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Synthesis of Porphyrinoids, BODIPYs and (Dipyrrinato) Ruthenium(II) Complexes from Pre-functionalized Dipyrromethanes

Benjamin F. Hohlfeld,[a][b][d] Keith J. Flanagan,[c] Nora Kulak,[b] Mathias O. Senge,[c] Mathias Christmann,[a] and Arno Wiehe*[a][d]

Dedicated to Professor Hans-Ulrich Reißig on the occasion of his 70th birthday.

Abstract: The introduction of functional groups into the meso-position of dipyrromethanes, boron-dipyrromethenes (BODIPYs) and porphyrinoids, is of fundamental importance in designing such dye systems for material sciences or photomedicine. One route that has proven to be particularly useful in this respect is the nucleophilic aromatic substitution (S_NAr) on porphyrinoids and their precursors carrying electron-withdrawing substituents. To further expand this methodology, the potential of the 4-fluoro-3-nitrophenyl and the 3,4,5-trifluorophenyl moieties for the synthesis of functionalized dipyrromethanes, BODIPYs, and porphyrinoids has been evaluated. The 3,4,5-trifluorophenyl moiety proved not to be applicable in the S_NAr with nucleophiles. The introduction of the 4-fluoro-3-nitrophenyl group, however, allowed fast and efficient S_NAr with various amine nucleophiles. The synthesized 4-amino-3-nitrophenyl-substituted dipyrromethanes were successfully applied in the synthesis BODIPYs and were tested in the synthesis of '*trans*'-A_2B_2 porphyrins and A_2B corroles. Furthermore, the dipyrromethanes - after oxidation to the dipyrromethenes - were found to be suitable ligands for metal ions giving access to functionalized ruthenium(II) metal complexes.

Introduction

Porphyrins and the related cyclic tetrapyrroles are fundamentally important components in essential biological processes.[1] The special characteristics of porphyrins and corroles such as their conformational flexibility,[2] which can be modified through peripheral substitution,[3] inner core modifications,[4] and the incorporation of metal centers,[5] enable diverse applications. They are characterized by intensive electronic absorption and emission, a low HOMO-LUMO gap, and the option to vary their redox properties *via* metalation.[6] Porphyrins and their metal complexes are used as catalysts,[7] in light-harvesting complexes, and as components of electronic sensors.[8] Metal complexes of corroles have found application as catalysts in the oxidation of hydrocarbons.[9] Due to their inherent properties, porphyrins and corroles have also found application in photomedicine, *e.g.* as photosensitizers in photodynamic therapy (PDT). Both compound classes show a strong absorbance at wavelengths with a deep light propagation in human tissue (red to near infrared region) while being harmless to the organism in their ground state.[10,11] Through light-excitation and the subsequent photophysical and chemical processes, tetrapyrrole-based dyes give eventually rise to reactive oxygen species which damage the diseased tissue in PDT by oxidation.[12]

Boron-dipyrromethenes (BODIPYs) are well established as fluorescence-imaging dyes in diagnostics[13] and share many characteristics with porphyrins and corroles, such as their intense color and fluorescence.[14] One subject of current research is to improve the BODIPY structure towards absorption at higher wavelengths and specifically to increase excited triplet state formation for an application in PDT.[15] This can *e.g.* be done by modifying the BODIPY backbone with halogen atoms[16,17,18] or through use of heavy-atom free BODIPY-anthracene dyads.[19]

Dipyrromethanes are of wide interest in organic synthesis and are commonly employed as building blocks for the selective synthesis of meso-substituted porphyrinoids as well as meso-substituted BODIPYs.[20,21,22] Specifically, BODIPYs are easily available from dipyrromethanes *via* a three-step one-pot synthesis.[23,24] The stability of meso-substituted dipyrromethanes strongly depends on the substitution in the meso-position. Electron-withdrawing substituents in this position stabilize the dipyrromethane against decomposition.[25] In addition, electron-withdrawing substituents render the dipyrromethane, or the final porphyrinoid, susceptible to S_NAr (whereas it is known that porphyrins in general are also

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[a] Benjamin F. Hohlfeld, Prof. Dr. Mathias Christmann, Dr. Arno Wiehe, Institut für Chemie u. Biochemie, Freie Universität Berlin Takustr. 3, 14195 Berlin, Germany

[b] Benjamin F. Hohlfeld, Prof. Dr. Nora Kulak, Institut für Chemie und Biochemie, Freie Universität Berlin, Fabeckstr. 34/36, 14195 Berlin, Germany

[c] Keith J. Flanagan, Prof. Dr. Mathias O. Senge, Medicinal Chemistry, Trinity Translational Medicine Institute, Trinity Centre for Health Sciences, Trinity College Dublin, The University of Dublin, St James's Hospital, Dublin 8, Ireland

[d] Dr. Arno Wiehe, biolitec research GmbH, Otto-Schott-Str. 15, 07745 Jena, Germany, arno.wiehe@biolitec.com, https://www.biolitec.de/

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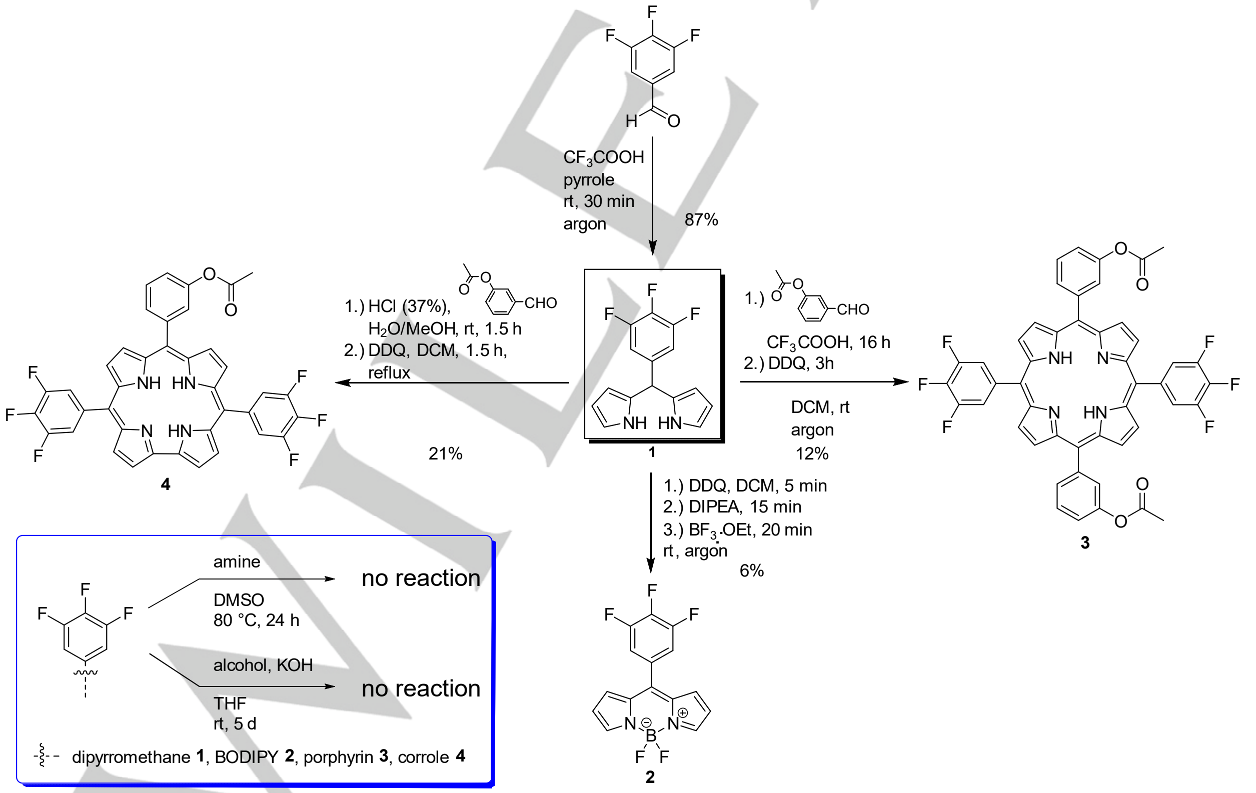
susceptible to a nucleophilic attack by strong nucleophiles like organolithium reagents[26]). One group that fulfills this criterion is the pentafluorophenyl group and hence it has been well studied in the synthesis of meso-substituted dipyrromethanes,[27] BODIPYs,[13,28] and porphyrins[29] using *e.g.* amines,[30] thiols,[31] and alkoxides[32] as nucleophiles for S_NAr.

Based on this, the 4-fluoro-3-nitrophenyl group presents itself as a good alternative to the well-established pentafluorophenyl substituent, with only a few S_NAr reactions on 4-fluoro-3-nitrophenyl-substituted BODIPYs[33] and 4-fluoro-3-nitrophenyl-substituted thiadiazole[34] already described in the literature. The electron-withdrawing effect of the fluoro and the nitro group should have a comparable stabilization effect on the dipyrromethane like the pentafluorophenyl substituent. The effect of the fluorine atoms in S_NAr, as well as the influence of the nitro group have been analysed in the literature.[35,36,37] The fluorine-substituted carbon atom adjacent to the electron-withdrawing nitro group is a suitable location for S_NAr at this position. Another alternative is the 3,4,5-trifluorophenyl group. The electron-withdrawing effect of the three fluorine atoms should still facilitate stabilization of the dipyrromethane and allow S_NAr; at the same time the reduced number of fluorine atoms, compared to the pentafluorophenyl moiety, can be beneficial for tentative medical applications. Fluorinations allow adjusting the hydrophobic/lipophilic character of chemical compounds.[38] In this respect, the reduced number of fluorine atoms can be of interest for better solubility in more polar solvents. Thus, the use of these two moieties in the synthesis and S_NAr modification of meso-substituted BODIPYs, porphyrinoids, and ruthenium(II) complexes were investigated.

Results and Discussion

Due to its similarity with the pentafluorophenyl moiety the investigations started with the 3,4,5-trifluorophenyl group as a possible substituent for S_NAr in dipyrromethanes, BODIPYs, porphyrins, and corroles. The lower number of fluorine atoms in the 3,4,5-trifluorophenyl moiety – compared to the pentafluorophenyl substituent – may lead to an improved solubility in polar solvents. In addition, possible side reactions with nucleophiles are excluded due to the absence of fluorine in the *ortho* positions, as observed with the pentafluorophenyl group.[32a]

Dipyrromethane **1** was readily synthesized from 3,4,5-trifluorobenzaldehyde and pyrrole according to standard dipyrromethane synthesis and was obtained in 87% yield (Scheme 1). Dipyrromethane **1** was then tested as a precursor for subsequent functionalizations and reactions. The syntheses of the corresponding BODIPY **2**, the '*trans*'-A_2B_2 porphyrin **3** and the A_2B corrole **4** were performed under standard reaction conditions for the respective compound (Scheme 1), the porphyrin being prepared under equilibrium conditions,[39] the



Scheme 1. Synthesis of a BODIPY, a 5,15-A_2B_2 porphyrin and an A_2B corrole incorporating the 3,4,5-trifluorophenyl substituent starting from dipyrromethane **1**.

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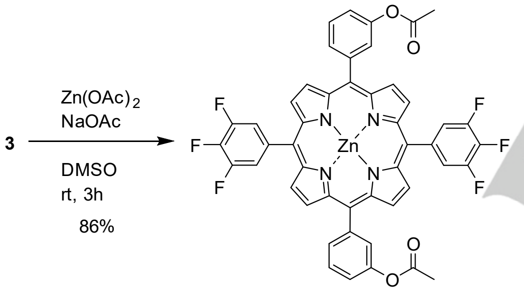
corrole in a two-step reaction as described by Gryko and co-workers,[40] and the BODIPY by the well-known oxidation-deprotonation-complexation sequence.[23,24,41] All three compounds were obtained in low to moderate yields.

In the next step, S_NAr was investigated on dipyrromethane **1** and on compounds **2**-**4** with a number of amines and alcohols, *e.g.*, *n*-butylamine, propargylamine, 1-butanol, and propargyl alcohol. However, a successful exchange of the *p*-fluorine atom was not observed with any of the tested nucleophiles, whether at room temperature or upon heating (Scheme 1; for details see Supporting Information). In all cases, the starting material was recovered, and no substitution products could be isolated. Perhaps, under more drastic conditions or special conditions such as microwave irradiation[42] an exchange of the p-fluorine atom may still be possible.

Chelation with metal ions can significantly affect the reactivity of the porphyrin macrocycle.[43] In the literature it has been described that complexation of a porphyrin (containing pentafluorophenyl groups at the meso-positions) with zinc(II) led to higher yields for the nucleophilic substitution at the *p*-position of the pentafluorophenyl substituent.[32a] Moreover, zinc(II) has the general advantage that it can easily be removed after the reaction under acidic conditions regenerating the free-base porphyrin.[44] Hence, free-base porphyrin **3** was treated with zinc acetate and sodium acetate in DMSO to obtain the desired zinc(II) complex **5** in 86% yield (Scheme 2).



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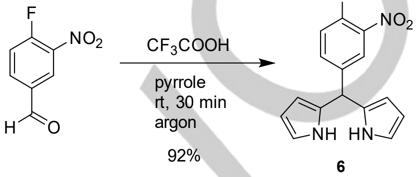
Scheme 2. Synthesis of the zinc porphyrin **5**.

The zinc(II) complex was subsequently reacted with *n*-butylamine and 1-butanol. However, only the starting material was recovered, and no substitution products were isolated (for details see Supporting Information). Hence, in contrast to the multitude of S_NAr reactions that have been described for the pentafluorophenyl substituent, the trifluorophenyl group is unsuitable for *p*-fluorine exchange under the conditions typically used for the pentafluorophenyl substituent.

Based on these findings, the investigations then focused on the 4-fluoro-3-nitrophenyl moiety. The 4-fluoro-3-nitrophenyl group has received little attention as a substituent in BODIPYs and porphyrinoids. Only a few reports incorporating a 4-fluoro-3-nitrophenyl group as part of BODIPYs and porphyrins have appeared.[33,45,46] Apart from some preliminary work related to the 5-(4-fluoro-3-nitrophenyl)dipyrromethene carried out in our group,[46] to the best of our knowledge only one publication has appeared on the S_NAr of 4-fluoro-3-nitrophenyl-substituted BODIPYs. Volkova and co-workers carried out substitutions on the 4-fluoro-3-nitrophenyl group of a BODIPY with amines and cyclic polyamines, however, this procedure required using quite harsh reaction conditions.[33] In the first step, the dipyrromethane **6** carrying the 4-fluoro-3-nitrophenyl substituent was synthesized from 4-fluoro-3-nitrobenzaldehyde and pyrrole according to our recently published procedure (Scheme 3).[46]



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Scheme 3. Synthesis of 5-(4-fluoro-3-nitrophenyl)dipyrromethane **6**.

This dipyrromethane **6**, unlike its 5-(3,4,5-trifluorophenyl)-substituted congener, was found to react readily with amines and hence served as the precursor for the synthesis of a wide range of amino-substituted dipyrromethanes (Table 1). In contrast to the harsher reaction conditions described by Volkova *et al.* (boiling acetonitrile) for the reaction with BODIPYs,[33] milder reaction conditions were employed for the S_NAr of dipyrromethane **6** with primary amines. In most cases, compound **6** was simply treated with an excess of the corresponding amine under solvent-free conditions. Using an excess of the amine also ensured a shift to the desired products. An inert gas atmosphere was used to prevent oxidation of the dipyrromethane. In all cases, the desired amino-substituted dipyrromethanes **7**-**14** (Table 1) were obtained in good to excellent yields, without the need for heating or catalytic support. All substitutions are performed at room temperature. Surprisingly, the reactions occurred in most cases within 1 hour. This is in contrast to S_NAr with amines on porphyrinoids with pentafluorophenyl moieties, which usually require elevated temperatures and longer reaction times.[47,48] These observations indicate that the 3-nitro group has a strong influence on the S_NAr of the 4-fluoro moiety, with high yields and short reaction times being facilitated by the electron-withdrawing character of the nitro group. Due to the similarities to the classical Meisenheimer complexes, a comparable stabilization of the intermediate after the attack of the nucleophile is conceivable. The stabilizing effect and the electron-withdrawing influence of the nitro group in such Meisenheimer complexes has been well studied in the literature.[49,50,51] In the nucleophilic substitution of **6**, nearly quantitative yields were achieved with amines carrying shorter residues, irrespective of additional functional groups, *e.g.,* the hydroxyl group or a prop-2-ynyl moiety (Table 1, entry 6 and 4). Amines carrying longer side chains still provided high yields (Table 1, entry 1 and 7). The reaction with the less nucleophilic aniline (Table 1, entry 8) required a prolonged reaction time and the addition of triethylamine to ensure a shift of the equilibrium

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towards the product; by this the successful formation of **14** was finally achieved. However, the product still contained aniline, which could not be completely removed.

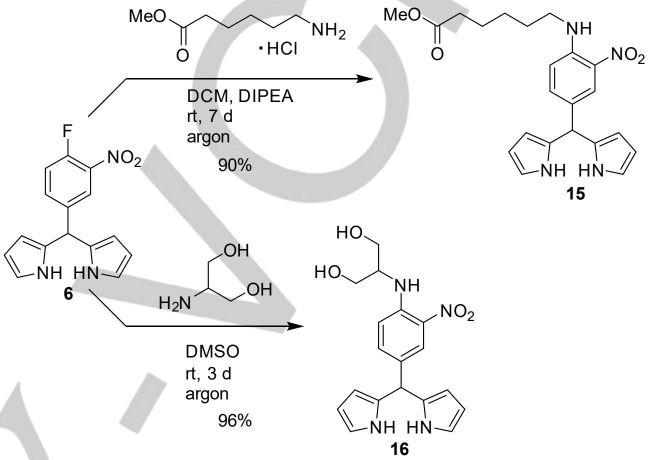
Table 1. Nucleophilic aromatic substitutions of **6** with amines.

Entry	Product	Time [h]	Yield [%]
1	**7**	1	87
2	**8**	48	61
3	**9**	1	95
4	**10**	1	96
5	**11**[a]	1	92
6	**12**	1	99
7	**13**	1	60
8[b]	**14**	30	63[c]

[a] The synthesis of **11** has been described in a previous publication.[46] [b] Triethylamine was added to ensure a shift to the product. [c] Approximate yield; product contained aniline which could not be completely removed.

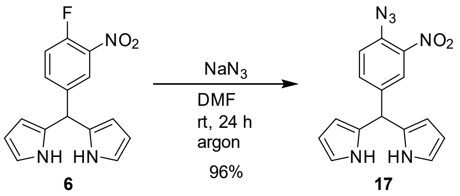
Besides primary amines with short residues, examples with the bulkier cyclohexyl group and a secondary amine (dibutylamine) were included. The increased reaction time in the case of **8** may be due to higher steric hindrance resulting from the two butyl residues (Table 1, entry 2). The functional groups introduced allow subsequent reactions, *e.g.*, the alkynyl groups give access to 1,3-dipolar cycloaddition reactions (“click” chemistry).[52] The hydroxyl groups and additional amino groups influence the polarity and solubility of the compounds. In fact, products **12** and **13** showed a significantly better solubility in *e.g.* methanol than the other functionalized dipyrromethanes.

In the case of solid amines, the reaction still works at room temperature in a suitable solvent, as exemplified by the reaction of **6** with methyl 6-aminohexanoate and serinol (Scheme 4). In both cases, the amino-substituted dipyrromethanes (**15** and **16**) were obtained in 90 and 96% yield, respectively. In the synthesis of **15**, *N*,*N*-diisopropylethylamine (DIPEA) was used to generate the free amine from the hydrochloric acid salt.



Scheme 4. Syntheses of the amino-substituted dipyrromethanes **15** and **16**.

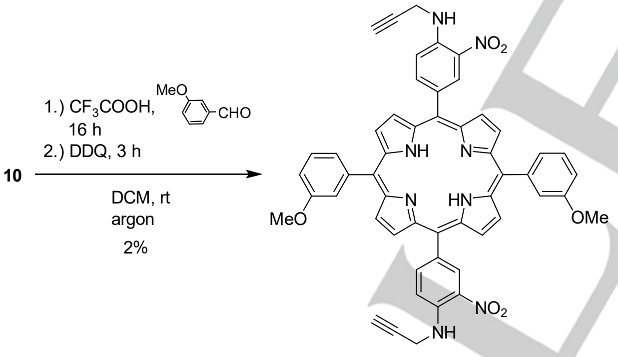
To increase the variety of nucleophiles, the introduction of an azide group was also tested. Under an argon atmosphere and at room temperature, sodium azide was added to compound **6** in DMF. After stirring for 24 h the azido-functionalized dipyrromethane **17** was obtained in excellent yield (Scheme 5), showing that both functional groups for the “click” chemistry, azide and alkynyl, can easily be introduced by S$_N$Ar into dipyrromethene **6**.



Scheme 5. Synthesis of the azido-substituted dipyrromethane **17**.

Alcohols are well established as suitable nucleophiles for S$_N$Ar, *e.g.*, in substitution reactions of the pentafluorophenyl group.[32a,28,47] Therefore, alcohols were also tested as possible nucleophiles for the fluorine exchange in the *p*-position. In comparison to other nucleophiles, alcohols are less nucleophilic and must be converted into their alkoxide. The deprotonated alcohol possesses a much stronger nucleophilic character. Often, metal hydrides have been used for their *in situ* generation.[32c,48] On the other hand, metal hydrides constitute fairly harsh conditions, with low yields being observed in some cases.[32c,54] A milder variant for the synthesis of alkoxides requires the addition of finely powdered potassium hydroxide (to increase the surface area) in THF or DMSO. The successful functionalization of the pentafluorophenyl group with various alcohols in the respective dipyrromethane and in diverse porphyrinoids has been reported.[28,55] Analogously to these reaction conditions, 1-butanol (in excess) was reacted with **6** and potassium hydroxide at room temperature for 24 h. While multiple unidentified products were formed in the reaction mixture, formation of the expected butyloxy-substituted dipyrromethane could not be observed (see the Supporting Information). This is most probably due to side reactions occurring between the alkoxide/hydroxide and the nitro group as mentioned in the literature for other nitro-substituted compounds.[56,57]

meso-Substituted dipyrromethanes are largely applied as building blocks in the synthesis of '*trans*' 5,15-A_2B_2 porphyrins and 5,15-A_2B corroles. The use of such synthons with a pre-determined arrangement of substituents increases the yield of the '*trans*'-A_2B_2 porphyrin and A_2B corrole, respectively, and decreases the yields of other possible tetrapyrroles which are usually observed as by-products in mixed condensation reactions.[58] Therefore, the new dipyrromethanes **7**, **9**, and **10** were investigated for their suitability as starting compounds for '*trans*'-A_2B_2 porphyrin synthesis. The dipyrromethanes were reacted in dichloromethane (DCM) under TFA acid catalysis with 3-methoxybenzaldehyde followed by oxidation with DDQ (2,3-dichloro-5,6-dicyano-*p*-benzoquinone) (see the example of dipyrromethane **10** in Scheme 6).[21a]



18

and other porphyrins

Scheme 6. Condensation of the pre-functionalized dipyrromethane **10** with 3-methoxybenzaldehyde.

However, with dipyrromethanes **7** and **9**, the expected '*trans*'-A_2B_2 porphyrins could not be separated by column chromatography. Instead, complex porphyrin mixtures were obtained. In the case of dipyrromethane **10**, the expected '*trans*'-A_2B_2 porphyrin **18** was isolated in only a 2% yield (Scheme 6). Other porphyrins were obtained as mixtures and were identified (*via* NMR and MS) as products (A_4, A_3B, and AB_3 porphyrins) that would typically arise from the mixed condensation reaction of the two aldehydes and pyrrole.

The increased formation of the by-products (A_4, A_3B, and AB_3 porphyrins) can be rationalized by the 'scrambling' mechanism. During 'scrambling', catalytic amounts of acid lead to an acidolysis of the porphyrin-precursor, *e.g.*, the dipyrromethane, the resulting fragments recombining to new cyclic compounds (porphyrinogens with a different substituent configuration). Afterward, the recombined compounds are oxidized and result in the observed porphyrin mixture.[59] The formation of product mixtures in porphyrin synthesis due to 'scrambling' has been reported for phenyl substituents with electron-donating substituents.[60,61] The amount of 'scrambling' can sometimes be reduced by maintaining certain reaction conditions, *e.g.* by decreasing the reaction temperature or by adjusting a slow reaction rate. Alternatively, dipyrromethanes with sterically demanding or electron withdrawing substituents in the meso-position can be employed.[25,59,61] In the present case, the electron-donating effect of newly introduced amino group in the *p*-phenyl-position of the dipyrromethane probably 'overcompensates' the stabilizing effect of the electron-withdrawing nitro group, thereby favoring the acidolysis of the dipyrromethane.

Dipyrromethanes **7** and **9** were also tested in a condensation reaction to yield corroles employing the reaction conditions developed by Gryko and Koszarna; *i.e.* the corresponding dipyrromethanes were reacted with 3-methoxybenzaldehyde in a water/MeOH mixture[40] under hydrochloric acid catalysis followed by oxidation with DDQ. However, again the dipyrromethanes proved to be unsuitable for this condensation reaction; no corrole could be isolated (for details see Supporting Information).

To experimentally verify the effect of the amino group on the condensation reaction, the '*trans*'-A_2B_2-porphyrin and the A_2B-corrole synthesis were repeated, this time using the 4-fluoro-3-nitrophenyl-substituted dipyrromethane **6**, which lacks the amino group, and 3-acetoxybenzaldehyde (Scheme 7).

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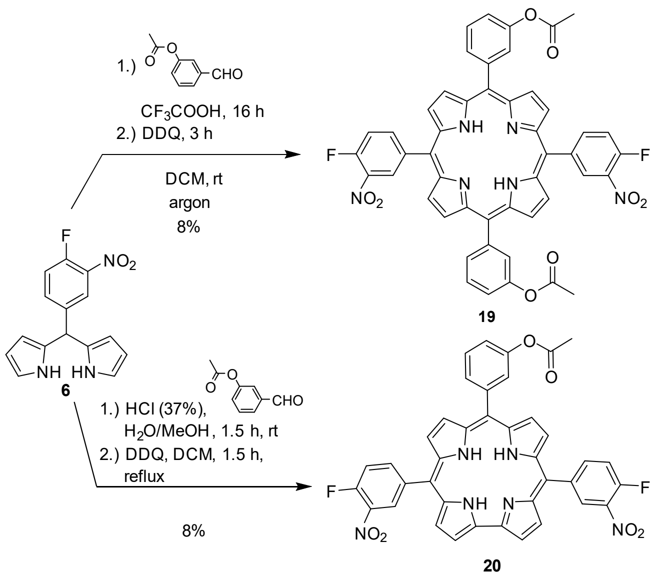
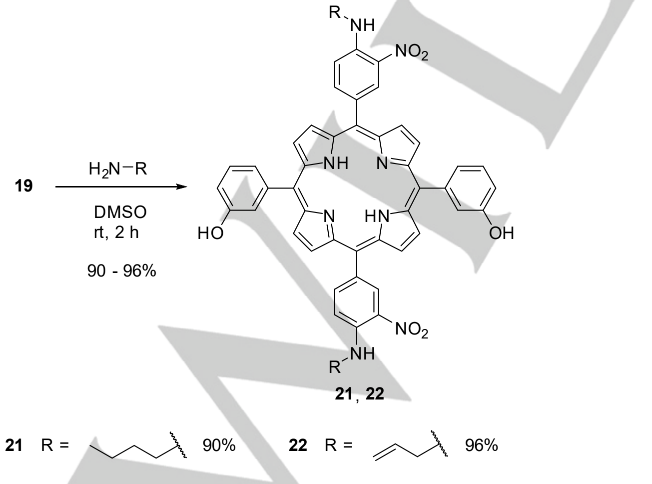


Scheme 7. Condensation of **6** with 3-acetoxybenzaldehyde to form '*trans*'-A_2B_2 porphyrin and A_2B corrole.

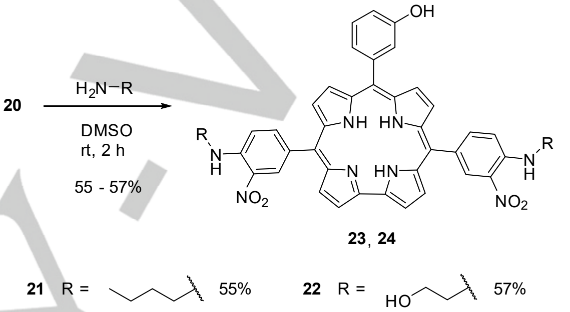
Indeed, in this case, the corresponding porphyrin **19** and the corrole **20** were obtained successfully in 8% yield for both compounds (Scheme 7). Other porphyrins were detected in significantly lower quantities. The successful synthesis of porphyrin **19** using the 4-fluoro-3-nitrophenyl-substituted dipyrromethane **6** indicates that the amino group is indeed responsible for the high degree of 'scrambling' observed with dipyrromethanes **7**,**9**, and **10**. Finally, the *p*-fluorine substitution with amines was performed with porphyrin **19** and corrole **20**. Porphyrin **19** was reacted with an excess of the respective primary amine in DMSO. The reactions proceeded in short reaction time and without any additional base at room temperature (Scheme 8).



Scheme 8. Nucleophilic aromatic substitution of **19** with amines.

The desired substituted porphyrins were obtained as expected. In these reactions, a simultaneous removal of the acetoxy protection group was observed, yielding the hydroxyl-substituted compounds. This cleavage of an acetoxy group *via* nucleophilic attack of an amine is well-known and has previously been described in the S_NAr reactions with amines on pentafluorophenyl-substituted porphyrins.[62,63,64] Excellent yields were observed when using *n*-butylamine and allylamine as nucleophiles (Scheme 8).

In a similar set of experiments, corrole **20** was reacted with a large excess of the primary amine in DMSO. Again, the S_NAr proceeded with a short reaction time and without any additional base, with the acetoxy group being simultaneously removed (Scheme 9).



Scheme 9. Nucleophilic aromatic substitution of **20** with amines.

After isolation and purification, the functionalized porphyrins and corroles **21**-**24** showed a poor solubility in common solvents (chloroform, acetone, DMSO, THF). Porphyrins **21** and **22** were therefore dissolved in deuterated acetic acid (forming the porphyrin dication) for NMR characterization. Corroles **23** and **24**, too, exhibited a poor solubility in common NMR solvents. Even in deuterated acetic acid the solubility was not sufficient to allow a characterization by NMR.

Dipyrromethanes have also extensively been employed in the synthesis of BODIPYs. Therefore, it seemed feasible to investigate the transformation of dipyrromethane **6** and its amino-substituted congeners (**6**-**16**) into BODIPYs. The reactions were performed according to the well-known three-step, one-pot procedure, involving oxidation to the dipyrromethene, deprotonation with a base, and finally reaction with $BF_3 \cdot OEt_2$ complex.[23,24,65] All meso-substituted dipyrromethanes were successfully converted into the corresponding BODIPYs (Table 2). Except for **29** (phenylamino substituent) and **33** (4-aminobutylamino substituent), all 8-substituted BODIPYs were obtained in good yields from their pre-functionalized dipyrromethane precursors (Table 2). Interestingly, in the case of dipyrromethane **12** the reaction yielded a mixture of product (**34**) and starting material, when DCM was used as a solvent. The expected BODIPY **34** was finally obtained in pure form by changing the solvent from DCM to THF. The experiments show that the amino- and azido-substituted dipyrromethanes provide an efficient entry for the synthesis of 8-substituted BODIPYs. Notably, the BODIPYs **33**

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and **34** showed good solubility in methanol, comparable to the good solubility of the functionalized dipyrromethanes **12** and **13** in polar solvents.

Table 2. Transformation of pre-functionalized dipyrromethanes into BODIPYs.

Entry	Starting Material	Substituent (R)	Solvent	Product	Yield [%]
1	**6**		DCM	**25**	25
2	**7**		DCM	**26**	38
3	**8**		DCM	**27**	41
4	**9**		DCM	**28**	20
5	**14**		DCM	**29**	4[a]
6	**11**		DCM	**30**[b]	39
7	**10**		DCM	**31**	44
8	**15**		DCM	**32**	33
9	**13**		DCM	**33**	1
10	**12**		DCM	**34**	n/a[c]
11	**12**		THF	**34**	25
12	**17**		DCM	**35**	26

[a] The yield refers to the entire reaction sequence, including functionalization of **6** with aniline. [b] The synthesis of **30** has been described in a previous publication.[46] [c] Obtained as a mixture (see text).

The absorption and emission maxima of **25**-**35**, showed only little variance (see Supporting Information). These minor differences in the spectra indicate that the functionalization in the *p*-position of the phenyl-substituent has only limited influence on the basic photophysical properties. The lower effect of meso-phenyl substitutions on the photophysical properties, compared to a substitution in 3,5- or 2,6-position of the BODIPY core, is well-known for other functionalized BODIPYs.[28] However, increased singlet oxygen quantum yields for meso-*p*-aminophenyl-substituted BODIPYs have been reported.[66]

For the 8-(4-aminobutyl-3-nitrophenyl)-substituted BODIPY **26**, crystals suitable for X-ray single crystal structure determination were obtained (Figure 1, Figure S1 shows the structure of **26** with all non-hydrogen atoms labeled). BODIPY **26** was solved in an orthorhombic space group with eight molecules present in the unit cell. One important feature is the tilt angle, which describes the orientation of the phenyl ring relative to the BODIPY framework. For **26** the tilt angle for these two structural elements is 44.5(8)°. It is probably because of this twisting of the phenyl ring relative to the BODIPY framework that the different substitutions in the *p*-position of the phenyl ring exert only a minor influence on the absorption and fluorescence spectra of the BODIPYs.

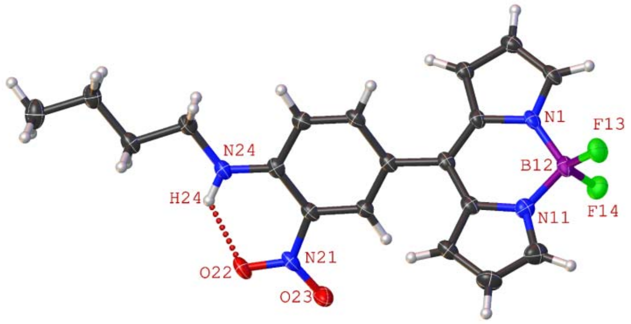

Figure 1. Molecular structure of **26** in the crystal showing the intramolecular interaction between N(24)–H(24)···O(22) (1.980(2) Å, 130.4(1)°) (thermal displacement 50%).

In the structure of **26**, the presences of an intramolecular the formation of a hydrogen bond between N(24)–H(24)···O(22) (1.980(2) Å, 130.4(1)°) is observed (Figure 1). This bond holds the nitro group in a co-planar conformation with regards to the benzene ring. This rigidity imposed on the amino group by hydrogen bonding to the nitro group may be one reason for the lower solubility observed for some of the compounds (see above). Additionally, in this structure the nitro group is seen to participate in a weak intermolecular hydrogen bond with the pyrrole ring through C(2)–H(2)···O(23) (2.509(2) Å, 145.2(2)°) and C(3)–H(3)···O(22) (2.579(4) Å, 126.7(2)°) which forms a linear network between the individual molecules (Figure S2). A second intermolecular interaction motif is seen is a bifurcated interaction between the fluorine atoms F14 pyrrole hydrogen atoms H9 (C(9)–H(9)···F(14) (2.472(2) Å, 150.7(2)°)) on one side and the phenyl hydrogen atoms H16 (C(16)–H(16)···F(14) (2.496(2) Å, 158.5(2)°)) on the other (Figure S3). Both these interactions cause the individual molecules to be rotated at ~90° to each other to form the twisted stacking pattern seen in Figure 2. In this arrangement, the nitro groups are stacked above each other.

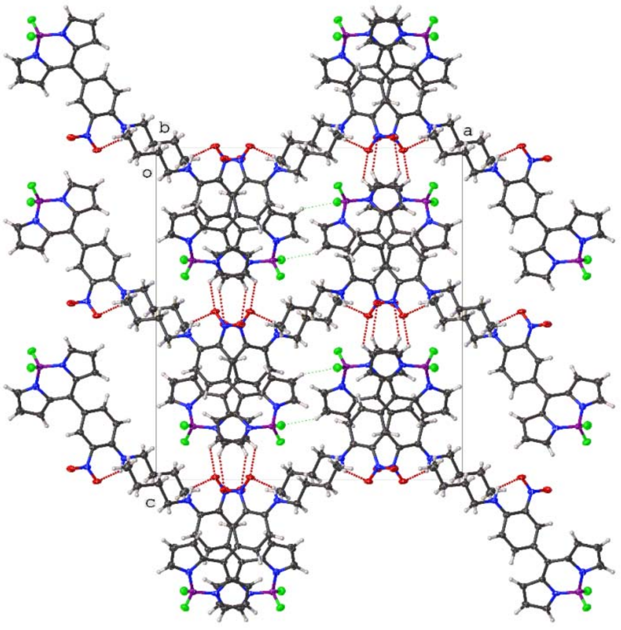

Figure 2. Crystal packing of **26** looking down the *b*-axis, showing the orientation of the BODIPY molecules.

The further functionalization of BODIPYs in the 3,5(*α*)- and 2,6(*β*)-positions to change their photochemical or physicochemical properties is a field of current interest.[67,68,69] Substituents comprise among others heavy atoms, *e.g.* bromine or iodine,[70] thiols,[71] and amines[72] as well as C-H acidic compounds, *e.g.* malonic esters.[73] C–H-acidic compounds readily react with the 3- and 5-position of BODIPYs *via* selective oxidative nucleophilic substitution of the hydrogen atom (ONSH), as first described by Dehaen *et al*.[46,73] Following our preliminary results in a previous publication,[46] investigations of the ONSH with dimethyl malonic ester on 4-amino-3-nitrophenyl-substituted BODIPYs were carried out with a number of other amino-substituted BODIPYs (Table 3). Following the published procedure,[46,73] the corresponding BODIPY was dissolved in DMF and a mild base (sodium carbonate) and a slight excess of dimethyl malonic ester were added. Atmospheric oxygen served as an oxidizing reagent (Table 3). All desired *α*-substituted BODIPYs (**36**-**40**) were formed as expected and in reasonable yields.

Table 3. Reactions of BODIPYs with dimethyl malonic ester.

Entry	Starting Material	Substituent (R)	Product	Yield [%]
1	**27**		**36**	53
2	**28**		**37**	35
3	**30**		**38**[a]	43
4	**31**		**39**	58
5	**34**		**40**	52

[a] The synthesis of **38** has been described in a previous publication.[46]

Apart from their use as ligands for boron difluoride, dipyrromethenes (dipyrrins) have also found attention as ligands for other metal ions, for example, ruthenium(II).[74,75] Therefore, it was investigated whether the new 4-amino-3-nitrophenyl-substituted dipyrromethanes could be employed in this context. The synthesis of the metal complexes initially requires the synthesis of the respective dipyrrins in pure form. Hence, selected amino-substituted dipyrromethanes (**7**, **11**, **12**, **15**, and **16**) were oxidized to the dipyrrins (Table 4). In these oxidations it was found that *p*-chloranil gave significantly higher yields than the stronger oxidant DDQ. Using *p*-chloranil, all meso-substituted dipyrromethanes were converted to their corresponding dipyrrins and obtained in good to excellent yields.

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Table 4. Oxidation of amino-substituted dipyrromethanes to the corresponding dipyrrins.

Entry	Starting Material	Substituent (R)	Product	Yield [%]
1	**7**		**41**	74
2	**11**		**42**[a]	85
3	**15**		**43**	65
4	**12**		**44**	98
5	**16**		**45**	75

[a] The synthesis of **42** has been described in a previous publication.[46]

The synthesis of the corresponding ruthenium complexes requires a base for deprotonating the dipyrrin and the di(μ-chlorido)bis[chlorido(*p*-cymene) ruthenium(II)].[76] Hence, the dipyrromethenes (**41**-**45**) were reacted with DIPEA and the di(μ-chlorido)bis[chlorido(*p*-cymene) ruthenium(II)] to obtain the corresponding chlorido(η^6-*p*-cymene)(dipyrrinato) ruthenium(II) complexes (**46**-**50**) (Table 5). All chlorido(η^6-*p*-cymene)(dipyrrinato) ruthenium(II) complexes were formed as expected in good yields.

Table 5. Synthesis of chlorido(η^6-*p*-cymene)(dipyrrinato) ruthenium(II) complexes.

Entry	Starting Material	Substituent (R)	Product	Yield [%]
1	**41**		**46**	43
2	**42**		**47**	44
3	**43**		**48**	48
4	**44**		**49**	43
5	**45**		**50**	42

For the {5-[4-(*N*-butylamino)-3-nitrophenyl]dipyrrinato}chlorido-(η^6-*p*-cymene) ruthenium(II) complex **46**, crystals suitable for X-ray single crystal structure determination were obtained. The molecular structure of **46** is represented in Figure 3 (Figure S4 shows the structure of **46** with all non-hydrogen atoms labeled). Complex **46** was solved in a triclinic space group with one molecule in the asymmetric unit. The tilt angle between phenyl moiety and the dipyrrin plane is 54.0(2)°, which is a moderate increase compared to BODIPY **26**. Similar to BODIPY **26**, there is an intramolecular interaction between the amine hydrogen atom and the nitro oxygen atom at a distance of O(2)···H(4A) distance of 2.006(6) Å and a N(4)–H(4A)···O(2) angle of 134.8(2)° (Figure 3). This moiety holds the nitro group in co-planar to the phenyl ring. In the crystal packing, there are two motifs which contribute to the crystal packing. The first motif is a π-stacked interaction between the η^6-*p*-cymene moieties at a centroid···centroid distance of 3.901(1) Å and a shift distance of 1.790(1) Å (Figure S5). This results in a head-to-head interaction which is coupled by the second motif which is a head-to-head overlap of the butylamino moieties on the opposite side of the macrocycle seen in Figure S6. On the opposite side to the molecule there is C(14)–H(14)···Cl(1) interaction between the benzene ring and the chlorine atom at a distance of 2.842(8) Å and an angle of 166.4(5)°.

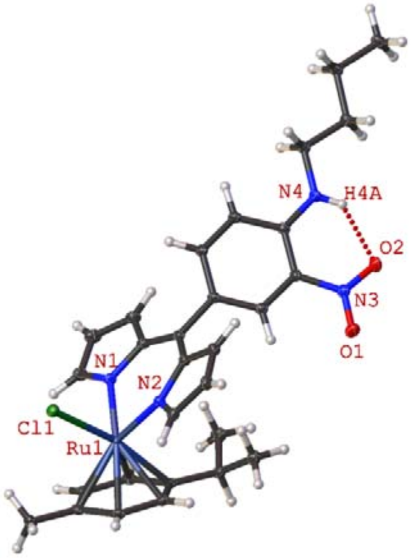

Figure 3. Molecular structure **46** in the crystal showing the intramolecular interaction between N(4)–H(4A)···O(2) (2.006(6) Å, 134.8(2)°) (thermal displacement 50 %).

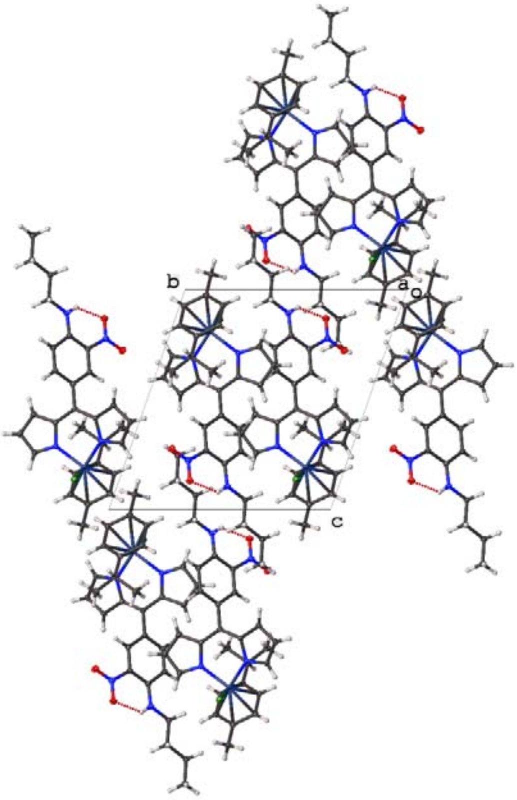

Figure 4. Crystal packing of **46** looking down the *a*-axis, showing the orientation of the dipyrrin molecules in the unit cell.

This forms a head-to-tail interaction between the molecules involving this interaction to be reciprocated between the two independent molecules (Figure S6). Combining the π-stacked interaction between the η^6-*p*-cymene moieties and the halogen-hydrogen interaction forms the basis of the crystal packing in the unit cell (Figure 4, Figure S7 shows a cross-section view of the combined interactions). In the crystal packing, while the nitro group appears to be in close contact with the butyl amino chain, no significant interactions are observed indicating this is a feature of close packing and not directive in the overall crystal packing (Figure 4).

Finally, reaction with 2,2′-bipyridine afforded the corresponding bis(2,2´-bipyridyl)(dipyrrinato) ruthenium(II) complexes.[77] Again, in all cases, the desired amino-substituted bis(2,2´-bipyridyl)(dipyrrinato) ruthenium(II) complexes (**51**-**55**) were obtained in good to excellent yields (Table 6).

Table 6. Synthesis of bis(2,2´-bipyridyl)(dipyrrinato) ruthenium(II) complexes.

Entry	Starting Material	Substituent (R)	Product	Yield [%]
1	**46**		**51**	74
2	**47**		**52**	77
3	**48**		**53**	81
4	**49**		**54**	85
5	**50**		**55**	90

Conclusions

In this publication, the potential of the 3,4,5-trifluorphenyl and the 4-fluoro-3-nitrophenyl substituent in the context of modifying

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porphyrins, corroles, BODIPYs, and their dipyrromethane precursors *via* S_NAr was evaluated. The 3,4,5-trifluorphenyl group proved to be unsuitable for a nucleophilic modification under conditions commonly applied for this reaction. The 4-fluoro-3-nitrophenyl substituent, however, readily reacted with amines under mild reaction conditions, affording the respective 4-amino-3-nitrophenyl-substituted porphyrins, corroles, and dipyrromethanes. The 4-amino-3-nitrophenyl-substituted dipyrromethanes exhibited extensive 'scrambling' in the synthesis of '*trans*'-A_2B_2-porphyrins. In this case functionalization *via* S_NAr on the stage of the 4-fluoro-3-nitrophenyl-substituted tetrapyrrole is preferable. The 4-amino-3-nitrophenyl-substituted dipyrromethanes were easily converted to the corresponding BODIPYs in good yields. Further modification of these BODIPYs *via* ONSH with C-H acidic malonate ester was possible. Moreover, the 4-amino-3-nitrophenyl-substituted dipyrromethanes could be oxidized to the respective dipyrromethenes which can serve as functionalized dipyrrinato ligands in metal complexes as exemplified with the synthesis of bis(bipyridyl)(dipyrrinato) ruthenium(II) complexes.

Experimental Section

General

All reactions were performed in standard round bottom flasks. Air-sensitive reactions were carried out under an argon gas protecting atmosphere. DCM, *n*-pentane, and methanol were purchased and used as received. Other solvents were purchased and distilled at reduced pressure. Purchased chemicals were used as received without further purification. All liquid reagents were added through syringes. Reactions were monitored by thin-layer chromatography (Merck, TLC Silica gel 60 F_{254} and visualized under UV light (254 nm and 366 nm). Flash column chromatography was performed on silica gel (Fluka silica gel 60M, 40-63µm). NMR spectra were recorded with JEOL ECX400, JEOL ECP500, Bruker Avance500, and Bruker Avance700. Multiplicity of the signals was assigned as follows: s = singlet, br s = broad singlet, d = doublet, t = triplet, dd = doublet of doublets, dt = doublet of triplets, dq = doublet of quartets, tt = triplet of triplets, ddd = doublet of doublets of doublets, ddt = doublet of doublets of triplets, sept = septet, m = multiplet, m_c = centered multiplet. Chemical shifts are reported relative to $CDCl_3$ (^{1}H: δ = 7.26 ppm, ^{13}C: δ = 77.2 ppm), acetone-d_6 (^{1}H: δ = 2.05 ppm, ^{13}C: δ = 29.8 ppm), acetic acid-d_4 (^{1}H: δ = 3.31 ppm, ^{13}C: δ = 49.0 ppm, THF-d_8 (^{1}H: δ = 3.58 ppm, ^{13}C: δ = 67.6 ppm), DMSO-d_6 (^{1}H: δ = 2.50 ppm, ^{13}C: δ = 39.5 ppm), and CD_2Cl_2 (^{1}H: δ = 5.32 ppm, ^{13}C: δ = 53.8 ppm). All ^{13}C NMR spectra are proton-decoupled and coupling constants are given in hertz (Hz). For a detailed peak assignment 2D spectra were measured (COSY, HMBC, and HMQC). HRMS analyses were carried out on an Agilent Technologies 6210 ESI-TOF (electrospray ionization, time of flight) instrument. IR spectra were measured with a JASCO FT/IR 4100 spectrometer equipped with a PIKE MIRacle^{TM} ATR instrument. UV/Vis spectra were recorded on a SPECORD S300 UV/Vis spectrometer (Analytic Jena) in quartz cuvettes (1 cm length). The fluorescence spectra of the BODIPYs were recorded with a JASCO FP 6500 spectrofluorometer in quartz cuvettes (1 cm length). Specified melting points were recorded on a Reichert Thermovar Apparatus and are not corrected. Compounds **6**, **11**, **30**, **38**, and **42** were prepared according to the literature.[46]

General Procedures

Preparation of 5-(3,4,5-trifluorophenyl)dipyrromethane (1). 3,4,5-Trifluorobenzaldehyde (10.00 g, 62.46 mmol, 1 equiv.) was dissolved in 150 mL pyrrole. Trifluoroacetic acid (480 µL, 6.25 mmol, 0.1 equiv.) was added and the reaction mixture was stirred under an argon atmosphere for 30 min at rt. After the indicated time, the remaining pyrrole was removed at 60 °C under reduced pressure. The crude product was purified by column chromatography (DCM/*n*-hexane = 3:1, v/v). Product **1** was obtained as a grey solid (15.02 g, 54.36 mmol, 87%). m.p. 70–78 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.41 (s, 1 H, H_{meso}), 5.89–5.90 (m, 2 H, $H_{pyrrole}$), 6.17–6.19 (m_c, 2 H, $H_{pyrrole}$), 6.73–6.74 (m, 2 H, $H_{pyrrole}$), 6.83 (dd, *J* = 8.4, 6.5 Hz, 2 H, Ar-H), 7.92 (br s, 2 H, NH) ppm. ^{13}C NMR (176 MHz, $CDCl_3$): δ = 43.4 (C_{meso}), 107.9 ($C_{pyrrole}$), 108.9 ($C_{pyrrole}$), 112.5 (dd, *J* = 16.7, 5.0 Hz, Ar-C_{ortho}), 118.1 ($C_{pyrrole}$), 130.95 ($C_{pyrrole}$), 138.7 (q, *J* = 6.2 Hz, Ar-C_{ipso}), 138.8 (dt, *J* = 250.9, 15.3 Hz, Ar-C_{para}), 151.3 (ddd, *J* = 250.2, 10.0, 4.0 Hz, Ar-C_{meta}) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -162.40 (tt, *J* = 20.9, 6.4 Hz, 1 F, CF_{para}), -133.90 (dd, *J* = 20.8, 8.0 Hz, 2F, CF_{meta}) ppm. IR (ATR): $\tilde{\nu}$ = 3380 [ν(NH)], 1610 [ν(C=N)], 1515 [ν(Ar-C)], 1440 [δ(Ar-C)], 1225 [ν(CF)], 715 [δ(HC=CH)] cm^{-1}.

Preparation of 8-(3,4,5-trifluorophenyl)-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene (2). Dipyrromethane **1** (2.21 g, 8.00 mmol, 1 equiv.) was dissolved in 15 mL of DCM. DDQ (1.82 g, 8.00 mmol, 1 equiv., suspended in 5 mL DCM) was added and the reaction mixture was stirred for 5 min at rt. After the indicated time, DIPEA (9.52 mL, 56.00 mmol, 7 equiv.) was added and stirred for 15 min. Afterwards, $BF_3 \cdot OEt_2$ (6.91 mL, 56.00 mmol, 7 equiv.) was added and the reaction mixture was stirred for additional 20 min at rt. Water was added to the mixture and extracted with DCM several times. The combined organic phases were washed again with water. The organic layer was dried with Na_2SO_4, filtrated, and evaporated to dryness. After purification by column chromatography (silica gel, DCM), product **2** was obtained as a red solid (157 mg, 0.49 mmol, 6%). m.p. 88–94 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.59 (d, *J* = 4.4 Hz, 2 H, $H_{pyrrole}$), 6.91 (d, *J* = 4.3 Hz, 2 H, $H_{pyrrole}$), 7.25 (dd, *J* = 7.5, 6.4 Hz, 2 H, Ar-H), 7.98 (s, 2 H, $H_{pyrrole}$) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 115.1 (dd, *J* = 17.1, 6.1 Hz, Ar-C_{ortho}), 119.5 ($C_{pyrrole}$), 129.5 (dt, *J* = 8.1, 4.9 Hz, Ar-C_{ipso}) 131.3 ($C_{pyrrole}$), 134.3 ($C_{pyrrole}$), 141.5 (dt, *J* = 257.9, 15.1 Hz, Ar-C_{para}), 142.99 (C_{meso}), 145.7 ($C_{pyrrole}$), 151.3 (ddd, *J* = 253.4, 10.1, 4.1 Hz, Ar-C_{meta}) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -162.39 (t, *J* = 21.3 Hz, 1 F, CF_{para}), -144.81 – -144.58 (m_c, 2 F, BF_2), -133.88 (dd, *J* = 19.7, 9.7 Hz, 2 F, CF_{meta}) ppm. HRMS: *m/z* calcd. for $C_{15}H_8BF_5N_2Na^+$ ([M+Na] $^+$) 345.0593, found 345.0609. IR (ATR): $\tilde{\nu}$ = 3125 [ν(NH)], 1610 [ν(C=N)], 1530 [ν(Ar-C)], 1480 [δ(Ar-C)], 1225 [ν(C-F)], 1070 [ν(B-F)], 725 [δ(HC=CH)] cm^{-1}. UV/Vis (DCM): λ_{max} [log (ε (L mol^{-1}cm^{-1})]: 508 nm [4.24]. Fluorescence (DCM): $\lambda_{em.}$ = 531 nm at $\lambda_{ex.}$ = 490 nm.

Preparation of 5,15-bis(3-acetoxyphenyl)-10,20-bis(3,4,5-trifluorophenyl)porphyrin (3). Dipyrromethane **1** (2.07 g, 7.50 mmol, 1 equiv.) was dissolved together with 3-acetoxybenzaldehyde (1.23 g, 7.50 mmol, 1 equiv.) in 1.5 L of DCM. Trifluoroacetic acid (570 µL, 7.50 mmol, 1 equiv.) was added, the reaction mixture was stirred under an argon atmosphere for 19 h at rt. For the reaction time, the flask was shielded from ambient light with aluminum foil. After the indicated time, DDQ (4.16 g, 15.00 mmol, 2 equiv., suspended in 50 mL DCM) was added and stirred again under an argon atmosphere for 2.5 h at rt. Triethylamine (1.00 mL, 7.50 mmol, 2 equiv.) was added to neutralize the reaction mixture. The mixture was concentrated under reduced pressure, and under UV light the red fluorescent product was isolated by filtration (DCM, then DCM/EtOAc = 9:1, v/v) over a silica gel filled glass frit. After column chromatography (DCM/*n*-hexane = 9:1, v/v, then DCM) and recrystallization (DCM/*n*-pentane), product **3** was obtained as a purple

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solid (356 mg, 0.43 mmol, 12%). m.p. > 280 °C. ^{1}H NMR (700 MHz, CDCl$_3$): *δ* = -2.89 (s, 2 H, NH), 2.42 (s, 6 H, Me), 7.59 (ddd, *J* = 8.4, 2.3, 1.0 Hz, 2 H, Ar$_1$-H$_{ortho}$), 7.80 (dd, *J* = 8.4, 7.4 Hz, 2 H, Ar$_1$-H$_{meta}$), 7.88 (t, *J* = 6.8 Hz, 4 H, Ar$_2$-H$_{ortho}$), 8.01 (s, 2 H, Ar$_1$-H$_{ortho}$), 8.11 (d, *J* = 7.3 Hz, 2 H, Ar$_1$-H$_{para}$), 8.88 (d, *J* = 4.7 Hz, 2 H, β-H), 9.01 (d, *J* = 4.7 Hz, 2 H, β-H) ppm. ^{13}C NMR (376 MHz, CDCl$_3$): *δ* = 21.4 (Me), 116.9 (Ar$_1$-C$_{meso}$), 118.9 (dd, *J* = 16.2, 4.3 Hz, Ar$_2$-C$_{ortho}$), 119.9 (Ar$_1$-C$_{ipso}$), 121.5 (Ar$_1$-C$_{ortho}$), 127.9 (Ar$_1$-C$_{meta}$), 128.2 (Ar$_1$-C$_{ortho}$), 132.3 (Ar$_1$-C$_{para}$), 137.9–138.0 (m, Ar$_2$-C$_{ipso}$), 140.4 (dt, *J* = 253.8, 15.1 Hz, Ar$_2$-C$_{para}$), 143.0 (Ar$_2$-C$_{meso}$), 149.5 (Ar$_1$-C$_{OAc}$), 149.8 (ddd, *J* = 251.4, 9.7, 3.9 Hz, Ar$_2$-C$_{meta}$), 169.8 (CO) ppm. ^{19}F NMR (376 MHz, CDCl$_3$): *δ* = -161.14 – -160.99 (m, 2 F, CF$_{para}$), -135.68 (dd, *J* = 20.4, 6.9 Hz, 4 F, CF$_{meta}$) ppm. HRMS: *m/z* calcd. for $C_{48}H_{29}F_6N_4O_4^+$ ([M+H]$^+$) 839.2088, found 839.2167. IR (ATR): $\tilde{\nu}$ = 3320 [*ν*(NH)], 1785 [*ν*(OAc)], 1620 [*ν*(C=N)], 1525 [*ν*(Ar-C)], 1475 [*δ*(Ar-C)], 1200 [*ν*(CF)], 725 [*δ*(HC=CH)] cm^{-1}. UV/Vis (DCM): *λ*$_{max}$ [log (*ε* (L mol^{-1}cm^{-1})] = 417 [5.40], 513 [4.28], 547 [3.98], 598 [3.83], 645 nm [3.53].

Preparation of 10-(3-acetoxyphenyl)-5,15-bis(3,4,5-trifluorophenyl)-corrole (4). Dipyrromethane **1** (2.07 g, 7.50 mmol, 2 equiv.) was suspended with 3-acetoxybenzaldehyde (615 mg, 3.75 mmol, 1 equiv.) into 350 mL of a water/methanol mixture (1:1, v/v). Hydrochloric acid (18.80 mL, 37%) was added and the reaction mixture was stirred for 1.5 h at rt. After the indicated time, the reaction was extracted with DCM and the combined organic phases were washed with water. The organic layer was concentrated and dissolved in 400 mL of DCM. DDQ (2.56 g, 11.25 mmol, 3 equiv., suspended in 50 mL DCM) was added and the reaction mixture was stirred under reflux for 1 h. The mixture was concentrated under reduced pressure, and under UV light the red fluorescent product was isolated by filtration (DCM) over a silica gel filled glass frit. After column chromatography (DCM/*n*-hexane = 9:1, v/v), product **4** was obtained as a black solid (553 mg, 0.80 mmol, 21%). m.p. 238–249 °C. ^{1}H NMR (CDCl$_3$, 400 MHz): *δ* = 2.42 (br s. 3 H, Me), 7.19–8.81 (m, 16 H, Ar$_1$-H, Ar$_2$-H, β-H) ppm. Signals for the NH groups were not detected. ^{13}C NMR (CDCl$_3$, 126 MHz): The signal to noise ratio of the recorded ^{13}C NMR spectrum did not allow a meaningful interpretation. ^{19}F NMR (CDCl$_3$, 376 MHz): *δ* = -162.12 – -161.94 (m, 2 F, CF$_{para}$), -134.63 – -134.61 (m, 4 F, CF$_{ortho}$) ppm. HRMS: *m/z* calcd. for $C_{39}H_{23}F_6N_4O_2^+$ ([M+H]$^+$) 693.1720, found 693.1711. IR (ATR): $\tilde{\nu}$ = 3330 [*ν*(NH)], 1770 [*ν*(OAc)], 1610 [*ν*(C=N)], 1525 [*ν*(Ar-C)], 1120 [*ν*(CF)], 725 [*δ*(HC=CH)] cm^{-1}. UV/Vis (DCM): *λ*$_{max}$ [log (*ε* (L mol^{-1}cm^{-1})] = 418 [4.94], 585 [4.33], 632 [4.23], 648 nm [4.18].

Preparation of [5,15-bis(3-acetoxyphenyl)-10,20-bis(3,4,5-trifluoro-phenyl)porphyrinato]zinc(II) (5). Porphyrin **3** (160 mg, 0.19 mmol, 1 equiv.) was dissolved in 30 mL of a DCM/MeOH mixture (4:1, v/v), zinc(II)-acetate dihydrate (16.71 g, 76.40 mmol, 400 equiv.), and sodium acetate (1.46 g, 12.03 mmol, 60 equiv.) were added. The reaction mixture was stirred for 3 h at rt. After the indicated time, 50 mL of DCM were added and the mixture was washed with water several times. The organic phase was dried over sodium sulfate, filtered, and evaporated to dryness. The crude product was purified by column chromatography (DCM) and recrystallized (DCM/*n*-pentane). Product **5** was obtained as a pink solid (415 mg, 0.16 mmol, 96%). m. p. > 280 °C. ^{1}H NMR (CDCl$_3$, 700 MHz): *δ* = 2.36 (s, 6 H, Me), 7.53 (ddd, *J* = 8.4, 2.3, 1.0 Hz, 2 H, Ar$_1$-H$_{ortho}$), 7.78 (t, *J* = 7.9 Hz, 2 H, Ar$_1$-H$_{meta}$), 7.87 (t, *J* = 6.6 Hz, 4 H, Ar$_2$-H), 7.96–7.97 (m, 2 H, Ar$_1$-H$_{ortho}$), 8.09–8.10 (m, 2 H, Ar$_1$-H$_{para}$), 8.96 (d, *J* = 4.6 Hz, 2 H, H$_{pyrrole}$), 9.08 (d, *J* = 4.6 Hz, 2 H, H$_{pyrrole}$) ppm. ^{13}C NMR (CDCl$_3$, 176 MHz): *δ* = 21.4 (Me), 117.9 (Ar$_1$-C$_{meso}$), 118.7 (dd, *J* = 15.9, Ar$_2$-C$_{ortho}$), 120.8 (Ar$_1$-C$_{ipso}$), 121.2 (Ar$_1$-C$_{ortho}$), 127.8 (Ar$_1$-C$_{meta}$), 128.0 (Ar$_1$-C$_{ortho}$), 131.8 (C$_{pyrrole}$), 132.2 (Ar$_1$-C$_{para}$), 132.97 (C$_{pyrrole}$), 138.6 (q, *J* = 7.7 Hz, Ar$_1$-C$_{ipso}$), 140.2 (dt, *J* = 253.6, 15.3 Hz, Ar$_2$-C$_{para}$), 143.7 (Ar$_2$-C$_{meso}$), 149.4 (C$_{pyrrole}$), 149.6 (ddd, *J* = 251.4, 9.5, 3.6 Hz, Ar$_2$-C$_{meta}$), 149.8 (Ar$_1$-C$_{OAc}$), 150.5 (C$_{pyrrole}$), 169.8 (CO) ppm. ^{19}F NMR (CDCl$_3$, 376 MHz): *δ* = -161.55 (tt, *J* = 20.5, 6.2 Hz, 2 F, CF$_{para}$), -136.05 (dd, *J* = 20.5, 7.6 Hz, 4 F, CF$_{meta}$) ppm. HRMS: *m/z* calcd. for $C_{48}H_{27}F_6N_4O_4Zn^+$ ([M+H]$^+$) 901.1222, found 901.1282. IR (ATR): $\tilde{\nu}$ = 1770 [*ν*(OAc)], 1610 [*ν*(C=N)], 1525 [*ν*(Ar-C)], 1450 [*δ*(Ar-C)], 1185 [*ν*(CF)], 725 [*δ*(HC=CH)] cm^{-1}. UV/Vis (DCM): *λ*$_{max}$ [log (*ε* (L mol^{-1}cm^{-1})] = 418 [5.76], 547 nm [4.69].

General procedure for the substitution of dipyrromethane 6 with amines to obtain 3-fluoro-4-amino-substituted dipyrromethanes 7-14. Dipyrromethane **6** (1 equiv.) was dissolved in the amine (40–50 equiv.). The reaction mixture was stirred under an argon atmosphere for 1 h at rt. Afterwards, the reaction mixture was diluted with DCM and the solution was washed with water several times. The organic phase was dried over sodium sulfate, filtered, and evaporated to dryness. The crude product was purified by column chromatography.

Preparation of 5,15-bis(3-acetoxyphenyl)-10,20-bis(4-fluoro-3-nitro-phenyl)porphyrin (19). Dipyrromethane **6** (2.50 g, 8.76 mmol, 1 equiv.) was dissolved together with 3-acetoxybenzaldehyde (1.44 g, 8.76 mmol, 1 equiv.) in 1.5 L of DCM. Trifluoroacetic acid (760 µL, 8.76 mmol, 1 equiv.) was added, the reaction mixture was stirred under an argon atmosphere for 19 h at rt. For the reaction time, the flask was shielded from ambient light with aluminum foil. After the indicated time, DDQ (3.98 g, 17.52 mmol, 2 equiv., suspended in 50 mL DCM) was added and stirred again under an argon atmosphere for 2.5 h at rt. Triethylamine (1.21 mL, 8.76 mmol, 2 equiv.) was added to neutralize the reaction mixture. The mixture was concentrated under reduced pressure, and under UV light the red fluorescent product was isolated by filtration filtered (DCM, then DCM/EtOAc = 9:1, v/v) over a silica gel filled glass frit. After column chromatography (DCM/*n*-hexane = 9:1, v/v, then DCM) and recrystallization (DCM/*n*-pentane), product **19** was obtained as a purple solid (296 mg, 0.35 mmol, 8%). m. p. >280 °C. ^{1}H NMR (700 MHz, CDCl$_3$): *δ* = -2.86 (s, 2 H, NH), 2.41 (s, 6 H, Me), 7.58 (d, *J* = 8.2 Hz, 2 H, Ar$_1$-H$_{ortho}$), 7.73 (t, *J* = 9.3 Hz, 1 H, Ar$_2$-H$_{meta}$), 7.77–7.81 (m, 2 H, Ar$_1$-H$_{meta}$), 8.00 (s, 2 H, Ar$_1$-H$_{ortho}$), 8.09 (d, *J* = 8.2 Hz, 2 H, Ar$_1$-H$_{para}$), 8.46–8.48 (m, 2 H, Ar$_2$-H$_{ortho}$), 8.80 (d, *J* = 4.9 Hz, 4 H, β-H), 8.91 (d, *J* = 5.1 Hz, 2 H, Ar$_2$-H$_{ortho}$), 9.01 (d, *J* = 4.9 Hz, 2 H, β-H) ppm. ^{13}C NMR (176 MHz, CDCl$_3$): *δ* = 21.3 (Me), 116.3 (Ar$_1$-C$_{meso}$), 117.12 (d, *J* = 20.7 Hz, Ar$_2$-C$_{meta}$), 120.1 (Ar$_1$-C$_{ipso}$), 121.5 (Ar$_1$-C$_{ortho}$), 127.97 (t, *J* = 11.6 Hz, (Ar$_1$-C$_{meta}$), 128.1–128.3 (m, Ar$_1$-C$_{ortho}$), 130.7 (Ar$_2$-C$_{ortho}$), 132.4 (β-C), 132.4 (Ar$_1$-C$_{para}$), 136.02 (d, *J* = 7.2 Hz)*, 139.1 (d, *J* = 4.5 Hz)*, 140.4 (d, *J* = 7.9 Hz, Ar$_2$-C$_{ortho}$), 142.9 (Ar$_2$-C$_{meso}$), 149.5 (Ar$_1$-CH$_{OAc}$), 155.7 (d, *J* = 267.2 Hz, Ar$_2$-C$_{para}$), 169.8 (CO) ppm. *These signals could not be assigned exactly to corresponding carbon atoms. They belong to the Ar$_2$-C$_{ipso}$ and the Ar$_2$-C$_{nitro}$ of the aryl residue.^{19}F NMR (376 MHz, CDCl$_3$): *δ* = -118.36 (s, 2 F, CF) ppm. HRMS: *m/z* calcd. for $C_{48}H_{31}F_2N_6O_8^+$ ([M+H]$^+$) 857.2166, found 857.2179. IR (ATR): $\tilde{\nu}$ = 3325 [*ν*(NH)], 1760 [*ν*(OAc)], 1620 [*ν*(C=N)], 1580 [*ν*$_{as}$(NO$_2$)], 1520 [*ν*(Ar-C)], 1340 [*ν*$_{sym}$(NO$_2$)], 1195 [*ν*(CF)], 730 [*δ*(HC=CH)] cm^{-1}. UV/Vis (DCM): *λ*$_{max}$ [log (*ε* (L mol^{-1} cm^{-1})] = 420 [4.34], 515 [4.03], 549 [3.88], 590 [3.86], 646 nm [3.57].

Preparation of 10-(3-acetoxyphenyl)-5,15-bis(4-fluoro-3-nitrophenyl)-corrole (20). Dipyrromethane **6** (1.14 g, 4.00 mmol, 2 equiv.) was suspended with 3-acetoxybenzaldehyde (328 mg, 2.00 mmol, 1 equiv.) into 200 mL of a water/methanol mixture (1:1, v/v). Hydrochloric acid (10.00 mL, 37%) was added and the reaction mixture was stirred for 1.5 h at rt. After the indicated time, the reaction was extracted with DCM and the combined organic phases were washed with water. The organic layer was concentrated and dissolved in 400 mL of DCM. DDQ (3 equiv., suspended in 50 mL DCM) was added and the reaction mixture was stirred under reflux for 1 h. The mixture was concentrated under reduced pressure, and under UV light the red fluorescent product was isolated by filtration over a silica gel filled glass frit. The reaction mixture was filtered (DCM, then DCM/EtOAc = 9:1, v/v). After column chromatography (DCM), product **20** was obtained as a black solid (103 mg, 0.15 mmol, 8%). m. p. 279–282 °C. ^{1}H NMR (CDCl$_3$, 400 MHz): *δ* = 2.42 (s, 3 H, Me), 7.53–8.02

(m, 6 H, Ar$_1$-H, Ar$_2$-H), 8.42–8.99 (m, 12 H, Ar$_2$-H, β-H) ppm. Signals for the NH groups were not detected. ^{13}C NMR (CDCl$_3$, 126 MHz): The signal to noise ratio of the recorded ^{13}C NMR spectrum did not allow a meaningful interpretation. ^{19}F NMR (CDCl$_3$, 376 MHz): δ = -119.48 (s, 2 F, CF) ppm. HRMS: *m/z* calcd. for $C_{39}H_{25}F_2N_6O_6^+$ ([M+H]$^+$) 711.1798, found 711.1810. IR (ATR): $\tilde{\nu}$ = 3314 [ν(NH)], 3090 [ν(Ar-H)], 1755 [ν(OAc)], 1620 [ν(C=N)], 1530 [δ(Ar-C)], 1335 [ν_{sym}(NO$_2$)], 1200 [ν(CF)] cm^{-1}. UV/Vis (DCM): λ_{max} [log (ε (L mol^{-1} cm^{-1})] = 418 [5.07], 573 [4.34], 620 [4.13], 647 nm [4.04].

General procedure for the substitution of 19 and 20 with amines. The corresponding porphyrin or corrole (1 equiv.) and the amine (100 equiv.) were dissolved in DMSO. The reaction mixture was stirred under an argon atmosphere for 2 h at rt. Afterwards, the reaction mixture was diluted DCM and was washed with water several times. The organic phase was dried over sodium sulfate, filtered, and evaporated to dryness. The crude product was purified by column chromatography and recrystallized.

General procedure for the preparation of BODIPYs from the 3-fluoro-4-amino-substituted dipyrromethanes 25-35. The corresponding dipyrromethane **6**-**16** (1 equiv.) was dissolved in 30 mL of DCM. DDQ (1 equiv., suspended in 5 mL DCM) was added, and the reaction mixture was stirred under an argon atmosphere for 5 min at rt. After the indicated time, DIPEA (7 equiv.) was added and stirred for 15 min at rt. Afterwards, $BF_3 \cdot OEt_2$ (7 equiv.) was added and stirred for additional 20 min at rt. Water was added, and the product was extracted with DCM. The combined organic phases were washed again with water. The organic phase was dried with sodium sulfate, filtered, and evaporated to dryness. The crude product was purified by column chromatography and recrystallized.

General procedure for the substitution of the 3-hydrogen in BODIPYs 36, 37, 39, and 40. Under oxygen atmosphere the corresponding BODIPY (1 equiv.) was dissolved in DMF. Dimethyl malonate (1.1 equiv.), Na$_2$CO$_3$ (2 equiv.) were added and the mixture was stirred for 3 d at rt. After the indicated time, the reaction mixture was diluted with DCM and washed with water several times. The organic layer was evaporated to dryness. The resulting oil was diluted with toluene and evaporated to dryness again (removing the DMF). The remaining solid was dissolved in DCM, dried with Na$_2$SO$_4$, filtrated and evaporated to dryness. The crude product was purified by column chromatography and recrystallization.

General procedure for the preparation of dipyrrins 41-45. The corresponding dipyrromethane **7**,**11**,**12**,**15** or **16** (1 equiv.) was dissolved in THF. *p*-Chloranil (1 equiv., dissolved in THF) was added and the reaction mixture was stirred for the 3 h at rt. Afterwards, THF was evaporated at reduced pressure and the remaining solid was diluted with EtOAc and filtered (EtOAc) over a silica gel filled glass frit. The filtrate was evaporated to dryness and purified by column chromatography.

General procedure for the preparation of (*p*-cymene)dipyrrinato ruthenium(II) complexes 46-50. The corresponding dipyrrin **41**-**45** (1 equiv.) and di(μ-chlorido)-bis[chlorido(η^6-*p*-cymene) ruthenium(II)] (0.5 equiv.) were dissolved in THF. The flask was shielded from ambient light with aluminum foil. DIPEA (14 equiv.) was added and the mixture was stirred for 24 h at rt. After the indicated time, saturated NaCl solution was added and extracted with DCM. The organic layer was dried with Na$_2$SO$_4$, filtrated and evaporated to dryness. The crude product was purified by column chromatography and recrystallized.

General procedure for the preparation of bis(2,2´-bipyridyl)dipyrrinato ruthenium(II) complexes 51-55. The corresponding (*p*-cymene)dipyrrinato ruthenium(II) complex **46**-**50** (1 equiv.) was dissolved in EtOH. 2,2´-bipyridine (2 equiv.) was added and the mixture was stirred under reflux for 24 h. After the indicated time, the mixture was allowed to cool down and was evaporated to dryness. The crude product was purified by column chromatography and recrystallized.

X-ray crystallography

Crystals were grown following the protocol developed by Hope by dissolving the compounds in DCM, and layering with MeOH for liquid diffusion.[78] Single crystal X-ray diffraction data for all compounds were collected on a Bruker APEX 2 DUO CCD diffractometer by using graphite-monochromated MoK$_\alpha$ (λ = 0.71073 Å) radiation. Crystals were mounted on a MiTeGen MicroMount and collected at 100(2) K by using an Oxford Cryosystems Cobra low-temperature device. Data were collected by using omega and phi scans and were corrected for Lorentz and polarization effects by using the APEX software suite.[79,80,81] Using Olex2, the structure was solved with the XT structure solution program, using the intrinsic phasing solution method and refined against $|F^2|$ with XL using least squares minimization.[82] Hydrogen atoms were generally placed in geometrically calculated positions and refined using a riding model. Details of data refinements can be found in Table S1. All images were prepared by using Olex2.[83]

Supporting Information

See footnote on the first page of this article: Synthesis details and ^{1}H, ^{13}C, and ^{19}F NMR and HRMS spectra for all new compounds. CCDC 1902788 (**26**) and CCDC 1902787 (**46**) 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.

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FULL PAPER

The 3,4,5-trifluorphenyl and the 4-fluoro-3-nitrophenyl substituent were evaluated for modifying porphyrins, corroles, BODIPYs, and their dipyrromethane precursors via S$_N$Ar. Specifically, the 5-(4-flouro-3-nitrophenyl)dipyrromethane was efficently substituted with different amines.These pre-fuctionalised dipyrromethanes served as precorsors for meso-substituded BODIPYs, dipyrrins, and their related ruthenium(II) complexes.

(Key Topic) BODIPYs, metal complexes

*Benjamin F. Hohlfeld, Keith J. Flanagan, Nora Kulak, Mathias O. Senge, Mathias Christmann, Arno Wiehe**

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Synthesis of Porphyrinoids, BODIPYs and (Dipyrrinato) Ruthenium(II) Complexes from Pre-functionalized Dipyrromethanes

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