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SYNTHESIS OF BROMO-SUBSTITUTED BICYCLIC OXALACTAM AND UNUSUAL ANIONIC DESALTING OLIGOMERIZATION OF ITS SODIUM SALT

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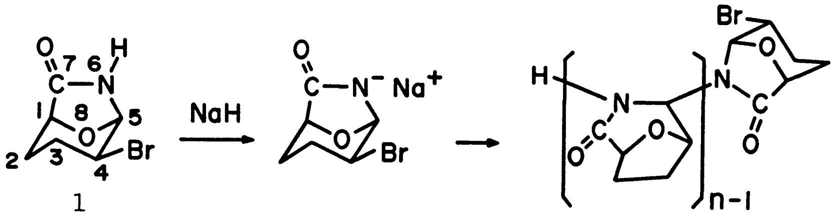
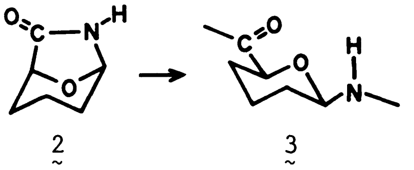
New bromo-substituted bicyclic oxalactam, 4(e)-bromo-8-oxa-6-azabicyclo[3.2.1]octan-7-one (1) was synthesized from sodium 3,4-dihydro-2*H*-pyran-2-carboxylate. Sodium salt of 1 was found to be oligomerized with the simultaneous desalting in dimethylformamide at 25 °C to give novel oligomers having a bicyclic oxalactam ring in each monomer unit.



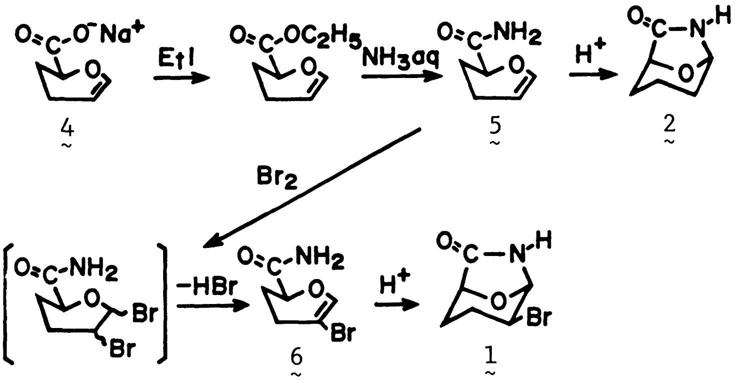
(1)



(2)

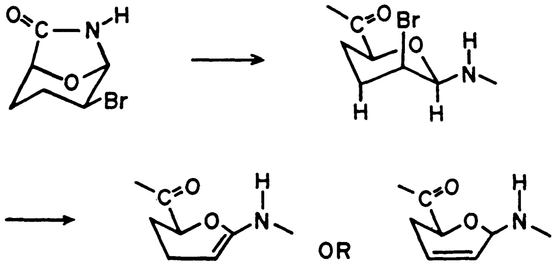
Anionic solution polymerization of a bicyclic oxalactam, 8-oxa-6-azabicyclo[3.2.1]octan-7-one (2), leads to give a high molecular weight polyamide (3). Polyamide 3 is easily cast to a hygroscopic membrane which has excellent permeability and permselectivity for water and solutes in aqueous solution, respectively.[1-8] The polyamide is also useful as a component for amphiphilic graft and block copolymers.[9-12] Such high polymerizability of 2 should be closely related to its molecular structure.[1,2,6,13,14] The effects of a polar substituent on the reactivity of the bicyclic oxalactam are important and attractive subjects as well as those in the case of bicyclic acetals.[15]

As shown in Scheme 1, a new bromo-substituted bicyclic oxalactam, 4(e)-bromo-8-oxa-6-azabicyclo[3.2.1]octan-7-one (1), was synthesized from sodium 3,4-dihydro-2*H*-pyran-2-carboxylate (4) which is also a starting material for the preparation of 2.[2] After the bromination of 3,4-dihydro-2*H*-pyran-2-carboxamide (5) in dimethylformamide below -25 °C, the reaction mixture was kept in the air for 2 h to give 5-bromo-3,4-dihydro-2*H*-pyran-2-carboxamide (6) in a high yield. Without isolating 6, the obtained solution was subsequently heated at 110 °C for 1 h to give colorless crystals of 1 (yield from 5, 40%). It is assumed that the hydrogen bromide eliminated and dissolved in the solution had catalyzed the intramolecular cyclization of the resulting amide 6. After recrystallization from the ethyl acetate solution, 1 was characterized as follows: mp , 146-147 °C. Elemental analysis. Found: C, 35.01; H, 3.85; N, 6.68%. Calcd for $C_6H_8NO_2Br$: C, 34.98; H, 3.91; N, 6.80%. Molecular weight, 206 (m/e of parent peak in mass spectrum, 205 and 207). IR ($CHCl_3$), 3444 and 3088 (νN-H, amide) and 1725 cm^{-1} (νC=O, five-membered lactam). The bromine atom in 1 was judged from the values of coupling constants in the 200 MHz ^1H-NMR spectrum[16] to be located at the equatorial position to the tetrahydropyran ring. This estimation was recently justified by the X-ray structural analysis of the crystal of 1.[17]



Scheme 1. Synthesis of 4(e)-bromo-8-oxa-6-azabicyclo[3.2.1]octan-7-one.

If 1 were polymerized anionically by the same mechanism as that for common lactams, the bromine atom, which had been located at the equatorial position to the tetrahydropyran in 1, would transfer to the axial position and be subsequently eliminated to give a dihydropyran ring as shown in Eq. 3. Since the base added as a catalyst, in that case, would be immediately consumed, the reaction would no longer proceed.



(3)

The sodium salt of 1 was prepared by the reaction of 1 with sodium hydride in tetrahydrofuran at room temperature under dry nitrogen atmosphere and isolated as white powder (yield, 93%). In dry nitrogen a dimethylformamide solution of the sodium salt (0.9 g/10 ml) was kept at 25 °C for 3 days to form an oligomer mixture containing mainly the trimer in a high conversion (see Fig. 1). From the mixture of 1 (0.9 g) and its sodium salt (1.07 g) the dimer was mainly obtained under the similar condition.

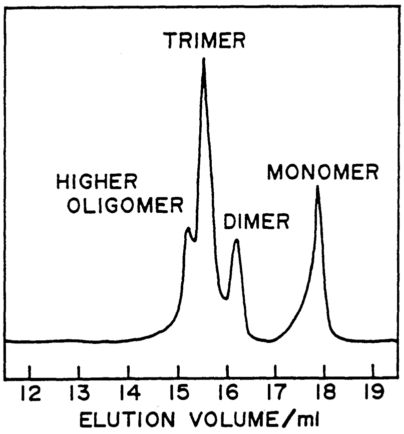


Fig. 1. GPC curve of a reaction mixture obtained by anionic desalting oligomerization of the sodium salt of 1 in dimethylformamide at 25 °C for 3 days (column, Shodex GPC KF-802, 8ϕ×600mm, chloroform).

After neutralization of the residual base in the latter reaction mixture with acetic acid, the fractional elution through the preparative silica gel column was carried out by using ethyl acetate-methanol mixed solvent as a developer. Consequently two kinds of dimers (major and minor fractions) and a trimer were isolated (yield: 0.77, 0.12, and 0.14 g, respectively).

From the data of elemental analysis[18] and molecular weight measurement,[19] hydrogen bromide is expected to have eliminated from each monomer unit except one terminal unit. Although the polymerization and oligomerization of lactams are generally accompanied with the ring-opening, the simultaneous elimination in the present oligomerization should bring about either of the formation of any unsaturated bond or another ring formation. The IR [20] and NMR spectra[21] (see Fig. 2) suggest that the isolated oligomers have no unsaturated bond except amide bonds. From the results of the detailed spectroscopic analyses together with X-ray crystallographic analysis[22] the molecular structures were determined as follows:[23]

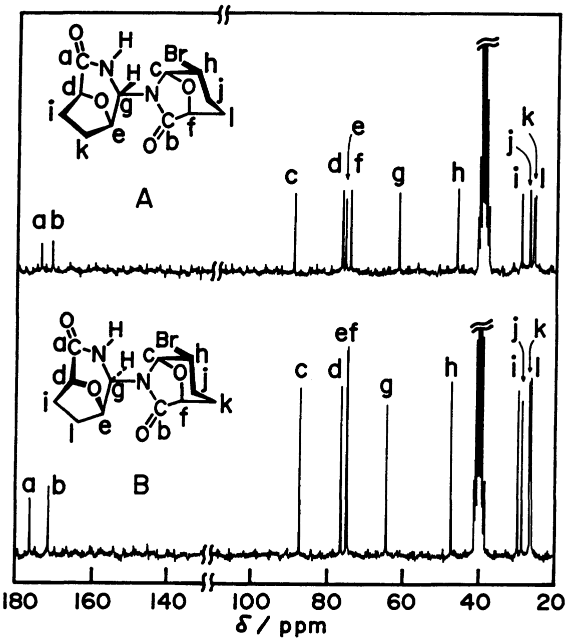
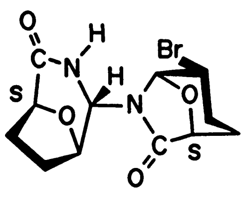
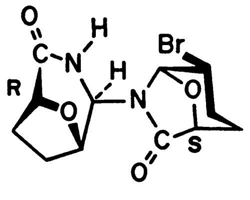


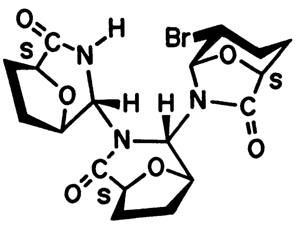
Fig. 2. ^{13}C-NMR spectra of dimers obtained by anionic desalting oligomerization of sodium salt of 1 (Me$_2$SO-d_6, TMS, 50 °C, 50 MHz). A, major dimer; B, minor dimer.



Major dimer, 7



Minor dimer, 8



Trimer, 9

It is noteworthy that each monomer unit in them has a bicyclic oxalactam skeleton. The one terminal unit has a five-membered oxalactam ring and a bromine atom in analogy with the fed monomer of 1. The other monomer units have six-membered oxalactam rings but no bromine atom. The novel molecular structures suggest that the anionic oligomerization proceeded with the simultaneous elimination of sodium bromide in dimethylformamide, which was quite different from the general mode of anionic ring-opening polymerization of lactams through the cleavage of the amide bonds.

From the configurations of the methine carbon atoms neighboring the carbonyl groups in each monomer unit of oligomers, the major dimer (7) and the trimer (9) are elucidated to be formed from either enantiomer of 1, and the minor dimer (8) from both enantiomers. The major dimer and the minor one are in the diastereomeric relation each other, and the yield ratio (87:13) suggests high enantiomer selectivity in the present unusual oligomerization. Taking into account of the configurational inversion, the detailed oligomerization mechanism will be discussed in the near future.

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16) ^{1}H-NMR (Me$_2$SO-d$_6$): δ 8.22(1H, amide), 5.28(1H, $^{5}\mathrm{C}\underline{\mathrm{H}}$), 4.36(1H, $^{4}\mathrm{C}\underline{\mathrm{H}}_{\mathrm{ax}}$, J($^{4}\mathrm{C}\underline{\mathrm{H}}_{\mathrm{ax}}$-$^{3}\mathrm{C}\underline{\mathrm{H}}_{\mathrm{ax}}$)=10.4 Hz, J($^{4}\mathrm{C}\underline{\mathrm{H}}_{\mathrm{ax}}$-$^{3}\mathrm{CH}_{\mathrm{eq}}$)=5.8 Hz, J($^{4}\mathrm{C}\underline{\mathrm{H}}_{\mathrm{ax}}$-$^{5}\mathrm{C}\underline{\mathrm{H}}$)=1.9 Hz), 4.06(1H, $^{1}\mathrm{C}\underline{\mathrm{H}}$), 2.30(1H, $^{3}\mathrm{C}\underline{\mathrm{H}}_{\mathrm{eq}}$), 1.80-2.16(2H, $^{2}\mathrm{C}\underline{\mathrm{H}}_{\mathrm{ax}}$ and $^{3}\mathrm{C}\underline{\mathrm{H}}_{\mathrm{ax}}$), and 1.72(1H, $^{2}\mathrm{C}\underline{\mathrm{H}}_{\mathrm{eq}}$).
17) Yuan-Xin Gu, T. Yamane, T. Ashida, K. Hashimoto, and H. Sumitomo, Bull. Chem. Soc. Jpn., in contribution.
18) Major dimer. Found: C, 43.36; H. 4.50; N, 8.47%. Calcd for $C_{12}H_{15}N_2O_4Br$: C, 43.52; H. 4.57; N, 8.46%. Minor dimer. Found: C, 43.56; H. 4.53; N, 8.37%. Calcd for $C_{12}H_{15}N_2O_4Br$: C, 43.52; H. 4.57; N, 8.46%. Trimer. Found: C, 47.49, H, 4.90; N, 9.22%. Calcd for $C_{18}H_{22}N_3O_6Br$: C, 47.38; H, 4.86; N, 9.21%.
19) Major dimer, 331 (m/e of parent peak in mass spectrum, 330 and 332). Minor dimer, 331 (330 and 332). Trimer, 456 (455 and 457).
20) Major dimer; 3396(νN-H), 1720(νC=O, five-membered lactam), 1693 cm^{-1}(νC=O, six-membered lactam). Minor dimer; 3390(νN-H), 1723(νC=O), 1692 cm^{-1}(νC=O). Trimer; 3390(νN-H), 1729(νC=O), 1685, and 1670 cm^{-1}(νC=O).
21) Trimer; δ 172.51, 170.96, 169.75(C=O); 91.50, 78.15, 76.69, 76.55, 75.50 73.90, 65.33, 65.11, 48.72($\underline{\mathrm{C}}\mathrm{H}$); 30.35, 29.95, 27.68, 26.61, 26.49, 25.10 ppm ($\underline{\mathrm{C}}\mathrm{H}_2$). Monomer: δ 174.19(C=O); 86.06, 73.24, 48.31($\underline{\mathrm{C}}\mathrm{H}$); 27.53, 26.17 ppm ($\underline{\mathrm{C}}\mathrm{H}_2$).
22) T. Yamane, M. Honda, T. Ashida, K. Hashimoto, and H. Sumitomo, to be published.
23) The oligomers prepared from the racemic monomer of **1** should be racemic. In these figures only one enantiomer for each of the oligomers is shown for the simplified expression.

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