Contracted Porphyrins

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Thiatriphyrin(2.1.1): A Core-Modified Contracted Porphyrin**

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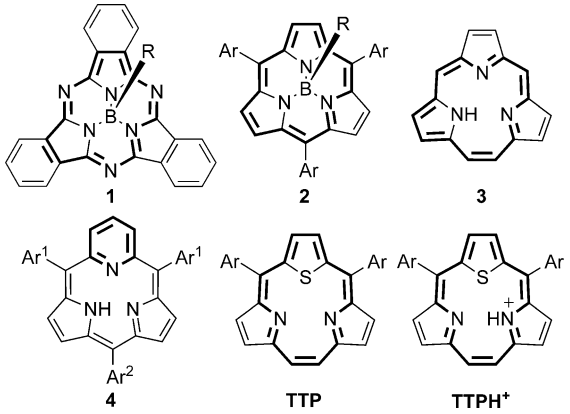
Dedicated to the memory of Christian Claessens

Triphyrins are porphyrin analogues that contain three pyrrole rings linked through *meso* sp^2-hybridized carbon atoms. They hold a unique position in porphyrin chemistry and are relative newcomers. Inevitably, all subphthalocyanines **1**[1] and subporphyrins **2**[2,3] have been boron complexes with nonplanar, dome-shaped conformations (Scheme 1). Triphyrins have demonstrated a variety of optoelectronic properties, such as nonlinear optical absorption[4] and high emission quantum yields,[4c,5] and have been applied in organic electronic devices, such as organic light-emitting diodes[6] and organic solar cells.[7] In 2008, we succeeded in preparing [14]triphyrin(2.1.1) (**3**) as a boron-free triphyrin with a near-planar structure. The triphyrin was synthesized by the acid-catalyzed condensation of a bicyclo[2.2.2]octadiene-fused pyrrole with an aryl aldehyde,[8] or by the intramolecular McMurry coupling of diformyltripyrrane.[9] Recently, the condensation of dipyrroethane and pentafluorobenzaldehyde to make a *meso*-tetraaryltriphyrin was reported.[10] [14]Triphyrins(2.1.1) have a 14π-electron aromatic system composed solely of pyrrole moieties and act as monovalent ligands. As a result of their boron-free composition, they can be converted into bowl-shaped Mn^I, Re^I, and Ru^{II} complexes.[8b,9]

It is well-known that remarkable changes in the optical and electrochemical properties and coordination abilities of porphyrins can be induced by the core modification of porphyrinoids.[11,12] It is therefore naturally expected that the core modification of triphyrins will also lead to new functionality. Subpyriporphyrin **4** (Ar^1 = mesityl, Ar^2 = phenyl) has one pyridine ring in place of one of the three pyrrole rings. Compound **4** and the corresponding subpyriporphyrin with a *p*-nitrophenyl group in place of the phenyl group are the only metal-free triphyrin(1.1.1) analogues reported to date.[13] The free-base form of this compound exhibits no aromaticity; however, a 14π-electron ring current is observed for its boron complex.



Scheme 1. Structures of subphthalocyanines **1**, subporphyrins **2**, [14]triphyrin(2.1.1) (**3**), subpyriporphyrins **4**, the thiatriphyrin(2.1.1) **TTP** (Ar = *p*-tolyl), and the protonated thiatriphyrin **TTPH**$^+$ (Ar = *p*-tolyl).

In this study, we attempted to synthesize a thiophene-containing triphyrin, the [14]thiatriphyrin(2.1.1) **TTP**, which should have a 14π-electron pathway within the macrocycle without an inner NH group. We reveal that the core-modified triphyrin is unstable in its neutral form and that thiatriphyrins with a *meso*-alkoxy substituent (ORTTPs) were readily formed. Interestingly, the treatment of these ORTTPs with acid led to the elimination of the alkoxy group and generated the protonated thiatriphyrin **TTPH**$^+$. Herein, we discuss the synthetic procedures as well as the unique reactivity, the crystal structures, and the optical properties of these thiatriphyrin derivatives.

The synthetic route to **TTP** is shown in Scheme 2. Among the reported synthetic methods for triphyrins, the intramolecular McMurry coupling turned out to be suitable for the preparation of thiatriphyrins from diformylthiatripyrranes such as **5**.[14] The McMurry coupling reaction of **5** gave 5,10-dihydro-5,10-di-*p*-tolylthiatriphyrin (**6**) in 50% yield. The direct oxidation of **6** with of 2,3-dichloro-5,6-dicyano-1,4-

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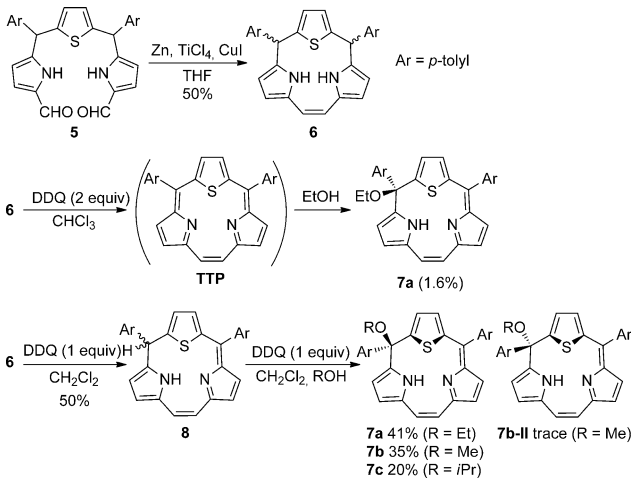

Scheme 2. Synthesis of **TTP** and its derivatives.

benzoquinone (DDQ; 2 equiv) in $CHCl_3$ was initially attempted and resulted in the formation of a small amount of the thiatriphyrin **7a** with an ethoxy group at the *meso* position. We assume that the ethoxy group is derived from ethanol present in the $CHCl_3$ solvent. Next, we examined a stepwise route. The oxidation of **6** with DDQ (1 equiv) in CH_2Cl_2 gave the 5-hydrothiatriphyrin **8** in 50% yield. Compound **8** is formally the partially oxidized triphyrinogen, and its structure was confirmed by ^{1}H NMR spectroscopy, 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 1).[15]

The subsequent oxidation of **8** with DDQ (1 equiv) in the absence of nucleophiles, such as ethanol, gave neither the desired product **TTP** nor the starting material, but only decomposition occurred. When the oxidation reaction was performed in CH_2Cl_2 in the presence of methanol, however, the methoxy-substituted product **7b** was obtained in 35% yield along with the corresponding isomeric product **7b-II** in very low yield. The addition of small amounts of either ethanol or 2-propanol to the CH_2Cl_2 solvent afforded **7a** and **7c** in 41 and 20% yield, respectively. The corresponding isomers **7a-II** and **7c-II** were not obtained. These results indicate that **TTP** is highly reactive at the *meso* position towards nucleophiles. To understand the high reactivity of **TTP**, the molecular orbitals of **TTP** were calculated at the B3LYP/6-31G** level (see Figure S1 in the Supporting Information).[16] Steric repulsion between the large sulfur atom and the two lone electron pairs of the imine nitrogen atoms in the small cavity make the **TTP** molecule nonplanar and reduce the aromatic stability. Furthermore, the molecular orbitals of the lone pairs of the inner nitrogen atoms were calculated to be close to each other at the HOMO level. This structure is unstable owing to the electronic repulsion of the lone pairs,[17] and as a result, **TTP** is unstable and highly reactive toward nucleophilic addition at the *meso* position. In contrast, macrocycles **7a–c** and **8** have a hydrogen bond between the inner nitrogen atoms, as indicated by the N–N distance and the orientation of the two pyrrole rings toward one another. This hydrogen bond is very important in the stabilization of these compounds (see Scheme S1 in the Supporting Information).

The structure of **7a** was characterized by ^{1}H NMR spectroscopy, high-resolution electrospray ionization time-of-flight (HR ESI-TOF) mass spectrometry, and X-ray crystal-structure analysis. The HR ESI-TOF mass spectrum of **7a** displays the parent-ion peak at m/z 489.1995 $[M+H]^+$ (calcd for $C_{32}H_{29}N_2OS$: 489.1922). The signals due to the thienyl hydrogen atoms in the ^{1}H NMR spectrum of **7a** were evident as two doublets at $\delta = 7.52$ and 6.95 ppm, and those of the pyrrole hydrogen atoms appeared around $\delta = 6.84$–6.02 ppm (Figure 2a). The signal for the inner NH hydrogen atom was observed at $\delta = 12.69$ ppm owing to hydrogen

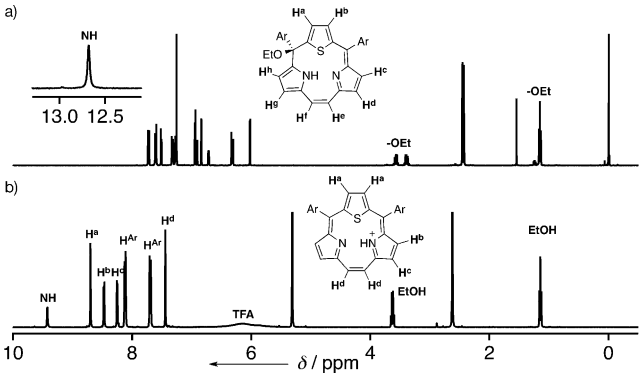

Figure 2. ^{1}H NMR spectra of **7a** a) in $CDCl_3$ without TFA and b) in CD_2Cl_2 with TFA (2.2 equiv) at −40 °C.

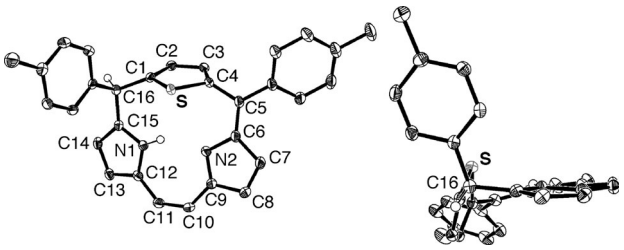

Figure 1. Crystal structure of **8**. Left: top view (hydrogen atoms except for N–H and C16–H are omitted for clarity); right: side view (hydrogen atoms except for C16–H are omitted for clarity). Thermal ellipsoids represent 50% probability.

bonding with the neighboring nitrogen atom. These data suggest that **7a** has no continuous conjugation around the three heterocyclic rings in its core structure. Single crystals of **7a** suitable for X-ray diffraction analysis were obtained by the slow evaporation of a solution in ethanol (Figure 3). 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 the structure of an imine (C9–N1: 1.320 Å), whereas the other has an amine structure (C12–N2: 1.409 Å); this observation suggests a hydrogen-bonding interaction between the two inner nitrogen atoms. The thiophene ring is significantly tilted out of the plane of

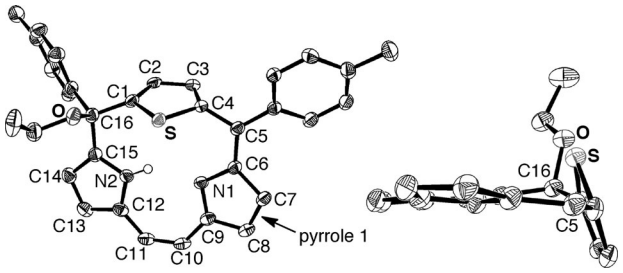

Figure 3. Crystal structure of **7a**. Left: top view (hydrogen atoms except for N–H are omitted for clarity); right: side view (hydrogen atoms and aryl groups are omitted for clarity). Thermal ellipsoids represent 50% probability.

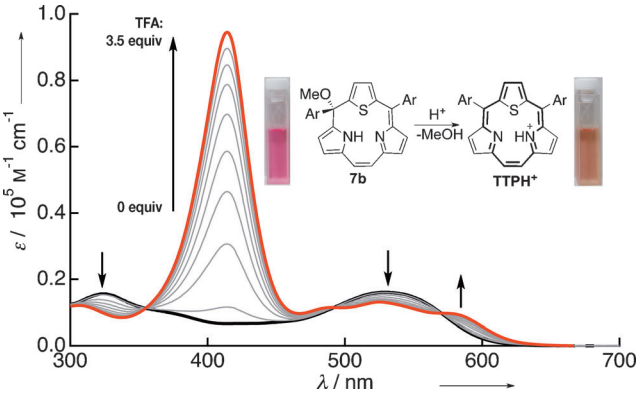

Figure 4. Changes in the absorption spectrum of **7b** in CH_2Cl_2 with increasing amounts of TFA (0.0, 0.2, 0.4, 0.6, 0.8, 1.0, 1.2, 1.4, 1.8, 3.5 equiv). Black line: 0 equivalents of TFA; red line: 3.5 equivalents of TFA.

the macrocycle, with a dihedral angle between the thiophene ring and pyrrole 1 (see Figure 3) of 69.53°.

During thermogravimetric analysis, **7b** exhibited an 8% mass loss at 162 °C (see 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. The heating of **7b** in a glass tube oven at 200 °C, however, produced only insoluble material rather than **TTP**. Interestingly, when a solution of **7b** in ethanol was heated at reflux for 12 h, **7a** was obtained in quantitative yield. When we attempted to obtain a single crystal of the structural isomer **7b-II** from a solution in CH_2Cl_2/methanol, only **7b** was obtained. These results indicate that methanol was removed to give **TTP** as an intermediate, but that the **TTP** reacted with methanol immediately on account of its instability to revert back to the substituted compound. According to DFT calculations at the B3LYP/6-31G** level, the total energy of **7a** is lower than that of its isomer **7a-II** (see Figure S3).

The elimination of methoxy groups under acidic conditions has been observed for subpyriporphyrins,[13a] an N-fused porphyrin–boron complex,[18] dithiaethyneporphyrin,[19] and a homoporphyrin–nickel complex.[20] We therefore checked the reactivity of **7b** for the production of protonated **TTP** (**TTPH**$^+$) under acidic conditions. The absorption spectrum of **7b** showed two broad bands at 325 and 530 nm (see Figure S4). Upon the addition of trifluoroacetic acid (TFA) to a solution of **7b** in CH_2Cl_2, the absorption spectrum changed according to the number of equivalents of TFA added, with isosbestic points at 355, 492, and 570 nm (Figure 4). The broad band at 530 nm decreased simultaneously with the increase in the Soret-like band at 414 nm and the Q-like bands at 490, 525, and 574 nm. After the addition of 3.5 equivalents of 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, the treatment of **TTPH**$^+$ with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in the presence of methanol in CH_2Cl_2 regenerated **7b** (see Figure S5). We also acquired the ^{1}H NMR spectrum of **TTPH**$^+$ formed from a mixture of **7a** and TFA (2.2 equiv) in CD_2Cl_2 at −40 °C (Figure 2b; see also Figure S6). A singlet peak corresponding to the thiophene moiety was observed at $\delta = 8.70$ ppm, and another due to the hydrogen atoms on the ethenyl bridge was observed at $\delta = 7.44$ ppm. The pyrrole signals were shifted downfield relative to those for **7a**. The NH signal was observed at $\delta = 9.42$ ppm, and was thus shifted upfield relative to that for **7a**. It disappeared upon the addition of D_2O (see Figure S6). In the H–H COSY spectrum, cross-peaks between the NH and pyrrolic signals were observed (see Figure S7). The chemical shifts of these hydrogen atoms reflect a diatropic ring current associated with the **TTPH**$^+$ macrocycle.

A single crystal of **TTPH**$^+$**[(CF$_3$COO)$_2$H]**$^-$ was obtained from a mixture of toluene, TFA, and water (Figure 5; see also Figure S9). The thiophene ring is again tilted out of the plane

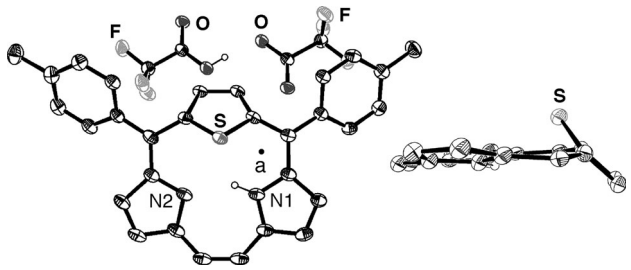

Figure 5. Crystal structure of **TTPH**$^+$**[(CF$_3$COO)$_2$H]**$^-$. Left: top view (hydrogen atoms except for N–H and solvent molecules are omitted for clarity); right: side view (hydrogen atoms, aryl groups, and solvent molecules are omitted for clarity). Thermal ellipsoids represent 30% probability.

of the macrocycle; the dihedral angles between the thiophene ring and the neighboring pyrrole rings are 50.28 and 48.61°, both of which are smaller than in **7a**. The lengths of the bonds between the *meso* carbon atoms and the α carbon atoms in the pyrrole and thiophene rings 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 that there is no bond alternation; the bonds are slightly longer than those of previously reported 14π-electron aromatic triphyrins.[8–10] We also estimated the nucleus-independent chemical shift (NICS(0)) values[21] of **TTPH**$^+$ at several points within the molecular plane on the basis of an optimized structure from

the X-ray diffraction data (see Figure S10). The NICS(0) value of **TTPH**$^+$ at point "a" in Figure 5 is $\delta = -11.37$ ppm, which indicates moderate aromaticity. Taken together, the changes in the UV and ^{1}H NMR spectra upon the addition of acid, the single-crystal X-ray analysis data, and the NICS(0) values suggest that the protonated compound **TTPH**$^+$ has a distinct 14π-electron aromatic structure.

When **8** was treated with TFA in CH_2Cl_2, a gradual decrease in the absorption band at 558 nm was accompanied by an increase in an absorption band at 640 nm (see Scheme S11). These results indicate that protonation of the second nitrogen atom (N2) occurred to generate **8H**$^+$. It thus appears that the alkoxy leaving groups play an important role during the conversion of **7a**, **7b**, or **7c** into **TTPH**$^+$ in the presence of an acid.

In summary, we have synthesized several alkoxy-group-substituted thiatriphyrins. Under acidic conditions, these compounds can be converted into protonated **TTPH**$^+$, which shows moderate aromaticity. **TTPH**$^+$ is the first reported example of the generation of aromaticity in a core-modified contracted porphyrin upon the protonation of its free-base form. It was also determined that these alkoxy-substituted thiatriphyrins have a stereogenic C16 center and a NNS coordination site. The results of studies concerning the control of the chirality and coordination abilities of these compounds will be reported in the near future.

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[1] a) A. Meller, A. Ossko, *Monatsh. Chem.* **1972**, *103*, 150 – 155; b) C. G. Claessens, D. González-Rodríguez, T. Torres, *Chem. Rev.* **2002**, *102*, 835 – 853.

[2] a) Y. Inokuma, J. H. Kwon, T. K. Ahn, M.-C. Yoo, D. Kim, A. Osuka, *Angew. Chem.* **2006**, *118*, 975 – 978; *Angew. Chem. Int. Ed.* **2006**, *45*, 961 – 964; b) Y. Inokuma, Z. S. Yoon, D. Kim, A. Osuka, *J. Am. Chem. Soc.* **2007**, *129*, 4747 – 4761; c) Y. Inokuma, A. Osuka, *Dalton Trans.* **2008**, 2517 – 2526; d) A. Osuka, E. Tsurumaki, T. Tanaka, *Bull. Chem. Soc. Jpn.* **2011**, *84*, 679 – 697.

[3] N. Kobayashi, Y. Takeuchi, A. Matsuda, *Angew. Chem.* **2007**, *119*, 772 – 774; *Angew. Chem. Int. Ed.* **2007**, *46*, 758 – 760.

[4] a) B. del Rey, U. Keller, T. Torres, G. Rojo, F. Agulló-López, S. Nonell, C. Martí, S. Brasselet, I. Ledoux, J. Zyss, *J. Am. Chem. Soc.* **1998**, *120*, 12808 – 12817; b) E. Tsurumaki, Y. Inokuma, S. Easwaramoorthi, J. M. Lim, D. Kim, A. Osuka, *Chem. Eur. J.* **2009**, *15*, 237 – 247; c) S. Easwaramoorthi, J.-Y. Shin, S. Cho, P. Kim, Y. Inokuma, E. Tsurumaki, A. Osuka, D. Kim, *Chem. Eur. J.* **2009**, *15*, 12005 – 12017.

[5] a) Y. Inokuma, S. Easwaramoorthi, S. Y. Jang, K. S. Kim, D. Kim, A. Osuka, *Angew. Chem.* **2008**, *120*, 4918 – 4921; *Angew. Chem. Int. Ed.* **2008**, *47*, 4840 – 4843.

[6] a) Y.-H. Chen, J.-H. Chang, G.-R. Lee, I.-W. Wu, J.-H. Fang, C.-I. Wu, T.-W. Pi, *Appl. Phys. Lett.* **2009**, *95*, 133302; b) G. E. Morse, M. G. Helander, J. F. Maka, Z.-H. Lu, T. P. Bender, *ACS Appl. Mater. Interfaces* **2010**, *2*, 1934 – 1944.

[7] a) K. L. Mutolo, E. I. Mayo, B. P. Rand, S. R. Forrest, M. E. Thompson, *J. Am. Chem. Soc.* **2006**, *128*, 8108 – 8109; b) N. Beaumont, S. W. Cho, P. Sullivan, D. Newby, K. E. Smith, T. S. Jones, *Adv. Funct. Mater.* **2012**, *22*, 561 – 566.

[8] a) Z.-L. Xue, Z. Shen, J. Mack, D. Kuzuhara, H. Yamada, T. Okujima, N. Ono, X.-Z. You, N. Kobayashi, *J. Am. Chem. Soc.* **2008**, *130*, 16478 – 16479; b) Z.-L. Xue, J. Mack, H. Lu, L. Zhang, X.-Z. You, D. Kuzuhara, M. Stillman, H. Yamada, S. Yamauchi, N. Kobayashi, Z. Shen, *Chem. Eur. J.* **2011**, *17*, 4396 – 4407.

[9] D. Kuzuhara, H. Yamada, Z.-L. Xue, T. Okujima, S. Mori, Z. Shen, H. Uno, *Chem. Commun.* **2011**, *47*, 722 – 724.

[10] K. S. Anju, S. Ramakrishnan, A. Srinivasan, *Org. Lett.* **2011**, *13*, 2498 – 2501.

[11] L. Latos-Grażyński in *The Porphyrin Handbook*, *Vol. 2* (Eds.: K. M. Kadish, K. M. Smith, R. Guilard), Academic Press, San Diego, **2000**, pp. 361 – 416.

[12] P. J. Chmielewski, L. Latos-Grażyński, *Coord. Chem. Rev.* **2005**, *249*, 2510 – 2533.

[13] a) R. Myśliborski, L. Latos-Grażyński, L. Szterenberg, T. Lis, *Angew. Chem.* **2006**, *118*, 3752 – 3756; *Angew. Chem. Int. Ed.* **2006**, *45*, 3670 – 3674; b) K. S. Kim, J. M. Lim, R. Myśliborski, M. Pawlicki, L. Latos-Grażyński, D. Kim, *J. Phys. Chem. Lett.* **2011**, *2*, 477 – 481.

[14] C. H. Lee, K. T. Oh, *Tetrahedron Lett.* **1999**, *40*, 1921 – 1924.

[15] CCDC 912982 (**8**), 912983 (**6a**), and 912984 (**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.

[16] Gaussian 09, M. Frisch, et al., Gaussian, Inc. Wallingford CT, **2009**.

[17] K. A. Brameld, B. Kuhn, D. C. Reuter, M. Stahl, *J. Chem. Inf. Model.* **2008**, *48*, 1 – 24.

[18] A. Młodzianowska, L. Latos-Grażyński, L. Szterenberg, M. Stępień, *Inorg. Chem.* **2007**, *46*, 6950 – 6957.

[19] a) A. Berlicka, L. Latos-Grażyński, T. Lis, *Angew. Chem.* **2005**, *117*, 5422 – 5425; *Angew. Chem. Int. Ed.* **2005**, *44*, 5288 – 5291; b) E. Nojman, A. Berlicka, L. Szterenberg, L. Latos-Grażyński, *Inorg. Chem.* **2012**, *51*, 3247 – 3260.

[20] H. J. Callot, E. Schaeffer, *J. Org. Chem.* **1977**, *42*, 1567 – 1570.

[21] P. R. Schleyer, C. Maerker, A. Dransfeld, H. Jiao, N. J. R. E. Hommes, *J. Am. Chem. Soc.* **1996**, *118*, 6317 – 6318.

