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Synthesis and pharmacological evaluation of pyrazoline derivatives as new anti-inflammatory and analgesic agents

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Abstract—A series of 3-(4-biphenyl)-5-substituted phenyl-2-pyrazolines (**2a**–**h**) and 1-benzoyl-3-(4-biphenyl)-5-substituted phenyl-2-pyrazolines (**3a**–**h**) were synthesized by condensation of chalcones with hydrazine hydrate in solvent system ethanol and DMF. The newly synthesized compounds were screened for their anti-inflammatory and analgesic activity, and were compared with standard drug. Among the compounds studied, compound **2e** showed more potent anti-inflammatory and analgesic activity than the standard drug, along with minimum ulcerogenic index.

Conventional non-steroidal anti-inflammatory drugs (NSAIDs) that non-selectively inhibit both major cyclooxygenase isoforms[1–4] (COX -1 and COX-2), are widely used to treat the signs and symptoms of inflammation, particularly arthritic pain. COX-1 is the constitutive isoform and is mainly responsible for the synthesis of cytoprotective prostaglandins in gastrointestinal (GI) tract; whereas COX-2 is inducible and plays a major role in prostaglandin biosynthesis in inflammatory cells.[5–7] It is believed that it is the inhibition of COX-1 that causes unfavourable GI side effects.[8] A high level of selective COX-2 inhibition represents, therefore, a therapeutic strategy to alleviate pain and inflammation without the untoward GI toxicity due to COX-1 inhibition. Therefore selective COX-2 inhibitors (coxibs) with better safety profile have been marketed as a new generation of NSAIDs.[9,10] But careful prospective examination of coxibs has revealed unexpected cardiovascular adverse effect.[11] Therefore development of novel compounds having anti-inflammatory-analgesic activity with an improved safety profile is still a necessity. Literature survey revealed that many pyrazoline derivatives have found their clinical application as NSAIDS. Antipyrine, 2,3-dimethyl-1-phenyl-3-pyrazolin-5-one, was the first pyrazolone derivative used in the management of pain and inflammation. Phenyl butazone and its potent metabolite oxyphenbutazone, a prototype of pyrazolinedione NSAIDs, are potent anti-inflammatory agents. However their use became restricted due to their GI side effects.[12] Feprazone, the 4-(methylbutenyl)-analogue, is comparable to phenylbutazone in efficacy, but with less side affects on GI tract.[13] Several related pyrazolidine-3,5-diones, pyrazolin-3-ones and pyrazolin-5-ones are also available as NSAIDs; examples are felcobuzone, mefobutazone, morazone, famprofazone, and ramifenazone.[14] Besides these many pyrazoline derivatives are also reported in literature as having potent anti-inflammatory activity.[15–17] In view of these observations and in continuation of our research programme on the synthesis of five membered heterocyclic compounds,[18–20] we report herein the synthesis of some new pyrazoline derivatives, which have been found to possess an interesting profile of anti-inflammatory and analgesic activity, with significant reduction in their ulcerogenic potential (Scheme 1).

3-Aryl-1-(4-biphenyl)propen-1-ones (**1a**–**h**) were synthesized by treating 4-acetyl biphenyl with aromatic aldehydes in the presence of methanol-dioxane and potassium hydroxide solution.[21] The chalcones thus prepared, when treated with hydrazine hydrate and few drops of concentrated HCl in a mixture of dimethyl formamide and ethanol, gave 3-(4-biphenyl)-5-substituted phenyl-2-pyrazolines[22] (**2a**–**h**). Treatment of compounds **2a**–**h** with benzoyl chloride in presence of pyrimidine gave 1-benzoyl-3-(4-biphenyl)-5-substituted phenyl-2-pyrazolines[23] (**3a**–**h**). The structure of the synthesized compounds was confirmed by elemental analysis and spectral data (IR, ^{1}H NMR, Mass).[24]

Keywords: Pyrazoline; Anti-inflammatory; Analgesic; Ulcerogenic; Lipid peroxidation.
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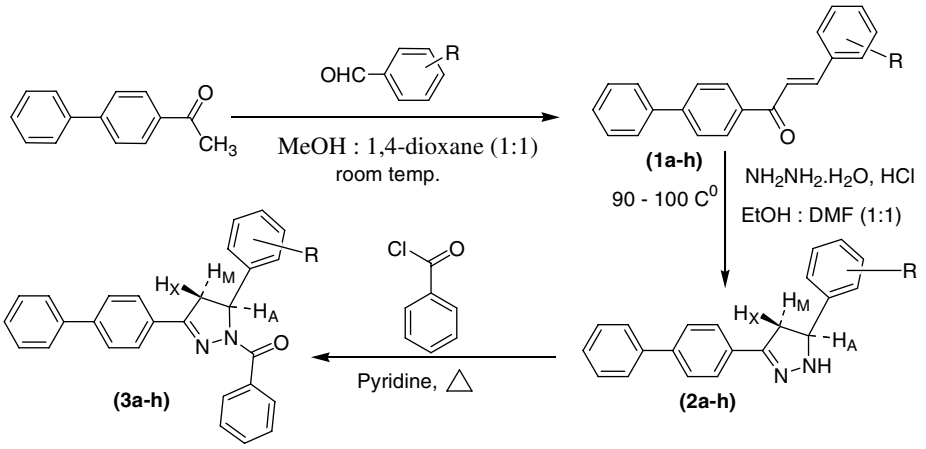

R = a : H; b : 2-Cl; c : 4-Cl; d: 4-N$(CH_3)_2$; e : 4CH_3; f : 4-OCH_3; g : 3,4-$(OCH_3)_2$; h : 2,4,6-$(OCH_3)_3$

Scheme 1.

The synthesized compounds **2a**–**h** and **3a**–**h** were tested for their anti-inflammatory activity[25] at an equimolar oral dose relative to 10 mg/kg (41 μmol/kg) flurbiprofen. % Inhibition was calculated both after 3 and 4 h, and since it was found to be more after 4 h, this was made the basis of discussion. The compounds showed anti-inflammatory activity ranging from 28.06% to 82.45% (Table 1), whereas standard drug flurbiprofen showed 80.29% inhibition after 4 h. The anti-inflammatory activity data showed that compounds having 4-methyl (**2e**) and 2,4,6-trimethoxy group (**2h**) in the phenyl ring at C-5 of pyrazoline nucleus possess highest activity (82.45%), greater than the standard drug flurbiprofen. Benzoylation of compound **2e** resulted in sharp decrease of activity 31.57% (**3e**), whereas benzoylation of compound **2h** showed slight decrease in anti-inflammatory activity 75.38% (**3h**). The rest of the pyrazoline derivatives showed moderate to weak anti-inflammatory activity.

The compounds **2e**, **2h**, and **3h** showing high anti-inflammatory activity were further screened for their analgesic activity[26] at an equimolar oral dose relative to 10 mg/kg (41 μmol/kg) flurbiprofen. Compounds showed analgesic activity ranging from 28.60% to 72.90%, whereas standard drug flurbiprofen showed 69.50% inhibition. It was observed that compound **2e** showing highest anti-inflammatory activity also exhibited highest analgesic activity 72.90% whereas compound **2h** showed sharp decrease in analgesic activity (28.60%), although it showed high anti-inflammatory activity (82.45%). The compound **3h** was found to have moderate analgesic activity (43.20%). These compounds were further screened for their acute ulcerogenic activity.[27] The compounds were tested at an equimolar oral dose relative to 30 mg/kg (123 μmol/kg) flurbiprofen. The maximum reduction in ulcerogenic activity (0.500 ± 0.00) was found in compound **2e** having 4-methylphenyl group at position 5 of pyrazoline ring. Rest of the tested compounds also showed better GI safety profile as compared to flurbiprofen, as illustrated in Table 2. All the compounds screened for ulcerogenic activity were also analyzed for lipid peroxidation.[28] Lipid peroxidation is measured as nanomole of malondialdehyde (MDA)/100 mg of gastric mucosa tissue. Flurbiprofen showed high lipid peroxidation (7.51 ± 0.68), whereas control group showed 3.25 ± 0.05. It was found that pyrazoline derivatives showing less ulcerogenic activity also showed reduction in lipid peroxidation (Table 2). Thus these studies showed that synthesized compounds have inhibited the induction of gastric mucosal lesion, and results further

Table 1. Anti-inflammatory activity of compounds (**2a**–**h** and **3a**–**h**)

Compound	Anti-inflammatory activity % inhibition ± SEM[a]		Compound	Anti-inflammatory activity % inhibition ± SEM[a]	
	After 3 h	After 4 h		After 3 h	After 4 h
2a	35.08 ± 3.23	38.60 ± 3.24*	**3a**	28.06 ± 4.23	33.32 ± 5.20*
2b	31.57 ± 5.26	31.57 ± 5.26*	**3b**	31.57 ± 4.51	38.59 ± 4.22*
2c	22.80 ± 3.51	28.06 ± 5.02*	**3c**	35.08 ± 5.28	42.10 ± 5.26*
2d	33.33 ± 2.20	36.84 ± 3.84*	**3d**	33.32 ± 3.51	35.08 ± 3.23*
2e	73.69 ± 3.60	82.45 ± 2.20	**3e**	29.82 ± 5.20	31.57 ± 5.92*
2f	35.08 ± 3.23	36.83 ± 3.84*	**3f**	40.34 ± 5.20	47.36 ± 5.44*
2g	35.08 ± 3.23	40.35 ± 4.44*	**3g**	28.06 ± 5.71	35.08 ± 7.40*
2h	80.70 ± 3.23	82.45 ± 2.21	**3h**	73.68 ± 3.60	75.38 ± 3.51*
Flurbiprophen	73.68 ± 4.51	80.69 ± 3.23	—	—	—

All compounds administered at an oral dose of 41 μmol/kg.

[a] Relative to standard and data were analyzed by ANOVA followed by Dunnett's multiple comparison test for $n = 6$.

* $P < 0.01$.

Table 2. Analgesic, ulcerogenic and lipid peroxidation activities of selected compounds

Compound	Analgesic activity[a]			Ulcerogenic activity (severity index ± SEM)[b]	nmol MDA content ± SEM/100 mg tissue[b]
	Pre-treatment/normal 0 h (s)	Post-treatment/after 4 h (s)	% Inhibition		
2e	1.22 ± 0.117	2.11 ± 0.136	72.90 ± 3.03*	0.500 ± 0.00**	5.04 ± 0.22**
2h	1.72 ± 0.183	2.22 ± 0.277	28.60 ± 2.81	0.833 ± 0.17**	5.58 ± 0.49
3h	1.76 ± 0.088	2.52 ± 0.113	43.20 ± 2.12*	0.583 ± 0.08**	5.18 ± 0.18**
Control	—	—	—	0.00	3.25 ± 0.05
Flurbiprofen	1.15 ± 0.060	1.95 ± 0.097	69.50 ± 1.88*	1.666 ± 0.24	7.51 ± 0.68

All compounds administered at an oral dose of 41 μmol/kg for analgesic activity and at 123 μmol/kg for ulcerogenic activity.
[a] Relative to normal (pre-treatment) and data were analyzed by paired Student's t test for $n = 6$.
[b] Relative to standard and data were analyzed by ANOVA followed by Dunnett's multiple comparison test for $n = 6$.
* $P < 0.0001$.
** $P < 0.01$.

Table 3. Effect of compounds on serum enzymes, total proteins and total albumin

Compound	SGOT[a] (U/mL)	SGPT[a] (U/mL)	Alkaline phosphatase[a]	Total protein[a] (g/dl)	Total albumin[a] (g/dl)
Control	148.67 ± 1.50	27.67 ± 0.84	13.06 ± 0.25	1.80 ± 0.01	1.67 ± 0.01
2e	147.50 ± 1.31	25.67 ± 0.67	12.08 ± 0.13	1.72 ± 0.05	1.63 ± 0.04
3h	143.67 ± 1.38*	25.33 ± 0.49	13.13 ± 0.21	1.77 ± 0.05	1.67 ± 0.04

[a] Relative to control and data were analyzed by ANOVA followed by Dunnett's multiple comparision test for $n = 6$.
* $P < 0.05$.

suggested that their protective effect be related to the inhibition of lipid peroxidation in the gastric mucosa.

Two compounds **2e** and**3h** showing potent anti-inflammatory and analgesic activities with reduced ulcerogenicity and lipid peroxidation, were further studied for their hepatotoxic effect. Both the compounds were studied for their effect on biochemical parameters[29–31] (serum enzymes, total protein, and total albumin) and histopathology of liver.[32] As shown in Table 3, both

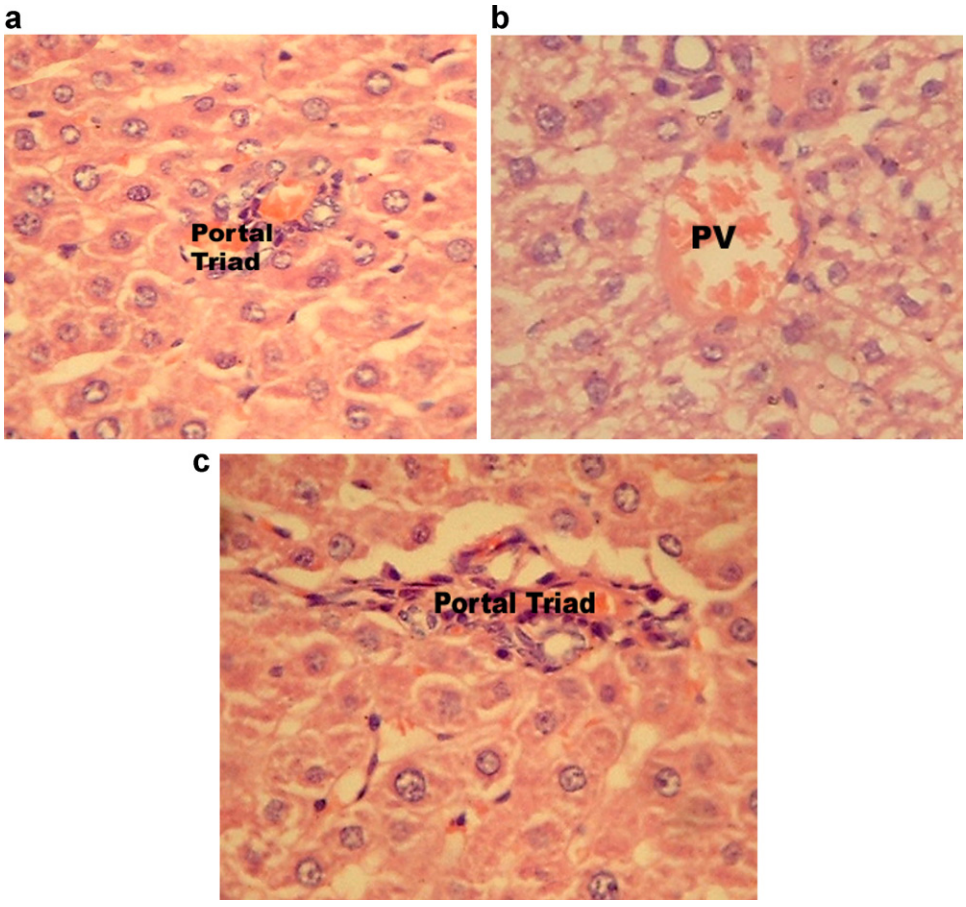

Figure 1. Histopathological studies of liver. Section of rat liver treated with compound **2e** (a) and compound **3h** (b), showing normal portal triad structure (400×). (c) Section of rat liver of control group, showing normal portal triad structure (400×).

the compounds did not show any significant variation in biochemical parameters in comparison to control. Histopathological studies of liver samples of the test compound **2e** (Fig.1a) and **3h** (Fig.1b) do not show any significant pathological changes in comparison to control group (Fig. 1c). No hepatocyte necrosis or degeneration was seen in any of the samples.

In summary, various pyrazoline derivatives were prepared with the objective of developing better anti-inflammatory agents with gastrosparing activity. It was interesting to note that three pyrazoline derivatives **2e**, **2h**, and **3h** were found to have significant anti-inflammatory activity. When these compounds were subjected to analgesic activity by tail immersion method in mice, compound **2e** showed high analgesic activity, more than standard drug flurbiprofen. These compounds were tested for ulcerogenic activity and they showed significant reduction in severity index than that of the standard drug. From these studies compound **2e**; 3-(4-biphenyl)-5-(4′-methyl phenyl)-2-pyrazoline has emerged as the lead compound, which showed maximum anti-inflammatory and analgesic activity. It also showed maximum reduction of severity index along with minimum lipid peroxidation, with no hepatocyte necrosis or degeneration. Thus the compound **2e** represents a fruitful matrix for development of a new class of non-acidic anti-inflammatory agent that would deserve further investigation and derivatisation.

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21. General procedure for synthesis of 3-aryl-1-(4-biphenyl)propen-1-ones: To a solution of 4-acetyl biphenyl (0.01 mol) in methanol and 1,4-dioxane (50 ml, 1:1), a concentrated solution of potassium hydroxide (5 ml) was added drop wise with stirring. Aromatic aldehydes (0.01 mol) were added to the above solution and the reaction mixture was stirred at room temperature for 12–14 h. It was slowly poured over crushed ice with constant stirring and the solid separated out was filtered, washed with water and recrystalised with ethanol, yield: 54–70% depending on aldehydes.
22. General procedure for synthesis of 3-(4-biphenyl)-5-substituted phenyl-2-pyrazolines: Compounds **1a**–**h** (0.001 mol), hydrazine hydrate (0.003 mol) and few drops of conc. hydrochloric acid were added to a mixture of DMF and ethanol (25 ml, 1:1). It was then heated in an oil bath at 90–100 °C for 4 h. The colour of the reaction mixture changed to yellowish green. The reaction mixture was allowed to cool at room temperature and was kept in refrigerator for 4–5 h. Fine crystals thus separated out were filtered, washed with cold ethanol, dried and recrystallised with ethanol, yield: 83–95% depending on substitution.
23. General procedure for synthesis of 1-benzoyl-3-(4-biphenyl)-5-substituted phenyl-2-pyrazolines: To compounds **2a**–**h** (0.001 mol) in pyridine (10 ml), benzoyl chloride (0.002 mol) was added. The reaction mixture was heated on water bath for 3 h and poured over crushed ice mixed with dil. hydrochloric acid. The solid separated out was filtered, washed with water, dried and recrystallised from ethanol, yield: 60–78% depending on substitution.
24. Physical and spectral data of selected compounds.
Compound **2a**: yield 86%, mp 102 °C; IR (KBr, ν cm^{-1}): 3233 (NH), 1620 (C=N); ^{1}H NMR ($CDCl_3$, δ): 3.21 (dd, J_{XM} = 9.7 Hz, J_{XA} = 5.6 Hz, 1H, CH_2 pyrazoline), 3.46 (dd, J_{MX} = 9.7 Hz, J_{MA} = 6.8 Hz, 1H, CH_2 pyrazoline), 5.23 (dd, J_{AX} = 5.6 Hz, J_{AM} = 6.8 Hz, 1H, CH pyrazoline), 7.09–7.46 (m, 14H, Ar-H), 8.95 (br s, 1H, NH); MS: *m/z* 298 (M^+); Anal. Calcd for $C_{21}H_{18}N_2$: C, 84.56; H, 6.04; N, 9.39. Found: C, 84.60; H, 6.09; N, 9.41.
Compound **2c**: yield 83%, mp 124 °C; IR (KBr, ν cm^{-1}): 3243 (NH), 1602 (C=N); ^{1}H NMR ($CDCl_3$, δ): 3.03 (dd, J_{XM} = 9.0 Hz, J_{XA} = 4.6 Hz, 1H, CH_2 pyrazoline), 3.51 (dd, J_{MX} = 9.0 Hz, J_{MA} = 6.9 Hz, 1H, CH_2 pyrazoline), 4.94 (dd, J_{AX} = 4.6 Hz, J_{AM} = 6.9 Hz, 1H, CH pyrazoline), 7.20–7.93 (m, 13H, ArH), 8.09 (br s, 1H, NH); MS: *m/z* 332 (M^+); Anal. Calcd for $C_{21}H_{17}ClN_2$: C, 75.78; H, 5.11; N, 8.42. Found: C, 75.84; H, 5.18; N, 8.46.

Compound **2d**: yield 93%, mp 166 °C; IR (KBr, ν cm^{-1}): 3231 (NH), 1590 (C=N); ^{1}H NMR ($CDCl_3$, δ): 2.43 (s, 6H, $(CH_3)_2$), 3.18 (dd, J_{XM} = 12.7 Hz, J_{XA} = 4.7 Hz, 1H, CH_2 pyrazoline), 3.61 (dd, J_{MX} = 12.7 Hz, J_{MA} = 6.9 Hz, 1H, CH_2 pyrazoline), 5.49 (dd, J_{AX} = 4.7 Hz, J_{AM} = 6.9 Hz, 1H, CH pyrazoline), 7.16–7.82 (m, 13H, ArH), 9.05 (br s, 1H, NH); MS: *m*/*z* 341 (M^+); Anal. Calcd for $C_{23}H_{23}N_3$: C, 80.93; H, 6.74; N, 12.31. Found: C, 80.99; H, 6.71; N, 12.28.

Compound **2e**: yield 88%, mp 164 °C; IR (KBr, ν cm^{-1}): 3273 (NH), 1590 (C=N); ^{1}H NMR ($CDCl_3$, δ): 2.32 (s, 3H, CH_3), 3.20(dd, J_{XM} = 12.9 Hz, J_{XA} = 4.7 Hz, 1H, CH_2 pyrazoline), 3.77 (dd, J_{MX} = 12.9 Hz, J_{MA} = 6.9 Hz, 1H, CH_2 pyrazoline), 5.50 (dd, J_{AX} = 4.7 Hz, J_{AM} = 6.9 Hz, 1H, C*H* pyrazoline), 7.16–7.82 (m, 13H, Ar*H*), 8.97 (br s, 1H, N*H*); MS: *m*/*z* 312 (M^+); Anal. Calcd for $C_{22}H_{20}N_2$: C, 84.61; H, 6.41; N, 8.97. Found: C, 84.66; H, 6.39; N, 8.94.

Compound **2f**: yield 85%, mp 158 °C; IR (KBr, ν cm^{-1}): 3260 (NH), 1610 (C=N),1255(C–O–C);^{1}H NMR ($CDCl_3$, δ): 3.19 (dd, J_{XM} = 12.0 Hz, J_{XA} = 4.7 Hz, 1H, CH_2 pyrazoline), 3.89–3.99 (m, 4H, OCH_3 & 1H of CH_2 pyrazoline), 5.48 (dd, J_{AX} = 4.7 Hz, J_{AM} = 6.9 Hz, 1H, CH pyrazoline), 7.14–8.01 (m, 13H, Ar-H), 8.90 (br s, 1H, NH); MS: *m*/*z* 328 (M^+). Anal. Calcd for $C_{22}H_{20}N_2O$: C, 80.48; H, 6.09; N, 8.53. Found: C, 80.37; H, 6.14; N, 8.48.

Compound **2g**: yield 83%, mp 128 °C; IR (KBr, ν cm^{-1}): 3235 (NH), 1583 (C=N), 1250(C–O–C); ^{1}H NMR ($CDCl_3$, δ): 3.22 (dd, J_{XM} = 12.8 Hz, J_{XA} = 4.8 Hz, 1H, CH_2 pyrazoline), 3.82–3.89 [m, 7H, $(OCH_3)_2$ & 1H of CH_2 pyrazoline], 5.48 (dd, J_{AX} = 4.8 Hz, J_{AM} = 6.9 Hz, 1H, CH pyrazoline), 6.77–7.83 (m, 12H, Ar-H), 8.99 (br s, 1H, NH); MS: *m*/*z* 358 (M^+); Anal. Calcd for $C_{23}H_{22}N_2O_2$: C, 77.09; H, 6.14; N, 7.82. Found: C, 77.01; H, 6.18; N, 7.89.

Compound **2h**: yield 92%, mp 190 °C; IR (KBr, ν cm^{-1}): 3233 (NH), 1589 (C=N), 1256(C–O–C); ^{1}H NMR ($CDCl_3$, δ): 3.24 (dd, J_{XM} = 12.8 Hz, J_{XA} = 4.8 Hz, 1H, CH_2 pyrazoline), 3.82–3.89 [m, 10H, $(OCH_3)_3$ & 1H of CH_2 pyrazoline], 5.50 (dd, J_{AX} = 4.8 Hz, J_{AM} = 6.8 Hz, 1H, CH pyrazoline), 6.77–7.83 (m, 11H, ArH), 9.04 (br s, 1H, NH); MS: *m*/*z* 388 (M^+); Anal. Calcd for $C_{24}H_{24}N_2O_3$: C, 74.22; H, 6.18; N, 7.21. Found: C, 74.29; H, 6.22; N, 7.23.

Compound **3d**: yield 71%, mp 154 °C; IR (KBr, ν cm^{-1}): 1634 (C=O), 1587 (C=N); ^{1}H NMR ($CDCl_3$, δ): 2.91 (s, 6H, $(CH_3)_2$), 3.21 (dd, J_{XM} = 13.05 Hz, J_{XA} = 4.3 Hz, 1H, CH_2 pyrazoline), 3.61 (dd, J_{MX} = 13.05 Hz, J_{MA} = 6.2 Hz, 1H, CH_2 pyrazoline), 5.74 (dd, J_{AX} = 4.3 Hz, J_{AM} = 6.2 Hz, 1H, CH pyrazoline), 7.03–8.08 (m, 18H, Ar-H); MS: *m*/*z* 445 (M^+); Anal. Calcd for $C_{30}H_{27}N_3O$: C, 80.89; H, 6.06; N, 9.43. Found: C, 80.81; H, 6.13; N, 9.37.

Compound **3e**: yield 64%, mp 104 °C; IR (KBr, ν cm^{-1}): 1669 (C=O), 1599 (C=N); ^{1}H NMR ($CDCl_3$, δ): 2.31 (s, 3H, CH_3), 3.19 (dd, J_{XM} = 13.44 Hz, J_{XA} = 4.2 Hz, 1H, CH_2 pyrazoline), 3.75 (dd, J_{MX} = 13.44 Hz, J_{MA} = 5.7 Hz, 1H, CH_2 pyrazoline), 5.50 (dd, J_{AX} = 4.2 Hz, J_{AM} = 5.7 Hz, 1H, C*H* pyrazoline), 7.15–8.14 (m, 18H, Ar*H*); MS: *m*/*z* 416 (M^+); Anal. Calcd for $C_{29}H_{24}N_2O$: C, 83.65; H, 5.76; N, 6.73. Found: C, 83.53; H, 5.69; N, 6.78.

Compound **3f**: yield 73%, mp 114 °C; IR (KBr, ν cm^{-1}): 1622 (C=O), 1569 (C=N), 1238(C–O–C); ^{1}H NMR ($CDCl_3$, δ): 3.03 (dd, J_{XM} = 10.5 Hz, J_{XA} = 5.6 Hz, 1H, CH_2 pyrazoline), 3.15 (dd, J_{MX} = 10.5 Hz, J_{AM} = 7.6 Hz, 1H, CH_2 pyrazoline), 3.89 (s, 3H, OCH_3), 4.94 (dd, J_{AX} = 5.6 Hz, J_{AM} = 7.6 Hz, 1H, CH pyrazoline), 7.20–7.87 (m, 18H, ArH); MS: *m*/*z* 432 (M^+); Anal. Calcd for $C_{29}H_{24}N_2O_2$: C, 80.55; H, 5.55; N, 6.48. Found: C, 80.62; H, 5.59; N, 6.51.

Compound **3g**: yield 73%, mp 98 °C; IR (KBr, ν cm^{-1}): 1647 (C=O), 1597 (C=N), 1234 (C–O–C); ^{1}H NMR ($CDCl_3$, 3.26 (dd, J_{XM} = 11.0 Hz, J_{XA} = 5.2 Hz, 1H, CH_2 pyrazoline), 3.80–3.88 [m, 7H, $(OCH_3)_2$ & 1H of CH_2 pyrazoline], 5.62 (dd, J_{AX} = 5.2 Hz, J_{AM} = 6.7 Hz, 1H, CH pyrazoline), 6.81–7.79 (m, 17H, Ar-H); MS: *m*/*z* 462 (M^+). Anal. Calcd for $C_{30}H_{26}N_2O_3$: C, 77.92; H, 5.62; N, 6.06; Found: C, 77.83; H, 5.67; N, 6.12.

Compound **3h**: yield 78%, mp 152 °C; IR (KBr, ν cm^{-1}): 1639 (C=O), 1590 (C=N), 1249 (C–O–C); ^{1}H NMR ($CDCl_3$, δ): 3.22 (dd, J_{XM} = 10.9 Hz, J_{XA} = 4.8 Hz, 1H, CH_2 pyrazoline), 3.81–3.89 [m, 10H, $(OCH_3)_3$ & 1H of CH_2 pyrazoline], 5.50 (dd, J_{AX} = 4.8 Hz, J_{AM} = 6.8 Hz, 1H, CH pyrazoline), 6.79–7.83 (m, 16H, Ar-H); MS: *m*/*z* 492 (M^+); Anal. Calcd for $C_{31}H_{28}N_2O_4$: C, 75.60; H, 5.69; N, 5.69. Found: C, 75.51; H, 5.73; N, 5.62.

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