International Journal for Pharmaceutical Research Scholars (IJPRS)

V-6, I-1, 2017 ISSN No: 2277 - 7873

RESEARCH ARTICLE

Synthesis, Characterization and Antimicrobial Activity of some 2, 6-di(coumarin-3-yl)-4-[1-aryl-3-(bezofuran-2-yl)-1*H*-pyrazol-4-yl]pyridines

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Manuscript No: IJPRS/V6/I1/00018, Received On: 04/03/2017, Accepted On: 07/03/2017

ABSTRACT

The synthesis of various 2,6-di(coumarin-3-yl)-4-[1-aryl-3-(bezofuran-2-yl)-1*H*-pyrazol-4-yl]pyridines **(5a-r)** has been carried out. The target compounds have been synthesized by reacting 3-{3-[1-aryl-3-(benzofuran-2-yl)-1*H*-pyrazol-4-yl]acryloyl}coumarins (coumarin chalcones) **(3a-f)** with 3-coumarinoyl methyl pyridinium bromide salts **(4a-c)** in the presence of ammonium acetate in glacial acetic acid under Krohnke's reaction condition. All the synthesized compounds were characterized by IR, ^{1}H-NMR, ^{13}C-APT and representative mass spectral analysis. All the compounds were screened for their antimicrobial activity.

KEYWORDS

Dicoumarinyl Pyridines, Benzofuran, *Krohnke* Reaction, Antimicrobial Activity

INTRODUCTION

Coumarins constitute an important class of benzopyrones, exhibiting a broad range of biological activities such as antioxidant[1], antibacterial[2], anticancer[3], anti-inflammatory[4] and anticoagulant[5]. Pyridyl substituted coumarins are reported to have interesting biological activities such as antifungal[6], antibacterial[7] and CNS depressant[8]. Among the five membered nitrogen containing heterocycles, pyrazole is important moiety. A large number of compounds having pyrazole nucleus in their structure are reported to have wide range of biological activities like antioxidant[9], antiviral[10] and are also used as agrochemicals[11] and dyestuffs[12]. The incorporation of pyrazole moiety in pyridine in a substitution form generates a pyrazolyl substituted pyridine heterocycles.

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In literature pyrazolyl substituted pyridine heterocycles derivatives are well documented and are reported to possess bioactivities like antimicrobial activity[13], DNA binding property[14], photophysical and electrochemiluminescence properties[15]. They are also used as a potent inhibitor of the transforming growth factor-β type I receptor kinase domain[16]. Benzofurans are oxygen containing heterocycles and are widely distributed in nature. Many benzofuran derivatives have been reported to have interesting biological activities like anti-tumour[17], anti-inflammatory[18], antimicrobial[19] and anti-alzheimer[20] activities. Encouraged by the interesting biological properties of pyridyl substituted coumarins, pyrazolyl pyridines and benzofuran it was thought worthwhile to incorporate these moieties in single scaffold so that it can exhibit better biological activities. Considering these objectives in mind, in the present work the synthesis of various dicoumarinyl substituted pyrazolyl pyridines using a *Krohnke's* reaction has been reported.

MATERIALS AND METHOD

All the melting points are uncorrected. All reactions were performed with commercially available reagents and they were used without further purification. Organic solvents were purified by standard methods and stored over molecular sieves. All the IR spectra (KBr disc) were recorded on Shimadzu FT-IR 8400-S spectrometer. ^{1}H NMR and ^{13}C APT spectra were recorded on Bruker Advance400 spectrometer operating at 400 MHz for ^{1}H NMR and 100 MHz for ^{13}C APT. The chemical shift (δ) is reported in ppm using chloroform-d as a solvent and calibrated standard solvent signal. Mass spectra were recorded on Shimadzu QP 2010 spectrometer. Column chromatography was performed with silica gel 60–120 mesh (Merck, Mumbai, India.). The reaction was monitored using silica gel 60 F254 TLC plates and their spots were visualized by exposure to a UV lamp, iodine vapour or $KMnO_4$ reagents.

Starting precursors 3-acetyl coumarins **(1a-b)**[21], pyrazole aldehydes **(2a-c)**[22] and 3-coumarinoyl methyl pyridinium bromide salts **(4a-c)**[23] were prepared using reported procedure.

General procedure for the synthesis of 3-{3-[3-(benzofuran–2-yl)–1–aryl-1*H*–pyrazol–4-yl] acryloyl} coumarins (3a-f)

In a 100 mL round bottom flask, an appropriate 3-acetyl coumarin(0.01 mol) and appropriate 3-(benzofuran-2-yl)-1-aryl-1*H*-pyrazole-4-carbaldehyde (0.01 mol) were taken in 50 mL of ethanol. Catalytic amount of piperidine (1.0 mL) was added and the reaction mixture was stirred for 10 minutes at room temperature. The reaction mixture was then refluxed on water bath for 4 hours. It was then allowed to cool to room temperature. A solid product separated out was filtered off, washed with cold ethanol and dried. It was recrystallized from ethanol.

Compound 3a : R_3 = R_4 = H, Yield = 76 %, Mp:220-222°C (lit[24] Mp:221-223°C)

Compound 3b : R_3 =H, R_4 =CH_3, Yield = 76 %, Mp:176-178°C

Molecular Formula : $C_{30}H_{20}N_2O_4$

Analysis	% C	% H	% N
Found	76.31	4.21	5.88
Calculated	76.26	4.27	5.93
IR (cm^{-1})	ν_{max} 1722 (C=O stretching of □-lactone of coumarin), 1662 (α,β unsaturated carbonyl group), 1602 and 1534 (aromatic C=C and C=N stretchings), 834 (C-H bending vibrations of p-disubstituted benzene ring), 3051 (aromatic C-H stretching), 2934 (aliphatic C-H stretching).		
^{1}H-NMR (δ, ppm) ($CDCl_3$)	2.45 (3H, singlet, CH_3), 7.03-8.73 (16H, multiplet, fourteen aromatic protons + two olefinic protons), 8.73 (1H, singlet, C_4–H of coumarin).		

Compound 3c: R_3 = H, R_4 = OCH_3, Yield = 78 %, Mp: 218-220°C (lit[25] Mp: 219-220°C)

Compound 3d: R_3 = OCH_3, R_4 = H, Yield = 74 %, Mp: 164-166°C (lit[24] Mp: 165°C)

Compound 3e: R_3 = OCH_3, R_4 = CH_3, Yield = 76 %, Mp: 182-184°C Molecular Formula: $C_{31}H_{22}N_2O_5$

Analysis	% C	% H	% N
Found	76.14	4.36	5.62
Calculated	76.09	4.41	5.57
IR (cm^{-1})	ν_{max} 1728 (C=O stretching of □-lactone of coumarin), 1666 (α,β unsaturated carbonyl group), 1606 and 1528 (aromatic C=C and C=N stretchings), 833 (C-H bending vibrations of p-disubstituted benzene ring), 3048 (aromatic C-H stretching), 2928 (aliphatic C-H stretching).		
^{1}H-NMR (δ, ppm) ($CDCl_3$)	2.48 (3H, singlet, CH_3), 4.10 (3H, singlet, OCH_3), 7.07-8.73 (15H, multiplet, thirteen aromatic protons + two olefinic protons), 8.73 (1H, singlet, C_4–H of coumarin).		

Compound 3f : $R_3 = OCH_3$, $R_4 = OCH_3$, Yield = 75 %, Mp:166-168°C (lit[25] Mp:167-169°C)

General procedure for the synthesis of 2,6-di(coumarin-3-yl)-4-[1-aryl-3-(bezofuran-2-yl)-1*H*-pyrazol-4-yl]pyridines (5a-r):

In a 100 mL round bottom flask equipped with a dropping funnel, condenser, guard tube and magnetic needle, appropriate 3-coumarinoyl methyl pyridinium bromide salt **(4a-c)** (0.003mol) in glacial acetic acid (15 mL) was taken. To this ammonium acetate (0.03mol) was added with stirring at room temperature. Then a solution of appropriate 3-{3-[3-(benzofuran–2-yl)–1–aryl-1*H*–pyrazol–4-yl] acryloyl} coumarin **(3a-f)** (0.003 mol) in glacial acetic acid (15 mL) was added with stirring at room temperature during 15 minutes. The reaction mixture was further stirred for 1 hour at room temperature and then it was refluxed for 8 hours at 140˚C. It was then allowed to come to room temperature and was poured into ice-cold water (75 mL). A crude solid obtained was extracted with chloroform (3 x 30 mL). The organic layer was washed with 5% sodium bicarbonate solution (3 x 20 mL), water (2 x 20 mL) and dried over anhydrous sodium sulfate. The removal of chloroform under reduced pressure gave crude material which was subjected to column chromatography using silica gel and chloroform-pet ether (7:3) as an eluent to give products **(5a-r)**. The compounds were recrystallized from chloroform-hexane.

The physical, analytical and spectral data for the compounds **(5a-r)** are given below.

Compound 5a: yellow solid; yield 70 %; mp 251-253°C; Anal. Calcd. for $C_{40}H_{23}N_3O_5$: C, 76.79; H, 3.71; N, 6.72%. Found: C, 76.84; H, 3.66; N, 6.66%. IR (KBr, ν_{max}, cm^{-1}); 1720 (C=O stretching of □-lactone of coumarin), 1605 and 1545 (aromatic C=C and C=N stretchings), 3063 (aromatic C-H stretching), 692 and 750 (C-H out of plane bending vibrations for mono substituted benzene ring); ^{1}H NMR (400MHz, $CDCl_3$, δ): 7.21-7.88 (18H, multiplet, aromatic protons), 8.27 (1H, singlet, C_5'''-H), 8.57 (2H, singlet, C_3-H and C_5-H), 8.81 (2H, singlet, C_4'-H and C_4''-H); ^{13}C APT (100MHz, $CDCl_3$, δ): 105.92(CH), 111.68(CH), 116.49(CH), 119.48(C), 119.68(CH), 121.25(CH), 121.30(C), 122.97(CH), 123.43(CH), 124.60(CH), 124.69(CH), 125.60(C), 127.36(CH), 128.26(CH), 128.57(C), 128.87(CH), 129.56(CH), 132.29(CH), 139.43(C), 141.62(C), 141.94(C), 142.74(CH), 148.96(C), 151.51(C), 154.05(C), 154.90(C) and 160.12(CO of coumarin). The mass spectrum of compound show M^+ peak at 626(1%) (m/z%) along with some fragments peaks at 558(1%), 83(18%) and 44(100%). The appearance of molecular ion peak at 626 mass unit supports the structure of compound 5a.

Compound 5b: yellow solid; yield 68 %; mp 268-270°C; Anal. Calcd. for $C_{41}H_{25}N_3O_5$: C, 76.99; H, 3.94; N, 6.57%. Found: C, 77.04; H, 3.89; N, 6.62%. IR (KBr, ν_{max}, cm^{-1}); 1718 (C=O stretching of □-lactone ring of coumarin), 1610 and 1547 (aromatic C=C and C=N stretchings), 3064 (aromatic C-H stretching), 2938 (aliphatic C-H stretching), 826 (C-H bending vibrations of p-disubstituted benzene ring); ^{1}H NMR (400MHz, $CDCl_3$, δ): 2.54 (3H, singlet, CH_3), 7.41-7.97 (17H, multiplet, aromatic protons), 8.41 (2H, singlet, C_3-H and C_5-H), 8.62 (2H, singlet, C_4'-H and C_4''-H), 8.96 (1H, singlet, C_5'''-H); ^{13}C APT (100MHz, $CDCl_3$, δ): 21.05 (CH_3), 105.99(CH), 111.04(CH), 116.15(CH), 119.05(C), 119.36(CH), 121.41(C), 121.84(CH), 122.05(CH), 123.58(CH), 124.26(CH), 124.70(CH), 125.09(C), 127.43(CH), 128.20(CH), 128.43(C) 128.89(CH), 129.67(CH), 132.15(C), 139.47(C), 141.05(C), 141.85(C), 142.66(CH), 148.48(C), 151.20(C), 154.25(C), 154.89(C), 160.11(CO of coumarin).

Compound 5c: yellow solid; yield 72 %; mp >300°C; Anal. Calcd. for $C_{41}H_{25}N_3O_6$: C, 75.11; H, 3.84; N, 6.41%. Found: C, 75.06; H, 3.79; N, 6.37%. IR (KBr, ν_{max}, cm^{-1}); 1728 (C=O stretching of □-lactone ring of coumarin), 1615 and 1545 (aromatic C=C and C=N stretchings), 3064 (aromatic C-H stretching), 2936 (aliphatic C-H stretching), 826 (C-H bending vibrations of p-disubstituted benzene ring); ^{1}H NMR (400MHz, $CDCl_3$, δ): 3.94 (3H, singlet, OCH_3), 7.10-7.86 (17H, multiplet, aromatic protons), 8.49 (2H, singlet, C_3-H and C_5-H), 8.65 (2H, singlet, C_4'-H and C_4''-H), 8.91 (1H, singlet, C_5'''-

H); ^{13}C APT (100MHz, $CDCl_3$, δ): 55.77(OCH_3), 108.54(C), 111.20(CH), 112.98(C), 115.18(CH), 115.74(C), 117.10(CH), 117.58(C), 118.15(C), 120.86(CH), 122.27(CH), 122.41(CH), 122.67(CH), 124.25(CH), 124.39(CH), 126.56(CH), 126.76(C), 130.49(CH), 136.51(CH), 136.73(C), 143.66(C), 145.44(C), 147.72(CH), 147.92(CH), 149.75(C), 154.07(C), 157.45(C), 160.12(CO of coumarin).

Compound 5d: yellow solid; yield 73 %; mp 275-277°C; Anal. Calcd. for $C_{41}H_{25}N_3O_6$: C, 75.11; H, 3.84; N, 6.41%. Found: C, 75.05; H, 3.79; N, 6.36%. IR (KBr, ν_{max}, cm^{-1}); 1724 (C=O stretching of □-lactone ring of coumarin), 1614 and 1543 (aromatic C=C and C=N stretchings), 3061 (aromatic C-H stretching), 2932 (aliphatic C-H stretching), 692 and 756 (C-H bending vibration of mono substituted benzene ring); ^{1}H NMR (400MHz, $CDCl_3$, δ): 4.01 (3H, singlet, OCH_3), 7.13-7.88 (17H, multiplet, aromatic protons), 8.28 (1H, singlet, C_5'''-H), 8.57-8.61 (2H, multiplet, C_3-H and C_5-H), 8.80 and 8.81 (2H, two singlets, C_4'-H and C_4''-H).; ^{13}C APT (100MHz, $CDCl_3$, δ): 55.49(OCH_3), 105.89(CH), 108.89(C), 111.69(CH), 114.04(CH), 116.49(CH), 119.51(C), 119.72(CH), 120.13(C), 120.26(CH), 121.31(CH), 122.94(CH), 123.51(CH), 124.46(CH), 124.59(CH), 124.68(CH), 125.65(C), 125.78(C), 127.35(CH), 127.68(CH), 128.31(CH), 128.57(C), 128.87(CH), 129.56(CH), 132.28(CH), 139.31(C), 139.46(C), 140.89(C), 141.67(C), 141.32(C), 141.98(C), 142.76(CH), 142.90(CH), 147.66(C), 149.08(C), 151.66(C), 154.16(C), 160.16(CO of coumarin).

Compound 5e: yellow solid; yield 72 %; mp 282-284°C; Anal. Calcd. for $C_{42}H_{27}N_3O_6$: C, 75.33; H, 4.06; N, 6.27%. Found: C, 75.28; H, 4.11; N, 6.33%. IR (KBr, ν_{max}, cm^{-1}); 1718 (C=O stretching of □-lactone ring of coumarin), 1607 and 1538 (aromatic C=C and C=N stretchings), 3060 (aromatic C-H stretching), 2932 (aliphatic C-H stretching), 835 (C-H bending vibrations of p-disubstituted benzene ring); ^{1}H NMR (400MHz, $CDCl_3$, δ): 2.38 (3H, singlet, CH_3) 3.98 (3H, singlet, OCH_3), 7.09-7.78 (16H, multiplet, aromatic protons), 8.27 (1H, singlet, C_5'''-H), 8.33 (2H, poorly resolved doublet, C_3-H and C_5-H), 8.72 and 8.75 (2H, two singlets, C_4'-H and C_4''-H); ^{13}C APT (100MHz, $CDCl_3$, δ): 21.37(CH_3), 56.65(OCH_3), 109.09(C), 109.97(C), 112.94(C), 114.93(C), 115.57(C), 116.07(C), 116.40(CH), 119.73(C), 120.16(CH), 121.65(CH), 121.89(CH), 122.40(C), 124.66(CH), 127.15(CH), 127.89(C), 128.37(CH), 129.01(CH), 129.20(CH), 129.39(CH), 129.47(CH), 129.91(CH), 130.15(CH), 130.76(CH), 131.09(CH), 132.28(C), 134.38(C), 135.20(C), 137.26(CH), 139.86(CH), 143.50(C), 148.30(C), 149.85(C), 153.67(C), 155.45(C), 160.20(CO of coumarin), 160.20(CO of coumarin).

Compound 5f: yellow solid; yield 75 %; mp 282-284°C; Anal. Calcd. for $C_{42}H_{27}N_3O_7$: C, 73.57; H, 3.97; N, 6.13%. Found: C, 73.62; H, 4.01; N, 6.08%. IR (KBr, ν_{max}, cm^{-1}); 1726 (C=O stretching of □-lactone ring of coumarin), 1612 and 1542 (aromatic C=C and C=N stretchings), 3059 (aromatic C-H stretching), 2935 (aliphatic C-H stretching), 833 (C-H bending vibrations of p-disubstituted benzene ring); ^{1}H NMR (400MHz, $CDCl_3$, δ): 3.86 (3H, singlet, OCH_3), 4.03 (3H, singlet, OCH_3), 6.93-8.36 (19H, multiplet, aromatic protons), 8.73 and 8.75 (2H, two singlets, C_4'-H and C_4''-H); ^{13}C APT (100MHz, $CDCl_3$, δ): 56.24(OCH_3), 57.06(OCH_3), 109.83(C), 112.18(C), 112.63(C), 113.61(C), 115.24(CH), 115.61(C), 116.02(CH), 116.78(C), 117.16(CH), 118.18(C), 118.44(C), 119.92(CH), 120.36(CH), 120.93(CH), 121.57(CH), 127.01(CH), 128.09(CH), 128.83(C) 129.71(CH), 129.91(CH), 130.22(CH), 130.43(CH), 130.63(CH), 130.87(CH), 131.02(C), 137.02(C), 139.55(CH), 141.59(CH), 143.09(CH), 145.78(C), 147.03(C), 148.63(CH), 149.63(C), 152.68(C), 154.22(C), 155.43(C), 161.63(CO of coumarin), 161.87(CO of coumarin).

Compound 5g: yellow solid; yield 69 %; mp 273-275°C; Anal. Calcd. for $C_{41}H_{25}N_3O_6$: C, 75.11; H, 3.84; N, 6.41%. Found: C, 75.06; H, 3.78; N, 6.36%. IR (KBr, ν_{max}, cm^{-1}); 1718 (C=O stretching of □-lactone of ring coumarin), 1611 and 1538 (aromatic C=C and C=N stretchings), 3064 (aromatic C-H stretching), 2935 (aliphatic C-H stretching), 696 and 769 (C-H bending

vibration of mono substituted benzene ring benzene ring); ^{1}H NMR (400MHz, $CDCl_3$, δ): 4.04 (3H, singlet, OCH_3), 7.13-7.87 (17H, multiplet, aromatic protons), 8.33 (2H, singlet, C3-H and C5-H), 8.37 (1H, singlet, C5'''-H), 8.73 and 8.74 (2H, two singlets, C4'-H and C4''-H); ^{13}C APT (100MHz, $CDCl_3$, δ): 56.42(OCH_3), 106.49(CH), 108.89(C), 111.69(CH), 114.04(CH), 116.49(CH), 119.51(C), 119.72(CH), 120.13(C), 120.26(CH), 121.31(CH), 122.94(CH), 123.51(CH), 124.46(CH), 124.59(CH), 124.68(CH), 125.65(C), 125.78(C), 127.35(CH), 127.31(CH), 128.31(CH), 128.57(C), 128.87(CH), 129.56(CH), 132.28(CH), 139.31(C), 139.46(C), 140.89(C), 141.32(C), 141.67(C), 141.98(C), 142.76(CH), 142.90(CH), 147.66(C), 149.08(C), 151.66(C), 154.16(C), 160.16(CO of coumarin).

Compound 5h: yellow solid; yield 70 %; mp 283-285°C; Anal. Calcd. for $C_{42}H_{27}N_3O_6$: C, 75.33; H, 4.06; N, 6.27%. Found: C, 75.28; H, 4.11; N, 6.31%. IR (KBr, ν_{max}, cm^{-1}); 1722 (C=O stretching of □-lactone ring of coumarin), 1621 and 1546 (aromatic C=C and C=N stretchings), 3064 (aromatic C-H stretching), 2933 (aliphatic C-H stretching), 831 (C-H bending vibrations of p-disubstituted benzene ring); ^{1}H NMR (400MHz, $CDCl_3$, δ): 2.38 (3H, singlet, CH_3) 3.98 (3H, singlet, OCH_3), 7.09-7.85 (16H, multiplet, aromatic protons), 8.27 (1H, singlet, C_5'''-H), 8.33 (2H, poorly resolved doublet, C_3-H and C_5-H), 8.72 and 8.75 (2H, two singlets, C_4'-H and C_4''-H); ^{13}C APT (100MHz, $CDCl_3$, δ) : 21.40(CH_3), 56.57(OCH_3), 109.07(C), 110.10(C), 112.89(C), 114.98(C), 115.59(C), 116.03(C), 118.47(CH), 119.77(C), 120.13(CH), 121.65(CH), 121.89(CH), 122.40(C), 124.66(CH), 127.15(CH), 127.89(C), 128.37(CH), 129.01(CH), 129.19(CH), 129.39(CH), 129.47(CH), 129.94(CH), 130.17(CH), 130.70(CH), 131.19(CH), 132.25(C), 134.34(C), 135.25(C), 137.21(CH), 139.81(CH), 143.56(C), 148.20(C), 149.75(C), 153.65(C), 155.48(C), 160.23(CO of coumarin), 160.79(CO of coumarin).

Compound 5i: yellow solid; yield 72 %; mp >300°C; Anal. Calcd. for $C_{42}H_{27}N_3O_7$: C, 73.57; H, 3.97; N, 6.13%. Found: C, 73.62; H, 4.02; N, 6.07%. IR (KBr, ν_{max}, cm^{-1}); 1721 (C=O stretching of □-lactone ring of coumarin), 1619 and 1548 (aromatic C=C and C=N stretchings), 3059 (aromatic C-H stretching), 2930 (aliphatic C-H stretching),), 828 (C-H bending vibrations of p-disubstituted benzene ring); ^{1}H NMR (400MHz, $CDCl_3$, δ): 3.76 (3H, singlet, OCH_3), 3.97 (3H, singlet, OCH_3), 6.96-8.61 (16H, multiplet, aromatic protons), 8.32 (2H, poorly resolved doublet, C_3-H and C_5-H), 9.01 (1H, singlet, C_5'''-H), 9.06 and 9.08 (2H, two singlets, C_4'-H and C_4''-H); ^{13}C APT (100MHz, $CDCl_3$, δ) : 56.18(OCH_3), 57.01(OCH_3), 109.88(C), 112.13(C), 112.76(C), 113.68(C), 115.18(CH), 115.61(C), 116.09(CH), 116.72(C), 117.26(CH), 118.17(C), 118.54(C), 119.99(CH), 120.36(CH), 120.93(CH), 121.57(CH), 127.01(CH), 128.09(CH), 128.83(C) 129.71(CH), 129.91(CH), 130.22(CH), 130.41(CH), 130.63(CH), 130.97(CH), 131.02(C), 137.09(C), 139.57(CH), 141.59(CH), 143.17(CH), 145.88(C), 147.53(C), 148.63(CH), 149.59(C), 152.66(C), 154.32(C), 155.49(C), 161.53(CO of coumarin), 161.78(CO of coumarin).

Compound 5j: yellow solid; yield 74 %; mp >300°C; Anal. Calcd. for $C_{42}H_{27}N_3O_7$: C, 73.57; H, 3.97; N, 6.13%. Found: C, 73.61; H, 4.01; N, 6.08%. IR (KBr, ν_{max}, cm^{-1}); 1724 (C=O stretching of δ-lactone ring of coumarin), 1615 and 1448 (aromatic C=C and C=N stretchings), 3062 (aromatic C-H stretching), 2942 (aliphatic C-H stretching), 675 and 766 (C-H bending vibrations of mono substituted benzene ring); ^{1}H NMR (400MHz, $CDCl_3$, δ): 4.05 (6H, singlet, 2 X OCH_3), 7.07-7.83 (16H, multiplet, aromatic protons), 8.58 (2H, poorly resolved doublet, C_3-H and C_5-H), 8.66 (2H, singlet, C_4'-H and C_4''-H), 8.94 (1H, singlet, C_5'''-H); ^{13}C APT (100MHz, $CDCl_3$, δ) : 56.60(OCH_3), 108.89(CH), 110.04(C), 111.15(CH), 112.93(C), 114.36(C), 115.75(C), 117.84(C), 118.05(CH), 118.58(C), 118.82(C), 120.70(CH), 121.09(CH), 121.43(CH), 122.39(CH), 124.26(CH), 126.24(CH), 126.67(CH), 128.15(C), 129.47(CH), 130.05(CH), 139.85(CH), 143.66(C), 145.41(C), 147.20(C), 148.25(CH), 149.89(C), 160.11(CO of coumarin).

Compound 5k: yellow solid; yield 71 %; mp 280-282°C; Anal. Calcd. for $C_{43}H_{29}N_3O_7$: C, 73.81; H, 4.18; N, 6.01%. Found: C, 73.76; H, 4.23; N, 5.96%. IR (KBr, ν_{max}, cm^{-1}): 1720 (C=O stretching of δ-lactone ring of coumarin), 1610 and 1442 (aromatic C=C and C=N stretchings), 3064 (aromatic C-H stretching), 2930 (aliphatic C-H stretching), 834 (C-H bending vibrations of p-disubstituted benzene ring); ^{1}H NMR (400MHz, $CDCl_3$, δ): 2.34 (3H, singlet, CH_3), 3.78 (6H, singlet, 2 X OCH_3), 6.98-8.01 (15H, multiplet, aromatic protons except), 8.31 (2H, C_3-H and C_5-H), 9.01 (1H, singlet, C_5'''-H), 9.09 (2H, singlet, C_4'-H and C_4''-H).; ^{13}C APT (100MHz, $CDCl_3$, δ): 21.67(CH_3), 56.58(OCH_3), 108.92(CH), 110.49(C), 111.49(CH), 112.48(C), 114.68(C), 115.25(C), 117.30(C), 118.43(CH), 118.60(C), 118.97(C), 120.69(CH), 121.60(CH), 121.87(CH), 122.26(C), 124.57(CH), 126.26(CH), 126.56(CH), 128.29(C), 129.43(CH), 130.62(CH), 139.94(CH), 143.74(C), 145.96(C), 147.51(C), 148.05(CH), 149.90(C), 160.05(CO of coumarin).

Compound 5l: yellow solid; yield 75 %; mp >300°C; Anal. Calcd. for $C_{43}H_{29}N_3O_8$: C, 72.16; H, 4.08; N, 5.87%. Found: C, 72.21; H, 4.13; N, 5.92%. IR (KBr, ν_{max}, cm^{-1}): 1726 (C=O stretching of δ-lactone ring of coumarin), 1616 and 1446 (aromatic C=C and C=N stretchings), 3058 (aromatic C-H stretching), 2928 (aliphatic C-H stretching), 834 (C-H bending vibrations of p-disubstituted benzene ring); ^{1}H NMR (400MHz, $CDCl_3$, δ): 3.85 (3H, singlet, OCH_3), 4.02 (6H, singlet, 2 X OCH_3), 6.92-7.86 (15H, multiplet, aromatic protons), 8.28 (1H, singlet, C_5'''-H), 8.35 (2H, C_3-H and C_5-H), 8.74 (2H, singlet, C_4'-H and C_4''-H); ^{13}C APT (100MHz, $CDCl_3$, δ): 55.73(OCH_3), 56.58(OCH_3), 105.29(CH), 108.29(CH), 111.16(CH), 112.96(C), 114.45(C), 115.09(CH), 115.80(C), 117.54(C), 117.90(CH), 118.77(C), 120.90(CH), 121.29(CH), 122.22(CH), 122.33(CH), 124.19(CH), 126.15(CH), 126.54(CH), 128.22(C), 142.20(C), 143.65(C), 145.33(C), 147.18(C), 148.03(CH), 149.85(C), 159.98(C), 160.40(C), 160.57(CO of coumarin).

Compound 5m: yellow solid; yield 68 %; mp 271-273°C; Anal. Calcd. for $C_{44}H_{25}N_3O_5$: C, 78.21; H, 3.73; N, 6.22%. Found: C, 78.16; H, 3.68; N, 6.16%. IR (KBr, ν_{max}, cm^{-1}): 1712 (C=O stretching of δ-lactone ring of coumarin), 1612 and 1448 (aromatic C=C and C=N stretchings), 3045 (aromatic C-H stretching), 662 and 765 (C-H bending vibrations of mono substituted benzene ring); ^{1}H NMR (400MHz, $CDCl_3$, δ): 7.21-8.38 (20H, multiplet, aromatic protons), 8.47 (2H, C_3-H and C_5-H), 8.77 (1H, singlet, C_5'''-H), 8.94 and 9.22 (2H, two singlets, C_4''-H and C_4'-H); ^{13}C APT (100MHz, $CDCl_3$, δ): 105.89(C), 107.53(CH), 108.27(C), 109.93(C), 112.06(C), 112.79(C), 113.53(C), 114.23(CH), 115.62(C), 116.09(CH), 116.91(CH), 118.27(C), 118.44(CH), 118.89(C), 119.77(CH), 120.29(CH), 121.32(CH), 121.41(CH), 121.47(CH), 127.02(CH), 128.06(CH), 128.77(CH) 129.57(CH), 129.77(CH), 129.90(CH), 130.16(CH), 130.71(CH), 130.82(C), 132.34(CH), 137.44(C), 139.57(CH), 142.94(CH), 143.46(C), 145.51(CH), 145.07(C), 147.07(C), 148.74(CH), 149.67(C), 152.72(C), 155.42(C), 160.44(CO of coumarin), 161.54(CO of coumarin).

Compound 5n: yellow solid; yield 71 %; mp 267-269°C; Anal. Calcd. for $C_{45}H_{27}N_3O_5$: C, 78.36; H, 3.95; N, 6.09%. Found: C, 78.41; H, 3.89; N, 6.14%. IR (KBr, ν_{max}, cm^{-1}): 1718 (C=O stretching of δ-lactone ring of coumarin), 1618 and 1439 (aromatic C=C and C=N stretchings), 3042 (aromatic C-H stretching), 2932 (aliphatic C-H stretching), 828 (C-H bending vibrations of p-disubstituted benzene ring); ^{1}H NMR (400MHz, $CDCl_3$, δ): 2.44 (3H, singlet, CH_3), 7.20-8.33 (20H, multiplet, aromatic protons), 8.41-8.46 (2H, multiplet, C_3-H and C_5-H), 8.74 and 9.55 (2H, two singlets, C_4''-H and C_4'-H); ^{13}C APT (100MHz, $CDCl_3$, δ): 21.48(CH_3), 105.53(C), 106.21(C), 107.56(CH), 109.73(CH), 111.76(CH), 113.58(C), 116.47(CH), 116.66(CH), 119.26(CH), 119.53(C), 120.21(C), 121.80(CH), 122.71(CH), 122.77(CH), 124.42(C), 124.58(CH), 125.81(C), 126.17(CH), 126.80(CH), 127.65(CH), 128.45(CH), 128.56(CH), 128.84(CH), 129.13(CH), 129.30(CH), 129.49(C), 129.54(C), 130.38(C), 132.22(CH), 133.69(CH), 138.17(C), 138.72(CH), 139.72(C), 142.54(C), 142.63(CH),

151.53(C), 151.76(C), 152.20(C), 153.93(C), 154.01(C), 160.06(CO of coumarin), 160.15(CO of coumarin).

Compound 5o: yellow solid; yield 68 %; mp 264-266°C; Anal. Calcd. for $C_{45}H_{27}N_3O_6$: C, 76.59; H, 3.86; N, 5.95%. Found: C, 76.64; H, 3.92; N, 5.89%. IR (KBr, ν_{max}, cm^{-1}): 1721 (C=O stretching of δ-lactone ring of coumarin), 1610 and 1437 (aromatic C=C and C=N stretchings), 3054 (aromatic C-H stretching), 2931 (aliphatic C-H stretching), 828 (C-H bending vibrations of p-disubstituted benzene ring); ^{1}H NMR (400MHz, $CDCl_3$, δ): 3.92 (3H, singlet, OCH_3), 7.22-8.38 (19H, multiplet, aromatic protons), 8.47 (2H, C_3-H and C_5-H), 8.76 (1H, singlet, C_5'''-H), 8.92 and 9.22 (2H, two singlets, C_4''-H and C_4'-H); ^{13}C APT (100MHz, $CDCl_3$, δ): 56.68(OCH_3), 105.18(C), 106.61(C), 108.61(CH), 110.24(C), 111.61(CH), 112.42(CH), 113.05(C), 113.29(C), 115.68(C), 115.88(C), 116.90(CH), 117.73(CH), 118.24(C), 118.64(CH), 118.71(CH), 119.11(C), 119.35(C), 120.05(CH), 120.27(CH), 120.83(CH), 121.52(CH), 122.57(CH), 124.57(CH), 126.21(CH), 126.61(CH), 128.32(C), 129.87(CH), 130.31(C), 131.43(CH), 132.19(CH), 132.63(CH), 133.35(C), 138.22(C), 138.78(CH), 142.63(C), 145.68(C), 147.22(C), 147.43(C), 148.63(CH), 160.05(CO of coumarin), 160.51(CO of coumarin).

Compound 5p: yellow solid; yield 72 %; mp 271-273°C; Anal. Calcd. for $C_{45}H_{27}N_3O_6$: C, 76.59; H, 3.86; N, 5.95%. Found: C, 76.64; H, 3.91; N, 6.01%. IR (KBr, ν_{max}, cm^{-1}): 1716 (C=O stretching of δ-lactone ring of coumarin), 1616 and 1446 (aromatic C=C and C=N stretchings), 3052 (aromatic C-H stretching), 2934 (aliphatic C-H stretching), 685 and 776 (C-H bending vibrations of mono substituted benzene ring); ^{1}H NMR (400MHz, $CDCl_3$, δ): 4.06 (3H, singlet, OCH_3), 7.15-8.46 (22H, multiplet, aromatic protons), 8.76 and 9.55 (2H, two singlets, C_4''-H and C_4'-H); ^{13}C APT (100MHz, $CDCl_3$, δ): 56.61(OCH_3), 105.25(C), 106.42(C), 108.45(CH), 110.19(C), 111.25(CH), 112.42(CH), 113.05(C), 113.29(C), 115.68(C), 115.88(C), 116.90(CH), 117.73(C), 118.24(CH), 118.64(CH), 118.71(CH), 119.11(C), 119.35(C), 120.05(CH), 120.27(CH), 120.91(CH), 121.52(CH), 122.49(CH), 124.34(CH), 126.21(CH), 126.61(CH), 128.32(C), 129.99(CH), 130.31(C), 131.46(CH), 132.19(CH), 132.75(CH), 133.35(C), 138.30(C), 138.78(CH), 142.95(C), 145.74(C), 147.16(C), 147.47(C), 148.51(CH), 159.75(CO of coumarin), 161.55(CO of coumarin).

Compound 5q: yellow solid; yield 69 %; mp 265-267°C; Anal. Calcd. for $C_{46}H_{29}N_3O_6$: C, 76.76; H, 4.06; N, 5.84%. Found: C, 76.81; H, 4.11; N, 5.79%. IR (KBr, ν_{max}, cm^{-1}): 1714 (C=O stretching of δ-lactone ring of coumarin), 1615 and 1439 (aromatic C=C and C=N stretchings), 3048 (aromatic C-H stretching), 2936 (aliphatic C-H stretching), 834 (C-H bending vibrations of p-disubstituted benzene ring); ^{1}H NMR (400MHz, $CDCl_3$, δ): 2.49 (3H, singlet, CH_3), 4.08 (3H, singlet, CH_3), 7.35-8.46 (18H, multiplet, aromatic protons), 8.50 (2H, singlet, C_3-H and C_5-H), 8.71 (1H, singlet, C_5'''-H), 8.93 and 9.21 (2H, two singlets, C_4''-H and C_4'-H); ^{13}C APT (100MHz, $CDCl_3$, δ): 21.53(CH_3), 56.58(OCH_3), 105.40(C), 106.57(C), 107.56(CH), 109.73(CH), 111.76(CH), 113.58(C), 116.47(CH), 116.66(CH), 119.26(CH), 119.53(C), 120.21(C), 121.80(CH), 122.09(CH), 122.76(CH), 124.28(C),124.38(C), 125.20(CH), 126.39(C), 126.47(C), 127.91(CH), 128.15(CH), 128.76(CH), 128.89(CH), 129.28(CH), 129.38(CH), 129.47(CH), 129.58(C), 130.89(C), 132.40(CH), 133.66(CH), 138.15(C), 138.89(CH), 139.37(C), 142.01(C), 142.20(CH), 151.39(C), 151.47(C), 152.20(C), 153.86(C), 154.05(C), 160.20(CO of coumarin), 160.26(CO of coumarin).

Compound 5r: yellow solid; yield 73 %; mp 275-277°C; Anal. Calcd. for $C_{46}H_{29}N_3O_7$: C, 75.09; H, 3.97; N, 5.71%. Found: C, 75.14; H, 4.02; N, 5.66%. IR (KBr, ν_{max}, cm^{-1}): 1715 (C=O stretching of δ-lactone ring of coumarin), 1618 and 1446 (aromatic C=C and C=N stretchings), 3051 (aromatic C-H stretching), 2930 (aliphatic C-H stretching), 832 (C-H bending vibrations of p-disubstituted benzene ring); ^{1}H NMR (400MHz, $CDCl_3$, δ): 3.92 (3H, singlet, OCH_3), 4.17 (3H, singlet, CH_3), 7.27-8.42 (18H, multiplet, aromatic protons), 8.51 (2H, singlet,

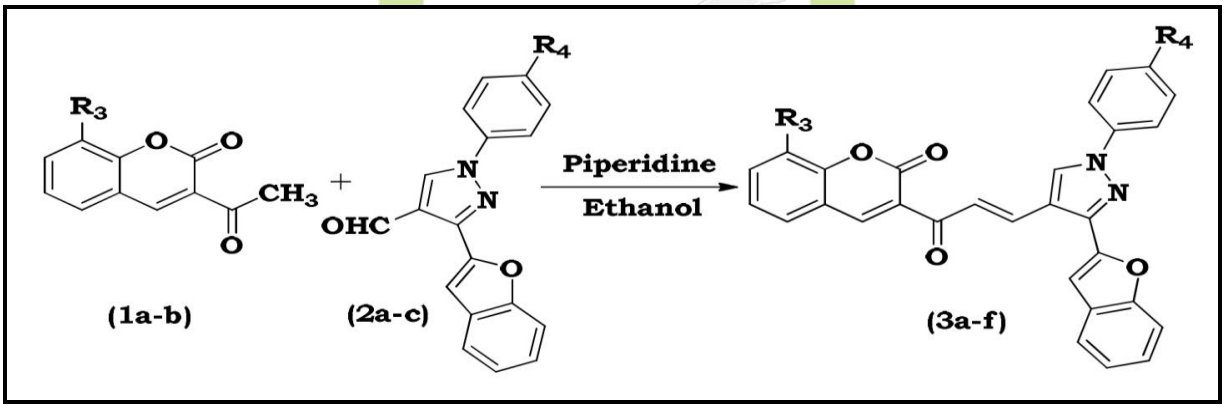
C_3-H and C_5-H), 8.85 (1H, singlet, C_5'''-H), 8.96 and 9.26 (2H, two singlets, C_4''-H and C_4'-H); ^{13}C APT (100MHz, $CDCl_3$, δ): 55.61(OCH_3), 56.77(OCH_3), 105.78(C), 107.56(CH), 108.18(C), 109.91(C), 112.06(CH), 112.92(C), 113.06(C), 114.76(CH), 115.58(C), 116.24(CH), 116.61(C), 118.02(CH), 118.44(C), 118.89(C), 119.77(CH), 120.44(CH), 121.36(CH), 121.58(CH), 121.93(CH), 127.57(CH), 128.01(CH), 128.09(CH), 129.71(CH), 129.83(CH), 129.91(CH), 130.22(CH), 130.43(C), 130.63(C), 132.87(CH), 137.02(C), 139.02(CH), 142.55(CH), 143.59(C), 145.09(CH), 145.78(C), 147.03(C), 148.63(C), 149.68(C), 152.72(C), 155.48(C), 160.24(CO of coumarin), 161.54(CO of coumarin).

In case of the compounds **5d, 5e, 5g, 5h** and **5o** the number of carbon signals in ^{13}C-APT spectra are less than expected (in case of compounds **5d, 5g** and **5o** one signal and in **5e** and **5h** two signals). This may be due to identical chemical shifts of certain carbons which may appear at same position.

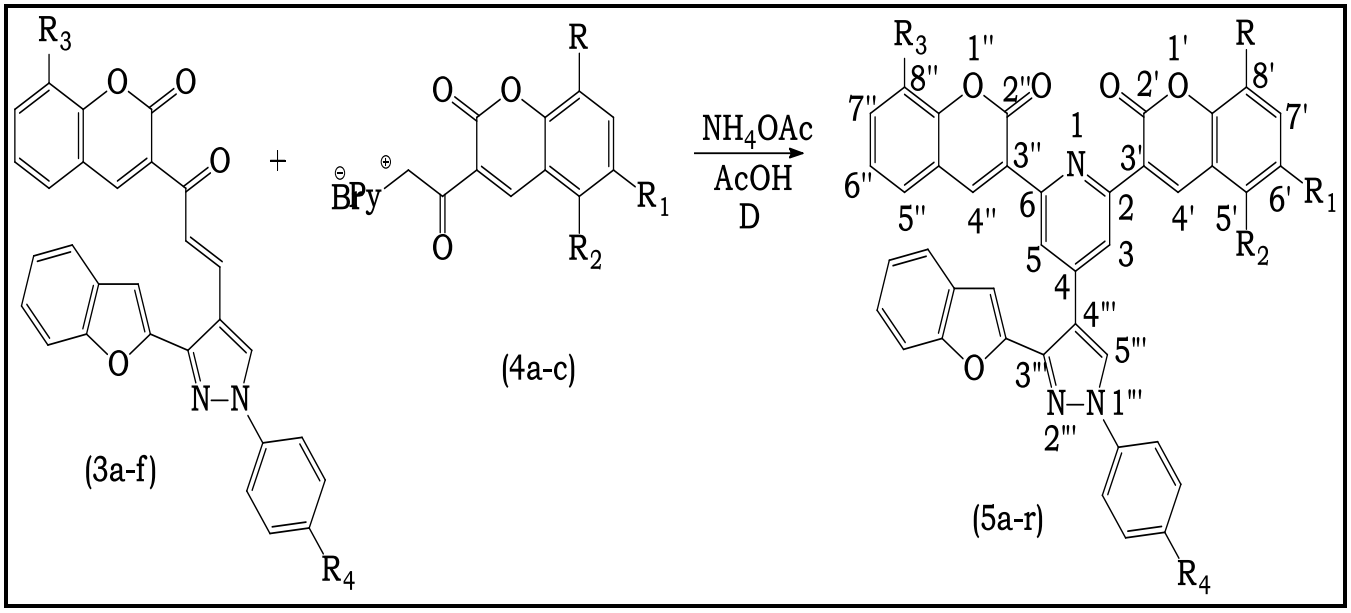
RESULTS AND DISCUSSION

Chemistry

In the present work, various 2,6-di(coumarin-3-yl)-4-[1-aryl-3-(bezofuran-2-yl)-1*H*-pyrazol-4-yl]pyridines **(5a-r)** have been synthesized by the reaction of 3-{3-[1-aryl-3-(benzofuran-2-yl)-1H-pyrazol-4-yl]acryloyl}coumarins **(3a-f)** with 3-coumarinoyl methyl pyridinium bromide salts **(4a-c)** in the presence of ammonium acetate in glacial acetic acid under Krohnke's reaction condition[26] **(Scheme 1)**. The starting material 3-{3-[1-aryl-3-(benzofuran-2-yl)-1*H*-pyrazol-4-yl]acryloyl}coumarins **(3a-f)** were prepared by the reaction of 3-acetyl coumarins **(1a-b)** with appropriate pyrazole aldehydes **(2a-c)** in the presence of piperidine in ethanol. The plausible mechanism for the formation of target compounds **(5a-r)** is shown in **Scheme 2.**



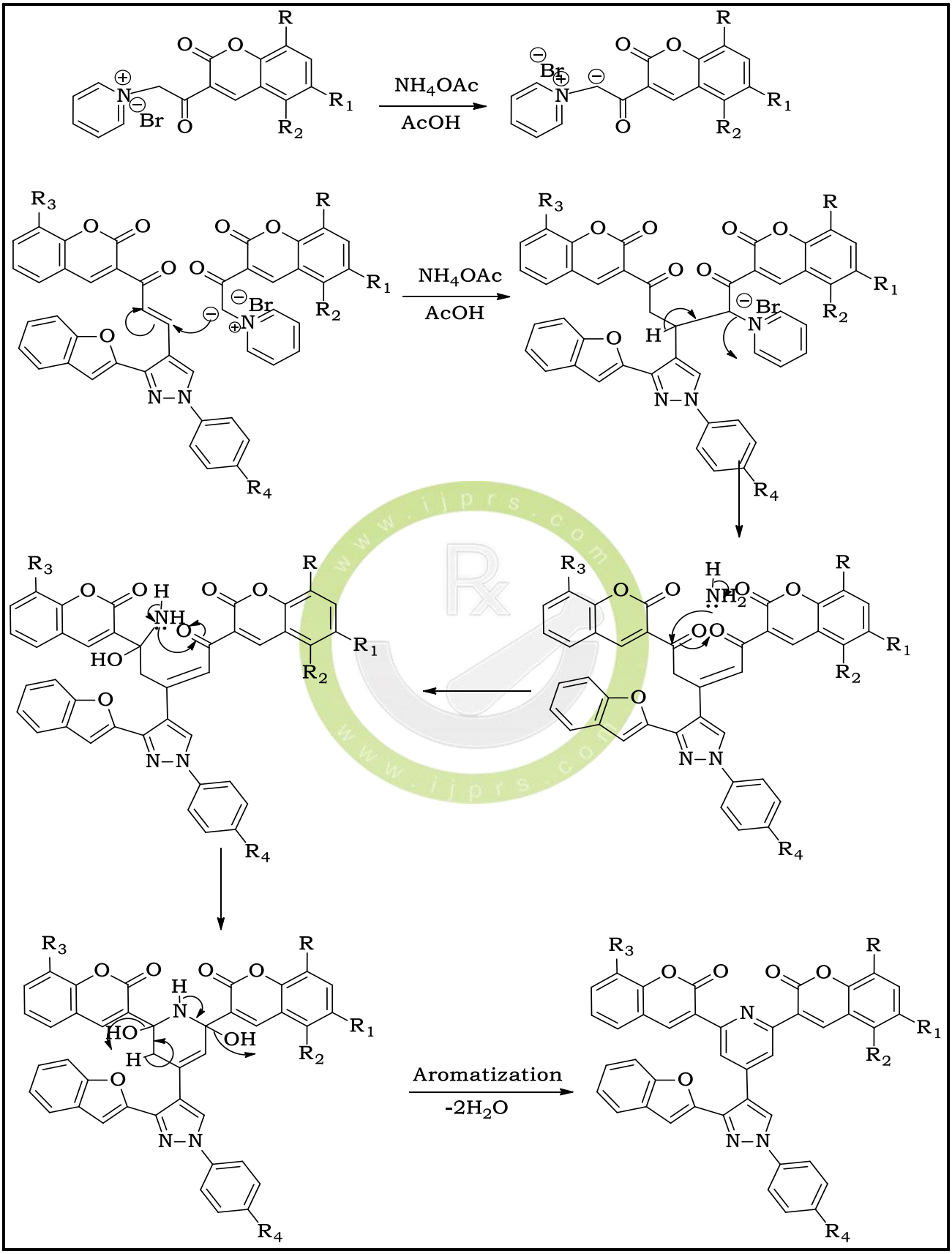
Compounds	R_3	Compounds	R_4	Compounds	R_3	R_4
1a	H	**2a**	H	**3a**	H	H
1b	OCH_3	**2b**	CH_3	**3b**	H	CH_3
		2c	OCH_3	**3c**	H	OCH_3
				3d	OCH_3	H
				3e	OCH_3	CH_3
				3f	OCH_3	OCH_3



Compounds	R	R_1	R_2
4a	H	H	H
4b	OCH_3	H	H
4c	H	Benzo	

Compounds	R	R_1	R_2	R_3	R_4	Compounds	R	R_1	R_2	R_3	R_4
5a:	H	H	H	H	H	**5j:**	OCH_3	H	H	OCH_3	H
5b:	H	H	H	H	CH_3	**5k:**	OCH_3	H	H	OCH_3	CH_3
5c:	H	H	H	H	OCH_3	**5l:**	OCH_3	H	H	OCH_3	OCH_3
5d:	H	H	H	OCH_3	H	**5m:**	H	benzo		H	H
5e:	H	H	H	OCH_3	CH_3	**5n:**	H	benzo		H	CH_3
5f:	H	H	H	OCH_3	OCH_3	**5o:**	H	benzo		H	OCH_3
5g:	OCH_3	H	H	H	H	**5p:**	H	benzo		OCH_3	H
5h:	OCH_3	H	H	H	CH_3	**5q:**	H	benzo		OCH_3	CH_3
5i:	OCH_3	H	H	H	OCH_3	**5r:**	H	benzo		OCH_3	OCH_3

Scheme 1: Synthetic scheme for compounds (5a-r)



Scheme 2: Plausible mechanism for the formation of target compounds (5a-r)

Biological Results

Antimicrobial Activity

The newly synthesized target compounds **(5a-r)** were evaluated for their *in vitro* antibacterial activity against two Gram positive bacteria *Staphylococcus aureus* (MTCC 96) and *Bacillus subtilis* (MTCC 441) and two Gram negative bacteria *Escherichia coli* (MTCC 443) and *Salmonella typhi* (MTCC 98). They were also evaluated for their *in vitro* antifungal activity against *Candida albicans* (MTCC 227) and *Aspergillus niger* (MTCC 282) as fungal strains. Broth dilution method was used for the determination of the antibacterial and antifungal activity as recommended by NCCLS[27]. Ampicillin, Chloramphenicol and Norfloxacin were used as standard antibacterial drugs, whereas Griseofulvin and Nystatin were used as standard antifungal drugs. All MTCC cultures were collected from Institute of Microbial Technology, Chandigarh and tested against above mentioned known drugs. Mueller-Hinton broth was used as the nutrient medium for the test bacteria and Sabouraud Dextrose broth was used for the test fungi. Inoculum size for the test strains was adjusted to 10^8 CFU (Colony Forming Unit per milliliter) per milliliter by comparing the turbidity. Each synthesized compound was diluted with DMSO so as to have the stock solution of 2000 $\mu g/$mL concentration as a stock solution. The results were recorded in the form of primary and secondary screening. The synthesized compounds **(5a-r)** were screened for their antibacterial and antifungal activity at the concentration of 1000, 500 and 250 $\mu g/$mL for the primary screening. The synthesized compound showing activity against microbes in the primary screening were further screened in a second set of dilution at concentrations of 200, 100, 62.5, 50 and 25 $\mu g/$mL. The suspention of 10 μL from each well were further incubated and growth was noted at 37°C after 24 hour for bacteria and 48 hour for fungi. The lowest concentration which showed no visible growth (turbidity) after spot subculture was considered as the minimum inhibitory concentration (MIC) for each compound.

The investigation of the data summarized in **(Table-1)** reveals that many compounds were found to be active against Gram-positive bacteria while some of the compounds were found to be active against Gram-negative bacterial and fungal species as compared to that of the standard antimicrobial drugs.

Antimicrobial Evaluation

The compounds **(5a-r)** were screened for their *in vitro* antibacterial and antifungal evaluation against various bacterial and fungal pathogens by broth dilution method. Ampicillin, Chloramphenicol, Norfloxacin, Griseofulvin and Nystatin were used as standard drugs. The values of MIC are summarized in **Table-1**.

Upon evaluating the antimicrobial activity data, it was observed that compound **5j** (MIC = 62.5$\mu g/$mL) exhibited excellent activity compared to Ampicillin (MIC = 250$\mu g/$mL) and Norfloxacin (MIC = 100$\mu g/$mL) against gram positive bacteria *B. subtilis.* Compounds **5e, 5g, 5l and 5p** (MIC = 100$\mu g/$mL) showed excellent activity towards the gram positive bacteria *B. subtilis* as compared to Ampicillin (MIC = 250$\mu g/$mL) and showed equipotent activity to Norfloxacin (MIC = 100$\mu g/$mL). Against gram positive bacteria *B. subtilis* compound **5q** (MIC = 125 $\mu g/$mL) showed better activity as compared to Ampicillin (MIC = 250$\mu g/$mL). Compounds **5a, 5c, 5d, 5f, 5i** and **5m** (MIC = 200$\mu g/$mL) showed better activity towards the gram positive bacteria *B. subtilis* as compared to Ampicillin (MIC = 250$\mu g/$mL). Compounds **5b, 5h, 5k, 5n, 5o** and **5r** (MIC = 250$\mu g/$mL) exerted equipotent activity against gram positive bacteria *B. subtilis*. Compound **5p** (MIC = 62.5$\mu g/$mL) and Compounds **5l, 5n, 5o** and **5r (**MIC = 100$\mu g/$mL) exhibited excellent activity compared to Ampicillin (MIC = 250$\mu g/$mL) against gram positive bacteria *S. aureus.* Compounds **5c, 5e, 5g** and **5j** (MIC = 125$\mu g/$mL) and Compounds **5f, 5h, 5m** and **5q (**MIC = 200$\mu g/$mL) exhibited better activity against gram positive bacteria *S. aureus* as compared to Ampicillin (MIC = 250$\mu g/$mL). Compounds 5**a, 5b, 5d, 5i** and **5k** (MIC = 250$\mu g/$mL) were found equipotent to Ampicillin (MIC = 250$\mu g/$mL) against gram

positive bacteria *S. aureus*. Compound **5e** (MIC = 62.5*μg/*mL) exhibited better activity compared to Ampicillin (MIC = 100*μg/*mL) against gram negative bacteria *E. coli*. Compounds **5c, 5o** and **5q** (MIC = 100*μg/*mL) were found equipotent compared to Ampicillin (MIC = 100*μg/*mL) against *E. coli*. Compounds **5i** and **5o** (MIC = 62.5*μg/*mL) exhibited better activity compared to Ampicillin (MIC = 100*μg/*mL) against gram negative bacteria *S. typhi*. Compounds **5d, 5g, 5j** and **5q** (MIC = 100*μg/*mL) were found equipotent compared to Ampicillin (MIC = 100*μg/*mL) against *S. typhi*. Compounds **5h** and **5l** (MIC = 250*μg/*mL) were found to be more active against *C. albicans* compared to Griseofulvin (MIC = 500*μg/*mL) whereas, compounds **5g, 5i, 5j, 5m** and **5r** (MIC = 500*μg/*mL) were found equipotent to Griseofulvin (MIC = 500*μg/*mL) against *C. albicans.* It is perceived from the antimicrobial data that almost all the tested derivatives **3a-l** were found to be potent against the gram positive bacterial strains. Among all the tested compounds, the compounds **5e, 5i, 5j, 5o** and **5p** were found to be more efficient members of the series.

Table 1: *In vitro* Antimicrobial activity of compounds (5a-r)

Compound	Minimum Inhibitory Concentration (MIC, $\mu g mL^{-1}$)						
	Gram +ve bacteria		Gram –ve bacteria		Fungi		
	B.s.	***S.a.***	***E.c.***	***S.t.***	***A.n.***	***C.a.***	
5a	**200**	**250**	250	250	1000	1000	
5b	**250**	**250**	200	250	1000	>1000	
5c	**200**	**125**	**100**	125	500	1000	
5d	**200**	**250**	250	**100**	250	>1000	
5e	**100**	**125**	**62.5**	200	250	1000	
5f	**200**	**200**	250	250	1000	>1000	
5g	**100**	**125**	200	**100**	1000	**500**	
5h	**250**	**200**	125	250	500	**250**	
5i	**200**	**250**	200	**62.5**	1000	**500**	
5j	**62.5**	**125**	125	**100**	500	**500**	
5k	**250**	**250**	200	250	1000	>1000	
5l	**100**	**100**	200	200	1000	**250**	
5m	**200**	**200**	125	250	>1000	**500**	
5n	**250**	**100**	200	250	250	1000	
5o	**250**	**100**	**100**	**62.5**	>1000	1000	
5p	**100**	**62.5**	250	125	500	>1000	
5q	**125**	**200**	**100**	**100**	500	1000	
5r	**250**	**100**	200	250	1000	**500**	
Ampicillin	250	250	100	100	-	-	
Chloramphenicol	50	50	50	50	-	-	
Ciprofloxacin	50	50	25	25	-	-	
Norfloxacin	100	10	10	10	-	-	
Gentamycin	1	0.25	0.05	5	-	-	
Griseofulvin	-	-	-	-	100	500	
Nystatin	-	-	-	-	100	100	

B.s.: *Bacillus subtilis,* ***S.a.:*** *Staphylococcus aureus,* ***E.c.:*** *Escherichia coli,* ***S.t.:*** *Salmonella typhi,* ***A.n.:*** *Aspergillus niger,* ***C.a.:*** *Candida albicans*

CONCLUSION

From present study, we summarized that employed synthetic strategy provide efficient route for the synthesis 2,6-di(coumarin-3-yl)-4-[1-aryl-3-(bezofuran-2-yl)-1*H*-pyrazol-4-yl]pyridines by Krohnke's protocol. Moreover the starting precursors were also easy to prepare from synthesis point of view. Antimicrobial study on target compounds concluded that the all the compounds exerted promising activity against gram positive bacteria and gram negative. Compounds **5e, 5i, 5j, 5o** and **5p** were found to be the most efficient members of the series.

ACKNOWLEDGEMENT

The authors are thankful to the Head, Department of Chemistry, Sardar Patel University for providing research facilities. Financial assistance to KNP from the UGC, New Delhi, India, is highly acknowledged.

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