobenzaldehyde (8.53 g, 31.4 mmol, 97%) as a pale yellow oil. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 0.80 (3H, s), 1.28 (3H, s), 3.64 (2H, d, $J$ = 10.9 Hz), 3.77 (2H, d, $J$ = 10.9 Hz), 5.36 (1H, s), 7.24 (1H, t, $J$ = 7.8 Hz), 7.42 (1H, d, $J$ = 7.7 Hz), 7.45−7.49 (1H, m), 7.68 (1H, t, $J$ = 1.8 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 22.1, 23.3, 30.5, 77.9, 100.9, 122.6, 125.1, 129.6, 130.1, 132.1, 140.9. HRMS (EI): calcd for $C_{12}H_{15}BrO_2$ 270.0255, found 270.0219.

**2-(5-Bromo-2-methoxyphenyl)-5,5-dimethyl-1,3-dioxane (13b).** 2,2-Dimethyl-1,3-propanediol (3.50 g, 33.6 mmol) and 5-bromo-2-anisaldehyde (6.00 g, 27.9 mmol) were reacted under the foregoing conditions. Recrystallization from ethanol gave the protected bromobenzaldehyde (8.12 g, 26.9 mmol, 96%) as a white powder, mp 112−114 °C. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 0.79 (3H, s), 1.32 (3H, s), 3.66 (2H, d, $J$ = 10.8 Hz), 3.75 (2H, d, $J$ = 10.8 Hz), 3.81 (3H, s), 5.71 (1H, s), 6.75 (1H, d, $J$ = 8.8 Hz), 7.40 (1H, dd, $J$ = 8.8, 2.6 Hz), 7.76 (1H, d, $J$ = 2.6 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 22.1, 23.3, 30.5, 56.1, 78.1, 96.3, 112.7, 113.4, 128.9, 130.5, 132.9, 155.8. Anal. Calcd for $C_{13}H_{17}BrO_3$: C, 51.84; H, 5.69. Found: C, 51.77; H, 5.96.

**2-(3-Bromo-4-methoxyphenyl)-5,5-dimethyl-1,3-dioxane (13c).** Using the previous method, 2-bromo-3-methoxybenzaldehyde (6.50 g, 30.2 mmol) was protected with 2,2-dimethyl-1,3-propanediol (3.80 g, 36.5 mmol). Recrystallization from ethanol yielded the **13c** (7.65 g, 25.4 mmol, 84%) as a white powder, mp 102−104 °C. $^1$H NMR (500 MHz, $CDCl_3$): 0.79 (3H, s), 1.28 (3H, s), 3.62 (2H, d, $J$ = 10.9 Hz), 3.74 (2H, d, $J$ = 10.9 Hz), 3.87 (3H, s), 5.31 (1H, s), 6.87 (1H, d, $J$ = 8.5 Hz), 7.40 (1H, dd, $J$ = 8.5, 2.1 Hz), 7.71 (1H, d, $J$ = 2.1 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 22.0, 23.2, 30.3, 56.4, 77.8, 100.7, 111.6, 126.6, 131.4, 132.6, 156.3. Anal. Calcd for $C_{13}H_{17}BrO_3$: C, 51.84; H, 5.69. Found: C, 51.94; H, 5.66.

**2-(5-Bromo-2,4-dimethoxyphenyl)-5,5-dimethyl-1,3-dioxane (13a).** 2,2-Dimethyl-1,3-propanediol (10.5 g, 100.8 mmol), 5-bromo-2,4-dimethoxybenzaldehyde (18.0 g, 74.36 mmol), and $p$-toluenesulfonic acid (23.0 mg) were reacted in benzene (175 mL) using the previous conditions. Recrystallization from ethanol afforded the protected dimethoxybenzaldehyde (20.91 g, 63.1 mmol, 86%) as a white powder, mp 197−198 °C. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 0.78 (3H, s), 1.31 (3H, s), 3.64 (2H, d, $J$ = 10.9 Hz), 3.73 (2H, d, $J$ = 10.9 Hz), 3.84 (3H, s), 3.89 (3H, s), 5.66 (1H, s), 6.43 (1H, s), 7.78 (1H, s). $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 22.1, 23.3, 30.4, 56.2, 56.6, 78.0, 96.43, 96.47, 102.6, 121.0, 131.7, 157.19, 157.24. Anal. Calcd for $C_{14}H_{19}BrO_4$: C, 50.77; H, 5.78. Found: C, 50.69; H, 5.74.

**3,3′-Bis(5,5-dimethyl-1,3-dioxanyl)benzophenone (14d).** In a 250 mL three-neck round-bottom flask fitted with a thermometer, a pressure-equalized addition funnel and a septum, 2.5 M $n$-butyllithium in hexanes (12.6 mL, 31.7 mmol) was mixed with THF (35 mL) at −78 °C and then stirred for 15 min. A solution of **13d** (8.60 g, 31.7 mmol) in THF (60 mL) was added dropwise, maintaining the temperature below −70 °C. Ethyl $N$,$N$-dimethylcarbamate (1.90 g, 16.2 mmol) in THF (10 mL) was added to the solution, maintaining the temperature below −60 °C, and the resulting mixture was stirred at −78 °C for 15 min and then at −20 °C for 1 h. A saturated ammonium chloride solution (35 mL) was added to quench the reaction, and the resulting inorganic precipitate was removed by suction filtration. The organic phase was separated and the aqueous solution extracted with ether. The combined organic layers were dried over sodium sulfate and the solvent evaporated under reduced pressure. The residue was recrystallized from ethanol to afford the benzophenone derivative (5.80 g, 14.1 mmol, 87%) as a white solid, mp 168−170 °C. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 0.80 (6H, s), 1.28 (6H, s), 3.66 (4H, d, $J$ = 10.9 Hz), 3.77 (4H, d, $J$ = 10.9 Hz), 5.44 (2H, s), 7.49 (2H, t, $J$ = 7.7 Hz), 7.73−7.77 (2H, m), 7.94 (2H, t, $J$ = 1.7 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 22.1, 23.3, 30.5, 77.9, 101.2, 128.2, 128.5, 130.3, 130.7, 137.8, 139.2, 196.4. Anal. Calcd for $C_{25}H_{30}O_5$: C, 73.15; H, 7.37. Found: C, 72.84; H, 7.37.

**3,3′-Bis(5,5-dimethyl-1,3-dioxan-2-yl)-4,4′-dimethoxybenzophenone (14b).** Protected bromobenzaldehyde **13b** (9.55 g, 31.7 mmol), 2.5 M $n$-butyllithium (12.6 mL, 31.7 mmol), and ethyl $N$,$N$-dimethylcarbamate (1.9 g, 16.2 mmol) were reacted using the foregoing procedure. Recrystallization from ethanol yielded the substituted benzophenone (5.44 g, 11.6 mmol, 73%) as a white solid, mp 214−215 °C. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 0.77 (6H, s), 1.28 (6H, s), 3.66 (4H, d, $J$ = 10.9 Hz), 3.73−3.75 (4H, d, $J$ = 10.9 Hz), 3.91 (6H, s), 5.75 (2H, s), 6.92 (2H, d, $J$ = 8.7 Hz), 7.79 (2H, dd, $J$ = 8.6, 2.3 Hz), 8.17 (2H, d, $J$ = 2.3 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 22.1, 23.3, 30.5, 56.1,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78.0, 96.8, 110.2, 126.8, 130.2, 130.9, 133.0, 159.9, 194.3. Anal. Calcd for $C_{27}H_{34}O_7$: C, 68.92; H, 7.28. Found: C, 68.81; H, 7.32.

**3,3′-Bis(5,5-dimethyl-1,3-dioxan-2-yl)-2,2′-dimethoxybenzophenone (14c).** Acetal **13c** (9.50 g, 31.5 mmol), 2.5 M *n*-butyllithium (12.6 mL, 31.7 mmol), and ethyl *N*,*N*-dimethylcarbamate (2.00 g, 17.0 mmol) were reacted under the previous conditions. Recrystallization from ethanol gave the ketone (4.43 g, 9.41 mmol, 60%) as a white powder, mp 135−136 °C. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 0.79 (6H, s), 1.38 (6H, s), 3.62 (4H, d, 11.2 Hz), 3.63 (6H, s), 3.74 (4H, d, $J$ = 11.2 Hz), 5.35 (2H, s), 6.90 (2H, d, $J$ = 8.2 Hz), 7.61−7.64 (4H, m). $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 22.1, 23.3, 30.4, 56.0, 77.9, 101.5, 111.6, 129.0, 129.9, 130.5, 131.0, 159.0, 194.5. Anal. Calcd for $C_{27}H_{34}O_7$: C, 68.92; H, 7.28. Found: C, 68.87; H, 7.40.

**3,3′-Bis(1,3-dioxolan-2-yl)-2,2′,4,4′-tetramethoxybenzophenone (12).** *p*-Toluenesulfonic acid (25 mg) was added to a solution of ethylene glycol (4 mL, 4.44 g, 71.5 mmol) and 5-bromo-2,4-dimethoxybenzaldehyde (6.10 g, 24.9 mmol) in benzene (50 mL), and the resulting mixture was heated under reflux overnight using a Dean−Stark apparatus to azeotropically remove water. The solution was cooled to room temperature and then washed consecutively with water, saturated aqueous sodium bicarbonate solution, and water. The aqueous layers were back-extracted with ether, and the combined organic layers were dried over sodium sulfate. The solvent was evaporated under reduced pressure to yield acetal **11** (6.84 g, 23.6 mmol, 95%) as a pale yellow oil. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 3.75 (3H, s), 3.78 (3H, s), 3.85−3.93 (2H, m), 3.96−4.05 (2H, m), 5.96 (1H, s), 6.35 (1H, s), 7.58 (1H, s). $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 56.0, 56.3, 65.2, 96.4, 98.6, 101.9, 119.7, 128.4, 157.3, 158.3. HRMS (EI): calcd for $C_{11}H_{12}BrO_4$ 286.9919, found 286.9927. The acetal is very unstable and was used immediately in the next step. A solution of the acetal (6.94 g, 24.0 mmol) in diethyl ether (50 mL) was added dropwise over a 15 min period to a stirred solution of 2.5 M *n*-butyllithium (11.5 mL, 28.9 mmol) in diethyl ether (30 mL), maintaining the temperature below −50 °C. The solution was stirred for 15 min before a solution of ethyl *N*,*N*-dimethylcarbamate (1.22 g, 10.4 mmol) in diethyl ether (10 mL) was added dropwise over a period of 10 min. The resulting mixture was stirred at −50 °C for 15 min and then at −20 °C for 1 h. The reaction was quenched by the addition of saturated aqueous ammonium chloride solution (30 mL), the layers were separated, and the aqueous phase was extracted with ether. The combined organic layers were washed with water and dried over sodium sulfate and the solvent evaporated under reduced pressure. The residue was recrystallized from ethanol to yield the protected dialdehyde (1.52 g, 3.4 mmol, 28%) as a white solid, mp 224−225 °C. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 3.69 (6H, s), 3.92 (6H, s), 3.97−4.02 (4H, m), 4.05−4.10 (4H, m), 6.10 (2H, s), 6.41 (2H, s), 7.70 (2H, s). $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 56.0, 56.2, 65.4, 95.2, 99.5, 118.3, 123.0, 130.6, 161.1, 161.5, 192.5. HRMS (EI): calcd for $C_{23}H_{26}O_9$ 446.1577, found 446.1577.

**Benzophenone-3,3′-dicarbaldehyde (9d).** Diacetal **14d** (14.00 g, 34.1 mmol) was dissolved in formic acid (150 mL) and stirred under reflux overnight. The resulting solution was taken up in 600 mL of ether and washed with water (200 mL × 3), followed by saturated sodium bicarbonate solution (200 mL). The organic layer was dried over sodium sulfate and filtered and the solvent evaporated under reduced pressure. The residue was recrystallized from 3:1 ethanol−water to give the dialdehyde (6.73 g, 28.2 mmol, 83%) as a light brown solid, mp 116−117 °C. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 7.72 (2H, t, $J$ = 7.7 Hz, 5,5′-H), 8.09 (2H, dt, $J$ = 7.7, 1.5 Hz, 6,6′-H), 8.16 (2H, dt, $J$ = 7.6, 1.4 Hz, 4,4′-H), 8.28 (2H, t, $J$ = 1.6 Hz, 2,2′-H), 10.11 (2H, s, 2 × CHO). $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 129.8, 131.2, 133.6, 135.5, 136.8, 138.0, 191.4, 194.5. Anal. Calcd for $C_{15}H_{10}O_3$: C, 75.62; H, 4.23. Found: C, 75.51; H, 4.08.

**4,4′-Dimethoxybenzophenone-3,3′-dicarbaldehyde (9b).** **14b** (5.05 g, 10.7 mmol) was dissolved in formic acid (55 mL) and stirred under reflux overnight. The resulting solution was taken up in 300 mL of chloroform and washed with water (150 mL × 3), followed by saturated sodium bicarbonate solution (150 mL). The organic layer was dried over sodium sulfate and filtered and the solvent evaporated under reduced pressure. The residue was recrystallized from 3:1 ethanol−water to give the benzophenone dialdehyde (2.67 g, 9.0 mmol, 84%) as a light brown solid, mp 174−175 °C. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 4.03 (6H, s, 2 × $OCH_3$), 7.12 (2H, d, $J$ = 8.7 Hz, 5,5′-H), 8.06 (2H, dd, $J$ = 8.7, 2.3 Hz, 6,6′-H), 8.18 (2H, d, $J$ = 2.3 Hz, 2,2′-H), 10.46 (2H, s, 2 × CHO). $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 56.4, 112.2, 124.4, 130.3, 131.1, 137.5, 164.8, 189.0, 193.1. Anal. Calcd for $C_{17}H_{14}O_5$: C, 68.45; H, 4.73. Found: C, 68.52; H, 4.67.

**6,6′-Dimethoxybenzophenone-3,3′-dicarbaldehyde (9c).** Using the foregoing procedure, **14c** (1.00 g, 2.1 mmol) was deprotected in formic acid (15 mL). Recrystallization from ethanol−water gave the dialdehyde (0.58 g, 1.9 mmol, 92%) as a light brown solid, mp 150−152 °C. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 3.74 (6H, s, 2 × $OCH_3$), 7.05 (2H, d, $J$ = 8.6 Hz, 5,5′-H), 8.04 (2H, dd, $J$ = 8.6, 2.2 Hz, 4,4′-H), 8.08 (2H, d, $J$ = 2.2 Hz, 2,2′-H), 9.94 (2H, s, 2 × CHO). $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 56.3, 111.8, 129.9, 130.3, 133.1, 134.4, 163.0, 190.4, 192.7. Anal. Calcd for $C_{17}H_{14}O_3$: C, 68.45; H, 4.73. Found: C, 68.30; H, 4.78.

**2,2′,4,4′-Tetramethoxybenzophenone (16).** In a 250 mL three-neck round-bottom flask fitted with a thermometer, a pressure-equalized addition funnel, and a septum, 2.5 M *n*-butyllithium (18.2 mL, 45.8 mmol) was added to diethyl ether (70 mL) at −78 °C and the mixture stirred for 15 min. A solution of 1-bromo-2,4-dimethoxybenzene (9.95 g, 45.8 mmol) in diethyl ether (80 mL) was then added dropwise while maintaining the reaction temperature below −70 °C. Ethyl *N*,*N*-dimethylcarbamate (2.80 g, 23.9 mmol) in diethyl ether (40 mL) was added to the solution, maintaining the temperature below −65 °C, and the resulting mixture was stirred at −78 °C for 15 min and then subsequently stirred at −20 °C for 1 h. Saturated ammonium chloride solution (35 mL) was added to quench the reaction, and the resulting inorganic precipitate was removed by suction filtration. The organic phase was separated and the aqueous solution extracted with ether. The combined organic solutions were washed with water and dried over sodium sulfate. The solvent was evaporated under reduced pressure, and the residue was recrystallized from ethanol to give the tetramethoxybenzophenone (4.33 g, 14.3 mmol, 63%) as a white solid, mp 138−140 °C (lit.[21] mp 138−142 °C). $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 3.66 (6H, s), 3.85 (6H, s), 6.42 (2H, d, $J$ = 2.3 Hz) 6.50 (2H, dd, $J$ = 8.5, 2.3 Hz), 7.50 (2H, d, $J$ = 8.5 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 55.6, 55.9, 98.7, 104.6, 124.1, 132.7, 160.3, 163.6, 193.1.

**4,4′,6,6′-Tetramethoxybenzophenone-3,3′-dicarbaldehyde (9a).** Phosphorus oxychloride (5 mL, 8.2 g, 53.5 mmol) was added dropwise to DMF (4 mL, 3.80 g, 51.9 mmol) in a 25 mL round-bottom flask, while maintaining the temperature of the mixture below 10 °C. A solution of 2,2′,4,4′-tetramethoxybenzophenone (1.00 g, 3.3 mmol) in DMF (14 mL) was added dropwise to the stirred mixture over a period of 10 min. The resulting mixture was heated at 95 °C for 3 h and then poured into 100 mL of ice−water and neutralized with triethylamine. The resulting precipitate was filtered and washed well with hot ethanol to yield the dialdehyde (0.99 g, 2.8 mmol, 84%) as a brown solid, mp 264−265 °C. $^1$H NMR (500 MHz, DMSO-$d_6$): $\delta$ 3.77 (6H, s, 6,6′-$OCH_3$), 4.03 (6H, s, 4,4′-$OCH_3$), 6.78 (2H, s, 5,5′-H), 7.79 (1H, s, 2,2′-H), 10.19 (1H, s, 2 × CHO). $^{13}$C NMR (125 MHz, DMSO-$d_6$): $\delta$ 57.0, 57.1, 96.5, 117.8, 123.1, 131.2, 165.2, 166.1, 187.6, 190.5. Anal. Calcd for $C_{19}H_{18}O_7$: C, 63.68; H, 5.06. Found: C, 63.31; H, 5.02.

**15,19-Diethyl-2,10-dimethoxy-14,20-dimethyl-6-oxo-*adj*-dibenziphlorin (7b).** In a 250 mL pear-shaped flask, dipyrrylmethanedicarboxylic acid **18** (123 mg, 0.39 mmol) was dissolved in TFA (5 mL) under nitrogen. The resulting solution was diluted with dichloromethane (185 mL), and dialdehyde **9b** (100 mg, 0.33 mmol) was added immediately. The resulting mixture was stirred under nitrogen at room temperature overnight. The solvent was then evaporated under reduced pressure and the residue dissolved in chloroform (15 mL). The solution was diluted with hexanes (200 mL) and placed in the refrigerator overnight. The resulting precipitate was suction-filtered and vacuum-dried to give the oxophlorin analogue TFA salt (165 mg, 0.27 mmol, 82%) as a red-purple powder, mp >300 °C. UV−vis (1% $Et_3N$−$CHCl_3$): $\lambda_{max}$ (log $\varepsilon$) 492 (4.03), 567 nm (3.86). UV−vis (1% TFA−$CHCl_3$): $\lambda_{max}$ (log $\varepsilon$) 550 (4.11), 631 nm (4.08). $^1$H NMR (500 MHz, $Et_3N$−$CDCl_3$): $\delta$ 1.13 (6H, t), 2.12 (6H, s), 2.44 (4H, q, $J$ = 7.6 Hz), 3.92 (6H, s), 5.29 (1H, s), 6.50 (2H, s), 7.03 (2H, d, $J$ = 8.7 Hz), 7.97 (2H, dd, $J$ = 8.7, 2.2 Hz), 8.55 (2H, d, $J$ = 2.2 Hz), 10.90 (1H, br s). $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 1.14 (6H, t, $J$ = 7.6 Hz, 2 × $CH_2CH_3$), 2.22 (6H, s,

14,20-$CH_3$), 2.50 (4H, q, $J$ = 7.7 Hz, 15,19-$CH_2$), 3.95 (6H, s, 2 × $OCH_3$), 5.54 (1H, s, 17-H), 6.87 (2H, s, 12,22-H), 7.08 (2H, d, $J$ = 8.8 Hz, 3,9-H), 8.06 (2H, dd, $J$ = 8.8, 2.0 Hz, 4,8-H), 8.62 (2H, d, $J$ = 2.0 Hz, 23,24-H). $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 10.1, 14.1, 17.7, 56.3, 84.8, 112.1, 114.7, 122.5, 130.1, 132.1, 134.6, 139.2, 143.0, 143.8, 161.4, 161.7, 193.5. HRMS (ESI): calcd for $C_{32}H_{33}N_2O_3$ 493.2491, found 493.2482.

**15,19-Diethyl-14,20-dimethyl-6-oxo-*adj*-dibenziphlorin (7d).** Dipyrrylmethanedicarboxylic acid **18** (79 mg, 0.25 mmol) and dialdehyde **9d** (50 mg, 0.21 mmol) were reacted as described above. After drying in vacuo, the oxodibenziphlorin TFA salt (56 mg, 0.10 mmol, 49%) was isolated as a dark purple solid, mp >300 °C. An analytical sample was obtained by dissolving the compound in chloroform and passing it through a flash silica column, eluting with 2:2:96 TFA−methanol−chloroform. UV−vis (2.5% $Et_3N$−$CHCl_3$): $\lambda_{max}$ (log $\varepsilon$) 330 (4.07), 491 (4.04), 568 nm (3.55). UV−vis (2.5% TFA−$CHCl_3$): $\lambda_{max}$ (log $\varepsilon$) 339 (4.07), 526 (4.16), 563 (4.31), 618 nm (3.82). $^1$H NMR (500 MHz, $Et_3N$−$CDCl_3$): $\delta$ 1.11 (6H, t, $J$ = 7.6 Hz), 2.10 (6H, s), 2.45 (4H, q, $J$ = 7.2 Hz), 5.49 (1H, s), 6.26 (2H, s), 7.42−7.44 (2H, m), 7.50 (2H, t, $J$ = 7.7 Hz), 7.88 (2H, dt, $J$ = 7.7, 1.5 Hz), 8.63 (2H, t, $J$ = 1.5 Hz). $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 1.15 (6H, t, $J$ = 7.7 Hz, 2 × $CH_2CH_3$), 2.21 (6H, s, 14,20-$CH_3$), 2.51 (4H, q, $J$ = 7.7 Hz, 15,19-$CH_2$), 5.58 (1H, s, 17-H), 6.67 (2H, s, 12,22-H), 7.51 (2H, d, $J$ = 7.8 Hz, 2,10-H), 7.60 (2H, t, $J$ = 7.7 Hz, 3,9-H), 7.99 (2H, d, $J$ = 7.8 Hz, 4,8-H), 8.74 (2H, s, 23,24-H). $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 10.0, 14.0, 17.7, 85.3, 119.0, 128.8, 130.5, 131.6, 134.3, 135.4, 139.2, 139.9, 142.9, 144.2, 161.9, 194.9. HRMS (ESI): calcd for $C_{30}H_{29}N_2O$ 433.2280, found 433.2288.

**15,19-Diethyl-2,4,8,10-tetramethoxy-14,20-dimethyl-6-oxo-*adj*-dibenziphlorin (7a).** In a 25 mL pear-shaped flask, trifluoroacetic acid (2 mL) was added to dipyrrylmethane **18** (100 mg, 0.32 mmol) and the mixture stirred under nitrogen for 2 min. The mixture was diluted with dichloromethane (18 mL), and a preprepared solution of 2,2′,4,4′-tetramethoxybenzophenone-3,3′-dicarbaldehyde (112 mg, 31 mmol) in trifluoroacetic acid (4 mL) was then added immediately. The solution was stirred in the dark under nitrogen for 2 h. The resulting mixture was diluted with dichloromethane and washed with water, saturated sodium bicarbonate solution, and brine. The organic layer was dried over sodium sulfate and the solvent evaporated under reduced pressure. The residue was passed through a grade 3 alumina column, with chloroform as eluent. The first fraction (purple) contained the product. The solvent was evaporated under reduced pressure and the residue recrystallized from chloroform−methanol to yield the oxophlorin analogue (60 mg, 10.9 mmol, 35%) as a purple solid, mp >300 °C. UV−vis ($CHCl_3$): $\lambda_{max}$ (log $\varepsilon$) 364 (4.50), 580 nm (4.16). UV−vis (1% TFA−$CHCl_3$): $\lambda_{max}$ (log $\varepsilon$) 311 (4.56), 649 nm (4.25). UV−vis (90% TFA−$CHCl_3$): $\lambda_{max}$ (log $\varepsilon$) 441 (4.24), 637 nm (3.92). $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 1.14 (6H, t, $J$ = 7.6 Hz, 2 × $CH_2CH_3$), 2.16 (6H, s, 14,20-$CH_3$), 2.50 (4H, q, $J$ = 7.6 Hz, 2 × $CH_2CH_3$), 3.92 (6H, s), 3.94 (6H, s) (4 × $OCH_3$), 5.53 (1H, s, 17-H), 6.54 (2H, s, 12,22-H), 6.60 (2H, s, 3,9-H), 8.09 (2H, s, 23,24-H), 9.91 (1H, v br, NH). $^1$H NMR (500 MHz, TFA-$CDCl_3$): $\delta$ 1.13 (6H, t, $J$ = 7.6 Hz, 2 × $CH_2CH_3$), 2.25 (6H, s, 14,20-$CH_3$), 2.52 (4H, q, $J$ = 7.6 Hz, 15,19-$CH_2$), 3.93 (6H, s, 4,8-$OCH_3$), 3.97 (6H, s, 2,10-$OCH_3$), 5.64 (1H, s, 17-H), 6.62 (2H, s, 3,9-H), 6.92 (2H, s, 12,22-H), 7.73 (2H, s, 23,24-H), 8.63 (2H, br s, 2 × NH). $^{13}$C NMR (125 MHz, TFA-$CDCl_3$): $\delta$ 10.1, 13.9, 17.6, 56.4, 56.5, 84.7, 96.9, 110.5, 115.1, 115.2, 121.7, 130.2, 139.5, 143.3, 144.0, 161.0, 163.8, 194.6. HRMS (EI): calcd for $C_{34}H_{36}N_2O_5$ 552.2624, found 552.2623.

## ■ ASSOCIATED CONTENT

### Ⓢ Supporting Information

Figures giving selected $^1$H NMR, $^1$H−$^1$H COSY, HSQC, $^{13}$C NMR, MS, and UV−vis spectra and tables giving Cartesian coordinates. This material is available free of charge via the Internet at http://pubs.acs.org.

## ■ AUTHOR INFORMATION

### Corresponding Author

*E-mail for T.D.L.: tdlash@ilstu.edu.

### Notes

The authors declare no competing financial interest.

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