December 2007 *Volume 3 Issue 4*

Trade Science Inc.

Organic CHEMISTRY

An Indian Journal

Full Paper

OCAIJ, 3(4), 2007 [220-223]

Synthesis and antibacterial activity of some α,β-unsaturated aromatic ketones and their derivatives

Kishor Kapadia, Pankit Solankee, Yogesh Prajapati, Hiral Patel, Sejal Solankee, Anjani Solankee*

Department of Chemistry, B.K.M. Science College, Valsad-396001, (INDIA)

E-mail: dranjani_solankee@yahoo.com

Received: 8th December, 2007 ; Accepted: 13th December, 2007

ABSTRACT

Chalcones, 2,4-bis-(phenylamino)-6-[4'-{3''-(phenyl / substituted phenyl)-2''-propenon-1''-yl} phenylamino]-*s*-triazines **(6a-e)** have been prepared from ketone **(5)** based on *s*-triazine nucleus. These chalcones **(6a-e)** on cyclisation with hydrazine hydrate in presence of glacial acetic acid and malononitrile in presence of ammonium acetate give the corresponding pyrazolines **(7a-e)** and cyanopyridines **(8a-e)** respectively. All the synthesized compounds have been screened for their antibacterial activity. The constitutions of newly synthesized compounds have been established on the basis of their elemental analysis, IR and ^{1}H NMR spectral data.

KEYWORDS

Chalcones;
Acetylpyrazolines;
Cyanopyridines.

INTRODUCTION

The chemistry of heterocycles that have been explored for developing pharmaceutically important molecules such as chalcones, pyrazolines and cyanopyridines have played a vital role in medicinal chemistry. The presence of reactive α,β-unsaturated keto function in chalcone is found to be responsible for their antifungal[1] and antibacterial[2] activities. Pyrazolines and cyanopyridines play an important role owing to their variety of therapeutic activities. Pyrazolines are reported to exhibit analgesic[3], antiviral[4], anticancer[5], antifungal[6], antibacterial[7], anti-inflammatory[8] and antitubercular[9] activities. It has been reported that introduction of acetyl group at 1-position enhances the molluscicidal[10] activity as well as increase the stability of pyrazolines. Cyanopyridines are well-known for their various biological activities such as anticancer, antifungal[11], antibacterial[12] and antitubercular[13] etc....

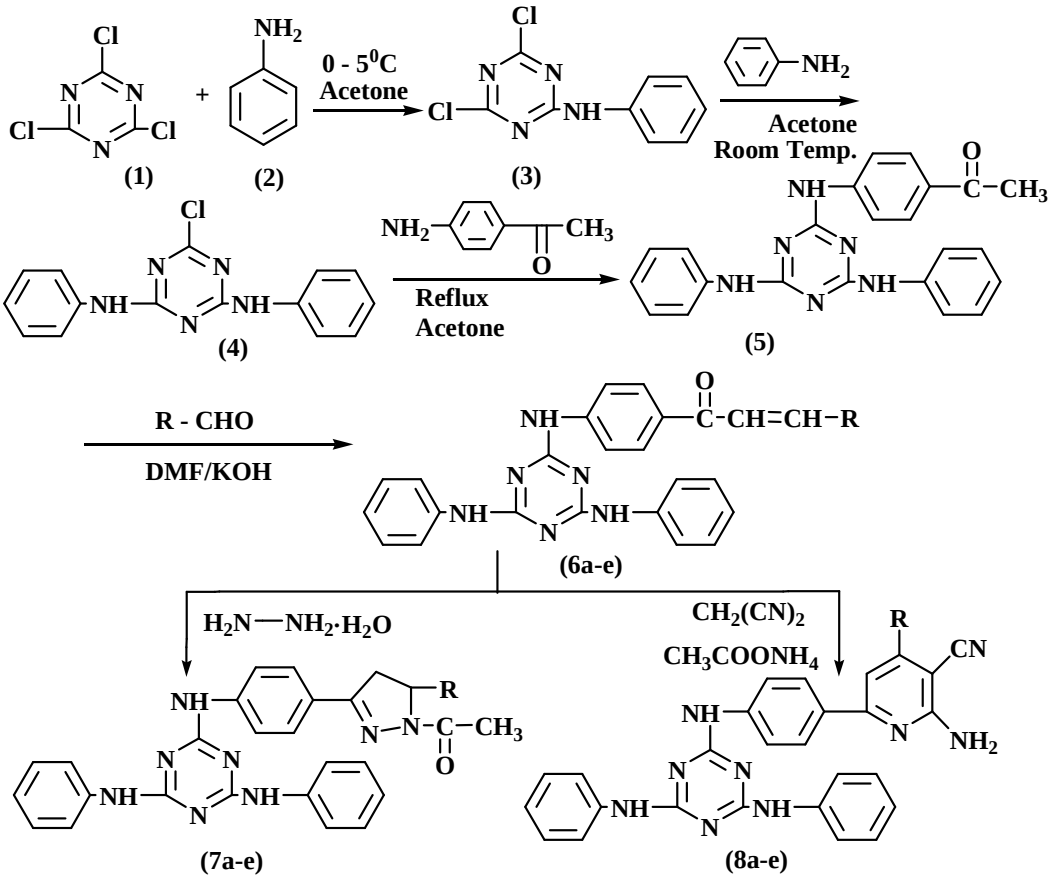
In the present communication, we report the reaction of 2,4-bis-(phenylamino)-6-(4'-acetylphenylamino) -s-triazine **(5)** with aromatic and different substituted aromatic aldehydes to form chalcones **(6a-e)**. Compound **(5)** is prepared by the condensation of cyanuric chloride and aniline at 0-5 ºC to form **(3)**, which further reacts with aniline at room temperature to form **(4)** which is treated with 4-aminoacetophenone to form compound **(5)**. Chalcones **(6a-e)** are cyclised with hydrazine hydrate in presence of glacial acetic acid and malononitrile in presence of ammonium acetate to form pyrazolines **(7a-e)** and cyanopyridines **(8a-e)** respectively (SCHEME).

Antibacterial activity

All the synthesized compounds were screened for

TABLE 1 : Physical and analytical data of compounds (6a-e), (7a-e) and (8a-e)

No.	R	M.P. (°C)	Yield (%)	Molecular formula	Elemental analysis found/(calcd.)%		
					C	H	N
6a	Phenyl	105	78	$C_{30}H_{24}N_6O$	74.34(74.38)	4.93(4.96)	17.39(17.36)
6b	2-Chlorophenyl	132	82	$C_{30}H_{23}N_6OCl$	69.44(69.43)	4.47(4.44)	16.19 (16.20)
6c	3-Chlorophenyl	116	76	$C_{30}H_{23}N_6OCl$	69.42(69.43)	4.46(4.44)	16.23 (16.20)
6d	2-Nitrophenyl	135	70	$C_{30}H_{23}N_7O_3$	68.07(68.05)	4.37(4.35)	18.54 (18.53)
6e	2-Methoxyphenyl	138	68	$C_{31}H_{26}N_6O_2$	72.38(72.37)	5.03(5.06)	16.35 (16.34)
7a	Phenyl	210	64	$C_{32}H_{28}N_8O$	71.09(71.11)	5.20(5.19)	20.75 (20.74)
7b	2-Chlorophenyl	219	67	$C_{32}H_{27}N_8OCl$	66.86(66.84)	4.71(4.70)	19.47 (19.50)
7c	3-Chlorophenyl	184	58	$C_{32}H_{27}N_8OCl$	66.81(66.84)	4.72(4.70)	19.52 (19.50)
7d	2-Nitrophenyl	146	62	$C_{32}H_{27}N_9O_3$	65.53(65.54)	4.60(4.62)	21.52 (21.54)
7e	2-Methoxyphenyl	159	64	$C_{33}H_{30}N_8O_2$	69.45(69.47)	5.24(5.26)	19.67 (19.65)
8a	Phenyl	80	68	$C_{33}H_{25}N_9$	72.37(72.39)	4.55(4.57)	23.01 (23.03)
8b	2-Chlorophenyl	116	61	$C_{33}H_{24}N_9Cl$	68.09(68.10)	4.16(4.13)	21.65 (21.67)
8c	3-Chlorophenyl	127	59	$C_{33}H_{24}N_9Cl$	68.13(68.10)	4.15(4.13)	21.69 (21.67)
8d	2-Nitrophenyl	162	58	$C_{33}H_{24}N_{10}O_2$	66.91(66.89)	4.06(4.05)	23.68 (23.65)
8e	2-Methoxyphenyl	145	66	$C_{34}H_{27}N_9O$	70.73(70.71)	4.70(4.68)	21.83 (21.84)



SCHEME

their antibacterial activity by using agar diffusion method[14] against *S.aureus* (MTCC 96), *B.subtilis* (MTCC 441) Gram positive and *E.coli*(MTCC 443), *S.paratyphi-B*(MTCC 733) Gram negative bacteria in nutrient agar medium. The sterilized agar media[2.4 %(w/v) agar-agar, 5%(w/v) NaCl, 3%(w/v) peptone, pH(6.8 to 7.0)] was poured into Petri dishes and allowed to solidify. On the surface of the media microbial suspension was spread over the agar plates to solidify. A stainless steel cylinder(pre-sterilized) was used to bore the cavities. All the synthesized compounds (100µg/ml) in DMF were placed serially in the cavities with the

Full Paper

TABLE 2: Antibacterial activity of compounds (6a-e), (7a-e) and (8a-e)

Comp. no.	R	Antibacterial activity Zone of Inhibition in mm			
		S.aureus (MTCC 96)	*B.subtilis* (MTCC 441)	*E.coli*(MTCC 443)	*S.aratyphi*-(MTCC733)
6a	Phenyl	10	15	12	14
6b	2-Chlorophenyl	10	17	18	10
6c	3-Chlorophenyl	11	20	14	11
6d	2-Nitrophenyl	10	14	16	19
6e	2-Methoxyphenyl	11	13	15	17
7a	Phenyl	10	-	-	-
7b	2-Chlorophenyl	11	-	12	10
7c	3-Chlorophenyl	10	-	10	10
7d	2-Nitrophenyl	13	13	16	20
7e	2-Methoxyphenyl	10	10	10	23
8a	Phenyl	13	10	-	-
8b	2-Chlorophenyl	-	12	-	-
8c	3-Chlorophenyl	10	-	14	-
8d	2-Nitrophenyl	15	11	16	22
8e	2-Methoxyphenyl	-	12	11	24
Standard drug	Ciprofloxacin	22	20	24	25

help of micropipette. It is then allowed to diffuse for 10 minutes in refrigerator. The plates were incubated at 37°C for 24 hours. After incubation the diameter of zone of inhibition was measured in mm. Under similar conditions controlled experiment was carried out by using Ciprofloxacin as standard drug for comparison. All the antibacterial data are represented in TABLE 2

EXPERIMENTAL

All the melting points were determined in an open capillary and are uncorrected. The IR spectra were recorded on Perkin-Elmer 237 spectrophotometer. ^{1}H NMR spectra on a Bruker Avance DPX 300MHz spectrometer with $CDCl_3$ as a solvent, using TMS as internal reference. Purity of the compounds were checked on TLC using silica gel-G. Elemental analysis was performed on Carlo Erba-1108 analyzer.

Preparation of 2-phenylamino-4,6-dichloro-s-triazine[15,16] (3)

Aniline(0.01mole) was added slowly to cyanuric chloride(0.01mole) in acetone (30ml) with constant stirring for 4 hours at 0 to 5°C. Then sodium carbonate (0.005mole) dissolved in water(10ml) was added dropwise to neutralize HCl evolved during the reaction. Finally the contents were poured into crushed ice. The solid separated out was filtered, washed with water, dried and recrystallized from alcohol to give (3).
Yield 86%; m.p. 196°C.

Preparation of 2,4-bis-(phenylamino)-6-chloro-s-triazine (4)

Aniline(0.01mole) was added slowly to compound **(3)** (0.01mole) in acetone(35ml) with constant stirring for 6 hours at room temperature. Then sodium carbonate (0.005mole) dissolved in water (10ml) was added dropwise to neutralize HCl evolved during the reaction. Finally the contents were poured into crushed ice. The solid separated out was filtered, washed with water, dried and recrystallized from alcohol to give (4).
Yield 80%; m.p. 179°C; IR(KBr) cm^{-1} : 772(C-Cl), 1359(C-N), 805(C-N, *s*-triazine); ^{1}H NMR($CDCl_3$) δ ppm : 7.20 to 7.80(m, 10 Ar-H and 2 NH).

Preparation of 2,4-bis-(phenylamino)-6-(4'-acetyl phenylamino)-s-triazine (5)

4-Aminoacetophenone(0.01mole) and compound **(4)** (0.01mole) were dissolved in acetone (40ml). The reaction mixture was refluxed for 6 hours, cooled and poured into crushed ice. Then sodium carbonate (0.005) dissolved in water(10ml) was added to neutralize HCl evolved during the reaction. The solid separated out was filtered, washed with water, dried and recrystallized from alcohol to give **(5)**.
Yield 75%; m.p. 218°C; IR (KBr)cm^{-1} : 1662(C=O), 1355(C-N), 805(C-N, *s*-triazine); ^{1}H NMR($CDCl_3$) δ ppm : 2.6 (s, 3H, -$COCH_3$), 7.0 to 7.95(m, 14 Ar-H and 3 NH).

Preparation of 2,4-bis-(phenylamino)-6-[4'-{3''-(2'''-methoxyphenyl)-2''-propenon-1''-yl}-phenyl amino]-s-triazine (6e)

Compound **(5)** (0.01mole) was dissolved in DMF

(30ml) and 2-methoxy benzaldehyde (0.01 mole) was added to it. Then solution of KOH (5ml of 40%) was added to the reaction mixture with constant stirring at room temperature. After 24 hours the reaction mixture was poured into crushed ice and neutralize with HCl. The product separated out was filtered, washed with water, dried and recrystallized from alcohol to give (6e). Yield 68%; m.p. 138°C; IR(KBr)cm^{-1}: 1647 (C=O), 1595(-CH=CH-, str.), 1340(C-N), 812(C-N, *s*-triazine); ^{1}H NMR ($CDCl_3$) δppm : 3.85(s, 3H, $-OCH_3$), 6.90(d, lH, -CO-CH=), 7.15 to 7.80(m, 18 Ar-H and 3NH), 8.05(d, 1H, Ar-CH=). Anal. Calcd for $C_{31}H_{26}N_6O_2$: C, 72.37; H, 5.06; N, 16.34. Found: C, 72.38; H, 5.03; N, 16.35.

Similarly the remaining compounds**(6a-d)** were prepared by this method. Their physical and analytical data are given in TABLE 1.

Preparation of 2,4-bis-(phenylamino)-6-[4'-{1''-acetyl-5''-(2'''-methoxyphenyl)-2''- pyrazolin-3''-yl}-phenylamino]-*s*-triazine (7e)

Compound **(6e)** (0.01mole) and hydrazine hydrate (0.01mole) in dioxane (25ml) was refluxed for 6 hours in presence of glacial acetic acid (15ml). The reaction mixture was then cooled, poured into crushed ice and product separated out was filtered, washed with water, dried and recrystallized from alcohol to give **(7e)**.
Yield 64%; m.p. 159°C; IR(KBr)cm^{-1}: 1573(C=N), 806(C-N, *s*-triazine), 1650(-$COCH_3$); ^{1}H NMR ($CDCl_3$) δ ppm : 2.42(s, 3H, -$COCH_3$), 3.15(dd, 1H, C_4-H_A), 3.65(dd, 1H, C_4-H_B), 3.80(s, 3H, $-OCH_3$), 5.60(dd, 1H, -CH-CH_2), 6.90 to 7.80(m, 18 Ar-H and 3 NH). Anal. Calcd for $C_{33}H_{30}N_8O_2$: C, 69.47; H, 5.26; N, 19.65. Found: C, 69.45; H, 5.24; N, 19.67.

Similarly the remaining compounds **(7a-d)** were prepared by this method. Their physical and analytical data are given in TABLE 1.

Preparation of 2,4-bis-(phenylamino)-6-[4'-{2''-amino-3''-cyano-4''-(2'''-methoxy phenyl)-pyridin-6''-yl}-phenylamino]-s-triazine (8e)

Compound **(6e)** (0.01mole) and malononitrile (0.01mole) in alcohol (40ml) was refluxed for 8 hours in presence of ammonium acetate (0.02mole). Then the reaction mixture was cooled and poured into crushed ice. The product separated out was filtered, washed with water, dried and recrystallized from alcohol to give **(8e)**.
Yield 66%; m.p. 145°C; IR(KBr)cm^{-1}: 3396(-NH_2), 2200(C=N), 806(C-N, *s*-triazine); ^{1}H NMR($CDCl_3$) δ ppm : 3.83(s, 3H, -OCH_3), 5.28(s, 2H, -NH_2), 6.90 to 8.20(m, 19 Ar-H and 3NH). Anal. Calcd for $C_{34}H_{27}N_9O$: C, 70.71; H, 4.68; N, 21.84. Found: C, 70.73; H, 4.70; N, 21.83.

Similarly the remaining compounds **(8a-d)** were prepared by this method. Their physical and analytical data are given in TABLE 1.

ACKNOWLEDGMENT

We are thankful to the principal and management of B.K.M. Science College, Valsad for providing research facilities and head of microbiology department for carrying out antibacterial activity.

REFERENCES

[1] A.K.Pedersen, G.A.Fitzgerald; J.Pharm.Sci.,**74**, 188 **(1985)**; Chem.Abstr., **103**, 87592m **(1985)**.
[2] J.Methew, A.V.Subba Rao, S.Rambhav; Curr.Sci., **53**, 576 **(1984)**.
[3] C.Fauran, M.G.Turin, B.Pourrias; Chem.Abstr., **84**, 59477y **(1976)**.
[4] C.Peter, H.Peter, S.Paup; Chem.Abstr., **126**, 74745p **(1997)**.
[5] A.Giovanni, B.Ezio; T.Lett, **37**, 7836 **(1996)**; Chem.Abstr., **126**, 19064r **(1997)**.
[6] S.Cihat, T.Ayla, S.Selma, Y.Naran; J.Indian Chem. Soc., **67**, 216775k **(1990)**.
[7] M.M.El-Kerdawy, A.A.El-Emam; J.Chem.Soc. Pak, **9**, 285 **(1987)**; Chem Abstr., **107**, 198165b **(1987)**.
[8] R.H.Udupi, A.R.Bhat; Indian J.Heterocycle Chem., **7**, 217 **(1998)**; Chem.Abstr., **128**, 308434g **(1998)**.
[9] H.M.Kanjariya, T.V.Radhakrishnan, K.R. Ramchandran, H.Parekh; Ind.J.Chem., **43B**,1569 **(2004)**.
[10] N.Mishriky, F.M.Asaad, Y.A.Ibrahim, A.S.Giris; Indian J.Chem., **35B**, 935 **(1996)**.
[11] N.Latif, N.Mishriky, N.S.Girgis; Indian J.Chem., **20B**, 147 **(1981)**.
[12] A.Streightoff; J.Bacteriol, **85**, 42-8 **(1963)**; Chem.Abstr., **58**, 4836a **(1963)**.
[13] Chem.Abstr., **63**, 6979 **(1965)**.
[14] A.L.Barry; Biol Abstr., **64**, 25183 **(1977)**.
[15] A.Solankee, I.Thakor; Indian J.Chem., **45B**, 517 **(2006)**.
[16] A.Solankee, J.Patel; Indian J.Chem., **43B**, 1580 **(2004)**.