2,7,12,17-Tetra(*p*-butylphenyl)-3,6,13,16-tetraazaporphycene: The First Example of a Straightforward Synthetic Approach to a New Class of Photosensitizing Macrocycles

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Selected on the basis of computational studies and synthetic feasibility, the title compound **9c** has been obtained by cross-coupling of 4,4′-bis(*p*-butylphenyl)-2,2′-biimidazole-5,5′-dicarbaldehyde (**28c**) followed by oxidative aromatization. The introduction of a Suzuki coupling protocol opens the way to 2,7,12,17-tetraryl-substituted 3,6,13,16-tetraazaporphycenes avoiding the development of a de novo synthesis whenever a new peripheral substituent is desired. As predicted by computational studies, oxidation of the non-aromatic precursor **33c** to yield the azaporphycene macrocycle **9c** is more favourable than in the case of porphycene itself. The absorption spectrum of **9c** shows a substantial bathochromic shift relative to porphycene **1a**, revealing a synergism between aza substitution in the macrocycle and phenyl substitution at its periphery.

Introduction

Tetrapyrrole macrocycles and related compounds continue to be the focus of intense research activity due to their particular optical and electric properties, which find applications in fields ranging from materials science to biomedicine. Specifically for the later applications, their photosensitizing ability is exploited in dermatology (treatment of psoriasis or acne),[1,2] ophthalmology (treatment of macular degeneration in the elderly),[3] inactivation of bacteria,[4,5] purification of blood to remove viruses such as HIV-1, herpes simplex, cytomegalovirus, and hepatitis-inducing virus,[6,7] as well as for cancer treatment.[8]

Photodynamic therapy (PDT) or photochemotherapy has arisen as an attractive therapeutic approach to cancer treatment based on the use of photosensitizing drugs that accumulate preferentially in tumour tissues. Thus, irradiation of the tumour area with red light induces the formation of highly reactive oxygen species (mainly singlet oxygen, $^1O_2$) that ultimately lead to cell death.

Several families of compounds are currently being investigated as PDT drugs,[9] such as porphyrins, chlorins, bacteriochlorins, azaporphyrins, purpurins, phthalocyanines, texaphyrins, and naphthalocyanines. Particularly relevant for this work are porphycenes (**1**), porphyrin isomers with much higher absorption coefficients above 600 nm, due to their lower symmetry. Porphycene **1a** (G = H, Po) was first synthesised by Vogel and co-workers in 1986 (Figure 1).[10]

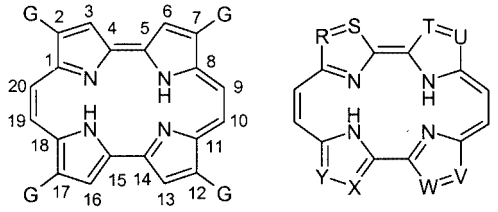

Figure 1. Porphycenes **1** and azaporphycenes **2**−**24** studied; R, S, T, U, V, W, X and Y are either CH or N (see text)

With perhaps the sole exception of symmetric phthalocyanines, the synthesis of most photosensitizers requires lengthy, multistep procedures. This is particularly true for aryl-substituted porphycenes.[11,12] Moreover, whenever new substituents need to be introduced — in order to modulate properties such as solubility, absorption spectra or redox potential — more often than not a de novo synthesis needs to be developed. When taken together, these are the main reasons precluding the use of combinatorial chemistry techniques for the development of novel photosensitizers.

Consequently, we set out to develop a new class of photosensitizing macrocycles that should be accessible by a synthetic itinerary eventually prone to a combinatorial approach. As a starting point, taking into account our pre-

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vious experience in the synthesis of 2,7,12,17-tetraphenylporphycene **1b** (G = Ph, TPPo) and its palladium complex ([PdTPPo]),[11−15] both of which are efficient at inactivating tumour cells in vitro, we studied which structural modifications would be required to allow for such an approach and, at the same time, would shift the absorption spectrum to the 700−800 nm region, where tissue is most transparent. This paper reports on the theoretical and experimental results obtained in that study.

Results and Discussion

Bearing in mind that the incorporation of nitrogen atoms to a conjugated macrocycle produces a bathochromic shift of the lowest energy band (often termed Q-band)[16] we investigated, by means of computational techniques, the effect of aza substitution on the position of the lowest-energy absorption band for 23 porphycene-like systems (**2**−**24**). Specifically, we calculated the Q-band shift $\Delta\lambda_{max}$ relative to porphycene **1a** (G = H, Po) (Figure 1). Azaporphycenes **2**−**24** were constructed by the formal stepwise substitution of the pyrrole units present in porphycene by imidazole and triazole rings. This procedure includes tautomeric isomers (cf. pairs **2**−**3**, **5**−**6**, **13**−**14**, **16**−**17** and **19**−**20**). Their geometries were optimised at the B3LYP/6−31G** level of theory,[17,18] followed by a TDDFT calculation at the same level in order to predict the UV/Vis spectra.[19]

The results obtained (Table 1) show that, as expected, the introduction of nitrogen atoms in the porphycene structure should cause a bathochromic shift (in the range 3−120 nm) depending on the number and position of the nitrogen atoms incorporated. The energy values of tautomeric azaporphycenes in turn reveals that the tautomers protonated at the less nitrogenated rings are more stable and have larger bathochromic shifts.

Azaporphycenes **2**−**24** could, in principle, be obtained by a McMurry coupling of the corresponding dialdehydes **25** and **26** (equal or different depending on the nature of R, S, T, U, V, W, X, and Y) followed by oxidative aromatization (spontaneous or chemically induced) of the reduced intermediate **27** (Scheme 1). Clearly, the most symmetrical azaporphycenes **9**, **10**, and **22** would be more easily accessible through this approach.

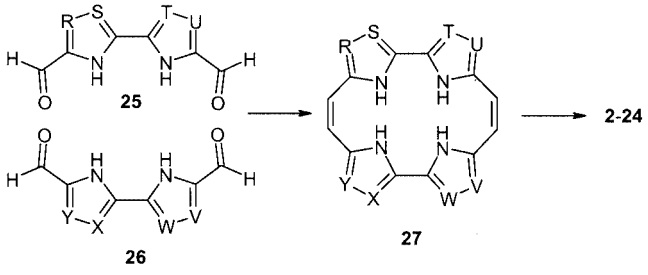
Rendering the macrocycle aromatic occurs at the expense of the aromaticity of three of the constitutive rings. This is a delicate balance and in related macrocycles the aromatic structure is often less stable than its reduced precursor. For instance, when two isoindole units were replaced by triazoles in the phthalocyanine macrocycle (formal introduction of four nitrogens) the triazolehemiporphyrazine obtained could not be rendered aromatic.[20] We assessed the feasibility of gas-phase oxidation of the annulenes **27** to symmetrical azaporphycenes **9**, **10**, and **22** relative to porphycene **1a** by means of calculations at the B3LYP/6−31G** level. We found the oxidation reaction to be more feasible for 3,6,13,16-tetraazaporphycene **9** than for porphycene **1a** (by −11.6 kcal/mol), comparable for 2,7,12,17-tetraazaporphycene **10** (+0.2 kcal/mol energy difference), and clearly less feasible for 2,3,6,7,12,13,16,17-octaazaporphycene **22** (by +16.7 kcal/mol) in line with the aforementioned triazolehemiporphyrazine case.[20] These results pointed to 3,6,13,16-tetraazaporphycene **9** as the synthetic candidate with the highest chance of being obtained. This is fortunate since, in addition, the synthesis of its precursor 2,2′-biimidazole can be achieved in one step from ammonia and glyoxal,[21] which is a significant advantage over the lengthy, multi-step synthesis of bipyrroles.[22]

Although the bathochromic shift expected for **9** is modest (ca. 10 nm, cf. Table 1), such a structure allows the introduction of further red-shifting substituents at positions C2, C7, C12, and C17, the ones with the least steric hindrance. Specifically, having observed previously that the presence of phenyl substituents in 2,7,12,17-tetraphenylporphycene (**1b**)

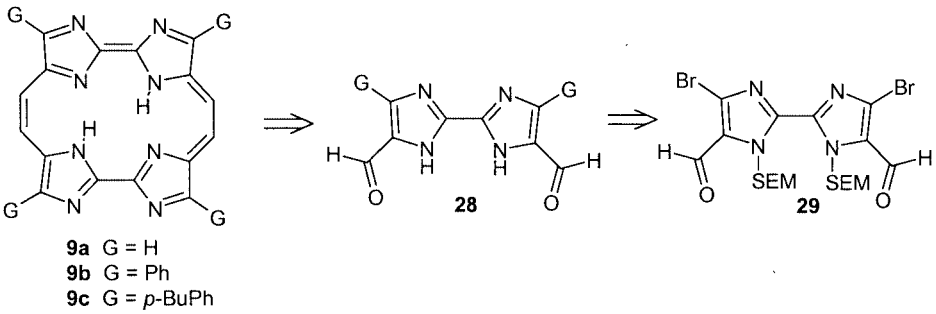
Table 1. Gas-phase energies (Hartrees) and $\Delta\lambda_{max}$ displacement differences[b] (nm) of selected azaporphycene cores.

	R	S	T	U	V	W	X	Y	Energy(H)[a]	$\Delta\lambda_{max}$
1a	CH	CH	CH	CH	CH	CH	CH	CH	−989.5513	0[b]
2	CH	N	CH	CH	CH	N	CH	CH	−1021.6696	19
3	CH	CH	N	CH	CH	CH	N	CH	−1021.6625	9
4	CH	CH	N	CH	CH	N	CH	CH	−1021.6659	12
5	N	CH	CH	CH	N	CH	CH	CH	−1021.6680	14
6	CH	CH	CH	N	CH	CH	CH	N	−1021.6617	−1
7	N	CH	CH	CH	CH	CH	CH	N	−1021.6648	3
8	N	CH	CH	N	N	CH	CH	N	−1053.7388	28
9	CH	N	N	CH	CH	N	N	CH	−1053.7471	10
10	N	CH	N	CH	N	CH	N	CH	−1053.7479	17
11	CH	N	CH	N	CH	N	CH	N	−1053.7476	15
12	N	CH	N	CH	CH	N	CH	N	−1053.7477	16
13	N	N	CH	CH	N	N	CH	CH	−1053.6986	53
14	CH	CH	N	N	CH	CH	N	N	−1053.6866	36
15	N	N	CH	CH	CH	CH	N	N	−1053.6935	12
16	N	CH	N	N	N	CH	N	N	−1085.7676	34
17	N	N	CH	N	N	N	CH	N	−1085.7731	44
18	N	CH	N	N	N	N	CH	N	−1085.7707	21
19	N	N	N	CH	N	N	N	CH	−1085.7646	54
20	CH	N	N	N	CH	N	N	N	−1085.7589	43
21	N	N	N	CH	CH	N	N	N	−1085.7621	30
22	N	N	N	N	N	N	N	N	−1117.7794	120
23	CH	CH	N	CH	CH	N	N	N	−1053.7122	17
24	N	N	CH	N	N	CH	CH	CH	−1053.7181	32

[a] All geometries and energies were calculated at the TDDFT-B3LYP/6−31G** level. [b] All values are relative to porphycene **1a** (λ_{max} = 553 nm), calculated at the TDDFT-B3LYP/6−31G** level.



Scheme 1. Synthetic itinerary for azaporphycenes **2**−**24** showing the oxidized intermediate **27**



Scheme 2. Retrosynthetic analysis for 2,7,12,17-tetrasubstituted 3,6,13,16-tetraazaporphycenes **9**

causes a bathochromic shift of 29 nm with respect to porphycene **1a**, we calculated the UV/Vis spectrum of the 2,7,12,17-tetraphenyl-substituted 3,6,13,16-tetrazaporphycene **9b** (G = Ph) at the TDDFT-B3LYP/3−21G level. Surprisingly, this calculation predicted a bathochromic shift of 106 nm with respect to porphycene **1a**, 80 nm with respect to 2,7,12,17-tetraphenylporphycene (**1b**), and 96 nm with respect to 3,6,13,16-tetraazaporphycene (**9**), i.e. a synergic effect of aza-substitution in the macrocycle and phenyl substitution in the periphery.

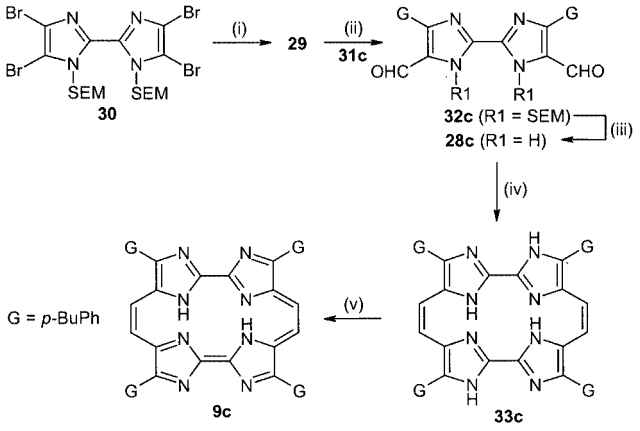
The retro-synthetic analysis depicted in Scheme 2 points to 4,4′-disubstituted 2,2′-biimidazole-5,5′-dicarbaldehydes **28** as the precursors needed to obtain 3,6,13,16-tetrazaporphycenes **9**.

As mentioned above, a general drawback of most current methods for the preparation of peripherally substituted porphyrinoids is the need to carry out a de novo synthesis whenever a new substituent is desired. In pursuing a synthetic methodology that would overcome this problem, thus allowing a combinatorial approach, we herewith propose 4,4′-dibromo-1,1′-bis[(trimethylsilyl)ethoxymethyl]-2,2′-biimidazole-5,5′-dicarbaldehyde (**29**) as the key intermediate (Scheme 2).

The SEM-protected 4,4′-dibromo-2,2′-biimidazole-5,5′-dicarbaldehyde **29** [SEM = (trimethylsilyl)ethoxymethyl], which should allow the introduction of almost any aryl and heteroaryl substituents at later stages of the synthesis by using Suzuki[23] or Stille[24,25] protocols, was easily accessible from tetrabromo-2,2′-biimidazole[26] (**30**) by treatment with BuLi in THF at −78 °C followed by addition of DMF (Scheme 3).

In order to incorporate G = *p*-butylphenyl (*p*-butyl substituent added to increase solubility in organic solvents) we treated **29** under Suzuki reaction conditions with the *p*-butylphenylboronic acid (**31c**) in toluene/ethanol/water in the presence of [tetrakis(triphenylphosphane)palladium(0)] and Na_2CO_3 to yield the corresponding 4,4′-bis(*p*-butylphenyl)-substituted SEM-protected dialdehyde **32c** (G = *p*-BuPh), which was deprotected with ethanolic HCl or tetrabutylammonium fluoride (TBAF) in THF to afford dialdehyde **28c** (G = *p*-BuPh) (Scheme 3).

Dialdehyde **28c** was deoxygenatively cross-coupled in the presence of the McMurry reagent[27−30] (low-valent titanium) to yield the corresponding 1,8,11,18-tetra-



Scheme 3. Synthetic route for azaporphycenes **9** applied to **9c** (G = *p*-BuPh): (i) BuLi/THF/−78 °C followed by DMF; (ii) *p*-butylphenylboronic acid (**31c**)/$[Pd(PPh_3)_4]$/Na_2CO_3/toluene/EtOH; (iii) HCl/EtOH/H_2O; (iv) $TiCl_4$/Zn(Cu)/THF; (v) O_2 in the presence of I_2

aza[20]annulene **33c** (G = *p*-BuPh), which was oxidized by molecular oxygen to the corresponding 2,7,12,17-tetrasubstituted 3,6,13,16-tetrazaporphycene **9c** (G = *p*-BuPh). Such oxidation could be accelerated by means of iodine vapour or 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ).

In this context, a bibliographic search revealed that the unsubstituted 3,6,13,16-tetraazaporphycene (**9a**) (G = H) was first cited in a communication to the 222nd ACS National Meeting (Chicago, 2001) by Sargent.[31] However, the synthesis of **9a** has not been published so far to the best of our knowledge. Other porphycene analogues containing external nitrogen atoms have been synthesised by Neidlein and co-workers. Specifically, this group reported the synthesis of the aromatic 21,23-dithia-3,13-diazaporphycenes (where two pyrrole rings of porphycene have been substituted by thiazoles, i.e., two external nitrogen atoms).[16] More significant for our work, the same group also described a macrocycle derived from 2,2′-bithiazole (i.e. containing four external nitrogen atoms) which, interestingly, could not be rendered aromatic.[32] The tetraazaporphycene **9c** described in this work is the first aromatic porphycene analogue containing four additional external nitrogens.

Consistent with our expectations, **9c** (G = *p*-BuPh) shows distinct absorption bands in the red (λ_{max} = 760 nm,

$\varepsilon = 2.4 \times 10^4$ M^{-1}cm^{-1}), which represents a red shift of about 130 nm relative to porphycene **1a**, and about 100 nm relative to 2,7,12,17-tetraphenylporphycene (**1b**)[13]. The position of this band is highly favourable for photodynamic therapy applications. Taken together, the absorption spectrum and the NMR spectroscopic data confirm a highly delocalised aromatic system. Compound **9c** is fluorescent ($\lambda_{max} = 777$ nm, quantum yield $\Phi_F = 0.03$) (Figure 2), forms a long-lived triplet state ($\tau_T = 40$ μs) and sensitizes the production of singlet oxygen, albeit with a low quantum yield ($\Phi_\Delta = 0.013$). All these properties suggest that tetraazaporphycenes **9** may be a new valuable class of photosensitizing compounds. A detailed photophysical characterisation of this compound will be published elsewhere.

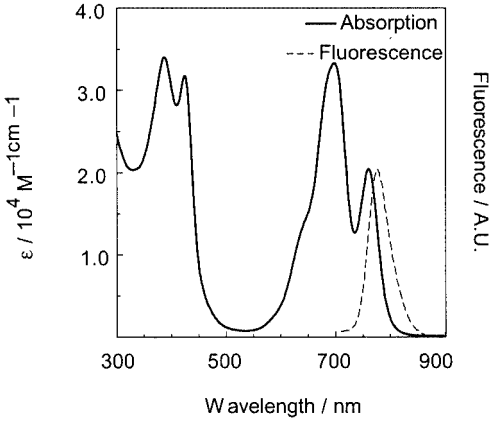


Figure 2. The UV/Vis absorption (−) and fluorescence (---) spectra of **9c** (G = *p*-BuPh)

Conclusion

In summary, by a combination of theoretical and experimental techniques, we have designed and developed a feasible synthetic route that opens the way to a new class of porphycene-like aromatic macrocycles amenable to a combinatorial approach. The approach followed may provide a cost-effective alternative for the development of new PDT drugs. Furthermore, the presence of the four outer nitrogen atoms opens the way to a new field of porphyrin chemistry based on the external coordination of metal ions[33,34] in addition to the conventional inner coordination. Work is currently in progress in such directions.

Experimental Section

General Remarks

Computational Details: Geometry optimisations and TDDFT[35−37] computations were carried out with the standard GAUSSIAN-98[38] quantum mechanical package. Calculations were performed on SGI workstations.

Experimental Details: All melting points were determined with a Büchi 530 capillary apparatus and are uncorrected. Infrared spectra were recorded on a Nicolet Magna 560 FTIR spectrophotometer. ^{1}H and ^{13}C NMR spectra were determined on a Varian Gemini-300 operating at a field strength of 300 and 75.5 MHz, respectively. Chemical shifts are reported in parts per million (δ) and coupling constants (*J*) in Hz, using in the case of ^{1}H NMR, TMS as an internal standard at δ = 0.00 ppm. All ^{13}C NMR spectra were referenced to the signal of the solvent (δ = 77.00 ppm, $CDCl_3$). Mass spectra (EI, 70 eV) were obtained on a VG AutoSpec while FAB(+)-HRMS were recorded at the Servicio de Espectrometría de Masas (Universidad de Córdoba) using a VG AutoSpec spectrometer (resolution 8000, 3-nitrobenzyl alcohol as matrix). Elemental microanalyses were obtained on a Carlo−Erba CHNS-O/EA 1108 analyzer and gave results for the elements stated with ±0.4% of the theoretical values. Thin-layer chromatography (TLC) was performed on precoated sheets of silica 60 Polygram SIL N-HR/UV254 (Macherey−Nagel, # 804023). Column chromatographies were performed using the "dry-column" flash technique.[39] THF was distilled from potassium/benzophenone immediately prior to use. Reagents were used without purification. Absorption spectra were recorded in a Varian Cary 4 spectrophotometer. Fluorescence spectra were recorded using a Jobin−Yvon Spex Fluoromax 2 spectrofluorometer.

4,4′-Dibromo-1,1′-bis[(trimethylsilyl)ethoxymethyl]-2,2′-biimidazole-5,5′-dicarbaldehyde (29): 5.3 mL (8.6 mmol) of a 1.6 M solution of BuLi in hexane was added to a solution of tetrabromo-2,2′-biimidazole (**30**; 2.8 g, 3.9 mmol)[26] in 120 mL of THF at −78 °C. The resulting mixture was stirred for 30 min and 1 mL of DMF was then added. The mixture was stirred for 2 h and allowed to warm to room temp. for 12 h. The reaction mixture was poured into 200 mL of a saturated solution of NH_4Cl and extracted with EtOAc. The organic layer was dried ($MgSO_4$), concentrated in vacuo and the resulting residue was chromatographed with a gradient of EtOAc/hexane as the eluent to yield 1.7 g (2.8 mmol, 71%) of **29** as slightly yellow needles; m.p. 66−67 °C. IR (KBr): $\tilde{\nu}$ = 3038, 2996, 2954, 2894, 2835, 1673, 1450, 1385, 1322, 1097, 864, 834, 771, 731 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.89 (s, 2 H, CHO), 6.27 (s, 4 H, N-CH_2), 3.57 (t, *J* = 8.4 Hz, 4 H, O−CH_2), 0.87 (t, *J* = 8.4 Hz, 4 H, Si−CH_2), −0.06 [s, 18 H, Si$(CH_3)_3$] ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 179.4, 140.3, 130.1, 127.7, 74.3, 66.8, 17.8, −1.5 ppm. $C_{20}H_{32}Br_2N_4O_4Si_2$ (608.5): calcd. C 39.48, H 5.30, N 9.21; found C 39.53, H 5.32, N 9.16.

4,4′-Bis(*p*-butylphenyl)-1,1′-bis[(trimethylsilyl)ethoxymethyl]-2,2′-biimidazole-5,5′-dicarbaldehyde (32c): *p*-Butylphenylboronic acid (**31c**; 1.0 g, 5.6 mmol), 15 mL of a 2 M aqueous solution of Na_2CO_3, and 6 mL of EtOH were added to a solution of of 4,4′-dibromo-1,1′-bis(trimethylsilylethoxymethyl)-2,2′-biimidazole-5,5′-dicarbaldehyde (**29**; (1.7 g, 2.8 mmol). The resulting mixture was degassed with a stream of dry nitrogen for 10 min. Then, 0.3 g of [tetrakis(triphenylphosphane)palladium] was immediately added and the resulting mixture was refluxed for 7 h under argon. The resulting mixture was cooled, diluted with EtOAc, dried ($MgSO_4$) and concentrated in vacuo. The residue obtained was column chromatographed with a gradient of EtOAc/hexane as the eluent to yield 1.1 g (1.54 mmol, 55%) of **32c** as colourless needles; m.p. 92−93 °C. IR (KBr): $\tilde{\nu}$ = 3081, 2954, 2924, 2872, 2856, 1665, 1489, 1339, 1250, 1087, 861, 833, 767, 730 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 10.01 (s, 2 H, CHO), 7.64 (d, *J* = 8.1 Hz, 4 H, Ph), 7.32 (d, *J* = 8.1 Hz, 4 H, Ph), 6.45 (s, 4 H, N−CH_2), 3.61 (t, *J* = 8.4 Hz, 4 H, O−CH_2), 2.69 (t, *J* = 7.8 Hz, 4 H, CH_2) 1.66 (q, *J* = 7.8 Hz, 4 H, CH_2) 1.39 (m, *J* = 7.8 Hz, 4 H, CH_2), 0.96 (t, *J* = 7.8 Hz, 6 H, CH_3), 0.87 (t, *J* = 8.4 Hz, 4 H, Si−CH_2), −0.11 [s, 18 H, Si$(CH_3)_3$] ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 181.1,

154.5, 144.7, 141.2, 129.3, 129.2, 128.9, 128.7, 127.2, 74.5, 66.4, 35.5, 33.5, 22.3, 17.9, 13.9, −1.5 ppm. MS (70 eV): *m/z* (%) = 715 (100) [M^+], 671 (58), 583 (65), 527 (98), 469 (53). $C_{40}H_{58}N_4O_4Si_2$ (715.1): calcd. C 67.19, H 8.18, N 7.83; found C 67.19, H 8.14, N 7.79.

4,4′-Bis(*p*-butylphenyl)-2,2′-biimidazole-5,5′-dicarbaldehyde (28c): A suspension of 4,4′-bis(*p*-butylphenyl)-1,1′-bis[(trimethylsilyl)ethoxymethyl]-2,2′-biimidazole-5,5′-dicarbaldehyde (**32c**; 1.96 g, 2.7 mmol) in 30 mL of a 1:1 mixture of 10% HCl and ethanol was stirred at reflux for 1 h under argon. The resulting mixture was cooled and carefully neutralised with a 10% aqueous solution of Na_2CO_3. The resulting solid was filtered and washed with hexane to yield 0.95 g (2.1 mmol, 76%) of **28c** as a white solid (hexane/CH_2Cl_2); m.p. > 250 °C. IR (KBr): $\tilde{\nu}$ = 3250, 3030, 2956, 2926, 2871, 2856, 1677, 1649, 1506, 1463, 1324, 1157, 938, 836, 775, 738 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 9.92 (s, 2 H, CHO), 7.59 (d, *J* = 7.8 Hz, 4 H, Ph), 7.30 (d, *J* = 7.8 Hz, 4 H, Ph), 2.68 (t, *J* = 7.5 Hz, 4 H, CH_2) 1.64 (q, *J* = 7.5 Hz, 4 H, CH_2) 1.37 (m, *J* = 7.5 Hz, 4 H, CH_2), 0.95 (t, *J* = 7.5 Hz, 6 H, CH_3) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 182.7, 145.3, 139.8, 129.2, 129.0, 128.5, 128.3, 124.6, 35.4, 33.3, 22.3, 13.8 ppm. MS (70 eV): *m/z* (%) = 455 (89) [M^+], 454 (100), 411 (15), 231 (27). HRMS calcd. for $C_{28}H_{30}N_4O_2$ 454.2369; found 454.2363.

2,7,12,17-Tetra(*p*-butylphenyl)-3,20:6,9:10,13:16,19-tetraimino-1,8,11,18-tetraaza[20]annulene (33c): $TiCl_4$ (2.3 mL, 19 mmol) was added dropwise to a suspension of Zn/Cu couple(5) (2.7 g, 41 mmol) in 500 mL of anhydrous THF cooled to 0 °C. Then, 1 mL of anhydrous pyridine was added and the mixture was heated at reflux for 2 h. A solution of 4,4′-bis(*p*-butylphenyl)-2,2′-biimidazole-5,5′-dicarbaldehyde (**28c**; 0.95 g, 2.1 mmol) in 250 mL of anhydrous THF was added dropwise to the resulting black suspension. The mixture was then heated at reflux for 1 h, allowed to cool to room temp. and filtered through Celite. The filtrate was hydrolysed with a 10% aqueous ammonia solution and extracted with EtOAc (500 mL). The organic layer was dried ($MgSO_4$), concentrated in vacuo and the resulting residue was chromatographed with a gradient of EtOAc/hexane as the eluent to yield 0.06 g (71 mmol, 7%) of **33c** as a yellow powder (EtOEt/CH_2Cl_2). IR (KBr): $\tilde{\nu}$ = 3437, 2954, 2926, 2856, 2532, 1796, 1614, 1505, 1453, 1415, 1219, 1115, 961, 835, 696 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.31 (d, *J* = 7.8 Hz, 8 H, Ph), 7.15 (d, *J* = 7.8 Hz, 8 H, Ph), 6.28 (s, 4 H, 9,10,19,20-H), 2.63 (t, *J* = 7.5 Hz, 8 H, CH_2), 1.63 (q, *J* = 7.5 Hz, 8 H, CH_2) 1.38 (m, *J* = 7.5 Hz, 8 H, CH_2), 0.96 (t, *J* = 7.5 Hz, 12 H, CH_3) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 142.3, 136.7, 131.5, 128.6, 128.5, 127.6, 127.5, 115.4, 35.5, 33.6, 22.5, 14.1 ppm. HRMS calcd. for $C_{56}H_{61}N_8$ [MH^+] 845.5019; found 854.5003.

2,7,12,17-Tetra(*p*-butylphenyl)-3,6,13,16-tetraazaporphycene (9c): A solution of 2,7,12,17-tetra(*p*-butylphenyl)-3,20:6,9:10,13:16,19-tetraimino-1,8,11,18-tetraaza[20]annulene (**33c**; 0.06 g, 71 mmol) in 10 mL of THF was stirred in a closed vessel saturated with I_2 vapour for 48 h. The resulting dark green coloured solution was column chromatographed with a gradient of EtOAc/hexane as the eluent to yield 0.04 g (43 mmol,60%) of **9c** as a dark emerald green solid. IR (KBr): $\tilde{\nu}$ = 3131, 2955, 2927, 2856, 1609, 1487, 1465, 1414, 1249, 1133, 992, 945, 838 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 9.62 (s, 4 H, 9,10,18,19-H), 7.53 (d, *J* = 7.5 Hz, 8 H, Ph), 7.57 (d, *J* = 7.5 Hz, 8 H, Ph), 2.89 (t, *J* = 7.8 Hz, 8 H, CH_2) 1.85 (q, *J* = 7.8 Hz, 8 H, CH_2) 1.55 (m, *J* = 7.8 Hz, 8 H, CH_2), 1.09 (t, *J* = 7.8 Hz, 12 H, CH_3) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 166.2, 145.2, 140.9, 138.6, 131.9, 131.2, 129.0, 116.7, 35.9, 33.7, 22.8, 14.2 ppm. UV/Vis (toluene): λ_{max} (ε) = 388 (3.44 × 10^4), 425 (3.31 × 10^4), 698 (3.86 × 10^4), 760 nm (2.37 × 10^4). HRMS calcd. for $C_{56}H_{59}N_8$ [MH^+] 843.4863; found 843.4843.

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