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ENSEMBLES OF RINGS WITH A COUMARIN UNIT. 1. SYNTHESIS OF 3-(2-R-THIAZOL-4-YL)- AND 3-(4-R-THIAZOL-2-YL)COUMARINS

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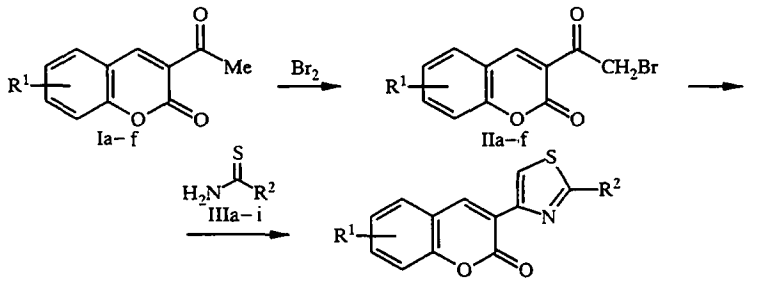
We have synthesized 3-(2-R-thiazol-4-yl)coumarins (R = H, CH_3, CH_2CN, Ar) by condensation of 3-(α-bromoacetyl)coumarins with thioamides. We obtained 3-(4-R-thiazol-2-yl)coumarins (R = H, Ar) by several methods. By reaction of 2-cyanomethyl-4-phenylthiazole with 2-hydroxybenzaldehydes, we synthesized 2-imino-3-(4-phenylthiazol-2-yl)coumarins, which were converted to the corresponding coumarins by acid hydrolysis. For 3-(2-R-thiazol-4-yl)coumarins (R = CH_2CN), we carried out reactions with aromatic aldehydes. We propose alternative methods for synthesis of 2-[2-aryl(hetaryl)-1-cyanoethenyl]-4-(coumarin-3-yl)thiazoles.

Ensembles of rings containing coumarin units have stimulated considerable interest among researchers. These compounds include active media for lasers with effective intramolecular energy transfer [1-3] and promising drugs [4-8]. In this paper, we present results of an investigation of synthesis routes for 3-(2-R-thiazol-4-yl) and 3-(4-R-thiazol-2-yl)coumarins.

Scheme 1



IVa-e, Va-d, VIa-f, VIIa-e, VIIIa-e, IXa-o

I, II a R^1 = H; b R^1 = 6-OMe; c R^1 = 7-OH; d R^1 = 7-NEt_2; e R^1 = 5,6-benzo; f R^1 = 6-n-C_6H_{13}, 7-OH; III a R^2 = H; b R^2 = CH_2CN; c R^2 = Me; d R^2 = Ph; e R^2 = p-$MeOC_6H_4$; f R^2 = p-$Me_2NC_6H_4$; g R^2 = p-ClC_6H_4; h R^2 = p-PhC_6H_4, i R^2 = p-(p-PhC_6H_4) C_6H_4; IV R^2 = H; VII R^2 = p-PhC_6H_4; VIII R^2 = p-(p-PhC_6H_4) C_6H_4; IV, VII, VIII a R^1 = H; b R^1 = 7-OH; c R^1 = 7-NEt_2; d R^1 = 5,6-benzo; e R^1 = 6-n-C_6H_{13}, 7-OH; V R^2 = CH_2CN; V a R^1 = H; b R^1 = 7-OH; c R^1 = 5,6-benzo; d R^1 = 6-n-C_6H_{13}, 7-OH; VI R^2 = Me; VI a R^1 = H; b R^1 = 6-OMe; c R^1 = 7-OH; d R^1 = 7-NEt_2; e R^1 = 5,6-benzo; f R^1 = 6-n-C_6H_{13}, 7-OH; IXa-f R^2 = Ph; a R^1 = H; b R^1 = 6-OMe; c R^1 = 7-OH; d R^1 = 7-NEt_2; e R^1 = 5,6-benzo; f R^1 = 6-n-C_6H_{13}, 7-OH; g-kR^2 = p-$MeOC_6H_4$; g R^1 = H; h R^1 = 7-OH; i R^1 = 7-NEt_2; j R^1 = 5,6-benzo; k R^1 = 6-n-C_6H_{13}, 7-OH; *l*, mR^2 = p-$Me_2NC_6H_4$; *l* R^1 = 7-NEt_2; mR^1 = 5,6-benzo; n, o R^2 = p-ClC_6H_4; n R^1 = H; o R^1 = H; o R^1 = 5,6-benzo.

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TABLE 1. Characteristics of Synthesized Compounds IVa-e, Va-d, VIa-f, VIIa-e, VIIIa-e, IXa-o, XVIa-m, XVIIIa,b

Compound	Empirical formula	Found N, % / Calculated N, %	T_{mp}, °C*	IR spectra, cm^{-1}	UV spectra, λ_{max}, nm	Fluorescence spectra, λ_{max}, nm	Yield, % (method)
1	2	3	4	5	6	7	8
IVa	$C_{12}H_7NO_2S$	6,10 / 6,11	160-161	3100, 1720	330,3	406,7	50 (A) 41 (B)
IVb	$C_{12}H_7NO_3S$	5,65 / 5,71	276-277	3250, 3090, 1715	363,9	420,4	30 (A) 17 (B)
IVc	$C_{16}H_{16}N_2O_2S$	9,28 / 9,33	134-136	3080, 1717	407,2	470,0	40 (A) 29 (B)
IVd	$C_{16}H_9NO_2S$	5,12 / 5,01	225-227	3095, 1722	374,5	430,4	35 (A) 31 (B).
IVe	$C_{18}H_{19}NO_3S$	4,37 / 4,25	192-194	3300, 3085, 1715	366,0	426,8	40 (A) 27 (B)
Va	$C_{14}H_8N_2O_2S$	—	157-159	3144, 2268, 1691	336,7	410,2	68
Vb	$C_{14}H_8N_2O_3S$	9,89 / 9,85	268-269	3336, 3143, 2264, 1696	358,2, 417,4	437,4, 474,8	37
Vc	$C_{18}H_{10}N_2O_2S$	8,93, 8,80	213-214	3133, 2262, 1708	375,4	431,4	55
Vd	$C_{20}H_{20}N_2O_3S$	7,64 / 7,60	192-193	3366, 3120, 2251, 1684	366,8, 435,9	432,5, 481,2	49
VIa	$C_{13}H_9NO_2S$	5,87, 5,76	178-180	3137, 1717	337,2	413,2	82
VIb	$C_{14}H_{11}NO_3S$	5,04 / 5,12	180-183	3135, 1711	355,9	417,7	67

TABLE 1 (continued)

1	2	3	4	5	6	7	8
VIc	$C_{13}H_9NO_3S$	5,45 / 5,40	237-238	3270, 3138, 1718	360,2, 418,8	424,8, 469,0	41
VId	$C_{17}H_{18}N_2O_2S$	8,87 / 8,91	163-165	3140, 1700	407,5	466,4	39
VIe	$C_{17}H_{11}NO_2S$	4,79 / 4,77	194-195	3134, 1715	375,4	433,3	81
VIf	$C_{19}H_{21}NO_3S$	4,00 / 4,08	199-200	3422, 3144, 1712	366,0, 432,2	431,0, 481,2	59
VIIa	$C_{24}H_{15}NO_2S$	3,71 / 3,67	206-207	3036, 1716	344,6	436,0	75
VIIb	$C_{24}H_{15}NO_3S$	3,50 / 3,52	318-320	3250, 3060, 1713	369,6	435,4	70
VIIc	$C_{28}H_{24}N_2O_2S$	6,25 / 6,19	170-171	3042, 1714	411,2	475,4	65
VIId	$C_{28}H_{17}NO_2S$	3,30 / 3,25	293-295	3044, 1720	382,6	444,8	85
VIIe	$C_{30}H_{27}NO_3S$	3,02 / 2,9	253-255	3290, 3965, 1715	372,0	438,4	72
VIIIa	$C_{30}H_{19}NO_2S$	3,01 / 3,06	277-280	3050, 1715	345,8	433,7	50
VIIIb	$C_{30}H_{19}NO_3S$	3,01 / 2,96	329-330	3240, 3075, 1710	368,2	437,5	65
VIIId	$C_{34}H_{21}NO_2S$	3,00 / 2,76	338-340	3050, 1720	409,5	542,1	75
VIIIe	$C_{36}H_{31}NO_3S$	2,70 / 2,51	267-269	3280, 3080, 1715	369,5	440,0	45
IXa	$C_{18}H_{11}NO_2S$	—	156-158	3144, 1740	344,4	421,6	77
IXb	$C_{19}H_{13}NO_3S$	4,20 / 4,18	181-183	3144, 1736	367,2	431,0	75

TABLE 1 (continued)

1	2	3	4	5	6	7	8
IXc	$C_{18}H_{11}NO_3S$	4,45 / 4,36	264-267	3254, 3130, 1700	366,6, 423,7	434,0, 478,0	44
IXd	$C_{22}H_{20}N_2O_2S$	—	153-155	3156, 1704	410,85	473,9	51
IXe	$C_{22}H_{13}NO_2S$	—	235-237	3131, 1719	380,5	442,1	83
IXf	$C_{24}H_{23}NO_3S$	3,51 / 3,45	230-232	3345, 3142, 1700	369,8, 440,9	436,7, 481,7	71
IXg	$C_{19}H_{13}NO_3S$	4,23 / 4,18	213-215	3152, 1736	352,9	470,4	82
IXh	$C_{19}H_{13}NO_4S$	4,01 / 3,99	283-286	3283, 3139, 1700	365,2, 424,1	456,2, 479,8	36
IXi	$C_{23}H_{22}N_2O_3S$	6,83 / 6,89	130-133	3151, 1710	497,5	469,5	43
IXj	$C_{23}H_{15}NO_3S$	3,57 / 3,63	216-217	3129, 1743	383,4	474,4	79
IXk	$C_{25}H_{25}NO_4S$	3,20 / 3,22	222-223	3295, 3147, 1704	373,1, 438,2	442,5, 482,2	67
IXl	$C_{24}H_{25}N_3O_2S$	10,07 / 10,02	180-183	3148, 1711	412,2	489,7	58
IXm	$C_{24}H_{18}N_2O_2S$	—	286-288	3133, 1736	—	—	70
IXn	$C_{18}H_{10}ClNO_2S$	—	197-198	3138, 1728	350,9	420,9	87
IXo	$C_{22}H_{12}ClNO_2S$	—	240-242	3119, 1712	381,1	440,5	89
XVIa	$C_{12}H_7NO_2S$	6,07 / 6,11	172-174	3120, 1715	352,4	423,4	35 (A), 51 (B)
XVIb	$C_{12}H_7NO_3S$	5,75 / 5,71	297-300	3325, 3115, 1720	381,1	449,8	45 (A), 49 (B)
XVIc	$C_{16}H_{16}N_2O_2S$	9,29 / 9,33	126-127	3100, 1717	435,9	490,8	30 (A), 47 (B)
XVId	$C_{16}H_9NO_2S$	5,03 / 5,01	263-265	3118, 1715	396,8	460,4	38 (A), 54 (B)

TABLE 1 (continued)

1	2	3	4	5	6	7	8
XVIe	$C_{18}H_{19}NO_3S$	4,28 / 4,25	220-221	3315, 3105, 1720	390,3	458,6	40 (A) 51 (B)
XVIf	$C_{18}H_{11}NO_2S$	—	149-150	3100, 1727	374,5	489,7	69 (A) 85 (B) 97 (D)
XVIg	$C_{19}H_{13}NO_3S$	4,07 / 4,18	245-246	3116, 1708	388,2	490,2	66 (A) 73 (B) 98 (D)
XVIh	$C_{22}H_{13}NO_2S$	4,01 / 3,94	255-256	3062, 1709	406,2	500	87 (A) 92 (B)
XVIi	$C_{24}H_{15}NO_2S$	3,65 / 3,67	240-242	3100, 1714	384,3	506,6	70 (A) 69 (B)
XVIj	$C_{24}H_{15}NO_3S$	3,48 / 3,52	309-310	3300, 3105, 1713	395,3	480,8	74 (A) 77 (B)
XVIk	$C_{28}H_{24}N_2O_2S$	6,11 / 6,19	205-207	3120, 1712	440,1	497,8	65 (A) 71 (B)
XVI*l*	$C_{28}H_{17}NO_2S$	3,24 / 3,25	297-298	3105, 1711	406,8	505,8	79 (A) 70 (B)
XVIm	$C_{30}H_{27}NO_2S$	2,94 / 2,91	267-270	3310, 3100, 1718	401,6	480,8	68 (A) 77 (B)
XVIIIa	$C_{18}H_{12}N_2OS$	9,17 / 9,20	184-185	3253, 3099, 1657	376,2	463,4	89
XVIIIb	$C_{19}H_{14}N_2O_2S$	8,35 / 8,38	153-154	3312, 3124, 1657	390,3	480,8	77

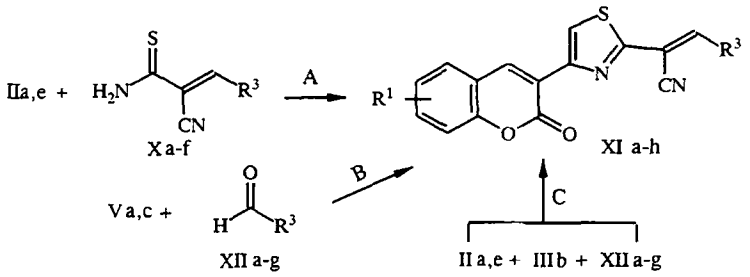
*Compounds IVa-e, Va, c, d, VIe, IXb, XVIa-e, XVIg, h, XVIIIa, b were recrystallized from *n*-BuOH; IXa, c, e, f were recrystallized from MeCN; IXi-k were recrystallized from aqueous DMF: Vb, VIa-d, f, IXd, g, h, *l*, XVIf were recrystallized from *i*-PrOH; VIIa-e, VIIIa-e, IXm-o, XVIi-m were recrystallized from DMF.

The most suitable method for building ensembles of rings containing coumarin and thiazole units is to combine a dielectrophilic $[C_2]_2^{2+}$ synthon with a dinucleophilic $[SN]_3^{2-}$ synthon. As the synthetic equivalents of the $[C_2]_2^{2+}$ synthon, we chose 3-(α-bromoacetyl)coumarins IIa-f [9], while as the equivalents of the $[SN]_3^{2-}$ synthon we chose thioformamide, thioacetamide, thiocyanoacetamide, and aromatic thioamides IId-i.

Condensation of coumarins IIa-f with thioamides IIIb-i was carried out with equimolecular amounts of reagents. The hydrogen halides formed in this case were converted to the free bases Va-d, VIa-f, VIIa-e, VIIIa-e, IXa-o by treatment with an aqueous ammonia solution. The 3-(thiazol-4-yl)coumarins IVa-e were synthesized both by reaction of IIa,c-f with thioformamide IIIa [11] (method A) and with the help of a modified Hantsch reaction, and the coumarin IIa,c-f was treated with formamide and phosphorus pentasulfide (method B) (Scheme 1). We found that in most cases, the use of thioformamide, despite its low stability, is preferred due to the elimination of secondary reactions of pentasulfide with 3-(α-bromoacetyl)coumarins. 4-Substituted thiobenzamides IIIe-g were obtained from the corresponding aldehydes by the method suggested in [12], while the thioamides IIId,h,i were obtained by treatment of the corresponding amides with phosphorus pentasulfide [13].

The use of 4-R-benzylidenecyanothioacetamides Xa-f [14] as the thioamide component allowed us to obtain 2-[2-aryl(hetaryl)-1-cyanoethenyl]-4-(coumarin-3-yl)thiazoles XIa-h (method A). With the goal of confirming the structure, we carried out alternate syntheses of compounds XIa-h by condensation of 3-(2-cyanomethylthiazol-4-yl)coumarins Va,c and aldehydes XIIa-g (method B) and three-component condensation of the derivatives IIa,e, IIIb and the aldehydes XIIa-g (method C) (Scheme 2).

Scheme 2

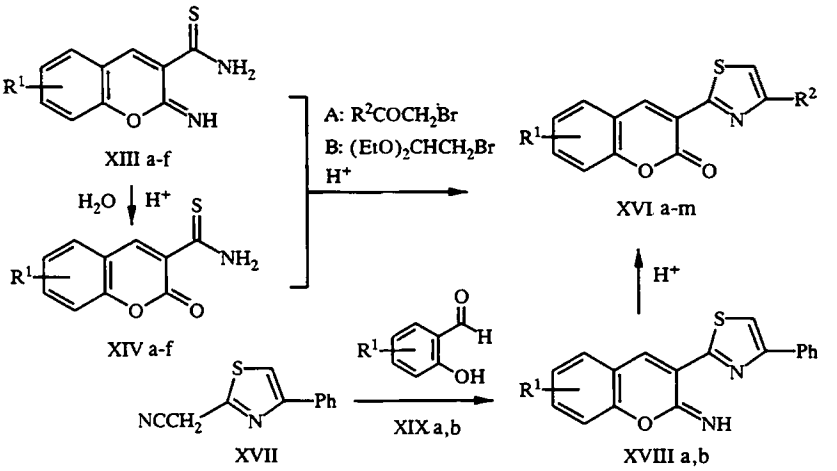


XIa-g R^1 = H; X, XI, XII a R^3 = 4-ClC_6H_4; b R^3 = 4-BrC_6H_4; c R^3 = 4-FC_6H_4; d R^3 = 4-$MeOC_6H_4$; e R^3 = 4-$O_2NC_6H_4$; f R^3 = 4-$Me_2NC_6H_4$; g R^3 = furfuryl-2; XI h R^1 = 5,6-benzo; R^3 = 4-ClC_6H_4

Upon reaction of 2-iminocoumarin-3-thiocarboxamides XIIIa-f [15] with α-halocarbonyl compounds XVa-c, the compounds XVIIIa-m are formed. However, this reaction may be complicated by hydrolysis of the imino group as a result of the hydrogen bromide and water liberated. Therefore, at the end of the reaction, complete conversion of the mixture of compounds formed XVIa-m and XVIIIa-m to coumarins XVIa-m was accomplished via acid hydrolysis. Synthesis of compounds XVIa-e, where the α-halocarbonyl component was bromoacetaldehyde, caused certain difficulties concerning purification of the compounds obtained because of the high reactivity and instability of bromoacetaldehyde. It was established that the use of the diethylacetal of bromoacetaldehyde XVd can also lead to the desired compounds; furthermore, when using the acetal, the synthesis is simplified and the yields are increased. If in the first stage the iminocoumarins XIIIa-f are hydrolyzed to the corresponding coumarins XIVa-f, then the end product of the reaction with haloketones XVa-c will be compounds XVIa-m.

In order to obtain 3-hetaryl-substituted 2-imino-2H-1-benzopyrans, the simplest and most elegant method is the Knoevenagel condensation [16,17] using salicylaldehydes and hetarylacetonitriles. For synthesis of 2-imino-3-(4-phenylthiazol-2-yl)coumarins XVIIIa,b, in the first stage the Hantsch reaction was carried out and 2-cyanomethyl-4-phenylthiazole (XVII) was obtained [18]; then 2-iminocoumarins XVIIIa,b were obtained by the Knoevenagel reaction. This synthesis route is preferred, since the process of closure of the iminocoumarin ring is not complicated by hydrolysis of the imino group. Upon boiling compounds XVIIIa,b in an alcohol–water–hydrochloride acid system, the compounds XVIf,g are formed in high yields (Scheme 3).

Scheme 3



XIII, XIV, XIX a R^1 = H; b R^1 = 6-OMe; c R^1 = 7-OH; d R^1 = 7-NEt_2; e R^1 = 5,6-benzo; f R^1 = 6-n-C_6H_{13}, 7-OH; XV a R^2 = H; b R^2 = Ph; c R^2 = 4-PhC_6H_4; XVIa-e R^2 = H; a R^1 = H; b R^1 = 7-OH; c R^1 = 7-NEt_2; d R^1 = 5,6-benzo; e R^1 = 6-n-C_6H_{13}, 7-OH; f-h R^2 = Ph; f R^1 = H; g R^1 = 6-OMe; h R^1 = 5,6-benzo; i-m R^2 = 4-PhC_6H_4; i R^1 = H; j R^1 = 7-OH; k R^1 = 7-NEt_2; *l* R^1 = 5,6-benzo; m R^1 = 6-n-C_6H_{13}, 7-OH; XVIII a R^1 = H; b R^1 = 6-OMe

In the IR spectra, among the characteristic bands confirming the structure of 2- and 4-(coumarin-3-yl)thiazoles IVa-e, Va-d, VIa-f, VIIa-e, VIIIa-e, IXa-o, XIa-h, XVIa-m we should pick out the vibrations of the lactone C=O group which appear at 1684-1743 cm^{-1} [19-21], and the absence of this absorption band for compounds XVIIIa,b; vibrations of the C−H bond of the thiazole ring are found in the range 3036-3156 cm^{-1} [22, 23] (Tables 1 and 3). The electronic absorption and fluorescence spectra of thiazolylcoumarins IVa-e, Va-d, VIa-f, VIIa-e, VIIIa-e, IXa-o, XVIa-i, XVIIIa,b have bands characteristic for 3-substituted coumarins, with pronounced vibronic structure (Table 1). Analysis of the PMR spectra of compounds Va, VIb, d, f, IXa, b, *l*, n, XIa-h, XVIb, XVIIIb showed (Tables 2 and 3) that the proton signals from these compounds are found in the region typical for coumarins and thiazoles [24]. In the mass spectra of compounds VIa-e, VIIa, c, e, and IXc, d, e, the peak for most of the molecular ions has maximum intensity (Table 4), which is typical for many bis-heteroaromatic compounds. Fragmentation of the molecular ion occurs according to a scheme typical for 2,4-disubstituted thiazoles: rupture of the 1−2 and 3−4 bonds of the thiazole ring with elimination of a molecule of the corresponding nitrile and localization of the charge on the sulfur-containing moiety is most characteristic.

EXPERIMENTAL

The IR spectra of the synthesized compounds were recorded on a Specord M-80 in KBr pellets. The electronic spectra were recorded on a Specord M-40 in 2-propanol. The fluorescence spectra were recorded on a Hitachi F-4010. The mass spectra were obtained on a Finnigan MAT-4615 B, ionization energy 70 eV, with ballistic heating of the sample. The PMR spectra were recorded on a Bruker WP-200 in DMSO-D_6, (compounds XIa-h, in $CDCl_3$), internal standard TMS.

The purity of the compounds was monitored by TLC on Silufol UV-254 plates in a 9:1 chloroform−ethanol system.

The physicochemical characteristics of the synthesized compounds IVa-e, Va-d, VIa-f, VIIa-e, VIIIa-e, IXa-o, XIa-h, XVIa-m, XVIIIa,b are presented in Tables 1-4.

General Procedure for Obtaining 3-(2-R-thiazol-4-yl)-2H-1-benzopyran-2-ones IVa-e, Va-d, VIa-f, VIIa-e, VIIIa-e, IXa-o (Table 1). A. Equimolecular amounts of 3-(α-bromoacetyl)coumarins IIa-f and the corresponding compound containing a thioamide group IIIa-i (0.01 moles) in 20-49 ml of 2-propanol or ethanol were boiled for 10-20 min (until a precipitate fell out of solution), then cooled and diluted with water and alkalized with an aqueous solution of ammonia or ammonium acetate up to pH ~7. The precipitate was separated and washed with water and ethanol on the filter, dried, and crystallized from an appropriate solvent.

TABLE 2. PMR Spectra of Compounds Va, VIb, d, f, IXa, b, *l*, n, XVIb, XVIIIb

Compound	Chemical shift, ppm, spin–spin coupling constant (*J*, Hz)			
	5'-H S (1H)	4-H S (1H)	Ar	other protons
Va	8,41	8,74	7,39 - 7,94 (4H, m)	4,64 (2H, s, CH_2)
VIb	8,25	8,77	7,50 (1H, d, 5-H; 2,5); 7,22 (1H, d.d, 7-H; 8,5; 2,5); 7,38 (1H, d, 8-H; 8,5)	2,73 (3H, s, CH_3); 3,82 (3H, s, 6-OCH_3)
VId	8,03	8,63	7,65 (1H, d, 5-H; 8,5); 6,76 (1H, d.d, 6-H; 8,5; 2,0); 6,60 (1H, d, 8-H; 2,0)	3,48 (4H, q, 7-$N(\underline{CH_2}CH_3)_2$); 1,16 (6H, t 7-$N(CH_2\underline{CH_3})_2$); 2,73 (3H, s, CH_3)
VIf	8,07	8,63	7,50 (1H, s, 5-H); 6,78 (1H, s, 8-H)	1,57 (2H, q, $CH_3(CH_2)_4\underline{CH_2}$); 1,29 (8H, s, $CH_3(\underline{CH_2})_4$); 0,87 (3H, t, $\underline{CH_3}(CH_2)_4CH_2$)
IXa	8,40	8,90	7,34 - 8,03 (9H, m)	—
IXb	8,44	8,92	7,20 - 8,06 (8H, m)	3,84 (3H, s, 6-OCH_3)
IX*l*	8,04	8,72	7,84 (2H, d; 8,5); 7,61 (1H, d, 5-H; 8,5); 6,80 (2H, d; 8,5); 6,70 (1H, d, d, 6-H; 8,5; 2,0); 6,57 (1H, d, 8-H; 2,0)	3,46 (4H, q, 7-$N(\underline{CH_2}CH_3)_2$); 1,17 (6H, t, 7-$N(CH_2\underline{CH_3})_2$); 3,00 (6H, s, 4-$N(CH_3)_2$)
IXn	8,42	8,88	7,62 - 8,05 (8H, m)	—
XVIb	8,27	9,05	7,27 - 8,09 (8H, m)	3,82 (3H, s, 6-OCH_3)
XVIIIb*	7,91	8,90	7,52 - 7,71 (8H, m)	4,07 (3H, s, 6-OCH_3)

*PMR spectrum in CF_3COOD.

B. 0.013 moles formamide and 0.003 moles phosphorus pentasulfide in 50 ml 1,4-dioxane were allowed to stand at room temperature for 1 h. 0.01 moles coumarin IIa-e was added to the mixture and then this was heated on a water bath for 1 h. The precipitate of compounds IVa-e was filtered off, washed with water and ethanol, dried, and crystallized from an appropriate solvent.

General Procedure for Obtaining 2-(Aryl-1-cyanoethenyl)-4-(coumarin-3-yl)thiazoles XIa-h (Table 3). A. Equimolecular amounts of coumarins IIa-f and the corresponding 4-R-benzylidenecyanothioacetamides Xa-f (0.01 moles) in 20 ml DMF were heated for 10-20 min at 80-90°C, cooled, diluted with water, and alkalized with an aqueous solution of ammonia or ammonium acetate up to pH ~7. The precipitate was separated, washed with water and ethanol on the filter, dried, and crystallized from a 1-butanol–DMF mixture.

B. Equimolecular amounts of 3-(2-cyanomethylthiazol-4-yl)coumarins Va,c and aldehydes XIIa-g (0.01 moles) were dissolved in 30-40 ml 2-propanol or ethanol, then 1-2 drops of piperidine were added. The reaction mixture was heated for 5 min at a temperature of 40-50°C, then stirred at room temperature until a precipitate fell out of solution. The precipitate was separated, washed with 2-propanol or ethanol on the filter, dried, and crystallized.

C. Equimolecular amounts of coumarins IIa-f, aldehydes XIIa-g, and 1 g thiocyanoacetamide IIIb (0.01 moles) in 20-30 ml 2-propanol or ethanol were boiled for 10 min, then 1-2 ml piperidine were added. The reaction mixture was heated for 5 min at a temperature of 50-60°C, then stirred at room temperature. The precipitate was separated, washed on the filter with 2-propanol or ethanol, dried, and crystallized from a 1-butanol–DMF mixture.

General Procedure for Obtaining 3-(4-R-thiazol-2-yl)-2H-1 of Benzopyran-2-ones XVIa-m (Table 1). A. Equimolecular amounts of 2-imino-2H-1-benzopyran-3-thiocarboxamides XIIIa-f and the corresponding α-halocarbonyl compounds XVa-c (0.01 moles) in 20-40 ml of 2-propanol or ethanol were boiled for 10-20 min (until a precipitate fell out of solution), then 10 ml each concentrated hydrochloric acid and water were added; this was boiled for 10-20 min more, cooled, diluted with water and alkalized with an aqueous solution of ammonia or ammonium acetate up to pH ~7. The precipitate was separated, washed on the filter with water and ethanol, dried, and crystallized from an appropriate solvent.

B. Equimolecular amounts of 2-imino-2H-1-benzopyran-3-thiocarboxamides XIIIa,c-f and diethylacetal of bromoacetaldehyde XVd (0.01 moles) in 20-40 ml 2-propanol or ethanol were boiled for 15-25 min (until a precipitate fell out of solution); 10 ml each concentrated hydrochloric acid and water were added and this was boiled for 15-20 min more, cooled, diluted with water and alkalized with an aqueous solution of ammonia or ammonium acetate up to pH ~7. The precipitate was separated, washed on the filter with water and ethanol, dried, and crystallized from an appropriate solvent.

TABLE 3. Physicochemical Characteristics of Synthesized Compounds XIa-h

Compound	Empirical formula	Found N, % / Calculated N, %	T_{mp}, °C	IR spectra, cm^{-1}	Chemical shift, ppm, spin–spin coupling constant (J, Hz)	Yield, % (method)
XIa	$C_{21}H_{11}ClN_2O_2S$	7,23 / 7,17	223-224	3127, 2231, 1712	8,56 (1H, s, 5'-H); 8,84 (1H, s, 4-H); 7,31...8,10 ($8H_{arom.}$ + 1H, m, CH=)	81 (A), 77 (B), 70(C)
XIb	$C_{21}H_{11}BrN_2O_2S$	6,40 / 6,44	225-227	3117, 2231, 1713	8,58 (1H, s, 5'-H); 8,84 (1H, s, 4-H); 7,32...8,08 ($8H_{arom}$ + 1H, m, CH=)	79 (A), 77 (B). 69 (C)
XIc	$C_{21}H_{11}FN_2O_2S$	7,43 / 7,48	199-200	3143, 2216, 1721	8,54 (1H, s, 5'-H); 8,84 (1H, s, 4-H); 7,31...8.10 ($8H_{arom}$ + 1H, m, CH=)	85 (A), 87 (B), 71 (C)
XId	$C_{22}H_{14}N_2O_3S$	7,19 / 7,25	207-208	3146, 2223, 1712	8,56 (1H, s, 5'-H); 8,88 (1H, s, 4-H); 7,04...8,36 ($8H_{arom}$ + 1H, m, CH=); 3,89 (3H, s, OCH_3)	81 (A), 73 (B), 71 (C)
XIe	$C_{21}H_{11}N_3O_4S$	10,39 / 10,47	260-261	3126, 2229, 1718	8,64 (1H, s, 5'-H); 8,84 (1H, s, 4-H); 7,31...8,37 ($8H_{arom}$ + 1H, m, CH=)	70 (A), 59 (B), 47 (C)
XIf	$C_{23}H_{17}N_3O_2S$	10,49 / 10,52	248-250	3136, 2215, 1719	8,41 (1H, s, 5'-H); 8,84 (1H, s, 4-H); 6,72...7,96 ($8H_{arom}$ + 1H, m, CH=); 3,10 (6H, s, 4-$N(CH_3)_2$)	69 (A), 67 (B), 41 (C)
XIg	$C_{19}H_{10}N_2O_3S$	8,08 / 8,09	214-216	3141, 2214, 1720	8,52 (1H, s, 5'-H); 8,82 (1H, s, 4-H); 7,29...7,98 ($7H_{arom}$ + 1H, m, CH=)	71 (A), 72 (B), 39 (C)
XIh	$C_{25}H_{13}ClN_2O_2S$	6,29 / 6,36	240-242	3127, 2213, 1719	8,60 (1H, s, 5'-H); 9,37 (1H, s, 4-H); 7,43...8,10 ($10H_{arom}$ + 1H, m, CH=)	77 (A), 71 (B), 52 (C)

TABLE 4. Mass Spectra of Compounds VIa-e, VIIa, c, e, IXc, d, e

Compound	m/z (I_{rel} %)
VIa	243 (M^+, 100), 215 (15), 202 (28), 174 (32), 174 (32), 146 (18), 145 (21), 130 (7), 101 (6), 102 (34)
VIb	273 (M^+, 100), 245 (13), 232 (9), 230 (7), 204 (10), 202 (12), 161 (11)
VIc	259 (M^+, 38), 231 (7), 218 (6), 205 (6), 204 (44), 190 (20), 189 (100), 162 (6), 161 (11), 134 (8), 105 (20)
VId	314 (M^+, 11), 299 (17), 260 (6), 259 (41), 245 (15), 244 (100), 216 (18)
VIe	293 (M^+, 100), 266 (6), 265 (35), 252 (6), 224 (29), 196 (5), 195 (26), 163 (7), 152 (24), 151 (14), 150 (8), 147 (6)
VIIa	381 (M^+, 100), 174 (20), 145 (14), 101 (15)
VIIc	452 (M^+, 65), 437 (45), 259 (70), 244 (100), 216 (50), 116 (95), 77 (80)
VIIe	481 (M^+, 40), 410 (70), 290 (55), 275 (100), 219 (95)
IXc	321 (M^+, 100), 293 (13), 259 (8), 244 (17), 218 (18)
IXd	376 (M^+, 85), 361 (100), 332 (34), 304 (13), 247 (10), 229 (41)
IXe	355 (M^+, 100), 328 (31), 244 (17), 224 (22), 219 (8)

*Peaks with $I_{rel} \geq 5\%$ are given.

C. Equimolecular amounts of 2-oxo-2H-1-benzopyran-3-thiocarboxamides XIVa-f and the corresponding α-halocarbonyl compound XVa-c (0.01 moles) in 20-40 ml of 2-propanol or ethanol were boiled for 10-20 min (until a precipitate fell out of solution); then this was cooled, diluted with water, and alkalized with an aqueous solution of ammonia or ammonium acetate up to pH ~7. The precipitate was separated, washed on the filter with water and ethanol, dried, and crystallized.

D. 0.01 moles of the corresponding 2-iminocoumarin XVIIIa, b was dissolved in 20 ml 1,4-dioxane, then 5-7 ml concentrated hydrochloric acid was added. The solution was heated for 5 min, diluted with 60 ml water, alkalized with an aqueous solution of ammonia up to pH ~7-8. The precipitate was filtered off and recrystallized from butanol.

General Procedure for Obtaining 2-Imino-3-(4-R-thiazol-2-yl)-2H-1-benzopyrans XVIIIa,b (Table 1). Equimolecular amounts of the corresponding salicylaldehyde XIXa, b and 2-cyanomethyl-4-phenylthiazole XVII (0.01 moles) was dissolved in 20-40 ml 2-propanol or ethanol, then 1-2 drops piperidine was added. The reaction mixture was heated for 5 min at a temperature of 40-50°C, and then was stirred at room temperature until a precipitate fell out of solution. The precipitate was separated, washed on the filter with 2-propanol or ethanol, dried, and crystallized from 1-butanol.

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