Tetrahedron Letters,Vol.30,No.50,pp 6989-6992,1989 0040-4039/89 $3.00 + .00
Printed in Great Britain Pergamon Press plc

HIGH YIELD SYNTHESIS OF 5,15-DIARYLPORPHYRINS

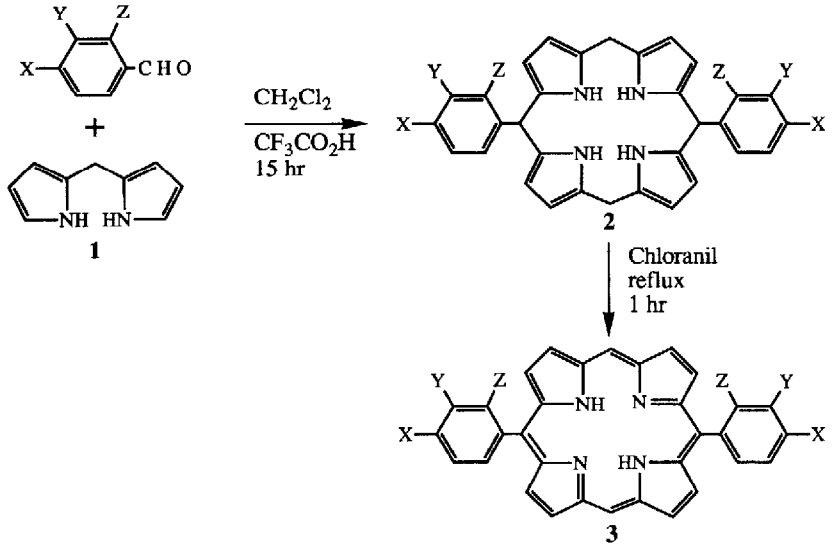
John S. Manka and David S. Lawrence*

Department of Chemistry, State University of New York
Buffalo, NY 14214

Abstract: The condensation of dipyrrylmethane with a variety of aromatic aldehydes furnishes, upon oxidation with chloranil, 5,15-diarylporphyrins in high yield (73-92%).

A multitude of structurally diverse porphyrins have been synthesized as mimics for heme-dependent proteins during the past two decades. The great majority of these are embellished derivatives of the basic tetraphenylporphyrin framework. Recently, researchers have recognized that the molecular architecture of 5,15-diarylporphyrins is more readily manipulated than that of the corresponding tetraarylporphyrins (1). Consequently, several reports of diarylporphyrins have appeared (2). To the best of our knowledge, the first example of a 5,15-diarylporphyrin was reported by Treibs and Haberle, who synthesized 5,15-diphenylporphine from benzaldehyde and dipyrrylmethane in 3% yield (3). Several 5,15-diaryl-2,3,7,8,12,13,17,18-octaalkylporphyrins have been subsequently synthesized in yields that range from 30% to 60% (1,2,4). We report herein that 5,15-diarylporphyrins can be prepared in high yield (73-92%) under reaction conditions that thermodynamically favor the formation of the intermediate porphyrinogen **2** (5).

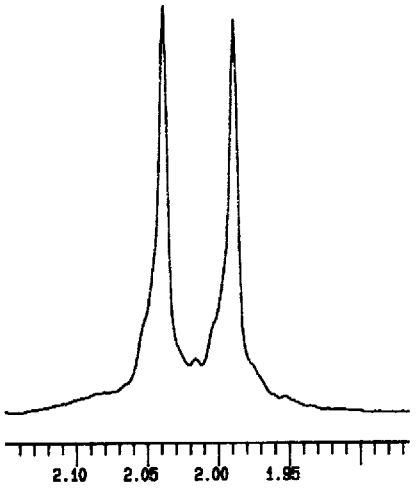
The porphyrins illustrated in the scheme below were prepared from the appropriate aromatic aldehyde and dipyrrylmethane **1**. The latter compound is readily available in three steps (40% overall yield) from pyrrole (6). Since dipyrrylmethane is prone to slight decomposition at room temperature over the course of a few days, we recommend that it be stored under an inert atmosphere at 0 °C. A typical experimental procedure is as follows: dipyrrylmethane (25 mg, 0.17 mmol) and one equivalent of aromatic aldehyde (0.17 mmol) were introduced into a 50 mL round bottomed flask (stirring bar, condenser) containing methylene chloride (30 mL) and trifluoroacetic acid (1 drop) and stirred at room temperature. The initial yellow solution became purple within a few hours, signaling the formation of porphyrinogen. The reaction was allowed to proceed for a total of 15 hr at which time chloranil (167 mg, 0.68 mmol) was added and the solution heated to reflux (1 hr). The reaction mixture was allowed to cool and the solvent was subsequently removed. The purple solid was dissolved in chloroform and chromatographed on a gravity column (silica gel, chloroform). In the case of the tolylporphyrins, we found it necessary to run a second gravity column (silica gel, 1:1 benzene:cyclohexane) to effect complete removal of the chloranil by-product. The yields provided in the scheme are those of purified porphyrin (7).



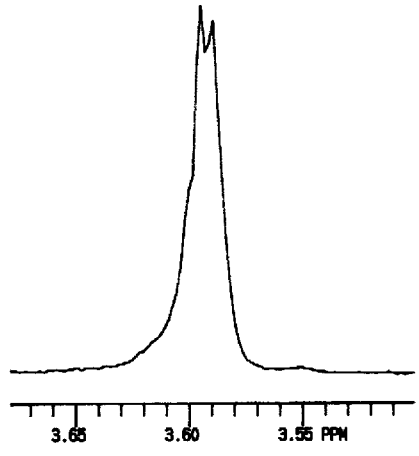
	X	Y	Z	Yield
3a	H	H	H	92%
3b	CH_3	H	H	89%
3c	H	CH_3	H	86%
3d	H	H	CH_3	81%
3e	H	H	Cl	80%
3f	Cl	H	Cl	79%
3g	H	H	OCH_3	85%
3h	H	H	NO_2	73%
3i	OCH_3	H	H	83%
3j	X = $OCH_2CH_2CH_2$Phthalimide			87%

Interestingly, with the exception of compound **3h**, the yields obtained for the porphyrins are nearly independent of the electron withdrawing or donating ability of the aromatic substituents. However, we did observe that the aromatic aldehyde component has a slight, yet noticeable, influence on the rate of porphyrinogen formation. Electron rich aldehydes produced the porphyrinogen intermediate (as assessed by the appearance of the characteristic purple color) more rapidly than their electron poor counterparts. In all cases, this portion of the reaction was allowed to proceed for an extended time period (15 hr) to ensure that formation of the porphyrinogen was complete. Subsequent chloranil oxidation, under the conditions employed, proceeded with equal facility for all compounds studied.

The ortho substituents in the compounds **3d-3h** should hinder rotation about the *meso C - aryl C* bond. Indeed, the ^{1}H NMR spectra shown below for the methyl (**3d**)- and methoxy-substituted porphyrins (**3g**) confirm the existence of atropisomers. The double methyl resonances in both cases are indicative of two conformational isomers. Analogous observations have been reported for tetra-o-tolylporphine (8). The chemical shift



Porphyrin 3d



Porphyrin 3g

differences (14.8 Hz for **3d**; 1.8 Hz for **3g**) appear to reflect the fact that the methyl substituent of the tolyl species is nearer the porphyrin core than its counterpart on the anisyl derivative.

In summary, 5,15-diarylporphyrins can be prepared in high yield under mild conditions. The protocol described in this paper is especially noteworthy in light of the recent interest in diarylporphyrins as model systems for biologically-important heme-dependent phenomena.

Acknowledgement

We thank the American Heart Association, National Center, for generous financial support.

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7. **3a**: ^{1}H NMR ($CDCl_3$, ppm): 10.3 (s,2H), 9.4 (d,4H), 9.1 (d,4H), 8.3 (d,4H), 7.8 (br, 6H), -3.2 (br, too broad to integrate); UV-vis ($CHCl_3$, nm): 639, 571, 530, 499, 405; MS: m/z = 462.18 (M^+) . **3b**: ^{1}H NMR: 10.3 (s,2H), 9.4 (d,4H), 9.2 (d,4H), 8.1(d,4H), 7.6 (d,4H), 2.7 (s,6H); UV-vis: 629, 574, 534, 502, 406; MS: m/z = 490.32 (M^+). **3c**: ^{1}H NMR: 10.3 (s,2H), 9.4 (d,4H), 9.1 (d,4H), 8.1 (br,4H), 7.7-7.6 (m,4H), 2.7 (s,6H), -3.2 (br,2H); UV-vis: 629, 574, 534, 500, 406; MS: m/z = 490.19 (M^+). **3d**: ^{1}H NMR: 10.2 (s,2H), 9.3 (d,4H), 8.8 (d,4H), 8.0-7.9 (m,4H), 7.7-7.5 (m,4H), 2.0 (d,6H), -3.16 (br,2H); UV-vis: 640, 572, 531, 499, 404; MS: m/z = 490.29 (M^+). **3e**: ^{1}H NMR: 10.3 (s,2H), 9.4 (d,4H), 8.9 (d,4H), 8.3-8.1 (m,2H), 7.9-7.6 (m,6H), -3.2 (br,1.5H); UV-vis: 640, 625, 571, 530, 498, 404; MS: m/z = 531.36 (M^+). **3f**: ^{1}H NMR: 10.3 (s,2H), 9.4 (d,4H), 8.9 (d,4H), 8.2-8.0 (m,2H), 7.9 (d,2H), 7.8-7.6 (m,2H), -3.3 (br,2H); UV-vis: 626, 571, 532, 499, 404; MS: m/z = 600.13 (M^+). **3g**: ^{1}H NMR: 10.2 (s,2H), 9.3 (d,4H), 9.0 (d,4H), 8.1 (d, 2H), 7.8 (t, 2H), 7.4 (q,6H), 3.6 (d,6H), -3.15 (br, too broad to integrate); UV-vis: 624, 574, 531, 500, 405; MS: m/z = 522.54 (M^+). **3h**: ^{1}H NMR: 10.3 (s,2H), 9.4 (d,4H), 8.8 (d,4H), 8.5 (m,2H), 8.3 (m,2H), 8.0 (m,4H), -3.1 (br, too broad to integrate); UV-vis: 628, 574, 533, 502, 406; MS: m/z = 552.29 (M^+). **3i**: ^{1}H NMR: 10.3 (s,2H), 9.4 (d,4H), 9.1 (d,4H), 8.2 (d,4H), 7.3 (d,4H), 4.1 (s,6H), -3.2 (br,1.2H); UV-vis: 636, 574, 536, 503, 409; MS: m/z = 522.36 (M^+). **3j**: ^{1}H NMR: 10.3 (s,2H), 9.4 (d,4H), 9.1 (d,4H), 8.1 (d,4H), 8.0-7.6 (m,8H), 7.2 (d,4H), 4.3 (t,4H), 4.1 (t,4H), 2.4 (p,4H), -0.6 (br,2H); UV-vis: 640, 575, 539, 503, 409, 395; MS: m/z = 868.72 (M^+).

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(Received in USA 11 August 1989)