New Synthetic Methodology For The Ethyl[2-(2H-Chromene-3yl)-4-Oxo-1,3-Thiazolidin-3-yl]Acetates

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ABSTRACT
2H-3-chromene carbaldehydes react with glycine ethyl ester hydrochloride salt, and mercapto acetic acid in the presence of diisopropylethylamine to give ethyl [2-(2H-chromene-3yl)-4-oxo-1,3-thiazolidin-3-yl]acetates. The products obtained in good yields and mechanism of this reaction was discussed.

Keywords: 2H-3-chromene carbaldehydes, Thiazolidinones, DIPEA, mercapto acetic acid and 2-(2H-chromene-3yl)-4-oxo-1,3-thiazolidin-3-yl]acetates.

INTRODUCTION
Chromene and its derivatives are biologically interesting compounds in addition to others (given in earlier Paper) exhibit antidepressant effects[1], inhibitory effect on influenza virus sialidases[2,3], DNA breaking activities and mutagenicity[4], antiviral activities[5] and act as sex pheromone homologues[6]. On the other hand thiazolidinones are one class of heterocycles that has attracted much attention because they have a wide range of biological activities including antifungal, anti-bacterial, antihistaminic, antimicrobial, and anti-inflammatory activities[7]. Thiazolidinone derivatives are well known in medicinal chemistry because of their diverse pharmaceutical action such as anticonvulsant[8], cardiovascular[9] and antihelminthic properties[10]. These are heterocyclic compounds that have an atom of sulfur at position 1, an atom of nitrogen at position 3, and a carbonyl group at position 4[11] Heterocyclic compounds are cyclic compounds with at least two different elements as ring member atoms[12]. They are the counter parts of homocyclic compounds, which have ring atoms from the same element. Thiazolidinone, a saturated form of thiazole, with a carbonyl group on the fourth carbon, has been considered to have a large number of biological activities. In view of the several biological activities of Chromene and thiazole derivatives, we are interested synthesis of ethyl [2-(2H-chromene-3yl)-4-oxo-1,3-thiazolidin-3-yl] acetate derivatives as shown in scheme-1.
Scheme 1. Synthesis of ethyl [2-(2H-chromene-3yl)-4-oxo-1,3-thiazolidin-3-yl]acetate derivatives (4-6).

MATERIALS AND METHODS

General methods: Reagents were purchased from commercial sources and were used as received. $^1$H NMR spectra were obtained on a Bruker AVANCE 400 spectrometer at 400 MHz or Bruker AVANCE 300 spectrometer at 300 MHz with tetramethylsilane used as an internal reference. $^{13}$C NMR spectra were obtained on a Bruker AVANCE 300 spectrometer at 100 MHz with the solvent peak used as the reference. Thin-layer chromatography (TLC) was performed using Whatman No. 4500-101 (Diamond No. MK6F silica-gel 60 Å) plates. Visualization of TLC plates was performed using UV light (254 nm). Mass spectra record on mass spectrometer.

General procedure for synthesis of substituted salicylaldehydes (2):
To a mixture of substituted phenol (1) (100 mmol), polyethylene glycol (PEG 400) (2.0 mL), CHCl$_3$ (20 mL), 50% aq. KOH (80 mL) was added during the period of 30 min. stirring was continued for an additional 30 min. The solvent was removed and the residue acidified with 2N H$_2$SO$_4$ (300 mL). After steam distillation and recrystallisation from hexane/chloroform (3:1), to furnish amidoxime (2) in good yields.

General procedure for synthesis of 2H-3-chromene-carbaldehydes (3):
To a solution of substituted salicylaldehyde (2) (100 mmol) in dioxane (80 mL) anhydrous K$_2$CO$_3$ (100 mmol) and acrolein (100 mmol) was added and refluxed on oil bath for 2 h. After completion of the reaction, the solvent was decanted and dioxane was distilled off under reduced pressure and the resultant crude was treated with crushed ice (100 g). The resultant solution was extracted with ether, dried and concentrated. It was column chromatographed over 60-120 mesh silica gel and eluted with chloroform to furnish amidoxime (3) in good yields.

2H-3-chromene-carbaldehyde (3a): Light yellowish liquid (10.4 g, 65% yield). IR (KBr): 1669 cm$^{-1}$ (C=O) and 1576 cm$^{-1}$ (C=C). UV (MeOH): 360 nm (log ε 4.4) and 288 nm (log ε 4.6). $^1$H NMR (CDCl$_3$, 400 MHz): δ 9.55 (s, CHO), 2.72 (m, H-4, 5.7), 6.91 (m, H-6), 6.81 (d, J = 8.3 Hz, H-8), 5.00 (s, OCH$_3$). $^{13}$C NMR (CDCl$_3$, 100 MHz): δ 189.8 (C0), 156.0 (C-8a), 141.2 (C-4), 133.2 (C-7), 131.6 (C-3), 130.8 (C-5).

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129.4 (C-5), 121.9 (C-6), 120.5 (C-4a), 11 63.1 (C-2). MS: m/z 160(M\(^+\)) (70), 13 1(100) and 104(15).

Analysis: Found C, 74.84, H, 5.11. C\(_{10}H_{10}O_2\) requires C, 74.99, H, 5.03%.

6-Chloro-2H-3-chromencarbaldehyde (3b):Pale yellow needles, mp 89°C.IR (KBr): 1672 cm\(^{-1}\)(C=O) and 1560 cm\(^{-1}\)(C=C).UV (MeOH): 384 nm (log \(\varepsilon\) 4.5) and 298 nm (log \(\varepsilon\) 4.7).\(^1\)H NMR (CDCl\(_3\), 400MHz): \(\delta\) 9.57 (s, CHO), 7.07-7.28 (m, H-4, 5, 7), 6.78 (d, \(J = 83\) Hz, H-8), 5.00 (s, OCH\(_3\)).\(^13\)C NMR (CDCl\(_3\), 100 MHz): \(\delta\) 189.4 (C=O), 154.3 (C-8a), 139.4 (C-4), 132.5 (C-7), 131.2 (C-3), 128.4 (C-5), 126.6 (C-6), 121.5 (C-4a), 117.8 (C-8), 63.4 (C-2). MS: m/z 194(M) (60), 165(80) and 13 1(10). Analysis: Found C, 61.89, H, 5.30%.

Ethyl 175(100), 145(45) and 131(50).

Thiazolidine carbaldehydes (3c): Pale yellow needles, mp 105 °C.IR (KBr): 1666 cm\(^{-1}\)(C=O) and 1560 cm\(^{-1}\)(C=C). UV (MeOH): 364 nm (log \(\varepsilon\) 4.2) and 250 nm (log \(\varepsilon\) 4.5).\(^1\)H NMR (CDCl\(_3\), 400MHz): \(\delta\) 9.58 (s, CHO), 7.24-7.39 (m, H-5, 7), 7.12 (s, H-4), 6.74 (d, \(J = 8.3\) Hz, H-8), 5.01(s, OCH\(_3\)).\(^13\)C NMR (CDCl\(_3\), 100 MHz): \(\delta\) 189.3 (C=O), 154.8 (C-8a), 139.2 (C-4), 135.4 (C-7), 132.3 (C-3), 131.3 (C-5), 122.1 (C-4a) 118.2 (C-8), 113.7 (C-6), 63.3 (C-2). MS: m/z 239(M\(^+\))(100), 211(95) and 131(30). Analysis: Found C, 50.41, H, 2.73.

General procedure for synthesis of ethyl [2-(2H-chromene-3-yl)-4-oxo-1,3-thiazolidin-3-ylacetates (4): A mixture of glycine ethyl ester hydrochloride salt (12 mmol), 2H-3-chromencarbaldehyde (24 mmol), mercaptoacetic acid (36 mmol) and diisopropylethylamine (15 mmol) in 50 mL of benzene was heated to reflux with a Dean-Stark trap for 18 h during which time about 0.5 mL of water was collected in the trap. The reaction mixture was cooled to room temperature and diluted with EtOAc. The organic phase was washed with saturated NaHCO\(_3\), 1N HCl and saturated NaCl. The organic solution was dried with MgSO\(_4\) and concentrated to give a light brownish oil, which was chromatographed over silica gel (60-120 mesh) by eluting with pet.ether: ethyl acetate (9:1) to afford


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Ethyl[2-(6-bromo-2H-chromene-3-yl)-4-oxo-1,3-thiazohdin-3-yl]acetate (77e): Light brown colored semi solid. (72% yield).IR (KBr): 1678 cm⁻¹(C=O). UV (MeOH): 338 nm (log ε 4.1), 281 nm (log ε 4.5) and 246 nm (log ε 4.1).¹H NMR (CDCl₃, 400 MHz): δ 7.21 (m, H-7'), 7.11 (d, J = 1.0 Hz, H-5'), 6.70 (d, J = 8.3 Hz, H-8'), 6.42 (s, H-5), 5.46 (s, H-2), 4.85 (d, J = 13.5 Hz, OCH of 2'-OCH₂), 4.59 (d, J = 13.5 Hz, OCH of 2'-OCH₂), 4.38 (d, J = 17.3 Hz, S-CH), 4.18 (q, J = 6.7 Hz, COOCH₂CH₃), 3.66 (q, J = 6.7 Hz, N-CH₂), 3.55 (d, J = 17.3 Hz, S-CH), 1.26 (t, J = 6.7 Hz, COOCH₂CH₃).¹³C NMR (CDCl₃, 100 MHz): δ 172.3 (C=O at C-4), 168.2 (COOCH₂CH₃), 154.8 (C-8a), 132.3 (C-3'), 130.7 (C-7'), 129.8 (C-5'), 129.3 (C-4'), 124.2 (C-4a), 112.6 (C-8'), 109.8 (C-6'), 64.8 (C-2'-OCH₂), 62.1 (C-2), 61.6 (COOCH₂CH₃), 41.5 (N-CH₂), 31.4 (S-CH₂), 14.0 (COOCH₂CH₃). MS: m/z 399[M+H]⁺.

Ethyl-2-(6-methyl-2H-chromene-3-yl)-4-oxo-1,3-thiazolidin-3-yl acetate (4d): Colorless semi solid. (68% yield).IR (KBr): 1690 cm⁻¹(C=O).UV (MeOH): 351 nm (log ε 4.4), 276 nm (log ε 4.3) and 233 nm (log ε 4.1).¹H NMR (CDCl₃, 400 MHz): δ 6.79-7.16 (m, H-5', 7, 8'), 6.48 (s, H-4'), 5.37 (s, H-2), 4.80 (d, J = 13.5 Hz, OCH of 2'-OCH₂), 4.54 (d, J = 13.5 Hz, OCH of 2'-OCH₂), 4.38 (d, J = 17.3 Hz, S-CH), 4.10 (q, J = 6.7 Hz, COOCH₂CH₃), 3.77 (s, 6'-CH₃), 3.52 (m, S-CH and N-CH₂), 1.26 (t, J = 6.7 Hz, COOCH₂CH₃).¹³C NMR (CDCl₃, 100 MHz): δ 172.5 (C=O at C-4), 168.4 (COOCH₂CH₃), 133.8 (C-6'), 150.1 (C-8a), 130.1 (C-3'), 126.3 (C-4'), 122.8 (C-4a), 117.0 (C-7'), 114.6 (C-5'), 112.2 (C-81), 64.6 (C-2'-OCH₂), 62.5 (C-2), 61.9 (COOCH₂CH₃), 55.4 (C-6'-CH₃), 41.8 (N-CH₂), 31.6 (S-CH₂), 14.0 (COOCH₂CH₃). MS: m/z 350[M+H].

Ethyl-2-(2-(2-methyl-2H-chromene-3-yl)-4-oxo-1,3-thiazoilcin-3-yl)acetate(4e):Light brown semi solid. (72% yield).IR (KBr): 1675 cm⁻¹(C=O).UV (MeOH): 360 nm (log ε 4.1), 285 nm (log ε 4.4) and 245 nm (log ε 4.5).¹H NMR (CDCl₃, 400 MHz): δ 6.75-7.20 (m, H-5', 6', 7', 8), 6.50 (s, H-4'), 5.49 (s, H-2'), 4.57 (d, J = 13.5 Hz, 2'-CH₃), 4.40 (d, J = 17.3 Hz, S-CH), 4.18 (q, J = 6.7 Hz, COOCH₂CH₃), 3.64 (m, S-CH and N-CH₂), 1.25 (t, J = 6.7 Hz, COOCH₂CH₃).¹³C NMR (CDCl₃, 100 MHz): δ 171.9 (C=O at C-4), 167.7 (COOCH₂CH₃), 154.1 (C-8a), 130.3 (C-7'), 128.8 (C-3), 127.2 (C-5'), 125.6(C-4), 121.7(C-3'), 121.4(C-4a), 111.9(C-8'), 115.9(C-8'), 115.8(C-2'-CH₃), 62.2(C-2), 61.7(COOCH₂CH₃), 44.0(N-CH₂), 32.0(S-CH₂), 14.0(COOCH₂CH₃). MS: m/z 333(M⁺)(20),260(35), 159(100).

Ethyl-2-(2-(6-chloro-2-methyl-2H-chromene-3-yl)-4-oxo-1,3-thiazolidin-3-yl)acetate(4f). Light brown Colored semi solid. (68% yield).IR (KBr): 2284 cm⁻¹(C=O).UV (MeOH): 345 nm (log ε 4.6), 275 nm (log ε 4.3) and 300 nm (log ε 4.2).¹H NMR (CDCl₃, 400MHz): δ 6.90-7.24 (m, H-5', 7', 8), 6.79 (d, J = 8.3 Hz, H-8'), 6.38 (s, H-4'), 5.39 (s, H-2), 4.77 (d, J = 13.5 Hz, 2'-CH₃), 4.32 (d, J = 17.3 Hz, S-CH), 4.09 (q, J = 6.7 Hz, COOCH₂CH₃), 3.58 (m, S-CH and N-CH₂), 1.17 (t, J = 6.7 Hz, COOCH₂CH₃).¹³C NMR (CDCl₃, 100MHz): δ 174.3 (C=O at C-4), 165.2 (COOCH₂CH₃), 155.7 (C-8a),132.5 (C-3'), 129.5 (C-7'), 128.9 (C-4), 127.5 (C-4a), 121.9 (C-5), 115.2 (C-8'), 64.8 (C-2'-CH₃), 62.1 (C-2), 61.5 (COOCH₂CH₃), 43.5(N-CH₂),32.6(S-CH₂),14.0(COOC₃CH₃).MS:m/z 367 [M+H]⁺.

Ethyl-2-(2-(6-bromo-2-methyl2H-chromrene-3-yl)-4-oxo-1,3-thiazhidin-3-yl)acetate(4g): Light brown colored semi solid. (75% yield). IR (KBr): 1878 cm⁻¹(C=O).UV (MeOH): 335 nm (log ε 4.1), 285 nm (log ε 4.5) and 250 nm (log ε 4.1).¹H NMR (CDCl₃, 400 MHz): δ 7.21 (m, H-7'), 7.11 (d, J = 3.0 Hz, H-5'), 6.75 (d, J = 8.3 Hz, H-8'), 6.43 (s, H-4'), 5.46 (s, H-2), 4.59 (d, J = 13.5 Hz, 2'-CH₃), 4.38 (d, J = 17.3 Hz, S-CH), 4.18 (q, J = 6.7 Hz, COOCH₂CH₃), 3.66 (q, J = 6.7 Hz, N-CH₂), 3.55 (d, J = 17.3 Hz, S-CH), 1.26 (t, J = 6.7 Hz, COOCH₂CH₃).¹³C NMR (CDCl₃, 100 MHz): δ 175.3 (C=O at C-4), 168.2 (COOCH₂CH₃), 155.8 (C-8a),132.3 (C-3'), 130.7 (C-7'), 129.8 (C-5'), 131.3 (C-4'), 124.2 (C-4a), 112.6 (C-8'), 64.8 (C-2'-OCH₂), 62.1 (C-2), 61.6 (COOCH₂CH₃), 42.5 (N-CH₂), 31.4 (S-CH₂), 15.0 (COOCH₂CH₃). MS: m/z 412[M+H]⁺.
Ethyl 2-(2-2,6-dimethyl-2H-chromene-3yl)-4-oxa- 1, 3-thiazolidin-3-yl] acetate (4h): Colorless semi solid. (70% yield). IR (KBr): 1690 cm\(^{-1}\)(C=O).UV (MeOH): 355 nm (log \(\varepsilon\) 4.4), 275 nm (log \(\varepsilon\) 4.3) and 245 nm (log \(\varepsilon\) 4.1); H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 6.75-7.15(m, H-5', 7, 8'), 6.48(s, H-4'), 5.37(s, H-2), 4.85(d, J = 13.5 Hz, CH\(_3\)), 4.38 (d, J = 17.3 Hz, S-CH), 4.10 (q, J = 6.7 Hz, COOCH\(_2\)CH\(_3\)), 3.75 (s, 6'-CH\(_3\)), 3.55 (m, S-CH and N-CH\(_3\)), 1.24 (t, J = 6.7 Hz, COOCH\(_2\)CH\(_3\)), \(^{13}\)C NMR (CDCl\(_3\), 100 MHz): \(\delta\) 175.5 (C=O at C-4), 165.4 (COOCH\(_2\)CH\(_3\)), 135.8 (C-6'), 150.1 (C-8a), 130.1 (C-3'), 126.3 (C-4'), 122.8(C-4a), 117.0 (C-7'), 114.6 (C-5'), 112.2 (C-81), 64.6 (C-2'-OCH\(_2\)), 62.5 (C-2), 61.9 (COOCH\(_2\)CH\(_3\)), 55.4(C-6'-OCH\(_3\)), 42.8(N-CH\(_3\)), 31.6(S-CH\(_3\)), 14.5(COOCH\(_2\)CH\(_3\)).MS: m/z 347[M+H].

RESULTS AND DISCUSSION

The synthesis of ethyl [2-(2H-chromene-3yl)-4-oxa-1,3-thiazolidin-3-yl] acetates (4a-h) by the reaction of 2H-3 hromencarbaldehydes (3a-h) with amino acid ethyl ester hydrochloride salts and mercaptoacetic acid in presence of diisopropylethylamine.

Synthesis of ethyl [2-(2H-chromene-3yl)-4-oxo-1,3-thiazolidin-3-yl]acetates (4a-h): Ethyl [2-(2H-chromene-3yl)-4-oxo-1,3-thiazolidin-3-yl]acetates (4a-h) were obtained directly from 2H-3 chromencarbaldehydes (3a-d). 2H-3-chromencarbaldehydes (3a-h) in a one-step reaction with glycine ester hydrochloride salt and mercaptoacetic acid in presence of diisopropylethylamine gave ethyl 12-(2H-chromene-3yl)-4-oxo-1,3-thiazolidin-3-yl]acetates (4a-h).

Synthesis of substituted salicylaldehydes (2a-d): Substituted phenols (1a-d) on reaction with excess of chloroform in alkali medium and polyethylene glycol-400, a phase transfer catalyst (Riemer-Tiemann reaction) gave a mixture of salicylaldehydes (2a-d).

Synthesis of 2H-3-chromencarbaldehydes (3a-d):Equimolar quantities of salicylaldehyde (2a), acrolein, K\(_2\)CO\(_3\) were refluxed in dioxane for 2 h. After completion of the reaction, solution was decanted and excess of dioxane was removed by distillation under reduced pressure, the crude product was treated with crushed ice, filtration and recrystallisation gave, 2H-3-chromencarbaldehyde (3a). Its structure was established by analytical and spectral data. The structure of 2H-3-chromencarbaldehydes (3a) is established by its spectral data as follows. Its IR spectrum showed peaks due to aldehyde C=O at 1669 cm\(^{-1}\), C=C at 1576 cm\(^{-1}\). Its UV (MeOH) spectrum showed absorption bands at 360 nm (log \(\varepsilon\) 4.4) and 288nm (log \(\varepsilon\) 4.6) indicating the presence of cinnamaldehyde chromophore. In the \(^1\)H NMR of 3a the aldehyde proton resonated at \(\delta\) 9.55 as singlet and the 2-OCH\(_3\) appeared as a singlet at 8.500. The H-4, 5, 7 appeared as a multiplet at 8 7.12-7.29, the H-8 appeared at \(\delta\) 6.81 as a doublet (J = 8.3 Hz) and H-6 appeared at \(\delta\) 6.91 as a multiplet. In its \(^13\)C NMR of 3a the aldehyde carbon resonated at \(\delta\) 189.8, the OCH\(_3\) carbon at \(\delta\) 63.1, C-4 at 6 141.2 and C-3 at 6 131.6. The aromatic carbon signal assignments are \(\delta\) 120.5(C-4a), 129.4(C5), 121.9(C6), 133.2(C7), 116.5(C-8), 156.0(C-8a). The El mass spectrum of 3a showed the molecular ion peak at m/z 160 (M\(^+\) (70%)). The other ions were observed at m/z 131(100) and 104 (15)

The other 2H-3-chromencarbaldehydes (3b-d) were prepared as described above by the reaction of the salicylaldehydes(3b-d) with acrolein. Their analytical and spectral data is given in experimental section.

Synthesis of ethyl [2-(2H-chromene-3yl)-4-oxo-1,3-thiazotidin-3y1] acetates (4a-h): A mixture of glycine ester hydrochloride salt, 2H-3-chromene carbaldehydes (3a-h), mercapto acetic acid and diisopropylethylamine in benzene was heated to reflux with Dean-Star trap for 18 h to give ethyl [2-(2H-chromene-3yl)-4-oxo-1,3-thiazotidin-3y1]acetates (4a-h).

Ethyl [2-(2H-chromene-3yl)-4-oxo-1,3-thiazotidin-3y1] acetate (4a) is characterized from its spectral data. In the IR spectrum of 4a, the carboxyl group of thiazolidinone showed absorption at 1673 cm\(^{-1}\) Its UV (MeOH) spectrum showed bands at 349 nm (log \(\varepsilon\) 4.1), 282 nm (log \(\varepsilon\) 4.4) and 235 nm (log \(\varepsilon\) 4.5). In the \(^1\)H NMR spectrum of 4a recorded in CDCl\(_3\) (400 MHz) H-2 in the new thiazolidinone ring appeared as a singlet at \(\delta\) 5.49. The CH\(_2\)-5 protons are diastereotopic, one H-5 appeared at \(\delta\) 4.40 as doublet (J =

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17.3 Hz) and the other H-S overlapped on the N-CH$_2$ protons appeared as a multiplet at δ 3.64. The chemical shifts and multiplicities of H-2, CH$_2$-5 suggests that a new thiazolidinone ring formed, which is pendent at C-3 of the chromene. The N-CH$_2$ protons overlapping with one H-S appeared at δ 3.64 as a multiplet. The OCH$_2$ of COOEt appeared as a quartet at δ 4.18 (J = 6.7 Hz) and the CH$_3$ appeared at δ 1.25 as a triplet (J = 6.7 Hz). The other signals in $^1$H NMR spectrum are due to the chromene moiety: The OCH$_2$ protons at C-2 are diastereotopic, one of the OCH$_2$ proton appeared at δ 4.57 as a doublet (J = 13.5 Hz) and other OCH$_2$ proton appeared as a doublet at δ 4.83 (J = 13.5 Hz). H-4' appeared at δ 4.83 as a singlet and H-5',6',7',8' protons appeared as a multiplet at δ 6.75-7.20. In the $^{13}$C NMR spectrum (CDCl$_3$) (100 MHz) of ethyl [2-(2H-chromene-3y1)-4-oxo-1, 3-thiazolidin-3y1) acetate (4a), the carbon signal assignments due to the thiazolidinone ring are as follows: the C-4 carbonyl resonated at δ171.9, C-2 at δ 63.2 and C-5 at δ 32.0. The N-CH$_2$ appeared at δ 44.0, the OCH$_2$ and CH$_3$ of the ester group appeared at δ 61.7 and 14.0. The carbon signal assignments in the 2H-3-chromene moiety are as follows: δ 63.8 (C-2'), 128.8 (C-3'), 125.6 (C-4'), 121.4 (C-4'a), 127.2 (C-5'), 121.7 (C- 6'), 130.3 (C-7'), 115.9 (C-8') and 154.1 (C-8'a). In the .El mass spectrum of 4a the molecular ion appeared at ring 319(20%) and the other ions observed at m/z 244 (33), 175 (100) and 131 (50). The structures of compounds 4b-h were characterized from their analytical and spectral data, which are given in the experimental section.

Mechanism of the formation of thiazolidinones (4a-h): The first step is the formation of imines 5 by the reaction of aldehydes (3) with glycine ethyl ester hydrochloride salt in the presence of disopropylethylamine (base). Nucleophilic attack of the SR of mercaptaoactic acid on the imine carbon gives an intermediate 6. Base catalyzed cyclization of 6 by the elimination of water gives rise to thiazolidinones (4) as shown in Scheme 2. The intermediates 5 and 6 could not be isolated.

![Scheme 2. Mechanism of the formation of thiazolidinones (4a-h)](image)

APPLICATIONS

The synthesized compounds have lot of important biological activities.

CONCLUSIONS

In conclusion we have developed new heterocyclic system chromene contain thiazolidinones from chromene aldehyde. Overall, the synthetic strategy described here could be useful in constructing library of
small molecules based on Chromene contain 2-substituted thiazole framework. Additionally, the Chromene contain 2-substituted thiazole heterocyclic framework presented here could be an attractive template for the identification of novel and potential biologically active compounds.

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