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Clay Mediated One Step Synthesis of Azo Dyes with 1,3-Benzoxazole Moiety

Bhagyashri A Lole and Pravina B Piste*

PG, Department of Chemistry, Yashavantrao Chavan Institute of Science, Satara, Maharashtra, India

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ABSTRACT

We have carried out synthesis of azo dyes of 4-(1,3-benzoxazol-2-yl) aniline (2a-j) in the presence of green and cost effective catalyst K10-Montmorillonite clay, using substituted phenols as coupling agents. The azo dyes were obtained in good isolated yield. The synthesized azo dyes have been evaluated in vitro for their antimicrobial activity against S. aureus and E. coli as bacterial strain and A. niger fungal strain. Some of the compounds displayed pronounced biological activity. The resulting compounds were characterized by IR, ^{1}H NMR, ^{13}CNMR and Mass spectroscopic analysis.

Keywords: Azo dyes; K10- montmorillonite clay; Antimicrobial evaluation

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INTRODUCTION

Azo compounds are a very important class of chemical compounds receiving attention in scientific research [1,2]. They are usually strongly colored compounds depending on the exact structure of the molecule. As a result of their color, azo compounds are tremendous interest as dyes and pigments for a long time [3]. It has been well known that they are the extensively used in various fields such as the dyeing of textile fibers, in biological–medical studies and advanced applications in organic synthesis [4]. Furthermore, they have been studied widely because of their excellent thermal and optical properties in applications such as optical recording medium, [5] toner, [6,7] ink-jet printing [8-10] and oil-soluble lightfast dyes [11]. Recently, azo metal chelates have also attracted increasing attention due to their interesting electronic and geometrical features in connection with their application for molecular memory storage, nonlinear optical elements and printing systems [12-14]. They also have wide range of pharmacological and medical potential applications [15], are known to be involved in a number of biological reactions such as inhibition of DNA, RNA, and protein synthesis, nitrogen fixation, and carcinogenesis [16]. The heterocyclic azo compounds are offering a wide spectrum of colors mainly due to the presence of chromophoric azo groups (–N=N–) blended with heterocycle and used in the manufacture of data storage devices such as CD, DVD [17-19]. In addition, these compounds are also utilized for coloring numerous consumer goods, such as clothes, leather, plastics, food, cosmetics and toys [20].

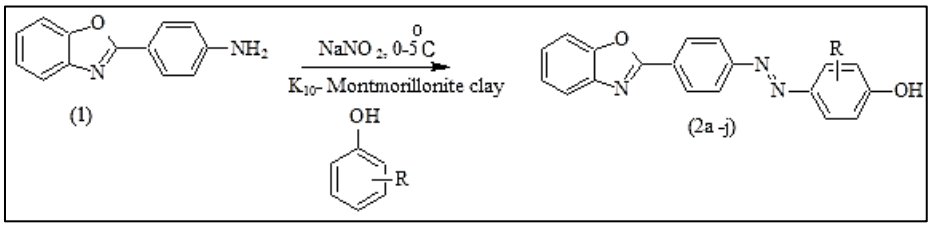
Montmorillonite clays as catalysts for chemical reactions constitute an exciting component of green chemistry. It is one of the most intensively explored catalytic materials in heterogeneous catalysis due to its low cost and eco-friendliness. Also, it possesses some unique properties like cation exchange capacity and swelling ability, thereby accommodating various guest species in its interlayer so, we intended to elaborate catalytic efficiency of K10 Montmorillonite clay in diazotization process for preparation of azo compounds. Hence, considering properties of hetero azo compounds have attracted our enormous interest in synthesis of azo dyes of 4-(1, 3-benzoxazol-2-yl) aniline in the presence of catalyst K10-Montmorillonite clay, using substituted phenols as coupling agents.

EXPERIMENTAL SECTION

Solvents and reagents were commercially sourced from local suppliers and used without further purification. Melting points were determined in an open capillary and are uncorrected. Products were recrystallized from ethanol as a solvent. The purity of compounds checked by the TLC on silica gel plates. The Infrared spectra were obtained on Perkin Elmer FT-IR spectrometer. The samples were examined as KBr discs 5% w/w.^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker AC (300/400 MHz for ^{1}H NMR and 100 MHz for ^{13}C NMR) spectrometer using $CDCl_3$/ DMSO as solvent and TMS as internal standard. The chemical shifts are reported in ppm.

General Procedure for 4-{(*E*)-(4-(1,3-benzoxazol-2-yl) diazenyl} Substituted Phenol (2a-j)

To a mixture of 4-(1,3-benzoxazol-2-yl) aniline(1) (5 mmol) in 15 mL water was added 25 mg of montmorillonite K10 clay. After stirring for 30 min 0.72 g $NaNO_2$ (10 mmol) in 10 mL water was added drop wise for a period of 30 min with continues stirring at 0°C. Then substituted phenol (5 mmol) was added to the diazonium-clay complex. Stirring was continued at room temperature for 1 hr. The reaction mixture was then filtered and the precipitated dye washed three times with cooled water. Finally, the azo dye was extracted with methanol to separate from montmorillonite clay and was recrystallized from methanol (Scheme 1).



Scheme 1: Synthesis of 4-{(*E*)-(4-(1,3-benzoxazol-2-yl) diazenyl} substituted phenol

RESULTS AND DISCUSSION

To pursue our objective of applying feasibility of Montmorillonite clay K10, we sought to explore the synthetic reactivity of 4-(1,3-benzoxazol-2-yl) aniline with various phenols for the generation of the azo compounds. From a synthetic perspective, we rationalized *in situ* formation of diazonium-clay complex of 4-(1,3-benzoxazol-2-yl) aniline followed by tandem reaction with substituted phenols thereby providing a facile access to azo derivatives.

Our preliminary study was focused on preparation of 4-(1,3-benzoxazol-2-yl) aniline from 2-amino phenol and 4-amino benzoic acid. The use natural acid catalyst in creation of (1) provides excellent yield 80%. To test the validity of the proposed hypothesis, a preliminary survey of reaction conditions and effect of catalyst loading was conducted using 4-(1,3-benzoxazol-2-yl) aniline(1), and phenol as model substrates (Table 1). As shown in Table 1, the yield of azo derivatives was increased with an increase in catalyst from 10 to 25 mg (Table 1, entries 1-4). However, further increase in amount of catalyst, did not show any considerable increase in product yield (Table 1, entries 5-7). Thus, 25 mg of catalyst loading was selected as optimum concentration for further studies.

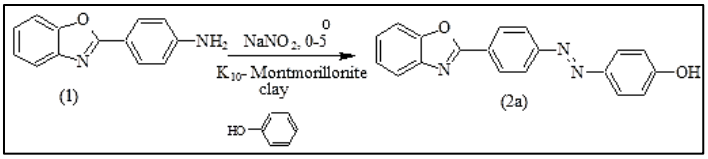


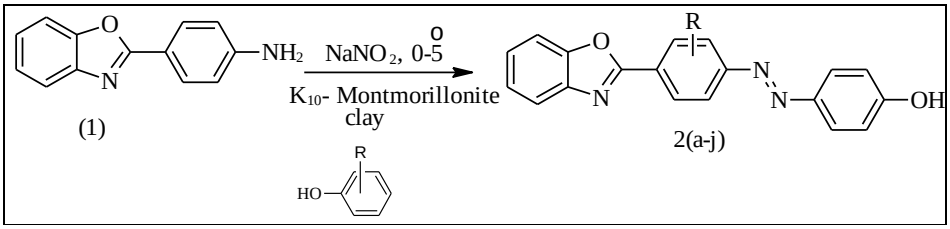
Table 1: Optimization of the reaction conditions[a]

Entry	Catalyst(mg)	Time(min.)	Yield[b](%)
1	10	150	64
2	15	120	67
3	20	100	72
4	25	60	80
5	30	60	81
6	40	55	78
7	50	55	79

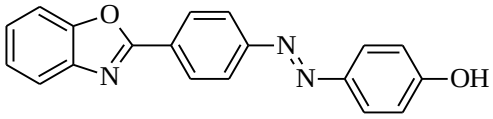
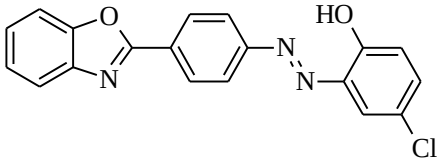
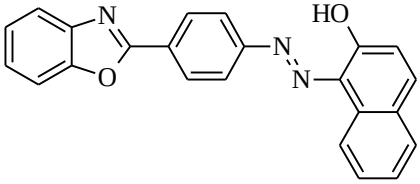
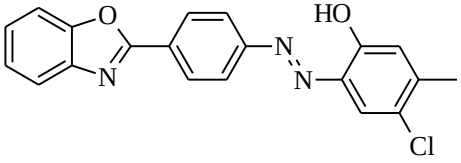
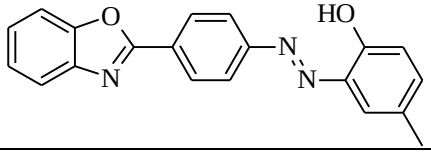
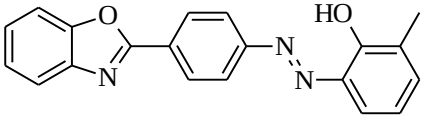
[a]Reaction condition: compound (1)(5 mmol), NaNO2 (10 mmol), phenol (5 mmol), catalyst in 15 mLwater,bYields of isolated product after recrystallization

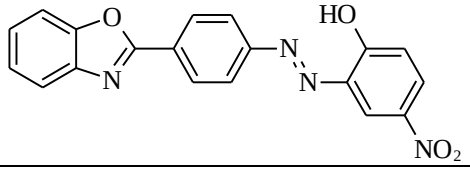
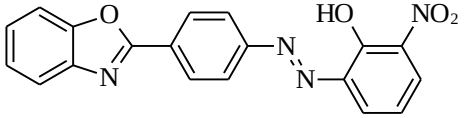
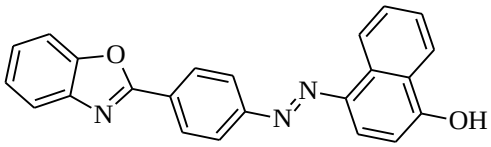
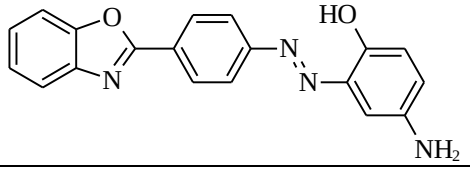
With this optimized reaction conditions, we scrutinized the generality of the protocol by reacting structurally diverse phenols. The results of reactions were summarized in Table 2. The reactions proceeded smoothly in all the cases affording the corresponding azo derivatives in excellent yields. It is noteworthy that electronic nature of substituents on the phenyl ring did not influence the reaction significantly. An interesting feature of the reaction is high reactivity of substrates bearing halide substituents thus providing opportunity for additional synthetic manipulation (Table 2, entry 3b, and 3d). The structures of the products were determined by IR, ^{1}H NMR and ^{13}C NMR spectroscopy as well as by mass spectrometry.

Table 2: Synthesis of azo compounds derives from4-(1,3-benzoxazol-2-yl) aniline[a] 2(a-j)



4-((E)-(4-(1,3-banzoxazol-2-yl)phenyl)diazenyl)phenol

Entry	Phenols	Product (2)	Yield[b] %	MP °C
a.	Phenol		80	107
b.	4-Chloro phenol		75	190
c.	β-Naphthol		78	86
d.	3-Methyl-4-chloro phenol		76	219
e.	4-Methyl phenol		80	169
f.	2-Methyl phenol		79	125

g.	4-Nitrophenol		76	135
h.	2-Nitrophenol		78	195
i.	α-Naphthol		80	125
j.	4-Amino phenol		79	163

[a]Reaction condition: compound (1)(5 mmol), $NaNO_2$ (10 mmol), phenol (5 mmol), catalyst (25 mg) in 15 mL water, [b]Yields of isolated product after recrystallization

Possible mechanism for diazotization and azo coupling is schematically described in Figure 1. Initially, clay is activated by losing water molecule to retain acidic and basic sites, in second step $NaNO_2$ adsorbs over the surface of the clay on acidic sites, further lone pairs on nitrogen atom initiates nucleophilic addition reaction with the adsorbed NO_2 to produce intermediate which on removal of water molecule produces diazonium salt and in final step diazo complex couples with the added coupling agent [21].

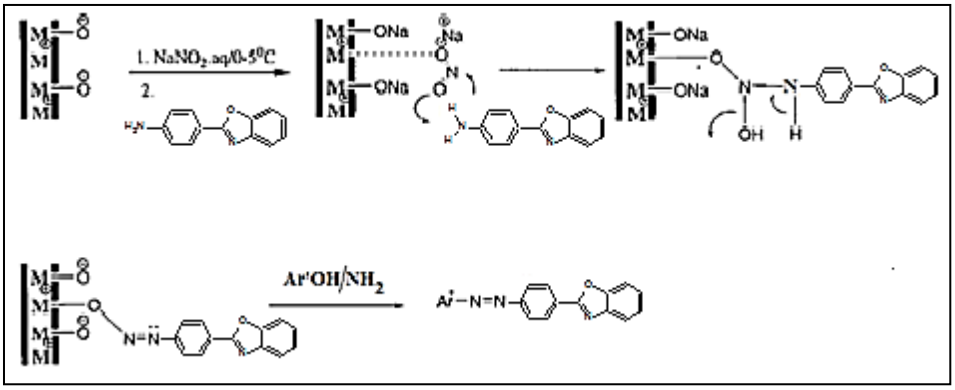


Figure 1: Plausible mechanism for clay mediated diazotization

Reusability Study of K10 Montmorillonite Clay Catalyst

For industrial and commercial use of any catalytic operation, r**e**cyclability study of catalyst is an important parameter. The reusability of the Montmorillonite K10 was tested on model reaction. On completion of reaction, the catalyst was isolated simply by filtration and washing with copious amount of acetone and drying in an oven. This oven dried catalyst was calcined at 250°C for 1hr and used for the next reaction. The recycled catalyst can be used up to five times without considerable loss of its catalytic activity for the model reaction (Figure 2).

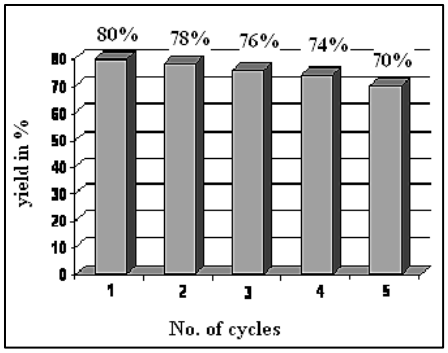


Figure 2: Reusability of K10 montmorillonite clay

Anti-Microbial Screening

The incorporation of heterocyclic moiety in azo dyes enhances the biological potential hence all the synthesized azo derivatives were examined for their pharmacologically potent anti-microbial activity at 100 µg/ml. The streptomycin and fluconazole is used as the standard and DMSO as the control. Results of the anti-microbial evaluation were summarized in Table 3, which showed moderate to good antibacterial activity of the synthesized azo derivatives against *S. aureus* and *E. coli* and anti-fungal activity against *A. niger*. As per previous reports halogenated compounds and electron donating groups are related with the good anti-microbial potential, we get the similar results here and found that compounds 3a,3c,3e, 3f,3g,3h have good anti-bacterial potential against *S. aureus*, on the other hand compounds 3a, 3b, 3c, 3g have significant anti-bacterial activity against *E. coli* as compared to that of the streptomycin. The compounds 3a, 3e, 3f, 3g, 3h, 3i, 3j shows good anti-fungal activity against fungal strain *A. niger* in comparison with fluconazole as standard. Thus azo derivatives with nitro 3g, 3h and halo 3b, 3d groups were showed good inhibitory activity. Remaining compounds possesses moderate anti-microbial activities.

Table 3: Anti-bacterial activity of synthesized compounds 2(a-j)

Comp. (100 g/ml)	Anti-bacterial activity(mm)		Anti-fungal activity
	S. aureus	*E. coli*	*Aspergillus niger*
3a	17	15	18
3b	14	16	16
3c	17	17	17
3d	15	12	17
3e	16	13	18
3f	16	12	18
3g	16	14	19
3h	16	13	20
3i	11	12	19
3j	12	13	18
Streptomycin	23	17	-
Flucanazole	-	-	22

Spectral Data of Representative Compounds

2-{(4-(1,3-benzoxazol-2-yl) phenyl) diazenyl}-4-chlorophenol(Table 2, entry 3b):

IR (KBr):υ_{max}=3258.60(-OH), 3072.92(-Ar-H), 1485 (-C=N-),1390.03(-N=N-).cm^{-1}

^{1}HNMR (400 MHz, DMSO):δ 9.8 (s, 1H,-OH), 8.00-8.39 (m, 4H),7.5 (m, 2H), 7.30-7.70 (m, 4H, Ar-H), 6.95(d,1H)ppm.

^{13}CNMR(100 MHz, DMSO):δ 167.2, 156.3, 153.6, 153.4, 138.5, 131.9, 129.1, 128.7, 124.8, 124.4, 123.1, 122.7, 122.2, 120.0, 117.0, 110.0 ppm.

1-{(4-(1,3-benzoxazol-2-yl) phenyl) diazenyl}naphthalen-2-ol (Table 2, entry 3c):

IR (KBr): υ_{max}=3232.57(-OH), 3078.05(-Ar-H), 1587(Ar-C=C<), 1511.09 (-C=N-), 1404.01 (-N=N-).cm^{-1}

^{1}HNMR (400 MHz, DMSO): δ 9.41 (s, 1H,-OH), 8.02-8.40 (m, 8H), 7.30-7.71 (m, 4H, Ar-H), 7.26-7.28 (m, 2H) ppm.

^{13}CNMR(100 MHz, DMSO):δ 162.2, 160.1, 155.3, 152.1, 146.7, 142.2, 128.2, 128.1, 127.6, 126.7, 126.1, 125.7, 124.0, 122.7, 119.3, 118.3, 117.0, 109.1 ppm.

2-{(4-(1,3-benzoxazol-2-yl) phenyl) diazenyl}-6-methylphenol (Table 2, entry 3f):
IR (KBr):υ_{max}=3240.35(-OH), 3062.92(-Ar-H), 1604.83, 1495.02 (-C=N-), 1415.07(-N=N-).cm^{-1}
^{1}HNMR (300 MHz, DMSO): δ 9.40 (s, 1H, -OH), 8.02-8.39 (m, 4H), 7.32-7.67 (m, 4H, Ar-H), 7.00-7.12 (m, 2H),6.95 (t, 1H), 2.11 (s, 3H) ppm.
^{13}CNMR (100 MHz, DMSO):δ 162.7, 152.0, 152.9, 153.1, 140.5, 134.7, 133.8, 130.7, 129.2, 126.0, 124.8, 124.6, 123.8, 122.5, 118.6, 110.5, 20.2 ppm.

2-{(4-(1,3-benzoxazol-2-yl) phenyl) diazenyl}-4-nitrophenol(Table 2, entry 3g):
IR (KBr):υ_{max}=3268.57(-OH), 3076.92(-Ar-H), 1501.02 (NO_2),1485.09 (-C=N-), 1390.13(-N=N-).cm^{-1}
^{1}HNMR (300 MHz, DMSO): δ 10.42 (s, 1H, -OH), 8.32 (m, 2H),7.11 (m, 1H), 8.05-8.39 (m, 4H), 7.30-7.69(m,4H,Ar-H) ppm.
^{13}CNMR(75 MHz, DMSO): δ 162.7, 156.3, 152.3, 153.1, 141.3, 140.5, 133.8, 130.7, 128.6, 127.1, 124.8, 124.6 123.8, 120.2, 118.6, 110.5 ppm.

CONCLUSION

We have carried out convenient synthesis of azo derivatives of 4-(1,3-benzoxazol-2-yl) aniline by using K10 Montmorillonite clay catalyst. The synthesized azo compounds screened for their anti-microbial activity. The azo dyes with 4-(1,3-benzoxazol-2-yl) aniline heterocyclic moiety shows significant anti-microbial activity. Easy workup, clean and simple procedure, cost effectiveness, high yield, reusability of catalyst, catalyst efficiency for diazotization are the merits of current synthesis. It can be concluded that the synthesized azo compounds hold greater promise in discovering a biologically potent anti-microbial agent.

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