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Synthesis and Structure of Benziodazoles

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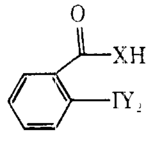
N-Alkylbenziodazoles **5a** and **5b** were prepared by dehydrochlorination of amides **3a** and **3b**. An X-ray structure determination showed **5b** to be a tricoordinate iodinane and not *N*-chloroamide **6b**. The chemical shift of the carbon α to iodine was found to be sensitive to the oxidation state of iodine. Preparation of a six-membered iodinane heterocycle, **12**, was unsuccessful.

Brief reports of iodinanes (tricoordinate iodine) with nitrogen and chlorine ligands have been made by several groups.[1,2] Naae and Gougoutas[2] have reported the preparation and crystal structure of a *N*-chlorobenziodazole. Only one *N*-alkylbenziodazole (**2b**) has been described and the structural assignment was not absolute.[2] This note outlines the synthesis of two *N*-alkylbenziodazoles **5a** and **5b**. An X-ray structure determination confirms that **5b** exists as a tricoordinate iodinane.

Results and Discussion

Aryl dichloroiodinanes are bright yellow highly crystalline compounds. Heating these materials in chloroform induces reductive elimination of chlorine to give the monovalent iodides.[3] Acid **1a** is a notable exception and with or without solvent cyclizes to **2a**.[4] Amide **1b** is reported to undergo a similar cyclization on heating in methanol.[2] No yield was reported. Our interest in *N*-alkylated benziodazoles, of which **5a** and **5b** are examples, led us to this method. Adding **4a** to boiling methanol gives reduced amide **3a** as the major product. Examination of the ^{13}C NMR spectrum of the crude reaction mixture indicates only a small amount (<5%) of **5a** is formed (see later text for ^{13}C assay technique). Cyclization does not compete favorably with reductive elimination of chlorine.



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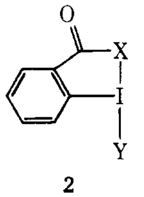
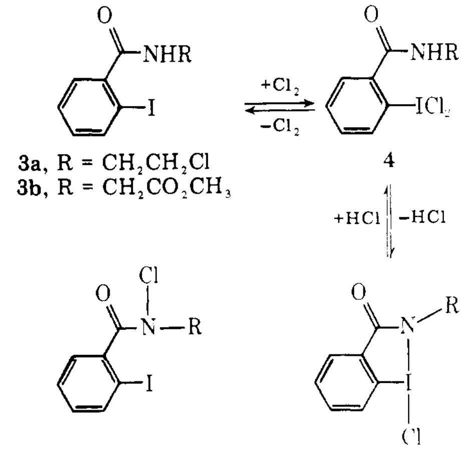


2

a, X = O; Y = Cl
b, X = NCH_3; Y = Cl
c, X = O; Y = OH

The 1-chloro-3-oxobenziodazoles **5a** and **5b** can be prepared in good yields if the respective dichloride (**4**) is added in portions to a stirred solution of acetic acid saturated with sodium acetate. The intense yellow color of the dichloride rapidly disappears and a white precipitate forms. Addition of cold water and filtration give **5a** and **5b** in yields of 79 and 84%, respectively.

Iodinanes **5a** and **5b** are stable at ambient temperature in the dark. These compounds are not hydrolyzed when washed with water and are unaffected by recrystallization from methanol. Bubbling HCl into a stirred mixture of **5a** and chloroform gives a homogeneous solution. Boiling this solution followed by removal of the solvent gives the reduction product **3a**.



3a, R = CH_2CH_2Cl
3b, R = $CH_2CO_2CH_3$
4
6
5

Field desorption mass spectra of **5a** and **5b** both exhibit strong molecular ions. Minor peaks are found for $M^{+\cdot} - Cl$. The proton spectra (Me_2SO-d_6) are characterized by low-field multiplets for the protons ortho to iodine. An absorption at δ 8.52 is observed for **5b** as compared with δ 7.89 for the same proton in the reduced species **3b**. This anisotropic effect of the I–Cl hypervalent bond is similar to that observed for the S–Cl bond in chlorosulfuranes.[5]

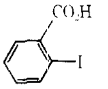
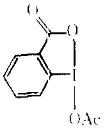
An X-ray structure determination described in the next section establishes an iodinane structure for **5b**, in the solid state. In solution this substance could exist in equilibrium with the *N*-chloro isomer **6b**. On obtaining a routine ^{13}C spectrum of **5b**, we have noticed a striking downfield shift of the carbon α to iodine, relative to the same carbon in the low valent precursor **3b** (see Table I). It should be noted that the carbon of monovalent aryl iodides is dramatically shielded relative to an unsubstituted carbon (note iodobenzene). NMR data on several compounds of known oxidation state are listed in Table I. Spectra of compounds **7–10** (structures of which are well defined in the literature[6]) clearly reflect the oxidation state of iodine. Chemical shift correlation of **5b** (also **5a**) with these standards is good and suggests a tricoordinate iodinane structure is predominant in solution. A rapid interchange between **5b** and a small amount of **6b** cannot, of course, be ruled out.[7]

Our efforts to prepare six-membered iodinane heterocycle **12** have failed. The procedure described above gives the *N*-chloro isomer **13** (26%) as confirmed by the chemical shift of the α carbon (δ 90.12). We have been unable to convert **13** to **12** either thermally or photochemically.

Molecular Structure of 5b. Pertinent intramolecular

0022-3263/79/1944-1447$01.00/0

Table I

compd	registry no.	chemical shift of carbon α to iodine (ppm)
C_6H_5I (7)	591-50-4	94.90
$C_6H_5I(OAc)_2$ (8)	3240-34-4	122.27
 (9)	88-67-5	94.15
 (10)	1829-26-1	118.52
3a	69238-58-0	93.5
5a	69238-59-1	116.54
3b	69238-60-4	92.16
5b	69238-61-5	116.47
11	13538-28-8	90.89
13	69258-28-2	90.12

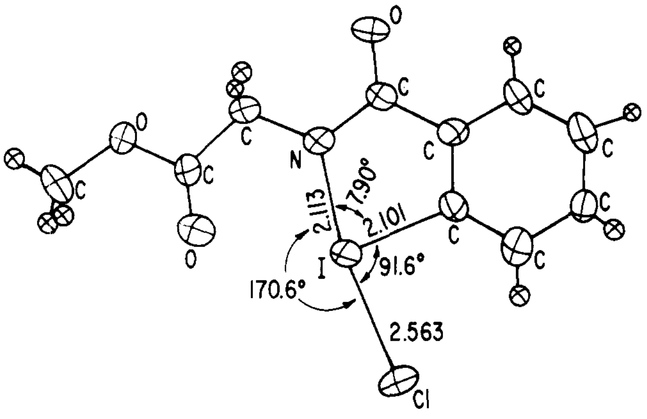
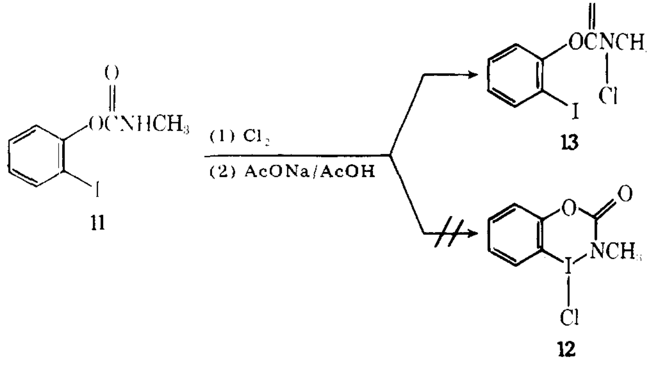


Figure 1. Pertinent bond distances and angles for **5b**. Estimated standard deviations for the bond distances are ±0.001 Å for I–Cl, ±0.004 Å for I–N, and ±0.006 Å for I–C. The thermal ellisoids for the hydrogen atoms are artificially small for clarity purposes.

bond distances and bond angles of **5b** are shown in Figure 1. The tricoordinate iodinane is slightly distorted from perfect TBP geometry. Mean-plane calculations for the iodine atom and the three coordinated atoms demonstrate the bonding geometry about iodine to be planar within ±0.05 Å. Similar planarity and ligand angle distortions have been found for **2c**.[8]

Of major interest is the hypervalent bond lengths. The I–N length is not notably different than the sum of normal covalent radii (2.08 Å). The I–Cl bond in contrast is significantly (0.24 Å) longer than the calculated sum. If the ligands were the same, hypervalent bonding theory would predict a slight elongation of both bonds.[9] That the I–Cl bond is long while the I–N bond is not can be explained on electronegativity differences. The formal negative charge on the apical ligands is best accommodated by Cl. The bond becomes more ionic in character and as a result is lengthened. This high polarizability of the iodine hypervalent bond is also observed[8,10] for **2c**. The endocyclic I–O bond is 0.31 Å longer than the sum of the covalent radii while the exocyclic I–O bond is in agreement with this calculated value.



Experimental Section

General. Melting points were determined on a Laboratory Devices Mel-temp apparatus and are uncorrected. NMR spectra were obtained on Varian T-60 and JEOLCO FX-100 spectrometers. Results are reported on the δ scale, parts per million (ppm) downfield from tetramethylsilane internal standard. Mass spectra were obtained on a Varian CH-7 mass spectrometer. Analyses were performed by Atlantic Microlab Inc.

***N*-(2-Chloroethyl)-2-iodobenzamide (3a).** To a CH_2Cl_2 (200 mL) solution of 2-iodobenzoyl chloride (14.12 g, 53.0 mmol) and 2-chloroethylamine hydrochloride (6.15 g, 53.0 mmol) was slowly added triethylamine (14.77 mL, 106 mmol). After being stirred 10 min, the solution was extracted with water, 10% HCl, and 10% NaOH and dried ($MgSO_4$) and the solvent was removed to give an oil. Crystallization from $CHCl_3$–hexane gave 13.1 g (42.3 mmol, 79.8%) of amide **3a:** mp 102–4 °C; ^1H NMR $CDCl_3$ δ 3.70 (m, 4, $-CH_2CH_2-$), 6.53 (s, 1, NH), 6.83–7.44 (m, 3), 7.77 (d, J = 9 Hz, 1); mass spectrum (70 eV) *m/e* 309 ($M^{+\cdot}$), 274 ($M^{+\cdot} - Cl$).

Anal. Calcd for C_9H_9ClINO: C, 34.92; H, 2.94; N, 4.53; Cl, 11.45. Found: C, 34.88; H, 2.97; N, 4.46; Cl, 11.56.

Methyl *N*-(2-Iodobenzoyl)glycinate (3b). To a stirred, cold (ice bath) mixture of glycine methyl ester hydrochloride (5.65 g, 45.03 mmol) in CH_2Cl_2 (300 mL) was slowly added triethylamine (12.55 mL, 90.06 mmol) and 2-iodobenzoyl chloride (12.0 g, 42.03 mmol). After being stirred for 1 h, water (200 mL) was added and the organic layer separated. This was washed with 10% HCl (1 × 100 mL) and 5% NaOH (2 × 75 mL). The solution was dried ($MgSO_4$) and the solvent removed to give a yellow-brown solid. Recrystallization from ethyl acetate–hexane gave 13.4 g (42.0 mmol, 93.3%) of amide **3b:** mp 100–2 °C; ^1H NMR ($CDCl_3$) δ 3.78 (s, 3, OCH_3), 4.19 (d, J = 5 Hz, 2, NCH_2), 6.57 (broad, s, 1, NH), 6.89–7.49 (m, 3), 7.89 (d, J = 8 Hz, 1); mass spectrum (70 eV) *m/e* 319 ($M^{+\cdot}$), 260 ($M^{+\cdot} - CO_2CH_3$).

Anal. Calcd for $C_{10}H_{10}INO_3$: C, 49.87; H, 3.59; N, 4.16. Found: C, 49.87; H, 3.58; N, 4.15.

1-Chloro-2-carbomethoxymethyl-1,3-dihydro-3-oxo-1,2-benziodazole (5b). Chlorine gas was bubbled into a stirred, cold CH_2Cl_2 (200 mL) solution of amide **3b** (9.0 g, 28.2 mmol). After 10 min, CCl_4 (100 mL) was added and the mixture stirred (5 °C) for 10 min longer. The yellow precipitate was collected and dried (15 min at 0.3 mm).

The dichloride was added in portions to acetic acid saturated with sodium acetate (175 mL). The heterogenous mixture was stirred for 1 h and ice (200 g) was added. After the ice melted, the mixture was filtered and the solid collected and washed with water. The powder was dried and washed well with ether to give 8.4 g (23.8 mmol, 84.3%) of iodinane **5b**: mp 170–3 °C dec; ^1H NMR (Me_2SO-d_6) δ 3.76 (s, 3, OCH_3), 4.54 (s, 2, NCH_2), 7.69–8.25 (m, 3), 8.52 (d, J = 8 Hz, 1); mass spectrum (FD) *m/e* 353 ($M^{+\cdot}$ for ^{35}Cl), 355 ($M^{+\cdot}$ for ^{37}Cl).

Anal. Calcd for $C_{10}H_9ClINO_3$: C, 37.64; H, 3.17; N, 4.39. Found: C, 37.66; H, 3.17; N, 4.40.

1-Chloro-2-(2-chloroethyl)-1,3-dihydro-3-oxo-1,2-benziodazole (5a). Chlorine gas was bubbled through a stirred, cold (ice bath) CH_2Cl_2 (150 mL) solution of amide **3a** (8.0 g, 25.8 mmol). After being stirred for 15 min, CCl_4 (100 mL) was added and the mixture was stirred at 5 °C for 15 min. The yellow dichloride was collected and dried (ca. 15 min at 0.4 mm).

The dichloride was added in portions to a stirred solution of acetic acid saturated with sodium acetate (200 mL). A white solid formed immediately. After the solution was stirred for 30 min, ice (200 g) was added. A white solid was collected and dried in vacuo. The powder was stirred in ether (100 mL) and the solid collected to give 7.03 g (20.4 mmol, 79.1%) of iodinane **5a:** mp 147–50 °C dec; ^1H NMR (Me_2SO-d_6) δ 3.94 (4, m, $-CH_2CH_2-$), 7.59–8.17 (m, 3), 8.44 (d, 1, J = 8 Hz, **H** ortho to I); mass spectrum (high-resolution field desorption) *m/e* 342.90047 (calcd for $C_9H_8Cl_2INO$, 342.90275).

Anal. Calcd for $C_9H_8Cl_2INO$: C, 31.41; H, 2.35; Cl, 20.61; I, 36.89; N, 4.07. Found: C, 31.62; H, 2.41; Cl, 20.39; I, 37.06; N, 4.14.

Table II. Summary of Crystal Data

formula	$C_{10}H_9ClINO_3$
formula wt	353.55
a, Å	9.007 (3)
b, Å	9.602 (3)
c, Å	7.818 (2)
α, deg	81.88 (2)
β, deg	109.48 (2)
γ, deg	116.99 (2)
V, Å	568.0
Z	2
density (calcd), g/cm^3	2.07
(obsd), g/cm^2	2.04
μ, cm^{-1}	30.8
space group	$P\bar{1}$
crystal size, mm	~cube 0.25
temp, °C	21 ± 2
radiation	Mo K$\bar{\alpha}$ (0.71069 Å) using graphite crystal monochromator
scan speed	variable Scan rate 2.0–18.0 deg/min for θ–2θ scans
scan ranges	Mo Kα_1 − 1.0° to Mo Kα_2 + 1.0°
ratio scan time/ background time	0.5
unique data	$1936 F_o > 2.0\sigma(F_o)$
final residuals	$R_1 = 0.033$, $R_2 = 0.046$
error in observation of unit wt	0.875

Reaction of Iodinane 5a with HCl. A tared flask was charged with iodinane **5a** (0.38 g, 1.10 mmol) and chloroform (20 mL). HCl gas was passed into the solution for 10 min and then the solution was boiled for 15 min. Removal of the solvent gave 0.334 g (1.08 mmol, 98%) of amide **3a**, identified by NMR and mixture melting point.

***O*-2-Iodophenyl *N*-Methylcarbamate (11).** Methyl isocyanate (1.53 g, 26.9 mmol) and 2-iodophenol (5.91 g, 26.9 mmol) were stirred in 5 mL of benzene and 0.2 mL of pyridine for 30 min. The solid which formed was dissolved in CCl_4 and extracted with 10% NaOH. Drying and solvent removal gave 6.9 g (24.9 mmol, 93%) of carbamate **11**: mp 105–6 °C; ^1H NMR ($CDCl_3$) δ 2.89 (d, 3, $NC\mathbf{H}_3$), 5.27 (s, 1 NH), 6.77–7.55 (m, 3), 7.83 (m, 1, **H** ortho to I); mass spectrum (80 eV) *m/e* 277 ($M^{+\cdot}$), 220 ($M^{+\cdot} - CH_2NCO$).

Anal. Calcd for $C_8H_8INO_2$: C, 34.68; H, 2.92; N, 5.06. Found: C, 34.63; H, 2.95; N, 5.01.

***O*-(2-Iodophenyl) *N*-Chloro-*N*-methylcarbamate (13).** Chlorine gas was passed through a cold (5 °C) CH_2Cl_2 (50 mL) solution of carbamate **11** (4.98 g, 18.0 mmol) until no more solid was formed. This was filtered and the yellow solid dried (0.3 mm) briefly. The dichloride was added in portions to acetic acid saturated with sodium acetate (75 mL). The solution became cloudy but no precipitate formed. Water (150 mL) and chloroform (150 mL) were added. The organic layer was separated and washed with water. Drying ($MgSO_4$) and solvent removal gave a brown oil. ^1H NMR indicated the oil was a mixture of starting **11** and a new product in a 2:3 ratio. Chromatography on Florisil (95:5, cyclohexane–ethyl acetate) gave 1.45 g (4.6 mmol, 25.9%) of pure **13** as a liquid: ^1H NMR ($CDCl_3$) δ 3.48 (s, 3, NCH_3), 6.78–7.53 (m, 3), 7.80 (d, 1, J = 8 Hz, **H** ortho to I); mass spectrum (FD) *m/e* 311 ($M^{+\cdot}$ for ^{35}Cl), 313 ($M^{+\cdot}$ for ^{37}Cl).

Anal. Calcd for $C_8H_7ClNO_2$: C, 30.84; H, 2.27; Cl, 11.38; I, 40.74; N, 4.50. Found: C, 30.66; H, 2.33; Cl, 11.46; I, 40.85; N, 4.41.

Crystallography. Data Collection. Crystal characterization and data collection procedures used the Syntex $P2_1$ Fortran Data Collection System[11] and the Syntex P2$_1$ Autodiffractometer. The crystal used for data collection, grown by slow solvent evaporation from a concentrated solution, was sealed in a thin-walled glass capillary, to prevent any possible decomposition during data collection, and optically centered on the four-circle goniometer. The lattice constants and orientation matrix used for data collection were obtained from the least-squares refinement of the diffraction geometry for 25 carefully centered reflections (5° < 2θ Mo Kα < 25°). Lattice constants and pertinent data collection parameters are given in Table II. θ–2θ scan data were collected having 0° ≤ 2θ Mo Kα ≤ 50.0°. The observed intensities for three standard reflections, measured every 150 reflections, showed no unusual deviations during data collection and the 2020 unique data were reduced to a set of relative $F_0{}^2$ after corrections for Lorentz and polarization effects. An empirical absorption correction was applied to all data.

Crystallography. Structural Solution and Refinement. The computer programs used for the structural solution and refinement were those of Syntex XTL Structure Determination System utilizing a Nova 1200 minicomputer. The atomic coordinates for the iodine and chlorine atoms were derived from a three-dimensional Patterson function. Their positional parameters were refined in one cycle of full-matrix least-squares refinement to give $R_1 = (\Sigma||F_o| - |F_c||)/\Sigma|F_o| = 0.36$ and $R_2 = [\Sigma\omega(|F_o| - |F_c|)^2/\Sigma|F_o|^2]^{1/2} = 0.39$. The remaining 13 non-hydrogen atom positions were located from a single difference Fourier synthesis using phases from the above refinement. These 16 atoms were refined first employing isotropic and then anisotropic thermal parameters to give $R_1 = 0.035$. Coordinates for the nine hydrogen atoms were located from a difference Fourier map and included in the final full-matrix least-squares refinement with fixed isotropic thermal parameters. The final refinement resulted in discrepancy indicators of $R_1 = 0.033$ and $R_2 = 0.046$. A final difference Fourier map failed to reveal anything of structural significance. A two-dimensional ORTEP drawing of the molecule may be seen in Figure 1. Pertinent bond distances and angles are illustrated on the drawing. See paragraph at the end of the paper concerning supplementary material for complete tables of positional and thermal parameters and bond distances and bond angles.

Registry No.—**4a**, 69238-62-6; **4b**, 69238-63-7; **11** dichloride, 69238-64-8; 2-iodobenzoyl chloride, 609-67-6; 2-chloroethylamine hydrochloride, 870-24-6; glycine methyl ester hydrochloride, 5680-79-5; methyl isocyanate, 624-83-9; 2-iodophenol, 533-58-4.

Supplementary Materials Available: Tables of thermal parameters, refined atomic coordinates, bond distances and angles, least-squares mean planes, and crystal data (Tables III–VI) and a perspective drawing of **5b** (6 pages). Ordering information is given on any current masthead page.

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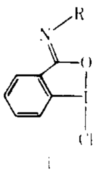

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