

Synthesis and Characterization of New 3,5-Dinaphthyl Substituted 2-Pyrazolines and Study of Their Antimicrobial Activity

Davood Azarifar* and Maseud Shaebanzadeh

Department of Chemistry, Faculty of Science, Bu-Ali Sina University, Zip Code 65174, Hamadan, Iran

* Author to whom correspondence should be addressed; e-mail azarifar@basu.ac.ir

Received: 12 March 2002; in revised form: 15 November 2002 / Accepted 17 November 2002 /

Published: 31 December 2002

Abstract: A number of chalcones were prepared by condensing either 1-acetylnaphthalene or substituted 1-acetylnaphthalenes with 1-naphthaldehyde or 4-dimethylamino-1-naphthaldehyde in ethanolic NaOH solutions. These chalcones were immediately reacted with hydrazine hydrochloride, phenyl hydrazine and semicarbazide hydrochloride in the presence of dry acetic acid to obtain the corresponding 2-pyrazolines. The synthesised heterocycles were characterized on the basis of their chemical properties and spectroscopic data. These compounds were tested for antimicrobial activity against a variety of test organisms: *Escherichia coli*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Shigella dysentery* and *Salmonella typhi*. The compounds containing chloro, hydroxo and dimethylamino -N(CH₃)₂ group as substituents on the naphthalene rings have been found to be very effective antimicrobial agents. In addition, the presence of a carboxamido -CONH₂ substituent group at the N-1 position of the 2-pyrazoline rings is shown to contribute substantially to the antimicrobial activity.

Keywords: Chalcones, (Naphthalene-/substituted naphthalene-1-yl)-2-pyrazolines, Aryl substituted pyrazolines, Pyrazolines, Antimicrobial activity, Heterocyclics

Introduction

Due to the interesting activity of variously substituted pyrazolines as biological agents considerable attention has been focused on this class. The pharmaceutical importance of these compounds lies in the fact that they can be effectively utilized as antibacterial, antifungal, antiviral, antiparasitic, anti-tubercular and insecticidal agents [1-6]. Some of these compounds have also antiinflammatory, anti-diabetic, anaesthetic and analgesic properties [7-10]. In addition, pyrazolines have played a crucial part in the development of theory in heterocyclic chemistry and also used extensively in organic synthesis [11-15].

Among the methods employed in synthesis of pyrazolines, condensation of a variety of substituted chalcones with hydrazine and its derivatives is commonly used [16-18]. 2-Pyrazolines can be conveniently synthesized by the treatment of α,β -unsaturated carbonyl compounds with hydrazine reagents in basic and acidic media [11,16,17]. In this method, hydrazones are formed as intermediates, which can be subsequently cyclized to 2-Pyrazolines in the presence of a suitable cyclizing reagent like acetic acid [19, 20].

As evident from the literature, in recent years a significant portion of research work in heterocyclic chemistry has been devoted to 2-pyrazolines containing different aryl groups as substituents. Baker *et. al.* have reported the formation of 1-phenyl-5-(2-hydroxy-4-methoxyphenyl)-3-methylpyrazoline from 2-hydroxy-4-methyl ketone on treatment with phenyl hydrazine [20]. Borkhade and Marathe have synthesized 3,5-diaryl-1-phenylpyrazoline by the action of phenyl hydrazine hydrochloride on 2'-hydroxy chalcones and flavanones in pyridine [22].

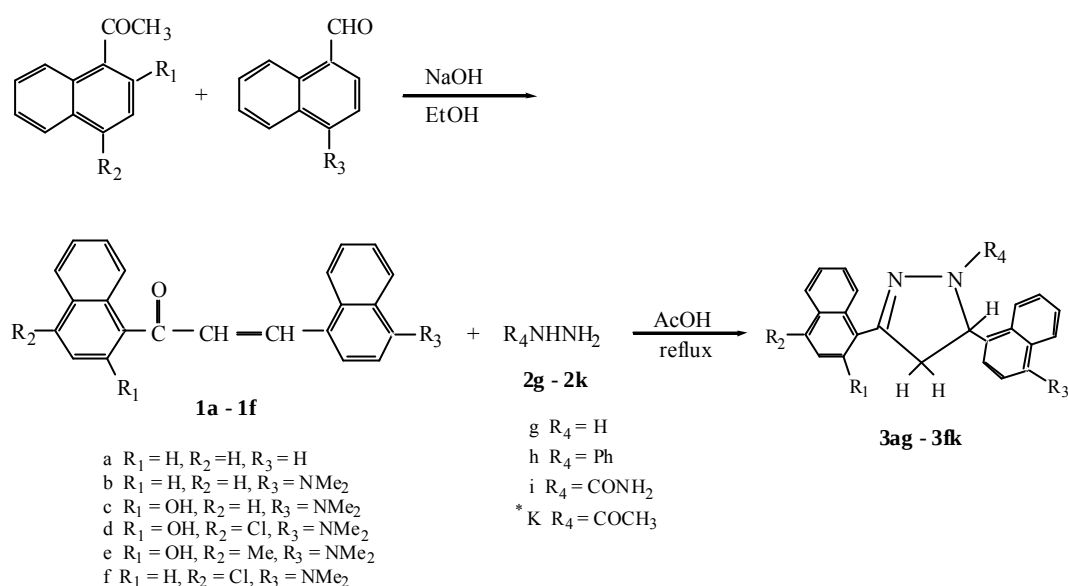
According to a literature survey, it was noted that very little research has been carried out regarding pyrazolines carrying naphthyl/substituted naphthyl groups as substituents on pyrazoline ring. In this area Dashi and Kadu have recently reported the synthesis and antimicrobial activity of some new naphthyl-substituted 2-pyrazolines [21].

Therefore, as a part of our program focused on 2-pyrazolines with biological activity, and in connection with our interest in the chemistry of arylated pyrazolines, in this paper we report the synthesis and anti-microbial properties of some new 3,5-dinaphthyl substituted 2-pyrazolines. A study of the effects of certain substituent groups attached both to naphthalene and pyrazoline rings on the antimicrobial activity of these compounds was also planned.

Results and Discussion

In this paper the syntheses of twenty-four 3,5-dinaphthalene-1-yl substituted 2-pyrazolines (**3ag-3fk**) containing certain groups as substituents both on the naphthalene and pyrazoline rings are described. These compounds were prepared by the action of hydrazine reagents **2g-2k** on chalcones **1a-1f**, in turn generated as intermediates by aldol condensation reactions between the corresponding 1-acetylnaphthalenes and 1-naphthaldehydes in ethanolic NaOH solution (Scheme 1).

Scheme 1



* Acetylation, *in situ*, occurs at prolonged refluxing times to convert the initially produced 2-pyrazolines (3ag - 3fg) mainly into their acetylated derivatives (3ak- 3fk).

Formation of the intermediate chalcones **1a-1f** was confirmed on the basis of their IR and $^1\text{H-NMR}$ data. They show a characteristic IR absorption peak at ν 1700-1650 cm^{-1} indicating the presence of a conjugated carbonyl group ($>\text{C}=\text{O}$). As their $^1\text{H-NMR}$ spectra suggest, the $\text{C}_\alpha\text{-H}$ and $\text{C}_\beta\text{-H}$ protons are considerably shifted downfield to the extent that they appear in the aromatic region (6.5-8.5). As a result, these protons can hardly be distinguished from those of the aromatic rings. This is probably associated with the joint deshielding resonance and anisotropic effects of the naphthalene groups bonded to β -carbon atom.

The chalcones **1a-1f** were then reacted with hydrazines **2g-2k** to give 2-pyrazoline compounds **3ag-3fk**. This reaction probably takes place through mediation of an appropriate α,β -unsaturated hydrazone, which immediately cyclizes to give a 2-pyrazoline ring in the presence of a suitable cyclizing agent like dry acetic acid under prolonged refluxing condition. Acetylation, *in situ*, to convert the initially obtained pyrazolines **3ag-3fg** into their N-1 acetylated derivatives **3ak-3fk** was observed under prolonged refluxing.

All the pyrazolines, in general, exhibited $\text{C}=\text{N}$ stretching vibrations in the ν 1687-1483 cm^{-1} range which can be difficult to identify due to large variations in intensity and their closeness to $\text{C}=\text{C}$ and $\text{C}=\text{O}$ vibrations when present. In addition, the absorption frequencies at ν 3583-3485(s), 3456-3220(m), 1677-1630(s) and 834-815(s) indicating the presence of $-\text{OH}$, $-\text{NH}_2$ (usually two bands), $>\text{C}=\text{O}$ and $-\text{Cl}$ groups, respectively, were also typical. $^1\text{H-NMR}$ spectra of these compounds generally exhibit an AMX pattern for the presence of two diastereotopic protons at C-4 and one single proton at the C-5 positions. These protons appear as three doublets of doublets, respectively, in the δ = 3.25-3.64, 3.92-4.67 and 5.31-6.28 ppm regions, each integrating for one proton (Table 1). It is interesting to note that, in all the $^1\text{H-NMR}$ spectra, a doublet integrating for one proton appears in the δ = 8.92-

9.56 ppm region. This probably belongs to the C₈-proton of the 3-naphthyl group which suffers a significant paramagnetic shift relative to other remaining aromatic protons. The large deshielding of this proton is attributed mainly to the anisotropy of C=N p-system in pyrazoline rings.

Antimicrobial activity

The compounds were tested in vitro for antimicrobial activity against the test organisms *Escherichia coli*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Shigella dysentery* and *Salmonella typhi* at a temperature of 37 °C (±1 °C). It was observed that 81% of the total samples tested show some antimicrobial activity. All the compounds showed activity against the test organisms *Klebsiella pneumoniae* and *Staphylococcus aureus*. Compounds **3cg**, **3eh**, **3ci**, **3di** and **3ei** positively acted against all six organisms. Among these, **3di** was found to be the most active since this compound could inhibit the microbial growth at lower concentrations. When a comparison is made between the compounds **3ag** and **3bg** and also between **3ah** and **3bh**, it appears that antimicrobial activity is enhanced due to the presence of an NMe₂ group as a substituent on the naphthalene ring. Furthermore, the comparison of MIC values of compounds in pairs **3bg/3cg**, **3bh/3ch** and also **3bh/3fh** indicates that the -OH and -Cl groups as substituents on the 3-naphthyl ring causes a substantial increase in antimicrobial activity. This fact is further supported by comparison of the MIC values of the compounds in pairs **3cg/3dg**, **3ch/3dh**, **3ck/3dk** and **3ci/3di**. On the contrary, the comparison of MIC values between the compounds in pairs **3ch/3eh**, **3ck/3ek** and **3ci/3ei** reveals that the presence of a methyl substituent group on the 3-naphthyl rings contributes almost nothing to the antimicrobial activity. Finally, on the basis of the comparison of MIC values of compounds **3ag-3dg** with those of compounds **3ah-3dh**, it was observed that the introduction of a Ph substituent group at the N-1 position of the pyrazoline ring results in no significant change in the antimicrobial activity. While on the other hand, from such a comparison between the compounds **3ag-3dg** and **3ak-3ek**, and also between the compounds **3ag-3dg** and **3ai-3ei**, it follows that COCH₃ and CONH₂ groups bonded to the N-1 position in the pyrazoline ring have moderate and strong effects on the antimicrobial activity, respectively. Accordingly, among the heterocyclics tested, it was found that compound **3di** possesses very high antimicrobial activity, which can be attributed to the simultaneous presence of -OH, -Cl, -NMe₂ and -CONH₂ substituent groups in this compound.

Therefore, on the basis of the observed MIC values of these compounds, it can be concluded that (i) the compounds containing -OH and -Cl groups in combination with a -NMe₂ group as substituents on the naphthalene rings can act as very effective antimicrobial agents; (ii) the dimethylamino (NMe₂), group exerts distinct antimicrobial activity which is independent of the presence of other substituents; (iii) a carboxamido (CONH₂) group attached to the N-1 position of the 2-pyrazoline ring presents a substantial contribution in the enhancement of antimicrobial activity; (iv) the general trend for activity in decreasing order can be given as: **3di**>**3ci**>**3ei**>**3cg**>**3eh**>**3dk**>**3dg**, **3eg**, **3dh**>**3fi**, **3ck**, **3bi**>**3fg**, **3ek**, **3fk**>**3fh**, **3ai**>**3bk**>**3bg**>**3ak**>**3ch**>**3bh**>**3ag**>**3ah**.

Acknowledgements

The authors acknowledge the financial support of the Bu-Ali Sina University, Chemistry Department, to carry out this research. They also wish to express their gratitude to Mrs. Hesami of the Microbiology Department, Bu-Ali Sina University, in connection with anti-bacterial tests.

Experimental

General

All melting points were determined on a Büchi 530 melting point apparatus, and are uncorrected. The ^1H -NMR spectra were recorded at ambient temperature for deuteriochloroform solutions using tetramethylsilane as the internal standard. Jeol FX (at 90 MHz) and Brüker AM (at 200 MHz) spectrometers were used. IR spectra were recorded on a Shimadzu IR-435U-04 instrument using potassium bromide pellets. Elemental analysis was performed at the Iran Polymer Research Center, Karaj, Iran. Antibacterial tests were performed at the Biology Department, Faculty of Science, Bu-Ali Sina University, Hamedan, Iran.

General procedure for the preparation of 3,5-dinaphthyl-2-pyrazoline derivatives (**3ag-3fk**).

Six 1,3-dinaphthyl bearing chalcones **1a-1f** were prepared by stirring a mixture of the appropriate 1-acetylnaphthalene and 1-naphthaldehyde derivative (0.1 mol of each) in ethanolic NaOH solution (80 mL) for several hours at room temperature until a yellow to orange color had developed. Then, the reaction mixture was filtered and the resulting precipitate was washed with 3% aqueous HCl. The crude material was recrystallized from ethanol (96%) to obtain a bright yellow crystalline product. The structures of these chalcones were established on the basis of their chemical properties and spectral data. Further, a solution of each of these chalcones **1a-1f** (0.05 mol), in dry acetic acid (100 mL) was then reacted with an appropriate hydrazine derivative for several hours at 90-100°C until the cyclization was complete and a deep orange color developed. The reaction mixture was then evaporated *in vacuo* to separate the acetic acid, and the residue was recrystallized from ethanol or acetonitrile to obtain the pure crystalline 2-pyrazolines **3ag - 3fi**. It was noticed that when these reactions were carried out with hydrazine itself, **2g**, under prolonged refluxing conditions, acetylation, *in situ*, occurred to convert the initially produced 2-pyrazolines **3ag-3fg** into their acetylated derivatives **3ak-3fk** (see Table 1 for melting points, yields and elemental data). The structures of these compounds were established on the basis of their chemical properties and spectral analysis (Table 2).

Table 1. Formulae, melting points, yields and analytical data of 2- pyrazolines

Compounds	Molecular Formula	M.P. (°C)	Yield (%)	Found (Calcd. %)		
				&	+	1
3ag	C ₂₃ H ₁₈ N ₂	195 - 196	82	85.68 (85.71)	5.53 (5.59)	8.48 (8.69)
3bg	C ₂₅ H ₂₃ N ₃	232 - 234	73	82.34 (82.19)	6.18 (6.30)	11.37 (11.51)
3cg	C ₂₅ H ₂₃ N ₃ O	285 - 286	65	78.57 (78.74)	6.13 (6.04)	10.87 (11.02)
3dg	C ₂₅ H ₂₂ ClN ₃ O	249 (decomp.)	82	72.12 (72.20)	5.18 (5.29)	9.76 (10.11)
3eg	C ₂₆ H ₂₅ ON ₃	278 - 280	68	78.75 (78.99)	6.25 (6.33)	10.49 (10.63)
3fg	C ₂₅ H ₂₂ N ₃ Cl	237 - 239	55	74.98 (75.09)	5.53 (5.51)	10.27 (10.51)
3ah	C ₂₉ H ₂₂ N ₂	225 - 226	78	87.05 (87.44)	5.57 (5.53)	7.21 (7.04)
3bh	C ₃₁ H ₂₇ N ₃	238(decomp.)	75	84.32 (84.35)	6.11 (6.12)	9.48 (9.52)
3ch	C ₃₁ H ₂₇ ON ₃	259 - 261	54	81.43 (81.40)	5.85 (5.91)	9.13 (9.19)
3dh	C ₃₁ H ₂₆ ON ₃ Cl	264 (decomp.)	73	75.52 (75.69)	5.15 (5.29)	8.52 (8.54)
3eh	C ₃₂ H ₂₉ ON ₃	238 - 239	74	81.51 (81.53)	5.74 (6.16)	8.81 (8.92)
3fh	C ₃₁ H ₂₆ N ₃ Cl	242 - 244	67	78.21 (78.23)	5.34 (5.47)	8.64 (8.83)
3ai	C ₂₄ H ₁₉ ON ₃	257 - 258	73	78.84 (78.90)	5.32 (5.20)	11.48 (11.51)
3bi	C ₂₆ H ₂₄ ON ₄	265 - 267	62	76.42 (76.47)	5.72 (5.88)	13.47 (13.72)
3ci	C ₂₆ H ₂₄ O ₂ N ₄	272 (decomp.)	68	73.46 (73.58)	5.37 (5.66)	13.84 (13.21)
3di	C ₂₆ H ₂₃ O ₂ N ₄ Cl	276 (decomp.)	65	67.39 (68.05)	5.08 (5.02)	12.63 (12.21)
3ei	C ₂₇ H ₂₆ O ₂ N ₄	280 - 282	85	73.64 (73.97)	5.92 (5.94)	12.81 (12.78)
3fi	C ₂₆ H ₂₃ ON ₄ Cl	270 - 272	74	70.28 (70.50)	5.12 (5.20)	12.53 (12.69)
3ak	C ₂₅ H ₂₀ ON ₂	207 - 208	75	82.18 (82.42)	5.58 (5.49)	7.89 (7.69)
3bk	C ₂₇ H ₂₅ ON ₃	236 - 238	58	79.33 (79.61)	6.08 (6.14)	10.45 (10.32)
3ck	C ₂₇ H ₂₅ O ₂ N ₃	243 - 245	72	76.54 (76.59)	5.83 (5.91)	9.65 (9.93)
3dk	C ₂₇ H ₂₄ O ₂ N ₃ Cl	237(decomp.)	68	70.85 (70.82)	5.64 (5.25)	9.33 (9.18)
3ek	C ₂₈ H ₂₇ O ₂ N ₃	226 - 228	78	76.78 (76.89)	6.21 (6.18)	9.67 (9.61)
3fk	C ₂₇ H ₂₄ ON ₃ Cl	241 - 242	47	73.25 (73.39)	5.32 (5.44)	9.85 (9.51)

Table 2. IR, ¹H-NMR and MS (ET) spectral data of the 2-pyrazoline products

Compounds	IR (cm ⁻¹)	¹ H-NMR (ppm)	Mass (m/z)
3ag	3448, 3230, 3080, 2928, 1652, 1598	3.35 (dd, 1H, >CHH _A), 4.15 (dd, 1H, >CH _B H), 5.75 (dd, 1H, >CHAr), 6.10 (s, 1H, NH), 6.5 - 8.2 (m, 13H, Ar), 9.45 (d, 1H, C' ₈ -H)	77, 91, 127, 153, 156, 168, 169, 195, 291, 304, 322
3bg	3180, 2925, 2812, 1585, 1578, 1310, 1205	2.85 (s, 6H, N(CH ₃) ₂), 3.32 (dd, 1H, >CHH _A), 4.12 (dd, 1H, >CH _B H), 5.64 (dd, 1H, >CHAr), 6.12 (s, 1H, NH), 6.2 - 8.5 (m, 12H, Ar), 9.43 (d, 1H, C' ₈ -H)	77, 91, 153, 158, 167, 170, 195, 197, 212, 291, 350, 365

3cg	3635, 3520, 3135, 2923, 1645, 1595, 1345, 1235, 1215	2.80 (s, 6H, N(CH ₃) ₂), 3.28 (dd, 1H, >CHH _A), 3.98 (dd, 1H, >CH _B H), 5.32 (dd, 1H, >CHAr), 5.76 (s, 1H, NH), 6.2 - 8.5 (m, 11H, Ar), 9.38 (d, 1H, C' ₈ -H), 11.10 (s, 1H, ArOH)	77, 91, 144, 169, 183, 197, 211, 350, 352, 364, 366, 381
3dg	3589, 3485, 3165, 2918, 1687, 1582, 1327, 1258, 1218, 815	2.78 (s, 6H, N(CH ₃) ₂), 3.25 (dd, 1H, >CHH _A), 3.92 (dd, 1H, >CH _B H), 5.31 (dd, 1H, >CHAr), 5.65 (s, 1H, NH), 6.5 - 9.10 (m, 10H, Ar), 9.35 (d, 1H, C' ₈ -H), 10.92 (s, 1H, ArOH)	77, 91, 183, 197, 203, 217, 218, 220, 245, 247, 354, 380, 386, 388, 402, 415, 417
3eg	3610, 3285, 3105, 2889, 1652, 1594, 1325, 1232	2.26 (s, 3H, Ar-CH ₃), 2.82 (s, 6H, N(CH ₃) ₂), 3.26 (dd, 1H, >CHH _A), 3.95 (dd, 1H, >CH _B H), 5.30 (dd, 1H, >CHAr), 5.73 (s, 1H, NH), 6.2 - 8.5 (m, 10H, Ar), 9.35 (d, 1H, C' ₈ -H), 10.87 (s, 1H, ArOH)	77, 91, 157, 183, 199, 225, 351, 362, 379, 380, 395
3fg	3165, 3100, 2905, 2825, 1605, 1500, 1280, 796	2.83 (s, 6H, N(CH ₃) ₂), 3.34 (dd, 1H, >CHH _A), 4.16 (dd, 1H, >CH _B H), 5.67 (dd, 1H, >CHAr), 6.15 (s, 1H, NH), 6.4 - 8.7 (m, 11H, Ar), 9.45 (d, 1H, C' ₈ -H)	77, 99, 187, 189, 203, 230, 355, 384, 386, 399, 401
3ah	3127, 2890, 1498, 1594, 1498, 1381, 1136, 772	3.42 (dd, 1H, >CHH _A), 4.22 (dd, 1H, >CH _B H), 5.91 (dd, 1H, >CHAr), 6.7 - 8.3 (m, 19H, Ar), 9.56 (d, 1H, C' ₈ -H)	77, 91, 127, 152, 165, 195, 241, 242, 291, 304, 398
3bh	3178, 2830, 1592, 1505, 1410, 1315, 1225	3.02 (s, 6H, N(CH ₃) ₂), 3.58 (dd, 1H, >CHH _A), 4.35 (dd, 1H, >CH _B H), 6.15 (dd, 1H, >CHAr), 6.2 - 8.5 (m, 18H, Ar), 9.56 (d, 1H, C' ₈ -H)	77, 91, 153, 167, 170, 195, 197, 244, 271, 334, 350, 441
3ch	3515, 3150, 2875, 1618, 1518, 1423, 1345, 1223	2.93 (s, 6H, N(CH ₃) ₂), 3.64 (dd, 1H, >CHH _A), 4.67 (dd, 1H, >CH _B H), 6.18 (dd, 1H, >CHAr), 6.5 - 8.2 (m, 17H, Ar), 8.95 (d, 1H, C' ₈ -H), 11.38 (s, 1H, ArOH)	77, 91, 169, 170, 183, 197, 211, 260, 350, 364, 366, 457, 459
3dh	3498, 3118, 2820, 1598, 1573, 1500, 1411, 1332, 1215, 825	2.91 (s, 6H, N(CH ₃) ₂), 3.63 (dd, 1H, >CHH _A), 4.67 (dd, 1H, >CH _B H), 6.15 (dd, 1H, >CHAr), 6.3 - 8.5 (m, 16H, Ar), 9.02 (d, 1H, C' ₈ -H), 11.12 (s, 1H, ArOH)	77, 99, 217, 219, 245, 247, 321, 384, 400, 402, 456, 474, 491, 493
3eh	3603, 3250, 2935, 2790, 1650, 1593, 1480, 1330, 1215	2.25 (s, 3H, Ar-CH ₃), 2.92 (s, 6H, N(CH ₃) ₂), 3.64 (dd, 1H, >CHH _A), 4.65 (dd, 1H, >CH _B H), 6.21 (dd, 1H, >CHAr), 6.5 - 8.0 (m, 16H, Ar), 8.92 (d, 1H, C' ₈ -H), 11.42 (s, 1H, ArOH)	77, 99, 183, 197, 225, 274, 301, 364, 454, 471
3fh	3135, 2878, 1612, 1585, 1434, 1325, 1218, 834	2.95 (s, 6H, N(CH ₃) ₂), 3.49 (dd, 1H, >CHH _A), 4.25 (dd, 1H, >CH _B H), 5.82 (dd, 1H, >CHAr), 6.5 - 8.7 (m, 16H, Ar), 9.47 (d, 1H, C' ₈ -H)	69, 77, 99, 201, 203, 228, 230, 278, 280, 368, 384, 386, 440, 475, 477
3ai	3456, 3200, 3085, 1677, 1650, 1582, 1505, 1468, 1391, 1106, 782	3.27 (dd, 1H, >CHH _A), 4.32 (dd, 1H, >CH _B H), 6.16 (dd, 1H, >CHAr), 6.61 (s, 2H, NH ₂), 7.3 - 8.3 (m, 14H, Ar), 9.25 (d, 1H, C' ₈ -H)	77, 115, 127, 141, 153, 168, 195, 196, 290, 292, 305, 323, 351, 366, 367
3bi	3465, 3250, 3100, 2815, 1668, 1635, 1580, 1500, 1458, 1117	2.86 (s, 6H, N(CH ₃) ₂), 3.28 (dd, 1H, >CHH _A), 4.34 (dd, 1H, >CH _B H), 6.12 (dd, 1H, >CHAr), 6.65 (s, 2H, NH ₂), 6.80 - 8.30 (m, 12H, Ar), 9.25 (d, 1H, C' ₈ -H)	77, 91, 127, 153, 168, 182, 184, 195, 238, 364, 393, 408
3ci	3632, 3410, 3182, 3110, 2865, 1670, 1610, 1480, 1455, 1238	2.82 (s, 6H, N(CH ₃) ₂), 3.23 (dd, 1H, >CHH _A), 4.31 (dd, 1H, >CH _B H), 6.08 (dd, 1H, >CHAr), 6.65 (s, 2H, NH ₂), 6.70 - 8.20 (m, 11H, Ar), 9.22 (d, 1H, C' ₈ -H), 10.95 (s, 1H, ArOH)	69, 97, 126, 143, 169, 184, 198, 211, 380, 409, 424
3di	3532, 3434, 3325, 3102, 2830, 1673, 1644, 1589, 1495, 1382, 1211, 815	2.82 (s, 6H, N(CH ₃) ₂), 3.23 (dd, 1H, >CHH _A), 4.33 (dd, 1H, >CH _B H), 6.12 (dd, 1H, >CHAr), 6.54 (s, 2H, NH ₂), 7.0 - 8.5 (m, 11H, Ar), 9.12 (d, 1H, C' ₈ -H), 11.02 (s, 1H, ArOH)	77, 91, 101, 177, 193, 197, 203, 217, 244, 384, 423, 441, 442, 443, 458, 460
3ei	3537, 3428, 3322, 2965, 2873, 1671, 1643, 1590, 1505, 1379, 1218	2.26 (s, 3H, Ar-CH ₃), 2.88 (s, 6H, N(CH ₃) ₂), 3.24 (dd, 1H, >CHH _A), 4.33 (dd, 1H, >CH _B H), 6.11 (dd, 1H, >CHAr), 6.57 (s, 2H, NH ₂), 7.2 - 8.5 (m, 11H, Ar), 9.16 (d, 1H, C' ₈ -H), 10.98 (s, 1H, ArOH)	77, 91, 157, 183, 197, 211, 364, 396, 421, 423, 424, 438, 440

3fi	3462, 3238, 3095, 2824, 1665, 1630, 1612, 1498, 1448, 1120, 785	2.85 (s, 6H, N(CH ₃) ₂), 3.29 (dd, 1H, >CHH _A), 4.36 (dd, 1H, >CH _B H), 6.14 (dd, 1H, >CHAr), 6.68 (s, 2H, NH ₂), 6.80 - 8.50 (m, 11H, Ar), 9.28 (d, 1H, C' ₈ -H)	77, 99, 126, 161, 187, 202, 216, 229, 398, 427, 442, 444
3ak	3033, 1667, 1506, 1415, 1390, 1150, 775	2.64 (s, 3H, COCH ₃), 3.39 (dd, 1H, >CHH _A), 4.13 (dd, 1H, >CH _B H), 6.28 (dd, 1H, >CHAr), 7.2 - 8.2 (m, 14H, Ar), 9.36 (d, 1H, C' ₈ -H)	83, 97, 127, 141, 152, 165, 167, 168, 194, 195, 290, 291, 321, 322, 349, 364
3bk	3028, 2850, 1659, 1610, 1485, 1432, 1280	2.62 (s, 3H, COCH ₃), 2.95 (s, 6H, N(CH ₃) ₂), 3.36 (dd, 1H, >CHH _A), 4.14 (dd, 1H, >CH _B H), 6.18 (dd, 1H, >CHAr), 6.80 - 8.00 (m, 12H, Ar), 9.32 (d, 1H, C' ₈ -H)	77, 91, 127, 153, 168, 224, 237, 364, 392, 407
3ck	3564, 3018, 2890, 1675, 1652, 1498, 1442, 1365, 1365, 1250	2.57 (s, 3H, COCH ₃), 2.98 (s, 6H, N(CH ₃) ₂), 3.28 (dd, 1H, >CHH _A), 4.25 (dd, 1H, >CH _B H), 6.04 (dd, 1H, >CHAr), 6.8 - 8.5 (m, 12H, Ar), 9.29 (d, 1H, C' ₈ -H), 11.13 (s, 1H, ArOH)	69, 97, 126, 143, 169, 170, 183, 210, 350, 366, 380, 381, 408, 423
3dk	3549, 3032, 2925, 1670, 1635, 1503, 1483, 1437, 1325, 1238, 780	2.63 (s, 3H, COCH ₃), 2.92 (s, 6H, N(CH ₃) ₂), 3.25 (dd, 1H, >CHH _A), 4.22 (dd, 1H, >CH _B H), 6.12 (dd, 1H, >CHAr), 7.10 - 8.6 (m, 11H, Ar), 9.17 (d, 1H, C' ₈ -H), 11.08 (s, 1H, ArOH)	77, 91, 177, 203, 217, 225, 244, 384, 414, 422, 442, 457, 459
3ek	3583, 3112, 2813, 1656, 1500, 1495, 1429, 1318, 1245	2.28 (s, 3H, ArCH ₃), 2.59 (s, 3H, COCH ₃), 2.92 (dd, 1H, >CH _B H), 6.02 (dd, 1H, >CHAr), 6.2 - 8.5 (m, 11H, Ar), 9.23 (d, 1H, C' ₈ -H), 11.10 (s, 1H, ArOH)	77, 91, 157, 183, 197, 225, 364, 380, 394, 420, 422, 437
3fk	3050, 2836, 1665, 1606, 1510, 1455, 1232, 795	2.58 (s, 3H, COCH ₃), 2.97 (s, 6H, N(CH ₃) ₂), 3.38 (dd, 1H, >CHH _A), 4.16 (dd, 1H, >CH _B H), 6.20 (dd, 1H, >CHAr), 7.00 - 8.20 (m, 11H, Ar), 9.35 (d, 1H, C' ₈ -H)	77, 99, 126, 161, 187, 202, 215, 383, 398, 426, 441, 443

Antimicrobial activity tests of the 2-pyrazolines

The above prepared 2-pyrazolines **3ag** - **3fk**, were assayed for their antimicrobial activities against six test organisms, *Escherichia coli*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Shigella dysentery* and *Salmonella typhii*, at a concentration of 100 mg/mL using the agar well technique [23]. Further, their MIC values against these organisms were determined by serial dilution method using DMF as a solvent and were compared with chloramphenicol as a standard antibiotic. The results obtained are given in Table 3.

Table 3. Antimicrobial activity of 2-pyrazolines

Compounds	MIC values (in mg/mL) against test organisms					
	<i>E. coli</i>	<i>S. aureus</i>	<i>K. pneumoniae</i>	<i>S. typhii</i>	<i>S. dysentary</i>	<i>P. mirabilis</i>
3,5-Bis (naphthalene -1- yl)-2-pyrazoline (3ag)	-	125	63	-	125	125
5-(4-dimethylaminonaphthalene -1- yl)-3-(naphthalene -1- yl)-2-pyrazoline (3bg)	125	63	125	63	125	-

3-(2-Hydroxynaphthalene -1- yl)-5-(4-dimethylaminonaphthalene-1- yl)-2-pyrazoline (3cg)	63	63	31	63	125	63
3-(2-Hydroxy-4-chloronaphthalene- 1-yl)-5-(4 -dimethylamino-naphthalene-1- yl)-2-pyrazoline (3dg)	63	31	63	125	-	31
3 - (2-Hydroxy - 4 -methylnaphthalene -1 -yl) -5- (4 –dimethylamino-naphthalene-1- yl) - 2 - pyrazoline (3eg)	63	31	63	-	125	31
3 - (4 -Chloro-naphthalene-1- yl) - 5 - (4 -dimethylamino-naphthalene-1- yl) - 2 - pyrazoline (3fg)	125	31	125	31	63	-
3,5 - Bis (naphthalene -1- yl) -1- phenyl- 2 -pyrazoline (3ah)	-	125	125	-	-	125
5 -(4 -Dimethylamino-naphthalene-1- yl) - 3 -(naphthalene -1-yl) - 1 -phenyl -2 - pyrazoline (3bh)	125	125	63	-	-	63
3 - (2 - Hydroxy -naphthalene -1- yl) - 5 - (4 - dimethylamino-naphthalene-1- yl) -1- phenyl- 2-pyrazoline (3ch)	-	63	31	125	-	125
3 - (2 -Hydroxy - 4 -chloro-naphthalene -1-yl) -5 - (4 –dimethylaminonaphthalene -1-yl) -1- phenyl - 2- pyrazoline (3dh)	63	31	31	-	125	63
3 - (2-Hydroxy -4-methyl-naphthalene -1-yl) -5 - (4 -dimethylamino-naphthalene-1 - yl)-1-phenyl- 2- pyrazoline (3eh)	125	63	125	31	63	63
3 - (4 -Chloro-naphthalene -1- yl) -5 - (4 - dimethylamino-naphthalene -1-yl) - 1- phenyl- 2– pyrazoline (3fh)	63	125	31	63	-	125
1-Acetyl -3,5- bis (naphthalene -1 -yl) -2- pyrazoline (3ak)	-	63	63	125	63	-
1 - Acetyl - 5 - (4-dimethylamino-naphthalene -1- yl) -3 -(naphthalene -1- yl) - 2 - pyrazoline (3bk)	125	125	31	63	125	-
1 - Acetyl -3 - (2 - hydroxy - naphthalene -1- yl)-5 - (4 - dimethyl amino-naphthalene -1- yl) - 2 - pyrazoline (3ck)	63	63	31	-	125	63

1 - Acetyl -3 - (2 - hydroxy - 4 - chloro - naphthalene -1-yl) -5 - (4 - dimethylamino - naphthalene - 1-yl) - 2- pyrazoline (3dk)	-	31	31	63	125	31
1 - Acetyl -3 - (2 - hydroxy - 4 - methyl - naphthalene -1-yl) - 5 - (4 - dimethylamino - naphthalene - 1-yl) - 2- pyrazoline (3ek)	-	125	63	31	125	31
1 - Acetyl - 5 - (4 - dimethylamino - naphthalene -1-yl) - 3 - (4 - chloro naphthalene -1-yl) - 2- pyrazoline (3fk)	125	31	63	125	31	-
1 - Carboxamido -3,5 - bis (naphthalene -1-yl) - 2 - pyrazoline (3ai)	125	63	31	-	63	125
1 - Carboxamido - 5 - (4 - dimethyl aminonaphthalene -1-yl) - 3 - (naphthalene - 1-yl) - 2 - pyrazoline (3bi)	63	63	31	63	-	125
1- Carboxamido -3 - (2 - hydroxy - naphthalene -1-yl) -5- (4 - dimethyl amino - naphthalene -1-yl) - 2 - pyrazoline (3ci)	63	31	16	125	63	31
1-Carboxamido -3- (2-hydroxy - 4 - chloro - naphthalene -1-yl) -5- (4 - dimethylamino - naphthalene -1-yl) - 2- pyrazoline (3di)	63	16	16	63	31	63
1-Carboxamido - 3 - (2 - hydroxy -4 - methyl naphthalene -1-yl) - 5 - (4 - dimethylaminonaphthalene -1-yl) - 2- pyrazoline (3ei)	125	31	63	31	63	63
1 - Carboxamido - 5 - (4 - dimethyl aminonaphthalene -1-yl) - 3 - (4 - chloronaphthalene -1-yl) - 2 - pyrazoline (3fi)	63	16	63	63	125	-
Chloramphenicol (standard antibiotic)	-	25	6	12	25	50

References

1. Roelfvan, S. G.; Arnold, C.; Wellnga, K. *J. Agric. Food Chem.* **1979**, *84*, 406.
2. Keats, G. H. *Brit. Pat.* 1,209,631, 1970.
3. Kedar, R. M.; Vidhale, N. N.; Chincholkar, M. M. *Orient. J. Chem.* **1997**, *13*, 143.
4. Singh, A.; Rathod, S.; Berad, B. N.; Patil, S. D.; Dosh, A. G. *Orient. J. Chem.* **2000**, *16*, 315.
5. Katri, H. Z.; Vunii, S. A. *J. Ind. Chem. Soc.* **1981**, *58*, 168.

6. Das, N. B.; Mittra, A. S. *Ind. J. Chem.* **1978**, *16B*, 638.
7. Garge, H. G.; Chandraprakash, J. *Pharm. Sc.* **1971**, *14*, 649.
8. Regaila, H. A.; El-Bayonk, A. K.; Hammad, M. *Egypt. J. Chem.* **1979**, *20*, 197.
9. Krishna, R.; Pande, B. R.; Bharthwal, S. P.; Parmar, S. S. *Eur. J. Med. Chem.* **1980**, *15*, 567.
10. Husain, M. I.; Shukla, S. *Ind. J. Chem.* **1986**, *25B*, 983.
11. Tomilovi, Yu. V.; Okonnishnikova, G. P.; Shulishov, E. V.; Nefedov, O. M. *Russ.Chem. Bt*, **1995**, *44*, 2114.
12. Klimova, E. I.; Marcos, M.; Klimova, T. B.; Cecilio, A. T.; Ruben, A. T.; Lena, R. R. *J. Organometallic Chem.* **1999**, *585*, 106.
13. Bhaskarreddy, D.; Padmaja, A.; Ramanareddy, P. V.; Seenaiiah, B. *Sulfur Lett.* **1993**, *16*, 227.
14. Padmavathi, V.; Sumathi, R. P.; Chandrasekhar, B. N.; Bhaskarreddy, D. *J. Chem. Research* **1999**, 610.
15. Bhaskarreddy, D.; Chandrasekhar, B. N.; Padmavathi, V.; Sumathi, R. P. *Synthesis*, **1998**, 491.
16. Knorr, L. *Ber. Dt. Chem. Ges.* **1893**, *26*, 100.
17. Thakare, V. G.; Wadodkar, K. N. *Ind. J. Chem. Sect. B* **1986**, *25*, 610.
18. Ankhiala, M. D.; Hathi, M. V. *J. Ind. Chem. Soc.* **1994**, *71*, 587.
19. Vounauwers, K.; Muller, *Ber. Dt. Chem. Ges.* **1908**, *41*, 4230.
20. Baker, A.; Butt, V. S. *J. Chem. Soc.* **1949**, 2142.
21. Kadu, V. B.; Dashi, A. G. *Orient. J. Chem.* **1997**, *13* (3), 285.
22. Borkhade, K. T.; Marathe, M. G. *Ind. J. Chem.* **1972**, *10*, 48.
23. Egorov, N. S. *Antibiotics, A Scientific Approach*, Mir Publishers: Moscow, 1985; pp 170-177.

Sample availability: Available from the authors.