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SYNTHESIS OF COUMARIN-COUPLED PYRAZOLE AND ISOXAZOLE COMPOUNDS

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ABSTRACT:
In the current study, we synthesised new compounds, namely 3-(substituted-(Furan-2-yl) acryloyl)-2H-chromen-2-one, 3-(5-substituted-(furan-2-yl)-4,5-dihydro-1H-pyrazol-3-yl)-2H-chromen-2-one, 3-(3-(5-substituted-furan-2-yl)-4,5-dihydro-1-(2,4-dinitrophenyl)-1H-pyrazol-5-yl)-2H-chromen-2-one, and 3-(5-(5-substituted-furan-2-yl)-4,5-dihydroisoxazol-3-yl)-2H-chromen-2-one, along with derivatives. These novel compounds were characterised using infrared (IR), ^{1}H NMR, ^{13}C-NMR spectroscopy, and elemental analysis. These reactions were conducted in the presence of sodium acetate as a catalyst and ethanol as the solvent.

KEYWORDS: 3-Acetylcoumarin, benzo-fused lactone, sodium acetate, chromen-2-one, pyrazole, isoxazole.

INTRODUCTION

Coumarin, classified as an oxygen-heterocyclic compound and also referred to as benzo-fused lactone, is a member of the lactone family characterised by a benzopyrones skeletal structure. It occurs naturally in several medicinal plants, including Tonga bean[i-ii], and can be synthesised in laboratory settings. Coumarin-containing plants are employed in traditional medicine, while synthetically derived coumarin derivatives find use in food additives[iii], chiroptical materials[iv], perfumes, cosmetics, pharmaceuticals[v], insecticides, optical brightening agents[vi], dispersed fluorescent and laser dyes[vii]. Furthermore, synthetically prepared coumarin and its fused derivatives have garnered significant attention in the realms of organic and medicinal chemistry, owing to their extensive utility in various pharmacological activities such as antimicrobial[viii], anticancer[ix], anti-inflammatory[x], anti-HIV[xi], antioxidant[xii], antimalarial[xiii], antitumor[xiv], anti-hyperlipidemic[xv], and antitubercular[xvi] functions. Reports indicate the importance of coumarin with a chalcone backbone, which serves as a precursor for synthesising heterocyclic compounds known for their substantial biological activity[xvii-xxiii].
In the investigation, Olayinka O. Ajan and colleagues undertook the synthesis of a diverse range of 3-(5-(substituted-phenyl)-4,5-dihydro-1H-pyrazol-3-yl)-2H-chromen-2-one

derivatives, which incorporate both coumarin and pyrazole skeletal frameworks. Importantly, these synthesised compounds exhibited potent antibacterial activity[xxiv]. In a related study, the same research group employed a structure-based approach to design and synthesise functionalised 3-(5-(s-phenyl)-4H-pyrazol-3-yl)-2H-chromene-2-one motifs in conjunction with indigenous plant extracts, highlighting their antimalarial potential[xxv]. Coumarin derivatives featuring pyrazole moieties have garnered substantial interest due to their utility in synthesising bioactive compounds[xxvi]. They are particularly relevant in inhibiting tumour cell growth owing to their distinctive chemical properties[xxvii] and agricultural applications[xxviii]. Notably, the synthesis of coumarin-pyrazolines as antimicrobial agents, with a specific target on bacterial D-alanine-D-alanine ligase, has shown promising antibacterial and antifungal activities[xxix]. Similarly, developing new derivatives of coumarin-containing pyrazoline compounds has demonstrated noteworthy antimicrobial potential[xxx]. Furthermore, coumarin derivatives that contain isoxazole moieties have demonstrated efficacy against pathogenic bacteria, including *S. aureus* and *E. coli*.[xxxi]. These findings underscore the versatile and valuable role of coumarin-based compounds in medicinal and agricultural applications, particularly in the context of antimicrobial and antitumor activities. The coupling of coumarin with pyrazole or oxazole has the potential to yield novel compounds. These unique compounds, featuring coumarin, pyrazole, or oxazole within a single motif, offer exciting prospects for developing bioactive compounds. Recognising the significance of coumarin, pyrazole, and oxazole in medicinal chemistry, we have successfully synthesised a distinct coumarin-based compound, paving the way for further exploration and potential applications in drug discovery.

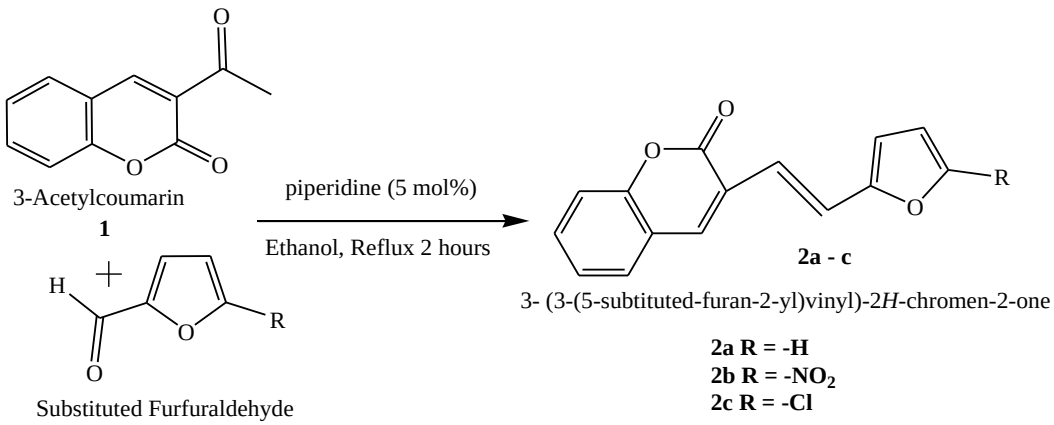
EXPERIMENTAL

Materials and methods

The reagents used were of analytical grade and utilised without purification. Ethyl acetoacetate and piperidine were purchased from Alfa Aesar. The Melting points of all the synthesised compounds were confirmed in an open capillary tube and are uncorrected. The reaction's progress was tracked through thin-layer chromatography (TLC) using silica plates. ^{1}H NMR spectra were recorded with an NMR predict proton $CDCl_3$ (BRUKER/TOPSPIN) spectrometer operating at 400 MHz using $CDCl_3$ solvent and ^{13}C-NMR at 100 MHz, $CDCl_3$ and element analysis was performed on BRUKER EUROEA at Indian Institute of Technology Hyderabad.

1. Procedure for synthesis of 3-(Substituted-(Furan-2-yl) acryloyl)-2H-chromen-2-one (2a-c):

3-Acetylcoumarin **1** was synthesised by the reported method[xxiv]. The mixture of 3-acetyl-coumarin **1** (10.6 mmol), substituted Furfuraldehyde (10.6 mmol), piperidine (5 mol%) and ethanol as solvent (20 mL) was taken in round bottom flask and the reactant mixture was refluxed for 2 hours to obtain 3-(substituted-(Furan-2-yl)acryloyl)-2H-chromen-2-one (**2a-c**). The complete reaction progress was monitored using thin-layer chromatography (TLC) with a solvent system comprising n-hexane and ethyl acetate. Once the reaction process was completed, the mixture was poured over crushed ice to obtain the desired compound. The resulting solid compound was filtered, dried, and recrystallised using ethanol as a solvent.



Scheme-I : Synthesis of 3-(3-(5-substituted-Furan-2-yl)acryloyl)-2H-chromen-2-one

1.1 3-(3-(Furan-2-yl) acryloyl)-2H-chromen-2-one (2a):

(Brown, MP- 139 ºC Yield- 2.52 g, 89%) IR (KBr): 1740, 1640, 1606, 1386 $cm^{-1.}$ 1H-NMR (CDCl3, 400 MHz): δ 6.88 (t, $^3J_{HH}$=7.7 Hz , 1H, Furan-H), 7.05 (d, 1H, $^3J_{HH}$= 8.7 Hz, CO=CH=CH), 7.70 (d, 1H, $^3J_{HH}$= 8.7 Hz, CO=CH=CH),7.40–7.85 (m, 5H, Ar-4H &Furan-1H),8.17 (d, $^3J_{HH}$=7.7 Hz 1H, Furan-H),8.58 (s, 1H, Coumarin-H). 13C-NMR (CDCl3, 400 MHz): δ 183.9 (C=O), 160 (C=O), 153.2, 151.8, 147.5, 143, 138.1, 134.2, 130.0, 128.5, 127.1, 124.8, 118.8, 116.7, 113.8, 113.2. Elemental analysis -: $C_{16}H_{10}O_4$ (266.06): Calcd. (%) C 72.18, H 3.79; Found (%) C 72.02, H 3.54

1.2 3-(3-(5-Nitrofuran-2-yl) acryloyl)-2H-chromen-2-one (2b):

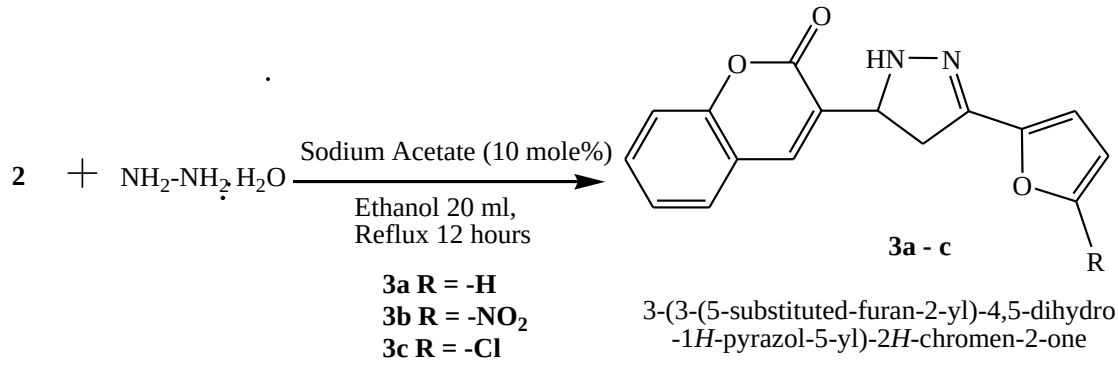
(Yellow, MP- 194-196 °C Yield-66.80%) (IR (KBr): 1734, 1680, 1605, 1370cm^{-1}. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ7.98 (d, $^3J_{HH}$=8.1 Hz , 1H, Furan-H), 7.05 (d, 1H, $^3J_{HH}$= 8.4 Hz, CO=CH=CH), 7.70 (d, 1H, $^3J_{HH}$= 8.4 Hz, CO=CH=CH),7.40–7.85 (m, 5H, Ar-4H &Furan-1H),8.58 (s, 1H, Coumarin-H). 13C-NMR (CDCl3, 400 MHz): δ 183.8 (C=O), 160.1 (C=O), 155.2, 155.8, 153.5, 147.4, 138.9, 134.2, 129.0, 128.5, 127.1, 125.8, 118.6, 117.7, 116.2, 114.2. Elemental analysis -: $C_{16}H_9NO_6$ (311.04): Calcd. (%) C 61.74, H 2.91, N 4.50; Found (%) C 60.90, H 2.70, N 4.10.

1.3 3-(3-(5-Chlorofuran-2-yl) acryloyl)-2H-chromen-2-one (2c):

(Green Color) MP- more than 300ºC Yield- 2.52 g, 59.20 %) IR (KBr): IR (KBr): 1740, 1655, 1600, 1380 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ6.89 (d, $^3J_{HH}$=8.7 Hz, 1H, Furan-H), 7. 23 (d, $^3J_{HH}$=8.7 Hz, 1H, Furan-H), 7.05 (d, 1H, $^3J_{HH}$= 9.5 Hz, CO=CH=CH), 7.70 (d, 1H, $^3J_{HH}$= 9.5 Hz, CO=CH=CH), 7.40–7.85 (m, 4H, Ar-4H), 8.58 (s, 1H, Coumarin-H). ^{13}C-NMR ($CDCl_3$, 400 MHz): δ 183.7 (C=O), 149.1 (C=O), 153.2, 151.8, 143.3, 138.9, 128.9, 134.2, 129.0, 128.5, 127.7, 125.4, 118.5, 116.2, 114.2, 109.6. Elemental analysis -: $C_{16}H_9ClO_4$ (300.02): Calcd. (%) C 63.91, H 3.02; Found (%) C 63.70, H 3.00.

2. Procedure for the Synthesis of 3-(5-substituted-(furan-2-yl)-4, 5-dihydro-1H-pyrazol-3-yl)-2H-chromen-2-one (3a-c):

A mixture of 3-(3-(5-substituted-Furan-2-yl)acryloyl)-2H-chromen-2-one **2** (1.87 mmole), 2, 4- dinitrophenylhydrazine hydrate (1.87 mmole), sodium acetate (10 mole%) as the catalyst, ethanol (20mL) as solvent was added in round bottom flask and mixture was refluxed for 4 to 5 hours. After some time interval, the reaction mixture was monitored by TLC. Once the reaction was finished, the mixture was poured onto the crushed ice. The precipitated solid compound was filtered, dried and recrystallised from ethanol to ensure the formation of compound **3** takes place.



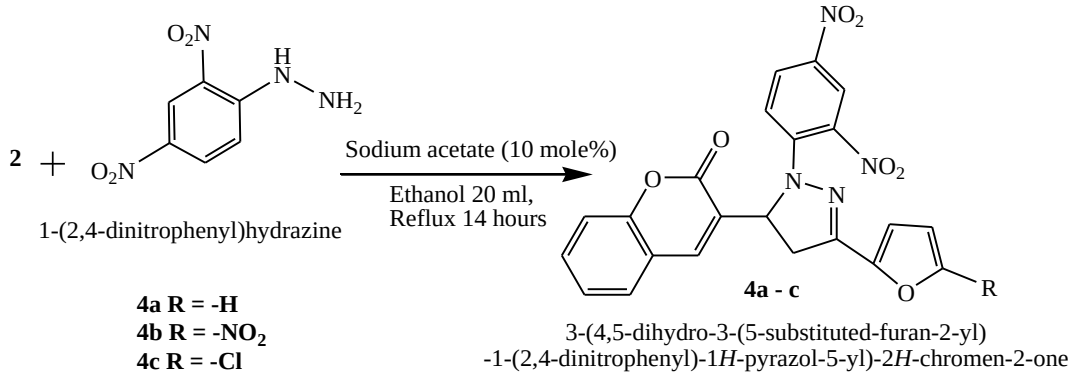
Scheme-II :- Synthesis of 3-(3-(5-substituted-(furan-2-yl)-4, 5-dihydro-1H-pyrazol-3-yl)-2H-chromen-2-on

2.1 3-(3-(furan-2-yl)-4, 5-dihydro-1H-pyrazol-3-yl)-2H-chromen-2-one (3a):
(MP 159 - 160 ºC) ^{1}HNMR(CDCl3- 400 MHz) δH: 8.45 (s, 1 H, Het-H),7.86–7.40 (m,, 4H, Coumarin H)7.67 (d, $^{3}J_{HH}$=7.7 Hz 1H, Furan-H),6.47 (t, $^{3}J_{HH}$=7.7 Hz , 1H, Furan-H),6.30 (d, $^{3}J_{HH}$=7.7 Hz , 1H, Furan-H), 6.93 (d, J =9.65 Hz, 1 H, NH-CH), 3.44–3.39 (m, 1 H, CH), 2.98 (d, J = 4.56 Hz, 2 H,CH_2-CH). ^{13}C-NMR (CDCl3, 400 MHz): δ 160.9 (C=O), 156.1 (C=N), 153.9, 152.2, 142.2, 134.5, 128.7, 127.6, 125.4, 123.8, 119.5, 116.6, 110.8, 109.5, 51.7, 38.8. Elemental analysis -: $C_{16}H_{12}N_2O_3$ (280.08): Calcd. (%) C 68.56, H 4.32, N 9.99; Found (%) C 68.20, H 4.10, N 9.85.

2.2 3-(5-(5-nitrofuran-2-yl)-4, 5-dihydro-1H-pyrazol-3-yl)-2H-chromen-2-one (3b):
(Yellow, MP – 134 - 136 ºC) ^{1}HNMR($CDCl_3$- 400 MHz) δ H: 8.45 (s, 1 H, Het-H),7.86–7.40 (m,,4H, Coumarin-H) ,7.55 (d, $^{3}J_{HH}$=7.1 Hz, 1H, Furan-H),6.58 (d, $^{3}J_{HH}$=7.1 Hz , 1H, Furan-H), 6.93 (d, J =9.65 Hz, 1 H, NH-CH), 3.40–3.40 (m, 1 H, CH), 3.01 (d, J = 4.56 Hz, 2 H,CH_2-CH). ^{13}C-NMR ($CDCl_3$, 400 MHz): δ 160.9 (C=O), 156.1 (C=N), 154.9, 153.2, 150.2, 134.5, 128.7, 127.6, 125.4, 123.8, 119.5, 116.6, 111.8, 109.5, 51.7, 38.7.Elemental analysis -: $C_{16}H_{12}N3O5$ (325.07): Calcd. (%) C 59.08, H 3.41, N 12.92; Found (%) C 58.90, H 3.10, N 12.05.

2.3 3-(5-(5-chlorofuran-2-yl)-4, 5-dihydro-1H-pyrazol-3-yl)-2H-chromen-2-one (3c):
(MP 214-219 ºC) ^{1}HNMR ($CDCl_3$- 400 MHz) δ H: 8.45 (s, 1 H, Het-H),7.86–7.40 (m,,4H, Coumarin-H),6.90 (d, $^{3}J_{HH}$=6.80 Hz, 1H, Furan-H),6.10 (d, $^{3}J_{HH}$=6.80 Hz , 1H, Furan-H), 6.93 (d, J =9.65 Hz, 1 H, NH-CH), 3.40–3.40 (m, 1 H, CH), 3.01 (d, J = 4.56 Hz, 2 H,CH_2-CH). ^{13}C-NMR (CDCl3, 400 MHz): δ 160.9 (C=O), 156.1 (C=N), 153.2, 151.5, 134.2, 133.5, 128.7, 127.6, 125.4, 123.8, 119.5, 116.6, 107.3, 109.5, 51.7, 38.7.Elemental analysis -: $C_{16}H_{12}ClN_2O_3$ (314.05): Calcd. (%) C 61.06, H 3.52, N 8.90; Found (%) C 60.92, H 3.30, N 8.30.

3. Procedure for the Synthesis of 3-(3-(5-substituted-furan-2-yl)-4, 5-dihydro-1-(2,4-dinitrophenyl)-1H-pyrazol-5-yl)-2H-chromen-2-one (4a-c):
A mixture of 3-(3-(5-substituted-Furan-2-yl)acryloyl)-2H-chromen-2-one **2** (1.87 mmole), 2, 4- dinitrophenylhydrazine (1.87 mmole), sodium acetate (10 mole%) as the catalyst, ethanol (20 mL) as solvent was added in round bottom flask and mixture was refluxed for 4 to 5 hours. After some time interval, the reaction mixture was monitored by TLC. Once the reaction was finished, the mixture was poured onto the crushed ice. The precipitated solid compound was filtered, dried and recrystallised from ethanol to afford the formation of compound **4**.



Scheme-III: Synthesis of 3-(3-(5-substituted-furan-2-yl)-4, 5-dihydro-1-(2,4-dinitrophenyl)-1*H*-pyrazol-5-yl)-2H-chromen-2-one

3.1 3-(1-(2, 4-dinitrophenyl)-5-(furan-2-yl)-4, 5-dihydro-1H-pyrazol-3-yl)-2H-chromen-2-one (4a):

(MP 141-143 ºC) ^{1}HNMR ($CDCl_3$- 400 MHz) δ H: 9.10 (s, 1H, Ar-NO_2),8.50 (d,$^{3}J_{HH}$=7.68 Hz 1H, Ar-NO_2),8.31 (s, 1 H, Het-H),7.20 (d,$^{3}J_{HH}$=7.68 Hz 1H, Ar-NO_2), 7.86–7.40 (m,, 4H, Coumarin-H), 7.65 (d, $^{3}J_{HH}$=7.7 Hz 1H, Furan-H),6.43(t, $^{3}J_{HH}$=7.7 Hz , 1H, Furan-H),6.35 (d, $^{3}J_{HH}$=7.7 Hz , 1H, Furan-H),5.40 (t, J =4.70 Hz,1 H, CH), 3.76 (d, J = 4.70 Hz, 2 H,CH_2-CH). ^{13}C-NMR ($CDCl_3$, 400 MHz): δ 159.3 (C=O), 155.1 (C=N), 153.9, 152.0, 141.8, 141.9, 137.8, 137.2, 133.7, 130.2, 128.7, 127.6, 125.4, 124.5, 123.1, 120.3, 118.5, 116.1, 110.5, 109.5, 58.9, 36.3.Elemental analysis -: $C_{22}H_{14}N_4O_7$ (280.08): Calcd. (%) C 59.20, H 3.16, N 12.55; Found (%) C 58.80, H 3.10, N 12.3

3.2 3-(1-(2,4-dinitrophenyl)-5-(5-nitrofuran-2-yl)-4,5-dihydro-1H-pyrazol-3-yl)-2H-chromen-2-one (4b):

(MP 220-223 ºC) ^{1}HNMR ($CDCl_3$- 400 MHz) ,δ H: 9.10 (s,1H,Ar-NO_2),8.50 (d,$^{3}J_{HH}$=7.68 Hz 1H,Ar-NO_2),8.31 (s, 1 H, Het-H),7.20 (d,$^{3}J_{HH}$=7.68 Hz 1H,Ar-NO_2), 7.86–7.40 (m,, 4H, Coumarin-H), 7.31(d, $^{3}J_{HH}$=7.3 Hz , 1H, Furan-H),6.81 (d, $^{3}J_{HH}$=7.3 Hz , 1H, Furan-H),5.41 (t, J =4.70 Hz,1 H, CH), 3.60 (d, J = 4.70 Hz, 2 H,CH_2-CH). 13C-NMR ($CDCl_3$, 400 MHz): δ 159.3 (C=O), 155.1 (C=N), 154.9, 153.3, 148.7, 141.9, 137.8, 137.2, 133.7, 130.2, 128.7, 127.6, 125.4, 124.5, 123.1, 120. 3,118.5, 116.1, 111.1, 108.1, and 58.9, 36.3.Elemental analysis -: $C_{22}H_{13}N_5O_9$ (491.07): Calcd. (%) C 53.78, H 2.67, N 14.25; Found (%) C 53.60, H 2.50, N 14.01.

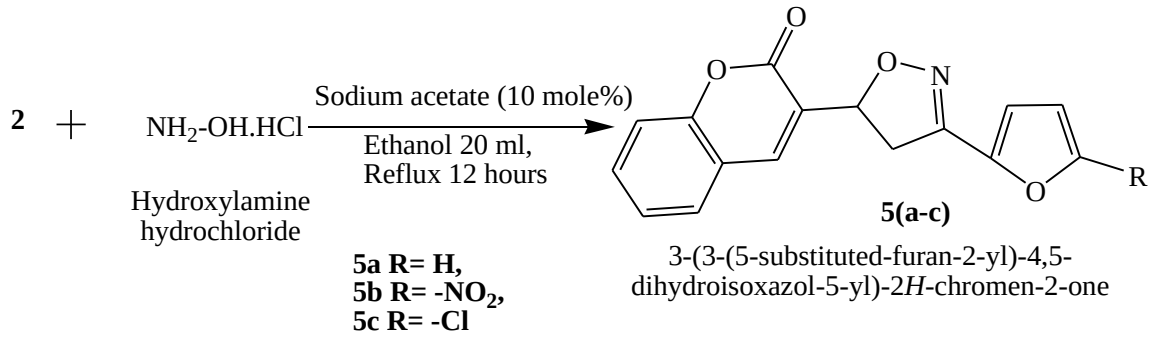
3.3 3-(5-(5-chlorofuran-2-yl)-1-(2, 4-dinitrophenyl)-4, 5-dihydro-1H-pyrazol-3-yl)-2H-chromen-2-one (4c):

(MP - 178-181 °C) ^{1}HNMR($CDCl_3$- 400 MHz) ,δ H: 9.10 (s,1H,Ar-NO_2),8.50 (d,$^{3}J_{HH}$=7.68 Hz 1H,Ar-NO_2),8.31 (s, 1 H, Het-H),7.20 (d,$^{3}J_{HH}$=7.68 Hz 1H,Ar-NO_2), 7.86–7.40 (m,, 4H, Coumarin-H), 6.67(d, $^{3}J_{HH}$=8.2 Hz , 1H, Furan-H),6.32 (d, $^{3}J_{HH}$=8.2 Hz , 1H, Furan-H),5.41 (t, J =4.70 Hz,1 H, CH), 3.60 (d, J = 4.70 Hz, 2 H,CH_2-CH). ^{13}C-NMR ($CDCl_3$, 400 MHz): δ 159.3 (C=O), 155.1 (C=N), 153.3, 151.6, 141.9, 137.8, 137.2, 134.2, 133.7, 130.2, 128.7, 127.6, 125.4, 124.5, 123.1, 120.3, 118.5, 116.1, 109.3, 107.1, 58.9, 36.1.Elemental analysis -: $C_{22}H_{13}ClN_4O_7$ (480.05): Calcd. (%) C54.96, H 2.73, N 11.65; Found (%) C 54.60, H 2.65, N 11.20.

4. Procedure for the Synthesis of 3-(5-(5-substituted-furan-2-yl)-4, 5-dihydroisoxazol-3-yl)-2H-chromen-2-one (5a–c):

The mixture of 3-(3-(5-substituted-Furan-2-yl)acryloyl)-2H-chromen-2-one (1.87 mmole), hydroxylamine hydrochloride (1.87 mmole), sodium acetate (10 mole%) as catalyst and ethanol (20 mL) as solvent was added in round bottom flask and mixture was refluxed for 12 hours. After monitoring the reaction mixture by TLC, it was transferred onto crushed ice upon

completion. The precipitated solid compound was filtered, dried and recrystallised from ethanol, forming compound **5**.



Scheme-IV: Synthesis of 3-(5-(5-substituted-furan-2-yl)-4, 5-dihydroisoxazol-3-yl)-2H-chromen-2-one

4.1 3-(5-(furan-2-yl)-4, 5-dihydroisoxazol-3-yl)-2H-chromen-2-one (5a):

^{1}H NMR ($CDCl_3$- 400 MHz),δ H: 8.32 (s, 1 H, Het-H), 7.82–7.42 (m, 4H, Coumarin-H),7.67 (d, $^3J_{HH}$=7.7 Hz 1H, Furan-H),6.47 (t, $^3J_{HH}$=7.7 Hz, 1H, Furan-H),6.35 (d, $^3J_{HH}$=7.7 Hz, 1H, Furan-H),4.8 (t, J = 4.56 Hz, 1 H, CH), 3.40 (d, J = 4.56 Hz, 2H, CH_2-CH).^{13}C-NMR (CDCl3, 400 MHz): δ 159.4 (C=O), 157.8 (C=N), 153.9, 153.2, 141.2, 137.5, 128.0, 127.6, 125.4, 125.0, 118.5, 116.3, 110.8, 109.9, 71.6, 23.6.Elemental analysis -: $C_{16}H_9NO_4$(279.04): Calcd. (%) C 68.82, H 3.25, N 5.02; Found (%) C 68.70, H 2.99, N 4.85.

4.2 3-(5-(5-nitrofuran-2-yl)-4, 5-dihydroisoxazol-3-yl)-2H-chromen-2-one (5b):

^{1}HNMR($CDCl_3$- 400 MHz)δ H: 8.32 (s, 1 H, Het-H), 7.82–7.42 (m, 4H, Coumarin-H),7.45 (d, $^3J_{HH}$=7.2 Hz, 1H, Furan-H),6.95 (d, $^3J_{HH}$=7.2 Hz, 1H, Furan-H),4.8 (t, J = 4.56 Hz, 1 H, CH), 3.40 (d, J = 4.56 Hz, 2H, CH_2-CH).^{13}C-NMR (CDCl3, 400 MHz): δ 159.4 (C=O), 157.8 (C=N), 156.2, 153.1, 147.3, 137.5, 128.1, 127.6, 125.4, 125.0, 118.5, 116.3, 110.8, 108.6, 71.6, 23.5.Elemental analysis -: $C_{16}H_{10}N_2O_6$(326.05): Calcd. (%) C 58.90, H 3.09, N 8.59; Found (%) C 58.60, H 2.90, N 8.20.

4.3 3-(5-(5-chlorofuran-2-yl)-4, 5-dihydroisoxazol-3-yl)-2H-chromen-2-one (5c):

^{1}HNMR($CDCl_3$- 400 MHz),δ H: 8.32 (s, 1 H, Het-H), 7.82–7.42 (m, 4H, Coumarin-H),6.42(d, $^3J_{HH}$=7.2 Hz, 1H, Furan-H),6.32 (d, $^3J_{HH}$=7.2 Hz, 1H, Furan-H),4.8 (t, J = 4.56 Hz, 1 H, CH), 3.40 (d, J = 4.56 Hz, 2H, CH_2-CH).^{13}C-NMR (CDCl3, 400 MHz): δ 159.4 (C=O), 157.8 (C=N), 154.1, 153.1, 137.5, 133.3, 128.1, 127.6, 125.4, 125.0, 118.5, 116.3, 109.9, 107.6, 71.5, 23.4.Elemental analysis -: $C_{16}H_{10}ClNO_4$ (315.03): Calcd. (%) C 60.87, H 3.19, N 4.44; Found (%) C 60.65, H 3.01, N 4.25.

RESULT AND DISCUSSION:

We have reported the synthesis of new coumarin-coupled pyrazole derivatives **3a-c**, **4a-c** and isoxazole derivatives **5a–c**. The synthesis of coumarin can be achieved in three steps through the condensation reaction of salicylaldehyde and ethyl acetoacetate using a catalytic amount of piperidine, following the standard procedure reported by N. Siddiqui *et al*., 2009[xxxii]. In the second step reaction of the aldol condensation reaction of coumarin and substituted furfural (for **2a** = furfural, for **2b** = 5- nitro-furfural and for **2c** = 5-chloro-furfural) to give coumarin-based chalcone **2a**; 89%, **2b**; 66.80% and **2c**; 59.20% respectively **(Scheme - I)**.

In the third step, These chalcone intermediates **2a–c** were reacted with hydrazine hydrate or 2, 4,-di-nitro-phenylhydrazine hydrate in solvent-ethanol to give [3 + 2] - cycloaddition products, 4, 5-dihydropyrazolo inserted coumarin **3a;** 72%**, 3b;** 74% and **3c;** 69% yield respectively **(Scheme - II)** and 2, 4-dinitro-N-phenyl substituted-4,5-dihydropyrazolo inserted coumarin **4a**; 65%, **4b**; 58% and **5c**; 57% yield respectively **(Scheme - III)**. Whereas similar reaction of

chalcone intermediates **2a–c** with hydroxylamine hydrochloride gives 4, 5-dihydroisoxazol inserted coumarin, **5a;** 71%, **5b;** 68% and **5c;** 69% yield respectively **(Scheme - IV).**

CONCLUSION

In summary, we achieved the efficient synthesis of coumarin-coupled pyrazole and isoxazole derivatives in a brief reaction period, yielding excellent results and characterised the compounds using IR, ^{1}H NMR, ^{13}C-NMR spectroscopy, and elemental analysis, employing sodium acetate as a catalyst and ethanol as the solvent.

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CONFLICT OF INTERESTS

The authors confirm no conflicts of interest.

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