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SYNTHESIS AND PROPERTIES OF 4-(3-AMINO-2-BENZOFURANYL)-COUMARINS

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The alkylation of o-cyanophenol by 4-chloromethylcoumarins and subsequent intramolecular condensation by the cyano and methylene groups gives substituted 4-(3-amino-2-benzofuranyl)coumarins. We studied the reactions of these compounds with acylating agents as well as with aldehydes, which lead to the 6H-[1]benzofuro[3,2-b]chromeno[4,3-d]pyridin-6-one system as the result of consecutive transformations.

Keywords: 4-(3-amino-2-benzofuranyl)coumarin, 6H-[1]benzofuro[3,2-*b*]chromeno[4,3-*d*]pyridin-6-one, 1,2-dihydropyridine, 4-chloromethylcoumarin, 5H-chromeno[3,4-*c*] pyridin-5-one, *o*-cyanophenol.

The healing properties of many plants have been long known and their present use is continuing to increase since an advantage of plant preparations is their low toxicity and the possibility of using them for long periods without the risk of side-reactions. The major groups of therapeutically active plants are alkaloids, steroid glycosides, saponins, flavonoids, coumarins, organic acids, and vitamins.

Derivatives of oxygen heterocycles are among the most common classes of natural products [1]. Compounds containing two or more oxygen heterocycles are encountered in nature much less frequently. Some of the most important such compounds are furocoumarins [2], linear and angular furochromones, coumestans, rotenoids [3], and coumarin and flavonoid derivatives containing a pyran ring fused to ring A or B [4, 5].

Coumarin derivatives containing a benzofuran ring possess anti-inflammatory, hypotensive, and analgesic action [6-9]. Thus, in a continuation of a study of the synthesis and properties of coumarin heteroanalogs, we investigated the preparation and reactivity of substituted 4-(3-amino-2-benzofuranyl)-coumarins. Special interest was found in the synthesis of condensed derivatives of pyridino[3,4-*c*]coumarins since such alkaloids have been isolated from *Schumanniophyton problematicum* [10]. Many alkaloids are known to be very valuable pharmaceutical products or serve as starting materials for the synthesis of such products.

The alkylation of salicylonitrile by 4-bromomethylcoumarin in acetone in the presence of potassium carbonate at room temperature leads to 4-(2-cyanophenoxymethoxy)coumarins, which are converted upon heating in ethanol at reflux in the presence of potassium carbonate into 4-(3-amino-2-benzofuranyl)coumarins [9].

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TABLE 1. Characteristics of Coumarin Derivatives **1-5** and **7**

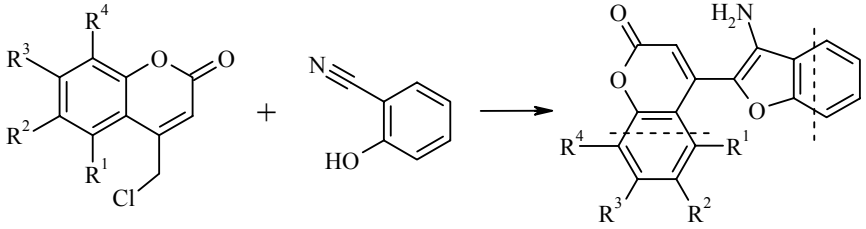
Compound	Empirical formula	Found, % / Calculated, %		mp, °C	Yield, %
		Hal	N		
1	2	3	4	5	6
1b	$C_{13}H_{13}ClO_2$	14.35 / 14.98		110-112	62
1c	$C_{10}H_6Cl_2O_2$	30.48 / 30.95		138-140	26
2a	$C_{19}H_{15}NO_3$		4.73 / 4.59	204-205	75
2b	$C_{20}H_{17}NO_3$		4.46 / 4.39	185-186	56
2c	$C_{17}H_{10}ClNO_3$	11.56 / 11.37	4.35 / 4.49	272-273	68
2d	$C_{18}H_{13}NO_3$		4.62 / 4.81	259-260	63
2e	$C_{19}H_{15}NO_3$		4.85 / 4.59	249-250	71
2f	$C_{20}H_{15}NO_3$		4.47 / 4.41	237-238	78
2g	$C_{18}H_{12}ClNO_3$	10.67 / 10.88	4.39 / 4.30	298-299	58
2h	$C_{19}H_{15}NO_3$		4.37 / 4.59	228-230	43
2i	$C_{19}H_{15}NO_3$		4.67 / 4.59	274-275	67
2j	$C_{19}H_{15}NO_3$		4.38 / 4.59	235-236	62
3a	$C_{23}H_{19}NO_4$		3.56 / 3.75	188-189	68
3b	$C_{24}H_{17}NO_5$		3.47 / 3.51	202-204	57
3c	$C_{28}H_{23}NO_5$		3.25 / 3.09	207-208	74
3d	$C_{19}H_{12}ClNO_4$	10.34 / 10.02	3.68 / 3.96	276-278	49
3e	$C_{23}H_{21}NO_4$		3.81 / 3.73	181-183	42
3f	$C_{23}H_{21}NO_4$		3.65 / 3.73	286-287	47
3g	$C_{27}H_{19}NO_6$		2.89 / 3.09	260-262	51
3h	$C_{29}H_{23}NO_6$		2.66 / 2.91	233-234	49
3i	$C_{26}H_{16}ClNO_6$	7.66 / 7.48	2.79 / 2.96	286-288	42
3j	$C_{22}H_{19}NO_4$		3.95 / 3.88	226-228	45
3k	$C_{24}H_{17}NO_5$		3.67 / 3.51	275-277	65
3l	$C_{29}H_{25}NO_7$		2.56 / 2.80	238-239	51
3m	$C_{26}H_{20}N_2O_4$		6.46 / 6.60	266-267	71
4a	$C_{29}H_{19}NO_7$		2.75 / 2.84	201-202	75
4b*	$C_{30}H_{21}NO_5S_2$		2.79 / 2.60	244-245	68
5a	$C_{23}H_{17}NO_3$		3.69 / 3.94	174-175	70
5b	$C_{24}H_{17}NO_3$		3.76 / 3.81	233-235	65
7a	$C_{28}H_{21}NO_5$		2.86 / 3.10	270-271	48

TABLE 1 (continued)

1	2	3	4	5	6
7b	$C_{29}H_{21}NO_5$		3.31 / 3.02	> 300	43
7c	$C_{20}H_{13}NO_3$		4.65 / 4.44	> 300	57
7d	$C_{27}H_{19}NO_3$		3.18 / 3.45	> 300	61
7e	$C_{26}H_{12}F_5NO_3$	19.76 / 19.73	3.12 / 2.91	> 300	47
7f	$C_{25}H_{16}N_2O_3$		7.22 / 7.14	> 300	36
7g	$C_{25}H_{16}N_2O_3$		7.36 / 7.14	232-234	40
7h	$C_{27}H_{20}N_2O_5$		5.88 / 6.19	268-270	32

Found, %: S 11.76; Calculated, %: S 11.88.

Hence, we studied the reaction of 4-chloromethylcoumarins **1a-j** with salicylonitrile in various solvents such as acetone, dioxane, and DMF at different temperatures. Thus, 4-(3-amino-2-benzofuranyl)coumarins **2a-j** were isolated when the reaction was carried out in anhydrous DMF with a four-fold excess of potassium carbonate upon stirring the reaction mixture at 80-100°C (Table 1). A one-step synthesis of these amines was developed by selecting the proper reaction conditions.



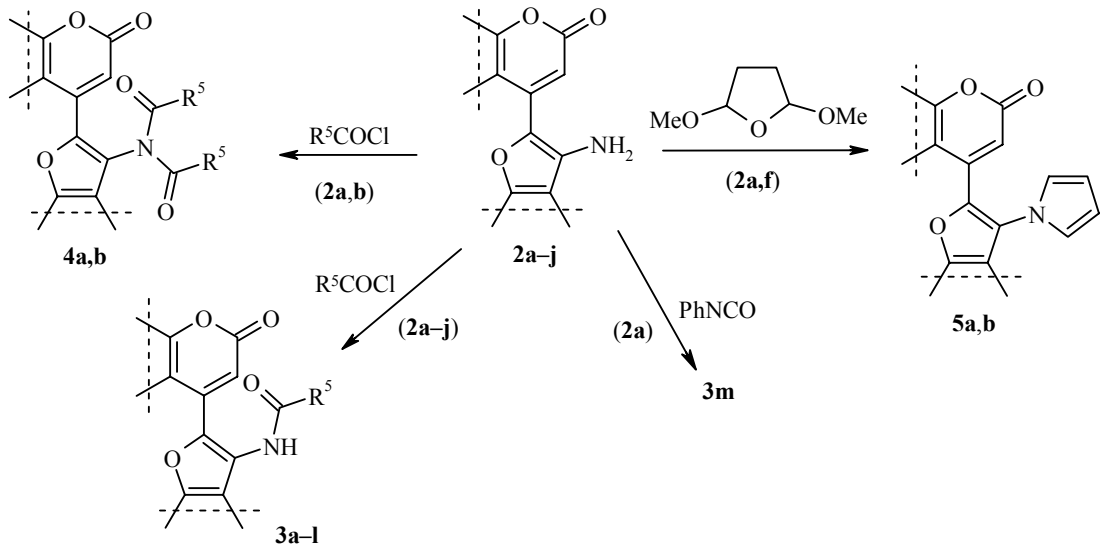
1a–j **2a–j**

1a–g, **2a–g** $R^1 = R^4 = H$; **1**, **2 a** R^2 = Et, $R^3 = H$; **b** R^2 = Pr-*i*; $R^3 = H$; **c** R^2 = Cl, $R^3 = H$; **d** $R^2 = H$, R^3 = Me; **e** $R^2 = R^3$ = Me; **f** $R^2R^3 = (CH_2)_3$; **g** R^2 = Cl, R^3 = Me; **h** $R^1 = R^3$ = Me, $R^2 = R^4 = H$; **i** $R^1 = R^2 = H$, $R^3 = R^4$ = Me; **j** $R^1 = R^3 = H$, $R^2 = R^4$ = Me

The presence of an amino group in **2a-j** was demonstrated by NMR spectroscopy (Table 2) and chemical transformations. Thus, a two-proton broadened singlet at 5.38-6.30 ppm is observed in the ^{1}H NMR spectra of substituted coumarins **2a-j**, which corresponds to the amino group.

We studied the acylation of the amino group in an investigation of the reactivity of 4-(3-amino-2-benzofuranyl)coumarins **2a-j**. Product amines **2a-j** are acylated by acid chloride derivatives of aliphatic, aromatic, and heterocyclic carboxylic acids upon prolonged heating at 50-60°C in dioxane in the presence of pyridine to give amides **3a-l**. Under analogous conditions, the reaction of amine **2a** with phenyl isocyanate gives urea derivative **3m**. Derivatives of bisacylation at the nitrogen atom **4a**,**b** are obtained when the acylation reaction of **2a**,**b** is carried out with a significant excess of the acid chloride of 2-furancarboxylic and 2-thiophenecarboxylic acids in pyridine.

Brief heating of **2a**,**f** with 2,5-dimethoxytetrahydrofuran in acetic acid leads to pyrroles **5a**,**b**, which contain a benzofuran substituent at C-1.



3a–i $R^1 = R^4 = H$, **a** R^2 = Et, $R^3 = H$, R^5 = cyclopropyl, **b** R^2 = Et, $R^3 = H$, R^5 = furyl-2, **c** R^2 = *i*-Pr, $R^3 = H$, $R^5 = C_6H_4OMe$-4, **d** R^2 = Cl, $R^3 = H$, R^5 = Me, **e** $R^2 = H$, R^3 = Me, R^5 = *t*-Bu, **f** $R^2 = R^3$ = Me, R^5 = *i*-Pr, **g** $R^2 = R^3$ = Me, $R^5 = C_6H_3(OCH_2O)$-3,4, **h** $R^2\ R^3 = CH_2CH_2CH_2$, $R^5 = C_6H_3(OMe)_2$-3,5, **i** R^2 = Cl, R^3 = Me, $R^5 = C_6H_3(OCH_2O)$-3,4, **j** $R^1 = R^3$ = Me, $R^2 = R^4 = H$, R^5 = Et, **k** $R^1 = R^2 = H$, $R^3 = R^4$ = Me, R^5 = furyl-2, **l** $R^1 = R^3 = H$, $R^2 = R^4$ = Me, $R^5 = C_6H_2(OMe)_3$-3,4,5, **m** $R^1 = R^3 = R^4 = H$, R^2 = Et, R^5 = NHPh, **4a**, **5a** $R^1 = R^3 = R^4 = H$, R^2 = Et; **4 a** R^5 = furyl-2, **b** $R^1 = R^3 = R^4 = H$, R^2 = *i*-Pr, R^5 = thienyl-2; **5b** $R^1 = R^4 = H$, $R^2R^3 = CH_2CH_2CH_2$

The synthesis of substituted 5H-chromeno[3,4-*c*]pyridin-5-ones has been studied by many workers and various methods have been reported for the preparation of these compounds, including the condensation of 3-cyano-4-(2-hydroxyphenyl)pyridine derivatives in PPA or HBr/HCl [11-14], of 4-(2-fluorophenyl)nicotinic acid upon heating [15], of salicylaldehyde, malononitrile, or ethyl cyanoacetate and ketones in the presence of ammonium acetate [16-21], of 4-dicyanomethylene-4H-1-benzopyrans with amines [22], and of 3-acetyl-coumarin with cyanoacetamide and ketones [23].

Heating amine **2a** with veratraldehyde in acetic acid in the presence of *p*-toluenesulfonic acid gave 6H-[1]benzofuro[3,2-*b*]chromeno[4,3-*d*]pyridin-6-one **7a**, whose structure was indicated by ^{1}H NMR spectroscopy (Table 3) and elemental analysis. Such polycyclic compounds have been obtained by Khan et al. [9] by [5+1] cycloaddition in the reaction of 4-(3-amino-2-benzofuranyl)coumarins with orthoesters of aliphatic acids.

The formation of chromenopyridone **7a** is possible through a sequence involving formation of a Schiff base, intramolecular cycloaddition of this base to give a condensed 1,2-dihydropyridine, which is oxidized by atmospheric oxygen to give the pyridine derivative. We isolated the proposed 1,2-dihydropyridine derivative **6a** from the reaction mixture and confirmed the structure of this intermediate by ^{1}H NMR spectroscopy.

A further study of the reactions of **2f**,**i** with various aldehydes led to the development of a new synthesis of 6H-[1]benzofuro[3,2-*b*]chromeno[4,3-*d*]pyridin-6-one derivatives containing residues of both aromatic and heteroaromatic aldehydes **7b-g**. Atmospheric oxygen proved the most suitable oxidizing agent in this case, though CrO_3 in acetic acid may also be used.

Thus, we have improved the synthesis of 4-(3-amino-2-benzofuranyl)coumarins and studied the reaction of these compounds with acylating agents. A new method was developed for the preparation of benzofurano-fused derivatives of 5H-chromeno[3,4-*c*]pyridin-5-ones, including previously unreported compounds possessing anti-inflammatory, analgesic, and antimicrobial effects.

TABLE 2. ^{1}H NMR Spectra of Compounds **2–5**

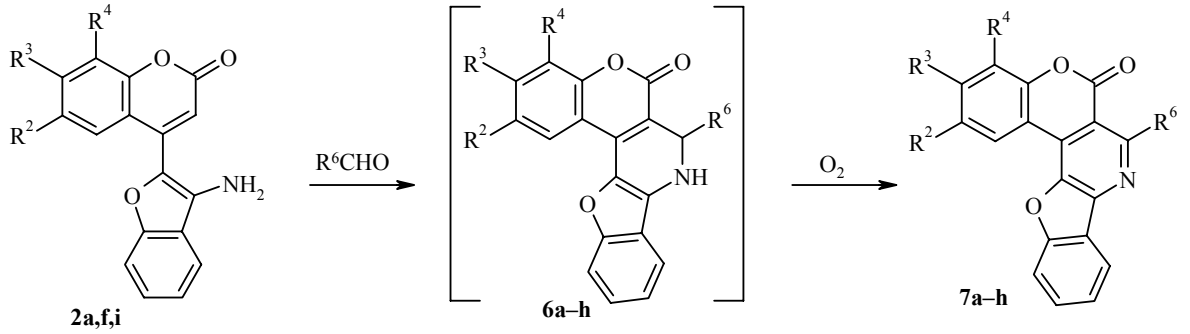
Compound	Chemical shifts, δ, ppm (*J*, Hz)									
	Coumarin residue					Benzofuran residue				
	H-3 (s)	5-R	6-R	7-R	8-R	3'-R	H-4' (m)	H-5' (m)	H-6' (m)	H-7' (m)
1	2	3	4	5	6	7	8	9	10	11
2a	6.50	8.23 (1H, m)	1.23 (3H, t, *J* = 7.0); 2.71 (2H, q, *J* = 7.0)	7.44 (1H, m)	7.36 (1H, m)	6.12 (2H, s)	7.98	7.30	7.49	7.58
2b	6.52	8.27 (1H, m)	1.26 (6H, m); 3.01 (1H, m)	7.55 (1H, m)	7.38(1H, m)	6.16 (2H, s)	8.00	7.31	7.47	7.58
2c	6.56	8.43 (1H, m)	—	7.70 (1H, m)	7.49 (1H, m)	6.30 (2H, s)	7.99	7.31	7.47	7.60
2d	6.47	8.34 (1H, m)	7.23 (1H, m)	2.44 (3H, s)	7.27 (1H, m)	6.17 (2H, s)	7.98	7.29	7.45	7.58
2e	6.44	8.18 (1H, m)	2.31 (3H, s)	2.34 (3H, s)	7.26 (1H, m)	6.13 (2H, s)	7.98	7.29	7.45	7.60
2f	6.44	8.19 (1H, m)	2.08 (2H, m); 2.96 (4H, m)		7. 30 (1H, m)	6.10 (2H, s)	7.97	7.29	7.44	7.58
2g	6.49	8.43 (1H, m)	—	2.44 (3H, s)	7.47 (1H, m)	6.30 (2H, s)	7.99	7.30	7.47	7.59
2h	6.49	2.37 (3H, s)	6.99 (1H, m)	2.06 (3H, s)	7.11 (1H, m)	5.38 (2H, s)	7.84	7.26	7.35	7.45
2i	6.47	8.15 (1H, m)	7.22 (1H, m)	2.32 (3H, s)	2.38 (3H, s)	6.12 (2H, s)	7.97	7.29	7.44	7.57
2j	6.50	8.00 (1H, m)	2.36 (3H, s)	7.34 (1H, m)	2.37 (3H, s)	6.06 (2H, s)	7.97	7.29	7.44	7.58
3a	6.66	7.73 (1H, m)	1.20 (3H, t, *J* = 7.5); 2.65 (2H, m)	7.27 (1H, m)	7.54 (1H, m)	0.64 (2H, m); 0.75 (2H, m); 1.81 (1H, m); 10.41 (1H, s)	7.71	7.39	7.50	7.53
3b	6.76	7.56 (1H, m)	1.03 (3H, t, *J* = 7.5); 2.53 (2H, m)	7.28 (1H, m)	7.40 (1H, m)	6.68 (1H, m); 7.50 (1H, m); 7.93 (1H, m); 10.50 (1H, s)	7.72	7.38	7.52	7.75
3c	6.75	7.57 (1H, m)	1.02 (6H, d, *J* = 7.2); 2.81 (2H, m)	7.52 (1H, m)	7.42 (1H, m)	3.82 (3H, s); 7.03 (2H, m); 7.91 (2H, m); 10.33 (1H, s)	7.75	7.39	7.52	7.72
3d	6.78	7.73 (1H, m)	—	7.73 (1H, m)	7.56 (1H, m)	2.03 (3H, s); 10.21 (1H, s)	7.75	7.39	7.50	7.73

TABLE 2 (continued)

1	2	3	4	5	6	7	8	9	10	11
3e	6.62	7.58 (1H, m)	7.22 (1H, m)	2.44 (3H, s)	7.34(1H, m)	1.19 (9H, s); 9.51 (1H, s)	7.73	7.38	7.49	7.73
3f	6.57	7.50 (1H, m)	2.24 (3H, s)	2.34 (3H, s)	7.31 (1H, m)	1.04 (6H, d, *J* = 7.2); 2.62 (1H, m); 9.96 (1H, s)	7.72	7.50	7.38	7.66
3g	6.66	7.54 (1H, m)	2.14 (3H, s)	2.29 (3H, s)	7.29 (1H, m)	7.04 (1H, m); 6.12 (2H, s); 7.43 (1H, m); 7.52 (1H, m); 10.29 (1H, s)	7.76	7.39	7.52	7.71
3h	6.67	7.60 (1H, m)	1.99 (2H, m); 2.77 (2H, m); 2.93 (2H, m)		7.35 (1H, m)	3.78 (6H, s); 7.02 (2H, m); 6.72 (1H, m); 10.37 (1H, s)	7.76	7.39	7.52	7.74
3i	6.77	7.75 (1H, m)	—	2.40 (3H, s)	7.43 (1H, m)	6.13 (2H, s); 7.05 (1H, d, *J* = 8.1); 7.53 (2H, m); 10.40 (1H, s)	7.77	7.40	7.53	7.75
3j	6.41	2.38 (3H, s)	7.01 (1H, m)	2.01 (3H, s)	7.18 (1H, m)	1.04 (3H, m); 2.35 (2H, m); 9.88 (1H, s)	7.70	7.36	7.43	7.63
3k	6.69	7.56 (1H, m)	7.15 (1H, d. *J* = 8.4)	2.36 (3H, s)	2.33 (3H, s)	6.70, 7.31, 7.94 (3H, 3m); 10.44 (1H, s)	7.74	7.39	7.51	7.70
3l	6.74	7.43 (1H, m)	2.22 (3H, s)	7.34 (1H, m)	2.36 (3H, s)	3.73 (3H, s); 3.82 (6H, s); 7.23 (2H, s); 10.34 (1H, s)	7.77	7.40	7.52	7.74
3m	6.75	7.70 (1H, m)	1.10 (3H, t, *J* = 7.6); 2.59 (2H, m)	7.50 (1H, m)	7.41(1H, m)	7.25 (3H, m); 7.37 (2H, m); 8.72 (1H, s); 8.87 (1H, s)	7.76	7.38	7.52	7.74
4a	6.49	7.60 (1H, m)	1.14 (3H, t, *J* = 7.8); 2.59 (2H, q, *J* = 7.8)	7.47 (1H, m)	7.37 (1H, d, *J* = 8.7)	6.61 (2H, m); 7.24 (2H, m); 7.85 (2H, m)	7.86	7.51	7.58	7.50
4b	6.31	7.35 (1H, m)	1.15 (6H, d, *J* = 7.2); 2.86 (2H, m)	4.78 (1H, m)	7.39 (1H, d, *J* = 8.7)	7.08 (2H, m); 7.53 (2H, m); 7.94 (2H, m)	7.87	7.58	7.61	7.56
5a	6.61	7.10 (1H, m)	1.04 (3H, t, *J* = 7.5); 2.44 (2H, m)	7.44 (1H, m)	7.35 (1H, m)	6.25 (2H, m); 7.10 (2H, m)	7.83	7.48	7.60	7.77
5b	6.42	7.30 (1H, s)	2.00 (2H, m); 2.73 (2H, m); 2.94 (2H, m)		7.21 (1H, s)	6.27 (2H, m); 7.05 (2H, m)	7.82	7.46	7.59	7.72

TABLE 3. ^{1}H NMR Spestra of Benzofuro[3,2-*b*]pyridino[3,4-*c*]coumarins **7a-h**

Com-pound	Shemisal shifts δ, ppm (*J*, Hz)								
	1-R	2-R	3-R	4-R	7-R	H-9 (m)	H-10 (m)	H-11 (m)	H-12 (m)
7a	8.82 (1H, m)	1.35 (3H, m); 2.86 (2H, m)	7.61 (1H, m)	7.42 (1H, m)	3.76 (3H, s); 3.85 (3H, s); 7.04 (1H, m); 7.15 (1H, m); 7.20 (1H, m)	8.26	7.61	7.81	8.05
7b	8.76 (1H, m)	2.12 (2H, m); 3.02 (4H, m)		7.29 (1H, m)	3.77 (3H, s); 3.85 (3H, s); 7.05 (1H, m); 7.13 (1H, m); 8.20 (1H, m)	8.24	7.58	7.79	8.03
7s	9.05 (1H, d, *J* = 8.2)	7.67 (1H, d, *J* = 8.2)	2.66 (3H, s)	2.58 (3H, s)	9.77 (1H, s)	8.51	7.85	8.13	8.13
7d	8.72 (1H, d, *J* = 8.2)	7.34 (1H, d, *J* = 8.2)	2.48 (3H, s)	2.42 (3H, s)	2.31 (3H, s); 7.26 (2H, d, *J* = 7.9); 7.45 (2H, d, *J* = 7.9)	8.22	7.57	7.78	7.96
7e	8.75 (1H, d, *J* = 8.2)	7.43 (1H, d, *J* = 8.2)	2.44 (3H, s)	2.32 (3H, s)	—	8.29	7.63	7.86	8.05
7f	8.68 (1H, d, *J* = 8.2)	7.36 (1H, d, *J* = 8.2)	2.37 (3H, s)	2.26 (3H, s)	7.50 (1H, m); 7.99 (1H, m); 8.66 (1H, m); 8.76 (1H, s)	8.24	7.59	7.80	7.99
7g	8.78 (1H, d, *J* = 8.2)	7.42 (1H, d, *J* = 8.2)	2.44 (3H, s)	2.34 (3H, s)	7.53 (2H, d, *J* = 5); 8.67 (2H, d, *J* = 5)	8.26	7.60	7.81	8.01
7h	8.84 (1H, d, *J* = 8.2)	7.49 (1H, d, *J* = 8.2)	2.46 (3H, s)	2.35 (3H, s)	2.46 (3H, s); 4.72 (1H, d, *J* = 12.4); 4.85 (1H, d, *J* = 12.4); 8.12 (1H, s)	8.31	7.62	7.85	8.10



7a R^2 = Et, R^3 = R^4 = H, R^6 = $C_6H_3(OMe)_2$-3,4, **b** R^2R^3 = $(CH_2)_3$, R^4 = H, R^6 = $C_6H_3(OMe)_2$-3,4, **c**–**g** R^2 = H, R^3 = R^4 = Me, **c** R^6 = H, **d** R^6 = C_6H_4Me-4, **e** R^6 = C_6F_5, **f** R^6 = pyridyl-3, **g** R^6 = pyridyl-4, **h** R^2 = H, R^3 = R^4 = Me, R^5 = 3-hydroxy-5-hydroxymethyl-2-methyl-pyridyl-4

EXPERIMENTAL

Monitoring of the reaction course and purity of the products were carried out by thin-layer chromatography on Silufol UV-254 and Merck 60 F_{254} plates with 9:1 and 95:5 chloroform-methanol as the eluent. The physicochemical constants and elemental analysis data for products **4-7** are given in Table 1. The ^{1}H NMR spectra were taken on a Varian VXR 300 spectrometer at 300 MHz with DMSO-d_6 as the internal standard.

Samples of starting 4-chloromethylcoumarins **1a-i** were obtained according to previous procedures [24-26].

4-Chloromethyl-6-isopropyl-coumarin (1b). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.23 (6H, d, *J* = 7.0, 6-(C<u>H</u>$_3$)$_2$CH); 2.99 (1H, m, *J* = 7.0, 6-(CH$_3$)C<u>H</u>); 5.06 (2H, s, 4-CH_2); 6.66 (1H, s, H-3); 7.36 (1H, d, *J* = 9.0, H-5); 7.55 (1H, dd, *J* = 9.0, *J* = 2.0, H-7); 7.68 (1H, d, *J* = 2.0, H-8).

6-Chloro-4-methylcoumarin (1c). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 4.99 (2H, s, 4-CH_2); 6.71 (1H, s, H-3); 7.44 (1H, d, *J* = 9.0, H-5); 7.65 (1H, dd, *J* = 9.0, *J* = 2.0, H-7); 7.88 (1H, d, *J* = 2.0, H-8).

Synthesis of Amines 2a-i (General Method). 4-Chloromethylcoumarin **1a-1i** (10 mmol) in DMF (10 ml) was added to a mixture of *o*-cyanophenol (10 mmol) and anhydrous potassium carbonate (40 mmol) in anhydrous DMF (20 ml) at 60-80°C, The reaction mixture was stirred for 3-4 h at 80-100°C; the end of the reaction was determined chromatographically. The mixture was then filtered hot. The solvent was evaporated off and the residue was crystallized from DMF–methanol.

Synthesis of Amides 3a-3l (General Method). Acid chloride (12 mmol) was added to a solution of 4-(3-amino-2-benzofuranyl)coumarin **2a-c** (10 mmol) and 20 ml pyridine in 50 ml dioxane at 50-60°C. The reaction mixture was maintained at this temperature for 3-4 h and cooled. Then, the mixture was diluted by adding 100 ml water and left to crystallize. The precipitate formed was filtered off, dried, and crystallized from ethanol.

N-[2-(6-Ethyl-2-oxo-2H-chromen-4-yl)-1-benzofuran-3-yl]-N'-phenylurea (3m) was synthesized analogously to amides **3a-l** from amine **2a** (0.6 g, 2 mmol) and phenyl isocyanate (0.26 ml, 2.4 mmol).

Synthesis of imides 4a and 4b (General Method). Acid chloride (30 mmol) was added to a solution of 4-(3-amino-2-benzofuranyl)coumarin **2a** or **2b** (2 mmol) in pyridine (10 ml) at 50-60°C. The reaction mixture was maintained at this temperature for 3-4 h, poured into water (150 ml), and brought to pH 4-5 by adding dilute hydrochloric acid. The precipitate formed was filtered off, dried, and crystallized from ethanol.

6-Ethyl-4-[3-(1H-pyrrol-1-yl)-1-benzofuran-2-yl]-2H-chromen-2-one (5a) and 4-[3-(1H-Pyrrol-1-yl)-1-benzofuran-2-yl]-7,8-dihydrocyclopenta[*g*]chromen-2(6H)-one (5b). Amine **2a** or **2f** (5 mmol) and 2,5-dimethoxytetrahydrofuran (1.3 ml, 9.6 mmol) in glacial acetic acid (20 ml) was heated at 90-100°C; the end of the reaction was determined chromatographically. The mixture was cooled and the solvent was distilled off on a rotary evaporator at reduced pressure. The residue was crystallized from methanol.

Synthesis of 6H-[1]Benzofuro[3,2-*b*]chromeno[4,3-*d*]pyridin-6-ones 7a-h (General Method). A mixture of 4-(3-amino-2-benzofuranyl)coumarin **2a,f** or **2i** (5 mmol), aromatic aldehyde (5 mmol) or 37% formalin (1 ml, 10 mmol), and *p*-toluenesulfonic acid (10 mg) in acetic acid (50 ml) was heated for 2-3 h at 60-70°C. The solution, which turns red, was stirred with the introduction of an air stream until there was no further oxidation and it assums a yellowish-hue (the end of the reaction was determined chromatographically) or 4 mmol CrO_3 was added and the mixture was stirred with heating for 60-90 min. The reaction mixture was cooled and diluted by adding cold water. The precipitate formed was filtered off, dried, and crystallized from DMF or dioxane.

Evaporation of the mother liquor after the crystallization of **7a** gave pyridone **6a**.

7-(3,4-Dimethoxyphenyl)-2-ethyl-7,8-dihydro-6H-benzofuro[3,2-*b*]chromeno[4,3-*d*]pyridin-6-one (6a). The yield of **6** was 15 mg, $C_{28}H_{23}NO_5$; mp 247-248°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.28 (3H, t, *J* = 7.4, 2-C<u>H</u>$_3$CH$_2$); 2.76 (2H, m, 2-CH$_3$C<u>H</u>$_2$); 3.65, 3.67 (6H, 2s, 3'-OCH$_3$ and 4'-OCH$_3$); 5.92 (1H, d, *J* = 3.4, H-7); 6.82, 7.08 (3H, 2m, H-2', H-5', and H-6'); 7.34 (2H, m, H-4 and H-10); 7.53 (2H, m, H-3 and H-11); 7.69 (1H, m, H-12); 7.90 (1H, m, H-9); 8.37 (1H, d, *J* = 3.4, 8-NH); 8.47 (1H, m, H-1).

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