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SHORT COMMUNICATION

An unusual synthesis of 3-(2-(arylamino)thiazol-4-yl)-2*H*-chromen-2-ones from ethyl 2-(chloromethyl)-2-hydroxy-2*H*-chromene-3-carboxylate via benzopyran ring opening

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Abstract
An unusual and unexpected synthesis of 3-(2-(arylamino)thiazol-4-yl)-2*H*-chromen-2-ones has been observed by the reaction of ethyl 2-(chloromethyl)-2-hydroxy-2*H*-chromene-3-carboxylate with various arylthioureas in ethanol under mild reaction conditions with excellent yields. The ambiguity in the structure of the obtained products has been solved by recording its single-crystal X-ray analysis. This protocol has been found to be a novel approach for the preparation of title compounds via benzopyran ring opening. A systematic plausible mechanism has been proposed for the formation of the product. Also, an efficient one-pot three-component method has been demonstrated for the formation of title compounds starting from salicylaldehyde.

Keywords Coumarins · Ethyl 2-(chloromethyl)-2-hydroxy-2*H*-chromene-3-carboxylate · Arylthioureas · X-ray crystallography · 3-(2-(Arylamino)thiazol-4-yl)-2*H*-chromen-2-ones

Introduction

Coumarin and its related compounds have found to have significant therapeutic, agricultural and material chemistry importance which has been reviewed by us recently [1]. Coumarin and its derivatives exhibited potential biological activities such as antimicrobial [2], anti-HIV [3], antioxidant [4], anti-tubercular [5], anti-mutagenic [6] and antibiotic [7]. Coumarins are also found be active pharmacophores in various drugs.

Furthermore, thiazoles and its derivatives have been also found to show various therapeutic activities such as anti-HIV [8], anti-tumor [9], insulin releasing [10], anti-convulsant [11], neuroprotective agent [12] and antimicrobial [13] agents. Some of the commercially available thiazole-based drugs are listed in Fig. 1.

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Different approaches have been reported in the recent literature for the synthesis of thiazoles by making use of various substrates and reagents. A gist of some of the recent highlights for the thiazole synthesis is as follows. Sheldrake et al. reported the synthesis of 5-arylthiazoles by the treatment of N,N-diformylaminomethyl aryl ketones with phosphorus pentasulfide and triethylamine in chloroform [14]. Tang et al. reported the synthesis of thiazoles by a copper-catalyzed [3 + 1 + 1]-type condensation of oximes, anhydrides and potassium thiocyanate in toluene at 120 °C [15]. Lingaraju et al. reported a base-induced cyclization of active methylene isocyanides such as tosylmethyl isocyanide, ethyl isocyanoacetate and arylmethyl isocyanides with methyl arene- and hetarenecarbodithioates to give 4,5-disubstituted thiazoles [16]. Miura et al. reported the reaction of 1-sulfonyl-1,2,3-triazoles with thionoesters in the presence of a rhodium(II) catalyst providing 3-sulfonyl-4-thiazolines, which subsequently aromatize into the corresponding of 2,5-disubstituted thiazoles [17]. Chen et al. reported the palladium(II) acetate catalyzed highly selective synthesis of 4-substituted 2-aminothiazoles from vinyl azides and potassium thiocyanate, where iron(III) bromide promotes the formation of 4-substituted 5-thiocyano-2-aminothiazoles [18]. Tang et al. reported the synthesis of 4,5-disubstituted 2-aminothiazoles by a copper-catalyzed coupling of oxime

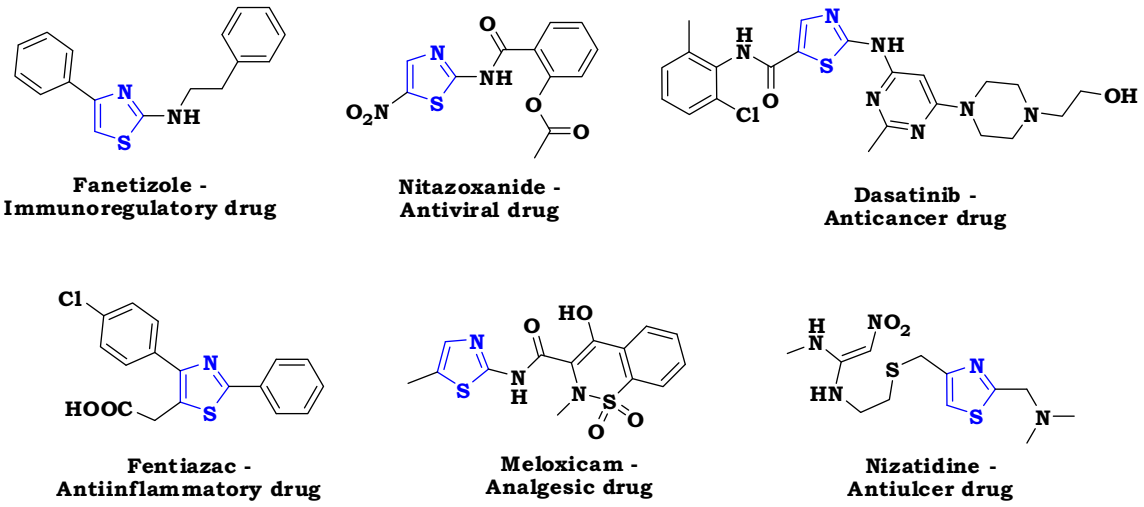
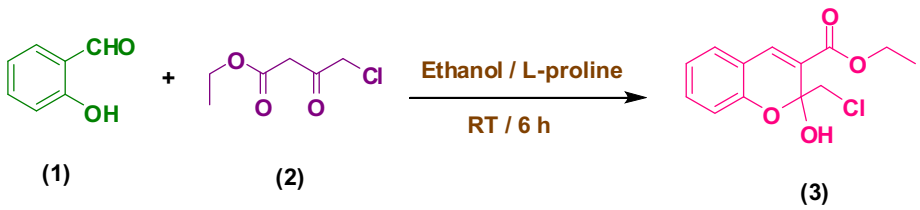


Fig. 1 Various commercially available thiazole-based drugs

Scheme 1 Synthesis of ethyl 2-(chloromethyl)-2-hydroxy-2H-chromene-3-carboxylate (**3**)



acetates with isothiocyanates under mild reaction conditions via copper-catalyzed N–O bond cleavage [19]. Castagnolo et al. reported a domino alkylation-cyclization reaction of propargyl bromides with thioureas and thio-pyrimidinones to give the 2-aminothiazoles [20]. Narender et al. outlined the preparation of 2-amino-4-arylthiazole-5-carboxylates and by α-halogenation of β-keto esters with *N*-bromosuccinimide, followed by cyclization with thiourea [21].

One of the most commonly used procedures for the synthesis of the thiazole ring that clubbed to coumarin is based on the reaction of 3-(2-bromoacetyl)-2*H*-chromen-2-one with thioureas. Siddiqui et al. reported the synthesis of thiazoles by treating 3-(2-bromoacetyl)-2*H*-chromen-2-one with thiourea and its derivatives in refluxing ethanol [22]. Rao et al. reported the tandem synthesis of 3-(2-(arylamino)thiazol-4-yl)-2*H*-chromen-2-ones by reacting 3-(2-bromoacetyl)-2*H*-chromen-2-ones with potassium thiocyanate for 1 h followed by further addition of arylamines at 60–65 °C for a period of 2 h [23]. Koti et al. reported the reaction between 3-(2-bromoacetyl)-2*H*-chromen-2-ones and substituted thiourea derivatives using ethanol as a solvent under reflux conditions for 12 h to give 3-(2-(arylamino)thiazol-4-yl)-2*H*-chromen-2-ones [24].

However, there is no report available for the preparation of 3-(2-(arylamino)thiazol-4-yl)-2*H*-chromen-2-ones by the reaction of ethyl 2-(chloromethyl)-2-hydroxy-2*H*-chromene-3-carboxylate with arylthioureas. As part of our ongoing research on synthesis of biologically important oxygen containing heterocyclic compounds, in particular, coumarins, this article describes an unexpected synthesis of 3-(2-(arylamino)thiazol-4-yl)-2*H*-chromen-2-ones via a benzopyran ring opening mechanism.

As shown in Scheme 1, reaction of salicylaldehyde (**1**) with ethyl-4-chloroacetoacetate (**2**) in ethanol containing catalytic amount of *L*-proline resulted in the formation of ethyl 2-(chloromethyl)-2-hydroxy-2*H*-chromene-3-carboxylate (**3**) which has been reported earlier in literature [25].

Reaction of ethyl 2-(chloromethyl)-2-hydroxy-2*H*-chromene-3-carboxylate (**3**) with 1-phenylthiourea (**4a**) in refluxing ethanol resulted in the formation of a compound which has been characterized on the basis of its spectral and analytical data. Thus, its IR (KBr) spectrum showed a strong, sharp peak at 1728 cm^{-1} due to a lactone C = O group and broad, medium peak in the range 3390–3430 cm^{-1} assignable to NH group. Its ^{1}H NMR (DMSO d_6/TMS) spectrum showed signals at δ 6.98 (d, 2H, Ar–**H**), 7.39–7.68 (complex, m, 6H, Ar–**H**), 7.72 (s, 1H, Ar–**H**), 7.96 (d, 1H, Ar–**H**), 8.67 (s, 1H, Ar–**H**), 10.15 (s, 1H, –N**H**). Its ^{13}C NMR (DMSO d_6/TMS) spectrum showed signals at δ 110.3, 116.3, 117.5, 119.7, 120.7, 121.9, 125.1, 129.4, 129.6, 132.1, 139.0, 141.4, 144.0, 152.7, 159.2, 162.9. Its HRMS showed the molecular ion ($M^+ + 1$) peak at *m/z* 321.0707 corresponding to its molecular weight of 320. Based on the above spectral and analytical data, there is an

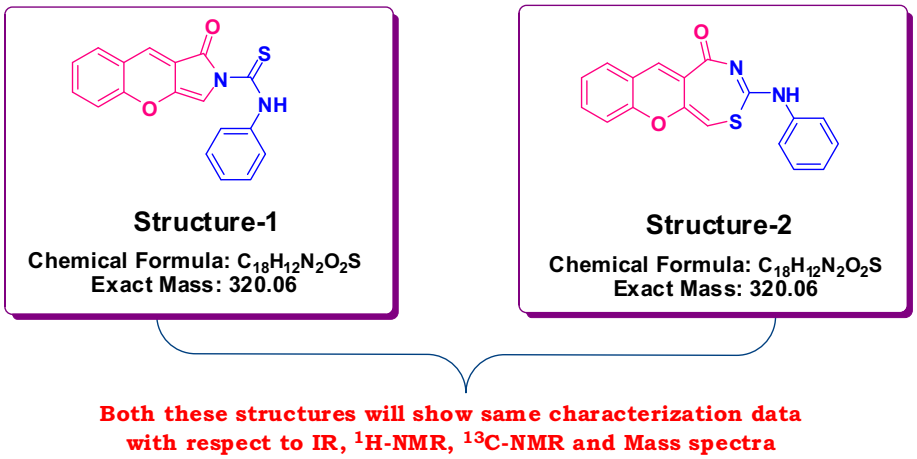


Fig. 2 Possible products for the reaction of **3** with 1-phenylthiourea (**4a**): an ambiguity

ambiguity in the structure of the product and we assumed there is possibility for the formation of two compounds and proposed the structures as shown in Fig. 2. Furthermore, in mechanistic way, structure 1 can be formed via an amide bond formation between ester group of **3** and amine from thioamide group of 1-phenylthiourea (**4a**) followed by internal cyclization and further dehydration to get a stabilized structure. Structure 2 can be possible by the reaction of 1-phenylthiourea (**4a**) in its thiol form with chloromethyl group of ethyl 2-(chloromethyl)-2-hydroxy-2*H*-chromene-3-carboxylate (**3**) to give a condensed compound followed by internal cyclization between ester group and amine from its thioamide group which further undergoes dehydration to obtain stability.

To resolve the ambiguity in the structure of the obtained product, we have crystallized the compound in a mixture of 1:1 chloroform and acetonitrile for several days and recorded its single-crystal X-ray crystallography (Fig. 3). Interestingly, the obtained structure kept us in still confusion. The structure is none of the above two possibilities but found to be as 3-(2-(phenylamino)thiazol-4-yl)-2*H*-chromen-2-one (**5a**) whose structure will also show same characterization data (Scheme 2).

The mechanism for this unusual conversion from **3** to thiazole skeleton (**5a**) was postulated to occur via the series of steps depicted in Scheme 3. To solve this mechanism, we have gone through the literature carefully and proposed a suitable mechanism which is quite closer to the ring opening of a quinoxaline-pyran system which was reported earlier [26]. In detail (Scheme 3), 1-phenylthiourea (**4a**) in its thiol form reacts with chloromethyl group of ethyl 2-(chloromethyl)-2-hydroxy-2*H*-chromene-3-carboxylate (**3**) to give a condensed compound **A** with a mole of hydrochloric acid which will undergo internal cyclization via a nucleophilic addition reaction to give an intermediate **B**. The latter will undergo benzopyran ring opening which is similar to ring opening of a quinoxaline-pyran system under acidic conditions to give an intermediate **C** which will undergo internal transesterification to give a stabilized structure, i.e., 3-(2-(phenylamino)thiazol-4-yl)-2*H*-chromen-2-one (**5a**).

With a view to optimize the reaction conditions for the formation of product in maximum yield, the reaction of **3** with 1-phenylthiourea (**4a**) was examined by treating equimolar amounts of the reactants in different solvents under reflux conditions to obtain **5a** (i.e., **5,** Ar = C_6H_5). Among all the conditions used, ethanol was found to be the best solvent for this synthesis in terms of reaction time and yield of the pure product formed without the use of column chromatography. Results of these studies are shown in Table 1.

Further, to evaluate the scope of this methodology, various arylthioureas (**4a–l**) have been taken and were treated with ethyl 2-(chloromethyl)-2-hydroxy-2*H*-chromene-3-carboxylate (**3**) in refluxing ethanol to give the desired products **(5a–l)** in good yields (Scheme 4).

Encouraged with the above results, having the optimization data in hand, it was thought of interest to prepare these compounds in a one-pot method and the best solvent i.e., ethanol as the solvent has been chosen. Thus, equimolar quantities of salicylaldehyde (**1**), ethyl-4-chloroacetoacetate (**2**), 1-phenylthiourea (**4a**) and catalytic amount of *L*-proline were reacted together in ethanol under refluxing conditions for 4–6 h. Interestingly, this reaction completed successfully to give the product **5a** in good yields (Scheme 5). Further, the scope of this reaction has been extended to various arylthiourea derivatives **(4a–l)** to obtain the title compounds **(5a–l)** in good to excellent yields.

The overall yield from the stepwise method for the formation of products **(5a–l)** has been calculated (Table 2) and compared with the yield obtained from the one-pot synthesis (Fig. 4). From this comparison, it has been clearly observed that one-pot synthesis is the most convenient and efficient method for the preparation of title compounds.

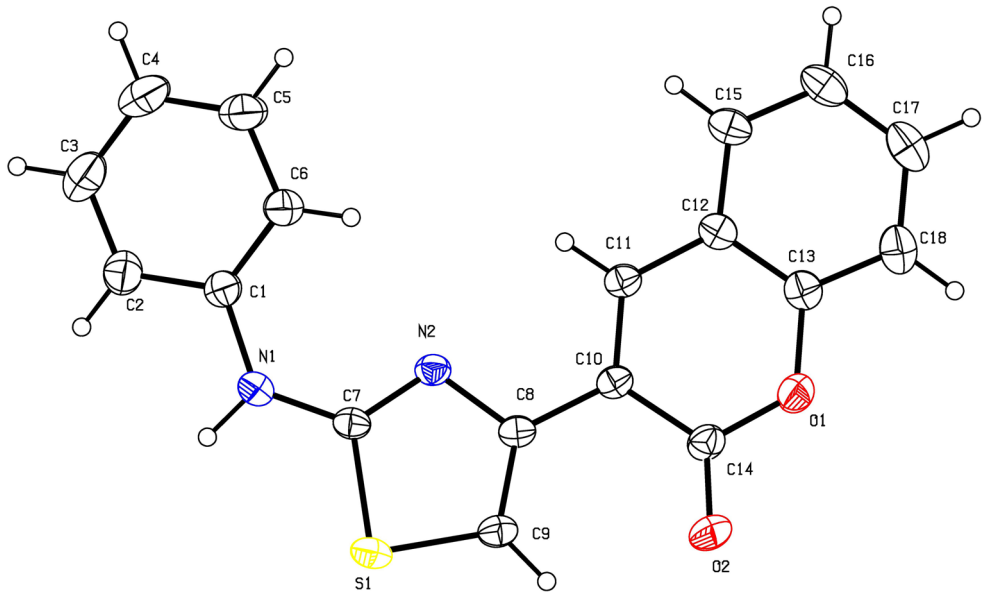
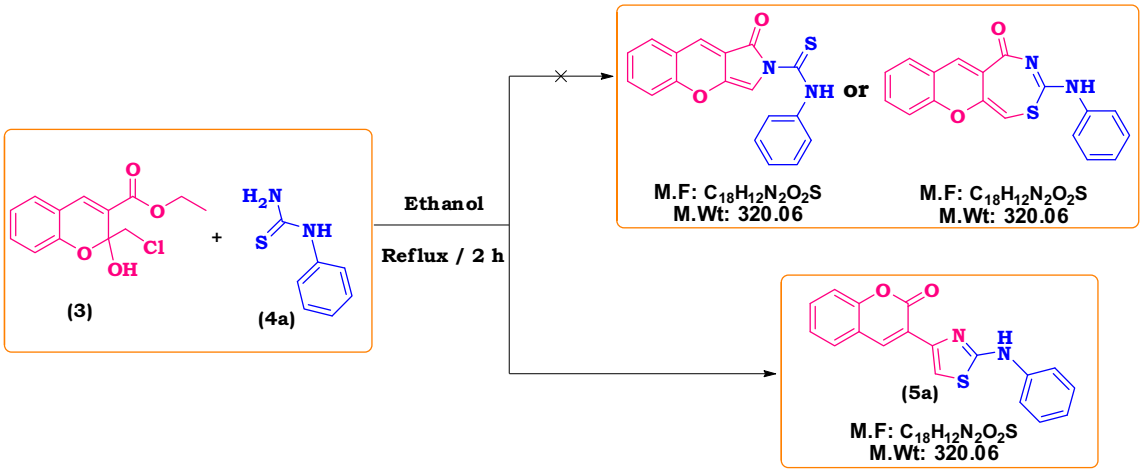


Fig. 3 ORTEP Diagram of compound **5a**



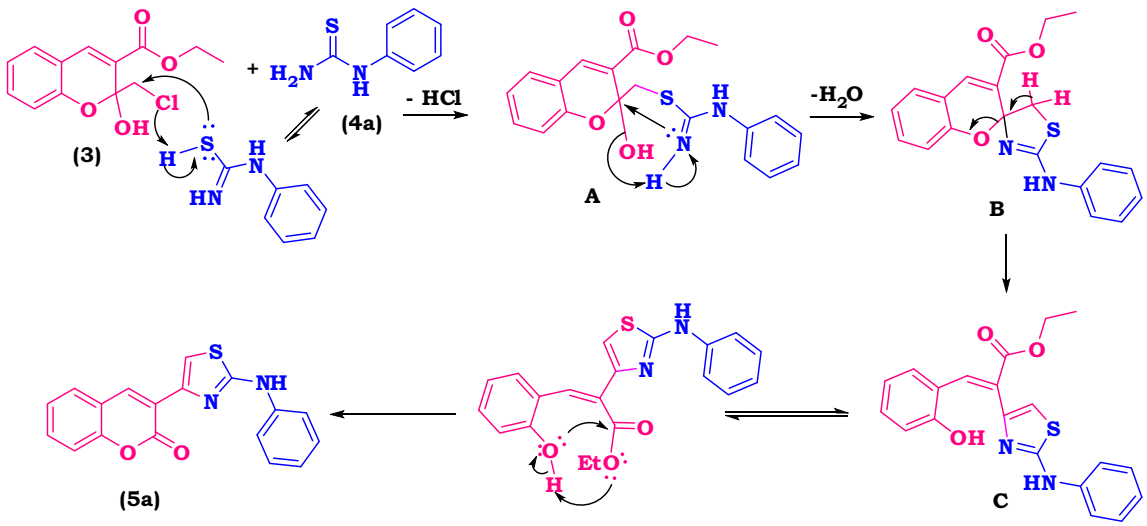
Scheme 2 An unusual synthesis of **5a**

Experimental section

Melting points are uncorrected and were determined in open capillary tubes using sulfuric acid bath. TLC analyses were done on silica gel-G coated sheets supplied by Merck Company, and visualization was done using UV lamp and iodine. ^{1}H NMR spectra were recorded on a Varian 400 MHz spectrometer in DMSO–d_6 using TMS as an internal standard. Mass spectra were recorded on Agilent 1100 LCMS instrument.

X-ray crystallography

Data for the compound **5a** was collected at room temperature on a Bruker D8 QUEST instrument with an IμS Mo microsource (λ = 0.7107 A) and a PHOTON-100 detector. The raw data frames were reduced and corrected for absorption effects using the Bruker Apex 3 software suite programs. The structure was solved using intrinsic phasing method and further refined with the SHELXL [27] program and expanded using Fourier techniques. Anisotropic displacement parameters were included for all non-hydrogen atoms. N bound H atoms were located in difference Fourier maps, and their positions and isotropic displacement parameters were refined. All C bound H atoms were positioned geometrically and treated as riding on their parent C atoms [C–H = 0.93–0.97 Å and $U_{iso}(H) = 1.5U_{eq}(C)$ for methyl H or $1.2U_{eq}(C)$ for other H atoms].

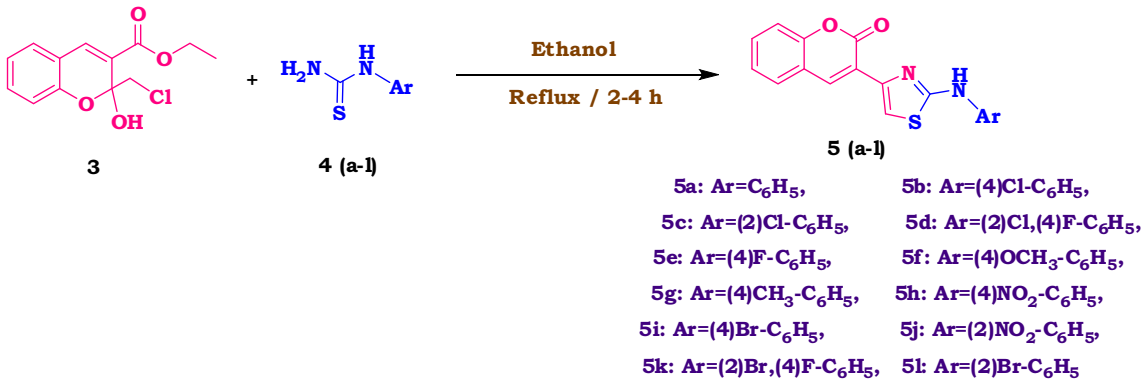


Scheme 3 Plausible mechanism for the formation of **5a** from **3** and **4a**

Table 1 Optimization data for the synthesis of **5a** from **3** and **4a**

S. no.	Solvent	Reaction condition	Reaction time	Yield[a] (%)
1	Ethanol	Reflux	2 h	91
2	Methanol	Reflux	2 h	89
3	Acetonitrile	Reflux	3 h	84
4	Acetone	Reflux	3½ h	79
5	Tetrahydrofuran	Reflux	2 h	82
6	1,4-dioxane	Reflux	4 h	68
7	Ethyl acetate	Reflux	3½ h	57
8	Isopropyl alcohol	Reflux	2½ h	76
9	Benzene	Reflux	7 h	35
10	Water	Reflux	8 h	21

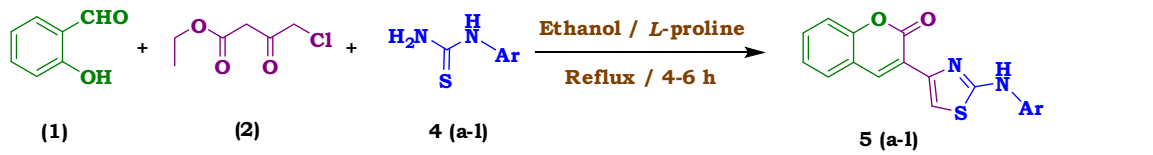
[a]Isolated yield



Scheme 4 Synthesis of 3-(2-(arylamino)thiazol-4-yl)-2*H*-chromen-2-ones (**5a–l**)

Preparation of 3 from 1 and 2

A mixture of **1** (20 mmol), **2** (20 mmol), L-proline (20 mol%) and ethanol (50 mL) was stirred at RT for 6 h. After the completion of reaction, the mixture was poured into ice-cold water (100 mL). The separated solid was filtered, washed with water (2 × 30 mL) and air-dried at RT. The crude product was recrystallized from methanol to obtain pure **3** white color solid. Yield: 4.12 g (77%). mp: 114–116 °C. Lit mp [25]: 113–115 °C.



(1) (2) 4 (a-l) 5 (a-l)

5a: Ar=C_6H_5, 5b: Ar=(4)Cl-C_6H_5,
5c: Ar=(2)Cl-C_6H_5, 5d: Ar=(2)Cl,(4)F-C_6H_5,
5e: Ar=(4)F-C_6H_5, 5f: Ar=(4)OCH_3-C_6H_5,
5g: Ar=(4)CH_3-C_6H_5, 5h: Ar=(4)NO_2-C_6H_5,
5i: Ar=(4)Br-C_6H_5, 5j: Ar=(2)NO_2-C_6H_5,
5k: Ar=(2)Br,(4)F-C_6H_5, 5l: Ar=(2)Br-C_6H_5

Scheme 5 One-pot synthesis of 3-(2-(arylamino)thiazol-4-yl)-2*H*-chromen-2-ones (**5a–l**)

Table 2 Comparison of yields of **5a–l** obtained in stepwise and one-pot methods

S. no.	Stepwise method			Yield of **5a–l** obtained in one-pot method
	Yield of **3** from **1** and **2**	Yield of **5a–l** from **3**	Overall yield of **5a–l**	
1	77	**5a**: 91	**5a**: 70	**5a**: 81
2	77	**5b**: 82	**5b**: 63	**5b**: 79
3	77	**5c**: 85	**5c**: 65	**5c**: 83
4	77	**5d**: 86	**5d**: 66	**5d**: 75
5	77	**5e**: 83	**5e**: 64	**5e**: 78
6	77	**5f**: 79	**5f**: 61	**5f**: 70
7	77	**5g**: 81	**5g**: 62	**5g**: 69
8	77	**5h**: 84	**5h**: 65	**5h**: 79
9	77	**5i**: 77	**5i**: 59	**5i**: 72
10	77	**5j**: 89	**5j**: 68	**5j**: 82
11	77	**5k**: 80	**5k**: 62	**5k**: 78
12	77	**5l**: 83	**5l**: 64	**5l**: 80

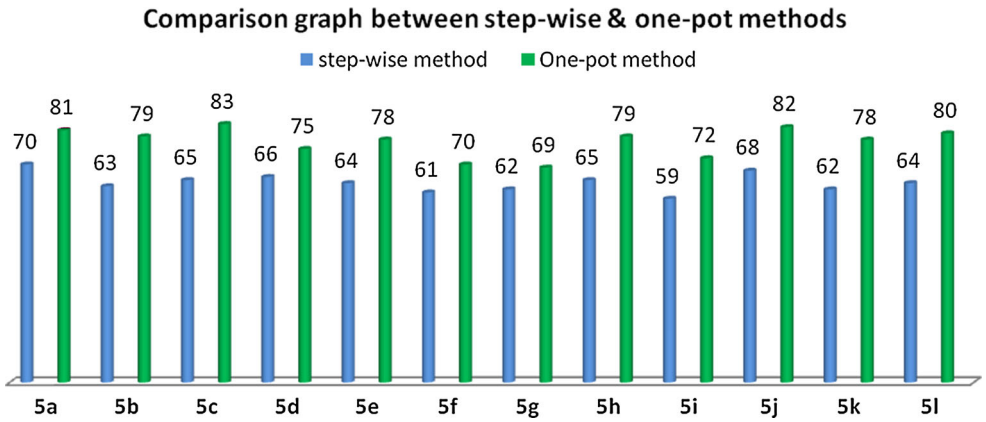


Fig. 4 Yield comparison of **5a–l** obtained in stepwise and one-pot methods

General procedure for the synthesis of 5 from 3 and 4

A mixture of **3** (10 mmol), **4** (10 mmol) and ethanol (30 mL) was refluxed for a period of 2–4 h. Progress of the reaction was monitored by thin layer chromatography. After the completion of the reaction, as shown by TLC analysis, the mixture was poured into ice-cold water (100 mL). The separated solid was filtered, washed with water (2 × 30 mL) and

air-dried at RT. The crude product was recrystallized from suitable solvent to obtain pure **5**.

3-(2-(Phenylamino)thiazol-4-yl)-2*H*-chromen-2-one (5a)

Yellow solid. Yield: 2.90 g (91%); mp 244–246 °C (Methanol); IR(KBr) νmax/cm^{-1}: 1728 cm^{-1} (strong, sharp, –CO of coumarin ring), 3390–3430 cm^{-1} (broad, medium, –NH group); ^{1}H-NMR (400 MHz, DMSO-d_6/TMS): δ = 6.98 (*d*, *J* = 8.8 Hz, 2H, Ar–**H**) 7.39–7.68 (complex, m, 6H, Ar–**H**), 7.72 (s, 1H, Ar–**H**), 7.96 (*d*, *J* = 6.8 Hz, 1H, Ar–**H**), 8.67 (s, 1H, Ar–**H**), 10.15 (s, 1H, –NH); ^{13}C-NMR (100 MHz, DMSO-d_6): 110.3, 116.3, 117.5, 119.7, 120.7, 121.9, 125.1, 129.4, 129.6, 132.1, 139.0, 141.4, 144.0, 152.7, 159.2, 162.9; HRMS calculated for $C_{18}H_{12}O_2N_2S$ $[M+H]^+$: 321.0697, Found: 321.0707.

Crystal data for 5a

$C_{18}H_{12}N_2O_2S$ (*M* = 320.36 g/mol): trigonal, space group R-3 (no. 148), *a* = 31.8600(3) Å, *c* = 7.6100(3) Å, *V* = 6689.7(3) $Å^3$, *Z* = 18, *T* = 293(2) K, μ(MoKα) = 0.229 mm^{-1}, *Dcalc* = 1.431 g/cm^3, 59,150 reflections measured (4.428° ≤ 2Θ ≤ 61.276°), 4585 unique (R_{int} = 0.0338, R_{sigma} = 0.0163) which were used in all calculations. The final R_1 was 0.0441 (I > 2σ(I)), and wR_2 was 0.1201 (all data). CCDC 1844833 contains supplementary Crystallographic data for the structure. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(0) 1223 336 033; email: deposit@ccdc.cam.ac.uk].

3-(2-((4-Chlorophenyl)amino)thiazol-4-yl)-2*H*-chromen-2-one (5b)

Yellow solid. Yield: 2.90 g (82%); mp 273–275 °C (Ethanol); IR(KBr) νmax/cm^{-1}: 1701 cm^{-1} (strong, sharp, –CO of coumarin ring), 3380–3460 cm^{-1} (broad, medium, –NH group); ^{1}H-NMR (400 MHz, DMSO-d_6/TMS): δ = 7.13 (*t*, *J* = 1.2 Hz, 1H, Ar–**H**), 7.36–7.66 (m, 5H, Ar–**H**), 7.82 (s, 1H, Ar–**H**), 7.92 (*d*, *J* = 1.2 Hz, 1H, Ar–H), 8.48 (*d*, *J* = 1.2 Hz, 1H, Ar–H), 8.71 (s, 1H, Ar–**H**) and 9.79 (s, 1H, –N**H**); ^{13}C-NMR (100 MHz, DMSO-d_6): 115.0, 115.3, 115.8, 118.8, 118.9, 119.2, 120.6, 124.2, 127.9, 130.8, 136.9, 138.2, 143.7, 152.3, 156.0, 159.1, 159.3, 163.0; HRMS calculated for $C_{18}H_{11}O_2N_2SCl$ $[M+H]^+$: 355.0308, Found: 355.0321.

3-(2-((2-Chlorophenyl)amino)thiazol-4-yl)-2*H*-chromen-2-one (5c)

Yellow solid. Yield: 3.00 g (85%); mp 154–156 °C (Ethanol); IR(KBr) νmax/cm^{-1}: 1720 cm^{-1} (strong, sharp, –CO of coumarin ring), 3390–3450 cm^{-1} (broad, medium, –NH group); ^{1}H-NMR (400 MHz, DMSO-d_6/TMS): δ = 7.11 (*t*, *J* = 7.6 Hz, 1H, Ar–**H**), 7.37–7.65 (complex, m, 5H, Ar–H), 7.82 (s, 1H, Ar–**H**), 7.91 (*d*, *J* = 7.6 Hz, 1H, Ar–**H**), 8.48 (*d*, *J* = 8.0 Hz, 1H, Ar–**H**), 8.61 (s, 1H, Ar–**H**) and 9.81 (s, 1H, –N**H**); ^{13}C-NMR (100 MHz, DMSO-d_6): 109.4, 115.5, 118.1, 119.0, 120.3, 124.0, 125.4, 127.8, 128.2, 130.7, 136.9, 137.0, 138.1, 139.3, 143.5, 152.1, 159.0, 162.1; HRMS calculated for $C_{18}H_{11}ClN_2O_2S$ $[M+H]^+$: 355.0308, Found: 355.0310.

3-(2-((2-Chloro-4-fluorophenyl)amino)thiazol-4-yl)-2*H*-chromen-2-one (5d)

Yellow solid. Yield: 3.19 g (86%); mp 124–126 °C (Ethanol); IR(KBr) νmax/cm^{-1}: 1713 cm^{-1} (strong, sharp, –CO of coumarin ring), 3360–3450 cm^{-1} (broad, medium, –NH group); ^{1}H-NMR (400 MHz, DMSO-d_6/TMS): δ = 6.98 (*d*, *J* = 9.2 Hz, 2H, Ar–**H**), 7.40 (*t*, *J* = 7.6 Hz, 1H, Ar–**H**), 7.47 (s, 1H, Ar–**H**), 7.61–7.68 (complex, m, 3H, Ar–**H**), 7.72 (s, 1H, Ar–**H**), 8.67 (s, 1H, Ar–**H**) and 10.15 (s, 1H, –N**H**); ^{13}C-NMR (100 MHz, DMSO-d_6): 117.7, 118.5, 119.6, 120.6, 125.2, 129.2, 132.1, 138.6, 139.6, 139.8, 143.9, 151.2, 152.7, 153.6, 159.1, 162.6; HRMS calculated for $C_{18}H_{10}ClFN_2O_2S$ $[M+H]^+$: 373.0213, Found: 373.0402.

3-(2-((4-Fluorophenyl)amino)thiazol-4-yl)-2*H*-chromen-2-one (5e)

Yellow solid. Yield: 2.80 g (83%); mp 126–128 °C (Methanol); IR(KBr) νmax/cm^{-1}: 1717 cm^{-1} (strong, sharp, –CO of coumarin ring), 3390–3450 cm^{-1} (broad, medium, –NH group); ^{1}H-NMR (400 MHz, DMSO-d_6/TMS): δ = 7.19–7.94 (complex, m, 8H, Ar–**H**), 7.96 (s, 1H, Ar–**H**), 8.69 (s, 1H, Ar–**H**) and 10.38 (s, 1H, –N**H**); ^{13}C-NMR (100 MHz, DMSO-d_6): 109.8, 115.4, 115.6, 115.8, 118.6, 118.6, 119.2, 120.2, 124.6, 128.9, 131.6, 137.4, 138.6, 143.5, 152.2, 155.7, 158.1, 158.7, 162.5; HRMS calculated for $C_{18}H_{11}IFN_2O_2S$ $[M+H]^+$: 339.0603, Found: 339.0599.

3-(2-((4-Methoxyphenyl)amino)thiazol-4-yl)-2*H*-chromen-2-one (5f)

Yellow solid. Yield: 2.76 g (79%); mp 192–194 °C (Acetonitrile); IR(KBr) νmax/cm^{-1}: 1720 cm^{-1} (strong, sharp, –CO of coumarin ring), 3395–3455 cm^{-1} (broad, medium, –NH group); ^{1}H-NMR (400 MHz, DMSO-d_6/TMS): δ = 3.75 (s, 3H, OC**H**$_3$), 6.96–7.94 (complex, m, 8H, Ar–**H**), 7.96 (s, 1H, Ar–**H**), 8.67 (s, 1H, Ar–**H**) and 10.16 (s, 1H, –N**H**); ^{13}C-NMR (100 MHz, DMSO-d_6): 55.1, 109.2, 114.3, 115.8, 118.9, 119.2, 120.2, 124.6, 128.9, 131.6, 134.4, 138.4, 143.4, 152.2, 154.2, 158.7, 163.1; HRMS calculated for $C_{19}H_{14}N_2O_3S$ [M + H]$^+$: 351.0803, Found: 351.0802.

3-(2-(4-Tolylamino)thiazol-4-yl)-2*H*-chromen-2-one (5g)

Yellow solid. Yield: 2.70 g (81%); mp 201–203 °C (Acetonitrile); IR(KBr) νmax/cm^{-1}: 1716 cm^{-1} (strong, sharp, –CO of coumarin ring), 3404–3450 cm^{-1} (broad, medium, –NH group); ^{1}H-NMR (400 MHz, DMSO-d_6/TMS): δ = 2.15 (s, 3H, -C**H**$_3$), 7.40–7.67 (m, 5H, Ar–**H**), 7.72 (s, 1H, Ar–**H**), 7.79–7.98 (complex, m, 3H, Ar–**H**), 8.71 (s, 1H, Ar–**H**) and 10.50 (s, 1H, –N**H**); ^{13}C-NMR (100 MHz, DMSO-d_6): 21.2, 110.0, 115.3, 119.1, 119.8, 120.8, 125.0, 128.1, 128.4, 133.2, 139.2, 140.1, 144.0, 152.4, 159.5, 162.2; HRMS calculated for $C_{19}H_{14}N_2O_2S$ [M + H]$^+$: 335.0855, Found: 335.0853.

3-(2-((4-Nitrophenyl)amino)thiazol-4-yl)-2*H*-chromen-2-one (5h)

Yellow solid. Yield: 3.07 g (84%); mp 170–172 °C (Methanol); IR(KBr) νmax/cm^{-1}: 1728 cm^{-1} (strong, sharp, –CO of coumarin ring), 3404–3430 cm^{-1} (broad, medium, –NH group); ^{1}H-NMR (400 MHz, DMSO-d_6/TMS): δ = 7.11 (*t*, *J* = 8.0 Hz, 1H, Ar–**H**), 7.37–7.65 (complex, m, 5H, Ar–**H**), 7.82 (s, 1H, Ar–**H**), 7.91 (*d*, *J* = 9.2 Hz, 1H, Ar–**H**), 8.48 (*d*, *J* = 7.6 Hz, 1H, Ar–**H**), 8.61 (s, 1H, Ar–**H**) and 9.81 (s, 1H, –N**H**); ^{13}C-NMR (100 MHz, DMSO-d_6): 110.7, 116.3, 119.0, 119.7, 120.6, 125.1, 129.3, 129.4, 132.1, 139.2, 140.3, 144.0, 152.7, 159.2, 162.6; HRMS calculated for $C_{18}H_{11}N_3O_4S$ [M + H]$^+$: 366.0549, Found: 366.0548.

3-(2-((4-Bromophenyl)amino)thiazol-4-yl)-2*H*-chromen-2-one (5i)

Yellow solid. Yield: 3.07 g (77%); mp 177–179 °C (Chloroform); IR(KBr) νmax/cm^{-1}: 1730 cm^{-1} (strong, sharp, –CO of coumarin ring), 3380–3438 cm^{-1} (broad, medium, –NH group); ^{1}H-NMR (400 MHz, DMSO-d_6/TMS): δ 7.43–7.48 (complex, m, 4H, Ar–**H**),7.63 (*d*, *J* = 6.8 Hz, 1H, Ar–**H**), 7.66 (s, 1H, Ar–**H**), 7.69 (*d*, *J* = 7.6 Hz, 1H, Ar–**H**), 7.82 (*t*, *J* = 8.8 Hz, 1H, Ar–**H**), 7.98 (*d*, *J* = 7.2 Hz, 1H, Ar–**H**), 8.73 (s, 1H, Ar–**H**) and 10.52 (s, 1H, –N**H**); ^{13}C-NMR (100 MHz, DMSO-d_6): 111.2, 115.5, 117.5, 118.0, 118.9, 119.3, 121.2, 124.7, 128.7, 130.9, 135.1, 139.0, 143.4, 151.8, 158.5, 163.6; HRMS calculated for $C_{18}H_{11}BrN_2O_2S$ [M + H] + : 398.9807, Found: 398.9802.

3-(2-((2-Nitrophenyl)amino)thiazol-4-yl)-2*H*-chromen-2-one (5j)

Yellow solid. Yield: 3.24 g (89%); mp 214–216 °C (Ethanol); IR(KBr) νmax/cm^{-1}: 1726 cm^{-1} (strong, sharp, –CO of coumarin ring), 3390–3440 cm^{-1} (broad, medium, –NH group); ^{1}H-NMR (400 MHz, DMSO-d_6/TMS): δ 7.12 (*t*, *J* = 7.2 Hz, 1H, Ar–**H**), 7.38–7.64 (complex, m, 5H, Ar–H), 7.84 (s, 1H, Ar–**H**), 7.93 (*d*, *J* = 6.8 Hz, 1H, Ar–**H**), 8.49 (*d*, *J* = 7.6 Hz, 1H, Ar–**H**), 8.61 (s, 1H, Ar–**H**) and 9.94 (s, 1H, –N**H**); ^{13}C-NMR (100 MHz, DMSO-d_6): 110.0, 115.2, 118.2, 119.1, 120.5, 123.9, 125.2, 128.0, 128.6, 130.9, 136.9, 137.2, 138.4, 139.4, 144.2, 152.2, 159.1, 162.2; HRMS calculated for $C_{18}H_{11}N_3O_4S$ [M + H] + : 366.0545, Found: 366.0548.

3-(2-(2-Bromo-4-fluorophenylamino)thiazol-4-yl)-2*H*-chromen-2-one (5k)

Yellow solid. Yield: 3.33 g (80%); mp 153–155 °C (Ethanol); IR(KBr) νmax/cm^{-1}: 1719 cm^{-1} (strong, sharp, –CO of coumarin ring), 3345–3480 cm^{-1} (broad, medium, –NH group); ^{1}H-NMR (400 MHz, DMSO-d_6/TMS): δ 6.95 (*d*, *J* = 8.0 Hz, 2H, Ar–**H**), 7.44 (*t*, *J* = 7.2 Hz, 1H, Ar–**H**), 7.49 (s, 1H, Ar–**H**), 7.64–7.69 (complex, m, 3H, Ar–**H**), 7.75 (s, 1H, Ar–**H**), 8.68 (s, 1H, Ar–**H**) and 10.13 (s, 1H, –N**H**); ^{13}C-NMR (100 MHz, DMSO-d_6): 116.9, 118.1, 119.4, 120.3, 125.1, 129.2, 131.9, 138.5, 139.5, 139.9, 144.0, 150.9, 152.6, 154.1, 159.2, 163.1; HRMS calculated for $C_{18}H_{10}BrFN_2O_2S$ [M + H]$^+$: 418.0325, Found: 418.0302.

3-(2-((2-Bromophenyl)amino)thiazol-4-yl)-2*H*-chromen-2-one (5l)

Yellow solid. Yield: 3.31 g (83%); mp 189–191 °C (Ethanol); IR(KBr) νmax/cm^{-1}: 1723 cm^{-1} (strong, sharp, –CO of coumarin ring), 3382–3460 cm^{-1} (broad, medium, –NH group); ^{1}H-NMR (400 MHz, DMSO-d_6/TMS): δ 7.14 (*t*, *J* = 8.2 Hz, 1H, Ar–**H**), 7.38–7.66 (complex, m, 5H, Ar–H), 7.83 (s, 1H, Ar–**H**), 7.91 (*d*, *J* = 7.2 Hz, 1H, Ar–**H**), 8.46 (*d*, *J* = 6.8 Hz, 1H, Ar–**H**), 8.60 (s, 1H, Ar–**H**) and 9.98 (s, 1H, –N**H**); ^{13}C-NMR (100 MHz, DMSO-d_6): 109.5, 115.6, 117.9, 119.1, 120.2, 123.9, 125.5, 128.0, 128.9, 131.5, 136.7, 137.1, 138.5, 139.8, 144.1, 152.8, 159.6, 162.5; HRMS calculated for $C_{18}H_{11}BrN_2O_2S$ [M + H] + : 398.9805, Found: 398.9802.

General procedure for the one-pot synthesis of 5 from 1, 2 and 4

A mixture of **1** (10 mmol), **2** (10 mmol), **4** (10 mmol), *L*-proline (20 mol%) and ethanol (30 mL) was refluxed for a period of 4–6 h. Progress of the reaction was monitored by thin layer chromatography. After the completion of the reaction, as shown by TLC analysis, the mixture was poured into ice-cold water (100 mL). The separated solid was filtered, washed with water (2 × 30 mL) and air-dried at RT. The crude product was recrystallized from suitable solvent to obtain pure **5**.

Conclusion

In conclusion, we have demonstrated an unusual and unexpected synthetic method for the preparation of various 3-(2-(arylamino)thiazol-4-yl)-2*H*-chromen-2-ones (**5**) from with ethyl 2-(chloromethyl)-2-hydroxy-2*H*-chromene-3-carboxylate (**3**). The scope of this reaction has been successfully extended to an efficient one-pot synthetic protocol for the synthesis of the same products and thus reduced the two steps process to a one-step process. Apart from all of these, a novel approach has been outlined for the synthesis of title compounds via benzopyran ring opening under mild reaction conditions with operational simplicity.

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