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 $\alpha,\beta$ -Unsaturated-1,2,5-thiadiazoles

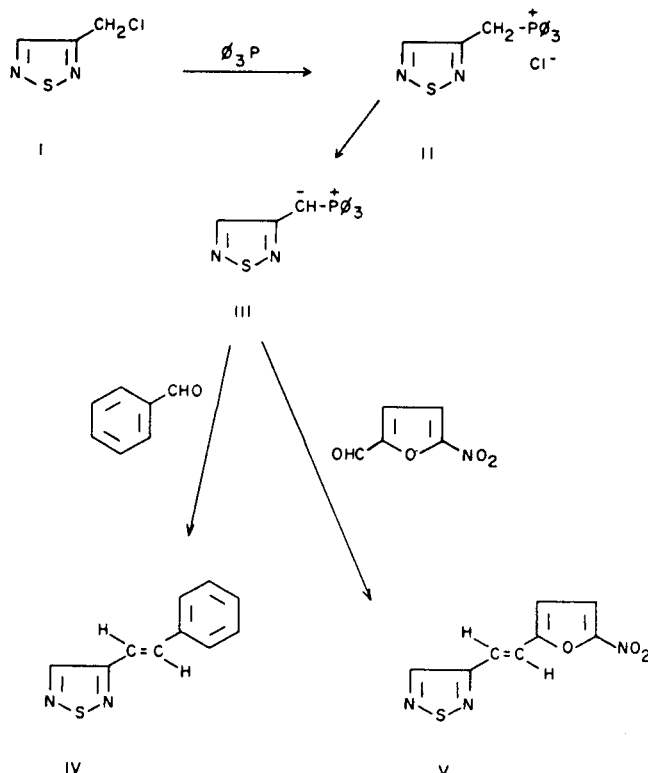
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In conjunction with our investigation of the chemistry of 1,2,5-thiadiazoles it was noted that few convenient synthetic routes to  $\alpha,\beta$ -unsaturated-1,2,5-thiadiazoles were available (1). We wish to report a facile synthesis of this class of 1,2,5-thiadiazoles employing the Wittig Reaction (2). The utilization of heterocyclic phosphoranes in the Wittig Reaction has received little attention in the literature, although Baker and Jordaan recently reported the successful condensation of 2-amino-4-hydroxy-5-phenylbutyl-6-pyrimidylmethylene triphenylphosphorane with several representative aldehydes (3).

The synthesis of 3-chloromethyl-1,2,5-thiadiazole (1) was readily effected by the procedure of Gill (1). In this procedure, 1,2,5-thiadiazole-3-carboxylic acid (4,5) is converted to the corresponding acid chloride. This in turn is reduced with sodium borohydride to the corresponding carbinol, which when treated with thionyl chloride affords good yields of 3-chloromethyl-1,2,5-thiadiazole (1). Condensation of halide I with triphenylphosphine took place smoothly in refluxing toluene, giving 3-(1,2,5-thiadiazolylmethyl)triphenylphosphonium chloride (II) in 66% yield. It was found most convenient to prepare 3-thiadiazolylmethylene triphenylphosphorane (III) by the addition of stoichiometric quantities of 2.5 *N* sodium hydroxide to an efficiently stirred mixture of benzene and aqueous phosphonium salt II. After drying, the benzene solution of the phosphorane may be treated with the desired aldehyde and refluxed for one hour to effect condensation. In this manner benzaldehyde yielded  $\beta$ -[3-(1,2,5-thiadiazolyl)]styrene (IV) in 52% yield; m.p., 51.5-52°. Pertinent infrared bands were: 1634  $\text{cm}^{-1}$  (C=C); 1575, 1495  $\text{cm}^{-1}$  (arom. C=C); 962  $\text{cm}^{-1}$  ( $\text{H}-\text{C}=\text{C}-\text{H}$ , *trans*). The N.M.R. spectrum of IV showed: AB quartet, 7.40 p.p.m.,  $J_{AB} = 12.0$  c.p.s.; multiplet, 7.39 p.p.m.; singlet, 8.65 p.p.m. The proximity of the olefinic and benzenoid protons precluded their separate integration, but their combined relative intensities were in the correct ratio to that of the lone thiadiazole proton (7/1).

Similarly, phosphorane III reacted smoothly with 5-nitro-2-furaldehyde to form  $\beta$ -[3-(1,2,5-thiadiazolyl)]-3-vinyl-5-nitrofuran (V) in 63% yield; m.p., 127-128°. Relevant infrared bands were noted at: 1569  $\text{cm}^{-1}$  (C=C). 1490, 1350  $\text{cm}^{-1}$  (arom.  $\text{NO}_2$ ); 958  $\text{cm}^{-1}$  ( $\text{H}-\text{C}=\text{C}-\text{H}$ ,

*trans*). N.M.R. spectrum: AB quartet, 7.46 p.p.m.,  $J_{AB} = 16$  c.p.s., rel. int. 2; AB quartet, 7.00 p.p.m.,  $J_{AB} = 4.0$  c.p.s., rel. int. 2; singlet, 8.69 p.p.m., rel. int. 1.



In both IV and V, the magnitude of the olefinic proton coupling constant reinforces the assigned *trans* configuration from infrared data.

## EXPERIMENTAL

Infrared spectra were determined as chloroform solutions on a Perkin-Elmer model 257 Spectrophotometer, and N.M.R. spectra on a Varian Associates model A-60A. All N.M.R. spectra were determined in deuteriochloroform employing tetramethylsilane as an internal standard.

## 3-Hydroxymethyl-1,2,5-thiadiazole (1).

A solution of 3.00 g. (0.023 mole) 1,2,5-thiadiazole-3-carboxylic acid (4,5) in 50 ml. of benzene was treated with 3.33 g. (0.028 mole) of thionyl chloride. The mixture was refluxed with stirring for 12 hours. The solvent was evaporated *in vacuo*, leaving a tan

oil, 3.13 g. (92%). This crude acid chloride was dissolved in 30 ml. of anhydrous dioxane and added dropwise with stirring to a suspension of 0.90 g. (0.023 mole) of sodium borohydride in 30 ml. of dioxane. The resulting mixture was refluxed with stirring for 18 hours. After cooling, the reaction mixture was treated with 40 ml. of 5% sodium carbonate solution and the mixture refluxed with stirring for 45 minutes. After cooling, this solution was extracted with 4 x 125 ml. of diethyl ether, the extracts dried over magnesium sulfate, and evaporated under reduced pressure leaving a yellow oil, 2.10 g. (86%) of crude 3-hydroxymethyl-1,2,5-thiadiazole. The infrared and N.M.R. spectra of this material were identical to those reported by Gill (1).

#### 3-Chloromethyl-1,2,5-thiadiazole (1) (I).

A solution of 2.00 g. (0.017 mole) of 3-hydroxymethyl-1,2,5-thiadiazole in 20 ml. of benzene was treated with 3.45 g. (0.028 mole) of thionyl chloride and the mixture refluxed with stirring for 17 hours. The brown solution was then evaporated under reduced pressure (water aspirator) at 35° leaving 2.04 g. (88%) of 3-chloromethyl-1,2,5-thiadiazole exhibiting infrared and N.M.R. spectra identical to those reported by Gill (1).

#### 3-(1,2,5-Thiadiazolylmethyl)triphenylphosphonium Chloride (II).

A mixture of 3-chloromethyl-1,2,5-thiadiazole (1), 2.00 g. (0.014 mole), triphenylphosphine, 4.00 g. (0.018 mole), and 30 ml. of anhydrous toluene was refluxed with stirring for four hours. After cooling to 5°, the off-white crystalline precipitate was isolated, washed with 10 ml. of toluene and dried. In this manner, 3.70 g. (66%) of phosphonium salt II was obtained, m.p., 280-284°. An analytical sample was prepared by recrystallization from acetonitrile and melted at 283.5-285°.

Pertinent infrared bands were: 1590, 1488  $\text{cm}^{-1}$  (C=C arom.), 1438, 1110, 995  $\text{cm}^{-1}$  (P-C, arom.).

The N.M.R. spectrum showed: singlet, 8.95 p.p.m., rel. int. 1; multiplet, 7.73 p.p.m., rel. int. 15; doublet 6.38 p.p.m., rel. int. 2, (J = 15 c.p.s.).

*Anal.* Calcd. for  $\text{C}_{21}\text{H}_{18}\text{ClN}_2\text{PS}$ : C, 63.55; H, 4.57; N, 7.06. Found: C, 63.27; H, 4.64; N, 7.23.

#### $\beta$ -[3-(1,2,5-Thiadiazolyl)]styrene (IV).

A separatory funnel was charged with a solution of 0.85 g. (0.0021 mole) of phosphonium salt II in 25 ml. of distilled water plus 50 ml. of benzene. To this mixture was added 2 ml. of 25 N sodium hydroxide and the solution shaken well. After separation of the benzene layer, the aqueous phase was re-extracted with two

30 ml. portions of benzene. The combined yellow benzene extracts were dried over magnesium sulfate and after filtering were stored under nitrogen. (Stored in this fashion, benzene solution of phosphorane III have been kept for several days with no observable deterioration). To the benzene solution of III was added 0.30 g. (0.0028 mole) of freshly distilled benzaldehyde and the mixture refluxed with stirring for one hour. The now colorless solution was evaporated to dryness under reduced pressure leaving a yellow oil. This mixture was chromatographed on Merck neutral alumina (1:1, v/v, hexane/benzene eluent) and afforded 0.21 g. (52%) of IV in fractions 5-7, m.p., 50-52°. Column dimensions were 24 x 3 cm. and fraction volumes were 50 ml. An analytical sample was obtained by recrystallization from aqueous methanol and melted at 51.5-52°.

*Anal.* Calcd. for  $\text{C}_{10}\text{H}_8\text{N}_2\text{S}$ : C, 63.80; H, 4.28; N, 14.89. Found: C, 63.66; H, 3.89; N, 14.92.

#### $\beta$ -[3-(1,2,5-Thiadiazolyl)]-2-vinyl-5-nitrofuran (V).

A dried benzene solution of phosphorane III was prepared as described above from 1.45 g. (0.0036 mole) of phosphonium salt II. To this solution was added 0.57 g. (0.0040 mole) of 5-nitro-2-furaldehyde and the mixture refluxed with stirring for one hour. The benzene was evaporated under reduced pressure leaving a gummy solid residue. This material was dissolved in 6 ml. of hot methanol and allowed to slowly cool. The precipitated yellow needles were isolated, washed with 2 ml. of cold methanol and air dried. In this manner 0.47 g. (63%) of V was obtained, m.p., 125-128°. A second recrystallization from methanol gave V melting at 127-128°.

*Anal.* Calcd. for  $\text{C}_8\text{H}_5\text{N}_3\text{O}_3\text{S}$ : C, 43.05; H, 2.26; N, 18.83. Found: C, 43.05; H, 2.10; N, 18.76.

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