NAPHTHO[1,2-c]PYRAZOLE, ISOXAZOLE AND NAPHTHO[1,2-d] PYRIMIDINE DERIVATIVES SYNTHESIS, SPECTRA AND BIOLOGICAL EVALUATION

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تم تشييد بعض مشتقات من كل من النفثو [2,1-C] بيرازول و الأيزوكسازول والنفثو [2,1-d] بيرميدينات الجديدة بتفاعل الإضافة التكاثفية لبعض مشتقات ٢-أريل ميثيلين-١-تترالون مع كواشف مناسبة. كما تم تدوين نتائج التحاليل الطيفيـــة والحيوية.

Naphtho[1,2-c]pyrazoles **2-4**, isoxazoles **5** and Naphtho[1,2-d]pyrimidines **6** were synthesised by the condensation of 2-arylmethylidene-1-tetralones **1** with the appropriate reagent. Spectra and biological evaluation of the prepared compounds were recorded.

INTRODUCTION

There is a considerable interest in the chemotherapeutic activity of pyrazole, oxazole and pyrimidine derivatives. They have been reported to exhibit broad spectrum of biological effects including analgesic [1], antimicrobial [2-5], anti-inflammatory [6-9], hypoglycemic [10-12] activity. On the other hand a wide variety of pharmacological properties are encountered with naphthalene derivatives [4]. Therefore, it was felt interesting to synthesise fused heterocyclic systems incorporating the naphthalene moiety and one of the above biologically active heterocycles with the two fold objective of preparing compounds of biological importance and studing the regiochemistry of the condensation process.

INVESTIGATIONS AND RESULTS

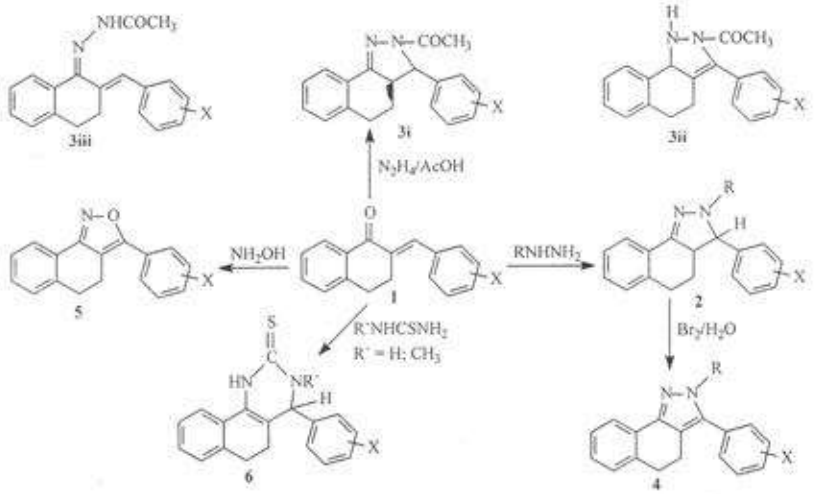
Synthesis of derivatives

Condensation of 2-arylmethylidene-1-tetralones **1** with hydrazine derivatives yielded the corresponding naphtho[1,2-c]pyrazoline derivatives **2** in good yields (Scheme 1). The ^{1}HNMR spectra of pyrazoline derivatives **2** exhibited beside the aromatic protons at δ 6.80-8.40, a doublet at δ 3.63-5.80, a triplet of doublets at δ 2.88-3.75, a doublet of doublets at δ 2.71-2.98 and two multiplets in the regions δ 1.08-1.96 and 1.88-2.28 for H-3, H-3a, H-5 (axial and equatorial), H-4(axial) and H-4 (equatorial) respectively, (Table 1). Here the coupling constants of 12.5-13 Hz, indicate vicinal protons in diaxial configurations, whilst values of 4.5-5.0 Hz are typical for axial-equatorial relationships [13]. As the multiplets show, the protons at δ 3.63-5.80 (H-3) couples with one axial proton (d; $J_{3,3a}$ (anti) ~ 13 Hz). The protons at δ 2.92-3.75 (H-3a) couples with two axial and one equatorial proton (td; $J_{3a,3}$ (anti) ~ 13 Hz, $J_{3a,4}$ (syn) ~ 5 Hz), whereas the protons at δ 2.71-2.98 (H-5) each couple with one axial and one equatorial protons (dd; $J_{4,5}$ (anti) ~ 13 Hz, $J_{3,4}$ (syn) ~ 5 Hz).

The structure of the above pyrazolines was further supported from their ^{13}C NMR spectra (Table 2). The physical and analytical data for all prepared compounds recorded in Table 3. The relative configuration of the two chiral centers in pyrazoline derivatives was confirmed by X-ray crystallography which showed an anti relationship between neighbouring protons H-3 and H-3a (Fig. 1).

Condensation of hydrazine hydrate with chalcones (1B, 1C, 1E and 1H) in ethanol gave brown oils from which no solid could be isolated. However, when the reaction was carried out in glacial acetic acid, crystalline products were isolated which from analytical data (Table 3) were shown to be either mixture of acetylpyrazoline derivatives **3i** and **3ii** or acetylhydrazone derivatives **3iii** (Scheme 1). The infrared spectra of the products showed a band characteristic of the carbonyl stretching frequency of solid amides in the range 1660-1667 cm^{-1} but no band characteristic of ν_{NH} group. Moreover, the ^1H NMR spectra exhibited two doublets at δ 4.95-5.04 and 5.70-5.78 for two H-3 as well as a mulliplet of two protons intensity at δ 2.95-3.00 for two H-3a as a result of the two diastereo-isomers present (Table 1). These spectral data completely rule out structures **3ii** and **3iii** and thus structure **3i** was assigned to be the reaction product.

It worthily to mention here that except in case of methyl and phenylhydrazines, the reaction of the 2-arylinethylidene-1-tetralones with hydra-zines afforded a mixture of two stereoisomers as could be observed clearly from their ^1H NMR and ^{13}C NMR spectral data (Tables 1 and 2). These are opposite in relative configuration on H-3 and H-3a, since the coupling constants are the same ($J_{3,3a}$ – 13Hz) in both isomers, this seems very unlikly that the N acetyl compound could be mixture of amide rotamers around the N atom in position 2.



X = A : H; B : m-Me; C : p-Me; D : p-MeO-; E : p-NO_2-; F : p-Cl; G : m-Br-; H : p-Br
R = H, Me, COMe, C_6H_5, p-ClC_6H_4, p-$NH_2SO_2C_6H_4$

Scheme 1

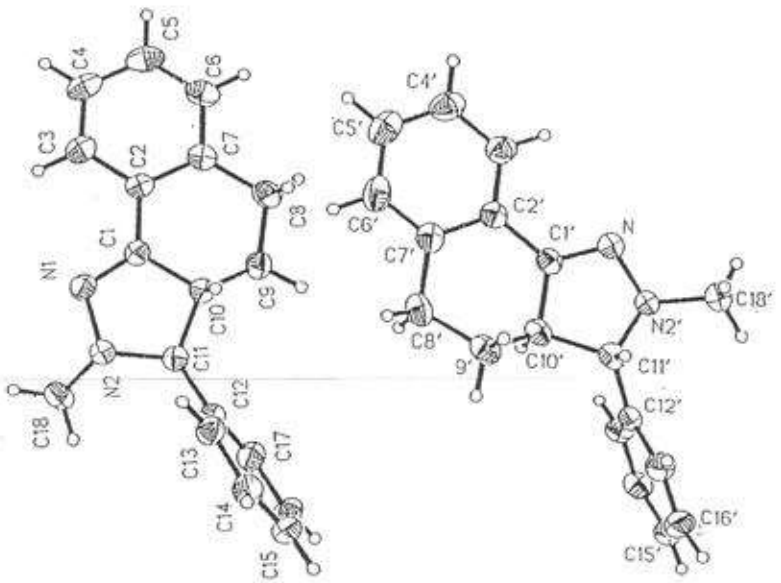


Figure 1: Molecular structure and atom numbering scheme for the two unique molecules of **2Ab**. Displacement ellipsoids are drawn at the 30% probability level and H-atoms are drawn as spheres of arbitary radius.

Mild oxidation of the pyrazoline derivatives **2** and **3** with bromine water afforded the corresponding naphthopyrazoles **4** (Scheme 1). In agreement with the suggested structures, the pyrazole derivatives lacked the signals characteristic of H-3 and H-3a in the corresponding pyrazolines and exhibited the aromatic protons as multiplets in the region δ 7.00-8.14 in addition to another multiplet of four proton intensity at δ 3.12-3.28 for H-4 and H-5 (Table 1).

Condensation of hydroxylamine with α,β-unsaturated ketones usually yields the corresponding isoxazolines and in some cases the product was found to be the isoxazole derivative [14]. However in our case the reaction of chalcones **1** with hydroxylamine hydrochloride in presence of sodium acetate yielded the corresponding isoxazole derivatives **5** as evidenced by ^{1}H NMR spectra. It exhibited beside the aromatic protons two multiplets each of two proton intensity at δ 3.04-3.06 and 3.12-3.25 for the H-4 and H-5 respectively.

In view of the usefulness of 2-mercapto-1,4-dihydropyrimidine as a vulcanizing accelerator agents and photography stabilizers [15], the condensation of the 2-arylmethylidene-1-tetralones **1** with thiourea and methylthiourea was effected in boiling enthanolic potassium hydroxide solution to yield the corresponding naphtho[1,2-d]pyrimidine-2-thione derivatives **6** (Scheme 1). Their IR spectra exhibited bands for NH, C = S supporting the given structures. The structures of these pyrimidine derivatives **6** were further supported by their ^{1}H NMR spectra (Table 1).

Table 1: ^{1}H NMR Spectral data[a] of Compounds (2-6)

Compd. No.	X	R or R'	H-3 (d,1H) (J=13Hz)	H-3a (td,1H) (J=13,13.5Hz)	H-4 (2mm,2H)	H-5 (dd,2H) (J=13.5Hz)	ArH (m)	Others CH_3 &/or CH_3O
2Ab	H	CH_3	3.70	3.15	1.85,2.15	2.87	7.10-7.98	2.82
2Ad	H	C_6H_5	4.64	3.29	1.75,2.21	2.90	6.80-8.18	
2Ae	H	p-ClC_6H_4	5.44,4.58	3.75,3.20	1.08,178[b]	2.98,2.85	6.98-8.10	
2Af	H	p-NH_2SO_2-C_6H_4	5.68,4.60	3.30[c]	1.12,230[b]	2.73[d]	6.88-8.00[e]	
2Cb	p-CH_3	CH_3	3.70	3.28	1.86,2.14	2.88	6.98-8.10	2.86,2.41
2Cd	p-CH_3	C_6H_5	4.65	3.18	2.24[f]	2.90	6.92-8.28	2.45
2Cc	p-CH_3	p-ClC_6H_4	5.35,4.55	2.92[a]	1.09,1.88[b]	2.83[d]	6.85-8.22	2.34,2.26
2Cf	p-CH_3	p-NH_2SO_2-C_6H_4	5.70,4.76	3.63[c]	1.12,200[b]	2.82[d]	6.98-8.28[e]	2.32,2.28
2Db	p-CH_3O	CH_3	3.63	3.10	1.82,2.12	2.88	6.95-7.95	2.80,3.84
2Dd	p-CH_3O	C_6H_5	4.78	3.27	2.25[f]	2.81	6.91-8.15	3.78
2De	p-CH_3O	p-ClC_6H_4	5.40,4.60	2.88[a]	1.07,1.78[b]	g	6.82-8.15	3.72,3.70
2Eb	p-NO_2	CH_3	3.86	3.14	1.80,2.20	2.87	7.10-8.40	2.82
2Fb	p-Cl	CH_3	3.65	3.08	1.83,2.11	2.86	7.10-7.96	2.78
2Ff	p-Cl	p-NH_2SO_2-C_6H_4	5.80,4.82	3.62[c]	1.15,2.19[b]	2.78[d]	6.91-8.30[e]	
2Ge	in-Br	p-ClC_6H_4	5.41,4.57	365[c]	1.15,228[b]	2.82[d]	6.94-8.28	
2Hb	p-Br	CH_3	3.68	3.10	1.80,2.15	2.88	7.00-8.12	2.80
2Hd	p-Br	C_6H_5	4.58	3.20	1.92,2.21	2.89	6.95-8.16	
2Hf	p-Br	p-NH_2SO_2-C_6H_4	5.78,4.78	3.65[c]	1.15,2.27[b]	280[d]	6.98-8.20[e]	
3Cc	p-CH_3	$COCH_3$	5.72,4.95	2.99[a]	1.18,1.98[b]	g	6.90-8.20	2.34,2.30, 2.48,2.40[h]
3Hc	p-Br	$COCH_3$	5.70,4.95	3.00[a]	1.16,1.89[b]	g	6.93-8.20	2.49,2.43[h]
4Ae	H	p-ClC_6H_4			3.28[b]	i	7.00-7.92[g]	
4Cf	p-CH_3	p-NH_2SO_2-C_6H_4			3.12[b]	i	7.10-8.14[e]	2.28
5B	m-CH_3				3.04	3.12	6.90-8.20	2.43
5H	p-Br				3.06	3.25	7.15-8.20	
6Aa	H	H	5.00[j]		2.10[k]	2.78[l]	7.00-7.92	9.00,9.35[m]
6Cb	p-CH_3	p-CH_3	4.85[n]		2.150[k]	2.82[l]	7.10-8.25	2.35,2.82

a: Solution in a mixture of $CDCl_3$ and DMSO-d_6, δ in ppm; b: 4H; c: Multiplet, 2H; d: m, 4H; j: d, H-4; e: NH overlapped by aromatic protons; f: Multiplets overlapped; g : Overlapped by H-3a; h: CH_3CO; i: overlapped by H-4; k: m,H-5; l: m,H-6; m: NH and n: s,H-4.

Table 2: ^{13}C NMR Spectral Data* of Compounds (2-5)

Compd. No.	X	R	C-3	C-3a	C-4	C-5	C-Ar	Other C
2Ab	H	CH_3	81.0	55.1	27.3	29.7	124.5, 127.0, 127.9, 128.3, 128.8, 129.1, 129.3, 129.4, 138.6, 140.1, 152.6	42.5 (N-CH_3)
2Ad	H	C_6H_5	73.6	56.5	27.8	29.7	115.5, 120.3, 124.6, 125.6, 126.0, 127.8, 128.4, 128.8, 129.3, 130.0, 134.2, 137.8, 142.4, 147.1, 150.7	
2Ae	H	p-ClC_6H_4	73.8 67.2	56.8 49.7	25.4 23.8	27.6 25.9	114.9, 116.4, 117.6, 118.5, 123.1, 124.2, 124.6, 125.0, 126.5, 127.0, 128.0, 128.1, 128.5, 128.8, 129.1, 129.4, 129.8, 132.6, 133.0, 137.0, 138.7, 138.8, 141.3, 142.0, 146.3, 147.1, 149.1, 151.0	
2Cb	p-CH_3	CH_3	80.1	SO.S	27.0	29.5	122.5, 123.4, 124.6, 125.0, 127.2, 127.8, 128.2, 129.1, 138.S, 140.0, 152.5	20.1 (CH_3), 42.0 (N-CH_3)
2Cd	p-CH_3	C_6H_5	73.2	56.0	27.4	29.4	115.4, 120.1, 124.0, 124.9, 126.2, 127.8, 128.0, 128.1, 129.5, 130.0, 133.7, 137.4, 143.S, 147.2, 150.8	21.7 (CH_3)
2Cf	p-CH_3	p-$NH_2SO_2C_6H_4$	70.1 6S.6	S6.S 48.8	26.8 23.6	29.0 28.3	111.7, 124.1, 126.2, 126.6, 127.2, 127.S, 127.7, 128.0, 128.6, 128.8, 128.9, 129.1, 129.4, 129.6, 129.8, 132.3, 132.6, 133.0, 134.3, 136.2, 138.1, 138.5, 142.9, 145.9, 150.7	21.1, 20.7(CH_3)
2Db	p-OCH_3	CH_3	80.7	52.1	27.6	28.9	123.0, 124.2, 126.3, 127.4, 128.1, 128.8, 129.5, 129.7, 138.1, 142.4, 153.2	42.2 (N-CH_3), 54.7 (OCH_3)

Table 2: Cont.

Compd. No.	X	R	C-3	C-3a	C-4	C-5	C-Ar	Other C
2Fb	p-Cl	CH_3	79.8	54.8	26.7	29.2	124.1,126.6, 128.7, 128.8, 128.9,129.0, 129.1, 133.5, 138.0,138.2, 152.0	42.0 ($N\text{-}CH_3$),
2Hb	p-Br	CH_3	80.1	50.5	27.0	29.5	123.4,125.0, 126.5, 127.2, 128.2,129.1, 130.5, 137.1, 138.5,140.0, 152.5	42.0 ($N\text{-}CH_3$),
2Hd	p-Br	C_2H_5	73.6	55.8	27.6	29.2	116.2,121.4, 124.3, 125.0, 126.7,127.2, 127.8, 128.0, 128.8,129.6, 133.0, 138.0, 144.0,146.3, 151.0	
3Hc	p-Br	$COCH_3$	67.1 62.7	55.7 48.6	27.3 24.4	28.8 28.0	124.9,125.1, 126.8, 127.2, 127.4,127.8, 128.2, 128.5, 129.2,130.6, 130.8, 131.6, 131.8,131.9, 133.6, 135.1, 136.5,139.7, 141.2, 155.8	22.2, 21.8 (CH_3CO), 168.5, 171.5, (CO)
4Ae	H	p-ClC_6H_4			29.5	30.1	115.5118.9, 121.4, 125.8, 126.2127.6, 128.0, 128.5 129.0,129.2, 129.2, 130.5, 131.5,133.7, 143.5, 147.1, 150.8	
5B	m-CH_3				28.9	29.8	116.6117.2, 121.1, 125.7, 126.0, 127.8, 128.3, 128.9 129.4, 130.5, 131.5, 132.4, 134.4, 136.2, 142.5, 148.3, 154.2	21.9(CH_3)

a:Solution in a mixture of $CDCl_3$ and DMSO-d_6.

Table 3: Physical and Analytical Data of Compounds (2-6)

Compd. no.	X	R or R'	Yield (%)	M.P. °C	Molecular Formula	Found %				Calc. %			
						C	H	N	S	C	H	N	S
2Ab	H	CH_3	78	136	$C_{18}H_{16}N_2$	82.21	6.66	10.45		82.44	6.87	10.69	
2Ad	H	C_6H_5	72	152	$C_{23}H_{18}N_2$	85.01	5.97	8.42		85.19	6.17	8.64	
2Ae	H	p-ClC_6H_4	70	186	$C_{23}H_{17}ClN_2$	77.08	5.14	7.65		76.99	5.30	7.81	
2Af	H	p-$SO_2NHC_6H_4$	88	235	$C_{23}H_{19}N_3O_2S$	68.40	5.21	10.62	8.02	68.51	5.24	10.41	7.93
2Bb	m-CH_3	CH_3	76	66	$C_{19}H_{18}N_2$	82.30	7.13	10.07		82.61	7.25	10.14	
2Bd	m-CH_3	C_6H_5	84	120	$C_{24}H_{20}N_2$	85.45	6.32	8.43		85.21	6.51	8.28	
2Be	m-CH_3	p-ClC_6H_4	81	143	$C_{24}H_{19}ClN_2$	77.12	5.48	7.39		77.32	5.64	7.52	
2Cb	p-CH_3	CH_3	73	150	$C_{19}H_{18}N_2$	82.32	7.52	10.32		82.61	7.25	10.14	
2Cd	p-CH_3	C_6H_5	96	131	$C_{24}H_{20}N_2$	85.06	6.64	8.42		85.21	6.51	8.28	
2Ce	p-CH_3	p-ClC_6H_4	80	200	$C_{24}H_{19}ClN_2$	77.15	5.47	7.43		77.32	5.64	7.52	
2Cf	p-CH_3	p-$SO_2NH_2C_6H_4$	71	202	$C_{24}H_{21}N_3O_2S$	68.95	5.42	10.11	7.78	69.06	5.52	10.07	7.67
2Db	p-CH_3	OCH_3	72	183	$C_{20}H_{20}N_2O$	77.96	6.64	9.38		78.08	6.85	9.59	
2Dd	p-CH_3	OC_6H_5	70	102	$C_{25}H_{22}N_2O$	81.52	6.03	7.76		81.36	6.21	7.91	
2De	p-CH_3O	p-ClC_6H_4	72	206	$C_{24}H_{19}ClN_2O$	74.36	5.21	7.06		74.13	5.41	7.21	
2Eb	p-NO_2	CH_3	71	241	$C_{19}H_{17}N_3O_2$	70.12	5.36	13.42		70.36	5.54	13.68	
2Ed	p-NO_2	C_6H_5	89	165	$C_{24}H_{19}N_3O_2$	74.65	4.96	11.15		74.80	5.15	11.38	
2Ee	p-NO_2	p-ClC_6H_4	75	189	$C_{24}H_{18}ClN_3O_2$	68.21	4.27	10.35		68.40	4.46	10.41	
2Eb	p-Cl	CH_3	72	193	$C_{19}H_{17}ClN_2$	72.63	5.51	9.28		72.85	5.73	9.44	
2Ed	p-Cl	C_6H_5	70	112	$C_{24}H_{19}ClN_2$	77.04	5.17	7.75		76.99	5.30	7.81	
2Fe	p-Cl	p-ClC_6H_4	68	152	$C_{24}H_{18}Cl_2N_2$	70.06	4.46	6.99		70.23	4.58	7.21	
2Ff	p-Cl	p-$SO_2NH_2C_6H_4$	78	252	$C_{23}H_{19}ClN_3O_2S$	63.30	4.73	9.75	7.46	63.09	4.57	9.60	7.31
2Gb	m-Br	CH_3	61	106	$C_{19}H_{17}BrN_2$	63.19	4.76	8.06		63.34	4.99	8.21	
2Gd	m-Br	C_6H_5	92	174	$C_{24}H_{19}BrN_2$	68.49	4.71	6.95		68.49	4.71	6.95	
2Ge	m-Br	p-ClC_6H_4	76	177	$C_{24}H_{18}BrClN_2$	63.12	3.99	6.31		63.09	4.11	6.40	
2Gf	m-Br	p-$SO_2NH_2C_6H_4$	73	264	$C_{23}H_{19}BrN_3O_2S$	57.12	4.47	8.58	6.59	57.26	4.15	8.71	6.64
2Hb	p-Br	CH_3	70	209	$C_{19}H_{17}BrN_2$	63.02	5.05	8.52		63.34	4.99	8.21	
2Hd	p-Br	C_6H_5	73	174	$C_{24}H_{19}BrN_2$	68.28	4.69	6.72		**68.49**	4.71	6.95	
2He	p-Br	p-ClC_6H_4	70	210	$C_{24}H_{18}BrClN_2$	63.41	4.21	6.42		63.09	4.11	6.40	
2Hf	p-Br	p-$SO_2NH_2C_6H_4$	75	240	$C_{23}H_{19}BrN_3O_2S$	57.52	3.99	8.86	6.37	57.26	4.15	8.71	6.64

Table 3: Cont.

Cmpd. no	X	R or R'	Yield (%)	M.P. °C	Molecular Formula	Found %				Calc. %			
						C	H	N	S	C	H	N	S
3Bc	m-CH_3	$COCH_3$	64	84	$C_{20}H_{20}N_2O$	78.82	6.75	9.42		78.95	6.58	9.21	
3Ce	p-CH_3	$COCH_3$	66	86	$C_{19}H_{18}N_2O$	79.1	6.39	9.06		78.95	6.58	9.21	
3Ee	p-NO_2	$COCH_3$	78	180	$C_{18}H_{17}N_3O_3$	68.16	4.99	12.87		68.06	5.07	12.54	
3Hc	p-Br	$COCH_3$	85	110	$C_{18}H_{17}BrN_2O$	61.79	4.32	7.64		61.79	4.61	7.59	
4Ae	H	p-ClC_6H_4	68	121	$C_{23}H_{17}ClN_2$	77.22	5.02	8.00		77.42	4.77	7.85	
4Cf	p-CH_3	p-$SO_2NH_2C_6H_4$	88	148	$C_{24}H_{23}N_3O_2S$	69.30	4.99	10.23	7.51	69.40	5.06	10.12	7.71
4Ff	p-Cl	p-$SO_2NH_2C_6H_4$	75	174	$C_{23}H_{20}ClN_3O_2S$	63.30	4.05	9.70	7.22	63.38	4.13	9.64	7.35
4Gf	m-Br	p-$SO_2NH_2C_6H_4$	77	142	$C_{23}H_{20}BrN_3O_2S$	57.13	4.00	8.56	6.98	57.50	3.75	8.75	6.67
4Hc	p-Br	$COCH_3$	72	100	$C_{16}H_{15}BrN_2O$	61.98	3.92	7.40		62.12	4.89	7.93	
5B	m-CH_3		48	89	$C_{17}H_{15}NO$	82.57	5.63	5.18		82.76	5.75	5.36	
5C	p-CH_3		42	117	$C_{17}H_{15}NO$	82.48	5.92	5.60		82.76	5.75	5.36	
5E	p-NO_2		57	182	$C_{17}H_{12}N_2O_3$	69.57	3.99	9.21		69.86	4.11	9.59	
5G	m-Br		42	90	$C_{17}H_{12}BrNO$	62.21	3.46	4.06		62.58	3.68	4.29	
5I	p-Br		40	151	$C_{17}H_{12}BrNO$	62.33	3.52	3.99		62.58	3.68	4.29	
6Aa	H	H	71	260	$C_{14}H_{10}N_2S$	73.77	5.52	9.32	11.00	73.97	5.48	9.59	10.95
6Cb	p-CH_3	CH_3	68	157	$C_{28}H_{20}N_2S$	74.87	6.00	8.92	10.22	75.00	6.25	8.75	10.00
6Fb	p-Cl	CH_3	70	147	$C_{28}H_{17}ClN_2S$	67.11	5.02	8.07	9.51	66.96	4.99	8.22	9.39
6Hb	p-Br	CH_3	66	177	$C_{28}H_{17}BrN_2S$	59.12	4.30	7.50	8.45	59.22	4.42	7.27	8.31

Antimicrobial activity:

Antimicrobial testing of the compounds **1-6** was carried out against gram-positive Staphylococcus aureus and gram-negative Escherichia coli. The antifungal testing was carried out against Candida albicans. It was found that all compounds were not significantly active towards the organisms used.

EXPERIMENTAL

Melting points were determined on Kofler hot stage apparatus and are uncorrected. IR spectra were recorded on a Nicolet FT-IR spectrometer Magna 520. ^1H & ^{13}C NMR spectra were scanned on a Varian EM-360L, or on Bruker DPX-400FT NMR spectrometers using TMS as internal standard. MS spectra were determined on a Kratos MS 30.

2,3-Disubstituted 3,3a,4,5-tetrahydronaphtho[1,2-c]pyrazoles 2

A solution of the appropriate 2-arylmethylidene-1-tetralone 1 (0.002 mol) in ethanol *(50* ml) was heated under reflux with the proper hydrazine derivative (0.0021 mol) for 41w. After concentration the pyrazole derivative separated and was recrystallized from ethanol as needles.

2Ab: ms m/z (relative abundance): 262 (M^+, 100), 185 (M-C_6H_5, 97), 144 (15), 130 (8), 118 (27), 116 (26), 115 (13), 91(44), 77(26), 65(15), 51(28).

2Ad: ms: m/z (relative abundance): 324 (M^+, 100), 247 (M-C_6H_5, 51), 232 (M-C_6H_5, 9), 218 (41), 206 (6), 180 (15), 144 (4), 130 (6), 104 (8), 118 (10), 116 (9), 115 (18), 91(34), 77 (53), 64 (15), 51(25).

2-Acetyl-3-aryl-3,3a,4,5-tetrahydronaphtho[1-,2-c]pyrazole 3

A mixture of the appropriate 2-arylmethylidene-1-tetralone (0.002 mole) and hydrazine hydrate (0.3m1) in glacial acetic acid (10 ml) was heated under reflux for 10 hrs. The reaction mixture was then cooled and poured into water, the acetylpyrazole which separated out was filtered off and recrystallized from methanol as cream needles.

2,3-Disubstituted 4,5-dihydronaphtho[1,2-c]-pyrazoles 4

To a suspension of **2** or **3** (0.002 mol) in water (10 ml), bromine water (5%, 20 ml) was gradually added (lhr.) with stirring at 25 °C. The pyrazole derivative that separated was recrystallized from ethanol as needles.

3-Substituted 4,5-dihydronaphtho[1,2-c]isoxazoles 5

A solution of the appropriate 2-arylmethylidene-1-tetralone **1** (0.002 mol) in ethanol (30 ml) was heated under reflux with a mixture of hydroxylamine (0.002 1 mol) and NaOAc (0.2g) in water (1 ml), for 4hr. The reaction mixture was then poured into water and the product which separated was filtered off and recrystallized from ethanol as needles.

5C: ms: m/z (relative abundance): 261(M^+,16); 247(79), 233(100); 215(4); 202(7); 129(13); 128(11); 115(13); 105(21); 101(11); 91(14); 89(11); 76(7); 60(49); 55(52).

3,4-Disubstituted 1,2,3,4,5,6-hexahydronaphtho[1,2-d] pyrimidine 6

A mixture of the appropriate aryl-methylidene-1-tetralone 2 (0.002 mol), the appropriate thiourea derivative (0.004 mol), KOH (0.3g), ethanol (50 ml) and water (2 ml) was heated under reflux for 5 hr. The reaction mixture was then cooled, poured into water and the solid which separated out was filtered off and recrystallized from ethanol-benzene mixture (2:1) as needles.

Biological testing

Compounds **1-6** were screened for antibacterial and antifungal activity by the agar-diffusion method [16], using gram-positive bacteria Staphylococcus aureus and gram-negative bacteria Escherichia coli. The antifungal testing was carried out against Candida albicans. A standard sterillized filter paper disc (5 mm dia) impregnated with a solution of the tested compound in C_2H_5OH (1 mg ml^{-1}) was placed on an agar plate seeded with the tested organism. The plates were incubated for 24h at 37 °C and the zone of inhibition of bacterial growth round the disc was observed.

Form the screening results, it was evident that all the compounds were not significantly active towards the organisms used (inhibition zone was found in the range 5.5-6 mm). Hence, no specific structure activity relationship could be established.

Crystal data for compound 2Ab:

$C_{18}H_{18}N_2$, M=262.34, Triclinic, Space group P1, a = 9.549(1), b = 10.168(1), c = 16.704(4) Å^3, Z = 4, Dc = 1.202 Mgm^{-3}, F(000) = 560, μ = 0.071 mm^{-3}, λ(Mo-Kα) = 0.7107Å.

The crystal used for data collection was a colourless block with the approximate dimensions 0.44 x 0.34 x 0.28 mm. Unit cell parameters were determined by least squares refinement of the optimised setting angles of 40 reflections in the range $5.2 < \theta < 12.4°$. Intensity data for 4689 reflections were measured on a Siemens P4 diffractometer at 190K using an ω scan method. The reflections were corrected for Lorentz and polarization effects to yield 4269 independant reflections (R_{int} = 0.012). The structure was solved by direct methods and refined by full-matrix least squares on F^2 using the program SHELXTL/PC[1] [17]. Two unique molecules were found in the unit cell with minor differences in the orientation of the aryl group such that the torsion angles N2-C11-C12-C13 and N2'-C11'-C12'-C13' of the two molecules are -48.7° and -58.1° respectively. All hydrogen atoms were included in calculated positions (C-H = 0.96Å) with isotropic displacement parameters set to 1.5 Ueq(C) for metyl groups and 1.2 Ueq(C) for remaining H atoms. All non-hydrogen atoms were refined with anisotropic displacement parameters. Final cycles of refinement gave R1 = 0.045, wR2 = 0.107 for all data, $R1 = \Sigma||Fo| - |Fc||/\Sigma|Fo|$, $wR2 = [\Sigma w(Fo^2 - Fc^2)^2/\Sigma w(Fo^2)^2]^{1/2}$, $w = 1/[\sigma^2(Fo^2) + (0.0432P)^2 + 0.26P]$ and $P = [\max(Fo^2, 0) + 2Fc^2]/3$. Goodness-of-fit, s = 1.004 and the maximum and minimum electron densities in the final ΔF map were 0.14 and -0.13 e Å^{-3} respectively.

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