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Synthesis of Some Triazole Derivatives as Potential Fungicides†

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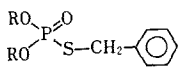
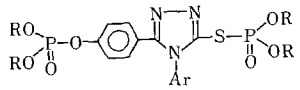
The biological importance of triazole derivatives is amply demonstrated by the fact that various triazoles exhibit anticholinesterase activity,[1] 3-amino-,[2,3] and 3-furfurylideneamino-1, 2, 4-triazoles[4] are herbicidal and wepsyn, a phosphoryl trisamide containing a triazole ring is very effective against powdery mildews.[5,6] The fungicidal value of thiolesters of phosphoric acid is evident from the performance of commercially important compounds like Kitazin (Ia)[7] and Kitazin-P (Ib)[8] which are especially suitable as rice fungicides.

In view of these facts, it was anticipated that *O, O*-dialkyl *S*-[3-(*p*-dialkoxyphosphinyloxy)phenyl-4-aryl-1, 2, 4-triazolyl-5] phosphorothioates (II) containing both a triazole and thiolester moieties might be effective antifungal agents. The synthesis and biological testing of compounds (II) described herein was undertaken with this objective.





Ia $R=R=C_2H_5$

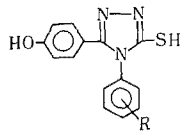
Ib $R=R=$iso-C_3H_7 (II)

EXPERIMENTAL

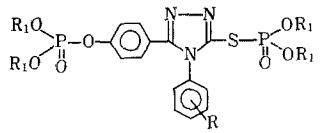
O, O-Dimethyl phosphorochloridate was prepared according to the method of Mastin *et al.*[9] by reacting phosphorusoxychloride (1 M) with methanol (2 M) in presence of pyridine.

O, O-Diethyl phosphorochloridate. was prepared by above method[9] from phosphorus oxychloride (1 M) and ethanol (2 M).

4-Aryl-3-p-hydroxyphenyl-5-mercapto-1, 2, 4-triazoles. were prepared by cyclising a mixture of *p*-hydroxybenzoylhydrazide (1 M) and aryl isothiocyanate (1 M) in alkaline medium.[10] These are recorded in Table I.



O, O-Dialkyl S-[3-(p-dialkoxyphosphinyloxy)phenyl-4-aryl-1, 2, 4-triazolyl-5 phosphorothioates. A mixture of 4-aryl-3-*p*-hydroxyphenyl-5-mercapto-1, 2, 4-triazole (0.1 M) and *O, O*-dialkylphosphorochloridate (0.2 M) was refluxed in acetone for 5~6 hr using pyridine as a catalyst. The reaction mixture was poured into water and product separating was isolated as usual. The compounds thus prepared are recorded in Table II.



Fungicidal test. Six compounds synthesised in the present investigation, were tested against two species of fungi, *viz.*, *A. flavus* and *H. oryzae* by agar-growth technique at three different concentrations and average percentage inhibition after three days was recorded. Most of the compounds were moderately toxic to both the fungal species. However, compound Nos. 3 and 4 were more toxic to *H. oryzae*. The results are recorded in Table III.

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TABLE I.

S. No.	R	Molecular formula	mp °C	%N		%S	
				Found	Calcd.	Found	Calcd.
1	H	$C_{14}H_{11}N_3OS$	183~4	15.63	15.61	11.83	11.89
2	4-CH_3	$C_{15}H_{13}N_3OS$	185	14.72	14.84	11.21	11.31
3	4-OCH_3	$C_{15}H_{13}N_3O_2S$	190	14.30	14.04	10.66	10.70
4	3-Cl	$C_{14}H_{10}N_3OSCl$	184~5	13.85	13.84	10.35	10.54

† Studies on Organophosphorus Pesticides. Part V.

TABLE II.

All melting points are uncorrected.

S. No.	R	R_1	Molecular formula	mp °C	%N		%P		%S		Significant bands (cm^{-1}) in IR absorption spectra			
					Found	Calcd.	Found	Calcd.	Found	Calcd.	P–O	P–O–C (phenyl)	P–S– (carbon)	C–N
1	H	CH_3	$C_{18}H_{21}N_3P_2O_7S$	190~1	8.58	8.66	12.65	12.78	6.54	6.58	1330	1220	560~620	1300
2	4–CH_3	CH_3	$C_{19}H_{23}N_3P_2O_7S$	200	8.41	8.43	12.43	12.45	6.37	6.41	1330	1220	560~620	1300
3	4–OCH_3	CH_3	$C_{19}H_{23}N_3P_2O_8S$	180	8.06	8.15	11.80	12.04	6.15	6.21	1330	1230	585	1260
4	3–Cl	CH_3	$C_{18}H_{20}N_3P_2O_7SCl$	194	8.00	8.08	11.86	11.94	6.08	6.16	—	—	—	—
5	H	C_2H_5	$C_{22}H_{29}N_3P_2O_7S$	195	7.84	7.76	11.52	11.46	6.00	5.91	—	—	—	—
6	4–CH_3	C_2H_5	$C_{23}H_{31}N_3P_2O_7S$	213~4	7.66	7.57	11.23	11.17	5.68	5.77	1330	1245	580	1270
7	4–OCH_3	C_2H_5	$C_{23}H_{31}N_3P_2O_8S$	185	7.38	7.35	11.00	10.86	5.61	5.60	—	—	—	—
8	3–Cl	C_2H_5	$C_{22}H_{28}N_3P_2O_7SCl$	192	7.37	7.30	10.88	10.77	5.62	5.56	1330	1240	610	1260

TABLE III. ANTIFUNGAL ACTIVITY

Compound No.	R	R_1	Average percentage inhibition after three days					
			Organism *A. flavus*			Organism *H. oryzae*		
			1:100	1:1000	1:10,000	1:100	1:1000	1:10,000
1	H	CH_3	52	30	21	73	50	40
3	4-OCH_3	CH_3	61	40	38	98	60	50
4	3-Cl	CH_3	57	43	36	98	73	46
6	4-CH_3	C_2H_5	53	43	29	73	50	32
7	4-OCH_3	C_2H_5	98	40	30	82	68	38
8	3-Cl	C_2H_5	40	30	20	77	55	36

assistance in evaluation of antifungal properties. The help received from C.D.R.I. Lucknow in recording IR spectra of some of the samples is gratefully acknowledged. One of us (Y.S.) is thankful to C.S.I.R. New Delhi for award of Senior Research Fellowship.

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