PORPHYRIN SYNTHESIS FROM a,c-BILADIENES. EVIDENCE FOR A COMMON MECHANISTIC PATHWAY IN THE ELECTROCHEMICAL AND CHEMICAL ROUTES. FORMATION OF NOVEL MACROCYCLES POSSESSING THE HOMOPORPHYRIN CARBON SKELETON*

ELECTROSYNTHESIS OF PORPHYRINS FROM a,c-BILADIENES‡

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CONDENSATION OF THE RESEARCH

PURPOSE OF THE STUDY  To establish the mechanistic pathway for the cyclization of 1, 19-dialkyl-a,c-biladiene salts to porphyrins

WHAT RESEARCHERS ACCOMPLISHED
• The authors described an electrochemical cyclization (1→3→4) of 1.19-dimethyl-a,c-biladiene (1; R1 = R2 = H) as an alternative to the standard cupric salt-catalyzed chemical cyclization (1→2→4) (Scheme 1).
• The researchers isolated structurally similar cyclic intermediates, thereby providing evidence for a common mechanistic pathway for both chemical and electrochemical processes.

RESEARCHERS’ APPROACH  The key step in the proposed pathway of the electrocyclization (Scheme 2) is the attack of a nucleophile on the angular methyl group of the cyclized intermediate 3. A similar intermediate has not hitherto been isolated from chemical cyclization. The cupric salt-catalyzed cyclization was therefore carried out on biladienes (1) that could produce corresponding intermediates (5), but that would not undergo nucleophilic reaction due to steric and or electronic reasons.

COMMENTARY ON THE RESEARCH

Since the discovery of the cupric salt-catalyzed cyclization of 1.19-dimethyl-a,c-biladienes by Johnson and Kay† and its subsequent generalization to prepare unsymmetrical porphyrins,‡§ Smith and co-workers have extended this method for the synthesis of several useful porphyrins.‡‖ Although the mech-
Scheme 1

Scheme 2
anism of this reaction has also been investigated \(^7,8\) and a plausible pathway suggested, until now, no intermediates have ever been isolated. By electrolyzing 1 (R1 = R2 = H) in N,N-dimethylformamide (DMF) at 0.8 V, the authors were able to isolate a blue-green intermediate (38-52%) whose structure (3) was established by high-resolution NMR and FAB mass spectroscopy. Further electrooxidation provided the porphyrin 4 (70%), suggesting the intermediiacy of 3 in the proposed pathway (Scheme 2). The key step is a nucleophilic attack on the angular methyl group of 3 leading to a phlorin 7 which autoxidizes to the porphyrin (4).

When 1,19-bis[2-(methoxycarbonyl)ethyl]-a,c-biladiene (1; R1 = R2 = CH$_2$CO$_2$CH$_3$) was cyclized in DMF (125°C; 5 min) in the presence of cupric salts, the cyclic tetrapyrrole copper complex 5 (R1 = R2 = CH$_2$CO$_2$CH$_3$) was obtained; demetalation in 1:1 sulfuric/trifluoroacetic acids gave 6 (R$^1$ = R$^2$ = CH$_2$CO$_2$CH$_3$). This is structurally similar to the intermediate 3 of electrocyclization. The unsymmetrically substituted biladiene 1 (R1 = CO$_2$C$_2$H$_5$; R$^2$ = CH$_2$CO$_2$CH$_3$) also produced the cyclic tetrapyrrole copper complex 5 (R$^1$ = CO$_2$C$_2$H$_5$; R$^2$ = CH$_2$CO$_2$CH$_3$), but attempted demetalation produced, surprisingly, a ring-expanded product with a homoporphyrin carbon skeleton. Structures of 5, 6, and the ring-expanded analog of 6 have been determined by X-ray crystallography.

REFERENCES