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Synthesis of novel push-pull fluorescent dyes – 7-(diethylamino)furo[3,2-*c*]coumarin and 7-(diethylamino)thieno[3,2-*c*]coumarin derivatives

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Abstract: Novel push-pull fluorescent dyes, 7-(diethylamino) furo[3,2-*c*]coumarin and 7-(diethylamino)thieno[3,2-*c*]coumarin derivatives, were designed and synthesized using formyl derivatives of furo- and thieno[3,2-*c*]coumarins as key intermediates. Electron absorption and emission spectra of the dyes were recorded in different solvents. The longest-wave bands in the electron absorption spectra of the dyes are suggested to be of push-pull nature.

Keywords: coumarin; electron absorption spectra; fluorescence; push-pull dyes.

Introduction

Push-pull chromophore systems contain strong electron acceptor(s) (A) and donor(s) (D) attached to a π-conjugated spacer [1]. Such organic compounds are widely used in biotechnology as labels and probes, medical diagnostics [2–4], analytical chemistry [5, 6], material science including optoelectronic [7] and optical data storage devices [8], functional polymers [9] and devices based on application of efficient nonlinear optics (NLO) fluorophores [10, 11]. Study of complex biochemical processes both *in vitro* and *in vivo*, particularly in a real-time manner, often requires the use of spectroscopic probes the fluorescent properties of which significantly change upon chemical reaction, non-covalent interaction or reversible binding with target analytes [12–15]. Various coumarin derivatives show high fluorescence quantum yields and large Stokes shifts [16]. Coumarin dyes are used as laser dyes [17, 18], organic photosensitizers in dye-sensitized solar cells (DSSC) [19–21] and fluorescent labels [22] in biochemistry [23] or in medicinal chemistry [24].

The examples discussed above mainly deal with non-fused coumarins, while spectral properties of 3,4-annulated coumarins have not been extensively studied. It has been mentioned, however, that some derivatives of thieno[3,2-*c*]coumarin possess high fluorescent quantum yields (close to 100%) and show bathochromic shift of absorption and emission bands as compared with non-condensed analogs [25]. Thus, it can be suggested that annulation of coumarin with five-membered heterocycles such as furan and thiophene may lead to a bathochromic shift of absorption and emission bands and greater Stokes shifts compared to non-fused coumarin derivatives. Herein we report synthesis of new furo[3,2-*c*]coumarin and thieno[3,2-*c*]coumarin derivatives with large delocalized π-electron systems that include π-conjugated donor and acceptor fragments forming together an asymmetrical push-pull fluorophore (Figure 1). More specifically, the electron-releasing diethylamino substituent is located at position 7 of coumarin fragment and different electron-withdrawing groups (EWG) are present at the furan or thiophene ring that is fused to the 3 and 4 coumarin atoms.

Results and discussion

Synthesis

The target push-pull dyes **1a–g** and **2a,b** were prepared as depicted in Schemes 1–3. For the synthesis of dyes **1a–g**, the key starting material, 7-(diethylamino)-4-hydroxycoumarin (**4** in Scheme 1) was prepared by Pechmann reaction [26] of diphenyl malonate **3** with 3-diethylaminophenol. The malonate **3** was prepared in a higher yield of 68% by modification of the earlier reported protocols

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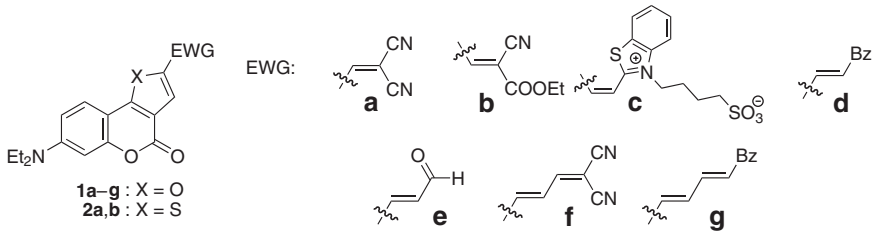
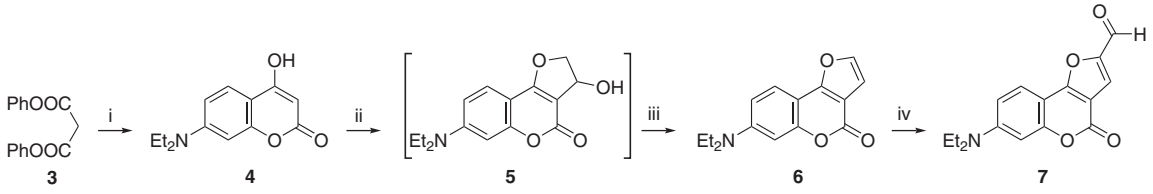


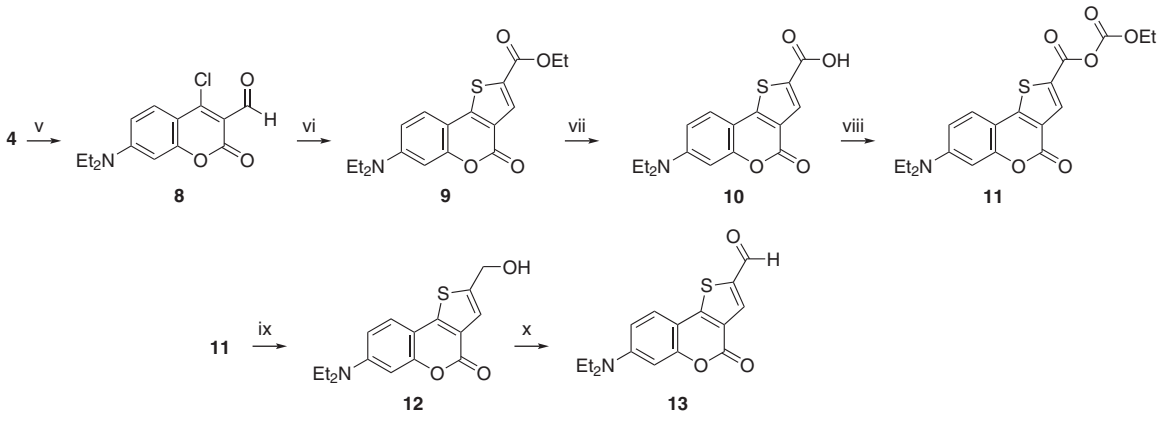
Figure 1 Push-pull fluorescent furocoumarin and thienocoumarin dyes **1a–g** and **2a,b**.

[27–29]. There are numerous methods of furocoumarins synthesis based on cross-coupling reactions of 3-substituted coumarins [30–32]. In this work, 7-(diethylamino)-furo[3,2-*c*]coumarin (**6**) was prepared following the earlier reported pathway (Scheme 1) [33]. Two-step reaction of the starting coumarin **4** with 2-chloroacetaldehyde in the presence of a potassium carbonate was conducted in one-pot manner without isolation of the intermediate product **5**. However, the diethylamino-substituted compound **6** was obtained with lower yield (40%) than the parent unsubstituted furo[3,2-*c*]coumarin reported earlier [34]. Vilsmeier-Haack formylation of compound **6** afforded product **7** in 45% yield.

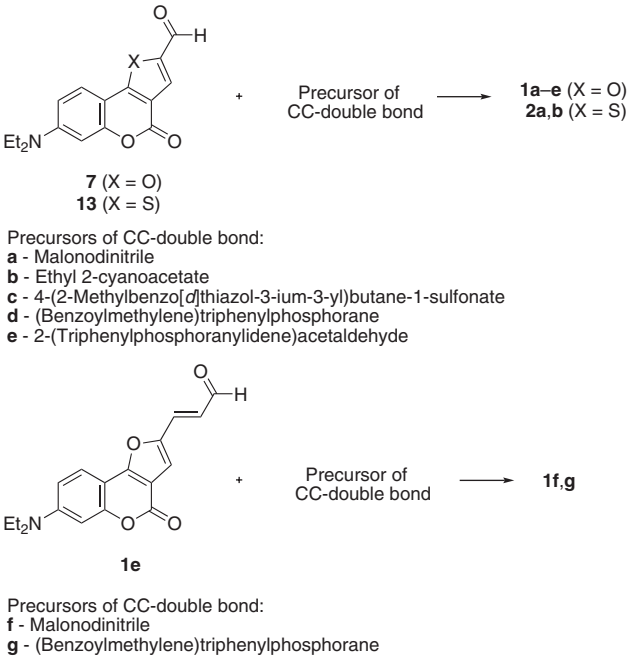
The synthetic route to push-pull dyes **2a,b** also started with substrate **4** but followed a different approach (Scheme 2). First, compound **4** was subjected to Vilsmeier-Haack formylation to give 4-chloro-3-formyl-7-diethylaminocoumarin (**8**) [29]. Then, reaction of compound **8** with ethyl 2-mercaptoacetate in dichloromethane in the presence of diisopropylethylamine (DIPEA) for 7 h afforded the thieno[3,2-*c*]coumarin **9** [34]. Since attempted reduction of ester **9** directly to the desired alcohol **12** using sodium borohydride failed, another methodology was applied. The successful approach to **12** involved hydrolysis of ester **9** followed by synthesis of a mixed anhydride **11** from the resultant acid **10** and the final reduction of compound **11**



Scheme 1 Reagents and conditions: (i) 3-diethylaminophenol, toluene, reflux, 8 h, yield 56%; (ii) 2-chloroacetaldehyde, aqueous K_2CO_3, 0°C; (iii) 40% HCl and (iv) DMF, $POCl_3$, 70°C, yield 45%.



Scheme 2 Reagents and conditions: (v) DMF, $POCl_3$, room temperature, yield 97%; (vi) ethyl 2-mercaptoacetate, DIPEA, dichloromethane, room temperature, yield 90%; (vii) (1) NaOH, EtOH/H_2O, reflux; (2) HCl, 91%; (viii) ethyl chloroformate, NEt_3, dichloromethane, room temperature, yield 94%; (ix) $NaBH_4$, THF, MeOH, yield 60% and (x) DMP, dichloromethane, room temperature, yield 75%.



Scheme 3 Synthesis of push-pull fluorescent furocoumarin and thienocoumarin dyes **1a–g** and **2a,b**.

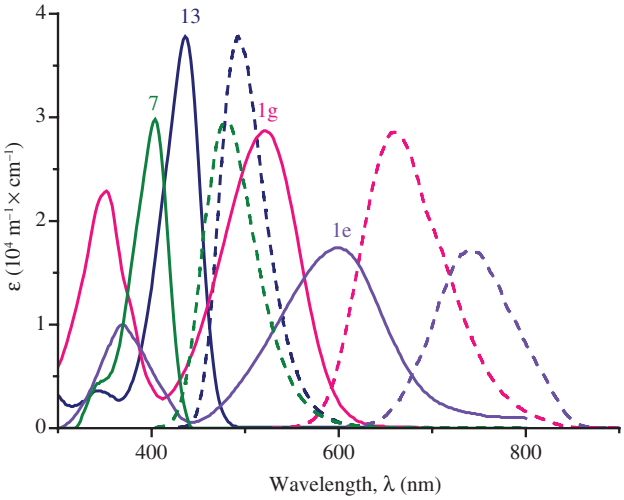


Figure 2 UV-vis absorption (solid lines) and fluorescence (dotted lines) spectra of new push-pull dyes in dichloromethane. Compound numbers are shown.

with sodium borohydride. Oxidation of the alcohol **12** by treatment with Dess-Martin reagent furnished aldehyde **13** in high yield and virtually no side products.

The furo[3,2-*c*]coumarin **7** (Scheme 1) and thieno[3,2-*c*]coumarin **13** (Scheme 2), obtained as discussed above, were the key precursors to the final products **1a–g** and **2a,b** (Scheme 3). Compounds **1a–c**,**f** and **2a,b** were prepared by the Knoevenagel condensation of **7** or **13** with various methylene compounds as CH-acids. Conversion of aldehyde **7** to conjugated carbonyl derivatives **1d,e** was carried out using Wittig reaction. Compound **1g** was also obtained by treatment of **1e** with a Wittig reagent.

Electron absorption and fluorescence spectra

Electron absorption spectra of the dyes in different solvents show an intense lowest energy charge-transfer (CT) absorption band in the near-UV-visible region. As expected, the location of this band is strongly influenced by the nature of electron-withdrawing substituent EWG attached to the 5-membered heterocycle [35–39]. Since the same electron-releasing group (diethylamino) is present in the coumarin core of all compounds, variation of electron-withdrawing groups at the five-membered ring is of interest for studying the absorption and emission spectra. For example, the absorption maximum of aldehyde **7** (λ_{abs} = 401 nm) is shifted bathochromically by 99 nm for α,β-unsaturated malonitrile **1a** (λ_{abs} = 500 nm) and further by 199 nm for α,β-unsaturated 2-benzothiazolium derivative **2c** (λ_{abs} = 600 nm). Fluorescence follows a similar pattern. Additional examples are shown in Figure 2. We are currently studying the molecular basis for these phenomena. It can be suggested that they are of push-pull nature.

Conclusions

Novel push-pull fluorescent dyes, 7-(diethylamino)-furo[3,2-*c*]coumarins and 7-(diethylamino)thieno[3,2-*c*]-coumarins, were synthesized using the corresponding formyl derivatives as starting materials. Effects of the structures on the spectral characteristics of the dyes are noted. The longest-wave transitions in electron absorption spectra of the new dyes are suggested to be of push-pull nature.

Experimental

Diphenyl malonate (**3**), 7-(diethylamino)-4-hydroxycoumarin (**4**) and 4-chloro-7-(diethylamino)-3-formylcoumarin (**8**) were prepared according to procedures reported by us previously [26]. All commercial reagents were used as received. Anhydrous toluene and dichloromethane were obtained by distillation over P_2O_5. Dry DMF was prepared by distillation over P_2O_5 under reduced pressure. Solvents used for UV-vis and fluorescence spectroscopy experiments were of spectral grade. Column chromatography was carried out using Macherey-Nagel Kieselgel 60 H silica gel. Analytical thin layer

chromatography was carried out using aluminum-backed plates coated with Macherey-Nagel Alugram SILG/UV_{254}; the compounds were visualized under UV light at 254 or 365 nm. Melting points were measured on a Stuart melting point apparatus SMP30 and are uncorrected. The ^{1}H NMR (500 MHz) and ^{13}C NMR (125 MHz) spectra were recorded on a Bruker spectrometer in solvents as indicated. The ESI-HR-MS data were obtained on a Bruker Daltonics MicroTof-Q II instrument operating in positive ionization mode. UV-vis absorption spectra were recorded using an SF-104 spectrophotometer (Interphotophysics LLC, Moscow, Russia).

7-(Diethylamino)-4*H*-furo[3,2-*c*]chromen-4-one (6)

Chloracetaldehyde (10 mmol, 1.27 mL in 20 mL H_2O) was added dropwise during 30 min to a stirred and cooled (0°C) solution of 7-(diethylamino)-4-hydroxycoumarin (**4**, 2.33 g, 10 mmol) in aqueous K_2CO_3 (2.76 g, 20 mmol, in 40 mL H_2O). The mixture was stirred at room temperature for 30 min, then treated with concentrated hydrochloric acid (4 mL) and stirred at room temperature for an additional 2 h. The mixture was neutralized with K_2CO_3 and extracted with dichloromethane. The extract was concentrated and the residue was chromatographed on silica gel eluting with dichloromethane to give yellow-pink crystals; yield 40%; mp 117–118°C; ^{1}H NMR ($CDCl_3$): δ 1.23 (6H, t, J = 7.0 Hz, 2× CH_3), 3.43 (q, 4H, q, J = 7.0 Hz, 2× CH_2), 6.64–6.69 (m, 2H, C(6)H, C(8)H), 6.91 (d, J = 2.1 Hz, 1H, CH-furo), 7.48 (d, J = 2.1 Hz, 1H, CH-furo), 7.64 (d, J = 8.6 Hz, 1H, C(5)H); ^{13}C NMR ($CDCl_3$): δ 11.9, 44.4, 97.8, 101.0, 105.6, 107.7, 108.6, 121.3, 142.3, 149.3, 154.7, 158.7, 158.8. HR-MS (ESI-TOF). Calcd for $C_{15}H_{15}NO_3$ [M + H]$^+$: *m/z* 258.1130. Found: *m/z* 258.1129.

7-(Diethylamino)-4-oxo-4*H*-furo[3,2-*c*]chromene-2-carbaldehyde (7)

$POCl_3$ (0.75 mL, 8 mmol) was added to a solution of 7-(diethylamino)furo[3,2-*c*]coumarin (**6**, 1.03 g, 4 mmol) in dry DMF (10 mL). The mixture was stirred at 80°C, analyzed by TLC and then poured onto aqueous NH_4OAc after completion of the reaction. The resulting precipitate was purified by silica gel chromatography using petroleum ether/EtOAc (2:1) as eluent to give yellow crystals; yield 45%; mp 143–145°C; ^{1}H NMR ($CDCl_3$): δ 1.26 (6H, t, J = 7.0 Hz, 2× CH_3), 3.47 (4H, q, J = 7.0 Hz, 2× CH_2), 6.63 (1H, d, J = 2.4 Hz, C(8)H), 6.72 (1H, dd, J = 2.4 Hz, J = 8.9 Hz, C(6)H), 7.68 (1H, s, CH-furo), 7.80 (1H, d, J = 8.9 Hz, C(5)H), 9.70 (1H, s, CHO); ^{13}C NMR ($CDCl_3$): δ 11.8, 44.5, 97.6, 99.2, 106.7, 109.1, 120.1, 122.9, 151.1, 151.3, 156.3, 157.4, 161.2, 176.1. HR-MS (ESI-TOF). Calcd for $C_{16}H_{15}NO_4$ [M + H]$^+$: *m/z* 286.1079. Found: *m/z* 286.1088.

General method for synthesis of compounds 1a–c

A solution of a C-H acid (1 equiv.) and a crystal of EDDA in ethanol was added dropwise to a hot solution of 7-(diethylamino)-4-oxo-4*H*-furo[3,2-*c*]chromene-2-carbaldehyde (**7**, 0.75–1 mmol) in ethanol (5 mL) and the mixture was stirred at room temperature for 2 h. The resultant precipitate was crystallized from ethanol.

2-((7-(Diethylamino)-4-oxo-4*H*-furo[3,2-*c*]chromen-2-yl)methylene)malononitrile (1a) This compound was obtained from **7** (285 mg, 1 mmol) and malonodinitrile (66 mg, 1 mmol) as a red powder; yield 70%; mp 208–210°C; ^{1}H NMR ($CDCl_3$): δ 1.28 (6H, t, J = 7.0 Hz, 2× CH_3), 3.49 (4H, q, J = 7.0 Hz, 2× CH_2), 6.61 (1H, d, J = 2.4 Hz, C(8)H), 6.73 (1H, dd, J = 2.4 Hz, J = 9.2 Hz, C(6)H), 7.46 (1H, s, CH-furo), 7.60 (1H, s, CH=), 7.74 (1H, d, J = 9.2 Hz, C(5)H); ^{13}C NMR ($CDCl_3$): δ 11.9, 44.7, 92.0, 97.5, 98.6, 108.0, 109.5, 112.4, 113.5, 121.7, 123.5, 140.0, 146.8, 151.7, 156.5, 156.6, 162.2. HR-MS (ESI-TOF). Calcd for $C_{19}H_{15}N_3O_3$ [M + H]$^+$: *m/z* 334.1192. Found: *m/z* 334.1207.

Ethyl 2-cyano-3-(7-(diethylamino)-4-oxo-4*H*-furo[3,2-*c*]chromen-2-yl)acrylate (1b) This compound was obtained from **7** (285 mg, 1 mmol) and ethyl 2-cyanoacetate (113 mg, 1 mmol) as an orange powder; yield 63%; mp 180–181°C; ^{1}H NMR ($CDCl_3$): δ 1.27 (6H, t, J = 7.0 Hz, 2× CH_3), 1.43 (3H, t, J = 7.0 Hz, CH_3), 3.48 (4H, q, J = 7.0 Hz, 2× CH_2), 4.41 (2H, q, J = 7.0 Hz, CH_2), 6.62 (1H, d, J = 2.4 Hz, C(8)H), 6.73 (1H, dd, J = 2.4 Hz, J = 9.2 Hz, C(6)H), 7.61 (1H, s, CH-furo), 7.80 (1H, d, J = 9.2 Hz, C(5)H), 7.99 (1H, s, CH=); ^{13}C NMR ($CDCl_3$): δ 11.8, 13.7, 44.6, 62.2, 97.6, 98.8, 99.2, 107.9, 109.3, 114.7, 119.8, 123.3, 136.8, 147.6, 151.2, 156.2, 157.0, 161.6, 162.0. HR-MS (ESI-TOF). Calcd for $C_{21}H_{20}N_2O_5$ [M + H]$^+$: *m/z* 381.1450. Found: *m/z* 381.1470.

4-(2-(2-(7-(Diethylamino)-4-oxo-4*H*-furo[3,2-*c*]chromen-2-yl)-vinyl)benzo[*d*]thiazol-3-ium-3-yl)butane-1-sulfonate (1c) This compound was obtained from **7** (214 mg, 0.75 mmol) and 4-(2-methylbenzo[*d*]thiazol-3-ium-3-yl)butane-1-sulfonate (203 mg, 0.75 mmol) in the presence of a crystal of EDDA in hot acetic acid (5 mL). The reaction mixture was heated under reflux for 8 h. The resulting precipitate was filtered off and purified by reverse-phase column chromatography using water/acetonitrile (10:1) as eluent to give dark-purple crystals; yield 69%; mp 237–239°C; ^{1}H NMR ($CDCl_3$/DMSO-d_6): δ 1.21 (6H, t, J = 7.3 Hz, 2× CH_3), 2.03 (2H, m, CH_2), 2.18 (2H, m, CH_2), 2.83 (2H, t, J = 6.7 Hz, CH_2), 3.47 (4H, q, J = 7.3 Hz, 2× CH_2), 4.97 (2H, t, J = 4.2 Hz, CH_2), 6.59 (1H, d, J = 2.4 Hz, C(8)H), 6.79 (1H, dd, J = 2.4 Hz, J = 8.2 Hz, C(6)H), 7.71 (1H), 7.78 (1H) (t, J = 8.9 Hz, *m,m′*-H(Ph)), 7.73 (1H, s, CH-furo), 8.04 (2H, s, CH=), 8.17 (1H, d, J = 8.2 Hz, C(5)H), 8.27 (2H, d, J = 8.9 Hz, *o,o′*-H(Ph)). ^{1}HR-MS (ESI-TOF). Calcd for $C_{28}H_{28}N_2O_6S_2$ [M + H]$^+$: *m/z* 553.1422. Found: *m/z* 553.1424.

General procedure for Wittig reaction of 7

A solution of aldehyde **7** (0.5–2 mmol) and a phosphorane reagent in dichloromethane was stirred at room temperature for 24 h under TLC control of the reaction. After removal of the solvent under reduced pressure, the oily residue was treated with ethanol (40 mL) and the resultant precipitate was crystallized from ethanol.

7-(Diethylamino)-2-(3-oxo-3-phenylprop-1-en-1-yl)-4*H*-furo-[3,2-*c*]chromen-4-one (1d) This compound was obtained from **7** (143 mg, 0.5 mmol) and (benzoylmethylene)triphenylphosphorane (209 mg, 0.55 mmol) as yellow crystals; yield 77%; mp 175–177°C; ^{1}H NMR ($CDCl_3$): δ 1.26 (t, J = 7.0 Hz, 6H, 2× CH_3), 3.46 (q, J = 7.0 Hz, 4H, 2× CH_2), 6.62 (d, J = 2.1 Hz, 1H, C(8)H), 6.70 (dd, J = 2.1 Hz, J = 8.9 Hz, 1H, C(6)H), 7.15 (s, 1H, CH-furo), 7.53–7.65 (m, 5H, $3H_{ar} + H_\alpha + H_\beta$), 7.76 (d, J = 8.9 Hz, 1H, C(5)H), 8.08 (d, J = 7.0 Hz, 2H, $2H_{ar}$); ^{13}C NMR ($CDCl_3$): δ 11.9, 44.4, 97.6, 99.8, 107.6, 108.7, 113.3, 120.0, 122.0, 128.0 (2C), 128.2 (2C), 129.0, 132.4, 137.5, 150.3, 151.2, 155.6, 157.8, 160.0,

188.9. HR-MS (ESI-TOF). Calcd for $C_{24}H_{21}NO_4$ $[M+H]^+$: *m/z* 388.1549. Found: *m/z* 388.1536.

(*E*)-3-(7-(Diethylamino)-4-oxo-4*H*-furo[3,2-*c*]chromen-2-yl)-acrylaldehyde (1e) This compound was obtained from **7** (570 mg, 2 mmol) and 2-(triphenylphosphoranylidene)acetaldehyde (608 mg, 2 mmol) as orange crystals; yield 71%; mp 198–199°C; ^{1}H NMR ($CDCl_3$): δ 1.25 (t, *J* = 7.0 Hz, 6H, 2× CH_3), 3.46 (q, *J* = 7.0 Hz, 4H, 2× CH_2), 6.62 (d, *J* = 2.1 Hz, 1H, C(8)H), 6.71–6.76 (m, 2H, d, *J* = 2.1 Hz, 1H, C(6)H + C_βH), 7.19 (s, 1H, CH-furo), 7.27 (d, *J* = 15.6 Hz, 1H, C_αH), 7.68 (d, *J* = 8.9 Hz, 1H, C(5)H), 9.70 (d, *J* = 7.9, 1H, CHO); ^{13}C NMR ($CDCl_3$): δ 11.9, 44.5, 97.7, 99.7, 107.7, 109.0, 114.0, 122.1, 126.4, 136.5, 150.0, 150.4, 155.6, 157.6, 160.4, 191.8. HR-MS (ESI-TOF). Calcd for $C_{18}H_{17}NO_4$ $[M+H]^+$: *m/z* 312.1236. Found: *m/z* 312.1251.

(*E*)-2-(3-(7-(Diethylamino)-4-oxo-4*H*-furo[3,2-*c*]chromen-2-yl)-allylidene)malononitrile (1f) A solution of malonodinitrile and a crystal of EDDA (0.5 mmol, 33 mg) in ethanol was added to a solution of (*E*)-3-(7-(diethylamino)-4-oxo-4*H*-furo[3,2-*c*]chromen-2-yl)-acrylaldehyde (**1e**, 156 mg, 0.5 mmol) in hot ethanol/chloroform (2:1, 6 mL). The mixture was stirred at room temperature for 2 h and the precipitated product was crystallized from toluene; purple powder; yield 46%; mp 249.5–250.5°C; ^{1}H NMR ($CDCl_3$): δ 1.27 (6H, t, *J* = 6.9 Hz, 2× CH_3), 3.48 (4H, q, *J* = 6.9 Hz, 2× CH_2), 6.61 (1H, d, *J* = 2.1 Hz, C(8)H), 6.72 (1H, dd, *J* = 2.1 Hz, *J* = 8.9 Hz, C(6)H), 7.05 (1H, d, *J* = 14.7 Hz, CH=), 7.18–7.27 (2H, m, CH-furo, CH=), 7.55 (1H, d, *J* = 11.9 Hz, CH=), 7.77 (1H, d, *J* = 8.9 Hz, C(5)H); ^{13}C NMR ($CDCl_3$): δ 11.8, 44.9, 81.7, 98.2, 99.8, 108.3, 109.5, 111.5, 113.2, 116.3, 120.5, 122.6, 132.5, 150.1, 150.5, 155.8, 157.2, 157.7, 161.0. HR-MS (ESI-TOF). Calcd for $C_{21}H_{17}N_3O_3$ $[M+H]^+$: *m/z* 360.1348. Found: *m/z* 360.1309.

7-(Diethylamino)-2-((1*E*,3*E*)-5-oxo-5-phenylpenta-1,3-dien-1-yl)-4*H*-furo[3,2-*c*]chromen-4-one (1g) (Benzoylmethylene)triphenylphosphorane (209 mg, 0.55 mmol) was added to a solution of aldehyde **1e** (0.5 mmol, 156 mg) in $CHCl_3$ (4 mL). The reaction mixture was stirred at 70°C for 48 h and occasionally analyzed by TLC. The solvent was removed under reduced pressure and an oily residue was treated with ethanol (10 mL) to give a precipitate that was crystallized from ethanol; orange crystals; yield 20%; mp 197.5–199°C; ^{1}H NMR ($CDCl_3$): δ 1.23 (t, *J* = 7.0 Hz, 6H, 2× CH_3), 3.43 (q, *J* = 7.0 Hz, 4H, 2× CH_2), 6.58 (d, *J* = 2.4 Hz, 1H, C(8)H), 6.67 (dd, *J* = 2.4 Hz, *J* = 8.9 Hz, 1H, C(6)H), 6.80 (d, *J* = 15.3 Hz, 1H), 7.15 (d, *J* = 15.3 Hz, 1H, (C_αH, C_γH)), 6.89 (s, 1H, CH-furo), 7.04–7.09 (dd, *J* = 15.3, *J* = 12.0 Hz, 1H, C_βH), 7.47–7.58 (m, 4H, (3CH_{ar} + C_γH)), 7.67 (d, *J* = 8.9 Hz, 1H, C(5)H), 7.93–8.01 (m, 2H, CH_{ar}); ^{13}C NMR ($CDCl_3$): δ 11.9, 44.3, 97.7, 100.1, 107.5, 108.6, 109.1, 121.7, 125.7, 126.2, 126.4, 127.9 (2C), 128.1 (2C), 132.2, 137.7, 143.0, 150.0, 152.0, 155.3, 158.0, 159.2, 189.6. HR-MS (ESI-TOF). Calcd for $C_{26}H_{23}NO_4$ $[M+H]^+$: *m/z* 414.1705. Found: *m/z* 414.1650.

Ethyl 7-(diethylamino)-4-oxo-4*H*-thieno[3,2-*c*]chromene-2-carboxylate (9)

DIPEA (1.1 mL, 10 mmol) and ethyl 2-mercaptoacetate (2.8 g, 10 mmol) were added to a solution of 4-chloro-7-(diethylamino)-3-formylcoumarin (**8**, 2.8 g, 10 mmol) in dichloromethane (15 mL). The mixture was stirred at room temperature for 7 h and then treated with ethanol (20 mL). The precipitated product was crystallized from ethanol; yellow crystals; yield 90%; mp 160–162°C; ^{1}H NMR ($CDCl_3$): δ 1.25 (t, *J* = 7.0 Hz, 6H, 2× CH_3), 1.42 (t, *J* = 7.2 Hz, 3H, CH_3), 3.45 (q, *J* = 7.0 Hz, 4H, 2× CH_2), 4.40 (q, *J* = 7.2 Hz, 2H, CH_2), 6.60 (d, *J* = 2.1 Hz, 1H, C(8)H), 6.68 (dd, *J* = 2.1 Hz, *J* = 8.9 Hz, 1H, C(6)H), 7.50 (d, *J* = 8.9 Hz, 1H, C(5)H), 8.19 (s, 1H, CH-furo); ^{13}C NMR ($CDCl_3$): δ 11.8, 13.7, 44.7, 61.1, 98.0, 105.0, 109.2, 120.8, 124.4, 129.9, 132.1, 149.8, 153.5, 153.9, 156.9, 161.1. HR-MS (ESI-TOF). Calcd for $C_{18}H_{19}NO_4S$ $[M+H]^+$: *m/z* 346.1113. Found: *m/z* 346.1113.

7-(Diethylamino)-4-oxo-4*H*-thieno[3,2-*c*]chromene-2-carboxylic acid (10)

Ethyl 7-(diethylamino)-4-oxo-4*H*-thieno[3,2-*c*]chromene-2-carboxylate (**9**) was added to a solution of sodium hydroxide (5 g, 125 mmol) in ethanol/water mixture (1:1). The resulting suspension was heated under reflux for 2 h and then vigorously stirred at room temperature for 12 h. The mixture was quenched with concentrated hydrochloric acid and the resultant precipitate was crystallized from ethanol; yellow crystals; yield 91%; mp 259–261°C; ^{1}H NMR ($CDCl_3$): δ 1.14 (t, *J* = 7.0 Hz, 6H, 2× CH_3), 3.37 (q, *J* = 7.0 Hz, 4H, 2× CH_2), 6.53 (br s, 1H, C(8)H), 6.65 (br d, *J* = 7.0 Hz, 1H, C(6)H), 7.43 (d, *J* = 8.9 Hz, 1H, C(5)H), 7.98 (s, 1H, CH-thieno); ^{13}C NMR ($CDCl_3$): δ 11.7, 13.5, 44.8, 98.0, 105.0, 109.5, 120.7, 124.5, 131.3, 131.5, 149.4, 153.3, 153.6, 156.8, 162.5. HR-MS (ESI-TOF). Calcd for $C_{16}H_{15}NO_4S$ $[M+H]^+$: *m/z* 318.0800. Found: *m/z* 318.0846.

(Ethyl carbonic) 7-(diethylamino)-4-oxo-4*H*-thieno[3,2-*c*]-chromene-2-carboxylic anhydride (11)

Triethylamine (1.5 mL, 10.9 mmol) was added to a suspension of 7-(diethylamino)-4-oxo-4*H*-thieno[3,2-*c*]chromene-2-carboxylic acid (**10**, 2.8 g, 8.8 mmol) in dichloromethane (40 mL). The mixture was then vigorously stirred at room temperature for 30 min, treated with ethyl chloroformate (1 mL, 10.6 mmol) and stirred at room temperature. After the reaction was completed as monitored by TLC analysis, water (200 mL) was added, and the organic layer was separated and concentrated under reduced pressure to give dark-yellow powder, yield 94%.

7-(Diethylamino)-2-(hydroxymethyl)-4*H*-thieno[3,2-*c*]-chromen-4-one (12)

MeOH (5 mL) was added to a suspension of the anhydride **11** (3.2 g, 8.2 mmol) in THF (55 mL) and mixture was vigorously stirred at room temperature for 30 min. Sodium borohydride (0.62 g, 16.4 mmol) was added and the mixture was further stirred at room temperature until gas evolution ceased. The resultant solution was washed with water (2×200 mL). The organic layer was separated, concentrated under reduced pressure, and the residue was subjected to silica gel chromatography using petroleum ether/EtOAc (2:1) as eluent; yellow crystals; yield 60%; mp 121–123°C; ^{1}H NMR ($CDCl_3$): δ 1.25 (t, *J* = 7.0 Hz, 6H, 2× CH_3), 3.45 (q, *J* = 7.0 Hz, 4H, 2× CH_2), 4.89 (s, 2H, CH_2), 6.65–6.90 (m, 2H, C(8)H + C(6)H), 6.78 (s, 1H), 7.41 (s, 1H, CH-thieno), 7.48 (d, *J* = 8.5 Hz, 1H, C(5)H), 14.50 (br s, 1H, OH). HR-MS (ESI-TOF). Calcd for $C_{16}H_{17}NO_3S$ $[M+H]^+$: *m/z* 304.1007. Found: *m/z* 304.1049.

7-(Diethylamino)-4-oxo-4*H*-thieno[3,2-*c*]chromene-2-carbaldehyde (13)

Dess-Martin periodinane in dichloromethane (15%, 5.4 mL, 2.23 mmol) was added to a solution of 7-(diethylamino)-2-(hydroxymethyl)-4*H*-thieno[3,2-*c*]chromen-4-one (**12**, 676 mg, 2.23 mmol) in dichloromethane (10 mL), and the mixture was stirred at room temperature. After TLC analysis confirmed the absence of substrate **12**, the organic solution was washed with aqueous $NaHCO_3$ (2×200 mL) and concentrated under reduced pressure. The residue was subjected to chromatography on silica gel using petroleum ether/EtOAc (2:1) as eluent; yellow crystals; yield 75%; mp 198–199°C; ^{1}H NMR ($CDCl_3$): δ 1.26 (6H, t, J = 7.2 Hz, 2× CH_3), 3.47 (4H, q, J = 7.2 Hz, 2× CH_2), 6.59 (1H, d, J = 2.1 Hz, C(8)H), 6.69 (1H, dd, J = 2.1 Hz, J = 8.9 Hz, C(6)H), 7.55 (1H, d, J = 8.9 Hz, C(5)H), 8.18 (1H, s, CH-thieno), 9.94 (1H, s, CHO); ^{13}C NMR ($CDCl_3$): δ 11.9, 44.6, 97.6, 104.6, 109.2, 120.8, 125.0, 136.0, 139.2, 150.6, 154.2, 155.4, 156.9, 181.8. HR-MS (ESI-TOF). Calcd for $C_{16}H_{15}NO_3S$ $[M+H]^+$: *m/z* 302.0851. Found: *m/z* 302.0901.

General method for synthesis of compounds 2a,b

Solution of a C-H acid (1 equiv.) and a crystal of EDDA in a solvent indicated below was added dropwise to a solution of 7-(diethylamino)-4-oxo-4*H*-thieno[3,2-*c*]chromene-2-carbaldehyde (**13**, 0.23–0.5 mmol) in hot ethanol (3 mL). The mixture was stirred at room temperature for 2 h and the resultant precipitate was crystallized from ethanol.

2-((7-(Diethylamino)-4-oxo-4*H*-thieno[3,2-*c*]chromen-2-yl)-methylene) malononitrile (2a) This compound was obtained from **13** (150 mg, 0.5 mmol) and malonodinitrile (33 mg, 0.5 mmol) in dichloromethane (10 mL) as bright-red crystals; yield 36%; mp 234–236°C; ^{1}H NMR ($CDCl_3$): δ 1.28 (6H, t, J = 7.0 Hz, 2× CH_3), 3.49 (4H, q, J = 7.0 Hz, 2× CH_2), 6.49 (1H, d, J = 2.3 Hz, C(8)H), 6.71 (1H, dd, J = 2.3 Hz, J = 9.0 Hz, C(6)H), 7.56 (1H, d, J = 9.0 Hz, C(5)H), 7.86 (1H, s, CH=), 8.05 (1H, s, CH-thieno); ^{13}C NMR ($CDCl_3$): δ 11.9, 44.7, 77.0, 97.6, 104.1, 109.6, 112.6, 113.3, 120.5, 125.5, 130.6, 139.4, 149.6, 151,3, 154.7, 156.0, 156.2. HR-MS (ESI-TOF). Calcd for $C_{19}H_{15}N_3O_2S$ $[M+H]^+$: *m/z* 350.0963. Found: *m/z* 350.0998.

Ethyl 2-cyano-3-(7-(diethylamino)-4-oxo-4*H*-thieno[3,2-*c*]chromen-2-yl)acrylate (2b) This compound was obtained from **13** (210 mg, 0.7 mmol) and ethyl 2-cyanoacetate (79 mg, 0.7 mmol) in dichloromethane (60 mL) as orange crystals; yield 87%; mp 235–237°C; ^{1}H NMR ($CDCl_3$): δ 1.27 (6H, t, J = 7.0 Hz, 2× CH_3), 1.42 (3H, t, J = 7.0 Hz, CH_3), 3.48 (4H, q, J = 7.1 Hz, 2× CH_2), 4.40 (2H, q, J = 7.1 Hz, CH_2), 6.62 (1H, d, J = 2.1 Hz, C(8)H), 6.72 (1H, dd, J = 2.1 Hz, J = 8.9 Hz, C(6)H), 7.58 (1H, d, J = 8.9 Hz, C(5)H), 8.06 (1H, s, CH-thieno), 8.35 (1H, s, CH=); ^{13}C NMR ($CDCl_3$): δ 11.8, 13.7, 45.0, 62.2, 98.1, 98.8, 104.9, 109.7, 115.2, 120.7, 125.3, 131.8, 138.2, 145.6, 150.3, 154.3, 155.0, 156.5, 162.0. HR-MS (ESI-TOF). Calcd for $C_{21}H_{20}N_2O_4S$ $[M+H]^+$: *m/z* 397.1222. Found: *m/z* 397.1192.

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