Tetrahedron Letters, Vol.31, No.19, pp 2685-2688, 1990
Printed in Great Britain

0040-4039/90 $3.00 + .00
Pergamon Press plc

NOVEL PERIPHERAL SUBSTITUENT MIGRATION REACTIONS IN TETRAPYRROLE MACROCYCLES

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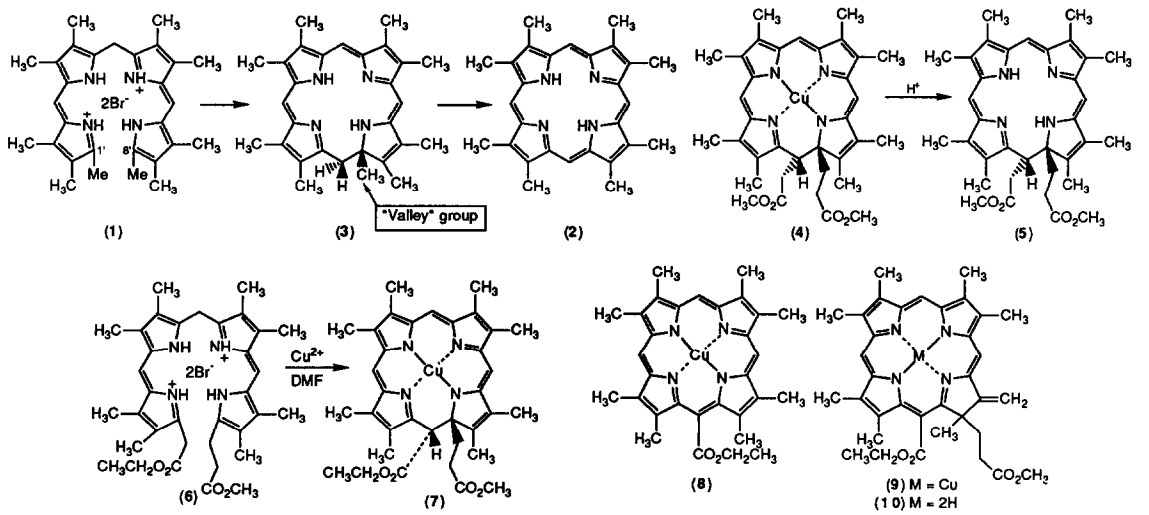
Abstract: *Copper(II) promoted cyclizations of a,c-biladiene salts bearing large terminal (1',8') substituents afford intermediates which suffer a variety of cleavage and cyclization reactions, in a stepwise manner, to yield mono-meso-substituted porphyrins, chlorins, and di-meso-substituted porphyrins via facile migration reactions.*

We recently showed[1] that electrochemical cyclization of 1',8'-dimethyl-a,c-biladiene salts (**1**) affords metal-free porphyrins (**2**) by way of a novel cyclic intermediate (**3**), which was isolated and fully characterized. This work was extended to show[2] that 1',8'-bis(2-methoxycarbonylethyl)-a,c-biladienes do not cyclize electrochemically to afford intermediates similar to (**3**), but if copper(II) salts are employed, a copper(II) macrocycle (**4**) is produced which is so stable that it can be demetalated in concentrated sulfuric acid to give the free-base (**5**). When the 1',8'-unsymmetrically disubstituted a,c-biladiene salt (**6**)[3] was heated at 130°C in dimethylformamide with copper(II) acetate the copper(II) macrocycle (**7**) (λ_{max} 321, 416, 842 nm) was obtained in good yield, along with minor amounts of a copper(II) porphyrin and a copper(II) chlorin.



(1) (3) (2) (4) (5)

(6) (7) (8) (9) M = Cu (10) M = 2H

Presumably the copper(II) porphyrin is obtained by cleavage of the "valley" group, as in the transformation of (**3**) into (**2**), and the copper(II) chlorin was obtained by migration of the "valley" substituent to a β-position of the tetrapyrrole. When the cyclization was carried out at room temperature, no copper(II) chlorin or porphyrin were obtained, and the only product was (**7**). Attempts to measure the melting point of the copper(II) complex (**7**) (>300°C) gave the copper(II) porphyrin (**8**) (spectrophotometry). Heating of (**7**) in dimethylformamide resulted only in recovery

of unchanged starting material. However, heating in dimethylformamide in the presence of copper(II) acetate gave almost equal amounts of a copper(II) porphyrin (**8**) (λ_{max} 399, 526, 564 nm) and copper(II) chlorin (**9**) (λ_{max} 410, 512, 552, 580, 626 nm), with no recovered starting material. The copper(II) chlorin (**9**) was demetalated with H_2SO_4/CF_3CO_2H to give (**10**) (λ_{max} 400, 498, 532, 600, 658 nm). Regiochemistry of the propionate migration was established with an X-ray structure (Figure 1) of the corresponding stereoselectively reduced (H_2; Pd-C) dihydro-derivative of (**9**).

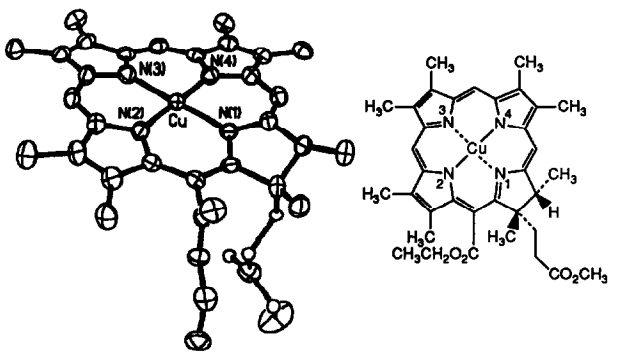
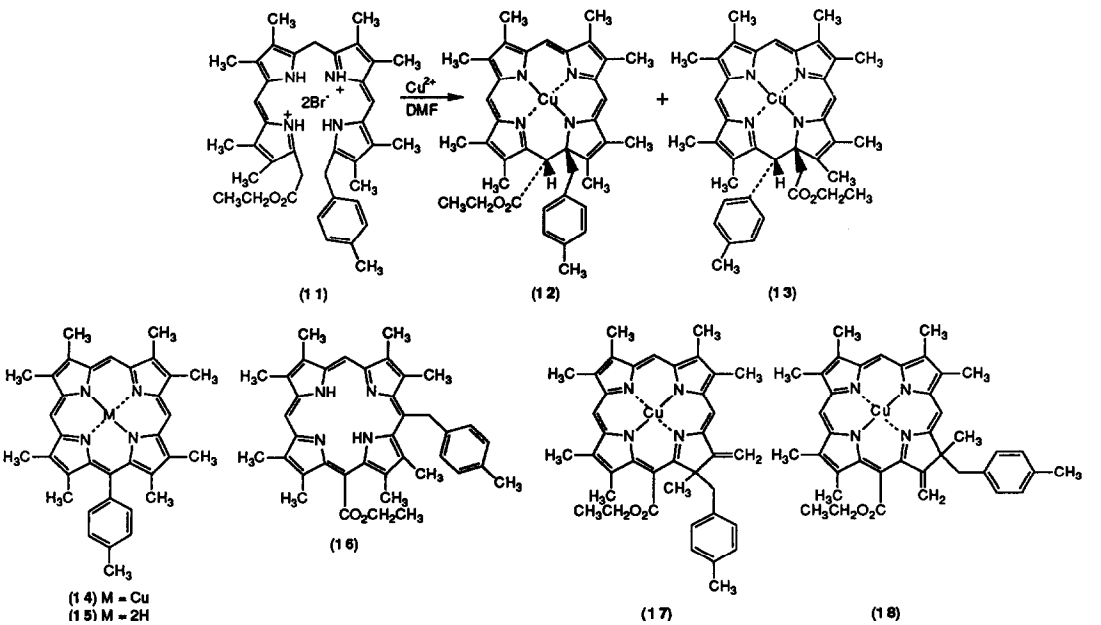


Figure 1: X-ray structure of dihydro-derivative of copper(II) chlorin (**9**)

Copper(II) promoted cyclization of the 1'-acetic-8'-(p-tolyl)methyl-a,c-biladiene (**11**) at 120°C gave similar, but more complicated results. The reaction afforded the anticipated copper(II) complex (**12**) along with three copper(II) porphyrins and two copper(II) chlorins. It seems likely that the copper(II) complex (**13**) was also a possible transient product because one of the copper(II) porphyrins was identified as the meso-p-tolyl copper(II) complex (**14**) [by demetalation to give (**15**)] while another, after demetalation was surprisingly shown to be (**16**) (vide infra). Upon chromatography, the copper(II) complex (**13**) appeared to decompose to give the two copper(II) chlorins and measurement of the melting point (242-245°C) caused the complex (**12,13**) to decompose to copper(II) porphyrin(s).



An X-ray structure showed one of the copper(II) chlorins [i.e. (**17**)] (Figure 2) to be the analogue of (**9**) produced via a 1,2 shift of the p-xylyl group. One possibility (vide infra) for the second copper(II) chlorin is (**18**).

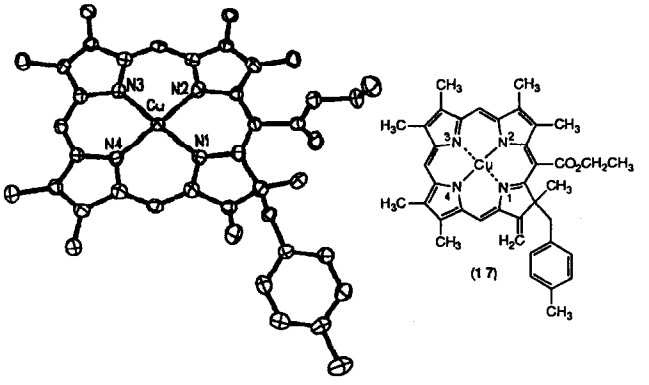


Figure 2: X-ray structure of copper(II) chlorin (**17**)

Equally intriguing results were obtained when the 1',8'-di(p-tolylmethyl)-a,c-biladiene salt (**19**) was cyclized in dimethylformamide at 140°C in presence of copper(II) acetate. The major product was the copper(II) porphyrin (**20**) (λ_{max} 400, 528, 562 nm) (characterized fully after demetalation with H_2SO_4/CF_3CO_2H), along with a small amount of a copper(II) chlorin (vide infra; λ_{max} 414, 516, 554, 582, 628 nm) and virtually no copper(II) macrocycle (**21**). Surprisingly, the copper(II) chlorin (**22**) was shown, by X-ray study (Figure 3), to have its migrated "valley" substituent sited in a 1,3 rather than 1,2 situation relative to its original position. Presumably, as with compound (**18**), steric congestion causes the p-xylyl group to undergo two successive 1,2 shifts, and in this case (because of the large size of the meso-tolyl group) it gives none of the chlorin (cf. **17**) which has undergone only one 1,2 shift of the "valley" group.

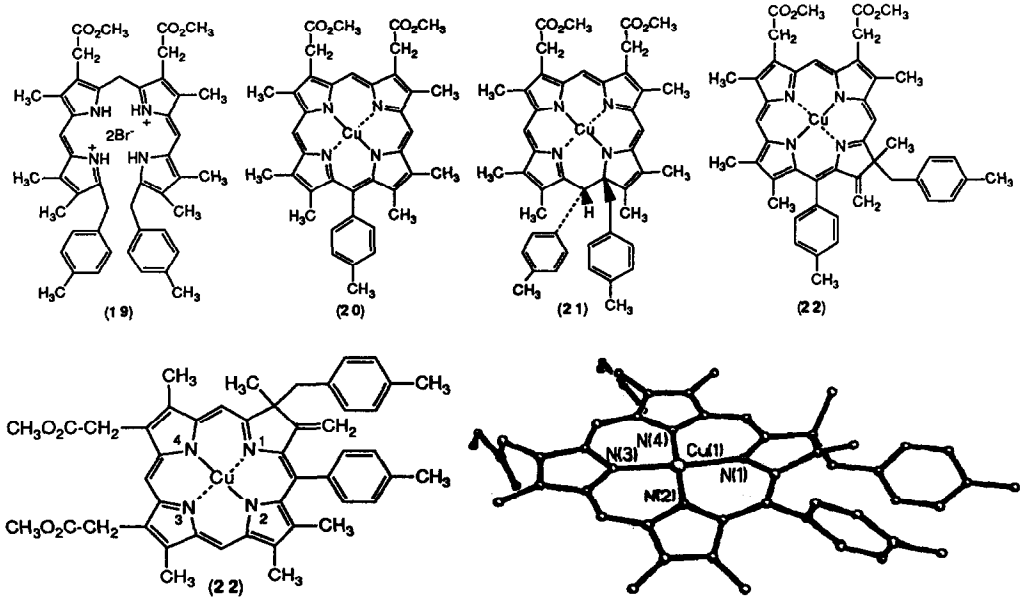
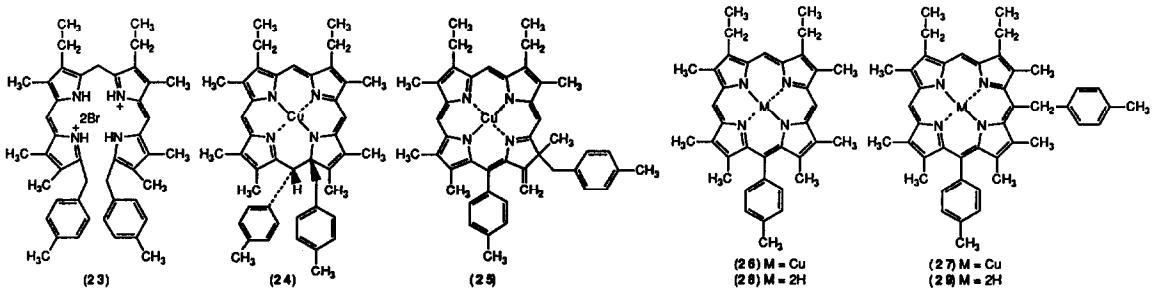


Figure 3: X-ray structure of copper(II) chlorin (**22**)

At lower temperatures (120°C) in dimethylformamide containing copper(II) acetate, the a,c-biladiene (**19**) once again gave copper(II) porphyrin (**20**), but this time the major product was indeed the copper(II) complex (**21**) and there was no copper(II) chlorin (**22**) present.

Similarly, when the a,c-biladiene salt (**23**) was cyclized in dimethylformamide at room temperature in presence of copper(II) acetate the major product was the copper(II) complex (**24**). The structure of this compound has been confirmed by an X-ray structure (not shown). At 100°C under otherwise similar conditions, the major product was still the copper(II) complex (**24**) but copper(II) porphyrins and copper(II) chlorin (**25**) were now apparent as minor products. At 120°C the copper(II) porphyrin and chlorin were in the majority, with only a minor amount of (**24**) isolated. Treatment of (**24**) with dimethylformamide at 120°C gave copper(II) porphyrin (**26**) (λ_{max} 400, 526, 562 nm) as the major product.



At 100°C in dimethylformamide containing copper(II) acetate, the a,c-biladiene (**23**) gave copper(II) chlorin (**25**) along with the copper(II) complex (**24**). Also isolated were the copper(II) porphyrins (**26**) and (**27**). Treatment of the pure copper(II) chlorin (**25**) with *o*-dichlorobenzene at 130°C for 24 hours, or at 140°C for only 10 minutes, gave the two copper(II) porphyrins (**26**) and (**27**), which were identified by proton NMR spectroscopy after demetalation with H_2SO_4/CF_3CO_2H [to give (**28**) and (**29**)]. Presumably, the second copper(II) porphyrin (**27**) is obtained by further 1,2 migrations of the p-xylyl group around the tetrapyrrole periphery.

Acknowledgments: We thank the National Institutes of Health (HL 22252) and the National Science Foundation (CHE-86-19034) for support of this research. Part of the diffraction and computing equipment was purchased under NSF grant CHE-88-02721.

References and Notes

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2 P. A. Liddell, M. M. Olmstead, and K. M. Smith, *J. Am. Chem. Soc.*, **1990**, *112*, in press.

3 Symmetrical a,c-biladienes were prepared by condensation of a pyrromethane with two moles of the appropriate 2-formylpyrrole. Unsymmetrically substituted a,c-biladiene salts were prepared via tripyrrenes: J. A. P. B. de Almeida, G. W. Kenner, J. Rimmer, and K. M. Smith, *Tetrahedron*, **1976**, *32*, 1793. K. M. Smith and G. W. Craig, *J. Org. Chem.*, **1983**, *48*, 4302.

Received in USA 26 February 1990)