Photochemical Synthesis of Diazacryptophane

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Azacryptophane was obtained by irradiation of the precursor diammonium chloride in the presence of γ-CD (γ-cycodextrin) in aqueous solution. In the liquid-liquid extraction, the azacryptophane showed a moderate affinity toward all alkali metal picrates without any significant selectivity, whereas it selectively extracted both Ag^+ and Pb^{2+} cations in a series of heavy metal nitrates.

Some methodologies have been developed to improve the complexing ability of crown ethers including stability constant and substrate selectivity. Adding a side arm is known good to increase stability constants toward alkali metal cations such as Na^+ and K^+ ions. Remarkable improvement of the stability constants was achieved by azacrown ether derivatives[1] and Okahara's C-pivot lariat ethers.[2] BiBLEs[3] or double armed crown compounds[4] also show unique complexing abilities by intramolecular cooperation of ligating side chains in equilibrium, extraction, and transport systems. Cryptands, three dimensional diazacrown ethers first prepared by Lehn, show extraordinarily high stability constants for various kind of cations, compared with those of the parent diazacrown ethers.[5] The cryptands, however, are not so easily prepared, since the synthetic route requires many steps including the high dilution method with the simultaneous addition of the coupling reagents.[6]

We have prepared prototypical crownophanes conveniently and efficiently by means of the intramolecular [2 + 2] photocycloaddition of styrene derivatives having oligo(oxyethylene) linkage.[7] Their sulfur analogs (thiacrownophanes) have also been prepared by the method and found to exhibit a high affinity to Ag^+ cation.[8]

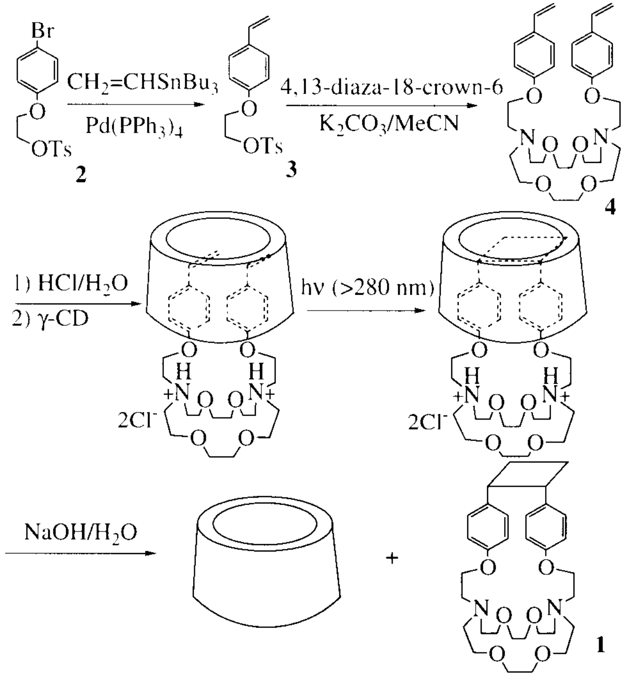
Recently we tried to prepare three dimensional diazacrown compounds (azacryptophanes) by the efficient photocycloaddition mentioned above, because the nitrogen-containing crownophanes are expected to show some interest complexing ability due to the unique crownophane skeleton.[7]

Although the irradiation of N,N-dimethylaminostyrene afforded cyclodimerized products,[9] crownophanes possessing amino groups in polyether linkages were not thought to be prepared by simply applying this method, since aliphatic tertiary amines, such as triethyl amine and tributyl amine, are known to act as a quencher for the S_1 state of styrene due to the formation of exciplex.[10]

In this communication, we would like to describe the synthesis of a crownophane possessing two amino groups in its polyether linkage under some modified conditions, and its complexing ability toward alkali and heavy metal cations.

Thus, diazacryptophane **1** was prepared according to Scheme 1. Compound **2** was obtained from hydroxyethylation of *p*-bromophenol by 2-chloroethanol in a basic aqueous solution, followed by tosylation. Using Stille reaction,[11] it was converted to vinyl derivative **3**. The reaction of **3** with diaza-18-crown-6 was accomplished in MeCN in the presence of K_2CO_3 at refluxing temperature for 7 h and gave **4** in 55% yield. We irradiated compound **4** in MeCN by a 400-W high pressure mercury lamp through Pyrex filter for 1.5 h, but we failed to obtain the desired product at all. This was because **4** acted as a quencher as mentioned above. Therefore, we tried to separate the quencher moiety from the styrene moieties by using γ-CD which has the space to be able to incorporate two naphthalene moieties in an aqueous solution.[12] Thus, the aqueous olefin solution was acidified to pH 3 by the addition of conc. HCl, and then irradiated in the presence of γ-CD (30 equiv.) in the same manner as mentioned above. Diazacryptophane **1** was obtained in 21% yield after neutralization, extraction with CH_2Cl_2, and then chromatographic separation over silica gel by using toluene-ethyl acetate as an eluent, whereas neither a control experiment without γ-CD nor that with β-CD afforded cryptophane **1**.

Scheme 1. Preparation of diazacryptophane.



The successful photoreaction can be explained as follows: As a results of incorporation of the vinylphenyl moieties into γ-CD cavity due to their lipophilicity, the reaction sites are well separated from quenching parts which are forced to be out of the CD cavity, and become closely adjacent at the same time. The explanation is also consistent with a recent report by Wenz, which showed that γ-CD efficiently worked as a reaction vessel for a stilbene derivative to afford its dimers in an aqueous solution.[13] Analytical data of new materials prepared are given.[14]

Azacryptophane was used as an extractant for alkali metal picrates in a liquid-liquid system together with reference compounds. A CH_2Cl_2 solution of the host compound (1×10^{-4} mol dm^{-3}, 5 ml) and an aqueous metal picrate solution

([MOH]=0.1 mol dm^{-3}, [picric acid]=1 x 10^{-5} mol dm^{-3}, 5 ml) were shaken in a 20-ml test tube equipped with a ground glass stopper at room temperature (20-22 °C) for 2 h. After two liquid phase were separated, percent extraction of metal picrates was measured by UV-Vis spectroscopy. Results are summarized in Table 1. Unsubstituted diaza-18-crown-6 ether (**5**) hardly extracted any cations in this system. Diazacryptophane **1** showed higher extractability toward all the cations except Li^+ ion without selectivity than conventional dibenzo-18-crown-6 **6**. Thus, the extractability was improved by the attachment of cyclophane bridge. The extractability, however, was still lower than that of cryptand[2.2.2] **7**, which showed high affinity to all the cations.

Table 1. Extraction of alkali metal picrates by ligand

Ligand	Extractability (%)^a				
	Li^+	Na^+	K^+	Rb^+	Cs^+
1	7	32	34	32	31
5	0	0	6	3	2
6	0	1	24	15	7
7	57	87	88	89	84

a) Extraction conditions: Aq. phase (5 ml), [metal hydroxide]= 0.1 mol dm^{-3}, [picric acid]=1.0 x 10^{-4} mol dm^{-3}; Org. phase, CH_2Cl_2, [ligand]=1.0 x 10^{-4} mol dm^{-3}; ca. 20 °C, shaken for 1 h. The values were based on the concentration of the crown compounds.

Extraction of heavy metal cations was also carried out in another liquid-liquid system. A CH_2Cl_2 solution of the host compound (1 x 10^{-4} mol dm^{-3}, 5 ml) and an aqueous metal nitrate solution (0.1 mol dm^{-3}, 5 ml), whose pH value was adjusted as high as possible not to precipitate the hydroxides, were shaken in a 20-ml test tube equipped with a ground glass stopper at room temperature (20-22 °C) for 2 h. After two liquid phases were separated, an aliquot (2 ml) of the organic phase was evaporated, and then aqueous HNO_3 solution (0.1 mol dm^{-3}, 2 ml) was added to the residue. The extracted cation in the acidic aqueous solution was analyzed by atomic absorption spectroscopy. Results are summarized in Table 2. As well known, crown ethers having amino moieties in the ring showed high affinity to Ag^+ and Pb^{2+} cations.[15, 16] Cryptophane **1** efficiently extracted both Ag^+ and Pb^{2+}, while cryptand[2.2.2] **7** showed higher affinity to Ag^+ cation than Pb^{2+} cation. Since ionic radii of the both cations are similar, the phenomenon cannot be explained by only the size-fitness argument between the cation and host. Other stereochemical factors besides the size can be responsible for the strength of complexing ability.[15] A macrocyclic compound-Ag^+ complex, however, is generally more lipophilic than a corresponding Pb^{2+}-complex, because the former complex is accompanied by only one hydrophilic counter anion, in contrast to two for the latter. Consequently, the distribution coefficient of the former to organic phase is larger than that of the latter. When the lipophilicity of host compound is high enough, there is no great difference of the distribution coefficient between the two complexes, resulting in similar percent extractions. In fact, in this case, the lipophilicity of **1** is considerably high in comparison with **7**.

In order to make the complex structures more clear, we examined the interaction between **1** and Ag^+ and Pb^{2+} cations in CD3CN by ^{13}C NMR titration method. The chemical shift of its aromatic carbon significantly changed with increasing the amount of $AgClO_4$ or $PbClO_4$ added to the host solution, until host/guest molar ratio became unity. It strongly suggests the 1:1 complexation.

Table 2. Extraction of heavy metal cations with ligands

Ligand	Extractability (%)^a						
	Ag^+	Pb^{2+}	Cu^{2+}	Mn^{2+}	Zn^{2+}	Ni^{2+}	Co^{2+}
1	42(6.3)	45(4.6)	0(4.2)	0(6.0)	0(6.1)	0(4.2)	0(6.2)
5	3(4.9)	0(4.5)	0(4.1)	0(6.4)	0(5.6)	0(4.5)	0(6.6)
7	47(6.0)	13(4.8)	0(4.4)	0(6.8)	2(6.1)	0(6.2)	0(6.7)

a) Extraction conditions: Aq. phase (5 ml), [metal nitrate]=1.0 x 10^{-1} mol dm^{-3}; Org. phase, CH_2Cl_2, [ligand]=1.0 x 10^{-4} mol dm^{-3}; ca. 20 °C, shaken for 1 h. The values were based on the concentration of the crown compounds. Values in parentheses were equilibrium pH of aqueous phase.

In conclusion, the [2 + 2] photocycloaddition was extended to the preparation of crownophane possessing aliphatic animo groups by using γ-CD in aqueous solution.

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14 All new compounds were colorless viscous liquids and gave satisfactory microanalytical data. ^{1}H NMR spectroscopic data ($CDCl_3$, 500 MH_Z): **1**: 6.74 (4H, Abq, J= 9.1), 6.61 (4H, ABq, J=9.1), 4.09 (4H, m), 3.90 (2H, m), 3.67 (8H, m), 3.62 (8H, m), 3.60 (4H, m), 3.48 (4H, m), 3.00 (4H, m), 2.39 (4H, m). **4**; 7.33 (4H, ABq, J=8.9), 6.86 (4H, Abq, J=8.9), 6.65 (2H, dd, J=17.0 & 12.0), 5.62 (2H, d, J=17.0), 5.15 (2H, d, J=12.0), 4.09 (4H, m), 3.62 (20H, m), 2.94 (8H, m).

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