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Synthesis of 2[2/-propen-1/-one,3/-(4-hydroxy,3-azophenyl) Phenyl] Pyrroles and 2[2/-propen-1/-one-3/- (3-hydroxy Naphthyl-1-azo) Phenyl] Pyrroles

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A facile synthesis of 2[2/-propene-1-one-3-(4-hydroxy, 3/-azophenyl) pheny] pyrroles (3a-h) and 2[2/-propene-1-one-3-(4/-hydroxy naphthyl-1-azo) pheny]pyrroles (6a-c) has been achieved by 2[4/-hydroxy benz-1(propane-1-one)] pyrrole 2 and 2[3/-amino benz-1(propene-1-one)] pyrrole 5 respectively The newly synthesized compounds structures have been supported by IR, ^{1}H NMR, spectral data. The antibacterial and antifungal activities of the compounds have also been evaluated.

Key words: Pyrrole, azo compounds, 4-hydroxy benzaldehyde.

A broad spectrum of biological activity is associated with both simple and fused pyrrole and a large number of natural and synthetic compounda containing such moieties find pharmaceutical applications[1-4]. Azo compounds have been found to possess wide spectrum of biodynamic properties. Many of them have been reported as antibacterial[5], antimicrobial[6], diagnostic aid[7], antineoplastic[8], urinary antiseptic[9] and topical dermatologic activities[10]. Several azo compounds have been proved useful for the colouration of cellulose acetat fibres.

RESULTS AND DISCUSSION

In view of these observations, it was thought worth-while to synthesize and investigate the compounds in which azo group have been linked with pyrrole moiety.

The reaction sequence leading to the formation of desired heterocyclic compounds are outlined in Scheme-I. The starting material 2-[4-hydroxy benz-1(propene-1-one)]Pyrrole (2) was prepared by the reaction of 2-acetyl pyrrole with 4-hydroxy benzaldehyde in presence of 40 % NaOH which on coupling with different aromatic amines in presence of $NaNO_{2-}$ and HCl at 0-5^{0}C yielded 2[2/-propene-1-one-3-(4-hydroxy, 3/-azophenyl) phenyl] pyrroles (3a-h) The nitro group present in compound (4) is reduced by Sn/HCl to yield 2[3/-amino benz-1(propene-1-one)] pyrrole (5) which was coupled with different aromatic hydroxy compounds in presence of $NaNO_{2-}$ and HCl at 0-5°C to give 2[2/-propene-1-one-3-(4/-hydroxy naphthyl-1-azo) phenyl]pyrroles (6a-d). The UV-Vis-spectra of the azo dyes (3a-h) and (6a-d) were recorded and the values of absorptions (λ max) and fastness properties are shown in Table 1. It is apparent that the wavelength of maximum absorptions azo compound was observed at 200-

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500nm in EtOH solutions. Variation in λ max is being attributed to structural variation of electron–rich aromatic compounds with N=N linkage used for the preparation of these azo compounds.

Structure proof for the synthesised compounds 3a-h , 6a-d was illusidated by IR and ^{1}HNMR studies. IR spectrum shows the presence of NH-pyrrole group at 3348cm^{-1}, C = 0 group at 16438cm^{-1}, N =N group at 1589cm^{-1}, OH group at 3410cm^{-1}, C-N group at 1587, C–Cl group at 755cm^{-1}, C-NO_2 group at 748. ^{1}HNMR spectrum showed be presence 8.1 (s, 1H, NH-pyrrole), 6.8 - 7.0(Ar-H), 5.3 (s, 1H, OH).

Pharmacological activities

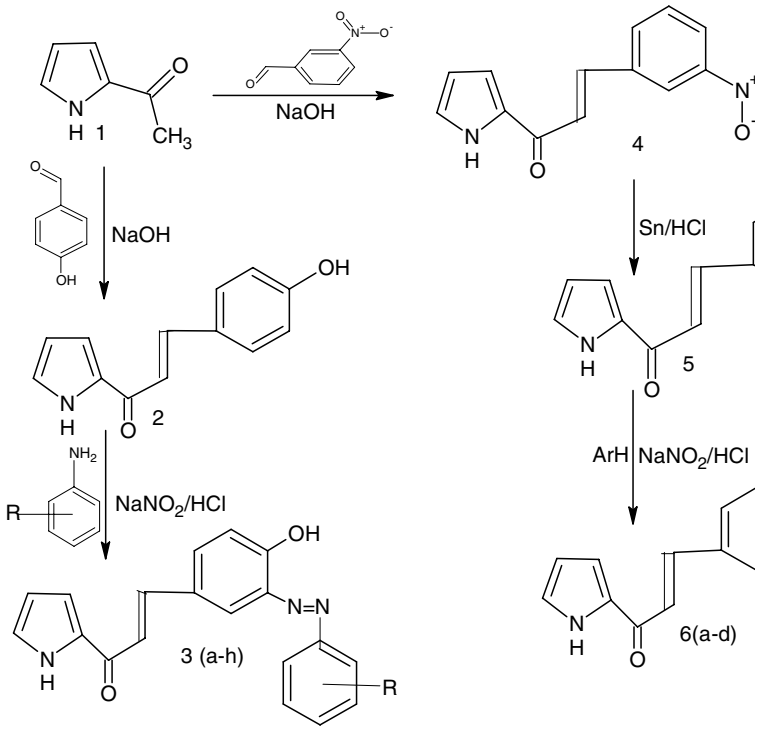
Comparative study of the 2 - acetyl pyrrole (1) and 2 [2′- propene -1-one - 3 - (4 – hydroxy , 3′- azo phenyl) phenyl] pyrroles (3 a –h) and 2 [2′- propene – 1 – one –3 – (4′- hydroxy naphthyl – 1 – azo) phenyl] pyrroles (6 a – d) has been observed by using Norfloxacin and Griseofulvine as standards.They show antibacterial activities against *E. Coil* and *S. Aureus* and antifungal activities against *A. niger* and *C. albicans* at 100 ug \ ml concentration as shown in Table (II).

EXPERIMENTAL

The melting points are uncorrected. Purity of the compounds was checked on silica gel G plates using iodine vapour as visualizing agent. Synthesized compound was characterized by IR spectra, run in KBr on a Perkin – Elmer infrared spectrophotometer. ^{1}H NMR spectra on Brucker AC–300F(300Hz) NMR spectrometer using DMSO-d_6 as a solvent and tetramethyl silane as internal standard

2[4′-hydroxy benz-1(propane-1-one)] pyrrole

2-acetyl pyrrole (0.01mol) and 4-hydroxy benzaldehyde (0.01mol) was dissolved in 100ml ethanol. To this solution, NaOH (40%, 10ml) was added dropwise with constant stirring at room temp. till a dark yellow mass was obtained.The reaction mixture was kept 7-8 hr and acidified with dil HCl. The solid obtained was washed with cold water. It



Scheme 1.

was filtered and dried. It was crystallized from ethanol. Yield 62% M.P 153^0

Preparation of 2[2-propene-1-one-3-(4-hydroxy-3-azophenyl) phenyl]pyrrole

Aniline (0.1mol)was dissolved in (20ml) 4% HCl and the solution was cooled to 0-5°C. To this saturated sodium nitrite solution was added dropwise followed by addition of compound (2) (0.1mol) in 20ml of 7% NaOH for a period of 10min till the coloured solution is obtained. The solution was stirred for 30min and then neutralized to pH 7 by adding 10% HCl, the solid separated out, filtered dried and crystalized from suitable sovent . Yield 65%:M.P.83°C: IR (KBr) : 3385(-OH), 3130 (NH-pyrrole), 1618 (C= 0), 1520(N=N), 1577cm^{-1} (C-N), 3144cm^{-1} (CH of pyrrole-); ^{1}H NMR (DMSO-d_6); 5.3 (s, 1H, OH), 6.8–8.2(Ar-H), 8.1(d, 1H, NH-pyrrole).

2[2-propene-1-one-3- (4-hydroxy-3-azo-2-chlorophenyl) phenyl]pyrrole

Yield 92%, M.Pt.68°C; IR (KBr);34229cm^{-1} (-OH), 3337cm^{-1} (NH-pyrrole), 1660cm^{-1} (C = 0), 1545cm^{-1} (C-N), 3143cm^{-1} (CH of pyrrole-) 1632cm^{-1} (N=N), 752cm^{-1} (C-Cl); ^{1}HNMR (DMSO-d_6) 9.7 (1H, s, NH-pyrrole), 5.3 (s, 1H, OH), 6.3-7.1 (Ar-H).

2[2-propene-1-one-3-(4-hydroxy-3-azo-3-chlorophenyl) phenyl]pyrrole

Yield 61%, M.Pt.59°C:IR (KBr) ; 34229cm^{-1} (-OH) 3335, (NH-pyrrole), 1683 (C = 0), 1585cm^{-1} (C-N), 3044cm^{-1} (CH of pyrrole-) 1635cm^{-1} (N=N) 755cm^{-1} (C-Cl); ^{1}HNMR (DMSO-*d*6) 8.7 (1H, s, NH-pyrrole), 6.3 (s, 1H, OH), 7.1 (Ar- H).

2[2-propene-1-one-3- (4-hydroxy-3-azo-4-chlorophenyl) phenyl]pyrrole

Yield 58% , M.P. 72° C; IR (KBr) ; 34229cm^{-1} (-OH), 3337 (NH-pyrrole) , 1683 (C = 0), 1547cm^{-1} (C-N), 3044cm^{-1} (CH of pyrrole-) 1635cm^{-1} (N=N) 742cm^{-1} (C-Cl) ; ^{1}HNMR (DMSO-*d*6) 9.2 (1H, s, NH-pyrrole), 5.7 (s, 1H, OH), 6.8 (Ar- H).

2[2-propene-1-one-3- (4-hydroxy-3-azo-2-nitrophenyl) phenyl]pyrrole

Yield 78% , M.P. 137° C; IR (KBr) ; 3422cm^{-1} (-OH), 3335 (NH-pyrrole) , 1683 (C = 0), 1587cm^{-1} (C-N), 3044cm^{-1} (CH of pyrrole-) 1635cm^{-1} (N=N), 742cm^{-1}(C-NO$_2$) ; ^{1}HNMR (DMSO-*d*6) 8.2 (1H, s, NH-pyrrole), 6.3 (s, 1H, OH), 6.9 (Ar- H).

2[2-propene-1-one-3- (4-hydroxy-3-azo-3-nitrophenyl) phenyl]pyrrole

Yield 68% , M.P. 149° C; IR (KBr) ; 34229cm^{-1} (-OH), 3335 (NH-pyrrole) , 1683 (C = 0), 1559cm^{-1} (C-N), 3044cm^{-1} (CH of pyrrole-) 1635cm^{-1} (N=N) 746cm^{-1}(C-NO$_2$); ^{1}HNMR (DMSO-*d*6) 8.7 (1H, s, NH-pyrrole), 6.8 (s, 1H, OH), 7.6 (Ar- H).

2[2-propene-1-one-3- (4-hydroxy-3-azo-4-nitrophenyl) phenyl]pyrrole

Yield 68% , M.P. 198° C; IR (KBr) ; 34229cm^{-1} (-OH), 3335 (NH-pyrrole) , 1683 (C = 0), 1587cm^{-1} (C-N), 3044cm^{-1} (CH of pyrrole-) 1635cm^{-1} (N=N) 744cm^{-1}(C-NO$_2$); ^{1}HNMR (DMSO-*d*6) 9.7 (1H, s, NH-pyrrole), 5.3 (s, 1H, OH), 6.3-7.1 (Ar- H).

2[2-propene-1-one-3- (4-hydroxy-3-azo-4-methylphenyl) phenyl]pyrrole

Yield 59% , M.P. 98° C; IR (KBr) ; 34229cm^{-1} (-OH), 3335 (NH-pyrrole) , 1683 (C = 0), 1548cm^{-1} (C-N), 3044cm^{-1} (CH of pyrrole-) 1635cm^{-1} (N=N); ^{1}HNMR (DMSO-*d*6) 9.5 (1H, s, NH-pyrrole), 6.6 (s, 1H, OH), 6.3 (Ar- H).

2[3′-nitro benz-1(propane-1-one)] pyrrole

2-acetyl pyrrole (0.01mol) and 3-nitro benzaldehyde (0.01mol) was dissolved in 100ml ethanol. To this solution, NaOH (40%, 10ml) was added dropwise with constant stirring at room temp. till a dark yellow mass was obtained .The reaction mixture was kept 7-8 hr and acidified with dil HCl. The solid obtained was washed with cold water. It was filtered and dried. It was crystallized from ethanol. Yield 62 % M.P 136^0

Preparation of 2[2-propene-1-one-3-(4-hydroxynaphthyl-1-azo) phenyl] pyrrole

0.1 mol of compound (5) was dissolved in (20ml) 3% HCl was cooled. The solution to 0-5°C and saturated solution of sodium nitrite was added dropwise maintaining ice cold temperature. The completion of reaction was checked by starch-iodine test. To this solution 0.1gm of a-naphthol in 20ml of 7% NaOH in a period of 10 min. was added. The coloured solution obtained was stirred for 30min. and then nuetralised to pH 7 by adding 10% HCl the solid was separated out, filter dried and crystallized from aqueous ethanol. Yield 68%; M.P. 163°C: IR (KBr) 3330(-OH), 3200(NH-pyrrole), 1672(C= 0), 1630(N=N), 1567cm^{-1} (C-N), 3010(CH-pyrrole) ^{1}HNMR (DMSO-d_6), 9.5 (1H, s, NH-pyrrole), 5.9 (s, 1H, OH), 6.3 (Ar- H).

Preparation of 2[2-propene-1-one-3-(2-hydroxynaphthyl-1-azo)phenyl] pyrrole

Yield 68%; M.P. 163°C: IR (KBr) 3330(OH), 3200(NH), 1672(C=0), 1630(N=N), 1577cm^{-1} (C-N), 3122(CH-pyrrole); ^{1}HNMR (DMSO-d_6), 8.5 (1H, s, NH-pyrrole), 6.5 (s, 1H, OH), 6.2 (Ar- H).

Preparation of 2[2-propene-1-one-3-(4-hydroxyphenyl-1-azo) phenyl] pyrrole

Yield 68%; M.P. 163°C: IR (KBr) 3330(OH), 3200(NH), 1672(C= 0), 1630(N=N), 1557cm^{-1} (C-N), 3011(CH-pyrrole) ^{1}HNMR (DMSO-d_6), 9.7 (1H, s, NH-pyrrole), 6.8 (s, 1H, OH), 5.9 (Ar- H).

Preparation of 2[2-propene-1-one-3-(4-hydroxyphenyl-1-azo) phenyl] pyrrole

Yield 68%; M.P. 163°C: IR (KBr) 3350(OH), 3250(NH), 1670(C= 0), 1631(N=N), 1540cm^{-1} (C-N),

Table 1. UV-VIS Section of Azo compound (3a –h)and (6a-d)and fastness properties

Code	Colour	lmax	Fastness properties			
			Silk		Wool	
			Light[a]	wash[b]	Light[a]	Wash[b]
3a	Red	475	2	3	2-3	3-4
3b	Brown	456	3-4	2-3	3-4	2
3c	Brown	442	2	4	2	3
3d	Brown	411	2-3	3-4	2-3	2-3
3e	Orange	422	4	2-3	3	3-4
3f	Orange	445	2-3	3-4	2-3	2-3
3g	Red	470	3-4	2-3	3-4	2
3h	Red	474	2	4	3	2-3
6a	Red	473	3	2-3	3-4	3
6b	Orange	457	3-4	3	2-3	2-3
6c	Orange	420	2	3	4	2-3
6d	Purple	483	4	3-4	2-3	3

IN EtOH solution (3a-h, 6a-d)
[a]Light-fastness: 1-minimum, 2-poor, 3-moderate, 4-fairly good, 5-good. 6-very good.
[b]wash-fastness: 1-poor, 2-fair, 3-good, 4-very good and 5-excellent.

Table 2. Data for in Vitro antibacterial and anti Fungal activities (in mm)

Comp	Minimum Inhibitory concentration's µg /ml			
	E. coli	*S. aureus*	*A. niger*	*C. albicans*
3a	13	15	17	12
3b	15	12	16	18
3c	12	14	15	14
3d	-	10	-	17
3e	10	12	15	18
3f	14	14	16	17
3g	NA	17	10	NA
3h	9	10	14	17
6a	13	12	17	16
6b	12	9	10	19
6c	NA	14	18	15
6d	14	11	21	14

NA -Not active
- = No inhibition of growth
Norfloxcin 100ug/ml used as standard against *E. coli,* and *S. aureus,* diameter of zone of inhibition is 20.
Grisefulvin 100ug/ml used as standard against *A. niger* and *C. albicans*, diameter of zone of inhibition is 32.

Table 3. Characterization data of newly synthesized compounds 3a-h, 6a-d

Comp	R	Mol Formula	M.P. (°C)	Yield (%)	Analysis formula (calcd)% (obs)		
					C	H	N
3a	- H	$C_{19}H_{14}O_2N_2$	83	65	75.2 (75.3)	4.9 (4.5)	9.2 (9.1)
3b	2-Cl	$C_{19}H_{14}O_2N_2Cl$	68	92	67.2 (67.74)	4.1 (4.0)	8.2 (8.3)
3c	3-Cl	$C_{19}H_{14}O_2N_2Cl$	59	61	67.2 (67.74)	4.1 (4.0)	8.2 (8.3)
3d	4-Cl	$C_{19}H_{14}O_2N_2Cl$	72	58	67.2 (67.74)	4.1 (4.0)	8.2 (8.3)
3e	2-NO_2	$C_{19}H_{14}O_4N_3$	137	78	65.5 (65.6)	4.0 (4.2)	12.0 (12.2)
3f	3-NO_2	$C_{19}H_{14}O_4N_3$	149	68	65.5 (65.6)	4.0 (4.2)	12.0 (12.2)
3g	4-NO_2	$C_{19}H_{14}O_4N_3$	198	68	65.5 (65.6)	4.0 (4.2)	12.0 (12.2)
3h	4-CH_3	$C_{20}H_{17}O_2N_2$	98	59	75.7 (75.6)	5.3 (5.1)	8.8 (8.7)
6a	a-$C_{10}H_7O$	$C_{23}H_{19}O_2N_2$	163	65	77.4 (77.4)	5.3 (5.0)	7.8 (7.6)
6b	b-$C_{10}H_7O$	$C_{23}H_{19}O_2N_2$	129	62	77.4 (77.4)	5.3 (5.0)	7.8 (7.6)
6c	-C_6H_5O	$C_{19}H_{15}O_2N_2$	122	65	75.2 (75.3)	4.9 (4.4)	7.8 (7.7)
6d	-$C_6H_6O_2$	$C_{19}H_{15}O_3N_3$	185	52	75.2 (75.6)	4.5 (4.4)	12.6 (12.7)

3020(CH-pyrrole); ^{1}HNMR (DMSO-d_6), 9.5 (1H, s, NH-pyrrole), 6.8 (s, 1H, OH), 6.1 (Ar- H).

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