RESEARCH ON PYRANES, THEIR ANALOGS, AND RELATED COMPOUNDS

XXII. 2-Acylaminochromones*

V. A. Zagorevskii, Sh. M. Glozman, V. G. Vinokurov,
and V. S. Troitskaya

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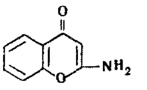
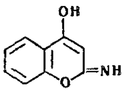
Reaction of sodium azide with chromone-2-carbonyl chloride or the action of nitrous acid on the hydrazide of chromone-2-carboxylic acid, existing in the cyclic form 3'-oxopyrazolidino[4', 5':2, 3]-chroman-4-one, gives the azide of chromone-2-carboxylic acid, the Curtius rearrangement of which is used to synthesize a number of 2-acylaminochromones.

Hitherto 2-aminochromones have been almost uninvestigated. Among other things the 2-aminochromone system (A) is interesting in that, because it contains a β-aminovinylketone grouping, it is tautomeric with 2-imino-4-hydroxycoumarin (B).

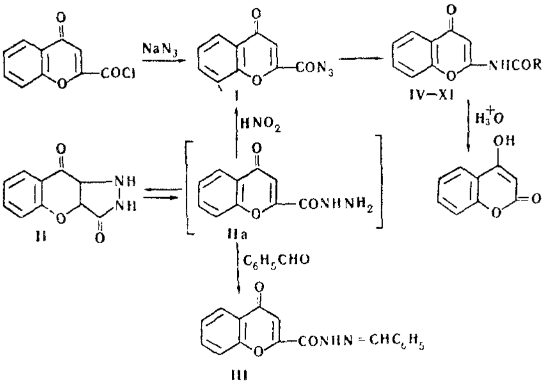


A



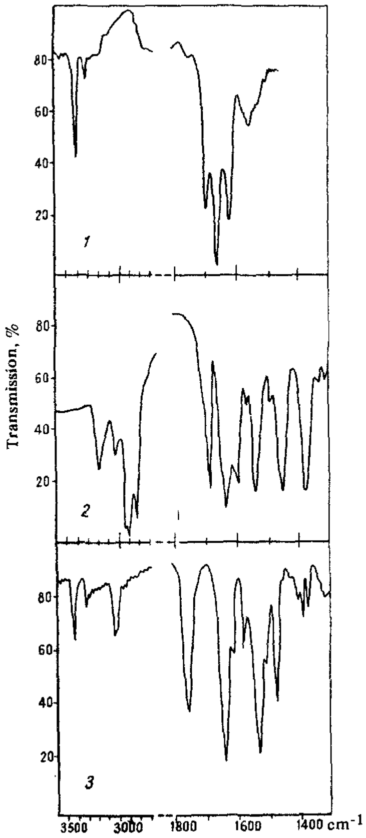
B

From their IR spectra, 2-aminoisoflavones were considered to have a chromone structure [2]. However, a hydroxy structure was ascribed to unsubstituted 2-aminochromone [3]. Since the carbon atom at position 2 of chromones carries a relatively large fractional positive charge (chromone-2-carboxylic acid is no less strong than trichloroacetic acid [4]), it may be assumed that 2-aminochromones will prove comparatively weak bases, and that the properties of the amino group will be comparable with those of aromatic amines. The Curtius rearrangement of the azide of chromone-2-carboxylic acid (I) has now been used to obtain hitherto unknown N-acyl derivatives of 2-aminochromones. Azide I can be synthesized either by reacting chromone-2-carbonyl chloride [5] with sodium azide, or by the action of nitrous acid on 3'-oxopyrazolidino [4', 5': 2, 3] chromanone-4 [6], the cyclic form of chromone-2-carbonyl azide (II).



IV–XI

IV $R=OC_2H_5$
V $R=CH_3$
VI $R=CCl_3$
VII $R=N(C_2H_5)_2$
VIII $R=NHC_6H_{11}$-cyclo
IX R=pyrrolidino
X R=piperidino
XI R=morpholino



IR spectra (UR-10): 1) 3'-oxopyrazolidino [4', 5': 2, 3] chromanone-4 (II) (in $CHCl_3$, c 0.001 M, d 1 cm); 2) N-(chromonoyl-2)-N'-benzalhydrazine (III) (in oil); 3) 2-ethoxycarbonylaminochromone (IV) (in $CHCl_3$, c 0.02 M, d 0.4 mm).

Previously [6] compound II was assumed to have an isomeric structure with two hydroxy groups. It is difficult to judge the structure of this compound from its IR spectrum in the crystalline state. However, the IR spectrum of a dilute chloroform solution of II (figure,

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*For Part XXI see [1].

plot 1) vibrations of free hydroxyl groups were not found in the 3500–3600 cm^{-1} region, suggesting the diketo structure. The bands at 3335 and 3445 cm^{-1} are assigned to vibrations of NH groups. The bands at 1665 and 1700 cm^{-1} are ascribed to carbonyl groups. However the first of them has too low a frequency to be ascribed to the carbonyl of the chromane portion or to the carbonyl of a γ-lactam. Possibly under the given conditions compound II is in the ordinary hydrazide form IIa; here it is to be assumed that the band of frequency 3445 cm^{-1} is the sum of 2 forms of vibration. It is of interest to note that reaction of hydrazide II with benzaldehyde gives a hydrazone (III), whose IR spectrum is not in contradiction with the structure indicated above (figure, plot 2).

2-Acylaminochromones (IV–XI) were obtained from azide I by the usual methods. Investigation of the IR spectrum of compound IV (figure, plot 3) leads to the conclusion that the chromone form probably corresponds to it; at 1635 cm^{-1} very intense vibrations are exhibited, characteristic of the carbonyl of the chromone system. The intense vibrations frequency 1758 cm^{-1} is to be ascribed to a carbonyl of an ester group. In the 3100–3600 cm^{-1} region there are two bands at 3410 and 3280 cm^{-1}, evidently due to vibrations of free and linked NH groups (in the spectrum observed in oil, the relative intensity of the vibration of the linked NH group at 3150 cm^{-1} is considerably increased). At high dilution (c 0.001 M), there remains in the stated region only one peak with frequency 3415 cm^{-1}. The intense vibrations frequency 1525 cm^{-1} most of all corresponds to the secondary amide band; such vibrations are lacking with ordinary chromones. The IR spectra of compounds IV, V, and VI (oil) in the regions considered above are similar to one another, whence it is possible to make a preliminary inference that their structures are similar, and that this extends to the other 2-acylaminochromones which we have prepared. Compounds VI and XI were submitted to acid hydrolysis, and gave 4-hydroxycoumarin. Since the general opinion is that 4-hydroxycoumarin has the hydroxy-form structure, it can be concluded, that the amino group, as compared with the hydroxyl group in the second position of the chromone system, to a large extent stabilizes the γ-pyrone form.

EXPERIMENTAL*

Chromone-2-carbonyl azide (I). A. A solution of 3.24 g $NaNO_2$ in 12 ml water was added dropwise to a solution of 9.6 g (0.047 mole) compound II [6] in 290 ml 10% HCl, and 280 ml water, cooled to −10°, the whole stirred and cooled for 1 hr, then stirred for 1 hr at about 20° C. The white precipitate formed was filtered off, washed with water, and vacuum dried over P_2O_5. Yield 8.17 g (99%) compound I, mp 136–137° (decomp, ex absolute EtOH). IR spectrum (in oil), cm^{-1}: 2152 (azide group), 1710 (C=O in CON_3), 1665 (pyrone C=O). Found: C 56.00, 55.69; H 2.47, 2.61; N 19.37, 19.41%, calculated for $C_{10}H_5N_3O_3$: C 55.81; H 2.34; N 19.53%.

B. A solution of 20.9 g (0.1 mole) chromane-2-carbonyl chloride [4] in 140 ml dry dioxane was added, with ice cooling, to a solution of 7.5 g NaN_3 in 30 ml water. The mixture was stirred for 30 min with cooling, and for 1 hr at about 20°, 300 ml water added, and the precipitate of azide I filtered off. Yield 20.2 g (94%), mp 135° (decomp). The IR spectrum showed the compound to be identical with a specimen obtained by method A.

N-(Chromonoyl-2)-N'-benzalhydrazine (III). 2.04 g (0.01 mole) compound II and 1.06 g (0.01 mole) benzaldehyde in 50 ml dry toluene were boiled together for 10 hr, the water being distilled off. The precipitate was filtered off, yield of hydrazone III 2.65 g (90.7%), mp 250–251° (ex BuOH). The compound did not give any coloration with $FeCl_3$, while with 10% NaOH it gave a salt of low solubility, evidently due to the acid hydrazide hydrogen. The IR spectrum (in oil), cm^{-1}: 3220 and 3080 (linked NH group), 1695 (>N−C=O); 1645 (pyrone C=O), 1550 (secondary amide band). Found: C 69.79, 70.03; H 4.21, 4.13; N 8.78, 9.50%, calculated for $C_{17}H_{12}N_2O_3$: C 69.85; H 4.14; N 9.59%.

2-Ethoxycarbonylaminochromone (IV). 2.15 g technical azide I was refluxed for 6 hr in 50 ml absolute EtOH, the resultant solution evaporated to dryness under vacuum, to give 2.27 g colorless crystals of IV.

2-Acetylaminochromone (V). 2.15 g technical azide I was heated for 3 hr in 50 ml dry benzene, 0.6 g glacial AcOH added to the cold solution (heat evolved). After about 16 hr the precipitate formed was filtered off, yield of V 2 g.

2-Diethylaminocarbonylaminochromone (VII). 2.15 g technical azide I was heated for 3 hr in 50 ml dry benzene, the solution cool-

2-Acylaminochromones

Compound	Mp, °C (solvent for crystallizing)	Formula	Found, %			Calculated, %			Yield, %*
			C	H	N	C	H	N	
IV	183—184 (decomp EtOH)	$C_{12}H_{11}NO_4$	61.76 61.64	4.83 4 81	5.88 6.00	61.79	4.75	6.04	91.5
V	289—290 (decomp BuOH)	$C_{11}H_9NO_3$	65.25 65.41	4.58 4.53	7.04 6.95	65.02	4.47	6.89	92.5
VI	187—190 (decomp absolute EtOH)	$C_{11}H_6Cl_3NO_3$**	43.01 42.75	1.98 1.97	4.57	43.10	1.97	4.57	88.6
VII	137—137.5 (benzone)	$C_{14}H_{16}N_2O_3$	—	—	10.61 10.58	—	—	10.76	75.5
VIII	224—225 (BuOH)	$C_{16}H_{18}N_2O_3$	67.41 67.29	6.27 6.35	9.95 10.03	67.12	6.33	9.78	76.8
IX	205.5—206 (BuOH)	$C_{14}H_{14}N_2O_3$	65 24 65.53	5.20 5.50	10.89 11.10	65.09	5.46	10.85	76.4
X	175—176 (benzone)	$C_{15}H_{16}N_2O_3$	66.18 66.42	5.89 5.90	10.60 10.42	66.13	5.92	10.42	75.9
XI	171—172 (benzone)	$C_{14}H_{14}N_2O_4$	—	—	10.07 10.13	—	—	10.22	88.7

*Calculated on the acid chloride taken for preparing the azide.

**Found: Cl 34.54; 34.58%. Calculated: Cl 34.72%.

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*With the assistance of L. A. Zhmurenko

ed, and 1 g Et_2NH added. The resultant precipitate was separated off (after about 15 min), yield of **VII** 2.05 g.

Other 2-acylaminochromones were prepared by the above methods. Data for compounds **IV-XI** are given in the table.

Hydrolysis of compounds VI and XI. 1 g compound **VI** in 10 ml 10% HCl and 20 ml EtOH was refluxed for 3 hr. The next day the products were vacuum evaporated to dryness, and the residue was dissolved in a small amount of 5% $NaHCO_3$. The solution was filtered, and acidified with 10% HCl. The precipitate formed was filtered off, yield of 4-hydroxycoumarin 0.4 g (75%), mp 207-208° (ex water). Undepressed mixed mp with a known specimen. Similarly hydrolysis of **XI** gave 4-hydroxycoumarin in 54% yield.

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Institute of Pharmacology
and Chemotherapy, Academy
of Medical Sciences USSR,
Moscow