# Synthesis and evaluation of the antimicrobial activity of schiff base and succinimide compounds

H.F. Fahmidha[a], M.H. Haroon[a]*, M.A. Baheej[c]

[a, b, c]Department of Chemical Sciences, Faculty of Applied Sciences, South Eastern University of Sri Lanka

([a]hfahamed4@gmail.com, [b]haroonnmh@fas.seu.ac.lk, [c]baheej2011@gmail.com)

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## Introduction

Schiff bases are organic compounds and were first reported by Hugo Schiff in 1864 [1]. These are usually formed by the condensation of primary amines with carbonyl compounds. They have a characteristic group -C=N-, which are called azomethines. The development of the new chemotherapeutic Schiff bases is now attracting the attention of medicinal chemists. It is known to exhibit a variety of powerful activities. Due to the presence of carbon-nitrogen double bond in Schiff bases they have significant biological activities. Such as antibacterial, antifungal [2], antioxidant [3] and anti-inflammatory [3] activities.

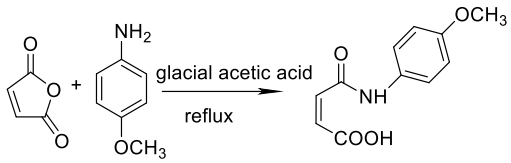
Succinimides are cyclic imides that have pharmaceutical applications. Due to the presence of both carbonyl and methylene groups, they have high chemical reactivity and biological activity. Succinimides are heterocyclic compounds. In recent years, heterocyclic compounds play an important role in the development of organic synthesis and their wide range of applications in the field of pharmaceuticals, agrochemicals, and veterinary products [4].

The current study has been conducted on synthesis of Schiff bases and Succinimide compounds, to check the purity of all compounds using thin-layer and column chromatography, and to evaluate the antimicrobial activity of each synthesized compound against pathogenic bacteria and fungi.

## Methodology

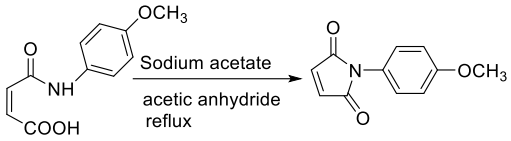
Scheme 01

Step 1: Preparation of maleanilic acid



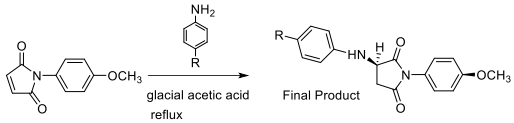

Finely powdered maleic anhydride 1.25 g, 1.36 g of para anisidine, and 10.00 ml of glacial acetic acid were placed in a 50.00 ml conical flask. The mixture was warmed over wire gauze and stirred with a glass rod for 30 minutes. The product was filtered at the pump, washed with a little (1 ml) ethanol, and drained well by suction for 45 minutes. 1.00 g of product was retained for step-2 and the remainder was recrystallized from a minimum volume of ethanol.

Step 2: Preparation of N-phenyl maleamide



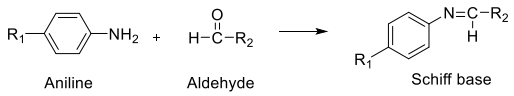

Above product 1.00 g (maleanilic acid), 0.25 g anhydrous sodium acetate, and 1.90 ml of acetic anhydride were placed in a 50.00 ml round bottom flask. The mixture was heated under reflux in a boiling water bath for 30 minutes with occasional shaking. The mixture was allowed to cool to RT (15 min) and was poured into cold water (15.00 ml) contained in a 100.00 ml conical flask and was stirred well. The product was collected at the pump, was washed well with water, and was drained well by suction. 0.50 g of product was retained for step-3 and the remainder was recrystallized from a minimum volume of cyclohexane.

Step 3: Preparation of Pyrrolidine-2, 5-dione derivatives




The above product 0.50 g (from step-2), 350.00 mg of 4-chloroaniline, and 2.50 ml glacial acetic acid were placed in a 50.00 ml round-bottomed flask and was refluxed gently over a wire gauze for 30 minutes. The mixture was cooled to RT. The product was collected at the pump, washed with little (1.00 ml) ethanol, and was drained well by suction. The remainder was recrystallized from a minimum volume of solvent. By changing the aniline derivatives six succinimide compounds were synthesized.

Scheme 02: Schiff base production




P-anisidine 1.00 mmol, benzaldehyde 1.20 mmol, 5.00 ml of ethanol, and 3-4 drops of glacial acetic acid were placed in a 50.00 ml round bottom flask. The mixture was heated under reflux in a boiling water bath for 2 hours with occasional shaking. The mixture was poured into crushed ice. The product was collected at the pump, was washed well with ethanol, and was drained well by suction [5]. By changing the aldehyde derivatives four Schiff bases were synthesized.

**Determination of antimicrobial bioassay.** Synthesized compounds were screened for antimicrobial activity against Escherichia coli, Bacillus spp, Aspergillus spp, and Trichoderma spp using the disc diffusion method. Three replicates were applied for the whole procedure.

The above bacterial and fungal colonies were taken separately onto a loop and transferred the growth to a test tube containing 2.00 ml of sterile normal saline. The test tube was vortexed thoroughly for 10 s to uniformly suspend the bacterial and fungal culture. The turbidity of the suspension was made to get equal to that of 0.5 McFarland standard. The Muller Hinton Agar plates were inoculated with 1.00 ml of the bacterial suspension. The Potato Dextrose Agar plates were inoculated with 1.00 ml of the fungal suspension. Petri dishes were rotated to ensure uniform spread and kept inside an oven at 44 °C for 15 minutes to dry completely.

Each synthesized compound (1.00 mg) was completely dissolved in 100.00 µL of DMSO and discs were soaked with 30.00 µL of the dissolved sample. The discs were allowed to air dry and placed on the previously prepared spread plate. Then, plates were incubated at 37 °C for 24 hours for antibacterial testing and the plates were incubated for 72 hours at 37 °C for antifungal testing. Finally, the plates were observed for a zone of inhibition and the diameter of the inhibition zone was measured along the two axes perpendicular to each other. The commercial antimicrobial agent gentamicin was used as the positive control and the effect of the solvent was also determined following the same procedure mentioned above using DMSO.

Randomized complete block design (RCBD) was used for the experimental design of the ZOI study and the number of samples per treatment was four.

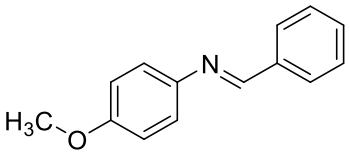
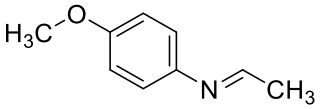
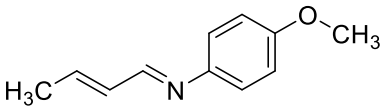
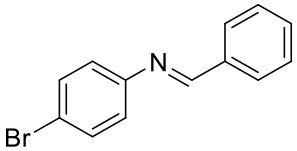
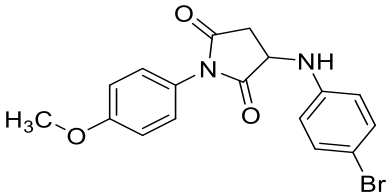
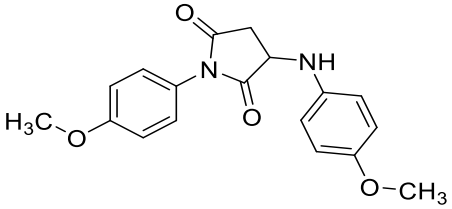
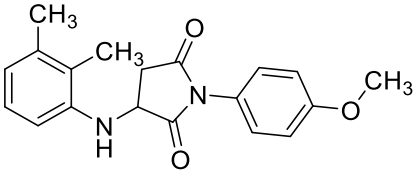
**Results and Discussion**

In the present study, 10 compounds were synthesized based on scheme 1 and scheme 2.

**Antimicrobial activity against pathogenic bacteria and fungi.** The Petri dishes were observed after 24 hours and the antimicrobial activity of synthesized compounds was calculated by measuring the diameter of the zone of inhibition of bacterial and fungal growth around the disc paper.

The literature survey has revealed that the Succinimide derivatives and Schiff bases exhibit good anticonvulsants, antimicrobial and anti-mutagenic activities. Hence, in the present study synthesized compounds have been evaluated for antibacterial and antifungal activities. Among synthesized compounds, compound 1 has been reported for its anti-platelet activity previously and Compound 4 has been reported for its antibacterial activity against *P. aeruginosa*.

**Table 1.** Show synthesized compounds with their yield percentage.

| Compound No | Product | Color of the final product | Percentage yield |
|---|---|---|---|
| 01 |  N-(4-methoxyphenyl)-1- phenylmethanimine | Gray | 69.73 |
| 02 |  N-(4-methoxyphenyl)ethanimine | Dark Brown | 74.62 |
| 03 |  N-(4-methoxyphenyl)but-2-en-1-imine | Dark Brown | 79.59 |
| 04 |  N-(4-bromophenyl)-1-phenylmethanimine | Gray | 97.72 |
| 05 |  3-((4-bromophenyl)amino)-1-(4-methoxyphenyl)pyrrolidine-2,5-dione | White | 9.99 |
| 06 |  1-(4-methoxyphenyl)-3-((4-methoxyphenyl)amino)pyrrolidine-2,5-dione | White | 4.54 |
| 07 |  3-((2,3-dimethylphenyl)amino)-1-(4-methoxyphenyl)pyrrolidine-2,5-dione | White | 6.43 |

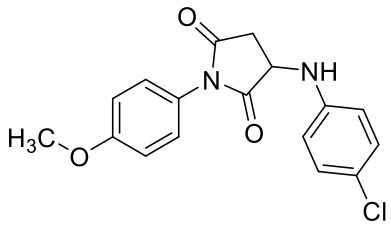
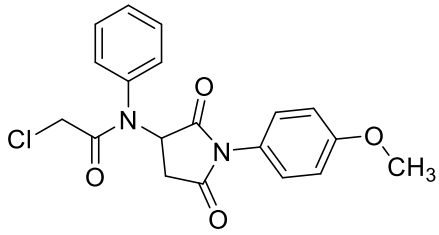
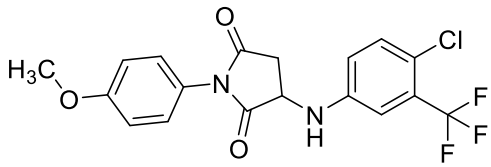
| | | | |
|---|---|---|---|
| 08 |  <br>3-((4-chlorophenyl)amino)-1-(4-methoxyphenyl)pyrrolidine-2,5-dione | White | 8.15 |
| 09 |  <br>2-chloro-N-(1-(4-methoxyphenyl)-2,5-dioxopyrrolidin-3-yl)-N-phenylacetamide | Yellow | 97.88 |
| 10 |  <br>3-((4-chloro-3-(trifluoromethyl)phenyl)amino)-1-(4-methoxyphenyl)pyrrolidine-2,5-dione | Pale Brown | 7.17 |

**Table 2.** Diameter of ZOI of synthesized compounds (in mm).

| **Compounds** | **Microorganisms** | | | |
|---|---|---|---|---|
| | ***Bacillus spp*** | ***Escherichia coli*** | ***Aspergillus spp*** | ***Trichoderma spp*** |
| 1 | - | - | - | 10.3 ± 0.4 |
| 2 | 7.6 ± 0.5 | 10.0 ± 0.2 | 8.0 ± 0.5 | 7.33 ± 0.2 |
| 3 | 12.0 ± 0.6 | 13.66 ± 0.5 | 9.0 ± 0.4 | - |
| 4 | - | - | - | - |
| 5 | 9.33 ± 0.34 | 8.0 ± 0.4 | - | - |
| 6 | 8.33 ± 0.13 | 7.66 ± 0.1 | - | - |
| 7 | 8.33 ± 0.2 | 9.0 ± 0.32 | - | - |
| 8 | - | 11.0 ± 0.1 | - | - |
| 9 | - | - | - | - |
| 10 | - | - | 8.0 ± 0.2 | 7.66 ± 0.3 |
| Gentamycin (Control) | 35.0 ± 0.4 | 31.7 ± 0.36 | 26.3 ± 0.42 | 25.8 ± 0.5 |

During the present investigation, Gentamycin was used as a positive control and DMSO (Dimethyl Sulphoxide) was used as a negative control. The inhibitory effect was observed, and

the antimicrobial activity of synthesized compounds was calculated by measuring the diameter of Zone of Inhibition (ZOI) of bacterial and fungal growth around the disc paper. Among them compounds 2, 3, 5, 6, 7, and 8 were showed a moderate level of inhibition against bacteria compared to standard drug gentamycin. And they were found to inhibit the growth of *Bacillus spp* and *Escherichia coli* with ZOI ranging from 7.6 – 12.0 mm and 7.66 - 13.66 mm respectively. Other compounds 1, 4, 9, and 10 were found to be inactive against tested bacteria. The compounds 1, 2, 3, and 10 were showed a moderate level of inhibition against fungi compared to standard drug gentamycin. And they were found to inhibit the growth of *Aspergillus spp* and *Trichoderma spp* with ZOI ranging from 8.0 – 9.0 mm and 7.33 – 10.3 mm respectively. The compounds 4 and 9 were showed no inhibition against tested bacteria and fungi.

## Conclusion

The present study mainly focused on the synthesis of Schiff base and Succinimide compounds. The compounds synthesized were screened against biological activities such as antibacterial and antifungal. This study showed that the synthesized compounds were inhibited bacterial growth and fungal growth too. Among the two bacteria, E. coli was more sensitive to all six compounds (2, 3, 5, 6, 7, and 8), than Bacillus spp, and also their effectiveness has differed. But both Aspergillus spp and Trichoderma spp showed approximately the same sensitivity to three compounds. These Schiff bases and Succinimide compounds could be synthesized and used as antibacterial and antifungal agents.

## Acknowledgment

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## References

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