

Synthesis, spectral properties, and IHR of 2,4,5-trisubstituted 3-oxo-2H-pyridazines

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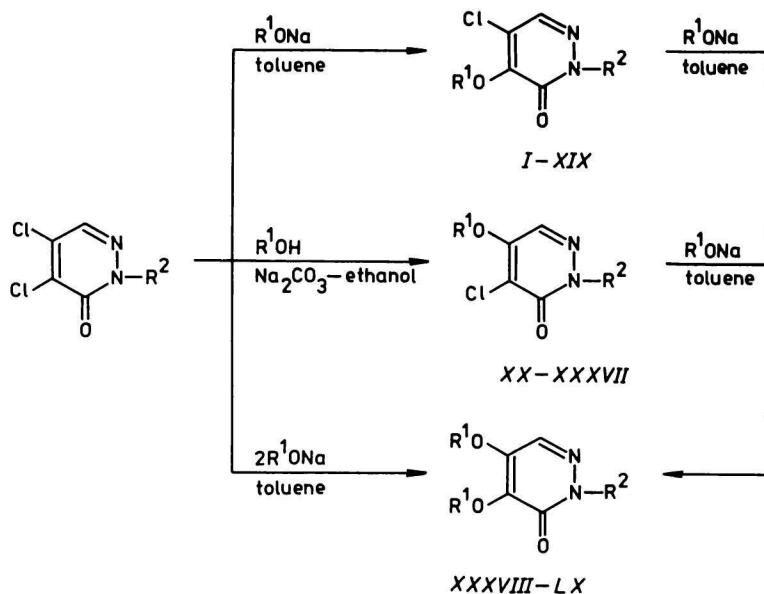
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The synthesis of 2-R²-4-alkoxy-5-chloro-, 2-R²-5-alkoxy-4-chloro-, and 2-R²-4,5-dialkoxy-3-oxo-2H-pyridazines by the reaction of 2-R²-4,5-dichloro- or 2-R²-4-chloro-5-alkoxy or 2-R²-5-alkoxy-4-chloro-3-oxo-2H-pyridazines with sodium alcoholate or alcohol in the presence of alkaline carbonate in aprotic or protic solvent is described. Infrared and ultraviolet spectra of the prepared compounds are interpreted. Prepared compounds were tested for fungicidal and herbicidal activity. In fungicidal activity none of the prepared compounds reached the activity of the standard Vitavax, in the inhibiting of the Hill reaction 2-cyclohexyl-4-methoxy-5-chloro-2-(3'-methylphenyl)-4-methoxy-5-chloro-, 2-(3'-chlorophenyl)-4-methoxy-5-chloro-, 2-cyclohexyl-4-chloro-5-methoxy-, 2-phenyl-4-chloro-5-methoxy-, 2-(3'-chlorophenyl)-4-chloro-5-methoxy-, 2-phenyl-4,5-dimethoxy-, 2-(3'-trifluoromethylphenyl)-4,5-dimethoxy-3-oxo-2H-pyridazines reached or surpassed the activity of the standard Pyrazon.

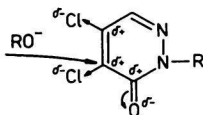
Описаны синтезы 2-R²-4-алкокси-5-хлор-, 2-R²-5-алкокси-4-хлор- и 2-R²-4,5-диалкокси-3-оксо-2H-пиридазинов посредством реакции 2-R²-4,5-дихлор- или 2-R²-4-хлор-5-алкокси- или 2-R²-5-алкокси-4-хлор-3-оксо-2H-пиридазинов с натриевым алкоголятом или спиртом в присутствии карбоната щелочного металла в апротонном или протонном растворителе. Исследованы инфракрасные и ультрафиолетовые спектры поглощения полученных соединений. У полученных соединений были проверены их фунгицидная и гербицидная активности. По фунгицидной активности ни одно из полученных соединений не достигало активности стандарта Витавакс, а по подавлению реакции Хилла 2-циклогексил-4-метокси-5-хлор-, 2-(3'-метилфенил)-4-метокси-5-хлор-, 2-(3'-хлорфенил)-4-метокси-5-хлор-, 2-циклогексил-4-хлор-5-метокси-, 2-фенил-4-хлор-5-метокси-, 2-(3'-хлорфенил)-4-хлор-5-метокси-, 2-фенил-4,5-диметокси-, 2-(3'-трифторметилфенил)-4,5-диметокси-3-оксо-2H-пиридазины достигали или превосходили активность стандарта Пиразон.

From 2,4,5-trisubstituted 3-oxo-2*H*-pyridazines only 2-phenyl-4-chloro-5-amino-3-oxo-2*H*-pyridazine (Pyrazon) found a practical use as a herbicide applied by cultivating the sugar beet [1]. The goal of this work was a synthesis of 2,4,5-trisubstituted 3-oxo-2*H*-pyridazines by the nucleophilic reactions of 2-substituted 4,5-dichloro-3-oxo-2*H*-pyridazines with alcohols or alkaline alkoxides in aprotic or protic solvents (Scheme 1).



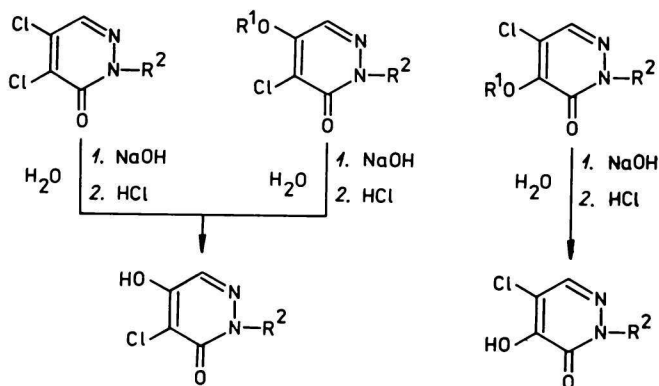
Scheme 1

Infrared and ultraviolet spectra of the prepared compounds were studied. Fungicidal activity and the activity on the Hill reaction in comparison with the Pyrazon standard were determined. Herbicidal activity with compounds showing high activity on the Hill reaction was determined under greenhouse conditions. In the nucleophilic substitution reaction of 2-substituted 4,5-dichloro-3-oxo-2*H*-pyridazine with alkaline alkoxide in aprotic solvents (toluene, xylene) the carbon atom in the position 4 was found more reactive due to the electron-withdrawing effect of the chlorine atoms and of the carbonyl group.



It was observed that besides 2-substituted 4-alkoxy-5-chloro-3-oxo-2*H*-pyridazines (Table 1) also 2-substituted 4-chloro-5-alkoxy-3-oxo-2*H*-pyridazines in yields up to 10 % are formed. These compounds were isolated by column chromatography. The structure of the prepared 2-substituted 4-alkoxy-5-chloro-3-oxo-2*H*-pyridazines (compounds *I*—*XIX*) was proved by spectral methods.

Infrared spectra of the prepared compounds showed the $\nu(\text{C}=\text{O})$ intense bands in the region of $\tilde{\nu} = 1654\text{—}1674\text{ cm}^{-1}$, the wavenumber of which being influenced mainly by the nature of the substituent R^2 . A significantly higher wavenumber of the $\nu(\text{C}=\text{O})$ bands in the spectra of compounds containing the phenyl group attached to the nitrogen atom in the position 2 of the pyridazine ring is caused by the mesomeric interaction of the aromatic ring with the carbonyl group. The structure of 2- R^2 -4-alkoxy-5-chloro-3-oxo-2*H*-pyridazines was proved by the fact that these compounds (e.g. *VII*, *IX*, *XV*) afforded in aqueous-alkaline medium corresponding 2- R^2 -4-hydroxy-5-chloro-3-oxo-2*H*-pyridazines (e.g. *LXI*, *LXII*, *LXIII* (Scheme 2)) in which the hydroxyl group is involved in strong intramolecu-



Scheme 2

lar hydrogen bonding with the carbonyl group of the pyridazine ring. In the infrared spectra of these compounds the $\nu(\text{O—H})$ bands are observed in the region of $\tilde{\nu} = 3370\text{—}3380\text{ cm}^{-1}$ [2].

In the ultraviolet spectra of compounds *I*—*XIX* (Table 4) two absorption bands in the region 212—216 nm and 290—320 nm are observed. The spectra of compounds containing the phenyl group in position 2 of the pyridazine ring showed a more significant bathochromic shift of the wavelength maximum.

In the tests on the Hill reaction compounds *VII*—*IX* reached equal or higher activity and compounds *XIII*, *XVII*, and *XVIII* a somewhat lower activity than the used standard Pyrazon. Compounds *VII*—*IX* were tested on herbicidal activity

Table 1

Characterization of the prepared 2-R²-4-alkoxy-5-chloro-3-oxo-2H-pyridazines

Compound	R ¹	R ²	w _i (calc.)/%		Yield	M.p./°C B.p./°C (p/Pa)	$\tilde{\nu}$ /cm ⁻¹ ν (C=O)	λ_{\max} /nm		IHR
			w _i (found)/%					%	log (ε/(dm ³ mol ⁻¹ cm ⁻¹))	
			N	Cl						
I	CH ₃	CH ₃	16.0	20.3	90	88—89	1660	214	290	0.0005
			16.2	20.4				4.34	4.05	
II	CH ₃	C ₃ H ₇	13.8	17.5	71	69(14)	1659	216	293	0.01
			13.9	17.6				4.44	3.89	
III	CH ₃	CH ₂ =CH—CH ₂	13.9	17.6	82	77(14)	1659	216	292	0.01
			14.1	17.8				4.39	3.90	
IV	CH ₃	C ₂ H ₅ OCH ₂	12.8	16.2	79	100—102	1662	215	298	0.05
			12.9	16.1				4.21	3.91	
V ^{a,d}	CH ₃	C ₂ H ₅ SCH ₂	11.9	15.1	43	92—93	1665	214	300	0.05
			11.8	15.0				4.06	3.95	
VI	CH ₃	C ₆ H ₁₁ (cyclo)	11.5	14.6	84	112(14)	1654	216	292	0.05
			11.7	14.5				4.42	3.90	
VII ^e	CH ₃	C ₆ H ₅	11.8	15.0	91	100—102	1672	215	306	1
			11.9	15.2				4.40	3.81	
VIII	CH ₃	3-CH ₃ —C ₆ H ₄	10.0	12.7	80	112—114	1673	212	301	1
			10.2	12.9				4.46	3.92	
IX	CH ₃	3-Cl—C ₆ H ₄	10.3	26.2	71	148—149	1674	212	301	1—5
			10.1	26.5				4.42	3.81	
X ^b	CH ₃	3-CF ₃ —C ₆ H ₄	9.2	11.6	84	68—69	1673	215	303	0.01
			9.4	11.8				4.26	3.79	
XI ^f	CH ₃	4-NO ₂ —C ₆ H ₄	14.9	12.6	68	205—208	1700	216	320	0.01
			15.1	12.8				4.43	4.05	
XII ^{c,g}	CH ₃	3-CF ₃ —4-Cl—C ₆ H ₃	8.4	21.3	76	126—127	1670	212	306	0.0005
			8.6	20.9				4.45	3.93	

Table 1 (Continued)

Compound	R ¹	R ²	w _i (calc.)/% w _i (found)/%		Yield %	M.p./°C B.p./°C (p/Pa)	$\tilde{\nu}$ /cm ⁻¹ ν (C=O)	λ_{\max} /nm log (ϵ /(dm ³ mol ⁻¹ cm ⁻¹))		IHR
			N	Cl						
			XIII	CH ₃				C ₆ H ₅ CH ₂	11.2 11.4	
XIV	C ₂ H ₅	CH ₃	14.9 15.1	18.8 19.0	92	30—32	1660	216 4.54	290 3.84	0.001
XV	C ₃ H ₇	CH ₃	13.8 14.0	17.5 17.4	85	80(14)	1663	216 4.44	290 3.77	0.005
XVI ⁱ	(CH ₃) ₂ CH	CH ₃	13.8 13.9	17.5 17.8	66	68(7)	1663	212 4.44	295 3.87	0.05
XVII ^h	C ₂ H ₅	C ₆ H ₅	11.1 11.3	14.1 14.0	89	74—76	1669	212 4.41	305 3.84	0.5
XVIII	C ₃ H ₇	C ₆ H ₅	10.6 10.8	13.4 13.6	80	132(14)	1668	213 4.51	305 3.96	0.1
XIX	(CH ₃) ₂ CH	C ₆ H ₅	10.6 10.7	13.4 13.5	71	128(14)	1672	216 4.45	304 3.76	0.0005

w_i(calc.)/%
w_i(found)/%

a)	S	b)	F	c)	F
	13.6		18.7		15.3
	13.9		19.0		15.5

λ_{\max} /nm(log (ϵ /(dm³ mol⁻¹ cm⁻¹))): d) 244(4.25); e) 268(3.73); f) 245(4.00), 270(4.03); g) 230(4.22), 270(3.84); h) 270(3.69); i) 270(3.76).
IHR — inhibition of the Hill reaction, the standard Pyrazon (PCA)=1.

Table 2

Characterization of the prepared 2-R²-4-chloro-5-alkoxy-3-oxo-2H-pyridazines

Compound	R ¹	R ²	w _i (calc.)/% w _i (found)/%		Yield %	M.p./°C	$\bar{\nu}/\text{cm}^{-1}$ $\nu(\text{C}=\text{O})$	$\lambda_{\text{max}}/\text{nm}$			IHR
			N	Cl				$\log(\epsilon/(\text{dm}^3 \text{mol}^{-1} \text{cm}^{-1}))$			
XX	CH ₃	CH ₃	16.0	20.3	89	154—155	1673	215	262	293	0.005
			16.1	20.3				4.41	3.66	3.65	
XXI	CH ₃	C ₃ H ₇	13.8	17.5	88	43—45	1663	216	262	295	0.1
			13.7	17.7				4.44	3.66	3.66	
XXII	CH ₃	CH ₂ =CH—CH ₂	13.9	17.6	73	65—66	1663	216	263	293	0.05
			14.1	17.8				4.41	3.67	3.68	
XXIII ^a	CH ₃	C ₂ H ₅ SCH ₂	11.9	15.1	62	70—71	1669	238	—	299	0.01
			11.8	14.9				4.19	—	3.99	
XXIV	CH ₃	C ₆ H ₁₁ (cyclo)	11.5	14.6	85	117—118	1657	217	262	296	5—10
			11.6	14.7				4.40	3.67	3.69	
XXV	CH ₃	C ₆ H ₅	11.8	15.0	90	154—156	1675	214	270	303	1
			11.7	15.1				4.38	3.82	3.74	
XXVI	CH ₃	3-CH ₃ —C ₆ H ₄	10.0	12.7	81	146—147	1677	213	270	302	1—5
			10.1	12.8				4.49	3.84	3.76	
XXVII	CH ₃	3-Cl—C ₆ H ₄	10.3	26.2	88	199—200	1676	215	270	303	1—5
			10.2	26.7				4.48	3.87	3.79	
XXVIII ^b	CH ₃	3-CF ₃ —C ₆ H ₄	9.2	11.6	89	146—148	1677	216	270	300	0.5
			9.3	11.8				4.38	3.86	3.73	
XXIX ^d	CH ₃	4-NO ₂ —C ₆ H ₄	14.9	12.6	86	226—228	1658	216	284	312	0.0005
			14.7	12.4				4.44	4.14	4.04	
XXX ^c	CH ₃	3-CF ₃ —4-Cl—C ₆ H ₃	8.4	21.3	86	146—147	1669	213	273	302	0.01
			8.2	20.9				4.39	3.96	3.82	
XXXI	CH ₃	C ₆ H ₅ CH ₂	11.2	14.1	87	98—99	1660	216	263	294	0.1
			11.2	14.2				4.42	3.96	3.64	

Table 2 (Continued)

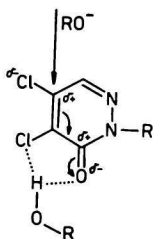
Compound	R ¹	R ²	w _i (calc.)/%		Yield	M.p./°C	$\bar{\nu}/\text{cm}^{-1}$ $\nu(\text{C}=\text{O})$	$\lambda_{\text{max}}/\text{nm}$			IHR
			w _i (found)/%					log ($\epsilon/(\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1})$)			
			N	Cl	%						
XXXII	C ₂ H ₅	CH ₃	14.9	18.8	78	105—107	1664	215	262	292	0.005
			14.8	18.9				4.39	3.64	3.63	
XXXIII	C ₃ H ₇	CH ₃	13.8	17.5	68	88—89	1657	216	262	292	0.01
			13.9	17.7				4.42	3.66	3.60	
XXXIV	(CH ₃) ₂ CH	CH ₃	13.8	17.5	59	111—113	1656	216	263	292	0.005
			14.0	17.8				4.42	3.65	3.63	
XXXV	C ₂ H ₅	C ₆ H ₅	11.1	14.1	96	140—141	1677	216	271	302	0.1
			11.4	14.3				4.41	3.85	3.74	
XXXVI	C ₃ H ₇	C ₆ H ₅	10.6	13.4	81	121—122	1676	215	271	302	0.05
			10.7	13.5				4.40	3.85	3.74	
XXXVII	(CH ₃) ₂ CH	C ₆ H ₅	10.6	13.4	74	119—121	1677	215	271	301	0.01
			10.8	13.6				4.40	3.76	3.70	

w_i(calc.)/%
w_i(found)/%

a)	S	b)	F	c)	F
	13.6		18.7		15.3
	13.8		18.9		15.4

d) IR spectra recorded in KBr; $\bar{\nu}/\text{cm}^{-1}$: 1351 $\nu_s(\text{NO}_2)$; 1520 $\nu_{\text{as}}(\text{NO}_2)$.

under greenhouse conditions. Nucleophilic substitution reactions proceed in protic solvent (alcohol, water) at the carbon atom in position 5 of the pyridazine ring (Table 2). This can be explained by the fact that the hydrogen of the protic solvent is involved in hydrogen bonding with oxygen of the carbonyl group and chlorine by which the interaction of π -electrons of the pyridazine ring with π -electrons of the carbonyl group is higher resulting in lowering of the electron density on the carbon atom in position 5 of the pyridazine ring.



Nucleophilic substitution reactions of 2-substituted 4,5-dichloro-3-oxo-2H-pyridazines were carried out:

- a) in alcohol medium in the presence of sodium or potassium alcoholate,
- b) in alcohol medium in the presence of sodium or potassium carbonate.

According to the (a) in dependence on the amount of sodium or potassium alcoholate an undesirable 2-substituted 4-chloro-5-hydroxy-3-oxo-2H-pyridazine is formed which is in the case of (b) not possible. With both procedures the formation of 2-substituted 4-alkoxy-5-chloro-3-oxo-2H-pyridazines was not observed.

In infrared spectra of the compounds XX—XXXVII the $\nu(\text{C}=\text{O})$ bands are observed in the region of $\tilde{\nu} = 1654\text{--}1677\text{ cm}^{-1}$. The wavenumber of these bands is higher than that of the $\nu(\text{C}=\text{O})$ bands of compounds I—XIX, which is evidently caused by the larger distance of the chlorine atom from the carbonyl group. The structure of 2-R²-4-chloro-5-hydroxy-3-oxo-2H-pyridazines was established by the fact that these compounds (e.g. XXI, XXVI, XXXV) in the aqueous-alkaline medium afforded corresponding 2-R²-4-chloro-5-hydroxy-3-oxo-2H-pyridazines (e.g. LXIV—LXVI), the hydroxyl group of which is involved in a weak intramolecular hydrogen bonding with the chlorine in position 4 of the pyridazine ring, $\nu(\text{OH})$ at $\tilde{\nu} = 3510\text{--}3520\text{ cm}^{-1}$ [2] (Scheme 2).

In ultraviolet spectra of the compounds prepared, excepting compound XXIII, three absorption bands are observed in the region of 213—217 nm, 262—284 nm, and 292—312 nm. Similarly as in the spectra of compounds I—XIX, compounds XX—XXXVII containing the phenyl group in the position 2 of the pyridazine ring absorb at the longest wavelengths.

In the test on the Hill reaction compounds XXIV—XXVII were equally or higher active as the used standard and therefore were an object of further study

— a testing under greenhouse conditions. A significantly lower activity showed the compounds *XXI*, *XXVIII*, *XXXI*, and *XXXV*. By the nucleophilic substitution of 2-substituted 4,5-dichloro-3-oxo-2*H*-pyridazines with sodium alkoxides in toluene 2-substituted 4,5-dialkoxy-3-oxo-2*H*-pyridazines were prepared (Table 3).

In the infrared spectra of compounds *XXXVIII*—*LX* the $\nu(\text{C}=\text{O})$ bands are at lower wavenumbers than in those of compounds containing chlorine in position 4 or 5 of the pyridazine ring. In ultraviolet spectra two bands are observed in the regions of 214—220 nm and 270—290 nm. These compounds absorb at shorter wavelengths than the compounds containing chlorine (compounds *I*—*XXXVII*), which is due to the effects of alkoxy groups lessening the conjugation.

In this group of compounds only *XLV* and *XLVI* reached in the Hill reaction test the level of activity of the standard Pyrazon. A remarkable activity was also observed with compounds *XXXIX*—*XLIII* and *XLIV*. In further stage of the research under greenhouse conditions compounds *XLV* and *XLVI* were included.

On the basis of the results obtained in the tests on the Hill reaction, compounds *VII*—*IX*, *XXIV*—*XXVII*, *XLV*, and *XLVI* were included in the study of the herbicidal activity under greenhouse conditions. Obtained results are summarized in Table 4. Tested compounds were treated as 50 % wettable powders and treatment of specimens on suspendability and sedimentation satisfied the condition ON 655711. Thus the differences in solubility were removed and the equal application conditions were achieved.

A remarkable herbicidal activity was found with compounds *XXIV*—*XXVII*, *XLV*, and *XLVI*, where *XLV* was the most active on *Avena fatua*, *XLV* and *XLVI* on *Echinochloa cruss-galli*, *XLV* on *Panicum miliaceum*, *XXVI* and *XLVI* on *Fagopyrum vulgare*, *XLV* and *XLVI* on *Sinapis alba*, *XXVI*, *XLV*, and *XLVI* on *Lepidium sativum*. Although the above-mentioned compounds showed high herbicidal activity, their principal drawback as compared with the used standard Pyrazon was that they attacked sugar beet as well.

From the results it unambiguously appeared that no direct dependence existed between the Hill reaction and herbicidal activities, many compounds were strong inhibitors of the photosynthesis only on the isolated chloroplasts level.

Experimental

Infrared spectra of the prepared compounds were recorded with an IR Specord 75 (Zeiss, Jena) instrument. The wavenumber calibration was checked against the spectrum of polystyrene. The spectra were recorded in tetrachloromethane and in trichloromethane ($c \approx 10^{-2}$ mol dm⁻³, cell thickness 0.1 mm). Ultraviolet spectra were recorded using Unicam SP 8000 instrument in methanol ($c = 2 \times 10^{-5}$ — 5×10^{-5} mol dm⁻³, cell thickness 1 cm).

Column chromatography was carried out on SiO₂ 100/160 mesh (Lachema, Brno) using toluene with the addition of acetone ($\varphi = 0$ —10 vol. %) as eluent agent. Silicagel was activated for 4 h at 140 °C before use.

Table 3

Characterization of the prepared 2-R²-4,5-dialkoxy-3-oxo-2H-pyridazines

Compound	R ¹	R ²	w _i (calc.)/% w _i (found)/%			Yield %	M.p./°C B.p./°C (p/Pa)	$\bar{\nu}/\text{cm}^{-1}$ $\nu(\text{C}=\text{O})$	$\lambda_{\text{max}}/\text{nm}$ $\log(\epsilon/(\text{dm}^3 \text{mol}^{-1} \text{cm}^{-1}))$		IHR
			C	H	N						
XXXVIII	CH ₃	CH ₃	49.4	5.9	16.5	85	59—60	1646	214	287	0.01
			49.6	6.0	16.4				4.46	4.01	
XXXIX	CH ₃	C ₂ H ₅	52.2	6.6	15.2	86	96(34)	1645	215	287	0.1
			52.3	6.5	15.4				4.37	3.63	
XL	CH ₃	(CH ₃) ₂ CH	54.5	7.1	14.1	76	98(27)	1646	215	288	0.1
			54.4	7.2	14.3				4.41	3.68	
XLI	CH ₃	C ₄ H ₉	56.6	7.6	13.2	71	108(40)	1645	216	288	0.5
			56.8	7.8	13.1				4.38	3.66	
XLII	CH ₃	C ₅ H ₁₁	58.4	8.0	12.4	50	106(27)	1644	215	288	0.5
			58.6	8.1	12.7				4.34	3.63	
XLIII	CH ₃	C ₆ H ₁₃	60.0	8.4	11.7	69	104(14)	1648	216	289	0.5
			60.3	8.5	11.9				4.37	3.72	
XLIV	CH ₃	C ₆ H ₁₁ (cyclo)	60.5	7.6	11.8	74	60—61	1646	216	288	0.001
			60.7	7.7	11.9				4.43	3.71	
XLV	CH ₃	C ₆ H ₅	62.1	5.2	12.1	96	141—142	1661	214	283	0.5—1
			62.3	5.4	12.3				4.35	3.74	
XLVI	CH ₃	3-CF ₃ -C ₆ H ₄	52.0	3.7	9.3	76	79—80	1665	217	284	1—5
			52.2	3.8	9.5				4.31	3.76	
XLVII	CH ₃	C ₆ H ₅ CH ₂	63.4	4.6	11.4	88	69—71	1648	216	290	0.1
			63.7	4.5	11.5				4.45	3.70	
XLVIII	C ₂ H ₅	CH ₃	54.5	7.1	14.1	67	93(27)	1650	215	288	0.001
			54.7	7.3	14.3				4.44	3.70	
XLIX	C ₂ H ₅	C ₄ H ₉	60.0	8.4	11.7	53	100(14)	1643	216	288	0.001
			60.3	8.5	11.9				4.41	3.70	

Table 3 (Continued)

Compound	R ¹	R ²	w _i (calc.)/% w _i (found)/%			Yield %	M.p./°C B.p./°C (p/Pa)	$\bar{\nu}$ /cm ⁻¹ ν (C=O)	λ_{\max} /nm log (ε/(dm ³ mol ⁻¹ cm ⁻¹))		IHR
			C	H	N						
L	C ₂ H ₅	C ₅ H ₁₁	61.4	8.3	11.0	57	109(14)	1644	216	288	0.00I
			61.5	8.5	11.2				4.43	3.70	
LI	C ₂ H ₅	C ₆ H ₁₃	62.6	9.0	10.4	58	112(14)	1643	216	289	0.01
			62.8	9.2	10.6				4.46	3.68	
LII	C ₂ H ₅	C ₆ H ₅	64.6	6.2	10.8	78	70—72	1661	217	278	0
			64.7	6.1	10.9				4.41	3.87	
LIII	C ₃ H ₇	CH ₃	58.4	8.0	12.4	77	92(14)	1648	216	288	0
			58.6	8.1	12.6				4.35	3.65	
LIV	C ₃ H ₇	C ₆ H ₅	66.6	7.0	9.7	78	143(27)	1664	218	294	0
			66.8	7.2	9.8				4.34	3.81	
LV	(CH ₃) ₂ CH	CH ₃	58.4	8.0	12.4	64	96(27)	1645	216	289	0
			58.3	8.3	12.5				4.38	3.70	
LVI	(CH ₃) ₂ CH	C ₄ H ₆	62.7	9.0	10.4	47	112(27)	1646	216	290	0
			62.9	9.2	10.3				4.37	3.72	
LVII	(CH ₃) ₂ CH	C ₆ H ₅	66.6	7.0	9.7	74	140(13)	1665	217	296	0
			66.9	7.1	9.9				4.28	3.66	
LVIII	C ₆ H ₅	C ₆ H ₅	74.1	4.5	7.9	68	124—126	1678	213	282	0.001
			74.4	4.4	8.1				4.49	3.96	
LIX	C ₆ H ₅ O(CH ₂) ₂	C ₆ H ₅	70.3	5.4	6.3	64	90—92	1648	220	270	0
			70.6	5.6	6.4				4.60	4.01	
LX	(CH ₃) ₂ C=N	C ₆ H ₅	61.1	5.7	17.8	71	138—140	1679	225	273	0.1—0.05
			61.4	5.9	17.9				4.59	4.04	

Table 4

Herbicidal activity of some compounds prepared

Testing object	Dose kg ha ⁻¹	Degree of herbicidal activity*																			
		preem. apl.								postem. apl.											
		VII	VIII	IX	XXIV	XXV	XXVI	XXVII	XLV	XLVI	Py ^a	VII	VIII	IX	XXIV	XXV	XXVI	XXVII	XLV	XLVI	Py ^a
<i>Avena fatua</i>	5	3	1	1	5	5	5	4	5	5	5	2	0	0	5	4	2	0	5	5	5
	1.58	1	0	0	5	5	4	1	5	5	5	0	0	0	4	3	1	0	4	4	4
	0.5	0	0	0	2	1	1	0	5	1	4	0	0	0	1	0	0	0	1	1	0
	0.158	0	0	0	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0
<i>Echinochloa crus-galli</i>	5	2	0	0	5	5	5	1	5	5	5	1	0	0	5	3	1	0	5	5	4
	1.58	0	0	0	4	4	2	0	5	5	5	0	0	0	2	1	0	0	1	5	1
	0.5	0	0	0	0	0	0	0	5	5	1	0	0	0	0	0	0	0	0	1	0
	0.158	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
<i>Panicum miliaceum</i>	5	1	0	1	5	5	5	1	5	5	5	1	0	0	5	2	1	0	5	5	1
	1.58	0	0	0	2	5	2	0	5	5	4	0	0	0	5	0	0	0	1	5	0
	0.5	0	0	0	0	0	0	0	4	1	1	0	0	0	1	0	0	0	0	1	0
	0.158	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
<i>Fagopyrum vulgare</i>	5	5	1	0	5	5	5	5	5	5	5	2	2	0	5	5	5	0	5	5	5
	1.58	1	0	0	5	5	5	2	5	5	5	1	0	0	5	3	1	0	4	5	5
	0.5	0	0	0	2	3	2	1	2	3	5	0	0	0	2	3	0	0	1	1	1
	0.158	0	0	0	1	1	0	0	0	0	3	0	0	0	1	0	0	0	0	0	0
<i>Sinapis alba</i>	5	4	0	1	5	5	5	5	5	5	5	3	1	0	5	5	4	1	5	5	5
	1.58	1	0	0	5	5	2	3	5	5	5	1	0	0	3	4	1	1	5	5	4
	0.5	0	0	0	1	1	0	1	5	5	5	0	0	0	1	1	0	0	4	4	3
	0.158	0	0	0	1	0	0	0	1	1	3	0	0	0	0	0	0	0	1	2	1
<i>Lepidium sativum</i>	5	5	0	1	5	5	5	5	5	5	5	N	1	0	5	5	5	1	5	5	5
	1.58	1	0	0	5	5	5	3	5	5	5	N	0	0	N	5	N	0	5	5	4
	0.5	0	0	0	3	5	1	1	5	5	5	N	0	0	N	1	0	0	4	4	3
	0.158	0	0	0	1	3	0	0	3	0	3	N	0	0	N	0	0	0	1	2	1
<i>Beta vulgaris</i>	5	5	5	1	5	5	5	5	5	5	5	4	2	0	5	5	5	0	5	5	2
	1.58	4	1	0	5	5	5	4	5	5	0	1	1	0	5	5	4	0	5	5	0
	0.5	2	0	0	3	5	4	4	5	5	0	0	0	0	1	3	2	0	3	4	0
	0.158	0	0	0	1	0	0	0	3	2	0	0	0	0	1	0	0	0	1	1	0

a) Py = the standard Pyrazon.

* 0 — no activity; 5 — 100 % activity; N — not tested.

Fungicidal activity of the prepared compounds was monitored by the *in vitro* methods on fungi of *Tilletia foetida*, *Botrytis cinerea*, *Fusarium avenaceum*, and *Alternaria alternata* according to the published method [3] using Vitavax, Euparen, captan, and dithiocy-

anatomethane as standards. A model test on the inhibition of the Hill reaction was monitored by the *in vitro* method according to the known procedure [4] using Pyrazon as a standard. Herbicidal activity was determined according to the known procedure [5].

2-R²-4-Alkoxy-5-chloro-3-oxo-2H-pyridazines

To 2-R²-4,5-dichloro-3-oxo-2H-pyridazine (0.1 mol) in toluene (300 cm³) sodium methanolate (0.1 mol) as a suspension in toluene (100 cm³) was added with stirring which was continued and the temperature of the reaction mixture reached 45 °C. After 40 min the reaction mixture was heated to reflux and then stirred for 4 h. A cold reaction mixture was treated by water (two times 200 cm³), dried and toluene was distilled off under reduced pressure. A remaining rest was purified by a column chromatography, the product was crystallized from hexane, cyclohexane or distilled under reduced pressure.

2-R²-4-Chloro-5-alkoxy-3-oxo-2H-pyridazines

To a suspension of sodium carbonate (0.1 mol) in alcohol (250 cm³) 2-R²-4,5-dichloro-3-oxo-2H-pyridazine (0.1 mol) was added under stirring and the stirring and heating was continued. After reaching the temperature of reflux the reaction mixture was stirred at reflux for 4 h. After cooling the reaction mixture was poured into water (600 cm³) under stirring. The excluded solid compound was separated and purified by crystallization from ethanol or cyclohexane.

2-R²-4,5-Dialkoxy-3-oxo-2H-pyridazines

To a suspension of sodium alkoxide (0.21 mol) in toluene (300 cm³) 2-R²-4-alkoxy-(chloro)-5-chloro(alkoxy)-3-oxo-2H-pyridazine (0.2 mol) or 2-R²-4,5-dichloro-3-oxo-2H-pyridazine (0.1 mol) was added under stirring. The reaction mixture was heated to reflux during 30 min and stirred for 8 h. After cooling sodium chloride was filtered off and from the filtrate toluene was distilled off under reduced pressure. The rest was purified by crystallization from cyclohexane, toluene or by distillation under reduced pressure.

2-R²-4-Hydroxy-5-chloro-3-oxo-2H-pyridazines

To the solution of sodium hydroxide (0.1 mol) in water (100 cm³) 2-R²-4-alkoxy-5-chloro-3-oxo-2H-pyridazine (compounds VII, IX, and XV) (0.05 mol) was added under stirring. The reaction mixture was stirred at the boiling point over 4–6 h and was acidified with concentrated hydrochloric acid to pH = 1. The excluded solid compound was filtered off, dried and purified by crystallization from toluene. By this route these compounds were obtained:

2-Methyl-4-hydroxy-5-chloro-3-oxo-2H-pyridazine (LXI), m.p. = 216—218 °C.

For $C_5O_2N_2Cl$ w_i (calculated): 22.1 % Cl, 17.5 % N; w_i (found): 22.2 % Cl, 17.6 % N.

IR (KBr), $\tilde{\nu}/cm^{-1}$: 1620 $\nu(C=O)$; 3380 $\nu(O-H)$.

2-Phenyl-4-hydroxy-5-chloro-3-oxo-2H-pyridazine (LXII), m.p. = 182—184 °C.

For $C_{10}H_7O_2N_2Cl$ w_i (calculated): 15.9 % Cl, 12.6 % N; w_i (found): 16.0 % Cl, 12.7 % N.

IR (KBr), $\tilde{\nu}/cm^{-1}$: 1600 $\nu(C=O)$; 3370 $\nu(O-H)$.

2-(3'-Chlorophenyl)-4-hydroxy-5-chloro-3-oxo-2H-pyridazine (LXIII), m.p. = 190—191 °C.

For $C_{10}H_6O_2N_2Cl_2$ w_i (calculated): 27.5 % Cl, 10.9 % N; w_i (found): 27.6 % Cl, 11.0 % N.

IR (KBr), $\tilde{\nu}/cm^{-1}$: 1605 $\nu(C=O)$; 3376 $\nu(O-H)$.

2-R²-4-Chloro-5-hydroxy-3-oxo-2H-pyridazines

To the aqueous solution (100 cm³) of sodium hydroxide (0.1 mol) 2-R²-4-chloro-5-alkoxy-3-oxo-2H-pyridazine (compounds XXI, XXVI, XXXV) (0.05 mol) was added under stirring. The reaction mixture was stirred at the boiling point for 8 h, then it was acidified by hydrochloric acid to pH = 1, the excluded solid was filtered off, dried and purified by crystallization from ethanol. These compounds were obtained by this route:

2-Methyl-4-chloro-5-hydroxy-3-oxo-2H-pyridazine (LXIV), m.p. = 257—259 °C.

For $C_5H_5O_2N_2Cl$ w_i (calculated): 22.1 % Cl, 17.5 % N; w_i (found): 22.3 % Cl, 17.7 % N.

IR (KBr), $\tilde{\nu}/cm^{-1}$: 1615 $\nu(C=O)$; 3510 $\nu(O-H)$.

2-Phenyl-4-chloro-5-hydroxy-3-oxo-2H-pyridazine (LXV), m.p. = 267—269 °C.

For $C_{10}H_7O_2N_2Cl$ w_i (calculated): 15.9 % Cl, 12.6 % N; w_i (found): 16.1 % Cl, 12.8 % N.

IR (KBr), $\tilde{\nu}/cm^{-1}$: 1615 $\nu(C=O)$; 3510 $\nu(O-H)$.

2-(3'-Chlorophenyl)-4-chloro-5-hydroxy-3-oxo-2H-pyridazine (LXVI), m.p. = 291—293 °C.

For $C_{10}H_6O_2N_2Cl_2$ w_i (calculated): 27.5 % Cl, 10.9 % N; w_i (found): 27.7 % Cl, 10.8 % N.

IR (KBr), $\tilde{\nu}/cm^{-1}$: 1618 $\nu(C=O)$; 3520 $\nu(O-H)$.

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