A NOVEL APPROACH TO THE SYNTHESIS OF SYMMETRICAL AND UNSYMMETRICAL PORPHYRIN DIMERS

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Abstract: Methodology for synthesis of symmetrical or unsymmetrical porphyrin dimers linked at the meso positions with phenyl or stillbene functionalities is reported; 5-porphyrinyl-dipyrromethanes are key intermediates in this approach.

Since the publication of the X-ray analyses of the bacterial photosynthetic reaction centers from *Rhodopseudomonas virdis*,^{1a,b} and *Rhodobacter spheroides*,^{1b,c} a variety of porphyrin monomers and dimers with different geometries and separation distances have been synthesized and studied by various investigators as models.^{2,3} From synthetic models, Gust et al.⁴ and Maruyama et al.⁵ have shown that close proximity is the important factor for efficient energy transfer. Distance, geometry, and orientation have been recognized as important factors for control of the efficiency of energy and electron transfer process.¹ Some porphyrin dimers with carbon-carbon linkages^{6,7} have also been reported as potential photosensitizers for photodynamic therapy, a new modality for the treatment of cancer.⁸ Despite the synthesis of a variety of porphyrin dimers, there are but few general and efficient synthetic methods for the preparation of unsymmetrical porphyrin dimers. Maruyama et al.⁹ reported the preparation of unsymmetrical porphyrin



dimers by condensation of an a,c-biladiene dihydrobromide with isophthaldehyde to give a porphyrin bearing a formyl group, which was then allowed to react with two equivalents of α -free pyrrole. The zinc(II) complex of the intermediate was further condensed with a dipyrromethane to give the unsymmetrical porphyrin dimer. However, the yield of the final product was extremely low. Recently Sessler et al.¹⁰ have reported the synthesis and characteristics of a variety of selectively mono-metalated mono-quinone substituted zinc containing octaalkyl porphyrin dimers, designed to mimic certain key electronic and structural aspects of the photosynthetic reaction centers, and Chang et al. have reported the synthesis of "PacMan" porphyrins^{2a} which may have interesting catalytic properties.

In this Communication, we report a general route for the synthesis of symmetrical porphyrin dimers 1 and 2 as well as an unsymmetrical porphyrin dimer 3. Bis-porphyrins of type 1 and 3, bearing a para- or meta-phenyl



interporphyrin tether have previously been reported by Sessler and coworkers.^{2c,10} For the preparation of symmetrical dimers 1 and 2, terephthaldehyde mono-(diethylacetal) 4 was first reduced to the corresponding alcohol 5 by reaction with lithium aluminum hydride^{11a} or sodium borohydride. It was then condensed with pyrrole 6^{12} to give the dipyrromethane 7^{10} in >90% yield. The formyl group from dipyrromethane 7 was regenerated by reaction with tetrapropylammonium per-ruthenate (TPAP) in dichloromethane/NMO^{13,14} and the resulting formyldipyrromethane 8 was isolated in 85% yield. Further reaction of dipyrromethane 8 with afree pyrrole 6 gave the bis-dipyrromethane 9¹⁰ in almost quantitative yield. Treatment of pyrromethane 9 with refluxing ethylene glycol/KOH gave 10 in excellent yield. It

was condensed with the known¹⁵ diformyldipyrromethane 11 following the standard MacDonald procedure,¹⁶ and the symmetrical porphyrin dimer was isolated in 22% yield along with a little coproporphyrin-II tetramethyl ester 12 (due to self condensation of the diformylpyrromethane 11).

In order to obtain the symmetrical bis-dipyrromethane 13, formyldipyrromethane 8 was dimerized with lowvalent titanium under McMurry conditions.¹⁷ We have previously shown that this methodology can also be applied successfully to the self-condensation of porphyrins bearing formyl substituents.¹⁸ Bis-dipyrromethane 13 was then converted into porphyrin dimer 2 in 18% yield by first refluxing with ethylene glycol/KOH (to give the tetracarboxylic acid 14 and then condensing with diformyldipyrromethane 11. The structure of 14 was further confirmed and the trans stereochemistry of the central double bond was established by a single crystal X-ray study.¹⁹



For the synthesis of the typical, totally unsymmetrical monometalated porphyrin dimer 3, the foregoing methodology was further modified; the key unsymmetrical bis-dipyrromethane dimer intermediate 15, containing both benzyl and ethyl ester protecting groups, was prepared as a key intermediate. For the synthesis of 15, terephthaldehyde



mono-(diethylacetal) 4 was first condensed with benzyl 3, 5-dimethylpyrrole-5-carboxylate 16²⁰ to give Reaction with TPAP/NMO 17. afforded the formyldipyrromethane 18 which was then condensed with two equivalents of pyrrole 6 and the desired unsymmetrical dipyrromethane dimer 15 was isolated in 82% yield. Hydrogenolysis of dipyrromethane 15 over Pd/C produced the bis-dipyrromethane dicarboxylic acid 19 in quantitative yield. Further reaction of 19 with diformyldipyrromethane 20^{21} gave the porphyrinyldipyrromethane 21 in 22% yield, along with porphyrin 22 as a minor contaminant.²² Treatment of 21 with Ni(acac)₂ in refluxing o-xylene produced the corresponding metal complex 23, which was subjected to hydrolysis by refluxing with ethylene glycol/KOH to give 24 and then condensed with diformyldipyrromethane 5 (Mac-Donald conditions); the desired dimer 3 was isolated in 15% yield.

Further developments and improvements of these approaches are in progress. Yields reported above, by and large, are unoptimized. All the new compounds were characterized by NMR, elemental analysis and/or high resolution mass spectrometry.

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- 21. Compound 20 was prepared by reaction of pyrrole 6 with benzaldehyde, followed by saponification of the ethyl esters and double Vilsmeier formylation.
- 22. Interestingly, previous syntheses of 5,15-diphenylporphyrins such as 22 have usually involved condensation of two moles of a dipyrromethane with two moles of benzaldehyde.^{2d,11b,23,24} In this case the approach is reversed, and involves serendipitous condensation of two moles of a 1,9-diformyl-5-phenyldipyrromethane. Conversion of 11 into 12 is another example of this same transformation.
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