N,N'-Di(8-quinolyl)glutaramide Exhibiting Highly Selective and Efficient Uphill Transport of Cu(II) through Liquid Membranes

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N,N'-Di(8-quinolyl)glutaramide has been found to be an excellent Cu(II) carrier in the transport through a chloroform liquid membrane. It can selectively and efficiently transport Cu(II) from a weakly acidic aqueous solution containing Cu(II), Zn(II), Ni(II), and Co(II). Several *N,N'*-di(8-quinolyl)glutaramide derivatives and their analogues have been prepared for comparison of this transport ability, which largely depends not only upon the structure of the carriers, but also upon the transport conditions.

Carrier-mediated continuous solvent extraction, i.e., transport through liquid membranes, of metal ions is not only an attractive method for the separation and recovery of valuable resources,[1] but also is of importance from the biological, medical, and environmental points of view. Although many carriers for the transport of alkali and alkaline earth metal ions through liquid membranes have been reported so far,[2] not many synthetic carriers for the highly selective and efficient uphill transport of heavy metal ions have been developed.[3–7] We preliminarily reported that *N,N'*-di(8-quinolyl)glutaramide(**4**) can transport Cu(II) with high selectivity and efficiency through liquid membranes.[8]

We report here on the Cu(II) transport behaviors of *N,N'*-di(8-quinolyl)glutaramide derivatives and their analogues through liquid membranes. The transport ability of **4** was investigated and compared with that of monoamide **1** and a series of diamides, **2**, **3**, and **5**. For comparison, commercially available 7-undecyl-8-quinolinol (Kelex 100) (**6**) was also used, which can work not only as a Cu(II) selective extractant in solvent extraction, but also as a Cu(II) selective carrier in the transport through liquid membranes.[9] Glutaramide derivatives, **7**—**11**, were also prepared to investigate the structural effect on Cu(II) transport.

n-C_5H_{11}-CONHQ

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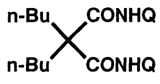

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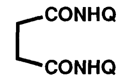

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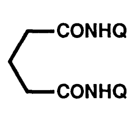

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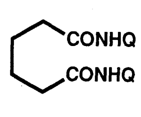

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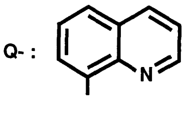

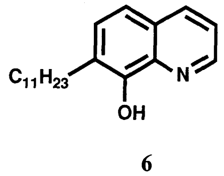

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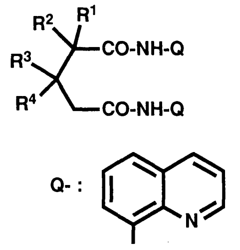
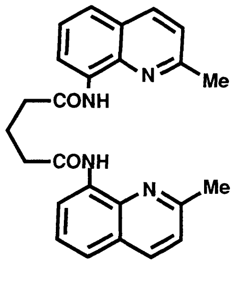


	R^1	R^2	R^3	R^4
7	Me	H	H	H
8	Me	Me	H	H
9	H	H	Me	H
10	H	H	Me	Me



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Experimental

General. The IR and UV spectra were recorded with a JASCO A-3 infrared and a Hitachi 330 spectrophotometer, respectively. The ^1H NMR spectra were recorded with a Bruker MSL-300 NMR spectrometer. The chemical shifts for $CDCl_3$ solution are reported relative to internal tetramethylsilane(TMS). The positions of the protons on the quinolyl group are depicted as Q-H^n. The high resolution mass spectra were measured with a Hitachi M-80B instrument.

Extra-pure grade benzene was dried by using molecular sieves(4 Å) which were purchased from Merck. Extra-pure grade triethylamine was dried over potassium hydroxide. 7-Undecyl-8-quinolinol(commercial name: Kelex 100) was obtained from Yokohama Kasei Co., Ltd. and distilled under vacuum (162 °C/0.1 mmHg 1mmHg=133.322 Pa; precise mass found: 299.224, calcd for $C_{20}H_{29}NO$: 299.225) by using a Kugelrohr. All other solvents and reagents were of extra-pure grade quality and were used without further purification.

General Procedure for the Preparation of *N*-(8-Quinolyl)carboxamide) Compounds (1—3 and 5). 8-Aminoquinoline and triethylamine(10 mmol each for hexanoyl chloride and 20 mmol each for the others) were added to the 10 ml of benzene solutions of acid chlorides(10 mmol) which were derived from hexanoic acid, 2,2-dibutylmalonic acid, succinic acid, and adipic acid. The mixture was then stirred at 80 °C overnight. After cooling to room temperature, the reaction mixture was poured into 50 ml of water and 50 ml of benzene, and extracted with benzene. The benzene layer was washed with water three times and dried over anhydrous magnesium sulfate. After the solvent and had been removed under reduced pressure, the residue was subjected to column chromatography on silica gel(300 mesh) with chloroform as eluent to give the corresponding *N*-(8-quinolyl)carboxamide derivatives.

***N*-(8-Quinolyl)hexanamide (1):** Yield 83%; colorless liquid (140 °C/0.5 mmHg); ^{1}H NMR (300 MHz, $CDCl_3$) δ=0.94 (3H, m, CH_3), 1.41 (4H, m, $CH_3C\underline{H}_2C\underline{H}_2CH_2CH_2$), 1.83 (2H, m, $CH_3CH_2CH_2C\underline{H}_2CH_2$, 2.56 (2H, t, *J*=6 Hz, CH_2CO), 7.44 (1H, dd, *J*=4 and 8 Hz, Q-H^3), 7.48 (1H, dd, *J*=2 and 8 Hz, Q-H^5), 7.53 (1H, t, *J*=8 Hz, Q-H^6), 8.15 (1H, dd, *J*=2 and 8 Hz, Q-H^4), 8.79 (1H, dd, *J*=2 and 7 Hz, Q-H^7), 8.80 (1H, dd, *J*=2 and 4 Hz, Q-H^2), and 9.81 (1H, s, NH). Precise mass, Found: *m*/*z* 242.139. Calcd for $C_{15}H_{18}N_2O$: M, 242.1421. IR (neat) 3360 and 1690 (C=O) cm^{-1}.

2,2-Dibutyl-*N*,*N′*-(8-quinolyl)malonamide (2): Yield 81%; mp 142—143 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ=0.87 (6H, t, *J*=7 Hz, CH_3), 1.41 (8H, m, $CH_3C\underline{H}_2C\underline{H}_2CH_2$), 2.32 (4H, m, $CH_3CH_2CH_2C\underline{H}_2$), 7.40 (2H, dd, *J*=4 and 8 Hz, Q-H^3), 7.48 (2H, dd, *J*=2 and 8 Hz, Q-H^5), 7.53 (2H, t, *J*=8 Hz, Q-H^6), 8.09 (2H, dd, *J*=2 and 8 Hz, Q-H^4), 8.86 (2H, dd, *J*=2 and 4 Hz, Q-H^2), 8.92 (2H, dd, *J*=2 and 7 Hz, Q-H^7), and 11.32 (2H, s, NH). Precise mass, Found: *m*/*z* 468.251. Calcd for $C_{29}H_{32}N_4O_2$: M, 468.2521. IR(KBr) 3340 (N–H) and 1685 (C=O) cm^{-1}.

***N*,*N′*-(8-Quinolyl)succinamide (3):** Yield 58%; mp 216—217 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ=3.09 (4H, s, CH_2CH_2), 7.43 (2H, dd, *J*=4 and 8 Hz, Q-H^3), 7.47 (2H, dd, *J*=2 and 7 Hz, Q-H^5), 7.50 (2H, t, *J*=7 Hz, Q-H^6), 8.13 (2H, dd, *J*=2 and 8 Hz, Q-H^4), 8.77 (2H, dd, *J*=2 and 8 Hz, Q-H^7), 8.79 (2H, dd, *J*=2 and 4 Hz, Q-H^2), and 9.99 (2H, s, NH). Precise mass, Found: *m*/*z* 370.142. Calcd for $C_{22}H_{18}N_4O_2$: M, 370.143. IR (KBr) 3320 (N–H) and 1670 (C=O) cm^{-1}.

***N*,*N′*-(8-Quinolyl)adipamide (5):** Yield 75%; mp 185—186 °C; ^{1}H NMR (300 MHz, $CDCl_3$), δ=1.98 (4H, m, $CH_2C\underline{H}_2C\underline{H}_2CH_2$), 2.65 (4H, m, $C\underline{H}_2CH_2CH_2C\underline{H}_2$), 7.41 (2H, dd, *J*=4 and 8 Hz, Q-H^3), 7.46 (2H, dd, *J*=2 and 8 Hz, Q-H^5), 7.50 (2H, t, *J*=8 Hz, Q-H^6), 8.12 (2H, dd, *J*=2 and 8 Hz, Q-H^4), 8.76 (2H, dd, *J*=2 and 4 Hz, Q-H^2), 8.78 (2H, dd, *J*=2 and 8 Hz, Q-H^7), and 9.83 (2H, s, NH). Precise mass, Found: *m*/*z* 398.172. Calcd for $C_{24}H_{22}N_4O_2$: M, 398.174. IR (KBr) 3350 (N–H) and 1670 (C=O) cm^{-1}.

General Procedure for the Preparation of *N*,*N′*-(8-Quinolyl)glutaramide Derivatives (4, 7—11). A mixture of glutaric acid or substituted glutaric acid (10 mmol) and 5 ml of thionyl chloride was heated at 60 °C for 5 h. Then, thionyl chloride was removed by evaporation in vacuo. The residual solid was dissolved in 30 ml of anhydrous benzene, and 8-aminoquinoline or 2-methyl-8-aminoquinoline (20 mmol) and triethylamine (20 mmol) were added to the solution. The mixture was then stirred at 80 °C overnight. After cooling to room temperature, the reaction mixture was poured into 50 ml of water and 50 ml of benzene, and extracted with benzene. The benzene layer was washed with water three times and dried over anhydrous magnesium sulfate. After the solvent had been removed under reduced pressure, the residue was subjected to column chromatography on silica gel (300 mesh) with chloroform as eluent to give the corresponding *N*,*N′*-di(8-quinolyl)glutaramide derivatives.

***N*,*N′*-Di(8-quinolyl)glutaramide (4):** Yield 82%; mp 147—148 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ=2.35 (2H, m, $C\underline{H}_2CH_2C\underline{H}_2$), 2.76 (4H, t, *J*=7 Hz, $CH_2C\underline{H}_2CH_2$), 7.37 (2H, dd, *J*=4 and 8 Hz, Q-H^3), 7.47 (2H, dd, *J*=2 and 8 Hz, Q-H^5), 7.52 (2H, t, *J*=8 Hz, Q-H^6), 8.10 (2H, dd, *J*=2 and 8 Hz, Q-H^4), 8.67 (2H, dd, *J*=2 and 4 Hz, Q-H^2), 8.78 (2H, dd, *J*=2 and 8 Hz, Q-H^7), and 9.87 (2H, s, NH) (Q=8-quinolyl). Precise mass, Found: *m*/*z* 384.159. Calcd for $C_{23}H_{20}N_4O_2$: M, 384.159. IR (KBr) 3350 (N–H), 1680, and 1690 (C=O) cm^{-1}.

2-Methyl-*N*,*N′*-di(8-quinolyl)glutaramide (7): Yield 43%; mp 119.5—120 °C; ^{1}H NMR (300 MHz, $CDCl_3$), δ=1.42 (3H, d, *J*=7 Hz, CH_3), 2.16 (1H, m, $CHC\underline{H}_2CH_2$), 2.29 (1H, m, $CHC\underline{H}_2CH_2$), 2.71 (2H, m, $CHCH_2C\underline{H}_2$), 2.86 (1H, m, $C\underline{H}CH_2CH_2$), 7.31 (2H, m, Q-H^3), 7.50 (2H, m, Q-H^5), 7.53 (2H, m, Q-H^6), 8.08 (2H, dd, *J*=2 and 8 Hz, Q-H^4), 8.54 (2H, m, Q-H^2), 8.77 (1H, dd, *J*=2 and 8 Hz, Q-H^7), 8.81 (1H, dd, *J*=2 and 8 Hz, Q-H^7), 9.83 (1H, s, NH), and 9.98 (1H, s, NH). Precise mass, Found: *m*/*z* 389.176. Calcd for $C_{24}H_{22}N_4O_2$: M, 398.174. IR (KBr) 3350 (N–H) and 1680 (C=O) cm^{-1}.

2,2-Dimethyl-*N*,*N′*-di(8-quinolyl)glutaramide (8): Yield 61%; mp 110—112 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ=1.52 (6H, s, CH_3), 2.27 (2H, m, $C(CH_3)_2C\underline{H}_2CH_2$), 2.69 (2H, m, $C\underline{H}_2CO$), 7.41 (2H, m, Q-H^3), 7.50 (4H, m, Q-H^5 and H^6), 8.11 (1H, dd, *J*=2 and 8 Hz, Q-H^4), 8.14 (1H, dd, *J*=2 and 7 Hz, Q-H^4), 8.69 (1H, dd, *J*=2 and 4 Hz, Q-H^2), 8.73 (1H, dd, *J*=2 and 7 Hz, Q-H^7), 8.77 (1H, dd, *J*=2 and 4 Hz, Q-H^2), 8.81 (1H, dd, *J*=2 and 7 Hz, Q-H^7), 9.80 (1H, s, NH), and 10.35 (1H, s, NH). Precise mass, Found: *m*/*z* 412.189. Calcd for $C_{25}H_{24}N_4O_2$: M, 412.190. IR (KBr) 3320 (N–H) and 1675 (C=O) cm^{-1}.

3-Methyl-*N*,*N′*-di(8-quinolyl)glutaramide (9): Yield 70%; mp 153—154 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ=1.27 (3H, d, *J*=7 Hz, CH_3), 2.62 (2H, q, *J*=7 Hz, CH_2), 2.80 (2H, q, *J*=7 Hz, CH_2), 2.86 (1H, m, CH_2–$C\underline{H}$–CH_2), 7.40 (2H, dd, *J*=4 and 8 Hz, Q-H^3), 7.48 (2H, dd, *J*=2 and 8 Hz, Q-H^5), 7.52 (2H, t, *J*=8 Hz, Q-H^6), 8.12 (2H, dd, *J*=2 and 8 Hz, Q-H^4), 8.72 (2H, dd, *J*=2 and 4 Hz, Q-H^2), 8.79 (2H, dd, *J*=2 and 8 Hz, Q-H^7), and 9.91 (2H, s, NH). Precise mass, Found: *m*/*z* 398.173. Calcd for $C_{24}H_{22}N_4O_2$: M, 398.174. IR (KBr) 3350 (N–H) and 1665 (C=O) cm^{-1}.

3,3-Dimethyl-*N*,*N′*-di(8-quinolyl)glutaramide (10): Yield 58%; mp 134.5—135.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$), δ=1.35 (6H, s, CH_3), 2.78 (4H, s, CH_2), 7.39 (2H, dd, *J*=4 and 8 Hz, Q-H^3), 7.49 (2H, dd, *J*=2 and 8 Hz, Q-H^5), 7.55 (2H, t, *J*=8 Hz, Q-H^6), 8.11 (2H, dd, *J*=2 and 8 Hz, Q-H^4), 8.71 (2H, dd, *J*=2 and 4 Hz, Q-H^2), 8.77 (2H, dd, *J*=2 and 8 Hz, Q-H^7), and 10.18 (2H, s, NH). Precise mass, Found: *m*/*z* 412.188. Calcd for $C_{25}H_{24}N_4O_2$: M, 412.190. IR (KBr) 3350 (N–H) and 1675 (C=O) cm^{-1}.

***N*,*N′*-Di(2-methyl-8-quinolyl)glutaramide (11):** Yield 62%; mp 127—129 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ=2.35 (2H, m, $CH_2C\underline{H}_2CH_2$), 2.60 (6H, s, CH_3), 2.78 (4H, t, *J*=7 Hz, $C\underline{H}_2CH_2C\underline{H}_2$), 7.24 (2H, d, *J*=8 Hz, Q-H^3), 7.43 (2H, d, *J*=8 Hz, Q-H^5), 7.46 (2H, t, *J*=8 Hz, Q-H^6), 7.99 (2H, d, *J*=8 Hz, Q-H^3), 8.76 (2H, dd, *J*=3 and 6 Hz, Q-H^7), and 9.93 (2H, s, NH). Precise mass, Found: *m*/*z* 412.192. Calcd for $C_{25}H_{24}N_4O_2$: M, 412.190. IR (KBr) 3350 (N–H) and 1670

(C=O) cm^{-1}.

Preparation of the Cu(II) Complex of *N,N'*-Di(8-quinolyl)glutaramide. Copper (II) acetate monohydrate (0.20 g, 1 mmol) was added to a solution (20 ml) of *N,N'*-di(8-quinolyl)glutaramide (0.19 g, 0.5 mmol) in ethanol. The reaction mixture was heated at 80 °C overnight and turned green-brown. Removal of the solvent under reduced pressure left a residue, which was subjected to column chromatography on silica gel (300 mesh) with a mixture of dichloromethane and methanol (9 : 1) as an eluent. The deep-green solid obtained was recrystallized from acetonitrile and dried in vacuo to give 0.16 g (yield 72%) of the Cu(II) complex of **4**. Mp>300 °C; elemental analysis, Found: C, 61.66; H, 4.43; N, 11.79%. Calcd for $C_{23}H_{18}N_4O_2Cu$ M, 445.97: C, 61.94; H, 4.07; N, 12.56%. UV($CHCl_3$) λ_{max}=398 nm, ε=4100. IR (KBr) 1600 (C=O) cm^{-1}.

Transport of Metal Ions through Liquid Membranes. The transport experiments were carried out by using a U-type glass cell (Fig. 1)$^{10)}$ across a chloroform liquid membrane from the buffered aqueous source phase containing either a single heavy metal ion or plural ions of Cu(II), Ni(II), Co(II), and Zn(II) to the receiving phase containing 0.05 M (1 M=1 mol dm^{-3}) sulfuric acid. The buffered aqueous source phase was adjusted to pH 6.2. The cell was kept at 25±0.2 °C and each phase was mechanically agitated at 200 rpm.

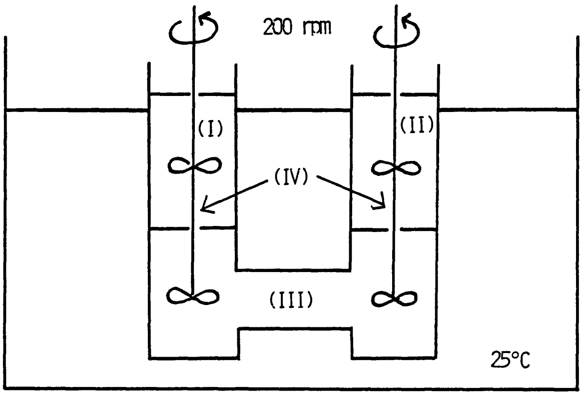
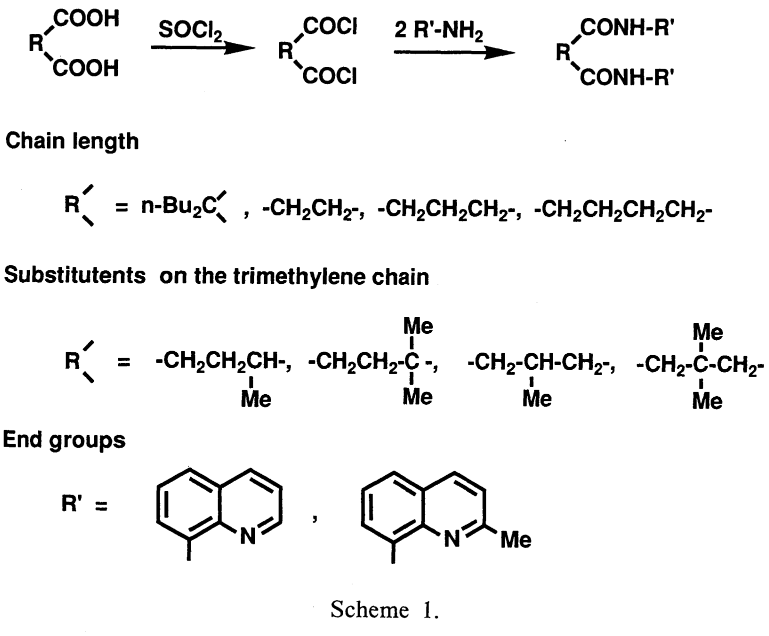


Fig. 1. Apparatus for measuring ion transport: (I) source phase. (II) chloroform membrane, (III) receiving phase, (IV) glass stirrer.

General Procedure of Solvent Extraction. 5 ml of an aqueous solution containing either 1 mM of each transition metal ion (Cu(II), Ni(II), Co(II), and Zn(II)) or 1 mM of a single transition metal ion (Cu(II), Ni(II), Co(II), or Zn(II)) and 5 ml of a chloroform solution containing 1 mM of diamide compound (or 2 mM of monoamide **1** and quinolinol **6**) was poured into a 20 ml sample tube with a crew cap. The aqueous solutions in the range from pH 6.2 to 1.4 were prepared by using both 1 M sodium acetate and 0.2 M acetic acid (or 1 M hydrochloric acid). The mixture was shaken vigorously for 24 h at 25 °C. The concentration of the remaining metal ions in the aqueous solution was determined by the atomic absorption spectroscopy. The concentration of the extracted metal ions was calculated from this value.

Results and Discussion

Synthesis of *N,N'*-Di(8-quinolyl)carboxamide Compounds. We have preliminarily reported that *N,N'*-di(8-quinolyl)glutaramide (**4**) can transport Cu(II) ion among transition metal ions selectively and efficiently through liquid membranes. In order to elucidate the relationship between the structure and the transport ability, homologues of **4** have been systematically prepared (Scheme 1). Compounds with different chain lengths binding the two amide groups, malonamide (**2**), succinamide (**3**), and adipamide (**5**), have been synthesized. The effect of the chain length upon the transport through liquid membranes and the extraction has been investigated by using these amide compounds. Monoamide **1** as a bidentate ligand was synthesized for comparison with the functions of these quadridentate



Scheme 1.

Table 1. Amount of Cu(II) Transport through Chloroform Phase after 2 Days[a)]

Carrier	Cu(II) transported to the receiving phase	Cu(II) remaining in the source phase	Cu(II) existing in chloroform[b)]
	% (mol)	% (mol)	% (mol)
1[c)]	0 (0)	100 (150)	0 (0)
2	0.2 (0.3)	94 (141)	5.8 (8.7)
3	29 (43.5)	63 (94.5)	8 (12)
4	63 (94.5)	35 (52.5)	2 (3)
5	6 (9)	93 (139.5)	1 (1.5)
6[c)]	34 (51)	0 (0)	66 (99)

a) Initial transport conditions (25°C): (source phase) 10 mM $Cu(OAc)_2$, pH 6.2, 15 ml/(liquid membrane) carrier (0.3 mmol for **2**—**5** or 0.6 mmol for **1** and **6**) in 30 ml of chloroform/(receiving phase) 0.05 M sulfuric acid, 15 ml. b) The values were calculated from Cu(II) amounts measured both in the receiving and source phase. c) Two equimolar amounts of **1** and **6** compared with the others were used because they are bidentate ligands.

ligands.

In order to investigate the substituent effect on the carbon chain of glutaramides, compounds **7**—**10** have been synthesized. Compound **11** has been prepared to investigate the substituent effect on the quinoline rings.

Transport of Transition Metal Ions through Liquid Membranes. Table 1 shows the results and conditions of Cu(II) transport after 2 d. Glutaramide derivative **4** apparently had the best Cu(II) transport ability among the carriers. The ability of Cu(II) transport decreased in the following order: **4**>**6**>**3**≫**5**>**2**≈**1**. The transport ability clearly depended on the structures of the diamides. It should be noticed here that **4** was superior to **6** in Cu(II) transport under the same conditions. Although malonamide **2** can extract Cu(II) with excellent selectivity as was recently reported,[11)] it has little ability to transport Cu(II) through liquid membranes because **2** forms stable 1 : 1 complex with Cu(II). Succinamide **3** seems to be a potent carrier, but it is soluble to some extent in the acidic receiving phase, and thus it is not appropriate as a carrier in the transport through liquid membranes.

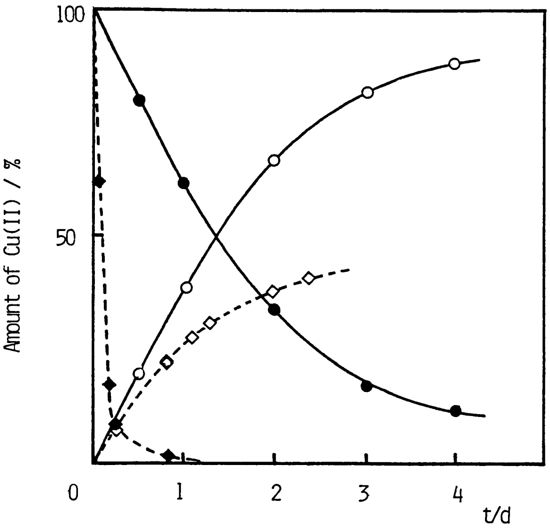


Fig. 2. Time dependence of Cu(II) transport through $CHCl_3$ membrane; transport conditions, see Table 1. **4**: —○— (Receiving phase) and —●— (Source phase), **6**: ---◇--- (Receiving phase) and ---◆--- (Source phase).

Figure 2 shows the time-dependence of the Cu(II) transport by amides **4** and **6**. Glutaramide derivative **4** can transport Cu(II) against its concentration gradient. The initial transport rate of **6** seemed comparable to that of **4**. However, the Cu(II) amount of transport by **4** increased almost linearly even after 2 d, whereas the rate of transport by **6** decreased with time. In addition, the decreasing rate of Cu(II) in the source phase by **6** was remarkably rapid compared with that by **4**. The curve of the decreasing amount with time by **4** in the source phase is symmetrical about the line corresponding to the increasing amount with time in the receiving phase, whereas the Cu(II) amount in the source phase decreases very rapidly by **6** and becomes nearly 0% after 1 d. Then, a large portion of Cu(II) exists in the chloroform phase where Cu(II) is slowly released to the receiving phase (see Table 1). This is supported by the observation that the color in chloroform containing **6** changes rapidly from colorless to yellowish brown and the color does not change during the transport experiment, while the color in chloroform containing **4** becomes only pale yellow even after two days. Furthermore, the single-ion transport of Ni(II), Co(II), and Zn(II) by **4** was attempted under the same conditions, but none of them could be transported at all. It should be noted in Fig. 2 that the amount of Cu(II) transported by **4** in the receiving phase after 1.5 d is apparently much more than that remaining in the source phase and yet continues to increase even after 1.5 d. This fact means that **4** can work as a highly selective and effective Cu(II) carrier for the uphill transport through liquid membranes.

In the competitive transport to Cu(II), Ni(II), Co(II), and Zn(II) by **4** and **6** from the source phase (pH 6.2) containing 10 mM of each metal ion, 0.3 mmol of glutaramide **4** in 30 ml of $CHCl_3$ transported only 54% of Cu(II) after 2 d under the same conditions described above, while 0.6 mmol of Kelex 100 (**6**) in 30 ml of $CHCl_3$ transported not only 20% of Cu(II), but also 34% of Zn(II), a small amount of Ni(II) (<1%), and a negligible amount of Co(II) (ca. 0%). Additionally, **4** transported only Cu(II) more than 90% after 2 d even from a solution

Table 2. Influence of Substituents of the Glutaramide Derivatives on the Cu(II)-Transport Ability[a]

Carrier	Cu(II) transported to the receiving phase	Cu(II) remaining in the source phase
	% (μmol)	% (μmol)
4	66 (9.9)	33 (5.0)
7	17 (2.6)	82 (12.3)
8	1 (0.15)	99 (14.9)
9	7 (1.1)	92 (13.8)
10	10 (1.5)	90 (13.5)
11	1 (0.15)	99 (14.9)

a) Initial transport conditions (25 °C): (Source phase) 1 mM $Cu(OAc)_2$, pH 6.2, 15 ml/(liquid membrane) 0.3 mmol of carrier in 30 ml of chloroform/(receiving phase) 0.05 M sulfuric acid, 15 ml.

Table 3. The Influence of the Acidity of the Receiving Phase on the Transport Ability of **4**[a]

Acidic condition in the receiving phase	Amount of Cu(II) after 2 days	
	Receiving phase	Source phase
	% (μmol)	% (μmol)
Lithium citrate buffered solution (pH 2.7)	27 (40.5)	72 (108)
0.025 M H_2SO_4 (pH 1.7)	36 (54)	61 (91.5)
0.05 M H_2SO_4 (pH 1.4)	63 (94.5)	35 (52.5)
0.1 M H_2SO_4 (pH 1.3)	64 (96)	36 (54)
0.5 M H_2SO_4 (pH 0.78)	20 (30)	76 (114)

a) Initial transport conditions (25 °C): (source phase) 10 mM $Cu(OAc)_2$, pH 6.2, 15 ml/(liquid membrane) 0.3 mmol of **4** in 30 ml of chloroform/(receiving phase) 15 ml of aqueous solution.

Table 4. Competitive Trabsport of Metal Ions by Glutaramide **4**

Initial concentration of metal ions in the source phase[a]	Amount of metal ions after 2 days			
	Receiving phase % (μmol)		Source phase % (μmol)	
	Cu(II)	Others	Cu(II)	Others
10 mM each Cu(II), Ni(II), Co(II), and Zn(II)	54 (81)	0 (0)	45 (67.5)	100 (150)
1 mM of Cu(II) and 10 mM each Ni(II), Co(II), and Zn(II)	94 (14.1)	0 (0)	5 (0.75)	100 (150)

a) Other transport conditions (25 °C): (Source phase) 15 ml buffered aqueous solution, pH 6.2/(chloroform membrane) 0.3 mmol of **4** in 30 ml of chloroform/(receiving phase) 0.05 M H_2SO_4, 15 ml.

containing a mixture of 1 mM Cu(II) and 10 mM Ni(II), Co(II), and Zn(II).

Effect of Substituents of Glutaramide Derivatives on the Ability of Transport. As described above, it has been found that glutaramide **4** was the best carrier among amides **1**—**5**. Next, the effect of substituents not only on the trimethylene group but also on the quinoline ring of glutaramides has been studied. The results of the Cu(II) transport by glutaramide derivatives **4, 7**—**11** are summarized in Table 2.

The transport ability of **7**—**11** drastically decreased compared with **4**. Apparently, the substituents on the trimethylene chain affect the Cu(II) transport ability. As a result, the substituents of the carriers are disadvantageous for Cu(II) transport. On the other hand, compound **11**, which has two 2-methyl-8-quinolyl groups, can hardly transport Cu(II) compared to **4**. It can be considered that the two methyl groups on the quinoline rings interfere with the formation of the stable Cu(II) complex. Inspecting the CPK model building, 2-methyl groups on the two quinoline rings interfere in the formation of a square-planar structure by four nitrogen atoms for the favorable conformation of the Cu(II) complex. In fact, the Cu(II) complex of **11** could not be obtained.

Influence of the Transport Conditions. It was found that glutaramide derivative **4** has an excellent transport ability of Cu(II) through liquid membranes which is comparable to that of commercially-available Kelex 100. We further investigated the transport ability under various conditions. In Table 3, the results of varying the acidity in the receiving phase are shown. When the acidity in the receiving phase became weaker than 0.05 M H_2SO_4, the Cu(II) amount transported after 2 d drastically decreased. On the other hand, when the receiving phase was adjusted to 0.5 M H_2SO_4, the transport rate again decreased drastically. In this case, since the acidity was too strong in the receiving phase, the carrier became soluble in the receiving phase. Thus, the amount of Cu(II) transported largely depended on the acidity in the receiving phase, and the optimum acidic condition for carrier **4**, was around 0.05 M to 0.1 M H_2SO_4.

To investigate the Cu(II) selectivity of glutaramide **4**, competitive transport experiments were performed by changing the amounts of the ions in the source phase. The results are shown in Table 4. It was observed that the amount of Cu(II) transported under the condition of 10 mM of each of four metal ions in the source phase was different from that in the single ion transport to result in a decrease of Cu(II) transported. Even when 1 mM of Cu(II) and 10 mM of each of the other metal ions (Ni(II), Co(II), and Zn(II)) existed in the source phase, carrier **4** transported only Cu(II). The other metal ions were not transported at all. As described above in the transport experiment of a single metal ion in the source phase, metal ions except Cu(II) could not be transported. Thus, **4** was shown to exhibit excellent selectivity and efficiency in the transport of Cu(II).

Relationship between the Transport Ability and the Extractability. In the ion transport through liquid membranes, it is well known that the following factors should be considered when evaluating transport ability: (1) uptake rate of ions at the boundary layer between the source phase and the organic phase, (2) solubility into the organic phase and diffusion rate of the complexes across it, and (3) release rate of ions from the organic phase to the receiving phase. In the transport system shown in Fig. 1, factor (2) does not seem serious because the Cu(II) complexes of these amides are soluble in $CHCl_3$ and each solution is stirred mechanically. Therefore, in order that ionophores for ion transport can work well, both factors (1) and (3) need to be satisfied. But, it is generally difficult for them to be consistent. This could be easily presumed because malonamide **2** exhibits good Cu(II) extractability, but not low ability of transport. Therefore, it is essentially important to control the balance between the thermodynamic stability of the complex and the ease of ion release from the complex.

In order to elucidate the reason why glutaramide **4** exhibits excellent Cu(II) transport, the ease of the complex formation and the pH dependence on the complexation have been investigated. Figure 3 shows the change of the UV spectrum of **4** dependent on the Cu(II) concentration. It is apparent that all of **4** could not completely change to the Cu(II) complex even in the presence of a three-fold Cu(II) concentration toward that of **4** under these experimental conditions. This means that the thermodynamic stability of the Cu(II) complex of **4** is apparently inferior to that of malonamide derivative **2** which can completely change to the Cu(II) complex then equimolar Cu(II) is present under the same conditions.[11] The absorption peak at around 400 nm is assigned to the Cu(II) complex of **4** because of the accordance with that of the isolated 1 : 1 Cu(II) complex which is deprotonated. The equilibrium between free amide **4** and the Cu(II) complex is kept as shown in Scheme 2 because these spectra have two isobestic points. A similar phenomenon has been confirmed in the case of the extraction of Cu(II) with **2**.[11]

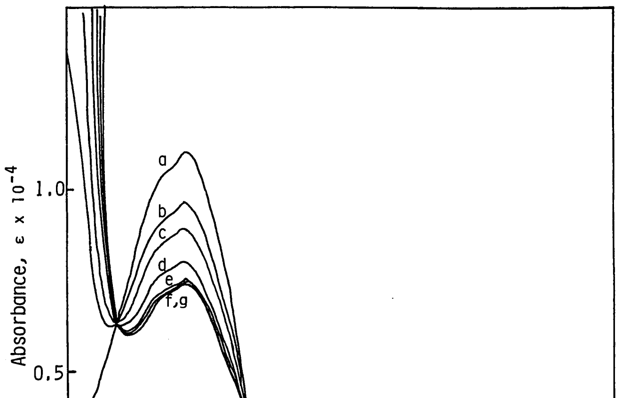
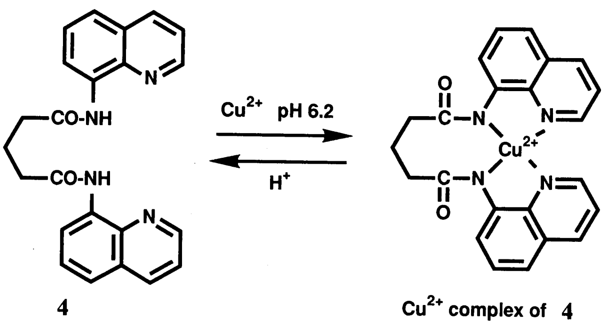


Fig. 3. Change in the absorption spectra of **4** ($=10^{-4}$ mol dm^{-3}) in $CHCl_3$ by complexation with Cu(II). a: **4**, b: Cu(II)/**4**=0.2, c: Cu(II)/**4**=0.3, d: Cu(II)/**4**=0.5, e: Cu(II)/**4**=0.67, f: Cu(II)/**4**=0.9, g: Cu(II)/**4**≥1.2. The values of Cu(II)/**4** indicate molar ratio of metal ion/ligand.



Scheme 2.

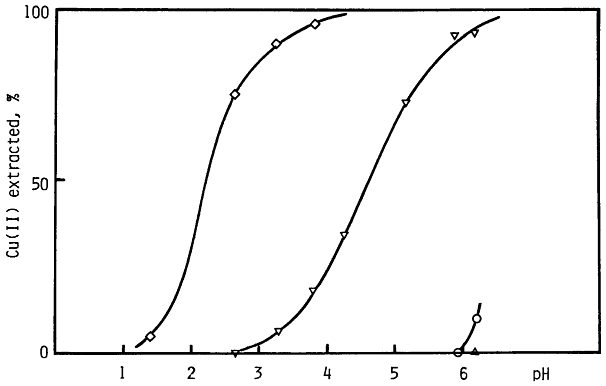


Fig. 4. pH-dependence of Cu(II) extraction with carriers. **2**: ▽, **4**: ○, **5**: △, **6**: ◇. Shaking time, 1 day, 25 °C.

The plots of the amount of Cu(II) after stirring for 1 day at 25 °C vs. pH are shown in Fig. 4. The order of the extractability among these carriers is: **6**>**2**>**4**>**5**. At pH 6.2, the Cu(II) extractability of **4** is relatively small, while **5** can hardly extract Cu(II) in the pH range studied. Surprisingly, in spite of the considerably small Cu(II)-extractability among these carriers, **4** can transport Cu(II) most efficiently as shown in Table 1. It is presumed that Cu(II) ions can be moderately removed into the organic layer from the nearly neutral aqueous layer and rapidly released at another boundary surface because of the relatively weak complexation of **4** with Cu(II). On the contrary, malonamide **2** has a considerable uptake rate of Cu(II), but the quadridentate Cu(II) complex of **2** is too stable to allow the release of Cu(II). In addition, it is also difficult for the 1 : 2 complex of Cu(II) with Kelex 100 (**6**) to release Cu(II) from the organic layer into the aqueous one, whereas **6** has a large Cu(II)-extractability at pH 6.2.[9] As a result, it could be interpreted that **4** exhibits almost the same ability of transport as Kelex 100 (**6**).

In conclusion, it was elucidated that glutaramide **4** can transport Cu(II) with high selectivity and efficiency through liquid membranes from the source phase in the range of nearly neutral pH to the acidic receiving phase, and the uphill transport of Cu(II) with **4** can be easily realized by keeping a pH difference between the source phase and the receiving phase. This compound could have potential use in Cu(II)-separation.

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