Reaction of N-Halosulfonamide. V. 1) Reaction of N,N-Dibromobenzene-
sulfonamide with Dihydropyran. (1) 2)

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Reaction of N,N-dibromobenzensulfonamide with dihydropyran in 1:1 molar ratio
was investigated. In the first step, unstable N-bromo addition product (III) was formed;
then the bromine atom at nitrogen was reduced by the treatment with ethanol or water
and a mixture of stereoisomers (IV and V) was obtained. The structures of IV and V
were established.

We have previously reported that N,N-dibromobenzensulfonamide reacts with cyclo-
hexene to give trans- and cis-2-bromo-1-benzensulfonamidocyclohexanes, trans-1,2-
dibromocyclohexane, and 1,3-cyclohexadiene as the major products. 4) It has also been
revealed that N-halosulfonamide cleaves the C-O linkage of aliphatic ether to produce aldehyde
and alkyl halide. 1)
These results prompted us to study the reactivity of N-halosulfonamide with dihydropyran which brings an ether bond and an olefinic bond. It would be of interest to investigate that N-halosulfonamide attacks either the ether bond or the double bond.

As a result of our experiments it was shown that the addition to the double bond predominate over the cleavage of the ether bond.

A rapid exothermic reaction occurred by addition (1:1 molar ratio) of dihydropyran (II) to the suspension of N,N-dibromobenzenesulfonamide (I) in carbon tetrachloride, and the crystalline product (III) was obtained. Since this product was labile and decomposed with liberation of bromine by light irradiation, it could not be purified further. III was presumed as N-bromo intermediate (Chart 1) because the lack of N-H streching vibration frequency in infrared region was observed.

Treatment of III with ethanol or water gave a mixture of two crystalline substances melting at 135° (IV) and 129° (V). Overall yield of the mixture was about 65%. This mixture was separated into IV and V by fractional recrystallization and the ratio of IV to V was found to be about 3:2.\(^5\)

The fact that IV and V have the same molecular formulas, \(\text{C}_{15}\text{H}_{14}\text{O}_2\text{NSBr}\) and the results of the comparison of solubilities and of the infrared (IR) spectra of them suggested that these compounds are stereoisomers each other.

Hydrolysis of IV with aqueous acid in the presence of 2,4-dinitrophenylhydrazine afforded an osazone (VI), mp 235—236.5° (decomp.), \(\text{C}_{15}\text{H}_{18}\text{O}_2\text{N}_8\). The disappearances of the bromine atom and the benzenesulfonylamide group from IV by the formation of osazone show that the said compound (VI) is 2,3-disubstituted tetrahydropyran, and it was further known that α-halogen atom on the tetrahydropyran ring readily reacts with silver nitrate solution at room temperature to precipitate silver halide whereas β-halogen atom does not.\(^6\) Since no precipitation occurred by shaking the chloroform solution of IV with aqueous silver nitrate, IV may give the structure of 2-benzenesulfonamido-3-bromotetrahydropyran.

The structure of IV was further established by following experiments: Reaction of 2,3-dibromotetrahydropyran (VII) with potassium salt of benzenesulfonamide gave a product identical with IV.

Treatment of IV with aqueous sodium hydroxide gave a hydroxy compound (VIII), mp 133—137°. Chronic acid oxidation of VIII gave a carbonyl compound (IX), mp 123—124°. IX is a six-membered lactone showing an absorption at 1740 cm\(^{-1}\) in its infrared spectrum. Compound (VIII) may therefore be 3-benzenesulfonamido-2-hydroxytetrahydropyran, and an intramolecular SN\(_2\) reaction occurred through aziridine intermediate (VII) in the formation of VIII from IV.

The configuration of the substituents in IV is probably trans on the basis of the above reaction process.

The nuclear magnetic resonance (NMR) spectrum (Fig. 1) of IV also supports the above presumption and

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5) An isomerization reaction between IV and V in polar solvent was found by us. The investigation on this problem will be reported later in detail.

that of V suggests cis structure. Both of IV and V showed signals as doublet of $H_A$ at 4.37 $\tau$ ($J = 10$ cps).

A triplet of $H_B$ at 5.23 $\tau$ ($J_{AB} = J_{BC} = 10$ cps) for IV whereas a quartet of $H_A$ at 5.23 $\tau$ ($J_{AB} = 10$ cps, $J_{BC} = 2$ cps) for V were observed. The resonance signals ($J_{AB}$) at 4.37 $\tau$ and 5.23 $\tau$ of both compounds disappeared by the treatment of them with deuterium oxide.

The difference between the coupling constants, $J_{BC}$ of $H_A$, for IV and V can be explained by Karplus' rule,\textsuperscript{7} i.e., the value ($J_{BC} = 10$ cps) for IV suggests that the dihedral angle of $H_A$–C–C–$H_C$ is about 180°, and the value (2 cps) for V suggests the said angle is about 60°.

Based on above spectral and chemical findings, the configuration of bormine and benzene-sulfonamide group on the pyran ring is effectively assigned as trans for IV and cis for V.

In the case of reacting two molar dihydroxypyrane with $N,N$-dibromobenzenesulfonamide gave adducts of bis type. The results of this case will be reported in detail in later paper.

Experimental

Reaction of $N,N$-Dibromobenzenesulfonamide (I) with 2,3-Dihydroxy (II) (Formation of IV and V)—A solution of II (4.33 g) in CCl$_4$ (25 ml) was dropwise added for 30 min to the suspension of I (16.37 g) in CCl$_4$ (75 ml). An exothermic reaction occurred. After standing for 10 min at room temperature, the mixture was gradually refluxed for 30 min. The crystals (III) separated out were filtered and washed with CCl$_4$ to give purified crystals, mp 147–150° (decomp.). $IR_{max}$ cm$^{-1}$: 1350, 1169 (sulfonamide).

The crystals were added to 95% EtOH (100 ml) and the mixture was refluxed for 30 min. The solution of CH$_2$CHO during this treatment was observed. After the whole was concentrated in vacuo to about 30 ml, H$_2$O (60 ml) was added and the mixture was stored in a refrigerator overnight. The crystals were collected by suction; the yield calculated as the crystals are mixture of stereoisomers was 64%. These crystals were separated into two kinds of compound by fractional recrystallization using CHCl$_3$, CCl$_4$, and MeOH. One of them, IV, mp 134–135° (4.1 g), was relatively insoluble in CHCl$_3$, CCl$_4$, and soluble in MeOH. $Anal.$ Calcd. for $C_{11}H_{10}O_4$.BrNS: C, 41.26; H, 4.41; N, 4.37. Found: C, 41.26; H, 4.16; N, 4.33. $IR_{max}$ cm$^{-1}$: 3330, 3220 (N–H), 1328, 1162 (sulfonamide). NMR: (Fig. 1).

The other compound, V, mp 127–128° (2.4 g), was obtained from the mixture as a material relatively soluble in CCl$_4$ and CHCl$_3$ and insoluble in MeOH. $Anal.$ Calcd. for $C_{11}H_{10}O_5$NSBr: C, 41.26; H, 4.41; N, 4.37. Found: C, 41.14; H, 4.36; N, 4.77. $IR_{max}$ cm$^{-1}$: 3200 (N–H), 1340, 1140 (sulfonamide). NMR: (Fig. 1).

trans-2-Hydroxy-3-benzenesulfonamidotetrahydropyran (VIII)—trans-2-Benzensulfonamidoo-3-bromo tetrahydropyran (IV) (1 g) was dissolved in acetone (10 ml), the solution was added to 10% aqueous NaOH (1.5 ml), and the mixture was refluxed for 5 min. An oil substance rapidly precipitated. After the addition of H$_2$O (15 ml), the oil was extracted with CHCl$_3$, and the extract was dried over Na$_2$SO$_4$. Removal of the solvent left an oil residue which was solidified on standing. It was recrystallized from C$_6$H$_4$ to give crystals, mp 131–136°, in 80% yield. $Anal.$ Calcd. for $C_{11}H_{11}O_4$.NS: C, 50.74; H, 5.90; N, 5.45. Found: C, 51.34; H, 6.08; N, 5.52. $IR_{max}$ cm$^{-1}$: 3200 (O–H, N–H), 1325, 1155 (sulfonamide).

2-Oxo-3-benzenesulfonamidotetrahydropyran (IX)—A solution of VIII (2.024 g) in MeOH (30 ml) was added to a mixture of CrO$_3$ (1.560 g) and AcOH (40 ml). After standing at room temperature for 30 min, the mixture was refluxed for 1 min. The solvent was removed in vacuo, the residue was extracted with CHCl$_3$, then the extract was washed with aqueous Na$_2$CO$_3$ and H$_2$O, and dried over Na$_2$SO$_4$. After the removal of CHCl$_3$ by distillation, the residue was changed to a solid by the treatment with aceticone, and the resulting solid was recrystallized from C$_6$H$_4$, mp 123–124°. The yield was 74% of the theory. $Anal.$ Calcd. for $C_{11}H_{13}$O$_4$NS: C, 51.76; H, 5.13; N, 5.49. Found: C, 51.56; H, 5.04; N, 5.28. $IR_{max}$ cm$^{-1}$: 3270 (N–H), 1740 (b-lactone), 1330, 1162 (sulfonamide).

3,4-Diiodoxypentose 2,4-Dinitrophenol (XI)—trans-3-Bromo-2-benzenesulfonamidotetrahydropyran (IV) (0.25 g) was dissolved in EtOH (30 ml), and the solution was added to a mixture of 2,4-dinitrophenylhydrazone (0.3 g), EtOH (10 ml), H$_2$O (10 ml), and conc. H$_2$SO$_4$ (5 ml). The mixture was heated on a water bath for 3.5 hr. After the mixture was cooled, the resulting precipitate was filtered by suction and recrystallized from EtOH–AcOEt to give a red-colored crystals, mp 235–236.5° (0.15 g). These were confirmed to be identical with authentic sample by the mixed melting point determination.

Synthesis of trans-2-Benzensulfonamido-3-bromotetrahydropyran—A solution of II (8.2 g) in CHCl$_3$ (40 ml) was added in dropwise to a solution of bromine (16 g) in CHCl$_3$ (60 ml) under vigorous stirring and

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cooling at $-5$ to $-10^\circ$ for a period of 1 hr. An excess of bromine was decolorized by addition of small amount of II (about 1.2 ml). Powdered KNSO$_2$C$_6$H$_5$ (19.6 g) was added to the above mixture, and the resulting suspension was heated, at $70^\circ$ under stirring for 30 min. The colored solution was filtered and the precipitate was washed with CHCl$_3$. The combined solution of the filtrate and the washing was evaporated under reduced pressure, and dark brown syrup (23 g) was remained. This was dissolved in EtOH, and fractionally precipitated from the EtOH solution by dilution with H$_2$O, and relatively insoluble crystalline substance was separated from the soluble oily by-products. The crystalline substance (10.1 g) was recrystallized from CHCl$_3$ to give crystals of mp $134-135^\circ$ which were identified with authentic sample by the mixed melting point determination and by the comparison of their IR spectra.