Aromaticity

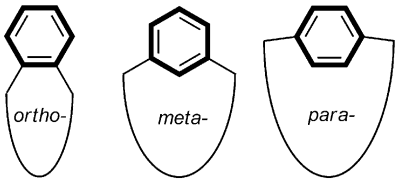
DOI: 10.1002/anie.201410595

Oxatriphyrins(2.1.1) Incorporating an *ortho*-Phenylene Motif**

Miłosz Pawlicki, Mateusz Garbicz, Ludmiła Szterenberg, and Lechosław Latos-Grażyński**

Abstract: *An understanding of fundamental aspects of archetypal organic structural motifs remains a key issue faced by the experimental and theoretical chemists. Two possible bonding modes for a disubstituted benzene ring, that is a meta and para, determines the π delocalization for oligomeric structures. When the less abundant ortho-substituted variant is introduced into a triphyrin(2.1.1) skeleton an aromatic molecule is obtained and the carbocyclic ring participates in the conjugation of the macrocycle. The two-electron reduction and introduction of boron(III) changes the aromatic character and results in an anti-aromatic structure which has been confirmed by single-crystal analysis and supported by theoretical calculations.*

Benzene, as an integral part of macrocyclic motifs brings to the light new aspects of carbocyclic reactivity enforced by the environment and type of substitution.[1] The bonding arrangement (Scheme 1) determines the properties of the target

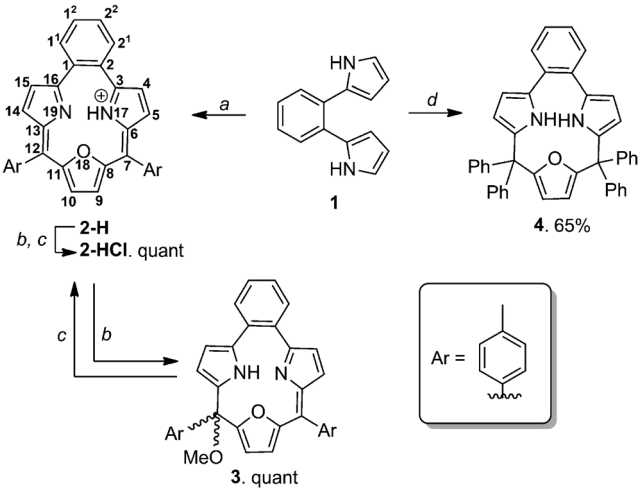


Scheme 1. Bonding modes for incorporation of benzene into macrocyclic loops.

molecules, noticeably distinguishing between the *ortho*-, *meta*-, and *para*-phenylenes incorporated into either a macrocycle[1c] or oligophenylene.[2]

In porphyrinoids the orientation of benzene modifies the conjugation, thus eventually determining the macrocyclic aromaticity. While the *para* isomer can be illustrated as an aromatic macrocycle,[3] the *meta* variant is mostly described as an example wherein *m*-phenyl blocks effective macrocyclic delocalization.[4] However, there are some exceptions documented for protonated structures.[5] The *ortho*-phenylene is rarely represented in porphyrinoids and reported for aromatic porphycenes[6] and texaphyrins,[7] as well as for non-aromatic calixpyrroles,[8] but it can potentially lead to a fully aromatic macrocyclic architecture and still remains an unexplored aspect of porphyrinoid reactivity.

Herein we present oxatriphyrins(2.1.1) with an *ortho*-phenylene motif serving as a C_2 meso-bridge. The initial step in formation of the desired structures requires the synthesis of **1** (Scheme 2) wherein a benzene ring is incorporated. By



Scheme 2. Formation of *ortho*-phenylene oxatriphyrins(2.1.1). Reaction conditions: a) 2,5-bis(hydroxymethyltolyl)furan, CH_2Cl_2, inert atmosphere, $BF_3{\cdot}Et_2O$, DDQ; b) MeOH/Et_3N (1:1); c) CH_2Cl_2, HCl; d) 2,5-bis(hydroxydiphenylmethyl)furan, CH_2Cl_2, inert atmosphere, $BF_3{\cdot}Et_2O$.

using the palladium-catalyzed Suzuki coupling for 1,2-dibromobenzene and N-Boc-pyrrol-2-yl-boronic acid,[9] followed by deprotection, **1** was obtained in 68% yield. The condensation of **1** with 2,5-bis(hydroxymethyltolyl)furan in equimolar ratio (Scheme 1) followed by oxidation with dichlorodicyano-*p*-quinone gave the oxatriphyrin(2.1.1) **2**-H, which was isolated solely in the monocationic form. The counterion, was identified as a dichlorodicyano-hydroquinone anion and replaced with a chloride by quantitative transformation into phlorin (**3**) followed by acidic removal of the methoxy substituent (Scheme 2), and finally giving **2**-HCl in 20% yield. The remarkable affinity of **2** toward protons reveals the structural suitability of the porphyrinoid core for formation of an intramolecular hydrogen bond. The behavior resembles that of other triphyrins(*n*.1.1).[10]

To explore the wider applicability of the presented synthetic approach, the calix-triphyrin **4** was synthesized and used here as an appropriate reference point to analyze

[*] Dr. M. Pawlicki, M. Garbicz, Dr. L. Szterenberg, Prof. L. Latos-Grażyński
Department of Chemistry, University of Wrocław
F. Joliot-Curie 14, 50383 Wrocław (Poland)
E-mail: milosz.pawlicki@chem.uni.wroc.pl
lechoslaw.latos-grazynski@chem.uni.wroc.pl
Homepage: http://llg.chem.uni.wroc.pl/

[**] Financial support from the Ministry of Science and Higher Education (Grant N N204 021939) and the National Science Centre (2012/04/A/ST5/00593) is kindly acknowledged. The DFT calculations were carried out at the Poznań Supercomputing Centre.

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201410595.

macrocyclic conjugation. The synthetic approach involves the same strategy as that applied for **2**-H, but using 2,5-bis(hydroxydiphenylmethyl)furan (Scheme 1). All synthetic steps are effective and lead to isolation of the desired macrocycles in good yields.

Based on the different structures one can expect drastically dissimilar electronic properties for all three of the oxatriphyrins(2.1.1) **2**-HCl, **3**, and **4.** **2**-HCl shows an aromatic character with downfield-shifted resonances for the perimeter hydrogen atoms. The ^{1}H NMR spectrum of **2**-H suggests a significant involvement of the carbocyclic fragment in π-delocalization of the macrocyclic as the AA′BB′ spin system characteristic for *ortho* benzene is shifted downfield [$\delta =$ 9.68 ppm (H1^1, H2^1) and 8.35 ppm (H1^2, H2^2)] (Figure 1 A) relative to the resonances for the non-aromatic **3** and **4** (Figure 1 B,C). A similar trend was previously reported for

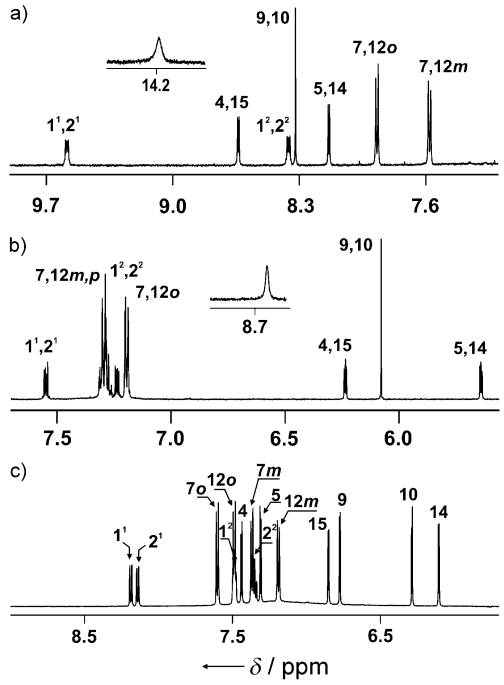


Figure 1. ^{1}H NMR spectra for a) **2**-HCl (MeOD, 300 K; inset presents NH group observed in $CDCl_3$), b) **4** (CD_2Cl_2, 300 K), and c) **3** (CD_2Cl_2, 300 K). The peak assignments follow the numbering scheme presented in Scheme 1.

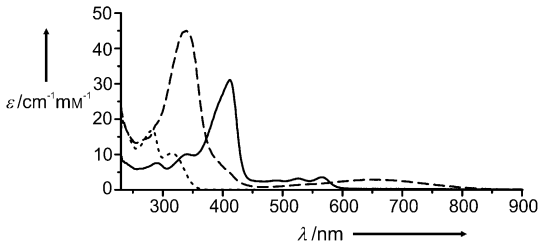
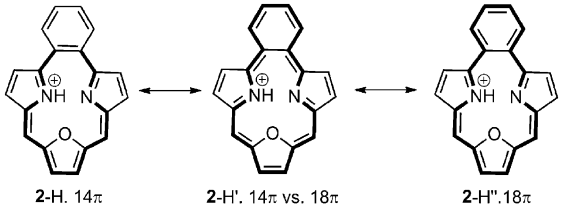


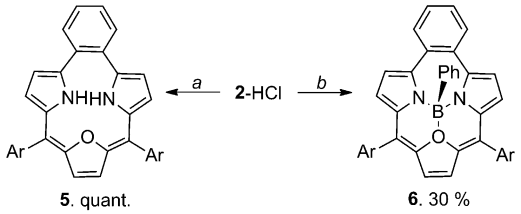
Figure 2. Absorption spectra for **2**-HCl (solid line), **4** (dotted line), and **6** (dashed line). All experiments performed in CH_2Cl_2 at 298 K.



Scheme 3. 14 π versus 18 π delocalization in **2**-H.

typical shape of 14 π triphyrins(2.1.1),[10c] but approaches the situation observed for thiophene-fused triphyrins(2.1.1).[9] The electronic spectrum for **4** reflects a complete blockage of the macrocyclic conjugation as the absorbance does not exceed $\lambda = 350$ nm.

The reduction of **2**-HCl with a zinc amalgam in an inert atmosphere (Scheme 4) affords **5**, the form which can be potentially described as an anti-aromatic compound with 16 π/20 π electron delocalization path. All β-resonances of **5** are similar to those of the non-aromatic **1** and **4**. Nevertheless the most informative structural fragment is the AA′BB′ spin



Scheme 4. Reactivity of **2**-HCl. Reaction conditions: a) Zn/Hg, $CDCl_3$, inert atmosphere; b) toluene (reflux), Et_3N, $PhBCl_2$, inert atmosphere.

ortho-phenylene incorporated into the porphycene skeleton.[6a] The β-hydrogen atoms of pyrroles and furan resonate at $\delta = 8.80$ ppm (H4, H15), 8.45 ppm (H9, H10), and 8.28 ppm (H5, H14) and are consistent with the aromaticity of **2**-HCl. A strongly downfield-shifted NH proton ($\delta \sim 14.2$ ppm) has a significant influence on the internal hydrogen bond which overshadows the upfield ring current contribution. Such an effect is typical for triphyrins(*n*.1.1).[9,10]

The electronic spectrum of **2**-H is consistent with the NMR-derived conclusions. An intense Soret-like band is accompanied by a set of Q-bands (Figure 2). The observed pattern suggests a contribution of both available delocalization paths (14 π/18 π; Scheme 3) as it does not present the system, of the *ortho*-phenylene, located at $\delta = 7.05$ ppm (H1^1, H2^1) and 6.80 ppm (H1^2, H2^2), which are shifted slightly upfield (by ca. 0.5 ppm) compared to those of **4** (Figure 1). Evidently a different spectroscopic picture was observed for the boron(III) complex of **5**, that is, **6** (Scheme 3) which was obtained by reaction of **2**-H with $PhBCl_2$ in the presence of Et_3N and using the procedure reported for thiophene-fused oxatriphyrins(2.1.1)[9] and for furan fused oxatriphyrin-(3.1.1).[12]

The insertion of boron(III) results in systematic upfield relocation of the β-hydrogen resonances of the pyrroles [$\delta =$ 5.84 ppm (H4, H15) and 5.61 ppm (H5, H14)] and furan [$\delta =$ 5.23 ppm (H9, H10); Figure 3 B]. Also the *ortho*-phenylene

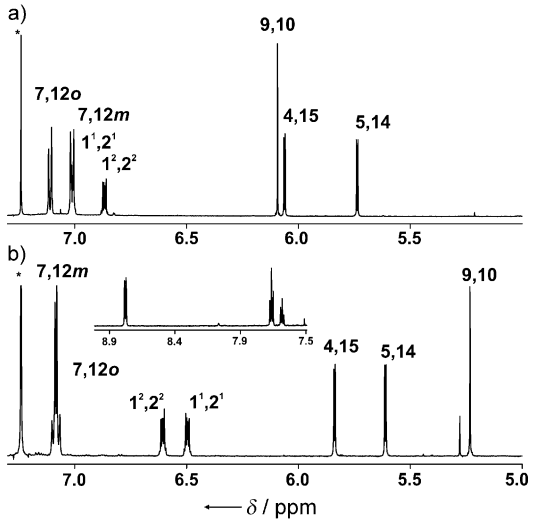


Figure 3. ^{1}H NMR ($CDCl_3$, 300 K, 600 MHz) spectra for a) **5** and b) **6** (inset presents the axial σ-phenyl resonances).

resonances move significantly upfield (ca. 1 ppm with respect to **4**) to $\delta = 6.61$ ppm ($H1^2$, $H2^2$) and 6.49 ppm ($H1^1$, $H2^1$). Significantly the paratropicity of **6** is reflected by a marked downfield relocation of the axially coordinated σ-phenyl (*o*-Ph: $\delta = 8.78$ ppm, *m*-Ph: $\delta = 7.66$ ppm, and *p*-Ph: $\delta = 7.58$ ppm).[9,11,12] The electronic properties recorded for **6** (Figure 2) resemble the picture characteristic of anti-aromatic delocalization in triphyrins,[9] tetraphyrins,[14] and expanded porphyrins.[15]

2-H crystalizes as a cation with a dichlorodicyano-hydroquinone dianion as the counteranion with an NH hydrogen atom entrapped within the macrocycle (Figure 4). Oxatriphyrin(2.1.1) presents a planar structure with hydrogen firmly held between two nitrogen atoms, thus confirming the hydrogen bond responsible for a downfield shift of the NH

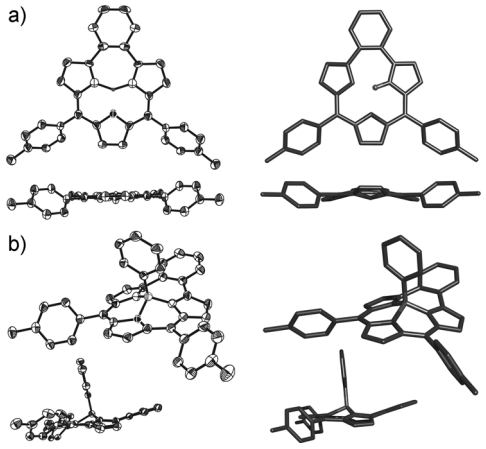


Figure 4. X-Ray structures[20] (left) and DFT models (right) for a) **2**-H and b) **6**. Thermal ellipsoids in crystal structures present at 50% probability. The NH hydrogen atoms in (A) are arbitrarily located. In the crystal structures oxygen atoms are presented as spheres with black filling, nitrogen atoms are presented as white spheres, and the central atoms (hydrogen for **2**-H and boron for **6**) are presented in gray.

proton in the ^{1}H NMR spectrum.[9,10a,11a,13] The N–N and N–O distances (2.550 Å and 2.490 Å, respectively) locate this hydrogen bond in the region of strong interaction which is characteristic of triphyrins,[9,10a,b,11a,13] but it is observed for a cavity introducing a new type of environment for a three-centered hydrogen bond which has not been reported before for triphyrins(2.1.1). The coordination of boron(III) distorts the planarity observed for **2**-H. The central boron(III) cation is displaced from the macrocyclic plane (defined by C3, C7, C12 and C16) by 0.7 Å, confirming the presence of a small cavity for this oxatriphyrin(2.1.1), which is similar to nitrogen analogues.[11b]

A careful analysis of bond lengths within the tri-heterocyclic portion of **2**-H and **6** (pyrrole-furan-pyrrole) clearly reflects the differences in electronic structure. The bond lengths of the furan fragment (C7–C8 1.432(7), C8–C9 1.389(7), C8–O 1.369(7), and C9–C10 1.382(10) Å) in **2**-H equalize, thus showing a delocalization, as compared to a free furan,[16] which is expected for macrocyclic aromaticity. Analogous bonds in **6** alternate (C7–C8 1.355(4), C8–C9 1.422(3), C9–C10 1.354(4), C10–C11 1.416(3) and C11–C12 1.355(4), C8–O 1.440(4), C11–O 1.431(4) Å) but in a fashion opposite to that of the free furan, thus reflecting the anti-aromatic features of **6**. Similar changes are observed for pyrroles linked directly to the benzene ring. The bonds between the benzene and pyrroles (C1–C16 1.470(7) for **2**-H and C1–C16 1.477(3) and C2–C3 1.475(3) Å for **6**) approach the distance of an $C(sp^2)$–$C(sp^2)$ bond (C(*meso*)–C(ipso): 1.485(7) Å for **2**-H and 1.480(3) Å for **6**), thus suggesting isolation of a benzene fragment from the rest of the macrocycle. Nevertheless the spectroscopically documented merging of benzene with the macrocyclic conjugation is supported by the bond lengths observed for the *ortho*-benzene fragment (from 1.386(11) to 1.420(10) for **2**-H and from 1.368(4) to 1.424(4) Å for **6**; see the Supporting Information), thus showing a significant difference when compared to the *meta* variant (1.378(2) to 1.399(2) Å) where isolation of the benzene ring from a macrocyclic conjugation has been documented.[4b,17] The data is similar to that of the *para* system (1.365(2) to 1.411(2) Å) which is shown to be part of the conjugated system.[3]

The DFT-optimized geometries of oxatriphyrins(2.1.1) (Figure 4; see the Supporting Information) present similar bond lengths and geometries as those observed for the crystal structures. The NICS (nucleus independent chemical shifts)[18] values calculated for the middle of macrocyclic plane for all four compounds [$\delta = -8.7$ ppm (**2**-H), -1.4 ppm (**4**), $+3.7$ ppm (**5**), and $+8.4$ ppm (**6**), NICS(0)] are consistent with ^{1}H NMR features. The NICS(0) values at the center of the *ortho*-phenylene ring [$\delta = -13.7$ ppm (**2**-H), -8.7 ppm (**4**), -5.5 ppm (**5**), and -3.3 ppm (**6**)] demonstrate a visible influence of the macrocycle on the properties of the carbocyclic unit.[18] The N17–N19, N17–O18, and N19–O18 distances (2.566 Å, 2.564 Å, and 2.566 Å, respectively) within the cavity of the theoretical models optimized for **2**-H are comparable with those observed for the crystal structures, thus supporting the origins of a strong hydrogen bond. The Wiberg indices[19] calculated in **2**-H (N17–H 0.5663, N19–H 0.1631, O18–H 0.0096) confirm a strong interaction within the

coordination cavity and a strong hydrogen bond observed for the N-O-N group within involving the neighboring oxygen atom.

In conclusion the skeleton of oxatriphyrin(2.1.1) has been significantly modified by integrating an *ortho*-phenylene fragment which merges with the macrocyclic π system. The molecule reveals either an aromatic or anti-aromatic macrocyclic π delocalization which is consistent with a significant contribution of either the corresponding 18π or 20π electronic system. Additionally a strong, three-centered hydrogen bond has been documented for the N-O-N surrounding.

Received: October 30, 2014
Published online: December 21, 2014

Keywords: aromaticity · boron · density functional calculations · macrocycles · structure elucidation

[1] a) B. Szyszko, L. Latos-Grażyński, L. Szterenberg, *Angew. Chem. Int. Ed.* **2011**, *50*, 6587 – 6591; *Angew. Chem.* **2011**, *123*, 6717 – 6721; b) B. Szyszko, K. Kupietz, L. Szterenberg, L. Latos-Grażyński, *Chem. Eur. J.* **2014**, *20*, 1376 – 1382; c) M. Stępień, L. Latos-Grażyński, *Acc. Chem. Res.* **2005**, *38*, 88 – 98.

[2] a) S. M. Mathew, C. S. Hartley, *Macromolecules* **2011**, *44*, 8425 – 8432; b) C. S. Hartley, *J. Org. Chem.* **2011**, *76*, 9188 – 9191; c) K. Matsuda, M. T. Stone, J. S. Moore, *J. Am. Chem. Soc.* **2002**, *124*, 11836 – 11837.

[3] M. Stępień, L. Latos-Grażyński, *J. Am. Chem. Soc.* **2002**, *124*, 3838 – 3839.

[4] a) K. Berlin, E. Breimaier, *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 1246 – 1247; *Angew. Chem.* **1994**, *106*, 1356 – 1357; b) M. Stępień, L. Latos-Grażyński, *Chem. Eur. J.* **2001**, *7*, 5113 – 5117.

[5] a) J. T. Szymanski, T. D. Lash, *Tetrahedron Lett.* **2003**, *44*, 8613 – 8616; b) T. D. Lash, J. T. Szymanski, G. M. Ferrence, *J. Org. Chem.* **2007**, *72*, 6481 – 6492.

[6] a) F. D'Souza, P. L. Boulas, M. Kisters, L. Sambrotta, A. M. Aukauloo, R. Guilard, K. M. Kadish, *Inorg. Chem.* **1996**, *35*, 5743 – 5746; b) W.-M. Dai, W. L. Mak, *Tetrahedron Lett.* **2000**, *41*, 10277 – 10280.

[7] J. L. Sessler, G. Hemmi, T. D. Mody, T. Murai, A. Burrell, S. W. Young, *Acc. Chem. Res.* **1994**, *27*, 43 – 50.

[8] B. Chandra, S. P. Mahanta, N. N. Pati, S. Baskaran, R. K. Kanaparthi, Ch. Sivasankar, P. K. Panda, *Org. Lett.* **2013**, *15*, 306 – 309.

[9] M. Pawlicki, K. Hurej, L. Szterenberg, L. Latos-Grażyński, *Angew. Chem. Int. Ed.* **2014**, *53*, 2992 – 2996; *Angew. Chem.* **2014**, *126*, 3036 – 3040.

[10] 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) K. S. Anju, S. Ramakrishnan, A. Srinivasan, *Org. Lett.* **2011**, *13*, 2498 – 2501; c) D. Kuzuhara, Y. Sakakibara, S. Mori, T. Okujima, H. Uno, H. Yamada, *Angew. Chem. Int. Ed.* **2013**, *52*, 3360 – 3363; *Angew. Chem.* **2013**, *125*, 3444 – 3447; d) A. Krivokapic, A. R. Cowley, H. L. Anderson, *J. Org. Chem.* **2003**, *68*, 1089 – 1096; e) M. Pawlicki, L. Latos-Grażyński, L. Szterenberg, *J. Org. Chem.* **2002**, *67*, 5644 – 5653; f) M. Pawlicki, D. Bykowski, L. Szterenberg, L. Latos-Grażyński, *Angew. Chem. Int. Ed.* **2012**, *51*, 2500 – 2504; *Angew. Chem.* **2012**, *124*, 2550 – 2554.

[11] a) R. Myśliborski, L. Latos-Grażyński, L. Szterenberg, T. Lis, *Angew. Chem. Int. Ed.* **2006**, *45*, 3670 – 3674; *Angew. Chem.* **2006**, *118*, 3752 – 3756; b) D. Kuzuhara, Z. L. Xue, S. Mori, T. Okujima, H. Uno, N. Aratani, H. Yamada, *Chem. Commun.* **2013**, *49*, 8955 – 8957.

[12] M. Pawlicki, A. Kędzia, D. Bykowski, L. Latos-Grażyński, *Chem. Eur. J.* **2014**, *20*, 17500 – 17506.

[13] a) H. Furuta, T. Ishizuka, A. Osuka, T. Ogawa, *J. Am. Chem. Soc.* **1999**, *121*, 2945 – 2946; b) H. Furuta, H. Maeda, A. Osuka, *J. Am. Chem. Soc.* **2001**, *123*, 6435 – 6436.

[14] a) J. A. Cissell, T. P. Vaid, G. P. A. Yap, *Org. Lett.* **2006**, *8*, 2401 – 2404; b) T. Kakui, S. Sugawara, Y. Hirata, S. Kojima, Y. Yamamoto, *Chem. Eur. J.* **2011**, *17*, 7768 – 7771.

[15] S. Cho, Z. S. Yoon, K. S. Kim, M.-C. Yoon, D.-G. Cho, J. L. Sessler, D. Kim, *J. Phys. Chem. Lett.* **2010**, *1*, 895 – 900.

[16] a) A. R. Katrizky, A. F. Pozharskii, *Handbook of Heterocyclic Chemistry*, 2nd ed., Elsevier Pergamon, Oxford, **2000**; b) J. A. Joule, K. Mills, *Heterocyclic Chemistry*, 5th ed., Wiley-Blackwell, Oxford, **2010**.

[17] E.-K. Sim, S.-D. Jeong, D.-W. Yoon, S.-J. Hong, Y. Kang, Ch.-H. Lee, *Org. Lett.* **2006**, *8*, 3355 – 3358.

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

[19] K. B. Wiberg, *Tetrahedron* **1968**, *24*, 1083 – 1096.

[20] Low-temperature (100 K) single-crystal diffraction data were collected on Nonius Kappa CCD diffractometer. Data were solved and refined with the SHELXS-97. Crystallographic data (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre [CCDC 1031417 (**2**-H) and 1031416 (**6**)] which 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. Single crystal X-ray diffraction data for **2**-H: $C_{34}H_{27}N_2O{\cdot}C_8N_2Cl_2$, $M_r = 707.40$, orthorhombic (*Pnma*), $a = 31.185(2)$ Å, $b = 30.231(2)$ Å, $c = 3.8539(4)$ Å, $\alpha = \beta = \gamma = 90.00°$, $V = 3633.2(5)$ Å^3, $Z = 4$, $\mu = 1.761$ mm^{-1}, $D_c = 1.293$ Mg m^{-3}, T = 100(2) K, 2956 independent reflections, $R_1 = 0.0736$, $wR_2 = 0.1997$ [$I > 2\sigma(I)$], $S = 0.807$; Single crystal X-ray diffraction data for **6**: $C_{40}H_{29}BN_2O$, $M_r = 564.46$, monoclinic ($P2_1/c$), $a = 7.8597(4)$ Å, $b = 22.9416(9)$ Å, $c = 16.5956(6)$ Å, $\alpha = 90.00°$, $\beta = 102.210(4)°$, $\gamma = 90.00°$, $V = 2924.7(2)$ Å^3, $Z = 4$, $\mu = 0.589$ mm^{-1}, $D_c = 1.282$ Mg m^{-3}, $T = 100(2)$ K, 6184 independent reflections, $R_1 = 0.0907$, $wR_2 = 0.2371$ [$I > 2\sigma(I)$], $S = 0.981$.

