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ORIGINAL PAPER

Synthesis and structure elucidation of some new azo dye from hydroxyquinolin-2(*1H*)-one derivatives and their antimicrobial evaluation

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Abstract
The aim of the work is synthesis of some novel azo dye from 1,2-dihydro-4-hydroxy-2-oxoquinoline-6-sulfonic acid (**3**), 4-hydroxy-6-methoxyquinolin-2(*1H*)-one (**4**), and 4-hydroxy-6-nitroquinolin-2(*1H*)-one (**5**). The prepared compounds were screened for antibacterial against *Staphylococcus aureus, Escherichia coli*, and antifungal activity against *Candida sp., Aspergillus multi* and *Aspergillus niger*. The structure of newly compounds was characterized by ^{1}H-NMR, IR and elemental analysis.

Keywords Antimicrobial activity · 4-Hydroxy-6-nitroquinolin-2(*1H*)-one · Azo dye and *Aspergillus niger*.

Introduction

Azo dyes are used to add colors or to change the characteristics of something and considered to be most important in chemical classes of industrial colorants [1]. Synthesis of Azo dyes done by coupling reactions and diazotization was studied more than any other classes of dyes [2]. Azo dyes are largely used in the food, textile, cosmetics, pharmaceutical, and paper industries [3]. The biological activities of coloring usually results from specific metabolic pathway. The in vivo studies showed the enzymatic-mediated reduction of azo bonds [4, 5], for example liver in mammals [6], bacteria in gastrointestinal tract [7–9] and staphylococcus aureus in the skin [10, 11]. Products of corresponding aromatic amines arising from azo dyes could be more or less toxic from other compounds, however, those processes may result in reduction or increasing of other toxic or carcinogenicity of these dyes [12, 13]. 4-Hydroxy-2-quinolones have attracted considerable attention in recent years due to their biological and pharmacological activities and use as chromosomes [14–19]. Novel azo dyes were synthesized by the reaction of 8-methyl-4-hydroxyl-2-quinolon with *p*-substituted aniline derivatives [20], and their applications on different fabrics. Therefore, we have synthesized novel new compounds azo dye by diazotization coupling methods.

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Experimental

Instruments and methods

Melting points were determined on Electro thermal IA 9100 series digital melting point apparatus in capillaries and are uncorrected. IR spectra were obtained in the solid state as potassium bromide disks using a Perkin-Elmer model 1430 spectrometer. ^{1}H-NMR spectra were recorded on a Varian/Gemini 400 MHz spectrometer in DMSO-d_6 as a solvent and TMS as an internal standard (chemical shifts in δ, ppm). Mass spectra were measured on an instrument VG-7035 at 70 or 15 eV. Elemental analyses have performed at the Micro analytical Centre, Cairo University, and Giza, Egypt.

General procedure for azo dye

Aromatic amines derivatives (**2a,b**) (3 mmol) was dissolved in glacial acetic acid (10 ml with 1 ml H_2SO_4) in 250-ml

beaker, and sodium nitrite (4 mmol)was dissolved in 15 ml of H_2O and added drop wise with stirring. The reaction mixture immersed in ice-salt bath and cooled to 0 °C until the reaction was complete. 4-hydroxy-quinolin-2(*1H*)-one derivatives (3 mmol) were dissolved in glacial acetic acid and 10% KOH. The solution was cooled to 0 °C in an ice-salt bath and then the prepared cold diazonium salt from above was stirred and added very slowly by the wall of the beaker with vigorous stirring. After the addition of the whole diazonium salt, the reaction mixture was left in the ice bath for further 12 h with occasional stirring, washed with cold water and dried.

4-(1,2-Dihydro-4-hydroxy-2-oxoquinoline-6-sulfonic acid-3-azo)sulfonic acid (6)

Dark red crystals. IR (KBr): 3446 (OH), 3203 (NH), 3079 (arom-H), 1689 (C=O). ^{1}H-NMR (400 MHz, DMSO): 15.33–14.50 (br, 1H, hydrazone, NH), 13. 06 (s, 1H,SO_3H), 10.93–10.7 (br, 1H, amide, NH), 7.95–7.89 (dd, 2H, $J=2.4$ Hz, Ar–H), 7.52–7.48 (dd, 2H, $J=2$ Hz, Ar–H), 7.85 (m, 3H, Ar–H). Anal. Calcd for: $C_{15}H_{13}N_3O_8S_2$ (427.41):C, 42.15; H, 3.07; N, 9.83; S, 15.00. found: C, 42.23; H, 3.17; N, 9.80; S, 15.12. Yield: 78%, Mp: 295–297 °C.

4-(4-Hydroxy-6-methoxyquinolin-2(*1H*)-one-3-azo) sulfonic acid (7)

Brown red crystals. IR (KBr): 3426 (OH), 3254 (NH), 3064 (arom-H), 1685 (C=O). ^{1}H-NMR (400 MHz, DMSO): 15.45–14.86 (br, hydrazone,1H, NH), 13.14 (s, 1H,SO_3H), 10.85–10.64 (br,1H, amide, NH), 7.85–7.89 (dd, 2H, $J=2.4$ Hz, Ar–H), 7.57–7.51 (dd, 2H, $J=2$ Hz, Ar–H), 7.77 (m, 3H, Ar–H), 2.34 (s, 3H, OCH_3). Anal. Calcd for: $C_{16}H_{13}N_3O_6S$ (375.36):C, 51.20; H, 3.49; N, 11.19; S, 8.54. found: C, 51.22; H, 3.51; N, 11.15; S, 8.49. Yield: 65%, Mp: 278–280 °C.

4-(4-Hydroxy-6-nitroquinolin-2(*1H*)-one-3-azo) sulfonic acid (8)

Red crystals. IR (KBr): 3443 (OH), 3205 (NH), 3089 (arom-H), 1687 (C=O), 1396–1523 (NO_2). ^{1}HNMR (400 MHz, DMSO): 15.03–14.56 (br,1H, hydrazone, NH), 10.86–10.79 (br, 1H, amide, NH), 7.85–7.69 (dd, 2H, $J=2.4$ Hz, Ar–H), 7.45–7.33 (dd, 2H, $J=2$ Hz,, Ar–H), 6.95 (m, 3H, Ar–H). Anal. Calcd for: $C_{15}H_{10}N_4O_7S$ (390.33):C, 46.16; H, 2.58; N, 14.35; S, 8.21. found: C, 46.19; H, 2.56; N, 14.38; S, 8.19. Yield: 68%, Mp: 265–267 °C.

(*Z*)-3-(2-(4-Methoxyphenyl)hydrazono)-1,2,3,4-tetrahydro-2,4-dioxoquinoline-6-sulfonic acid (9)

Brown red crystals. IR (KBr): 3420 (OH), 3234 (NH), 3075 (arom-H), 1689 (C = O). ^{1}H-NMR (400 MHz, DMSO): 15.53–14.79 (br, 1H, hydrazone, NH), 13.02 (s, 1H,SO_3H),10.25–10.43 (br, 1H, amide, NH), 7.82–7.89 (dd, 2H, $J=2.4$ Hz, Ar–H), 7.50–7.53 (dd, 2H, $J=2$ Hz, Ar–H), 7.77 (m, 3H, Ar–H), 2.15 (s, 1H, OCH_3). Anal. Calcd for $C_{16}H_{13}N_3O_6S$ (375.36):C, 51.20; H, 3.49; N, 11.19; S, 8.54. Found: C, 51.18; H, 3.51; N, 11.21; S, 8.51. Yield: 60%, Mp: 270–272 °C.

(*Z*)-3-(2-(4-Methoxyphenyl) hydrazono)-6-methoxyquinoline-2,4(*1H,3H*)-dione (10)

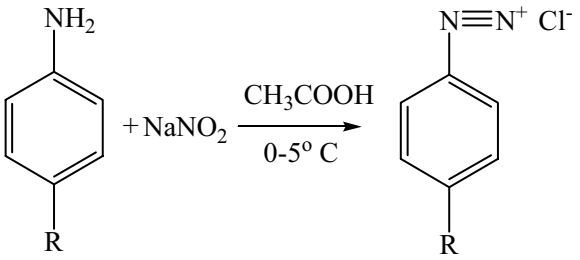
Red crystals. IR (KBr): 3526 (OH), 3120 (NH), 3086 (arom-H), 1692 (C=O). ^{1}HNMR (400 MHz, DMSO): 15.33–14.21 (br, hydrazone, NH), 13.32 (s, 1H,SO_3H),10.23–9.86 (br, amide, NH), 7.76–7.59 (dd, 2H, $J=2.4$ Hz, Ar–H), 7.32–7.02 (dd, 2H, $J=2$ Hz), 8.95 (m, 3H, Ar–H), 2.52 (s,3H, OCH_3), 3.78 (s,3H, OCH_3). Anal. Calcd for: $C_{17}H_{15}N_3O_4$ (325.32):C, 62.76; H, 4.65; N, 12.92. Found: C, 62.65; H, 4.64; N, 12.94. Yield: 57%, Mp: 293–295 °C.

(*Z*)-3-(2-(4-Methoxyphenyl)hydrazono)-6-nitroquinoline-2,4 (*1H,3H*)-dione (11)

Red crystals. IR (KBr): 3456 (OH), 3120 (NH), 3054 (arom-H), 1689 (C=O). ^{1}HNMR (400 MHz, DMSO): 15.12–14.43 (br, hydrazone, NH), 10.45–10.32 (br, amide, NH), 6.85–6.69 (dd, 2H, $J=2.4$ Hz, Ar–H), 7.23–7.12 (dd, 2H, $J=2$ Hz, Ar–H), 8.95 (m, 3H, Ar–H), 2.76 (s, 3H, OCH_3). Anal. Calcd for:$C_{16}H_{12}N_4O_5$ (340.29):C, 56.47; H, 3.55; N, 16.46. Found: C, 56.40; H, 3.51; N, 16.52. Yield: 65%, Mp: 286–288 °C.

(*Z*)-3-(2-*p*-tolylhydrazono)-6-methoxyquinoline-2,4(*1H,3H*)-dione

Red crystals. IR (KBr): 3310 (NH), 3087 (arom-H), 1686 (C=O). ^{1}HNMR (400 MHz, DMSO): 14.96–14.43 (br, hydrazone, NH), 10.45–9.97 (br, amide, NH), 6.80–6.67 (dd, 2H, $J=2.4$ Hz, Ar–H), 7.33–7.19 (dd, 2H, $J=2$ Hz, Ar–H), 8.95–7.86 (m, 3H, Ar–H), 3.52 (s, 3H, OCH_3), 2.01(s, 3H, OCH_3). Anal. Calcd for:$C_{17}H15N_3O_3$ (309.32): C, 66.01; H, 4.89; N, 13.58. Found: C, 66.04; H, 4.92; N, 13.56. Yield: 56%, Mp: 276–278 °C.

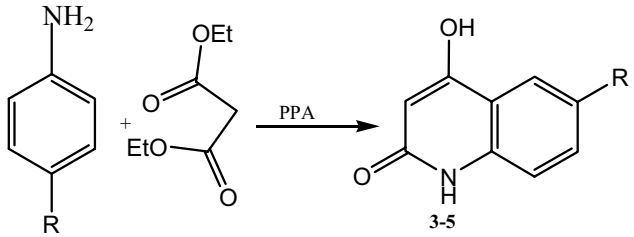


1a,b,c

R=
a= SO_3H
b= OCH_3
c =CH_3

2a,b,c

Scheme 1 Synthesis of diazonium salts **2a–c**



3 R= SO_3H
4 R= OCH_3
5 R= NO_2

Scheme 2 Synthesis of 4-hydroxy-2(*1H*)-quinolone derivatives **3–5**

(*Z*)-3-(2-*p*-tolylhydrazono)-6-nitroquinoline-2,4(*1H,3H*)-dione

Red crystals. IR (KBr): 3198 (NH), 3123 (arom-H), 1679 (C=O). ^{1}HNMR (400 MHz, DMSO): 15.21–14.44 (br, hydrazone, NH), 10.40-10.29 (br, amide, NH), 6.79–6.60 (dd, 2H, $J=2.4$ Hz, Ar–H), 7.12–6.98 (dd, 2H, $J=2$ Hz, Ar–H), 8.87–7.62 (m, 3H, Ar–H), 2.06 (s, 3H, CH_3). Anal. Calcd for: $C_{16}H_{12}N_4O_4$ (324.29): C, 59.26; H, 3.73; N, 17.28. Found: C, 59.29; H, 3.70; N, 17.30. Yield: 63%, Mp: 269–270 °C.

Results and discussion

Chemistry

The first aniline derivatives (**1a–b**) were dissolved in glacial acetic acid and diazotized using concentrated sulphuric acid and sodium nitrite in ice bath containing methanol at 0–5 °C to form diazo compounds (**2a–c**) according to a published procedure [21] (Scheme 1).

4-Hyroxy-2(*1H*)-quinolone derivatives were synthesized by condensation of aniline derivatives with diethylmalonoate and polyphosphoric acid (phosphorous oxy chloride with phosphoric acid) [22]. We chose 4-Hyroxy-2(*1H*)-quinolone derivatives in synthesized azo dye due to the third position in 4-Hyroxy-2(*1H*)-quinolone ring being highly activated that it also has both electrophilic and nucleophilic properties (Scheme 2).

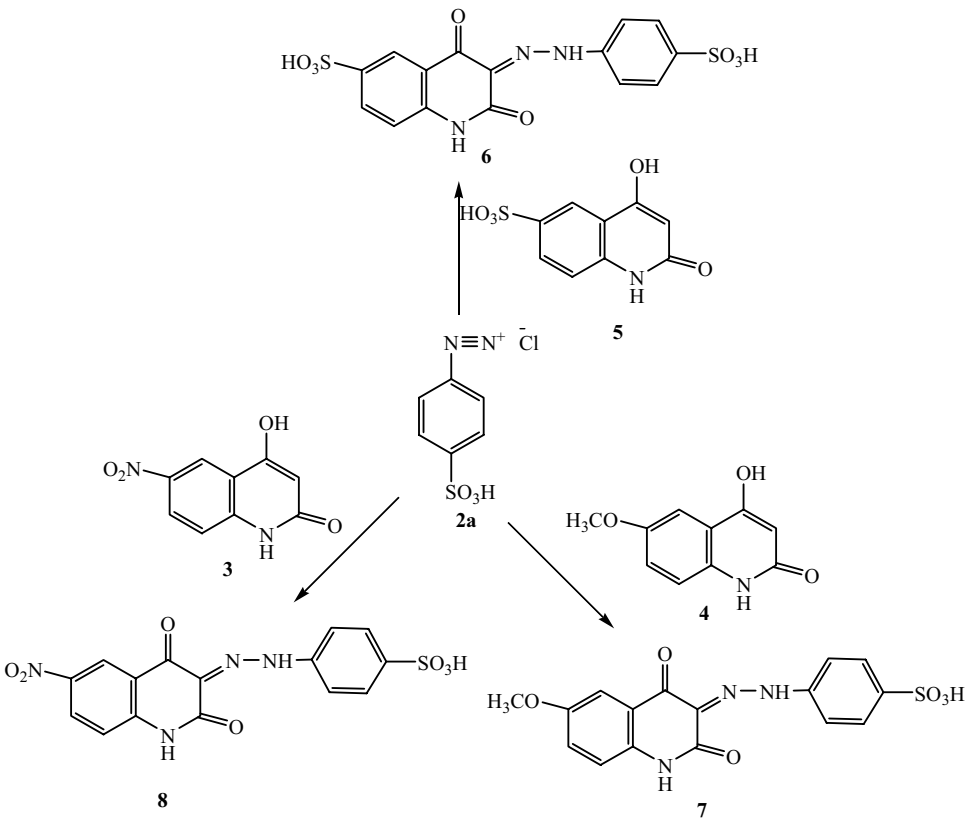
4-Diazobenzenesulfonic acid (**2a**) was coupled with various substituted 1,2-dihydro-4-hydroxy-2-oxoquinoline-6-sulfonic acid (**3**), 4-hydroxy-6-methoxyquinolin-2(*1H*)-one (**4**), and 4-hydroxy-6-nitroquinolin-2(*1H*)-one (**5**) in alkaline medium of potassium hydroxide (10%) to synthesize azo dye compounds 4-(1,2-dihydro-4-hydroxy-2-oxoquinoline-6-sulfonic acid-3-azo)sulfonic acid (**6**), 4-(4-hydroxy-6-methoxyquinolin-2(*1H*)-one-3-azo) sulfonic acid (**7**) and 4-(4-hydroxy-6-nitroquinolin-2(*1H*)-one-3-azo) sulfonic acid (**8**), respectively. The IR spectrum of all dyes in KBr showed abroad band at 3500–3275 cm^{-1} which confirms the presence of hydroxyl group (OH) and another band at 1418–1438 cm^{-1} due to (*N*=*N*) group. The new series of compounds were characterized on the basis of ^{1}H-NMR (Scheme 3).

Also the diazonium salt of 4-anisidine **(2b)** was coupled with the same 4-hydroxy-quinoline-*4H*-one derivatives **3, 4** and **5** yielded (*Z*)-3-(2-(4-methoxyphenyl) hydrazono)-1,2,3,4-tetrahydro-2,4-dioxoquinoline-6-sulfonic acid **(9)** (*Z*)-3-(2-(4-methoxyphenyl) hydrazono)-6-methoxyquinoline-2,4(*1H,3H*)-dione **(10)** and (*Z*)-3-(2-(4-methoxyphenyl) hydrazono)-6-nitroquinoline-2,4 (*1H,3H*)-dione **(11)** (Scheme 4).

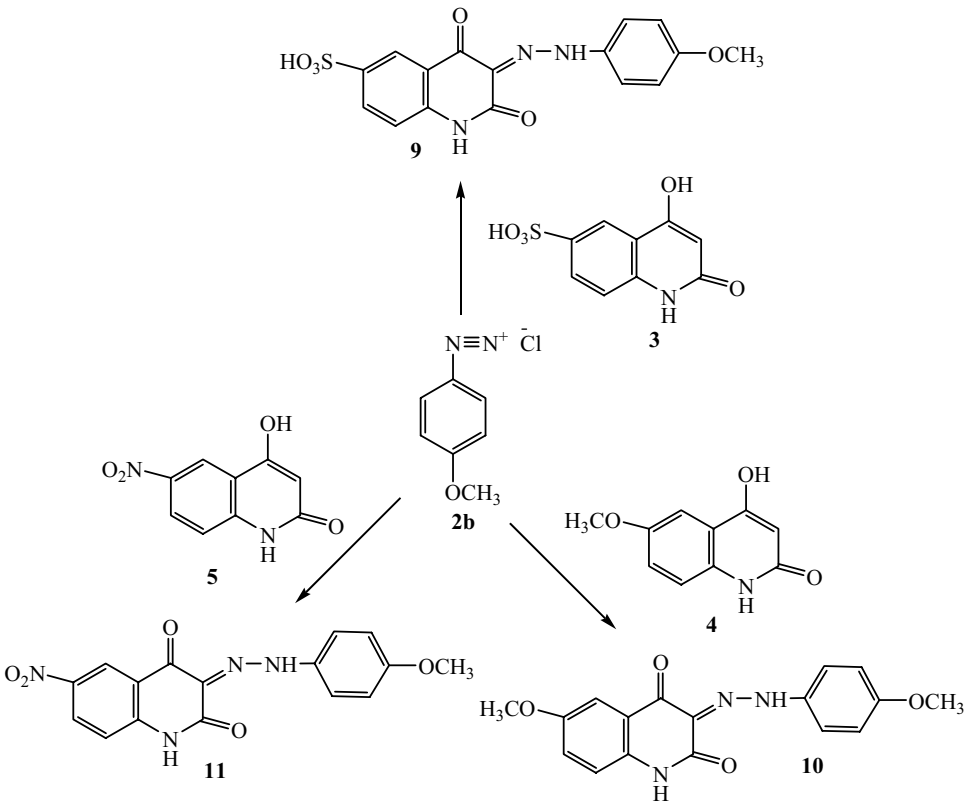
Synthesis of azo dyes (**12) and** (**13**) was produced by reaction of 4-methylbenzenediazonium **(2c) with** 4-hydroxy-quinoline-*4H*-one derivatives **(3, 4)** in aqueous solution (scheme 5).

Mechanism for synthesized azo dye compounds.

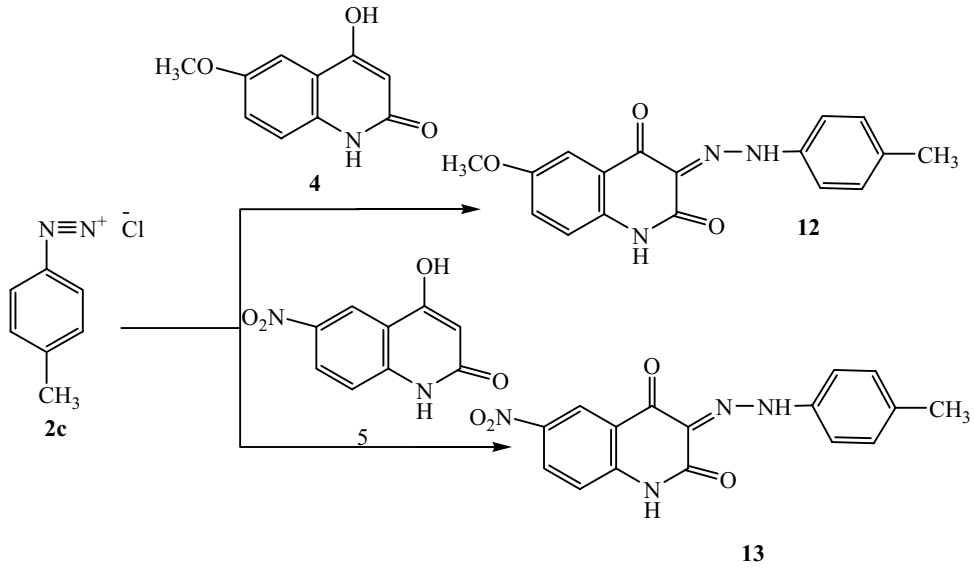
Scheme 3 Synthesized azo dye compounds **6, 7** and **11**

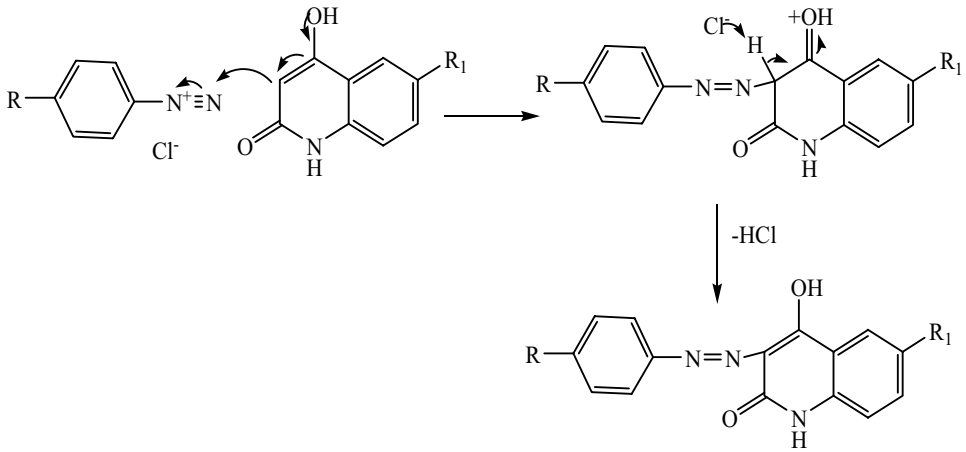


Scheme 4 Synthesized azo dye compounds **9, 10** and **11**



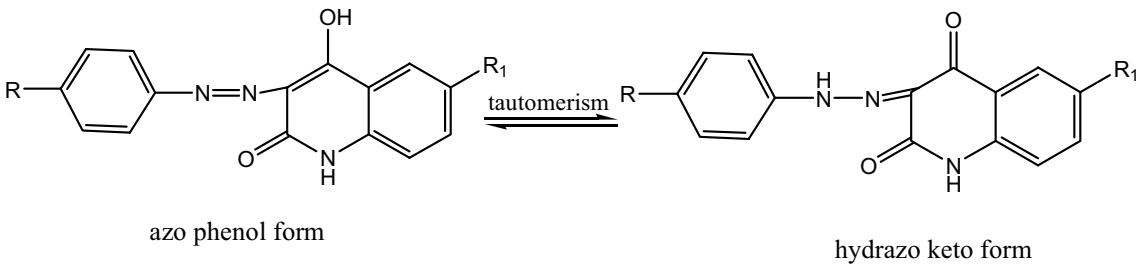
Scheme 5 Synthesized azo dye compounds **12** and **13**





R:a=SO_3H; b=OCH_3; c= CH_3

R_1: SO_3H; NO_2; OCH_3



azo phenol form

hydrazo keto form

Fig. 1 Possible tautomeric structure of azo dye

Table 1 Antibacterial activity of synthesized compounds (**6–11**), zone of inhibition (mm)

Compounds	*Staphylococcus aureus* Zone of inhibition	*Escherichia coli* Zone of inhibition
6	24	18
7	23	16
8	25	21
9	10	13
10	17	19
11	22	18
Ampicillin (10ug/ml)	26	26

Table 2 Antifungal activity of synthesized compounds (**6–11**), zone of inhibition (mm)

Compounds	*Candida sp.* Zone of inhibition	*Aspergillus multi* Zone of inhibition	*Aspergillus niger* Zone of inhibition
6	14	9	12
7	16	11	14
8	12	12	13
9	10	13	8
10	13	6	9
11	11	10	15
Ketoconazole (10ug/ml)	17	17	16

As shown in Fig. 1, compounds under accurate examination can have two possible tautomeric structures.

Antimicrobial activities

All the synthesized compounds were screened for antifungal and antibacterial activities using agar diffusion methods [23] against *Staphylococcus aureus*, *Escherichia coli* as antibacterial and *Candida sp., Aspergillus multi, and Aspergillus niger as antifungal*. Antimicrobial activities were tested by measuring the diameter of inhibition zone in mm. Ampicillin and Ketoconazole were used as standard drug against bacteria and fungi, respectively. The results of antibacterial activity are shown in Table 1 and antifungal activity in Table 2. The synthesized compounds showed high activity against *Staphylococcus aureus, Candida sp and Aspergillus niger*.

Conclusion

In this manuscript, synthesis of six new heterocyclic azo dyes by diazotization coupling methods was performed. Their compounds were established by ^{1}H-NMR and FT-IR spectra. All the dyes tested had some effective properties on bacterial growth.

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Compliance with ethical standards

Conflict of interest All authors have none to declare.

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