Chemistry of Natural Compounds, Vol. 34, No. 4, 1998

5,7-DIHYDROXY-3-PHENOXYCHROMONES: SYNTHESIS AND PROPERTIES

M. M. Garazd,[a] A. S. Ogorodniichuk,[a] V. V. Shilin,[a] S. A. Vasil'ev,[b] A. V. Turov,[b] and V. P. Khilya[b]

UDC 547.814.5

A series of 5,7-dihydroxy-3-phenoxychromones and their 2-methyl analogs has been obtained by the heterocyclization of α-aryloxy-2,4,6-trihydroxyacetophenones. Their acylation, alkylation, and aminoacylation reactions have been studied.

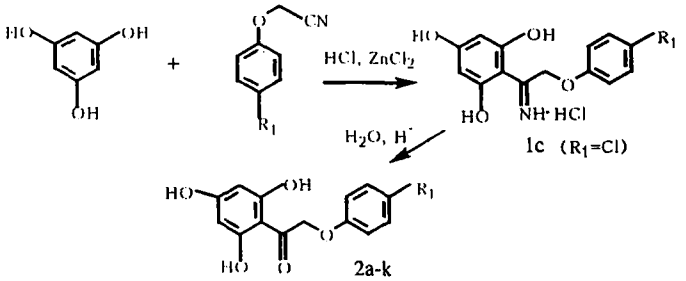
Interest in the synthesis of compounds containing a chromone ring is due to the fact that they form a broad group of natural compounds with a wide spectrum of biological action, thanks to which they have found use in medical practice [1]. Together with the use of drugs isolated from natural raw material [2] (thus, capillarin — 5,7-dihydroxy-2-(4-hydroxyphenoxy)-6-methoxychromone has been isolated from *Artemisia capillaris*), synthetic products containing a phenoxy fragment linked with a chromone nucleus are acquiring ever-increasing importance. Such compounds possess antitubercular [3], antimicrobial [4], herbicidal, fungicidal and insecticidal [5], and neuroleptic and hypoglycemic [6] activities.

It is known that among natural flavonoids the most common orientation of phenolic hydroxyls is the phloroglucinol type. We have therefore synthesized 3-phenoxy analogs of 5,7-dihydroxychromone.

The initial compounds for the synthesis of the 3-phenoxy-5,7-dihydroxychromones — α-aryloxy-2,4,6-trihydroxyacetophenones — were obtained by the Houben–Hoesch condensation of aryloxyacetonitriles with phloroglucinol in benzene-ether in the presence of $ZnCl_2$ at 0°C [6]. The acylating agent was the complex $[ArCH_2C^+{=}NH]ZnCl_3^-$ and the reaction product a ketimine hydrochloride.

In contrast to the ketimine hydrochlorides obtained from resorcinol, the hydrochlorides of ketimines of α-aryloxy-2,4,6-trihydroxyacetophenones proved to be stable compounds, which permitted them to be isolated and characterized. They did not give an intense coloration with an alcoholic solution of $FeCl_3$, since no formation of an intramolecular chelate complex is possible. In the PMR spectra measured in DMSO-d_6, the protons of the hydroxy groups and the imino groups resonated in the weak field at 10.9-11.0 ppm. Quantitative analysis for nitrogen and chlorine fully confirmed the structures of the ketimine hydrochloride (**1c**).

In view of the high stability of the ketimine hydrochlorides, the hydrolysis of the reaction mixture was conducted under more severe conditions than usual (2 h at 100°C). As a result, the α-aryloxy-2,4,6-trihydroxyacetophenone (**2a-k**) were obtained.



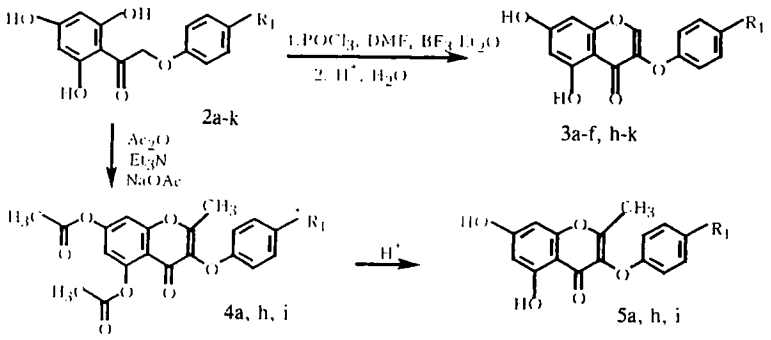
a: R_1=H; b: R_1=F; c: R_1=Cl; d: R_1=Br; e: R_1= I; f: R_1=Et; g: R_1=COOMe; h: R_1=COOPr; i: R_1=OMe; j: R_1=OEt; k: R_1=NO_2

a) Institute of Bioorganic Chemistry and Petrochemistry, National Academy of Sciences, Ukraine, 253660, Kiev, ul. Murmanskaya, 1. b) Kiev Taras Shevchenko University, 252033, Kiev, ul. Vladimirskaya, 64. Translated from Khimiya Prirodnykh Soedinenii, No. 4, pp. 466-474, July-August, 1998. Original article submitted April 1, 1998.

0009-3130/98/3404-0435$20.00

Ketones (**2a-k**) were high-melting colorless substances giving an intense coloration with an alcoholic solution of $FeCl_3$ owing to the formation of an intramolecular complex of the chelate type. The structure of these ketones was determined on the basis of the results of quantitative analysis and PMR spectroscopy. Thus, in the PMR spectra of the α-aryloxy-2,4,6-trihydroxyacetophenones measured in DMSO-d_6 a weak-field two-proton singlet at 12.10 ppm was assigned to the two protons of the hydroxy groups in positions 2 and 6, which are capable of participating in the formation of an intramolecular hydrogen bond with the carbonyl group of the compound concerned. The OH-4 proton resonated in a stronger field, at 10.50 ppm, since it does not form an intramolecular hydrogen bond. The signals of the aromatic protons in positions 3 and 5 fused into a single peak at 5.86 ppm, which is due to a concerted positive mesomeric effect of the three hydroxy groups, while a two-proton singlet of the α-methylene unit appeared at 5.22-5.50 ppm. The physicochemical constants of compounds (**2a-k**) are given in Table 1.

The heterocyclization of the ketones was effected by adding boron trifluoride etherate (BTE) to solutions of the α-aryloxy-2,4,6-trihydroxyacetophenones in DMFA, followed by the addition of $POCl_3$ at a ratio of the reactants (in moles) of ketone:DMFA:BTE:$POCl_3$ = 1:2:3:1.2, followed by keeping the reaction mixture at 60-70°C for 30-40 min and subsequent hydrolysis. As a result of the synthesis the 5,7-dihydroxy-3-phenoxychromones (**3a-f, h-k**) were obtained.



To synthesize the 5,7-dihydroxy-2-methyl-3-phenoxychromones (**5a, h, i**) we used the interaction of Ac_2O and the ketones in Et_3N with heating in the presence of anhydrous NaOAc. As a result of the reaction the diacetates (**4a, h, i**) were formed. The acetate groups were eliminated by boiling an alcoholic solution with hydrochloric acid.

All the above-mentioned 3-aryloxychromones gave a dark brown coloration with an alcoholic solution of $FeCl_3$. It must be mentioned that the coloration was more intense with the chromones than with the corresponding ketones.

The structure of the chromones obtained was established on the basis of PMR spectroscopy and elementary analysis. In the PMR spectra of the 5,7-dihydroxy-3-aryloxychromones (**3a-f, h-k**) measured in DMSO-d_6 the following differences from the spectra of the initial ketones were observed:

the two-proton singlet of the α-methylene unit had disappeared and a sharp singlet of the H-2 proton had appeared at 8.60-8.70 as a result of the formation of the chromone ring;

in place of the weak-field two-proton singlet of the 2- and 6-hydroxy groups, a one-proton singlet remained of the proton of the 5-hydroxy group of the chromone, which formed an intramolecular hydrogen bond;

distinct positions were observed for the signals of the aromatic protons because of a disturbance to the symmetry of the ketone molecule and changes in the environments of the protons.

For the protons of the 7-hydroxy group and the phenoxyl fragment the resonance pattern had scarcely changed. In the case of the 3-aryloxy-5,7-dihydroxy-2-methylchromones, each PMR spectrum had a three-proton singlet of the 2-methyl group of the chromone at 2.30-2.40 ppm. The physicochemical constants of chromones (**3a-f, h-k**) and (**5a, h, i**) are given in Table 2.

The chemical properties of the 3-aryloxy-5,7-dihydroxychromones obtained were studied in acylation, alkylation, and aminoacylation reactions.

The acylation of the 5,7-dihydroxychromones was conducted by boiling their pyridine solutions with acetic anhydride. The hydroxy groups present in the composition of the chromones synthesized are nonequivalent in reactivity, which is a consequence of different effects of electron-donating and spatial factors and also of intramolecular hydrogen bonds. Thus, according to TLC, the 7-O-acetyl derivative was formed on brief boiling, while more prolonged boiling led to exhaustive acetylation; i.e., selective acetylation is possible under the appropriate conditions.

TABLE 1. Properties of the α-Aryloxy-2,4,6-trihydroxyacetophenones

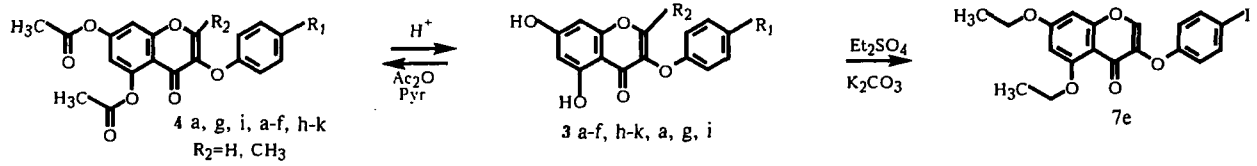
Compound	Empirical formula	Yield, %	mp, °C	PMR spectrum, δ, ppm, solvent – DMSO-d_6						
				protons of the phenol moiety				protons of the phenoxy moiety		
				OH-2, OH-6, s	OH-4, s	H-3, H-5,s	α-CH_2, s	H-2,H-6,d	H-3,H-5, d	R_1
2a	$C_{14}H_{12}O_5$	80	234	12.10	10.48	5.86	5.29	7.3 (m)		7.3 (H)
2b	$C_{14}H_{11}FO_5$	81	242	12.13	10.52	5.86	5.28	7.0 (m)		F
2c	$C_{14}H_{11}ClO_5$	85	251	12.09	10.57	5.86	5.31	6.87	7.30	Cl
2d	$C_{14}H_{11}BrO_5$	82	256	12.15	10.20	5.84	5.37	7.03	7.53	Br
2e	$C_{14}H_{11}IO_5$	80	269	12.10	10.46	5.85	5.29	6.72	7.55	I
2f	$C_{16}H_{16}O_5$	88	247	12.05	10.55	5.85	5.25	6.75	7.08	2.52; 1.13 (Et)
2g	$C_{16}H_{14}O_7$	83	258	12.10	10.60	5.87	5.41	6.48	7.88	3.81(COOMe)
2h	$C_{18}H_{18}O_7$	86	255	12.13	10.55	5.85	5.39	6.45	7.85	4.22; 1.75;0.94 (COOPr)
2i	$C_{15}H_{14}O_6$	78	259	12.15	10.60	5.86	5.22	6.82 (s)		3.68 (OMe)
2j	$C_{16}H_{16}O_6$	81	223	12.16	10.50	5.86	5.22	6.80 (s)		3.92; 1.29 (OEt)
2k	$C_{14}H_{11}NO_7$	87	295	12.07	10.50	5.87	5.50	7.08	8.17	NO_2

TABLE 2. Properties of the 3-Aryloxy-5,7-dihydroxychromones

Compound	Empirical formula	Yield, %	mp, °C	PMR spectrum, δ, ppm, solvent – DMSO-d_6							
				chromone protons					phenoxyl protons		
				OH-5, s	OH-7, s	R_2-2, s	H-6, d	H-8, d	H-2, H-6, d	H-3, H-6, d	R_1
3a	$C_{15}H_{10}O_5$	88	214	12.18	10.98	H 8.60	6.25	6.45	7.0; 7.03 (m)		7.3 (H)
3b	$C_{15}H_9FO_5$	84	198	12.15	10.98	H 8.60	6.25	6.45	7.13	7.07	F
3c	$C_{15}H_9ClO_5$	82	212	12.11	11.00	H 8.64	6.25	6.46	7.35	7.07	Cl
3d	$C_{15}H_9BrO_5$	85	229	12.11	11.00	H 8.63	6.25	6.45	7.47	7.02	Br
3e	$C_{15}H_9IO_5$	85	255	12.10	11.00	H 8.63	6.25	6.45	7.61	6.90	I
3f	$C_{17}H_{14}O_5$	69	201	12.20	10.96	H 8.57	6.24	6.45	7.13	6.93	2.55; 1.14 (Et)
3g	$C_{19}H_{16}O_7$	91	197	12.06	11.01	H 8.69	6.26	6.47	7.91	7.15	4.20; 1.70; 0.94 (COOPr)
3h	$C_{16}H_{12}O_6$	72	195	12.23	10.95	H 8.53	6.24	6.43	6.90 (s)		3.70 (OMe)
3i	$C_{17}H_{14}O_6$	78	219	12.23	10.96	H 8.52	6.24	6.41	6.90 (s)		3.95; 1.29 (OEt)
3j	$C_{15}H_9NO_7$	85	285	11.98	11.04	H 8.74	6.27	6.48	7.30	8.20	NO_2
5a	$C_{16}H_{12}O_5$	76	191	12.28	10.90	Me 2.33	6.22	6.42	7.0; 7.3 (m)		7.3 (H)
5g	$C_{18}H_{14}O_6$	72	208	12.05	10.95	Me 2.31	6.25	6.47	7.85	7.12	4.05 (COOMe)
5i	$C_{17}H_{14}O_6$	83	185	12.13	10.97	Me 2.33	6.24	6.44	6.90 (s)		3.75 (OMe)

TABLE 3. Properties of the 3-Aryloxy-5,7-diacetoxychromone Derivatives

Compound	Empirical formula	Yield, %	mp, °C	PMR spectrum, δ, ppm, solvent – $CDCl_3$							
				chromone protons					phenoxyl protons		
				OAc-5 s	OAc-7 s	R_2-2 s	H-6 d	H-8 d	H-2 H-6 d	H-3 H-6 d	R_1
6a	$C_{19}H_{14}O_7$	80	160	2.37	2.34	H 7.87	6.86	7.25	7.0; 7.03 (m)		7.30 (H)
6b	$C_{19}H_{13}FO_7$	88	147	2.37	2.35	H 7.87	6.86	7.25	6.99	6.92	F
6c	$C_{19}H_{13}ClO_7$	79	169	2.37	2.35	H 7.94	6.90	7.26	7.26	6.90	Cl
6d	$C_{19}H_{13}BrO_7$	84	173	2.37	2.35	H 7.94	6.84	7.25	7.44	6.88	Br
6e	$C_{19}H_{13}IO_7$	86	189	2.37	2.34	H 7.95	6.87	7.27	7.57	6.72	I
6f	$C_{21}H_{18}O_7$	89	129	2.38	2.34	H 7.81	6.85	7.24	6.90	7.12	2.61; 1.20 (Et)
6h	$C_{23}H_{20}O_9$	76	145	2.34	2.33	H 8.01	6.87	7.28	7.99	6.95	4.24; 1.77; 1.00(COOPr)
6i	$C_{20}H_{16}O_8$	81	142	2.40	2.34	H 7.73	6.83	7.25	6.90 (m)		3.77 (OMe)
6j	$C_{21}H_{18}O_8$	88	132	2.40	2.33	H 7.73	6.88	7.24	6.88 (s)		3.98; 1.39 (OEt)
6k	$C_{19}H_{13}NO_9$	79	195	2.35	2.34	H 8.09	6.90	7.31	7.01	8.18	NO_2
7e	$C_{19}H_{17}IO_5$	95	195	EtO 4.05; 1.35	EtO 3.95; 1.35	H 7.93	6.90	7.25	6.90	7.12	I
4a	$C_{20}H_{16}O_7$	88	141	2.35	2.35	Me 2.35	6.85	7.25	6.9; 7.3 (m)		7.3 (H)
4g	$C_{22}H_{18}O_9$	91	155	2.35	2.35	Me 2.35	6.88	7.23	7.85	7.10	4.05 (COOMe)
4i	$C_{21}H_{18}O_8$	89	131	2.36	2.36	Me 2.36	6.82	7.26	6.82 (s)		3.76 (OMe)



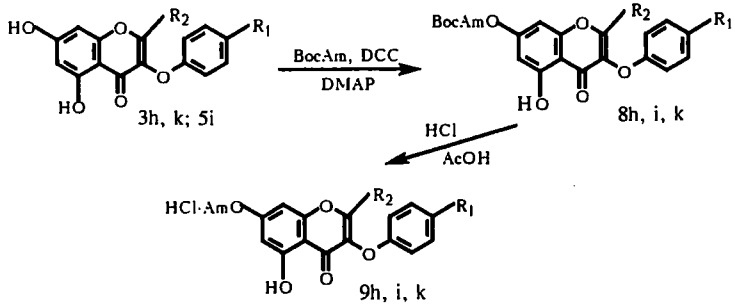
4 a, g, i, a-f, h-k
R_2=H, CH_3

3 a-f, h-k, a, g, i

7e

TABLE 4. Properties of the 7-Aminoacyloxy Derivatives of the 3-Aryloxychromones

Compound	Empirical formula	Yield, %	mp, °C	PMR spectrum, δ, ppm								
				chromone protons				phenoxyl protons			protons of the aminoacyl residue	solvent
				OH-5 s	R_2-2 s	H-6 d	H-8 d	H-2 H-6 d	H-3 H-5 d	R_1		
7a	$C_{27}H_{29}NO_{10}$	86	125	12.10	H 8.12	6.81	6.98	7.88	7.05	4.22; 1.75; 1.02(COOPr)	1.48; 5.12; 4.53; 1.58 Boc NH CH CH_3	$CDCl_3$
7i	$C_{31}H_{31}NO_9$	81	121	12.34	Me 2.44	6.32	6.68	6.88 (s)		3.77 (OMe)	1.46; 5.05; 4.80; 3.23; 7.3 Boc NH CH CH_2 Ph	$CDCl_3$
7k	$C_{26}H_{28}N_2O_9$	95	138	11.93	H 8.18	6.33	6.87	7.07	8.22	NO_2	1.47; 5.06; 4.47;1.12 2.01;1.05 Boc NH CH CH_2 CH $(CH_3)_2$	$CDCl_3$
9h	$C_{22}H_{22}ClNO_8$	75	200 dec.	12.14	H 8.92	6.83	7.19	7.92	7.25	4.21; 1.65; 0.94(COOPr)	8.90; 4.40; 1.61 HCl NH_2 CH CH_3	DMSO-d_6
9i	$C_{26}H_{24}ClNO_7$	81	195 dec.	12.08	Me 2.36	6.24	6.62	6.91 (s)		3.72 (OMe)	9.11; 4.55; 3.40; 7.30 HCl NH_2 CH CH_2 Ph	DMSO-d_6
9k	$C_{21}H_{21}ClN_2O_8$	71	210 dec.	12.05	H 8.97	6.82	7.21	7.38	8.21	NO_2	8.97; 4.18; 1.57; 2.10; 1.02 HCl NH_2 CH CH_2 CH $(CH_3)_2$	DMSO-d_6



Alkylation of the 5,7-dihydroxychromones was conducted by boiling their acetone solutions with diethyl sulfate in the presence of potassium carbonate. By analogy with acetylation, the 7-hydroxy group of the chromone underwent alkylation first, and exhaustive alkylation of the hydroxy groups took place under the action of an excess of alkylating agent and prolonged boiling.

The diacetates (**4a, g, i**) and (**6a-f, h-k**) and the diethoxy derivative (**7e**) that were obtained did not give a characteristic coloration with alcoholic $FeCl_3$ solution. The acetates were deacetylated by boiling an alcoholic solution in the presence of hydrochloric acid.

The structures of the derivatives obtained were confirmed by PMR spectroscopy. In contrast to the spectra of the initial chromones, in the PMR spectra of the acetates and of the O-ethyl derivative the signals of the protons of the hydroxy groups had disappeared, and the signals of acetoxy and ethoxy groups had appeared in their place. The physicochemical constants of the chromone derivatives are given in Table 3.

The possibility of the selective acylation of the 5,7-dihydroxychromones was shown in the aminoacylation reaction. Since the 5-hydroxy group of a chromone is bound by an intramolecular hydrogen bond, it is exclusively the hydroxy group in position 7 that undergoes acylation. The known methods for the synthesis aminoacyl analogs of flavonoids at a phenolic hydroxyl are based on the use of the methods of symmetrical and mixed anhydrides of alkoxycarbonylamino acids and phosphoric acid derivatives [7, 8]. To obtain 7-O-aminoacyl derivatives of the 3-aryloxy-5,7-dihydroxychromones, N-*tert*-butoxycarbonylamino acids (BocAm's) (the alanine, isoleucine, and phenylalanine derivatives) were first brought into reaction with dicyclohexylcarbodiimide (DCC), and their symmetrical anhydrides so produced were condensed with the chromones in the presence of 4-dimethylaminopyridine (DMAP) in THF solution at room temperature. The protection was removed from the amino function by acidolysis under the action of a 3 M solution of dry HCl in glacial acetic acid.

The structure of the aminoacyl derivatives (**8**) and (**9**) was confirmed by spectral and analytical findings. In the PMR spectra of the protected 7-aminoacyloxychromones (**8**) we observed a broadened doublet of the amide group at 5.0-5.10 ppm, the signal of the Boc group at 1.45-1.50 ppm, and the signal of the protons of the amino acid residue. The formation of hydrochlorides was confirmed by the absence of the signals of the protons of the protective group and the amide group and also by the presence of amino group protons in the weak field at 9.0 ppm. The physicochemical constants of the compounds obtained, (**8**) and (**9**), are given in Table 4.

EXPERIMENTAL

The course of the reactions was followed and the purity of the compounds obtained was checked by TLC on Silufol UV-254 plates in the chloroform–methanol (9:1) and benzene–ethanol (9:1) systems. PMR spectra were taken on a Bruker WP-100 SY instrument (Germany) in DMSO-d_6 and $CDCl_3$ relative to TMS (internal standard).

2,4,6-Trihydroxy-α-(4-chlorophenoxy)acetophenone Ketimine Hydrochloride (1c). A current of dry HCl was passed into a solution of 4-chloroacetonitrile in 100 ml of dry benzene for 15 min, after which a solution of 17 g (0.125 mole) of freshly calcined $ZnCl_2$ and 37.8 g (0.30 mole) of phloroglucinol in 125 ml of dry ether was added. The temperature was maintained between 0 and 5°C, and, with vigorous stirring, a current of dry HCl was passed in until the reaction mixture thickened (1 h). After 12 h the precipitate that had deposited was filtered off and crystallized from acetone. Yield 89%, mp 280°C (decomp.). Empirical formula: $C_{14}H_{13}Cl_2NO_4$. Found %: Cl 21.41; N 4.32. Experimental %: Cl 21.52; N 4.24. PMR spectrum (100 MHz, DMSO-d_6): 5.51 (2H, s, α-CH_2); 6.25 (2H, s, H-3, H-5); 7.14 (2H, d, H-3′, H-5′); 7.42 (2H, d, H-2′, H-6′); 10.9-11.2 (broadened signal, OH-2, OH-4, OH-6, =NH).

General Procedure for the Synthesis of the α-Aryloxy-2,4,6-trihydroxyacetophenones (2a-k). A current of dry HCl was passed into a solution of 0.25 mole of an aryloxyacetonitrile in 100 ml of dry benzene for 15-30 min, after which a solution of 17 g (0.125 mole) of freshly calcined $ZnCl_2$ and 37.8 g (0.30 mole) of phloroglucinol in 125 ml of dry ether was added. The temperature was maintained between 0 and 5°C and, with vigorous stirring, a current of dry HCl was passed through until the mixture thickened (2 h). After a day, the reaction mixture was poured into 500 ml of 10% H_2SO_4 and the resulting mixture was boiled for 2 h. After cooling, the precipitate was filtered off and crystallized from 70% ethanol.

General Procedure for the Synthesis of the 3-Aryloxy-5,7-dihydroxychromones (3a-f, h-k). With cooling and vigorous stirring, 53 ml (150 mmole) of $BF_3 \cdot Et_2O$ was added dropwise to a solution of 50 mmole of an α-aryloxy-2,4,6-trihydroxyacetophenone (**2a-f, h-k**) in 75 ml (100 mmole) of DMFA. The cooling was stopped, and 5.3 ml (60 mmole) of $POCl_3$ was added dropwise. After the mixing of all the components, the reaction mixture was kept at 60-70°C for 30 min

and was then poured into 400 ml of acidified water. After cooling, the precipitate was filtered off and crystallized from ethanol.

General Procedure for the Synthesis of the 3-Aryloxy-5,7-diacetoxy-2-methylchromones (4a, g, i). A mixture of 10 mmole of an acetophenone (**2a, g, i**), 5.5 ml (60 mmole) of freshly distilled Ac_2O, 8.4 ml (60 mmole) of Et_3N, and 2 g of freshly calcined NaOAc was kept at 130-140°C for 4 h. After cooling, the reaction mixture was poured into 200 ml of ice water, and the precipitate was filtered off and crystallized from propan-2-ol.

General Procedure for the Synthesis of the 3-Aryloxy-5,7-dihydroxy-2-methylchromones (5a, g, i). A solution of 5 mmol of a diacetoxychromome (**4a, g, i**) in the minimum amount of ethanol was treated with 1-3 ml of hydrochloric acid and the mixture was boiled. The end of the reaction was determined by TLC. The resulting precipitate was filtered off and crystallized from alcohol.

Compounds (**3a-f, h-l**) were obtained from (**6a-f, h-k**) analogously.

General Procedure for the Synthesis of the 3-Aryloxy-5,7-diacetoxychromones (6a-f, h-k). A solution of 10 mmole of a 3-aryloxy−5,7-dihydroxychromone (**3a-f, h-l**) in 10 ml of pyridine and 5.5 ml of freshly distilled acetic anhydride was kept at 100-110°C for 30-50 min. After cooling, the reaction mixture was poured into 200 ml of acidified ice-water, and the precipitate was filtered off and crystallized from propan-2-ol.

3-(4-Iodophenoxy)-5,7-diethoxychromone (7e). A boiling solution of 1 g (2.5 mmole) of the 5,7-dihydroxychromone (**3e**) in 15 ml of absolute acetone was treated with 2.1 g (15 mmole) of freshly calcined potassium carbonate, and then, with stirring and heating (50-56°C), 0.78 ml (6 mmole) of diethyl sulfate was added dropwise. The reaction mixture was kept for 4 h (the end of the reaction was determined by TLC). After cooling, it was poured into 100 ml of acidified ice water, and the precipitate was filtered off and crystallized from ethanol.

General Procedure for the Synthesis of the 7-(*tert*-Butoxycarbonylaminoacyloxy)-3-aryloxy-5-hydroxychromones (8h, i, k). A solution of 5 mmole of the appropriate N-Boc-amino acid in 10 ml of THF cooled to 0°C was treated with 0.5 g (2.5 mmole) of dicyclohexylcarbodiimide and the reaction mixture was stirred at 0°C for 20-30 min. The dicyclohexylurea that precipitated was filtered off, and a solution of 2 mmole of a chromone (**3k, 4a, i**) in the minimum amount of THF (10-20 ml) and 5 mg of DMAP were added to the mother solution. The reaction mixture was stirred at 0°C for 20-30 min, the end of the reaction being determined by TLC. The solvent was distilled off in vacuum, the residue was dissolved in 50 ml of ethyl acetate, and the solution was washed successively with 5% $NaHCO_3$ solution (2 × 25 ml), water (25 ml), and saturated NaCl solution (25 ml). The organic phase was dried with anhydrous $MgSO_4$, the solvent was distilled off in vacuum, and the residue was crystallized from propan-2-ol.

General Procedure for the Synthesis of Hydrochlorides of 7-Aminoacyloxy-3-aryloxy-5-hydroxychromones (9h, i, k). A solution of 2 mmole of a 7-*tert*-butoxycarbonylaminoacyloxy-3-aryloxy-5-hydroxychromone (**8a, i, k**) in 5 ml of absolute THF was treated with 10 ml of a 3 M solution of hydrogen chloride in glacial acetic acid, and the mixture was kept at 20°C for 30 min. The end of the reaction was determined by TLC. The reaction mixture was diluted with 100 ml of absolute ether and the resulting precipitate was filtered off and dried.

REFERENCES

1. A. Kazakov, V. P. Khilya, V. V. Mezheretskii, and D. Litkei, Natural and Modified Isoflavonoids [in Russian], Rostov-na-Donu, Izd. RGU (1985).
2. T. Namba, M. Hattori, and Y. Takehana, Phytochemistry, **22**, No. 4, 1057 (1983).
3. J. R. Merchant and A. S. Gupta, Chem. Ind. (London), No. 16, 628 (1978).
4. J. R. Gupta and J. R. Merchant, Indian J. Chem., **17B**, No. 4, 410 (1979).
5. M. Lacova, J. Chovancova, and V. Konecny, Chem. Pap., No. 1, 121 (1968).
6. S. A. Vasil'ev, V. G. Pivovarenko, and V. P. Khilya, Dokl. Akad. Nauk UkrSSR, Ser. B., No. 4, 34 (1989).
7. T. Mori and K. Nishimura, Chem. Pharm. Bull., **36**, No. 1, 338 (1988).
8. N. V. Gorbulenko, O. V. Gaiduk, A. S. Ogorodniichuk, V. P. Khilya, and V. V. Shilin, Dokl. Akad. Nauk UkrSSR, No. 9, 144 (1991).