TÜBİTAK

Turkish Journal of Chemistry

http://journals.tubitak.gov.tr/chem/

Research Article

Turk J Chem
(2013) 37: 383 – 393

doi:10.3906/kim-1204-81

A two-component protocol for synthesis of 3-(2-(substituted phenylamino)thiazol-4-yl)-2*H*-chromen-2-ones

Aamer SAEED,[1,*] **Mubeen ARIF,**[1] **Madiha IRFAN,**[1] **Michael BOLTE**[2]
[1] Department of Chemistry, Quaid-I-Azam University, Islamabad, Pakistan
[2]Institute of Inorganic and Analytical Chemistry, Goethe University, Frankfurt/Main, Germany

Received: 28.04.2012 • **Accepted:** 13.03.2013 • **Published Online:** 10.06.2013 • **Printed:** 08.07.2013

Abstract: An efficient 2-component synthesis of a series of 3-(2-(substituted phenylamino)thiazol-4-yl)-2*H*-chromen-2-ones (**3a–j**) was achieved by the reaction of 3-(2-thiocyanatoacetyl)-2*H*-chromen-2-one (**1**) with a variety of suitably substituted anilines in 1:1 molar ratio in ethanol. The structures of the products were established by elemental analyses, and UV-vis, FTIR, ^{1}H and ^{13}C NMR, and mass spectroscopy. 3-(2-(4-Methylphenylamino)thiazol-4-yl)-2*H*-chromen-2-one (**3j**) was further characterized by single crystal X-ray diffraction study. This compound, $C_{19}H_{14}N_2OS$, crystallizes in the orthorhombic space group Pna21, with $Z = 4$, and unit cell parameters $a = 13.0785(11)$, b = 25.746(2), c = 4.7235(3) Å, $\alpha = \beta = \gamma = 90^\circ$.

Key words: 3-Thiazolcoumarins, crystal structure

1. Introduction

Coumarins, also called benzo-α-pyrones, comprise a very large and important family of compounds that occur widely in nature. They are found in a wide range of plants such as tonka bean, vanilla grass, cinnamon, sweet clover, strawberries, apricots, and cherries. A number of coumarin derivatives are used in the pharmaceutical industry as precursor molecules for the synthesis of many synthetic pharmaceutical compounds including anticoagulants and vitamin K antagonists, while others are used in the treatment of lymphedema.[1] Coumarin derivatives exhibit antibacterial, antifungal,[2,3] anticancer,[4] anti-HIV,[5,6] antitubercular,[7] antiacylcholineestrase,[8] antimutagenic,[9] anthelmintic,[10] anticoagulant,[11] anti-inflammatory, antihepatitis C,[12] and analgesic[13] properties.

Moreover, many coumarin derivatives are used as inhibitors of heat shock protein,[14] nonpeptidic protease inhibitors,[15] inhibitors of 17β-hydroxysteroid dehydrogenase (17β-HSD) type 1,[16] TNF-α inhibitors,[17] and monoamine oxidase inhibitors.[18] 4-Methylcoumarins bearing different functionalities are well-known antioxidant and radical scavengers.[19]

Thiazole derivates have been isolated and synthesized in view of their versatile pharmacological activities. Some thiazole analogues are used as fungicidal,[20] cardiotonic,[21] bactericidal,[22] anti-inflamatory,[23] antiviral,[24] anti-arrhythmic,[25] and antitumor[26] agents. Thiazoles are used as drugs for the treatment of hypertention[27] HIV infections,[28] and pain.[29] Many thiazoles are fibrinogin receptor antagonists with antithrombotic activity,[30] inhibitors of bacterial DNA gyrase B,[31] and lypoxygenase inhibitors.[32] Aminothiazoles are known to be ligands

*Correspondence: aamersaeed@yahoo.com

of estrogen receptors[33] as well as a novel class of adenosine receptor antagonists.[34] The thiazoline ring present in vitamin B_1 serves as an electron sink and its coenzyme form is important for the decarboxylation of alpha-ketoacids.[35]

Both coumarins and thiazoles exhibit a wide range of fluorescence emission properties.[36,37] Coumarins can be used as memory media in different devices,[38] as colorimetric chemosensors,[39] and as dyes for efficient dye-sensitized solar cells.[40] Similarly, thiazole derivatives have a wide range of applications as ferroelectric displays[41] and optical brighteners[42] and in flow cytometry[43] and DNA detection.[44] Coumarins also exhibit interesting fluorescence properties. These properties have led to their widespread application as sensitive fluorescent probes in a wide range of systems. Furthermore, photobiological properties of coumarins were also studied.

Coumarins are also known as tannin activators. They block out short-wave radiation (280 to 315 nm) but allow the longer wave radiation that gives a nice tan. In addition, studies have shown that coumarins are rapidly and extensively absorbed through human, rat, and mouse skin, and that the compounds remain metabolically unchanged during absorption.

Taking into account the aforesaid biological and synthetic significance of coumarins on one hand and the multifunctional value of the thiazole ring in drug design on the other, the endeavor of the current work was the synthesis of some new thiazolyl-bearing coumarins to combine their valuable effects in a single structural entity.

2. Experimental

R_f-values were determined using aluminum pre-coated silica gel plates Kieselgel 60 F_{254} from Merck (Germany). Melting points were determined using a Gallenkamp melting point apparatus (MP-D) and are uncorrected. Infrared spectra were recorded using an FTS 3000 MS, Bio-Rad Marlin (Excalibur Model) spectrophotometer. ^{1}H NMR spectra were obtained using a Bruker 300 NMR MHz spectrometer in $CDCl_3$, DMSO-d_6, and C_3D_6O solutions using TMS as an internal reference. Chemical shifts are given in δ-scale (ppm). Abbreviations *s, d, dd, t,* and *at* are used for singlet, doublet, double doublet, triplet, and apparent triplet, respectively; *m* stands for a multiplet. ^{13}C NMR spectra (75 MHz) were measured in $CDCl_3$, DMSO-d_6, and C_3D_6O solutions. LCMS spectra were recorded using an EI source of 70 eV on an Agilent Technologies 6890N. Ultraviolet-visible (UV-vis) spectra were measured on a Shimadzu Pharma-spec 1700 UV-Visible Spectrophotometer.

Data were collected on a STOE IPDS II 2-circle diffractometer with graphite-monochromated Mo$K\alpha$ radiation. Empirical absorption correction was performed using MULABS[46] in PLATON.[47] The structure was solved by direct methods using the program SHELXS and refined against F2 with full-matrix least-squares techniques using the program SHELXL-97.[48] H atoms bonded to C were refined using a riding model. The H atom bonded to N was freely refined; 5383 reflections measured, 2623 unique (R int = 0.0385), R1 = 0.0379, wR2 = 0.0821 for all data, GooF = 1.074, highest peak in final difference map 0.181 e-/Å3. The absolute structure was determined: Flack-x-parameter –0.02(8).

3-(2-Thiocyanatoacetyl)-2*H*-chromen-2-one (**1**) was prepared by treating 3-(2-bromoacetyl)-2*H*-chromen-2-one with KSCN in dry acetone. The solid separated was purified by recrystallization in ethanol.

General procedure for the synthesis of 3-(2-(substituted phenylamino)thiazol-4-yl)-2*H*-chromen-2-ones (3a–j)

To a stirred solution of 3-(2-thiocyanatoacetyl)-2*H*-chromen-2-one (**1**) (1 mmol) in 30 mL of ethanol was added portionwise suitably substituted aniline (1.2 mmol) and the reaction mixture was refluxed for 4–5 h. The

progress of the reaction was monitored with TLC using petroleum ether:ethyl acetate (4:1). The solid products appeared either by cooling the reaction mixture or by pouring it on ice-cold water. The solid separated was purified by recrystallization in ethanol.

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

Mp 249–251 °C, (Lit[45] 150–151 °C), yield 70%. R_f: 0.4 (a). IR (pure cm^{-1}): 3303 (N-H), 3154 (Csp^2-H), 1707 (C=O), 1603 (C=N), 1557 (C=C aromatic). ^{1}H NMR (300 MHz, C_3D_6O) in δ (ppm) and J (Hz): 9.78 (1H, s, NH), 8.73 (1H, s, Ar-H), 8.12 (1H, d, J = 7.5 Hz, Ar-H), 7.89 (1H, s, thiazole H-5), 7.86 (1H, dd, ^1J = 1.51 Hz, ^2J = 7.2 Hz, Ar-H), 7.76–7.70 (2H, m, Ar-H), 7.59–7.52 (2H, m, Ar-H) 7.51–7.46 (2H, m, Ar-H). ^{13}C NMR: (75 MHz, C_3D_6O) in δ (ppm): 162.3 (C=N), 157.9 (C=O), 152.2, 144.7, 144.4, 137.1, 130.5, 129.7, 127.6, 126.2, 124.7, 123.0, 119.6, 118.5, 116.0, 115.5, 113.6, 110.3. UV-Vis λmax/nm (chloroform) 296. LCMS m/z $[M\text{-}H]^+$: 355 g/mol. Found C, 60.99; H, 3.21; Cl, 9.84; N, 7.98; S, 9.12. Calc. for $C_{18}H_{11}ClN_2O_2S$: C, 60.93; H, 3.12; Cl, 9.99; N, 7.90; S, 9.04%.

3-(2-(3-Chlorophenylamino)thiazol-4-yl)-2*H*-chromen-2-one (3b)

Mp 255–257 °C (Lit[45] 134–135 °C), yield 72%. R_f: 0.39 (a). IR (pure cm^{-1}): 3316 (N-H), 3135 (Csp^2-H), 1702 (C=O), 1610 (C=N), 1597–1503 (C=C aromatic). ^{1}H NMR (300 MHz, C_3D_6O) in δ (ppm) and J (Hz): 9.72 (1H, s, NH), 8.75 (1H, s, Ar-H), 8.02 (1H, at, Ar-H), 7.93 (1H, s, thiazole H-5), 7.86–7.83 (1H, m, Ar-H), 7.79–7.76 (1H, m, Ar-H), 7.69–7.63 (1H, m, Ar-H) 7.46–7.37 (3H, m, Ar-H) 7.08–7.04 (1H, m, Ar-H). ^{13}C NMR: (75 MHz, C_3D_6O) in δ (ppm): 162.4 (C=N), 158.5 (C=O), 152.1, 145.4, 144.0, 139.0, 136.0, 130.0, 129.2, 128.0, 124.6, 122.7, 119.7, 119.0, 118.9, 115.5, 113.4, 110.3. UV-Vis λmax/nm (chloroform) 299. LCMS m/z $[M\text{-}H]^+$: 355 g/mol. Found C, 61.89; H, 3.40; Cl, 10.02; N, 7.71; S, 9.28%. Calc. for $C_{18}H_{11}ClN_2O_2S$: C, 60.93; H, 3.12; Cl, 9.99; N, 7.90; S, 9.04%.

3-(2-(4-Chlorophenylamino)thiazol-4-yl)-2*H*-chromen-2-one (3c)

Mp 269–273 °C (Lit[45] 186–188 °C); yield 73%. R_f: 0.41 (a). IR (pure cm^{-1}): 3293 (N-H), 3079 (Csp^2-H), 1695 (C=O), 1604 (C=N), 1536 (C=C aromatic). ^{1}H NMR (300 MHz, DMSO-d_6) in δ (ppm) and J (Hz): 10.5 (1H, s, NH), 8.71 (H, s, Ar-H), 7.07 (1H, d, J = 6.6 Hz, Ar-H), 7.83–7.80 (3H, m, Ar-H), 7.47–7.39 (5H, m, Ar-H, thiazol H-5). ^{13}C NMR (75 MHz, DMSO-d_6) in δ (ppm): 162.6 (C=N), 159.2 (C=O), 152.7, 144.0, 140.3, 139.2, 132.2 (2C), 129.4, 129.4, 125.1, 120.6, 120.0, 119.7, 119.0 (2C), 116.3, 110.7. UV-Vis λmax/nm (chloroform) 295. LCMS m/z $[M\text{-}H]^-$ 353 g/mol. Found C, 61.04; H, 3.21; Cl, 9.9.92; N, 7.85; S, 9.11. Calc. for $C_{18}H_{11}ClN_2O_2S$: C, 60.93; H, 3.12; Cl, 9.99; N, 7.90; S, 9.04%.

3-(2-(2-Methylphenylamino)thiazol-4-yl)-2*H*-chromen-2-one (3d)

Mp 231–233 °C, (Lit[45] 174–175 °C), yield 73%. R_f 0.41 (a). IR (pure cm^{-1}): 3309 (N-H), 3172 (Csp^2-H), 1709 (C=O), 1608 (C=N), 1581 (C=C aromatic). ^{1}H NMR (300 MHz, DMSO-d_6) in δ (ppm) and J (Hz): 10.20 (1H, s, NH), 8.62 (1H, s, Ar-H), 7.62 (1H, d, J = 6.9 Hz, Ar-H), 7.56 (1H, dd, ^1J = 1.2 Hz, ^2J = 7.6 Hz, Hz, Ar-H), 7.49–7.43 (4H, m, Ar-H), 7.38–7.32 (2H, m, Ar-H), 2.31 (3H, s, methyl). ^{13}C NMR: (75 MHz, DMSO-d_6) in δ (ppm): 163.6 (C=N), 159.7 (C=O), 152.5, 143.6, 139.1, 137.7, 132.8, 131.4, 130.1, 129.2,

128.2, 125.4, 120.6, 119.5, 118.7, 118.5, 116.3, 111.8, 20.64. UV-Vis λmax/nm (chloroform) 300. LCMS m/z $[M\text{-}H]^+$ 335 g/mol. Found C, 68.17; H, 4.29; N, 8.428; S, 9.51. Calc. for $C_{19}H_{14}N_2O_2S$: C, 68.24; H, 4.22; N, 8.38; S, 9.59%.

3-(2-(4-Methylphenylamino)thiazol-4-yl)-2*H*-chromen-2-one (3e)

Mp 208–210 °C, yield 75% R_f: 0.39 (a). IR (pure cm^{-1}): 3301 (N-H), 3194–3078 (Csp2-H), 1698 (C=O), 1602 (C=N), 1506 (C=C aromatic). ^{1}H NMR (300 MHz, $CDCl_3$) in δ (ppm) and J (Hz): 8.56 (1H, s, Ar-H), 7.85 (1H, s, thiazole H-5), 7.59–7.56 (2H, m, Ar-H), 7.38–7.28 (5H, m, Ar-H, NH), 7.19 (2H, d, J = 8.4 Hz, Ar-H), 2.359 (3H, s, methyl). ^{13}C NMR: (75 MHz, $CDCl_3$) in δ (ppm): 164.6 (C=N), 159.7 (C=O), 152.8, 143.8, 138.8, 137.5, 133.5, 131.3, 130.0 (2C), 128.2, 124.5, 120.7, 119.6, 119.2, 116.3 (2C), 109.8, 20.84. UV-Vis λmax/nm (chloroform) 299. LCMS m/z $[M\text{-}H]^+$ 335 g/mol. Found C, 68.31; H, 4.29; N, 8.8.29; S, 9.63. Calc. for $C_{19}H_{14}N_2O_2S$: C, 68.24; H, 4.22; N, 8.38; S, 9.59%.

3-(2-(3-Nitrophenylamino)thiazol-4-yl)-2*H*-chromen-2-one (3f)

Mp 193–195 °C, (reported 168–170 °C), yield 70%. R_f 0.21 (a). IR (pure cm^{-1}): 3135 (N-H), 3066 (Csp^2-H), 1711 (C=O), 1603 (C=N), 1579–1489 (C=C aromatic). ^{1}H NMR (300 MHz, DMSO-d_6) in δ (ppm) and J (Hz): 10.963 (1H, s, NH), 9.06 (1H, s, Ar-H), 8.72 (1H, s, thiazole H-5), 7.98 (1H, d, J = 7.2 Hz, Ar-H), 7.86–7.801 (3H, m, Ar-H), 7.68–7.63 (2H, m, Ar-H), 7.49–7.44 (2H, m, Ar-H). ^{13}C NMR: (75 MHz, DMSO-d_6) in δ (ppm): 162.5 (C=N), 158.5 (C=O), 150.4, 149.1, 145.6, 144.23, 131.2, 129.4, 127.5, 126.2, 124.7, 122.5, 120.5, 114.5, 111.2, 110.7. UV-Vis λmax/nm (chloroform) 275. LCMS m/z $[M\text{-}H]^+$: 366 g/mol. Found C, 59.11; H, 3.11; N, 11.58; S, 8.69. Calc. for $C_{18}H_{11}N_3O_4S$: C, 59.17; H, 3.03; N, 11.50; S, 8.78%.

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

Mp 179–181 °C, (reported 158–160 °C), yield 75%. R_f: 0.41 (a); IR (pure cm^{-1}): 3226 (N-H), 3137 (Csp^2-H), 1710 (C=O), 1605 (C=N), 1570 (C=C aromatic). ^{1}H NMR (300 MHz, $CDCl_3$) in δ (ppm) and J (Hz): 8.64 (1H, s, Ar-H), 8.13–8.10 (1H, m, Ar-H), 7.91 (1H, s, thiazole H-5), 7.84 (1H, s, NH), 7.67–7.64 (1H, m, Ar-H), 7.57–7.53 (1H, m, Ar-H), 7.39–7.38 (2H, m, Ar-H), 7.11–7.02 (2H, m, Ar-H), 6.96–6.93 (1H, m, Ar-H), 3.95 (3H, s, methoxy). ^{13}C NMR: (75 MHz, $CDCl_3$) in δ (ppm): 162.8 (C=N), 159.7 (C=O), 152.9, 147.5, 143.9, 138.9, 131.2, 129.7, 124.5, 122.3, 121.1, 120.8, 116.3, 110.2, 110.1, 55.77. UV-Vis λmax/nm (chloroform) 303. LCMS m/z $[M\text{-}H]^-$: 349 g/mol Found C, 65.06; H, 4.12; N, 7.87; S, 9.21. Calc. for $C_{19}H_{14}N_2O_3S$: C, 65.13; H, 4.03; N, 7.99; S, 9.15%.

3-(2-(4-Methoxyphenylamino)thiazol-4-yl)-2*H*-chromen-2-one (3h)

Mp 196–199 °C, yield 78%. R_f 0.28 (a). IR (pure cm^{-1}): 3219 (N-H), 3135 (Csp^2-H), 1715 (C=O), 1564 (C=C aromatic), 1601 (C=N). ^{1}H NMR (300 MHz, DMSO-d_6): δ 10.1 (1H, s, NH), 8.67 (1H, s, Ar-H), 7.95 (1H, d, J = 7.5 Hz, Ar-H), 7.68–7.60 (3H, m, Ar-H), 7.47–7.38 (2H, m, Ar-H), 7.72 (1H, s, thiazole H-5), 6.97 (2H, d, J = 7.3 Hz, Ar-H). ^{13}C NMR: (75 MHz, DMSO-d_6) in δ (ppm): 162.5 (C=N), 159.0 (C=O), 150.9, 150.3, 146.2, 140.0, 135.7, 129.0, 127.9, 126.6, 124.0, 121.5, 120.1, 116.5 (2C), 115.2 (2C), 112.9, 55.7. UV-Vis

λmax/nm (chloroform) 302. LCMS m/z [M-H]$^-$: 349 g/mol Found C, 65.19; H, 4.07; N, 8.03; S, 9.09. Calc. for $C_{19}H_{14}N_2O_3S$: C, 65.13; H, 4.03; N, 7.99; S, 9.15%.

3-(2-(2,3-Diflourophenylamino)thiazol-4-yl)-2*H*-chromen-2-one (3i)

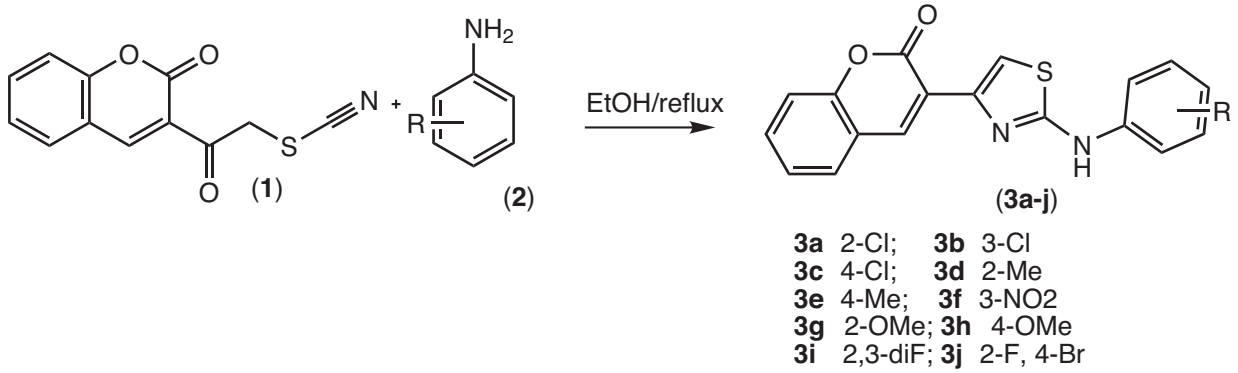
Mp 195–197 °C, yield 71%. R_f 0.53 (a). IR (pure cm^{-1}): 3284 (N-H), 3132 (Csp^2-H), 1712 (C=O), 1606 (C=N), 1567 (C=C aromatic). ^{1}H NMR (300 MHz, C_3D_6O) in δ (ppm) and J (Hz): 10.1 (1H, s, NH), 8.63 (1H, s, Ar-H), 8.61–8.55 (1H, m, Ar-H), 7.92 (1H, dd, ^1J = 1.2 Hz, ^2J = 7.8 Hz, Ar-H), 7.79 (1H, s, thiazole H-5), 7.65–7.59 (1H, m, Ar-H), 7.45–7.29 (3H, m, Ar-H), 7.19–7.12 (1H, m, Ar-H). ^{13}C NMR (75 MHz, C_3D_6O) in δ (ppm): 163.6 (C=N), 159.2 (C=O), 152.7, 143.6, 139.0, 132.1, 129.4, 126.1, 125.1, 121.6, 120.6, 119.7, 116.3, 111.9, 111.6, 111.3, 104.4, 104.0. UV-Vis λmax/nm (chloroform) 305. LCMS m/z [M-H]$^-$: 355 g/mol. Found C, 60.59; H, 2.89; F, 10.71; N, 7.79; S, 9.06. Calc. for $C_{18}H_{10}F_2N_2O_2S$: C, 60.67; H, 2.83; F, 10.66; N, 7.86; S, 9.00%.

3-(2-(4-Bromo-2-flourophenylamino)thiazol-4-yl)-2*H*-chromen-2-one (3j)

Mp 233–235 °C, yield 69%. R_f 0.53 (a). IR (pure cm^{-1}): 3309 (N-H), 3145, 3061 (Csp^2-H), 1708 (C=O), 1610 (C=N), 153 (C=C aromatic). ^{1}H NMR (300 MHz, C_3D_6O) in δ (ppm) and J (Hz): 9.53 (1H, s, NH), 8.81 (1H, s, Ar-H), 8.89–8.83 (1H, m, Ar-H), 7.99 (1H, s, thiazole H-5), 7.89–7.86 (1H, m, Ar-H), 7.69–7.66 (1H, m, Ar-H), 7.49–7.39 (5H, m, Ar-H). ^{13}C NMR: (75 MHz, C_3D_6O): in δ (ppm): 162.2 (C=N), 159.5 (C=O), 159.0, 150.6, 146.2, 140.2, 129.2, 128.7, 128.0, 127.5, 126.9, 125.3, 122.6, 121.7, 121.2, 119.5, 114.9, 113.2. UV-Vis λmax/nm (chloroform) 303. LCMS m/z [M-H]$^-$: 416 g/mol Found C, 51.88; H, 2.51; Br, 19.11; F, 4.47; N, 6.78; S, 7.60. Calc. for $C_{18}H_{10}BrFN_2O_2S$: C, 51.81; H, 2.42; Br, 19.15; F, 4.55; N, 6.71; S, 7.68%.

3. Results and discussion

The reaction sequence leading to the formation of thiazolyl-2*H*-chromen-2-ones is depicted in the Scheme. The starting material 3-(2-thiocyanatoacetyl)-2*H*-chromen-2-one (**1**) is readily accessible via the reaction of 3-(2-bromoacetyl)-2*H*-chromen-2-one with potassium thiocyanate in dry acetone.[28] Treatment of the latter with an equimolar quantity of a variety of suitably substituted anilines (**2a**–**j**) in ethanol furnished the title thiazolyl-2*H*-chromen-2-ones (**3a**–**j**).



Scheme. Synthesis of 3-(2-(substituted phenylamino)thiazol-4-yl)-2*H*-chromen-2-ones.

All 3-(2-(substituted phenylamino)thiazol-4-yl)-2*H*-chromen-2-ones were characterized using spectroscopic analysis including IR, ^{1}H NMR, ^{13}C NMR, and UV and in some cases by mass spectrometry. All the compounds are fluorescent under UV-light. Their fluorescent properties were studied using a luminescence spectrophotometer and emitted wavelengths were recorded.

IR spectra of all compounds had strong N-H absorptions at about 3316–3219 cm^{-1} and displayed absorptions at about 1715–1695 cm^{-1} and 1610–1601 cm^{-1} assigned to C=O and C=N functions, respectively. In the UV-vis spectra λ_{max} are observed at 287.5–302.0 nm.

In the ^{1}H NMR spectral data for all the compounds, there was a characteristic singlet in the range 10.5–8.50 ppm, indicative of NH. A thiazolyl proton appeared in the range 8.00–7.30 ppm and the remaining protons appeared at their respective chemical shift values. Compounds **3c**, **3e**, and **3h** are para substituted with electron-donating substituents. The protons of the aniline ring are making part of an AB system. In the case of compound **3c** there is a 4-proton multiplet at 7.47–7.39 showing that these protons have close chemical shifts, and in **3e** signals at 7.38–7.28 and 7.19 ppm for 2 protons each, clearly indicating an AB system. ^{13}C NMR spectral data show significant peaks for C=N of thiazole moiety and C=O in the range 164.6–162.0 ppm and 159.9–158.3 ppm, respectively. The deshielded value of C=N of the thiazole skeleton can be justified by the 2 neighboring electron-withdrawing sulfur and nitrogen atoms.

The structure of **3e** was unequivocally confirmed by single crystal X-ray analysis (Figure 1).[46] Single crystals suitable for X-ray diffraction studies were obtained by slow evaporation of ethanol. Figures 2 and 3 show the packing diagrams with a view onto the bc-plane and the ab-planes respectively. Hydrogen bonds are drawn as dashed lines. The molecule is almost planar (r.m.s. deviation for all non-H atoms 0.076 Å). Bond lengths and angles are in the usual ranges. The molecules are connected by N-H...O hydrogen bonds to zigzag chains running along [2 0 1].

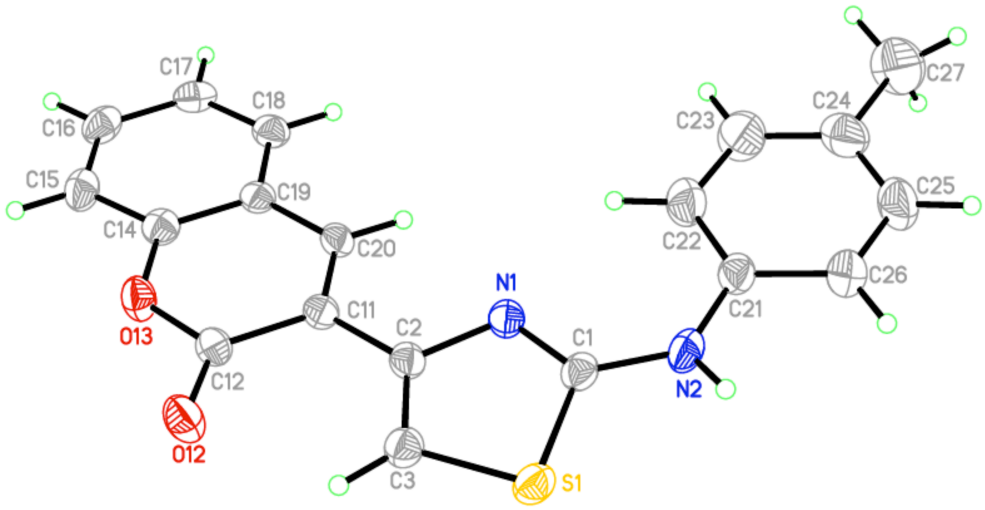


Figure 1. Molecular structure with displacement ellipsoids at the 50% probability level.

3.1. Photophysical properties

Absorption properties of the synthesized compounds were determined in dilute chloroform solution and the results are given in the Table. In the absorption spectra of the compounds 2 bands appear from 270 to 430 nm. The major absorption band is due to $\pi-\pi^*$ transition from the basic coumarin skeleton. The addition of phenyl

substituted thiazole at position 3 of coumarin moiety causes the shoulder, which is shifted bathochromically according to the nature and position of the substituents. According to the common rule, electron-donating groups shifted the absorption to longer wavelengths, while electron-withdrawing substituents did the opposite. [49]

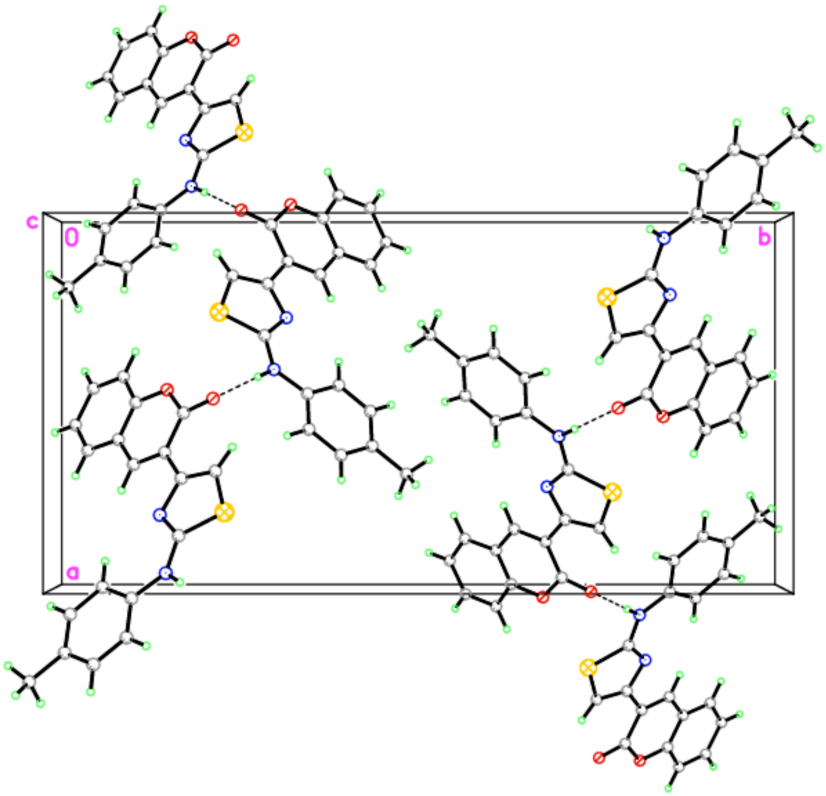


Figure 2. Packing diagram with view onto the bc-plane. Hydrogen bonds are drawn as dashed lines.

The maximum shift in absorption wavelength observed for (-OMe) substituents is due to their high electron donating nature, while the minimum was observed for (-NO_2) group and the rest showed a similar trend. The shift to longer wavelength can also be attributed to formation of aggregates of H-type and J-type. [50,51]

Fluorescence is a form of photoluminescence and these studies were performed to determine the wavelength of emitted light. Fluorescence was measured in dilute chloroform solution. Compounds **(3b, 3c, 3j)**

Table. Absorption data of compounds **3a**–**3j**.

Sr. no.	Compound	R	λ_{max} (nm)
1	**3a**	2-Cl	296, 343
2	**3b**	3-Cl	299, 363
3	**3c**	4-Cl	295, 367
4	**3d**	2-Me	300, 367
5	**3e**	4-Me	299, 362
6	**3f**	3-NO2	275, 356
7	**3g**	2-OMe	303, 372
8	**3h**	4-OMe	302, 364
9	**3i**	2,3-difloro	305, 352
10	**3j**	4-Br-2-F	303, 362

show their emitted wavelength in the range 392–424 nm with the appearance of 2 emission bands. The marked difference from the absorption maxima may be due to the intermolecular charge transfer (ICT) from the nitrogen donor to the carbonyl acceptor of the coumarin moiety.[52] Moreover, the observed difference of **3c** from **3b** and **3j** was because of the presence of a donor group, i.e. halogen, at the para position of nitrogen, accumulating the charge, which might cause a little disturbance in aggregation. The color of emitted light is in the blue region (Figure 5). The fluorescent properties of these compounds are enhanced and shifted to the blue region due to attachment of thiazole moiety to the third position of coumarin, which is emitted up to 350–380 nm. The fluorescent properties of the compounds indicate that they can be used as chemical sensors, fluorescent labeling, dyes, and biological detectors and in fluorescent lamps.

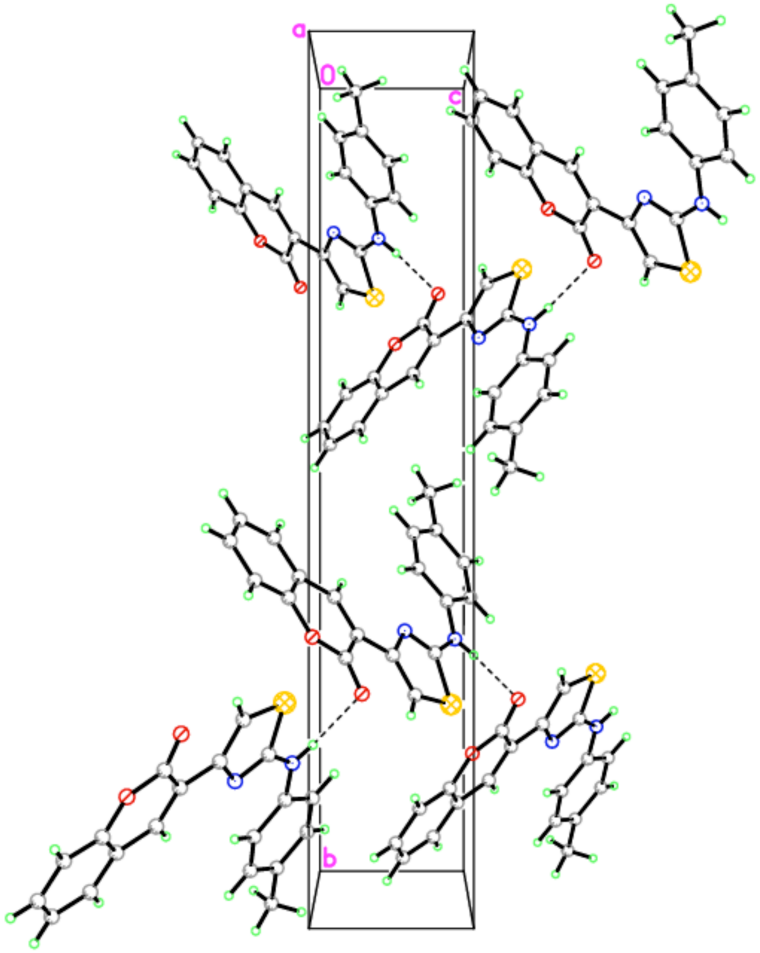


Figure 3. Packing diagram with view onto the ab-plane. Hydrogen bonds are drawn as dashed lines.

Their use as chemosensors is due to the chelating ability of C=N and C=O groups and it is known that these groups exhibit a high affinity to transition and posttransition metal cations but less binding affinity toward alkali metal and alkaline earth metal cations.[53–56]

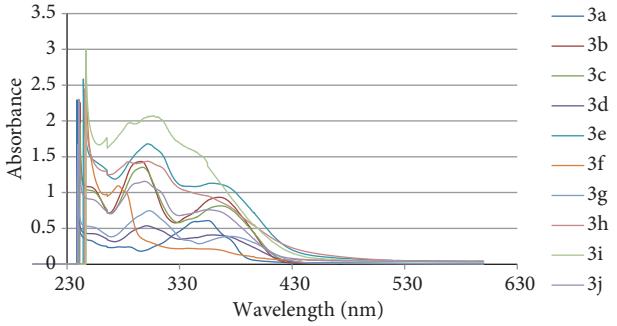


Figure 4. UV/Vis absorption spectra of **3a-3j** in $CHCl_3$.

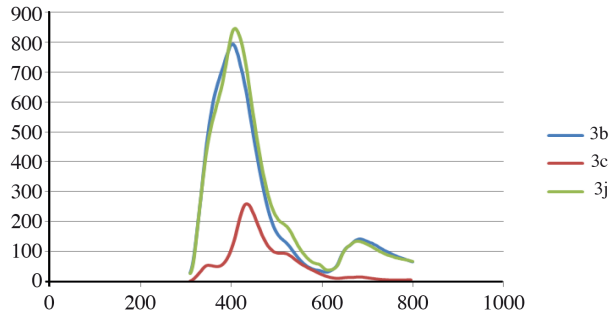


Figure 5. Photoluminescence spectra of some selected compounds in $CHCl_3$ at 10^{-5} M.

References

1. Wagner B. D. *Molecules* **2009**, *14*, 210–237.
2. Smyth, T.; Ramachandran, V. N.; Smyth, W. F. *Int. J. Antimicrob. Agents.* **2009**, *33*, 42–48.
3. Dekić, V.; Radulović, N.; Vukicević, R.; Dekić, B.; Stojanović-Radi, Z.; Palić, R. *Afr. J. Pharma. Pharmacol.* **2011**, *5*, 371–375.
4. Belluti, F.; Fontana, G.; Bo, L. D.; Carenini, N.; Giommarelli, C.; Franco Zunino, F. *Bioorg. Med. Chem.* **2010**, *18*, 3543–3550.
5. Al-Soud, Y. A.; Al-Sa'doni, H. H.; Amajaour. H. A. S.; Salih, K. S. M.; Mubarak, M. S.; Al-Masoudi, N. A.; Jaber, I. H., *Z. Naturforsch.* **2008**, *63b,* 83–90.
6. Manvar, A.; Malde, A.; Verma, J.; Virsodia, V.; Mishra, A.; Upadhyay, K.; Acharya, H.; Coutinho, E.; Shah, *Eur. J. Med. Chem.* **2008**, *43*, 2395–2403.
7. Zhou, X.; Wang, X. B.; Wang, T.; Kong, L. Y. *Bioorg. Med. Chem.* **2008**, *16*, 8011–8021.
8. Edenharder, A.; Speth, C.; Decker, M.; Kolodziej, H.; Kayser, O.; Platt, K. L. *Mutat. Res.* **1995**, *345*, 57–62.
9. Lee, B. H.; Clothier, M. F.; Dutton, F. E.; Conder, G. A.; Johnson, S. S. *J. Ethnopharmacol.* **2005**, *97*, 293–299.
10. Hoult, J. R. S.; Paydt, M. *Gen. Pharmac.* **1996**, *27*, 713–718.
11. Hwu, J. R.; Singha, R.; Hong, S. C.; Chang, Y. H.; Das, A. R.; Vliegen, I.; Clercq, E. D.; Neyts, J. *Antiviral Res.* **2008**, *77*, 157–162.
12. Kalkhambkar, R. G.; Kulkarni, G. M.; Kamanavalli, C. M.; Premkumar, N.; Asdaq, S. M. B.; Sun, C. M. *Eur. J. Med. Chem.* **2008**, *43*, 2178–2188.
13. Radanyi, C.; Bras, G. L.; Messaoudi, S.; Bouclier, C.; Peyrat, J. F.; Brion, J. D.; Marsaud, V.; Renoir, J. M.; Alami, M. *Bioorg. Med. Chem. Lett.* **2008**, *18*, 2495–2498.
14. Wood, W. J. L.; Patterson, A. W.; Tsuruoka, H.; Jain, K. R.; Ellman, J. A. *J. Am. Chem. Soc.* **2005**, *127*, 15521–15529.
15. Starcevic, S.; Kocbek, P.; Hribar, K. G.; Rizner, T. L.; Gobec, S. *Chem. Biol. Interact.* **2011**, *191*, 60–65.
16. Cheng, J. F.; Ishikawa, A.; Ono, Y.; Arrhenius, T.; Nadzan, A. *Bioorg. Med. Chem. Lett.* **2003**, *13*, 3647–3650.
17. Chimenti, F.; Secci, D.; Bolasco, A.; Chimenti, P.; Granese, A.; Befani, O.; Turini, P.; Alcaroc, S.; Ortuso, F. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 3697–3703.
18. Raj, H. G.; Parmar, V. S.; Jain, S. C.; Goel, S.; Poonam.; Himanshu.; Malhotra, S.; Singh, A.; Olsen, C. E.; Wengeld, J. *Bioorg. Med. Chem.* **1998**, *6*, 833–839.
19. Sarojini, B. K.; Krishna, B. G.; Darshanraj, C. G.; Bharath, B. R.; Manjunatha, H. *J. Eur. Med. Chem.* **2010**, *45*, 3490–3496.

20. Andreani, A.; Rambaldi, M.; Leoni, A.; Locatelli, A.; Bossa, R.; Chiericozzi, M.; Galatulas, I.; Salvator, G. *J. Eur. Med. Chem.* **1996**, *31*, 383–387.
21. El-Gaby, M. S. A. *J. Chin. Chem. Soc.-Taip.* **2004**, *51*, 125–132.
22. Clemence, F.; Marter, O. L.; Delevalle, F.; Benzoni, J.; Jouanen, A.; Jouquey, S.; Mouren, M.; Deraedt, R. *J. Med. Chem.* **1988**, *31*, 1453–1461.
23. Dawane, B. S.; Konda, S. G. *Int. J. Pharm. Sci. Rev. Res.* **2010**, *3(2)*, 96–98.
24. Abdel-Aziz, H. A.; Abdal-Wahab, B. F.; El-Sharief, M. A. S. S.; Abdulla, M. M. *Monatsh. Chem.* **2009**, *140*, 431–437.
25. Plouvier, B.; Houssin, R.; Hecquet, B.; Colson, P.; Houssier, C.; Waring, M. J.; Henichart, J. P; Bailly, C. *Bioconjugate Chem.* **1994**, *5,* 475–482.
26. Patt, W. C.; Hamilton, H. W.; Taylor, M. D.; Ryan, M. J.; Taylor, D. G. Jr.; Connolly, C. J. C.; Doharty, A. M.; Klutchko, S. R.; Sircar, I.; Steinbaugh, B. A. *J. Med. Chem.* **1992**, *35*, 2562–2570.
27. Bell, F. W.; Cantrell, A. S.; Hoberg, M.; Jaskunas, S. R.; Johansson, N. G.; Jordon, C. L.; Kinnick, M. D.; Lind, P.; Morin, J. M. Jr.; Noreen, R. *J. Med. Chem.* **1995**, *38*, 4929–4937.
28. Kalkhambkar, R. G.; Kulkarni, G. M.; Shivkumar, H.; Rao, R. N. *Eur. J. Med. Chem.* **2007**, *42*, 1272–1276.
29. Vijesh, A. M.; Isloor, A. M.; Prabhu, V.; Ahmad, S.; Malladi, S. *Eur. J. Med. Chem.* **2010**, *45*, 5460–5464.
30. Rudolph, J.; Theis, H.; Hanke, R.; Endermann, R.; Johannsen, L.; Geschke, F. U. *J. Med. Chem.* **2001**, *44*, 619–625.
31. Geronikaki, A.; Hadjipavlov-Litina, D.; Zablotskaya, A.; Segal, I. *Bioinorg. Chem. Appl.* **2007**, Article ID 92145, 7 pages doi:10.1155/2007/92145.
32. Fink, B. A.; Mortensen, D. S.; Stauffer, S. R.; Aron, Z. D.; Katzenellenbogen, J. A. *Chem. Biol.* **1999**, *6*, 205–209.
33. Muijlwijk-Koezen, J. Ev.; Timmerman, H.; Vollinga, R. C.; Von Drabbe Kunzel, J. F.; De Groote, M.; Visser, S.; Ijzerman, A. P. *J. Med. Chem.* **2001**, *44*, 749–754.
34. Breslow, R. *J. Am. Chem. Soc.* **1958**, *80*, 3719–3727.
35. Wagner, B. D. *Molecules* **2009***, 14,* 210–237.
36. Kaloyanova, S; Ivanova, I; Tchorbanov, A; Dimitrova, P; Deligeorgiev, T. *J. Photochem. Photobiol. B* . **2011**, *103*, 215–221.
37. Flašík, R; Stankovičová, H; Gáplovský, A; Donovalová, J. *Molecules* **2009**, *14*, 4838–4848.
38. Lim, N. C.; Schuster, J. V.; Porto, M. C.; Tanudra, M. A.; Yao, L.; Freake, H. C.; Brückner, C. *Inor. Chem.* **2005**, *44*, 2018–2027.
39. Hara, K.; Sato, T.; Katoh, R.; Furube, A.; Ohga, Y.; Shinpo, A.; Suga, S.; Sayama, K.; Sugihara, H.; Arakawa, H. *J. Phys. Chem. B* **2003**, *107,* 597–603.
40. Mills, J. T.; Gleeson, H. F.; Goodby, J. W.; Hird, M.; Seed, A. *J. Mater. Chem.* **1998**, *8,* 2385–2390.
41. Dear, K. M.; Bedfordshire, L.; Jeffreys, R. A.; Thomas, D. A. 3,630,738. *US*, **1971**.
42. Nebe-von-Caron, G.; Stephens, P. J.; Hewitt, C. J.; Powell, J. R.; Badley, R. A. *J. Microbiol Meth.* **2000**, *42*, 97–114.
43. Rye, H. S.; Yue, S.; Wemmer, D. E.; Quesada, M. A.; Haugland, R. A.; Mathies, R. A.; Glazer, A. N. *Nucleic Acids* Res. **1992**, *20*, 2803–2812.
44. Yoon, S.; Albers, A. E.; Wong, A. P.; Chang, C. J. *J. Am. Chem. Soc.* 2005, *127*, 16030–16039.
45. Koti, R. J.; Koloavi, G. D.; Hegde, V. S.; Khazi, I. M. *Syn. Comun.,* **2007**, *37*, 99–105.
Full crystallographic data have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-867181. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.or by e-mailing data_request@ ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK.

46. Blessing, R. H. *Acta Cryst.* **1995**, *A51*, 33–38.

47. Spek, A. L. *J. Appl. Cryst.* **2003**, *36*, 7–13.

48. Sheldrick, G. M. *Acta Cryst.* **2008**, *A64*, 112–122.

49. Donovalová, J.; Cigáň, M.; Stankovičová, H.; Gašpar, J.; Danko, M.; Gáplovský, A.; Hrdlovič, P. *Molecules* **2012**, *17*, 3259–3276.

50. Yao, H.; Domoto, K.; Isohashi, T.; Kimura, K. *Langmuir* **2005**, *21*, 1067–1073.

51. García-Báez, E. V.; Martínez-Martínez, F. J.; Höpfl, H.; Padilla-Martínez, I. I. *ARKIVOC* **2003**, *xi*, 100–111.

52. Lee, S. H.; Helal, A.; Kim, H. S. *Bull. Korean. Chem. Soc.* **2010**, *31*, 615–619.

53. Yanxi, S.; Zhen, C.; Hongqi, L. *Curr. Org. Chem.* **2012**, *16*, 2690–2707.

54. Helal, A.; Harun-Or-Rashid, M.; Choi, C. H.; Kim, H. S. *Tetrahedron* **2011**, *67*, 2794–2802.

55. Mizukami, S.; Okada, S.; Kimura, S.; Kikuchi, K. *Inorg. Chem.* **2009**, *48*, 7630–7638.

56. Lin, W.; Yuan, L.; Cao, X.; Tan, W.; Feng, Y. *Eur. J. Org. Chem.* **2008**, *2008*(29), 4981–4987.