Positioning dependent anion recognition by thiourea-based chromoionophores *via* hydrogen bonding in aqueous vesicle solutions†

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A cationic vesicle interface exhibited a filter function for less hydrophobic anions, and highly selective anion recognition *via* hydrogen bonding was achieved by thiourea-based chromoionophores (C_n-TU) located deep inside the vesicle.

Selective recognition and *in situ* sensing of biologically important anions are of current interest in host-guest chemistry.[1,2] Several synthetic neutral receptors possessing amide,[3] urea[4] and thiourea moieties[5] as a binding site for anion recognition have been reported, in which the binding takes place exclusively *via* hydrogen bonding interaction. Recently we have shown that thiourea-based chromoionophore (C_1-TU) interacts strongly with anions *via* formation of hydrogen bonds in non-aqueous media (Fig. 1) and produces a readily observable color change with a selectivity of $MeCO_2^-$ > $H_2PO_4^-$ > Cl^- >> ClO_4^-, reflecting anion basicity.[6] For anion sensing in aqueous media, however, the hydrogen bonding interaction of the binding site encounters significant interference from anion hydration. In biological systems, hydrophobic microenvironments produced by the supramolecular structure of receptors are cleverly utilized for ion recognition.[7] Thus, a simple strategy to achieve anion recognition in water is to incorporate the chromoionophore into hydrophobic regions, such as vesicle media, to shield their binding site from water.[8–10]

To develop an anion sensing system in water using a chromoionophore/vesicle complex as a mimic of a biological system, two factors are important: (i) the positioning of the thiourea binding site inside the vesicle, and (ii) the role of the cationic vesicle interface in anion recognition. To elucidate these factors, we have designed novel thiourea-based chromoionophores having various length of alkyl chains (C_n-TU)[11] and examined their anion recognition function in cationic vesicle solutions. We report here, the first positioning-dependent anion recognition by C_n-TU chromoionophore/vesicle complexes in water.

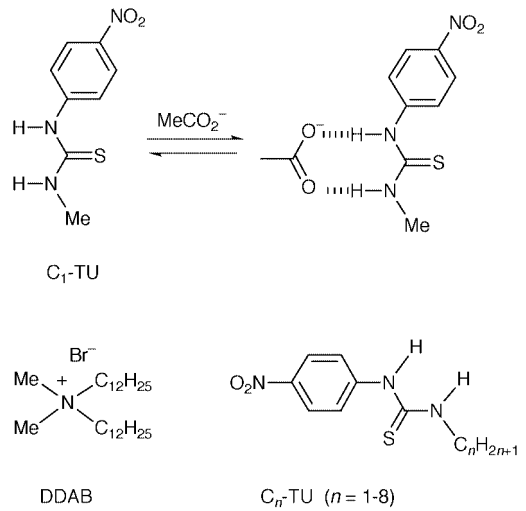

Fig. 1 Anion recognition by thiourea-based chromoionophores.

As a well known cationic amphiphile which forms single lamellae vesicles in water, didodecyldimethylammonium bromide (DDAB) was selected.[12] Films of C_n-TU/DDAB (1:10 mol%) were prepared by evaporation of a chloroform solution containing 1.0×10^{-5} mol C_n-TU and 1.0×10^{-4} mol DDAB on the inside of 100 mL-round bottomed flask. The films were left under vacuum for 1 day, followed by hydration with 10 mL of pure water at 40 °C by vortex mixing. The solution temperature was maintained at 40 °C while being probe-sonicated for 3 min using a power of 30–40 W. The resultant clear solution of C_n-TU/DDAB was diluted 20× with 0.01 M 2-[4-(2-hydroxyethyl)-1-piperazinyl]ethanesulfonic acid buffer (HEPES, pH 7.50) containing guest anions as sodium salts.

In acetonitrile, all C_n-TU show the same UV-VIS spectra with λ_{max} at 340 nm ($\varepsilon = 1.4 \times 10^4$ M^{-1} cm^{-1}), which can be assigned as an intramolecular charge transfer (CT) absorption band, despite the difference in their alkyl chain lengths (n = 1–8). However in DDAB solution, the λ_{max} of C_n-TU shifts monotonously to higher wavelengths with an increase in alkyl chain lengths from 338 nm (ε = 1.1 x10^4 $M^{-1}cm^{-1}$) for C_1-TU to 361 nm (ε = 1.5 x10^4 M^{-1} cm^{-1}) for C_8-TU (Fig. 2). The CT absorption bands generally show a bathochromic shift when the solvent polarity is increased.[13] Thus the results in Fig. 2 clearly reveal that the positioning of chromophore binding sites is controlled by the alkyl chain length of C_n-TU; the binding site of C_n-TU bearing a long alkyl chain is located on the surface of the cationic vesicle (hydrophilic microenvironment), whereas that of C_n-TU bearing a short alkyl chain is positioned deep within the vesicle (hydrophobic microenvironment).

The thiourea proton associated with the *p*-nitrophenyl unit dissociates under basic conditions and a new peak in the UV–VIS spectrum appears at 450 nm. Thus the apparent pK_a of C_n-TU in DDAB solution can be assessed by pH titration analysis.[14] Observed pK_a values are 9.9 ± 0.1 for C_1-TU and 9.5 ± 0.1 for C_8-TU. The larger pK_a value observed for C_1-TU supports the finding that the binding site of C_1-TU is located in the hydrophobic microenvironment. In DMSO-d_6, the ^{1}H NMR spectra of the vicinal phenyl protons in all C_n-TU show the same chemical shifts at δ 7.80/8.16. However in DDAB–D_2O solution, the chemical shifts of these phenyl protons are δ 8.00/8.21 for C_1-TU and δ 8.22/8.39 for C_8-TU. The chemical shifts of C_1-TU observed at higher magnetic fields are ascribed

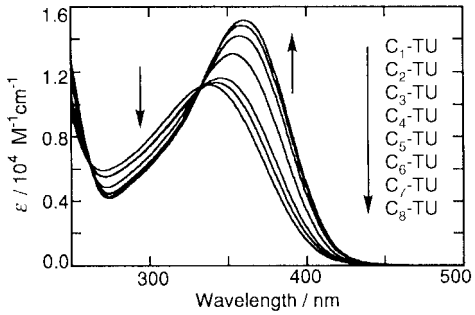

Fig. 2 UV-VIS spectra of C_n-TU in DDAB; [C_n-TU] = 5.0×10^{-5} M in 5.0×10^{-4} M DDAB solution, pH = 5.5–6.0 at 25 °C.

† Electronic supplementary information (ESI) available: response profiles of C_n-TU in DDAB upon addition of Cl^- and their equilibrium analysis. See http://www.rsc.org/suppdata/cc/a9/a909758i/

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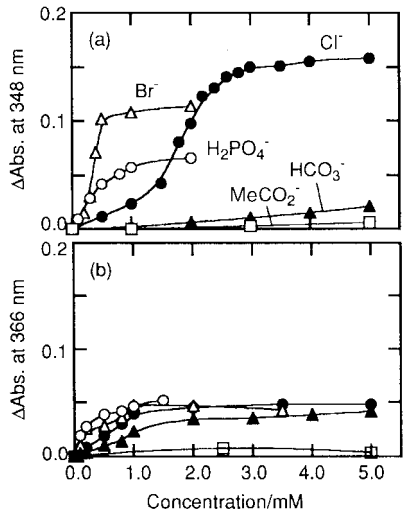

Fig. 3 Effect of anion concentration upon the spectral response of (a) C_1-TU and (b) C_8-TU in DDAB. (○) $H_2PO_4^-$, (△) Br^-, (●) Cl^-, (▲) HCO_3^-, (□) $MeCO_2^-$. [C_n-TU] = 5.0×10^{-5} M in 5.0×10^{-4} M DDAB solution. pH = 7.5 (adjusted by HEPES buffer at 25 °C).

to the hydrophobic effect,[15] which is additional evidence that C_1-TU is present deep within the vesicle.

The spectral responses of C_n-TU/DDAB complexes in water upon addition of anions were examined at pH 7.5 (Fig. 3). Increasing the anion concentration produced a bathochromic shift in λ_{max} with an enhanced molar absorptivity. These spectral changes are ascribed to (i) complex formation of anions with the thiourea moiety *via* hydrogen bonding as reported in acetonitrile,[6] and/or (ii) changes in the location of the chromophore within the vesicle due to the hydrophilic nature of the anion complexes. It is interesting that C_n-TU/DDAB complexes in water exhibit no response for $MeCO_2^-$, which differs from the response selectivity recorded in acetonitrile.[6] Since $MeCO_2^-$ is strongly hydrated in water,[16] the low binding affinity of $MeCO_2^-$ on the surface of DDAB vesicle may cause this poor response. This is a unique filter function of the cationic vesicle interface. The observed selectivity for C_1-TU/DDAB complex is Br^- > $H_2PO_4^-$ > Cl^- >> HCO_3^-, $MeCO_2^-$, reflecting a Hofmeister series [Fig. 3(a)].[16] On the other hand, no distinct selectivity is recorded for the C_8-TU/DDAB complex [Fig. 3(b)]. The spectral change (ΔAbs) upon addition of HCO_3^- is even larger for C_8-TU than for C_1-TU. This indicates that the binding of fewer hydrophobic anions takes place mainly on the vesicle surface. For C_n-TU with alkyl chain lengths from n = 2 to 7, an intermediate response between those of C_1-TU and C_8-TU is clearly observed.†

Thus it is apparent that the response selectivity is strongly affected by the positioning of C_n-TU in DDAB vesicles (Fig. 4).

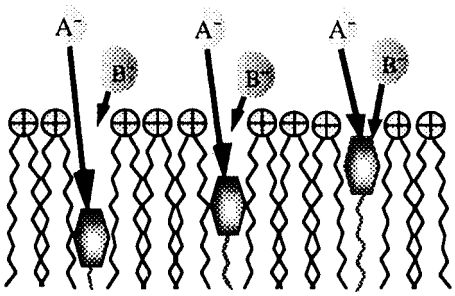

Fig. 4 Positioning-dependent anion recognition by C_n-TU in DDAB.

This is the first report that positioning dependent anion recognition can be carried out in aqueous vesicle solution.

In summary, the shifts in λ_{max}, pK_a, and ^{1}H NMR resonances revealed that the positioning of chromophore binding sites in DDAB was successfully controlled by the alkyl chain length of C_n-TU. This first report of positioning-dependent anion recognition *via* hydrogen bonding has been achieved by use of C_n-TU/DDAB complexes in water. Based on the filter function of the vesicle interface as well as the depth dependent distribution of the chromoionophores, this molecular assembled system should provide a new methodology for specific ion and molecule recognition in aqueous solutions.

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