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Short communication

Synthesis of some thiazolyl-pyrazoline derivatives and preliminary investigation of their hypotensive activity

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Abstract – Some 1-(4-arylthiazol-2-yl)-3,5-diaryl-2-pyrazoline derivatives were synthesized by reacting 1-thiocarbamoyl-3,5-diaryl-2-pyrazoline derivatives with phenacetylbromide in ethanol. The structural elucidation of the compounds were performed by IR, ^{1}H-NMR and Mass spectral data and elemental analyses. The hypotensive activities of 13 compounds were evaluated by using the tail-cuff method. All examined compounds showed appreciable hypotensive activities. Clonidine was used as reference substance in the pharmacological evaluation. © 2000 Éditions scientifiques et médicales Elsevier SAS

thiazol / pyrazoline / thiazolyl-pyrazoline / chalcone / hypotensive activity

1. Introduction

Compounds including a pyrazole nucleus are known to possess analgesic, anti-inflammatory, antipyretic, antiarrhythmic, tranquillizing, muscle relaxant, psychoanaleptic, anticonvulsant, hypotensive, monoamine oxidase inhibitor, antidiabetic and antibacterial activities [1–9].

Some thiazol derivatives have been reported to possess tuberculostatic, antibacterial and antifungal activities [10–14].

It was also reported that one of the modified forms of clonidine **I**, thiazolo-imidazoline derivative **II**, is as potent as clonidine itself [15]. This result encouraged us to study several thiazolyl-pyrazoline derivatives **III** bearing structural and isosteric relationships to **I** and **II** (*figure 1*).

In this study, 39 1-(4-aryl-thiazol-2-yl)-3,5-diaryl-2-pyrazoline derivatives were synthesized and the hypotensive activities of 13 of them were studied in rats by using tail-cuff method.

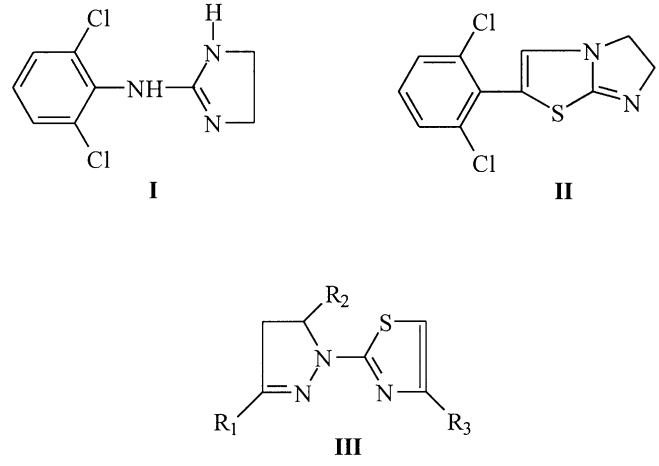

Figure 1. Structures of I–III.

2. Chemistry

The synthesis of the new compounds was carried out as outlined in *figure 2*. 1-Thiocarbamoyl-3,5-diaryl-2-pyrazoline derivatives **III** were synthesized by the reac-

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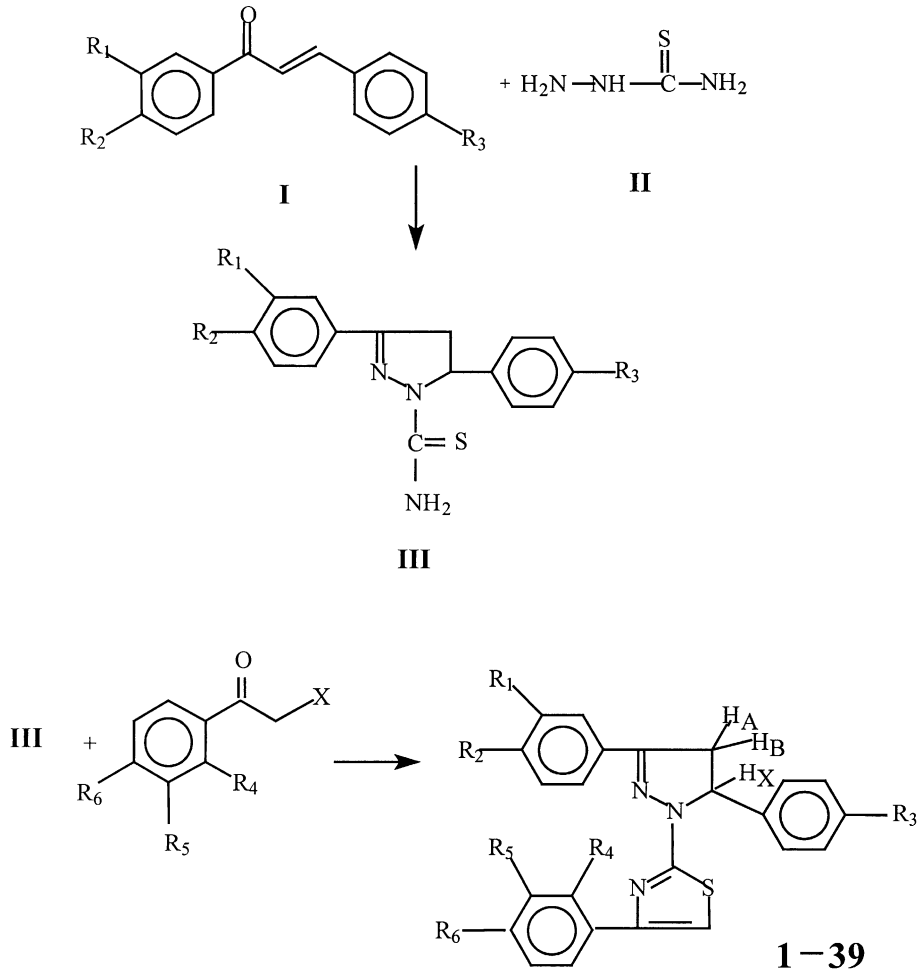

Figure 2. Synthesis of 1-(4-arylthiazol-2-yl)-3,5-diaryl-2-pyrazoline.

tion of 1,3-diaryl-2-propen-1-ones (chalcones) **I** with thiosemicarbazide **II** in accordance with the method described in literature [16].

1-(4-Arylthiazol-2-yl)-3,5-diaryl-2-pyrazoline derivatives **1–39** were obtained by reacting compounds **III** with phenacetylbromide in ethanol (*figure 2*). Some characteristics of the compounds are presented in *table I*.

3. Pharmacology

The hypotensive activity of 13 compounds chosen randomly was determined in vivo. Albino rats of either sex weighing 200 ± 10 g were used in this study. There were seven animals in each group. The compounds were dissolved in DMSO. The arterial blood pressures of the conscious rats were measured by the tail-cuff method [17, 18] and using an indirect blood pressure recorder. The blood pressure of each rat was measured before and 30 min after the intraperitoneal injection of the compounds. Each compound was given at 20 mg/kg dose in 0.1 mL volume. The same volume of DMSO was administered to the animals in the control group. Clonidine (0.5 mg/kg) was used as a reference drug. The reduction of blood pressures between two measurements were recorded as mm Hg. The results were expressed as mean ± SEM. Student's *t*-test was used for statistical analysis (*table II*).

The tested compounds showed hypotensive activity. The magnitude of their effects after acute i.p. administration of single doses (20 mg/kg) was less pronounced than

Table I. Physico-chemical data of the compounds.

	R_1	R_2	R_3	R_4	R_5	R_6	M.p. °C	Yield %	Mol. For.
1	H	H	H	H	H	H	215	72	$C_{24}H_{19}N_3S$
2	H	H	H	H	H	NO_2	233	81	$C_{24}H_{18}N_4O_2S$
3	H	H	H	H	NO_2	H	217	80	$C_{24}H_{18}N_4O_2S$
4	H	H	H	OH	H	H	219	75	$C_{24}H_{19}N_3OS$
5	H	H	H	OH	H	OCH_3	227	72	$C_{25}H_{21}N_3O_2S$
6	Cl	H	H	H	H	H	186	72	$C_{24}H_{18}ClN_3S$
7	Cl	H	H	H	H	NO_2	251	75	$C_{24}H_{17}ClN_4O_2S$
8	Cl	H	H	H	H	Cl	189	68	$C_{24}H_{17}Cl_2N_3S$
9	Cl	H	H	H	NO_2	H	207	74	$C_{24}H_{17}ClN_4O_2S$
10	Cl	H	H	OH	H	H	222	75	$C_{24}H_{18}ClN_3OS$
11	OCH_3	H	H	H	H	H	213	77	$C_{25}H_{21}N_3OS$
12	OCH_3	H	H	OH	H	H	212	71	$C_{25}H_{21}N_3O_2S$
13	OCH_3	H	H	OH	H	OCH_3	220	65	$C_{26}H_{23}N_3O_3S$
14	CH_3	CH_3	H	H	H	H	191	82	$C_{26}H_{22}N_3S$
15	CH_3	CH_3	H	H	H	NO_2	235	77	$C_{26}H_{22}N_4O_2S$
16	CH_3	CH_3	H	H	H	Cl	166	73	$C_{26}H_{21}ClN_3S$
17	CH_3	CH_3	H	H	H	CH_3	197	70	$C_{27}H_{24}N_3S$
18	CH_3	CH_3	H	OH	H	H	214	65	$C_{26}H_{22}N_3OS$
19	CH_3	CH_3	H	OH	H	OCH_3	192	62	$C_{27}H_{24}N_3O_2S$
20	CH_3	CH_3	H	H	NO_2	H	237	78	$C_{26}H_{22}N_4O_2S$
21	H	H	OCH_3	H	H	H	184	60	$C_{25}H_{21}N_3OS$
22	H	H	OCH_3	OH	H	OCH_3	192	62	$C_{26}H_{23}N_3O_3S$
23	$-(CH_2)_3-$		H	H	H	H	201	70	$C_{27}H_{23}N_3S$
24	$-(CH_2)_3-$		H	H	H	NO_2	228	74	$C_{27}H_{22}N_4O_2S$
25	$-(CH_2)_3-$		H	H	H	Cl	179	68	$C_{27}H_{22}ClN_3S$
26	$-(CH_2)_3-$		H	H	H	OCH_3	222	68	$C_{28}H_{25}N_3OS$
27	$-(CH_2)_3-$		H	H	H	CH_3	181	70	$C_{28}H_{25}N_3S$
28	$-(CH_2)_3-$		H	H	NO_2	H	207	76	$C_{27}H_{22}N_4O_2S$
29	$-(CH_2)_3-$		H	OH	H	H	225	73	$C_{27}H_{23}N_3OS$
30	$-(CH_2)_3-$		H	OH	H	Cl	226	67	$C_{27}H_{22}ClN_3OS$
31	$-(CH_2)_3-$		H	OH	H	OCH_3	191	75	$C_{28}H_{25}N_3O_2S$
32	$-(CH_2)_3-$		H	CH_3	H	OH	83	65	$C_{28}H_{25}N_3OS$
33	$-(CH_2)_4-$		H	H	H	H	191	74	$C_{28}H_{25}N_3S$
34	$-(CH_2)_4-$		H	H	H	NO_2	186	77	$C_{28}H_{24}N_4O_2S$
35	$-(CH_2)_4-$		H	H	NO_2	H	197	75	$C_{28}H_{24}N_4O_2S$
36	$-(CH_2)_4-$		H	OH	H	H	224	68	$C_{28}H_{25}N_3OS$
37	$-(CH_2)_4-$		H	OH	H	OCH_3	184	67	$C_{29}H_{27}N_3O_2S$
38	$-(CH_2)_4-$		H	OH	H	Cl	208	60	$C_{28}H_{24}N_3ClOS$
39	$-(CH_2)_4-$		H	CH_3	H	OH	88	58	$C_{29}H_{27}N_3OS$

that of an optimal dosage of the reference drug clonidine (0.5 mg/kg) in the same experimental conditions.

4. Results, discussion and conclusions

In the present work, 39 new compounds were synthesized. The structures of all compounds were confirmed by IR, ^{1}H-NMR, Mass spectra and elemental analyses. IR spectra of the compounds showed C=N and C=C stretching bands at 1 630 cm^{-1} and 1 580 cm^{-1}, respectively. In the ^{1}H-NMR spectra, H_A, H_B, H_X protons of pyrazoline ring were seen as doublets of doublets at 3.10–3.30, 4.00–4.10 and 5.60–5.70 ppm (J_{AB} = 17.07, J_{AX} = 6.30, J_{BX} = 11.05 Hz), respectively. The protons belonging to the aromatic ring and phenyl substituents were observed at expected chemical shift and integral values. The 5-H proton of thiazole was observed as a singlet between 7.20 and 7.70 ppm.

According to the results shown in *table II* an increase in the hypotensive activity of the compounds **5**, **19**, **22** and **31** has been observed. It can be concluded that the addition of a hydroxyl group to R_4 and a methoxy group

Table II. Hypotensive activity of compounds.

Compound	Reduction of arterial blood pressure (mm Hg) (X ± SEM)	*n*	Student's *t*-test
1	13.80 ± 3.45	7	$P < 0.05$
3	12.29 ± 3.41	7	$P < 0.05$
5	33.29 ± 6.23	7	$P < 0.05$
9	8.57 ± 1.69	7	$P < 0.05$
16	16.29 ± 4.12	7	$P < 0.05$
19	29.57 ± 9.43	7	$P < 0.05$
20	34.29 ± 8.69	7	$P < 0.05$
21	17.43 ± 4.05	7	$P < 0.05$
22	35.57 ± 10.36	7	$P < 0.05$
31	25.57 ± 7.15	7	$P < 0.05$
34	16.57 ± 3.48	7	$P < 0.05$
35	20.43 ± 6.17	7	$P < 0.05$
36	16.14 ± 7.47	7	$P < 0.05$
Clonidine (0.5 mg/kg)	63.00 ± 4.56	7	$P < 0.001$
Control (DMSO)	3.86 ± 1.038	7	$P < 0.05$

to R_6 leads to an increase in the hypotensive activity of the above compounds. Besides this, compound **20** shows hypotensive activity due to the nitro group at R_5.

5. Experimental protocols

5.1. Chemistry

Melting points were determined by using a Gallenkamp apparatus. Spectroscopic data were recorded by the following instruments: IR, Shimadzu IR-435 spectrophotometer; ^{1}H-NMR, Bruker 250 MHz NMR spectrometer; MS, fast atom bombardment mass spectra (MS-FAB$^+$) were obtained by VG Quattro Mass spectrometer; microanalyses, Leco CHNS elemental analyses apparatus.

5.1.2. General procedure

5.1.2.1. Preparation of 1-thiocarbamoyl-3,5-diaryl-2-pyrazoline derivatives **III**

A mixture of chalcone (0.01 mol), thiosemicarbazide (0.01 mol) and NaOH (0.025 mol) was refluxed in ethanol (25 mL) for 8 h. The solution was poured into ice-water. The precipitate was filtered and crystallized from methanol.

5.1.2.2. 1-Thiocarbamoyl-3-(3′,4′-dimethylphenyl)-5-phenyl-2-pyrazoline

^{1}H-NMR (DMSO-d_6, δ, ppm): 3.10 (1H, dd, H_A), 3.80 (1H, dd, H_B), 5.80 (1H, dd, H_X), 7.00–7.60 (8H, m, aromatic protons), 7.80–8.00 (2H, two s, NH_2), (J_{AB} = 17.94, J_{AX} = 2.85, J_{BX} = 11.30 Hz).

5.1.2.3. 1-Thiocarbamoyl-3-(5′,6′,7′,8′-tetrahydronaphthalene-2′-yl)-5-phenyl-2-pyrazoline

^{1}H-NMR (DMSO-d_6, δ, ppm): 1.70 (4H, s, CH_2), 2.70 (4H, s, CH_2), 3.10 (1H, dd, H_A), 3.80 (1H, dd, H_B), 5.90 (1H, dd, H_X), 7.00–7.60 (8H, m, aromatic protons), 7.80–8.00 (2H, two s, NH_2), (J_{AB} = 18.00, J_{AX} = 3.09, J_{BX} = 11.40 Hz).

5.1.2.4. Preparation of 1-(4-arylthiazol-2-yl)-3,5-diaryl-2-pyrazoline derivatives **1–39**

To a solution of **III** (0.01 mol) in ethanol (30 mL) phenacetylbromide (or w-chloroacetyl substituted phenol) (0.01 mol) was added. The resulting mixture was refluxed for 1 h. After cooling, the solid which separated was recrystallized from ethanol. **1–39**: IR (KBr, cm^{-1}); 1 630 (C=N), 1 580 (C=C).

5.1.2.5. 1-(4-Phenylthiazol-2-yl)-3,5-diphenyl-2-pyrazoline **1**

^{1}H-NMR (DMSO-d_6, δ, ppm): 3.20–3.40 (1H, m, H_A), 4.10 (1H, dd, H_B), 5.70 (1H, dd, H_X), 7.20–7.80 (16H, m, aromatic protons), (J_{AB} = 17.05, J_{AX} = 6.35, J_{BX} = 11.08 Hz). MS (FAB$^+$): M + 1: m/z: 382.

5.1.2.6. 1-[4-(4′-Nitrophenyl)thiazol-2-yl]-3,5-diphenyl-2-pyrazoline **2**

^{1}H-NMR (DMSO-d_6, δ, ppm): 3.30 (1H, dd, H_A), 4.00 (1H, dd, H_B), 5.70 (1H, dd, H_X), 7.20–8.50 (15H, m, aromatic protons), (J_{AB} = 17.25, J_{AX} = 6.37, J_{BX} = 11.88 Hz). MS (FAB$^+$): M + 1: m/z: 427.

5.1.2.7. 1-[4-(3′-Nitrophenyl)thiazol-2-yl]-3,5-diphenyl-2-pyrazoline **3**

^{1}H-NMR (DMSO-d_6, δ, ppm): 3.20–3.40 (1H, m, H_A), 4.05 (1H, dd, H_B), 5.70 (1H, dd, H_X), 7.30–8.50 (15H, m, aromatic protons), (J_{AB} = 17.32, J_{AX} = 6.34, J_{BX} = 10.98 Hz). MS (FAB$^+$): M + 1: m/z: 427.

5.1.2.8. 1-[4-(2′-Hydroxyphenyl)thiazol-2-yl]-3,5-diphenyl-2-pyrazoline **4**

^{1}H-NMR (DMSO-d_6, δ, ppm): 3.10–3.30 (1H, m, H_A), 4.15 (1H, dd, H_B), 5.70 (1H, dd, H_X), 7.10–7.70 (15H, m, aromatic protons), 10.60 (1H, s, OH), (J_{AB} = 17.15, J_{AX} = 6.45, J_{BX} = 11.00 Hz). MS (FAB$^+$): M + 1: m/z: 398.

5.1.2.9. 1-[4-(2′-Hydroxy-4′-methoxyphenyl)thiazol-2-yl]-3,5-diphenyl-2-pyrazoline **5**

^{1}H-NMR (DMSO-d_6, δ, ppm): 3.30–3.50 (1H, m, H_A), 3.75 (3H, s, OCH_3), 3.95–4.10 (1H, m, H_B), 5.70 (1H, dd, H_X), 6.30–7.70 (14H, m, aromatic protons), 10.75 (1H, s, OH), (J_{AX} = 6.35, J_{BX} = 11.95 Hz).

5.1.2.10. 1-(4-Phenylthiazol-2-yl)-3-(3″-chlorophenyl)-5-phenyl-2-pyrazoline **6**

^{1}H-NMR (DMSO-d_6, δ, ppm): 3.20–3.40 (1H, m, H_A), 4.00–4.10 (1H, m, H_B), 5.70 (1H, dd, H_X), 7.20–7.70 (15H, m, aromatic protons), (J_{AX} = 6.72, J_{BX} = 11.35 Hz). MS (FAB$^+$): M + 1: m/z: 416.

5.1.2.11. 1-[4-(4′-Nitrophenyl)thiazol-2-yl]-3-(3″-chlorophenyl)-5-phenyl-2-pyrazoline **7**

^{1}H-NMR (DMSO-d_6, δ, ppm): 3.40–3.60 (1H, m, H_A), 4.15 (1H, dd, H_B), 5.70 (1H, dd, H_X), 7.40–8.60 (14H, m, aromatic protons), (J_{AB} = 17.42, J_{AX} = 6.57, J_{BX} = 11.30 Hz). MS (FAB$^+$): M + 1: m/z: 461.

5.1.2.12. 1-[4-(4′-Chlorophenyl)thiazol-2-yl]-3-(3″-chlorophenyl)-5-phenyl-2-pyrazoline **8**

^{1}H-NMR (DMSO-d_6, δ, ppm): 3.30–3.50 (1H, m, H_A), 4.05 (1H, dd, H_B), 5.70 (1H, dd, H_X), 7.10–7.90 (14H, m, aromatic protons), (J_{AB} = 17.22, J_{AX} = 6.37, J_{BX} = 11.00 Hz). MS (FAB$^+$): M + 1: m/z: 450.

5.1.2.13. 1-[4-(3′-Nitrophenyl)thiazol-2-yl]-3-(3″-chlorophenyl)-5-phenyl-2-pyrazoline **9**

^{1}H-NMR (DMSO-d_6, δ, ppm): 3.40–3.60 (1H, m, H_A), 4.15 (1H, dd, H_B), 5.80 (1H, dd, H_X), 7.40–8.40 (14H, m, aromatic protons), (J_{AB} = 18.02, J_{AX} = 6.45, J_{BX} = 11.32 Hz). MS (FAB$^+$): M + 1: m/z: 461.

5.1.2.14. 1-[4-(2′-Hydroxyphenyl)thiazol-2-yl]-3-(3″-chlorophenyl)-5-phenyl-2-pyrazoline **10**

^{1}H-NMR (DMSO-d_6, δ, ppm): 3.30 (1H, dd, H_A), 4.15 (1H, dd, H_B), 5.70 (1H, dd, H_X), 7.10–8.00 (14H, m, aromatic protons) 11.00 (1H, s, OH), (J_{AB} = 17.37, J_{AX} = 6.41, J_{BX} = 11.77 Hz). MS (FAB$^+$): M + 1: m/z: 432.

5.1.2.15. 1-(4-Phenylthiazol-2-yl)-3-(3″-methoxyphenyl)-5-phenyl-2-pyrazoline **11**

^{1}H-NMR (DMSO-d_6, δ, ppm): 3.30–3.50 (1H, m, H_A), 3.65 (3H, s, OCH_3), 3.90–4.10 (1H, m, H_B), 5.60 (1H, dd, H_X), 6.60–7.70 (15H, m, aromatic protons), (J_{AX} = 6.20, J_{BX} = 11.35 Hz).

5.1.2.16. 1-[4-(2′-Hydroxyphenyl)thiazol-2-yl]-3-(3″-methoxyphenyl)-5-phenyl-2-pyrazoline **12**

^{1}H-NMR (DMSO-d_6, δ, ppm): 3.20–3.45 (1H, m, H_A), 3.55 (3H, s, OCH_3), 3.95–4.10 (1H, m, H_B), 5.60 (1H, dd, H_X), 6.75–7.80 (14H, m, aromatic protons), 10.80 (1H, s, OH), (J_{AX} = 6.20, J_{BX} = 11.35 Hz) MS (FAB$^+$): M + 1: m/z: 428.

5.1.2.17. 1-[4-(2′-Hydroxy-4′-methoxyphenyl)thiazol-2-yl]-3-(3″-methoxyphenyl)-5-phenyl-2-pyrazoline **13**

^{1}H-NMR (DMSO-d_6, δ, ppm): 3.30–3.50 (1H, m, H_A), 3.65 (3H, s, OCH_3), 3.80 (3H, s, OCH_3), 3.90–4.10 (1H, m, H_B), 5.60 (1H, dd, H_X), 6.30–7.70 (13H, m, aromatic protons), 10.70 (1H, s, OH), (J_{AX} = 6.20, J_{BX} = 11.35 Hz).

5.1.2.18. 1-(4-Phenylthiazol-2-yl)-3-(3′,4′-dimethylphenyl)-5-phenyl-2-pyrazoline **14**

^{1}H-NMR (DMSO-d_6, δ, ppm): 2.25 (6H, s, CH_3), 3.10–3.20 (1H, m, H_A), 4.00 (1H, dd, H_B), 5.60 (1H, dd, H_X), 6.80–7.70 (14H, m, aromatic protons), (J_{AX} = 6.40, J_{BX} = 11.22 Hz) MS (FAB$^+$): M + 1: m/z: 409.

5.1.2.19. 1-[4-(4′-Nitrophenyl)thiazol-2-yl]-3-(3″,4″-dimethylphenyl)-5-phenyl-2-pyrazoline **15**

^{1}H-NMR (DMSO-d_6, δ, ppm): 2.25 (6H, s, CH_3), 3.20–3.30 (1H, m, H_A), 4.20 (1H, dd, H_B), 5.80 (1H, dd, H_X), 7.25–8.60 (13H, m, aromatic protons), (J_{AX} = 6.55, J_{BX} = 10.42 Hz) MS (FAB$^+$): M + 1: m/z: 455.

5.1.2.20. 1-[4-(4′-Chlorophenyl)thiazol-2-yl]-3-(3″,4″-dimethylphenyl)-5-phenyl-2-pyrazoline **16**

^{1}H-NMR (DMSO-d_6, δ, ppm): 2.25 (6H, s, CH_3), 3.10–3.20 (1H, m, H_A), 4.00–4.20 (1H, m, H_B), 5.60 (1H, dd, H_X), 6.80–7.80 (13H, m, aromatic protons), (J_{AX} = 6.60, J_{BX} = 11.53 Hz) MS (FAB$^+$): M + 1: m/z: 443.

5.1.2.21. 1-[4-(4′-Methylphenyl)thiazol-2-yl]-3-(3″,4″-dimethylphenyl)-5-phenyl-2-pyrazoline **17**

^{1}H-NMR (DMSO-d_6, δ, ppm): 2.22 (3H, s, CH_3), 2.25 (6H, s, CH_3), 3.15–3.30 (1H, m, H_A), 4.00–4.15 (1H, m, H_B), 5.70 (1H, dd, H_X), 6.70–7.70 (13H, m, aromatic protons), (J_{AX} = 6.75, J_{BX} = 12.03 Hz) MS (FAB$^+$): M + 1: m/z: 423.

5.1.2.22. 1-[4-(2′-Hydroxyphenyl)thiazol-2-yl]-3-(3″,4″-dimethylphenyl)-5-phenyl-2-pyrazoline **18**

^{1}H-NMR (DMSO-d_6, δ, ppm): 2.25 (6H, s, CH_3), 3.15–3.30 (1H, m, H_A), 4.00–4.10 (1H, m, H_B), 5.70 (1H, dd, H_X), 6.40–7.80 (13H, m, aromatic protons) 10.80 (1H, s, OH), (J_{AX} = 6.70, J_{BX} = 11.42 Hz) MS (FAB$^+$): M + 1: m/z: 425.

5.1.2.23. 1-[4-(2′-Hydroxy-4′-methoxyphenyl)thiazol-2-yl]-3-(3″,4″-dimethylphenyl)-5-phenyl-2-pyrazoline **19**

^{1}H-NMR (DMSO-d_6, δ, ppm): 2.25 (6H, s, CH_3), 3.10–3.30 (1H, m, H_A), 3.75 (3H, s, OCH_3), 4.00–4.10 (1H, m, H_B), 5.60 (1H, dd, H_X), 6.30–7.80 (12H, m, aromatic protons) 10.70 (1H, s, OH), (J_{AX} = 6.40, J_{BX} = 11.22 Hz) MS (FAB$^+$): M + 1: m/z: 455.

5.1.2.24. 1-[4-(3′-Nitrophenyl)thiazol-2-yl]-3-(3″,4″-dimethylphenyl)-5-phenyl-2-pyrazoline **20**

^{1}H-NMR (DMSO-d_6, δ, ppm): 2.25 (6H, s, CH_3), 3.20–3.30 (1H, m, H_A), 4.20 (1H, m, H_B), 5.80 (1H, dd,

H_X), 7.25–8.60 (13H, m, aromatic protons), (J_{AX} = 6.55, J_{BX} = 10.42 Hz) MS (FAB^+): M + 1: m/z: 455.

5.1.2.25. 1-(4-Phenylthiazol-2-yl)-3-phenyl-5-(4′-methoxyphenyl)-2-pyrazoline **21**

^{1}H-NMR (DMSO-d_6, δ, ppm): 3.25–3.50 (1H, m, H_A), 3.70 (3H, s, OCH_3), 4.00 (1H, dd, H_B), 5.65 (1H, dd, H_X), 6.50–7.90 (15H, m, aromatic protons), (J_{AB} = 17.02, J_{AX} = 6.22, J_{BX} = 11.09 Hz). MS (FAB^+): M + 1: m/z: 412.

5.1.2.26. 1-[4-(2′-Hydroxy-4′-methoxyphenyl)thiazol-2-yl]-3-phenyl-5-(4″-methoxyphenyl)-2-pyrazoline **22**

^{1}H-NMR (DMSO-d_6, δ, ppm): 3.25–3.50 (1H, m, H_A), 3.65 (3H, s, OCH_3), 3.80 (3H, s, OCH_3), 4.00 (1H, dd, H_B), 5.60 (1H, dd, H_X), 6.70–7.70 (13H, m, aromatic protons), (J_{AB} = 17.02, J_{AX} = 6.22, J_{BX} = 11.09 Hz), 10.80 (1H, s, OH), MS (FAB^+): M + 1: m/z: 458.

5.1.2.27. 1-(4-Phenylthiazol-2-yl)-3-(indan-5″-yl)-5-phenyl-2-pyrazoline **23**

^{1}H-NMR (DMSO-d_6, δ, ppm): 2.00–2.10 (2H, m, CH_2), 2.90 (4H, br, CH_2), 3.30 (1H, dd, H_A), 4.00 (1H, dd, H_B), 5.70 (1H, dd, H_X), 6.80–7.80 (14H, m, aromatic protons), (J_{AB} = 17.35, J_{AX} = 6.65, J_{BX} = 11.85 Hz) MS (FAB^+): M + 1: m/z: 422.

5.1.2.28. 1-[4-(4′-Nitrophenyl)thiazol-2-yl]-3-(indan-5″-yl)-5-phenyl-2-pyrazoline **24**

^{1}H-NMR (DMSO-d_6, δ, ppm): 2.00–2.10 (2H, m, CH_2), 2.90 (4H, br, CH_2), 3.30 (1H, dd, H_A), 4.00 (1H, dd, H_B), 5.70 (1H, dd, H_X), 7.20–8.40 (13H, m, aromatic protons), (J_{AB} = 17.65, J_{AX} = 6.85, J_{BX} = 11.80 Hz) MS (FAB^+): M + 1: m/z: 467.

5.1.2.29. 1-[4-(4′-Chlorophenyl)thiazol-2-yl]-3-(indan-5″-yl)-5-phenyl-2-pyrazoline **25**

^{1}H-NMR (DMSO-d_6, δ, ppm): 2.00–2.10 (2H, m, CH_2), 2.90 (4H, br, CH_2), 3.30 (1H, dd, H_A), 4.00 (1H, dd, H_B), 5.70 (1H, dd, H_X), 6.90–7.60 (13H, m, aromatic protons), (J_{AB} = 17.35, J_{AX} = 7.05, J_{BX} = 12.00 Hz) MS (FAB^+): M + 1: m/z: 456.

5.1.2.30. 1-[4-(4′-Methoxyphenyl)thiazol-2-yl]-3-(indan-5″-yl)-5-phenyl-2-pyrazoline **26**

^{1}H-NMR (DMSO-d_6, δ, ppm): 2.00–2.10 (2H, m, CH_2), 2.90 (4H, br, CH_2), 3.30 (1H, dd, H_A), 3.65 (3H, s, OCH_3), 4.00 (1H, dd, H_B), 5.70 (1H, dd, H_X), 7.20–8.00 (13H, m, aromatic protons), (J_{AB} = 17.28, J_{AX} = 6.35, J_{BX} = 11.06 Hz) MS (FAB^+): M + 1: m/z: 452.

5.1.2.31. 1-[4-(4′-Methylphenyl)thiazol-2-yl]-3-(indan-5″-yl)-5-phenyl-2-pyrazoline **27**

^{1}H-NMR (DMSO-d_6, δ, ppm): 2.00–2.10 (2H, m, CH_2), 2.24 (3H, s, CH_3), 2.90 (4H, br, CH_2), 3.35 (1H, dd, H_A), 4.10 (1H, dd, H_B), 5.70 (1H, dd, H_X), 7.10–7.90 (13H, m, aromatic protons), (J_{AB} = 17.85, J_{AX} = 6.95, J_{BX} = 11.90 Hz) MS (FAB^+): M + 1: m/z: 436.

5.1.2.32. 1-[4-(3′-Nitrophenyl)thiazol-2-yl]-3-(indan-5″-yl)-5-phenyl-2-pyrazoline **28**

^{1}H-NMR (DMSO-d_6, δ, ppm): 2.00–2.10 (2H, m, CH_2), 2.90 (4H, br, CH_2), 3.30 (1H, dd, H_A), 4.00 (1H, dd, H_B), 5.70 (1H, dd, H_X), 7.20–8.50 (13H, m, aromatic protons), (J_{AB} = 17.18, J_{AX} = 6.55, J_{BX} = 11.86 Hz) MS (FAB^+): M + 1: m/z: 467.

5.1.2.33. 1-[4-(2′-Hydroxyphenyl)thiazol-2-yl]-3-(indan-5″-yl)-5-phenyl-2-pyrazoline **29**

^{1}H-NMR (DMSO-d_6, δ, ppm): 2.00–2.10 (2H, m, CH_2), 2.90 (4H, br, CH_2), 3.30 (1H, dd, H_A), 4.00 (1H, dd, H_B), 5.70 (1H, dd, H_X), 6.80–7.70 (13H, m, aromatic protons), 10.70 (1H, s, OH), (J_{AB} = 17.17, J_{AX} = 6.56, J_{BX} = 11.86 Hz).

5.1.2.34. 1-[4-(2′-Hydroxy-4′-chlorophenyl)thiazol-2-yl]-3-(indan-5″-yl)-5-phenyl-2-pyrazoline **30**

^{1}H-NMR (DMSO-d_6, δ, ppm): 2.00–2.10 (2H, m, CH_2), 2.90 (4H, br, CH_2), 3.30 (1H, dd, H_A), 4.00 (1H, dd, H_B), 5.70 (1H, dd, H_X), 7.00–7.90 (12H, m, aromatic protons), 10.90 (1H, s, OH), (J_{AB} = 17.22, J_{AX} = 6.86, J_{BX} = 11.00 Hz).

5.1.2.35. 1-[4-(2′-Hydroxy-4′-methoxyphenyl)thiazol-2-yl]-3-(indan-5″-yl)-5-phenyl-2-pyrazoline **31**

^{1}H-NMR (DMSO-d_6, δ, ppm): 2.00–2.10 (2H, m, CH_2), 2.90 (4H, br, CH_2), 3.30 (1H, dd, H_A), 3.70 (3H, s, OCH_3), 4.00 (1H, dd, H_B), 5.70 (1H, dd, H_X), 6.80–7.70 (12H, m, aromatic protons), 10.70 (1H, s, OH), (J_{AB} = 17.22, J_{AX} = 6.86, J_{BX} = 11.00 Hz) MS (FAB^+): M + 1: m/z: 468.

5.1.2.36. 1-[4-(2′-Methyl-4′-hydroxyphenyl)thiazol-2-yl]-3-(indan-5″-yl)-5-phenyl-2-pyrazoline **32**

^{1}H-NMR (DMSO-d_6, δ, ppm): 2.00–2.10 (2H, m, CH_2), 2.23 (3H, s, CH_3), 2.90 (4H, br, CH_2), 3.30 (1H, dd, H_A), 4.10 (1H, dd, H_B), 5.70 (1H, dd, H_X), 6.70–7.50 (12H, m, aromatic protons), 10.70 (1H, s, OH), (J_{AB} = 17.45, J_{AX} = 7.06, J_{BX} = 11.20 Hz) MS (FAB^+): M + 1: m/z: 452.

5.1.2.37. 1-4-(Phenylthiazol-2-yl)-3-(5″,6″,7″,8″-tetrahydronaphthalene-2″-yl)-5-phenyl-2-pyrazoline **33**

^{1}H-NMR (DMSO-d_6, δ, ppm): 2.00–2.10 (4H, m, CH_2), 2.90 (4H, br, CH_2), 3.20–3.40 (1H, m, H_A), 4.00 (1H, dd, H_B), 5.65 (1H, dd, H_X), 7.20–7.80 (14H, m, aromatic protons), (J_{AB} = 17.41, J_{AX} = 6.42, J_{BX} = 11.45 Hz) MS (FAB^+): M + 1: m/z: 436.

5.1.2.38. 1-[4-(4′-Nitrophenyl)-thiazol-2-yl]-3-(5″,6″,7″,8″-tetrahydronaphthalene-2″-yl)-5-phenyl-2-pyrazoline **34**

^{1}H-NMR (DMSO-d_6, δ, ppm): 2.00–2.10 (4H, m, CH_2), 2.90 (4H, br, CH_2), 3.20–3.40 (1H, m, H_A), 4.00 (1H, dd, H_B), 5.70 (1H, dd, H_X), 7.20–0–8.50 (13H, m, aromatic protons), (J_{AB} = 17.27, J_{AX} = 6.32, J_{BX} = 11.75 Hz) MS (FAB$^+$): M + 1: m/z: 481.

5.1.2.39. 1-[4-(3′-Nitrophenyl)-thiazol-2-yl]-3-(5″,6″,7″,8″-tetrahydronaphthalene-2″-yl)-5-phenyl-2-pyrazoline **35**

^{1}H-NMR (DMSO-d_6, δ, ppm): 2.00–2.10 (4H, m, CH_2), 2.90 (4H, br, CH_2), 3.20–3.40 (1H, m, H_A), 4.00 (1H, dd, H_B), 5.70 (1H, dd, H_X), 7.10–0–8.40 (13H, m, aromatic protons), (J_{AB} = 17.20, J_{AX} = 6.42, J_{BX} = 11.95 Hz) MS (FAB$^+$): M + 1: m/z: 481.

5.1.2.40. 1-[4-(2′-Hydroxy-phenyl)thiazol-2-yl]-3-(5″,6″,7″,8″-tetrahydronaphthalene-2″-yl)-5-phenyl-2-pyrazoline **36**

^{1}H-NMR (DMSO-d_6, δ, ppm): 2.00–2.10 (4H, m, CH_2), 2.90 (4H, br, CH_2), 3.10–3.30 (1H, m, H_A), 4.10 (1H, dd, H_B), 5.65 (1H, dd, H_X), 6.70–0–7.80 (13H, m, aromatic protons), 10.90 (1H, s, OH), (J_{AB} = 18.07, J_{AX} = 6.65, J_{BX} = 11.65 Hz) MS (FAB$^+$): M + 1: m/z: 452.

5.1.2.41. 1-[4-(2′-Hydroxy-4′-methoxyphenyl)thiazol-2-yl]-3-(5″,6″,7″,8″-tetrahydronaphthalene-2″-yl)-5-phenyl-2-pyrazoline **37**

^{1}H-NMR (DMSO-d_6, δ, ppm): 2.00–2.10 (4H, m, CH_2), 2.90 (4H, br, CH_2), 3.10–3.30 (1H, m, H_A), 3.65 (3H, s, OCH_3), 4.15 (1H, dd, H_B), 5.75 (1H, dd, H_X), 6.80–0–7.90 (12H, m, aromatic protons), 11.05 (1H, s, OH), (J_{AB} = 17.80, J_{AX} = 6.95, J_{BX} = 11.85 Hz) MS (FAB$^+$): M + 1: m/z: 482.

5.1.2.42. 1-[4-(2′-Hydroxy-4′-chlorophenyl)thiazol-2-yl]-3-(5″,6″,7″,8″-tetrahydronaphthalene-2″-yl)-5-phenyl-2-pyrazoline **38**

^{1}H-NMR (DMSO-d_6, δ, ppm): 2.00–2.10 (4H, m, CH_2), 2.90 (4H, br, CH_2), 3.10–3.30 (1H, m, H_A), 4.15 (1H, dd, H_B), 5.70 (1H, dd, H_X), 6.85–0–7.80 (12H, m, aromatic protons), 11.00 (1H, s, OH), (J_{AB} = 17.80, J_{AX} = 6.95, J_{BX} = 11.85 Hz) MS (FAB$^+$): M + 1: m/z: 486.

5.1.2.43. 1-[4-(2′-Methyl-4′-hydroxyphenyl)thiazol-2-yl]-3-(5″,6″,7″,8″-tetrahydronaphthalene-2″-yl)-5-phenyl-2-pyrazoline **39**

^{1}H-NMR (DMSO-d_6, δ, ppm): 2.00–2.15 (4H, m, CH_2), 2.25 (3H, s, CH_3), 2.80 (4H, br, CH_2), 3.10–3.30 (1H, m, H_A), 4.00 (1H, dd, H_B), 5.65 (1H, dd, H_X), 7.20–8.20 (12H, m, aromatic protons), 10.80 (1H, s, OH), (J_{AB} = 17.27, J_{AX} = 6.32, J_{BX} = 11.75 Hz) MS (FAB$^+$): M + 1: m/z: 466.

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