SASAPOS, not Sisyphos: Highly Efficient 20-Step One-Pot Synthesis of a Discrete Organic–Inorganic Ion Cluster with a Porphyrin Core

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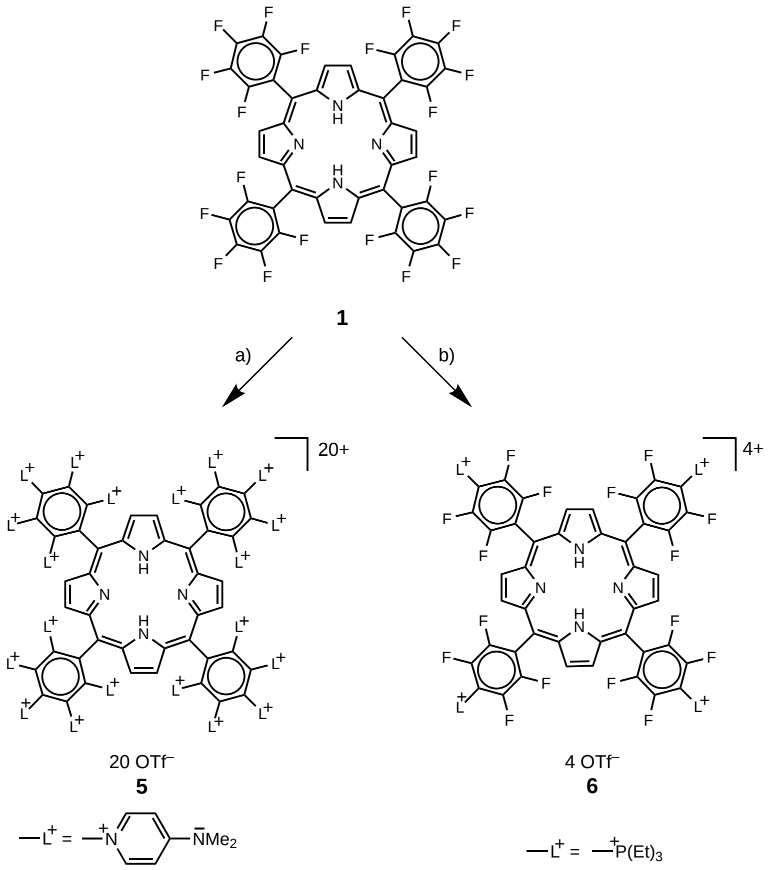
As a result of their central role in coordination chemistry, porphyrins have been functionalized in many ways, mostly by the combination of synthetic building blocks, and to a lesser extent by electrophilic (S_E) or radical (S_R) substitution.[1] Modifications by nucleophilic substitution (S_N) are limited to the replacement of fluorine atoms at the *para* positions of *meso*-tetrakis(pentafluorophenyl)porphyrin **1** with R_2N-, RS-, and RO-groups.[2]

More recently, the introduction of cationic substituents has become an area of interest, because cationic porphyrins have been shown to be biologically active.[3] In this context, up to four phosphonio[4] or 4-pyridinio[5] substituents have been introduced to peripheral positions of porphyrin derivatives by quaternization reactions. An electrochemical route that involves the oxidative addition of phosphonio-[6] and 1-pyridinio substituents[7] in the β or *meso* positions of porphyrin derivatives has recently also been successful for the first time. To date, there have been no reports of the direct introduction of cationic substituents into porphyrin derivatives by nucleophilic aromatic substitution (S_N(Ar)). We have now accomplished this through the development of Me_3SiOTf-assisted, selfactivated polyonio substitution of polyhalogenated (preferably fluorinated) substrates.[8] We refer to this highly efficient method by the acronym SASAPOS (*s*elf-*a*ctivated *s*ilyl-*a*ssisted *p*oly*o*nio *s*ubstitution), in which the first attribute refers to the increasingly electrostatically facilitated addition steps, and the second to the energy-releasing elimination steps of the addition/elimination cascade.

We were thus able to synthesize the first peronio-substituted benzene derivative by the reaction of hexafluorobenzene with 4-dimethylaminopyridine (DMAP; **2**) and trimethylsilyl triflate (**3**) in a SASAPOS cascade to form the hexatriflate.[8a] The concurrent energy-releasing formation of Me_3SiF causes this S_N(Ar) reaction sequence to be strongly exothermic overall, resulting in a characteristic lack of intermediate products. Once we found that pentafluorobenzene reacts in a similar fashion,[8a] we undertook the conversion of more complex pentafluorophenyl-substituted compounds. We have had an initial success by using **1** as a model compound.

Compound **1** was treated with **2** or triethylphosphane (**4**) in the presence of an equal amount of **3** in boiling chlorobenzene. Regardless of the initial quantity of the reagents used, exclusively icosakis- **5** or tetrakisonio-substituted **6** precipitated out of the organic solvent as analytically pure, dark violet salts. The yields were nearly quantitative when stoichiometric amounts of the reactants were used (Scheme 1).

Compounds such as **6** were recently synthesized for the first time by a relatively complex total synthesis.[4] The structure of **6** can be unequivocally determined from its analytical and spectroscopic data (see Experimental Section). The introduction of the phosphonio substituents at the 4-positions is as we expected.[2] A further SASAPOS cascade (beginning with the 3,5-positions of the phenyl rings) is apparently sterically hindered. Such a steric block of thermodynamically favorable S_N(Ar) reaction sequences did not occur when we tried the reaction with disk-shaped and strongly nucleophilic **2**.



Scheme 1. SASAPOS-cascades on **1**: a) + 20 DMAP, + 20 Me_3SiOTf; − 20 Me_3SiF; PhCl, Δ, 4 days, 99%; b) + 4 PEt_3, + 4 Me_3SiOTf; − 4 Me_3SiF; PhCl, Δ, 2 days, 97%.

We obtained porphyrin derivative **5**, with 20 cationic substituents, in high purity and were thus able to perform a crystallographic analysis. Unfortunately, four of the triflate ions were only detected as diffuse electron densities.[9] The

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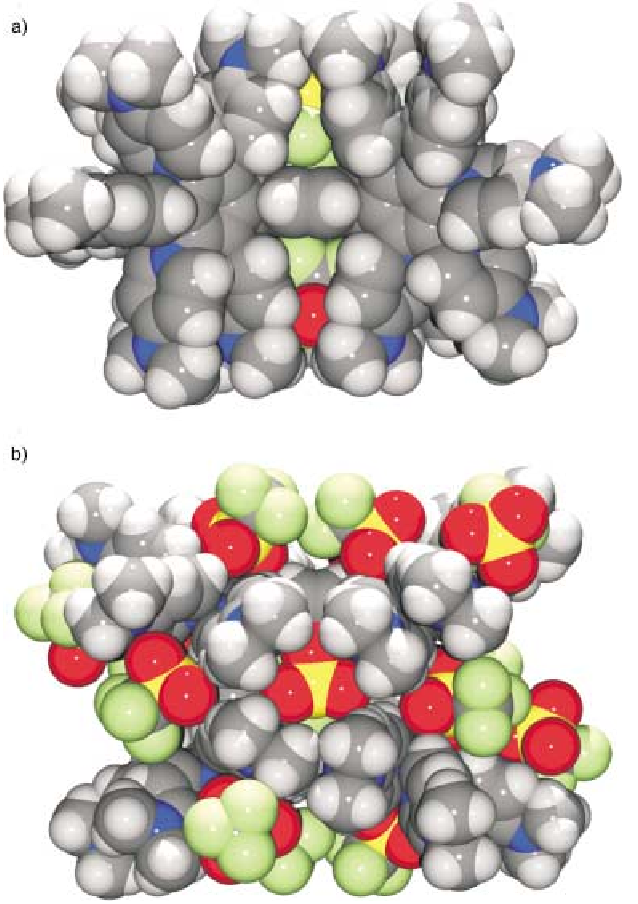

Figure 1. a) Cation of **5** with two centrally enclosed triflate ions (viewed parallel to the porphyrin plane). b) Cation of **5** with 16 triflate ions (viewed perpendicular to the porphyrin plane).

structure shown thus includes the icosakis(cation) and only 16 of the 20 triflate ions present (Figures 1 a and b).

The phenyl rings are twisted by 70–80° relative to the porphyrin framework; the dmap$^+$ ligands are twisted relative to the phenyl rings by a similar angle. The resulting structure of the polycation in **5** is marked by the following characteristics:

a) Large cavities are formed above and below the porphyrin π-electron system as a result of the four onio substituents at the 2,6-positions of the *meso* phenyl groups.
b) There are four large indentations between the four pentakis(onio)phenyl groups.
c) Vicinal onio ligands form many binding cavities on the periphery of the polycation.

A characteristic feature of the overall structure of the 1:20-electrolyte **5** is that the high positive potential of the polycation causes the 20 counterions to be massively attracted to it, resulting in discrete organic–inorganic ion clusters within the crystal. Thus each of the central cavities is filled by one anion, while each of the peripheral indentations contains two; spatial constraints cause the latter to be arranged alternately one above the other or next to each other. Aside from these ten anions within the cluster, six more were found to be within the local spheres of influence of the individual pentakisoniophenyl groups; of these, four were within binding cavities between vicinal onio ligands. The four anions that were detected as diffuse electron densities occupied positions on the periphery of the ion cluster (Figures 1 a and b). Overall, **5** can be described as a "penetrated ion cluster",[10] in which we can qualitatively recognize a shell-like gradation of the electrostatic anion stabilization within the cluster.

A characteristic of the NMR spectrum of **5** is the upfield shift, on average by 0.5–0.9 ppm (see Experimental Section), of all of the proton signals of the eight dmap$^+$ ligands bound at the 2,6-positions. This is as a result of the location of the ligands within the influence of the ring-current effect of the porphyrin π electrons (Figures 1 a and 1 b). Furthermore, **5** and **6** were analyzed by FAB mass spectrometry. Under these conditions, both ion clusters lose a triflate ion and are detected with high relative intensities as monocations with the expected m/z ratios of 5870 (**5**) or 1816 (**6**). This result is especially remarkable for **5**, and can be taken as direct evidence for the high stability of this type of discrete ion cluster.

The massive electrostatic effects of the onio substituents in **5** and **6** should significantly influence the redox potentials of the porphyrin framework. We looked into this by examining **5**.[11] The half-wave potentials for *meso*-tetraphenylporphyrin (**7**), the perfluorinated analogue **1**, and the ion cluster **5**, which are summarized in Table 1, illustrate this influence.[12] Usually, porphyrin derivatives have two oxidation and two reduction steps. We were unable to detect the second oxidation step (OX(2)) for **5**. The redox potentials for **5** are each shifted towards a more positive potential by about 800 mV relative to **7** (Table 1). This impressively demonstrates the electrostatic effect of the 20 cationic substituents in **5** on the central porphyrin π-electron system, and leads us to expect stable reduction products.

Table 1. Redox potentials of selected porphyrin derivatives[a]

	OX(2) [V]	OX(1) [V]	RED(1) [V]	RED(2) [V]
7[b]	+1.34	+1.10	−1.10	−1.48
1[c]	+1.54	+1.20	−0.97	−1.40
5[b]	-	+1.90	−0.26	−0.72

[a] All values are reported relative to the standard calomel electrode. [b] In CH_3CN. [c] In CH_2Cl_2.

The results we have described herein open up a myriad of approaches for the variation of the structures of ion clusters based on porphyrins:

a) by variation of the type, number, and arrangement of per- or partially fluorinated aryl substituents
b) by exchange reactions of the resulting ion clusters with the assistance of protic nucleophiles H–Nu
c) by anion metathesis
d) by NH double deprotonation and synthesis of corresponding metal complexes.

We are close to being able to replace the porphyrin system with other organic and inorganic building blocks, thus opening routes for the rational design of new types of ion clusters. Further investigations are currently underway.

Experimental Section

All work was carried out under a nitrogen atmosphere with purified and dried solvents.

5: A solution of *meso*-tetrakis(pentafluorphenyl)porphyrin (94 mg, 0.10 mmol), DMAP (305 mg, 2.50 mmol), and Me$_3$SiOTf (0.40 mL, 2.20 mmol) in chlorobenzene (25 mL) was stirred at reflux for 4 days; a precipitate begins to form after 5 h. The precipitate was separated, washed with dichloromethane ($5 \times \approx 5$ mL), and dried at 0.05 Torr to yield an intensely violet powder (577 mg, 99 %). ^{1}H NMR (400.05 MHz, CD$_3$NO$_2$): $\delta = -3.29$ (s, 2H; NH porphyrin), 2.81 (s, 48H; CH$_3$ *o*-dmap), 3.30 (s, 48H; CH$_3$ *m*-dmap), 3.38 (s, 24H; CH$_3$ *p*-dmap), 6.16 (d, ^3J(H,H) = 8.1 Hz, 16H; 3/5-H *o*-dmap), 7.06 (d, ^3J(H,H) = 8.1 Hz, 16H; 3/5-H *m*-dmap), 7.15 (d, ^3J(H,H) = 8.1 Hz, 8H; 3/5-H *p*-dmap), 7.86 (br d, ^3J(H,H) = 7.9 Hz, 16H; 2/6-H *o*-dmap), 8.32 (d, ^3J(H,H) = 8.1 Hz, 16H; 2/6-H *m*-dmap), 8.60 (br d, ^3J(H,H) = 7.8 Hz, 8H; 2/6-H *p*-dmap), 9.95 ppm (br m, 8H, C-H porphyrin); ^{13}C NMR (100.50 MHz, CD$_3$NO$_2$): $\delta = 41.37$ (s; CH$_3$), 41.64 (s; CH$_3$), 41.68 (s; CH$_3$), 108.27 (s; *meso*-C porphyrin), 109.74 (s; C3/5 dmap), 110.85 (s; C3/5 dmap), 111.11 (s; C3/5 *p*-dmap), 122.00 (q, $|^1J(\mathrm{C,F})| = 325.4$ Hz; CF$_3$), 140.14 (s; phenyl), 140.58 (s; phenyl), 140.63 (s; C2/6 *p*-dmap), 141.54 (s; C2/6 dmap), 141.60 (s; C2/6 dmap), 142.26 (br s; porphyrin), 142.97 (s; phenyl), 144.72 (s; phenyl), 156.73 (s; C4 dmap), 156.96 (br s; C-H porphyrin), 157.60 (s; C4 dmap), 157.77 ppm (s; C4 dmap); UV/Vis (CH$_3$CN): $\lambda_{\max}$ (ε) = 300 (345000), 437 (236000), 525 (25000), 595 nm (9000 mol^{-1} dm^3 cm^{-1}); FABMS (NBA): *m*/*z*: 5870 $[M-\mathrm{OTf}]^+$, 5720 $[M-\mathrm{HOTf}-\mathrm{OTf}]^+$, 5571 $[M-\mathrm{HOTf}-\mathrm{OTf}-\mathrm{OTf}]^+$, 2860 $[M-2\,\mathrm{OTf}]^{2+}$, 2786 $[M-\mathrm{HOTf}-2\,\mathrm{OTf}]^{2+}$, 1808 $[M-\mathrm{HOTf}-3\,\mathrm{OTf}]^{3+}$; elemental analysis (%): calcd. (M+6H$_2$O): C 39.99, H 3.65, N 10.06, S 10.46; found: C 40.12, H 3.66, N 9.90, S 10.32.

6: The same procedure as for **5**, but with **1** (128 mg, 0.13 mmol), PEt$_3$ (0.12 mL, 0.78 mmol), and Me$_3$SiOTf (0.12 mL, 0.65 mmol); reaction time: 2 days; precipitate formation after 1 h. Yield: 251 mg, 97 %, intensely violet powder. ^{1}H NMR (400.05 MHz, CD$_3$NO$_2$): $\delta = -2.92$ (s, 2H; NH Porphyrin), 1.63 (dt, ^3J(H,H) = 7.6, ^3J(H,P) = 20.8 Hz, 36H; CH$_3$), 3.07 (dq, ^3J(H,H) = 7.6, ^2J(H,P) = 19.8 Hz, 24H; CH$_2$), 9.36 ppm (br s, 8H, CH porphyrin); ^{13}C NMR (100.50 MHz, CD$_3$NO$_2$): $\delta = 4.43$ (d, ^2J(C,P) = 5.5 Hz; CH$_3$), 15.32 (d, ^1J(C,P) = 47.8 Hz; CH$_2$), 101.54 (dt, $|^2J(\mathrm{C,F})| = 18.3$, ^1J(C,P) = 70.5 Hz; C4 phenyl), 105.17 (s; *meso*-C porphyrin), 122.49 (q, $|^1J(\mathrm{C,F})| = 321.7$ Hz; CF$_3$), 129.06 (t, $|^2J(\mathrm{C,F})| = 19.3$ Hz; C1 phenyl), 148.66 (dm, $|^1J(\mathrm{C,F})| = 251.9$ Hz; CF phenyl), 149.94 (dm, $|^1J(\mathrm{C,F})| = 244.5$ Hz; CF phenyl), 156.74 ppm (s; CH porphyrin); ^{31}P NMR (161.70 MHz, CD$_3$NO$_2$): $\delta = 45.22$ ppm (m); FABMS (NBA): *m*/*z*: 1818 $[M-\mathrm{OTf}]^+$, 1668 $[M-\mathrm{HOTf}-\mathrm{OTf}]^+$, 1640 $[M-\mathrm{C_2H_5}-2\,\mathrm{OTf}]^+$, 1552 $[M+\mathrm{H}-\mathrm{PEt_3}-2\,\mathrm{OTf}]^+$; elemental analysis (%): calcd. (M+2H$_2$O): C 43.16, H 3.72, N 2.80, S 6.40; found: C 43.08, H 3.70, N 2.71, S 6.43.

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[1] L. Jaquinod in *The Porphyrin Handbook, Vol. 1* (Eds.: K. M. Kadish, K. M. Smith, R. Guilard), Academic Press, San Diego, **2000**, chapt. 5.

[2] P. Battioni, O. Brigaud, H. Desvaux, D. Mansuy, T. G. Taylor, *Tetrahedron Lett.* **1991**, *32*, 2893 – 2896.

[3] a) D. T. Croke, L. Perrouault, M. A. Sari, J. P. Battioni, D. Mansuy, C. Melene, *J. Photochem. Photobiol. B* **1993**, *18*, 41 – 50; b) B. Mestre, A. Jakobs, G. Pratviel, B. Meunier, *Biochemistry* **1996**, *35*, 9140 – 9149.

[4] G. Märkl, M. Reiß, P. Kreitmeier, H. Nöth, *Angew. Chem.* **1995**, *107*, 2439 – 2442; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 2230 – 2234.

[5] a) V. H. Houlding, K. Kalyansundra, M. Gratzel, L. R. Milgrom, *J. Phys. Chem.* **1983**, *87*, 3175 – 3184; b) I. Willner, Y. Degani, *J. Chem. Soc. Chem. Commun.* **1982**, 1249 – 1251; c) A. Harriman, G. Porter, M.-C. Richoux, *J. Chem. Soc. Faraday Trans. 2* **1982**, *78*, 1955 – 1961.

[6] L. Ruhlmann, A. Giraudeau, *Chem. Commun.* **1966**, 2007 – 2008.

[7] A. Giraudeau, L. Ruhlmann, L. El Kahef, M. Gross, *J. Am. Chem. Soc.* **1996**, *118*, 2969 – 2979.

[8] a) R. Weiss, B. Pomrehn, F. Hampel, W. Bauer, *Angew. Chem.* **1995**, *107*, 1446 – 1148; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1319 – 1321; b) R. Weiss, S. Engel, *Angew. Chem.* **1992**, *104*, 239 – 240; *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 216 – 217; c) R. Weiss, J. Seubert, *Angew. Chem.* **1994**, *106*, 900 – 901; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 891 – 893; d) R. Weiss, J. Seubert, F. Hampel, *Angew. Chem.* **1994**, *106*, 2038 – 2039; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 1952 – 1953; e) R. Weiss, R. May, B. Pomrehn, *Angew. Chem.* **1996**, *108*, 1319 – 1321; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1232 – 1234; f) R. Weiss, F. Pühlhofer, F. Hampel, *Z. Naturforsch. B* **2001**, *56*, 1209 – 1216; g) R. Weiss, F. Pühlhofer, *Z. Naturforsch. B* **2001**, *56*, 1360 – 1368.

[9] Crystal structure analysis: single crystals were obtained by diffusion of diethyl ether into a solution of **5** in acetonitrile. A crystal of **5** was mounted on a glass fiber in perfluorinated oil and was measured in a stream of cold gas. Intensity data were obtained with a Bruker AXS area detector[13] at −70 °C (Mo$_{\mathrm{K}\alpha}$ radiation, $\lambda = 0.71073$ Å, ω scan, scan range [°]: $1.80 < \theta < 22.50$). Compound **5** ($\mathrm{C_{210}H_{222}N_{44}O_{60}F_{60}S_{20}}\cdot 4\,\mathrm{CH_3CN}$): monoclinic, $P2_1/n$, $a = 21.789(3)$, $b = 29.575(4)$, $c = 23.712(3)$ Å, $\beta = 101.542(3)°$, $V = 14972(4)$ Å^3, $Z = 2$, $\mu = 0.909$ mm^{-1}, crystal size: $0.5 \times 0.5 \times 0.3$ mm^3, $F(000) = 6220$, $\rho_{\mathrm{calcd}} = 1.342$ Mg m^{-3}, data collection of 60456 intensities ($2\theta_{\max} = 45°$), 19483 independent, 11348 observed $[F_o > 4\sigma(F_o)]$, structure solution by direct methods (SHELXS 97),[14] refinement on F^2 with all measured reflections (SHELXL 97),[14] 1736 parameters. Diffuse electron densities of two disordered triflate ions were located by using the PLATON/SQUEEZE[15] program module, but could not be unambiguously refined. The positions of the H atoms were calculated and were considered isotropically, using a riding model. $R_1 = 0.1137$, $wR_2 = 0.3278$. CCDC-179729 contains the detailed crystallographic data for this publication. The data may be obtained free of charge from www.ccdc.cam.ac.uk/conts/retrieving.html (or they can be requested from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB21EZ; Fax: (+44)1223-336-033; or deposit@ccdc.cam.ac.uk).

[10] For more information on the concept of “penetrated ion pairs”, see: G. Boche, *Angew. Chem.* **1992**, *104*, 742 – 743; *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 731 – 732.

[11] The measurements were carried out in solutions of (NBu$_4$)BF$_4$ in acetonitrile (0.1N) with a concentration of **5** of 0.7 mmol L^{-1} and a feed rate of 100 mV s^{-1}.

[12] K. M. Kadish, G. Royal, E. van Caemelbecke, L. Gueletti in *The Porphyrin Handbook, Vol. 9* (Eds.: K. M. Kadish, K. M. Smith, R. Guilard), Academic Press, San Diego, CA, **2000**, pp. 1 – 212.

[13] Siemens, SMART, and SAINT. Area detector control and integration software. Siemens Analytical X-ray Instruments Inc. Madison, WI, USA, **1996**.

[14] Siemens, SHELXTL. Version 5.10/DOS/WIN95/NT, Siemens Analytical X-ray Instruments Inc. Madison, WI, USA, **1996**.

[15] “PLATON/SQUEEZE”: P. van der Sluis, A. L. Spek, *Acta Crystallogr. Sect. A* **1990**, *46*, 194 – 198.