ISSN 1070-3632, Russian Journal of General Chemistry, 2014, Vol. 84, No. 11, pp. 2248–2256. © Pleiades Publishing, Ltd., 2014.

One Pot Multicomponent Synthesis of 3',5-Diaryl-1'-phenyl-3,4-dihydro-1'*H*,2*H*-3,4'-bipyrazoles and Their Antimicrobial Activity[1]

D. Ashok[a], Arram Ganesh[a], S. Ravi[a], B. Vijaya Lakshmi[a], and B. Ramesh[b]

[a] *Department of Chemistry, Osmania University, Hyderabad, India*

[b] *Department of Chemistry, Degree and P. G. College, Siddipet, India*
e-mail: ashokdou@gmail.com

Received October 7, 2014

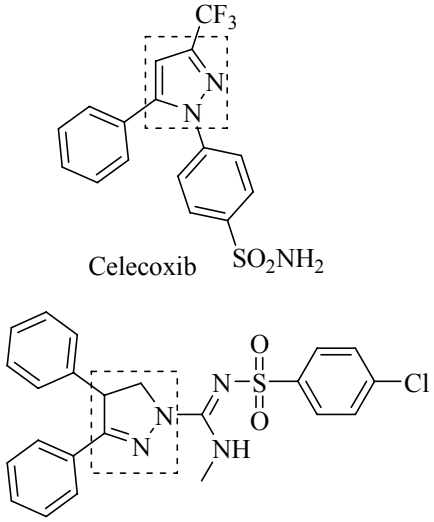
Abstract—One pot multicomponent synthesis of 3',5-Diaryl-1'-phenyl-3,4-dihydro-1'*H*,2*H*-3,4'-bipyrazoles from 1-(1-methoxynaphthalen-2-yl)ethanone/1-(2-methoxynaphthalen-1-yl)ethanone, 3-aryl-1-phenyl-1*H*-pyrazole-4-carbaldehyde and hydrazines in the presence of basic alumina under conventional heating, ultrasound and microwave irradiation methods is presented. All newly synthesized compounds were evaluated for their in vitro antibacterial activity against bacterial strains Gram-positive (*Staphylococcus aureus*), Gram-negative (*Escherichia coli*) and strains (*Aspergillus niger* and *Candida metapsilosis*). The results of anti-bacterial and antifungal studies revealed that all compounds exhibited good antimicrobial activity. All synthesized analogues were characterized by IR, ^{1}H and ^{13}C NMR, and mass spectral data and elemental analysis.

Keywords: pyrazoline, pyrazole, microwave irradiation, ultrasound irradiation, antimicrobial activity

DOI: 10.1134/S1070363214110346

The pyrazole core is one of the important five membered nitrogen heterocyclic motifs embedded in several natural products and drugs (see figure) [1, 2]. Pyrazole derivatives possess significant biological activities including antimicrobial [3], antiviral [4], antitumor [5, 6], antihistaminic [7], antidepressant [8], insecticides [9], fungicides [9], 5α-reductase inhibitor [10], anti-proliferative [11], anti-parasitic [12], herbicides [13], anti-inflammatory [14], and antiprotozoal [15, 16].

Considerable attention has been focused on substituted pyrazolines due to their antifungal [17], anti-depressant [18] anticonvulsant [19] anti-inflammatory [20], antibacterial [21] and antitumor [22] and some other [23–25] activities. Synthetic methods for such compounds have some disadvantages such as long reaction time, organic solvents media and others. Recently, K_2CO_3 mediated microwave irradiation has been shown to be an efficient synthetic approach to pyrazolines [26]. Ultrasound and microwave irradiation methods have increasingly been used in organic synthesis in the last few decades at the expense of conventional heating methods. The ultrasound and microwave irradiation procedures are more simple, need shorter reaction time, mild reaction conditions and give high yields of products. We report here development of the ongoing study of ultrasound and microwave irradiation in organic synthesis, specifically the one pot synthesis of 3',5-Di-aryl-1'-phenyl-3,4-dihydro-1'*H*,2*H*-3,4'-bipyrazoles and their antimicrobial activity (see Schemes 1, 2 and table).



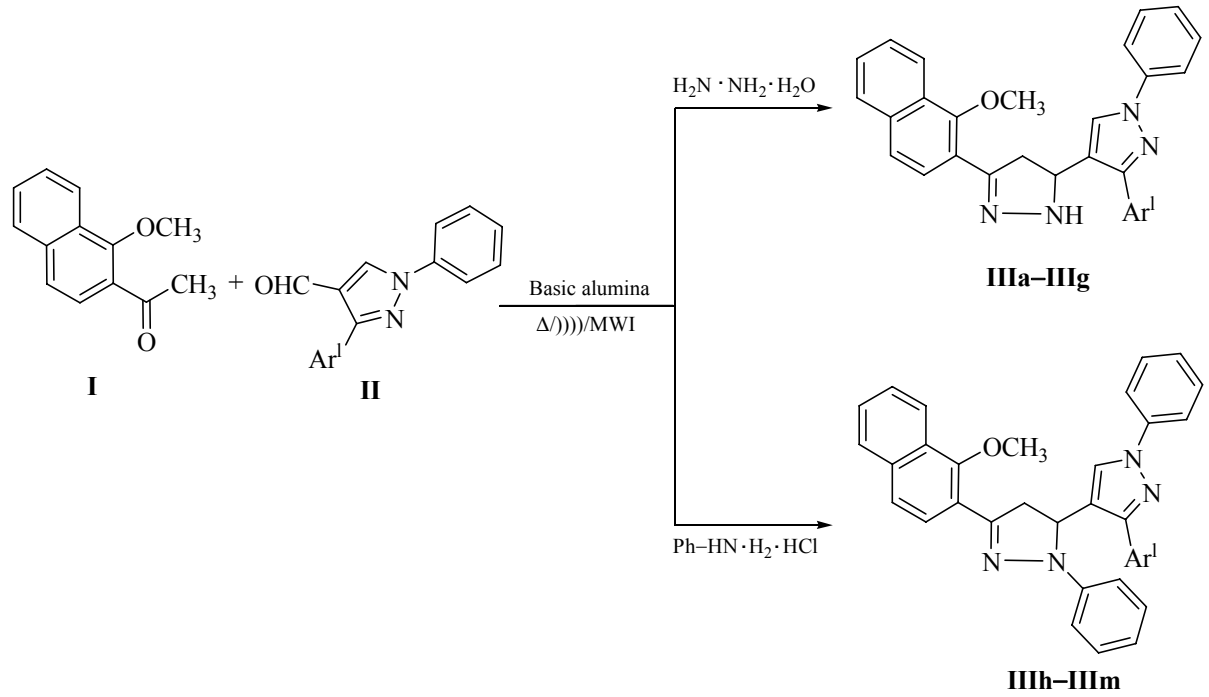
Celecoxib

Ibipinabant

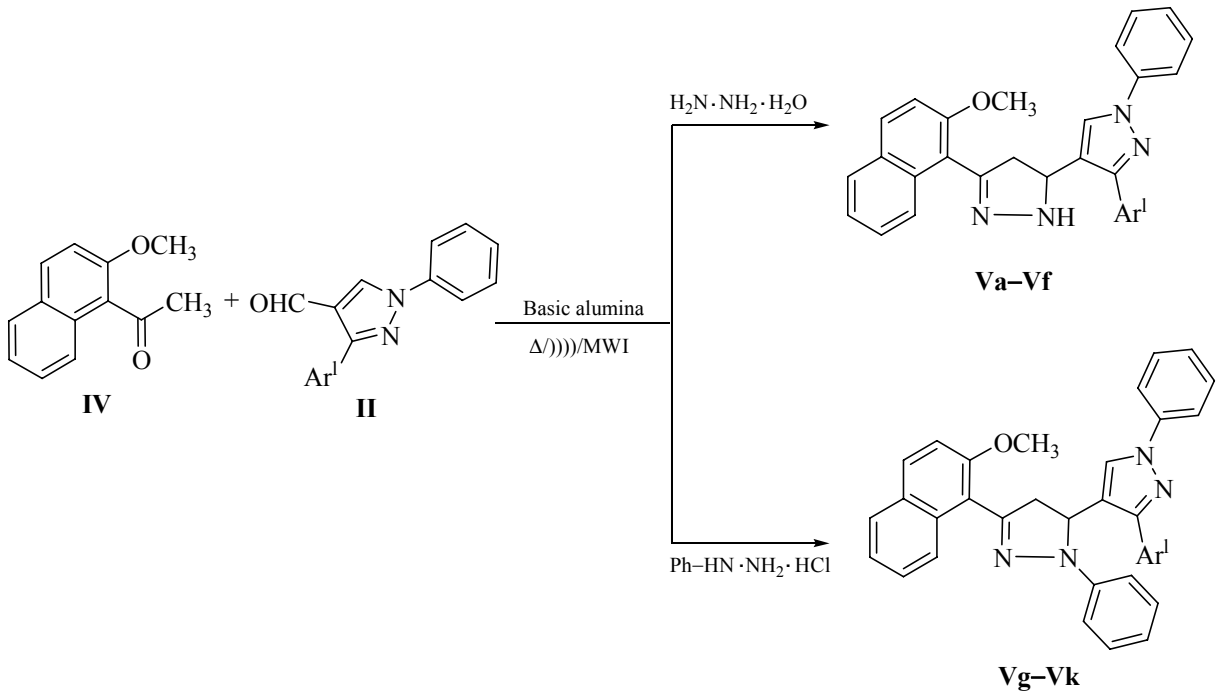
Pyrazole and pyrazoline core embedded drugs.

[1] The text was submitted by the authors in English.

Scheme 1.



Scheme 2.



Ar^1 = phenyl (**IIa**), 4-methylphenyl (**IIb**), 4-methoxyphenyl (**IIc**), 4-chlorophenyl (**IId**), 4-bromophenyl (**IIe**), 4-nitrophenyl (**IIf**), thienyl (**IIg**). Ar^1 = phenyl (**IIIa, IIIh**), 4-methylphenyl (**IIIb, IIIi**), 4-methoxyphenyl (**IIIc, IIIj**), 4-chlorophenyl (**IIId**), 4-bromophenyl (**IIIe, IIIk**), 4-nitrophenyl (**IIIf, IIIl**), thienyl (**IIIg, IIIm**). Ar^1 = phenyl (**Va, Vg**), 4-methylphenyl (**Vb, Vh**), 4-methoxyphenyl (**Vc, Vi**), 4-bromophenyl (**Vd, Vj**), 4-nitrophenyl (**Ve, Vk**), thienyl (**Vf**).

Conditions for the synthesis of 3',5-di-aryl-1'-phenyl-3,4-dihydro-1'*H*,2*H*-3,4'-bipyrazoles **IIIa–IIIm** and **Va–Vk**

Comp.no.	mp, °C	Reaction time			Yield, %		
		Conventional heating, h	USI[a], h	MWI[b], min	Conventional heating	USI[a]	MWI[b]
IIIa	152	4.5	2.5	3.5	63	71	80
IIIb	138	4.5	2.0	3.0	66	74	84
IIIc	120	4.0	2.0	3.0	65	73	85
IIId	159	5.0	3.0	3.5	62	70	83
IIIe	148	5.0	3.0	4.0	65	72	80
IIIf	127	4.0	3.0	4.0	60	70	82
IIIg	131	5.0	2.5	3.0	65	76	85
IIIh	153	4.5	3.0	4.0	61	72	80
IIIi	202	4.5	2.5	3.0	63	74	82
IIIj	119	5.0	2.5	3.0	64	75	83
IIIk	170	5.0	3.0	4.0	60	72	82
IIIl	146	4.5	3.0	4.0	62	70	80
IIIm	122	4.5	2.5	3.5	64	76	84
Va	133	4.5	3.0	4.0	60	72	84
Vb	202	4.5	2.5	3.5	63	75	88
Vc	119	4.0	2.5	3.5	64	78	90
Vd	170	5.0	3.0	4.0	62	74	86
Ve	146	5.0	3.0	4.0	60	72	84
Vf	122	4.0	2.5	3.0	66	76	90
Vg	126	5.0	3.0	3.5	62	70	83
Vh	140	4.5	2.5	3.5	64	74	85
Vi	137	4.5	2.5	3.5	64	75	88
Vj	125	5.0	3.0	4.0	61	74	86
Vk	156	5.0	3.0	4.0	60	70	84

[a] Ultrasound irradiation. [b] Microwave irradiation.

Antibacterial activity. All products were screened for their *in vitro* antibacterial activity against *Escherichia coli,* and *Staphylococcus aureus* using Ampicillin as standard drug. The activity was determined using cup plate agar diffusion method by measuring the zone of inhibition in mm. The compounds were screened at the concentrations of 25, 50, and 100 μg/mL in DMSO. From the screening studies it is evident that the synthesized compounds **IIIc, IIIj**, **IIIm, Vc,** and **Vj** exhibited higher activity than the standard drug against all tested organisms.

Antifungal activity. All products were screened for their antifungal activity in vitro against *Aspergillus niger* and *Candida metapsilosis* using Grieseofulvin as standard drug. The activity was determined using the method presented in the section above. The study made it evident that the synthesized compounds **IIIa,**

IIIe, **IIIm, Vb, Vi,** and **Vk** had higher activity than the standard drug against all tested organisms.

EXPERIMENTAL

Melting points were measured in open capillary tubes. Purity of compounds was monitored by TLC on silica gel plates 60 F254 (Merck). Reactions under microwave irradiation were carried out in milestone multi SYNTH microwave system. Sonication was performed in Shanghai BUG40-06 ultrasonic cleaner (frequencies 25, 40, and 59 kHz and nominal power 250 W). IR (KBr) spectra were recorded on a Shimadzu FT-IR-8400s spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were measured on Bruker Avance II 400 MHz spectrometer (TMS internal standard). Mass spectra were measured on a GCMS-QP 1000EX mass spectrometer. Elemental analysis was carried out by a Thermo Finnigan CHNS analyzer.

General procedure for the synthesis of 3',5-diaryl-1'-phenyl-3,4-dihydro-1'*H*,2*H*-3,4'-bipyrazoles IIIa–IIIm and Va–Vk. *a. Conventional heating method.* A mixture of arylmethyl ketones **I, IV** (1 mmol), 3-aryl-1-phenyl-1*H*-pyrazole-4-carbaldehydes **II** (1 mmol), substituted hydrazines (1.2 mmol), and basic alumina (2 mg) in ethanol (5 mL) was loaded in a round bottom flask and refluxed for 4–5 h. Progress of the reaction was monitored by TLC, upon completion of the reaction, the product was extracted with ethyl acetate (2 × 20 mL). The solvent was removed under reduced pressure and the crude solid purified by column chromatography on silica-gel (petroleum ether : ethyl acetate, 8 : 2, v/v) to yield the title compounds **IIIa–IIIm and Va–Vk**.

b. Ultrasonic irradiation method. A mixture of arylmethyl ketones **I, IV** (1 mmol), 3-aryl-1-phenyl-1*H*-pyrazole-4-carbaldehydes **II** (1 mmol), substituted hydrazines (1.2 mmol), and basic alumina (2 mg) in ethanol (5 mL) was loaded in a conical flask and it was subjected to ultrasound irradiation for 2–3 h at 60°C. Progress of the reaction was monitored by TLC. Upon completion of the reaction the product was extracted with ethyl acetate (2 × 20 mL). The solvent was removed under reduced pressure and the crude solid was purified by column chromatography on silica-gel (hexane : ethyl acetate 8 : 2, v/v) to yield the title compounds **IIIa–IIIm and Va–Vk**.

c. Microwave irradiation method. Basic alumina (2 mg) was added to a mixture of aryl methyl ketones **I, IV** (1 mmol), 3-aryl-1-phenyl-1*H*-pyrazole-4-carbaldehydes **II** (1 mmol), and substituted hydrazines (1.2 mmol) in ethanol (10 mL). Ethanol was removed under vacuum and the mixture was irradiated under microwave for 3–4 min at 160 W with 30 s intervals. Progress of the reaction was monitored by TLC. Upon completion of the reaction, the product was extracted with ethyl acetate (2 × 20 mL). Ethyl acetate was removed under reduced pressure and the crude solid was purified by column chromatography on silica-gel (hexane : ethyl acetate 8 : 2, v/v) to yield the title compounds **IIIa–IIIm** and **Va–Vk**.

Compound IIIa. IR spectrum, ν, cm^{-1}: 1597 (C=N), 1623 (C=C), 3051 (C–H), 3297 (N–H). ^{1}H NMR spectrum, δ, ppm: 3.25–3.31 d.d (1H, CH_2, J = 7.2, 16.4 Hz), 3.44–3.51 d.d (1H, CH_2, J = 9.6, 16.4 Hz), 3.96 s (3H, O–CH_3), 5.50–5.53 d.d (1H, CH_2, J = 7.2, 10 Hz), 6.05 br.s (1H, NH), 7.30–7.49 m (8H, ArH), 7.77–7.81 m (4H, ArH), 7.88–7.90 d (1H, ArH), 8.02–8.04 d (2H, ArH), 8.13–8.15 d (1H, ArH), 8.23 s (1H, pyrazol proton). ^{13}C NMR spectrum, δ_C, ppm: 44.4, 55.5(N–CH), 56.4 (O–CH_3), 112.8, 116.4, 118.9, 123.5, 123.9, 124.7, 126.2, 126.4, 127.2, 128.0, 128.1, 128.2, 128.7, 129.2, 129.4, 130.6, 132.9, 133.1, 140.0, 151.1, 155.4. Found, %: C 78.42, H 5.40, N 12.53. $C_{29}H_{24}N_4O$. Calculated, %: C 78.36, H 5.44, N 12.60. M 445 $[M + H]^+$.

Compound IIIb. IR spectrum, ν, cm^{-1}: 1598 (C=N), 1621 (C=C), 3052 (C–H), 3332 (N–H). ^{1}H NMR spectrum, δ, ppm: 2.45 s (3H, CH_3), 3.24–3.30 d.d (1H, CH_2, J = 7.2, 16.4 Hz), 3.43–3.50 d.d (1H, CH_2, J = 9.6, 16.4 Hz), 3.96 s (3H, O–CH_3), 5.49–5.53 d.d (1H, CH_2, J = 7.2, 9.6 Hz), 6.05 br.s (1H, NH), 7.27–7.39 m (5H, ArH), 7.44–7.49 m (3H, ArH), 7.65–7.67 d (2H, ArH), 7.76–7.81 m (3H, ArH), 7.88–7.91 d (1H, ArH), 8.12–8.14 d (1H, ArH), 8.31 s (1H, pyrazol proton). ^{13}C NMR spectrum, δ_C, ppm: 21.3 (CH_3), 44.4, 55.5 (N–CH), 56.4 (O–CH_3), 112.8, 116.5, 118.9, 123.4, 123.9, 124.7, 126.1, 126.3, 127.2, 128.0, 128.1, 128.2, 128.7, 129.2, 129.4, 130.2, 130.6, 132.9, 137.9, 140.1, 151.2, 155.4. Found, %: C 78.54, H 5.78, N 12.28. $C_{30}H_{26}N_4O$. Calculated, %: C 78.58, H 5.72, N 12.22. M 490 $[M + H]^+$.

Compound IIIc. IR spectrum, ν, cm^{-1}: 1597 (C=N), 1614 (C=C), 3053 (C–H), 3332 (N–H). ^{1}H NMR spectrum, δ, ppm: 3.25–3.31 d.d (1H, CH_2, J = 6.8, 16.4 Hz), 3.43–3.50 d.d (1H, CH_2, J = 9.8, 16.8 Hz), 3.84 s (3H, OCH_3), 3.96 s (3H, O–CH_3), 5.49–5.53 d.d (1H, CH_2, J = 7.2, 9.6 Hz), 6.05 br.s (1H, NH), 6.84–

6.86 d (2H, ArH), 7.28–7.50 m (5H, ArH), 7.54–7.56 d (2H, ArH), 7.72–7.74 d (2H, ArH), 7.78–7.82 d.d (2H, ArH), 7.87–7.90 d (1H, ArH), 8.08–8.10 d (1H, ArH), 8.26 s (1H, pyrazol proton). ^{13}C NMR spectrum, δ_C, ppm: 21.3 (CH_3), 44.3, 55.3 (N–CH), 56.4 (O–CH_3), 112.8, 115.9, 119.0, 122.8, 124.0, 123.5, 123.9, 124.7, 126.3, 126.5, 127.3, 128.0, 128.8, 129.1, 129.4, 129.6, 130.2, 130.6, 132.8, 139.9, 151.4, 152.3, 155.4, 156.6. Found, %: C 75.86, H 5.58, N 11.78. $C_{30}H_{26}N_4O_2$. Calculated, %: C 75.93, H 5.52, N 11.81. *M* 475 $[M + H]^+$.

Compound IIId. IR spectrum, ν, cm^{-1}: 1599 (C=N), 1622 (C=C), 3054 (C–H), 3335 (N–H). ^{1}H NMR spectrum, δ, ppm: 3.22–3.28 d.d (1H, CH_2, *J* = 6.8, 16.2 Hz), 3.43–3.49 d.d (1H, CH_2, *J* = 10, 16.4 Hz), 3.96 s (3H, OCH_3), 5.16–5.21 d.d (1H, CH_2, *J* = 6.8, 10.4 Hz), 6.05 br.s (1H, NH), 7.29–7.33 m (2H, ArH), 7.34–7.39 m (2H, ArH), 7.45–7.49 d (3H, ArH), 7.72–7.77 m (4H, ArH), 7.79–7.81 d (2H, ArH), 7.88–7.90 d (1H, ArH), 8.11–8.13 d (1H, ArH), 8.31 s (1H, pyrazol proton). ^{13}C NMR spectrum, δ_C, ppm: 44.4, 55.4 (N–CH), 56.4 (O–CH_3), 112.8, 116.2, 118.9, 123.4, 123.9, 124.6, 126.5, 126.6, 127.3, 128.0, 128.9, 129.1, 129.4, 129.5, 130.7, 131.7, 132.9, 134.1, 139.9, 149.9, 151.2, 155.4. Found, %: C 72.64, H 4.91, N 11.65. $C_{29}H_{23}ClN_4O$. Calculated, %: C 72.72, H 4.84, N 11.70. *M* 479 $[M + H]^+$.

Compound IIIe. IR spectrum, ν, cm^{-1}: 1598 (C=N), 1621 (C=C), 3049 (C–H), 3309 (N–H). ^{1}H NMR spectrum, δ, ppm: 3.23–3.29 d.d (1H, CH_2, *J* = 6.8, 16.6 Hz), 3.45–3.50 d.d (1H, CH_2, *J* = 9.6, 16.4 Hz), 3.93 s (3H, OCH_3), 5.20–5.25 d.d (1H, CH_2, *J* = 6.8, 9.4 Hz), 6.05 br.s (1H, NH), 7.26–7.37 m (3H, ArH), 7.44–7.49 m (3H, ArH), 7.58–7.60 d (2H, ArH), 7.64–7.66 d (2H, ArH), 7.75–7.79 m (3H, ArH), 7.87–7.89 d (1H, ArH), 8.11–8.13 d (1H, ArH), 8.33 s (1H, pyrazol proton). ^{13}C NMR spectrum, δ_C, ppm: 44.4, 55.5 (N–CH), 56.4 (O–CH_3), 112.8, 116.2, 118.9, 122.3, 123.4, 123.9, 124.6, 126.5, 126.6, 127.3, 128.0, 128.9, 129.1, 129.5, 129.7, 130.7, 131.9, 132.1, 132.9, 139.9, 149.9, 151.2, 155.4. Found, %: C 66.48, H 4.47, N 10.75. $C_{29}H_{23}BrN_4O$. Calculated, %: C 66.54, H 4.43, N 10.70. *M* 523 $[M + H]^+$.

Compound IIIf. IR spectrum, ν, cm^{-1}: 1599 (C=N), 1622 (C=C), 3049 (C–H), 3372 (N–H). ^{1}H NMR spectrum, δ, ppm: 3.22–3.28 d.d (1H, CH_2, *J* = 8, 16 Hz), 3.46–3.53 d.d (1H, CH_2, *J* = 10, 16.8 Hz), 3.96 s (3H, OCH_3), 5.23–5.25 d.d (1H, CH_2, *J* = 8, 10 Hz), 6.05 br.s (1H, NH), 7.26–7.36 m (2H, ArH), 7.35–7.39 m (2H, ArH), 7.48–7.52 m (3H, ArH), 7.78–7.82 d.d (2H, ArH), 7.89–7.91 d (1H, ArH), 8.01–8.05 m (2H, ArH), 8.12–8.14 d (1H, ArH), 8.33–8.37 s (3H, pyrazol proton and ArH). ^{13}C NMR spectrum, δ_C, ppm: 44.3, 55.5 (N–CH), 56.4 (OCH_3), 112.8, 115.2, 118.7, 123.9, 124.7, 125.9, 126.1, 127.2, 128.1, 128.7, 129.2, 129.3, 129.6, 129.6, 130.5, 132.1, 132.9, 139.7, 140.2, 146.5, 151.4, 155.4. Found, %: C 71.08, H 4.79, N 14.28. $C_{29}H_{23}N_5O_3$. Calculated, %: C 71.15, H 4.74, N 14.31. *M* 490 $[M + H]^+$.

Compound IIIg. IR spectrum, ν, cm^{-1}: 1595 (C=N), 1621 (C=C), 3067 (C–H), 3319 (N–H). ^{1}H NMR spectrum, δ, ppm: 3.24–3.30 d.d (1H, CH_2, *J* = 7.2, 16.6 Hz), 3.49–3.56 d.d (1H, CH_2, *J* = 10, 16.6 Hz), 3.94 s (3H, OCH_3), 5.49–5.53 t (1H, CH_2, *J* = 7.2, 9.8 Hz), 6.05 br.s (1H, NH), 7.14–7.16 d.d (1H, ArH), 7.27–7.38 m (4H, ArH), 7.44–7.49 m (4H, ArH), 7.74–7.76 d (2H, ArH), 7.79–7.81 d (1H, ArH), 7.88–7.90 d (1H, ArH), 8.13–8.15 d (1H, ArH), 8.25 s (1H, pyrazol proton). ^{13}C NMR spectrum, δ_C, ppm: 43.9, 55.5 (N–CH), 56.4 (O–CH_3), 112.8, 116.5, 118.9, 122.9, 123.9, 124.2, 124.7, 125.4, 125.6, 126.4, 126.6, 127.2, 127.7, 128.0, 129.2, 129.5, 130.7, 132.9, 135.3, 139.8, 145.4, 151.1, 155.5. Found, %: C 71.88, H 4.96, N 12.51, S, 7.08. $C_{27}H_{22}N_4OS$. Calculated, %: C 71.98, H 4.92, N 12.44, S, 7.12. *M* 451 $[M + H]^+$.

Compound IIIh. IR spectrum, ν, cm^{-1}: 1595 (C=C), 1623 (C=N), 3055 (C–H). ^{1}H NMR spectrum, δ, ppm: 3.55–361 d.d (1H, CH_2, *J* = 6.8, 17.4 Hz), 3.86 s (3H, OCH_3), 4.06–4.14 d.d (1H, CH_2, *J* = 12, 17.4 Hz), 5.23–5.76 d.d (1H, CH_2, *J* = 6.8, 12 Hz), 6.81–6.84 t (1H, ArH), 7.14–7.16 d (1H, ArH), 7.20–7.25 m (4H, ArH), 7.38–7.40 m (2H, ArH), 7.45–7.52 m (4H, ArH), 7.61–7.66 m (5H, ArH), 7.72–7.73 (dd, 1H, ArH), 7.82 s (1H, pyrazol proton); 7.82–7.84 d.d (2H, ArH), 8.09–8.10 d (1H, ArH). ^{13}C NMR spectrum, δ_C, ppm:45.4, 56.8 (OCH_3), 63.0 (N–CH), 113.8, 118.9, 119.5, 121.9, 122.4, 123.0, 124.3, 124.7, 125.8, 126.3, 126.4, 126.5, 126.7, 128.1, 128.3, 128.4, 128.8, 129.0, 129.3, 133.2, 135.2, 139.8, 144.7, 146.2, 150.2, 154.6. Found: C 80.70, H 5.48, N 10.71. $C_{35}H_{28}N_4O$. Calculated, %: C 80.74, H 5.42, N 10.76. *M* 521 $[M + H]^+$.

Compound IIIi. IR spectrum, ν, cm^{-1}: 1596 (C=C), 1620 (C=N), 3051 (C–H). ^{1}H NMR spectrum, δ, ppm: 2.42 s (3H, CH_3), 3.36–3.42 d.d (1H, CH_2, *J* = 6.8, 17.2 Hz), 3.85–3.94 m (4H, OCH_3, CH_2), 5.51–5.56 d.d (1H, CH, *J* = 6.8, 11.8 Hz), 6.78–6.82 t (1H, ArH), 7.12–7.18 m (3H, ArH), 7.16–7.22 m (2H, ArH), 7.28–7.37 m (3H, ArH), 7.38–7.40 m (4H, ArH), 7.43–7.51 m (3H, ArH), 7.68–7.75 m (2H, ArH), 7.78–7.91 m (1H, ArH), 7.98 s (1H, pyrazol proton); 8.24–8.26 d (1H, ArH). ^{13}C NMR spectrum, δ_C, ppm: 21.3 (CH_3),

47.1, 56.4 (O–CH_3), 56.7 (N–CH), 112.9, 113.8, 115.9, 118.8, 119.3, 123.0, 124.7, 126.3, 126.4, 127.3, 127.9, 128.1, 128.9, 129.2, 129.3, 129.5, 130.4, 130.8, 132.8, 138.0, 139.9, 145.4, 146.9, 150.4, 155.8. Found, %: C 80.82, H 5.71, N 10.42. $C_{36}H_{30}N_4O$. Calculated, %: C 80.87, H 5.66, N 10.48. *M* 535 $[M + H]^+$.

Compound IIIj. IR spectrum, ν, cm^{-1}: 1595 (C=C), 1620 (C=N), 3051 (C–H). ^1H NMR spectrum, δ, ppm: 3.34–3.45 d.d (1H, CH_2, *J* = 6.8, 17.2 Hz), 3.74–3.82 d.d (1H, CH_2, *J* = 6.8, 11.8 Hz), 3.84 s (3H, OCH_3), 3.88 s (3H, OCH_3), 5.79–5.84 d.d (1H, CH_2, *J* = 6.8, 11.8 Hz), 6.94–6.96 d (2H, ArH), 7.21–7.26 m (2H, ArH), 7.37–7.41 m (2H, ArH), 7.50–7.57 m (3H, ArH), 7.59–7.61 d (2H, ArH), 7.64–7.69 m (3H, ArH), 7.81–7.88 m (4H, ArH), 7.98 s (1H, pyrazol proton), 8.24–8.26 d (1H, ArH). ^{13}C NMR spectrum, δ_C, ppm: 55.3, 56.4 (O–CH_3), 56.7 (N–CH), 112.3, 113.8, 114.2, 118.8, 119.5, 119.7, 123.5, 124.1, 124.4, 124.8, 126.6, 127.5, 127.0, 129.0, 130.5, 131.4, 132.5,132.8, 140.2, 145.5, 147.0, 149.7, 155.6. Found, %: C 78.57, H 5.55, N 10.14. $C_{36}H_{30}N_4O_2$. Calculated, %: C 78.52, H 5.49, N 10.17. *M* 551 $[M + H]^+$.

Compound IIIk. IR spectrum, ν, cm^{-1}: 1596 (C=C), 1623 (C=N), 3052 (C–H). ^1H NMR spectrum, δ, ppm: 3.51–3.58 d.d (1H, CH_2, *J* = 7.2, 17.2 Hz), 3.86 s (3H, OCH_3), 4.05–4.13 d.d (1H, CH_2, *J* = 12, 17 Hz), 5.49–5.53 d.d (1H, CH_2, *J* = 6.8, 12 Hz), 6.81–6.85 t (1H, ArH), 7.12–7.18 m (2H, ArH), 7.16–7.15 m (3H, ArH), 7.20–7.25 m (2H, ArH), 7.36–7.40 m (2H, ArH), 7.47–7.53 m (2H, ArH), 7.58–7.65 m (3H, ArH), 7.70–7.72 d (2H, ArH), 7.96–7.98 m (2H, pyrazol proton and ArH), 8.07–8.09 d (1H, ArH). ^{13}C NMR spectrum, δ_C, ppm: 45.3, 56.7 (OCH_3), 62.9 (NCH), 113.7, 118.9, 119.6, 121.7, 122.4, 122.5, 123.0, 124.3, 125.7, 126.4, 126.6, 126.7, 126.8, 128.4, 127.9, 128.0, 129.0, 129.4, 129.5, 132.1, 132.1, 135.2, 139.6, 144.6, 146.2, 148.9, 154.3. Found, %: C 70.17, H 4.58, N 9.30. $C_{35}H_{27}BrN_4O$. Calculated, %: C 70.12, H 4.54, N 9.35. *M* 599 $[M + H]^+$.

Compound IIIl. IR spectrum, ν, cm^{-1}: 1597 (C=C), 1623 (C=N), 3048 (C–H). ^1H NMR spectrum, δ, ppm: 3.53–3.59 d.d (1H, CH_2, *J* = 6.8, 17.2 Hz), 3.87 s (3H, O–CH_3), 4.12–4.19 d.d (1H, CH_2, *J* = 12, 17 Hz), 5.55–5.60 d.d (1H, CH_2, *J* = 6.8, 11.6 Hz), 6.84–6.87 t (1H, ArH), 7.13–7.15 d.d (2H, ArH), 7.21–7.26 m (2H, ArH), 7.28–7.30 d (1H, ArH), 7.40–7.44 m (2H, ArH), 7.50–7.54 m (2H, ArH), 7.62–7.64 d (1H, ArH), 7.65–7.68 d.d (2H, ArH), 7.83–7.85 d.d (1H, ArH), 7.86 s (1H, pyrazol proton); 8.02–8.10 m (4H, ArH), 8.35–8.38 d (2H, ArH). ^{13}C NMR spectrum, δ_C, ppm: 45.3, 56.7 (OCH_3), 64.1 (NCH), 119.3, 119.6, 122.9, 124.0, 124.3, 124.6, 125.9, 126.8, 126.9, 127.1, 127.2, 127.8, 128.1, 128.2, 128.3, 128.9, 129.5, 129.7, 129.9, 133.9, 138.2, 139.6, 142.5, 147.8, 148.2, 156.7. Found, %: C 74.27, H 4.85, N 12.43. $C_{35}H_{27}N_5O_3$. Calculated, %: C 74.32, H 4.81, N 12.38. *M* 566 $[M + H]^+$.

Compound IIIm. IR spectrum, ν, cm^{-1}: 1596 (C=C), 1623 (C=N), 3051 (C–H). ^1H NMR spectrum, δ, ppm: 3.55–3.61 d.d (1H, CH_2, *J* = 6.8, 17.6 Hz), 3.87 s (3H, O–CH_3), 4.13–4.20 d.d (1H, CH_2, *J* = 12, 17.4 Hz), 5.60–5.65 d.d (1H, CH_2, *J* = 6.8, 11.8 Hz), 6.82–6.85 t (1H, ArH), 7.14–7.17 d.d (2H, ArH), 7.17–7.19 d.d (1H, ArH), 7.22–7.25 d.d (1H, ArH), 7.28–7.32 m (2H, ArH), 7.35–7.41 m (2H, ArH), 7.44–7.49 m (2H, ArH), 7.62–7.64 d (1H, ArH), 7.65–7.68 d.d (2H, ArH), 7.84–7.86 d.d (1H, ArH), 7.88 s (1H, pyrazol proton); 8.09–8.11 d (2H, ArH), 8.19–8.22 d (1H, ArH), 8.29–8.31 d (1H, ArH). ^{13}C NMR spectrum, δ_C, ppm: 45.0, 56.7 (O–CH_3), 62.9 (N–CH), 113.2, 117.3, 119.6, 120.3, 122.8, 124.3, 124.5, 125.3, 123.5, 125.8, 126.3, 126.8, 126.9, 127.1, 127.5, 127.8, 128.1, 128.9, 129.5, 129.9, 134.3, 139.6, 144.2, 146.6, 148.9, 154.9. Found, %: C 75.20, H 4.92, N 10.69, S, 6.12. $C_{33}H_{26}N_4OS$. Calculated, %: C 75.26, H 4.98, N 10.64, S, 6.09. *M* 527 $[M + H]^+$.

Compound Va. IR spectrum, ν, cm^{-1}: 1595 (C=C), 1623 (C=N), 3055 (C–H), 3330 (N–H). ^1H NMR spectrum, δ, ppm: 3.34–3.40 d.d (1H, CH_2, *J* = 9.4, 16.6 Hz), 3.72–3.79 d.d (1H, CH_2, *J* = 10, 16.8 Hz), 3.87 s (3H, O–CH_3), 5.14–5.20 d.d (1H, CH_2, *J* = 7.2 Hz, 9.6 Hz), 6.05 br.s (1H, NH), 7.29–7.33 m (2H, ArH), 7.37–7.54 m (6H, ArH), 7.60–7.62 m (2H, ArH), 7.72–7.79 m (2H, ArH), 7.82–7.84 d.d (2H, ArH), 7.92–7.94 d (1H, ArH), 8.09 s (1H, pyrazol proton), 8.10–8.11 d (1H, ArH). ^{13}C NMR spectrum, δ_C, ppm: 44.4, 55.5 (N–CH), 56.4 (O–CH_3), 112.8, 116.4, 118.9, 123.5, 123.9, 124.7, 126.2, 126.4, 127.2, 128.0, 128.1, 128.2, 128.7, 129.2, 129.4, 130.6, 132.9, 133.1, 140.0, 151.1, 155.4. Found, %: C 78.42, H 5.40, N 12.53. $C_{29}H_{24}N_4O$. Calculated, %: C 78.36, H 5.44, N 12.60. *M* 445 $[M + H]^+$.

Compound Vb. IR spectrum, ν, cm^{-1}: 1596 (C=N), 1621 (C=C), 3052 (C–H), 3339 (N–H). ^1H NMR spectrum, δ, ppm: 2.34 s (3H, CH_3), 3.35–3.45 d.d (1H, CH_2, *J* = 9.4, 16.8 Hz), 3.80–3.87 m (4H, CH_2, OCH_3), 5.15–5.22 d.d (1H, CH_2, *J* = 7.2, 9.6 Hz), 6.05 br.s (1H, NH), 7.07–7.09 d (1H, ArH), 7.14–7.16 d (2H, ArH), 7.30–7.49 m (6H, ArH), 7.59–7.76 m (3H,

ArH), 7.82–7.92 m (2H, ArH), 8.05 s (1H, ArH), 8.11–8.14 d (1H, ArH). ^{13}C NMR spectrum, δ_C, ppm: 43.2, 56.4 (O–CH_3), 63.0 (N–CH), 114.2, 118.9, 122.1, 122.4, 122.7, 124.1, 125.7, 125.8, 126.3, 126.4, 126.5, 128.0, 128.1, 128.4, 129.4, 130.0, 135.3, 139.9, 151.0, 154.4, 159.7. Found, %: C 78.54, H 5.78, N 12.28. $C_{30}H_{26}N_4O$. Calculated, %: C 78.58, H 5.72, N 12.22. *M* 459 $[M + H]^+$.

Compound Vc. IR spectrum, ν, cm^{-1}: 1598 (C=N), 1621 (C=C), 3056 (C–H), 3330 (N–H). ^{1}H NMR spectrum, δ, ppm: 3.34–3.40 d.d (1H, CH_2, *J* = 9.4, 16.8 Hz), 3.71–3.78 d.d (1H, CH_2, *J* = 10, 16.8 Hz), 3.86 s (3H, O–CH_3), 3.87 s (3H, O–CH_3), 5.13–5.18 d.d (1H, CH_2, *J* = 7.2, 9.6 Hz), 6.05 br.s (1H, NH), 7.00–7.02 d (2H, ArH), 7.26–7.28 m (1H, ArH),7.41–7.45 m (1H, ArH), 7.50–7.55 m (1H, ArH), 7.60–7.62 d (2H, ArH), 7.67–7.69 m (2H, ArH), 7.71–7.75 d.d (2H, ArH), 7.82–7.84 d.d (2H, ArH), 7.91–7.93 d (1H, ArH), 8.07 s (1H, pyrazol proton), 8.11–8.13 d (1H, ArH). ^{13}C NMR spectrum, δ_C, ppm: 43.0, 56.4 (O–CH_3), 55.3 (O–CH_3), 63.0 (N–CH), 116.7, 119.6, 122.2, 122.7, 123.6, 124.0, 125.1, 125.8, 126.3, 126.5, 128.0, 128.2, 128.9, 129.4, 130.2, 135.2, 139.7, 149.6, 157.6. Found, %: C 75.86, H 5.58, N 11.78. $C_{30}H_{26}N_4O_2$. Calculated, %: C 75.93, H 5.52, N 11.81. *M* 475 $[M + H]^+$.

Compound Vd. IR spectrum, ν, cm^{-1}: 1596 (C=N), 1622 (C=C), 3054 (C–H), 3320 (N–H). ^{1}H NMR spectrum, δ, ppm: 3.40–3.46 d.d (1H, CH_2, *J* = 9.6, 16.8 Hz), 3.78–3.84 d.d (1H, CH_2, *J* = 10, 16.4 Hz), 3.89 s (3H, O–CH_3), 5.14–5.21 d.d (1H, CH_2, *J* = 7.2, 9.6 Hz), 6.05 br.s (1H, NH), 7.12–7.20 m (3H, ArH), 7.27–7.29 m (2H, ArH), 7.41–7.49 d (2H, ArH), 7.61–7.89 m (2H, ArH), 7.84–7.86 m (2H, ArH), 7.92–7.94 m (3H, ArH), 8.09–8.12 d (1H, ArH), 8.10 s (1H, pyrazol proton). ^{13}C NMR spectrum, δ_C, ppm: 45.8, 56.5 (O–CH_3), 63.1 (N–CH), 114.5, 116.7, 119.0, 122.3, 123.4, 123.9, 124.8, 125.6, 126.0, 127.2, 128.8, 129.5, 129.7, 132.4, 133.7, 139.3, 141.3, 145.2, 157.5. Found, %: C 66.50, H 4.52, N 10.77. $C_{29}H_{23}BrN_4O$. Calculated, %: C 66.54, H 4.43, N 10.70. *M* 523 $[M + H]^+$.

Compound Ve. IR spectrum, ν, cm^{-1}: 1599 (C=N), 1621 (C=C), 3056 (C–H), 3330 (N–H). ^{1}H NMR spectrum, δ, ppm: 3.32–3.39 d.d (1H, CH_2, *J* = 9.6, 16.8 Hz), 3.77–3.83 d.d (1H, CH_2, *J* = 10, 16.4 Hz), 3.87 s (3H, O–CH_3), 5.13–5.18 d.d (1H, CH_2, *J* = 7.2, 9.6 Hz), 6.05 br.s (1H, NH), 7.32–7.36 m (1H, ArH), 7.46–7.54 m (3H, ArH), 7.62–7.64 d (2H, ArH), 7.74–7.76 d.d (2H, ArH), 7.84–7.86 d.d (2H, ArH), 7.92–7.94 d (1H, ArH), 7.98–8.00 d (1H, ArH), 8.11–8.13 d (1H, ArH), 8.15 s (1H, pyrazol proton), 8.33–8.35 d (2H, ArH). ^{13}C NMR spectrum, δ_C, ppm: 44.4, 55.5 (O–CH_3), 63.0 (N–CH), 112.8, 115.2, 118.7, 123.9, 124.7, 125.9, 126.1, 127.2, 128.1, 128.7, 129.2, 129.3, 129.6, 129.6, 130.5, 132.1, 132.9, 139.7, 140.2, 146.5, 151.4, 159.4. Found, %: C 71.19, H 4.68, N 14.24. $C_{29}H_{23}N_5O_3$. Calculated, %: C 71.15, H 4.74, N 14.31. *M* 490 $[M + H]^+$.

Compound Vf. IR spectrum, ν, cm^{-1}: 1598 (C=N), 1621 (C=C), 3066 (C–H), 3336 (N–H). ^{1}H NMR spectrum, δ, ppm: 3.34–3.41 d.d (1H, CH_2, *J* = 8.8, 16.8 Hz), 3.78–3.85 d.d (1H, CH_2, *J* = 10, 16.8 Hz), 3.88 s (3H, O–CH_3), 5.25–5.30 d.d (1H, CH_2, *J* = 8.6, 9.6 Hz), 6.05 br.s (1H, NH), 7.00–7.02 d (2H, ArH), 7.26–7.69 m (6H, ArH), 7.71–7.75 d.d (2H, ArH), 7.82–7.84 d.d (2H, ArH), 7.91–7.93 d (1H, ArH), 8.07 s (1H, pyrazol proton), 8.11–8.13 d (1H, ArH). ^{13}C NMR spectrum, δ_C, ppm: 49.9, 55.3 (O–CH_3), 63.1 (N–CH), 118.9, 119.4, 119.0, 125.5, 126.3, 126.4, 126.5, 126.7, 127.4, 127.6, 128.1, 128.4, 129.4, 129.6, 130.0, 135.3, 139.9, 151.0, 154.4, 159.7. Found, %: C 71.86, H 4.90, N 12.49, S, 7.09. $C_{27}H_{22}N_4OS$. Calculated, %: C 71.98, H 4.92, N 12.44, S, 7.12. *M* 451 $[M + H]^+$.

Compound Vg. IR spectrum, ν, cm^{-1}: 1596 (C=C), 1621 (C=N), 3053 (C–H). ^{1}H NMR spectrum, δ, ppm: 3.33–3.39 d.d (1H, CH_2, *J* = 6.8, 17.2 Hz), 8.50 s (1H, pyrazol proton), 3.87–3.91 d.d (4H, O–CH_3, CH_2), 5.48–5.53 d.d (1H, CH_2, *J* = 6.8, 11.8 Hz), 6.80–6.84 t (1H, ArH), 7.09–7.12 d (2H, ArH), 7.18–7.29 m (2H, ArH), 7.40–7.50 m (3H, ArH), 7.43–7.51 m (3H, ArH), 7.61–7.63 m (4H, ArH), 7.68–7.70 m (4H, ArH), 7.79–7.89 m (2H, ArH), 8.24–8.26 d (1H, ArH). ^{13}C NMR spectrum, δ_C, ppm: 47.1, 56.4 (O–CH_3), 56.7 (N–CH), 112.9, 113.8, 115.9, 118.8, 119.3, 123.0, 124.7, 126.3, 126.4, 127.3, 127.9, 128.1, 128.9, 129.2, 129.3, 129.5, 130.4, 130.8, 132.8, 138.0, 139.9, 145.4, 146.9, 150.4, 155.8. Found, %: C 80.70, H 5.37, N 10.71. $C_{35}H_{28}N_4O$. Calculated, %: C 80.74, H 5.42, N 10.76. *M* 521 $[M + H]^+$.

Compound Vh. IR spectrum, ν, cm^{-1}: 1598 (C=C), 1622 (C=N), 3054 (C–H). ^{1}H NMR spectrum, δ, ppm: 2.48 s (3H, CH_3), 3.36–3.42 d.d (1H, CH_2, *J* = 6.8, 17.2 Hz), 3.87–3.92 d.d (4H, O–CH_3, CH_2), 5.51–5.56 d.d (1H, CH_2, *J* = 6.8, 11.8 Hz), 6.76–6.80 m (2H, ArH), 6.95–6.98 m (2H, ArH), 7.12–7.46 m (12H, ArH), 7.69–8.00 m (6H, ArH), 8.26–8.28 d (1H, ArH), 8.49 s (1H, pyrazol proton), ^{13}C NMR spectrum, δ_C, ppm: 21.3 (CH_3), 47.1, 55.9 (OCH_3), 56.7 (N–CH),

113.3, 113.9, 114.3, 118.9, 122.2, 123.4, 123.8, 124.2, 124.5, 124.6, 126.4, 126.7, 126.9, 127.5, 127.9, 128.1, 128.4, 128.5, 128.8, 129.3, 129.4, 130.4, 131.2, 143.1, 144.5, 150.9, 153.9. Found, %: C 80.92, H 5.62, N 10.43. $C_{36}H_{30}N_4O$. Calculated, %: C 80.87, H 5.66, N 10.48. *M* 535 $[M + H]^+$.

Compound Vi. IR spectrum, ν, cm^{-1}: 1596 (C=C), 1620 (C=N), 3053 (C–H). ^1H NMR spectrum, δ, ppm: 3.81–3.91 d.d (7H, 2XOCH_3, CH_2), 3.36–3.42 d.d (1H, CH_2, *J* = 6.8, 17.2 Hz), 5.49–5.54 d.d (1H, CH_2, *J* = 6.8, 11.8 Hz), 6.81–7.50 m (7H, ArH), 7.72–7.99 m (12H, ArH), 8.26–8.28 d (1H, ArH), 8.52–8.54 m (3H, pyrazol proton), ^{13}C NMR spectrum, δ_C, ppm: 47.0, 55.4 (OCH_3), 56.4 (OCH_3), 56.6 (NCH), 112.6, 112.9, 113.3, 113.8, 114.2, 118.7, 119.9, 122.8, 123.6, 123.9, 124.7, 124.8, 126.2, 126.4, 126.7, 126.9, 127.2, 127.9, 128.1, 128.9, 129.1, 129.2, 129.3, 129.6, 130.8, 131.2, 145.4, 146.9, 150.2, 155.8, 159.6. Found, %: C 78.49, H 5.56, N 10.12. $C_{36}H_{30}N_4O_2$. Calculated, %: C 78.52, H 5.49, N 10.17. *M* 551 $[M + H]^+$.

Compound Vj. IR spectrum, ν, cm^{-1}: 1596 (C=C), 1622 (C=N), 3052 (C–H). ^1H NMR spectrum, δ, ppm: 3.32–3.39 d.d (1H, CH_2, *J* = 6.8, 17.2 Hz), 3.84–3.90 d.d (4H, OCH_3, CH_2), 5.47–5.52 d.d (1H, CH_2, *J* = 6.8, 11.8 Hz), 6.82–6.84 t (1H, ArH), 7.09–7.28 m (4H, ArH), 7.36–7.50 m (4H, ArH), 7.61–7.89 m (8H, ArH), 8.00 s (1H, pyrazol proton), 8.25–8.27 d (1H, ArH), ^{13}C NMR spectrum, δ_C, ppm: 46.9, 56.4 (OCH_3), 56.6 (NCH), 112.8, 113.9, 118.8, 119.0, 119.5, 119.7, 123.9, 124.5, 124.6, 126.6, 126.8, 127.3, 127.9, 128.1, 129.1, 129.5, 129.6, 130.4, 130.9, 131.4, 131.8, 131.9, 139.7, 145.4, 146.9,156.8. Found, %: C 70.06, H 4.50, N 9.31. $C_{35}H_{27}BrN_4O$. Calculated, %: C 70.12, H 4.54, N 9.35. *M* 599 $[M]^+$.

Compound Vk. IR spectrum, ν, cm^{-1}: 1597 (C=C), 1625 (C=N), 3055 (C–H). ^1H NMR spectrum, δ, ppm: 3.34–3.40 d.d (1H, CH_2, *J* = 6.8, 17.2 Hz), 3.89–4.00 m (4H, OCH_3, CH_2), 5.54–5.59 d.d (1H, CH_2, *J* = 6.8, 11.6 Hz), 6.82–6.87 t (1H, ArH), 7.11–7.50 m (10H, ArH), 7.72–7.74 m (2H, ArH), 7.80–7.82 d (2H, ArH), 7.88–7.90 m (1H, ArH), 8.02–8.06 m (3H, ArH), 8.34–8.37 d (2H, ArH). ^{13}C NMR spectrum, δ_C, ppm: 47.5, 55.2 (OCH_3), 57.0 (NCH), 112.3, 113.8, 119.1, 122.4, 123.1, 123.9, 124.1, 124.5, 124.7, 125.4, 126.6, 126.8, 128.1, 128.6, 129.0, 129.6, 129.9, 130.4, 130.8, 130.9, 131.8, 139.3, 145.5, 147.0, 155.8, *M* 566 $[M]^+$. Found, %: C 74.28, H 4.85, N 12.36. $C_{35}H_{27}N_5O_3$. Calculated C 74.32, H 4.81, N 12.38.

ACKNOWLEDGMENTS

The authors are thankful to the Head, Department of Chemistry for providing laboratory facilities. The authors are also thankful to the Director, Central Facilities for Research and Development (CFRD), Osmania University for providing IR and NMR spectral analysis. Financial support from UGC, New Delhi for one of the authors AG is gratefully acknowledged.

REFERENCES

1. Primo, F.T. and Froehlich, P.E., *Acta farm. Bonaer.,* 2005, vol. 24, no. 3, p. 421.
2. Fong, T.M. and Heymsfield, S.B., *Int. J. Obes. (Lond),* 2009, vol. 33, no. 9, p. 947.
3. Pimerova, E.V. and Voronina, E.V., *J. Pharm. Chem.*, 2001, vol. 35, p. 18.
4. Janus, S.L., Magdif, A.Z., Erik, B.P., and Claus, N., *Monatsh. Chem.*, 1999, vol. 130, p. 1167.
5. Park, H.J., Lee, K., Park, S., Ahn, B., Lee, J.C., Cho, H.Y., and Lee, K.I., *Bioorg. Med. Chem. Lett.*, 2005, vol. 15, p. 3307.
6. Bouabdallah, I., Mbarek, L.A., Zyad, A., Ramadan, A., Zidane, I., and Melhaoui, A., *Nat. Prod. Res.*, 2006, vol. 20, p. 1024.
7. Yildirim, I., Ozdemir, N., Akcamur, Y., Dincer, M., and Andac, O., *Acta Cryst.*, 2005, vol. 61, p. 256.
8. Bailey, D.M., Hansen, P.E., Hlavac, A.G., Baizman, E.R., Pearl, J., Defelice, A.F., and Feigenson, M.E., *J. Med. Chem.*, 1985, vol. 28, p.256.
9. Chu, C.K. and Cutler, J., *J. Heterocycl. Chem.,* 1986, vol. 23, p. 289.
10. Amr, A.E.E., Abdel-Latif, N.A., and Abdlla, M.M., *Acta Pharm.,* 2006, vol. 56, p. 203.
11. Chimichi, S., Boccalini, M., Hassan, M.M.M., Viola, G., Dall Acqua F., and Curini, M., *Tetrahedron*, 2006, vol. 62, p. 90.
12. Henry, T.A., *The Plant Alkoloids*, Anmol Publicaion Pvt. Ltd., 1999.
13. Kobayashi, Hisafumi, Kato, Motto, Nitani, and Fumio, *Chem. Abstr.*, 1989, vol. 106, p. 297008.
14. Nugent, R.A., Murphy, M., Schlachter, S.T., Dunn, C.J., Smith, R.J., Staite, N.D., Galinet L.A., Shields, S.K., Aspar, D.G., and Richard, K.A., *J. Med. Chem.*, 1993, vol. 361, p. 134.
15. Hantoon, M.A., *Minnesota Medicine*, 2001, vol. 84, p. 102.

16. Zhang, X., Li, X., Allan, G.F., and Sbriscia, T., *J. Med. Chem.,* 2007, vol. 50, no. 16, p. 3857.
17. Korgaokar, S.S., Patil, P.H., Shah, M.J., and Parekh, H.H., *Indian J. Pharm. Sci.,* 1996, vol. 58, p. 222.
18. Palaska, E., Aytemir, M., Uzbay, I.T., and Erol, D., *Eur. J. Med. Chem*., 2001, vol. 36, p. 539.
19. Ruhogluo, O., Ozdemir, Z., Calis, U., Gumusel, B., and Bilgin, A.A., *Arzneimittelforschung,* 2005, vol. 55, p. 431.
20. Udupi, R.H., Kushnoor, A.S., Bhat, A.R., *Indian J. Heterocycl. Chem*., 1998, vol. 8, p. 63.
21. Nauduri, D., and Reddy, G.B., *Chem. Pharm. Bull. Tokyo,* 1998, vol. 46, p. 1254.
22. Taylor, E.C. and Patel, H.H., *Tetrahedron,* 1992, vol. 48, p. 8089.
23. Fischer, E., and Knövenagel, O., *Ann. Chem.,* 1887, vol. 239, p. 194.
24. Powers, D.G., Casebier, D.S., Fokas, D. and Ryan, W.J., *Tetrahedron,* 1998, vol. 54, p. 4085.
25. Levai, A., *ARKIVOC,* vol. IX 2005 p. 344.