Inorg. Chem. **2006**, *45*, 8288–8296

Inorganic Chemistry
Article

Chromogenic Indicator for Anion Reporting Based on an N-Substituted Oxoporphyrinogen

Jonathan P. Hill,*,† Amy Lea Schumacher,‡ Francis D'Souza,*,‡ Jan Labuta,§,£ Carl Redshaw,‖ Mark R. J. Elsegood,⊥ Masaru Aoyagi,▽ Takashi Nakanishi,§ and Katsuhiko Ariga§

International Center for Young Scientists, National Institute for Materials Science, 1-1 Namiki, Tsukuba, Ibaraki 305-0044, Japan, Department of Chemistry, Wichita State University, 1845 Fairmount, Wichita, Kansas, 67260-0051, Supermolecules Group, Organic Nanomaterials Center, National Institute for Materials Science, 1-1 Namiki, Tsukuba, Ibaraki 305-0044, Japan, Faculty of Mathematics and Physics, Charles University, V Holesovickach 2, 180 00 Prague 8, Czech Republic, Department of Chemical Sciences and Pharmacy, University of East Anglia, Norwich, Norfolk, NR4 7TJ, U.K., Chemistry Department, Loughborough University, Leicestershire, LE11 3TU, U.K., Nanoarchitectonics Research Center (NARC), National Institute of Advanced Industrial Science and Technology (AIST), Tsukuba Central 5, Higashi 1-1-1, Tsukuba, Ibaraki 305-8565, Japan

Received June 25, 2006

5,10,15,20-Tetrakis-3,5-di-*tert*-butyl-4-oxocyclohexadienylidene porphyrinogen and its di-N-benzylated derivative are solvatochromic dyes capable of binding anionic species. The influence of solvent polarity and hydrogen bonding on their electronic absorption spectra was observed. Hydrogen bonding by the porphyrinogen amine protons of acetone solvent molecules could be observed in the solid state. The acetone solvate of $N_{21}N_{23}$-dibenzyl-5,10,15,20-tetrakis-3,5-di-*tert*-butyl-4-oxocyclohexadienylidene porphyrinogen crystallized under anhydrous conditions in the space group $P\bar{1}$ with cell dimensions $a = 12.1693(11)$ Å, $b = 17.5849(13)$ Å, $c = 21.0965(17)$ Å, $\alpha = 69.870(4)°$, $\beta = 78.140(4)°$, $\gamma = 82.865(5)°$. These porphyrinogens are capable of binding a variety of anions and can be used to distinguish fluoride chromogenically from the other halide anions. Solvatochromism was combined with anion binding in an attempt to provide more selective tests for anions. The anion binding properties were investigated using UV/vis spectrophotometry and ^{1}H NMR spectroscopy.

Complexation of anionic species by molecules containing an appropriate binding site is an area of recent substantial interest in supramolecular chemistry.[1,2] Additionally, binding of a particular anion is involved in the activity or inhibition of activity of some proteins.[3] The specificity of this interaction is a desirable characteristic for synthetic derivatives, and many small molecules have been investigated in relation to this. The ability to complex and report the presence of several environmentally deleterious or toxic anions would be a valuable means for determination of those anions. Certain types of molecules lend themselves well to anion complex-

---

* To whom correspondence should be addressed. Phone: +81-29-860-4399 (J.P.H.). Fax: +81-29-860-4832 (J.P.H.). E-mail: Jonathan.Hill@nims.go.jp (J.P.H.); francis.dsouza@wichita.edu (F.D.).

† International Center for Young Scientists, National Institute for Materials Science.

‡ Wichita State University.

§ Organic Nanomaterials Center, National Institute for Materials Science.

£ Charles University.

‖ University of East Anglia.

⊥ Loughborough University.

▽ Nanoarchitectonics Research Center.

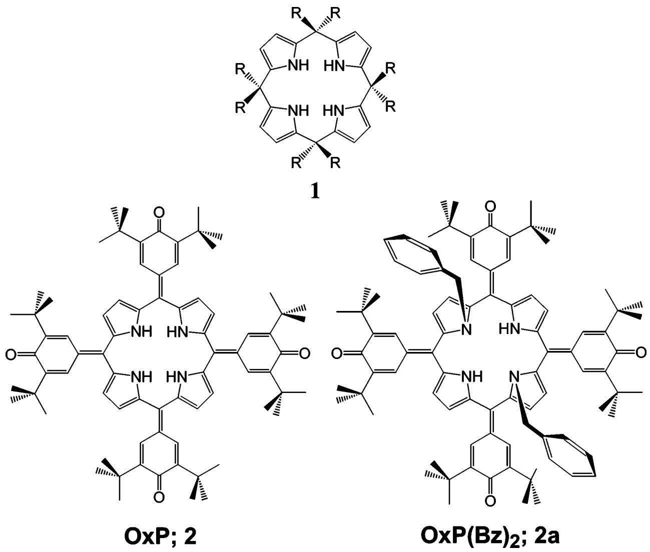
(1) (a) Gale, P. A. *Coord. Chem. Rev.* **2000**, *199*, 181. (b) *Supramolecular Chemistry of Anions*; Bianchi, A., Bowman-James, K., Garcia-Espana, E., Eds.; VCH: Weinheim, 1997. (c) Choi, K.; Hamilton, A. D. *Coord. Chem. Rev.* **2003**, *240*, 101−110. (d) Bowman-James, K. *Acc. Chem. Res.* **2005**, *38*, 671−678.

(2) (a) Koskela, S. J. M.; Fyles, T. M.; James, T. D. *Chem. Commun.* **2004**, 945−947. (b) Arimori, S.; Davidson, M. G.; Fyles, T. M.; Hibbert, T. G.; James, T. D.; Kociok-Koehn, G. I. *Chem. Commun.* **2004**, 1640−1641. (c) Choi, K.; Hamilton, A. D. *J. Am. Chem. Soc.* **2001**, *123*, 2456−2457.

(3) (a) Zak, O.; Ikuta, K.; Aisen, P. *Biochemistry* **2002**, *41*, 7416−7423. (b) Doyle, D. A.; Cabral, J. M.; Pfuetzner, R. A.; Kuo, A.; Gulbis, J. M.; Cohen, S. L.; Chait, B. T.; MacKinnon, R. *Science* **1998**, *280*, 69−77. (c) Sato, M.; Kubo, M.; Aizawa, T.; Kamo, N.; Kikukawa, T.; Nitta, K.; Demura, M. *Biochemistry*, **2005**, *44*, 4775−4784. (d) Bekker, E. G.; Creagh, A. L.; Sanaie, N.; Yumoto, F.; Lau, G. H. Y.; Tanokura, M.; Haynes, C. A.; Murphy, M. E. P. *Biochemistry* **2004**, *43*, 9195−9203. (e) Miller, A.-F.; Sorkin, D. L.; Padmakumar K. *Biochemistry* **2005**, *44*, 5969−5981.

10.1021/ic0611591 CCC: $33.50

Scheme 1



1

OxP; 2

$OxP(Bz)_2$; 2a

ation applications, notable examples being polyamide macrocycles,[4] calixarenes[5] and the calix[4]pyrroles.[6−8] Certain of these have been found to bind specific anions with great selectivity, permitting speculation on their applications.[7]

The calix[4]pyrroles (**1**) have been investigated intensively from the point of view of anion binding.[6−8] They are ideal for this purpose, being available in high yield from a relatively simple synthesis. Their appeal is furthered by availability of various post-macrocyclization modifications[9] and because unsymmetrical derivatives can be prepared, facilitating, for instance, the introduction of a fluorophoric reporting group.[10] Anion-binding properties of the calix[4]pyrroles depend on hydrogen-bonding interactions between the pyrrole NH groups and the analyte anion with the inherent flexibility of their porphyrinogen skeleton allowing the calix[4]pyrroles to exist in conformations somewhat analogous with the calixarenes, hence the term calix[4]pyrroles.

A species related to the calix[4]pyrroles is the 4-oxocyclohexadienylidene-substituted porphyrinogen **2**,[11,12] which, although bearing essential similarities in its structure with the calix[4]pyrroles, can be distinguished from them by an increased macrocyclic rigidity as a result of its conjugated electronic system. Another novel feature of the extended π-electronic system is an intense color in all of its derivatives. After adventitiously observing an effect (red-shift) related to the presence of an anionic species (perchlorate) in the electronic absorption spectra of the cyclohexadienylidene-substituted porphyrinogens during spectroelectrochemical analyses,[13] we were encouraged to investigate their behavior in the presence of a wider range of substrate anions. Since these compounds possess intense electronic absorptions, we hoped to obtain an anion-dependent chromogenic response.[14] In addition to this, these molecules bear a moderate solvatochromism, which we believed could improve anion differentiation.

Experimental Section

Materials. The compounds **2** and **2a** used in this study were prepared by previously reported methods.[13] Solvents used for spectroscopic measurements were obtained from Wako Chemical Co. or Aldrich Chemical Co. Tetra-*n*-butylammonium salts for anion binding studies were obtained from Aldrich Chemical Co., Tokyo Kasei Chemical Co., and Wako Chemical Co. Electronic absorption spectra were measured using a JASCO V-570 UV/vis/NIR spectrophotometer, a Princeton Applied Research (PAR) diode-array rapid scanning spectrometer, or a Shimadzu UV/vis spectrophotometer. ^{1}H NMR spectra were obtained using JEOL AL300BX or Bruker Avance 400 spectrometers. Variable-temperature measurements were performed using either instrument equipped with the appropriate liquid nitrogen cooling apparatus.

X-ray Crystallography. Crystals of the acetone solvate of compound **2a** were grown by refrigeration ($T = -20$ °C) of a solution of **2a** in anhydrous acetone. Very thin purple plates, which had appeared after 2−3 weeks, were subjected to X-ray crystallographic analysis using a rotating-anode Mo Kα source. A suitable crystal was selected and mounted on a glass fiber using perfluoropolyether oil. This was placed in the cold stream of the diffractometer (Bruker-Nonius Kappa CCD) at 120K prior to data collection.

Crystal data for 2a·acetone. $C_{93}H_{110}N_4O_5$, $M = 1363.85$, triclinic, $P\bar{1}$, $a = 12.1693(11)$ Å, $b = 17.5849(13)$ Å, $c =$

---

(4) (a) Kang, S. O.; Llinares, J. M.; Powell, D.; VanderVelde, D.; Bowman-James, K. *J. Am. Chem. Soc.* **2003**, *125*, 10152−10153. (b) Kang, S. O.; Hossain, M. A.; Powell D.; Bowman-James K. *Chem. Commun.* **2005**, 328−330. (c) Choi, K.; Hamilton, A. D. *J. Am. Chem. Soc.* **2003**, *125*, 10241−10249. (d) Hossain, M. A.; Llinares, J. M.; Powell, D.; Bowman-James, K. *Inorg. Chem.* **2001**, *40*, 2936−2937.

(5) (a) Evans,A. J.; Matthews, S. E.; Cowley, A. R.; Beer P. D. *Dalton Trans.* **2003**, 4644−4650. (b) Cooper, J. B.; Drew, M. G. B.; Beer P. D. *J. Chem. Soc., Dalton Trans.* **2000**, 2721−2728. (c) Gale, P. A.; Sessler, J. L.; Lynch V.; Sansom, P. I. *Tetrahedron Lett.* **1996**, *37*, 7881. (d) Blazejczyk, A.; Szczupak, M.; Wieczorek, W.; Cmoch, P.; Appetecchi, G. B.; Scrosati, B.; Kovarsky, R.; Golodnitsky, D.; Peled E. *Chem. Mater.* **2005**, *17*, 1535−1547.

(6) (a) Sessler, J. L.; Gale, P. A. In *The Porphyrin Handbook*; Kadish, K. M., Smith, K. M., Guilard, R., Eds.; Academic Press: San Diego, CA, Burlington, MA, 2000; Vol. 6, pp 257−278. (b) Camiolo, S.; Gale P. A. *Chem. Commun.* **2000**, 1129−1130. (c) Gale, P. A.; Sessler, J. L.; Král, V.; Lynch, V. *J. Am. Chem. Soc.* **1996**, *118*, 5140.

(7) Sessler, J. L.; Gale, P. A.; Genge, J. W. *Chem.−Eur. J.* **1998**, *4*, 1095.

(8) (a) Sessler, J. L.; Cho, W.-S.; Gross, D. E.; Shriver, J. A.; Lynch, V. M.; Marquez, M. *J. Org. Chem.* **2005**, *70*, 5982−5986. (b) Sessler, J. L.; An, D.; Cho, W.-S.; Lynch, V.; Yoon, D.-W.; Hong, S.-J.; Lee, C.-H. *J.* Org. Chem. **2005**, *70*, 1511−1517. (c) Gale, P. A.; Anzenbacher, P., Jr.; Sessler, J. L. *Coord. Chem. Rev.* **2001**, *222*, 57−102. (d) Schmidtchen, F. P. *Org. Lett.* **2002**, 4, 431−434.

(9) Woods, C. J.; Camiolo, S.; Light, M. E.; Coles, S. J.; Hursthouse, M. B.; King, M. A.; Gale, P. A.; Essex, J. W. *J. Am. Chem. Soc.* **2002**, *124*, 8644−8652.

(10) (a) Miyaji, H.; Kim, H.-K.; Sim, E.-K.; Lee, C.-K.; Cho, W.-S.; Sessler, J. L.; Lee, C.-H. *J. Am. Chem.* Soc. **2005**, *127*, 12510−12512. (b) Nishiyabu, R.; Anzenbacher, P. *J. Am. Chem. Soc.* **2005**, *127*, 8270−8271.

(11) (a) Milgrom, L. R.; Hill, J. P. *J. Heterocyclic Chem.* **1993**, *30*, 1629−1633. (b) Milgrom, L. R.; Hill, J. P.; Flitter, W. D. *J. Chem. Soc., Perkin Trans. 2* **1994**, 521−524. (c) Milgrom, L. R.; Hill, J. P.; Yahioglu, G. *J. Heterocyclic Chem.* **1995**, *32*, 97−101. (d) Milgrom, L. R.; Hill, J. P.; Dempsey, P. F. *Tetrahedron* **1994**, *50*, 13477−13484. (e) Milgrom, L. R. *Tetrahedron* **1983**, *39*, 3895−3898.

(12) (a) Hill, J. P.; Hewitt, I. J.; Anson, C. E.; Powell, A. K.; McCarty, A. L.; Karr, P. A.; Zandler, M. E.; D'Souza, F. *J. Org. Chem.* **2004**, *69*, 5861−5869. (b) Dolušić, E.; Toppet, S.; Smeets, S.; Meervelt, L. V.; Tinant, B.; Dehaen, W. *Tetrahedron* **2003**, *59*, 395−400.

(13) Hill, J. P.; Schmitt, W.; McCarty, A. L.; Ariga, K.; D′Souza, F. *Eur. J. Org. Chem.* **2005**, 2893−2902.

(14) Examples of chromogenic anion reporters: (a) Ros-Lis, J. V.; Martínez-Máñez, R.; Soto, J. *Chem. Commun.* **2005**, 5260−5262. (b) Aldakov, D.; Palacios, M. A.; Anzenbacher, P. *Chem. Mater.* **2005**, *17*, 5238−5241. (c) He, X.; Hu, S.; Liu, K.; Guo, Y.; Xu, J.; Shao, S. *Org. Lett.* **2006**, 8, 333−336. (d) R. Martínez-Máñez and F. Sancenón, *Chem. Rev.* **2003**, 103, 4419. (e) Chen, C.-F.; Chen, Q.-Y. *New J. Chem.* **2006**, *30*, 143−147.

Table 1. Donor Numbers and β Values of the Employed Solvents and Optical Absorption Spectral Data for the Investigated Porphyrinogens in Different Solvents

solvent	donor number[a]	β[b]	OxP, **2**	OxP(Bz)$_2$, **2a**
hexane	0.0	0.00	330, 364, 538(sh), 660	322, 486, 552(sh)
benzene	0.1	0.10	343, 514, 583(sh)	329, 503, 569(sh)
nitrobenzene	4.4	0.30	530, 592(sh)	521, 585(sh)
benzonitrile	11.9	0.41	342, 531, 594(sh)	339, 522, 589(sh)
acetonitrile	14.1	0.31	367, 543, 682	344, 519, 586
dioxane	14.8	0.37	350, 512.5, 584(sh)	338, 504, 574(sh)
acetone	17.0	0.48	360, 524, 590(sh)	352, 516, 580(sh)
ethyl acetate	17.1	0.45	356, 521, 602(sh)	348, 510, 583(sh)
ethanol	19.2	0.77	360, 535, 604(sh)	353, 517, 588(sh)
diethyl ether	19.2	0.47	343, 500, 577(sh)	344, 497
tetrahydrofuran	20.0	0.55	356, 521, 598(sh)	349, 507, 575(sh)
dimethylformamide	26.6	0.69	372, 535, 637	360, 534, 586, 757
dimethylsulfoxide	29.8	0.76	371, 544, 625	365, 536, 606(sh)
pyridine	33.1	0.64	389, 537, 631	374, 532(sh), 601, 679

[a] Taken from ref 16. [b] Taken from ref 17.

21.0965(17) Å, α = 69.870(4)°, β = 78.140(4)°, γ = 82.865(5) °, V = 4141.3(6) Å^3, Z = 2, D_c = 1.094 g cm^{-3}, μ(Mo Kα) = 0.067 mm^{-1}, crystal size 0.12 × 0.10 × 0.02 mm^3, 56 176 reflections measured of which 10 799 were independent, R_{int} = 0.193, data corrected for absorption on the basis of symmetry equivalent and repeated data (min and max transmission factors: 0.992, 0.999) and for Lp effects, structure solved by direct methods, F^2 refinement, R1 = 0.117 for 6377 data with $F^2 > 2\sigma(F^2)$, wR2 = 0.180 for all data, 946 parameters, largest difference map features ±0.23 e Å^{-3}.

Results and Discussion

Solvatochromism. Solvatochromism is the term for changes in electronic spectra of compounds when dissolved in different media and is related to changes in the electronic structure in the subject molecules caused by variation of solvent polarity or other interactions, especially hydrogen bonding.[15] For compounds **2** and **2a**, absorption maxima in different solvents appear in the range 400−900 nm, and this is illustrated by the spectra shown in Figure 1 while the positions of the absorption maxima in different solvents are summarized in Table 1. Low solubility of **2** in several of the solvents used here did not prevent us from observing the trends in its electronic absorption spectrum. However, **2a** proved soluble in a greater variety of solvents. Hexane is the least polar of the solvents employed and gives λ_{max} for **2a** at 486 nm. Increasing the polarity of the solvent results in a red-shift so that λ_{max} for 1,4-dioxane occurs at 504 nm. Other non-hydrogen-bonding solvents with comparable polarities, such as chloroform and dichloromethane, have λ_{max} of similar value. When solvents capable of H-bonding are used new absorption bands appear at 600 and 750 nm, the relative intensity of which varies with the solvent polarity and may be a measure of how strongly the hydrogen bonding interaction occurs with the oxoporphyrinogens, **2** and **2a**. The original 'Soret'-type band at 500 nm reduces in intensity with increasing solvent polarity. Variation of solvent polarity could also be accomplished using a binary mixture. Spectra were measured in dichloromethane−dimethylformamide mixtures of various ratios. Even at high CH$_2$Cl$_2$−DMF ratios, there is a notable color change from pink to violet with a gradual attainment of the blue color (see Supporting Information).

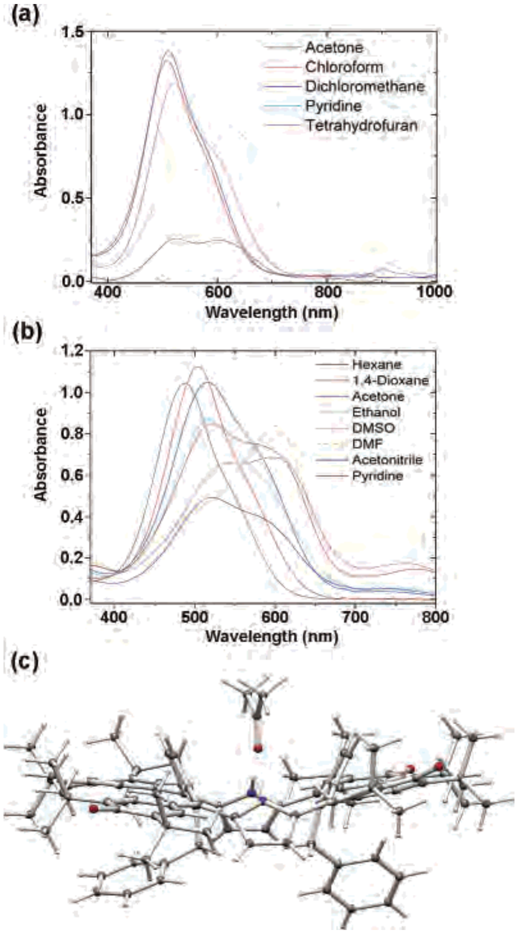


Figure 1. Solvatochromism in **2** and **2a**: (a) and (b) electronic absorption spectra of **2** and **2a**, respectively, in solvents of various polarities, and (c) molecular structure of the acetone solvate of **2a**. (For the molecular structure of the water solvate see ref 12a). **2a**, acetone hydrogen bond N−O distance: 2.904 Å.

To emphasize the possibility of hydrogen bonding involving the pyrrolic NH groups and solvent molecules, the crystal

---

(15) (a) Dodsworth, E. S.; Hasegawa, M.; Bridge, M.; Linert, W. *Comprehensive Coord. Chem. II* **2004**, *2* 351−365. (b) Karelson, M. In *Handbook of Solvents*; Wypych, G., Ed.; ChemTec: Toronto, 2001; pp 639−679. (c) Nigam, S.; Rutan, S. *Appl. Spectrosc.* **2001**, *55* (11), 362A-370A. (d) Carr, P. W. *Microchem. J.* **1993**, *48(1)*, 4−28. (e) Sone, K.; Fukuda, Y. *Rev. Inorg. Chem.* **1990**, *11* (2−4), 123−53. (f) Buncel, E.; Rajagopal, S. *Acc. Chem. Res.* **1990**, *23* (7), 226−31.

structure of the acetone solvate of **2a** was determined. Figure 1c shows the inclusion of acetone at the binding site of **2a** in the compound **2a·acetone**. Notably, crystals of **2a·acetone** are purple, which represents a departure from the usual green-red dichroism in crystals of these compounds. However, the purple color of the crystals is consistent with the observed solvatochromism of **2a**. When compared with the known structures of di-N-alkylated **2**,[12a,13] the most obvious difference is the displacement of the water molecule from the binding site between the pyrrolic NH groups. The $N_{22}-O_{acetone}$ distance in **2a·acetone** is 2.90 Å compared to 3.02 Å for the case where water is hydrogen bonded. This is one of the factors affecting the dihedral angles subtended between the pyrrole groups and the macrocyclic least squares plane, so that while the angle between benzyl-substituted pyrroles is similar in both water and acetone solvates, the angle subtended by the pyrroles involved in the H-bonding interaction is lower in the acetone solvate (41° and 43° against 47° and 52.4° for the water solvate[12a]).

Qualitatively, the solvatochromism of **2** and **2a** results in a color change from red-pink in nonpolar solvents through violet to blue for the most polar solvents used here (*N*,*N*-dimethylformamide, dimethyl sulfoxide). For the fully N-substituted derivatives of **2**, there is predictably no substantial change in the electronic spectrum upon variation of solvent polarity since the possibilities for hydrogen bonding and protic tautomerism have been effectively negated by complete N-alkylation.

Several models have been developed in the literature to visualize the linear solvation energy relationships.[15,16] A comprehensive collection of solvatochromic parameters and methods for simplifying the generalized solvatochromic equations has been reported by Kamlet et al.[17] In the present study, we utilized solvent donor number (quantitative measurement of Lewis basicity) and the β scale of HBA (hydrogen-bond acceptor) basicities to seek linear solvation energy relationships. The β scale provides a measure of the solvent's ability to accept a proton (donate an electron pair) in a solute-to-solvent hydrogen bond. Figure 2 illustrates the relationships between the solvent donor number, the β values, and the spectral shifts of compounds **2** and **2a**. The correlation coefficients for these plots were found to be 0.85, 0.97, 0.73, and 0.90, respectively, for plots a–d. The linear trend in the plots suggests that solute–solvent hydrogen bonding is primarily responsible for the observed solvatochromic effect of porphyrinogens.

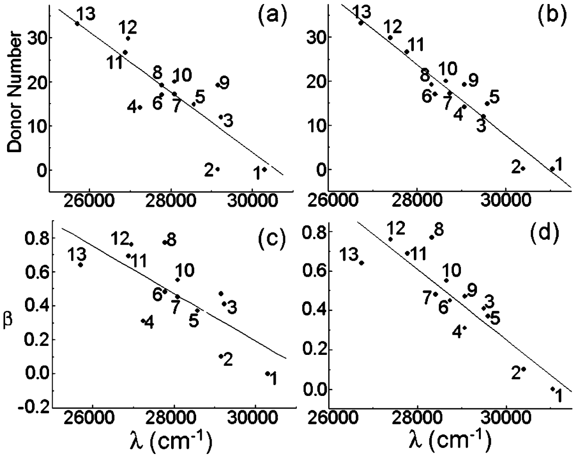


Figure 2. Plots of donor number versus absorption peak maxima (a and b), and β versus absorption peak maxima (c and d) for **2** (plots a and c) and **2a** (plots b and d). Solvents: 1 (hexane); 2 (benzene); 3 (benzonitrile); 4 (acetonitrile); 5 (1,4-dioxane); 6 (acetone); 7 (ethyl acetate); 8 (ethanol); 9 (diethyl ether); 10 (tetrahydrofuran); 11 (dimethylformamide); 12 (dimethyl sulfoxide); 13 (pyridine).

UV/Vis Spectrophotometry of Anion Binding for 2 and 2a. The potential of polytopic hydrogen-bonding sites can be exploited by assessing their anion binding properties. We observed previously that the electronic absorption spectra of the 4-oxocyclohexadienylidene porphyrinogens are modified by the presence of perchlorate and other anions. Therefore, electronic absorption spectroscopy was used to quantify the binding of halides and several other anions.

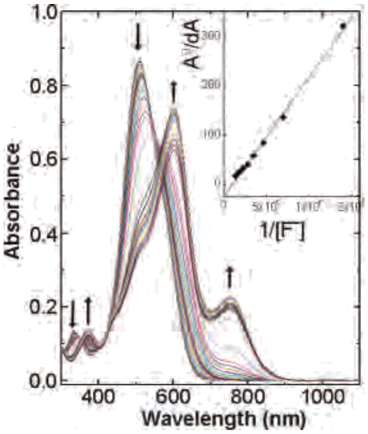


Figure 3. Spectral changes observed during titration of **2a** with tetrabutylammonium fluoride in dichloromethane. The figure inset shows the Benesi–Hildebrand plot constructed for determination of the binding constants

Figure 3 illustrates the spectral changes observed during the titration of tetrabutylammonium fluoride against a solution of **2a** in dichloromethane. During the titration, absorption bands located at 333 and 509 nm underwent a red-shift to 374 and 604 nm, respectively. In addition, a new intense band was observed at 753 nm. An isosbestic point was observed at 420 nm, suggesting the presence of one equilibrium process in solution. Similar spectral changes were observed for all of the anions investigated. The Job's plot of the method of continuous variation yielded a 1:1 stoichiometry for the porphyrinogen(**2a**)/anion complexes. The anion binding constants were evaluated using the spectral data by construction of Benesi–Hildebrand plots[18] (Figure 3, inset). Linear plots were observed for all of the studied anions, and the binding constants thus calculated are summarized in Table 2.

Interestingly, since compound **2** has the ability to bind two anions, two sets of spectral changes were observed during anion titrations (See Supporting Information for

---

(16) Gutman, V. *Coord. Chem. Rev.* **1976**, *18*, 225–255.

(17) Kamlet, M. J.; Abboud, J.-L. M.; Abraham, M. H.; Taft, R. W. *J. Org. Chem.* **1983**, *48*, 2877–2887.

(18) Benesi, H. A.; Hildebrand, J. H. *J. Am. Chem. Soc.* **1949**, *71*, 2703.

Table 2. Anion[a] Binding Constants for OxP, **2** and $OxP(Bz)_2$, **2a** Receptors Determined from the Absorption Titration Method in Dichloromethane at Room Temperature

	OxP, **2**			$OxP(Bz)_2$, **2a**	
anion	$\Delta\lambda$, $cm^{-1,\,b}$	K_1, M^{-1}	K_2 M^{-1}	$\Delta\lambda$, cm^{-1}	K, M^{-1}
F^-	821	1.0×10^5	2.7×10^4	854	1.2×10^5
Cl^-	647	8.3×10^4	3.2×10^4	521	5.1×10^4
Br^-	534	8.2×10^4	2.4×10^4	247	1.9×10^4
I^-	83	4.8×10^4	1.6×10^3	58	3.5×10^3
PF_6^-	15	1.2×10^4	1.5×10^3	8	3.2×10^3
ClO_4^-	19	1.5×10^4	2.1×10^3	62	7.9×10^3
NO_3^-	383	9.7×10^4	2.7×10^4	548	8.2×10^4
$C_2H_3O_2^-$	554	6.6×10^4	3.3×10^4	526	6.1×10^4
$H_2PO_4^-$	520	3.3×10^4	2.3×10^4	570	6.1×10^4

[a] Tetrabutylammonium salts were utilized. [b] For the first set of spectral changes.

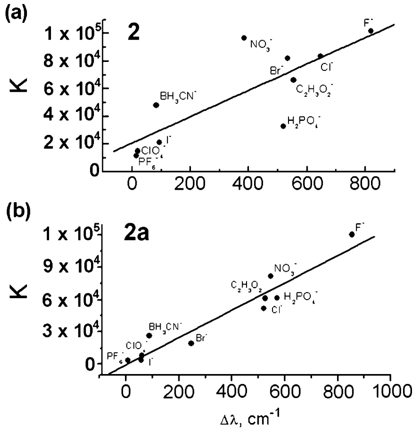


Figure 4. Plots of binding constant of different anions versus spectral shift for (a) **2** and (b) **2a**.

relevant figures of fluoride binding and for the Job's plot). Using this spectral data, the binding constants were evaluated and are also given in Table 2. The magnitudes of *K* values suggest stable anion binding by both porphyrinogens, which for halides follows the trend: $I^- < Br^- < Cl^- < F^-$. However, for polyatomic anions, no clear tread could be observed perhaps due to different modes of binding of these anions to the porphyrinogen pyrrolic NH groups. In general, porphyrinogen **2** shows higher *K* values compared to **2a** for a given anion (K_1 was utilized for comparison). The spectral shifts of the UV band were correlated with the *K* values, as shown in Figure 4. Good trends were observed for both of the investigated porphyrinogen derivatives. On the basis of the results of solvatochromic studies in Figure 2 and the results of Figure 4, one can conclude that hydrogen-bonding interactions are primarily responsible for these observations. Further ^1H NMR studies were performed to confirm the hydrogen-bonding interactions for solvent and anions by the investigated porphyrinogens.

^{1}H NMR Spectroscopy. In general, it is possible to detect hydrogen-bonding interactions during binding of an anion by a small molecule using ^1H NMR spectroscopy. Observation of the interaction is preferred in a solvent, such as dimethyl sulfoxide or acetonitrile, where formation of an ion pair by the anion salt (e.g., tetra-*n*-butylammonium fluoride) is not favored. For derivatives of **2**, which are poorly soluble in these solvents, this presented a problem. However, in the presence of excesses of the analyte anion, the compounds are somewhat solubilized, permitting measurement of their NMR spectra. This solubilization is evidently caused by anion complexation.

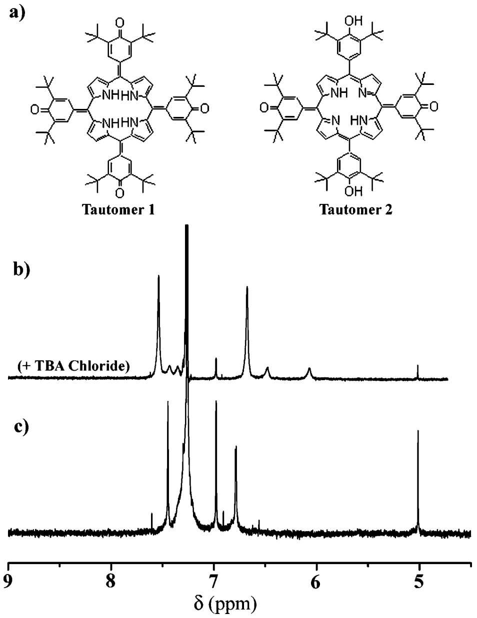


Figure 5. ^1H NMR spectra of **2** in $CDCl_3$ in the absence and presence of excess tetra-*n*-butylammonium chloride. (a) Structures of the two tautomers of **2** (Tautomer 1: porphyrinogen form, Tautomer 2: porphodimethene form). (b) ^1H NMR spectrum of **2** in the presence of excess tetra-*n*-butylammonium chloride revealing binding of chloride by the porphyrinogen form. (c) ^1H NMR spectrum of **2** in the absence of excess tetra-*n*-butylammonium chloride indicating its existence as the porphodimethene form.

Proton NMR spectra of **2** in the absence and presence of chloride ions in $CDCl_3$ are shown in Figure 5. We interpret the spectra with reference to the known protic tautomerization of **2**. The tautomerism is illustrated together with the ^1H NMR spectrum of a $CDCl_3$ solution of the tautomers in admixture. The NH and OH peaks assigned to the porphyrinogen (Figure 5b) and porphodimethene (Figure 5c) forms, respectively, are present. In the aromatic region, the peak due to residual chloroform obscures one of the peaks. It is notable that increasing the temperature of measurement shifts the tautomeric equilibrium to the porphyrinogen form. Stabilization of the porphyrinogen form can also be accomplished by introduction of a hydrogen-bonded guest species such as a halide or other anion. In the presence of anions the peaks due to the porphodimethene form are diminished, as illustrated in Figure 5b.

In the case of **2a** in $CDCl_3$, the complexation of an anion is again obviated not only by a downfield shift of the pyrrolic NH protons but by variations in the chemical shifts of the pyrrolic *β*-proton resonances. The downfield shift of the NH proton peak is a result of hydrogen bonding with the substrate anion. For the more strongly interacting fluoride, cyanide, and acetate anions, the resonance due to the NH protons gradually broadens with a slight downfield shift. Shifts in the positions of the *β*-proton resonances are also more pronounced than for the other anions studied because of larger macrocyclic perturbations. For instance, complexation

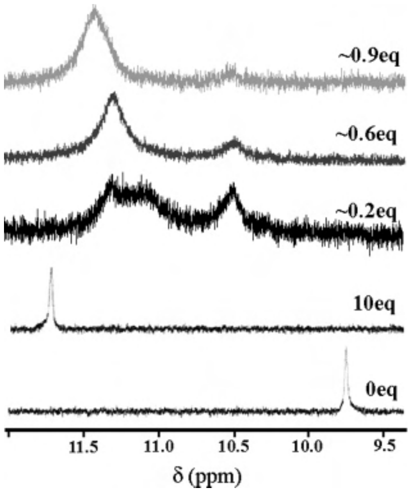


Figure 6. Low-temperature NMR data for **2a** in $CDCl_3$ solution at −70 °C and in the presence an increasing proportion (as indicated) of tetra-*n*-butylammonium fluoride.

by the smaller fluoride ion must cause more serious macrocyclic deformations, and this is born out by the substantial red-shift in the electronic spectrum. The potential coupling between proton and fluorine nuclei could not be initially observed in **2a**, although NMR spectra at depressed temperatures (Figure 6) indicate the presence of more than one species in solution assigned to complexed and noncomplexed **2a**. A third peak observed during the low-temperature measurements could be due to complexation of one fluoride ion by two molecules of **2a**. When dichloromethane was used as solvent, the complexation by fluoride ion can be more easily observed, and a titration of **2a** against fluoride ions in CD_2Cl_2 is shown in Figure 7. During the titration and for low proportions of fluoride ion, there appear two distinct NH resonances As fluoride ion concentration is increased the NH peak at lower field (assigned to the **2a**$\cdot F^-$ complex) increases then diminishes until, at proportions above 1 equiv, it disappears from the spectrum altogether, presumably because of anionic exchange. In the initial stages of the titration involving very low concentrations of fluoride ion, the NH resonance becomes significantly broadened although the NH peak(s) reappear at higher fluoride concentrations. The peak at higher field is due to the anion-free **2a**.

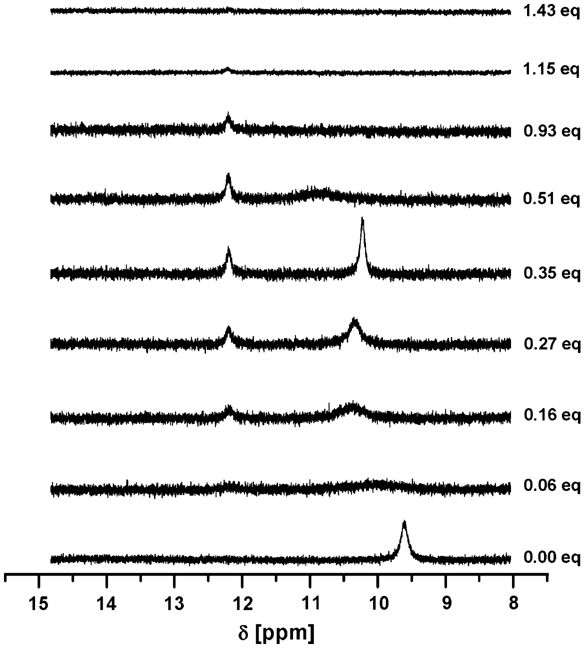


Figure 7. Titration of **2a** against fluoride ions perfomed in CD_2Cl_2 solution at room temperature.

Anion Selectivity by a Combination of Anion Binding and Solvatochromic Effects. The effect of the solvatochromism of **2** and its di-N-benzylated derivative **2a** on their electronic spectra in the presence of complexing anions was observed. This is intended as a qualitative assessment of the colorimetric responses of **2** and **2a** to anions in various solvents. For **2**, accessible solvents for this study were dichloromethane, chloroform, tetrahydrofuran, and pyridine. For several other solvents, **2** was virtually insoluble except in the presence of excesses of the more strongly interacting anions (see Supporting Information). Electronic absorption spectra indicate the effect of anion binding and solvent identity on the color of the solutions. The most attractive example of this for **2** is in dichloromethane solution where changing the identity of the anions gives relatively well-defined changes in the UV/vis spectrum. Tetrafluoroborate anions interact weakly and do not perturb the spectrum of the parent significantly. Binding of the halides gradually increases the intensity of a new band at 665 nm passing from iodide to chloride. However, when fluoride is present, the absorption spectrum departs much more significantly from that of the parent. A broad band appears at 758 nm, as was noted previously. This band is significant in that it would allow monitoring for the presence of fluoride at around 860 nm without interference from the other anions studied. In acetone, the response of **2** to different anions is similar to that in dichloromethane. In acetone, however, cyanide and acetate anions give a response almost identical with that of fluoride ions (see Supporting Information). For pyridine and tetrahydrofuran, the spectra are overlapping, although iodide ions in tetrahydrofuran introduce a new absorption band at 358 nm. The effect of the presence of particular anions on the color of solutions of **2** is summarized in Figure 8. It is interesting to note in Figure 8 that an apparent isosbestic point appears in the spectra containing nonidentical anions. This is because the mode of binding of the anion is similar for those participating in this phenomenon.

For **2a**, fluoride ions could be easily distinguished from the other halides in most solvents while they could also be distinguished from acetate and cyanide by variation of the solvent. In solvents of higher polarity, differentiation of fluoride became increasingly unlikely because the diagnostic color for fluoride ions coincides increasingly with the native color of **2a** in those solvents. Generally, the ions acetate, cyanide, and fluoride can be differentiated from the other ions by the blue color of their solutions. The presence of other anions tends to result in violet solutions. The most notable color differences are for fluoride in pyridine and cyanide in chloroform. Electronic absorption spectra of solutions containing individual anions, **2a**, and in selected solvents are shown in Figure 9 (Data for other solvents are

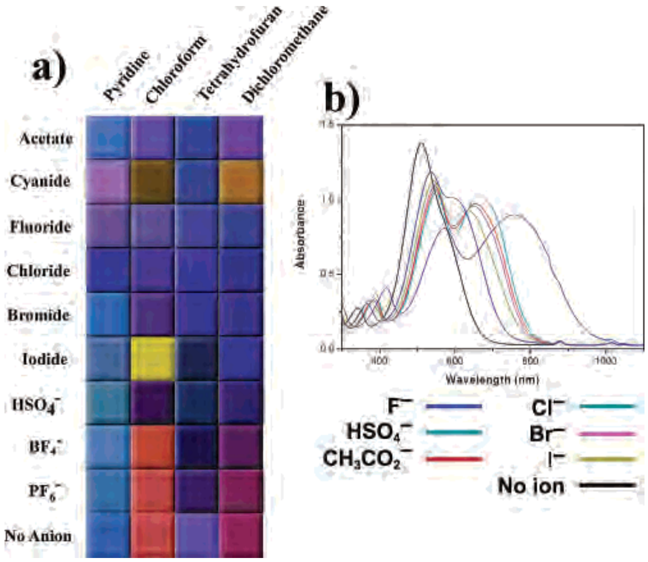


Figure 8. Colors of solutions of **2** in the presence of various anions and in the solvents indicated. The electronic spectra of **2** in dichloromethane and in the presence of the indicated anions are shown as an example (see Supporting Information for other spectra and the photograph from which the tile pattern was generated).

in the Supporting Information). Acetone is a typical case where the spectra of **2a** in the presence of fluoride, cyanide, or acetate are similar and contain a substantial absorption band at 728 nm. For the other ions, the spectra are similar to the parent except for the halides where a shoulder at 600 nm increases in intensity passing from iodide to chloride. The most notable separation of anion response comes in dichloromethane where fluoride can be distinguished from all the other ions studied by virtue of the absorption band at 750 nm. Also, notable is the response to cyanide which results in an intense new absorption band at 300 nm. This response may be due to some chemical reaction. Cyanide ions may be distinguished from the others studied using ethanol as solvent. In that case, it is the lack of response from other anions which enables almost unobstructed observation of an absorption band at 756 nm. Finally, iodide ions give a variety of responses depending on solvent. Often a new absorption band(s) is observed in the UV spectrum around 380 nm. Where propionic acid is the solvent, iodide is the only analyte to illicit a distinct response from **2a**. In the UV/vis spectrum, this manifests itself as intense new absorption bands at 350 and 440 nm with a less intense band at 785 nm which does not overlap with the absorption bands in the spectra of solutions containing other anions. The tiling representation in Figure 10 illustrates the colors of dilute solutions ($\sim 10^{-6}$ M) of **2a** in various solvents and in the presence of excesses of the respective anions. The solvents are arranged in order of their polarities, while the anions are arranged approximately by the apparent strengths of interaction with the anion complexing agent according to the color changes.

Finally, anomalous effects are obtained when solvents containing peroxides are employed.[19] In propionic acid, no chromogenic response can be observed except in the case of iodide ions. The intense yellow color replaces the dark pink of noncomplexed **2**. However, although the effect is intense, no change is observed in the electronic absorption band of **2**. The lack of response by the other anions simply serves to emphasize a chromogenic response in propionic acid. This result suggests further that specific responses can be observed if a third party reagent is present.

Discussion

The anion binding by **2** and its N-substituted derivatives is not only of interest from the point of view of determination of ions but also has connotations for the actual N-alkylation reaction leading to those derivatives. In our case, we routinely use solvent ethanol with anhydrous potassium carbonate as the base during these preparations. The fact that **2** is poorly soluble in ethanol (and other polar solvents) had evaded us until we embarked on the study of anion binding in these compounds. However, in the presence of carbonate anions, **2** is sufficiently solubilized in ethanol, albeit at elevated temperature, presumably by binding of the carbonate anion and the consequent higher polarity of the anion complex, that the N-alkylation reaction is promoted. In this way, the use of 18-crown-6 as a promoter is not required since **2** itself

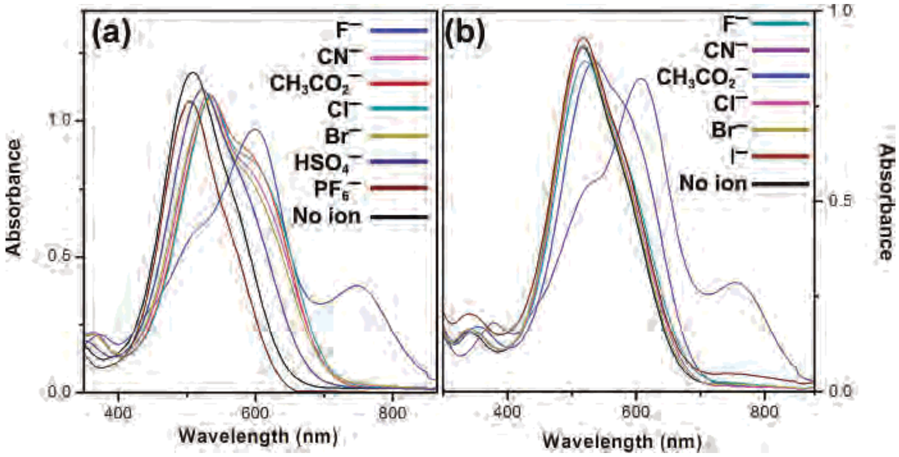


Figure 9. Electronic spectra of **2a** in dichloromethane or ethanol and in the presence of the indicated anions.

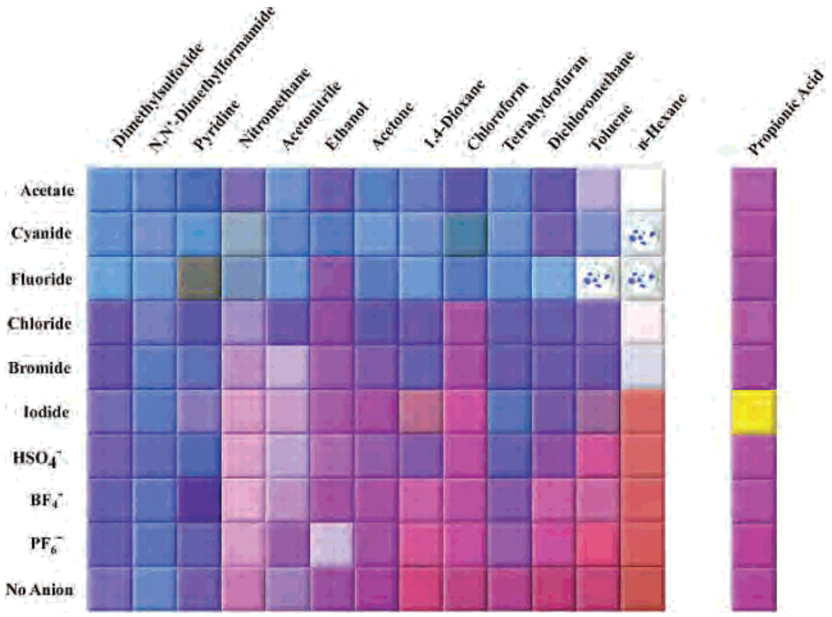


Figure 10. Tiling representation of the colors of dilute (~10^{-6} M) solutions of **2a** in several solvents and in the presence of the anions studied (see Supporting Information for photograph from which the tile pattern was generated).

acts as a phase-transfer catalyst by binding of carbonate. It is also now likely that anion binding of carbonate influences the distribution of the N-alkylates obtained from the reaction between **2** and alkyl bromides. Hence, N-benzylation of **2** should displace a bound carbonate anion resulting in N_{21}-benzyl-**2**. Carbonate ions interact weakly with the single NH group at N_{23} increasing the rate of reaction between this pyrrole group and a subsequent alkylating species. Thus, N_{21},N_{23}-dibenzyl-**2** is obtained as one major product. A similar situation occurs for N_{21},N_{23}-dibenzyl-**2** at its unalkylated face where displacement of the carbonate by N_{22}-alkylation enhances reactivity at N_{24}. We also considered that the carbonate anion binding may effectively prevent formation of the other isomers of multiple substitution products by fixing the macrocyclic conformation, although the puckered structure of **2** already ensures this. In addition, use of other bases apparently does not affect the identity of the resulting N-alkylates although variation of base *and* solvent can lead to changes in the distribution of products obtained from the alkylation reaction.[12b]

The interaction with carbonate ions of the di-N-substituted products also implicates an acidic workup for the isolation of these compounds. One case where binding of the carbonate anion is suspected to have been observed is during the N-alkylation of **2** using a porphyrinyl benzyl bromide giving mono-N-porphyrinyl compound **3** among others.[20] In that case, an acidic workup of the reaction was not performed and column chromatography allowed isolation of compounds,

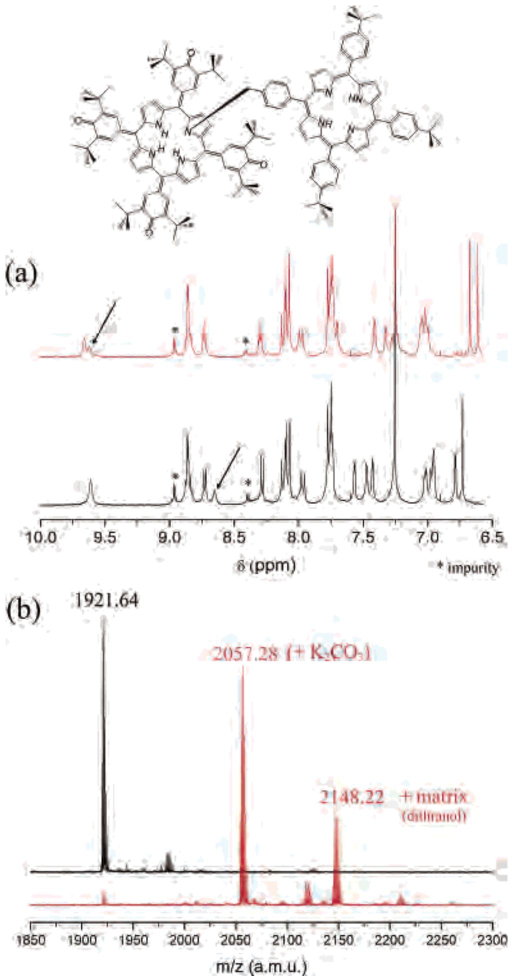


Figure 11. Possible binding of carbonate in the porphyrinyl-appended oxoporphyrinogen **3**. (a) ^{1}H NMR of the aromatic region for the bound and nonbound forms. (b) MALDI-TOF mass spectrum contains a major peak assigned to the potassium carbonate complex (m/z = 2057.28;). **3** has a molecular ion m/z = 1921.64.

---

(19) In the absence of **2**, traces (~10 ppm) of peroxides cause a yellow discoloration in solutions of iodide ions in tetrahydrofuran, propionic acid, or 1,4-dioxane. The yellow color is an accepted indicator for the presence of peroxides, which are in this case present because of the use of stabilizer-free solvents. Discoloration of the solutions generally occurs on a time scale of minutes.

(20) Hill, J. P.; Sandanayaka, A. S. D.; McCarty, A. L.; Karr, P. A.; Zandler, M. E.; Charvet, R.; Ariga, K.; Araki, Y.; Ito, O.; D'Souza, F. *Eur. J. Org. Chem.* **2006**, 595−603.

including what appears to be a carbonate bound mono-N-porphyrinyl compound. Unfortunately, X-ray-quality crystals of this compound did not become available on the time scale of this work although the MALDI-MS analysis (Figure 11b) is highly suggestive of the existence of a potassium carbonate complex. Other analyses support this assignment especially the proton NMR spectrum (Figure 11a), where one NH resonance is shifted downfield, inferring anion binding at the substituted face of the molecule. The infrared spectrum is also supportive of this given the appearance of a shoulder in the carbonyl stretching region and minor changes in the NH stretching absorptions. The electronic spectrum is almost unchanged, although this is expected given the weaker interaction of other anions such as hydrogensulfate.

Conclusion

In conclusion, we have found that the 4-oxocyclohexadienylidene porphyrinogens, **2**, are capable of binding anionic species such as the halides and other more complex anions. Further, there is some specificity in the chromogenic response illicited by **2** and its derivatives when in the presence of certain anions. Thus, fluoride ions can be distinguished from the other halides by the more substantial change in color that occurs upon fluoride ion binding. This difference is even more substantial in spectrophotometric terms with fluoride ion binding resulting in a strong absorption band at longer wavelength. In addition, derivatives of **2** exhibit solvatochromism allowing some chromogenic distinction between other ions, such as acetate or cyanide and fluoride. Both solvatochromic and anion binding effects are influenced by the hydrogen-bonding ability of the pyrrolic NH groups so that increased H-bonding between **2**, **2a**, and the solvent obscures the effect of anion binding. Hydrogen bonding by **2a** to solvent acetone molecules was observed in the crystal structure of that solvate. Furthermore, **2** tends to undergo a tautomerism which can be weighted in favor of the porphyrinogen form by complexation with appropriate anions. Currently, we are examining the effect of porphyrinogen N-substitution on the anion binding properties of this system.

Acknowledgment. The authors are thankful to the National Science Foundation (Grant No. 0453464 to F.D.), the donors of the Petroleum Research Fund administered by the American Chemical Society. The authors are also grateful for support received from the Special Coordination Funds for Promoting Science and Technology from Ministry of Education, Culture, Sports, Science and Technology (MEXT), Japan, through an ICYS Fellowship (J.P.H.) and thank the EPSRC UK National Crystallography Service for X-ray data collection of the acetone solvate **2a·acetone**. This work was also supported by a Grant-in-Aid for Science Research in a Priority Area “Super-Hierarchical Structures” from the Ministry of Education, Culture, Sports, Science and Technology (MEXT), Japan. The authors also thank the Ministry of Education, Youth and Sports of the Czech Republic for support (MSM0021620835).

Supporting Information Available: CIF for **2a·acetone**; additional electronic absorption spectra; and photographs used to generate the color tiling illustrations of the solvatochromism and anion binding. This material is available free of charge via the Internet at http://pubs.acs.org.

IC0611591