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Research Article

SYNTHESIS AND BIOLOGICAL SCREENING OF SOME NEW SULFANILAMIDE SCHIFFS BASE

SOFIAN SALEH MOHAMED[1], ASMA ABO-BAKER[2], SALAH M. BENSABER[3], MOUSA I. JAEDA[3], TARIQ ALMOG[3]*

[1]National Center for Medical Research, Medicinal Chemistry Department, Zawia,-Libya, [2]National Center for Medical Research, Microbiology Department, Zawia – Libya, [3]Department of Medicinal and Pharmaceutical Chemistry, Faculty of Pharmacy, University of Tripoli, Tripoli-Libya. Email: elmoug@hotmail.com

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ABSTRACT

Synthesis and antimicrobial activity of some new sulfanilamide Mono-Schiff's base derivatives II-VIII were described. The purity of the new synthesized compounds were checked by performing TLC using appropriate solvent and the spots were visualized in the UV light. The chemical structure of the compounds were confirmed by FT-IR, ^{1}H and [13]C-NMR spectroscopy. Synthetic compounds were screened in vitro for their antimicrobial activity against: *Staphylococcus aureus ATCC 29213, Escherichia coli ATCC 25922* and *Candida albicans ATCC 10231.* The best result obtained at the concentration 5µg molar with VI, V, and VI compounds against fungus (*Candida albicans ATCC*), VI compound against gram positive bacteria (*Staphylococcus aureus ATCC 29213*) while no compound was active against gram negative bacteria (*Escherichia coli ATCC 25922*).

Keywords: Synthesis; Schiff's base; Sulfanilamide; Antimicrobial activity

INTRODUCTION

Hugo Shiff was a pioneer discovered Schiff base and imines[1]. Schiff base is the compound which containing an azomethazine group (-CH=N-) in their structure, these are usually resulted by react a primary amine with carbonyl compound as in the following reaction[2]

$$R\text{-}CHO + H_2NR' \longrightarrow R\text{-}CH{=}NR' + H_2O$$

Where, R can be an aliphatic or an aromatic group. It was reported that, the Schiff base resulted from an aliphatic aldehydes are relatively unstable and readily polymerizable[3], while those formed from aromatic aldehyde are more stable due to their conjugated system. Schiff base serve as a back bone for the synthesis of various heterocyclic compounds having a versatile use and a wide range of application such as antibacterial[4-12], antifungal[4,6,9-13], antiviral[14], anthelmintic[15], as anti-malarial[16], ant-tuberculosis[12], anticancer[17], analgesic, anti-inflammatory[18] and antihyperlipidemic activity[19]. The presence of azomethine and sulfonamide functional group is responsible for antimicrobial activity, which can be altered depending upon the type of substituent present on the aromatic rings. In view of these above biological importance of Schiff bases, A simple and efficient synthesis under microwave irradiation was applied.

MATERIALS AND METHODS

Chemical synthesis of the Schiff base

Materials and solvents

All chemical materials and solvents used in chemical synthesis of Schiff base were highest purity and used without further Purification, purchased from sigma Aldrich chemical company and fluka analytical company, UK.

Instruments

Synthesis of compounds was performed in microwave (start E) from mileston company, Italy. Thin layer chromatographic (TLC) analyses were performed on pre-coated aluminum plates (silica gel 60778, fluka analytical). TLC spots were visualized with UV light. Melting points were measured in open capillary tubes on an electrothermal SMP30 melting point apparatus (stuart), UK. The IR spectra of samples were recorded in region 4000-400cm^{-1} by Varian FT-IR spectrophotometer 660, Australia. ^{1}H,[13]C-NMR spectra (400MHz) recorded in DMSO by employing TMS as an internal standard on ultra shield Bruker 400 NMR spectrometer.

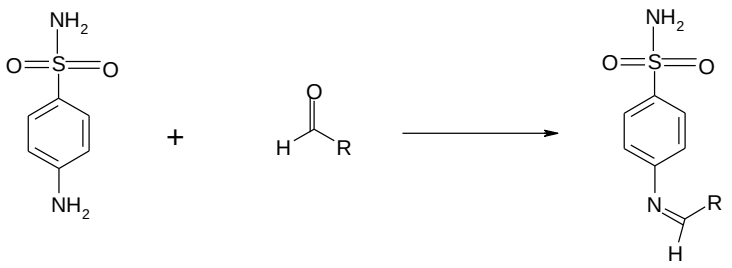
General procedure for Synthesis of Schiff base

The Schiff base was prepared by reaction of equimolar (0.01 M) of sulfanilamide and substituted aromatic aldehydes. The mixture were transferred to a clean, dry Teflon vessel, and triturated to form uniform mixture, then drops of ethanol were added. This mixture was irradiated to microwave (400 watt) for 0.5-1 minutes in 60 C°. After the reaction was completed, it allowed to cool, the crude solid product was collected through filtration and washed several times with ethanol then dried using a vacuum. The product was re-dissolved in ethanol for recrystallization and then dried to give a pure product II-VIII (scheme 1).

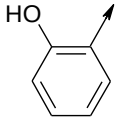
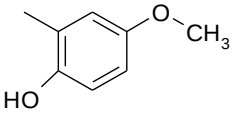
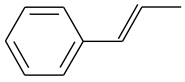
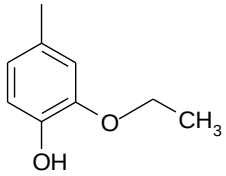
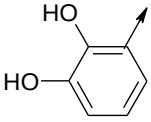
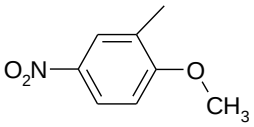
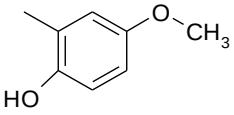
Antimicrobial activity

The antimicrobial activity of all synthesized compounds (II-VIII) were screened against different standard organism obtained from the American type of cell culture collection (ATCC), including *Staphylococcus aureus* (ATCC 29213), *Escherichia coli* (ATCC 25922) and *Candida albicans* (ATCC 10231). Agar diffusion technique at the concentration level of 5µg molar was applied. Ciprofloxacin and Ketoconazole were used as reference compounds for antibacterial and antifungal activities respectively.

Fig. 1: Scheme for the synthesis of Schiff's bases II-VIII



Sulfanilamide Aldehyde Schiff's base II-VIII

Compound. No.	R-CHO	Compound. No.	R-CHO
II		**VI**	
III		**VII**	
IV		**VIII**	
V			

RESULTS AND DISCUSTION

Chemical part

The Schiff's bases **II-VIII** was prepared by react sulfanilamide with aromatic aldehydes at ratio (1:1). Microwave irradiation reported to be an efficient, rapid, eco-friendly, fewer amounts of solvent required and cost effective for synthesis of some chemical compounds[20], so the advantages of this technique encouraged us to synthesize of some Schiff's base compound. The purity of the synthesized compounds were controlled by using TLC. Physical properties of synthesize compounds **II-VIII** were presented in table 1.

Table 1: physical properties of synthesize compounds II-VIII.

Compound. No.	M.WT	M.P(c°)	YILED (%)
II	276.31	222	88
II	288.36	203	90
IV	292.31	286	78
V	276.31	180	78
VI	320.36	185	90
VII	326.36	274	85
VIII	335.33	224	92

The structures of the synthesized compounds were determined on the basis of their FT-IR, ^{1}H and [13]C-NMR data were as a following

***4-[(2-Hydroxy-benzylidene)-amino]-benzenesulfonamide* II**

FT-IR (cm^{-1}): 1614(HC=N), 3239(N-H str), 1151(S=O asym), 1307(S=O sym), 3335(O-H str), 1570(phenolic OH). ^{1}H-NMR (400MHz, DMSO-d_6): δ [ppm] 12.7(s, 1H, OH), 9(s, 1H, HC=N), 7.90-7.40(m, 8H, Ar-H). [13]C-NMR (400MHz, DMSO-d_6): δ [ppm] 164.97(HC=N), 160.21, 151.19, 141.93, 133.89, 132.51, 127.04, 121.79, 119.33, 119.27, 116.68.

***4-(3-Phenyl-propylideneamino)-benzenesulfonamide* III**

FT-IR (cm^{-1}): 3176(C-H aromatic), 1621(HC=N), 1575(C=C aromatic), 3306(N-H str), 1150(S=O asmy), 1330(S=O sym). ^{1}H-NMR (400MHz, DMSO-d_6): δ [ppm] 9.70(d, 1H, HC=N), 8.45-6.6(m, 9H, Ar-H). [13]C-NMR (400MHz, DMSO-d_6): δ [ppm] 164.02(HC=N), 154.30, 145.62, 140.92, 135.12, 129.83, 128.91, 127.95, 127.69, 126, 84, 121.02.

***4-[(2,3-Dihydroxy-benzylidene)-amino]-benzenesulfonamide* IV**

FT-IR (cm^{-1}): 3248(N-H str), 1617(HC=N), 1572(C=C aromatic), 1148(S=O asmy), 1328(S=O sym), 1209(C-O phenolic), 1273(OH). ^{1}H-NMR (400MHz, DMSO-d_6): δ [ppm] 8.55(s, 1H, HC=N), 7.95-7.1(m, 7H, Ar-H). [13]C-NMR (400MHz, DMSO-d_6): δ [ppm] 165.4(HC=N), 150.54(C-OH), 149.1(C-OH), 145.5, 141.53, 127, 121.52, 119.3, 118.9.

***4-{[(Z)-(2-hydroxyphenyl)methylidene]amino}benzenesulfonamide* V**

FT-IR (cm^{-1}): 3246(N-H str), 1618(HC=N), 1156(S=O asym), 1275(S=O sym). ^{1}H-NMR(400MHz,DMSO-d_6): δ [ppm] 12(s,1H,OH), 8.95(s,1H, HC=N), 7.92- 6.92(m,10H,Ar-H), 3.42(s,6H,OCH_3). [13]C-NMR (400MHz, DMSO-d_6): δ [ppm] 164.26(HC=N), 154.29, 151.92, 151.56, 141.82, 127.06, 121.71, 121.25, 119.21, 117.64, 114.54, 55.49(OCH_3).

***4-[(3-Ethoxy-4-hydroxy-benzylidene)-amino]-benzenesulfonamide* VI**

FT-IR (cm^{-1}): 3271(N-H str), 1598(HC=N), 1518(C=C aromatic), 1145(S=O asym), 1330(S=O sym), 1286(C-O phenolic), 1192(OH). ^{1}H-NMR(400MHz,DMSO-d_6): δ [ppm] 9.76(s,2H,SO_2 -NH_2), 8.46(s,1H,HC=N), 7.85-6.6 (m,7H,Ar-H), 5.83(s,3H, OCH_3).

[13]C-NMR (400MHz, DMSO-d_6): δ [ppm] 162.13(HC=N), 154.83, 151.88, 150.91, 145.15, 140.05, 129.93, 127.39, 126.89, 124.55, 121.14, 115.42, 112.38, 111.65, 63.7(OCH_3).

***4-[(2-Hydroxy-naphthalen-1-ylmethylene)-amino]-benzenesulfonamide* VII**

FT-IR (cm^{-1}): 3023(C-H aromatic), 3165(N-H str), 1621(HC=N), 1587(C=C aromatic), 1310(S=O sym), 1292(OH). ^{1}H-NMR (400MHz, DMSO-d_6): δ [ppm] 15.5(s, 1H, NH2), 10.82(s, 1H, HC=N), 9.70-7(m, 10H, Ar-H). [13]C-NMR (400MHz, DMSO-d_6): δ [ppm] 156.38(HC=N), 146.62, 141.34, 137.70, 133.07, 129.07, 128.28, 127.39, 127.16, 126.74, 123.79, 122.17, 120.71, 120.50, 112.37, 108, 74.

***4-{[(E)-(2-methoxy-4-nitrophenyl)methylidene]amino} benzenesulfonamide* VIII**

FT-IR (cm^{-1}): 3289(N-H str), 3029(C-H aromatic), 1620(HC=N), 1579(C=C aromatic), 1258(C-O phenlic), 1334(S=O sym), 1153(S=O asym), 1378(NO_2). ^{1}H-NMR (400MHz, DMSO-d_6): δ [ppm] 8.90(s, 1H, HC=N), 8.25-7.25(m, 7H, Ar-H), 4.05(s, 3H, OCH_3).

[13]C-NMR (400MHz, DMSO-d_6): δ [ppm] 159.41(HC=N), 156.02, 153.86, 141.03, 150.33, 141.73, 128.98, 127.30, 128.16, 126.93, 121.32, 115.59, 107.15, 56.61(OCH_3).

The IR spectra of the synthesized compounds confirmed by the presence of C=N stretching bands at 1500-1690 cm^{-1}, absence of C=O at 1700 cm^{-1} and the bands due to asymmetric and symmetric SO_2 group are shifted to lower frequencies, while NH is disappeared or hidden under the broad bands at 3450-3300cm^{-1} in Schiff's base.

The ^{1}H, [13]C-NMR spectra of the synthesized compounds were recorded in DMSO-d_6. The chemical shifts (δ), expressed in part per million (ppm) downfield form tetamethylsilane. The signals for the methane protons of the azomethine group, **-**N=CH- were observed between 6.90 and 10.82 ppm.

Antimicrobial Part

The antimicrobial activity of all the synthesized compounds (II -VIII) were examined against different Gram-positive (*Staphylococcus aureus)* and Gram-negative (*Escherichia coli*) and fugal strains *Candida albicans* organisms by measuring zone of inhibition (diameter, mm). The antimicrobial activity was performed by Agar diffusion method**.** In accordance with the data obtained from antimicrobial activity. The compounds **IV,V** and **VI** have shown excellent activity against *C. albicans* comparison to the reference compound (Ketoconazole), while compound **VI** has shown similar activity against *S. aurous* as the reference compound Ciprofloxacine. All the synthesized compounds have no shown activity against *E. coli* (table 2).

Table 2: Zone of inhibition (mm) data of synthesized compounds

Compound. No	**Antibacterial activity**		**Antifungal activity**
	S. aurous	***E. coli***	***C. albicans***
II	10	-	20
III	-	-	12
IV	-	20	25
V	-	12	30
VI	27	-	25
VII	25	-	-
VIII	-	-	-
Ciprofloxacin	27	33	-
Ketoconazole	-	-	23

(-) No effect

CONCLUSION

In accordance with the data obtained from antimicrobial activity of the synthesized Schiff bases, some of them have good activity against the tested microbes comparison with ciprofloxacin and ketoconazole as references drugs.

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