Journal of Pharmaceutical and Scientific Innovation
www.jpsionline.com
Research Article

SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL EVALUATION OF SCHIFF'S BASES

Omran Fhid*, Talal Zeglam, Asma Gebril
Department of Pharmaceutical Chemistry, Faculty of pharmacy, Tripoli University, Tripoli-Libya
*Corresponding Author Email: Ofhid@yahoo.com
DOI: 10.7897/2277-4572.03197
Published by Moksha Publishing House. Website www.mokshaph.com

Received on: 25/12/13 Revised on: 21/01/14 Accepted on: 05/02/14

ABSTRACT
Keeping in view of the biological potential of Schiff bases attached to heterocyclic ring system; a series of novel Schiff's base derivatives were synthesized 1-8 successfully in appreciable yields. The structures of all the synthesized derivatives were confirmed by physical and spectral analysis. Furthermore, all synthesized compounds were evaluated for antifungal activity against different strains of fungal organisms. Some of the compounds exhibited appreciable antifungal activity comparing to the reference compound (Nystatine).
Keywords: heterocyclic ring system, Schiff's base, antifungal activity.

INTRODUCTION

Schiff's bases are condensation product of primary amines and aromatic aldehydes , they are known to exhibit a potent antibacterial, anticonvulsant, and Ant inflammatory activity[1]. In addition some Schiff bases show pharmacologically useful activities like anticancer[2], anti hypertensive and hypnotic[3] activities. Clinically, candidiasis and aspergillosis account for between 80 % and 90 % of systemic fungal infections in immune compromised patients. While there is a multiple choice of drugs for the treatment of candidiasis, only amphotericin B and itraconazole[4-6] come into consideration in the case of infections due to *Aspergillus fumigatus*. Although the research toward a new azole continues at an unabated pace, with examples such as TAK-187,[7] ER-30346,[8] Sankyo's amido alcohol,4 UR- 9825,[9] and most notably voriconazole6 and SCH-56592 (posaconazole)[10] having been reported, the discovery and development of new structural types of antifungal compounds are no less desirable. There is a real perceived need for the discovery of new compounds that are endowed with antibacterial and antifungal activities, possibly acting through mechanism of actions, which are distinct from those of well known classes of antimicrobial agents to which many clinically relevant pathogens are now resistant[11]. Heterocyclic compounds like substituted benzoic acid, indoleamine arouse great interest due to diverse type of biological activity associated with it, viz. anti malarial, anticancer, anticonvulsant and antibacterial[12]. The constitution of all compounds synthesized was established by physical and spectral analysis. Selected compounds were evaluated for antibacterial and antifungal activates.

MATERIAL AND METHODS

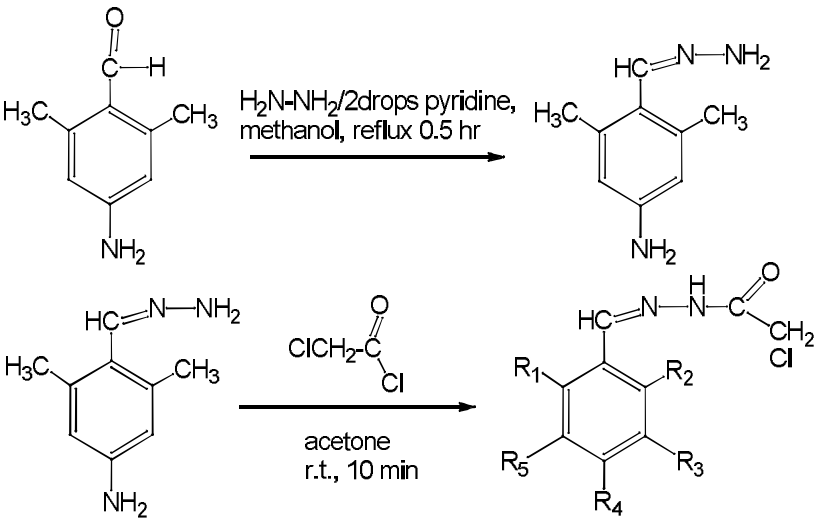
Experimental

All chemicals and solvents, reagents used in the present study were of analytical grade purchased from Sigma, Fischer. All the solvents were used after distillation. The melting points were determined by open capillary method and were uncorrected. The purity of compounds was confirmed by thin layer chromatography using Silica coated aluminium sheets (silica gel 60 F_{254}). IR spectra were recorded using KBr on FTIR Shimadzu. The elemental analysis was performed on Perkin-Elmer.

Synthesis

General procedure for synthesis of compounds 1-5

The Schiff bases were prepared by reaction of equimole of substituted benzaldehyde and hydrazine in methanol and few drops of pyridine yielded 4-hydrazonomethyl-3, 5-dimethylaniline (Intermediate product). This upon treatment with 2-chloracetyl chloride in acetone under refluxed for 10 minutes in r.t. The precipitate was filtered off, washed with water and then purified by re crystallization from 96^{o} EtOH respectively (Scheme1, Table 1).

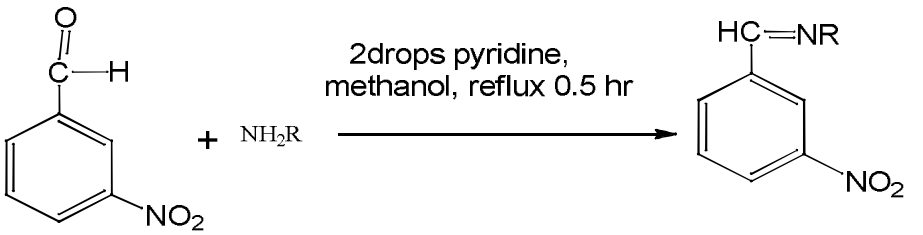


Scheme 1: Synthesis of compounds 1-5

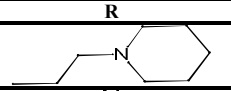
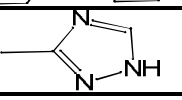
Comp. No	R1	R2	R3	R4	R5
1	CH3	CH3	H	NH2	H
2	H	H	NO2	H	H
3	H	H	H	Cl	H
4	H	OH	H	H	NH2
5	NO2	H	NO2	H	H

General procedure for synthesis of compounds 6 and 7

Schiff bases were prepared by reacting the Substituted benzaldehyde with substituted primary amine in equimolar, were taken in methanol and few drops of pyridine. Both the solutions were mixed and refluxed for 0.5 h. The reaction mixture was cooled; the precipitate was filtered off, washed with water and then purified by re crystallization from 96^{o} EtOH, (Scheme2, Table 1).

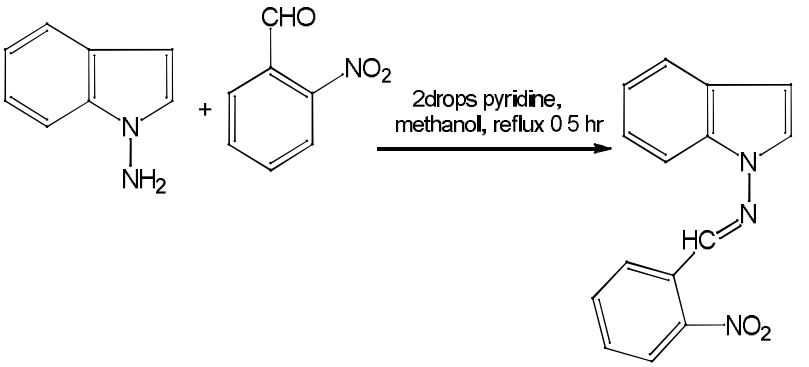


Scheme 2: Synthesis of compounds 6, 7

Comp. No	R
6	
7	

Synthesis of N-(3-nitrobenzylidene)-1 h-indole-1-amine 8

0.01 mol of indolamine, 0.01 mol of m. nitroaniline and few drops of pyridine in methanol; The mixture was refluxed for 0.05 h. cool, The dried solid product was filtered off, and re crystallized from EtOH (Scheme3, Table 1)



Scheme 3: Synthesis of compound 8

Table 1: Represent the physical data of the compounds (1-8)

Compounds	M. formula	M.P C°	Yield %
(*Z*)-*N*'-(4-amino-2,6-dimethylbenzylidene)-2-chloroacetohydrazide **1**	$C_{11}H_{15}N_3O$ (205.26)	65-67	48
(*Z*)-2-chloro-*N*'-(3-nitrobenzylidene)acetohydrazide **2**	$C_9H_9N_3O3$ (207.19)	204-206	70.2
(*Z*)-2-chloro-*N*'-(4-chlorobenzylidene)acetohydrazide **3**	$C_9H_9N_2O.Cl$ (196.64)	213-215	57
(*Z*)-*N*'-(4-amino-2-hydroxybenzylidene)-2-chloroacetohydrazide **4**	$C_9H_{11}N_3O2$ (193.21)	210-212	45
(*Z*)-2-chloro-*N*'-(2,4-dinitrobenzylidene)acetohydrazide **5**	$C_9H_8N_4O5$ (252.19)	118-120	52
N-(3-nitrobenzylidene)-2-(piperidin-1-yl)ethanamine **6**	$C_9H_8N_4O5$ (252.19)	60-62	30
(*E*)-*N*-(3-nitrobenzylidene)-1*H*-1,2,4-triazol-5-amine **7**	$C_{15}H_{20}N_2O_2$ (260.34)	64-66	40.7
N-(3-nitrobenzylidene)-1*H*-indol-1-amine **8**	$C_{15}H_{11}N_3O_2$ (265.27)	110-112	55

***In vitro* Antifungal screening**

The compounds 1-8 were evaluated against *Candida albicans* by diffusion method using Nystatine 100µ g/disc. Compound 8 exhibited activity against *Candida albicans*, while compounds 2 and 7 showed moderate activity against *C. albicans* comparable with the reference compound Table 2.

Table 2: *In vitro* antifungal activity of the title compounds (1-9) against *C. albicans*

Compounds	Conc (100 µg/100 ml)	Inhibition Zone (0.4 cm)				
		C. albicans Code No				
		669	1047	1057	660	772
1	(100 µg/100 ml)	0.4	0.4	0.4	1.2	0.4
2	(100 µg/100 ml)	1.3	**2.5**	**2.5**	**2.5**	**2.6**
3	(100 µg/100 ml)	0.4	0.4	1.0	1.0	0.4
4	(100 µg/100 ml)	0.4	0.4	1.0	1.0	0.4
5	(100 µg/100 ml)	0.4	0.4	1.0	1.0	0.4
6	(100 µg/100 ml)	1.4	2.3	1.4	2.0	**2.6**
7	(100 µg/100 ml)	1.3	2.1	1.5	2.0	**2.4**
8	(100 µg/100 ml)	**2.3**	**3.5**	**3.1**	**3.4**	**3.1**
Nystatine	100 µg/100 ml	1.6	2.0	2.0	1.9	2.0

RESULT AND DISCUSION

All the prepared compounds (1-8) are crystalline solids, and all the physicochemical data of the compounds are described in the Table 1. The antifungal activity exhibited by the compounds 2, 6-8 can be attributed to the presence of Schiff base (N = CH) linkage present in them[13]. Further, attachment of the Schiff's base linkage can greatly enhance the antifungal activity of the compounds. During Schiff's base formation the primary amino group condenses with aromatic aldehydes. The nature and position of the substituents of the aromatic aldehydes greatly influences the antifungal activity of the Schiff's bases. Generally the substituent's that causes activity are 3-nitro and 4-nitro groups in the aromatic ring. To conclude, the Schiff's bases formulated from the heterocyclic ring system containing in dole moiety have given satisfactory results for its antifungal activity. Schiff's bases can be converted into moieties like different aromatic aniline, indolemine, triazolamine. It can be concluded that this class of compounds certainly holds great promise towards good active leads in medicinal chemistry.

REFERENCES

1. Spasov AI, Phensoitiva. Tet Hed. Lett, 1971, 571, Keeping in view of the biological potential of Schiff bases Chemical Abst, 77 (s).
2. Takanyangani, Takeo, Japan Kokai, Takyo, Kolio, 8045, 608. Synthesis And Anti Microbial Studies of Certain Schiff Bases. Chem. Abst 1980, 2042. (s)
3. Ibid, 1972, 3: 668, 196, Chem Abst, 77, 1972, 26404 F (s)
4. Bonner JCDP. Recent Developments in Pradimycin-benacomycin and Triazole Antibiotics Expert Opin. Invest. Drugs 1997; 6: 129-145. http://dx.doi.org/10.1517/13543784.6.2.129
5. Tasaka A, Kitazaki T, Tamura N, Tsuchimori N, Matsushita Y, Hayashi R, Okonogi K, Itoh K. Optically Active Antifungal Azoles. VII. Synthesis and Antifungal Activity of Stereoisomers of 2-[(1R,2R)-2-(2,4-Difluorophenyl)- 2-hydroxy-1-methyl-3-(1H-1,2,4-triazol-1-yl)propyl]-4-[(2,2,3,3- tetrafluoropropoxy)phenyl]-3-(2H,4H)-1,2,4-triazolone (TAK 187). Chem. Pharm. Bull 1997; 45: 321-326. http://dx.doi.org/10.1248/cpb.45.321
6. Naito T, Hata K, Tsuruoka. For a review on ER-30346 (licensed to Bristol-Myers Squibb; the new laboratory code for this compound is BMS-207,-147). A. Drugs Future 1996; 21: 20-24.
7. Konosu T, Tajima Y, Takeda N, Miyaoka T, Kasahara M, Yasuda H, Oida S. Triazole Antifungals. IV. Synthesis and Antifungal Activities of 3-Acylamino-2-aryl-2-butanol Derivatives. Chem. Pharm. Bull 1991; 39: 2581-2589. http://dx.doi.org/10.1248/cpb.39.2581
8. Bartroli J, Turmo E, Alguero M, Boncompte E, Vericat ML, Conte L, Ramis J, Merlos M, Garcı A Rafanell J, Forn J. New Azole Anti fungals. 3. Synthesis and Antifungal Activity of 3-Substituted-4(3H)-quinazolinones. J. Med. Chem 1998; 41: 1869-1882. http://dx.doi.org/10.1021/jm9707277
9. Voriconazole (UK-109496). Drugs Future for fungi 1997; 22: 326-327.
10. Cacciapuoti A, Loebenberg D, Corcoran E, Menzel F Jr, Moss EL Jr, Norris C, Michalski M, Raynor K, Halpern J, Mendrick C, Arnold B, Antonacci B, Parmegiani R, Yarosh Tomaine T, Miller GH, Hare RS. *In vitro* and *in vivo* activities of SCH-5692 (posaconazole), a new triazole antifungal agent, against *Aspergillus* and *Candida*. Anti microb. Agents Chemother 2000; 44: 2017-2022. http://dx.doi.org/10.1128/AAC.44.8.2017-2022.2000
11. Sharma D, Narasimhan B, Kumar P, Jalbout A. Synthesis and QSAR Evaluation of (2-(Substituted Phenyl)-1H-Benzimidazol-1-yl)-Pyridin-3-yl-Metahnones. Eur. J. Med. Chem 2009; 44: 1119-1127. http://dx.doi.org/10.1016/j.ejmech.2008.06.009
12. Kalsi Ind. Synthesis and anti-inflammatory activity of indolyl azetidinones. J. Pharm. Sci 1990; 52(3): 129-134 (s).
13. Nair R, Shah A, Baluja S and Chanda SV, Medicinal Chemistry Research 2002; 11(8): 463-479 (s)

Source of support: Nil, Conflict of interest: None Declared

QUICK RESPONSE CODE	ISSN (Online) : 2277 –4572
	Website http://www.jpsionline.com

How to cite this article:

Omran Fhid, Talal Zeglam, Asma Gebril. Synthesis, characterization and biological evaluation of Schiff's bases. *J Pharm Sci Innov*. 2014;3(1):10-13 http://dx.doi.org/10.7897/2277-4572.03197