Pergamon

Tetrahedron Letters, Vol. 38, No. 22, pp. 3935-3938, 1997

0040-4039/97 $17.00 + 0.00

PII: S0040-4039(97)00783-1

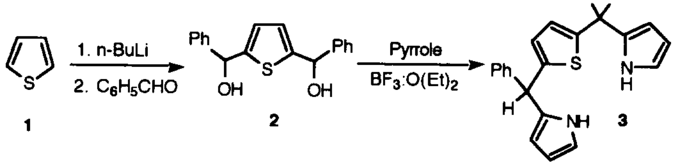
SYNTHESIS OF *meso*-TETRAPHENYLTHIAPORPHYRINS BEARING ONE INVERTED PYRROLE

Chang-Hee Lee* and Han-Je Kim
*Department of Chemistry, Kangwon National University, Chun-Cheon 200-701, Korea

2-Aza-21-thia-23-carba-5,10,15,20-tetraphenylporphyrin and its N-methylated analogue were synthesized and characterized. The synthesis utilizes [3+1] condensation of thiatripyrrin with 2,4-bis(α-hydroxy-α-phenylmethyl)pyrrole or 2,4-bis(α-hydroxy-α-phenylmethyl)-N-methylpyrrole in the presence of acid catalyst. This convenient process gives predominently the titled porphyrin. Reinversion of the pyrrole unit is observed by prolonging the reaction time.

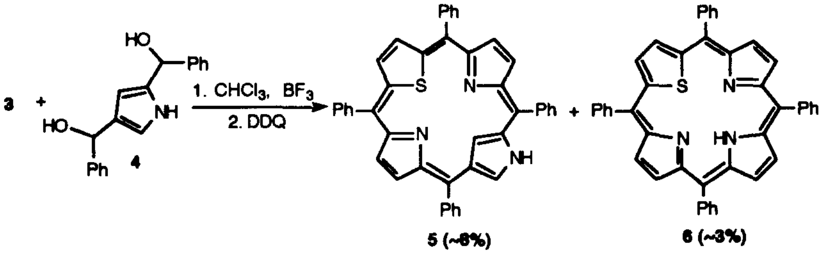
As part of continuous effort to develop synthetic methods for the preparation of core-modified porphyrins with fixed arrangement of core-ligands, we recently reported a synthesis of 1,14-unsubstituted tetrahydrotripyrrins by acid-catalyzed condensation of 2,4-bis(α-hydroxy-α-phenylmethyl)pyrrole, 2,5-bis(α-hydroxymethyl)furan or 2,5-bis(α-hydroxymethyl)thiophene with excess pyrrole.[1] This simple synthesis provided a stepwise synthesis of porphyrins bearing core ligands other than nitrogen and prompted us to investigate a related method for synthesizing various core-modified porphyrins with predesignated orientation of the core ligands. The porphyrin isomer 2-aza-21-carba-5,10,15,20-tetraphenylporphyrin (so called 'N-confused porphyrin') was previously isolated as a side product from a normal porphyrin forming reaction between benzaldehyde and pyrrole.[3] To date, we are not aware of any reports concerning the directed synthesis of pyrrole inverted porphyrins. We report the stepwise synthesis of a core-modified porphyrin bearing one inverted pyrrole unit and the selective replacement of one nitrogen with sulfur. Modification of the core by the introduction of other atoms (O, S, C) for the pyrrole nitrogens produces a new class of macrocycles with potential interesting properties. For example, Kunitake et al[4] recently reported that tetraphenylporphyrin with one inverted pyrrole (NC-TPP) recognize halides anion at air-water interface.

Scheme 1



The 5,10-diphenyl-16-thia-5,10,15,17-tetrahydrotripyrrin **3** was synthesized by reacting 2,5-bis(α-hydroxy-α-phenylmethyl)thiophene **2** with excess pyrrole in the presence of Lewis acid catalyst such as BF_3:$O(Et)_2$.[1] The high reactivity of 2-α-hydroxymethylated 5-membered aromatic heterocycles toward nucleophilic substitution in the presence of acid catalysts is well known.[5] We found that the yields of tripyrrins varied depending on the purity of the starting materials. Usually the maximum yields were obtained when BF_3:$O(Et)_2$ was used as the catalyst and more than 40 equivalents of distilled pyrrole were used as the reaction solvent.[1] TLC analysis of **3** showed no other appreciable products formed except small amount of polymeric material at the origin. Condensation of **3** with 2,4-bis(α-hydroxy-α-phenylmethyl)pyrrole was carried out in chloroform in the presence of BF_3:$O(Et)_2$. The isolated products contained two different porphyrin components. One was identified as carbaporphyrin **5** (SNCN) and the other was thiaporphyrin **6** (SNNN).

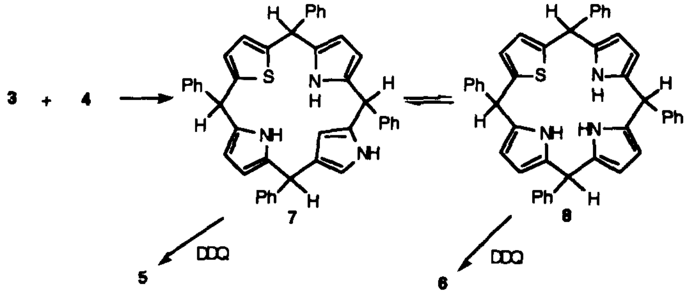
Scheme 2



The formation of thiaporphyrin **6** (SNNN) indicates that the 2,4-substituted pyrrole unit originally used in the condensation rearranges into the 2,5-substituted pyrrole unit during the condensation. The twisting of the pyrrole unit may occur as a result of acid catalysed ring opening of the initially formed porphyrinogen.[6] The amount of porphyrins **6** that formed is incresed when the reaction was run for more than 1 hour. The ratio of **5**/**6** formed in this case is 1/1 judging from proton nmr spectra. Stirring the reactants (**3** and **4**) alone in the presenceof $BF_3{:}O(Et)_2$ in chloroform or trifluoroacetic acid in methylene chloride did not result in any detectable amount of porphyrin-like components.

Each porphyrin component isolated was easily identified by ^1H NMR spectroscopy; ^1H NMR spectrum of **6** (SNNN) was simple due to its symmetry. Silica TLC analysis showed that porphyrin **6** is less polar than **5**. The ^1H NMR spectrum of porphyrin **6** showed that the inner N-H proton has a broad signal at -2.78 ppm which is completely disappears upon addition of TFA-d. The protons on the thiophene appeared as a singlet at 9.68 ppm. The β-pyrrolic protons located trans from the thiophene appeared as a singlet at 8.86 ppm. The other four β-pyrrolic protons appeared as two distictive doublet at 8.62, 8.53 ppm. Due to low solubility of porphyrin **5** in organic solvent, the proton nmr spectrum was taken after adding small amount of deuterated trifluoroacetic acid and the spectrum was rather complex due to the unsymmetric nature of the compound. For example, the inner C-H proton was shown at -1.65 ppm and the outer β-H of the flipped pyrrole was obscured by aromatic protons and other β-pyrrolic protons were shown as two doublets at 8.76, 8.66 ppm and at 8.42-8.40 ppm as multiplet. The inner C-H proton peak shown at -1.65 ppm was not exchanged upon exposure to acidic deuterium oxide over a 36 hour period. The N-H proton signal was not observed due to acidic nature of experiemntal condition.[7] The Soret band of the porphyrin **5** appeared at 445 nm and at 428 nm for porphyrin **6**. The large red shifts of the Soret band indicates that the structure of **5** is more flexible and distorted from porphyrin plane possibly due to the repulsion between inner C-H hydrogen and sulfur. On the other hand, porphyrin **6** is rather closer to planarity due to the presence of one less inner hydrogen but larger size of sulfur may cause small distortion. From a mechanistic point of view for the retwisting of pyrrole unit, one can consider the sum of all the internal bond angles of each porphyrinogen. Structure **5** takes up a greater portion of the sum of internal angles than does **6**. This is because the imaginary angle which is formed by extrapolation of 2- and 5-alkyl substitutents in the pyrrole unit is 133°, while 2- and 4-alkyl substituents is 151°.[8] The porphyrinogen **7** has increased size of the macrocycle due to the inversion of one pyrrole unit. This inversion causes increased ring strain and the acid catalyzed reversible cleavage of the inverted pyrrole will release the strain somewhat. Acid catalyzed recyclization after rotation of pyrrole unit will result in porphyrinogen **8**. Thiophene unit has smaller CSC angle than CNC angle in pyrrole. Thus substitution of thiophene would not result any appreciable angle strain. Sessler and Latos-Grazynski have suggested that the formation of N-confused porphyrin is the result of macrocyclization of filpped pyrrole.[9] But current results indicate that normal macrocyclization is thermodynamic while 'flipped' macrocyclization is kinetic in nature. The results obtained here agree with our previous observations.[6] In general, the flipping of pyrrole must be thermodynamically favorable and inherent characteristics of pyrrole nuclei in porphyrin forming reactions.

Scheme 3

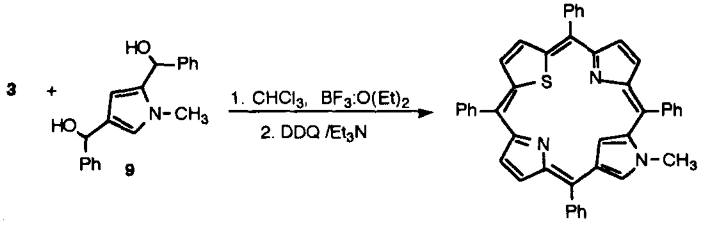


This is why the thermodynamic equilibration between **7** through **8** must be prefered than normal porphyrinogen **8**. If the reaction is trapped by oxidation before the equilibration reaches, **7** will be formed and consequently results in porphyrin **5** as predominant product.

On the contrary, the condensation of N-methyl-2,4-bis(α-hydroxy-α-phenylmethyl)pyrrole **9** with tripyrane **3** resulted only porphyrin **10** in 30 % yield as shown in scheme 4. The yield of **10** seems not decreasing by extending reaction time. N-Methylated **4** obviously favor the one-side condensation and retwisting is unfavorable due to steric repulsion. The UV-Vis spectrum of **10** is slightly red-shifted by cal 8 nm compare to the **5**. but the spectral shape and intensity is almost identical. This observation indicates the favorable isomerc form is the one which the proton on the nitrogen resides outside the core. This is because twice larger size of sulfur and core hydrogen attched to the carbon is already sterically crowded. This observation is contrary with the porphyrin which sulfur in the porphyrin **10** is substituted with oxygen. The hydrogen resides in the core and inner hydrogen was well observed by proton nmr spectroscopy in this case.[6] The ^{1}H NMR spectrum of porphyrin **10** showed that the inner C-H proton has a doublet at 2.06 ppm which is shifted to -1.38 ppm upon addition of TFA-d. Unusual high field shift of C-H proton indicates that the porphyrin plane is much more flexible and the 'flipped' pyrrole is out of plane due to steric repulsion. But the protonation on the outer pyrrolic nitrogen forces the pyrrole ring to tilt back toward core due to severe steric repulsion between meso-phenyl and N-methyl group. The protons on the thiophene also shifted from 8.30 to 9.22 ppm.

The obvious advantages of the present syntheses are their wide applicabilities in synthesizing porphyrins having different ligands in the core in the regiospecific manner. The synthetic approaches presented with this article also could be applied to the synthesis of regiospecific inversion of pyrrole unit. Replacement of the nitrogen atoms in the porphyrin core with other ligands produces unique macrocycles with different cavity sizes and complexing abilities.[10] Our demonstration for the synthesis of core-modified porphyrins in simple manner will be applicable in designing various model systems. Currently, we are investigating the possibility of synthesizing other core-modified porphyrins and expanded porphyrins using the same analogy. The chemistry for preparing these new porphyrin family and their metal complexes is now in hand and physical and electronic properties are under investigation also.

Scheme 4



10 (~30%)

Acknowledgement

We gratefully thank for the financial support from Korea Science and Engineering Foundation (961-0302-014-2). and partial financial support from Ministry of Education (BSRI-96-3401).

References and notes

1. Lee C. H.; Lindsey, J. S.*Tetrahedronn* **1994**, *50*, 11427.
2. Heo, P. Y. and Lee, C. H. *Tetrahedron Lett.* **1996**, 197.
3. Furuta, H.; Asano, T.; Ogawa, T. *J. Am. Chem. Soc.* **1994,** *116*, 767.
4. Ariga, K.; Kunitake, T and Furuta, H. *J. Chem. Soc. Perkin Trans. 2*, **1996**, 667
5. "*Porphyrins and Metalloporphyrins*", Smith, K. M., Ed.; Elsevier: Amsterdam, **1975.**
6. Heo, P. Y. and Lee, C. H. *Bull. Korean Chem. Soc.* **1996**, *17*, 778.
7. Spectroscopic data for the new compounds are follow: ^{1}H NMR ($CDCl_3$/TFA-d) for **5** δ 9.22 (t, 2H, thiophene-H), 8.77 and 8.65 (two doublets, 2H, pyrrole-H), 8.42-8.41 (m, 2H, pyrrole-H), 8.40-8.25 (m, 8H, Ar-H), 8.12-7.95 (m, 13H, Ar-H), -1.65 (s, 1H, inner C-H); FAB-MS Calc. for $C_{44}H_{29}N_3S$ 631.2, Found 631.0 (M^+, base), 264, 236, 173 ; **6** ($CDCl_3$) δ 9.80 (s, 2H, thiophene-H), 8.93 (s, 2H, pyrrole-H), 8.71 and 8.60 (two doublets, 4H, pyrrole-H), 8.29-8.19 (m, 8H, Ar-H), 7.9-7.73 (m, 12H, Ar-H), -2.7 (s, 1H, N-H); FAB-MS Calc. for $C_{44}H_{29}N_3S$ 631.2, Found 631.0 (M^+, base), 554, 121; **10** ($CDCl_3$,without TFA-d), δ 8.31 and 8.29 (two doublets, 2H, thiopene-H), 7.83 and 7.74 (two doublets, 2H, pyrrolic-H), 7.52 and 7.47 (two doublets, 1H, pyrrolic-H), 7.32 (d, 1H, pyrrole-H), 7.91-7.90 (m, 4H, Ar-H), 7.85-7.84 (m, 4H, Ar-H), 7.65-7.57 (m, 12H, Ar-H), 3.37 (s, 3H, N-methyl), 2.06 (d, 1H, inner C-H); ($CDCl_3$/TFA-d), δ 9.02 and 9.03 (two doublets, 2H, J = 5 Hz, thiopene-H), 8.57 and 8.37 (two doublets, 2H, J = 4 Hz, pyrrolic-H), 8.17 and 8.13 (two doublets, 2H, J = 5 Hz, pyrrolic-H), 8.31-8.25(m, 4H, Ar-H), 8.19-8.16 (m, 4H, Ar-H), 8.07-8.00 (m, 6H, Ar-H), 7.93-7.89 (m, 6H, Ar-H), 7.45 (s, 1H, pyrrolic-H), 3.60 (s, 3H, N-methyl), -1.38 (s, 1H, inner C-H); FAB-MS Calc. for $C_{45}H_{31}N_3S$ 645.2, Found 645.1 (M^+).
8. Franck, B. and Nonn, A. *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1795.
9. a).Sessler, J. L. *Angew. Chem. Int. Ed. Engl.* **1994,** *33*, 1348. b). Chmilewski, P. J.; Latos-Grazynski, L.; Rachlewicz, K. and Glowiak, T. *Angew. Chem.* **1994,** *106*, 805. c). Chmilewski, P. J.; Latos-Grazynski, L.; Rachlewicz, K. and Glowiak, T. *Angew. Chem. Int. Ed. Eng.* **1994,** *33*, 779.
10. a). Grazynski, L. L.; Lisowski, J.; Olmstead, M. M. and Balch, A. L., *J. Am. Chem. Soc.* **109**, 4428 (1987), b). Ulman, A.; Manassen, J.; Frolow, F.; Rabinovich, D. *J. Am. Chem. Soc.* **1979**, *101*, 7055. c). Ulman, A.; Manassen, J. *J. Am. Chem. Soc.* **1975**, *97*, 6540. c). Berlin, K.; Breitmaier, E. *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 219.

(*Received in Japan* 11 *March* 1997; *revised* 17 *April* 1997; *accepted* 21 *April* 1997)