ogenated chemicals against the toxicity of organophosphates.

Registry No. DEP, 598-02-7; DETP, 2465-65-8; lindane, 58-89-9; parathion, 56-38-2; *p*-nitrophenol, 100-02-7; aminoparathion, 3735-01-1.

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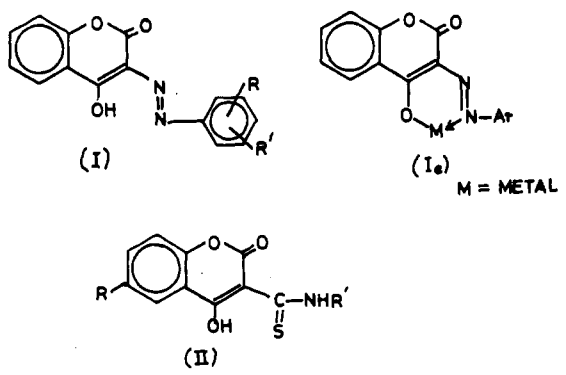
Fungicidal and Molluscicidal Activity of Some 3-Substituted 4-Hydroxycoumarin Derivatives

Somari Giri* and Awadhesh Kumar Mishra

A number of derivatives comprising 3-(arylazo)-4-hydroxycoumarins (I) and 3-*N*-arylthiocarbamoyl)-4-hydroxycoumarins (II) have been synthesized. Eleven such compounds have been screened for their fungitoxicity against *Alternaria tenuis* and *Helminthosporium oryzae*, and two of them have been tested for their molluscicidal activity against *Lymnea acuminata*. The results have been compared with two commercial fungicides, Dithane M-45 and Bavistin, tested under similar conditions.

A number of coumarin and isocoumarin derivatives have been synthesized as insecticides (Beriger, 1976) and fungicides (Maikawa and Yoshikawa, 1979; Giri and Singh, 1978; Nakajima et al., 1979). The 4-hydroxyoumarin derivatives such as dicoumarol (O'Connor, 1948), warfarin (Overman et al., 1944), and coumachlor (Reiff and Weismann, 1951) are well-known rodenticidal agents. A number of azo compounds have been found to be active acaricides (Metcalf, 1955). Several azo dyes exhibit fungicidal activity (Silk and Summers, 1963). In view of these observations, it was anticipated that a compound of the structure I having a combination of an azo linkage with a 4-hydroxycoumarin moiety would possess interesting pesticidal properties. This is because the structure I would very well serve as a suitable ligand to chelate the essential metals involved in fungal metabolism as shown in Ie.

The importance of the N–C–S linkage as the active toxophore (Metcalf, 1955; Goldsworthy, 1942; Joshi and Giri, 1963) in a number of pesticides has been well stressed. 3-(*N*-Substituted carbamoyl)-4-hydroxycoumarins have been patented (Beriger, 1976) as an insecticide; it was expected that the analogous compounds (II) might also be active pesticidal agents.



The 3-(arylazo)-4-hydroxycoumarins (I) were prepared by reacting different aryldiazonium salts with 4-hydroxycoumarin in the presence of anhydrous CH_3COONa and

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Table I. 3-(Arylazo)-4-hydroxycoumarins (Vide Structure I)

compd no.	R	R′	mp, °C	yield, %	molecular formula	R_f[a]	C, % found	C, % calcd	H, % found	H, % calcd	N, % found	N, % calcd
1	H	4-Cl	176–178	55.5	$C_{15}H_9N_2O_3Cl$	0.55	59.82	60.00	2.87	3.00	8.57	9.33
2	H	4-OCH_3	218–220 (d)	55	$C_{16}H_{12}N_2O_4$	0.46	64.67	64.86	3.85	4.05	9.36	9.48
3	2-CH_3	3-CH_3	169–170	44	$C_{17}H_{14}N_2O_3$	0.68	69.17	69.32	4.63	4.76	9.39	9.52

Significant Bands (cm^{-1}) in IR Spectra (KBr Disk)

aromatic rings	N=N of azo compound	phenolic O–H	=CH–C(=O)–OR	substituted phenyl rings
3100, 1430	1590	1280	1160	760

^1H NMR Spectrum of 2 in $CDCl_3$[b]

type of protons	no. of protons	chemical shift, (δ)	multiplicity
ar H, benzenoid	8	7.2	singlet
–O–H, phenolic	1	3.8	singlet
–O–CH_3, alkyl	3	3.6	singlet

[a] Solvent system for TLC: ethyl acetate–chloroform–benzene (1:3:3). [b] Low resolution.

Table II. 3-(*N*-Arylthiocarbamoyl)-4-hydroxycoumarins (Vide Structure II)

compd no.	R	R′	mp, °C	yield, %	molecular formula	R_f	C, % found	C, % calcd	H, % found	H, % calcd	N, % found	N, % calcd
4	H	*s*-$C_6H_2Br_3$	126–128	78	$C_{16}H_8NSO_3Br_3$	0.43[b]	35.67	35.96	1.31	1.50	2.48	2.62
5	H	$-C_6H_5$	137–139	84	$C_{16}H_{11}NSO_3$	0.56[a]	64.52	64.67	3.51	3.7	4.43	4.71
6	H	$-CH_2-CH=CH_2$	196–200	84	$C_{13}H_{11}NSO_3$	0.65[b]	65.71	65.82	4.49	4.64	5.16	5.9
7	H	$-C_6H_4OCH_3$-*p*	182–184	53.5	$C_{17}H_{13}NSO_4$	0.47[a]	62.48	62.38	3.67	3.97	4.02	4.28
8	H	$-C_6H_4CH_3$-*p*	169–170	78	$C_{17}H_{13}NSO_3$	0.7[a]	65.47	65.59	4.00	4.18	4.32	4.5
9	H	$-C_6H_4OC_2H_5$-*p*	160–161	69	$C_{18}H_{15}NSO_4$	0.6[b]	63.12	63.34	4.12	4.39	3.95	4.11
10	Cl	$-C_1H_4OC_2H_5$-*p*	156–158	64	$C_{18}H_{14}NSO_4Cl$	0.52[b]	57.46	57.60	3.59	3.73	3.63	3.73
11	Cl	$-C_6H_4CH_3$-*p*	176–178	58.8	$C_{17}H_{12}NSO_3Cl$	0.58[a]	58.98	59.13	3.33	3.48	3.84	4.06

Significant Bands (cm^{-1}) in IR Spectra (KBr Disk)

compd	aromatic rings	NH stretching	C=S linkage	C–O–C stretching	substituted aromatic ring
4	1610, 1450	3300	1075	1290	880
9	1610, 1545, 1505	3200	1050	1240	
11	1590, 1480	3100	1020	1140	1540

^1H NMR Spectrum of 4 in $CDCl_3$

type of proton	no. of protons	chemical shift, δ	multiplicity
Ar H, benzenoid	6	7.4	singlet
–O–H, phenolic	1	4.55	singlet
–N–H, secondary amine	1	3.6	singlet

[a] Solvent system: chloroform–benzene (1:1). [b] Solvent system: ethyl acetate–chloroform–benzene (1:3:3).

glacial acetic acid. The IR spectra of I showed absorption bands in the regions 1590 cm^{-1} (N=N stretching vibration), 1280 cm^{-1} (phenolic O–H stretching), 1160 cm^{-1} (=CH–C=O–OR stretching), and 3100 and 1430 cm^{-1} (aromatic rings).

3-(*N*-Arylthiocarbamoyl)-4-hydroxycoumarins (II) have been prepared by refluxing a mixture of 4-hydroxycoumarin with aryl isothiocyanates in DMF containing a few drops of pyridine (Dave et al., 1960).

All the compounds prepared were screened for antifungal activity against *Helminthosporium oryzae* and *Alternaria tenuis*. The compounds under investigation are comparable with the fungicidal power of commercial fungicides, dithane M-45 and bavistin, at higher concentrations. Two of these compounds were found to cause mortality of snails in varying numbers at three different concentrations.

EXPERIMENTAL SECTION

4-Hydroxycoumarins. These compounds have been prepared by heating appropriate phenol (1.0 M) and malonic acid (1.0 M) in the presence of a $ZnCl_2$–$POCl_3$ mixture at 60–65 °C for 30–35 h (Shah et al., 1960; Dallacker and Kratzer, 1961): R = H, mp 208–210 °C (Shah et al., 1960); R = Cl_3 mp 227–228 °C.

3-(Arylazo)-4-hydroxycoumarins (I). 4-Hydroxycoumarin (1.0 M) was mixed with anhydrous sodium acetate and glacial acetic acid and kept in ice so that the temperature remains below 10 °C. Different aromatic amines (1.1 M) were dissolved in diluted HCl and kept at 5–10 °C. this was diazotized by a cold solution of $NaNO_2$ below 10 °C. The diazotized solution was mixed slowly to the paste of coumarin and sodium acetate and shaken thoroughly. The precipitate thus obtained was filtered, dried, and purified by repeated crystallization and performing TLC (benzene, ethyl acetate, and chloroform). The compounds thus prepared are recorded in Table I.

3-(*N*-Arylthiocarbamoyl)-4-hydroxycoumarin (II). These compounds were prepared by refluxing 4-hydroxycoumarin (1.0 M) with different aryl isothiocyanates (1.0 M) in dimethylformamide with a few drops of pyridine for 4 h. It was then cooled and poured into ice water. The precipitate separating was filtered, dried, repeatedly crystallized from ethanol, and purified by TLC using the benzene–chloroform–ethyl acetate solvent system. The compounds synthesized are recorded in Table II.

Fungicidal Test. The fungicidal activity of 11 compounds synthesized in the present investigation was evaluated by the agar-growth technique against two different species of fungi used as the test organism. The

Table III. Fungicidal Data

compd no.[a]	average % inhibition after 96 h					
	A. tenuis concentration used			*H. oryzae* concentration used		
	1:1000	1:10 000	1:100 000	1:1000	1:10 000	1:100 000
1	88.1	78.7	68.0	90.0	73.5	53.3
2	84.6	71.0	60.6	87.3	69.3	37.3
3	80.0	64.0	41.4	73.5	62.3	34.2

[a] Numbers of the compounds correspond to that given in Table I.

Table IV. Fungicidal Data

compd no.[a]	average % inhibition after 96 h					
	A. tenuis concentration used			*H. oryzae* concentration used		
	1:1000	1:10 000	1:100 000	1:1000	1:10 000	1:100 000
4	92.0	87.1	81.1	85.2	68.2	56.1
5	84.4	78.7	68.0	84.3	68.2	49.2
6	96.6	88.6	81.1	95.8	87.3	70.6
7	86.1	74.7	59.7	90.0	81.0	58.8
8	88.1	81.7	54.3	81.9	69.3	34.1
9	86.1	69.6	50.5	88.0	73.5	53.6
10	92.0	82.9	69.6	96.9	79.4	62.3
11	94.2	84.6	70.4	96.2	87.3	66.1
Bavistin	98.9	96.6	94.7	94.2	91.2	84.3
Dithane M-45	99.1	98.5	94.9	96.7	93.2	85.7

[a] Numbers of the compounds correspond to that given in Table II.

Table V. Molluscicidal Data

no. of animals	compd no.	dose, mg/L	% mortality (mean ± SE) at indicated time intervals after treatment		
			24 h	48 h	96 h
60	3	1.0	8.33 ± 3.37	21.67 ± 5.24	28.33 ± 5.24
60	3	o.0	31.67 ± 3.37	41.67 ± 3.37	53.33 ± 4.63
60	3	5.0	58.33 ± 4.41	68.33 ± 5.24	76.67 ± 5.43
60	4	1.0	31.67 ± 3.37	45.0 ± 3.75	50.0 ± 2.83
60	4	3.0	41.67 ± 3.37	51.67 ± 3.37	60.0 ± 5.67
60	4	5.0	63.33 ± 4.63	63.33 ± 4.63	76.67 ± 4.63

[a] Numbers of the compounds correspond to that given in Tables I and II.

fungus was planted in agar medium mixed with the test compound. The diameter of the fungus colony was measured with a millimeter scale at three different concentrations. Inhibition of fungus growth was determined as the difference in growth between control plates and those treated with the toxicant. Three repetitive experiments were performed for each concentration of the compound under investigation, and same number of replicates of controls was provided. The percentage inhibition was calculated as

$$\% \text{ inhibition} = \frac{(C - T)}{C} \times 100$$

where C = the average diameter of the fungus colony (in mm) on the control plate and T = the average diameter of the fungus colony (in mm) on the treated plate. The fungicidal performance of test compounds was compared with that of two commercial fungicides, Dithane M-45 and Bavistin, by using similar conditions and same fungus species. The fungicidal data are recorded in Tables III and IV.

Molluscicidal Activity Test. The molluscicidal activity of two compounds was evaluated against a snail, *Lymnea acuminata*. The aquarium containing the snails was intoxicated by different concentrations of the chemicals, and the mortality studies were carried out after different time intervals. Each aquarium contained 10 experimental animals. Six aquariums were set up for each concentration of the toxicant. Equal numbers of control animals were kept in a similar manner without the chemical (toxicant). The snails were exposed to three different concentrations of each chemical for a period of different hours. The results obtained were worked up to their percentage mortality by mathematical calculation, which is given in Table V.

RESULTS AND DISCUSSION

Among 3-(arylazo)-4-hydroxycoumarins the most active compound was the one having a chloro group (no. 1) followed by the compound incorporating a methoxy group (no. 2) when tested against *A. tenuis*. All these compounds were less active against *H. oryzae*.

The 3-(*N*-arylthiocarbamoyl)-4-hydroxycoumarins (no. 4–11) were fairly toxic to both fungus species at concentrations of 1000 and 100 ppm. However, upon dilution (10 ppm) only compound no. 4, 6, and 11 could maintain the fungitoxicity against *H. oryzae* to a better level. It is to be noted that these compounds contain halo or alkenyl groups, which appear to induce greater fungitoxicity in compounds under investigation than other groups.

The molluscicidal activity appears to depend both on dose and on time. At minimum doses, the compounds bring about least mortality after 24 h, but as the time of exposure lengthens, the mortaility rate of the test animals increases. If the starting dose is increased, there is considerable mortality even after 24 h, the minimum recorded time in the present investigation.

CONCLUSION

The 3-(arylazo)-4-hydroxycoumarins with chloro and methoxy substituents appear to be promising fungicides and need further screening on a wider range of fungi. The 3-(*N*-substituted thiocarbamoyl)-4-hydroxycoumarins seem

to be a weeker class of fungicides compared to the above compounds.

The molluscicidal power of coumarin derivatives depends on the concentration of the samples and time of exposure of test animals.

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Registry No. 1, 68454-11-5; 2, 89999-02-0; 3, 89999-03-1; 4, 89999-04-2; 5, 26004-25-1; 6, 89999-05-3; 7, 89999-06-4; 8, 68266-19-3; 9, 89999-07-5; 10, 89999-08-6; 11, 89999-09-7.

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Fungicidal and Molluscicidal Activity of Some Heteroarylcarbinols and Ethylenes

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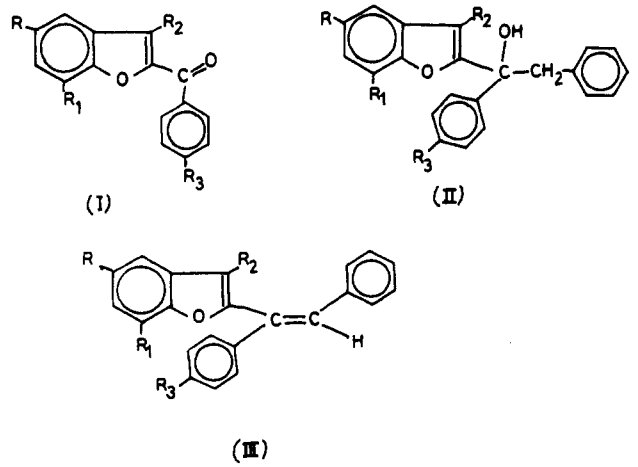
A number of derivatives comprising 1-aryl-1-(substituted benzofur-2-yl)-2-benzylcarbinols (II) and 1-aryl-1-(substituted benzofur-2-yl)-2-phenylethylenes (III) have been synthesized. Ten such compounds have been screened for their fungitoxicity against *Alternaria tenuis* and *Helminthosporium oryzae*, and two of them have been tested for their molluscicidal activity against *Lymnea acuminata*, a snail. The results have been compared with two commercial fungicides, Dithane M-45 and Bavistin, tested under similar conditions.

A number of benzofuran derivatives have been developed as insecticides (Boell et al., 1974) and fungicides (Grinev et al., 1979; Brooke et al., 1971). Some unsaturated and cyclic alcohols and their ethers have strong insecticidal, fungicidal, bactericidal, and acaricidal (Metcalf, 1948) effects. In view of these observations, it was presumed that the carbinols (II) containing benzofuryl and benzyl moieties should be effective pesticides. The pesticidal properties of some halogenated alkenes is well-known (Melnikov, 1971). Some acrolein (Grassberger and Reinshagm, 1975) and butene (Saikawa and Takano, 1970) derivatives containing a nitrofuryl substituent have been patented as fungicidal, protozoacidal, and antibacterial agents. In view of these records, the alkenes of type III have been synthesized with the anticipation that they might be useful pesticidal agents.



1-Aryl-1-(substituted benzofur-2-yl)-2-benzylcarbinols (II) have been prepared by a general procedure described in the literature (Fuson et al., 1941). Freshly prepared benzylmagnesium chloride in an extremely anhydrous condition was added dropwise to a solution of 2-benzoylbenzofuran in sodium-dried ether. The reaction mixture was kept refluxing in a warm water bath for 2–3 h. After the complex was decomposed with ice and NH_4Cl, the product contained in the ethereal layer was isolated as usual. The IR spectrum of II showed absorption bands in the regions 1600 cm^{-1} (aromatic –C=C– stretching), 1050 cm^{-1}, 815 cm^{-1} (benzofuran ring), 3500 cm^{-1}, 1300 cm^{-1} (tertiary –OH group), and 1445 cm^{-1} ($-CH_2-$ bending).

The triarylethylenes (III) have been obtained in good yield by dehydration of triarylcarbinols (II) using acetic anhydride as the dehydrating agent. The IR spectrum of III reveals the following signals at 3100 cm^{-1} (C–H of the benzofuran ring), 1580 cm^{-1}, 1480 cm^{-1}, 1450 cm^{-1} (aromaticity), 1010 cm^{-1}, 815 cm^{-1} (characteristic of benzofuran), 900 cm^{-1} (C–H bending of trans-substituted alkene), and 1760 cm^{-1} (–C=C– bond stretching of trans-

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