Rearrangements

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From 21,23-Dioxaporphyrin to a 3-Pyranone Dioxacorrole Skeleton: The Achmatowicz Rearrangement in the Porphyrin Frame**

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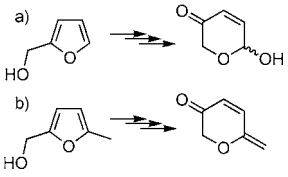
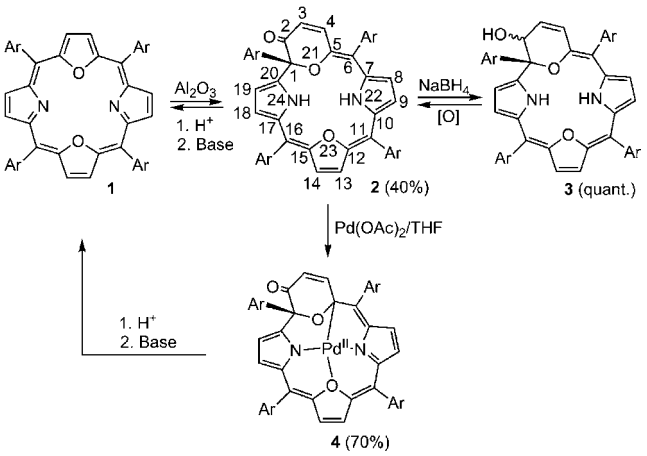
Solid-supported organic reactions are an important aspect of current research as they cover broadly defined environment-concerned reactions applicable to obtain a wide scope of valuable molecules.[1] In this field aluminium oxide is a significant carrier and supporting material for several oxidative and catalytic processes.[2] A pivotal aspect of organic reactions often observed is the reactivity of furan rings as this heterocycle plays a special role in the extensively surveyed areas of natural product synthesis,[3] the creation of combinatorial libraries of potential therapeutics,[4,5] or molecular electronic applications (formation of extended π systems).[6] Furan with different functions can be obtained by heterocyclic modifications starting from the classical aromatic electrophilic substitution,[7] through oxidative processes leading to other heterocycles (O→N, S, Se exchange),[8] and ending at building blocks of large structures. The oxidative processes with formation of open dicarbonyl structures (i.e. the Paal–Knorr reaction[7] or the Achmatowicz reaction,[9] Scheme 1) are fundamental when considering natural product



Scheme 1. The Achmatowicz rearrangement.

syntheses. They are of significance in macrocyclic chemistry, however reactivity was observed solely for systems in which local aromaticity of the isolated furan was sustained, that is, calix[*n*]furans.[8] Built in macrocyclic aromatic structures (i.e. oxaporphyrins,[10] O-confused oxaporphyrin,[11] or oxaporphycenes[12]) the character of an individual furan ring is deeply modified and the heterocycle shows features adopted to the demands imposed by the macrocycle. Widely defined porphyrinoids suit as a unique environment that allows observing a specific metal–carbon interaction (carbaporphyrinoids)[13] or stabilization of a less abundant oxidation states of transition metals (hetero-porphyrinoids).[10,14] The studies which address the profound rearrangement of the separate heterocycle (carbocycle) entrapped in the porphyrinoid are rather rare and limited to a few examples.[15]

Here, we report on an unprecedented route of the Achmatowicz rearrangement which is encompassed within the 5,10,15,20-tetratolyl-21,23-dioxaporphyrin frame, leading to a 3-pyranone dioxacorrole skeleton. The created macrocycle provides a carbaporphyrinoidal coordination cavity effective in palladium(II) coordination and formation of a Pd–C(sp^3) bond (Scheme 2).



Scheme 2. The Achmatowicz rearrangement in the dioxaporphyrin **1** frame (Ar—*p*-tolyl; THF = tetrahydrofuran).

The aromatic, symmetrical, and rather polar 5,10,15,20-tetratolyl-21,23-dioxaporphyrin **1** (orange) placed on the basic alumina GII converts to a green compound, which is subsequently readily eluted with dichloromethane. The electronic spectrum observed for the new macrocycle (Figure 1) shows features of porphyrinoids with absent macrocyclic π delocalization. Actually the product is the dioxaporphyrin derivative formally formed by an addition of a water molecule as confirmed by mass spectrometry (m/z = 691.2921). The ^{1}H NMR spectrum of the new compound reflects the π-conjugated, nonaromatic electronic structure (Figure 2, trace A). A specific AB system (6.96 and 6.08 ppm) with an extraordinary coupling constant for porphyrinoids (^3J = 10.1 Hz) but characteristic for an alkene unit has been identified. Four further signals (four doublets of doublets, two AB systems) that showed scalar correlations (COSY map) to

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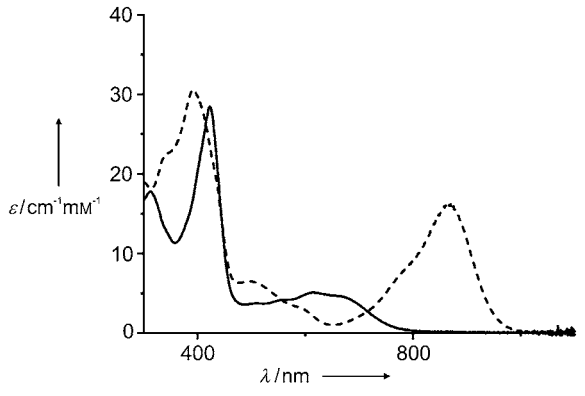


Figure 1. Electronic spectra of **2** (solid) and **4** (dashed) in CH_2Cl_2.

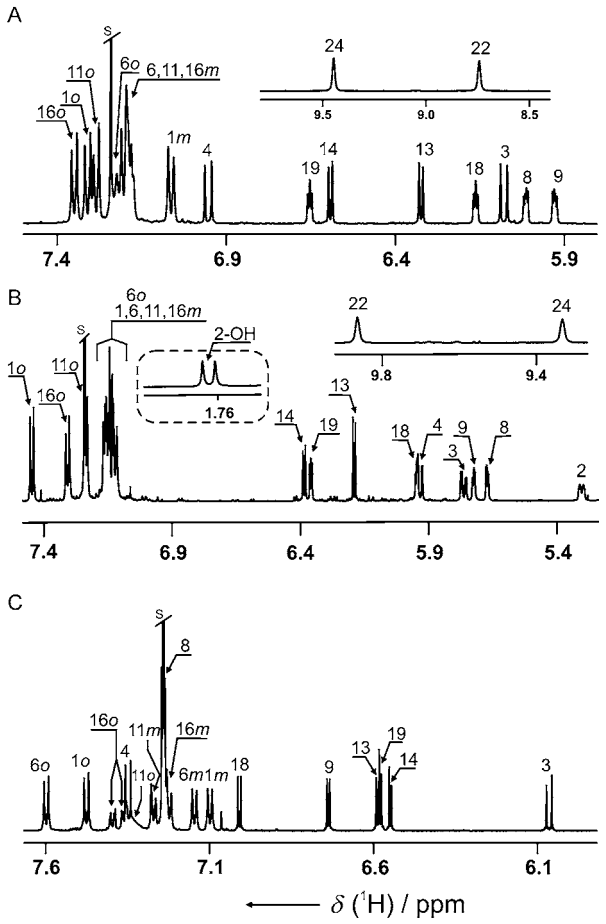


Figure 2. ^{1}H NMR ($CDCl_3$, 300 K, 600 MHz) spectra of **2** (A), **3** (B), and **4** (C). Numbering as in Scheme 2.

strongly downfield-shifted, broad signals (8.85 and 9.48 ppm) were readily assigned to the β-pyrrolic protons and the broad signals to the NH groups. The fourth, unchanged spin system (6.35 and 6.62 ppm) is assigned to the furan ring that remained intact. Further ^{13}C NMR characterization has shown the presence of a tetrahedral C(1) carbon ($\delta =$ 85.1 ppm) and a carbonyl C(2) atom ($\delta = 190.2$ ppm).

All these premises led to the conclusion that **1** underwent a significant change during reaction, affording 3-pyranone dioxacorrole **2** (Scheme 2). The cyclic structure was established by a careful analysis of a complementary picture provided by a combination of ^{1}H–^{1}H NOESY and ^{1}H–^{13}C HMBC connectivities. The NOESY experiment indicated a dipolar interaction between (1-*o*)H and both NH hydrogen atoms as expected from structural constrains imposed by the macrocyclic product of the Achmatowicz rearrangement. The DFT-optimized geometry (Figure 3 A) of **2** showed a proximity of the (1-*o*)H and NH protons in the macrocycle. The theoretical calculations showed that feasible isomers of **2**, that is, **1**-H_2O (5-hydroxyisodioxaphlorin—water addition product of **1**) and **2**-CH are evidently unstable relatively to **2** as the energy difference equals 16.0 and 22.0 kcal mol^{-1}, respectively (Scheme 3, Figure 3).

The mechanistic considerations suggest that the dioxaporphyrin **1** adsorbed on the basic alumina surface converts initially to **1**-OH (unprotonated form of **1**-H_2O) with a benzyl hydroxyl group that is a key intermediate in the Achmatowicz rearrangement. In contrast to the classic variant (Scheme 1) this reaction does not require the presence of an external oxidant as an aromatic macrocycle allows an intramolecular redox process (Scheme 4) in which the bottom part (triheterocyclic brace) is reduced while in the same moment the reacting furan is oxidized (Scheme 4). The further steps eventually afforded **2**.

The formation of **2** is reversible and **1** can be fully recovered (0.5 h, 298 K) by an acid-catalyzed transformation of **2** into **1** (retro-Achmatowicz rearrangement, see Figure S8 in the Supporting Information) without any reducing agent. This is an independent proof for the fully intramolecular mechanism elaborated for formation of **2**.

The six-membered-ring of pyranone, a product of the Achmatowicz rearrangement, takes an important place in the natural product synthesis as it can be readily derivatized.[5] In this light the reversibility of the formation process of **2** shows a similar modifiability. The presence of a carbonyl group at the macrocyclic periphery along with the mechanism of the reaction (including reversibility) and standard derivatization of the pyranone ring open a way for further modification. For instance, a straightforward conversion of **2** by reduction with $NaBH_4$ resulted in a quantitative formation of **3** (Scheme 1), that is, the reduction of 3-pyranone dioxacorrole afforded 3-pyranol dioxacorrole. The NMR analysis of **3** showed a resonance for the additional H(2) hydrogen (5.30 ppm) adjacent to the alkene fragment which was accompanied by the well-defined scalar-coupled OH resonance (1.76 ppm) all contributing to the ABCD spin system of the {OH,H(2),H(3),H(4)} set (Figure 2 B). The tetrahedral geometry around C(1) ($\delta = 82.5$ ppm) has been proved with the ^{1}H–^{13}C HMBC experiment as the correlations similar to **2** were preserved. The H(2) hydrogen is also bound to the tetrahedral carbon atom as reflected by the ^{13}C chemical shift of C(2) ($\delta =$ 69 ppm) determined by ^{1}H–^{13}C HSQC.

The reduction is reversible and **2** is recovered by spontaneous oxidation due to its exposition to air.

The reaction of **2** with palladium(II) acetate gave a neutral complex proving the ability of **2** for coordination. The ^{1}H and

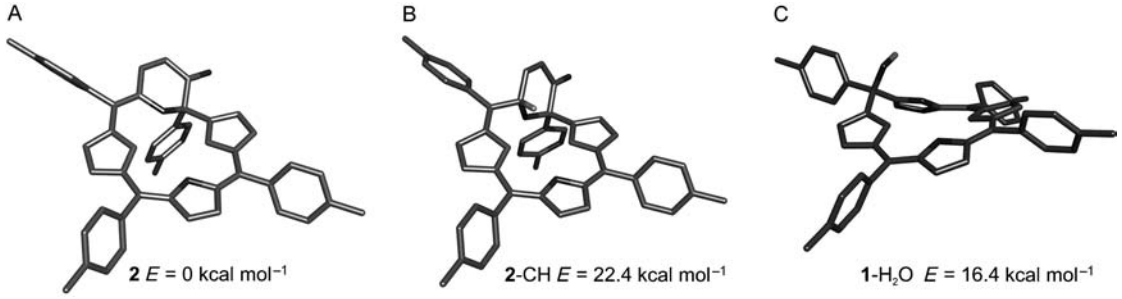
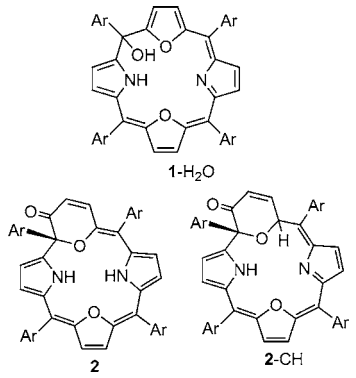
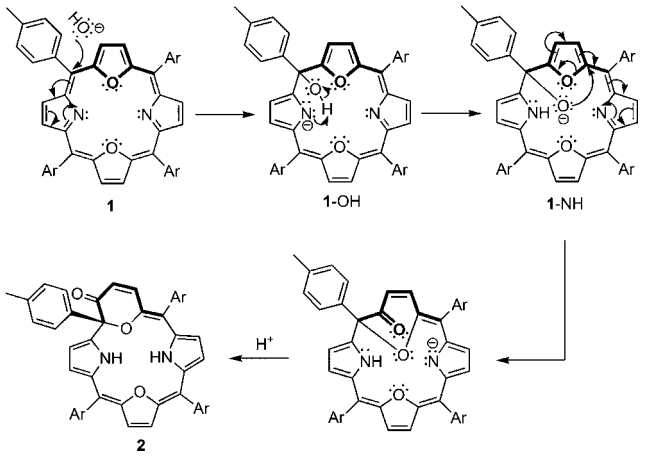


Figure 3. DFT-optimized geometries of isomeric **2**, **2**-CH, and **1**-H_2O (5-hydroxyphlorin). The shown energies are related to **2**.



Scheme 3. Selected isomers of **2**.



Scheme 4. Formation of **2** with an intramolecular redox process (the bottom, the triheterocyclic brace is reduced while the upper furan (bold) is formally oxidized).

^{13}C NMR analyses have shown a sustained carbon skeleton as the unusual coupling constant ($^3J = 9.9$ Hz, Figure 2C) was preserved along with a characteristic tetrahedral atom (C(1), $\delta = 90.4$ ppm) and a carbonyl group (C(2), $\delta = 192.2$ ppm). In addition the ^{13}C NMR experiments showed the formation of a second sp^3 carbon center ($\delta = 92.4$ ppm) which implies significant structural changes within the macrocycle during the insertion. The cavity size obtained from the DFT-optimized models of **2** (Figure 3) suggested two possible coordination modes. The first one, characteristic for **2** in which the coordination engages two oxygen atoms and two nitrogen donors {ONON}, and the second, less obvious in which the adjacent carbon (C(5)) is involved yielding an organometallic compound affording the {CNON} coordination core (**2**-CH, Figure 3B). The second coordination mode requires a formal prearrangement of **2** into the less stable (22.4 kcal mol^{-1}) **2**-CH in which one of the NH hydrogen atoms is relocated on the tetrahedral, rehybridized C(5) atom (Scheme 3, Figure 3B). Noticeably, considering the mechanism of metal ion insertion into **2** to form **4**, one can include a preorganization step envisaged by a transformation of **2** into **2**-CH—the structure of the ligand satisfies the requirements imposed by the inserted metal in **4**. This preorganization may contribute to the overall activation energy of metal insertion.[16]

The correlation experiments (^{1}H–^{1}H-NOESY, ^{1}H–^{13}C HMBC) confirmed the formation of palladium(II)–carbon(5) bond (Scheme 1) and showed an entrapment of **2**-CH by coordination.

X-ray crystallographic analysis showed that **4** creates a carbaporphyrinoidal environment and the metal center is located at the {CNON} coordination core. The bonds lengths in the palladium(II) surrounding (Figure 4) remain in a good agreement relative to other organometallic complexes of palladium(II) in macrocyclic environment.[11,15d] As observed in the NMR experiments the presence of the Pd–C bond forces the formation of two sp^3 carbon atoms. Both positions, C(1) and C(5), are tetrahedral as the angles proximate the values characteristic for sp^3 hybridization (Figure 4B). Furthermore the coordination forces the ligand to acquire an extraordinary conformation in which the 3-pyranone ring is almost perpendicular to the plane of the rest of the macrocycle (Figure 4A) visualized for the DFT-optimized, ruffled structure of **2**-CH.

As seen in Scheme 1 and Figure 3 **2** is a chiral compound with one stereogenic center. The optical activity of **2** was confirmed by an HPLC experiment with a chiral column in which two fractions were observed with different retention times (see Figure S10 in the Supporting Information) eluted for a spectrally pure compound. The UV/Vis and NMR spectra recorded for both fractions were identical. In fact insertion of palladium(II) into **2** results in the formation of a second stereogenic center. Only a single pair of enantiomers has been identified by HPLC (chiral column). Thus a stereoselective rearrangement of the molecular frame (**2**-*R* into **4**-*RR*, **2**-*S* into **4**-*SS*) of **2** occurred during the insertion. In

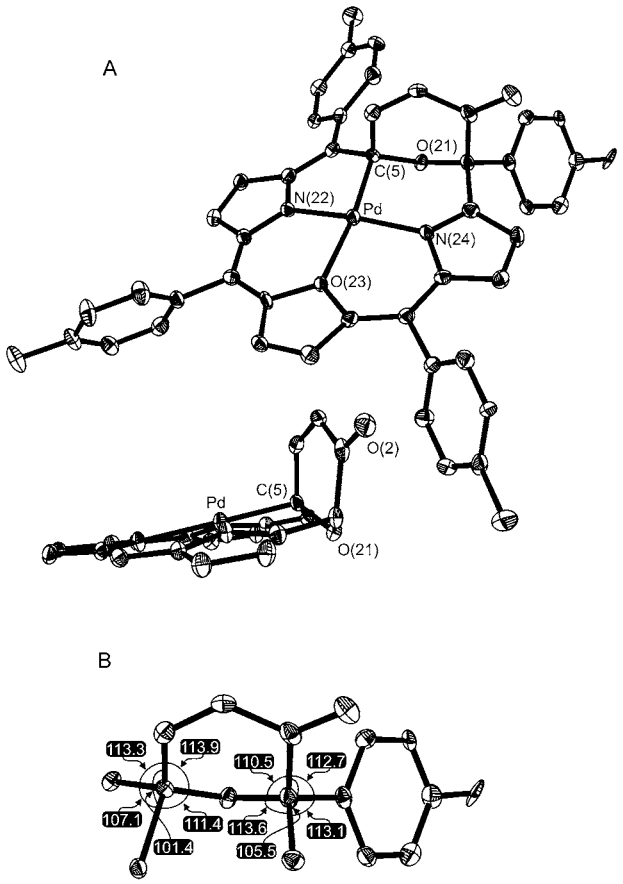


Figure 4. The X-ray molecular structure of **4**. A) Overall geometry of the molecule and the projection emphasizing the perpendicular orientation of the 3-pyranone ring enforced by coordination [Pd(1)-C(5) 1.995(3), Pd(1)-N(22) 1.924(2), Pd(1)-O(23) 2.107(2), and Pd(1)-N(24) 1.979(2). B) Selected bond angles around two sp^3 carbon atoms C(1) and C(5)].[17]

a simplified model of insertion the initial binding of palladium(II) by the NON pincer exposes palladium(II) to the inner side of originally trigonally hybridized C(5), which forces the detected stereoselectivity.

In conclusion, a unique example of the solid-supported Achmatowicz rearrangement in a macrocyclic environment has been encountered. 21,23-Dioxaporphyrin undergoes conversion to a contracted, flexible macrocycle with a 3-pyranone subunit built in the skeleton. The insertion of palladium(II) triggers the ligand accompanied by formation of a carbon–metal bond, showing the ability of 3-pyranone to adopt its behavior to the demands of the central metal. The presence of the 3-pyranone subunit opens a path for sophisticated modifications as shown in the test reduction with quantitative formation of 3-pyranol-dioxacorrole.

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[17] CCDC 859245 contains 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.

