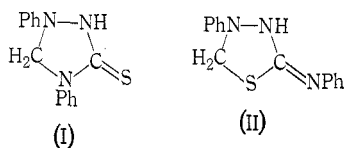


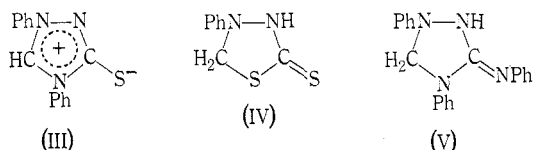
THE REACTION OF 1,4-DIPHENYLTHIOSEMICARBAZIDE AND 1,5-DIPHENYLTHIOCARBAZIDE WITH ALDEHYDES*

By G. W. EVANS† and B. MILLIGAN†

Reaction of 1,4-diphenylthiosemicarbazide with formaldehyde in aqueous dioxan gave two isomers, $C_{14}H_{13}N_3S$, presumably (I) and (II).



Oxidation of the major product with chromic acid gave a compound, $C_{14}H_{11}N_3S$, identical with that prepared by Busch and Schneider¹ from 1,4-diphenylthiosemicarbazide and formic acid. The skeletal structure of this oxidation product, a so-called meso-ionic compound, has been proposed as (III) in the preceding paper.² Hence it follows that the major product of reaction of formaldehyde and 1,4-diphenylthiosemicarbazide has the structure (I) and presumably the minor product is (II).



These assignments are supported by the mass spectral results. The isomer (II) affords a fragmentation peak at m/e 163, corresponding to the loss of the ion $PhNH^+$, whereas no such peak is derived from (I). Moreover, treatment of (I) with methyl iodide, followed by alkali, gives rise to methanethiol (identified by gas chromatography), behaviour typical of a thioamide.

Comparison of the p.m.r. spectra of (I) and (II) with those of the model compounds (IV) and (V) did not assist in the assignment of structures, since the absorption peaks of the methylene group protons of (I) and (II) are much closer together (at δ 5.10 and 5.08 p.p.m., respectively) than those of (IV) and (V) (δ 5.41 and δ 5.20 p.p.m., respectively).

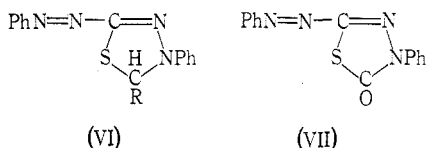
* Manuscript received February 23, 1967.

† Division of Protein Chemistry, CSIRO Wool Research Laboratories, Parkville, Vic.

¹ Busch, M., and Schneider, S., *J. prakt. Chem.*, 1903, **67**, 246.

² Evans, G. W., and Milligan, B., *Aust. J. Chem.*, 1967, **20**, 1779.

Reaction of 1,5-diphenylthiocarbazine with formaldehyde yielded a bright red compound (VI; R = H), rather than the expected dihydro compound.



This oxidation, albeit in the presence of formaldehyde, is perhaps not so surprising considering the ease of oxidation of 1,5-diphenylthiocarbazine to dithizone. The structure of (VI; R = H) was confirmed by oxidation with chromic acid to the known thiadiazolinone³ (VII). The phenyl derivative of (VI; R = Ph) was also prepared from 1,5-diphenylthiocarbazine by reaction with benzaldehyde.

Experimental

Proton magnetic resonance spectra were determined on a Varian A60 spectrometer operating at 60 Mc/s (tetramethylsilane as internal standard) using 10% solutions.

Reaction of 1,4-Diphenylthiosemicarbazide with Formaldehyde

A solution of 1,4-diphenylthiosemicarbazide (9.0 g) in dioxan (20 ml) was shaken with formaldehyde (36%, 40 ml) at room temperature for 24 hr. The pink oil which separated was extracted with ethyl acetate, and the extract washed well with water. Evaporation gave a crude product (9.1 g) from which 1,4-diphenyl-1,2,4-triazolidine-3-thione (I) (3.7 g) was isolated as colourless prisms, m.p. 91°, after several recrystallizations from benzene/light petroleum (Found: C, 66.5; H, 5.3; N, 16.1; S, 12.9. $\text{C}_{14}\text{H}_{13}\text{N}_3\text{S}$ requires C, 65.9; H, 5.1; N, 16.5; S, 12.6%). The p.m.r. spectrum (CDCl_3) showed a multiplet at δ 6.8–7.5 p.p.m. (10 aromatic protons), a broad singlet at δ 6.2 p.p.m. (–NH–), and a singlet at δ 5.05 p.p.m. (–CH₂–). In dimethyl sulphoxide the latter peak was shifted to δ 5.10 p.p.m. The mother liquors were combined and evaporated. On addition of ethanol (25 ml) 4-phenyl-2-phenylamino-1,3,4-thiadiazolidine (II, 0.15 g) separated; after recrystallization from acetone it had m.p. 154–155° (Found: C, 66.5; H, 5.3; S, 12.4. $\text{C}_{14}\text{H}_{13}\text{N}_3\text{S}$ requires C, 65.9; H, 5.1; S, 12.6%). The p.m.r. spectrum (in dimethyl sulphoxide at 86°) showed a singlet at δ 5.08 p.p.m. (–CH₂–) and a complex multiplet at δ 6.7–7.7 p.p.m. (10 aromatic protons). No absorption peak due to NH was observed in the p.m.r. spectrum but the occurrence of an absorption band at c. 3400 cm^{-1} in the infrared spectrum (KBr) confirms its presence.

On adding picric acid to the ethanolic mother liquors of (II), the picrate of 1,4-diphenyl-1,2,4-triazolidine-3-thione (I) (3.8 g) separated. It had m.p. 134–135° (from ethyl acetate) (Found: C, 49.6; H, 3.5; N, 17.4; S, 6.8. $\text{C}_{26}\text{H}_{16}\text{N}_6\text{O}_7\text{S}$ requires C, 49.6; H, 3.3; N, 17.3; S, 6.6%). A suspension of the picrate in ethyl acetate was shaken with 1M sodium carbonate solution for 2 hr. The organic layer was dried (Na_2SO_4) and passed through a column of alumina (pH 10). Evaporation of the eluate, and crystallization of the residue from cyclohexane, gave (I) (89%).

Oxidation of 1,4-Diphenyl-1,2,4-triazolidine-3-thione (I)

A solution (35%) of chromium trioxide in 18N sulphuric acid was added dropwise to a solution of (I) (0.35 g) in acetone (10 ml) until the red colour persisted. The product (0.20 g) was isolated by dilution with water, and, after recrystallization from chloroform/ethanol, had m.p. 216–217° (Found: C, 66.2; H, 4.5; N, 16.5; S, 12.7. Calc. for $\text{C}_{14}\text{H}_{11}\text{N}_3\text{S}$: C, 66.4; H, 4.4; N, 16.6; S, 12.7%). The m.p. was undepressed on admixture with the product of

³ Freund, M., and Kuh, F., *Ber. dt. chem. Ges.*, 1890, **23**, 2821.

reaction of 1,4-diphenylthiosemicarbazide and formic acid, m.p. 216–217°, prepared according to Busch and Schneider.¹

Spectra

The mass spectrum of (I) showed a molecular-ion peak at m/e 255 and fragmentation peaks at 208, 146, 135, 118, 105, 91, 77, 66, and 51. The isomer (II) gave all of the above peaks, and also one at m/e 163.

The p.m.r. spectrum (in dimethyl sulphoxide) of 4-phenyl-1,3,4-thiadiazolidine-2-thione (IV), m.p. 115–116° (lit.⁴ 112°), showed a singlet at δ 5.41 p.p.m. ($-\text{CH}_2-$) and a complex multiplet at δ 6.9–7.6 p.p.m. (5 aromatic protons). No peak due to $-\text{NH}-$ was discernible. The p.m.r. spectrum (in CDCl_3) of 1,4-diphenyl-2-phenylamino-1,3,4-triazolidine (V), m.p. 127–128° (lit.⁵ 128°), showed a singlet at δ 5.17 p.p.m. ($-\text{CH}_2-$), a broad singlet at δ 5.70 p.p.m. ($-\text{NH}-$), and a complex multiplet at δ 6.7–7.7 p.p.m. (15 aromatic protons). In dimethyl sulphoxide the band attributed to $-\text{CH}_2-$ was shifted to δ 5.20 p.p.m.

3-Phenyl-5-phenylazo-1,3,4-thiadiazoline (VI; R = H)

Formaldehyde (36% w/v, 50 ml) was added to a cold solution of 1,5-diphenylthiocarbazine (4 g) in ethanol (500 ml). After a few minutes the red solution was evaporated to a low volume and the product (0.5 g, 20%) was filtered off. The yield was not improved by prolonging the time of reaction. The compound crystallized from ethanol as red plates, m.p. 162° (Found: C, 63.0; H, 4.8; N, 20.5; S, 12.3. $\text{C}_{14}\text{H}_{12}\text{N}_4\text{S}$ requires C, 62.7; H, 4.5; N, 20.9; S, 12.0%). The p.m.r. spectrum (in CDCl_3) showed a singlet ($-\text{CH}_2-$) at δ 5.37 p.p.m. and a complex multiplet (10 aromatic protons) at δ 7.0–8.0 p.p.m. The u.v. spectrum (in ethanol) showed maxima at λ 263, 287, and 498 $m\mu$.

3-Phenyl-5-phenylazo-1,3,4-thiadiazolin-2-one (VII)

A solution of (VI) in acetone was oxidized with chromic acid as described above. The mixture was diluted with water and the oxidation product (VII) isolated by extraction with ether. It crystallized from methanol as orange needles, m.p. 146–147°; lit.³ 140° (Found: C, 59.5; H, 3.7; N, 19.6; S, 11.2. Calc. for $\text{C}_{14}\text{H}_{10}\text{N}_4\text{O}_2\text{S}$: C, 59.6; H, 3.6; N, 19.9; S, 11.4%). The m.p. was undepressed on admixture with an authentic sample, m.p. 146–147°, prepared by treating 1,4-diphenylthiosemicarbazide with phosgene in toluene.³

2,3-Diphenyl-5-phenylazo-1,3,4-thiadiazoline (VI; R = Ph)

Benzaldehyde (30 ml) was added to a solution of 1,5-diphenylthiocarbazine (2.3 g) in ethanol (150 ml), giving a dark green solution. After 12 hr the solution was shaken with saturated sodium bisulphite solution, and the resulting bisulphite addition compound was filtered off. Water was added to the dark red filtrate, and the crude product (0.3 g) was extracted with ether. After four recrystallizations from ethanol, the product was obtained as red granules, m.p. 159° (Found: C, 69.7; H, 4.8; N, 16.1; S, 9.3. $\text{C}_{20}\text{H}_{16}\text{N}_4\text{S}$ requires C, 69.7; H, 4.7; N, 16.3; S, 9.3%). The u.v. spectrum (in ethanol) showed maxima at λ 262, 307, and 492 $m\mu$. The p.m.r. spectrum (in CDCl_3) showed a singlet at δ 6.92 p.p.m. ($-\text{CH}-$) and a complex multiplet at δ 7.1–8.0 p.p.m. (15 aromatic protons).

Acknowledgments

We thank Messrs J. Oocolowitz, Defence Standard Laboratories, and J. L. Little, Division of Applied Chemistry, CSIRO Chemical Research Laboratories, for recording the mass and p.m.r. spectra, respectively. We also thank Professor J. M. Swan for his advice and encouragement.

⁴ Busch, M., *Ber. dt. chem. Ges.*, 1895, **28**, 2635.

⁵ Busch, M., and Mehrtens, G., *Ber. dt. chem. Ges.*, 1905, **38**, 4049.