Synthesis and Structure of 1-Alkynyl-1,2-benziodoxol-3(1*H*)-ones

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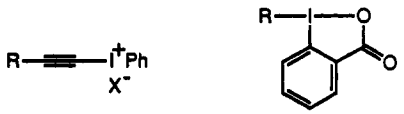
1-Alkynyl-1,2-benziodoxol-3(1*H*)-ones **3** were synthesized by the reaction of 1-alkynyltrimethylsilanes with 1-hydroxybenziodoxolone **4** in the presence of BF_3·Et_2O. The IR and NMR spectra of **3** and the X-ray structure of 1-(cyclohexylethynyl)benziodoxolone **3a** are in good agreement with the cyclic benziodoxolone structure in solution as well as in the solid state. The *A* value of the substituted ethynyl group of **3a** was determined to be 1.33 kcal/mol by the dynamic ^1H NMR.

Alkynylphenyliodonium salts containing a variety of counterions, such as tetrafluoroborates,[1] tosylates,[2] triflates,[3] phosphates,[4] and halides[5] have been synthesized and well-characterized. It seems to be difficult, however, to synthesize the corresponding alkynyliodonium carboxylates **1**, since they readily undergo Michael-type addition of the carboxylates to the electron-deficient carbon–carbon triple bond in an intra- or an intermolecular fashion. Stang and co-workers have reported that the reaction of [(diacyloxy)iodo]benzene with lithium acetylides and the anion exchange reaction of alkynylphenyliodonium tosylates with carboxylates involve an intermediate formation of alkynylphenyliodonium carboxylates **1**, which decompose to the acetylenic carboxylates and iodobenzene through Michael-type addition of the carboxylate nucleophile.[4a,6] We have reported that the reaction of alkynylphenyliodonium tetrafluoroborates **2** with sodium acetate or acetic acid in the presence of water affords α-acetoxy ketones through Michael-type addition of an acetoxy group.[7] On the other hand, alkynyliodonium trifluoroacetates have been isolated as a crystalline compound, presumably due to the relatively low nucleophilicity of the counterion, which would decrease the rate of decomposition of the iodonium trifluoroacetates.[8]



1: X = $R'CO_2$
2: X = BF_4

3a: R = cyclo-$C_6H_{11}C{\equiv}C$
3b: R = n-$C_8H_{17}C{\equiv}C$
3c: R = t-Bu$C{\equiv}C$
4: R = OH
5: R = Ph

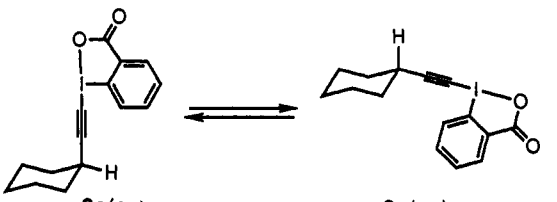
Cyclic aryliodinanes have been shown to be more stable than their acyclic analogues, preumably due to conjugative overlap of the lone pairs of electrons on the iodine atom with π-orbitals of the aromatic nucleus.[9] It occurred to us that the presence of an ortho carboxyl moiety on the aromatic ring of alkynylaryliodinanes would make it possible to form a five-membered iodoxolone heterocycle, as shown in **3**, and thereby intramolecular conjugate addition of the carboxylate group to the triple bond might become unfavorable. Hypervalent organoiodinanes containing the iodoxolone nucleus are well-known.[10] We report herein a synthesis and characterization of 1-alkynylbenziodoxolone **3**.

Results and Discussion

Treatment of (cyclohexylethynyl)trimethylsilane with 1-hydroxybenziodoxolone **4** in the presence of BF_3·Et_2O in dichloromethane at room temperature, followed by heating the resulting pale yellow powder in methanol at 60 °C, gave, after chromatographic purification using silica gel, 1-(cyclohexylethynyl)benziodoxolone **3a** in 34% yield as colorless crystals. Similarly, 1-decynyl- **3b** and 1-(3,3-dimethyl-1-butynyl)benziodoxolones **3c** were prepared from the corresponding 1-alkynyltrimethylsilanes, albeit in low yields. These iodoxolones **3** are easily purified by silica gel chromatography.

In the infrared (IR) spectra of benziodoxolones, such as 1-hydroxy- (**4**), 1-methoxy-, 1-acetoxy-, and 1-phenyl-1,2-

Scheme I



3a(ax) **3a**(eq)

Table I. ^{13}C NMR Data for 1-Alkynyliodinane, $R{-}C_\beta{\equiv}C_\alpha{-}I$(III), and 1-Decynyl Iodide (6)

compd	^{13}C shifts, δ (ppm) C_α	C_β
2a, R = c-C_6H_{11}	16.1	117.0
2b, R = n-C_8H_{17}	15.6	113.5
3a	39.0	113.6
3b	39.2	109.7
6	−3.3	96.8

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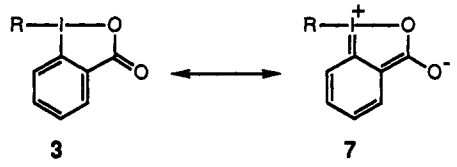
0022-3263/91/1956-5511$02.50/0

Scheme II



3 7

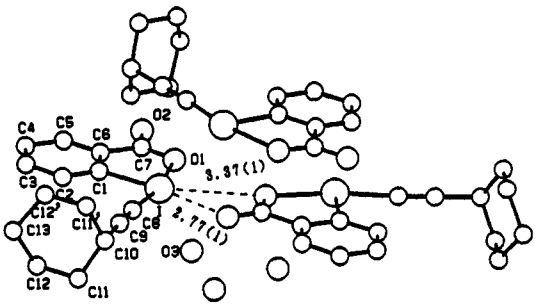


Figure 1. Molecular arrangement of **3a** around a 3-fold axis. The atoms except C11 and C12 lie on the mirror plane at $z/c = 1/4$: C11′ and C12′ are related to C11 and C12, respectively, by the mirror. Water of crystallization, O3, is at $z/c = -1/4$.

benziodoxol-3(1*H*)-ones (**5**), the carbonyl absorption bands generally appear in the range of 1650–1615 cm^{-1} because of the considerable ionic nature of the endocyclic I–O bonds.[11] The carbonyl frequency of 1645 cm^{-1} for **3a** is in a good agreement with the cyclic structure. The ^1H NMR spectra of **3a** in dichloromethane-d_2 had characteristic signals at δ 8.30, 8.21, and 7.77 assigned to the aromatic protons. The propargylic proton appeared at δ 2.79 as a triplet of triplets (J = 9.2 and 3.9 Hz). When the sample was cooled to −90 °C, this multiplet was well-resolved into two signals: δ 3.38 (a broad singlet with a small half-band width of 11.2 Hz) and 2.76 (a broad triplet with a half-band width of 26.2 Hz). These results indicate the presence of two conformers in solution, and the former, lower field signal was assigned to the equatorial methine proton of the axial ethynyl isomer **3a**(ax) and the latter one to the axial methine proton of the equatorial isomer **3a**(eq) (Scheme I).[12] The conformational ratio **3a**(ax)/**3a**(eq) of 17:83 corresponds to a value of ΔG of 1.33 kcal/mol for the substituted ethynyl group.

The ^{13}C NMR chemical shifts of acetylenic carbons of benziodoxolones **3a,b** and the corresponding phenyliodonium tetrafluoroborates **2a,b**[1a] are shown in Table I. Heavy-atom effects of iodine lead to the anomalously high shielding of α-acetylenic carbons of these organoiodinanes and 1-decynyl iodide (**6**).[13] Both α- and β-acetylenic carbons of **2b** and **3b** show downfield shifts in the range 13–43 ppm relative to those of **6**. This can be accounted for by the increasing −I and −M effects and by the decreasing +M effect of the aryliodine(III) groups.[14] It is of interest that the α-carbons of **3a,b** are much more deshielded compared to those of **2a,b**. As mentioned earlier, the conjugative overlap of lone pairs on the iodine with π-orbitals of the aromatic nucleus of **3**, which is less effective in acyclic analogues **2** because of the unfavorable steric arrangement,[15] makes participation of the zwitterion structure **7** possible to some extent. This may be responsible in part for the large deshielding of α-carbons of **3** (Scheme II).

Table II. Selected Bond Distances (Å) and Bond Angles (deg)[a]

(A) Bond Distances			
I–O1	2.34 (1)	I–C1	2.14 (1)
I–C8	2.03 (2)	C1–C6	1.40 (2)
C6–C7	1.49 (2)	C7–O1	1.28 (2)
C7–O2	1.24 (2)	C8–C9	1.19 (3)
(B) Bond Angles			
C1–I–O1	75.8 (4)		
C1–I–C8	90.9 (6)		
O1–I–C8	166.7 (5)		

[a] Numbers in parentheses are esd values.

In order to determine the stereostructure of **3a**, single-crystal X-ray diffraction analysis was carried out.[16] The structure of the trimer formed in the crystal, which contains water of crystallization, is shown in Figure 1. All the atoms of the trimer, other than C11, C11′, C12, and C12′, are in the same plane as the ring C1–C6, which is parallel to the plane consisting of water, with a distance of 3.556 Å. Interestingly, in the solid state the ethynyl substituent occupies an axial position of the cyclohexane chair conformer. The distorted T-shape geometry around the iodine is in good agreement with the results obtained in X-ray crystallographic studies of closely related benziodoxolones.[10,17] The selected intramolecular bond distances and bond angles are summarized in Table II.

The I–O1 bond distance of 2.34 Å is significantly longer than the computed covalent single-bond length of 1.99 Å,[18] which indicates a highly ionic nature of the bond. This bond is slightly longer than the I–O bond in **4** (2.30 Å),[17a] but considerably shorter than that in **5** (2.478 (4) Å).[17d] The I–C8 length of 2.03 Å is comparable to the corresponding ones of phenyl(3,3-dimethyl-1-butynyl)iodonium periodate (2.006 (13) Å)[19] and phenyl[(trimethylsilyl)-ethynyl]iodonium tetrafluoroborate (1.987 (6) Å).[20] The crystal structure contains two secondary bonds[21] between the iodine and the two oxygen atoms (O1 and O2) (3.37(1) and 2.77(1) Å, respectively). The deviation of O1–I–C8 bond angle of 166.7 (5)° from the ideal value of 180° for the hypervalent bond may be partly interpreted in terms of the presence of these secondary bonds.

Experimental Section

Melting points were determined with a Yanaco micro melting point apparatus and are uncorrected. IR spectra were recorded on a JASCO A-202 spectrophotometer. NMR spectra were recorded on either a Varian VXR 200, JEOL JNM-GX 270, or JEOL JNM-GX 400 spectrometer. Chemical shifts (^1H, ^{13}C) were reported in parts per million (ppm) downfield from internal tetramethylsilane. Mass spectra (MS) were taken on a JEOL

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(15) In acyclic aryliodinanes $ArIX_2$ the plane of the aromatic ring is generally perpendicular to the hypervalent I(III)–X bonds.[9]

(16) Crystal data for **3a**: $C_{15}H_{15}O_2I \cdot H_2O$, M = 372.20, $P6_3/m$, a = 19.700 (2) Å, c = 7.111 (2) Å, Z = 6, V = 2390.0 (6) Å^3, ρ_c = 1.552 g cm^{-3}, R = 0.057 for 956 reflections.

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JMS-D300 spectrometer. Preparative thin-layer chromatography (TLC) was carried out on precoated plates of silica gel (Merck, Silica gel F-254).

General Procedure for Synthesis of 1-Alkynylbenziodoxolones 3. To a stirred suspension of 1-alkynyltrimethylsilane (3 mmol) and commercially available 1-hydroxybenziodoxolone 4 (6.6 mmol) in freshly distilled dichloromethane (30 mL) was added dropwise $BF_3{\cdot}Et_2O$ (6.6 mmol) at room temperature under nitrogen, and the mixture was stirred for 2 days. A pale yellow color developed. After the removal of the solvent under reduced pressure, diethyl ether (30 mL) was added. A pale yellow precipitate was collected, washed with diethyl ether, and dried in vacuo. A mixture of the precipitate in methanol (60 mL) was heated at 60 °C for 45 min to give a clear solution. After the removal of the solvent under reduced pressure, dichloromethane (100 mL) was added. The resulting precipitate was filtered off, and the filtrate was concentrated to give an oil, which was purified by silica gel column chromatography or by preparative TLC to give 1-alkynyliodoxolone 3.

1-(Cyclohexylethynyl)-1,2-benziodoxol-3(1*H*)-one (3a). The benziodoxolone 3a was prepared from (cyclohexylethynyl)-trimethylsilane in 34% yield according to the general procedure: colorless prisms (recrystallized from dichloromethane–hexane); mp 70–73 °C dec; IR ($CHCl_3$) 3430, 3000, 2940, 2860, 2160, 1645, 1440, 1320, 1290, 830, 585 cm^{-1}; ^1H NMR (400 MHz, CD_2Cl_2) δ 8.30 (dd, J = 7.1, 2.0 Hz, 1 H), 8.21 (dd, J = 7.9, 1.3 Hz, 1 H), 7.81–7.72 (m, 2 H), 2.79 (tt, J = 9.2, 3.9 Hz, 1 H), 1.98–1.88 (m, 2 H), 1.82–1.70 (m, 2 H), 1.67–1.51 (m, 3 H), 1.46–1.32 (m, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 166.7, 134.6, 132.3, 131.6, 131.4, 126.1, 115.6, 113.6, 39.0, 32.2, 30.7, 25.5, 24.7; MS m/z (relative intensity) 354 (2, M^+), 351 (8), 248 (13), 231 (100), 203 (20), 76 (33); HRMS calcd for $C_{15}H_{15}O_2I$ (M^+) 354.0118, found 354.0097. Anal. Calcd for $C_{15}H_{15}O_2I{\cdot}H_2O$: C, 48.40; H, 4.60. Found: C, 48.10; H, 4.35.

1-(1-Decynyl)-1,2-benziodoxol-3(1*H*)-one (3b). The benziodoxolone 3b was prepared from 1-decynyltrimethylsilane in 22% yield according to the general procedure: colorless oil; ^1H NMR (270 MHz, $CDCl_3$) δ 8.44–8.38 (m, 1 H), 8.22–8.15 (m, 1 H), 7.80–7.72 (m, 2 H), 2.60 (t, J = 7.1 Hz, 2 H), 1.73–1.20 (12 H), 0.89 (t, J = 6.8 Hz, 3 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 166.6, 134.6, 132.3, 131.5, 131.4, 126.1, 115.6, 109.7, 39.2, 31.7, 29.1, 28.9, 28.9, 28.2, 22.6, 20.4, 14.0; MS m/z (relative intensity) 384 (<1, M^+), 351 (4), 248 (10), 231 (100), 203 (18), 76 (25).

1-(3,3-Dimethyl-1-butynyl)-1,2-benziodoxol-3(1*H*)-one (3c). The benziodoxolone 3c was prepared from (3,3-dimethyl-1-butynyl)trimethylsilane in 35% yield according to the general procedure: colorless needles (recrystallized from dichloromethane–hexane); mp 206–208 °C dec; IR ($CHCl_3$) 2980, 2900, 2160, 1645, 1440, 1320, 1290, 1210, 830 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.45–8.38 (m, 1 H), 8.16–8.10 (m, 1 H), 7.80–7.72 (m, 2 H), 1.38 (s, 9 H); MS m/z (relative intensity) 313 (1, M^+ – Me), 269 (35), 248 (14), 231 (40), 208 (54), 193 (91), 142 (88), 141 (73), 81 (100), 76 (53); HRMS calcd for $C_{12}H_{10}O_2I$ (M^+ – Me) 312.9728, found 312.9768.

Registry No. 3a, 135226-07-2; 3b, 135226-08-3; 3c, 135226-09-4; 4, 131-62-4; (cyclohexylethynyl)trimethylsilane, 66270-60-8; 1-decynyltrimethylsilane, 54559-17-0; (3,3-dimethyl-1-butynyl)-trimethylsilane, 14630-42-3.

Supplementary Material Available: Tables of crystallographic details, atomic coordinates and isotropic temperature factors, anisotropic thermal parameters, bond lengths, and bond angles of 3a; ^1H and ^{13}C NMR spectra of 3a and 3b; and ^1H NMR spectrum of 3c (12 pages). Ordering information is given on any current masthead page.

Reactions of (*E*)-*O*-Arylbenzaldoximes with Secondary Amines in Acetonitrile. Competition between E2 and S_NAr Reactions

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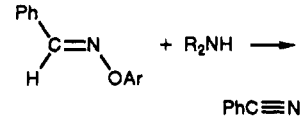
Reactions of (*E*)-*O*-arylbenzaldoximes in which the *O*-aryl group is 2,4-dinitrophenyl (1) and picryl (2) with secondary amines in acetonitrile have been studied kinetically. The reactions proceed via competing E2 and S_NAr mechanism. The second rate-determining step of the S_NAr reactions involves both uncatalyzed and base-catalyzed pathways. The sensitivity of the S_NAr reaction to base catalysis was greater for 2 and increased with base strength. The rates of E2 and S_NAr reactions increased by approximately 10^3 and 10^4 fold, respectively, with the variation of the substrate from 1 to 2. The yield of S_NAr product increased with base concentration, electron-withdrawing ability of *O*-aryl group, and base strength. From these results, factors that influence the competition between E2 and S_NAr reaction pathways are assessed.

Recently we reported a competition between base-promoted elimination and nucleophilic aromatic substitution reactions of (*E*)-*O*-arylbenzaldoximes 1 and 2 under various conditions. Thus, when hydroxide ion in 60% aqueous DMSO was used as the promoting base, 1 produced elimination products, whereas 2 yielded S_NAr products exclusively.[1] On the other hand, the reactions of both 1 and 2 with tertiary amines proceeded by an E2 mechanism.[2] It appears that the nature of attacking base and the electron-withdrawing ability of the *O*-aryl substituent play important roles in these reactions.

To understand the factors that influence the competition between these two reactions, it seems necessary to conduct the reactions under conditions where both of these processes proceed at comparable rates. We found that the reactions of 1 and 2 with secondary amines in acetonitrile produced both elimination and substitution products (eq 1). To probe these two competing mechanisms, we have investigated the effects of varying base concentration, base strength, and steric bulk, as well as *O*-aryl substituents. The results of these studies are reported here.



$$PhC{\equiv}N + PhCH{=}NOH + ArO^- + R_2NAr \quad (1)$$

Ar	R_2NH
1 2,4-dinitrophenyl	pyrrolidine
2 picryl	piperidine
	tetrahydroisoquinoline
	morpholine

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