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Arylazomethylene Derivatives as Molluscicides

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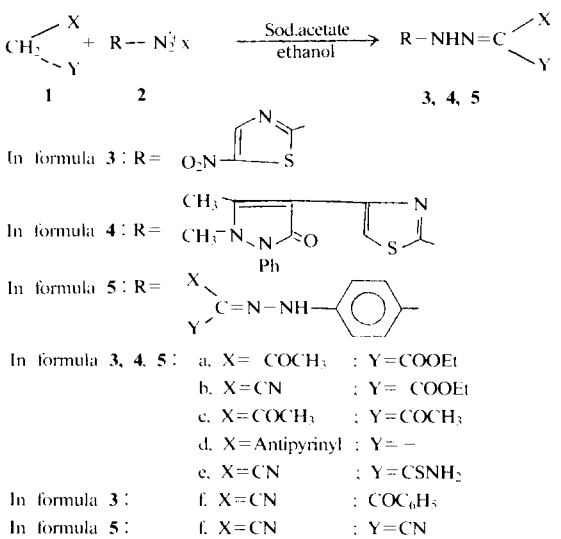
Abstract Arylazomethylene derivatives as molluscicides were synthesized from heterocyclic amines

Keywords Molluscicides, snails, *Biomphlaria alexandrina*, arylazomethylene.

Schistosomiosis is one of the most dangerous diseases in Egypt, and in most tropical and substropical countries[1]. For rapid control of the disease, the lift cycle of the parasite may be broken through snail control to reduce or eliminate the factors essential for the completion of the life cycle[2].

The molluscicidal and schistosomicidal activities of 5-nitrothiazole derivatives[3,4], *p*-phenylenediamine and azobenzene[1] as well as the bacteriostatic, fungistatic and trichomonostatic effects of arylazomethylenes[5,6] encouraged the synthesis of some arylazomethylene derivatives as molluscicides.

Thus, the arylazomethylene derivatives which have in general structures **3a-f**, **4a-e** and **5a-e** (Scheme 1) were synthesized in very good yields *via* reaction of active methylenes **1** such as ethyl acetoacetate, ethyl cyanoacetate, acetylacetone, antipyrine, 2-cyanothioacetamide, ω-cyanoacetophenone and malononitrile with a diazotized solution of primary amines **2** such as 2-amino-5-nitrothiazole, aminophenazonylthiazole and *p*-phenylenediamine in ethanol in the presence of sodium acetate. Structures **3**, **4** and **5** were established on the basis of microanalytical data of the isolated products as well as their spectral data which are in good agreement with these structures (cf Table III).



Scheme 1

MOLLUSCICIDAL TESTING AND RESULTS

Biompharia alexandrina snails were collected from irrigation canals in Giza Governarate-Egypt that have not been treated with molluscicides. They were kept under laboratory conditions (dechlorinated tap water pH 7.0-7.5, 26± 1C) for four weeks before being used in bioassay tests. The synthesized compounds were screened for their molluscicidal activity against adult snails of 10± 2 mm in diameter according to the W.H.O. method[7]. The exposure period was 24 hours, followed by recovery of 24 hours. Ehylene glycol is used as a detergent for compounds **3a-f** while twin 20 is used for compounds **4a-e** and **5a-e**.

Comparative study of the molluscicidal activity

Table I. Susceptibility of *B. alexandrina* to compounds 3a-f after 24 hours of exposure using ethylene glycol as a solvent

Comp.	Concentration (ppm)				
	25	50	75	100	150
3a	10	30	30	90	100
b	0	40	30	30	60
c	10	20	30	30	90
d	20	20	30	50	50
e	0	0	10	0	20
f	20	40	60	60	80
Control	0	0	0	0	0

Table II. Susceptibility of *B. alexandrina* to compounds 4a-e and 5a-e after 24 hours of exposure using Twin 20 as a solvent

Comp.	Concentration (ppm)						
	10	20	30	40	50	60	70
4a	0	0	0	0	0	0	0
b	0	0	0	0	0	0	0
c	0	0	0	0	0	0	0
d	0	0	0	0	0	0	20
e	0	0	0	0	10	60	80
5a	0	0	0	20	80	100	100
b	0	20	20	40	40	100	100
c	0	0	0	0	0	0	0
d	0	0	0	0	0	0	0
e	20	60	90	100	100	100	100
Control	0	0	0	0	0	0	0

of the synthesized compounds **3a-f**, **4a-e** and **5a-f** indicated that **5e** was the most toxic one as it killed the snails at 40 ppm., also compounds **3a-d**, **3f** and **5b** have marked activity against the snails. However, compounds **4a-e** show inactivity against the snails (cf Tables I and II).

EXPERIMENTAL METHODS

All melting points are uncorrected. IR spectra were recorded in KBr discs on a shimadzu 408 spectrophotometer. Microanalytical data were obtained from the microanalytical unit at Cairo University.

Synthesis of the arylazomethylenes 3a-f, 4a-e and 5a-f

Table III. Analytical data of the synthesized compounds

Comp.*	M.P.C°	Yield	Formula (mol.wt)	Calc./found C %	H %	N %	S %
3a	182	80	$C_9H_{10}N_4O_3S$	37.76	3.99	19.58	11.19
			(286)	38.1	3.8	19.3	11.0
b	205	77	$C_8H_7N_5O_4S$	35.69	2.60	26.02	11.84
			(269)	35.8	2.6	26.1	11.6
c	241	85	$C_8H_8N_4O_4O_4S$	37.50	3.13	21.87	12.50
			(256)	37.8	3.4	21.5	12.3
d	195	86	$C_{14}H_{13}N_6O_3S$	48.69	3.76	24.35	9.28
			(345)	48.5	3.7	24.5	9.6
e	267	80	$C_6H_4N_6O_2S_2$	28.13	1.56	32.81	25.00
			(256)	28.3	1.7	33.1	24.8
f	215	80	$C_{12}H_7N_4O_3S$	50.17	2.44	19.51	11.15
			(287)	50.4	2.5	19.6	11.0
4a	171	75	$C_{20}H_{21}N_5O_4S$	56.20	4.92	16.39	4.99
			(427)	56.4	4.6	16.2	4.7
b	159	80	$C_{19}H_{18}N_6O_3S$	55.61	4.39	20.4	7.80
			(410)	55.7	4.5	20.3	7.5
c	123	77	$C_{19}H_{19}N_5O_3S$	57.43	4.78	17.32	8.06
			(397)	57.3	4.8	17.3	8.2
d	140	73	$C_{25}H_{24}N_5O_2S$	61.72	4.93	20.16	6.58
			(486)	61.9	5.2	20.3	6.7
e	187	81	$C_{17}H_{15}N_7OS_2$	51.38	3.77	24.68	16.12
			(397)	51.3	3.9	24.8	16.3
5a	133	72	$C_{18}H_{22}N_4O_6$	55.38	5.64	14.35	–
			(390)	55.7	5.2	14.5	–
b	101	70	$C_{16}H_{16}N_6O_4$	53.93	4.49	23.59	–
			(356)	53.8	4.7	23.8	–
c	196	63	$C_{16}H_{18}N_4O_4$	58.18	5.45	16.96	–
			(330)	58.0	5.6	17.1	–
d	161	52	$C_{28}H_{28}N_8O_2$	66.14	5.51	22.05	–
			(508)	66.4	5.7	21.8	–
e	150	65	$C_{12}H_{10}N_8S_2$	43.63	3.03	33.93	–
			(330)	43.9	3.5	34.2	–
f	113	70	$C_{12}H_6N_8$	54.96	2.29	42.75	–
			(206)	55.2	2.5	42.9	–

*All synthesized compounds were purified through silica gel column chromatography. Also satisfactory IR spectra were considered.

General procedure

The corresponding quantity of the activated methylene compound (0.01 mol) in ethanol/sod. acetate mixture was added to a stirred solution of the corresponding amine diazonium salt (prepared from the amine hydrochloride or sulfate and the corresponding quantity of sodium nitrite) (0.01 mol). The reaction mixture was left in a refrigerator for 24

hours and the resulting solid product was then collected by filtration and identified as **3a-f**, **4a-e** and **5a-f**, (cf Table III).

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