Organic & Biomolecular Chemistry

Cite this: *Org. Biomol. Chem.*, 2012, **10**, 2692

www.rsc.org/obc

PAPER

Direct C–H cross-coupling approach to heteroaryl coumarins†

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Received 20th December 2011, Accepted 23rd January 2012
DOI: 10.1039/c2ob07137a

A Pd-catalyzed direct cross-coupling of 3-bromocoumarins with heteroarenes provided an efficient route to synthesizing 3-heteroarylcoumarins. The reaction scope for the transformation was fairly broad, affording modest to good yields of various 3-heteroarylcoumarin scaffolds, which are privileged structures and prevalent motifs in many biologically active compounds and fluorophores.

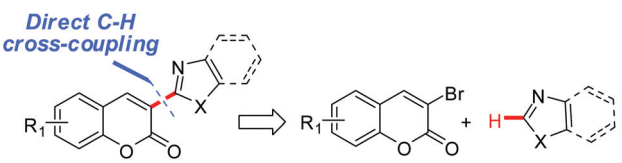
Introduction

Coumarins constitute a major class of naturally occurring compounds and privileged medicinal scaffolds that exhibit a broad range of biological and pharmaceutical properties, including anti-HIV, anti-tumor, anti-hypertension, anti-arrhythmia, anti-inflammatory, anti-osteoporosis, antiseptic, analgesic and anti-coagulant activities.[1] Coumarins are also most a important class of fluorophores, and they have been extensively investigated as powerful tools for biological applications, especially for live cell imaging.[2] Significant efforts have been directed toward developing efficient synthetic approaches to coumarin derivatives.[3] Among the compounds with valuable optical properties and biological activities are the 3-heteroarylcoumarins containing benzothiazole, benzoxazole and thiazole residues.[4] In this regard, developing more efficient methods for the construction of this structural motif is a topic of immense importance. Although many strategies for the synthesis of 3-heteroarylcoumarins have been developed,[4] the scope of such condensation reactions has been somewhat limited due to their harsh conditions, multistep synthesis, poor substituent tolerance, or low chemical yield, and therefore, the synthesis of some derivatives continues to pose a challenge. In this regard, developing alternative efficient methods for the construction of this structural motif is a topic of immense importance.

The direct functionalization of C–H bonds in heteroarenes is an exceedingly valuable process in the context of contemporary organic synthesis. In particular, direct arylation and vinylation of heteroarenes using transition-metal catalysts has found widespread use in synthesis for the construction of complex frameworks.[5] Inspired by the recent advances in this area, we envisaged that the development of a generally applicable synthetic strategy for preparing 3-heteroarylcoumarins *via* direct C–H cross-coupling of a coumarin core with benzothiazoles, benzoxazoles, thiazoles or caffeine would be highly desirable for a practical route to focused chemical libraries of coumarin derivatives (Scheme 1). In carrying out these efforts, we established an efficient protocol and investigated the photophysical properties of the synthesized coumarin derivatives, and herein report the details of these studies.

Results and discussion

At the outset, the direct C–H cross-coupling reaction conditions were optimized by employing 3-bromocoumarin (**1**) and benzothiazole (**2**) as model substrates. CuI in the absence of palladium catalysts could carry out the coupling reaction but exhibited only negligible activity (Table 1, entries 1–2). A catalytic system comprising both $Pd(OAc)_2$ and CuI improved the reaction efficiency (entry 4). The addition of PPh_3 has been shown to enhance the yield significantly for the coupling reaction (entry 5), indicating the pivotal role of a phosphine ligand in the catalytic cycle. Reaction optimization revealed that, at 110 °C, $Pd(PPh_3)_4$ (2.5 mol%) with CuI (3 equiv), Cs_2CO_3 (2 equiv) and 1,4-dioxane, was the most efficient in providing the desired product. These reaction conditions provided an 84% yield of **3a** (entry 6). An excess of the benzothiazole (2 equiv) was needed to ensure complete conversion of the 3-bromocoumarin. Reactions conducted under other bases, temperatures, solvents or lower amount of CuI provided lower yields of the cross-coupled product. Interestingly, replacing CuI with other copper(I) compounds significantly reduced the reactivity (entry 7).



Scheme 1 Synthetic strategy for construction of 3-heteroarylcoumarins *via* direct C–H cross-coupling.

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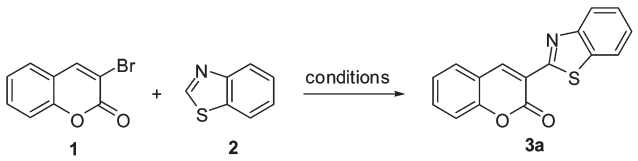
†Electronic supplementary information (ESI) available: ^1H and ^{13}C NMR spectra. See DOI: 10.1039/c2ob07137a

Table 1 Development of cross-coupling of coumarin with benzothiazole[a]



Entry	Catalyst (2.5 mol%)	Additive (equiv)	Solvent	Yield[b] (%)
1	None	CuI (3)	1,4-Dioxane	Trace
2	None	CuI (3); Phen (0.2)	1,4-Dioxane	7
3	$Pd(OAc)_2$	None	1,4-Dioxane	5
4	$Pd(OAc)_2$	CuI (3)	1,4-Dioxane	27
5	$Pd(OAc)_2$	CuI (3); PPh_3 (3)	1,4-Dioxane	58
6	$Pd(PPh_3)_4$	CuI (3)	1,4-Dioxane	84
7	$Pd(PPh_3)_4$	CuCl (3)	1,4-Dioxane	6
8	$Pd(PPh_3)_4$	Cu(Xantphos)I (3)	1,4-Dioxane	72
9	$Pd(PPh_3)_4$	CuI (3)	DMF	15
10	$Pd(PPh_3)_4$	CuI (3)	Toluene	62

[a] Reactions were conducted with coumarin (1 equiv), benzothiazole (2 equiv), and Cs_2CO_3 (2 equiv) at 110 °C for 6 h. [b] Yields are reported after isolation and purification by flash silica gel chromatography. Phen = 1,10-phenanthroline.

No beneficial effects were observed when either Xantphos[6] (entry 8) or *t*-$BuCO_2H$, were employed.

The scope of the Pd-catalyzed direct cross-coupling procedure was investigated using substituted coumarins and benzothiazoles or benzoxazoles as coupling partners. Gratifyingly, the reaction scope using this catalyst system was broad, and all coupling reactions went to completion in less than 12 h with modest to good yields (Table 2). These derivatives yielded broad fluorescence emission spectra over 400–500 nm, associated with high quantum yields, as summarized in Table 2. The photophysical and spectroscopic properties of coumarins can be readily modified by introducing substituents into the coumarin core.[4c] The addition of electron-donating groups such as OMe and NEt_2 at position 7 on the coumarin core triggers a bathochromic shift and enhances the photophysical properties. Furthermore, a comparative analysis of the values in Table 2 revealed that the substituent in the benzothiazole or benzoxazole affected the absorption/emission wavelength. For example, a direct comparison of **3a** (λ_{em} = 451 nm, Φ_F = 0.15) with **4d** (λ_{em} = 491 nm, Φ_F = 0.45) or **4e** (λ_{em} = 486 nm, Φ_F = 0.43) clearly revealed that introduction of OMe or phenyl groups to the C-6 position on the benzothiazole ring gave rise to notably red-shifted maxima and increased the value of Φ_F.

Because the photophysical properties also depended on the substituents on the benzothiazole ring, we carried out a study to investigate the synergistic effects, if any, on the photoluminescence efficiency by incorporating substituents on both the coumarin core and the benzothiazole ring. To this end, 7-OMe or NEt_2 substituted coumarins were coupled to 6-OMe or phenyl substituted benzothiazoles, respectively, under the reaction conditions, to provide the desired products **5a–5d** with modest yields (Table 3). The emission maxima of these compounds were slightly red shifted relative to the emission maxima of the corresponding unsubstituted benzothiazolyl coumarins **3e** and **3g**.

To diversify the 3-heteroarylcoumarin derivatives further, our method was explored using other heteroarenes. We were pleased to observe that this synthetic strategy was suitable for the synthesis of 3-thiazolylcoumarins. For example, thiazole and 4,5-dimethylthiazole participated in a cross-coupling reaction with 3-bromocoumarins to afford the corresponding coupling products in modest to good yields as summarized in Table 4. The 3-thiazolylcoumarin derivatives **6a–6f** were found to possess similar fluorescence properties as those of the corresponding 3-benzothiazolylcoumarins.

Because some xanthine derivatives are biologically active and fluorescent,[7] we further probed our synthetic method for its utility toward coupling of 3-bromocoumarins with caffeine. Indeed, the addition of the caffeine group to the 3 position of the coumarin core was expected to induce a red-shift in the emission wavelength, by extending the electronic conjugation and introducing electron-withdrawing effects. To our delight, caffeine was compatible with the coupling reaction conditions, and modest to good yields of the desired products were obtained as shown in Table 5. Furthermore, these new derivatives **7a–7c** exhibited strong photonic luminescence (Table 5) and appeared to be promising in their potential for further modification to yield biologically active compounds with high photoluminescence efficiencies.

Conclusions

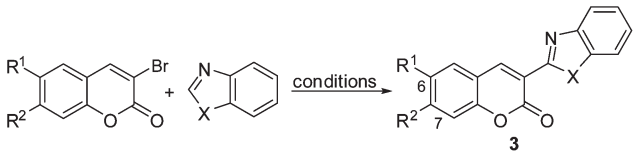
We developed an efficient method for the direct cross-coupling of a coumarin core and various heteroarenes *via* a palladium-catalyzed C–H functionalization reaction. The reaction scope for the transformation was fairly broad, affording good yields of a wide range of 3-heteroaryl coumarins, which are privileged structures in many biologically active compounds and fluorophores. In addition, our synthetic strategy led to the discovery of new caffeine-based derivatives that show intense photonic luminescence.

Experimental

General methods and materials

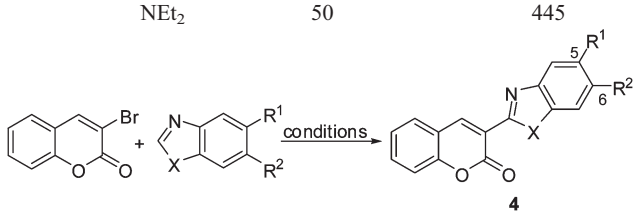
Unless stated otherwise, reactions were performed in flame-dried glassware under a positive pressure of nitrogen using freshly distilled solvents. Analytical thin layer chromatography (TLC) was performed on precoated silica gel 60 F254 plates and visualization on TLC was achieved by UV light (254 and 354nm). Flash column chromatography was undertaken on silica gel (400–630 mesh). ^{1}H NMR spectra were recorded at 400 MHz or 300 MHz and chemical shifts were quoted in parts per million (ppm) referenced to the appropriate solvent peak or 0.0 ppm for tetramethylsilane. The following abbreviations were used to describe peak splitting patterns when appropriate: br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublet. Coupling constants, *J*, were reported in hertz (Hz). ^{13}C NMR spectra were recorded at 100 MHz and were fully decoupled by broad band proton decoupling. Chemical shifts were reported in ppm referenced to the center line of a triplet at 77.0 ppm of chloroform-d. Mass spectral data were obtained from the KAIST Basic Science Institute by using EI

Table 2 Pd-catalyzed direct cross-coupling of various coumarins with benzoxazole or benzothiazole[a]



3

Compd	X	R^1	R^2	Yield[b] (%)	λ_{abs}[c] (nm)	λ_{em}[d] (nm)	ϕ_F[e]
3a		H	H	84	361	451	0.15
3b		OMe	H	56	393	461	0.07
3c		Me	H	47	368	449	0.28
3d	S	Cl	H	61	367	458	0.11
3e		H	OMe	64	379	465	0.55
3f		OMe	OMe	40	408	476	0.73
3g		H	NEt_2	48	462	496	0.93
3h		H	H	76	353	448	0.49
3i		Cl	H	46	367	451	0.32
3j	O	OMe	H	64	382	460	0.03
3k		H	OMe	55	374	446	0.64
3l		OMe	OMe	43	393	462	0.60
3m		H	NEt_2	50	445	481	0.93

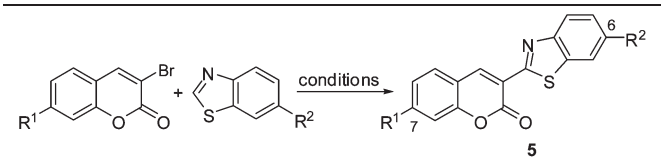


4

Compd	X	R^1	R^2	Yield[b] (%)	λ_{abs}[c] (nm)	λ_{em}[d] (nm)	ϕ_F[e]
4a		Cl	H	42	364	443	0.10
4b		H	Me	48	370	465	0.40
4c	S	H	Cl	33	366	454	0.49
4d		H	OMe	48	371	491	0.45
4e		H	Ph	44	376	486	0.43
4f		Cl	H	81	378	441	0.52
4g	O	Me	H	59	362	450	0.61
4h		Ph	H	72	363	461	0.64

[a] Reactions were conducted with coumarin (1 equiv), benzothiazole (2 equiv), $Pd(PPh_3)_4$ (2.5 mol%), CuI (3 equiv) and Cs_2CO_3 (2 equiv) in 1,4-dioxane at 110 °C over 6–12 h. [b] Yields are reported after isolation and purification by flash silica gel chromatography. [c] Only the longest absorption maxima are shown. [d] Excited at the maximum excitation wavelength. [e] Absolute fluorescence quantum yield.

Table 3 Pd-catalyzed direct cross-coupling of substituted coumarins and benzothiazoles[a]



5

Compd	R^1	R^2	Yield (%)	λ_{abs} (nm)	λ_{em} (nm)	ϕ_F
5a	OMe	OMe	42	407	489	0.46
5b		Ph	40	404	485	0.47
5c	NEt_2	OMe	36	451	502	0.76
5d		Ph	51	454	503	0.78

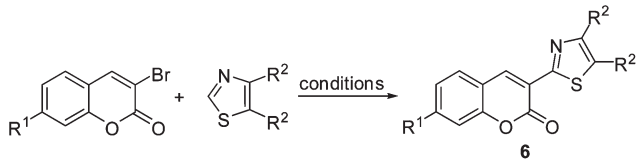
[a] Reactions were conducted with coumarin (1 equiv), benzothiazole (2 equiv), $Pd(PPh_3)_4$ (2.5 mol%), CuI (3 equiv) and Cs_2CO_3 (2 equiv) in 1,4-dioxane at 110 °C for 6 h.

methods. Commercial grade reagents and solvents were used without further purification except as indicated below. Dichloromethane was distilled from calcium hydride. THF was distilled from sodium. Unless otherwise stated, all commercial reagents and solvents were used without additional purification.

General procedure (GP) for synthesis of 3-heteroarylcoumarins

Bromocoumarins (1 eq.), heteroarene (2 eq.), $Pd(PPh_3)_4$ (2.5 mol %), CuI (3 eq.) and Cs_2CO_3 (2 eq.) were combined in 1,4-dioxane under air. The reaction mixture was heated to 110 °C with stirring. The reaction was monitored by TLC using 25% EtOAc and 75% *n*-hexane as the mobile phase. After disappearance of starting material (coumarins), the reaction mixture was diluted and filtered through Celite with CH_2Cl_2. After removal of solvent, the residue was purified by flash chromatography on silica gel to give desired product.

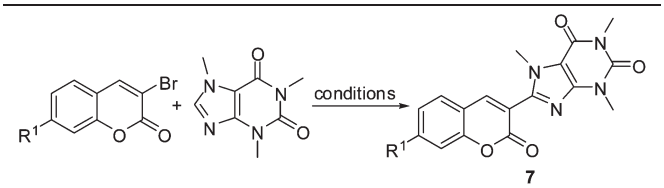
Table 4 Pd-catalyzed direct cross-coupling of coumarins with thiazoles[a]



Compd	R^1	R^2	Yield (%)	λ_{abs} (nm)	λ_{em} (nm)	ϕ_F
6a	H		60	349	423	0.60
6b	OMe	H	78	375	444	0.70
6c	NEt_2		82	434	484	0.73
6d	H		64	366	456	0.63
6e	OMe	Me	67	390	464	0.61
6f	NEt_2		75	438	489	0.70

[a] Reactions were conducted with coumarin (1 equiv), benzothiazole (2 equiv), $Pd(PPh_3)_4$ (2.5 mol%), CuI (3 equiv) and Cs_2CO_3 (2 equiv) in 1,4-dioxane at 110 °C for 6 h.

Table 5 Pd-catalyzed direct cross-coupling of coumarins with caffeine[a]



Compd	R^1	Yield (%)	λ_{abs} (nm)	λ_{em} (nm)	ϕ_F
7a	H	46	352	479	0.37
7b	OMe	43	360	472	0.53
7c	NEt_2	72	420	481	0.57

[a] Reactions were conducted with coumarin (1 equiv), caffeine (2 equiv), $Pd(PPh_3)_4$ (2.5 mol%), CuI (3 equiv) and Cs_2CO_3 (2 equiv) in 1,4-dioxane at 110 °C for 6 h.

3-(Benzo[*d*]thiazol-2-yl)-2*H*-chromen-2-one (3a). Yield 84% (13.6 mg); mp 221–223 °C; IR (KBr): 2926, 1716, 1604, 1187, 756 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.08 (s, 1H), 8.08 (d, J = 8.1 Hz, 1H), 7.96 (d, J = 8.1 Hz, 1H), 7.72 (dd, J = 7.7, 1.5 Hz, 1H), 7.64–7.62 (m, 1H), 7.54–7.50 (m, 1H), 7.43–7.39 (m, 2H), 7.37 (td, J = 7.6, 0.8 Hz, 1H); ^{13}C NMR δ (100 MHz, $CDCl_3$): 116.7, 118.9, 120.2, 121.7, 122.9, 125.2, 125.5, 126.6, 129.4, 133.3, 137.8, 141.6, 152.3, 153.9, 159.8, 159.9; HRMS (EI+) m/z calcd for $C_{16}H_9NNaO_2S^+$ $[M + Na]^+$: 302.0246, found: 302.0269.

3-(Benzo[*d*]thiazol-2-yl)-6-methoxy-2*H*-chromen-2-one (3b). Yield 56% (13.4 mg); mp 213–215 °C; IR (KBr): 1712, 1455, 839, 754 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.07 (s, 1H), 8.08 (d, J = 8.2 Hz, 1H), 7.96 (d, J = 8.2 Hz, 1H), 7.52 (td, J = 8.2, 1.2 Hz, 1H), 7.41 (td, J = 8.2, 1.1 Hz, 1H), 7.35 (d, J = 9.1 Hz, 1H), 7.20 (dd, J = 9.1 2.9 Hz, 1H), 7.11 (d, J = 2.9 Hz, 1H); ^{13}C NMR δ (100 MHz, $CDCl_3$): 55.9, 110.7, 117.8, 119.3, 119.9, 121.8, 121.8, 122.6, 125.6, 126.7, 136.5, 141.9, 148.5, 151.6, 156.6, 159.9, 160.2; HRMS (EI+) m/z calcd for $C_{17}H_{11}NNaO_3S^+$ $[M + Na]^+$: 332.0352, found: 332.0399.

3-(Benzo[*d*]thiazol-2-yl)-6-methyl-2*H*-chromen-2-one (3c). Yield 47% (11.6 mg); mp 230–232 °C; IR (KBr): 1737, 1496, 1264, 821 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.01 (s, 1H), 8.07 (d, J = 8.1 Hz, 1H), 7.96 (d, J = 8.1 Hz, 1H), 7.53–7.47 (m, 2H), 7.43–7.40 (m, 2H), 7.31 (d, J = 8.4 Hz, 1H), 2.44 (s, 3H); ^{13}C NMR δ (100 MHz, $CDCl_3$): 21.6, 116.8, 119.0, 120.2, 121.4, 122.3, 125.2, 128.4, 129.4, 133.2, 135.9, 136.9, 141.3, 150.2, 153.8, 158.9, 159.8; HRMS (EI+) m/z calcd for $C_{17}H_{11}NNaO_2S^+$ $[M + Na]^+$: 316.0403, found: 316.0407.

3-(Benzo[*d*]thiazol-2-yl)-6-chloro-2*H*-chromen-2-one (3d). Yield 61% (14.9 mg); mp 250–252 °C; IR (KBr): 1727, 1481, 1252, 1194, 812 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.98 (s, 1H), 8.09 (d, J = 8.1 Hz, 1H), 7.98 (d, J = 8.1 Hz, 1H), 7.68 (d, J = 2.4 Hz, 1H), 7.58–7.52 (m, 2H), 7.46–7.37 (m, 2H); HRMS (EI+) m/z calcd for $C_{16}H_8ClNNaO_2S^+$ $[M + Na]^+$: 335.9856, found: 335.9853.[8]

3-(Benzo[*d*]thiazol-2-yl)-7-methoxy-2*H*-chromen-2-one (3e). Yield 64% (15.5 mg); mp 232–235 °C; IR (KBr): 1712, 1594, 1281, 838, 750 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.03 (s, 1H), 8.06 (d, J = 8.2 Hz, 1H), 7.95 (d, J = 8.2 Hz, 1H), 7.60 (d, J = 8.8 Hz, 1H), 7.52–7.48 (m, 1H), 7.41–7.37 (m, 1H), 6.93 (dd, J = 8.8, 2.4 Hz, 1H), 6.89 (d, J = 2.4 Hz, 1H); ^{13}C NMR δ (100 MHz, $CDCl_3$): 56.1, 100.6, 112.7, 114.1, 115.9, 121.8, 122.2, 125.4, 126.7, 130.9, 135.9, 142.7, 151.2, 156.2, 160.1, 160.9, 164.7; HRMS (EI+) m/z calcd for $C_{17}H_{11}NNaO_3S^+$ $[M + Na]^+$: 332.0352, found: 332.0371.

3-(Benzo[*d*]thiazol-2-yl)-6,7-dimethoxy-2*H*-chromen-2-one (3f). Yield 40% (9.4 mg); mp 260–262 °C; IR (KBr): 1713, 1619, 1004, 840, 755 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.03 (s, 1H), 8.05 (d, J = 8.1 Hz, 1H), 7.96 (d, J = 7.7 Hz, 1H), 7.51 (t, J = 7.1 Hz, 1H), 7.40 (t, J = 7.4 Hz, 1H), 7.05 (s, 1H), 6.93 (s, 1H), 3.99 (s, 3H), 3.95 (s, 3H); HRMS (EI+) m/z calcd for $C_{18}H_{13}NNaO_4S^+$ $[M + Na]^+$: 362.0457, found: 362.0467.[4c]

3-(Benzo[*d*]thiazol-2-yl)-7-(diethylamino)-2*H*-chromen-2-one (3g). Yield 48% (8.6 mg); mp 213–215 °C; IR (KBr): 2922, 1709, 1191, 754 cm^{-1}; ^1H NMR (300 MHz, CD_2Cl_2) δ 8.92 (s, 1H), 7.97 (t, J = 7.4 Hz, 1H), 7.54–7.46 (m, 2H), 7.37 (t, J = 8.2 Hz, 1H), 6.72 (dd, J = 9.0, 2.5 Hz, 1H), 6.59 (d, J = 2.4 Hz, 1H), 3.49 (q, J = 7.1 Hz, 4H), 1.27 (t, J = 7.1 Hz, 6H); HRMS (EI+) m/z calcd for $C_{20}H_{18}N_2NaO_2S^+$ $[M + Na]^+$: 373.0981, found: 373.0985.[8]

3-(Benzo[*d*]oxazol-2-yl)-2*H*-chromen-2-one (3h). Yield 76% (9.8 mg); mp 179–181 °C; IR (KBr): 1733, 686 cm^{-1}; ^1H NMR δ (300 MHz, DMSO-d_6): 9.07 (s, 1H), 8.00 (dd, J = 7.7, 1.4 Hz, 1H), 7.87–7.76 (m, 3H), 7.51–7.42 (m, 4H) ; HRMS (EI^+) m/z calcd for $C_{16}H_9NNaO_3^+$ $[M + Na]^+$: 286.0475, found: 286.0486.[9]

3-(Benzo[*d*]oxazol-2-yl)-6-chloro-2*H*-chromen-2-one (3i). Yield 46% (6.9 mg); mp 204–206 °C; IR (KBr): 1746, 1250, 814, 674 cm^{-1}; ^1H NMR δ (400 MHz, CD_2Cl_2): 8.71 (s, 1H), 7.85–7.83 (m, 1H), 7.70 (d, J = 2.4 Hz, 1H), 7.68–7.63 (m, 1H), 7.62 (dd, J = 8.8, 2.5 Hz, 1H), 7.47–7.39 (m, 2H), 7.38 (d, J =

8.8 Hz, 1H); ^{13}C NMR δ (100 MHz, CD_2Cl_2): 111.2, 116.7, 118.6, 119.8, 121.0, 125.4, 126.6, 128.6, 130.5, 133.9, 142.1, 144.2, 151.1, 153.3, 156.2, 158.2; HRMS (EI$^+$) *m/z* calcd for $C_{16}H_8ClNNaO_3^+$ [M + Na]$^+$: 320.0085, found: 320.0096.

3-(Benzo[*d*]oxazol-2-yl)-6-methoxy-2*H*-chromen-2-one (3j). Yield 64% (7.4 mg); mp 193–195 °C; IR (KBr): 1728, 1256 cm^{-1}; ^{1}H NMR δ (400 MHz, CD_2Cl_2): 8.74 (s, 1H), 7.82–7.81 (m, 1H), 7.65 (d, *J* = 7.0 Hz, 1H), 7.44–7.40 (m, 2H), 7.34 (d, *J* = 9.0 Hz, 1H), 7.25 (dd, *J* = 9.1 Hz, 3.0, 1H), 7.12 (d, *J* = 2.9 Hz, 1H), 3.88 (s, 3H); ^{13}C NMR δ (100 MHz, CD_2Cl_2): 56.3, 111.0, 111.1, 115.9, 118.1, 119.2, 120.9, 122.3, 125.3, 126.4, 142.2, 145.5, 149.6, 151.1, 156.9, 156.9, 158.9; HRMS (EI$^+$) *m/z* calcd for $C_{17}H_{11}NNaO_4^+$ [M + Na]$^+$: 316.0580, found: 316.0593.

3-(Benzo[*d*]oxazol-2-yl)-7-methoxy-2*H*-chromen-2-one (3k). Yield 55% (8.3 mg); mp 188–190 °C; IR (KBr): 1746, 1613, 1283, 1229, 773, 740 cm^{-1}; ^{1}H NMR δ (400 MHz, CD_2Cl_2): 8.72 (s, 1H), 7.80–7.78 (m, 1H), 7.64–7.62 (m, 1H), 7.60 (d, *J* = 8.6 Hz, 1H), 7.43–7.36 (m, 2H), 6.96–6.93 (m, 1H), 6.89 (d, *J* = 1.9 Hz, 1H), 3.92 (s, 3H); ^{13}C NMR δ (100 MHz, CD_2Cl_2): 56.5, 100.9, 111.0, 111.8, 112.6, 113.9, 120.6, 125.1, 126.0, 130.8, 142.3, 145.8, 151.0, 157.1, 157.3, 159.3, 165.2; HRMS (EI$^+$) *m/z* calcd for $C_{17}H_{11}NNaO_4^+$ [M + Na]$^+$: 316.0580, found: 316.0592.

3-(Benzo[*d*]oxazol-2-yl)-6,7-dimethoxy-2*H*-chromen-2-one (3l). Yield 43% (6.8 mg); mp 261–263 °C; IR (KBr): 1726, 1248, 739 cm^{-1}; ^{1}H NMR δ (400 MHz, CD_2Cl_2): 8.72 (s, 1H), 7.81–7.79 (m, 1H), 7.65–7.63 (m, 1H), 7.41–7.38 (m, 2H), 7.04 (s, 1H), 6.92 (s, 1H), 3.97 (s, 3H), 3.92 (s, 3H); ^{13}C NMR δ (100 MHz, CD_2Cl_2): 56.7, 56.9, 100.1, 109.2, 111.0, 111.5, 111.9, 120.6, 125.1, 125.9, 142.4, 142.9, 145.7, 147.5, 151.0, 151.9, 155.7, 157.4; HRMS (EI$^+$) *m/z* calcd for $C_{18}H_{13}NNaO_5^+$ [M + Na]$^+$: 346.0686, found: 346.0690.

3-(Benzo[*d*]oxazol-2-yl)-7-(diethylamino)-2*H*-chromen-2-one (3m). Yield 50% (8.4 mg); mp 179–181 °C; IR (KBr): 1740, 1587, 1230, 770, 739 cm^{-1}; ^{1}H NMR δ (300 MHz, CD_2Cl_2): 8.61 (s, 1H), 7.75 (br, 1H), 7.60 (br, 1H), 7.46 (d, *J* = 8.9 Hz, 1H), 7.36–7.34 (m, 2H), 6.68 (dd, *J* = 8.9, 2.3 Hz, 1H), 6.54 (s, 1H), 3.47 (q, *J* = 7.1 Hz, 4H), 1.25 (t, *J* = 7.1 Hz, 6H); HRMS (EI$^+$) *m/z* calcd for $C_{20}H_{18}N_2NaO_3^+$ [M + Na]$^+$: 357.1210, found: 357.1206.[10]

3-(5-Chlorobenzo[*d*]thiazol-2-yl)-2*H*-chromen-2-one (4a). Yield 42% (14.6 mg); mp 271–273 °C; IR (KBr): 1726, 965, 750 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.07 (s, 1H), 8.05 (d, *J* = 1.8 Hz, 1H), 7.87 (d, *J* = 8.5 Hz, 1H), 7.73 (dd, *J* = 7.6, 1.1 Hz, 1H), 7.65 (td, *J* = 8.5, 1.3 Hz, 1H), 7.43 (d, *J* = 8.3 Hz, 1H), 7.40–7.37 (m, 2H); HRMS (EI+) *m/z* calcd for $C_{16}H_8ClNNaO_2S^+$ [M + Na]$^+$: 335.9856, found: 335.9858.[8]

3-(6-Methylbenzo[*d*]thiazol-2-yl)-2*H*-chromen-2-one (4b). Yield 48% (7.0 mg); mp 219–221 °C; IR (KBr): 1722, 1262, 806 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.03 (s, 1H), 7.95 (d, *J* = 8.4 Hz, 1H), 7.74 (s, 1H), 7.70 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.59 (td, *J* = 7.1, 1.5 Hz, 1H), 7.42 (d, 8.3 Hz, 1H), 7.38–7.31 (m, 2H), 2.50 (s, 3H); ^{13}C NMR δ (100 MHz, $CDCl_3$): 21.6, 116.8, 119.0, 120.2, 121.4, 122.3, 125.2, 128.4, 129.4, 133.2, 135.9, 135.9, 136.9, 141.3, 150.2, 153.8, 158.9, 159.8; HRMS (EI+) *m/z* calcd for $C_{17}H_{11}NNaO_2S^+$ [M + Na]$^+$: 316.0403, found: 316.0412.

3-(6-Chlorobenzo[*d*]thiazol-2-yl)-2*H*-chromen-2-one (4c). Yield 33% (9 mg); mp 229–231 °C; IR (KBr): 1725, 1195, 813, 744 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.09 (s, 1H), 7.99 (d, *J* = 8.8 Hz, 1H), 7.93 (d, *J* = 2 Hz, 1H), 7.73 (dd, J = 7.8, 1.5 Hz, 1H), 7.66–7.63 (m, 1H), 7.49–7.38 (m. 3H); ^{13}C NMR δ (100 MHz, $CDCl_3$): 116.9, 118.9, 119.7, 121.3, 123.5, 125.4, 127.6, 129.6, 131.6, 133.6, 137.8, 142.2, 150.4, 153.9, 159.8, 160.6; HRMS (EI+) *m/z* calcd for $C_{16}H_8ClNNaO_2S^+$ [M + Na]$^+$: 335.9856, found: 335.9846.

3-(6-Methoxybenzo[*d*]thiazol-2-yl)-2*H*-chromen-2-one (4d). Yield 48% (12.8 mg); mp 199–201 °C; IR (KBr): 1726, 1603, 821, 758 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.02 (s, 1H), 7.95 (d, *J* = 8.9 Hz, 1H), 7.77 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.64 (t, *J* = 1.6 Hz, 1H), 7.46–7.40 (m, 3H), 7.14 (dd, *J* = 8.9, 2.5 Hz, 1H), 3.91 (s, 3H); ^{13}C NMR δ (100 MHz, $CDCl_3$): 55.8, 103.4, 116.7, 116.9, 119.0, 120.2, 123.4, 125.2, 129.3, 133.1, 138.2, 140.8, 146.6, 153.7, 157.4, 158.1, 159.9; HRMS (EI+) *m/z* calcd for $C_{17}H_{11}NNaO_3S^+$ [M + Na]$^+$: 332.0352, found: 332.0344.

3-(6-Phenylbenzo[*d*]thiazol-2-yl)-2*H*-chromen-2-one (4e). Yield 44% (13.7 mg); mp 256–258 °C; IR (KBr): 1738, 1260, 797 cm^{-1}; ^{1}H NMR (300 MHz, CD_2Cl_2) δ 9.12 (s, 1H), 8.22 (d, *J* = 1.4 Hz, 1H), 8.13 (d, *J* = 8.5 Hz, 1H), 7.80 (dd, *J* = 8.5, 1.8 Hz, 2H), 7.73–7.66 (m, 3H), 7.53–7.40 (m, 5H); ^{13}C NMR δ (100 MHz, CD_2Cl_2): 117.0, 119.5, 120.2, 120.8, 123.4, 125.6, 126.6, 127.7, 127.9, 129.9, 133.6, 138.0, 139.1, 140.9, 141.9, 152.4, 154.3, 160.2, 160.4; HRMS (EI+) *m/z* calcd for $C_{22}H_{13}NNaO_2S^+$ [M + Na]$^+$: 378.0559, found: 378.0561.

3-(5-Chlorobenzo[*d*]oxazol-2-yl)-2*H*-chromen-2-one (4f). Yield 81% (11.9 mg); mp 239–241 °C; IR (KBr): 1756, 1000, 802, 754 cm^{-1}; ^{1}H NMR δ (300 MHz, $CDCl_3$): 8.79 (s, 1H), 7.83 (s, 1H), 7.70–7.66 (m, 2H), 7.56 (d, *J* = 8.3 Hz, 1H), 7.44–7.37 (m, 3H); HRMS (EI$^+$) *m/z* calcd for $C_{16}H_8ClNNaO_3^+$ [M + Na]$^+$: 320.0085, found: 320.0097.[9]

3-(5-Methylbenzo[*d*]oxazol-2-yl)-2*H*-chromen-2-one (4g). Yield 34% (10.0 mg); mp 161–163 °C; IR (KBr): 1739, 754 cm^{-1}; ^{1}H NMR δ (400 MHz, CD_2Cl_2): 8.77 (s, 1H), 7.71 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.66 (d, *J* = 7.3 Hz, 1H), 7.60 (s, 1H), 7.52 (d, *J* = 8.3 Hz, 1H), 7.42–7.38 (m, 1H), 7.24 (d, *J* = 9.4 Hz, 1H), 2.49 (s, 3H); ^{13}C NMR δ (100 MHz, CD_2Cl_2): 21.6, 110.5, 115.8, 117.0, 118.9, 120.6, 125.3, 127.6, 129.6, 134.1, 135.4, 142.4, 145.5, 149.3, 155.0, 156.8, 158.8; HRMS (EI$^+$) *m/z* calcd for $C_{17}H_{11}NNaO_3^+$ [M + Na]$^+$: 300.0631, found: 300.0650.

3-(5-Phenylbenzo[*d*]oxazol-2-yl)-2*H*-chromen-2-one (4h). Yield 72% (12.2 mg); mp 174–176 °C; IR (KBr): 1748, 757 cm^{-1}; ^{1}H NMR δ (400 MHz, $CDCl_3$): 8.82 (s, 1H), 8.02 (d, *J* = 1.4 Hz, 1H), 7.73 (dd, *J* = 1.5 Hz, 1H), 7.72–7.65 (m, 5H), 7.50–7.47 (m, 2H), 7.44–7.37 (m, 3H); ^{13}C NMR δ (100 MHz, $CDCl_3$): 111.2, 115.5, 117.0, 118.8, 119.1, 125.4, 125.9, 127.8, 129.3, 129.7, 134.3, 139.1, 141.1, 142.8, 145.8, 149.5, 150.6,

155.0, 156.7, 159.4; HRMS (EI$^+$) *m/z* calcd for $C_{22}H_{13}NNaO_3^+$ [M + Na]$^+$: 362.0788, found: 362.0799.

7-Methoxy-3-(6-methoxybenzo[*d*]thiazol-2-yl)-2*H*-chromen-2-one (5a). Yield 42% (11.0 mg); mp 205–207 °C; IR (KBr): 1719, 827, 816, 767 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.99 (s, 1H), 7.95 (d, J = 8.8 Hz, 1H), 7.60 (d, J = 8.6 Hz, 1H), 7.37 (d, J = 2.3 Hz, 1H), 7.11 (dd, J = 8.9, 2.5 Hz, 1H), 6.94–6.88 (m, 2H), 3.90 (s, 3H), 3.89 (s, 3H); ^{13}C NMR δ (100 MHz, $CDCl_3$): 55.9, 56.0, 100.6, 103.5, 112.8, 113.9, 116.4, 116.7, 122.9, 130.6, 137.7, 141.4, 155.9, 157.9, 158.2, 160.2, 164.3; HRMS (EI+) *m/z* calcd for $C_{18}H_{13}NNaO_4S^+$ [M + Na]$^+$: 362.0457, found: 362.0461.

7-Methoxy-3-(6-phenylbenzo[*d*]thiazol-2-yl)-2*H*-chromen-2-one (5b). Yield 40% (12.0 mg); mp 268–270 °C; IR (KBr): 1714, 1019, 767, 760 cm^{-1}; ^{1}H NMR (300 MHz, CD_2Cl_2) δ 9.06 (s, 1H), 8.20 (s, 1H), 8.09 (d, J = 8.4 Hz, 1H), 7.78 (d, J = 9.4 Hz, 1H), 7.71–7.67 (m, 3H), 7.49 (t, J = 7.3 Hz, 2H), 7.39 (t, J = 7.3 Hz, 1H), 6.99–6.95 (m, 2H); ^{13}C NMR δ (100 MHz, CD_2Cl_2): 56.1, 77.3, 77.6, 100.5, 112.8, 113.8, 119.8, 122.7, 125.9, 127.3, 127.5, 128.9, 130.7, 137.4, 138.2, 140.5, 141.7, 151.9, 156.1, 164.4; HRMS (EI+) *m/z* calcd for $C_{23}H_{15}NNaO_3S^+$ [M + Na]$^+$: 408.0665, found: 408.0658.

7-(Diethylamino)-3-(6-methoxybenzo[*d*]thiazol-2-yl)-2*H*-chromen-2-one (5c). Yield 36% (9.1 mg); mp 200–203 °C; IR (KBr): 1705, 1256, 1014, 801, 790 cm^{-1}; ^{1}H NMR (400 MHz, CD_2Cl_2) δ 8.83 (s, 1H), 7.86 (d, J = 8.9 Hz, 1H), 7.50 (d, J = 8.9 Hz, 1H), 7.41 (d, J = 2.5 Hz, 1H), 7.08 (dd, J = 8.9 Hz, 2.5 Hz, 1H), 6.70 (dd, J = 8.9, 2.5 Hz, 1H), 6.57 (d, J = 2.4 Hz, 1H), 3.89 (s, 3H), 3.47 (q, J = 7.1 Hz, 4H), 1.25 (t, J = 7.1 Hz, 6H); ^{13}C NMR δ (100 MHz, CD_2Cl_2): 12.6, 45.4, 56.2, 97.2, 104.0, 108.9, 110.3, 112.9, 116.1, 123.1, 131.0, 138.1, 141.6, 147.7, 152.5, 157.3, 157.8, 159.6, 161.4; HRMS (EI+) *m/z* calcd for $C_{21}H_{20}N_2NaO_3S^+$ [M + Na]$^+$: 403.1087, found: 403.1092.

7-(Diethylamino)-3-(6-phenylbenzo[*d*]thiazol-2-yl)-2*H*-chromen-2-one (5d). Yield 51% (10.7 mg); mp 212–215 °C; IR (KBr): 1728, 1275, 760 cm^{-1}; ^{1}H NMR δ (400 MHz, CD_2Cl_2): 8.92 (s, 1H), 8.16 (d, J = 1.8 Hz, 1H), 8.02 (d, J = 8.5 Hz, 1H), 7.73 (dd, J = 8.5, 1.9 Hz, 1H), 7.70–7.68 (m, 2H), 7.52 (d, J = 8.9 Hz, 1H), 7.48 (t, J = 7.4 Hz, 2H), 7.38–7.36 (m, 1H), 6.71 (dd, J = 8.9, 2.5 Hz, 1H), 6.58 (d, J = 2.4 Hz, 1H), 3.47 (q, J = 7.1 Hz, 4H), 1.25 (t, J = 7.1 Hz, 6H). ^{13}C NMR δ (100 MHz, CD_2Cl_2): 12.6, 45.5, 97.2, 109.0, 110.5, 112.6, 120.1, 122.5, 126.1, 127.6, 127.7, 129.3, 131.3, 137.4, 138.0, 141.1, 142.4, 152.5, 152.7, 157.5, 161.3, 162.4; HRMS (EI$^+$) *m/z* calcd for $C_{26}H_{22}N_2NaO_2S^+$ [M + Na]$^+$: 449.1294, found: 449.1284.

3-(Thiazol-2-yl)-2*H*-chromen-2-one (6a). Yield 60% (12.0 mg); mp 148–151 °C; IR (KBr): 1730 cm^{-1}; ^{1}H NMR (400 MHz, CD_2Cl_2) δ 8.91 (s, 1H), 7.97 (d, J = 3.2 Hz, 1H), 7.73 (dd, J = 7.7, 1.4 Hz, 1H), 7.63–7.61 (m, 1H), 7.56 (d, J = 3.2 Hz, 1H), 7.44–7.38 (m, 2H); ^{13}C NMR δ (100 MHz, CD_2Cl_2): 116.9, 119.6, 120.8, 122.6, 125.4, 129.6, 132.9, 139.5, 143.5, 153.9, 159.5, 160.2; HRMS (EI+) *m/z* calcd for $C_{12}H_7NNaO_2S^+$ [M + Na]$^+$: 252.0090, found: 252.0098.

7-Methoxy-3-(thiazol-2-yl)-2*H*-chromen-2-one (6b). Yield 78% (15.4 mg); mp 188–190 °C; IR (KBr): 1710, 1254, 844, 723 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.83 (s, 1H), 7.92 (d, J = 3.2 Hz, 1H), 7.55 (d, J = 8.5 Hz, 1H), 7.47 (d, J = 3.2 Hz, 1H), 6.92–6.87 (m, 2H), 3.89 (s, 3H). ^{13}C NMR δ (100 MHz, $CDCl_3$): 55.9, 100.5, 112.7, 113.8, 116.8, 121.5, 130.2, 139.6, 142.5, 155.5, 159.8, 160.1, 163.8; HRMS (EI+) *m/z* calcd for $C_{13}H_9NNaO_3S^+$ [M + Na]$^+$: 282.0195, found: 282.0203.

7-(Diethylamino)-3-(thiazol-2-yl)-2*H*-chromen-2-one (6c). Yield 82% (12.1 mg); mp 125–128 °C; IR (KBr): 1706, 1616, 819 cm^{-1}; ^{1}H NMR δ (400 MHz, CD_2Cl_2): 8.71 (s, 1H), 7.86 (d, J = 3.2 Hz, 1H), 7.46 (d, J = 8.9 Hz, 1H), 7.40 (d, J = 3.2 Hz, 1H), 6.68 (dd, J = 8.9, 2.5 Hz, 1H), 6.56 (d, J = 2.5 Hz, 1H), 3.46 (q, J = 7.1 Hz, 4H), 1.23 (t, J = 7.1 Hz, 6H); ^{13}C NMR δ (100 MHz, CD_2Cl_2): 12.6, 45.4, 97.2, 108.8, 110.2, 113.3, 120.3, 130.7, 140.2, 142.7, 152.1, 157.0, 161.2, 161.2; HRMS (EI$^+$) *m/z* calcd for $C_1H_{16}N_2NaO_2S^+$ [M + Na]$^+$: 323.0825, found: 323.0842.

3-(4,5-Dimethylthiazol-2-yl)-2*H*-chromen-2-one (6d). Yield 64% (14.1 mg); mp 190–192 °C; IR (KBr): 1713, 1220, 1191, 944, 758 cm^{-1}; ^{1}H NMR (400 MHz, CD_2Cl_2) δ 8.75 (s, 1H), 7.68 (dd, J = 7.6 , 1.6 Hz, 1H), 7.61–7.56 (m, 1H), 7.40–7.33 (m, 2H), 2.42 (s, 3H), 2.38 (s, 3H); ^{13}C NMR δ (100 MHz, CD_2Cl_2): 11.4, 14.9, 116.8, 119.7, 120.9, 125.3, 129.2, 130.9, 132.4, 137.6, 149.6, 153.6, 154.0, 160.1; HRMS (EI+) *m/z* calcd for $C_{14}H_{11}NNaO_2S^+$ [M + Na]$^+$: 280.0403, found: 280.0411.

3-(4,5-Dimethylthiazol-2-yl)-7-methoxy-2*H*-chromen-2-one (6e). Yield 67% (15.0 mg); mp 166–168 °C; IR (KBr): 1717, 1016, 813 cm^{-1}; ^{1}H NMR (400 MHz, CD_2Cl_2) δ 8.70 (s, 1H), 7.58 (d, J = 8.5 Hz, 1H), 6.94–6.89 (m, 2H), 3.09 (s, 3H), 2.41 (s, 3H), 2.37 (s, 3H); ^{13}C NMR δ (100 MHz, CD_2Cl_2): 11.4, 14.9, 56.3, 100.8, 113.4, 113.7, 117.7, 129.9, 130.3, 138.1, 149.2, 154.7, 155.6, 160.5, 163.8; HRMS (EI+) *m/z* calcd for $C_{15}H_{13}NNaO_3S^+$ [M + Na]$^+$: 310.0508, found: 310.0510.

7-(Diethylamino)-3-(4,5-dimethylthiazol-2-yl)-2*H*-chromen-2-one (6f). Yield 75% (12.2 mg); mp 196–198 °C; IR (KBr): 1705, 816, 768 cm^{-1}; ^{1}H NMR δ (400 MHz, CD_2Cl_2): 8.58 (s, 1H), 7.43 (d, J = 8.9 Hz, 1H), 6.66 (dd, J = 9.0, 2.5 Hz, 1H), 6.54 (d, J = 2.5 Hz, 1H), 3.44 (q, J = 7.1 Hz, 4H), 2.36 (d, J = 13.9 Hz, 6H), 1.22 (t, J = 7.1 Hz, 6H); ^{13}C NMR δ (100 MHz, CD_2Cl_2): 11.3, 12.6, 14.9, 45.3, 97.2, 109.0, 110.1, 113.7, 128.2, 130.4, 138.7, 148.5, 151.8, 155.9, 156.7, 161.1; HRMS (EI$^+$) *m/z* calcd for $C_{18}H_{20}N_2NaO_2S^+$ [M + Na]$^+$: 351.1138, found: 351.1147.

1,3,7-Trimethyl-8-(2-oxo-2*H*-chromen-3-yl)-3,4,5,7-tetrahydro-1*H*-purine-2,6-dione (7a). Yield 46% (13.7 mg); mp 294–296 °C; IR (KBr): 1718, 1656, 760 cm^{-1}; ^{1}H NMR (300 MHz, CD_2Cl_2) δ 8.23 (s, 1H), 7.71–7.68 (m, 2H), 7.45–7.39(m, 2H), 3.95 (s, 3H), 3.56 (s, 3H), 3.37(s, 3H); ^{13}C NMR δ (100 MHz, CD_2Cl_2): 28.1, 29.9, 34.2, 109.6, 117.1, 118.1, 125.5, 129.4, 133.9, 146.7, 147.7, 148.4, 151.9, 154.9, 155.8, 158.7; HRMS (EI+) *m/z* calcd for $C_{17}H_{14}N_4NaO_4^+$ [M + Na]$^+$: 361.0907, found: 361.0919.

8-(7-(Diethylamino)-2-oxo-2*H*-chromen-3-yl)-1,3,7-trimethyl-1*H*-purine-2,6(3*H*,7*H*)-dione (7c). Yield 72% (14.5 mg); mp 241–243 °C; IR (KBr): 1706, 1663, 1600, 1250, 760 cm^{-1}; ^{1}H

NMR δ (400 MHz, CD_2Cl_2): 8.02 (s, 1H), 7.39 (d, J = 8.9 Hz, 1H), 6.67 (dd, J = 8.9, 2.5 Hz, 1H), 6.54 (d, J = 2.4 Hz, 1H), 3.91 (s, 3H), 3.55 (s, 3H), 3.47 (q, J = 7.1 Hz, 4H), 3.36 (s, 3H), 1.24 (t, J = 7.1 Hz, 6H); ^{13}C NMR δ (100 MHz, CD_2Cl_2): 12.6, 28.0, 29.8, 34.0, 45.4, 97.2, 108.4, 109.0, 110.0, 130.5, 147.7, 148.4, 148.6, 152.0, 152.6, 155.7, 158.0, 159.7; HRMS (EI^+) m/z calcd for $C_{21}H_{23}N_5NaO_4^+$ $[M + Na]^+$: 432.1642, found: 432.1660.

Absolute quantum yield measurement

Absolute quantum yields (Φ_F) were measured by a combination system of a spectrophotometer (V-530 UV/Vis Spectrophotometer, JASCO, Inc.) with a fluorimeter (RF-5301PC Spectrofluorophotometer, SHIMADZU Corp.) Samples were prepared as solutions by dilution of the fluorescent compound in DCM. Absorption λ_{max} was measured with a spectrophotometer scanning the 700–250 range wavelength while fluorescence emission λ_{max} and integrated intensity were analyzed with OriginPro 8 software. The absolute quantum yield of a known fluorescent dye – fluorescein – was obtained to determine those of the samples precisely (Φ_F = 0.925 ± 0.015 in 0.1 N NaOH aqueous solution).

Acknowledgements

This research was supported by National Research Foundation of Korea (NRF) funded by the Ministry of Education, Science and Technology (NRF-2010-0022179, 2011-0020322 and 2011-0016436).

Notes and references

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