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Synthesis, antimicrobial evaluation and spectroscopic characterization of novel imidazolone, triazole and triazinone derivatives

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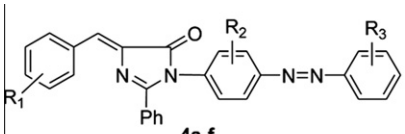
HIGHLIGHTS

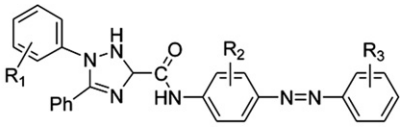
- Synthesized compounds were characterized by analytical and spectral data.
- Compounds were screened for their antibacterial activity and antifungal activity.
- Compounds **10f**, **14b** and **14c** showed a significant activity.

GRAPHICAL ABSTRACT



4a-f

4a, $R_1 = R_2 = R_3 = H$
4b, $R_1 = H$, $R_2 = CH_3$-*o*, $R_3 = NO_2$-*p*
4c, $R_1 = H$, $R_2 = OCH_3$-*o*, $R_3 = NO_2$-*p*
4d, $R_1 = OCH_3$-*p*, $R_2 = R_3 = H$
4e, $R_1 = OCH_3$-*p*, $R_2 = CH_3$-*o*, $R_3 = NO_2$-*p*
4f, $R_1 = OCH_3$-*p*, $R_2 = OCH_3$-*o*, $R_3 = NO_2$-*p*



10a-f

10a, $R_1 = R_2 = R_3 = H$
10b, $R_1 = H$, $R_2 = CH_3$-*o*, $R_3 = NO_2$-*p*
10c, $R_1 = H$, $R_2 = OCH_3$-*o*, $R_3 = NO_2$-*p*
10d, $R_1 = OCH_3$-*p*, $R_2 = R_3 = H$
10e, $R_1 = OCH_3$-*p*, $R_2 = CH_3$-*o*, $R_3 = NO_2$-*p*
10f, $R_1 = OCH_3$-*p*, $R_2 = OCH_3$-*o*, $R_3 = NO_2$-*p*

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ABSTRACT

The reactions of 2-phenyl-4-arylmethylene-2-oxazolin-5-ones (**1a**, **b**) and 2-phenyl-4-arylazo-2-oxazolin-5-ones (**8a**, **b**) with *p*-aminoazobenzene derivatives (**2a–c**) gave the corresponding imidazolone derivatives (**4a–f**) and triazole derivatives (**10a–f**), respectively. Also, the reaction of **1a** with *o*-aminophenol to give the imidazolone derivative **5** was studied. The reaction of **1a** with 2,4-dinitrophenylhydrazine gave the corresponding 1,2,4-triazine derivatives **14a–c**, respectively. The newly synthesized compounds were screened for their antibacterial activity against Gram-positive (*Bacillus subtilis* and *Bacillus thuringiensis*), Gram-negative bacteria (*Escherichia coli* and *Pseudomonas aeruginosa*) and in vitro antifungal potential against *Fusarium oxysporum* and *Botrytis fabae* fungal strains. The results revealed that the investigated compounds exhibited antibacterial and a significant antifungal activity.

Introduction

The interesting and medicinal activities of imidazole and 1,2,4-triazine moieties stimulated considerable recent research directed to synthesis of derivatives of this ring system [1–4]. The incorporation of arylazo or arylhydrazone is known to have diverse pharmacological properties including antibacterial, antiviral, antiallergic and antineoplastic [5,6].

In continuation of the project concerning the development of new procedure for the synthesis of different heterocycles with potential biological activities [7–10], I have now synthesized new imidazolinones and their triazinone derivatives.

Results and discussion

Chemistry

Thus, it was found that 2-phenyl-4-arylmethylene-2-oxazoline-5-one derivatives **1a**, **b** react with *p*-aminoazobenzene derivatives **2a–c**, I found that the products obtained depend on the reaction conditions. Thus, when the reaction was carried out in refluxing ethanol, we obtained the corresponding carboxamide derivatives **3a–f** through the oxazolone ring opening at C_5, while when the reaction was carried out under fusion condition and in the

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presence of freshly fused sodium acetate, we obtained the corresponding imidazolone derivatives **4a–f**, which are formed through oxazolone ring opening at C_5, followed by cyclization to the corresponding imiazolone derivatives **4a–f**. The chemical structures of compounds **3a–f** and **4a–f** were confirmed by spectral and elemental analyses. The IR spectra of **3a–f** in general showed absorption bands at 3350, 1691, 1620 and 1550 cm^{-1} corresponding to stretching frequencies of (NH), (CO, amidic), (C=C) and (N=N) groups, respectively. While, the ^1H NMR spectrum of **3b** showed signals at δ 2.3 (s, 3H, CH_3), 7.1–8.2 (m, 17H, Ar–H), 8.4 (s, 1H, CH=C), 10.1 (s, 1H, NH) and 10.5 ppm (s, 1H, NH). On the other hand, the IR spectra of compounds **4a–f** showed bands at 1700, 1610 and 1551 cm^{-1} corresponding to (CO, amidic), (C=C) and (N=N) functions, respectively. The ^1H NMR spectrum of **4b** showed signals at δ 2.27 (s, 3H, CH_3), 7.0–8.2 (m, 17H, Ar–H), 8.3 ppm (s, 1H, PhCH=C).

In addition, it was found that heating compounds **3a–f** in glacial acetic acid containing a catalytic amount of freshly fused sodium acetate gave product identical in all respects (IR, ^1H NMR and mass spectra) to **4a–f** (**Scheme 1**). Moreover, fusion of *o*-aminophenol with **1a** afforded (*Z*)-4-benzylidine-1-(2-hydroxyphenyl)-2-phenyl-1*H*-imidazol-5(4*H*)-one (**5**). The ^1H NMR spectrum of compound **5** showed a characteristic singlet signal at δ 7.85 ppm for (CH=C) proton.

Derivatives of 4-phenylazophenol are well known as dyes [11]. Recently, some details dealing with the synthesis and dyeing behavior of 4-arylazophenol dyes with mercaptotriazine, thiadiazine and indole moieties on different fibers have been reported [11]. Consequently, the coupling of various diazotized arylamines with imidazolone derivative **5** was explored in order to synthesize some new arylazophenol derivatives of biological interest. Therefore, it has been found that, reaction of **5** with different diazotized arylamines (**6a–c**) afforded the corresponding 4-arylazo-2-(*Z*)-4-benzylidene-2-phenyl-1*H*-imidazol-5(4*H*)-ones **7a–c** (**Scheme 2**).

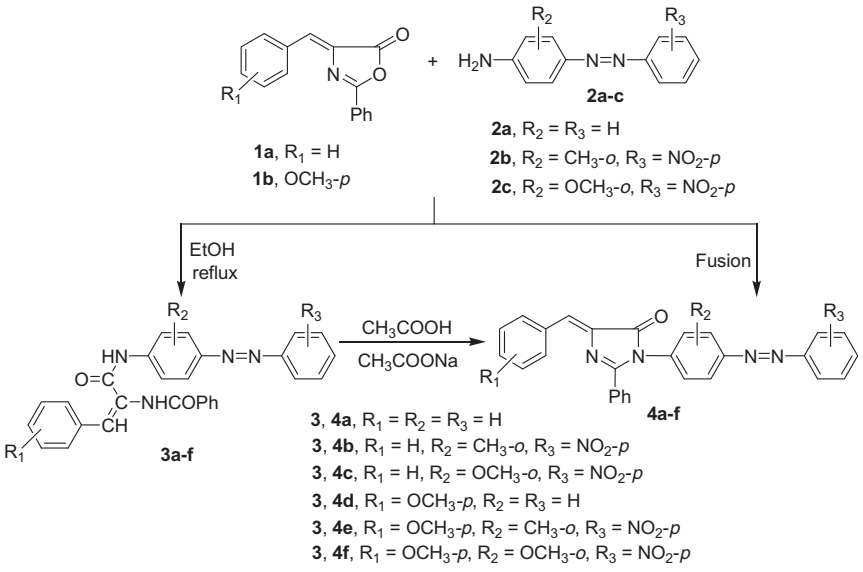
From the infrared measurements of the prepared arylazo derivatives **7a–c**, bands at 1580 cm^{-1} (–N=N–, stretching), 1610 cm^{-1} (conjugated C=N group), 3300 cm^{-1} (NH absorption) and 3430 cm^{-1} (OH stretching) were recorded. Compounds **7a–c** can exist in the tautomeric forms (**A** and **B**) as shown in **Scheme 2**.

On the other hand, the reaction of 2-phenyl-4-arylazo-2-oxazolin-5-one derivatives **8a**, **b** toward *p*-aminoazobenzene derivatives **2a–c** in different reaction conditions was studied. Thus, heating of **8a** with **2a–c** in refluxing ethanol afforded the corresponding carboxamide derivatives **9a–c**, while when the reaction was carried out by fusion of **8a**, **b** conditions and in the presence of freshly fused sodium acetate, the corresponding triazole derivatives **10a–f** were obtained. The chemical structures of products **9a–c** and **10a–f** were confirmed by spectral and elemental analyses. The IR spectra of compounds **9a–c** in general showed absorption frequencies at 3200 cm^{-1} (NH), 1695 cm^{-1} (CO), 1620 cm^{-1} (C=N). The ^1H NMR spectrum of **9b** revealed signals at δ 1.75 for 2H (2C(OH) =N), at δ 2.65 for CH_3 protons and at δ 6.7–8.5 ppm for aromatic protons and one NH proton. On the other hand, The IR spectra of the triazole derivatives **10a–f** showed absorption bands at 3400 cm^{-1} (NH), 1670 cm^{-1} (CO) and 1625 cm^{-1} (C=N). The ^1H NMR spectrum of **10b** showed signals at δ 1.9 for enolic OH, δ 2.17 ppm for methyl protons and at δ 6.8–8.5 ppm as multiplet signals due to aromatic protons.

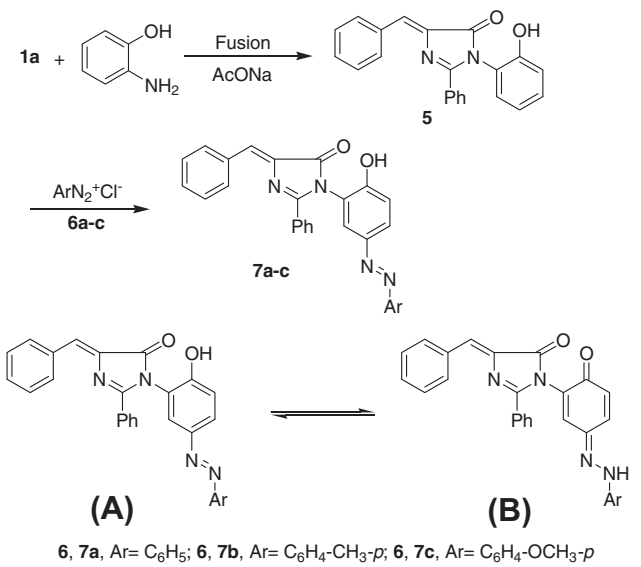
Generally, the change in color of these dyes results from the nature and orientation of substituents in the diazonium components. Further, the UV spectra of the diazonium coupling products of **7a–c** provide additional evidence that such compounds gave the tautomeric relationship with benzoquinone monohydrazones.

Most of the dyes show three absorption bands in the region 210–370 nm. The relatively small difference in λ_{max} may be due to the polarity change of the absorbing system caused by solvent interactions due to the general solvent effect [12]. It has been reported that the UV spectra of mono-phenylazo compounds differ from those of mono-phenylhydrazones. The azo compounds generally show two absorption bands at 400–410 and 290–300 nm, corresponding to n–$\pi*$ and π–$\pi*$ transitions, respectively [12]. On the other hand, monophenyl hydrazones show three intense bands in the 220–230, 250–280 and 330–390 nm regions [12]. It is clear that these dyes exhibit three bands; of these, the medium and high wavelength bands seem to be affected by the nature of the polar substituent in the arylazo group, and the low wavelength band is unaffected. The 250 nm band of the parent imidazole exhibits a profound hyposochromic shift, often disappearing from the measurable region, which is conceivably caused by the cis arrangement of the imidazolylphenol.

Heating of **1a** with 2,4-dinitrophenyl hydrazine in refluxing ethanol afforded the corresponding (*Z*)-*N*-(3-(2-(2,4-dinitrophenyl)hydrazinyl)-3-oxo-1-phenylprop-1-en-2-yl) benzamide (**11**). Its IR spectrum showed absorption bands at 3350–



Scheme 1. Reactions of 2-phenyl-4-arylmethylene-2-oxazolin-5-ones (**1a**, **b**) with arylazoaniline derivatives (**2a–c**).



6, **7a**, Ar= C_6H_5; **6**, **7b**, Ar= C_6H_4-CH_3-*p*; **6**, **7c**, Ar= C_6H_4-OCH_3-*p*

Scheme 2. Synthesis of (Z)-4-benzylidene-1-(5-((E)-aryldiazenyl)-2-hydroxy-phenyl)-2-phenyl-1H-imidazol-5(4H)-one derivatives (**7a–c**).

3360 cm^{-1} (NH absorption), 1610 cm^{-1} (C=C group), 1682 cm^{-1} (CO, amidic), 1530, 1350 (NO_2). The ^1H NMR spectrum of **11** showed a characteristic three singlet signals at δ 7.5, 7.96, and 9.8 ppm attributable to (α-amido, NH), (CH=C) and (2NH) protons, respectively.

When compound **11** was subjected to heat in glacial acetic acid in the presence of a catalytic amount of freshly fused sodium acetate afforded the corresponding triazine derivative **12** in good yield (**Scheme 4**). The IR spectrum of **12** showed absorption frequencies at 3310 cm^{-1} (NH), 1690 cm^{-1} (CO), 1630 cm^{-1} (C=N), 1610 cm^{-1} (C=C), 1531, 1335 cm^{-1} (NO_2). When compound **12** was heated with zinc dust in the presence of glacial acetic acid, it was reduced to the corresponding (*Z*)-5-benzylidene-2-(2,4-diamino-phenyl)-3-phenyl-1,2-dihydro-1,2,4-triazine-6(5*H*)-one (**13**). The IR spectrum of **13** showed absorption bands at 3450 cm^{-1} (NH_2), 3352 cm^{-1} (NH), 1690 cm^{-1} (CO) and the absence of any bands due to NO_2 groups. In addition, its ^1H NMR spectrum gives a more confirmation to this structure, which showed singlet signals at δ 5.69 (CH, benzene ring), 6.27 ($2NH_2$) and δ 7.8 ppm (CH=C), also, showed doublet signal at δ 5.91 and 6.33 ppm due to (2CH benzene ring).

Diazonium salts undergo coupling reactions with compound **13** to give (5*Z*)-5-benzylidene-2-(2,4-diamino)-5-(aryldiazenyl)phenyl)-3-phenyl-1,2-dihydro-1,2,4-triazin-6(5*H*)-ones **14a–c**. However, no details, regarding the synthesis and antimicrobial evaluation of these compounds have been reported.

Structures **14a–c** were elucidated from their spectral and elemental analyses. The IR spectra showed similar spectra to that of compound **13**, in addition to stretching vibration at 1550 cm^{-1} due to (–N=N–) group. While, the ^1H NMR spectra showed four singlet signals at δ 5.89, 6.27, 7.0 and 7.83 ppm due to CH, $2NH_2$, CH and CH=C protons, respectively. The doublet signal at δ 5.91 and 6.33 ppm was disappeared.

Antimicrobial evaluation

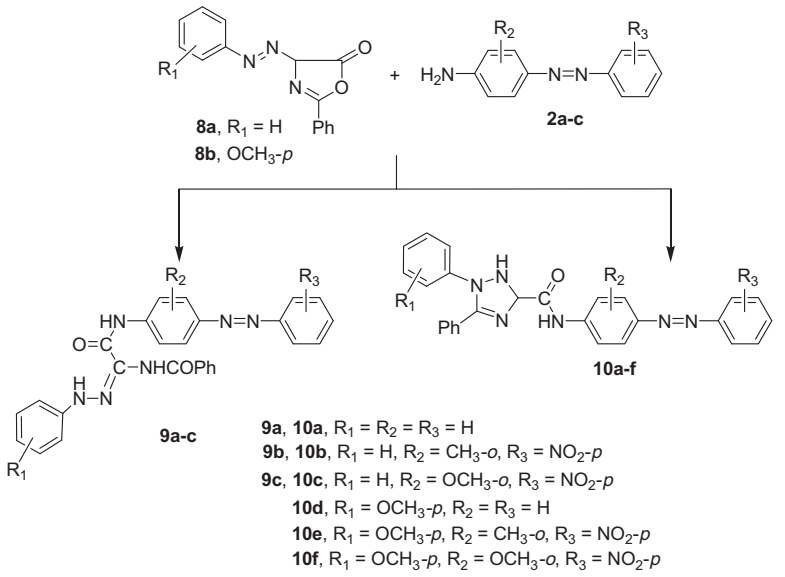
Twenty one of the newly synthesized target compounds were evaluated for their in *vitro* antibacterial activity against *Bacillus subtilis* and *Bacillus thuringiensis* as examples of Gram-positive bacteria and *Escherichia coli* and *Pseudomonas aeruginosa* as examples of Gram-negative bacteria. They were also evaluated for their *in vitro* antifungal potential against *Fusarium oxysporum* and *Botrytis fabae* fungal strains.

Agar-diffusion method [13] was used for the determination of the preliminary antibacterial and antifungal activity. Chloroam-

Table 1
Minimal inhibitory concentration (MIC, μg/mL) and inhibition zone (mm) of some new synthesized compounds.

Compound No.	MIC[a] in μg/mL and inhibition zone (mm) Bacteria				Fungi	
	Gram (+) bacteria		Gram (−) bacteria			
	B. subtilis	*B. thuringiensis*	*E. coli*	*P. aeruginosa*	*F. oxysporum*	*B. fabal*
4a	50 (20)	100 (15)	100 (15)	100 (15)	100 (15)	50 (20)
4b	25 (26)	50 (20)	100 (14)	100 (15)	100 (14)	50 (19)
4c	25 (28)	50 (19)	50 (18)	100 (16)	100 (15)	100 (15)
4d	50 (20)	100 (14)	100 (15)	100 (15)	100 (16)	100 (14)
4e	25 (27)	25 (28)	50 (19)	100 (15)	50 (19)	50 (19)
4f	25 (26)	50 (21)	100 (16)	100 (15)	50 (18)	100 (15)
5	100 (15)	100 (14)	100 (15)	100 (15)	100 (15)	100 (14)
7a	25 (26)	25 (27)	50 (18)	50 (18)	25 (26)	100 (15)
7b	25 (27)	25 (26)	50 (19)	100 (15)	100 (15)	100 (15)
7c	25 (26)	25 (26)	50 (18)	100 (16)	100 (14)	50 (19)
10a	12.5 (32)	25 (25)	100 (15)	100 (17)	12.5 (30)	25 (26)
10b	6.25 (37)	12.5 (33)	50 (18)	100 (16)	100 (14)	50 (20)
10c	6.25 (38)	12.5 (31)	25 (26)	50 (19)	50 (18)	50 (19)
10d	12.5 (31)	12.5 (30)	100 (15)	100 (15)	12.5 (31)	100 (15)
10e	6.25 (38)	12.5 (32)	50 (19)	25 (26)	50 (20)	50 (21)
10f	3.125 (42)	6.25 (39)	50 (18)	25 (26)	50 (18)	50 (19)
12	6.25 (37)	6.25 (38)	100 (15)	6.25 (37)	6.25 (31)	25 (27)
13	12.5 (30)	12.5 (32)	100 (14)	25 (26)	25 (26)	50 (19)
14a	6.25 (38)	6.25 (37)	50 (18)	50 (18)	50 (20)	100 (15)
14b	3.125 (42)	6.25 (37)	50 (19)	6.25 (37)	50 (20)	6.25 (26)
14c	3.125 (41)	6.25 (38)	50 (18)	50 (19)	25 (26)	12.5 (31)
Chloramphenicol	3.125 (42)	3.125 (44)	6.25 (38)	6.25 (37)	NT[b]	NT
Cephalothin	6.25 (36)	6.25 (37)	6.25 (37)	6.25 (38)	NT	NT
Cycloheximide	NT	NT	NT	NT	3.125 (41)	3.125 (42)

[a] MIC: Minimal inhibitory concentration values SEM = 0.02.
[b] NT: Not tested.



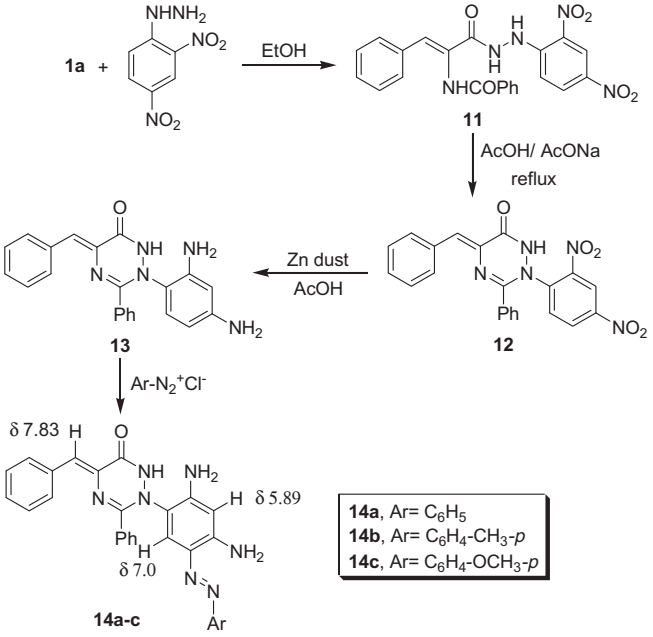
Scheme 3. Reactions of 2-phenyl-4-arylazo-2-oxazolin-5-ones (**8a**, **b**) with arylazoaniline derivatives (**2a**–**c**).

phenicol, cephalothin and cycloheximide were used as reference drugs. The results were recorded for each tested compound as the average diameter of inhibition zones (IZ) of bacterial or fungal growth around the disks in mm. The minimum inhibitory concentration (MIC) measurement was determined for compounds showed significant growth inhibition zones (>14 mm) using two fold serial dilution method [14]. The MIC (μg/mL) and inhibition zone diameters values are recorded in Table 1.

The results depicted in Table 1 revealed that most of tested compounds displayed variable inhibitory effects on the growth of the tested Gram-positive and Gram-negative bacterial strains, and also against antifungal strains.

In general, most of the tested compounds revealed better activity against the Gram positive rather than the Gram-negative bacteria. It would be also noticed that compounds belonging to the triazole and triazin-6-one series (Schemes 3 and 4) exhibited better antibacterial potentials than members of the imidazol-5-one (Schemes 1 and 2). Regarding the structure–activity relationship of the triazin-6-one against Gram positive bacteria, the results revealed that compounds **12**, **14a**, and **14c** exhibited broad spectrum antibacterial profile against the tested organisms. Compounds with electron withdrawing groups such as CO, $C_6H_3(NO_2)_2$, C_6H_5 and N=N recorded higher activity. In this view, compounds **10f**, **14b** and **14c** were equipotent to chloroamphenicol in inhibiting the growth of *B. subtilis* (MIC 3.125 μg/mL), while its activity was 50% lower than of chloroamphenicol against *B. thuringiensis*. Compounds **10b**, **10c**, **12** and **14a** showed 50% of the activity of chloroamphenicol (MIC 6.25 μg/mL) but they were equipotent to cephalothin in inhibiting the growth of *B. subtilis* and *B. thuringiensis* (MIC 6.25 μg/mL).

On the other hand, compounds **4a–f**, **5** and **7a–c** exhibited weak to moderate growth inhibitory activity against Gram-positive bacteria as revealed from their MIC values (25–100 μg/mL). Among these compounds **10a**, **10d** and **13** showed relatively good growth inhibitory profiles against *B. subtilis* (MIC 12.5 μg/mL) which were about 25% of the activity of chloroamphenicol and 50% of cephalothin against the same organism. Moreover, distinctive anti-Gram-positive profile was displayed by compounds **10f**, **14b** and **14c** where it proved to be equipotent as chloroamphenicol against *B. subtilis* (MIC 3.125 μg/mL) together with a significant activity against *B. thuringiensis* (MIC 6.25 μg/mL). Concerning the antibacterial activity of the compounds **4c**, **4e**, **7a–c**, **10b**, **10e**, **10f** and **14a–c** revealed weak growth inhibitory against the tested



Scheme 4. Synthesis of (Z)-5-benzylidene-2-(2,4-diamino-5-((E)-aryldiazenyl) phenyl)-3-phenyl-1,2-dihydro-1,2,4-triazin-6(5H)-ones (**14a**–**c**).

Gram-negative bacteria (MIC 50 μg/mL). On the other hand, compounds **12** and **14b** showed equipotent activity as chloroamphenicol and cephalothin (MIC 6.25 μg/mL) against *E. coli* and *P. aeruginosa*.

Regarding the activity triazinone, triazolone and imidazolone, against antifungal strains, the results revealed that compounds **12** and **14b** were 50% lower than cycloheximide in inhibitory the growth of *B. fabae* and *F. oxysporum* (MIC 6.25 μg/mL), while the reactivity of compounds **3b**, **10a**, **10d** and **14c** were 25% lower than cycloheximide against *F.oxysporum* (MIC 12. 5 μg/mL).

The substitution pattern was also crucial. It is worth mentioning that incorporation of arylazo group to triazinone and triazole nucleus at position 4 directly produced a high antimicrobial activity. Conversion of compound **13** to *N*-arylazo derivatives **14a–c** enhanced also the antimicrobial activity.

On the other hand, incorporation of 4-arylazophenol and *N*-arylazo moieties, 1,4-benzothiazine and/or 1,4-benzoxazine to pyrazole nucleus at position 4 in compounds **4a–f** and **7a–c** unfortunately produced weak antimicrobial activity. High biological activity can be correlated with low electron density of ring systems.

Conclusion

In conclusion, the objective of the present study was to synthesize and investigate the antimicrobial activities of some new functionalized *N*-arylazo-imidazolone/triazole and *N*-arylazotriazinone with the hope of discovering new structure leads serving as potent antimicrobial agents.

Our aim has been verified by the synthesis of three different groups of structure hybrids comprising basically the arylazo moiety attached to either imidazolone, triazole and triazinone derivatives counter parts through various linkages of synthergistic purpose. The obtained results clearly revealed that compounds derived from triazinone and triazole exhibited better antimicrobial activity than their imidazolone structure variants.

Experimental

Instruments

All melting points are recorded on Gallenkamp electrothermal melting point apparatus. The IR spectra were recorded for KBr disc on a Mattson 5000 FTIR spectrophotometer. The ^{1}H NMR spectra were measured on a Bruker AC 300 (300 MHz) in DMSO-d_6 as solvent, using TMS as an internal standard, and chemical shifts are expressed as δ_{ppm}. The mass spectra were determined on Finnigan Incos 500 (70 eV). Elemental analyses were carried out at the Microanalytical Unit of the Faculty of Science, Cairo University, Giza, Egypt.

Reactions of 2-phenyl-4-arylmethylene-2-oxazolin-5-ones (1a, b) or 2-phenyl-4-arylazo-2-oxazolin-5-ones (8a, b) with arylazoaniline derivatives (2a-c)

(a) Reflux conditions: general procedures
A solution of an equimolar amounts of **1a**, **b** or **8a**, **b** (0.01 mol) and aryl azoaniline derivatives **2a–c** (0.01 mol) in absolute ethanol (35 mL) was refluxed for 3–4 h. After cooling the formed precipitate was collected and crystallized from ethanol.

(b) Fusion conditions: general procedures
A mixture of **1a**, **b** or **8a**, **b** (0.01 mol), aryl azoaniline derivatives **2a–c** (0.01 mol) and freshly fused sodium acetate (0.02 mol) was fused at 150–160 °C for 1.5–2 h, then boiled with 25 mL dilute HCl, filtered while hot. After cooling the precipitated product was collected and crystallized from ethanol.

N-((1E)-3-Oxo-1-phenyl-3-(4-(phenyldiazenyl)phenylamino)prop-1-en-2-yl) benzamide (3a). Yield (68%); m.p. 173 °C; IR (KBr): ν/cm^{-1} = 3350 (NH), 1691 (CO amidic), 1620 (C=C), 1550 (N=N); ^{1}H NMR (DMSO-d_6) δ (ppm): 6.77 (s, 1H, CH=C), 7.25–8.31 (m, 19H, Ar–H), 8.4 (s, 1H, NH), 10.12 (s, 1H, NH); MS (EI, 70 eV) *m/z* (%) = 446 (M$^+$, 67). Anal. Calcd. for $C_{28}H_{22}N_4O_2$ (446.5): C, 75.32; H, 4.97; N, 12.55%. Found: C, 75.12; H, 4.85; N, 12.44%.

N-((1E)-3-(2-Methyl-4-((4-nitrophenyl)diazenyl)phenylamino)-3-oxo-1-phenylprop-1-en-2-yl)benzamide (3b). Yield (71%); m.p. 182 °C; IR (KBr): ν/cm^{-1} = 3350 (NH), 1685 (CO), 1618 (C=C), 1556 (N=N), 1530, 1356 (NO_2); ^{1}H NMR (DMSO-d_6) δ (ppm): 2.3 (s, 3H, CH_3), 6.73 (s, 1H, CH=C), 7.1–8.2 (m, 17H, Ar–H), 8.4 (s, 1H, NH), 10.1 (s, 1H, NH); ^{13}C–NMR(DMSO-d_6) δ (ppm): 17.5 (CH_3), 108.1, 115.2 (CH=C), 120.9 (2C), 121.4 (C), 124.2 (2C), 124.7 (C), 127.5 (2C), 127.8 (C), 127.9 (C), 128.5–128.8 (6C), 132.1–133.2 (2C), 134.2 (C), 134.6 (C), 136.9 (C–NH), 148.2 (C–N=N), 150.1 (C–NO2), 155.5 (N=N–C), 166.2 (C=O), 167.5 (C=O); MS (EI, 70 eV) *m/z* (%) = 505 (M$^+$, 46). Anal. Calcd. for $C_{29}H_{23}N_5O_4$ (505.52): C, 68.90; H, 4.59; N, 13.85%. Found: C, 68.73; H, 4.48; N, 13.73%.

N-((1E)-3-(2-Methoxy-4-((4-nitrophenyl)diazenyl)phenylamino)-3-oxo-1-phenyl prop-1-en-2-yl)benzamide (3c). Yield (68%); m.p. 210 °C; IR (KBr): ν/cm^{-1} = 3350 (NH), 1690 (CO), 1622 (C=C), 1553 (N=N), 1536, 1347 (NO_2); ^{1}H NMR (DMSO-d_6) δ (ppm): 3.81 (s, 3H, OCH_3), 6.77 (s, 1H, CH=C), 7.33–8.3 (m, 17H, Ar–H), 8.41 (s, 1H, NH), 10.12 (s, 1H, NH); MS (EI, 70 eV) *m/z* (%) = 521 (M$^+$, 82). Anal. Calcd. for $C_{29}H_{23}N_5O_5$ (521.52): C, 66.79; H, 4.45; N, 13.43%. Found: C, 66.73; H, 4.39; N, 13.33%.

N-((1E)-1-(4-Methoxyphenyl)-3-oxo-3-(4-(phenyldiazenyl)phenyl amino)prop-1-en-2-yl)benzamide (3d). Yield (77%); m.p. 271 °C; IR (KBr): ν/cm^{-1} = 3351 (NH), 1688 (CO), 1620 (C=C), 1547 (N=N); ^{1}H NMR (DMSO-d_6) δ (ppm): 3.83 (s, 3H, OCH_3), 4.1 (s, 1H, NH), 6.21 (s, 1H, CH=C), 6.51–8.25 (m, 17H, Ar–H), 10.22 (s, 1H, NH); MS (EI, 70 eV) *m/z* (%) = 476 (M$^+$, 91). Anal. Calcd. for $C_{29}H_{24}N_4O_3$ (476.53): C, 73.09; H, 5.08; N, 11.76%. Found: C, 73.13; H, 5.11; N, 11.84%.

N-((1E)-1-(4-Methoxyphenyl)-3-(2-methyl-4-((4-nitrophenyl)diazenyl) phenyl-amino)-3-oxoprop-1-en-2-yl)benzamide (3e). Yield (80%); m.p. 216 °C; IR (KBr): ν/cm^{-1} = 3355 (NH), 1693 (CO), 1625 (C=C), 1560 (N=N), 1546, 1350 (NO_2); ^{1}H NMR (DMSO-d_6) δ (ppm): 2.12 (s, 3H, CH_3), 3.81 (s, 3H, OCH_3), 4.01 (s, 1H, NH), 6.22 (s, 1H, CH=C), 7.2–8.3 (m, 16H, Ar–H), 10.2 (s, 1H, NH); MS (EI, 70 eV) *m/z* (%) = 535 (M$^+$, 100). Anal. Calcd. for $C_{30}H_{25}N_5O_5$ (535.55): C, 67.28; H, 4.71; N, 13.08%. Found: C, 67.34; H, 4.73; N, 13.16%.

N-((1E)-3-(2-Methoxy-4-((4-nitrophenyl)diazenyl)phenylamino)-1-(4-methoxy phenyl)-3-oxoprop-1-en-2-yl)benzamide (3f). Yield (76%); m.p. 183 °C; IR (KBr): ν/cm^{-1} = 3351 (NH), 1686 (CO), 1620 (C=C), 1561 (N=N), 1535, 1346 (NO_2); ^{1}H NMR (DMSO-d_6) δ (ppm): 3.80 (s, 6H, 2OCH_3), 4.02 (s, 1H, NH), 6.81–8.33 (m, 16H, Ar–H), 10.2 (s, 1H, NH); MS (EI, 70 eV) *m/z* (%) = 551 (M$^+$, 62). Anal. Calcd. for $C_{30}H_{25}N_5O_6$ (551.55): C, 65.33; H, 4.57; N, 12.70%. Found: C, 65.37; H, 4.63; N, 12.76%.

(4Z)-4-Benzylidene-2-phenyl-1-(4-(phenyldiazenyl)phenyl)-1H-imidazol-5(4H)-one (4a). Yield (81%); m.p. 280 °C; IR (KBr): ν/cm^{-1} = 1700 (CO), 1610 (C=C), 1551 (N=N); ^{1}H NMR (DMSO-d_6) δ (ppm): 7.33–8.31 (m, 19H, Ar–H), 7.82 (s, 1H, CH=); ^{13}C–NMR (DMSO-d_6) δ (ppm): 114.6, 130.1 (C=C), 157.2 (N=C, pyrazole ring), 140.1 (N–C), 151.0 (C–N=N), 152.7 (N=N–C), 170.1 (C=O), 123.2–135.2 (4 benzene rings); MS (EI, 70 eV) *m/z* (%) = 428 (M$^+$, 17). Anal. Calcd. for $C_{28}H_{20}N_4O$ (428.48): C, 78.49; H, 4.70; N, 13.08%. Found: C, 78.21; H, 4.67; N, 13.0%.

(4Z)-4-Benzylidene-1-(2-methyl-4-((4-nitrophenyl)diazenyl)phenyl)-2-phenyl-1H-imidazol-5(4H)-one (4b). Yield (75%); m.p. 222 °C; IR (KBr): ν/cm^{-1} = 1700 (CO amidic), 1615 (C=C), 1555 (N=N), 1535, 1347 (NO_2); ^{1}H NMR (DMSO-d_6) δ (ppm): 2.27 (s, 3H, CH_3), 7.0–8.2 (m, 17H, Ar–H), 8.3 (s, 1H, CH=C); MS (EI, 70 eV) *m/z* (%) = 487 (M$^+$, 15). Anal. Calcd. for $C_{29}H_{21}N_5O_3$ (487.51): C, 71.45; H, 4.34; N, 14.37%. Found: C, 71.33; H, 4.31; N, 14.30%.

(4Z)-4-Benzylidene-1-(2-methoxy-4-((4-nitrophenyl)diazenyl)phenyl)-2-phenyl-1H-imidazol-5(4H)-one (4c). Yield (77%); m.p. 270 °C; IR (KBr): ν/cm^{-1} = 1700 (CO), 1620 (C=C), 1551 (N=N), 1530, 1346 (NO_2); ^{1}H NMR (DMSO-d_6) δ (ppm): 3.85 (s, 3H, OCH_3), 7.33–8.3 (m, 17H, Ar–H), 7.83 (s, 1H, CH=C); MS (EI, 70 eV) *m/z* (%) = 503 (M^+, 70). Anal. Calcd. for $C_{29}H_{21}N_5O_4$ (503.51): C, 69.18; H, 4.20; N, 13.91%. Found: C, 69.01; H, 4.10; N, 13.82%.

(4Z)-4-(4-Methoxybenzylidene)-2-phenyl-1-(4-(phenyldiazenyl) phenyl)-1H-imidazol-5(4H)-one (4d). Yield (66%); m.p. 187 °C; IR (KBr): ν/cm^{-1} = 1710 (CO), 1615 (C=C), 1551 (N=N); ^{1}H NMR (DMSO-d_6) δ (ppm): 3.85 (s, 3H, OCH_3), 6.95–8.33 (m, 18H, Ar–H), 7.85 (s, 1H, CH=C); MS (EI, 70 eV) *m/z* (%) = 458 (M^+, 70). Anal. Calcd. for $C_{29}H_{22}N_4O_2$ (458.51): C, 75.97; H, 4.84; N, 12.22%. Found: C, 75.91; H, 4.75; N, 12.01%.

(4Z)-4-(4-Methoxybenzylidene)-1-(2-methyl-4-((4-nitrophenyl)diazenyl)phenyl)-2-phenyl-1H-imidazol-5(4H)-one (4e). Yield (63%); m.p. 261 °C; IR (KBr): ν/cm^{-1} = 1700 (CO), 1610 (C=C), 1553 (N=N), 1527, 1347 (NO_2); ^{1}H NMR (DMSO-d_6) δ (ppm): 2.10 (s, 3H, CH_3), 3.80 (s, 3H, OCH_3), 6.95–8.31 (m, 16H, Ar–H), 7.85 (s, 1H, CH=C); MS (EI, 70 eV) *m/z* (%) = 517 (M^+, 10). Anal. Calcd. for $C_{30}H_{23}N_5O_4$ (517.53): C, 69.62; H, 4.48; N, 13.53%. Found: C, 69.59; H, 4.37; N, 13.49%.

(4Z)-1-(2-Methoxy-4-((4-nitrophenyl)diazenyl)phenyl)-4-(4-methoxy-benzyl-idene)-2-phenyl-1H-imidazol-5(4H)-one (4f). Yield (60%); m.p. 253 °C; IR (KBr): ν/cm^{-1} = 1701 (CO), 1615 (C=C), 1551 (N=N), 1537, 1346 (NO_2); ^{1}H NMR (DMSO-d_6) δ (ppm): 3.84 (s, 3H, OCH_3), 7.01–8.34 (m, 16H, Ar–H), 7.81 (s, 1H, CH=C); MS (EI, 70 eV) *m/z* (%) = 533 (M^+, 17). Anal. Calcd. for $C_{30}H_{23}N_5O_5$ (533.53): C, 67.53; H, 4.35; N, 13.13%. Found: C, 67.44; H, 4.29; N, 13.05%.

N-((1E)-2-Oxo-2-(4-(phenyldiazenyl)phenylamino)-1-(2-phenyl hydrazono)ethyl) benzamide (9a). Yield (81%); m.p. 217 °C; IR (KBr): ν/cm^{-1} = 3200 (NH), 1695 (CO), 1620 (C=C), 1620 (C=N), 1550 (N=N); ^{1}H NMR (DMSO-d_6) δ (ppm): 6.80–8.21 (m, 19H, Ar–H), 8.1 (s, 1H, NH), 8.21 (s, 1H, NH), 10.2 (s, 1H, NH); ^{13}C–NMR (DMSO-d_6) δ (ppm): 113.9–140.2 (4 benzene rings), 152.6 (N=C), 160.9 (C=O), 167 (C=O); MS (EI, 70 eV) *m/z* (%) = 462 (M^+, 67). Anal. Calcd. for $C_{27}H_{22}N_6O_2$ (462.5): C, 70.12; H, 4.79; N, 18.17%. Found: C, 70.09; H, 4.68; N, 18.01%.

N-((1E)-2-(2-Methyl-4-((4-nitrophenyl)diazenyl)phenylamino)-2-oxo-1-(2-phenyl hydrazono)ethyl)benzamide (9b). Yield (78%); m.p. 216 °C; IR (KBr): ν/cm^{-1} = 3250 (NH), 1701 (CO), 1615 (C=N), 1551 (N=N), 1535, 1347 (NO_2); ^{1}H NMR (DMSO-d_6) δ (ppm): 2.09 (s, 3H, CH_3), 6.85–8.34 (m, 17H, Ar–H), 8.1 (s, 1H, NH), 8.23 (s, 1H, NH), 10.09 (s, 1H, NH); MS (EI, 70 eV) *m/z* (%) = 521 (M^+, 15). Anal. Calcd. for $C_{28}H_{23}N_7O_4$ (521.53): C, 64.48; H, 4.45; N, 18.80%. Found: C, 64.39; H, 4.39; N, 18.77%.

N-((1E)-2-(2-Methoxy-4-((4-nitrophenyl)diazenyl)phenylamino)-2-oxo-1-(2-phenylhydrazono)ethyl)benzamide (9c). Yield (68%); m.p. 270 °C; IR (KBr): ν/cm^{-1} = 3250 (NH), 1688 (CO), 1615 (C=N), 1551 (N=N), 1535, 1347 (NO_2); ^{1}H NMR (DMSO-d_6) δ (ppm): 3.85 (s, 3H, OCH_3), 6.8–8.3 (m, 17H, Ar–H), 8.0 (s, 1H, NH), 8.19 (s, 1H, NH), 10.2 (s, 1H, NH); MS (EI, 70 eV) *m/z* (%) = 537 (M^+, 13). Anal. Calcd. for $C_{28}H_{23}N_7O_5$ (537.53): C, 62.56; H, 4.31; N, 18.24%. Found: C, 62.44; H, 4.29; N, 18.19%.

1,5-Diphenyl-N-(4-(phenyldiazenyl)phenyl)-2,3-dihydro-1H-1,2,4-triazole-3-carboxamide (10a). Yield (57%); m.p. 281 °C; IR (KBr): ν/cm^{-1} = 3400 (NH), 1670 (CO), 1625 (C=N), 1550 (N=N); ^{1}H NMR (DMSO-d6) δ (ppm): 2.0 (s, 1H, HO–C=N), 6.9–8.29 (m, 19H, Ar–H), 7.23 (s, 1H, NH); ^{13}C–NMR(DMSO-d6) δ (ppm): 87.2 (C, triazole ring), 119.3–152.7 (4 benzene rings), 140.7 (NH–C, benzene ring), 150.0, 152.6 (C–N=N–C), 157.9 (C=N, triazole ring), 168.2 (C=O); MS (EI, 70 eV) *m/z* (%) = 446 (M+, 20). Anal. Calcd. for C27H22N6O (446.5): C, 72.63; H, 4.97; N, 18.82%. Found: C, 72.57; H, 4.88; N, 18.78%.

N-(2-Methyl-4-((4-nitrophenyl)diazenyl)phenyl)-1,5-diphenyl-2,3-dihydro-1H-1,2,4-triazole-3-carboxamide (10b). Yield (62%); m.p. 266 °C; IR (KBr): ν/cm^{-1} = 3400 (NH), 1681 (CO), 1622 (C=N), 1551 (N=N), 1537, 1348 (NO_2); ^{1}H NMR (DMSO-d_6) δ (ppm): 1.9 (s, 1H, OH enolic), 2.17 (s, 3H, CH_3), 7.4–8.3 (m, 17H, Ar–H), MS (EI, 70 eV) *m/z* (%) = 503 (M^+-2, 11). Anal. Calcd. for $C_{28}H_{23}N_7O_3$ (505.53): C, 66.52; H, 4.59; N, 19.39%. Found: C, 66.47; H, 4.54; N, 19.32%.

N-(2-Methoxy-4-((4-nitrophenyl)diazenyl)phenyl)-1,5-diphenyl-2,3-dihydro-1H-1,2,4-triazole-3-carboxamide (10c). Yield (71%); m.p. 277 °C; IR (KBr): ν/cm^{-1} = 3410 (NH), 1690 (CO), 1620 (C=N), 1551 (N=N), 1539, 1348 (NO_2); ^{1}H NMR (DMSO-d_6) δ (ppm): 3.85 (s, 3H, OCH_3), 7.35–8.33 (m, 17H, Ar–H), 9.15 (s, 1H, NH); MS (EI, 70 eV) *m/z* (%) = 521 (M^+, 27). Anal. Calcd. for $C_{28}H_{23}N_7O_4$ (521.53): C, 64.48; H, 4.45; N, 18.80%. Found: C, 64.43; H, 4.39; N, 18.74%.

1-(4-Methoxyphenyl)-5-phenyl-N-(4-(phenyldiazenyl)phenyl)-2,3-dihydro-1H-1,2,4-triazole-3-carboxamide (10d). Yield (67%); m.p. 282 °C; IR (KBr): ν/cm^{-1} = 3350 (NH), 1690 (CO), 1621 (C=N), 1555 (N=N); ^{1}H NMR (DMSO-d_6) δ (ppm): 3.81 (s, 3H, OCH_3), 7.41–8.33 (m, 18H, Ar–H), 9.2 (s, 1H, NH); MS (EI, 70 eV) *m/z* (%) = 476 (M^+, 10). Anal. Calcd. for $C_{28}H_{24}N_6O_2$ (476.53): C, 70.57; H, 5.08; N, 17.64%. Found: C, 70.50; H, 5.03; N, 17.58%.

1-(4-Methoxyphenyl)-N-(2-methyl-4-((4-nitrophenyl)diazenyl)phenyl)-5-phenyl-2,3-dihydro-1H-1,2,4-triazole-3-carboxamide (10e). Yield (71%); m.p. 199 °C; IR (KBr): ν/cm^{-1} = 3340 (NH), 1685 (CO), 1620 (C=N), 1551 (N=N), 1537, 1350 (NO_2); ^{1}H NMR (DMSO-d_6) δ (ppm): 2.19 (s, 3H, CH_3), 3.80 (s, 3H, OCH_3), 7.4–8.3 (m, 18H, Ar–H), 9.2 (s, 1H, NH); MS (EI, 70 eV) *m/z* (%) = 535 (M^+, 72). Anal. Calcd. for $C_{29}H_{25}N_7O_4$ (535.55): C, 65.04; H, 4.71; N, 18.31%. Found: C, 64.96; H, 4.67; N, 18.25%.

N-(2-Methoxy-4-((4-nitrophenyl)diazenyl)phenyl)-1-(4-methoxyphenyl)-5-phenyl-2,3-dihydro-1H-1,2,4-triazole-3-carboxamide (10f). Yield (65%); m.p. 275 °C; IR (KBr): ν/cm^{-1} = 3360 (NH), 1690 (CO), 1620 (C=N), 1550 (N=N), 1540, 1350 (NO_2); ^{1}H NMR (DMSO-d_6) δ (ppm): 3.85 (s, 6H, 2OCH_3), 6.99–8.3 (m, 18H, Ar–H), 9.22 (s, 1H, NH); MS (EI, 70 eV) *m/z* (%) = 551 (M^+, 19). Anal. Calcd. for $C_{29}H_{25}N_7O_5$ (551.55): C, 63.15; H, 4.57; N, 17.78%. Found: C, 63.08; H, 4.53; N, 17.70%.

Synthesis of (Z)-4-benzylidene-1-(2-hydroxyphenyl)-2-phenyl-1H-imidazol-5(4H)-one (5). A mixture of **1a** (0.02 mol), *o*-aminophenol (0.02 mol) and 0.5 g of freshly fused sodium acetate was heated in pressure tube at 120 °C in an silicon oil bath for 1.5 h. the reaction mixture was washed with dilute HCl. The precipitated solid material was then washed with water and crystallized from ethanol-DMF mixture (1:1). Yield (45%); m.p. 210 °C; IR (KBr): ν/cm^{-1} = 3250 (OH), 1700 (CO), 1630 (C=N); ^{1}H NMR (DMSO-d_6) δ (ppm): 5.4 (s, 1H, OH), 7.82 (s, 1H, CH=C), 6.93–7.6 (m, 14H, Ar–H); MS (EI, 70 eV) *m/z* (%) = 340 (M^+, 32). Anal. Calcd. for $C_{22}H_{16}N_2O_2$ (340.37): C, 77.63; H, 4.74; N, 8.23%. Found: C, 77.57; H, 4.68; N, 8.20%.

General method for the synthesis of (Z)-4-benzylidene-1-(5-((E)-aryldiazenyl)-2-hydroxyphenyl)-2-phenyl-1H-imidazol-5(4H)-one derivatives 7a-c. To ice cold solution of **5** (0.02 mol) in ethanol (25 mL) containing a catalytic amount of sodium acetate (0.5 g), in an ice-bath, was added a cold solution of aryldiazonium chloride (0.02 mol) solution dropwise with continuous stirring at 0 °C. After complete coupling reaction, the reaction mixture was stirred for extra half hour at room temperature. The precipitated solid material was filtered off, dried and crystallized from ethanol.

(Z)-4-Benzylidene-1-(2-hydroxy-5-((E)-phenyldiazenyl)phenyl)-2-phenyl-1H-imidazol-5(4H)-one (7a). Yield (61%); m.p. 180 °C; IR (KBr): ν/cm^{-1} = 3350 (OH), 1685 (CO), 1620 (C=N), 1560 (N=N); ^{1}H NMR (DMSO-d_6) δ (ppm): 5.41 (s, 1H, OH), 7.4–8.0 (m, 18H, Ar–H), 7.84 (s, 1H, CH=); MS (EI, 70 eV) *m/z* (%) = 444 (M$^+$, 42). Anal. Calcd. for $C_{28}H_{20}N_4O_2$ (444.48): C, 75.66; H, 4.54; N, 12.60%. Found: C, 75.60; H, 4.51; N, 12.58%.

(Z)-4-Benzylidene-1-(2-hydroxy-5-((E)-p-tolyldiazenyl)phenyl)-2-phenyl-1H-imidazol-5(4H)-one (7b).. Yield (81%); m.p. 166 °C; IR (KBr): ν/cm^{-1} = 3410 (OH), 1700 (CO), 1620 (C=N), 1558 (N=N); ^{1}H NMR (DMSO-d6) δ (ppm): 2.35 (s, 3H, CH3), 7.33–8.1 (m, 18H, Ar–H), 7.86 (s, 1H, CH=C); MS (EI, 70 eV) *m/z* (%) = 442 (M+, 60). Anal. Calcd. for C29H22N4O2 (458.51): C, 75.97; H, 4.84; N, 12.22%. Found: C, 75.92; H, 4.79; N, 12.17%.

(Z)-4-Benzylidene-1-(2-hydroxy-5-((E)-(4-methoxyphenyl)diazenyl) phenyl)-2-phenyl-1H-imidazol-5(4H)-one (7c). Yield (63%); m.p. 230 °C; IR (KBr): ν/cm^{-1} = 3400 (OH), 1700 (CO), 1615 (C=N), 1551 (N=N); ^{1}H NMR (DMSO-d_6) δ (ppm): 3.81 (s, 3H, OCH_3), 7.33–8.1 (m, 18H, Ar–H), 7.82 (s, 1H, CH=C); MS (EI, 70 eV) *m/z* (%) = 474 (M$^+$, 17). Anal. Calcd. for $C_{29}H_{22}N_4O_3$ (474.51): C, 73.40; H, 4.67; N, 11.81%. Found: C, 73.37; H, 4.62; N, 11.74%.

Synthesis of (Z)-N-(3-(2-(2,4-dinitrophenyl)hydrazinyl)-3-oxo-1-phenylprop-1-en-2-yl)benzamide (11). A solution of the oxazoline **1a** (0.1 mol) and 2,4-dinitrophenylhydrazine (0.1 mol) in ethanol (50 mL) was heated for 3 h and cooled. A solid product was obtained which was recrystallized from acetic acid as colorless crystals. Yield (67%); m.p. 169 °C; IR (KBr): ν/cm^{-1} = 3310 (NH), 1700 (CO), 1600 (C=C), 1530, 1347 (NO_2); ^{1}H NMR (DMSO-d_6) δ (ppm): 4.0 (s, 1H, NH), 5.91 (s, 1H, CH=C), 7.33–8.97 (m, 13H, Ar–H); MS (EI, 70 eV) *m/z* (%) = 447 (M$^+$, 15). Anal. Calcd. for $C_{22}H_{17}N_5O_6$ (447.4): C, 59.06; H, 3.83; N, 15.65%. Found: C, 59.0; H, 3.79; N, 15.61%.

Cyclization of hydrazide 11 to triazine 12

The hydrazide **11** (0.1 mol) in glacial acetic acid (20 mL) in the presence of fused sodium acetate (0.5 g) was heated under reflux for 3 h and cooled. Dilution with water gave the corresponding 1,2,4-triazine derivative **12** which crystallized from acetic acid. Yield (72%); m.p. 211 °C; IR (KBr): ν/cm^{-1} = 3310 (NH), 1690 (CO), 1630 (C=N), 1610 (C=C), 1531, 1335 (NO_2); ^{1}H NMR (DMSO-d_6) δ (ppm): 7.33–9.02 (m, 13H, Ar–H), 7.82 (s, 1H, CH=C); MS (EI, 70 eV) *m/z* (%) = 429 (M$^+$, 81). Anal. Calcd. for $C_{22}H_{15}N_5O_5$ (429.39): C, 61.54; H, 3.52; N, 16.31%. Found: C, 61.44; H, 3.50; N, 16.01%.

Synthesis of (Z)-5-benzylidene-2-(2,4-diaminophenyl)-3-phenyl-1,2-dihydro-1,2,4-triazin-6(5H)-one (13)

To a solution of **12** (0.1 mol) in glacial acetic acid (30 mL) was added zinc dust (0.1 mol) and the reaction mixture was heated under reflux condition for 2 h. the reaction mixture was filtered while hot, and the filtrate was left to cool at room temperature overnight. The precipitated solid was filtered and recrystallized from dilute acetic acid. Yield (68%); m.p. 260 °C; IR (KBr): ν/cm^{-1} = 3450, 3352 (NH_2), 1693 (CO), 1620 (C=N); ^{1}H NMR (DMSO-d_6) δ (ppm): 5.69 (s, 1H, NH_2C=CH), 5.91 (d, 1H, NH_2–C=CH–CH), 6.27 (s, 4H, 2NH_2), 6.33 (d, 1H, NH_2–C=CH–CH), 7.80 (s, 1H, CH=), 7.33–7.89 (m, 10H, Ar–H), 8.3 (s, 1H, NH); MS (EI, 70 eV) *m/z* (%) = 369 (M$^+$, 77). Anal. Calcd. for $C_{22}H_{19}N_5O$ (369.42): C, 71.53; H, 5.18; N, 18.96%. Found: C, 71.49; H, 5.0; N, 18.88%.

General procedure for the synthesis of (Z)-5-benzylidene-2-(2,4-diamino-5-((E)-aryldiazenyl)phenyl)-3-phenyl-1,2-dihydro-1,2,4-triazin-6(5H)-ones (14a-c)

It was prepared by the general procedure for the preparation of compounds (**7a–c**).

(Z)-5-Benzylidene-2-(2,4-diamino-5-((E)-phenyldiazenyl)phenyl)-3-phenyl-1,2-dihydro-1,2,4-triazin-6(5H)-one (14a). Yield (71%); m.p. 214 °C; IR (KBr): ν/cm^{-1} = 3451, 3330 (NH_2, NH), 1680 (CO), 1620 (C=N), 1550 (N=N); ^{1}H NMR (DMSO-d_6) δ (ppm): 5.89 (s, 1H, CH, Ar–H), 6.27 (s, 4H, 2NH_2), 7.0 (s, 1H, CH, Ar–H), 7.33–8.0 (m, 15H, Ar–H), 7.82 (s, 1H, CH=); MS (EI, 70 eV) *m/z* (%) = 473 (M$^+$, 17). Anal. Calcd. for $C_{28}H_{23}N_7O$ (473.53): C, 71.02; H, 4.90; N, 20.71%. Found: C, 71.0; H, 4.87; N, 20.65%.

(Z)-5-Benzylidene-2-(2,4-diamino-5-((E)-p-tolyldiazenyl)phenyl)-3-phenyl-1,2-dihydro-1,2,4-triazin-6(5H)-one (14b). Yield (64%); m.p. 185 °C; IR (KBr): ν/cm^{-1} = 3450, 3335 (NH_2, NH), 1690 (CO), 1620 (C=N), 1551 (N=N); ^{1}H NMR (DMSO-d_6) δ (ppm): 2.34 (s, 3H, CH_3), 5.89 (s, 1H, CH, Ar–H), 6.31 (s, 4H, 2NH_2), 7.0 (s, 1H, CH, Ar–H), 7.34–8.01 (m, 14H, Ar–H), 7.85 (s, 1H, CH=); MS (EI, 70 eV) *m/z* (%) = 487 (M$^+$, 67). Anal. Calcd. for $C_{29}H_{25}N_7O$ (487.56): C, 71.44; H, 5.17; N, 20.11%. Found: C, 71.29; H, 5.01; N, 20.01%.

(Z)-5-Benzylidene-2-(2,4-diamino-5-((E)-(4-methoxyphenyl)diazenyl)phenyl)-3-phenyl-1,2-dihydro-1,2,4-triazin-6(5H)-one (14c).. Yield (45%); m.p. 218 °C; IR (KBr): ν/cm^{-1} = 3450, 3331 (NH_2, NH), 1691 (CO), 1622 (C=N), 1553 (N=N); ^{1}H NMR (DMSO-d_6) δ (ppm): 3.83 (s, 3H, OCH_3), 5.89 (s, 1H, CH, Ar–H), 6.31 (s, 4H, 2NH_2), 7.1 (s, 1H, CH, Ar–H), 7.30–8.09 (m, 14H, Ar–H), 7.81 (s, 1H, CH=); MS (EI, 70 eV) *m/z* (%) = 503 (M$^+$, 67). Anal. Calcd. for $C_{29}H_{25}N_7O_2$ (503.55): C, 69.17; H, 5.00; N, 19.47%. Found: C, 69.01; H, 4.93; N, 19.37%.

Antimicrobial evaluation

Standard sterilized filter paper disks (5 mm diameter) impregnated with a solution of the test compound in DMF (1 mg/mL) was placed on an agar plate seeded with the appropriate test organism in triplicates. The utilized test organisms were: *B. subtilis* and *B. thuringiensis* as examples of Gram-positive bacteria and *E. coli* and *P. aeruginosa* as examples of Gram-negative bacteria. They were also evaluated for their in *vitro* antifungal potential against *F. oxysporum* and *B. fabae* fungal strains. Chloroamphenicol, cephalothin and cycloheximide were used as standard antibacterial and antifungal agents, respectively. DMF alone was used as control at the same above-mentioned concentration. The plates were incubated at 37 °C for 24 h for bacteria and for 48 days for fungi. Compounds that showed significant growth inhibition zones (>14 mm) using the twofold serial dilution technique, were further evaluated for their minimal inhibitory concentrations (MICs).

Minimal inhibitory concentration (MIC) measurement

The microdilution susceptibility test in Müller–Hinton Broth (Oxoid) and Sabouraud Liquid Medium (Oxoid) was used for the determination of antibacterial and antifungal activity, respectively. Stock solutions of the tested compounds, chloroamphenicol, cephalothin and cycloheximide were prepared in DMF at concentration

of 1000 μg/mL followed by twofold dilution at concentrations of (500, 250, 3.125 μg/mL). The microorganism suspensions at 10^6 CFU/mL (Colony Forming U/mL) concentrations were inoculated to the corresponding wells. Plates were incubated at 36 °C for 24–48 h and the minimal inhibitory concentrations (MIC) were determined. Control experiments were also done.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.saa.2012.04.068.

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