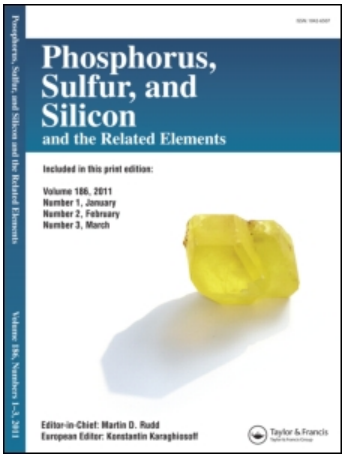

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REACTION OF DIALKYL PHOSPHITES AND THIOL ACIDS WITH UNSATURATED 5-(4-PYRIDYL)-1,3,4 OXADIZOL DERIVATIVES

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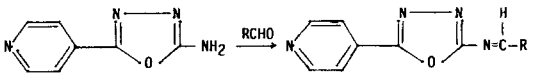
Diethyl phosphite and diphenylphosphinodithioic acid add to carbon-nitrogen double bonds in compounds 4-[5-[(P-methoxybenzylidene) amino]-1,3,4-oxadiazol 2-yl] pyridine I, 4-[5-[(2-thenylidene) amino]-1,3,4-oxadiazol-2-yl] pyridine II and 4-[5-(piperonylidene) amino] 1,3,4-oxadiazol-2-yl] pyridine III to give the corresponding phosphonates I_a, II_a, III_a; and diphenyl phosphinodithioates I_b, II_b, III_b, respectively. The given structures were based upon analytical, chemical and spectroscopic results.

Key Words: 1,3,4-Oxadiazols; Schiff bases; Phosphonates; Diphenyl phosphinodithioates.

RESULTS AND DISCUSSION

1,3,4-Oxa- and thiadiazol derivatives are of great practical significance primarily in drug synthesis. Interesting pharmacological properties[1] are exhibited by 2-amino-5-substituted 1,3,4-oxadiazols[2] and 1,3,4-thiadiazols,[3] which were taken as starting materials to extend the work in this field.

5-(4-Pyridyl)-2-amino-1,3,4-oxadiazol,[4] reacted with aromatic aldehydes, namely 4-methoxy benzaldehyde, 2-thiophene aldehyde, and piperonaldehyde to yield 4-[5-[(*P*-methoxybenzylidene) amino]-1,3,4-oxadiazol-2-yl] pyridine I, 4-[5-[(2-thenylidene) amino]-1,3,4-oxadiazol-2-yl] pyridine II, and 4-[5-(piperonylidene) amino 1,3,4-oxadiazol-2-yl] pyridine III.



I, R = P-anisyl
II, R = 2-thenyl
III, R = piperonyl

Compounds I, II, and III were allowed to react with diethyl phosphite (DEP) in the absence of solvent at 100°C to give the diethylphosphonate adducts I_a, II_a, and III_a. The mechanism involved the addition of the phosphite radical to the double bond followed by hydrogen abstraction from the phosphite ester.[5] The I.R. spectrum of compound II_a (using kBr) as an example was quite consistent with the assigned structure. It showed bands at 3400 cm^{-1} (–NH), 1600 cm^{-1}

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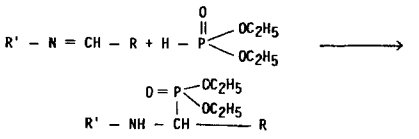
(aromatic band), 1250 cm^{-1} (P=0), and at 1050 cm^{-1} (P—O C_2H_5). Its NMR showed aromatic protons (7 H) in the region δ8.0–δ9.0 ppm, methine proton at δ4.1 ppm; signals at δ3.6 ppm (4 H, ethoxy CH_2, q), δ1.6 ppm (6 H, ethoxy CH_3, t), and at δ12.7 ppm a signal due to the NH proton.



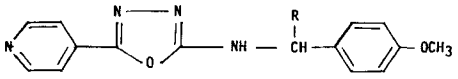
I, R = anisyl
II, R = 2-thenyl
III, R = piperonyl

R' = 5(4-pyridyl)-1,3,4-oxadiazol-2-yl

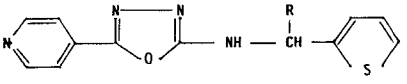
The addition of phosphorus compounds containing the >P(S)SH grouping to the carbon–carbon multiple linkage has been used to prepare varieties of sulphides,[6] a number of which are important potential insecticides.[7] Diphenylphosphinodithioic acid now has been found to add to the exocyclic conjugated carbon-nitrogen double bond in I, II, and III yielding coloured crystalline 1:1 adducts formulated as I_b, II_b, and III_b.

The structures of the aforementioned compounds were confirmed by elemental analyses (Table I), molecular weight determination (MS), I.R., and ^{1}H NMR spectra.

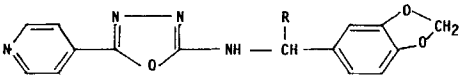
The I.R. spectrum (using kBr) of adduct III_b was identical to the proposed structure: It revealed the absence of the (>C=N–) absorption band and disclosed the presence of an (–NH) band at 3300 cm^{-1}. The NMR spectrum of



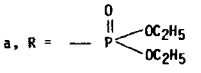
$I_{a,b}$



$II_{a,b}$



$III_{a,b}$

a, R = 

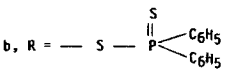
b, R = 

TABLE I

Physical constants and analytical data of the new compounds

Comp.	M.P. °C	Solvent of crystallization	Yield %	Formula Mol. wt.	Analysis Calc./Found C	H	N	S	P
I	162	Methanol water	75	$C_{15}H_{12}N_4O_2$ (280)	64.29 63.85	4.29 4.01	20.00 19.65	— —	— —
II	229	Ethanol	70	$C_{12}H_8N_4OS$ (256)	56.25 55.82	3.13 2.95	21.88 21.26	12.50 12.20	— —
III	227	Ethanol	70	$C_{15}H_{10}N_4O_3$ (294)	61.23 61.52	3.40 3.51	19.05 18.70	— —	— —
I_a	190	Benzene	60	$C_{19}H_{23}N_4O_5P$ (418)	68.90 68.63	5.50 5.38	13.40 13.18	— —	7.42 7.22
II_a	245	Chloroform ether	65	$C_{16}H_{19}N_4O_4SP$ (394)	48.73 48.32	4.82 4.29	14.21 13.80	8.12 7.72	7.89 7.36
III_a	170	Benzene pet-ether	60	$C_{19}H_{21}N_4O_6P$ (432)	52.78 52.96	4.86 4.42	12.97 12.60	— —	7.18 6.88
I_b	183	Ethanol	80	$C_{27}H_{23}N_4S_2O_2P$ (530)	61.13 61.40	4.34 3.95	10.57 10.22	12.08 11.58	5.85 5.71
II_b	187	Ethanol	85	$C_{24}H_{19}N_4S_3OP$ (506)	56.92 57.29	3.16 3.03	11.07 10.86	18.97 18.52	6.13 5.91
III_b	190	Ethanol	85	$C_{27}H_{21}N_4S_2O_3P$ (544)	59.56 59.34	3.86 3.71	10.29 10.01	11.77 11.42	6.98 6.71

the same compound III_b in $CDCl_3$ showed that aromatic protons fall in the region δ6.9–δ8.8 ppm (17 H), a methine proton at δ4.7 ppm, methylene protons at δ6.1 ppm, and at δ12.0 ppm, a broad singlet due to the NH proton.

Taking adduct III_b as an example, this compound regenerated the starting material III when heated above its melting point or upon treatment with alcoholic hydrochloric acid.

EXPERIMENTAL

All melting points were uncorrected. Benzene (thiophene free) and petroleum ether (60–80°) were dried over sodium. Dialkyl phosphite was prepared according to an established procedure[8] and twice distilled before use. Diphenylphosphinodithioic acid was freshly prepared[9] and twice crystallized before use.

The I.R. spectra (run in kBr and expressed in cm^{-1}) were recorded with a Beckmann 4220 Infracord Model and the 'H NMR spectra were measured (in $CDCl_3$ or DMSO-d_6 and expressed in the δ-scale) at 60 MHZ or 90 MHZ on a Varian instrument using TMS as an internal standard. The mass spectra were performed at 70 eV using a Varian MAT 112 Mass spectrometer.

Action of aldehydes on 2-amino-5-(4-pyridyl)-1,3,4-oxadiazol. To a solution of 2-amino-5-(4-pyridyl)-1,3,4-oxadiazol (0.1 mol) in absolute ethanol (20 ml), 2 drops of triethylamine and *p*-methoxybenzaldehyde (0.1 mol) were added. The reaction mixture was refluxed for 6 hrs, cooled, and the precipitate that formed was filtered and crystallized from the proper solvent to give compound I.

The I.R. spectrum of compound I (using kBr) showed characteristic bands at 1650 cm^{-1} (>C=N–), 1600 cm^{-1} (aromatic band), and 2840–2820 cm^{-1} (–OCH_3).[10]

The NMR spectrum of compound I (in DMSO-d_6), taken as an example for 'H NMR, showed 8 aromatic protons in the region between δ7.8–δ8.8 ppm, δ3.3 ppm (–OCH_3), and the methine proton at δ4.1 ppm.[11]

In a similar manner, compounds II and III were obtained by the addition of 2-thiophene aldehyde and piperonaldehyde respectively (Table I).

Diethyl [∝-[(*5-(4-pyrdiyl)-1,3,4-oxadiazol-2-yl*] *amino*] *P-anisyl phosphonate* I_a. A mixture of 4-[5-[(*P*-methoxybenzylidene) amino)-1,3,4-oxadiazol-2-yl] pyridine I (0.005 mol) and diethyl phosphite (0.05 mol) was heated at 100°C for 12 hrs. After removal of the volatile materials in vacuo, the residual substance was collected and recrystallized from the proper solvent to give adduct I_a.

By the same procedure adducts II_a and III_a were obtained by reaction of II and III respectively (Table I).

Adducts I_a, II_a, and III_a gave a negative ferric chloride colour reaction and were insoluble in aqueous sodium hydroxide.

∝-[[*5-(4-Pyridyl-1,3,4-oxadiazol-2-yl*)] *amino*]-*P-anisyl diphenylphosphinodithioate* I_b. To a solution of I (0.1 mol) in benzene (50 ml) was added diphenylphosphinodithioic acid (0.1 mol). The reaction mixture was boiled under reflux for 12 hrs. The mixture was left to cool and the product so obtained was filtered and crystallized to give adduct I_b.

In a similar manner, adducts II_b and III_b were obtained by the reaction of II and III respectively (Table I).

Degradation experiments with dithioates III

a) *Thermolysis.* Compound III_b, taken as example (0.2 g) was heated at 230° (bath temperature) for 30 minutes. The residue was extracted with hot ethanol. After cooling, the ethanol solution deposited a pale yellow crystalline substance which was identified as 4-[5-(piperonylidene) amino]-1,3,4-oxadiazol-2-yl] pyridine III (m.p. and mixed m.p.).

b) *Action of hydrochloric acid.* Adduct III_b (0.2 g) was refluxed with alcoholic hydrochloric acid (5 ml of hydrochloric acid sp. gr. 1.18 and 15 ml ethanol) for 6 hrs. The reaction mixture was cooled and the precipitate which separated after neutralization with sodium bicarbonate was collected and crystallized from ethanol to give 4-[5-(piperonylidene) amino]-1,3,4-oxadiazol-2-yl] pyridine III (m.p. and mixed m.p.).

REFERENCES

1. E. H. Northey, "The Sulfonamides and Allied Compounds", Reinhold Publishing Corp. New York, 1948, pps. 35, 36, 92, 93, 408.
2. R. B. Pathak, U. Strivastava and S. C. Bahel, *J. Indian Chem. Soc.*, **59,** 776 (1982).
3. G. Malcolm Dyson and Perry May, "May's Chemistry of Synthetic Drugs". 5th Ed., Longmans, 1959, p. 481.
4. S. G. Boots and C. C. Cheng, J. Heterocyclic Chem., 4, 272 (1967), W. R. Sherman, *J. Org. Chem.*, **26,** 88 (1961).
5. A. R.. Stiles, W. E. Vanghan and F. F. Rust, *J.. Am. Chem. Soc.*, **80,** 714 (1958).
6. A. C. Cope, Organic Reactions "Vol. XIII", John Wiley and Sons Inc., New York, N.Y., p. 150 (1963).
7. W. H. Mueller and A. A. Oswald, *J. Org. Chem.*, **31,** 1894 (1966).
8. A. H. Ford Moore and J. Perry, *Organic Syntheses,* **31,** 111 (1951).
9. Wm. A. Higgins, P. W. Vogel and W. G. Graig, *J. Am. Chem. Soc.*, **77,** 1864 (1955).
10. L. J. Bellamy, "The Infrared Spectra of Complex Molecules", John Wiley, New York, p. 311 (1964).
11. F. Ramirez, O. P. Madan and S. R. Heller, *J. Am. Chem. Soc.*, **87,** 731 (1965).