Formation of *p*-Aminostyrene Cyclic Tetramer

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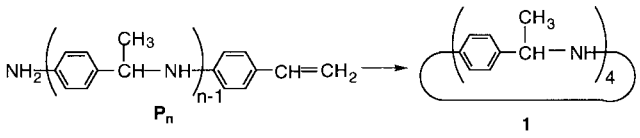
(Received March 12, 2001; CL-010216)

Two isomers (**1a** and **1b**) of *p*-aminostyrene cyclic tetramer (1,9,17,25-tetramethyl-2,10,18,26-tetraaza[2.2.2.2]paracyclophane, **1**) were produced from the linear oligomer $\mathbf{P_n}$ by passing it through a silica gel column. These are stereochemical isomers (**1a**: *RSRS*, *meso* and **1b**: *RRSS*, *meso*) and stable in solution. They include two solvent molecules in their crystalline states; **1a** includes benzene and **1b** includes ethanol.

We have recently reported[1–3] that *p*-aminostyrene (PAS) is easily oligomerized by various Brønsted acids to give polyaddition products $\mathbf{P_n}$ whose backbones are composed of phenylene, ethylidene and secondary amine groups. The reaction proceeds stepwise to yield the linear oligomer $\mathbf{P_n}$ (n = 4–8) at the end of the reaction via the formation of dimer $\mathbf{P_2}$ and trimer $\mathbf{P_3}$.[2,3] When this oligomer was eluted through a silica gel column (Wakogel C-300, Wako Co. Ltd., pH: 5.5–7.0) using hexane-ethyl acetate mixed solvent (9:1), we found that one fraction of



the effluent unexpectedly included *p*-aminostyrene cyclic tetramer **1**. From this fraction, two isomers **1a** and **1b** were separated as crystals by a fractional crystallization. **1a** was obtained as plate or needle-like crystals from chloroform–benzene system, while **1b** as needle-like crystals from chloroform–ethanol system. The yields of **1a** and **1b** were 44 and 12%, respectively. The residue on the column after elution contained structurally undefined oligomer more than pentamer with no polycyclic compound except cyclic tetramer. The ^{1}H NMR spectra[4] of **1a** and **1b** in Figure 1 were measured for the samples without solvents, which were prepared from the ethyl acetate–hexane solvent system. The spectrum of **1a** in Figure 1(a) shows a simple pattern and is easily assigned to the methyl, –NH, methine protons and phenylene protons with an A_2B_2 spin system, and consistent with its structure. In contrast, the ^{1}H NMR spectrum of **1b** in Figure 1(b) is a more complicated and parts of the signals are separated into two groups, i. e., the signals of the methyl, methine and phenyl protons adjacent to $CHCH_3$ are measured as two signals with the same patterns having equivalent intensities. This can be understood by noting that in the cyclic tetramer, two units are in a different environment from the other two units in a symmetrical way. To clarify the crystalline structures of the isomers, X-ray analysis was carried out. In Figures 2, the X-ray crystalline structures[5] of **1a** and **1b** are shown, respectively. Molecule **1a** has two-fold rotational symmetry, while **1b** has a center of symmetry, and they include two molecules of benzene or ethanol outside of the cavity. From the stereochemistry of four –NH–CH–CH_3 fragments in the tetramers, their structures are *RSRS* and *RRSS* for **1a** and **1b**, respectively. This is consistent with the ^{1}H NMR spectra. Both are *meso*-isomers and were confirmed to be optically inactive from ORD and CD measurements.

1 is probably produced via the formation of a linear tetramer cation $\mathbf{P_4}^+$ and the subsequent intramolecular cyclization due to the electrophilic addition of the carbocation to its own primary amino end group. Many macropolycyclic (cage)

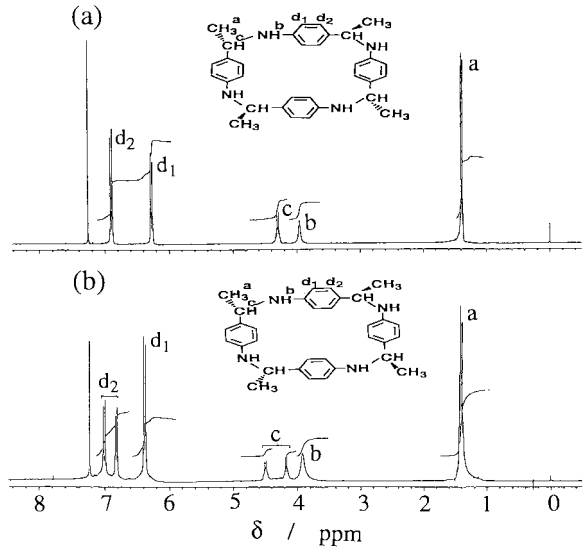


Figure 1. ^{1}H NMR spectra of (a) **1a** and (b) **1b** (in $CDCl_3$, Varian 300 MHz).

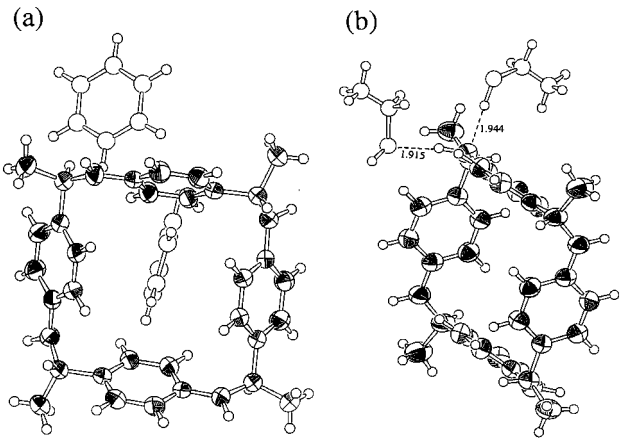
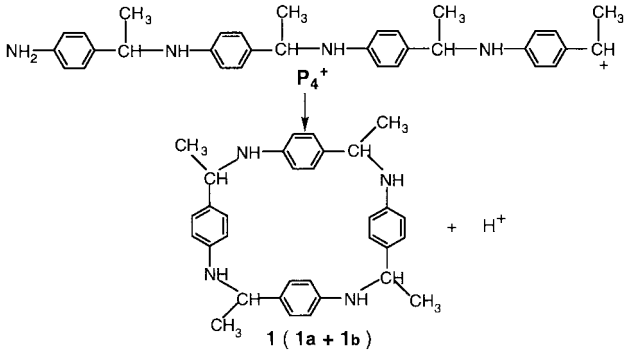


Figure 2. ORTEP drawings of (a) **1a** and (b) **1b**. Radii of the atoms of solvent molecules are arbitrary. For **1b**, the methylene groups of ethyl alcohols are disordered. For clarity, the disorder is not illustrated. The lengths of the intermolecular hydrogen bonds for N-H---O and O-H---N are 1.915 and 1.944 Å, respectively.



compounds have been so far synthesized as complexing agents for various inorganic and organic substrates.[6] Among them, nitrogen-bridged cage-type polyazacyclophanes have been recently noted as useful receptors of cation, neutral or anion compounds.[7,8] Compound **1** prepared in this paper might be expected to be a source of such a cage compound as well as paracyclophanes like a tetraaza[3.3.3.3]paracyclophane[9,10] and tetraaza[6.1.6.1]paracyclophane.[11]

A striking finding in this paper is the unusual production of the cyclic tetramer **1** from oligomer $\mathbf{P_n}$ in high yield by passing through silica gel column. It could not be obtained by passing through an alkaline alumina column (Wako Co. Ltd., Aluminum oxide 010–01525, pH: 9.0–11.0) So, this reaction seems to occur on an acidic solid catalyst. This is an example of a rare reaction on chromatography adsorbents.[12–15] At present it is not possible to provide a concise explanation for this unusual reaction on the silica gel column. The detailed mechanism is now under study.

We are grateful to Dr. T. Takahashi for many useful discussions.

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4 Structural analyses: **1a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.38 (d, J = 6.9 Hz, 12H, $-CH_3$), 3.96 (br s, 4H, –NH), 4.30 (q, J = 6.9 Hz, 4H, –CH), 6.27 (AA'BB', J_{AB} = 8.4 Hz, 8 aromaticH, *o*–H to –NH), 6.90 (AA'BB', J_{AB} = 8.4 Hz, 8 aromaticH, *m*–H to –NH). IR (KBr): 3409, 2976, 2959, 2920, 2865, 1616, 1518, 1318, 1287, 1179, 820, 565 cm^{-1}. Anal. Calcd for $C_{32}H_{36}N_4$: C, 80.67; H, 7.56; N, 11.76%. Found: C, 80.73; H, 7.63; N, 11.72%. ES-MS: m/z 477. **1b**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.40 (d, J = 6.9 Hz, 6H, $-CH_3$), 1.43 (d, J = 6.9 Hz, 6H, $-CH_3$), 3.94 (br s, 4H, –NH), 4.18 (q, J = 6.9 Hz, 2H, –CH), 4.50 (q, J = 6.9 Hz, 2H, –CH), 6.38 (AA'BB', J_{AB} = 8.4 Hz, 8 aromaticH, *o*-H to -NH), 6.82 (AA'BB', J_{AB} = 8.4 Hz, 4 aromaticH, *m*-H to –NH). 7.01 (AA'BB', J_{AB} = 8.4 Hz, 4 aromaticH, *m*-H to –NH). IR (KBr): 3410, 2963, 2922, 2866, 1615, 1518, 1318, 1287, 1254, 1181, 820, 563 cm^{-1}. Anal. Found: C, 80.45; H, 7.38; N, 11.65%. ES-MS: *m/z* 477.

5 Crystal data for **1a**: $C_{32}H_{36}N_4 \cdot 2C_6H_6$, fw = 632.9, monoclinic, space group $C2/c$, a = 27.018(4), b = 9.615(1), c = 16.903(2) Å, β = 122.065(4), V = 3720.9(8) Å^3, Z = 4. D_c = 1.130 g/cm^3. μ = (Cu Kα) = 5.03 cm^{-1}. T = 296 K. A crystallographic asymmetric unit $0.5(C_{32}H_{36}N_4)\cdot 0.5(C_6H_6)\cdot 0.5(C_6H_6)$. The number of measured reflections 3018, unique reflections 2872 (R_{int} = 0.015), used reflections for full matrix least squares 2206 ($I > 2\sigma(I)$). R = 0.056 (R_w = 0.078), S = 2.53 on F. **1b**: $C_{32}H_{36}N_4 \cdot 2\,C_2H_5OH$, fw = 568.8, monoclinic, space group $P21/n$, a = 10.631(2), b = 8.0871(7), c = 18.910(4) Å, β = 97.64(1)°, V = 1611.4(4) Å^3, Z = 4. D_c = 1.172 g/cm^3. μ = (Cu Kα) = 5.68 cm^{-1}. T = 296 K. A crystallographic asymmetric unit $0.5(C_{32}H_{36}N_4)\cdot C_2H_5OH$ (disordered). The number of measured reflections 2732, unique reflections 2237 (R_{int} = 0.037), used reflections for the refinement 1731 ($I > 2\sigma(I)$). R = 0.054 (R_W = 0.065), S = 1.90 on F.

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