A Novel Heterocycle. Crystal Structure and Formation of *N*-Chloro-3-aza-3*H*,2,1-benzoxiodol-1-yl Chloride from the Dichloride of *o*-Iodobenzamide

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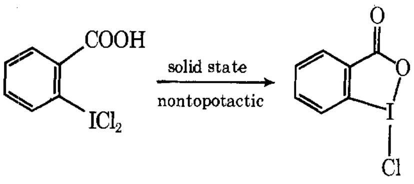
During the course of our studies of topotactic transformations involving organic polyvalent iodine compounds[1] we investigated the solid state cyclization of the iododichloride **1** to the chlorobenzoxiodole **2**.[2,3] However, **2** was found to form as a polycrystalline phase[4] of no preferred orientation relative to the single crystal structure of the parent dichloride **1** (a nontopotactic transformation) and we therefore examined the behavior of the corresponding iododichlorides **3** and **4**. These studies led to the isolation of a novel heterocycle, *N*-chloro-3-aza-3*H*,2,1-benzoxiodol-1-yl chloride (**5**), the crystal structure of which is described in this report.



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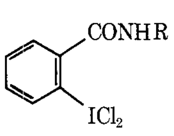
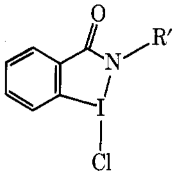


3, R = H
4, R = CH_3



5, R′ = Cl
6, R′ = H
7, R′ = CH_3

Results and Discussion

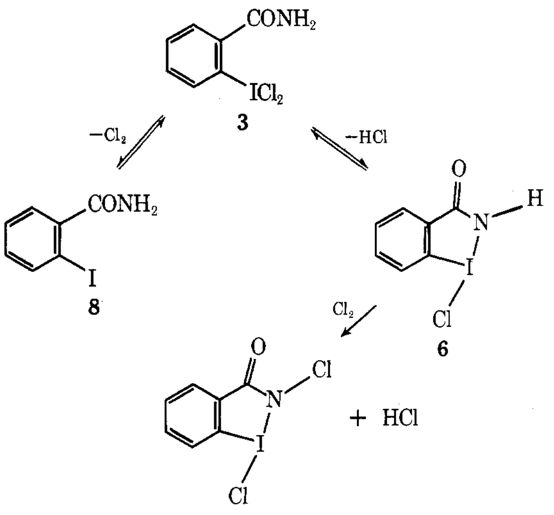
In contrast to the facile formation of crystalline **2** with loss of HCl from single crystals of **1** at room temperature, single crystals of **3** slowly lose chlorine when exposed to the atmosphere and are transformed to polycrystalline *o*-iodobenzamide (**8**). Crystals of **4**, and also the methyl ester of **1**, similarly evolve chlorine at room temperature and are converted to the parent monovalent iodine compounds.

The mode of decomposition of the crystalline dichlorides also is variable in the presence of pure solvents in which they have some solubility. Thus, the formation and subsequent crystallization of **2** occurs within a few seconds after the addition of methanol (~22°) to crystalline **1**. **4** is relatively insoluble at this temperature, but it dissolves readily in boiling methanol. The bright yellow color of **4**, which is common to all of these iododichlorides, fades upon dissolution and a nearly colorless substance, **7**, crystallizes upon cooling. Both **2** and **7** can be recrystallized from boiling methanol without appreciable decomposition. We have tentatively formulated **7** as the trivalent iodine heterocycle rather than as the isomeric *N*-chloro-*N*-methyl-*o*-iodobenzamide, primarily on the basis of its infrared carbonyl absorption which is bathochromically shifted by 26 cm^{-1} relative to that of *N*-methyl-*o*-iodobenzamide (1636 cm^{-1}). The crystal structure and solid state behavior of **7** are under investigation.

Attempts to dissolve **3** in boiling methanol or chloroform led to isolation of only **8**. However, **3** dissolves slowly in warm (<60°) methanol or chloroform to give clear yellow solutions which deposit the intensely yellow monoclinic crystals of **5** when stored at room temperature for several days, or overnight at −20°. Variable amounts of **3** and/or **8** also crystallize from the cooled solutions but the direct cyclization product, **6**, could not be isolated in this manner. An impure, nearly colorless precipitate which appears to consist primarily of **6** was obtained by acidification of an aqueous buffered solution of **3**. Attempts to recrystallize the precipitate have been unsuccessful. It disproportionates in warm methanol and approximately equal amounts of **5** and **8** are formed.

These observations are consistent with the equilibria shown in Scheme I. Similar equilibria between **1**, **2**, and *o*-$\mathrm{IC_6H_4COOH}$ have been proposed by Andrews and Keefer.[2]

Scheme I



Crystal Structure of 5. The intramolecular bond distances and angles observed in the crystal structure of **5** are shown in Figure 1. The distorted T-shape geometry of the three covalent bonds to iodine in this essentially planar molecule is similar to that in **2**[4] and several other closely related benzoxiodole structures.[5] The crystal structures of trivalent iodine compounds in our studies invariably have been found to contain intermolecular coordination bonds between the relatively electropositive trivalent iodine and some nucleophilic atom in a neighboring molecule. In most structures an oxygen coordinates with iodine, as is the case in the three polymorphs of **1** which, despite their different crystal structures, contain similar coordination bonds involving the carbonyl oxygen atom. The geometry of oxygen coordination has been found to be remarkably constant.[6] Monovalent halogen atoms also can coordinate with the trivalent iodine[5] and it is this coordination mode which is present in the crystal structure of **5**. Atom Cl-2 closely approaches (3.36 Å) the iodine of a screw-related molecule resulting in an approximately square planar arrangement of the four atoms, C-1, N, Cl-2, and Cl-2 (intermolecular) about iodine (Figure 1).

Since these coordination bonds are established between molecules related by a screw axis, the crystal structure consists of infinite chiral chains of coordinated molecules extending along the crystallographic *b* axis. The space group is $P2_1$ and therefore a single crystal is *chiral* and contains only one of the enantimorphs of the chiral chains; however,

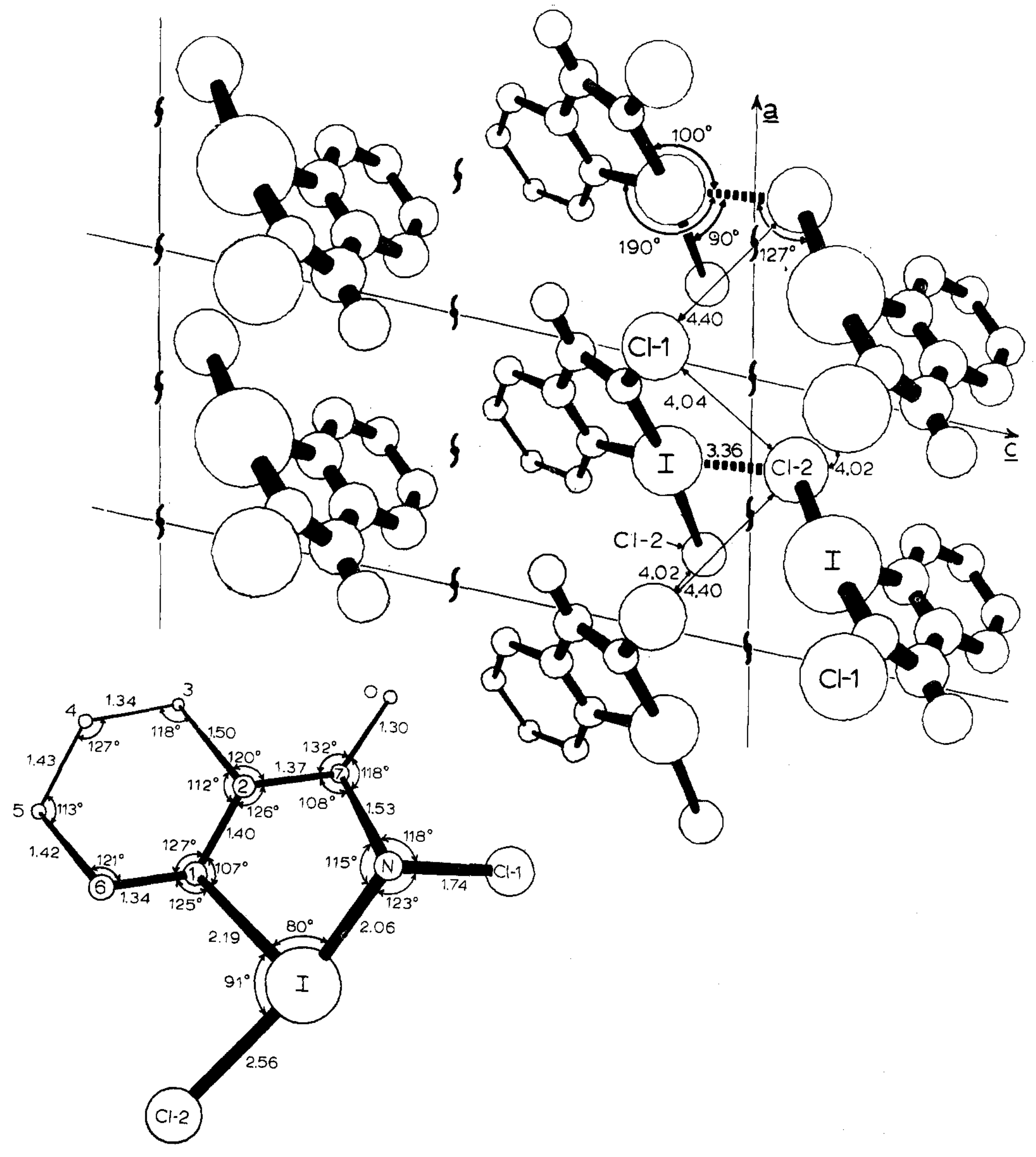


Figure 1. The crystal structure of **5**, viewed along the *b* axis. The coordination bond between I and Cl-2 of a screw related molecule is indicated by a broken line. Distances are given in ångstroms. Lower left: bond distances and angles in **5**. Esd values for bonds to I fall in the range 0.02–0.05 Å. The esd is 0.05 Å for the N–Cl bond, and 0.07–0.11 Å for the other bonds. Esd values for bond angles about I are ~1°, while those about the lighter atoms are 2–5°.

we have not attempted to establish the absolute configuration of the crystal used in the analysis. Intermolecular contacts between chains are dominated by Cl–Cl contacts ranging from 3.33 to 4.40 Å.

Experimental Section

Preparation of the Dichlorides 3 and 4. The preparation of **3** from **8** by chlorination in chloroform has been reported;[7] **4** was prepared in an analogous manner, mp 135–142° dec. Anal. Calcd: I, 38.25. Found: I, 38.9.

Formation of 5 from 3. 3 (50 mg) was dissolved slowly in 5 ml of warm (<60°) methanol. Yellow plates (8 mg) of **5** were isolated after cooling the methanolic solution overnight at −20°: mp 187–192° dec; ir (KBr) no λ_{max} from 4000 to 3100 cm^{-1}, 1660 (s), 1588 (m), 1565 (m), 1452 (s), 1440 (s), 1283 (s), 1234 (s), 1142 (s), 1114 (m), 1000 (m), 780 (m), 730 (s), 650 cm^{-1} (m). The mass spectrum exhibited the molecular ion peak at 315. Anal. Calcd: I, 40.19. Found: I, 39.90.

Preparation of 6. 3 (0.5 g) was dissolved slowly in aqueous pH ~7 phosphate buffer. The solution was filtered to remove a small amount of insoluble material. Acidification of the filtrate with dilute HCl gave a nearly colorless precipitate which was dried over P_2O_5 in vacuo, mp 127–129°. The mass spectrum exhibited a peak (*m/e* 281) corresponding to the molecular ion of **6**. This material rapidly oxidized a KBr disk which then displayed an ir spectrum similar to that of **8**.

Formation of 5 from 6. Fifty milligrams of the above precipitate (**6**) were dissolved in 8 ml of hot methanol and the solution was allowed to evaporate to dryness at room temperature. The crystalline residue was contained in two separate zones on the walls of the test tube. The first, 21 mg (75%) of yellow crystals, was identified as **5** by ir and TLC. The second zone consisted of ~18 mg (80%) of colorless crystals of **8**.

Preparation of 7. 4 dissolves readily in boiling methanol. Colorless needles of **7** were obtained after cooling the solution overnight: mp 182–186°; ir (KBr) 1610 (s), 1586 (m), 1568 (m), 1455 (m), 1439 (m), 1356 (m), 1028 (w), 1008 (m), 975 (m), 772 (w), 728 (s), 653 cm^{-1} (m). The mass spectrum exhibited the molecular ion peak for **7** at 295. Anal. Calcd: I, 42.98. Found: I, 42.81.

Crystal Structure Determination. The unit cell constants a = 5.78 (1), b = 6.49 (1), c = 12.88 (2) Å, and β = 101.7 (1)° were determined from Al-calibrated Weissenberg photographs. The diffraction symmetry and systematically absent reflections (0*k*0, *k* odd), together with the measured crystal density (2.27 g cm^{-3}), suggested either space group $P2_1$ or $P2_1/m$ with Z = 2. Of the 731 intensities measured on a Pailred diffractometer (monochromatic Cu Kα), 597 with intensity $\geq 3\sigma(I)$ were used for the solution and refinement of structure. The statistical distribution of these intensities (corrected for absorption, μ = 330 cm^{-1}) and the successful progress of the structure analysis verified our initial assignment of crystalline **5** to space group $P2_1$.

The structure was solved by Patterson and Fourier methods but no attempt was made to locate the hydrogen atoms. Least-squares refinements of the atomic coordinates and thermal parameters (anisotropic for I and Cl and isotropic for C, N, and O) converged to R = 0.07. Various refinements of the multiplicities of C-7, O, and N in the final stages of the analysis confirmed the presence of the *N*-chloro lactam moiety in **5**.

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Registry No.—**3**, 5152-34-1; **4**, 27305-20-0; **5**, 27305-23-3; **6**, 3580-04-9; **7**, 27305-21-1.

Supplementary Material Available. Tables of fractional coordinates and temperature factors will appear following these pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105 × 148 mm, 24× reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Journals Department, American Chemical Society, 1155 16th St., N.W., Washington D. C. 20036. Remit check or money order for $4.00 for photocopy or $2.50 for microfiche, referring to code number JOC-75-2129.

References and Notes

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Unusual Reaction of 4-Mercapto-1,2,3-benzotriazine with *N*-(2,4-Dibromophenyl)benzohydrazonyl Bromide

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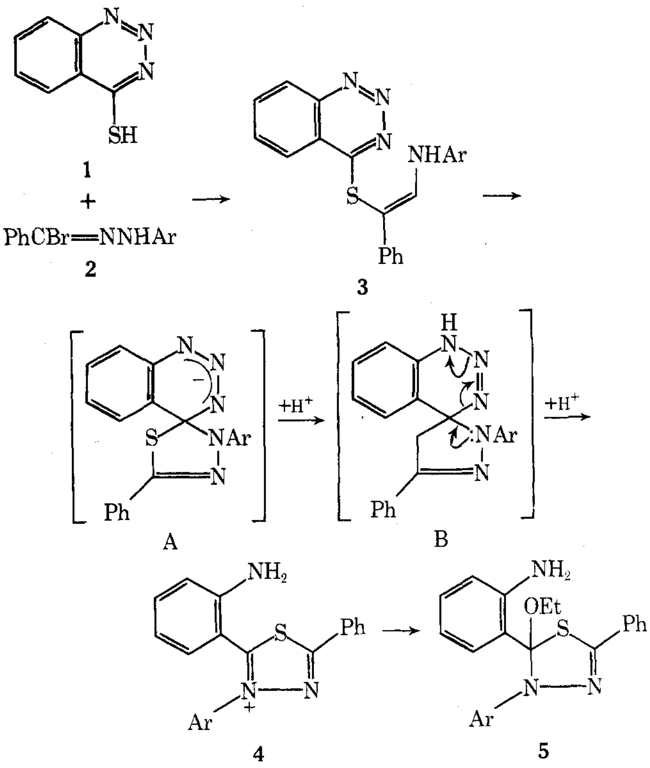
During the course of studies on hydrazonyl halides, we have noted an unusual reaction between 4-mercapto-1,2,3-benzotriazine (**1**), *N*-(2,4,-dibromophenyl)benzohydrazonyl bromide (**2**, Ar = 2,4-$Br_2C_6H_3$), and ethanol in the presence of triethylamine.

Reactions of aryl mercaptans with hydrazonyl halides in the presence of base give aryl thiohydrazonates which are normally stable under the conditions of formation.[1] In the present case we envisage deprotonation by triethylamine of the thiohydrazonate **3** formed from **1** and **2**, followed by intramolecular nucleophilic addition of the anion to C-4 of the triazine.[2] Reversible protonation of the spirocyclic intermediate A at N-1 or N-3 of the triazine to give, e.g., B may now be followed by aromatization of the newly formed ring, opening of the triazine ring with loss of N-3 and N-2 as nitrogen, and protonation of N-1 to give the thiadiazolium ion **4**. We have confirmed[3] that such thiadiazolium ions add ethoxide ion equivalent at C-2(5) when treated with ethanolic sodium ethoxide or ethanol–triethylamine and so progression of **4** to the observed product **5** is readily understood. The ease of reaction is notable in view of the stability of simple aryl thiohydrazonates.[1]

This case and the recently reported[4] formation of 2-(2-aminophenyl)-5-mercapto-1,3,4-thiadiazole from 4-hydrazinoquinazoline and CS_2 in the presence of KOH represent unusual Smiles-type rearrangements[5] in which the migrating aryl ring (1,2,3-benzotriazin-4-yl or quinazolin-4-yl) collapses while the cyclic transition state for the migration is consolidated as a new ring (1,3,4-thiadiazole), closure occurring by C–N or C–S bond formation as appropriate.



Experimental Section

NMR data were obtained with a Varian A-60 spectrometer (tetramethylsilane as internal standard).

4-Mercapto-1,2,3-benzotriazine was conveniently prepared from 1,2,3-benzotriazin-4-one and phosphorus pentasulfide in pyridine or toluene.[6]

5-(2-Aminophenyl)-4-(2,4-dibromophenyl)-5-ethoxy-2-phenyl-Δ^2-1,3,4-thiadiazoline (5). A mixture of 1.63 g (0.01 mol) of **1**, 4.33 g (0.01 mol) of **2**,[7] and 30 ml of ethanol was stirred at room temperature and 2 ml of triethylamine was added. There was an immediate evolution of gas. After 30 min, solvent was removed in vacuo and the pale brown solid was washed with water and dried to give 2.8 g (53%) of **5** which crystallized from hexane as fawn needles: mp 136–137°; ir (Nujol–hexachlorobutadiene mulls) 3500 and 3400 (NH), 1600, 1570, 1550, and 1480 (aromatic C=C and C=N),[8] 1460 and 1375 (aliphatic CH), 1325, 1300, 1220, 1150, 1105, 1075, 1060, 1050, 980, 970; 870, 820, 765, 745, 725, and 690 cm^{-1} (aromatic C–H; mono-, 1,2-di-, and 1,2,4-trisubstituted benzene); NMR ($CDCl_3$) δ 7.90–6.42 (m, 12 H), 4.39 (s, br, 2 NH, exchangeable with D_2O), 3.82 (m, 2 H), and 1.35 ppm (t, 3 H).

Anal. Calcd for $C_{22}H_{19}Br_2N_3OS$: C, 49.5; H, 3.6; Br, 30.0; N, 7.9. Found: C, 49.8; H, 3.8; Br, 30.5; N, 7.7.

Registry No.—**1**, 2536-88-1; **2** (Ar = 2,4-$Br_2C_6H_3$), 2516-46-3; **5** (Ar = 2,4-$Br_2C_6H_3$), 55298-74-3.

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