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150. Yoshio Ueno, Shoji Takemura, Yoshiko Ando, and Hiromi Terauchi*2 : Reaction of N-Halosulfonamide.*1 I. Reaction of N,N-Dihalobenzenesulfonamide with Cyclohexene. (1).

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Reaction between N,N-dihalobenzenesulfonamide (I) and cyclohexene (II) was studied. Addition products, DL-*cis*- and DL-*trans*-2-halo-1-benzenesulfonamidocyclohexanes (III and IV), and by-products, DL-*trans*-1,2-dihalocyclohexane (V), 1,3-cyclohexadiene (VI), 1-cyclohexen-3-one (VIII) and benzenesulfonamide (VII) were isolated and identified from the reaction mixture. A presumption on this reaction was also drawn.

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It has previously been reported by Kharasch and Priestley,[1] and Buckles and Probst[2] that N,N-dibromo- and N-bromo-N-methyl derivatives of aromatic sulfonamides react with alkenes such as styrene to produce addition products. Recently, Oehlschlager and Zalkow[3] reported the addition of N,N-dibromobenzenesulfonamide to norbornylene.

It appeared still of interest to investigate the scope and mechanism of the reaction of N,N-dihalosulfonamide with various alkenes comparing with those of the reaction of N-bromosuccinimide which is well-known as a reagent for allylic bromination with alkene. The present paper relates to the reaction of N,N-dichlorobenzenesulfonamide (Ia) and N,N-dibromobenzenesulfonamide (Ib) with cyclohexene (II), and also to the identification of the isolated products. These reactions were outlined in Chart 1.

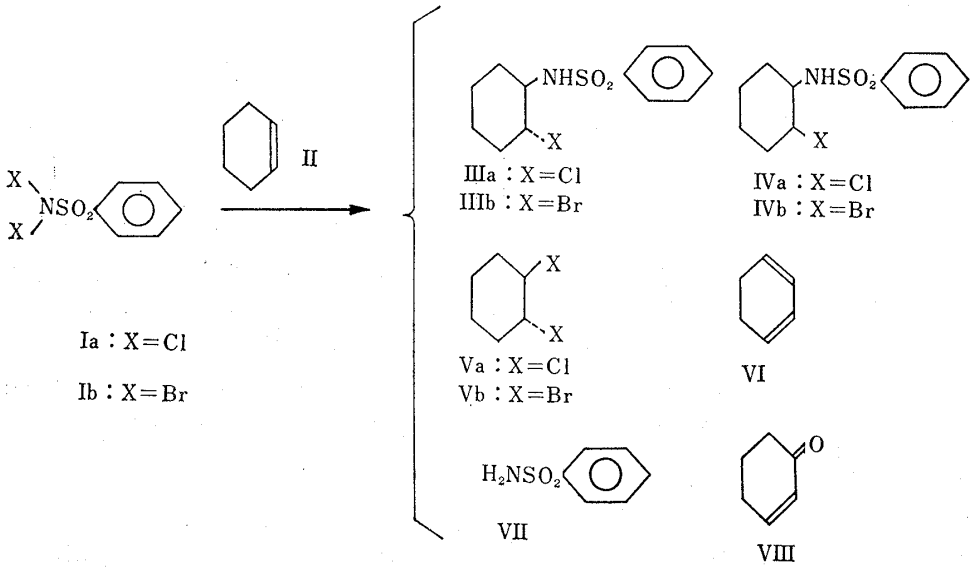

Chart 1.

*1 A communication on these studies appeared in This Bulletin, **13**, 1369 (1965).

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1) M. S. Kharasch, H. M. Priestly : J. Am. Chem. Soc., **61**, 3425 (1936).

2) R. E. Buckles, W. J. Probst : J. Org. Chem., **22**, 1728 (1957).

3) A. C. Oehlschlager, L. H. Zalkow : Tetrahedron Letters, **1964**, 2663; A. C. Oehlschlager, C. D. Kennedy, L. H. Zalkow : J. Org. Chem., **31**, 1682 (1966).

When N,N-dichlorobenzenesulfonamide (Ia) and an excess of cyclohexene (II) were mixed in carbon tetrachloride at room temperature, an exothermic reaction occurred and, after the reaction subsided, the mixture was gently refluxed. The resulted mixture was distilled to collect the fraction boiling below 82°, which was used for examination of its content. The result will be described below. From the residue, crystals (IIIa), m.p. 155°, $C_{12}H_{16}O_2NSCl$, were collected in 50% yield*[3] and were identified with the authentic DL-*trans*-2-chloro-1-benzenesulfonamidocyclohexane prepared by the reaction of DL-*trans*-2-chlorocyclohexylamine[4] with benzenesulfonyl chloride.

After the removal of IIIa, the mother liquor was chromatographed on an alumina column and the following five products were isolated : DL-*trans*-1,2-dichlorocyclohexane (Va), $b.p_{30}$ 85~89°, in 41% yield,*[4] being identified with an authentic sample[5]; 1-cyclohexen-3-one (VIII) in 3% yield,*[4] being identified as its 2,4-dinitrophenylhydrazone, m.p. 164°[6]; DL-*cis*-2-chloro-1-benzenesulfonamidocyclohexane (IVa), $C_{12}H_{16}O_2NSCl$, crystals of m.p. 115°, in 2% yield,*[4] being identified with a sample prepared by the reaction of benzenesulfonyl chloride with DL-*cis*-2-chlorocyclohexylamine[7] in alkaline solution; additional crop of IIIa; and benzenesulfonamide (VII), m.p. 156°.

On reaction of the above-mentioned low-boiling fraction with maleic anhydride, the presence of 1,3-cyclohexadiene (VI) in the products was confirmed by the formation of the Diels-Alder adduct, *i.e.* 3,6-ethano-Δ^4-tetrahydrophthalic anhydride,[8] m.p. 147°: the yield of VI was found to be 47%*[4] by a gas chromatographic measurement (Fig. 1).

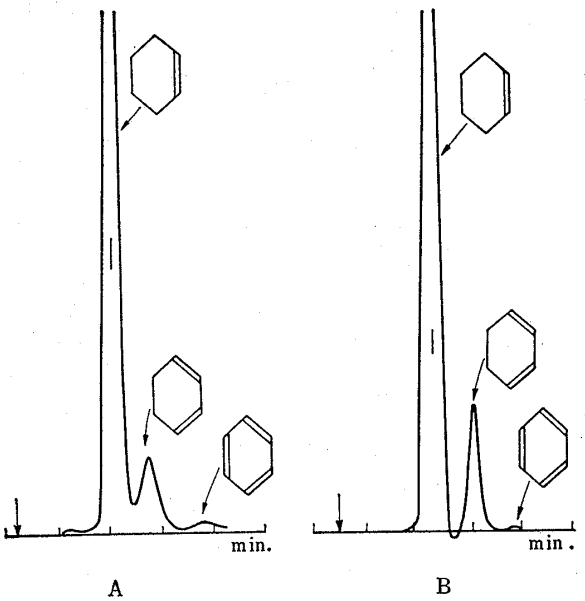

Fig. 1. Gas Chromatogram of Low-boiling Fraction from the Reaction Mixture of N,N-Dihalobenzenesulfonamide (A : the chloro derivative, B : the bromo derivative) with Cyclohexene.

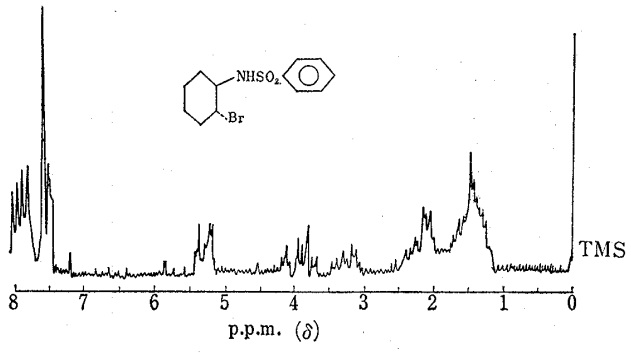

Fig. 2. Nuclear Magnetic Resonance Spectrum of DL-*trans*-2-Bromo-1-benzenesulfonamidocyclohexane (IIIb).

The reaction of the bromo analog, N,N-dibromobenzenesulfonamide (Ib), with II and isolation of the products were then carried out in a similar manner as in the case of

*[3] Overall yield including each crop on calculation from the Ia used.
*[4] Yield calculated from I used.
4) F. Winternitz : Bull. soc. chim. France, **1956**, 382.
5) M. W. Markownikow : Ann., **302**, 29 (1898).
6) A. Guillemonat : Compt. rend., **205**, 67 (1937).
7) G. E. McCasland, *et al.* : J. Am. Chem. Soc., **71**, 637 (1949).
8) O. Diels, K. Alder : Ann., **460**, 98 (1928).

chloro analog. The products isolated were as follows: DL-*trans*-2-bromo-1-benzenesulfonamidocyclohexane (IIIb), m.p. 166°, $C_{12}H_{16}O_2NSBr$ (75~91%), in whose nuclear magnetic resonance spectrum (Fig. 2), signals of 1-H and 2-H in cyclohexane ring appeared at 6.7τ and 6.02τ, respectively, and one proton of N-H exhibits at 4.63τ; the *cis*-isomer of IIIb (IVb), m.p. 116~117°, $C_{12}H_{16}O_2NSBr$ (6~13%*4); DL-*trans*-1,2-dibromocyclohexane (Vb), b.p_{30} 91~105° (41~49%*4); 1,3-cyclohexadiene (VI) (49%*4) which was converted into 3,6-ethano-Δ^4-tetrahydrophthalic anhydride[8] by the action of maleic anhydride on the low-boiling fraction obtained from the reaction mixture, and was detected directly by gas chromatography (Fig. 1); benzenesulfonamide (VII) (8%*4) and 1-cyclohexen-3-one (VIII) (2%*4).

In view of the above facts, the most reasonable presumption to be drawn is that a simple addition in a 1:1 molar ratio between I and II occurs giving some intermediates in the reaction pathway and then the intermediates react with excess II to give the final products.

In order to obtain an evidence for the above presumption, Ib and II were allowed to react in various molar ratios and the yield of IIb produced were compared (Table I).

TABLE I. Yield of IIIb and Color of Mixtures obtained by Reaction of Ib and II in Various Molar Ratios

Molar ratio Ib:II	Yield (1st crop) (%)	Color of reaction mixture	Molar ratio Ib:II	Yield (1st crop) (%)	Color of reaction mixture
1:1	22	Orange	1:4	34	Pale yellow
1:2	29	Orange-yellow	1:10	35	Pale yellow

In the case of the reactions in 1:1 and 1:2 molar ratios, the reactions did not seem to be completed since the reaction mixtures are still positive for KI-starch tests. Addition of excess II to these uncompleted reaction mixtures resulted in color change to pale yellow and increased in the yields of IIIb. Further, thin-layer chromatograms of the reaction mixtures in the above reactions were more complicated than in the case of 1:4 molar mixture. The chromatograms after additions of II to the former mixtures were similar to that in latter case.

Subsequent experiments on the intermediates and mechanism of this reaction will be reported in the following paper.

Experimental

N,N-Dihalobenzenesulfonamide (Ia and Ib) was prepared by a modified procedure of the known method.[9]

N,N-Dichlorobenzenesulfonamide (Ia)——Chlorine gas was bubbled through a solution of benzenesulfonamide (20 g.) in 4% aq. NaOH (300 ml.) and chilled to 0° for 3 hr. to complete the reaction. The separated white solid was collected, washed with H_2O, and extracted with hot $CHCl_3$ (150 ml.). The $CHCl_3$ extract was dried over anhydrous Na_2SO_4, evaporated *in vacuo* to 1/5 volume, and to the residue was added *n*-hexane to give white plates (Ia), m.p. 76° (23 g.).

N,N-Dibromobenzenesulfonamide (Ib)——To a cooled solution of benzenesulfonamide (40 g.) in 4% aq. NaOH (600 ml.), Br_2 (104 g.) was added under stirring. The separated orange crystals were collected, washed with H_2O, and dissolved in hot $CHCl_3$ (300 ml.). After removal of separated aqueous layer, the solution was dried over anhydrous Na_2SO_4, evaporated *in vacuo* to 1/3 volume, and *n*-hexane (200 ml.) was added to obtain orange crystals (Ib), m.p. 113~114° (decomp.) (72.8 g.).

Reaction of Ia with II: Isolation of IIIa, IVa, Va, VI, VII, and VIII——Under external cooling below 10°, Ia (5.6 g.) was added to II (10 ml.) in small portions. A gentle refluxing for 10 min. and subsequent heating at 50° for 30 min. were required to complete the reaction, *i.e.* the mixture became negative to the

9) A. A. Petrov: C. A. **32**, 5370 (1938); M. V. Lithosherstov, V. A. Sklavrov: C. A., **32**, 4521 (1938).

KI-starch test. The reaction mixture was then distilled and the distillate boiling below 82°(low-boiling fraction) was collected.

1) DL-*trans*-2-Chloro-1-benzenesulfonamidocyclohexane (IIIa): After removal of the low-boiling fraction, CCl_4 (50 ml.) was added to the residue, the mixture was chilled to 0°, and separated crystals (IIIa)(2.5 g.) were collected. M.p. 155°(EtOH)(2.0 g.), IR ν_{max}^{Nujol} cm^{-1}: 3220 (ν_{N-H}), 1320, 1155 (ν_{SO_2NH}). *Anal.* Calcd. for $C_{12}H_{16}O_2NSCl$: C, 52.71; H, 5.90; N, 5.12. Found: C, 52.89; H, 5.77; N, 4.88. The crystals were identical with the authentic specimen (prepared by the method described later) by spectral comparison and by a mixed fusion.

2) 1-Cyclohexen-3-one (VIII): The mother liquor of IIIa was evaporated to dryness, the residue was dissolved in CCl_4 (30 ml.), and chromatographed on neutral Al_2O_3. Elution of the column with CCl_4 gave at first an oily mixture and then an oil with crystals. The crystals in the latter eluate were collected, washed with CCl_4, and the washing was combined with the first eluate. The combined solutions were evaporated to dryness. A part of the residue (VIII)(0.2 g.) was converted into a 2,4-dinitrophenylhydrazone and the hydrazone was purified by passing a solution of it in $CHCl_3$ through a small silica gel column to obtain orange-yellow needles, m.p. 164°(70 mg.), which were identical with the authentic sample.[6]

3) DL-*trans*-1,2-Dichlorocyclohexane (Va): The mother liquor after the filtration of the 2,4-dinitrophenylhydrazone of VIII was evaporated to dryness and the residue was extracted with $CHCl_3$ (each 10 ml., three times). The extracts combined were dried over Na_2SO_4 and then the $CHCl_3$ was removed by distillation. The residue was dissolved in *n*-hexane, purified by passing the resulting solution through a small Al_2O_3 column, and the column was eluted with *n*-hexane. The combined eluates were distilled to obtain an oil (Va), b.p_{30} 85~89°(31 mg.), which was proved to be identical with an authentic sample[5] by comparison of IR spectra.

4) DL-*cis*-2-Chloro-benzenesulfonamidocyclohexane (IVa): The crystals obtained from the above-mentioned (in the item 2) second eluate were recrystallized from EtOH to give colorless needles (IVa), m.p. 115~118°(150 mg.). IR ν_{max}^{Nujol} cm^{-1}: 3240 (ν_{N-H}), 1330, 1163 (ν_{SO_2NH}). *Anal.* Calcd. for $C_{12}H_{16}O_2NSCl$: C, 52.71; H, 5.90; N, 5.12. Found: C, 52.38; H, 5.85; N, 4.99. These were identified with authentic sample by the comparison of IR spectra and by a mixed fusion.

5) Benzenesulfonamide (VII) and Additional Crop of IIIa: The foregoing alumina column was subsequently eluted with $CHCl_3$ to obtain an additional crop of IIIa as white needles, m.p. 152°(0.2 g.). The column was then finally eluted with MeOH, crude benzenesulfonamide (VII), m.p. 156°(MeOH-H_2O)(0.3 g.) was obtainned.

6) 1,3-Cyclohexadine (VI): A part (1 ml.) of the above-metioned low-boiling fraction from the reaction mixture was mixed with *n*-hexane (3 ml.), then maleic anhydride (100 mg.) was added thereto, and the mixture was kept standing for 36 hr. at room temperature. The solvent was evaporated to one-half the original volume and the separated solid was recrystallized from ligroin to give colorless prisms, m.p. 147°(22 mg.). These were proved to be identical with 3,6-ethano-Δ^4-tetrahyrophthalic anhydride by comparison of the IR spectra and determination of a mixed melting point.

Reaction of Ib and II: Isolation of IIIb, IVb, and Vb——A mixture of II (32 g.) and CCl_4 (15 g.) was allowed to react with a small portion of Ib (31.5 g.) under cooling below 10° and then the whole was refluxed on a water bath for 1 hr. until it became negative to the KI-starch test.

1) DL-*trans*-2-Bromo-1-benzenesulfonamidocyclohexane (IIIb): The reaction mixture was cooled to room temperature and the separated crystals (IIIb) were collected by suctional filtration to give the product (18.5 g.), m.p. 164~166°(from EtOH). IR ν_{max}^{Nujol} cm^{-1}: 3250 (ν_{N-H}), 1325, 1159 (ν_{SO_2NH}). NMR (Fig. 2). *Anal.* Calcd. for $C_{12}H_{16}O_2NSBr$: C, 45.17; H, 5.07; N, 4.40; O, 10.06. Found: C, 44.87; H, 4.97; N, 4.19; O, 10.23. This product was identified with an authentic sample by a mixed melting point determination and by IR spectral comparison.

2) DL-*cis*-2-Bromo-1-benzenesulfonamidocyclohexane (IVb): After removal of the first crop of IIIb, the mother liquor was evaporated and the residue was extracted with *n*-hexane (30 ml.). The second crop of IIIb (2.5 g.) was obtained by allowing the *n*-hexane-insoluble liquid to stand. The preceding extract with *n*-hexane was evaporated, and the residue was combined with the mother liquor from the filtrate of the second crop of IIIb. The mixture was repeatedly treated with *n*-hexane and 8.9 g. of *n*-hexane-insoluble and 15.4 g. of soluble fractions were obtained. The former fraction was chromatographed on an alumina column and eluted with CCl_4 to give a main crystalline fraction as colorless needles (IVb), m.p. 116~117° (from benzene-*n*-hexane) (4.2 g.); IR ν_{max}^{Nujol} cm^{-1}: 3240 (ν_{N-H}), 1327, 1156 (ν_{SO_2NH}). *Anal.* Calcd. for $C_{12}H_{16}O_2NSBr$: C, 45.17; H, 5.07; N, 4.40. Found: C, 45.33; H, 4.99; N, 3.98. This product was identical with authentic DL-*cis*-2-bromo-1-benzenesulfonamidocyclohexane by comparison of IR spectra and by a mixed melting point determination.

3) DL-*trans*-1,2-Dibromocyclohexane (Vb): A part of the above *n*-hexane-soluble fraction (6.3 g.) was chromatographed on a neutral alumina column. The fraction eluted with *n*-hexane was evaporated to leave an oil (4.5 g.) which was rectified to collect the main fraction (Vb) of b.p_{30} 118~120°. It was identical with authentic sample[10] by comparison of IR spectra.

Isolation of IIIb, IVb, VI, and VII——Cyclohexene (II) (16 g.) and Ib (15.9 g.) were allowed to react in

10) H. R. Snyder, L. A. Brooks: Org. Syntheses, Coll. Vol. 2, 171 (1943).

CCl_4 (7.5 g.) as described above, the reaction mixture was distilled, and the fraction boiling below 82° (low-boiling fraction) was separated. After the addition of CCl_4 (20 ml.) to the residue, the solid material was collected by filtration and recrystallized from EtOH to IIIb (8.9 g.).

The filtrate was evaporated to obtain a sirupy material (18.9 g.). A part (5.8 g.) of this material was mixed with alumina (5 g.) and *n*-hexane (15 ml.), the mixture was charged on the top of a column of neutral alumina-*n*-hexane, and the column was developed and eluted with *n*-hexane. The eluate was distilled to collect a fraction of b.p_{30} 119~120° (2.0 g.) which was found to be identical with a sample of Vb by comparison of IR spectra. The column was then developed with CCl_4 to give IVb (0.3 g.); further development with $CHCl_3$ gave an additional crop of IIIb (1.7 g.). Final development with MeOH gave white plates, m.p. 156° (from EtOH-H_2O), which were identical with authentic benzenesulfonamide (VII).

The low-boiling fraction (1 ml.), UV $\nu_{max}^{n\text{-hexane}}$ mμ : 256, separated previously was dissolved in benzene (3 ml.), maleic anhydride (100 mg.) was added, and the mixture was allowed to stand for 36 hr. at room temperature. After evaporation of the solvent to one-half volume, the solution was cooled. The separated solid was crystallized from ligroin to colorless prisms, m.p. 147° (22 mg.), which were identical with authentic 3,6-ethano-Δ^4-tetrahydrophthalic anhydride by IR spectral comparison and by a mixed melting point determination.

Gas Chromatography of the Low-boiling Fractions——The low-boiling fractions obtained from the reaction mixtures of Ia and Ib with II were analyzed separately by gas chromatography (Fig. 2) under the following condition : Column, Polyethyleneglycol 6000 (30~60 mesh, 2 m., 80°); detector, hydrogen ionization detector; samples, 1 μl.; carrier, He.

DL-*trans*-2-Chloro-1-benzenesulfonamidocyclohexane (IIIa)——A cooled mixture of DL-*trans*-2-chlorocyclohexylamine hydrochloride (0.369 g.), H_2O (10 ml.), and 10% aq. NaOH (1.73 ml.) was allowed to react with $C_6H_5SO_2Cl$ (0.3 ml.) under stirring for 30 min. at 0°. The separated solid was triturated with $CHCl_3$ and recrystallized from $CHCl_3$ to give IIIa, m.p. 153° (64 mg.).

DL-*cis*-2-Chloro-1-benzenesulfonamidocyclohexane (IVa)——DL-*cis*-2-Chlorocyclohexylamine hydrochloride (0.208 g.), 10% aq. NaOH (4.9 ml.), and $C_6H_5SO_2Cl$ (0.321 g.) were allowed to react as same as above to give IVa, m.p. 113~115° (0.120 g.).

DL-*trans*-2-Bromo-1-benzenesulfonamidocyclohexane (IIIb)——Cyclohexenimine[11] (2.5 g.) was dissolved in dry Et_2O (30 ml.) and dry HBr was passed through the solution so that DL-*trans*-2-bromocyclohexylamine hydrobromide was separated therefrom as a white solid. Purification of this material was unsuccessful. The crude hydrobromide (4.2 g.) was dissolved in pyridine (15 ml.) and $C_6H_5SO_2Cl$ (2.1 ml.) was added dropwise to the solution during 30 min. under stirring at 0°. After the addition of H_2O, the separated solid (0.9 g.) was recrystallized from MeOH to white needles, m.p. 164~166°.

DL-*cis*-2-Bromo-1-benzenesulfonamidocyclohexane (IVb)——To a cooled and stirred solution of DL-*cis*-2-bromocyclohexylamine hydrochloride[12] (0.430 g.) in H_2O (20 ml.) and $C_6H_5SO_2Cl$ (0.5 ml.) and *N* NaOH (8 ml.) were added dropwise in 30 min. The solution was extracted with $CHCl_3$, the $CHCl_3$ extract was evaporated *in vacuo*, EtOH (5 ml.) was added to the residue, and H_2O was cautiously added to produce white needles, m.p. 106~108° (0.163 g.). Repeated purification from aq. MeOH afforded a sample melting at 125°.

11) O. E. Paris, P. E. Fanta : J. Am. Chem. Soc., **74**, 3007 (1952).
12) *cis*-Compound : A. F. Osterberg, E. L. Kendall : *Ibid.*, **42**, 2616 (1920).