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Switching the ligand-exchange reactivities of chloro-bridged cyclopalladated azobenzenes for the colorimetric sensing of thiocyanate†

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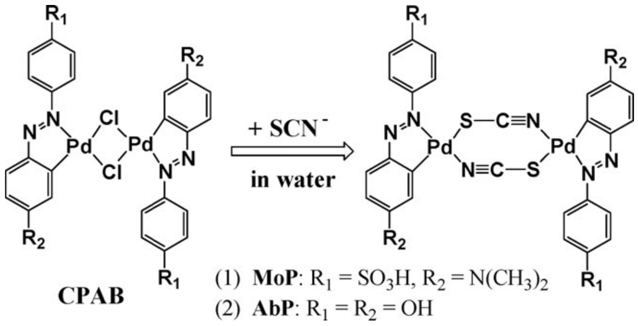
A dinuclear cyclopalladated complex of methyl orange shows a sensitive chromogenic response towards thiocyanate over a series of other anions in aqueous solution at physiological pH.

Metal–ligand interactions are usually utilized as the recognition driving force in assembling molecular chemosensors, affording high selectivity and operability in aqueous solution. In this respect, many coordination complexes of transition metals have been employed as luminescent or chromogenic chemosensors for environmental or physiological anion species,[1] with the ultimate objective of convenient detection or imaging applications. Although the design of optical sensing ensembles for cyanide is attracting considerable interest because of its high toxicity, few examples of thiocyanate chemosensors have been reported.[2] Thiocyanate is the end product of the detoxification of cyanide compounds, and it has a strong tendency to bind proteins as a non-competitive inhibitor for iodine.[3] Thiocyanate in urine, saliva or serum has been considered as a biomarker for the evaluation of cyanide contamination and for distinguishing smokers from non-smokers.[4] Chronically elevated levels of thiocyanate in body fluids are known to be toxic and related to local goitre, vertigo or unconsciousness.[5] Herein, we report a highly selective and sensitive colorimetric chemosensor for thiocyanate based on a simple cyclopalladated azobenzene (**CPAB**).

The peculiar electronic and steric properties of cyclometalated platinum group complexes make them suitable for interesting applications in functional materials. Due to their facile preparation, many "H-shaped" halo-bridged dinuclear azobenzene Pd(II) complexes have been investigated for organometallic liquid-crystalline materials.[6] Originating from a H-shaped chloro-bridged dimer, a series of dinuclear **CPAB**s were synthesized through the ligand-exchange reaction of the chloride bridge with different organic or inorganic anions.[7,8] Different mesomorphous and photophysical properties of **CPAB**s were obtained through the facile alteration of the bridging groups. Based on the photoactive bridge-exchange reaction and the relatively high molar absorption coefficient of **CPAB**s, we posed a question as to whether it was possible to achieve ion-selective chromophores through the rational design of the azo ligands of **CPAB**s. Since it has been reported that the ligand-exchange reactivity of cyclopalladated compounds is greatly affected by its "metalloaromaticity",[9] H-shaped chloro-bridged dinuclear **CPAB**s $[(H\text{-Azo})\mathrm{Pd}(\mu\text{-Cl})_2]$, synthesized by both symmetrically and unsymmetrically-substituted azobenzene, were employed in a comparative anion-sensing study due to their differences in "aromaticity" and photophysical properties.

The investigated **CPAB**s, **AbP** and **MoP** (Scheme 1), were synthesized by the simple treatment of the corresponding azobenzenes with potassium tetrachloropalladate(II) in a dioxane–water mixture.[10] Nematic symmetrically-substituted 4,4′-bis(hydroxy)-azobenzene derivatives have been widely used as the azo ligands for mesomorphous **CPAB**s.[7,8] Methyl orange was chosen as the comparative unsymmetrically-substituted ligand due to its typical donor–π-acceptor conjugated structure. The optical responses of both **AbP** and **MoP** towards a variety of anions were tested in aqueous solutions at physiological pH. As shown in Fig. 1(a) and Fig. 2, the addition of thiocyanate induced rapid and remarkable color and spectral changes to the **MoP** solution, whereas no such phenomenon occurred with other anions, including fluoride, chloride, bromide, iodide, nitrate, phosphate, nitrite, sulfate, carbonate, benzoate, acetate, sulfide and sulfite. Although **MoP** exhibited an enhancement in absorbance in the presence of cyanide, no color shift was observed in the sensing solution. In a parallel and comparative study, **AbP** displayed different chromogenic responses toward the anions tested (Fig. 1(b)). The color of the **AbP** solution changed from purple ($\lambda_{\max}$ = 530 nm, $\varepsilon_{530\ \mathrm{nm}} = 1.07 \times 10^4\ \mathrm{cm^{-1}\ mol^{-1}\ L}$) to yellow ($\lambda_{\max}$ = 360 nm, $\varepsilon_{360\ \mathrm{nm}} = 2.33 \times 10^4\ \mathrm{cm^{-1}\ mol^{-1}\ L}$), orange ($\lambda_{\max}$ = 495 nm, $\varepsilon_{495\ \mathrm{nm}} = 1.90 \times 10^4\ \mathrm{cm^{-1}\ mol^{-1}\ L}$) and colorless upon addition of sulfide, sulfite and thiocyanate anions, respectively (Fig. 2). Besides their color and spectral



Scheme 1 Structures and proposed thiocyanate-sensing reactions of the **CPAB**s.

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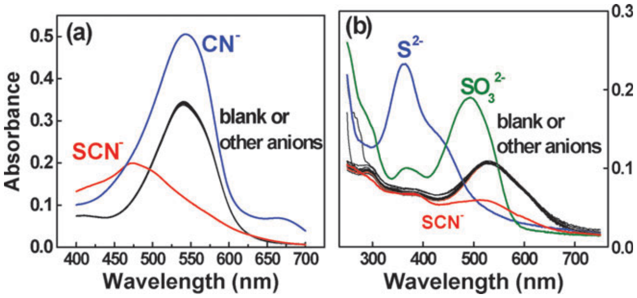

Fig. 1 Spectral responses of (a) **MoP** and (b) **AbP** toward a variety of anions in aqueous solution at pH 7.4. [**CPAB**]: 1.0 × 10^{-5} mol L^{-1}; anions (1.0 × 10^{-4} mol L^{-1}): F^-, Cl^-, Br^-, I^-, NO_3^-, SCN^-, NO_2^-, SO_4^{2-}, HCO_3^-, $PhCO_2^-$, $CH_3CO_2^-$, CN^-, S^{2-} and SO_3^{2-}; pH buffer: 0.02 mol L^{-1} phosphates.

Fig. 2 Colour responses of (top) **MoP** and (bottom) **AbP** toward a variety of anions in aqueous solution at pH 7.4. [**CPAB**]: 1.0 × 10^{-5} mol L^{-1}; anions (1.0 × 10^{-4} mol L^{-1}, from a to o): blank, F^-, Cl^-, Br^-, I^-, NO_3^-, SCN^-, NO_2^-, SO_4^{2-}, HCO_3^-, $PhCO_2^-$, $CH_3CO_2^-$, CN^-, S^{2-} and SO_3^{2-}; pH buffer: 0.02 mol L^{-1} phosphates.

responses to thiocyanate, **AbP** solutions showed considerably sensitive responses to sulfide and sulfite. Furthermore, no absorption response was observed in an **AbP** solution titrated with cyanide. All of these facts support our presumption that the chromogenic anion-binding reactivities of [(*H*-Azo)Pd(μ-Cl)$_2$] can be influenced by changing the substituted azobenzene ligands. For selectivity considerations, we chose **MoP** as a colorimetric chemosensor for thiocyanate in the following study.

Ghedini *et al.*[8] have reported the possibility of tuning the spectroscopic properties of [(*H*-Azo)Pd(μ-Cl)$_2$] by a ligand-exchange reaction of the chloride bridge with various organic or inorganic anions, including thiocyanate. The different nature of the bridging group allows the variation of the distance between the palladium atoms and the bonding environment experienced by the metal centers, explaining the different optical responses of **AbP** toward sulfide, sulfite and thiocyanate. The difference in the bridge substitution reactivities of **AbP** and **MoP** was attributed to their metalloaromaticity, tuned by the substitution groups on the azobenzene ligands. According to the literature,[9] an enhancement in the metalloaromaticity of cyclopalladated compounds usually results in a decrease of their ligand-exchange reactivities. As deduced from a comparison between **AbP** and **MoP**, [(*H*-Azo)Pd(μ-Cl)$_2$] with a donor–π-acceptor conjugated ligand such as methyl orange showed a thermodynamic preference for bridge-substitution by thiocyanate over that with the symmetrically substituted ligand. It must be noted that the hydroxyl groups on **AbP** are partially deprotonated at pH 7.4. Therefore, we expected that complete deprotonation of the hydroxyl groups would result in a further decrease in the thiocyanate-binding reactivity of **AbP** due to its symmetrically-substituted ligand. As evidence, an **AbP** solution at pH 9.5 hardly showed any spectral response toward thiocyanate (Fig. 3). The spectral responses of **AbP** toward sulfide and sulfite were less susceptible to this pH change than that towards thiocyanate. The fact that the spectral responses of **AbP** to sulfide and sulfite still occurred at pH 9.5 indicates that the absorption changes of **AbP** in water are induced by sulfide and sulfite anions, and not by H_2S and SO_2 gaseous molecules. Thus, the ligand-exchange of bridge bonds, but not axial coordination, is thought to be responsible for the binding of sulfide and sulfite to **AbP**.

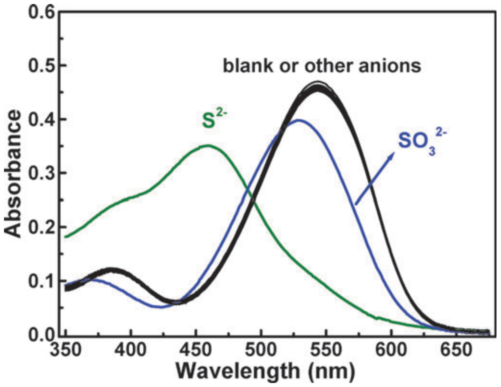

Fig. 3 Spectral responses of **AbP** toward a variety of anions in aqueous solution at pH 9.5. [**AbP**]: 2.0 × 10^{-5} mol L^{-1}; anions (1.0 × 10^{-4} mol L^{-1}): blank, F^-, Cl^-, Br^-, I^-, NO_3^-, SCN^-, NO_2^-, SO_4^{2-}, HPO_4^{2-}, $PhCO_2^-$, $CH_3CO_2^-$, CN^-, S^{2-} and SO_3^{2-}; pH buffer: 0.02 mol L^{-1} carbonates.

MoP could be employed for thiocyanate detection with a high selectivity. The effect of co-existing anions on the thiocyanate sensing response was examined in aqueous solution at pH 7.4. As shown in Fig. 4, a 400-fold excess of common inorganic anions, including chloride, bromide, iodide, nitrate, phosphate, nitrite, sulfate and carbonate, did not affect the absorption change of **MoP** upon adding thiocyanate. A 50-fold excess of benzoate, acetate, sulfide or sulfite was also tolerated by the chromogenic response towards thiocyanate. Although cyanide had the potential to form a new product with an enhancement in the absorbance of **MoP** (Fig. 1), the color of the sensing solution changed from red to yellow upon adding thiocyanate with the co-existence of equivalent cyanide. This indicates that **MoP** has a binding preference for thiocyanate over cyanide. The concentration levels of thiocyanate in body fluids are far higher than those of cyanide. For example, the salivary cyanide and thiocyanate levels of tobacco smokers were determined to be (0.66 ± 0.52) × 10^{-9} and (1.66 ± 0.84) × 10^{-6} mol L^{-1}, respectively.[11] Therefore, **MoP** is still regarded as an efficient thiocyanate probe for potential biochemical applications.

To examine the possibility of applying **MoP** to biochemical analysis, the absorption changes of **MoP** induced by a titration

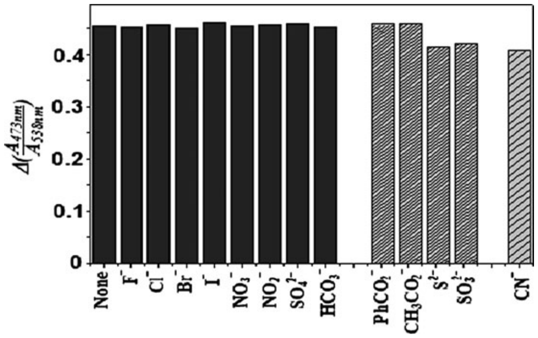

Fig. 4 The thiocyanate-sensing signals of **MoP** in the presence of different anions in aqueous solution at pH 7.4. [**MoP**]: 1.0×10^{-5} mol L^{-1}; [SCN^-]: 1.0×10^{-5} mol L^{-1}; [anion]: 4.0×10^{-3} mol L^{-1} (solid), 5.0×10^{-4} mol L^{-1} (dense), 1.0×10^{-5} mol L^{-1} (sparse); pH buffer: 0.02 mol L^{-1} phosphates. The thiocyanate-sensing signals were measured as the increase of the absorbance ratio at 473 nm compared to 538 nm after titration with thiocyanate.

with thiocyanate were investigated in the presence of artificial co-existing anions. During the addition of thiocyanate, the UV-vis absorption peak of **MoP** decreased at 538 nm and increased at 473 nm in aqueous solution at pH 7.4 (Fig. 5(a)), with a gradual color change from red ($\varepsilon_{538\ nm} = 3.41 \times 10^4\ cm^{-1}\ mol^{-1}$ L) to yellow ($\varepsilon_{473nm} = 2.01 \times 10^4\ cm^{-1}\ mol^{-1}$ L). There was a good linear correlation between the characteristic absorbance ratio ($A_{473\ nm}/A_{538\ nm}$) of the sensing solution and the concentration of thiocyanate over a range from 2.0×10^{-7} to 1.8×10^{-5} mol L^{-1}, and the detection limit was 1.7×10^{-7} mol L^{-1}, obtained from three times the standard deviation of the reagent blank divided by the slope of the linear regression equation. This is deemed to be a sensitive spectrometric method without the need for complex chromogenic derivation.

A Jot plot (Fig. S7, ESI†) confirmed the 1 : 2 binding stoichiometry between **MoP** and thiocyanate, which was also supported by IR spectra of potassium thiocyanate before and after a reaction with 0.5 equiv. of **MoP** (Fig. S4, ESI†). Although two thiocyanate-substituted sites in **MoP** complicate the possible substitution course of thiocyanate, the clear linearity of the calibration curve (Fig. 5(b)) indicates that only one chromogenic product is yielded, even at low thiocyanate concentration levels. If single substitution is thermodynamically preferred when binding thiocyanate, different absorption bands should be observed in the visible region upon adding a low concentration (<1 equiv. of **MoP**, Fig. 5) and excess thiocyanate (Fig. 1), respectively. However, only one new absorption peak appeared and increased with the further addition of thiocyanate. It is therefore concluded that double substitution occurred during the sensing of thiocyanate with **MoP**. The described substitution mode is assumed to result from the structural differences between the bridging anions. The length mismatch between a thiocyanate group and a chloride ion prevents them from cooperatively bridging the two Pd atoms in **MoP** (Scheme 1), explaining the thermodynamic preference of double substitution over single substitution.

In summary, highly selective and sensitive colorimetric sensing of thiocyanate in aqueous solution could be achieved using a simple **CPAB**. The possibility of tuning the ligand-exchange reactivities of **CPAB**s by changing the chelate azo ligands was reported. This could be applied to other designs of **CPAB**-based optical chemosensors for important anionic or gaseous species in further studies.

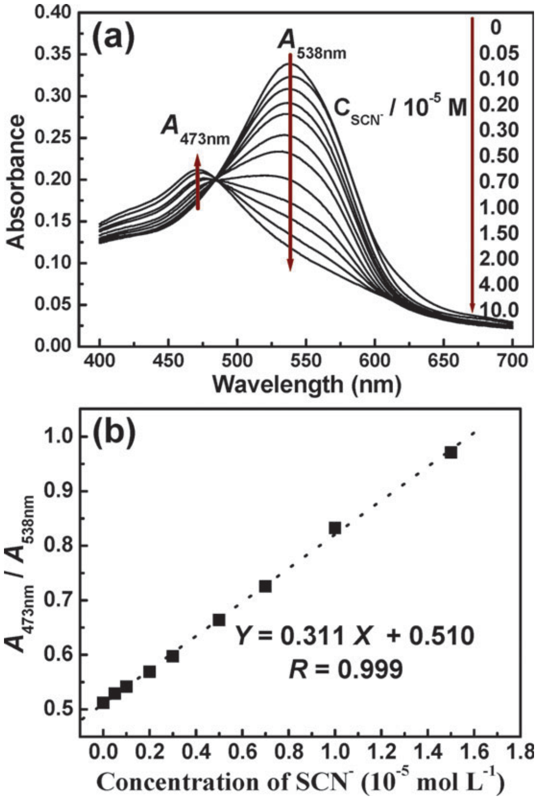

Fig. 5 (a) The absorption evolution of an **MoP** solution upon titration with sodium thiocyanate at pH 7.4. (b) The calibration curve plotted by the absorbance ratio at 473 nm compared to 538 nm *vs.* the concentration of thiocyanate. The sensing solutions of **MoP** were prepared as aqueous mixtures of **MoP** (1.0×10^{-5} mol L^{-1}), NaCl (0.1 mol L^{-1}), Na_2SO_4 (0.02 mol L^{-1}), $NaHCO_3$ (0.03 mol L^{-1}), NaF (1.0×10^{-4} mol L^{-1}), KI (1.0×10^{-4} mol L^{-1}), $NaNO_2$ (2.0×10^{-4} mol L^{-1}), KNO_3 (1.0×10^{-3} mol L^{-1}), CH_3CO_2Na (2.0×10^{-4} mol L^{-1}), $PhCO_2Na$ (1.0×10^{-4} mol L^{-1}) and buffer phosphates.

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Experimental

General remarks

Potassium tetrachloropalladate(II) (Aldrich) and methyl orange (TCI) were purchased and used as received. All other reagents were of analytical grade or better and used without further purification. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance II 400 MHz NMR spectrometer. Chemical shifts are reported in parts per million (ppm) relative to the residual DMSO peak (2.50 ppm in the ^{1}H NMR and 39.43 ppm in the ^{13}C NMR) and coupling constants (*J*) are reported in Hertz (Hz). Matrix-assisted laser desorption ionisation (MALDI) time-of-flight (TOF) mass spectra were recorded on a Bruker-Dalton Reflex III mass spectrometer. X-Ray photoelectron spectra were recorded on a VG ESCA LAB MK-2 instrument. Elemental analysis data were obtained on a Thermo Quest Italia S.P.A. EA 1110 instrument. Absorption spectra were recorded on a Varian CARY-300 UV-vis spectrophotometer. IR spectra were recorded on a Nicolet Avatar 360 spectrophotometer.

Synthesis

MoP. MoP was prepared as we have reported elsewhere.[10a] A 5 mL aqueous solution of potassium tetrachloropalladate(II) (66 mg, 0.2 mmol) was slowly added to a solution of methyl orange (100 mg, 0.3 mmol) in a 30 mL dioxane–water (1 : 1) mixture. The reaction mixture was stirred at room temperature for one week to give a claret-coloured solution. The solvent was evaporated to *ca*. 1.5 mL under vacuum. The precipitate was collected, and washed with ethanol and diethyl ether. The obtained solid was dried under vacuum to give the potassium salt of **MoP** (53 mg, 52% yield). Potassium tetrachloropalladate(II) was used in the form of needle crystals in this preparation. Selected ^{1}H NMR (400 MHz, DMSO-d_6) data of the product: 2.50 (DMSO), 3.17 (s, 6 H, N–CH_3), 6.77 (d, 2 H, Ph–H, J_{HH} = 9 Hz), 6.85 (d, 1 H, Ph–H, J_{HH} = 9 Hz), 7.72 (s, 1 H, Ph–H), 7.80 (d, 2 H, Ph–H, J_{HH} = 9 Hz) and 7.88 (d, 2 H, Ph–H, J_{HH} = 9 Hz).

AbP. In a typical preparation, 4,4′-bis(hydroxy)-azobenzene (44 mg, 0.2 mmol) and potassium tetrachloropalladate(II) (66 mg, 0.2 mmol) were dissolved in a 30 mL dioxane–water (1 : 1) mixture. The mixture was stirred at room temperature for one week to give a brown-coloured solution. The solvent was evaporated to *ca*. 1.5 mL under vacuum. The precipitate was collected, and washed with ethanol and diethyl ether, respectively. The obtained solid was dried under vacuum to give 62 mg of **AbP**·$3H_2O$ (76% yield). Elemental analysis calc. for $C_{24}H_{24}N_4O_7Cl_2Pd_2$: N, 7.33; C, 37.72; H, 3.17. Found: N, 7.00; C, 37.77; H, 3.06%. XPS: Pd (4d, 3p, MNV, $3d_{5/2}$ = 337.9 eV, $3d_{3/2}$ = 343.1 eV), Cl (2p, $2d_{3/2}$ = 198.6 eV, $2d_{1/2}$ = 200.1 eV), C (1s), N (1s) and O (1s). ^{1}H NMR (400 MHz, DMSO-d_6): 2.50 (DMSO), 3.35 (H_2O), 6.59 (d, 1 H, Pd–Ph–*H*), 6.82 (d, 2 H, Ph–*H*), 7.10 (s, 1 H, Pd–Ph–*H*), 7.60 (d, 2 H, Ph–*H*), 7.66 (d, 1 H, Pd–Ph–*H*), 10.09 (s, 1 H, O–*H*) and 10.52 (s, 1 H, O–*H*). ^{13}C NMR (100 MHz, DMSO-d_6): 114.80, 115.11, 115.42, 125.68, 125.83, 131.14, 143.96, 156.95, 159.42 and 159.75. MALDI-TOF MS: m/z = 708.75 $[M - H]^-$ and 726.99 $[M + OH]^-$.

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