

# Efficient and selective up-hill transport of anions by pH-induced affinity switching of a copper complex carrier

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The copper(II) complex of 6,6'-bis(4-hexylbenzoylamino)-2,2'-bipyridine served as a new type of functional carrier in efficient and selective up-hill transport of anions across an organic liquid membrane. Reversible deprotonation of the amide groups of the ligand regulated the uptake and release of anions by alteration of the anion affinity of the complex, and affinity switching of the carrier by the pH of external aqueous solutions induced efficient up-hill transport of  $\text{SCN}^-$  and toluene-*p*-sulfonate by coupling with a small pH difference across the membrane. The high thiocyanate selectivity of the carrier was ascribed to preferential axial co-ordination of  $\text{SCN}^-$  to the complex which possesses an  $\text{N}_2\text{O}_2$  square-planar structure.

Carrier-mediated transport across an artificial membrane has been investigated extensively as a model of biological membrane-transport systems.<sup>1</sup> There are varieties of naturally occurring<sup>2</sup> and synthetic cation carriers,<sup>3</sup> but relatively few anion carriers have been reported.<sup>4</sup> Recently, much effort has been devoted to the development of highly functional carrier molecules which show higher substrate selectivity, controlled uptake and release, *etc.* in order to mimic the characteristic functions of biological membranes.<sup>5</sup> Among them, active transport with high substrate selectivity is the major target of such studies. To achieve high transport efficiency, high substrate affinity of the carrier is required in the extraction process, while low affinity is favourable for the release process. Therefore, affinity switching of the carrier during the transport process can achieve highly efficient transport, leading to active transport when alteration of the affinity is sufficiently large.<sup>6</sup>

We previously reported<sup>7</sup> a new efficient anion carrier, the copper(II) complex of 6,6'-bis(4-hexylbenzoylamino)-2,2'-bipyridine ( $\text{H}_2\text{L}$ ). The pH-induced dissociation-association of the amide proton(s) of the ligand is suggested to regulate uptake and release of  $\text{SCN}^-$  by switching the anion affinity of the carrier, and efficient and selective up-hill transport of  $\text{SCN}^-$  was mediated by coupling with a small pH difference across the organic liquid membrane. We report here the structure, properties, anion affinity and transport mechanism of this new class of carrier.

## Experimental

Thermal analyses were carried out by using a Mettler FP90 thermo system and by a Rigaku Thermo Plus TG-DTA system. The IR spectra were recorded with a Perkin-Elmer 1600 series FTIR spectrometer, ESR spectra with a JEOL JES-FE3X spectrometer operated at X band, and electronic spectra on a Shimadzu UV-2200 spectrophotometer at 20 °C.

Solvents and other chemicals were obtained commercially, and were purified by routine methods if necessary.

## Syntheses

**6,6'-Bis(hexylbenzoylamino)-2,2'-bipyridine ( $\text{H}_2\text{L}$ ).** This compound was prepared from 6,6'-diamino-2,2'-bipyridine and 4-hexylbenzoyl chloride according to the reported procedure.<sup>8</sup> Recrystallization from benzene yielded white plates of  $\text{H}_2\text{L}$  (0.479 g, 80%), m.p. 211–212 °C (Found: C, 76.8; H, 7.7; N, 9.7.  $\text{C}_{36}\text{H}_{42}\text{N}_4\text{O}_2$  requires C, 76.85; H, 7.5; N, 9.95%);  $\tilde{\nu}_{\text{max}}/\text{cm}^{-1}$

1436vs and 1567m (bipy); 1293m, 1535s and 3306w (NH); 1649s (CO); 1372s and 2925m (hexyl).

**$[\text{Cu}(\text{H}_2\text{L})(\text{H}_2\text{O})][\text{NO}_3]_2$ .** A mixture of  $\text{H}_2\text{L}$  (0.120 g, 0.21 mmol) and  $\text{Cu}(\text{NO}_3)_2 \cdot 3\text{H}_2\text{O}$  (0.063 g, 0.26 mmol) in methanol (10  $\text{cm}^3$ ) was stirred at room temperature until the mixture became a homogeneous blue solution. After evaporation of the solvent, the residual blue solid was recrystallized from methanol to give light blue plates of  $[\text{Cu}(\text{H}_2\text{L})(\text{H}_2\text{O})][\text{NO}_3]_2$  (0.116 g, 71%),  $\text{H}_2\text{O}$  lost at 112.5 °C (TG), m.p. 182.7–184.9 °C (decomp.) (Found: C, 56.1; H, 5.7; N, 10.9.  $\text{C}_{36}\text{H}_{44}\text{CuN}_6\text{O}_9$  requires C, 56.3; H, 5.75; N, 10.95%);  $\tilde{\nu}_{\text{max}}/\text{cm}^{-1}$  1430w and 1567w (bipy); 1237w, 1541w and 3448m (NH); 1612s (CO); 1384s and 2927w (hexyl).

**$[\text{CuL}]$ .** To a solution of  $[\text{Cu}(\text{H}_2\text{L})(\text{H}_2\text{O})][\text{NO}_3]_2$  (0.0588 g, 0.077 mmol) in dichloromethane (15  $\text{cm}^3$ ) was added dropwise methanol containing 0.1 mol  $\text{dm}^{-3}$  KOH. The resultant precipitate was filtered off and recrystallized from benzene to give green needles of  $[\text{CuL}]$  (0.0467 g, 97%), m.p. 205.6–209.7 °C (Found: C, 69.3; H, 6.4; N, 8.7.  $\text{C}_{36}\text{H}_{40}\text{CuN}_4\text{O}_2$  requires C, 69.25; H, 6.45; N, 8.95%);  $\tilde{\nu}_{\text{max}}/\text{cm}^{-1}$  1417s and 1556m (bipy); 1378w and 2924w (hexyl).

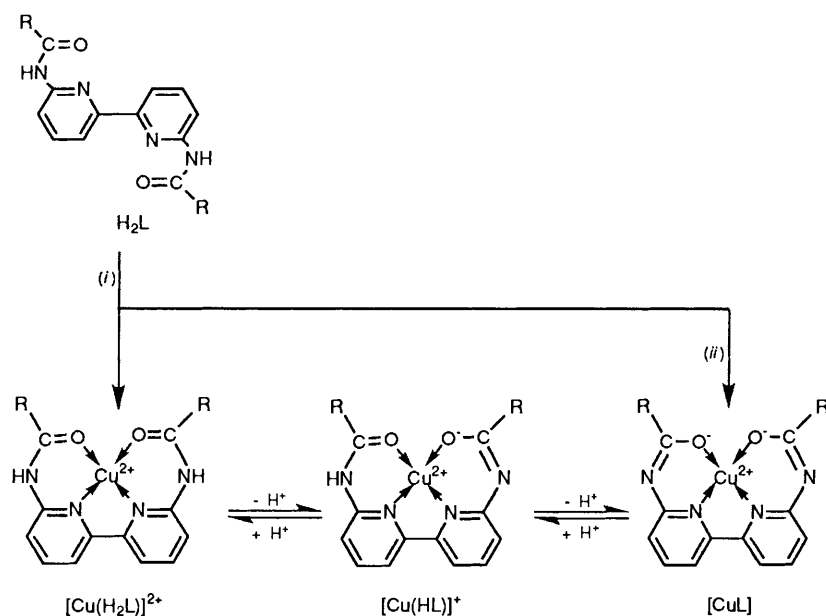
## Anion uptake and release in two-phase systems

All the experiments were carried out at room temperature.

**Uptake.** A buffer solution (5  $\text{cm}^3$ , Kolthoff's buffer solutions; mixtures of 0.05 mol  $\text{dm}^{-3}$  sodium succinate and 0.05 mol  $\text{dm}^{-3}$  sodium tetraborate, pH 3.0, 4.0 and 6.0) containing  $4 \times 10^{-3}$  mol  $\text{dm}^{-3}$  sodium salts and a dichloromethane solution (5  $\text{cm}^3$ ) containing  $2 \times 10^{-3}$  mol  $\text{dm}^{-3}$   $[\text{Cu}(\text{H}_2\text{L})(\text{H}_2\text{O})][\text{NO}_3]_2$  was placed in a cylindrical capped bottle (20  $\text{cm}^3$ ). After 60 min of mixing of the two layers by a Yamato model MD-21 (200 revolutions  $\text{min}^{-1}$ ) shaker, the bottle was left to stand for 30 min.

**Release.** A portion (3  $\text{cm}^3$ ) of the organic layer from the uptake experiments and a fresh buffer solution (3  $\text{cm}^3$ , pH 6.0) were placed in a cylindrical bottle (10  $\text{cm}^3$ ) and the two layers were mixed by the above procedure.

The amounts of the anion extracted from the aqueous layer into the organic layer and released from the organic layer into the aqueous layer were determined by the following methods:  $\text{SCN}^-$  by colorimetric method according to the standard procedure,<sup>9</sup> bromide by anion-selective electrode (Br-125, Toa



Scheme 1 R = 4-Hexylphenyl. (i)  $Cu(NO_3)_2 \cdot 3H_2O$ , MeOH; (ii) KOH, MeOH

**Table 1** The ESR parameters of the copper(II) complexes in  $CH_2Cl_2$  at 77 K<sup>a</sup> ( $G = 10^{-4}$  T)

Complex	$g_{\parallel}$	$g_{\perp}$	$A_{\parallel}/G$
$[Cu(H_2L)]^{2+}$	2.25	2.00	160
$[CuL]$	2.22	2.06	175
$[Cu(H_2L)]^{2+} + NBu_4SCN^b$	2.25	2.01	160

<sup>a</sup>  $1.0 \times 10^{-3}$  mol  $dm^{-3}$   $[Cu(H_2L)]^{2+}$ . <sup>b</sup>  $NBu_4SCN : [Cu(H_2L)]^{2+} = 2 : 1$ .

Electronics Ltd., Tokyo), and toluene-*p*-sulfonate by absorbance at 261 nm.

### Transport experiment in three-phase systems

All transport experiments were carried out at 20 °C. A cylindrical glass cell (diameter 4 cm, height 6 cm) was divided into two parts by a glass plate, except for the bottom portion (1 cm).<sup>10</sup> The two aqueous layers were separated from each other by the glass plate and the organic layer ( $CH_2Cl_2$ ) was placed at the bottom. During the transport experiment the organic layer was slowly stirred with a small magnetic stirrer to allow the interface of the aqueous and organic layers to swirl slowly (*ca.* 80 revolutions  $min^{-1}$ ).

## Results

### Properties of the copper(II) complex of $H_2L$

The copper(II) complex obtained from  $H_2L$  and copper(II) nitrate was recrystallized from methanol to give light blue plates of  $[Cu(H_2L)(H_2O)][NO_3]_2$ . Addition of KOH to a dichloromethane solution of the complex  $[Cu(H_2L)]^{2+}$  yielded green needles of the amide-deprotonated complex  $[CuL]$  (Scheme 1). Their IR spectra were essentially the same as those of the copper(II) complexes of 6,6'-bis(benzoylamino)-2,2'-bipyridine.<sup>8</sup> An  $N_2O_2$  square-planar structure of the complex was confirmed by the ESR parameters (Table 1). The complexes  $[Cu(H_2L)]^{2+}$  and  $[CuL]$  in  $CH_2Cl_2$  showed typical axial-type spectra with five superhyperfine splittings due to the two nitrogens in the copper co-ordination sphere. Therefore, introduction of the hexyl group to the benzyl units has had little effect on the structure of the complexes.

However, the hexyl group did increase the hydrophobicity

of the complexes. Though the non-deprotonated complex of 6,6'-bis(benzoylamino)-2,2'-bipyridine was soluble in water,  $[Cu(H_2L)]^{2+}$  and  $[CuL]$  were sufficiently soluble in organic solvents like  $CH_2Cl_2$  and  $CHCl_3$  but not at all in water.

Electronic spectra of metal-free  $H_2L$  and its copper(II) complexes in  $CH_2Cl_2$  are shown in Fig. 1(a). The complexes showed absorption bands at around 350–500 nm presumably due to ligand-centred  $\pi-\pi^*$  transitions.<sup>8</sup> Addition of small amounts of methanolic NaOH solution to the  $[Cu(H_2L)]^{2+}$ – $CH_2Cl_2$  solution showed a clear two-step spectral change [Fig. 1(b)], which is ascribed to stepwise deprotonation of the complex (Scheme 1) through a monodeprotonated complex,  $[Cu(HL)]^+$  [ $NaOH$ :complex molar ratio = 1:1, Fig. 1(b)(i)], to the fully deprotonated complex,  $[CuL]$  [ $NaOH$ :complex = 2:1, Fig. 1(b)(ii)]. Deprotonation of the amide units of the complex was confirmed to be reversible by repeated addition of methanolic HCl and NaOH.

### Anion affinity of the complexes in dichloromethane

Electronic spectra of the complexes between 280 and 500 nm were measured in the presence of tetra-*n*-butylammonium bromide, toluene-*p*-sulfonate and thiocyanate in  $CH_2Cl_2$  at 20 °C. The spectrum of the deprotonated complex  $[CuL]$  was little affected by the presence of any of the  $NBu_4^+$  salts, suggesting no direct interaction with these anions. The bromide and toluene-*p*-sulfonate salts caused no detectable change in the spectrum of  $[Cu(H_2L)]^{2+}$ . However, a small but clear change was observed when  $SCN^-$  was present (Fig. 2). Increase of  $[SCN^-]$  resulted in a two-step alteration with isosbestic points at 331, 358, 378 and 410 nm for the first step {Fig. 2(a),  $SCN^- : [Cu(H_2L)]^{2+}$  molar ratio = 1:1} and 420 nm for the second {Fig. 2(b),  $SCN^- : [Cu(H_2L)]^{2+}$  molar ratio = 2:1}, respectively. The complex-formation constant for the first step ( $K_{s1}$ ) was too large to be determined from the spectral change by the Rose-Drago plot,<sup>11</sup> but that for the second step ( $K_{s2}$ ) was determined to be  $\log K_{s2} = 4.53$  from the absorbance at 305 nm.

The d–d bands of the complexes also showed a similar anion-dependent spectral change. For these experiments, 5% v/v of methanol was added in order to increase solubility of the complex ( $1.0 \times 10^{-3}$  mol  $dm^{-3}$ ). The d–d bands of  $[Cu(H_2L)]^{2+}$  and  $[CuL]$  in  $CH_2Cl_2$  without  $NBu_4^+$  salts appeared at 638 ( $\epsilon = 156$ ) and 554 nm ( $\epsilon = 219$   $dm^3$   $mol^{-1}$   $cm^{-1}$ ), respectively. The presence of any of the  $NBu_4^+$  salts had little effect on the band of  $[CuL]$ . On the other hand,

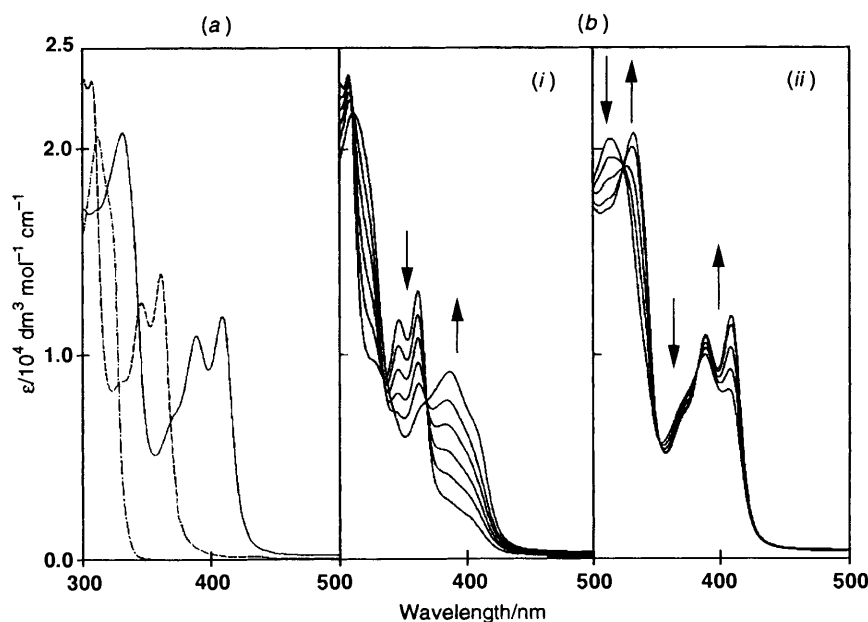


Fig. 1 Electronic spectra of  $H_2L$  and its copper(II) complexes ( $7.10 \times 10^{-5} \text{ mol dm}^{-3}$ ) in dichloromethane at  $20^\circ\text{C}$ . (a)  $H_2L$  (— · — · —),  $[Cu(H_2L)(H_2O)](NO_3)_2$  (----) and  $[CuL]$  (—); (b) spectral change of  $[Cu(H_2L)(H_2O)](NO_3)_2$  upon addition of small amounts of methanolic NaOH, where NaOH: complex molar ratios were 0–1:1 (i) and 1–2:1 (ii)

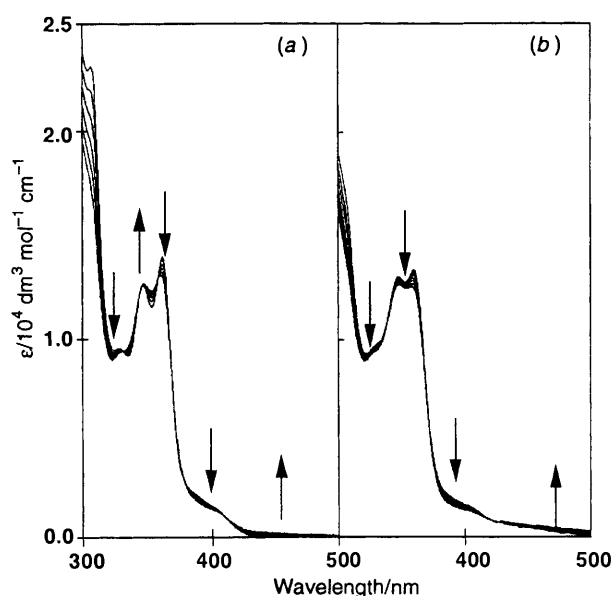


Fig. 2 Spectral changes of  $[Cu(H_2L)(H_2O)](NO_3)_2$  ( $5.00 \times 10^{-5} \text{ mol dm}^{-3}$ ) in  $CH_2Cl_2$  upon addition of  $NBu_4SCN$  at  $20^\circ\text{C}$ , where the  $NBu_4SCN$ : complex molar ratios were 0–1:1 (a) and 1–2:1 (b)

addition of  $NBu_4SCN$  caused a red-shift of the band of the  $Cu(H_2L)]^{2+}$  from 638 to 665 and 694 nm at  $NBu_4SCN$ : $[Cu(H_2L)]^{2+}$  molar ratios of 1.0 and 2.0:1, respectively. No spectral change was observed when the bromide or toluene-*p*-sulfonate salt was added.

#### Uptake and release of anions in the two-phase system

Electronic spectra of  $[Cu(H_2L)]^{2+}-CH_2Cl_2$  solutions ( $2.0 \times 10^{-3} \text{ mol dm}^{-3}$ ) after vigorous mixing with the same volume of aqueous Kolthoff's buffer solutions (mixtures of 0.05  $\text{mol dm}^{-3}$  sodium succinate and 0.05  $\text{mol dm}^{-3}$  sodium tetraborate, pH 3.0 and 6.0) containing  $NaSCN$  ( $4.0 \times 10^{-3} \text{ mol dm}^{-3}$ ) are shown in Fig. 3(a). When the pH of the aqueous solution was 6.0 the complex was exclusively in the fully deprotonated form  $[CuL]$ , whereas the spectra after contact with the pH 3.0 buffer solution indicated that the major component was  $[Cu(H_2L)]^{2+}$  (molar fraction = 0.84) though  $[Cu(HL)]^+$  (0.01) and  $[CuL]$  (0.15) were simultaneously

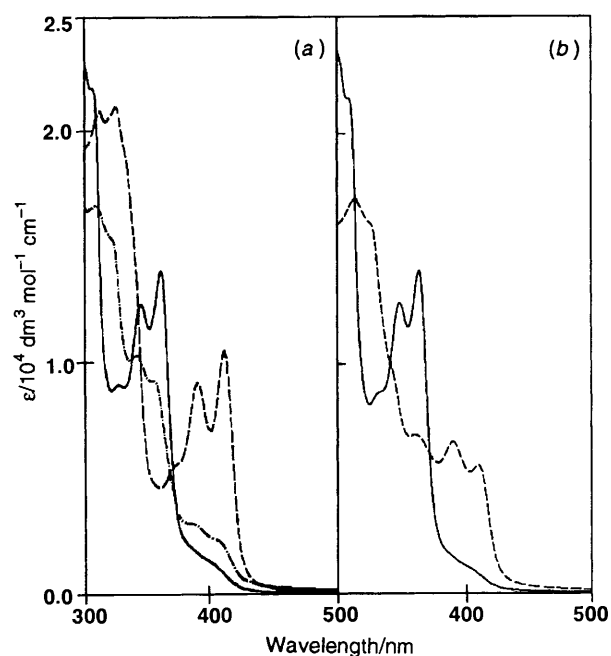


Fig. 3 (a) Electronic spectra of the  $[Cu(H_2L)(H_2O)](NO_3)_2$  ( $2.0 \times 10^{-3} \text{ mol dm}^{-3}$ ) in  $CH_2Cl_2$  before (—) and after contact with the same volume of aqueous  $NaSCN$  ( $4.0 \times 10^{-3} \text{ mol dm}^{-3}$ ) solution adjusted to pH 3.0 (— · — · —) and 6.0 (----). (b) Spectral change of  $[Cu(H_2L)]^{2+}$  ( $1.11 \times 10^{-4} \text{ mol dm}^{-3}$ ) in the  $CH_2Cl_2$  layer before (—) and after 3 h (----) of the transport experiment (for experimental conditions, see Table 3, no. 1)

present in the organic layer. Use of  $H_2L$  in the organic and  $Cu(NO_3)_2$  in the aqueous layers separately gave essentially the same results. No sign of leakage of  $H_2L$  or its copper(II) complex into the aqueous solution was observed spectrophotometrically, showing the hydrophobic nature of the hexylbenzoyl group.

To study the effect of anions in the aqueous solution, the organic solution containing  $[Cu(H_2L)(H_2O)](NO_3)_2$  was mixed with the same volume of pH 3.0–6.0 buffer solutions containing sodium bromide, toluene-*p*-sulfonate or thiocyanate. The amounts of anions transferred to the organic layer are summarized in Table 2. In the absence of the complex in the

**Table 2** Uptake (0% for NaBr) and release of the anions (percent, relative to the initial concentration of anion in the buffer solution)<sup>a</sup>

pH	Anion (NaX) (%)			
	NaSCN		NaO <sub>3</sub> SC <sub>6</sub> H <sub>4</sub> Me- <i>p</i>	
	Uptake	Release <sup>b</sup>	Uptake	Release <sup>b</sup>
3.0	54.8	48.5	<sup>c</sup>	
4.0	25.8	17.3	12.3	10.8
6.0	7.2	1.4	0.0	0.0

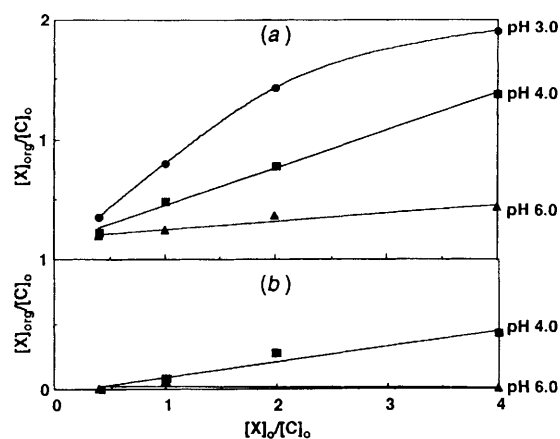
<sup>a</sup> [Complex] =  $2.0 \times 10^{-3}$ , [NaX] =  $4.0 \times 10^{-3}$  mol dm<sup>-3</sup>; see Experimental section for details. <sup>b</sup> Organic layers after extraction were mixed with fresh pH 6.0 buffer solutions. See Experimental section for details. <sup>c</sup> A small amount of precipitate was observed at the interface after the aqueous and organic solutions were mixed.

organic layer, negligible amounts of anions were transferred from the aqueous layer to the organic layer. In the presence of the complex, however, SCN<sup>-</sup> was efficiently extracted from the aqueous pH 3.0 solution. The lipophilic anion, toluene-*p*-sulfonate, was also transferred to the organic layer by the complex, but hydrophilic bromide anion was not extracted at all. Fig. 4 shows the effect of the initial SCN<sup>-</sup> or toluene-*p*-sulfonate concentrations ([X]<sub>0</sub>) in aqueous solutions on the concentration of the extracted anion ([X]<sub>org</sub>) in the organic layer. Increase of the SCN<sup>-</sup> concentration in the aqueous pH 3.0 solution increased the SCN<sup>-</sup>:complex molar ratio in the organic layer *ca.* to 2:1. Therefore, a twice molar amount of SCN<sup>-</sup> was incorporated into the organic layer by the complex. As the complex was mostly in the [Cu(H<sub>2</sub>L)]<sup>2+</sup> form when the organic layer was mixed with a pH 3.0 buffer containing SCN<sup>-</sup>, the results are in good agreement with the findings in the previous section that the complex interacts with two SCN<sup>-</sup> in the organic layer. From the aqueous layer at pH 6.0, negligible amounts of SCN<sup>-</sup> and toluene-*p*-sulfonate were extracted into the organic layer. Since the complex after contact with the aqueous pH 6.0 solution was in the fully deprotonated form the results also confirmed the poor anion affinity of [CuL].

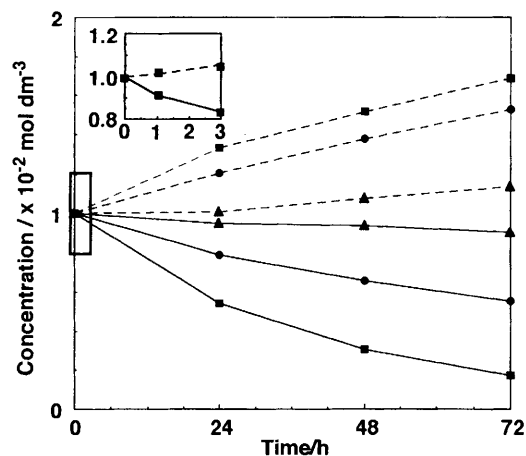
The organic layer after extraction of anions from aqueous solutions was subjected to contact with fresh pH 6.0 buffer solutions. The amounts of anions released into the aqueous solutions are also included in Table 2. Both SCN<sup>-</sup> and toluene-*p*-sulfonate were released back to the aqueous pH 6 solutions.

#### Anion transport in a three-phase system

Transport experiments were carried out at 20 °C using a three-phase system, where two aqueous buffer solutions were separated by a [Cu(H<sub>2</sub>L)]<sup>2+</sup>-CH<sub>2</sub>Cl<sub>2</sub> layer ( $1.11 \times 10^{-4}$  mol dm<sup>-3</sup>, 30 cm<sup>3</sup>). The aqueous layers I (pH 3.0–5.0) and II (pH 6.0) were identical in their volume (10 cm<sup>3</sup>) and NaSCN concentration ( $1.00 \times 10^{-2}$  mol dm<sup>-3</sup>), though their pH values were different. When the pH of I was 4.0 or 3.0 (Fig. 5) efficient up-hill transport of SCN<sup>-</sup> was mediated from I to II against the concentration gradient, but only a slow transport was observed from the pH 5.0 solution. When the pH of I was 3.0, the SCN<sup>-</sup> concentration of II after 72 h was approximately 10 times higher than that of the I, and simultaneously the pH of I and II shifted to 3.71 and 5.21, respectively. Use of H<sub>2</sub>L in the organic and Cu(NO<sub>3</sub>)<sub>2</sub> in the aqueous layers separately instead of dissolving [Cu(H<sub>2</sub>L)]<sup>2+</sup> in the organic layer gave essentially the same results. No transport of SCN<sup>-</sup> was observed in the absence of any one of Cu(NO<sub>3</sub>)<sub>2</sub>, H<sub>2</sub>L or a pH difference between the two aqueous layers. These results confirmed that the copper(II) complex of H<sub>2</sub>L was the carrier, and the up-hill transport was mediated by coupling with the pH difference across the membrane. It should be noted that no transport of



**Fig. 4** Effect of the initial anion concentrations in the aqueous layer on the concentration of the extracted anions in the organic layer; [C]<sub>0</sub>, [X]<sub>0</sub> and [X]<sub>org</sub> represent the concentrations of initial [Cu(H<sub>2</sub>L)]<sup>2+</sup>, in CH<sub>2</sub>Cl<sub>2</sub>, initial anion in the buffer solution, and extracted anion in CH<sub>2</sub>Cl<sub>2</sub>, respectively. See Experimental section for detailed conditions. X = SCN<sup>-</sup> (a), *p*-MeC<sub>6</sub>H<sub>4</sub>SO<sub>3</sub><sup>-</sup> (b)



**Fig. 5** Time course of the concentration of SCN<sup>-</sup> in aqueous layers I (—) and II (---) during the up-hill transport across the CH<sub>2</sub>Cl<sub>2</sub> layer mediated by [Cu(H<sub>2</sub>L)]<sup>2+</sup> ( $1.11 \times 10^{-4}$  mol dm<sup>-3</sup>) at 20 °C. The initial concentrations of the anions in both aqueous layers were  $1 \times 10^{-2}$  mol dm<sup>-3</sup>. Layer II was set at pH 6.0, while pH of layer I was 3.0 (■), 4.0 (●) or 5.0 (▲)

the buffer anions (succinate and borate) was observed during the transport experiments.

Electronic spectra of the organic layer before and after 3 h of the transport experiment are shown in Fig. 3(b). From the spectra the molar fractions of the complexes [Cu(H<sub>2</sub>L)]<sup>2+</sup>, [Cu(HL)]<sup>+</sup> and [CuL] after 3 h were estimated to be 0.41, 0.19 and 0.39, respectively.

Lipophilic toluene-*p*-sulfonate was also transported across the organic layer, but hydrophilic bromide was not transported at all, indicating that hydrophobicity of the anion is the important factor for mediating up-hill transport. When the sulfonate and SCN<sup>-</sup> were present simultaneously in the aqueous layers, SCN<sup>-</sup> having higher co-ordination ability was selectively transported (Table 3).

## Discussion

### Structure of the complex and mode of anion binding in organic media

The results shown in Fig. 5 demonstrated that the copper(II) complex of H<sub>2</sub>L served as the carrier for the efficient and selective up-hill transport of SCN<sup>-</sup> by coupling with the pH difference across the liquid membrane. Introduction of the *n*-hexyl group into the ligand moiety increased the lipophilicity of the complex.

The complex in  $\text{CH}_2\text{Cl}_2$  undergoes reversible amide deprotonation (Scheme 1), and either in the non-deprotonated or deprotonated form has an  $\text{N}_2\text{O}_2$  square-planar structure as shown from their electronic and ESR spectra. Since the d-d band of the fully deprotonated complex  $[\text{CuL}]$  is blue-shifted (84 nm) compared to that of  $[\text{Cu}(\text{H}_2\text{L})]^{2+}$  it has the stronger square-planar ligand field.

The non-deprotonated complex  $[\text{Cu}(\text{H}_2\text{L})(\text{H}_2\text{O})][\text{NO}_3]_2$  is present as a divalent cation, and counter anions bind to it primarily by electrostatic forces. The presence of the bromide or toluene-*p*-sulfonate salt of  $\text{NBu}_4^+$  did not affect the electronic spectra of  $[\text{Cu}(\text{H}_2\text{L})]^{2+}$ , indicating that these anions did not co-ordinate directly to the metal. However,  $\text{SCN}^-$  having high co-ordination ability resulted in a small but clear two-step change (Fig. 2). The additional presence of the toluene-*p*-sulfonate or bromide salt had little effect on this change. Since this spectral change is relatively small and the ESR parameters are not different from those in the absence of  $\text{NBu}_4\text{SCN}$  (Table 1), it is concluded that the non-deprotonated complex retains the square-planar symmetry even in the presence of  $\text{SCN}^-$ .<sup>12</sup> Therefore, the observed spectral change is not due to ligand exchange of  $\text{H}_2\text{L}$  with  $\text{SCN}^-$  but is ascribed to the stepwise co-ordination of two  $\text{SCN}^-$  molecules to the metal in axial positions. Evidence in support of this was provided by the red shift of the d-d band of  $[\text{Cu}(\text{H}_2\text{L})]^{2+}$  from 638 to 665  $\{[\text{NBu}_4\text{SCN}]:[\text{Cu}(\text{H}_2\text{L})]^{2+} = 1:1\}$  and 694 nm (2:1) on addition of  $\text{NBu}_4\text{SCN}$ , because the weaker square-planar ligand field decreases the d-d transition energy of the copper complex.<sup>13</sup> Association of  $\text{SCN}^-$  with the complex is almost quantitative for the first step, demonstrating the high affinity of  $\text{SCN}^-$  for the complex.

In the case of the deprotonated complex having no formal charge no electrostatic interaction with anions is expected. Indeed, the presence of any of the  $\text{NBu}_4^+$  salts did not result in any detectable change in the electronic spectrum, confirming the poor anion affinity of  $[\text{CuL}]$  for even  $\text{SCN}^-$  having high co-ordination ability. This poor axial co-ordination of  $\text{SCN}^-$  to the complex is in good agreement with the fact that  $[\text{CuL}]$  has a stronger square-planar ligand field. Thus, it is confirmed that the non-deprotonated complex has high anion affinity, while the fully deprotonated complex shows poor anion affinity, and reversible amide deprotonation causes a drastic alteration of the anion affinity of the carrier complex.

#### Anion extraction by the complex in the two-phase system

In the two-phase system the complex is exclusively in the fully deprotonated form after contact with the aqueous pH 6.0 solution, but  $[\text{Cu}(\text{H}_2\text{L})]^{2+}$  is the major component after contact with the aqueous pH 3.0 solution. Therefore, the reversible deprotonation of the complex in the organic layer is controlled by the pH of the aqueous solution.

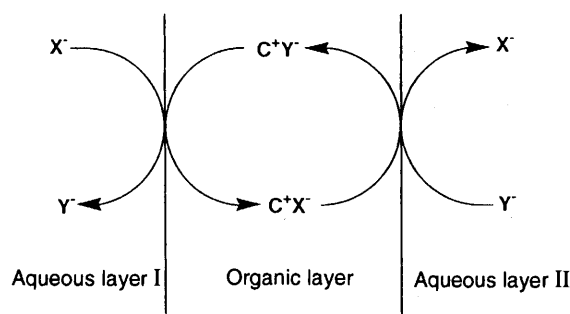
In the presence of the complex in the organic layer, lipophilic toluene-*p*-sulfonate was transferred to some extent into the organic layer from the pH 4.0 aqueous solution but not from the pH 6.0 aqueous solution (Table 2). Therefore, the non-deprotonated or monodeprotonated complex is responsible for extraction of this anion into the organic layer. Hydrophilic bromide was not transferred into the organic layer at all. These anions have poor co-ordination ability, and do not co-ordinate directly to the metal. Since nitrate is the counter anion of the non-deprotonated complex before contact with the buffer, the lipophilic sulfonate is extracted into the organic layer by ion exchange with hydrophilic nitrate, showing the importance of the lipophilicity of the anion.

However,  $\text{SCN}^-$  is much more effectively transferred from the aqueous pH 3.0 and 4.0 solutions. This is ascribed to its high affinity for  $[\text{Cu}(\text{H}_2\text{L})]^{2+}$  due to the axial co-ordination. It is likely that this axial co-ordination allows efficient extraction into organic layer. The extracted anions are released back to the aqueous pH 6.0 solution. Therefore, the results demonstrated that affinity switching of the carrier complex can control uptake and release of  $\text{SCN}^-$  and toluene-*p*-sulfonate.

#### Mechanism of anion transport

The carrier complex mediated highly efficient up-hill transport of  $\text{SCN}^-$ . When the initial pH of the aqueous layer I was 3.0 the  $\text{SCN}^-$  concentration in the aqueous layer II after 72 h was  $1.69 \times 10^{-2} \text{ mol dm}^{-3}$ , nearly 10 times higher than that of the  $1.7 \times 10^{-3} \text{ mol dm}^{-3}$  in I. Though the up-hill transport became considerably slower after 72 h it still persisted (Fig. 5). During the transport experiments the pH of layer I increased to 3.71. Titration with concentrated  $\text{NaOH}$  showed that  $9 \times 10^{-3} \text{ mol dm}^{-3}$  of  $\text{H}^+$  had to be consumed in order to increase the pH of the buffer solution to 3.71. This value is in good agreement with the decrease in the amount of  $\text{SCN}^-$  in layer I ( $8.3 \times 10^{-3} \text{ mol dm}^{-3}$ ), and, therefore, up-hill transport of  $\text{SCN}^-$  is effectively coupled with symport of  $\text{H}^+$  from layer I to II.

It is worth noting that only a small pH difference is sufficient to mediate efficient up-hill transport of  $\text{SCN}^-$ . The difference

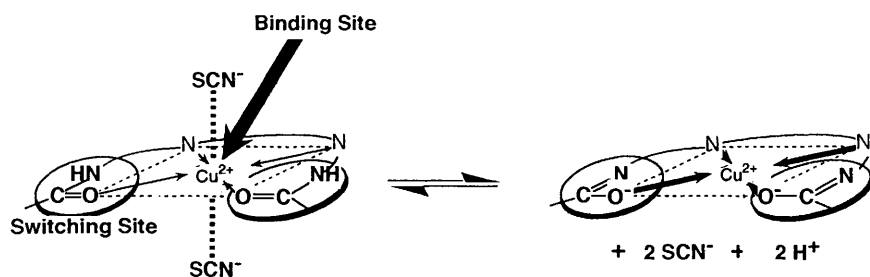


Scheme 2

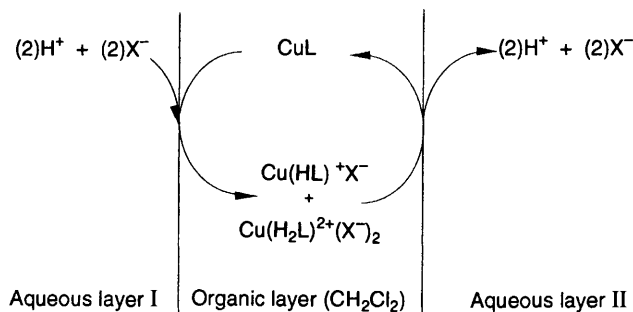
**Table 3** Anion transport from aqueous layer I ( $10 \text{ cm}^3$ ) to II ( $10 \text{ cm}^3$ ) across the  $\text{CH}_2\text{Cl}_2$  layer containing  $[\text{Cu}(\text{H}_2\text{L})]^{2+}$  ( $1.11 \times 10^{-4} \text{ mol dm}^{-3}$ ,  $30 \text{ cm}^3$ ) at  $20^\circ\text{C}$ <sup>a</sup>

Experiment	Anion	pH	Concentration after 72 h/ $10^{-2} \text{ mol dm}^{-3}$		
			Layer I	Layer II (pH 6.0)	Turnover <sup>b</sup>
1	$\text{SCN}^-$	3.0	0.17	1.69	10.0
2		4.0	0.55	1.53	8.0
3		5.0	0.90	1.13	2.0
4	$\text{Br}^-$	4.0	1.00	1.00	0.0
5	$p\text{-MeC}_6\text{H}_4\text{SO}_3^-$	4.0	0.77	1.21	3.0
6 <sup>c</sup>	$p\text{-MeC}_6\text{H}_4\text{SO}_3^-$	4.0	0.88	1.03	0.5
	$\text{SCN}^-$		0.50	1.45	7.0

<sup>a</sup> Initial anion concentrations in layers I and II were  $1.00 \times 10^{-2} \text{ mol dm}^{-3}$ . <sup>b</sup> Turnover of the carrier after 72 h based on the assumption that a twice molar amount of anion is transported by the carrier. <sup>c</sup> The aqueous layers contained both  $p\text{-MeC}_6\text{H}_4\text{SO}_3^-$  and  $\text{SCN}^-$ .



Scheme 3



Scheme 4

in the proton chemical potentials of layers I and II after 72 h at 20 °C is calculated to be 8.4 kJ mol<sup>-1</sup> by assuming that the concentrations can be used as activities, while that of SCN<sup>-</sup> after 72 h generated by the carrier is -5.6 kJ mol<sup>-1</sup>. The results confirm the effective coupling of the proton and SCN<sup>-</sup> transports not only quantitatively but also energetically, and the small pH difference is sufficient to induce up-hill transport of SCN<sup>-</sup>. Conventional carrier-mediated transport involves ion exchange at both sides of the membrane (Scheme 2). As discussed in the Introduction section, higher substrate affinity of the carrier is favourable for the uptake process, but is unfavourable for the release process. Therefore, most of the pH-driven up-hill transport requires a large pH difference across the membrane in order to establish efficient uptake and release simultaneously.<sup>14</sup> In the case of the carrier reported here, protonation of the deprotonated complex is coupled with uptake of counter anion(s), while deprotonation of the mono- or non-deprotonated complex induces concomitant release of the counter anion(s). As the anion-binding and affinity-switching sites are different within the carrier complex, strong anion binding to the carrier does not interfere with deprotonation of the amide groups and release of the bound anion(s) (Scheme 3). Thus, affinity switching of the carrier can easily be controlled by the pH of the aqueous layer, and a pH difference sufficient to induce affinity switching of the carrier can mediate up-hill transport.

The transport mechanism of this system is illustrated in Scheme 4. After 3 h of the SCN<sup>-</sup> transport the proportions of [Cu(H<sub>2</sub>L)]<sup>2+</sup>, [Cu(HL)]<sup>+</sup> and [CuL] in the organic membrane layer are estimated to be 0.41, 0.19 and 0.39, respectively, from Fig. 4. Therefore, the carrier in the system is either the non-deprotonated or the monodeprotonated complex, and the contribution of [Cu(H<sub>2</sub>L)]<sup>2+</sup> is higher in the SCN<sup>-</sup> transport. On the basis of the assumption that a twice molar amount of anion is transported by the carrier complex the turn-over of the carrier can be estimated and is included in Table 3.

The carrier complex shows excellent anion selectivity in transport. This is explained by the two factors lipophilicity and

co-ordination ability of anions, in the uptake process. Anions having poor co-ordination ability are extracted in the organic layer as a counter anion of the carrier complex, where higher lipophilicity is favourable for extraction. However, direct co-ordination of SCN<sup>-</sup> to the metal is much more advantageous in the extraction process. As shown in Table 3, SCN<sup>-</sup> is selectively transported even in the presence of toluene-*p*-sulfonate.

In conclusion, the copper(II) complex of H<sub>2</sub>L having an N<sub>2</sub>O<sub>2</sub> square-planar structure served as a new type of functional carrier in the pH-induced up-hill transport of anions. Reversible deprotonation of the amide groups of the complex was effectively coupled with uptake and release of anions, and affinity switching of the carrier by the pH of the aqueous layers induced efficient up-hill transport by coupling with symport of H<sup>+</sup>. The high transport selectivity of the carrier toward SCN<sup>-</sup> was explained by its preferential axial co-ordination to the metal.

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