Journal of Engineering and Applied Sciences 14 (6): 1760-1764, 2019
ISSN: 1816-949X

Antimicrobial Activity of Some Derivatives of 2-Arylidene-1-Benzosuberone

Nawal H. Al-Bahtiti
Department of Basic Science, University of Applied Science Private, 1193 Amman, Jordan

Abstract: Natural products containing a benzosuberone nucleus are important class of medicinal and pharmaceutical compounds and have recently attracted a considerable amount of attention due to their remarkable broad-spectrum biological activity and antioxidant, anticancer agent. The minimum inhibitory concentration values for a group of 2-arylidene-1-benzosuberone their dibromides and their pyrazolines derivatives were determined for gram-positive and gram negative bacteria and yeast. Some compounds exhibited significant activity against *S. aureus, S. epidermidis* and *B. licheniformis*. The structural activity of these compounds is discussed. We hope in future to study the effect of these compounds on growth and morphology.

Key words: Chalcones, benzosuberones, 2-arylidene-1-benzosuberone, biological activity, compounds, pyrazolines

INTRODUCTION

Different organic compounds can act as antibacterial or antifungal agents. Many chalcones and their derivatives showed a good antimicrobial activity (Alvarez-Builla and Barluenga, 2011; Verma and Saraf, 2008; Azab *et al*., 2013; Al Bahtiti, 2005, 2008, 2007; El-Gohary, 2014; Pati *et al*., 2007; Bahbahani *et al*., 2018; Monostory *et al*., 2003; El-Rayyes and Ramadan, 1987 and El-Salam *et al*., 2017). The benzosuberone unit constitutes the core structure of several natural products such as colchicines, isocolchicine, allocolchicine, theaflavin, bussealin E, demethylsalvicanol and feveline (Fig. 1) where all these natural products are clinically reported as anti-tumor agents (Stretton and Manson, 1973). several synthetic benzosuberones cited in this article exhibited wide range of therapeutic activities such as bacteriostatic, anti-inflammatory, antidepressants and anti-tumor activities (Farghaly *et al*., 2016). The most important example of these chalcones is the 3-indolylidene-acetophenone. The new technology enables the synthesis of alpha-benzosuberone with a benzene ring and seven cyclic ketones a new pharmaceutical and agrochemical intermediate as anticonvulsant and a drug for treating density (Stretton and Manson, 1973). Because of this we decided to study the antibacterial activity of a series of 2-arylidene-1-benzosuberones and their derivatives; Compounds prepared previously were evaluated *in vitro* for their antifungal activity (Al Bahtiti, 2007).

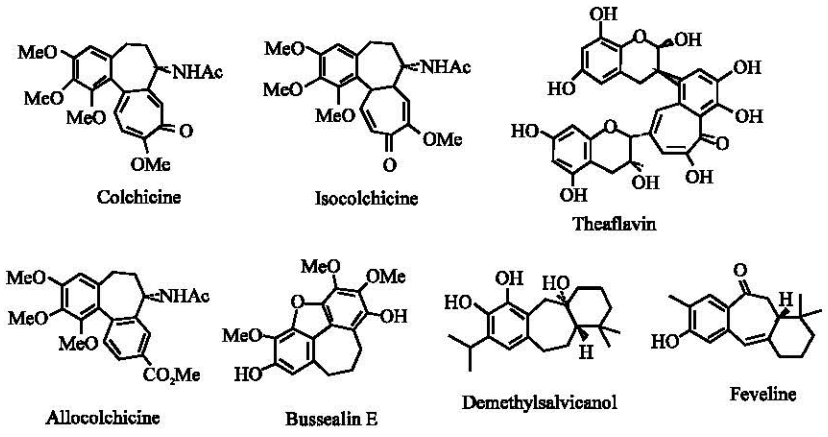

Fig. 1: Some benzosuberone-based natural products

MATERIALS AND METHODS

The organism used in this study for the determination of antimicrobial activity were; *S. epidermidis* (ATCC 12228), *S. aureus* (ATCC25923), *S. faecalis* (ATCC 19433), *S. faecalis* (ATCC 33186), *S. subtilis* (NCIB 3610), *B. licheniformis* (NCIB 1097), *K. pneumoniae* (ATCC 13883), *P. vulgaris* (ATCC 25922), *A. calcoaceticus* (ATCC 19606), *E. colaceticus* (ATCC 13048), *E. aerogenes* (ATCC 23355) and *C. albicans* (Table 1-4).

Chemicals: The starting materials, namely, atetralone, benzosuberone, aryl aldehydes and hydrazine derivatives were obtained from flukaAG, buchs-swiss. 2-arylidene-benzosuberone was prepared from condensation of benzosuberone with corresponding aryl aldehydes in alkaline medium, the pyrazoline were prepared from the condensation of hydrazine and hydrazine deraratives with corresponding 2-arylidene-1-benzosuberone (Al Bahtiti, 2008; Al Bahtiti, 2008).

Table 1: Minimum Inhibitory Concentration (MIC) of chalcones of the general formula Ar^1-CH = CH = CO-3-indolyl

Microorganims	MIC of compounds µg/mL Ar^1				
1-Gram+ve bacteria	C_4H_3O	m-Cl-C_6H_4	p-Cl-C_6H_4	$C_{10}H_7$	C_8H_7
S. epidermidis ATCC 1228	>2000	250	32.5	>2000	250
S. aureus ATCC 25923	>2000	250	65	>2000	250
S. faecalis ATCC 33186	>2000	2000	>2000	>2000	125
S. faecalis ATCC 19433	>2000	2000	32.5	>2000	125
B. subtilis NCIB 3610	>2000	250	2000	>2000	250
2-Gram-ve bacteria					
B. licheniformis NCIB 1097	>2000	2000	250	>2000	250
K. pneumoniae ATCC 13883	>2000	2000	2000	>2000	1000
P. vulgaris ATCC 25922	>2000	1000	2000	>2000	500
S. sonnei ATCC 25931	>2000	500	>2000	>2000	1000
P. aeroginose ATCC 27853	>2000	2000	>2000	>2000	250
Yeast					
C. albicans	>2000	2000	>2000	>2000	>2000

Table 2: Minimum Inhibitory Concentration (MIC) of chalconesdibromides (XIII)

Microorganims	MIC of compounds (µg/mL)				
1-Gram+ve bacteria	IIa	IIk	III	IIm	XIIIo
S. epidermidis ATCC 1228	>2000	2000	2000	2000	500
S. aureus ATCC 25923	>2000	2000	2000	1000	65
S. faecalis ATCC 19433	2000	2000	2000	2000	500
B. subtilis NCIB 3610	2000	2000	2000	2000	65
2-Gram-ve bacteria					
B. licheniformis NCIB 1097	2000	1000	250	>2000	250
K. pneumoniae ATCC 13883	2000	2000	2000	>2000	1000
P. vulgaris ATCC 25922	2000	1000	2000	>2000	500
S. sonnei ATCC 25931	2000	2000	>2000	>2000	1000
P. aeroginose ATCC 27853	2000	2000	>2000	>2000	250
Yeast					
C. albicans	2000	2000	>2000	>2000	>2000

Table 3: Minimum Inhibitory Concentration (MIC) of pyrazolines (5,6) and pyrazoles (9 and 10)

Microorganims	MIC of compounds (µg/mL)				
1-Gram+ve bacteria	IXf	IXj	Vf	VIb	Xb
S. epidermidis ATCC 1228	125	500	2000	2000	960
S. aureus ATCC 25923	2000	250	2000	1000	65
S. faecalis ATCC 19433	32.5	2000	2000	2000	250
B. subtilis NCIB 3610	125	2000	2000	2000	250
2-Gram-ve bacteria					
B. licheniformis NCIB 1097	32.5	250	2000	>2000	250
A. colaceticus ATCC 19606	65	500	500	65	125
E. colaceticus ATCC 13048	2000	250	2000	2000	125
S. marescens ATCC 8100	2000	2000	2000	2000	500
P. aeroginose ATCC 27853	2000	2000	2000	500	1000
Yeast					
C. albicans	2000	2000	>2000	>2000	>2000

The compounds were tested for their antimicrobial testing *in vitro* by the agar dilution techniques. All compounds were dissolved in DMSO for their antibacterial test solutions were sterilized by membrane filtration. Aliquots of compounds were diluted with melted typtic soya or agar, tryptone, soytone, sodiumchloride, agar for bacteria or saturateddextrose agar for yeast to give concentration of 2000, 1500.1000, 500.250.125, 62.5 and 31.3 ug/mL. The MIC values were noted after 24 h at 37°C.

Table 4: Key of compounds (Table 2 and 3)

Compounds	Ar
I-XV a	p-OCH_3-C_6H_4
I-XV b	p-NO_2-C_6H_4
I-XV f	1-naphthyl
I-XV j	C_5H_4N (3-pyridyl)
I-XV k	C_5H_7N (1-methylpyrrolyl)
I-XV l	C_8H_7 (3-indolyl)
I-XV m	2,6-$Cl_2C_6H_4$
I-XV o	$C_7H_6O_2$ (3 and 4-methylene-dioxy phenyl)

RESULTS AND DISCUSSION

Antimicrobial activity screening tests were carried out for chalcones-2-arylidene1-benzosuberone-dibromides and derivatives. Chalcones derived from 3-indolyllidene-acetophenone showed biological activity against Gram-positive bacteria more than Gram-negative bacteria or yeast (Table 1 and Fig. 2). The maximum inhibitory activity was shown by 3-indolylidene-(p-chloroacetophenone), i.e., 32.5 µg/mL of it against *Streptococcus faecalis* (ATCC, 19433) and (12228). This compound showed slight activity against *S aureus* ATCC (25923). Other substituted compounds derived from 3-indolyidene-acetophenone did not exibit any microbiological activity. On the other hand, 2-arylidene-1-benzosuberone did not show any biological activity against *S. epidermidts, S. faecalis* and *B. licheniformis*. It can be concluded at this respect that

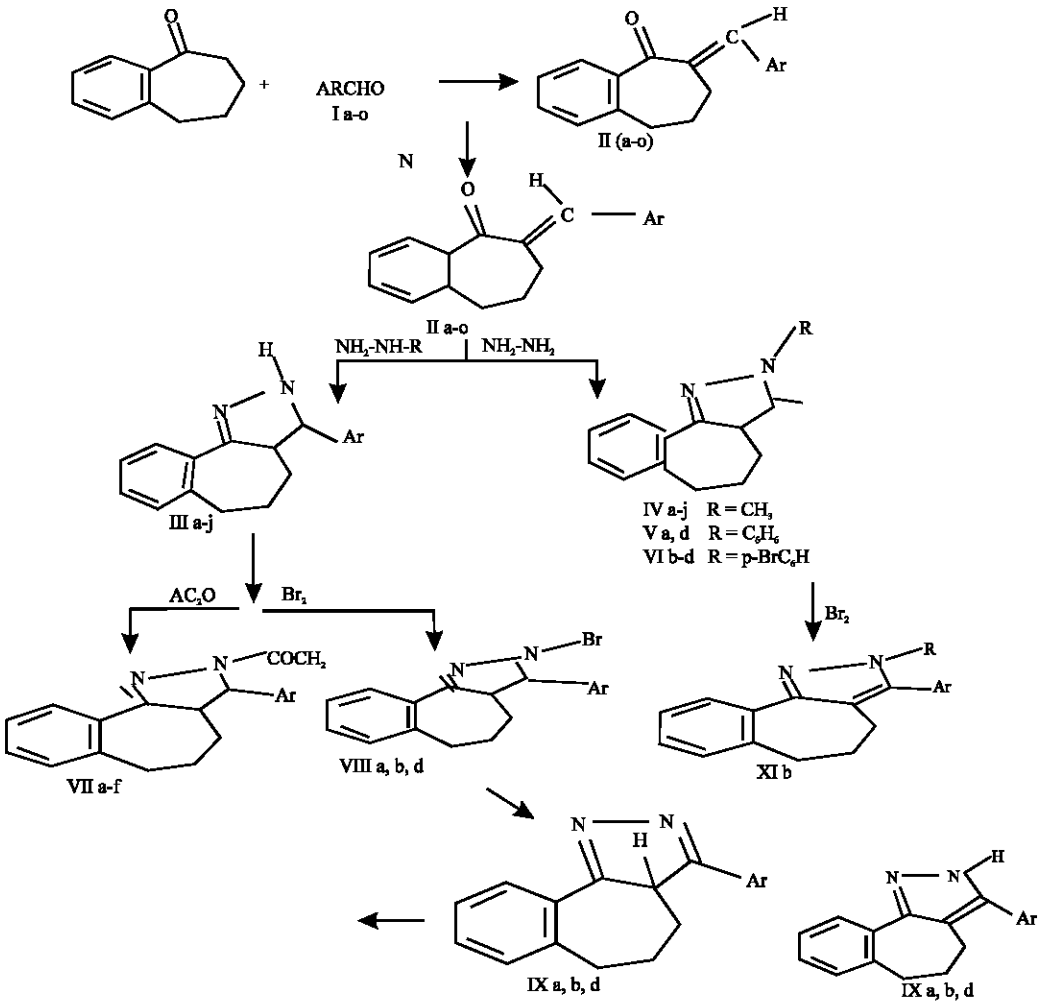

Fig. 2: Synthesis routes to the pyrazolines and pyrazoles compounds

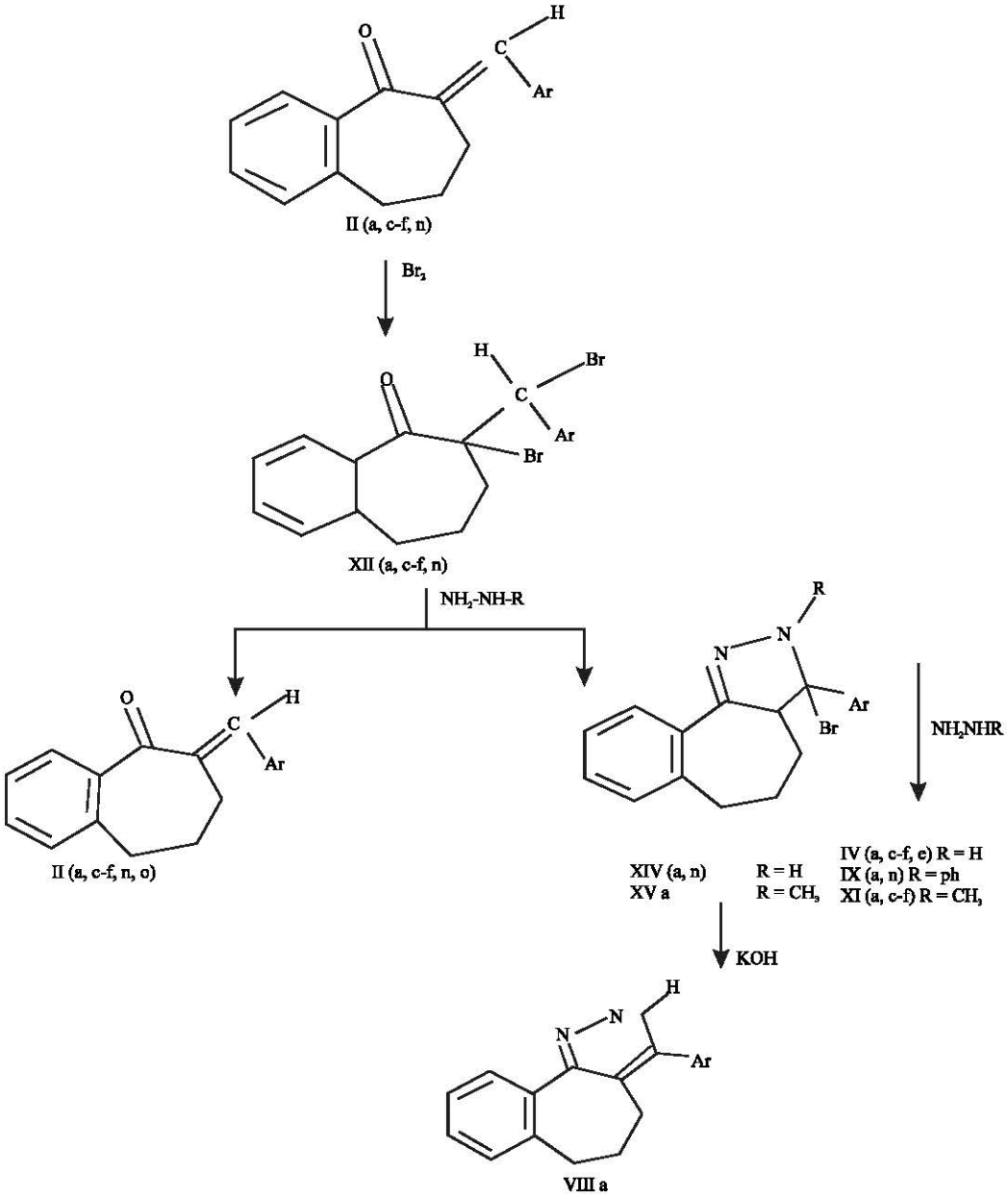

Fig. 3: Synthis routes to the pyrazolines from dibromo-2-arylidene-1-benzosuberone

the bromine enhances the antibacterial activity shown by the en-one function in the chalcone (Table 2) (Fig. 2 and 3).

The pyrazolines derived from chalcones 4-8 were screened for their microbiological activity and their MIC values showed significant activity against *S. aureus, S. epidermidis, D. faecalism, B. subtilis* and *B. licheniformis* molecular modifications of 2-arylidene-1-indanones leading toincreased cytotoxic potencies (Farghaly *et al*., 2012). It was also shown that the pyrazole (Xb) has an activity against *S aureus* two times higher than against *B. lichiniformis,* creating another double bond in the system and 4-nitrophenyl substitueted group in pyrazole (Xb) may help in inhibitory effect shown (Table 3).

CONCLUSION

In general we can say that compounds (2-10) having active sites as en-one, imine and amine group, show biological activity against microorganisms. Other studies are needed to predict their effect on the inhibition of

growth of microorganisms. We think that such compounds may inhibit the bacterial cell membrane and reduce the uptake of glucose which leads to a less or none cellular acid production. A similar observation has been made by Stretton and Manson (1973) for bronopol (Turek *et al*., 2017).

ACKNOWLEDGEMENTS

The researcher acknowledges Applied Science Private University, Amman, Jordan for the fully financial support granted of this research article. Sincere thanks to all my colleagues at basic science department for creating inspiring conditions for researchers.

REFERENCES

Al Bahtiti, H., 2008. Biological activity of alcoholic extract of Jordanian Propolis Nawal. Arabian J. Chem., 1: 333-336.

Al Bahtiti, N., 2005. Antimicrobial activity of some heterocyclic derivatives of chalcones. Jordan J. Appl. Sci. Nat., 7: 51-57.

Al-Bahtiti, N.H., 2007. Synthesis, characterization and antibacterial activity of some 5-aryl-1, 3-Diphenyl 1-4, 5-dihydro-1H-Pyrazoles. Arab Gulf J. Sci. Res., 25: 1-5.

Alvarez-Builla, J. and J. Barluenga, 2011. An introduction of medical heterocyclic compounds. J. Heterocycl. Compd. Chem., 1: 1-9.

Azab, M.E., M.M. Youssef and E.A. El-Bordany, 2013. Synthesis and antibacterial evaluation of novel heterocyclic compounds containing a sulfonamido moiety. Mol., 18: 832-844.

Behbehani, H., K.M. Dawood and T.A. Farghaly, 2018. Biological evaluation of benzosuberones. Expert Opin. Ther. Pat., 28: 5-29.

El-Gohary, N.S., 2014. Arylidene derivatives as synthons in heterocyclic synthesis. Open Access Library J., 1: 1-47.

El-Salam, O.I.A., A.S. Alsayed, K.A. Ali, A.A.A. Elwahab and A.E.G.E. Amr, *et al*., 2017. Antimicrobial activities of some newly synthesized substituted Benzosuberone and its related derivatives. Biomed. Res., 28: 157-163.

El-Rayyes, N.R. and H.M. Ramadan, 1987. Heterocycles part X. synthesis of new pyrimidine systems. J. Heterocycl. Chem., 24: 589-596.

Farghaly, T.A., M.A. Abdallah and M.R. Abdel Aziz, 2012. Synthesis and antimicrobial activity of some new 1,3,4-Thiadiazole derivatives. Molecules, 17: 14625-14636.

Farghaly, T.A., S.M. Gomha, K.M. Dawood and M.R. Shaaban, 2016. Synthetic routes to benzosuberone-based fused-and spiro-heterocyclic ring systems. RSC. Adv., 6: 17955-17979.

Monostory, K., V. Tamasi, L. Vereczkey and P. Perjesi, 2003. A study on CYP1A inhibitory action of E-2-(4-methoxybenzylidene)-1-benzosuberone and some related chalcones and cyclic chalcone analogues. Toxicol., 184: 203-210.

Pati, H.N., U. Das, E.D. Clercq, J. Balzarini and J.R. Dimmock, 2007. Molecular modifications of 2-arylidene-1-indanones leading to increased cytotoxic potencies. J. Enzyme Inhib. Med. Chem., 22: 37-42.

Stretton, R.J. and T.W. Manson, 1973. Some aspects of the mode of action of the antibacterial compound bronopol (2-bromo-2-nitropropan-1, 3-diol). J. Appl. Bacteriol., 36: 61-76.

Turek, M., D. Szczesna, M. Koprowski and P. Balczewski, 2017. Synthesis of 1-indanones with a broad range of biological activity. Beilstein J. Org. Chem., 13: 451-494.

Verma, A. and S.K. Saraf, 2008. 4-Thiazolidinone-A biologically active scaffold. Eur. J. med. Chem., 43: 897-905.