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Synthesis and anti-microbial evaluation of novel 3-(arylideneamino)-3a,8a-dihydroxy-1,3,3a,8a-tetrahydroindeno[1,2-d]imidazole-2,8-diones and their 2-thioxo analogues

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Synthesis and anti-microbial evaluation of novel 3-(arylideneamino)-3a,8a-dihydroxy-1,3,3a,8a-tetrahydroindeno[1,2-*d*]imidazole-2,8-diones and their 2-thioxo analogues

Yeshwinder Saini[1], Rajni Khajuria[1], Ramneet Kaur[1], Sanjana Kaul[2], Tanwi Sharma[2], Suruchi Gupta[2], Vivek K. Gupta[3], Rajni Kant[3], Kamal K. Kapoor[1]

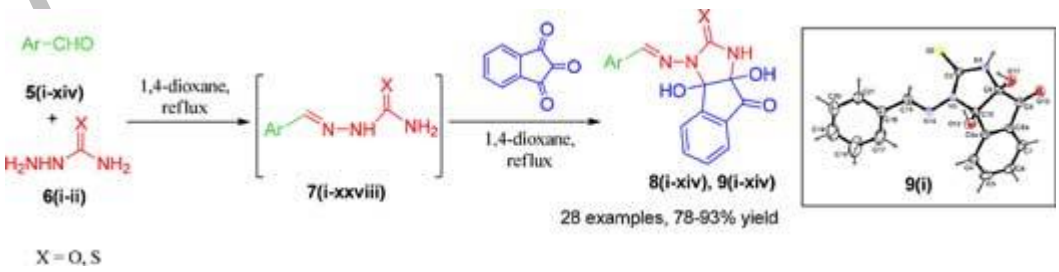
[1]Department of Chemistry, University of Jammu, Jammu, India, [2]School of Biotechnology, University of Jammu, Jammu, India, [3]Department of Physics & Electronics, University of Jammu(X-ray crystallography group), Jammu, India

Corresponding Author: Kamal K. Kapoor, Email: k2kapoor@yahoo.com; Sanjana Kaul, Email: sanrozie@rediffmail.com

Abstract

The preparation of some novel 3-(arylideneamino)-3a,8a-dihydroxy-1,3,3a,8a-tetrahydroindeno[1,2-*d*]imidazole-2,8-diones **8(i-xiv)** and 3-(arylideneamino)-3a,8a-dihydroxy-2-thioxo-1,3,3a,8a-tetrahydroindeno[1,2-*d*]imidazol-8(*2H*)-ones **9(i-xiv)** have been reported *via* one-pot catalyst-free reaction of aldehydes, semicarbazide hydrochloride/thiosemicarbazide with ninhydrin. All the synthesized compounds have been screened for anti-microbial activity and some of them were observed to possess broad spectrum anti-bacterial potential as well as significant antagonistic potential against fungal pathogens.

Graphical Abstract:



KEYWORDS: Ninhydrin, tetrahydroindenoimidazoledione, 2-thioxotetrahydro indenoimidazolone, anti-bacterial, anti-fungal.

INTRODUCTION

Hydrazones (semicarbazones and thiosemicarbazones) **1** play significant role in the synthesis of biologically important heterocyclic compounds[1]. They are of immense biological significance and are known to exhibit anti-cancer[2], anti-malarial[3], anti-viral[4], anti-fungal[5], anti-bacterial[6], anti-tubercular[7] and anti-inflammatory [8] properties. Ninhydrin has been employed in the synthesis of a variety of biologically active imidazole derivatives[9]. For example, compound **2** obtained by the reaction of ninhydrin with thiourea, exhibited promising anti-microbial activity against gram positive and gram negative bacteria and a fungus *Candida albicans*[10]. Compound **3**, a hydrophobic analogue of **2** is devoid of two H-bond donors. Obtained[11] by the reaction of ninhydrin with diphenylthiourea, compound **3** has shown improvement in activity against some bacterial strains (*Bacillus subtilis, Streptococcus pneumoniae, Pseudomonas aeruginosa*) and loss against some other strains (*Shigella flexneri, Escherichia coli*). Loss in anti-fungal activity of compound **3** against *C. albicans* was also noticed[10, 11]. In view of this irregular trend in activity, we wished to maintain a balance between hydrophilicity and hydrophobicity by retaining one H-bond donor and this led us to design a compound **4** possessing the attributes of hydrazones as well as tetrahydroindeno[1,2-*d*]imidazolones **(Figure 1)**.

RESULTS AND DISCUSSION

Chemistry

Benzaldehyde **5(i)** (1 mmol) was reacted with semicarbazide hydrochloride **6(i)** (1 mmol) in ethanol to yield the corresponding semicarbazone **7(i)** (96%), which upon reaction with ninhydrin (1.2 mmol) in ethanol (TLC) at reflux led to the formation of 3-(benzylideneamino)-3a,8a-dihydroxy-1,3,3a,8a-tetrahydroindeno[1,2-*d*]imidazole-2,8-dione **8(i)** (77%) (overall yield 74%) **(Scheme 1)**.

In another set of experiment, one-pot reaction was carried out. Initially, benzaldehyde **5(i)** (1 mmol) and semicarbazide hydrochloride **6(i)** (1 mmol) were reacted in refluxing ethanol (30 min) and noticing the completion of reaction (TLC), ninhydrin (1.2 mmol) was added and refluxing was continued. After 90 minutes, the reaction got completed and 8% increase in the yield of the desired product **8(i)** was noticed. Replacing ethanol with various solvents **(Table 1)** led us to conclude that 1,4-dioxane was the best solvent for this reaction.

Further, replacement of semicarbazide hydrochloride **6(i)** with thiosemicarbazide **6(ii)** yielded the expected 3-(benzylideneamino)-3a,8a-dihydroxy-2-thioxo-1,3,3a,8a-tetrahydroindeno[1,2-*d*]imidazol-8(2*H*)-one **9(i)** in 87% yield. The structure of **9(i)** was supported by single-crystal X-ray crystallographic study **(Figure 2)**. The ORTEP diagram of **9(i)** clearly indicates that the two hydroxyl groups are in *cis*-conformation.

A variety of aromatic aldehydes bearing electron donating and electron withdrawing groups led to the successful formation of the desired products **8(i-xiv)** and **9(i-xiv)** (**Scheme2**). The plausible mechanism for the formation of 3-(arylideneamino)-3a,8a-dihydroxy-1,3,3a,8a-tetrahydroindeno[1,2-*d*]imidazole-2,8-diones **8(i-xiv)** and 3-(arylideneamino)-3a,8a-dihydroxy-2-thioxo-1,3,3a,8a-tetrahydroindeno[1,2-*d*]imidazol-8(*2H*)-ones **9(i-xiv)** is shown in **Scheme 3**. The terminal nitrogen of semi/thiosemicarbazone **7(i-xxviii)**, formed *in situ*, underwent nucleophilic addition reaction with ninhydrin to form hydrazine carboxamide/carbothioamide intermediate (**A**) and this was followed by attack from the same side of the internal nitrogen to yield the desired *cis*-products **8(i-xiv)/9(i-xiv)** as illustrated in **Scheme 3**. It is pertinent to mention that attack from the same side lead to the exclusive formation of *cis*-product since it is well established [12] that *cis*-biquinane systems are far more stable than their *trans*-counterparts.

BIOLOGICAL EVALUATION

Anti-Bacterial And Anti-Fungal Bioassays (*In Vitro*)

The anti-bacterial screening of the test compounds **8(i-xiv)** and **9(i-xiv)** was done against eight bacterial strains at concentrations of 100 μg/ml, 250 μg/ml, 500 μg/ml, 750 μg/ml and 1000 μg/ml. No inhibitory activity was observed for the test compounds at 100 μg/ml, 250 μg/ml, 500 μg/ml and 750 μg/ml. At 1000 μg/ml concentration, the test compounds displayed perceptible potential against the screened bacterial strains (**Table 2**, **Figure 3)**. The results clearly indicate that twenty-four out of the twenty-eight compounds showed activity against one or more strains. Compounds **8(viii, xii)** and **9(v)**

possessed broad spectrum anti-bacterial activity against all the tested strains whereas **8(ix)** and **9(vi)** were found active against seven test cultures. **9(vii)** and **9(xii)** displayed moderate inhibitory potential against five tested strains. Compounds **8(viii)** and **9(vi)** were active against four, **8(xii)** against three, **8(xiv)** against two and **8(ix)**, **9(v)**, **9(x)** and **9(xiii)** against one bacterial strain. Four compounds **8(v, x)** and **9(xi, xiv)** did not exhibit anti-bacterial activity against any of the organisms screened.

Anti-fungal potential of the test compounds **8(i-xiv)** and **9(i-xiv)** was represented as percentage inhibition values (**Table 3**, **Figure 4**). The investigation of anti-fungal screening of these compounds revealed their varying degrees of activity against all the tested microorganisms. Compound **9(viii)** exhibited very good anti-fungal activity with 70% and 78% growth inhibition against *Fusarium oxysporum and Alternaria alternata respectively*. Compound **8(viii)** displayed 71.43% growth inhibition against *Alternaria alternata.* Rest of the test compounds showed varying degrees of % inhibition of tested fungal pathogens ranging from 2.86 to 68%. Species of *Alternaria* and *Fusarium* are reported to cause broad spectrum infections in humans and mostly affect immune compromised patients. Therefore, the compounds showing significant activity against these fungi can serve as potential candidates for anti-fungal therapy.

EXPERIMENTAL

General

All the experiments were performed in an oven dried glass apparatus. All the commercially available reagents were purchased from *Aldrich* and were used

without further purification. Melting points (°C) were measured in open glass capillaries using Perfit melting point apparatus and are uncorrected. The progress of reaction was monitored by thin layer chromatography (TLC) using silica gel pre-coated aluminum sheets (60 F254, Merck). Visualization of spots was effected by exposure to ultraviolet light (UV) at 365 nm and 254 nm, iodine vapours and 2% 2,4-dinitrophenylhydrazine solution in methanol containing few drops of H_2SO_4 and draggendroff reagent. IR spectra (ν, cm^{-1}) were recorded on Perkin-Elmer FTIR spectrophotometer using KBr discs. ^1H and ^{13}C NMR were recorded on Bruker AC-400 spectrometer operating respectively at 400 MHz and 100 MHz with tetramethylsilane (TMS) as an internal standard. The chemical shifts are expressed in δ (ppm) downfield from TMS. *J* values are given in Hertz (Hz). The abbreviations s, bs, d, t, q and m in ^1H NMR spectra refer to singlet, broad singlet, doublet, triplet, quartet and multiplet respectively. Electron impact mass spectra (EIMS) were recorded on Micro Mass VG-7070 H mass spectrometer at 70eV. Elemental analysis was performed on Leco CHNS 932 analyzer. Solvents were removed using Heidolph rotary evaporator. Column chromatography was performed using a gradient of ethylacetate and petroleum ether.

The synthesized 3-(arylideneamino)-3a,8a-dihydroxy-1,3,3a,8a-tetrahydroindeno[1,2-*d*]imidazole-2,8-diones **8(i-xiv)** and 3-(arylideneamino)-3a,8a-dihydroxy-2-thioxo-1,3,3a,8a-tetrahydroindeno[1,2-*d*]imidazol-8(2*H*)-ones **9(i-xiv)** were screened for their *in vitro* anti-bacterial activity using agar well diffusion method[13]. The test pathogens used in the study included four gram positive bacteria [*Bacillus subtilis* (MTCC 441),

Staphylococcus aureus (MTCC 3160), *Klebsiellapneumoniae* (MTCC 109), *Bacillus cereus* (MTCC 430)] and four gram negative bacteria [*Escherichia coli* (MTCC 40), *Enterococcus faecalis* (MTCC 439), *Pseudomonas aeruginosa* (MTCC 1934) and *Pseudomonas alcaligenes* (MTCC 493)]. For anti-bacterial assay, test pathogens were revived by growing overnight at 37°C and 100 rpm. Test compounds were prepared by dissolving in DMSO at concentrations of 100μg/ml, 250μg/ml, 500μg/ml, 750μg/ml and 1000μg/ml whereas the standard drug chloramphenicol was used at a concentration of 100 μg/ml. DMSO was used as negative control. Sterile petri-plates were poured with 35ml of Nutrient agar medium. 100 μl of bacterial suspension was spread on the solidified plates. Wells were bored in the plates with the help of borer of 6 mm diameter. 100 μl of prepared compounds were added to labeled wells. Results were observed as diameter of zone of inhibition after incubating the plates at 37°C overnight.

Anti-fungal activity of these compounds was evaluated against *Fusarium oxysporum* (MTCC 2485) and *Alternaria alternata* (MTCC 2724) by poison food technique [14]. 1000 μg of each compound was added in sterile luke warm Potato dextrose agar medium before pouring. Fungal agar plug of five days old test culture was placed at the centre of the medium plate. Plates were incubated at 28ºC for seven days. Percentage inhibition of fungal culture in presence of test compounds was assessed by comparing mycelia growth diameter on poisoned (media + compound) and non-poisoned (media + DMSO) plates and calculated using the formula

$$\%\ \text{age inhibition} = \left[\left(R1 - R2 \right) / R1 \right] \times 100$$

R1 means radial growth of test fungi in non-poisoned plate; R2 means radial growth of same in poisoned plate.

General Procedure For The Synthesis Of 8(I-Xiv) And 9(I-Xiv)

A mixture of aldehyde (**5i-5xiv**, 1mmol) and semicarbazide hydrochloride **6(i)** (0.11g, 1mmol)/thiosemicarbazide **6(ii)** (0.09g, 1mmol) in 1,4-dioxane (10 ml) was refluxed for the time mentioned in **Scheme 2** to achieve the complete formation of the desired semicarbazones/thiosemicarbazones (TLC). At this stage, ninhydrin (0.21g, 1.2 mmol) was added to the reaction mixture and refluxing was continued till the completion of reaction (time given in **Scheme2**). The reaction mixture was poured into ice-cold water (50 ml) and kept in refrigerator overnight. The solid separated was filtered, dried and column chromatographed to obtain the pure product [**8(i-xiv)**; **9(i-xiv)**; 78-93% yield].

Spectral Characterization Of (8i) And (9i)

3-(Benzylideneamino)-3a,8a-dihydroxy-1,3,3a,8a-tetrahydroindeno[1,2-*d*]imidazole-2,8-dione **(8i)**; white solid; m.p: 185 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.02 (bs, 2H), 7.98 – 7.77 (m, 3H), 7.72 -7.63 (m, 4H), 7.53 – 7.34 (m, 3H), 7.05 (bs, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 195.5, 152.6, 151.6, 145.7, 137.7, 135.5, 132.1, 131.1, 130.1, 129. 2, 127.1, 125.5, 124.2, 89.8, 84.5; IR (KBr)ν_{max}/cm^{-1}: 3365.78, 1724.36, 1695.48; *Anal.* calcd. for $C_{17}H_{13}N_3O_4$: C, 63.16; H, 4.05; N, 13.00; found C, 63.12; H, 4.07; N, 12.96; ESI-MS *m/z* : $[M+H]^+$ = 324.

3-(Benzylideneamino)-3a,8a-dihydroxy-2-thioxo-1,3,3a,8a-tetrahydroindeno[1,2-*d*]imidazol-8(2*H*)-one **(9i);** yellow crystalline solid; m.p: 203 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.28 (bs, 1H), 9.58 (s, 1H), 8.14-8.07 (d, *J* = 8 Hz, 1H), 7.97 – 7.86 (m, 4H), 7.79-7.69 (d, *J* = 8.0 Hz, 2H), 7.55 (s, 3H), 7.40 (bs, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 196.1, 174.9, 156.1, 148.4, 137.3, 134.4, 133.2, 131.5, 131.4, 129.4, 128.1, 127.4, 124.3, 92.7, 86.8; IR (KBr)ν_{max}/cm^{-1}: 3365.32, 1711.14, 1707.34,1285.10; *Anal*. calcd. for $C_{17}H_{13}N_3O_3S$: C, 60.17; H, 3.86; N, 12.38; S, 9.45; found C, 60.01; H, 3.69; N, 12.84; S, 9.61; ESI-MS *m/z* : $[M+H]^+$ = 340.

CONCLUSION

A series of novel 3-(arylideneamino)-3a,8a-dihydroxy-1,3,3a,8a-tetrahydroindeno[1,2-*d*]imidazole-2,8-diones and 3-(arylideneamino)-3a,8a-dihydroxy-2-thioxo-1,3,3a,8a-tetrahydroindeno[1,2-*d*]imidazol-8(2*H*)-ones have been synthesized *via* one-pot, catalyst-free reaction of aldehydes, semicarbazide hydrochloride/thiosemicarbazide with ninhydrin and screened for anti-microbial activity. Some of the synthesized compounds showed promising results.

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SUPPORTING INFORMATION

Experimental data, X-ray crystallographic data, ^{1}H NMR and ^{13}C NMR spectra of all the synthesized compounds can be accessed at publisher's website.

REFERENCES

1. Banerjee, S.; Mondal, S.; Chakraborty, W.; Sem, S.; Gachhui, R.; Butcher, R. J.; Slawin, A. M.; Mandal, C.; Mitra, S. Z. *Polyhedron* **2009**, *28*, 2785.

2. (a) Despaigne, A. A. R.; Parrilha, G. L.; Izidoro, J. B.; da Costa, P. R.; dos Santos, R. G.; Piro, O. E.; Castellano, E. E.; Rocha, W. R.; Beraldo, H. *Eur. J. Med. Chem.* **2012**, *50*, 163; (b) Dandawate, P.; Khan, E.; Padhye, S.; Gaba, H.; Sinha, S.; Deshpande, J.; Swamy, K. V.; Khetmalas, M.; Ahmad, A.; Sarkar, F. H. *Bioorg. Med. Chem. Lett.* **2012,** *22*, 3104; (c) Mohareb, R. M.; Al-Omran, F. *Steroids* **2012**, *77*, 1551; (d) Aydin, S.; Kaushik Basu, N.; Arora, P.; Basu, A.; Nichols, B. D.; Talele, T. T.; Akkurt, M.; Celik, I.; Buyukgungor, O.; Kucukguzel, S. G. *Marmara Pharm. J.* **2013,** *17*, 26.

3. (a) Fattorusso, C.; Campiani, G.; Kukreja, G.; Persico, M.; Butini, S.; Romano, M. P.; Altarelli, M.; Ros, S.; Brindisi, M.; Savini, L.; Novellino, E.; Nacci, V.; Fattorusso, E.; Parapini, S.; Basilico, N.; Taramelli, D.; Yardley, V.; Croft, S.; Borriello, M.; Gemma, S. *J. Med. Chem.* **2008**, *51*, 1333; (b) Acharya, B. N.; Saraswat, D.; Kaushik, M. P. *Eur. J. Med. Chem.* **2008**, *43*, 2840.

4. (a) el-Sabbagh, Ol.; Rady, H. M. *Eur. J. Med. Chem.***2009,** *44*, 3680; (b) Tian, B.; He, M.; Tang, S.; Hewlett, I.; Tan, Z.; Li, J.; Jin, Y.; Yang, M. *Bioorg. Med. Chem. Lett.* **2009,** *19*, 2162.

5. (a) Secci, D.; Bizzarri, B.; Bolasco, A.; Carradori, S.; D' Ascenzio, M.; Rivanera, D.; Mari, E.; Polletta, L.; Zicari, A. *Eur. J. Med. Chem.* **2012,** *53*, 246; (b) Maillard, L. T.; Bertout, S.; Quinonera, O.; Akalin, G.; Turan-Zitouni, G.; Fulcrand, P.; Demirci, F.; Martinez, J.; Masurier, N. *Bioorg. Med. Chem. Lett.* **2013,** *23*, 1803; (c) Altintop, M. D.; Ozdemir, A.; Turan Zitouni, G.; llgin, S.; Atli, O.; lscan, G.; Kaplancikli, Z. A. *Eur. J. Med. Chem.* **2012,** *58*, 299; (d) Kocyigit-Kaymakcioglu, B.; Oruc-Emre, E. E.; Unsalan, S.; Tabanca, N.; Khan, S. I.; Wedge, D. E.; Iscan, G.; Demirci, F.; Rollas, S. *Med. Chem. Res.* **2012**, *21*, 3499.

6. (a) Abdel-Aziz, H. A.; Mekawey, A. A. *Eur. J. Med. Chem*. **2009**, *44*, 4985; (b) Abdel-Wahab, B. F.; Awad, G. E.; Badria, F. A. *Eur. J. Med. Chem*. **2011**, *46*, 1505; (c) Khan, S. A. *Eur. J. Med. Chem.* 2008, *43*, 2040.

7. (a) Telvekar, V. N.; Belubbi, A.; Bairwa, V. K.; Satardekar, K. *Bioorg. Med. Chem. Lett.* **2012** *22*, 2343; (b) Gemma, S.; Savini, L.; Altarelli, M.; Tripaldi, P.; Chiasserini, L.; Coccone, S. S.; Kumar, V.; Camodeca, C.; Campiani, G.; Novellino, E.; Clarizio, S.; Delogu, G.; Butini, S.; *Bioorg. Med. Chem*. **2009**, *17*, 6063 (c) Imramovsky, A.; Polanc, S.; Vinsova, J.; Kocevar, M.; Jampilek, J.; Reckova, Z. *Bioorg. Med. Chem.* **2007**,*15*, 2551.

8. (a) Gokce, M.; Utku, S.; Kupeli, E. *Eur. J. Med. Chem.* **2009,** *44*, 3760; (b) Khan, K. M.; Khan, M.; Ali, M.; Taha, M.; Rasheed, S.; Perveen, S.; Choudhary, M. I. *Bioorg. Med. Chem.* **2009**, *17*, 7795; (c) Moldovan, C. M.; Oniga, O.; Parvu, A.; Tiperciuc, B.; Verite, P.; Pirnau, A.; Crisan, O.; Bojita, M.; Pop, R. *Eur. J. Med. Chem*. **2011**, *46*, 526.

9. (a) Alizadeh, A.; Zarei, A.; Rezvanian, A. *Helv. Chim. Acta* **2011**, *94*, 802; (b) Das, S.; Frohlich, R.; Pramanik, A. *Org. Lett.* **2006,** *8*, 426; (c) Seyfi, S.; Hossaini, Z.; Rostami-Charati, F. *Comb. Chem. High Throughput Screen.* **2013,** *16***,** 652.

10. Ghalib, R. M.; Hashim R.; Alshahateet, S. F.; Mehdi, S. H.; Sulaiman, O.; Murugaiyah, V.; Aruldass, C. A. *J. Mol. Struct.* **2011,** *1005*, 152.

11. Ghalib, R. M.; Hashim, R.; Alshahateet, S. F.; Mehdi, S. H.; Sulaiman, O.; Chan, K. –L.; Murugaiyah, V.; Jawad, A. J. *Chem. Crystallogr*. **2012**, *42*, 783.

12. (a) Chang, S. –J.; McNally, D.; Shary-Tehrany, S.; Hickey, S. M. J.; Boyd, R. H. *J. Am. Chem. Soc.* **1970**, *92*, 3109; (b) Kim, W. –Y.; Kim, B. G.; Kang, T.; Lee, H. –Y. *Chem. Asian J*. **2011**, *6*, 1931.

13. Rahman, A. -U.; Choudhary, M. I.; Thomsen, W. J. *In Bioassay Techniques for Drug Development, Harwood Academic Publishers: The Netherlands* **2001**,16.

14. Das, K.; Tiwari, R. K. S.; Shrivastava, D. K. *J. Med. Plants Res.* **2010**, ***4***, 104-111.

Table 1. Optimization of solvent.

Entry	Solvent	Yield (%)
1	CH_3CN	80
2	**1,4-Dioxane**	**90**
3	1,2-DCE	77
4	DMF	70
5	Toluene	72
6	THF	75
7	Benzene	73
8	EtOH	82

Table 2. Anti-bacterial activity of test compounds **8(i-xiv)** and **9(i-xiv)**.

Test Compound	Diameter of Inhibition Zone Against pathogens (mm)							
	B.s	*B.c*	*S.a*	*K.p*	*E.c*	*E.f*	*P.a*	*P.al*
8 (i)	-	10	11	-	9	12	-	-
8 (ii)	12	11	12	-	-	-	11	-
8 (iii)	-	13	11	-	-	-	-	11
8 (iv)	11	-	-	12	10	-	12	-
8 (v)	-	-	-	-	-	-	-	-
8 (vi)	-	11	10	-	12	-	12	-
8 (vii)	-	11	-	-	-	-	-	-
8 (viii)	15	14	14	13	12	13	14	12
8 (ix)	14	13	13	12	13	11	13	-
8 (x)	-	-	-	-	-	-	-	-
8 (xi)	-	-	11	-	11	-	-	-
8 (xii)	12	11	15	14	13	12	15	11
8 (xiii)	-	12	12	-	11	-	11	-
8 (xiv)	15	-	14	-	12	9	-	-
9 (i)	12	-	-	12	-	-	13	-
9 (ii)	-	13	-	-	-	11	-	12
9 (iii)	-	-	-	-	12	-	11	12
9 (iv)	13	-	-	11	-	-	10	-
9 (v)	13	14	12	12	11	13	13	13

9 (vi)	13	-	14	15	13	15	16	11
9 (vii)	12	11	13	-	-	12	13	-
9 (viii)	-	-	12	-	10	-	12	13
9 (ix)	13	12	-	-	11	-	12	-
9 (x)	-	-	14	-	9	6	-	12
9 (xi)	-	-	-	-	-	-	-	-
9 (xii)	-	11	12	-	12	-	13	13
9 (xiii)	12	-	13	-	-	14	-	-
9 (xiv)	-	-	-	-	-	-	-	-
+ve Control (SD)	19	19	20	19	15	20	21	19
-ve Control	-	-	-	-	-	-	-	-

+ve Control = Chloramphenicol (at 100µg/ml concentration); -ve Control = DMSO; Test compounds (at 1000 µg/ml concentration)

B.s, *Bacillus subtilis*; *B.c*, *Bacillus cereus*; *S.a*, *Staphylococcus aureus*; *K.p*, *Klebsiella pneumoniae*; *E.c*, *Escherichia coli*; *E.f*, *Enterococcus faecalis*; *P.a*, *Pseudomonas aeruginosa*; *P.al*, *Pseudomonas alcaligenes*.

'-' sign indicates absence of clear zone; Weaker = 6–10 mm; Moderate = 10-13 mm, above 13 mm = good.

Table 3. Anti-fungal activity of test compounds **8(i-xiv)** and **9(i-xiv)**

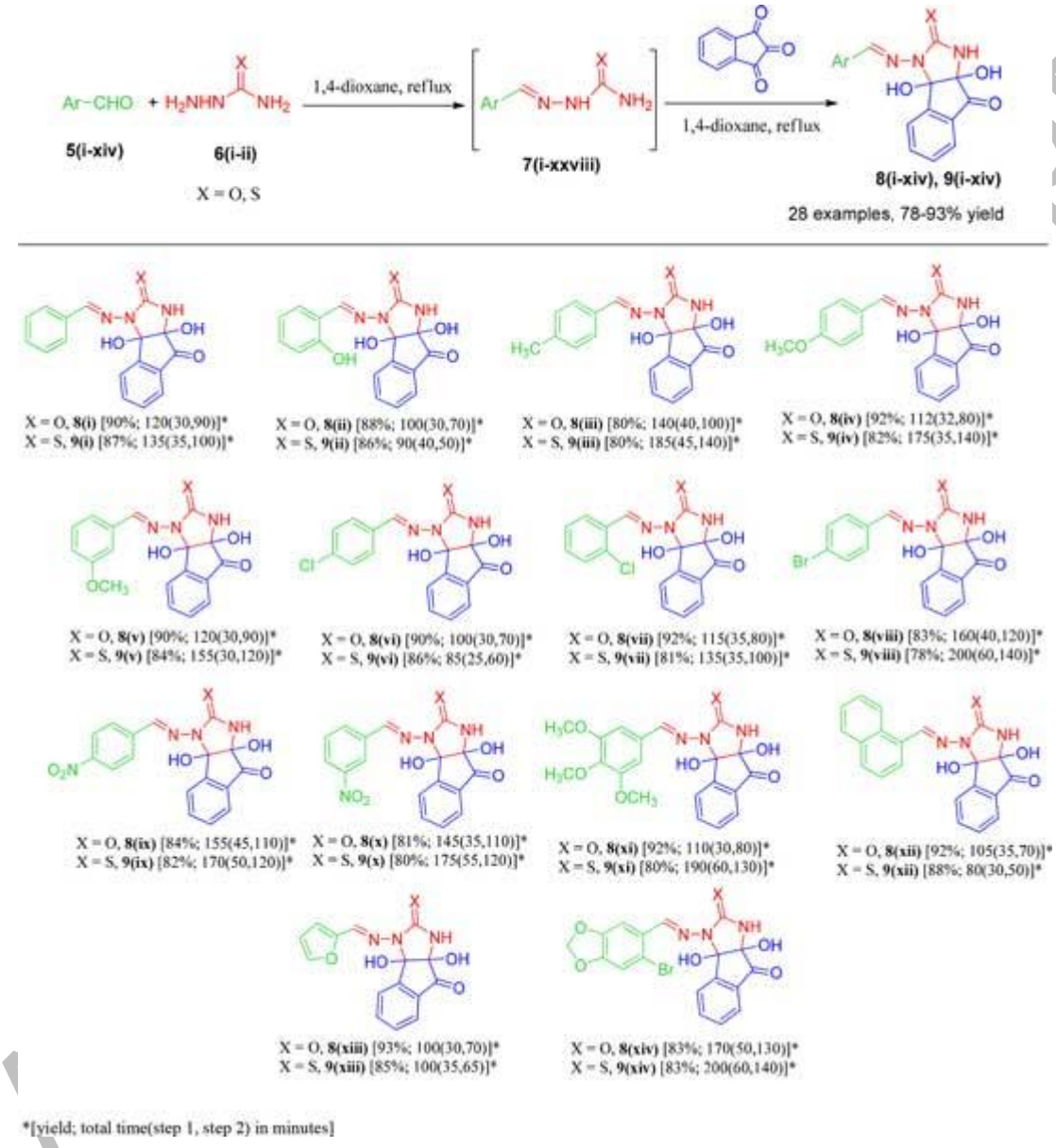
Test	% inhibition of test fungal pathogens	
Compound	*Fusariumoxysporum*	*Alternaria alternata*
8 (i)	24.21	52.86
8 (ii)	43.22	64.28
8 (iii)	41.00	51.57
8 (iv)	51.67	67.14
8 (v)	58.00	21.24
8 (vi)	17.21	68.00
8 (vii)	29.70	34.28
8 (viii)	47.22	71.43
8 (ix)	21.90	2.86
8 (x)	21.12	-
8 (xi)	29.00	62.14
8 (xii)	42.00	39.00
8 (xiii)	29.33	64.28
8 (xiv)	12.80	34.28
9 (i)	31.21	19.32
9 (ii)	38.63	33.12
9 (iii)	54.00	60.00
9 (iv)	40.00	43.00
9 (v)	14.24	18.21
9 (vi)	22.12	33.00

9 (vii)	29.00	29.22
9 (viii)	70.00	78.00
9 (ix)	45.42	52.10
9 (x)	37.61	32.70
9 (xi)	39.80	32.32
9 (xii)	32.12	36.00
9 (xiii)	17.98	33.00
9 (xiv)	49.5	36.43

Test compounds (at 1000 μg/ml concentration)

Scheme 1. Synthesis of 3-(benzylideneamino)-3a,8a-dihydroxy-1,3,3a,8a-tetrahydroindeno[1,2-*d*]imidazole-2,8-dione **8(i)**.

Scheme 2. One-pot synthesis of indeno-3-(arylideneamino)-3a,8a-dihydroxy-1,3,3a,8a-tetrahydroindeno[1,2-*d*]imidazole-2,8-diones **8(i-xiv)** and their 2-thioxo analogues **9(i-xiv)**.



*[yield; total time(step 1, step 2) in minutes]

Scheme 3. Plausible mechanism for the formation of **8(i-xiv)** and **9(i-xiv)**

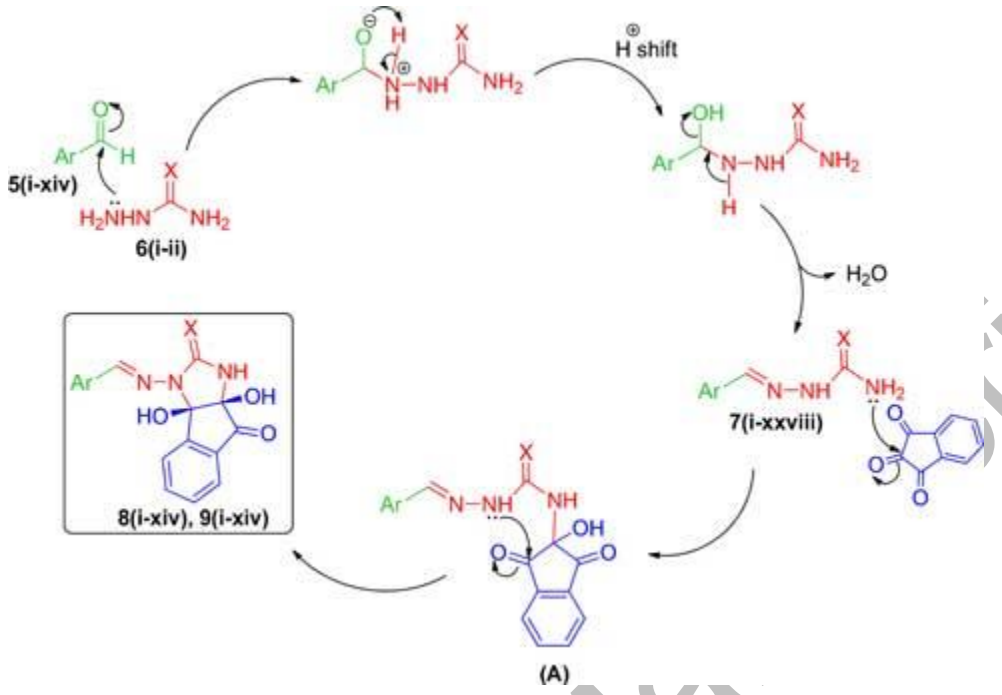


Figure 1.

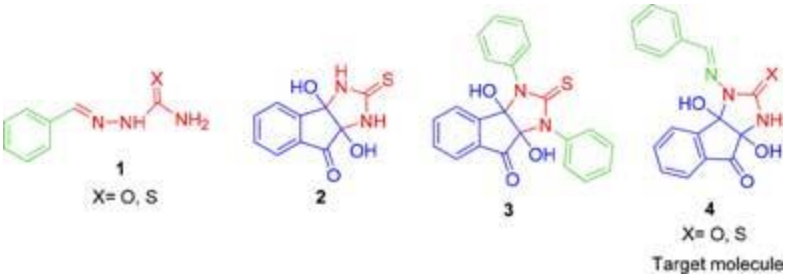


Figure 2. ORTEP diagram of 3-(benzylideneamino)-3a,8a-dihydroxy-2-thioxo-1,3,3a,8a-tetrahydroindeno[1,2-*d*]imidazol-8(2*H*)-one **(9i)**.

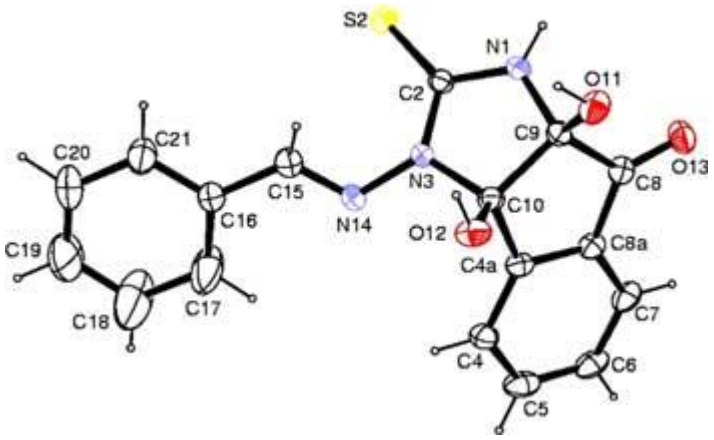


Figure 3. Comparison of anti-bacterial activity of **8(i-xiv)** and **9(i-xiv)** with the standard drug **(**chloramphenicol).

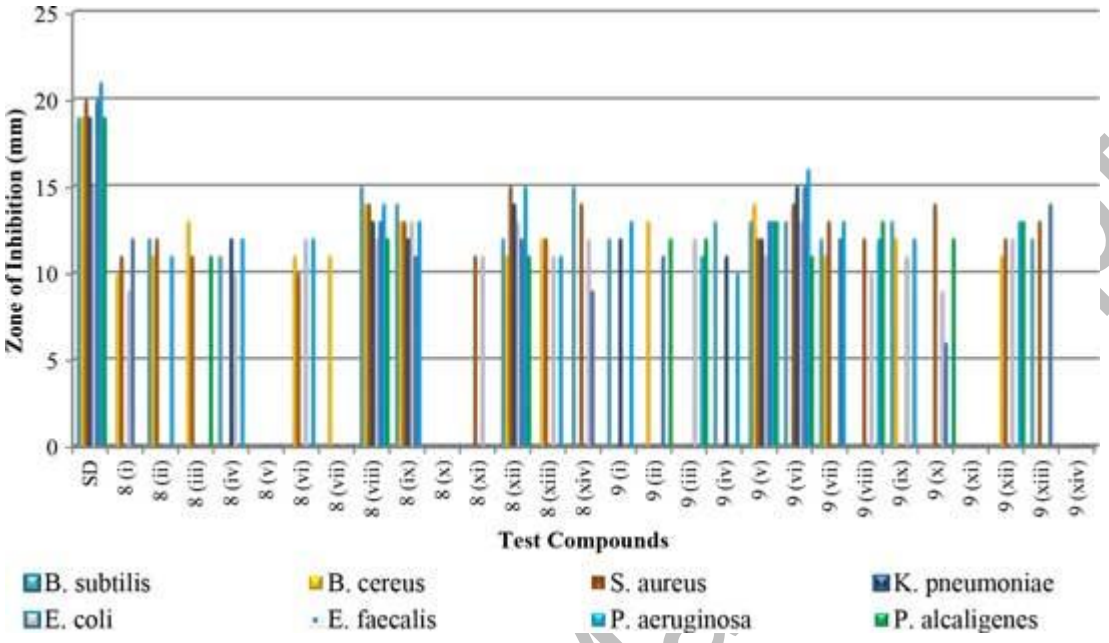


Figure 4. Anti-fungal potential of test compounds.