

Mercuriphilic 1-(8,8-Dicyanoheptafulven-3-yl)aza-15-crown-5 Ether. Synthesis, X-Ray Structural Analysis, and Fixation of Its Derivative on a Polymer

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Mercurophilic 1-(8,8-Dicyanoheptafulven-3-yl)aza-15-crown-5 Ether. Synthesis, X-Ray Structural Analysis, and Fixation of Its Derivative on a Polymer

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Mercurophilic 1-(8,8-dicyanoheptafulven-3-yl)aza-15-crown-5 ether and its homologs were synthesized by substitution of 3-bromo-8,8-dicyanoheptafulvene with 1-azacrown ethers. By the condensation with malononitrile these heptafulvene derivatives yielded 1-(2-amino-1,3-dicyanoazulen-5-yl)azacrown ethers. The Merrifield Resin carrying 1-(2-amino-1,3-dicyanoazulenyl)azacrown unit irreversibly formed a complex with mercury (II) ion. The X-ray crystallographic analysis with aza-15-crown-5 derivative revealed a head-to-tail association of two nearly parallel heptafulvene rings; the bond lengths of the atoms in the conjugated system indicated a highly polar electronic structure.

During our current studies on the tropone- and heptafulvene-incorporated dithiocrown derivatives,¹⁾ we have shown that effective mercurophilic compounds should have five ethereal heteroatoms for coordination.²⁾ In order to keep reversibility of complexation-liberation processes, cation-forming seven-membered conjugated segments are essential, and therefore, 1-aza-crown derivatives with a substituent of seven-membered conjugated systems might be good functional compounds for this aim.³⁾

Herein described is a facile synthesis of such 8,8-dicyanoheptafulvene derivatives (**1a** and **1b**), from easily available 3-bromo-8,8-dicyanoheptafulvene (**2**).⁴⁾

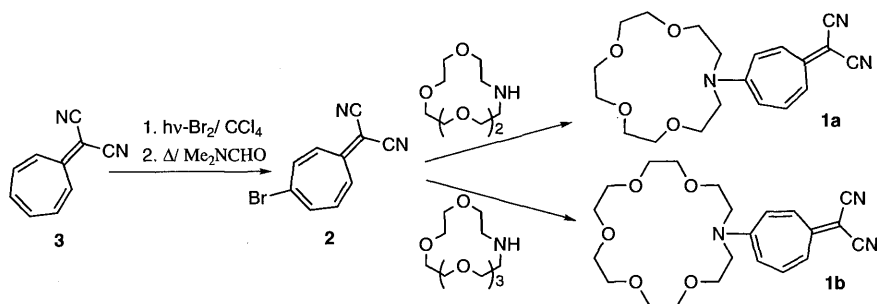
Results and Discussion

Synthesis of Aza-crown Derivatives. Required 3-bromo-8,8-dicyanoheptafulvene (**2**) was obtained by bromination and dehydrobromination of 8,8-dicyanoheptafulvene (**3**).⁴⁾ Thermal reaction of **2** with 1-aza-15-crown-5 ether (Az-5) in benzene and pyridine (1:1 in volume) for 2 h gave 3-(1-aza-15-crown-5)-8,8-dicyanoheptafulvene (**1a**). The ¹H NMR spectrum of **1a** indicated a considerable isolated double bond character for C(1)=C(2) bond; *vic*-coupling constants, $J_{1,2}$, $J_{5,6}$ and $J_{6,7}$, were 13.2, 10.3, and 10.9 Hz, respectively, showing an averaged magnitude of coupling constants for $J_{5,6}$ and $J_{6,7}$. Thus, mesomeric effects of dimethylamino and dicyano groups are significant. An extremely high-field shifted ¹³C NMR signal of C-8, $\delta = 58.4$, was parallel to this view.⁵⁾

Similar treatment of **2** with 1-aza-18-crown-6 ether (Az-6) gave 3-(1-aza-18-crown-6)-8,8-dicyanoheptafulvene (**1b**).

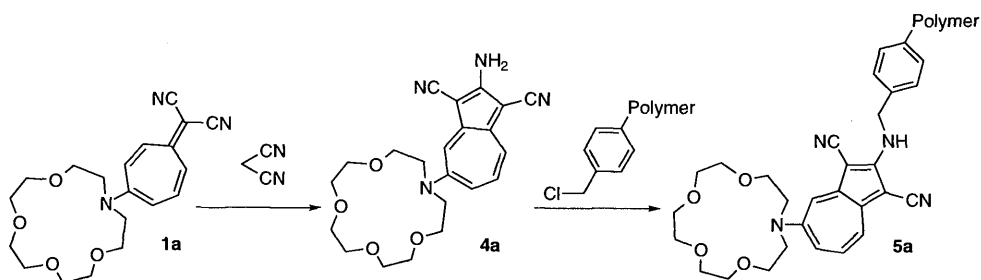
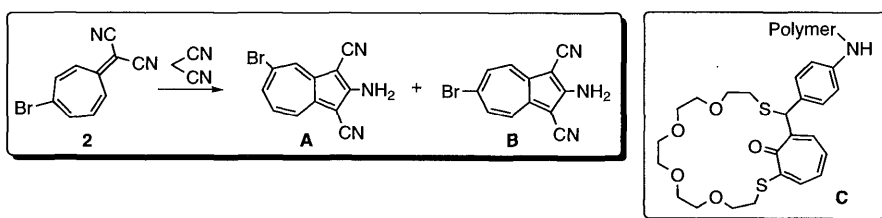
It would be interesting to convert these heptafulvene derivatives into azulene derivatives.⁶⁾ Previously, Oda *et al.* have examined the conversion of **2** to observe concom-

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Scheme 1

itant formation of isomers, 2-amino-5-bromo-1,3-dicyanoazulene and 2-amino-6-bromo-1,3-dicyanoazulene (**A** and **B**).⁴⁾ Should the mesomeric effect of aza-crown substituents be significant, these derivatives should furnish the single azulene derivatives in each case. This was the case when **1a** and malononitrile were condensed with base. The sole product identified was 2-amino-1,3-dicyano-5-(dimethylamino)azulene (**4a**).



Scheme 2

X-Ray Structural Analysis. The single crystal of **1a** was obtained by crystallization from CH_3CN , as a red prism, mp $134\text{--}135.5^\circ\text{C}$ (in a sealed tube), $\text{C}_{20}\text{H}_{25}\text{O}_4\text{N}_3$ ($M=371.44$), which was monoclinic with the space group $P2_1/a$; the cell dimensions were $a=14.330(1)$, $b=16.390(3)$, $c=8.484(1)\text{ \AA}$, $\beta=97.40(1)^\circ$, and $V=1966.1(4)\text{ \AA}^3$, with $Z=4$ and $D_x=1.25\text{ g cm}^{-3}$.

The structure was solved by direct method (SIR88)⁷⁾ and difference Fourier syntheses. Using the 2564 reflections having intensities greater than 3.0 times their standard deviation, for 311 variable parameters, the structure was refined in full-matrix least squares. At the

final stage, it showed $R=0.060$ and $wR=0.086$.

At first, **1a** revealed some noticeable features; the heptafulvene ring was nearly planar and any bisected angles of any two planes constructed by any three or four atoms in the conjugated ring system were smaller than 6° . An ethereal oxygen atom, O-3, is disordered with its counterpart, O-3' in the ratio of 7:3. The relatively large thermal factors of C-15 and C-16 are probably due to this disordered nature of this oxygen atom. Highly polarized

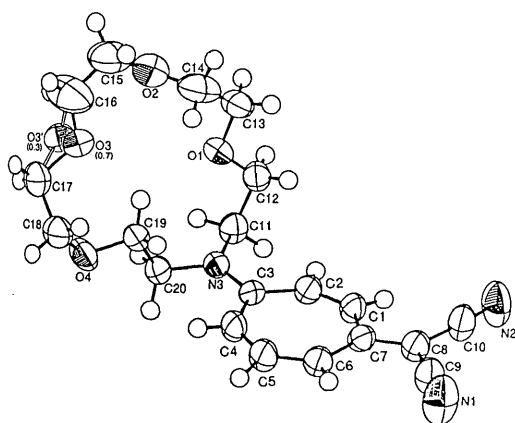


Fig. 1 The ORTEP drawing of molecular structure of **1a**.

nature of **1a** was reflected on the bond length of C-N of the azacrown group; the observed value, 1.356 \AA is between the typical values of C=N (1.287 \AA) and C-N (1.512 \AA). Being consistent with this, the bond lengths of CN groups were 1.145 and 1.137 \AA , which are considerably longer than the typical values for cyano groups. Interestingly, the bond alternation of the seven-membered system of **1a** was disturbed by the electromeric effect of the azacrown nitrogen atom; the bond lengths of C-1-C-7 and C-7-C-6 were 1.435 and 1.403 \AA , respectively, and the difference, $\Delta d_a = 0.032 \text{ \AA}$, was more than the experimental error. Even larger differences in the bond lengths were observed for C-1-C-2 (1.340 \AA) and C-5-C-6 (1.378 \AA), $\Delta d_b = 0.038 \text{ \AA}$, and for C-2-C-3 (1.430 \AA) and C-4-C-5 (1.375 \AA), $\Delta d_r = 0.055 \text{ \AA}$. These values are explained in terms of the polarized electronic structure of **1a** with enhanced isolated double bond character for C-1-C-2 bond.

The ORTEP diagram is illustrated in Fig. 1.

Complex Formation with Various Metal Ions. In a comparative viewpoint, complexation of these heptafulvenes with various metal ions was investigated.³⁾ Thus, the UV spectrophotometric analysis with metal ions, Hg^{2+} , Na^+ , Li^+ , K^+ , NH_4^+ , Ca^{2+} , Mg^{2+} , Ba^{2+} , Zn^{2+} , and Cd^{2+} , in acetonitrile solutions revealed no detectable change to rule out a complexation. However, extractions of various metal ions into the chloroform-*d* solutions from aqueous solutions containing **1a** and **1b** were positive, according to ^1H NMR spectroscopy, only with mercury(II) ion; all other metal ions examined, such as Hg^{2+} , Na^+ , Li^+ , NH_4^+ , Ca^{2+} , Mg^{2+} , Ba^{2+} , Fe^{3+} , Co^{2+} , Ni^{2+} , Zn^{2+} , Cu^{2+} , and Ag^+ , remained in aqueous solutions.

Thus, according to experiments using a U-type cell⁸⁾, **1a** and **1b** transported mercury(II) ion selectively, and, in parallel to the previous cases, copper(II) ion did not interfere the transport. Moreover, zinc(II), nickel(II), and silver(I) ions were not transported under the same conditions. The amount of mercury(II) ions transported was determined photometrically as compiled in Table 1, where the relative rates of transport, $T(\text{M})$, of mercury(II) ion with ethers having different sizes are expressed; the term, T , denotes a total amount (micromol per hour) of ions transported by means of a U-type cell under the specified conditions (See Experimental). Due to the highly polarized nature of the molecules,

aqueous solutions, particularly with the receiving part, were colored in deep red, indicating a considerable dissolution of **1a** and **1b** into the aqueous solutions. This led to an incompleteness of the transport (Fig. 2). In fact, after a period of 100 h, only 50% and 90% of **1a** and **1b** were recovered from the organic layer. Also included in Table 1 was a result obtained by **4a**; it was also soluble in water, and the extraction was not completed. Certainly, liberation of mercury (II) ion by acidification should not be effective since **1** and **4a** have the protonation sites at the remote positions from the site of complexation, and these sites are connected with polarized conjugated heptafulvene and azulene systems.

It is also noteworthy that the transport efficiency dropped sharply when **1a** or **1b** was used; the transport rate for **1b** was less than 30% of that for **1a** as could be seen in Table 1.

Fixation of an Azacrown Derivative on the Merrifield Resin. Consequently, increased hydrophilic properties of aza-crown function made the completion difficult. This should be overcome by introduction of hydrophobic substituents, or even by fixation as a pendant on the polymer chain. Taking these points into account, we made a fixation of **4a** onto the Merrifield Resin; the IR spectrum of the resultant black powder showed a strong ν_{CN} band at 2230 cm^{-1} . An attempted liberation of the complexed mercury (II) ion from the Resin by acidification was unsuccessful being confirmed by the UV spectrophotometry. In a previous example of polymer-supported dithiocrown ether (**C**), liberation was quantitative for every repeated acid treatment. There are several differences from the present case; a) the site of protonation was different as the previous **C** has a tropone carbonyl being close to the site of complexation, while **4a** has two cyano groups on the remote position with the neighboring benzyl-amino group. Therefore, an effect of protonation in regard of the Coulomb repulsion may not be significant.

In conclusion, aza-crown derivatives showed a strong mercuriphilicity, but due to a presence of protonation sites in the molecule, these water soluble derivatives have a restriction for a practical use.

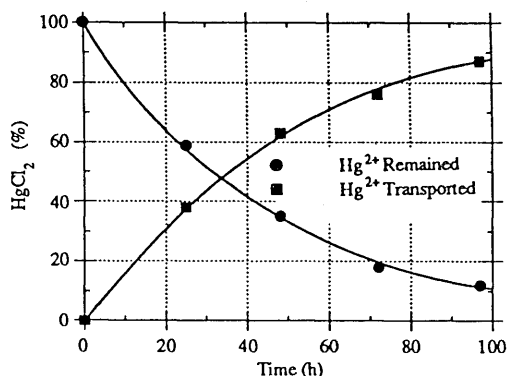


Fig. 2 The U-Type cell transport of Hg(II) ion with **1a**.

Table 1 Transport Experiments of Several Metal Ions by Use of Aza-Crown Heptafulvene Derivatives.

Crown deriv.	1a	1b	4a
T(Ca ²⁺) ^{a)}	—	—	—
T(Ba ²⁺) ^{b)}	—	—	—
T(Zn ²⁺) ^{c)}	—	—	—
T(Hg ²⁺) ^{a)}	3.18	0.79	0.64
T(Ag ⁺) ^{a)}	—	—	—

a) diphenylthiocarbazone

b) sodium diethyldithiocarbamate

c) 1-(2-pyridylazo)-2-naphthol.

Experimental

The melting points were measured with a Yanagimoto Micro Melting Point Apparatus and are uncorrected. The NMR spectra were measured by means of JEOL FX 100 Model and GSX 270H Model spectrometers in CDCl_3 ; the chemical shifts are expressed in units of δ . The mass spectra were measured with a JEOL 01SG-2 spectrometer, except for FAB-MS measurements of high-resolution molecular weight determinations which were performed by a JEOL JMS SX 102A model spectrometer being controlled by a JEOL DA-7000 Data System (Tokyo), of the Pharmaceutical School of Kyushu University. The IR spectra were taken as KBr disks for crystalline compounds or as liquid films inserted between NaCl plates for oily compounds, using a JASCO IR-A 102 spectrometer. The UV spectra were measured using Hitachi U-3200 and U-3410 spectrophotometers. The stationary phase for column chromatography was Wakogel C-300 and the eluent was a mixture of ethyl acetate and hexane.

Reaction of 2 with Az-5 or Az-6 in Benzene and Pyridine to Form 1 (General Method). An anhydrous Ac_2O solution (2 cm^3) of **2** (80-90 mg) and Az (60 mg) was heated under N_2 atmosphere at $130\text{--}140^\circ\text{C}$ for 1-3 h. The mixture was then heated in vacuo to remove volatile materials, and the residue thus obtained was chromatographed on a silicagel column to give **1**.

1a: Red crystals, mp $134\text{--}135.5^\circ\text{C}$, 85%. ^1H NMR $\delta=3.62$ (4H, s), $3.63\text{--}3.84$ (16H, m), 6.13 (1H, dd, $J=10.3, 2.9\text{ Hz}$), 6.84 (1H, dd, $J=10.9, 2.6\text{ Hz}$), 6.96 (1H, dd, $J=10.9, 10.3\text{ Hz}$), 7.08 (1H, dd, $J=13.2, 2.9\text{ Hz}$), and 7.43 (1H, dd, $J=13.2, 2.6\text{ Hz}$) ^{13}C NMR $\delta=54.5$ (2C), 58.4 , 68.0 (2C), 69.9 (2C), 70.5 (2C), 71.2 (2C), 112.1 , 117.4 , 117.7 , 122.2 , 129.9 , 130.0 , 136.1 , 139.7 , 156.7 and 159.8 . MS m/z (%), 371 (M^+ , 100), 196 (8), 194 (13), 141 (61), 126 (9), 114 (11), 56 (38), and 54 (14). IR ν : 2866 , 2190 , 2162 , 1633 , 1543 , 1507 , 1469 , 1449 , 1420 , 1400 , 1379 , 1358 , 1343 , 1324 , 1306 , 1260 , 1227 , 1118 , 1105 , 983 , 937 , 873 , 856 , 839 , and 772 cm^{-1} . UV $\lambda_{\text{max}}^{\text{CHCl}_3}=254.5\text{ nm}$ ($\epsilon=18000$), 331.0 (8500), 349.2 (7100), and 471.4 (29900). Found: C, 64.48; H, 6.76; N, 11.24%. Calcd for $\text{C}_{20}\text{H}_{25}\text{O}_4\text{N}_3$: C, 64.67; H, 6.78; N, 11.31%.

1b: Red crystals, mp $103.5\text{--}104.5^\circ\text{C}$, 33%. ^1H NMR $\delta=3.61\text{--}3.82$ (24H, m), 6.16 (1H, dd, $J=10.6, 3.1\text{ Hz}$), 6.82 (1H, dd, $J=10.6, 2.6\text{ Hz}$), 6.94 (1H, t, $J=10.6\text{ Hz}$), 7.20 (1H, dd, $J=13.2, 3.1\text{ Hz}$), and 7.43 (1H, dd, $J=13.2, 2.6\text{ Hz}$) ^{13}C NMR $\delta=52.7$ (2C), 57.9 , 68.2 (2C), 70.6 (2C), 70.78 (2C), 70.81 (2C), 71.1 (2C), 111.8 , 117.6 , 117.9 , 121.9 , 130.1 , 135.9 , 139.8 , 157.2 , and 159.7 . MS m/z (%), 417 (M^++2 , 24), 416 (M^++1 , 98), 415 (M^+ , 100), 414 (51), 141 (49), 96 (22), 58 (23), and 57 (49). IR ν : 2884 , 2186 , 2158 , 1629 , 1556 , 1502 , 1481 , 1461 , 1421 , 1358 , 1346 , 1280 , 1248 , 1230 , 1173 , 1122 , 1094 , 1025 , 947 , 894 , 865 , 831 , 785 , and 548 cm^{-1} . UV $\lambda_{\text{max}}^{\text{CHCl}_3}=251.7\text{ nm}$ ($\epsilon=8400$), 311.5 (6300), 332.3 (8100), 352.5 (6500), 448.5 (22300, sh), 472.5 (28900), and 485.9 (25200, sh). Found: C, 63.83; H, 6.73; N, 10.34%. Calcd for $\text{C}_{22}\text{H}_{29}\text{O}_5\text{N}_3$: C, 63.59; H, 7.04; N, 10.11%.

Conversion of 1a to Azulene (4a). An EtOH solution (10 cm^3) of malononitrile (30.1 mg) was treated with NaH (154 mg) and stirred at room temperature for 30 min. To the mixture was added **1a** (154 mg) at room temperature, and stirred for 12 h. After

removing the solvent *in vacuo*, the residue was diluted with water and extracted with CHCl_3 and chromatographed on a silica-gel column to give **4a** [red crystals, mp 195–197 °C, 145 mg; 54%. ^1H NMR δ = 3.63 (4H, s), 3.68–3.97 (16H, m), 5.68 (2H, br s), 7.08 (1H, ddd, J = 10.3, 2.9, 1.8 Hz), 7.29–7.41 (2H, m), and 7.56 (1H, d, J = 2.9 Hz). ^{13}C NMR δ = 54.7 (2C), 68.2 (2C), 69.6 (2C), 70.5 (2C), 71.0 (2C), 77.3, 116.1, 116.5, 116.6, 119.6, 122.0, 131.6, 146.2, 146.3, 152.2, and 160.7. MS m/z (%), 411 ($\text{M}^+ + 1$, 54), 410 (M^+ , 100), 235 (26), 221 (27), 220 (29), 206 (32), 180 (37), and 165 (23). IR ν : 3346, 3240, 2872, 2180, 1638, 1611, 1574, 1534, 1501, 1461, 1420, 1346, 1297, 1281, 1231, 1203, 1119, 1103, 985, 942, and 865 cm^{-1} . UV $\lambda_{\text{max}}^{\text{CH}_3\text{CN}}$ = 211 nm (ϵ = 19300), 242 (19300), 273 (16400), 340 (50000), 354 (33900), 394 (12500), 410 (9100), and 502 (1200). Found: C, 61.84; H, 6.20; N, 12.97%. Calcd for $\text{C}_{22}\text{H}_{26}\text{O}_4\text{N}_4 \cdot \text{H}_2\text{O}$: C, 61.67; H, 6.59; N, 13.08%].

Fixation of 4a onto Merrifield Resin. A pyridine solution (1.5 cm^3) of **4a** (27.5 mg) and Merrifield Resin (50 mg) was refluxed for 24 h. After cooling, the mixture was filtered and the residue was washed with MeOH and EtOAc and dried on a desiccator to obtain the constant weight. Black resin, **5a** [IR ν = 2184 cm^{-1} , 56 mg (82%)].

Transport Experiment of Various Metal Ions with 1a and 1b Using a U-Type Cell. By similar procedures as described in the previous paper,¹⁾ spectrophotometric determinations of metal ions before and after the transport *via* complexation with **1a** and **1b** were carried out:

Ni²⁺ ion: 10 cm^3 of aqueous NiCl_2 solution (0.05 mol/dm^3) was employed, and determined UV-spectrometrically at a λ_{max} of 570 nm as a complex with 1-(2-pyridylazo)-2-naphthol.⁹⁾

Zn²⁺ ion: 10 cm^3 of aqueous ZnCl_2 solution (0.05 mol/dm^3) was employed, and determined UV-spectrometrically at a λ_{max} of 535 nm as a complex with diphenylthiocarbazone.¹⁰⁾

Ag⁺ ion: 10 cm^3 of aqueous AgNO_3 solution (0.05 mol/dm^3) was employed, and determined UV-spectrometrically at a λ_{max} of 470 nm as a complex with diphenylthiocarbazone.¹¹⁾

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