Synthesis of 3-(aryl-X-)coumarins and their pesticidal and antifungal activity

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3-(Aryl-X-)coumarins, where X is oxygen or —C(O)NH— group, have been prepared by Perkin synthesis from aryl-X-ethanoic acids and 2-hydroxybenzaldehyde at 180—200 °C. They were tested for herbicidal, fungicidal, and insecticidal activities as well as for activity against dermatophytes.

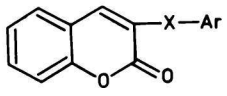
3-(Арил-X-)кумарины, где X – кислород или —C(O)NH— группа были получены посредством синтеза Перкина из арил-X-этановых кислот и 2-гидроксибензальдегида при 180—200 °C. У полученных соединений были проверены их гербицидная, фунгицидная и инсектицидная активности, а также активность против дерматофитов.

For synthesis of 3-(aryl-X-)coumarins 13 variously substituted aryloxyethanoic and 3 benzamidoethanoic acids were used. Aryloxyethanoic acids, mainly those substituted by halogens, are known as inhibitors or stimulators of plant growth and have been used as agents for plant protection [1]. Therefore, they have been subjected to many studies concerning their biological activity. Reactivity of their methylene group in aldol syntheses has received little attention so far [2—6]. It is known that the yields of aldol condensations with aryloxyethanoic acids are severalfold lower than with arylethanoic and arylthioethanoic acids. Therefore, these syntheses are of little significance from preparative standpoint, however, it is the only way to prepare such types of compounds as the biologically very active 3-aryloxymethylenephthalides [7, 8], 3-aryloxymethylenephthalimidines [9], esters of 2-aryloxyacetylbenzoic acids, which are highly phytotoxic and inhibit metamorphosis of juvenile forms of insect, and 2-aryloxy-1,3-indandiones.

There is only one work [6] in the literature publishing the synthesis of 3-phenoxycoumarin by condensation of 2-hydroxybenzaldehyde with phenoxy-

Table 1

3-(Aryl-X)coumarins



Compound	X Aryl	Formula M_r	w_i(calc.)/% w_i(found)/%				M.p./°C	IR $\tilde{\nu}$/cm^{-1}	^{1}H NMR δ/ppm
			C	H	N	Cl			
I	O	$C_{15}H_{10}O_3$	75.65	4.19	—	—	114—115	1725 ν(CO)	7.00—7.65 (10H, m)
	Phenyl	238.2	75.53	4.11					
II	O	$C_{16}H_{12}O_3$	76.21	4.76	—	—	104—105	1730 ν(CO)	2.250 (3H, s)
	3-Methylphenyl	252.3	76.12	4.81					6.75—7.70 (9H, m)
III	O	$C_{17}H_{14}O_3$	76.68	5.38	—	—	135—136	1730 ν(CO)	3.425 (6H, s)
	3,5-Dimethylphenyl	266.3	76.20	5.30					6.77—7.62 (8H, m)
IV	O	$C_{15}H_9NO_5$	63.60	3.18	4.94	—	172—173	1721 ν(CO), 1520 ν(NO_2),	7.17—8.10 (8H, m)
	2-Nitrophenyl	283.2	63.64	3.07	4.91			1344 ν(NO_2)	7.750 (1H, s)
V	O	$C_{15}H_9NO_5$	63.60	3.18	4.94	—	174—176	1728 ν(CO), 1538 ν(NO_2),	7.22—8.05 (8H, m)
	3-Nitrophenyl	283.2	63.78	3.04	4.82			1356 ν(NO_2)	7.850 (1H, s)
VI	O	$C_{15}H_9NO_5$	63.60	3.18	4.94	—	221—222	1716 ν(CO), 1580 ν(NO_2),	8.05—8.25 (4H, d), 7.950 (1H, s)
	4-Nitrophenyl	283.2	63.74	3.01	4.82			1350 ν(NO_2)	7.12—7.75 (4H, m)
VII	O	$C_{15}H_9O_3Cl$	66.07	3.32	—	13.00	178—180	1725 ν(CO)	6.75—7.70 (9H, m)
	4-Chlorophenyl	272.7	66.04	3.26		12.84			
VIII	O	$C_{16}H_{10}O_5$	68.09	3.57	—	—	127	1700 ν(CO)	—
	2-Carboxyphenyl	282.3	67.95	3.94				1742 ν(CO)	
IX	O	$C_{16}H_{11}O_3Cl$	67.02	3.86	—	12.36	124—126	1728 ν(CO)	2.175 (3H, s)
	2-Methyl-4-chlorophenyl	286.7	66.90	3.86		12.05			6.82—7.62 (8H, m)

Table 1 (Continued)

Compound	X Aryl	Formula M_r	w_i(calc.)/% w_i(found)/%				M.p./°C	IR $\tilde{\nu}$/cm^{-1}	^{1}H NMR δ/ppm
			C	H	N	Cl			
X	O	$C_{15}H_7O_3Cl_3$	52.73	1.94	—	31.13	172—173	1710 ν(CO)	7.825 (1H, s), 7.725 (1H, s)
	2,4,5-Trichlorophenyl	341.6	52.74	2.06		31.87			7.625 (1H, s), 7.25—7.57 (4H, m)
XI	O	$C_{19}H_{18}O_3$	77.54	6.16	—	—	172—173	1730 ν(CO)	1.175 (3H, s), 1.250 (3H, s)
	2-Isopropyl-4-methyl-phenyl	294.3	77.81	6.24					2.300 (3H, s), 3.35 (1H, m) 6.75—7.30 (8H, m)
XII	O	$C_{19}H_{12}O_3$	79.16	4.19	—	—	115	1725 ν(VO)	7.07—8.12 (12H, m)
	1-Naphthyl	288.3	79.42	4.41					
XIII	O	$C_{19}H_{12}O_3$	79.16	4.19	—	—	173—175	1728 ν_S(CO)	7.25—8.00 (12H, m)
	2-Naphthyl	288.3	79.23	4.15				1714 sh ν(CO)	
XIV	NHCO	$C_{16}H_{11}O_3N$	72.43	4.15	5.28	—	176	1726, 1705, 1684 ν(CO)	7.25—8.00 (9H, m), 8.625 (1H, s)
	Phenyl	265.3	72.35	4.12	5.28			3370 ν(NH)	9.350 (1H, s)
XV	NHCO	$C_{16}H_{10}O_5N_2$	61.94	3.25	9.03	—	283	1710, 1698, 1670 ν(CO)	—
	3-Nitrophenyl	310.3	62.30	3.18	9.04			3377 ν(NH)	
XVI	NHCO	$C_{16}H_{10}O_5N_2$	61.94	3.25	9.03	—	313—314	1708, 1690, 1670 ν(CO)	—
	4-Nitrophenyl	310.3	61.80	3.18	9.14			3380 ν(NH)	

ethanoic acid at the conditions of Perkin synthesis. The yields in this synthesis were reported to be only 30 %.

The aim of the present work was to find some favourable conditions in order to increase the yield of the mentioned reaction and test the prepared compounds for biological activity because not only the aryloxy group is a part of biologically active systems but also derivatives of coumarins occur in several natural compounds and some of the synthesized types are anticoagulants or show antimicrobial properties [10].

3-Aryloxycoumarins were prepared by the classical Perkin synthesis at modified conditions using mixed aryloxyethanoic and ethanoic anhydrides *in situ*, prepared prior to condensation itself, and three bases, namely potassium acetate, pyridine, and triethylamine, applied at the same time. This procedure afforded 50—60 % yields of 3-aryloxycoumarins.

It was found that for the preparation of coumarins substituted in the position 3 by aryloxoamino group aryloxoaminoethanoic acids were suitable, which gave 80—90 % yields. In this reaction acetic anhydride as dehydration agent could not be used since, in its presence, aryloxoaminoethanoic acids would dehydrate to cyclic anhydrides, *i.e.* 2-aryl-5-oxazolones.

The infrared spectra of the prepared compounds proved their structures. The band belonging to ν(CO) appeared in the region of $\tilde{\nu} = 1710$—$1730\ \mathrm{cm}^{-1}$. ^{1}H NMR spectra were measured with the compounds sufficiently soluble (Table 1).

The compounds *I*, *VI*—*IX*, *XIII*, and *XV* were tested for herbicidal activity on *Avena sativa*, *Fagopyrum vulgare*, *Sinapis alba*, *Panicum miliaceum*, and *Lepidium sativum*. The tests showed that the compounds were not phytotoxic even in the maximum area density 1.5 g m^{-2} applied. The results of tests led to a recognition that highly phytocidal acids, such as 2,4,5-trichlorophenoxyethanoic, 4-chlorophenoxyethanoic, 2-methyl-4-chlorophenoxyethanoic, and 2-naphthyloxyethanoic acids on introduction into the coumarin skeleton lost their phytotoxicity.

In standard fungicidal tests on *Erysiphe graminis*, *Phytophtora infestans*, *Tilletia caries*, *Fusarium avenaceum*, and *Botritis cinerea* the compounds showed 25—50 % activity when compared to the standards used.

Insecticidal tests were carried out on *Musca domestica*, *Calandra granaria*, *Tetranychus urticae*, *Aphis fabae* (contact application on imago). Ovicidal activity was followed on *Tetranychus urticae* and *Aphis fabae*. Tests in contact application were on the level of the control, while ovicidal tests showed 5—20 % inhibition.

The compounds *I*—*XV* were tested for antifungal activity on *Trichophyton rubrum*, *T. gypseum*, *T. mentagrophytes var. interdigitale*, *Microsporum gypseum*, *M. cookei*, and *Epidermophyton floccosum*. The compounds *IX* and *XI* inhibited the growth of these cultures in 50 μg cm^{-3} concentration and that of *E. floccosum* in 100 μg cm^{-3}. The rest of the compounds tested showed no inhibition on these microorganisms even when applied in 100 μg cm^{-3} concentration.

Experimental

Infrared spectra of the compounds in paraffin oil were measured with a Specord 75 IR spectrophotometer in the region of $\tilde{\nu} = 400—4000$ cm^{-1}. ^{1}H NMR spectra were measured in a saturated DMSO solution with a Tesla BS 487 A apparatus at 80 MHz.

Tests for herbicidal activity were carried out according to [7], for fungicidal activity according to [11], for insecticidal activity according to [12], and tests for activity against dermatophytes according to [13].

3-Aryloxycoumarins (I—XIII)

Aryloxyethanoic acid (0.05 mol) and acetic anhydride (0.1 mol) were refluxed for 30 min and the volatile components were distilled off thoroughly. Then 2-hydroxybenzaldehyde (0.06 mol), melted CH_3COOK (0.005 mol), pyridine (0.05 mol), and triethylamine (0.05 mol) were added and the mixture was heated to reflux for 1 h. The reaction temperature was elevated to 190—200 °C which, at stirring and distillation of volatile components, was maintained for 60—90 min till all the reaction water was distilled off. Then the hot mixture was poured into cold water (200 cm^3). The excess aldehyde was removed by addition of $NaHSO_3$ solution, while the excess acid was removed by washing the precipitate with $NaHCO_3$ solution. The insoluble portion was sucked or decanted, washed with water several times, and crystallized from ethanol or ethanoic acid. The compounds prepared are presented in Table 1.

3-(Aryloxoamino)coumarins (XIV—XVI)

The mixture of aryloxoaminoethanoic acid (0.05 mol), 2-hydroxybenzaldehyde (0.06 mol), CH_3COOK (0.005 mol), pyridine (0.05 mol), and triethylamine (0.05 mol) was heated to reflux for 1 h. Then the temperature was elevated to 180 °C and maintained for 1 h at simultaneous distillation of the volatile components. The hot mixture was poured into cold water and the products were isolated and purified similarly as in the previous case. The compounds prepared are presented in Table 1.

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