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Reactions with hydrazonoyl halides 66: Synthesis of some new 1,3,4-thiadiazoles, triazolino[4,3-*a*]pyrimidines and isoxazolo[3,4-*d*]pyridazines containing coumarin moiety

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ABSTRACT

2,3-Dihydro-1,3,4-thiadiazoles, triazolino[4,3-*a*]pyrimidines, isoxazoles and isoxazolo[3,4-*d*]pyridazines containing coumarin moities were synthesized from the reactions of methyl (or benzyl) carbodithioate, pyrimidine-2-thione and 3-(3-(dimethylamino)acryloyl)-2*H*-chromen-2-one derivatives with *C*-coumarinoyl-*N*-phenylhydrazonoyl bromide. The structures of all the newly synthesized compounds were confirmed by elemental analyses and spectral data.

1. Introduction

Coumarin derivatives constitute an important class of heterocyclic compounds with anticoagulant [1,2], anticoagulant rodenticide [3], insecticide [4] and antibacterial [5,6] pharmacolgical activities. On the other hand, 1,3,4-thiadiazole derivatives have become very useful compound in medicine, agriculture and in many fields of technology [7]. As an extension of our study [8,9-15] and a part of our program aiming at the synthesis of different heterocyclic derivatives, herein we report the convenient synthesis of 2,3-dihydro-1,3,4-thiadiazoles, triazolino[4,3-*a*]pyrimidines and isoxazolo[3,4-*d*]pyridazines containing coumarins moities.

2. Experimental

2.1. Instrumentation

All melting points were determined on an electrothermal apparatus and are uncorrected. IR spectra were recorded (KBr disc) on a Shimadzu FT-IR 8201 PC spectrophotometer. ^{1}H NMR spectra were recorded in $CDCl_3$ and $(CD_3)_2SO$ solutions on a Varian Gemini 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. Electronic absorption was recorded on Shimadzo 3101 PC spectrophotometer. Elemental analyses were carried out at the Microanalytical Center of Cairo University. Hydrazonoyl halides [16,17-19], 2-acetylbenzo[*f*]2H-chromen-3-one [20], 3-(2-bromoacetyl)-2*H*-chromen-2-one [21] and alkyl carbodi-thioates [22] were prepared as previously reported.

2.2. Synthesis of 3-{5-[(arylidene)-hydrazono]-4-phenyl-4,5-dihydro-[1,3,4]thiadiazole-2-carbonyl}-chromen-2-one (7a-j)

A mixture of the appropriate methyl (or benzyl) carbodithioate **3a-j** or **4a-j** (5 mmol), C-coumarin-3-oyl-*N*-phenylhydrazonoyl bromide, **1** (1.86 g, 5 mmoles), and triethylamine (0.75 mL, 5 mmol) in ethanol (20 mL) was stirred for 2 hrs at room temperature. The resulting solid was collected and recrystallized to give 2,3-dihydro-1,3,4-thiadiazoles, **7a-j** (Scheme 1).

Benzaldehyde [5-(2-oxo-2H-chromen-3-yl)-3-phenyl-1,3,4-thiadiazol-2(3H)-ylidene]hydrazone (7a): Yellow crystals from AcOH. Yield: 77%. M.p.: 192-194 °C. FT-IR (KBr, cm^{-1}): 3055 ν(CH), 1732, 1654 ν(CO's), 1624 ν(C=N), 1612 ν(C=N),1589 ν(C=C). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 7.42-7.46 (m, 7H, ArH's), 7.47-7.55 (m, 4H, ArH's), 7.76-7.94 (m, 3H, ArH's), 8.52 (s, 1H, ArH), 8.85 (s, 1H, CH=). MS (EI, *m/z* (%)): 453 (M+1, 17.84), 335 (11.45), 173 (38.35), 135 (12.08), 101 (14.50), 89 (100), 77 (28.84), 69 (10.08), 63 (14.38), 63 (14.38). UV (EtOH, λ_{max}, nm): 320, 419.5. Anal. calcd. for $C_{25}H_{16}N_4O_3S$ (452.48): C, 66.36; H, 3.56; N, 12.38. Found: C, 66.48; H, 3.67; N, 12.41%.

4-Methylbenzaldehyde [5-(2-oxo-2H-chromen-3-yl)-3-phenyl-1,3,4-thiadiazol-2(3H)-ylidene]hydrazone (**7b**): Orange crystals from dioxane. Yield: 78 %. M.p.: 244-248 °C. FT-IR (KBr, cm^{-1}): 3051, 2981 ν(CH), 1735, 1647 ν(CO's), 1604 ν(C=N), 1565 ν(C=C), 1365 ν(CH_3). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 2.34 (s, 3H, 4-$CH_3C_6H_4$), 7.28 (d, 2H, *J* = 8 Hz, ArH's), 7.44-7.94 (m, 11H, ArH's), 8.48 (s, 1H, ArH), 8.85 (s, 1H, CH=). MS (EI, *m/z* (%)): 465 (M-1, 43.3), 335 (33.3), 334 (13.3), 302 (20), 185 (20), 184 (16.7), 173 (53.3), 172 (46.7), 162 (26.7), 161 (13.3), 145 (20), 135 (30), 131 (26.7), 117 (13.3), 102

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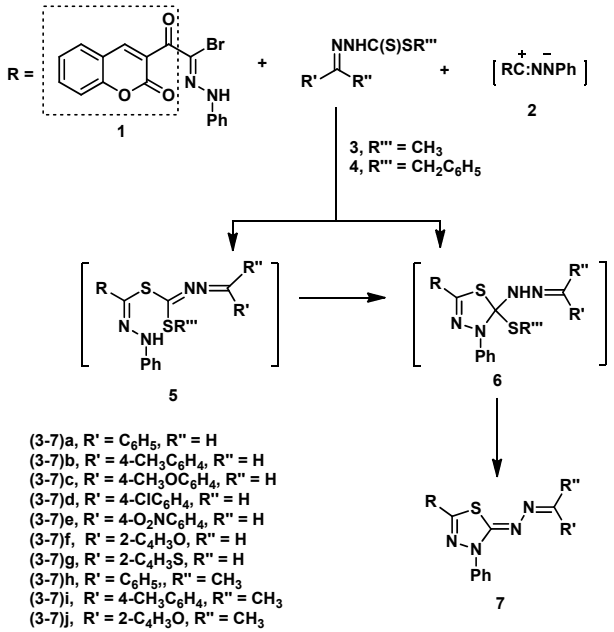


Scheme 1

(33.3), 101 (66.7), 100 (13.01), 99 (10.0), 91 (20), 90 (33.3), 89 (50), 78 (43.3), 77 (66.7), 75 (23.3), 74 (16.7), 73 (26.7), 72 (16.7), 83 (16.7). UV (EtOH, λ_{max}, nm): 322, 417. Anal. calcd. for $C_{26}H_{18}N_4O_3S$ (466.51): C, 66.94; H, 3.89; N, 12.01; S, 6.87. Found: C, 67.12; H, 3.98; N, 12.22; S, 6.78%.

4-Methoxylenzaldehyde [5-(2-oxo-2H-chromen-3-yl)-3-phenyl-1,3,4-thiadiazol-2(3H)-ylidene]hydrazone (**7c**): Red crystals from dioxane. Yield: 78.8 %. M.p.: 228-230 °C. FT-IR (KBr, cm^{-1}): 3042, 2981 ν(CH), 1736, 1652 ν(C=O), 1614 ν(C=N), 1589 ν(C=C), 1365 ν(CH_3). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 3.82 (s, 3H, 4-$CH_3OC_6H_4$), 7.14-7.77 (m, 13H, ArH's), 8.48 (s, 1H, ArH), 8.85 (s, 1H, CH=). MS (EI, *m/z* (%)): 484 (M+2, 9.76), 483 (M+1, 16.70), 482 (M^+, 30.50), 336 (10.34), 335 (4.49), 310 (3.92), 174 (13.64), 173 (91.22), 145 (18.93), 135 (21.06), 134 (18.13), 120 (97.75), 119 (15.68), 105 (21.26), 104 (19.38), 101 (36.26), 96 (32.41), 95 (20.85), 91 (100), 89 (63.94), 77 (75.45), 70 (10.65), 65 (16.29), 63 (33.03), 62 (18.08), 35 (25.86). UV (EtOH, λ_{max}, nm): 328, 423. Anal. calcd. for $C_{26}H_{18}N_4O_4S$ (482.51): C, 64.72; H, 3.76; N, 11.61; S, 6.65. Found: C, 64.64; H, 3.68; N, 11.51; S, 6.53%.

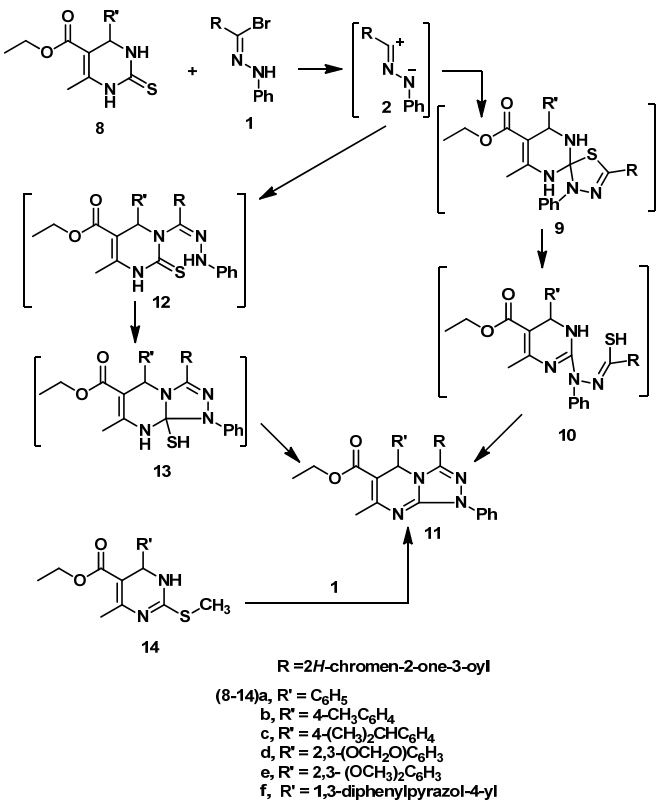
4-Chlorobenzaldehyde [5-(2-oxo-2H-chromen-3-yl)-3-phenyl-1,3,4-thiadiazol-2(3H)-ylidene]hydrazone (**7d**): Yellow crystals from dioxane. Yield: 79 %. M.p.: 226-228 °C. FT-IR (KBr, cm^{-1}): 3058 ν(CH), 1739, 1658 ν(CO's), 1616 ν(C=N), 1569 ν(C=C). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 7.39-7.57 (m, 7H, ArH's), 7.63-7.49 (m, 6H, ArH's), 8.52 (s, 1H, ArH), 8.85 (s, 1H, CH=). MS (EI, *m/z* (%)): 191 (9.8), 189 (43.9), 173 (43.9), 172 (26.8), 171 (12.2), 170 (8.5), 160 (13.9), 147 (13.4), 133 (8.5), 132 (18.3), 130 (36.6), 129 (18.3), 119 (13.4), 117 (17.1), 105 (31.7), 104 (26.8), 103 (13.4), 102 (24.4), 99 (12.2), 93 (11), 91 (24.4), 87 (40.2), 86 (24.4), 77 (100), 65 (23.2), 61 (51.2). UV (EtOH, λ_{max}, nm): 333.5, 417.5. Anal. calcd. for $C_{25}H_{15}ClN_4O_3S$ (486.93): C, 61.67; H, 3.10; N, 11.51; S, 6.59. Found: C, 61.81; H, 3.22; N, 11.74; S, 6.70%.

4-Nitrobenzaldehyde [5-(2-oxo-2H-chromen-3-yl)-3-phenyl-1,3,4-thiadiazol-2(3H)-ylidene]hydrazone (**7e**): Orange crystals from AcOH. Yield: 79 %. M.p.: 248-250 °C. FT-IR (KBr, cm^{-1}): 3074 ν(CH), 1732, 1654 ν(CO's), 1624 ν(C=N), 1589 ν(C=C), 1531, 1338 ν(NO_2). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 7.41-7.58 (m, 5H, ArH's), 7.76-7.94 (m, 5H, ArH's), 9.03 (d, 1H, *J* = 8Hz, ArH), 8.29 (d, 2H, *J* = 8 Hz, ArH's), 8.636 (s, 1H, ArH), 8.867 (s, 1H, CH=). MS (EI, *m/z* (%)): 499 (M+2, 1.5), 498 (M+1, 9.4), 497 (M^+, 26), 496 (M-1, 25), 335 (12.1), 334 (11.6), 173 (82), 135 (30.6), 134 (21.8), 101 (26), 90 (12.13), 89 (100), 88 (22.8), 77 (39.6), 76 (25.5), 65 (7.7), 63 (40.6), 62 (11.9). UV (EtOH, λ_{max}, nm): 276.5, 364.5, 422.5. Anal. calcd. for $C_{25}H_{15}N_5O_5S$ (497.48): C, 60.36; H, 3.04; N, 14.08; S, 6.45. Found: C, 60.42; H, 2.89; N, 14.14; S, 6.35%.

2-Furaldehyde [5-(2-furyl)-3-phenyl-1,3,4-thiadiazol-2(3H)-ylidene]hydrazone (**7f**): Red crystals from AcOH. Yield: 77 %. M.p.: 176-180 °C. FT-IR (KBr, cm^{-1}): 3074 ν(CH), 1732, 1654 ν(CO's), 1624 ν(C=N), 1589 ν(C=C). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 6.66 (s, 1H, furan H_3), 6.99 (s, 1H, ArH), 7.31-8.82 (m, 10H, ArH's and furan protons), 8.83 (s, 1H, ArH), 8.84 (s, 1H, CH=). MS (EI, *m/z* (%)): 443 (M+1, 70.12), 335 (66.23), 173 (100), 145 (13.11), 135 (22.33), 108 (42.06), 101 (33.83), 89 (33.20), 80 (66.92), 77 (39.17), 65 (27.7), 62 (13.60). UV (EtOH, λ_{max}, nm): 331.5, 418.5. Anal. calcd. for $C_{23}H_{14}N_4O_4S$ (442.45): C, 62.44; H, 3.19; N, 12.66; S, 7.25. Found: C, 62.35; H, 3.22; N, 12.79; S, 7.32%.

Thiophene-2-carbaldehyde [5-(2-furyl)-3-phenyl-1,3,4-thiadiazol-2(3H)-ylidene]-hydrazone (**7g**): Red crystals from AcOH. Yield: 78 %. M.p.: 196-198 °C. FT-IR (KBr, cm^{-1}): 3074 ν(CH), 1734, 1653 ν(CO's), 1614 ν(C=N), 1589 ν(C=C). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 7.39-8.00 (m, 13H, ArH's and thiophene protons), 8.84 (s, 1H, CH=). MS (EI, *m/z* (%)): 459 (30.13), 335 (18.12), 256 (12.36), 220 (10.48), 206 (12.44), 174 (42.64), 173 (55.84), 145 (15.55), 135 (32.31), 110 (38.39), 109 (27.32), 101 (23.22), 96 (100), 89 (62.23), 77 (55.15), 69 (61.86), 65 (22.43). UV (EtOH, λ_{max}, nm): 341, 424.5. Anal. calcd. for $C_{23}H_{14}N_4O_3S_2$ (458.5): C, 60.25; H, 3.08; N, 12.22; S, 13.99. Found: C, 60.32; H, 3.14; N, 12.45; S, 14.12%.

5-(2-Oxo-2H-chromen-3-yl)-3-phenyl-1,3,4-thiadiazol-2(3H)-one[(1-phenylethyl-idene]-hydrazone (**7h**): Orange crystals from AcOH. Yield: 78 %. M.p.: 192-194 °C. FT-IR (KBr, cm^{-1}): 3074 ν(CH), 1731, 1654 ν(CO's), 1614 ν(C=N), 1589 ν(C=C). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 2.34 (s, 3H, CH_3), 7.20-8.01 (m, 14H, ArH's), 8.35 (s, 1H, ArH). MS (EI, *m/z* (%)): 467 (10.0), 335 (11.68), 234 (9.62), 173 (6.76), 135 (16.24), 117 (10.51), 10 (90.24), 111 (15.55), 135 (32.31), 110 (38.39), 109 (27.32), 101 (23.22), 96 (100), 89 (25.46), 91 (13.77), 89 (20.36), 77 (61.46). UV (EtOH, λ_{max}, nm): 328.5, 421.5.



Scheme 2

Anal. calcd. for $C_{26}H_{18}N_4O_3S$ (466.51): C, 66.94; H, 3.89; N, 12.01; S, 6.87. Found: C, 67.15; H, 3.92; N, 12.14; S, 6.75%.

5-(2-Oxo-2H-chromen-3-yl)-3-phenyl-1,3,4-thiadiazol-2(3H)-one[(1-4-methyl-phenylethylidene]hydrazone (**7i**): Red crystals from AcOH. Yield: 79 %. M.p.: 208-210 °C. FT-IR (KBr, cm^{-1}): 3074 ν(CH), 1733, 1655 ν(CO's), 1604 ν(C=N), 1589 ν(C=C). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 2.36 (s, 3H, CH_3), 2.43 (s, 3H, CH_3) 7.27-8.00 (m, 13H, ArH's), 8.84 (s, 1H, ArH). MS (EI, *m/z* (%)): 481 (14.47), 173 (100), 145 (11.19), 135 (23.53), 118 (44.98), 115 (38.07), 101 (33.87), 94 (41.65), 77 (46.96), 65 (84.59), 55 (18.35). UV (EtOH, λ_{max}, nm): 321, 425.5. Anal. calcd. for $C_{27}H_{20}N_4O_3S$ (480.54): C, 67.48; H, 4.20; N, 11.66; S, 6.67. Found: C, 67.54; H, 4.31; N, 11.75; S, 6.72%.

5-(2-Oxo-2H-chromen-3-yl)-3-phenyl-1,3,4-thiadiazol-2(3H)-one[1-(2-furyl)-ethylidene]hydrazone (**7j**): Red crystals from AcOH. Yield: 79 %. M.p.: 180-182 °C. FT-IR (KBr, cm^{-1}): 3074 (CH), 1735, 1654 ν(CO's), 1612 ν(C=N), 1579 ν(C=C). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 2.35 (s, 3H, CH_3), 6.35 (s, 1H, furan H-3), 7.20-7.79 (m, 11H, ArH's), 8.44 (s, 1H, ArH). MS (EI, *m/z* (%)): 457 (1.0), 173 (5.72), 144 (6.09), 135 (11.89), 101 (12.61), 94 (62.93), 88 (13.20), 77 (15.14), 65 (42.36). UV (EtOH, λ_{max}, nm): 332, 429. Anal. calcd. for $C_{24}H_{16}N_4O_4S$ (456.47): C, 63.15; H, 3.53; N, 12.27; S, 7.02. Found: C, 63.23; H, 3.71; N, 12.15; S, 6.89%.

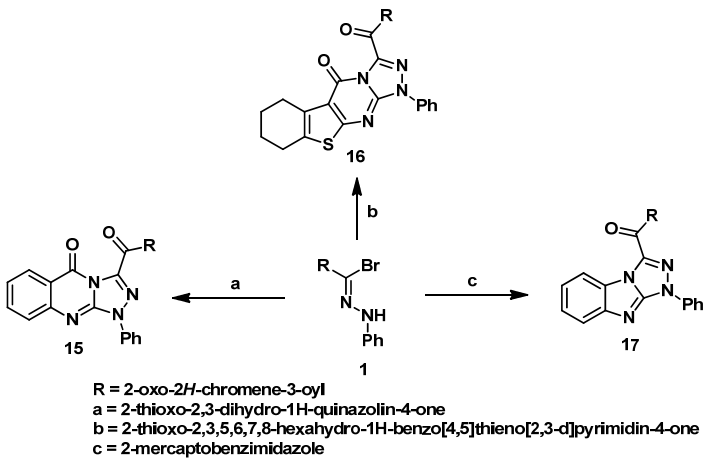
2.3. Synthesis of triazolino[4,3-a]pyrimidines (11a-f), [1,2,4]triazolo[3,4-b]quinazolin-5-one (15) 1H-benzo[4,5] imidazo[2,1-c][1,2,4]triazol-3-yl)-methanone (16) and 1,2,3a,10-tetraaza-cyclopenta[b]fluoren-4-one (17)

***Method A*:** A mixture of the hydrazonoyl bromide, **1**, (1.86 g, 5 mmol) and the appropriate of pyrimidine-2-thione derivatives [23] **8a-f**, 2-thioxo-2,3-dihydro-1*H*-quinazolin-4-one, 2-thioxo-2,3,5,6,7,8-hexahydro-1*H*-benzo[4,5]thieno[2,3-*d*]-pyrimidin-4-one, or 2-mercaptobenzimidazole (5 mmol) in chloroform (20 mL) containing triethylamine (0.5 g (0.75 mL), 5 mmol) was refluxed for 20 h. Chloroform was evaporated under reduced pressure and the remaining solid was crystallized from the proper solvent to givel **11a-f**, and **15**-**17**, respectively (Scheme 2 and 3).

***Method B*:** A mixture of the appropriate hydrazonoyl bromide, **1** (1.68 g, 5 mmol), the appropriate of **14a-e** [22] (5 mmol), and sodium ethoxide (0.34 g, 5 mmol) in ethanol (20 mL) was refluxed for 3 hrs. The reaction mixture was cooled and the resulting solid was collected and crystallized from the proper solvent gave products identical in all aspects (m.p., mixed m.p., and spectra) with corresponding products obtained by Method A.

Ethyl 7-methyl-3-(2-oxo-2H-chromene-3-carbonyl)-1,5-diphenyl-1,5-dihydro-[1,2,4]triazolo[4,3-a]pyrimidine-6-carboxylate (**11a**): Brown crystals from AcOH. Yield: 82 %. M.p.: 250-252 °C. FT-IR (KBr, cm^{-1}): 3062, 2977 ν(CH), 1720 ν(CO), 1608 ν(C=N), 1550 ν(C=C), 1450 (CH_2), 1373 (CH_3). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 1.01 (t, J = 7.5 Hz, 3H, CH_2CH_3), 2.09 (s, 3H, CH_3), 4.11 (q, J = 7.5 Hz, 2H, CH_2CH_3), 5.4 (s, 1H, pyrimidine H-4), 6.91-7.73 (m, 15H, ArH). MS (EI, *m/z* (%)): 532 (0.37), 152 (5.71), 150 (15.39), 139 (12.68), 104 (18.11), 97 (27.38), 95 (17.47), 93 (16.42), 91 (19.60), 89 (14.97), 85 (23.06), 83 (36.06), 81 (34.82), 79 (27.56), 76 (93.30), 71 (57.99), 69 (57.88), 67 (36.52), 65 (24.19). UV (EtOH, λ_{max}, nm): 285.5, 591. Anal. calcd. for $C_{31}H_{24}N_4O5$ (532.55): C, 69.92; H, 4.54; N, 10.52. Found: C, 70.08; H, 4.45; N, 10.72%.

Ethyl 7-methyl-3-(2-oxo-2H-chromene-3-carbonyl)-5-phenyl-1-p-tolyl-1,5-dihydro-[1,2,4]triazolo[4,3-a]pyrimidine-6-carboxylate (**11b**): Brown crystals from dioxane. Yield: 83 %. M.p.: 226-230 °C. FT-IR (KBr, cm^{-1}): 3062, 2974 ν(CH), 1739 ν(CO), 1624 ν(C=N), 1558 ν(C=C), 1473 ν(CH_2), 1392 ν(CH_3).



Scheme 3

^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 1.24 (t, 3H, *J* = 7.5 Hz, CH_2CH_3), 2.18 (s, 3H, CH_3), 2.27 (s, 3H, CH_3), 4.11 (q, *J* = 7.5 Hz, 2H, CH_2CH_3), 5.4 (s, 1H, pyrimidine H-4), 7.27-7.73 (m, 11H, ArH), 8.16 (d, 2H, *J* = 8 Hz, ArH's), 8.38 (s, 1H, ArH). MS (EI, *m/z* (%)): 547 (M+1, 0.42), 546 (M^+, 0.85), 349 (30.49), 378 (29.28), 323 (32.21), 318 (34.14), 321 (22.04), 302 (15.88), 276 (27.92), 258 (31.48), 217 (14.90), 202 (8.15), 199 (12.47), 184 (14.37), 173 (13.22), 158 (23.38), 156 (17.00), 144 (33.18), 143 (61.35), 135 (11.99), 127 (35.70), 118 (74.32), 115 (63.66), 102 (10.23), 101 (24.67), 91 (100), 86 (59.45), 77 (95.66), 65 (62.31). UV (EtOH, λ_{max}, nm): 285.5, 606. Anal. calcd. for $C_{32}H_{26}N_4O_5$ (546.57): C, 70.32; H, 4.79; N, 10.25. Found: C, 70.21; H, 4.95; N, 10.41%.

Ethyl 5-(4-isopropyl-phenyl)-7-methyl-3-(2-oxo-2H-chromene-3-carbonyl)-1-phenyl-1,5-dihydro-[1,2,4]triazolo[4,3-a]pyrimidine-6-carboxylate (**11c**): Brown crystals from DMF. Yield: 83 %. M.p.: 292-294 °C. FT-IR (KBr, cm^{-1}): 3070, 2958 ν(CH), 1720 ν(CO), 1612 ν(C=N), 1550 ν(C=C), 1446 ν(CH_2), 1369 ν(CH_3). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 1.16 (t, *J* = 7.5 Hz, 3H, CH_2CH_3), 1.17 (d, 6H, $(CH_3)_2CH$), 2.18 (s, 3H, CH_3), 2.77 (sept., 1H, $(CH_3)_2CH$, 4.07 (q, *J* = 7.5 Hz, 2H, CH_2CH_3), 5.35 (s, 1H, pyrimidine H-4), 7.27-7.78 (m, 13H, ArH's), 8.10 (s, 1H, ArH). MS (EI, *m/z* (%)): 575 (0.44), 505 (11.06), 431 (13.85), 378 (24.96), 377 (38.97), 347 (66.21), 332 (31.61), 330 (71.78), 304 (100), 289 (68.99), 287 (12.07), 260 (12.14), 257 (52.73), 244 (24.82), 229 (26.91), 217 (15.89), 211 (18.07), 199 (12.42), 184 (24.28), 179 (16.04), 143 (59.71), 135 (19.86), 128 (55.56), 118 (40.82), 114 (24.23), 102 (31.85), 91 (43.57), 85 (11.20), 76 (33.72). UV (EtOH, λ_{max}, nm): 286.5, 622. Anal. calcd. for $C_{35}H_{30}N_4O_5$ (574.22): C, 71.07; H, 5.26; N, 9.75. Found: C, 71.15; H, 5.34; N, 9.89%.

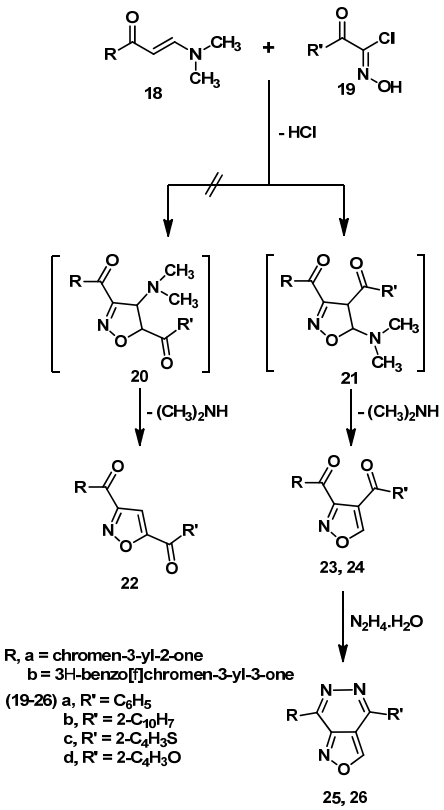
Ethyl 5-benzo[1,3]dioxol-4-yl-7-methyl-3-(2-oxo-2H-chromene-3-carbonyl)-1-phenyl-1,5-dihydro-[1,2,4]triazolo[4,3-a]pyrimidine-6-carboxylate (**11d**): Brown crystals from DMF. Yield: 83 %. M.p.: 190-192 °C. FT-IR (KBr, cm^{-1}): 3070, 2900 ν(CH), 1712 ν(CO), 1608 ν(C=N), 1566 ν(C=C), 1442 ν(CH_2), 1373 ν(CH_3). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 1.12 (t, *J* = 7.5 Hz, 3H, CH_2CH_3), 2.25 (s, 3H, CH_3), 4.07 (q, *J* = 7.5 Hz, 2H, CH_2CH_3), 5.35 (s, 1H, pyrimidine H-4), 5.96 (s, 2H, OCH_2O), 7.15-7.37 (m, 13H, ArH). MS (EI, *m/z* (%)): 576 (M^+, 0.35), 377 (5.71), 146 (5.07), 145 (6.52), 144 (5.41), 143 (6.22), 118 (25.56), 115 (29.93), 101 (21.92), 92 (15.70), 91 (36.58), 88 (41.63), 86 (16.65), 76 (100), 69 (16.67), 66 (14.44), 65 (26.24), 63 (62.04). UV (EtOH, λ_{max}, nm): 286.5, 510, 621.5. Anal. calcd. for $C_{32}H_{24}N_4O_7$ (576.56): C, 66.66; H, 4.20; N, 9.72. Found: C, 66.75; H, 4.18; N, 9.89%.

Ethyl 5-(2,3-dimethoxy-phenyl)-7-methyl-3-(2-oxo-2H-chromene-3-carbonyl)-1-phenyl-1,5-dihydro-[1,2,4]triazolo[4,3-a]pyrimidine-6-carboxylate (**11e**): Brown crystals from DMF. Yield: 83 %. M.p.: 160-162 °C. FT-IR (KBr, cm^{-1}): 3070, 2935 ν(CH), 1712 ν(CO), 1608 ν(C=N), 1566 ν(C=C), 1485 ν(CH_2), 1369 ν(CH_3). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 1.16 (t, *J* = 7.5 Hz, 3H, CH_2CH_3), 2.09 (s, 3H, CH_3), 3.85 (s, 3H, OCH_3), 3.91 (s, 3H, OCH_3), 4.13 (q, *J* = 7.5 Hz, 2H, CH_2CH_3), 5.35 (s, 1H, pyrimidine H-4), 7.15-7.37 (m, 13H, ArH's). MS (EI, *m/z* (%)): 593 (M^+, 0.87), 396 (37.70), 394 (17.31), 380 (9.92), 364 (21.94), 362 (40.49), 322 (16.86), 321 (100), 304 (20.39), 302 (25.91), 261 (17.30), 258 (29.58), 233 (14.37), 184 (18.65), 150 (13.17), 144 (21.83), 134 (10.04), 117 (26.85), 102 (18.78), 91 (30.79), 76 (22.79). UV (EtOH, λ_{max}, nm): 281.5, 598.5. Anal. calcd. for $C_{33}H_{28}N_4O_7$ (592.6): C, 66.88; H, 4.76; N, 9.45. Found: C, 66.98; H, 4.57; N, 9.61%.

Ethyl 5-(1,3-diphenyl-1H-pyrazol-4-yl)-7-methyl-3-(2-oxo-2H-chromene-3-carbonyl)-1-phenyl-1,5-dihydro-[1,2,4]triazolo [4,3-a]pyrimidine-6-carboxylate (**11f**): Brown crystals from AcOH. Yield: 85 %. M.p.: 160-162 °C. FT-IR (KBr, cm^{-1}): 3070, 2935 ν(CH), 1712 ν(CO), 1608 ν(C=N), 1566 ν(C=C), 1485 ν(CH_2), 1369 ν(CH_3). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 1.16 (t, *J* = 7.5 Hz, 3H, CH_2CH_3), 2.09 (s, 3H, CH_3), 4.13 (q, *J* = 7.5 Hz, 2H, CH_2CH_3), 5.35 (s, 1H, pyrimidine H-4), 7.15-7.37 (m, 21H, ArH's and pyrazole H-5). MS (EI, *m/z* (%)): 674 (M-1, 3.03), 478 (11.05), 478 (25.23), 476 (19.05), 403 (20.79), 402 (11.20), 119 (11.07), 104 (14.13), 103 (7.67), 102 (5.99), 78 (10.28), 77 (100). UV (EtOH, λ_{max}, nm): 283. Anal. calcd. for $C_{40}H_{30}N_6O_5$ (674.7): C, 71.21; H, 4.48; N, 12.46. Found: C, 71.34; H, 4.51; N, 12.64%.

3-(2-Oxo-2H-chromene-3-carbonyl)-1-phenyl-1H-[1,2,4] triazolo[3,4-b]quinazolin-5-one (**15**): Brown crystals from AcOH. Yield: 79 %. M.p.: 150-152 °C. FT-IR (KBr, cm^{-1}): 3070 ν(CH), 1701, 1666 ν(CO's), 1608 ν(C=N), 1566 ν(C=C), 1485 ν(CH_2), 1369 ν(CH_3). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 6.90-7.83 (m, 10H, ArH), 8.10-8.14 (m, 2H, ArH's), 8.30-8.35 (m, 2H, ArH's). MS (EI, *m/z* (%)): 435 (M+1, 1.09), 254 (10.98), 237 (100), 120 (19.54), 119 (28.44), 92 (25.40), 90 (27.49), 77 (20.04), 63 (40.77). UV (EtOH, λ_{max}, nm): 289.5, 467.5. Anal. calcd. for $C_{25}H_{14}N_4O_4$ (434.4): C, 69.12; H, 3.25; N, 12.90. Found: C, 69.23; H, 3.41; N, 13.11%.

3-(2-Oxo-2H-chromene-3-carbonyl)-1-phenyl-5,6,7,8-tetra hydro-1H-9-thia-1,2,3a,10-tetraaza-cyclopenta[b]fluoren-4-one (**16**): Brown crystals from EtOH. Yield: 75 %. M.p.: 156-158 °C. FT-IR (KBr, cm^{-1}): 3070, 2935 ν(CH), 1712 ν(CO), 1608 ν(C=N), 1566 ν(C=C), 1485 ν(CH_2), 1369 ν(CH_3). ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm): 1.61-1.64 (m, 4H, $2CH_2$), 2.80-2.98 (m, 4H, $2CH_2$), 7.17-7.24 (m, 2H, ArH's), 7.37-7.43 (m, 3H, ArH's), 7.54 (d, 1H, *J* = 8 Hz, ArH), 7.73-7.77 (m, 1H, ArH's), 8.10-8.14 (m,



Scheme 4

2H, ArH's), 8.39 (d, 1H, *J* = 8 Hz, ArH). MS (EI, *m/z* (%)): 491 (M-2, 0.15), 225 (38.17), 287 (3.88), 267 (21.68), 179 (100), 151 (67.92), 135 (23.01), 125 (22.52), 123 (25.74), 120 (33.78), 115 (23.92), 108 (10.40), 104 (10.83), 100 (25.17), 96 (29.64), 93 (11.35), 90 (51.03), 85 (31.84), 83 (11.15), 80.60 (14.36), 78 (34.29), 76 (89.18), 71 (10.96), 65 (53.62). UV (EtOH, λ_{max}, nm): 320.5, 468. Anal. calcd. for $C_{27}H_{18}N_4O_4S$ (494.52): C, 65.58; H, 3.67; N, 11.33; S, 6.48. Found: C, 65.73; H, 3.71; N, 11.45; S, 6.60%.

3-(1-Phenyl-1H-benzo[4,5]imidazo[2,1-c][1,2,4]triazole-3-carbonyl)-chromen-2-one (**17**): Dark brown crystals from AcOH. Yield: 77 %. M.p.: 242-244 °C. FT-IR (KBr, cm^{-1}): 3055, 2923 ν(CH), 1747 ν(CO), 1604 ν(C=N), 1566 ν(C=C), 1438 ν(CH_2), 1373 ν(CH_3). ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm): 7.31-8.34 (m, 11 H, ArH's), 8.10-8.14 (m, 2H, ArH's), 8.39 (d, 1H, *J* = 8 Hz, ArH). MS (EI, *m/z* (%)): 408 (M+2, 11.02), 357 (13.32), 301 (8.31), 227 (17.58), 177 (12.20), 174 (11.13), 151 (10.19), 142 (13.83), 139 (14.59), 137 (10.60), 120 (15.27), 117 (12.60), 116 (16.61), 115 (10.18), 105 (15.34), 103 (13.38), 102 (13.81), 101 (13.85), 99 (10.92), 94 (10.95), 92 (14.19), 91 (26.22), 88 (25.19), 82 (29.89), 78 (30.40), 77 (45.78), 76 (98.26), 75 (37.03), 74 (20.66), 73 (15.95), 69 (39.71), 65 (57.38), 63 (80.72). UV (EtOH, λ_{max}, nm): 236.5, 302, 464. Anal. calcd. for $C_{24}H_{14}N_4O_3$ (406.39): C, 70.93; H, 3.47; N, 13.79. Found: C, 71.12; H, 3.53; N, 13.97%.

2.4. Synthesis of isoxazoles (23a-d) and (25a-d)

Method A: Triethylamine (0.5 g (0.75 mL), 5 mmol) was added dropwise to equimolar a mount of **18a** (or **18b**) and the appropriate hydroximoyl chloride [25,26-28] **19a-d** (5 mmol, each) in dry toluene (20 mL) while stirring. The reaction mixture was stirred for 6 hrs.; evaporate the solvent and then triturated with petroleum ether (40-60 °C). The resulting solid was collected and crystallized gave **23a-d** and **25a-d**, respectively (Scheme 4).

Method B: Equimolar a mount of **18a** (or **18b**) and the appropriate hydroximoyl chloride **19a-d** (5 mmol, each) in dry toluene (20 mL) were heated under reflux for 18 h. The reaction mixture was filtered off and the filtrate was evaporated and triturated with petroleum ether (40-60 °C). The resulting solid was collected and crystallized to give products identical in all aspects (mp. mixed mp. and spectra) with **23a-d**.

3-(3-Benzoylisoxazole-4-carbonyl)-chromen-2-one (**23a**): Brown crystals from AcOH. Yield: 81 %. M.p.: 170-172 °C. FT-IR (KBr, cm^{-1}): 3070 ν(CH), 1724, 1678 ν(CO's), 1608 ν(C=N), 1562 ν(C=C). ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm): 7.33-8.64 (m, 7H, ArH's), 8.60-8.62 (d, 3H, *J* = 8 Hz, ArH's), 8.97 (s, 1H, isoxazole H5). MS (EI, *m/z* (%)): 345 (M^+, 4.45), 344 (M-1, 76.57), 340 (58.62), 173 (12.88), 163 (8.30), 150 (7.89), 142 (6.24), 115 (11.04), 105 (58.81), 102 (10.80), 101 (15.22), 100 (5.78), 92 (12.16), 88.60 (34.60), 87 (19.94), 77 (85.96), 74 (40.64), 62 (64.76). UV (EtOH, λ_{max}, nm): 278.5, 296.5, 349.5. Anal. calcd. for $C_{20}H_{11}NO_5$ (345.31): C, 69.57; H, 3.21; N, 4.06. Found: C, 69.74; H, 3.32; N, 4.11%.

3-[3-(Naphtha-2-oyl)-isoxazole-4-carbonyl]-chromen-2-one (**23b**): Deep brown crystals from AcOH. Yield: 83 %. M.p.: 184-186 °C. IR (KBr): 3058 ν(CH), 1724, 1678 ν(CO's), 1608 ν(C=N), 1570 ν(C=C). ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm): 7.33-8.79 (m, 12H, ArH's), 8.97 (s, 1H, isoxazole H-5). MS (EI, *m/z* (%)): 395 (M^+, 0.22), 356 (51.65), 329 (33.91), 271 (5.00), 243 (5.11), 155 (29.45), 127 (100), 113 (15.27), 75 (10.19). UV (EtOH, λ_{max}, nm): 288.5, 351.5. Anal. calcd. for $C_{24}H_{13}NO_5$ (395.36): C, 72.91; H, 3.31; N, 3.54. Found: C, 73.12; H, 3.54; N, 3.33%.

3-[3-(Thieno-2-oyll)-isoxazole-4-carbonyl]-chromen-2-one (**23c**): Deep brown crystals from AcOH. Yield: 83 %. M.p.: 164-166 °C. FT-IR (KBr, cm^{-1}): 3058 ν(CH), 1724, 1678 ν(CO's), 1608 ν(C=N), 1570 ν(C=C). ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm):

7.18-8.17 (m, 7H, ArH's and thiophene protons), 8.56 (s, 1H, ArH), 8.99 (s, 1H, isoxazole H5). MS (EI, *m/z* (%)): 351 (M^+, 15.60), 128 (10.99), 113 (33.91), 111 (100), 101 (11.85), 88 (25.40), 82 (25.76), 62 (15.70). UV (EtOH, λ_{max}, nm): 304. Anal. calcd. for $C_{18}H_9NO_5S$ (351.33): C, 61.53; H, 2.58; N, 3.99; S, 9.13. Found: C, 61.53; H, 2.58; N, 3.99; S, 9.13%.

3-[3-(Furan-2-carbonyl)-isoxazole-4-carbonyl]-chromen-2-one (**23d**): Brown crystals from AcOH. Yield: 80 %. M.p.: 208-210 °C. FT-IR (KBr, cm^{-1}): 3058 ν(CH), 1715, 1651 ν(CO's), 1604 ν(C=N), 1570 ν(C=C). ^1H NMR (300 MHz, $CDCl_3$, δ, ppm): 6.62 (s, 1H, furan H-3), 7.18-8.17 (m, 6H, ArH's and furan protons), 8.56 (s, 1H, ArH), 8.99 (s, 1H, isoxazole H-5). UV (EtOH, λ_{max}, nm): 299. Anal. calcd. for $C_{18}H_9NO_6$ (335.27): C, 64.48; H, 2.71; N, 4.18. Found: C, 64.57; H, 2.68; N, 4.35%.

2-(3-Benzoyl-isoxazole-4-carbonyl)-benzo[f]chromen-3-one (**24a**): Yellow crystals from AcOH. Yield: 83 %. M.p.: 140-142 °C. FT-IR (KBr, cm^{-1}): 3093 ν(CH), 1720, 1662 ν(CO's), 1643 ν(C=N), 1596 ν(C=C). ^1H NMR (300 MHz, $CDCl_3$, δ, ppm): 7.28-8.00 (m, 8H, ArH's), 8.51-8.62 (m, 4H, ArH's), 8.99 (s, 1H, isoxazole H-5). MS (EI, *m/z* (%)): 396 (M^{+1}, 12.41), 177 (5.79), 151 (16.03), 139 (34.28), 105 (100), 77 (78.02). UV (EtOH, λ_{max}, nm): 259.5, 391. Anal. calcd. for $C_{24}H_{13}NO_5$ (395.36): C, 72.91; H, 3.31; N, 3.54. Found: C, 73.11; H, 3.42; N, 3.31%.

2-[3-(Naphthalene-2-carbonyl)-isoxazole-4-carbonyl]-benzo[f]chromen-3-one (**24b**): Dark brown crystals from AcOH. Yield: 87 %. M.p.: 204-206 °C. FT-IR (KBr, cm^{-1}): 3020 ν(CH), 1724, 1685 ν(CO's), 1624 ν(C=N), 1596 (C=C). ^1H NMR (300 MHz, DMSO-d_6, δ, ppm): 7.38-8.42 (m, 13H, ArH's), 8.65 (s, 1H, ArH), 9.04 (s, 1H, isoxazole H-5). MS (EI, *m/z* (%)): 445 (M^+, 0.12), 155 (26.57), 139 (10.42), 127 (100), 101 (10.28), 87 (5.47), 77 (14.33), 75 (15.32), 62 (12.68), 50 (12.55). UV (EtOH, λ_{max}, nm): 255, 296. Anal. calcd. for $C_{28}H_{15}NO_5$ (445.1): C, 75.50; H, 3.39; N, 3.14. Found: C, 75.37; H, 3.45; N, 3.28%.

2-{[3-(2-thienylcarbonyl)isoxazol-4-yl]carbonyl}-3H-benzo[f]chromen-3-one (**24c**): Yellow crystals from AcOH. Yield: 87 %. M.p.: 222-224 °C. FT-IR (KBr, cm^{-1}): 3089 ν(CH), 1716, 1647 ν(CO's), 1593 ν(C=C). ^1H NMR (300 MHz, DMSO-d_6, δ, ppm): 7.13-7.94 (m, 8H, ArH's), 8.51 (d, 1H, ArH), 8.65 (s, 1H, ArH), 9.04 (s, 1H, isoxazole H-5). MS (EI, *m/z* (%)): 404 (M^+, 100), 223 (18.33), 189 (22.07), 176 (23.51), 163 (10.97), 151 (53.98), 89 (17.09), 86 (18.93), 82 (52.65), 74 (12.16), 62 (13.35). UV (EtOH, λ_{max}, nm): 266, 392. Anal. calcd. for $C_{22}H_{11}NO_5S$ (401.04): C, 65.83; H, 2.76; N, 3.49; S, 7.99. Found: C, 65.75; H, 2.62; N, 3.51; S, 8.14%.

2-{[3-(2-furoyl)isoxazol-4-yl]carbonyl}-3H-benzo[f]chromen-3-one (**24d**): Yellow crystals from AcOH. Yield: 82 %. M.p.: 240-242 °C. FT-IR (KBr, cm^{-1}): 3097 ν(CH), 1716, 1654 ν(CO's), 1593 ν(C=C). ^1H NMR (300 MHz, DMSO-d_6, δ, ppm): 6.64 (s, 1H, furan H-3), 7.13-7.33 (m, 4H, ArH's), 7.94-7.97 (m, 3H, ArH's), 8.32 (d, 2H, *J* = 8 Hz), ArH), 9.04 (s, 1H, isoxazole H-5). MS (EI, *m/z* (%)): 385 (M^+, 5.7), 223 (13.0), 222 (9.1), 139 (10.6), 112 (15.2), 95 (100), 94 (20.8), 89 (17.09), 86 (18.93), 82 (52.65), 74 (12.16), 62 (13.35). UV (EtOH, λ_{max}, nm): 281.5, 291, 390.5. Anal. calcd. for $C_{22}H_{11}NO_6$ (385.33): C, 68.57; H, 2.88; N, 3.64. Found: C, 68.66; H, 3.10; N, 3.48%.

2.5. Synthesis of isoxazolo[3,4-d]pyridazines (25a-d) and (26a-d)

Equimolar a mount of each of the appropriate isoxazoles (**23a-d**, **24a-d**) (5 mmol) and hydrazine hydrate (1 mL, 99%) in ethanol (20 mL) was boiled under reflux for 2h. The resulting solid was collected and crystallized to give isoxazolo[3,4-*d*]pyridazines, **25a-d**, **26a-d** (Scheme 4).

3-(7-Phenyl-isoxazolo[3,4-d]pyridazin-4-yl)-chromen-2-one (**25a**): Beige crystals from EtOH. Yield: 85 %. M.p.: >300 °C. FT-IR (KBr, cm^{-1}): 3058 ν(CH), 1685 ν(CO), 1612 ν(C=N), 1566 ν(C=C). ^1H NMR (300 MHz, DMSO-d_6, δ, ppm): 7.27-7.56 (m, 7H, ArH's), 7.94 (d, 2H, *J* = 8 Hz, ArH's), 8.55 (s, 1H, isoxazole H-5), 875 (s, 1H, pyran H-4). MS (EI, *m/z* (%)): 342 (M+1, 0.12), 284 (23.73), 225 (22.25), 197 (48.30), 168 (24.92), 141 (37.45), 115 (100), 101 (24.34), 89 (21.91), 86 (20.97), 77 (13.59), 75 (30.23), 62 (29.28). UV (EtOH, λ_{max}, nm): 302, 335, 349. Anal. calcd. for $C_{20}H_{11}N_3O_3$ (341.32): C, 70.38; H, 3.25; N, 12.31. Found: C, 70.50; H, 3.42; N, 12.48%.

3-(7-Naphthalen-2-yl-isoxazolo[3,4-d]pyridazin-4-yl)-chromen-2-one (**25b**): Brown crystals from AcOH. Yield: 87 %. M.p.: 224-226 °C. FT-IR (KBr, cm^{-1}): 3058 ν(CH), 1685 ν(CO), 1612 ν(C=N), 1566 ν(C=C). ^1H NMR (300 MHz, DMSO-d_6, δ, ppm): 7.27-7.32 (m, 2H, ArH's), 7.45-7.61 (m, 4H, ArH's), 7.65-8.74 (m, 5H, ArH's), 8.12 (s, 1H, isoxazole H-5), 8.65 (s, 1H, pyran H-4). MS (EI, *m/z* (%)): 391 (M^+, 0.62), 253 (56.02), 225 (26.88), 197 (40.04), 168 (15.27), 141 (34.75), 115 (84.29), 100 (11.01), 98 (18.90), 91 (27.20), 89 (47.44), 87 (38.86), 83 (12.73), 77 (64.68), 65 (24.13), 62 (100). UV (EtOH, λ_{max}, nm): 286, 330, 353.5. Anal. calcd. for $C_{24}H_{13}N_3O_3$ (391.38): C, 73.65; H, 3.35; N, 10.74. Found: C, 73.51; H, 3.48; N, 10.68%.

3-[7-(2-thienyl)isoxazolo[3,4-d]pyridazin-4-yl]-2H-chromen-2-one (**25c**): Brown crystals from EtOH. Yield: 86 %. M.p.: 240-242 °C. FT-IR (KBr, cm^{-1}): 3058 ν(CH), 1681 ν(CO), 1612 ν(C=N), 1566 ν(C=C). ^1H NMR (300 MHz, DMSO-d_6, δ, ppm): 7.27-7.32 (m, 3H, ArH's), 7.55-7.62 (m, 2H, ArH's), 7.71-7.73 (d, 1H, *J* = 8 Hz, ArH's), 8.38 (s, 1H, thiophene H-3), 8.65 (s, 1H, isoxazole H-5), 8.78 (s, 1H, pyran H-4). MS (EI, *m/z* (%)): 347 (M^+, 0.89), 330 (11.55), 284 (24.53), 269 (13.53), 253 (71.95), 225 (63.57), 213 (10.26), 197 (33.75), 168 (14.73), 152 (40.57), 146 (14.99), 141 (30.43), 140 (44.78), 127 (32.00), 118 (18.96), 111 (49.49), 109 (18.92), 107 (21.97), 101 (34.64), 97 (35.83), 93 (34.62), 91 (32.52), 89 (39.72), 87 (37.03), 81 (34.84), 76 (42.42), 69 (28.07), 62 (89.59). UV (EtOH, λ_{max}, nm): 261, 335, 351. Anal. calcd. for $C_{18}H_9N_3O_3S$ (347.35): C, 62.24; H, 2.61; N, 12.10; S, 9.23. Found: C, 62.41; H, 2.74; N, 12.25; S, 9.18%.

3-[7-(2-furyl)isoxazolo[3,4-d]pyridazin-4-yl]-2H-chromen-2-one (**25d**): Beige crystals from EtOH. Yield: 85 %. M.p.: >300 °C. FT-IR (KBr, cm^{-1}): 3058 ν(CH), 1695 ν(CO), 1616 ν(C=N). ^1H NMR (300 MHz, DMSO-d_6, δ, ppm): 6.91 (s, 1H, furan H-3), 7.27-7.71 (m, 5H, ArH's), 8.92 (s, 1H, ArH), 9.12 (s, 1H, isoxazole H-5), 8.78 (s, 1H, pyran H-4). UV (EtOH, λ_{max}, nm): 280.5. Anal. calcd. for $C_{18}H_9N_3O_4$ (331.28): C, 65.26; H, 2.74; N, 12.68. Found: C, 65.42; H, 2.84; N, 12.75%.

2-(7-Phenylisoxazolo[3,4-d]pyridazin-4-yl)-7,10-dihydro-3H-benzo[f]chromen-3-one (**26a**): Yellowish green crystals from DMF. Yield: 87 %. M.p.: 292-294 °C. FT-IR (KBr, cm^{-1}): 3058 ν(CH), 1685 ν(CO), 1620 ν(C=N). ^1H NMR (300 MHz, DMSO-d_6, δ, ppm): 7.41-7.94 (m, 11H, ArH's), 8.25 (d, 1H, *J* = 8Hz, ArH), 8.55 (s, 1H, isoxazole H-5). MS (EI, *m/z* (%)): 392 (M^+, 0.11), 323 (7.66), 170 (47.61), 152 (7.25), 143 (13.51), 141 (17.94), 127 (29.56), 115 (100), 101 (6.85), 88 (21.20), 77 (6.16). UV (EtOH, λ_{max}, nm): 314, 357, 407. Anal. calcd. for $C_{24}H_{13}N_3O_3$ (391.38): C, 73.65; H, 3.35; N, 10.74. Found: C, 73.55; H, 3.52; N, 10.89%.

2-(7-Naphthylisoxazolo[3,4-d]pyridazin-4-yl)-7,10-dihydro-3H-benzo[f]chromen-3-one (**26b**): Brown crystals from DMF. Yield: 89 %. M.p.: 276-278 °C. FT-IR (KBr, cm^{-1}): 3058 ν(CH), 1628 ν(C=N). ^1H NMR (300 MHz, DMSO-d_6, δ, ppm): 7.41-8.35 (m, 13H, ArH's), 8.55 (s, 1H, isoxazole H-5), 8.78 (s, 1H, ArH). MS (EI, *m/z* (%)): 442 (M^+, 20.16), 380 (19.95), 168 (28.36), 140 (22.52), 127 (34.50), 119 (24.52), 114 (34.52), 111 (23.96), 89 (27.04), 82 (20.08), 79 (21.48), 77 (47.82), 76 (31.32), 75 (19.95), 74 (24.52), 63 (61.89), 62 (34.08), 57 (42.31). UV (EtOH, λ_{max}, nm): 273, 330, 404. Anal. calcd. for $C_{28}H_{15}N_3O_3$ (441.44): C, 76.18; H, 3.42; N, 9.52. Found: C, 76.23; H, 3.52; N, 9.78%.

2-[7-(2-thienyl)isoxazolo[3,4-d]pyridazin-4-yl]-7,10-dihydro-3H-benzo[f]chromen-3-one (**26c**): Beige crystals from DMF. Yield: 88 %. M.p.: 304-306 °C. FT-IR (KBr, cm^{-1}): 3058 ν(CH), 1628 ν(C=N). ^1H NMR (300 MHz, DMSO-d_6, δ, ppm): 7.32-7.85 (m, 8H, ArH's), 8.12 (d, 1H, *J* = 8Hz, ArH), 8.39 (s, 1H, thiophene H-3), 8.62 (s, 1H, isoxazole H-5). MS (EI, *m/z* (%)): 397 (M^+,

0.01), 183 (5.29), 170 (100), 154 (11.30), 152 (19.21), 127 (81.44), 101 (18.41), 88 (41.71), 77 (9.26), 75 (8.37), 65 (9.55), 63 (17.59). UV (EtOH, λ_{max}, nm): 327, 411. Anal. calcd. for $C_{22}H_{11}N_3O_3S$ (397.41): C, 66.49; H, 2.79; N, 10.57; S, 8.07. Found: C, 66.62; H, 2.85; N, 10.75; S, 7.85%.

2-[7-(2-furyl)isoxazolo[3,4-d]pyridazin-4-yl]-7,10-dihydro-3H-benzo[f]chromen-3-one (**26d**): Yellow crystals from DMF. Yield: 87 %. M.p.: > 300 °C; IR (KBr): 3058 ν(CH), 1628 ν(C=N). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 6.85 (s, 1H, furan H-3), 7.32-7.85 (m, 8H, ArH's), 8.12 (d, 1H, *J* = 8Hz, ArH), 8.62 (s, 1H, isoxazole H-5). MS (EI, *m/z* (%)): 381 (M^+, 0.01), 183 (5.29), 170 (100), 154 (11.30), 152 (19.21), 127 (81.44), 101 (18.41), 88 (41.71), 77 (9.26), 75 (8.37), 65 (9.55), 63 (17.59). UV (EtOH, λ_{max}, nm): 302, 313, 344, 356. Anal. calcd. for $C_{22}H_{11}N_3O_4$ (381.34): C, 69.29; H, 2.91; N, 11.02. Found: C, 69.42; H, 3.15; N, 10.89%.

3. Results and discussion

Methyl *N'*-(4-Methyl-benzylidene)-hydrazine carbodithioate (**3b**) reacted with 3-aza-2-bromo-1-(2-oxo(2H-chromen-3-yl)-3-(phenylamino)prop-2-en-1-one (**1**) to afford 3-{5-[(4-methyl-benzylidene)-hydrazono]-4-phenyl-4,5-dihydro-[1,3,4]-thiadiazole-2-carbonyl}-chromen-2-one (**7b**) (Scheme 1). Structure **7b** was confirmed by elemental analysis, spectra and alternative synthetic route. Thus, treatment of benzyl *N'*-(4-Methyl-benzylidene)-hydrazine carbodithioate (**4b**) with **1** gave a product identical in all aspects (M.p., mixed m.p. and spectra) with **7b**. The formation of **7b** is assumed to proceed *via* 1,3-addition of thiol tautomer of carbodithioate **3b** (or **4b)** to nitrilium imide **2** (generated in situ by treatment of **1** with triethylamine) can give **6a**, nucleophilic cyclization to yield **5b**. Alternatively, 1,3-cycloaddition of nitrilium imide **2** to the C=S of carbodithioate **3b** (or **4b)** can give **6b** directly, and then afforded **7b** by loss of alkyl mercaptan (Scheme 1). Analogously, treatment of **1** with the appropriate **3a, c-j** in ethanolic triethylamine gave thiadiazoline derivatives **7a, c-j**, respectively.

Also, treatment of **1** with the pyrimidine-2-thione **8b** in boiling chloroform gave triazolino[4,3-*a*]pyrimidines **11b** in a good yields (Scheme 2). Structure of **11b** was elucidated by elemental analysis, spectral data and alternative synthetic route. Thus, ^{1}H NMR spectrum of **11b** showed signals at δ: 2.24 (s, CH_3, 4-$CH_3C_6H_4$), 5.05 (s, 1H, pyrimidine H-4), 7.44-8.24 (m, 19H, ArH's). Its IR spectrum revealed bands at 1702 (CO ester), 1650 (CO conjugated) and 1615 (C=N). Compound **11b** was obtained from the reaction of ethyl 6-methy-2-methylthio-4-phenyl-3,4-dihydropyrimidine-5-carboxylate, **14b** with **1** in boiling sodium ethoxide solution. The mechanism outlined in Scheme 2 seems to be the most plausible pathway for the formation of **11** from the reaction of **1** with **8** or **14**.

1. 1,3-addition of the thiol tautomer **8** to the nitrilium imide **2** to give the thiohydrazonate ester **9** which undergoes nucleophilic cyclization to yield spiro compounds **10**. The latter ring open and cyclized to yield **11** by loss hydrogen sulfide; and
2. 1,3-cycloaddition of nitrilium imide **2** to C=S double bond of **8** to give directly **10** (Scheme 2). Attempts to isolate the thiohydrazonate ester **9** or intermidate **10** did not succeed even under mild conditions as they readily undergo *in situ* cyclization followed by elimination of hydrogen sulfide to give the final product **11** in Scheme 2.

Analogously, reactions of 2-thioxo-2,3-dihydro-1*H*-quinazolin-4-one [29], 2-thioxo-2,3,5,6,7,8-hexahydro-1*H*-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one [30], 2-mercaptobenzimidazole or with hydrazonoyl bromide **1** were carried out in refluxing chloroform in presence of TEA gave 3-(2-oxo-2*H*-chromene-3-carbonyl)-1-phenyl-1*H*-[1,2,4]triazolo[3,4-b]quinazolin-5-one **15**, 3-(2-oxo-2*H*-chromene-3-carbonyl)-1-phenyl-5,6,7,8-tetrahydro-1*H*-9-thia-1,2,3a,10-tetraaza-cyclopenta[*b*]fluoren-4-one, **16** and 3-(1-phenyl-1H-benzo[4,5]imidazo[2,1-c][1,2,4]triazole-3-carbonyl)-chromen-2-one, **17**, respectively (Scheme 3).

Finally, treatment of 3-(3-(dimethylamino)acryloyl)-2*H*-chromen-2-one (**18**) with 2-chloro-2-(hydroxyimino)-1-phenylethanone (**19a**) in dry toluene and presence of triethylamine at 0 °C afforded one isolable product identified as 3-(3-benzoyl-isoxazole-5-carbonyl)chromen-2-one (**22a**) or 3-(3-benzoyl-isoxazole-4-carbonyl)-chromen-2-one (23a) Scheme 4. Structure **23a** was elucidated by elemental analysis, spectra, alternative synthetic route and chemical transformation.

Formation of **23** can be explained via reaction of nitrile oxide, which formed in situ from the appropriate hydroximoyl chlorides **19** and triethylamine, with the appropriate **18** to afford cyclo adduct intermediate **20** or **21**, and then eliminate dimethylamine to give isoxazole as final product **22** or oxazole **23**.

The later was ruled out on the basis of the formation of isoxazolo[4,3-*d*] pyridazine 25. Other isoxazolo[4,3-*d*] pyridazines **25b-e** were obtained in a good yield from boiling the appropriate isoxazole **23a-e** with hydrazine in boiling ethanol. Structures **25b-e** were elucidated on the basis of elemental analysis and spectral data. Analogously, treatment of 2-(3-(dimethylamino)acryloyl)-3*H*-benzo[*f*]chromen-3-one (**18b**) with appropriate hydroximoyl chlorides **19a-e** gave isoazoles 24a-e, which it converted to isoxazolo[3,4-*d*]pyridazines **26a-e** (Scheme 4).

4. Conclusion

The 1,3,4-thiadiazoline, triazolo[4,3-a]pyrimidines, isoxazole and isoxazolo[3,4-d]pyridazine derivatives containing the coumarin moiety in a good yields were synthesized by reaction of hydrazonoyl halides and hydroximoyl chlorides with alkyl carbodithioates, pyrimidine-2-thiones and enaminones.

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