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Research Article

One pot conventional synthesis and biological activity of some novel double schiff bases

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ABSTRACT

In this work, we report the synthesis and biological activity of some new double Schiff bases derived from ethylene diamine with 2-acetylnaphthalene and 2-acetylpyridine and were characterised by using UV-Visible, FTIR, ^{1}HNMR and ^{13}C NMR spectroscopy studies. All of the synthesized compounds gave satisfactory analytical and spectroscopic data.

We explored the antibacterial activity of the synthesized compounds against *Esherichia coli, Staphylococcus aureus* and *Pseudomonas aeruginosa* and the results showed that the compounds exhibits appreciable activity against the selected bacterial strains. The investigation of antifungal screening of the compounds against *Aspergillus niger, Candida albicans and Cryptococcus* explored that the Schiff bases showed a significant activity against the selected fungal strains.

Keywords: Schiff bases; ethylene diamine; 2-acetylnaphthalene; 2-acetylpyridine; biological activity.

INTRODUCTION

A Schiff base (or azomethine) is a functional group that contains a carbon nitrogen double bond (C=N) with the nitrogen atom connected to an aryl or alkyl group but not to hydrogen [1]. Schiff bases are of the general formula $R_1R_2C=NR_3$, where R_3 is an aryl or alkyl group that makes the Schiff base a stable imine[2]. The importance of Schiff bases in organic synthesis has increased over the past few decades because they are among the most versatile organic synthetic intermediates. The wide use of antibiotics in man and animals and their extensive use in areas other than the treatment made many bacterial strains to become resistant to the available drugs. Various strategies have been worked out and tried upon to cope with the resistance problem and enhance the activity, or broaden the spectrum of drugs [3]. The Schiff base structure provides for a greater choice and flexibility and complexation with a metal element adds to stability and versality of the molecule [4]. It has been suggested that the azomethine linkage might be responsible for the biological activities displayed by Schiff bases [5].

Schiff bases have been reported to posses the pharmacological activities such as anti-fungal [6], anti-microbial [7], anti-tumor [8], anti-malarial [9], anti-cancer [10], anti-tubercular [11], anti-viral [12], herbicidal [13], anti-bacterial [14], anti-convulsant [15], anti inflammatory activities [16]. In addition some Schiff bases have been reported to exhibit anti-hypertensive [17], anti-HIV [18] and hypnotic activities [19]. They are also known to be neo-plasm inhibitors [20] and as plant growth regulators [21]. They serve as models for biologically important species and find applications in biomimetic catalytic reactions [22]. Furthermore, schiff bases are reported to show a variety of some other interesting biological actions, including anti-mouse hepatitis virus (MHV) [23], inhibition of simplex virus type I (HSV-1) [24], adenovirus type 5 (Ad 5) [25] and anti-mosquito larvae[26].

EXPERIMENTAL

Materials and Methods

All the chemicals and solvents used for the syntheses were of reagent grade and were obtained commercially from Merck Company. The UV spectra (λ_{max} nm) of the synthesized Schiff bases were recorded on a Techcomp 8500 UV spectrometer. The infrared spectra (υ cm^{-1}) of the Schiff bases were recorded on a Shimadzu FT-IR spectrometer as KBr disks. ^{1}H NMR and ^{13}C NMR spectral measurements were carried out on a Jeol Spectroscopy Advance 500 MHz ultrashield spectrometer using DMSO – d_6 as solvent and TMS as an internal reference.

General procedure for the synthesis of Compound A and B

Ethylenediamine (20 mmol) was added to a solution of 2-acetylnaphthalene (40 mmol) in absolute ethanol (60 mL)

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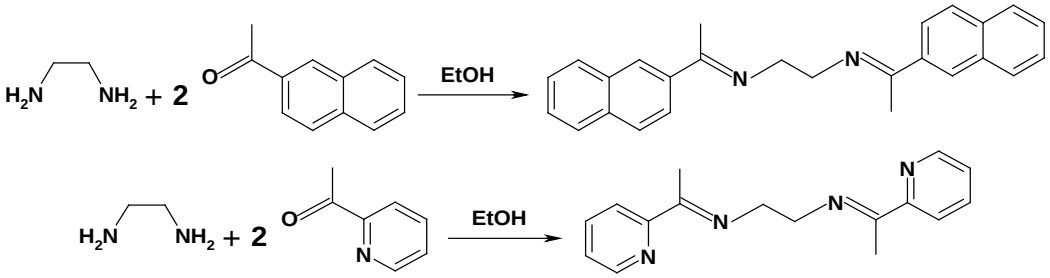
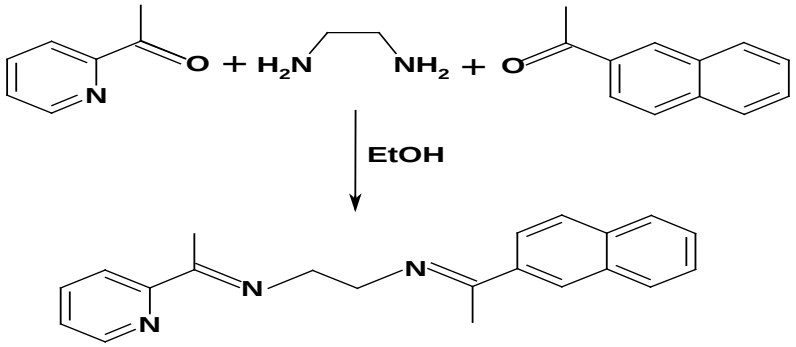
or 2-acetylpyridine (40 mmol) in absolute ethanol (60 mL) in 1:2 ratio. The reaction mixture was refluxed at 140-150°C for 4-5 hours. The clear solution was left to overnight and the resulting yellow solid product was extracted with absolute ethanol. The solution was concentrated to dryness to afford the desired Schiff base. The purity of compounds was checked routinely by TLC (0.5 mm thickness) using silica gel-G coated aluminium plates (Merks) and spots were visualized by exposing the dry plates in iodine vapours and exposing to UV light.



Scheme 1: Synthetic route to Symmetrical Schiff bases

General procedure for the synthesis of Compound C

Ethylenediamine (20 mmol) was added to a solution of 2-acetylnaphthalene (20 mmol) in absolute ethanol (30 mL) and 2-acetylpyridine (20 mmol) in absolute ethanol (30 mL) in 1:1:1 ratio. The reaction mixture was refluxed at 140-150°C for 4-5 hours and process as above.



Scheme 2: Synthetic route to Unsymmetrical Schiff base

Antibacterial and Antifungal studies

The main characteristics of the medium were to support the growth of the organisms normally tested and not contain antagonist of antimicrobial activity. The medium must allow free diffusion of plant extract from the well.

The sterilized medium was poured into a Petri dish in a uniform thickness and kept aside for solidification. Using sterilized swabs, even distribution of lawn culture was prepared using bacteria and fungi chosen in Muller Hinton Agar (MHA) plates and Sabouraud's dextrose (SDA) agar, respectively [30].

Compound A: Yield: 75%; UV (λ_{max} nm): 200, 285; IR (υ cm^{-1}): 725, 1606, 2895, 3047; ^{1}H NMR (δ ppm): 1.13, 2.67, 3.89, 7.59-8.09, 8.28; ^{13}C NMR (δ ppm): 14.04, 28.99, 58.59, 120.60, 122.47, 124.34, 136.90, 137.04, 158.05, 166.32.

Compound B: Yield: 73%; UV (λ_{max} nm): 200, 285; IR (υ cm^{-1}): 771, 1450, 1637, 3059; ^{1}H NMR (δ ppm): 1.25, 1.36, 2.31, 3.55, 3.83, 7.59-8.25, 8.56; ^{13}C NMR (δ ppm): 14.31, 26.14, 28.98, 58.41, 120.06, 122.06, 124.55, 124.98, 136.90, 137.04, 148.78, 149.74, 158.13, 166.32.

Compound C: Yield: 70%; UV (λ_{max} nm): 195, 275; IR (υ cm^{-1}): 748, 1448, 1620, 3059; ^{1}H NMR (δ ppm): 1.25, 1.34, 1.77, 2.46, 2.67, 3.87, 7.50-8.09, 8.64; ^{13}C NMR (δ ppm): 14.31, 28.70, 58.02, 120.77, 122.92, 124.55, 128.18, 137.07, 148.47, 148.78, 149.74, 157.30, 166.32, 167.01.

RESULTS AND DISCUSSSION

A peak at 195-200 nm is observed which is due to π- π* transition of C=N and benzene. A broad band at 275-285 nm is observed which is due to n- π* transition.

A peak at 1606-1637 cm^{-1} corresponds to C=N stretching absorption [27, 28, 29]. A sharp peak at 3047-3059 cm^{-1} is characteristic of C-H stretching absorption of aromatic hydrocarbon. A band at 2895-2999 cm^{-1} is due to C-H stretching absorption in CH_2 and CH_3.

In the nuclear magnetic resonance spectra the signals of the respective protons of the compound A is verified on the basis of its chemical shifts, multiplicities and coupling constants. The spectra showed the aromatic proton at 7.5-8.0 ppm, the imine proton (N=C-H) at 8.2-8.6 ppm, methyl proton at 2.3-2.6 ppm and methylene proton at 3.8 ppm [29].

The ^{13}C NMR spectrum showed a signal at 137.05 ppm which indicates the presence of C=N group in the structure.

The *in-vitro* antibacterial activities was evaluated against a series of bacterial strains namely (Gram positive: *Staphylococcus aureus*; Gram negative: *Esherichia* coli, *Pseudomonas aeruginosa*) with the *Ciprofloxacin* as standard reference broad antibiotic. The data of antibacterial activity of the reported compounds are given in Table (1 & 3) [27, 28]. The results showed that the tested double Schiff bases containing pyridine moiety are in general capable of inhibiting the growth of bacteria to an appreciable extent.

The *in-vitro* antifungal screening effect of the synthesized double Schiff bases were evaluated against *Aspergillus niger, Candida albicans and Cryptococcus* using *Ketoconazole* as standard antifungal reference by well diffusion technique. The data of antifungal activity of the reported compounds are given in Table (2 & 4). The results showed that the tested double Schiff bases exhibited potent inhibitory activity against all the three fungal strains.

Table – 1: Antibacterial activity of compounds A, B & C

S.No.	Organism (Bacteria)	Zone of Inhibition (mm)			
		A (AN)	B (AP)	C (ANAP)	Ciprofloxacin
1.	*E. coli*	-	16	10	17
2.	*Pseudomonas Aeruginosa*	-	10	5	8
3.	*Staphylococcus Aerues*	5	15	9	10

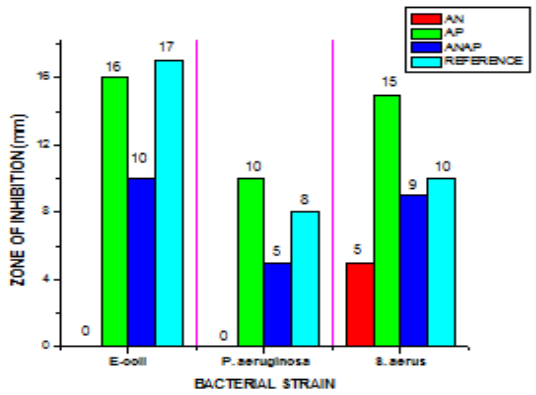


Chart-1: Graphical representation of the Anti-bacterial activity

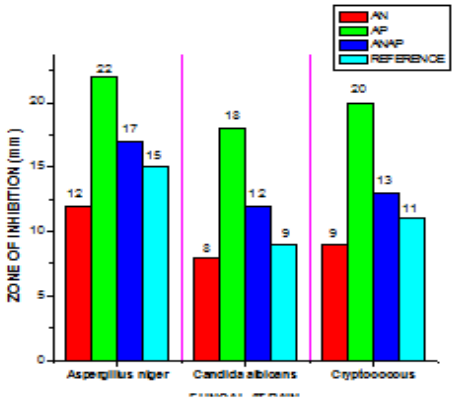


Chart-2: Graphical representation of the Anti-fungal activity

Table – 2: Antibacterial activity of compounds A, B & C

S.No.	Organism ((Fungus)	Zone of Inhibition (mm)			
		A (AN)	B (AP)	C (ANAP)	Ketoconazole
1.	*Aspergillus niger*	12	22	17	15
2.	*Candida albicans*	8	18	12	9
3.	*Cryptococcus*	9	20	13	11

Table – 3: Effect of Schiff Bases on the Growth of Tested Bacteria

S.No.	Compound	Bacteria		
		Gram Negative		Gram Positive
		Escherichia Coli	*Pseudomonas aeruginosa*	*Staphylococcus Aureus*
1.	*Ciprofloxacin*	+++	+	++
2.	A (AN)	-	-	+
3.	B (AP)	+++	++	+++
4.	C (AN AP)	++	+	+

Key to symbols:
Highly active = + + + (inhibition zone > 14 mm).
Moderately active = + + (inhibition zone 10-14 mm)
Slightly active = + (inhibition zone 5-9 mm)
Inactive = - (inhibition zone < 5 mm)

Table – 4: Effect of Schiff Bases on the Growth of Tested Fungus

S.No.	Compound	Fungus		
		Aspergillus niger	*Candida albicans*	*Cryptococcus*
1.	*Ketoconazole*	+++	+	++
2.	A (AN)	++	+	+
3.	B (AP)	+++	+++	+++
4.	C (AN AP)	+++	++	++

CONCLUSION

In summary, some novel double Schiff bases have been designed and prepared from ethylenediamine, 2-acetylnaphthalene and 2-acetylpyridine. The synthesized compounds were characterized by using UV-Visible, FT-IR, ^{1}H NMR and ^{13}C NMR spectra.

We explored the antibacterial activity of the synthesized compounds against *Escherichia coli, Staphylococcus aureus*

and *Pseudomonas aeruginosa* and the results showed that the compounds (B) and (C) exhibits appreciable activity against the selected bacterial strains. The investigation of antifungal screening of the compounds against *Aspergillus niger, Candida albicans and Cryptococcus* explored that the Schiff bases (A), (B) and (C) showed a significant activity against the selected fungal strains.

REFERENCES

1. Jerry M, *Advanced Organic chemistry Reactions: Mechanisms and Structure*; 4th Ed., John wiley & sons: New York, 1992, 896.

2. Henry P. M. and Lange G. L., *The chemistry of double bonded functional* groups, S. Patai , Interscience, New York, suppl. A, part 2, 1977, pp 1067.

3. Brown, A.G. and S.M. Roberts, (Ed.), Recent advances in the Chemistry of β -lactam antibiotics, *The Royal Society of Chemistry*, London, 1984.

4. Forghieri, F., C. Preti, G. Toshi and P. Sonnini, *Aust. J. Chem*., 36: 1125.

5. Phatak, P.; Jolly, V. S.; Sharma, K. P. *Orient. J. Chem.* 2000, 16, 493-494.

6. Pandey S.N, Lakshmi VS and Pandey A., *Indian J Pharm Sci*. 2003, 65, 213-222.

7. Wadher. J, Puranik. M. P, Karande. N. A. and Yeole. P. G., *International Journal of Pharm. Tech. Research* 2009, 1, 22-33.

8. Pandeya S N and Sriram D, *Acta Pharmaceutica Turcica,* 1998, 40(1), 33-38.

9. Li Y, Yang ZS, Zhang H, Cao BJ and Wang FD, Artemisinin, *Bio org and Med Chem.* 2003, 11, 4363-4368.

10. Villar R,Encio I, Migliaccio M, Gil MG, Martinez-Merino V., *Bioorga and Med Chem*. 2004, 12, 963-968.

11. Bhat M.A, Imran M, Khan SA and Siddiqui N., *J Pharm Sci*., 2005, 67, 151-159.

12. Karthikeyan M.S, Dasappa Jagadeesh Prasad, Boja Poojary Subrahmanya Bhat K, Bantwal Shivaram Holla,. *Bioorg and Med Chem*. 2006; 14, 7482-7489.

13. Panneerselvam P, Nair R R and Vijayalakshmi G, *Eur J Med Chem*., 2005, 40(12), 225-229.

14. Venugopal KN, Jayashree BS.Microwave-induced synthesis of Schiff bases of bromcoumarins as antibacterials. *Indian J Pharm. Sci*. 2008; 70, 88-91.

15. Pandeya S N and Sriram D, *Acta Pharmaceutica Turcica,* 1998, 40(1), 33-38.

16. Chandra, T.; Garg, N.; Lata, S.; Saxena, K.K.; Kumar, A., *Eur. J. Med. Chem.*2010, 45, 1772-1776.

17. Kalla, R.; Zablocki, J. Chapter 13 *Recent Advances in Adenosine Receptor* (AR) Ligands in Pulmonary Diseases. *Annu. Rep. Med. Chem.* 2009, 44, 265-277.

18. Deacon, S.W.; Beeser, A.; Fukui, J.A.; Rennefahrt, U.E.E.; Myers, C.; Chernoff, J.; Peterson, J.R., *Chem. Biol.* 2008, 15, 322-331.

19. More. P. G, Bhalvankar. R. B, and Patter S. C. *J. Ind. Chem. Soc* 2001 78, 474.

20. Sur B, Chatterjee S P, sur P, Maity t & Choudhury S R , *Oncology,* 1990, 47 (5), 433.

21. Regine D., Pierre H, Jean H Y & Claude V, *CR Acad Sci.* Paris, 1969 265 (25), 1952.

22. Canpolat. E and Kaya M, *J. Coord. Chem.2004,* 57 1217.

23. Wang, P-H.; Keck, J. G.; Lien, J.; Lai, M. M. C. *J. Med. Chem.* 1990, *33*, 608-614.

24. Das, A.; Trousdale, M. D.; Ren, S.; Lien, E. J. *Antiviral Res.* 1999, *44*, 201-208.

25. Das, B. P.; Choudhury, R. T.; Das, K. G.; Choudhury, D. N.; Choudhury, B. *Chem. Environ. Res.*1994, 3, 19-23.

26. Samadhiya, S.; Halve, A. *Orient. J. Chem.* 2001, 17, 119-122.

27. Syed Tajudeen S., Radha E., *Asian J. of Chemistry*, 2009, 21, 313

28. Syed Tajudeen S., Manjunathan., Dastageer. M.S., *Asian J. of Chemistry*, 2009, 21 317

29. Maria T. Cocco et. al European J of Medicinal Chemistry, 34 (1999) 1071-1076.

30. Syed Tajudeen S., et. al., *J. Phar. Research*., 2010, 3(11) 2759-2760