Synthesis, Structure, Fungicidal and Herbicidal Activity of *S*-(2,6-Dialkylanilido)carbonylmethyl Esters of *N,N*-Disubstituted Dithiocarbamic Acid

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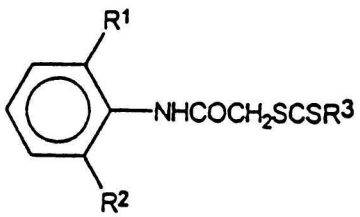
The synthesis of 15 novel *S*-(2,6-dialkylanilido)carbonylmethyl esters of dithiocarbamic acid by the reaction of *N*-chloroacetyl-2,6-dialkylanilines with alkaline dithiocarbamates is described. The structures of prepared esters were confirmed by spectral methods. Fungicidal and herbicidal activity of title esters was assessed and found lesser than those of commercial preparations.

N,N-Disubstituted 2,6-dialkylanilines are one of the most important organic moieties in the design of plant protective agents. Some of these compounds, for instance *alachlor* (*N*-methoxymethyl-2,6-diethylchloroacetanilide), *dimetachlor* (*N*-2-methoxyethyl-2,6-dimethylchloroacetanilide), and *metolachlor* (*N*-methoxyisopropyl-2-ethyl-6-methylchloroacetanilide) [1—3] have already been used as commercial herbicides. Likewise, *metalaxyl* and *benalaxyl* (*N*-(2,6-dimethylphenyl)-*N*-(methoxyacetyl)alanine and *N*-(2,6-dimethylphenyl)-DL-α-alanine) [4, 5] are commercial fungicides. On the other hand, derivatives of dithiocarbamic acid, mainly the Mn^{2+} and Zn^{2+} salts of *N,N'*-ethylenebis(dithiocarbamic) acid belong also to the core inventory of fungicidal preparations [6].

In order to combine and enhance the biological effects, we set out to prepare compounds harbouring both the 2,6-dialkylaniline and dithiocarbamic acid substructures in their molecules and test the resulting fungicidal and herbicidal activity.



I—XV

Formula 1

The prepared target compounds, listed in Table 1, were characterized by the spectral data, summarized in Table 2. The presence of thiocarbonyl group manifested itself by causing nonequivalence of methyl protons in the dimethylamino group and in methylene protons in other substituents. The difference in chemical shifts of a dimethylamino group was thus found to be 0.15, that of a diethylamino group 0.25 (compounds *I, VI, XI*). Alkylamino substituents exert virtually no influence on methylene protons of the —S—CH_2—CO— group, the difference being mere 0.04. Signals of aromatic protons are found at $\delta = 6.7$—7.3.

Infrared spectra of the prepared compounds display a band belonging to carbonyl group ν(C=O) at $\tilde{\nu} = 1705$ cm^{-1} and N—H bands at $\tilde{\nu} = 3260$—3280 cm^{-1}. In the ultraviolet spectra there are $\pi \rightarrow \pi^*$ type maxima at $\lambda = 244$—252 nm and $n \rightarrow \pi^*$ type band at $\lambda = 275$—281 nm. Bathochromic shift of both maxima is decreasing in the order dimethylamino, diethylamino, ethylbutylamino, piperidino, and morpholino substituents, with virtually no effect on the band intensity.

The prepared compounds were tested for contact and systemic fungicidal and herbicidal activity. They showed much less of that activity than the used standards.

EXPERIMENTAL

Melting points were determined with the Mettler apparatus, model SP-8000. ^{1}H NMR spectra of 10 % deuterochloroform solutions were taken with the Tesla

Table 1. Characterization of the Prepared *S*-(2,6-Dialkylanilido)carbomethyl Esters of *N,N*-Disubstituted Dithiocarbamic Acid

Compound	R^1	R^2	R^3	Formula	M_r	w_i(calc.)/% w_i(found)/%		Yield	M.p.
						N	S	%	°C
I	CH_3	CH_3	$(CH_3)_2N$	$C_{13}H_{18}N_2OS_2$	282.40	9.91	22.70	86.0	169.4
						9.80	22.57		
II	CH_3	CH_3	$(C_2H_5)_2N$	$C_{15}H_{22}N_2OS_2$	310.44	9.02	20.65	90.2	98.4
						8.89	20.50		
III	CH_3	CH_3	EtBuN	$C_{15}H_{26}N_2OS_2$	338.46	8.27	18.94	50.0	38.6
						8.15	18.72		
IV	CH_3	CH_3	1-Piperidyl	$C_{16}H_{22}N_2OS_2$	322.42	8.68	19.88	90.8	163.2
						8.80	19.64		
V	CH_3	CH_3	4-Morpholinyl	$C_{15}H_{20}N_2O_2S_2$	324.40	8.63	19.76	92.3	192.3
						8.78	19.94		
VI	CH_3	C_2H_5	$(CH_3)_2N$	$C_{14}H_{20}N_2OS_2$	296.42	9.45	21.63	70.4	144.3
						9.59	21.72		
VII	CH_3	C_2H_5	$(C_2H_5)_2N$	$C_{16}H_{24}N_2OS_2$	324.46	8.63	19.76	72.2	100.6
						8.51	19.68		
VIII	CH_3	C_2H_5	EtBuN	$C_{18}H_{28}N_2OS_2$	352.50	7.94	18.19	61.3	34.1
						7.80	18.26		
IX	CH_3	C_2H_5	1-Piperidyl	$C_{17}H_{24}N_2OS_2$	336.44	8.32	19.05	69.0	149.1
						8.39	19.57		
X	CH_3	C_2H_5	4-Morpholinyl	$C_{16}H_{22}N_2O_2S_2$	338.42	8.27	18.94	69.2	167.6
						8.40	19.07		
XI	C_2H_5	C_2H_5	$(CH_3)_2N$	$C_{15}H_{22}N_2OS_2$	310.44	9.02	20.65	69.0	143.7
						9.22	20.60		
XII	C_2H_5	C_2H_5	$(C_2H_5)_2N$	$C_{17}H_{26}N_2OS_2$	338.48	8.27	18.94	61.1	70.6
						8.13	18.85		
XIII	C_2H_5	C_2H_5	EtBuN	$C_{19}H_{30}N_2OS_2$	366.52	7.42	17.49	64.8	85.9
						7.58	18.00		
XIV	C_2H_5	C_2H_5	1-Piperidyl	$C_{18}H_{26}N_2OS_2$	350.43	8.00	18.29	74.2	146.5
						8.13	18.40		
XV	C_2H_5	C_2H_5	4-Mopholinyl	$C_{17}H_{24}N_2O_2S_2$	352.44	7.94	18.19	75.5	180.1
						7.83	18.08		

spectrometer, model BS 467 (80 MHz) using HMDS as internal standard. Infrared spectra were recorded with the Specord IR-71 instrument (Zeiss, Jena) in tetrachloromethane solutions ($c \approx 0.03$ mol dm^{-3}, cell thickness 1.03 mm). Poorly soluble compounds, such as *I*, *V*, *X*, and *XV* were measured as saturated tetrachloromethane solutions. Ultraviolet spectra of methanolic solutions ($c = 4 \times 10^{-5}$ mol dm^{-3}) in 10 mm cells were taken with a Unicam spectrophotometer, model SP-8000.

The antifungal activity of the prepared compounds was tested against standards Dithane M 45 (a complex of Zn and Mn salts of ethylenebis(dithiocarbamic acid)), Euparen 50 (*N'*-dichlorofluoromethylthio-*N,N*-dimethyl-*N'*-phenylsulfamide), Fundazol 50 (*N*-[1-(butylcarbamoyl)benzimidazolyl]-*O*-methylcarbamate), Bayleton 25 (1-(4-chlorophenoxy)-3,3-dimethyl-1-(1,2,4-triazol-1-yl)butan-2-one) according to established procedures [7]. The tests were performed with phytopathogenic fungi *Phytophthora infestans* DE BY, *Alternaria* species CCM 938, *Botrytis cinerea* CCM 16, and *Fusarium nivale* CCM 570. The herbicidal activity was determined by preemergent into soil and postemergent application on leaves of the following plant species: *Avena sativa* L., *Lepidium sativum* L., *Panicum miliaceum* L., *Fagopyrum vulgare* L. according to the published procedure [8].

The starting *N*-chloroacetyl-2,6-dialkylanilines were prepared by treating the corresponding 2,6-dialkylanilines with chloroacetyl chloride in toluene in the presence of sodium carbonate [9].

N-Chloroacetyl-2,6-dimethylaniline, yield = 90 %, m.p. = 148.3 °C. For $C_{10}H_{12}ClNO$ (M_r = 197.64) w_i(calc.): 17.94 % Cl, 7.08 % N; w_i(found): 18.01 % Cl, 7.12 % N.

N-Chloroacetyl-2-ethyl-6-methylaniline, yield = 88.5 %, m.p. = 114.2 °C. For $C_{11}H_{14}ClNO$ (M_r = 211.66) w_i(calc.): 16.75 % Cl, 6.62 % N; w_i(found): 16.81 % Cl, 6.82 % N.

N-Chloroacetyl-2,6-diethylaniline, yield = 87 %, m.p. = 131.8 °C. For $C_{12}H_{16}ClNO$ (M_r = 225.68) w_i(calc.): 15.70 % Cl, 6.20 % N; w_i(found): 15.79 % Cl, 6.31 % N.

S-(2,6-Dialkylanilido)carbonylmethyl Esters of *N,N*-Disubstituted Dithiocarbamic Acid *I*—*XV*

To the stirred solution of *N*-chloroacetyl-2,6-dialkylaniline (0.05 mol) in 80 cm^3 of acetone the

Table 2. Spectral Data of the Prepared Compounds

Compound	^{1}H NMR, δ								UV	
	$CH_{3\,arom}$ (s)	$CH_3CH_{2\,arom}$ (t)	$CH_3CH_{2\,arom}$ (q)	CH_3N (s)	CH_3CH_2N (t)	CH_3CH_2N (q)	SCH_2CO (s)	CONH	λ_{max}/nm	$\log(\varepsilon/(m^2\ mol^{-1}))$
I	2.17	–	–	3.38	–	–	4.25	8.25	275	3.97
				3.53					244	4.01
II	2.17	–	–	–	1.27	3.76	4.27	8.37	278	3.99
						4.01			248	4.00
III	2.17	–	–	–	1.25	3.76	4.26	8.40	278	3.98
						4.01			248	3.98
IV[a]	2.18	–	–	–	–	–	4.29	8.33	279	4.05
									250	4.02
V[b]	2.18	–	–	–	–	–	4.29	8.13	281	4.05
									252	4.02
VI	2.18	1.10	2.56	3.38	–	–	4.25	8.28	275	3.97
				3.53					244	4.00
VII	2.18	1.22	2.57	–	1.27	3.77	4.27	8.42	278	3.99
						4.02			248	3.98
VIII	2.19	1.12	2.57	–	1.25	3.78	4.27	8.43	278	4.00
						4.03			248	3.99
IX[a]	2.18	1.12	2.57	–	–	–	4.13	8.38	279	4.05
									250	4.00
X[b]	2.18	1.12	2.57	–	–	–	4.30	8.20	281	4.04
									252	4.00
XI	–	1.10	2.55	3.38	–	–	4.27	8.30	275	3.97
				3.53					244	3.99
XII	–	1.11	2.57	–	1.24	3.77	4.28	8.43	278	3.98
						4.02			248	3.98
XIII	–	1.12	2.57	–	1.25	3.78	4.28	8.43	279	4.01
						4.03			249	4.00
XIV[a]	–	1.10	2.55	–	–	–	4.28	8.37	279	4.03
									250	3.98
XV[b]	–	1.11	2.55	–	–	–	4.30	8.17	281	4.03
									252	3.99

δ: *a*) 1.65—1.68 (CH_2), *b*) 3.9—4.5 (CH_2O), 3.5—3.9 (CH_2N), 6.7—7.3 (H_{arom}).

sodium salt of *N,N*-dialkyldithiocarbamic acid (0.055 mol) was added. The reaction mixture was stirred and refluxed for another 3 h, cooled to 10 °C and poured onto ice water (300 cm^3). The precipitated solid was removed, dried and crystallized from either cyclohexane or toluene.

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