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**RESEARCH ARTICLE**

# Reactions and Antimicrobial activity of (3-(3-(4-Methoxyphenyl)acryloyl)-2*H*-Chromen-2-one

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## *Abstract*

Several pyridine derivatives, pyrazolines were synthesized via reaction of 3-(3-(4-methoxyphenyl)acryloyl)-2*H*-chromen-2-one with different reagents. Structures of newly synthesized compounds were confirmed by elemental analysis, spectral data, chemical transformation and alternative synthetic route whenever possible. Also, the newly synthesized compounds were screen towards some microorganism.

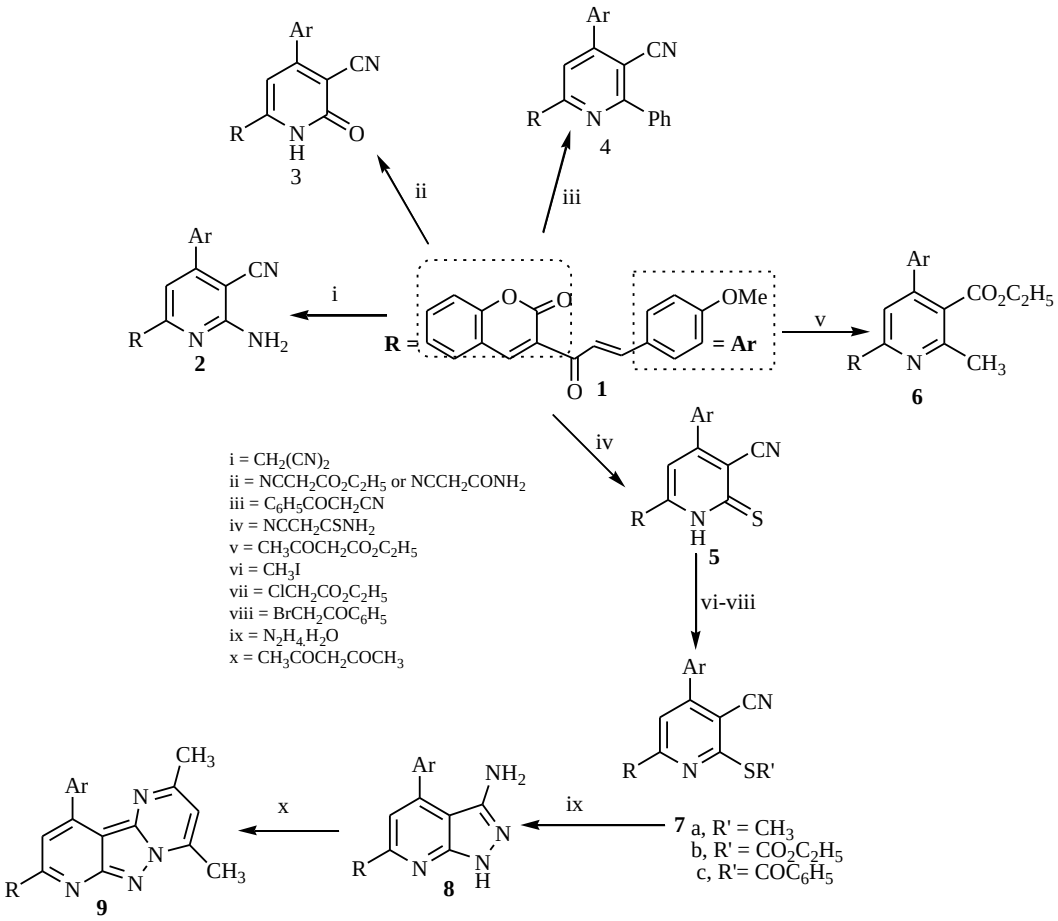


## 1. Introduction

The chalcones are associated with different biological activities like insecticidal [1], anticancer [2], anti-inflammatory [3], bactericidal [4], fungicidal [5], antiviral [6], antitumor [7], antimalarial [8] and antiulcer [9]. Literature shows that lieochalcone and oxygenated chalcone has strong antileishmanial activity [10, 11]. It is reported that chalcones exhibited potent activity against human malarial parasite [12]. Also, many workers have reported the different pharmaceutical activities of chalcones and its derivatives [13-22].

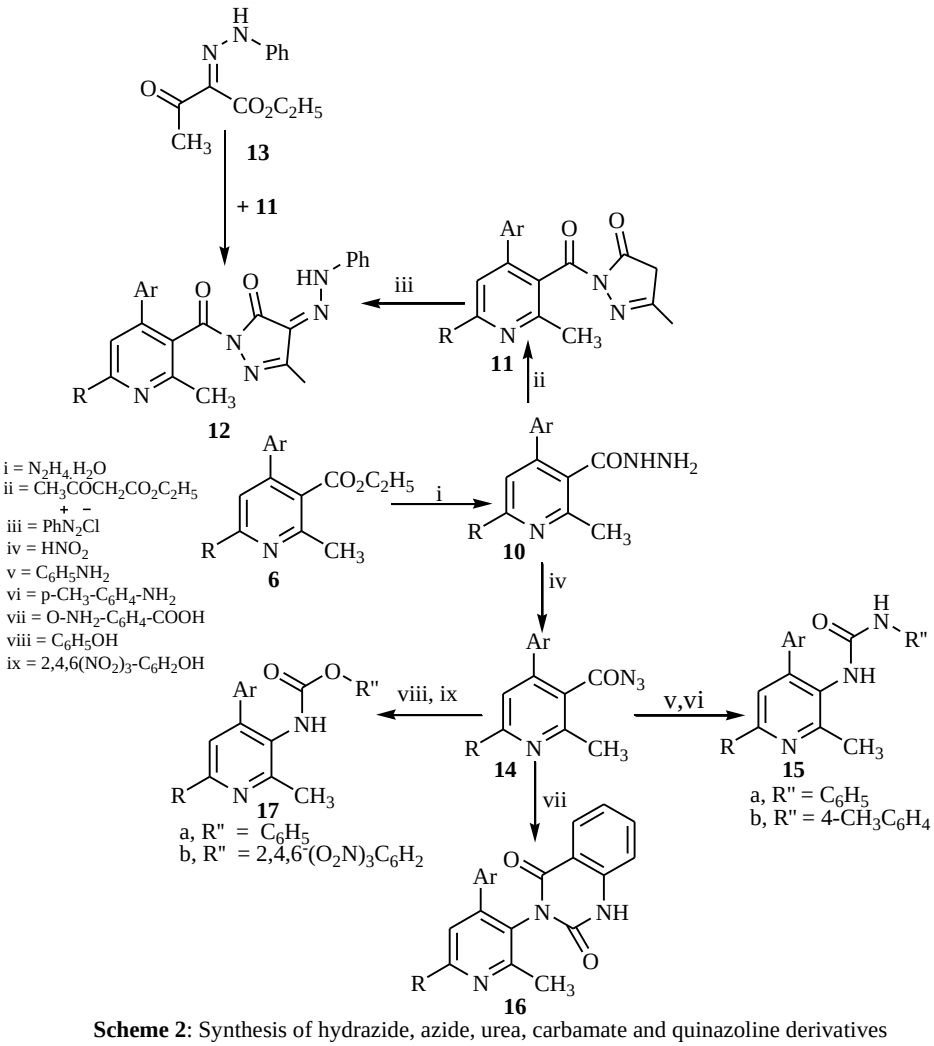
## 2. Results and Discussion

The present work deals with the exploitation of the reaction 3-(3-(4-methoxyphenyl)acryloyl)-2*H*-chromen-2-one [23] (**1**) with each of malononitrile, ethyl cyanoacetate, benzoylacetonitrile, cyanothioacetamide, and ethyl acetoacetate in butanol containing ammonium acetate afforded pyridine derivatives **2-6**, respectively Scheme 1. Structures **2-6** were elucidated on the basis of elemental analysis, spectral data and chemical transformation. Thus, 2-mercapto-4-(4-methoxyphenyl)-6-(2-oxo-2*H*-chromen-3-yl)-2,3-dihydropyridine-3-carbonitrile (**5**) was reacted with iodomethane in potassium hydroxide gave corresponding 4-(4-methoxyphenyl)-2-(methylthio)-6-(2-oxo-2*H*-chromen-3-yl)-2,3-dihydropyridine-3-carbonitrile (**7a**), which converted to 3-(3-amino-4-(4-methoxyphenyl)-1*H*-pyrazolo[3,4-*b*]pyridin-6-yl)-2*H*-chromen-2-one (**8**) via its boiling with hydrazine hydrate. Compound **8** was confirmed via elemental analysis, spectral data and its reaction with acetylacetone in acetic acid afforded 3-(10-(4-methoxyphenyl)-2,4-dimethylpyrido[2',3':3,4]-pyrazolo[1,5-*a*]pyrimidin-8-yl)-2*H*-chromen-2-one (**9**) Scheme 1.




**Scheme 1: Synthesis of pyridine, 3-(3-amino-4-(4-methoxyphenyl)-1*H*-pyrazolo[3,4-*b*]pyridin-6-yl)-2*H*-chromen-2-one and 3-(10-(4-methoxyphenyl)-2,4-dimethylpyrido[2',3':3,4]-pyrazolo[1,5-a]pyrimidin-8-yl)-2H-chromen-2-one derivatives**

On the other hand, treatment of **6** with hydrazine hydrate gave 4-(4-methoxyphenyl)-2-methyl-6-(2-oxo-2*H*-chromen-3-yl)nicotinohydrazide (**10**). Structure of **10** was confirmed by elemental analysis, spectral data and chemical transformation. Thus, **10** was reacted with each of ethyl acetoacetate and nitrous acid afforded 1-(4-(4-methoxyphenyl)-2-methyl-6-(2-oxo-2*H*-chromen-3-yl)nicotinoyl)-3-methyl-1*H*-pyrazol-5(4*H*)-one (**11**) and 4-(4-methoxyphenyl)-2-methyl-6-(2-oxo-2*H*-chromen-3-yl) nicotinoyl azide (**14**), respectively (Scheme 2). Structure **11** was elucidated by elemental analysis, spectral data and chemical transformation. Thus, benzenediazonium chloride was reacted with **11** in ethanolic sodium acetate solution at $0^oC$ afforded 1-(4-(4-methoxyphenyl)-2-methyl-6-(2-oxo-2*H*-chromen-3-yl) nicotinoyl)-3-methyl-4-(2-phenylhydrazono)-1*H*-pyrazol-5(4*H*)-one (**12**). Also, compound **12** was obtained by reaction of **10** with the ethyl 2-(2-phenylhydrazono)-3-oxobutanoate (**13**) in acetic acid Scheme 2.

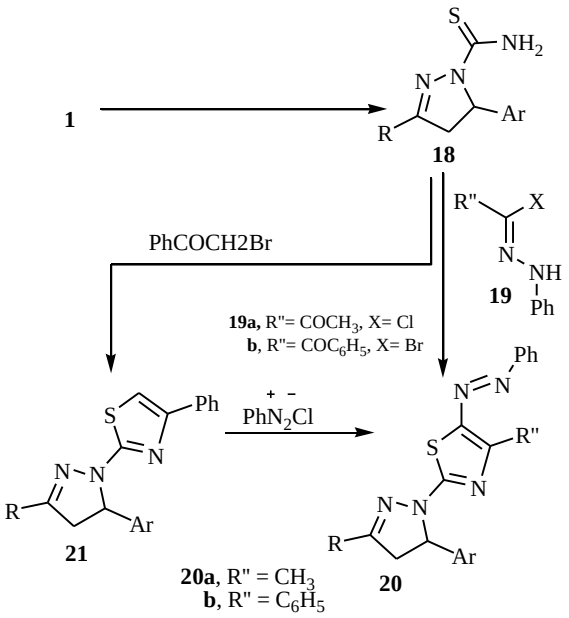



**Scheme 2**: Synthesis of hydrazide, azide, urea, carbamate and quinazoline derivatives

Compound **14** was reacted with the appropriate aniline, 4-toluidine, anthranilc acid, phenol and picric acid afforded urea derivatives **15a**, **15b**, 3-(4-(4-methoxyphenyl)-2-methyl-6-(2-oxo-2*H*-chromen-3-yl)pyridin-3-yl)quinazoline-2,4(1*H*,3*H*)-dione (**16**) and aryl (4-(4-methoxyphenyl)-2-methyl-6-(2-oxo-2*H*-chromen-3-yl)pyridin-3-yl)carbamate **17a** and **17b**, respectively.

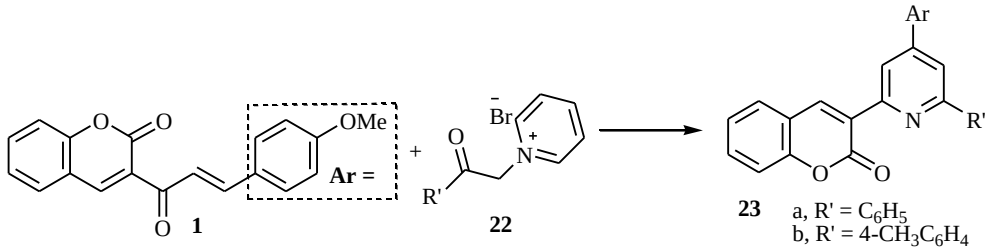
Treatment of 3-(3-(4-methoxyphenyl)acryloyl)-2*H*-chromen-2-one (**1**) with thiosemicarbazide in boiling ethanolic sodium hydroxide gave 5-(4-methoxyphenyl)-3-(2-oxo-2*H*-chromen-3-yl)-4,5-dihydro-1*H*-pyrazole-1-carbothioamide (**18**). Compound **18** reacted with the appropriate hydrazonoyl halides **19a,b** in boiling ethanol containing catalytic amount of triethylamine to give 3-(5-(4-methoxyphenyl)-1-(4-methyl-5-(phenyldiazenyl)thiazol-2-yl)-4,5-dihydro-1*H*-pyrazol-3-yl)-2*H*-chromen-2-one (**20a**) and 3-(5-(4-methoxyphenyl)-1-(4-phenyl-5-(phenyldiazenyl)thiazol-2-yl)-4,5-dihydro-1*H*-pyrazol-3-yl)-2*H*-chromen-2-one (**20b**), respectively (Scheme 3).

Structure **20b** was confirmed by elemental analysis, spectral data, and alternative synthetic route. Thus, benzenediazonium chloride reacted with 3-(5-(4-methoxyphenyl)-1-(4-phenylthiazol-2-yl)-4,5-dihydro-1*H*-pyrazol-3-yl)-2*H*-chromen-2-one (**21**) which prepared *via* reaction of **18** with ω-bromoacetophenone, in ethanol to give products identical in all aspects (mp., mixed mp. and spectra) with **20b** (Scheme 3).




**Scheme 3:** Synthesis of pyrazoline, thiazole and 5-phenylazothiazole derivatives

3-(4-(4-Methoxyphenyl) -6-substituted pyridin-2-yl)-2*H*-chromen-2-one **23a** and **23b** were also prepared in good yields by Krohnke reaction *via* treatment of **1** with 1-(2-oxo-2-substituted ethyl)pyridinium bromides **22a, b** in glacial acetic acid (Scheme 4).




**Scheme 4**: Synthesis of pyridine derivatives **23**

## Antimicrobial activity

All the compounds synthesized in the present investigation were tested for their antimicrobial activity. An examination of the data in Table 1 it is revealed that most of compounds showed moderate to good inhibition zone. Compound **1** has lowest activity against *Salmonela typhimurium* (as Gram-negative bacteria) and *Candida albicans* as antifungal.

Structure and biological activity relationship of title compounds (**2**, **6**, **7a**) showed that presence pyridine moiety and biologically active groups like, –CN, COOEt, $SCH_3$ with coumarine nucleus enhanced the antibacterial activity. Cyclization of compound **7a** to pyrazole ring as in compound **8** enhances the activity.

Compound **14** have intermediate activity when it reacts with phenol gives compound **15a** that increases the antibacterial and antifungal activity while its reaction with amine as in compound **17b** decrease the activity, compounds **15b**, **16** and **17a** have no activity against all tested microorganisms. Further, reaction of chalcone with thiosemicarbazide (compound **18**) increase the activity against most tested microorganisms due to the formation of pyrazoline ring. In addition, reaction of **18** with hydrazonoyl halides increase the activity due to the presence of biologically active moieties as thiazole and N=N-Ph (compounds **20a**, **b**). The minimum inhibitory concentration (MIC) of the biologically active compounds was measured by a two-fold serial dilution method. The results are depicted in Table 2.

These preliminary results of biological screening of the tested compounds could offer encouraging framework in this filed that may lead to the discovery of novel antimicrobial agent.

**Table 1: Antimicrobial activity data of the chalcone and it's cyclized products.**

| Organism | Mean* of zone diameter, nearest whole mm. | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Gram - positive bacteria | | | | Gram - negative bacteria | | | | Yeast and Fungi | | | |
| | *S. aureus* (ATCC 25923) | | *B. subtilis* (ATCC 6635) | | *S. typhimurium* (ATCC 14028) | | *E. coli* (ATCC 25922 | | C. Albicans (ATTCC 10231) | | *A.Fumigatus* | |
| Conc. Sample | 1 mg/ ml | 0.5 mg/ ml | 1 mg/ ml | 0.5 mg/ ml | 1 mg/ ml | 0.5 mg/ Ml | 1 mg/ ml | 0.5 mg/ Ml | 1 mg/m l | 0.5 mg/ ml | 1 mg/ ml | 0.5 mg/ ml |
| **1** | - | - | - | - | 3 L | - | - | - | 2 L | - | - | - |
| **2** | - | - | 5L | 3L | 6 L | 3 L | - | - | 4 L | 2 L | - | - |
| **3** | - | - | - | - | 5 L | 3 L | - | - | - | - | - | - |
| **4** | - | - | 2L | - | - | - | - | - | 2 L | - | - | - |
| **5** | - | - | - | - | - | - | - | - | - | - | - | - |
| **6** | 2L | - | 7L | 4L | 2 L | - | 3 L | - | 2 L | - | - | - |
| **7a** | - | - | 5L | 3L | 3 L | - | - | - | - | - | - | - |
| **8** | - | - | 11L | 8L | - | - | - | - | 9 L | 7 L | - | - |
| **9** | - | - | 2L | - | 2 L | - | - | - | 3 L | - | - | - |
| **10** | - | - | - | - | 4 L | 2 L | - | - | 2 L | - | - | - |
| **11** | - | - | 16I | 13I | - | - | - | - | 9 L | 7 L | - | - |
| **12** | - | - | - | - | - | - | - | - | - | - | - | - |
| **14** | 2L | - | 10L | 6L | 2 L | - | 2 L | - | 11 L | 7 L | - | - |
| **15a** | 3L | - | 16I | 12I | - | - | 9 L | 6 L | 20 I | 15 I | 10L | 6L |
| **15b** | - | - | - | - | - | - | - | - | - | - | - | - |
| **16** | - | - | - | - | - | - | - | - | - | - | - | - |
| **17a** | - | - | - | - | - | - | - | - | - | - | - | - |
| **17b** | - | - | - | - | 3 L | - | - | - | 4 L | 2 L | - | - |
| **18** | 5L | 3L | 3L | - | 5 L | 3 L | - | - | 4 L | 2 L | - | - |
| **20a** | - | - | 6L | 3 L | 5 L | 2 L | - | - | 4 L | 2 L | - | - |
| **20b** | - | - | 7L | 3 L | 7 L | 5 L | - | - | 3 L | - | - | - |
| **23a** | - | - | 7L | 3 L | 7 L | 5 L | - | - | 3 L | - | - | - |
| **23b** | - | - | - | - | - | - | - | - | 2 L | - | - | - |
| Control# | 35 | 26 | 35 | 25 | 36 | 28 | 38 | 27 | 35 | 28 | 37 | 26 |

* = Calculate from 3 values, ** = identified on the basis of routine culture, morphological and microscopical characteristics. – = No effect. L: Low activity = Mean of zone diameter ≤ 1/3 of mean zone diameter of control., I: Intermediate activity = Mean of zone diameter ≤ 2/3 of mean zone diameter of control. H: High activity = Mean of zone diameter > 2/3 of mean zone diameter of control., #: Chloramphenicol in the case of Gram-positive bacteria, Cephalothin in the case of Gram-negative bacteria and cycloheximide was used as standard reference in the case of yeasts and fungi.

**Table 2: MIC of newly synthesized compounds**

| Organism | Mean* of zone diameter, nearest whole mm. | | | | | |
|---|---|---|---|---|---|---|
| | Gram - positive bacteria | | Gram - negative bacteria | | Yeast and Fungi | |
| | *S. aureus* (ATCC 25923) | *B. subtilis* (ATCC 6635) | *S. typhimurium* (ATCC 14028) | *E. coli* (ATCC 25922 | C. Albicans (ATTCC 10231) | *A.Fumigatus* |
| **11** | ND | $\leq$256 | ND | ND | >32 | ND |
| **15a** | ND | $\leq$ 128 | ND | ND | ND | ND |

ND= Not determined

# 3. Experimental

### *3.1. Instrumentation*

All melting points were determined on an electrothermal apparatus and are uncorrected. IR spectra were recorded (KBr discs) on a Shimadzu FT-IR 8201 PC spectrophotometer. $^{1}H$ and $^{13}C$ NMR spectra were recorded in CDCl3 and $(CD_3)_2SO$ solutions on Mercury-300 MHz spectrometer and chemical shifts are expressed in δ ppm units using TMS as an internal reference. Mass spectra were recorded on a GC-MS QP1000 EX Shimadzu. Elemental analyses were carried out at the Microanalytical Center of Cairo University. Hydrazonoyl halides [24, 25] and 3-(3-(4-methoxyphenyl)acryloyl)-2*H*-chromen-2-one [23] were prepared as previously reported.

### *3.2. Synthesis*

#### *3.2.1. Pyridine derivatives 2-6*.

A mixture of 3-(3-(4-methoxyphenyl)acryloyl)-2*H*-chromen-2-one (**1**) (1.53 g, 5 mmol), the appropriate malononitrile, ethyl acetoacetate, ethyl cyanoacetate (or cyanoacetamide), benzoylacetonitrile, cyanothioacetamide, and ammonium acetate (0.38 g, 5 mmol), was heated in acetic acid (10 mL) under reflux for 3 h. on cooling, the separated solid was filtered, washed with *water* and crystallized from the proper solvent to afford **2-6**, respectively.

***2-Amino-4-(4-methoxyphenyl)-6-(2-oxo-2H-chromen-3-yl)nicotinonitrile (2).*** Color: Brownish yellow Crystals from dilute ethanol Yield: 75%. M.p.:140-42°C. FT-IR (KBr, ν, $cm^{-1}$): 3344, 3220 ($NH_2$), 3082 (CH), 2191 (CN), 1724 (CO), 1625 (C=N), 1608 (C=C). $^{1}H$ NMR: (300 MHz, DMSO-*d*6, δ, ppm): 3.75 (s, 3H, $OCH_3$), 6.52 (s, br., 2H, $NH_2$), 7.28-7.81 (m, 9H, ArH's), 8.81 (s, 1H, coumarine H-4). MS (EI, *m/z* (%): 369 ($M^+$, 7), 356 (66), 327 (23), 252 (13), 238 (12), 225 (24), 188 (17), 155 (22), 143 (30), 127 (42), 114 (40), 100 (41), 88 (56), 76 (93). Anal. calcd. for $C_{22}H_{15}N_2O_4$: C, 71.54; H, 4.09; N, 11.38. Found: C, 71.44; H, 4.00; N, 11.27%.

***4-(4-Methoxyphenyl)-2-oxo-6-(2-oxo-2H-chromen-3-yl)-1,2-dihydropyridine-3-carbonitrile (3).*** Color: Yellow Crystals from dilute ethanol Yield: 90%. M.p.: 120-22 °C. FT-IR (KBr, ν, $cm^{-1}$): 3460 (NH), 3056 (CH), 2218 (CN), 1728 (CO), 1685 (CO), 1620 (C=N), 1589 (C=C). $^{1}H$ NMR: (300 MHz, DMSO-*d*6, δ, ppm): 3.82 (s, 3H, $OCH_3$), 6.98-7.72 (m, 10H, ArH's), 12.57 (s, 1H, NH). MS (EI, *m/z* (%): 370 ($M^+$, 10), 356 (95), 327 (42), 252 (21), 225 (39), 189 (49), 151 (39), 143 (52), 127 (64), 114 (48), 101 (34), 88 (67), 76 (100). Anal. calcd. for $C_{22}H_{14}N_2O_4$: C, 71.35; H, 3.81; N, 7.56. Found: C, 71.24; H, 3.97; N, 7.45%.

***4-(4-Methoxyphenyl)-6-(2-oxo-2H-chromen-3-yl)-2-phenylnicotinonitrile*** **(4).** Color: Pale yellow Crystals from dilute ethanol Yield: 85%. M.p.: 237-40 °C. FT-IR (KBr, ν, $cm^{-1}$): 3055, 2927, 2843 (CH), 2218 (CN), 1728 (CO), 1608 (C=N), 1570 (C=C). $^{1}H$ NMR: (300 MHz, DMSO-*d*6, δ, ppm): 3.75 (s, 3H, $OCH_3$), 7.25-7.48 (m, 12H, ArH's), 8.40-8.42 (d, 2H, *J* = 8Hz, ArH's), 8.84 (s, 1H, coumarine H-4). MS (EI, *m/z* (%)): 430 ($M^+$, 100), 416 (13), 400 (10), 387 (19), 356 (16), 329 (18), 242 (6), 214 (12), 165 (25). Anal. calcd. for $C_{28}H_{18}N_2O_3$: C, 78.13; H, 4.21; N, 6.51. Found: C, 78.00; H, 4.05; N, 6.43%.

***4-(4-Methoxyphenyl)-6-(2-oxo-2H-chromen-3-yl)-2-thioxo-1,2-dihydropyridine-3-carbonitrile*** **(5).** Color: Brownish red Crystals from ethanol Yield: 80%. M.p.: 180-81 °C. FT-IR (KBr, ν, $cm^{-1}$): 3410 (NH), 3056, 2923, 2854 (CH), 2216 (CN), 1712 (CO), 1610 (C=N), 1583 (C=C). $^{1}H$ NMR: (400 MHz, DMSO-*d*6, δ, ppm): 3.75 (s, 3H, $OCH_3$), 7.28-7.81 (m, 10H, ArH's and NH), 8.81 (s, 1H, coumarine H-4). Anal. calcd. for $C_{22}H_{14}N_2O_3S$: C, 68.38; H, 3.65; N, 7.25; S, 8.30. Found: C, 68.17; H, 3.55; N, 7.18; S, 8.11%.

***Ethyl 4-(4-methoxyphenyl)-2-methyl-6-(2-oxo-2H-chromen-3-yl)nicotinate (6).*** Color: Yellow Crystals from ethanol Yield: 50%. M.p.: 188-90 °C. FT-IR (KBr, ν, $cm^{-1}$): 1724, 6385 (CO's), 1620 (C=N), 1577 (C=C). $^{1}H$ NMR: (300 MHz, DMSO-*d*6, δ, ppm): 1.31 (t, 3H, *J* = 7.5 Hz, $CH_2\mathbf{CH_3}$), 2.63 (s, 3H, $CH_3$), 3.78 (s, 3H, $OCH_3$), 4.21 (q, 2H, *J* = 7.5 Hz, $\mathbf{CH_2}CH_3$), 6.97-7.77 (m, 9H, ArH's), 8.80 (s, 1H, coumarine H-4). MS (EI, *m/z* (%): 416 (76), 402 (30), 400 (51), 387 (80), 358 (80), 329 (83), 303 (21), 215 (40), 200 (21), 171 (54), 165 (100), 151 (37), 137 (22), 126 (22), 113 (46), 102 (49)88 (45), 76 (73), 63 (70). Anal. calcd. for $C_{25}H_{21}NO_5$: C, 72.28; H, 5.10; N, 3.37. Found: C, 72.15; H, 4.98 N, 3.20%.

#### *3.2.2. Pyridine derivatives 7a-c*

A mixture of 2-mercapto-4-(4-methoxyphenyl)-6-(2-oxo-2*H*-chromen-3-yl)nicotinonitrile **(5)** (1.93 g, 5 mmol), potassium hydroxide (0.28 g, 5 mmol) in *N, N*-dimethylformamide (10 mL) was stirred for 2 hrs. The appropriate of iodomethane, ethyl chloroacetate and 2-bromo-l-phenylethanone (5 mmol) was added while stirring. Stirring was continued for 2 hrs. The resulting solid was collected and crystallized to afford **7a-c**, respectively.

***4-(4-Methoxyphenyl)-2-(methylthio)-6-(2-oxo-2H-chromen-3-yl)nicotinonitrile (7a).*** Color: Black Crystals from ethanol Yield: 50%. M.p.: 210-12 °C. FT-IR (KBr, ν, $cm^{-1}$): 3057, 2922, 2856 (CH), 2214 (CN), 1710 (CO), 1612 (C=N), 1585 (C=C). $^1$H NMR: (300 MHz, DMSO-*d*6, δ, ppm): 2.82 (s, 3H, $SCH_3$), 3.75 (s, 3H, $OCH_3$), 7.20-7.58 (m, 9H, ArH's), 8.80 (s, 1H, coumarine H-4). Anal. calcd. for $C_{23}H_{16}N_2O_3S$: C, 68.98; H, 4.03; N, 7.00; S, 8.0. Found: C, 68.88; H, 4.00; N, 6.97: S, 8.11 %.

***Ethyl 2-(3-cyano-4-(4-methoxyphenyl)-6-(2-oxo-2H-chromen-3-yl)pyridin-2-yl)thio)acetate (7b).*** Color: Yellow Crystals from ethanol Yield: 70%. M.p.: 126-28 °C. FT-IR (KBr, ν, $cm^{-1}$): 3068, 2923, 2854 (CH), 2210 (CN), 1728, 1681 (CO's), 1612 (C=N), 1579 (C=C). $^1$H NMR: (300 MHz, DMSO-*d*6, δ, ppm): 1.25 (s, 3H, *J* = 7.5 Hz, $CH_2\mathbf{CH_3}$), 3.99 (q, 2H, *J* = 7.5 Hz, $\mathbf{CH_2}CH_3$), 3.75 (s, 3H, $OCH_3$), 4.21 (s, 2H, $CH_2$), 6.82-7.63 (m, 9H, ArH's), 8.78 (s, 1H, coumarine H-4). Anal. calcd. for $C_{26}H_{20}N_2O_5S$: C, 66.09; H, 4.27; N, 5.93; S, 6.79. Found: C, 66.00; H, 4.15; N, 5.87: S, 7.12 %.

***4-(4-Methoxyphenyl)-2-(2-oxo-2-phenylethyl)thio)-6-(2-oxo-2H-chromen-3-yl)nicotinonitrile (7c).*** Color: Brown. Crystals from ethanol Yield: 60%. M.p.: 146-48 °C. FT-IR (KBr, ν, $cm^{-1}$): 3068, 2923, 2854 (CH), 2210 (CN), 1686 (CO's), 1608 (C=N), 1579 (C=C). $^1$H NMR: (300 MHz, DMSO-*d*6, δ, ppm): 3.75 (s, 3H, $OCH_3$), 4.56 (s, 2H, $CH_2$), 7.28-7.70 (m, 14H, ArH's), 8.81 (s, 1H, coumarine H-4). Anal. calcd. for $C_{30}H_{20}N_2O_4S$: C, 71.41; H, 4.00; N, 5.55; S, 6.36. Found: C, 71.52; H, 4.17; N, 5.47; S, 6.51%.

***3.2.3. 3-(3-Amino-4-(4-methoxyphenyl)-1H-pyrazolo[3,4-b]pyridin-6-yl)-2H-chromen-2-one* (8)**. A mixture of **7a** (1.9 g, 5 mmol) and hydrazine hydrate (0.5 g, 10 mmol) in ethanol (10 mL) was heated under reflux for 5 hrs. The solid formed after cooling was collected and crystallized to afford **8** as Pale yellow color. Crystals from ethanol Yield: 85%. M.p.: 160-61 °C. FT-IR (KBr, ν, $cm^{-1}$): 3480, 3370 ($NH_2$) 2923, 2854 (CH), 1681 (CO), 1570 (C=C). $^1$H NMR: (300 MHz, DMSO-*d*6, δ, ppm): 3.79 (s, 3H, $OCH_3$), 6.88-7.38 (m, 9H, ArH's), 8.39 (s, br., 3H, NH, $NH_2$), 8.78 (s, 1H, coumarine H-4). Anal. calcd. for $C_{22}H_{16}N_4O_3$: C, 68.74; H, 4.20; N, 14.58. Found: C, 68.92; H, 3.98; N, 14.67%.

***3.2.4. 3-(10-(4-Methoxyphenyl)-2,4-dimethylpyrido[2',3':3,4]pyrazolo[1,5-a]pyrimidin-8-yl)-2H-chromen-2-one* (9)**. A mixture of **8** (1.9 g, 5 mmol) and acetylacetone (0.5 g, 5 mmol) in acetic acid (10 mL) was heated under reflux for 20 minutes. The solid formed after cooling was collected and crystallized to afford **9** as Color: Yellow Crystals from acetic acid Yield: 55%. M.p.: > 300 °C. FT-IR (KBr, ν, $cm^{-1}$): 3067, 2923, 2854 (CH), 1681 (CO), 1620 (C=N), 1585 (C=C). $^1$H NMR: (300 MHz, $CDCl_3$, δ, ppm): 2.37 (s, 3H, $CH_3$), 2.42 (s, 3H, $CH_3$), 3.75 (s, 3H, $OCH_3$), 6.35 (s, 1H, pyrimidine H-4), 7.28-7.51 (m, 9H, ArH's), 8.82 (s, 1H, coumarine H-4). Anal. calcd. for $C_{27}H_{20}N_4O_3$: C, 72.31; H, 4.49; N, 12.49. Found: C, 72.45; H, 4.37; N, 12.58%.

***3.2.5. 4-(4-Methoxyphenyl)-2-methyl-6-(2-oxo-2H-chromen-3-yl)nicotinohydrazide (10).***

A mixture of ethyl 4-(4-methoxyphenyl)-2-methyl-6-(2-oxo-2H-chromen-3-yl)nicotinate **(6)** (2.207 g, 5 mmol) and hydrazine hydrate (1g, 1 mL, 20 mmol) in ethanol (20 mL) was heated under reflux for 3 hr. The solid formed was collected and recrystallized from ethanol to afford **10** as yellow crystals from dilute ethanol Yield: 75%. M.p.: 116-18 °C. FT-IR (KBr, ν, $cm^{-1}$): 3420, 3370, 3193.(NH, $NH_2$) 3070, 2920, 2850 (CH), 1685 (CO), 1608 (C=N), 1566 (C=C). $^1$H NMR: (300 MHz, $CDCl_3$, δ, ppm): 2.78 (s, 3H, $CH_3$), 3.75 (s, 3H, $OCH_3$), 6.52 (s, br., 3H, NH, $NH_2$), 6.85-7.72 (m, 8H, ArH's), 7.75 (s, 1H, ArH), 8.81 (s, 1H, coumarine H-4). Anal. calcd. for $C_{23}H_{19}N_3O_4$: C, 68.82; H, 4.77; N, 10.47. Found: C, 69.00; H, 4.85; N, 10.65%.

***3.2.6. 1-(4-(4-Methoxyphenyl)-2-methyl-6-(2-oxo-2H-chromen-3-yl)nicotinoyl)-3-methyl-1H-pyrazol-5(4H)-one (11).***

Equimolar amount of **10** and ethyl acetoactate (5 mmol each) in ethanol was heated for 1 hr. The solid was collected and crystallized from ethanol to afford **11** as Orange Crystals. Yield: 75%. M.p.: 182-85 °C. FT-IR (KBr, ν, $cm^{-1}$): 3057, 2923, 2854 (CH), 1705, 1681 (CO's), 1610 (C=N), 1585 (C=C). $^1$H NMR: (300 MHz, DMSO-*d*6, δ, ppm): 2.11 (s, 3H, $CH_3$), 2.68 (s, 3H, $CH_3$), 3.41 (s, 2H, CH), 3.75 (s, 3H, $OCH_3$), 6.82-7.48 (m, 8H, ArH's),7.88 (s, 1H, ArH), 8.81 (s, 1H, coumarine H-4). Anal. calcd. for $C_{27}H_{21}N_3O_5$: C, 69.37; H, 4.53; N, 8.99. Found: C, 69.85; H, 4.35; N, 9.12%.

***3.2.7. 1-(4-(4-Methoxyphenyl)-2-methyl-6-(2-oxo-2H-chromen-3-yl)nicotinoyl)-3-methyl-4-(2-phenyl hydrazono)-1H-pyrazol-5(4H)-one (12).***

**Method A**: Dropwise addition of benzenediazonium chloride (5 mmol), which was prepared *via* reaction of aniline (0.46 g. 5 mmol), hydrochloric acid (3 mL, 6 M) and sodium nitrite (0.37 gm, 5 mmole) at 0-5°C to a mixture of **11** (2.35 g, 5 mmole) and sodium acetate (0.41 gm, 5 mmole) in ethanol

(30 mL) at 0-5°C, while stirring. The reaction mixture was stirred for 3 hrs. The resulting solid, was collected, washed with water and recrystallized from acetic acid to give **12**.

**Method B**: A mixture of **10** (2.05 g, 5 mmol) and ethyl 2-(2-phenylhydrazono)-3-oxobutanoate (**13**) (1.27 g, 5 mmol) in ethanol (20 mL) and catalytic amount of acetic acid (2 drops) was refluxed for 2 hrs. The resulting solid, so formed, was collected and recrystallized from acetic acid to give products identical in all aspects to those obtained from method A.

Color: red Crystals from ethanol Yield: 80%. M.p.: 120-22 °C. FT-IR (KBr, ν, $cm^{-1}$): 3372 (NH), 3056, 2923, 2854 (CH), 1702, 1685 (CO's), 1610 (C=N), 1584 (C=C). $^1$H NMR: (300 MHz, DMSO-*d*6, δ, ppm): 2.10 (s, 3H, $CH_3$), 2.71 (s, 3H, $CH_3$), 3.75 (s, 3H, $OCH_3$), 6.82-7.75 (m, 14H, ArH's), 7.87 (s, 1H, ArH), 8.81 (s, 1H, coumarine H-4). Anal. calcd. for $C_{33}H_{25}N_5O_5$: C, 69.34; H, 4.41; N, 12.25. Found: C, 69.44; H, 4.62; N, 12.41%.

***3.2.8. 4-(4-Methoxyphenyl)-2-methyl-6-(2-oxo-2H-chromen-3-yl)nicotinoyl azide (14).***
To a stirred solution of **10** (2.05 g, 5 mmol) in hydrochloric acid (15 mL, 6M) at 0-5°C, sodium nitrite was added portion wise tell effervescence ended. The reaction mixture was stirred for 1hr. The resulting solid, was collected, filtered, washed with water and recrystallized from acetic acid to give **14** as orange. Crystals from ethanol Yield: 85%. M.p.: 170-72 °C. FT-IR (KBr, ν, $cm^{-1}$): 3054, 2923, 2854 (CH), 2191 ($CN_3$), 1680 (CO), 1610 (C=N). $^1$H NMR: (300 MHz, DMSO-*d*6, δ, ppm): 2.79 (s, 3H, $CH_3$), 3.75 (s, 3H, $OCH_3$), 6.84-7.55 (m, 8H, ArH's), 7.89 (s, 1H, ArH), 8.81 (s, 1H, coumarine H-4). Anal. calcd. for $C_{23}H_{16}N_4O_4$: C, 66.99; H, 3.91; N, 13.59. Found: C, 67.08; H, 3.78; N, 13.62%.

***3.2.9. Urea derivatives 15a and 15b.***
A mixture of appropriate aniline or *p*-toluidine, (5 mmol) and azido compound **14** (2.06 g, 5 mmol) in dry dioxane (20 mL) was refluxed for 4 hrs. The resulting solid, so formed, was collected and recrystallized to give **15a** and **15b,** respectively.

***1-(4-(4-Methoxyphenyl)-2-methyl-6-(2-oxo-2H-chromen-3-yl)pyridin-3-yl)-3-phenylurea (15a)***. Color: Yellow Crystals from benzene Yield: 65%. M.p.: 150-52 °C. FT-IR (KBr, ν, $cm^{-1}$): 3271 (NH), 2931, 2842 (CH), 1681, 1658 (CO's), 1610 (C=N), 1581 (C=C). $^1$H NMR: (300 MHz, DMSO-*d*6, δ, ppm): 2.17 (s, 3H, $CH_3$), 3.85 (s, 3H, $OCH_3$), 6.69-7.99 (m, 16H, ArH's and NH), 8.81 (s, 1H, coumarine H-4). Anal. calcd. for $C_{29}H_{23}N_3O_4$: C, 72.94; H, 4.85; N, 8.80. Found: C, 73.00; H, 4.95; N, 8.99 %.

***1-(4-(4-Methoxyphenyl)-2-methyl-6-(2-oxo-2H-chromen-3-yl)pyridin-3-yl)-3-(p-tolyl)urea (15b).*** Color: Yellow Crystals from dioxane Yield: 60 %. M.p.: 170-71 °C. FT-IR (KBr, ν, $cm^{-1}$): 3278 (NH), 2923, 2854 (CH), 1681 (CO's), 1612 (C=N), 1570 (C=C). $^1$H NMR: (300 MHz, $CDCl_3$, δ, ppm): 2.11 (s, 3H, $CH_3$), 2.25 (s, 3H, $CH_3$), 3.75 (s, 3H, $OCH_3$), 6.69-8.05 (m, 15H, ArH's), 8.81 (s, 1H, coumarine H-4). Anal. calcd. for $C_{30}H_{25}N_3O_4$: C, 73.30; H, 5.13; N, 8.55. Found: C, 73.12; H, 5.00; N, 8.34%.

***3.2.10. 3-(4-(4-Methoxyphenyl)-2-methyl-6-(2-oxo-2H-chromen-3-yl)pyridin-3-yl)quinazoline-2,4(1H, 3H)-dione (16).***
A mixture of appropriate methyl anthranilate or anthranilic acid (5 mmol) and azido compound **14** (2.06 g, 5 mmol) in dry dioxane (20 mL) was refluxed for 4 hrs. The resulting solid, so formed, was collected and recrystallized from ethanol gave **16** as brown crystals. Yield: 65%. M.p.: 170-71 °C. FT-IR (KBr, ν, $cm^{-1}$): 3363(NH), 3070, 2923, 2850 (CH), 1670 (CO), 1608 (C=N), 1570 (C=C). $^1$H NMR: (300 MHz, DMSO-*d*6, δ, ppm): 2.51 (s, 3H, $CH_3$), 3.75 (s, 3H, $OCH_3$), 6.78-8.10 (m, 13H, ArH's), 8.81 (s, 1H, coumarine H-4), 10.59 (s, br., 1H, NH). Anal. calcd. for $C_{30}H_{21}N_3O_5$: C, 71.56; H, 4.20; N, 8.35. Found: C71.66; H, 4.11; N, 8.55%.

***3.2.11. Aryl carbamates 17a and 17b.***
A mixture of **14** (2.06 g, 5 mmol) and the appropriate phenol or picric acid (5 mmol) in dry benzene (20 mL) was refluxed for 4 hrs. The resulting solid, so formed, was collected and recrystallized from the proper solvent to give **17a** and **17b**, respectively.

***Phenyl-(4-(4-methoxyphenyl)-2-methyl-6-(2-oxo-2H-chromen-3-yl)pyridin-3-yl)carbamate (17a).***
Color: Pale brown Crystals from ethanol Yield: 70%. M.p.: 134-35 °C. FT-IR (KBr, ν, $cm^{-1}$): 3365 (NH), 3078, 2923, 2854 (CH), 1680 (CO), 1605 (C=N), 1562 (C=C). $^1$H NMR: (300 MHz, DMSO-*d*6, δ, ppm): 2.17 (s, 3H, $CH_3$), 3.85 (s, 3H, $OCH_3$), 5.15 (s, br., 1H, NH), 6.81-8.10 (m, 15H, ArH's and NH), 8.81 (s, 1H, coumarine H-4). Anal. calcd. for $C_{29}H_{22}N_2O_5$: C, 72.79; H, 4.63; N, 5.85. Found: C, 72.94; H, 4.82; N, 5.91%.

***2,4,5-Trinitrophenyl-(4-(4-methoxyphenyl)-2-methyl-6-(2-oxo-2H-chromen-3-yl)pyridin-3-yl) carbamate* (17b).** Color: Brown Crystals from ethanol Yield: 80%. M.p.: 235-36 °C. FT-IR (KBr, ν, $cm^{-1}$): 3350 (NH), 3065, 2923, 2854 (CH), 1681 (CO), 1612 (C=N), 1570 (C=C), 1553, 1372 ($NO_2$). $^1H$ NMR: (300 MHz, DMSO-*d*6, δ, ppm): 2.25 (s, 3H, $CH_3$), 3.75 (s, 3H, $OCH_3$), 7.28-7.81 (m, 12H, ArH's and NH), 8.81 (s, 1H, coumarine H-4). Anal. calcd. for $C_{29}H_{19}N_5O_{11}$: C, 56.78; H, 3.12; N, 11.42. Found: C, 56.91; H, 3.00; N, 11.27%.

### *3.2.12. 5-(4-Methoxyphenyl)-3-(2-oxo-2H-chromen-3-yl)-4,5-dihydro-1H-pyrazole-1-carbothioamide (18).*

A mixture of 3-(3-(4-methoxyphenyl)acryloyl)-2H-chromen-2-one (**1**) (1.53 g, 5 mmol), and thiosemicarbazide (0.46 g, 5 mmol) in ethanol (20 mL) was heated under refluxed for 3 h. The resulting solid was collected and recrystallized from ethanol. to give **18** as Yellow Crystals Yield: 70%. M.p.: 190-91 °C. FT-IR (KBr, ν, $cm^{-1}$): 3390, 3263, 3155 ($NH_2$), 3043, 2920, 2850 (CH), 1720 (CO), 1604 (C=N), 1500 (C=C). $^1H$ NMR: (300 MHz, DMSO-*d*6, δ, ppm): 2.78 (q, 1H, *J* = 8Hz, $CH_2$), 3.47 (q, 1H, *J* = 12Hz, $CH_2$), 3.74 (s, 3H, $OCH_3$), 5.81 (q, 1H, *J* = 8Hz, 12Hz, CH), 6.98-7.79 (m, 7H, ArH's), 7.85 (t, 1H, ArH), 8.12 (m, br., 3H, $NH_2$, AH). Anal. calcd. for $C_{20}H_{17}N_3O_3S$: C, 63.31; H, 4.52; N, 11.07; S, 8.45. Found: C, 63.22; H, 10.95; N, 8.32%.

### *3.2.13. 5-Phenylazothiazole derivatives 20a and 20b.*

**Method A**: A mixture of **18** (2.12 g, 5 mmol), the appropriate hydrazonoyl halides **19a** and **19b** (5 mmol) and triethylamine (0.75 mL, 5 mmol) in ethanol (20 mL) were boiled under reflux for 3 hr. The resulting solid was collected and recrystallized from acetic acid to give **20a** and **20b**, respectively.

**Method B**: Benzenediazonium chloride (5 mmol), which prepared from aniline (0.45 mL, 5 mmol), hydrochloric acid (6 N, 6 mL), and sodium nitrite (0.35g, 5 mmol), was added dropwise with stirring to a cold solution of a mixture of **21** (1.81 g, 5 mmol) and sodium acetate trihydrate (1.3 g, 10 mmol) in ethanol (50 ml). The resulting solid was collected and recrystallized to give product identical with **20b**.

***3-(5-(4-Methoxyphenyl)-1-(4-methyl-5-(phenyldiazenyl)thiazol-2-yl)-4,5-dihydro-1H-pyrazol-3-yl)-2H-chromen-2-one (20a)***. Color: Deep brown Crystals from ethanol Yield: 60%. M.p.: 110-12 °C. FT-IR (KBr, ν, $cm^{-1}$): 3065, 2939, 2881 (CH), 1680 (CO), 1608 (C=N), 1597 (C=C). $^1H$ NMR: (400 MHz, DMSO-*d*6, δ, ppm): 2.46 (s, 3H, $CH_3$), 3.25 (q, 1H, *J* = 8Hz, $CH_2$), 3.60 (q, 1H, *J* = 12Hz, *J* = 8Hz, 12Hz, $CH_2$), 3.75 (s, 3H, $OCH_3$), 5.47 (q, 1H, *J* = 8Hz, 12Hz, CH), 6.87-7.81 (m, 13H, ArH's), 8.81 (s, 1H, coumarine H-4). Anal. calcd. for $C_{29}H_{23}N_5O_3S$: C, 66.78; H, 4.44; N, 13.43; S, 6.15. Found: C, 66.95; H, 4.32; N, 13.31; S, 6.00 %.

***3-(5-(4-Methoxyphenyl)-1-(4-phenyl-5-(phenyldiazenyl)thiazol-2-yl)-4,5-dihydro-1H-pyrazol-3-yl)-2H-chromen-2-one (20b).*** Color: Red Crystals from Benzene Yield: 70%. M.p.: 178-80 °C. FT-IR (KBr, ν, $cm^{-1}$): 3062, 2920, 2850 (CH), 1724 (CO), 1602 (C=N), 1570 (C=C). $^1H$ NMR: (300 MHz, DMSO-*d*6, δ, ppm): 3.25 (q, 1H, *J* = 8Hz, $CH_2$), 3.60 (q, 1H, *J* = 12Hz, *J* = 8Hz, 12Hz, $CH_2$), 3.75 (s, 3H, $OCH_3$), 5.47 (q, 1H, *J* = 8Hz, 12Hz, CH), 6.87-7.81 (m, 18H, ArH's), 8.12 (s, 1H, coumarine H-4). MS (EI, *m/z* (%): 583 (4), 463 (100), 439 (17), 413 (40), 386 (15), 356 (40), 328 (18), 279 (37), 251 (45), 236 (27), 210 (37), 172 (73). Anal. calcd. for $C_{34}H_{25}N_5O_3S$: C, 69.97; H, 4.32; N, 12.00; S, 5.49. Found: C, 70.12; H, 4.51; N, 11.89; S, 5.32 %.

### *3.2.14. 3-(5-(4-Methoxyphenyl)-1-(4-phenylthiazol-2-yl)-4,5-dihydro-1H-pyrazol-3-yl)-2H-chromen-2-one (21).*

Equivalent amount of carbothioamide **18** (2.12 g, 5 mmol) and ω-bromoacetophenone (1 g, 5 mmol) and triethylamone (0.75 mL, 5 mmol) in ethanol (20 mL) were boiled under reflux for 2 hr. The resulting solid was collected and recrystallized from ethanol to give **21** as brown crystals Yield: 70%. M.p.: 146-47 °C. FT-IR (KBr, ν, $cm^{-1}$): 3062, 2920, 2850 (CH), 1716 (CO), 1604 (C=N), 1571 (C=C). $^1H$ NMR: (300 MHz, DMSO-*d*6, δ, ppm): 3.25 (q, 1H, *J* = 8Hz, $CH_2$), 3.60 (q, 1H, *J* = 12Hz, *J* = 8Hz, 12Hz, $CH_2$), 3.75 (s, 3H, $OCH_3$), 5.47 (q, 1H, *J* = 8Hz, 12Hz, CH), 6.87-7.81 (m, 14H, ArH's and thiazole H-5), 8.12 (s, 1H, coumarine H-4). Anal. calcd. for $C_{28}H_{21}N_3O_3S$: C, 70.13; H, 4.41; N, 8.76; S, 6.69. Found: C, 70.00; H, 4.23: N, 8.60: S, 6.82%.

### *3.2.15. 1,3,5-trisubstituted Pyridines 23a and 23b*

A mixture of 3-(3-(4-methoxyphenyl)acryloyl)-2H-chromen-2-one (**1**) (1.53 g, 5 mmol), the appropriate l-(2-oxo-2-substituted ethyl)pyridinium bromides **22a** and **22b** (5 mmol) and ammonium acetate (0.38 g, 5 mmol), was heated in acetic acid (10 mL) under reflux for 4 hrs. The resulting solid, which formed after cooling, was collected, washed with water and crystallized from the proper solvent to give **23a** and **23b**.

***3-(4-(4-Methoxyphenyl)-6-phenylpyridin-2-yl)-2H-chromen-2-one (23a).*** Color: Paige crystals from ethanol Yield: 90%. M.p.: 146-47°C. FT-IR (KBr, ν, $cm^{-1}$): 3056, 2920, 2850 (CH) 1724, 1678 (CO),

1608 (C=N), 1542 (C=C). $^1$H NMR: (300 MHz, DMSO-*d*6, δ, ppm): 3.80 (s, 3H, $OCH_3$), 6.55-7.89 (m, 15H, ArH's), 8.81 (s, 1H, coumarine H-4). MS (EI, *m/z* (%): 405 (038), 327 (3), 139 (5), 111 (14), 97 (35), 82 (61), 71 (47). Anal. calcd. for $C_{27}H_{19}NO_3$: C, 79.98; H, 4.72; N,3.45. Found: C, 80.11; H, 4.65; N, 3.55%.

***3-(4-(4-Methoxyphenyl)-6-(p-tolyl)pyridin-2-yl)-2H-chromen-2-one (23b).*** Color: Paige crystals from ethanol Yield: 90%. M.p.: 146-47 °C. FT-IR (KBr, ν, $cm^{-1}$): 3055, 2923, 2854 (CH), 1724, 1678 (CO), 1608 (C=N), 1542 (C=C). $^1$H NMR: (400 MHz, DMSO-*d*6, δ, ppm): 2.34 (s, 3H, $CH_3$), 3.75 (s, 3H, $OCH_3$), 6.89-8.11 (m, 14H, ArH's), 8.79 (s, 1H, coumarine H-4). Anal. calcd. for $C_{28}H_{21}NO_3$: C, 80.17; H, 5.05; N, 3.34. Found: C, 80.11; H, 4.95; N, 3.29%.

## 4. Antimicrobial activity:

Screening of antimicrobial activity was performed at a Microbiology Lab in Faculty of Agriculture, Al-Azhar University, Cairo, Egypt. Antimicrobial activity of the newly synthesized compounds was determined *in vitro* by standardized disc – agar diffusion method [26]. Cultures of two fungal species, namely, *Aspergillusfumigatus* and one yeast fungus; *Candida albicans*, as well as four bacterial species, namely, Gram- positive bacteria: *Staphylococcus aureus (ATCC 25923)* and *Bacillus subtilis (ATCC 6635),* Gram-negative bacteria: *Escherichia coli (ATCC 25922)* and *Salmonela typhimurium (ATCC 14028),* were used to investigate the antimicrobial activity of the newly synthesized compounds.

***Preparation of tested compound***

The tested compounds were dissolved in dimethyl formamide (DMF) solvent an in two concentrations; 100 and 50 mg/ml and then 10 µl of each preparation was drooped on disk of 6 mm in diameter and the concentrations became 1 and 0.5 mg/disk respectively. In case of insoluble compounds, the compounds were suspended in DMF and vortexes men processed.

***Testing for anti-bacterial and yeasts activity:***

Bacterial cultures were grown in nutrient broth medium at 30 °C. After 16h of growth microorganism, at a concentration of $10^8$ cells / mL, was inoculated on the surface of Muller-Hinton agar plates using sterile cotton swab. Subsequently, uniform size lifter paper disks (6 mm in diameter) were impregnated by equal volume (10 µl) from the specific concentration of dissolved compounds and carefully placed on surface of each inoculated plate. The plates were incubated in the upright position at 36°C for 24 hours. Three replicates were carried cut for each extract against each of the test organism. Simultaneously, addition of the respective solvent instead of dissolved compound was carried out as negative controls. After incubation, the diameters of the growth inhibition zones formed around the disc were measured with transparent ruler in millimeter, averaged and the mean values were tabulated. The results are depicted in Table 1.

***Testing for anti-fungal activity:***

Active inoculum for experiments "were prepared by transferring many loopfuls of spores from the stock cultures to test tubes of sterile distilled water (SDW) that were agitated and diluted with sterile distilled water to achieve optical density corresponding to 2.0 x $10^5$ spore/ml, inoculum of 0.1 % suspension was swabbed uniformly and the inoculum was allowed to dry for 5 minutes then the same procedure was followed as described above. The results are depicted in Table 1.

**Measurement of minimal inhibition concentration (MIC)**

MIC values of the synthesized compounds were determined using agar dilution technique (Andrews 2001). Each compound with high or intermediate antimicrobial effect shown in the disk diffusion test was further diluted with DMF to 25.6, 12.8, 6.4, 3.2, 1.6, 0.8, 0.4, 0.2, and 0.1 mg/ml respectively. Then 100 µl of each diluted compound and 100 µl of 108 cells/mL of specific organism was mixed with 10 ml of cooled (50 °C) melted Mueller-Hinton agar and then plated into 6 cm sterile Petri dish. The concentrations of the compounds became 256, 128, 64, 32, 16, 8, 4, 2, and 1 µg/ml respectively. Each dilution was prepared in duplication. Each concentration was prepared for 2 dishes. All plates were incubated at 33°C for 24 hours. MIC of each compound was measured from the plate with the lowest concentration with no visible growth of specific organism. The results are depicted in Table 2.

## 5. Conclusion

A convenient, efficient and rapid method was developed for synthesis of pyridines, pyrazolines and thiazolines. The structures of the newly synthesized compounds were confirmed by spectral data and elemental analyses. Also, the newly synthesized were screen towards some microorganism.

## 6. References

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