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Anion Recognition by Urea Derivatives of Anthraquinone: Dihydrogen Phosphate Ion Selective Neutral Receptors

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Three urea derivatives of anthraquinone were synthesized and they showed a high selectivity for dihydrogen phosphate ions.

Keywords: Anthraquinone; Dihydrogen phosphate; Urea derivative; Anion recognition

INTRODUCTION

Anthraquinones play an important role in the various photochemical and colorimetric sensor system [1–3]. Recently Sessler and his coworker [4] reported the important colorimetric anion sensors with 1,2- and 1,8-diaminoanthraquinone. They observed dramatic spectral changes with anions, particularly in the case of 1,2-diaminoanthraquinone, in which solutions initially yellow in color ($\lambda_{max} =$ 478 nm) became dark purple ($\lambda_{max} = 555$ nm), red ($\lambda_{max} = 519$ nm), reddish orange ($\lambda_{max} = 513$ nm), orange ($\lambda_{max} = 499$ nm), purple ($\lambda_{max} = 548$ nm), and orange ($\lambda_{max} = 493$ nm) when exposed to fluoride, chloride, bromide, iodide, phosphate, and sulfate ions, respectively.

Many successful positively charged receptors have been reported [5–9]. Though neutral receptor compounds for inorganic and organic phosphates have attracted attention due to their many possible applications in aprotic media, they are still very limited. Xanthene urea and thiourea derivatives [10] showed dihydrogen phosphate selectivity over acetate and chloride. In nature sulfate and phosphate binding proteins are very important receptors for active transport systems in cell [11–13]. Also, phosphate ions play an important role in many biological systems. In the pursuit of effective phosphate binding with neutral chromoionophore, we combined a phosphate anion selective xanthene framework with the chromophoric properties of anthraquinone. Three urea derivatives of anthraquinone **2**, **3** and **4** were synthesized and their anion binding properties were investigated with NMR and UV titration. These novel neutral anion receptors **2**, **3**, and **4** bind anions through hydrogen bonding and show a high selectivity with $H_2PO_4^-$ over $CH_3CO_2^-$, Cl^- and HSO_4^-.

MATERIAL AND METHODS

Unless otherwise noted, starting materials were obtained from commercial suppliers and used without further purification. Infrared (IR) spectra were determined on a FT-IR spectrometer. Nuclear magnetic resonance (NMR) spectra were recorded on a 300 MHz spectrometer. UV-absorption spectra were obtained on a HP 8453 spectrophotometer. Thin layer chromatography (TLC) analyses were carried out on silica gel plates.

1,8-Bis(*N*-phenylureido)-4,5-dihydroxyanthraquinone (2)

To a 0.1 g (0.37 mmol) of anthraquinone **1** in 15 ml of THF (10 ml) and DMF (5 ml) solution, 0.5 ml (5 mmol) of phenylisocyanate was added and the mixture was refluxed for one day. After removing the

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solvent, the residue was triturated with $CHCl_3$ yielding a pure purple solid (0.14 g, 74%) mp 292–293°C. ^{1}H NMR (DMSO-d_6) δ 12.68 (s, 2H, –OH), 11.39 (s, 2H, –NH), 10.03 (s, 2H, –NH), 8.70 (d, 2H, ArH, $J = 8.7$ Hz), 7.53 (d, 4H, ArH, $J = 7.2$ Hz); 7.45 (d, 2H, ArH, $J = 9.9$ Hz), 7.31 (t, 4H, ArH, $J = 7.2$ Hz), 7.01 (t, 2H, ArH, $J = 7.2$ Hz); ^{13}C NMR (DMSO-d_6) δ 195.7 and 191.9 (–CO), 157.7 (–NHCONH–), 163.1, 144.8, 142.8, 136.9, 134.3, 131.6, 127.9, 124.2, 121.1 and 118.9 (Ar); FAB MS m/z 508.4 (M^+, Calcd 508.5). Anal. Calcd for $C_{28}H_{20}N_4O_6$: C, 66.14; H, 3.96; N, 11.02. Found: C, 65.81; H, 3.91; N, 11.15.

1,8-Bis(*N*-phenylureido)-4,5-dimethyloxyanthraquinone (3)

To a 0.1 g (0.2 mmol) of anthraquinone **2** and 0.4 g (2.9 mmol) of K_2CO_3 in 15 ml of THF (10 ml) and DMF (5 ml) solution, 0.2 ml (3.2 mmol) of CH_3I was added and the mixture was stirred at room temperature for 20 h. After removing the solvent, the residue was taken up in $CHCl_3$ (100 ml) and washed with 0.1 N HCl (100 ml) and water. $CHCl_3$ was evaporated and the residue was purified by column chromatography (eluent, $CHCl_3$: MeOH = 20 : 1) to yield a dark red solid (64 mg, 60%) mp 285–286°C. ^{1}H NMR (DMSO-d_6) δ 10.53 (s, 2H, –NH), 9.80 (s, 2H, –NH), 8.47 (d, 2H, ArH, $J = 9.3$ Hz), 7.57 (d, 2H, ArH, $J = 9.6$ Hz), 7.52 (d, 4H, ArH, $J = 7.8$ Hz), 7.29 (t, 4H, ArH, $J = 7.5$ Hz, 6.99 (t, 2H, ArH, $J = 7.5$ Hz), 3.89 (s, 6H, $-CH_3$); ^{13}C NMR (DMSO-d_6) δ 188.8 and 182.0 (–CO), 152.5 (–NHCONH–), 152.4, 139.5, 134.3, 128.7, 126.8, 122.9, 120.9, 119.8 and 118.6 (Ar), 56.5 ($-CH_3$); FAB MS m/z 536.9 (M^+, Calcd 536.5). Anal. Calcd for $C_{30}H_{24}N_4O_6$; C, 67.16; H, 4.51; N, 10.44. Found: C, 67.21; H, 4.32; N, 10.47.

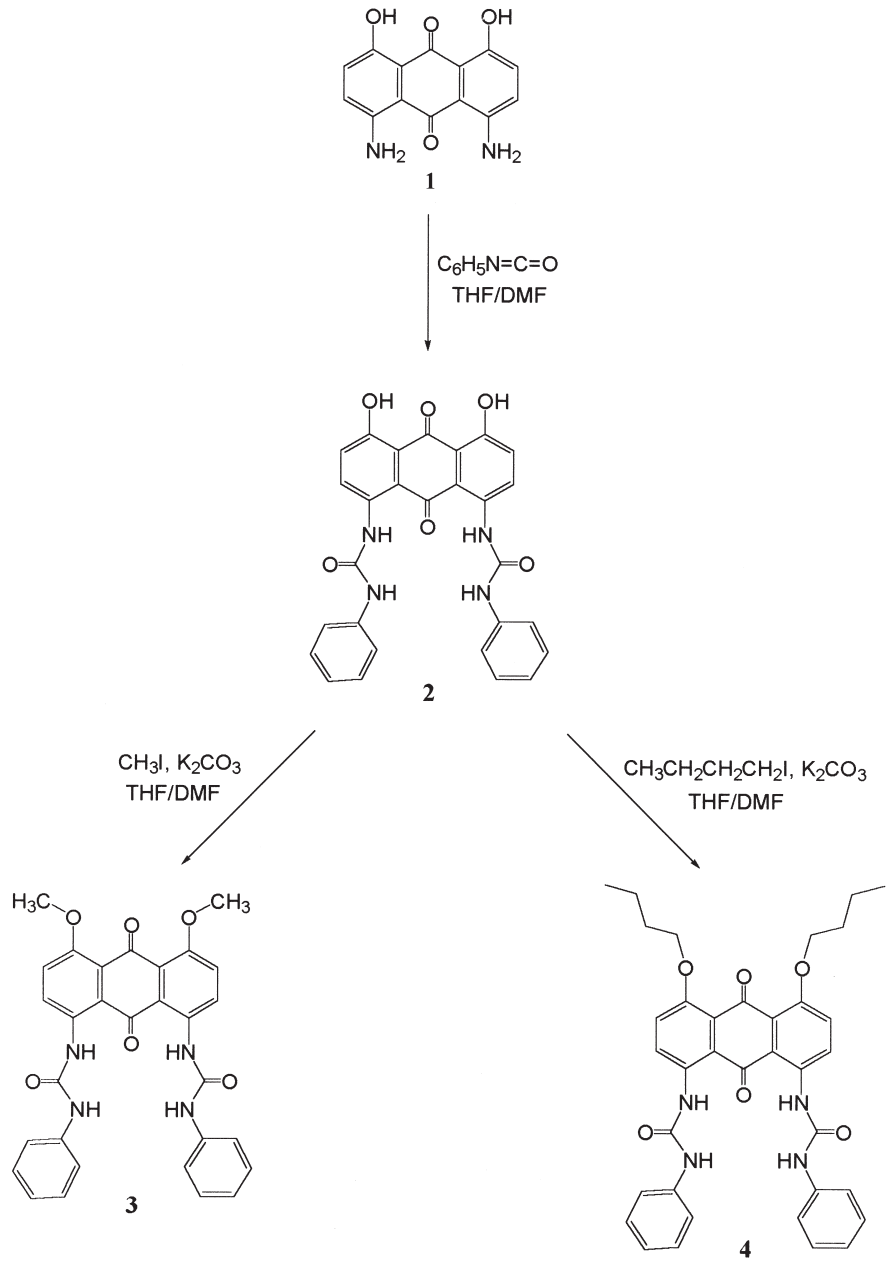
1,8-Bis(*N*-phenylureido)-4,5-dibuthyloxyanthraquinone (4)

To a 0.1 g (0.2 mmol) of anthraquinone **2** and 0.4 g (2.9 mmol) of K_2CO_3 in 15 ml of THF (10 ml) and DMF (5 ml) solution, 0.2 ml (1.76 mmol) of *n*-butyl iodide was added and the mixture was refluxed for 5 h. After removing the solvent, the residue was taken up in $CHCl_3$ (100 ml) and washed with 0.1 N HCl (100 ml) and water. $CHCl_3$ was evaporated and the crude products were purified by column chromatography (eluent, $CHCl_3$: Acetone = 20 : 1) to yield a dark red solid (67 mg, 54%). mp 237–238°C. ^{1}H NMR (DMSO-d_6) δ 10.53 (s, 2H, –NH), 9.79 (s, 2H, –NH), 8.42 (d, 2H, ArH, $J = 9.6$ Hz), 7.52 (m, 6H, ArH), 7.28 (t, 4H, ArH, $J = 7.5$ Hz), 6.98 (t, 2H, ArH, $J = 7.2$ Hz), 4.08 (t, 4H, $-OCH_2-$, $J = 6.0$ Hz), 1.72 (m, 4H, $-CH_2-$, $J = 6.3$ Hz), 1.52 (m, 4H, $-CH_2-$, $J = 7.5$ Hz), 0.94 (t, 6H, $-CH_3$, $J = 7.5$ Hz); ^{13}C NMR (DMSO-d_6) δ 189.2 and 182.5 (–CO), 152.8 (–NHCONH–), 152.2, 139.9, 134.8, 129.2, 126.9, 124.1, 122.8, 122.6, 120.1 and 119.0 (Ar), 69.5 ($-OCH_2-$), 31.3 and 19.0 ($-CH_2-$), 14.1 ($-CH_3$); FAB MS m/z 621.2 (M^+ Calcd 620.7). Anal. Calcd for $C_{36}H_{36}N_4O_6$: C, 69.66; H, 5.85; N, 9.03. Found: C, 69.19; H, 5.56; N, 9.02.

RESULTS AND DISCUSSION

The urea anthraquinone derivative **2** was prepared from the reaction of 1,8-diamino-4,5-dihydroxyanthraquinone **1** and phenylisocyanate. In order to block the hydroxy group a simple alkylation of **2** was carried out with methyl iodide and *n*-butyl bromide in the presence of potassium carbonate, which provided the two alkyl analogs **3** and **4** as shown in Scheme 1.

The anion binding properties were investigated by proton NMR titration in DMSO-d_6 solution in the presence of various anions such as tetrabutylammonium (TBA) chloride, dihydrogen phosphate, hydrogen sulfate, and acetate. In proton NMR experiments a large down field shift of two singlets NH proton resonances were observed upon the addition of TBA $H_2PO_4^-$ anions to a host **3** solution as shown in Fig. 1. Also, the slight up and down field shift of phenyl and anthraquinone resonances was noticeable. Particularly, two singlets at δ 10.53 and 9.80 for the urea NH signals shifted rapidly at around δ 12.3 and 11.2 upon addition of **1** equivalent TBA $H_2PO_4^-$. Further addition of $H_2PO_4^-$ caused only a very slight downfield shift. Any further significant change was not observed after one equivalent of TBA $H_2PO_4^-$, suggesting that **3** complexed with dihydrogen phosphate ion in a 1:1 solution stoichiometry. A large chemical shift of the NH protons in the presence of anions indicated that the anions bind to the urea protons directly. The association constants of the various anions to the receptors are obtained from the resulting titration curves using EQ–NMR [14]. These values are presented in Table I. A high selectivity for dihydrogen phosphate anion over acetate, chloride and hydrogen sulfate was observed particularly for host **2**. Receptors **3** and **4** showed a similar selectivity order, but acetate binding constant increased about 10-fold (5320 and 5100, respectively) with receptor **3** and **4** compared with receptor **2** (510). Acetate is a relatively strong base and could react with hydroxy protons in anthraquinone, which could compete with the anion binding site in the case of receptor **2**. This could be the reason for weak binding in the case of receptor **2** with acetate anion. But receptor **3** and **4** do not have acidic protons reacting with acetate, therefore acetate binding was increased. Methyl derivative **3** was not soluble in $CDCl_3$. Butyl derivative **4** was synthesized for the investigation in less polar solvents such as chloro-



SCHEME 1 Urea derivatives of anthraquinone chromoionophore.

form, but showed no particular difference for anion binding properties with receptor **3**.

In order to investigate the chromophoric shift in the presence of anions, anion binding properties were examined by the UV–Vis spectrophotometer. When acetate ion was added to receptor **2** in DMSO solution, the color of the solution changed from purple to blue (λ_{max} 558 and 590 nm to 638 and 689 nm). The same color change was also observed when dihydrogen phosphate was added (λ_{max} 558 and 590 nm to 631 and 682 nm). A similar change in color was noticed when bases such as triethylamine and pyridine were added. On the other hand, exposure to weak bases compared with phenoxide, such as chloride and hydrogen sulfate anions, did not lead to any noticeable change in color (Fig. 2), indicating that color change resulted in hydrogen proton abstraction instead of anion binding. In

TABLE I Stability constant data ($K/dm^3\,mol^{-1}$) of urea derivatives of anthraquinone in DMSO

Ligand	$H_2PO_4^-$*	$CH_3CO_2^-$	Cl^-	HSO_4^-
2	11,000	510	56	Weak†
3	10,100	5320	145	78
4	9830	5100	150	60

*Tetrabutylammonium salts. Errors estimate to be <10%. †Very weak binding, a stability constant value could not be calculated in this solvent.

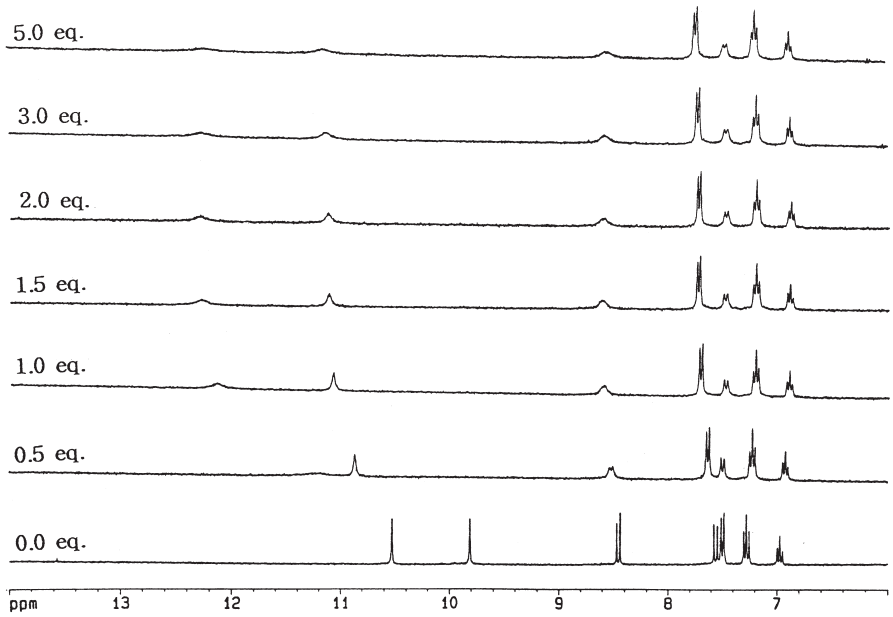


FIGURE 1 The partial ^{1}H NMR spectra of **3** in the presence of TBA (tetrabutylammonium) $H_2PO_4^-$ in DMSO-d_6. Numbers at the left side indicate the equivalents amounts of $H_2PO_4^-$ added.

the case of host **3**, when acetate, chloride and hydrogen sulfate anions were added in DMSO solution, the UV spectrum did not change at all. But when dihydrogen phosphate anion was added, λ_{max} shifted from 490 to 460 nm (from orange to pale yellow) as shown in Fig. 3, with a decrease in molar absorptivity. Receptor **3** does not possess any hydroxy protons, suggesting that it is not an acid–base interaction. Hypsochromic shift of neutral chromophore was reported [15,16] previously when metal was complexed with an electron donor (on a metal binding site)-acceptor (on a chromophoric site) system. The 30 nm blue shift in the presence of dihydrogen phosphate could result in an interaction between chromopore **3** and dihydrogen phosphate anion. Photoexcitation of **3** could cause a net electronic charge transfer from the nitrogen to the oxygen within the chromophore (Fig. 4). Thus, the effect of the anion binding to the chromophore is to destabilize an excited state more than the electronic ground state with respect to the corresponding electronic state in the uncomplexed chromophore. The result is a hypsochromic band shift in the absorption maxima upon anion complexation with a concurrent reduction in molar absorptivity. When acetate ion was added, spectrum changes were not observed at all. Even though acetate ion was bound strongly (K_a 5000), it did not effect changes in chromophoric anthraquinone moiety.

For effective complexation, bent acetate ions require two acidic NH protons. Many successful acetate receptors have been reported [6,7]. On the other hand, tetrahedral shape dihydrogen phosphate ions require four acidic protons for effective

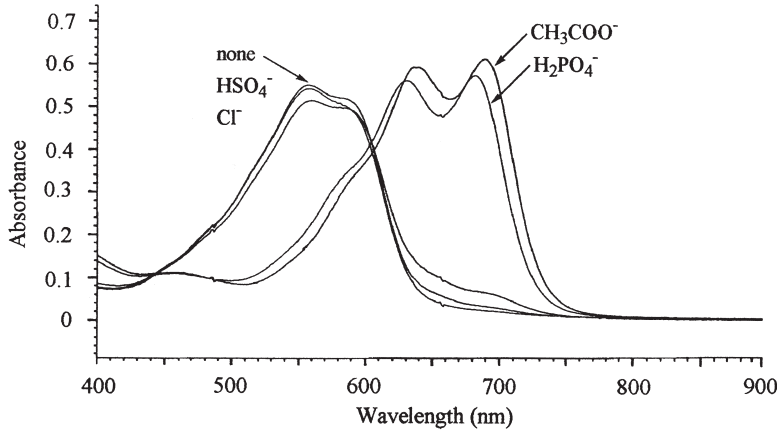


FIGURE 2 Absorption spectra of **2** recorded in DMSO (3×10^{-5} M) after the addition of 100 equivalents of representative anions.

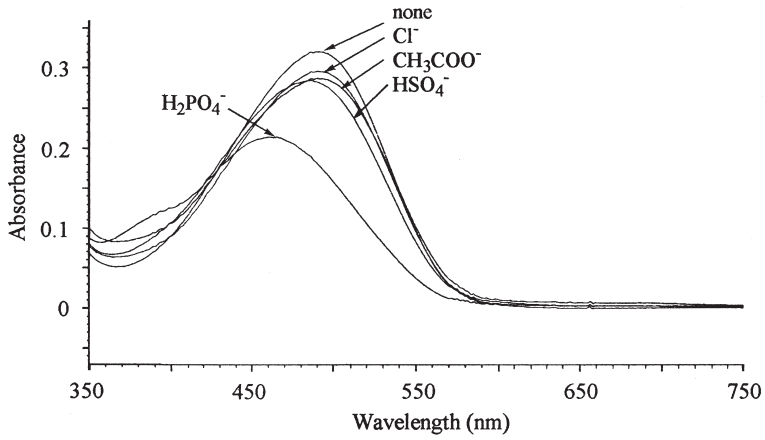


FIGURE 3 Absorption spectra of **3** recorded in DMSO (3×10^{-5} M) after the addition of 500 equivalents of representative anions.

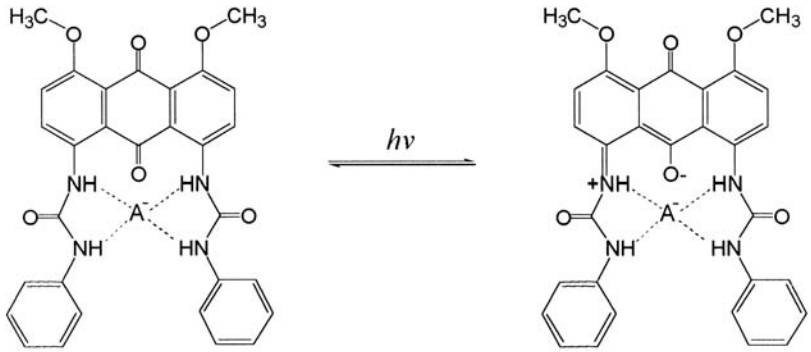


FIGURE 4 Change in structure upon light absorption by an anion-complexed neutral chromoionophore.

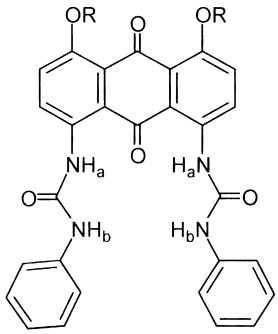


TABLE II Chemical shift of the urea NH protons of receptor **3** and **4** upon increasing the concentration of $H_2PO_4^-$ and CH_3COO^- in DMSO-d_6

Ligand	Anion		0.0 eq.	0.5 eq.	1.0 eq.	1.5 eq.	2.0 eq.	3.0 eq.	$\Delta\delta$ (3.0 −0.0 eq.)
3	$H_2PO_4^-$*	NH_a	10.53	10.86	11.07	11.11	11.12	11.13	0.60
		NH_b	9.82	11.18	12.13	12.28	12.29	12.29	2.47
	CH_3COO^-	NH_a	10.53	10.70	10.80	10.83	10.83	10.84	0.31
		NH_b	9.82	11.22	12.16	12.42	12.51	12.56	2.74
4	$H_2PO_4^-$	NH_a	10.53	10.81	11.04	11.12	11.13	11.14	0.61
		NH_b	9.80	10.94	11.97	12.34	12.34	12.34	2.54
	CH_3COO^-	NH_a	10.53	10.68	10.80	10.84	10.85	10.85	0.32
		NH_b	9.80	11.00	12.11	12.51	12.60	12.64	2.84

*Tetrabutylammonium salts.

complexation [10]. Chemical shift of two NH protons showed an interesting change in the presence of anions. Chemical shift of $N-H_b$† in receptor **3** was downfield shifted by δ 2.47 ppm when three equivalents of dihydrogen phosphate were added as seen in Table II. When three equivalents of acetate were added, chemical shift of $N-H_b$ in receptor **3** was downfield shifted by δ 2.74 ppm, presumably resulting in the basicity difference between two anions. When three equivalents of dihydrogen phosphate were added, chemical shift of $N-H_a$ in receptor **3** was downfield shifted by δ 0.60 ppm. But only δ 0.31 ppm downfield shift was observed when three equivalents of acetate were added, indicating that dihydrogen phosphate binds with NH_a protons more strongly than acetate ions. Similar changes occurred when anions were added to receptor **4**. This observation strongly suggest that hypsochromic shift of anthraquinone could have occurred when $N-H_a$ was complexed with anions, which was seen here with dihydrogen phosphate ion.

In summary, we synthesized three urea derivatives of anthraquinone. They showed a high selectivity for dihydrogen phosphate ion. In the UV–Vis spectrum a 30 nm hypsochromic shift of receptor **3** or **4** was observed upon the addition of dihydrogen phosphate ion with decrease in molar absorptivity.

Acknowledgements

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References

[1] Delgado, M., Gustowski, D.A., Yoo, H.K., Gatto, V.J., Gokel, G.W. and Echegoyen, L. (1988), *J. Am. Chem. Soc.* **110**, 119.
[2] Chen, Z., Schall, D.F., Alcala, M., Li, Y., Gokel, G.W. and Echegoyen, L. (1992), *J. Am. Chem. Soc.* **114**, 444.
[3] Miyaji, H., Sato, W. and Sessler, J.L. (2000), *Angew. Chem. Int. Ed.* **39**, 1777.
[4] Miyaji, H. and Sessler, J.L. (2001), *Angew. Chem. Int. Ed.* **40**, 154.
[5] Izatt, R.M., Pawlak, K., Bradshaw, J.S. and Bruening, R.L. (1991), *Chem. Rev.* **91**, 1721.
[6] Beer, P.D., Drew, M.G.B., Hesek, D. and Nam, K.C. (1997), *Chem. Commun.* **107**.
[7] Beer, P.D., Drew, M.G.B., Hodacova, J. and Stokes, S.E. (1995), *J. Chem. Soc. Dalton Trans.*, 3447.
[8] Szemes, F., Hesek, D., Chem, Z., Dent, S.W., Drew, M.G.B., Golden, A.J., Graydon, A.R., Grieve, A., Mortimer, R.J., Wear, T., Weightman, J.S. and Beer, P.D. (1996), *Inorg. Chem.* **35**, 5868.
[9] Beer, P.D. and Dent, S.W. (1998), *Chem. Commun.*, 825.
[10] Buhlmann, P., Nishizawa, S., Xiao, K.P. and Umezawa, T. (1997), *Tetrahedron* **53**, 1647.
[11] Pflugrath, J.W. and Quiocho, F.A. (1985), *Nature* **314**, 257.
[12] Kanyo, Z.F. and Christianson, D.W. (1991), *J. Biol. Chem.* **266**, 4264.
[13] Thatcher, G.R.J., Cameron, D.R., Nagelkerke, R. and Schmitke, J. (1992), *J. Chem. Soc. Chem. Commun.*, 386.
[14] Hynes, M.J. (1993), *J. Chem. Soc. Dalton Trans.*, 311.
[15] Dix, J.P. and Vogtle, F. (1978), *Angew. Chem.* **90**, 893.
[16] Dix, J.P. and Vogtle, F. (1980), *Chem. Ber.* **113**, 457.

†$N-H_a$ and $N-H_b$ were assigned based on the chemical shifts difference of two kind of urea N–H protons. Presumably $N-H_a$ could make an intramolecular hydrogen bond with carbonyl oxygen. Therefore downfield singlet at δ 10.58 was designated as $N-H_a$ and a singlet at δ 9.80 was designated as $N-H_b$.