5-Benzyloxy-4-oxo-4*H*-pyran-2-carboxisopropylamide (*VIII*)

VI (0.0018 mol) was dissolved in minimum of absolute acetone. Isopropylamine (0.16 cm^3) and triethylamine (0.27 cm^3) were added. Mixture was stirred at laboratory temperature for 1 h, then mixed with excess of water and extracted with benzene. Evaporation of solvent gave solid product. Raw material was crystallized from benzene.

N-(4-Methylphenyl) amide of 5-benzyloxy-4-oxo-4*H*-pyran-2-carboxylic acid (*IX*) was prepared by analogous method.

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Synthesis and Antimycobacterial Effect of 3-Formylchromone *N*-Aroyl- or *N*-Alkylcarbonylhydrazones

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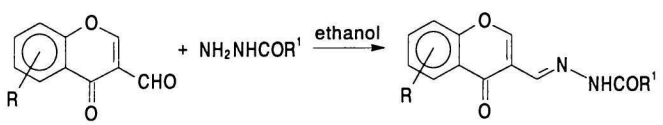
3-Formylchromone *N*-aroyl- or *N*-alkylcarbonylhydrazones were prepared by condensation reaction of 3-formylchromones with hydrazine derivatives in ethanol and toluene-*p*-sulfonic acid as catalyst. Some of the prepared compounds were tested against typical and atypical *Mycobacterium tuberculosis*.

Biological activities of chromone derivatives render them of considerable pharmaceutical and chemical interest [1]. In this work we describe the synthesis of 3-formylchromone *N*-aroylhydrazones and 3-formylchromone *N*-alkylcarbonylhydrazones because many of hydrazide derivatives are of pharmacological importance [2], and also 3-formylchromones show interesting pharmacological activities [3—5], so we were interested to synthesize some new derivatives of chromones with prediction of new pharmacological activities.

4-Oxo-4*H*-1-benzopyrans in their reactions with phenylhydrazine behave like α,β-unsaturated ketones



I *II* *III*

	R	R^1
a	H	2-OH-C_6H_4
b	H	4-C_5H_4N
c	6-CH_3	$(CH_2)_3CH_3$
d	6-CH_3	$(CH_2)_{14}CH_3$
e	6-CH_3	2-OH-C_6H_4
f	6-CH_3	3,4,5-$(OH)_3$-C_6H_2
g	6-CH_3	4-C_5H_4N
h	6-Cl	4-C_5H_4N
i	6-OH	$(CH_2)_3CH_3$
j	6-OH	$(CH_2)_{14}CH_3$
k	6-OH	2-OH-C_6H_4
l	6-OH	3,4,5-$(OH)_3$-C_6H_2
m	6-OH	4-C_5H_4N
n	7,8-$(OH)_2$	4-C_5H_4N
o	6-(n-C_6H_{13})-7-OH	4-C_5H_4N
p	7-OH	2-OH-C_6H_4

Scheme 1

and the nucleophile attacks at C-2 (Michael addition) with the opening of the pyrone ring to give pyrazole derivatives [6, 7].

In our study we found that the 3-formylchromones (*I*) were reacted with hydrazide derivatives (*II*) in ethanol and toluene-*p*-sulfonic acid as catalyst at temperature 50—60 °C to give 3-formylchromone *N*-aroyl- or *N*-alkylcarbonylhydrazones (*IIIa—IIIp*) (Scheme 1). The starting aldehydes for compounds *IIIn*, *IIIo,* and *IIIp* were prepared according to [8].

The structure of compounds *IIIa—IIIp* was confirmed by IR spectra (Table 1) and ^{1}H NMR spectra

Table 1. Characteristic Data of Compounds *III* and *IV*

Compound	Formula	w_i(calc.)/%			Yield	M. p.	IR*, $\tilde{\nu}$/cm^{-1}		
		w_i(found)/%					ν(CO) (s)	ν(CO)	ν(NH)
	M_r	C	H	N	%	°C	Pyrone	Amide	
IIIa	$C_{17}H_{12}N_2O_4$	66.23	3.92	9.09	58	222—224	1620	1653	3251
	308.29	66.35	3.95	8.96					
IIIb	$C_{16}H_{11}N_3O_3$	65.53	3.78	14.33	50	198—201	1642	1700	3200
	293.28	65.64	3.73	14.41					
IIIc	$C_{16}H_{18}N_2O_3$	67.12	6.34	9.78	61	218—220	1634	1690	3280
	286.33	67.15	6.32	9.99					
IIId	$C_{27}H_{40}N_2O_3$	73.60	9.15	6.36	45	145—147	1628	1687	3280
	440.63	73.70	8.94	5.98					
IIIe	$C_{18}H_{14}N_2O_4$	67.07	4.38	8.69	56	220—222	1618	1641	3236
	322.32	67.28	4.22	8.58					
IIIf	$C_{18}H_{14}N_2O_6$	61.02	3.98	7.91	50	215—217	1627	1647	3251
	354.32	61.09	4.03	7.74					
IIIg	$C_{17}H_{13}N_3O_3$	66.44	4.26	13.67	52	207—209	1634	1671	3184
	307.31	66.69	4.38	13.48					
*IIIh***	$C_{16}H_{10}ClN_3O_3$	58.64	3.07	12.82	56	208—210	1644	1687	3279
	327.73	58.38	3.16	12.94					
IIIi	$C_{15}H_{16}N_2O_4$	62.49	5.59	9.72	61	223—225	1620	1664	3213
	288.30	62.53	5.69	9.89					
IIIj	$C_{26}H_{38}N_2O_4$	70.56	8.65	6.33	46	199—201	1621	1665	3221
	442.60	70.42	8.86	6.15					
IIIk	$C_{17}H_{12}N_2O_5$	62.96	3.73	8.64	50	240—242	1617	1649	3153
	324.29	62.98	3.73	8.24					
IIIl	$C_{17}H_{12}N_2O_7$	57.31	3.39	7.86	49	239—240	1629	1645	3144
	356.29	57.54	3.48	8.14					
IIIm	$C_{16}H_{11}N_3O_4$	62.14	3.58	13.58	50	250—252	1625	1694	3267
	309.28	61.80	3.58	13.12					
IIIn	$C_{16}H_{11}N_3O_5$	59.08	3.39	12.92	64	254—255	1615	1690	3260
	325.3	58.84	3.40	12.68					
IIIo	$C_{22}H_{23}N_3O_4$	67.20	5.85	10.69	71	231—233	1618	1688	3156
	393.3	66.90	5.77	10.36					
IIIp	$C_{17}H_{12}N_2O_5$	62.96	3.70	8.64	62	262—263	1612	1649	3150
	324.3	62.63	3.71	8.39					3065
IVa	$C_{11}H_{10}N_2O_3$	60.55	4.58	12.84	73	279—281	–	–	–
	218.1	60.28	4.56	12.72					
*IVb****	$C_{10}H_8N_2O_4$	54.55	3.63	12.72	68	304—306	–	–	–
	220.18	54.20	3.67	12.42					

*In paraffin oil. **% Cl w_i(calc.), w_i(found): 10.82, 10.87. ***IR for *IVb* $\tilde{\nu}$/cm^{-1}: 3332 (br), 3465 (br) ν(OH); 1610, 1615 ν(C=N).

Table 2. ^{1}H NMR spectra of Compounds *IIIe*, *IIIg*, *IIIh*, *IVa*, and *IVb*

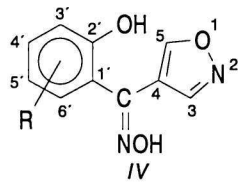
Compound	δ
IIIe	11.96 (s, 1H, NH), 8.80 (s, 1H, H-2), 8.63 (s, 1H, H-9), 6.92—8.06 (m, 7H, H_{arom}), 2.45 (s, 3H, CH_3)
IIIg	12.11 (s, 1H, NH), 8.65—8.82 (m, 4H, H-2, H-9, H-15), 7.64—7.91 (m, 5H, H_{arom}), 2.45 (s, 3H, CH_3)
IIIh	12.15 (s, 1H, NH), 8.74—8.89 (m, 4H, H-2, H-9, H-15), 7.84—8.06 (m, 5H, H_{arom})
IVa	10.4 (br, 1H, OH-2′), 9.64 (s, 1H, H-5), 9.02 (br, 1H, NOH), 7.79 (d, 1H, H-6′), 7.49 (dd, 1H, H-4′, $J_{6',4'}$ = 2.1 Hz, $J_{4',5'}$ = 8.4 Hz), 7.37 (s, 1H, H-3), 7.29 (d, 1H, H-3′), 2.40 (s, 3H, CH_3)
IVb	10.48 (br, 1H, OH-2′), 9.89 (br, 1H, OH-5′), 9.65 (s, 1H, H-5), 8.92 (br, 1H, NOH), 7.36 (s, 1H, H-3), 7.33 (d, 1H, H-6′), 7.27 (d, 1H, H-3′), 7.09 (dd, H-4′, $J_{6',4'}$ = 3.0 Hz, $J_{4',3'}$ = 7.9 Hz)

Compounds *IIIe*, *IIIg*, *IIIh* were measured on Tesla BS 487 A instrument (80 Hz) in DMSO. Compounds *IVa*, *IVb* were measured on Varian VXR-300 apparatus in DMSO.

(Table 2). The IR spectra of *N*-(2-hydroxybenzoyl)-hydrazones (*IIIa*, *IIIe*, *IIIk*, *IIIp*) indicated strong band at $\tilde{\nu}$ = 1617—1620 cm^{-1} for carbonyl group of pyrone, band at $\tilde{\nu}$ = 1641—1653 cm^{-1} of ν(CO) amide and broad band centred at $\tilde{\nu}$ = 3153—3251 cm^{-1} of ν(NH) and ν(OH) groups. The other derivatives of *III* possess the similar IR values.

The ^{1}H NMR spectra of *N*-(2-hydroxybenzoyl)-hydrazone (*IIIe*) showed a singlet signal at δ = 8.80 of H-2 and a singlet signal at δ = 8.63 of H-9. Also the ^{1}H NMR spectra of hydrazones *IIIg*, *IIIh* showed multiplet signals at δ = 8.65—8.89 of H-2, H-9, and H-15.

In our study we found that the reaction between equimolar quantities of hydrazones *IIIg* or *IIIm* and hydroxyammonium chloride in pyridine gave derivatives of isoxazole *IVa* and *IVb* after removal of the hydrazide group (Formula 1).



IV

a R = CH_3-5′
b R = OH-5′

Formula 1

The structure of prepared isoxazole derivatives was confirmed by ^{1}H NMR spectra (Table 2).

Some derivatives of the prepared compounds were tested against *Mycobacterium tuberculosis* ($H_{37}R_V$), *Mycobacterium kansasii* (PKG_8), *Mycobacterium avium* (80/72), and *Mycobacterium fortuitum* (1021).

In the test we used six compounds (*IIIb*, *IIIf*, *IIIg*, *IIIi*, *IIII*, *IIIm*) at concentrations ρ/(μg cm^{-3}) 1, 10, 25, 50, and 100 using Isoniazid as compared sample. The results of the test on typical and atypical mycobacteria showed that the *N*-(4-pyridinecarbonyl)-hydrazone derivatives *IIIb*, *IIIg*, *IIIm* exhibit activity against typical *Mycobacterium* ($H_{37}R_V$) as Isoniazid and the other derivatives *IIIf*, *IIIi*, *IIII* are inactive.

EXPERIMENTAL

The IR spectra were measured on a Specord 75 IR (Zeiss, Jena) apparatus in the region $\tilde{\nu}$ = 400—4000 cm^{-1} using suspension in paraffin oil. Instruments for measurements of ^{1}H NMR spectra are given in Table 2.

The experimental method for testing on typical and atypical mycobacteria was used according to the published method [9].

3-Formylchromone *N*-Aroyl- or *N*-Alkylcarbonylhydrazones *IIIa—IIIp*

To solutions of 3-formylchromones (0.01 mol) in least amount of ethanol, solution of hydrazide derivatives (0.01 mol) in least amount of ethanol and one crystal of toluene-*p*-sulfonic acid were added. The mixture was stirred at temperature 50—60 °C for 30 min, filtered off, and the solid produced was boiled in ethanol, filtered off on hot to give *IIIa—IIIp* (Tables 1 and 2).

4-[(2-Hydroxyaryl)hydroxyiminomethyl]-isoxazoles (*IVa*, *IVb*)

A mixture of *IIIg*, *IIIf* or *IIIk* (0.022 mol) in pyridine (3 cm^3) and hydroxylammonium chloride (0.15 g; 0.22 mol) in water (1 cm^3) was refluxed for 4 h. The cooled mixture was poured over crushed ice and acidified with acetic acid and the solid that separated, was filtered off and recrystallized from cyclohexane or dioxane.

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Preparation and Pesticide Properties of Some 1-Substituted (1*H*)-1,2,4-Triazoles

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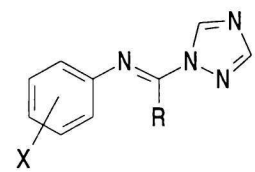
The preparation, infrared and ^{1}H NMR spectra of five types of substituted 1-imidoyl-(1*H*)-1,2,4-triazoles are described. Herbicidal, fungicidal, and growth-regulating properties, tested on selected plants, are given.

So far, numerous pesticidally active compounds possessing the 1-substituted (1*H*)-1,2,4-triazole ring system have been prepared, and commercialized [1]. Triazoles with an imidoyl moiety have recently been added to this family of compounds (Formulas 1 and 2). Some diarylformamidinoyltriazoles [2] have been found to possess good fungicidal and nematocidal activity (type *II,* Formula 1), structures containing sulfonamide group were good herbicides [3], *S*-benzoylthiourea-substituted derivatives (type *V*, Formula 2) displayed bactericidal and fungicidal properties [4].

In our effort to enlarge the family of 1-substituted (1*H*)-1,2,4-triazoles we described the synthesis and biological properties of some azolylquinazolines [5], in which the imidoyl moiety was built in the pyrimidine ring. Now we describe another five types of imidoyltriazoles, namely four *N*-phenylbenzimidoyltriazoles *Ia—Id,* nine *N*-phenylformamidinoyltriazoles *IIa—IIi,* and four bis-triazolyl derivatives, formally guanidines *IIIa—IIId*. Compounds *IVa, IVb* are derivatives of *O*-methylthiourea, *Va, Vb* can be classified as *N*-phenylhydroxamoyltriazoles.



	R	Z	X
Ia	C_6H_4-Z	H	H
Ib	C_6H_4-Z	H	4-Cl
Ic	C_6H_4-Z	3,4-di-Cl	4-Cl
Id	C_6H_4-Z	H	2-CH_3
IIa	morpholinyl		H
IIb	morpholinyl		4-Cl
IIc	piperidinyl		4-Cl
IId	diethylamino		4-Cl
IIe	piperidinyl		2,4-di-Cl
IIf	morpholinyl		2,3,4,5,6-penta-Cl
IIg	morpholinyl		4-Br
IIh	piperidinyl		4-Br
IIi	diethylamino		4-Br
IIIa	1,2,4-triazol-1-yl		4-Cl
IIIb	1,2,4-triazol-1-yl		2,4-di-Cl
IIIc	1,2,4-triazol-1-yl		2,3,4,5,6-penta-Cl
IIId	1,2,4-triazol-1-yl		4-Br
IVa	OCH_3		4-Cl
IVb	OCH_3		4-Br

Formula 1