Note

Synthesis of Some *O*-Alkyl *O*-(2-Methoxycarbonylphenyl) *N*-Substituted Phosphoramidates as Fungicides

S. GIRI and NIZAMUDDIN

Chemistry Department, University of Gorakhpur, Gorakhpur, U. P., India

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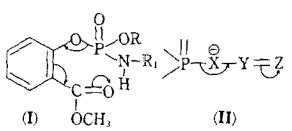
The organophosphorus toxicants act by inhibition of esterases by phosphorylation mechanism of active sites of the enzymes. The intense physiological activity of important pesticides like DDVP, parathion and several others, is in fact related to their high phosphorylating potential.[1] A phosphoramidate of the structure (I) may apparently have enhanced phosphorylating potential by process of weakening of phosphorus-acyloxygen bond as shown and consequently the compound should be an interesting biotoxic agent. The situation obtained in (I) is comparable to P-XYZ system (II)[2] in which the electronegativity of Z, whether self or induced by electrophilic agents and sp^2 hybridised nature of Y tend to enhance the phosphorylating potential of the compound due to weakening of P-X bond.



(I) (II)

In view of these considerations and guided by the fact that some phosphoramidates have wide spectrum of activity possessing at the same time insecticidal, fungicidal and herbicidal properties[3] and that certain 1,2,4-thiadiazolyl phosphates and thiazolyl phosphoramidates have already been introduced as effective pesticides,[4,5] it was presumed that the title compounds might be of interest as pest-control agents. The synthesis and biological testing of compounds described herein were undertaken with this objective.

EXPERIMENTAL

2-Amino-5-aryl-1,3,4-thiadiazoles. These were prepared by cyclisation of arylthiosemicarbazides in the presence of conc. H_2SO_4 following the method of Maffii *et al.*[6]

Substituted-2-aminothiazoles. A mixture of appropriate ketone (0.1 mol), thiourea (0.2 mol) and iodine (0.1 mol) was heated for several hours and the thiazole compound isolated as usual.[7]

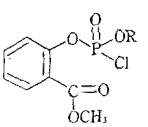
O-Alkyl O-(2-methoxycarbonylphenyl) phosphorochloridates. To methyl salicylate (0.1 mol) dissolved in aqueous sodium hydroxide (10%) was added *O*-alkyl phosphorodichloridate[8] (0.1 mol) slowly. The mixture was kept at room temperature for several hours. The product separating was extracted with ether, washed with dilute $NaHCO_3$ solution followed by water and dried over anhydrous sodium sulfate. After removing ether, the product was distilled. The compounds thus prepared are recorded in Table I.

O-Alkyl O-(2-methoxycarbonylphenyl) N-(5-substituted-1,3,4-thiadiazolyl-2) phosphoramidates. A mixture of 2-amino-5-aryl-1,3,4-thiadiazole (0.01 mol) and *O*-alkyl *O*-(2-methoxycarbonylphenyl) phosphorochloridate (0.01 mol) in pyridine was refluxed on a water bath for 4 hr. It was cooled and poured into water. The precipitated product was filtered and recrystallised from aqueous ethanol. The compounds thus prepared are recorded in Table II.

The corresponding substituted *N*-thiazolyl-2-phosphoramidates were prepared by similar procedure and are recorded in Table II.

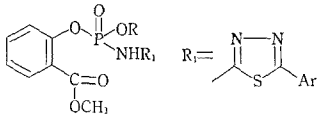
Fungicidal Test. The fungicidal activity of eight

TABLE I. *O*-ALKYL *O*-(2-METHOXYCARBONYLPHENYL) PHOSPHOROCHLORIDATES

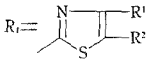


S. No.	R	BP °C	Molecular formula	% Cl Found	% Cl Calcd.
1	O_2H_5	220~26	$C_{10}H_{12}O_5ClP$	12.2	12.7
2	CH_3	195~99	$C_9H_{10}O_5ClP$	13.2	13.4
3	*n*-C_4H_9	201~5	$C_{12}H_6O_5ClP$	11.4	11.5

TABLE II. *O*-ALKYL *O*-(2-METHOXYCARBONYLPHENYL) *N*-(THIADIAZOL/THIAZOL-2-YL) PHOSPHORAMIDATES



S.N.	Ar	R	MP °C	Molecular formula	N (%) Found	N (%) Calcd.	S (%) Found	S (%) Calcd.	Significant bands (cm^{-1}) in IR spectra (KBr disc) P–NH	C=O	C=N	P=O	P–O–C	Aromatic ring
1	Ph	C_2H_5	184	$C_{19}H_{19}O_5N_3PS$	9.81	10.02	7.32	7.63	—	—	—	—	—	—
2	2-ClPh	C_2H_5	170	$C_{18}H_{17}O_5N_3PSCl$	9.00	9.26	6.82	7.05	3000	1680	1620	1290	1030	1590,1450,1460
3	2-ClPh	CH_3	169	$C_{17}H_{15}O_5N_2PSCl$	9.41	9.55	7.00	7.26	3125	1660	1640	1280	985	1580,1500,1460
4	Ph	CH_5	210	$C_{17}H_{16}O_5PN_3S$	10.11	10.37	7.61	7.9	3240	1680	1640	1285	1000	1590,1570,1450
5	Ph	C_4H_9	192	$C_{20}H_{22}O_5PN_3S$	9.20	9.39	6.89	7.11	—	—	—	—	—	—



	R^1	R_2	R	MP °C	Molecular formula	N (%) Found	N (%) Calcd.	S (%) Found	S (%) Calcd.						
6	4-BrPh	H	CH_3	160	$C_{18}H_{16}N_2O_5BrPS$	5.51	5.80	6.42	6.63	—	—	—	—	—	—
7	Ph	H	CH_3	155	$C_{18}H_{17}N_2O_5PS$	6.72	6.94	7.80	7.91	3200	1650	1600	1280	1020	— 1570,1460
8	CH_3	CH_3	CH_3	139	$C_{14}H_{17}N_2O_5PS$	6.63	7.86	8.69	8.89	3100	1660	1620	1300	1030	1595,1490,1442
9	Ph	H	C_2H_5	161	$C_{19}H_{19}N_2O_5PS$	6.52	6.71	7.50	7.67	3200	1680	1620	1260	1060	1600,1560,1450
10	4-BrPh	H	C_2H_5	126	$C_{19}H_{18}N_2O_5BrPS$	5.42	5.64	6.21	6.45	—	—	—	—	—	—

TABLE III.

S. No.	Average percentage inhibition after 96 hr					
	C. miyabeanus Concentration used (ppm)			*A. flavus* Concentration used (ppm)		
	1000	100	10	1000	100	10
1*	62.1	32.3	24.1	65.4	44.8	32.6
2	73.2	43.1	30.2	68.6	56.3	43.1
3	74.4	48.2	28.4	76.4	58.0	49.4
4	61.2	36.6	30.3	72.3	49.4	36.3
5	70.2	32.4	14.2	66.3	51.4	34.6
7	58.3	34.1	15.0	54.4	32.2	19.9
9	50.3	30.2	12.8	48.3	28.4	12.1
10						
Maneb	90.2	79.4	68.0	93.2	80.2	63.4
Carbendazim	82.4	70.3	64.6	96.3	78.0	65.3

* S. No. of compounds corresponds to that in Table II.

compounds was evaluated by agar-growth technique on two organisms, *Cochliobolus miyabeanus* and *Aspergillus niger*. The fungi were allowed to grow on the synthetic agar medium mixed with the test compound. The experiments were repeated in triplicate for each concentration of the compound and a fair number of replicates of the controls were provided. The diameter of the fungus colony after 96 hr was taken as standard for calculating percentage inhibition according to the equation

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

where, C=Diameter of fungus colony (in mm) in control plates

T=Diameter of fungus colony (in mm) in treated plates.

With a view to comparing the results, two commercial fungicides, maneb (Dithane M45) and carbendazim (Baristin) were tested under similar conditions against same fungi. The fungicidal data are recorded in Table III.

RESULTS AND DISCUSSION

Both thiadiazole and thiazole rings possess versatile biological properties and hence it was anticipated that in combination with phosphoramidate entity, they would give compounds of enhanced fungicidal properties. The results obtained herein indicate that three compounds from thiadiazolyl phosphoramidate (Nos. 2, 3, 4) are quite active against *A. flavus* at all concentrations. Although these were also toxic to *C. miyabeanus* at higher concentration, their fungitoxicity diminishes on dilution. Chloro- and bromo-substituents along with a hydrocarbon radical tend to enhance the fungi toxicity of both *N*-thiadiazolyl and *N*-thiazolyl phosphoramidates. This is evident from the fungicidal data of compound Nos. 2, 3, 6 and 10. The *N*-thiazolyl compounds were in general weaker in fungicidal performance, yet those having halo and alkyl substituents were relatively stronger fungicides (Nos. 6 and 10). The commercial fungicides, Dithane M-45 and Bavistin, were far more superior in fungicidal actions against both fungi as compared to the compounds under investigation.

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