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Colorimetric anion sensing by porphyrin-based anion receptors

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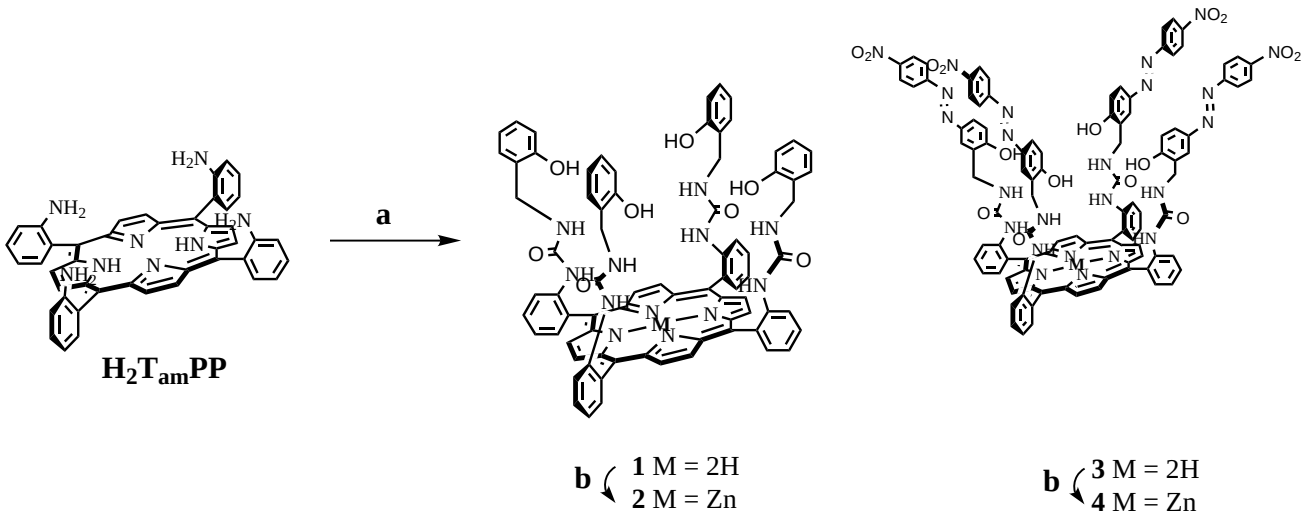
Abstract—Porphyrin derivatives **1**–**4** with H-bond donors and/or color-reporting chromophoric unit were synthesized and studied as anion-binding receptors. **1** and **2** exhibited binding selectivity in the order of $AcO^- > H_2PO_4^- \gg Cl^-$, Br^-, I^- in DMSO-d_6. Color change tests with several different anions for colorimetric anion sensors (**3** and **4**) resulted in selectivities for F^-, AcO^- and $H_2PO_4^-$ in organic solution. While **1** and **2** exhibited good selectivities for AcO^- and $H_2PO_4^-$, **3** and **4** showed a dramatic color change for F^- due to increased interaction with a nitrophenylazo phenolic OH group.

The development of synthetic receptors for anion recognition has attracted considerable attention in recent decades within the field of supramolecular chemistry due to the fact that a large number of biological processes involve molecular recognition of anionic species.[1] Selective colorimetric anion sensing is particularly challenging since visual detection can give immediate qualitative information, while absorption spectroscopy gives quantitative information.[2] Most of these sensors have the chromophore covalently attached to the anion recognition unit.[3] However, there are only a few reported colorimetric sensors available for anionic substrates.[2,3] In this paper we present colorimetric anion sensing by porphyrin-based receptors. In addition to the biologically important functions of the porphyrin as the prosthetic group of heme proteins, porphyrins constitute a suitable framework for artificial receptors due to their several unique characteristics.[4] We used a porphyrin scaffold as a rigid spacer for the multiple hydrogen bond donors to be predisposed on favorable positions for anion binding above a porphyrin plane.[5] It turns out that the receptors **3** and **4** act as colorimetric sensors for selected anions by means of hydrogen bonding interactions.



$H_2T_{am}PP$

Scheme 1. (a) Triphosgene, TEA, CH_2Cl_2, rt, **6** (or **7**), 76% (79%); (b) $Zn(OAc)_2$, CH_2Cl_2, MeOH, rt, 95%.

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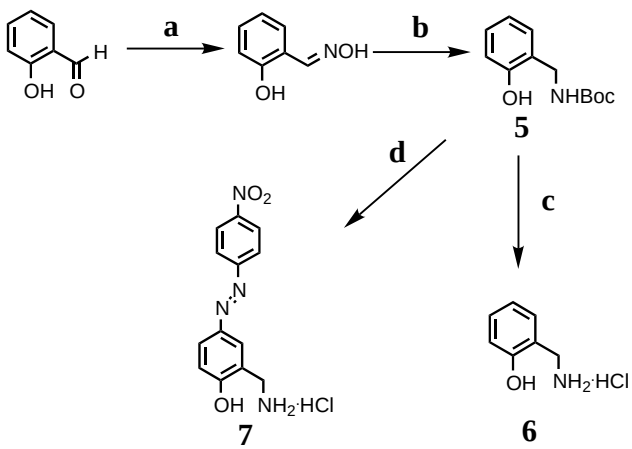
The syntheses of receptors **1**–**4** are outlined in Scheme 1. Compounds **5** and **6** were prepared by the standard methods in Scheme 2. Attachment of a *p*-nitrophenylazo group on the *para* position of the phenolic OH of **5** was accomplished by a general azo-coupling method[6] and then removal of a Boc protecting group gave **7** (Scheme 2). The synthesis of 5,10,15,20-*meso*-tetrakis(*o*-aminophenyl)porphyrin (H_2T-$_{am}$PP) was accomplished using the Collman's method,[7] from which the α,α,α,α-isomer of $H_2T_{am}PP$ was obtained using Lindsey's atropisomerization method.[8] To a stirred solution of $H_2T_{am}PP$ and TEA in CH_2Cl_2 was added 1.33 equiv. triphosgene under N_2 with subsequent stirring for 1 h. The resulting mixture was treated with **6** and stirred for 1 h to give free-base porphyrin receptor **1**.[9] Receptor **3**[10] was prepared following the above methodology[11] in which **7** was used instead of **6**. Zn insertion was accomplished by stirring the CH_2Cl_2 solution of **1** or **3** with methanol saturated with zinc acetate for 2 h to give rise to receptors **2**[12] and **4**.[13] Compounds **1** and **2** have urea groups and additional phenol groups as H-bond donors for anionic guest molecules. The association of **1** and **2** with various anion guests in DMSO-d_6 was studied by ^{1}H NMR spectroscopy. Downfield shifts of urea N*H* resonances (0.3–0.5 ppm) were detected upon complexation with AcO^- and $H_2PO_4^-$. When 0.2 equiv. of AcO^- and $H_2PO_4^-$ was added, the phenol O*H* peak became broad and almost disappeared. These shifts indicated



Scheme 2. (a) $NH_2OH{\cdot}HCl$, TEA, MeOH, 1 h, 98%; (b) (i) LAH, THF, 2 h, (ii) di-*tert*-butyl dicarbonate, H_2O, THF, 2 h, 44%; (c) HCl bubbling, 99%; (d) (i) aq. NaOH, MeOH, RT, (ii) *p*-nitroaniline, $NaNO_2$, aq. HCl, MeOH, 0°C, (iii) HCl bubbling, 60%.

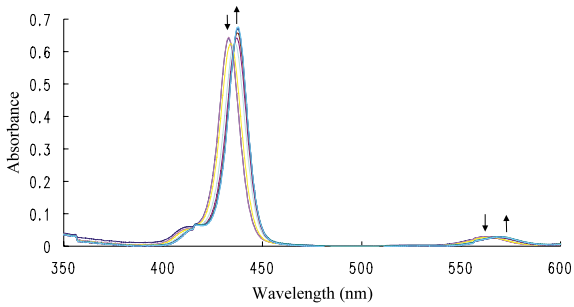


Figure 1. UV–vis titration of **2** with $H_2PO_4^-$ in DMSO ([**2**] = 2×10^{-6} M, [$H_2PO_4^-$] = 0–520 equiv.).

that urea and phenol groups play an essential role in the anion recognition process via hydrogen bonding.

Anion binding to **1** and **2** was also investigated with UV–vis spectroscopy. UV–vis spectral changes for the receptors were induced by the addition of anion guests in DMSO. UV–visible titration spectra revealed anion binding through perturbation of the Soret and visible Q-bands. The original Soret band at 433 nm shifted to 438 nm when $H_2PO_4^-$ was added to **2** and isosbestic points were observed in the spectra (Fig. 1), indicating 1:1 complexation between host and guest molecules. The formation constants of complexes between 2 and various anions were calculated by fitting the binding curve of absorbance at λ_{max} as a function of change in anion concentration (Table 1).

The selectivity trends in binding affinities of anions for **1** and **2** were determined to be $AcO^- > H_2PO_4^- \gg Cl^-$, Br^-, I^-. The selectivity for AcO^- and $H_2PO_4^-$ can be rationalized based on the guest basicity and structure of the complex. This result contrasts with those for Burn's urea-appended porphyrin which complexes more strongly with spherical chloride.[4c] This finding shows that the phenol unit as an additional H-bond site is important in anion recognition. As expected from the basicity of anions,[14] AcO^- and $H_2PO_4^-$ form stronger complexes than other anions. These results lead to the idea that by introducing another chromophore azophenol, **3** and **4** might cause color changes suitable for the visual detection of selected anions.[3d–f] UV–vis spectra of **3** and **4** with anions show different patterns from those of **1** and **2**. Upon addition of $H_2PO_4^-$ to **3** in DMSO, the absorbance of the original Soret band decreased with little shift of λ_{max}, and increased in a new peak at about 600 nm (Fig. 2). This results from the stronger basicity of the *p*-nitrophenyl-azophenolic OH of **3**. As can be expected from UV–vis data, a color

Table 1. Association constants (M^{-1}) for complexes of **1**–**3** with anionic guests[a]

	F^-	$H_2PO_4^-$	AcO^-	HSO_4^-	Cl^-
1	NDT	4.5×10^4 [b]	NDT	1.6×10^5 [b]	ND
2	NDT	2.0×10^4 [b] (1.6×10^4)[c]	4.4×10^4 [b] (6.4×10^4)[c]	9.5×10^4 [b] (9.7×10^4)[c]	2400[c]
3	(3.6×10^4)[d]	1.4×10^4 [b] (2.5×10^5)[d]	3.5×10^4 [b] (3.3×10^5)[d]	(4.1×10^4)[d]	ND

[a] Anions were added as their tetrabutylammonium salts except for Cl^-, which was used as tetraethylammonium salt. Association constants were determined by UV–vis titration in [b] DMSO, [c] DMSO:H_2O = 93:7, [d] $CHCl_3$ at rt. NDT = not determined (binding constants are too large to determine), ND = not detected. In case of **4**, UV-titration curves for all anions were not well fitted to 1:1 binding isotherm.

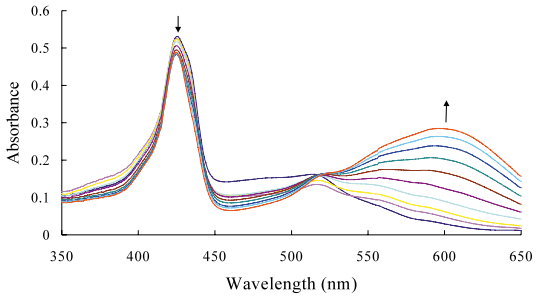


Figure 2. UV–vis titration of **3** with $H_2PO_4^-$ in DMSO ([**3**]= 2×10^{-6} M, [$H_2PO_4^-$]=0–520 equiv.).

change occurs by addition of anions to the solution of **3** and **4**. More pronounced spectral changes for **3** and **4** were induced by addition of F^-, $H_2PO_4^-$ and AcO^- in CH_3CN (Fig. 4). Similarly, F^-, $H_2PO_4^-$ and AcO^- induced the most distinguishable color changes upon complexation in CH_3CN. However, no detectable color changes were observed upon addition of excess HSO_4^-, Cl^-, Br^- or I^- to the CH_3CN solution of **3** (Fig. 3).

The absorption intensities of F^--**3**, AcO^--**3** and $H_2PO_4^-$-**3** are well correlated with the intensity of the color change in the order of $F^->AcO^->H_2PO_4^-$ (Figs. 3 and 4). While **1** and **2** have the greatest binding affinity for AcO^-, **3** and **4** have a detectable selectivity for F^- because F^- interacts more effectively with azophenol groups. The selectivity trends of anion-induced color changes for **3** and **4** were determined to be $F^->AcO^->H_2PO_4^-\gg HSO_4^-$, Cl^-, Br^-, I^-. As a result of the basicity order of anions, F^-, $H_2PO_4^-$ and AcO^- form stronger complexes than other anions and show noticeable color changes compared to other anions.

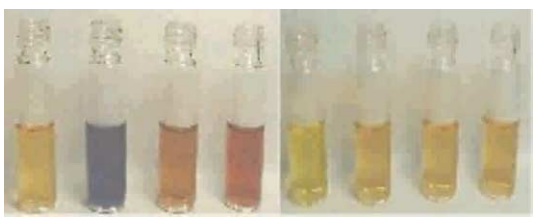


Figure 3. Color changes of **3** in CH_3CN. [**3**]=2.0×10^{-5} M, [anion]=5 equiv.; (a) **3** only; (b) F^-; (c) $H_2PO_4^-$; (d) AcO^-; (e) HSO_4^-; (f) Cl^-; (g) Br^-; (h) I^-.

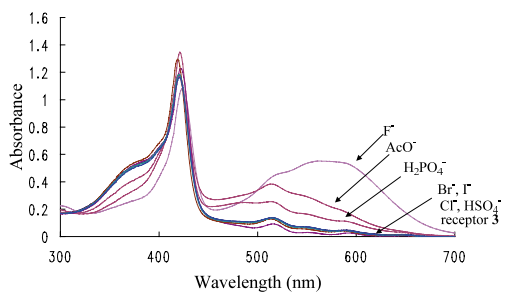


Figure 4. UV–vis changes of **3** operated in CH_3CN (5.0×10^{-6} M) after the addition of 20 equiv. of anions.

In summary, we have developed new colorimetric azophenolurea-introduced porphyrin sensors for anions, which show a selective coloration for F^-, $H_2PO_4^-$ and AcO^-. Color responses for selected anions (F^-, $H_2PO_4^-$, AcO^-) arise from basicity of the anions and effective binding between the azophenolic OH function of **3** (or **4**) and the anion.

Acknowledgements

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9. Selected spectral data for **1**: ^{1}H NMR (300 MHz, DMSO-d_6, ppm): δ −2.69 (s, 2H), 3.85–3.87 (d, 8H), 6.38 (br, 4H), 6.48–6.51 (t, 4H), 6.57–6.59 (d, 4H), 6.74–6.77 (d, 4H), 6.86–6.88 (t, 4H), 7.29–7.31 (t, 4H), 7.51–7.56 (m, 8H), 7.73–7.76 (t, 4H), 8.44–8.47 (d, 4H), 8.71 (s, 8H), 9.32 (s, 4H); ^{13}C NMR (75 MHz, DMSO-d_6, ppm): δ 38.96, 115.76, 116.70, 119.48, 121.81, 122.00, 126.07, 128.83, 129.65, 129.96, 131.50, 132.40, 136.46, 140.38, 155.59, 156.46; LR FAB-MS (*m*-NBA) $m/z=1271$ (found), 1270.48 (calculated for $[C_{76}H_{62}N_{12}O_8]^+$); UV–vis λ_{max} (DMSO, nm): 433 (Soret), 519, 563.
10. Selected spectral data for **3**: ^{1}H NMR (300 MHz, DMSO-d_6, ppm): δ −2.67 (s, 2H), 3.81 (s, 8H), 6.43 (br, 4H), 6.68–6.71 (d, 4H), 6.71–7.52 (m, 36H), 8.19–8.22 (d, 8H), 8.36–8.39 (d, 4H), 8.75 (s, 8H), 10.58 (br, 4H); ^{13}C NMR (75 MHz, DMSO-d_6, ppm): δ 38.76, 116.38, 116.60, 122.12, 123.56, 124.22, 124.46, 125.61, 125.86, 127.62, 130.02, 131.83, 136.33, 140.21, 145.66, 148.31, 156.09, 156.38, 160.59; MALDI-TOF-MS $m/z=1866.27$ (found), 1866.57 (calculated for $[C_{100}H_{74}N_{24}O_{16}]$); UV–vis λ_{max} ($CHCl_3$, nm): 424 (Soret), 518, 591.
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12. Selected spectral data for **2**: ^{1}H NMR (300 MHz, DMSO-d_6, ppm): δ 3.75 (s, 8H), 6.26 (br, 4H), 6.39–6.44 (t, 4H), 6.53–6.56 (d, 4H), 6.61–6.63 (d, 4H), 6.81–6.86 (t, 4H), 7.07 (s, 4H), 7.30–7.35 (t, 4H), 7.69–7.74 (m, 8H), 8.40–8.43 (d, 4H), 8.68 (s, 8H), 9.27 (s, 4H); ^{13}C NMR (75 MHz, DMSO-d_6, ppm): δ 37.84, 114.80, 115.60, 118.50, 120.62, 120.78, 125.32, 127.72, 128.32, 128.56, 131.62, 131.84, 135.31, 139.42, 149.63, 154.52, 155.46; LR FAB-MS (*m*-NBA) $m/z=1334$ (found), 1332.39 (calculated for major isotope peak for $[C_{76}H_{60}N_{12}O_8Zn]^+$); UV–vis λ_{max} (DMSO, nm): 433 (Soret), 563.
13. Selected spectral data for **4**: ^{1}H NMR (300 MHz, DMSO-d_6, ppm): δ 3.68 (s, 8H), 6.28 (br, 4H), 6.66–6.69 (d, 4H), 6.95 (s, 4H), 7.27–7.49 (m, 12H), 7.62–7.75 (m, 16H), 8.18–8.21 (d, 8H), 8.31–8.34 (d, 4H), 8.71 (s, 8H), 10.47 (s, 4H); ^{13}C NMR (75 MHz, DMSO-d_6, ppm): δ 37.74, 115.40, 115.54, 120.82, 122.71, 123.40, 124.71, 126.82, 128.53, 131.71, 131.98, 135.15, 139.29, 144.85, 147.44, 149.63, 155.24, 155.31, 159.55; LR FAB-MS (*m*-NBA) $m/z=1931$ (found), 1928.48 (calculated for major isotope peak for $[C_{100}H_{72}N_{24}O_{16}Zn]^+$); UV–vis λ_{max} (DMSO, nm): 433 (Soret), 518.
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