Thiatriphyrin(2.1.1): A Novel Core-Modified Contracted Porphyrin
Daiki Kuzuhara, Yuka Sakakibara, Shigeki Mori, Tetsuo Okujima, Hidemitsu Uno and Hiroko Yamada

(Dedication---optional)

Triphyrins are porphyrin analogues that contain three pyrrole rings linked through meso-sp² carbon atoms. They hold a unique position in the porphyrin chemistry and they are relatively newcomers. Inevitably, all the subphthalocyanines 1[13] and subporphyrins 2[23] have been boron complexes with nonplanar, dome-shaped conformations (Figure 1). Triphyrins have also demonstrated a variety of opto-electronic properties such as non-linear optical absorption,[4] higher emission quantum yields,[46,5] and have been applied for organic electronic devices such as organic light emitting diodes (OLED)[6] and organic solar cells (OSC).[7] In 2008, we succeeded in preparing [14]triphyrin(2.1.1) 3 as the boron-free triphyrin with near-planar structure. The triphyrin was synthesized by the acid-catalyzed condensation of a bicyclo[2.2.2]octadiene (BCOD)-fused pyrrole with an arylaldehyde,[8] or the intramolecular McMurry coupling of diformyltripyrane.[9] Recently the condensation reaction of dipyrroethene and pentfluorobenzaldehyde to make meso-tetraaryltriphyrin was reported.[10] [14]Triphyrins(2.1.1) have a 14π-electron aromatic system composed solely of pyrrole moieties and act as a monovalent ligand. As a result of their boron-free composition, they can be converted to bowl-shaped Mn(I), Re(I) and Ru(II) complexes.[8,9]

It is well known that remarkable changes in the optical and electrochemical properties and coordination abilities of porphyrins can be induced by core-modification of porphyrinoids.[11,12] In light of this, it is naturally expected that the core-modification of triphyrins will also give them new functionality. Subpyriporphyrin 4 has one pyridine ring in place of one of the three pyroles and is the only metal-free triphyrin(1.1.1) analogue reported to date.[13] The free base form of this compound exhibits no aromaticity, while 14 π-electron ring current is observed in its boron complex.

Here, we have attempted to synthesize a thiophene containing triphyrin, [14]thiatriphyrin(2.1.1) (TTP), which should have a 14 π-electron pathway within the macrocycle without inner NH. It is revealed that the core-modified triphyrin is unstable as a neutral form and meso-alkoxy-attached thiatriphyrins (ORTTP) were easily formed. Interestingly, the treatment of ORTTP with acid led to the elimination of the alkoxy group and generated the protonated thiatriphyrin TTP+. In this paper we discuss the synthetic procedures as well the unique reactivity, the crystal structures, and the optical properties of these thiatriphyrin derivatives.

![Figure 1. Structures of subphthalocyanine (1), subporphyrin (2), [14]triphyrin(2.1.1) (3), subpyriporphyrin (4), thiatriphyrin(2.1.1) (TTP) and protonated thiatriphyrin (TTP+)](image)

The synthetic route to TTP is shown in Scheme 1. Among the reported synthetic methods for triphyrins, the intramolecular McMurry coupling method is turned out to be suitable for the preparation of thiatriphyrins from diformylthiatripyrane 5.[14] The McMurry coupling reaction of 6 gave 5,10-dihydro-5,10-ditolylthiatripyrane 6 in 50% yield. The direct oxidation of 6 with 2 eq. of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in CHCl₃.
was initially attempted and resulted in the formation of small amount of the thiatriphyrin 7a with an ethoxy group at the meso position, which we assume came from the presence of ethanol in the CHCl₃. Then, we examined the step-wise route. The oxidation of 6 with 1 eq. of DDQ in CH₂Cl₂ gave 5-hydrothiatriphyrin (8) in 50% yield. Compound 8 is formally the partially oxidized tripyrrologen, the structure of which was confirmed by ¹H NMR, mass spectrometry and X-ray diffraction analysis. The crystal structure of 8 showed that the tolyl group at the C16 position was oriented in the same direction as the sulfur atom (Figure 2).[15]

Scheme 1. Synthesis of thiatriphyrin (TTP) and its derivatives.

Figure 2. Crystal structure of 8. Left: top view, right: side view. At the top view, hydrogen atoms expect for NH proton and C16-H are omitted for clarity. At the side view, hydrogen atoms expect for C16-H are omitted for clarity. Thermal ellipsoids represent 50% probability.

The subsequent oxidation of 8 with 1 eq. of DDQ in the absence of nucleophiles such as ethanol did not give the desired product TTP nor the starting material, but only decomposition occurred. When the same oxidation was performed in CH₂Cl₂ with methanol, however, the methoxy-attached product 7b was obtained in 35% yield, in addition to the corresponding isomeric product 7b-II in very low yield. The addition of small amounts of either ethanol or 2-propanol to the CH₂Cl₂ afforded 7a and 7e in 41% and 20% yields respectively. The corresponding isomers 7a-II and 7e-II were not obtained. These results indicate that the TTP is highly reactive with nucleophile reaction at the meso position. To understand the high reactivity of TTP, molecular orbital of TTP was calculated at the B3LYP/6-31G** (Figure S1).[16] TTP has steric repulsion between the large sulfur atom and two lone electron pairs of the imine nitrogen atoms in a small cavity, which make the TTP molecule non-planar and reduce the aromatic stability. Furthermore the molecular orbitals of lone pairs of inner nitrogen atoms were calculated to be close to each other at HOMO level. This structure is unstable due to the electric repulsion of lone pairs[17] which make TTP unstable and high reactive to the nucleophylic addition at meso-position. On the contrary, the macrocycle, 7a-c and 8 have a hydrogen bond between inner nitrogen atoms which can be observed by the N-N distance and the mutual direction of two pyrrolys. This hydrogen bond is very important for stabilizing these compounds. (Scheme S1).

The structure of 7a was characterized by ¹H NMR, high-resolution electrospray ionization time-of-flight (HR-ESI-TOF) mass spectrum and X-ray crystal analysis. HR-ESI-TOF mass spectrum of 7a displays the parent ion peak at m/z 489.1995, (calcd. for C₂₂H₂₆N₄O₅S = 489.1922 [M + H]+). The ¹H NMR spectrum of 7a is shown in Figure 3a. The signals due to the thienyl protons were evident as two doublets at 7.52 and 6.95 ppm and pyrrole protons appear around 6.84~6.02 ppm. The inner NH proton was observed at 12.69 ppm due to the hydrogen bonding with its neighboring nitrogen atoms. These data suggest that 7a have no continuous conjugation around tripyrrolic framework. Single crystals of 7a suitable for X-ray diffraction analysis were obtained by slow evaporation of an ethanol solution (Figure 4). The ethoxy group at the C16 position is oriented in the same direction as the sulfur atom relative to the plane of the macrocycle. The bond lengths in the pyrrole moieties indicate that one of the pyrrole units has an imine (C9-N1: 1.320 Å) while the other is an amine structure (C12-N2: 1.409 Å), suggesting the hydrogen-bonding interaction between the two inner nitrogen atoms. The thiophene ring is largely tilted away from the plane of the macrocycle, with a dihedral angle between the thiophene and pyrrole 1 ring of 69.53°.

Figure 3. ¹H NMR spectra of 7a a) in CDCl₃ without TFA and b) in CD₂Cl₂ with 2.2 eq. of TFA at -40 ºC.
During thermogravimetric analysis, 7b exhibited an 8% mass loss at 162 °C (Figure S2), which is in good agreement with the predicted value of 7% expected for the elimination of methanol from 7b to form TTP on heating. Heating of 7b in a glass tube oven at 200 °C, however, produced only insoluble material rather than TTP. Interestingly, reflux of an ethanol solution of 7b for 12 h gave 7a in quantitative yield. When attempting to obtain a single crystal of the structural isomer 7b-II from a CH2Cl2/methanol solution, only 7b was obtained. These results indicate that methanol was removed to give TTP as an intermediate, but the TTP reacted with methanol immediately due to its instability thereafter to revert back to the substituted compound. According to DFT calculations based on the B3LYP/6-31G** level, total energy of 7a is more stable than that of its isomer 7a-II (Figure S3).

The elimination of methoxy groups under acidic conditions has been observed for subpyrroporphyrin,[13a] an N-fused porphyrin boron complex,[18] dithiaethyneporphyrin,[19] and a homoporphyrin nickel complex.[20] According to these reports, we checked the reactivity of 7b to produce protonated TTP (TTPH+) under acidic conditions. The absorption of 7b showed two broad bands at 325 and 530 nm (Figure S4). Upon the addition of trifluoroacetic acid (TFA) to a solution of 7b in CH2Cl2, the absorption spectrum changed relative to the equivalents of TFA added, with isosbestic points at 355, 492 and 570 nm (Figure 5). The broad band at 530 nm decreased simultaneously with the increase of the Soret-like band at 414 nm and the Q-like bands at 490, 525 and 574 nm. After addition of 3.5 eq. TFA, there were no further changes and the spectrum was similar to that reported for protonated triphyrins.[8a,10] These spectral changes suggested that TTPH+ was generated from 7b in response to the addition of the acid. Moreover, treatment of TTPH+ with DBU in the presence of methanol in CH2Cl2 regenerated 6b (Figure S5). We also acquired the 1H NMR spectrum of TTPH+ resulting from a mixture of 7a and 2.2 eq. TFA in CD2Cl2 at -40 °C (Figure 2b and Figure S6). Singlet peaks were observed at 8.70 ppm corresponding to the thiophene moiety, and at 7.44 ppm due to the ethynyl bridge protons. The pyrrole signals exhibit down-field shifts compared to 7a. The NH signal was observed at 9.42 ppm which exhibited up-field shift compared to 7a and disappeared by adding D2O (Figure S6). From H-H COSY, cross peaks between NH and pyrrolic signals were observed (Figure S7). The chemical shifts of these protons reflect a diatropic ring current associated with the TTPH+ macrocycle.

Fortunately, a single crystal of TTPH+·[CF3CO2]2H+ was obtained from a mixture of toluene, TFA and water (Figure 6 and S9). The thiophene ring is again tilted away from the plane of the macrocycle and the dihedral angles between the thiophene ring and the neighboring pyrroles were 50.28° and 48.61°, both of which are smaller than in 7a. The bond lengths between the meso and pyrrolic α-carbons were 1.434(4) Å for C4-C5, 1.415(4) Å for C5-C6, 1.401(4) Å for C15-C16 and 1.456(3) Å for C16-C1. These values indicate there is no bond alternation and are slightly longer than those of previously reported 14π-electron aromatic triphyrins.[8-10]

We also estimated the nucleus-independent chemical shift (NICS) values of TTPH+ at several points within the molecular plane based on an optimized structure from the X-ray diffraction data (Figure S10). The NICS (0) value of TTPH+ at point (a) in Figure 6 is -11.37 ppm, which indicates moderate aromaticity. Taken together, the changes in UV and 1H NMR spectra on the addition of acid, X-ray single crystal analysis data, as well as NICS (0) values suggest that the protonated compound TTPH+ exhibits a distinct 14 π-electron aromatic structure.
When 8 was treated with TFA in CH$_2$Cl$_2$, absorption band at the 558 nm was gradually decreased, accompanied by an increase at 640 nm (Scheme S11). These results indicate that protonation of the nitrogen occurred to generate 8H$^+$. It thus appears that the alkoxy leaving groups play an important role during the acid conversion of 7a, 7b or 7c to TTPH$^+$. In summary, we have synthesized several alkoxy group-substituted triatriphyrins. Under acidic conditions, these can be converted to protonated TTPH$^+$, which shows moderate aromaticity. TTPH$^+$ is the first reported instance of aromaticity in a core-modified, contracted porphyrin upon protonation of its free-base form. It was also determined that these alkoxy-substituted triatriphyrins have a chiral center at the C16 carbon and a NNS coordination site. The results of studies concerning control of the chirality and coordination abilities of these compounds will be reported in the near future.

Received: ((will be filled in by the editorial staff))
Published online on ((will be filled in by the editorial staff))

**Keywords:** triphyrin · core-modification · acid conversion · aromaticity · porphyrinoids

[15] CCDC 912982 (8), 912983 (6a) and 912983 (TTPH$^+$) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
Thiatriphyrin(2.1.1): A Novel Core-Modified Contracted Porphyrin

(The core-modified, contracted porphyrin thiatriphyrin(2.1.1) was prepared by intramolecular McMurry coupling. This thiatriphyrin readily reacts with alcohols and was converted to a variety of alkoxy-substituted analogues. On reaction with TFA, each of these compounds formed protonated thiatriphyrin(2.1.1), which exhibited moderate aromaticity.)