EurJOC
European Journal of Organic Chemistry

Chemistry Europe
European Chemical Societies Publishing

Accepted Article

Title: SNAr Reaction toward the Synthesis of Fluorinated Quinolino[2,3,4-at]porphyrins

Authors: Damaris Thuita, Matthew J. Guberman-Pfeffer, and Christian Brueckner

To be cited as: *Eur. J. Org. Chem.* 10.1002/ejoc.202001347

Link to VoR: https://doi.org/10.1002/ejoc.202001347

WILEY-VCH

10.1002/ejoc.202001347

WILEY-VCH

FULL PAPER

S_NAr Reaction toward the Synthesis of Fluorinated Quinolino[2,3,4-at]porphyrins

Damaris Thuita[a], Matthew J. Guberman-Pfeffer[a,b], and Christian Brückner[a],*

Abstract: An intramolecular S_NAr displacement of one *o*-fluorine atom of a *meso*-pentafluorophenyl-substituted porphyrin metal complex by a neighboring β-amino functionality generated the corresponding *meso*-fluorophenyl-substituted metallo-quinolino[2,3,4-at]porphyrins that are not accessible using established quinoline-annulation methodologies. The Cu(II), Ni(II), and Zn(II) complexes were thus prepared. The parent free base quinolino[2,3,4-at]porphyrin is accessible only by demetallation of the copper or zinc complex. A strong through-space NMR-spectroscopic coupling between the remaining *o*-fluorine atoms on the annulated *meso*-aryl group and the β-hydrogen atom on the adjacent pyrrole moiety provide a clear spectroscopic signature for the annulation. Quinoline-annulation alters the optical properties significantly. On account of the presence of the β-amino functionality, all quinoline-annulated porphyrins show strong halochromic responses with Brønsted acids and bases, the prerequisite for their potential use in chemosensing applications.

Introduction

The introduction of functional groups to the periphery of porphyrins and their analogues is an attractive approach to, for example, generate chemosensors that take advantage of their frequently bright fluorescence emission or strong UV-vis absorbance.[1] In this context, the introduction of amino groups is central since they can be flexibly converted to a range of functionalities and their inherent ability to interact with metal ions and protons.[2] Amino groups have been introduced to a range of positions on the porphyrin,[3] often through nitration reactions or the synthesis of porphyrins with nitrated components.[2b, 2d, 4]
One class of β-aminoporphyrins are the quinoline-annulated porphyrins (quinolino[2,3,4-at]porphyrins), such as **1**/**1M** through **3**/**3M**.[2a, 2b, 2d, 4b, 5] Compound **1** and closely related compound **2** contain an sp^3-hybridized β-amino group, whereby the corresponding nitrogen atom in **3** is sp^2-hybridized. All possess significantly red-shifted optical spectra.[4b, 5d, 6] Compounds **2M** were also shown to have the ability to coordinate to transition metals, as shown for its Pd(II) complex **$(2Ni)_2Pd$**.[2a, 2b, 7] Compound **3** showed unique photoacoustic properties and a biocompatible derivative was utilized as a photoacoustic imaging agent in a mouse tumor model.[8]
While there are multiple ways to introduce a β-amino group, a common feature in all quinoline-annulated systems is that the bond between the β-nitrogen atom and the flanking *meso*-aryl group was formed via harsh, thermally induced, oxidative bond formation conditions or S_EAr reactions.[2a, 2b, 2d, 4b, 5]

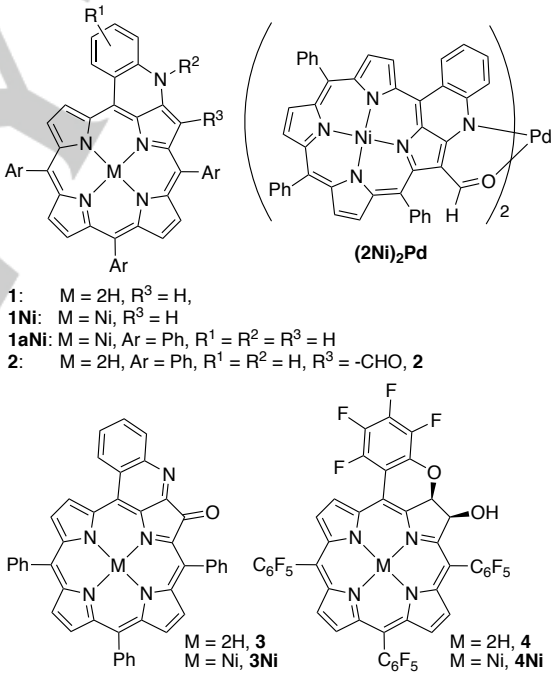


Figure 1. Literature-known quinoline-annulated porphyrins (**1** through **3**) and chromene-annulated chlorin **4**.

We introduced chromene-annulated chlorin **4** and related chromophores that were formed by an S_NAr displacement of an *ortho*-fluorine atom of a *meso*-pentafluorophenyl group by a neighboring β-hydroxy functionality under relatively mild conditions (warming in DMF).[9] The S_NAr displacement of *p*- and *o*-fluorine atoms of *meso*-pentafluorophenyl-substituted porphyrinoids by a range of *N*-, *O*-, or *S*-nucleophiles is well-known,[10] and was used to introduce solubilizing groups,[11]

[a] Prof. Dr. C. Brückner, D. Thuita, Dr. M.J. Guberman-Pfeffer
Department of Chemistry
University of Connecticut, Unit 3060
Storrs, CT 06268-3060, U.S.A.
E-mail: c.bruckner@uconn.edu
Homepage: http://bruckner.research.uconn.edu

[b] Current address:
Department of Molecular Biophysics and Biochemistry and the Microbial Science Institute
Yale University
New Haven CT 06520, U.S.A.

Supporting information for this article is given via a link at the end of the document.

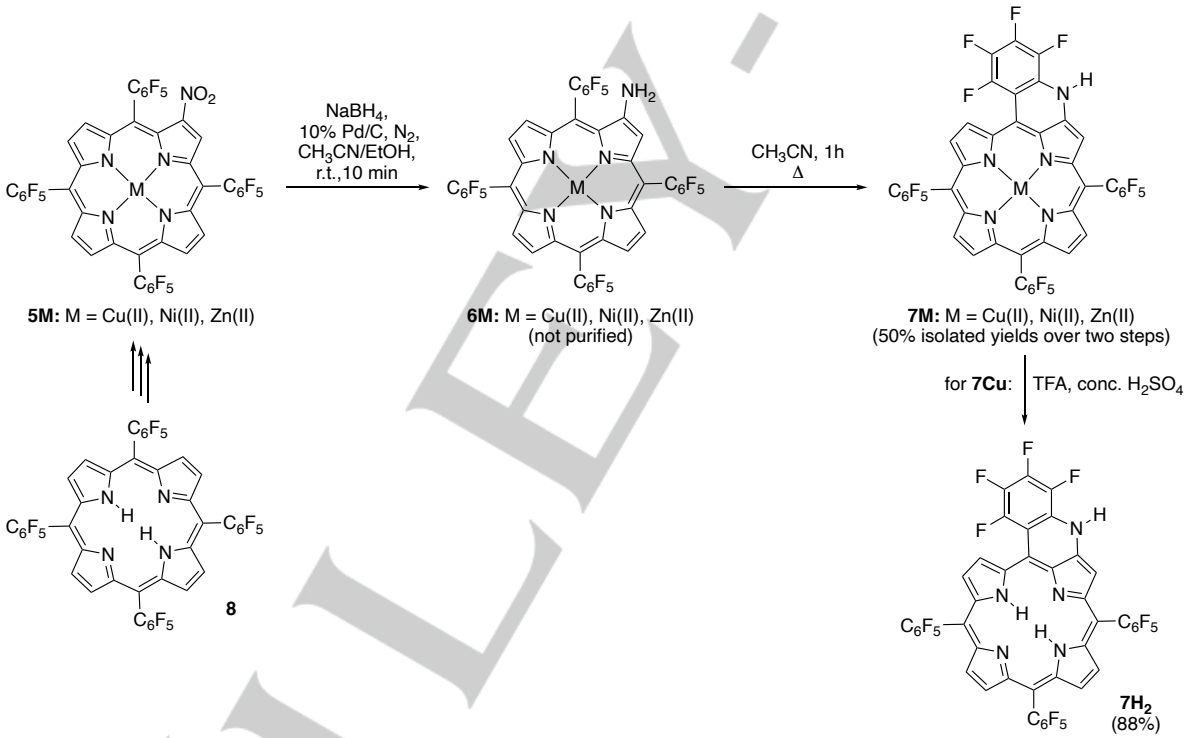
though the utilization of this reaction for intramolecular annulations is relatively rare.[9, 12]

We report here an addition to the number of methods known to form quinolino[2,3,4-at]porphyrins using an intramolecular S_NAr displacement of an *o*-fluorine atom of a *meso*-pentafluorophenyl-substituted porphyrin by a neighboring β-amino functionality. This method is complementary to the existing methods in that it allows the generation of *meso*-pentafluorophenyl-substituted quinoline-annulated porphyrins hitherto not accessible using the traditional methodologies.

Results and Discussion

Formation of Quinolino[2,3,4-at]porphyrins. The synthesis of known β-aminoporphyrin complexes **6M** (M = Cu(II), Ni(II), Zn(II)) proceeded as described previously via reduction of the corresponding β-nitroporphyrin complexes **5M**, themselves generated by nitration of *meso*-tetrakis(pentafluorophenyl)-porphyrinato metal complexes,[13] but with some variations in the particular reduction conditions used (Scheme 1).[14] The crude β-aminoporphyrin complexes **6M** were then subjected to the intramolecular S_NAr-type annulation reaction by simply heating in acetonitrile (b.p. = 82 °C). This quantitatively converted the starting materials within 1 h to generate a major product **7M** of lower polarity, in 50% isolated yields (over two steps). All products showed a composition (as per ESI^- HR-MS) corresponding to the starting materials less one equivalent of HF, as expected for the annulated target compound.

This reaction was only suitable for the reasonably stable β-aminoporphyrin metal complexes **6M**. The use of the corresponding free base β-aminoporphyrin failed to provide a major product and, instead, generated a myriad of intractable compounds. Thus, access to the free base annulated derivative was possible only via acid-induced demetallation of the copper or zinc complexes, **7Cu** or **7Zn**, respectively.



Scheme 1. Formation of title compounds **7M** and **$7H_2$** from the ultimate starting porphyrin, *meso*-tetrakis(pentafluorophenyl)porphyrin **8**.

The facility of the intramolecular annulation reaction was already presaged by the ESI^- mass spectra of the precursor β-amino-metalloporphyrins, as shown for the spectrum for **6Cu** (Figure 2). Under standard MS conditions (100% CH_3CN, 30 V cone voltage), the peak corresponding to the annulated product $[M\text{-}H\text{-}HF]^-$ is more intense than the parent $[M\text{-}H]^-$ peak. The observation of annulations of *meso*-fluoro-alkyl and -arylporphyrins resulting from the intramolecular loss of HF are not uncommon, but frequently require more forcing tandem MS conditions.[15]

The aryl groups in *meso*-arylporphyrins are in idealized perpendicular arrangements to the mean plane of the porphyrin.[16] In contrast, the β-to-*o*-aryl bond formation forces the *meso*-aryl group into much greater co-planarity with the porphyrin ring.[17] This brings the *o*-fluorine atom on the annulated *meso*-aryl group opposite of the annulation site into close proximity to the

β-hydrogen atom on the adjacent pyrrole moiety. As we discovered for chromene-annulated chlorins (like **4**),[9a] this proximity leads to a diagnostic strong coupling between these two atoms, as seen in a strong correlation peak in the ^{1}H-^{19}F HOESY spectra of the *meso*-fluoroaryl quinolino[2,3,4-at]porphyrins and their diamagnetic metal complexes (as shown for **7Zn**, Figure 3).

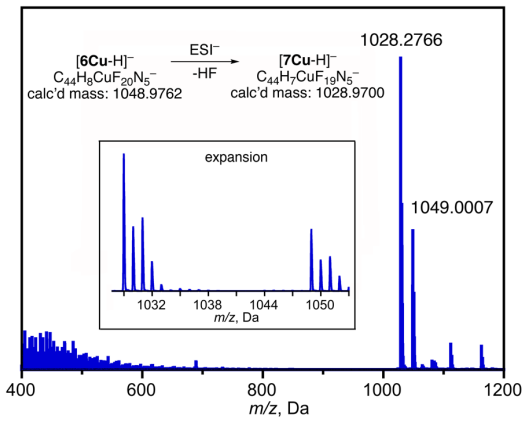


Figure 2. HR-MS (ESI⁻, 100% CH_3CN, TOF) spectrum of **6Cu** highlighting the proposed origin of the [M-H-HF]⁻ peak. The isotope patterns match those of the compositions indicated, see ESI.

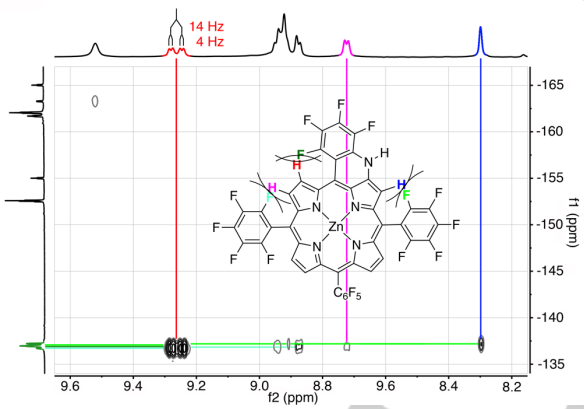


Figure 3. ^{1}H-^{19}F HOESY ($CDCl_3$) spectrum of **7Zn**, showing the diagnostic signal for the formation of β-to-*o*-aryl linkage in *meso*-pentafluorophenyl-derived porphyrins in comparison to related correlations.

Since this ^{1}H-^{19}F correlation is diagnostic for the annulation and might provide also a clear probe for the conformation of the macrocycle, we performed a relaxed potential energy scan for a simplified model of **7Zn** (Figure 4). The distance-dependent ^{1}H-^{19}F NMR spin coupling constant and relative energies were determined (see computational details in the ESI).

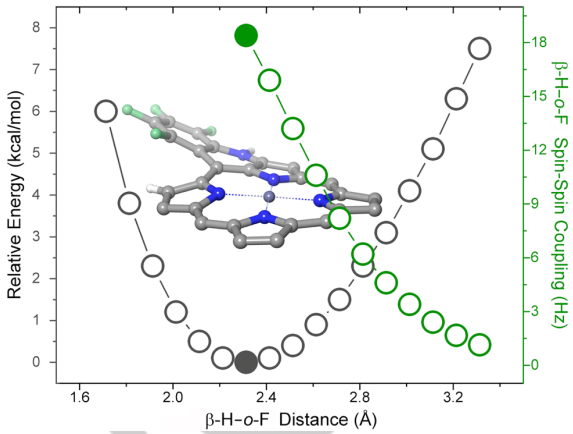


Figure 4. Computed relaxed potential energy scan relationship over the β-H–*o*-F distance in 0.1 Å increments to shorter and longer lengths than the 2.31 Å separation found in the minimum energy conformer, plotting relative energies and ^{1}H–^{19}F nuclear spin-spin coupling constants (at the PBEPBE/def2-TZVP level of theory), for the simplified model of **7Zn** shown. B3LYP-D3/[SDD level of theory for Zn and 6-31G(d) level for H, C, N, F; the conformationally little restricted, non-annulated *meso*-aryl groups were omitted for simplicity; for details, see ESI.

The equilibrium β-H–*o*-F distance was computed to be 2.31 Å at the minimum energy point, correlating to a computed 18 Hz coupling constant between these atoms. The experimental coupling value for **7Zn** is slightly lower, 14 Hz, suggesting that either the computed coupling constant or the degree of conformational distortion of the macrocycle are slightly over-estimated. Using the computed Boltzmann-weighted average of the coupling constants (15.6 Hz) over the thermally accessible distances reduces the minor discrepancy down to insignficant values. The experimental values for the nickel complex **7Ni** are 11.3 Hz and for the free base **7H₂** 12 Hz, suggesting that the H-F distances in these two compounds are larger than for the zinc complex.

The computation of the model for **7Zn** also suggests that the annulation introduces a modest ruffling-type distortion to the porphyrin macrocycle, with some minor saddling, doming and waving contributions (see ESI). The conformation of nickel porphyrins is, on account of the presence of the small square planar coordinated, diamagnetic d^8 nickel(II) ion, often dominated by a strongly ruffled conformation.[18] In fact, the crystal structures of the closely related, non-fluorinated *meso*-phenyl-substituted nickel complex **1aNi** (CCDC codes ERATIA and VIDRAC) show these strongly ruffled conformations (see ESI),[2b, 2d] albeit the distance between the β-C(H)–*o*-C(H) carbon atoms (of 3.07 Å) is shorter than the corresponding computed carbon-carbon atom distance in the model of **7Zn** (3.17 Å).

In the previously investigated chromene-annulated chlorins,[9] a computed H–F distance of 2.5 Å corresponded to an experimental coupling constant of 9.7 Hz; the value computed for this distance we also (at 13 Hz), overestimated by the same 3-4 Hz as above, but the general larger distance-smaller coupling constant relationship holds.

We conclude from these analyses that while the >10 Hz β-H–*o*-F coupling is a reliable indicator for the presence of an *o*-annulated *meso*-pentafluorophenyl ring, a numerical interpretation of the experimental coupling constant in terms of β-H–*o*-F distances or even conformational modes is, in light of the small data set available and in the absence of a thorough error analysis, as yet tenuous.

Optical Properties of Quinolino[2,3,4-at]porphyrins. Similarly to the non-fluorinated derivatives,[2b, 2d] annulation leads to significantly altered metalloporphyrin-like UV-vis spectra of the quinolino[2,3,4-at]porphyrins **7M** compared to those of the corresponding 2-amino-porphyrins, as illustrated for the copper complexes (Figure 5A) (see also ESI). Upon annulation, the Soret band is markedly red-shifted (404 to 442 nm) but the longest wavelengths of absorption (λ_{max}) is red-shifted to a lesser degree (599 to 622 nm). We attribute these shifts to the altered conformation of the annulated chromophore and, to a smaller extent, to the increased co-planarity (and associated greater π-conjugation) of the annulated *meso*-aryl group. The optical changes upon annulation of this all-sp^2-hybridized porphyrinic macrocycle are much more pronounced than upon annulation of the chlorin precursor to **4**,[9a, 19] suggesting that the conformational changes imposed by the quinoline-annulation reaction of the porphyrin are more extensive than upon chromene-annulation of the chlorin.

The annulated free base **7H₂** possesses a (red-shifted) porphyrin-like UV-vis spectrum (Figure 5C). Remarkably, both the free base **7H₂** (Figure 5C) and its metal complexes **7M** (shown for **7Ni**, Figure 5B) show strong halochromic responses, both of which we attribute to the presence of the C_6F_4-substituted β-amino functionality. The response to strong base may set these fluorinated derivatives apart from their non-fluorinated congeners,[2b, 2d] though their halochromic response was not reported. We also note that we observe the formation of the M^- ions in the ESI mass spectra of the metallocomplexes that are also most readily explained with the facile deprotonation of the β-amino group.

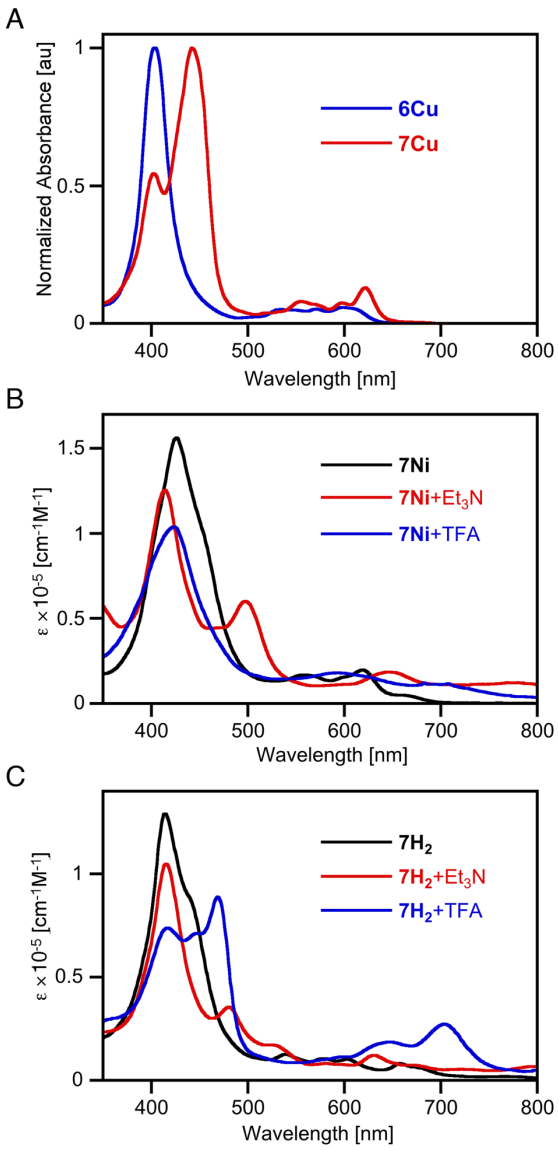


Figure 5. UV-vis spectra of the compounds indicated in CH_2Cl_2 (black trace), CH_2Cl_2 + 1% TFA (blue trace), and CH_2Cl_2 + 1% Et_3N (red trace). Spectra for **7Ni** and **7H₂** under acidic and basic conditions in the range between 300 and 1100 nm included in the ESI.

Conclusions

We reported here the intramolecular S_NAr reaction of a β-amino-porphyrin with a flanking *meso*-pentafluorophenyl-group to form quinolinometalloporphyrins in acceptable yields in two simple steps from the corresponding *meso*-pentafluorophenyl-2-nitro-metalloporphyrin. The free base is accessible via the demetallation of the copper or zinc complexes. Clear spectroscopic signatures for the annulation could be detected. This method is complementary to existing methods of generating quinoline-annulated porphyrinoids in that it allows the formation of *meso*-pentafluorophenyl-substituted systems that were

unavailable along established routes that rely on oxidative methods or S_NAr reactions. This is important because *meso*-pentafluorophenyl-substituted porphyrinoids were shown to be most versatile in the generation of functionalized, water-soluble and/or biologically active porphyrinoids.

Experimental Section

Materials and Instruments:

All solvents and reagents (Sigma-Aldrich, St. Louis, MO, USA and Acros, Fair Lawn, NJ, USA) were used as received. *meso*-Tetrakis(pentafluorophenyl)porphyrin was either synthesized according to the literature procedure[20] or obtained commercially. *meso*-Tetrakis(pentafluorophenyl)-2-nitro-porphyrins **5Cu**, **5Ni**, and **5Zn** were synthesized according to literature procedures.[13]

Aluminum-backed, silica gel 60, 250 μm thickness analytical plates were used for analytical TLC; Either 20 × 20 cm, glass-backed, silica gel 60, 500 μm thickness preparative TLC plates or standard grade, 60 Å, 32-63 μm flash column silica gel were used for the chromatographic purification of the products.

^{1}H and ^{19}F NMR spectra were recorded on a Bruker 400 MHz instrument in the solvents indicated, and were referenced to residual solvent peaks. All UV-vis spectra were recorded on Cary 50 or 100 UV-vis spectrometers (Varian). FT_IR spectra were recorded on a Bruker Alpha ATR instrument with diamond window. High-resolution mass spectra were recorded from CH_3CN solutions (~10^{-6} M) using an AB Sciex QStar Elite Quadrupole-TOF mass spectrometer at the Mass Spectrometry Facility, Department of Chemistry, University of Connecticut.

Step 1: General Procedure for the Formation of 2-Aminometallo-porphyrins (6M) via Reduction of 2-Nitrometalloporphyrins (5M). Reduction method adopted from the literature:[14] In a 50 ml three-neck round bottom flask equipped with a stir bar and capped with septa, a nitrogen inlet and outlet, 10% Pd/C was stirred in ethanol (EtOH) and the suspension was purged with dry N_2. $NaBH_4$ was dissolved in EtOH and added slowly to the solution via syringe and the reaction mixture was kept under an inert atmosphere using a N_2-filled balloon. Nitroporphyrin **5M** was dissolved in acetonitrile (CH_3CN) and solution added dropwise over ~10 min to the reductant mixture via syringe. A noticeable color change from magenta to deep green took place during this time. Once no starting material could be detected by TLC, the organic phase was filtered through a short plug of diatomaceous earth (Celite®), and the filter cake rinsed with CH_3CN. The volume of the solution was reduced by rotary evaporation and the solution of the crude 2-aminometalloporphyrin **6M** was immediately used as is for the annulation step.

Step 2: General Procedure for the Annulation of 2-Aminometallo-porphyrins (6M). The crude product from Step 1 was diluted with CH_3CN (to 25 ml) and transferred to a 50 ml round-bottom flask equipped with stir bar and condenser. The reaction mixture was stirred and heated to reflux. The reaction monitored by TLC. Upon consumption of the starting material after ~1 h, the reaction was allowed to cool to ambient temperature and diluted with CH_2Cl_2 (25 ml). The reaction mixture was transferred into a separatory funnel, the solution was washed with water (25 ml), dried over anhyd. Na_2SO_4, and evaporated to dryness using rotary evaporation. The residue was purified by flash column or preparative plate chromatography.

Quinolino[2,3,4-at]porphyrinato]Ni(II) (7Ni). Nitroporphyrin **5Ni** (7.6 × 10^{-5} mol, 82 mg) dissolved in CH_3CN (10−15 mL) was reduced with 10% Pd/C (0.10 g) and $NaBH_4$ (1.0 × 10^{-2} mol, 390 mg) in EtOH (2−5 mL) according to the general Step 1 procedure to produce crude **6Ni**. R_f of **6Ni** = 0.38 (silica-40% hexane/CH_2Cl_2). Quinoline-annulated porphyrin **7Ni** was produced and isolated by chromatography (silica, 25% hexane/CH_2Cl_2) as a green-coloured solid in 50% yield (3.8 × 10^{-5} mol, 39 mg) according to the general Step 2 procedure. R_f (silica−25% hexane/CH_2Cl_2) = 0.88. ^{1}H NMR (400 MHz, $CDCl_3$, *δ*) 9.60 (s, 1H), 9.25 (dd, ^3J = 11.3, $^{H\text{-}F}J$ = 5.0 Hz, 1H), 8.70 (q, ^3J = 6.1 Hz, 4H), 8.64 (s, 1H), 8.13 (s, 1H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$, δ): 147.5, 145.0, 143.0, 142.7, 142.1, 141.1, 140.2, 139.2, 138.8, 138.3, 136.4, 133.6, 133.1, 132.2, 131.85, 131.5, 130.9, 130.5, 114.6, 104.2, 102.7, 100.2, 99.3, 99.0 ppm. ^{19}F NMR (376 MHz, $CDCl_3$, *δ*): –136.08 to –137.52 (m, 6F), –137.67 (dt, ^3J = 21.1, ^4J = 10.4 Hz, 1F), –151.95 (q, ^3J = 19.6 Hz, 3F), –154.16 (t, ^3J = 20.7 Hz, 1F), –161.20 (s, 2F), –161.41 to –161.59 (m, 4F), –162.19 (dd, ^3J = 20.0, ^4J = 9.8 Hz, 1F), –164.26 to –164.38 (m, 1F) ppm. UV-vis (CH_2Cl_2) λ_{max} (log ε): 425.1 (4.19), 550.9 (3.10), 619.0 (3.28) nm. FT-IR (neat, diamond ATR): $\nu_{N\text{-}H}$ = 3436.5 cm^{-1}. HR-MS (ESI$^-$, 100% CH_3CN, TOF): *m/z* calc'd for $C_{44}H_7F_{19}N_5Ni$ $[M\text{-}H]^-$ 1023.9757; found 1023.9792.

Quinolino[2,3,4-at]porphyrinato]Zn(II) (7Zn). Nitroporphyrin **5Zn** (4.42 × 10^{-5} mol, 48 mg) dissolved in CH_3CN (10 mL) was reduced with 10% Pd/C (0.10 g) and $NaBH_4$ (1.0 × 10^{-2} mol, 390 mg) in EtOH (2−5 mL) according to the general Step 1 procedure to produce crude known **6Zn**.[21] R_f of **6Zn** = 0.22 (silica-40% hexane/CH_2Cl_2). Quinoline-annulated porphyrin **7Zn** was produced and isolated by chromatography (silica, 25% hexane/CH_2Cl_2) a green-coloured solid in 50% yield 2.9 × 10^{-5} mol, 30 mg) according to the general Step 2 procedure. R_f (silica−25% hexane/CH_2Cl_2) = 0.42. ^{1}H NMR (400 MHz, $CDCl_3$, *δ*): 9.49 (s, 1H), 9.24 (dd, ^3J = 13.7, $^{H\text{-}F}J$ = 4.2 Hz, 1H), 8.91 (dd, ^3J = 7.5, ^4J = 4.5 Hz, 3H), 8.85 (d, ^3J = 4.5 Hz, 1H), 8.70 (d, ^3J = 4.4 Hz, 1H), 8.27 (s, 1H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$, δ): 151.0, 150.8, 150.5, 150.4, 150.1, 147.8, 147.6, 147.1, 146.0, 145.6, 143.0, 141.0, 140.0, 138.6, 137.15, 136.6, 132.4, 132.3, 132.2, 132.0, 131.8, 131.6, 131.5, 131.1, 131.0, 130.2, 130.0, 129.0, 128.7, 116.6, 105.1, 105.0, 99.2 ppm**.** ^{19}F NMR (376 MHz, $CDCl_3$, *δ*): –136.72 (s, 1F), –136.96 (d, ^3J = 17.4 Hz, 4F), –137.22 (dd, ^3J = 23.5, ^4J = 6.9 Hz, 2F), –152.58 (q, ^3J = 22.4 Hz, 3F), –155.02 (t, ^3J = 20.6 Hz, 1F), -161.71 (td, ^3J = 22.3, ^4J = 6.6 Hz, 2F), –161.99 to –162.15 (m, 4F), -163.29 (d, ^3J = 11.9 Hz, 1F), –165.04 (t, ^3J = 21.4 Hz, 1F) ppm. UV-vis (CH_2Cl_2): λ_{max} (log ε) 407.1 (5.18), 441.9 (5.42), 561.0 (4.31), 603.0 (4.30), 627.9 (4.57) nm. FT-IR (neat, diamond ATR): $\nu_{N\text{-}H}$ = 3414.4 cm^{-1}. HR-MS (ESI$^-$, 100% CH_3CN, TOF): *m/z* calc'd. for $C_{46}H_{12}F_{19}N_5O^{65}Zn^-$ $[M\text{-}H]^-$ 1075.9852; found 1075.9836; $C_{44}H_7F_{19}N_5Zn$ $[M\text{-}H]^-$ 1029.9696; found 1029.9753.

Quinolino[2,3,4-at]porphyrinato]Cu(II) (7Cu). Nitroporphyrin **5Cu** (9.10 × 10^{-5} mol, 98 mg) dissolved in CH_3CN (10 mL) was reduced with 10% Pd/C (0.10 g) and $NaBH_4$ (1.0 × 10^{-2} mol, 390 mg) in EtOH (4 mL) according to the general Step 1 procedure to produce crude known **6Cu**.[13b] R_f of **6Cu** = 0.58 (silica-50% hexane/CH_2Cl_2). Quinoline-annulated porphyrin **7Cu** was produced and isolated by chromatography (silica, 25% hexane/CH_2Cl_2) as a green-coloured solid in 50% yield (4.6 × 10^{-5} mol, 47 mg) according to the general Step 2 procedure. R_f (silica−50% hexane/CH_2Cl_2) = 0.30. UV-vis (CH_2Cl_2) λ_{max} (log ε): 403.0 (4.80), 442.0 (5.06), 554.9 (3.96), 622.0 (4.17) nm. FT-IR (neat, diamond ATR): $\nu_{N\text{-}H}$ = 3415.3 cm^{-1}. HR-MS (ESI$^-$, 100% CH_3CN, TOF): *m/z* calc'd for $C_{44}H_7CuF_{19}N_5$ $[M\text{-}H]^-$ 1028.9700; found 1028.9856.

Quinolino[2,3,4-at]porphyrin (7H$_2$). In a 25 ml round-bottom flask, crude [quinolinoporphyrinato]Cu(II) (**7Cu**) (prepared from 9.10 × 10^{-5} mol **5Cu**) was dissolved in trifluoracetic acid (CF_3CO_2H, 2–4 ml). Concentrated H_2SO_4 (2 mL) was then added dropwise to the solution. Alternatively, crude [quinolinoporphyrinato]Zn(II) (**7Zn**) (prepared from 4.42 × 10^{-5} mol **5Zn**) was dissolved in CF_3CO_2H (2–4 ml) and chloroform ($CHCl_3$, 5 ml).

Concentrated HCl (2 mL) was then added dropwise to the solution. The reactions were stirred at room temperature for ~1.5 h after which the mixture was poured onto water (100 mL). The water phase was extracted with CH_2Cl_2 (5 × 5 mL). The combined organic layers were washed with water (2 × 25 mL) and dried over anhydrous Na_2CO_3 and evaporated to dryness by a rotary evaporation. The residue was purified by flash column or preparative plate chromatography (silica, 50% hexane/CH_2Cl_2) to produce **7H₂** as a dark brown-coloured solid in 88% yield (77 mg, 7.97 × 10^{-5} mol). R_f (silica−25% hexane/CH_2Cl_2) = 0.75. ^{1}H NMR (400 MHz, $CDCl_3$, δ): 9.95 (s, 1H), 9.43 (dd, ^3J = 4.4, $^{H\text{-}F}J$ = 12 Hz, 1H), 8.96 (s, 2H), 8.78 (t, ^3J = 4.9 Hz, 2H), 8.71 (d, ^3J = 4.8 Hz, 1H), 8.36 (s, 1H), –1.85 (s, 2H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$, δ): 147.5, 145.6, 143.3, 141.3, 137.5, 136.6, 132.4, 130.0, 128.2. ^{19}F NMR (376 MHz, $CDCl_3$, *δ*): –135.85 (dd, ^3J = 21.5, ^4J = 9.7 Hz, 1F), –136.59 (dd, ^3J = 23.6, ^4J = 7.9 Hz, 4F), –136.87 (dd, ^3J = 23.5, ^4J = 7.9 Hz, 2F), –151.75 to –152.04 (m, 3F), –154.35 (t, ^3J = 20.3 Hz, 1F), –161.31 (td, ^3J = 22.1, ^4J = 7.0 Hz, 2F), –161.64 (qd, ^3J = 21.6, ^4J = 6.5 Hz, 4F), –162.92 (s, 1F), –164.65 to –164.76 (m, 1F) ppm. UV-vis (CH_2Cl_2) λ_{max} (log ε): 412.0 (6.40), 414.5 (6.39), 536.5 (5.35), 575.0 (5.24), 603.0 (5.15), 657.5 (5.09) nm. FT-IR (neat, diamond ATR): $\nu_{N\text{-}H}$ = 3426 cm^{-1}. HR-MS (ESI$^-$, 100% CH_3CN, TOF): *m/z* calc'd for $C_{44}H_9F_{19}N_5^-$ $[M–H]^-$ 968.0560; found 968.0663.

Acknowledgments

Funding for this work was provided by the U.S. National Science Foundation (NSF) through grant CHE-1800361 and the UConn Vice President for Research through the Research Excellence Program. We thank Hayley Piepho and Bionca Feagin for preliminary experiments.

Keywords: Porphyrinoids • S_NAr Reaction • β-Aminoporphyrin • Annulation reaction

References

[1] a) D. B. Papkovsky, G. V. Ponomarev, O. S. Wolfbeis, *Spectrochim. Acta, Part A* **1996**, *52A*, 1629–1638; b) Y. Ding, W.-H. Zhu, Y. Xie, *Chem. Rev*. **2017**, *117*, 2203–2256; c) M. Biesaga, K. Pyrzynska, M. Trojanowicz, *Talanta* **2000**, *51*, 209–224.

[2] a) S. Richeter, C. Jeandon, J.-P. Gisselbrecht, R. Ruppert, H. J. Callot, *J. Am. Chem. Soc.* **2002**, *124*, 6168–6179; b) S. Richeter, C. Jeandon, J.-P. Gisselbrecht, R. Graff, R. Ruppert, H. J. Callot, *Inorg. Chem.* **2004**, *43*, 251–263; c) C. M. A. Alonso, M. G. P. M. S. Neves, A. C. Tome, A. M. S. Silva, J. A. S. Cavaleiro, *Tetrahedron* **2005**, *61*, 11866–11872; d) D.-M. Shen, C. Liu, Q.-Y. Chen, *Eur. J. Org. Chem.* **2007**, *2007*, 1419–1422 (see also correction to this paper: *Eur. J. Org. Chem.* **2007**, 2888.); e) T. Bruhn, F. Witterauf, D. C. G. Götz, C. T. Grimmer, M. Würtemberger, U. Radius, G. Bringmann, *Chem.–Eur. J.* **2014**, *20*, 3998–4006. f) A. Abdulaeva, K. P. Birin, J. Michalak, A. Romieu, C. Stern, A. Bessmertnykh-Lemeune, R. Guilard, Y. G. Gorbunova, A. Y. Tsivadze, *New J. Chem.* **2016**, *40*, 5758–5774.

[3] a) A. Bousfiha, A. K. D. Dime, A. Mankou-Makaya, J. Echaubard, M. Berthelot, H. Cattey, A. Romieu, J. Roger, C. H. Devillers, *Chem. Commun.* **2020**, *56*, 884–887. b) M. C. Balaban, C. Chappaz-Gillot, G. Canard, O. Fuhr, C. Roussel, T. S. Balaban, *Tetrahedron* **2009**, *65*, 3733–3739.

[4] a) M. J. Crossley, L. G. King, S. M. Pyke, C. W. Tansey, *J. Porphyrins Phthalocyanines* **2002**, *6*, 685–694; b) A. M. V. M. Pereira, C. M. A. Alonso, M. G. P. M. S. Neves, A. C. Tome, A. M. S. Silva, F. A. A. Paz, J. A. S. Cavaleiro, *J. Org. Chem.* **2008**, *73*, 7353–7356; c) S. Ostrowski, D. Szerszen, M. Ryszczuk, *Synthesis* **2005**, 819–823; d) V. I. V. Serra, S. M. G. Pires, C. M. A. Alonso, M. G. P. M. S. Neves, A. C. Tomé, J. A. S. Cavaleiro, *Topics Heterocycl. Chem.* **2013**, *33*, 35–78. e) A. Mikus, M. Zając, S. Ostrowski, *Org. Chem. Front.* **2018**, *5*, 2840–2844.

[5] a) A. M. V. M. Pereira, M. G. P. M. S. Neves, J. A. S. Cavaleiro, J.-P. Gisselbrecht, C. Jeandon, R. Ruppert, *J. Porphyrins Phthalocyanines* **2011**, *15*, 575–582; b) J. Akhigbe, M. Zeller, C. Brückner, *Org. Lett.* **2011**, *13*, 1322–1325; c) A. M. V. M. Pereira, S. Richeter, C. Jeandon, J.-P. Gisselbrecht, J. Wytko, R. Ruppert, *J. Porphyrins Phthalocyanines* **2012**, *16*, 464–478; d) J. Akhigbe, M. Luciano, M. Zeller, C. Brückner, *J. Org. Chem.* **2015**, *80*, 499–511; e) A. J. Jimenez, N. S. Mesa, A. M. V. M. Pereira, M. Jean, B. Vincent, C. Jeandon, J.-P. Gisselbrecht, R. Ruppert, *Asian J. Org. Chem.* **2015**, *4*, 1294–1300; f) A. M. V. M. Pereira, P. S. S. Lacerda, B. N. M. Silva, M. G. P. M. S. Neves, A. M. S. Silva, B. V. Silva, F. C. da Silva, V. F. Ferreira, A. C. Pinto, J. A. S. Cavaleiro, *Dyes Pigm.* **2017**, *139*, 247–254.

[6] J. Akhigbe, M. Luciano, A. O. Atoyebi, S. Jockusch, C. Brückner, *J. Porphyrins Phthalocyanines* **2020**, *24*, 386–393.

[7] S. Richeter, J. Christophe, G. Jean-Paul, R. Romain, in *Handbook of Porphyrin Science, Vol. 3* (Eds.: K. M. Kadish, K. M. Smith, R. Guilard), World Scientific Publishing Company, Hackensack, NJ, **2010**, pp. 429–483.

[8] a) A. Abuteen, S. Zanganeh, J. Akhigbe, L. P. Samankumara, A. Aguirre, N. Biswal, M. Braune, A. Vollertsen, B. Röder, C. Brückner, Q. Zhu, *Phys. Chem. Chem. Phys.* **2013**, *15*, 18502–18509; b) M. Luciano, M. Erfanzadeh, F. Zhou, H. Zhu, T. Bornhütter, B. Röder, Q. Zhu, C. Brückner, *Org. Biomol. Chem.* **2017**, *15*, 972–983.

[9] a) M. A. Hyland, M. D. Morton, C. Brückner, *J. Org. Chem.* **2012**, *77*, 3038–3048; b) M. A. Hyland, N. Hewage, K. Walton, A. Nimthong Roldan, M. Zeller, M. Samaraweera, J. A. Gascon, C. Brückner, *J. Org. Chem.* **2016**, *81*, 3603–3618.

[10] a) S. J. Shaw, K. J. Elgie, C. Edwards, R. W. Boyle, *Tetrahedron Lett.* **1999**, *40*, 1595–1596; b) D. Samaroo, M. Vinodu, X. Chen, C. M. Drain, *J. Comb. Chem.* **2007**, *9*, 998–1011; c) T. Bříza, R. Kaplánek, M. Havlík, B. Dolenský, Z. Kejík, P. Martásek, V. Král, *Supramol. Chem.* **2008**, *20*, 267–242; d) J. I. T. Costa, A. C. Tomé, M. G. P. M. S. Neves, J. A. S. Cavaleiro, *J. Porphyrins Phthalocyanines* **2011**, *15*, 1116–1133; e) N. Hewage, B. Yang, A. G. Agrios, C. Brückner, *Dyes Pigm.* **2015**, *121*, 159–169; f) H. R. A. Golf, H.-U. Reissig, A. Wiehe, *Eur. J. Org. Chem.* **2015**, 1548–1568. g) R. Weiss, F. Puhlhofer, N. Jux, K. Merz, *Angew. Chem. Int. Ed.* **2002**, *41*, 3815–3817. h) H. C. Sample, M. O. Senge, *Eur. J. Org. Chem.* **2020**, 10.1002/ejoc.202001183 (review).

[11] M. Luciano, C. Brückner, *Molecules* **2017**, *22*, 980.

[12] a) M. Suzuki, R. Taniguchi, A. Osuka, *Chem. Commun.* **2004**, 2682–2683; b) S. Tokuji, J.-Y. Shin, K. S. Kim, J. M. Lim, K. Youfu, S. Saito, D. Kim, A. Osuka, *J. Am. Chem. Soc.* **2009**, *131*, 7240–7241.

[13] a) P. Wyrębek, S. Ostrowski, *J. Porphyrins Phthalocyanines* **2007**, *11*, 822–828; b) M. G. H. Vicente, M. G. P. M. S. Neves, J. S. Cavaleiro, H. K. Hombrecher, D. Koll, *Tetrahedron Lett.* **1996**, *37*, 261–262; c) M. E. Lipińska, D. M. D. Teixeira, C. A. T. Laia, A. M. G. Silva, S. L. H. Rebelo, C. Freire, *Tetrahedron Lett.* **2013**, *54*, 110–113.

[14] G. E. F. Lejarazo, S. S. Elvira, S. T. Sara, *J. Chem. Chem. Eng.* **2018**, *12*, 74–82.

[15] a) K. S. F. Lau, M. Sadilek, G. E. Khalil, M. Gouterman, C. Brückner, *J. Am. Soc. Mass Spectrom.* **2005**, *16*, 1915–1920; b) K. S. F. Lau, M. Sadilek, G. E. Khalil, M. Gouterman, C. Brückner, *J. Am. Soc. Mass Spectrom.* **2006**, *17*, 1306–1314; c) R. A. Izquerido, C. M. Barros, M. G. Santana-Marques, A. J. F. Correia, A. M. G. Silva, A. C. Tome, A. Silva, M. G. P. M. S. Neves, J. A. S. Cavaleiro, *Rapid Commun. Mass Spectrom.* **2004**, *18*, 2601–2611.

[16] M. O. Senge, in *The Porphyrin Handbook, Vol. 10* (Eds.: K. M. Kadish, K. M. Smith, R. Guilard), Academic Press, San Diego, **2000**, pp. 1–218.

[17] a) S. Fox, R. W. Boyle, *Tetrahedron* **2006**, *62*, 10039–10054. b) S. Banerjee, A. A. Phadte, *ChemistrySelect* **2020**, *5*, 11127–11144.

[18] a) X.-Z. Song, W. Jentzen, S.-L. Jia, L. Jaquinod, D. J. Nurco, C. J. Medforth, K. M. Smith, J. A. Shelnutt, *J. Am. Chem. Soc.* **1996**, *118*, 12975–12988; b) T. Wondimagegn, A. Ghosh, *J. Phys. Chem. B* **2000**, *104*, 10858–10862.

[19] B. Yang, N. Hewage, M. J. Guberman-Pfeffer, T. Wax, J. A. Gascón, J. Zhao, A. G. Agrios, C. Brückner, *Phys. Chem. Chem. Phys.* **2018**, *20*, 18233–18240.

[20] P. J. Spellane, M. Gouterman, A. Antipas, S. Kim, Y. C. Liu, *Inorg. Chem.* **1980**, *19*, 386–391.

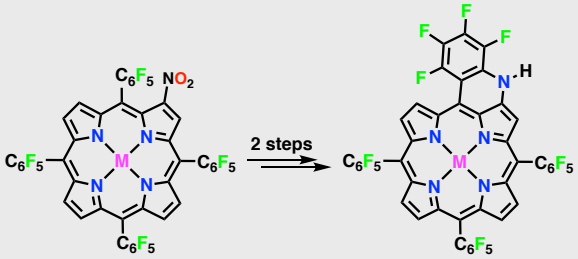
[21] Ol'shevskaya, V. A.; Alpatova, V. M.; Radchenko, A. S.; Ramonova, A. A.; Petrova, A. S.; Tatarskiy, V. V.; Zaitsev, A. V.; Kononova, E. G.; Ikonnikov, N. S.; Kostyukov, A. A.; Egorov, A. E.; Moisenovich, M. M.; Kuzmin, V. A.; Bragina, N. A.; Shtil, A. A., β-Maleimide substituted meso-arylporphyrins: Synthesis, transformations, physico-chemical and antitumor properties. *Dyes Pigm.* **2019**, *171*, 107760.

10.1002/ejoc.202001347

WILEY-VCH

Entry for the Table of Contents (Please choose one layout)

FULL PAPER



Porphyrin Modification*

*Damaris Thuita, Matthew J. Guberman-Pfeffer, and Christian Brückner**

Page No. – Page No.

S_NAr Reaction Toward the Synthesis of Fluorinated Quinolino[2,3,4-at]porphyrins

An intramolecular S_NAr displacement reaction of an *o*-fluorine atom on a *meso*-pentafluorophenyl group by the β-amino-group in *meso*-tetrakis(pentafluorophenyl)-2-amino-metalloporphyrin (M = Cu(II), Ni(II), Zn(II)) provides a novel pathway toward quinoline-annulated metalloporphyrins. The corresponding free base chromophore is available by demetallation.