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PEG-600 mediated one-pot reaction of 3-acetyl-2*H*-chromen-2-one with heterylthiols and phenylthioureas using Tetrabutylammonium Tribromide as an efficient green reagent

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Abstract: A facile method for the one-pot reaction of 3-acetyl-2*H*-chromen-2-one with different heterylthiols and phenylthioureas has been described under green conditions using tetrabutylammonium tribromide (TBATB) as an efficient reagent. 3-acetyl-2*H*-chromen-2-one reacted with TBATB in acetic acid to give 3-(2-bromoacetyl)-2*H*-chromen-2-one. PEG-600 was found to be the effective solvent for this reaction. Thus, one-pot reaction of equimolar amounts of 3-acetyl-2*H*-chromen-2-one, TBATB & heterylthiols/phenylthioureas independently, resulted in the formation of heterylthioacetylcoumarins and coumarinylthiazoles respectively. Effect of solvent on these reactions has been studied. The merits of this preparation are mild reaction conditions, easy workup, good yields and use of PEG-600 as green reaction media.

Keywords: 3-Acetyl-2*H*-chromen-2-one, tetrabutylammonium tribromide, heterylthiols, phenylthioureas and PEG-600.

INTRODUCTION

Coumarin is one of the important parent compounds found in many plants and could be used as an important component of various functional materials and shown diverse pharmacological properties.[1] Some of the important activities include antitumor,[2] anti-inflammatory,[3] anti-coagulant,[4] and anti-oxidant[5] etc. Coumarins containing other heterocycles

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such as thiazole, imidazole, and oxazole have been reported to possess various biological activities[6-10] which requires 3-(2-bromoacetyl)-2*H*-chromen-2-one as a starting material. Also 3-(2-bromoacetyl)-2*H*-chromen-2-one is a very attractive synthetic intermediate since it has been used for a variety of organic transformations especially for the synthesis of thiadiazines[11], pyrans,[12] pyridines,[13] thiadiazoles,[14] oxadiazoles,[15] selenazoles,[16] phosphonates and phosphates,[17] etc.

3-(2-bromoacetyl)-2*H*-chromen-2-one is generally prepared by the reaction of 3-acetyl-2*H*-chromen-2-one with liquid bromine.[18] However, bromine is a corrosive, toxic, maintenance of stoichiometry is difficult and special care is required for its storage and transportation, it is very important for various organic transformations. Therefore there has been a search for benign reagents which can act as bromine alternatives. A number of such alternatives have been reported in literature for the synthesis of 3-(2-bromoacetyl)-2*H*-chromen-2-one in recent days.

Shaikh et al. reported[19] the synthesis of 3-(2-bromoacetyl)-2*H*-chromen-2-one by the reaction of 3-acetyl-2*H*-chromen-2-one with copper(II)bromide in 1:1 ethyl acetate and chloroform under reflux conditions for 12 h in 90 % yield. Abdolali et al. reported[20] the synthesis of 3-(2-bromoacetyl)-2*H*-chromen- 2-one from 3-acetyl-2*H*-chromen-2-one by its reaction with N-bromosuccinimide in 1:5 ratio of acetonitrile and chloroform using p-toluenesulfonic acid as a catalyst under refluxing conditions in 70% yield. Wang et al. reported[21] the treatment of 3-acetyl-2*H*-chromen-2-one with N-bromosuccinimide in the presence of p-toluenesulfonic acid in acetonitrile at 50 °C for 5 h to give 3-(2-bromoacetyl)-2*H*-chromen- 2-one in 75% yield.

Among all the bromine alternatives that have been developed so far, a group of reagents that have become popular are the quaternary ammonium tribromides which are having numerous applications in various organic transformations such as bromination reactions,[22,23] synthesis of

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acetals,[24,25] heterocyclic synthesis,[26] sulfide oxidations,[27] multi-component reactions,[28] oxidative cyclizations,[29] etc. Moreover, most of these tribromides are stable up to 200 °C temperatures,[30,31] and thus can be used for reactions at higher temperature, making them reagents of choice over liquid bromine at elevated temperatures.[32,33] Among all these, Tetrabutylammonium tribromide (TBATB) has drawn the attention of researchers because of its stability, easier method of preparation and has certain advantages over liquid bromine.[34] TBATB was first synthesized by Buckles et al. from tetrabutylammonium bromide and liquid bromine.[35]

One-pot synthesis is an important strategy to improve the efficiency of a chemical reaction whereby a reactant is subjected to successive chemical reactions just in one reaction vessel. This is much desired by chemists because avoiding lengthy processes and purifications of the intermediate compounds would save time and resources with enhancing the product yield.

Rao et al. reported[36] the one-pot synthesis of aminothiazole by heating a mixture of 3-acetyl-2*H*-chromen-2-one, iodine and phenylthioureas on water bath for 24 h. Gouda et al. described[37] the one-pot reaction of 3-acetyl-2*H*-chromen-2-one with iodine and thiourea to yield the corresponding aminothiazole in refluxing ethanol for 8 h. It was reported[38] from our laboratory, a one-pot reaction of 3-acetyl-2*H*-chromen-2-one, 1*H*-benzo[d]imidazole-2-thiol & iodine in isopropyl alcohol at room temperature for 4-5 h to give the corresponding condensed products.

Thus, based on the above literature reports and in continuation of our research work [39,40] it was considered worthwhile to develop an alternative method which avoids the use of liquid bromine or the use of iodine for the one-pot reaction of 3-acetyl-2*H*-chromen-2-ones with heterylthiols and phenylthioureas.

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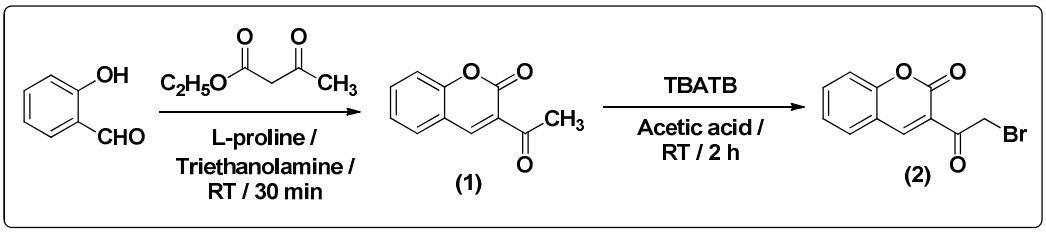
RESULTS AND DISCUSSION:

Commercially available salicylaldehyde was treated with ethyl acetoacetate in triethanolamine containing catalytic amount of *L*-proline at RT for 30 min to yield 3-acetyl-2*H*-chromen-2-one (**1**). The later, on bromination, using tetrabutylammonium tribromide (TBATB) in acetic acid, at room temperature for 2 h afforded 3-(2-bromoacetyl)-2*H*-chromen-2-one (**2**) (Scheme 1).



Scheme 1. Synthesis of 3-(2-bromoacetyl)-2*H*-chromen-2-one (**2**)

With a view to optimize the reaction conditions for the formation of compound **2** in maximum yield & in shorter reaction time, the reaction of **1** with TBATB was examined by treating equimolar amounts of the reactants in different solvents (Table 1).

Table 1. Optimization of reaction conditions for the synthesis of **2** from **1** using TBATB at RT

S. No.	Solvent	Time	Yield[#] (%)
1	Acetic acid	2 h	92
2	Ethanol	4 h	83
3	Glycerol	2 ½ h	78
4	**PEG-600**	**1 ½ h**	**96**
5	Methanol	4 h	86
6	Acetonitrile	3 h	61
7	Isopropyl alcohol	5h	70

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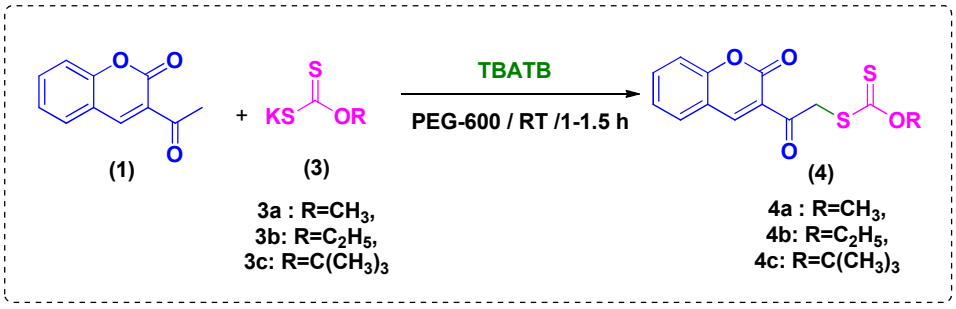
8	Tetrahydrofuran	3 ½ h	81
9	1,4-Dioxane	6 h	56
10	Water	10 h	Nil

[#] Isolated yield.

Among all these conditions PEG-600 was found to be the best solvent in terms of reaction time and yield. So, keeping this best result in hand, we have utilized PEG-600 for the one-pot reaction of 3-acetyl-2*H*-chromen-2-one (**1**) with various nucleophiles.

Initially, the one-pot reaction was performed between 3-acetyl-2*H*-chromen-2-one (**1**) and xanthate salt i.e., potassium O-methyl carbonodithioate **3a** (i.e., **3,** R=CH_3) in PEG-600 without the use of any base or any phase transfer catalyst (PTC) to check whether the reaction is forwarding or not. Surprisingly, the reaction completed just in 1 h to result in the formation of corresponding condensed product O-methyl S-(2-oxo-2-(2-oxo-2H-chromen-3-yl)ethyl) carbonodithioate, **4a** (i.e., **4,** R=CH_3) in good yields. It was found that in this reaction PEG-600 found to play the dual role as a base and also as a PTC which was reported earlier in literature.[40-41] This reaction was also extended to other xanthate salts i.e., potassium O-ethyl carbonodithioate **3b** (i.e., **3,** R=C_2H_5), potassium O-isopropyl carbonodithioate **3c** (i.e., **3,** R=$C(CH_3)_3$) to obtain the compounds **4b** and **4c** respectively (Scheme 2).



Scheme 2. One-pot reaction of 3-acetyl-2*H*-chromen-2-one, TBATB & xanthate salts.

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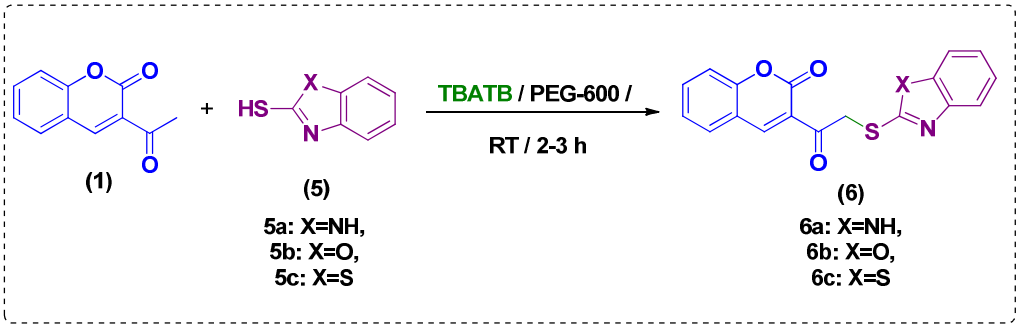
Encouraging with the above positive result, one-pot reaction between 3-acetyl-2*H*-chromen-2-one (**1**), TBATB and different heterylthiols performed independently in PEG-600. Reaction was completed successfully in 2-3 h at RT itself to give the corresponding condensed products, i.e., **6(a-c)** (Scheme 3).



Scheme 3. One-pot reaction of **1**, TBATB & **5** to give **6**

In order to check the effect of solvent on this reaction, we have optimized the reaction conditions for the reaction between 3-acetyl-2*H*-chromen-2-one (**1**), TBATB & 1*H*-benzo[d]imidazole-2-thiol (**5a**) using different solvents (Table 2). Form the optimization studies it was found that PEG-600 as the best reaction medium for the reaction to occur in lesser time and in maximum product yield.

Table 2. Optimization of reaction conditions for the synthesis of **6a** from **1, 5a** & TBATB at RT

S. No.	Solvent	Time	Yield[#] (%)
1	Ethanol	6 h	63
2	Glycerol	4 h	78
3	**PEG-600**	**2 ½ h**	**84**
4	Methanol	7 h	60
5	DMF	4 ½ h	64

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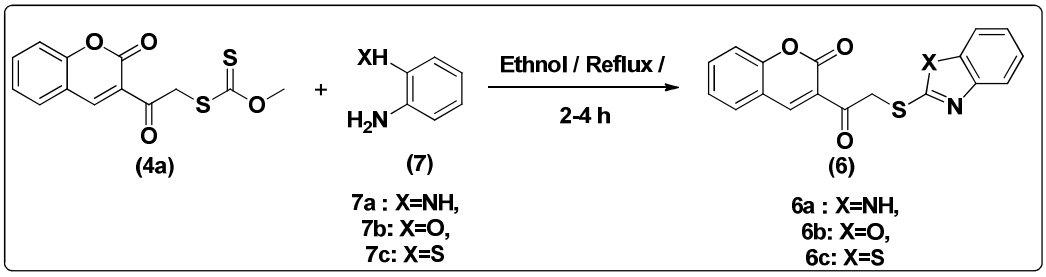
6	Isopropyl alcohol	5 h	57
7	Tetrahydrofuran	6 ½ h	70
8	1,4-Dioxane	8 h	51
9	Acetic acid	10 h	Nil
10	Water	10 h	Nil

[#] Isolated yield.

The above products **6** could also be prepared alternatively by the reaction of **4a** with each of o-phenylenediamine (**7a**), o-aminophenol (**7b**) & o-aminothiophenol (**7c**) independently in refluxing ethanol for 2-4 h, but in lower yields. Thus, these compounds **6**, prepared in this route were found to be identical with the ones that obtained in the earlier route in all respects such as mp, mmp and co-TLC (Scheme 4).



Scheme 4. Alternative method for the preparation of **6**.

From the above set of reactions, TBATB has been found to be an effective reagent for the direct reaction of 3-acetyl-2*H*-chromen-2-one (**1**) with sulfur nucleophiles. The efficiency of this reagent was extended to test a reaction between 3-acetyl-2*H*-chromen-2-one (**1**) and phenylthiourea **8a** (i.e., **8,** Ar=C_6H_5) under the same reaction conditions. Thus a mixture of equimolar amounts of **1**, TBATB, phenylthiourea in PEG-600 was stirred at RT. Interestingly, the reaction was completed just in 2 h to yield a product which was characterized as 3-(2-

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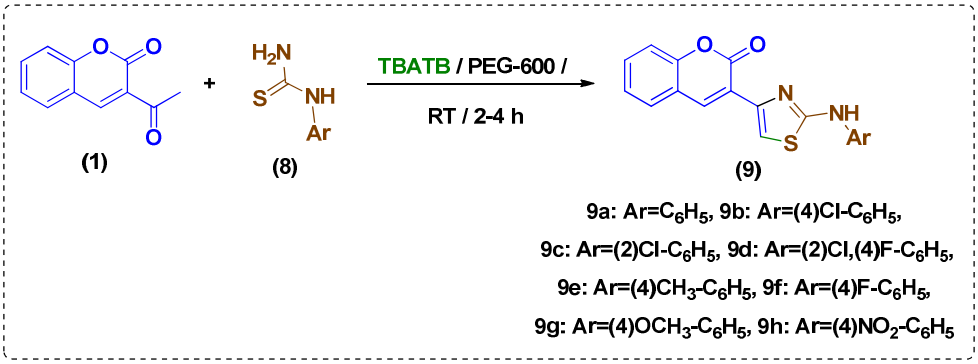
(phenylamino)thiazol-4-yl)-2H-chromen-2-ones (**9**) that was found to be identical with the product obtained by the reaction of 3-(2-bromoacetyl)-2*H*-chromen-2-one (**2**) with phenylthiourea in ethanol under reflux conditions, a reaction that is usually known as Hantzsch thiazole synthesis. Thus, this one-pot reaction of **1** with TBATB and phenylthiourea in PEG-600 was found to be a general one and was extended to other substituted phenylthioureas (Scheme 5).



Scheme 5. One-pot synthesis of 3-(2-(phenylamino)thiazol-4-yl)-2*H*-chromen-2-ones (**9**)

The scope of formation of product **9a** in maximum yield & in lesser reaction time was further studied using various solvents (Table 3). From this optimization study, we came to a conclusion that PEG-600 is the best reaction medium for the one-pot reaction of 3-acetyl-2*H*-chromen-2-one (**1**), TBATB & various nucleophiles in terms of reaction time & product yield.

Table 3. Optimization of reaction conditions for the synthesis of **9a** from **1, 8a** & TBATB at RT

S. No.	Solvent	Time	Yield[#] (%)
1	Ethanol	7 ½ h	61
2	Glycerol	6 ½ h	65
3	**PEG-600**	**3 h**	**88**
4	Methanol	9 h	58
5	DMF	7 ½ h	60

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6	Isopropyl alcohol	7 h	57
7	Tetrahydrofuran	8 h	53
8	1,4-Dioxane	9 h	46
9	Acetic acid	10 h	Nil
10	Water	10 h	Nil

[#] Isolated yield.

The mechanism for these one-pot reactions was studied and it was found from literature that TBATB known to release anhydrous HBr in an alcoholic medium and in other organic solvents.[42-44] TBATB can be considered as a general brominating agent which can be used in brominations that ordinarily performed with molecular bromine. Thus, it reacts with 3-acetyl-2*H*-chromen-2-one (**1**) in PEG-600 to give the corresponding 3-(2-bromoacetyl)-2*H*-chromen-2-one (**2**), HBr and tetrabutylammonium bromide (TBAB). **2**, thus formed reacts in-situ with heterylthiols (**5)** or phenylthioureas (**8**) to give the corresponding products **6** or **9**. The beauty of this reaction is, TBATB during its reaction generates TBAB and will be in the reaction mass, act as a Phase Transfer Catalyst and further enhances the progress of reaction in-situ (Scheme 6).

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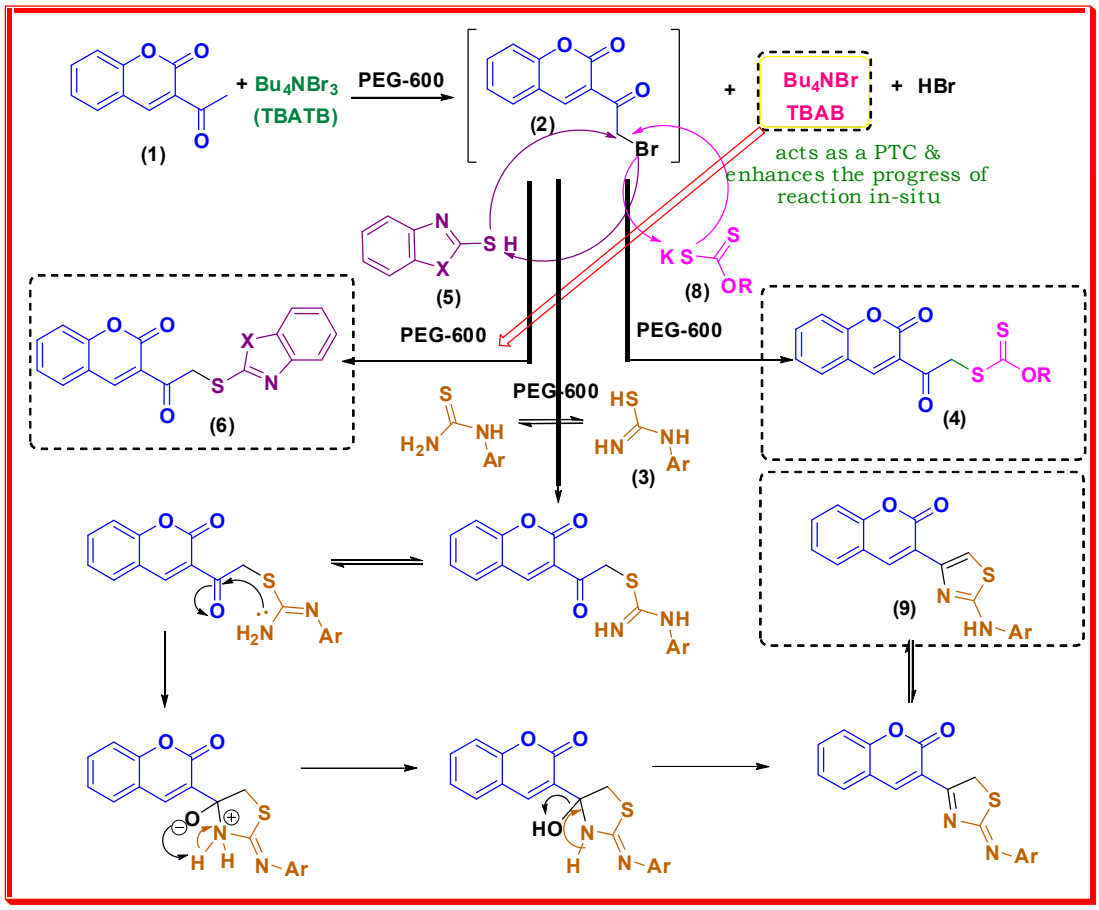

Scheme 6. Plausible mechanism for the one-pot reaction.

Characterization of TBATB:

Even though the formation of the reagent was compared with the available literature data, further characterization is always an added advantage. Keeping this in view, we characterized the reagent with SEM–EDX analysis, powder XRD analysis.

SEM–EDX analysis of TBATB:

To study the surface morphology of the reagent, i.e., TBATB, SEM micrograph of the reagent was recorded. The SEM images of the reagent (Fig. 1) showed an even distribution and in a proper alignment which was recorded at 10 μm. Further, EDX analysis (Fig. 2) is generally

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carried out to know the elemental composition of the material of our interest. For TBATB, EDX analysis showed the presence of C, N and Br elements.

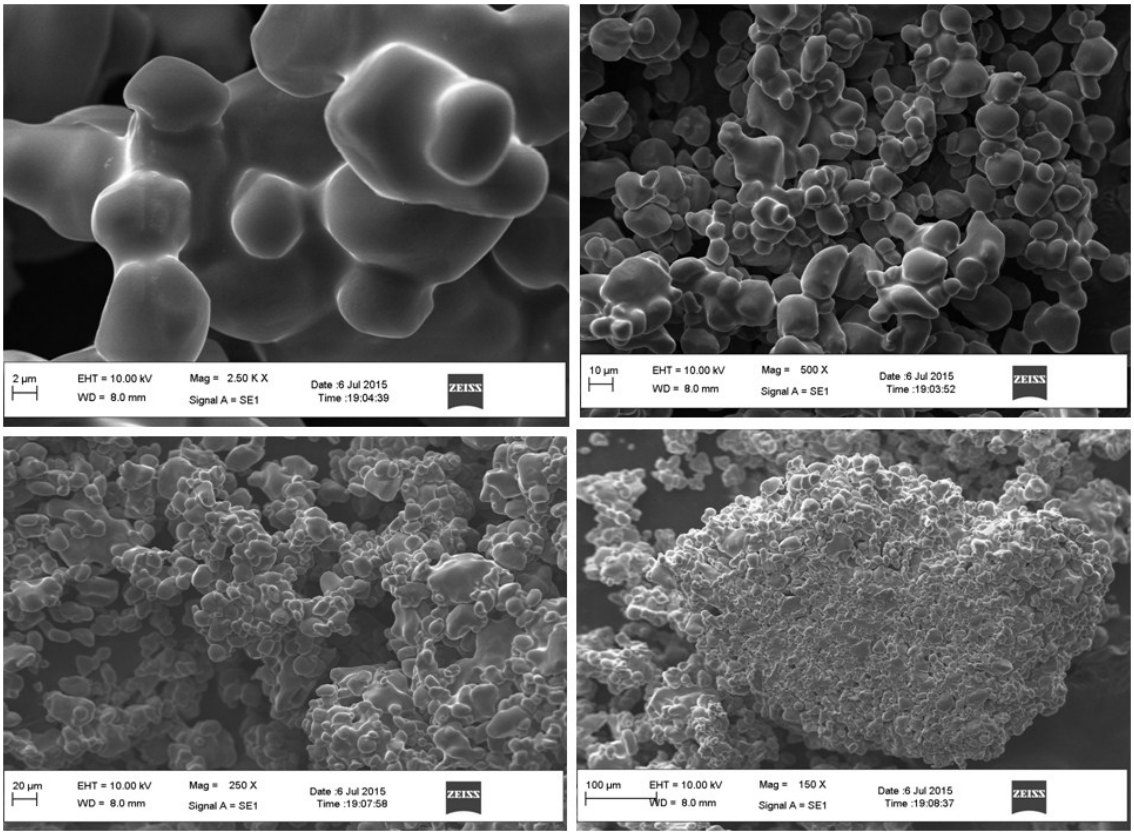

Fig. 1 SEM image of TBATB at different magnifications

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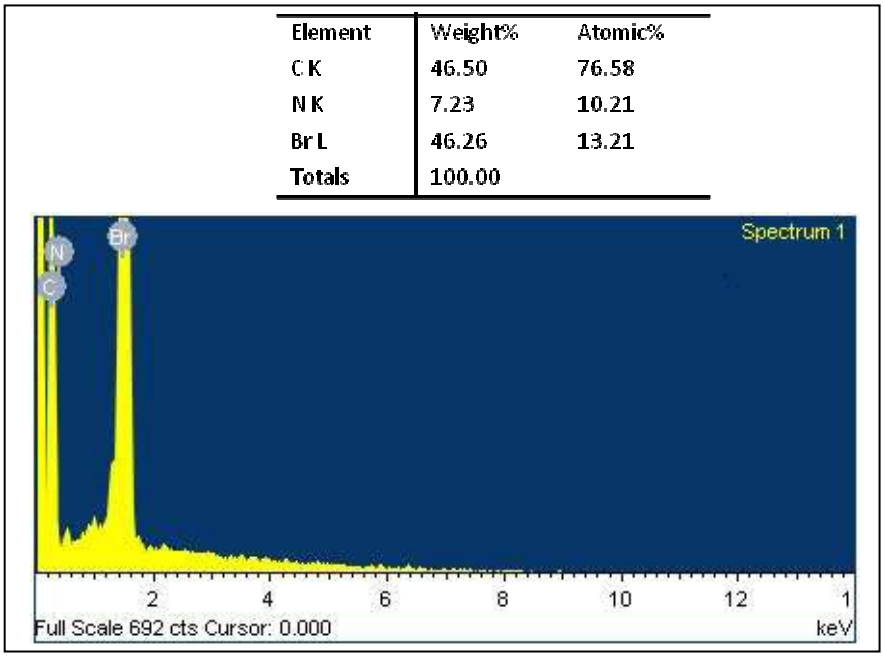

Fig. 2: EDX analysis of TBATB

Powder X-ray diffraction (XRD) analysis of TBATB:

The nature of the prepared reagent (TBATB) was identified by powder XRD. X-ray patterns of the reagent was recorded at 2 theta = 10–80° range (Fig. 3). A broad peak centered at 2 theta angle showed strong crystalline peaks in the range 10–60° confirmed the nature of the TBATB reagent as crystalline.

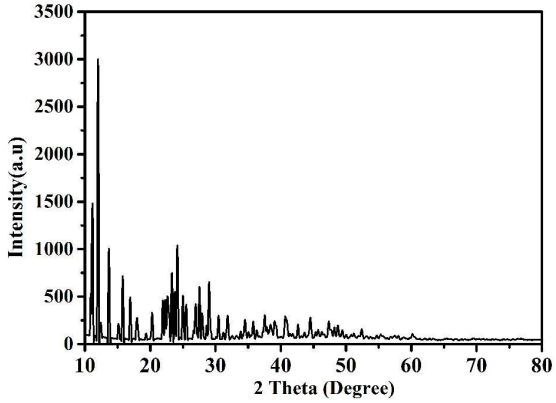

Fig. 3: Powder X-ray diffraction analysis of TBATB

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Experimental Section

Melting points are uncorrected and were determined in open capillary tubes using hot sulphuric 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. IR spectra were recorded using Perkin Elmer model-446 FTIR in KBr.^{1}H NMR spectra were recorded in DMSO–d_6 using TMS as an internal standard using Varian 400-MHz spectrometer instrument. Mass spectra were recorded on Agilent-LCMS instrument. Starting materials salicyladehydes, ethyl acetoacetate, liquid bromine and solvents like PEG-600 were obtained from commercial suppliers and were used as such.

General procedure for the preparation of 1 from salicylaldehyde:

A mixture of a salicylaldehyde (10 mM), ethyl acetoacetate (12 mM) and 25 mol% of L-proline in triethanolamine (5 mL) was stirred at RT for 30 min. The progress of the reaction was monitored by TLC. After the completion of reaction, the mixture was poured into ice-cold water (30 mL). The separated solid was filtered, washed and dried. The crude product was recrystallized from a methanol to obtain pure **1**.

Yield 1.80 g (96%). m.p.121-123 °C.

General procedure for the preparation of 4 from 1:

A mixture of **1** (1.88 g, 10 mmol), tetrabutylammonium tribromide (TBATB) (4.82 g, 10 mmol), xanthate salt (**3**) (10 mmol) and PEG-600 (30 mL) was stirred at RT for 1-1½ h. After completion of reaction, as indicated by TLC, 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 **4**.

O-methyl S-(2-oxo-2-(2-oxo-2H-chromen-3-yl)ethyl) carbonodithioate (4a)

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Yield = 2.58 g (88%); mp 196–198 °C (Chloroform); IR (KBr): 1263 cm^{-1} (strong, sharp, -C=S), 1690 cm^{-1} (strong, sharp, -CO of $-COCH_3$), 1715 cm^{-1} (strong, sharp, -CO of coumarin ring); ^{1}H-NMR (400 MHz, *DMSO-d_6*/ TMS): δ 3.72 (s, 3H, OC**H**$_3$), 4.90 (s, 2H, -C**H**$_2$), 4.80 (s, 2H, -C**H**$_2$), 7.43-8.08 (m, 4H, Ar-**H**), 8.84 (s, 1H, Ar-**H**); ^{13}C NMR (100 MHz, *DMSO-d_6*): 52.261, 55.211, 119.088, 119.255, 124.649, 128.892, 131.597, 134.409, 152.261, 158.761, 139.084, 194.649, 208.741; HRMS calculated for $C_{13}H_{10}O_4S_2$ $[M+H]^+$: 295. 0098, Found: 295.0103.

O-ethyl S-(2-oxo-2-(2-oxo-2H-chromen-3-yl)ethyl) carbonodithioate (4b)

Yield = 2.64 g (86%); M.P: 131–133 ^{0}C (Methanol); IR (KBr): 1236 cm^{-1} (strong, sharp, -C=S), 1695 cm^{-1} (strong, sharp, -CO of $-COCH_3$), 1733 cm^{-1} (strong, sharp, -CO of coumarin ring); ^{1}H-NMR (400 MHz, *DMSO-d_6*/TMS): δ 1.28 (t, 3H, C**H**$_3$), 4.58 (q, 2H, -OC**H**$_2$), 4.80 (s, 2H, -C**H**$_2$), 7.41-8.08 (m, 4H, Ar-**H**), 8.80 (s, 1H, Ar-**H**); ^{13}C NMR (100 MHz, *DMSO-d_6*): 22.322, 51.340, 73.478, 116.543, 118.180, 125.049, 127.291, 128.345, 131.257, 137.300, 153.061, 159.881, 197.208, 210.171; HRMS calculated for $C_{14}H_{12}O_4S_2$ $[M+H]^+$: 309.0255, Found: 309.0390

O-isopropyl S-(2-oxo-2-(2-oxo-2H-chromen-3-yl)ethyl) carbonodithioate (4c)

Yield = 2.89 g (90%); M.P: 173–175 ^{0}C (Ethanol); IR (KBr): 1236 (strong, sharp, -C=S), 1695 cm^{-1} (strong, sharp, -CO of $-COCH_3$), 1724 cm^{-1} (strong, sharp, -CO of coumarin ring); ^{1}H-NMR (400 MHz, *DMSO-d_6*/TMS): δ 1.30 (d, 6H, -C**H**$_3$), 4.75 (s, 2H, -C**H**$_2$), 5.60 (m, 1H, -C**H**), 7.43-8.02 (m, 4H, Ar-**H**), 8.79 (s, 1H, Ar-**H**); ^{13}C NMR (100 MHz, *DMSO-d_6*): 21.512, 21.536, 52.234, 67.098, 110.165, 118.567, 125.438, 127.954, 128.398, 131.271, 137.092, 154.042, 158.976, 196.841, 209.897; HRMS calculated for $C_{15}H_{14}O_4S_2$ $[M+H]^+$: 323.0411, Found: 323.0398

General procedure for the preparation of 6 from 1:

A mixture of **1** (1.88 g, 10 mmol), tetrabutylammonium tribromide (TBATB) (4.82 g, 10 mmol),

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corresponding heterylthiol (**5**) (10 mmol) and PEG-600 (30 mL) was stirred at RT for 2-3 h. After completion of reaction, as indicated by TLC, 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 **6**.

3-(2-((1H-benzo[d]imidazol-2-yl)thio)acetyl)-2H-chromen-2-one (6a): Yield = 2.82 g (84%); M.P: 161–163 ^{0}C (Ethanol); IR (KBr): 1684 cm^{-1} (strong, sharp, -CO of –$COCH_2$), 1745 cm^{-1} (strong, sharp, -CO of coumarin ring), 3420-3440 cm^{-1} (broad, medium, -NH group); ^{1}H-NMR (400 MHz, *DMSO-d_6*/TMS): δ 4.82 (s, 2H, -C**H**$_2$), 7.04-8.16 (m, 8H, Ar-**H**), 8.33 (s, 1H, Ar-**H**), 11.02 (s, 1H, -N**H**); ^{13}C-NMR (100 MHz, *DMSO-d_6*/TMS): 49.0, 119.8, 120.0, 126.1, 126.2, 126.9, 127.5, 128.0, 128.8, 129.6, 134.1, 135.2, 139.8, 147.0, 152.4, 161.2, 196.1; HRMS calculated for $C_{18}H_{12}N_2O_3S$ $[M+H]^+$: 337.0646, Found: 337.0650

3-(2-(Benzo[d]oxazol-2-ylthio)acetyl)-2H-chromen-2-one (6b): Yield = 2.93 g (87%); M.P: 157–159 ^{0}C (Methanol); IR (KBr): 1684 cm^{-1} (strong, sharp, -CO of –$COCH_2$), 1727 cm^{-1} (strong, sharp, -CO of coumarin ring); ^{1}H-NMR (400 MHz, *DMSO-d_6*/TMS): δ 5.16 (s, 2H, -C**H**$_2$), 7.11-8.03 (m, 8H, Ar-**H**), 8.86 (s, 1H, Ar-**H**); ^{13}C NMR (100 MHz, *DMSO-d_6*): 45.621, 110.642, 116.178, 118.196, 119.429, 123.988, 124.286, 125.690, 127.900, 128.316, 131.231, 137.685, 141.290, 151.873, 153.084, 159.465, 165.023, 197.031; HRMS calculated for $C_{18}H_{11}NO_4S$ $[M+H]^+$: 338.0487, Found: 338.0518.

3-(2-(Benzo[d]thiazol-2-ylthio)acetyl)-2H-chromen-2-one (6c): Yield = 2.83 g (80%); M.P: 238–240 ^{0}C (Acetone); IR (KBr): 1675 cm^{-1} (strong, sharp, -CO of –$COCH_2$), 1725 cm^{-1} (strong, sharp, -CO of coumarin ring); ^{1}H-NMR (400 MHz, *DMSO-d_6*/TMS): δ 5.20 (s, 2H, -C**H**$_2$), 7.15-8.03 (m, 8H, Ar-**H**), 8.88 (s, 1H, Ar-**H**); ^{13}C NMR (100 MHz, *DMSO-d_6*): 46.082, 109.487, 115.998, 118.763, 120.193, 123.075, 124.656, 126.560, 127.785, 128.676, 131.441, 139.993,

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142.054, 152.873, 154.128, 160.002, 166.163, 196.987; HRMS calculated for $C_{18}H_{11}NO_3S_2$ $[M+H]^+$: 354.0253, Found: 354.0258.

Alternative method for the preparation of 6 from 4a:

A mixture of 4a (1.88 g, 5 mmol), 5 mmol each of o-phenylenediamine (**7a**), o-aminophenol (**7b**) & o-aminothiophenol (**7c**) independently was refluxed in ethanol (30 mL) for a period of 2-4 h on a water bath. After completion of reaction, as indicated by TLC, the mixture was poured into ice-cold water (60 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 **6**.

6a: Yield = 0.65 g (39%);

6b: Yield = 0.74 g (42%);

6c: Yield = 0.74 g (44%);

General procedure for the preparation of 9 from 1:

A mixture of **1** (1.88 g, 10 mmol), tetrabutylammonium tribromide (TBATB) (4.82 g, 10 mmol), corresponding phenylthiourea (**8**) (10 mmol) and PEG-600 (30 mL) was stirred at RT for 2-4 h. After completion of reaction, as indicated by TLC, 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 **9**.

3-(2-(Phenylamino)thiazol-4-yl)-2H-chromen-2-one (9a)

Yellow solid, Yield = 2.81 g (88%); 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, 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, -NH); ^{13}C NMR (100 MHz, *DMSO-d_6*): 110.366, 116.336, 117.570, 119.754, 120.792, 121.925, 125.162, 129.470, 129.601,

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132.140, 139.084, 141.440, 144.088, 152.775, 159.291, 162.993; HRMS calculated for $C_{18}H_{12}O_2N_2S$ $[M+H]^+$: 321.0697, Found: 321.0707.

3-(2-((4-Chlorophenyl)amino)thiazol-4-yl)-2H-chromen-2-one (9b)

Yellow solid, Yield = 2.86 g (81%); mp > 250 °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, 1H, Ar-**H**), 7.36-7.66 (m, 5H, Ar-**H**), 7.82 (s, 1H, Ar-**H**), 7.92 (d, 1H, Ar-H), 8.48 (d, 1H, Ar-H), 8.71 (s, 1H, Ar-**H**) and 9.79 (s, 1H, -N**H**); ^{13}C NMR (100 MHz, *DMSO-d_6*): 115.035, 115.334, 115.823, 118.820, 118.984, 119.276, 120.624, 124.213, 127.952, 130.844, 136.960, 138.273, 143.706, 152.363, 156.010, 159.196, 159.341, 163.057; 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)-2H-chromen-2-one (9c)

Yellow solid, Yield = 279 g (79%); mp 154-156 °C (Ethanol); IR(KBr) νmax/ cm^{-1}: 1720 cm^{-1} (strong, sharp, -CO of coumarin ring), 3390-3450cm^{-1} (broad, medium, -NH group); ^{1}H NMR (400 MHz, *DMSO-d_6*/ TMS): δ 7.11 (t, 1H, Ar-**H**), 7.37-7.65 (complex, m, 5H, Ar-H), 7.82 (s, 1H, Ar-**H**), 7.91 (d, 1H, Ar-**H**), 8.48 (d, 1H, Ar-**H**), 8.61 (s, 1H, Ar-**H**) and 9.81 (s, 1H, -N**H**); ^{13}C NMR (100 MHz, *DMSO-d_6*): 109.473, 115.574, 118.147, 119.033, 120.364, 124.051, 125.445, 127.819, 128.265, 130.707, 136.960, 137.077, 138.120, 139.308, 143.537, 152.136, 159.056, 162.153; 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)-2H-chromen-2-one (9d)

Yellow solid, Yield = 3.08 g (83%); 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, 2H, Ar-**H**), 7.40 (t, 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

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NMR (100 MHz, *DMSO-d_6*): 117.731, 118.595, 119.698, 120.685, 125.219, 129.245, 132.189, 138.627, 139.653, 139.850, 143.921, 151.210, 152.773, 153.600, 159.189, 162.633; HRMS calculated for $C_{18}H_{10}ClFN_2O_2S$ $[M+H]^+$: 373.0213, Found: 373.0402.

3-(2-(4-Tolylamino)thiazol-4-yl)-2H-chromen-2-one (9e)

Yellow solid, Yield = 2.83 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*): 21.243, 110.012, 115.322, 119.123, 119.854, 120.839, 125.055, 128.152, 128.460, 133.223, 139.228, 140.126, 144.074, 152.456, 159.569, 162.243; LCMS (CI): m/z = 335 $[M^{\cdot+}+1]$.

3-(2-((4-Fluorophenyl)amino)thiazol-4-yl)-2H-chromen-2-one (9f)

Yellow solid, Yield = 2.70 g (80%); mp 126–128 °C (Methanol); IR(KBr) νmax/ cm^{-1}: 1728 cm^{-1} (strong, sharp, -CO of coumarin ring), 3385-3445 cm^{-1} (broad, medium, -NH group); ^{1}H NMR (400 MHz, *DMSO-d_6*/ TMS): δ 7.41-7.47 (complex, m, 4H, Ar-**H**),7.62 (d, 1H, Ar-**H**), 7.64 (s, 1H, Ar-**H**), 7.67 (d, 1H, Ar-**H**),7.81(t, 3H, Ar-**H**), 7.97 (d, 1H, Ar-**H**), 8.71 (s, 1H, Ar-**H**) and 10.50 (s, 1H, -N**H**); ^{13}C NMR (100 MHz, *DMSO-d_6*): 110.373, 115.847, 117.009, 117.222, 118.135, 119.114, 120.201, 124.711, 128.743, 131.691, 138.128, 138.562, 143.420, 152.273, 158.676, 162.114; LCMS (CI): m/z = 339 $[M^{\cdot+}+1]$.

3-(2-((4-Methoxyphenyl)amino)thiazol-4-yl)-2H-chromen-2-one (9g)

Yellow solid, Yield = 2.83 g (81%); mp 192-194 °C (Acetonitrile); IR(KBr) νmax/ cm^{-1}: 1716 cm^{-1} (strong, sharp, -CO of coumarin ring), 3386-3448 cm^{-1} (broad, medium, -NH group); ^{1}H NMR (400 MHz, *DMSO-d_6*/ TMS): δ 3.18 (s, 1H, OC**H**$_3$), 6.98 (d, 1H, Ar-**H**), 7.39-7.68 (m, 5H,

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Ar-**H**), 7.72 (s, 1H, Ar-**H**), 7.95 (d, 1H, Ar-**H**), 8.67 (s, 1H, Ar-**H**) and 10.17 (s, 1H, -N**H**); ^{13}C NMR (100 MHz, *DMSO-d_6*): 55.211, 109.235, 114.336, 115.821, 119.088, 119.253, 120.246, 124.649, 128.892, 131.597, 134.409, 138.488, 143.342, 152.261, 154.333, 158.767, 163.234; HRMS calculated for $C_{19}H_{14}N_2O_3S$ $[M+H]^+$: 351.0803, Found: 351.0809.

3-(2-((4-Nitrophenyl)amino)thiazol-4-yl)-2H-chromen-2-one (9h)

Yellow solid, Yield = 3.17 g (75%); 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, 1H, Ar-**H**), 7.37-7.65 (complex, m, 5H, Ar-**H**), 7.82 (s, 1H, Ar-**H**), 7.91 (d, 1H, Ar-**H**), 8.48 (d, 1H, Ar-**H**), 8.61 (s, 1H, Ar-**H**) and 9.81 (s, 1H, -N**H**); ^{13}C NMR (100 MHz, *DMSO-d_6*): 110.789, 116.347, 119.048, 119.754, 120.690, 125.155, 129.352, 129.460, 132.183, 139.228, 140.326, 144.074, 152.796, 159.269, 162.633; LCMS (CI): m/z = 366 $[M^{\cdot+}+1]$.

CONCLUSION:

In summary, we have demonstrated a simple and efficient one-pot method for the direct reaction of 3-acetyl-2*H*-chromen-2-one with different heterylthiols, phenylthioureas & their derivatives by employing TBATB as a reagent in PEG-600. The notable advantages of the present protocol are excellent yields, shorter reaction times, easy & safe handling of reagent. Due to its operational simplicity, generality and efficacy this method is expected to have wider applicability for the preparation of various other compounds with other acetophenone derivatives. Thus, TBATB was found to be the most benign alternative for the toxic bromine and are capable of facilitating a host of organic transformation reagents on a wide variety of substrates.

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PEG-600 mediated one-pot reaction of 3-acetyl-2*H*-chromen-2-one with heterylthiols and phenylthioureas using Tetrabutylammonium Tribromide as an efficient green reagent

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GRAPHICAL ABSTRACT