Extraction of Metal Picrates by Lipophilic Hexamide and Hexamine Derivatives of Azacrown [18]-N$_6$

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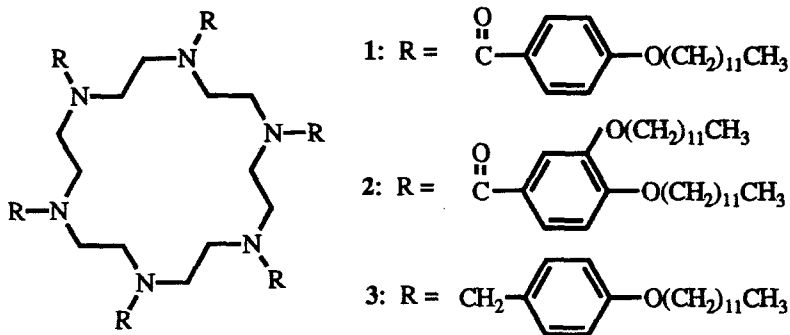
Abstract. To determine the metal ion complexing ability of high molecular weight macrocyclic polyamines and polyamides, lipophilic derivatives of azacrown [18]-N$_6$ (hexacyclen) were prepared. Transition and heavy metal picrates, but not alkali and alkaline earth picrates, were extracted from water into chloroform and transported from water through chloroform into a second water phase by the hexa-4-dodecyloxybenzoyl and hexa-3,4-bis-dodecyloxybenzoyl amide derivatives **1** and **2** and by the hexa-4-dodecyloxybenzyl amine derivative **3** of [18]-N$_6$ (hexacyclen). The relative amounts of picrates extracted by hexamine **3** from a pH 5 aqueous solution were $Cu^{2+} \sim Ag^+ \sim Pb^{2+} > Hg^{2+} > Zn^{2+} > Co^{2+} > Ni^{2+} \sim Cd^{2+}$. Using a pH 7 receiving phase, none of the metal ions were transported rapidly through chloroform, and only Co^{2+}, Cu^{2+}, and Pb^{2+}, were transported rapidly into a pH 11 aqueous phase. The hexamide **2**, but not hexamide **1**, extracted significant amounts of the picrates of Cu^{2+}, Ag^+, and Hg^{2+}, and transported Cu^{2+} and Ag^+ but not Hg^{2+}.

Key words: Azacrown, [18]-N$_6$, hexacyclen, extraction, transport, metal ion, picrate.

1. Introduction

The extraction of metal salts from water into organic solvents by crown ethers and related macrocycles was studied first by Pedersen [1]. Since then hundreds of macrocycle extractions of metal salts have been reported [2, 3]. In general oxygen macrocycles, such as crown ethers, are effective for extraction of alkali and alkaline earth metal salts but not transition metal salts, and their nitrogen analogues [4–16] are effective for transition metal salts, but not alkali metal salts. We have prepared azamacrocyclic [18]-N$_6$ derivatives **1–3** for study of their thermotropic liquid crystalline and metal ion complexation properties. Compounds **1** and **2** and related macrocyclic amides have discotic liquid crystal phases, due to a combination of flexibility of the long alkoxy chains and the rigidity of the benzamide groups attached to the central macrocycle [17–23]. Hexamine **3** is not liquid crystalline by itself, but forms liquid crystalline complexes with metal salts [24, 25]. In this paper we report extraction of a wide variety of metal picrates, and picrates of two amino acid esters, from water into chloroform solutions of azamacrocycles **1–3**, and transport of the picrates through chloroform solutions of the azamacrocycles.

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$$1: R = \overset{O}{\underset{\parallel}{C}} - \bigcirc - O(CH_2)_{11}CH_3$$

$$2: R = \overset{O}{\underset{\parallel}{C}} - \bigcirc \begin{array}{c} O(CH_2)_{11}CH_3 \\ O(CH_2)_{11}CH_3 \end{array}$$

$$3: R = CH_2 - \bigcirc - O(CH_2)_{11}CH_3$$

2. Experimental

Reagent grade metal salts and dibenzo-18-crown-6 ether (**DB18C6**) were obtained from Aldrich and used without further purification. Macrocycles **1** and **2** were prepared by acylation of [18]-N_6 [23], and **3** was prepared by LiAlH$_4$ reduction of **1** [19]. Glycine ethyl ester hydrochloride (GlyOEt·HCl) and L-phenylalanine ethyl ester hydrochloride (PheOEt·HCl) were from Sigma. An aqueous solution of picric acid (J.T. Baker Co.) was standardized with sodium hydroxide.

2.1. EXTRACTION

Distilled deionized water of resistivity 1.6×10^6 ohm cm was decarbonated by boiling and was saturated with chloroform, and the chloroform was saturated with water, in order to minimize the volume change on mixing. An aqueous solution containing 0.1 mM picric acid and 10.0 mM metal salt was adjusted from about pH 3.5 to pH 5.0 with a few drops of aqueous tetramethylammonium hydroxide (Aldrich). Five mL of a 1.0 mM chloroform solution of the macrocycle and 5 mL of the pH 5 picric acid solution were mixed with a Wrist-Action shaker for 20 min at $23 \pm 1^\circ$C, and the concentration of picrate ion in the aqueous phase was determined spectrophotometrically at 355 nm. The amount of picrate in the chloroform phase was calculated from the concentrations in the aqueous phase before and after extraction. No detectable picrate was transferred to the chloroform phase in the absence of macrocycles. The amount of picrate extracted from a pH 5 sodium picrate solution with hexamine **3** was measured in three independent experiments to be 24.5, 25.7, and 28.4%, and so we estimate the accuracy of the percent of picrate extracted to be ±3%. The other experiments were performed only once because of the small amounts of macrocycles available.
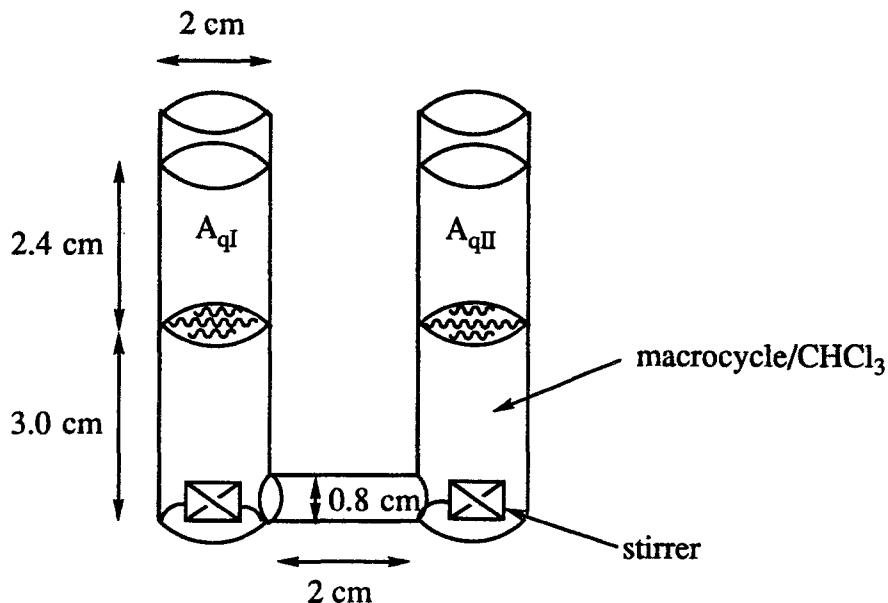
Fig. 1. Apparatus for transport experiments.

2.2. TRANSPORT

Transport of the picrates from a pH 5 aqueous solution (Aq$_I$, identical with that used in the extraction experiments) through chloroform containing 1.0 mM macrocycle and into a second aqueous phase (Aq$_{II}$), adjusted initially to pH 3, 7, or 11 with HCl or tetramethylammonium hydroxide was measured at 23 ± 2°C. A glass cell, illustrated in Figure 1 and designed after that of Tsukube [16], was filled with 12 mL of a chloroform solution of the macrocycle and 5 mL of the aqueous solutions Aq$_I$ and Aq$_{II}$ in the two vertical tubes. The chloroform phase was stirred at 500±50 rpm with two 9 mm star-shaped magnets (VWR Scientific Co., model 400 HPS) located directly under the vertical tubes. The average path length through chloroform was 8.5 cm. The interfacial areas of about 2 cm^2 were not affected by the stirring. After stirring for one hour the concentrations of picrate in the two aqueous phases were determined spectrophotometrically, and the amount of picrate in the chloroform phase was calculated by difference. In control experiments without macrocycle in the chloroform phase no K$^+$ or Cu^{2+} picrate ion pair was transported from Aq$_I$ to Aq$_{II}$. The change in pH of aqueous phases I and II after the transport process was ≤ 0.2 units. In three independent experiments using K$^+$ picrate and **DB18C6** we found 40.7, 37.2, and 39.3% of the picrate in Aq$_I$ and 45.0, 38.9, and 42.1% of the picrate in Aq$_{II}$. Thus the amounts of picrate extracted in the other experiments, which were performed only once because of the small amounts of macrocycles available, are estimated to be accurate to ±3%.

TABLE I. Extraction of picric acid into chloroform with hexamine 3^a

pH	4.2	5.0	6.0	7.0	8.0	9.0	10.0
% extracted^b	58	35	28	28	25	19	7

^{a} Conditions: 5 mL of 1.0 mM hexamine 3 in chloroform and 5 mL of 0.1 mM aqueous
picric acid; pH was adjusted with tetramethylammonium hydroxide before extraction.
^{b} Estimated errors are $\pm 3\%$ (see Section 2).

3. Results

3.1. EXTRACTION

The amount of picrate ion extracted was analyzed by the difference in UV spec-
trophotometric absorbances of the aqueous solutions before and after extraction
with a chloroform solution of the macrocycle. We used dibenzo-18-crown-6 ether
(DB-18-C-6) as a control macrocycle to test the method. DB-18-C-6 extracted
sizeable amounts of the picrates of only K^+ and the organic amino acid ester
cations, in agreement with previous reports [1, 2], and small amounts of Cu^{2+},
Ag^+, Hg^{2+}, and Pb^{2+} picrates. Hexamine 3 extracted picric acid into chloroform,
and the amount extracted decreased with increasing pH of the aqueous phase, as
shown in Table I. Less of the Li, Na, K, and Ca picrates than of picric acid were
extracted from a pH 5 aqueous phase, as shown in Table II. Hexamine 3 extracted
large amounts of all transition and heavy metal ions tested, as shown in Table II.

Hexamides 1 and 2 and DB18C6 extracted small amounts of picric acid from
a pH 5 aqueous solution into chloroform, as shown in Table II. Extraction of
chloroform solutions of the macrocycles 1-3 with equal volumes of water showed
no evidence of extraction of any macrocycle into water at pH 4 or pH 7. Using
the amount of picric acid extracted as a reference, the results of Table II show
extraction of amounts of picrate in excess of the amount extracted as picric acid
only with PheOEt cation by hexamide 1, and with Cu^{2+}, Hg^{2+}, Pb^{2+}, GlyOEt, and
the PheOEt cations by hexamide 2.

3.2. TRANSPORT

Transport of picrate ion from an aqueous phase (Aq_I) containing picric acid and
metal salts at pH 5 through a chloroform solution of macrocycle into a second
aqueous phase (Aq_{II}) were carried out with solutions stirred at a constant standard
speed in a U-tube, as shown in Figure 1. The results are reported in Table III as the
percentage distribution of picrate ion among the three phases. Except for the Co^{2+}
and perhaps the Hg^{2+} experiments, the amounts of metal picrates transported out
of Aq_I in one hour were less than the amounts extracted into chloroform during
20 min of vigorous shaking. Since the volumes of the phases, the concentrations
of the solutes, the type of stirring bar, and the stirring speed were all carefully

TABLE II. Extraction of picrate from pH 5 aqueous solution into chloroform by macrocycles[a]

Metal salt	Cation radius[b] Å	% extracted by[c]			DB18C6
		1	**2**	**3**	
none		6	9	35	5
LiCl	0.76	6	7	29	5
NaCl	1.02	7	4	26	6
KCl	1.38	4	6	21	29
CaCl$_2$	1.00	4	9	28	5
CoCl$_2$	0.75	9	6	68	8
NiCl$_2$	0.69	5	6	55	4
CuCl$_2$	0.77	8	17	99	12
ZnCl$_2$	0.74	4	6	77	5
AgNO$_3$	1.15	9	11	99	10
CdCl$_2$	0.95	5	4	56	5
HgCl$_2$	1.19	10	18	88	12
Pb(OAc)$_2$	1.19	9	10	99	11
GlyOEt		6	16	97	28
PheOEt		69	67	99	76

[a] Conditions: 5.0 mL of 1.0 mM macrocycle in chloroform and 5.0 mL of 0.1 mM picric acid and 10 mM metal salt in water adjusted to pH 5.0 with tetramethylammonium hydroxide at 25 ± 2°C.
[b] Ref. 2b.
[c] Estimated errors are ±3% (see Section 2).

controlled, the relative rates of transport of the metal picrates are reliable, but the absolute rates depend on the U-tube design and the efficiency of stirring.

4. Discussion

The results in Tables I–III point to several important conclusions.

(1) Picrate is extracted from a pH 5 aqueous solution into chloroform containing macrocycle **3** as H$^+$ (picrate)$^-$. In water at pH 5 the hexaethyl hexamine analogous to **3** is present mainly as the (+3)-cation [13]. The stronger binding of H$^+$ than of alkali metal ions to **3** leads to more picrate extraction from a metal-free aqueous solution than from one containing Li, Na, K, or Ca ions, as shown in Table II.

(2) When transition and heavy metal ions assist the extraction of picrate into chloroform, there is no correlation between the percent extracted and the ionic radius. The small Cu^{2+} and large Pb^{2+} are 99% extracted by **3**, whereas the small Co^{2+}, Ni^{2+}, and Zn^{2+} are not.

The relative amounts of metal picrates extracted by hexamine **3** (Cu$^{2+} \sim$ Ag$^+$ $\sim$ Pb$^{2+} >$ Hg$^{2+} >$ Zn$^{2+} >$ Co$^{2+} >$ Ni$^{2+} \sim$ Cd^{2+}), differ from those reported by Izatt and coworkers [13] for the hexaethyl [18]-N$_6$ in organic solution (Hg$^{2+} >$ Ni$^{2+} >$ Zn$^{2+} \sim$ Cd$^{2+} >$ Pb$^{2+} >$ Ag$^+$), and for a silica-bound pentaethyl [18]-

TABLE III. Transport of metal picrates through a chloroform membrane containing macrocycle[a]

| Macrocycle | Metal salt | pH of Aq_{II} | -----------% of picrate[b] in----------- | | |
			Aq_I	Aq_{II}	Chloroform
1	$CuCl_2$	7	94	2.4	4
1	$CuCl_2$	11	94	2.8	3
1	$AgNO_3$	11	77	7	17
2	$CuCl_2$	7	88	2.6	10
2	$CuCl_2$	11	80	9	11
2	$NiCl_2$	7	94	2.1	4
2	$AgNO_3$	7	86	6	8
2	$AgNO_3$	11	64	18	18
2	$HgCl_2$	7	86	4	10
3	KCl	7	90	1.4	9
3	$CoCl_2$	3	12	0.7	87
3	$CoCl_2$	7	33	0.9	66
3	$CoCl_2$	11	30	9	61
3	$CuCl_2$	7	16	0.3	84
3	$CuCl_2$	11	45	30	26
3	$NiCl_2$	7	63	1.6	36
3	$NiCl_2$	11	90	2.5	8
3	$ZnCl_2$	11	86	4	10
3	$AgNO_3$	11	69	0.4	31
3	$HgCl_2$	3	8	0.1	92
3	$HgCl_2$	7	13	1.7	85
3	$HgCl_2$	11	12	0.3	88
3	$Pb(OAc)_2$	7	22	0.2	78
3	$Pb(OAc)_2$	11	64	16	20
3	GlyOEt	7	21	0.1	79
3	GlyOEt	11	46	27	27
DB18C6	KCl	7	39	42	19
DB18C6	$CuCl_2$	7	92	0.8	7
DB18C6	$CuCl_2$	11	90	5	6
DB18C6	$NiCl_2$	7	96	1.4	3
DB18C6	$HgCl_2$	7	90	2.6	7
DB18C6	GlyOEt	11	48	24	29

[a] Conditions: 5.0 mL of aqueous phase I containing 10 mM metal salt and 0.10 mM picric acid adjusted to pH 5 with tetramethylammonium hydroxide, 5.0 mL of aqueous phase II with pH adjusted by HCl or tetramethylammonium hydroxide, 12.0 mL of chloroform containing 1.0 mM macrocycle.

[b] Distribution of picrate after 1.0 h at $23 \pm 2°C$. Estimated errors are $\pm 3\%$ (see Section 2).

N_6 (Hg^{2+} > Cu^{2+} > Pb^{2+} > Cd^{2+} > Ni^{2+} ~ Zn^{2+} ~ Ag^+). The selectivity differences between **3** and its lower molecular weight analogues may be due to different conformations of the central 18-membered ring.

(3) The extraction of Cu^{2+} and Hg^{2+} picrates into chloroform by hexamide **2** is the first example of which we are aware of a macrocyclic polyamide extracting metal cations from an aqueous solution. Since hexamide **2** is more effective than hexamide **1** for extraction of Cu^{2+} and Hg^{2+}, and the structural difference between **1** and **2** is the second alkoxy group on each aromatic ring of **2**, complexation by **2** may be due to the pairs of ether oxygen atoms on the benzene rings. The extraction of protonated amino acid ester picrates by **1** and **2** is similar to the extraction of the analogous perchlorates by macrocyclic amides reported by Tsukube [12].

(4) Lesser fractions of picrate in the chloroform phase in the transport experiments than in the extraction experiments of Table II indicate that the transport is kinetically controlled. The transport data in Table III show both transfer from the original aqueous phase Aq_I to the chloroform phase, and transfer from chloroform into the receiving phase Aq_{II}. Transport into Aq_{II} requires favorable transfer rates at both water-chloroform interfaces. An extraction equilibrium that favors metal picrate in the organic phase slows the rate of transfer into the aqueous receiving phase, as discussed earlier for crown ethers and cryptands [2, 3, 26]. We observe greater extraction and faster transport of Cu^{2+} than of Hg^{2+} by **3**. In contrast, hexabenzyl [18]-N_6 was found before to transport Cu^{2+} faster than Hg^{2+} but extract more Hg^{2+} than Cu^{2+} [27]. Further evidence of kinetic control is that greater amounts of Cu^{2+} to pH 7 Aq_{II} and of Ag^+ to pH 11 Aq_{II} were transported by hexamide **2** than by hexamine **3**. Kinetic control of rates of transport of metal salts from water through chloroform to water using different complexing agents has been reported before [2, 3, 16, 26, 29]. Presumably the macrocycle lies at the water-chloroform interface during metal ion transfer, as illustrated in Figure 2, and the Co^{2+}, Cu^{2+}, and Pb^{2+} picrates pass through the interface faster than the other metal ions.

(5) Our transport experiments differ from most others by having a neutral or basic, rather than an acidic receiving phase. With acidic Aq_{II} transport of metal ions is driven from Aq_I to Aq_{II} by the counter transport of H^+. Since our experiments show little picrate either in the chloroform phase with hexamine **3** or in Aq_{II}, transport of $H^+(\text{picrate})^-$ is kinetically controlled at the Aq_I-chloroform interface.

The faster rates of transport of metal picrates into pH 11 Aq_{II} is probably driven by the formation of metal hydroxides in Aq_{II}. We observed precipitates at the interface of pH 11 Aq_{II} and chloroform in the Ag^+ and Hg^{2+} experiments, but not in the other experiments, although solubility product constants [28] suggest that insoluble metal hydroxides should have been formed at pH 11 with all of the transition and heavy metal ions investigated. There may have been small amounts of colloidal metal hydroxides in the pH 11 Aq_{II} phases that we did not detect by visual observation.
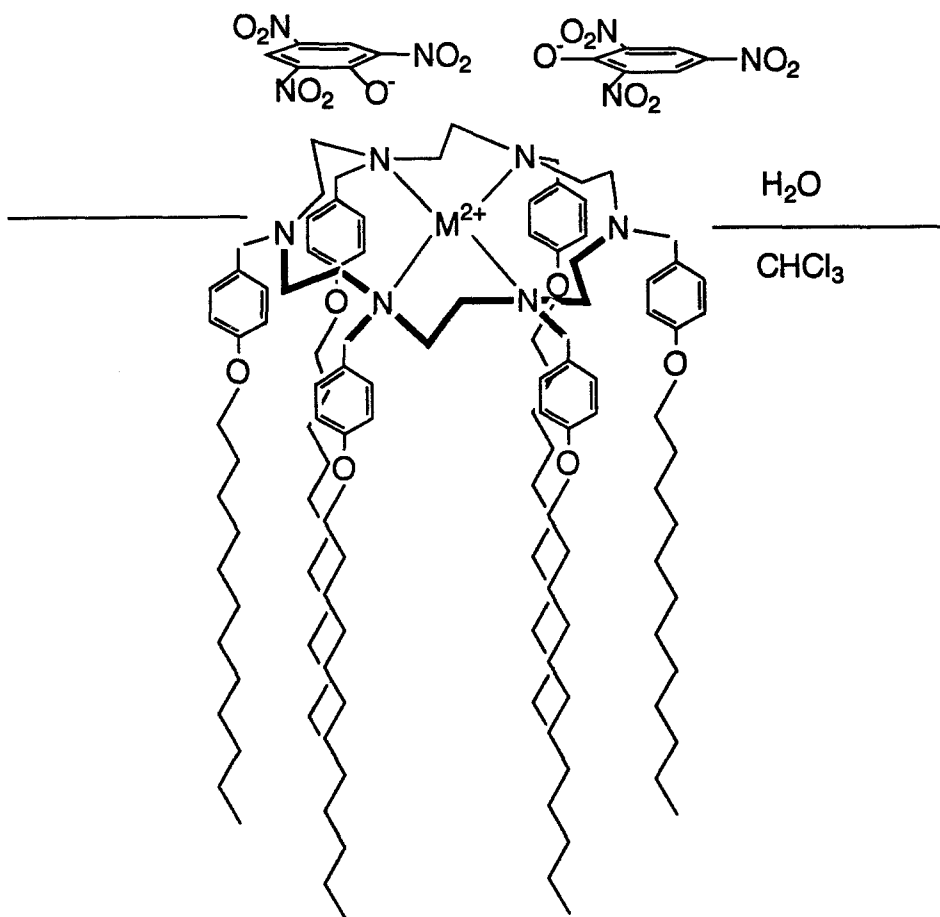
Fig. 2.   Model of a lipophilic macrocycle (3)-metal ion complex at a water-chloroform interface.

In contrast to the results in Table III, the order of picrate transport rates using the hexabenzyl analogue of 3 lacking the dodecyloxy chains and metal acetates is $Zn^{2+} > Ni^{2+} > Cu^{2+} > Co^{2+}$ [16]. The selectivity of 3 for transport of Co^{2+}, Cu^{2+}, and Pb^{2+} picrates must be due to faster transfer across the water-chloroform interfaces.

5. Conclusions

The relative amounts of metal picrates extracted from water into chloroform and transported through chloroform by hexamine 3 differ from those extracted and transported by less lipophilic derivatives of [18]-N_6. The lipophilic hexamide 2 is the first amide shown to extract and transport any metal picrates from water.

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References

1. C.J. Pedersen: *J. Am. Chem. Soc.* **89**, 7017 (1967).
2. B.G. Cox and H. Schneider: *Coordination and Transport Properties of Macrocyclic Compounds in Solution*, Elsevier, 1992.
3. R.M. Izatt, J.S. Bradshaw, S.A. Nielsen, J.D. Lamb, and J.J. Christensen: *Chem. Rev.* **85**, 271 (1985).
4. M. Kodama, E. Kimura, and S. Yamaguchi: *J. Chem. Soc. Dalton Trans.* 2536 (1980).
5. A. Bencini, A. Bianchi, M. Micheloni, P. Paoletti, E. Garcia-Espana, and M.A. Nino: *J. Chem. Soc. Dalton Trans.* 1171 (1991).
6. L.Y. Martin, C.R. Sperati, and D.H. Busch: *J. Am. Chem. Soc.* **99**, 2968 (1977).
7. R. Nagai and M. Kodama: *Inorg. Chem.* **23**, 4184 (1984).
8. M. Kato and T. Ito: *Inorg. Chem.* **24**, 504 (1985).
9. M. Kato and T. Ito: *Inorg. Chem.* **24**, 509 (1985).
10. H. Tsukube: *J. Chem. Soc., Chem. Commun.* 970 (1983).
11. H. Tsukube, K. Takagi, T. Higashiyama, T. Iwachido, and N. Hayama: *J. Chem. Soc. Perkin Trans.* 2 1541 (1985).
12. H. Tsukube: *J. Coord. Chem.* **16**, 101 (1987).
13. R.M. Izatt, R.L. Bruening, B.J. Tarbet, L.D. Griffin, M.L. Bruening, K.E. Krakowiak, and J.S. Bradshaw: *Pure Appl. Chem.* **62**, 1115 (1990).
14. D. Cordier and M.W. Hosseini: *New J. Chem.* **14**, 611 (1990).
15. H. Tsukube: *J. Chem. Soc. Perkin Trans. 1* 615 (1985).
16. H. Tsukube, Y. Kubo, T. Toda, and T. Araki: *J. Polym. Sci.: Polym. Lett. Ed.* **23**, 517 (1985).
17. J.-M. Lehn, J. Malthete, and A.-M. Levelut: *J. Chem. Soc. Chem. Commun.* 794 (1985).
18. C. Mertesdorf and H. Ringsdorf: *Liq. Cryst.* **5**, 1757 (1989).
19. S.H.J. Idziak, N.C. Maliszewskyj, P.A. Heiney, J.P. McCauley, Jr., P.A. Sprengeler, and A.B. Smith, III: *J. Am. Chem. Soc.* **113**, 7666 (1991).
20. S.H.J. Idziak, N.C. Maliszewskyj, G.B.M. Vaughan, P.A. Heiney, C. Mertesdorf, H. Ringsdorf, J.P. McCauley, Jr., and A.B. Smith: *J. Chem. Soc., Chem. Commun.* 98 (1992).
21. G. Lattermann: *Mol. Cryst. Liq. Cryst.* **182B**, 299 (1990).
22. J. Malthete, A.-M. Levelut, and J.-M. Lehn: *J. Chem. Soc., Chem. Commun.* 1434 (1992).
23. M. Zhao, W.T. Ford, S.H.J. Idziak, N.C. Maliszewskyj, and P.A. Heiney: *Liq. Cryst.* (in press).
24. A. Liebmann, C. Mertesdorf, T. Plesnivy, H. Ringsdorf, and J.H. Wendorff: *Angew. Chem. Int. Ed. Engl.* **30**, 1375 (1991).
25. M. Zhao: Ph.D. Dissertation, Oklahoma State University, 1993.
26. J.D. Lamb, J.J. Christensen, J.L. Oscarson, B.L. Nielsen, B.W. Asay, and R.M. Izatt: *J. Am. Chem. Soc.* **102**, 6820 (1980).
27. K. Maruyama, H. Tsukube, and T. Araki: *J. Am. Chem. Soc.* **102**, 3246 (1980).
28. T.R. Hogness and W.C. Johnson: *Qualitative Analysis and Chemical Equilibrium*, 4th ed., Henry Holt and Co., 1954, pp. 563–564.
29. F.M. Menger and J.-J. Lee: *J. Org. Chem.* **58**, 1909 (1993).