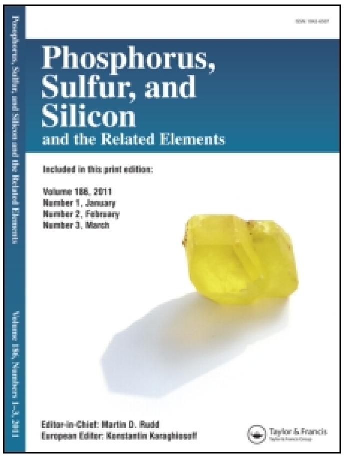

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THE BEHAVIOR OF 5-(4-PYRIDYL)-2-THIONO-1,3,4-OXADIOAZOLE TOWARDS WITTIG-HORNER REAGENTS

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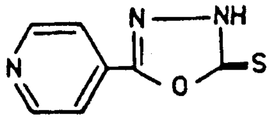
Wittig-Horner reagents (**2a–c**) react with 5-(4-pyridyl)-2-thiono-1,3,4-oxadiazole (**1**) yielding the new adducts (**3a–c**). Structural reasoning for compounds **3** was based on compatible analytical and spectral data. The mechanism that accounts for the formation of **3** is discussed.

Key words: 5-(4-Pyridyl)-2-thiono-1,3,4-oxadiazole; Wittig-Horner reagents; 5-(4-pyridyl)-2-cyanomethylene-diethyl phosphonate-1,3,4-oxadiazole; methylacetate-5-(4-pyridyl)-B-methylacetate-2-propene-1,3,4-oxadiazole; and 5-(4-pyridyl)-2-ethylacetate-1,3,4-oxadiazole.

INTRODUCTION

It has been reported that substituted 1,3,4-oxadiazole derivatives possess antibacterial, fungicidal and pharmacological properties,[1–5] hence the synthesis of new compounds incorporating such nuclei was undertaken in view of possible bactericidal and fungicidal activity. Our continuing interest in the reaction of Wittig and Wittig-Horner reagents for the production of novel, synthetically useful ylides and new heterocyclic systems[6–12] led us to investigate the reactivity of 5-(4-pyridyl)-2-thiono-1,3,4-oxadiazole (**1**) towards a number of Wittig-Horner reagents of type (**2**).



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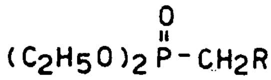

$$(C_2H_5O)_2\overset{O}{\overset{\|}{P}}-CH_2R$$

2a, R = CN
b, R = $COOCH_3$
c, R = $COOC_2H_5$

RESULTS AND DISCUSSION

When 5-(4-pyridyl)-2-thiono-1,3,4-oxadiazole (**1**) was treated with one equivalent of diethyl (cyanomethyl) phosphonate (**2a**) in the presence of alcoholic sodium

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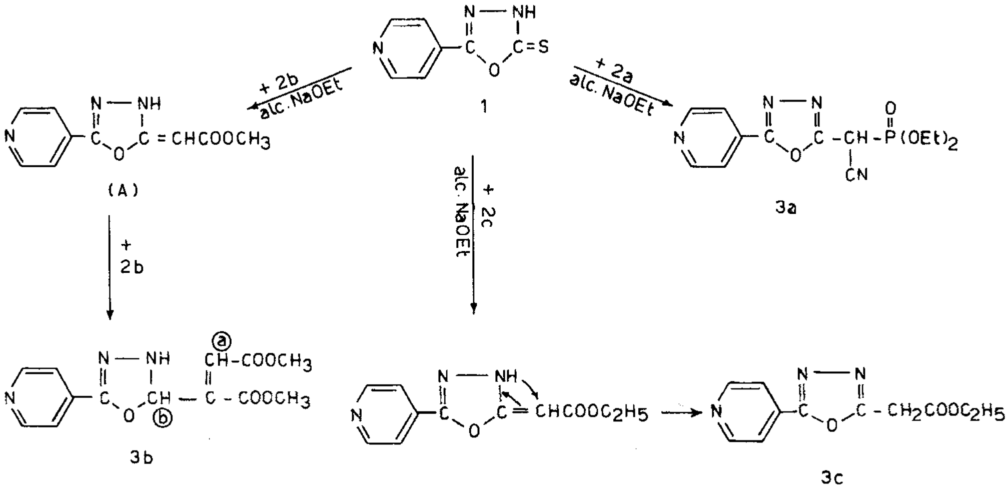
ethoxide solution at 60–70°C for 4 hours, adduct **3a** was isolated in good yields (Scheme I). The structure of the new compound **3a** is assignable from its analysis, IR, ^{1}H NMR and mass spectroscopic data. Elemental and mass spectral analyses for compound **3a** corresponded to an empirical formula of $C_{13}H_{15}N_4O_4P$. Its IR spectrum, in KBr, exhibits strong absorption bands at 1610 cm^{-1} (C=N), 1620 (C=N), 1230 cm^{-1} (P=O, bonded)[13] and at 1050 cm^{-1} (P—O—C_2H_5). Moreover, the $\rangle$C=S band present around 1260 cm^{-1} in the spectrum of **1** was absent in the IR spectrum of **3a**. ^{1}H NMR spectrum of 5-(4-pyridyl)-2-cyanomethylene-diethyl phosphonate-1,3,4-oxadiazole (**3a**) showed signals at δ = 0.85 (3H, CH_3 ethoxy, t), 1.3 (3H, CH_3-ethoxy-t), 4.45 (4H, two CH_2-ethoxy, m) corresponding to the two ethoxy groups attached to the phosphorus atom. Moreover, the ^{1}H NMR spectrum of compound **3a** showed signals centered at 2.95 ppm (d with J_{HP} = 10 Hz) for the methylene protons attached to phosphorus. The four methylene protons of the pyridyl ring appeared as two doublets centered at δ = 7.9 and 8.3 with coupling constant value of 6.05 Hz.[14] The mass spectrum of compound **3a** showed the molecular ion peak at m/e 322. The mechanism proposed to account for the formation of adduct **3a** is shown in (Scheme I). 5-(4-Pyridyl)-2-thiono-1,3,4-oxadiazole (**1**) reacts with one mol of diethyl (cyanomethyl) phosphonate (**2a**) to give the stable-phosphonate **3a** through loss of hydrogen sulfide (Scheme I).

The reaction of **1** with methyl diethylphosphonoacetate (**2b**) was also investigated. When **1** was allowed to react with one equivalent of **2b** in the presence of alcoholic sodium ethoxide solution at 60–70°C for 5 hours, adduct **3b** and some unchanged oxadiazole **1** were isolated. Carrying out the reaction using two mols of Wittig-Horner reagent (**2b**) instead of one, led to the formation of **3b** in good yields. Reasons for structure **3b** were: (a) Correct elemental analysis; (b) the IR spectrum of methylacetate-5-(4-pyridyl)-B-methylacetate-2-propene-1,3,4-oxadiazole (**3b**) shows bands at 1620 (C=N), 3010 (NH) and at 1690, 1700 cm^{-1} (C=O). The ^{1}H NMR spectrum of **3b** shows two singlets at 6.8 and 7 ppm corresponding



Scheme I

to the two methine protons (a) and (b), respectively (Scheme I). The four methylene protons of the pyridyl ring appeared as two doublets centered at 7.9 and 8.3 ppm with J_{HH} = 6 Hz. The exchangeable (D_2O) proton (NH) appears as a broad singlet at 8.53 ppm. The mass spectrum of compound **3b** showed the molecular ion peak at m/e 291.

Adduct **3b** can be obtained via thiocarbonyl olefination by one mole of Wittig-Horner reagent (**2b**) to give the intermediate (A) which adds another molecule of methyldiethylphosphonoacetate (**2b**) by Michaelis addition followed by expulsion of dialkyl phosphate ion to yield the final product **3b** (Scheme I).

We have found that the reaction of triethylphosphonoacetate (**2c**) with 5-(4-pyridyl)-2-thiono-1,3,4-oxadiazole (**1**), in the presence of alcoholic sodium ethoxide solution, proceeds at 60–70°C to give a chromatographically pure adduct formulated as **3c** (Scheme I). The structure of the new compound **3c** is assignable from its analysis, IR, ^1H NMR and mass spectral data. Elemental and mass spectral analyses for compound **3c** corresponded to an empirical formula of $C_{11}H_{11}N_3O_3$. Its IR spectrum, in KBr, exhibits strong absorption bands at 1610 cm^{-1} (C=N), 1620 (C=N) and at 1690 cm^{-1} characteristic for the ester carbonyl band.

On the other hand, the C=S band present around 1260 cm^{-1} in the spectrum of **1** was absent in the IR spectrum of **3c**. ^1H NMR spectrum of 5-(4-pyridyl)-2-ethylacetate-1,3,4-oxadiazole (**3c**) showed signals at δ = 1.5 (3H, ethoxy-CH_3, t), at 3.35 (2H, ethoxy-CH_2, q) and at 1.8 (2H, CH_2, s). The mass spectrum of compound **3c** showed the molecular ion peak at m/e 233. A possible explanation for the course of the reaction of triethylphosphonoacetate (**2c**) with **1** is shown in (Scheme I). Adduct **3c** can be obtained via thiocarbonyl olefination by one molecule of the Wittig-Horner reagent (**2c**) to give the olefinic adduct **3c** and dialkylphosphate ion.

The significance of these findings is not only the discovery of a new pattern of Wittig-Horner reaction but also the establishment of a novel method for the synthesis of products **3a–c**. Noteworthy is that 5-(4-pyridyl)-2-thiono-1,3,4-oxadiazole (**1**) behaves towards Wittig-Horner reagents in a manner different from that already reported by us with Wittig reagents.[15]

EXPERIMENTAL

All melting points are uncorrected. Wittig-Horner reagents were prepared by means of the Michaelis-Arbuzov reaction.[16] The IR spectra were measured in KBr, on a Perkin-Elmer Infracord Spectrometer Model 157 (Grating). The ^1H NMR spectra were run on a "Varian Spectrophotometry" at 200 MHz, using TMS an an internal reference. The mass spectra were run at 70 eV on a Kratos MS-50 equipment provided with a data system.

Reaction of diethyl (cyanomethyl) phosphonate (**2a**) *with 5-(4-pyridyl)-2-thiono-1,3,4-oxadiazole* (**1**). A solution of 2 mols of sodium ethoxide in absolute ethanol was treated with an equimolar amount of the phosphonate (**2a**), after a while 1 mol of the starting compound (**1**) was added and the resulting reaction mixture was allowed to heat on a water bath at 60–70°C for 4 hr. The reaction mixture was allowed to cool to room temperature, then poured on a small amount of water, extracted with chloroform (3 × 20 ml), and the extract was evaporated under reduced pressure. The residual material was recrystallized from chloroform/pet. ether b.r. 60–80°C to give 5-(4-pyridyl)-2-cyanomethylene-diethyl phosphonate-1,3,4-oxadiazole (**3a**) as pale yellow crystals in 72% yield m.p. 63–65°C.

Anal. Calcd. for $C_{13}H_{15}N_4O_4P$ (322.255) C, 48.45; H, 4.69; N, 17.39; P, 9.61. Found: C, 48.41; H, 4.60; N, 17.37 P, 9.63.

Reaction of methyl diethylphosphonoacetate (**2b**) *with 5-(4-pyridyl)-2-thiono-1,3,4-oxadiazole* (**1**). The same method was used to react the phosphonate (**2b**) (0.002 mol) with the starting material (0.001 mol) (**1**) to give methylacetate-5-(4-pyridyl)-B-methylacetate-2-propene-1,3,4-oxadiazole (**3b**) as yellowish brown crystals (from chloroform/pet. ether) in 67% yield, m.p. 55–57°C.

Anal. Calcd. for $C_{13}H_{13}N_3O_5$ (291.262) C, 53.61; H, 4.50; N, 14.43. Found: C, 53.55; H, 4.58; N, 14.45.

Reaction of triethylphosphonoacetate (**2c**) *with 5-(4-pyridyl)-2-thiono-1,3,4-oxadiazole* (**1**). To a suspension of oxadiazole (**1**) (0.34 g, 0.002 mol) in ethanol (10 ml), was added phosphonate (**2c**) (0.44 g, 0.002 mol) and an equimolecular amount of sodium ethoxide. The reaction mixture was refluxed on a water bath for 5 hrs, then cooled to room temperature, poured on a small amount of water, extracted twice with ethyl acetate. The extract was evaporated till dryness and the residue was recrystallized from acetone/pet. ether to give 5-(4-pyridyl)-2-ethylacetate-1,3,4-oxadiazole (**3c**) as deep yellow crystals, in 75% yield, m.p. 78–80°C.

Anal. Calcd. for $C_{11}H_{11}N_3O_3$ (233.222) C, 56.65; H, 4.75; N, 18.02. Found: C, 56.60; H, 4.78; N, 18.00.

REFERENCES

1. W. R. Shermann, *J. Org. Chem.*, **26,** 88 (1961).
2. A. E. Wilder-Smith, E. Frommel and S. Arzneimittel, *Forsch*, **13,** 388 (1963).
3. M. I. Siddiqui and M. T. Comrie, *J. Chem. Soc.*, 2798 (1971).
4. D. J. Jones, S. Squires and K. R. H. Wooldrig, *J. Med. Chem.*, **8,** 676 (1965).
5. A. K. Bhat, *Indian J. Chem.*, **5,** 397 (1967).
6. L. S. Boulos and M. H. N. Arsanious, *Phosphorus and Sulfur*, **36,** 23 (1988).
7. L. S. Boulos and M. H. N. Arsanious, *Phosphorus and Sulfur*, **42,** 47 (1989).
8. L. S. Boulos, Y. O. El-Khoshnieh and M. H. N. Arsanious, *Phosphorus and Sulfur*, **47,** 199 (1990).
9. L. S. Boulos, Atef. G. Hanna, I. T. Hennawy and M. H. N. Arsanious, *Phosphorus and Sulfur*, **57,** 181 (1991).
10. A. A. El-Kateb, L. S. Boulos, I. T. Hennawy and H. A. Abdel. Malek, *Phosphorus and Sulfur*, **60,** 275 (1991).
11. L. S. Boulos and Naglaa M. Abd El-Rahman, *Phosphorus and Sulfur*, **62,** 163 (1991).
12. L. S. Boulos and Naglaa M. Abd El-Rahman, *Phosphorus and Sulfur*, **68,** 241 (1992).
13. L. J. Bellamy, "The Infra-red Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, p. 311 (1964).
14. R. N. Silverstein and G. C. Bassler, "Spectroscopic Identification of Organic Compounds (2nd Edition, p. 145), Wiley, New York (1967).
15. L. S. Boulos and I. T. Hennaway, *Phosphorus and Sulfur*, **56**, 65 (1991).
16. G. M. Kosolapoff, "Organophosphorus Compounds," 1st ed. J. Wiley and Sons, Inc., New York, N.Y., Chap. 7 (1950).