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Facile synthesis of *N*,*N*′-dimethylated *N*-confused porphyrins

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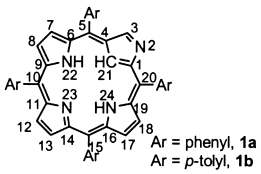
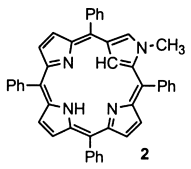
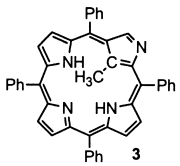
Abstract—*N*-Confused tetraarylporphyrins react with CH_3I in the presence of Na_2CO_3 to give, in high yield, *N*,*N*′-dimethylated *N*-confused porphyrin salts, which are mixtures of structural isomers. The structures of the major isomers were determined by X-ray diffraction and NMR spectroscopic analyses. These *N*,*N*′-dimethylated *N*-confused tetraarylporphyrin salts generate singlet oxygen when irradiated at long wavelengths in the visible region, and therefore, are potential sensitizers for photodynamic therapy.

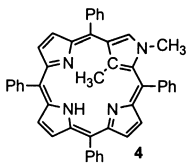
1. Introduction

In 1994, the groups of Furuta and Latos-Grazynski independently reported on the synthesis of *N*-confused porphyrins **1a**, **1b**.[1,2] Since then the outer *N*-methylated *N*-confused porphyrin **2**, the *C*-methylated *N*-confused porphyrin **3**, the *C*,*N*-dimethylated *N*-confused porphyrin **4**, and their nickel(II) derivatives have also been prepared by Latos-Grazynski et al.[3,4] We report here on the synthesis of *N*,*N*′-dimethylated *N*-confused porphyrins and their ability to generate singlet oxygen.









1a N-confused tetraphenylporphyrin
1b N-confused tetra(*p*-tolyl)porphyrin
2 2-aza-2-methyl-5,10,15,20-tetraphenyl-21-carbaporphyrin
3 2-aza-21-methyl-5,10,15,20-tetraphenyl-21-carbaporphyrin
4 2-aza-2,21-dimethyl-5,10,15,20-tetraphenyl-21-carbaporphyrin

Keywords: *N*,*N*′-dimethylated *N*-confused porphyrin; *N*-confused porphyrin; methylation; singlet oxygen.

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2. Results and discussion

2.1. Formation of *N*,*N*′-dimethylated *N*-confused porphyrins

The methylation of **1a** with CH_3I in CH_2Cl_2 yields compound **2**.[3] It is assumed that protonation of compound **2** by HI generated from the methylation reaction prevents subsequent inner *N*-methylation. Therefore, addition of a base, such as Na_2CO_3, might neutralize the protonated intermediate, making the inner nitrogens more nucleophilic towards methylation and resulting in *N*,*N*′-dimethylation. In fact, near-quantitative dimethylation of *N*-confused porphyrins, as shown by TLC, was carried out in CH_2Cl_2 solution using CH_3I and Na_2CO_3. The *N*,*N*′-dimethylated *N*-confused porphyrin salts have a broad absorption around 790 nm ($\sim$20000 M^{-1} cm^{-1}), and therefore, will be of interest for their use as photosensitizers in photodynamic therapy (PDT).[5]

However, each of the *N*,*N*′-dimethylated *N*-confused porphyrin salts **5**(**a**–**e**) may have three structural isomers (I–III, Scheme 1), since there are three possible positions, N-22, N-23, and N-24, for inner *N*-methylation. Separation of the isomers using various chromatographic techniques was not successful in our hands. Only the major isomer of compounds **5**(**a**–**d**) could be isolated by recrystallization.

2.2. Crystal structure of compound 5a-III

Compound **5a-III** (Fig. 1) is the major isomer of *N*,*N*′-dimethylated 2-aza-5,10,15,20-tetraphenyl-21-carbaporphyrin·HI (**5a**). When the I^- was exchanged for $CF_3SO_3^-$ in **5a-III**, the structure was determined by X-ray crystallography, which confirms that the porphyrin is *N*,*N*′-dimethylated.

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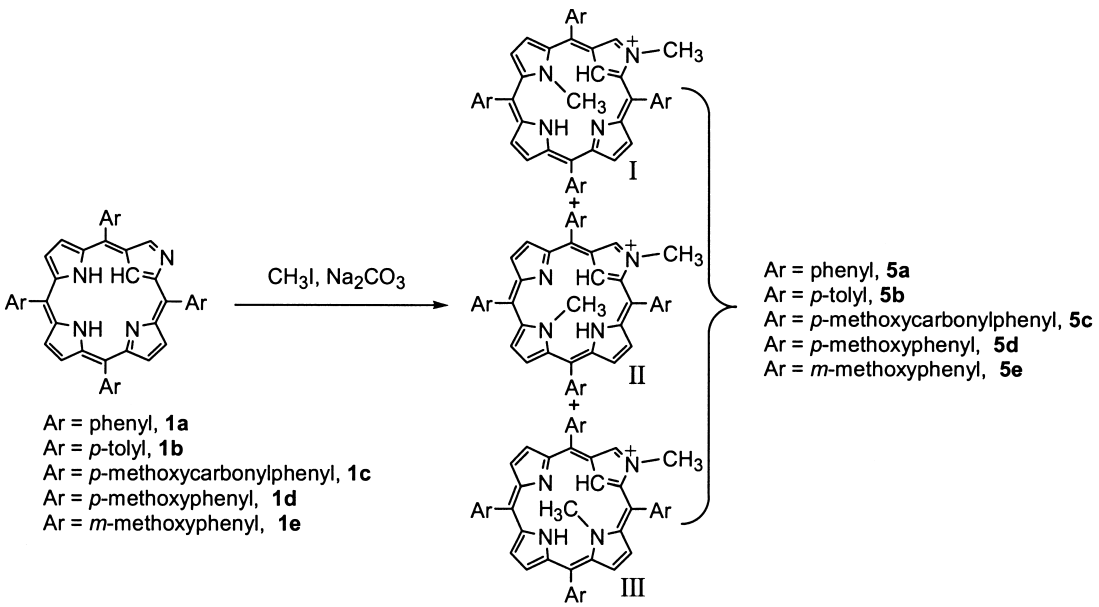

Scheme 1. The synthesis of *N*,*N*′-dimethylated 2-aza-5,10,15,20-tetraphenyl-21-carbaporphyrin·I⁻ (**5a**), *N*,*N*′-dimethylated 2-aza-5,10,15,20-tetra(*p*-tolyl)-21-carbaporphyrin·I⁻ (**5b**), *N*,*N*′-dimethylated 2-aza-5,10,15,20-tetrakis(*p*-methoxycarbonylphenyl)-21-carbaporphyrin·I⁻ (**5c**), *N*,*N*′-dimethylated 2-aza-5,10,15,20-tetrakis(*p*-methoxyphenyl)-21-carbaporphyrin·I⁻ (**5d**) and *N*,*N*′-dimethylated 2-aza-5,10,15,20-tetrakis(*m*-methoxyphenyl)-21-carbaporphyrin·I⁻ (**5e**).

2.3. Structural determination by NMR spectroscopy

The structure of **5d-III**, the major isomer of **5d**, was determined by NMR spectroscopic analyses (^{1}H, ^{13}C, selective NOE, HMQC and HMBC (Fig. 2)). The ^{1}H 3.81 ppm peak was assigned to H-25 based on the observed cross peak with the ^{13}C 39.5 ppm peak using HMQC. Selective NOE experiments showed correlations of H-25 (3.81 ppm) with H-43a (8.40 ppm) and H-43b (8.04 ppm), correlations of H-43a with H-43b and H-18 (7.56 ppm) and correlation of H-18 with H-17 (7.16 ppm). The 2-*N*-methyl group hinders rotation of the adjacent *p*-methoxyphenyl group. The rotation is slow and H-43a and H-43b can be distinguished by NMR spectroscopy. However, there is still some rotation, which results in H-43a and H-43b being interchangeable and their peaks broadened. The negative peak at 8.04 ppm, upon irradiation at 8.40 ppm, showed that the two hydrogens are interchangeable. The −1.47 ppm peak was assigned to the inner methyl group, as suggested by the chemical shift and integration. The observed cross peaks of ^{13}C 150.8 ppm with H-17 (7.16 ppm), H-18 (7.56 ppm) and H-26 (−1.47 ppm) in an HMBC experiment clearly showed that the inner methyl group is connected to the pyrrole unit containing H-17 and H-18.

The structures of the major isomers of compounds **5b** and **5c** were determined in a similar way by NMR spectroscopic analysis. In each case, the inner methylation occurs on N-24, the same as for **5a-III** and **5d-III**.

Because the 2-*N*-methyl group hinders rotations of the adjacent *m*-methoxyphenyl group, compounds **5e** has

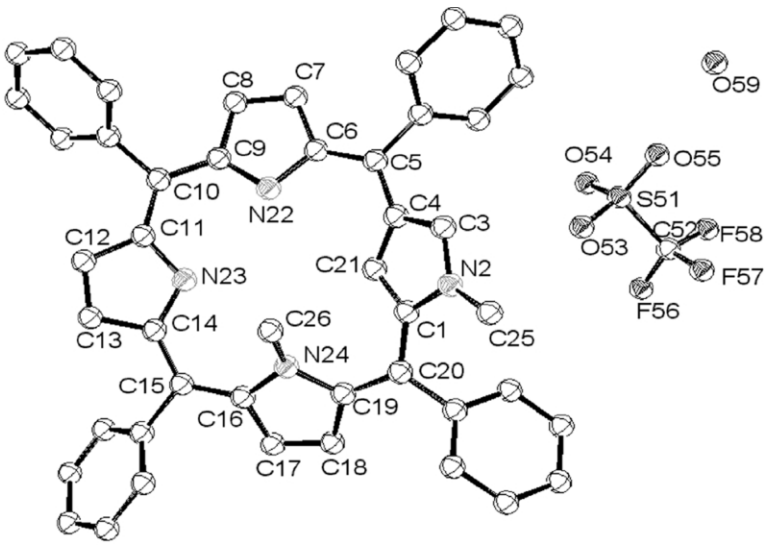

Figure 1. ORTEP drawing of compound (**5a-III**) showing atomic labeling and thermal ellipsoids at the 50% probability level.

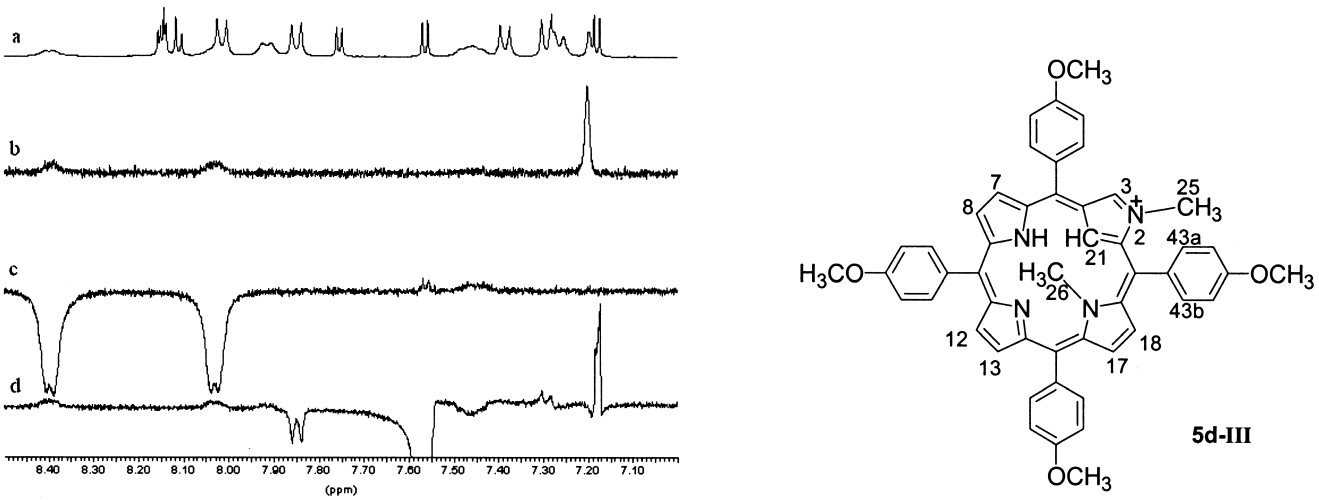

Figure 2. ^{1}H NMR spectra of **5d-III** in CD_2Cl_2: (a) no irradiation; (b) upon irradiation at 3.81 ppm; (c) upon irradiation at 8.40 ppm; (d) upon irradiation at 7.56 ppm.

atropisomers in addition to structural isomers, making it a more complicated mixture than compound **5**(**a**–**d**). Purification by recrystallization was not successful in this case.

2.4. Generation of singlet oxygen

1,3-Diphenylisobenzofuran (DPBF)[6] was used to determine the ability of these *N*,*N*′-dimethylated *N*-confused porphyrin salts to generate singlet oxygen. DPBF reacts quickly with singlet oxygen and its absorption decay around 418 nm can be readily monitored. The reaction products of DPBF have no absorption in the visible region and do not quench singlet oxygen. A solution containing DPBF (~18 μM) and *N*,*N*′-dimethylated *N*-confused porphyrin salts (e.g. **5b**, ~13 μM) was irradiated with a halogen lamp using a filter (700 nm) and monitored by UV–vis spectroscopy at 418 nm. Substantial decay of the UV–vis signal at 418 nm was observed confirming that *N*,*N*′-dimethylated *N*-confused porphyrin salts generate singlet oxygen (Fig. 3).

3. Conclusions

A series of *N*,*N*′-dimethylated *N*-confused tetraarylporphyrin salts were synthesized through methylation of *N*-confused tetraarylporphyrins using CH_3I in the presence of Na_2CO_3. The inner methylation of the major isomers occurs on N-24, as determined by X-ray diffraction and NMR spectroscopic analyses. These compounds have a broad absorption around 790 nm (~20,000 M^{-1} cm^{-1}). It has also been shown that *N*,*N*′-dimethylated *N*-confused tetraarylporphyrin salts can generate singlet oxygen when irradiated, suggesting that they are potential sensitizers for PDT.

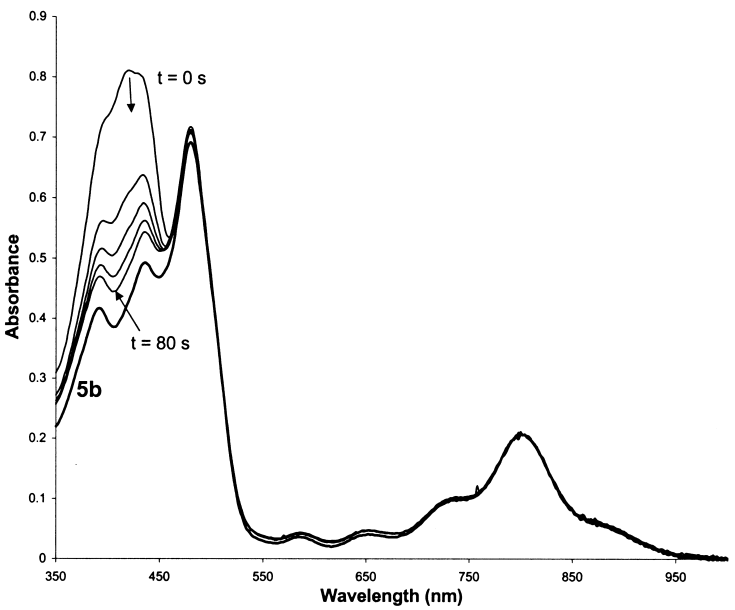

Figure 3. UV–vis spectra of a solution of DPBF and compound **5b** before and after irradiation (irradiation intervals at 20 s). The UV–vis spectrum of pure compound **5b** is shown in a thicker line.

4. Experimental

4.1. General information

Pyrrole (Acros) was distilled from CaH_2 before use. The silica gel was 230–400 mesh (Silicycle). Activity III basic alumina was obtained by adding 6% water to activity I Brockman basic alumina, 60–325 mesh (Fisher). All other materials and solvents were used as received. The NMR spectra were recorded on a Bruker WH-400, a Bruker AV-400 or a Bruker AMX-500 in the solvents indicated and were referenced to residual solvent peaks. Elemental analyses were performed on a Carlo Erba Elemental Analyzer1108. The UV–vis spectra were measured on a Cary 50. Mass spectra were determined on a KRATOS Concept IIHQ hybrid mass spectrometer. Irradiations were carried with a 250 W Osram HLX 64655 arc lamp in an Oriel lamp housing (model 66184). The light output passed through a filter: P70-700-S-Corion.

4.2. *N*-Confused porphyrins

N-Confused porphyrins were synthesized using a modification of Lindsey's procedure.[7] To a solution of pyrrole (0.52 mL, 7.5 mmol) and arylaldehyde (7.5 mmol) in CH_2Cl_2 (750 mL) was added methanesulfonic acid (MSA) (0.34 mL, 5.2 mmol). The mixture was stirred for 30 min after which DDQ (1.50 g, 6.6 mmol) was added. After 1 min, triethylamine (1.5 mL) was added. The crude reaction mixture was chromatographed with silica gel (14×4.4 cm) under vacuum and eluted with CH_2Cl_2. CH_2Cl_2/1.2% methanol eluted the product with impurities. The fractions were collected and concentrated under vacuum and then absorbed onto 7.5 g of activity III basic alumina. The absorbed sample was added to the top of a column with 150 g activity III basic alumina in 2:1 hexanes/CH_2Cl_2. The polarity of the eluant was increased from 2:1 to 1:1 to 1:2 hexanes/CH_2Cl_2, the *N*-confused porphyrins were eluted with 1:2 hexanes/CH_2Cl_2 (in the case of compounds **1c** and **1d**, the polarity of the eluant was increased from CH_2Cl_2 to CH_2Cl_2/0.2% methanol to elute the product). The solvent was removed under vacuum and the residue was triturated with CH_2Cl_2/hexanes to yield the product. Compound **1a**, yield: 373 mg (32%); compound **1b**, yield: 274 mg (22%); compound **1c**, yield: 259 mg (16%); compound **1d**, yield: 208 mg (15%); compound **1e**, yield: 316 mg (23%).

4.2.1. 2-Aza-5,10,15,20-tetrakis(*p*-methoxycarbonylphenyl)-21-carbaporphyrin (1c). R_f (silica–CH_2Cl_2/5% CH_3OH/2% Et_3N) 0.46; ^1H NMR (400 MHz, CD_2Cl_2) δ=−5.24 (s, 1H), −2.56 (br s, 2H), 4.08 (d, 12H), 8.18–8.58 (m, 19H), 8.60 (d, *J*=4.7 Hz, 1H), 8.70 (s, 1H), 8.84 (d, *J*=4.7 Hz, 1H), 8.94 (d, *J*=4.7 Hz, 1H); UV–vis (CH_2Cl_2) λ_{max}/nm (log ε) 444 (5.31), 544 (4.07), 586 (4.22), 728 (4.15); MS (LSIMS) 847 (MH^+, 100%); HRMS (LSIMS) *m*/*e* calcd for $C_{52}H_{39}N_4O_8$: 847.27679, found 847.27667 (MH^+). Anal. calcd for $C_{52}H_{38}N_4O_8$: C, 73.75; H, 4.52; N, 6.62. Found: C, 73.95; H, 4.49; N, 6.72.

4.2.2. 2-Aza-5,10,15,20-tetrakis(*p*-methoxyphenyl)-21-carbaporphyrin (1d). R_f (silica–CH_2Cl_2/5% CH_3OH/2% Et_3N) 0.38; ^1H NMR (400 MHz, CD_2Cl_2) δ=−4.92 (s, 1H), −2.31 (br s, 2H), 4.04 (s, 3H), 4.07 (s, 6H), 4.09 (s, 3H), 7.25–7.49 (m, 8H), 8.00–8.13 (m, 4H), 8.25 (d, *J*=8.6 Hz, 4H), 8.55 (d, *J*=5.2 Hz, 3H), 8.61 (d, *J*=4.7 Hz, 1H), 8.64 (s, 1H), 8.89 (d, *J*=4.4 Hz, 1H), 8.97 (d, *J*=4.7 Hz, 1H); UV–vis (CH_2Cl_2) λ_{max}/nm (log ε) 442 (5.38), 514 (sh), 548 (sh), 592 (4.32), 736 (4.24); MS (LSIMS) 735 (MH^+, 100%); HRMS (LSIMS) *m*/*e* calcd for $C_{48}H_{39}N_4O_4$: 735.29713, found 735.29721 (MH^+). Anal. calcd for $C_{48}H_{38}N_4O_4$: C, 78.45; H, 5.21; N, 7.62. Found: C, 78.11; H, 5.10; N, 7.71.

4.2.3. 2-Aza-5,10,15,20-tetrakis(*m*-methoxyphenyl)-21-carbaporphyrin (1e). R_f (silica–CH_2Cl_2/5% CH_3OH/2% Et_3N) 0.50; ^1H NMR (400 MHz, CD_2Cl_2) δ=−5.12 (s, 1H), −2.45 (br s, 2H), 3.98 (s, 6H), 4.02 (s, 3H), 4.06 (s, 3H), 7.22–7.45 (m, 4H), 7.58–7.82 (m, 8H), 7.82–8.00 (m, 4H), 8.55–8.66 (m, 3H), 8.68 (d, *J*=4.7 Hz, 1H), 8.78 (s, 1H), 8.96 (d, *J*=4.7 Hz, 1H), 9.05 (d, *J*=5.2 Hz, 1H); UV–vis (CH_2Cl_2) λ_{max}/nm (log ε) 440 (5.34), 540 (4.06), 582 (4.13), 726 (4.11); MS (LSIMS) 735 (MH^+, 100%); HRMS (LSIMS) *m*/*e* calcd for $C_{48}H_{39}N_4O_4$: 735.29713, found 735.29827 (MH^+). Anal. calcd for $C_{48}H_{38}N_4O_4$: C, 78.45; H, 5.21; N, 7.62. Found: C, 78.44; H, 5.18; N, 7.71.

4.3. General method for synthesis of the *N*,*N*′-dimethylated *N*-confused porphyrins

N-Confused porphyrin (100 mg) was dissolved in a minimal amount of CH_2Cl_2 (about 10 mL). To this solution, CH_3I (8 mL) and Na_2CO_3 (250 mg) were added. The mixture was stirred for 2 days in the absence of light, then filtered through Celite. The filtrate was evaporated to dryness under vacuum and the residue was triturated with CH_2Cl_2/hexanes to yield the products.

4.3.1. *N*,*N*′-Dimethylated 2-aza-5,10,15,20-tetraphenyl-21-carbaporphyrin·I^- (5a). Yield: 110 mg (88%). R_f (silica–CH_2Cl_2/5% CH_3OH/2% Et_3N) 0.36; ^1H NMR (400 MHz, CD_2Cl_2) δ=−1.62 (d, *J*=1.4 Hz, 0.65H), −1.57 (d, *J*=1.5 Hz, 0.35H), −1.48 (s, 3×0.65H), −1.39 (s, 3×0.35H), 3.62 (s, 3×0.35H), 3.82 (s, 3×0.65H), 7.18–8.54 (m, 27H); UV–vis (CH_2Cl_2) λ_{max}/nm (log ε) 382 (sh), 476 (4.85), 582 (3.79), 650 (3.73), 724 (sh), 788 (4.39); MS (LSIMS) 643 (M^+, 100%); HRMS (LSIMS) *m*/*e* calcd for $C_{46}H_{35}N_4$: 643.28617, found 643.28623 (M^+). Anal. calcd for $C_{46}H_{35}N_4{\cdot}I{\cdot}1.5H_2O$: C, 69.26; H, 4.80; N, 7.02; I, 15.91. Found: C, 68.96; H, 4.76; N, 6.86; I, 15.82.

4.3.2. 2-Aza-2,24-dimethyl-5,10,15,20-tetraphenyl-21-carbaporphyrin·$CF_3SO_3^-$ (5a-III). Compounds **5a** (86 mg) was dissolved in 20 mL of CH_2Cl_2. Silver triflate (1.3 g) was added and the solution was stirred for 2 h. The mixture was chromatographed through a silica gel column (10×2.5 cm) and eluted with CH_2Cl_2 under vacuum. CH_2Cl_2/1% CH_3OH eluted the porphyrin triflate salts. The compound was recrystallized three times with CH_2Cl_2/hexanes giving **5a-III** (29 mg). Crystals of **5a-III** were obtained by solvent diffusion of hexanes into CH_2Cl_2. R_f (silica–CH_2Cl_2/5% CH_3OH/2% Et_3N) 0.36; ^1H NMR (400 MHz, CD_2Cl_2) δ=−1.60 (s, 1H), −1.49 (s, 3H), 3.81 (s, 3H), 7.24 (d, *J*=5.0 Hz, 1H), 7.43 (s, 1H), 7.62 (d, *J*=5.0 Hz, 1H), 7.70–8.13 (m, 20H), 8.16 (d, *J*=5.1 Hz, 1H), 8.20 (d, *J*=5.1 Hz, 1H), 8.33 (d, *J*=4.8 Hz, 1H), 8.47 (d,

J=6.4 Hz, 1H); UV–vis (CH_2Cl_2) λ_{max}/nm (log ε) 385 (sh), 475 (4.85), 580 (3.74), 650 (3.67), 724 (sh), 790 (4.41); MS (LSIMS) 643 (M^+, 100%). Anal. calcd for $C_{46}H_{35}N_4{\cdot}CF_3SO_3{\cdot}1.5H_2O$: C, 68.85; H, 4.67; N, 6.83; S, 3.91. Found: C, 68.99; H, 4.61; N, 6.78; S, 4.00.

Crystal data for **5a-III**. $C_{47}H_{35}N_4SO_3F_3{\cdot}H_2O$, M=810.89, triclinic, a=11.922(2) Å, b=13.505(2) Å, c=15.090(3) Å, α=110.043(6)°, β=94.106(6)°, γ=113.859(7)°, V=2023.9(6) Å^3, T=198.2 K, space group $P\bar{1}$ (#2), Z=2, μ(Mo K_α)=1.44 cm^{-1}, 11514 reflections measured, 5815 unique (R_{int}=0.056) which were used in all calculations. The final $Rw(F^2)$ was 0.176 (all data).

4.3.3. *N*,*N*′-Dimethylated 2-aza-5,10,15,20-tetrakis-(*p*-tolyl)-21-carbaporphyrin·I$^-$ (5b). Yield: 105 mg (85%). R_f (silica–CH_2Cl_2/5% CH_3OH/2% Et_3N) 0.36; ^{1}H NMR (400 MHz, CD_2Cl_2) δ=−1.53 (d, J=1.7 Hz, 0.65H), −1.48 (s, 3×0.65H), −1.45 (d, J=1.7 Hz, 0.35H), −1.34 (s, 3×0.35H), 2.65 (m, 12H), 3.61 (s, 3×0.35H), 3.81 (s, 3×0.65H), 7.1–8.5 (m, 23H); UV–vis (CH_2Cl_2) λ_{max}/nm (log ε) 392 (sh), 478 (4.85), 588 (3.64), 646 (3.69), 798 (4.22); MS (LSIMS) 699 (M^+, 100%); HRMS (LSIMS) *m/e* calcd for $C_{50}H_{43}N_4$: 699.34877, found 699.34859 (M^+). Anal. calcd for $C_{50}H_{43}N_4{\cdot}I{\cdot}0.5H_2O$: C, 71.85; H, 5.31; N, 6.70. Found: C, 71.85; H, 5.41; N, 6.70.

4.3.4. 2-Aza-2,24-dimethyl-5,10,15,20-tetrakis(*p*-tolyl)-21-carbaporphyrin·I$^-$ (5b-III). Compounds **5b** (109 mg) was recrystallized three times with CH_2Cl_2/hexanes to give the major isomer (34 mg). R_f (silica–CH_2Cl_2/5% CH_3OH/2% Et_3N) 0.36; ^{1}H NMR (400 MHz, CD_2Cl_2) δ=−1.55 (d, J=1.7 Hz, 1H), −1.49 (s, 3H), 2.63 (s, 6H), 2.66 (s, 6H), 3.82 (s, 3H), 7.22 (d, J=5.2 Hz, 1H), 7.33 (d, J=1.3 Hz, 1H), 7.51–8.05 (m, 17H), 8.15 (d, J=5.2 Hz, 1H), 8.18 (d, J=5.2 Hz, 1H), 8.29 (d, J=4.7 Hz, 1H), 8.34 (br s, 1H); UV–vis (CH_2Cl_2) λ_{max}/nm (log ε) 390 (sh), 435 (sh), 480 (4.78), 585 (3.54), 650 (3.56), 800 (4.26); MS (LSIMS) 699 (M^+, 100%). Anal. calcd for $C_{50}H_{43}N_4{\cdot}I{\cdot}H_2O$: C, 71.08; H, 5.37; N, 6.63; I, 15.02. Found: C, 71.05; H, 5.31; N, 6.58; I, 14.95.

4.3.5. *N*,*N*′-Dimethylated 2-aza-5,10,15,20-tetrakis-(*p*-methoxycarbonylphenyl)-21-carbaporphyrin·I$^-$ (5c). Yield: 103 mg (87%). R_f (silica–CH_2Cl_2/5% CH_3OH/2% Et_3N) 0.36; ^{1}H NMR (400 MHz, CD_2Cl_2) δ=−1.79 (m, 1H), −1.49 (m, 3H), 3.65 (s, 3×0.27H), 3.87 (s, 3×0.73H), 4.05 (m, 12H), 7.20–8.73 (m, 23H); UV–vis (CH_2Cl_2) λ_{max}/nm (log ε) 386 (sh), 478 (4.84), 576 (3.86), 652 (3.81), 726 (sh), 792 (4.24); MS (LSIMS) 875 (M^+, 100%); HRMS (LSIMS) *m/e* calcd for $C_{54}H_{43}N_4O_8$: 875.30809, found 875.30815 (M^+). Anal. calcd for $C_{54}H_{43}N_4O_8{\cdot}I{\cdot}2.5H_2O$: C, 61.89; H, 4.62; N, 5.35. Found: C, 61.99; H, 4.42; N, 5.20.

4.3.6. 2-Aza-2,24-dimethyl-5,10,15,20-tetrakis(*p*-methoxycarbonylphenyl)-21-carbaporphyrin·I$^-$ (5c-III). Compounds **5c** (78.5 mg) was recrystallized three times with CH_2Cl_2/hexanes to give the major isomer (29 mg). R_f (silica–CH_2Cl_2/5% CH_3OH/2% Et_3N) 0.36; ^{1}H NMR (400 MHz, $CDCl_3$) δ=−1.45 (d, 4H), 3.91 (s, 3H), 4.06 (s, 12H), 7.19 (s, 1H), 7.52 (s, 2H), 7.82–8.85 (m, 20H); UV–vis (CH_2Cl_2) λ_{max}/nm (log ε) 385 (sh), 480 (4.83), 585 (3.67), 655 (3.16), 725 (sh), 790 (4.26); MS (LSIMS) 875 (M^+, 100%). Anal. calcd for $C_{54}H_{43}N_4O_8{\cdot}I{\cdot}H_2O$: C, 63.53; H, 4.44; N, 5.49; I, 12.43. Found: C, 63.26; H, 4.55; N, 5.48; I, 12.20.

4.3.7. *N*,*N*′-Dimethylated 2-aza-5,10,15,20-tetrakis-(*p*-methoxyphenyl)-21-carbaporphyrin·I$^-$ (5d). Yield: 112 mg (92%). R_f (silica–CH_2Cl_2/5% CH_3OH/2% Et_3N) 0.36; ^{1}H NMR (400 MHz, CD_2Cl_2) δ=−1.43 (s, 3×0.7H), −1.37 (d, J=1.5 Hz, 1×0.7H), −1.22 (d, 4×0.3H), 3.60 (s, 3×0.3H), 3.82 (s, 3×0.7H), 4.00–4.14 (m, 12H), 7.07–8.50 (m, 23H); UV–vis (CH_2Cl_2) λ_{max}/nm (log ε) 436 (4.82), 486 (4.97), 592 (3.62), 662 (3.82), 818 (4.40); MS (LSIMS) 763 (M^+, 100%). Anal. calcd for $C_{50}H_{43}N_4O_4{\cdot}I{\cdot}1.5H_2O$: C, 65.43; H, 5.05; N, 6.10. Found: C, 65.67; H, 4.88; N, 5.98.

4.3.8. 2-Aza-2,24-dimethyl-5,10,15,20-tetrakis(*p*-methoxyphenyl)-21-carbaporphyrin·I$^-$ (5d-III). Compounds **5d** (89 mg) was recrystallized three times with CH_2Cl_2/hexanes to give the major isomer **5d-III** (37 mg). R_f (silica–CH_2Cl_2/5% CH_3OH/2% Et_3N) 0.36; ^{1}H NMR (500 MHz, $CDCl_3$) δ=−1.47 (s, 3H), −1.44 (s, 1H), 3.81 (s, 3H), 4.01–4.13 (m, 12H), 7.16 (d, J=4.9 Hz, 1H), 7.19 (s, 1H), 7.28 (m, 4H), 7.38 (d, J=8.6 Hz, 2H), 7.46 (m, 2H), 7.56 (d, J=4.9 Hz, 1H), 7.75 (d, J=4.7 Hz, 1H), 7.84 (d, J=8.7 Hz, 2H), 7.91 (d, J=7.0 Hz, 2H), 8.04 (m, 3H), 8.11 (d, J=5.1 Hz, 1H), 8.14 (d, J=4.6 Hz, 1H), 8.15 (d, J=5.1 Hz, 1H), 8.40 (d, J=6.4 Hz, 1H); UV–vis (CH_2Cl_2) λ_{max}/nm (log ε) 436 (4.78), 486 (4.91), 590 (3.56), 658 (3.74), 824 (4.37); MS (LSIMS) 763 (M^+, 100%); HRMS (LSIMS) *m/e* calcd for $C_{50}H_{43}N_4O_4$: 763.32843, found 763.32857 (M^+). Anal. calcd for $C_{50}H_{43}N_4O_4{\cdot}I$: C, 67.40; H, 4.87; N, 6.29; I, 14.25. Found: C, 67.11; H, 4.97; N, 6.16; I, 14.09.

4.3.9. *N*,*N*′-Dimethylated 2-aza-5,10,15,20-tetrakis-(*m*-methoxyphenyl)-21-carbaporphyrin·I$^-$ (5e). Yield: 99 mg (82%). R_f (silica–CH_2Cl_2/5% CH_3OH/2% Et_3N) 0.36; ^{1}H NMR (400 MHz, CD_2Cl_2) δ=−1.61 (m, 1H), −1.48 (d, 3×0.7H), −1.39 (s, 3×0.3H), 3.68 (s, 3×0.3H), 3.86 (s, 3×0.7H), 3.95–4.17 (m, 12H), 7.21–8.42 (m, 23H); UV–vis (CH_2Cl_2) λ_{max}/nm (log ε) 378 (sh), 478 (4.95), 584 (3.81), 654 (3.74), 724 (sh), 788 (4.38); MS (LSIMS) 763 (M^+, 100%); HRMS (LSIMS) *m/e* calcd for $C_{50}H_{43}N_4O_4$: 763.32843, found 763.32854 (M^+). Anal. calcd for $C_{50}H_{43}N_4O_4{\cdot}I{\cdot}0.5H_2O$: C, 66.74; H, 4.93; N, 6.23; I, 14.10. Found: C, 66.72; H, 4.93; N, 6.30; I, 13.97.

4.4. Singlet oxygen tests

A solution containing DPBF and an *N*,*N*′-dimethylated *N*-confused porphyrin salt (one of compounds **5**(**a**–**e**) or the major isomer of **5**(**a**–**d**)) (OD=0.8–1.0 at 418 nm, OD=0.1–0.2 at irradiation wavelength) was prepared and the UV–vis spectra were measured. The solution was then irradiated with a halogen lamp using a filter (700 nm) for four 20 s intervals and UV–vis spectra were taken after each interval. Substantial decay of the signal around 418 nm was observed in each case. No change in UV–vis spectra was observed after a sample containing DPBF and an *N*,*N*′-dimethylated *N*-confused porphyrin salts was left in the dark for 10 min, and there is also no change in UV–vis

spectra after irradiating a solution containing only DPBF or an *N*,*N*′-dimethylated *N*-confused porphyrin salts for 1 min.

4.5. Supporting information available

Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Center as supplementary publication number CCDC 169756.

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References

1. Furuta, H.; Asano, T.; Ogawa, T. *J. Am. Chem. Soc.* **1994**, *116*, 767–768.
2. Chmielewski, P. J.; Latos-Grazynski, L.; Rachlewicz, K.; Glowiac, T. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 779–781.
3. Chmielewski, P. J.; Latos-Grazynski, L. *J. Chem. Soc., Perkin Trans. 2* **1995**, 503–509.
4. Chmielewski, P. J.; Latos-Grazynski, L.; Glowiak, T. *J. Am. Chem. Soc.* **1996**, *118*, 5690–5701.
5. (a) MacDonald, I. J.; Dougherty, T. J. *J. Porphyr. Phthalocya.* **2001**, *5*, 145–158. (b) Sternberg, E.; Dolphin, D. *Curr. Med. Chem.* **1996**, *3*, 293–324.
6. Spiller, W.; Kliesch, H.; Wohrle, D.; Hackbarth, S.; Roder, B.; Schnurpfeil, G. *J. Porphyr. Phthalocya.* **1998**, *2*, 145–158.
7. Geier, III., G. R.; Haynes, D. M.; Lindsey, J. S. *Org. Lett.* **1999**, *1*, 1455–1458.