# Metal-Catalyzed Oxidative Cyclizations of *a,c*-Biladiene Salts Bearing 1- and/or 19-Arylmethyl Substituents: Macrocyclic Products and Their Chemistry

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Several 1-mono- and 1,19-bis(*p*-arylmethyl)-*a,c*-biladiene salts were prepared and subjected to either copper(II)- or chromium(III)-assisted oxidative cyclization to yield numerous products in which the 1- or 19- substituent is adapted, eliminated, or rearranged to other points on the tetrapyrrole. For example, cyclization using copper(II) acetate of 19-((ethoxycarbonyl)methyl)-2,3,7,8,12,13,17,-18-octamethyl-19-(*p*-tolylmethyl)-*a,c*-biladiene dihydrobromide (**25**) yielded the copper(II) 20-((ethoxycarbonyl)methyl)-1-(*p*-tolylmethyl)-2,3,7,8,12,13,17,18-octamethyl-1,20-dihydroporphyrin (**42**), copper(II) 20-(ethoxycarbonyl)-3-methylidene-2,3,7,8,12,13,17,18-octamethyl-2-(*p*-tolylmethyl)-chlorin (**44**), copper(II) 20-(ethoxycarbonyl)-2-methylidene-2,3,7,8,12,13,17,18-octamethyl-3-(*p*-tolylmethyl)chlorin (**45**), and three porphyrins: copper(II) 20-(ethoxycarbonyl)-2,3,7,8,12,13,17,18-octamethylporphyrin (**3**), copper(II) 2,3,7,8,12,13,17,18-octamethyl-20-*p*-tolylporphyrin (**50**), and copper(II) 20-(ethoxycarbonyl)-2,3,7,8,12,13,17,18-octamethyl-5-(*p*-tolylmethyl)porphyrin (**47**). Formation of porphyrin **47** and the intermediate chlorins **44** and **45** suggests the stepwise migration of the arylmethyl group from the 1-position in compound **42**. The isolation of products from cyclization reactions of various 1,19-arylmethyl-substituted *a,c*-biladiene salts provides further insight into the mechanisms of metal-assisted oxidative cyclization of *a,c*-biladiene salts to give cyclic tetrapyrroles. Macrocyclizations of *a,c*-biladienes such as **25** using chromium(III) afford good yields of the metal-free 1-substituted compounds such as **43**.

## Introduction

In a recent paper we showed[1] that metal ion [e.g., copper(II), chromium(III)] promoted oxidative cyclizations of *a,c*-biladiene salts substituted at the 1- and 19-positions (e.g., **1**; Scheme 1) with various aliphatic substituents gave a variety of novel macrocyclic products, including 1-substituted substances **2**, copper(II) porphyrins **3**, copper(II) chlorins **4**, and so-called homoporphyrins **5**. The chemistry reported paralleled the electrochemical synthesis of porphyrins from *a,c*-biladiene salts[2,3] and enabled a deeper understanding of the mechanistic pathways[4,5] from *a,c*-biladienes to copper(II) porphyrins[6,7] and to metal-free porphyrins using the chromium procedure recently described by Boschi and coworkers.[8] Other studies have also probed the nature of the metal salt oxidant used,[9] as well as methodology for generalization of the synthetic route through the preparation of unsymmetrically substituted *a,c*-biladienes and porphyrins therefrom.[10,11] Parallel synthetic and mechanistic studies of the synthesis of porphyrins from *b*-bilenes have also been reported by Clezy and coworkers,[12−14] and their results are broadly in agreement with our own conclusions for *a,c*-biladienes.

In the present paper we describe our results on the copper(II)-catalyzed cyclization of *a,c*-biladiene salts bearing at least one *arylmethyl* substituent at positions 1 or 19. The presence of the arylmethyl substituent, it will be shown, results in novel substituent migrations around the tetrapyrrole macrocycle.

## Results and Discussion

**Preparation of Tripyrrenes and *a,c*-Biladienes.** Symmetrical *a,c*-biladienes bearing 1,19-bis(*p*-tolylmethyl) substituents were prepared by addition of 2 molar equiv of formylpyrrole **7** to a mole of dipyrromethanedicarboxylic acid **16** (**17** or **18**) to give *a,c*-biladiene dihydrobromide **19** (**20** or **21**) in 84% (84% and 78%) yield (Scheme 2).

Unlike the synthesis of *a,c*-biladienes such as **19**, a stepwise approach was neccessary for the preparation of the unsymmetrical *a,c*-biladienes. 2-(Acetoxymethyl)-

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(1) Liddell, P. A.; Gerzevske, K. R.; Lin, J. J.; Olmstead, M. M.; Smith, K. M. *J. Org. Chem.* **1993**, *58*, 6681.
(2) Jeyakumar, D.; Snow, K. M.; Smith, K. M. *J. Am. Chem. Soc.* **1988**, *110*, 8562.
(3) Swanson, K. L.; Snow, K. M.; Jeyakumar, D.; Smith, K. M. *Tetrahedron Lett.* **1991**, *47*, 685.
(4) Smith, K. M.; Minnetian, O. M. *J. Org. Chem.* **1985**, *50*, 2073.
(5) Smith, K. M.; Kehres, L. A. *J. Chem. Soc., Perkin Trans. 1* **1983**, 2329.
(6) Johnson, A. W.; Kay, I. T. *J. Chem. Soc.* **1961**, 2418.
(7) (a) Smith, K. M. In *Porphyrins and Metalloporphyrins*; Smith, K. M., Ed.; Elsevier: Amsterdam, 1975; pp 29−55. (b) Smith, K. M. In *Porphyrins and Metalloporphyrins*; Smith, K. M., Ed.; Elsevier: Amsterdam, 1975; p 764. (c) Smith, K. M. In *Porphyrins and Metalloporphyrins*; Smith, K. M., Ed.; Elsevier: Amsterdam, 1975; p 763. (d) Improved syntheses of pyrroles **12** and **13** have recently been reported: Lash, T. D.; Bellettini, J. R.; Bastian, J. A.; Couch, K. B. *Synthesis* **1994**, 170. Burns, D. H.; Jabara C. S.; Burden, M. W. *Synth. Commun.* **1995**, *25*, 379. (e) Jackson, A. H.; Pandey, R. K.; Rao, K. R. N.; Roberts, E. *Tetrahedron Lett.* **1985**, *26*, 793.
(8) Boschi, T.; Paolesse, R.; Tagliatesta, P. *Inorg. Chim. Acta* **1990**, *168*, 83.
(9) Smith, K. M.; Minnetian, O. M. *J. Chem. Soc., Perkin Trans. 1* **1986**, 277.
(10) Almeida, J. A. P. B.; Kenner, G. W.; Rimmer, J.; Smith, K. M. *Tetrahedron* **1976**, *32*, 429.
(11) Smith, K. M.; Craig, G. W. *J. Org. Chem.* **1983**, *48*, 4307.
(12) Clezy, P. S.; Ravi, B. N.; Thuc, L. V. *Aust. J. Chem.* **1986**, *39*, 419.
(13) Atkinson, E. J.; Brophy, J. J.; Clezy, P. S. *Aust. J. Chem.* **1990**, *43*, 383.
(14) Clezy, P. S. *Aust. J. Chem.* **1991**, *44*, 1163.

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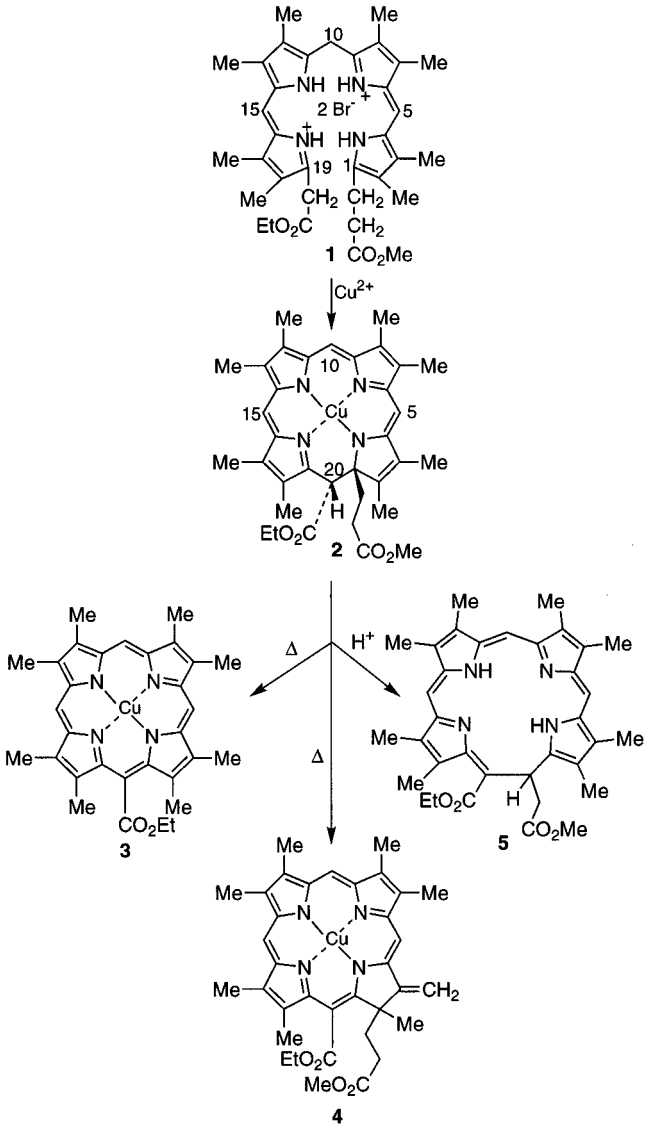
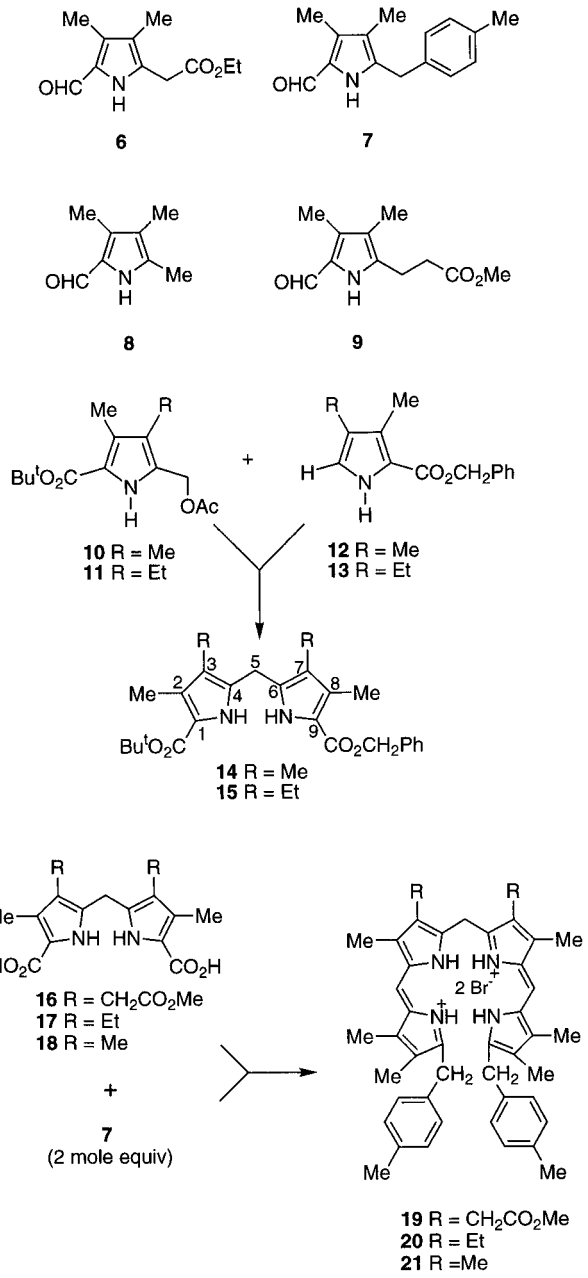
**Scheme 1. Formation of Novel Macrocycles from Copper(II)-Catalyzed Oxidative Cyclization of *a,c*-Biladiene Dihydrobromide (1)[1]**




pyrrole **10**[7c] was treated with 2-unsubstituted pyrrole **12**[1,7d] in the presence of Montomorillite K-10 Clay[7e] to afford the dipyrromethane **14**[1] in 80% yield (Scheme 2). There are two possible routes for conversion of unsymmetrically substituted dipyrromethanes into tripyrrenes and then on to *a,c*-biladienes; these involve selective and sequential cleavage of either the *tert*-butyl or the benzyl ester on the dipyrromethane. Catalytic debenzylation of dipyrromethane **14** followed by acid-catalyzed condensation with formylpyrrole **7** afforded the tripyrrene hydrobromide **22** in 81% yield. Treatment of tripyrrene **22** with acid followed by addition of 2-formylpyrrole **8** gave the *a,c*-biladiene **25** (Scheme 3). The alternative pathway through tripyrrene required the removal of the *tert*-butyl ester from dipyrromethane **15** (or **14**) with acid. The dipyrromethane was condensed with 1 molar equiv of pyrrole **7** under acidic conditions to give tripyrrene **24** (or **23**). Hydrolysis and decarboxylation of the benzyl ester with 30% HBr/acetic acid and trifluoroacetic acid[11] gave the tripyrrene hydrobromide **24** (or **23**) which readily underwent condensation with another 2-formylpyrrole (**8**) to give the unsymmetrical *a,c*-biladiene dihydrobromide **28** in yields ranging from 76 to 85%.

**Copper(II)-Promoted Oxidative Cyclization of *a,c*-Biladiene Salts.** Heating of *a,c*-biladiene **19** in

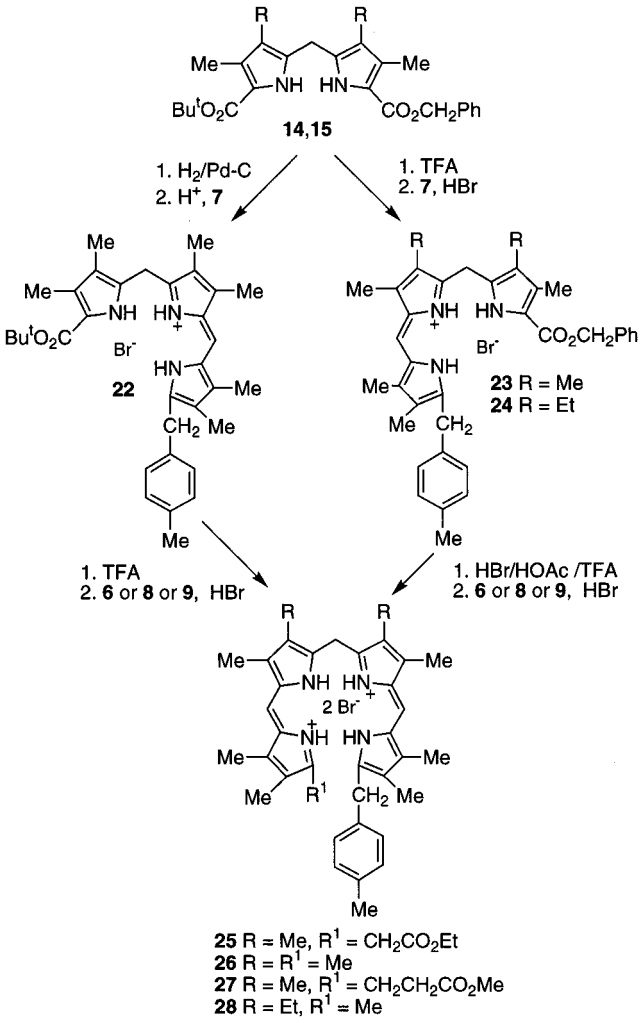
**Scheme 2. Preparation of Dipyrromethanes 14 and 15 and *a,c*-Biladienes 19−21**




DMF at 145 °C in the presence of copper(II) acetate (Scheme 4) afforded the copper(II) porphyrin **36** as the major product (characterized as **37** after demetalation), together with a very small amount of a copper(II) chlorin which was shown, by X-ray crystallography (Figure 1), to be the 2-methylidene compound **33** rather than the isomer **41**; presumably, steric congestion between the 1- and 20-substituents in **41** caused it to be unstable, under the reaction conditions, compared with its further migration product, compound **33**. When the reaction was performed in DMF with copper(II) acetate at 120 °C, the copper(II) porphyrin was again the major product, but the 1-substituted copper(II) complex **30** was also isolated, thereby demonstrating its intermediacy in the reaction at 145 °C; the milder reaction conditions resulted in none of the copper(II) chlorins **33** or **41** being observed or isolated. Figure 2 shows the X-ray structure of the copper(II) 1-(*p*-tolylmethyl)-20-*p*-tolyl macrocycle **30**.

Copper(II)-catalyzed cyclization of *a,c*-biladiene dihydrobromide **20** in DMF at room temperature resulted in formation of the copper(II) 1-substituted compound **29**

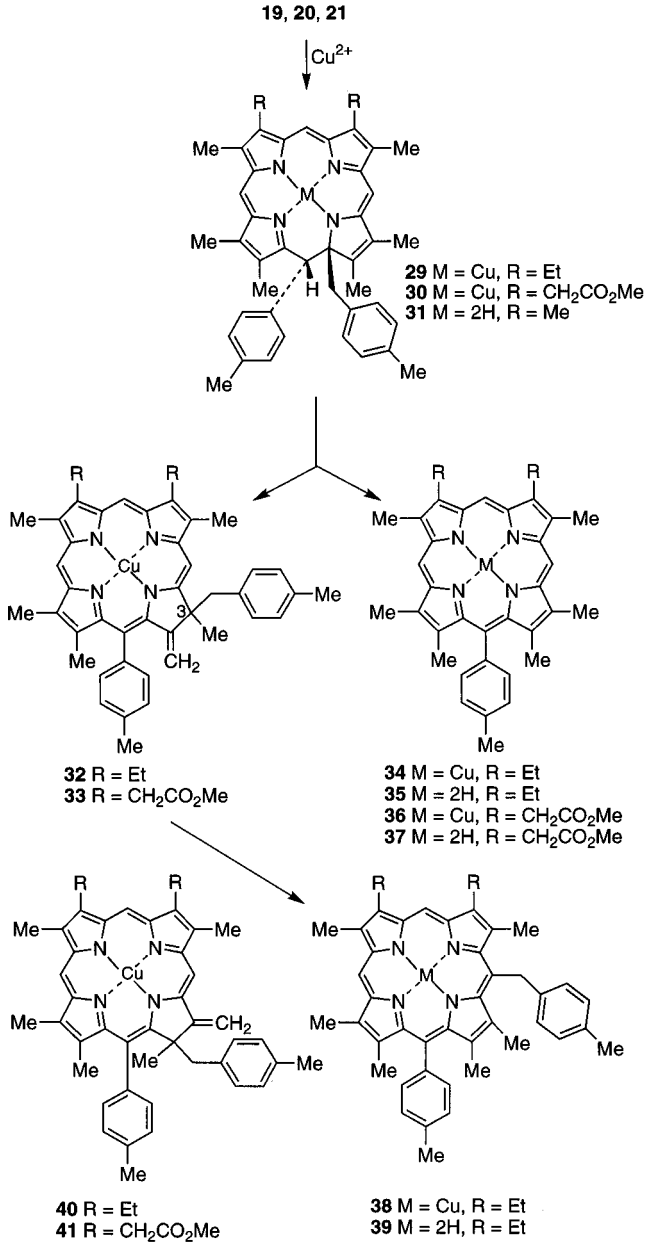
**Scheme 3. Synthetic Approaches to Unsymmetrical *a,c*-Biladienes 25−28**




as the major product, in 81% yield. Its structure was confirmed by X-ray crystallography (not shown, but deposited with CCDC). When the same reaction was performed at 120 °C, several products were isolated, including copper(II) compound **29** (8%), the copper(II) 2-methylidenechlorin **32** (4%), and the copper(II) porphyrins **34** (30%) and **38** (3%) (both characterized by NMR spectroscopy after demetalation in sulfuric/trifluoroacetic acids to give **35** and **39**, respectively). The regiochemistry of the migrated *p*-tolylmethyl group was assigned on the basis of the structure of the similar chlorin **33**, determined by X-ray crystal analysis as previously reported.[15] Perhaps the most surprising product was the copper(II) porphyrin **38** in which the *p*-tolylmethyl substituent had migrated from the 1-position in **29** (presumably) completely across the macrocyclic A ring to the 5-position. Further examples elucidating the migratory effect of the *p*-tolylmethyl moiety will be seen with cyclization of *a,c*-biladiene **25** (vide infra).

The roles as intermediates, in the migration process, of the 1-substituted compound **29** and chlorin **32** were further investigated. Compound **29** was subjected to cyclization conditions (copper acetate and *N,N*-dimethylformamide) for 15 min at 140 and 120 °C. At 140 °C, **29** provided copper(II) porphyrin **34** as the major product. In addition, porphyrin **38** and chlorin **32** were isolated in 3% and 1% yields, respectively. The product distribution is comparable to the yield of these macrocycles isolated by cyclizing *a,c*-biladiene **20** at 120 °C, further substantiating product **29** as the intermediate that provides the migration products. Heating of compound **29** under similar conditions at 120 °C provided an increase in yield of the chlorin **32** over porphyrins **34** and **38**, from 1% to 11%. When the copper(II) 2-methylidenechlorin **32** was heated in *o*-dichlorobenzene (at 140 °C for 120 min), a mixture of the copper(II) porphyrins **34** and **38** was obtained, with porphyrin **38** as the major product (78% yield). Table 1 summarizes the results obtained from **29** and **32**.

**Scheme 4. Products from Copper(II)-Catalyzed Oxidative Cyclization of *a,c*-Biladiene Dihydrobromides 19, 20, and 21**




When *a,c*-biladiene **25** was treated with copper(II) acetate in DMF at 120 °C, the 1-*p*-tolylmethyl-substituted copper(II) complex **42** was isolated, along with three copper(II) porphyrins and two copper(II) chlorins (Scheme 5). The pathway for this migration became clearer once the two copper(II) chlorins were isolated, purified, and characterized as the migration intermediates **44** and **45**, along with porphyrin **47**; compounds **42**, **44**, **45**, and **47** (and experiments described above with **19** and **20**)

(15) Liddell, P. A.; Olmstead, M. M.; Smith, K. M. *Tetrahedron Lett.* **1990**, *31*, 2685.

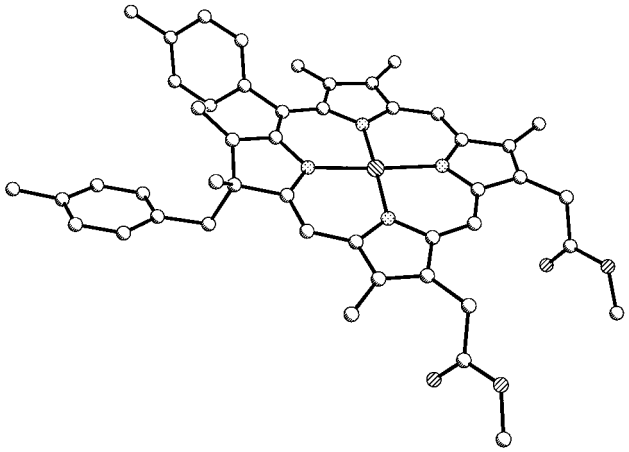


**Figure 1.** Molecular structure of copper(II) chlorin **33**. Hydrogen atoms have been omitted for clarity.

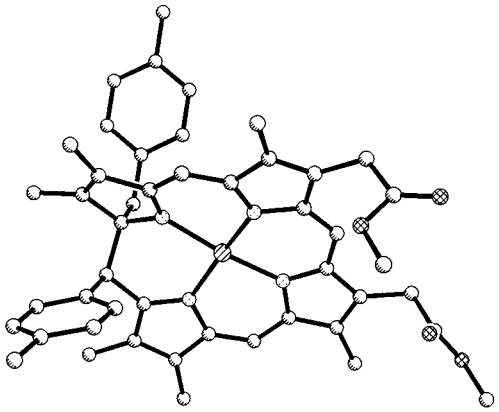


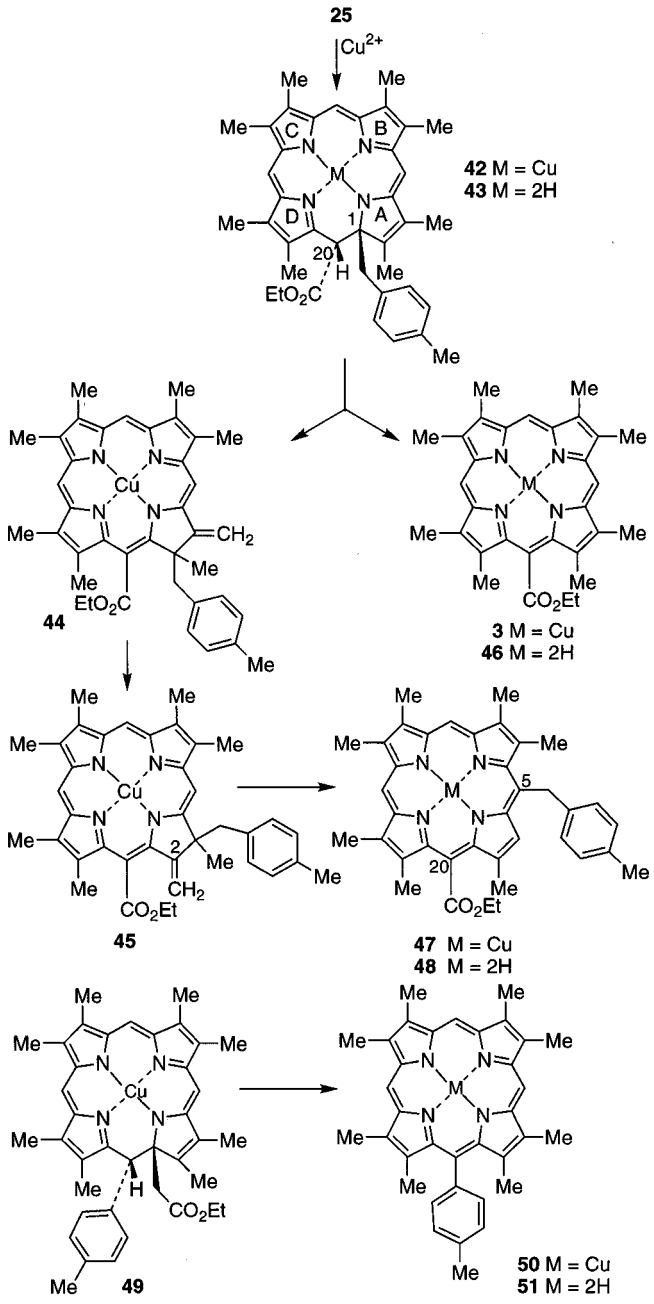
**Figure 2.** Molecular structure of the copper(II) complex **30**. Hydrogen atoms have been omitted for clarity.

**Table 1. Results from Rearrangement Experiments Using Compounds 29 and 32**

| | | product yield (%) | | | |
|---|---|---|---|---|---|
| compd | temp (°C) | 1-subd prod | porphyrin **34** | chlorin **32** | porphyrin **38** |
| **29** | 140 | | 33 | 1 | 3 |
| | 120 | | 21 | 11 | 2 |
| | 100 | 42 | 29 | 1 | 1 |
| **32** | 140 | | 12 | 21 | 78 |

confirmed the stepwise migration of *p*-tolylmethyl from the 1-positon to positions 2, 3, and 5. Figure 3A shows the X-ray structure for chlorin **45**, while the crystal structure of chlorin **44** is shown in Figure 3B. The second copper(II) porphyrin was identified as the 20-*p*-tolylporphyrin **50** by demetalation and characterization of the metal-free product **51**. This led us to the conclusion that the 1-(ethoxycarbonyl)methyl compound **49** must also have been a product from the cyclization of *a,c*-biladiene **25** since the methylene carbon in the 1-*p*-tolylmethyl group had been used to provide the 20-carbon in **49** (and **50**); cleavage of acetic side chains from such 1-substituted substances is not uncommon,[1] and the fact that we had not isolated compound **49** suggests that it was so labile under the reaction conditions that it was transformed into **50** *in situ*. Even during chromatography the 1-substituted compound **42** could be observed to decompose into the two chlorins **44** and **45**, and when the compound **42** (obtained from reaction of **6** at 100 °C in DMF, and therefore presumably contaminated with some **49**) was heated above 145 °C, copper(II) porphyrins were produced. Instability of the copper(II) complex **49** could be

**Scheme 5. Products from Copper(II)-Catalyzed Oxidative Cyclization of *a,c*-Biladiene Dihydrobromide 25**




attributed to the presence of the acetic side chain as indictated by the results obtained in cyclizations of the 19-propionic 1-((ethoxycarbonyl)methyl)-*a,c*-biladiene **1**.[1]

Copper(II)-promoted cyclization of **27** at 120 °C, afforded four products, namely, two copper(II) porphyrins and two copper(II) 1-substituted compounds. The major product was identified as the 1-propionic 20-*p*-tolyl copper(II) complex **52** (Scheme 6); Figure 4 shows the X-ray structure of **52**. The less abundant 1-substituted compound was deduced (from mass spectral data) to be the 20-acetic 1-*p*-tolylmethyl isomer **54** of compound **52**. The most abundant porphyrin was identified as the copper(II) 20-arylporphyrin **50**. Although not enough material was isolated for complete characterization, the second porphyrin isolated was deduced to be copper(II) porphyrin **55**, obtained by aryl elimination from the corresponding copper(II) 1-substituted compound. Table 2 shows the results obtained under variable conditions

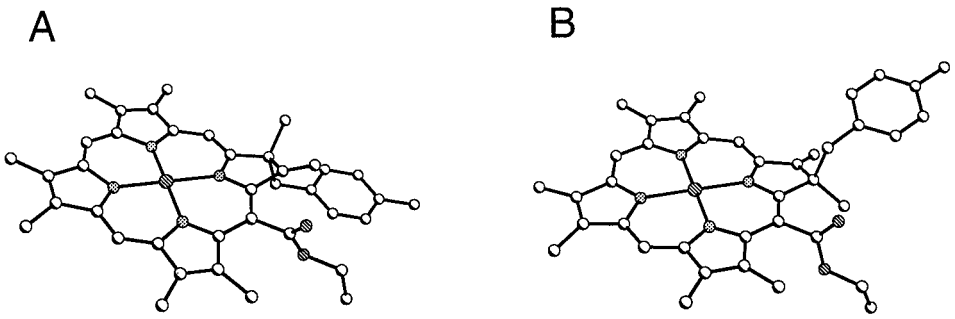
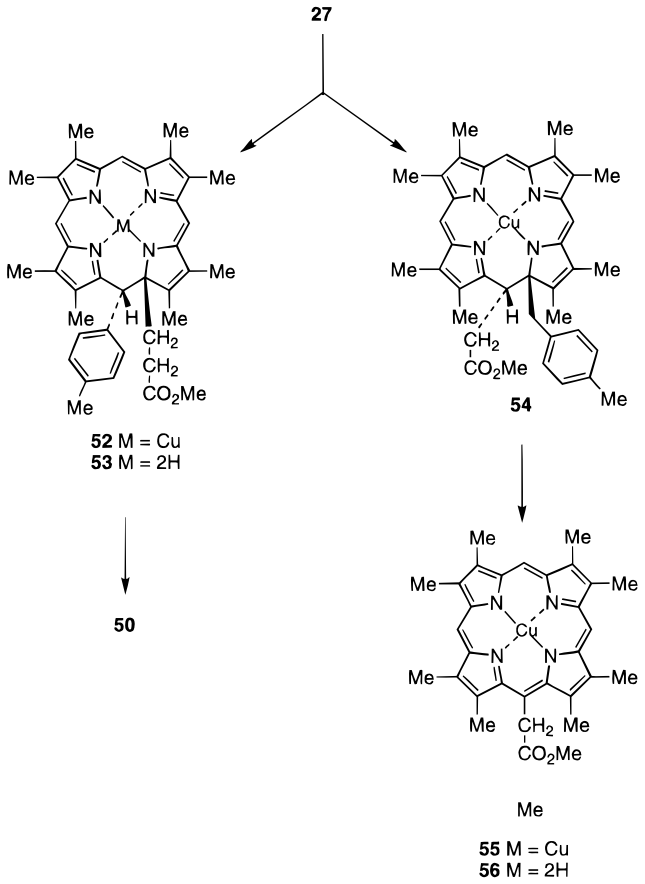



**Figure 3.** Molecular structure of (A) copper(II) chlorin **45** and (B) copper(II) chlorin **44**. Hydrogen atoms have been omitted for clarity.

**Scheme 6. Products from Copper(II)-Catalyzed Oxidative Cyclization of *a,c*-Biladiene Dihydrobromide 27**




during cyclization reactions of *a,c*-biladienes **19**, **20**, **25**, **27**, and **28**.

Low-temperature/room temperature cyclization of *a,c*-biladiene **28** gave two porphyrins, **34** and **60**, in yields of 8% and 2%, respectively; no significant amounts of 1-substituted intermediates **57** and **58** were isolated. At 125 °C, cyclization of **28** afforded porphyrin **34** as the major product, with again an insignificant amount of 1-substituted compound. Cyclization was then carried out at 100 °C, and this afforded three products, the two porphyrins (**34**, **60**) and a 1-substituted intermediate, believed to be **58** (Scheme 7). The identity of **60** was further confirmed by demetalation to give **61**. The precise structure of **58** was established using X-ray crystallography (Figure 5). At room temperature, copper(II) cyclization of **28** afforded only copper(II) porphyrins, with no 1-substituted products being isolated. Significant amounts of 1-substituted compounds were only observed at higher temperature (100 °C); at this temperature,

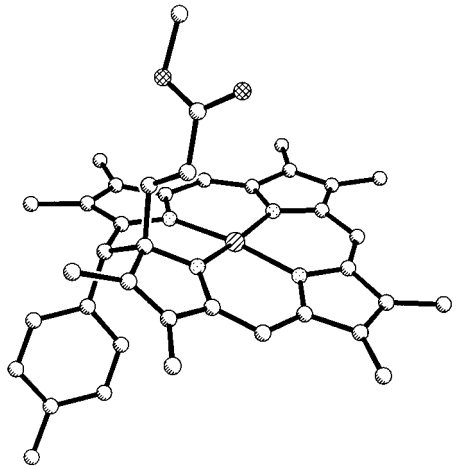


**Figure 4.** Molecular structure of the copper(II) complex **52**. Hydrogen atoms have been omitted for clarity.

**Table 2. Summary of *a,c*-Biladienes Studied, Reaction Conditions, and Products**

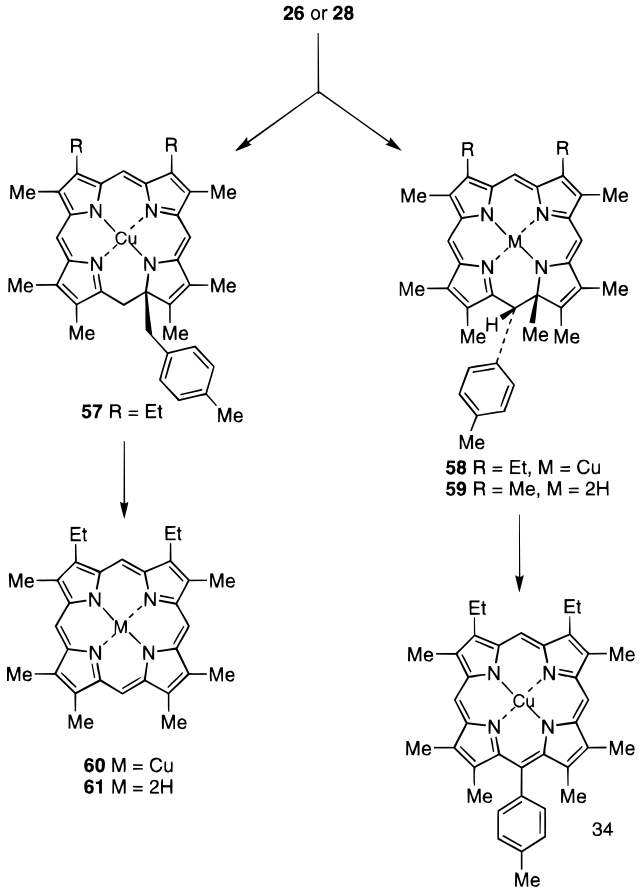
| | | product and yield (%) | | | |
|---|---|---|---|---|---|
| *a,c*-biladiene | temp (°C) | 1-subd prod | porphyrin (mono-*meso*-) | chlorin | porphyrin (di-*meso*-) |
| **19** | 120 | **30** (71) | **36** (4) | **33** (0) | a |
| | 145 | **30** (45) | **36** (14) | **33** (2.5) | a |
| **20** | 25 | **29** (81) | **34** (<1) | **32** (*a*) | **38** (*a*) |
| | 120 | **29** (8) | **34** (30) | **32** (4) | **38** (3) |
| **25** | 120 | **42** (33) | **50** (3) | **44** (0.5) | **47** (1) |
| | | | **3** (7) | **45** (1) | |
| **27** | 120 | **52** (41) | **50** (1) | a | a |
| | | **54** (4) | **55** (<1) | | |
| **28** | 25 | **58** (--) | **34** (9) | a | a |
| | 100 | **58** (18) | **34** (47) | a | a |
| | | | **60** (12) | | |
| | 125 | **58** (<1) | major product | a | a |

[a] No product isolated.

some 1-(*p*-tolyl)-20-methyl macrocycle **57** appeared to be produced, but it decomposed during chromatography to give copper (II) porphyrin **60**.

**Chromium(III)-Promoted Oxidative Cyclization of *a,c*-Biladiene Salts.** Boschi and co-workers[8] have shown that metal-free porphyrins can be obtained from the cyclization of *a,c*-biladienes using chromium(III) acetate in hot buffered ethanol or DMF. In the same study they concluded that when the 1,19 groups are other than methyl (e.g., ethyl or propionic methyl ester) an alternative mechanism to that established for copper(II)-promoted cyclization must be dominant. We have shown that if a modification of Boschi's method using mild chromium(III) cyclization conditions is employed, then intermediates (such as the metal free analogue of **2**) were isolated.[16] Our original studies concentrated on *a,c*-

**Scheme 7. Products from Copper(II)-Catalyzed Oxidative Cyclization of *a,c*-Biladiene Dihydrobromides 26 and 28**




biladienes with alkyl groups in the terminal 1,19-positions. In the present study the *a,c*-biladienes chosen for cyclization are again extended to substances with at least one arylmethyl group in the two terminal positions. The results clearly demonstrate mechanistic similarities between the copper(II)- and chromium(III)-promoted cyclizations.

The main advantage of the chromium(III) method over the copper(II) approach is the formation of metal-free intermediates and porphyrins during the cyclization process. Many of the 1-substituted cyclized intermediates which we have isolated as copper(II) complexes have proven unstable to the harsh acidic ($H_2SO_4$/TFA) conditions of demetalation,[1] and we have needed to depend upon X-ray diffraction analysis of the copper(II) complexes to accurately characterize the products; however, the chromium(III) reaction offers an attractive alternative because metal-free reaction intermediates and porphyrins are isolated, and proton NMR characterization is therefore available.

To initiate this study, *a,c*-biladiene **21** was chosen as the substrate for cyclization (due to the simplicity of its proton NMR spectrum). Cyclization at 100 °C in DMF for 60 min unexpectedly provided the metal-free 1-*p*-tolylmethyl compound **31** as the only product, in 52% yield.

Chromium(III)-promoted cyclization of *a,c*-biladiene **27** in DMF at 100 °C also yielded the 1-substituted compound as the major product. Although decomposition was evident, with several trace decomposition products

(16) Gerzevske, K. R.; Lin, J. J.; Smith, K. M. *Heterocycles* **1994**, *37*, 207.

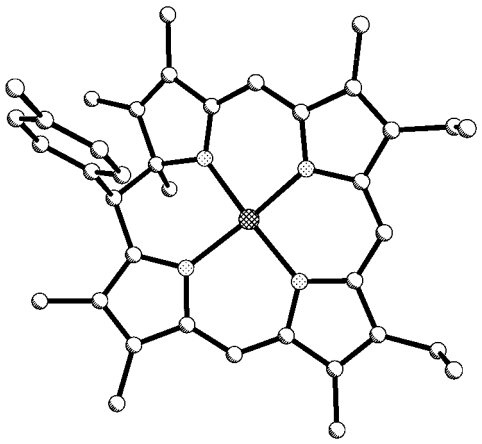


**Figure 5.** Molecular structure of chlorin **58**. Hydrogen atoms have been omitted for clarity.

observable (TLC), the major product isolated (but in only 4% overall yield) was a blue green compound identified as the metal-free analogue **53** of compound **52**. The structure of the product was determined by proton NMR spectroscopy (comparing three singlets in the meso region at 6.23, 5.42, and 4.81 ppm with earlier decoupling experiments[2]). This result provided further evidence for the similarity in cyclization mechanisms between the traditional copper(II) and newer chromium(III) methods. Interestingly, none of the isomeric 1-(*p*-tolylmethyl)-20-((methoxycarbonyl)methyl) compound **54** was isolated. As in other examples of compounds containing a 1- or 19-propionic methyl ester,[1] the chromium(III) cyclization method resulted in a product in which the alkyl ester is situated in the 1-position. Steric interactions may play a role in the cyclization with the chromium(III) method; in contrast, however, the copper(II) method yielded a small amount of isomer **54** (vide supra).

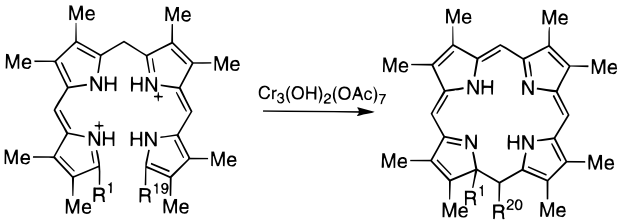
Chromium-assisted cyclization of *a,c*-biladiene **25** under conditions similar to those used for synthesis of compound **21** resulted only in decomposition products. A reaction at 0 °C gave metal-free 1-substituted compound **43** as the only product, in 13% yield. *a,c*-Biladiene **26** was also oxidized under the same conditions as used for *a,c*-biladiene **21** to provide the 1-substituted compound **59** as the only product. Table 3 summarizes the products observed in the chromium(III) cyclizations of *a,c*-biladienes.

## Conclusions

*a,c*-Biladienes bearing 1- and/or 19-(*p*-tolylmethyl) substituents can be cyclized using copper(II) oxidation methodology to give numerous products in which the 1- or 19-substituents are adapted, eliminated, or rearranged to other points on the tetrapyrrole macrocycle. Copper(II)-assisted cyclization of *a,c*-biladiene **25** provided the most impressive example of the overall phenomenon; after cyclization to give a 1-*p*-tolylmethyl macrocycle, stepwise migration of the 1-substituent to adjacent carbons gives the chlorins **44** and **45** and finally the 5-(*p*-tolylmethyl)-substituted porphyrin **47**. *a,c*-Biladienes **19** and **20** demonstrated product distribution upon copper(II)-promoted cyclization; for example, *a,c*-biladiene **20** afforded the copper(II) 1-(*p*-tolylmethyl)-20-*p*-tolyl macrocycle **29**, the copper(II) 2-methylidenechlorin **32**, and copper(II) porphyrins **34** and **38**.

19-((Methoxycarbonyl)ethyl)-1-(*p*-tolylmethyl)-*a,c*-biladiene **27** afforded four products upon copper(II)-promoted

**Table 3. Structures of *a*,*c*-Biladienes Studied, with Reaction Conditions and Products[a]**




| *a*,*c*-biladiene | | | reaction conditions | | products | | | |
|---|---|---|---|---|---|---|---|---|
| compd | $R^1$ | $R^{19}$ | temp (°C) | solvent | compd | $R^1$ | $R^{20}$ | yield (%) |
| **21** | PX | PX | 100 | DMF | **31** | PX | *p*-$C_6H_4Me$ | 50 |
| **26** | PX | Me | 140 | DMF | **59** | Me | *p*-$C_6H_4Me$ | 51 |
| | | | 100 | | **59** | Me | *p*-$C_6H_4Me$ | 40 |
| **27** | PX | $P^{Me}$ | 100 | DMF | **53** | $P^{Me}$ | *p*-$C_6H_4Me$ | 13 |
| **25** | PX | $AE^E$ | 0 | EtOH aq | **43** | PX | $CO_2Et$ | 30 |

[a] PX = $CH_2(C_6H_4)$-*p*-Me; $AE^E$ = $CH_2CO_2Et$; $P^{Me}$ = $CH_2CH_2CO_2Me$.

oxidation, and none of them showed any substituent migration; the major products are macrocycles with the *p*-tolylmethyl contributing a carbon atom to form the bridge in **52** and in porphyrin **50**. Thus, the *p*-tolylmethyl group showed more tendency to contribute its methylene to become the macrocyclic bridging carbon than did the propionic side chain. Similarly, 19-methyl-1-(*p*-tolylmethyl)-*a*,*c*-biladiene **28** showed the same distribution of products as did *a*,*c*-biladiene **27**, again indicating that the *p*-tolylmethyl group is also more likely than methyl to contribute the interpyrrolic carbon atom in the cyclization process. The results of the earlier copper(II)-promoted cyclization studies using only alkyl groups[1] and data from the present work complement the chromium(III) cyclization results, which concluded that the 1- or 19-substituent most likely to provide the interpyrrolic (20-) carbon follows the order (ethoxycarbonyl)methyl > *p*-tolylmethy > methyl > (methoxycarbonyl)ethyl.[16] Finally, metal-free 1-substituted macrocycles (e.g., **31, 43, 53, 59**) can be prepared from oxidative cyclization of *a*,*c*-biladienes using the Boschi chromium-(III) procedure.

## Experimental Section

General details are as previously described.[17] Mass spectra were measured at the Mass Spectrometry Facility, University of California, San Francisco.

**Pyrrole. 2-Formyl-3,4-dimethyl-5-(*p*-tolylmethyl)pyrrole (7).** Benzyl 3,4-dimethyl-5-(*p*-tolylmethyl)pyrrole-2-carboxylate[18,19] (3.0 g, 0.90 mol) in THF (110 mL) containing 10% Pd−C (229 mg) and triethylamine (2 drops) was hydrogenated at rt overnight. The catalyst was filtered off through a bed of Celite which was rinsed with a small amount of DMF and THF, and the filtrate was evaporated to give an oil. After the solution was cooled to 0 °C under $N_2$, cold TFA (8.7 mL) was added. After 10 min, triethyl orthoformate (8.7 mL) was added, and the mixture was stirred for 0.5 h before being diluted with $CH_2Cl_2$ and treated with 10% aqueous sodium carbonate. The organic layer was washed with 10% aqueous sodium carbonate and brine before being dried over anhydrous sodium sulfate. The organic phase was filtered through an anhydrous sodium sulfate plug and then evaporated. Crystallization from $CH_2Cl_2$/*n*-hexane afforded 1.35 g (66% yield) of the title pyrrole: mp 136−137 °C; $\delta$ ($CDCl_3$) 9.45 (s, 1H), 8.65 (br s, 1H), 7.12, 7.04 (each d, $J$ = 7.8 Hz, 2H), 3.87 (s, 2H), 2.32, 2.25, 1.97 (each s, 3H). Anal. Calcd for $C_{15}H_{17}NO$: C, 79.25; H, 7.54; N, 6.17. Found: C, 78.92; H, 7.36; N, 6.11.

**Dipyrromethane. *tert*-Butyl 9-((Benzyloxy)carbonyl)-3,7-diethyl-2,8-dimethyl-dipyrromethane-1-carboxylate (15).** *tert*-Butyl 5-(acetoxymethyl)-4-ethyl-3-methylpyrrole-2-carboxylate[7c] (1.15 g, 4.09 mmol) and benzyl 4-ethyl-3-methylpyrrole-2-carboxylate[17] (1.96 g, 8.06 mmol) under $N_2$ were stirred with dichloromethane (100 mL) and Montmorillite K-10 clay (3.00 g) for 24 h at rt. The clay was then filtered off and rinsed with dichloromethane (600 mL). Evaporation gave a brownish oil which was flashed-chromatographed on silica gel, eluting with dichloromethane, to give an oily residue which solidified to afford 1.52 g (80% yield) of the title dipyrromethane: mp 58−60 °C; $\delta$ ($CDCl_3$) 8.47, 8.34 (each br s, 1H), 7.38 (m, 5H), 5.27, 3.84 (each s, 2H), 2.40 (m, 4H), 2.29, 2.25 (each s, 3H), 1.53 (s, 9H), 1.05 (m, 6H). Anal. Calcd for $C_{28}H_{36}N_2O_4$: C, 72.37; H, 7.81; N, 6.03. Found: C, 72.43; H, 7.70; N, 6.04.

**Tripyrrenes. *tert*-Butyl 1-(*p*-Tolylmethyl)-2,3,7,8,12,-13-hexamethyl-5-tripyrrene-14-carboxylate Hydrobromide (22).** *tert*-Butyl 9-((benzyloxy)carbonyl)-2,3,7,8-tetramethyldipyrromethane-1-carboxylate (**14**)[1] (6.0 g, 13.7 mmol) in dry THF (100 mL) containing 10% Pd−C (500 mg) was hydrogenated at rt and atmospheric pressure overnight. The catalyst was filtered off through a bed of Celite which was washed with distilled THF. The filtrate was evaporated to give a white solid which was dried under high vacuum. The dipyrromethanecarboxylic acid and formylpyrrole **7** (3.16 g, 15.12 mmol) were dissolved in distilled $CH_2Cl_2$ (200 mL). Next, TsOH (5.75 g) in distilled MeOH (20 mL) was added over a period of 15 min, and the mixture was stirred at rt for 45 min (solution turned from clear to a deep yellow orange). The mixture was diluted with $CH_2Cl_2$ (200 mL) and washed with aqueous saturated $NaHCO_3$ (200 mL), and the organic phase was dried over anhydrous sodium sulfate. The solvent was immediately removed (at 30 °C) using a benzene chaser to eliminate any residual water and MeOH. The residue was placed under high vacuum for several hours before being dissolved in dichloromethane (40 mL) and (after cooling to 0 °C) having a slow stream of HBr(g) pass through the solution for 5 s (solution turned bright orange). The solvent was removed immediately over low heat, and a benzene chaser was added and removed. The residue was dissolved in dichloromethane (130 mL) and MeOH (10 mL) before addition of ether (200 mL). The solution was placed at −20 °C and then at −40 °C before being filtered to give the title compound (4.85 g, 81% yield). Proton NMR integration indicated an approximate 10% loss of the *tert*-butyl protecting group; therefore, a portion was subjected to further HBr(g) treatment and crystallized as the monocarboxylic acid for analysis: mp 192−211 °C; $\lambda_{max}$ ($CH_2Cl_2$) 277 nm ($\epsilon$ 28 500), 372 (14 000), 500 (88 700); $\delta$ ($CDCl_3$) 13.32, 13.23, 10.42 (each br s, 1H), 7.27, 7.10 (d, $J$ = 8.0 Hz, 4H), 7.07 (s, 1H), 4.41 (s, 2H), 4.31 (s, 2H), 2.29, 2.23, 1.90 (each s, 3H), 2.21, 2.04 (each 6H, s), 1.55 (s, 9H). Anal. Calcd for $C_{33}H_{42}BrN_3O_2$: C, 66.68; H, 7.16; N, 7.11. Found: C, 66.68; H, 7.02; N, 6.97.

**Benzyl 2,3,7,8,12,13-Hexamethyl-1-(*p*-tolylmethyl)-5-tripyrrene-14-carboxylate Hydrobromide (23).** *tert*-Butyl

(17) Wallace, D. M.; Leung, S. H.; Senge, M. O.; Smith, K. M. *J. Org. Chem.* **1993**, *58*, 7245.
(18) Gerzevske, K. R. Ph.D. Dissertation, University of California, Davis, 1994.
(19) Gribble, G. W.; Kelly, W. J.; Emery, S. E. *Synthesis* **1978**, 763.

9-((benzyloxy)carbonyl)-2,3,7,8-tetramethyldipyrromethane-1-carboxylate[1] (**15**) (769 mg, 1.76 mmol) was dissolved in cold TFA (4.4 mL) and stirred under dry nitrogen in an ice bath for 30 min before formylpyrrole **7** (444 mg, 1.95 mmol) in MeOH (21 mL) was introduced. The solution was stirred for an additional 1 h before a slow stream of HBr gas was passed through the solution for 10 s, followed by addition of diethyl ether to precipitate out the product. Isolation of the title compound (792 mg, 72%) was achieved through suction filtration and washing the product with cold ether: mp 193−5 °C; $\lambda_{max}$ ($CH_2Cl_2$) 280 nm ($\epsilon$, 28 800), 376 (12 900), 500 (91 600); $\delta$ ($CDCl_3$) 13.25, 13.18, 10.58 (each br s, 1H), 7.48, 7.08 (each d, $J$ = 7.5 Hz, 2H), 7.32 (m, 5H), 7.07 (s, 1H), 5.29, 4.38, 4.33-(each s, 2H), 2.21 (s, 6H), 2.28, 2.24, 2.03, 2.00, 1.91 (each s, 3H). Anal. Calcd for $C_{36}H_{40}BrN_3O_2$: C, 69.09; H, 6.45; N, 6.72. Found: C, 68.86; H, 6.36; N, 6.71.

**Benzyl 8,12-Diethyl-2,3,7,13-tetramethyl-1-(*p*-tolylmethyl)-5-tripyrrene-14-carboxylate Hydrobromide (24).** *tert*-Butyl 9-((benzyloxy)carbonyl)-3,7-diethyl-2,8-dimethyldipyrromethane-1-carboxylate (**14**) (498 mg, 1.07 mmol) was dissolved in cold TFA (3.4 mL) and stirred under nitrogen and in an ice bath for 20 min before formylpyrrole **7** (279 mg, 1.22 mmole) in MeOH (14 mL) was added. The mixture was stirred for an additional 1 h before being treated with a slow stream of HBr gas for 10 s, followed by precipitation with cold ether to give 483 mg (69%) of the title compound: mp 200−205 °C; $\lambda_{max}$ ($CH_2Cl_2$) 500 nm ($\epsilon$, 100 000); $\delta$ ($CDCl_3$) 13.26, 13.23, 10.53 (each br s, 1H), 7.48, 7.06 (each d, $J$ = 8.1 Hz, 2H), 7.31 (m, 5H), 7.22 (s, 1H), 5.30 (s, 2H), 4.39, 4.33 (each s, 2H), 2.33, 2.49 (each q, $J$ = 7.5 Hz, 2H), 2.28, 2.21, 2.17, 2.02 (each s, 3H), 1.91 (s, 3H), 1.14, 1.03 (each t, $J$ = 7.5 Hz, 3H). Anal. Calcd for $C_{38}H_{44}BrN_3O_2 \cdot H_2O$: C, 68.85; H, 6.85; N, 6.34. Found: C, 69.06; H, 6.59; N, 6.24.

***a,c*-Biladiene Salts. 8,12-Diethyl-2,3,7,13,17,18-hexamethyl-1,19-bis(*p*-tolylmethyl)-*a,c*-biladiene Dihydrobromide (20).** 3,7-Diethyl-2,8-dimethyldipyrromethane-1,9-dicarboxylic acid[7b] (**17**) (500 mg, 1.00 mmol) in THF (30 mL) was hydrogenated over 10% Pd−C (70 mg). After uptake of hydrogen ceased, the catalyst was filtered off through a bed of Celite, and the filtrate was concentrated (at 40 °C) under vacuum. The resulting white solid (**31**) was dissolved in TFA (6 mL) and stirred at rt for 15 min before being cooled to 0 °C followed by rapid addition of formylpyrrole **7** (620 mg, 2.7 mmol) over a 3 min period. After the solution was stirred for 1 h, a slow stream of HBr gas was passed for 10 s through the solution; then ether (100 mL) was added dropwise to initiate precipitation. The flask was placed at −20 °C for 4 h before the product was filtered, washed with cold ether, and dried (683 mg, 84%): mp > 300 °C; $\lambda_{max}$ ($CH_2Cl_2$) 456 nm ($\epsilon$ 136 000), 534 (103 000); $\delta$ ($CDCl_3$) 13.44, 13.37 (each br s, 2H), 7.33, 7.10 (each d, $J$ = 7.8 Hz, 2H), 7.12 (s, 2H), 5.24 (s, 2H), 4.42 (s, 4H), 2.57 (q, $J$ = 7.2 Hz, 4H), 2.29 (s, 6H), 2.24 (s, 12H), 1.93 (s, 6H), 0.67 (t, $J$ = 7.5 Hz, 3H); HRMS calcd for $[C_{45}H_{54}BrN_4]^+$ 729.353, found 729.354. Anal. Calcd for $C_{45}H_{54}Br_2N_4$: C, 66.81 ; H, 6.73; N, 6.91. Found: C, 66.87; H, 6.73; N, 6.91.

**8,12-Bis((methoxycarbonyl)methyl)-2,3,7,13,17,18-hexamethyl-1,19-bis(*p*-tolylmethyl)-*a,c*-biladiene Dihydrobromide (19).** The title *a,c*-biladiene was prepared in 84% yield from 3,7-bis((methoxycarbonyl)methyl)-2,8-dimethyldipyrromethane-1,9-dicarboxylic acid[7b] (**16**) (2.28 g, 4.57 mol) in THF (100 mL) with 10% Pd−C (400 mg) and treatment with TFA (20 mL) and formylpyrrole **7** (2.20 mg, 9.68 mmol) in MeOH (30 mL), followed by HBr gas and ether (250 mL) precipitation, to give (3.75 g): mp >290 °C dec; $\lambda_{max}$ ($CH_2Cl_2$) 452 nm ($\epsilon$ 90 000), 528 (131 000); $\delta$ ($CDCl_3$) 13.56, 13.50 (each br s, 2H), 7.34, 7.11 (each d, $J$ = 8.0 Hz, 2H), 7.15 (s, 2H), 5.26 (s, 2H), 4.45(s, 4H), 3.80 (s, 4H), 3.30 (s, 6H), 2.30, 2.27, 2.24, 1.93 (each s, 6H). Anal. Calcd for $C_{47}H_{54}Br_2N_4O_4 \cdot H_2O$: C, 62.30; H, 6.12; N, 6.19. Found: C, 62.01; H, 5.88; N, 6.09.

**2,3,7,8,12,13,17,18-Octamethyl-1,19-bis(*p*-tolylmethyl)-*a,c*-biladiene Dihydrobromide (21).** 2,3,7,8-Tetramethyldipyrromethane-1,9-dicarboxylic acid[3] (**18**) (178 mg, 0.613 mmol) was dissolved in TFA (2.4 mL) and stirred at rt for 5 min before rapid addition of formylpyrrole **7** (350 mg, 1.53 mmol) in MeOH (4 mL). Stirring was continued for a further 1 h before HBr gas was bubbled into the solution for 10 s. Ether (50 mL) was added dropwise to initiate precipitation, and the flask was placed at −20 °C overnight before the product was filtered off, washed with cold ether, and dried to give the title compound (365 mg, 76%): mp > 250 °C dec; $\lambda_{max}$ ($CH_2Cl_2$) 456 nm ($\epsilon$ 144 000), 532 (90 000); $\delta$ ($CDCl_3$) 13.45, 13.31 (each br s, 2H), 7.32, 7.10 (each d, $J$ = 8.0 Hz, 2H), 7.11 (s, 2H), 5.21 (s, 2H), 4.41 (s, 4H), 2.29, 2.23, 2.22, 1.93, 1.92 (each s, 6H). Anal. Calcd for $C_{43}H_{50}Br_2N_4$: C, 65.99; H, 6.44; N, 7.16. Found: C, 65.72; H, 6.40; N, 6.96.

**1-((Ethoxycarbonyl)methyl)-2,3,7,8,12,13,17,18-octamethyl-19-(*p*-tolylmethyl)-*a,c*-biladiene Dihydrobromide (25).** Tripyrrene **22** (3.20 g, 5.40 mmole) was dissolved in dry TFA (30 mL) under $N_2$ and stirred at rt for 5 min before being cooled to 0 °C and then the addition of formylpyrrole **6**[1] (1.36 g, 6.48 mmol) in EtOH (25 mL). After 3 min of stirring, HBr gas was bubbled into the solution for 1 min, and stirring was continued at rt for 4 h. The solvent was removed under vacuum, and the residue was azeotropically distilled with a portion of benzene (200 mL). The solid was redissolved in dichloromethane (35 mL) and treated with diethyl ether (300 mL). The solid was collected and recrystallized again from $CH_2Cl_2$ (30 mL) and MeOH (15 mL) and ether to afford the title *a,c*-biladiene (3.30 g, 80%) after filtering, washing with cold ether, and drying under vacuum: mp >195 °C dec; $\lambda_{max}$ ($CH_2Cl_2$) 454 nm ($\epsilon$ 116 000), 530 (82 000); $\delta$ ($CDCl_3$) 13.47, 13.41, 13.30, 13.21 (each br s, 1H), 7.32, 7.09 (each d, $J$ = 7.8 Hz, 2H), 7.16 (each s, 1H), 5.20 (s, 2H), 4.41 (s, 2H), 4.23 (s, 2H), 4.20 (q, $J$ = 7.2 Hz, 2H), 2.30, 2.29, 2.10, 1.98, 1.93, 1.92, 1.90 (each s, 3H), 2.23 (s, 6H), 1.28 (t, $J$ = 7.2 Hz, 3H). Anal. Calcd for $C_{38}H_{48}Br_2N_4O_2$: C, 60.64; H, 6.43; N, 7.44. Found: C, 60.41; H, 6.12; N, 7.55.

**19-((Methoxycarbonyl)ethyl)-2,3,7,8,12,13,17,18-octamethyl-1-(*p*-tolylmethyl)-*a,c*-biladiene Dihydrobromide (27).** This compound was prepared similarly to *a,c*-biladiene **25** from benzyl 1-(*p*-tolylmethyl)-2,3,7,8,12,13-hexamethyl-5-tripyrrene-14-carboxylate hydrobromide (**23**) (370 mg, 0.590 mmol); the tripyrrene was first treated with 30% HBr/$CH_3CO_2H$ (5 mL) for 1 h at 0 °C and then with TFA (10 mL) for 1 h. The mixture was stirred at rt for an additional 1 h, before being cooled in an ice bath and then addition of formylpyrrole[1] **9** (200 mg, 0.956 mmol) in MeOH (12 mL). The product (378 mg, 84%) was obtained after filtering, washing with cold ether, and drying under vacuum, mp > 200 °C dec; $\lambda_{max}$ ($CH_2Cl_2$) 454 nm ($\epsilon$ 122 000), 530 (84 000); $\delta$ ($CDCl_3$) 13.46, 13.41, 13.32, 13.07 (each br s, 1H), 7.32, 7.10 (each d, $J$ = 7.8 Hz, 2H), 7.12, 7.11 (each s, 1H), 5.20 (s, 2H), 4.42 (s, 2H), 3.67 (s, 3H), 3.28 (t, $J$ = 7.3 Hz, 2H), 3.00 (t, $J$ = 7.3 Hz, 2H), 2.29, 2.28, 2.23, 2.22, 2.21, 2.05, 1.90 (each s, 3H), 1.91 (s, 6H). Anal. Calcd for $C_{38}H_{48}Br_2N_4O_2$: C, 60.64; H, 6.43; N, 7.44. Found: C, 60.80; H, 6.33; N, 7.52.

**8,12-Diethyl-1,2,3,7,13,17,18-heptamethyl-19-(*p*-tolylmethyl)-*a,c*-biladiene Dihydrobromide (28).** Under $N_2$, tripyrrene **24** (0.396 g, 0.607 mmol) was dissolved in 30% HBr/acetic acid (5 mL) and stirred at 0 °C for 1 h. TFA (10 mL) was added, and the solution was stirred for another 1 h at 0 °C. The solution was then stirred at rt for an additional 1 h while being warmed up to rt. Finally the solution was cooled again (0 °C), formylpyrrole **8**[4] (0.110 g, 0.803 mmol) in MeOH (13 mL) was added, and the mixture was stirred for 90 min before being treated for 10 s with a stream of HBr gas. Precipitation with ether gave the title compound (338 mg; 85%) after filtering, washing with cold ether, and drying, mp > 210 °C dec; $\lambda_{max}$ ($CH_2Cl_2$) 454 nm ($\epsilon$, 115 000), 530 (91 000); $\delta$ ($CDCl_3$) 13.43, 13.36 13.22 13.19 (each br s, 1H), 7.32, 7.11 (each d, $J$ = 7.5 Hz, 2H), 7.10, 7.08 (each s, 1H), 5.20 (s, 2H), 4.42(s, 2H), 2.68 (s, 3H), 2.28, 2.29 (each s, 3H each), 2.23 (s, 9H), 2.56 (m, 4H), 2.00 (s, 3H), 1.93 (s, 3H), 0.646 (m, 6H). Anal. Calcd for $C_{38}H_{48}Br_2N_4 \cdot 1.5H_2O$: C, 61.19; H, 6.90; N, 7.52. Found: C, 61.12; H, 6.43; N, 7.35.

**2,3,7,8,12,13,17,18,19-Nonamethyl-1-(*p*-tolylmethyl)-*a,c*-biladiene Dihydrobromide (26).** This compound was prepared using a method similar to that used for *a,c*-biladiene **28** from benzyl 2,3,7,8,12,13-hexamethyl-1-(*p*-tolylmethyl)-5-tripyrrene-14-carboxylate hydrobromide (**23**) (248 mg, 0.396 mmol) in 30% HBr/HOAc (7 mL) with TFA (8 mL) and 2-formyl-3,4,5-trimethylpyrrole (**8**) (62 mg, 0.452 mmol) in MeOH (12 mL). The title *a,c*-biladiene (208 mg, 76% yield) **26** was filtered off, washed with cold ether, and dried under

vacuum, mp > 185 °C dec; $\lambda_{max}$ ($CH_2Cl_2$) 452 nm ($\epsilon$, 139 000), 530 (71 800); $\delta$ ($CDCl_3$) 13.41, 13.28, 13.22, 13.11 (each br s, 1H), 7.32, 7.10 (each d, $J$ = 7.8Hz, 2H), 7.11, 7.09 (each s, 1H), 5.17 (s, 2H), 4.22 (s, 2H), 2.67, 2.29, 2.28, 2.23, 1.99, 1.93 (each s, 3H), 2.22, 1.92 (each s, 6H). Anal. Calcd for $C_{36}H_{44}Br_2N_4 \cdot 0.5H_2O$: C, 61.95; H, 6.45; N, 8.20. Found: C, 61.63; H, 6.47; N, 7.99.

**Copper(II)-Promoted Oxidative Cyclizations. Cyclization of 1-((Ethoxycarbonyl)methyl)-2,3,7,8,12,13,17,18-octamethyl-19-(*p*-tolylmethyl)-a,c-biladiene Dihydrobromide (25).** Copper(II) acetate (3.10 g, 0.017 mol) was added to DMF (40 mL) under $N_2$. The mixture was heated at 120 °C for 5 min before the *a,c*-biladiene **25** (0.765 g, 1.00 mmol) was added all at once and stirred an additional 3 min before cooling. The mixture was diluted with a biphasic mixture of iced water and dichloromethane. After the two layers were separated, the aqueous layer was washed with more dichloromethane (2 × 100 mL). The combined organic layer was washed with brine (100 mL) and dried over anhydrous sodium sulfate before being filtered and concentrated. Residual DMF was removed under high vacuum. The reaction was repeated under the same conditions with identical amounts of reactants, and the crude mixtures were combined for separation. To remove the base-line impurities, a flash silica gel column, eluting with 10% cyclohexane and 0.05% MeOH in dichloromethane, afforded the mixture of products. Further flash silica gel chromatography, eluting with a solvent gradient from 33% cyclohexane in toluene to pure toluene, afforded 84 mg of the least polar porphyrin *copper(II) 2,3,7,8,12,13,17,18-octamethyl-20-(p-tolylmethyl)porphyrin* (**50**) [mp 292−295 °C dec; $\lambda_{max}$ ($CH_2Cl_2$) 330 nm ($\epsilon$ 19 200), 402 (207 000), 528 (16 600), 564 (20 400); LRMS calcd for $[C_{35}H_{34}CuN_4]^+$ 573.207, found 573.6. Anal. Calcd for $C_{35}H_{34}CuN_4 \cdot 0.5H_2O$: C, 72.14; H, 6.06; N, 9.62. Found: C, 72.59; H, 6.10; N, 9.62], a mixture of chlorins and porphyrins, and 436 mg of *copper(II) 20-(ethoxycarbonyl)-2,3,7,8,12,13,17,18-octamethyl-1-(p-tolylmethyl)-1,20-dihydroporphyrin* (**42**) [mp 242−245 °C dec to porphyrin; $\lambda_{max}$ ($CH_2Cl_2$) 321 nm ($\epsilon$ 23 700), 416 (45 200), 764 (8500), 837 (14 100). Anal. Calcd for $C_{39}H_{41}CuN_4O_2$: C, 70.83; H, 6.25, N, 8.47; Found: C, 70.63; H, 6.39; N, 8.33]. Finally, 40 mg of the most polar *compound copper(II) 2,3,7,8,12,13,17,18-octamethyl-20-(ethoxycarbonyl)porphyrin* (**3**) was obtained [mp > 300 °C; $\lambda_{max}$ ($CH_2Cl_2$) 332 nm ($\epsilon$, 15 500), 399 (154 400), 526 (100 200), 564 (14 300). Anal. Calcd for $C_{31}H_{32}N_4O_2Cu \cdot H_2O \cdot CH_3OH$: C, 63.45; H, 6.33; N, 9.25. Found: C, 63.40; H, 5.95; N, 8.95]. Removal of the copper from **50** was accomplished using the standard method of $H_2SO_4$/TFA, to yield the metal-free porphyrin *2,3,7,8,12,13,17,18-octamethyl-20-p-tolylporphyrin* (**51**) [mp > 300 °C; $\lambda_{max}$ ($CH_2Cl_2$) 400 nm ($\epsilon$ 175 000), 501 (22 000), 534 (14 500), 570 (13 400), 622 (9700); $\delta$ ($CDCl_3$) 10.11 (s, 2H), 9.88 (s, 1H), 7.91, 7.54 (each d, $J$ = 7.8 Hz, 2H), 3.59, 3.56, 3.52 (each s, 3H), 2.73 (s, 3H), 2.47 (s, 6H), −3.20 (br s, 2H); LRMS calcd for $[C_{35}H_{36}N_4]^+$ 512.294, found 512.5. Anal. Calcd for $C_{35}H_{36}N_4$: C, 81.98 H, 7.08; N, 10.93. Found: C, 81.69; H, 6.94; N, 10.99]. Removal of copper ($H_2SO_4$/TFA) from a small amount of porphyrin **3** gave *2,3,7,8,-12,13,17,18-octamethyl-20-(ethoxycarbonyl)porphyrin* (**46**) [mp > 300 °C; $\lambda_{max}$ ($CH_2Cl_2$) 398 nm ($\epsilon$, 106 100), 500 (15 000), 532 (12 400), 568 (10 300), 622 (9700); $\delta$ ($CDCl_3$) 10.36 (s, 2H), 10.29 (s, 1H), 5.04 (q, $J$ = 7.2 Hz, 2H), 3.51 (s, 12H), 3.41, 3.16 (each s, 6H), 1.76 (t, $J$ = 7.2 Hz, 3H), −1.80 (br s, 2H). Anal. Calcd for $C_{31}H_{34}N_4O_2 \cdot H_2O$: C, 72.62, H, 7.08, N, 10.93. Found: C, 72.88, H, 6.86, N, 10.88]. Further separation of the mixed porphyrin/chlorin band (above) was accomplished by flash silica gel chromatography, eluting first with a solvent gradient (33% $CH_2Cl_2$ in cyclohexane to 33% cyclohexane in $CH_2Cl_2$) and then using a second column eluting with 2% ethyl acetate in cyclohexane. The least polar band gave 6 mg of the copper(II) 3-methylidenechlorin *copper(II) 20-(ethoxycarbonyl)-2,7,8,12,13,17,18-heptamethyl-3-methylidene-2-(p-tolylmethyl)-chlorin* (**44**) [mp 224−226 °C; $\lambda_{max}$ ($CH_2Cl_2$) 310 nm ($\epsilon$, 17 100), 410 (133 400), 514 (9400), 552 (12 400), 582 (10 800), 628 (38 400)], the band of medium polarity gave 12 mg of the copper(II) 2-methylidenechlorin *copper(II) 20-(ethoxycarbonyl)-2,7,8,,12,13,17,18-heptamethyl-2-methylidene-3-(p-tolylmethyl)-chlorin* (**45**) [mp 216−8 °C; $\lambda_{max}$ ($CH_2Cl_2$) 310 nm ($\epsilon$, 19 000), 406 (146 700), 508 (9000), 548 (12 000), 582 (12 400), 626 (41 700)], and the most polar band gave 12 mg of *copper(II) 20-(ethoxycarbonyl)-2,3,7,8,12,13,17,18-octamethyl-5-(p-tolylmethyl)porphyrin* (**47**) [mp 240−242 °C dec; $\lambda_{max}$ ($CH_2Cl_2$) 408 nm ($\epsilon$, 221 500), 538 (15 500), 572 (16 300); LRMS calcd for $[C_{39}H_{40}CuN_4O_2]^+$ 659.2, found 659.2. Anal. Calcd for $C_{39}H_{40}CuN_4O_2 \cdot 0.5H_2O$: C, 70.33; H, 6.18; N, 8.38. Found: C, 70.19; H, 6.01; N, 8.34]. Using the standard demetalation protocol, 10 mg of **47** was used to obtain 6 mg of the metal-free product, *20-(ethoxycarbonyl)-2,3,7,8,12,13,17,18-octamethyl-5-(p-tolylmethyl)-porphyrin* (**48**) [mp > 217 °C dec; $\lambda_{max}$ ($CH_2Cl_2$) 408 nm ($\epsilon$, 158 900), 508 (16 200), 540 (12 000), 582 (11 800), 630 (8200); $\delta$ ($CDCl_3$) 9.80, 9.74 (each s, 1H), 6.97, 6.94 (each d, $J$ = 8.4 Hz, 2H), 6.19 (s, 2H), 5.00 (m, 2H), 3.46 (s, 6H), 3.45, 3.38, 3.26, 3.16, 3.11, 3.08 (each s, 3H), 2.27 (s, 3H), 1.67 (t, $J$ = 7.2 Hz, 3H), −3.15 (br s, 2H). Anal. Calcd for $C_{39}H_{42}N_4O_2Cu \cdot {}^2/_3H_2O$: C, 76.68; H, 7.16; N, 9.18. Found: C, 76.38; H, 6.79; N, 9.22.

**Cyclization of 19-((Methoxycarbonyl)ethyl)-2,3,7,8,12,-13,17,18-octamethyl-1-(*p*-tolylmethyl)-*a,c*-biladiene Dihydrobromide (27).** This reaction was repeated three times (with identical quantities of reactants and solvents) to obtain sufficient quantities of material. It was performed as for *a,c*-biladiene **25**, using the *a,c*-biladiene **27** (0.765 g, 1.00 mmol) and copper(II) acetate (3.10 g, 17.0 mmol) in DMF (40 mL) at 120 °C for 3 min. The combined residue of the three reactions was purified by flash silica gel chromatography, eluting with 1−10% ethyl acetate in cyclohexane. The least polar band was 21 mg of copper(II) 20-*p*-tolylporphyrin **50** [LRMS calcd for $[C_{35}H_{34}CuN_4]^+$ 573.208, found 573.6]. The second band isolated was 84 mg of *copper(II) 2,3,7,8,12,13,17,18-octamethyl-20-((methoxycarbonyl)methyl)-1-(p-tolylmethyl)-1,20-dihydroporphyrin* (**54**) [mp 224−225 °C; $\lambda_{max}$ ($CH_2Cl_2$) 420 nm ($\epsilon$, 34 300), 750 (8100), 828 (13 900); LRMS calcd for $[C_{39}H_{43}CuN_4O_2]^+$ 661.3, found 661.3], the isomer of copper(II) 1-(2-(methoxycarbonyl)ethyl)-2,3,7,8,12,13,17,18-octamethyl-20-*p*-tolyl-1,20-dihydroporphyrin (**52**) which was obtained in 41% yield (819 mg) [mp 235−238 °C dec to porphyrin; $\lambda_{max}$ ($CH_2Cl_2$) 322 nm ($\epsilon$ 24 100), 421 (42 400), 753 (8600), 832 (16 500); LRMS calcd for $[C_{47}H_{46}CuN_4O_4]^+$ 661.260, found 661.2 (see Figure 2)]. The most polar compound isolated was a trace of *copper(II) 2,3,7,8,12,13,17,18-octamethyl-5-(2-(methoxycarbonyl)ethyl)porphyrin* (**55**) [mp > 300 °C; $\lambda_{max}$ ($CH_2Cl_2$) 399 nm ($\epsilon$ 165 800), 524 (14 600), 560 (23 800). Anal. Calcd for $C_{31}H_{32}CuN_4O_2$: C, 67.01; H, 5.81; N, 10.09. Found: C, 67.30; H, 5.57; N, 10.48]. A small amount of porphyrin **55** was taken through standard TFA/$H_2SO_4$ demetalation protocols, but yielded a mixture of porphyrins. One of these porphyrins was identified as *2,3,7,8,12,13,17,18-octamethyl-20-((methoxycarbonyl)methyl)porphyrin* (**56**) using MS [HRMS calcd for $[C_{31}H_{34}CuN_4O_2]^+$ 494.2682, found 494.2674]. Because of the low solubilities of the porphyrins in the mixture, further analysis was not pursued.

**Cyclization of 8,12-Bis((methoxycarbonyl)methyl)-2,3,7,13,17,18-hexamethyl-1,19-bis(*p*-tolylmethyl)-*a,c*-biladiene Dihydrobromide (19).** The reaction was performed as for *a,c*-biladiene **27**, using *a,c*-biladiene **19** (450 mg; 0.50 mmol) and copper(II) acetate (1.56 g, 8.60 mmol) in DMF (30 mL) at 120 °C for 3 min. The products were separated by flash silica gel chromatography, eluting with 20−30% ethyl acetate in cyclohexane. Two products were isolated. The least polar compound isolated was 285 mg *of copper(II) 8,12-bis((methoxycarbonyl)methyl)-2,3,7,13,16,17-hexamethyl-1-(p-tolylmethyl)-20-(p-tolyl)-1,20-dihydroporphyrin* (**30**) [mp 190−198 °C dec to porphyrin; $\lambda_{max}$ ($CH_2Cl_2$) 325 nm ($\epsilon$ 26 800), 419 (50 000), 749 (9500), 825 (17 100); HRMS calcd for $[C_{47}H_{49}CuN_4O_4]^+$ 796.305, found 796.308. Anal. Calcd for $C_{47}H_{48}CuN_4O_4$: C, 70.88; H, 6.07; N, 7.03. Found: C, 71.03; H, 6.13; N, 6.99]. The most polar compound isolated was 14 mg of *copper(II) 8,12-bis((methoxycarbonyl)methyl)-2,3,7,13,16,17-hexamethyl-20-(p-tolyl)porphyrin* (**36**) [mp 296 °C dec; $\lambda_{max}$ ($CH_2Cl_2$) 402 nm ($\epsilon$ 341 000), 528 (25 700), 564 (28 000); HRMS calcd for $[C_{39}H_{38}CuN_4O_4]^+$ 689.219, found 689.222. Anal. Calcd for $C_{39}H_{38}CuN_4O_4 \cdot {}^2/_3H_2O$: C, 66.74; H, 5.65; N, 7.99. Found: C, 66.76; H, 5.65; N, 7.85]. The whole sample of porphyrin was demetalated using standard acidic conditions, affording 10 mg of *8,12-bis((methoxycarbonyl)methyl)-2,3,7,13,16,17-hexamethyl-20-p-tolylporphyrin* (**37**) [mp 297 °C dec; $\lambda_{max}$ ($CH_2Cl_2$) 404 nm

($\epsilon$, 199 000), 502 (26 000), 536 (18 000), 572 (17 800), 624 (13 200); $\delta$ ($CDCl_3$) 10.15 (s, 2H), 10.00 (s, 1H), 7.90, 7.54 (each d, $J$ = 7.8 Hz, 2H), 5.04 (s, 2H), 3.79, 3.65, 3.51, 2.47 (each s, 6H), 2.73 (s, 3H), −3.22 (br s, 2H). Anal. Calcd for $C_{39}H_{40}N_4O_4 \cdot H_2O$: C, 73.43; H, 6.48; N, 8.79. Found: C, 73.25; H, 6.37; N, 8.70]. The reaction was repeated at 145 °C giving a different distribution of products: after a similar workup as in the previous reaction, the products were separated by flash silica gel chromatography, eluting with 60:10:30 mixture of cyclohexane:ethyl acetate:$CH_2Cl_2$. Three products were isolated, and the least polar was 184 mg of compound **30**. The product from the band of medium polarity was 10 mg of *copper(II) 8,12-bis((methoxycarbonyl)methyl)-3,7,13,17,18-pentamethyl-2-methylidene-3-(p-tolylmethyl)-20-p-tolylchlorin* (**33**) [mp 118−120 °C; $\lambda_{max}$ ($CH_2Cl_2$) 414 nm ($\epsilon$, 186 500), 516 (5700), 554 (7300), 582 (7800), 628 (33 500); LRMS calcd for $[C_{47}H_{46}CuN_4O_4]^+$ 793.282, found 793.6. Anal. Calcd for $C_{47}H_{46}CuN_4O_4 \cdot H_2O$: C, 69.52; H, 5.96; N, 6.90. Found: C, 69.41; H, 5.98; N, 6.99].

**Cyclization of 8,12-Diethyl-2,3,7,13,17,18-hexamethyl-1,19-bis(*p*-tolylmethyl)-*a,c*-biladiene Dihydrobromide (20).** This reaction was performed as for *a,c*-biladiene **27**, using the *a,c*-biladiene **20** (0.618 g, 0.762 mmol) and copper(II) acetate (4.59 g, 25.4 mmol) in DMF (35 mL) at 120 °C for 6 min. The products were separated by chromatography on Brockmann Grade II alumina (eluting with 1:1 petroleum ether/$CH_2Cl_2$). Four fractions were separated and products were isolated. Fraction 1 contained 18 mg of *copper(II) 8,12-diethyl-2,3,7,-13,17,18-hexamethyl-20-p-tolyl-1-(p-tolylmethyl)-1,20-dihydroporphyrin* (**29**) [mp 210−212 °C; $\lambda_{max}$ ($CH_2Cl_2$) 416 nm ($\epsilon$ 28 200), 750 (5800), 812 (10 000). Anal. Calcd for $C_{45}H_{48}CuN_4 \cdot 0.5H_2O$: C, 75.33; H, 6.88; N, 7.81. Found: C, 75.43; H, 6.76; N, 7.92]. Fraction 2 contained 17 mg of *copper(II) 8,12-diethyl-2,3,7,13,17,18-hexamethyl-20-p-tolyl-5-(p-tolylmethyl)porphyrin* (**38**) [mp 226−227 °C; $\lambda_{max}$ ($CH_2Cl_2$) 412 nm ($\epsilon$ 250 300), 540 (25 500), 571 (22 000); LRMS calcd for $C_{45}H_{46}CuN_4$ 705.3018, found 705.3. Anal. Calcd for $C_{45}H_{46}CuN_4 \cdot 0.5H_2O$: C, 71.95; H, 6.85; N, 7.25. Found: C, 71.97; H, 6.85; N, 7.47]. A small portion of **38** was demetalated in acid for proton NMR confirmation of the metal-free porphyrin *8,12-diethyl-2,3,7,-13,17,18-hexamethyl-20-p-tolyl-5-(p-tolylmethyl)porphyrin* (**39**) [mp 140−142 °C dec to porphyrin **35**; $\lambda_{max}$ ($CH_2Cl_2$) 418 nm ($\epsilon$ 129 400), 516 (16 900), 554 (12 400), 590 (13 000), 644 (9900); $\delta$ ($CDCl_3$) 9.67, 9.64 (each s, 1H), 7.95, 7.54 (each d, $J$ = 7.2 Hz, 2H), 6.95, 6.93 (each d, $J$ = 8.1 Hz, 2H), 6.30 (s, 2H), 3.91 (m, 4H), 3.48, 3.33, 3.16, 2.94, 2.70, 2.03 (each s, 3H), 2.27, 2.26 (each s, 3H), 1.18, 1.65 (each t, $J$ = 7.5 Hz, 3H), −2.66 (s, 2H). Porphyrin **39** was found to decompose when heated to give porphyrin **34**; thus, this compound could not be subjected to normal thermal preparation prior to elemental analysis. HRMS: calcd for $C_{45}H_{48}N_4$ 644.3879, found 644.3901]. Fraction 3 provided 10 mg of *copper(II) 8,12-diethyl-3,7,13,-17,18-pentamethyl-2-methylidene-20-p-tolyl-3-(p-tolylmethyl)chlorin* (**32**) [mp 223−225 °C; $\lambda_{max}$ ($CH_2Cl_2$) 412 nm ($\epsilon$ 185 700), 513 (23 300), 552 (24 000), 630 (55 100). Anal. Calcd for $C_{45}H_{46}CuN_4 \cdot 0.5H_2O$: C, 75.60; H, 6.63; N, 7.84. Found: C, 75.46; H, 6.56; N, 7.63]. Fraction 4 contained 193 mg of *copper(II) 8,12-diethyl-2,3,7,13,17,18-hexamethyl-20-p-tolylporphyrin* (**34**) [mp >296 °C dec; $\lambda_{max}$ ($CH_2Cl_2$) 400 nm ($\epsilon$ 276 500), 526 (19 700), 562 (23 800). Anal. Calcd for $C_{37}H_{40}CuN_4$: C, 73.85; H, 6.37; N, 9.32. Found: C, 73.85; H, 6.62; N, 9.19]. For proton NMR characterization, a small portion of **34** was demetalated in acid to give *8,12-diethyl-2,3,7,13,17,18-hexamethyl-20-p-tolylporphyrin* (**35**) [mp > 300 °C; $\lambda_{max}$ ($CH_2Cl_2$) 402 nm ($\epsilon$ 123 400), 501 (16 300), 531 (14 000), 568 (14 200); $\delta$ ($CDCl_3$) 10.16 (s, 2H), 9.95 (s, 1H), 7.91, 7.54 (each d, $J$ = 7.8 Hz, 2H), 4.08 (q, $J$ = 7.5 Hz, 4H), 3.64, 3.53, 2.48 (each s, 6H), 2.73 (s, 3H), 1.89 (t, $J$ = 7.5 Hz, 6H), −3.17, −3.30 (each s, 1H); LRMS calcd for $[C_{37}H_{40}N_4]^+$ 540.3, found 540.0. Anal. Calcd for $C_{37}H_{40}N_4$: C, 82.17; H, 7.46; N, 10.37. Found: C, 81.91; H, 7.54; N, 10.47].

**Rearrangement Studies Using Copper(II) 8,12-Diethyl-2,3,7,13,17,18-hexamethyl-20-*p*-tolyl-1-(*p*-tolylmethyl)-1,20-dihydroporphyrin (29).** Apart from the difference in reaction temperatures (140 °C, 120 °C) conditions were the same for each reaction; compound **29** and copper(II) acetate (1.0 g, 5 mmol) in DMF (15 mL) were heated under $N_2$ for 15 min. The solution was then poured into a biphasic mixture of ether and ice−water. The organic products were extracted with diethyl ether (4 × 50 mL), and the combined organic layers were washed with deionized water and then brine (100 mL), dried over anhydrous sodium sulfate, and evaporated to dryness. The residue was chromatographed on a column of Brockmann Grade II alumina (elution with 1:1 petroleum ether/$CH_2Cl_2$). The least polar band contained the copper(II) 5,20-disubstituted porphyrin **38**, followed by the copper(II) 2-methylidenechlorin **32**, and finally the 20-*p*-tolylporphyrin **34**. **At 140 °C:** compound **29** (110 mg, 0.155 mmol) yielded 3.4 mg of porphyrin **38**, 1.4 mg of chlorin **32**, and 30.4 mg of porphyrin **34**. **At 120 °C:** compound **29** (123 mg, 0.173 mmol) afforded 6.0 mg of **38**, 14.0 mg of chlorin **32**, and 22.0 mg of 20-*p*-tolylporphyrin **34**.

**Rearrangement Studies Using Copper(II) 8,12-Diethyl-3,7,13,17,18-pentamethyl-2-methylidene-20-*p*-tolyl-3-(*p*-tolylmethyl)chlorin (32).** The copper(II) chlorin **32** (13.0 mg) was combined with 10 mL of *o*-dichlorobenzene under dry $N_2$ and then heated at 140 °C for 2 h. The solvent was evaporated, and the residue was chromatographed on a Brockmann Grade II alumina column (elution with 1:1 petroleum ether/$CH_2Cl_2$). The least polar compound was identified as porphyrin **38** (8 mg, 78%), and this was followed by the starting material **32** (2.8 mg). Finally, the 20-*p*-tolylporphyrin **34** (1.3 mg) was collected.

**Cyclization of 8,12-Diethyl-1,2,3,7,13,17,18-heptamethyl-19-(*p*-tolylmethyl)-*a,c*-biladiene Dihydrobromide (28). At 100 °C:** the *a,c*-biladiene **28** (338 mg, 0.469 mmol) and copper(II) acetate (3.24 g, 16.2 mmol) in DMF (35 mL) were heated for 5 min. After the usual workup the crude product was chromatographed on a Brockmann Grade II alumina column (elution with 1:1 petroleum ether/$CH_2Cl_2$). Three fractions were isolated: the first fraction yielded 53 mg of *copper(II) 8,12-diethyl-2,3,7,13,17,18-hexamethyl-1-(p-tolylmethyl)-1,20-dihydroporphyrin* (**58**) (see Figure 5) [mp 241−242 °C dec; $\lambda_{max}$ ($CH_2Cl_2$) 416 nm ($\epsilon$ 47 600), 742 (11 700), 820 (18 800); LRMS calcd for $[C_{38}H_{42}CuN_4]^+$ 617.27, found 617.3]. The second fraction contained 133 mg of *copper(II) 8,12-diethyl-2,3,7,13,-17,18-octamethyl-20-p-tolylporphyrin* (**34**). The most polar fraction provided 29 mg of *copper(II) 3,7-diethyl-2,8,12,13,17,-18-hexamethylporphyrin* (**60**) [mp dec > 280 °C; $\lambda_{max}$ ($CH_2Cl_2$) 397 nm ($\epsilon$ 336 500), 524 (32 600), 560 (41 700). Anal. Calcd for $C_{30}H_{32}CuN_4 \cdot 0.5H_2O$: C, 69.20; H, 6.39; N, 10.77. Found: C, 68.98; H, 6.40; N, 10.54]. A small quantity of compound **60** was demetalated for proton NMR analysis, to give *8,12-diethyl-2,3,7,13,17,18-hexamethylporphyrin* (**61**) [mp > 300 °C; $\lambda_{max}$ ($CH_2Cl_2$) 397 nm ($\epsilon$ 88 400), 496 (10 200), 530 (8800), 566 (7400), 620 (6200), $\delta$ ($CDCl_3$) 10.52 (s, 4H), 4.04 (q, $J$ = 7.2 Hz, 4H), 3.06 (s, 18H), 1.96 (t, $J$ = 7.2 Hz, 6H), −2.70 (br s, 1H); HRMS calcd for $[C_{30}H_{34}N_4]^+$ 450.2783, found 450.2783. Anal. Calcd for $C_{30}H_{34}N_4 \cdot 0.5H_2O$: C, 78.38; H, 7.68; N, 12.20. Found: C, 78.61; H, 7.43; N, 12.22]. **At 20 °C:** *a,c*-biladiene **28** (78.3 mg, 0.109 mmol) and copper(II) acetate (1.00 g, 5.01 mmol) in DMF (15 mL) were stirred under $N_2$ for 20 h. After chromatography, three major products were isolated. The first fraction contained **58** (< 1 mg), the second fraction provided copper(II) porphyrin **34** (5.8 mg), and the most polar band provided copper(II) porphyrin **60** (1 mg).

**Chromium(III)-Promoted Oxidative Cyclizations. Cyclization of 2,3,7,8,12,13,17,18-Octamethyl-1,19-bis(*p*-tolylmethyl)-*a,c*-biladiene Dihydrobromide (21).** Dry DMF (50 mL) and triethylamine (0.5 mL) were heated at 100 °C under nitrogen for 5 min before *a,c*-biladiene dihydrobromide **21** (48.6 mg, 0.0621 mmol) and $Cr_3(OAc)_7(OH)_2$ (55.8 mg, 0.0925 mmol) were added simultaneously. The reaction was protected from light during the 3 h reaction time. After cooling, the mixture was diluted with $CH_2Cl_2$ (100 mL) and water (100 mL) before being separated and extracted with $CH_2Cl_2$. The combined organic layer was evaporated, and the residue was diluted with ether (100 mL) and washed with water (4 × 100 mL) and then brine (100 mL) to drive off remaining DMF. After drying over anhydrous sodium sulfate and filtering, the solution was concentrated. Alumina chromatography (Brockmann Grade III; elution with 1:1 $CH_2Cl_2$ and petroleum ether) afforded (20 mg, 52%) of *20-p-tolyl-2,3,7,8,12,13,17,18-octamethyl-1-p-tolyl-1,20-dihydroporphy-*

*rin* (**31**), mp ~180 °C dec to give compound with $\lambda_{max}$ 442 nm; $\lambda_{max}$ ($CH_2Cl_2$) 304 nm ($\epsilon$ 19 000), 383 (48 000), 655 (7900), 711 (9700); $\delta$ ($CDCl_3$) 14.35, 13.58 (each br s, 1 H), 7.54, 7.12, 6.96, 6.89 (each d, $J$ =7.8 Hz, 2H), 6.28, 5.46, 4.67 (each s, 1H), 4.04, 2.99 (each d, $J$ = 13.2 Hz, 1H), 3.75 (each s, 1H), 2.23, 2.22, 2.03, 1.98, 1.72, 1.18 (each s, 3H), 1.96, 1.83 (each s, 6H); HRMS calcd for $[C_{43}H_{46}N_4^+]$ 618.3723, found 618.3710; calcd for $[C_{43}H_{47}N_4]^+$ 619.3801, found 619.3830. Anal. Calcd for $C_{43}H_{46}N_4 \cdot H_2O$: C, 81.09; H, 7.60; N, 8.80. Found: C, 81.46; H, 7.55; N, 8.82.

**Cyclization of 1-((Ethoxycarbonyl)methyl)-2,3,7,8,12,-13,17,18-octamethyl-19-(*p*-tolylmethyl)-*a*,*c*-biladiene Dihydrobromide (25).** Ethanol, (95% 25 mL) was degassed with $N_2$ in an ice bath before sodium acetate (259 mg, 3.15 mmol) and $Cr_3(OAc)_7(OH)_2$ (109 mg, 0.180 mmol) were added all at once. The *a*,*c*-biladiene **25** (51.8 mg, 0.0688 mmol) was added, and the mixture was stirred, in the dark at 0 °C. The reaction was completed after 3.5 h (spectrophotometry). $CH_2Cl_2$ (50 mL) and water (50 mL) were added, and the organic layer was separated. The organic layer was washed with water (2 × 100 mL) and aqueous saturated sodium bicarbonate (100 mL) and then brine (100 mL). After being dried over anhydrous sodium sulfate and filtered, the solution was concentrated, and the residue was quickly chromatographed on an alumina column (Brockmann Grade III, elution with 30% $CH_2Cl_2$ in petroleum ether). The major band isolated (13.9 mg, 40%) was *20-(ethoxycarbonyl)-2,3,7,8,12,13,17,18-octamethyl-1-(p-tolylmethyl)-1,20-dihydroporphyrin* (**43**), mp >180 °C dec to compound with $\lambda_{max}$ 436 nm; $\lambda_{max}$ ($CH_2Cl_2$) 304 nm ($\epsilon$ 17 600), 380 (47 200), 653 (8100), 703 (8600); $\delta$ ($CDCl_3$) 14.6, 14.2 (each br s, 1H), 7.11, 6.90 (each d, $J$ = 7.8 Hz, 2H each), 6.15, 5.22, 4.66 (each s, 1H), 4.17, 4.04 (each m, 1H), 3.99, 2.76 (each d, $J$ = 12.6 Hz, 1H), 3.50 (s, 1H), 2.22, 2.00, 1.97, 1.86, 1.39 (each s, 3H), 1.87, 1.79 (each s, 6H), 1.19 (t, $J$ = 7.2 Hz, 3H); HRMS calcd for $[C_{39}H_{45}N_4O_2]^+$ 601.3542, found 601.3548. Anal. Calcd for $C_{39}H_{44}N_4O_2 \cdot 0.5H_2O$: C, 76.82; H, 7.44; N, 9.19. Found: C, 76.42; H, 7.43; N, 8.92.

**Cyclization of 2,3,7,8,12,13,17,18,19-Nonamethyl-1-(*p*-tolylmethyl)-*a*,*c*-biladiene Dihydrobromide (26).** The *a*,*c*-biladiene **26** (49.4 mg, 0.0713 mmol) and $Cr_3(OAc)_7(OH)_2$ (97.2 mg, 0.0161 mmol) in DMF (25 mL) and triethylamine (0.5 mL) were refluxed for 5 min. The crude product was subjected to chromatography on an alumina column (Brockmann Grade III; elution with 1:1 $CH_2Cl_2$/petroleum ether), to give 18 mg (50%) of *1,2,3,7,8,12,13,17,18-nonamethyl-20-p-tolyl-1,20-dihydroporphyrin* (**59**): mp > 180 °C dec; $\lambda_{max}$ ($CH_2Cl_2$) 304 nm ($\epsilon$ 19 400), 381 (47 100), 655 (7900), 708 (9800); $\delta$ ($CDCl_3$) 14.25, 13.50 (each br s, 1H), 7.52, 6.97 (each d, $J$ = 7.8 Hz, 2H), 6.26, 5.44, 4.84 (each s, 1H), 3.61 (s, 1H), 2.24, 2.01, 1.96, 1.85, 1.79, 1.77, 1.66, 1.45 (each s, 3H), 1.93 (s, 6 H); HRMS calcd for $[C_{36}H_{41}N_4]^+$ 529.3331, found 529.3348. Anal. Calcd for $C_{36}H_{40}N_4 \cdot 0.5H_2O$: C, 80.41; H, 7.69; N, 10.42. Found: C, 80.67; H, 7.55; N, 10.32. When the reaction was repeated at 100 °C the identical compound was isolated in 40% yield ($^1$H NMR data).

**Cyclization of 19-((Methoxycarbonyl)ethyl)-2,3,7,8,12,-13,17,18-octamethyl-1-(*p*-tolylmethyl)-*a*,*c*-biladiene Dihydrobromide (27).** $Cr_3(OAc)_7(OH)_2$ (319 mg, 0.529 mmol) and *a*,*c*-biladiene **27** (152 mg, 0.202 mmol) in DMF (75 mL) and triethylamine (1.5 mL) were heated at 100 °C for 1 h (spectrophotometric monitoring). After an aqueous workup the residue was chromatographed on alumina (Brockmann grade III, elution with 1:1 $CH_2Cl_2$/petroleum ether) followed by chromatography on a silica gel column, eluting with 1% acetone in $CH_2Cl_2$. Many minor decomposition bands were observed, but the major product (5.0 mg, 4% yield) was *1-(2-(methoxycarbonyl)ethyl)-2,3,7,8,12,13,17,18-octamethyl-20-p-tolyl-1,20-dihydroporphyrin* (**53**), mp ~165 °C dec to porphyrin; $\lambda_{max}$ ($CH_2Cl_2$) 304 nm ($\epsilon$ 20 700), 383 (50 300), 654 (8500), 716 (10 100); $\delta$ ($CDCl_3$) 14.24, 13.47 (each br s, 1 H), 7.51, 6.97 (each d, $J$ = 7.8 Hz, 2H), 6.23, 5.42, 4.81 (each s, 1H), 3.61 (s, 3H), 3.59 (s, 1H), 3.23, 2.32 (each m, 2H), 2.24, 1.99, 1.93, 1.92, 1.91, 1.85, 1.75, 1.71, 1.43 (each s, 3 H); HRMS calcd for $[C_{39}H_{45}N_4O_2]^+$ 601.3542, found 601.3541. Anal. Calcd for $C_{39}H_{44}N_4O_2 \cdot 0.5H_2O$: C, 76.82; H, 7.44; N, 9.19. Found: C, 76.98; H, 7.32; N, 8.95.

**Crystallographic Structure Determination.**[20] All crystals were grown from $CH_2Cl_2$/*n*-hexane. **29:** crystal data for $C_{45}H_{48}N_4Cu$ at 130 K (Cu Kα radiation, $\lambda$ = 1.541 78 Å, $2\theta_{max}$ = 115°), triclinic, space group $P\bar{1}$, $a$ = 13.672(2) Å, $b$ = 14.475-(3) Å, $c$ = 18.968(4) Å, α = 84.67(2)°, $\beta$ = 87.22(2)°, $\gamma$ = 82.30-(2)°, $V$ = 3701.1(12) Å$^3$, $Z$ = 4, $R$ = 0.0541, wR = 0.069, $S$ = 0.94 for 8643 reflections with $F > 4.0\sigma(F)$ and 896 parameters. **30:** crystal data for $C_{53}H_{62}CuN_4O_4$ at 130 K (Mo Kα radiation, $\lambda$ = 0.710 73 Å, $2\theta_{max}$ = 50°), monoclinic, space group $P2_1/n$, $a$ = 14.966(4) Å, $b$ = 16.786(3) Å, $c$ = 19.608(3) Å, $\beta$ = 110.97-(2)°, $V$ = 4599.7(16) Å$^3$, $Z$ = 4, $R$ = 0.067, wR = 0.0966, $S$ = 0.82 for 3955 reflections with $F > 4.0\sigma(F)$ and 395 parameters. **33:** crystal data for $C_{47}H_{46}CuN_4O_4$ at 130 K (Cu Kα radiation, $\lambda$ = 1.541 78 Å, $2\theta_{max}$ = 115°), triclinic, space group $P\bar{1}$, $a$ = 11.104(4) Å, $b$ = 13.138(4) Å, $c$ = 14.681(5) Å, α = 65.55(2)°, $\beta$ = 84.18(3)°, $\gamma$ = 76.03(2)°, $V$ = 1892(1) Å$^3$, $Z$ = 2, $R$ = 0.0579, wR = 0.079, $S$ = 1.52 for 4750 reflections with $F > 4.0\sigma(F)$ and 415 parameters. **44:** crystal data for $C_{39}H_{44}CuN_4O_2$ at 130 K (Cu Kα radiation, $\lambda$ = 1.541 78 Å, $2\theta_{max}$ = 115°), triclinic, space group $P\bar{1}$, $a$ = 7.438(2) Å, $b$ = 14.857(4) Å, $c$ = 14.830(3) Å, α = 96.03(2)°, $\beta$ = 97.64(2)°, $\gamma$ = 103.66(2)°, $V$ = 1562.4(7) Å$^3$, $Z$ = 2, $R$ = 0.0524, wR = 0.0689, $S$ = 1.12 for 3865 reflections with $F > 4.0\sigma(F)$ and 415 parameters. **45:** crystal data for $C_{39}H_{40}CuN_4O_2$ at 130 K (Mo Kα radiation, $\lambda$ = 0.710 73 Å, $2\theta_{max}$ = 42°), monoclinic, space group $P2_1/c$, $a$ = 9.200(6) Å, $b$ = 14.220(11) Å, $c$ = 25.514(9) Å, $\beta$ = 103.20(4)°, $V$ = 3249(3) Å$^3$, $Z$ = 4, $R$ = 0.0823, wR = 0.08, $S$ = 1.53 for 1790 reflections with $F > 4.0\sigma(F)$ and 190 parameters. **52:** crystal data for $C_{39}H_{42}CuN_4O_2$ at 130 K (Mo Kα radiation, $\lambda$ = 0.710 73 Å, $2\theta_{max}$ = 55°), monoclinic, space group $P2_1/c$, $a$ = 12.591(9) Å, $b$ = 18.03(2) Å, $c$ = 14.726(10) Å, $\beta$ = 101.070(1)°, $V$ = 3329(5) Å$^3$, $Z$ = 4, $R$ = 0.0892, wR = 0.1244, $S$ = 1.50 for 3510 reflections with $F > 4.0\sigma(F)$ and 320 parameters. **58:** crystal data for $C_{38}H_{42}CuN_4$ at 130 K (Cu Kα radiation, $\lambda$ = 1.541 78 Å, $2\theta_{max}$ = 114°), monoclinic, space group $P2_1/c$, $a$ = 18.285(4) Å, $b$ = 13.324(3) Å, $c$ = 13.177(3) Å, α = 65.55(2)°, $\beta$ = 84.18-(3)°, $\gamma$ = 76.03(2)°, $V$ = 3179.4(11) Å$^3$, $Z$ = 4, $R$ = 0.047, wR = 0.1191, $S$ = 1.063 for 3875 reflections with $F > 4.0\sigma(F)$ and 387 parameters.

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