[Chem. Pharm. Bull. 19(8)1606—1610(1971)]

UDC 547.541.04 : 547.592.2.04

Reaction of N-Haloamide. XIII.[1] The Coupled Reaction of N,N-Dibromobenzenesulfonamide and Formamide or Dimethylformamide with Cyclohexene

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(Received January 5, 1971)

The reaction of N,N-dibromobenzenesulfonamide (I) with cyclohexene (II) in formamide or dimethylformamide were studied. The reaction of I with II in formamide gave a major product, *trans*-2-bromo-1-cyclohexyl N-benzenesulfonylformimidate (III), and minor products, *trans*-1,2-dibromocyclohexane (IV), *trans*-2-bromocyclohexyl formate (V), *trans*-2-bromocyclohexanol (VI) and benzenesulfonamide (VII).

The reaction in dimethylformamide, contrary to that in formamide, gave another type of product, N,N-dimethyl-N'-benzenesulfonylformamidine (IX), IV, V and VI were also obtained as by-products.

The mechanism to form these products was discussed.

The reaction of N,N-dibromobenzenesulfonamide with cyclohexene in non-polar solvent gives adducts (*trans*- and *cis*-2-bromo-1-benzenesulfonamidocyclohexanes, *trans*-1,2-dibromocyclohexane) and other by-products.[3]

Turner, *et al.*[4] observed a coupled reaction of olefin with N,N-dichlorourethane in acetonitrile which results N-β-chloroalkyl-N'-chlorocarbethoxyacetamidine and Theilacker[5] reported the similar reaction of olefin with N,N-dichlorobenzenesulfonamide in acetonitrile. Other coupled reactions of olefins with N-haloamide in acetic acid or alcohols giving β-haloacetoxy or β-haloalkoxy compounds respectively were also reported.[6-9]

The possibility of the participation of coexisting substance such as formamide to the reaction system of olefin with N-haloamide appeared to be of interest to investigate.

As the result of the reaction of N,N-dibromobenzenesulfonamide (I), cyclohexene (II), and formamide, a major product, *trans*-2-bromo-1-cyclohexyl N-benzenesulfonylformimidate (III), and minor products, *trans*-1,2-dibromocyclohexane (IV), *trans*-2-bromocyclohexylformate (V), *trans*-2-bromocyclohexanol (VI), and benzenesulfonamide (VII) were obtained.

Addition of II to the solution of I in formamide under a mild condition gave crystals of mp 94—95° (III) which had a molecular formula, $C_{13}H_{16}O_3NSBr$. Absorption bands ($\nu_{C=N}$ at 1591 cm^{-1} and ν_{SO_2N} at 1158 and 1316 cm^{-1}) were observed in the infrared (IR) spectrum.

In order to clarlify the structure of III, it was hydrolyzed in acetone-water mixture at room temperature and *trans*-2-bromocyclohexylformate (V), benzenesulfonamide (VII), and *trans*-2-bromocyclohexanol (VI) were obtained. The formate (V) was converted to VI by longer period of hydrolysis (Chart 2).

1) Part XII: S. Takemura, and Y. Kamiya, *Chem. Pharm. Bull.* (Tokyo), **18**, 848 (1970).
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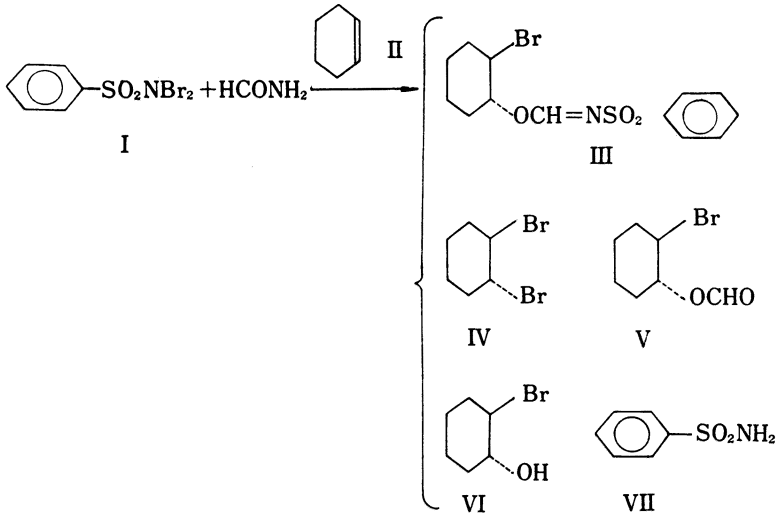


Chart 1

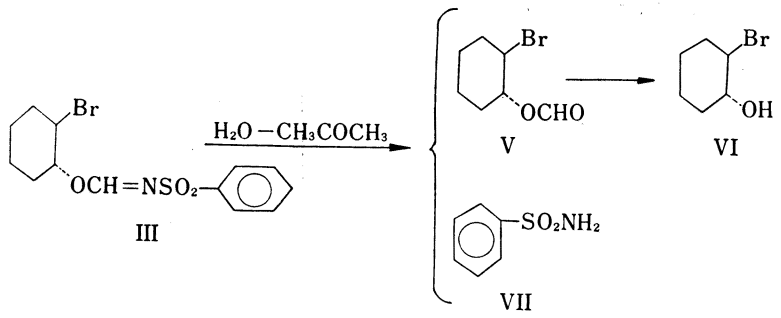


Chart 2

From the above results, the structure of III is estimated to be 2-bromo-1-cyclohexyl N-benzenesulfonylformimidate and the configuration found to be *trans*.

In the nuclear magnetic resonance (NMR) spectrum of III, two multiplet signals at 6.02 τ and 5.0 τ are assigned to the protons geminal to bromine and oxygen respectively by reason that the protons geminal to bromine and oxygen exhibit together in the region of 5.8—6.7 τ as a complex signal in VI, and the signals of the corresponding protons in V appear at 4.95 τ (multiplet) and 6.02 (multiplet).

When I was added to formamide, the yellow color of I disappeared and colorless crystals (mp 60—61° (decomp.)) which were supposed to be an intermediate were separated, but they could not be purified further due to lability of them. The analytical data of the crystals suggests that the substance is probably a complex of formamide with I in 2:1 molar ratio. Reaction of it with II also gave the same results as shown in Chart 1.

The results of the reaction of I with II in dimethylformamide are illustrated in Chart 3.

Cyclohexene (II) was dropwise added to the solution of N,N-dibromobenzenesulfonamide (I) in dimethylformamide. The crystalline substance, mp 128—129°, which separated out from the reaction mixture was given a structure IX. The elemental analysis of it agreed with $C_9H_{12}O_2N_2S$, and the IR spectrum showed the presence of C=N (1610 cm^{-1}) and SO_2N bondings (1330, 1140 cm^{-1}). The NMR shows two doublets due to methyl groups at 6.87 τ

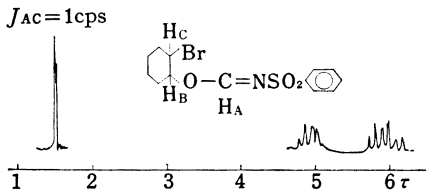


Fig. 1. Nuclear Magnetic Resonance Spectrum of III in $CDCl_3$

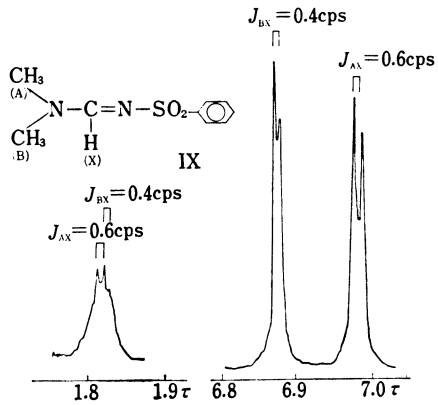


Fig. 2. Nuclear Magnetic Resonance Spectrum of IX in $CDCl_3$

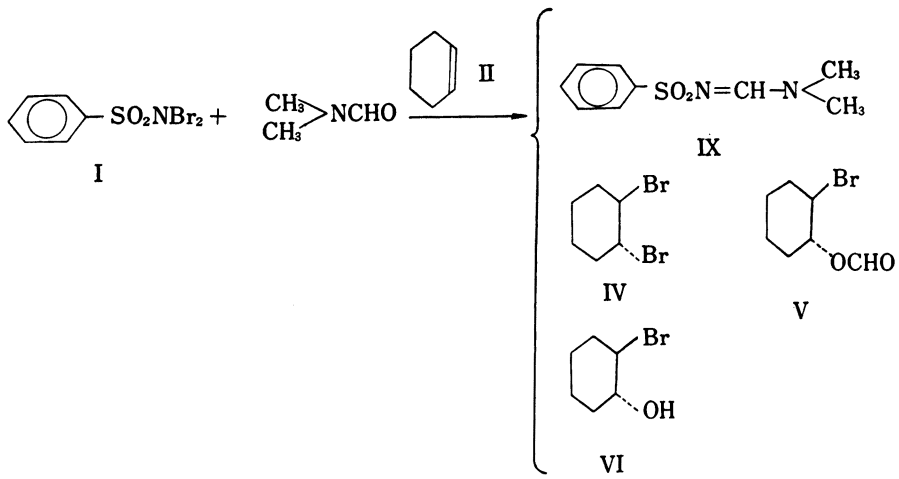


Chart 3

(J_{BX}=0.4 cps) and 6.98 τ (J_{AX}=0.6 cps) and a triplet appeared at 1.82 τ which might be assigned to an amidine-C proton.

This compound was completely agreed with the authentic N,N-dimethyl-N′-benzenesulfonylformamidine prepared from VII, benzenesulfonyl chloride, and dimethylformamide by the method of Pettit and Kadunce.[9]

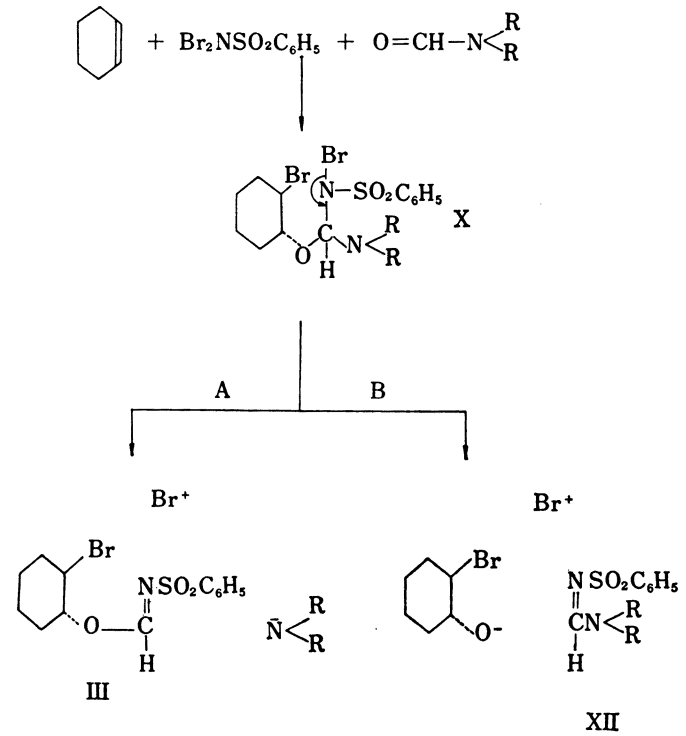
The splitting of the two methyl signals in NMR is probably due to the hindrance of the intramolecular rotation similarly to that of dimethylformamide.[10]

In order to examine whether II participates in the formation of IX or not, I was treated with dimethylformamide in the absence of II and no IX was obtained. Therefore, the participation of II for the formation of IX is evident. By-products, IV, V, and VI were also isolated from the mother liquor after the removal of IX, and III was detected too in the liquor by thin-layer chromatography (TLC).

These results are accounted for by the following mechanism, *i.e.*, I and formamides react to give an intermediate X, and the elimination of Br^+ by the E-effect of sulfonyl group fol-

10) A. Pines and M. Rabinovits, *Tetrahedron Letters*, **1968**, 3529; *J. Am. Chem. Soc.*, **91**, 1585 (1969).

lows two couses, one is the fission of the C–N bonding (A), and another is one of the C-O bonding (B). In the case of R=H, reaction with formamide, the reaction through (A) is predominant and that with dimethylformamide causes (B) by the I-effect of methyl group. The bromohydrin and its formyl derivative were probably formed by the hydrolysis of XI or III with small amount of water in the reaction system.



R=H or CH_3

Chart 4

Experimental

Reaction of N-N-Dibromobenzenesulfonamide (I) with Cyclohexene (II) in Formamide——i) *trans*-2-Bromo-1-cyclohexyl N-Benzenesulfonylformimidate (III): I (16 g) was added to formamide (40 ml), and II (15 ml) was dropwise added in the stirring mixture at room temperature during a period of about one hour. The separated solid was recrystallized from $CHCl_3$–*n*-hexane and colorless crystals (III), mp 94—95° (5.5 g, 32%) were obtained. *Anal.* Calcd. for $C_{13}H_{16}O_3$ NSBr: C, 45.09; H, 4.66; N, 4.05. Found: C, 44.95; H, 4.66; N, 3.75. IR cm^{-1} (Nujol): ν_{C-N} 1951; ν_{SO_2N} 1316, 1158. NMR: Fig. 1. III was soluble in $CHCl_3$ and CH_2Cl_2 and insoluble in MeOH, CCl_4 and *n*-hexane.

ii) *trans*-1,2-Dibromocyclohexane (IV): After the removal of III, the mother liquor was extracted with CH_2Cl_2. The CH_2Cl_2–layer was evaporated to remove the solvent and the residue was dissolved in *n*-hexane and chromatographed on a silica gel column. An eluate with 10% CCl_4 in *n*-hexane was freed from the solvent and the residue was distilled to obtain an oil of bp_{12} 100—110° (bath temperature) (0.38 g, 3%), which was identified with authentic IV by the comparison of IR spectra.

iii) *trans*-2-Bromo-1-cyclohexyl Formate (V): The column was eluted with 40% $CHCl_3$ in CCl_4, and the eluate was evaporated to remove the solvent, and the residue was distilled *in vacuo* to yield an oil, bp_{17} 122—126° (bath temperature) (0.4 g, 2%), which was identical with authentic sample by the comparison of IR and the *Rf* value of thin-layer chromatography.

iv) *trans*-2-Bromo-1-cyclohexanol (VI): The final fraction which was eluted from the column with 50% $CHCl_3$ in CCl_4 was evaporated and the residue was distilled under reduced pressure to yield an oil, bp_{20} 88—89° (0.93 g, 5%), which was agreed with authentic sample in the comparison of IR.

v) Benzenesulfonamide (VII): The formamide layer of the above CH_2Cl_2-extraction was added to H_2O (60 ml) and the separated crystals were recrystallized from MeOH to give colorless crystals, mp 151—152° (0.83 g, 11%), which showed no depression by mixed fusion with authentic VII.

Hydrolysis of III——Water was added to the hot acetone solution of III (1 g) until it became turbid. The mixture was allowed to stand for 3 days at room temperature and condensed *in vacuo* to separate a colorless solid, which was filtered and recrystallized from MeOH to obtain crystals of VII, mp 150—152° (0.1 g). The filtrate was then extracted with $CHCl_3$. The $CHCl_3$-layer was dried over anhydrous Na_2SO_4, the solvent was removed, an the residue was extracted with *n*-hexane. The *n*-hexane solution was charged on a silica gel column which was eluted with 40% $CHCl_3$ in CCl_4 to obtain an oil, bp_{13} 118—120° (bath temperature) (87 mg). The oil was identical with V by IR and TLC examinations. The column was then eluted with 50% $CHCl_3$ in CCl_4 to give next fraction of oil, bp_{13} 102—104° (bath temperature) (68 mg). This oil was identical with VI by IR and TLC comparisons.

Reaction of VIII with Cyclohexene (II)——Formamide (3 ml) was dropwise added to a mixture of I (16 g) and $CHCl_3$ (10 ml) with stirring. The separated crystals (VIII), mp 60—61° (decomp.) was filtered. *Anal.* Calcd. for $2HCONH_2 \cdot C_6H_5O_2NSBr_2$: C, 23.70; H, 2.74; Br, 39.46. Found: C, 22.92; H, 2.72; Br, 40.54. Formamide (25 ml) was added to VIII (16 g), and II (10 ml) was dropwise added to the mixture with chilling and stirring. The reaction mixture was extracted with CH_2Cl_2 and the solvent was distiled off. The residue was extracted with *n*-hexane and it was separated into *n*-hexane-insoluble and soluble parts. The insoluble part was dissolved in $CHCl_3$ and chromatographed on silica gel. $CHCl_3$-eluate was condensed and the residue was purified from $CHCl_3$–*n*-hexane to obtain crystals, mp 95° (1.68 g, 9.7%), which was identical with III by IR, TLC, and mixed fusion. The *n*-hexane-soluble part was chromatographed on a silica gel column to give IV, bp_{25} 110° (bath temperature) (0.32 g), V, bp_{25} 109—110° (0.5 g) and VI, bp_{26} 104—106° (1.1 g).

The above described formamide-layer, *i.e.* a residue after extracting with CH_2Cl_2, was diluted with H_2O to separate VII mp 150—151° (0.47 g). All products, IV, V, VI, and VII were identified with authentic samples respectively.

Reaction of I with II in Dimethylformamide——i) N,N-Dimethyl-N′-benzenesulfonylformamidine (IX): II (7 ml) was dropwise added to the mixture of I (4 g) and dimethylformamide (6 ml) with stirring at room temperature. The separated solid was recrystallized from MeOH to give colorless crystals, mp 128—129° (0.85 g, 31%). IR cm^{-1}: $\nu_{C=N}$ 1610; ν_{SO_2N} 1330, 1140. *Anal.* Calcd. for $C_9H_{12}O_2N_2S$: C, 50.93; H,5.70; N, 13.20. Found: C, 50.97; H, 5.59; N, 13.18. NMR: Fig. 2.

ii) *trans*-1,2-Dibromocyclohexane (IV): After the removal of IX, the mother liquor was evaporated to remove the solvent, the residue was dissolved in $CHCl_3$ and the solution was charged on a silica gel column, and eluted with $CHCl_3$. The solvent was removed from the eluate and the residue was extracted with *n*-hexane. The extract was chromatographed through a silica gel column. Elution of the column with 5% CCl_4 in *n*-hexane gave an oil, bp_{24} 108° (0.41 g, 13%), which was identified with authentic VI by the comparison of IR spectra.

iii) *trans*-2-Bromo-1-cyclohexyl Formate (V): The said column was subsequently eluted with 20% $CHCl_3$ in *n*-hexane, and the first eluate was distilled on a water bath to remove the solvent. The residue was distilled to obtain an oil, bp_{24} 136—137° (0.25 g, 5%), which was identical with authentic V by the comparison of IR and *Rf* value of TLC.

iv) *trans*-2-Bromo-1-cyclohexanol (VI): The second fraction was eluted with 20% $CHCl_3$ in *n*-hexane. It contained an oil of bp_{25} 98° (0.34 g, 7%). This agreed with authentic VI by the compairson of IR.