

Oxidative Coupling

C,C- and N,C-Coupled Dimers of 2-Aminotetraphenylporphyrins: Regiocontrolled Synthesis, Spectroscopic Properties, and Quantum-Chemical Calculations

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Abstract: β , β' -Bisporphyrins are intrinsically chiral porphyrin dimers with fascinating properties. The configurational stability at their axes can be directed by variation of the central metal atoms. Herein, we present a regioselective functionalization of the monomeric 2-amino-tetraphenyl-porphyrin as a versatile substrate for dimerization by oxidative coupling. By simple variation of the reaction conditions (solvent and oxidant), the oxidation selectively gave either the axially chiral C,C-coupled diaminobisporphyrin in high yields or,

Introduction

Chiral porphyrins are increasingly important as chelating ligands, as metal catalysts in asymmetric synthesis,^[1,2] and as substrates for chiral recognition.^[3,4] The origin of chirality in such systems can be manifold. In addition to the introduction of stereogenic centers or axes, or planar chirality in the periphery of the tetrapyrrole macrocycles,^[5] there is also the possibility to link porphyrins through a chiral bridge.^[6] Documented examples of chiral axes caused by a direct porphyrin–porphyrin linkage are quite rare, but are gaining attention.^[7,8] We described the synthesis of the first β , β' -bisporphyrins with intrinsic axial chirality, by using a Suzuki coupling with moderate to good yields, providing the dimers with a large variety of central metals.^[9,10] The determination of their absolute configurations was accomplished on the basis of quantum-chemical CD calculations in combination with HPLC-CD measurements.^[10]

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under Ullmann conditions, the twofold N,C-linked achiral dimer, also in good yields. A generalized mechanism for the coupling reaction is proposed based on DFT calculations. The axially chiral β , β' -coupled porphyrin dimers were isolated as racemic mixtures, but can be resolved by HPLC on a chiral phase. TDDFT and coupled-cluster calculations were used to explain the spectroscopic properties of the amino-porphyrins and their dimers and to elucidate the absolute configurations of the C,C-coupled bisporphyrins.

More detailed kinetic investigation on the atropisomerization process showed that the choice of the central metal has a high impact on the stereochemical stability of the axis. Additional amino substituents in the proximity of the porphyrinporphyrin axis should not only increase the rotational barrier of such β , β' -dimers, but would also provide possibilities for further functionalization of the system. Thus, exocyclic amino functions might offer the possibility to construct multimodalcoordinated metal centers on the periphery of the porphyrin,^[11,12] in analogy to the related, but smaller, molecule 2,2'-diamino-1,1'-binaphthalene (BINAM), which is used as a ligand in palladium-catalyzed coupling reactions.^[13] In this paper, we report the highly regioselective synthesis of C,C- or N,C-linked porphyrin dimers, controlled by simple variation of the reaction conditions, and on the spectroscopic and chiroptical properties of the dimers thus obtained.

Results and Discussion

In a first approach we wanted to synthesize such β , β' -diaminobisporphyrins by homocoupling of the respective monomers under Ullmann conditions (Scheme 1). This approach has been achieved for the synthesis of biaryls and heterobiaryls previously,^[14] however, only for aromatic substrates with amides or with secondary or tertiary amino functions, not with primary amino groups. Moreover, no direct Ullmann coupling of porphyrins had been described. It was therefore important to prepare the previously unknown 2-bromo-3-aminotetraphenylporphyrin **2** as a promising precursor for coupling reactions.

The β -positions in monosubstituted tetraphenylporphyrins (TPPs) are electronically (and sterically) difficult to differentiate,

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Scheme 1. Planned synthesis of β,β' -diaminobisporphyrins 3 under Ullmann conditions.

| Table 1. Regioselective synthesis of the halogenated $\beta\mbox{-aminoporphyrin}$ 2. | | | | | | | |
|---|-------|----|-----|----|-------------------|--|--|
| Entry | Educt | м | NXS | х | Yield [%] | | |
| 1 | 1a | Ni | NBS | Br | 97 (2 a) | | |
| 2 | 1a | Ni | NCS | Cl | 76 (2 b) | | |
| 3 | 1a | Ni | NIS | I. | decomp. | | |
| 4 | 1 b | Cu | NBS | Br | 94 (2 c) | | |
| 5 | 1 b | Cu | NCS | CI | 92 (2 d) | | |

making regioselective β -functionalization of unsymmetric TPPs very challenging.^[15] Thus, the first synthetic goal to establishing a route towards the 2-bromo-3-amino-TPPs 2 from 2-aminoporphyrins such as 1 (Table 1), did not initially seem very promising. Nevertheless, bromination of the common nickelated 2-amino-TPP (1 a) with N-bromosuccinimide (NBS) quantitatively gave a single monobrominated compound (entry 1), and even chlorination of 1 a with NCS succeeded in yields of 76% (entry 2). The structure of 2a, which confirmed the regioselective β -functionalization of **1a** adjacent to the amino group, was established on the basis of COSY-NMR spectroscopic analysis (see the Supporting Information). The same halogenation reactions with 2-amino CuTPP (1b) by using NBS or NCS gave the respective halides 2c and 2d in yields of more than 90% (entries 4 and 5), with the same remarkable regioselectivity. All attempts to isolate the analogous 2-iodo-3-amino-TPP failed (entry 3), probably due to the sensitivity of the resulting iodinated porphyrins to light and oxidants. The regioselective high-yield synthesis of the halogenated β -aminoporphyrins 2 was an important prerequisite for the planned bisporphyrin syntheses, but these novel intermediates are clearly of value for other functionalization reactions on porphyrin monomers in general.

Attempts to couple the now easily available key intermediate **2a** were performed under mild Ullmann conditions^[14] at room temperature, using *N*-methyl-2-pyrrolidinone (NMP) as the solvent and 2.5 equivalents of copper(I) thiophene-2-car-

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Scheme 2. Attempted coupling of the brominated aminoporphyrin 2 a under Ullmann type coupling conditions leading to the pyrazine-bridged dimer 4.

boxylate (CuTC) as the coupling agent. However, instead of the desired C,C-coupling to give 3a, the formation of a twofold N,C-coupled dimer was observed (Scheme 2). The main product was characterized as the pyrazine-fused porphyrin dimer 4a, which was formed in 58% yield. Under the more common conditions for an Ullmann coupling,^[16] viz. treatment of the nickelated 2-bromo-3-amino-TPP (2a) with Cu powder (freshly activated) in N,N-dimethylformamide (DMF) at room temperature, the pyrazine-fused porphyrin dimer 4 was obtained in as much as 78% yield. The synthesis of 4 by an oxidative coupling using 2,3-dichloro-5,6-dicyano-1,4-benzoguinone (DDQ) had previously been described by Shinokubo et al., but was formed in low yields, with low selectivity, and was accompanied by formation of the C,C-coupled β , β' -diaminobisporphyrin 3a.^[17] The latter coupling protocol had been adapted from Osuka et al., who had built up meso, meso-coupled porphyrin dimers under these conditions.^[18] More recently, Mandoj and co-workers synthesized the biszincated derivative of 4 in moderate yields by condensation of a Zn^{II} diaminoporphyrin with diethyl oxalate or with a $Zn^{\parallel} \alpha$ -dioneporphyrin derivative; however, in this case two different buildings blocks were required.^[19]

As an alternative approach, the synthesis of **3a** was attempted by directed C,C-coupling of the respective aminoporphyrins **2**; to this end, a Suzuki protocol was chosen (not shown), as described by us for the synthesis of β , β' -dimers.^[9,10] However, the additional amino group present in **2a** increased the steric bulk in the β -position, so that instead of borylation of the brominated aminoporphyrin **2a**, only hydrodebromination was observed.

With the results described above in hand, an oxidative approach was again considered for the synthesis of the desired β , β' -diaminobisporphyrin **3a**. Surprisingly, treatment of the halogen-free aminoporphyrin **1a** with AgPF₆, as previously used for the *meso,meso*-coupling of ZnDPP^[18] (and likewise for C,C-linkage), exclusively provided the desired β , β' -diaminobisporphyrin **3a** in high yields. For the success of the reaction the use of anhydrous solvent and an inert gas atmosphere was critical, otherwise decomposition of the starting material occurred.

To further enhance the yields and to gain more insight into the reasons for the regioselectivity of this reaction, several con-

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| Table 2. C,C- versus N,C-coupling of aminoporphyrin 1 a (50 mg,72.8 μmol; at RT) to give bisporphyrin 3 a and/or pyrazine-bridged dimer4. | | | | | | | |
|---|-----------------------------------|---------|---------|----------------|-------------|---------------------------|--------------------------|
| Entry | Oxidant | [Equiv] | Solvent | Volume [mL] | Time [h] | Yield of 3a [%] | Yield of 4 [%] |
| 1 | AgPF ₆ | 1.2 | CHCl₃ | 15 | 4 | 54 | 0 |
| 2 | $AgPF_6$ | 1.2 | CHCl₃ | 80 | 3 | 93 | 0 |
| 3 | $AgPF_6$ | 0.6 | CHCl₃ | 80 | 36 | 94 | 0 |
| 4 ^[a] | $AgPF_6$ | 0.6 | THF | 80 | 36 | 20 | 6 |
| 5 | AgPF ₆ | 1.2 | THF | 15 | 4 | 50 | 0 |
| 6 | $AgPF_6$ | 1.2 | THF | 80 | 68 | 32 | 10 |
| 7 | $AgCO_2CF_3$ | 1.2 | CHCl₃ | 15 | 20 | 34 | 16 |
| 8 | AgCO ₂ CF ₃ | 1.2 | CHCl₃ | 80 | 42 | 14 | 16 |
| 9 | $AgCO_2CF_3$ | 1.2 | THF | 80 | 200 | 0 | 16 |
| 10 | AgCO ₂ CF ₃ | 5.0 | THF | 80 | 5 | 0 | 16 |
| 11 | FeCl₃ | 1.0 | CHCl₃ | 15 | 5 | 76 | 0 |
| 12 | FeCl₃ | 1.0 | CHCl₃ | 80 | 2.5 | 85 | 0 |
| 13 | FeCl₃ | 0.6 | CHCl₃ | 80 | 3.5 | 95 | 0 |
| 14 | FeCl₃ | 1.2 | THF | 80 | 160 | 22 | 8 |
| 15 ^[b] | $AgPF_6$ | 0.6 | CHCl₃ | 80 | 20 | 0 | 24 |
| 16 ^[b] | $AgPF_{6}$ | 5.0 | CHCl₃ | 80 | 36 | 0 | 16 |
| 17 ^[c] | $AgPF_6$ | 1.0 | CHCl₃ | 80 | 30 | 44 | 14 |
| [a] 25 mg (50%) starting material recovered. [b] 200 μL of NEt_3 were added. [c] 500 μL of DIPEA were added. | | | | | | | |

ditions were tested (Table 2). All the parameters were found to have significant influence on the outcome of the reaction. In general, higher amounts (one equivalent or more) of the oxidizing agents clearly decreased the reaction times but also gave slightly lower yields, probably due to decomposition by over-oxidation. The best yields (up to 95%) were achieved when 0.6 equivalents of AgPF₆ or FeCl₃ (entries 3 and 13) were used in a diluted chloroform solution. With tetrahydrofuran (THF) as the solvent the N,C-coupled annulated system **4** was formed as a by-product (entries 4 and 6). Compound **4** was also found under all tested reaction conditions when AgCO₂CF₃ was used (entries 7–10). With THF as the solvent it was even formed as the main product, albeit with low yield (16%; entries 9 and 10).

Clearly, the solvent had a large impact on the outcome of the reaction. In THF, generally, both coupling types were observed. In chloroform, however, C,C-coupling was found almost exclusively, whereas addition of NEt₃ or Hünig's base (DIPEA) to the chloroform again led either to N,C-coupling (Table 2, entries 15 and 16) or to both coupling types (entry 17), when using AgPF₆ as the oxidant. Interestingly, just half the stoichiometric amount of oxidant (e.g., 0.6 equiv) was sufficient to obtain the high coupling yields. It is possible that, under these conditions, only the radical cation of the dimer was formed during the synthesis and the fully oxidized dimer was formed during workup. Investigations on this topic are ongoing.

Having optimized the reaction conditions for the dimerization of metalated aminoporphyrin **1a**, several derivatives of **3** differing in their central metals were synthesized (Table 3) starting from the respective metalated aminoporphyrins **1b**–**d**, which were prepared according to published procedures.^[20,21] For the Cu^{II} dimer **3b** and the Pd^{II} dimer **3c** the reactions succeeded with high yields above 90% (entries 1–7). Whereas the



synthesis of **3b** gave comparable conversion rates using AgPF₆ or FeCl₃ (entries 1–4), the coupling of **1c** and **1d** was better accomplished with FeCl₃ (entries 5–9). The Zn^{II} dimer **3d** was, however, only accessible in 30% yield (entry 9); in this case, a smaller amount (up to 0.6 equiv) of the oxidizing agent was used because the Zn^{II} derivative **1d** was highly sensitive to oxidation and/or light and easily decomposed during the reaction.

Crystals of **3a** and **3c** that were suitable for X-ray structure analysis were obtained when the respective solution in chloroform was layered with *n*-hexane (Figure 1). Both axially chiral



Figure 1. ORTEP plot (thermal ellipsoids at 50% probability) of dimers **3a** (top) and **3c** (below), arbitrarily only the *M*-atropo-enantiomers are shown. The outer phenyl substituents and all hydrogen atoms have been omitted for clarity.

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compounds crystallized as a racemic mixture in the space group P1. In contrast to a previously published crystal structure of **3a**,^[17] the crystals obtained in this case contained a molecule of water instead of chlorobenzene in the asymmetric unit of the crystal. A comparison of our crystal structure with the published structure revealed some significant differences, which proved to stem from an imprecise description in that article.[17] A direct comparison with the crystal structure data from the CCDC showed fewer differences. Therefore, prior to comparing the structure of 3a with that of 3c, we here first describe the most important (revised) structural features of 3 a. Remarkably, the geometries of the two subunits of the nickelated porphyrin 3a were significantly different, and thus the molecule clearly deviated from C_2 symmetry in the crystal structure. One porphyrin moiety showed a ruffled conformation, whereas the second had a distorted but clearly saddleshaped ring structure. The phenyl substituents directly adjacent to the axis displayed clear π -stackings with the neighboring macrocycles, with average distances between the respective pyrroles and phenyls of 3.486 and 3.265 Å. This is confirmed by the clearly shifted ¹H NMR peaks of the corresponding phenyl substituents. The angle at the central axis, when defined as that between the porphyrin subunits, was found to be about 54°, but, when defined as the dihedral angle between the directly connected pyrroles, was 76°.

In the bispalladated dimer **3c**, the porphyrin subunits were nearly planar and only slightly saddled, and the phenyl substituents at the β , β '-axis were no longer centered above the macrocycles as in **3a**, but rather peripheral. Nevertheless, the average distances of these phenyl groups to the macrocycle of 3.428 and 3.388 Å evidenced a clear π -stacking (also visible in the ¹H NMR spectra). The angle between the porphyrin moieties of **3c** was 60° and the dihedral angle between the pyrrole units at the axis was 84°, thus both angles were significantly larger than in **3a**. The sizes of the angles at the central axis are reflected in the UV spectra of the β , β '-diaminobisporphyrins **3**, which we discuss below.

Synthesis of β , meso-dimers and β , meso, β -trimers

Because the conditions used for oxidative β , β' -couplings were similar to those used for the previously described^[18] *meso,meso*-couplings, the construction of a directed β ,*meso*-linkage seemed to be a rewarding task. Indeed, treatment of an equimolar mixture of the nickelated aminoporphyrin **1a** and a triarylporphyrin (viz. the zincated tris(3,5-di-*tert*-butylphenyl)porphyrin **5a**) with AgPF₆ (Scheme 3) led to the formation of the symmetrical β , β' -diaminobisporphyrin **3a** in 36% yield and the β ,*meso*-coupled dimer **6** (A₃- β TAP type^[24]) in 15% yield. Interestingly, no *meso,meso*-dimer was found. The use of an excess (3 equiv) of the *meso*-precursor **5a** increased the yield of the unsymmetrical β ,*meso*-coupled compound **6** to 45%, whereas the β , β' -diaminobisporphyrin **3a** was isolated in only trace amounts; the remaining starting material **5a** (2 equiv) was reisolated nearly completely.

It seemed that **1a** was not only oxidized more easily than **5a**, but also that the nucleophilicities of the two educts were





Scheme 3. Agl-mediated directed cross-coupling to the $\beta, \textit{meso-porphyrin}$ dimer 6.

different, otherwise meso, meso-coupling would also be expected. Such directed oxidative cross-couplings of aromatic compounds had been reported before.^[22] The mixed coupling of 1 a and 5 a was clearly influenced by the metal atom in the meso-building block. Whereas the zincated triarylporphyrin 5 a reacted very well, no reaction to a β , meso-dimer was observed in the case of the nickelated derivative 5b, for which only the β , β' -diaminobisporphyrin **3a** was formed. Similar observations had previously been made for meso, meso-couplings of diphenylporphyrins (DPP) with Ni^{II} as the central atom.^[18] A simple explanation was found by analyzing the orbital coefficients of NiDPP and ZnDPP and their averaged localized ionization energy (ALIE) surfaces^[23] (see the Supporting Information); thus, only in the zincated educt were the HOMO and an ionization energy minimum clearly located at the meso-positions, so that nucleophilic attack from the meso-position could only occur for this DPP.

The successfully established β , meso-linkage encouraged us to use this reaction principle to elaborate an easy access even to β ,meso, β -trimers. Such achiral and chiral trimers, as previously prepared by a twofold Suzuki coupling,^[24] are of interest because, even when achiral, they can occur as stable cis/transatropo-diastereoisomers. For the synthesis of the envisaged β ,meso, β -coupled porphyrin trimer **9** (Scheme 4), aminoporphyrin **1** a was used as the β -building block and ZnDPP (7) as the meso-unsubstituted precursor. As expected from the previous results, again no meso, meso-homocoupling was observed in this reaction. In addition to the symmetric β , β' -diaminobisporphyrin 3a (12%) and the cross-coupled intermediate β ,meso-dimer **8** (29%), the desired β ,meso, β -trimer **9** (β TAP-5,15-A₂- β TAP type^[24]) was found in a yield of 10%. The latter was isolated as a single diastereomer, most probably the sterically less demanding trans-isomer, however, this could not be proven by NMR spectroscopic analysis due to the symmetry of the molecule.[24]



Scheme 4. Synthesis of the $\beta, \textit{meso}, \beta\text{-coupled trimer 9}$ and the intermediate dimer 8.

Mechanism

The results described above permit several conclusions to be drawn regarding the mechanism of the oxidative coupling. In the initial halogenation step from 1 to 2, the amino group already has a strong directing influence, with the electrophile exclusively attacking the carbon atom next to the carbon bearing the amino function (i.e., C-3), showing that this enamine carbon had by far the highest nucleophilicity in the 2-aminoporphyrins 1. It has been reported that oxidative coupling in the meso-position of DPP takes place via a DPP radical cation, with subsequent C,C-bond formation by its electrophilic attack to an unoxidized porphyrin, and final oxidation of the primary coupling product to give the meso, meso-dimer.^[18, 25] In the case of 2-aminoporphyrin 1, the reaction of the corresponding radical cation should occur exclusively at C-3, that is, the β -carbon atom next to the carbon carrying the amino function. However, as shown above, not only C,C-, but also N,C-coupling can occur upon oxidation, that is, there are two positions from which the electrophilic attack of the 2-aminoporphyrin radical cation can take place. These positions can be rationalized by the mesomeric structures of the intermediate radical cation I (Scheme 5), which show that spin density can be expected at the amino nitrogen (Scheme 5, Ib) and at the enamine carbon, that is, in the 3-position (Scheme 5, Ic, Id).

To validate these conclusions and to further clarify the mechanism, the spin density in the radical cation I of 1a was determined by quantum-chemical calculations by using the



Scheme 5. Possible mechanism for the formation of 3 and 4.



Figure 2. Calculated spin densities of the intermediate radical cation I a) in the absence or b) in the presence of a chloride anion (green sphere), and c) average local ionization energy (ALIE) surface of the nucleophilic educt **1 a**.

 ω B97X-D/6-31G* (6-311G* for Ni) method. Surprisingly, the spin density was mainly present at the amino group, and none was found at C-3 (Figure 2a). Because the experimental results had shown an influence of the solvent, the anion of the oxidizing agent, and of the additives to the oxidative coupling, their roles were investigated by further calculations. Including the

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solvents THF and chloroform in the calculations, as expected, showed no influence on the spin densities, whereas computations in the presence of an additional chloride anion in the proximity of the radical revealed spin density at the β -carbon C-3 (Figure 2b).

To assess the nucleophilicity of the second reaction partner, the nonoxidized aminoporphyrin **1a**, the average local ionization energy (ALIE)^[23] surface was calculated from the ω B97X-D/ 6-31G*-optimized structures. These results were in agreement with the experimental findings, confirming clearly that the only position expected to undergo electrophilic attack was the carbon atom next to the carbon having the amino function, that is, C-3 (Figure 2c).

For the outcome of the reaction merely the distribution of the spin density was decisive: When the spin was exclusively localized on the nitrogen atom (Scheme 5, **Ib** and Figure 2a), only the N,C-coupling was possible, whereas in the other cases (Scheme 5, **Ic**, **Id** and Figure 2b) the thermodynamically preferred C,C-coupling occurred. The ALIE surfaces showed no clear dependence of the nucleophilicities on the different type of central metal atoms in the aminoporphyrins **1**, in contrast to the cases of NiDPP and ZnDPP (see the Supporting Information).

The fact that treatment of aminoporphyrin **1a** with AgPF₆ in THF also gave rise to a small amount of N,C-coupling, might be explained by the known^[26] complex formation of the silver salt with THF. This complexation has been reported to lower the oxidation potential of the silver salt.^[26] The absence of the anion as a consequence of the complexation significantly changes the position of the spin density in the radical cation I (as shown in Figure 2 a and 2 b for I with and without a chloride anion). Addition of NEt₃ to AgPF₆ in chloroform had a similar effect and, thus, again N,C-coupling occurred. It is well-known that oxidative aromatic coupling is very sensitive to the electron density of the substrate^[27] and in the case of the aminoporphyrins it is clearly possible to easily change the spin density by varying the solvent and/or the oxidizing agent.

Spectroscopic properties

The UV spectrum of diaminobisporphyrin 3a in CH_2CI_2 (Figure 3) had a broadened Soret band at 421 nm, which was red-shifted by 10 nm compared with that of the aminoporphyrin monomer 1a (411 nm). The Davydov splitting of the



Figure 3. UV spectra of the dimers 3a-d in CH_2CI_2 .



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Soret band, as clearly observed in most β , β' -bisporphyrins without amino functions, did not occur in the UV spectra of the nickelated or palladated dimers 3a and 3c. The absorptions of the metalated porphyrin dimers **3 b-d** were quite similar to that of 3a, although the Pd^{II} dimer 3c had a slightly less broadened Soret band and the Cu^{II} dimer **3b** showed a small shoulder at 420 nm and a lower intensity of the Soret band. The shoulder in the Soret band was also observed for 3d and may hint at a Davydov splitting in these 2-aminoporphyrin dimers. As in previous cases,^[28,29] the angle between the porphyrin subunits had a strong impact on the UV spectrum of β , β' -bisporphyrins: the smaller this angle, the more broadened the expected Soret band. The crystal structures of 3a and 3c explained the observed differences in the Soret band: 3c had a larger angle than 3a and thus it displayed a narrower absorption band.

As described above, the additional amino group should increase the rotational barrier at the central axis of the β , β' -coupled dimers **3**, making it possible to resolve the presumed racemic mixtures of **3** by HPLC on a chiral phase. After intense optimization of the chromatographic system, the resolution of all dimers **3a-d** succeeded with a Chiralpak IA phase (Daicel Chemical Industries, Ltd.; **3a-c**: CH₂Cl₂/*n*-hexane 20:80; flow: 1.0 mLmin⁻¹; **3d**: CH₂Cl₂/*n*-hexane 40:60; flow: 1.2 mLmin⁻¹), permitting measurement of full CD spectra of the enantiomers by HPLC-CD in the stopped-flow mode. This made it rewarding to likewise calculate the CD curves for the enantiomers of **3a** quantum-chemically and to compare with these experimental CD spectra, to assign their absolute configurations.

To find a suitable computational method, we first calculated the UV spectra with different density functionals. When computing the UV spectra of the monomer **1a** and of the dimer **3a** using TDCAM-B3LYP in combination with the 6-31G* (for Ni 6-311G*) basis set, severe problems were found in reproducing the experimental UV spectrum for the monomer, although this method had been used successfully for the computation of excited states of porphyrins before.^[28,30] The calculated spectrum had a general blueshift of 47 nm and two excitations (calculated at 397 and 385 nm) were observed that had an even higher intensity than the Soret band. Electron-density difference plots showed that these excitations had a charge-transfer (CT) character, with transitions from the amino group and the corresponding pyrrole to the porphyrin macrocycle, which might explain the problems of the TDDFT method.

To gain a deeper insight into whether these CT excitations really exist and if at least their calculated energies were correct, RI-SCS-CC2 calculations were performed. Although this coupled-cluster method showed a high hypsochromic shift of 50 nm, the overall agreement with the experiment was much better. The additional transitions found in the TDDFT computations also occurred when applying the RI-SCS-CC2 method at comparable energies but with a much lower intensity in the absorption spectrum (see the Supporting Information). This high-level method showed that the CT character of the excitations was slightly overestimated by TDCAM-B3LYP but the general level of agreement of the excitation energy with the RICC2 result was acceptable. However, the TDDFT oscillator strengths



were highly overestimated and this problem was also observed in the dimer calculations, for which RICC2 computations were not feasible. Thus, the determination of a reliable UV shift, simply by comparison of the experimental UV spectra with the calculated spectra, was difficult. This problem was solved by identifying the calculated Soret bands by analyzing the main configurations of the excitations. Transitions from HOMO and HOMO-1 to LUMO and LUMO + 1 contribute to a high extent to the Soret band, as is known porphyrins, nonaminated for making it easy to find the correct excitations and to determine a reliable UV shift.



Figure 4. Determination of the absolute configuration of the two enantiomers of dimer 3 a by comparison of their CD spectra measured online with those calculated quantum-chemically.

The TDCAM-B3LYP/6-31G*//

 ω B97X-D/6-31G* (6-311G* for Ni) calculations of the *M*-configured diaminobisporphyrin **3a** yielded a CD spectrum that gave a very good match with the experimental spectrum of the faster eluting enantiomer, whereas the curve of the more slowly eluting compound fit very well with the spectrum calculated for the *P*-enantiomer (Figure 4). Clearly, the calculated rotational-strength values did not suffer from the problem identified for the oscillator-strength values.

In a similar way, guantum-chemical calculations were performed for the dimers with Pd^{II}, Cu^{II}, or Zn^{II} as the central metal atoms. All CD curves of the faster eluting peaks showed nice agreement with the CD spectra calculated for the respective M-configured enantiomers, whereas the CD curves of the more slowly eluting peaks matched nearly perfectly with those calculated for the P-enantiomers (see Figure 5 and Figure S1-S3 in the Supporting Information). The enantiomeric similarity indices^{[31]} ($\Delta_{\text{ESI}\prime}$ calculated in the range from 350 to 500 nm) were above 90% for 3a-c and above 60% for 3d, showing the high reliability of these configurational assignments by using CD calculations. Interestingly, the metal centers had a substantial impact on the intensity of the CD curves. The palladated dimer 3c showed the strongest signal and the nickelated bisporphyrin 3a the weakest, whereas the CD intensities of 3b (M=Cu) and 3d (M=Zn) were in between.

All attempts to conduct TDB3LYP and TDBHLYP calculations did not yield a satisfactory agreement between the calculated and the experimental CD curves. At first glance the computed UV curves showed a better match because the 'CT' excitations mentioned above had a significantly lower absorption, but their excitation energies were much lower (closer to the Q bands) in the case of the TDB3LYP calculation and much higher in the case of TDBHLYP (even higher than the Soret band). This eventually corrupted the computed CD spectra to such an extent that a reliable determination of the absolute configuration by comparison of the experimental spectra with



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Figure 5. Experimental CD spectra (offline) of the faster eluting *M*-configured enantiomers of **3 a–d**.

the TDB3LYP or TDBHLYP calculated spectra was impossible (see the Supporting Information).

The CD spectra of the *M*-configured β , β' -diaminobisporphyrins **3** were nearly mirror images of the curves of the *M*-configured and rotationally stable β , β' -bisporphyrins without amino substituents^[10] (see the Supporting Information). Thus, the common method used to elucidate the absolute configuration by comparison of the CD spectra of new compounds with those of structurally closely related compounds would have led to wrong results in this case, highlighting the importance of quantum-chemical CD calculations.

To gain more detailed insight into the stereochemical stability of the axis, the resolved pure enantiomers of **3a** were inves-



tigated by HPLC at different temperatures after different intervals, but even at 100 °C no rotation was observed and at higher temperatures the dimers decomposed. This already showed that, in comparison to the (stereochemically unstable) β -unsubstituted nickelated porphyrin dimers,^[10] the rotational barrier had been significantly increased by the additional β -amino groups.

Conclusion

A series of novel metalated β , β' -coupled diaminobisporphyrins **3** were synthesized in excellent yields and high regioselectivities by the simple methodology of an oxidative coupling of 2-aminoporphyrins **1**. These are most valuable substrates because they can be halogenated in a highly regioselective manner. In a similar way, the amino group has a strong directing influence in oxidative coupling reactions, which can be selectively directed towards N,C-coupling, leading to pyrazine-fused dimers **4**, or to C,C-coupling to give axially chiral bisporphyrins **3**. This regioselectivity can be convincingly rationalized by ALIE-surface and spin-density calculations.

The β , β' -coupled, intrinsically chiral aminoporphyrin dimers **3** were found to be rotationally stable at the central axis. Resolution of their enantiomers was achieved by HPLC with a chiral phase. By HPLC-CD coupling, in combination with quantum-chemical CD calculations, the absolute configurations of the enantiomers were determined. Investigations on the rotational barrier showed the high impact of the additional amino groups. Whereas the nickelated β , β' -bisporphyrins without amino groups have been reported to racemize at room temperature,^[10] the pure enantiomers of the novel diamino-substituted analogue **3a** were found to be stereochemically stable.

 β , β' -Diaminobisporphyrins might find use as ligands for metal coordinations as described for N-inverted porphyrin dimers^[11] or even as catalysts in metal-assisted coupling reactions with the porphyrin dimer as a kind of "super BINAM".^[13]

Experimental Section

General experimental procedures

UV/Vis spectra were obtained with a Cary 50 spectrophotometer (Varian). IR spectra were recorded with a JASCO FTIR-410 spectrometer. ¹H and ¹³C NMR spectra were taken with Bruker Avance 400 or DMX 600 (400 and 600 MHz) spectrometers using CDCl₃ as internal standard (CDCl₃; $\delta =$ 7.26 and 77.00 ppm, respectively). HRMS (ESI) spectra were obtained with a microTOF-focus mass spectrometer (Bruker Daltonik GmbH) equipped with an APCI ion source (Agilent G1947-60101). Due to the isotopic distribution over a broad m/z region caused by zinc and palladium, the signal of monoisotopic signals was too small in intensity for some compounds for an accurate mass measurement. In these cases, typically the most intense signal (X+n) of this isotopic distribution was taken as described and compared to the respective calculated value. Enantiomeric resolutions on an analytical scale were performed with a Jasco HPLC system (pump PU1580, gradient unit LG-980-02S, degasser DG-2080-53, UV detector MD-2010Plus) equipped with a Chiralpak IA column (Chiral Technologies Europe, 4.6×250 mm) as the chiral phase and coupled to a Jasco 715 spectropolarimeter for the online-CD investigations (scanning rate: 200 nm min⁻¹, bandwidth: 1.0 nm, response time: 0.25 s, number of accumulations: 3). All enantiomeric resolutions were carried out at RT with a constant flow rate using an isocratic solvent system consisting of dichloromethane and *n*-hexane. Semipreparative resolutions of the racematic mixtures were performed with a Jasco HPLC system (pump PU1580, gradient unit LG-2080–04, degasser DG-2080–54, UV detector MD-1510) equipped with a Chiralpak IA column (Chiral Technologies Europe, 10×250 mm, 5μ m) as the chiral phase.

Unless otherwise noted, materials obtained from commercial suppliers were used without further purification except for *N*-bromosuccinimide, which was recrystallized from H₂O. Anhydrous CHCl₃ was obtained by distillation from CaH₂. Column chromatography was performed on silica gel (0.063–0.2 mm). Thin-layer chromatography was carried out on aluminum sheets coated with fluorescence-active silica gel 60 F254 (Merck).

Computational details

All optimizations were performed by using the $\omega\text{B97X-D}^{\scriptscriptstyle[32]}$ functional in combination with the 6-31G*[33] basis set for C, H, and O atoms, 6-311G*^[34] for Ni, Cu, Zn, and Cl, and SDD^[35] (and pseudo potentials) for Pd. The conformers arising from different dihedral angles at the phenyl axes were ignored as they had no impact on the CD behavior. Thus, for most of the dimers only one significant conformation was found. Dimer **3a** was the only exception, with two possible conformers, for which the spectra were added up after a Boltzmann-statistical weighting.^[36] For the optimizations of the radical cations, solvent effects were considered (CPCM, [37] solvent = chloroform). Subsequently, TDCAM-B3LYP^[38] calculations were done using the same combinations of basis sets and CPCM (solvent = dichloromethane) for solvent effects. In case of the RI-SCS-CC2^[39] calculations, def2-SV(P)^[40] (def2-TZVP^[40] for Ni) was utilized. All computations were done with Gaussian09^[41] except for the coupled-cluster approach, which was performed with Turbomole.^[42] Visualization of the spin densities was carried out with Avogadro^[43] in combination with PovRay. ALIE surfaces were calculated using Multiwfn 3.1,^[44] and visualized with VMD^[45] and PovRay. Processing of the TD calculations and comparison with the experimental spectra was done with SpecDis.^[31,46] The following UV shifts $^{\rm [36]}$ and σ values were used: 32 nm and 0.14 eV for 3a, 45 nm and 0.1 eV for 3 b, 40 nm and 0.11 eV for 3 c, 47 nm and 0.16 eV for 3 d.

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Keywords: atropisomerism · configuration determination · oxidative coupling · porphyrins · quantum-chemical calculations

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