2,4,4-Trimethyl-1,3-dioxanium Perchlorate (I). A total of 1 ml (0.01 mole) of 70% $HClO_4$ solution was added dropwise to a mixture (prepared at −5°) of 4 ml of acetic anhydride and 1.16 g (0.01 mole) of 4,4-dimethyl-1,3-dioxane. After 10 min, the mixture was diluted with ether, during which an oil was liberated. The oil crystallized rapidly when the mixture was stirred. Workup gave 1.71 g (75%) of a product with mp 52-54° (methylene chloride, ether). Found: C 33.2; H 5.6; Cl 16.0%. $C_6H_{11}ClO_6$. Calculated: C 33.6; H 5.6; Cl 16.6%. Perchlorates I-IV, VII, and VIII were similarly obtained.

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SYNTHESIS OF 4-ETHOXYFLAVYLIUM SALTS AND FLAVONES

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4-Ethoxybenzopyrylium salts, which are converted to the corresponding flavones in quantitative yields by refluxing with water, were synthesized by condensation of o-hydroxyacetophenones with aromatic aldehydes in the presence of ethyl orthoformate and 70% perchloric acid.

The previously described methods for the synthesis of 4-alkoxybenzopyrylium salts were based on the reaction of ethyl orthoformate with o-hydroxychalcones [1] or of ethyl orthoformate with (ω-acyl)hydroxyacetophenones [2] in the presence of 70% perchloric acid. We have recently proposed a method for the preparation of 4-ethoxyflavylium salts on the basis of acid condensation of o-hydroxyacetophenones with aromatic aldehydes in the presence of ethyl orthoformate and 70% perchloric acid [3]. As compared with other methods [1, 2], this method for the synthesis of 4-ethoxyflavylium salts is the simplest method, is satisfactorily reproducible, and is convenient for the preparation of natural flavones and their synthetic analogs, which find application as regulators of the nervous system, stimulators of the activity of the heart muscles, and have p-vitamin activity [4].

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TABLE 1. 4-Ethoxyflavylium Salts I

R	R′	R″	mp, °C[a]	Absorption bands in the IR spectra, cm^{-1}	Found, %			Empirical formula	Calc., %			Yield, %
					C	H	Cl		C	H	Cl	
OH	H	H	195	1640 1610 1530 1510 1090	55,6	4,2	9,8	$C_{17}H_{15}ClO_7$	55,7	4,1	9,4	16
OH	OH	H	188	1630 1525 1600 1510 1080	53,6	4,0	9,6	$C_{17}H_{15}ClO_8$	53,3	3,9	9,3	50
OH	OCH_3	OCH_3	205	3450 1620 1600 1530 1080	53,9	4,2	8,0	$C_{19}H_{19}ClO_9$	53,5	4,5	8,3	73
OH	OH	OCH_3	163	1630 1600 1540 1500 1080	52,2	4,2	8,2	$C_{18}H_{17}ClO_9$	52,4	4,1	8,6	98
OH[b]			232	3300 1640 1600 1100	48,6	3,8	9,5	$C_{15}H_{13}ClO_7S$	48,3	3,5	9,5	72
OH	OCH_2O		207	3400 1640 1600 1540	53,0	3,9	9,1	$C_{18}H_{15}ClO_9$	52,6	3,7	8,6	98
Cl	OCH_2O		132[c]	1630 1605 1550 1505 1090	50,8	3,3	16,1	$C_{18}H_{14}Cl_2O_8$	50,4	3,3	16,5	54
Cl	OCH_3	H	162	1640 1600 1530 1080	52,5	3,9	17,1	$C_{18}H_{16}Cl_2O_7$	52,1	3,9	17,3	75
Cl	$OCOCH_3$	H	212[d]	1705 1620 1550 1510 1610 1100	51,5	4,0	15,9	$C_{19}H_{16}ClO_8$	51,4	3,6	15,9	78
Cl	OCH_3	OCH_3	145[c]	1630 1600 1530 1090	50,9	4,2	15,5	$C_{19}H_{18}Cl_2O_8$	51,0	4,1	15,9	83
Cl	OH	OCH_3	107	1620 1600 1530 1070	50,6	3,7	16,6	$C_{18}H_{16}Cl_2O_8$	50,1	3,7	16,4	83
Cl	H	H	112	1620 1610 1550 1500 1090	53,0	4,0	18,3	$C_{17}H_{14}Cl_2O_6$	53,1	3,7	18,4	12

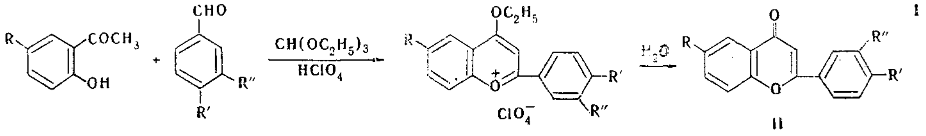
[a] From glacial acetic.

[b] 2-(α-Thienyl)-4-ethoxy-6-hydroxychromylium perchlorate. Found: S 8.6%. Calculated: S 8.6%.

[c] From nitromethane.

[d] From acetic anhydride.

In order to make a further study of the range of application of this method, we investigated the condensation of 2,5-dihydroxy and 2-hydroxy-5-chloroacetophenones with a number of aromatic aldehydes and ethyl orthoformate in the presence of perchloric acid. As expected, this reaction led to the formation of 4-ethoxyflavylium salts I in good yields (Table 1).



All of the synthesized 4-ethoxybenzopyrylium salts are converted to the corresponding flavones (Table 2) in quantitative yields when they are refluxed with water.

The IR spectra of perchlorates I contain absorption bands of the pyrylium cation (1620-1640, 1530-1540 cm^{-1}), the benzene ring (1590-1610 cm^{-1}), and the ClO_4^- anion (1080-1100 cm^{-1}). An absorption band at 1630-1660 cm^{-1} (pyrone ring ν_{CO}) is present in the IR spectra of the flavones.

The hydroxyl group undergoes acylation during crystallization of 4-ethoxy-6-chloro-4′-hydroxyflavylium perchlorate from acetic anhydride, as evidenced by the appearance in the IR spectrum of an absorption band of an ester group at 1765 cm^{-1}.

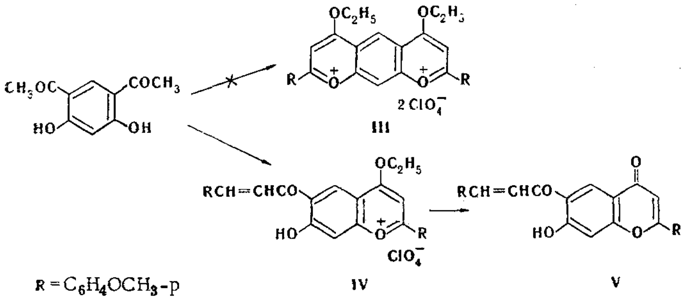


TABLE 2. Flavones II

R	R′	R″	mp, °C	Absorption bands in the IR spectra, cm^{-1}	Empirical formula	Found, %			Calculated, %		
						C	H	Cl	C	H	Cl
OH	H	H	230[5]	3320 1635 1500 1600	$C_{15}H_{16}O_3$						
OH	OH	H	320[6]	3240 1640 1590 1500	$C_{15}H_{16}O_4$						
OH	OCH_3	OCH_3	215[a]	3300 1640 1600 1510	$C_{17}H_{14}O_5$	68,8	4,8		68,4	4,7	
OH	OH	OCH_3	202[a]	3500 1660 1600	$C_{16}H_{12}O_5$	67,9	4,5		67,6	4,2	
OH[b]			320[c]	3420 1630 1600	$C_{13}H_8O_3$	63,5	4,1		63,9	3,7	
OH		OCH_2O	320[c]	3300 1660 1640 1610	$C_{16}H_{10}O_5$	67,9	3,43		68,1	3,54	
Cl		OCH_2O	272[7]	1650 1600 1510	$C_{16}H_9ClO_4$						
Cl	OCH_3	H	182[d]	1660 1600 1510	$C_{16}H_{11}ClO_3$	67,5	3,7	12,8	67,0	3,9	12,4
Cl	$OCOCH_3$	H	190[a]	1750 1645 1610 1510	$C_{17}H_{11}ClO_4$	64,9	3,6	10,7	64,9	3,5	11,2
Cl	OCH_3	OCH_3	195[7]	1640 1600 1520	$C_{17}H_{13}ClO_4$						
Cl	OH	OCH_3	244[d]	3320 1630 1600 1550	$C_{16}H_{11}ClO_4$	63,7	3,6	11,2	63,5	3,7	11,7
Cl	CH	H	178	1660 1600 1500	$C_{15}H_9ClO_2$						

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[a] From ethanol.

[b] 2-(α-Thienyl)-6-hydroxychromone. Found: S 12.9%. Calculated: S 13.1%.

[c] Decomposes above 320°.

[d] From DMF.

The reaction of resodiacetophenone with anisaldehyde and ethyl orthoformate proceeds in a peculiar manner. Instead of the expected diperchlorate III, pyrylium salt IV, which is converted to flavone V when it is refluxed with water, is formed. The IR spectrum of V (in nitromethane) contains the absorption band of a hydroxyl group at 3600 cm^{-1}.

The condensation of o-hydroxy ketones with α-formylthiophene, which leads to the formation of 2-(α-thienyl)-4-ethoxy-6-hydroxychromylium perchlorate (Table 1), proceeds similarly.

EXPERIMENTAL

The IR spectra of mineral oil pastes of the compounds were recorded with a UR-20 spectrometer.

4-Ethoxy-6-hydroxy-4'-methoxyflavylium Perchlorate. A 0.2-ml sample of 70% perchloric acid was added dropwise to a mixture of 0.31 g (0.002 mole) of 2,5-dihydroxyacetophenone, 0.84 g (0.006 mole) of veratraldehyde, and 2.8 ml of freshly distilled ethyl orthoformate, and the mixture was allowed to stand at room temperature for 3 h. The precipitated crystals of the perchlorate were removed by filtration to give 0.63 g (81%) of a product with mp 224° (from acetic acid). IR spectrum: 3330, 1630, 1560, and 1100 cm^{-1}. Found: C 55.0; H 4.28; Cl 9.2%. $C_{18}H_{17}ClO_8$. Calculated: C 54.5; H 4.3; Cl 8.9%. The remaining compounds of the I type were similarly prepared.

4-Ethoxy-6-(p-methoxycinnamoyl)-7-hydroxy-4'-methoxyflavylium Perchlorate (IV). A total of 2 ml of 70% perchloric acid was added dropwise to a mixture of 1.96 g (0.01 mole) of resodiacetophenone, 12.2 g (0.06 mole) of anisaldehyde, and 28 ml of ethyl orthoformate, and the mixture was allowed to stand at room temperature for 3 h. The precipitated crystals of the perchlorate were removed by filtration to give 3.7 g (66%) of a product with mp 230° (from nitromethane). IR spectrum: 1645, 1610, 1520, 1500, and 1080 cm^{-1}. Found: C 61.0; H 4.9; Cl 6.0%. $C_{28}H_{25}ClO_{10}$. Calculated: C 60.4; H 4.5; Cl 6.4%.

6-Hydroxy-4'-methoxyflavone. Water (100 ml) was added to 0.78 g of 4-ethoxy-6-hydroxy-4'-methoxyflavylium perchlorate, and the mixture was refluxed for 2-4 min. The colorless precipitate was removed by filtration and air dried to give 0.5 g (91%) of a product with mp 236° (from ethanol). IR spectrum: 3360, 1645, 1600, and 1500 cm^{-1}. Found: C 72.8; H 4.4%. $C_{16}H_{12}O_4$. Calculated: C 72.9; H 4.3%. The remaining flavones of the II type were similarly prepared.

6-(p-Methoxycinnamoyl)-7-hydroxy-4'-methoxyflavone (V). A 0.56-g (0.001 mole) sample of perchlorate IV was mixed with 100 ml of water and the mixture was refluxed for 5 min. The colorless precipitate was removed by filtration and air dried to give 0.41 g (96%) of a product with mp 244° (from ethanol). IR spectrum: 3600, 1670, 1640, 1610, and 1520 cm^{-1}. Found: 72.4; H 5.1%. $C_{26}H_{20}O_6$. Calculated: C 72.9; H 4.7%.

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