SYNTHESIS AND BIOLOGICAL ACTIVITY OF FURAN, PYRIDINE, AND BENZIMIDAZOLE ANALOGS OF ISOFLAVONES

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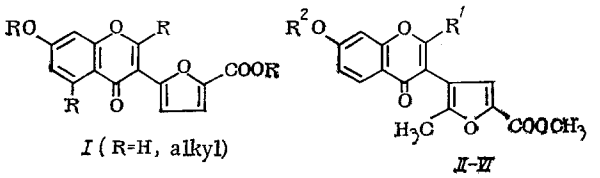
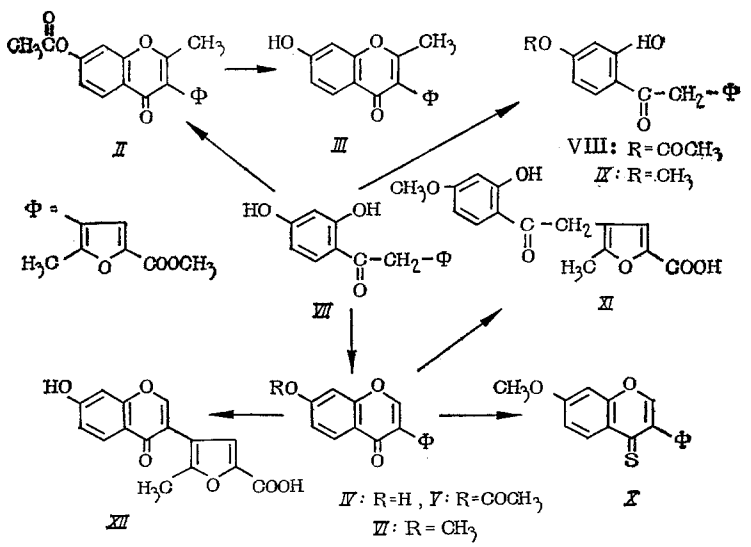
It is known [1] that furan analogs of flavones possess biological activity, with an effect on the living organism similar to that of khellin, a natural furochromone which shows strong antispasmodic action. In an earlier study of physiological activity, we prepared the furan analogs of isoflavones (I) [2, 3], and found that several of them showed heart regulatory activity in mice. The present work describes the first preparation of new furan analogs of isoflavones II-VI, isomers of compounds of type I, and also several derivatives of 3-(2-furyl)chromones, 3-(2-pyridyl)chromones, and 3-(2-benzimidazolyl)chromones, as well as a study of their biological properties.



I (R=H, alkyl) *II-VI*

Ketone VII was used as starting material for the synthesis of chromones II-VI [4]. We studied several reactions of compound VII, and prepared chromones based upon them. Treatment of VII with excess acetic anhydride and triethyl amine gave the acetyl derivative II, from which the 7-hydroxychromone III was obtained by stirring with dilute base. The action of orthoformic ester on ketone VII in pyridine gave chromone IV. Treatment of the latter with acetic anhydride in the cold resulted in transformation into compound V. Heating IV with dimethyl sulfate in acetone gave the methoxychrome VI. Reaction of compound VII with



II *III* VIII: R=$COCH_3$ *IV*: R=CH_3 *VII* *XI* *XII* *IV*: R=H, *V*: R=$COCH_3$ *VI*: R=CH_3 *X*

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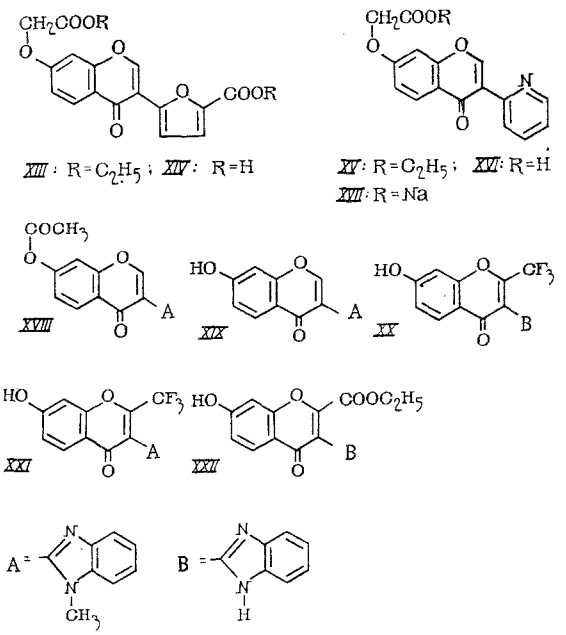
acetic anhydride in xylene acylated the hydroxyl in position 4 to give compound VIII. Similarly, reaction of ketone VII with dimethyl sulfate gave the 4-methoxy derivative, compound IX. The structures of compounds II-IX were confirmed by their PMR spectra. In Table 1 are given the chemical shifts for the aromatic proton signals of the phenolic portion of the chromones II-VI, for the -OH, $-OCOCH_3$, and $-OCH_3$ groups, and for the protons of the furan nucleus. In the PMR spectra of ketones VIII and IX, the singlets corresponding to the 2-OH group lie at a weaker field strength (12-17, 60 ppm) than the signal corresponding to the 7-OH group of chromones, which is explained by the ability of the 2-OH group in acetophenone to form intramolecular hydrogen bonds. In addition, the open structure of compounds VIII and IX have been proven by chemical reactions: these compounds are easily soluble in 2 N aqueous base (a sign of phenolic hydroxyls) and show a yellowish red complex with an alcoholic ferric chloride solution.

The thiochromone X was prepared by heating the 7-methoxychromone VI with excess phosphorus pentasulfide.

The action of base on several of the furan and benzofuran analogs of isoflavones has been studied [5]. In continuing this investigation, we tested the reaction of VI with a four-fold excess of 5% sodium hydroxide solution, which brought about the opening of the pyrone ring and the formation of the ketone XI. This same substance was obtained by a reverse synthesis from the 4-methoxyacetophenone IX. Boiling 7-acetoxychromone V with an equivalent quantity of 5% base leads to deacylation as well as to saponification of the ester group resulting in the production of compound XII.

We studied the influence of the carbomethoxy derivatives of the furan and pyridine isoflavone analogs XIV and XVII on heart activity in mice by the hemodynamic method.

In addition, the antimicrobial activity of the benzimidazole isoflavone analogs XVIII-XXII was studied [6].



EXPERIMENTAL PHARMACOLOGICAL PART

A discussion of the shifts of hemodynamic properties observed on introduction of the heterocyclic isoflavone analogs has important practical significance, since it allows the expansion of concepts of some pharmacological activities of the group of compounds in question, and the planning of further goal-directed syntheses [7, 8].

The experiments were carried out on rabbits weighing 2.0-2.2 kg. The basic hemodynamic properties were established by thermal dilution. The instantaneous blood volume (IBV in milliliters) is calculated by the formula:

$$IBV = \frac{V_t \cdot \Delta T \cdot 60}{S} \cdot K,$$

TABLE 1. Properties of 3-(2-Methyl-methoxycarbonyl-3-furyl)chromones

Compound	Yield, %	Melting point, °C	Found, %		Empirical formula	Calculated, %		PMR Spectral data (δ, ppm)								IR Spectral data (ν, cm⁻¹)			
								chromone ring protons					furan ring protons						
			C	H		C	H	2-R	5-H	6-H	7-R	8-H	2-CH_3	4-H	5-$COOCH_3$	Chromone C=O	Chromone C=O	Ester C=O	OH
II	95	203	63,8	4,8	$C_{18}H_{16}O_7$	64,0	4,5	CH_3; 2,47 or 2,38	8,21	7,14	$OCOCH_3$; 2,38 or 2,47	7,28	2,47 or 2,38	7,17	3,99				
III	95	220	63,9	4,4	$C_{17}H_{14}O_6$	65,0	4,5	CH_3; 2,35 or 2,40	7,90	6,94	OH; 10,77	6,88	2,40 or 2,35	7,29	3,94				
IV	94	260 with decomposition	64,4	4,4	$C_{16}H_{12}O_6$	64,0	4,0	H; 8,33	7,96	6,96		6,89	2,50	7,32	3,92	1620	1575	1725	3200
V	95	215	62,9	4,5	$C_{18}H_{14}O_7$	63,2	4,1	H; 7,92	8,27	7,02	$OCOCH_3$; 2,44 or 2,50	7,32	2,50 or 2,44	7,28	3,97	1660	1580 1620	1712 1772	
VI	80	164 with decomposition	64,7	4,4	$C_{17}H_{14}O_6$	65,0	4,5	H; 7,87	8,14	6,99	OCH_3; 4,05 or 4,01	6,90	2,54	7,34	4,01 или 4,05	1612	1572 1592	1735	
X	31	184	S9,30		$C_{17}H_{14}O_5S$	S9,70													
XII	80	>300	62,5	3,9	$C_{15}H_{10}O_6$	62,9	3,5												

Note: the PMR spectra of compounds II, V, VI were obtained in deuterochloroform, and of compounds III and IV in deuteriodimethyl sulfoxide.

TABLE 2. Influence on Hemodynamic Properties of the Sodium Salt of 3-(2-pyridyl)-7-carboxymethoxychromone (M ± m)

Hemodynamic Property	Control	Dose, mg/kg						
		1				10		
		Time, min						
		1	5	10	30	1	5	10
Pulse Volume	1,77 ± 0,15	1,66 ± 0,2	1,71 ± 0,22	1,67 ± 0,21	1,74 ± 0,22	1,62 ± 0,29	1,65 ± 0,18	1,6 ± 0,19
Instantaneous Vol., ml/min	427,10 ± 48,49	426,37 ± 40,47	453,49 ± 63,92	435,39 ± 60,41	461,63 ± 62,94	406,09 ± 83,68	414,15 ± 63,66	391,66 ± 46,95
Cardiac Index, ml/m²/min	2 053,76 ± 266,92	2 042,46 ± 266,39	2 175,82 ± 327,01	2 111,97 ± 314,782	2 251,85 ± 325,42	1 968,84 ± 420,96	1 979,88 ± 291,59	1 858,13 ± 261,04
Systolic Index, ml/m²	8,50 ± 0,89	7,64 ± 0,98	8,19 ± 1,16	8,11 ± 1,05	8,49 ± 1,18	7,91 ± 1,50	7,92 ± 1,00	7,60 ± 1,00
Left Ventricle Work Index, kg-m/m²/min	1 841,19 ± 303,33	1 816,33 ± 345,66	2 026,20 ± 379,90	1 889,81 ± 388,02	1 950,42 ± 319,66	1 667,39 ± 471,50	1 749,63 ± 364,70	1 572,16 ± 263,05
General Peripheral Resistance, dyn/sec/cm⁻⁵	14 221,71 ± 2216,12	13 927,36 ± 2250,33	13 048,70 ± 1715,32	12 808,88 ± 1131,52	13 015,11 ± 2190,04	13 956,55 ± 2219,80	11 475,0 ± 1431,40	12 900,91 ± 2282,68
Arterial Pressure, mm Hg	66,87 ± 4,34	63,12 ± 4,34	66,00 ± 2,85	64,25 ± 3,22	62,50 ± 4,96	58,12 ± 6,83	59,0 ± 6,21	58,50 ± 6,21

Hemodynamic Property	Dose, mg/kg								
	10	50				100			
	Time, min								
	30	1	5	10	30	1	5	10	30
Pulse Volume	1,45 ± 0,27	1,79 ± 0,3	1,46 ± 0,25	1,34 ± 0,34	1,56 ± 0,32	2,21 ± 0,52	2,01 ± 0,84	1,42 ± 0,18	1,64 ± 0,46
Instantaneous Vol., ml/min	364,43 ± 80,43	442,98 ± 86,26	356,48 ± 73,20	339,65 ± 98,43	380,47 ± 92,16	520,65 ± 149,8	623,02 ± 177,16	324,28 ± 36,25	358,67 ± 82,63
Cardiac Index, ml/m²/min	1 768,67 ± 406,39	2 136,42 ± 420,83	1 708,92 ± 365,29	1 617,36 ± 477,21	1 599,46 ± 800,30	2 578,66 ± 761,57	3 070,00 ± 823,84	1 586,30 ± 195,32	1,753,34 ± 468,03
Systolic Index, ml/m²	7,07 ± 1,43	8,64 ± 1,47	6,98 ± 1,28	6,68 ± 1,63	7,53 ± 1,700	10,82 ± 2,71	13,03 ± 3,13	6,96 ± 0,60	8,09 ± 2,06
Left Ventricle Work Index, kg-m/m²/min	1 352,32 ± 690,61	1 580,29 ± 547,21	1 525,23 ± 459,11	1 216,09 ± 586,01	1 382,10 ± 621,99	1 610,80 ± 919,94	1 945,31 ± 1066,31	924,85 ± 300,50	1 105,75 ± 219,14
General Peripheral Resistance, dyn/sec/cm⁻⁵	14 729,48 ± 2494,86	12 110,25 ± 3535,52	12 705,03 ± 1758,17	12 989,85 ± 4744,24	11 546,04 ± 2351,61	7 133,12 ± 2714,46*	6 396,86 ± 2135,23*	11 608,98 ± 3624,84	14 093,67 ± 5585,0
Arterial Pressure, mm Hg	53,87 ± 5,71	53,12 ± 7,45	60,00 ± 6,21	47,85 ± 8,37	49,71 ± 8,37	39,6 ± 10,96*	41,2 ± 10,96	43,60 ± 10,96	50,0 ± 7,28

*Here and in Table 3, the difference from the corresponding control value is significant.

TABLE 3. Influence on Hemodynamic Properties of 3-(5-carboxy-2-furyl)-7-carboxymethoxychromone (XIV) (M ± m)

Hemodynamic Property	Control	Dose, mg/kg							
		1				10			
		Time, min							
		1	5	10	30	1	5	10	30
Pulse Volume	2,07±0,33	1,46±0,17	1,27±0,25	1,67±0,20	1,84±0,88	1,27±0,13	1,08±0,20	1,66±0,18	1,37±0,40
Instantaneous Vol. ml/min	550,65 ±94,51	388,12 ±60,28	327,24 ±56,05	436,94 ±111,58	473,36 ±221,92	329,02 ±15,13	280,64 ±64,86	427,05 ±73,09	331,08 ±97,30
Cardiac Index, $ml/m^2/min$	2464,88 ±324,85	1767,55 ±316,00	1510,62 ±313,27	2014,46 ±566,24	2044,25 ±116,57	1503,58 ±160,35	1254,63 ±271,01*	1909,62 ±184,11	1462,67 ±349,12
Systolic Index, ml/m^2	9,29±0,95	6,66±1,06	5,85±1,42	7,67±1,91	8,09±3,24	5,85±0,86	7,05±0,82	7,45±0,62	6,09±1,45
Left Ventricle Work Index, $kg\text{-}m/m^2/min$	2491,07 ±415,01	1861,17 ±170,77	1505,65 ±328,72	1947,15 ±276,90	2374,08 ±1123,0	1586,22 ±159,98	1330,82 ±246,23	2104,53 ±413,13	1668,44 ±568,33
General Peripheral Resistance, $dyn/sec/cm^{-5}$	11 416,57 ±2001,60	17 360,80 ±3410,37	19 082,13 ±3626,14	16 202,96 ±8903,72	18 203,63 ±6769,76	19 233,96 ±1912,55	25 554,46 ±8069,59	15 513,50 ±1989,79	21 564,10 ±3619,79
Arterial Pressure, mm Hg	75,00±5,11	80,00±6,82	75,00±8,53	76,33 ±11,60	81,66±8,53	79,00±7,50	80,00 ±10,23	81,00±9,55	81,66±8,53

TABLE 3. (continued)

Hemodynamic Property	Control	Dose, mg/kg							
		50				100			
		Time, min							
		1	5	10	30	1	5	10	30
Pulse Volume	2,07±0,33	1,62±0,39	1,56±0,52	1,33±0,25	1,86±0,6	0,82±0,42	1,65±1,3	1,51±0,15	1,50±0,35
Instantaneous Vol. ml/min	550,65 ±94,51	390,20 ±95,24	376,25 ±126,52	316,31 ±65,00	425,61 ±137,88	183,64 ±100,76	384,92 ±325,81	347,52 ±58,34	327,51 ±97,31
Cardiac Index, $ml/m^2/min$	2464,88 ±324,85	1753,12 ±398,29	1727,78 ±624,58	1409,65 ±220,56	1869,71 ±465,63	792,94 ±340,72*	1615,36 ±1234,67	1554,48 ±43,8	1447,72 ±233,52
Systolic Index, ml/m^2	9,29±0,95	7,30±1,65	7,19±2,6	5,94±0,84	8,20±2,04	3,54±1,41*	6,96±4,85	6,82±0,25	6,67±0,61
Left Ventricle Work Index, $kg-m/m^2/min$	2491,07 ±415,01	1907,74 ±372,79	1836,93 ±506,33	1531,89 ±335,92	1989,59 ±658,04	1015,83 ±528,27	1929,48 ±1525,33	1766,26 ±156,58	1563,53 ±252,20
General Peripheral Resistance, $dyn/sec/cm^{-5}$	11 416,57 ±2001,60	18 491,86 ±5023,58	21 500,70 ±7837,40	22 509,03 ±4698,87	16 340,03 ±6958,56	48 101,55 ±22 314,68	32 574,90 ±26 792,12	13 032,10 ±2133,93	20 688,05 ±8477,67
Arterial Pressure, mm Hg	75,00±5,11	81,66±5,11	83,00±7,84	81,33±10,7	76,66 ±10,23	92,50±5,11	87,00±3,75	84,0±5,0	80,0±0

TABLE 4. Antimicrobial Activity (in μg/ml) of 3-(2-Benzimidazolyl)chromones*

Compound	Staphylococcus aureus 209	E. coli	Candida albicans 62	Aspergillus niger	Trichophyton gupseum
XVIII	200	40	25	50	12,5
XIX	200	40	50	50	50
XX	200	200	50	—	50
XXI	200	40	50	—	50
XXII	200	200	—	—	50

*The indicated concentration is that at which the growth of the microorganism was depressed.

where V_i = quantity of indicator (0.9% sodium chloride solution) introduced; ΔT = difference between blood temperature and indicator temperature; S = amount of temperature variation in each second after introduction of the indicator; coefficient K is the ratio between the derived specific heat capacities of the injected solution and the blood.

The level of arterial pressure was measured in the femoral artery, and rhythm was obtained by EKG. The IBV value was used for calculating other hydrodynamic properties (blood pulse volume, cardiac index, systolic index, general peripheral resistance, left ventricle work index).

The heteryl chromones XIV and XVII were introduced in a dose of 1-100 mg/kg intravenously [9], resulting in several positive effects. Thus, the 3-pyridylchromone XVII showed a favorable influence on the hemodynamics (reduction of arterial pressure 1 min after introduction, decrease of general and peripheral resistance 1 and 5 min after introduction of a dose of 100 mg/kg, Table 2). The activity of the furan isoflavone analog XIV on the properties studied showed it to be significantly weaker than compound XVII (decrease of cardiac index 5 min after injection at a dose of 10 mg/kg, and 1 min after introduction of a dose of 100 mg/kg; decrease of the systolic index within 1 min at a dose of 100 mg/kg, Table 3).

Thus, searches for new compounds showing a normalizing influence on hemodynamic properties should be carried out among isoflavone analogs containing a nitrogen heterocycle in position 3.

The antimicrobial activity of compounds XVIII-XXII was studied by serial dilution in a titration series. The test organisms were from the Stamm collection (Table 4), The results of examination of the bacteriostatic and fungistatic activity show that all tested compounds possess antimicrobial activity against *Staphylococcus aureaus* and *E. coli* in concentrations of 200-40 μg/ml, and show strong fungistatic activity against the dermatophyte *Trichophyton gupseum* and the yeastlike fungus *Candida albicans 62*.

EXPERIMENTAL CHEMICAL PART

PMR spectra were determined in 0.25 M solutions with a ZKR-60 spectrometer using tetramethylsilane as an internal standard, and IR spectra were determined in potassium bromide on a UR-10 spectrometer. The purity of the compounds prepared was controlled by thin layer chromatography on Silufol. A mixture of chloroform and methanol (9:1) was used as eluent.

2-Methyl-3-(2-methyl-5-methoxycarbonyl-3-furyl)-7-acetoxychromone (II). A mixture of 4.06 g (14 mmole) of ketone, 7.14 g (70 mmole) of acetic anhydride, and 5.66 g (56 mmole) of triethyl amine was maintained at 120-130°C for 2-3 h and added to 100 ml of ice water containing 98 mmole of concentrated hydrochloric acid. The resulting oil which solidified on rubbing was filtered off, washed several times with water, and recrystallized from alcohol.

2-Methyl-3-(2-methyl-5-methoxycarbonyl-3-furyl)-7-hydroxychromone (III). A 5% solution of sodium hydroxide (1.6 ml, 2 mmole) was added dropwise to a hot solution of 0.71 g

(2 mmole) of II in 20 ml of ethanol. The solution was boiled 2-3 sec, diluted with 2 volumes of water, and boiled again for 5 min. The solution was neutralized with dilute hydrochloric acid, the resulting residue was filtered off, and recrystallized from aqueous alcohol.

3-(2-Methyl-5-methoxycarbonyl-3-furyl)-7-hydroxychromone (IV). A mixture of 1.25 g (3.5 mmole) of ketone VII, 3.5 ml of orthoformic ester, 3.5 ml of pyridine, and 12 drops of piperidine was maintained at 120-130°C for 5 h. The reaction mixture was kept at 0°C overnight and the resulting crystals were filtered off and recrystallized from alcohol.

3-(2-Methyl-5-methoxycarbonyl-3-furyl)-7-acetoxychromone (V). To a solution of 1 g (3.3 mmole) of IV in the minimum quantity of pyridine was added 1.84 g (18 mmole) of acetic anhydride and the reaction mixture was kept overnight at 0°C. The resulting precipitate was filtered off and recrystallized from alcohol.

3-(2-Methyl-5-methoxycarbonyl-3-furyl)-7-methoxychromone (VI). To a hot solution of 1.92 g (6.4 mmole) of IV in absolute acetone was added 0.93 ml (9.8 mmole) of dimethyl sulfate and 3.7 g of calcined potassium carbonate. The mixture was boiled 6 h, the inorganic precipitate was filtered off, and the filtrate was acidified with 2 drops of glacial acetic acid. The acetone was distilled and the residue was recrystallized from alcohol.

α-(2-Methyl-5-methoxycarbonyl-3-furyl)-2-hydroxy-4-acetoxyacetophenone (VIII). A solution of 0.5 g (1.72 mmole) of VII and 0.35 ml (3.8 mmole) of acetic anhydride in the minimum quantity of absolute xylene was kept at 140°C for 3 h. The resulting precipitate was filtered off. Yield 53% of colorless needles, mp 162°C (from alcohol). Found, %: C 61.85, H 5.19. $C_{17}H_{16}O_7$. Calculated, %: C 61.60, H 4.85. The PMR spectrum was determined in deuteriochloroform (δ, ppm): CH_2, 4.12; 2-OH, 12.17; 3-H, 6.79; 4-$OCOCH_3$, 2.40; 5-H, 6.71; 6-H, 7.81; furan ring protons: 2-CH_3, 2.42; 4-H, 7.07; 5-$COOCH_3$, 3.95.

α-(2-Methyl-5-methoxycarbonyl-3-furyl)-2-hydroxy-4-methoxyacetophenone (IX). To a hot solution of 1 g (3.5 mmole) of VII in 43 ml of absolute benzene was added 0.5 ml (5.2 mmole) of dimethyl sulfate and 2 g (14.2 mmole) of freshly calcined potassium carbonate, and the mixture was boiled for 6 h. The inorganic precipitate was filtered off, and the filtrate was acidified with 2 drops of glacial acetic acid. The solution was concentrated to give 76% yield of colorless needles, mp 125°C (from methanol). Found, %: C 62.92, H 5.69. $C_{16}H_{18}O_6$. Calculated, %: C 63.29, H 5.30. The NMR spectrum was determined in deuteriochloroform (δ, ppm): CH_2, 4.06; 2-OH, 12.60; 3-H, 6.47; 4-OCH_3, 3.91; 5-H, 6.53; 6-H, 7.73; furan ring protons: 2-CH_3, 2.40; 4-H, 7.15; 5-$COOCH_3$, 3.91.

3-(2-Methyl-5-methoxycarbonyl-3-furyl)-4-thioxo-7-methoxychromone (X). A solution of 0.61 g (1.98 mmole) of VI and 0.266 g (1.1 mmole) of phosphorus pentasulfide in 12 ml of absolute pyridine was kept at 100-110°C for 4 h and added to 50 ml of water. The precipitate was filtered off and crystallized from methanol in orange needles.

α-(2-Methyl-5-carboxy-3-furyl)-2-hydroxy-4-methoxyacetophenone (XI). Method A. To a hot solution of 0.2 g (0.66 mmole) of IX in 15 ml of alcohol and 15 ml of water was added 1.06 g (1.32 mmole) of 5% aqueous sodium hydroxide. The solution was boiled 30 min, acidified to pH 2.0-3.0, and the precipitate was filtered off.

Method B. To a hot solution of 0.2 g (0.64 mmole) of VI in 15 ml of alcohol and 15 ml of water was added 1.94 ml (2.56 mmole) of 5% aqueous sodium hydroxide. The mixture was boiled for 30 min, acidified to pH 2.0-3.0 and the precipitate was filtered off and crystallized from aqueous alcohol.

3-(2-Methyl-5-carboxy-3-furyl)-7-hydroxychromone (XII). To a solution of 4.5 g (13.5 mmole) of V in 200 ml of absolute acetone was added 32.4 ml (40 mmole) of 5% sodium hydroxide solution, the mixture was boiled 2-3 sec, and diluted 2-fold with water. The product (3 g) was filtered from the cold solution.

3-(5-Ethoxycarbonyl-2-furyl)-7-ethoxycarbonylmethoxychromone (XIII) was obtained analogously to compound VI from 3 g (10 mmole) of 3-(5-ethoxycarbonyl-2-furyl)-7-hydroxychromone [10] in 600 ml of absolute acetone, 4.5 ml (40 mmole) of ethyl bromoacetate and 4.8 g (35 mmole) of freshly calcined potassium carbonate. Yield 3.2 g (96%) of colorless needles, mp 144°C (from alcohol). Found, %: C 61.79, H 5.00. $C_{20}H_{18}O_8$. Calculated, %: C 62.19, H 4.69.

3-(5-Carboxy-2-furyl)-7-carboxymethoxychromone (XIV). To a hot solution of 2.1 g (5.4 mmole) of XIII in a minimum quantity of acetone was added dropwise 8.25 ml of 5% aqueous

sodium hydroxide and the solution was boiled for 1 min. The reaction mixture was then diluted 2-fold with water and boiled for 3-4 min. After acidification to pH 2.0-3.0, the precipitate was filtered off from the cold solution. Yield 1.7 g (95%) of colorless needles, mp 214°C (from alcohol). Found, %: C 57.84, H 3.56. $C_{16}H_{10}O_6$. Calculated, %: C 57.18, H 3.05.

3-(2-Pyridyl)-7-ethoxycarbonylmethoxychromone (XV). A mixture of 0.48 g (2 mmole) of 3-(2-pyridyl)-7-hydroxychromone [11], 1.34 g (5 mmole) of ethyl bromoacetate and 0.83 g (3 mmole) of freshly calcined potassium carbonate in 200 ml of dry acetone was boiled for 6 h. The inorganic precipitate was filtered from the hot solution, the filtrate was concentrated, and the residue was washed with cold alcohol. Yield 0.5 g (84%) of colorless needles, mp 133°C (from alcohol). Found, %: N 4.26. $C_{18}H_{15}NO_5$. Calculated, %: N 4.30.

3-(2-Pyridyl)-7-carboxymethoxychromone (XVI). To a hot solution of 0.325 g (1 mmole) of XV in 10 ml of alcohol was added dropwise 0.8 ml of 5% aqueous sodium hydroxide. The solution was boiled for 1 min, diluted 2-fold with water and boiled for 3-4 min more. The reaction mixture was acidified with dilute hydrochloric acid to pH 7.0 and the resulting product was filtered off. Yield, 0.25 g (80%) of colorless needles, mp 194°C (from alcohol). Found, %: N 4.58. $C_{17}H_{11}NO_5$. Calculated, %: N 4.72.

Sodium Salt of 3-(2-pyridyl)-7-carboxymethoxychromone (XVII). To a warm solution of 0.59 g (2 mmole) of XVI in the minimum quantity of alcohol was added 1.6 ml (2 mmole) of 5% aqueous sodium hydroxide at 40°C. The solution was cooled and the resulting precipitate was filtered off and washed with alcohol and ether. Yield, 0.54 g (84%) of yellow crystals, mp 265°C (from propanol). Found, %: N 4.58. $C_{16}H_{10}NO_5Na$. Calculated, %: N 4.39.

LITERATURE CITED

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