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Synthesis and characterization of some novel hetrecyclic compounds containig pyrazoline moiety

CHIRAG K. NAIK and VIKAS A. DESAI*

Department of Chemistry B.K.M. Science College, Valsad - 396 001 (India).

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ABSTRACT

The pyrazoline are having several interesting applications in the field of medicinal chemistry. We have synthesized a series of 3-{3'-(6"-methoxy-naphthalen-2"-yl)-5'-2"-hydroxy-4"-methoxy phenyl)-4'5'-dihydro-1h-pyrazol-1-y1}-5-(phenyl/submitted phenyl/2'-furyl)-2-pyrazoline (5a-1). The structures of pyrazoline have been characterized on bases of elemental analysis an spectral data. The compounds were screened for their in vitro anatibacterial activity using gram-positive bacteria and gram negative bacteria.

Key words: Pyrazoline chalocone, antibacterial activity, heterocylic synthesis.

INTRODUCTION

The chemistry and wide range of pharmaceutical properties of pyrazoline derivatives have been sited in literature[1-2]. Considerable interest has been caused on pyrazoline structure, which in known to possess a broad spectrum of biological activity. Pyrazoline have fungicidal, insecticidal antibacterial activity[3-6]. Pyrazoline are found in drugs and dyes[7-8]. In view of the fact that many pharmacological activities such as antibacterial[9], antifungal[10] antidibetic[11] antitubercular[12] were associated with pyrazoline nucleus.

In this study 6-methoxy-2-acetyl naphthalene on condensation with 4-methoxy-2-hydroxy benazaldehyde according to Claisen-Schmidt condensation[13-14] gives chalcone (1), which on reaction with hydrazine hydrate afforded 3-(6'-methoxy-naphthalene-2'-yl)-5-(4'-methoxy-2-'hydroxy phenyl) pyrazoline (2) this compound on further reaction with glacial acetic 15-17 gives 1-acetyl-3-(6'-methoxy-naphthalene-2-'-yl)-5-(4'-methoxy-2'-hyroxy phenyl) pyrazoline (3) the resulting compound (3) on condensed with various aromatic aldehydes in presence of 10% KOH solution afforded corresponding 1-[3'-(6"-methoxy-naphthalene-2-"-yl)-5-(4'-methoxy-2"- hydroxyl phenyl) pyrazoline] -3- (substituted phenyl) – 2-propene -1-one (4a-1). This different chalcones on cyclo-condensation with hydrazine hydrate gives respectively pyrazolo pyrazoline derivatives (5a-1).

EXPERIMENTAL

All melting points were determine in an open capillary tube and are uncorrected. The infra red (IR) spectra were recorded on a FTIR -8400 Shimadzu using potassium bromide pellets. Proton nuclear magnetic resonance (^{1}HNMR) Spectra were recorded on a Bruker avance dpx-200 (at 200 MHz) with $CdCl_3$ as a solvent using tetra methyl silane as internal standard chemical shift are expressed in part per million (ppm) down field form internal standard, the coupling standard are in Hz, and signal are quoted as s(singlet), d(doublet), t(triplet),q(quartlet), or m(multiplet). All reagents were of highest purity commercially available. Element analysis of C,H. and N was performed by CDRI, Lucknow and results are within ±0.4% of the calculated value. Thin layer chromatography was carried out using silica gel kieselgel 60 (Merck) to

monitor the reaction and to check the purity of compounds. The eluent was a mixture of toluene and methanol in ration of (60:40) and spot were visualized with UV (254 nm) or Iodine to check the purity of compound.

Preparation of 1-(6'-methoxy-naphalene-2-'yl)-3-(4'-methoxy-2'-hydroxy phenyl)-2-propane – 1-one (1)

6-methoxy-2-acetyl napththalene (0.01 mole) and 4-methoxy-2- hydroxyl benzaldehyde (0.01 mole) in methanol (30 ml) stirred at 35°C for 45 min, then add 10% KOH (4 ml) added in it and stir for more 6 hours After that reaction mixture was kept of 24 hrs. at room temperature. The reaction mixture was then poured in to ice-cold water and acidified wit dilute. HCI. The separated precipitate was filter of was with distilled water and crystallized from ethanol to get desire product m.p. 160°C yield 65.0% (found : C:75,45, H:5.36, calculated $C_{21}H_{18}O_4$:for C:75,43,H:5.34)

Preparation of 3-(6'-methoxy-naphalene-2-'yl)-5-(4'-methoxy-2'-hydroxy phenyl) pyrazoline (2)

A mixture of 1-(6'-methoxy naphthalene-2-'-yl)-3-(4'-methoxy 2'-hydroxyphenyl)-2-propen-1-ones (0.01 mol) and hydrazine hydrate (0.01 mole) kin ethanol (25 ml) were refluxed on water bath for 12 hrs. then reaction mixture was cooled and poured in to crushed ice. The resulting product 3-(6'methoxy naphthalene-2-'-yl)-5-(4'-methoxy 2'-hydroxyphenyl) pyrazoline separated was filtered washed with water and recrystallised from ethanol M.P. -106°C, yield: 73%,

Table 1: Physical data and elemental analysis data for the new Pyrazolines 5a-i

No	R	Molecular formula	m.p. (°C)	Yield	Elemental analysis		
					% of C found (Calcd)	% of H found (Calcd)	% of N found (Calcd)
5a	2,4,6 Trimethoxyphenyl	$C_{33}H_{34}N_4O_6$	153	56	68.05 (68.03)	5.90 (5.88)	9.65 (9.62)
5b	3-Phenoxyhenyl	$C_{33}H_{34}N_4O_4$	173	49	73.92 (73.95)	5.54 (5.52)	9.62 (9.62)
5c	4-Methoxyphenyl	$C_{31}H_{30}N_4O_4$	158	57	71.24 (71.25)	5.83 (5.79)	10.74 (10.72)
5d	2-Chloropenyl	$C_{30}H_{27}N_4O_3$	175	59	68.36 (68.37)	5.10 (5.12)	10.60 (10.63)
5e	4-Hydroxyphenyl	$C_{30}H_{28}N_4O_4$	169	63	70.87 (70.85)	5.52 (5.55)	10.99 (11.02)
5f	2'-furyl	$C_{28}H_{26}N_4O_4$	163	58	69.68 (69.69)	5.41 (5.43)	11.64 (11.61)
5g	4-hydroxy-3-methoxy phenyl	$C_{31}H_{30}N_4O_5$	164	68	69.16 (69.13)	5.58 (5.61)	10.38 (10.40)
5h	2-Nitrophenyl	$C_{30}H_{27}N_5O_5$	142	63	67.03 (67.03)	5.02 (5.06)	13.00 (13.03)
5i	4-N,N-Dimethylaminophenyl	$C_{32}H_{33}N_5O_3$	176	61	71.78 (71.75)	6.19 (6.21)	13.11 (13.07)
5j	2.4-Dihydroxy phenyl	$C_{30}H_{28}N_4O_5$	184	54	68.66 (68.69)	5.36 (5.38)	10.66 (10.68)
5k	Phenyl	$C_{30}H_{28}N_4O_3$	171	51	73.17 (73.15)	5.71 (5.73)	11.40 (11.37)
5l	3-NitrophenyL	$C_{30}H_{27}N_5O_5$	149	56	67.01 (67.03)	5.04 (5.06)	13.02 (13.03)

Preparation of 1-acetyl-3- (6'-methoxy-naphalene-2-'yl)-5-(4'-methoxy-2'-hydroxy phenyl) pyrazoline (3)

A mixture of 3-(6'-methoxy-naphalene-2-'yl)-5-(4'-methoxy-2'-hydroxy phenyl) pyrazoline (0.01 mole)in glacial acetic acid (25ml) was refluxed for 4 hrs. Then reaction mixture concentrated, on cooling resulting solid obtained was filtered washed with water and recrystallised from ethanol M.P.-121°C, yield: 68%,

Synthesis of 1—3- (6'-methoxy-naphalene-2-'yl)-5-(4'-methoxy-2'-phenoxy phenyl) -4'5'-dihydro-1H-pyrazol-1-'-yl} phenyl)-3-(3'phenoxyphenyl)-2-propane – 1- one (4b)

1-acetyl-3-(6'-methoxynaphthalene-2'-yl) -5-(4'-methoxy-2'-hydroxy phenyl) pyrazoline (0.01 mol) was dissolved in ethanol (30 ml) and 25% KOH solution was added to reaction mass. 3-phenoxy benzaldehyde (0.01 mol) in ethanol (20 ml) was added with constant string at room temperature in above reaction mass. After 24 hrs reaction mixture was poured in to crushed ice and neutralized with dil HCL. The resulting product, 1-{-3-{6-methoxy -naphalene-2-'yl)-5-(4'-methoxy-2'-hydroxyphenyl)-4', 5'-dihydro-1H- pyrazol-1'-yl} -3-(phenyl / submitted phenyl / 2'-furyl)-2-propen-1-one separated out was filter washed with water and recrystallised from alcohol. M.P. 149°C. Yield 49.0% (found: C:75:78, H:5.33: N:4.92, calculated for $C_{36}H_{30}N_2O_5$, C:75.77, H:5.33, N:4.91%) IR: = CH (3160 CM-1 C=C(1505 cm^{-1}), C=N (pyrazoline ring, 1580 cm^{-1}), -C-O-C-(1225 cm^{-1}). 1H NMR: δ:3.2 (1h, dd. –CH2a) 3.65 (1H, dd, -CH2b), 3.97 (6H, s, -OCH3), 5.8 (1H, t, -CH_2-CH), 7.1-8.1-(20H, m, Ar-H & CO-CH & CH-Ar),

Similarly other compounds of series (4a-1) were synthesized (Table 1).

Synthesis of 3–{3- (6'-methoxy-naphalene-2-'yl)-5-(4'-methoxy-2'-hydroxy phenyl) -4'5'-dihydro-1H-pyrazol-1-'-yl} phenyl)-5-(3'phenoxy phenyl)-2-propane. (5b)

A mixture of 1-3–{3- (6'-methoxy-naphalene-2-'yl)-5-(4'-methoxy-2'-hydroxy phenyl) -4'5'-dihydro-1H-pyrazol-1-'-yl}-3-(3'phenoxyphenyl)-2-propane – 1- one (0.01 mol) and hydrazine hydrate (0.011 mol) in ethanol (25 ml) were refluxed on water bath for 12hrs. than reaction mixture was then cooled and poured in crushed ice. The resulting product -3–{3- (6'-methoxy-naphalene-2-'yl)-5-(4'-methoxy-2'-hydroxy phenyl) -4'5'-dihydro-1H-pyrazol-1-'-yl} -5-(3'phenoxy phenyl)-2-pyrazoline separated out was filter, washed with water and recrystallised from alcohol. IR: = CH (3080 cm^{-1}), C=C(1495 cm^{-1}), C=N (pyrazoline ring, 1640 cm^{-1}), -C-O-C-

Table 2: Antibacterial activity of Synthesized compound

No.	Compounds	Antibacterial activity Diameter of Zone of Inhibition (in mm)			
		S. aureus	***S.paratyphi-A***	***E.coli***	***B.subtilis***
5a	2,4,6,Trimethoxyphenyl	18	15	15	14
5b	3-Phenoxyphenyl	7	10	11	10
5c	4-Methoxyphenyl	17	9	17	13
5d	2-Chloropenyl	10	9	12	15
5e	4-hydroxy phenyl	15	16	16	10
5f	2-furyl	8	12	12	3
5g	4-hydroxy-3-methoxy phenyl	13	13	9	9
5h	2-Nitrophenyl	15	7	13	8
5i	4-N,N- Dimethylaminophenyl	9	15	13	4
5j	2.4-Dihydroxy phenyl	13	12	6	12
5k	Phenyl	13	10	14	10
5L	3-Nitrophenyl	7	10	11	10
STD	Ampicillin	40	28	38	30

(1040 cm^{-1}). –NH (3300 cm^{-1}) ^1H NMR: δ:3.15 (1H, dd. $–CH_{2a}$) 3.72 (1H, dd, $-CH_{2b}$), 3.98 (6H, s, $-OCH_3$), 5.82 (1H, t, $-CH_2-CH$), 6.8-8.4(18H, m, Ar-H) 9.8 (1H, s, -NH).

Similarly other compounds of series (5a-1) were synthesized (Table 1).

Antibacterial activity

The target molecules were tested for antibacterial activity against the variety of test organisms *E. coli, B. substillis* (Gram – negative bacteria) and *S. aureus*, *S.paratyphi*-A(Gram – positive bacteria) bacteria. Screening was carried out in acetone solution at concentration of 40 µg/ml. Cup plate method18 was employed using nutrient agar culture medium. Under the similar condition, control experiment was carried out using chlomphanicol as a standard drug for comparison. The antibacterial screening results are given in Table 2 all compound were active against both gram-positive and gram-negative bacteria at concentration of 40 µg/ml. the degree of inhibition varied with the test compound as well as with bacterium.

From the activity data it may be concluded than compounds nos. 5a, 5e and 5k shows good activity.

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REFERENCES

1. Pathak, M: Jain, R, *Indian J. chem*. **32B**: 505 (1993)
2. Amir, M:, Agarwal, R, *J. Indian Chem Soc*. **74**: 154 (1997).
3. Dighade, S.R. Chincholkar, M.M. *Oriental Journal of Chem*, **17**(1): 151 (2001).
4. EI-Kerdawy, M.M:E-Emam, A.A.: *J Chem Soc. Pak,* **9**: 285 (1987): *Chem. Abstr*. **107**: 198165b(1987).
5. Ankhiwala, M.D. Naik, H.B. *J. Indian Chem Soc,* **67**(5): 176 (1989).
6. Vonhes, R: Crossurt, A.C. *Chem Abstr.* **78**(7): 10728 (1982).
7. Nisbat, H.B. J. *Indian Chem Soc* 1568 (1930).
8. Velyeshka, N.A. Debishika, I. T: Zhobshah, Khim, **23**: 230 (1983)
9. Upadhyay, J: Daveand, D.N. Parekh H: *J.Inst. Chem* **64**: 72 (1992)
10. Sorathiya, S.D. Patel V.B. Parikh A.R. *Indian J. Chem* **36**(B): 630 (1997).
11. Husain, M.I. Kumar, A:, *Indian Drugs* **24**: 187 (1987).
12. Karti, H.I. Avunii, S,J: *Indian Chem Soc* **58**: 168 (1981)
13. Dawey, W.: Tivey D.J.J. *Chem Soc*. 1320 (1958)
14. Kohler, H.M. Chadwell, H: Gilman, H,: Blatt, A.H.:(Eds) Organic Synthesis: Wiley: New York, (Coll. Vol. I) P 78 (1967).
15. Beech, S.G. Trunbull, J.H: Wilson, W:J. *Chem. Soc*. 4686 (1952).
16. Jurd, L.: *Tetrahedron*, **31**: 2884 (1975).
17. Sayed G.H. *Indian J. Chem*. **19(B)**: 364 (1980).
18. Barry, A.L. The Antimicrobial Susceptibility Test: Principle and practice edited by Illuslea & febiger, (Philadelphia Pa USA). P. 180(1976)[*Biol, Abstr.* 6) 25183 (1977)].