SHORT PAPER

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Hypervalent iodine in synthesis 69: an efficient synthesis of 2-arylbenzoxazoles via the palladium-catalysed carbonylation and condensation of diaryliodonium salts and *o*-aminophenols

Tao Zhou and Zhen-Chu Chen*

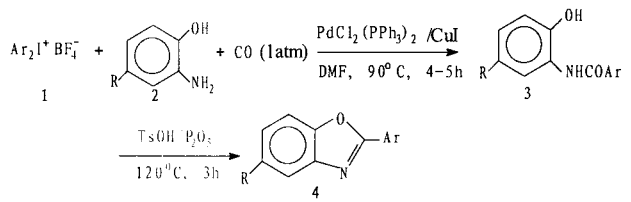
Department of Chemistry, Zhejiang University (Xixi Campus), Hangzhou, 310028, P. R. China

An efficient synthetic method is reported in which 2-arylbenzoxazoles have been prepared in good to excellent yields under mild reaction conditions by the palladium-catalysed carbonylation of diaryliodonium salts with *o*-aminophenols followed by dehydrative cyclisation.

Keywords: hypervalent iodine, 2-arylbenzoxazoles

Benzoxazole derivatives have wide applications in medicine and agriculture.[1] 2-Arylbenzoxazoles are commonly made in two ways: (1) by the condensation of an aromatic carboxylic acid or its derivatives with an *o*-aminophenol,[2] or by the reaction of *o*-aminophenol and allenic or acetylenic nitriles,[3] or by the reaction of *o*-aminophenol and trihalomethyl aromatic compound.[4] (2) by the oxidation cyclization of Schiff' bases derived from aldehydes and *o*-aminophenol by various oxidants such as lead tetraacetate,[5] nickel peroxide,[6] active manganese dioxide,[7] barium manganate,[8] iodobenzene diacetate,[9] copper(I) chloride in the presence of dioxygen,[10] and by photochemical ring-closure.[11] One limitation of the former conventional methods is the unavailability of starting materials. The latter method also have limitations such as long syntheses and the, unavailability of certain aryl aldehydes. Recently, a preparation for the title compounds via the palladium-catalysed carbonylation and condensation of aromatic halides and *o*-aminophenols was developed,[12] but a high pressure of carbon monoxide was needed in this method.

As part of our effort to extend the application of diaryliodonium salts in organic synthesis and our interest in the synthesis of heterocyclic compounds, we wish to report an efficient one-pot synthesis of 2-arylbenzoxazoles by the palladium-catalysed carbonylation and condensation of diaryliodonium salts and *o*-aminophenols. In the presence of palladium catalyst and cuprous iodide cocatalyst, diaryliodonium salts react with *o*-aminophenols under one atmosphere of carbon monoxide to produce a hydroxy-amide **3**. These were not isolated but were subjected to dehydrative cyclisation to give 2-arylbenzoxazoles **4** in the presence of dehydrating agent (Scheme 1). The products were characterized by ^{1}H NMR, IR and m.p. which are consistent with the literature data. The results are summarised in Table 1.



Scheme 1

We found that in the absence of CuI, the reaction proceeded smoothly and but it only gave a moderate yield (Entry 2). The addition of CuI increased the yields. In order to enhance the dehydrative cyclisation of amido-phenols **3**, two dehydrating agents including P_2O_5 and *p*-toluenesulfonic acid were tested. We found that **3** was cyclised to **4** in moderate yields within 3h by using each of the dehydrating agents (Entry 4, 5), but the yields were not further increased even after 12h. Using both of them together improved the yields. The reaction was found to be general. Several diaryliodonium salts and o-aminophenols with various substituents such as methyl, methoxy, bromo and chloro were successful reacted in good to excellent yields.

In conclusion, palladium-catalysed carbonylation of diaryliodonium salts with *o*-aminophenols and subsequent cyclization took place readily under mild reaction conditions. With the obvious advantages of simple manipulation, mild conditions, no need of using high pressure of carbon monoxide and accessible starting materials, our route affords an efficient preparation for 2-arylbenzoxazoles and nicely compliments the existing methods.

Experimental

Melting points were uncorrected. ^{1}H NMR spectra were obtained on PMK-60 Spectrometer using CCl_4 as the solvent with TMS as an internal standard. IR spectra were determined on PE-683 Infrared Spectrometer with KBr pallet.

General procedure for preparation of 2-arylbenzoxazoles: A mixture of diaryliodonium salt **1** (1 mmol), *o*-aminophenol **2** (1.5 mmol), K_2CO_3 (2mmol), $PdCl_2(PPh_3)_2$ (5 mol%), CuI (10 mol%), and DMF (5 ml) was stirred under CO atmosphere (1 atm) at 90°C for 4–5h. The reaction mixture was diluted with DMF (5 ml), treated with $TsOH{\cdot}H_2O$ (4 mmol) and P_2O_5 (4 mmol), and stirred at 120°C for 3h. Then the reaction mixture was neutralized with concentrated NH_4OH, diluted with saturated NH_4Cl (20 ml), and extracted with diethyl ether (3×15 ml). The combined organic phases were washed with brine, dried over anhydrous Na_2SO_4. After the removal of solvent under reduced pressure, the residue was purified with TLC on silica gel using cyclohexane/ethyl acetate (8:1) as an eluent to give pure product **4**.

Physical and Spectroscopic Data: *2-Phenyl benzoxazole* (**4a**): m.p. 101–103°C (lit.[13] 102–103°C). ^{1}H NMR δ_H 7.05–7.8 (m, 7H), 8.0–8.3 (m, 2H). IR 1615, 1550, 1450, 1240, 1050, 745, 700, 685 cm^{-1}.

2-(4-Methylphenyl)benzoxazole (**4b**): m.p. 110–112°C (lit.[14] 110–112°C). ^{1}H NMR δ_H 2.33 (s, 3H), 7.1–7.8 (m, 6H), 8.0–8.3 (d, 2H). IR 1630, 1510, 1460, 1250, 1055, 745 cm^{-1}.

2-(4-Chlorophenyl) benzoxazole (**4c**): m.p. 144–146°C (lit.[15] 146-148°C). ^{1}H NMR δ_H 7.1–7.8 (m, 6H), 8.0–8.3 (m, 2H). IR 1620, 1485, 1450, 1405, 1245, 1090, 1055, 1010, 735 cm^{-1}.

2-(4-Methoxyphenyl)benzoxazole (**4d**): m.p. 99–101°C (lit.[9] 101°C). ^{1}H NMR δ_H 3.73 (s, 3H), 6.7–7.7 (m, 6H), 7.9–8.2 (m, 2H). IR 1620, 1500, 1450, 1250, 1170, 1020, 740 cm^{-1}.

* To receive any correspondence.

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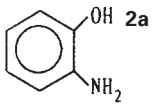
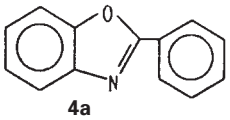
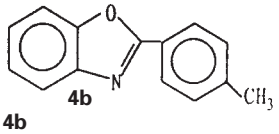
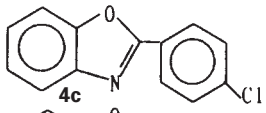
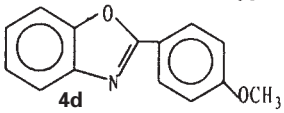
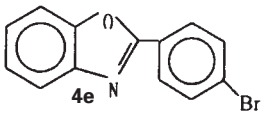
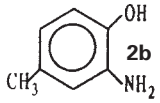
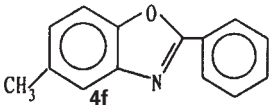
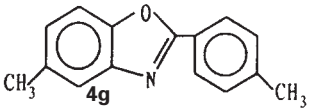
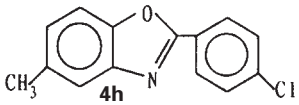
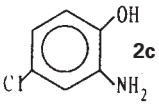
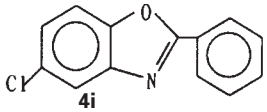
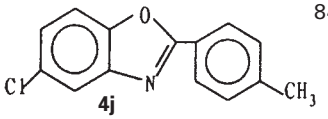
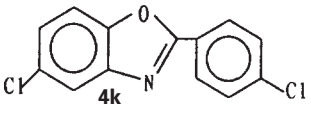
Table 1. Benzoxazoles from diaryliodonium salts and o-aminophenols

Entry	Diaryliodonium salts	o-Aminophenols	Products	Yield (%)[a]
1	$Ph_2I^+BF_4^-$ **1a**	 **2a**	 **4a**	87
2[b]	**1a**	**2a**	**4a**	67
3	$(Tol)_2I^+BF_4^-$ **1b**	**2a**	 **4b**	92
4[c]	**1b**	**2a**	**4b**	77
5[d]	**1b**	**2a**	**4b**	62
6	$(p\text{-}ClC_6H_4)_2I^+BF_4^-$ **1c**	**2a**	 **4c**	82
7	$(p\text{-}CH_3OC_6H_4)_2I^+BF_4^-$ **1d**	**2a**	 **4d**	90
8	$(p\text{-}BrC_6H_4)_2I^+BF_4^-$ **1e**	**2a**	 **4e**	87
8	**1a**	 **2b**	 **4f**	88
9	**1b**	**2b**	 **4g**	98
10	**1c**	**2b**	 **4h**	82
11	**1a**	 **2c**	 **4i**	80
12	**1b**	**2c**	 **4j**	84
13	**1c**	**2c**	 **4k**	75

[a]Isolated yield based on diaryliodonium salt. [b]CuI was absence. [c]8mmol P_2O_5 was used. [d]8mmol $TsOH{\cdot}H_2O$ was used.

2-(4-Bromophenyl)benzoxazole (**4e**): m.p. 155–157°C (lit.[16] 158°C). ^1H NMR δ_H 7.1–7.8 (m, 6H), 8.0–8.3 (m, 2H). IR 1620, 1485, 1455, 1400, 1245, 1070, 1010, 830, 760 cm^{-1}.

5-Methyl-2-phenyl benzoxazole (**4f**): 102–104°C (lit.[9] 103°C). ^1H NMR δ_H 2.35 (s, 3H), 7.0–7.55 (m, 6H), 8.0–8.3 (m, 2H). IR 1620, 1550, 1475, 1450, 1265, 1200, 1055, 1020, 800, 700, 685 cm^{-1}.

5-Methyl-2-(4-methylphenyl)benzoxazole (**4g**): m.p. 133–135°C (lit.[17] 135.5–136°C). ^1H NMR δ_H 2.33 (s, 3H), 2.40 (s, 3H), 7.0–7.5 (m, 5H), 7.9–8.2 (m, 2H). IR 1610, 1555, 1500, 1260, 1055, 795, 725 cm^{-1}.

2-(4-Chlorophenyl)-5-methyl benzoxazole (**4h**): m.p. 148–150°C (lit.[18] 150–151°C). ^1H NMR δ_H 2.43 (s, 3H), 7.1–7.8 (m, 5H), 8.0–8.4 (m, 2H). IR 1615, 1595, 1550, 1480, 1400, 1260, 1090, 1050, 795, 730 cm^{-1}.

5-Chloro-2-phenylbenzoxazole (**4i**): m.p. 99–101°C (lit.[19] 101.1–102.1°C). ^1H NMR δ_H 7.3–7.9 (m, 6H), 8.15–8.45 (m, 2H). IR 1615, 1550, 1450, 1270, 1055, 805, 700, 680 cm^{-1}.

5-Chloro-2-(4-methylphenyl)benzoxazole (**4j**): m.p. 142–144°C (lit.[18] 143–145°C). ^1H NMR δ_H 2.40 (s, 3H), 7.1–7.8 (m, 5H), 8.0–8.3 (m, 2H). IR 1615, 1555, 1500, 1450, 1260, 1060, 800, 725, 700 cm^{-1}.

5-Chloro-2-(4-chlorophenyl)benzoxazole (**4k**): m.p. 189–191°C (lit.[6(a)] 192-193°C). ^1H NMR δ_H 7.1–7.9 (m, 5H), 8.1–8.4 (m, 2H). IR 1650, 1610, 1595, 1480, 1450, 1270, 1090, 1060, 800, 750 cm^{-1}.

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