

# Reaction of N-Haloamide. X.<sup>1)</sup> Reaction of N,N-Dichlorobenzamide with Cyclohexene<sup>2)</sup>

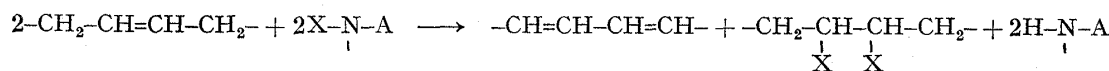
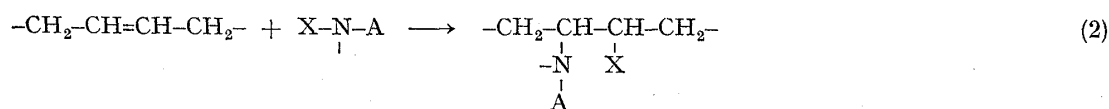
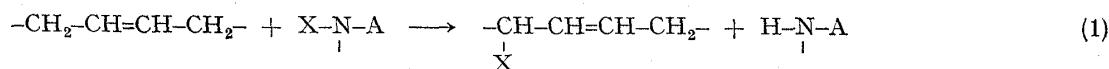
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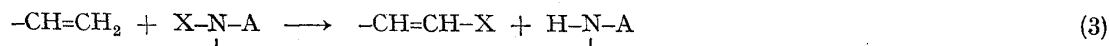
(Received August 7, 1968)

The reaction of N,N-dichlorobenzamide (I) with cyclohexene (II) was investigated and *trans*-2-chloro-1-benzamidocyclohexane (IV), 3-chloro-1-cyclohexene (V), and N-mono-chlorobenzamide (III) were obtained. Discussion of these results in comparison with that of the reaction between N,N-dichlorobenzenesulfonamide with II was made.

The mode of reaction of N-haloamide with olefin is classified into following three types: (1) Halogenation at allylic position (Wohl-Ziegler reaction). (2) Addition of N-haloamide to double bond. (3) Simultaneous dehydrogenation and halogen addition on the substrate molecule or molecules.



or



The tendency which course predominants depends on the structure of olefin and it is interesting to examine the effects of acidic group in reagent.

In the reaction of N,N-dihalobenzenesulfonamide with olefin,<sup>4)</sup> addition reaction of the second type was predominant.

This paper concerns the reaction of N,N-dichlorobenzamide with cyclohexene to compare the effects of sulfonyl with carbonyl groups.

Datta and Ghosh<sup>5)</sup> obtained N,N-dichlorobenzamide by the chlorination of benzamide in water or in diluted acetic acid. Their method requires long period to complete the reaction. Recently, Foglia and Swern<sup>6)</sup> prepared N,N-dichlorourethane by bubbling chlorine in the suspension of urethane in acetic acid-sodium acetate solution. A satisfactory result was obtained by chlorinating a suspension of benzamide in a buffer solution.

1) Part IX: *J. Med. Chem.*, **11**, 1269 (1968).

2) A part of the work was presented at the 88th Annual Meeting of the Pharmaceutical Society of Japan, Tokyo, April 1968.

3) Location: Kowakae, Higashi-Osaka, Osaka.

4) Y. Ueno, S. Takemura, Y. Ando, and H. Terauchi, *Chem. Pharm. Bull.* (Tokyo), **15**, 1193, 1198, 1328 (1967).

5) R.L. Datta and T. Ghosh, *J. Am. Chem. Soc.*, **35**, 1044 (1913).

6) T.A. Foglia and B. Swern, *J. Org. Chem.*, **31**, 3625 (1966).

An exothermic reaction occurred by the addition of cyclohexene to a solution of N,N-dichlorobenzamide (I) in carbon tetrachloride, and the crystals of N-monochlorobenzamide (III) separated out. After the removal of (III), new colorless crystals, mp 166° (IV) were obtained by alumina chromatography of the mother liquor. An oil, bp 36—37° (20 mmHg), was also obtained by the distillation under reduced pressure of the same liquor from another lot.

The crystals (IV) which have a molecular formula of  $C_{13}H_{16}ONCl$  was expected to be 2-chloro-1-benzamidocyclohexane on the analogy of the reaction of N,N-dihalobenzenesulfonamide. The expected compound (IV) was synthesized by the action of hydrogen chloride on cyclohexenimine and subsequent condensation of the resulted *trans*-2-chlorocyclohexyl ammonium chloride with benzoyl chloride. The structure of IV was examined by direct identification with this authentic sample.

The oil (V) was identical with the authentic sample of 3-chloro-1-cyclohexene.

The yields of III, IV, and V were 46%, 12%, and 14.6%, respectively.

The reaction of N,N-dichlorobenzamide and N,N-dichlorobenzenesulfonamide with cyclohexenes were illustrated in Chart 1.

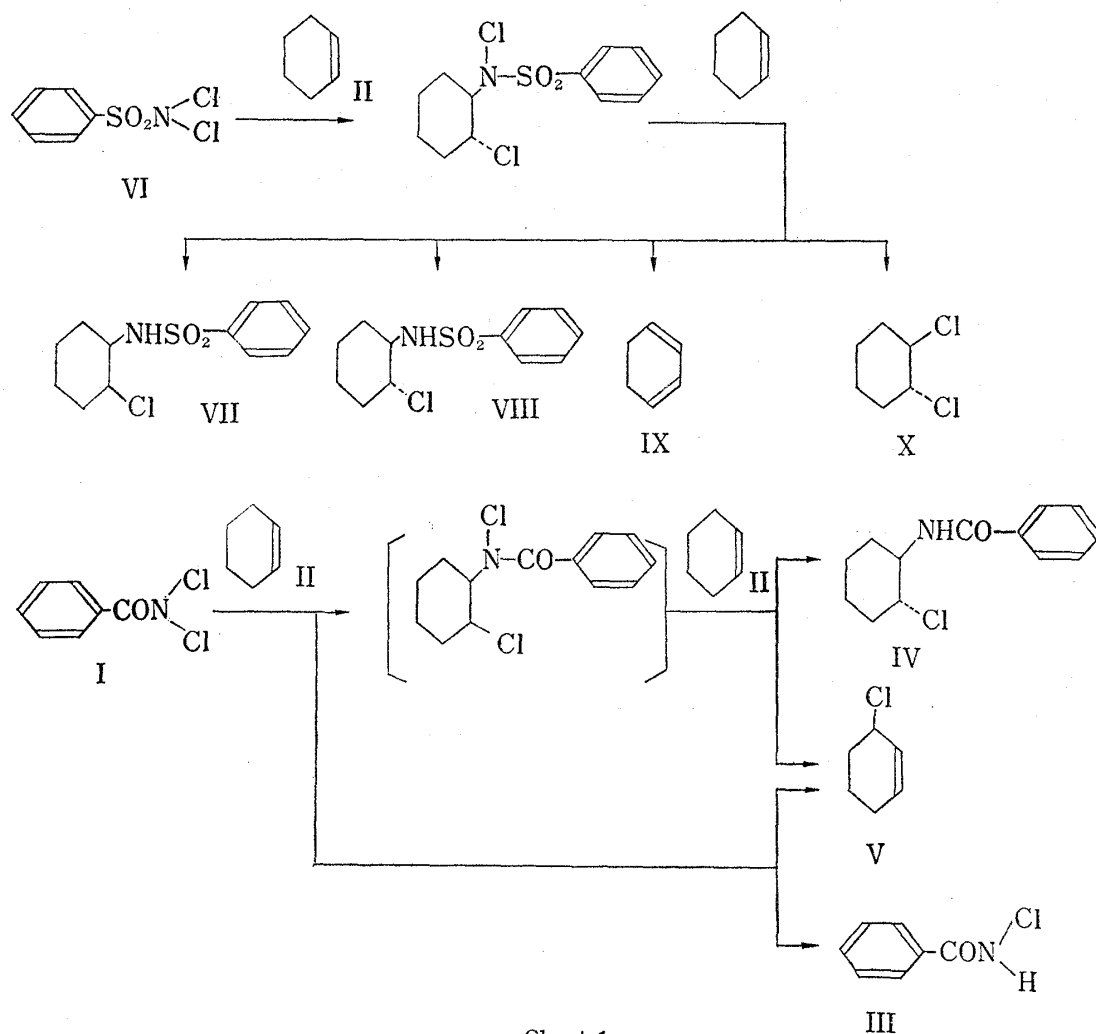


Chart 1

The difference between both reactions are first almost complete addition reaction occurred in the reaction of II with N,N-dichlorobenzenesulfonamide (VI) while, only a part of I added to II, in the case of reacting II with I, more over, *cis* and *trans* isomers (VII and VIII) were afforded in the former case, however, the formation of *cis* isomer did not found in the latter case.

We pointed out<sup>4)</sup> that N-chloro intermediate<sup>7)</sup> which formed by the reaction of II with VI reacted with excess of olefin to cause dehydrogenation and addition of chlorine to olefin molecules producing diene (IX) and dichloro compound (X), however, in the reaction of II with I any diene was not found even the reaction mixture was examined by gas chromatography and this results indicate that an allylic chlorination only occurred.

In the case of reacting I with II, monochlorobenzamide (III) was recovered and III did not further react with II by the refluxing for a long period, contrary to this, in the reaction of II with VI, slight amount of benzenesulfonamide was obtained and monochlorobenzene-sulfonamide have never been isolated.

### Experimental

**N,N-Dichlorobenzamide**—Benzamide (4.1 g, 1.125 mole), NaOAc (7 g, 2.5 mole), H<sub>2</sub>O (30 ml), and AcOH (0.7 g, 0.35 mole) were mixed, and gaseous Cl<sub>2</sub> was bubbled through the mixture with stirring until the solid changed to yellow oil. It required about 5 min. The oil was pipetted out. The residual aqueous solution was saturated with NaCl and was extracted with CHCl<sub>3</sub>. The CHCl<sub>3</sub> solution was combined with the oil and the mixture was dried over Na<sub>2</sub>SO<sub>4</sub>. After the evaporation of the solvent *in vacuo*, the residual oil was subjected to the next process. The yield of the oil was 93% of the theoretical amount. The purity of this oil was examined and found that it showed no N-H stretching band in the infrared spectrum. The active chlorine of it was determined to be 95%.

**Reaction of N,N-Dichlorobenzamide with Cyclohexene**—N,N-Dichlorobenzamide (7.1 g, 0.037 mole) was mixed with CCl<sub>4</sub> (20 ml), and the solution of cyclohexene (30 g, 0.37 mole) in CCl<sub>4</sub> (5 ml) was dropwise added to the mixture with cooling and stirring. During the addition of cyclohexene, colorless crystals separated out. After the addition was over, the reaction mixture was stirred for 30 min. Then the crystals were filtered (2.7 g, 46%), and they were recrystallized from CH<sub>2</sub>Cl<sub>2</sub>, mp 114–116°. The pure product was identified with authentic N-chlorobenzamide by the comparison of IR spectra and the mixed melting point determination.

After the removal of N-chlorobenzamide, the filtrate was condensed under reduced pressure to leave an oil (6.9 g) which was chromatographed on an alumina column. Elution of the column with CHCl<sub>3</sub> gave a crystalline substance which was purified by recrystallization from EtOH to give 1.2 g of colorless crystals, mp 166–168°. The sample was identified with authentic *trans*-2-chloro-1-benzamidocyclohexane by the comparison of IR spectra and the admixed melting point determination. *Anal.* Calcd. for C<sub>13</sub>H<sub>16</sub>ONCl: C, 65.70; H, 6.74; N, 5.90. Found: C, 65.68; H, 6.78; N, 5.89.

Another lot which was obtained by the reaction of I with II followed by the displacement of N-chlorobenzamide by filtration was fractionally distilled under reduced pressure. The first fraction bp 20–27.5° (40 mmHg) was gas chromatographed and it was found to contain the solvent (CCl<sub>4</sub>) and the excess of cyclohexene. The second fraction, bp 36–37° (20 mmHg) (12%) was identified with the authentic 3-chloro-1-cyclohexene by gas chromatography and the comparison of IR spectra.

***trans*-2-Chloro-1-benzamidocyclohexane**—*trans*-2-Chlorocyclohexyl ammonium chloride (1 g) which was obtained by the method of Winternitz<sup>8)</sup> from cyclohexenimine was dissolved in dry pyridine (10 ml), and C<sub>6</sub>H<sub>5</sub>COCl (0.7 ml) was added thereto with vigorous stirring and ice cooling. After the addition of the chloride, the stirring was continued more 10 min. H<sub>2</sub>O was then added to the mixture until any more crystals did not separated. After standing overnight, the mixture was filtered, and the resulting crystals were recrystallized from CH<sub>2</sub>Cl<sub>2</sub>, mp 166–168°. These were identified with authentic sample by the comparison of IR spectra and the mixed melting point determination.

7) Recently, W. Theilacker and H. Wessel reported that the intermediate chlorinates allyl position of II (*Ann.*, 703, 34 (1967)). According to their communication to us, however, their reaction condition is different from ours; *i.e.*, they carried out the reaction of II with VI at 35°, and obtained crystalline N-chloro compound. This was further made to react with II and 3-chloro-1-cyclohexene was obtained in 38% yield from the reaction mixture.

8) F. Winternitz, *Bull. Soc. Chim. France*, 1956, 382.