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Synthesis of Some New 3-(Substituted phenyl)-5-(9-anthryl)-2-pyrazolines, 1-Phenyl-3-(substituted phenyl)-5-(9-anthryl)-2-pyrazolines and 2-(9-Anthryl)-4-(substituted phenyl)-1,5-benzothiazepines as Antibacterial Agents

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The title compounds have been synthesized from the corresponding 1-(substituted phenyl)-3-(9-anthryl)-2-propen-1-one (**I**) by condensation with hydrazine hydrate, phenyl hydrazine and 2-amino-thiophenol. The structures of the new compounds were established on the basis of analytical and spectral data. All the compounds have been screened for their antibacterial activity.

Key Words: Synthesis of substituted pyrazoline, N-Phenyl pyrazoline, Benzothiazepine, Antibacterial agents.

INTRODUCTION

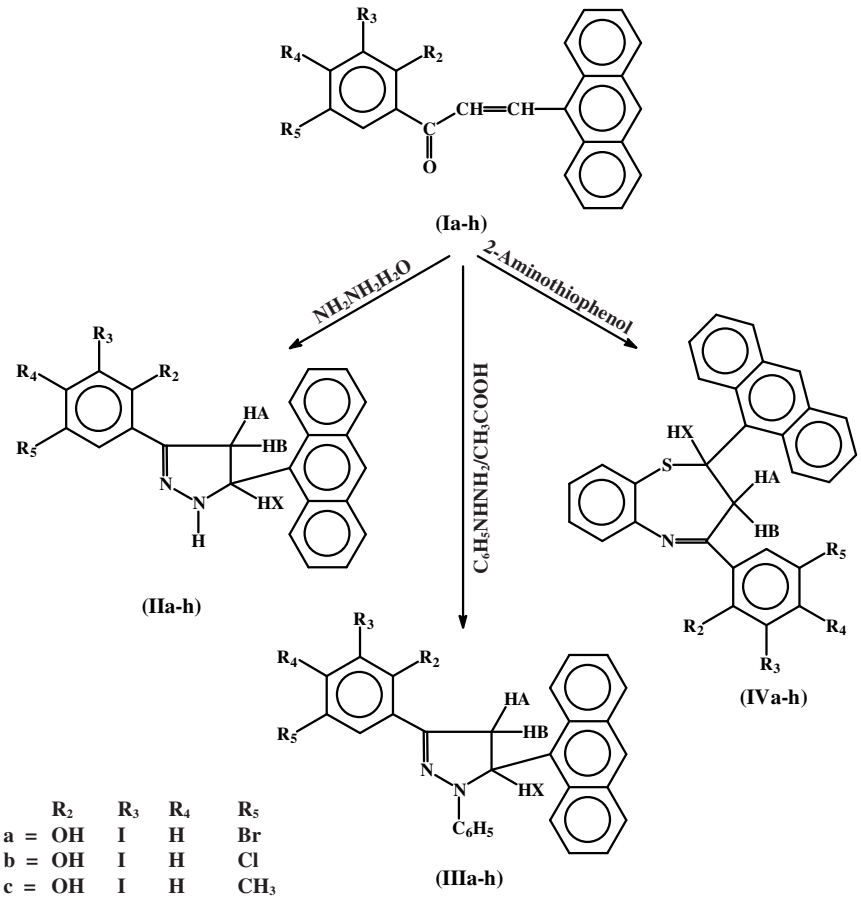
Pyrazolines are prominent nitrogen containing heterocylic compounds. Numerous pyrazoline type compounds have been found to possess useful bioactivity such as fungicidal[1,2], local anaesthetics[3], anticonvulsant[4], antifertile[5], CNS stimulant[6], antidiabetics[7], antiinflammatory[8], cardiovascular[9] agents. Benzothiazepine systems are known to be biologically active and are important constituents of many pharmaceutical role as anticoagulant[10], antihypertensive[11] and antidepressant[12] compounds. The exploitation of simple molecules of heterocycles is a worthy contribution to the field of medicinal chemistry. This contribution prompted us to synthesize different pyrazolines and benzothiazepine with a view of obtaining antibacterial agents.

The most common synthetic approach to pyrazoline synthesis involved cyclization of chalcones[13] with hydrazine hydrate (**IIa-h**) and phenyl hydrazine (**IIIa-h**). 1,5-Benzothiazepines were obtained by the condensation of chalcones with 2-amino thiophenol (**IVa-h**).

The structure of the synthesized compounds have been characterized by their elemental analysis, IR and ^{1}H NMR spectral data.

EXPERIMENTAL

Melting points were determined in open capillary tubes and are uncorrected. All the chemicals and solvents used are of laboratory grade and solvents were purified. Completion of the reaction was monitored by TLC, silica gel GF_{254} (E. Meck). The final products were purified by column chromatography. IR (KBr, cm^{-1}) were recorded on Perkin-Elmer spectrometer. The ^1H NMR spectra were scanned on Hitachi NMR-12 at 300 MHz using TMS as internal standard (chemical shift in δ ppm) in $CDCl_3$ and DMSO-d_6. All the synthesized compounds gave satisfactory C, H and N analyses.



	R_2	R_3	R_4	R_5
a =	OH	I	H	Br
b =	OH	I	H	Cl
c =	OH	I	H	CH_3
d =	OH	Cl	H	I
e =	OH	I	CH_3	Cl
f =	OH	I	H	I
g =	OH	I	Cl	CH_3
h =	OH	Cl	H	Cl

Scheme-I

Synthesis of 3-(2′-hydroxy-3′-iodo-4′-methyl-5′-chlorophenyl)-5-(9-anthryl)-2-pyrazoline (IIe): A mixture of 1-(2′-hydroxy-3′-iodo-4′-methyl-5′-chlorophenyl)-5-(9-anthryl)-2-propen-1-one (0.001 mol) and hydrazine hydrate (0.002 mol) in ethanol (20 mL) was refluxed for 6 h. The progress of the reaction was monitored by TLC. After completion of the reaction, the contents were poured in ice water. The solid obtained was filtered and recrystallized from rectified spirit to gave compounds (**IIe**).

IR spectra of all pyrazolines showed absorption band in the region 1260-1215 cm^{-1} due to (N-N-C) of pyrazoline ring, near at 1570 cm^{-1} due to (N-N-bending), 1625-1590 cm^{-1} due to (C=N), ^1H NMR data shows ABX pattern of signals, attributed to methine and methylene protons.

All compounds (**IIa-h**) were prepared similarly and their characterization data are given in Table-1.

Synthesis of 1-phenyl-3-(2′-hydroxy-3′-iodo-4′-methyl-5′-chlorophenyl)-5-(9-anthryl)-2-pyrazoline (IIIe): A mixture of 1-(2′-hydroxy-3′-iodo-4′-methyl-5′-chlorophenyl)-5-(9-anthryl)-2-propen-1-one (0.001 mol) and phenyl hydrazine (0.001 mol) in ethanol (20 mL) and acetic acid (5 mL) was refluxed for 6 h. The reaction was monitored by TLC, on completion of the reaction the contents were poured in ice water. The solid obtained was filtered, washed with water and recrystallized from rectified spirit to gave compounds (**IIIe**).

The IR spectra of all N-phenyl pyrazolines showed (C=N) stretch in the region of 1625-1590 cm^{-1} indicating the conversion (>C=O) into (>C=N), 1270-1210 cm^{-1} is due to (-N-N-C-) of pyrazoline. ^1H NMR data shows ABX pattern of signals, attributed to methine and methylene protons.

All compounds (**IIIa-h**) were prepared and their charaterization data are given in Table-1.

Synthesis of 2-(9-anthryl)-4-(2′-hydroxy-3′-iodo-4′-methyl-5′-chlorophenyl)-1,5-benzothiazepine (IVe): A mixture of 1-(2′-hydroxy-3′-iodo-4′-methyl-5′-chlorophenyl)-5-(9-anthryl)-2-propen-1-one (0.01 mol) and 2-aminothiophenol (0.01 mol) in ethanol (25 mL) and few drops of piperidine was added and the reaction mixture was refluxed for 2 h on steam bath. It was acidified with glacial acetic acid (10 mL) and further refluxed for 3 h and cooled. The reaction mixture was left over night at room temperature. Solid thus obtained was then filtered and recrystallized from ethanol.

The IR spectra of all 1,5-benzothiazepines showed a band of near 1610 cm^{-1} (C=N), 3190 cm^{-1} (-OH broad). ^1H NMR data contain ABX pattern of signals, attributed to methine and methylene protons.

All other compounds (**IVa-h**) were prepared and their characterization data are given in Table-1.

TABLE-1
CHARACTERIZATION DATA AND ANTIBACTERIAL ACTIVITIES OF **II, III, IV (a-h)**

Compd.*	m.p. (ºC)	Yield (%)	Characterization data		Antibacterial activity**	
			IR	^{1}H NMR	*E. coli*	*S. aureus*
IIa	204	70	3190 br ν(OH), 3200 ν(NH), 1605 ν (C=N)	2.68 (dd, 1H, HA), 3.70 (dd, 1H, HB), 5.2 (t, 1H, HX) 8.20 (s, 1H, NH), 12.10 (s, 1H, Ar-OH), 7.2-8 (m, 11H, Ar-H)	–	10
IIb	168	75	3245 ν(NH), 3150 br ν(OH), 1608 ν(C=N)	2.56 (dd, 1H, HA), 3.49 (dd, 1H, HB), 5.12 (t, 1H, HX) 8.09 (s, 1H, NH), 12.15 (s, 1H, Ar-OH), 7.15-8.05 (m, 11H, Ar-H)	18	10
IIc	149	70	3230 ν(NH), 3195 br ν(OH), 1616 ν(C=N)	2.62 (dd, 1H, HA), 3.58 (dd, 1H, HB), 5.16 (t, 1H, HX) 1.38 (s, 3H, CH_3), 8.06 (s, 1H, NH), 11.98 (s, 1H, Ar-OH), 7.08-8.16 (m, 11H, Ar-H)	16	–
IId	174	70	–	–	12	10
IIe	190	75	3205 ν(NH), 3160 br ν(OH), 1603 ν(C=N)	2.57 (dd, 1H, HA), 3.48 (dd, 1H, HB), 5.20 (t, 1H, HX) 1.29 (s, 3H, CH_3), 7.98 (s, 1H, NH), 11.87 (s, 1H, Ar-OH) 7.98-8.28 (m, 11H, Ar-H)	–	18
IIf	178	75	–	–	28	–
IIg	151	75	–	–	12	8
IIh	164	70	–	–	8	15
IIIa	182	65	1610 ν(C=N), 3175 br ν(OH)	2.69 (dd, 1H, HA), 3.84 (dd, 1H, HB), 5.31 (t, 1H, HX) 11.35 (s, 1H, Ar-OH), 7.2-8.5 (m, 16H, Ar-H)	–	4
IIIb	178	70	1622 ν(C=N), 3200 br ν(OH)	2.61 (dd, 1H, HA), 3.94 (dd, 1H, HB), 4.98 (t, 1H, HX) 11.15 (s, 1H, Ar-OH), 7.4-8.3 (m, 16H, Ar-H)	20	1
IIIc	163	75	–	–	4	16

Compd.*	m.p. (ºC)	Yield (%)	Characterization data		Antibacterial activity**	
			IR	^{1}H NMR	*E. coli*	*S. aureus*
IIIe	208	70	1616 ν(C=N), 3280 br ν(OH)	2.58 (dd, 1H, HA), 4.01 (dd, 1H, HB), 4.98 (t, 1H, HX) 12.00 (s, 1H, Ar-OH), 1.53 (s, 3H, CH_3), 7.2-8.4 (m, 16H, Ar-H)	–	3
IIIf	182	65	–	–	20	13
IIIg	158	70	1621 ν(C=N), 3240 br ν(OH)	2.62 (dd, 1H, HA), 3.91 (dd, 1H, HB), 5.01 (t, 1H, HX) 11.98 (s, 1H, Ar-OH), 1.76 (s, 3H, CH_3), 7.2-8.4 (m, 15H, Ar-H)	–	3
IIIh	145	75	–	–	11	4
IVa	202	65	1610 ν(C=N), 3350 br ν(OH)	2.81 (dd, 1H, HA), 4.03 (dd, 1H, HB), 5.31 (t, 1H, HX) 11.41 (s, 1H, Ar-OH), 6.9-8.24 (m, 15H, Ar-H)	13	3
IVb	165	70	–	–	18	4
IVc	149	75	1605 ν(C=N), 3240 br ν(OH)	2.61 (dd, 1H, HA), 4.28 (dd, 1H, HB), 5.28 (t, 1H, HX) 11.58 (s, 1H, Ar-OH), 1.5 (s, 3H, CH_3) 7.00-8.30 (m, 14H, Ar-H)	19	13
IVd	173	70	–	–	28	21
IVe	188	65	–	–	27	18
IVf	154	65	–	–	17	23
IVg	169	70	1615 ν(C=N), 3280 br ν(OH)	2.78 (dd, 1H, HA), 4.02 (dd, 1H, HB), 5.54 (t, 1H, HX) 12.00 (s, 1H, Ar-OH), 7.2-8.28 (m, 15H, Ar-H)	26	–
IVh	194	70	–	–	21	18
Ampicillin	–	–	–	–	36	28

*All compounds gave satisfactory elemental analysis; **Diameter of Zone of inhibition in mm.

RESULTS AND DISCUSSION

All the synthesised compounds were screened for their antibacterial activity against *S. aureus* and *E. coli* at various concentrations such as 25, 50 and 100 µg/mL. The activity was carried out using cup plate agar diffusion method[14]. The zone of inhibition was measured in mm. DMF was used as solvent. The activities of the compounds were compared with stantard ampicillin drug, under identical conditions from Table-1, it was concluded that the compounds pyrazoline derivatives **IIf**, **IIId**, **IIIf** and benzothiazepines derivatives **IVd**, **IVe**, **IVg** and **IVf** are moderately active.

The activity of above compounds is significant against the bacterial strains. This might be due to the presence of halo groups in aryl nucleus. Though the compounds possess antibacterial activity against various species, none can reach the activity of the standard drug.

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