

A novel preparation of 2-aryl-5-methoxyoxazoles[†]

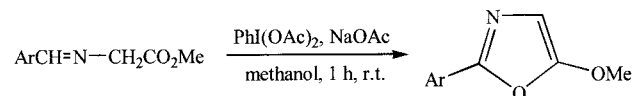
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2-Aryl-5-methoxyoxazoles can be synthesized by oxidation of Schiff's bases with (diacetoxyiodo) benzene in good yields under mild conditions.

Oxazoles are important organic heterocyclic compounds and have found widespread application in the synthesis of medicines, chemicals and pigments. They are also of interest as Diels–Alder dienes in the synthesis of furans¹ and pyridines², and as protecting groups³. Some methods for the preparation and 4- and 5-substituted⁴ and 2-substituted oxazoles⁵ exist. However, there have been few reports on the generation of 2-aryl-5-methoxyoxazoles.⁶

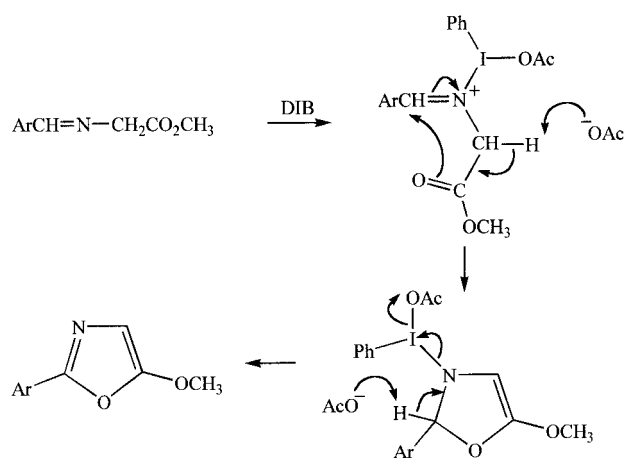
Recently hypervalent iodine compounds have been attracting much interest in organic synthesis. Among the various species of hypervalent iodine compounds, (diacetoxyiodo)benzene (DIB) is a very useful reagent which can be used as an efficient oxidant for many kinds of organic substrates.⁷ Dai and co-workers reported that 1,3,4-oxadiazoles could be produced smoothly in the presence of methanol or methylene chloride by oxidative cyclization under acetate anion catalysis⁸. This inspired us to attempt the synthesis of 2-aryl-5-methoxyoxazoles by oxidizing the Schiff's bases of aryl aldehydes and glycine methyl esters with DIB (Scheme 1).



Scheme 1

We found the reaction access readily for a range of the substrate and gives good yields within 1 hour at room temperature in methanol containing NaOAc. The results are shown in Table 1. These indicate that acetate anion catalysis improves the yield significantly. The electronic effect of aryl substituents had no great influence on the reaction; with either electron-donating or electron-withdrawing groups the reaction takes place well.

A possible mechanism of the reaction (Scheme 2) involves



Scheme 2

an initial exchange of an acetoxy ligand of DIB forming a hypervalent iodine intermediate A, which through an intramolecular carbonyl oxygen attack cyclizes to generate hypervalent iodine intermediate B. This may undergo an acetate anion catalyzed intramolecular reductive elimination of PhI to provide the 2-aryl-5-methoxyoxazole.

In conclusion, we offer here a novel method to prepare 2-aryl-5-methoxyoxazoles by oxidative cyclization with DIB under mild conditions and in good yields.

Experimental

General procedure for preparation of Schiff's base: At room temperature, the mixed solution of glycine methyl ester hydrochloride (2.0 mmol) in methylene chloride (20 ml) with arylaldehyde (2.2 mmol) in the presence of triethylamine (3 ml) and anhydrous magnesium sulfate (2 g) was stirred. After filtration, the filtrate was washed with water (8 ml). The organic layer was dried over anhydrous magnesium

Table 1 Preparation of 2-aryl-5-methoxyoxazoles using DIB

Entry	Ar	Yield(%)	mp (°C)	Lit. ^{6b} m.p. (°C)	IR $\nu_{C=N}$ (cm ⁻¹)	¹ H-NMR (80 Hz/CDCl ₃) δ (ppm) (H _{MeO} H _{C4})
1 ^a	Ph	81	oil	oil	1620	3.79, 6.07
2 ^a	<i>p</i> -CH ₃ OC ₆ H ₄	84	82–84	84	1620	3.82, 6.03
3 ^a	<i>p</i> -CH ₃ C ₆ H ₄	88	42–43	44–45	1620	3.82, 6.07
4 ^a	<i>p</i> -ClC ₆ H ₄	76	65–67	68	1615	3.86, 6.10
5 ^a	<i>p</i> -NO ₂ C ₆ H ₄	71	145–146	148	1625	3.90, 6.20
6 ^{a,c§}	<i>p</i> -C ₂ H ₅ C ₆ H ₄	82	47–49	–	1625	3.82, 6.02
7 ^b	<i>p</i> -CH ₂ C ₆ H ₄	55	42–43	44–45	1620	3.82, 6.07
8 ^b	Ph	51	oil	oil	1620	3.79, 6.07

^aThe reaction was carried out with 1.2 mmol DIB and 1.0 mmol Schiff's base in the presence of 2.0 mmol NaOAc at room temperature for 1 hour; ^bThe reaction was carried out in the absence of 2.0 mmol NaOAc, the other conditions being the same; ^cAnal. Calcd. for C₁₂H₁₃NO₂ C 74.08, H 5.73, N 6.17; Found C 73.93, H 5.61, N 6.16; [§] isolated yields.

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† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M)*.

sulfate and the solvent was removed to give the Schiff's base which could be purified by recrystallization with 95% alcohol and stored for several months in a freezer.

General procedure for preparation of 2-aryl-5-methoxyoxazoles with DIB: At room temperature, DIB (1.2 mmol) and NaOAc (2.0 mmol) are added in one portion into the solution of Schiff's base (1.0 mmol) of the arylaldehyde in methanol (10 ml). The mixture was reacted for 1 hour and was then filtered. The solvent was removed under reduced pressure and the product was isolated by TLC (silica gel) using EtOAc/*n*-hexane (1:5) as eluant.

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