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Electrosynthesis, Electrochemical behaviour, Antibacterial and Antifungal Activity of Novel azo Schiff's Bases*

KEYWORDS: Electrochemical reduction, zinc cathode, platinum anode, antimicrobial potential.2-[(E) -{4-[(E) -(2-hydroxybenzylidene) amino] phenyl} diazenyl] phenol, reductive coupling.

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ABSTRACT *The Schiff's bases containing azo group were synthesized at a cathode surface in an aqueous methanol solution containing sodium hydroxide. The synthesis was carried out at DC source voltage of 3.5- 9.5V using zinc cathode, platinum anode and calomel electrode. The products were characterized by spectroscopic techniques. In vitro, antimicrobial potential of Schiff's base was assessed by well-in agar method. The Schiff's base exhibited potent antibacterial and antifungal activities against most of the tested pathogenic bacteria and fungi in 10% concentration itself.*

Introduction

The brief review about electro organic synthesis was introduced by chemist and it is expected to be an important organic synthetic tool in the future because of its diverse application in industry.[1,2] The importance of the electrochemical measurement of potential or current to characterize an analyt's chemical reactivity. The current is a measure of the rate of the analyt's reduction, the reduction of nitro group to amine group consumes electrons, which was drawn from the electrode. The flow of electrons between the electrodes provides a measurable current. The chemists have studied electrochemical behaviour of *o*-, *m*- and *p*-nitroaniline by the cyclic voltametric method. The reduction behaviour of nitro compounds also studied in the presence of other organic molecule. There have been relatively a very few studies concerning the electrochemical behaviour of *o*-nitroaniline and *p*-nitroaniline in the presence of salicylaldehyde in aqueous methanol media. The reduction of nitro compound has been shown that, there were four electrons and proton transfer which convert the nitro group into amine group. The amine group generally condensed with aldehyde to form Schiff's base. However, the hydrolysis of Schiff's base into the parent carbonyl compound complicates the situation in practice mode. Hydrolysis was complete for all pH values, but rapid in an acidic medium. Schiff's bases were useful synthetic molecules which are used in various fields such as medicine, corrosion inhibition. Schiff's base macrocycles have electronic and optical properties.[3-6]

They have the pharmacological activities such as antiviral, antibacterial, antifungal, anti -malarial, anti-inflammatory, anti cancerous and anti convulsant activity.[7] The reduction of nitro compounds was very important in electro chemistry.[8] The organic electronics that utilize carbon based molecules as conductor. They are appreciated for low costs, light weight and rubbery flexibility. The electrical properties are used in organic electronics, particularly in OLED.[9] The active groups like $-NH_2$ and -OH on the Schiff's base molecule changes the physical and chemical properties. But the introduction of these groups to Schiff's base by conventional method requires more energy and time. The chemists have used the electrochemical method for synthesizing organic molecule.[10-14]

The pollution of the atmosphere opens the door of green chemistry. Several chemists carried out electro reduction of electro active groups by cyclic voltametric method.[15] Some chemists have synthesized Schiff's base of 5-aminosalicylic acid which is a useful drug in an effective treatment of inflammatory, bowel disease.[16,17] We designed one pot synthesis of azo Schiff's bases by electro reductive coupling method. In our previous work, the Schiff's bases were synthesized and their structures elucidated by using spectroscopic methods.[18] The electrochemical behaviour of imine group was studied by cyclic voltametry by many researchers.[19-21] However, there have been no reports of the electrochemical one pot synthesis of 2-[(E)-{4-[(E)-(2-hydroxybenzylidene)amino]phenyl}diazenyl]phenol.

Experimental

All chemicals were analytical reagent grade materials. These chemicals were used without further purification. Before performing the experiment, the cell with electrodes were cleaned by rinsing with acetone and washed with distilled water.

Apparatus

The reaction equipments were the glassware electrolytic cell equipped with platinum anode, zinc cathode and calomel electrode.

Experimental procedure

A solution of *p*-nitroaniline (1.38g, 0.01 mmol) was taken in an undivided cell along with 50 ml of methanol and 40 ml of water. To this mixture salicylaldehyde(1.22g, 0.01 mmol) and an 10% aqueous solution of sodium hydroxide (1g) was added dropwise at room temperature. The undivided cell was equipped with a zinc cathode (4X4 cm^2), platinum anode (Pt^+) and calomel electrode. The constant potential

Volume : 4 | Issue : 10 | October 2014 | ISSN - 2249-555X

was supplied with DC power supply (9.5V, 300mA). The reaction was electrolysed with constant stirring using a magnetic stirrer for 20 minutes and the progress of the reaction was monitored by TLC. The solution was evaporated and recrystallised from ethanol to get orange coloured product. The isolated yield was 98%.

The recrystallized products were characterized by the spectroscopic method.

2-[(E) -{4-[(E) -(2-hydroxybenzylidene) amino] phenyl} diazenyl] phenol:M.P.158-160^{0}C;λ/nm360; IR(KBr) ν/cm^{-1} 3443, 1613,1599,1585,1565,1508,1483,1373,1242,1171,1108,756;^{1}H NMR (400MHz, DMSO) δ 6.9-7.9 (m, 16H,Ph-H), 8.3(s, 2H, CH=N), 10.6 (s, 1H, -OH hydrogen bonded); Elemental analysis $C_{26}H_{20}N_4O_2$ (in percentage): Found C, 64.28; H, 4.07; N, 11.72. Theoretical C, 64.8; H, 4.2; N, 11.72.

Table-1: IR spectra of the synthesized derivatives in cm-1

Functional group	Product (a)	Product (b)	Product (c)	Product (d)
-OCH_3	-	2838	-	-
-N=CH-	1613	1681	1628	1672
-N=N-	1565	1599	1569	1571
-OH	3443	-	3477	-
-C=C-	-	-	-	1624
Ar-H	3069	3222	3200	3175

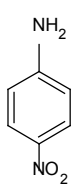
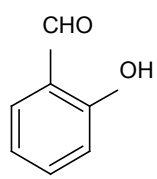
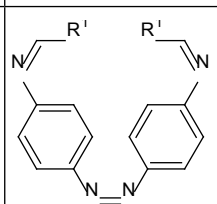
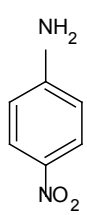
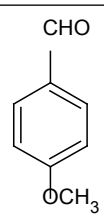
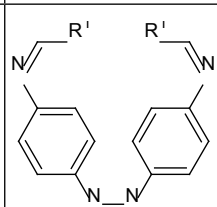
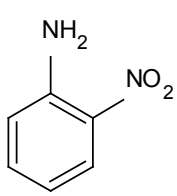
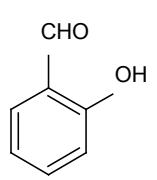
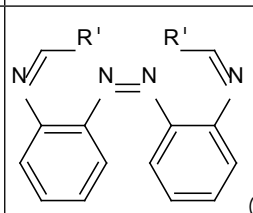
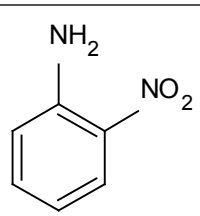
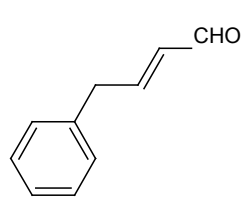
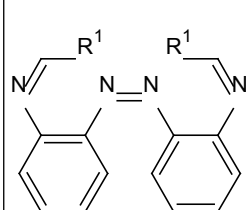
Note: '-'functional groups not existing in the molecules

Results and Discussion

The present study was carried out to develop a simple, rapid and precise electrochemical method for the synthesis of azo Schiff's bases and to study the electrochemical behaviour of reductive coupling. The N=N group is sensitive for reduction in acidic condition, as pH increases the reduction tendency of N=N decreases.[22]

The derivatives of azobenzenes were synthesised by electroreductive coupling of substituted nitro aniline, but it requires 6-13 hours for the completion of the raction.[12] The higher product yield with comparatively lesser reaction time in the aqueous methanol clearly indicates the superiority of the present method (Table-2 and 3). The reaction time and the yield of the products remain almost same in all the reactions (Table 2 and 3), except in the case of *o*-nitroaniline due to steric hindrance. The electroreductive coupling was also extended for the electrosynthesis of 2-[(E)-{4-[(E)-(2-hydroxybenzylidene)amino]phenyl}diazenyl] phenol and their derivatives.

Table-2: Synthesis of azoschiff's base

Entry	Substrate	R^1	product	Yield %
1			 (a)	98
2			 (b)	90
3			 (c)	30
4			 (d)	45

Volume : 4 | Issue : 10 | October 2014 | ISSN - 2249-555X

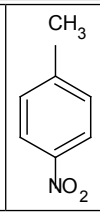
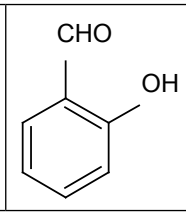
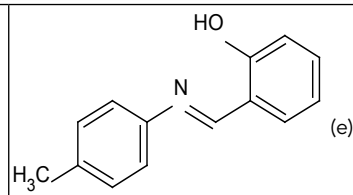
5			 (e)	70

Table-3: Optimized conditions for the synthesis of azos-chiffbase at zinc cathode.

Entry	Nitro com-pounds	Solvent	Time/ min	D C source voltage (V)
1	p-nitroani-line	Water, methanol (80:20)	20	9.5
2	p-nitroani-line	Water, methanol (80:20)	30	9.5
3	o-nitroani-line	Water, methanol (80:20)	40	3.5
4	o-nitroani-line	Water, methanol (80:20)	45	3.5
5	p-nitrotol-uene	Water, methanol (80:20)	40	8.0

The electrolysis reaction was carried out in aqueous alkaline solution of methanol containing *p*-nitroaniline and salicylaldehyde at the surface of Zn-cathode using a Pt-anode and DC source voltage of 9.5V. The reaction was preceded in two steps (Scheme 1 and 2), which involves condensation and the reductive coupling; both the steps were completed in 20 to 45 minutes (Table 3). cyclic Voltammetry (CV) curves ofschiff base at the scan rate of 0.5V /S

The Schiff base of Entry No.5 was prepared by condensation reaction of salicyaldehyde and p-methyl aniline in the ethanol medium for about three hours [24].

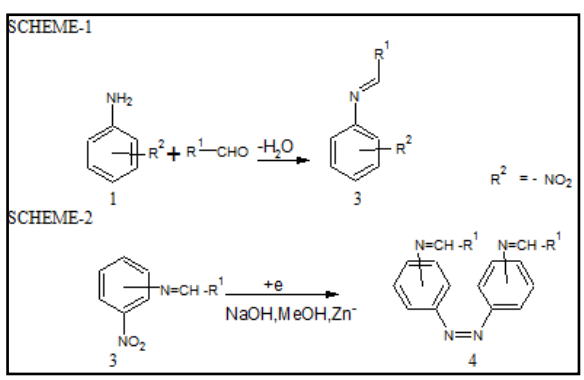
In the present work above Schiff base was prepared by electrochemical method in aqueous methanol medium for about 40 minutes. Copper and platinum were used as cathode and anode for this reaction. This electrochemical reaction was eight times faster than the conventional condensation method

The *p*-nitrotoluene in absence of salicylaldehyde undergoes reductive coupling in THF,[12] but the electrolysis of *p*-nitrotoluene in the presence of salicylaldehyde in aqueous methanol yields Schiff's base (Table 2, entry 5). The electrolysis reaction of nitro aniline in the absence and presence of various aromatic aldehydes in aqueous methanol containing sodium hydroxide was shown in the Figure 1 and 2. The S-shaped character of the plot (Fig. 1) was typical of the electrochemical events here after indicating that there was some chemical transformation.[23] The electroreduction of nitroaniline in absence and presence of cinnamaldehyde was shown in the figure 1. It was observed that in the absence and presence of cinnamaldehyde, reduction occurs at -0.90V and -0.92V respectively. The Figure 2 indicated many different conditions that were without imine group, imine group with salicylaldehyde moiety, imine group with cinnamaldehyde moiety. The current density and time taken were different for these three reactions. The withdrawing groups increase the reduction time and the reduction potential shift towards more negative potential (Fig. 1). The current density depends upon the nature of the reaction mixture (Fig. 2). The rate of reaction, r_A, as the rate of conversion of the reactant per unit time per unit area of electrode, it follows from Faraday·s law that:

$r_A = ai/nF$----------(1)

$i = (nFr_A)/a$----------(2)

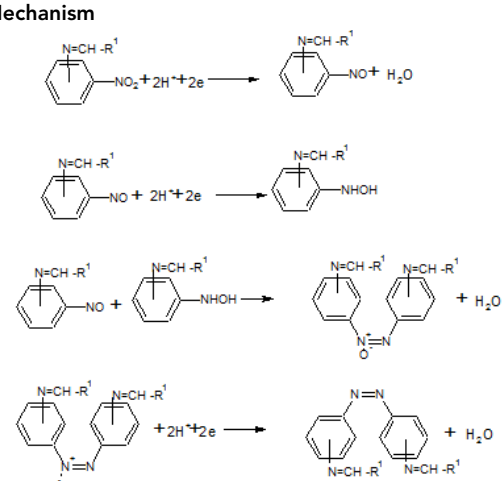
where a is the stoichiometric coefficient of the reactant. The current density for an electrochemical reaction is therefore equivalent to the rate of the reaction. In case of the reaction mixture containing *o*-nitroaniline and salicylaldehyde, current density increases which correspond to the first reaction. The further increase in current density was due to the starting of another reaction. In the second plot corresponds the reaction mixture contain *o*-nitroaniline in which only one reaction is possible. But in the third plot two reactions were taking place at low current density when compare to that of first and second plots.



The chemist have established the reductive coupling mechanism[12] and in the present work same mechanism was given for the reductive coupling of R^1 and R^2 substituted nitro compounds.

It was as follows.

Mechanism



Volume : 4 | Issue : 10 | October 2014 | ISSN - 2249-555X

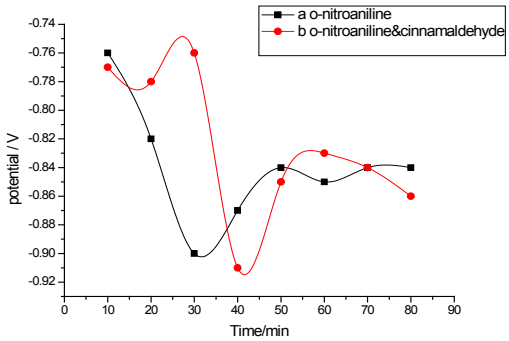


Figure 1: Graph showing the variation of potential with time for two different reactions.

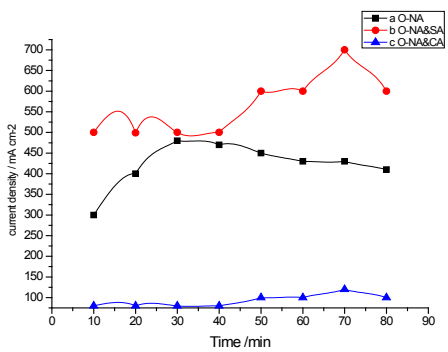


Figure 2: Graph showing the variation of current density with time for three different reactions (o-NA:o-nitroaniline , SA:salicylaldehyde, CA: cinnamaldehyde).

The structures of compounds were confirmed by FTIR, ^{1}H NMR and CHN analysis. The FTIR spectrum of a compound showed in the Table 1, peaks around 3443 cm^{-1}, 3069 cm^{-1}, 1613 cm^{-1} and 1483 cm^{-1} which were assigned to -OH, -C-H aromatic, -C=N- and –N=N- vibrations respectively. H^1 NMR spectrum of 2-[(E)-{4-[(E)-(2-hydroxybenzylidene) amino]phenyl}diazenyl]phenol showed signals at δ 6.9-7.9, 8.3 and 10.8 due to resonance of imine, aromatic and hydroxyl protons respectively.

Antibacterial and antifungal activity of 2-[(E) -{4-[(E) -(2-hydroxybenzylidene) amino] phenyl} diazenyl] phenol.
The *in-vitro* antibacterial activity carried out by well diffusion method using nutrient agar as the medium, DMSO as the control and chloramphenicol used as a standard bactericide and fluconazole as standard fungicide. The newly synthesized compounds were screened for antimicrobial activity against Staphylococcus aureus. Bacillus aureus, Streptococcus Sp, Proteus mirabilis, Staphylococcus epidermidis, Enterobacter aerogenes, Shigella flexneri, Klebsiella pneumonia, Vibriocholerae and species of fungi that was against Aspergillus Flavius, Aspergillus Niger, Cryptococcus. neaformens, Curvularia Sp, Trichosporon Sp, Candida albicans Well-in agar method. The synthesized compounds (1mg mL^{-1}) and the controlled drugs were dissolved in redistilled DMSO for determining the both antibacterial and antifungal activity. The zones of inhibition were determined at the end of an incubation period of 24 hours at 37°C. During this period, the test solution defused and the growth of inoculated microorganism was affected. The antifungal activities were determined at 26-28 °C.

The Schiff's base showed good antibacterial and antifungal activity and its benzoylated product less activity. The reduced activity was due to the protection of –OH group by benzoyl group. The zone of inhibition is given in Table 4 and 5.

Table-4: Antifungal activity (zone of inhibition in mm)

Sl. No.	Type of fungi	Zone of inhibition in mm	
		S1	S2
1	Aspergillus flavius	36	36
2	Aspergillus niger	15	33
3	Cryptococcus.neaformens	55	40
4	Curvularia sp	16	35
5	Trichosporon sp	15	32
6	Candida albicans	38	36

S1: 2-[(E) -{4-[(E) -(2-hydroxybenzylidene) amino] phenyl} diazenyl] phenol

S2: Benzoyl derivative of 2-[(E) -{4-[(E) -(2-hydroxybenzylidene) amino] phenyl} diazenyl] phenol

Table-5: Antibacterial activity (zone of inhibition in mm)

Sl. No.	Bacterial trains used	Zone of inhibition in mm	
		S1	S2
1	Staphylococcus.aureus	36	36
2	Bacillus cereus	15	33
3	Streptococcus sp	55	40
4	Proteus mirabilis	16	35
5	Staphylococcus epidermidis	15	32
6	Enterobacter aerogenes	38	36
7	Shigella flexneri	39	18
8	Klebsiella pneumoniae	55	19
9	Vibriocholerae	39	37

Conclusions
The results of this work shows that the Schiff's' bases of nitro aniline yield azo Schiff's bases by electro reductive coupling. The electrochemical behaviour of Schiff's bases of nitro aniline is very clear at zinc electrodes in aqueous methanol medium. The syntheses of azo Schiff's bases utilize less time. The azo Schiff's bases show good biological activity.

Volume : 4 | Issue : 10 | October 2014 | ISSN - 2249-555X

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