Acta Pharmaceutica Sciencia
52: 505-510 (2010)

Synthesis and *in vitro* antimicrobial activity of some novel chalcones containing 5-phenyl tetrazole

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Abstract

5-phenyl 1-acetyl tetrazole were allowed to react separately with different aromatic aldehydes in presence of alkaline medium to yield corresponding 5-phenyl tetrazole 1- substituted chalcones. The compounds were identified by spectral data and screened evaluated for *in vitro* antimicrobial and antifungal activity.

Keywords: 5-phenyl tetrazole, chalcone, anti-microbial activity

Introduction

Tetrazole, an heterocyclic compound, possess various biological activities like antibacterial (Mulwad et al. 2008), antifungal (Upadhaya et al. 2004, Rajasekaran et al. 2006), analgesic (Bachar and Lahiri 2004), anti-inflammatory (Ray et al. 1990), antitubercular activity (Adamec et al. 2005), antinociceptive (Rajsekaran et al. 2005). Chalcones are products of condensation of simple or substituted aromatic with simple or substituted acetophenones in presence of alkali (Felipe et al. 1998). Chalcone constitute an impartment group of natural products and some of them possess a wide range of biological activities such as antimicrobial (Prasad et al. 2008), anticancer (Jevwon et al. 2005), antitubercular (Shivakumar et al. 2005), antiviral (Churkin et al. 1982) and anti-inflammatory activity (Herencia et al. 1998) etc. Walton et al. (1945) during their chemical studies in the structure of clavicin found that a structural feature which was responsible for antibacterial activity in clavicin was α, β unsaturated keto functional group which is similar to the structure of chalcones. The diverse biological properties of chalcones have prompted us to synthesize them in order to study their antimicrobial activity (Vogel et al. 2000 and 2002). The present work deals with the reaction of 5-phenyl tetrazole (1) with acetic anhydride to yield 5-phenyl 1-acetyl tetrazole (2) which on further reaction with different aromatic aldehydes to form chalcones (3a-h) and the structure of all the various synthesized compounds were assigned on the basis of elemental analysis, IR and ^{1}H NMR spectral data. These compounds were screened for their antimicrobial activity.

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Materials and Methods

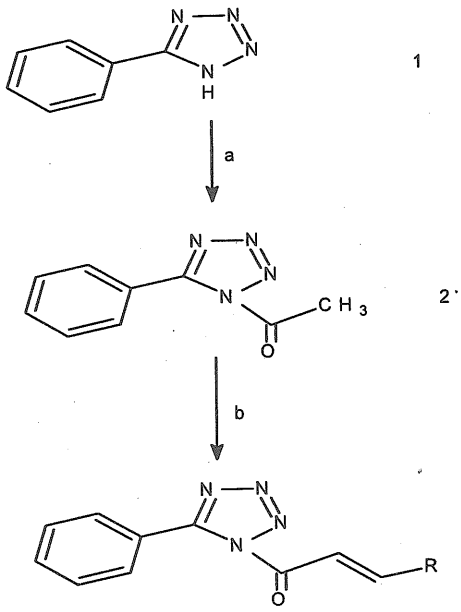
Melting points were determined with open capillary. FTIR spectra were recorded on a Shimadzu FT-IR model 8010 spectrophotometer. ^{1}H NMR spectra were recorded in DMSO on a Varian mercury FT-NMR model YH- 300 instrument using TMS as internal standard.

Synthesis of 5-phenyl 1-acetyl tetrazole

A solution of 5-phenyl tetrazole (12.8g, 0.08 moles) and acetic anhydride (0.08 moles) and 2-3 drops of concentrated sulphuric acid was warmed for 15-20 min on water bath. It was cooled and poured into ice cold water. The product separated was filtered and dried. It was further purified by crystallization from ethanol.

General procedure for the preparation of 3-aryl-1-(5-phenyl-1H-tetrazol-1-yl) prop-2-en-1-one (chalcones) (3a-j)

A solution of 5-phenyl 1-acetyl tetrazole (85g, 0.005 moles) and aromatic aldehydes (0.005 moles) in ethanol (12 mL) was cooled to 5 to 10°C in an ice bath. The cooled solution was treated with dropwise addition of aqueous sodium hydroxide (2.5, 50%). The resulting reaction mixture was magnetically stirred for 30 min and then left over night. The resulting dark solution was diluted with ice water and carefully acidified using diluted hydrochloric acid. The tetrazole analogue of chalcone crystallized out and was collected by filtration after washing with sodium bicarbonate and water. It was further purified by crystallization from ethanol.



a. $(CH_3CO)_2O$/GAA; **b.** R-CHO/NaOH

Figure 1. Synthesis of Chalcones

Table 1. Physical data of compounds

Comp no	R	Mole. Formula	MW	% Yield	M.P.^{0}C	Rf.	Found (Calcd) %		
							C	H	N
3a	C_6H_5	$C_{16}H_{12}N_40$	276	72	198	0.67	69.58 (69.55)	4.40 (4.38)	2.30 (20.28)
3b	2-Cl-C_6H_5	$C_{16}H_{11}ClN_40$	310	66	222	0.68	61.90 (61.84)	3.59 (3.57)	17.99 (18.03)
3c	4-Cl-C_6H_5	$C_{16}H_{11}ClN_40$	310	66	224	0.68	61.90 (61.84)	3.59 (3.57)	17.99 (18.03)
3d	4- Br -C_6H_5	$C_{16}H_{11}BrN_40$	355	72	248	0.72	54.01 (54.10)	3.08 (3.12)	15.75 (15.77)
3e	4-OCH3-C_6H_5	$C_{17}H_{14}N_40_2$	306	64	235	0.77	66.56 (66.66)	4.62 (4.61)	18.30 (18.29)
3f	2-NO2-C_6H_5	$C_{16}H_{11}N_50_3$	321	59	252	0.71	59.91 (59.81)	3.48 (3.45)	21.85 (21.80)
3g	4-NO2-C_6H_5	$C_{16}H_{11}N_50_3$	321	59	250	0.69	59.91 (59.81)	.48 (3.45)	21.85 (21.80)
3h	4-(CH3)N-C_6H_5	$C_{18}H_{17}N_50$	319	60	230	0.65	67.73 (67.70)	5.30 (5.37)	21.85 (21.80)
3i	4-CH3-C_6H_5	$C_{17}H_{14}N_40$	290	54	218	0.81	70.25 (70.33)	4.80 (4.86)	19.38 (19.30)
3j		$C_{14}H_{10}N_40_2$	266	70	188	0.62	65.10 (63.15)	3.82 (3.79)	21.10 (21.04)

IR (KBr δ cm–1) and 1H NMR (DMSO, ö ppm)

3a: 3-phenyl -1-(5-phenyl-1*H*-tetrazol-1-yl) prop-2-en-1-one

FT-IR:,1285(N-N=N-),1108 and 1138(Tetrazole ring) ,1735(C=O), 1630(C=C), 3054(Ar-CH).

^{1}H NMR:6.61(1H,d,-CO-CH=),7.05(1H,d,=CH-Ar), 7.14-7.80 (10H, m, Ar-H).

3b: 3-(2-chlorophenyl)-1-(5-phenyl-1*H*-tetrazol-1-yl) prop-2-en-1-one

FT-IR: 1285(N-N=N-),1108 and 1138(Tetrazole ring) ,1733(C=O), 1627(C=C), 3052(Ar-CH), 785(C-Cl).

^{1}H NMR: 6.62(1H,d,-CO-CH=),7.06(1H,d,=CH-Ar), 7.14-7.75 (9H, m, Ar-H).

3c: 3-(4-chlorophenyl)-1-(5-phenyl-1*H*-tetrazol-1-yl) prop-2-en-1-one

FT-IR: 1284(N-N=N-),1108 and 1138(Tetrazole ring) ,1734(C=O), 1632(C=C), 3050(Ar-CH), 785(C-Cl).

^{1}H NMR: 6.63(1H,d,-CO-CH=),7.06(1H,d,=CH-Ar), 7.14-7.80 (9H, m, Ar-H).

3d: 3-(4-bromophenyl)-1-(5-phenyl-1*H*-tetrazol-1-yl) prop-2-en-1-one

FT-IR: 1283(N-N=N-),1108 and 1138(Tetrazole ring) ,1735(C=O), 1630(C=C), 3055(Ar-CH), 652(C-Br),

^{1}H NMR: 6.5(1H,d,-CO-CH=),7.03(1H,d,=CH-Ar), 7.14-7.81 (9H, m, Ar-H).

3e: 3-(4-methoxyphenyl) -1-(5-phenyl-1*H*-tetrazol-1-yl) prop-2-en-1-one

FT-IR: 1285(N-N=N-),1108 and 1138(Tetrazole ring) ,1736(C=O), 1635(C=C),

3058(Ar-CH),1251(-OCH3)

^{1}H NMR: 6.58(1H,d,-CO-CH=),7.02(1H,d,=CH-Ar), 7.14-7.75 (9H, m, Ar-H).

3f: 3-(2-nitrophenyl)-1-(5-phenyl-1*H*-tetrazol-1-yl) prop-2-en-1-one

FT-IR: 1285(N-N=N-),1108 and 1138(Tetrazole ring) ,1734(C=O), 1630(C=C),

3055(Ar-CH), 1578(-NO2).

^{1}H NMR: 6.60(1H,d,-CO-CH=),7.01(1H,d,=CH-Ar), 7.14-7.68 (9H, m, Ar-H).

3g: 3-(4-nitrophenyl)-1-(5-phenyl-1*H*-tetrazol-1-yl) prop-2-en-1-one

FT-IR: 1285(N-N=N-),1108 and 1138(Tetrazole ring) ,1735(C=O), 1630(C=C),

3054(Ar-CH).,1578(-NO2).

^{1}H NMR: 6.61(1H,d,-CO-CH=),7.01(1H,d,=CH-Ar), 7.14-7.70 (9H, m, Ar-H).

3h: 3-(4-dimethylaminophenyl)-1-(5-phenyl-1*H*-tetrazol-1-yl) prop-2-en-1-one

FT-IR: 1285(N-N=N-),1108 and 1138(Tetrazole ring) ,1735(C=O), 1630(C=C),

3054(Ar-CH),1321(-N(CH3)2.

^{1}H NMR: 2.9(6H,d,CH_3)6.63(1H,d,-CO-CH=),7.03(1H,d,=CH-Ar), 7.14-7.50 (9H, m, Ar-H).

3i: 3-(4-methylphenyl)-1-(5-phenyl-1*H*-tetrazol-1-yl) prop-2-en-1-one

FT-IR: 1285(N-N=N-),1108 and 1138(Tetrazole ring) ,1733(C=O), 1630(C=C),

3054(Ar-CH),1365(CH3).

^{1}H NMR: 3.72(3H,CH3)6.62(1H,d,-CO-CH=),7.02(1H,d,=CH-Ar), 7.14-7.50 (9H, m, Ar-H).

3j: 3-(furan-2yl) -1-(5-phenyl-1*H*-tetrazol-1-yl) prop-2-en-1-one

FT-IR: 1285(N-N=N-),1108 and 1138(Tetrazole ring) ,1734(C=O), 1630(C=C),3077(Furan)

^{1}H NMR: 6.60(1H,d,-CO-CH=),7.01(1H,d,=CH-Ar),6.25-7.40(3H,m,Furyl)

Antimicrobial Activity

Table 2. Antibacterial and Antifungal data of chalcones

Compound	Zone of inhibition in mm							
	Staphylococcus aureus		*Escherichia coli*		*Candida albicans*		*Aspergillus niger*	
	50 µg	100 µg	50 µg	100 µg	50 µg	100 µg	50 µg	100 µg
3a	12	15	09	12	12	15	10	12
3b	14	15	14	13	17	20	15	16
3c	15	16	14	15	18	20	13	15
3d	12	14	10	12	16	18	11	13
3e	11	14	08	10	19	22	20	22
3f	12	15	08	11	12	15	08	11
3g	13	15	10	11	13	15	10	12
3h	12	13	10	12	15	17	09	11
3i	13	17	09	13	12	14	11	12
3j	10	11	11	12	10	13	11	13
Ciprofloxacin	19	24	20	24	-	-	-	-
Griseofulvin	-	-	-	-	21	24	21	24

All the newly synthesized compounds were screened for antimicrobial activity against both gram positive *S. aureus* and gram negative *E. coli* bacteria and antifungal activity against *C. albicans* and *A. niger* according to cup plate method (Vagdevi et al. 2006) at a concentration 50 µg and 100 µg, respectively. Streptomycin and Griseofulvin (William. et al 2000) were used as standard for comparison of antibacterial and antifungal activity (Indian Pharmacopoeia 1996, Kumar 1996). Dimethyl sulphoxide (DMSO) was used as control. The results of screening are given in Table 2.

Results and Discussion

From the results of antibacterial screening, it is evident that most of the compounds are very weakly active and few are moderately active against *S. aureus* and *E. coli* but compounds 3b, 3c and 3i possess very good activity against *S. aureus* and *E. coli* at concentration of 100µg. Similarly from the results of antifungal screening, it is evident that the compounds 3b, 3c and 3e possess very good activity against fungi *Candida albicans* and *Aspergillus niger* and compound 3d showed moderate activity all bacteria and fungi tested.

Acknowledgments

We are highly thankful to Principal M.E.S. College Pharmacy, Sonai and Prashant Patil Gadakh , Secreatary ,Mula Education Society for providing excellent research facilities

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Received: 21.12.2009
Accepted: 02.03.2010