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# Antibacterial Potential Assessment of Schiff Bases Derived from 1-Aminoanthracene-9, 10-Dione

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**Abstract.** A variety of Schiff bases **1-17** of 1-aminoanthracene-9, 10-dione were synthesized using a reported catalytic method and evaluated for their antibacterial potential against *Staphylococcus aureus* multidrug resistant (MDR), *Escherichia coli* (MDR), *Klebsiella* species (MDR), *Salmonella typhimurium* (MDR), *Pseudomonas aeruginosa* (MDR), *Escherichia coli* ATCC-8739, *Staphylococcus aureus* ATCC-25923, *Staphylococcus aureus, Escherichia coli, Klebsiella* species and *Pseudomonas aeruginosa.* Compounds **2**, **3, 4, 13** and **14** were found to be potent against (MDR) bacterial strains when compared with the cefotaxime standard, however compound **8** exhibited good activities against *S. aureus* and *Klebsiella* species. Compounds **2** and **15** were found to be good to moderately active against *P. aeruginosa* and compounds **4** and **15** demonstrated moderate activity against *S. aureus*. All the remaining compounds except **11** and **17** showed weak antimicrobial activity against non-MDR strains of bacterial isolates.

**Keywords:** Schiff base, 1-aminoanthracenedione, antibacterial activity, multidrug resistant

## Introduction

The fast growing resistance of bacteria towards available antibiotics is a foremost medical issue. Increasing resistance against known antibiotics that causes severe infections is directly linked with the dramatic increase in mortality rate (daSilva *et al*., 2011). The bacterial resistance against multiple available antibiotics is due to their toxicity and different modes of action. In order to cope with the growing human pathogen resistance, there is an urgent medical need to discover some additional antibacterial drugs that have no adverse effects due to their unusual mode of action (Alekshun and Levy, 2017; Rice, 2006).

Schiff bases or imines are the compounds bearing azomethine (-C=N-) functionality (Fareed *et al*., 2013) with numerous biological applications including antibacterial, antifungal, antiviral, antioxidant, anti-tuberculosis, analgesic and anti-inflammatory activities (Kajal *et al*., 2013; daSilva *et al*., 2011; Piotr *et al*., 2009). Several natural and non-natural compounds with imine group are biologically active. The presence of imine functionality in such compounds is responsible for their significant biological potential (Guo *et al*., 2007; Souza *et al*., 2007; Bringmann *et al*., 2004).

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Derivatives of anthracene-9, 10-dione have attracted the attention of medicinal chemists due to a wide spectrum of significant pharmacological activities such as anti-tumour (Ashnagar *et al*., 2010; Ge and Russell, 1997), anti-inflammatory (Yadav *et al*., 2010), anti-malarial (Osman *et al*., 2010; Yadav *et al*., 2010), antioxidants, antimicrobial (Yadav *et al*., 2010; Xiang *et al*., 2008), antifungal (Rath *et al*., 1995), antileukemic (Chang and Lee, 1984), antiviral and anti-HIV properties (Alves *et al*., 2004; Schinazi *et al*., 1990). It has also been reported that derivatives of aminoanthracene-9, 10-dione show considerably increased antitumor activities (Nor *et al*., 2013). In view of the wide interest of medicinal chemists towards imines and anthracenedione, synthesis and antibacterial activities of the Schiff bases have been reported here.

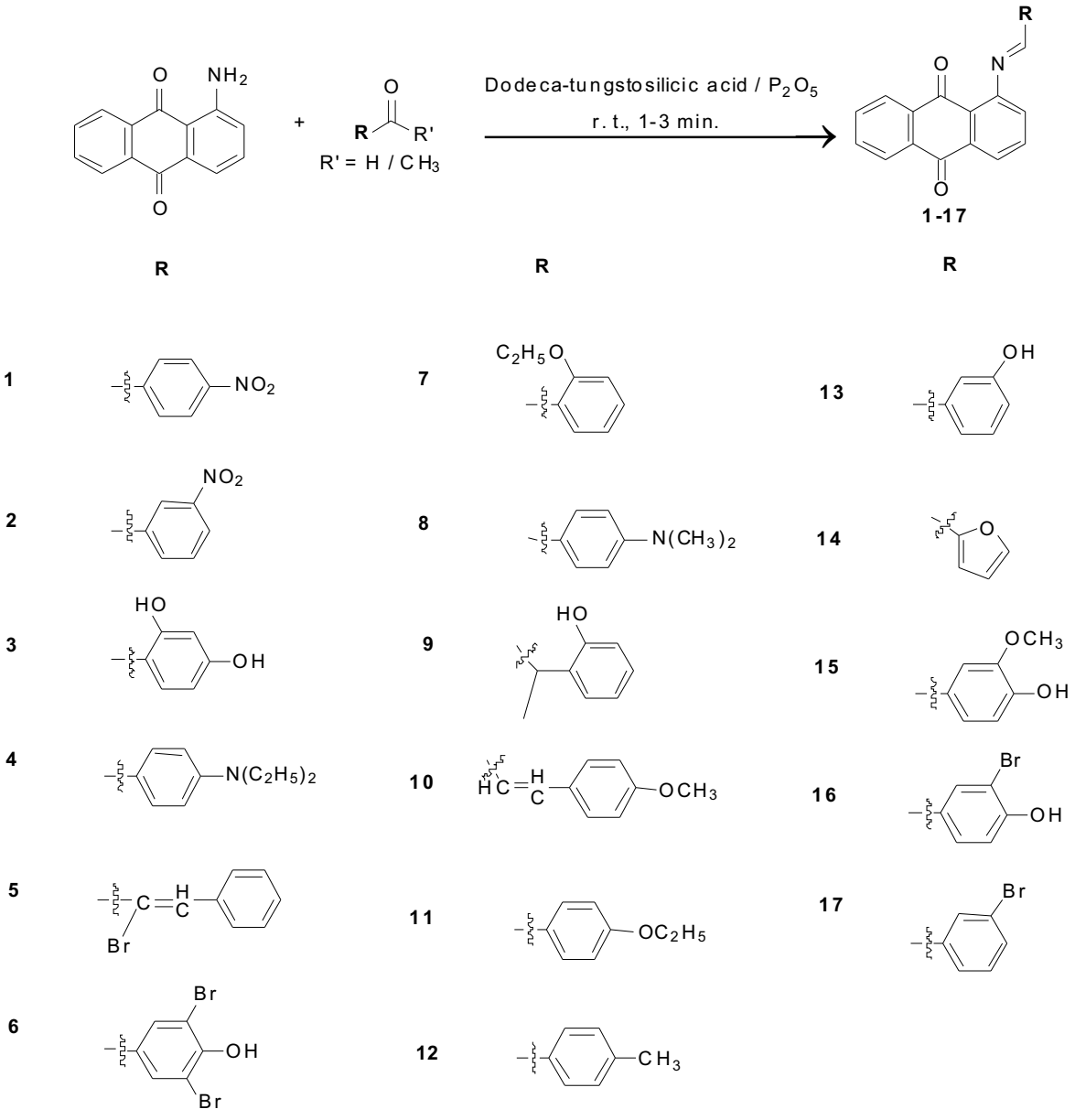
## Materials and Methods

The melting points were recorded in a glass capillary using Gallenkamp MF-370 melting point apparatus and are uncorrected. $^{1}$H-NMR (300MHz) and $^{13}$C-NMR (75MHz) spectra were recorded on Bruker AV-300 NMR Spectrometer in DMSO-$d_6$ with trimethyl silane (TMS) as an internal standard. IR spectra were recorded on Nicolet Avatar 300 DTGS. Mass spectra were recorded on a Finnigan LCQ Advantage Max. Elemental

analysis were conducted on a Carlo Erba Strumentazion-Mod-1106 instrument.

**General method for the synthesis of Schiff bases 1-17.** A mixture of 1-aminoanthracene-9,10-dione (1 mmol), variety of aromatic carbonyl compounds (1 mmol) and *dodeca*-tungstosilicic acid/$P_2O_5$ (0.2 g, 1 mol% of 1-aminoanthraquinone/$P_2O_5$) as a catalyst was ground in mortar with a pestle under solvent free conditions at room temperature for 1-3 min (Scheme 1). The reaction mixture turned to paste like material which indicated the completion of the reaction. Crushed ice was added to afford precipitates of the Schiff bases. In order to remove catalyst, the product was washed several times with ice cooled water. The solid products were obtained in excellent yield (Fareed *et al*., 2013).

***In vitro* antibacterial assay.** *In vitro* antimicrobial activity was performed by determining MIC of compounds by broth micro dilution method (Wayn, 2012) against multidrug resistant (MDR) and normal strains *viz*., methicillin resistant *Staphylococcus aureus*




**Scheme 1**. Structures of synthesized Schiff bases **1-17**

(MRSA), *Escherichia coli* (MDR), *Klebsiella* species (MDR), *Salmonella typhimurium* (MDR), *Pseudomonas aeruginosa* (MDR), *E. coli* ATCC 8739*, Staphylococcus aureus* ATCC 25923*, Staphylococcus aureus, Escherichia coli, Klebsiella* species, and *Pseudomonas aeruginosa.* Stock solution was prepared by dissolving 5 mg of compounds in 1ml of sterile DMSO. 100 µL from the stock solution of each compound was taken in first rows of well then serially half dilution were made by taking Mueller Hinton broth. The bacterial suspensions were adjusted with sterile saline to a concentration of $1.0\times10^5$ CFU/mL then 10 µL inocula were taken and added in each well. Micro titer plates were incubated for 24 h at 37 °C to check the results. Well showed no visible growth was taken as MIC of compound. Each experiment was performed in triplicate to authenticate the results.

## Results and Discussion

**Antibacterial activity.** Schiff bases **1-17** were synthesized by condensation of 1-aminoanthracene-9,10-dione with variety of aromatic and aliphatic carbonyl compounds using reported catalytic method (Fareed *et al*., 2013).

The antibacterial tests of the compounds **1-17** were carried out to determine MIC (Minimum Inhibitory Concentration) against multidrug resistant (MDR) strains *viz*., *S. aureus*, *E. coli* , *Klebsiella* species , *S. typhimurium*, *P. aeruginosa*, *E. coli* ATCC 8739, *S. aureus* ATCC-25923, and non-MDR strains of *S. aureus, E. coli, Klebsiella* species, and *P. aeruginosa.* The antibacterial studies were performed by broth micro dilution method by means of CLSI (Clinical and Standards Institute, 2012) formerly NCCLS (National Committee for Clinical Laboratory Standards) guidelines. All the isolates were isolated from various clinical samples (pus, urine, ear swabs, wound swabs, blood, fluid) of patients attending various hospitals in Karachi. The results were compared with Cefotaxime, which was used as standard drug. The results are depicted in Table 1.

Compounds **2**, **3, 4, 13** and **14** were found to be potent against multidrug resistant (MDR) bacterial strains when compared with the Cefotaxime standard, however compound **8** exhibited good activities against *S. aureus* and *Klebsiella* species. Compounds **2** and **4** exhibited lower MIC (250 µg/mL) against MDR *S. typhinurium*. Compound **14** showed MIC (250 µg/mL) against MDR *S. typhinurium*, *E. coli* and *P. aeruginosa*. Compounds **2** and **5** were found to have MIC (31.25 µg/mL) against

**Table 1.** Antibacterial activity of synthesized schiff bases **1-17**

| Name of bacteria/compound no. | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** | **10** | **11** | **12** | **13** | **14** | **15** | **16** | **17** | Cefotaxime |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *Staphylococcus aureus* (MDR) | - | 250 | 500 | 250 | - | - | - | 1000 | - | - | - | - | 1000 | 750 | - | - | - | >800 |
| *Escherichia coli* (MDR) | - | 500 | 750 | 500 | - | - | - | 1000 | - | - | - | - | 750 | 250 | - | - | - | >800 |
| *Klebsiella* species (MDR) | - | 1000 | 500 | 500 | - | - | - | 750 | - | - | - | - | 500 | 500 | - | - | - | >800 |
| *Salmonella typhimurium* (MDR) | - | 250 | 500 | 250 | - | - | - | 750 | - | - | - | - | 500 | 250 | - | - | - | >800 |
| *Pseudomonas aeruginosa* (MDR) | - | 500 | 500 | 1000 | - | - | - | 1500 | - | - | - | - | 500 | 250 | - | - | - | >800 |
| *Escherichia coli* ATCC-8739 | 500 | 250 | 500 | 750 | 250 | 500 | 62.5 | 1000 | 250 | 125 | - | 500 | 500 | 125 | 500 | 1000 | - | 3 |
| *Staphylococcus aureus* ATCC-25923 | 250 | 250 | 125 | 125 | 125 | 250 | 125 | 750 | 250 | 250 | - | 250 | 750 | 125 | 250 | 500 | - | 3 |
| *Staphylococcus aureus* | 250 | 500 | 125 | 62.5 | 31.25 | - | 250 | 1000 | 125 | 250 | - | 500 | 500 | 750 | 62.5 | 500 | - | 6 |
| *Escherichia coli* | - | 250 | 500 | 1000 | 125 | 500 | 750 | 250 | 250 | 125 | - | 500 | 750 | 62.5 | 500 | 750 | - | 5 |
| *Klebsiella* species | 250 | 62.5 | 500 | 250 | 31.25 | 500 | 1000 | 500 | 500 | 750 | - | 750 | 1000 | 125 | 500 | 1000 | - | 6 |
| *Pseudomonas aeruginosa* | 250 | 31.25 | 1500 | 125 | 500 | 250 | 500 | 250 | 750 | 500 | - | 1000 | 1500 | 125 | 62.5 | 500 | - | 6 |

Results are presented as MIC value; MIC (µg/mL) = minimum inhibitory concentration; No. of isolates = 11.

non-MDR *P. aeruginosa* and *S. aureus* and *Klebsiella* species, respectively. Compounds **2** and **15** were found to be good to moderately active against *P. aeruginosa* with MIC values 31.25 µg/mL and 62.5 µg/mL, respectively and compounds **4** and **15** showed moderate activity against *S. aureus* with MIC 62.5 µg/mL. All the remaining compounds except **11** and **17** showed weak antimicrobial activity against non-MDR strains of bacterial isolates. Therefore, pharmacodynamic studies would be required to make them useful as potential antimicrobial agents.

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