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A. DE MUNNO (\*), V. BERTINI (\*\*)

ACTION OF N-BROMOSUCCINIMIDE  
ON 3-METHYL-1, 2, 5-THIADIAZOLE (\*\*\*)

**Riassunto** — *Azione della N-bromosuccinimide sul 3-metil-1,2,5-tiadiazolo.* Viene esaminata la reazione di bromurazione del 3-metil-1,2,5-tiadiazolo con N-bromosuccinimide che fornisce miscele di 3-bromometil-1,2,5-tiadiazolo, 3-dibromometil-1,2,5-tiadiazolo e 3-tribromometil-1,2,5-tiadiazolo. I bromometilderivati ottenuti vengono esaminati dal punto di vista delle loro proprietà chimiche e fisiche.

**Abstract** — The radical bromination of 3-methyl-1,2,5-thiadiazole which yields mixtures of 3-bromomethyl-1,2,5-thiadiazole, 3-dibromomethyl-1,2,5-thiadiazole, and 3-tribromomethyl-1,2,5-thiadiazole is reported. Some chemical and physical properties of the obtained bromomethyl derivatives are examined.

**Key words:** N-bromosuccinimide; 3-methyl-1,2,5-thiadiazole.

As a part of a continuing study on the chemistry of 1,2,5-thiadiazoles and with the aim to obtain functionalized compounds of synthetic usefulness, we have studied the bromination reaction of 3-methyl-1,2,5-thiadiazole with N-bromosuccinimide (NBS). The reaction in carbon tetrachloride with benzoyl peroxide gives, besides the unreacted substrate, mixtures of 3-bromomethyl-1,2,5-thiadiazole (I) (KARJYONE et Al., 1974), 3-dibromomethyl-1,2,5-thiadiazole (II), and, for the more severe bromination conditions, 3-tribromomethyl-1,2,5-thiadiazole (III) (Scheme 1), in a ratio which depends on the reaction conditions employed (see experimental section). The reaction involves the benzylic position, meanwhile the thiadiazole ring remains unaltered also for prolonged reaction time, confirming the remarkable stabilization of such nucleus.

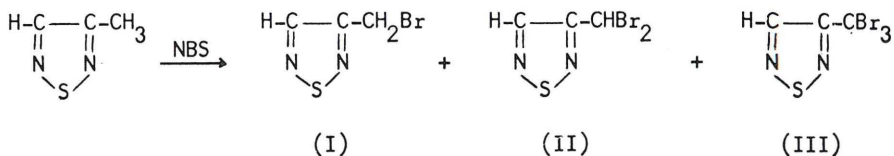
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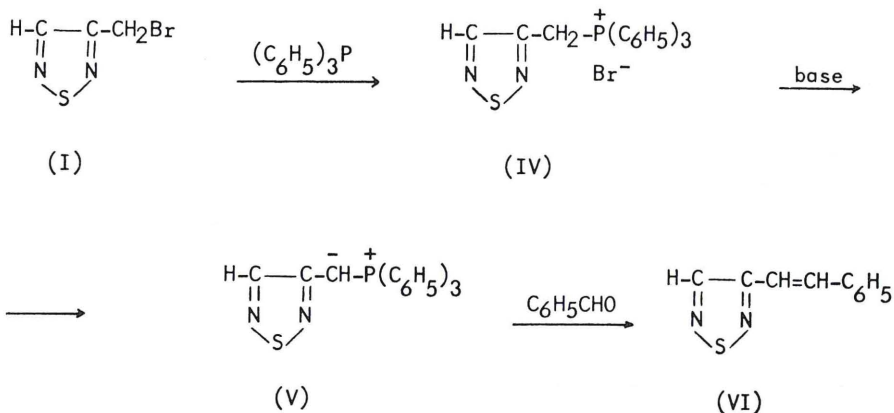
SCHEME 1



Elemental analysis, I.R., and N.M.R. spectral data are consistent with the assigned structures.

Compound I was transformed into 3-(1,2,5-thiadiazolymethyl)-triphenylphosphonium bromide (IV), then into 1,2,5-thiadiazolymethylenetriphenylphosphorane (V) (MULVEY et Al., 1967) (Scheme 2).

SCHEME 2



The formation of V from IV was easily carried out with various basic reagents, nevertheless the preparation of pure V required selected conditions.

The action of dilute aqueous alkalis is efficient in the formation of V, but in such hydrolysing conditions V is gradually decomposed with formation of phosphin oxide and 3-methyl-1,2,5-thiadiazole. As no traces of 3-methyl-1,2,5-thiadiazole are found in the reaction with saturated potassium hydroxide (see later), the possibility of a direct substitution of hydroxyl ion at the phosphorus atom (GRAYSON et Al., 1960) is excluded.

With *n*-butyllithium IV produces V together with di-*n*-butyl-

thioether even if the nucleophile is added dropwise to IV so that it never is present in excess. The formation of thioether indicates that the  $\alpha$ -elimination reaction is accompanied by the cleavage of the thiadiazole ring through the nucleophilic attack at the sulphur atom (BERTINI et Al., 1974).

Finley powdered sodamide in ethereal suspension transforms IV into V very slowly, meanwhile the addition of few percent of sodium ethoxide very much increases the reaction rate.

With saturated aqueous potassium hydroxide in presence of methylene chloride and of pellets of the solute, the phosphonium salt IV behaves as an efficient phase transfer catalyst, and releases in the organic layer the yellow phosphorane remarkably pure. Such procedure was preferred for preparative purposes.

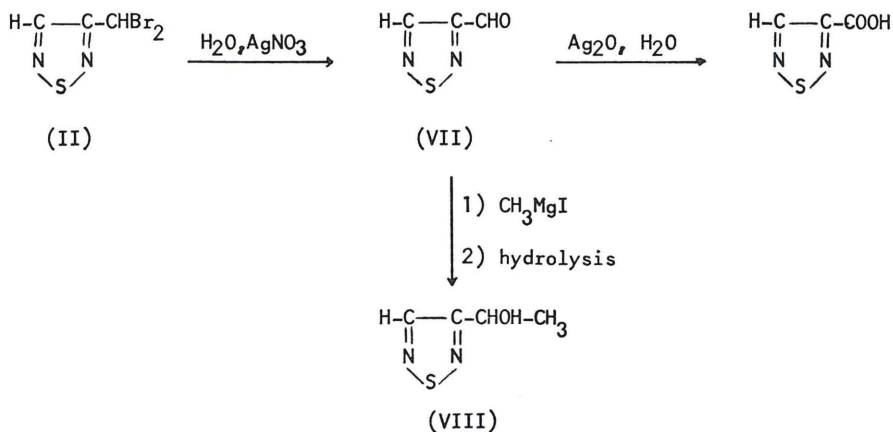
Compound V yielded yellow crystals rather stable under anhydrous conditions, according to a remarkable electron-withdrawing effect of the thiadiazole ring. The phosphorane V easily reacts with benzaldehyde at room temperature giving the known  $\beta$ -[3-(1,2,5-thiadiazolyl)]styrene (VI) (MULVEY et Al., 1967). In spite of the stability of V, its easy transformation into VI by reacting with benzaldehyde allows us to suppose that the reaction may occur also with other less reactive carbonyl compounds, making accessible by this way various thiadiazol substituted alkenes.

Compound II was hydrolysed to the 3-formyl-1,2,5-thiadiazole (VII) (GILL, 1964) (Scheme 3). The hydrolysis was tested under several conditions owing to the high fragility of the aldehyde which may be largely destroyed before its recovering. It was found most convenient to carry out the reaction with an aqueous solution of stoichiometric silver nitrate in presence of ethanol, followed by extraction with ether. The colorless liquid aldehyde obtained by rapid distillation under nitrogen at reduced pressure and collection at  $-70^{\circ}\text{C}$  spontaneously and promptly affords resins when allowed to heat at room temperature. The oxidation of VII with silver oxide in water gave the 1,2,5-thiadiazol-3-carboxylic acid. Samples of VII yielded the corresponding 4-nitrophenylhydrazone (GILL, 1964) and 2,4-dinitrophenylhydrazone.

Compound VII treated dropwise with methylmagnesium iodide yielded the 1-[3-(1,2,5-thiadiazolyl)]ethanol (VIII) (GILL, 1964) and no dimethylthioether. This fact, showing that the carbonyl group of the compound VII is a more reactive center towards Grignard reagents than the sulphur atom (BERTINI et Al., 1974),

opens the way to the exploitation of the reaction between VII and carbanionic nucleophiles for the synthesis of various 1,2,5-thiadiazol derivatives.

SCHEME 3



## EXPERIMENTAL SECTION

M.p.s, where no otherwise indicated, were determined with a Kofler apparatus and are uncorrected. I.R. Spectra were recorded on a Perkin Elmer Mod. 225 spectrophotometer. N.M.R. Spectra were run on a DA-60 IL Varian instrument ( $\text{Me}_4\text{Si}$  as internal standard). Elemental analyses were carried out at the Microanalysis Laboratory of the Istituto di Chimica farmaceutica dell'Università di Pisa.

### *Bromination of 3-methyl-1,2,5-thiadiazole*

#### *General procedure*

Experiments were carried out with a 10 molar solution of 3-methyl-1,2,5-thiadiazole in carbon tetrachloride by refluxing it under stirring from 1 to 15 hours with benzoyl peroxide (1% in moles) and NBS (from 1 to 2 moles of NBS per mole of thiadiazole derivative). The reaction mixtures were filtered, in order to remove the solid succinimide, distilled up to elimination of the solvent and tested by gas-chromatography on 2 m silicon columns. The crude residue yielded pure samples of unreacted substrate, I, II, and eventually III, by preparative G.P.C. on silicon columns. Results of typical experiments are reported in table 1.



TABLE 1 - Bromination of 3-methyl-1,2,5-thiadiazole.

moles methylthiadiazole moles NBS	hours	Products %			
		unreacted thiadiazole	I	II	III
1 : 1	2.5	29	50	21	—
1 : 1.5	6	2	45	46	7
1 : 2	9	1	29	40	30

The separation and purification of the products for preparative purposes was carried out by fractional distillation at reduced pressure for compound I and by repeated crystallizations from ether at low temperature for compounds II and III.

Compound I is a lachrymatory liquid with b.p. 105°/18 Torr;  $n_D^{25} = 1.5899$ ;  $\nu_{\max}$  (film) 3075 (CH), 3030 (CH<sub>2</sub> asym.), 2970 (CH<sub>2</sub> sym.), 826, 790, 625, 517 cm<sup>-1</sup> (ring);  $\delta$  (CCl<sub>4</sub>) 8.51 (1H, s, ring proton), and 4.55 (2H, s, CH<sub>2</sub>). Found: C, 20.25; H, 1.78; Br, 44.52; N, 15.45; S, 17.80. C<sub>3</sub>H<sub>3</sub>BrN<sub>2</sub>S requires C, 20.13; H, 1.69; Br, 44.63; N, 15.65; S, 17.91%.

Compound II shows m.p. 37° in sealed tube;  $\nu_{\max}$  (film) 3090 (CH ring), 3015 (aliphatic CH), 840, 791, 615, 516 cm<sup>-1</sup> (ring);  $\delta$  (CCl<sub>4</sub>) 8.57 (1H, s, ring proton), 6.72 (1H, s, aliphatic CH). Found: C, 14.05; H, 0.87; Br, 62.04; N, 10.75; S, 12.35. C<sub>3</sub>H<sub>2</sub>Br<sub>2</sub>N<sub>2</sub>S requires C, 13.97; H, 0.78; Br, 61.96; N, 10.86; S, 12.43%.

Compound III shows m.p. 48° in sealed tube;  $\nu_{\max}$  (KBr) 3085 (CH), 854, 801, 620, 517 cm<sup>-1</sup> (ring);  $\delta$  (CCl<sub>4</sub>) 8.94 (1H, s). Found: C, 10.90; H, 0.34; Br, 71.36; N, 8.44; S, 9.42. C<sub>3</sub>HBr<sub>3</sub>N<sub>2</sub>S requires C, 10.70; H, 0.30; Br, 71.17; N, 8.32; S, 9.52%.

### 3-(1,2,5-Thiadiazolymethyl)triphenylphosphonium bromide (IV)

A solution of 17.43 g (66.45 mmol) of triphenylphosphine in 150 ml of anhydrous benzene was added to a solution of 11.32 g (63.23 mmol) of 3-bromomethyl-1,2,5-thiadiazole (I) in 50 ml of anhydrous benzene, then the mixture was refluxed under stirring for 4 hours. After cooling the crystals of IV were filtered, washed with 20 ml of acetone, and crystallized from methylene chloride,



(27.15 g; 61.52 mmol). The washing with acetone and crystallization from methylene chloride was repeated three times obtaining a product with m.p. 238°.  $\nu_{\max}$  (KBr) 1107, 991 (P-C, arom.), 521  $\text{cm}^{-1}$  (heterocyclic ring). Found: C, 57.08; H, 4.08; Br, 18.20; N, 6.44; S, 7.22.  $\text{C}_{21}\text{H}_{18}\text{BrN}_2\text{PS}$  requires C, 57.15; H, 4.11; Br, 18.11; N, 6.35; S, 7.26%.

### *1,2,5-Thiadiazolylmethylenetriphenylphosphorane (V)*

#### *Method a*

A mixture of 150 ml of saturated aqueous potassium hydroxide containing solid pellets of the solute, 300 ml of anhydrous methylene chloride and 13.24 g (30.00 mmol) of 3-(1,2,5-thiadiazolylmethyl)-triphenylphosphonium bromide (IV) was shaken for about 2 minutes in a separatory funnel, then it was separated and the aqueous layer was extracted twice with 100 ml portions of methylene chloride. The intensely yellow organic phase was shaken for 15 minutes with pellets of potassium hydroxide, then it was decanted, distilled up to the removal of the solvent and dried two hours at 40°/0.01 Torr. The residue (10.56 g; 29.30 mmol) by a double recrystallization from anhydrous methylene chloride under nitrogen at low temperature yielded yellow crystals of V (m.p. in sealed tube 109-110°). Less good results were obtained using anhydrous ether or benzene in place of methylene chloride as reaction solvent.  $\nu_{\max}$  (nujol) 1103, 996, 907, 836, 778, 527  $\text{cm}^{-1}$ .

#### *Method b*

A mixture of 5.85 g (150 mmol) of commercial powdered sodamide, 2000 ml of anhydrous ether, and 0.14 g (3.04 mmol) of absolute ethanol was stirred under nitrogen at room temperature for half an hour, then it was treated with 13.24 g (30.00 mmol) of IV and stirred for other 25 hours. The yellow ethereal phase, after filtering and removal of the solvent, yielded 8.65 g (24.00 mmol) of V which was recrystallized as described under method a.

#### *Method c*

A 1.19 N solution of *n*-butyllithium in ether (25.2 ml) was added by drops, in about 23 minutes, to a mixture of 13.24 g (30.00 mmol) of IV and 28 ml of anhydrous ether maintained at -70°

under nitrogen and vigorous stirring, so the colour turned deep orange. Fifteen minutes after the addition, the temperature was allowed to rise at 0°. The reaction mixture, which showed yellow lemon colour and smell of *n*-butylthioether, by reaction with benzaldehyde gave in 49% yields on respect to IV the  $\beta$ -[3-(1,2,5-thiadiazolyl)]-styrene (VI) (MULVEY et A., 1976) identical to that obtained from a pure sample of the phosphorane V prepared according to the method a.

### *3-Formyl-1,2,5-thiadiazole* (VII)

A solution of 11.43 g (44.31 mmol) of 3-dibromomethyl-1,2,5-thiadiazole (II) in 40 ml of ethanol, under nitrogen and continuous stirring, was treated dropwise with 15.07 g (88.71 mmol) of silver nitrate in 70 ml of water, then the temperature was raised to 75° for about 3 hours. The reaction mixture was extracted with ether and the extracts were dried over anhydrous sodium sulphate. After removal of the solvent the residue was distilled under nitrogen (40°/4 Torr) and the distillate was collected in a vessel cooled at -70°. Grams 4.68 of crude VII were obtained. Samples of VII allowed to rise the room temperature spontaneously underwent decomposition with formation of resins.

A 0.095 g (0.83 mmol) sample of VII in 2 ml of ethanol was added to the silver oxide obtained from 0.3 g of silver nitrate and 0.14 g of sodium hydroxide in 4 ml of water. After 30 minutes stirring, the mixture was filtered and the liquid acidified with hydrochloric acid. By extracting with ether, drying over anhydrous sodium sulphate, and removal of the solvent, the reaction liquors yielded 0.101 g (0.77 mmol) of 1,2,5-thiadiazol-3-carboxylic acid which, after sublimation, exhibited melting point and I.R. spectrum coincident with those known (WEINSTOCK, 1959).

The compound VII yielded the 4-nitrophenylhydrazone (GILL 1964) (m.p. after crystallization from ethanol 196-198°) and the 2,4-dinitrophenylhydrazone (m.p. after crystallization from ethanol 252-254°); Found: C, 36.70; H, 2.03; N, 28.48; S, 10.98.  $C_9H_6N_6O_4S$  requires C, 36.74; H, 2.06; N, 28.56; S, 10.90%.

### *1-[3-(1,2,5-Thiadiazolyl)]ethanol* (VIII)

A solution of 2.58 g of crude 3-formyl-1,2,5-thiadiazole (VII) in 40 ml of anhydrous ether, stirred under nitrogen at -70°, was

treated dropwise with the ethereal solution of methylmagnesium iodide prepared from 0.46 g (18.93 mmol) of magnesium and 2.69 g (18.95 mmol) of methyl iodide in 10 ml of ether. After the addition, the stirring was continued for about half an hour allowing the temperature to rise the room value, then the mixture was hydrolysed and extracted with ether. The extracts, washed with a dilute solution of sodium sulphite and dried over anhydrous sodium sulphate yielded, by distillation at reduced pressure, after removal of the solvent, 1.69 g of VIII exhibiting I.R. spectrum coincident with that known (GILL, 1964). The compound VIII gave the 3,5-dinitrobenzoate (GILL, 1964) melting at 105-106°, after crystallization from methanol.

## REFERENCES

- BERTINI V., DE MUNNO A., MENCONI A., FISSI A. (1974) - Nucleophilic cleavage of the 1,2,5-thia- and -selenadiazole rings. *J. Org. Chem.*, **39**, 2294-2296.
- GILL J. M. (1964) - Chemistry of 1,2,5-thiadiazoles. *Dissertation Abstracts*, **24**, 2690; Univ. Microfilms, Ann Arbor, Michigan, No. 64-468.
- GRAYSON M., KEOUGH P. T. (1960) - Phosphonium compounds II. Decomposition of phosphonium alkoxides to hydrocarbons, ether and phosphine oxide. *J. Am. Chem. Soc.*, **82**, 3919-3924.
- KARIYONE K., TANAKA K., TAKAI K. (1974) - Thiadiazolecarboxylic acids. Japan Kokai 7424, 963; *Chem. Abstr.*, **81**, 49686q.
- MULVEY D. M., WEINSTOCK L. M. (1967) -  $\alpha$ ,  $\beta$ -Unsaturated-1,2,5-thiadiazoles. *J. Heterocyclic Chem.*, **4**, 445-446.
- WEINSTOCK L. M. (1959) - Synthesis and properties of 1,2,5-thiadiazole and its derivatives. *Dissertation Abstracts*, **19**, 3136; Univ. Microfilms, Ann Arbor, Michigan, No. 58-2947.

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