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Hypervalent Iodine Oxidation of Phenolic Schiff's Bases: Synthesis of 2-Arylbenzoxazoles

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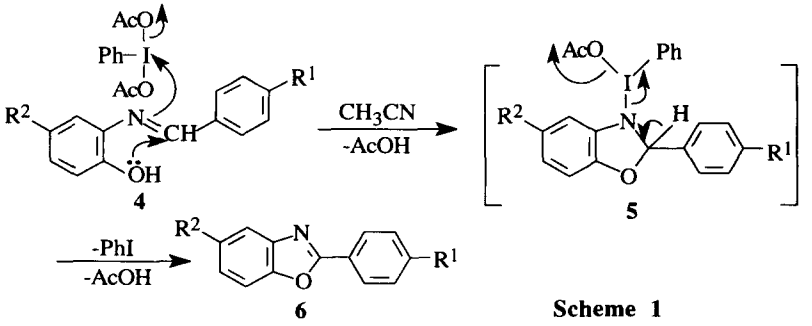
Abstract: 2-Arylbenzoxazoles, **6**, are synthesized, rapidly and in high yields, *via* the oxidative intramolecular cyclization of phenolic Schiff's bases, **4**, using iodobenzene diacetate (IBD) as an oxidant in acetonitrile or methanol at room temperature. © 1997 Elsevier Science Ltd.

The use of organohypervalent iodine reagents as oxidizing agents has been demonstrated in organic synthesis.[1] Schiff's bases, **1**, derived from aldehydes, on reaction with iodobenzene diacetate (IBD) undergo oxidative rearrangement with the formation of acylal **2** (hydrolyzing to an aldehyde) and azo compound **3** (*via* dimerization of nitrene intermediate, ArN:) (Eqn. 1).[2]

$$\underset{\mathbf{1}}{ArCH{=}NAr'} \xrightarrow{IBD} \underset{\mathbf{2}}{ArCH(OAc)_2} + \underset{\mathbf{3}}{Ar'N{=}NAr'} \qquad \text{Eqn. 1}$$

In view of our ongoing program on the application of hypervalent iodine reagents in organic synthesis[1b,c,g] and because of the recent interest in benzoxazole ring system,[3-5] we explored the oxidation of Schiff's bases **4**, readily accessible from arylaldehydes and *o*-aminophenol, with IBD. The aim is to ascertain the influence of *o*-hydroxy group on the course of this reaction and hopefully to achieve a concise synthesis of benzoxazoles *via* intramolecular cyclization. The oxazole derivatives find application mainly in agriculture, and medicine.[6] As a recent example, the ring system is key part of the antitumor metabolite, UK-1, produced by *Streptomyces* sp. 517-02.[4] Among the known methods for the synthesis of 2-arylbenzoxazoles,[5] the general approach involves the oxidative cyclization of **4** by oxidants such as barium manganate,[7] lead tetraacetate,[8] nickel peroxide,[9] copper(I) chloride in the presence of dioxygen,[10] and thianthrene cation radical.[3]



Scheme 1

We wish to report that the oxidation of **4** with IBD, in either acetonitrile or methanol, leads to a facile intramolecular cyclization providing a convenient route to the synthesis of 2-arylbenzoxazoles, **6.** Interestingly, the intramolecular cyclization is preferred to the oxidative rearrangement that may result in the formation of an acylal derivative. The general procedure involves the addition of 1.1 equivalents of IBD at room temperature to a stirred solution of **4** in acetonitrile or methanol. The reaction is completed rapidly in 4-5 min as followed by TLC examination (hexane:EtOAc, 9:1, v/v). The solvent is removed under reduced pressure and the residue is neutralized with aqueous sodium bicarbonate solution. The crude product is extracted into dichloromethane and purified by column chromatography to afford **6**. The reaction proceeds with equal efficiency in methanol or acetonitrile and the procedure appears to be of general preparative value since it tolerates a variety of functional groups. As described previously for other oxidative protocols, the substrates bearing electron withdrawing functionalities afford better yields. Our results for various benzoxazoles are summarized in the **Table**.

Mechanistically, the plausible pathway for transformation **4—>6** involves the formation of N-I(III) cyclic adduct, **5**, by intramolecular participation of *o*-hydroxy group. The elimination of iodobenzene and acetic acid affords the 2-arylbenzoxazoles, **6** (**Scheme 1**).

Table: Preparation of 2-arylbenzoxazoles, 6 from phenolic Schiff's bases

Entry	R^1	R^2	m.p. (°C)	Yield[a] (%)
1	H	H	102	83
2	Me	H	113-14	87
3	OMe	H	101	82
4	Cl	H	147	87
5	NO_2	H	266-68	93
6	H	Me	103	85

[a]Unoptimized yields of isolated pure products that exhibited physical and spectral properties in accord with the assigned structures.

In conclusion, oxidative intramolecular cyclization of phenolic Schiff's bases, **4**, leads to the rapid formation of 2-arylbenzoxazoles, **6**, in high yields using iodobenzene diacetate (IBD) under mild conditions. The influence of other ortho substituents and the associated reaction conditions for intramolecular cyclization to useful heterocycles are currently being explored.

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